chapter-I

synthesis of furoisoflavones

section-I

CHAPTER - I

SYNTHESIS OF FUROISOFLAVONES

SECTION - I

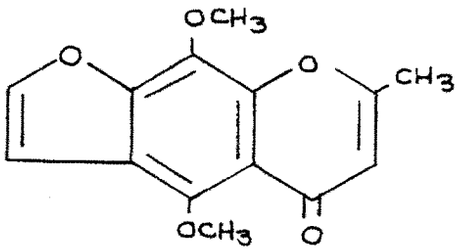
Many of the naturally occuring polyphenolics viz. coumarins, chromones bear furan ring system. Furochromones of furcbenzo- ɣ -pyrones occuring mainly in the fruits and seeds of Ammi Visanaga L. a re of the linear type of and are limited in number. Khellin (1), visanagin (2), Khellol (3) are a few important furochromones isolated as natural products having physiological properties.

In isoflavonoids, there are a few natural products viz. Nepsudin (4), Dehydroneotenone (5), Neo-Rautenone (6), Ambonone (7) which also bear unsubstituted furan ring system.

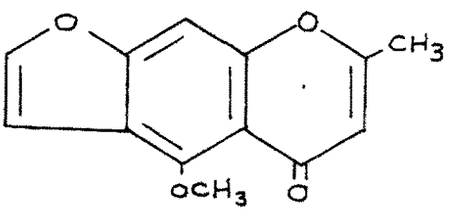
Physiological activities of Furobenzo- ɣ -pyrone derivatives

Khellin (1) has pronounced physiological activity. It has selective antispasmodic effect upon ureter,[3,4] gall blader,[5] and bile duct.[6] A bronchodilating action of (1) has been reported.[7,8] It is used as potent coronary vasodilator[9-11] and in whopping cough.

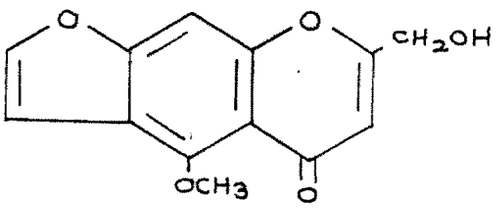
Khellin has been used for a variety of pharmacological indications including hypertension, renal and biliary colic and stomach disorders. The recent discovery of Khellin's lipid-altering activity in man and antiatherosclerotic activity in animal mcdels has renewed interest in Khellin analogues.[12] Recently khellin was employed



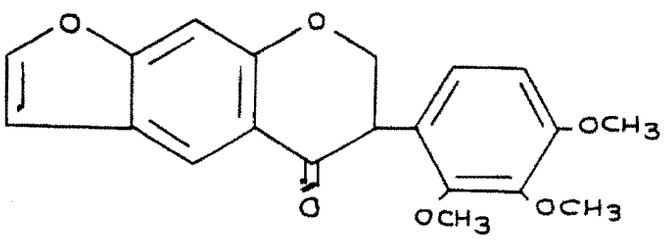
Khellin



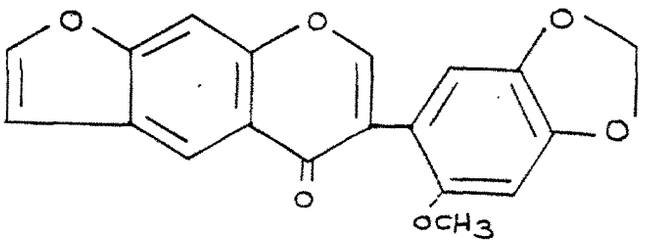
Visanagin



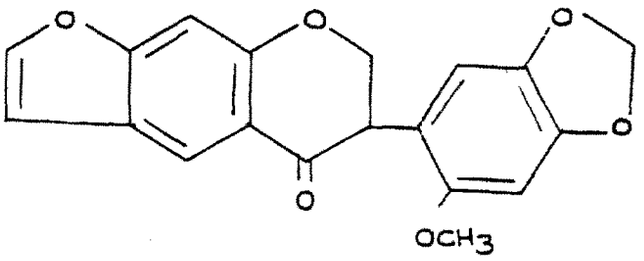
Khellol



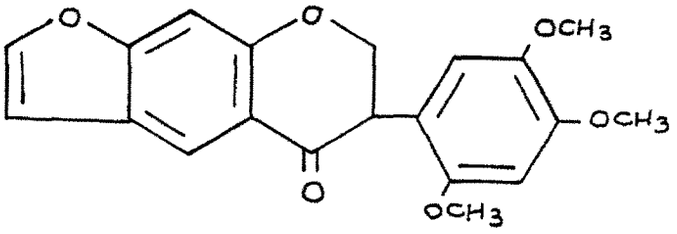
Nepsudin



Dehydroneotenone



Neo-Rautenone



Ambonone

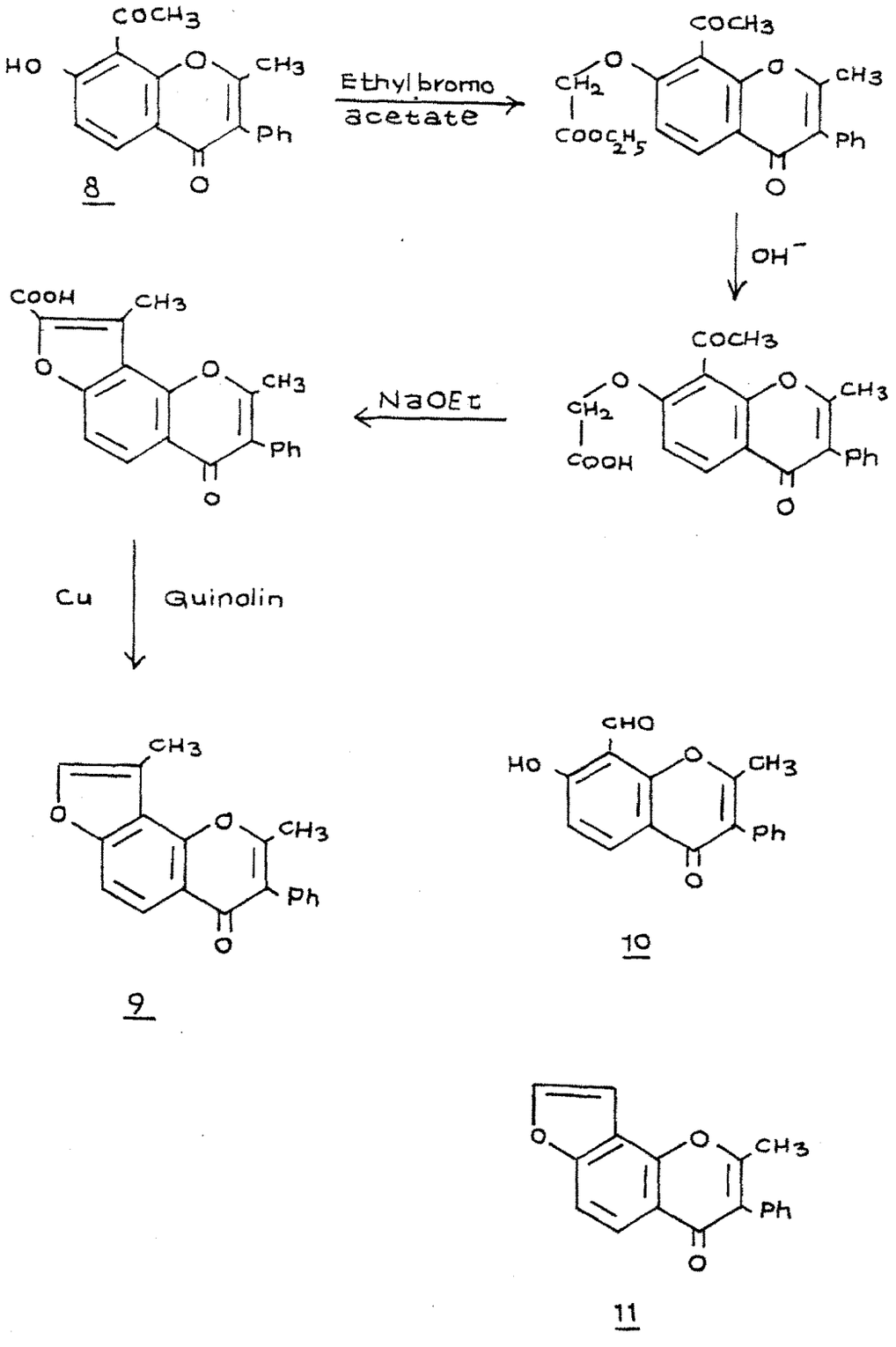
for the photochemotherapy of Vitiligo[13,14] an idiopatic disease characterized by the lack of pigmentation of some areas of the human skin. It has been demonstrated that Khellin, unlike psoralene, is not phototoxic & consequently, the treatment by this drug and sunlight is considered safe.[15]

Khellol glucoside, khellinin exert a simulating action on the heart and increases the coronary flow. It is not converted into khellin in the digestive tractor in the body tissue.[16] Schonberg and Sina[17] studied antispasmodic activity of a number of furochromones with the relation to their chemical constitutions.

Methods of Synthesis of Furoisoflavones

Different methods are described in the literature to build up furan ring system on the aromatic nucleus. Row and Seshadri[18] carried out the Fries migration of 7-acetoxy-2-methyl isoflavone and obtained 8-acetyl-7-hydroxy-2-methyl isoflavone, which on condensation with ethyl bromoacetate and subsequent hydrolysis followed by cyclization of the acid gave furancarboxylic acid which was decarboxylated to 3",2-dimethyl furo (5",4":7,8) isoflavone (9). (Scheme-I)

Scheme I : Row and Seshadri [18]



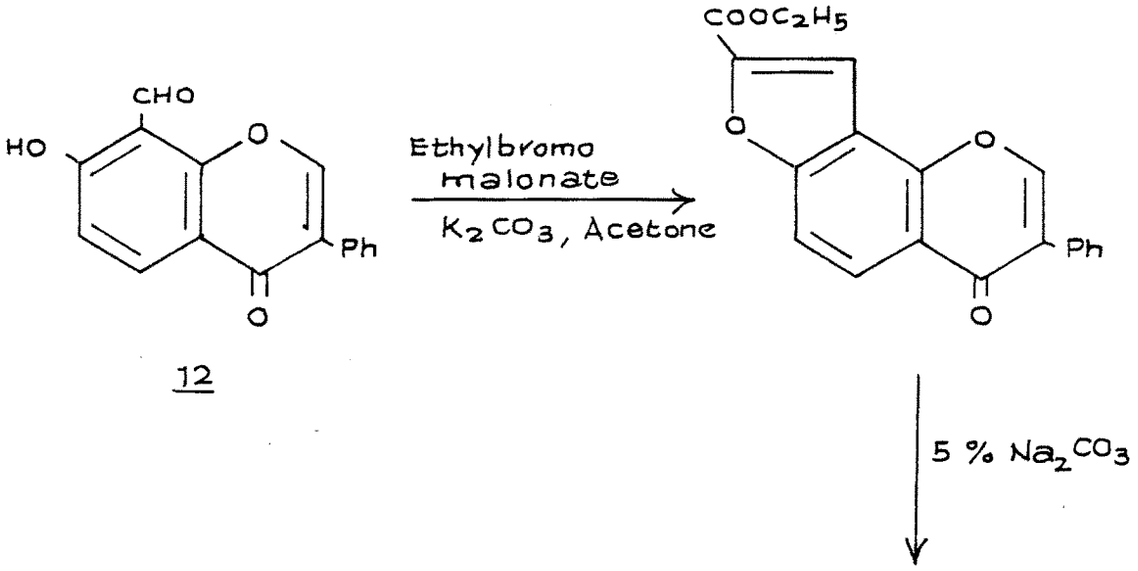
Using this procedure, they also synthesised 2-Methyl furo (5",4":7,8) isoflavone (11) starting from 8-formyl-7-hydroxy-2-methyl isoflavone (10). Matsumato et al.[19] also prepared the same furo isoflavone (11) from 8-formyl-7-hydroxy-2-methyl isoflavone using ethyl bromomalonate instead of ethyl bromoacetate.

Fukui and Kawase[20] synthesised furo (5",4":7,8) isoflavone (13) by condensing 8-formyl-7-hydroxy isoflavone (12) with ethylbromomalonate in acetone solution in presence of anhydrous potassium carbonate followed by hydrolysis and decarboxylation. (Scheme-II).

Sarin, Segal and Seshadri[21] prepared 2",2-dimethyl 4'-methoxy furo (5",4":7,8) isoflavone (14). Bromination of the 8-allyl derivative was carried out using mixtureof HBr and acetic acid which was further cyclized and dehydrogenated by treating with N-bromosuccinimide in CCl_4 to obtain furoisoflavone. (Scheme-III)

Seshadri, Chandrashekar and Krishnamurti[22] synthesized dehydroelliptone (16) starting from 7-hydroxy-2',4',5'-trimethoxy isoflavone (15) which was allylated and then subjected to Claisen rearrangement to give 8-allyl compound. Oxidation of this with OsO_4 gave 8-acetaldehyde derivative

Scheme II : Fukui and Kawase[20]



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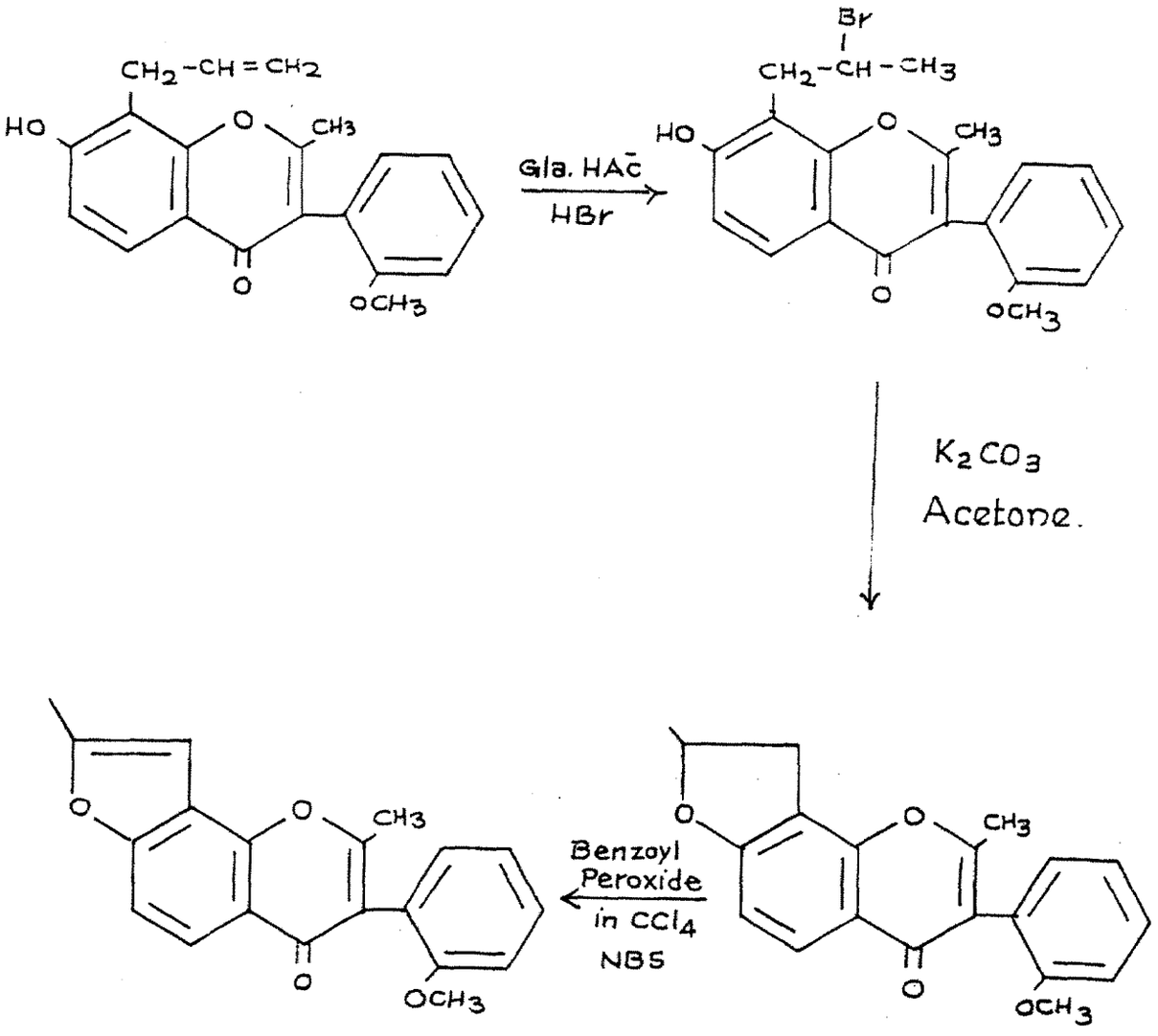
Scheme III : Sarin et al[21]



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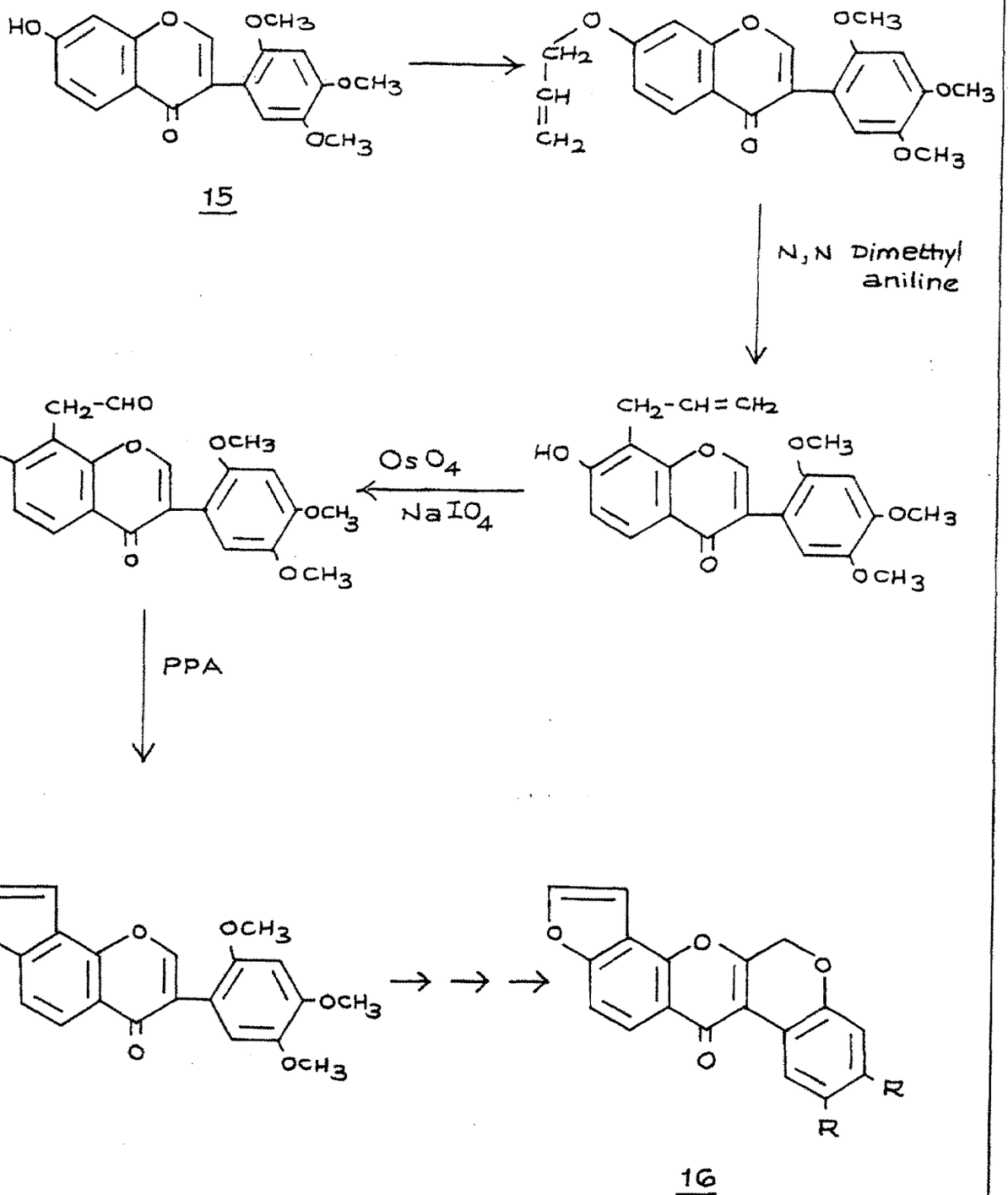
which on treatment with PPA gave elliptol isoflavone. (Scheme-IV)

Linear furoisoflavones are difficult to synthesize as migration of 7-allyloxy isoflavone takes place regiospecifically at position 8 only and not at position 6, the reason being fixation of double bond between position 7 and 8.[23] Seshadri, Chandrashekar and Krishnamurti[24] synthesized a linearly fused isoelliptol isoflavone (18) starting from corresponding ketone (17). It was allylated at hydroxyl group of position 4 and then methylated at hydroxyl group at position 2, which when subjected to Claisen rearrangement gave regiospecific 5-allyl derivative. It was further demethylated and isoflavone ring was then built up. Treatment with OsO_4 and ring closer with PPA gave isoelliptol isoflavone (18). (Scheme-V)

pardanani and Trivedi[25] synthesized linear furoisoflavone namely 2,9-dimethyl-6-phenyl-5-oxo-5H-furo (3,2-g) benzopyran (21) starting with 7-hydroxy-8-methyl isoflavone (19). Allylation of (19) followed by the Claisen rearrangement furnished 6-allyl-8-methyl-7-hydroxyisoflavone. Cyclization with 80% H_2SO_4 gave 2,9-dimethyl 2,3-dihydro-6-phenyl furo(3,2-g) benzopyran-[5H]-one (20). Dehydrogenation of (20) with Pd/C (10%) afforded 2,9-dimethyl-

Scheme IV : Seshadri et al[22]



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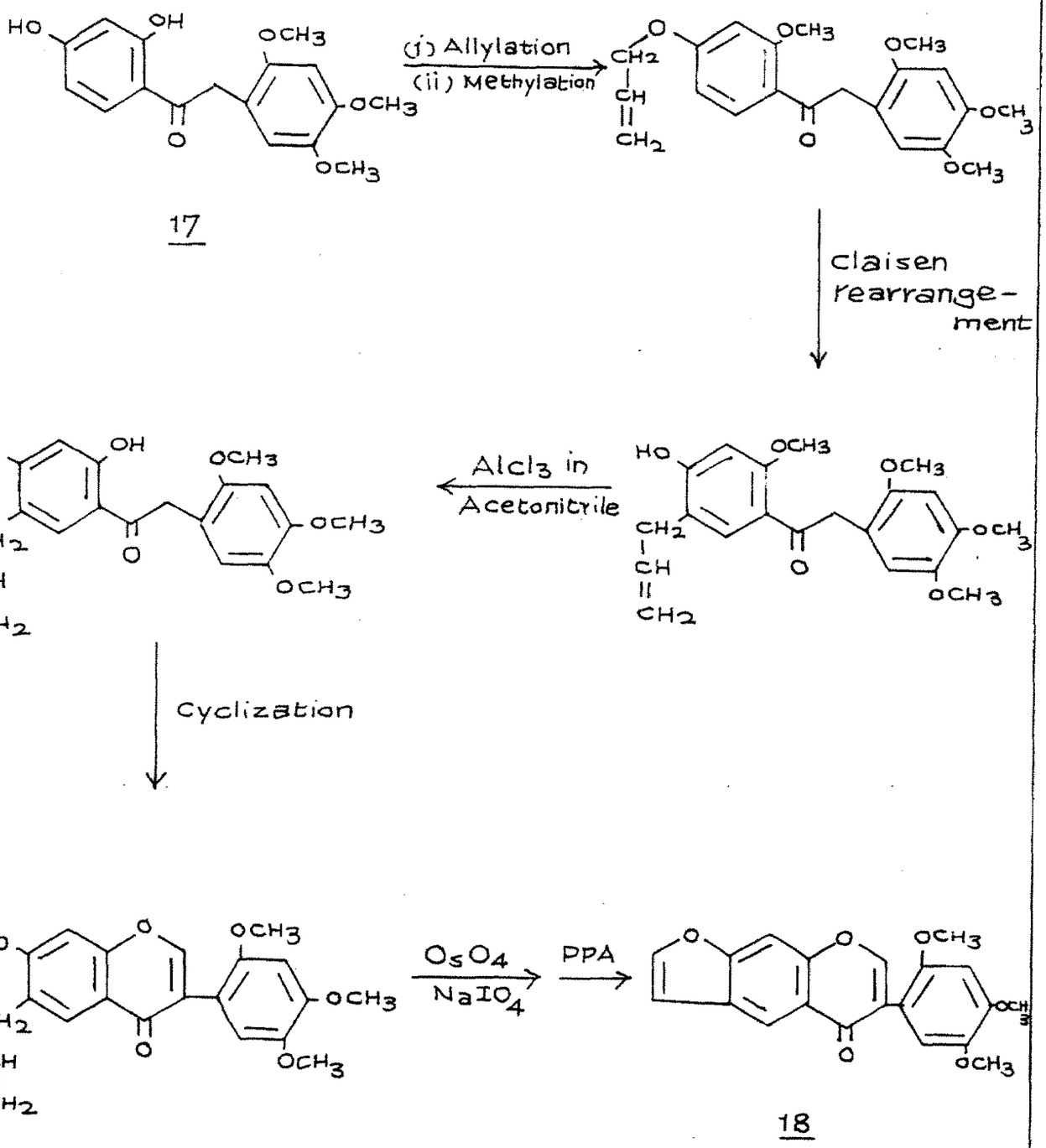
Scheme V : Seshadri and coworkers[24]



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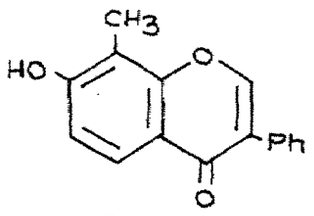
Scheme VI : Pardanani and Trivedi[25]



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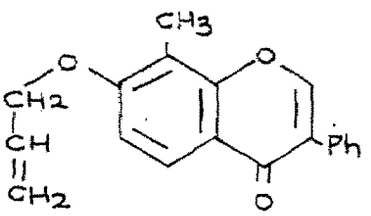
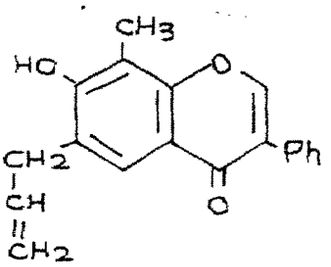
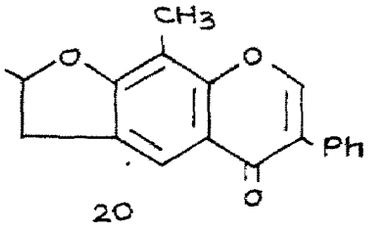
Allyl bromide
K_2CO_3, Acetone



Claisen rearrangement



80 %
H_2SO_4



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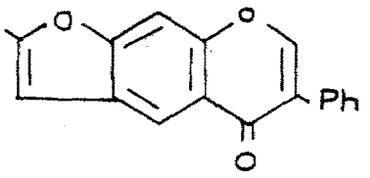
Pd/C



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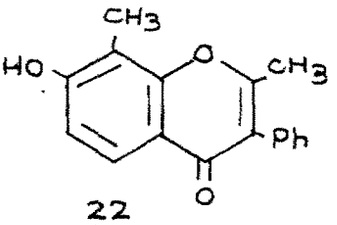

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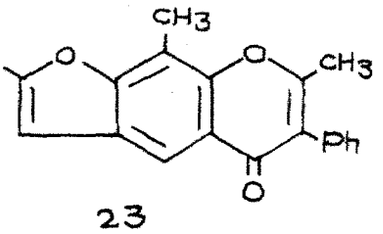


23

-6-phenyl furo (3,2-g) benzopyran (23) starting with 2,8-dimethyl-7-hydroxy isoflavone (22) by the same route. (Scheme VI)

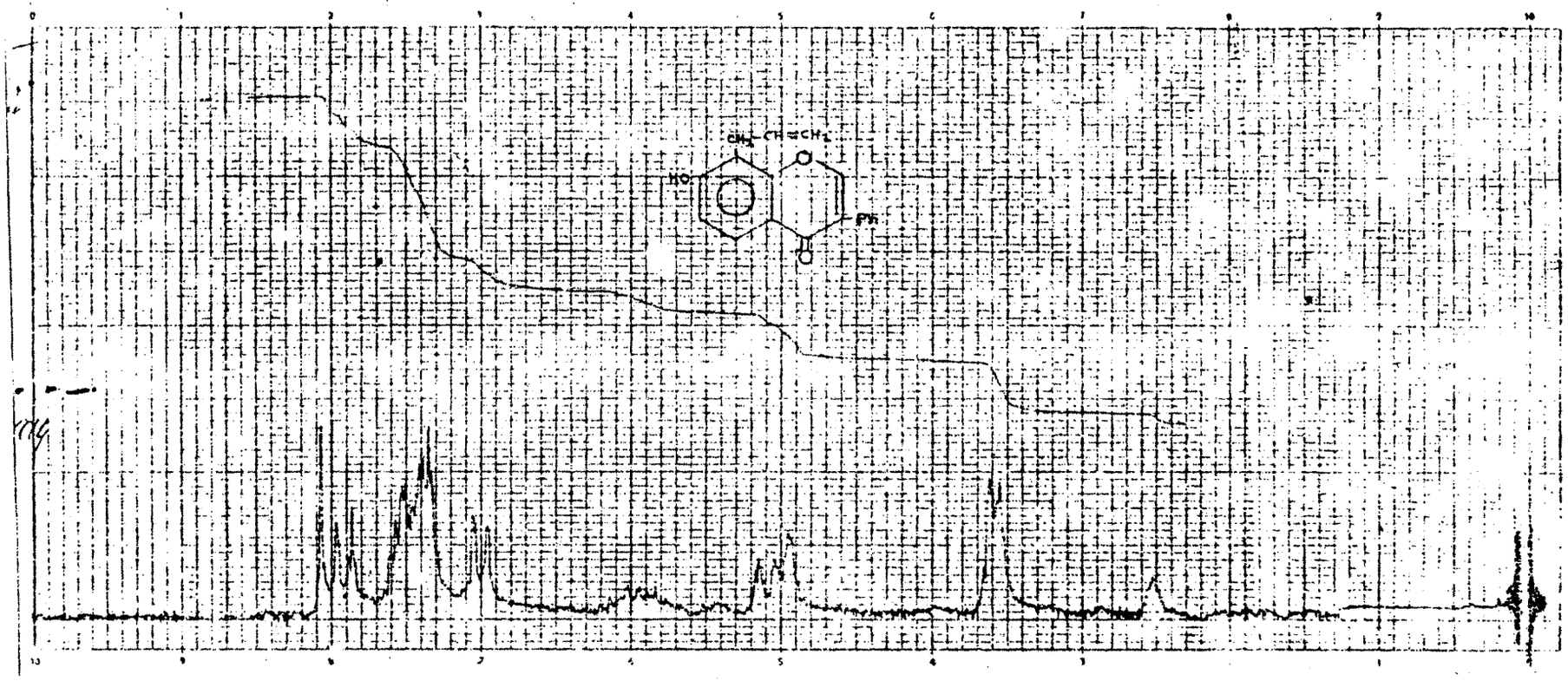
Present work

In continuation of the work carried out by Pardanani and Trivedi [25] different linear as well as angular furo-isoflavones are synthesized.

