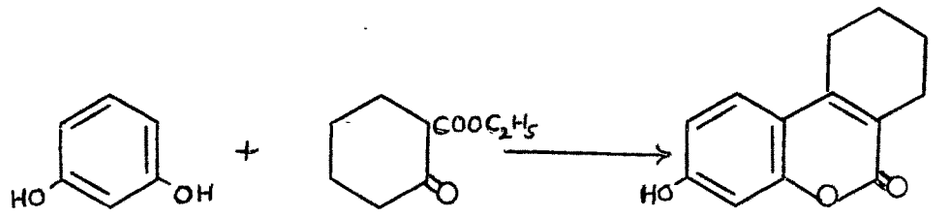
CHAPTER II

REACTIONS ON 7-HYDROXY-3,4-CYCLOHEXENOCOUMARIN

Reactions on 7-hydroxy-3,4-cyclohexenocoumarin

Dieckmann[1] in 1907, condensed resorcinol (1) with cyclic-β-ketonic esters and assumed the formation of benzo-α-pyrones (2) in this reaction. Sen and Basu[2] studied the above reaction by taking different phenols and obtained the corresponding benzo-α-pyrones using concentrated sulphuric acid as condensing agent.



(1) (2)

Desai and coworkers[3] condensed resacetophenone with ethyl-cyclohexanone-2-carboxylate, ethyl-4- and 5-methyl-cyclohexanone-2-carboxylate and ethyl trans-β-decalone-3-carboxylate in the presence of phosphorus oxychloride and obtained 7-hydroxy-6-acetyl derivatives of cyclohexeno- and octalino-coumarins. They also condensed various dihydric and trihydric phenols with ethyl-cyclohexanone-2-carboxylate in the presence of aluminium chloride or concentrated sulphuric acid.

Ahmad and Desai[4] studied the effect of the cyclohexeno group in the 3,4-positions of the coumarin ring. Thus mercuration of 7-hydroxy cyclohexeno(1',2',4,3) coumarin with mercuric acetate gave a 6,8,x-triacetoxy

mercury derivative. In a similar manner 5,7-dihydroxy cyclohexeno(1',2',4,3)coumarin and 5-hydroxy-7-methyl-cyclohexeno(1',2',4,3)coumarin were mercurated. In all the cases, triacetoxy mercuri derivatives were obtained. Two of the mercuric acetate groups occupy the 6- and 8-positions while the actual position of the third group was unknown.

So far, there is no report regarding the reactivity of 7-hydroxy-3,4-cyclohexenocoumarin and its derivatives. It was thought of interest to study the pattern of substitution in 7-hydroxy-3,4-cyclohexeno-coumarin derivatives. The reactivity of the compound is expected to be similar with that of 7-hydroxycoumarin derivatives and hence a brief outline of the reactions on 7-hydroxycoumarin derivatives is described here.

Bromination : Fries and Lindemann[5] obtained a mono bromo derivative from 7-hydroxy-4-methylcoumarin which they claimed to be the 8-bromo derivative. This was latter disproved by Dalvi and Sethna[6] who found this compound to be the 3-bromo derivative. They also carried out the bromination of 7-hydroxy-4-methylcoumarin with two molecules of bromine and obtained the 3:6- and the 3:8-dibromo compound, the former being in preponderating yield.

Formylation : Pailer[7] obtained the 8-formyl-7-hydroxy-coumarin from 7-hydroxycoumarin by using hexamethylene tetramine. Similarly Rangaswami and Seshadri[8] obtained the

8-formyl derivative from 7-hydroxy-4-methylcoumarin. The structure of the formyl derivative was proved by converting it into 7-hydroxy-4,8-dimethylcoumarin which was prepared from 2-methyl resorcinol.

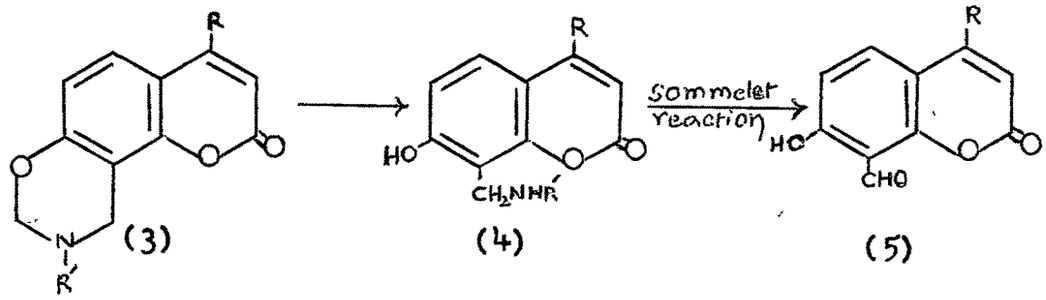
Fries migration and Friedel-Craft's reaction : Thakor and Shah[9] studied Fries migration of 7-acetoxy- and 7-benzoyloxy-4-methylcoumarin and obtained the corresponding 8-acyl derivatives. Only traces of the 6-isomers were also obtained. Parikh and Thakor[10] studied the Friedel Craft's acetylation and benzoylation of 7-hydroxy-4-methylcoumarin and obtained corresponding 8-acyl derivatives.

Mannich reaction : Gupta et al.[11] prepared Mannich bases from 7-hydroxy- and 7-hydroxy-4-methylcoumarin and found them to be powerful stimulants of nervous and respiratory systems.

Desai[12] studied the Mannich reaction on 7-hydroxy-coumarins with several amines. He isolated the oxazino derivatives in cases where primary amines were used.

Sethna and coworkers[13,14] have also studied this reaction on a number of coumarin derivatives such as 6-hydroxy, 7-hydroxy and 8-hydroxycoumarin and obtained the Mannich bases where secondary amines were used and the oxazinocoumarins such as (3) where primary amines such as benzylamine and aniline were used. The oxazino

derivatives were decomposed with dilute hydrochloric acid and the Mannich bases (4) obtained. The Mannich bases were converted into the corresponding formyl derivatives (5) by Sommelet reaction.



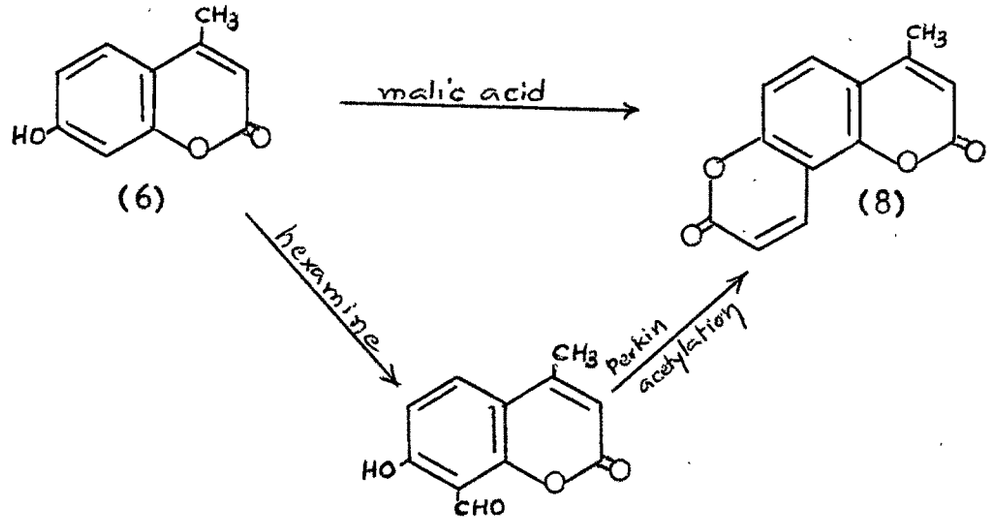
(3) (4) (5)

R = H or CH_3,

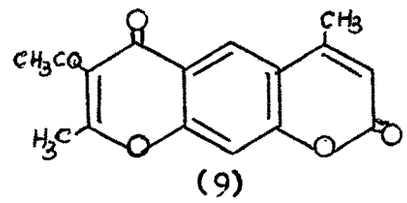
R' = $CH_2C_6H_5$, C_6H_5 etc.

Pechmann reaction : Sen and Chakravarti[15] condensed 7-hydroxycoumarin and 7-hydroxy-4-methylcoumarin with malic acid in the presence of sulphuric acid and obtained coumarino-7,8-α-pyrone and 4-methylcoumarino-7,8-α-pyrone (8). They, however, did not prove the structures of the coumarino-α-pyrones formed. Rangaswami and Seshadri[16] showed that when 7-hydroxycoumarin is condensed with malic acid both the angular and the linear coumarino-α-pyrones are formed but the latter is obtained in poor yield. Under the same experimental conditions 7-hydroxy-4-methylcoumarin (6) gives only the angular coumarino-α-pyrone (8). They proved the structure of coumarino-7,8-α-pyrone by its synthesis from 7-hydroxy-8-formyl-coumarin by Perkin reaction. In a similar way the

constitution of 4-methylcoumarino-7,8-α-pyrone was also proved, by its preparation which was prepared from 7-hydroxy-8-formyl-4-methylcoumarin (7).



