CHAPTER-IV

SOME REACTIONS OF 3,4-DIHYDRO COUMARINS

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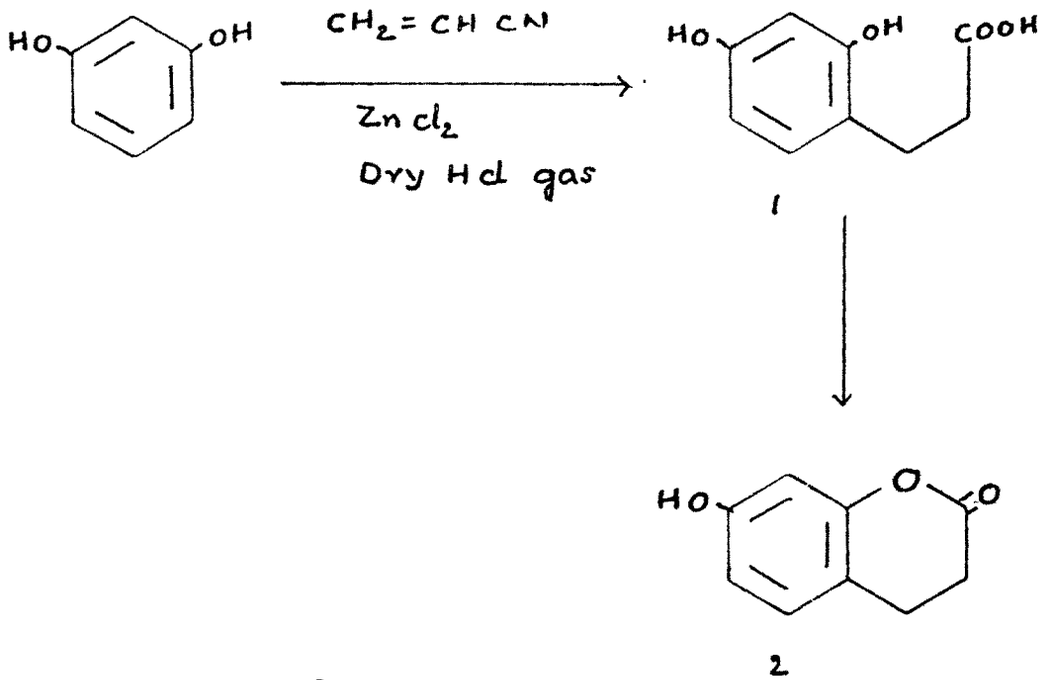
It is well established that majority of the coumarins occurring in nature are C-6 substituted but in the case of 7-hydroxycoumarin derivatives, the substitution and migration are regiospecifically directed to C-8 position with traces of C-6 isomer. This regiospecificity is changed to C-6 position in the case of 7-hydroxy-3,4-dihydrocoumarin system. Keeping in the view of the regiospecificity of 3,4-dihydrocoumarin system it was thought of interest to prepare some C-6 substituted coumarins which are are difficult to obtain by other known methods and also they can be used as starting materials for linear furocoumarins.

Synthesis of 7-hydroxy-3,4-dihydrocoumarins

Langley and Adams[1] synthesised 7-hydroxy-3,4-dihydrocoumarin (2) by the action of acrylonitrile upon resorcinol. Dry HCl is passed through the solution mixture of resorcinol, acrylonitrile, freshly fused $ZnCl_2$ in dry ether till the solution get saturated with dry HCl. The separated product gave on hydrolysis β-(2,4-dihydroxy) phenylpropionic acid (1). 7-Hydroxy-3,4-dihydrocoumarin (2) is obtained on heating the (1) above its melting point. [Scheme-1]

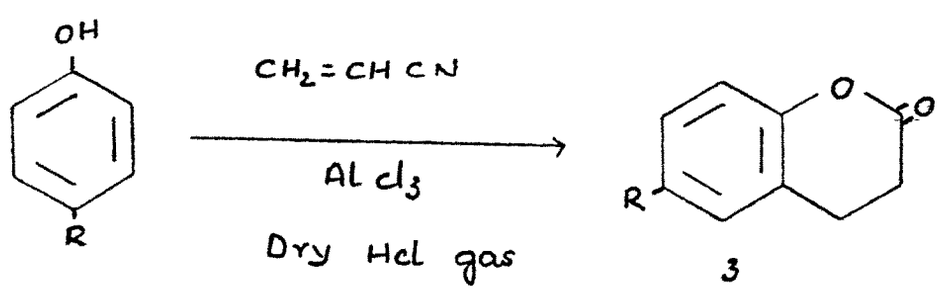
SCHEME-1

Langley and Adams[1]



SCHEME-2

K. Sato et al[2]



R = $-CH_3$, $-OCH_3$, cl

They also prepared 5,7-dihydroxy and 5-methyl-7-hydroxy-3,4-dihydrocoumarins by taking phloroglucinol and orcinol respectively.

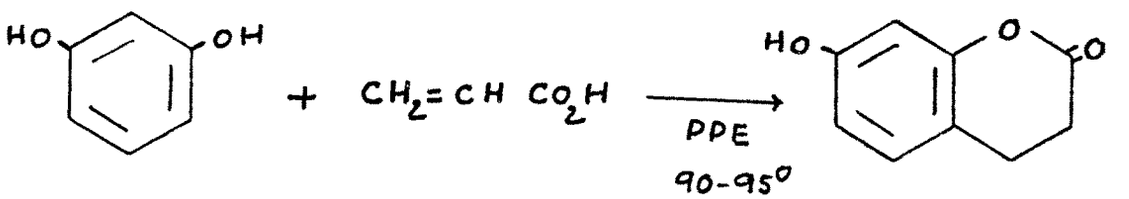
K. Sato et al.[2] also synthesised dihydrocoumarins or 6-substituted dihydrocoumarins in one step by the condensation of phenol or the parasubstituted phenols with acrylonitrile in the presence of anhydrous $ALCl_3$. Dry HCl gas is passed through the mixture of p-cresol, acrylonitrile and anhydrous $AlCl_3$ maintained at 10-15°. The reaction mixture was slowly heated to turn into a fluid and heating was continued at 140-145° for 3 hr. keeping the passage of dry HCl. The mixture was then decomposed with dil. HCl and extrated with ethyl acetate to give 6-methyl-3,4-dihydrocoumarin (3). [Scheme-2]

Sato and coworkers[3] also reported the use of PPE (Ethyl ester of poly phosphoric acid). They observed that resorcinol reacts smoothly with acrylic acid in PPE at 90-95° giving good yield of dihydrocoumarin along with malelotic acid (4). [Scheme-3]

The malelotic acid (4) thus obtained is converted to 7-hydroxy-3,4-dihydrocoumarin by heating it at 160-170° for 2 hr.

SCHEME-3

Sato and coworkers[3]



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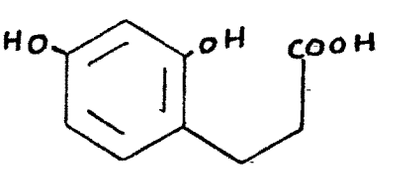
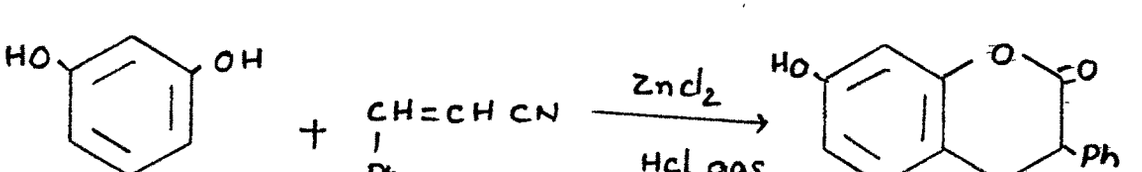


4

SCHEME-4

Dasgupta and coworkers[4]



5

Das Gupta and coworkers[4] synthesised 3-phenyl-3,4-dihydrocoumarins by the condensation of resorcinol with 2-phenylacrylonitrile. Dry HCl gas is passed through a mixture of resorcinol, α-phenylacrylonitrile, containing hydroquinone, zinc chloride in dry ether for 2 hr. The product obtained was distilled in vacuum (180-200°/0.3 mm) to obtain the product (5). [Scheme-4]

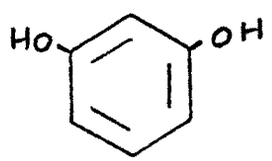
4-Phenyl, 3,4-diphenyl dihydrocoumarins were also synthesised in a similar way using methyl cinnamate and 2-phenylcinnamonitrile in the presence of $AlCl_3$/HCl or $ZnCl_2$/HCl respectively. They carried out the dehydrogenation of 3-3-phenyl, 4-phenyl and 3,4-diphenyl 3,4-dihydrocoumarins with pd/c in diphenyl ether to give respective 7-hydroxycoumarin derivatives.

T. Matsui[5] used polyphosphoric acid as condensing agent to synthesise dihydrocoumarins effectively. Resorcinol on condensation with trans-cinnamic acid in the presence of L-PPA [P_2O_5 and 85% phosphoric acid (1:2)] at 85-95° afforded 7-hydroxy-4-phenyl-3,4-dihydrocoumarin (6) in 47%. [Scheme-5]

This condensation gives a mixture of two compounds 7-hydroxy-4-phenyl-3,4-dihydrocoumarin in 21.3% and 7-hydroxy flavone (7) in 12.7% when H-PPA (Equal proportions of P_2O_5 85% phosphoric acid) is used.

SCHEME-5

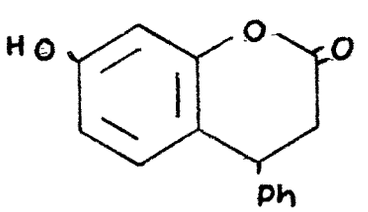
T. Matsui[5]



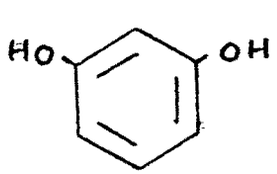
+ Ph - CH=CH COOH

L-PPA

85-95°



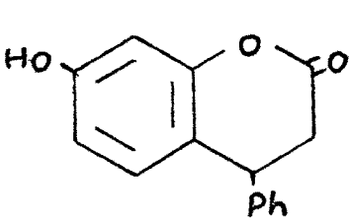
6 47%



+ Ph - CH=CH COOH

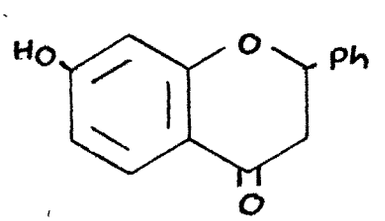
H-PPA

85-95°



21.3%

+



7 12.7%

Reactions with 3,4-dihydrocoumarins

Sen and coworkers[6] conveniently synthesised C-6 substituted derivatives of umbelliferone which is an important intermediate for the synthesis of linear furano and pyranocoumarins. 7-Hydroxy-3,4-dihydrocoumarin on allylation gave 7-allyloxy-3,4-dihydrocoumarin (8) which on Claisen rearrangement and subsequent acid catalysed cyclisation furnished 2-methyl-2,3,5,6-tetrahydrofuro(3,2-g)benzopyran-7(H)-one (10). [Scheme-6]

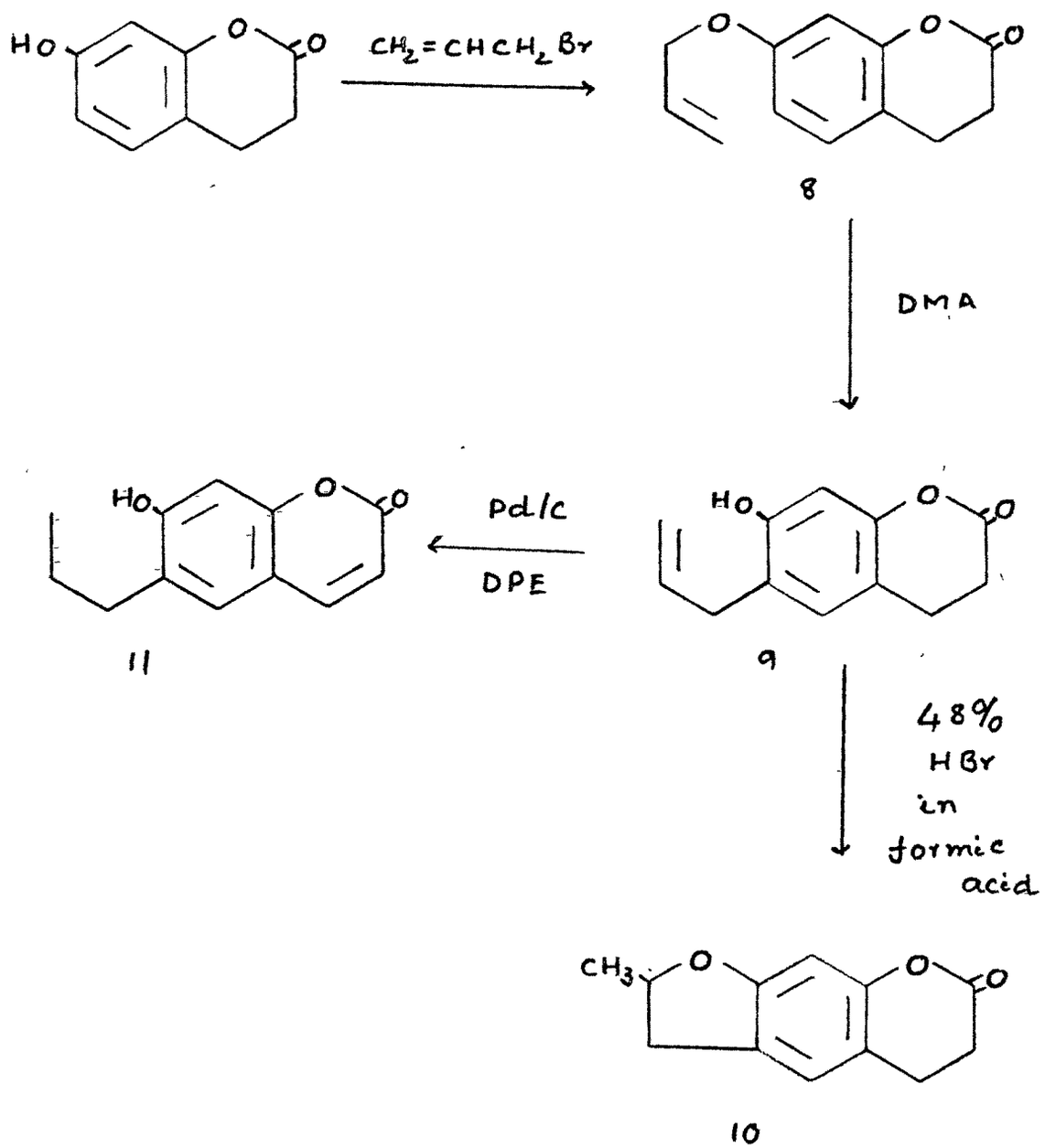
They also prepared 7-hydroxy-6-propylcoumarin (11) by refluxing (9) with Pd/c in diphenyl ether for 13 hr. hydrogenation of double bond taking place during the reaction.

A new synthesis of 6-allylumbelliferone which is a synthetic precursor of psoralen was developed by Sen and coworkers[7] 7-Hydroxy-3,4-dihydrocoumarin which when subjected to Claisen rearrangement afforded 7-hydroxy-6-allyl-3,4-dihydrocoumarin. This on treatment with DDQ in dry benzene gave 6-allyl-7-hydroxycoumarin (12).

They further established the structure of the compound (12) by cyclising it to 2-methyl-2,3-dihydrofuro(3,2-g) benzopyran-7(H)-one (13) with 48% hydrobromic acid. [Scheme-7]

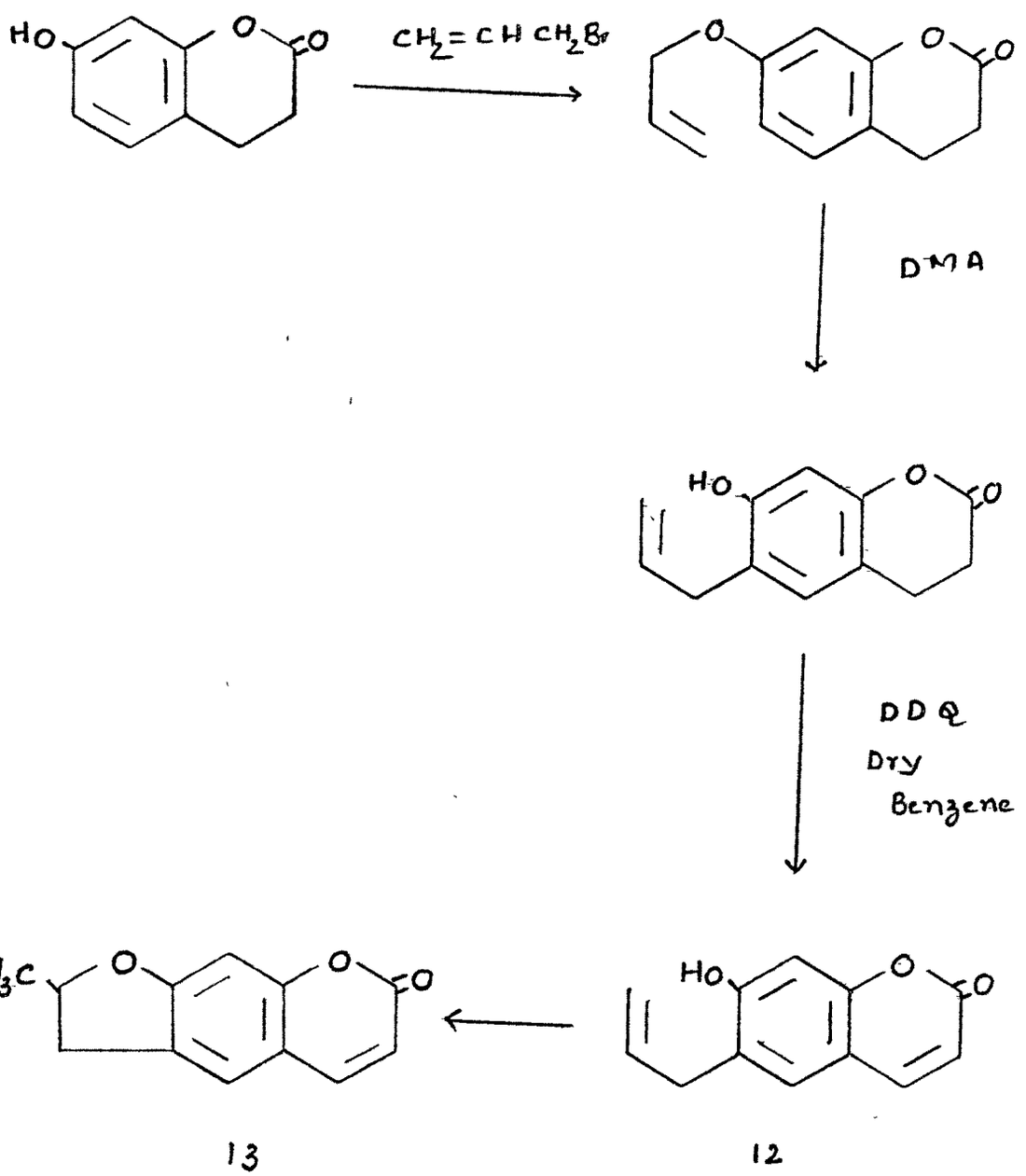
SCHEME-6

Sen and coworkers[6]



SCHEME-7

Sen and coworkers[7]



