CHAPTER-II

SYNTHESIS

OF

FUROBENZOPYRANS

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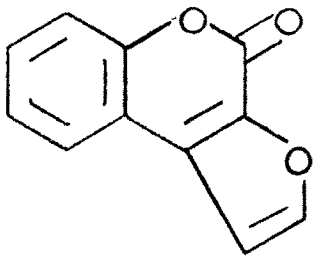
Many naturally occuring coumarins contain furan ring system. Furocoumarins also known as Furobenzopyran-2-ones occur mainly in Psoralea Corylifolia, Xanthoxylum flavum or Angelica archangelica or Bergamot fruit.[1] There are 8 different isomeric forms of furocoumarins found in literature. They can be synthesised by starting with suitably substituted coumarin derivative and then building up furan ring on it.

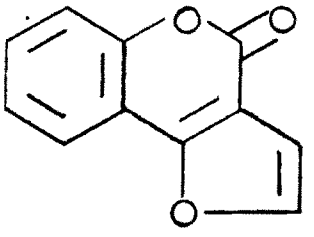
PHYSIOLOGICAL ACTIVITIES OF FUROBENZOPYRAN-2-ONES

Furocoumarins of type (6) known as psoralens have received considerable attention on account of their therapeutic propeerties. Psoralen derivatives are used as Photochemotherapeutical drugs in PUVA (Psoralen Ultraviolet-A) therapy of dermatological disorders like Psoriasis,[2] vitiligo,[3] atropic eczema[4] and micosis fungoides[5] in tumour stage. Such compounds are useful tools for studying the structures of nucleic acid in molecular biology.

Xanthotoxin or 8-methoxypsoralen (10) (8-MOP) is a fish poison[6] but is non-toxic to mammals. Schonberg and Latif[7] observed that it possesses moluscicidal activity. Currently it is the only PUVA drug in general clinical use. However,



(1)



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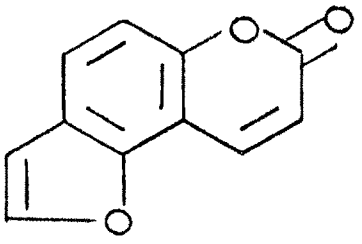

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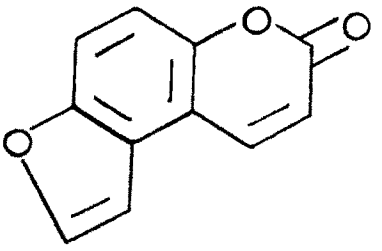

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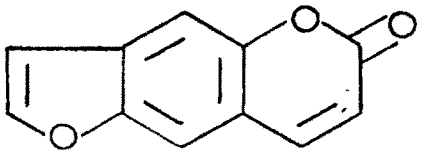

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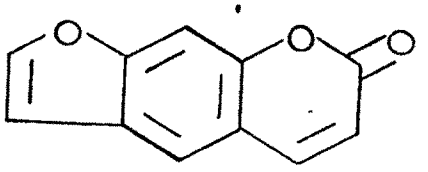


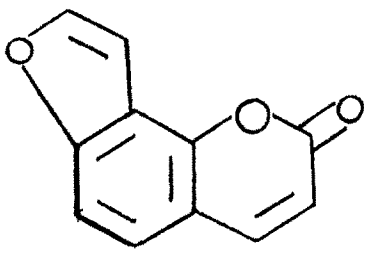
(6)

it is reported that 8-MOP produces unwarranted side effects in patients. Elwi[8] demonstrated that it produces fatty degradation of liver and adrenal haemorrhage if it is administreted in large doses to mammals, 8-MOP is used in treatment of leucoderma.[9] It has erythermal response to ultra violet light, a property which has been used clinically to prevent sunsburns.[10] 8-MOP in connection with UV-A erradiation has moderate mutagenic properties and was found to be carcinogenic[11] under certain conditions.

Pathak and Fellman[12] have studied the activating and fluroscent wavelengths of 37 furocoumarins and their biological photosensitizing action was investigated. Furocoumarins which induced definite photosensitized erythermal response on mammalian skin showed activation peaks in the region of 340-380 mμ and concomitantly the fluroscent peaks in the region of 420-460 mμ. The inactive furocoumarins did not show these specific activating fluroscent peaks.

STRUCTURE-ACTIVITY RELATIONSHIP

A study of structure activity relationship of erythermal activity of furocoumarins [13a,b] indicated that maximum photosensitizing activity lies in the parent compound Psoralen and its various derivatives have more or less reduced activity depending upon the nature and position of substituents. Free phenolic group inactivates molecule whereas the methyl



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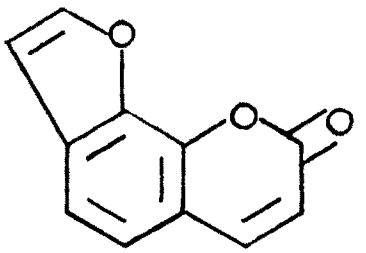

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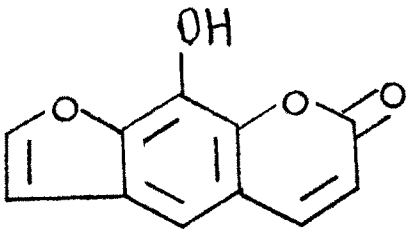

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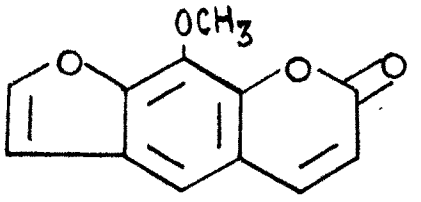
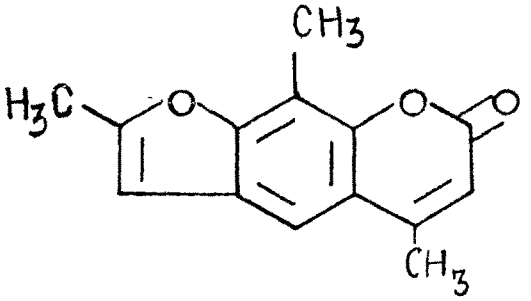


(10a)



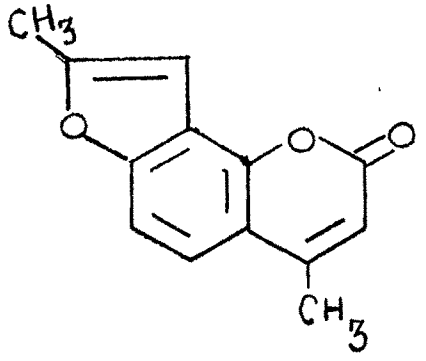
(10b)

ether is active, eg. xanthotoxol (9) is inactive whereas its methylether xanthotoxin (10a) is active.

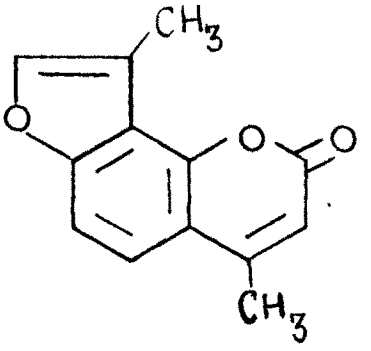
MODE OF ACTION

Psoralen (6) (7-H-furo(3,2-g)[1]-benzopyran-2-one), 8-methoxypsoralen (8-MOP) (10a), 4,5',8-trimethyl psoralen (10b) (TMP), 4,5'-dimethylangelicin[14a] (11a), 4,4'-dimethyl-angelicin[14b] (11b) and 6,4'-dimethyl angelicin[14b] (11c) are some photodynamically active furocoumarins. From these coumarins, 8-MOP and TMP are used in photochemotherapy.[2] These compounds are stable in dark, however, under UV-A irradiation they undergo modification. They can act through two mechanisms (i) The drug, on absorption of light quanta in the UV-visible region is promoted to electronically excited (singlet excited) state. It may decay to ground state through radiative or non-radiative pathways or (ii) It can be converted to triplet excited state, having longer life time and has a greater intrinsic activity. Triplet state can also decay to ground state through radiative and non-radiative pathway.

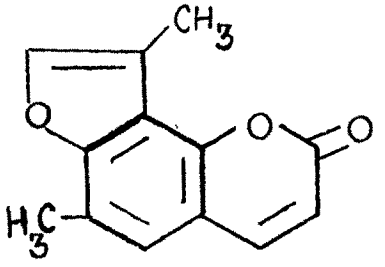
Psoralen photoreacts with DNA according to type (i) mechanism. It forms mono and diadducts through 3,4 and 4',5' double bonds. These double bonds are photoreactive sites in psoralen and can engage in reactions of C_4 cycloaddition with various substrates. Psoralen is intercalated between two base pairs of DNA and form monocycloadducts or diadducts with thyamine.[15,16,17] (A, B, C)



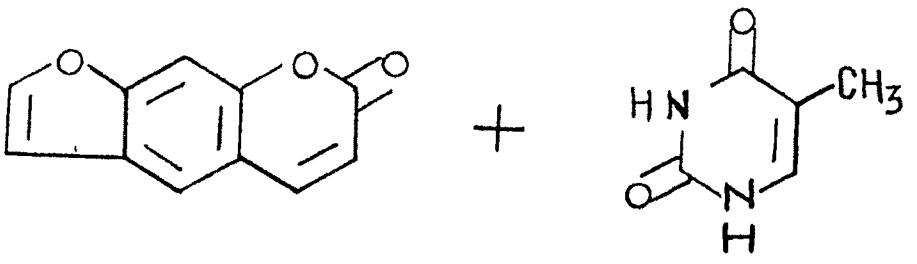
(11a)



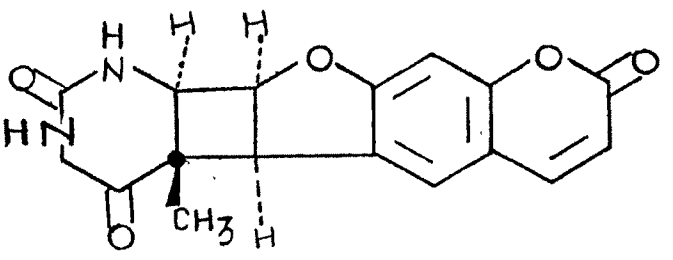
(11b)



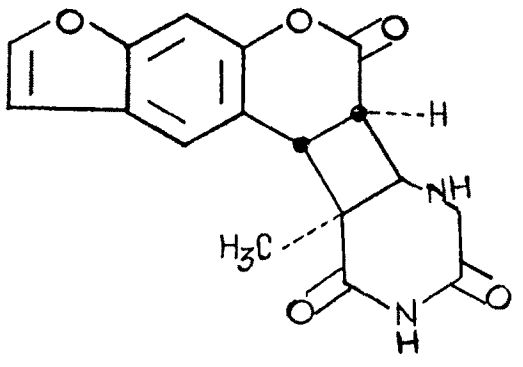
(11c)



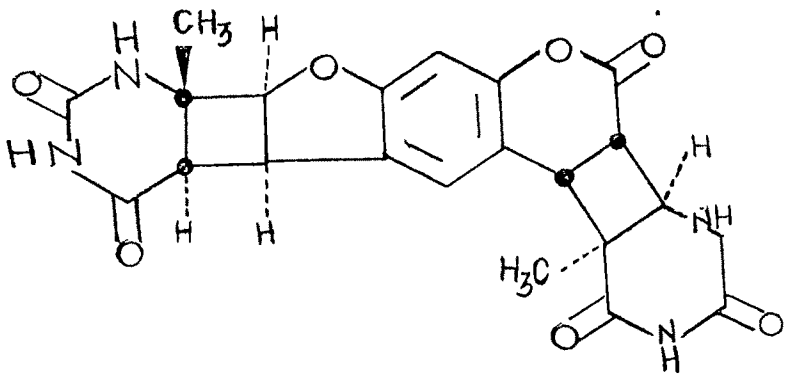
Psoralen + Thyamine



(A)



(B)



(C)

In this way an interstrand crosslinkage is formed which convalently conjugates the two chains of the DNA molecule[18] The capacity of various furocoumarins to form interstrand crosslinkages is different. There is correlation between the rate constant of formation of crosslinkages and the ability to induce skin erythema in the large series of Psoralens.[19,20]

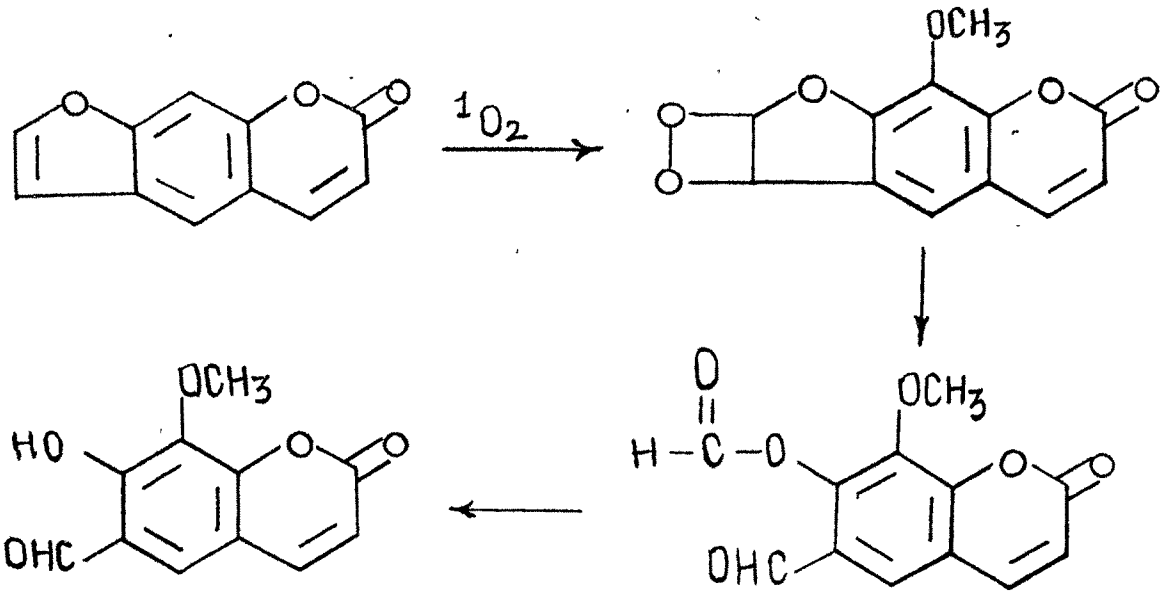
The repair of interstrand crosslinkage is much less effective than repair of monofunctional adducts. This mechanism of action is responsible for the antiproliferative, mutagenic and photocarcinogenic effects or alteration of the immune system.

Psoralens can accomplish their photosensitizing effects involving type (ii) mechanism by generation of singlet oxygen ($^1O_2$).[21] 8-MOP when irradiated at 365 nm in solution undergoes photodegradation as shown in Scheme-1. This photodegradation can be mediated by singlet oxygen and lead to the formation of 6-formyl-7-hydroxy-8-methoxy coumarin[22] (12) [Scheme-1].

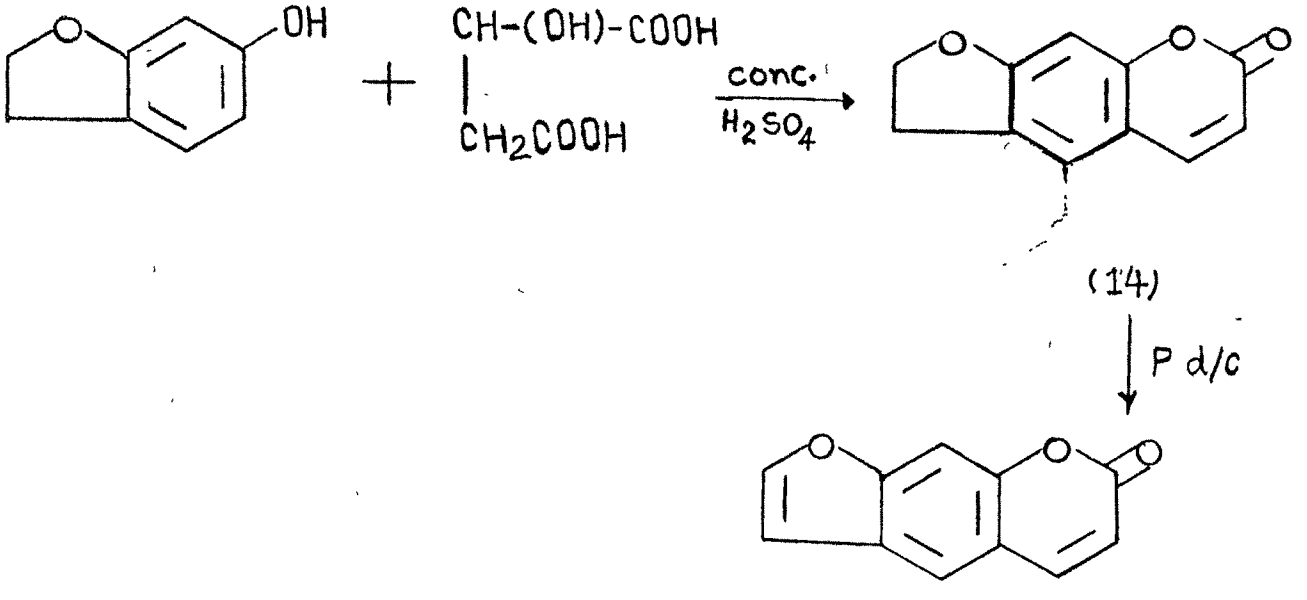
Due to the undesirable side effects of Psoralens used in photochemotherapy, search for new drugs in which acute or cronic side effects of Psoralens are reduced or eliminated was carried out.

The new monofunctional drugs, such as 3-carbethoxy psoralens or pyridopsoralens, which cannot form interstrand

Scheme-1



Scheme-2 Spath and Pailer[25]



crosslinkage in DNA, because of steric hinderance of 3-carbethoxy group[23] or pyridine ring,[24] do not usually have skin phototoxicity. Therefore, synthesis of such psoralens is needed.

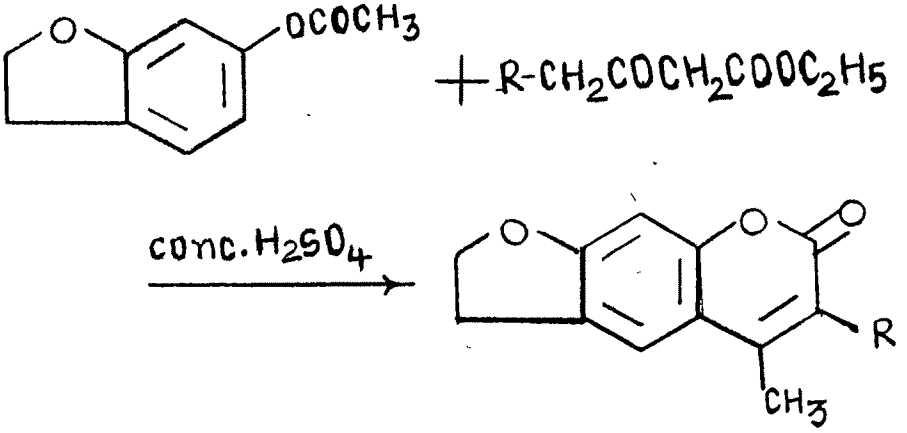
METHODS OF SYNTHESIS OF PSORALENS

There are different methods described in literature for the synthesis of psoralen and its derivatives. Spath and Pailer[25] carried out the condensation of 6-hydroxy coumarin (13) with malic acid in the presence of conc. H_2SO_4 & obtained 2,3-dihydropsoralen (14) which on dehydrogenation gave psoralen (15) [Scheme-2].

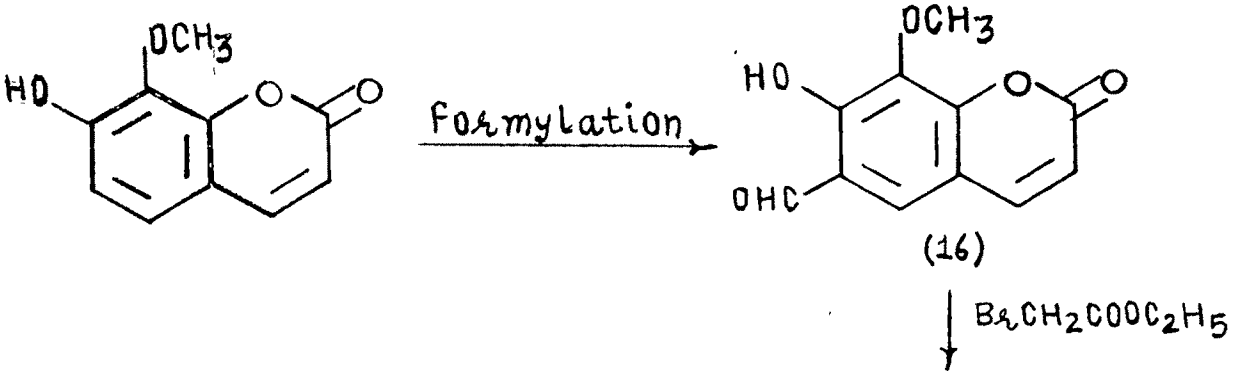
Later Horning and Reisner[26] prepared different 5-substituted 2,3-dihydropsoralen derivatives by condensing 6-acetoxycoumaran with variety of β-ketonic esters in presence of conc. H_2SO_4. [Scheme-3] Esse and Chirstenson[27] have extended this reaction to obtain 6-alkyl-2,3-dihydro-5-methylpsoralen by condensing apropriate α-alkyl-β-ketonic esters with 6-acetoxy coumaran. The main drawback in this method is that the dehydrogenation of dihydropsoralen derivatives with palladised charcoal gives poor yields of psoralen.

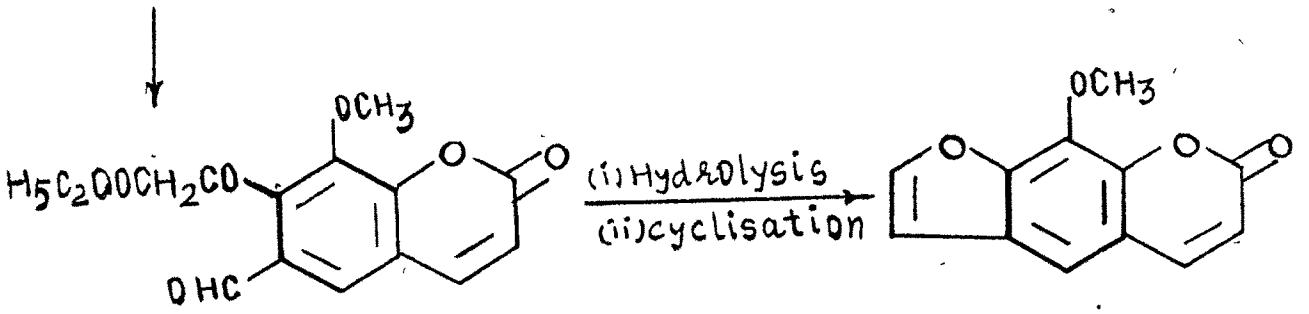
Rodighiero and Antonello[28] have synthesised8-methoxy psoralen by preparing 7-hydroxy-8-methoxy-6-formylcoumarin

Scheme-3 Horning and Reisner[26]

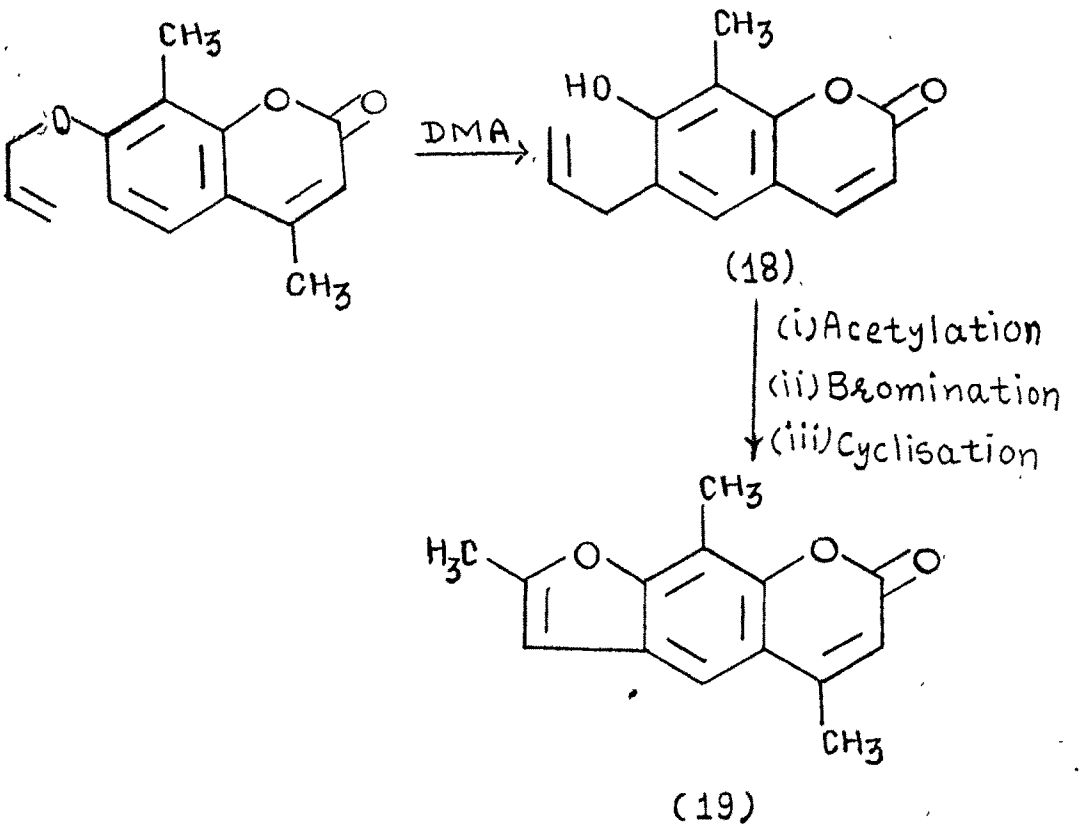


Scheme -4 Rodighiero and Antonello[28]





Scheme-5 Kaufmann et al[31]



(16) and then treating with ethylbromoacetate followed by hydrolysis and cyclisation. (Scheme4)

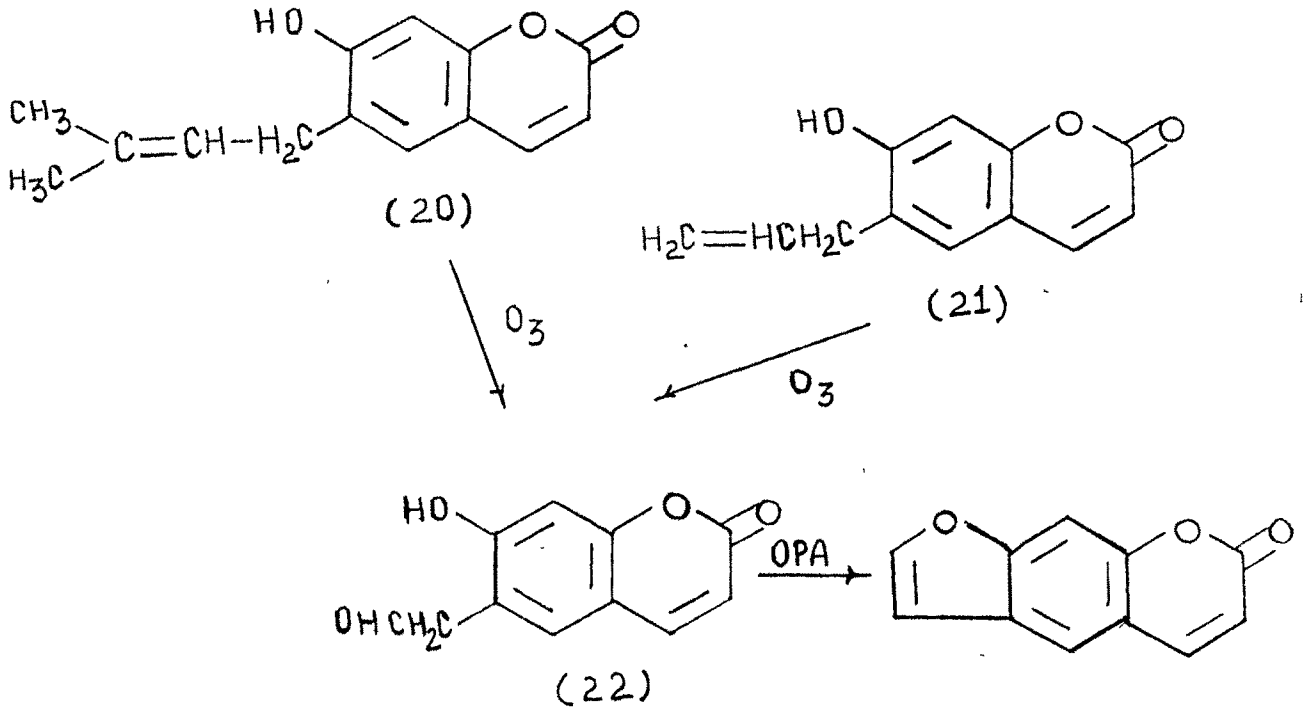
Limaye and Gangal[29] had synthesised 3',4'-dimethylpsoralen from 7-hydroxy-6-acetyl-4-methyl coumarin. Foster et al.[30] synthesised psoralen by first subjecting 6-hydroxy coumaran to Gatterman aldehyde synthesis and then condensing 6-hydroxy-5-formyl coumaran with cyanoacetic acid followed by hydrolysis of cyno group, decarboxylation and dehydrogenation.

Kaufmann[31] had prepared 4,5',8-trimethylpsoralen (19) by Claisen rearrangement of 7-allyloxy-4,8-dimethyl coumarin (17) followed by acetylation, bromination and cyclisation of compound (18). [Scheme-5]

Seshadri and coworkes[32] had obtained psoralen by ozonolysis of 6-dimethylallyl 7-hydroxycoumarin (20) and 6-allyl-7-hydroxy coumarin (21) followed by cyclisation of aldehyde (22) with o-phosphoric acid [Scheme-6].

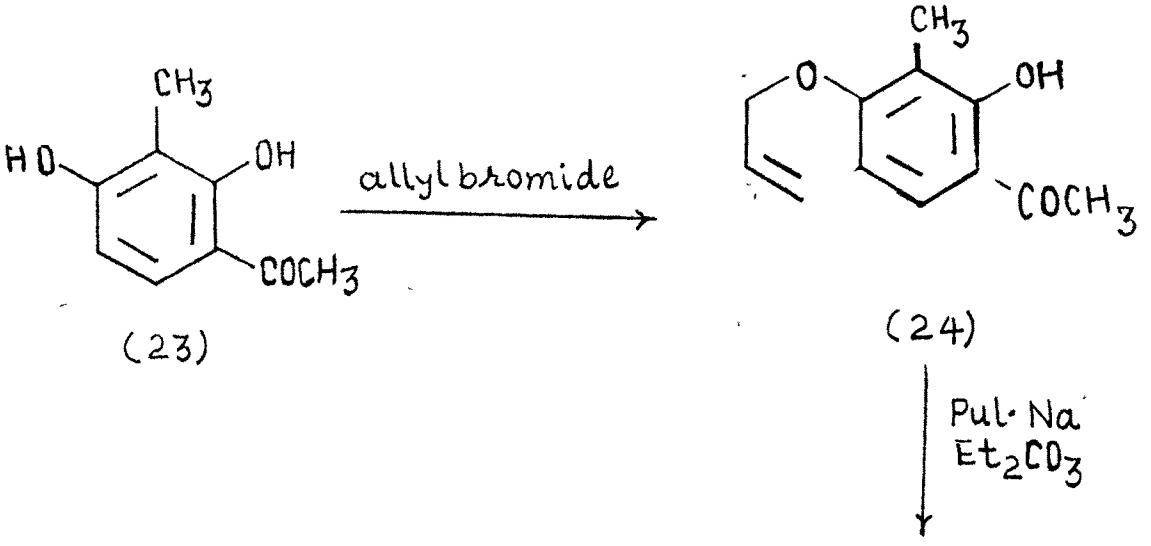
Dholakia and Trivedi[33] had synthesised 4-methoxy-5'-8-dimethylpsoralen (29) and 4-hydroxy-5',8-dimethylpsoralen (30), 2,4-dihydroxy-3-methyl acetophenone (23) was allylated with allylbromide to 4-allyloxy-2-hydroxy-3-methylacetophenone (24) which on treatment with pulverised Na & diethylcarbonate gave 4-hydroxy-7-allyloxy-8-methyl coumarin (25). This was

Scheme-6 Seshadri and coworkers[32]



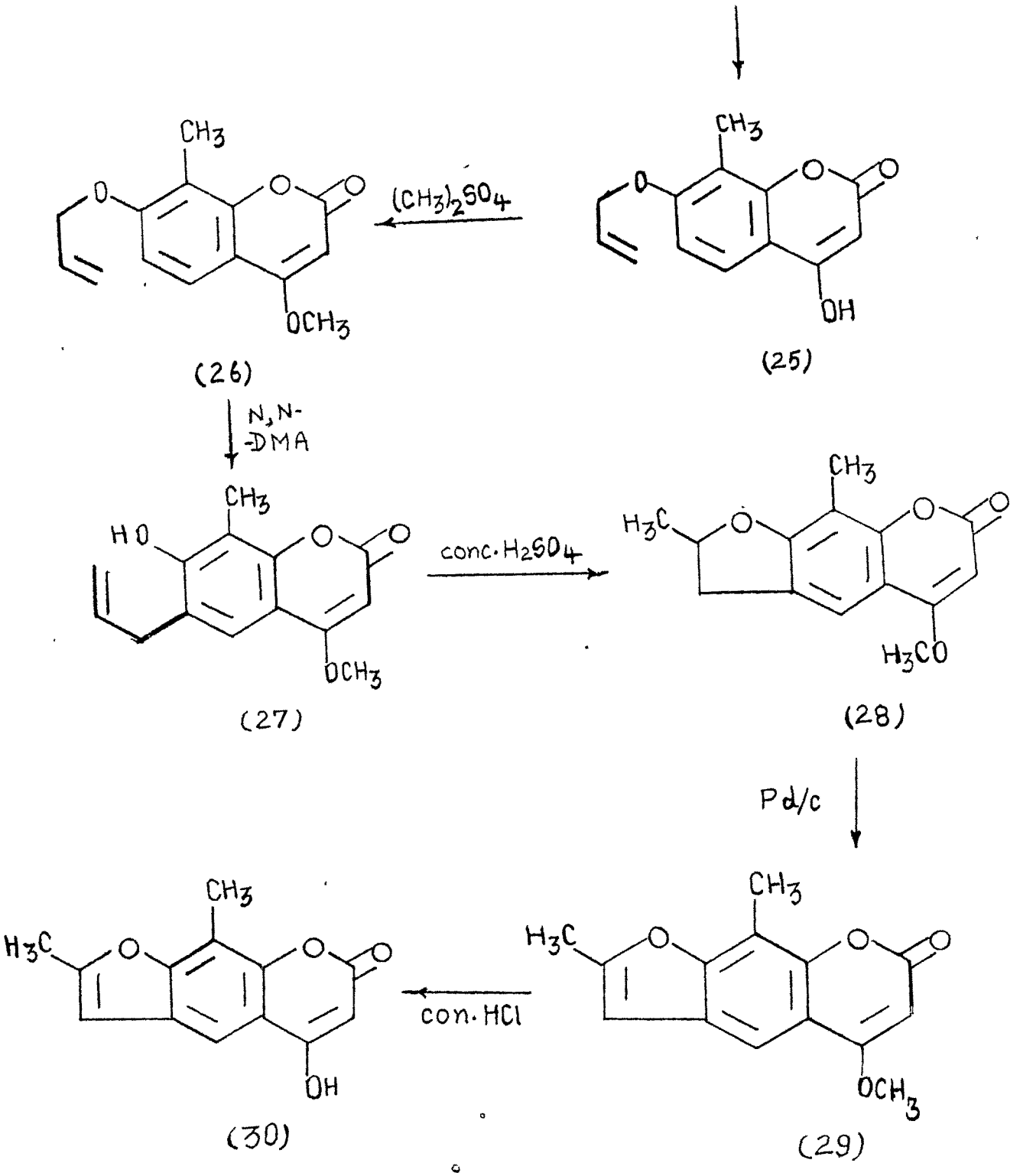
(22)

Scheme-7 Dholakia and Trivedi[33]



(23)

(24)


CH3
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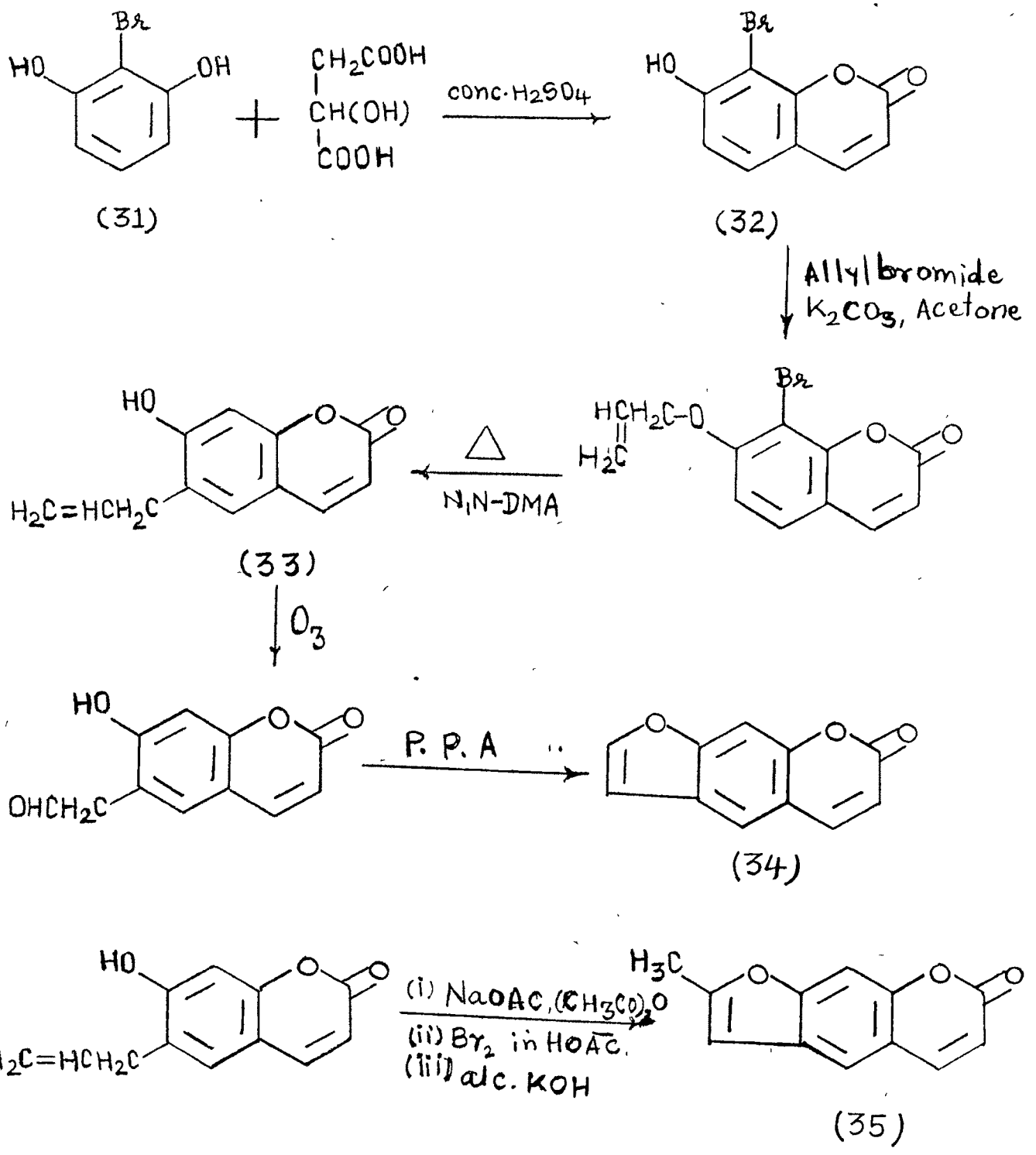
O
O
OCH3
(26)
(CH3)2SO4
CH3
O
O
O
OH
(25)
N,N-
-DMA
CH3
HO
O
O
OCH3
(27)
conc.H2SO4
CH3
H3C
O
O
O
H3CO
(28)
Pd/c
CH3
H3C
O
O
O
OCH3
(29)
con.HCl
CH3
H3C
O
O
O
OH
(30)

methylated and the methylether (26) was subjected to Claisen rearrangement to yield 4-methoxy-6-allyl-7-hydroxy-8-methyl coumarin (27) which on cyclisation with conc. H_2SO_4 gave 4-methoxy-5',8-dimethyl-4',5'-dihydropsoralen (28) which on dehydrogenation with Palladium charcoal gave compound (29) [Scheme-7]. The demethylation of (29) was carried out by refluxing it with conc. HCl to give (30). [Scheme-7]

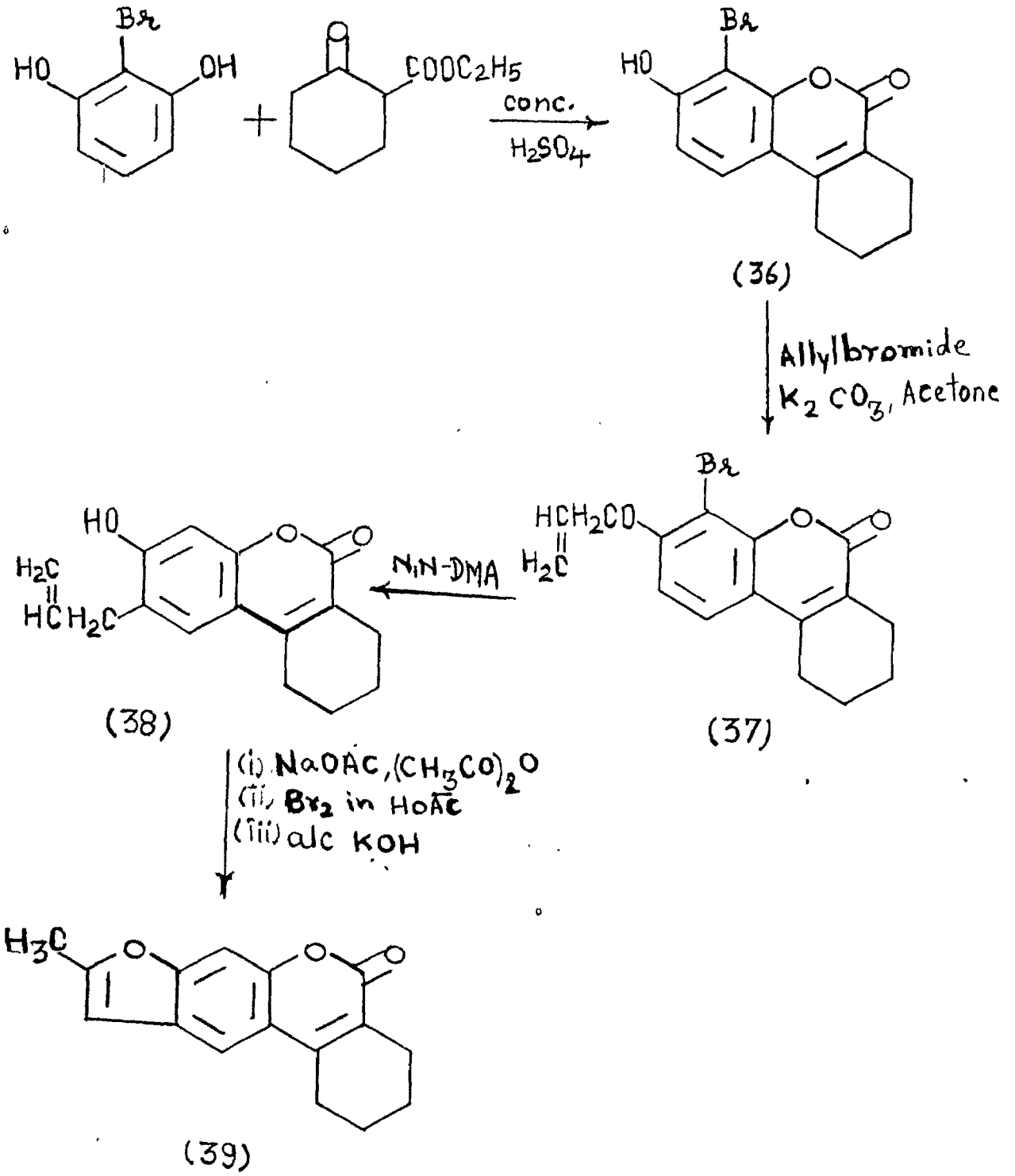
Pardanani and Trivedi[34] synthesised Psoralen (34) and 5'-methyl psoralen (35) by starting with 2-bromoresorcinol (31) which on condensation with malic acid gave 7-hydroxy-8-bromocoumarin (32). This on condensation with allylbromide followed by Claisen rearrangement gave 6-allyl-7-hydroxy coumarin (33), which on ozonolysis, followed by cyclisation gave psoralen (34). (33) on acetylation followed by bromination and cyclisation gave 5'-methyl psoralene (35), [Scheme -8].