Kostanecki-Robinson acylation of 7-hydroxy-8- and -6-acylcoumarin : Desai and Hamid[17] carried out the Kostanecki-Robinson acetylation of 7-hydroxy-6-acetyl- and 7-hydroxy-8-acetyl-4-methylcoumarin and obtained 4,2'-dimethyl-3'-acetylcoumarino-7,6-γ-pyrone (9) and 4,2'-dimethyl-3'-acetylcoumarino-7,8-γ-pyrone (10) respectively.



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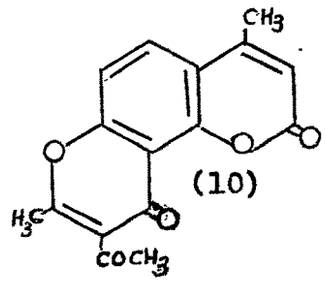
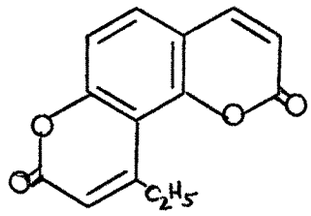


(10)

Shah and Contractor[18] similarly carried out the Kostanecki-Robinson acylation of 7-hydroxy-8-propionyl and 7-hydroxy-8-butyrylcoumarin and assigned the 4'-ethylcoumarino-7,8-α-pyrone (11) and 4'-propyl-coumarino-7,8-α-pyrone (12) respectively structures to the products obtained.



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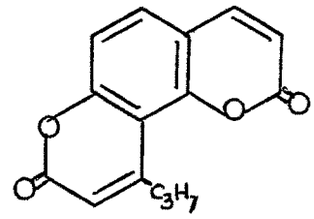
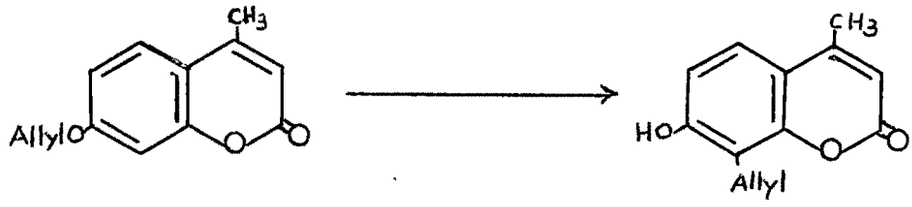


(12)

Claisen Rearrangement : Baker and Lothian[19] studied the Claisen rearrangement of 7-allyloxy-4-methylcoumarin (13) and obtained 7-hydroxy-8-allyl-4-methylcoumarin(14).



(13) (14)

Furocoumarins : This subject is described in details in the III rd chapter " Coumarino-α-pyrones and Furocoumarins ".

The present work deals with the reactions on 7-hydroxy-3,4-cyclohexenocoumarin and the study of its

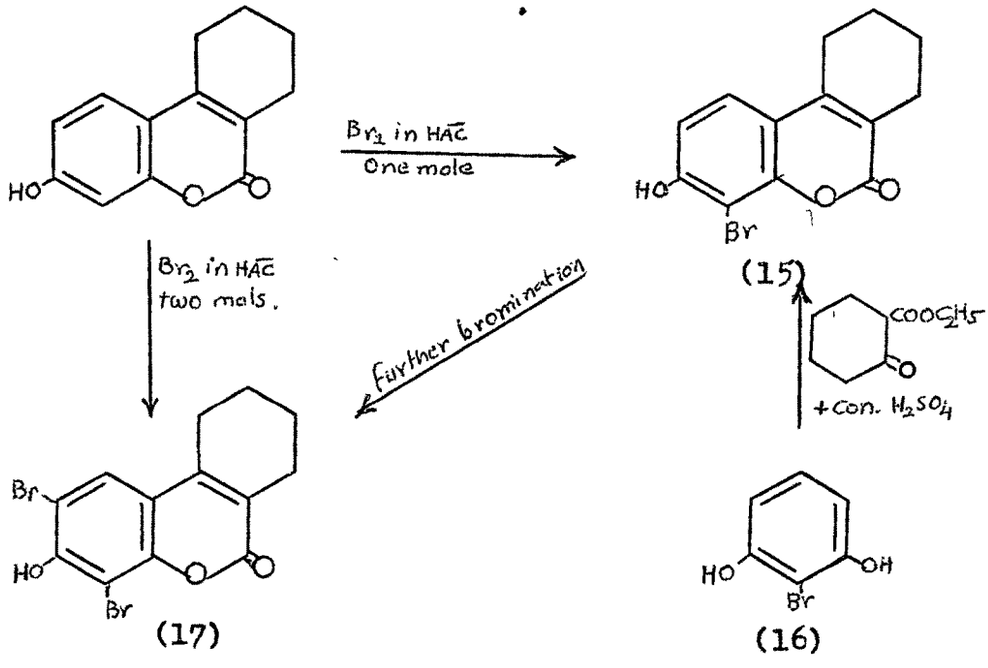
pattern of substitution.

Synthesis of 7-hydroxy-3,4-cyclohexenocoumarin :

The compound was obtained in purer and good yield by the revised method of Sen and Basu[2]. Resorcinol and ethyl cyclohexanone-2-carboxylate were mixed slowly with concentrated sulphuric acid and the mixture, after two hours, was worked out as usual. The yield of 7-hydroxy-3,4-cyclohexenocoumarin was almost quantitative.

Bromination of 7-hydroxy-3,4-cyclohexenocoumarin :

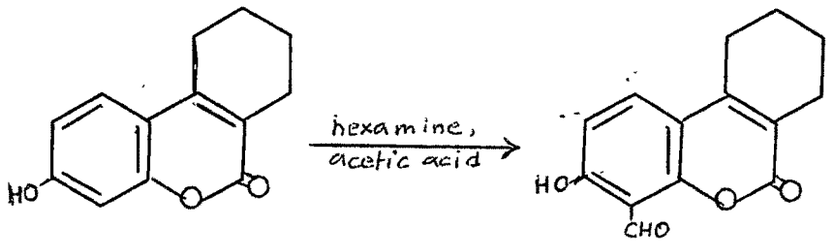
7-Hydroxy-3,4-cyclohexenocoumarin on bromination with one mole of bromine gave 8-bromo derivative (15). The structure of 7-hydroxy-8-bromo-3,4-cyclohexenocoumarin was proved by its synthesis from 2-bromoresorcinol(16) and ethyl cyclohexanone-2-carboxylate in the presence of concentrated sulphuric acid. Both the compounds were found to be identical.



With two moles of bromine, 7-hydroxy-3,4-cyclohexenocoumarin gave 7-hydroxy-6,8-dibromo-3,4-cyclohexenocoumarin (17), which was compared with the dibromo derivative obtained by further bromination of 7-hydroxy-8-bromo-3,4-cyclohexenocoumarin.

Formylation of 7-hydroxy-3,4-cyclohexenocoumarin by Duff's method : 7-Hydroxy-8-formyl-3,4-cyclohexenocoumarin (18) :

7-Hydroxy-3,4-cyclohexenocoumarin when treated with hexamethylene tetramine gave 7-hydroxy-8-formyl-3,4-cyclohexenocoumarin (18), the structure of which was proved by NMR spectra (Table I) which showed ortho-splitting of the aromatic protons of position 5 and 6, thus indicating that the formyl group is in the 8-position and not in the 6-position.