13 12

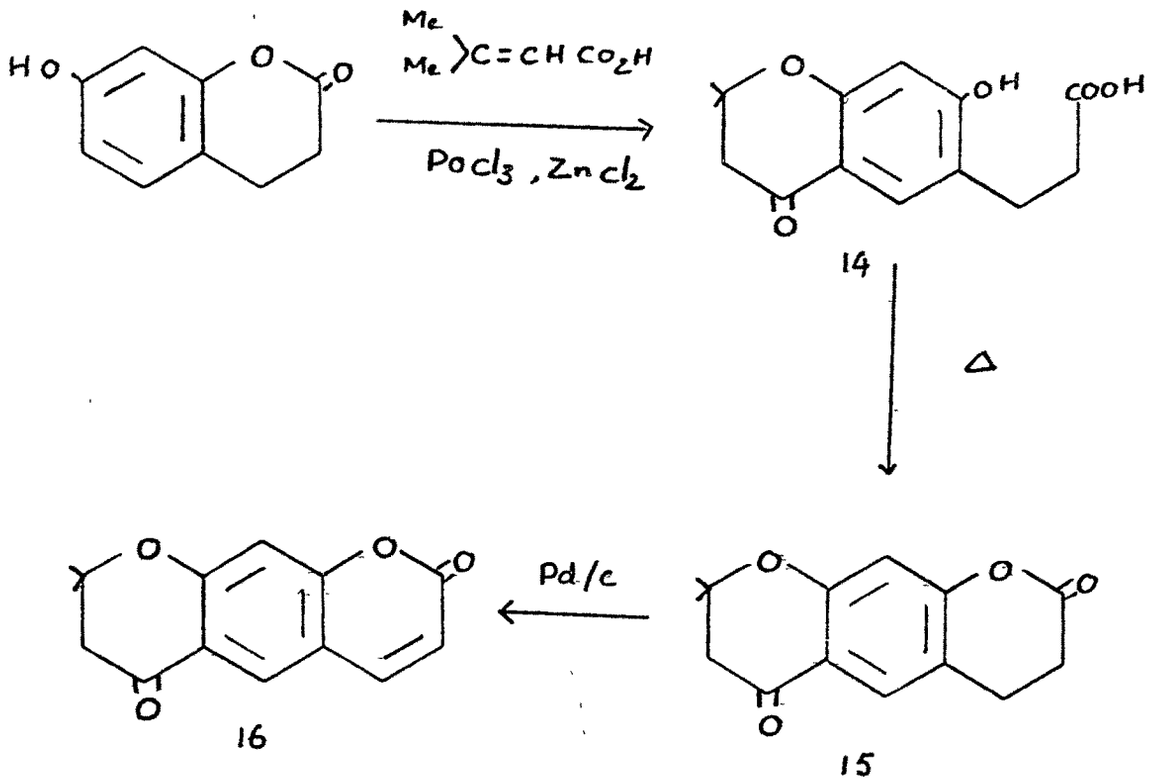
Majumdar and Usgaonkar[8] synthesised 7,8-dihydro-8,8-dimethyl benzo(1,2-b : 5,4-b) dipyran-2,6-dione (16) a naturally occuring compound from 3,4-dihydrocoumarin in three steps in good yield. 7-Hydroxy 3,4-dihydrocoumarin on condensation with β,β-dimethylacrylic acid in the presence of $POCl_3$ and zinc chloride gave a chromanone derivative (14), which cyclised to 3,4,7,8-tetrahydro-8,8-dimethyl benzo (1,2-b : 5,4-b') dipyran-2,6-dione (15) readily on heating. (16) is obtained on dehydrogenating the compound (15) with Pd/c in diphenylether. [Scheme-8]

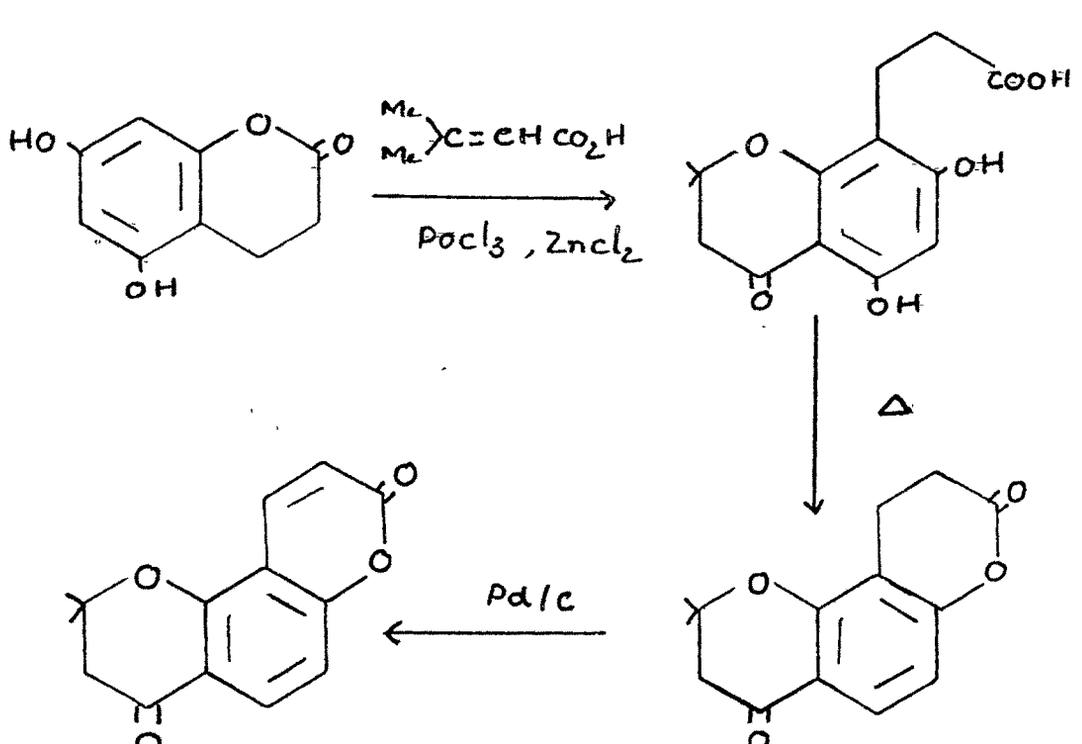
The same reaction failed to give corresponding linear product when 3,4-dihydro-5,7-dihydroxycoumarin is condensed with β,β-dimethylacrylic acid, instead it gave an angular isomer (17), a naturally occuring clausenin. [Scheme-8]

Mujumdar and Usgaonkar[9] also studied the Pechmann condensation of 7-hydroxy-3,4-dihydrocoumarin with malic acid and ethylacetoacetate. 7-Hydroxy-3,4-dihydrocoumarin on Pechmann condensation with malic acid or ethylacetoacetate in presence of conc. H_2SO_4 afforded 7-hydroxycoumarin-6-propionic acid (18) which lactonised by heating to give corresponding dihydrobenzodipyrandione (19). Linearbenzodipyrandiones (20) are obtained by refluxing (19) in diphenyl ether with Pd/c.

SCHEME-8

Mujumdar and Usgaonkar[8]





In the case of 5-methyl-7-hydroxydihydrocoumarin, the condensation with malic acid gave a linear isomer (21) while with ethylacetoacetate an angular isomer was obtained. [Scheme-9]

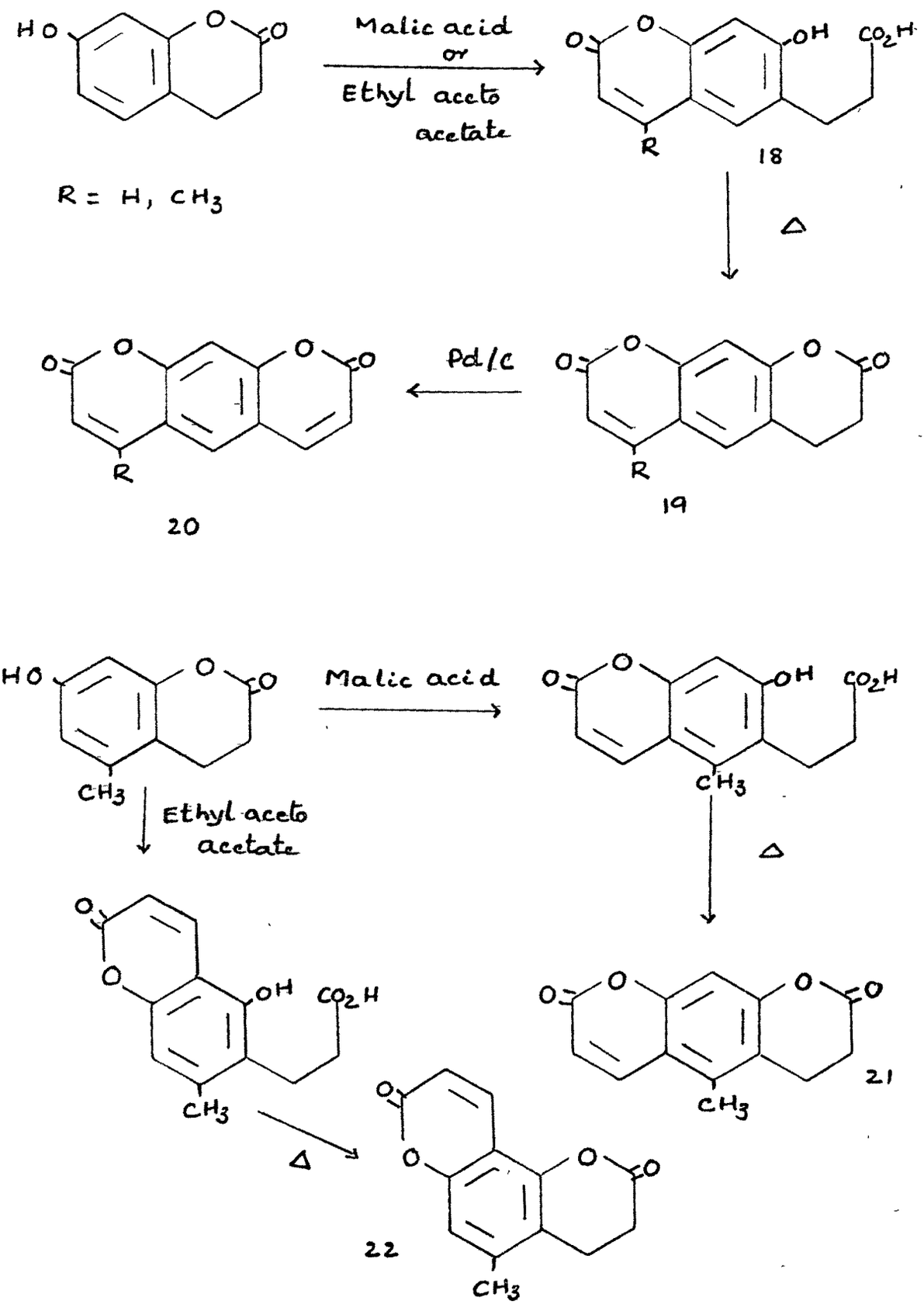
In this Chapter the synthesis of C-6 substituted coumarin derivatives are described using Friedel-Crafts method. Some naturally occuring coumarins like graveolone, xanthyletin and their derivatives have also been synthesised keeping the regiospecificity of 3,4-dihydrocoumarin ring system in view.

6-Acetyl umbelliferone a useful starting material is difficult to obtain in substantial amount by Fries migration of 7-acetoxycoumarin and apart from, the product obtained by this method contain some 8-acetylcoumarin.

Chatterji and coworkers[10] synthesised first 6-acetyl dihydrocoumarin by passing dry HCl gas through the solution mixture of 7-hydroxy-3,4-dihydrocoumarin, acetic anhydride, aluminium chloride in ether. After the solution becomes saturated with HCl gas, ether was removed and then the mixture was heated at 155-60° for 3 to 4 hr. continuing the flow of dry HCl gas. 6-Acetyl-3,4-dihydrocoumarin (24) was obtained after decomposing the mixture in cold dil. HCl followed by the vacuum sublimation of the product. [Scheme-10]

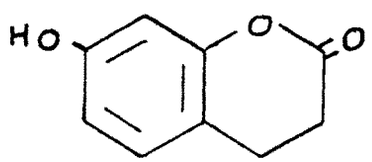
SCHEME-9

Majumdar and Usgaonkar[9]



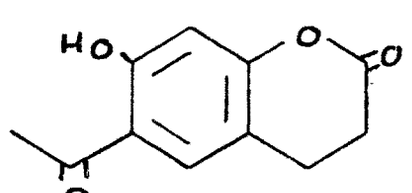
SCHEME-10

Chatterjee and coworkers[10]



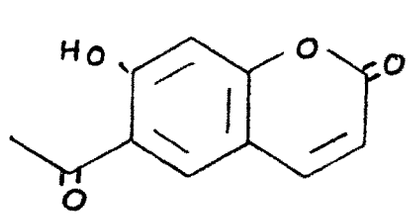
+ Ac_2O

1. $Alcl_3$
   Dry Hcl gas
   ether
2. 150-60°



24

Pd/c



25

6-Acetyl-7-hydroxycoumarin (25) was prepared by refluxing the dihydrocoumarin in diphenylether with Pd/c.

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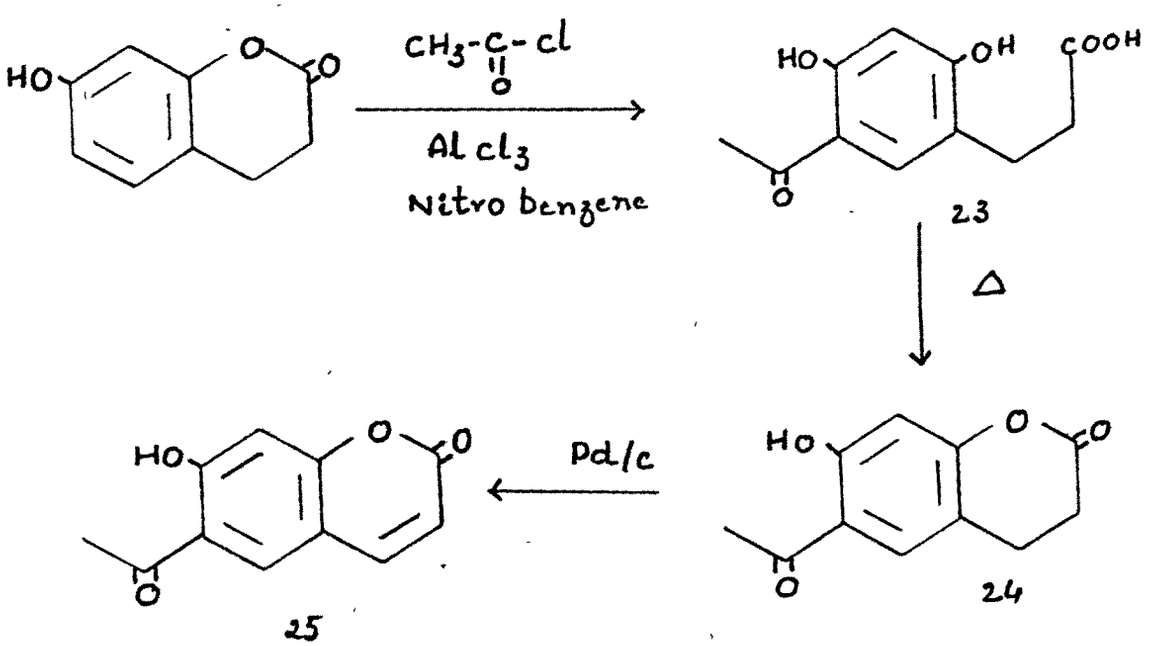
6-Acetyl-7-hydroxybenzopyran-2(H)-one (25)

6-Acetylumbelliferone was conveniently synthesised by Friedel-Crafts acetylation of 7-hydroxy-3,4-dihydrocoumarin followed by its dehydrogenation. [Scheme-11]

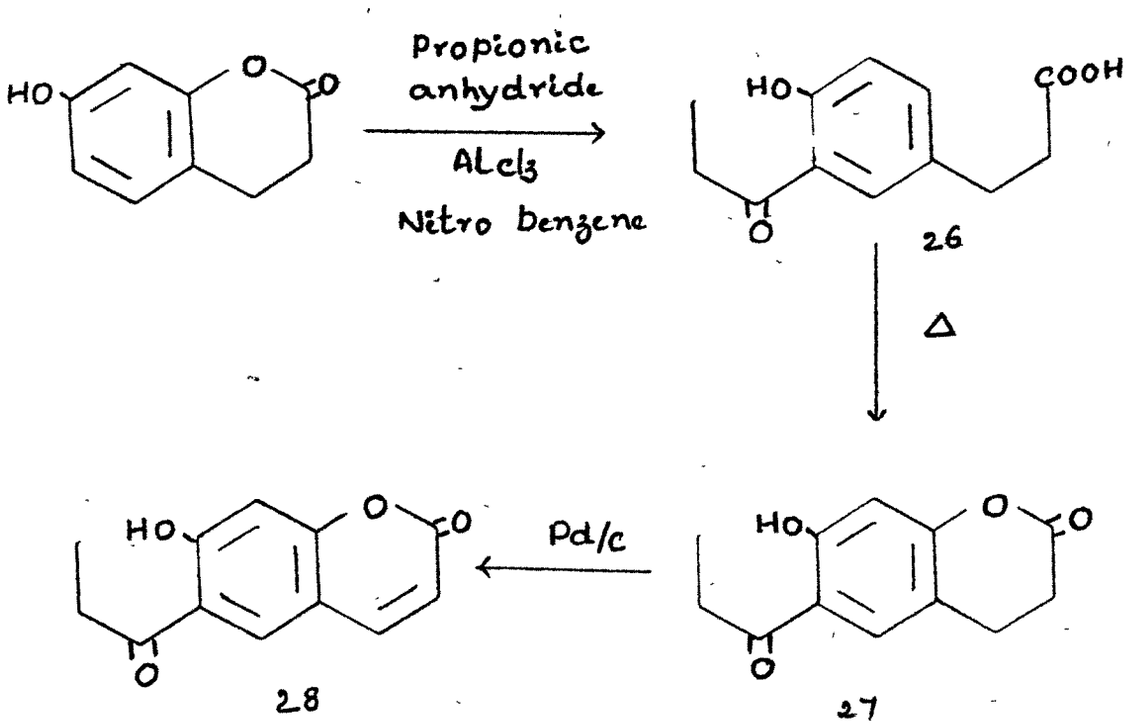
7-Hydroxy-3,4-dihydrocoumarin dissolved in nitrobenzene was treated with aluminium chloride and the mixture was heated with acetyl chloride on steam bath for 6 hr. On working up of the reaction mixture 2,4-dihydroxy-5-acetyl phenyl propionic acid (23) was obtained. (23) on heating in an oil bath at 180-200° for 40-50 min. till it ceases to give effervescence, afforded 7-hydroxy-6-acetyl-3,4-dihydrocoumarin (24). The structure of the compound (24) was established by PMR spectra which exhibited signals in $CDCl_3$ at δ 2.6 for three protons of the $-COCH_3$ group at C-6, a multiplet at δ 2.7-3.1 for four protons at C-3 and C-4, a singlet at δ 6.65 for one proton at C-5, another singlet at δ 7.65 for a proton at C-8 and the hydroxyl proton at C-7 appeared at δ 12.3. (Fig. 1)

The compound (24) on dehydrogenation with Pd/c (10%) in refluxing diphenylether gave 6-acetyl-7-hydroxycoumarin (25) m.p. 175° lit.[10] m.p. 175° the structure of which was

