CHAPTER-IV

Section-1

Claisen rearrangement and Wittig reactions of Cinnamylated benzopyran-2H-ones

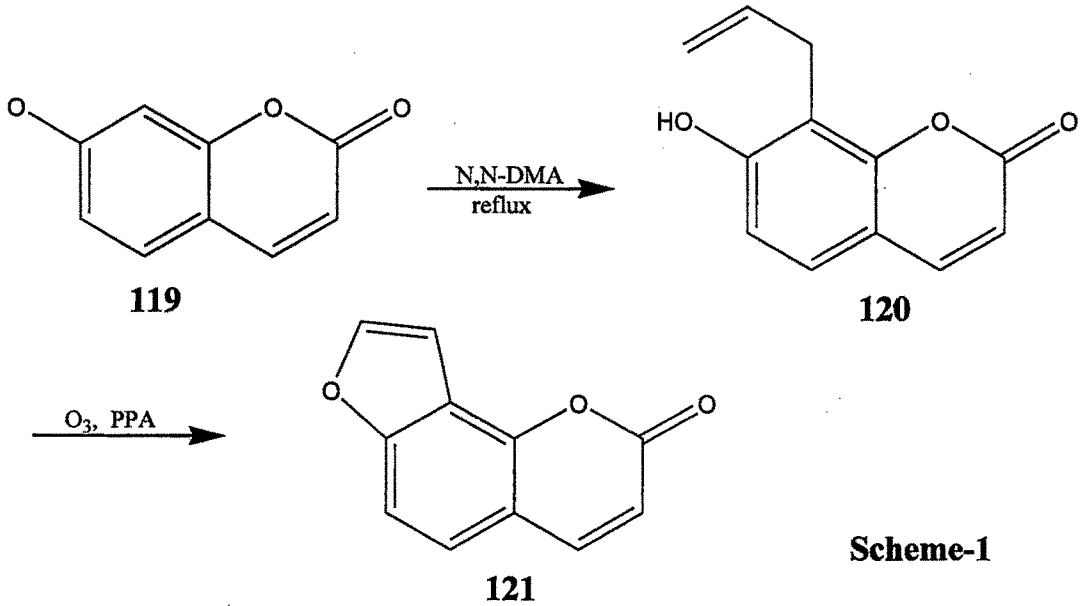
Section:1 Claisen rearrangement and Wittig reaction of cinnamylated 2H-1-benzopyran-2-one

IV.1 Introduction

Studies and synthesis of furobenzopyran derivatives have been elaborated in details. It was found that the electron withdrawing groups such as –CN, -COOEt, -$COCH_3$ etc. at 3-position facilitated the formation of linearly fused furobenzopyrones[1]. Studies on allylation and Claisen rearrangement of 2H-1-benzopyran-2-ones as the key step have been reported earlier[7]. In present work, cinnamylation and prenylation studies and the formation of novel cyclic compounds using amino alcohols have been planned with a view to understanding the chemistry and synthetic aspects of these compounds.

Trivedi and Madhava Rao[2] studied the Claisen rearrangement of cinnamyloxy benzopyrone derivatives and reported the formation of normal and abnormal products, their mechanism, geometry and spatial arrangement.

Aneja *et al*[3] synthesized angularly furofused benzopyrone **121** via Claisen rearrangement of 7-allyloxy-2H-1-benzopyran-2-one **119** to 7-hydroxy-8-allyl-2H-1-benzopyran-2-one **120.** On ozonolysis and subsequent cyclisation with polyphosphoric acid, compound **120** afforded angularly furofused benzopyrone **121** (Scheme-1).

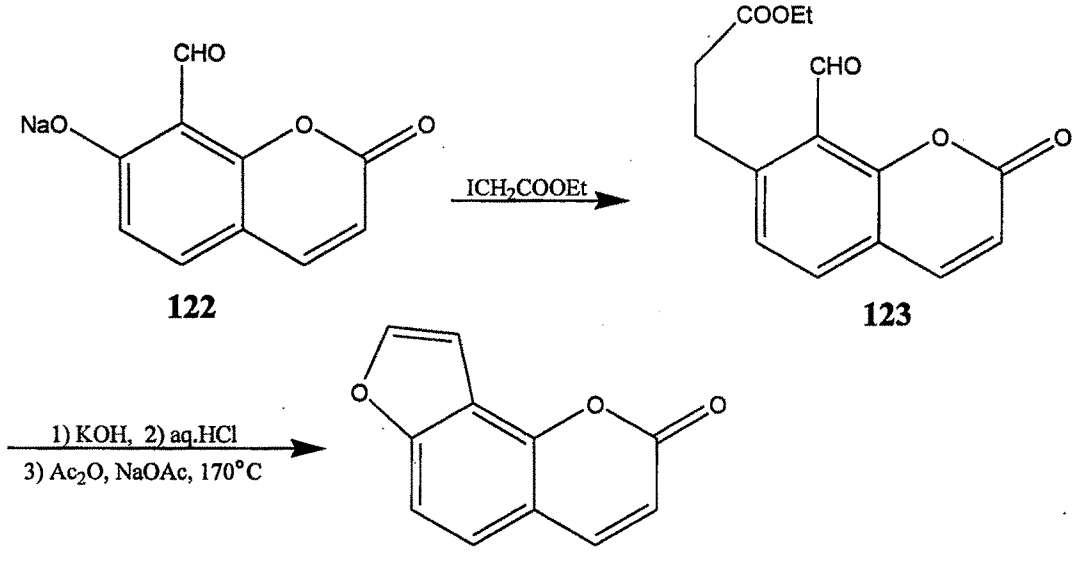


119 **120**

121

Scheme-1

Spath and Pailer[4] synthesized furofused benzopyrone **121** by condensation of sodium salt of 8-formyl-7-hydroxy-2H-1-benzopyran-2-one **122** with iodo acetic ester followed by decarboxylative cyclisation of corresponding ether **123** with sodium acetate and acetic anhydride (Scheme-2).