(18)

Fries migration of 7-acetoxy-3,4-cyclohexenocoumarin : 7-Hydroxy-8-acetyl- and 7-hydroxy-6-acetyl-3,4-cyclohexenocoumarin (20, 21) :

7-Acetoxy-3,4-cyclohexenocoumarin (19) on Fries migration with anhydrous aluminium chloride gave

Table I

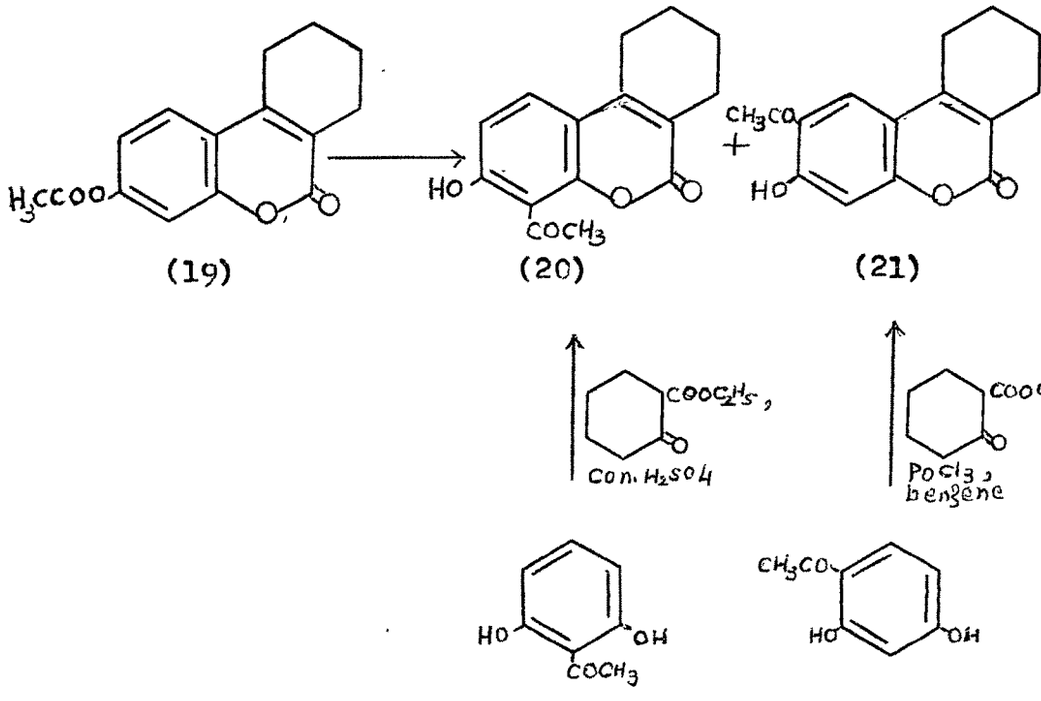
NMR spectra of 7-hydroxy-3-formyl-3,4-cyclohexenocoumarin

(60 MC. $CDCl_3$)

Shift (δ)	Coupling constant J (C/Sec)	Signals	Assignment
7.7	8	doublet	1 H } (aromatic)
6.85	8	doublet	1 H }
2.7 - 1.7	-	multiplet	8 H cyclohexene ✓
10.5	-	singlet	1 H -CHO group
12.1	-	singlet	1 H OH (chelated)

7-hydroxy-8-acetyl-(20) and 7-hydroxy-6-acetyl-3,4-cyclohexenocoumarin (21). The structures of both isomers were established by their individual synthesis. Desai et al.[20] carried out the above reaction and obtained only 7-hydroxy-8-acetyl-3,4-cyclohexenocoumarin. In Fries migration of 7-acetoxy-4-methylcoumarin the yield of 7-hydroxy-6-acetyl-4-methylcoumarin was in traces but in the above case, the yield of 7-hydroxy-6-acetyl-3,4-cyclohexenocoumarin was comparatively better.

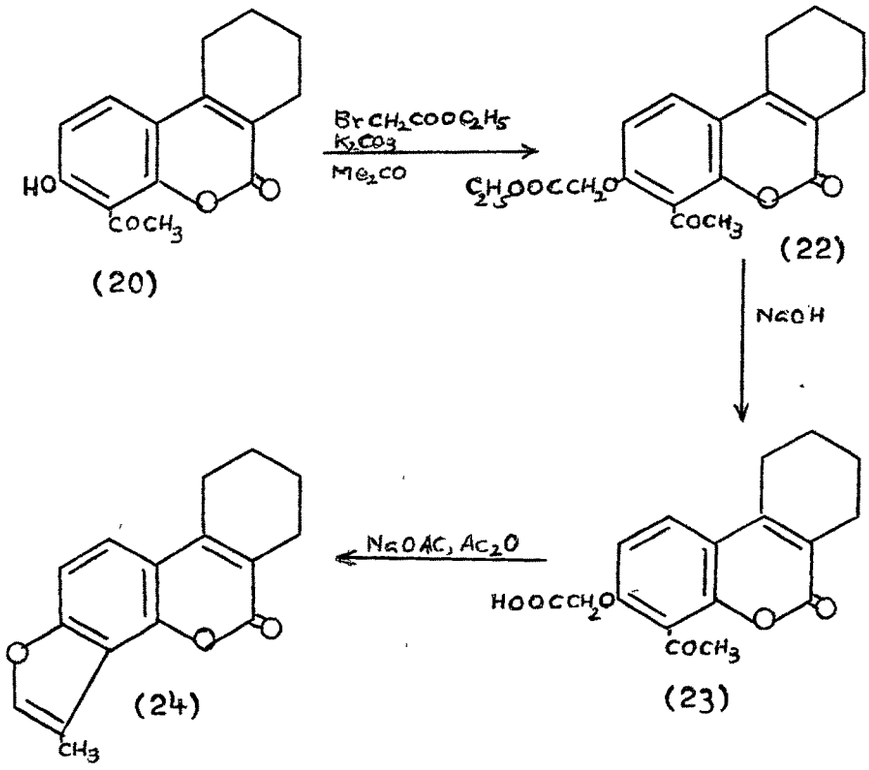
7-Hydroxy-8-acetyl-3,4-cyclohexenocoumarin was synthesised by the condensation of 2-acetylresorcinol and ethyl-cyclohexanone-2-carboxylate in the presence of concentrated sulphuric acid. Similarly, the known 7-hydroxy-6-acetyl-3,4-cyclohexenocoumarin was synthesised



by the condensation of resacetophenone and ethyl cyclohexanone-2-carboxylate in the presence of phosphorus oxychloride and benzene according to Desai et al.[21] Mixed m.pts. of the above isomers with the related compounds obtained by independent synthesis were not depressed.

Synthesis of 11-methyl-2H-furo(2,3-h)-3,4-cyclohexenobenzopyran-2-one (24) :

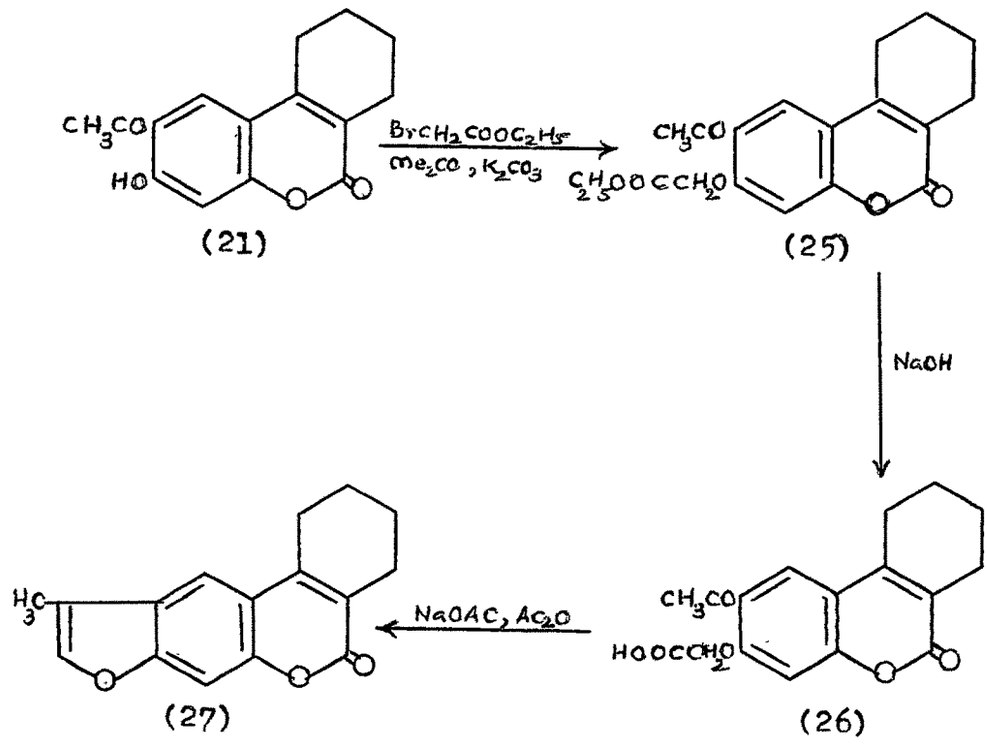
7-Hydroxy-8-acetyl-3,4-cyclohexenocoumarin (20) was condensed with ethylbromoacetate in boiling acetone in the presence of anhydrous potassium carbonate when ethyl 8-acetyl-3,4-cyclohexeno-7-coumarinyloxyacetate(22) was obtained. The ester on hydrolysis with dilute sodium hydroxide solution gave 8-acetyl-3,4-cyclohexeno-7-coumarinyloxyacetic acid (23). The cyclisation of this



acid with acetic anhydride and freshly fused sodium acetate gave 11-methyl-2H-furo(2,3-h)-3,4-cyclohexeno-benzopyran-2-one (24).