SCHEME - 11



SCHEME - 12



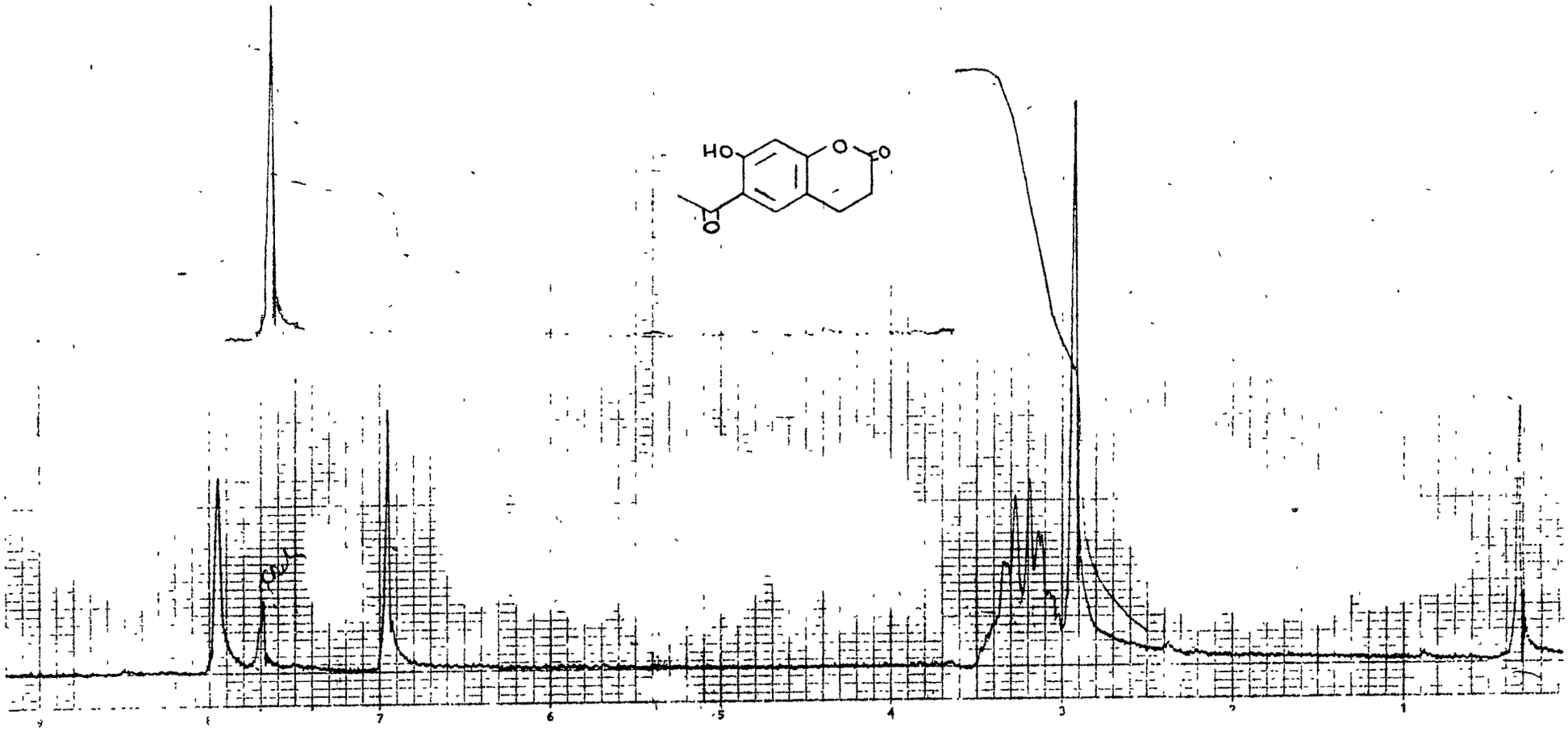


FIG-1

established byPMR spectra in $CDCl_3$ which show signals at δ2.65, a singlet for three protons of $-COCH_3$ group at C-6, a doublet J=9Hz at δ6.3 for a proton at C-3, a singlet at δ6.85 for a proton at C-5, another doublet J=9Hz at δ7.6 for a proton at C-4, another singlet for C-8 proton appeared at δ7.9 and the hydroxyl proton of C-7 appeared as a singlet at δ12.6. (Fig. 2)

6-Propionyl-7-hydroxybenzopyran-2(H)-one (28)

6-Propionyl-7-hydroxycoumarin was also synthesised by Fridel-Crafts method. 7-Hydroxy-3,4-dihydrocoumarin in nitrobenzene, aluminium chloride and propionic anhydride were heated on steam bath for 6 hr. After the usual work up it gave 2,4-dihydroxy-5-propionyl phenyl propionic acid (26). The compound (26) could not be isolated in pure state hence it washeated at 180-200° in an oil bath for 40-50 min.to obtain 6-propionyl-7-hydroxy-3,4-dihydrocoumarin (27).

Dehydrogenation of the compound (27) with Pd/c in diphenylether gave 6-propionyl-7-hydroxybenzopyran-2(H)-one (28). [Scheme-12] Its PMR showed signals in $CDCl_3$ at δ1.4, a triplet for three methyl protons in the propionyl group at C-6, quartet at δ3.2 for two methylene protons of the propionyl at C-6, a doublet J=9Hz at δ6.35 for the proton at C-3, a singlet at δ6.9 for the proton at C-5, another doublet J=9Hz at δ7.65 for C-4 proton and a singlet at

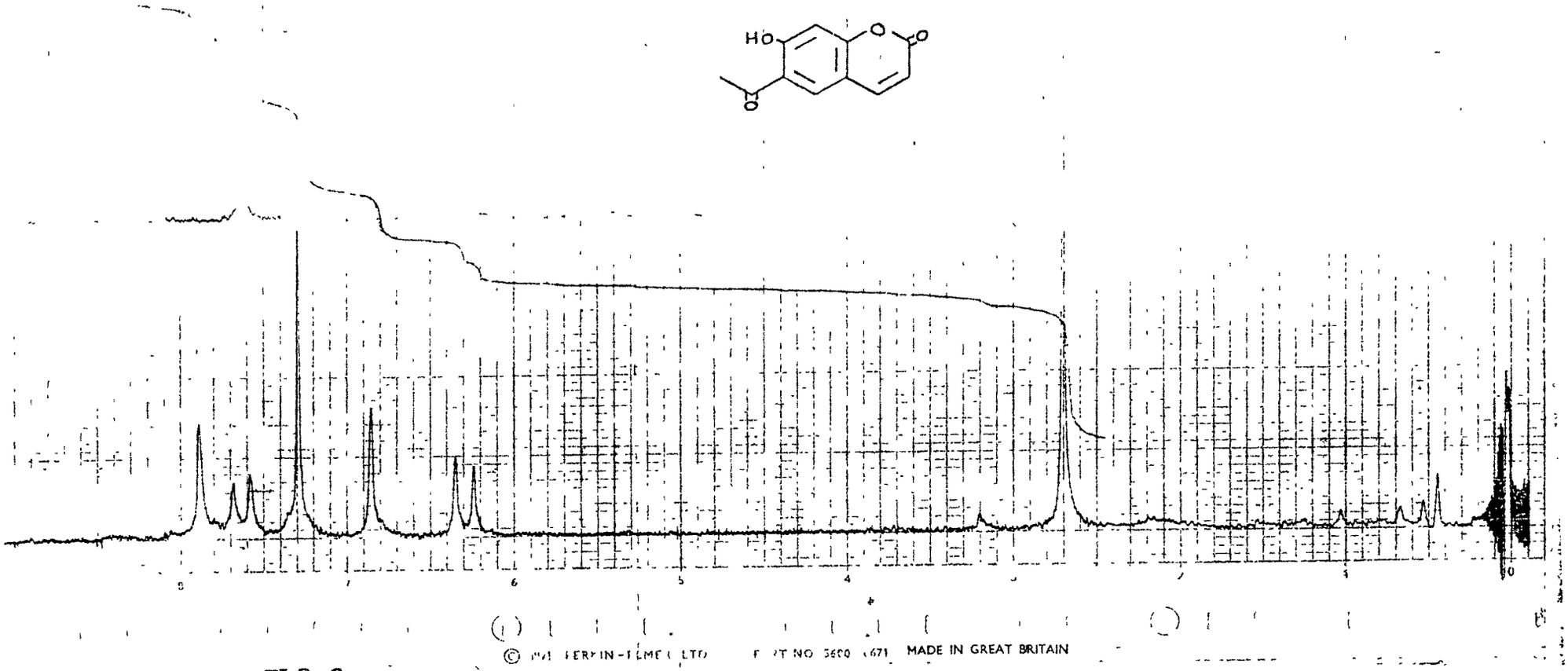


FIG-2

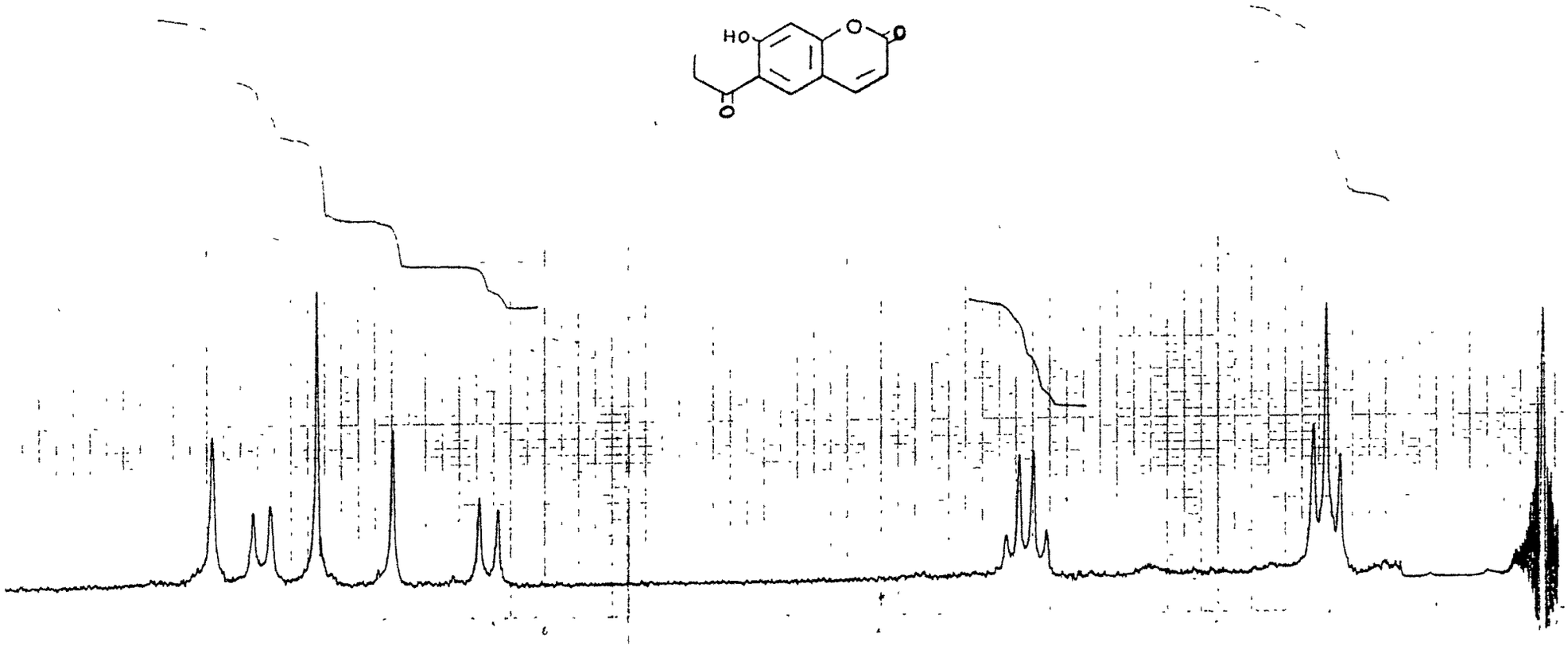


FIG-3

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δ 7.95 for the proton at C-8. (Fig. 3)

6-Acetyl-7-hydroxy-4-phenylbenzopyran-2(H)-one (31)

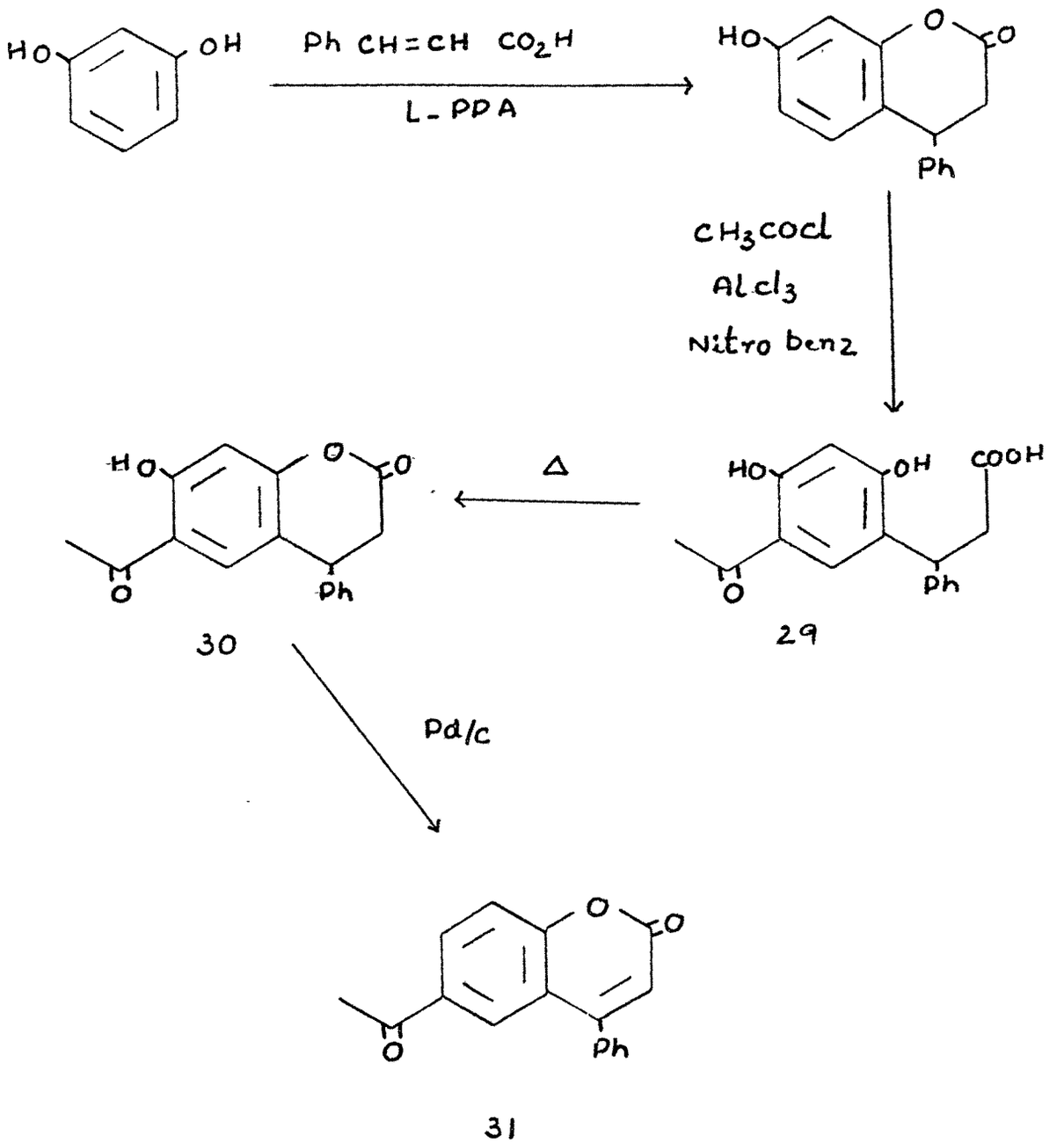
7-Hydroxy-4-phenyl-3,4-dihydrocoumarin, which was prepared by condensing resorcinol with cinnamic acid using L-PPA, in nitrobenzene was heated with acetylchloride on steam bath for 6 hr. in the presence of anhydrous $AlCl_3$. After the usual work up, it gave the propionic acid derivative (29) which when heated in an oil bath for 40-50° min. at 180-200° furnished 7-hydroxy-6-acetyl-4-phenyl-3,4-dihydrocoumarin (30).

Its PMR showed signals in $CDCl_3$ at δ2.45, a singlet for three $-COCH_3$ protons at C-6, a multiplet at δ 3.1 for two protons at C-3, a triplet at δ 4.4 for a proton at C-4, at δ 6.7 a singlet appeared for C-5 proton, the multiplet at δ 7.1-7.4 for five phenyl protons at C-4 got mixed up with the C-8 proton while the hydroxyl proton at C-7 appeared at δ12.6. (Fig. 4)

(30) was also obtained by condensing resacetophenone with cinnamic acid in the presence of L-PPA, thus confirming the structure of (30).

Compound (30) on dehydrogenation with Pd/c gave (31) [Scheme-13]. The structure of the compound was confirmed

SCHEME - 13


HO
OH
Ph CH=CH CO2H
L-PPA
HO
O
O
Ph
CH3COCl
AlCl3
Nitro benz
HO
OH
COOH
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Ph
30
29
Pd/C
O
O
O
Ph
31