Later on Shah and Trivedi[35] synthesised 3,4-cyclohexenopsoralene using the above procedure.8-Bromo-7-hydroxy-3,4-cyclohexenocoumarin (36), on allylation gave 7-allyloxy-8-bromo-3,4-cyclohexeno coumarin (37) [Scheme-9]. This on Claisen rearrangement in N,N-dimethylaniline gave 6-allyl-7-hydroxy-3,4-cyclohexenocoumarin (38). (38) on acetylation followed by bromination and cyclisation gave 2-methyl-3,4-cyclohexeno psoralene (39). [Scheme-9]

Scheme - 8 Paradnani and Trivedi[34]



Scheme-9 Shah and Trivedi

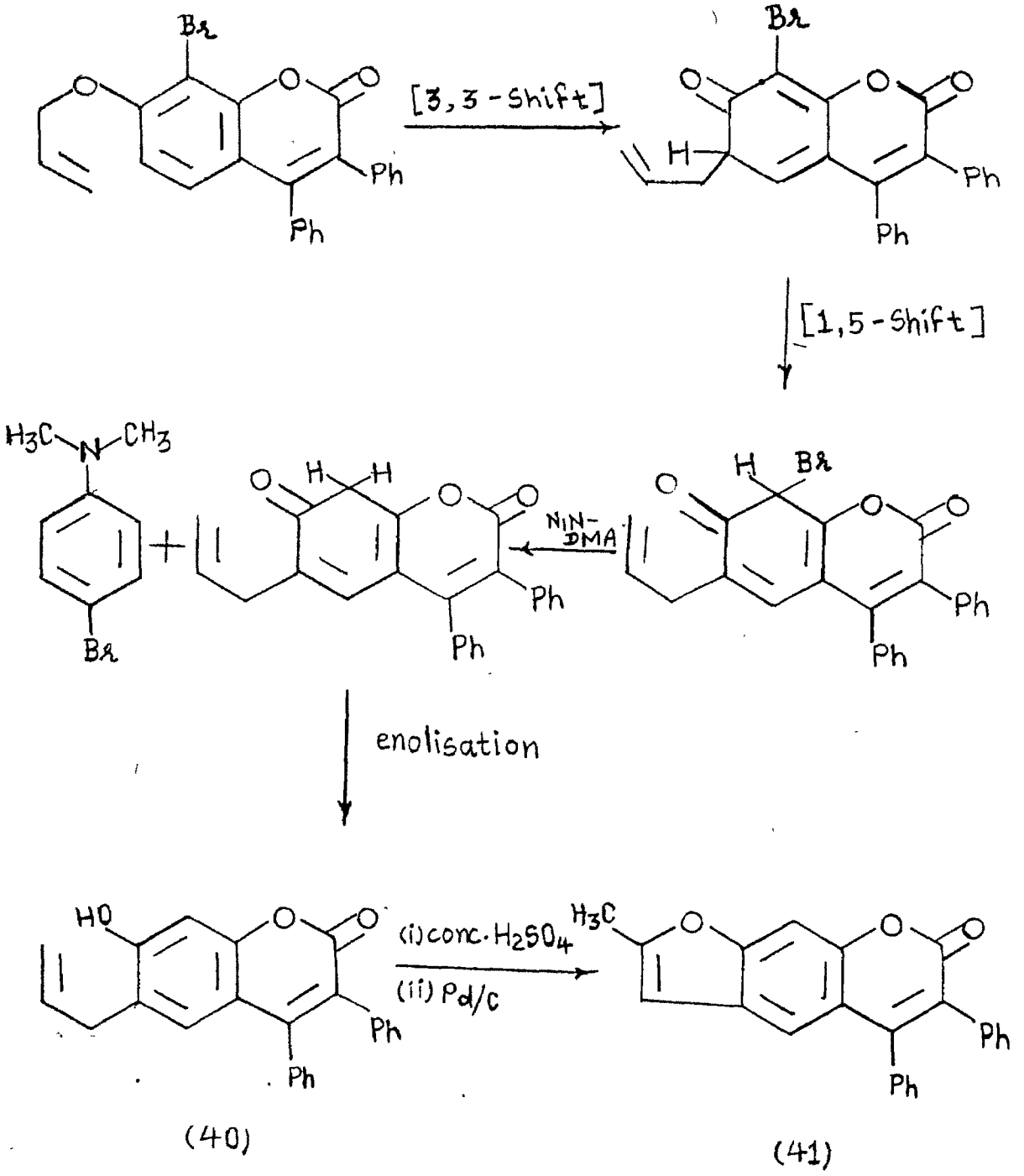


Similarly Desai and Trivedi[36] carried out Claisen rearrangement of 7-allyloxy-8-bromo-3,4-diphenyl coumarin and obtained 6-allylisomer (40), thus establishing the regiospecificity of this reaction for C-6 isomer. They explained the mechanism of elimination of bromine as shown in [Scheme-10]. (40) on cyclisation with conc. H_2SO_4 followed by dehydrogenation by Palladium charcoal gave compound (41).

Parekh and Trivedi[37] synthesised 4,5',8-trimethyl psoralen (42) by Claisen rearrangement of 7-allyloxy-4,8-dimethylcoumarin, which was further cyclised with conc. H_2SO_4 and dehydrogenation with palladised charcoal to give the product (42) [Scheme-11]

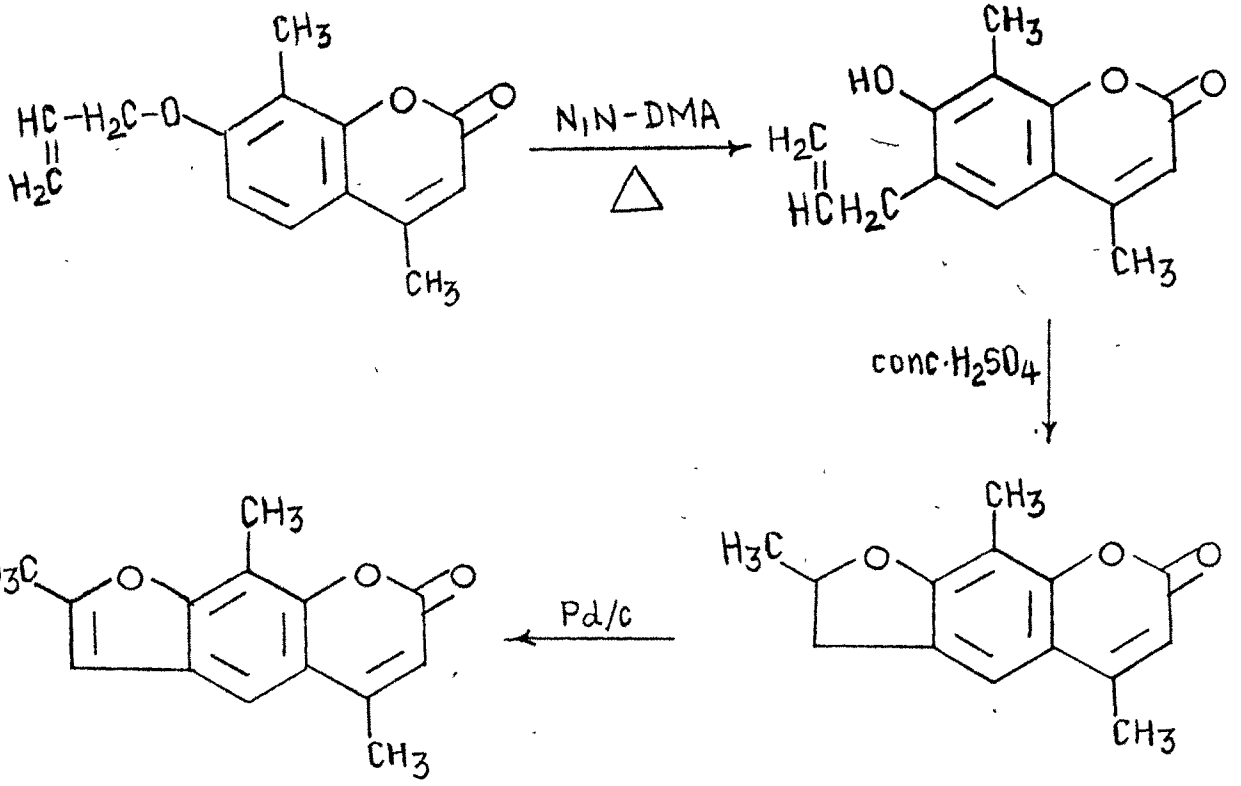
These are the methods by which bifunctional psoralens were synthesised. Shaikh and Trivedi[38] had synthesised 3,4-benzopsoralen (47) and 3,4-cyclohexenopsoralen (49) by starting with 2-methylresorcinol and condensing it with ethylcyclohexanone-2-carboxylate to give 3,4-cyclohexeno-7-hydroxy-8-methylcoumarin (43) which on allylation gave 7-allyloxy-8-methyl-3,4-cyclohexenocoumarin (44). This on Claisen rearrangement gave 6-allyl-7-hydroxy-8-methyl-3,4-cyclohexeno coumarin (45), which on cyclisation with conc. H_2SO_4 (80%) gave (46) and was further dehydrogenated with palladised charcoal to give compound (47). Compound (45) on treatment with OSO_4 and potassium periodate gave (48) which was further cycised with PPA to give (49) [Scheme-12].

Scheme - 10 Desai and Trivedi[36]



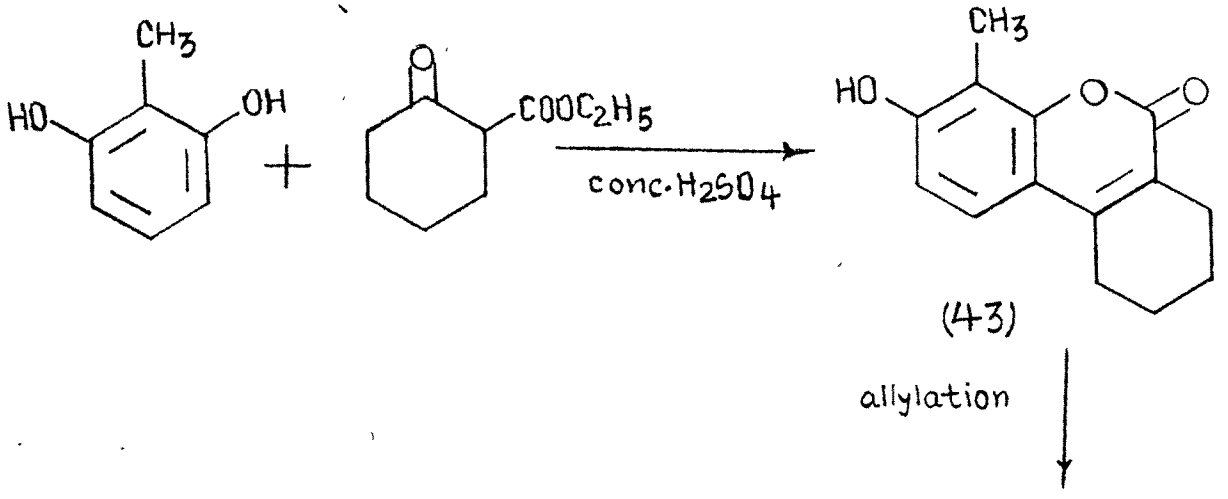
(40) (41)

Scheme-11 Parekh and Trivedi[37]



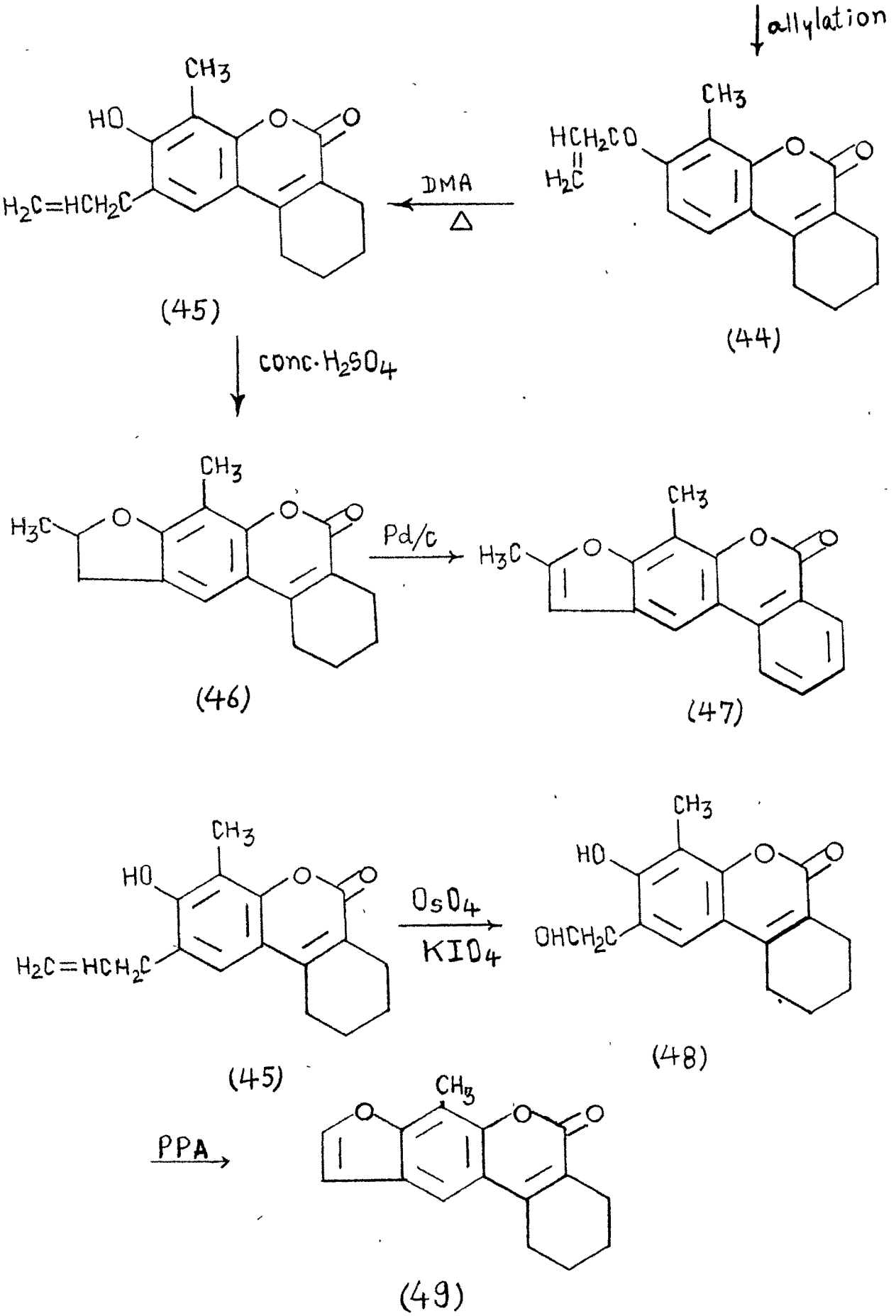
(42)

Scheme-12 Shaikh and Trivedi[38]



(43)

allylation


allylation
DMA
Δ
conc. H_2SO_4
Pd/C
OsO_4
KIO_4
PPA
(45)
(44)
(46)
(47)
(48)
(49)

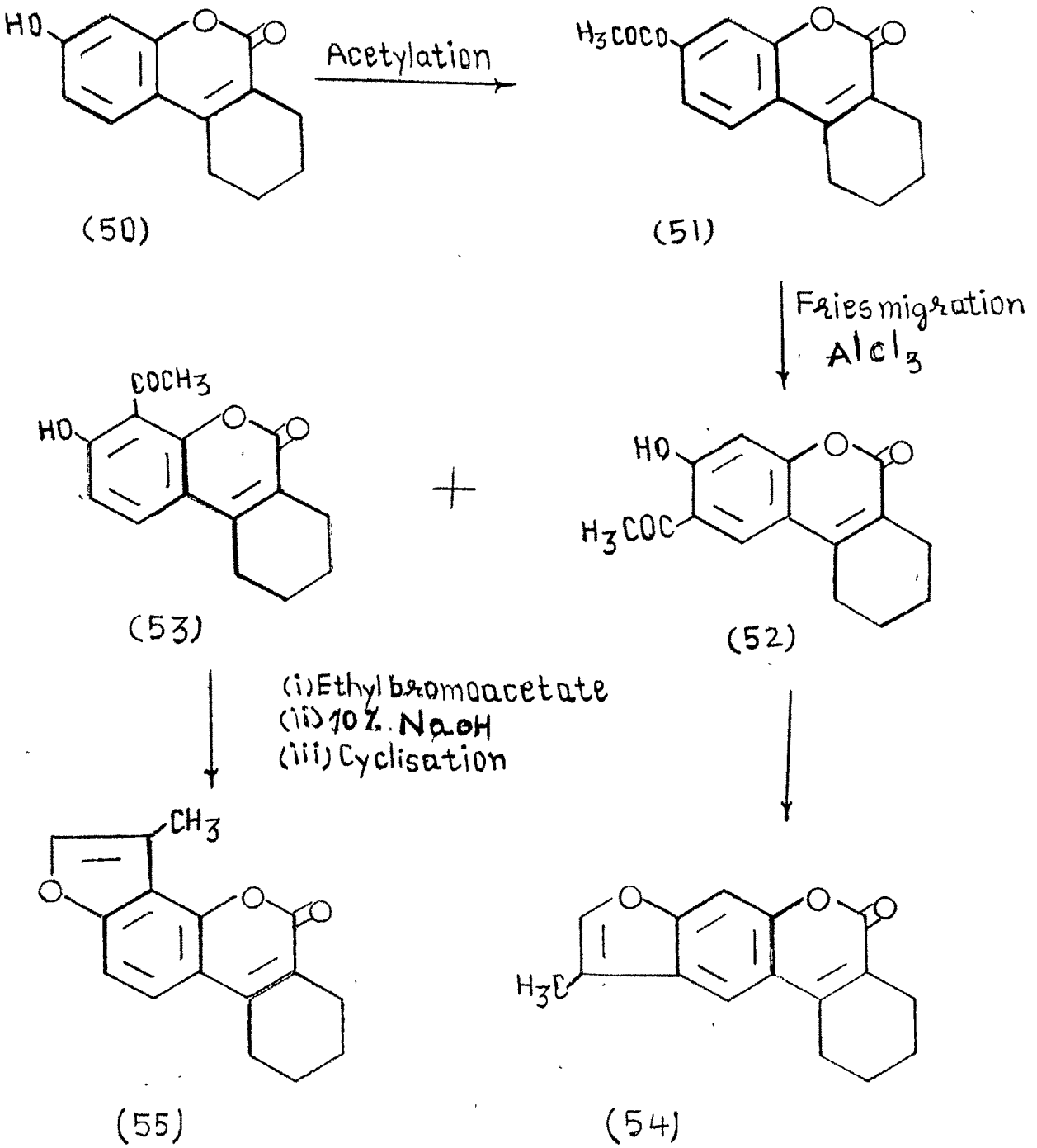
Parekh and Trivedi[39] have also synthesised monofunctional psoralens, 3,4-cyclohexenopsoralen (54) and 3,4-cyclohexeno angelicine (55) by starting with 7-hydroxy-3,4-cyclohexeno coumarin (50) which on acetylation gave its acetoxy derivative (51). The Fries migration of this acetoxycoumarin gave two isomers6-acetyl-3,4-cyclohexeno-7-hydroxycoumarin (52) and 8-acetyl-3,4-cyclohexeno-7-hydroxycoumarin (53). (52) and (53) both on condensation with ethylbromoacetate, followed by hydrolysis and cyclisation gave 3,4-cyclohexenopsoralen (54) and 3,4-cyclohexenoangelicin (55). [Scheme-13].

Bisgani et al.[40] have synthesised 3-carbethoxy psoralen (57) by starting with 2-hydroxy-4-methoxy-benzaldehyde (56) [Scheme-14]. Bisgani et al.[41] have also synthesised 3,4-pyridopsoralen (59) by condensing 6-acetoxy-7-alkylcoumarin (58) with 1-benzyl-3-ethoxy carbonyl piperidine-4-one [Scheme-15]. Here 3,4 position of coumarin ring is substituted by pyridine ring.

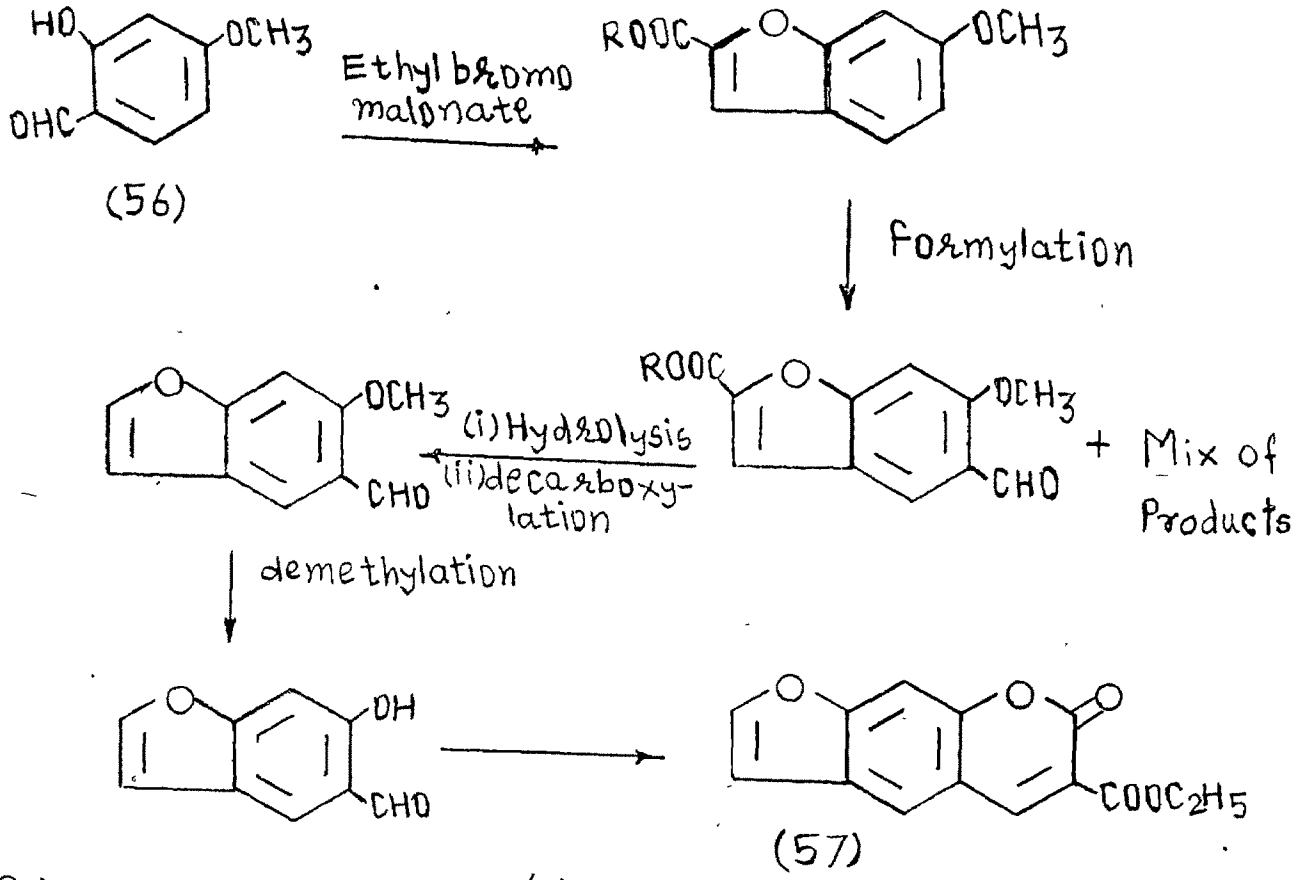
PRESENT WORK

In continuation of the work carried out by Shah and Trivedi, different linear furocoumarins are synthesised with methoxy group at 8-position of coumarin ring which increases its activity.

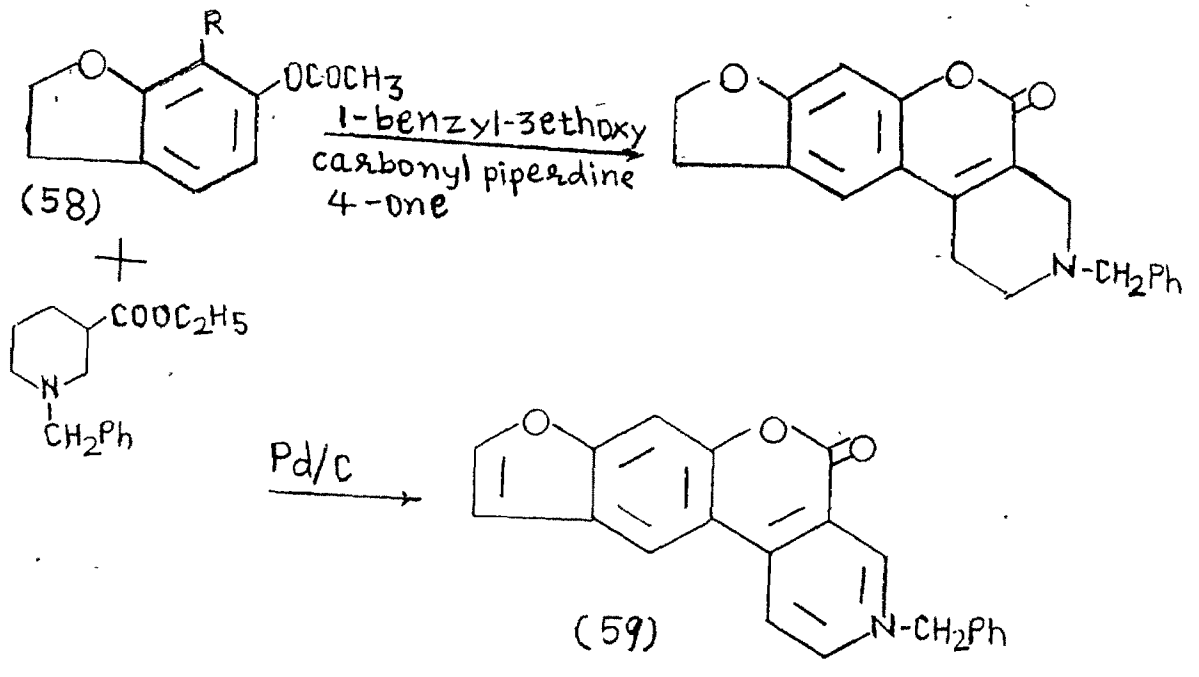
Scheme -13 Parekh and Trivedi[39]



Scheme-14 Bisgani et al[40]



Scheme-15 Bisgani et al[41]



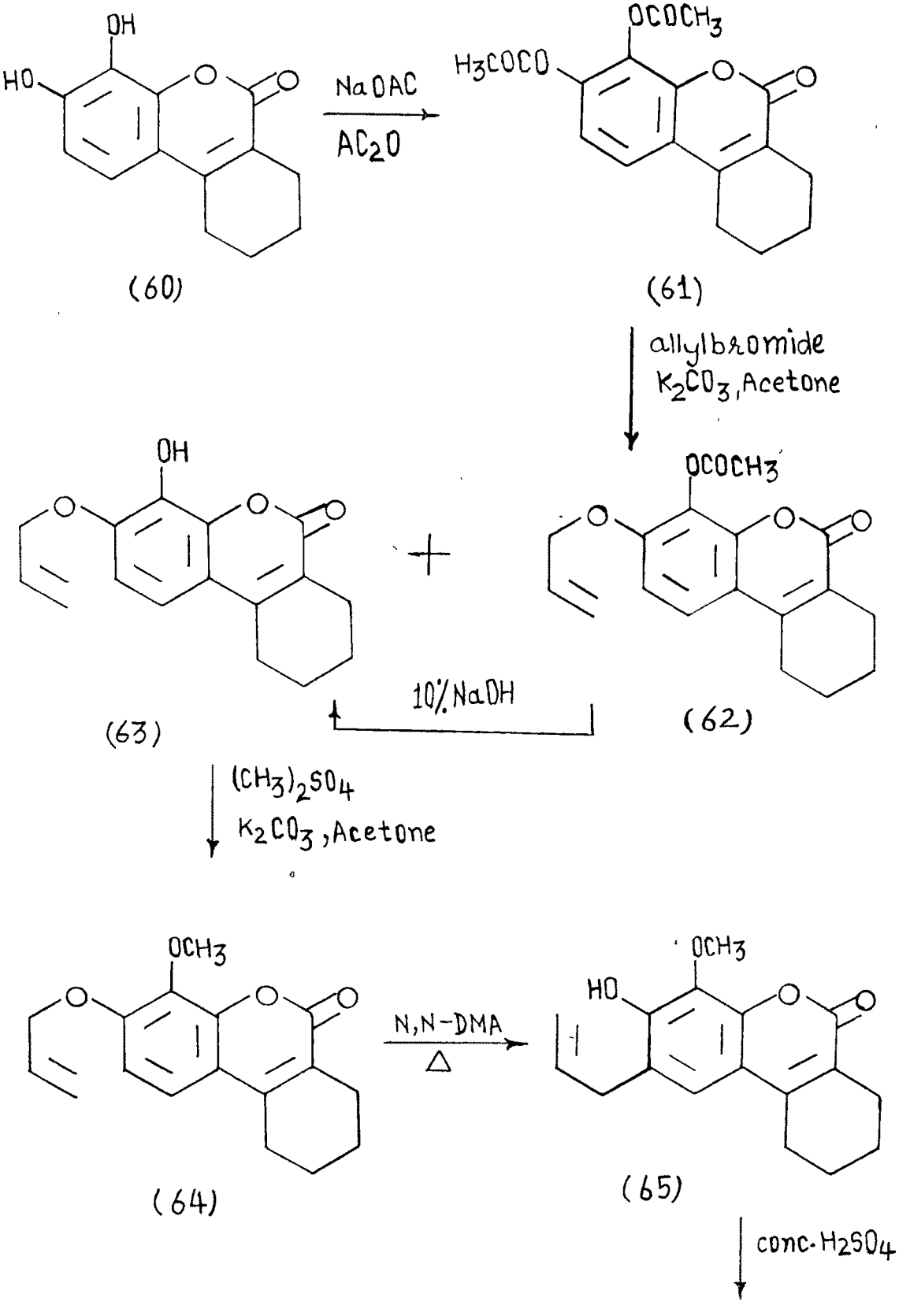
Synthesis of 7-methoxy-9-methyl-5-oxo-5H-benzofuro (6,5-c)-[2]-benzopyran (67)

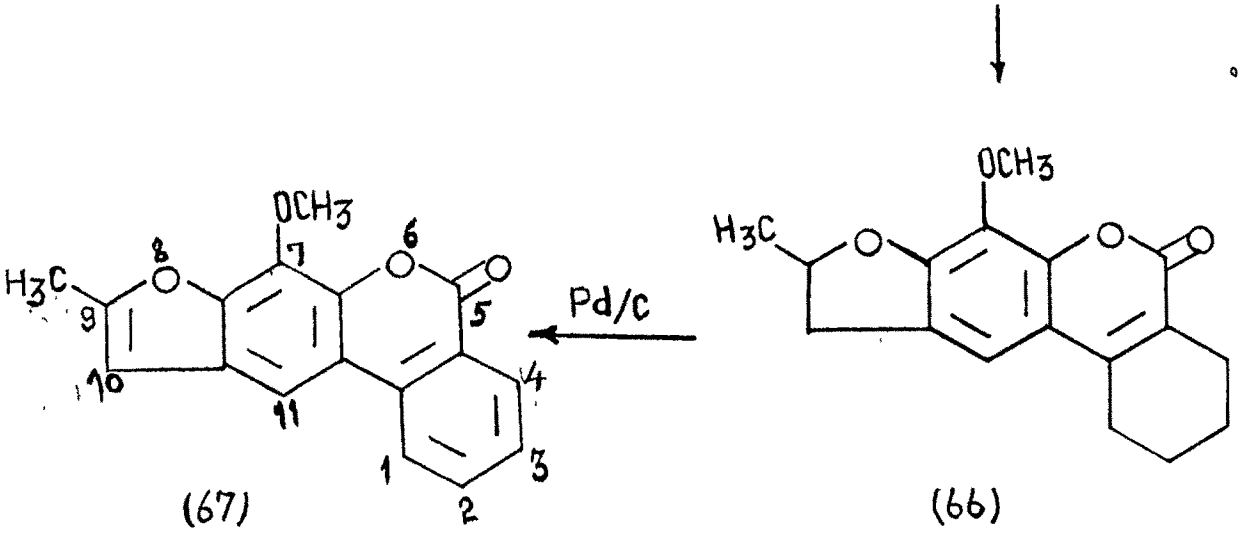
Pyrogallol on Pechmann[42] condensation with ethyl-2-cyclohexanonecarboxylate in presence of conc. sulfuric acid gave 3,4-dihydroxy-7,8,9,10-tetrahydro-6H-dibenzo(b,d)-pyran-6-one (60) which on acetylation with sodium acetate and acetic anhydride gave 3,4-diacetoxy-7,8,9,10-tetrahydro-6H-dibenzo (b,d)-pyran-6-one (61). The NMR spectra showed two singlets at δ 2.3 and 2.4 for acetoxy group at C-3 and C-4 positions. Compound (61) when reacted with one mole of allylbromide in presence of anhydrous potassium carbonate and dry acetone gave two products, one aqueous sodium hydroxide insoluble 3-allyloxy-4-acetoxy7,8,9,10-tetrahydro-6H-dibenzo (b,d)-pyran-6-one (62) and another aqueous sodium hydroxide soluble, 3-allyloxy-4-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo-(b,d)-pyran-6-one (63) [Scheme-16]. The NMR spectra of compound (62) exhibited singlet at δ 2.4 for $-OCOCH_3$ group and three signals at δ 4.65, 5.3 and 5.8-6.1 for allyl group indicating the presence of allyl and acetoxy group. [illegible]

Compound (62) on hydrolysis with 10% alcoholic sodium hydroxide gave compound which has same m.p., and m.m.p. as compound (63).

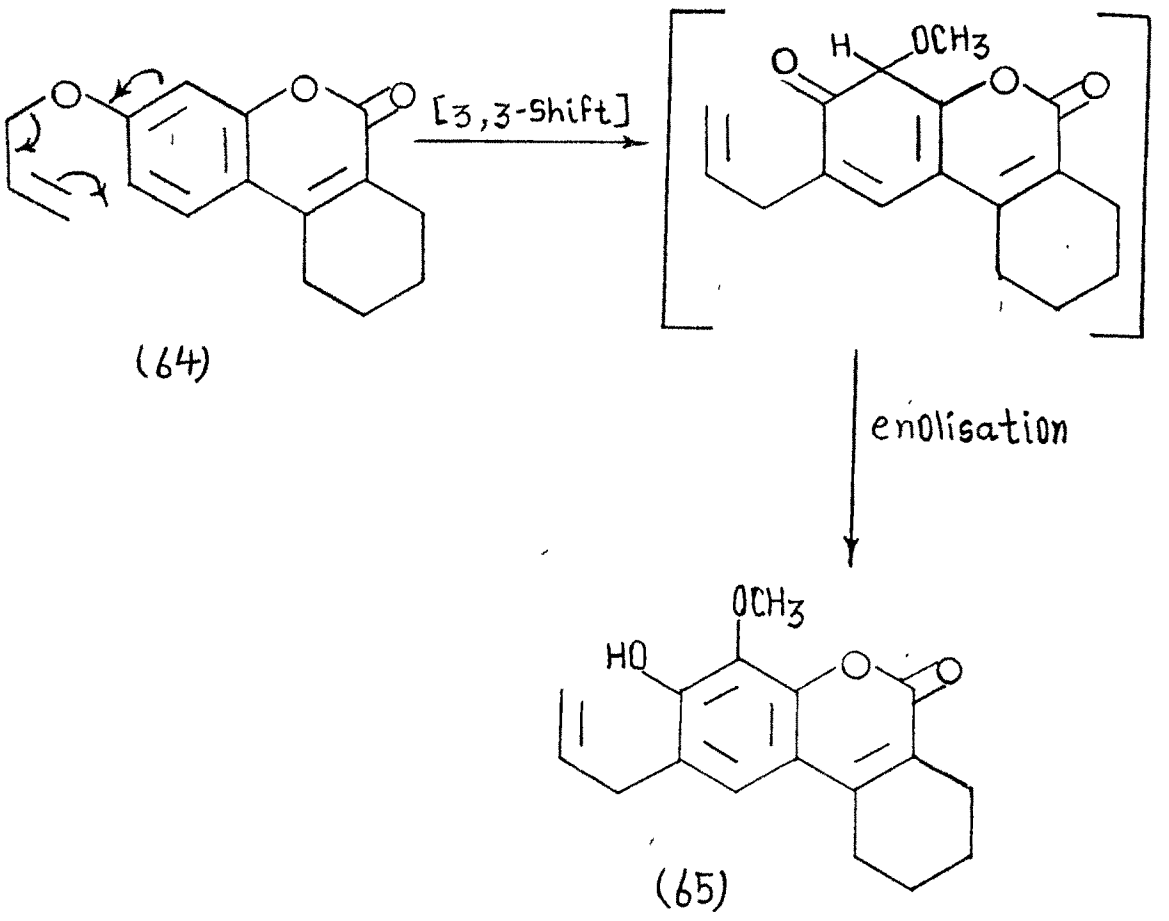
This compound (63) on condensation with dimethylsulfate

Scheme -16


OH
HO
NaOAC
AC_2O
$OCOCH_3$
H_3COCO
(60)
(61)
allylbromide
K_2CO_3, Acetone
OH
$OCOCH_3$
10% NaOH
(63)
(62)
$(CH_3)_2SO_4$
K_2CO_3, Acetone
OCH_3
N,N-DMA
Δ
OCH_3
HO
(64)
(65)
conc. H_2SO_4



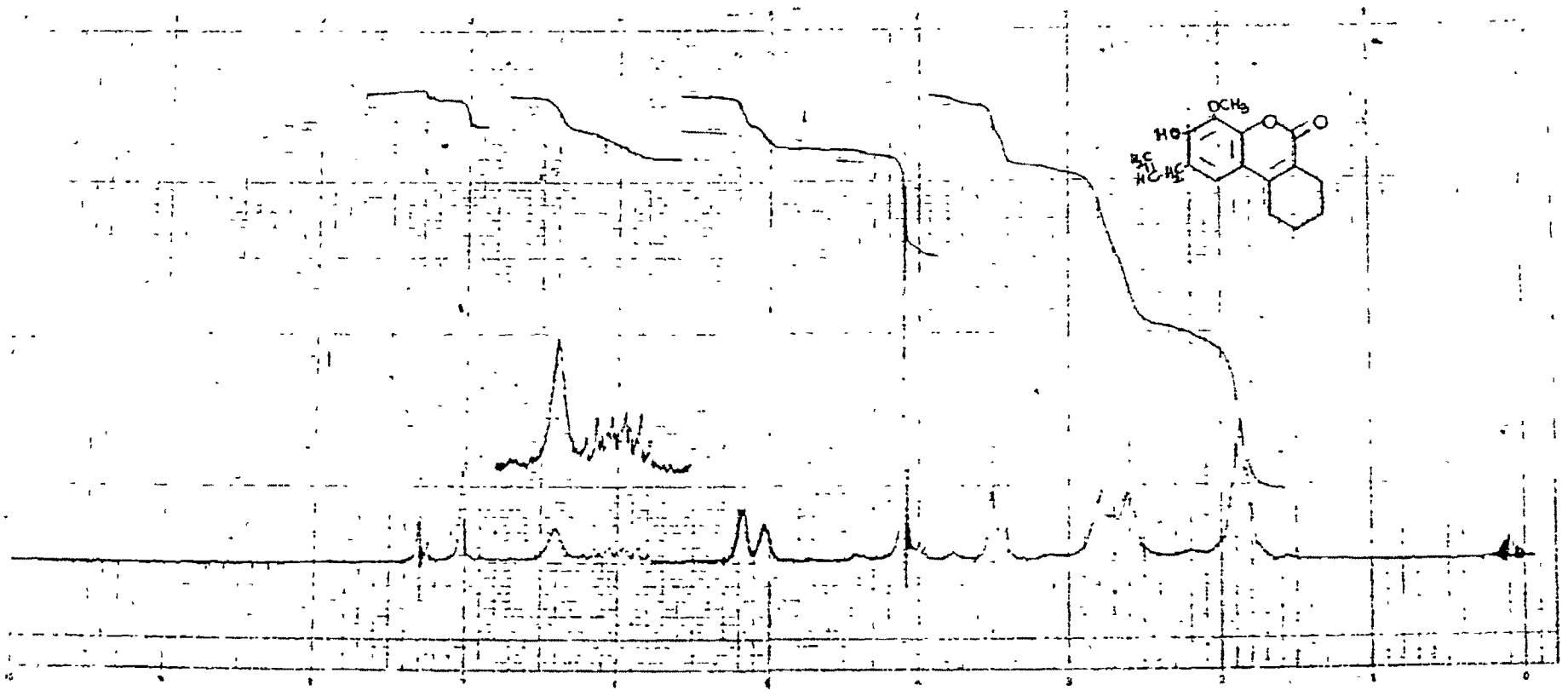
Scheme -17 Mechanism of Claisen Rearrangement



and anhydrous potassium carbonate in dry acetone gave 3-allyloxy-4-methoxy-7,8,9,10-tetrahydro-6H-dibenzo(b,d)-pyran-6-one (64). The NMR spectra of (64) exhibited the signals at δ 3.95 as singlet for $-OCH_3$ group. Signals of allyl group are as usual at δ 4.65, 5.2 and 5.8-6.1. Two doublets, one at δ 6.8 (J=9Hz) for proton at C-1 and another at δ 7.2 for proton at C-2 (J=9Hz) indicating that position 1 and 2 on aromatic nucleus are free to couple.