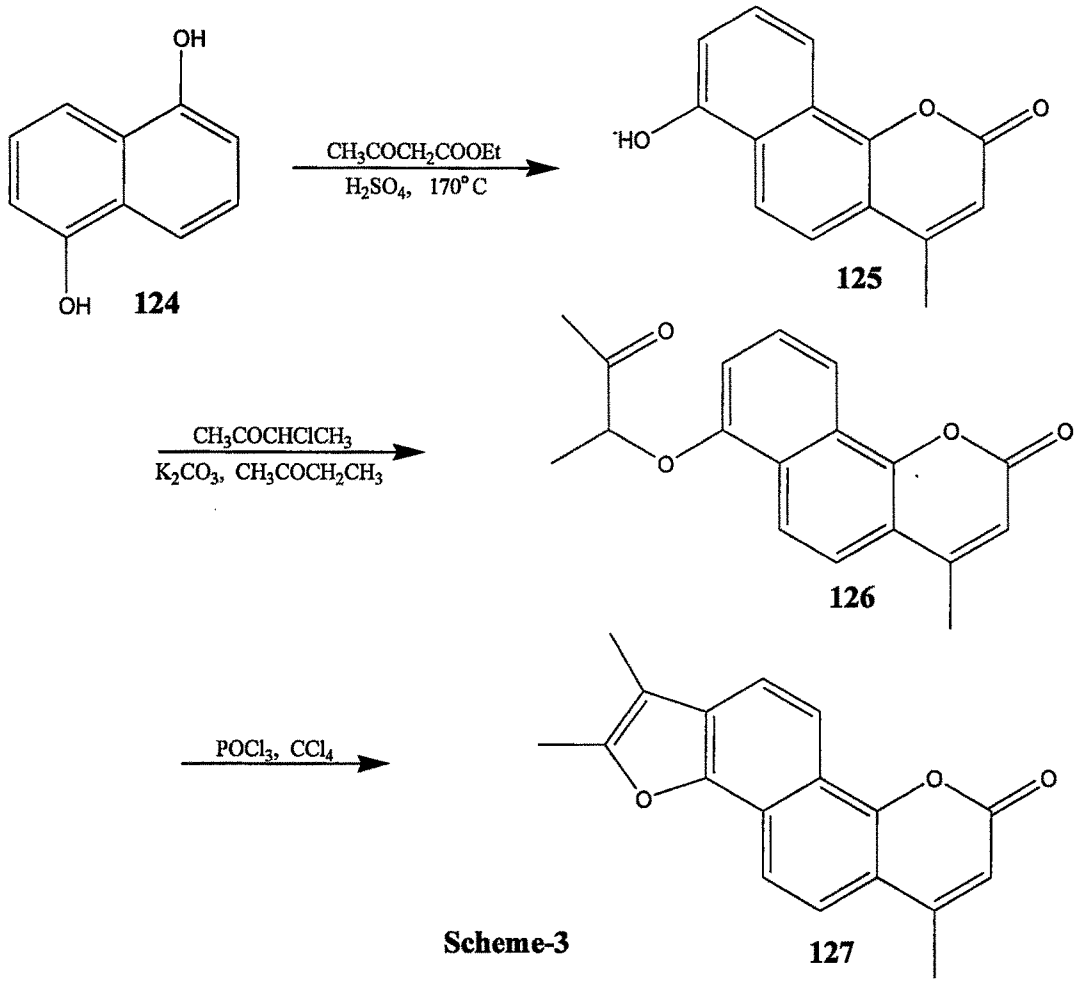


122 **123**

121

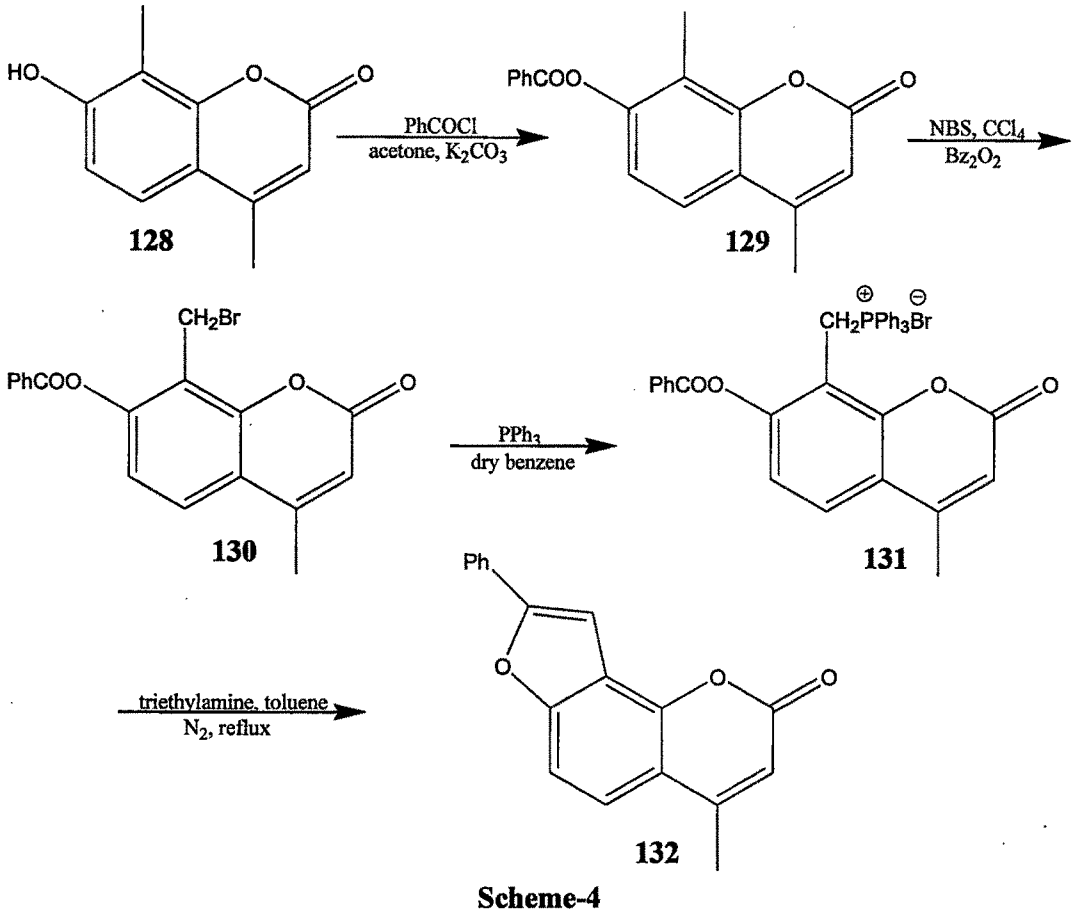
Scheme-2

Furonaphthopyrone **127** was prepared by Adam *et al*[5] from 1,5-naphthalenediol **124**. Conversion of diol **124** into naphthopyrone **125** was carried out by Pechmann condensation then hydroxyl group was converted into ether **126** which on cyclisation with $POCl_3$ gave furonaphthopyrone **127** (Scheme-3).



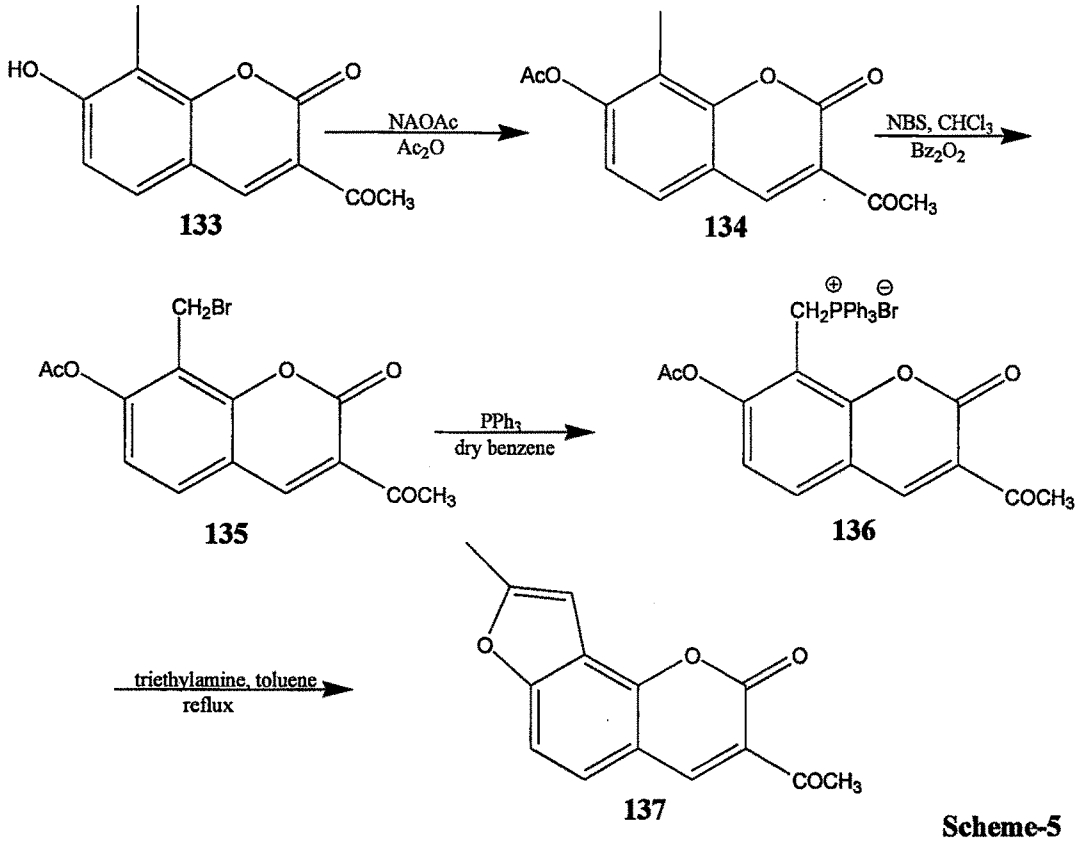
Scheme-3

Intramolecular Wittig reaction was utilized[6] to prepare angularly furofused benzopyrone **132** from 7-hydroxy-4,8-dimethyl-2H-1-benzopyran-2-one **128.** Bromination of **129** by NBS, followed by reaction with triphenylphosphine in dry benzene afforded a ylide **131** which *in situ* with triethylamine under nitrogen atmosphere yielded furofused benzopyrone **132** (Scheme-4).