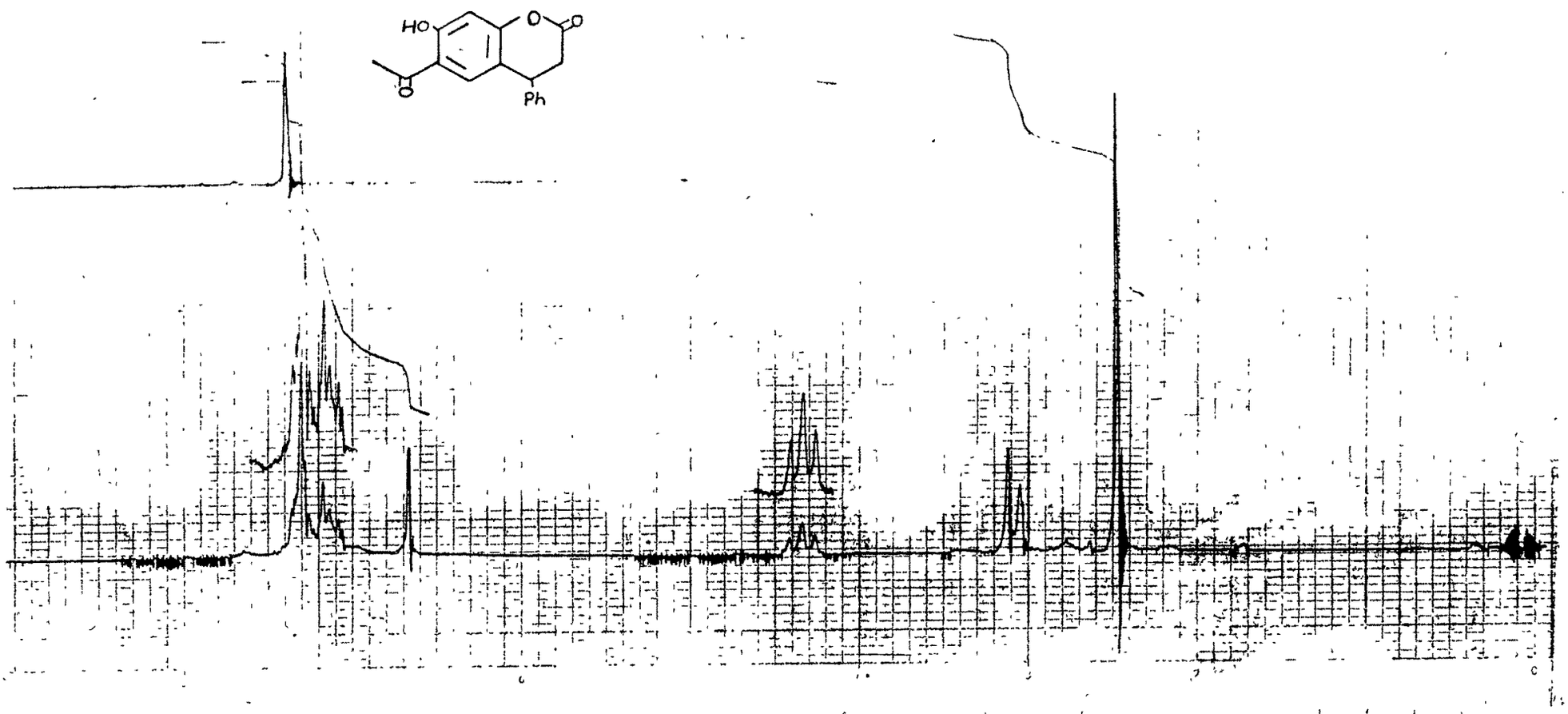


FIG-4

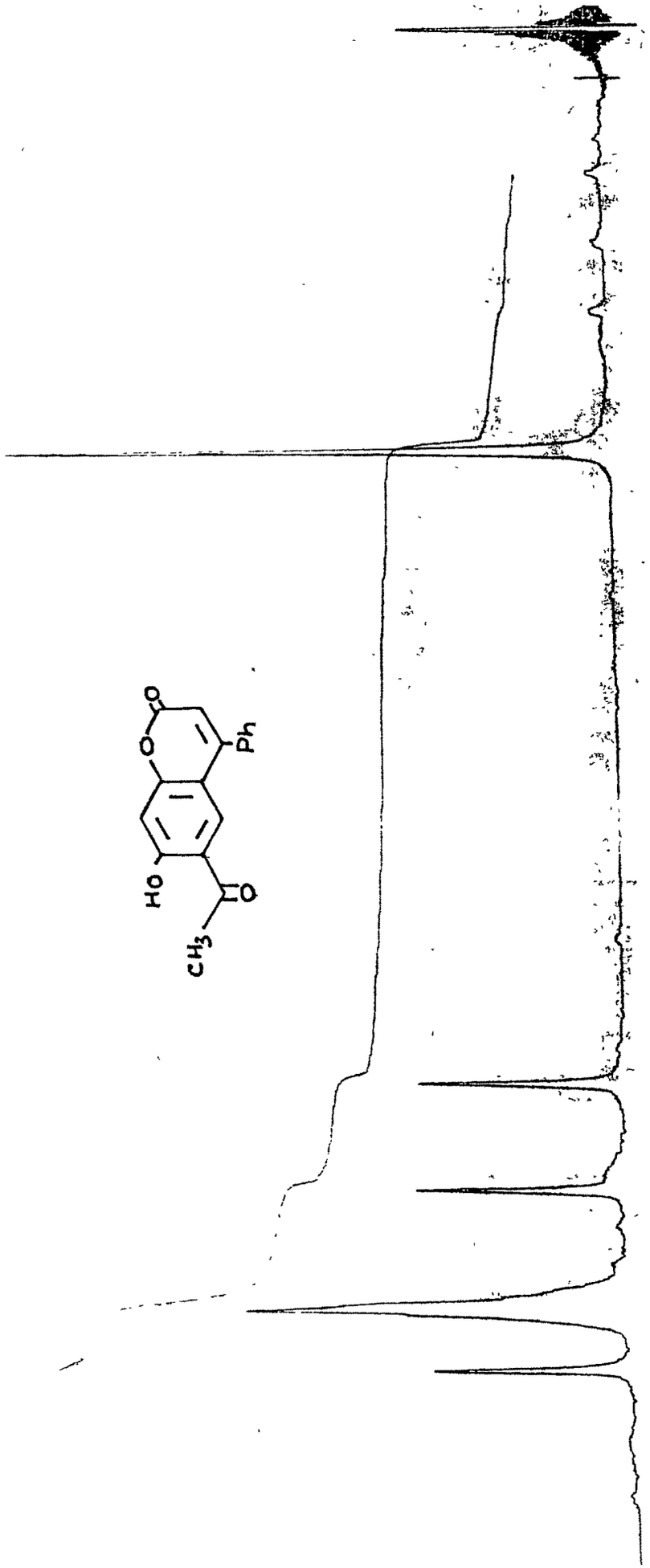


FIG-5

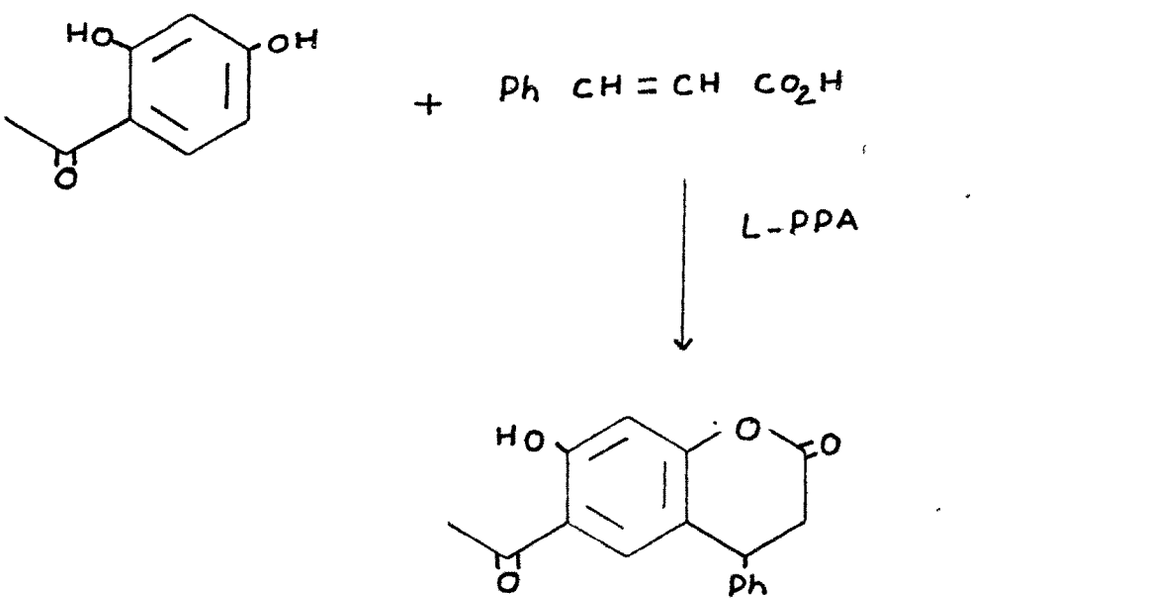
by PMR which showed signals in $CDCl_3$ at δ2.45 for three protons of $-COCH_3$ group at C-6, a singlet at δ6.15 for vinylic proton at C-3, a singlet at δ6.75 for a proton at C-5, a broad peak at δ7.45 for five phenyl protons at C-4 and a singlet for a proton at C-8 appeared at δ7.85. (Fig. 5)

6-Propionyl-7-hydroxy-4-phenylbenzopyran-2(H)-one (34)

6-Propionyl-7-hydroxy-4-phenylcoumarin was prepared by first heating the mixture of 7-hydroxy-4-phenyl-3,4-dihydrocoumarin in nitrobenzene, aluminium chloride and propionic anhydride on a steam bath for 5-6 hr. to give a propionic acid derivative (32) on work up. (32) on heating in an oil bath at 180-200° for 40-50 min. furnished 7-hydroxy-6-propionyl-4-phenyl-3,4-dihydrocoumarin (33).

The structure of the compound was confirmed by PMR spectra which showed signals in $CDCl_3$ at δ1.05, a triplet for three methyl protons in the propionyl group at C-6, a quartet at δ2.75 for the two methylene protons in the propionyl at C-6, a doublet at δ3.0 for the two protons at C-2, a triplet at δ4.3 for one proton at C-4, a singlet appeared at δ6.65 for C-5 proton and a multiplet at δ6.95-7.4 for five phenyl protons and a proton at C-8. (Fig. 6)

SCHEME - 14


HO
OH
O
+
Ph CH = CH CO2H
L-PPA
HO
O
O
O
Ph
HO
O
O
Ph
Propionic anhydride
AlCl3, Nitro benz
HO
OH
COOH
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Pd/c
HO
O
O
O
Ph
34

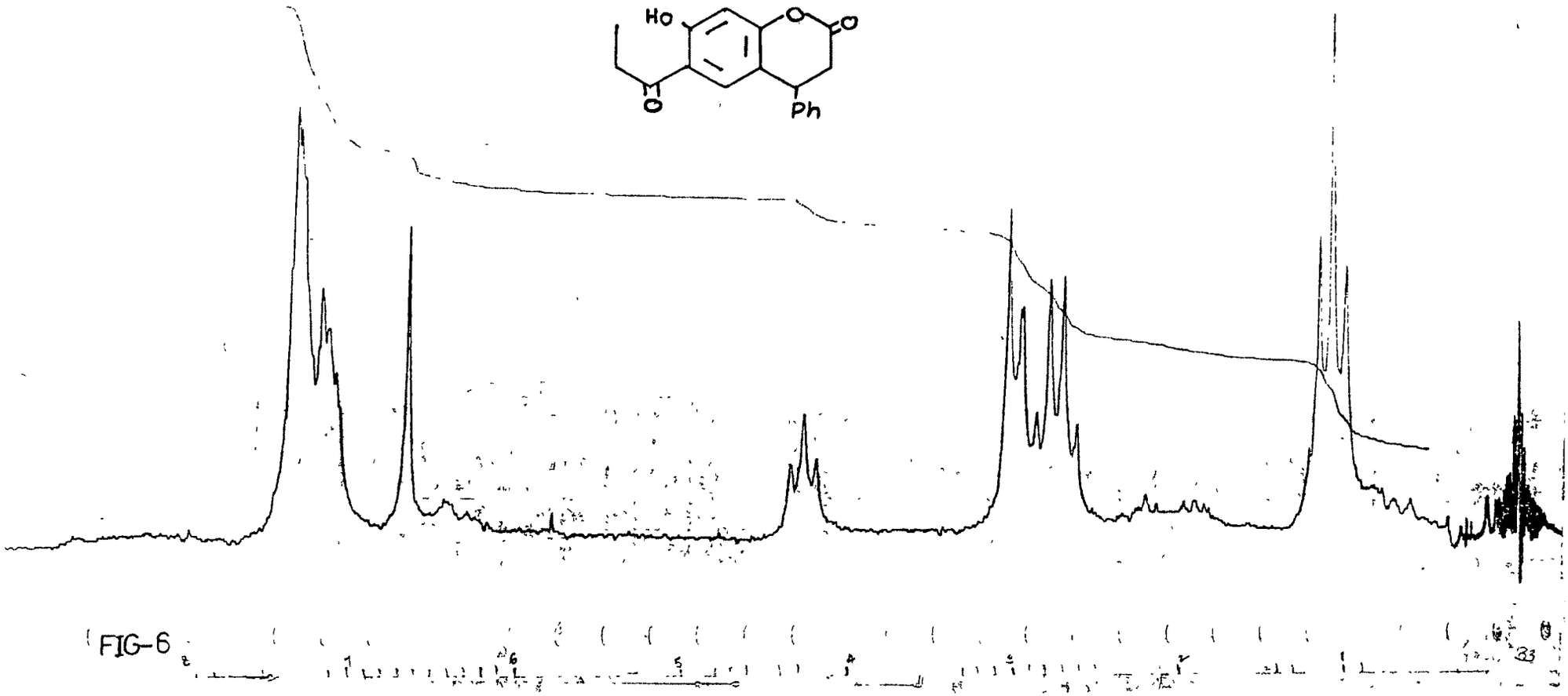


FIG-6

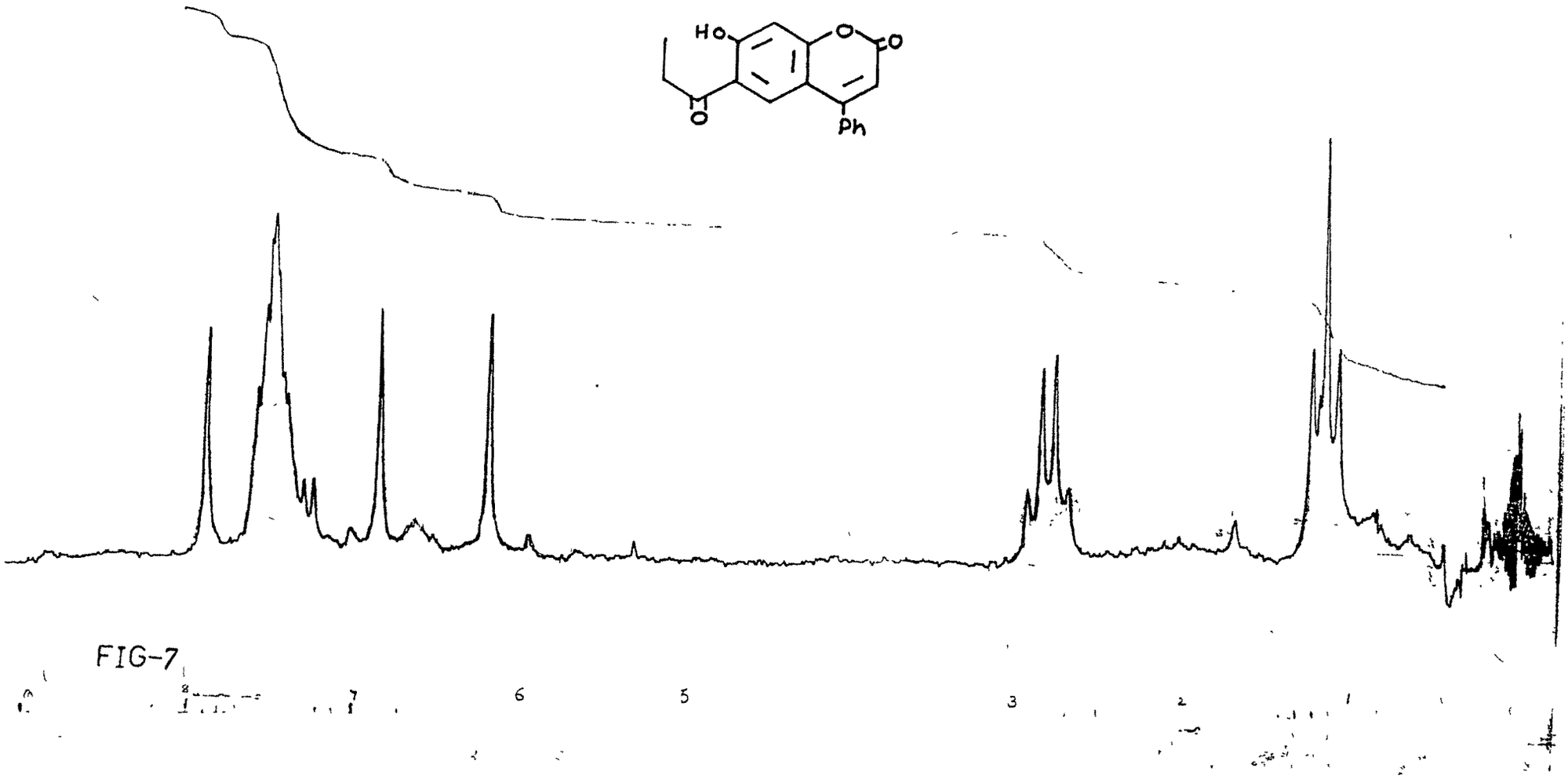


FIG-7

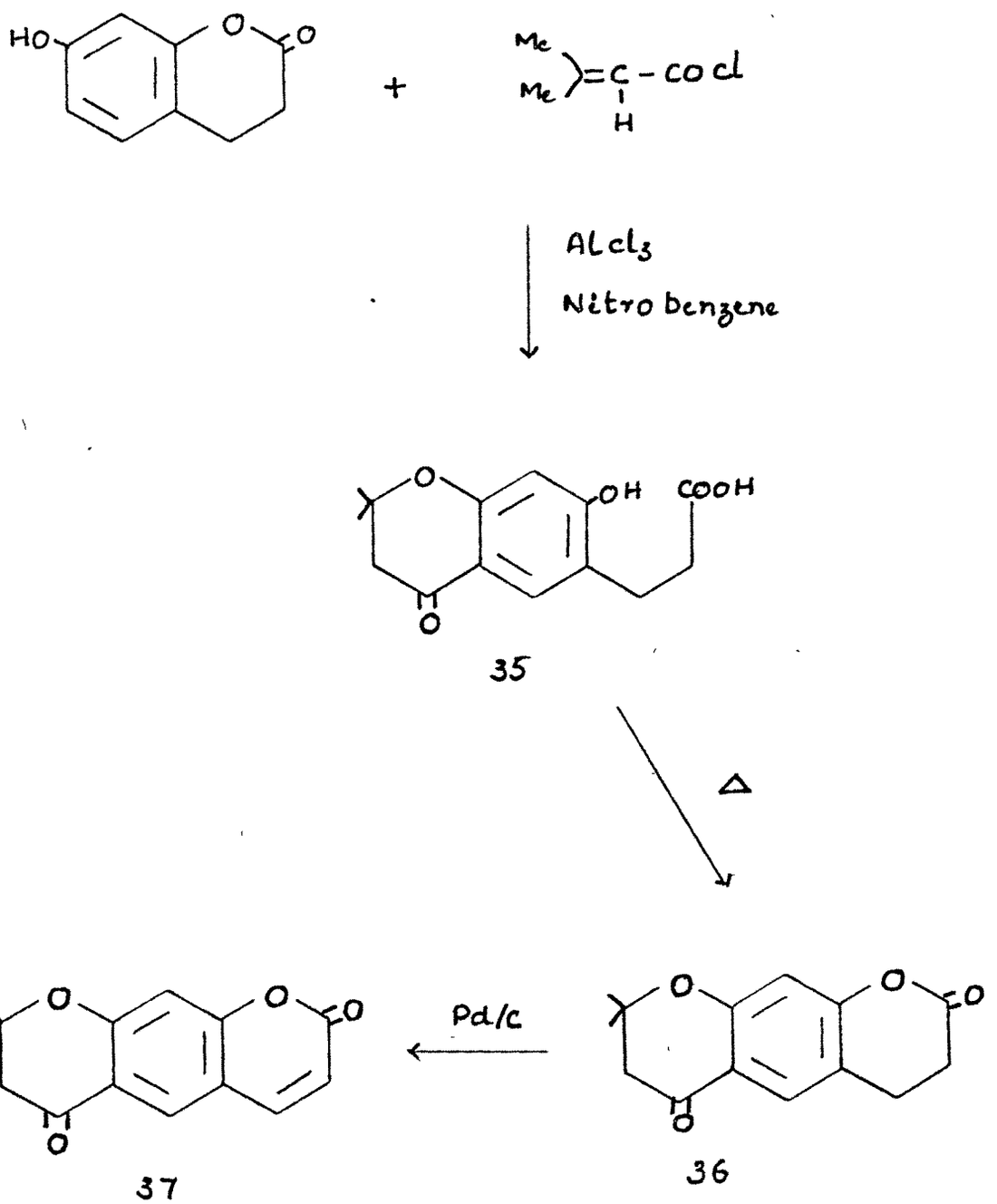
The compound (33) on dehydrogenation with Pd/c in diphenylether afforded 7-hydoxy-6-propionyl-4-phenyl-benzopyran-2(H)-one (34) [Sheme-14] which showed signals in $CDCl_3$ at δ1.15, a triplet for three methyl protons in the propionyl function at C-6, a quartet at δ2.85 for two methylene protons of the propionyl at C-6, a singlet at δ6.15 for a vinylic proton at C-3, a singlet at δ6.85 for a proton at C-5, five aromatic protons at C-4 appeared as a multiplet at δ 7.25-7.6 and a singlet appeared for C-8 proton at δ 7.9. (Fig. 7)

8,8-Dimethylpyrano(3,2-g)benzopyran-2(H)-6(H)-dione (Graveolone) (37)

8,8-Dimethylpyrano(3,2-g)benzopyran-2(H)-6(H)-dione, a naturally occuring coumarin, Graveolone was synthesised using Friedel-Crafts method. 7-Hydroxy-3,4-dihydrocoumarin in nitrobenzene and aluminium chloride were heated with β,β-dimethylacryloylchloride on steam bath for 5 to 6 hr. After the usual work up it gave 7-hydroxy-2,2-dimethyl chromanone-6-propionic acid (35).