Compound (64) when subjected to Claisen rearrangement in N,N-dimethylaniline furnished 2-allyl-3-hydroxy-4-methoxy-7,8,9,10-tetrahydro-6H-dibenzo(b,d)-pyran-6-one (65). The mechanism isshown in Scheme-17. NMR spectra of this compound showed only one singlet at δ 6.95 for proton at C-1 indicating the migration took place at C-2 position. (Two doublets present inprevious spectra disappeared). Singlet at δ 6.3 disappeared on adding D_2O indicated the presence of free -OH group. (Fig.1)

(65) on tituration with H_2SO_4 (80%) furnished 7-methoxy-9-methyl-1,2,3,4,9,10-hexahydro-5-oxo-5H-benzofuro (6,5-c)-benzopyran (66), the structure of which was established by NMR spectrum ($CDCl_3$) which exhibited characteristic double doublets for two geminal protons at position 10, one at δ 2.8 (J=18,8Hz) and another at δ 3.2 (J=18,8Hz). This signal is overlapped by signals of C-3 and C-4 protons. The methyl group at C-9 appeared as doublet at δ 1.5 and proton at C-9

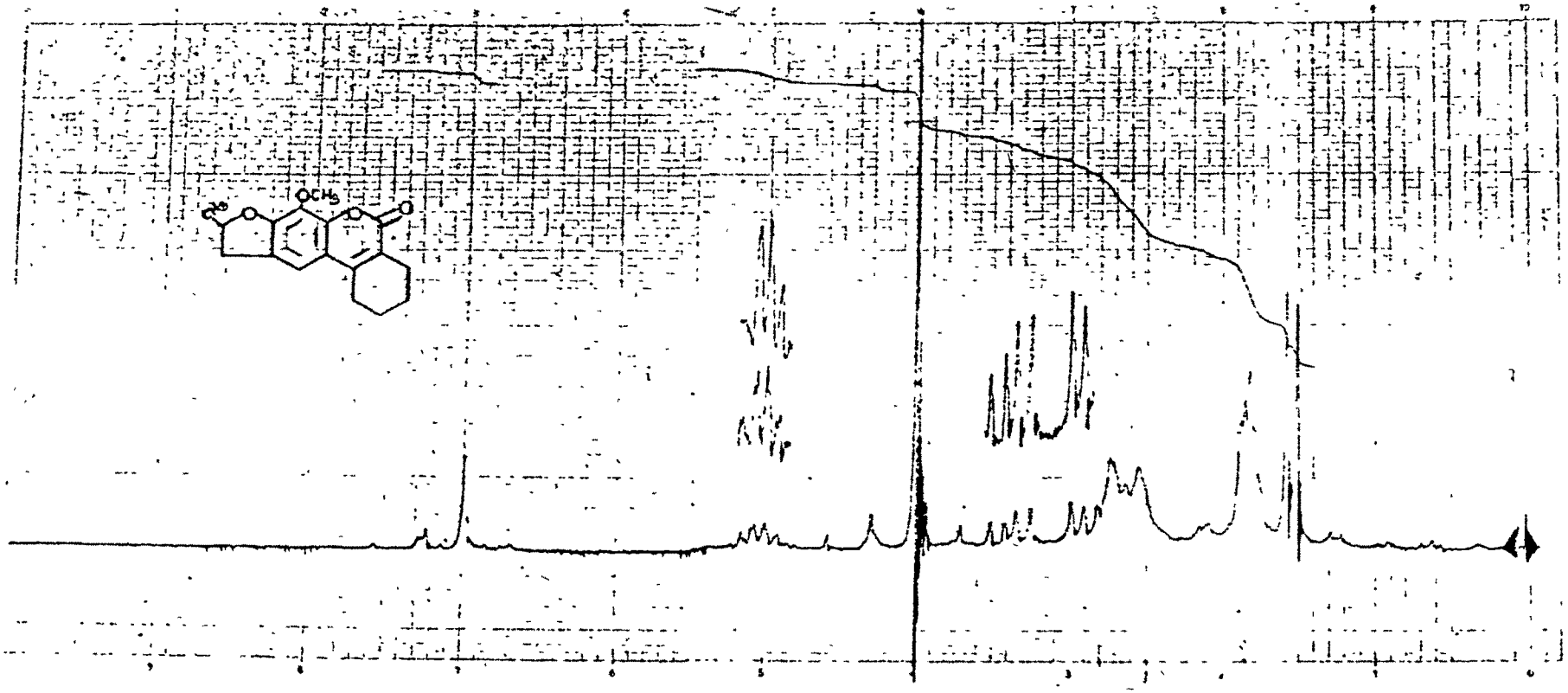


(fig-1) 2-Allyl-3-hydroxy-4-methoxy-7,8,9,10-tetrahydro-dibenzo-(b,d)-pyran-6(H)-one (65)

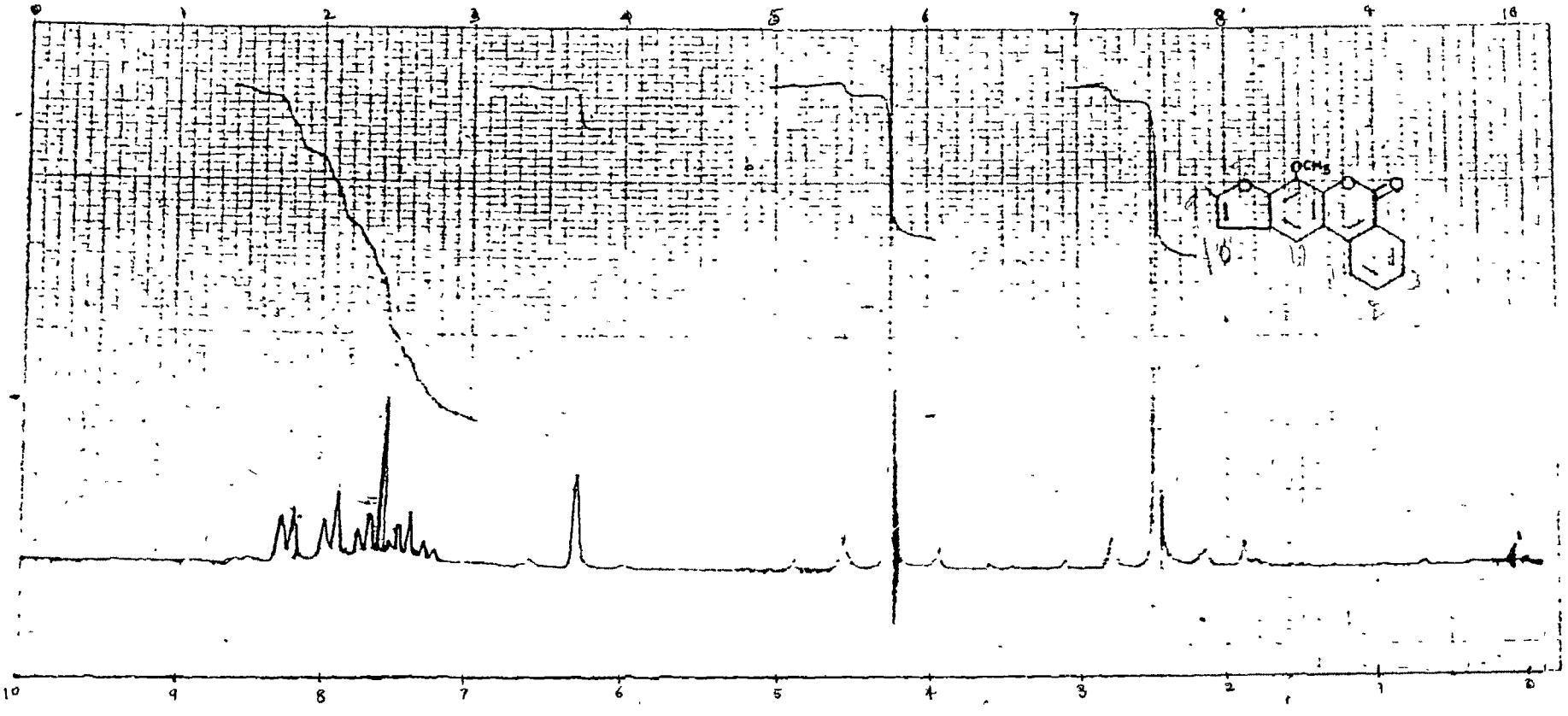
appeared as multiplet at δ 5.0. Singlet at δ 6.95 in down field region indicated the presence of only one aromatic proton at C-11. Methoxy group at C-7 appeared as singlet at δ 3.95 (Fig. 2). Compound (66) when refluxed with diphenyl ether with palladised charcoal (10%) underwent dehydrogenation to yield 7-methoxy-9-methyl-5-oxo-5H-benzofuro (6,5-c)-benzopyran (67), the structure of which was established by PMR spectrum ($CDCl_3$) exhibiting signals at δ 2.4, singlet for methyl group at C-9, one singlet at δ 4.1 for methoxy group at C-7, and one singlet at δ 6.2 for proton at C-10. The proton at C-11 appeared as singlet at δ 7.45. The protons at C-2 and C-1 appeared as two doublets at δ 7.6 (J=9Hz) and 7.8 (J=9Hz) respectively. Proton at C-4 couples with C-2 and C-3 proton and appeared downfield at δ 8.1 as dd J=8, 1.5Hz. Proton at C-3 appeared as multiplet at δ 7.3 - 7.45, indicating the ortho coupling with C-2 and C-4 proton (Fig. 3). Here disappearance of two multiplets from upfield region and signals in aromatic region indicated that cyclohexene ring at 3 and 4 position of coumarin ring also get dehydrogenated. To get only furan ring dehydrogenated, method due to Kaufmann[31] is used which involves first acetylation of hydroxy group of Claisen rearrangement product (65) then addition of bromine to allylic double bond which follows subsequent ring closure.

Synthesis of 7-methoxy-9-methyl-1,2,3,4-tetrahydro-5-oxo-5H-benzofuro (6,5-c)-benzopyran (70)

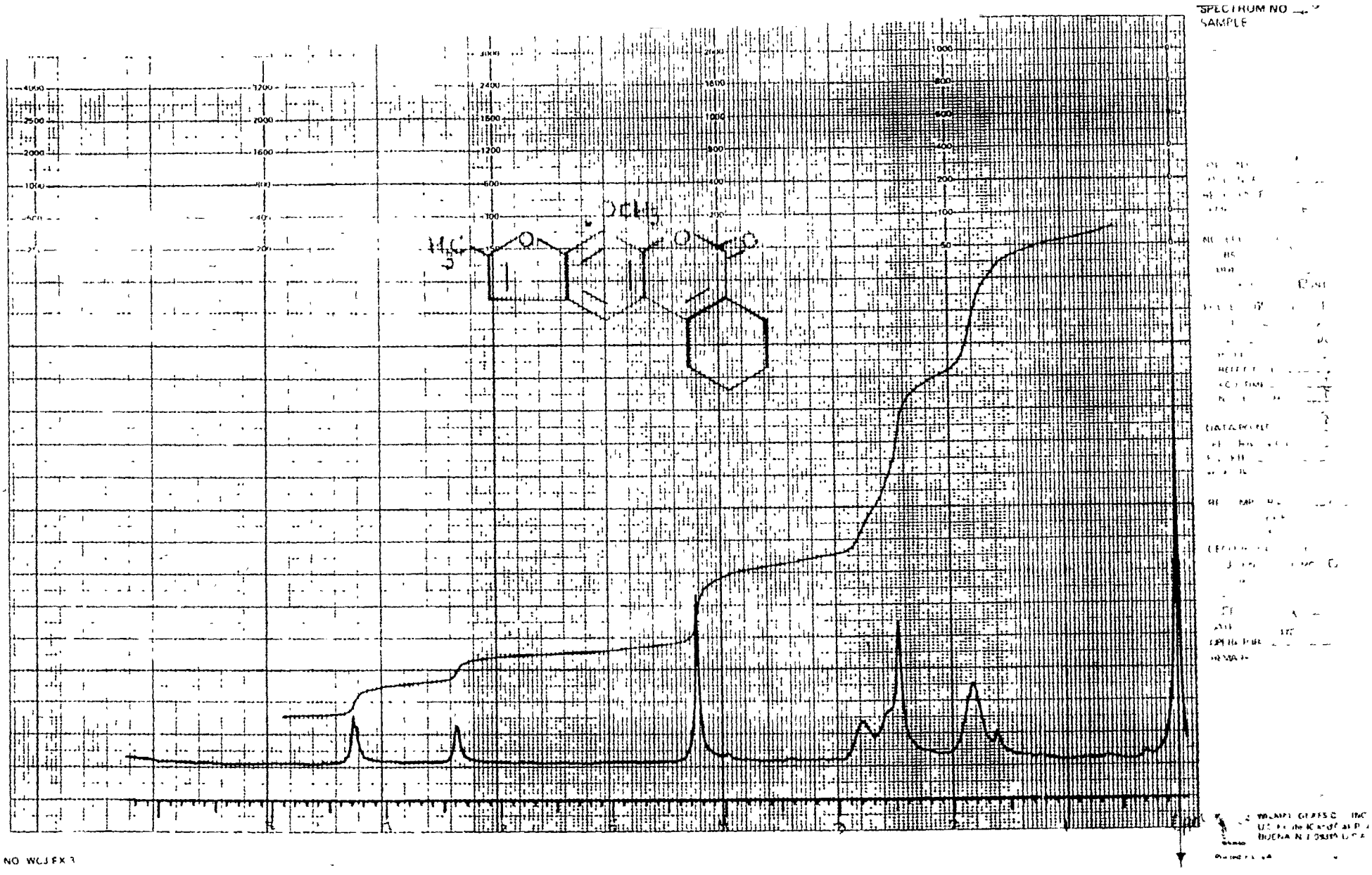
Compound (65) on acetylation with sodium acetate and



(fig-2) : 7-methoxy-9-methyl-1,2,3,4,9,10-hexahydro-5-oxo-5H-benzofuro(6,5-c)-benzopyran (66).



(fig-3) : 7-methoxy-9-methyl-5-oxo-5H-benzofuro (6,5-c)-2-benzopyran (67)



(fig-4): 7-methoxy-4-methyl-1,2,3,4-tetrahydro-5-oxo-5H-(6,5-c) benzopyran. (70)

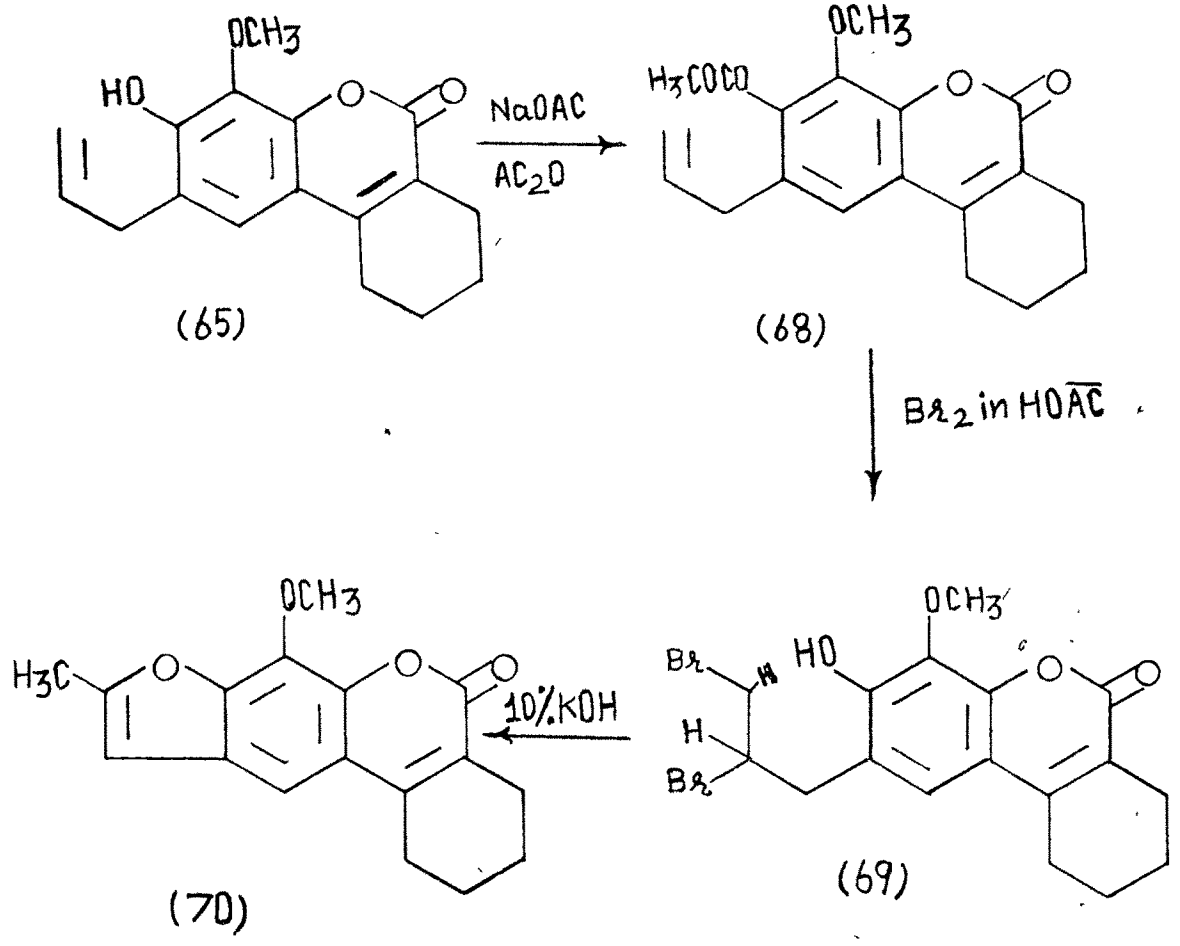
acetic anhydride gave 2-allyl-3-acetoxy-4-methoxy-7,8,9,10-tetrahydro-6H-dibenzo(b,d)-pyran-6-one (68) which on addition of bromine in acetic acid gave 3-acetoxy-2-(2',3'-dibromopropyl)-4-methoxy-7,8,9,10-tetrahydro-6H-dibenzo(b,d)-pyran-6-one (69) [Scheme-18] .

Compound (69) on cyclisation with alcoholic potassium hydroxide gave 7-methoxy-9-methyl-1,2,3,4-tetrahydro-5-oxo-5H-benzofuro (6,5-c)-benzopyran (70). The structure of which was established by its PMR spectra taken in ($CDCl_3$) exhibited thetwo multiplets at δ 1.6-2.0 and 2.5-2.9 for protons indicating the presence of cyclohexene ring. The singlet at δ 2.5 indicated the prsence of $-CH_3$ group at C-9 which is mixed with the multiplet of cyclohexene ring. Singlet at δ 4.25 is appeared for $-OCH_3$ group at C-7. Singlets at δ 6.4 and δ 7.3 are for protons at C-10 and C-11 respectively. (Fig. 4)

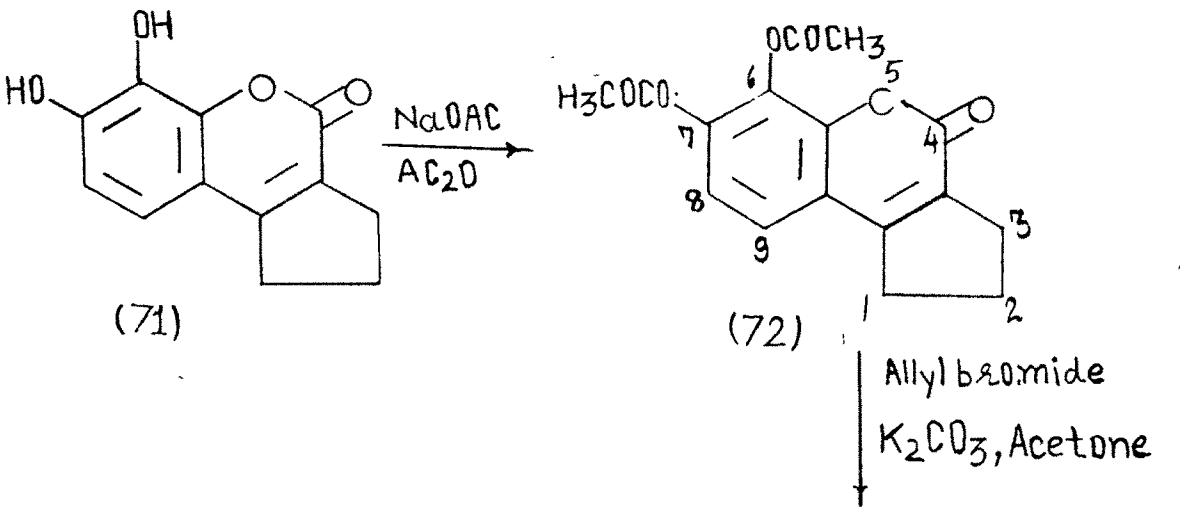
Synthesis of 8-methyl-6-methoxy-1,2,3-trihydrocyclopenta-[C]-furo (3,2-g) [1]-benzopyran-4-one (78)

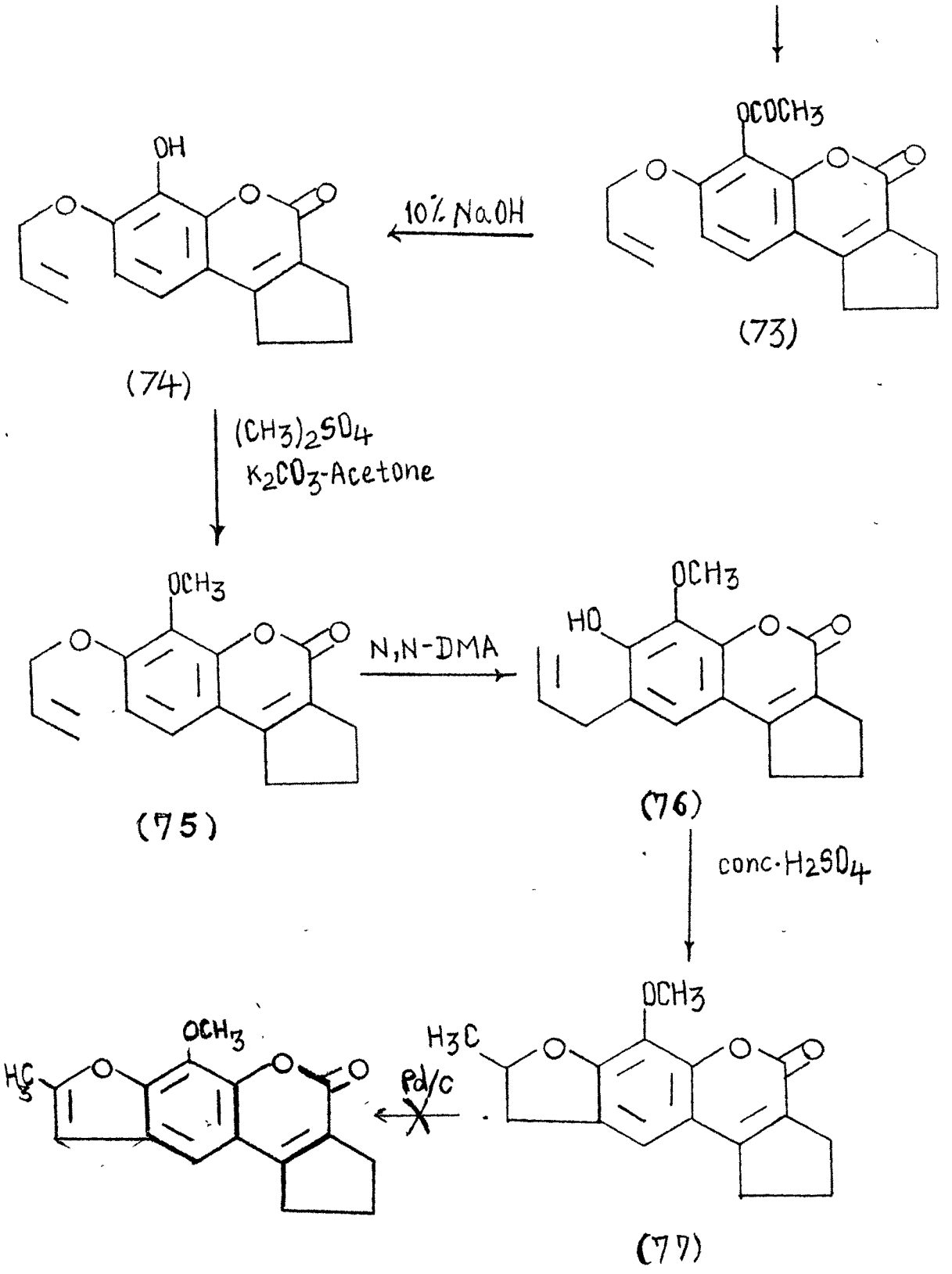
Pyrogallol on Pechmann[42] condensation with ethyl-2-cyclopentanone carboxylate in presence of conc. H_2SO_4 gave 6,7-dihydroxy-1,2,3-trihydrocyclopenta (C) (1)-benzopyran-4-one (71), which on acetylation with sodium acetate and acetic anhydride gave 6,7-diacetoxy-1,2,3-trihydro-cyclopenta (C) [1]benzopyran-4-one (72). The PMR spectrum showed two multiplets at δ 1.95-2.2 and 2.7-3.2 for protons of cyclopentene

Scheme -18



Scheme -19

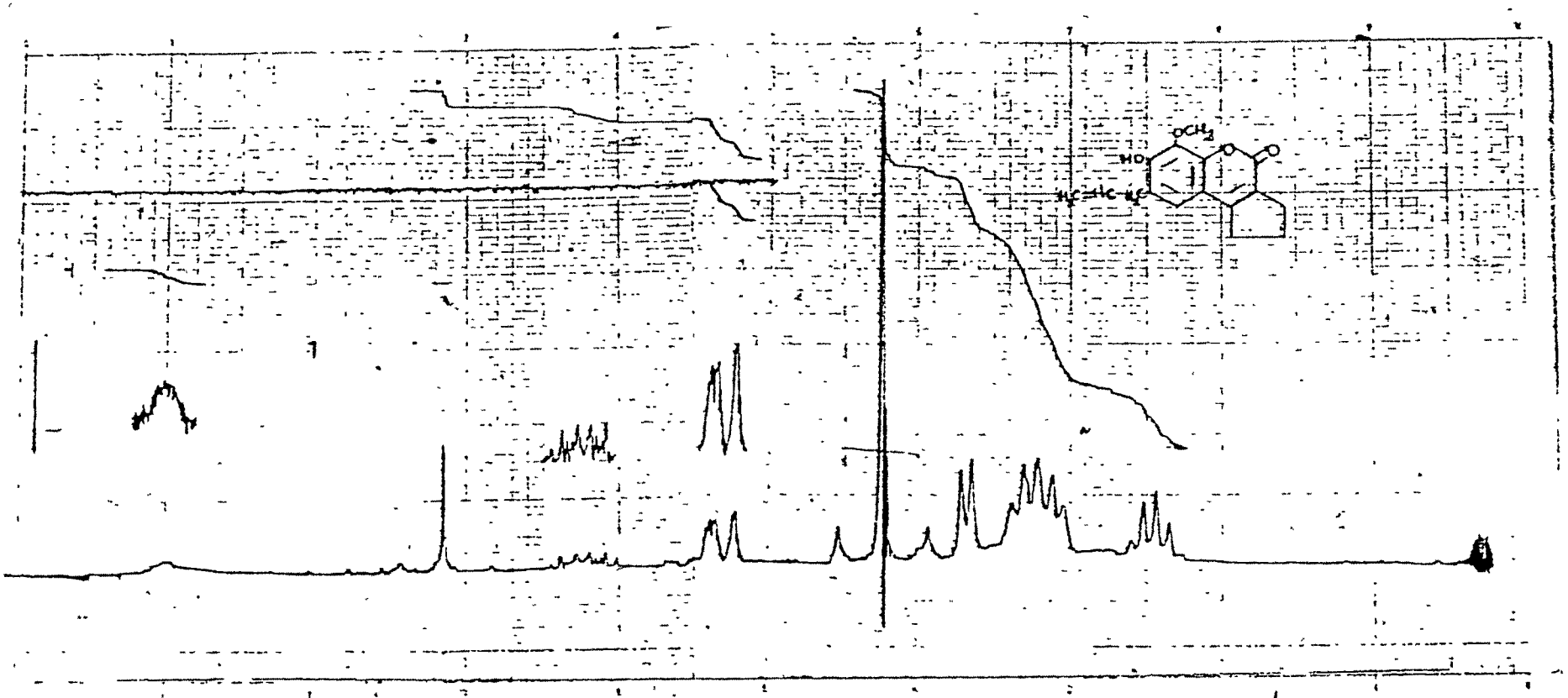



OCOCH3
OH
10% NaOH
(73)
(74)
(CH3)2SO4
K2CO3-Acetone
OCH3
N,N-DMA
HO
(75)
(76)
conc.H2SO4
OCH3
H3C
Pd/C
OCH3
H3C
(77)

ring. Two singlets at δ 2.3 and 2.4 indicated the presence of two acetoxy groups at C-6 and C-7. Two doublets located at δ 7.1 (J=9Hz) and 7.3(J=9Hz) indicated coupling of two aromatic protons located at C-8 and C-9.

Compound (72) on allylation with one mole of allylbromide in presence of anhydrous potassiumcarbonate in dry acetone gave 6-acetoxy-7-allyloxy-1,2,3-trihydrocyclopenta [C]-[1]-benzopyran-4-one (73). The PMR spectrum taken in ($CDCl_3$) exhibited the multiplets at δ 4.5, 5.1-5.4 and 5.7-6.1 for allyl group protons located at C-7. Singlet at δ 2.3 for three protons indicated the presence of acetoxy group at C-6. The other signals are same as in previous spectra. Compound (73) on hydrolysis with alcoholic potassium hydroxide (10%) gave 7-allyloxy-6-hydroxy-1,2,3-trihydrocyclopenta [C]-[1]-benzopyran-4-one (74) which on methylation with dimethyl sulfate in presence of anhydrous potassium carbonate in dry acetone gave 7-allyloxy-6-methoxy-1,2,3-trihydro-cyclopenta [C]-[1]-benzopyran-4-one (75). [Scheme-19.]

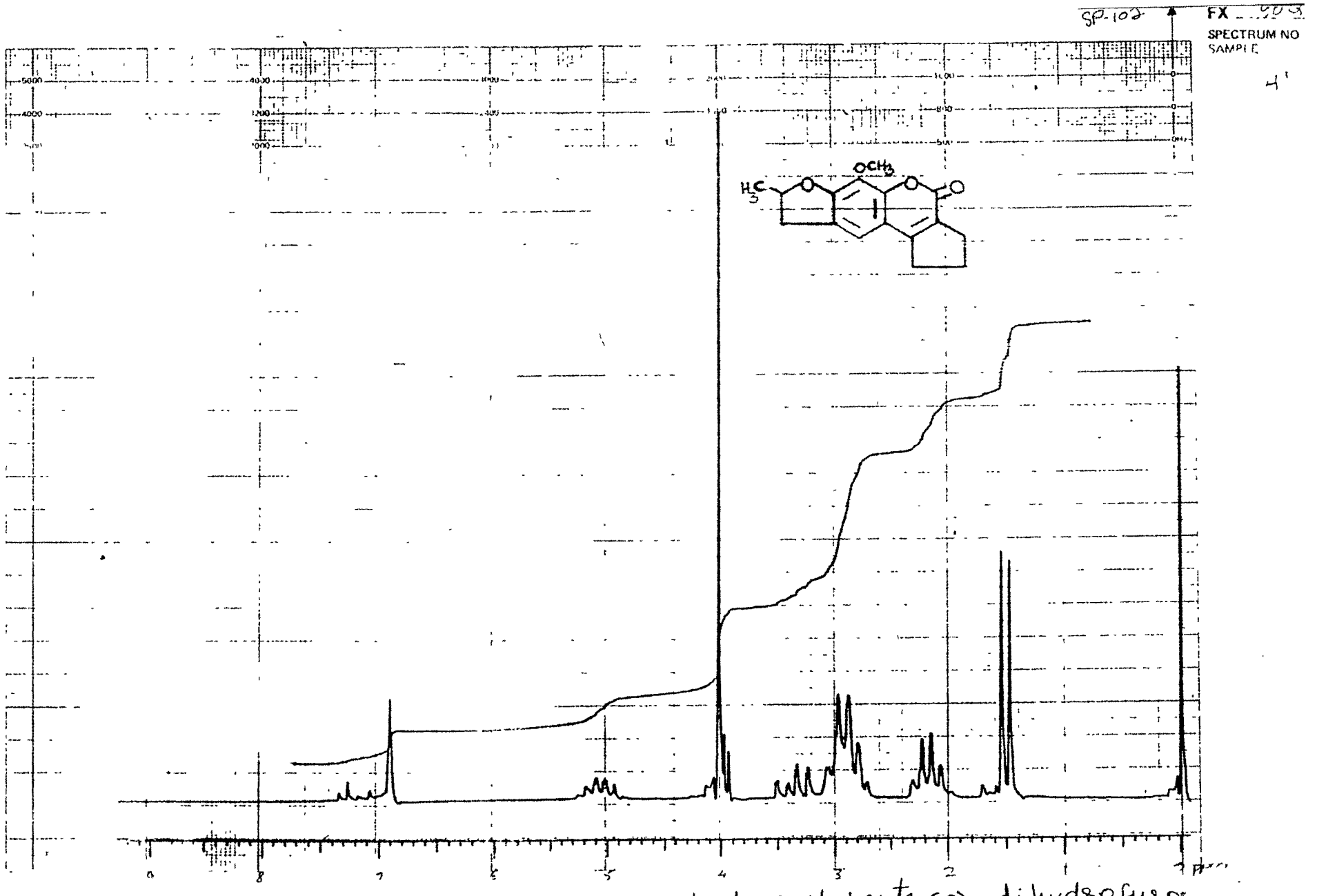
Compound (75) on Claisen rearrangement in N,N-dimethylaniline gave 8-allyl-7-hydroxy-6-methoxy-1,2,3-trihydrocyclopenta [C]-[1]-benzopyran-4-one (76). Due to the presence of methoxy group at position 6, allyl group migrated to 8-position only. The PMR spectrum taken in $CDCl_3$ exhibited only one aromatic proton at δ 7.1, singlet due to the proton at C-9. Other signals are as usual (Fig.5"). Compound (76)



(fig-5): 8-Allyl-7-hydroxy-6-methoxy-1,2,3-trihydro-cyclopenta (c) (1)-benzopysan-4-one (76)

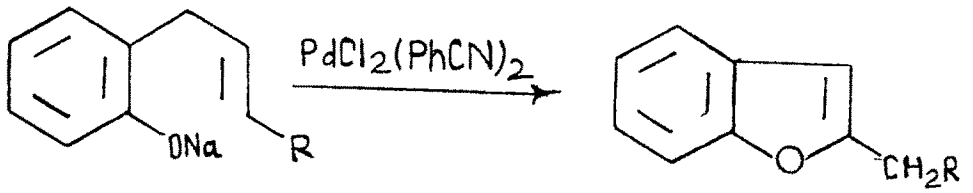
on trituration with conc. H_2SO_4 (80%) gave the cyclised product, 8-methyl-6-methoxy-1,2,3-trihydrocyclopenta [C]-dihydrofuro (3,2-g) [1]-benzopyran-4-one (77). The PMR signals exhibited doublet at δ 1.5 indicated he presence of methyl group at C-8. Multiplet at δ 2.2 and 3.0 indicated the presence of cyclohexene ring at 3 and 4 position. The double doublet or rather multiplet at δ 3.3 indicated proton at C-9. Singlet at δ 4.0 indicated $-OCH_3$ group at C-6. Multiplet at δ 5.1 indicated proton at C-8. Singlet at δ 7.0 indicated one aromatic proton at C-10. (Fig. 6) (77) on refluxing in diphenyl ether with palladised charcoal (10%) did not give the dehydrogenated product. This might be due to the presence of cyclopentene ring at 3,4-position of coumarin ring. The furan ring was built up by making use of palladium chloride benzonitrile complex method.[43] T. Hosokawa et al[44] had prepared benzofuran bythe reaction of sodium salt of allylphenols anddichlorobis (benzonitrile)-palladium [Scheme-20]. They had also prepared different naphthofurans[45] and chromene[46] using the same method.