Scheme-4

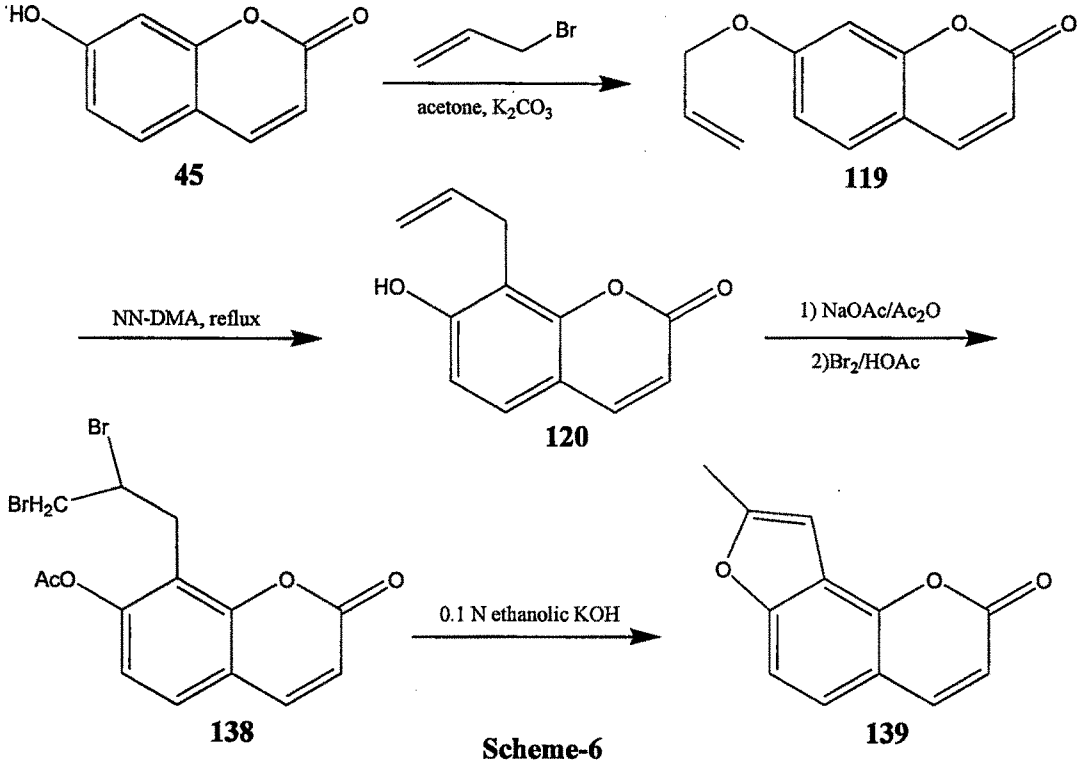
Furofused benzopyrone **137** was synthesized[7] using Wittig reaction from 3-acetyl-7-hydroxy-8-methyl-2H-1-benzopyran-2-one **133.** In this synthesis acetoxy compound **134** was first brominated and then converted into a ylide **136** which on treatment with triethylamine under nitrogen atmosphere in toluene yielded furofused benzopyrone **137** (Scheme-5).



133 **134** **135** **136** **137**

Scheme-5

Angularly fused methyl furo benzopyrone **139** has also been reported in literature[7]. 8-Allyloxy-7-hydroxy-2H-1-benzopyran-2-one **120,** obtained from 7-hydroxy-2H-1-benzopyran-2-one **45**, was acetylated and then brominated in acetic acid to give dibromoderivative **138** which on cyclisation with ethanolic KOH gave angularly furo fused benzopyrone **139** (Scheme-6).



Scheme-6

IV.2 Results and Discussion:

2,4-Dihydroxybenzaldehyde was subjected to Knoevenagel condensation with diethylmalonate in presence of pyridine and piperidine to give ethyl-7-hydroxy-2H-1-benzopyran-2-one-3-carboxylate **140**, followed by cinnamylation in dry DMF affording cinnamylated product **141**. In refluxing N,N-dimethylaniline for eight hours compound **141** did not show any rearrangement and was recovered (Scheme-7).

Then Wittig strategy was employed as follows. 2,4-Dihydroxybenzaldehyde was condensed with cinnamyl chloride in dry acetone which afforded monocinnamyloxy **142** and dicinnamyloxy **143** derivatives (Scheme-8). Monocinnamyloxy derivative **142** on refluxing with N,N-dimethylaniline did not give any product and was recovered unchanged. Then both mono and dicinnamyloxy derivatives were subjected separately to tandem-Wittig reaction followed by Claisen rearrangement in N,N-dimethylaniline with equimolar proportion of ylide, carboethoxy methylene triphenyl phosphorane. The dicinnamyloxy derivative **143** gave two products **144** and **145**.

In this approach 2,4-dihydroxybenzldehyde **54** was condensed with cinnamyl chloride. On work up TLC showed two spots. The spot (compound **143**) having higher R_f value was eluted out with petroleum ether (60-80°C) in relatively low yield and second compound **142** was eluted with petroleum ether (60-80°C)- ethyl acetate (98:2) mixture. Compound **142** was soluble in alkali and showed a weak IR band at 3650 cm^{-1} for hydroxyl group and 1645 cm^{-1} for carbonyl group [Figure-49]. This may be attributed to strong intramolecular hydrogen bonding in compound **142,** also –OH proton appeared at much down field in NMR.

PMR spectrum of ethyl 7-(3-phenylprop-2-enoxy)-2H-1-benzopyran-2-one-3-carboxylate **141** exhibited a triplet for three methyl protons of ethyl group of ester at δ 1.40, a quartet at δ 4.39 for two methylene protons of ethyl group, a doublet at δ 4.80 for two protons in cinnamyl chain –$OC\underline{H}_2CH$=CH- at C-7, a double doublet at δ 6.42 for -$OCH_2C\underline{H}$=CH- alkene proton, a doublet at δ 6.80 for a proton of cinnamyl chain Ar$C\underline{H}$=CH-, a doublet at δ 6.90 for C-5 proton, a multiplet at δ 7.28-7.52 for six protons of aromatic ring and a C-4 proton and finally singlet at δ 8.53 for C-9 [Figure-48].

PMR of compound **142** exhibited a double doublet (J=5.8 & 0.7) at δ 4.72-4.77 for two $C\underline{H}_2O$- protons,, a double doublet (J_1=J_2=5.9 Hz) at δ 6.36 for an olefinic proton, an another double doublet (J_1=J_2=5.9 Hz) at δ 6.40 for an olefinic proton, a doublet (J=2.1 Hz) at δ 6.49 for a proton, a double doublet (J=8.6 and 2.2 Hz) at δ 6.58-6.62 for an olefinic proton, a doublet (J=16 Hz) at δ 6.72-6.76 for a proton, a multiplet at δ 7.27-7.33 for three aromatic protons overlapping, two doublets one (J=9.8 Hz) at δ 7.42 and another at δ 7.43 (J=11.2 Hz), a singlet at δ 9.72 for an aldehyde proton and finally a singlet at δ 11.45 for H-bonded proton [Figure-50]. Downshift of –OH signal in PMR supports the intramolecular H-bond in the compound **142.**

PMR of compound **143** exhibited a double doublet (J=5.8 & 0.7) at δ 4.75-4.86 for four $C\underline{H}_2O$- protons, a multiplet at δ 6.40 for two protons, a double doublet (J_1=J_2=0.9 Hz) at δ 6.58-6.62 for two olefinic protons, another double doublet (J_1=J_2=8.6 Hz) at δ 6.72-6.80 for two olefinic protons, a doublet (J=16 Hz) at δ 7.23-7.28 for two protons, a singlet for C-3 proton overlapping, a multiplet at δ 7.33-7.85 for eight phenyl protons and finally a singlet at δ 10.38 for aldehyde proton [Figure-52].

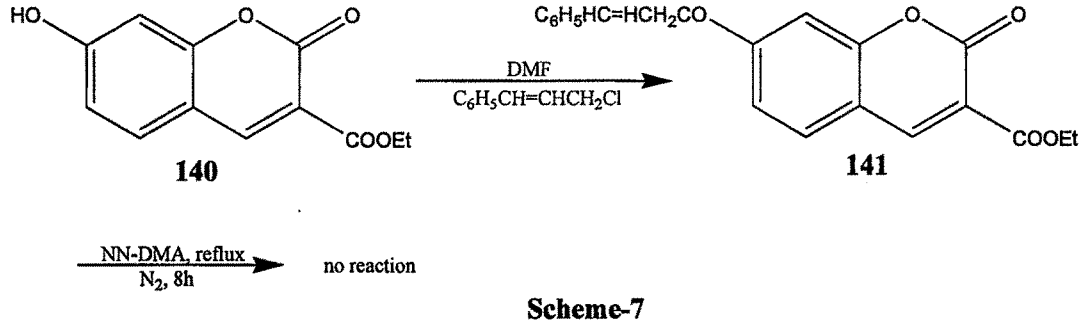
Compound **143** was heated with equimolar proportions of the ylide, carboethoxy methylene triphenyl phosphine, at 195 – 200 °C in DMA for 8 hours then contents were cooled and poured in cold dil HCl. Crude product obtained was chromatographed, two compounds were isolated (Scheme-9). First compound **144** was eluted out with pet. ether-ethyl acetate (95:5) mixture. IR of compound **144** showed bands at 1728 cm^{-1} and 1601 cm^{-1} suggesting formation of pyrone ring [Figure-53]. Elemental analysis suggested incorporation of one cinnamyl group. The second compound **145** was eluted out with pet. ether (60-80°C)-ethyl acetate (50:50) mixture. IR spectrum of compound **145** showed absorption bands at 1718 cm^{-1} and 1601 cm^{-1} indicating formation of pyrone ring [Figure-55]. Elemental analysis revealed incorporation of two cinnamyl groups.