The crude product was directly cyclised by heating at 180-200° for 40-50 min. to give 8,8-dimethylpyrano(3,2-g) 3,4-dihydrobenzopyran-2(H)-6(H)-dione (36), m.p.138°, Lit. m.p. 136-37°. PMR of the compound showed signals in $CDCl_3$ at δ1.45 a singlet corresponding to six protons of two

SCHEME - 15



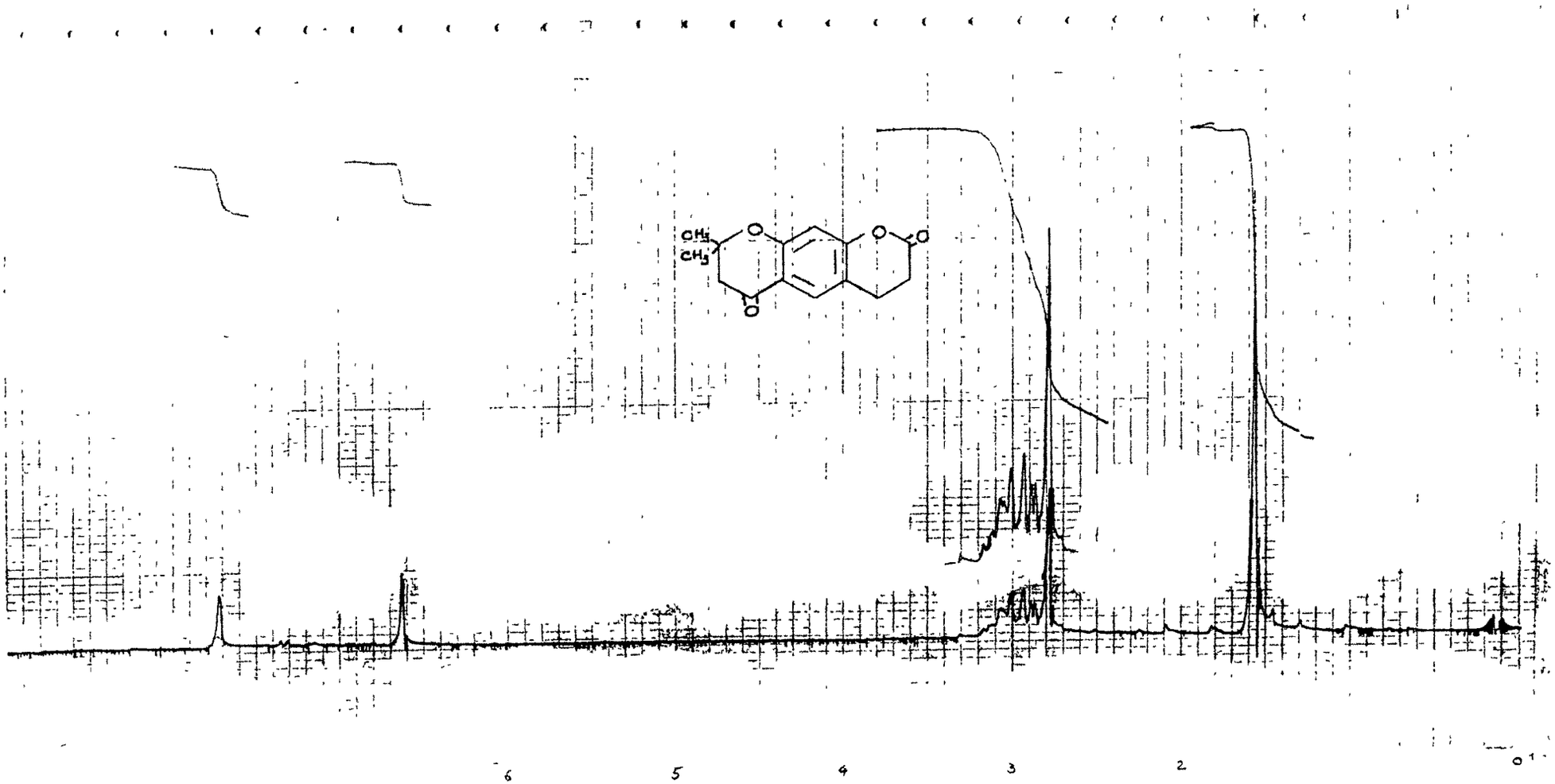


FIG-8

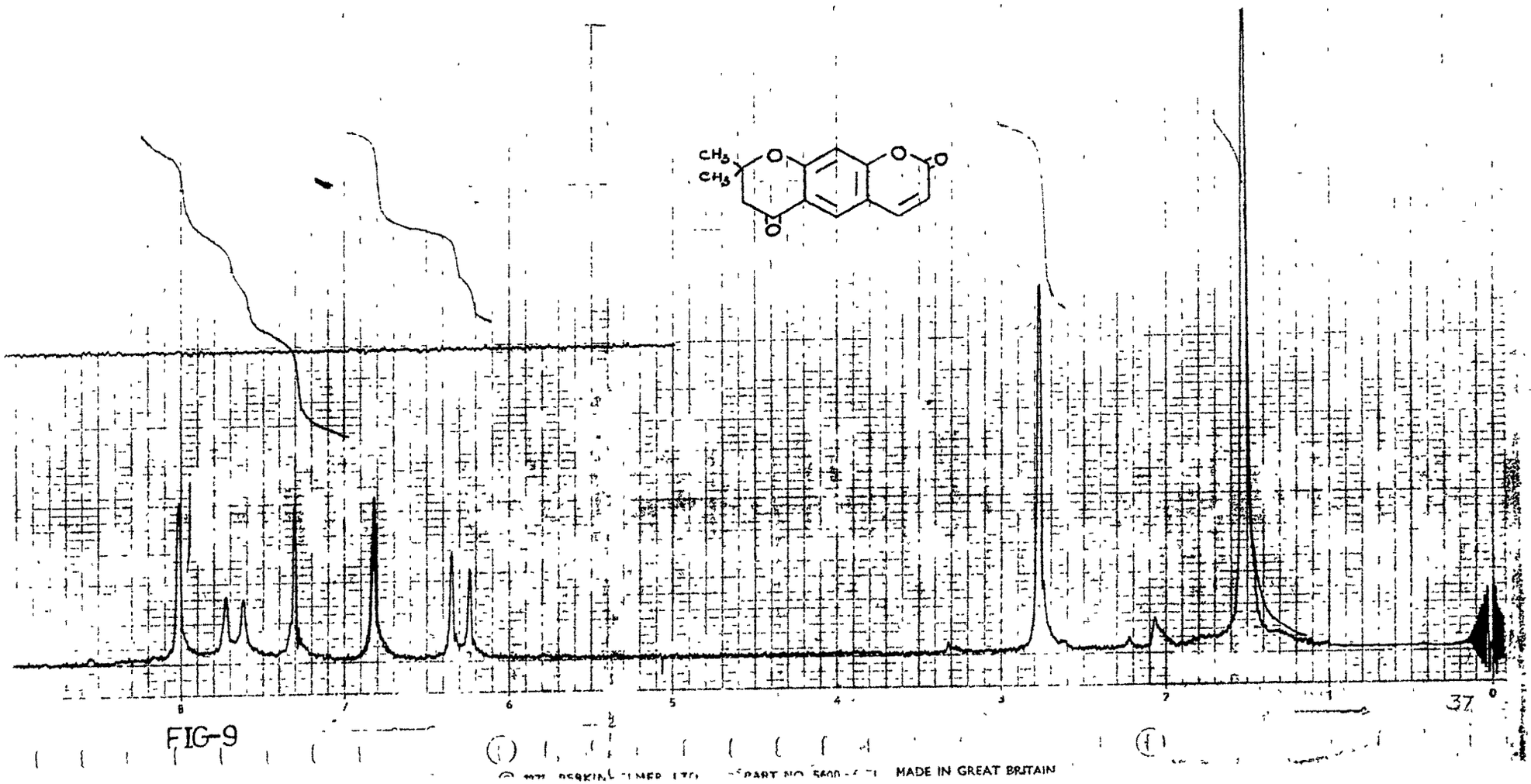


FIG-9

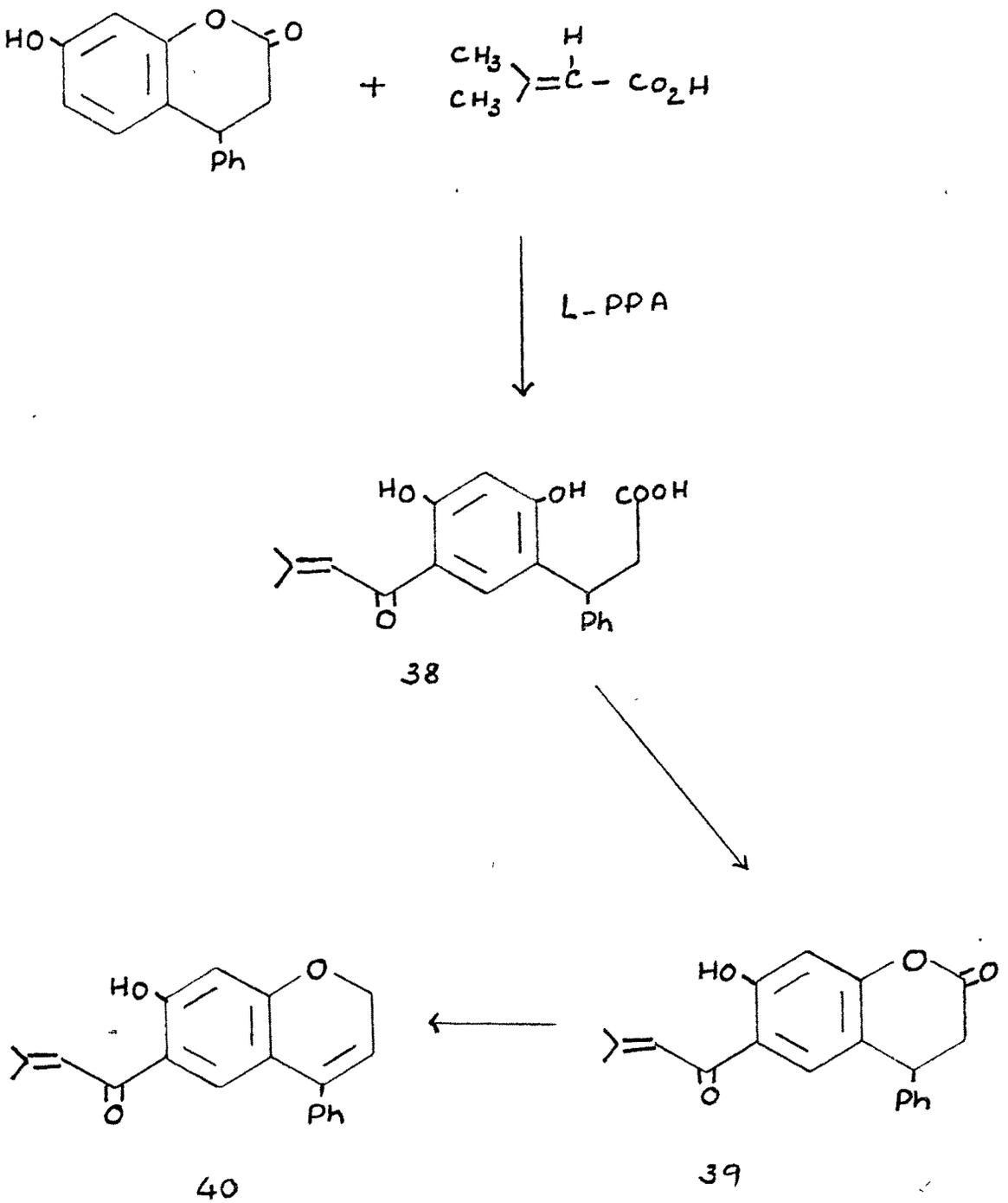
methyl groups at C-8, another singlet at δ2.7 for the two protons at C-7, a multiplet for four protons of C-3 and C-4 at δ 2.75-3.0 and two singlets at δ6.5 and 7.6 for C-10 and C-5 protons respectively. (Fig. 8)

The compound (36) on dehydrogenation with Pd/c in diphenylether gave the product (37). [Scheme-15] m.p. 176°, Lit.[8] m.p. 175-76°. Its PMR in $CDCl_3$ exhibited signals at δ1.5, a singlet for six protons of two methyl groups at C-8, another singlet at δ2.8 for two protons at C-7, a doublet J=9Hz at δ6.3 for a proton at C-3, at δ6.8 a singlet for C-10 proton, another doublet J=9Hz at δ7.7 for a proton at C-4 and a singlet at δ8.0 for a proton at C-5. (Fig. 9)

7-Hydroxy-6-(β,β-dimethylacryloyl)-4-phenylbenzopyran-2(H)-one (40)

7-Hydroxy-4-phenyl-3,4-dihydrocoumarin, was stirred with β,β-dimethyl acrylic acid in L-PPA at 120° for 1 hr. The reaction mixture was decomposed by pouring over cold dil. HCl. Separated propionic acid derivative (38) was directly heated at 180°-200° for 1 hr. to yield 7-hydroxy-6-(β,β-dimethylacryloyl)-4-phenyl-3,4-dihydrocoumarin (39). PMR of the compound exhibited signals in $CDCl_3$ at δ1.3, a singlet for six protons of two methyl groups in the dimethyl acryloyl function at C-6, a multiplet at δ3.0 for two protons