Synthesis of 8-methyl-2H-furo(3,2-g)-3,4-cyclo-hexenobenzopyran-2-one (27) :

7-Hydroxy-6-acetyl-3,4-cyclohexenocoumarin (21) on a similar condensation with ethyl bromoacetate, anhydrous potassium carbonate and acetone gave ethyl 6-acetyl-3,4-cyclohexeno-7-coumarinyloxyacetate (25) which on hydrolysis with alkali afforded 6-acetyl-3,4-cyclohexeno-7-coumarinyloxyacetic acid (26). The cyclisation of the acid was affected by refluxing it



(21) (25) (27) (26)

with acetic anhydride and freshly fused sodium acetate. Simultaneous decarboxylation and ring closure took place and 8-methyl-2H-furo(3,2-g)-3,4-cyclohexeno-benzopyran-2-one (27) was obtained.

Synthesis of 10-methyl-furo(2,3-h)-3,4-benzo-coumarin (31)

The Claisen rearrangement has proved very useful in getting the intermediates for the syntheses of furo-coumarins. 7-Allyloxy-4-methylcoumarin on Claisen rearrangement gave 8-allyl-7-hydroxy-4-methylcoumarin[22]. Similarly 7-hydroxy-3,4-cyclohexenocoumarin was employed for the synthesis of (31) as follows.

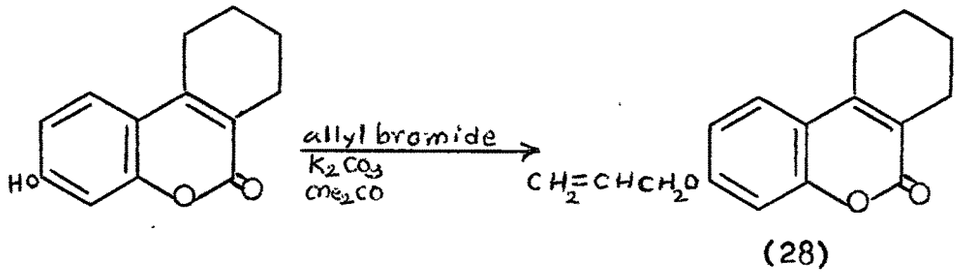
7-Hydroxy-3,4-cyclohexenocoumarin was refluxed with allylbromide and anhydrous potassium carbonate in acetone where 7-allyloxy-3,4-cyclohexenocoumarin (28) was obtained. The Claisen rearrangement of the above allyl ether was carried out by refluxing it with dimethylaniline. The product is assigned 7-hydroxy-8-allyl-3,4-cyclohexenocoumarin structure (29) on the basis of the analogy with allyl migration of 7-allyloxy-4-methylcoumarin derivative. It is further confirmed by NMR spectra (Table II) which showed ortho-splitting of the aromatic protons of position 5 and 6. This proved that the allyl migration has taken place in

Table II

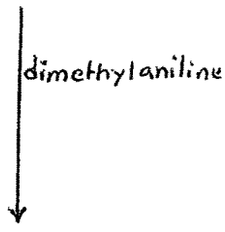
NMR spectra of 7-hydroxy-8-allyl-3,4-cyclohexenocoumarin

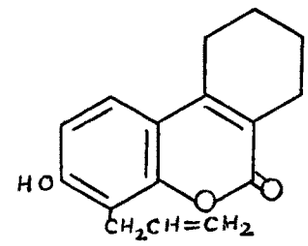
(60 MC, DMSO-d_6)

Shift (δ)	Coupling constant J (C/Sec)	Signals	Assignment
7.3	8	doublet	1 H } (aromatic)
6.85	8	doublet	1 H } (aromatic)
6.2 - 5.8	-	multiplet	1 H } ($-CH_2=CH-CH_2$)
5.2 - 4.8	-	triplet	2 H } ($-CH_2=CH-CH_2$)
3.5	-	doublet	2 H } ($-CH_2=CH-CH_2$)
2.7 - 1.7	-	multiplet	8 H cyclohexene
9.98	-	singlet	1 H OH

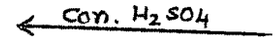

allyl bromide
K_2CO_3
Me_2CO
HO
$CH_2=CHCH_2O$

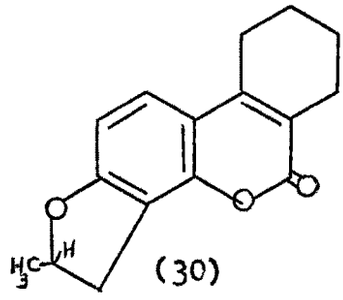
(28)


dimethylaniline

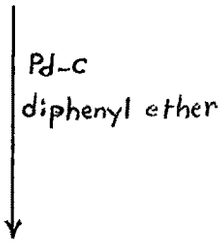

HO
$CH_2CH=CH_2$

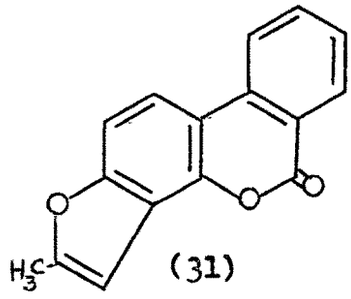
(29)


Con. H_2SO_4


H_3C
H

(30)


Pd-C
diphenyl ether

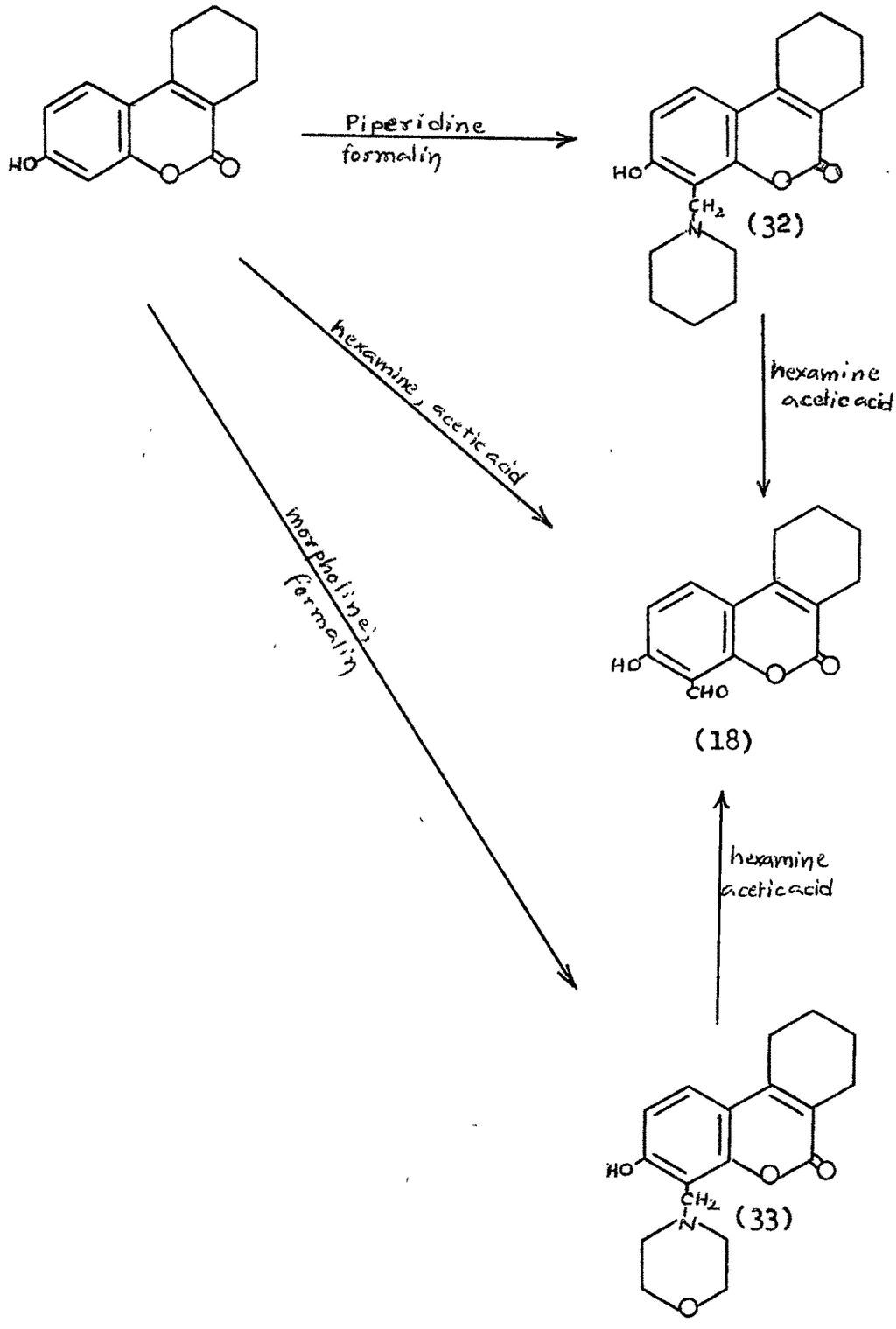

H_3C

(31)