PMR spectrum of compound **144** exhibited a doublet (J=8 Hz) at δ 1.31 for three methyl protons, a doublet (J=7.8 Hz) at δ 2.91 for a C-9 proton, a multiplet at δ 3.63-3.81 for a C-8 proton, a doublet (J=9.8 Hz) at δ 7.10 for two C-3 and C-4 protons, a multiplet at δ 7.21-7.41 for five aromatic protons and finally a doublet (J=8.4 Hz) at δ 7.54 for C-5 and C-6 protons [Figure-54].

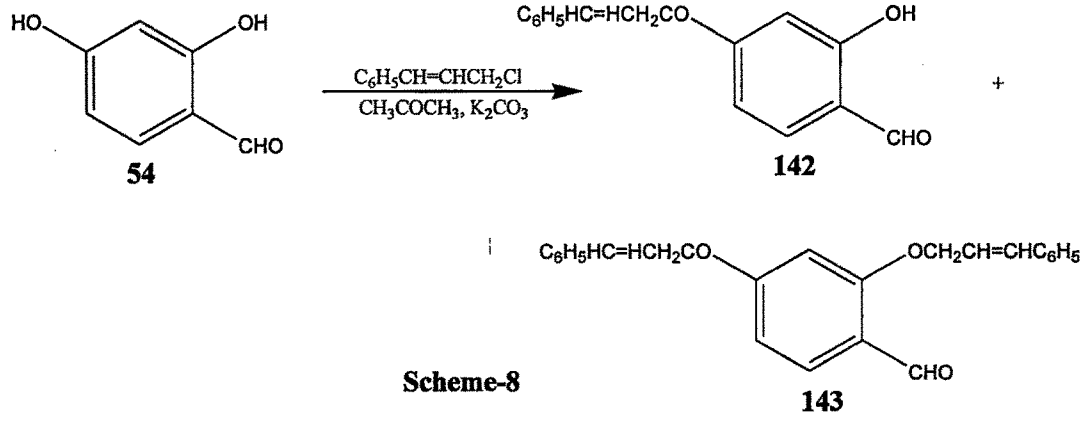
PMR spectrum of compound **145** exhibited a doublet (J=8 Hz) at δ 1.35 for three methyl protons, a doublet (J=4.8 Hz) at δ 2.79 for a C-9 proton, an another doublet (J=4.8 Hz) at δ 2.94 for a Ar-C<u>H</u>=CH- proton, a multiplet at δ 3.84 for a –OC<u>H</u>- proton, a multiplet at δ 4.17 for CH_2=C<u>H</u>- olefinic proton, a double doublet(J_1=J_2=0.9Hz) at δ 5..12 for an olefinic proton, another double doublet (J_1=J_2=0.9Hz) at δ 5..21 for an olefinic proton, a multiplet at δ 7.38-7.42 for two aromatic protons, a singlet at δ 7.43 for C-5 proton, a doublet (J=9.3 Hz) at δ 7.48 for C-3 proton, an another doublet (J=9.3 Hz) at δ 7.52 for C-4 proton and finally a multiplet at δ 7.73-7.92 for eight aromatic protons [Figure- 56].

It can be revealed from the above information that the cinnamyl group at C-2 migrated initially to C-3 to facilitate the formation of pyrone ring. Now cinnamyl group at C-4 in compound **143** tend to migrate to its angular position but the position is occupied, therefore it has two options either it can knock off from the molecule to give compound **144** or migrate to the next vacant position to form **145**.

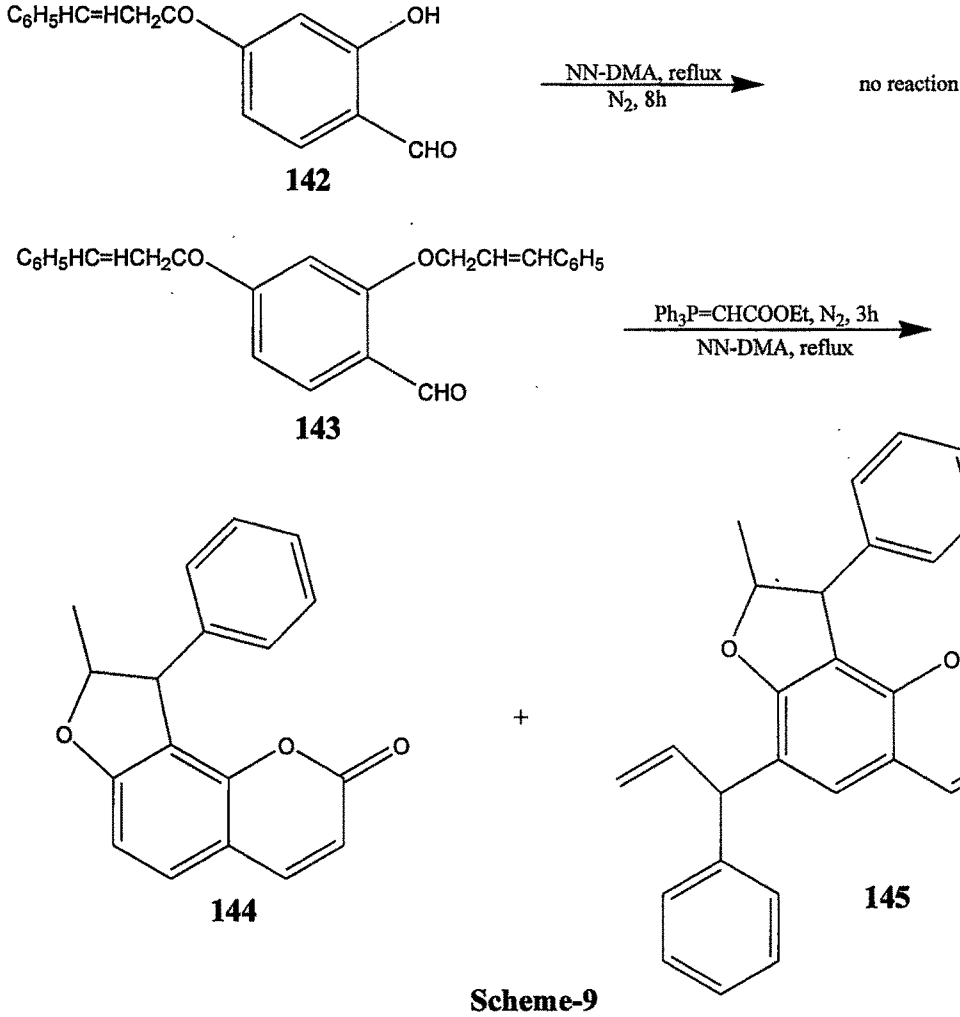
It can be attributed from the Claisen rearrangement that compound **143** has undergone step by step or simultaneous transformations (1) ortho migration of cinnamyl group from C-2 to C-3 and C-4 to C-5, then the formation of pyron ring eliminating ethanol molecule (2) formation of angular dihydrofuran ring.



Scheme-7



Scheme-8


C6H5HC=HCH2CO
OH
CHO
NN-DMA, reflux
N2, 8h
no reaction
142
C6H5HC=HCH2CO
OCH2CH=CHC6H5
CHO
Ph3P=CHCOOEt, N2, 3h
NN-DMA, reflux
143
O
O
O
144
+
O
O
O
145

Scheme-9

IV.3 Experimental:

Synthesis of ethyl-7-(3-phenylprop-2-enoxy)-2H-1-benzopyran-2-one-3-carboxylate, 141

Ethyl 7-hydroxy-2H-1-benzopyran-2-one-3-carboxylate **140** (4.6g, 0.0196mol) was refluxed with cinnamyl chloride (2.9g, 0.0196mol) in presence of anhydrous K_2CO_3 (10g, 0.072mol) and pinch of KI in dry N,N-dimethylformamide (35ml) for 8 hours. Mixture was cooled and N,Ndimethylformamide was decanted into crushed ice (200g) carefully and content was stirred for about half an hour. The solid thus obtained was dried and purified by column chromatography using petroleum ether(40-60C) with few drops of toluene and recrystallised from ethanol.