SCHEME – 16


HO
O
O
Ph
+
CH3
CH3
H
C – CO2H
L-PPA
HO
OH
COOH
O
Ph
38
HO
O
O
Ph
39
HO
O
O
Ph
40

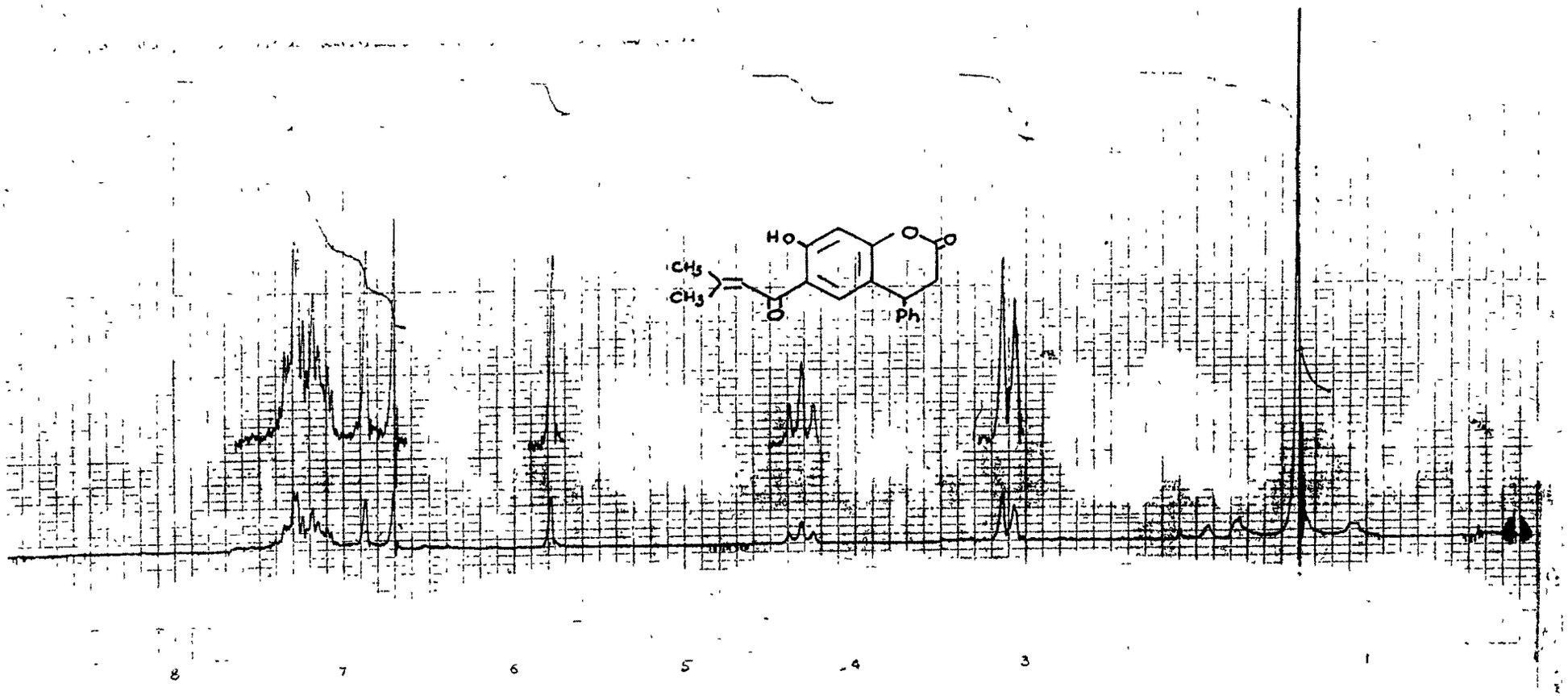


FIG-10

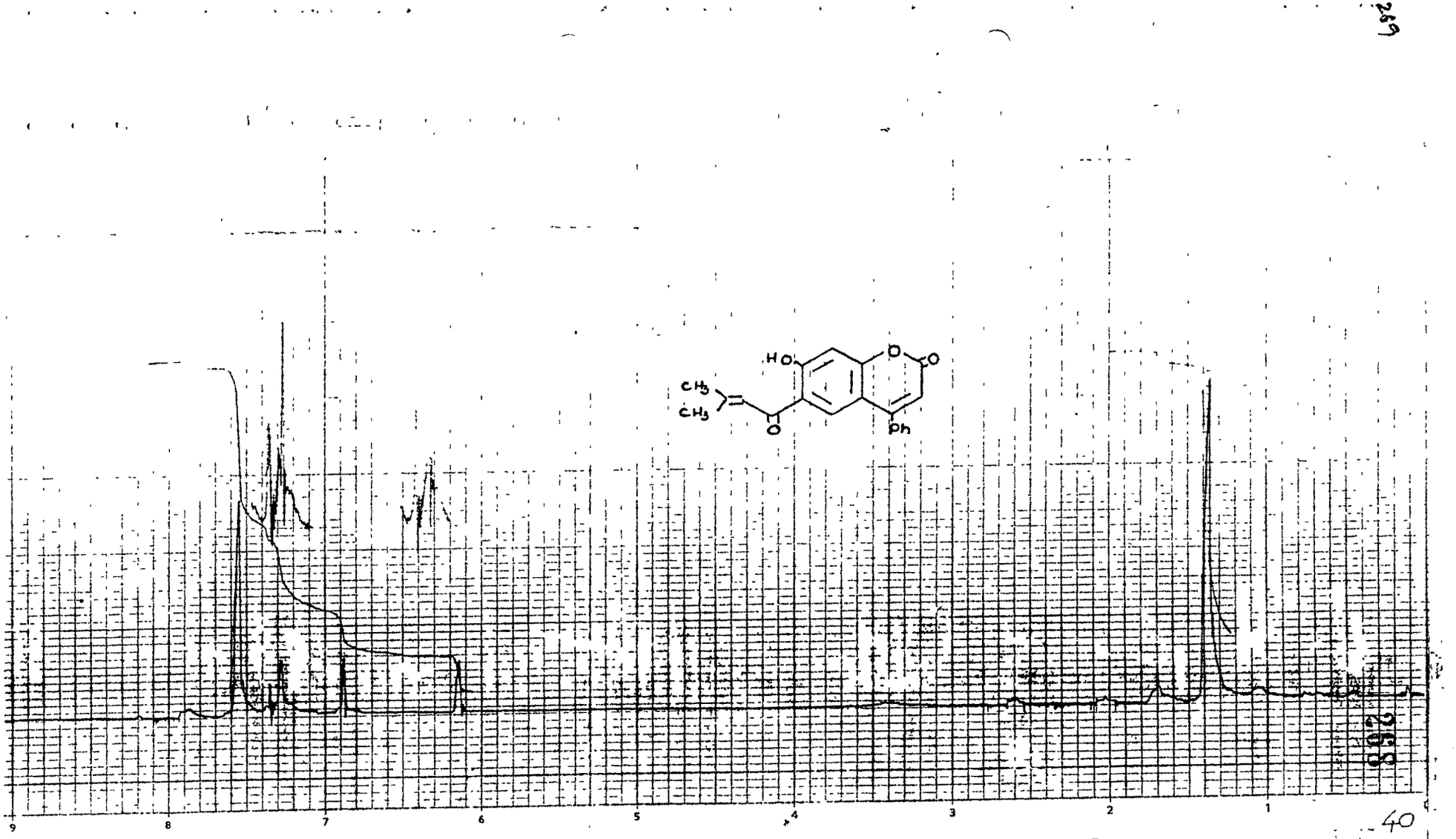


FIG-11

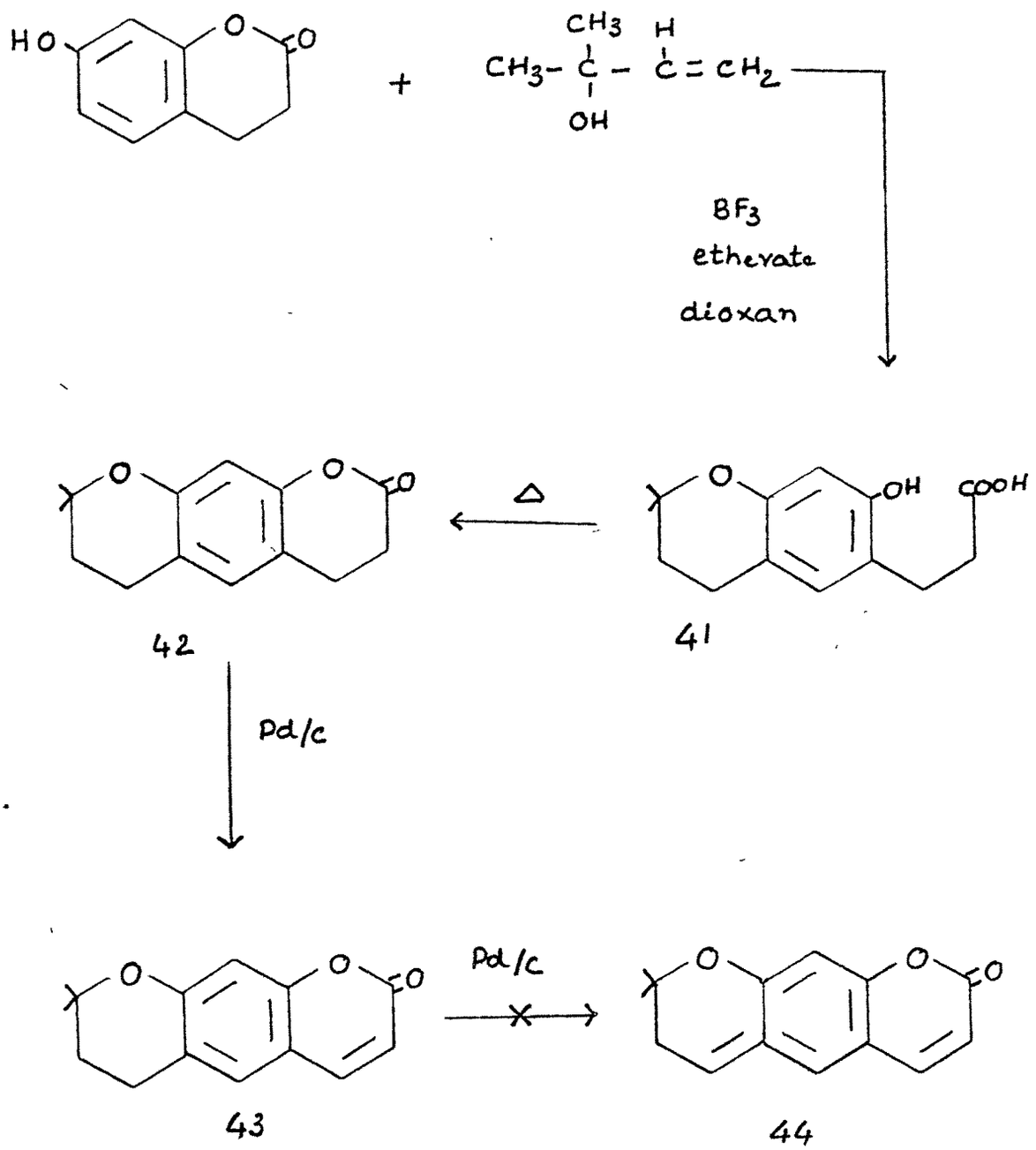
at C-3, a triplet at δ4.2 for a single proton at C-4, a singlet at δ5.7 for a proton in the dimethyl acryloyl group >C-H at C-6, two singlets at δ 6.6 and δ 6.75 for two protons at C-5 and C-8 and a multiplet corresponds to five phenyl protons appeared at δ7-7.25. (Fig. 10)

Dehydrogenation of the compound (39) with Pd/c in diphenylether gave 7-hydroxy-6-(β,β-dimethylacryloyl)-4-phenyl benzopyran-2(H)-one (40). [Scheme-16] The structure of the compound (40) was established by PMR spectra which exhibited signals at δ1.25, a singlet for six protons of two methyl groups in the dimethyl acryloyl moiety at C-6, a singlet at δ6.05 for the vinylic proton at C-4, two singlets at δ6.8 and 7.2 for the two protons at C-5 and C-8 and a singlet for five phenyl protons at C-4 appeared at δ7.45 (Fig. 11)

8,8-Dimethyl-6,7-dihydropyrano(3,2-g)benzopyran-2(H)-one (43)

7-Hydroxy-3,4-dihydrocoumarin in dioxane was condensed with 2-methyl-3-butene-2-ol in the presence of BF_3 etherate in dioxane gave 2-hydroxy-5,5-dimethyl-6,7-dihydropyrano(3,2-g) phenyl propionic acid (41). The compound was directly heated at 180-200° for 1 hr. furnished 8,8-dimethyl-3,4,6,7-tetrahydro pyrano(3,2-g)benzopyran-2(H)-one (42), m.p. 156° Lit.[11] m.p. 153-54°. Its PMR exhibited signals in $CDCl_3$ at δ1.25

SCHEME - 17


HO
O
O
+
CH3
H
CH3- C - C = CH2
OH
BF3
etherate
dioxan
O
O
O
42
Δ
O
OH
COOH
41
Pd/c
O
O
O
43
Pd/c
O
O
O
44

272

271

FIG-12

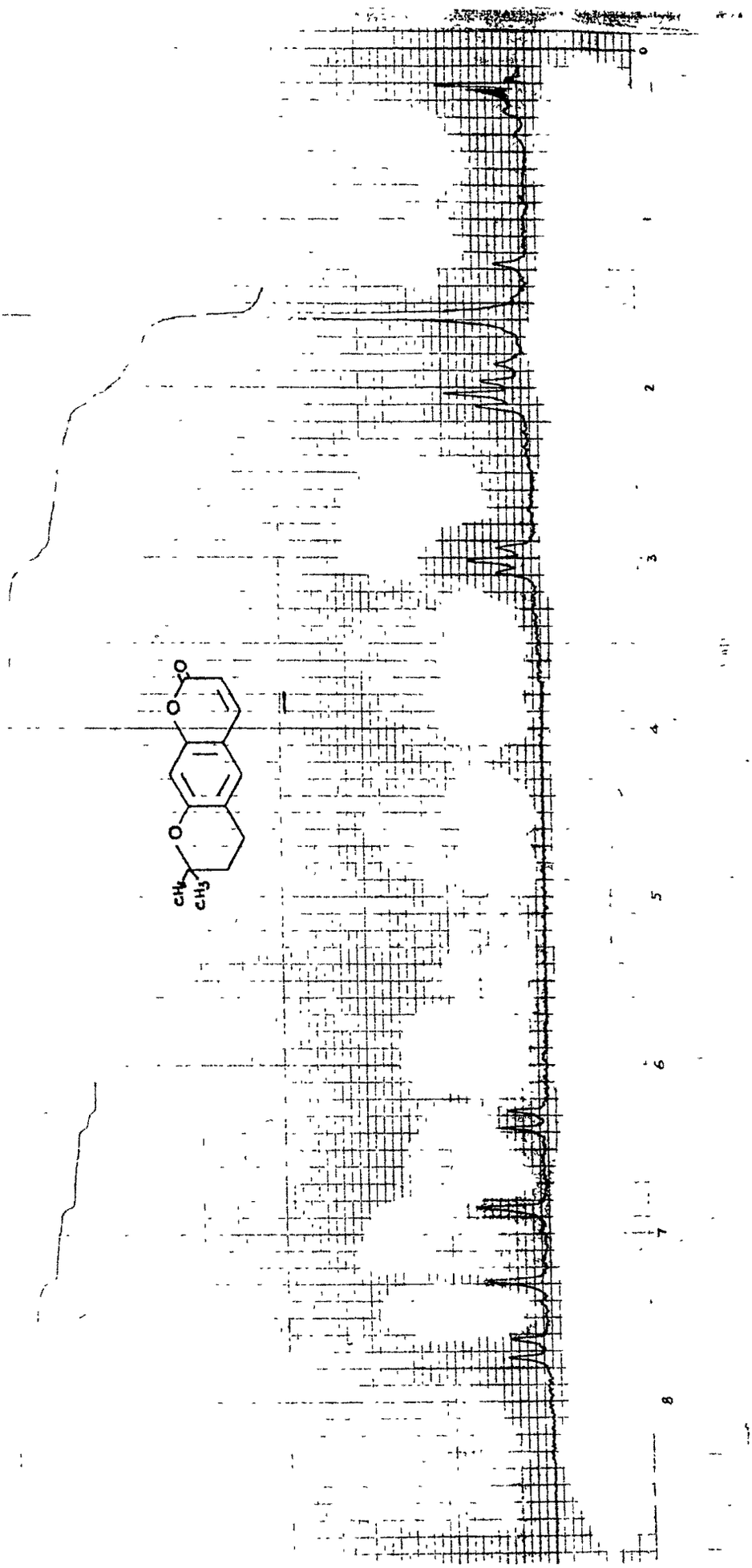


FIG-13

for six protons of two methyl groups at C-8, a triplet at δ1.75 for two protons at C-7, a multiplet appeared at δ2.6-2.9 for six protons, two protons each of C-3, C-4 and C-6 and two singlets appeared at δ6.5 and 6.95 for two protons at C-5 and C-10 respectively. (Fig. 12)

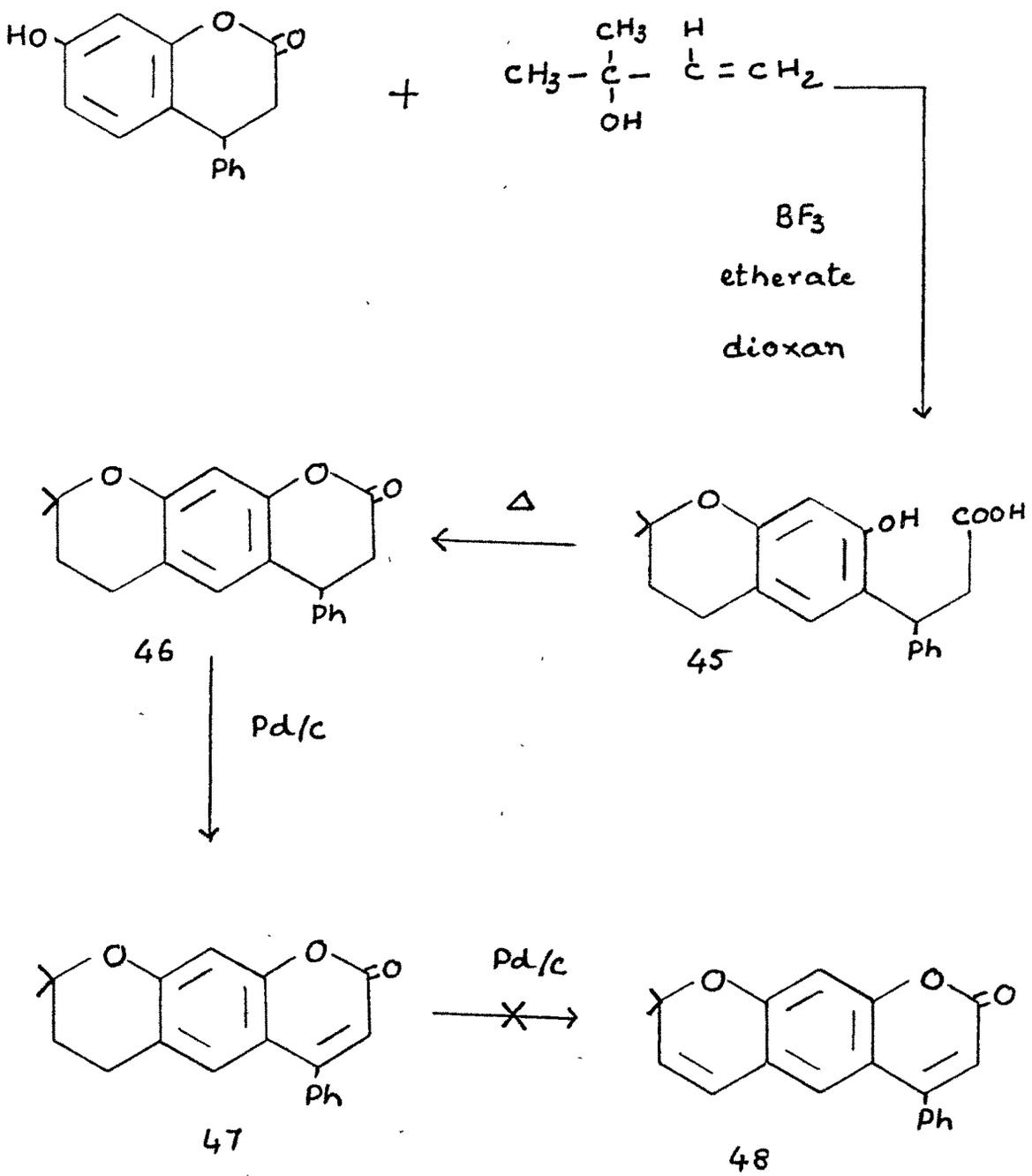
Dehydrogenation of the compound (42) with Pd/c in diphenyl-ether gave 8,8-dimethyl-6,7-dihydropyrano(3,2-g)benzopyran-2(H)-one (43), m.p. 118° Lit.[11] m.p. 122-23°. The structure of the compound was confirmed by PMR which exhibited signals at δ1.4, a singlet for six protons of two methyl groups at C-8, a triplet at δ1.8 for two protons at C-7, another triplet for two protons at C-6 appeared at δ 2.8, a doublet, J=9Hz at δ 6.15 for a proton at C-3, a singlet at δ6.65 corresponds to one proton at C-5, another singlet at δ 7.1 for a proton at C-10, another doublet J=9Hz for a proton at C-4 appeared at δ7.5. (Fig. 13)

Attempts to further dehydrogenate (43) with palladised charcoal (10%) failed to give (44). [Scheme-17]

<u>8,8-Dimethyl-4-phenyl-6,7-dihydropyrano(3,2-g)benzopyran-2(H)-one</u> (47)

A mixture of 7-hydroxy-4-phenyl-3,4-dihydrocoumarin, 2-methyl-3-butene-2-ol in dioxane was stirred with BF_3 etherate in dioxane for 5 hr. which gave a propionic acid (45) on

SCHEME - 18


HO
O
O
Ph
+
CH3
H
CH3 – C – C = CH2
OH
BF3
etherate
dioxan
O
O
O
Ph
46
Δ
O
OH
COOH
Ph
45
Pd/c
O
O
O
Ph
47
Pd/c
O
O
O
Ph
48

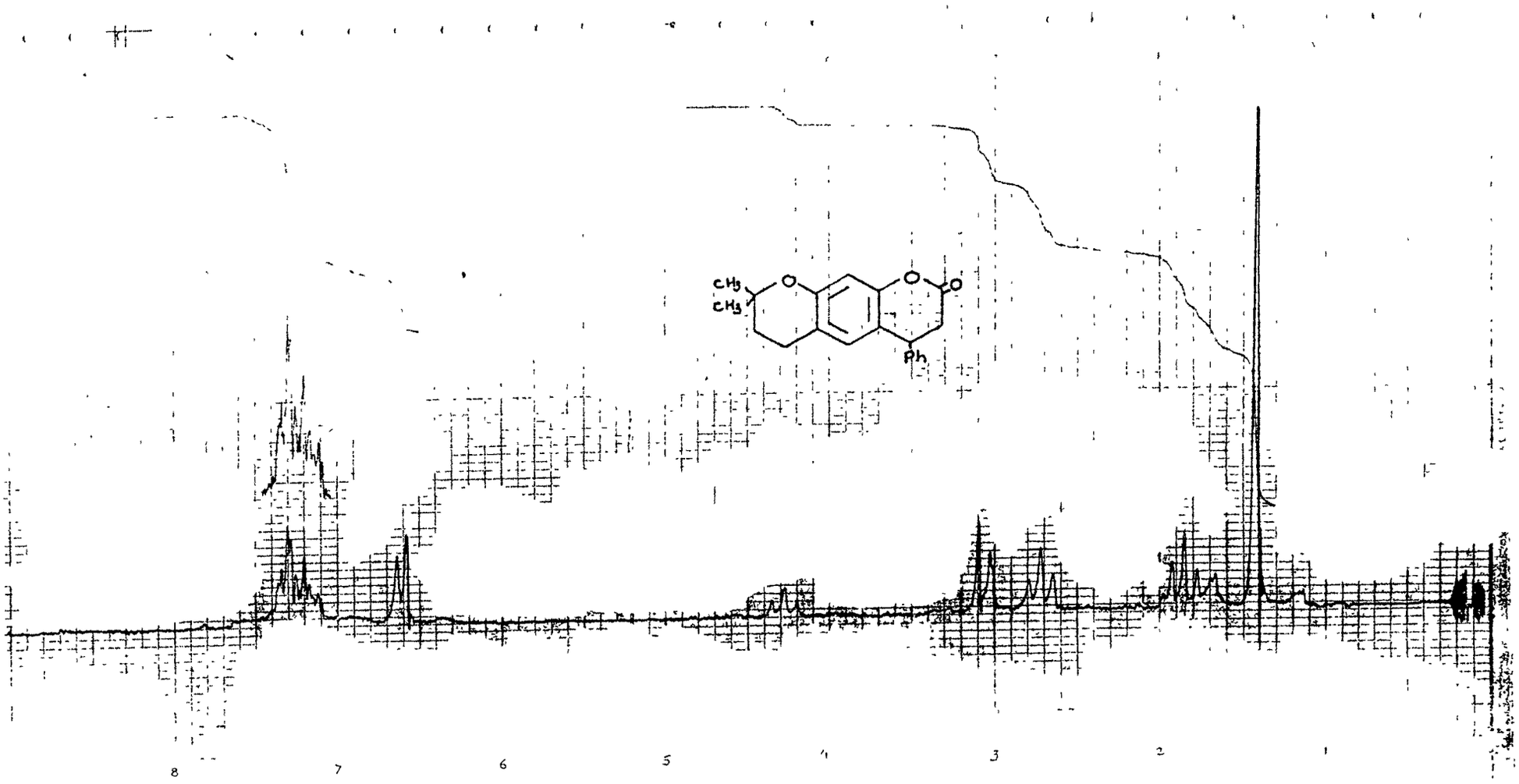


FIG-14

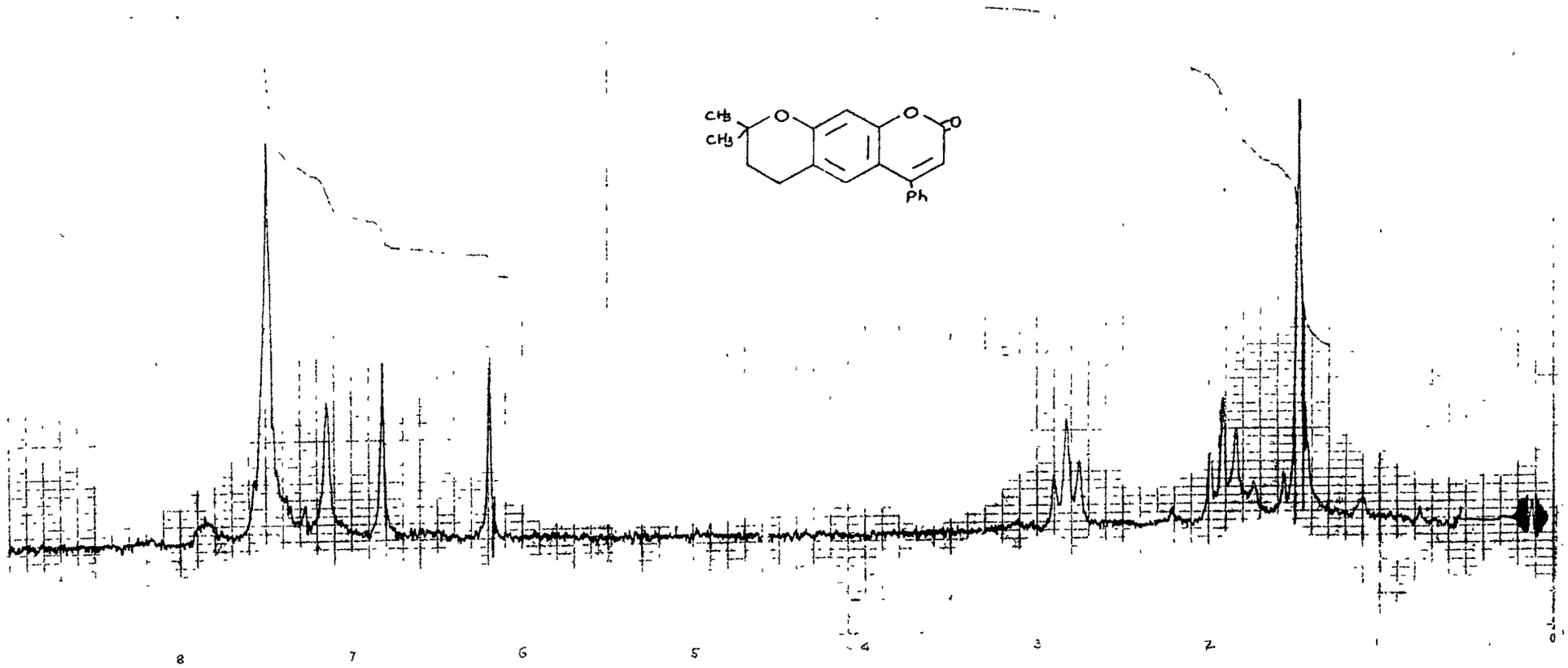


FIG-15

work up. As the compoundcould not be isolated, (45) was heated at 180°-200° for an hr. to furnish 8,8-dimethyl-4-phenyl-3,4,6,7-tetrahydropyrano(3,2-g)benzopyran-2(H)-one (46). The structure of the compound was confirmed by PMR which exhibited signals at δ1.3, a singlet for 6 protons of two methyl groups at C-8 position, a triplet at δ1.75 for two protons at C-7, another triplet at δ2.6 for two protons at C-6, a doublet appeared at δ3.0 for two protons at C-3, a triplet at δ4.3 for a single proton at C-4, two singlets at δ6.4 and 6.45 for the two protons at C-5 and C-10 and a multiplet appeared at δ7.0-7.25 for five phenyl protons at C-4. (Fig. 14)