Synthesis of 2-Methyl-6-phenylfuro (2,3-h)-1-benzopyran-7(H)-one (28)

7-Hydroxy isoflavone (24) on allylation with allyl bromide and anhydrous potassium carbonate in dry acetone gave 7-allyloxyisoflavone (25) which when subjected to Claisen rearrangement by refluxing in N,N-dimethylaniline furnished 8-allyl-7-hydroxyisoflavone (26) as TLC pure product.

The PMR spectra (26) exhibited two doublets one at δ 7.9 for proton at C-5 (J=9Hz) and another at δ 7.0 for proton at C-6 (J=9Hz) indicating that position 5th and 6th on the aromatic nucleus are free to couple and migration took place at position 8 rather than at position 6 of the isoflavone ring. (Fig.1) This is because of the fact that there is fixation of double bond between position 7 and 8 of the isoflavone ring. The allyl isoflavone on tituration

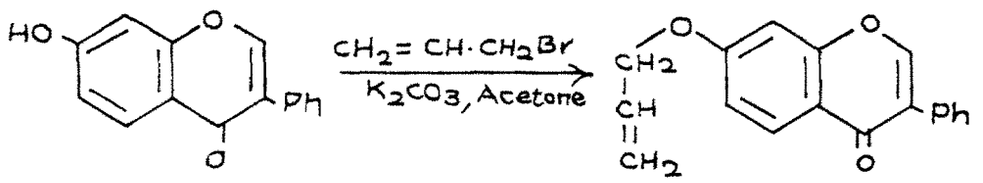


(Fig.1) 7-Hydroxy-8-allyl isoflavone (26)

with H_2SO_4 (80%) furnished 2,3-dihydro-2-methyl-6-phenyl furo (2,3-h)-1-benzopyran-7(H)-one (27) the structure of which was established by PMR spectrum ($CDCl_3$) which exhibited characteristic double doublets for two geminal protons at position 3, one at δ 3.0 (J=18,8Hz) and another at δ 3.5 (J=18,8Hz). The signal for the proton at C-2 appeared as multiplet at 5.2 while the protons at C-5 and C-8 appeared as singlets and doublet, J=9Hz in downfield region at δ 7.9 and 8.15 respectively. (Fig.2) (27) was also formed when (21) was heated with a mixture of acetic acid and hydrobromic acid followed by cyclization with potassium carbonate in dry acetone. (27) when refluxed with diphenyl ether with Pd/C (10%) underwent dehydrogenation to furnish 2-methyl-6-phenylfuro (2,3-h)[1]-benzopyran-7(H)-one. (28) the structure of which was established by PMR spectrum ($CDCl_3$) exhibiting signals at δ 2.6, singlet for methyl group at C-2, one singlet at δ 6.8 for proton at C-3. The protons at C-8 and C-9 appeared as two doublets at 8.2 and 7.35 (J=9Hz) respectively, five protons of aromatic nucleus appeared as multiplet in downfield region at 7.5, one singlet at 8.1 appeared for proton at C-5. (Scheme-VII) (Fig.3)

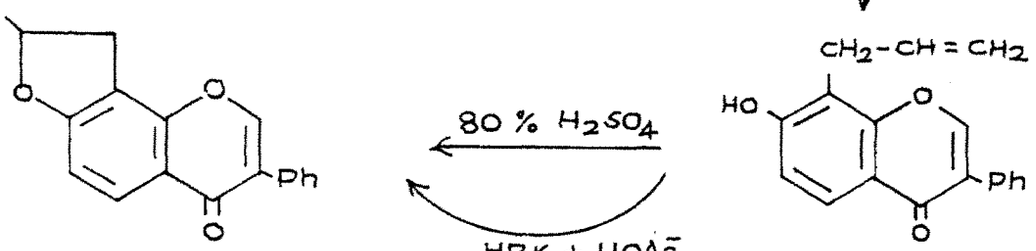
Ozonolysis of (26) followed by hydrogenation furnished 7-hydroxy-8-(2-oxoethyl)isoflavone (29) which was cyclized

Scheme VII



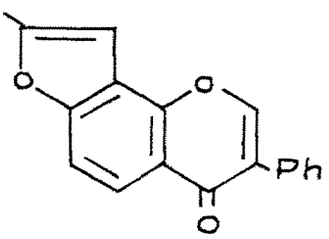
24 25

DMA



27 26

Pd/c



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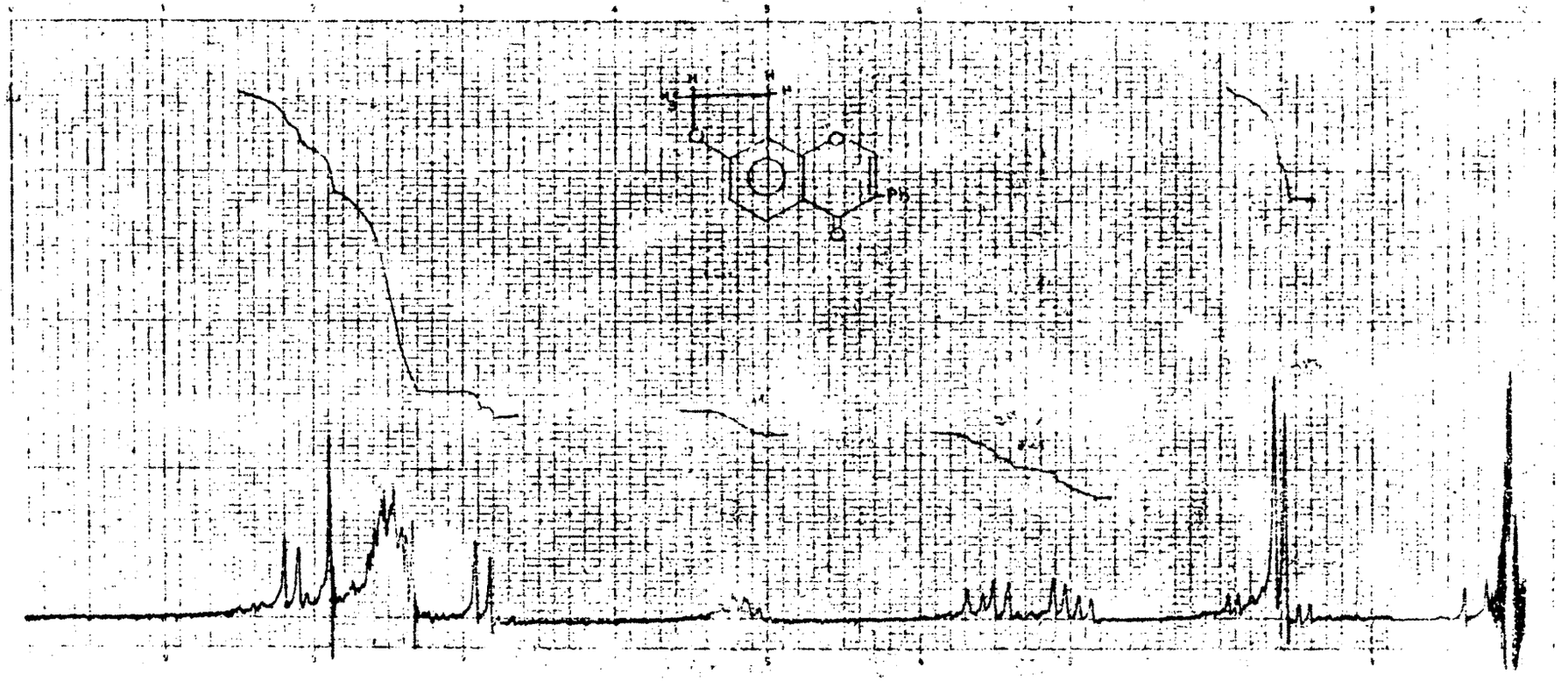
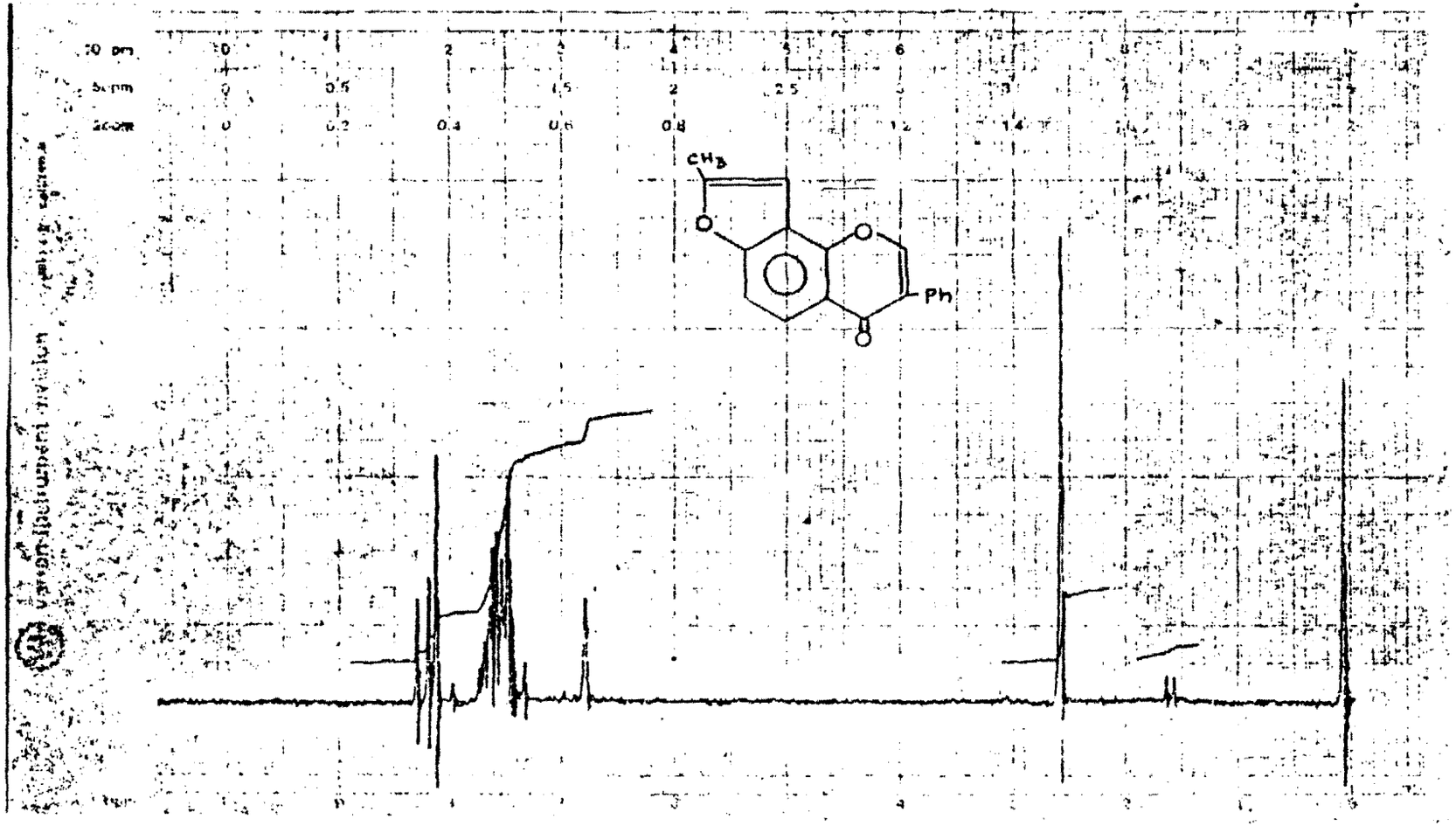


2,3-Dihydro-2-methyl-6-phenyl furo(2,3-h)-1-benzopyran-(7H)-one (27)

(Fig. 2)



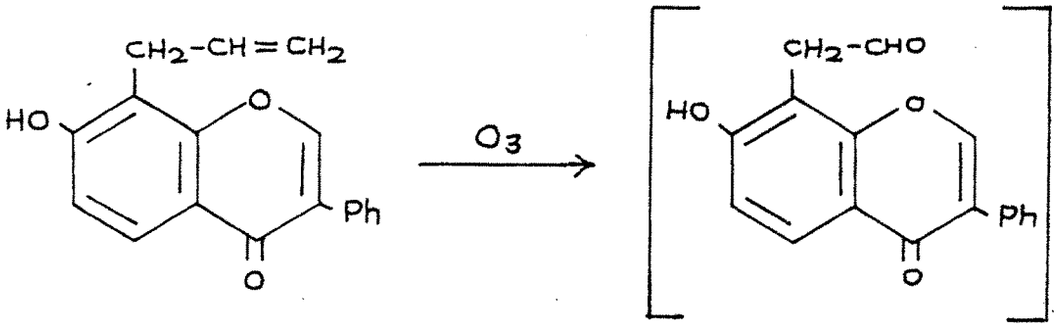
2-Methyl-6-phenyl furo(2,3-h)-1-benzopyran-(7H)-one (28) (Fig. 3)

with polyphosphoric acid to give 6-phenylfuro(2,3-h)-1-benzopyran-7(H)-one (30). M.p. 150°. The same compound was synthesized by Fukui et al[20] and reported m.p. 152°. PMR ($CDCl_3$) exhibited the signal at δ 7.1 (J=3Hz) as doublet for proton at C_3-H and another doublet at δ 7.7 (J=3Hz) for proton at C_2-H, multiplet at 7.4 for 5 protons of aromatic nucleus and one proton at C_9-H, singlet for one proton at C_5-H at δ 8.0 a doublet (J=9Hz) for proton at C_8-H at δ 8.1. (Scheme-VIII) (Fig. 4)

In order to synthesize linear furoisoflavones, it was thought of interest to utilize the stratagy developed by Pardanani and Trivedi[26] to synthesize Psoralene - a linear furocoumarin and Patel and Trivedi[27] to synthesize linear furoxanthones. In this stratagy, position 8 of 7-hydroxycoumarin was blocked by bromine and 7-allyloxy-8-bromocoumarin (31) was subjected to Claisen rearrangement which afforded 6-allyl-7-hydroxycoumarin (32) bromine being eliminated during course of the reaction. Compound (32) was converted to Psoralene (33) by subjecting it to ozonolysis followed by cyclization with orthophosphoric acid. (Scheme-IX)

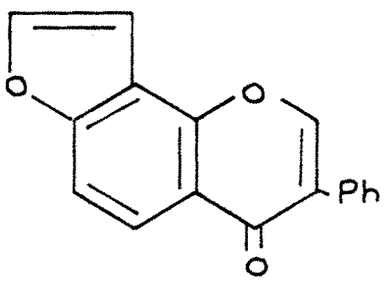
Shah and Trivedi[28] carried out the Claisen rearrangement of several 4-substituted 7-allyloxy-8-bromocoumarin

Scheme VIII



26 29

PPA



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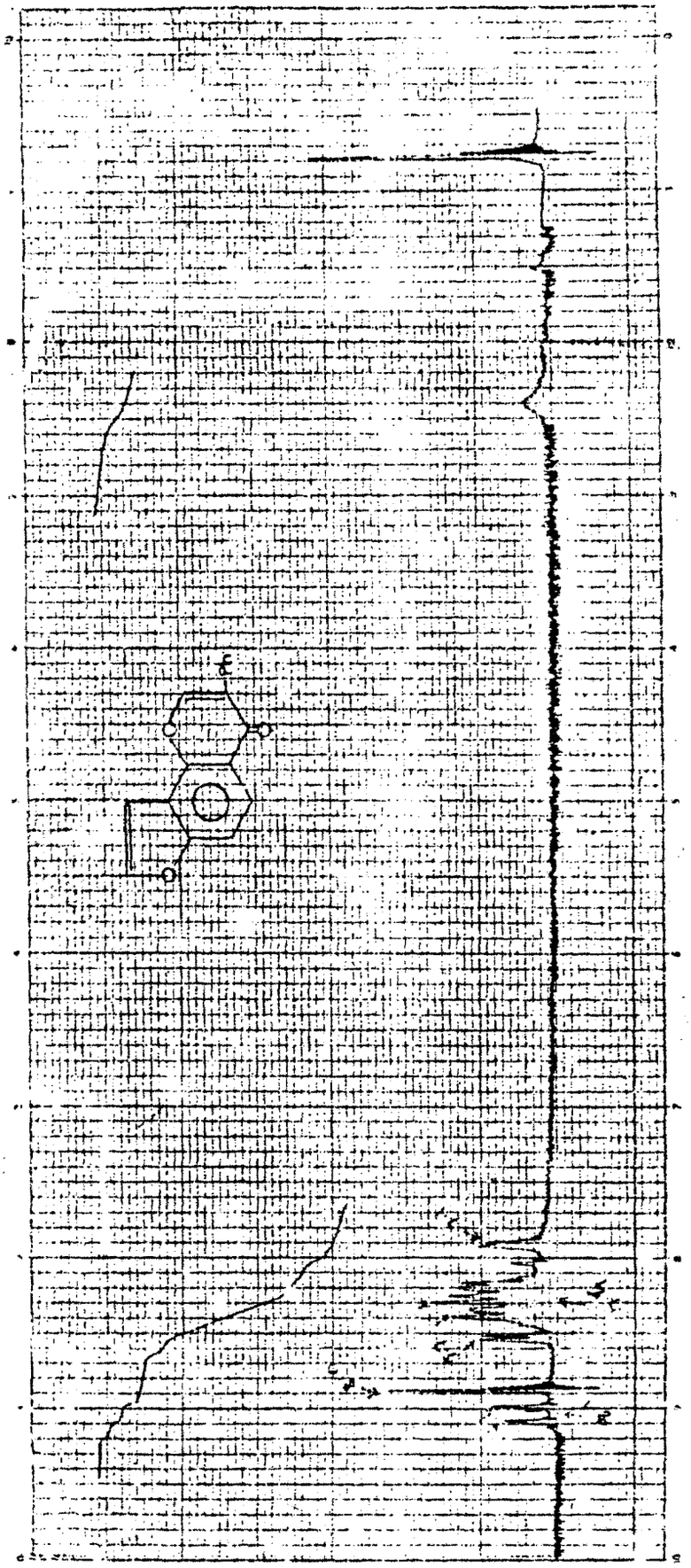
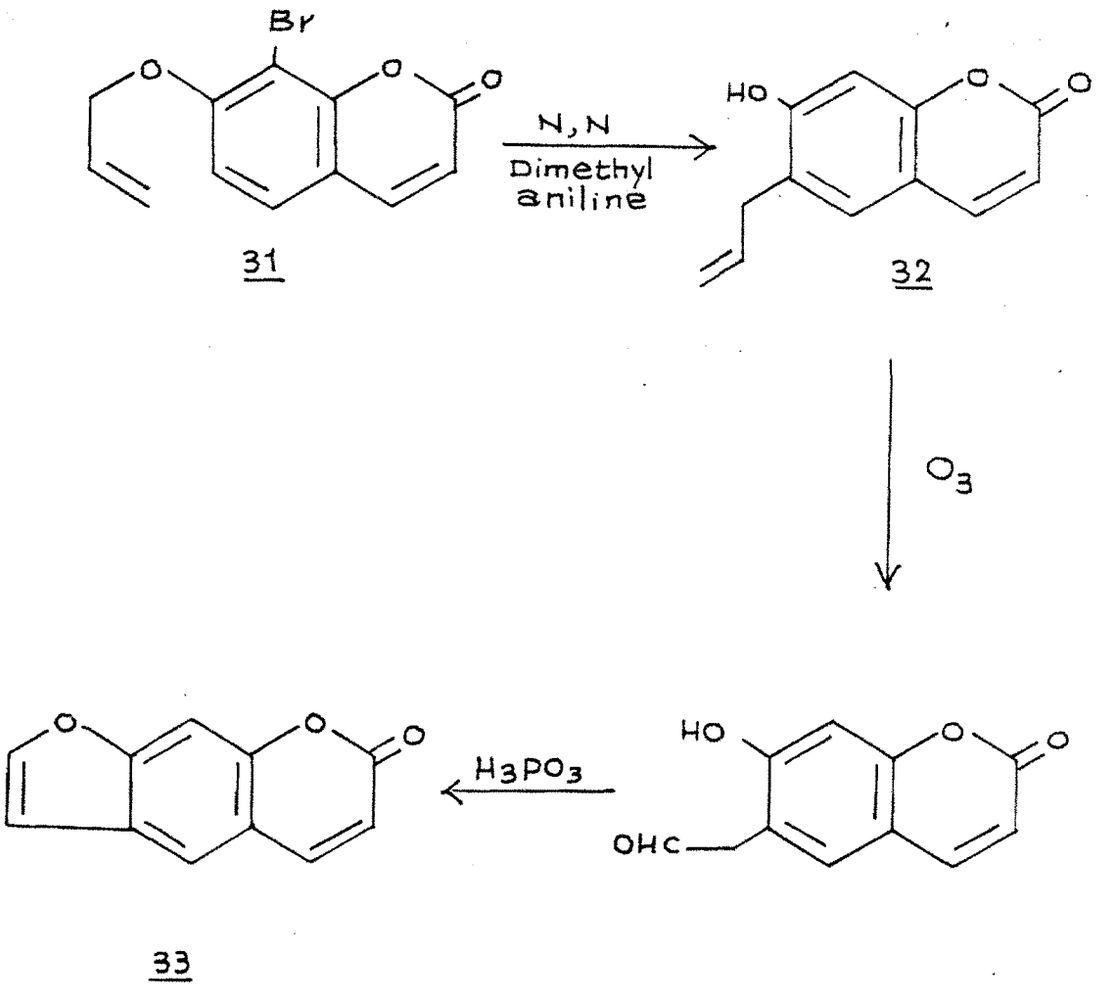


6-Phenyl furo(2,3-h)-1-benzopyran-(7H)-one (30) (Fig. 4)

Scheme IX : Pardanani and Trivedi[26]



31 32

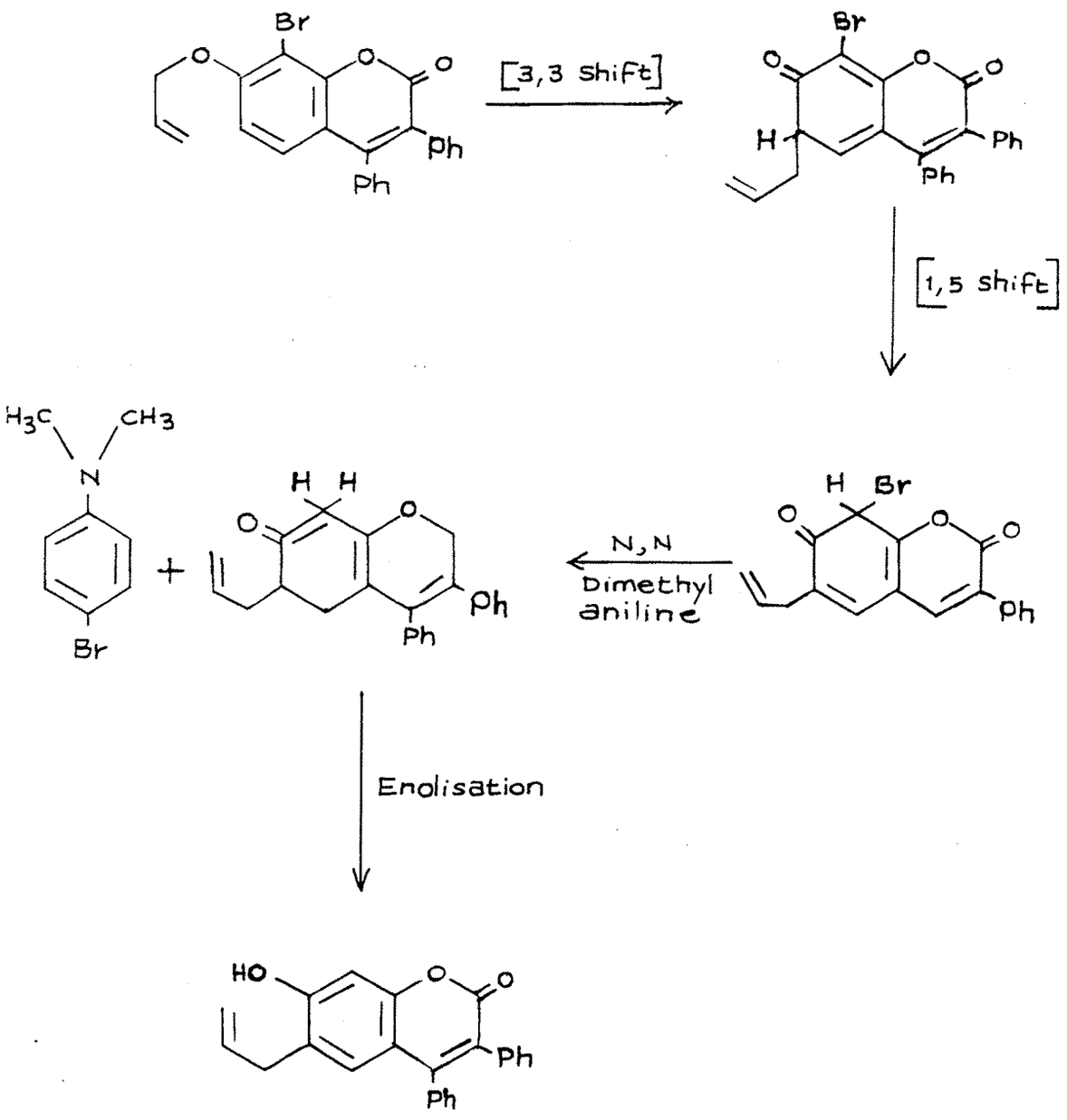
33

and obtained 6-allyl-7-hydroxy-4-substituted coumarins thus establishing the regiospecificity of this reaction for C-6 isomer.

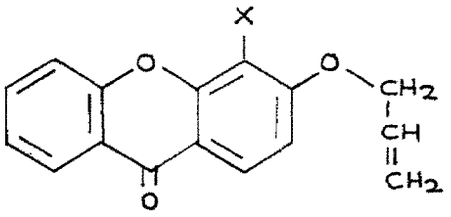
Desai and Trivedi[29] carried out the Claisen rearrangement of 7-allyloxy-8-bromo-3,4-diphenylcoumarin & obtained the 6-allyl isomer. They also explained the mechanism of elimination of bromine as shown in the (Scheme-X). This work was extended on the xanthone nucleus by Patel and Trivedi.[27] 3-Allyloxy-4-bromo xanthone was subjected to Claisen rearrangement to give 2,3-dihydro-2-methyl furo xanthone (36), 3-hydroxy-2-allyl xanthone (34) & 3-hydroxy-4-allyl xanthone (35). 3-Allyloxy-4-iodoxanthone gave similar products as those of bromo derivatives. (Scheme-XI). On changing the solvent from DMA to decalin, one more product 2-allyl-4-bromo-3-hydroxy xanthone (37) alongwith (35) was obtained.

Thus even in the case of xanthone, this stratagy was fruitful for getting 2-allyl-3-hydroxyxanthone. It was therefore thought of interest to apply this stratagy to synthesize linear furoisoflavcnes by subjecting 7-allyloxy -8-bromoisoflavones to Claisen rearrangement followed by ring closer and dehydrogenaticn.

Scheme X : Desai and Trivedi[29]

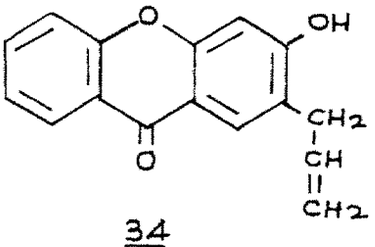


Scheme XI : Patel and Trivedi[27]



X = Br, I

N,N Dimethyl aniline →



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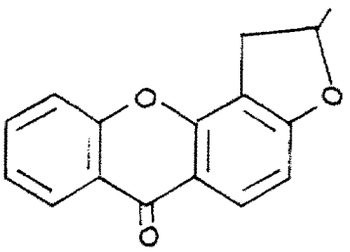
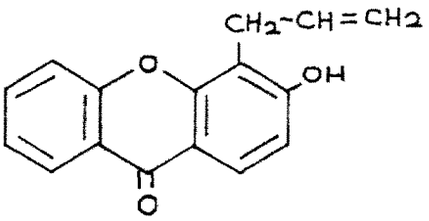
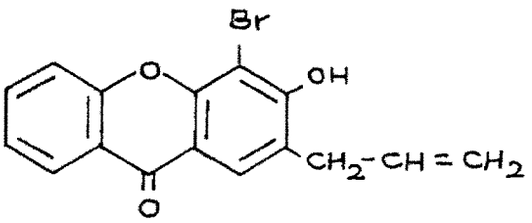


36

+



35



37

Claisen rearrangement of 7-allyloxy-8-bromo isoflavone

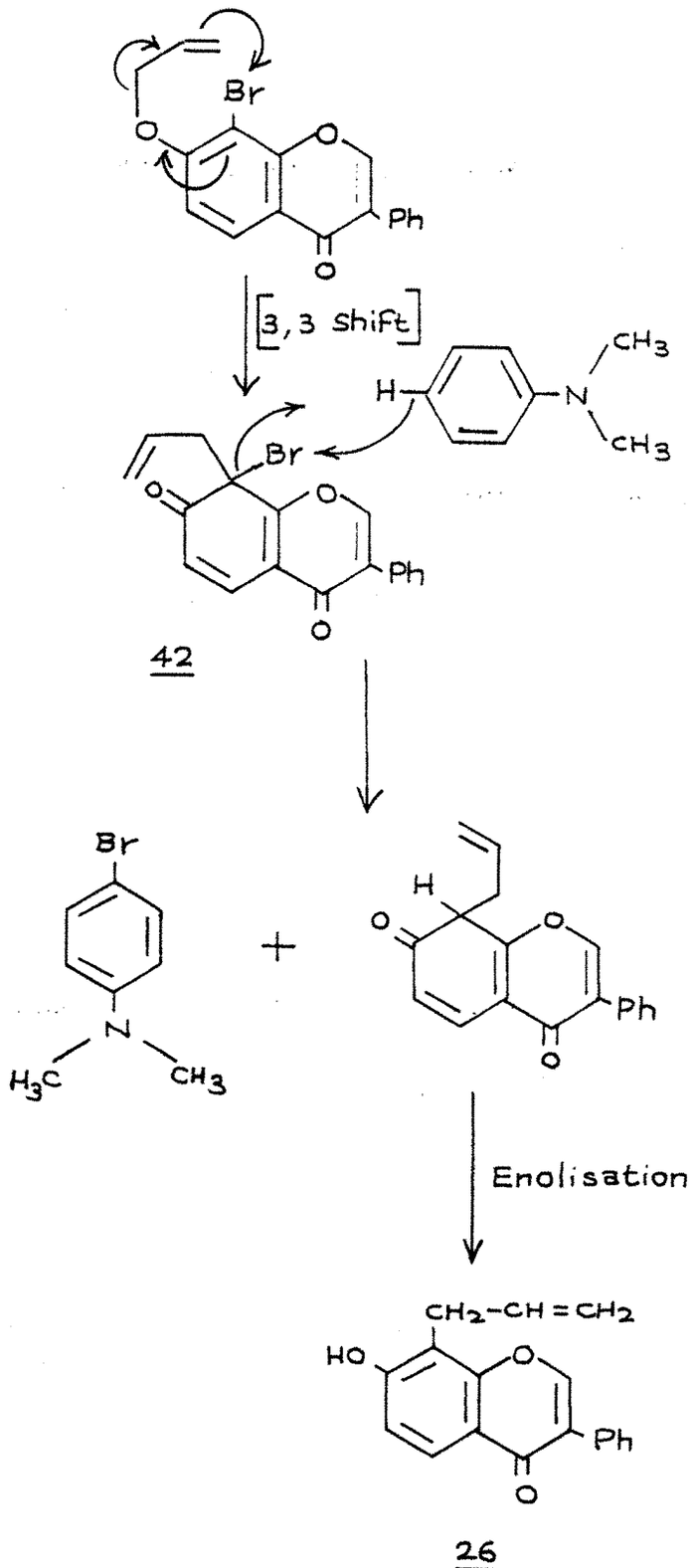
Allylation of 7-hydroxy-8-bromo isoflavone[30] (38) gave 7-allyloxy-8-bromoisoflavone (39) which was subjected to Claisen rearrangement by refluxing in N,N-dimethylaniline On working up the reaction mixture, 8-allyl-7-hydroxyisoflavone (26) along with p-bromo-N,N-dimethylaniline were isolated. Efforts to isolate 6-allyl-7-hydroxyisoflavone met with failure. The formation of p-bromo-N,N-dimethylaniline can be explained on the basis of the attack of N,N-dimethylaniline on p-bromo cyclohexadienone intermediate (42) formed after 3,3 shift rearrangement of allyl group in the position 8. (Scheme-XII)