the 8-position and not in the 6-position. On triturating 7-hydroxy-8-allyl-3,4-cyclohexenocoumarin with concentrated sulphuric acid for five minutes, it cyclised to 10-methyl-2H-10,11-dihydro-furo(2,3-h)-3,4-cyclohexeno-benzopyran-2-one (30) in good yield. The product was sufficiently pure for the further reaction. Earlier methods[23] of cyclisation of o-allyl phenols to benzopyran derivatives by hydrobromic acid or pyridine hydrochloride gives poor yield, and sometimes requires vacuum sublimation. Thus this method of cyclisation with concentrated sulphuric acid has got distinct advantages over the hydrobromic acid or pyridine hydrochloride method. This compound (30) was then dehydrogenated by refluxing it with diphenyl ether in the presence of palladised charcoal (5 %) to 10-methyl-2H-furo(2,3-h)-3,4-benzo-benzopyran-2-one (31). Dehydrogenation of cyclohexene ring also occurred simultaneously.

Mannich reaction on 7-hydroxy-3,4-cyclohexeno-coumarin with formalin and piperidine :

The Mannich reaction has proved to be an important tool in the field of synthetic organic chemistry. The resulting products of the Mannich reaction may be further transformed into a variety of compounds. Some of the Mannich bases and their reduction products have proved to be important medicinal agents.


HO
Piperidine
formalin
HO
CH2
N
(32)
hexamine, acetic acid
morpholine,
formalin
hexamine
acetic acid
HO
CHO
(18)
hexamine
acetic acid
HO
CH2
N
(33)

7-Hydroxy-3,4-cyclohexenocoumarin, formaldehyde and piperidine in equimolecular quantities gave a product to which 7-hydroxy-8-piperidinomethyl-3,4-cyclohexenocoumarin (32) structure has been assigned because on treatment with hexamethylenetetramine it gave 7-hydroxy-8-formyl-3,4-cyclohexenocoumarin (18). This was identical with the compound obtained by the direct formylation of 7-hydroxy-3,4-cyclohexenocoumarin with hexamethylenetetramine and acetic acid.

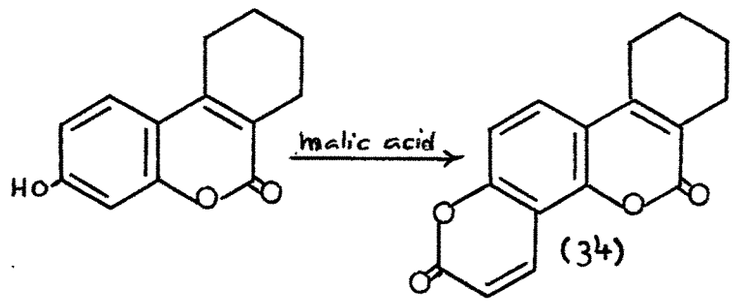
Mannich reaction on 7-hydroxy-3,4-cyclohexenocoumarin with formalin and morpholin :

7-Hydroxy-3,4-cyclohexenocoumarin on similar reaction with morpholin and formalin gave 7-hydroxy-8-morpholinomethyl-3,4-cyclohexenocoumarin (33). This on Sommelet reaction with hexamine and acetic acid gave the above 7-hydroxy-8-formyl-3,4-cyclohexenocoumarin.

Pechmann reaction of 7-hydroxy-3,4-cyclohexenocoumarin with malic acid :

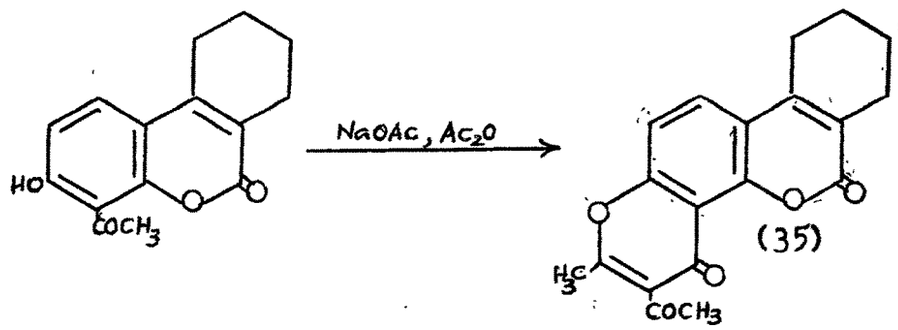
7-Hydroxy-3,4-cyclohexenocoumarin on condensation with malic acid in the presence of concentrated sulphuric acid furnished the compound to which 2H,10H-pyrano(2,3-h)-3,4-cyclohexenobenzopyran-2,10-dione (34) structure was assigned. on the basis of the analogy with compounds obtained by Pechmann

condensation of malic acid with 7-hydroxycoumarin derivatives. As the compound was insoluble in common organic solvents, NMR spectra could not be recorded.



Kostanecki-Robinson acetylation on 7-hydroxy-8-acetyl-3,4-cyclohexenocoumarin : 10-Methyl-11-acetyl-2H-12H-pyrano(2,3-h)-3,4-cyclohexenobenzopyran-2,12-dione (35) :

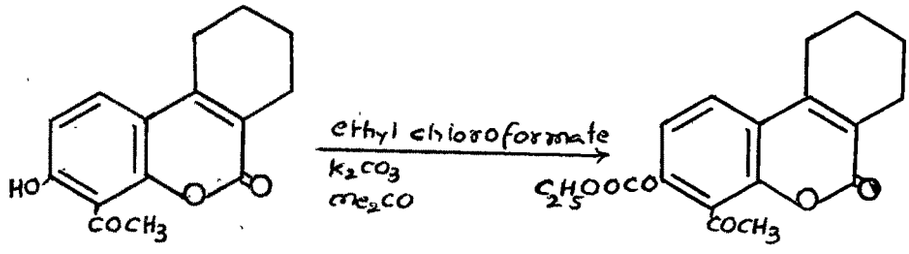
7-Hydroxy-8-acetyl-3,4-cyclohexenocoumarin on Kostanecki-Robinson acetylation with sodium acetate and acetic anhydride gave a product which was insoluble in cold dilute alkali and did not give alcoholic ferric chloride colouration. On the basis of these properties



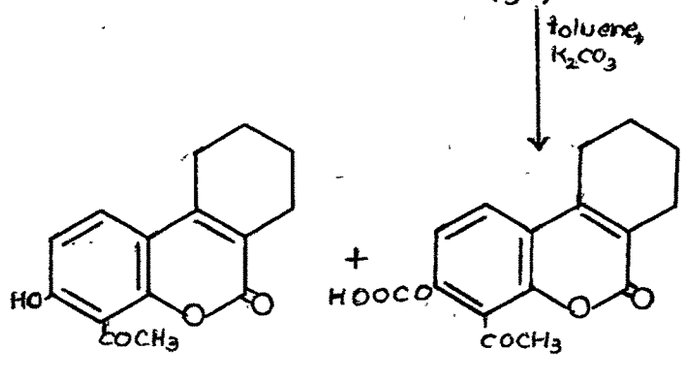
and the analytical results it has been assigned the 10-methyl-11-acetyl-2H-12H-pyrano(2,3-h)-3,4-cyclohexenobenzopyran-2,12-dione (35)structure. This is further proved by taking its i.r.spectra.

Condensation of 7-hydroxy-8-acetyl-3,4-cyclohexenocoumarin with ethylchloroformate :

7-Hydroxy-8-acetyl-3,4-cyclohexenocoumarin on refluxion with ethylchloroformate in dry acetone and anhydrous potassium carbonate gave the compound which was found to be insoluble in bicarbonate and alkali solution and was given the structure ethyl-8-acetyl-3,4-cyclohexeno-7-coumarinyloxyformate (36) on the basis of the analytical results.