Dehydrogenation of the compound (46) with Pd/c in diphenylether furnished 8,8-dimethyl-6,7-dihydropyrano(3,2-g)benzopyran-2(H)-one (47), m.p. 200° Lit.[12] m.p. 199-200°. PMR spectra confirmed the structure of the compound (47) which exhibited signals in $CDCl_3$ at δ1.35, singlet for six protons of two methyl groups at C-8, a triplet at δ1.75 for two protons at C-7, another triplet for two protons at C-6 appeared at δ2.65, a singlet appeared at δ6.05 for a vinylic proton at C-3, two singlets for C-5 and C-10 protons showed at δ6.65 and 7.0 respectively and the phenyl group at C-4 showed a singlet for five protons at δ7.35. (Fig. 15)

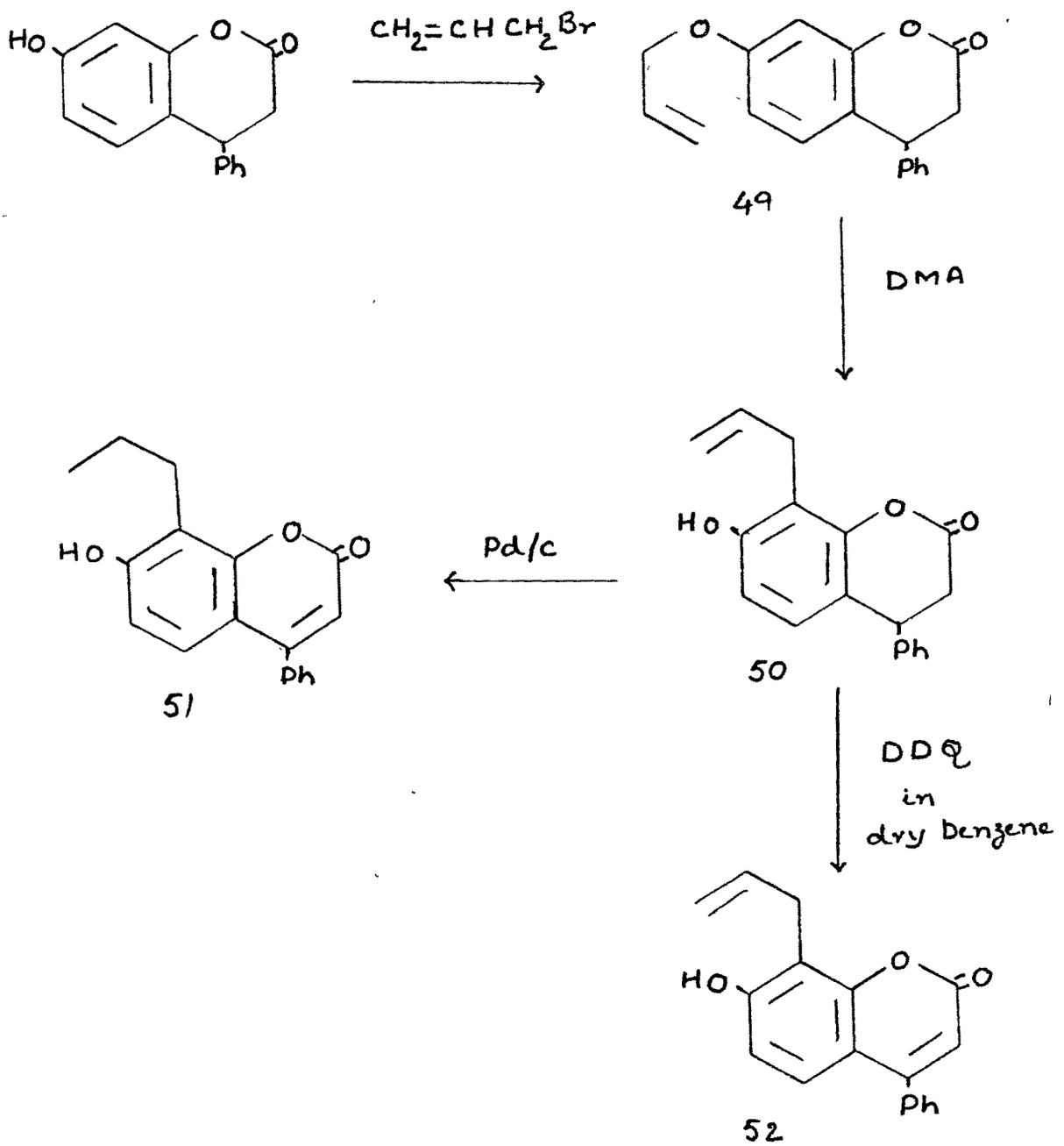
Attempts to further dehydrogenate (47) with Pd/c (10%) failed to give (48). [Scheme-18]

Attempted synthesis of 5'-methyl-4-phenyl psoralen

It was thought of interest to prepare some psoralen derivatives taking the advantage of the regiospecificity of 3,4-dihydrocoumarin moiety. 7-Hydroxy-4-phenyl-3,4-dihydrocoumarin on allylation with allylbromide in presence of potassium carbonate in dry acetone gave 7-allyloxy-4-phenyl-3,4-dihydrocoumarin (49) (Fig. 16) which when subjected to Claisen migration in N,N-dimethylaniline did not furnish C-6 isomer but instead a C-8 isomer 8-allyl-7-hydroxy-4-phenyl-3,4-dihydrocoumarin (50). The structure of the compound was confirmed by PMR which showed signals at δ2.95, a doublet for two protons at C-3, a multiplet at δ3.5 for two protons in the allylic function CH_2=CH-$\underline{CH}_2$- at C-8, a triplet at δ4.2 for a single proton at C-4, another mutiplet appeared at δ5.0-5.2 for the two protons in the allylic function $\underline{CH}_2$=CH-CH_2 at C-8, a singlet for exchangeable hydroxyl proton at C-7 appeared at δ5.3, a multiplet at δ5.7-6.15 for single proton in the allylic function CH_2=$\underline{CH}$-CH_2- at C-8, a doublet J=9Hz at δ6.45 for a proton at C-5 and another doublet J=9Hz at δ6.6 for a proton at C-6 indicate that C-5 and C-6 are ortho coupled with one another and a multiplet for five phenyl protons at C-4 appeared at δ7.0-7.3. (Fig. 17)

Compound (50) on refluxing in diphenyl ether with Pd/c gave 7-hydroxy-8-propyl-4-phenyl coumarin (51) instead of 7-hydroxy-8-allyl-4-phenylcoumarin (52) trans hydrogenation

SCHEME - 19


HO
O
O
Ph
$CH_2=CHCH_2Br$
49
DMA
50
HO
Ph
Pd/c
51
HO
Ph
DDQ
in
dry Benzene
52
HO
Ph

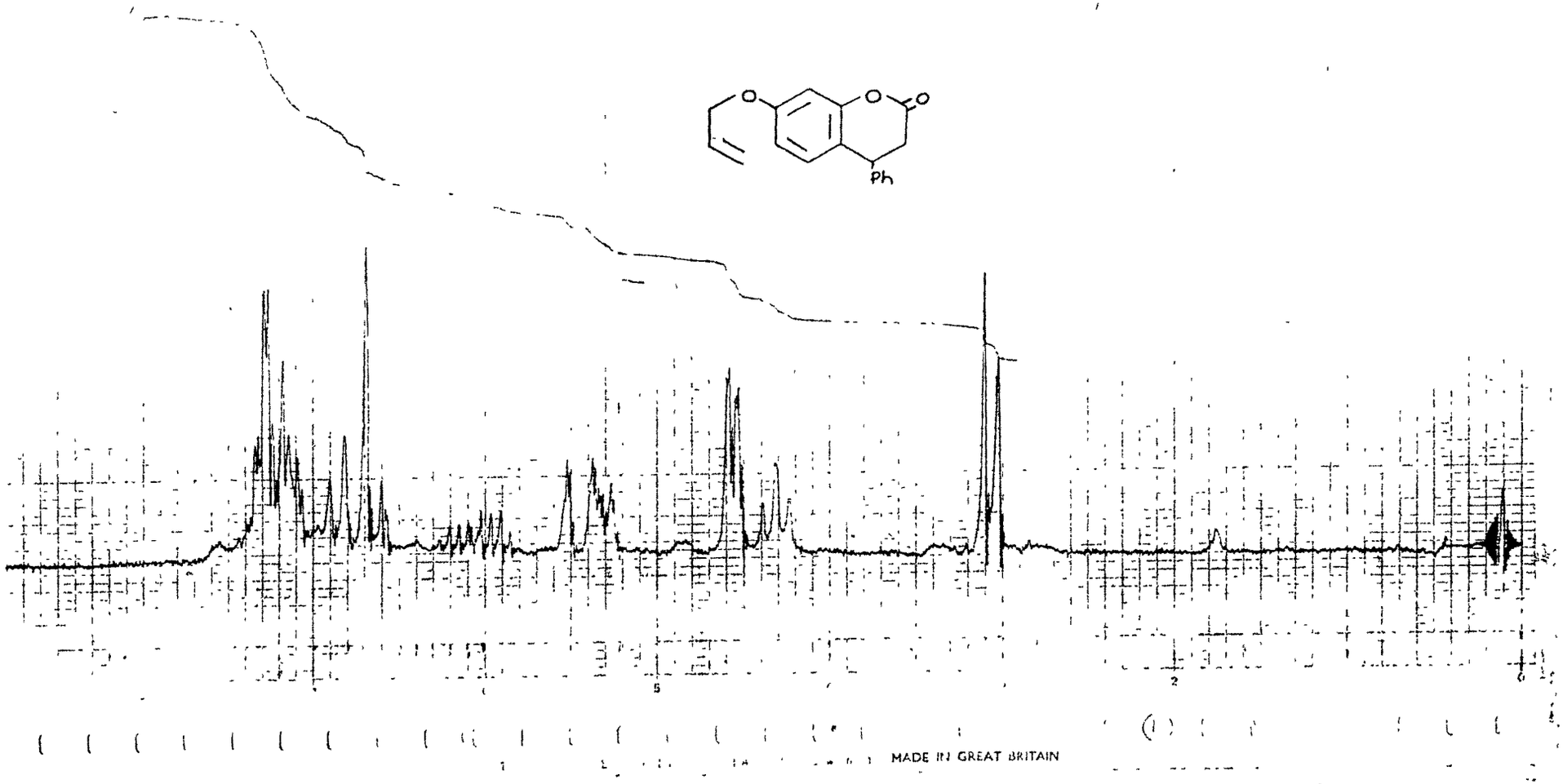


FIG-16

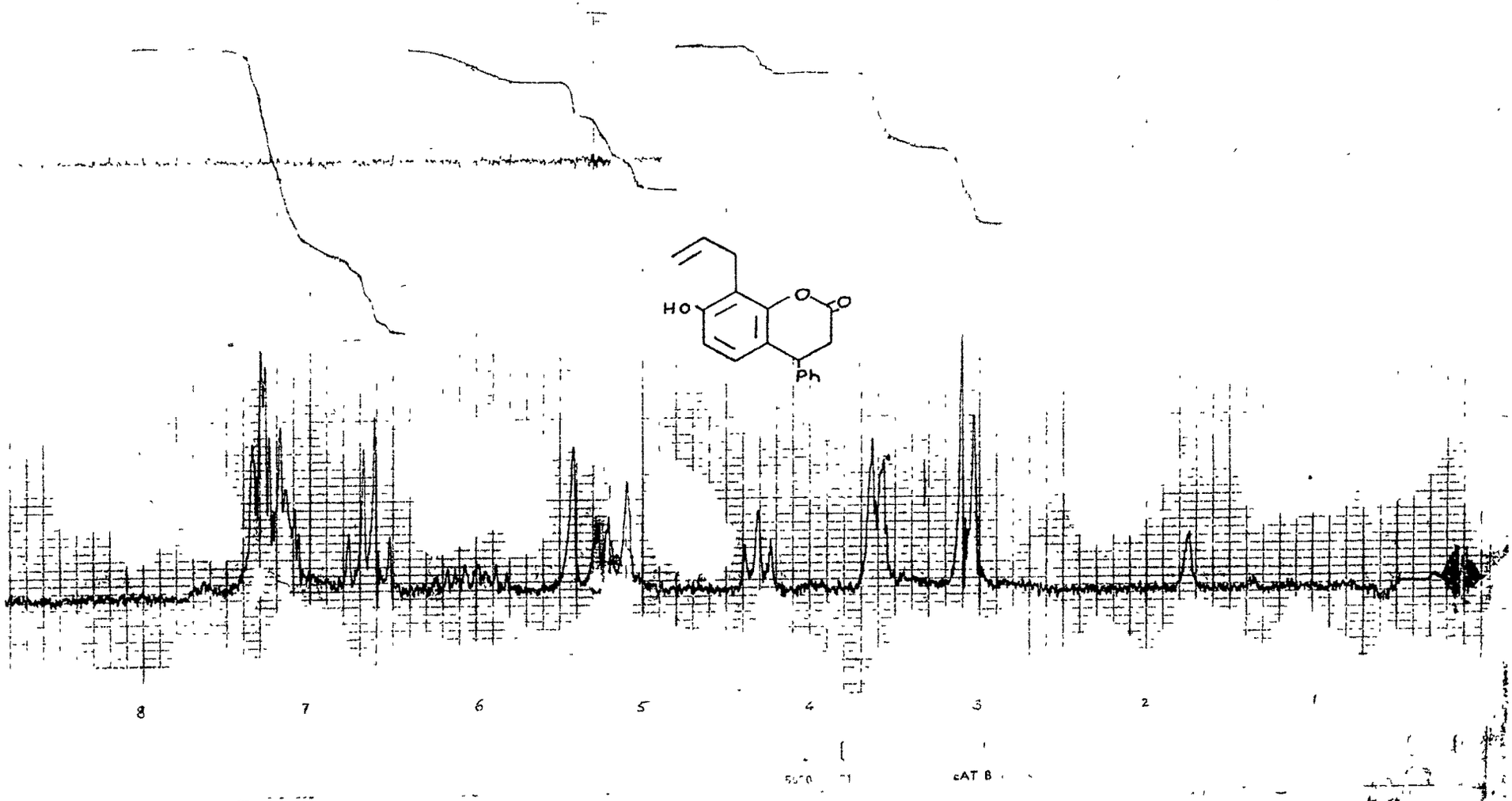


FIG-17

taking place during the course of the reaction. PMR of (51) showed signals in DMSO-D_6 at δ1.0 a triplet for a methyl group in the propyl function at C-8, a quartet at δ1.65 for two methylene protons in the propyl function CH_3-$\underline{CH}_2$-CH_2- at C-8, another triplet at δ2.8 for two methylene protons at C-8, a singlet at δ6.0 for vinylic proton at C-3. (Fig. 18)

This indicates that the reaction of (50) with Pd/c in diphenylether not only dehydrogenated 3,4 positions but also hydrogenated the double bond in the allyl group. The compound (50) was refluxed with DDQ in dry benzene which yielded a known compound 7-hydroxy-8-allyl-4-phenylcoumarin (52). (Fig. 19) The structure of the compound was confirmed by comparing the m.p. and mix m.p. with authentic sample.