7-Allyloxy-8-iodoisoflavone[30] (41) also gave (26) alongwith p-iodo-N,N-dimethylaniline, 7-Allyloxy-8-bromoisoisoflavone (39) when subjected to Claisen rearrangement using decalin as solvent furnished (26) by elimination of bromine atom at position 8.(Scheme-XIII)

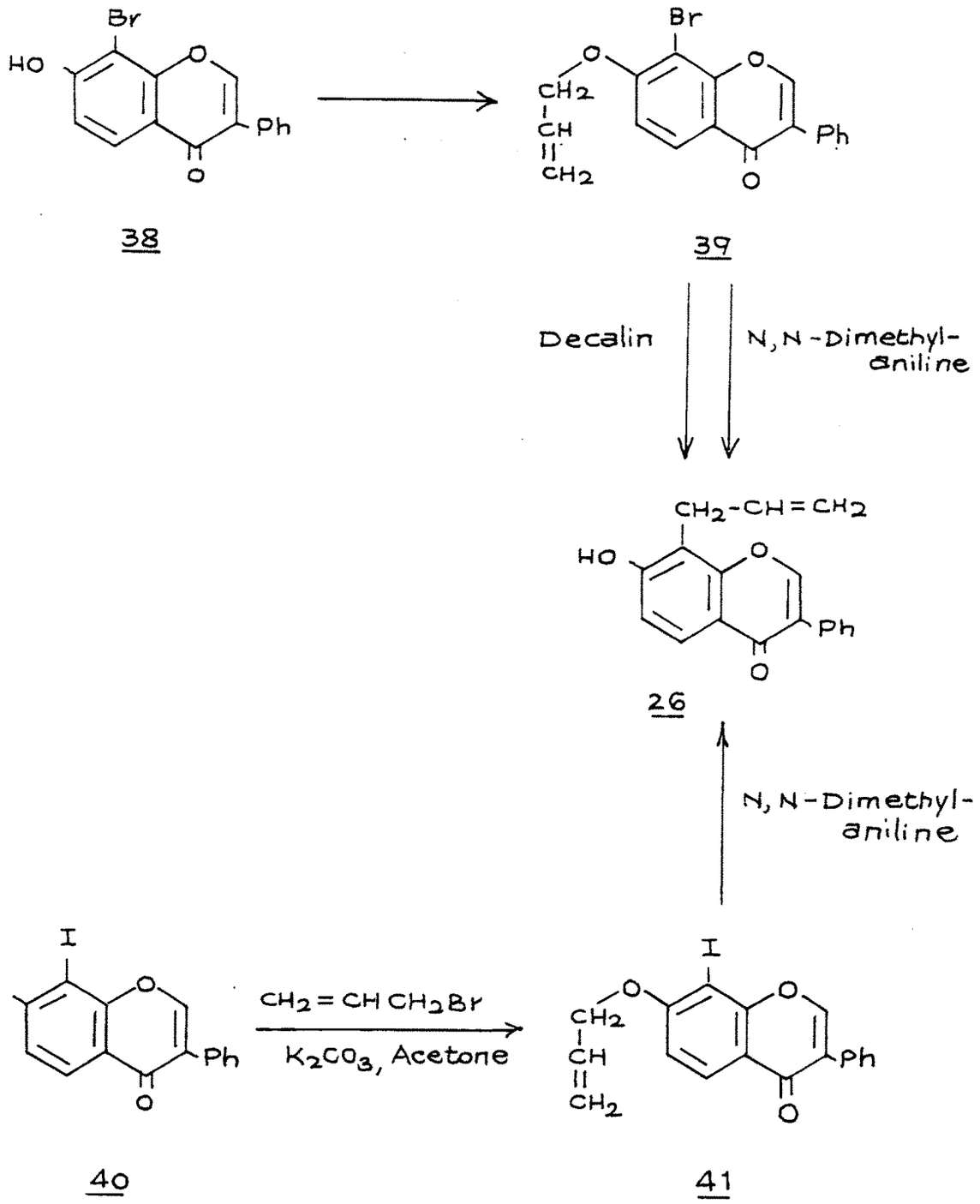
Claisen rearrangement of 7-allyloxy-6,8-dibromoisoflavone

Patel and Trivedi[27] made a novel observation on the Claisen rearrangement of 3-allyloxy-2,4-dibromoxanthone (43). When (43) was refluxed with N,N-dimethylaniline, it gave two products viz. 4-allyl-2-bromo-3-hydroxyxanthone (44) and 2-bromo-4',5'-dihydro-5'-methylfuro (2',3':3,4)

Scheme XII:


Br
O
O
Ph
O
[3,3 shift]
H
N
CH3
CH3
Br
O
O
Ph
O
42
Br
N
H3C
CH3
+
H
O
O
Ph
O
Enolisation
CH2-CH=CH2
HO
O
Ph
O
26

Scheme XIII:


Br
HO
O
Ph
O
38
Br
O
CH2
CH
CH2
O
O
Ph
O
39
Decalin
N,N-Dimethyl-aniline
CH2-CH=CH2
HO
O
Ph
O
26
N,N-Dimethyl-aniline
I
HO
O
Ph
O
40
CH2=CH CH2Br
K2CO3, Acetone
I
O
CH2
CH
CH2
O
Ph
O
41

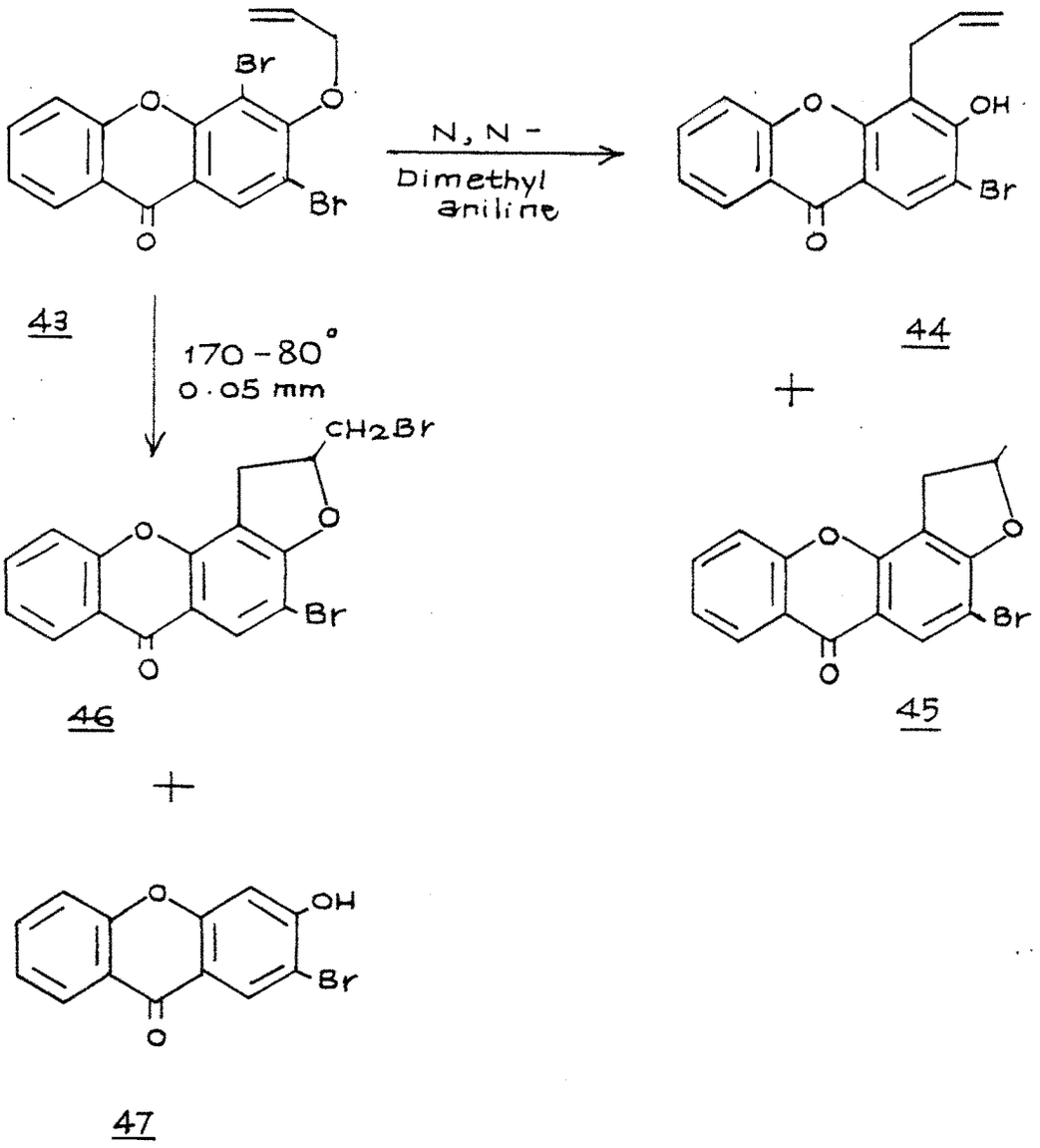
xanthone (45). Claisen rearrangement of (43) under reduced pressure at 170-80°C also gave two products 2-bromo-5'-bromomethyl-4',5'-dihydrofuro (2',3':3,4)xanthone (46) and 2-bromo-3-hydroxyxanthone (47). Formation of (46) is a novel observation in the Claisen rearrangement. (Scheme-XIV)

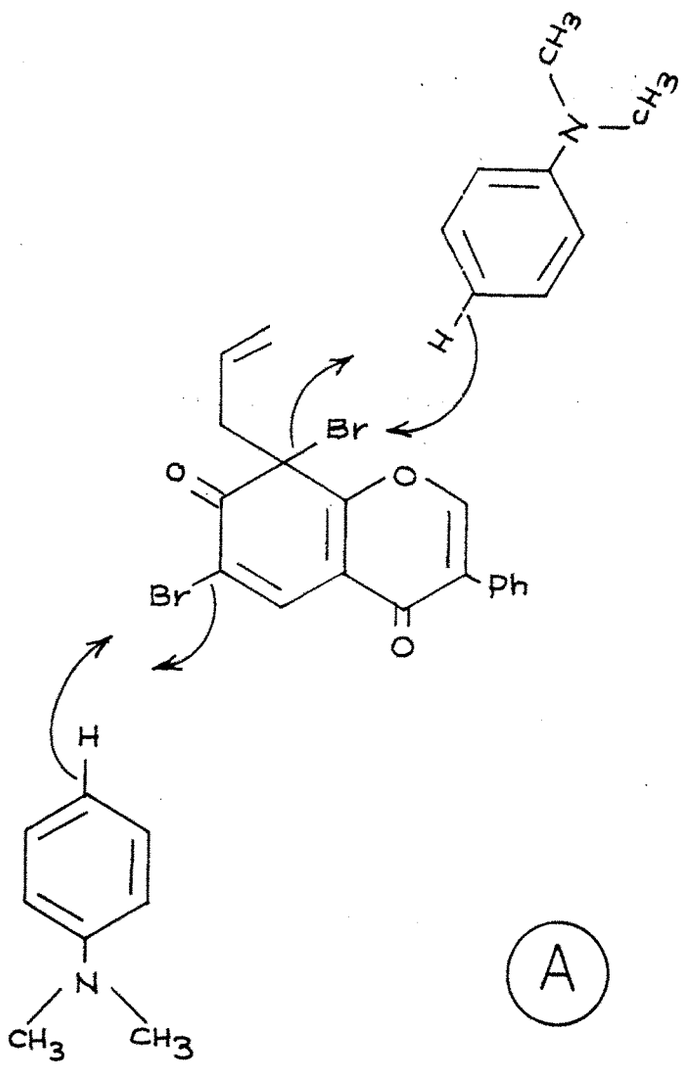
In view of above observations, it was thought of interest of study the Claisen rearrangement of 7-allyloxy-6,8-dibromo isoflavone (48).

Allylation of 6,8-dibromo-7-hydroxyisoflavone[28] (48) gave 7-allyloxy-6,8-dibromoisoflavone (49), which was subjected to Claisen rearrangement by refluxing in N,N-dimethylaniline.

On working up the reaction mixture, 8-allyl-7-hydroxy-isoflavone (26) and p-bromo-N,N-dimethylaniline were isolated, both the bromine at position 6 and 8 being eliminated during the course of the reaction. Elimination of bromine from position 6 and 8 can be explained by the attack of N,N-dimethylaniline on dibromocyclohexadienone intermediate formed after the [3,3] shift of the allyl group on poisiton 8, as shown in structure (A) (Scheme-XV)

Scheme XIV: Patel and Trivedi [27]





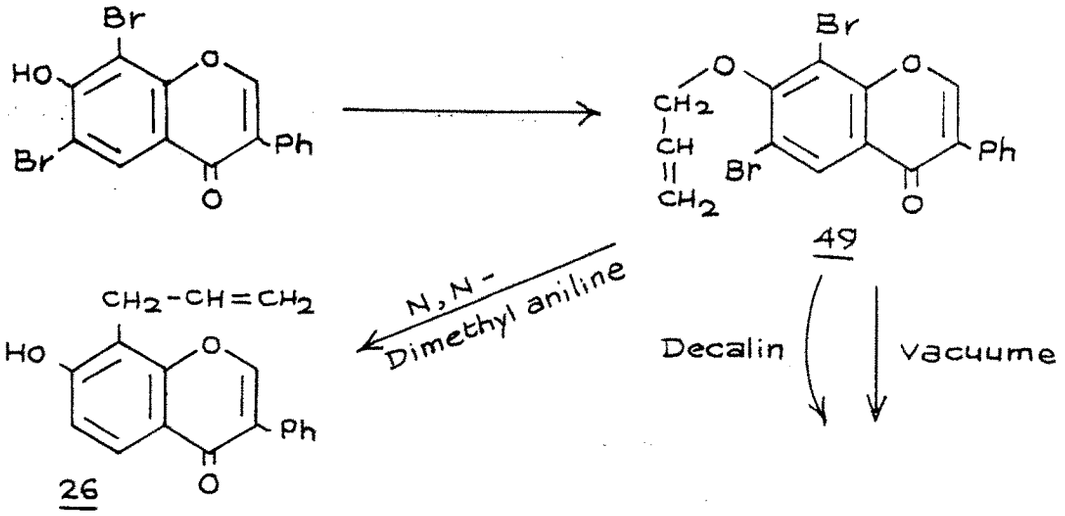
A

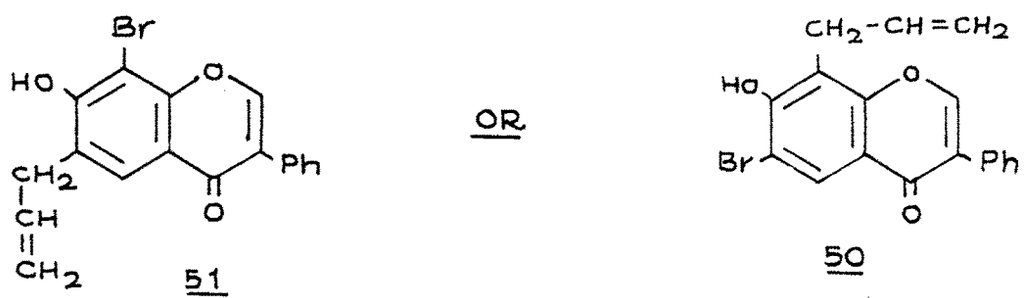
Both the bromine atoms being adjacent to carbonyl group in cyclohexadiene structure are labile & are therefore eliminated during the course of the reaction.

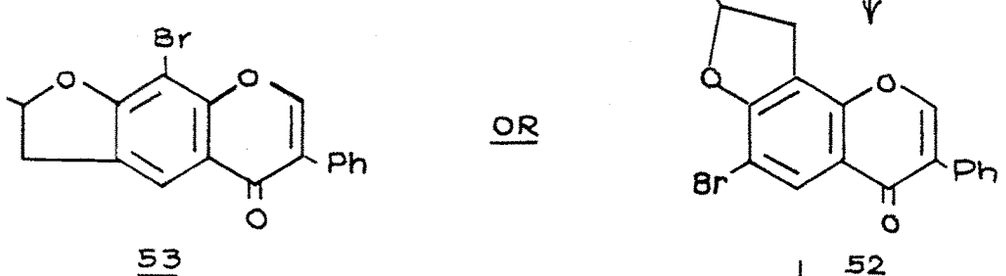
Claisen rearrangement of 7-allyloxy-6,8-dibromoisoflavone (49) was then carried out using decalin as solvent. On working up the reaction mixture, only one product was isolated. From the microanalysis data, it was found to contain one bromine atom on the ring and so the structure of product could be 8-allyl-6-bromo-7-hydroxyisoflavone (50) or 6-allyl-8-bromo-7-hydroxyisoflavone (51). The compound (50) exhibited following signals in PMR spectrum ($CDCl_3$) δ 3.7 doublet (J=7Hz) for methylene protons of allyl group $Ar-CH_2-$; one multiplet at 5.0 - 5.15 for two vinylic protons $=CH_2$; another multiplet in the region 5.8 - 6.2 for one vinylic proton of allylmoiety $-CH=CH_2$ five aromatic protons appear as multiplet in downfield region at δ 7.4 two singlets at 7.95 and 8.3 for protons at C-2 and C-5 respectively. (Scheme XV) (Fig. 5)

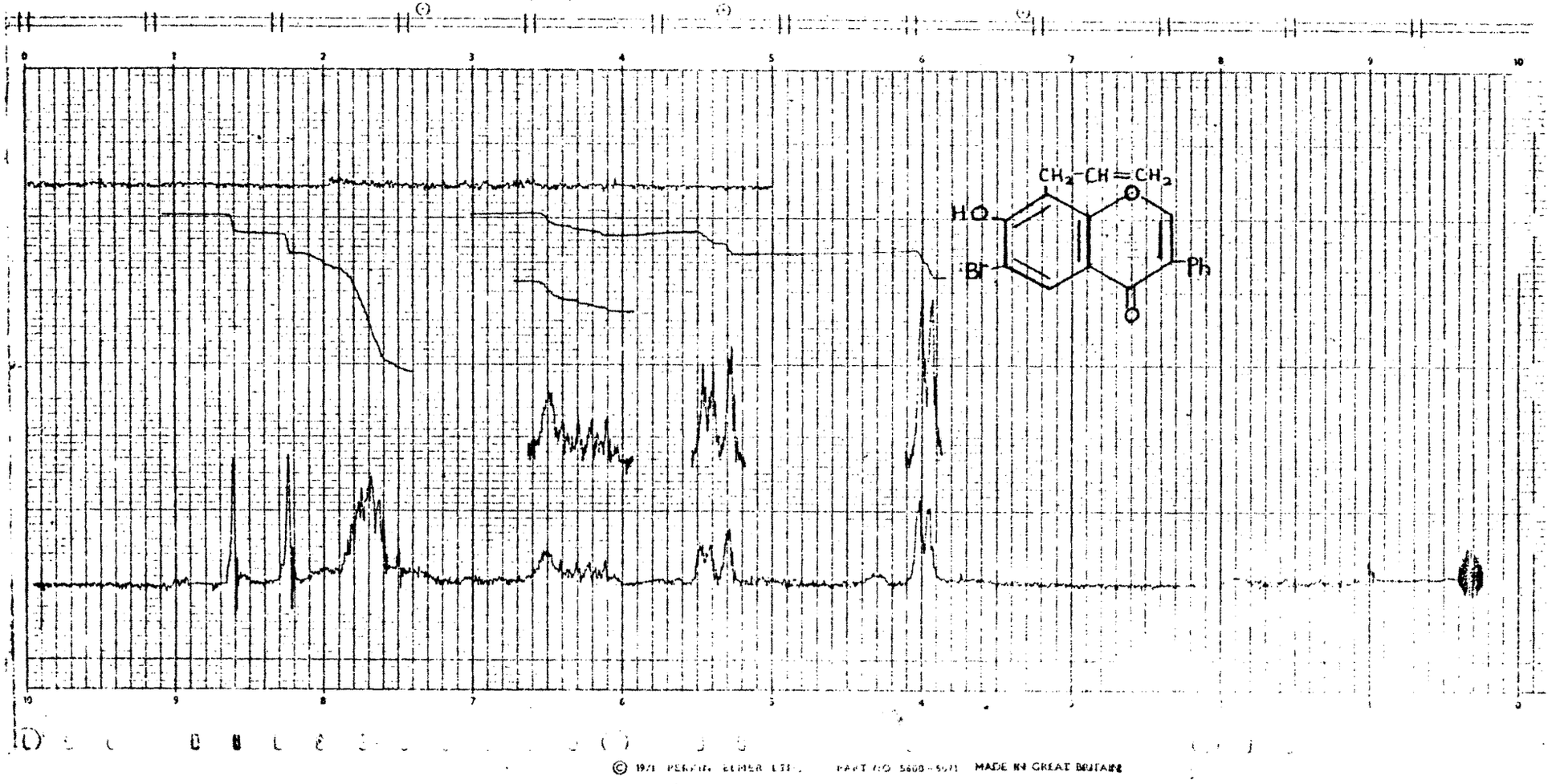
The PMR data could not distinguish between the two structures 8-allyl-6-bromo-7-hydroxyisoflavone (50) and 6-allyl-7-hydroxy-8-bromo isoflavone (51). In order to confirm the exact to position of bromine atom, the compound was cyclized with sulfuric acid (80%) to give either 2,3-dihydro-9-bromo-2-methyl-6-phenylfuro (2,3-h)benzopyran-

Scheme XV :


Br
HO
Br
Ph
O
CH2
CH
CH2
49
N,N-
Dimethyl aniline
CH2-CH=CH2
26
Decalin
Vacuume


Br
HO
CH2
CH
CH2
51
OR
CH2-CH=CH2
Br
50


Br
53
OR
CH3
Br
52
Pd/C
28

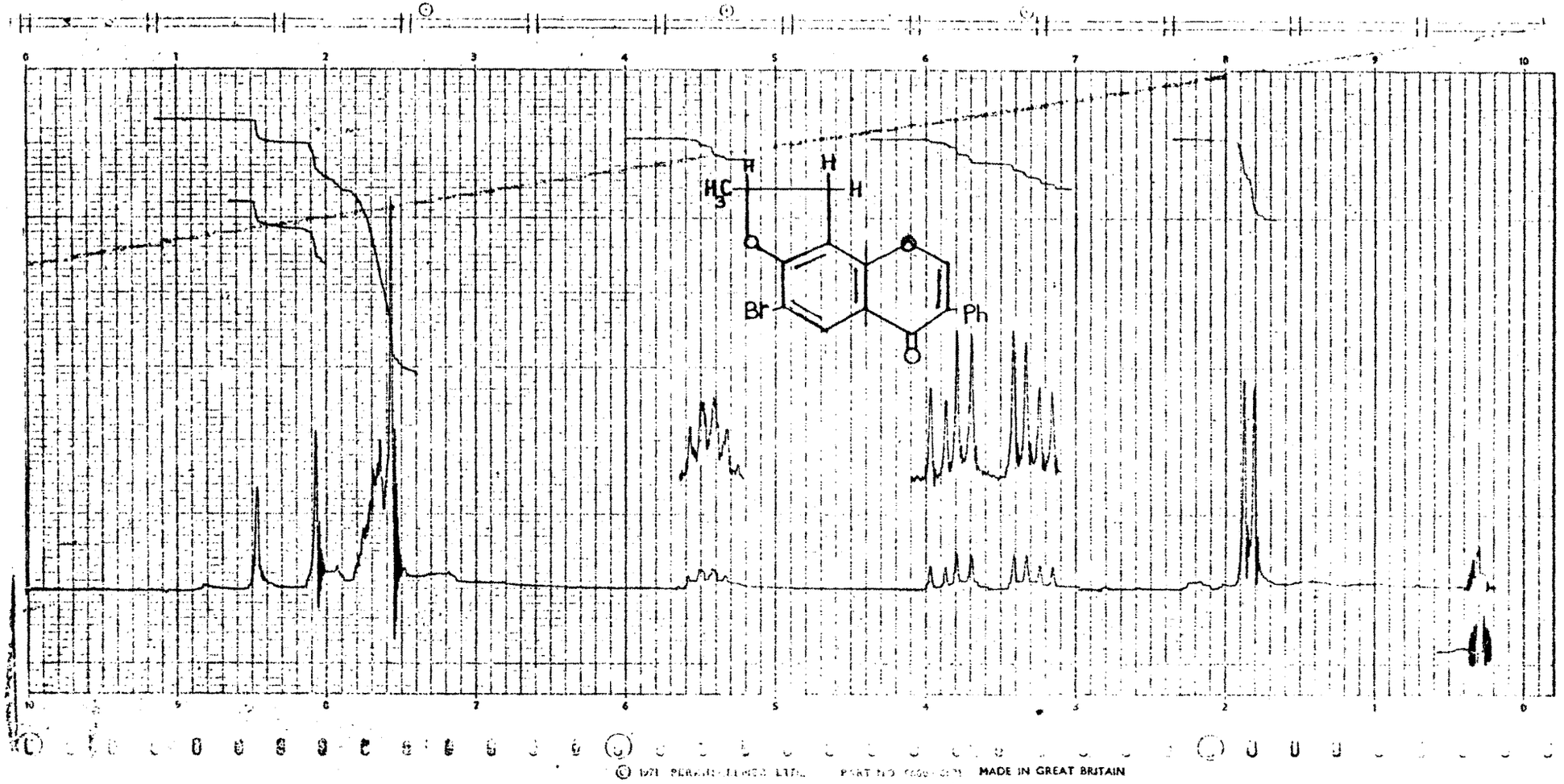


8-allyl-7-hydroxy-6-bromo isoflavone (50) (Fig. 5)

-7(H)-one (52) or 2,3-dihydro-9-bromo-2-methyl-6-phenylfuro (2,3-g)benzopyran-5(H)-one (53).

The PMR ($CDCl_3$) spectrum of the above compound exhibited doublet at δ 1.55 (J=8Hz) for 3 protons of methyl group at C-2, two double doublets at 3.0 and 3.5 (J=18,8Hz) for two geminal protons at C-3, multiplet at 5.2 for proton at C-2, 7.4, multiplet for five aromatic protons, two singlets at 7.8 and 8.15 for protons at C-8 and C-5.(Fig.6)

In this case also the PMR data could not distinguish between the two structures (52) and (53). In order to establish the exact position of bromine atom on the isoflavone ring, bromination of known 2,3-dihydro-2-methyl-6-phenylfuro (2,3-h) benzopyran-7(H)-one (27) obtained by the cyclization of 8-allyl-7-hydroxyisoflavone (26) was carried out and the structure of product obtained was 2,3-dihydro-9-bromo-2-methyl-6-phenylfuro (2,3-h)benzopyran-7(H)-one (52) and not the isomeric 2,3-dihydro-9-bromo-2-methyl-6-phenylfuro (2,3-g) benzopyran-5(H)-one (53) as its PMR spectra exhibited two singlets at δ 7.8 and 8.15 for protons at C-8 and C-5 respectively. The product was identical with (52) with respect to its m.p. and mixed m.p. and TLC behaviour. This observation firmly established the structure of the product obtained by Claisen rearrange-



2-methyl-9-bromo-6-phenyl 2,3-dihydrofuro(2,3-h) benzopyran-7H-one (52) (Fig. 6)

ment of 7- allyloxy-6,8-dibromoisoflavone as 8-allyl-6-bromo-7-hydroxyisoflavone, bromine being eliminated from the position 8.

Dehydrogenation of (52) with Pd/C (10%) in diphenyl ether gave 2-methyl-6-phenylfuro (2,3-h) benzopyran 7(H)-one (28) instead of 9-bromo-2-methyl-6-phenylfuro (2,3-h)benzo-pyran-7(H)-one (54), bromine being eliminated during the course of the reaction, m.p. and m.m.p. with authentic sample (28) are identical. When 7-allyloxy-6,8-dibromo-isoflavone (49) was heated in vacuume (5 mm) at 140°C for 2 hr. it underwent Claisen rearrangement to give 8-allyl-6-bromo-7-hydroxyisoflavone (50) as only isolable product, one bromine atom being eliminated during the course of the reaction.

experimental

EXPERIMENTAL

All melting points are uncorrected. PMR spectrum recorded on Perkin-Elmer R-32 Spectrometer (90 MHz) using TMS as internal standard. Silica gel used for column chromatography with mesh size 60-120.

7-Allyloxy isoflavone (25)

A mixture of 7-hydroxyisoflavone (24) (2.4 gm, 0.01 mole) Allyl bromide (1.2 gm, 0.01 mole) and anhydrous potassium carbonate (10 gm) was refluxed in dry acetone (200 ml) in waterbath for 10 hr. The reaction mixture poured into cold water, separated solid filtered washed with dilute sodium hydroxide solution. The product crystallized from benzene + petroleum ether mixture (2 gm, 72%) M.p. 160°

Analysis : Found : C, 77.3 ; H, 5.4

$C_{18}H_{14}O_3$: requires : C, 77.7 ; H, 5.4%

7-Hydroxy-8-allyl isoflavone (26)

7-Allyloxy isoflavone (25) (1 gm) was refluxed with N,N-dimethylaniline (5 ml) for 8 hr. The reaction mixture poured in cold dilute HCl and extracted with solvent ether, which was further washed with dilute sodium hydroxide solution. On acidification of it with conc. HCl gave

7-hydroxy-8-allyl isoflavone (26). It crystallized from benzene alcohol mixture as colourless crystals. M.p. 225°, yield 800 mg, 80%.

Analysis : Found : C, 78.1 ; H, 4.7

$C_{18}H_{14}O_3$: requires : C, 77.7 ; H, 5.0%

PMR (DMSO/D_6 TMS) δ 3.6, doublet, 2H, J=7Hz, Ar$\underline{CH_2}$-CH=CH_2 ; 5.0, m, 2H, Ar-CH_2-CH=CH_2 ; 6.0, m, 1H, Ar-CH_2-CH=CH_2 ; 7.0 d, 1H, J=9Hz, C-6 ; 7.4, m, 5H, Ar-H ; 7.9, d, 1H, J=9Hz, C-5 8.1, s, 1H, C_2-H.

2-Methyl-6-phenyl-2,3-dihydrofuro (2,3-h)benzopyran-7(H)-one (27)

7-Hydroxy-8-allyl isoflavone (26) (700 mg) was titurated with 80% H_2SO_4 (4 ml) and heatd on water bath for 15 min. The content was pouredon crushed ice, separated solid filtered and washed with dilute sodium hydroxide solution. Residue crystallized from benzene. M.p. 140°, yield 400 mg, 57%.

Analysis : Found : C, 77.6 ; H, 5.0

$C_{18}H_{14}O_3$: requires : C, 77.7 ; H, 5.0%

UV(MeOH)(log ϵ) : 202 (5.14), 246 (4.68) and 300 nm ($_4$.38)

2-Methyl-6-phenyl-2,3-dihydrofuro (2,3-h)benzopyran-7(H)-one (27)

7-Hydroxy-8-allyl isoflavone (26) (2 gm) was heated with glacial HOAc (30 ml) and HBr (20 ml, 48%) on waterbath for 8 hr. The mixture was cooled and poured over crushed ice, separated solid filtered and dried at room temperature. The crude was taken in dry acetone (100 ml) and fused potassium carbonate (4 gm) and refluxed for 10 hr. Reaction mixture worked up and the product crystallized from benzene M.p. and m.m.p. with authentic sample was 140°. Yield 700 mg, 35%.