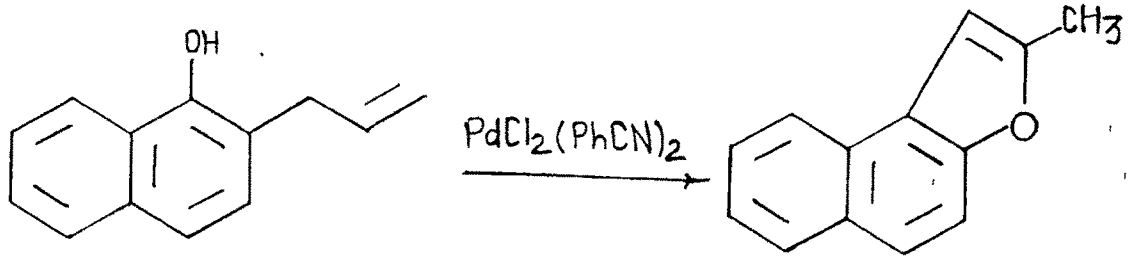
Sodium salt of compound (76) was mixed with dichlorobis (benzonitrile) palladium and refluxed in waterbath which gave 8-methyl-6-methoxy-1,2,3-trihydrocyclopenta [C]-furo-(3,2-g)[1]-benzopyran-4-one (78). [Scheme-21]. The PMR spectra taken in ($CDCl_3$) showed two mutiplets at δ 1.7-2.0 and 2.5-2.9 for 6-protons indicating the presence of cyclo-

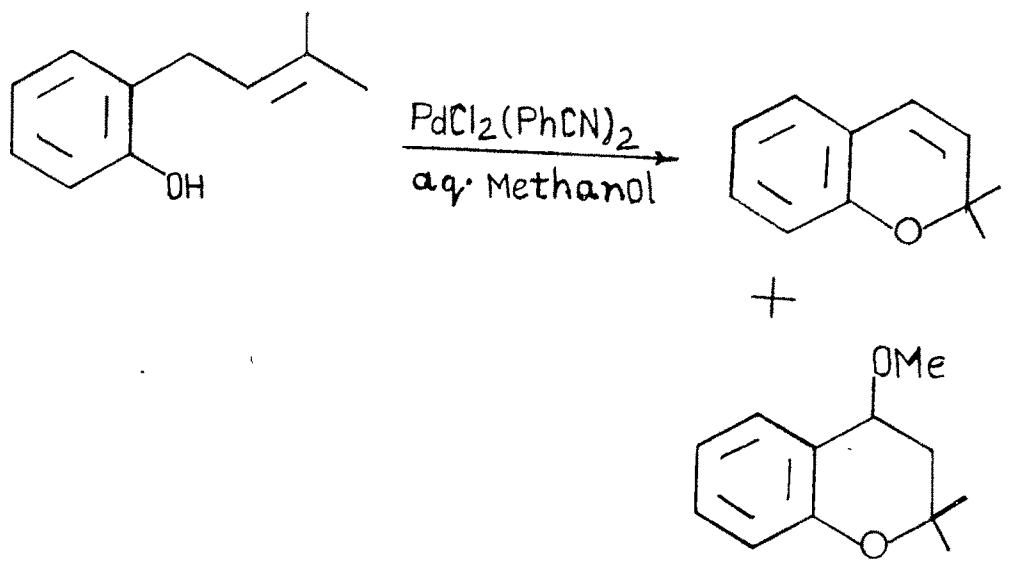


(fig-6): 8-Methyl-6-methoxy-1,2,3-trihydrocyclopenta (c)-dihydrofuro (3,2-g)-(1)benzopyran-4-One. (77)

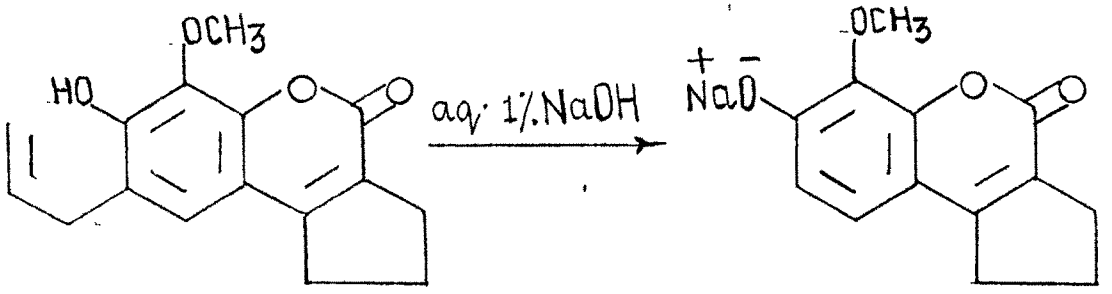
Scheme-20 Hosokawa et al[44-46]





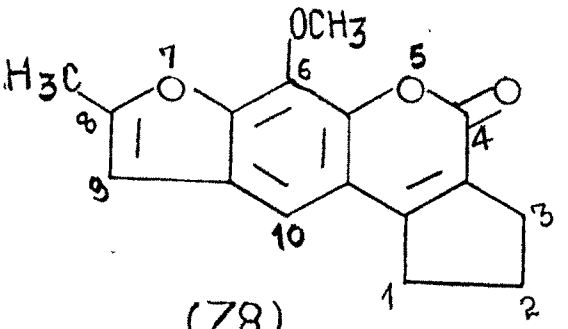


Scheme -21



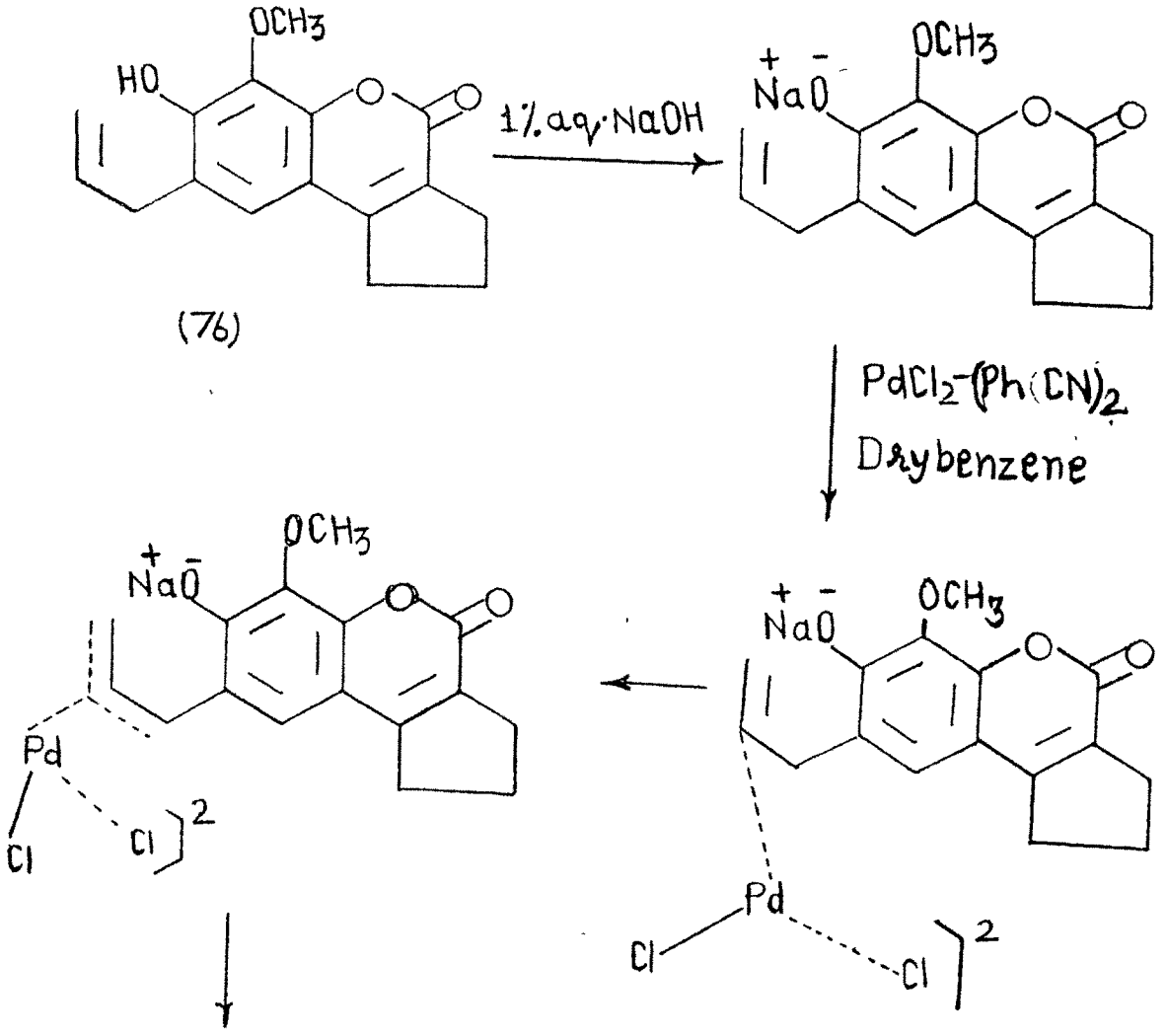
(76)

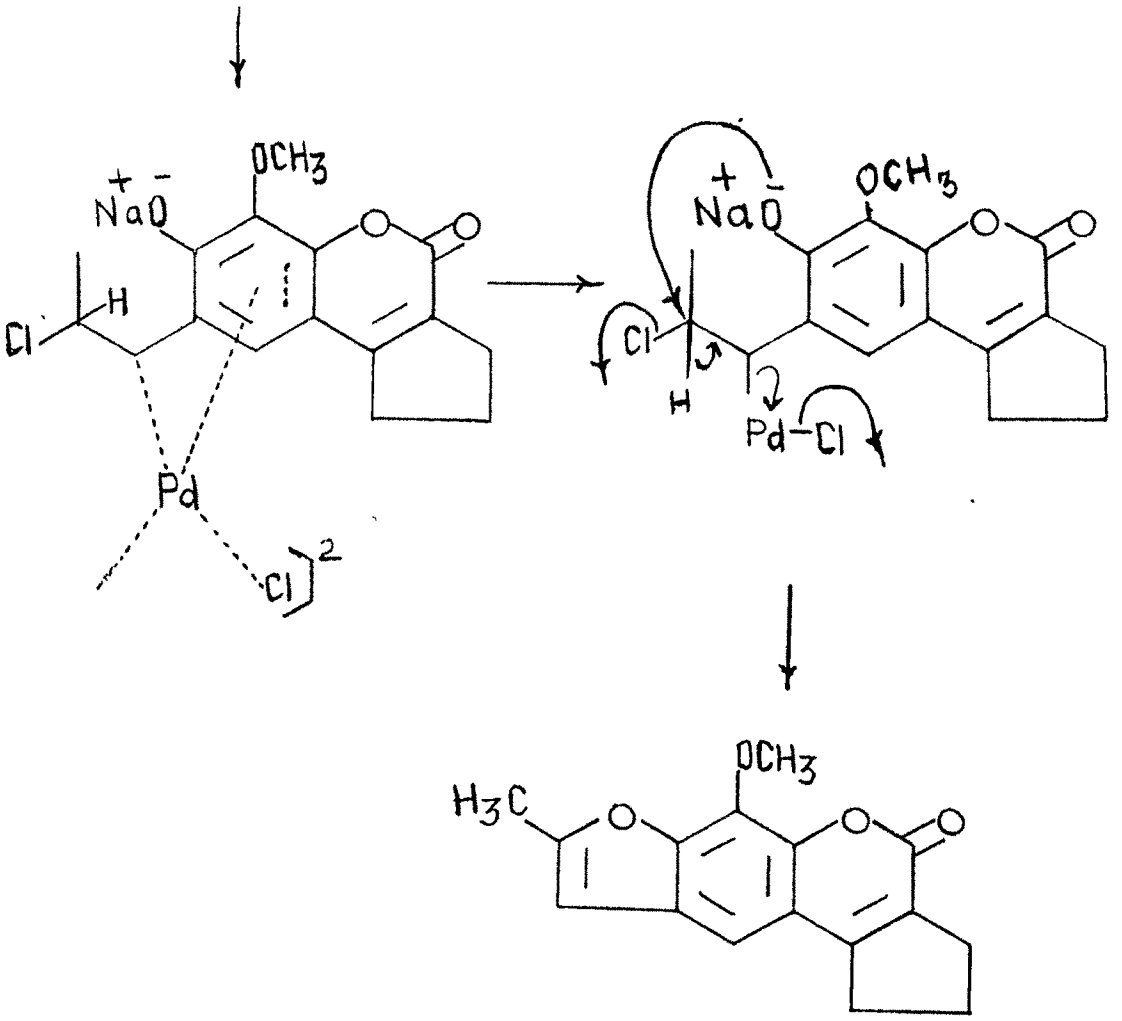
$PdCl_2$-(Ph CN)$_2$
Drybenzene



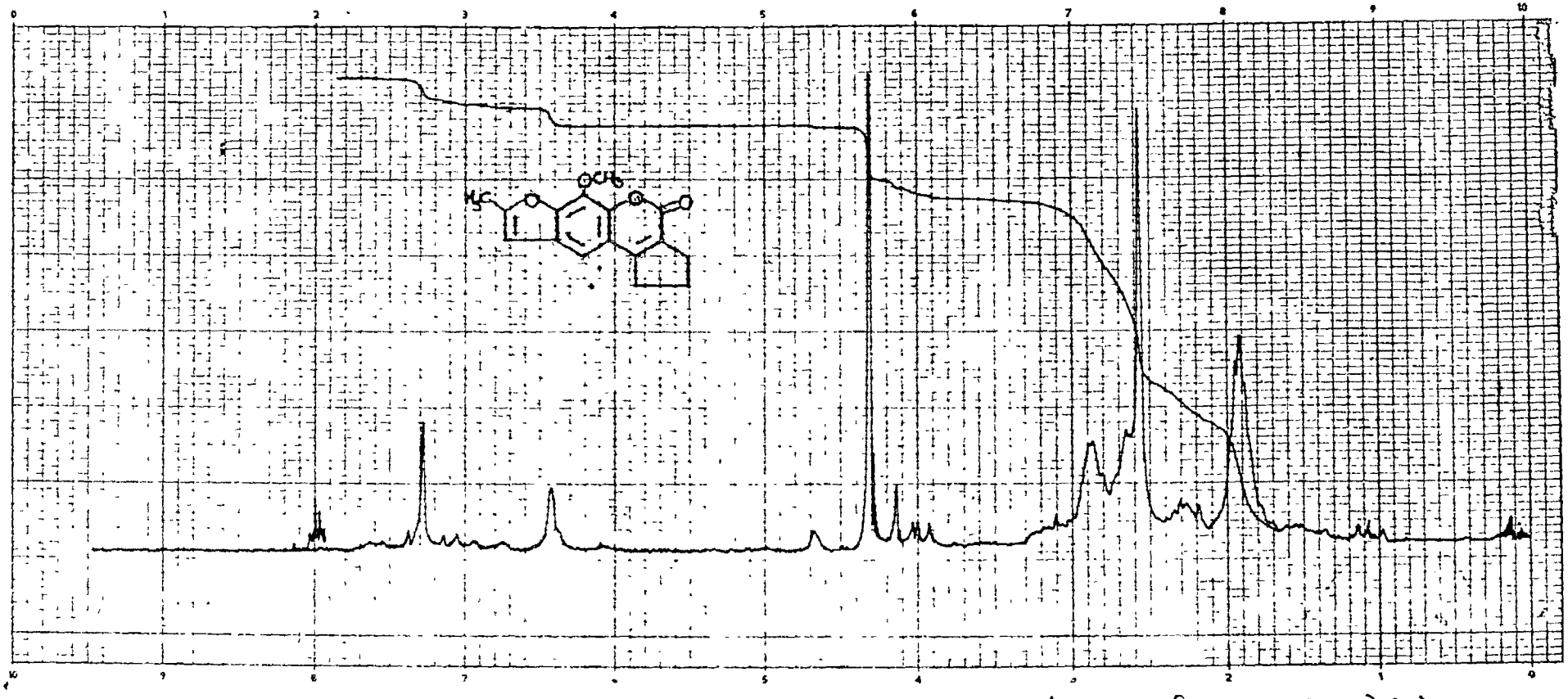
(78)

Scheme - 22 Mechanism of Dehydrogenation by Palladium Chloride-benzonitrile Complex Method





(78)



(f.g-7): 8-Methyl-6-methoxy-1,2,3-trihydro cyclopenta (c)-furo (3,2-g)(1)-benzopyran-4-one (78).

pentane ring. Singlet at δ 2.5 and 4.2 indicated the presence of methyl group at C-8 and methoxy group at C-6 respectively. Singlet at δ 6.3 for one proton indicated the presence of dehydrogenated proton of furan ring at C-9 and singlet at 7.2 indicated the aromatic proton at C-10 (Fig. 7). The mechanism of this reaction is shown in [Scheme-22].

SYNTHESIS OF DIFURANOCOUMARINS

As we have seen earlier, introduction of furan ring in coumarin nucleus can be brought about by Claisen rearrangement of suitably substituted allyloxy coumarins and then cyclisation of it, followed by dehydrogenation.

Synthesis of furocoumarins is widely occuring in literature, while synthesis of difurocoumarins is rarely reported in literature. Similar to furocoumarins, difurocoumarins can be synthesised by Claisen rearrangement of suitably substituted diallyloxy coumarins, followed by subsequent ring closure. It is interesting to observe Claisen rearrangement of diallyloxy coumarins. Since two allyl groups are there, we may get both the allylgroups migrated or one group migrated and one group cyclised or both groups cyclised or loss of one group with migration of other group.

Seshadri and Coworkers [47] have demonstrated Claisen rearrangement of 5,7-diallyloxy-4-phenyl coumarin (79).

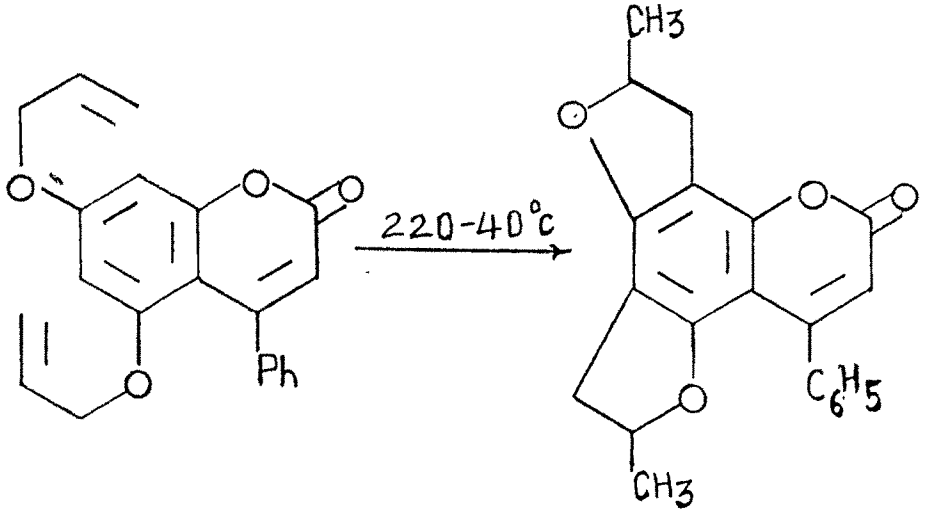
After heating at 220-40°C, they have reported both the allyl groups get cyclised as major product (80), while one group cyclised and one group migrated product (81) was in traces [Scheme-23].

Sanghavi and Trivedi[48] have synthesised different difuranocoumarin derivatives by carrying out Claisen rearrangement of 4,7-diallyloxy coumarin [Scheme-24] 4,7-diallyloxy-8-methylcoumrin [Scheme-25] and 4,6-diallyloxy coumarin [Scheme-26].

7-Allyloxy resacetophenone was condensed with diethylcarbonate and pulverised sodium to give 4-hydroxy-7-allyloxy coumarin (82) which on condensation with allylbromide gave 4,7-diallyloxy coumarin (83). This on Claisen rearrangement gave 2-methyl-6-allyl-7-hydroxy-dihydrofuro (2,3-c)-benzopyran-4(H)-one (84), which on cyclisation with conc. H_2SO_4 (80%), gave 2,7-dimethyl-dihydrofuro (3,2-c;2',3'-h)-benzopyran-4(H)-one (85). This on dehydrogenation with palladised charcoal (10%) gave 2,7-dimethyl-difurano (3,2-c; 2',3'-h)benzopyran 4(H)-one (86). [Scheme-24].

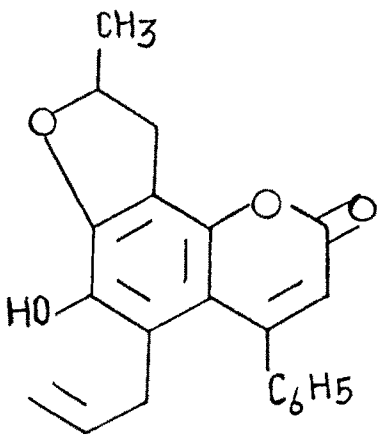
In case of Claisen rearrangement of 4,7-diallyloxy-8-methyl coumarin (87) obtained by starting with 2-methylresorcinol, migration of C-7 allyl group took place at 6-position and obtained linear furan ring.

Scheme -23 Seshadri and Coworkers[47]



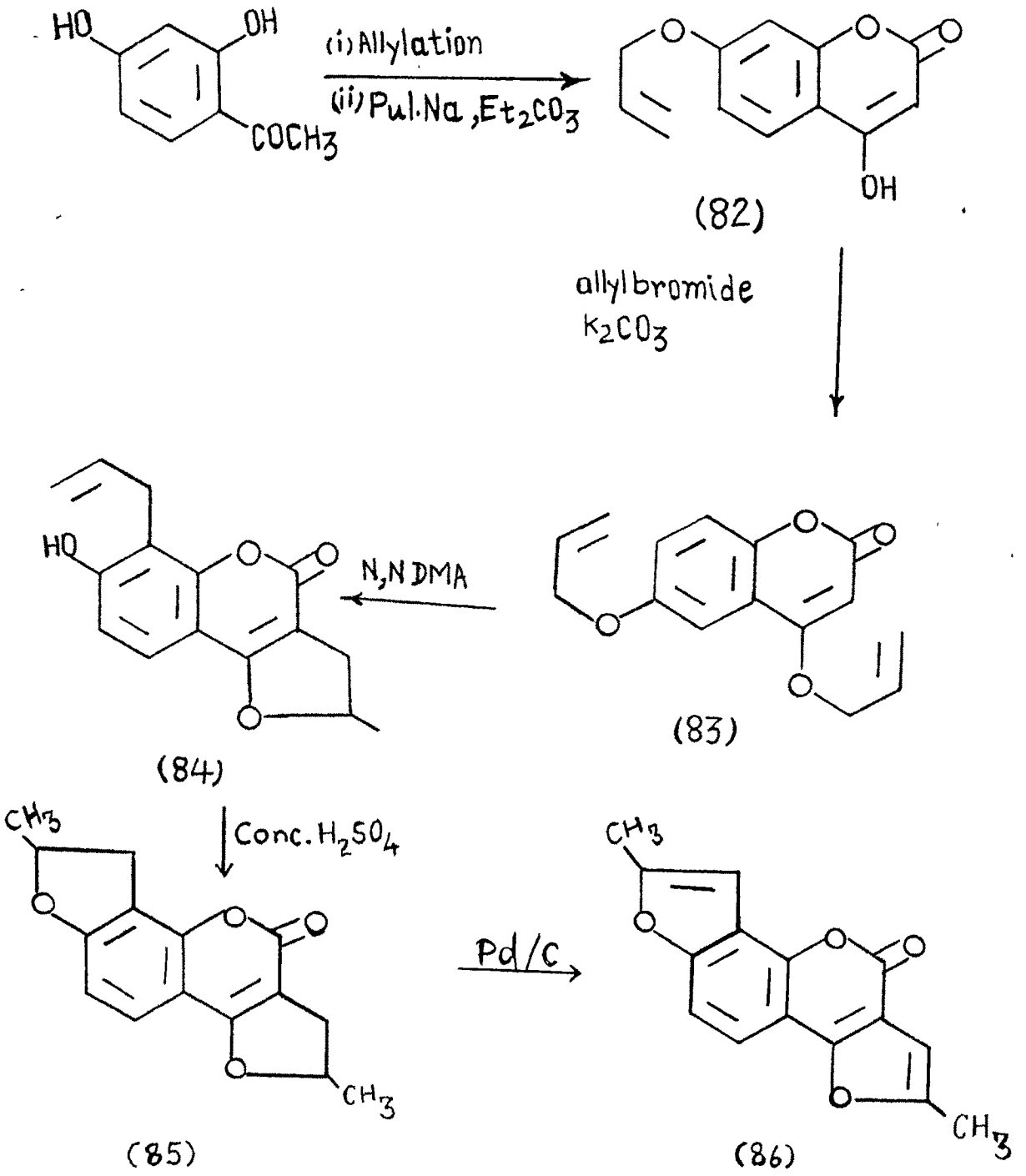
(80)
60%

+

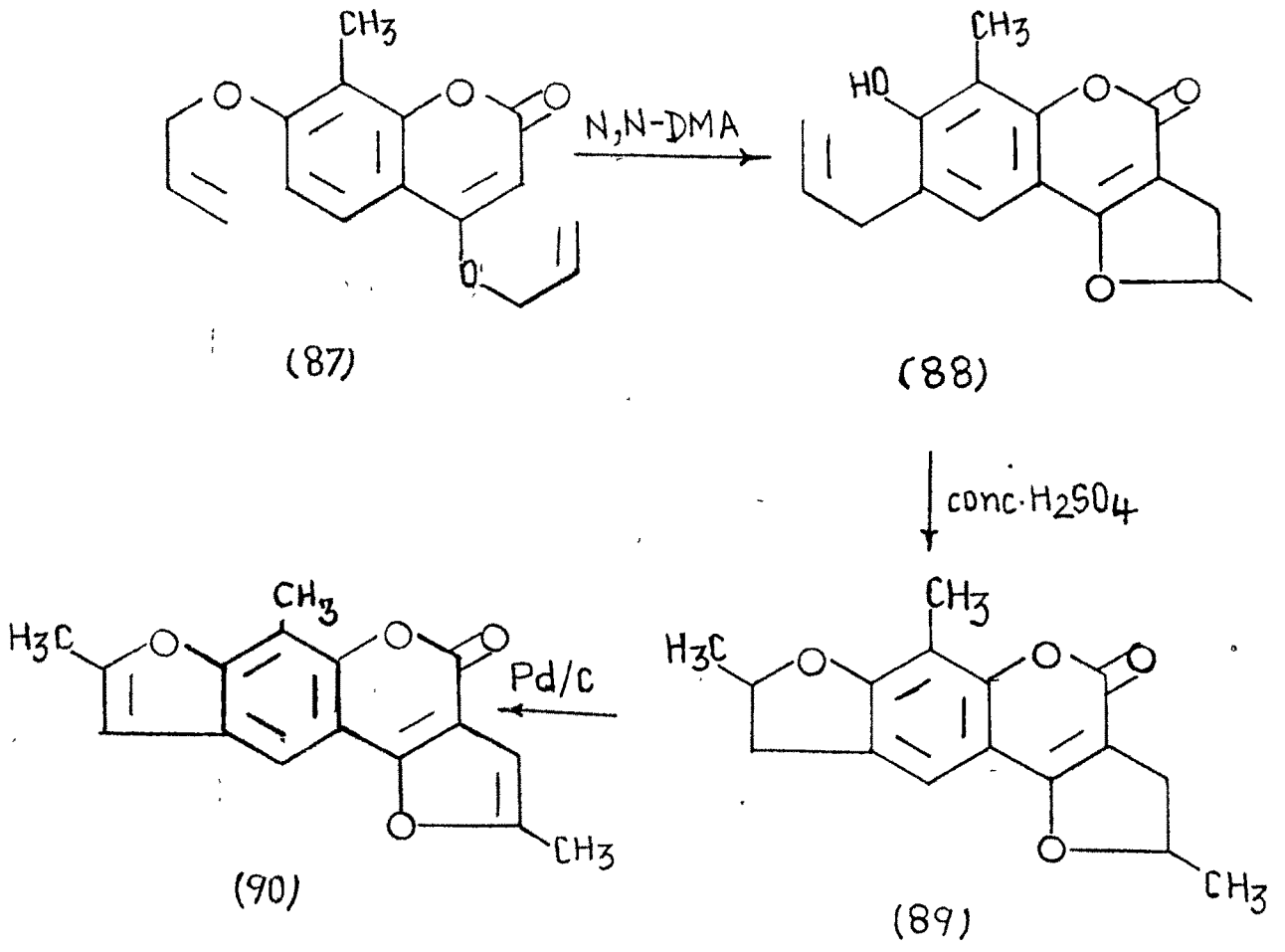


(81)
2-5%

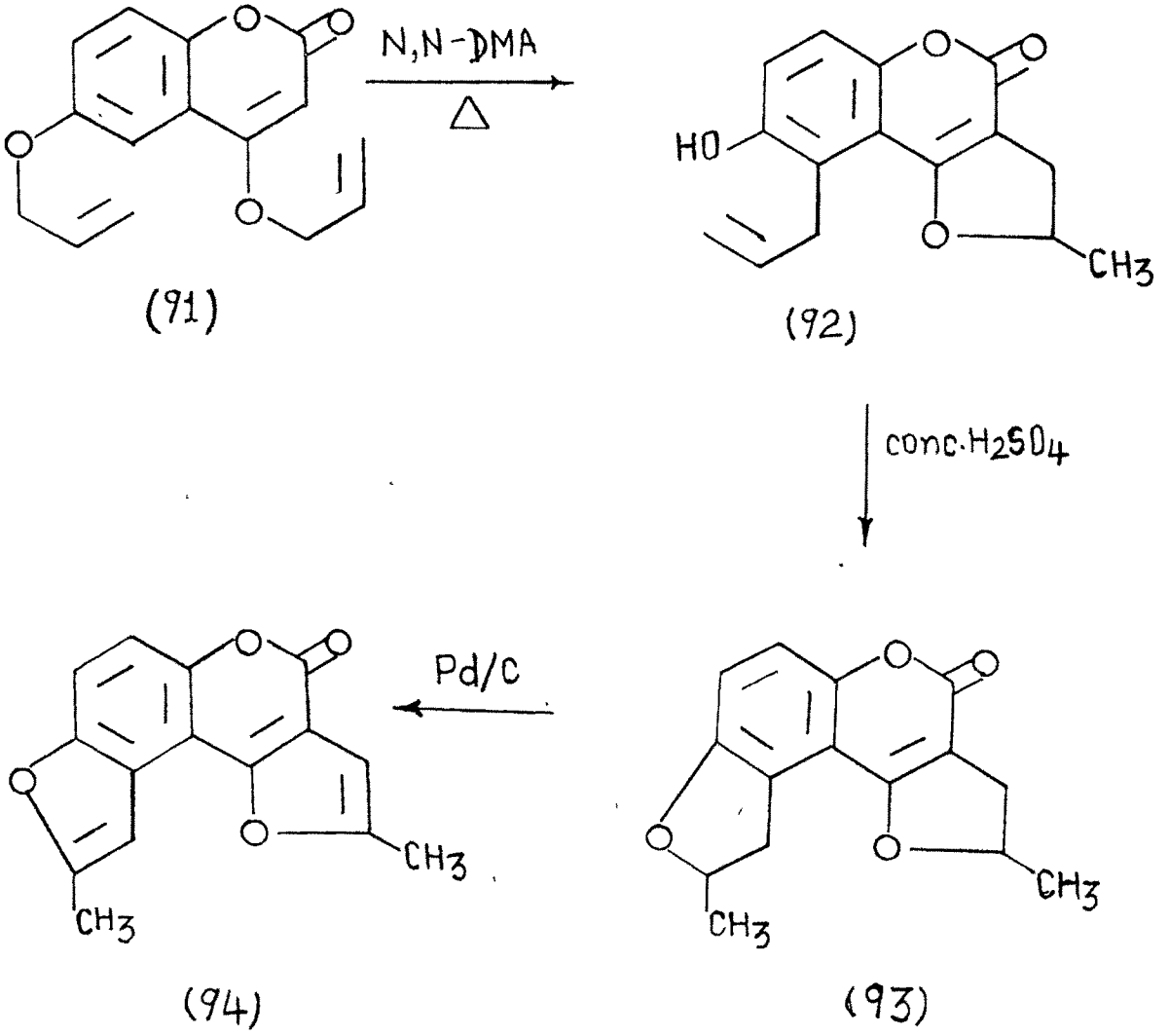
Scheme - 24 Sanghvi and Trivedi[48]



Scheme-25 Sanghvi and Trivedi[48]



Scheme - 26 Sanghvi and Trivedi[48]



The allyl group at C-4 got cyclised. [Scheme-25]. 4,6-diallyloxy coumarin (91) when subjected to Claisen rearrangement, allyl group at C-4 got cyclised and allyl group at C-6 is migrated to C-5 and the product obtained was 2-methyl-9-allyl-8-hydroxy-dihydrofuro (2,3-c) benzopyran-4(H)-one (92) which on cyclisation with con. H_2SO_4 (80%) gave compound (93) which was further dehydrogenated with palladised charcoal (10%) to obtain 2,7-dimethyl-difurano (2,3-c, 2',3'-f) benzopyran-4(H)-one (94) [Scheme- 26]

PRESENT WORK

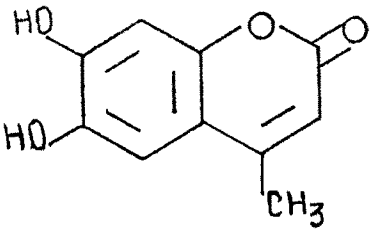
Present work deals with Claisen rearrangement of 6,7-diallyloxy and 7,8-diallyloxy-4-methyl coumarin.

Allylation of 6,7-dihydroxy-4-methyl coumarin

In continuation of the work carried out by Sanghvi and Trivedi, we have studied Claisen rearrangement of 6,7-diallyloxy-4-methyl coumarin.

6,7-dihydroxy-4-methyl coumarin (95) was condensed with 2-moles of allylbromide in presence of anhydrous potassium carbonate in dry acetone to obtain 6,7-diallyloxy-4-methyl coumarin (96). This compound was subjected to Claisen rearranement in N,N-dimethylaniline gave the product which could have either structure (97(a), 97(b), 97(c) or (98) [Scheme-27]. The possibility of structure 97(c) or 98 was ruled out on the basis of PMR spectrum which indicated the presence

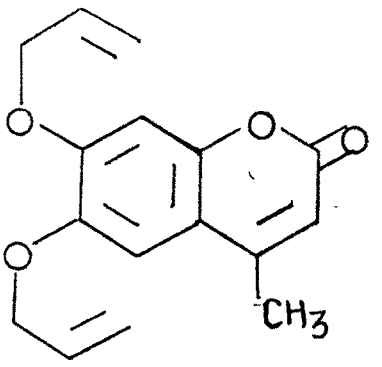
Scheme -27



(95)

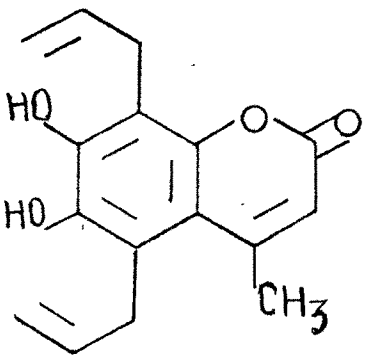
allyl bromide

K_2CO_3, Acetone

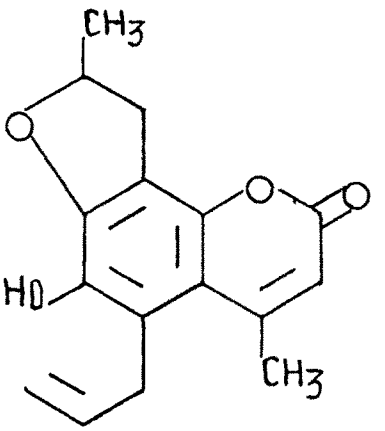


(96)

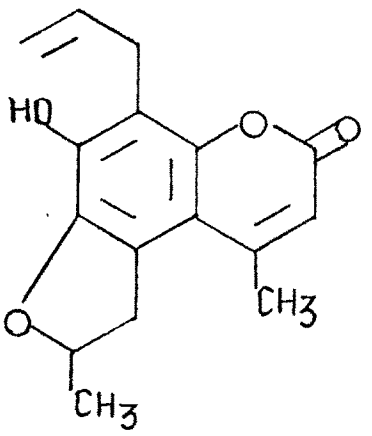
N,N-DMA



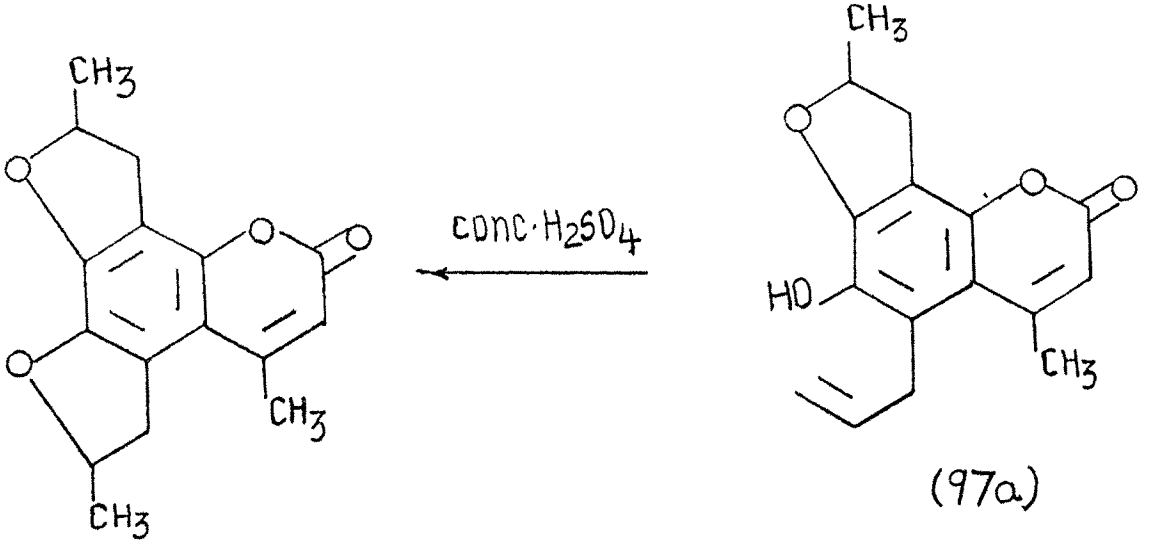
(97b)



(97a)

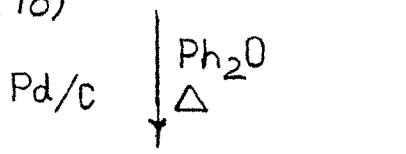


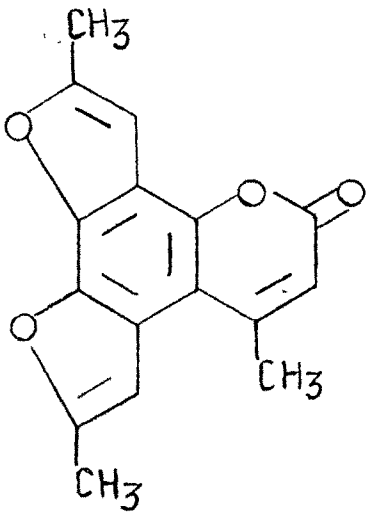
(97c)



(97a)

(98)



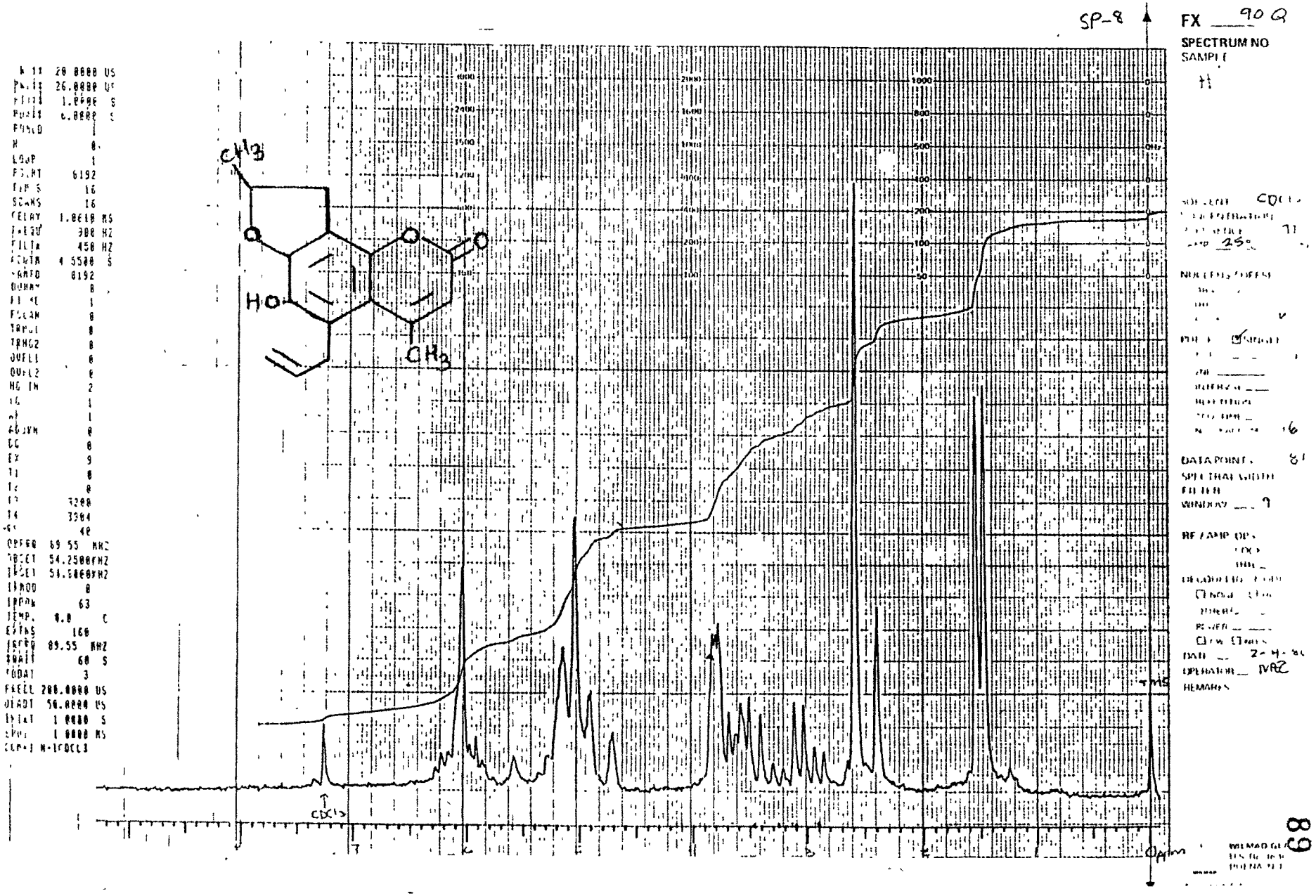


(99)

of dihydrofurano ring system and free allyl group. It also did not develop green colouration with neutral ferric chloride solution. The PMR spectrum taken in $CDCl_3$ (Fig. 18) exhibited doublet at δ 1.5 (J=7Hz) for three protons indicated the presence of methyl group at C-2 of dihydrofurano ring. Singlet at δ 2.8 indicated the methyl group at C-7. The double doublet at δ 3.0 (J=18,8Hz) indicated the presence of protons at C-3. The another double doublet at δ 3.4 (J=18,8Hz) indicated the presence of other proton at C-3 of dihydrofuro ring. Multiplets at δ 3.75, 5.0 and 5.6 indicated the presence of free allyl group at C-8. Multiplet at δ 5.0 also indicated the presence of proton at C-2, which is mixed with the signal of allyl group proton. Singlet at δ 6.0 is for proton at C-6.