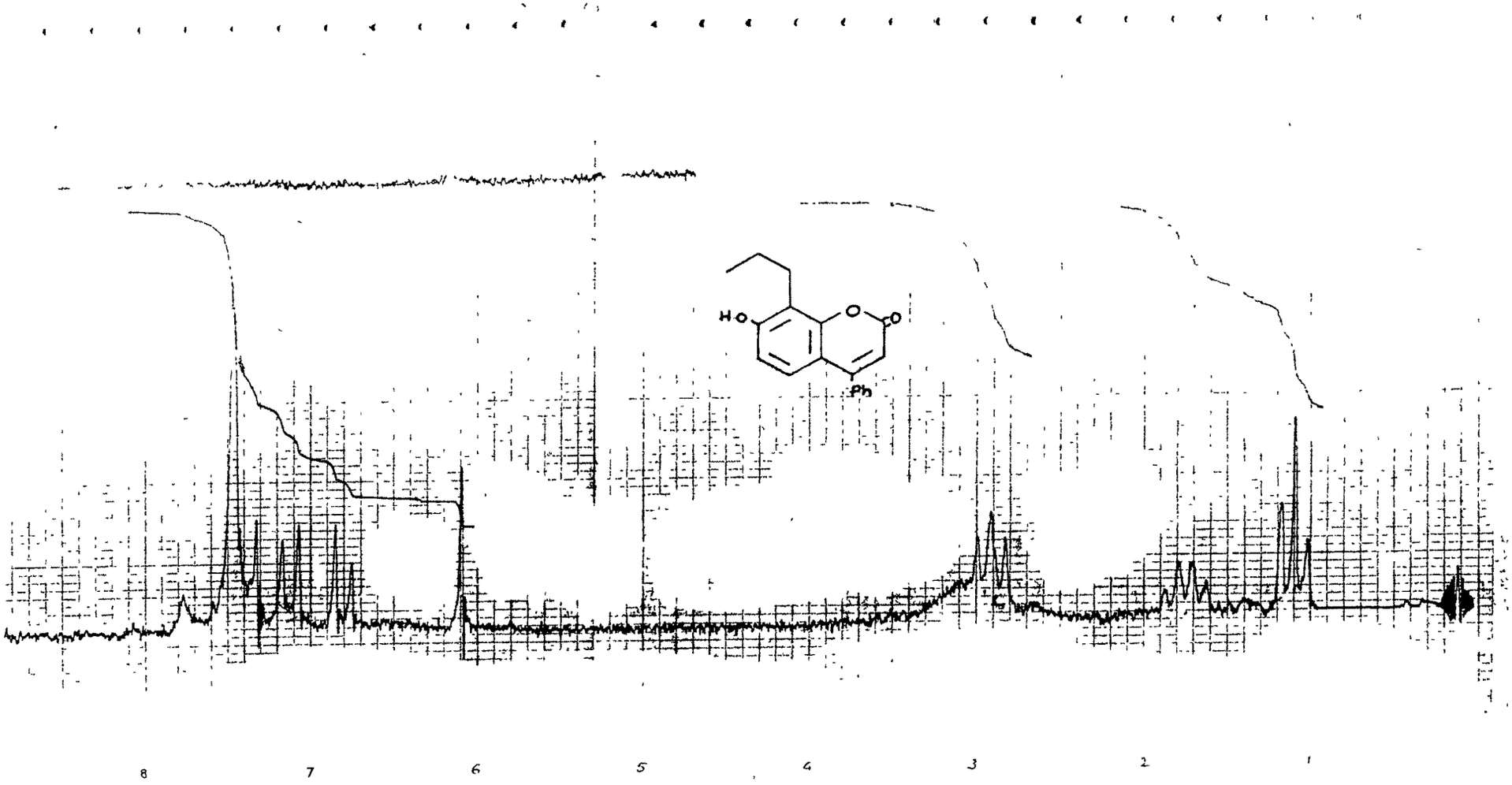


FIG-18

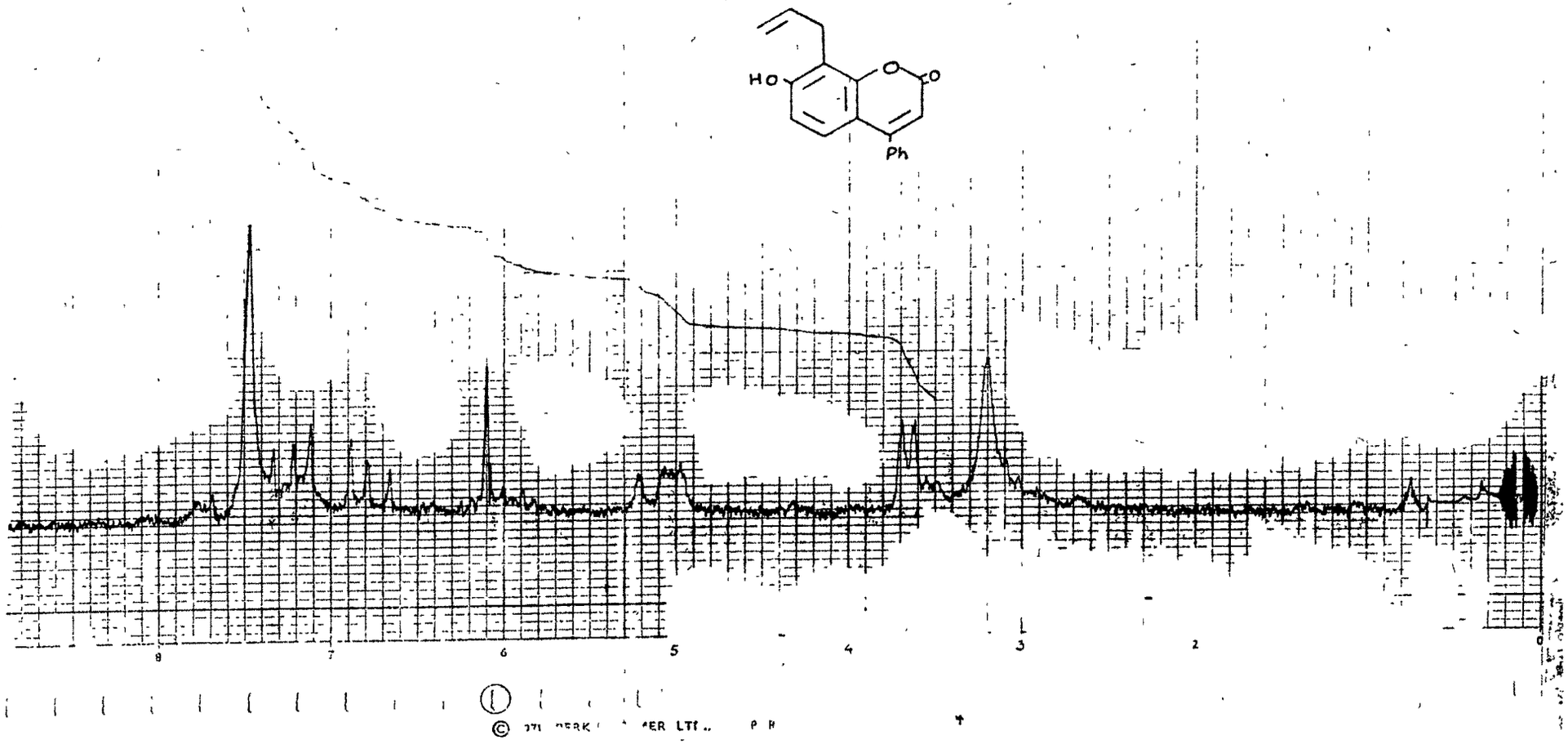


FIG-19

EXPERIMENTAL

EXPERIMENTAL

All melting points are uncorrected. PMR spectra recorded on Perkin-Elmer R-32 Spectrometer (90 MHz) using TMS as internal standard.

6-Acetyl-7-hydroxy-3,4-dihydrobenzopyran-2(H)-one (24)

7-Hydroxy-3,4-dihydrocoumarin (5 g) in distilled nitrobenzene (75 ml) was treated with aluminium chloride (10 g) in small portions and acetyl chloride (5 ml) was added tod the reaction mixture which was then heated on steamd bath for 8 hr. The reaction mixture was cooled and poured into dil. HCl. The title product was obtained by heating the separated compound at 180-200° in an oil bath till it ceases to give effervescence, for 40 min. It was purified by column chromatography, the product crystallised from benzene (3 g) m.p. 148°.

Analysis	:	Found	:	C, 64.50 ; H, 5.03%
$C_{11}O_4H_{10}$	:	requires	:	C, 64.07 ; H, 4.85%

6-Acetyl-7-hydroxy benzopyran-2(H)-one (25)

7-Hydroxy-6-acetyl 3,4-dihydrocoumarin (0.5 g) in diphenyl ether (8 ml) was refluxed with palladised charcoal (Pd/c 10%, 0.5 g) for 5 hr. The reaction mixture was filtered hot and diluted with pet. ether (40°-60°) (5 ml). Separated

product crystallised from benzene (0.3 g), m.p. 175°.Lit. m.p. 175°.

Analysis	:	Found	: C, 65.10%	; H, 3.96%
$C_{11}O_4H_8$	:	requires	: C, 64.71%	; H, 3.92%

6-Propionyl-7-hydroxy-3,4-dihydrobenzopyran-2(H)-one (27)

7-Hydroxy-3,4-dihydrocoumarin (5 g) in nitrobenzene (75 ml) aluminium chloride (10 g) was heated on a steam bath with propionic anhydride (8 ml) for 5 to 6 hr. The reaction mixture was worked up as usual. The product obtained was heated at 180°-200°C in an oil bath to yield the title product which was purified by column chromatography. The product crystallised from alcohol (3.5 g), m.p. 108°

Analysis	:	Found	: C, 65.34%	; H, 5.84%
$C_{12}H_{12}O_4$	:	requires	: C, 65.64%	; H, 5.45%

6-Propionyl-7-hydroxy benzopyran-2(H)-one (28)

6-Propionyl-7-hydroxy-3,4-dihydrobenzopyran-2(H)-one (0.5 g) and palladised charcoal (0.5 g) in diphenyl ether (8 ml) was refluxed for 6 hr. The reaction mixture was filtered hot and diluted with pet. ether (40°-60°) (5 ml) to get the product. Separated product filtered and crystallised from benzene (0.2 g), m.p. 154°.

Analysis	:	Found	: C, 65.70%	; H, 4.70%
$C_{12}H_{10}O_4$	:	requires	: C, 66.05%	; H, 4.58%

6-Acetyl-7-hydroxy-4-phenyl-3,4-dihydrobenzopyran-2(H)-one (30)

7-Hydroxy-4-phenyl-3,4-dihydrobenzopyran-2(H)-one (2.4 g) in nitrobenzene (25 ml) was treated with aluminium chloride (3.5 g) in small portions. Then the reaction mixture was heated on steam bath for 6 hr. after the addition of acetyl chloride (1.5 ml). After the completion of the reaction it was cooled and poured over cold dil. HCl. The product obtained on ether extraction of the solution mixture was heated on oil bath at 180°-200° for 45 min. which was then purified by column chromatography and crystallised from benzene and few drops of pet. ether (40°-60°) (1.5 g), m.p. 136°.

Analysis	:	Found	: C, 72.52%	; H, 4.94%
$C_{17}H_{14}O_4$	:	requires	: C, 72.34%	; H, 4.95%

6-Acetyl-7-hydroxy-4-phenyl benzopyran-2(H)-one (31)

6-Acetyl-7-hydroxy-4-phenyl-3,4-dihydrobenzopyran-2(H)-one (0.5 g) in diphenyl ether (8 ml) was refluxed with palladised charcoal (0.5 g) for 6 hr. The reaction mixture was filtered hot and diluted with pet. ether (40°-60°) (5 ml).

separated product filtered and crystallised from benzene and few drops of pet. ether (0.2 g), m.p. 176°.

Analysis	:	Found	: C, 73.25%	; H, 4.49%
$C_{17}H_{12}O_4$	:	requires	: C, 72.85%	; H, 4.28%

6-Propionyl-7-hydroxy-4-phenyl-3,4-dihydrobenzopyran-2(H)-one (33)

A mixture of 7-hydroxy-4-phenyl-3,4-dihydrocoumarin (2.4 g) in nitrobenzene (25 ml), aluminium chloride (3.5 g) and propionic anhydride (2.6 ml) was heated on steam bath for five hours. The reaction was worked up as usual. The product obtained was heated on oil bath at 180°-200°C to get the product (33) which was purified by column chromatography and it crystallised from benzene and few drops of pet. ether (1.8 g), m.p. 118°

Analysis	:	Found	: C, 73.37%	; H, 5.44%
$C_{18}H_{16}O_4$	:	requires	: C, 72.97%	; H, 5.40%

6-Propionyl-7-hydroxy-4-phenyl benzopyran-2(H)-one (34)

6-Propionyl-7-hydroxy-4-phenyl-3,4-dihydro-benzopyran-2(H)-one (0.5 g) in diphenyl ether (8 ml) was refluxed with palladised charcoal (0.5 g) for 5 hr. The reaction was worked up

as usual. Product crystallised from benzene (0.3 g), m.p. 173°.

Analysis	:	Found	:	C, 73.82%	;	H, 4.91%
$C_{18}H_{14}O_4$	:	requires	:	C, 73.46%	;	H, 4.76%

8,8-Dimethyl pyrano(3,2-g) 3,4-dihydrobenzopyran-2(H), 6(H)-dione (36)

A mixture of 7-hydroxy-3,4-dihydrocoumarin (5 g) in nitrobenzene (75 ml) was treated with aluminium chloride (10 g) and then the reaction mixture was heated on steam bath adding 3,3-dimethyl acryloyl chloride (7.5 ml) for 6 hr. The reaction was worked up as usual. The product obtained was heated on oil bath at 180°-200°C to obtain the (36) which was purified by column chromatography and crystallised frombenzene and few drops of petroleum ether (40°-60°) (1.5 g), m.p. 138°. Lit. m.p. 136-37°.

Analysis	:	Found	:	C, 67.90%	;	H, 5.35%
$C_{14}H_{14}O_4$	:	requires	:	C, 68.3%	;	H, 5.6%

8,8-Dimethylpyano(3,2-g)benzopyran-2(H)-6(H)-dione (37)

8,8-Dimethylpyrano(3,2-g) 3,4-dihydrobenzopyran-2(H), 6(H)-dione (0.5 g) and Pd/c (0.5 g) was refluxed in diphenyl ether (8 ml) for 5 hr. The reaction mixture was filtered

hot and diluted with pet. ether (40°-60°) (5 ml). Separated product crystallised from benzene and few drops of pet. ether (0.2 g), 176°. Lit. m.p. 175-76°.

Analysis	:	Found	:	C, 68.45%	;	H, 4.60%
$C_{14}H_{12}O_4$	:	requires	:	C, 68.84%	;	H, 4.91%

7-Hydroxy-6-(3,3-dimethylacryloyl)-4-phenyl-3,4-dihydrobenzopyran-2(H)-one (39)

A mixture of 7-hydroxy-4-phenyl-3,4-dihydrocoumarin (2.4 g) and 3,3-dimethylacrylic acid (1 g) was stirred in L-PPA at 120° for an hour. The reaction mixture was cooled and poured over cold dil. HCl. Separated product was heated at 180-200° to furnish 7-hydroxy-6-(3,3-dimethylacryloyl)-4-phenyl-3,4-dihydrocoumarin (39). The product obtained was purified by column chromatography which crystallised from benzene (1.5 g), m.p. 188°.

Analysis	:	Found	:	C, 74.88%	;	H, 5.20%
$C_{20}H_{18}O_4$	:	requires	:	C, 74.53%	;	H, 5.59%

7-Hydroxy-6-(3,3-dimethylacryloyl)-4-phenylbenzopyran-2(H)-one (40)

7-Hydroxy-6-(3,3-dimethylacryloyl)-4-phenyl-3,4-dihydro-

coumarin (0.5 g) in diphenyl ether (8 ml) was refluxed with Pd/c (0.5 g) for 6 hr. The reaction mixture was filtered hot and diluted with pet. ether (40°-60°) (5 ml) after cooling. Separated product crystallised from the mixture of benzene and alcohol (0.4 g), m.p. 290°.

Analysis	: Found	: C, 75.45%	; H, 5.40%
$C_{20}H_{16}O_4$	: requires	: C, 75.00%	; H, 5.00%

8,8-Dimethyl-3,4,6,7-tetrahydropyrano(3,2-g)benzopyran-2(H)-one (42)

A mixture of 7-hydroxy-3,4-dihydrocoumarin (2.5 g) in dioxane (30 ml), BF_3 etherate (1.2 ml) in dioxane (30 ml) and 2-methyl-3-butene-2-ol (1.2 ml) was stirred for 5 to 6 hr Then the reaction mixture was poured into ice water. The obtained product on extraction with ether was heated on oil bath at 180°-200° to get the product (42) which was purified by column chromatography and crystallised from benzene and few drops of pet. ether (40°-60°) (0.8 g), m.p. 156°. Lit. m.p. 153-54°.

Analysis	: Found	: C, 72.00%	; H, 6.92%
$C_{14}H_{16}O_3$	: requires	: c, 72.41%	; H, 6.89%

8,8-Dimethyl-6,7-dihydropyrano(3,2-g)benzopyran-2(H)-one (43)

8,8-Dimethyl-3,4,6,7-tetrahydropyrano(3,2-g)benzopyran-

2(H)-one (0.5 g), palladised charcoal (0.5 g) was refluxed in diphenyl ether (8 ml) for 5 hr. The reaction mixture was filtered hot and diluted with pet. ether (40°-60°) (5 ml) Separated product crystallised from benzene (0.2 g), m.p. 118°. Lit. m.p. 122-23°.

Analysis	:	Found	:	C, 73.45%	;	H, 6.12%
$C_{14}H_{14}O_3$	:	requires	:	C, 73.04%	;	H, 6.08%

8,8-Dimethyl-4-phenyl-3,4,6,7-tetrahydropyrano(3,2-g)benzopyran-2(H)-one (46)

7-Hydroxy-4-phenyl-3,4-dihydrocoumarin (2.4 g) in dioxane (15 ml), BF_3 etherate (0.6 ml) in dioxane (15 ml), was stirred with 2-methyl-3-butene-2-ol (0.85 ml) for 5 hr. The reaction mixture was then poured over ice water.

Next day the solution mixture was extracted with ether. The product thus obtained was heated at 180°-200° gave the product (46) which was purified by column chromatography, crystallised from benzene and few drops of pet. ether (1 g), m.p. 162°.

Analysis	:	Found	:	C, 77.47%	;	H, 6.38%
$C_{20}H_{20}O_3$	:	requires	:	C, 77.92%	;	H, 6.49%

8,8-Dimethyl-4-phenyl-6,7-dihydropyrano(3,2-g)benzopyran-2(H)-one (47)

8,8-Dimethyl-4-phenyl-3,4,6,7-tetrahydropyrano(3,2-g) benzopyran-2(H)-one (0.5 g) in diphenyl ether (8 ml) was refluxed with palladised charcoal (0.5 g) for 5 hours. The reaction was worked up as usual. The product obtained crystallised from benzene (0.3 g), m.p. 200°. Lit. m.p. 199-200°

Analysis : Found : C, 78.00% ; H, 5.48%

$C_{20}H_{18}O_3$: requires : C, 78.43% ; H, 5.88%

7-Allyloxy-4-phenyl-3,4-dihydrobenzopyran-2(H)-one (49)

A mixture of 7-hydroxy-4-phenyl-3,4-dihydrocoumarin (2.4 g), allylbromide (1.5 ml) in dry acetone (60 ml) was refluxed with anhydrous potassium carbonate (10 g) for 5 to 6 hr. After the reaction the acetone was decanted and the excess of acetone was distilled out. The product was purified by crystallisation which crystallised from petroleum ether (40°-60°) and few drops of benzene (2.0 g), m.p. 65-70°.

Analysis : Found : C, 76.78% ; H, 5.87%

$C_{18}H_{16}O_3$: requires : C, 77.13% ; H, 5.71%

7-Hydroxy-8-allyl-4-phenyl-3,4-dihydrobenzopyran-2(H)-one (50)

7-Allyloxy-4-phenyl-3,4-dihydrocoumarin (2 g) was refluxed in N,N-dimethylaniline (15 ml) for 8 hr. The reaction mixture was cooled and poured over cold dil. HCl and extracted with chloroform. The excess of chloroform was removed and subjected to column chromatography using benzene as eluent. The product obtained crystallised from benzene and few drops of pet. ether (40°-60°) (1.0 g), m.p. 141°.

Analysis	:	Found	:	C, 76.80%	;	H, 5.75%
$C_{18}H_{16}O_3$	:	requires	:	C, 77.17%	;	H, 5.71%

7-Hydroxy-8-propyl-4-phenylbenzopyran-2(H)-one (51)

7-Hydroxy-8-allyl-4-phenyl-3,4-dihydrobenzopyran-2(H)-one (0.5 g) in diphenylether (8 ml) was refluxed with Pd/c (10%, 0.5 g) for 8 hr. The reaction mixture was filtered hot, cooled and diluted with pet. ether (40°-60°) (5 ml). Separated product was filtered and crystallised from benzene and few drops of pet. ether (0.2 g), m.p. 188°.

Analysis	:	Found	:	C, 77.45%	;	H, 5.83%
$C_{18}H_{16}O_3$	:	requires	:	C, 77.17%	;	H, 5.71%

7-Hydroxy-8-allyl-4-phenylbenzopyran-2(H)-one (52)

7-Hydroxy-8-allyl-4-phenyl-3,4-dihydrobenzopyran-2(H)-

one (0.5 g) in drybenzene was refluxed with DDQ (0.5 g) in dry benzene for 10 hr. The reaction mixture was filtered hot and the excess of benzene was distilled. The compound was further purified by column chromatography and it crystallised from benzene (0.3 g), m.p. 194°.

Analysis	:	Found	:	C, 78.05%	;	H, 5.43%
$C_{18}H_{14}O_3$	:	requires	:	C, 77.69%	;	H, 5.03%

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