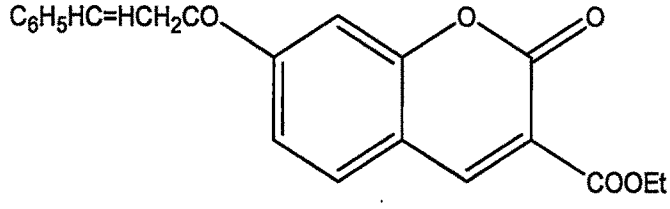
Synthesis of 4-cinnamyloxy-2-hydroxybenzaldehyde, 142 and 2,4-dicinnamyloxy benzaldehyde, 143

2,4-Dihydroxy benzaldehyde **54** (4.2g, 0.03mol) was refluxed with cinnamyl chloride (4.57g, 0.03mol) in presence of anhydrous K_2CO_3 (10g, 0.072mol) and a pinch of solid KI in dry acetone (100ml) for 7 hours. Monitoring with TLC showed two spots. Mixture was poured in crushed ice (200g) and left overnight. The solid thus obtained was filtered, dried and subjected to column chromatography using petroleum ether(40-60C) with few drops of toluene. First five fractions gave a solid compound **143** having melting point 91°-92° C. There after the polarity of toluene-petrolium ether eluent was increased to 12% which showed a faint spot on TLC. Then polarity was increased to 20% which afforded a solid compound **142** having melting point 98° C. Both compound **142** and **143** were recrystallised from benzene.

Synthesis of 8-methyl-9-phenyl-8,9-dihydro-2H-furo[2,3-h]-1-benzopyran-2-one, 144 and 8-methyl-9-phenyl-6-(1-phenylprop-2-enyl)-8,9-dihydro-2H-furo[2,3-h]-1-benzopyran-2-one, 145

2, 4 – Cinnamyloxy benzaldehyde **143** (1.5g, 0.004mol) and carboethoxy methylene triphenyl phosphorane (1.5g, 0.004mol) was refluxed in dry N,N-dimethylaniline (25ml) under atmosphere of nitrogen using three-necked flask for 10 hours. Completion of reaction was checked by TLC. Mixture was poured in crushed ice (200g) and 36% aq.HCl(50ml) with constant stirring and left overnight. The solid thus obtained was filtered, dried and subjected to chromatography using pet.ether eluent but no spot was detected on TLC. Then 20% toluene-pet.ether mixture was used as eluent but no spot was found even for it. There after 10% pet.ether-ethyl acetate mixture was used as eluent which afforded a compound having MP 145° C and IR spectrum was compared and found similar to triphenyl phosphine oxide ($Ph_3P=O$). On elution with 50% pet.ether-ethyl acetate mixture a semisolid compound was obtained which on thoroughly washing with pet.ether gave a brown solid residue and on TLC this brown solid residue showed two spots. On subjecting to column chromatography using ethyl acetate eluent, the brown solid residue in first five fractions gave compound **144** and remaining fractions afforded compound **145**. Both the compound **144** and **145** were recrystallised from ethanol.

Ethyl-7-(3-phenylprop-2-enoxy)-2H-1-benzopyran-2-one-3-carboxylate, **141:**



State : yellowish solid

Molecular Formula : $C_{21}H_{18}O_5$

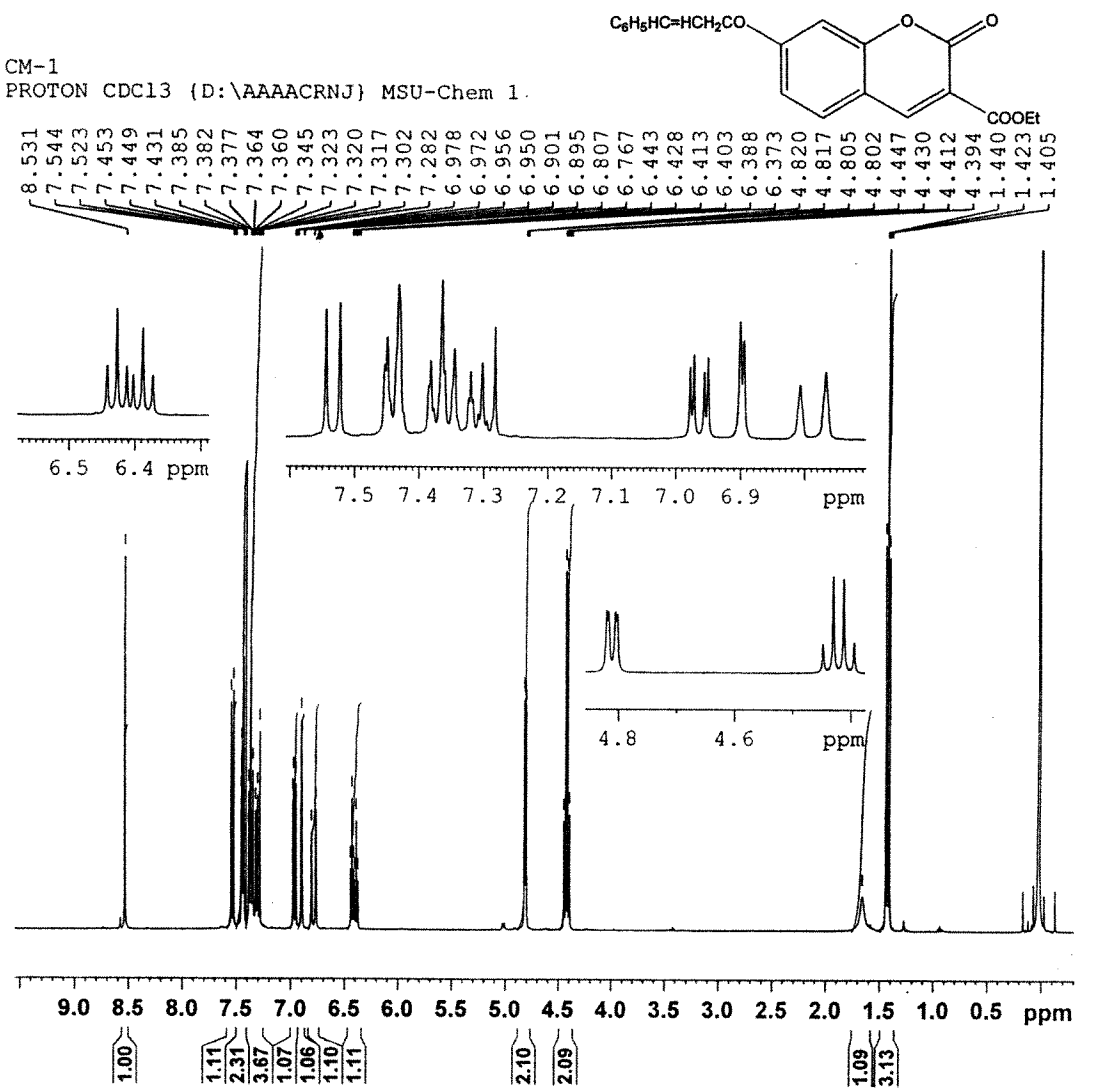
Melting Point : 110 °C

% Yield : 80

%C,H,N analysis (calculated) : C : 72.00 H : 5.14

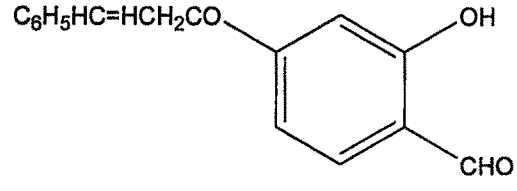
%C,H,N analysis (found) : C : 71.91 H : 5.19

PMR data (400MHz, $CDCl_3$) δ ppm: 1.40(t, 3H, $-CH_3$), 4.39(q, 2H, $-C\underline{H}_2CH_3$), 4.80(d, J=8 Hz, 2H, $-C\underline{H}_2O$), 6.42(dd, 1H, alkene proton), 6.80(d, 1H, Ar$C\underline{H}$=CH), 6.90(d, J=8 Hz, 1H, C-5), 6.95(d, J=8 Hz, 1H, C-6), 7.28-7.52(m, 6H, aromatic and C-4 protons), 8.53(s, 1H, C-9).