The UV spectrum of this compound was also taken which was as follows. UV(methanol)[49] λmax. 340 nm (log ϵ 5.2), 1M NaOH λmax 400 nm (log ϵ 2.4). The increase in λmax, with the decrease in ϵ value with the addition of NaOH indicated the presence of hydroxyl group[49] at C-6 and not at C-7 of coumarin ring which indicated the possibility of structure 97(a) and not 97(b). The identity of structure (97a) was finally confirmed by its unambigous synthesis. Compound (97a) when titurated with conc. H_2SO_4 (80%) gave 2,7,9-trimethyl-2,3,8,9-tetrahydrofuro (2,3-h , 2',3'-f) [1]-benzopyran-5(H)-one (98). The structure of this compound was established by

(fig-8) : 8-Allyl-2,7-dimethyl-dihydrofuro (2, 3-b)-(1)-benzopyran 5(H)-one (97a)

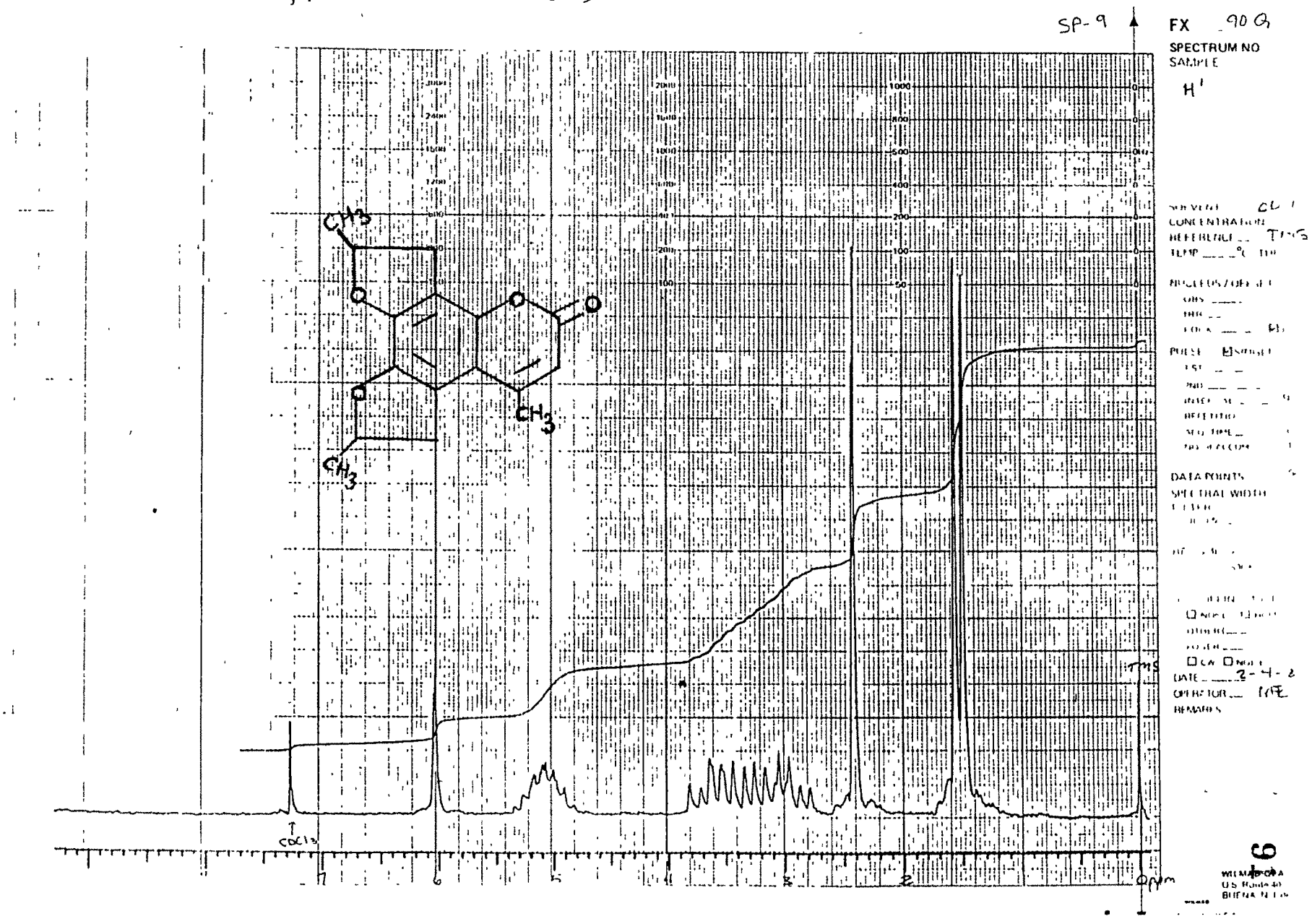


PMR spectrum taken in $CDCl_3$ (Fig. 9.). It exhibited the doublet at δ 1.5 (J=7Hz) for 6 protons indicated the presence of two methyl groups at C-2 and C-9. Singlet at δ 2.4 is for methyl group at C-7. Two double doublets or rather one can say multiplet at δ 2.8-3.8 (J=18,8Hz) for four protons indicated two protons each at C-3 and C-8. Multiplet at δ 5.1 indicated two protons at C2 and c-9. Singlet at δ 6.0 is for proton at C-6. Compound (98) on refluxing in diphenyl ether with palladised charcoal (10%) gave 2,7,9-trimethyl-difurano (2,3-h , 2',3'-f)[1]-benzopyran-5(H)-one (99). The PMR spectrum taken in $CDCl_3$ (Fig. 10) showed two singlets at δ 2.5 and 2.6 for methyl groups at C-2, C-9 and C-7 respectively. Singlet at δ 6.2 indicated proton at C-6 and singlet at δ 6.8 indicated two protons at C-3 and C-8.

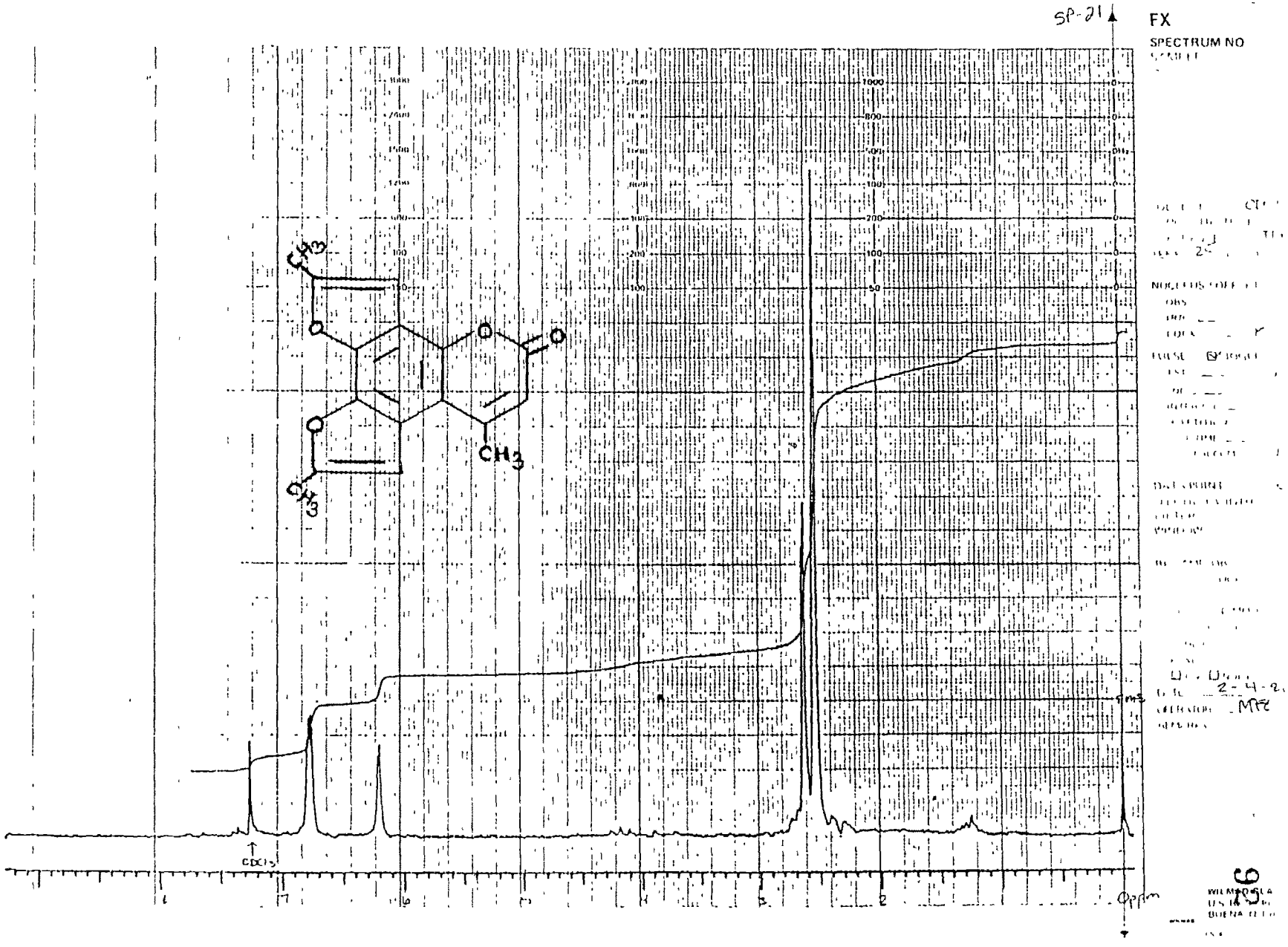
To prove the structure of (97a), it was synthesised unambigously as follows [Scheme-28]

6,7-Dihydroxy-4-methyl coumarin (95) on acetylation with sodium acetate and acetic anhydride gave 6,7-diacetoxy-4-methyl coumarin (100). This on condensation with one mole of allylbromide in presence of anhydrous potassium carbonate and dry acetone gave 6-acetoxy-7-allyloxy-4-methyl coumarin (101). The structure (101) was assigned on the basis of analogy of allylation of 6,7-diacetoxy coumarin.[50] The Claisen rearrangement of (101) in boiling N,N-dimethylaniline

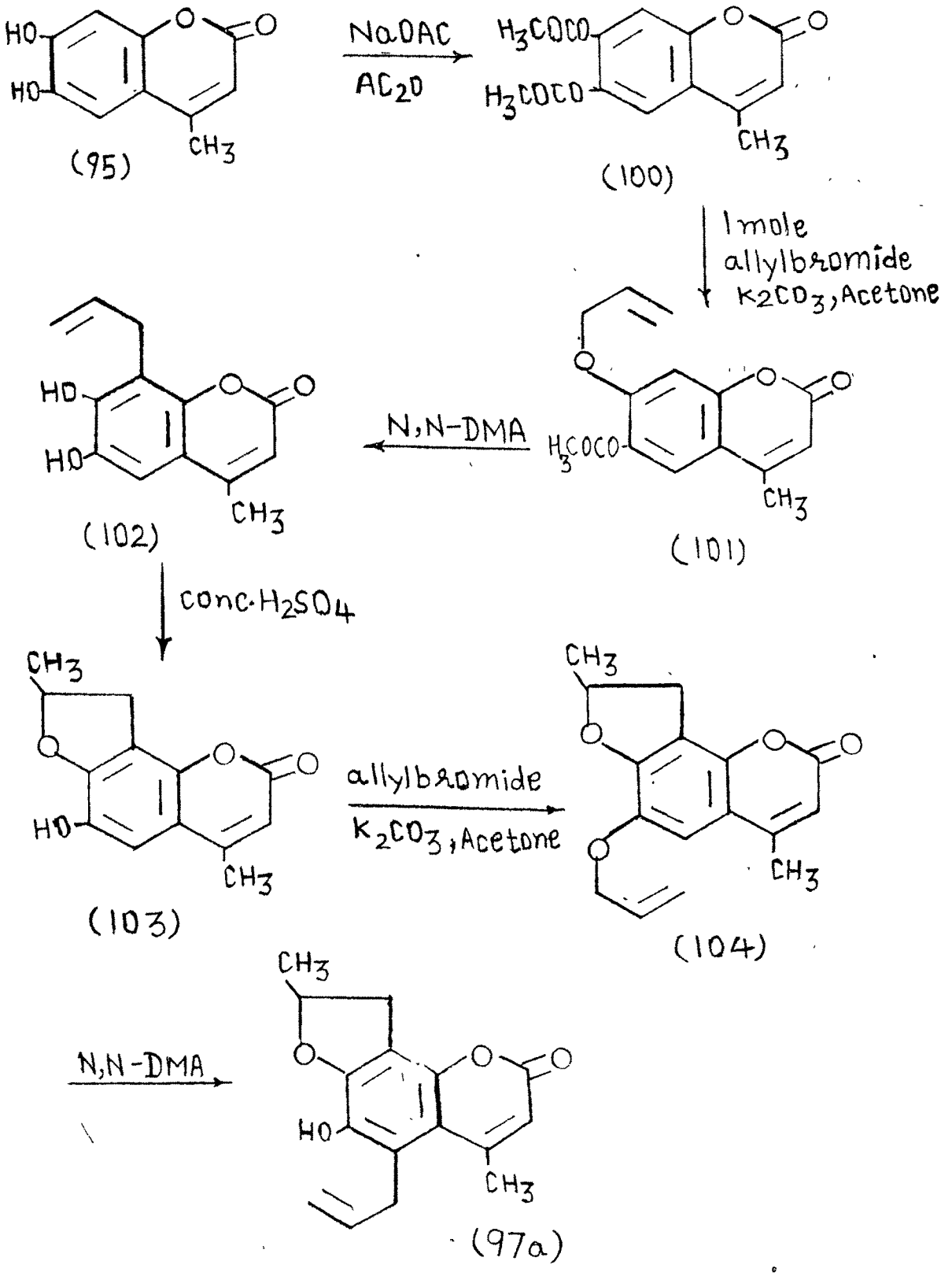
(fig-9): 2,7,9-trimethyl-2,3,8,9-tetrahydrofuro-(2,3-h : 2',3'-f)(1)-benzopyran-5(H)-one. (98)



(fig-10): 2,7,9-trimethyl-difurano (2',3':b : 2',3'-f) (1)-benzopyran-5(H)-one (gg)



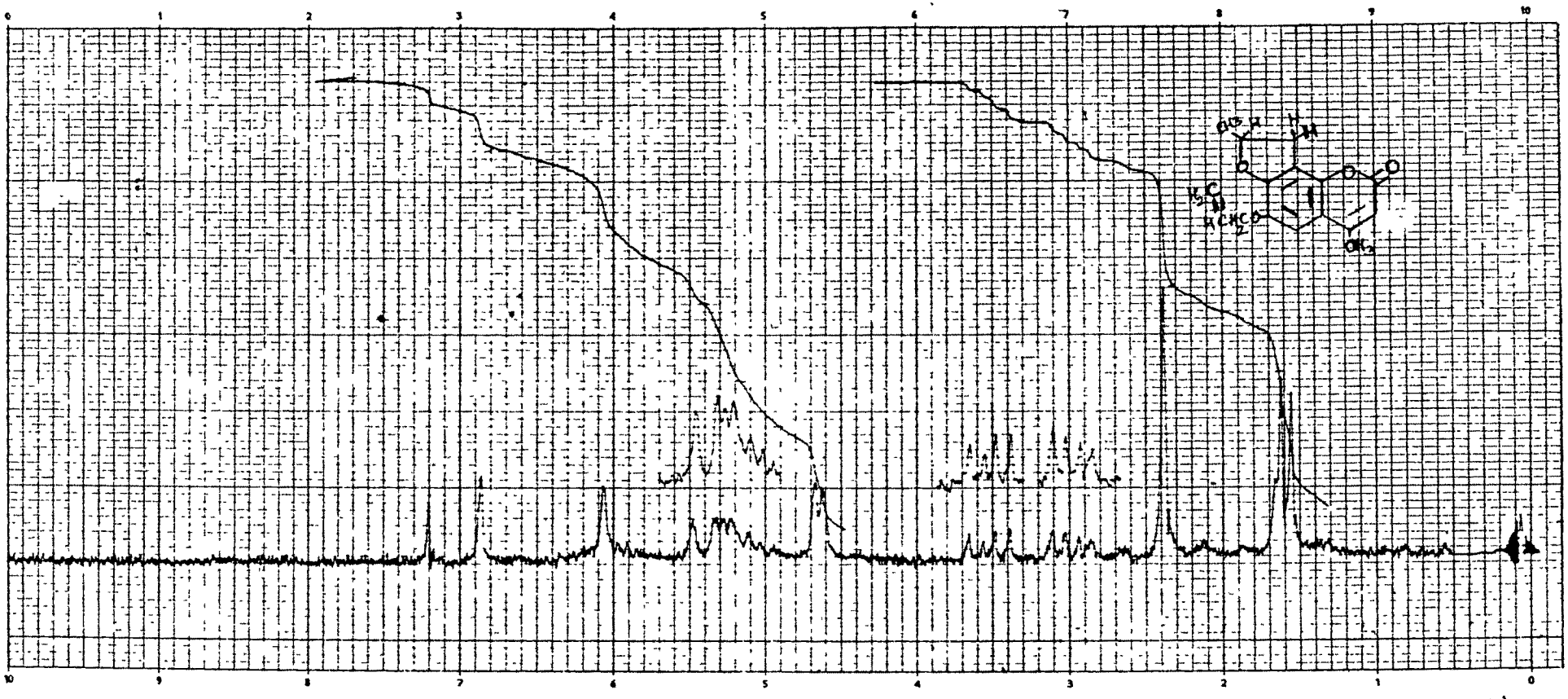
Scheme - 28


HO
HO
CH3
(95)
NaOAC
AC2O
H3COCO
H3COCO
CH3
(100)
1 mole
allylbromide
K2CO3, Acetone
HO
HO
CH3
(102)
N,N-DMA
H3COCO
CH3
(101)
conc. H2SO4
CH3
HO
CH3
(103)
allylbromide
K2CO3, Acetone
CH3
CH3
(104)
N,N-DMA
CH3
HO
CH3
(97a)

gave 8-allyl-6,7-dihydroxy-4-methyl coumarin (102). The structure of this compound was established by PMR spectrum taken in DMSO-d_6. It exhibited the singlet at δ 2.5 for methyl group at C4. Three multiplets at δ 3.4, 5.0 and 5.65 indicated allyl group at C-8. Two singlets at δ 6.0 and 6.9 are for protons at C-3 and C-5 respectively. Moreover, this compound gave green colouration with neutral ferric chloride indicating the presence of two free ortho hydroxy groups.

Compound (102) on tituration with con. H_2SO_4 (80%) gave 2,7-dimethyl-9-hydroxy-dihydrofurano(2,3-h) (1)-benzopyran-5(H)one (103). The structure of this compound was established by PMR spectrum taken in DMSO-d_6, which indicated the presence of dihydrofurano ring. Doublet at δ 1.4 (J=7Hz) indicated methyl group at C-2 and singlet at δ 2.4 indicated methyl group at C-7. The double doublets at δ 2.8-3.2 (J=18,8Hz) mixed with DMSO-d_6 signal indicated two protons at C-3. One multiplet at δ 5.1 indicated the presence of proton at C-2. Two singlets at δ 6.1 and 6.9 indicated presence of two protons at C-6 and C-8 respectiely.

Compound (103) on condensation with allylbromide in presence of anhydrous potassium carbonate in dry acetone gave 9-allyloxy-2,4-dimethyldihydrofuro (2,3-h)[1]-benzopyran-5(H)-one (104). The structure of (104) was established by its PMR spectrum (Fig. 11) which exhibited doublet at δ 1.5



(fig-11): 9-Allyloxy-2,4-dimethyl dihydrofuro (2,3-h) (1)-benzopyran-5(H)-one (104)

(J=7Hz) indicating the presence of methyl group at C-2. Singlet at δ 2.3 indicated methyl group at C-7. Multiplet at δ 2.8-3.8 indicated two protons at C-3 and two protons of allyl group, two multiplets at δ 4.5 and 5.1 indicated the presence of other allyl protons and proton at C-2. Two singlets at δ 6.1 and 6.95 indicated the presence of two protons at C-6 and C-8 respectively.

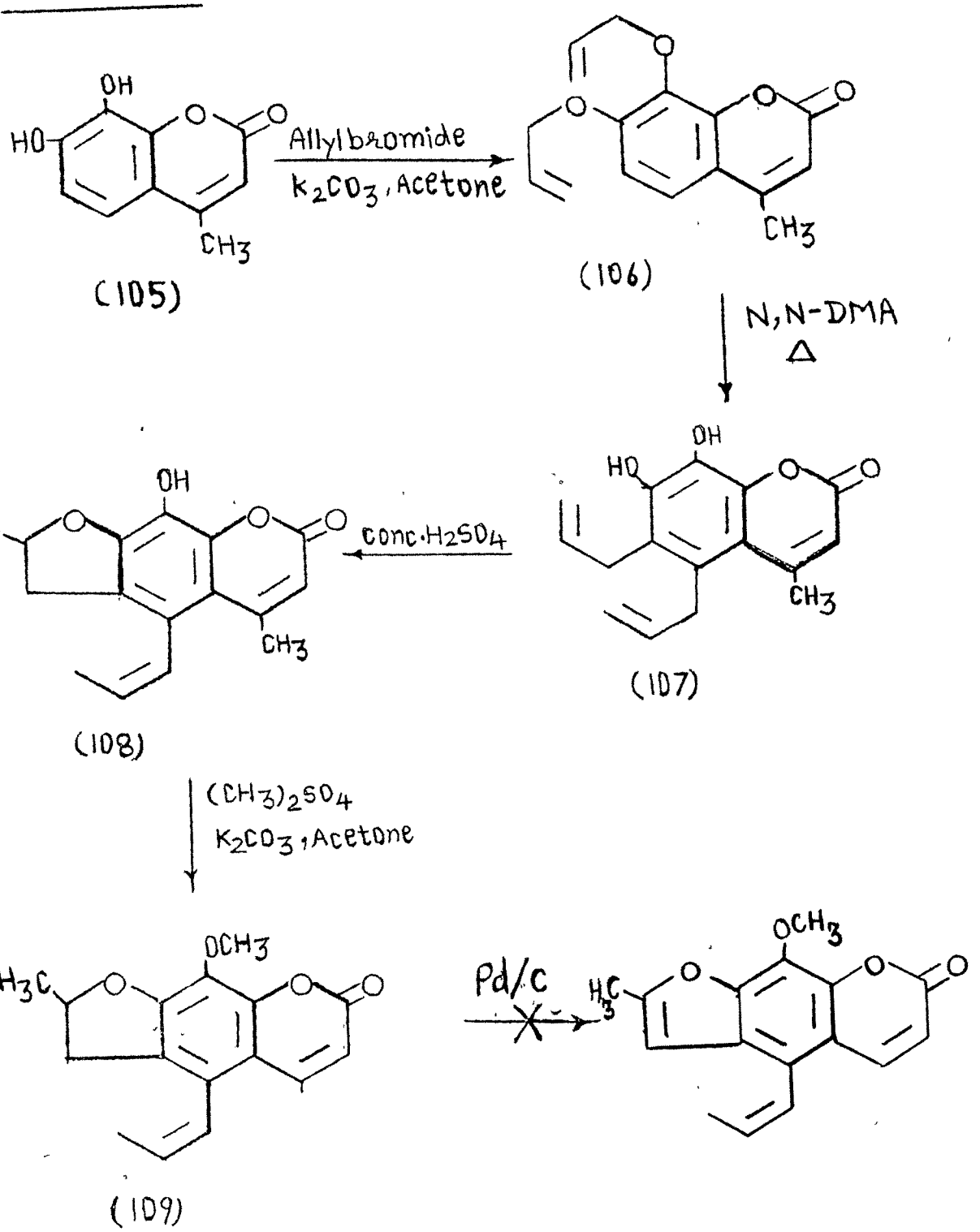
This compound (104) on Claisen rearrangement in boiling N,N-dimethylaniline gave 2,7-dimethyl-8-allyl-9-hydroxy (2,3-h) [1]-benzopyran-5(H)-one which was identical with (97a) by mixed m.p. and Co-TLC. It also showed PMR spectrum same as that of (97a) [Scheme- 28]

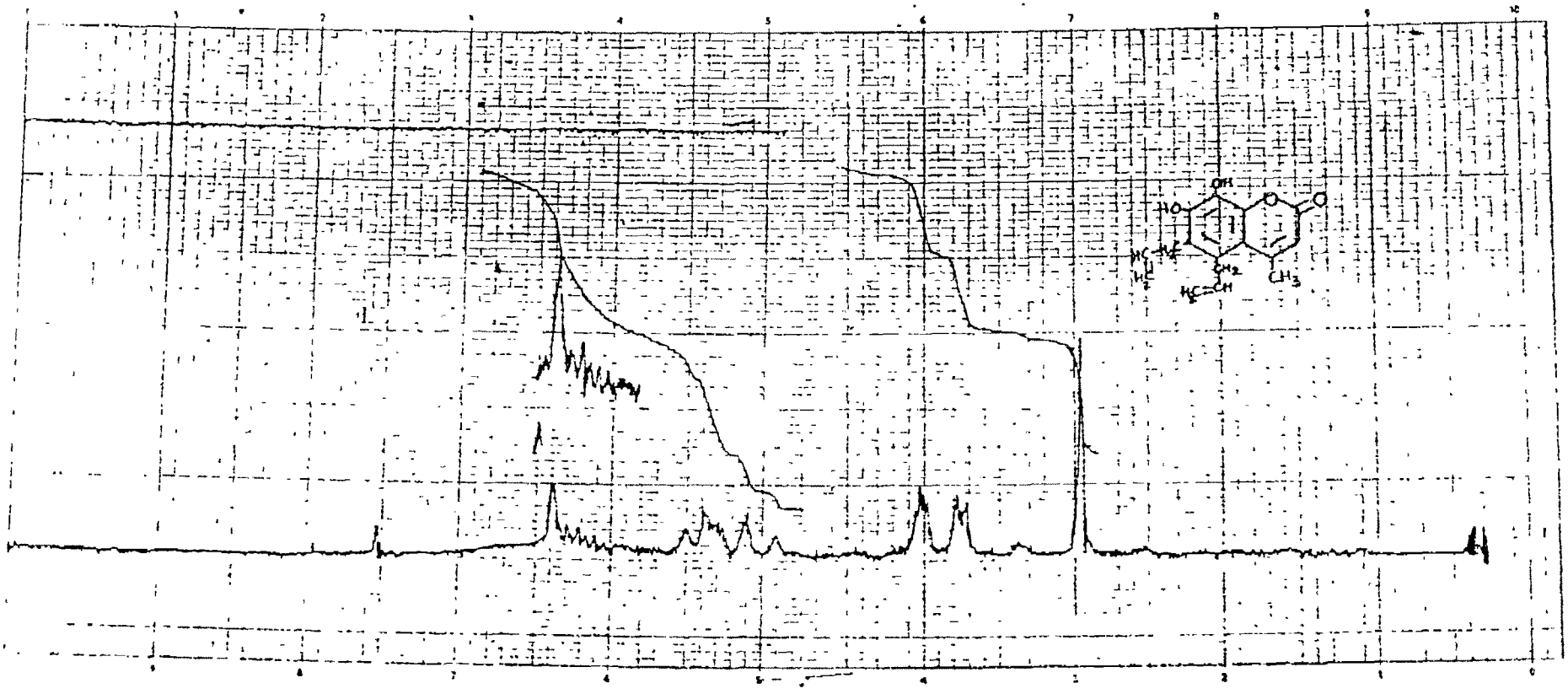
Allylation of 7,8-dihydroxy-4-methyl coumarin

After carrying out the Claisen rearrangement of 6,7-diallyloxy-4-methyl coumarin, it was thought of interest to carry Claisen rearrangement of 7,8-diallyloxy-4-methyl coumarin.

7,8-dihydroxy-4-methyl coumarin (105) on condensation with 2-moles of allylbromide in presence of anhydrous potassium carbonate in dry acetone gave 7,8-diallyloxy-4-methyl coumarin (106). This compound when subjected to Claisen rearrangement in boiling N,N-dimethylaniline gave 5,6-diallyl-7,8-dihydroxy-4-methyl coumarin (107). The structure of this compound was established by PMR spectrum taken in $CDCl_3$ (Fig. 12).

Scheme-29

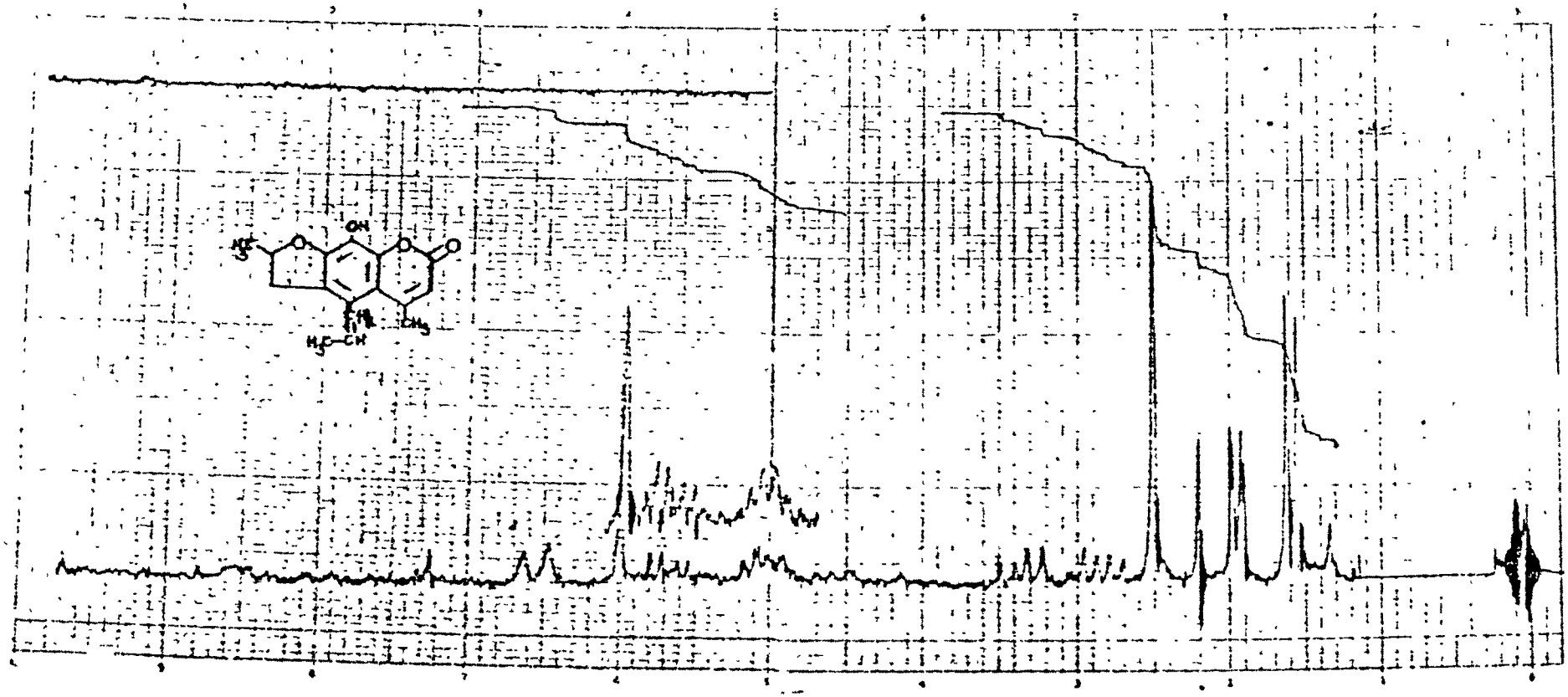

OH
HO
CH3
(105)
Allylbromide
K2CO3, Acetone
(106)
N,N-DMA
Δ
OH
HO
CH3
(107)
conc.H2SO4
OH
H3C
CH3
(108)
(CH3)2SO4
K2CO3, Acetone
OCH3
H3C
(109)
Pd/C
OCH3
H3C



(fig-12): 5,6-diallyl-7,8-dihydroxy-4-methyl coumarin (107)

The singlet at δ 2.7 indicated the presence of methyl group at C-4. Multiplet at δ 3.4 indicated two protons of allyl group ($-\underline{CH_2}-CH=CH_2$) at C-5. Other multiplet at δ 3.75 indicated two protons of allyl group ($-\underline{CH_2}-CH=CH_2$) at C-6. Two multiplets at δ 4.6-4.7 and 4.8-5.2 indicated two terminal protons of allyl group ($-CH_2-CH=\underline{CH_2}$) at C-5 and C-6 respectively. One multiplet at δ 5.5-6.0 indicated two protons of ~~a-1~~ allyl group ($-CH_2-\underline{CH}=CH_2$) at C-5 and C-6. Singlet at δ 6.01 indicated proton at C-3. Moreover, this compound gave green colouration with neutral ferric chloride which indicated the presence of two free ortho hydroxy groups [Scheme-29]

(107) when titurated with conc. H_2SO_4 (80%) one allyl group at C-6 [illegible] cyclised and other allyl group at C-5 underwent rearragement. The product obtained was 4-(propen-2-yl)2,5 dimethyl-9-hydroxy-dihydrofurano (2,3-g)-[1]-benzopyran-7(H)-one (108). The structure of this compound was established by PMR spectrum taken in $CDCl_3$ (Fig. 13). The doublet exhibited at δ 1.55 (J=7Hz) is of methyl group at C-2. The doublet at δ 1.9 is of terminal methyl group of allyl group at C-4 ($-CH=CH-\underline{CH_3}$) which indicated that allyl group at C-4 underwent prototropic shift. Singlet at δ 2.5 is of methyl group at C-5. The double doublets observed at δ 2.9 (J=18,8Hz) and 3.4 (J=18,8Hz) indicated the two protons at C-3. The multiplet at δ 5.0 for two protons indicated one proton of allyl group ($CH=\underline{CH}-CH_3$) at C-4 and other proton at C-2 of dihydrofurano



(fig-13): 4-(Propen-2-yl)-2,5-dimethyl-9-hydroxy-dihydrofusano(2,3-g)-(1)-benzopyran-7(H)-one(108)

ring. Multiplet at δ 5.8 indicated one proton of allyl group (-CH=CH-CH_3) at C-4. Singlet at δ 5.95 indicated proton at C-6.

This compound (108) when methylated with dimethylsulfate in presence of anhydrous potassium carbonate and dry acetone gave 4-(propen-2-yl)-2,7-dimethyl-9-methoxy-dihydrofuro (2,3-g) -[1]-benzopyran-7(H)-one (109). The structure of this compound was established by PMR spectrum taken in $CDCl_3$. All the signals were same as in the spectrum of compound (108) except the extra singlet at δ 4.0 indicating the presence of methoxy group at C-9. The dehydrogenation of compound (110) with palladised charcoal (10%) in boiling diphenylether failed.

Synthesis of Furocoumarins by Intramolecular Wittig Reaction

Different methods are available for the synthesis of furocoumarins, but intramolecular Wittig reaction for the synthesis of furocoumarins is still not reported. Moreover it is regiospecific method.

Wittig and Geissler[51] first time found that reaction of benzophenone with methylene triphenylphosphorane gave 1,1-diphenylethylene and triphenylphosphine oxide in almost quantitive yield. The phosphorane was prepared from triphenyl phosphonium bromide and phenyl lithium [Scheme-30].

This discovery led to the development of new method

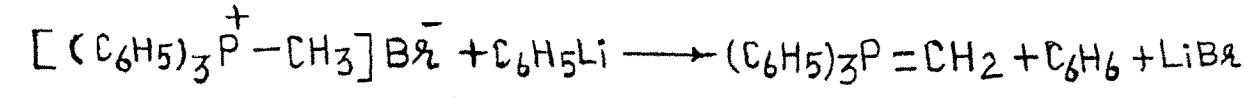
for the synthesis of different olefins[52-54] under the name of Witting reaction. The advantage of this new method was, the carbonyl group was specifically replaced by carbon carbon double bond, without the formation of isomers. It also gave total control over double bond.

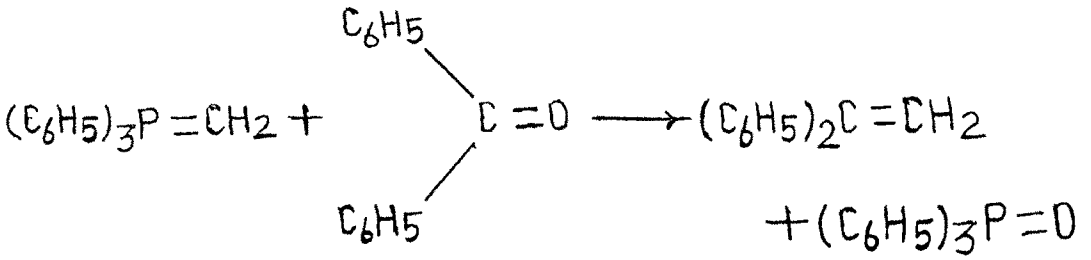
The mechanism can be explained as shown in [Scheme-31] Witting reaction forms both σ and π bonds in one reaction so the disconnection is at the double bonds with a nearly free choice of which end comes from alkylhalide and which comes from carbonyl compounds. But generally the stable phosphoranes are known to provide major amounts of trans-olefins and minor amounts of Cis-olefins.

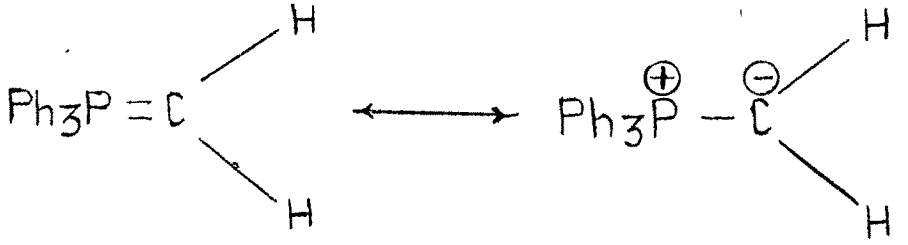
Phosphorous ylides are most commonly prepared by deprotonation of Phosphonium salts with a base. Bestmann and coworkers[55] have extensively studied these ylides and reported various application of these reagents. They are useful for converting cyclic ketones to exocyclic olefins.[56] Several heterocyclic compounds have also been prepared by making use of these ylides.[57]

This method is proved to be especially valuable tool in synthetic organic chemistry. It has been used for the synthesis of various olefinic, Carbocyclic and heterocyclic compounds. Among the compounds synthesised are terpenoids,[58] alkaloids,[59] Vitamins,[60] carotenoids,[61] Steroids[62] and several

Scheme-30 Wittig and Geissler[51]

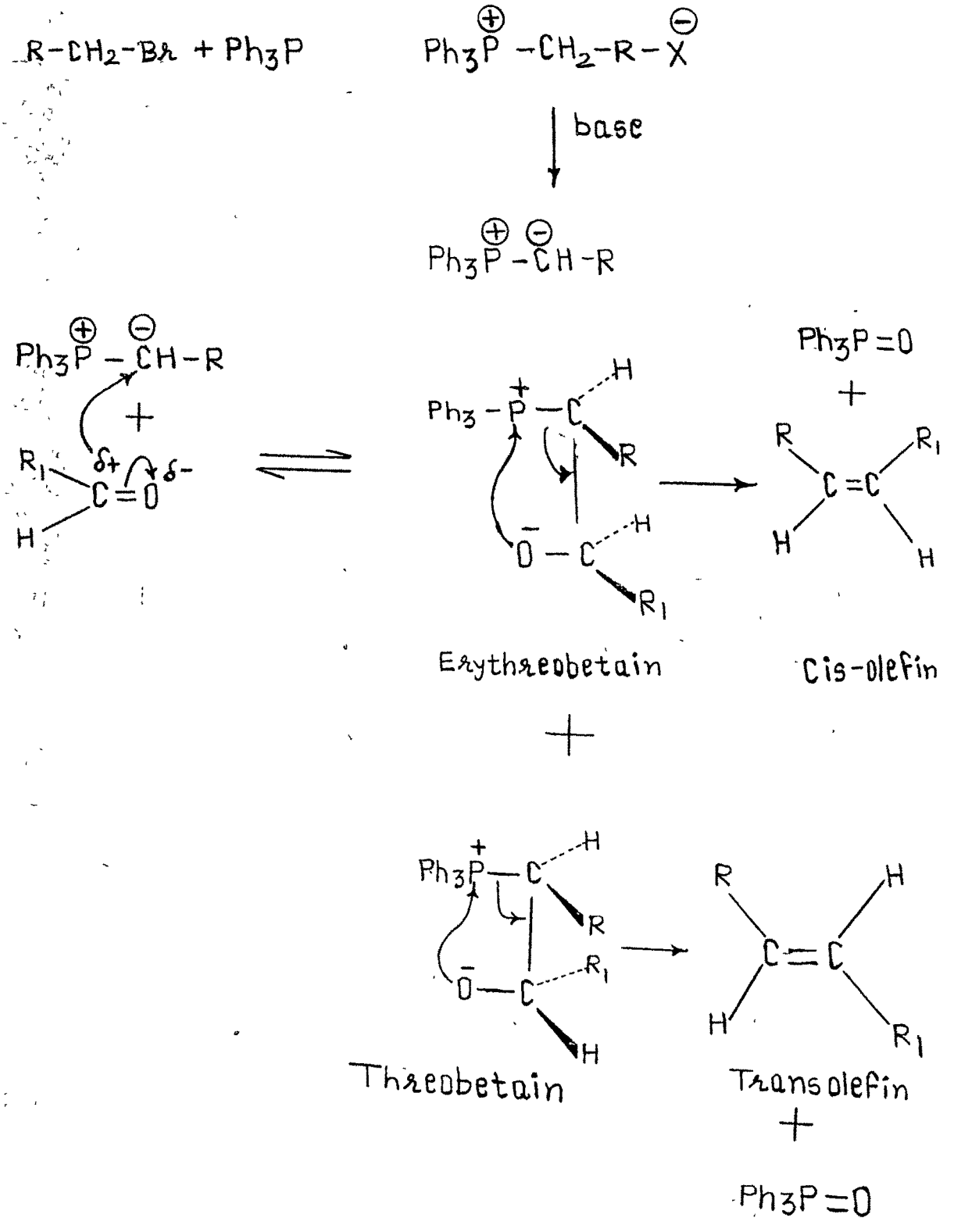






Ylene Form Ylide Form

Scheme -31


R-CH2-Br + Ph3P
Ph3P⊕ -CH2-R-X⊖
base
Ph3P⊕ ⊖CH-R
Ph3P⊕ ⊖CH-R
+
R1 δ+ δ- C=O
H
Ph3 - P+ - C
H
R
O⁻ - C
H
R1
Erythreobetain
Ph3P=O
+
R
R1
C=C
H
H
Cis-olefin
+
Ph3P+ — C
H
R
O⁻ — C
R1
H
Threobetain
R
H
C=C
H
R1
Trans olefin
+
Ph3P=O

other natural products like pheromones[63] and Prostaglandins[64] etc.