2-Methyl-6-phenyl furo (2,3-h)benzopyran-7(H)-one (28)

A mixture of 2-Methyl-6-phenyl-2,3-dihydrofuro (2,3-h) benzopyran-7(H)-one (27) (500 mg) and Pd/C (500 mg, 10%) was refluxed in boiling diphenyl ether solvent for 12 hr. Solvent was removed and separated solid dissolved in benzene and passed through the column of silica gel. Crystallization from benzene gave colourless crystals of 2-Methyl-6-phenyl furo (2,3-h)benzopyran-7(H)-one (28) M.p. 180°, yield 200 mg, 40%.

Analysis : Found : C, 78.4 ; H, 4.6

$C_{18}H_{12}O_3$: requires : C, 78.3 ; H, 4.3%

6-Phenylfuro (2,3-h)benzopyran-7(H)-one (30)

Though the ice-cold solution of 7-hydroxy-8- allyl isoflavone (26) (700 mg) in ethyl acetate, a stream of ozon gas with oxygen was passed for 2 hr. To decompose the ozonoid, Pd/C (300 mg, 10%) was mixed and reaction mixture stirred in the atmosphere of hydrogen gas. Reaction mixture worked up and pasty mass obtained was taken in PPA and heated in oil bath at 140° for 30 min. Reaction mixture poured over crushed ice and separated solid filtered off, crystallization was done from benzene. M.p. 150° yield 150 mg, 23%.

Analysis : Found : C, 77.4 ; H, 4.3

$C_{17}H_{10}O_3$: requires : C, 77.8 ; H, 3.8%

7-Allyloxy-8-bromo isoflavone (39)

A mixture of 7-hydroxy-8-bromo isoflavone (38) (2.5 gm, 0.08 mole), Allyl bromide (1 gm, 0.08 mole) & anhydrous potassium carbonate (12 gm) was refluxed in dry acetone (300 ml) for 11 hr. Reaction mixture worked up as usual. The product crystallized from benzene. M.p. 118°, yield 2 gm, 71%.

Analysis : Found : C, 61.0 ; H, 4.0

$C_{18}H_{13}O_3Br$: requires : C, 60.5 ; H, 3.6%

7-Allyloxy-8-bromo isoflavone + DMA

7-Allyloxy-8-bromo isoflavone (1 gm) was refluxed with N,N-dimethylaniline (5 ml) for 8 hr. The reaction mixture poured into cold conc. HCl and crude extracted with solvent ether whhich was further washed with dilute alkali solution. On acidification it gave 7-hydroxy-8-allyl isoflavone. M.p. and m.m.p. with authentic sample was 225°, yield 600 mg, 77%.

Some solid condensed on the upper layer of air condenser was scratched and identified as p-bromo N,N-dimethylaniline.

7-Allyloxy-8-bromo isoflavone + Decalin

7-Allyloxy-8-bromo isoflavone (1 gm) was refluxed with Decalin (6 ml) for 6 hr. Solvent was removed by vacuume distillation and product separated. It dissolved in solvent ether and washed with dilute alkali solution. On acidification with con. HCl gave 7-hydroxy-8-allyl isoflavone. M.p. and m.m.p. with authentic sample was 225°, yield 500 mg, 64%.

7-Allyloxy8-iodo isoflavone (41)

A mixture of 7-hydroxy-8-iodo isoflavone (2 gm,

0.005 mole), allyl bromide (0.6 gm, 0.005 mole) & anhydrous potassium carbonate (12 gm) was refluxed in dry acetone (300 ml) for 15 hr. The reaction mixture worked up as usual. The product crystallized from benzene. M.p. 105°, yiled 1.3 gm, 50%.

Analysis : Found : C, 53.9 ; H, 3.4

$C_{18}H_{13}O_3I$: requires : C, 53.5 ; H, 3.2%

6,8-Dibromo-7-allyloxy isoflavone (49)

A mixture of 7-hydroxy-6,8-dibromo isoflavone (4 gm 0.01 mole), allyl bromide (1.2 gm, 0.01 mole) and fused potassium carbonate (12 gm) was refluxed indry acetone (400 ml) for 10 hr. Reaction mixture worked up and product crystallized from benzene petrcleum ether mixture. M.p. 135°, yield 3 gm, 51%.

Analysis : Found : C, 50.0 ; H, 3.0

$C_{18}H_{12}O_3Br_2$: requires: C, 49.5 ; H, 2.7%

6,8-Dibromo-7-allyloxy isoflavone + DMA

1 gm of (49) was refluxed with N,N-dimethylaniline (7 ml) for 8 hr. Reaction mixture worked up as usual. Alkali soluble product was found to be 7-hydroxy-8-allyl isoflavone (26). M.p. and m.m.p. with authentic sample was 225°, yield 500 mg, 78%

6-Bromo-7-hydroxy-8-allyl isoflavone (50)

1 gm of (49) was refluxed with decalin (5 ml) for 3 hr. Reaction mixture was cooled and solid separated. It was filtered and washed with light petroleum ether and crystallized from petroleum ether. M.p. 177-8°, yield 450 mg, 55%.

Analysis : Found : C, 60.8 ; H, 4.0

$C_{18}H_{13}O_3Br$: requires : C, 60.5 ; H, 3.6%

2-Methyl-6-phenyl-9-bromo-2,3-dihydro furo (2,3-h)benzopyran -7(H)-one (52)

6-Bromo-7-hydroxy-8-allyl isoflavone (50) (500 mg) was titurated with 80% H_2SO_4 (3 ml) and heated in water bath for 30 min. Reaction mixture poured over crushed ice, product was filtered and dried. It crystallized from benzene. M.p. 165°, yield 150 mg, 30%

Analysis : Found : C, 60.1 ; H, 3.6

$C_{18}H_{11}O_3Br$: requires : C, 60.5 ; H, 3.6%

2-Methyl-6-phenyl furo (2,3-h)benzopyran 7(H)-one (28)

(50) (700 mg) was refluxed in diphenyl ether solvent (700 ml) with Pd/C (500 mg, 10%) for 7 hr. Reaction mixture

was cooled and filtered. On working up the reaction mixture product obtained was found to contain no bromine atom in the molecule thus become identical to (28). M.p. and m.m.p. with authentic sample was 180°.

Analysis : Found : C, 78.0 ; H, 4.5

$C_{18}H_{12}O_3$: requires : C, 78.3 ; H, 4.3%

6-Bromo-7-hydroxy-8-allyl isoflavone (50)

(49) (500 mg) was subjected to vacuume (5 mm) at 140° for 2 hr in oil bath. The reactionmixture was cooled and dissolved in benzene, then washed with dilute alkali solution. On acidificatin the solid obtained which crystallized from light petroleum ether (200 mg, 37%). M.p. and m.m.p. with authentic sample was 177-8°C.

7-Hydroxy-8-allyl isoflavone (26)

7-Allyloxy-8-iodo isoflavone (41) (1 g) was refluxed with N,N-dimethylaniline (5 ml) for 8 hr. Reaction mixture worked up as usual and the product obtained was 7-hydroxy-8-allyl isoflavone. M.p. and m.m.p. with authentic sample was 225°, yield 400 mg, 60%.

section - II

CHAPTER - I

SYNTHESIS OF FUROISOFLAVONES

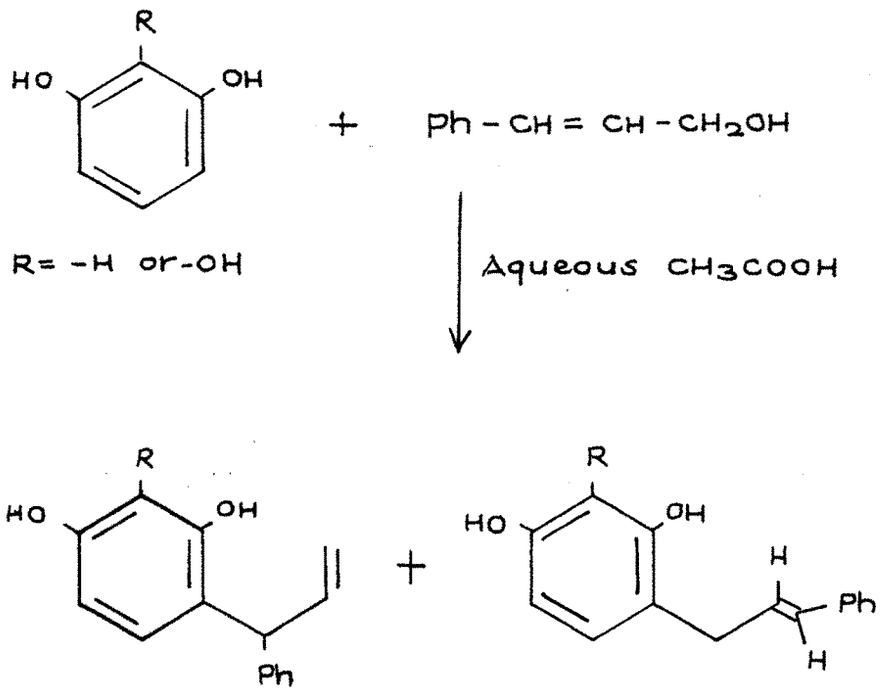
SECTION - II

CINNAMYLATION OF ISOFLAVONES

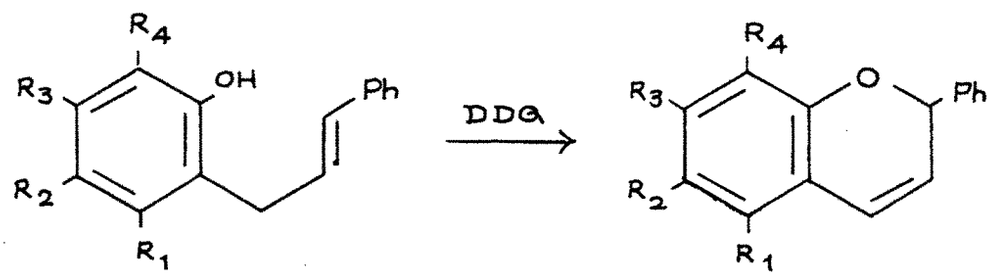
Some natural polyphenolics have a cinnamyl unit present in various forms. Mention may be made of two groups of natural products called neoflavonoids and cinnamylphenols[31] occuring in species of Dalbergia & Machaerium. Introduction of a cinnamyl unit in a polyphenol can be brought about by two ways. First method consists of direct cinnamylation of phenols with cinnamyl alcohol in presence of aqueous organic acid such as acetic acid, formic acid etc. Jurd[32] carried out the cinnamylation of phenols such as pyragallol, resorcinol etc. and obtained benzyl styrene derivatives and isomeric neoflavanoids. (Scheme-I)

Meri lini and coworkers[33] have demonstrated the conversion of o-cinnamylphenols to flav-3-enes by DDQ. (Scheme II) The second method involves the o-cinnamylation of polyphenol with cinnamyl bromide or chloride in the presence of K_2CO_3 followed by Claisen migration.H. Schmid & coworkers[34] have carried out a detailed study of Claisen rarrangement of 3'-(aryl substituted) allylphenol in $PhNEt_2$. 2-(1'-

Scheme I : Jurd et al.[32]



Scheme II : Merlini and coworkers[33]

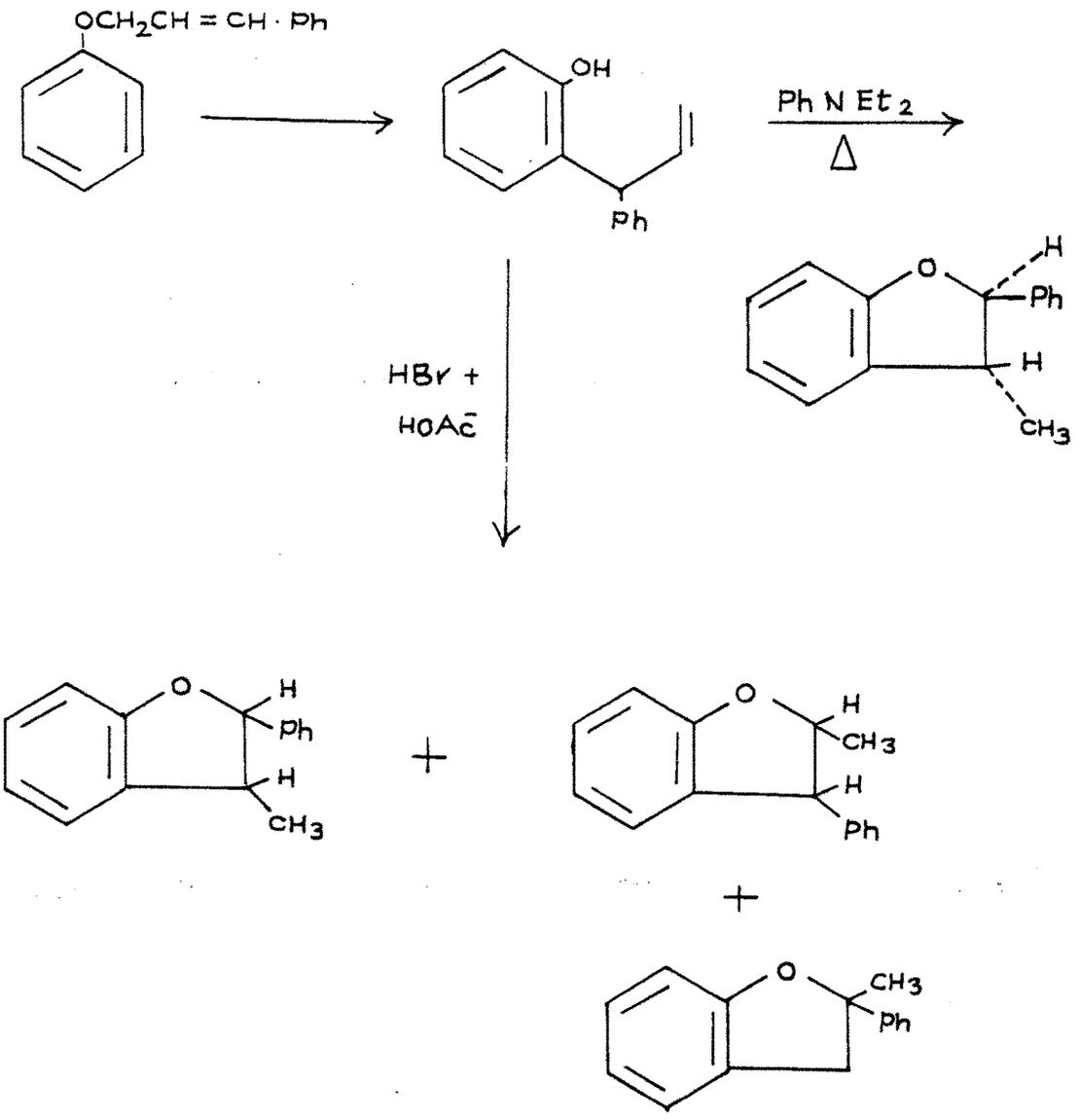


arylallyl) phenols thus obtained are transformed on heating in $PhNEt_2$ into trans-2-aryl-3-methylcoumarans in excellent yields. The same 2-(1'-arylallyl) phenols when refluxed under acidic condition (HBr + HOAc) gave a mixture of 3-aryl-2-methylcoumarans, 2-aryl-3-methylcoumarans and 2-aryl-2-methylcoumaran. (Scheme-III)

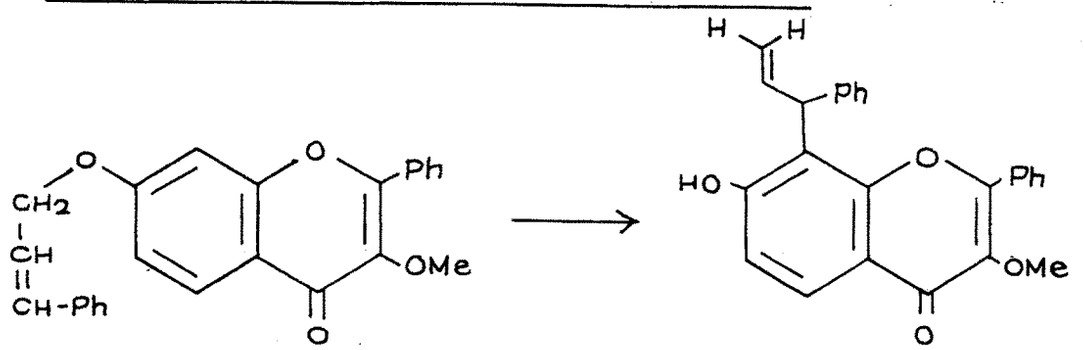
The present work deals with the Claisen rearrangement of cinnamyloxy isoflavone to obtain (1-phenyl-1-propenyl)-hydroxy isoflavones and their conversion to dihydrofurano isoflavones followed by their dehydrogenation to furano-isoflavones. C-cinnamylation of o-hydroxyphenylbenzyl ketone is also carried out and products are converted to cinnamyl isoflavones and 2-phenylpyrano isoflavones. Jain, Tuli and Kumar[35] subjectd to 7-cinnamyloxy-3-methoxy-flavones (1) and 4-methyl-7-cinnamyloxy coumarin (2) to to Claisen rearrangement to get two different types of rearranged products viz. 3-(1-phenyl-1-propenyl)-7-hydroxy-3-methoxyflavone in first case and 4-methyl-8-(1-phenyl-1-propenyl)-7-hydroxy coumarin in second case. (Scheme-IV)

Jain and Gupta[36] also studied cinnamylation reaction on different chromone derivatives and obtained different products. Claisen rearrangement of 7-cinnamyloxy noreugenin

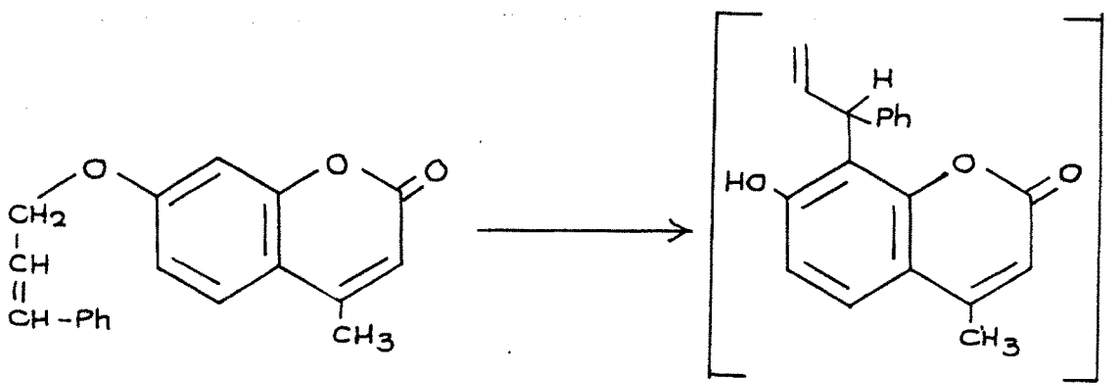
Scheme III : E. Schmid et al [34]



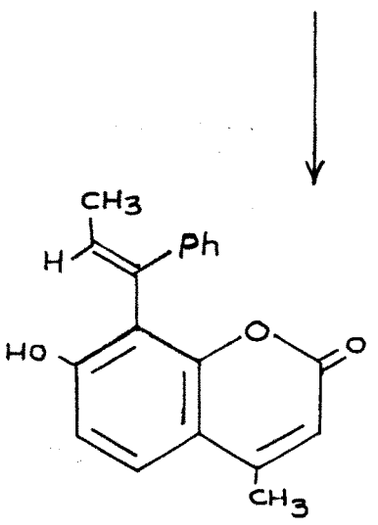
Scheme IV : Jain, Tuli and Kumar [35]



(1)



(2)



(3) yielded 4',5'-dihydro-5-hydroxy-2,4'-dimethyl-5'-phenyl furo (2',3':7,8) chromone (4), while 7-cinnamyoxy flavone (5) gave 4'-phenyl-5'-methylfuro (2',3':7,8) flavone (6) (Scheme-V). Dehydrogenation of these products gave the corresponding furochromones. (Scheme-V)

Jain and Tuli[37] also subjected 7-cinnamyloxy-5-hydroxy isoflavone to Claisen rearrangement & obtained two products with linearly as well as angularly fused furan ring. However, they could not assign the positions of phenyl and methyl groups on furan ring. Compounds have been tentatively assigned structure (7) and (8). (Scheme-VI)

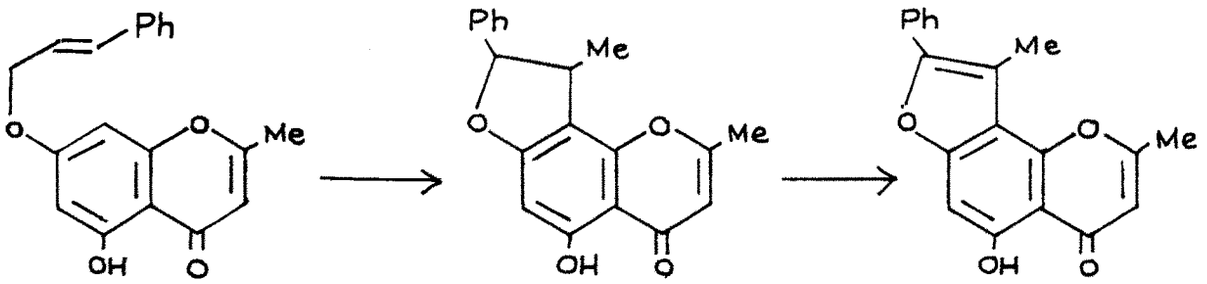
Jain, Tuli and Kumar[38] studied cinnamylation reactions on flavones, coumarins and isoflavones. 7-Cinnamyloxyisoflavone, (10) when subjected to Claisen rearrangement gave 8-(1-phenyl-1-propenyl)-7-hydroxy isoflavone (12).

PRESENT WORK

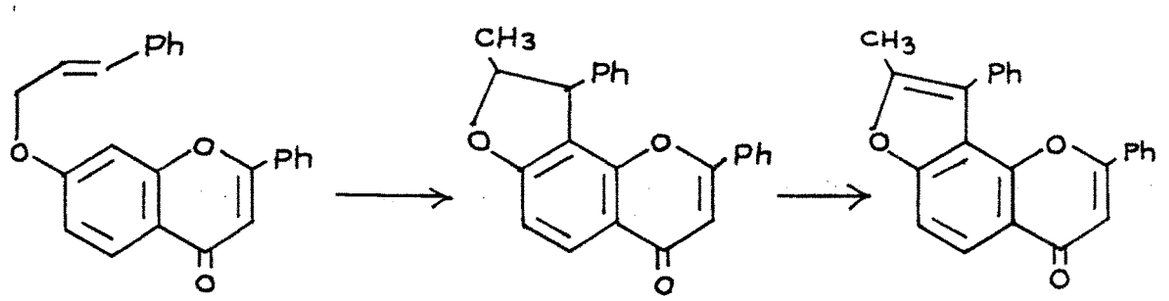
Cinnamylation of 7-Hydroxyisoflavone (9)

In view of above work carried out by Jain, Tuli and Kumar[38] which is rather an incomplete investigation of Claisen rearrangement of cinnamyloxy derivatives, it was thought of interest to study these rearrangements systematically and establish the mechanism and structures of the final products obtained in this rearrangement.

Scheme V: Jain and Gupta[36]

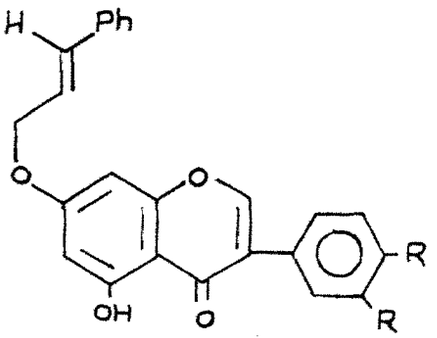


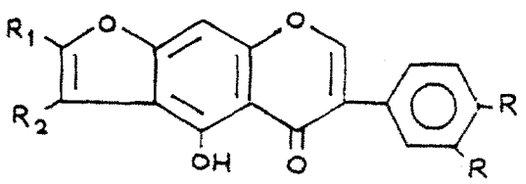
(3) (4)



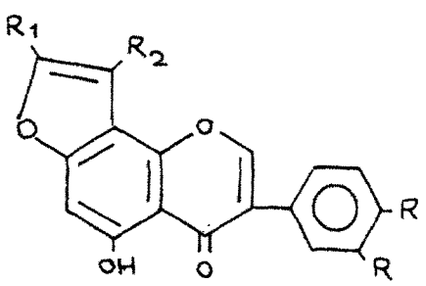
(5) (6)

Scheme VI : Jain and Tuli [37]





(7)



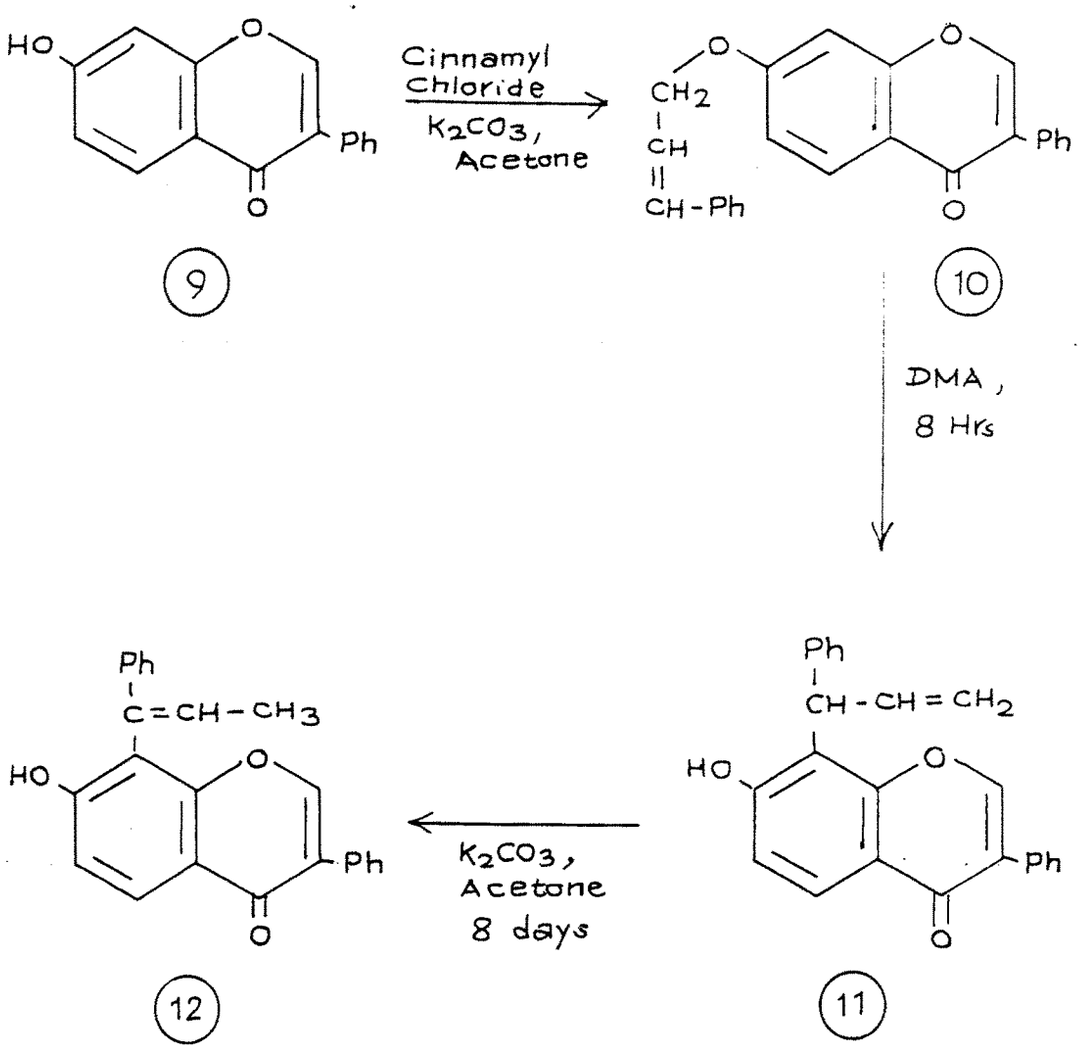
(8)