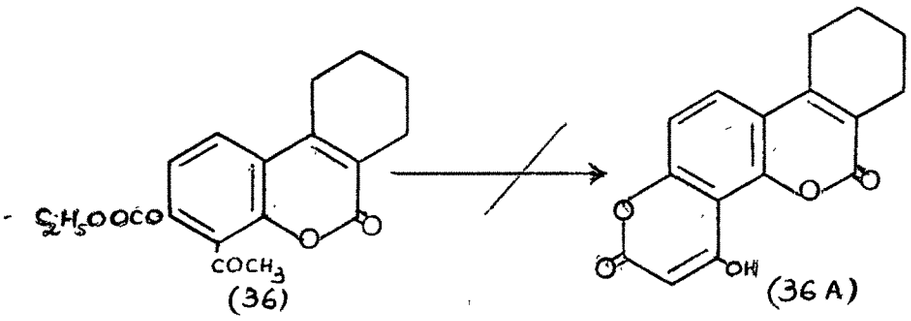
(36)



(37)

Attempted cyclisation of ethyl-8-acetyl-3,4-cyclohexeno-7-coumarinyloxyformate (36) to 4'-hydroxy-α-pyrono(5',6',7,8)-3,4-cyclohexenocoumarin (36 A):

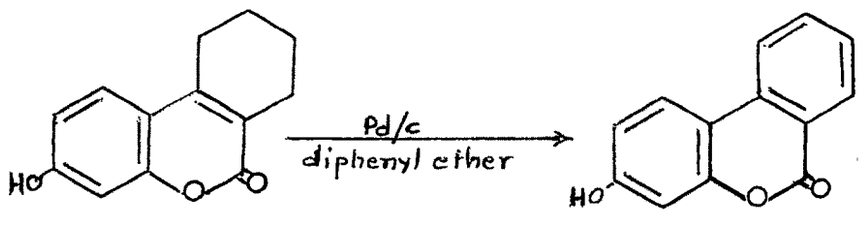
The above ester (36) was refluxed in the presence of anhydrous potassium carbonate in toluene for a long time. The product could not be condensed even after refluxing for long time. On working out the reaction mixture it was found to be the mixture of 7-hydroxy-8-acetyl-3,4-cyclohexenocoumarin and 8-acetyl-3,4-cyclohexeno-7-coumarinyloxy formic acid (37).



(36) (36 A)

Catalytic dehydrogenation of 7-hydroxy-3,4-cyclohexeno-coumarin to 7-hydroxy-3,4-benzocoumarin

7-Hydroxy-3,4-cyclohexenocoumarin on dehydrogenation with palladium charcoal and diphenyl ether gave the known 7-hydroxy-3,4-benzocoumarin (38) which has been prepared by the condensation of resorcinol and ortho bromobenzoic acid[24].



(38)

EXPERIMENTAL

7-Hydroxy-3,4-cyclohexenocoumarin :

Resorcinol (1.2 g.) and ethyl-2-cyclohexanone-2-carboxylate (2 g.) were intimately mixed and the mixture was slowly treated with concentrated sulphuric acid (6 ml.) allowing the temperature to rise slowly. The flask was shaken after each addition. After two hours the deep red solution was poured over ice. The compound was crystallised from dilute alcohol, m.p. 202°. The yield was theoretical. It was soluble in dilute alkali or sodium carbonate solution and did not give colouration with alcoholic ferric chloride solution.

Bromination of 7-hydroxy-3,4-cyclohexenocoumarin :

7-Hydroxy-8-bromo-3,4-cyclohexenocoumarin :

7-Hydroxy-3,4-cyclohexenocoumarin (2.16 g. ; 0.01 M) was dissolved in acetic acid by warming and to this solution bromine in acetic acid (10 % ; 16 ml. ; 0.01 M) was added. The mixture was left overnight at room temperature. The solid which separated out was crystallised from dilute acetic acid in colourless needles, m.p. 238°. Yield 2 g.

Analysis : Found : Br, 27.61 %.

$C_{13}H_{11}O_3Br$ requires : Br, 27.12 %.

The above compound was also prepared as follows : To a mixture of 2-bromoresorcinol (1.9 g. ; 0.01 M) and

ethyl-cyclohexanone-2-carboxylate (2.03 g. ; 0.012 M), sulphuric acid (80 % ; 10 ml.) was slowly added. The reaction mixture was allowed to stand overnight at the room temperature. The solid which separated on pouring the reaction mixture over crushed ice, was purified through sodium hydroxide solution. It crystallised from acetic acid in colourless needles, m.p. 238-40°. Yield 1.8 g. Mixed m.p. with the above compound was not depressed.

7-Hydroxy-6,8-dibromo-3,4-cyclohexenocoumarin :

7-Hydroxy-3,4-cyclohexenocoumarin (0.216 g. ; 0.001 M) was dissolved in acetic acid by warming . Bromine in acetic acid (10 % ; 6.4 ml ; 0.004 M) was added slowly with shaking. The reaction mixture was then heated on a steam bath for 4 hours. The product which separated on keeping the reaction mixture overnight, was crystallised from acetic acid in colourless needles, m.p. 218°. Yield 0.2 g.

Analysis : Found : Br, 42.75 %.

$C_{13}H_{10}O_3Br_2$ requires : Br, 42.78 %.

The dibromo compound was also prepared by further bromination of 7-hydroxy-8-bromo-3,4-cyclohexenocoumarin (1 M) with bromine in acetic acid (4 M) with the above condition. Mixed m.p. with the above compound was not depressed.

Formylation of 7-hydroxy-3,4-cyclohexenocoumarin :

7-Hydroxy-8-formyl-3,4-cyclohexenocoumarin :

A mixture of 7-hydroxy-3,4-cyclohexenocoumarin (2.16 g. ; 0.01 M), hexamethylenetetramine (2.5 g.) and glacial acetic acid (20 ml.) was gently refluxed on a sand bath for 5 hours. Dilute hydrochloric acid (25 ml. ; 1:1) was then added and the whole reaction mixture was heated on a steam bath for 2 hours. It was cooled and extracted with ether. On removal of ether a yellow solid was obtained. This was crystallised from ethanol in yellow shining plates, m.p. 172°. It gave reddish colouration with alcoholic ferric chloride solution.

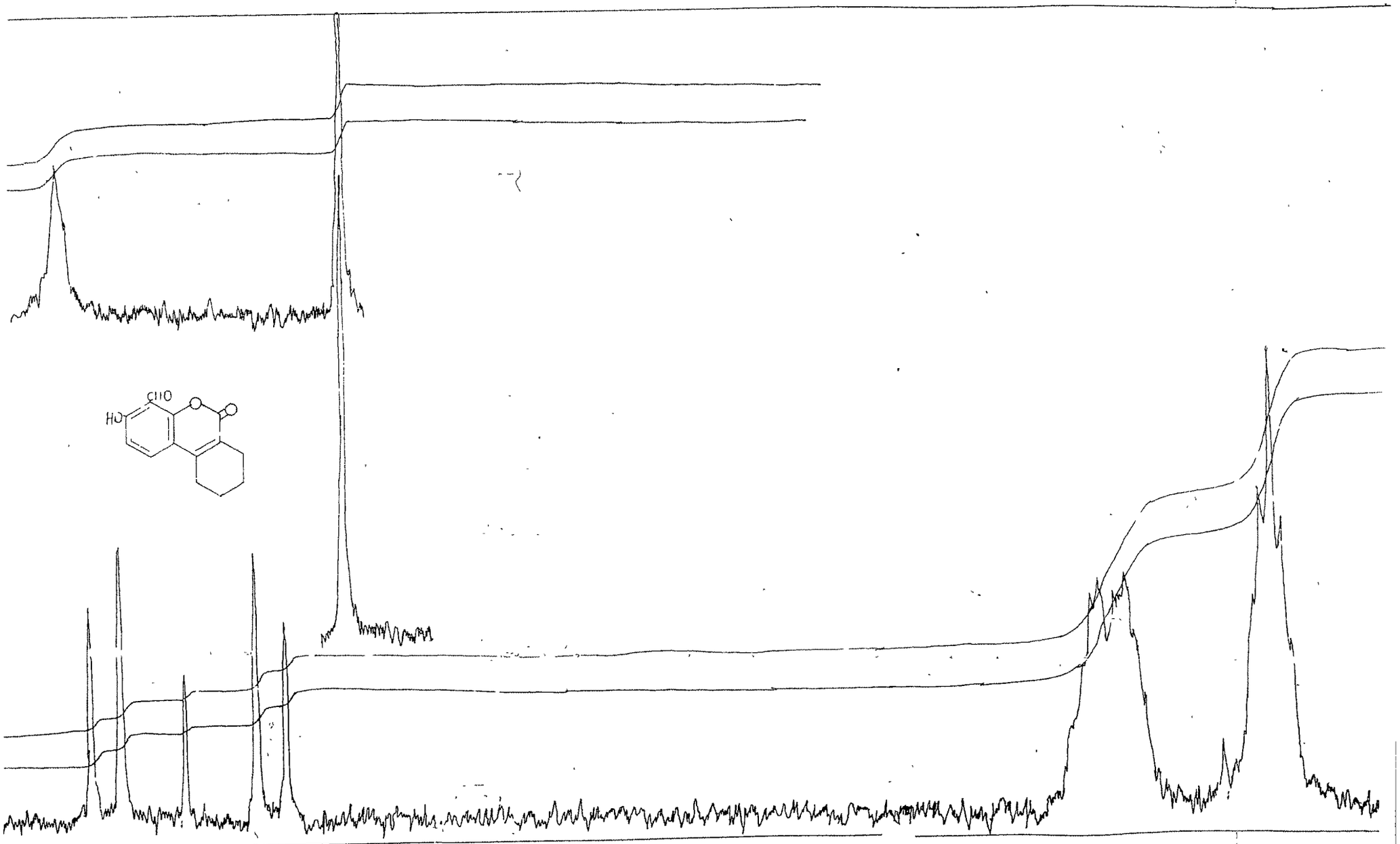
Analysis : Found : C,68.55 ; H,5.06 %.