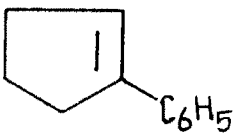
Cyclic compounds were prepared by intramolecular Wittig reactions. Biber and Eisman[65] had prepared 1-phenylcyclopentene (111) by intramolecular Wittig reaction [Scheme-32] Griffin and Witschard[66] had synthesised 1,4-diphenyl-1,4-cyclohexadiene (112) from 2-benzoylethylidenetriphenyl phosphorane by intramolecular condensation of two molecules of phosphorane [Scheme-32]

Several workers[67-71] had used Witting reaction for the synthesis of heterocyclic compounds. The compounds synthesised are presented in the following [Scheme-33]

Hidekazu and Massashi[72] and M. Le Corre et al.[73] had synthesised chromones by intramolecular Wittig reaction.

Wittig reaction had also been applied to number of other classes of natural products such as furocoumarins, furobenzopyrans, indoles etc. M.Le Corre et al.[74,75,76] had synthesed benzofurans (114) from o-hydroxybenzyltriphenylphosphonium bromide (113) and acid chloride or acid anhydride in presence of base by intramolecular Wittig reaction [Scheme-34]. He had also synthesised isochromenes (115) by the reaction of monophosphonium salts derived from α,α-dibromo-o-xylene with sodium carboxylates in presence of base [Scheme-36]

Scheme -32 Biber and Eismann[65]

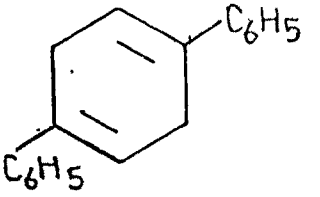
$(C_6H_5)_3P=CH(CH_2)_3COC_6H_5$ $\xrightarrow[\text{Wittig Reaction}]{\text{Intramolecular}}$ 

(111)

+

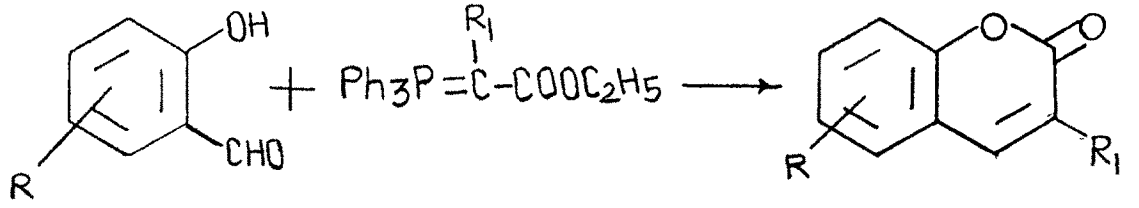
$C_6H_5P=O$

Griffin and Witschard[66]

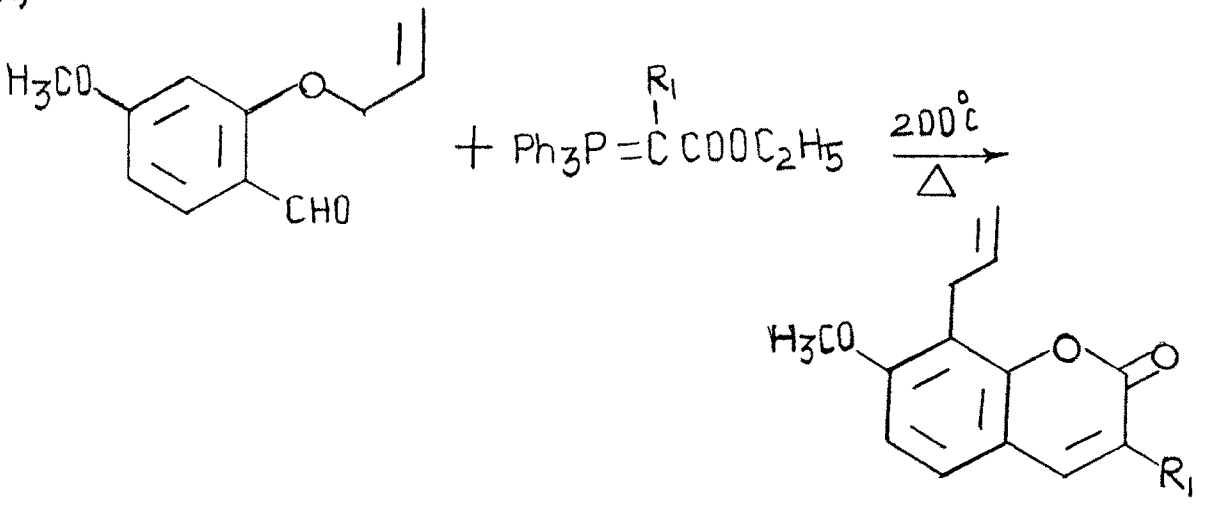
$2(C_6H_5)_3P=CH-CH_2-COC_6H_5$ $\xrightarrow[\text{Wittig Reaction}]{\text{Intramolecular}}$ 

(112)

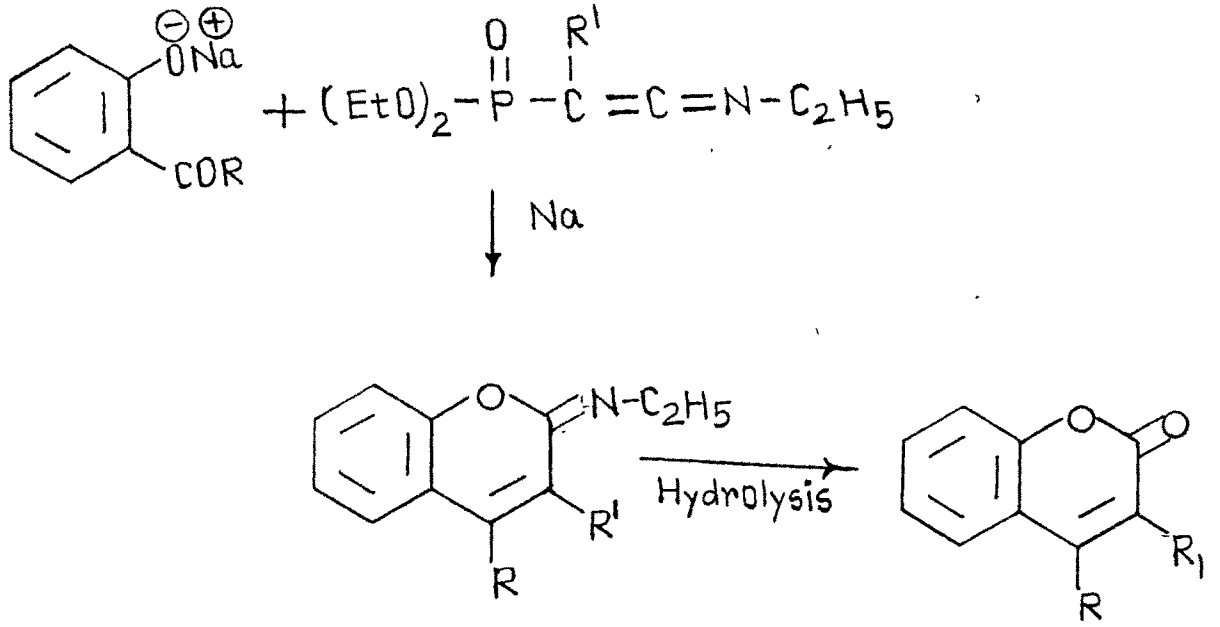
Scheme -33 Mali and Coworkers[67]



(a)

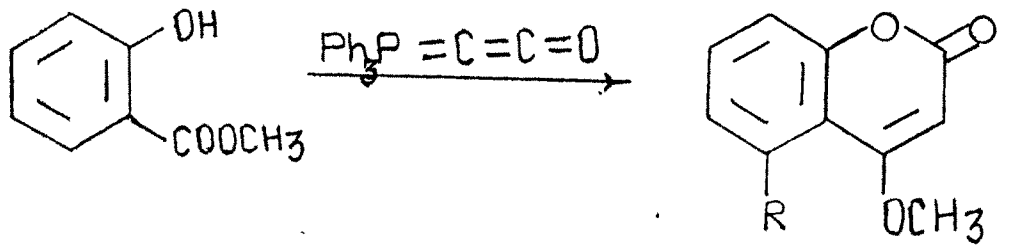


Scheme - 33 M. Jiro et al[68]



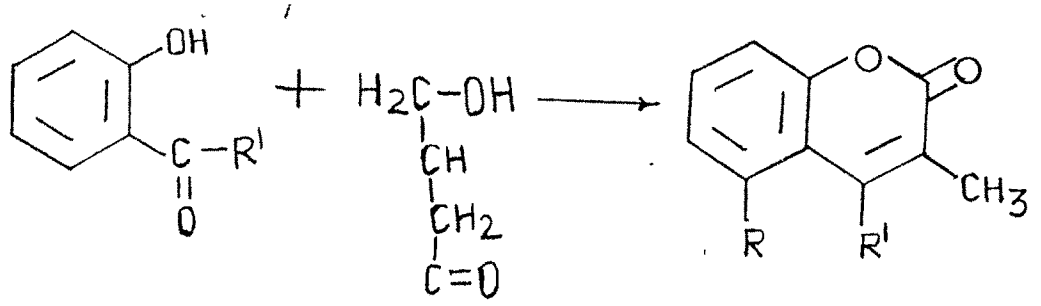
Scheme - 34 K. Niekish et al[69]

(a)

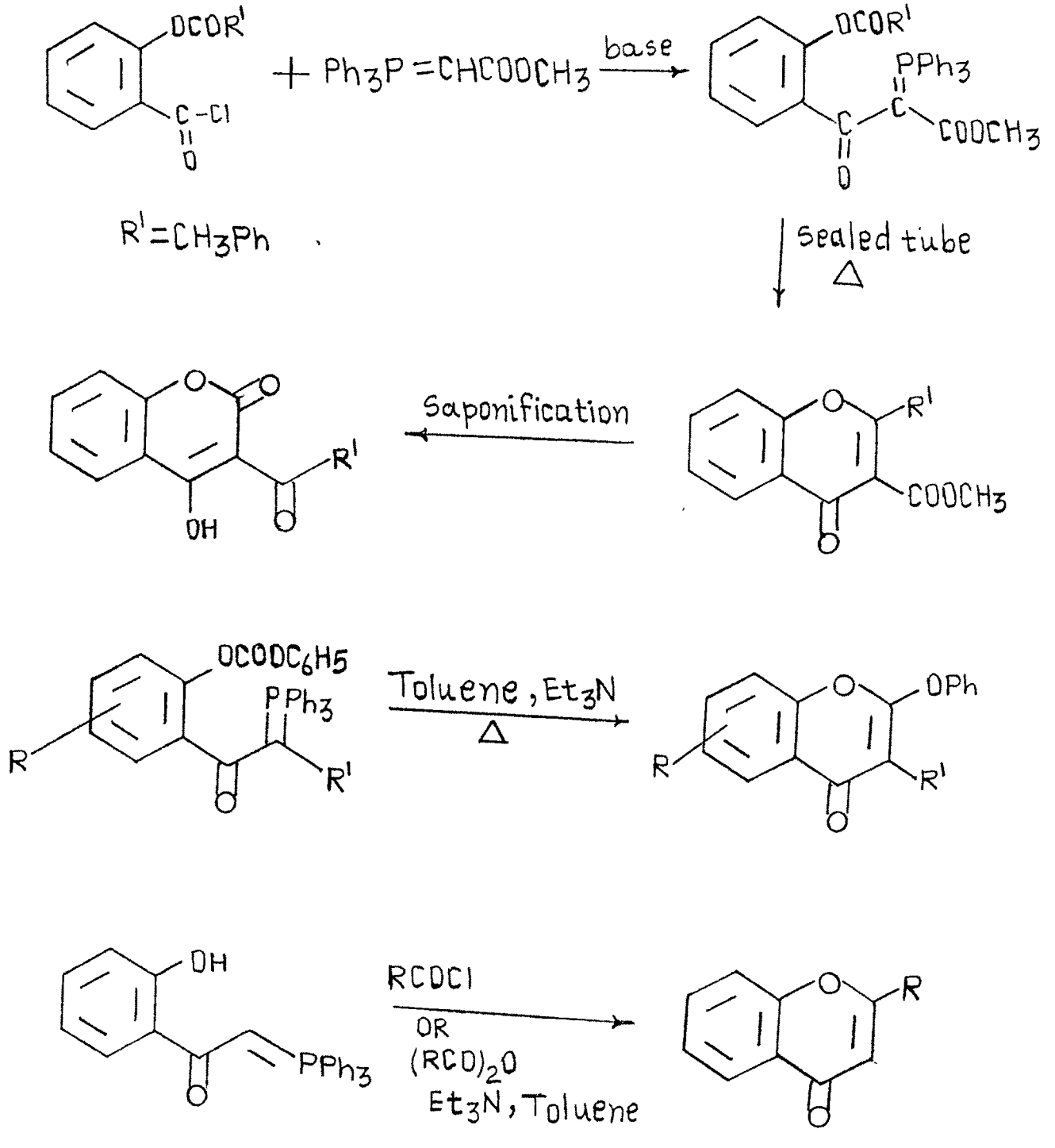


F Gibachino et al[70]

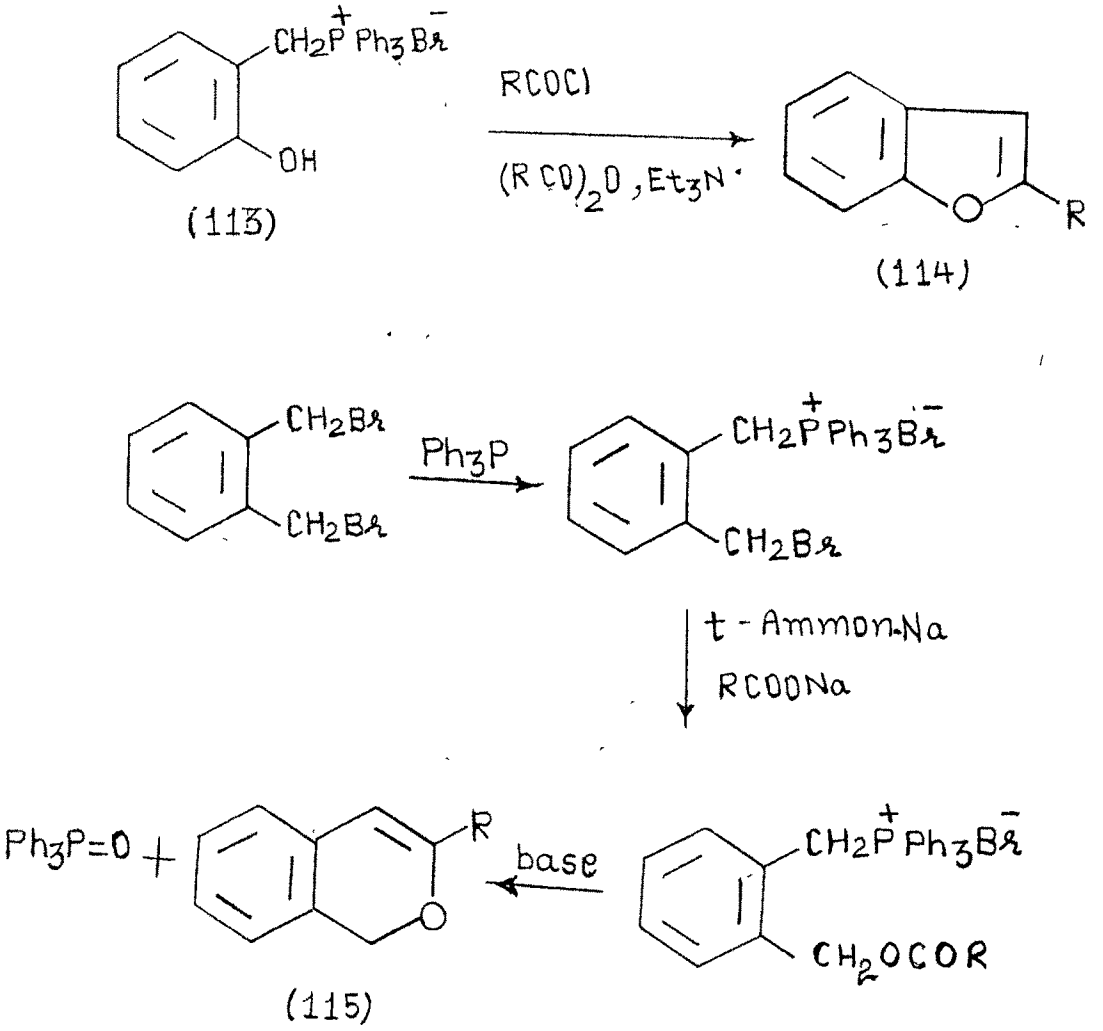
(b)



Scheme - 35 Babin et al[71]



Scheme-36 M·Corre et al[74,75]



He had also synthesised benzofurans (117) from o-acyloxy benzylidene triphenylphosphoranes by intramolecular Wittig reaction [Scheme-37] (116).

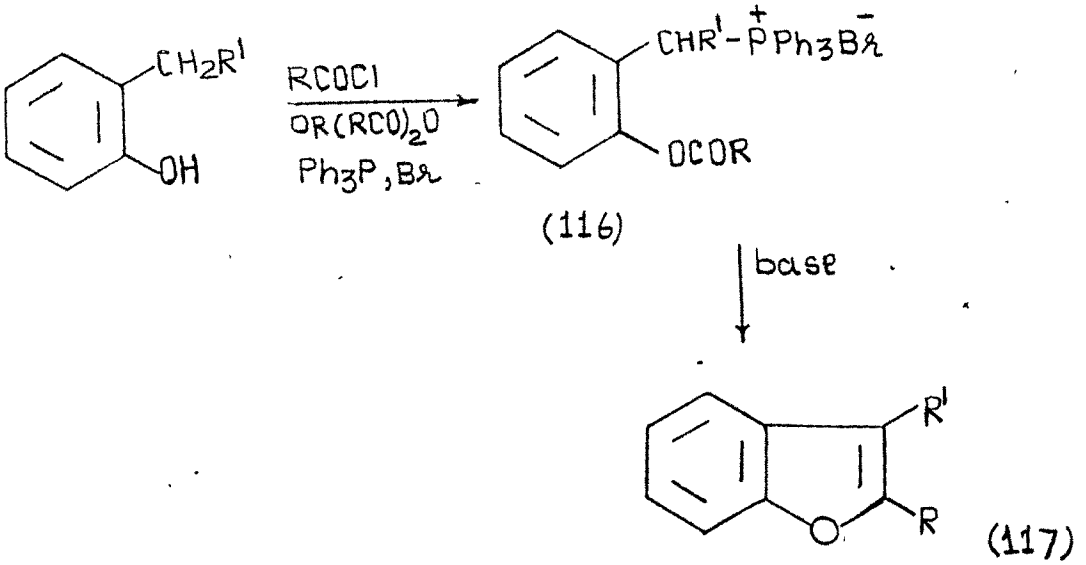
B. Mackittrick and R. Stevenson[77] had synthesised aryl-benzofuran (119) constituent of Sophora tomentosa. In this synthesis the key step is formation of benzofuran which was obtained by intramolecular Witting reaction of an o-bromo-methylphenylaryol ester (118) [Scheme-38]

He had also synthesised Acamelin (122)[78] a natural product from 3-methoxypyrocatechol. Here the key step is the formation of 2-methyl benzofuran (121) using o-acetoxybenzylbromide (120) [Scheme- 39]. He had also synthesised some natural lignans,[79] a group of eupomatenoids and yeast antioxidant benzofuran analogs by this method.

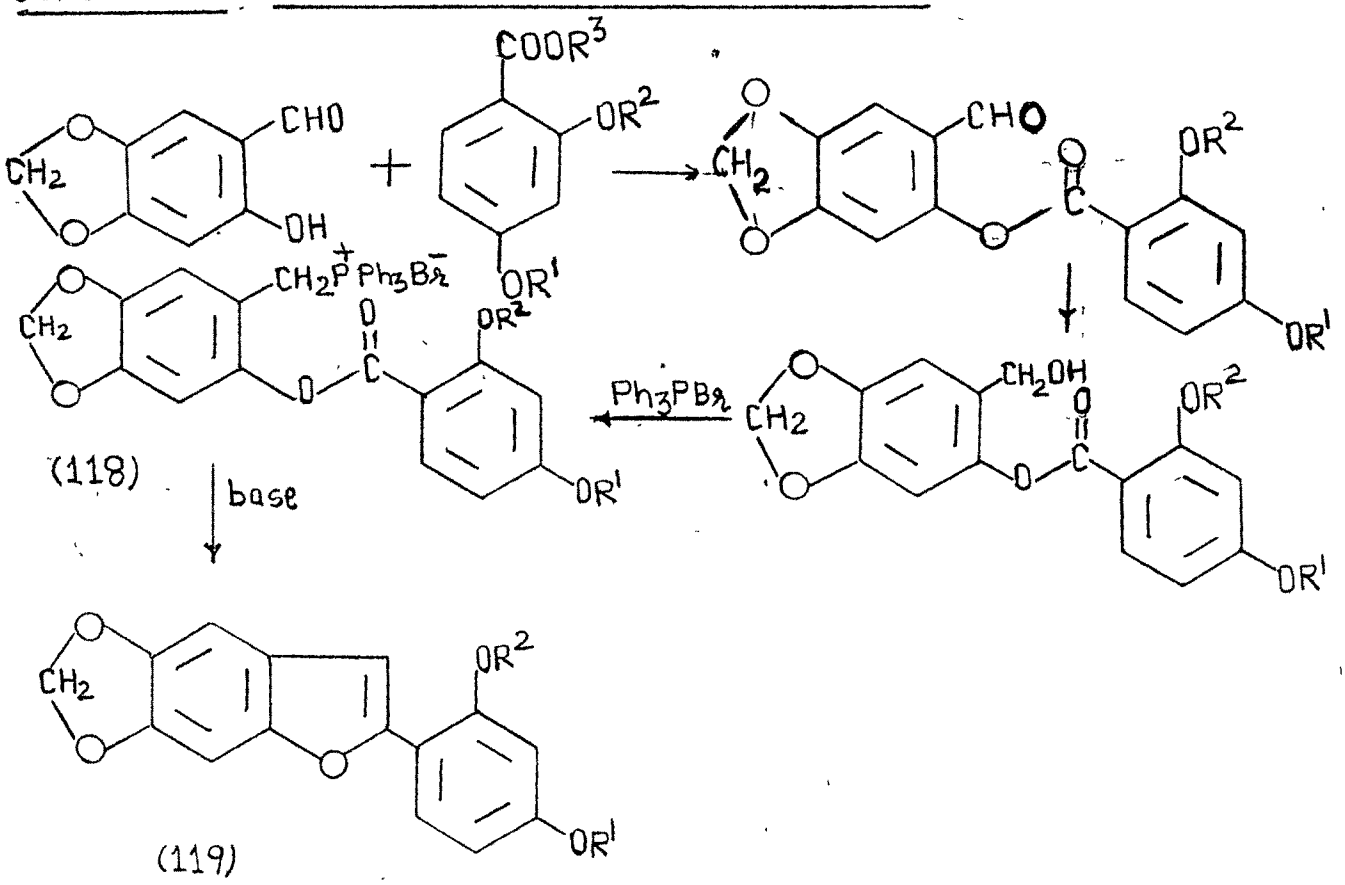
M.Le. Corre et al.[80] had used intramolecular Wittig reaction for the synthesis of indoles (124) in good yields, from amidocarbonyl group (123) [Scheme- 40]

In view of all these reactions, it was thought of interest to synthesise some furocoumarins using intramolecular Wittig Reaction. Because of its regiospecificity and quantitative yields use of this reaction for the synthesis of some linear and angular furocoumarins is reported here. Number of steps in this method are reduced andbecause as a rule Wittig reagents

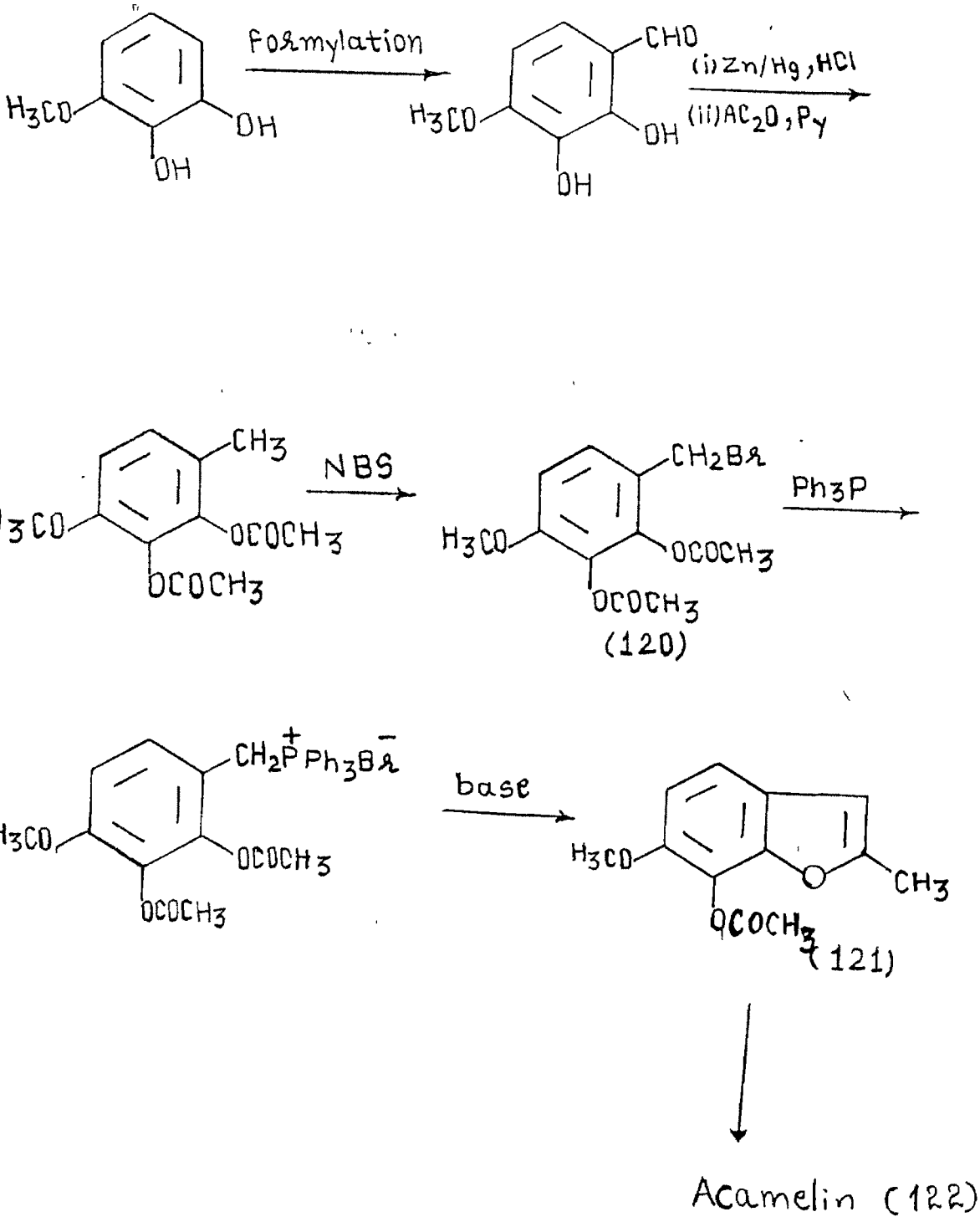
Scheme -37 M. Corre et al[76]



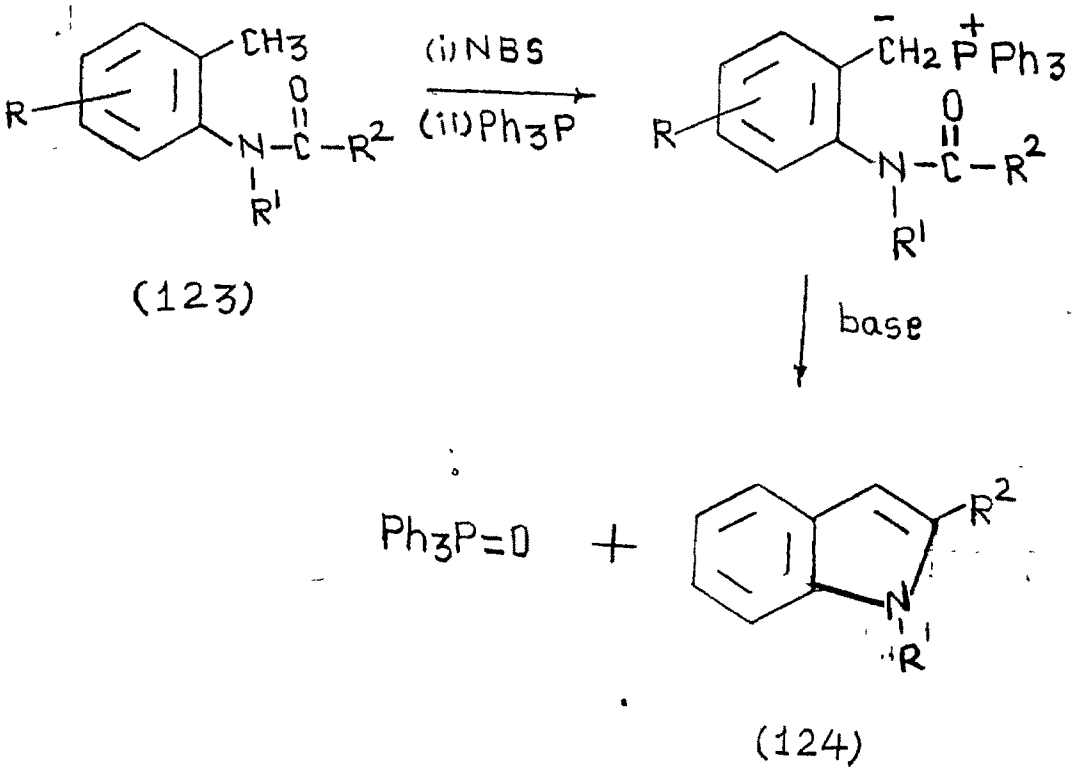
Scheme -38 B. Mackittrick and R. Stevenson[77]



Scheme - 39 B. Mackittrick and R. Stevenson[78]



Scheme - 40 M. Le. Corre et al[80]



(123)

(124)

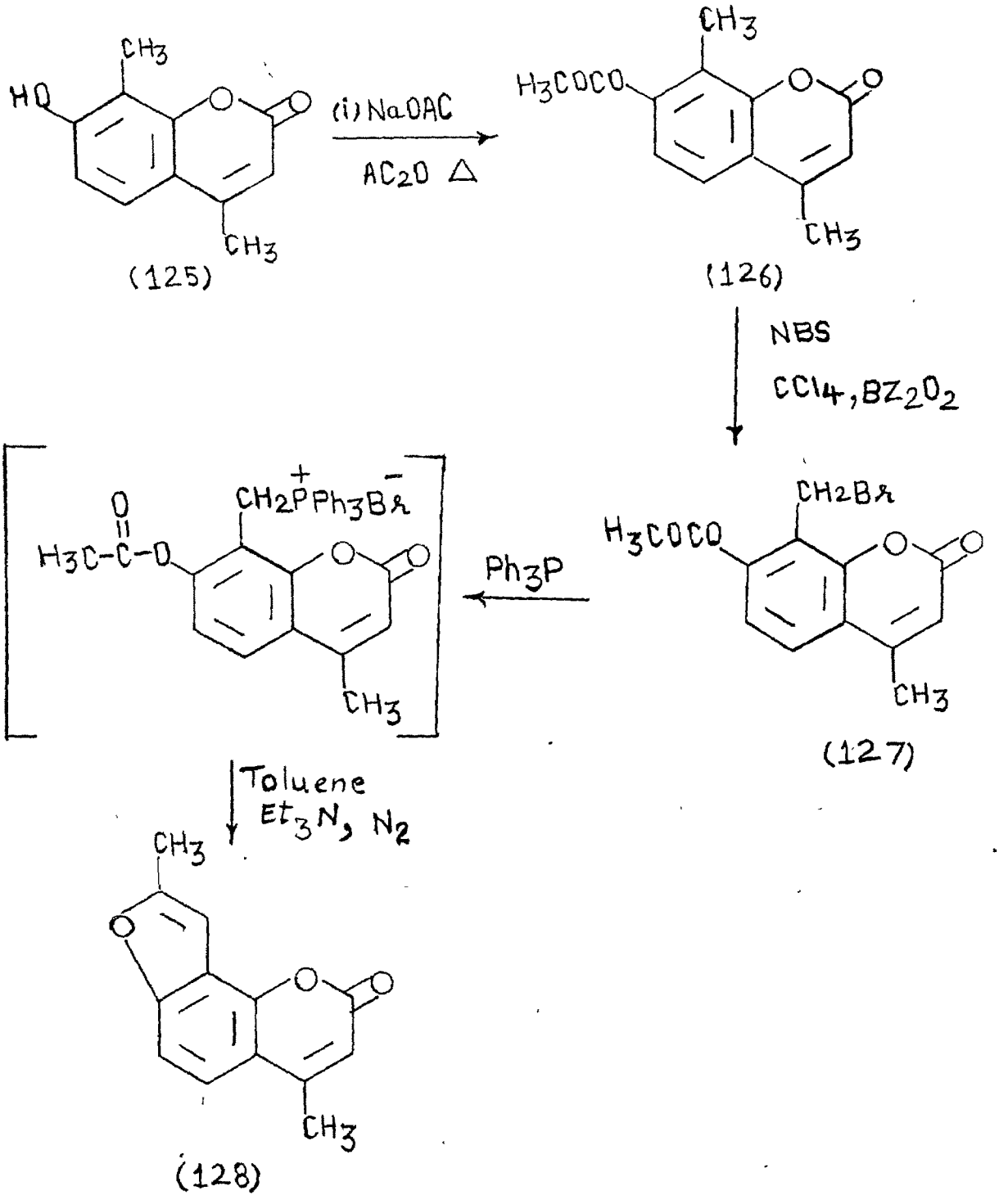
are not isolated, immediately following their generation, they are allowed to react with carbonyl compounds in the same reaction flask. It is easier to prepare linear furocoumarins in very good yields by this method when compare with the other standard methods for the synthesis of psoralens.

Synthesis of 2,7-dimethyl-furo (2,3-h)-benzopyran-5(H)-one (128)

2-Methyl resorcinol on Pechmann condensation with ethylacetoacetate in conc. H_2SO_4 gave 4,8-dimethyl-7-hydroxy coumarin (125). This compound on acetylation with sodium acetate and acetic anhydride gave 7-acetoxy-4,8-dimethyl coumarin (126). This when reacted with N-bromosuccinimide gave 7-acetoxy-8-bromomethyl-4-methyl coumarin (127). The structure of this compound was established by its PMR spectrum taken in $CDCl_3$. This singlet at δ 2.45 for 6 protons indicated the presence of methyl group at C-4 and acetoxy group at C-7. Singlet at δ 4.45 indicated the presene of $-CH_2$ group at C-8. Singlet at δ 6.25 is for one proton at C-3 and two doublets at δ 7.2 and 7.35 (J=9Hz) indicated the ortho coupling of two aromatic protons at C-5 and C-6.

Compound (127) when allowed to react with triphenylphosphine in dry benzene gave 7-acetoxy-4-methyl-8-bromotriphenyl phosphosnium coumarin, which was not isolated. The oil obtained after distilling dry benzene was used directly

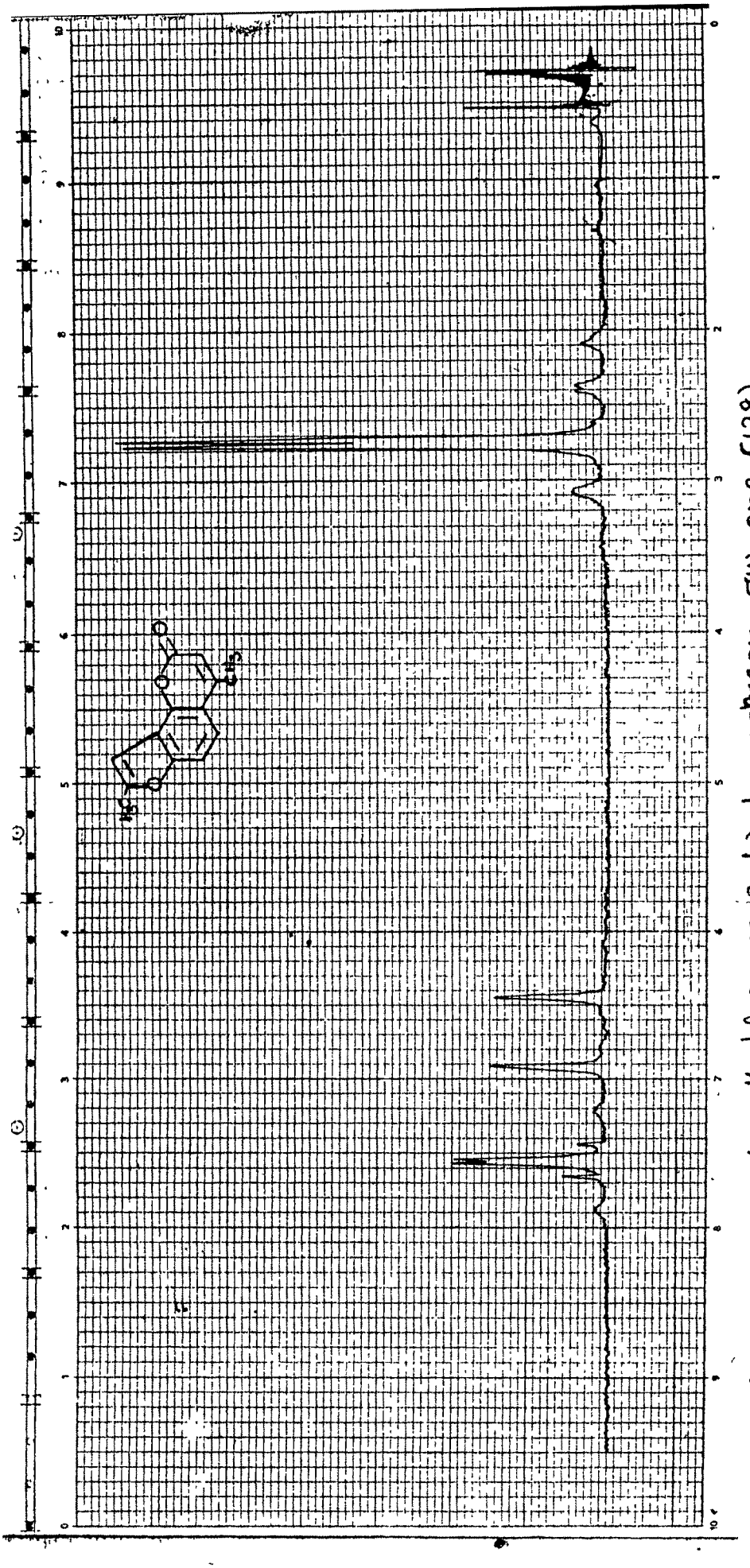
Scheme-41


HO
CH3
(i) NaOAC
AC2O Δ
H3COCO
(125)
(126)
NBS
CCl4, BZ2O2
CH2BR
(127)
Ph3P
CH2PPh3Br
Toluene
Et3N, N2
(128)

for further reaction. The oil was suspended in dry toluene and triethylamine as a base was added to it, and the reaction was carried out under the atmosphere of N_2. On working up of the reaction mixture it gave 2,7-dimethylfuro (2,3-h)benzo-pyran-5(H)-one (128) [Scheme- 41]. The mechanism of this reaction is shown in [Scheme- 42]. The structure of this compound was established by its PMR spectrum taken in $CDCl_3$ Two singlets at δ 2.5 indicated two methyl groups at C-2 and C-7. Disappearance of peak at δ 4.4 indicated that Wittig reaction had taken place. Singlet at δ, 6.15 indicated proton at C-6. Singlet at δ 6.65 indicated C-3 proton ; i.e. furan ring proton. Two doublets at δ 7.2 and 7.35 (J=9Hz) indicated orthocoupling of two aromatic protons at C-8 and C-9 (Fig. 14). The structure of this compound was further confirmed by taking mixed m.p. of the authentic sample of (128).