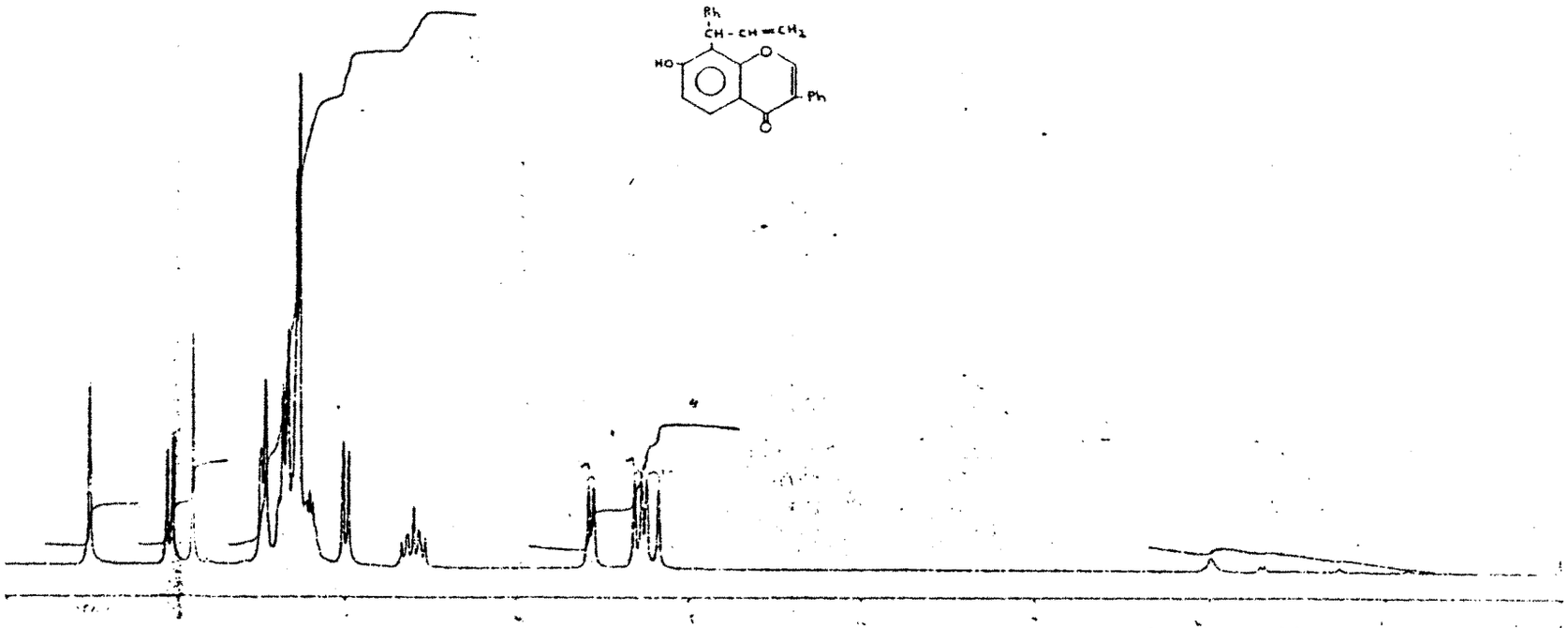
If R_1 = Me , R_2 = Ph

If R_1 = Ph , R_2 = Me

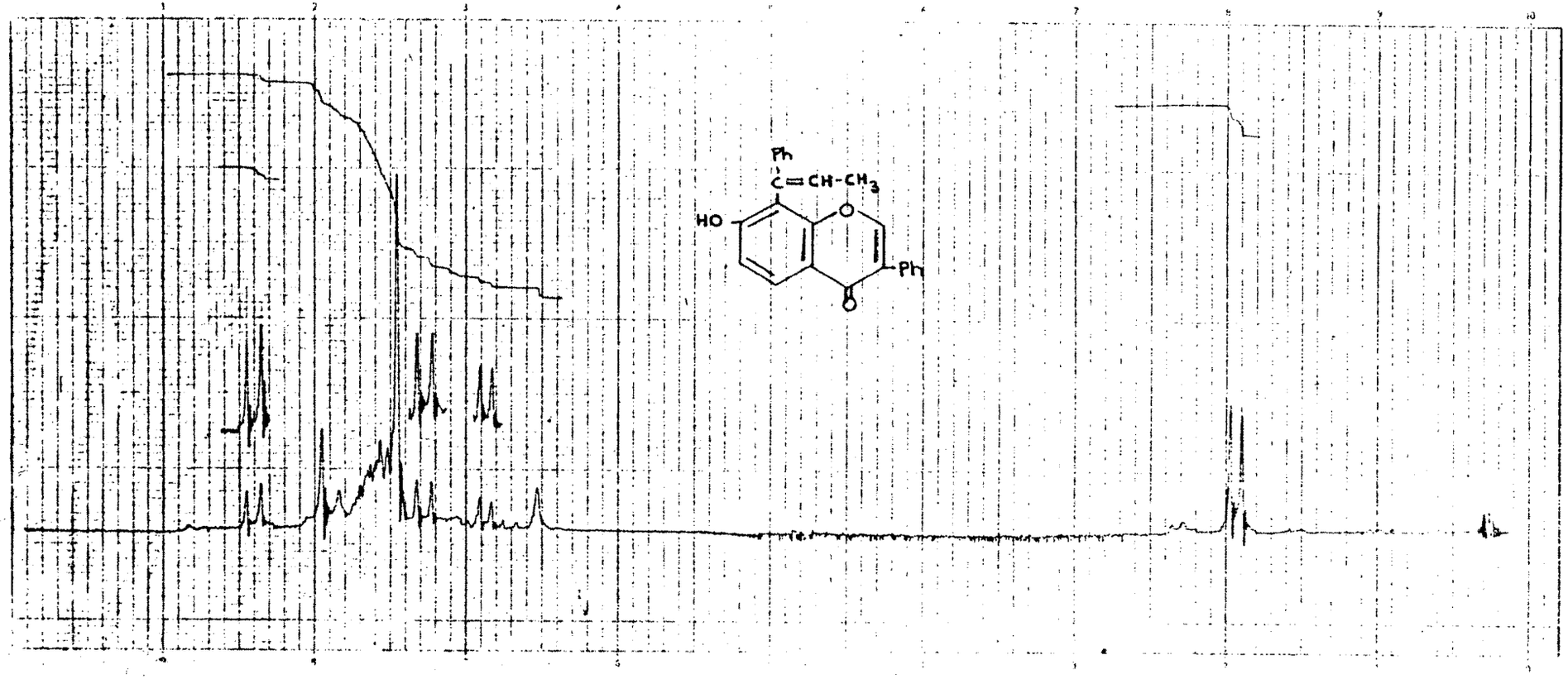
7-Hydroxyisoflavone (9) was condensed with cinnamyl chloride in the presence of fused potassium carbonate in acetone with few crystals of potassium iodide in it, to obtain 7-cinnamyloxy isoflavone (10). On repeating the work of Jain et al.[38] under identical conditions of refluxing 7-cinnamyloxyisoflavone (10) in dimethylaniline for 8 hr, a product (11) m.p. 190-2° (lit. m.p.[33] 192°C) was isolated. The structure of (11) was established by pmr spectra which showed it to be 8-(1-phenyl-2-propenyl)-7-hydroxyisoflavone (11) and not 8-(1-phenyl-1-propenyl) 7-hydroxyisoflavone (12) as reported by Jain et al.[38] It exhibited double doublet for two allylic protons of side chain at δ 5.25, J=18,8Hz. Another doublet was also observed at δ 5.5, J=8Hz for single benzylic proton of the side chain. The other vinylic proton appeared as multiplet at 6.55. Two doublets were observed at 8.15 and 7.0, J=9Hz for two aromatic protons at C-5 and C-6 ; multiplet for five aromatic protons of the phenyl ring at 3-position appeared at 7.25 while signal for proton at C-2 appeared as singlet at 7.95. No signal appeared at δ 1.7, for the methyl group as reported by Jain and coworkers.[38] (Fig. 1) It is observed that compound (11) is first formed in the Claisen rearrangement which isomerises to give the compound (12). In order to prepare (12), 7-hydroxy-8-(1-phenyl-2-propenyl)-isoflavone (11) was refluxed in acetone for 8 days in the presence of potassium carbonate

Scheme VII : Jain, Tuli and kumar[38]





7-Hydroxy-8-(1-phenyl-2-propenyl) isoflavone (11) (Fig.1)

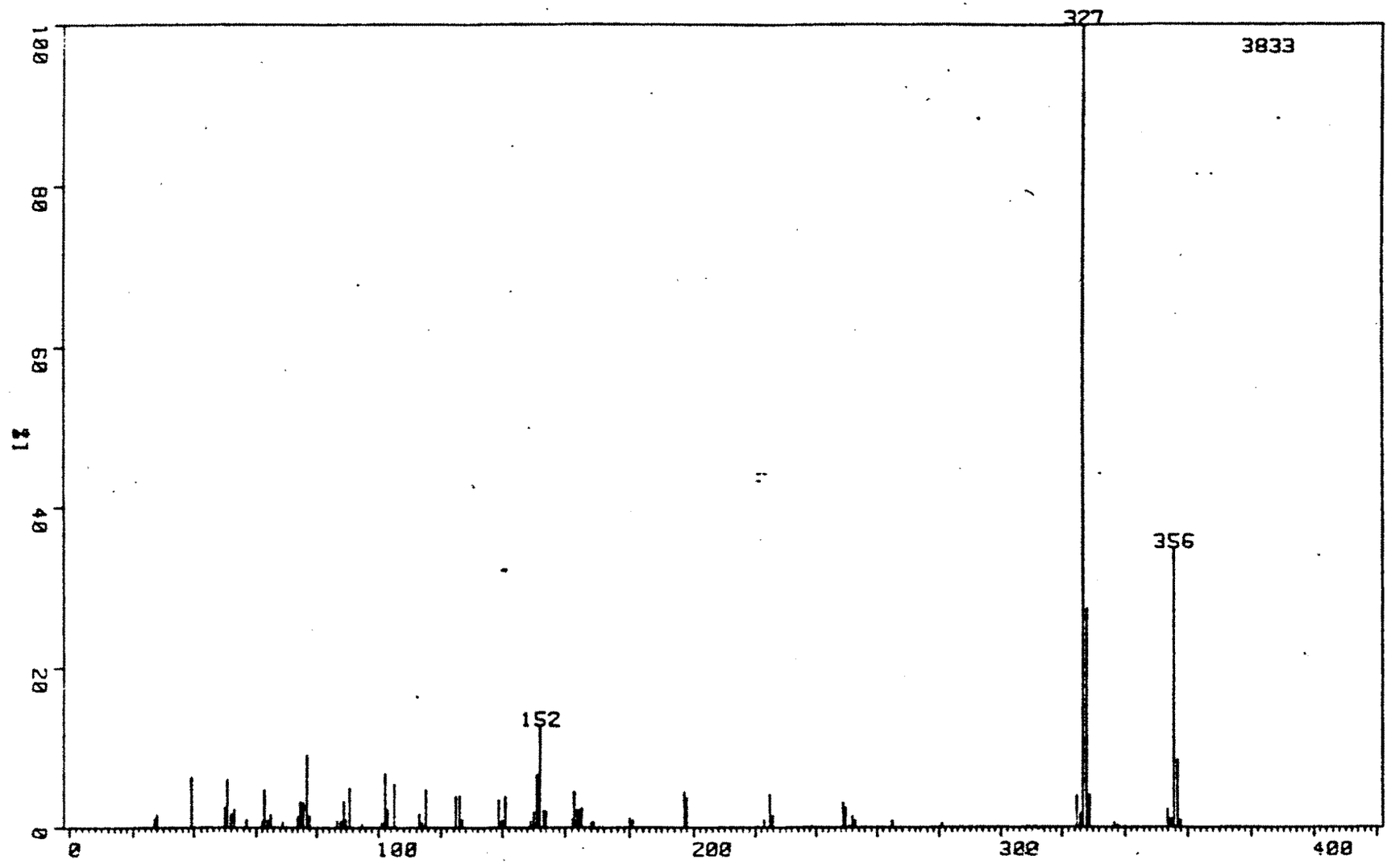


7-Hydroxy-8-(1-phenyl-1-propenyl) isoflavone (12) (Fig. 2)

to give 7-Hydroxy-8-(1-phenyl-1-propenyl) isoflavone (12) M.p. 181-2°C. The structure (12) was established by PMR spectrum ($CDCl_3$) which exhibited following signals, a doublet, J=7Hz, for a methyl group at δ 1.68, the vinylic proton of the side chain appeared as a quartet J=7Hz at 6.6 five aromatic protons and one proton at C_6.H appeared as multiplet at 7.15 ; while another group of five aromatic protons showed multiplet at 7.3 ; 7.65, singlet for proton at C-2, one downfield doublet for proton at C-5 appeared at 8.15 with J=9Hz. (Scheme-VII) (Fig. 2)

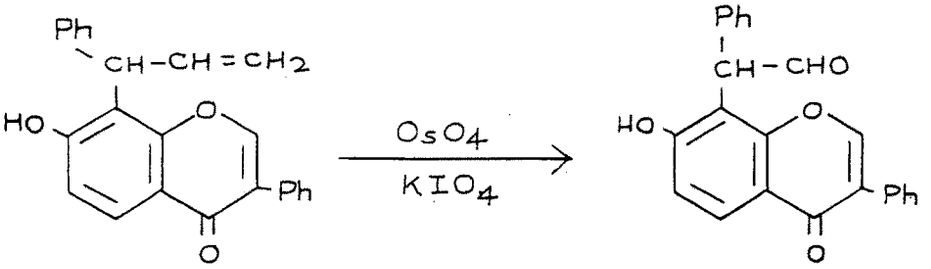
To establish the position of double bond in the side chain in (11) it was reacted with OsO_4 in ethylacetate in the presence of potassium periodate. On working up the reaction mixture 7-Hydroxy-8-(2'-phenyl-2'-oxoethyl) isoflavone (17) was isolated. PMR was not recorded as it was not soluble in any organic solvent at room temperatur. Mass spectrum showed molecular ion peak at m/e 356 and characteristic (M-1) peak at 355 for aldehydic function. (Scheme-VIII)(Fig.3A)

Compound (17) underwent cyclodehydrogenation when heated with polyphosphoric acid at 200°C to give the product 3,6-diphenylfuro (2,3-h) benzopyran-7(H)-one (18). Structure (18) was confirmed by PMR spectrum showing following signals ($CDCl_3$) : δ 7.0, doublet with J=9Hz for proton at C-9



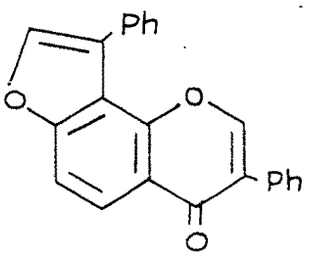
7-Hydroxy-8-(2'-phenyl-2'-oxoethyl)isoflavone (17) (Fig.3A)

Scheme VIII :

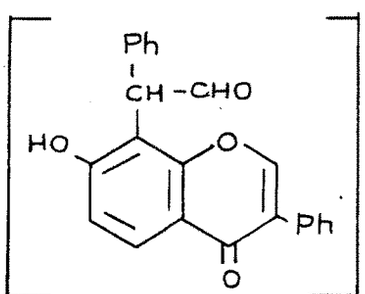


(11) (17)

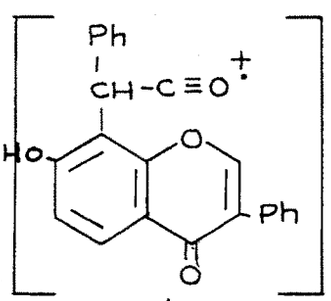
PPA



(18)

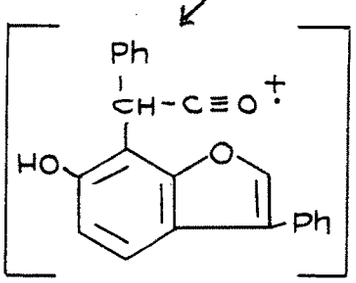


(M^+) 356

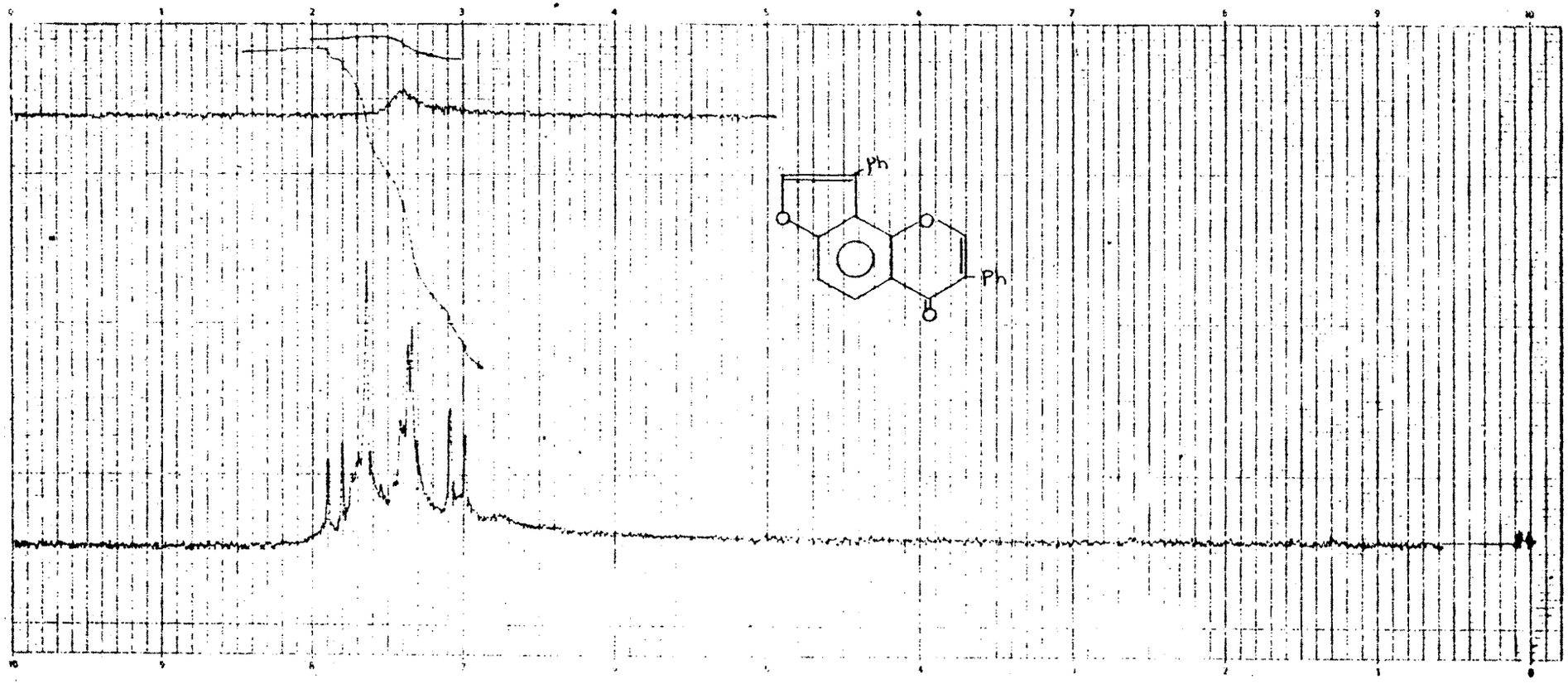


$(M-1)^+$ 355

-CO



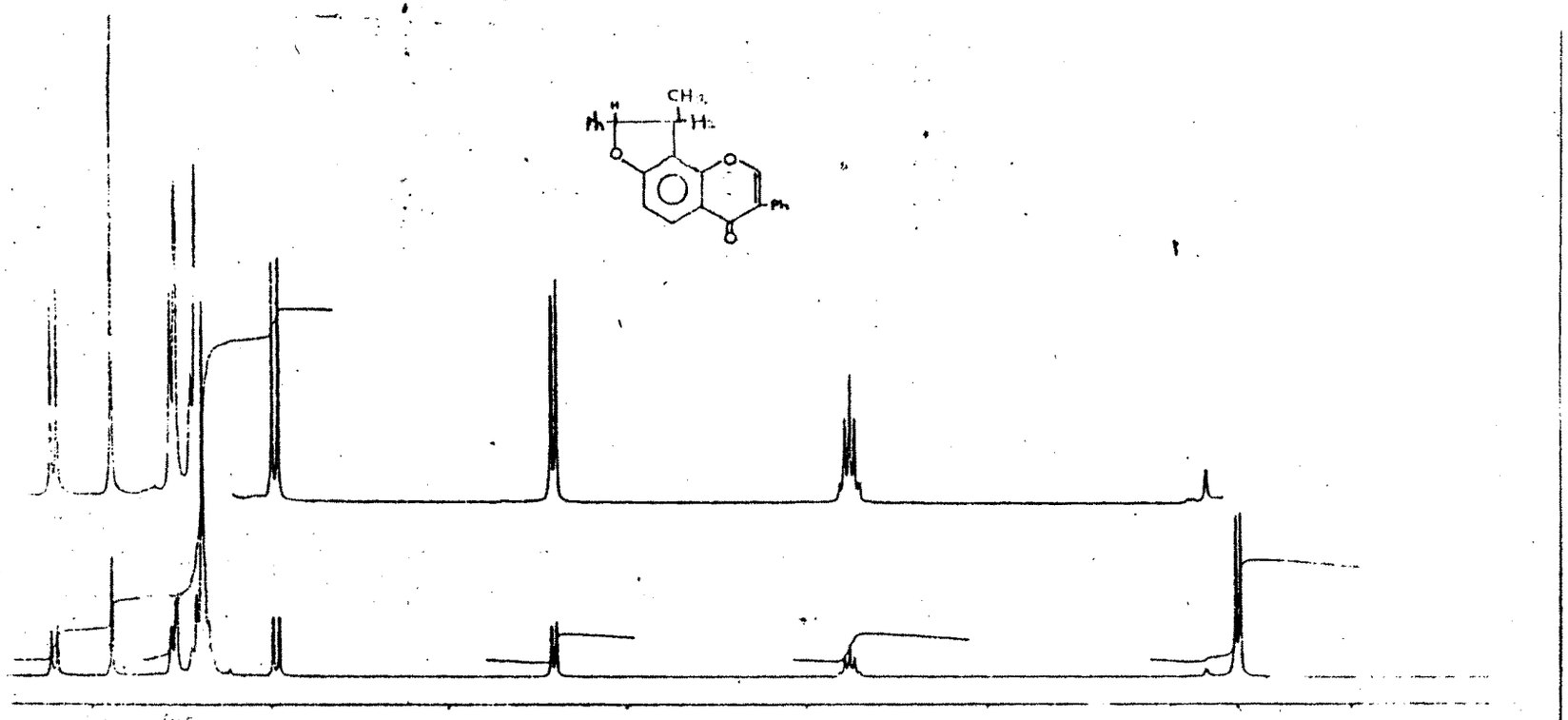
m/e 327



3,6-Diphenyl furo(2,3-h)-benzopyran-7(H)-one (18) (Fig.3)

multiplet appeareda at 7.4 for five aromatic protons of phenyl ring at C-3 ; another multiplet appeared at 7.65 for five aromatic protons of phenyl ring at C-6 and one aromatic proton at C_9-H ; a singlet at 7.65 for one proton at C-5 ; one doublet in the downfield region appeared at 7.85 with J=9Hz for proton at C-8. This sequence of reactions established the structure of (11).(Fig. 3)

It is observed that in Claisen rearrangements different products are obtained on changing the heating period of the reaction. When heating period of the above reaction was extended, cyclized product alongwith open chain compound was obtained. In the present case of Claisen rearrangement of 7-cinnamyloxy isoflavone the reaction mixture was refluxed for 12 hrs. On working up the reaction mixture, crude product was washed with alkali solution and filtered. Filtrate was acidified to obtain the product (11) whose mixed m.p. with authentic sample prepared earlier was not depressed. Alkali insoluble product was characterized as 2,6-diphenyl-3-methyl-2,3-dihydrofuro (2,3-h)benzopyran-7(H)-one (13). Structure of (13) was established by PMR spectrum which exhibited following signals. ($CDCl_3$) : δ 1.6, doublet for methyl protons with J=7Hz at C-3 ; the proton at C-3 showed multiplet at 3.7 ; proton at C-2 appeared as doublet with J=7Hz at 5.3 ; another down-



2,6-Diphenyl-3-methyldihydrofuro(2,3-h)-benzopyran-7(H)-one (13) (Fig.4)

field doublet was observed at 7.0 with J=9Hz for C-9 proton. Five aromatic protons showed multiplet at 7.3 ; singlet for proton at C-5 appeared at 7.8 ; downfield doublet with J=9Hz occured at 8.2 for proton at C_8-H. (Scheme IX) (Fig.4)

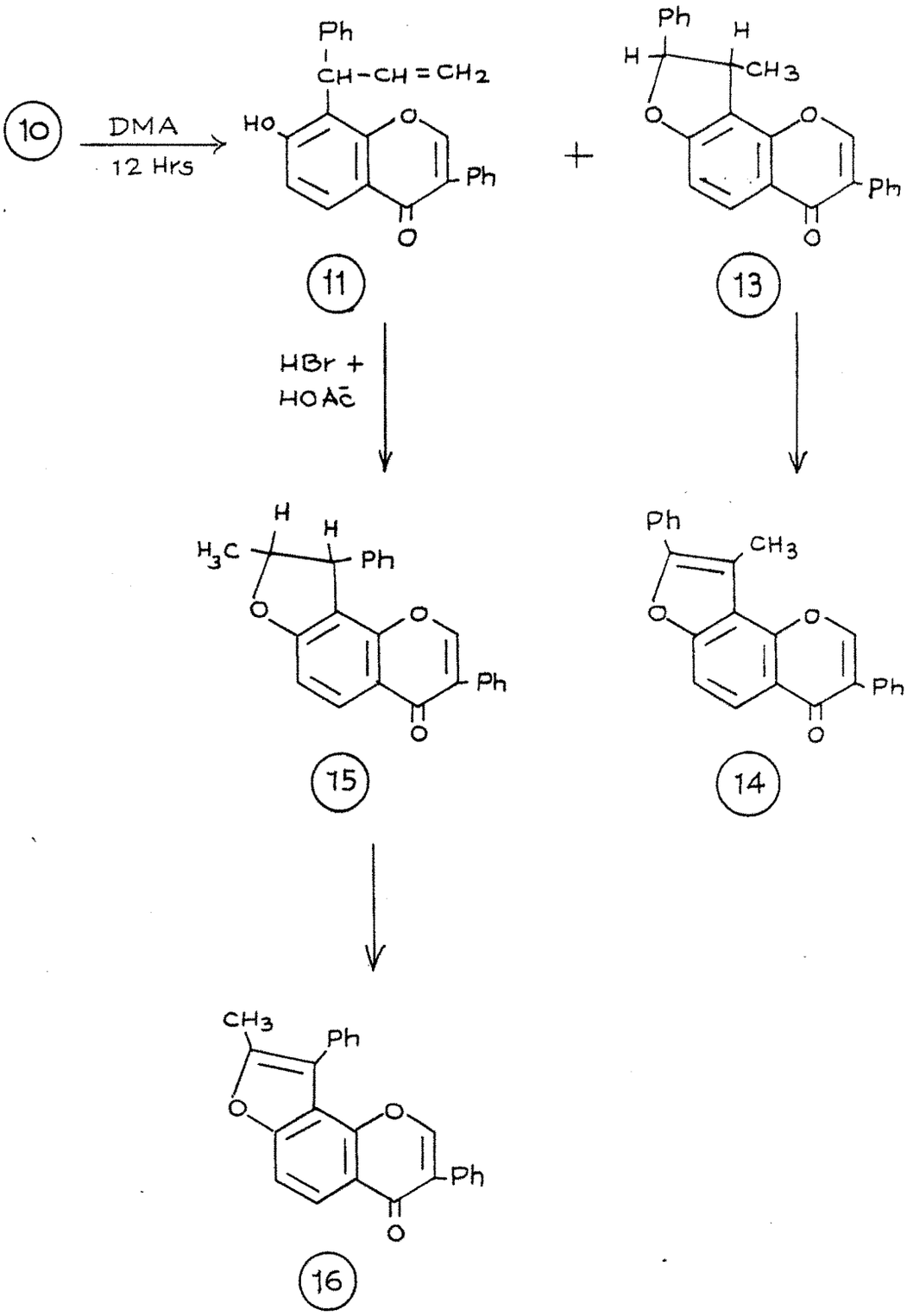
The isomeric structure (15) is eliminated on the basis that the doublet of proton at C-2 appears downfield at δ 5.3 in comparison to proton at C-3 which appears as multiplet at 3.7. If the isomeric structure (15) was present, then the doublet of proton at C-3 would have appeared upfield in comparison with multiplet of proton at C-2. The isomeric product (15) is prepared from (11) and is discussed later.

Mechanism of formation of (13) is shown in the (Scheme-X).

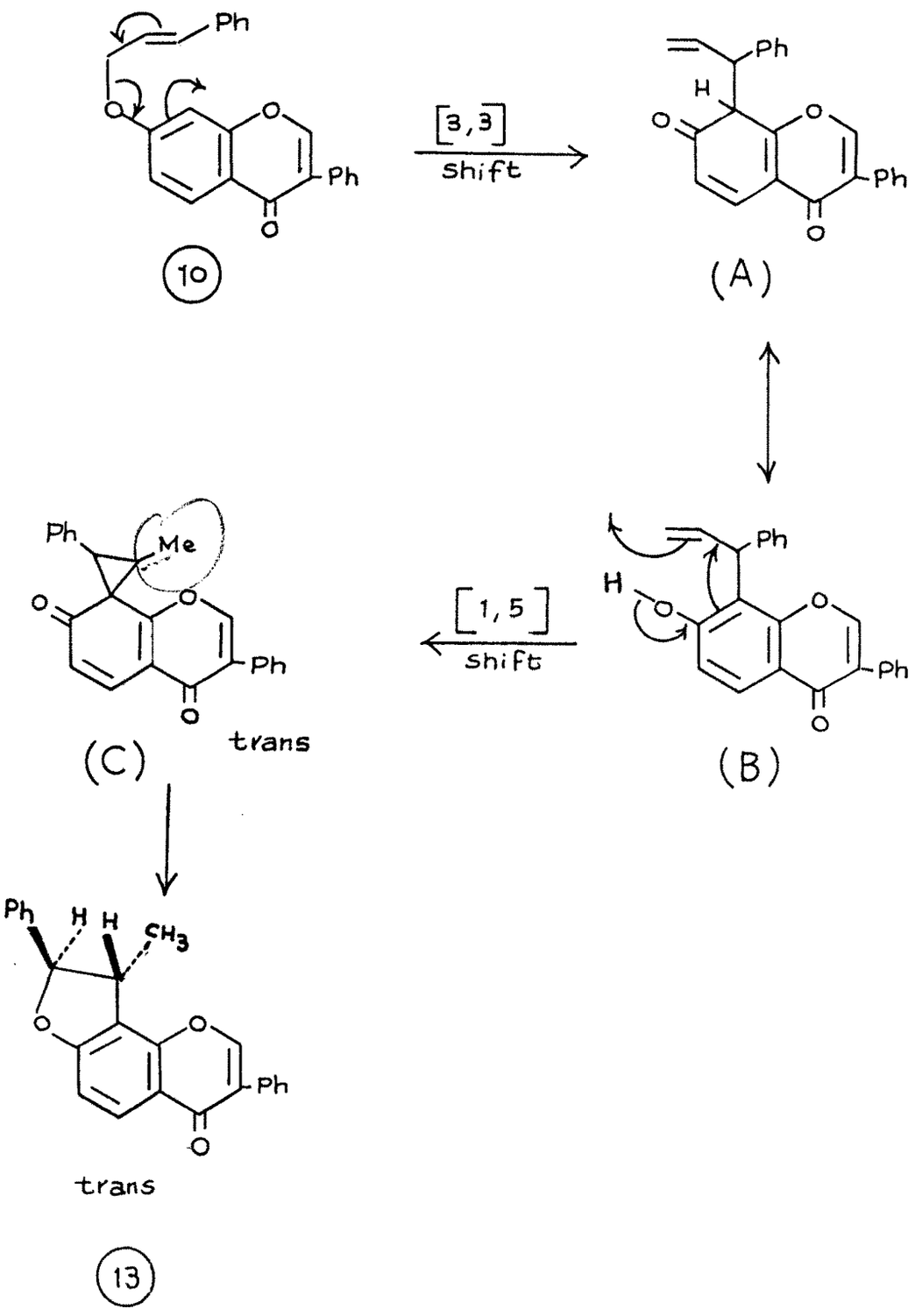
The Claisen rearrangement of 7-cinnamyloxy isoflavone takes in normal way to give structure (A) which undergoes cyclization to form cyclopropane intermediate (C) which then opens up to give trans-2,6-diphenyl-3-methyl-2,3-dihydro (2,3-h)benzopyran-(7H)-one (13).

The mechanism of formation of (15) is shown in the (Scheme-XI).