$C_{14}H_{12}O_4$ requires : C,68.85 ; H,4.91 %.

Fries migration of 7-acetoxy-3,4-cyclohexenocoumarin :

7-Hydroxy-8-acetyl-3,4-cyclohexenocoumarin and 7-hydroxy-6-acetyl-3,4-cyclohexenocoumarin :

7-Acetoxy-3,4-cyclohexenocoumarin (1.5 g.) was intimately mixed with anhydrous aluminium chloride (7.5 g.) and heated at 160° for one hour. It was then treated with hydrochloric acid (1:1). The solid obtained was found to be the mixture of 7-hydroxy-8-acetyl-3,4-cyclohexenocoumarin and 7-hydroxy-6-acetyl-3,4-cyclohexenocoumarin.


HO
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The mixture was then taken in minimum quantity of acetic acid from which 7-hydroxy-6-acetyl-3,4-cyclohexenocoumarin was separated. It was crystallised from acetic acid in colourless needles, m.p. 237°. Yield 0.3 g. The mother liquor was diluted and the product was crystallised from alcohol in colourless needles, m.p. 171°. Yield 0.6 g. This was found to be 7-hydroxy-8-acetyl-3,4-cyclohexenocoumarin.

The above compounds were also synthesised as follows :

2-Acetylresorcinol (1.5 g.) was treated with ethyl-4-cyclohexanone-2-carboxylate (2 g.) and concentrated sulphuric acid (6 ml.). On working up the reaction mixture as usual, gave the 7-hydroxy-8-acetyl-3,4-cyclohexenocoumarin.

Resacetophenone was condensed with the above ester in the presence of phosphorus oxychloride and dry benzene by refluxing the mixture for 3 hours. 7-Hydroxy-6-acetyl-3,4-cyclohexenocoumarin was extracted in benzene and was crystallised from dilute alcohol. Both the compounds were identical with the isomers isolated in Fries migration.

Synthesis of 11-methyl-2H-furo(2,3-h)-3,4-cyclohexeno-benzopyran-2-one : Ethyl-8-acetyl-3,4-cyclohexeno-7-coumarinyloxyacetate :

7-Hydroxy-8-acetyl-3,4-cyclohexenocoumarin

(2.58 g. ; 0.01 M), ethylbromoacetate (1.67 g. ; 0.01 M) and anhydrous potassium carbonate (1.38 g. ; 0.01 M) were refluxed in acetone for 8 hours. The product obtained after evaporation of acetone was washed with dilute sodium hydroxide solution and crystallised from acetic acid in colourless needles, m.p. 161°. Yield 1.5 g.

Analysis	Found	: C,65.80 ; H,5.78 %.
$C_{19}H_{20}O_6$	requires	: C,66.27 ; H,5.81 %.

8-Acetyl-3,4-cyclohexeno-7-coumarinyloxyacetic acid :

The above ester (1 g.) on hydrolysis by warming it with sodium hydroxide solution (4 % ; 10 ml.) and leaving overnight gave the product which was purified with bicarbonate solution. On acidification it gave 8-acetyl-3,4-cyclohexeno-7-coumarinyloxyacetic acid which was crystallised from acetic acid in colourless needles, m.p. 200°. Yield 0.5 g.

Analysis :	Found	: C,64.18 ; H,5.07 %.
$C_{17}H_{16}O_6$	requires	: C,64.55 ; H,5.06 %.

11-Methyl-2H-furo(2,3-h)-3,4-cyclohexenobenzopyran-2-one :

The above acid (3.16 g. ; 0.01 M) was heated with sodium acetate (1 g. ; 0.01 M) and acetic anhydride (3 ml. ; 0.02 M) on a sand bath for two hours. The product, obtained on pouring the reaction mixture into ice cold water, was filtered, washed with bicarbonate

solution and was crystallised from acetic acid in colourless needles, m.p. 145°. Yield 1.5 g.

Analysis : Found : C,75.25 ; H,5.54 %.

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

Synthesis of 8-methyl-2H-furo(3,2-g)-3,4-cyclohexenobenzopyran-2-one : Ethyl 6-acetyl-3,4-cyclohexeno-7-coumarinyloxyacetate :

7-Hydroxy-6-acetyl-3,4-cyclohexenocoumarin (2.5 g. ; 0.01 M), ethylbromoacetate (1.6 g. ; 0.01 M) and anhydrous potassium carbonate (1.4 g. ; 0.01 M) were refluxed in acetone for 8 hours. The product was washed with dilute alkali and crystallised from alcohol in shining plates, m.p. 183°. Yield 1.8 g.

Analysis : Found : C,65.89 ; H,5.64 %.

$C_{19}H_{20}O_6$ requires : C,66.27 ; H,5.85 %.

6-Acetyl-3,4-cyclohexeno-7-coumarinyloxyacetic acid:

The above ester (1 g.) on hydrolysis by warming with sodium hydroxide solution (4 % ; 10 ml.) and leaving overnight at the room temperature gave the product which was crystallised from acetic acid in colourless crystals, m.p. 242°. Yield 0.7 g.

Analysis : Found : C,64.07 ; H,5.01 %.

$C_{17}H_{16}O_6$ requires : C,64.55 ; H,5.10 %.

8-Methyl-2H-furo(3,2-g)-3,4-cyclohexenobenzopyran-2-one :

6-Acetyl-3,4-cyclohexeno-7-coumarinyloxyacetic acid (3.16 g. ; 0.01 M) was heated with sodium acetate (1 g. ; 0.01 M) and acetic anhydride (3 ml. ; 0.02 M) on a sand bath for 3 hours. The product, obtained on pouring the reaction mixture into ice cold water, was filtered, washed with bicarbonate solution and was crystallised from alcohol in colourless needles, m.p. 202°. Yield 1.8 g.

Analysis : Found : C,75.60 ; H,5.46 %.
$C_{16}H_{14}O_3$ requires : C,75.57 ; H,5.55 %.

Synthesis of 10-methyl-2H-furo(2,3-h)-3,4-benzobenzopyran-2-one : 7-Allyloxy-3,4-cyclohexenocoumarin :

7-Hydroxy-3,4-cyclohexenocoumarin (1 g.) was mixed with allylbromide (1 ml.), anhydrous potassium carbonate (2 g.) and dry acetone (40 ml.). The reaction mixture was refluxed on a steam bath for 6 hours. The compound obtained after evaporation of acetone was washed with dilute alkali and crystallised from alcohol in silky needles, m.p. 121°. Yield 0.9 g.

Analysis : Found : C,74.54 ; H,5.81 %.
$C_{16}H_{16}O_3$ requires : C,74.98 ; H,6.29 %.

7-Hydroxy-8-allyl-3,4-cyclohexenocoumarin :

7-Allyloxy-3,4-cyclohexenocoumarin (1 g.) was refluxed with dimethylaniline (3 ml.) on a wire gauze for 6 hours. The mixture was cooled and filtered. The separated product was washed with petroleum ether, dried and purified through dilute alkali solution. It was crystallised from alcohol in shining needles, m.p. 194°. Yield 0.6 g.