[Figure-48]: Ethyl-7-(3-phenylprop-2-enoxy)-2H-1-benzopyran-2-one-3-carboxylate, 141

4-Cinnamyloxy-2-hydroxybenzaldehyde, **142:**



State : brownish solid

Molecular Formula : $C_{16}H_{14}O_3$

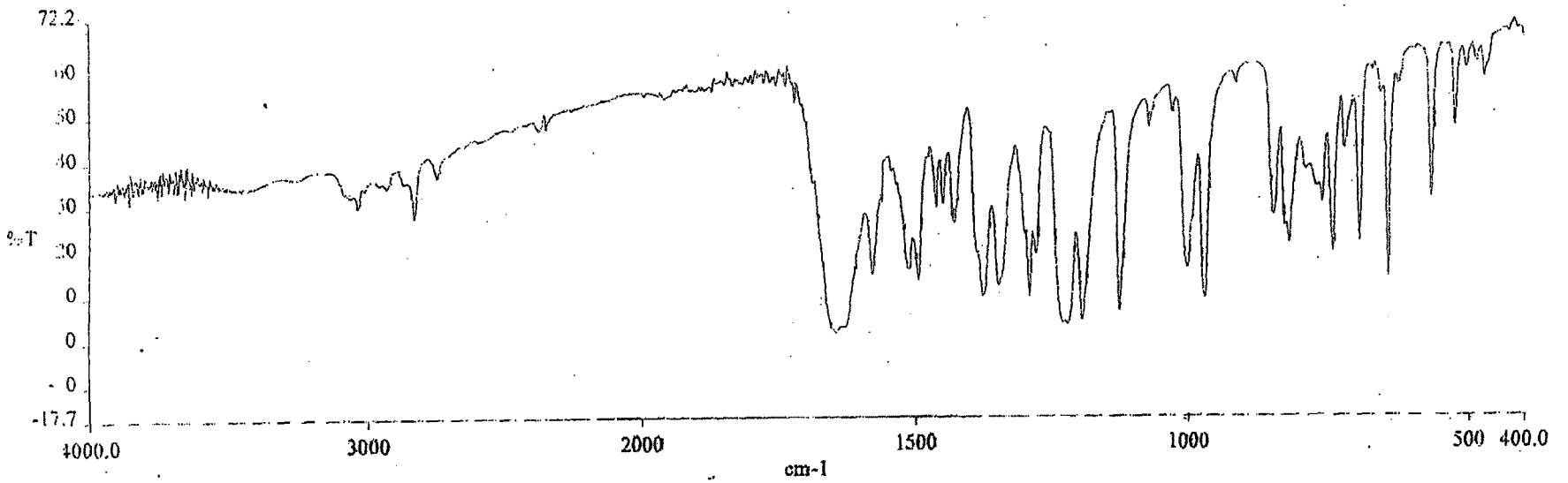
Melting Point : 98 °C

% Yield : 51

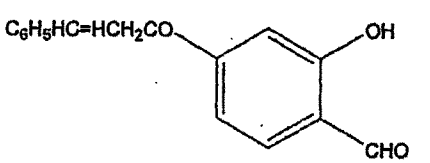
%C,H,N analysis (calculated) : C : 75.59 H : 5.51

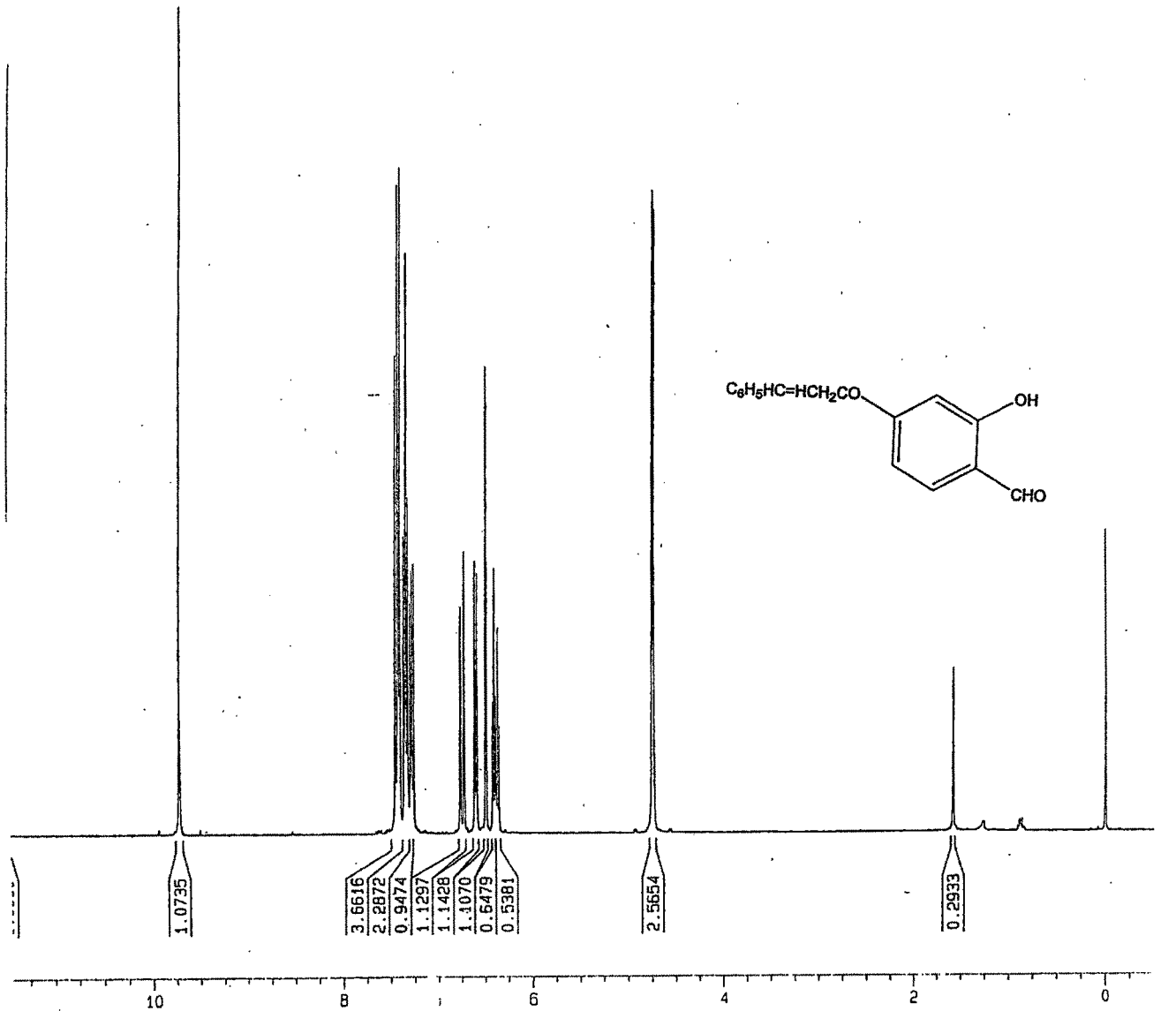
%C,H,N analysis (found) : C : 75.21 H : 5.78

PMR data (400MHz, $CDCl_3$) δ ppm: 4.72-4.77(dd, J=5.8 & 0.7 Hz, 2H, -CH_2O), 6.36(dd, J_1=J_2=5.9 Hz, 1H, phenyl ring), 6.40(dd, J1=J2=5.9 Hz, 1H), 6.49(d, J=2.1 Hz, 1H, olefinic proton), 6.58-6.62(dd, J=8.6, 2.2 Hz, 1H olefinic), 6.71-6.77(d, J=16 Hz, 1H), 7.27-7.33(m, 3H, a overlaping), 7.42(d, J=9.8 Hz, 1H), 7.43(d, J=11.2 Hz, 1H, x), 9.72(s, 1H, -CHO), 11.45(s, 1H, H-bonded –OH).