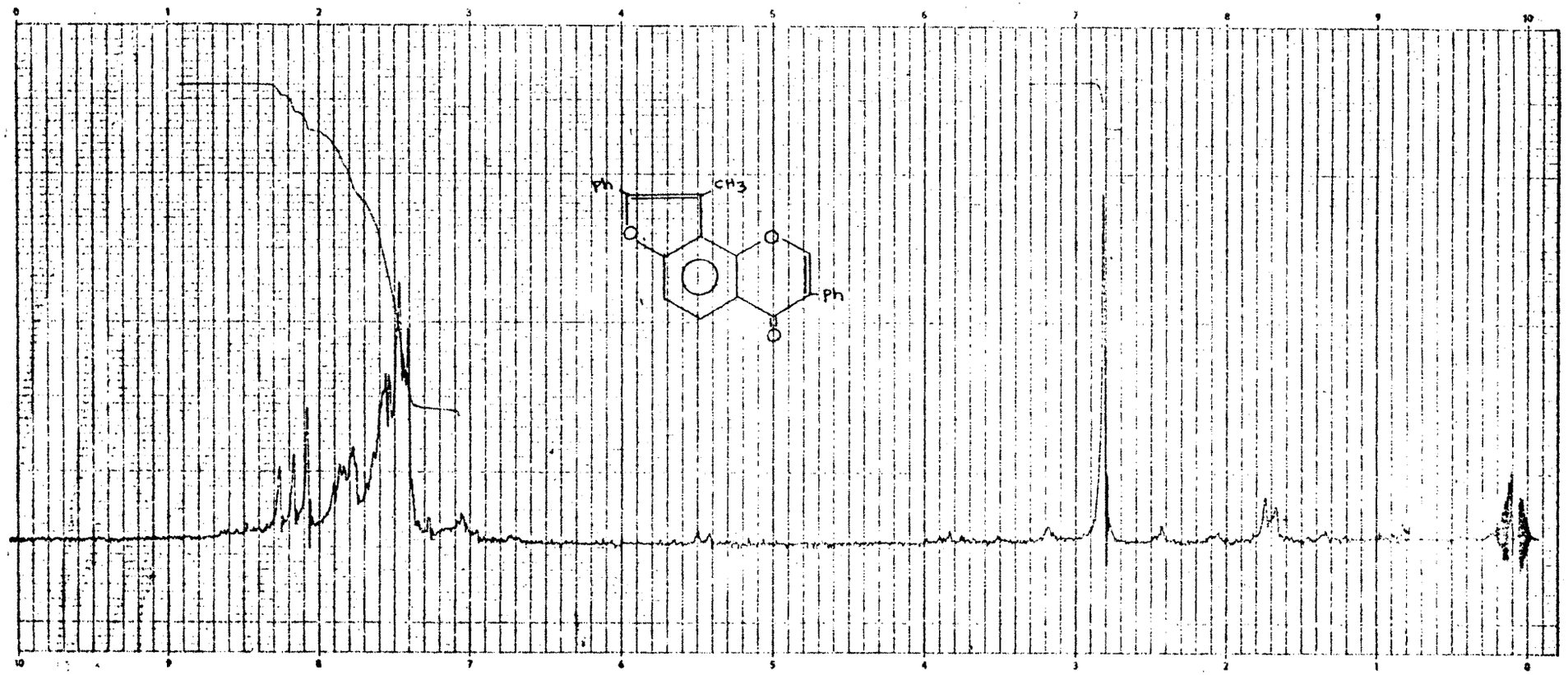
Scheme IX :


10
DMA
12 Hrs
Ph
CH-CH=CH2
HO
O
Ph
O
11
+
Ph
H
H
CH3
O
O
Ph
O
13
HBr +
HOAc
H
H
H3C
Ph
O
O
Ph
O
15
Ph
CH3
O
O
Ph
O
14
CH3
Ph
O
O
Ph
O
16

Scheme X

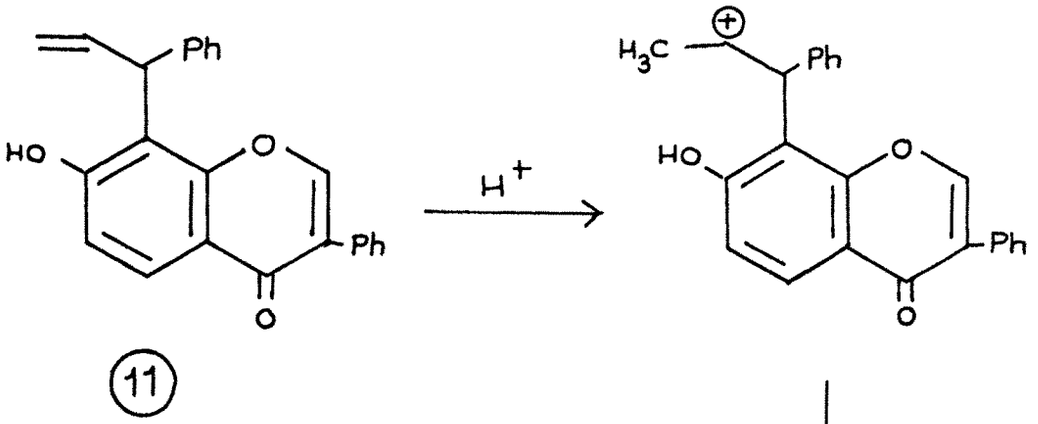

Ph
O
O
Ph
O
10
[3,3]
shift
Ph
H
O
O
Ph
O
(A)
(B)
Ph
H
O
O
Ph
O
[1,5]
shift
Ph
Me
O
O
Ph
O
(C)
trans
Ph
H
H
CH3
O
O
Ph
O
trans
13

Dehydrogenation of (13) was carried out by refluxing it in diphenylether in the presence of Pd/C (10%). Product obtained was 2,6-diphenyl-3-methylfuro (2,3-h)benzopyran-7(H)-one (14). Structure was confirmed by pmr spectrum giving following signals ($CDCl_3$) : δ 2.7, singlet for three protons of methyl group at C-3 ; multiplet for five aromatic protons of phenyl ring and one proton at C_9-H appeared at 7.4 ; another multiplet for a group of five aromatic protons appeared at 7.7 ; one downfield singlet occured at 8.0 for proton at C-5 ; proton at C-8 showed doublet with J=9Hz at 8.15.(Fig.5) Cyclization of (11) was carried out by heating it with a mixture of glacial acetic acid and hydrobromic acid to obtain 3,6-diphenyl-2-methyl-2,3-dihydrofuro (2,3-h) benzopyran-7(H)-one (15). The pmr spectrum of the compound showed it to be a mixture of cis and trans isomers ($CDCl_3$) : δ 1.15, doublet with J=10Hz for three protons of methyl group at C-2. This signal was from cis isomer of the furan moiety. Another doublet at 1.6 with J=8Hz for three protons of methyl group at C-2 from trans isomer. Single proton doublet at 4.45 with J=7Hz was due to C_3-H from trans isomer, while doublet at 4.75 with J=9.5 was shown by C_3-H from cis isomer. Similarly there were two multiplets existing at different positions for protcn at C-2 from twoisomers. Multiplet at 4.95 was due to trans isomer while at 5.3

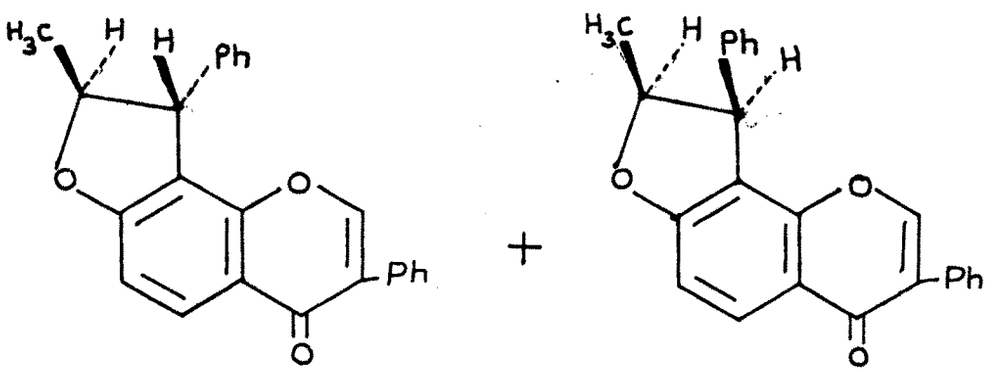


2,6-Diphenyl-3-methyl furo(2,3-h)-benzopyran-7(H)-one (14) (Fig.5)

Scheme XI



(11)



trans
(15)

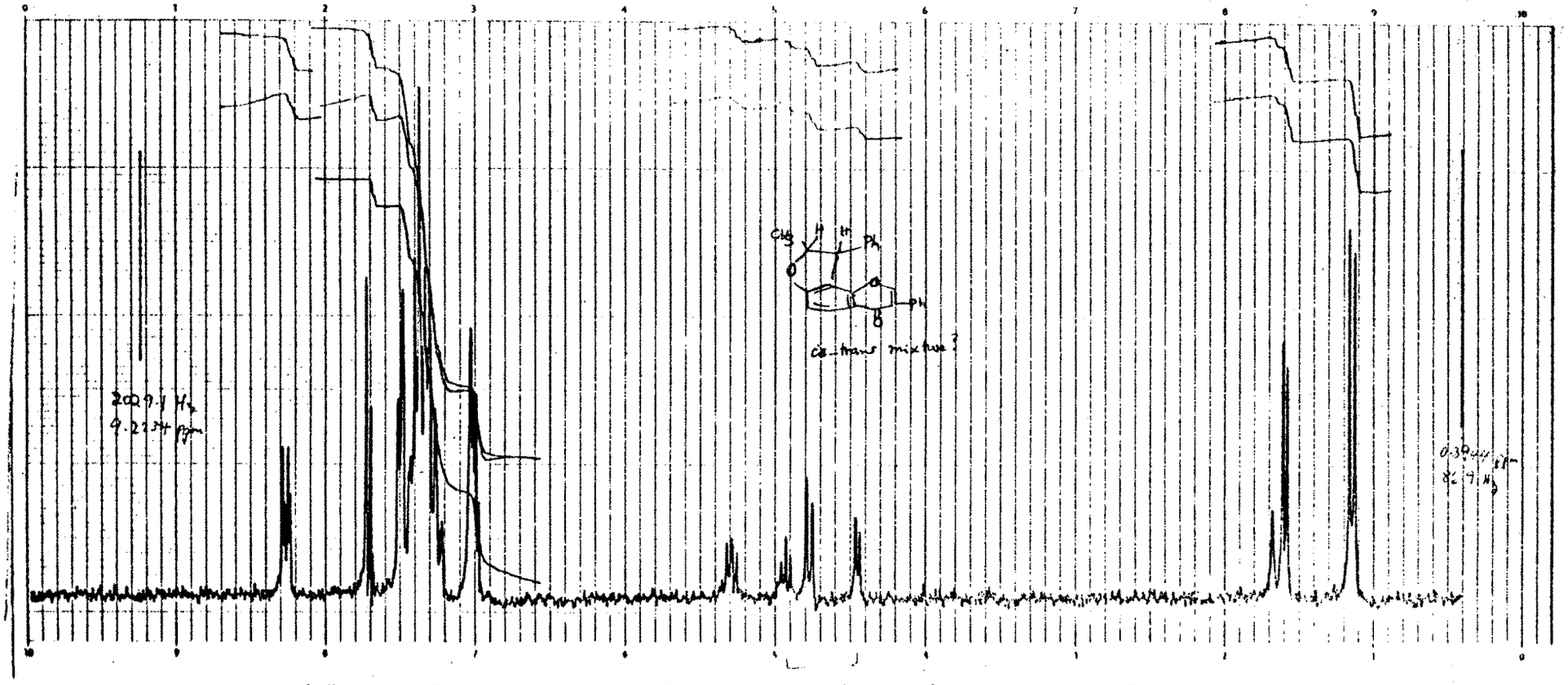
cis
(15)

was due to cis isomer. Ten aromatic protons showed multiplet din the downfield region from 7.0 - 7.3. One downfield doublet at 7.5 with J=9Hz appeared due to proton at C-9 and another doublet with J=9Hz at 7.7 was due to proton at C-8. At 8.25 and 8.28 there were two singlets for proton at C-5 from cis and trans isomers.(Fig. 6)

It was observed from pmr spectrum that there were two isomers of the same molecule giving signals at two different positions for the same proton. In order to decide the exact chemical shift of eachproton from cis as well as trans isomer, decoupling study was carried out for this molecule.

When C_2-H giving multiplet at δ 5.3 was irradiated, doublet at δ 1.1 appeared as singlet and doublet at 4.8 also changed to a singlet. Hence doublet at 1.1 for --CH_3 at C-2, doublet at 4.8 for C_3-H and the multiplet at 5.3 for C_2-H was from the same isomer.

When C_2-H giving multiplet at δ 4.9, was irradiated, doublet at 1.6 was changed to singlet and also doublet at 4.45 became singlet. Hence doublet at 1.6 for -CH_3 at C-2 ; doublet at 4.45 for C_3-H and multiplet at 4.9 for C_2-H were from the same isomer.



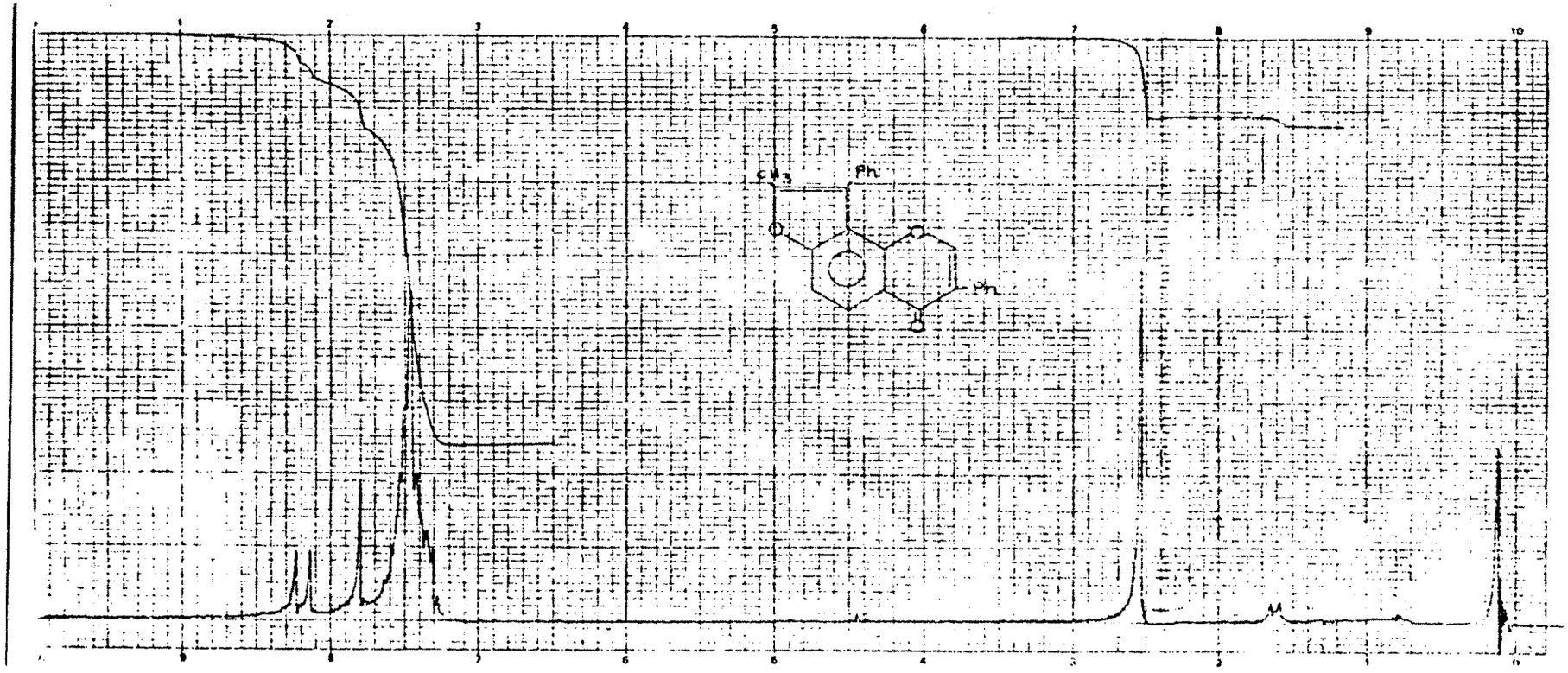
3,6-Diphenyl-2-methyl 2,3-dihydro furo(2,3-h)-benzopyran-7(H)-one (15) (Fig.6)

It was difficult to separate this mixture of cis-trans isomers with the help of TLC as it was showing only one spot on the chromatographic plate.

Dehydrogenation of (15) was carried out with Pd/C (10%) by refluxing it in diphenyl ether. After usual workig up of the reaction mixture, 3,6-diphenyl-2-methyl furo(2,3-h)benzopyran-7(H)-one (16) was dobtained. Structure was confirmed by pmr spectrum ($CDCl_3$) : δ 2.45 singlet for three protons of methyl group at C-2 ; multipet in the downfield region at 7.4 appeared for 10 protons of the aromatic region + one protonat C_9-H. One singlet at 7.7 occured due to proton at C-5. Downfield doublet at 8.1 with J=9Hz appeared for proton at C-8.(Fig.7)

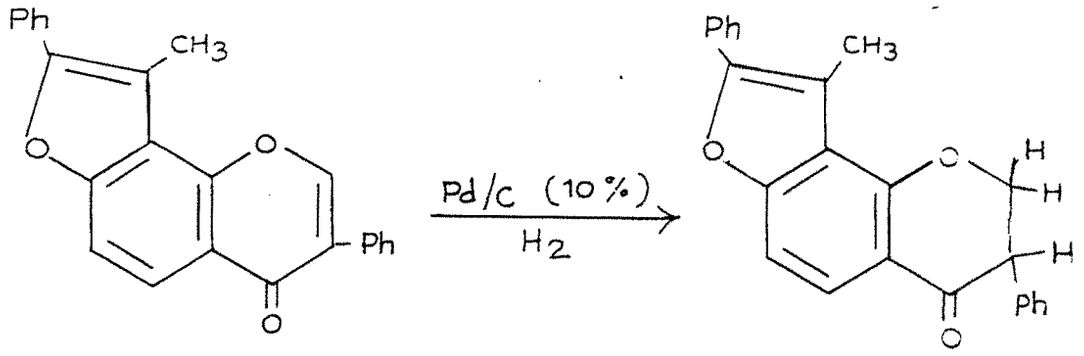
In order to study the stereochemistry of dihydrofuro isoflavone, hydrogenation of furoisoflavone was carried out as hydrogenation with Pd/C would furnish stereospecifically cis isomer only. (Scheme-XII)

Hydrogenationof (14) was carried out using Pd/C (10%) as a catalyst. On working up of the reaction mixture, the product obtaining was purified and its pmr spectrum was recorded which showed following signals ($CDCl_3$) : δ 2.4, singlet for three protons of methyl group at C-3 ; 3.9, multiplet for proton at C-6 ; protons at C-5 appeared as doublet

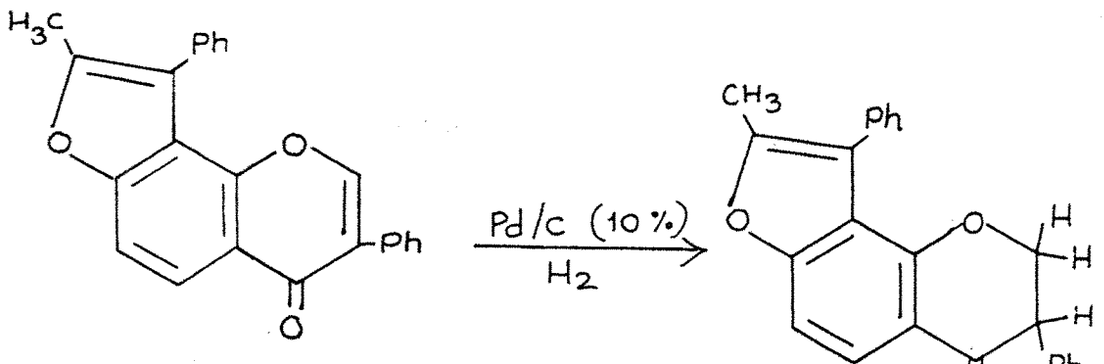


3,6-Diphenyl-2-methyl Furo(2,3-h)-benzopyran-7(H)-one (16) (Fig.7)

Scheme XII



(14) (19)



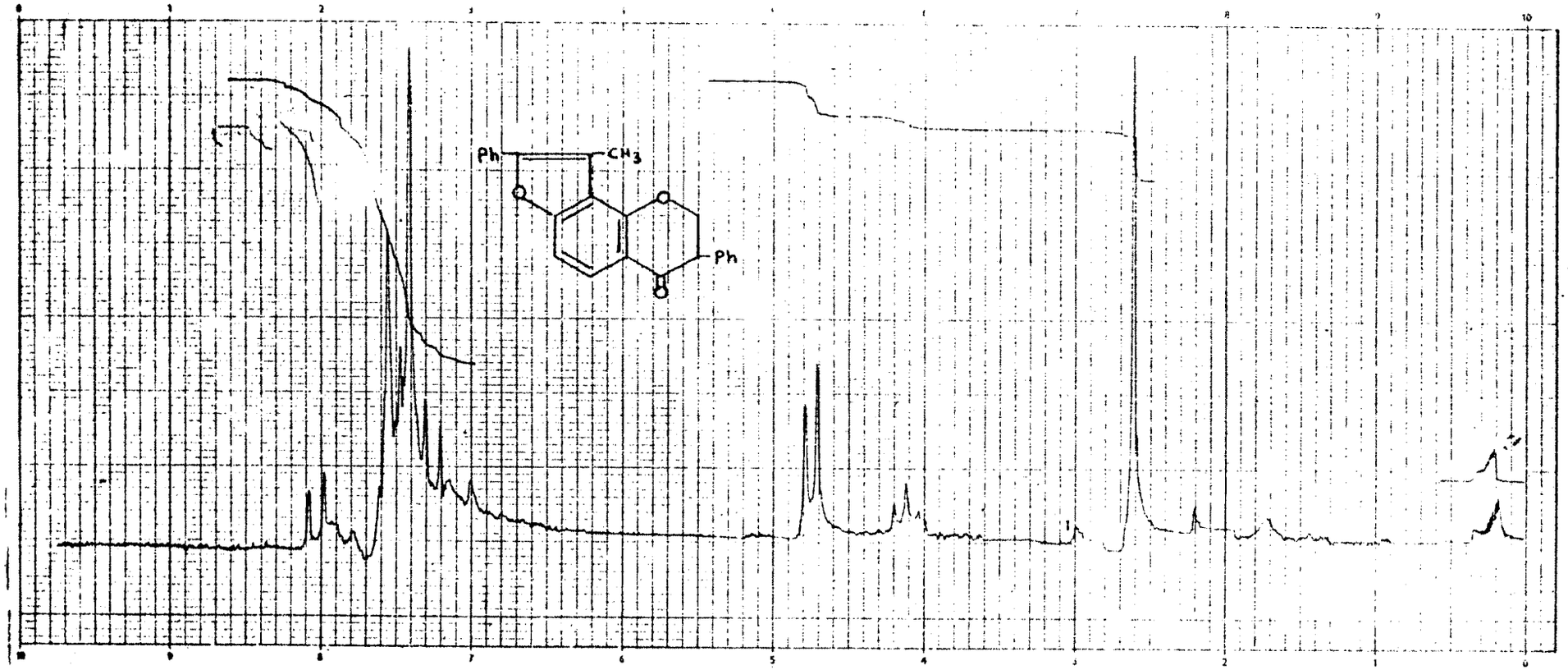
(16) (20)

with J=8Hz at 4.55 ; another doublet at 7.05 with J=9Hz was due to one proton at C-9. Ten aromatic protonsshowed multiplet at 7.25 ; a downfield doublet appeared at 7.8 with J=9Hz for proton at C-8.(Fig.8)

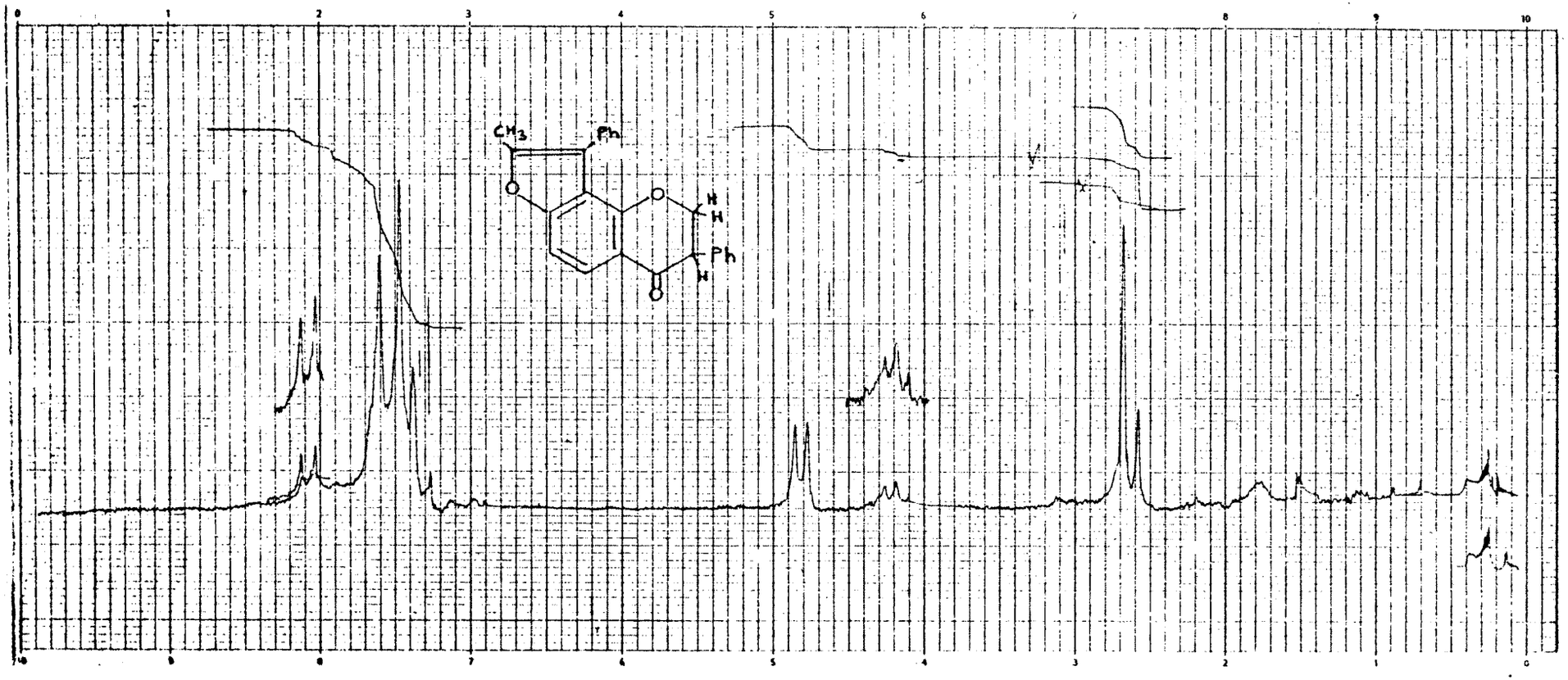
From the above pmr spectra it appears that the structure of the compound (19) is 3-methyl-2,6-diphenyl-5,6-dihydrofuro (2,3-h)benzopyran-7(H)-one (19) and not cis-2,6-diphenyl-3-methyl-2,3-dihydro furo (2,3-h)benzopyran -7(H)-one (D). Thus it is clear that double bond of the γ-pyrone ring was hydrogenated while that of furan ring remained unaffected.

Similarly hydrogenation of (16) was carried out using Pd/C (10%). It furnished the product 2-methyl-3,6-diphenyl-5,6-dihydro furo(2,3-h)benzopyran-7(H)-one (20) and not cis-2methyl-3,6-diphenyl-2,7-dihydro furo (2,3-h)benzopyran--7(H)-one (E) ($CDCl_3$) : δ 2.45, singlet for three protons of methyl group at C-2 ;multiplet at 3.95 for proton at C-6 ; two protons at C-5 gave doublet with J=8Hz at 4.55 six aromatic protons showed multiplet at 7.25 ; another multiplet at 7.35 for five aromatic protons ; one downfield doublet at 7.8 for proton at C-9 with J=9Hz.(Fig.9)

From these two hydrogenated products, stereochemistry of the dihydrofuro isoflavones could not be assigned as



2,6-Diphenyl-3-methyl-5,6-dihydro furo(2,3-h)-benzopyran-7(H)-one (19) (Fig.8)



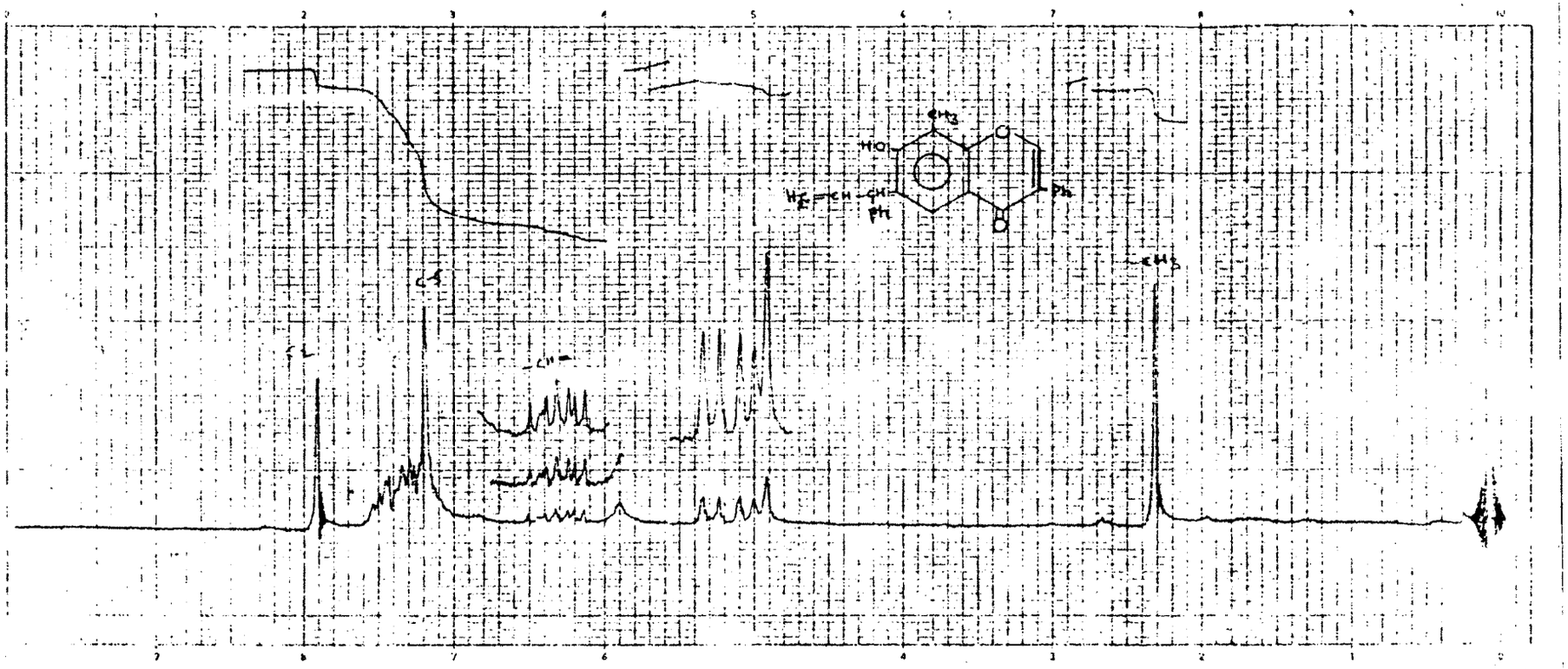
3,6-Diphenyl-2-methyl-5,6-dihydro furo(2,3-h)-benzopyran-7(H)-one (20) (Fig.9)

in both the cases, furan ring remain uunaffected towards hydrogenation reaction.