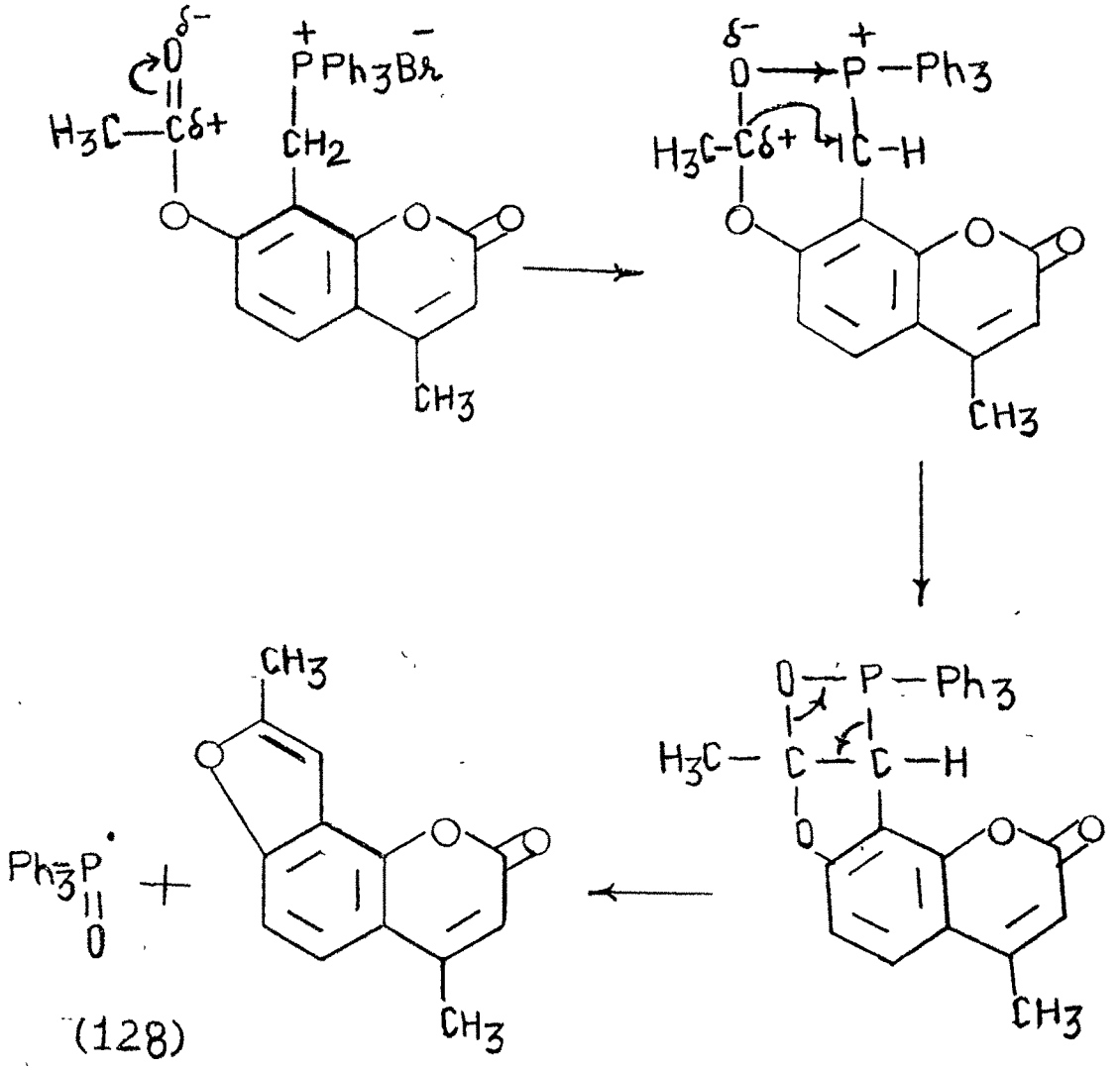
Synthesis of 2,5-dimethyl-furo(2,3-g)-benzopyran-7(H)-one (132)

4-Methyl resorcinol on Pechmann condensation with ethyl-acetoacetate in conc. H_2SO_4 gave 4,6-dimethyl-7-hydroxy coumarin (129). This compound on acetylation with anhydrous sodium acetate and acetic anhydride gave 7-acetoxy-4,6-dimethyl-coumarin (130). Compound (130) on reaction with N-bromo-succinimide in carbon tetrachloride gave 7-acetoxy-6-bromo methyl-4-methyl coumarin (131). The structure of this compound



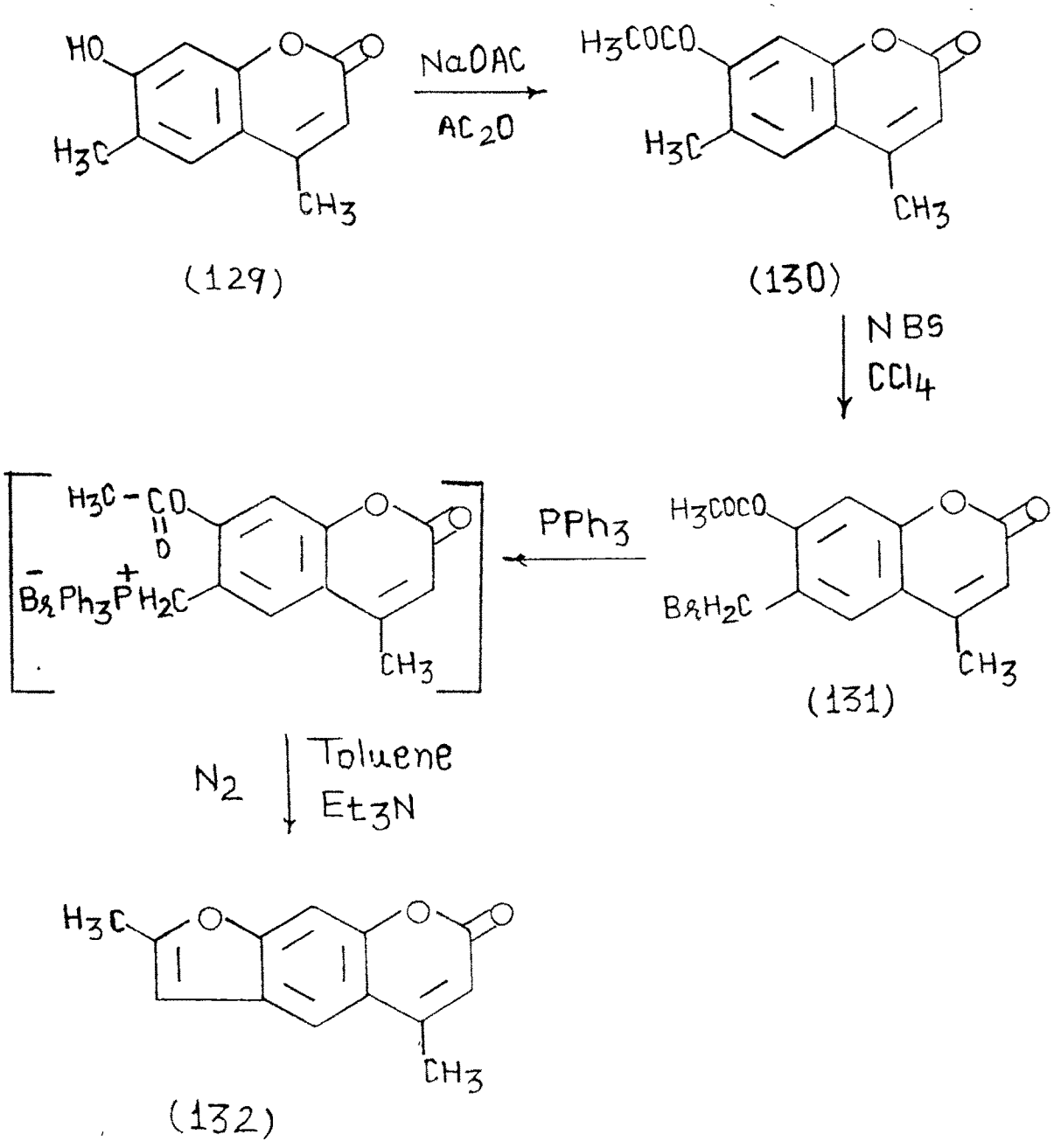
(fig-14) : 2,7-dimethylfuro (2,3-h)-benzopyran-5(4)-one. C(28).

Scheme-42 Mechanism of Wittig Reaction



(128)

Scheme-43

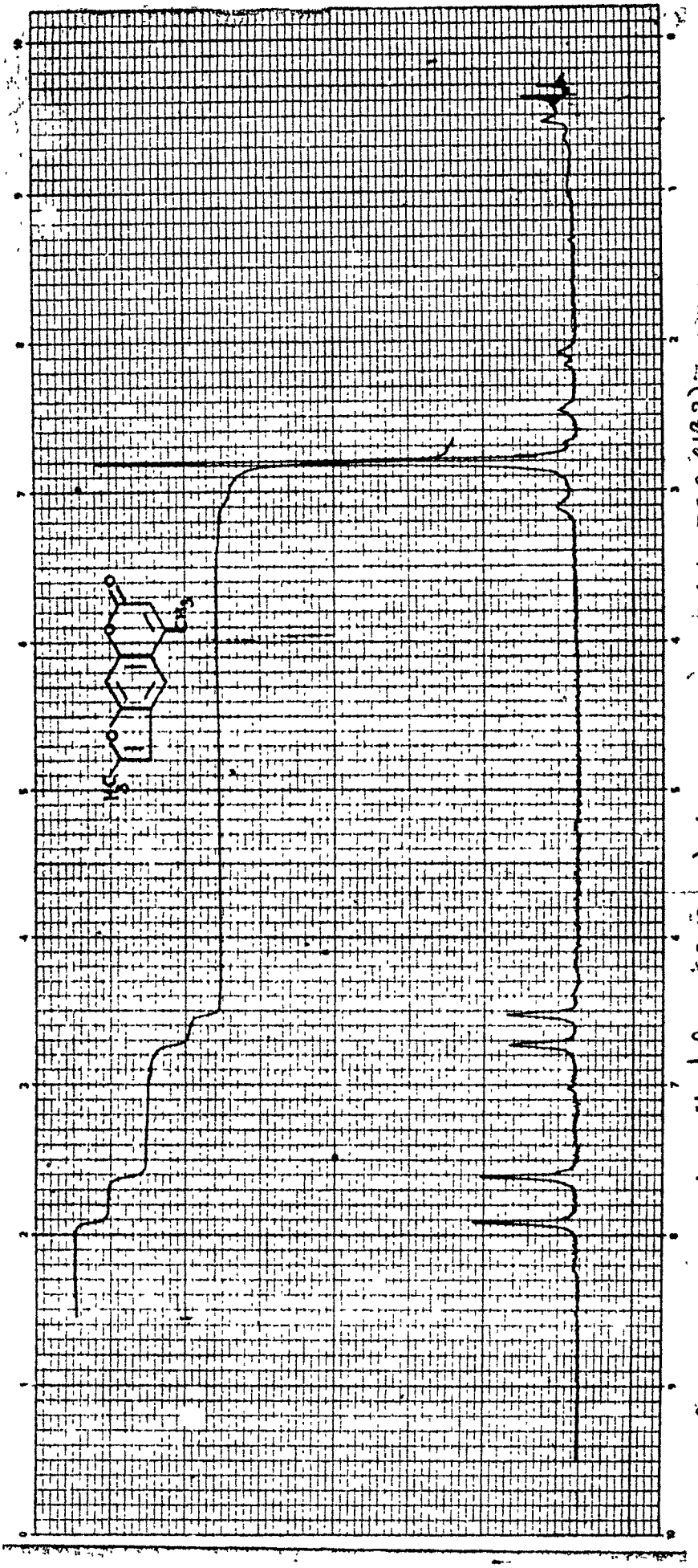

HO
H3C
CH3
NaOAC
AC2O
H3COCO
H3C
CH3
(129)
(130)
NBS
CCl4
H3C-CO
O
BrPh3P+H2C
CH3
PPh3
H3COCO
BrH2C
CH3
(131)
N2
Toluene
Et3N
H3C
CH3
(132)

was established by its PMR spectrum taken in ($CDCl_3$). (Fig.14) The singlet at δ 2.45 for six protons indicated methyl group at C-4 and acetoxy group at C-7. Singlet at δ 4.45 indicated $-CH_2$ group at C-6; singlet at δ 6.25 indicated proton at C-3 Two singlets at δ 7.15 and 7.65 indicated protons at C-8 and C-5 respectively.

Compound (131) when reacted with triphenylphosphine in dry benzene gave its corresponding phosphonium salt which on Wittig reaction carried out in the atmosphere of Nitrogen, gave the product 2,5-dimethyl-furo (3,2-g)-benzopyran-7(H)-one (132) [Scheme-43], the structure of which was established by its PMR spectrum taken in ($CDCl_3$). The singlet at δ 2.45 for 6 protons indicated two methyl groups atC-2 and C-5. Singlet at δ 6.2 indicated proton at C-6, singlet at δ 6.4 indicated furan ring proton at C-3 ; two singlets at δ 7.25 and 7.4 indicated protons at C-4 and C-9 respectively. (Fig.15) and also by mixed m.p. with authentic sample.

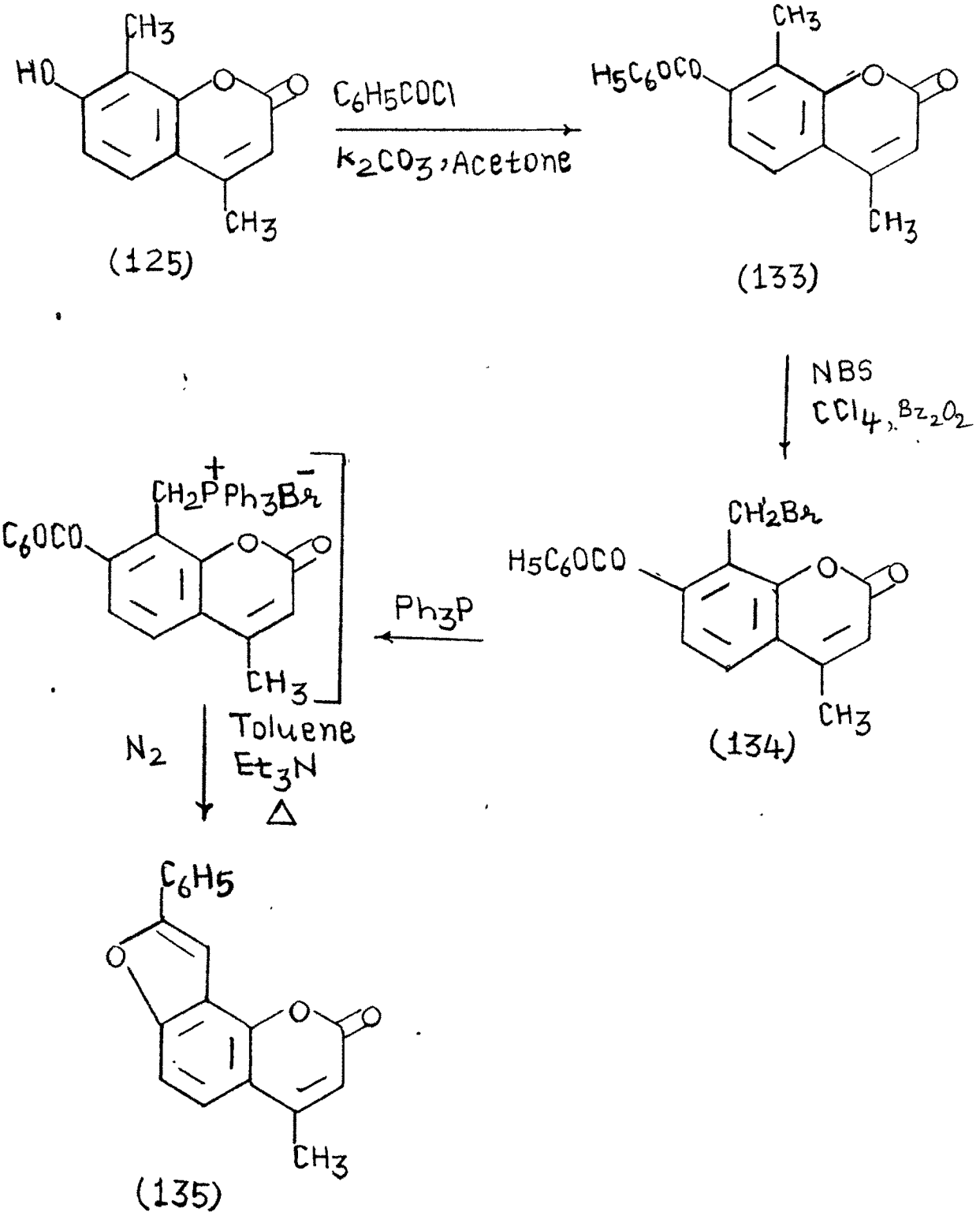
Synthesis of 7-methyl-2-phenyl-furo (2,3-h)-benzopyran-5(H) one (135)

7-Hydroxy-4,8-dimethyl coumarin (125) on condensation with benzoylchloride in presence of anhydrous potassium carbonate and dry acetone gave 7-benzoyloxy-4,8-dimethyl coumarin (133) which on bromination with N-bromosuccinimide gave 7-benzoyloxy-8-bromomethyl-4-methyl coumarin (134). The structure



(Fig-15) : 2,5-dimethyl furo(3,2-g)-benzopyran-7(H)-one (132)

Scheme - 44

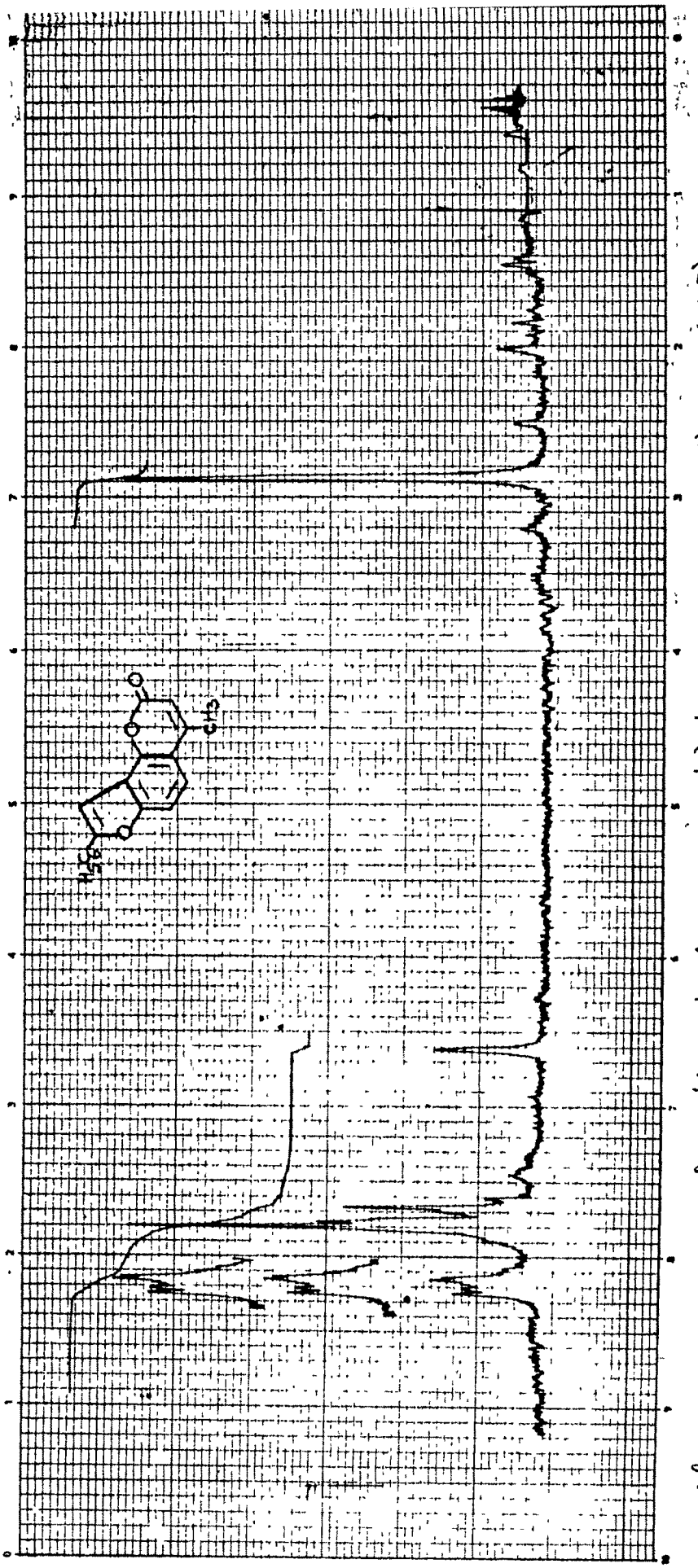

HO
CH3
CH3
(125)
C6H5COCl
K2CO3, Acetone
H5C6OCO
CH3
CH3
(133)
NBS
CCl4, Bz2O2
CH2Br
H5C6OCO
CH3
(134)
Ph3P
CH2P+Ph3Br−
H5C6OCO
CH3
N2
Toluene
Et3N
Δ
C6H5
CH3
(135)

of this compound was established by its PMR spectrum taken in $CDCl_3$ (Fig. 16). The singlet at δ 2.45 indicated methyl group at C-4. Singlet at δ 4.7 indicated two protons of methylene group at C-8. Singlet at δ 6.15 indicated proton at C-3. Two doublets at δ 7.2 and 7.55 (J=9Hz) indicated ortho coupling of aromatic protons of C-5 and C-6. This signal is mixed with multiplet at δ 7.5-8.2 of aromatic protons of bezoyloxy group at C-7.

This compound (134) when reacted with triphenylphosphine in dry benzene gave its corresponding phosphonium salt which on Wittig reaction carried out in the atmosphere of nitrogen, gave 7-methyl-2-phenyl-furo-(2,3-h)-benzopyran-5(H)-one (135). [Scheme-44]. The structure of this compound was established by its PMR spectrum taken in $CDCl_3$. Singlet at δ 2.5 indicated the methyl group at C-7. Singlet at δ 6.2 indicated proton at C-6. Multiplet from δ 7.2 to 8.25 indicated all aromatic protons with proton of furan ring at C-3 (Fig. 17).

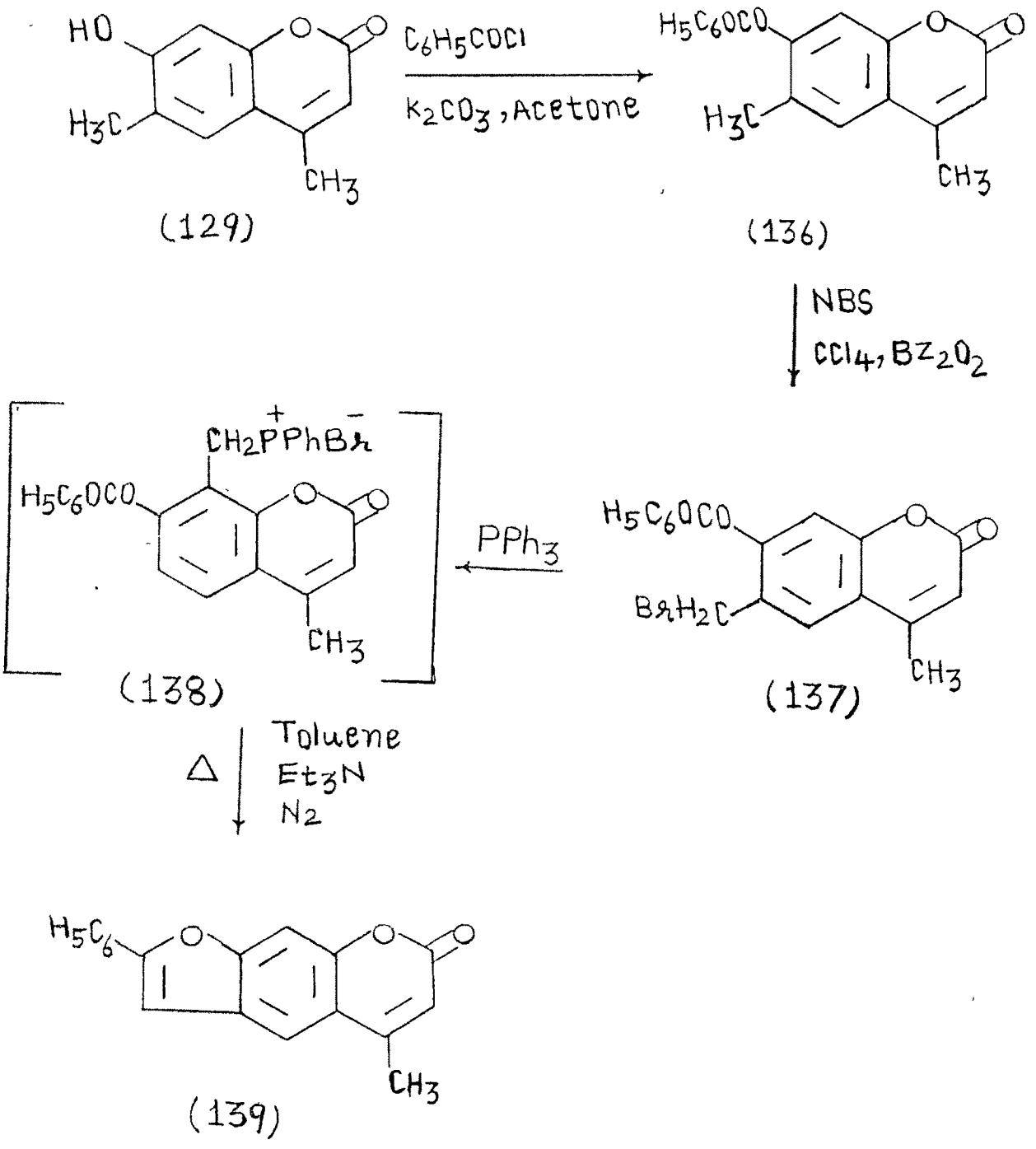
Synthesis of 5-methyl-2-phenyl (3,2-g)-benzopyran-7(H)-one (139)

4,6-Dimethyl-7-hydroxy coumarin (129) on condensation with benzoylchloride gave 7-benzoyloxy-4,6-dimethyl coumarin (136). This compound on bromination with N-bromosuccinimide gave 7-benzoyloxy-6-bromomethyl-4-methyl coumarin (137). The structure of this compound was established by its PMR



(fig-18) : 7-Methyl-2-phenyl-furo (2,3-b)-benzopyran-5(H)-one (135).

Scheme - 45



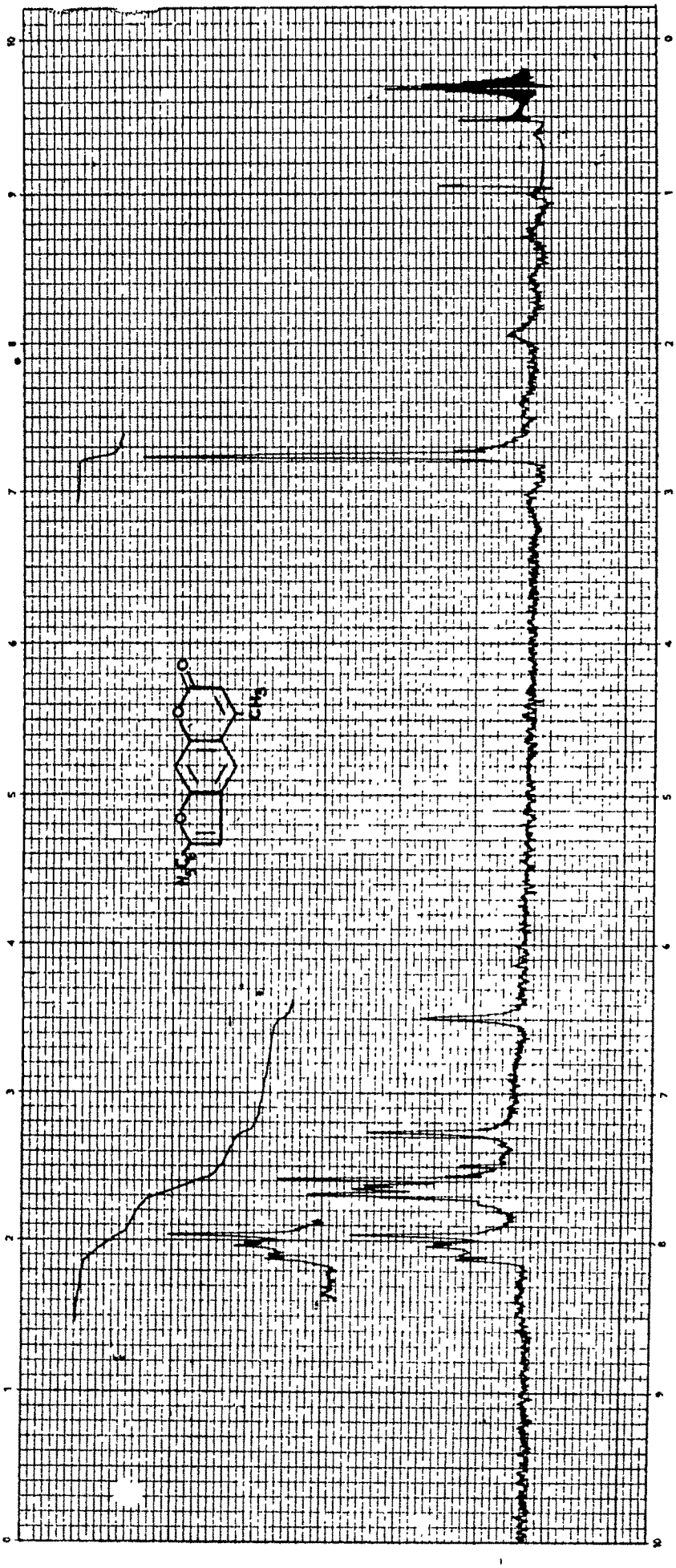
(129) (136) (138) (137) (139)

spectrum taken in $CDCl_3$. Singlet at δ 2.45 indicated the presence of methyl group at C-4. Singlet at δ 4.5 indicated methyene group at C-6. Singlet at δ 6.2 indicated proton at C-3. Multilet at δ 7.3 to 7.6 indicated five aromatic protons of benzoyloxy group at C-7. Two doublets at δ 8.1 and 8.2 (J=2Hz) indicated protons at C-5 and C-8 respectively. (Fig. 1

Compound (137) on reaction with triphenylphosphine in dry benzene gave its corresponding phosphonium salt (138), which on Wittig reaction was carried out in the atmosphere of nitrogen gave 2-phenyl-5-methyl-furo (3,2-g)-benzopyran-7(H)-one (139) [Scheme-45]. The structure of this compound was established by its PMR spectrum taken in ($CDCl_3$). Singlet at δ 2.4 indicated methyl group at C-5. Singlet at δ 6.2 indicated proton at C-6. Singlet at δ 6.9 indicated proton of furan ring at C-3. Broad multiplet at δ 7.2 to 7.9 indicated five aromatic protons of phenyl group at C-2 and two protons at C-4 and C-9. (Fig. 17).

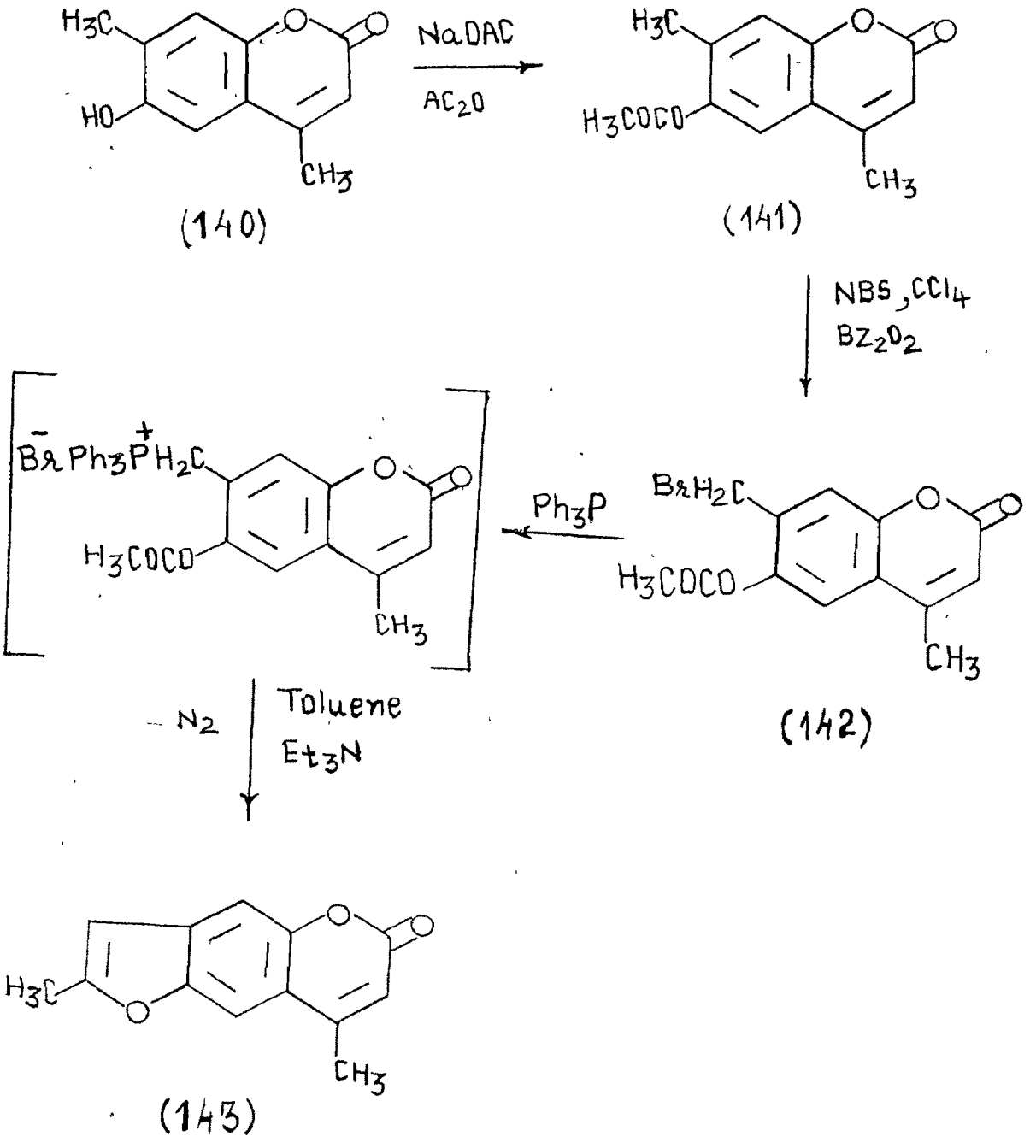
Synthesis of 2,8-dimethyl-furo(2,3-g)-benzopyran-6(H)-one (143)

Methylhydroquinone on Pechmann condensation with ethyl-acetoacetate in conc. H_2SO_4 gave 4,7-dimethyl-6-hydroxycoumarin (140). This was condensed with anhydrous sodium acetate and acetic anhydride gave 6-acetoxy-4,7-dimethyl coumarin (141). The structure of this compound was established by its PMR spectrum taken in DMSO-d_6. Three singlets at δ 2.25, 2.35 and 2.4 are for two methyl groups and one acetoxy group.



(Fig - 17) : 2-Phenyl-5-methyl-furo (3, 2-g) - benzopyran-5(H)-one (139)

Scheme - 46



(140) (141) (142) (143)

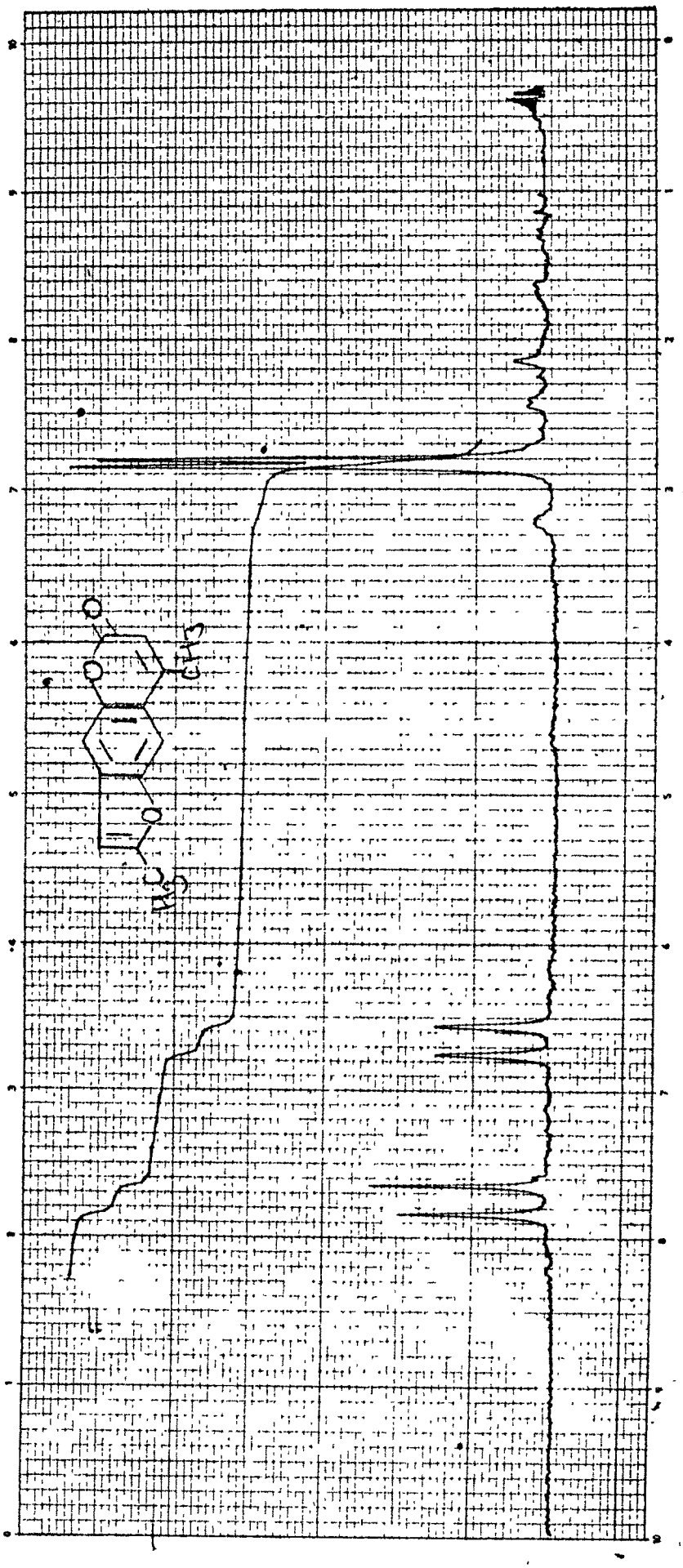
Singlet at δ 6.4 is for proton at C-3. Two singlets at δ 7.35 and 7.45 are for protons at C-5 and C-8.

Compound (141) on bromination with N-bromosuccinimide in presence of light gave 6-acetoxy-7-(bromomethyl)-4-methyl coumarin (142) [Scheme-46]. The structure of this compound was assigned on the basis of its PMR spectrum taken in ($CDCl_3$) [illegible]. The singlet at δ 2.35 indicated methyl group at C-4 and acetoxy group at C-6. The singlet at δ 4.35 indicated two protons of $-CH_2$ group at C-7. Singlet at δ 6.2 indicated proton at C-3. Singlet at δ 7.25 indicated two aromatic protons at C-5 and C-8.

Compound (142) when reacted with triphenylphosphine in dry benzene gave its corresponding phosphonium salt, which on Wittig reaction carried out in the atmosphere of nitrogen gave the product 2,8-dimethyl-furo (2,3-g)-benzopyran-6(H)-one (143). The structure of this compound was assigned on the basis of PMR spectrum taken in ($CDCl_3$). (Fig. 18) Two singlets at δ 2.5 indicated two methyl groups at C-2 and C-8. Singlet at δ 6.2 indicated proton at C-7. Singlet at δ 6.4 indicated proton at C-3. Two singlets at δ 7.3 and 7.5 indicated two protons at C-4 and C-9 respectively.

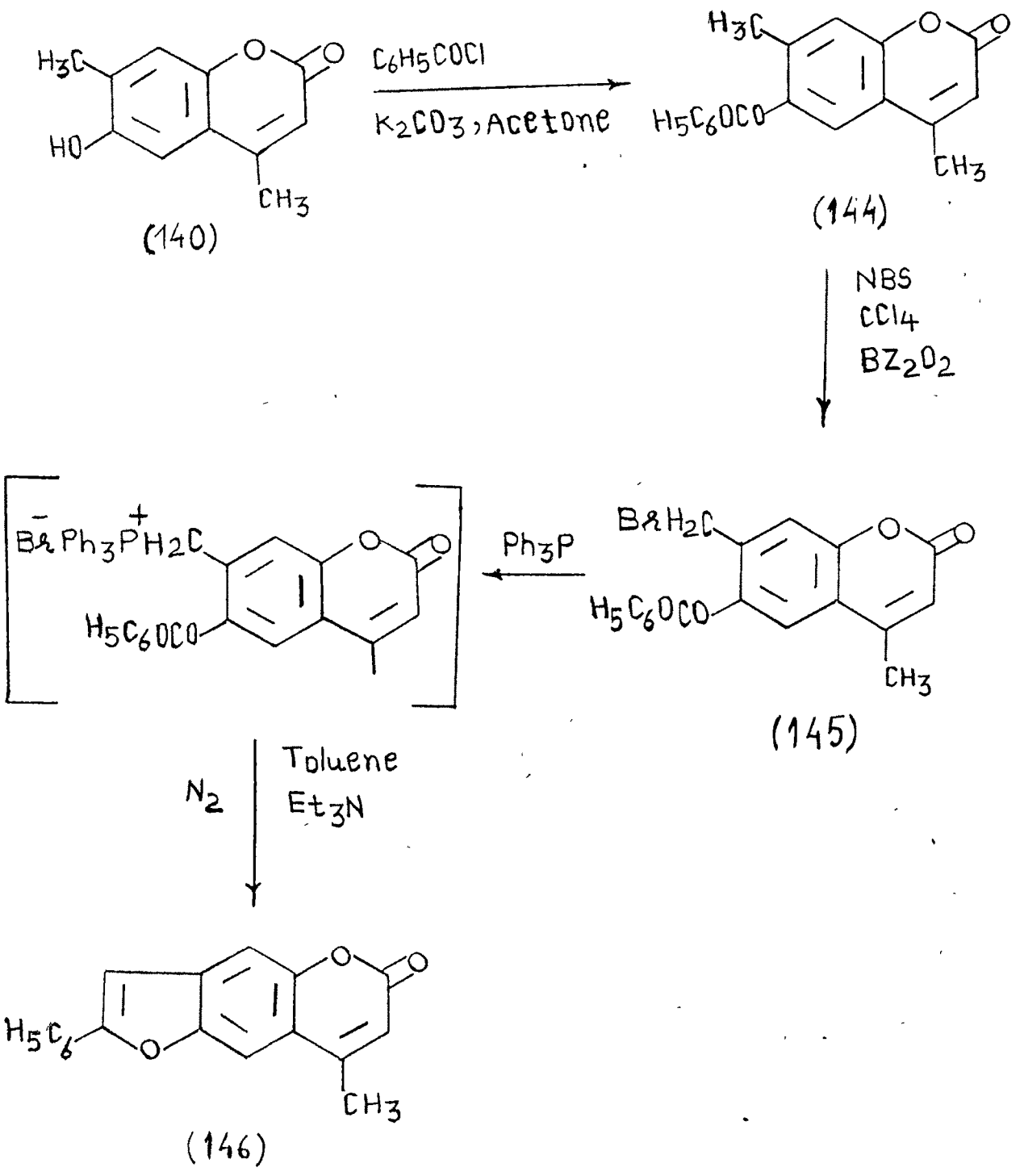
Synthesis of 2-phenyl-8-methyl-furo-(2,3-g)-benzopyran-6(H)-one (146)

4,7-Dimethyl-6-hydroxy coumarin (140), was condensed



(fig-18) : 2,8-dimethyl-furo c2,3-g)-benzopyran-6(H)-one (143).