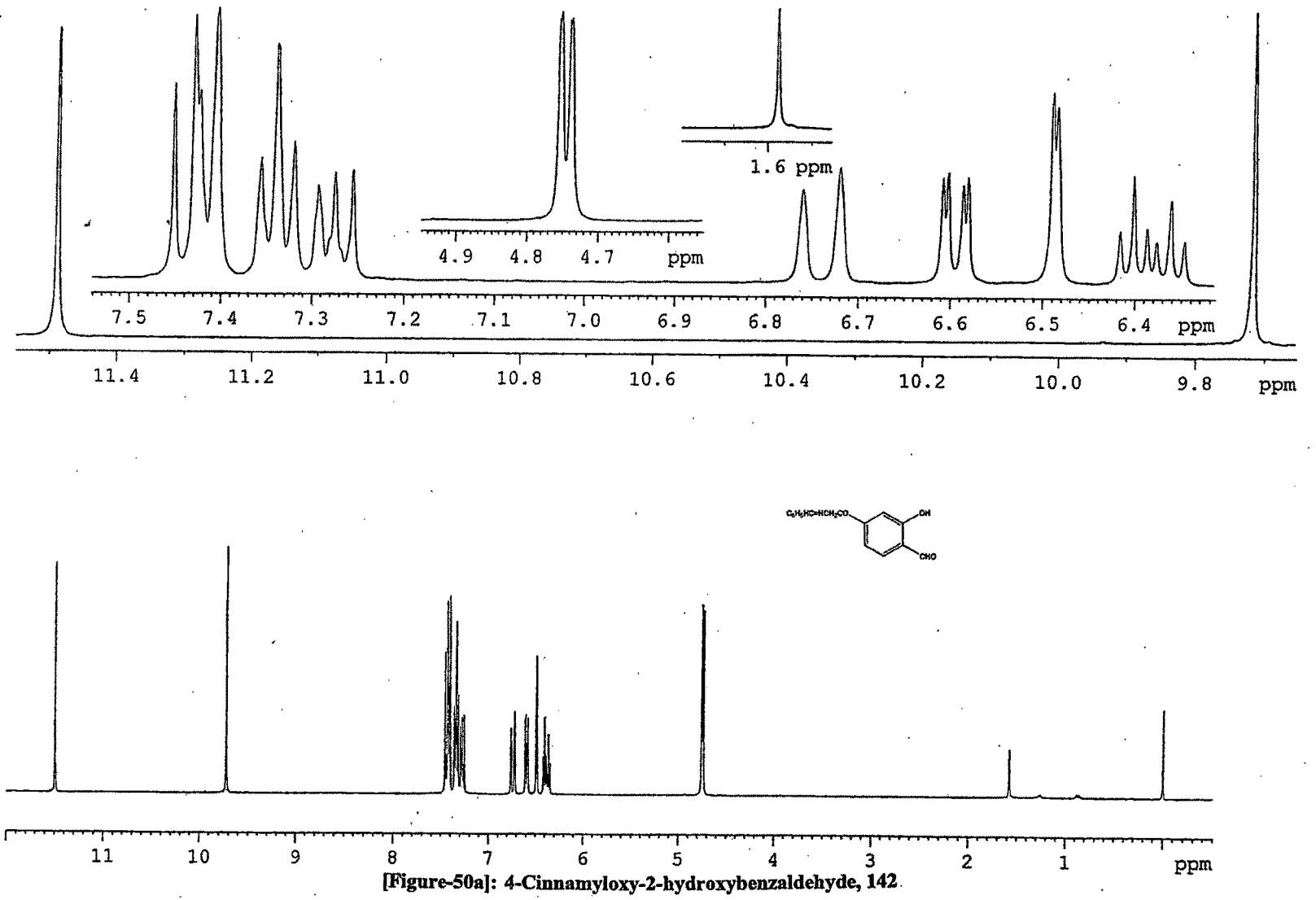


[Figure-49]: 4-Cinnamyloxy-2-hydroxybenzaldehyde, 142



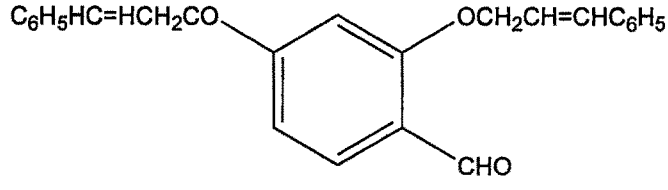


[Figure-50]: 4-Cinnamyloxy-2-hydroxybenzaldehyde, 142



[Figure-50a]: 4-Cinnamyloxy-2-hydroxybenzaldehyde, 142

2,4-Dicinnamyloxybenzaldehyde, **143:**



State : light yellow solid

Molecular Formula : $C_{25}H_{22}O_3$

Melting Point : 92 °C

% Yield : 31

%C,H,N analysis (calculated) : C : 81.08 H : 5.94

%C,H,N analysis (found) : C : 81.48 H : 6.11

PMR data (400MHz, $CDCl_3$) δ ppm: 4.75-4.98(dd, J=5.8 & 0.7 Hz, 4H, 2x-$C\underline{H}_2O$), 6.40(m, 2H, phenyl ring), 6.58-6.62(dd, $J_1=J_2=0.9$ Hz, 2H, olefinic proton), 6.72-6.80(dd, J=8.6 & 2.2 Hz, 2H olefinic protons), 7.23-7.28(d, J=16 Hz, 2H, z), 7.32(s, 1H, C-3, overlaping), 7.33-7.85(m, 8H, aromatic phenyl protons), 10.38(s, 1H, -CHO).

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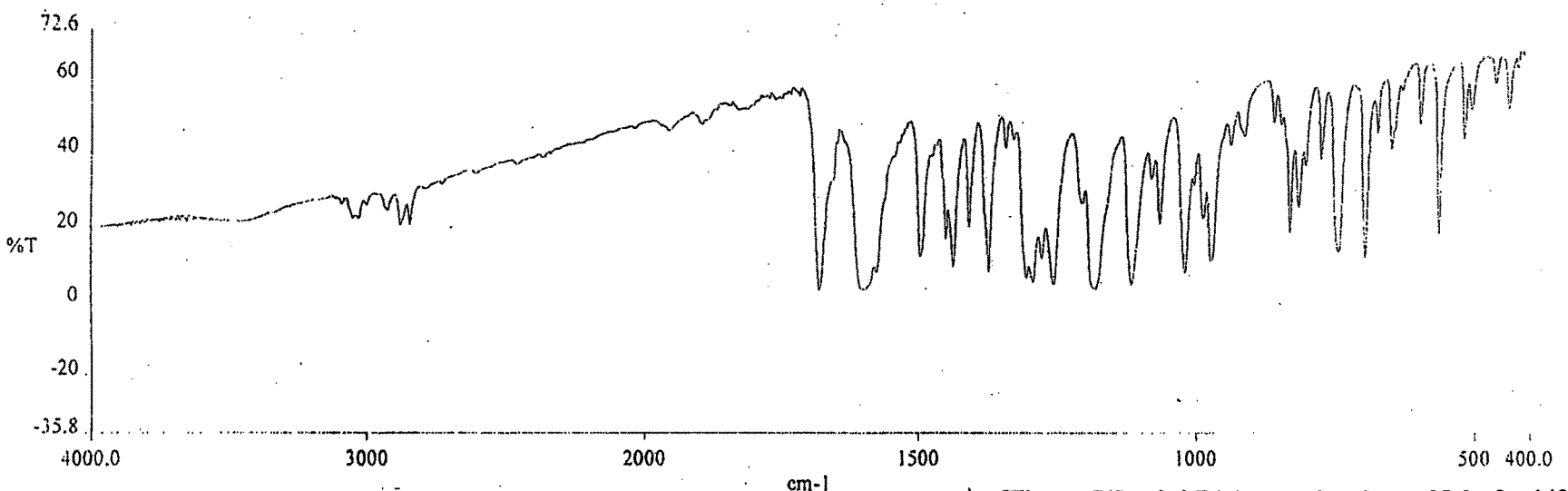
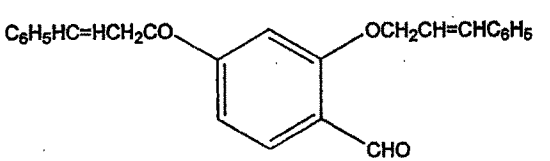
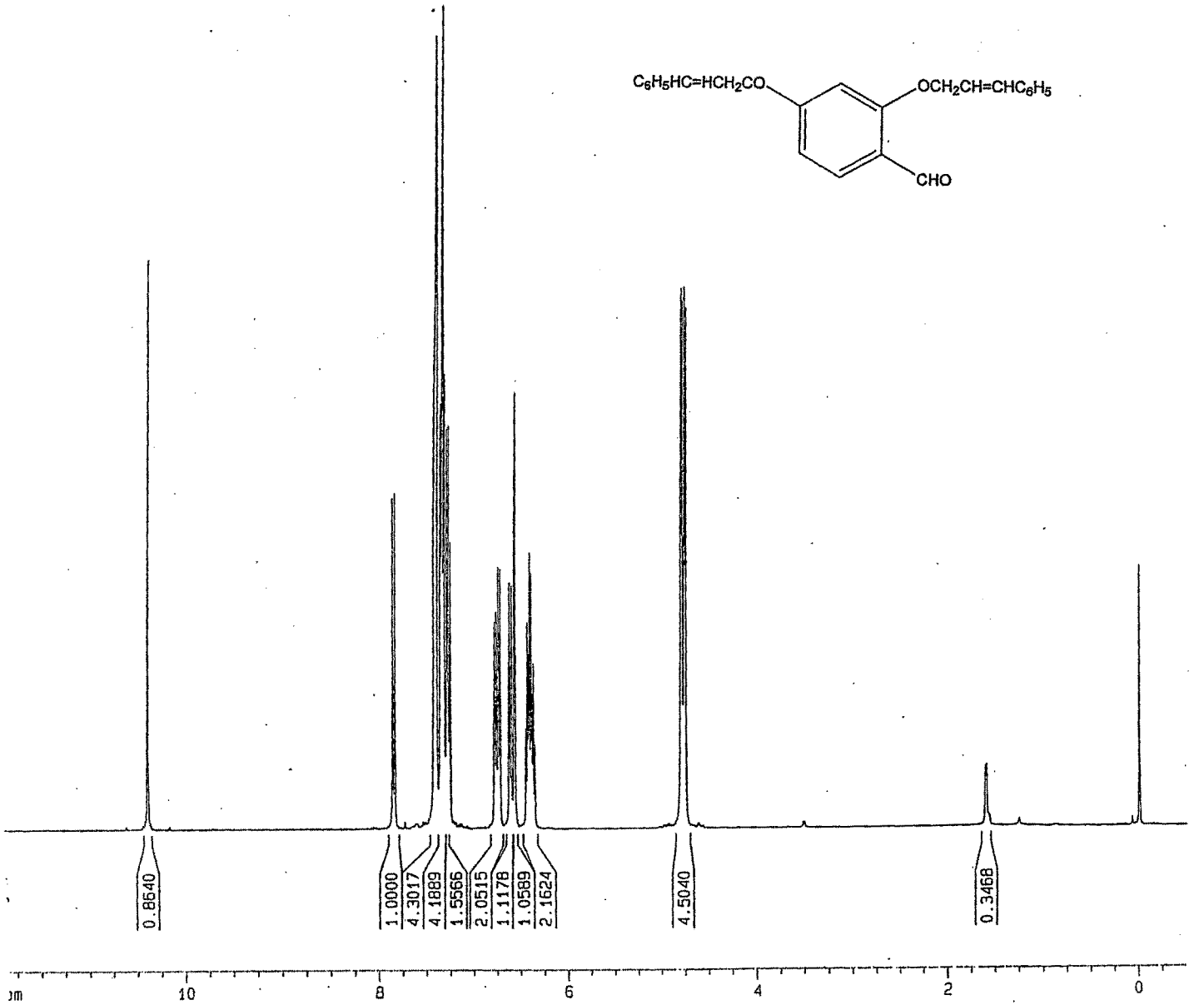
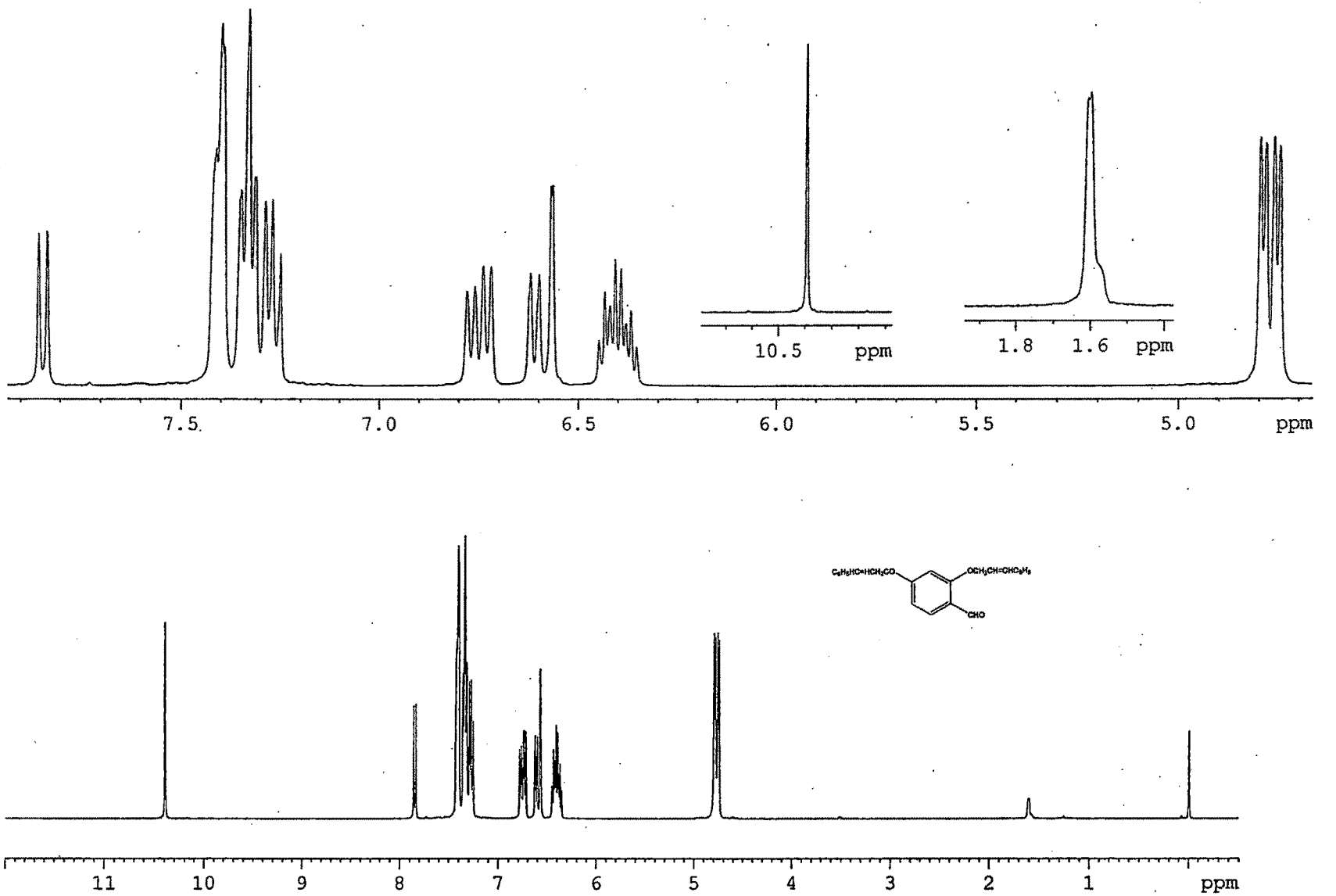