2,9-Dimethyl-3,6-diphenylfuro(3,2-g)benzopyran-5(H)-one (25)

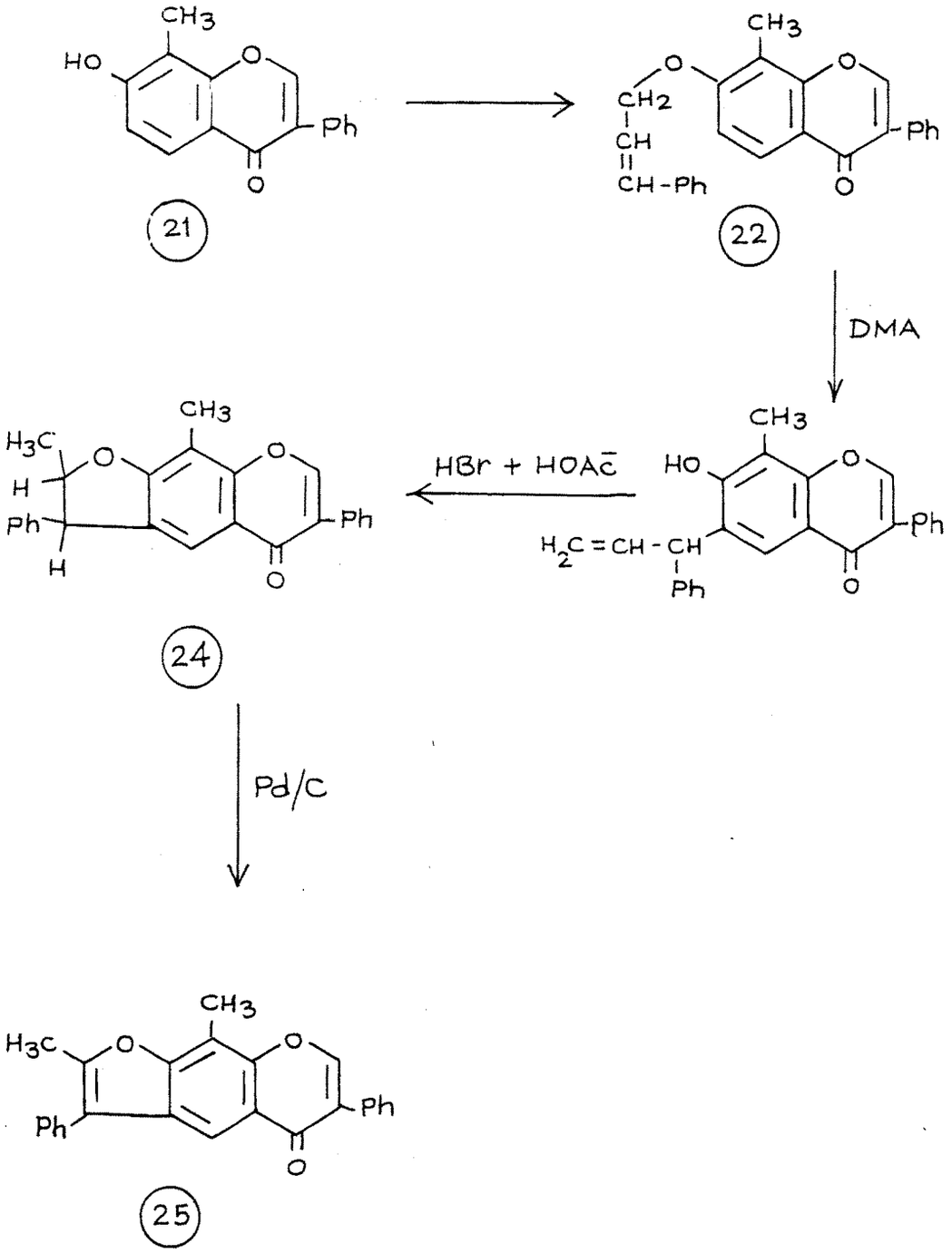
7-Hydroxy-8-methylisoflavone (21) was condensed with cinnamyl chloride inthe presence of anhydrous potassium carbonate and dry acetone to furnish 7-cinnamyloxy-8-methylisoflavone (22) (Scheme-XIII). It underwent Claisen rearrangement when refluxed with N,N-dimethylaniline. Reaction mixture worked up as usual to obtain only alkali soluble product 6-(1-phenyl-2-propenyl)-7-hydroxy-8-methyl-isoflavone (23). Structure was established by pmr spectrum giving following signals ($CDCl_3$) : δ 2.3, singlet three protons of methyl group at C-8 ; 5.0, multiplet for two vinylic protons = CH_2 ; one allylic proton gave doublet with J=10Hz at 5.3, Ar-CH-C= ; multiplet appeared due to one vinylic proton at 6.3, Ar-CH-CH= ; 7.2, singlet for proton at C-5 ; five aromatic protons showed multiplet at 7.3 ; one downfield singlet at 7.9 appeared for proton at C-2. (Fig. 10)

Cyclization was carried out by refluxing (23) in the mixture of acetic acid and hydrobromic acid solution. On usual working up of the reaction mixture the product obtained was 2,9-dimethyl-3,6-diphenyl-2,3-dihydrofuro (3,2-g) benzopyran-5(H)- one (24). (Scheme-XIII)



7-Hydroxy-6-(1-phenyl-2-propenyl)-8-methylisoflavone (23) (Fig. 10)

Scheme XIII

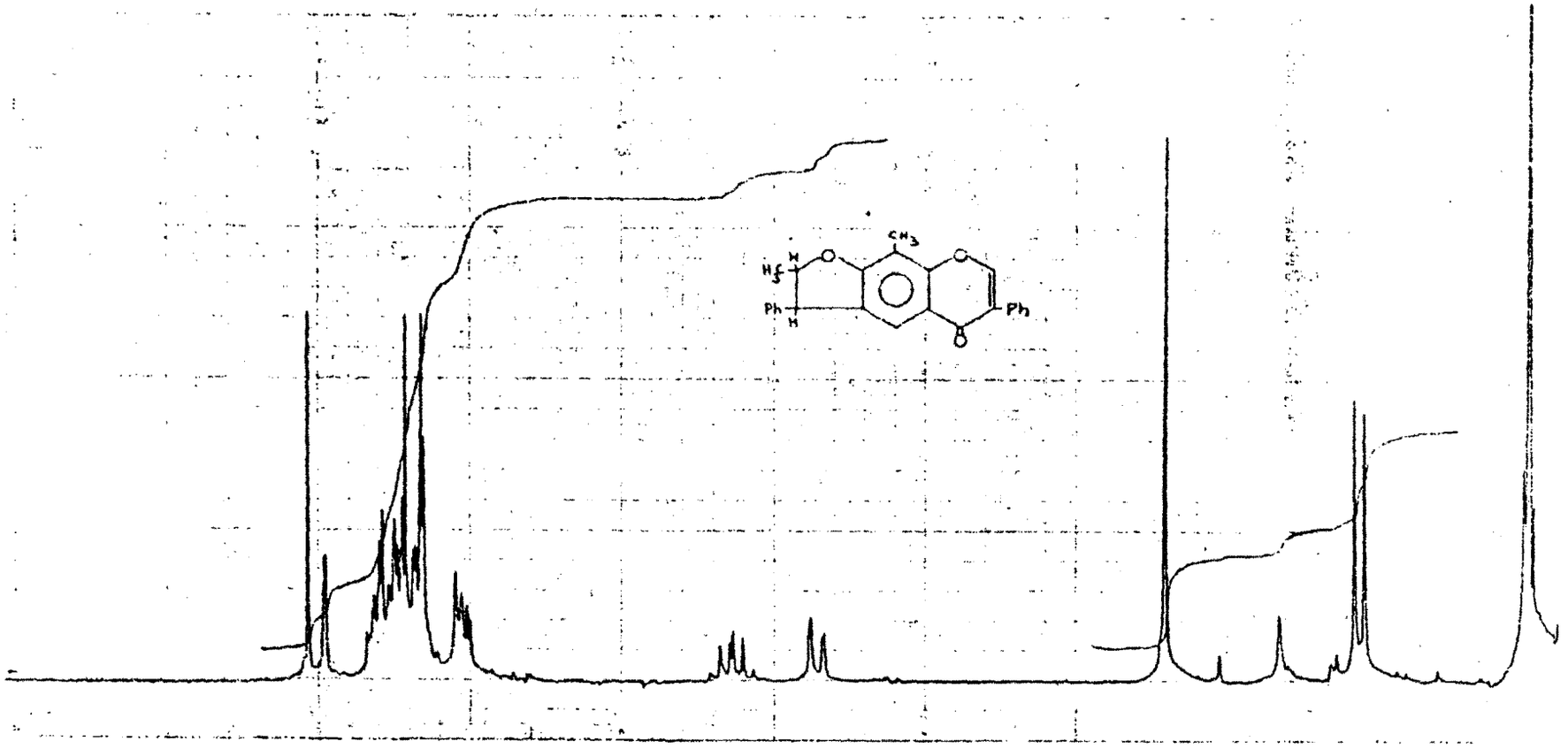

CH3
HO
O
Ph
O
21
CH3
O
O
CH2
CH
CH-Ph
Ph
O
22
DMA
CH3
HO
O
Ph
H2C=CH-CH
Ph
O
HBr + HOAc
CH3
H3C
O
O
H
Ph
Ph
H
O
24
Pd/C
CH3
H3C
O
O
Ph
Ph
O
25

PMR spectrum of (24) showed following signals ($CDCl_3$) δ 1.1, doublet with J=7Hz for three protons of methyl group at C-2 ; 2.4, singlet for methyl group protons at C-9 ; proton at C-3 showed doublet with J=10Hz at 4.7 multiplet for single proton at C-2 appeared at 5.3 ; 7.0 - 7.5 multiplet for ten aromatic protons ; two downfield singlets appeared at 7.95 and 8.1 for protons at C-4 and C-7 respectively. (Fig.11)

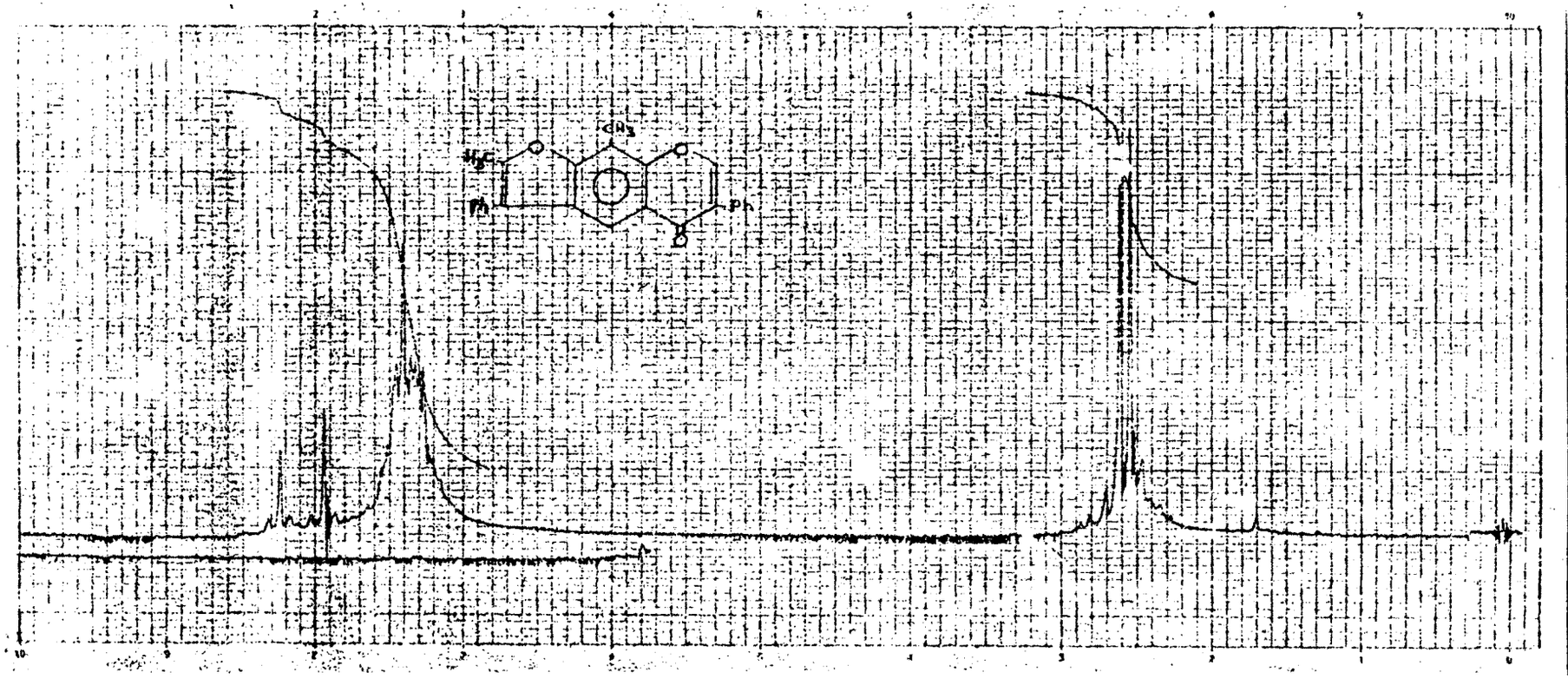
(24) was refluxed in diphenyl ether with Pd/C (10%) for dehydrogenation. Excess of solvent was removed and product crystallized to furnish 2,9-dimethyl-3,6-diphenyl furo (3,2-g) benzopyran-5(H)-one (25). Structure was confirmed by pmr spectrum ($CDCl_3$) : δ 2.55, singlet for three methyl protons at C-2 ; another singlet for three methyl protons at C-9 appeared at 2.6 ; multiplet at 7.4 for ten aromatic protons ; 7.9, singlet for proton at C-7 and another downfield singlet at 8.2 for proton at C-4. (Fig.12)

Stereochemistry of 2,3-dihydrofuro isoflavone : NOE difference spectra :

NOEs are much more easily detected by substracting in the computer the normal spectrum from a spectrum taken with the irradiating signal on, and printing only the



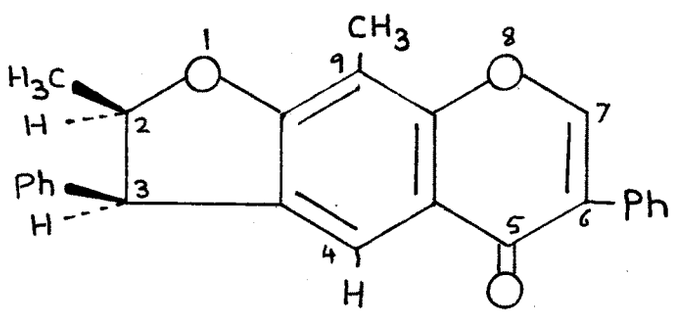
2,9-Dimethyl-3,6-diphenyl-2,3-dihydro furo(3,2-g)-benzopyran-5(H)-one (24) (Fig. II)



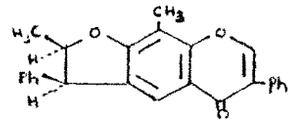
2,9-Dimethyl-3,6-diphenyl furo(3,2-g)-benzopyran-5(H)-one (25) (Fig.12)

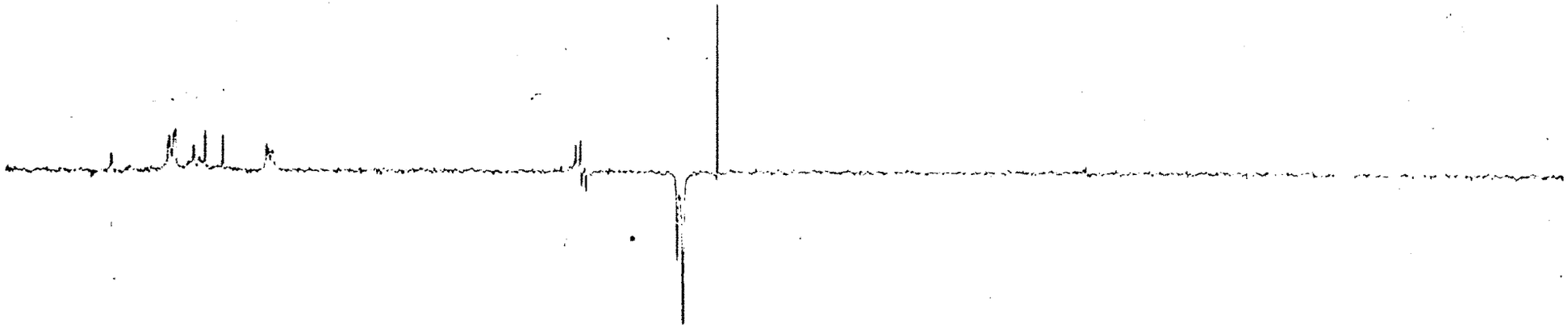
difference between the two spectra. All the unaffected signals simply disappear and all that shown is the enhancement of signals of neighbouring protons in the same place. Using difference spectra, it is easy to detect 1% enhancemet or even less, with the result that NOEs in methyl groups are now quite commonly measurable.

In order to assign the stereochemistry of 2,9-dimethyl-3,6-diphenyl 2,3-dihydrofuro (3,2-g)benzofuro-(5H)-one (24), this technique of NOE difference spectra was applied. NOE difference spectra of (24) shows the enhancement of signals for the proton at C-2, proton on the phenyl ring at C-3 and the proton at C-4, while the proton at C-3 shows negative NOE and is relaying NOE to the proton at C-4.



(24)





Cis - 2,9-Dimethyl-3,6-diphenyl-2,3-dihydro furo(3,2-g)-benzofuran-5(H)-one (24) (Fig. 13)

Thus there is NOE between C_2-H and C_3-H, between C_3-H and C_4-H and also between $-CH_3$ group at C-2 with aromatic proton of the phenyl ring, at C-3. Thus this compound has methyl group and phenyl ring cis to one another. This is also evident from the chemical shift of C_2-CH_3 group. In the case of 2,3-dihydrofurano compounds when there is no phenyl ring in the 3 position, the normal chemical shift of C_2-CH_3 group is in the region of δ 1.5. In the present case C_2-CH_3 and C_3-phenyl ring are cis to one another and hence the C_2-CH_3 group is shielded by the phenyl ring and therefore the chemical shift of C_2-methyl moves upfield at δ 1.1. When the methyl group and phenyl ring are trans to one another, the chemical shift of methyl group is observed around δ 1.6 - 1.7. Thus the structure of (24) is cis-2,9-dimethyl-3,6-diphenyl-2,3-dihydrofuro (3,2-g)benzopyran-(5H)-one. (Fig. 13)

Based on this arguments the stereochemistry of (13) and (29) can be assigned as trans-2,6-diphenyl-3-methyl-2,3-dihydrofuro (2,3-h)benzopyran-(7H)-one and trans-3,5-dimethyl-2,6-diphenyl-2,3-dihydrofuro (2,3-h) benzopyran-(7H)-one as the chemical shift of methyl protons occured at δ 1.6 in both the cases.

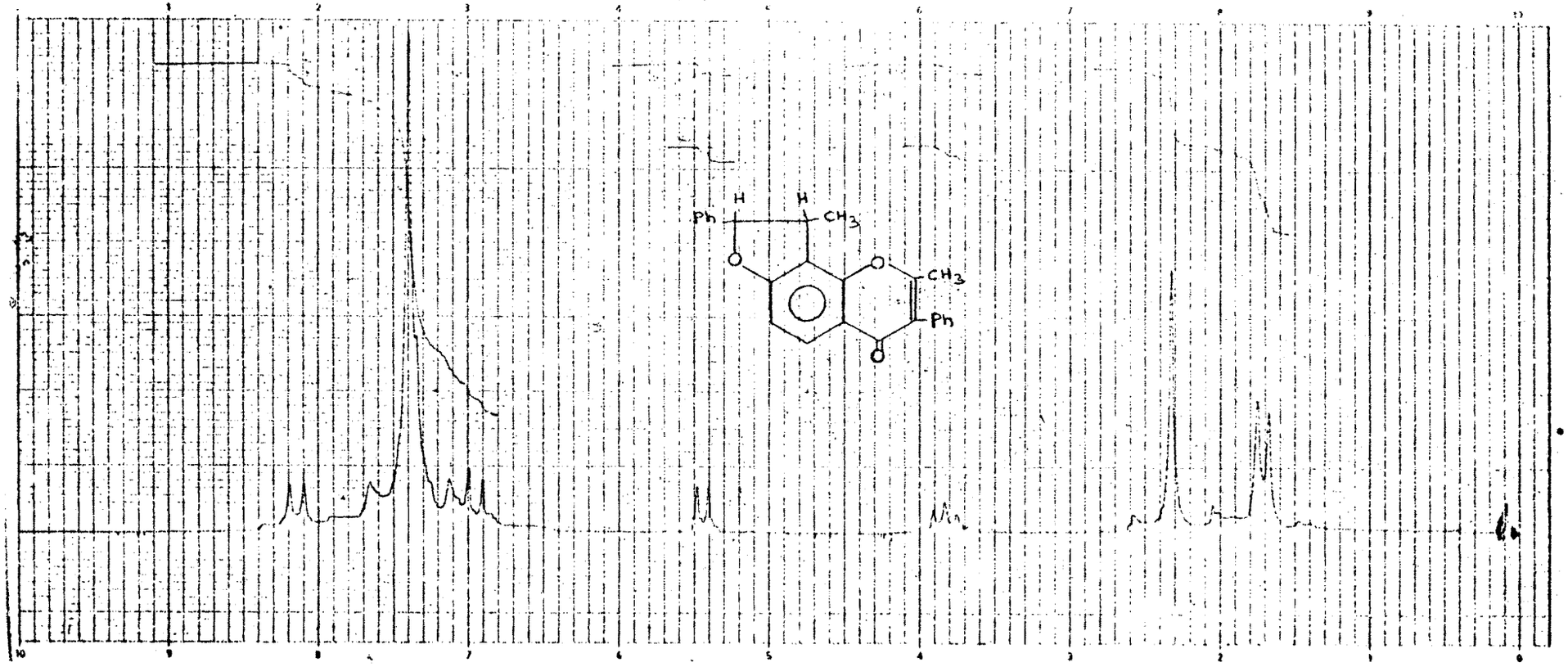
Cinnamylation of 7-Hydroxy-2-methyl isoflavone (26)

7-Cinnamyloxy-2-methylisoflavone (27) was obtained

by treating 7-hydroxy-2-methylisoflavone (26) with cinnamyl chloride in the presence of K_2CO_3 & KI in the mild alkaline medium.

7-Cinnamyloxy-2-methylisoflavone (27) was refluxed with N,N-dimethylaniline for 8 hr. Reaction mixture was worked up by usual method. On washing the crude product with dilute alkali and on acidification two products were obtained, one alkali soluble and another alkali insoluble (Scheme-XIV). Alkali insoluble product was characterized as 3,5-dimethyl-2,6-diphenyl-2,3-dihydrofuro (2,3-h) benzo-pyran-7(H)-one (29) on the basis of pmr spectrum ($CDCl_3$) : δ 1.6, doublet with J=8Hz for three protons of methyl group at C-3 ; another set of methyl group protons at C-5 appeared at 2.2 ; multiplet at 3.7 occured for proton at C-3 ; proton at C-2 showed doublet with J=8Hz at 5.3 another doublet with J=9Hz appeared at 6.85 for proton at C-8 ; Ten aromatic protons showed multiplet at 7.3 ; one doublet in the downfield region appeared at 8.05 with J=9Hz for proton at C-9.(Fig.14)

Attempt to dehydrogenate either (29) with Pd/C or with DDQ met with failure and unreacted product was obtained back.



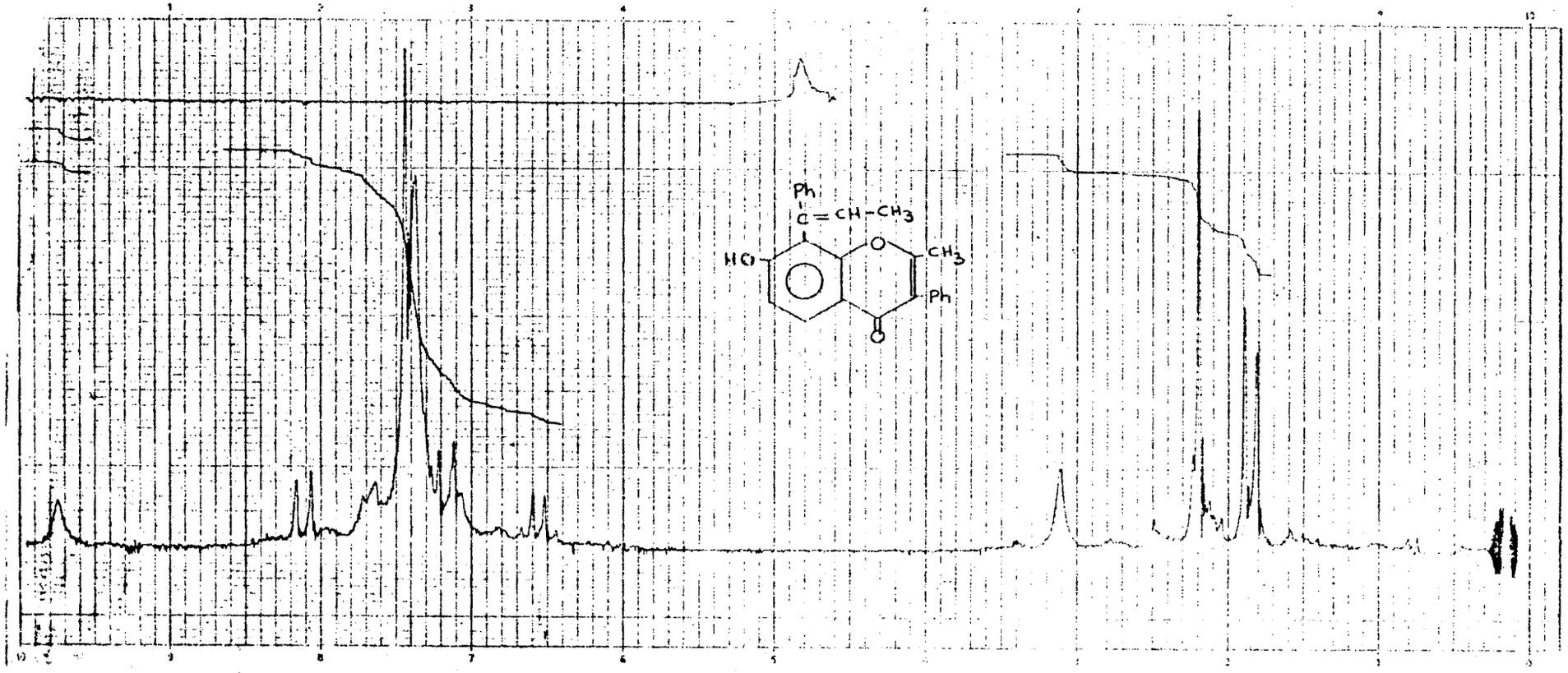
3,5-Dimethyl-2,6-diphenyl-2,3-dihydrofuro(2,3-h)-benzopyran-7(H)-one (29) (Fig. 14)

Alkali soluble product was assigned 8-(1-phenyl-1-propenyl)-7-hydroxy-2-methylisoflavone structure (28), on the basis of pmr spectrum giving following signals ($CDCl_3$) : δ 1.7, doublet with J=8Hz for three protons of terminal methyl group ; another methyl group protons at C-2 appeared as singlet at 2.0 ; one vinylic proton showed quarter at 6.3 = $CH-CH_3$; doublet with J=9Hz for for proton at C-6 appeared at 7.0 ; ten aromatic protons showed multiplet at 7.2 ; one doublet in the downfield region with J=9Hz occured for C-5 proton at 7.9 ; hydroxyl proton appeared as singlet at 9.55.(Fig. 15)

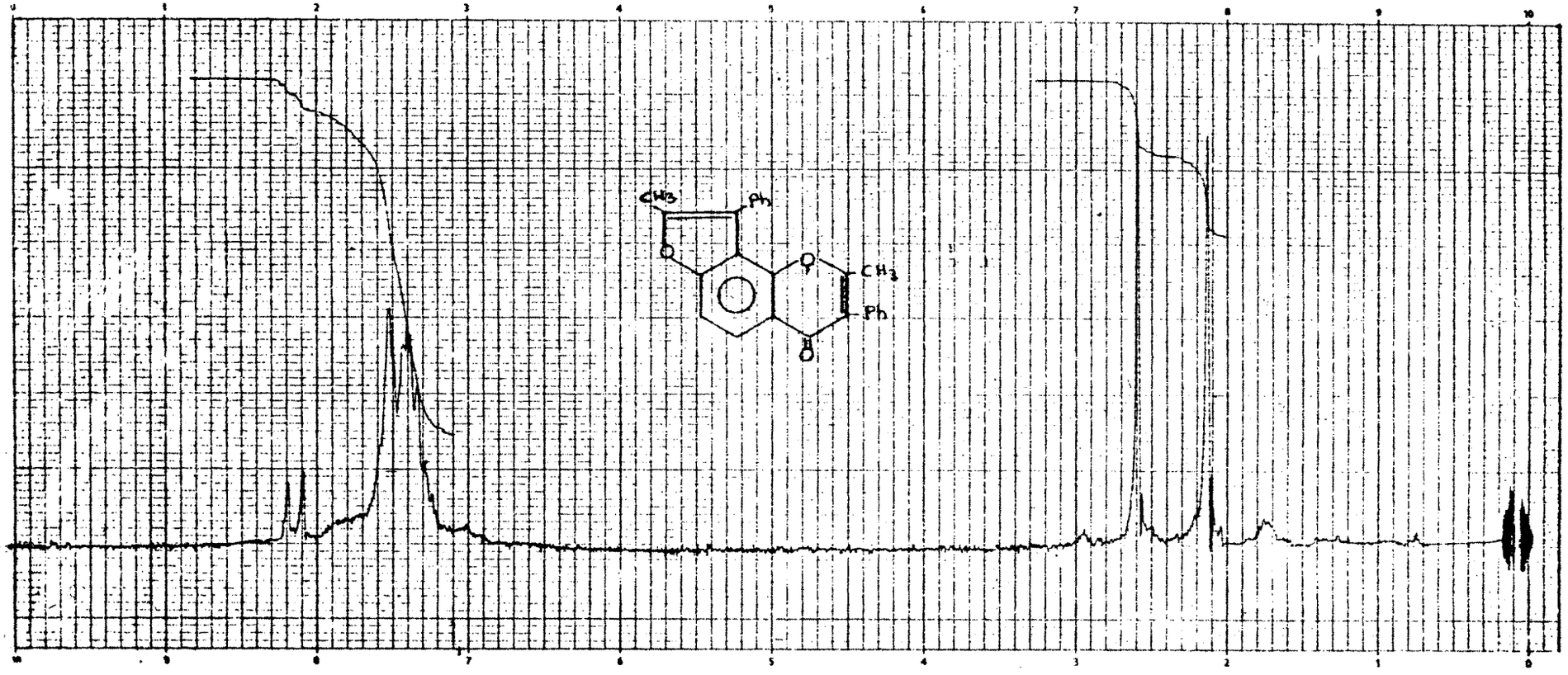
Cyclization of (28) with a mixture of hydrobromic acid and glacial acetic acid gave the product 2,5-dimethyl-3,6-diphenyl furo (2,3-h)benzopyran-7(H)-one (30). PMR spectrum of (30) exhibited following signals ($CDCl_3$) : δ 2.0, singlet for methyl protons at C-5 ; another singlet for methyl protons at C-2 appeared at 2.5 ; ten aromatic protons Ar-H + C_9-H exhibited multiplet in the downfield region from 7.2 to 7.4 ; one doublet with J=9Hz appeared at 8.05 for proton at C-8. Thus cyclohedrogenation occured during this reaction.(Fig. 16)

C-Cinnamylation of 2,4-Dihydroxyphenylbenzyl ketone (31)

2,4-Dihydroxy phenylbenzyl ketone (31) was condensed



7-Hydroxy-8-(1-phenyl-1-propenyl)-2-methylisoflavone (28) (Fig. 15)