Scheme- 47

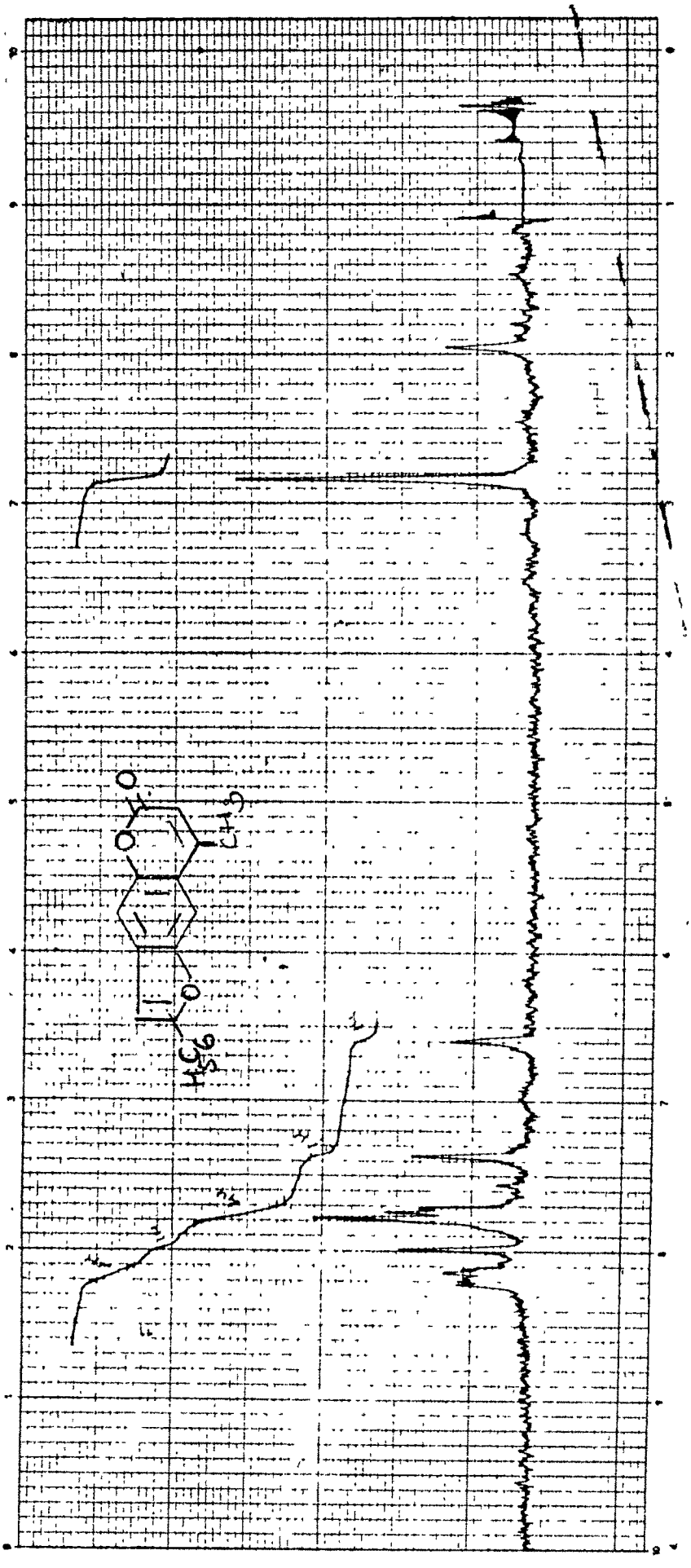

H3C
HO
CH3
(140)
C6H5COCl
K2CO3, Acetone
H3C
H5C6OCO
CH3
(144)
NBS
CCl4
BZ2O2
Br H2C
H5C6OCO
CH3
(145)
Ph3P
Br Ph3P H2C
H5C6OCO
N2
Toluene
Et3N
H5C6
CH3
(146)

with benzoylchloride to give 6-benzoyloxy-4,7-dimethyl coumarin (144). The structure of this compound was assigned on the basis of PMR spectrum taken in ($CDCl_3$). Two singlets at δ 2.35 are due to methyl and acetoxy groups at C-4 and C-6 respectively. Singlet at δ 6.2 indicated proton at C-3. Two singlets at δ 7.15 and 7.3 indicated two aromatic protons at C-5 and C-8. Triplet at δ 7.5 indicated protons at C-3' C-4' and C-5' of benzoyloxy group. Doublet at δ 8.1 indicated two protons at C-2' and C-6' of benzoyloxy group. Doublet at δ 8.1 indicated two protons at C-2' and C-6' of benzoyloxy group.

Compound (144) on bromination with N-bromosuccinimide in the presence of Bz_2O_2 and light gave 6-benzoyloxy-7-bromomethyl-4-methyl coumarin (145) [Scheme-47]. The structure of which was assigned on the basis of PMR spectrum taken in $CDCl_3$. [illegible]. The singlet at δ 2.4 indicated methyl group at C-4. Singlet at δ 4.5 indicated two protons of methylene group singlet at δ 6.3 indicated C-3 proton. The multiplet from δ 7.4-7.7 indicated protons at C-5 and C-8 and C-3', C-4', C-5' protons. Doublet at δ 8.2 indicated C-2' and C-6' protons.

Compound (145) when reacted with triphenylphosphine in dry benzene gave the corresponding phosphonium salt, which was suspended in toluene and triethylamine and reaction was carried out in the atmosphere of nitrogen to give the product 2-phenyl-8-methyl-furo-(2,3-g)-benzopyran-6(H)-one (146).

[Scheme-47]. The structure of this compound was established by its PMR spectrum taken in ($CDCl_3$) (Fig. 19). Singlet at δ 2.5 is for methyl group at C-8. Singlet at δ 6.25 is for proton at C-7. Singlet at δ 7.0 is for proton at C-3. Multiplet at δ 7.35-7.55 indicated two protons at C-4, C-9 and two protons of phenyl ring at C-2. Singlet at δ 7.65 indicated proton at C-4' of phenyl group at C-2. Multiplet at δ 7.75-7.9 indicated two protons of phenyl ring at C-2' and C-6'.



(fig-19) : 2-Phenyl-8-methyl furo (2, 3-g)-benzopyran-6(H)-one (146).

EXPERIMENTAL

EXPERIMENTAL

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

3,4-Dihydroxy-7,8,9,10-tetrahydro-6H-dibenzo(b,d)-pyran-6-one (60)

Pyrogallol (5.0 g) was added to the ice-cold mixture of ethyl-2-cyclohexanone carboxylate (5.2 ml) and conc. H_2SO_4 (8 ml). It was kept overnight and then poured into ice-cold water. The solid obtained was crystallised from ethanol. M.p. 276°C, yield (6.5 g).

3,4-Diacetoxy-7,8,9,10-tetrahydro-6H-dibenzo-(b,d)-pyran-6-one (61)

A mixture of 3,4-dihydroxy-7,8,9,10-tetrahydro-6H-dibenzo (b,d)-pyran-6-one (5.0 g), anhydrous sodium acetate (10 g) and acetic anhydride (10 ml) was heated in water bath for 12 hrs. It was poured in ice-cold water, filtered, washed with dil. aqueous NaOH and crystallised from benzene. White crystals showed M.p. 162°C, yield(6.2 g).

Analysis	:	Found	:	C, 64.71%	;	H, 5.06
$C_{17}H_{16}O_6$	:	requires	:	C, 64.56%	;	H, 4.87%

3-Allyloxy-4-acetoxy-7,8,9,10-tetrahydro-6H-dibenzo-(b,d)-pyran-6-one (62)

A mixture of 3,4-diacetoxy-7,8,9,10-tetrahydro-6H-dibenzo (b,d)-pyran-6-one (3.16 g), anhydrous potassium carbonate (12.0 g), allyl bromide (1.2 ml) and dry acetone (150 ml) was refluxed in water bath for 10 hours. The excess of acetone was removed and poured into ice cold water. The solid obtained was treated with aq. NaOH. The product insoluble in aq. NaOH, it crystallised from benzene. M.p. 132°C, yield (2.0 g)

Analysis : Found : C, 68.38% ; H, 5.66%

$C_{18}H_{18}O_5$: requires : C, 68.79% ; H, 5.73%

The product soluble in aq. NaOH was reppted by adding conc. HCl was 3-allyloxy-4-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo-(b,d)-pyran-6-one crystallised from ethanol. M.p. 205°C, yield (0.8 g).

3-Allyloxy-4-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo-(b,d)-pyran-6-one (63)

4-Acetoxy-3-allyloxy-7,8,9,10-tetrahydro-6H-dibenzo (b,d)-pyran-6-one (2.0 g) was dissolved in ethanol (10 ml) and 10% aq. NaOH (20 ml) was added and left overnight. Alcohol was distilled out, poured into ice-cold water and acidified with conc. HCl. The solid was filtered and filtrate extracted with ether. Combined product was crystallised from ethanol. M.p. 205°C, yield (1.1 g).

Analysis : Found : C, 70.62% ; H, 5.41%

$C_{16}H_{16}O_4$: requires : C, 70.59% ; H, 5.88%

3-Allyloxy-4-methoxy-7,8,9,10-tetrahydro-6H-dibenzo-(b,d)-pyran-6-one (64)

A mixture of 3-allyloxy-4-hydroxy-7,8,9,10-tetrahydro-6H-dibenzo-(b,d)-pyran-6-one (2.0 g), anhydrous potassium carbonate (8.0 g), dimethyl sulfate (2.3 ml) and dry acetone (100 ml) was refluxed in waterbath for 8 hours. It was worked out as usual. The solid obtained was filtered, washed with aq. NaOH and crystallised from benzene. M.p. 96°C, yield (1.4 g).

Analysis : Found : C, 71,75% ; H, 6.69%

$C_{17}H_{18}O_4$: requires : C, 71.32% ; H, 6.29%

2-Allyl-3-hydroxy-4-methoxy-7,8,9,10-tetrahydro-6(H)-dibenzo-(b,d)-pyran-6-one (65)

3-Allyloxy-4-methoxy-7,8,9,10-tetrahydro-6(H)-dibenzo-(b,d)-pyran-6-one (64) was refluxed in N,N-dimethylaniline (10 ml) for 6 hours and poured into (1:1) HCl. The solid obtained was treated with aq. NaOH. On acidification with conc. HCl, the solid obtained was filtered, and purified by column chromatography using benzene as eluting solvent and crystallised from benzene. M.p. 180°C, yield (0.6 g).

Analysis : Found : C, 71.39% ; H, 5.96%

$C_{17}H_{18}O_4$: requires : C, 71.33% ; H, 6.29%

7-Methoxy-9-methyl-1,2,3,4,9,10-hexahydrofuro-5-oxo-5(H)-benzofuro (6,5-c)-benzopyan (66)

2-Allyl-3-hydroxy-4-methoxy-7,8,9,10-tetrahydro-6(H)-dibenzo (b,d)-pyran-6-one (1.0 g) was triturated with conc. H_2SO_4, then heated in waterbath for 10 minutes and poured into crushed ice. The solid obtained was filtered and purified by column chromatography using benzene as eluting solvent, then crystallised from benzene. M.p. 146°C, yield 0.5 g.

Analysis : Found : C, 71.76% ; H, 6.10%

$C_{17}H_{18}O_4$: requires : C, 71.33% ; H, 6.29%

7-Methoxy-9-methyl-5-oxo-5(H)-benzofuro (6,5-c)-2-benzopyran (67)

A mixture of 7-methoxy-9-methyl-1,2,3,4,9,10-hexahydro-5-oxo-5(H)-benzofuro (6,5-c)-benzopyran (0.5 g), palladised charcoal (10%) (0.4 g) and diphenyl ether (10 ml) was refluxed for 18 hr. It was filtered hot, diphenyl ether was removed and the product obtained was purified by preparative TLC using benzene as running solvent phase, crystallised from benzene, showed blue fluoroscence in UV light. M.p. 173°C, yield 0.3 g.

Analysis : Found : C, 72.76% ; H, 4.18%

$C_{17}H_{12}O_4$: requires : C, 72.86% ; H, 4.29%

3-Acetoxy-2-allyl-4-methoxy-7,8,9,10-tetrahydro-6(H)-dibenzo (b,d)-pyran-6-one (68)

A mixture of 2-allyl-3-hydroxy-4-methoxy-7,8,9,10-tetrahydro-6(H)-dibenzo (b,d)-pyran-6-one (1.0 g), anhydrous sodium acetate (2.0 g) and acetic anhydride (5 ml) was heated in waterbath for 8 hr. then poured into ice-cold water. The solid obtained was filtered and crystallised from benzene. M.p. 115°C, yield (1.0 g).

Analysis : Found : C, 69.10% ; H, 6.11%

$C_{19}H_{20}O_5$: requires : C, 69.50% ; H, 6.09%

3-Acetoxy-2-(2',3'-dibromopropyl)-4-methoxy-7,8,9,10-tetrahydro-6(H)-dibenzo-(b,d)-pyran-6-one (69)

3-Acetoxy-2-allyl-4-methoxy-7,8,9,10-tetrahydro-6H-dibenzo-(b,d)-pyran-6-one (1.0 g) dissolved in acetic acid (1-2 ml) and bromine in acetic acid (2 ml) was added dropwise with constant stirring and left overnight. Next day poured into ice-cold water, filtered and crystallised from benzene. M.p. 130°C, Yield (0.9 g).

Analysis : Found : C, 47.09% ; H, 4.11%

$C_{19}H_{20}O_5Br_2$: requires : C, 46.72% ; H, 4.10%

7-Methoxy-9-methyl-1,2,3,4-tetrahydro-5-oxo-%H-benzofuro (6,5-c) benzopyran (70)

3-Acetoxy-2-(2',3'-dibromopropyl)-4-methoxy-7,8,9,10-tetrahydro-6H-dibenzo-(b,d)-pyran-6-one (1.0 g) was dissolved in

ethanol (25 ml) and potassium hydroxide (0.5 g) was added and refluxed in waterbath for 8 hrs. The excess of alcohol was distilled out, poured into icecold water and acidified by conc. HCl. It was filtered and purified by column chromatography using benzene as eluting solvent, then crystallised from benzene. M.p. 132°C, Yield (0.4 g).

Analysis : Found : C, 71.37% ; H, 5.73%

$C_{17}H_{16}O_4$: requires : C, 71.83% ; H, 5.64%

6,7-Dihydroxy-1,2,3-trihydrocyclopenta (C)[1]-benzopyran-4-one (71)

Pyrogallol (5.0 g) was added slowly to the ice-cold mixture of ethylcyclopentanone-2-carboxylate (5.1 ml) and conc. H_2SO_4 (10 ml). It was left overnight, next day poured into ice-cold water, filtered, crystallised from ethanol. M.p. 272°C, yield (5.3 g).

6,7-Diacetoxy-1,2,3-trihydrocyclopenta(C)[1]-benzopyran-4-one (72)

A mixture of 6,7-dihydroxy-1,2,3-trihydrocyclopenta (C)[1]-benzopyran-4-one (10 g), anhydrous sodium acetate (20 g) and acetic anhydride (15 ml) was heated in waterbath for 16 hr. then poured into ice-cold water. The product obtained was filtered, washed with aq. NaOH and crystallised from benzene. M.p. 194°C, yield (12.4 g).

Analysis : Found : C, 64.00% ; H, 4.53%

$C_{16}H_{14}O_6$: requires : C, 63.57% ; H, 4.64%

7-Allyloxy-6-acetoxy-1,2,3-trihydro-cyclopenta-(C) [1]-benzopyran-4-one (73)

A mixture of 6,7-diacetoxy-1,2,3-trihydrocyclopenta (C)[1]-

benzopyran-4-one (3.0 g), anhydrous potassium carbonate (12.0 g), allylbromide (1.2 ml) and dry acetone (150 ml) was refluxed in waterbath for 12 hr. The excess of acetone was distilled out and poured into ice-cold water. The product obtained was crystallised from benzene. M.p. 158°C, yield (2.5 g).

Analysis	:	Found	:	C, 67.59%	;	H, 5.38%
$C_{17}H_{16}O_5$	:	requires	:	C, 68.00%	;	H, 5.33%

7-Allyloxy-6-hydroxy-1,2,3-trihydrocyclopenta (C)[1]-benzopyran-4-one (74)

6-Acetoxy-7-allyloxy-1,2,3-trihydrocyclopenta (C)[1]-benzopyran-4-one (5.0 g) was dissolved in ethanolic (50 ml) sodium hydroxide (2.5 g) and left overnight. Next day the excess of alcohol was distilled out, poured into ice-cold water and acidified with conc. HCl. The product obtained was filtered, dried and crystallised from ethanol. M.p. 230°C, yield (3.0 g).

Analysis	:	Found	:	C, 69.94%	;	H, 5.24%
$C_{15}H_{14}O_4$	:	requires	:	C, 69.77%	;	H, 5.43%

7-Allyloxy-6-methoxy-1,2,3-trihydrocyclopenta (C)[1]-benzopyran-4-one (75)

A mixture of 7-allyloxy-6-hydroxy-1,2,3-trihydrocyclopenta (C)[1]-benzopyran-4-one (2.0 g), anhydrous potassium carbonate

(8.0 g), dimethylsulfate (1.5 ml) and dry acetone (100 ml) was refluxed in waterbath for 8 hr. It was worked out as usual. The product obtained was filtered, washed with aq. dil. NaOH and purified by column chromatography using benzene as eluting solvent, crystallised from benzene. M.p. 98°C, yield (1.55 g).

Analysis : Found : C, 70.23% ; H, 6.18%

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

8-Allyl-7-hydroxy-6-methoxy-1,2,3-trihydrocyclopenta (C)[1]-benzopyran-4-one (76)

7-Allyloxy-6-methoxy-1,2,3-trihydrocyclopenta (C)[1]-benzopyran-4-one (2.0 g) was refluxed in N,N-dimethylaniline (10 ml) for 6 hr. It was worked out as usual. The product obtained was filtered, dried and purified by column chromatography using benzene, crystallised from benzene. M.p. 175°C, yield (1.35 g).

Analysis : Found : C, 71.00% ; H, 6.01%

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

6-Methoxy-8-methyl-1,2,3-trihydrocyclopenta (C)[1]-dihydrofuro (3,2-g)-benzopyran-4-one (77)

5-Allyl-7-hydroxy-6-methoxy-1,2,3-trihydro-cyclopenta (C)[1]-benzopyran-4-one (1.0 g) was triturated with conc.

H_2SO_4 (80%) and then heated inwaterbath for 10 minutes. It was poured into ice-cold water. The product was filtered, washed with aq. dil. NaOH and then with water, purified by column chromatography using benzene as eluting solvent ; crystallised from benzene. M.p. 137°C, yield (0.65 g).

Analysis	:	Found	:	C, 70.60%	;	H, 6.26%
$C_{16}H_{16}O_4$	:	requires	:	C, 70.58%	;	H, 5.88%

6-Methoxy-8-methyl-1,2,3-trihydrocyclopenta (C)[1]-furo (3,2-g) benzopyran-4-one (78)

Sodium salt of 8-allyl-7-hydroxy-6-methoxy-1,2,3-trihydrocyclopenta (C)[1]-benzopyran-4-one (1.0 g) and dichlorobis (benzonitrile) palladium (1.5 g) was suspended in benzene and stirred at room temperature for ½ hr. Suspension became clear and developed intense red colour during stirring, then reluxed for 2 hr. The palladium metal separated out and solution turned colourless. It was filtered and filtrate concentrated and chromatographed on silica gel. First elution with pet. ether gave benzonitrile and subsequent elution with benzene gave the product, which crystallised from benzene. M.p. 240°C, yield (0.6 g).

Analysis	:	Found	:	C, 70.18%	;	H, 5.99%
$C_{16}H_{14}O_4$	:	requires	:	C, 69.77%	;	H, 5.43%

6,7-Diallyloxy-4-methyl coumarin (96)

A mixture of 6,7-dihydroxy-4-methyl coumarin (3.8 g), anhydrous potassium carbonate (12 g) and allylbromide (5.0 ml) and dry acetone (100 ml) was refluxed in waterbath for 12 hr. The excess of acetone was distilled out and poured in ice-cold water, the product was filtered, washed with aq. dil. NaOH and crystallised from benzene. M.p. 102°C, yield(4.1 g)

Analysis : Found : C, 71.03% ; H, 6.23%

$C_{16}H_{16}O_4$: requires : C, 70.59% ; H, 5.88%

8-Allyl-2,7-dimethyl-9-hydroxy-dihydrofuro (2,3-h)-[1]-benzo-pyran-5(H)-one (97a)

6,7-Diallyloxy-4-methyl coumarin (2.0 g) and N,N-dimethyl-aniline (10 ml) was refluxed for 6 hr. The reaction mixture was poured into (1:1) ice-cold HCl. The reppted product was filtered, dried and purified by column chromatography using benzene and crystallised from benzene. M.p. 144°C, yield (1.2 g).

Analysis : Found : C, 70.21% ; H, 5.81%

$C_{16}H_{16}O_4$: requires : C, 70.59% ; H, 5.88%

2,7,9-Trimethyl-2,3,8,9-tetrahydro (2,3-h : 2',3'-f)[1]-benzo-pyran-5(H)-one (98)

8-Allyl-2,7-dimethyl-9-hydroxy-dihydrofuro (2,3-h)-[1]-

benzopyran-5(H)-one (1.0 g) was triturated with conc. H_2SO_4 (80%) andthen heated in waterbath for 10 minutes, poured in ice-cold water. The product was filtered, washed with aq. dil. NaOH and then with water, purified by column chromatography using benzene and crystallised from benzene. M.p. 182°C, yield (0.6 g).

Analysis : Found : C, 70.39% ; H, 6.04%

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

2,7,9-trimethyl-difurano (2,3-h ; 2',3'-f)-[1]-benzopyran-5(H)-one (99)

2,7,9-Trimethyl-2,3,8,9-tetrahydrodifurano (2,3-h ; 2',3'-f) [1]-benzopyran-5(H)-one (0.5 g) palladised charcoal (10%) (0.4 g) and diphenyl ether (10 ml) was refluxed for 20 hr. It was filtered, hot, diphenyl ether was removed and product obtained was purified by preparative TLC using benzene. The compound, with yellow fluoroscence in UV light, and finally crystallised from benzene. M.p. 212°C, yield (200 mg).

Analysis : Found : C, 71.22% ; H, 4.24%

$C_{16}H_{14}O_4$: requires : C, 71.64% ; H, 4.48%

6,7-Diacetoxy-4-methyl coumarin (100)

A mixture of 6,7-dihydroxy-4-methyl coumarin (5.0 g), anhydrous sodium acetate (10 g) and acetic anhydride (10ml)

was heated in waterbath for 8 hr. poured into ice-cold water. The product obtained was filtered, washed with dil. NaOH and then with water and crystallised from benzene. M.p. 154°C, yield (6.5 g).

Analysis : Found : C, 60.72% ; H, 4.12%

$C_{14}H_{12}O_6$: requires : C, 60.87% ; H, 4.35%

6-Acetoxy-7-Allyloxy-4-methyl coumarin (101)

A mixture of 6,7-diacetoxy-4-methyl coumarin (2.76 g), anhydrous potassium carbonate (9.0 g), allylbromide (1.2 ml) (0.01 mole) and dry actone (100 ml) was refluxed for 10 hrs. The excess of acetone was distilled out and poured in ice-cold water. The product obtained was filtered dried and crystallised from benzene. M.p. 140°C, yield (1.9 g).

Analysis : Found : C, 65.20% ; H, 4.96%

$C_{15}H_{14}O_5$: requires : C, 65.69% ; H, 5.11%

8-Allyl-6,7-dihydroxy-4-methyl coumarin (102)

6-Acetoxy-7-allyloxy-4-methyl coumarin (1.0 g) and N,N-dimethylaniline (10 ml) was refluxed for 6 hrs. It was then poured into (1:1) ice-cold HCl. The product was treated with aq. NaOH. On acidification with HCl, it was reprecipitated. It was filtered and purified by column chromatography using benzene. M.p. 225°C, yield (0.5 g).

Analysis : Found : C, 67.82% ; H, 4.96%

$C_{15}H_{12}O_4$: requires : C, 67.24% ; H, 5.17%

2,7-Dimethyl-9-hydroxy-dihydrofurano (2,3-h)-[1]-benzopyran-5(H)-one (103)

6,7-Dihydroxy-8-allyl-4-methyl coumarin (1.0 g) was triturated with con. H_2SO_4 (80%) and then heated in waterbath for 10 min. Then it was poured into ice. The product obtained was filtered and crystallised from benzene. M.p. 202°C, yield (0.6 g).

Analysis : Found : C, 67.34% ; H, 5.37%

$C_{13}H_{12}O_4$: requires : C, 67.24% ; H, 5.17%

9-Allyloxy-2,7-dimethyl-dihydrofurano (2,3-h)-[1]-benzopyan-5(H)-one (104)

A mixture of 2,7-dimethyl-9-hydroxy-dihydrofuro (2,3-h) [1]-benzopyran-5(H)-one (2.5 g), anhydrous potassium carbonate (9.0 g) allylbromide (1.2 ml) (0.01 mole) and dry actone (70 ml) was refluxed for 10 hr. It was worked out as usual. The product obtained was filtered, washed with aq. dil. NaOH and then with water, dried and crystallised from benzene. M.p. 130°C, yield (1.5 g).

Analysis : Found : C, 70.96% ; H, 5.76%

$C_{16}H_{16}O_4$: requires : C, 70.59% ; H, 5.88%

8-Allyl-2,7-dimethyl-9-hydroxy-dihydrofuro (2,3-h)-[1]-benzopyran-5(H)-one (97a)

9-Allyloxy-2,7-dimethyl-dihydrofuro (2,3-h)[1]-benzopyran-5(H)-one (1.0 g) and N,N-dimethylaniline (10 ml) was refluxed for 6 hr. It was worked out as usual. The product obtained was purified by column chromatography using benzene and then crystallised from benzene. M.p. 144°C, yield (0.5 g). This compound is same as (97a) by m.m.p. and CO-TLC.

Analysis : Found : C, 70.21% ; H, 5.81%

$C_{16}H_{16}O_4$: requires : C, 70.59% ; H, 5.88%

7,8-Diallyloxy-4-methyl coumarin (106)

A mixture of 7,8-dihydroxy-4-methyl coumarin (4.0 g), anhydrous potassium carbonate (12.0 g), allylbromide (7.5 ml) and dry acetone (100 ml) was refluxed in waterbath for 14 hr. The excess of acetone was distilled out and poured into ice-cold water. The oil obtained was separated and washed with dil. NaOH. It was purified by column chromatography. The solid product is obtained on trituration with pet. ether, finally crystallised from Pet. ether. M.p. 51°C, Yield (5.2 g).

Analysis : Found : C, 71.00% ; H, 5.63%

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

5,6-Diallyl-7,8-dihydroxy-4-methyl coumarin (107)

7,8-Diallyloxy-4-methyl coumarin (4.0 g) and N,N-dimethyl-

aniline (15 ml) were refluxed for 6 hr. It was poured in 1:1 ice-cold HCl. The oil obtained was dissolved in aq. NaOH and then reppted with HCl. It was filtered and purified by column chromatography using benzene and crystallised from benzene. M.p. 160°C, yield (1.1 g).

Analysis : Found : C, 70.82% ; H, 5.83%

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

4-(Propen-2-yl)-2,5-dimethyl-9-hydroxy-dihydrofurano (2,3-g)-[1]-benzopyran-7(H)-one (108)

5,6-Diallyl-7,8-dihydroxy-4-methyl coumarin (1.0 g) was triturated with conc. H_2SO_4 (80%) and then heated in water-bath for 10 minutes. It was poured into ice-cold water. The solid obtained was filtered, dried and purified by column chromatography using benzene and crystallised from benzene. M.p. 202°C, yield (0.4 g).

Analysis : Found : C, 70.84% ; H, 5.58%

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

4-(Propen-2-yl)-2,5-dimethyl-9-methoxy-dihydrofuro (2,3-g)-[1]-benzopyran-7(H)-one (109)

A mixture of 4-(Propen-2-yl)-2,5-dimethyl-9-hydroxy-dihydrofuro (2,3-g)-[1]-benzopyran-7(H)-one (1.5 g), anhydrous potassium carbonate (5.0 g), dimethyl sulfate (1.4 ml) and dry acetone

(100 ml) was refluxed for 8 hrs. The excess of acetone was removed and poured into ice-cold water. The product obtained was filtered, washed with aq. dil. NaOH and then with water, purified by column chromatography and finally crystallised from benzene. M.p. 137°C, yield (1.0 g).

Analysis	: Found	: C, 70.93%	; H, 6.61%
$C_{17}H_{18}O_4$	: requires	: C, 71.33%	; H, 6.29%

7-Hydroxy-4,8-dimethyl coumarin (125)

2-Methyl resorcinol (5.0 g) was added at 0-5°C to the mixture of ethylacetoacetate (4.8 ml) and conc. H_2SO_4 (10 ml). It was left overnight. Next day poured in ice-cold water. The product was filtered and crystallised from ethanol. M.p. 256°C,[42] yield (6.5 g).

7-Acetoxy-4,8-dimethyl coumarin (126)

A mixture of 7-hydroxy-4,8-dimethyl coumarin (3.0 g) anhydrous sodium acetate (3.0 g) and acetic anhydride (10 ml) was heated for 8 hr. It was then poured in ice-cold water. The product was filtered washed with aq. dil. NaOH and finally crystallised from benzene. M.p. 128°C, yield (3.2 g).

Analysis	: Found	: C, 66.86%	; H, 5.28%
$C_{13}H_{12}O_4$	: requires	: C, 67.24%	; H, 5.17%

8-Bromomethyl-7-actoxy-4-methyl coumarin (127)

7-Acetoxy-4,8-dimethyl coumarin (2.0 g) dissolved in CCl_4 (200 ml), N-bromosuccinimide (1.78 g) and benzoylperoxide (0.3 g) were added to it and refluxed under light for 8 hr. It was filtered and solvent was removed by distillation. The product obtained was purified by column chromatography using benzene, finally crystallised from benzene. M.p. 162°C, yield (1.3 g).

Analysis	:	Found	:	C, 50.58%	;	H, 3.96%
$C_{13}H_{11}O_4Br$	:	requires	:	C, 50.16%	;	H, 3.54%

2,7-Dimethyl-furo-(2,3-h)-benzopyran-5-one (128)

A mixture of 8-bromomethyl-7-hydroxy-4-methyl coumarin (1.0 g) and triphenylphosphine (1.2 g) was dissolved in benzene (60 ml) and refluxed for 6 hr. Then benzene was distilled out and semi solid obtained was triphenylphosphonium salt of coumarin. It was suspended in dry toluene (100 ml), triethylamine (2.0 ml) was added and refluxed under the atmosphere of N_2 for 16 hrs. It was filtered hot and toluene was distilled out. The semisolid obtained was purified by column chromatography using benzene, finally crystallised from benzene. M.p. 180°C, yield (0.65 g).

Analysis	:	Found	:	C, 72.48%	;	H, 4.92%
$C_{13}H_{10}O_3$	:	requires	:	C, 72.90%	;	H, 4.67%

4,6-Dimethyl-7-hydoxy coumarin (129)

4-Methyl resorcinol (5.0 g) was added slowly to the mixture of ethylacetoacetate (4.4 ml) and conc. H_2SO_4 (20 ml) at 0-5°C. It was kept overnight. Next day poured into ice-cold water. The product was filtered and crystallised from ethanol : water (1:1). M.p. 210°C, yield (4.0 g).

Analysis : Found : C, 69.30% ; H, 5.20%

$C_{11}H_{10}O_3$: requires : C, 69.47% ; H, 5.26%

7-Acetoxy-4,6-dimethyl coumarin (130)

A mixture of 7-hydroxy-4,6-dimethyl coumarin (2.0 g) anhydrous sodium acetate (3.0 g) and acetic anhydride (10 ml) was heated for 10 hr. It was poured into ice-cold water. The product obtained was filtered, washed with dil. NaOH and crystallised from benzene. M.p. 161°C, yield (2.5 g).

Analysis : Found : C, 66.86% ; H, 5.19%

$C_{13}H_{12}O_4$: requires : C, 67.24% ; H, 5.17%

7-Acetoxy-6-bromomethyl-4-methyl coumarin (131)

7-Acetoxy-4,6-dimethylcoumarin (2.0 g) was dissolved in carbon tetrachloride (200 ml). N-bromosuccinimide (1.78 g) and benzoylperoxide (0.3 g) were added to it and refluxed under light for 12 hrs. It was filtered hot, solvent was removed and product obtained was purified by column chromatography using benzene. It was crystallised from benzene. M.p. 186°C, yield (1.5 g).

Analysis : Found : C, 49.74% ; H, 3.68%

$C_{13}H_{11}O_4Br$: requires : C, 50.16% ; H, 3.54%

2,5-Dimethyl-furo (3,2-g)-benzopyran-7-one (132)

7-Acetoxy-6-bromomethyl-4-methyl coumarin (1.0 g) and triphenylphosphine (1.1 g); were dissolved in dry benzene (60 ml) and refluxed for 8 hr. Then benzene was distilled out and the oil obtained was suspended in dry toluene (30 ml). Triethylamine (2-3 ml) was added and refluxed under the atmosphere of N_2 for 16 hr. It was filtered hot and toluene was distilled out. The product obtained was purified by column chromatography using benzene. and finally crystallised from benzene. M.p. 162°C, Yield (0.6 g).

Analysis : Found : C, 73.29% ; H, 5.04%

$C_{13}H_{10}O_3$: requires : C, 72.89% ; H, 4.67%

7-Benzoyloxy-4,8-dimethyl coumarin (133)

A mixture of 7-hydroxy-4,8-dimethyl coumarin (2.5 g), anhydrous potassium carbonate (10 g), benzoyl chloride (2.5 ml) and dry acetone (150 ml) was refluxed in waterbath for 8 hr. The excess of acetone was distillled out and poured in ice-cold water. It crystallised from benzene. M.p. 202°C, yield (2.4 g).

Analysis : Found : C, 73.87% ; H, 5.11%

$C_{18}H_{14}O_4$: requires : C, 73.47% ; H, 4.76%

7-Benzoyloxy-8-bromomethyl-4-methyl coumarin (134)

7-Benzoyloxy-4,8-dimethyl coumarin (2.90 g, 0.01 mole) was dissolved in CCl_4 (200 ml) and N-bromosuccinimide (1.78 0.01 mole) and benzoyl peroxide (0.2 - 0.3 g) were added to it and refluxed under light for 10 hrs. It was filtered and solvent was removed by distillation. On evaporation of last few cc fraction, the crude solid obtained was purified by column chromatography using benzene. It was crystallised from benzene. M.p. 145°C, yield (1.6 g).

Analysis : Found : C, 57.49% ; H, 3.95%

$C_{18}H_{13}O_4Br$: requires : C, 57.91% ; H, 3.49%

7-Methyl-2-phenyl-furo (2,3-h)-benzopyran-5-one (135)

7-Benzoyloxy-8-bromomethyl-4-methyl coumarin (1.0 g) and triphenylphosphine (1.1 g) were dissolved in dry benzene (80 ml) and refluxed for 6 hrs. The benzene was removed by distillation and the semisolid obtained was suspended in dry toluene (80 ml) and triethylamine (2-3 ml) was added to it. It was refluxed under the atmosphere of N_2 for 16 hrs. It was filtered hot, toluene was distilled out and solid obtained was purified by column chromatography using benzene. It crystallised from benzene. M.p. 191°C, yield (0.6 g).

Analysis : Found : C, 77.89% ; H, 4.75%

$C_{18}H_{12}O_3$: requires : C, 78.26% ; H, 4.35%

7-Benzoyloxy-4,6-dimethyl coumarin (136)

A mixture of 4,6-dimethyl-7-hydroxy coumarin (2.5 g) anhydrous potassium carbonate (10 g), benzoylchloride (2.5 ml) was refluxed in dry acetone (150 ml) for 8 hrs. The excess of acetone was distilled out and poured into ice-cold water. The product obtained was filtered, dried and crystallised from benzene. M.p. 190°C, yield (2.3 g).

Analysis	:	Found	:	C, 73.41%	;	H, 5.15%
$C_{18}H_{14}O_4$	:	requires	:	C, 73.47%	;	H, 4.76%

7-Benzoyloxy-6-bromomethyl-4-methyl coumarin (137)

7-Benzoyloxy-4,6-dimethyl coumarin (2.9 g, 0.01 mole) was dissolved in CCl_4 (200 ml) and N-bromosuccinimide (1.78 g, 0.01 mole) and benzylperoxide (0.2-0.3 g) were added to it and refluxed under light for 10 hrs. It was filtered and solvent was removed by distillation. On evaporation of last few cc. of solvent, the crude solid obtained was purified bycolumn chromatography using benzene. It crystallised from benzene. M.p. 166°C, yield (1.6 g).

Analysis	:	Found	:	C, 57.80%	;	H, 3.91%
$C_{18}H_{13}O_4Br$	:	requires	:	C, 57.91%	;	H, 3.49%

5-Methyl-2-phenyl-furo (2,3-g)-benzopyran-7-one (139)

7-Benzoyloxy-6-bromomethyl-4-methyl coumarin (1.0 g) & triphenyl

phosphine (1.1 g) were dissolved in dry benzene (80 ml) and refluxed for 6 hrs. Benzene was removed by distillation and the semi solid obtained was suspended in dry toluene (80 ml) and triethylamine (2-3 ml) was added to it. It was refluxed under atmosphere of N_2 for 16 hrs. It was filtered hot, toluene was distilled out and solid obtained was purified by column chromatography. It crystallised from benzene. M.p. 212°C, yield (0.6 g).

Analysis	:	Found	:	C, 77.79%	;	H, 4.77%
$C_{18}H_{12}O_3$	:	requires	:	C, 78.26%	;	H, 4.34%

6-Acetoxy-4,7-dimethyl coumarin (141)

A mixture of 6-hydroxy-4,7-dimethyl coumarin (2.0 g), anhydrous sodium acetate (3.0 g) and acetic anhydride (10 ml) was heated for 10 hrs. It was poured into ice-cold water. The product obtained was filtered, washed with aq. NaOH to remove unreacted compound. It was crystallised from alcohol M.p. 208°C, yield (2.2 g).

Analysis	:	Found	:	C, 66.79%	;	H, 5.46%
$C_{13}H_{12}O_4$	:	requires	:	C, 67.24%	;	H, 5.17%

6-Acetoxy-7-bromomethyl-4-methyl coumarin (142)

6-Acetoxy-4,7-dimethyl coumarin (2.32 g) was dissolved in carbon tetrachloride and chloroform mixture (200 ml), N-bromosuccinimide (1.78 g) and benzoylperoxide (0.3 g) were

added to it and refluxed under light for 12 hrs. It was filtered hot, solvent was removed and the product obtained was purified by column chromatography using benzene, finally crystallised from benzene. M.p. 156°C, yield (1.8 g).

Analysis : Found : C, 50.35% ; H, 4.00%

$C_{13}H_{11}O_4Br$: requires : C, 50.16% ; H, 3.54%

2,8-Dimethyl-furo (2,3-g)-6(H)-benzopyran-2-one (143)

6-Acetoxy-7-bromomethyl-4-methyl coumarin (1.0 g) and triphenylphosphine (0.9 g) were dissolved in dry benzene (60 ml) and refluxed for 8 hrs. Then benzene was distilled out and the solid obtained was suspended in dry toluene (30 ml) and triethylamine (2-3 ml) was added and refluxed under the atmosphere of nitrogen for 16 hrs. It was filtered hot, solvent was removed and the product obtained was purified by preparative TLC using benzene. It was crystallised from benzene. M.p. 168°C, yield (0.6 g).

Analysis : Found : C, 72.61% ; H, 5.09%

$C_{13}H_{10}O_3$: requires : C, 72.89% ; H, 4.67%

6-Benzoyloxy-4,7-dimethyl coumarin (144)

A mixture of 6-hydroxy-4,7-dimethyl coumarin (2.5 g), anhydrous potassium carbonate (10 g), benzoylchloride (2.4 ml) was refluxed in dry acetone (150 ml) for 8 hrs. It was worked out as usual. The product obtained was filtered

and washed with aq. dil. NaOH to remove unreacted compound. It was crystallised from benzene. M.p. 158°C, yield (2.3 g)

Analysis : Found : C, 73.06% ; H, 5.08%

$C_{18}H_{14}O_4$: requires : C, 73.47% ; H, 4.76%

6-Benzoyloxy-7-bromomethyl-4-methyl coumarin (145)

6-Benzoyloxy-4,7-dimethyl coumarin (2.5 g) was dissolved in chloroform and carbon tetrachloride mixture (200 ml). N-bromosuccinimide (1.6 g) and benzoylperoxide (0.3 g) were added to it and refluxed under light for 10 hrs. It was filtered and solvent was removed. The product obtained was purified by column chromatography using benzene. M.p. 152°C, yield (2.0 g).

Analysis : Found : C, 58.37% H, 3.89%

$C_{18}H_{13}O_4Br$: requires : C, 57.91% ; H, 3.49%

2-Phenyl-8-methyl-furo-(2,3-g)-6-(H)-benzopyran-6-one (146)

6-Benzoyloxy-7-bromomethyl-4-methyl coumarin (1.0 g) and triphenylphosphine (1.0 g) were dissolved in dry benzene (80 ml) and refluxed for 6 hrs. Then benzene was removed and the product obtained was suspended in dry toluene (30 ml) and triethylamine (2-3 ml) and refluxed under atmosphere of nitrogen for 16 hrs. It was filtered hot and solvent was removed by distillation. The product obtained was purified by column chromatography using benzene. M.p. 228°C, yield (0.7 g)

Analysis : Found : C, 77.81% ; H, 4.82%

$C_{18}H_{12}O_3$: requires : C, 78.26% ; H, 4.35%

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