Analysis : Found : C,75.08 ; H,6.26 %.

$C_{16}H_{16}O_3$ requires : C,74.98 ; H,6.29 %.

10-Methyl-2H-10,11-dihydro-furo(2,3-h)-3,4-cyclohexenobenzopyran-2-one :

7-Hydroxy-8-allyl-3,4-cyclohexenocoumarin (1 g.) was mixed with concentrated sulphuric acid (2 ml.) with constant shaking for 10 minutes. The clear reaction mixture on adding into ice cold water gave the alkali insoluble product which on crystallisation with ethanol gave colourless crystals, m.p. 167°. Yield 0.7 g.

Analysis : Found : C,75.30 ; H,6.48 %.

$C_{16}H_{16}O_3$ requires : C,74.98 ; H,6.29 %.

10-Methyl-2H-furo(2,3-h)-3,4-benzo-benzopyran-2-one :

10-Methyl-2H-10,11-dihydro-furo(2,3-h)-3,4-cyclohexenobenzopyran-2-one (0.5 g.) was mixed with diphenyl ether (3 ml.) and palladised charcoal (10 % ; 0.2 g.). The mixture was refluxed for 8 hours and

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OFFSET

filtered hot. On cooling, the crystals were separated, washed with petroleum ether and crystallised from alcohol in colourless needles, m.p. 222°. Yield 0.2 g.

Analysis : Found : C,76.38 ; H,3.50 %.

$C_{16}H_{10}O_3$ requires : C,76.81 ; H,4.00 %.

Mannich reaction on 7-hydroxy-3,4-cyclohexenocoumarin with formalin and piperidine : 7-Hydroxy-8-piperidinomethyl-3,4-cyclohexenocoumarin :

7-Hydroxy-3,4-cyclohexenocoumarin (2.16 g.) in ethanol, formalin (0.3 g.), piperidine (0.85 g.) were heated on a water bath for 3 hours. The residue obtained after recovering the solvent was washed with benzene and crystallised from benzene-petroleum ether in colourless crystals, m.p. 170°. Yield 1.6 g.

Analysis : Found : C,72.84 ; H,7.12 ; N,4.69 %.

$C_{19}H_{23}O_3N$ requires : C,72.84 ; H,7.34 ; N,4.47 %.

Sommelet reaction on 7-hydroxy-8-piperidinomethyl-3,4-cyclohexenocoumarin : 7-Hydroxy-8-formyl-3,4-cyclohexenocoumarin :

7-Hydroxy-8-piperidinomethyl-3,4-cyclohexenocoumarin (1 g.) was refluxed with acetic acid (10 ml.) and hexamethylene-tetramine (1 g.) for 4 hours on a wire gauze. Concentrated hydrochloric acid (10 ml.) was added and the mixture was refluxed further for one hour. It was then added to water (500 ml.) and the solution was

extracted with ether. The residue, on removal of ether was crystallised from alcohol in shining plates, m.p. 172°. Mixed m.p. with the compound prepared by the direct formylation of 7-hydroxy-3,4-cyclohexenocoumarin was not depressed.

Mannich reaction on 7-hydroxy-3,4-cyclohexenocoumarin with formalin and morpholine : 7-Hydroxy-8-morpholinomethyl-3,4-cyclohexenocoumarin :

The mixture of 7-hydroxy-3,4-cyclohexenocoumarin (2.16 g.) in ethanol (c.c) formalin (0.3 g.) and morpholine (0.9 g.) was heated on a water bath for 3 hours. The separated product was crystallised from alcohol in colourless crystals, m.p. 180°. Yield 1.3 g.

Analysis	: Found	: C, 68.22 ; H, 6.55 ; N, 4.83 %.
$C_{18}H_{21}O_4N$	requires	: C, 68.55 ; H, 6.71 ; N, 4.44 %.

Sommelet reaction on 7-hydroxy-8-morpholinomethyl-3,4-cyclohexenocoumarin : 7-Hydroxy-8-formyl-3,4-cyclohexenocoumarin :

7-Hydroxy-8-morpholinomethyl-3,4-cyclohexenocoumarin (1 g.) was refluxed with acetic acid (10 ml.) and hexamethylenetetramine (1 g.) for 5 hours on a wire gauze. Concentrated hydrochloric acid (10 ml.) was added and the mixture was refluxed further for one hour. It was worked up as usual and the 7-hydroxy-8-formyl-3,4-cyclohexenocoumarin was crystallised from alcohol in colourless crystals, m.p. 172°.

Pechmann reaction of 7-hydroxy-3,4-cyclohexenocoumarin with malic acid : 2H-10H-Pyrano(2,3-h)-3,4-cyclohexenobenzopyran-2,10-dione :

7-Hydroxy-3,4-cyclohexenocoumarin (1 g.) was mixed with malic acid (1 g.) and concentrated sulphuric acid (3 ml.). The reaction mixture was heated on a steam bath for 3 to 4 hours till the effervescence ceased. The mixture on decomposition with ice water gave a yellow compound which was digested with ammonia and filtered. The compound was crystallised from large quantities of glacial acetic acid in colourless needles, m.p. 315°. Yield 0.3 g.

Analysis : Found : C,71.21 ; H,4.18 %.
$C_{16}H_{12}O_4$ requires : C,71.64 ; H,4.48 %.

K.R. Acetylation on 7-hydroxy-8-acetyl-3,4-cyclohexenocoumarin : 10-Methyl-11-acetyl-2H-12H-pyrano-(2,3-h)-3,4-cyclohexenobenzopyran-2,12-dione :

7-Hydroxy-8-acetyl-3,4-cyclohexenocoumarin (0.5 g.) was mixed with freshly fused sodium acetate (1 g.) and acetic anhydride (3 ml.). The reaction mixture was heated at 180-90° for 8-9 hours. It was then cooled at the room temperature and decomposed in ice-water. The product was filtered and washed with dilute alkali solution. It was crystallised from acetic acid in silky crystals, m.p. 240°. Yield 0.2 g.

The i.r.spectra showed three strong bands in the carbonyl region, viz. 1720 cm^{-1} (lactonyl >C=O group), 1698 cm^{-1} (γ-pyronyl >C=O group), 1655 cm^{-1} (acetyl group at position 11).

Analysis : Found : C,70.20 ; H,4.95 %.
$C_{19}H_{16}O_5$ requires : C,70.36 ; H,4.98 %.

Condensation of 7-hydroxy-8-acetyl-3,4-cyclohexenocoumarin with ethyl chloroformate : Ethyl 8-acetyl-3,4-cyclohexeno-7-coumarinyloxyformate

7-Hydroxy-8-acetyl-3,4-cyclohexenocoumarin (2.58 g. ; 0.01 M), ethyl chloroformate (1.09 g. ; 0.01 M) and anhydrous potassium carbonate (2 g.) were refluxed in boiling acetone for 15 hours. The compound obtained on evaporation of acetone was washed with dilute alkali solution. It was crystallised from alcohol in shining plates, m.p. 155°. Yield 0.5 g.

Analysis : Found : C,65.65 ; H,5.12 %.
$C_{18}H_{18}O_6$ requires : C,65.45 ; H,5.45 %.

Attempted cyclisation of ethyl 8-acetyl-3,4-cyclohexeno-7-coumarinyloxyformate :

The above ester (0.5 g.) was mixed with dry toluene (40 ml.) and refluxed in the presence of anhydrous potassium carbonate for 40 hours. The compound obtained on evaporation of the solvent was found to be the mixture of 8-acetyl-3,4-cyclohexeno-7-coumarinyloxy formic acid and 7-hydroxy-8-acetyl-3,4-cyclohexeno-

coumarin. The mixture was taken in bicarbonate solution and filtered. The filtrate on acidification gave the above acid which was crystallised from glacial acetic acid in shining needles, m.p. 265°.

Analysis : Found : C,63.95 ; H,4.73 %.

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

Dehydrogenation of 7-hydroxy-3,4-cyclohexenocoumarin : 7-Hydroxy-3,4-benzocoumarin :

The mixture of 7-hydroxy-3,4-cyclohexenocoumarin (1 g.),diphenyl ether (5 ml.) and palladised charcoal (10 % ; 0.5 g.) was refluxed for 6 to 8 hours. It was filtered hot and the filtrate was cooled. The separated product was washed with petroleum ether and crystallised from ethanol in colourless needles, m.p. 235°. Hurtley et al.[24] reported m.p. 232°.

Analysis : Found : C,73.16 ; H,3.68 %.

$C_{13}H_8O_3$ requires : C,73.58 ; H, 3.77 %.

Calc for $C_{15}H_{10}O_3$ which is previously reported & analysed

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