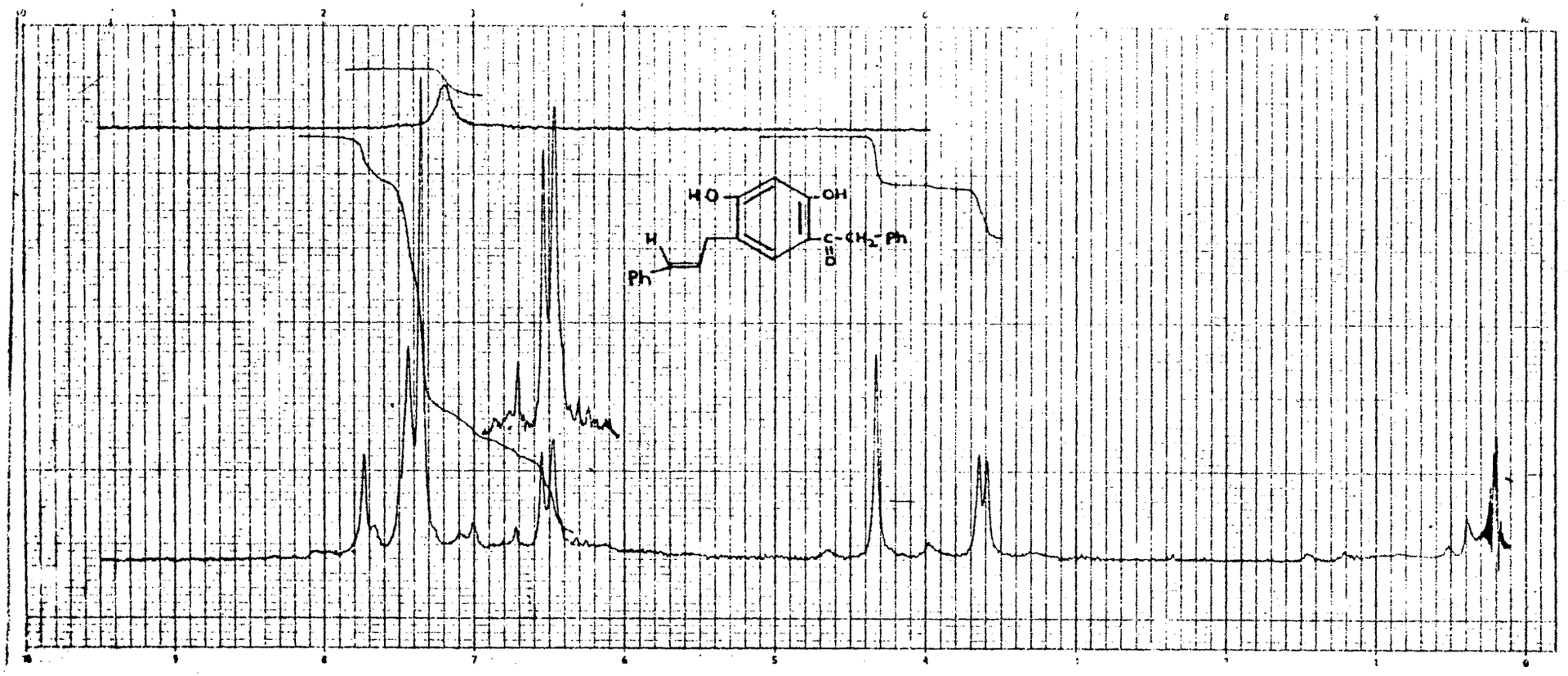


2,5-Dimethyl-3,6-diphenyl furo(2,3-h)-benzopyran-7(H)-one (30) (Fig. 16)

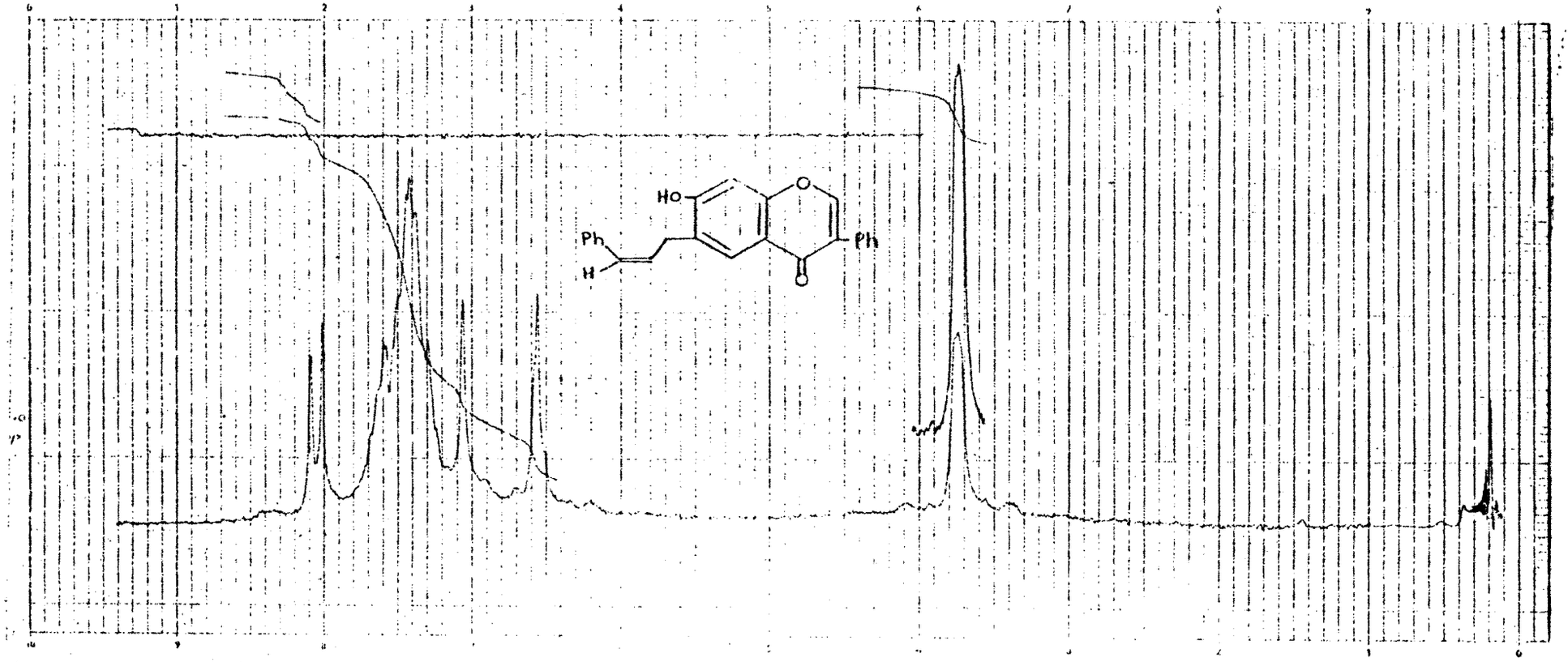
with cinnamyl alcohol in the presence of formic acid (80%) The product obtained was assigned the structure 2,4-dihydroxy-5-cinnamylphenylbenzyl ketone (32) which was confirmed by pmr spectrum giving following spectrum ($CDCl_3$) : δ 3.4, doublet with J=6Hz for two methylene protons of the side chain at C-5 ; singlet appeared at 4.1 for two protons of methylene group $-COCH_2Ph$. Onevinylic proton H_B of the side chain appeared as a broad doublet at 6.2 while H_A gave doublet at 6.5, JAB = 16Hz ; eleven aromatic protons gave multiplet at 7.2 ; one downfield singlet appeared at 7.5 for proton at C-6. (Fig. 17)

Isoflavone ring was then built up on the above ketone (32) by refluxing it in the mixture of pyridine, piperidine and triethylorthoformate. Reaction mixture worked up as before the product was purified to furnish 7-hydroxy-6-cinnamylisoflavone (33). (Scheme-XV)

Structure of (33) was confirmed by pmr spectrum ($CDCl_3$); δ 3.6, broad singlet for methylene proton attached to aromatic nucleus $Ar-CH_2-$; two vinylic protons showed multiplet at 6.4 -CH=CH- ; proton at C-8 appeared as singlet at 6.9 ; ten aromatic protons exhibited multiplet in the region 7.2 to 7.5 ; two singlets appeared in the downfield region at 7.85 and 7.9 for two aromatic protons C-2 and C-5 respectively. (Fig. 18)



2,4-Dihydroxy-5-cinnamyl phenyl benzyl ketone (32) (Fig. 17)

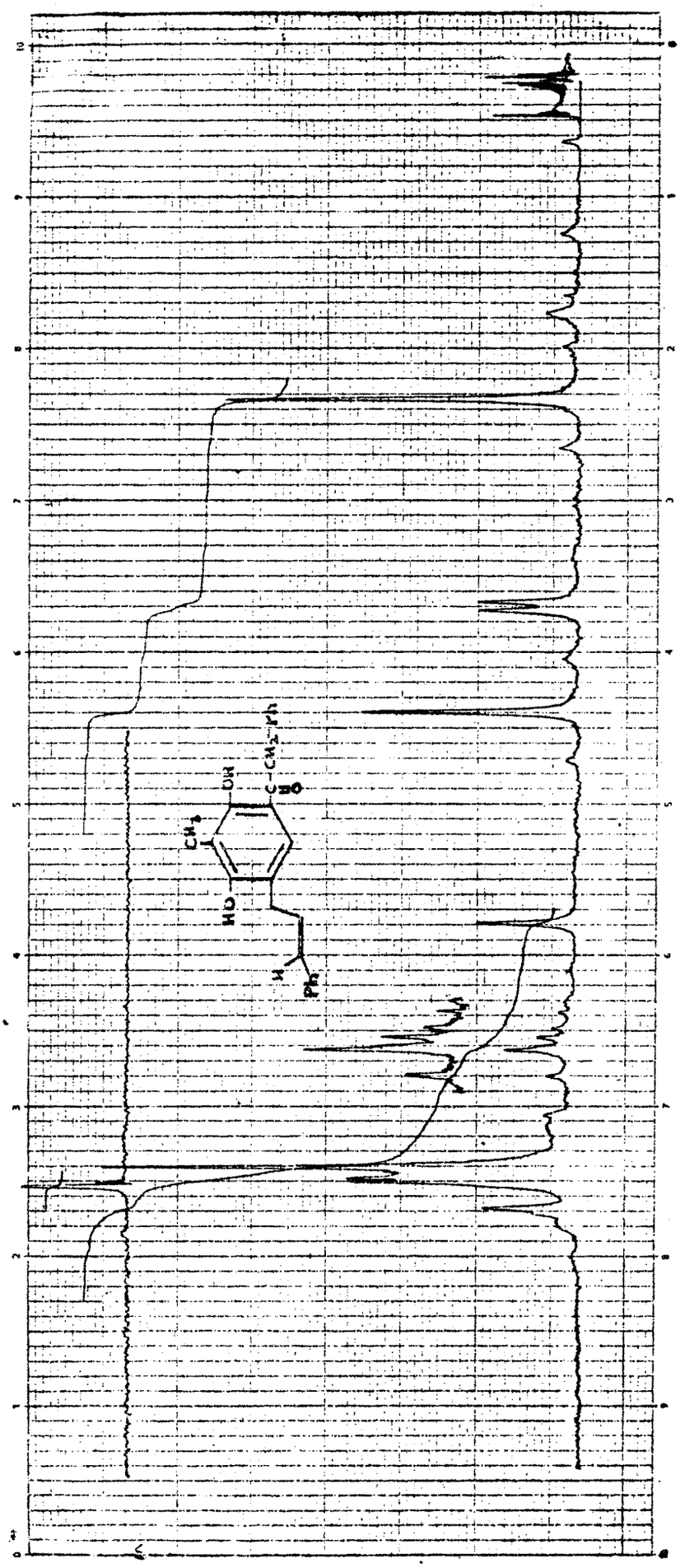


6-Cinnamyl-7-hydroxyisoflavone (33) (Fig. 18)

C-Cinnamylation of 2,4-Dihydroxy-3-methylphenylbenzyl ketone (34)

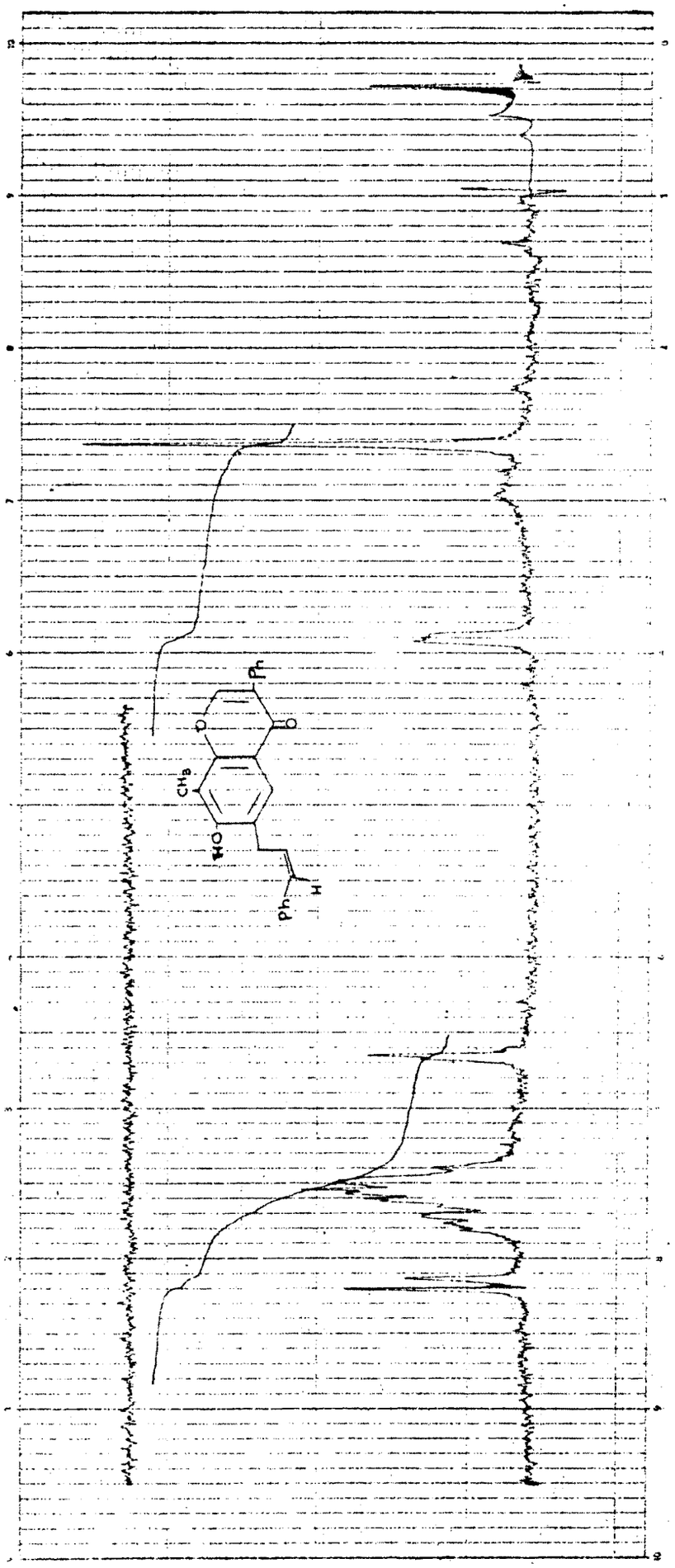
2,4-Dihydroxy-3-methylphenylbenzyl ketone (34) was subjected to C-cinnamylation by reacting it with cinnamyl alcohol and formic acid solution (80%) for 25 hr. Reaction mixture worked up as before to furnish 2,4-dihydroxy-3-methyl-5-cinnamylphenylbenzyl ketone (35). Structure was assigned by pmr spectrum giving following signals ($CDCl_3$) ; δ 2.1, singlet for methyl protons ; doublet appeared at 3.5 with J_{BX}=6Hz for methylene protons attached to aromatic nucleus Ar-CH_2- at C-5 ; another methylene protons exhibited singlet at 4.2 - CO-CH_2-Ph ; hydroxyl proton at C-2 showed singlet at 5.6. Vinylic proton H_B appeared as broad doublet at 6.2 while another proton HA appeared doublet at 6.5, JAB=16Hz ; broad multiplet in downfield region from 7.1 to 7.3 was appeared for ten aromatic protons ; one singlet for C-6 proton occured at 7.5 ; another chelated hydroxyl proton showed singlet in the far downfield region at 13.0. (Scheme XVI) (fig. 19)

Conversion of (35) to corresponding isoflavone was carried out by refluxing it in the mixture of triethylorthoformate, pyridine and piperidine. Reaction mixture worked up by the usual procedure. Solid was purified to obtain 6-cinnamyl-7-hydroxy-8-methylisoflavone (36). Structure



6-Cinnamyl-2,4-dihydroxy-3-methylphenylbenzylketone (35) (Fig. 19)

was assigned by pmr spectrum giving signals ($CDCl_3$) ; δ 2.3, singlet for methyl protons at C-8 ; methylene protons attached to aromatic nucleus exhibited doublet at 3.6 Ar-CH_2- ; multiplet appeared at 6.35 for two vinylic protons of the side chain -CH=CH- ; another multiplet occured in the region from 7.1 to 7.4 for ten aromatic protons ; Aromatic protons at C-5 and C-2 exhibited two singlets in the downfield region at 7.9 & 7.8 respectively. (Fig. 20)



6-Cinnamyl-7-hydroxy-8-methylisoflavone (36) (Fig. 20)

experimental

EXPERIMENTAL

All melting points are uncorrected. NMR spectrum recorded on Perkin-Elmer (R-32) (70 MHz) spectrometer using TMS as internal standard. Silica gel used for column chromatography with mesh size 60-120.

Cinnamylation reaction

7-Cinnamyloxy isoflavone (10)

A mixture of 7-hydroxy isoflavone (9) (4.8 gm, 0.02 mole), cinnamyl chloride (4.1 gm, 0.02 mole), anhydrous potassium carbonate (15 gm) and few crystals of potassium iodide was refluxed in dry acetone (300 ml) for 15 hr. The reaction mixture was poured over crushed ice, separated product filtered and washed with dilute alkali solution to remove any unreacted material. The compound was dried and titurated with light petroleum ether to remove any unreacted reagent, if present. It crystallised from benzene. M.p. 154° (lit. 150-155°C) yield 3.5 gm, 49%.

Analysis : Found : C, 81.21 ; H, 4.8

$C_{24}H_{14}O_3$: requires: C, 81.3 ; H, 5.08%

7-Hydroxy-8-(1-phenyl-2-propenyl)isoflavone (11)

7-Cinnamyloxy isoflavone (10) (1 gm) was refluxed with N,N-dimethylaniline (10 ml) for 8 hr. Reaction mixture

was poured into cold con. HCl and solid separated. It was dissolved in solvent ether, which was further washed with dilute alkali solution. On acidification with conc. HCl, it gave 7-hydroxy-8-(1-phenyl-2-propenyl) isoflavone. It crystallized from benzene + petroleum ether. M.p. 190-2°C., yield 700 mg, 70%. Etheral layer on evaporation gave black oil as impurity containing some unreacted reagent.

Analysis : Found : C, 81.77 ; H, 4.9

$C_{24}H_{18}O_3$: requires : C, 81.35 ; H, 5.08%

C-Cinamyloxy isoflavone + DMA (11) + (13)

7-Cinnamyloxy isoflavone (10) (1 gm) was refluxed with N,N-dimethylaniline (10 ml) for 12 hr. The reaction mixture was cooled and poured into cold conc. HCl. Solid separated was filtered and dissolved into solvent ether. Etheral solution was washed with dilute alkali solution. On acidification with conc. HCl, solid separated which was filtered, dried and purified. It was 7-hydroxy-8-(1-phenyl-2-propenyl)isoflavone (11) which crystallized from benzene + pet. ether mixture. M.p. and m.m.p. with authentic sample was 190-92°.

Etheral layer on evaporation gave 2,6-diphenyl-3-methyl-2,3-dihydro furo (2,3-h)benzopyran-7(H)-one (13).

It crystallized from benzene. M.p. 155°, yield 400 mg, 40%.

Analysis : Found : C, 81.56 ; H, 5.35

$C_{24}H_{18}O_3$: requires : C, 81.35 ; H, 5.08%

2,6-Diphenyl-3-methylfuro (2,3-h) benzopyran-7(H)-one (14)

A mixture of (13) (700 mg) and palladium on charcoal (500 mg, 10%) was refluxed in diphenyl ether solvent for 18 hr. Reaction mixture was filtered hot, excess of solvent removed and product obtained was 2,6-diphenyl-3-methyl furo (2,3-h)benzopyran-7(H)-one (14). It crystallized from benzene. M.p. 195°, yield 250 mg, 36%.

Analysis : Found : C, 82.24 ; H, 4.44

$C_{24}H_{16}O_3$: requires : C, 81.81 ; H, 4.54%

2-Methyl-3,6-diphenyl-2,3-dihydrofuro (2,3-h)benzopyran-7(H)-one (15)

7-Hydroxy-8-(1-phenyl-2-propenyl)isoflavone (11) (1.1gm) was refluxed in the mixture of glcial acetic acid (12 ml) and hydrobromic acid (8 ml, 48%) for 8 hr. Reaction mixture poured over crushed ice, separated solid was filtered, dried and purified by column chromatography using benzene as eluent. It crystallized from benzene M.p. 170°, yield 550 mg, 55%.

Analysis : Found : C, 80.98 ; H, 4.7

$C_{24}H_{18}O_3$: requires : C, 81.35 ; H, 5.08%

2-Methyl-3,6-diphenyl furo (2,3-h)benzopyran-7(H)-one (16)

700 mg of (15) was mixed with Pd/C (600 mg, 10%) and refluxed with diphenyl ether for 18 hr. Reaction mixture filtered hot, excess of solvent removed and product separated. It was dissolved in benzene and passed through the column of silica gel for purification. It crystallized from benzene to give (16). M.p. 180°, yield 300 mg, 43%.

Analysis : Found : C, 82.27 ; H, 4.87

$C_{24}H_{16}O_3$: requires : C, 81.81 ; H, 4.54%

7-Hydroxy-8-(1-phenyl-1-propenyl)isoflavone (12)

1 gm of (11) was dissolved in 400 ml of dry acetone and 4 gm of anhhdrous potassium carbonate was added in it. Reaction mixture refluxed for 70-72 hrs. then filtered, excess of solvent was removed and product obtained . It crystallized from benzene. M.p. 181-2°, yield 800 mg, 80%.

Analysis : Found : C, 81.74 ; H, 5.45

$C_{24}H_{18}O_3$: requires : C, 81.35 ; H, 5.0%

7-Hydroxy-8-(phenyl ethanol) isoflavone (17)

7-Hydroxy-8-(1-phenyl-2-propenyl) isoflavone ( ) (700 mg) in ethyl acetate (30 ml) and O O (50 mg) in water (10 ml) were vigorously stirred for 15 min. potassium periodate (1.5 gm) was added in small quantities to the dark solution over a period of 2 hr. The reaction mixture was stirred 1 hr more. The ethyl acetate layer was separated, washed with water, dried with sodium sulfate and distilled. The residue was crystallized from glacial acetic acid. M.p. 240°, yield 200 mg, 28%.

Analysis : Found : C, 77.56 ; H, 4.4

$C_{23}H_{16}O_4$: requires : C, 77.52 ; H, 4.5%

3,6-Diphenyl furo (2,3-h)benzopyran-7(H)-one (18)

200 mg of above compound taken in polyphosphoric acid (5 ml) and heated in oil bath at 200° for 2 hr. Reaction mixture was cooled and poured over crushed ice. Solid separated was filtered, dried and crystallized from benzene. M.p. 210°, yield 60 mg, 32%.

Analysis : Found : C, 81.43 ; H, 4.58

$C_{23}H_{14}O_3$: requires : C, 81.65 ; H, 4.14%

3-Methyl-2,6-diphenyl-5-hydrofuro (2,3-h)benzopyran-7(H) -one (19)

(14) (185 mg) was mixed with Pd/C (100 mg, 10%) and added to ethyl acetate as solvent. Reaction mixture was stirred in the atmosphere of hydrogen for 4 hr. then it was filtered and excess of solvent was distilled off. The solid obtained was crystallized from ethyl acetate + petroleum ether mixture. M.p. 175-8°, yield 130 mg, 70%.

Analysis : Found : C, 81.8 ; H, 5.3

$C_{24}H_{18}O_3$: requires : C, 81.3 ; H, 5.0%

2-Methyl-3,6-diphenyl-5-hydrofuro (2,3-h)benzopyran-7(H)-one (20)

145 mg (16) was mixed with Pd/C (100 mg, 10%) and added to ethyl acetate solvent. Reaction mixture was stirred for 4 hr in the atmosphere of hydrogen then it was filtered and excess of solvent was distilled off. The solid separated was crystallized from ethyl acetate + petroleum ether mixture. M.p. 125-8°, yield 110 mg, 75%.

Analysis : Found : C, 81.8 ; H, 5.44

$C_{24}H_{18}O_3$: requires : C, 81.35; H, 5.0%

7-Cinnamyloxy-8-methyl isoflavone (22)

A mixture of 7-hydroxy-8-methyl isoflavone (21) (2.5 gm, 0.01 mole), cinnamyl chloride (2.0 gm, 0.01 mole) anhydrous potassium carbonate (10 gm) and few crystals of potassium iodide was refluxed in dry acetate (300 ml) for 10 hr. Reaction mixture was added in water, solid separated was filtered and washed with dilute sodium hydroxide solution to remove any unreacted compound solid was dried and scratched with light petroleum ether to remove any uunreacted reagent. It crystallized from benzene to give white shining needles. M.p. 145°, yield 2.0 gm, 55%.

Analysis : Found : C, 82.00 ; H, 5.7

$C_{25}H_{20}O_3$: requires : C, 81.5 ; H, 5.4%

7-Hydroxy-8-methyl-6-(1-phenyl-2-propenyl) isoflavone (23)

7-Cinnamyloxy-8-methyl isoflavone (22) (1.5 gm) was refluxed in N,N-dimethylaniline (7 ml) for 8 hr. Reaction mixture was poured into cold conc. HCl and solid obtained was dissolved in solvent ether. Etheral solution was washed with dilute sodium hydroxide solution. On acidification with con. HCl it gave 7-hydroxy-8-methyl-6-(1-phenyl-2-propenyl) isoflavone (23). It crystallized from benzene. M.p. 101°, yield 1 gm, 66%.

Etheral layer on evaporation gave black oil as impurity

Analysis : Found : C, 81.17 ; H, 5.3

$C_{24}H_{20}O_3$: requires : C, 8C.89 ; H, 5.6%

2,9-Dimethyl-3,6-diphenyl 2,3-dihydrofuro (3,2-g)benzopyran-5(H)-one (24)

1 gm of (23) was refluxed with the mixture of glacial acetic acid (12 ml) and hydrobromic acid (8 ml, 48%) for 8 hr. Reaction mixture was poured over crushed ice. Solid obtained was washed with dilute alkali solution to remove any unreacted compound. It purified by column chromatography using benzene eluent crystallized from benzene + petroleum ether to give (24). M.p. 190°, yield 450 mg, 45%.

Analysis : Found : C, 81.85 ; H, 5.3

$C_{25}H_{20}O_3$: requires : C, 81.52 ; H, 5.4%

2,9-Dimethyl-3,6-diphenyl furo (3,2-g)benzopyran-5(H)-one (25)

A mixture of (24) (700 mg) and palladium on charcoal (600 mg, 10%) was refluxed in diphenyl ethersolvent for 20 hr. Reaction mixture filtered hot, excess of solvent removed and solid obtained which was crystallized from

benzene to furnish (25). M.p. 195°, yield 250 mg, 36%.

Analysis : Found : C, 82.4 ; H, 4.9

$C_{25}H_{18}O_3$: requires : C, 81.96; H, 4.9%

7-Cinnamyloxy-2-methylisoflavone (27)

A mixture of 7-hydroxy-2-methyl isoflavone (26) (2.5 gm, 0.01 mole), cinnamyl chloride (2 gm, 0.01 mole) anhydrous potassium carbonate (10 gm) and few crystals of potassium iodide was refluxed in dry acetone (300 ml) for 10 hr. Reaction mixture was added in cold water, solid separated was filtered, and washed with dilute alkali solution to remove any unreacted compound. Crude was dried and titurated with petroleum ether to remove unreacted reagent, if any. It crystallized from benzene to obtain (27). M.p. 153-55°, yield 2.2 gm, 60%.

Analysis : Found : C, 81.64 ; H, 5.7

$C_{25}H_{20}O_3$: requires : C, 81.5 ; H, 5.4%

7-Cinnamyloxy-2-methyl isoflavone + DMA

7-Cinnamyloxy-2-methyl isoflavone (27) (1 gm) was refluxed with N,N-dimethylaniline (10 ml) for 8 hr. The reaction mixture was cooled and poured into cold conc. HCl solid separated was filtered and dissolved into solvent ether. Etheral solution was washed with dilute alkali

solution. On acidification with conc. HCl, solid separated which was filtered, dried and crystallized from benzene + alcohol mixture to furnish (28).

Analysis : Found : C, 81.7 ; H, 5.8

$C_{25}H_{20}O_3$: requires : C, 81.5 ; H, 5.4%

Etheral layer on evaporation gave solid which was crystallized from benzene to furnish (29). M.p. 150°, yield 600 mg, 30%.

Analysis : Found : C, 82.0 ; H, 5.6

$C_{25}H_{20}O_3$: requires : C, 81.5 ; H, 5.4%

2,5-Dimethyl-3,6-diphenyl furo (2,3-h)benzopyran-7(H)-one (30)

1 gm (28) was refluxed with the mixture of glacial acetic acid (5 ml) and hydrobromic acid (9 ml, 48%) for 8 hr. Reaction mixture was poured over crushed ice, solid obtained was washed with dilute alkali solution to remove any unreacted compound. It was crystallized from benzene. M.p. 185°, yield 500 mg, 50%.

Analysis : Found : C, 81.6 ; H, 4.7

$C_{25}H_{18}O_3$: requires : C, 81.9 ; H, 4.9%

2,4-Dihydroxy-5-cinnamylphenylbenzyl ketone (32)

To a solution of 2,4-dihydroxyphenylbenzyl ketone (31) (2.4 gm) in formic acid (80%) (30 ml), cinnamyl alcohol (8 gm) was added. Reaction mixture was refluxed with continuous stirring for 4 hr. then poured into excess by ice-cold water. Solid crystallized from benzene to furnish (32). M.p. 130°, yield 2 g.

Analysis : Found : C, 79.8 ; H, 6.3

$C_{23}H_{20}O_3$: requires : C, 80.0 ; H, 5.8%

7-Hydroxy-6-cinnamyl isoflavone (33)

2,4-Dihydroxy-5-cinnamylphenylbenzyl ketone (32) (1 gm), dry pyridine (5 ml), piperidine (0.5 ml) and redistilled triethyl orthoformate (3 ml) were refluxed together for 8 h. and then reaction mixture left overnight. Next day it was decomposed in ice and con. HCl mixture. Solid separated, filtered, dried and crystallized from benzene + ethanol mixture. M.p. 220°, yield 0.5 g.

Analysis : Found : C, 81.4 ; H, 5.5

$C_{24}H_{18}O_3$: requires : C, 81.3 ; H, 5.1%

2,4-Dihydroxy-3-methyl-6-cinnamylisoflavone (35)

To a solution of 2,4-dihydroxy-3-methylphenylbenzyl ketone (34) (2.4 g) in formic acid (80%) (30 ml), cinnamyl alcohol (1.4 g) was added. Reaction mixture was refluxed with continuous stirring for 25 hr. then poured into excess of ice-cooled water. Separated crude was subjected to column chromatography and product obtained by eluting light petroleum ether + benzene (60:40) mixture. Solid was crystallized from a mixture of benzene & light petroleum ether, to obtain (35). M.p. 118°, yield (1.8 g).

Analysis : Found : C, 80.2 ; H, 6.5

$C_{24}H_{22}O_3$: requires : C, 80.4 ; H, 6.1%

6-Cinnamyl-7-hydroxy-8-methylisoflavone (36)

2,4-Dihydroxy-3-methyl-6-cinnamylisoflavone (35) (1 gm) dry pyridine (5 ml), piperidine (0.5 ml) and redistilled triethylorthoformate (3 ml) were refluxed together for 8 h. and the reaction mixture left overnight. Next day it was decomposed in ice and conc. HCl mixture. Solid separated, filtered, dried and crystallized from benzene + ethanol mixture. M.p. 200°, yield 0.6 g.

Analysis : Found : C, 81.4 ; H, 5.4

$C_{25}H_{20}O_3$: requires : C, 81.5 ; H, 5.4%.

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