[Figure-51]: 2,4-Dicinnamyloxybenzaldehyde, 143



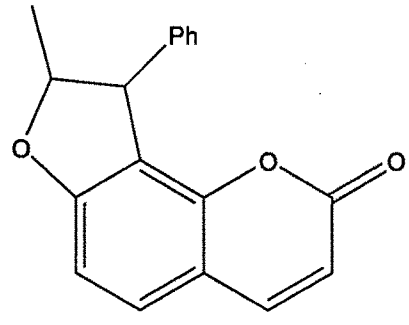


[Figure-52]: 2,4-Dicinnamyloxybenzaldehyde, 143



[Figure-52a]: 2,4-Dicinnamyloxybenzaldehyde, 143

8-Methyl-9-phenyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, **144:**



State : light brownish crystalline solid

Molecular Formula : $C_{18}H_{14}O_3$

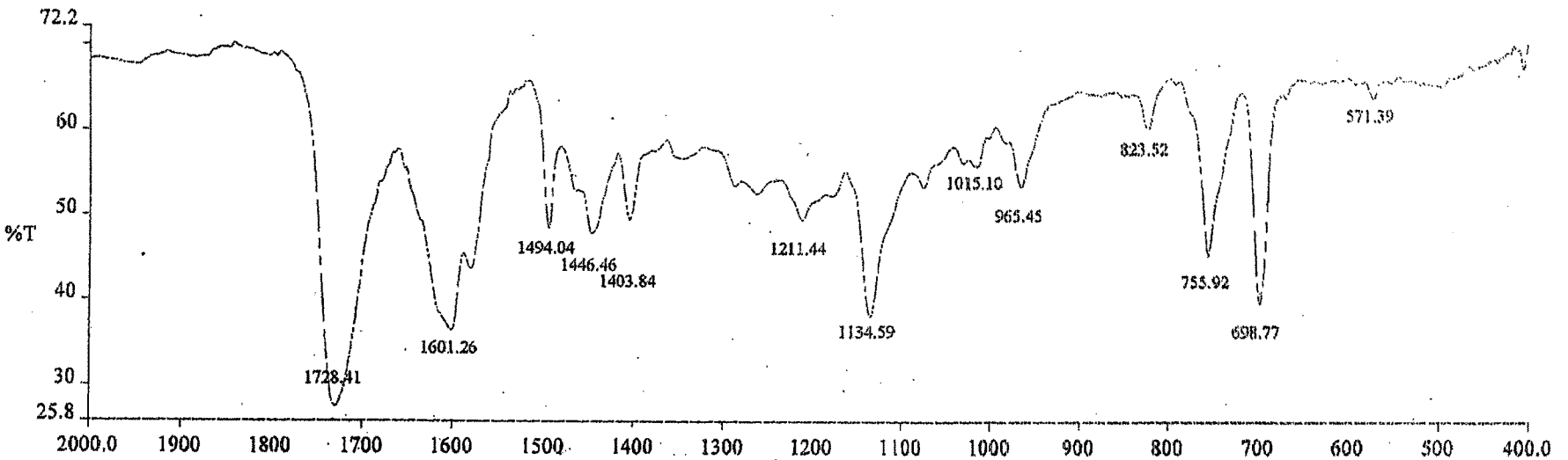
Melting Point : 135°C

% Yield : 30

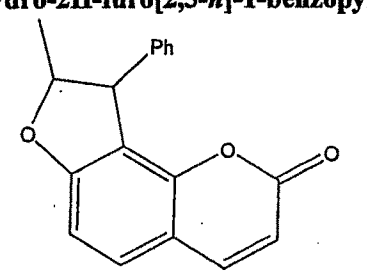
%C,H,N analysis (calculated) : C : 77.70 H : 5.03

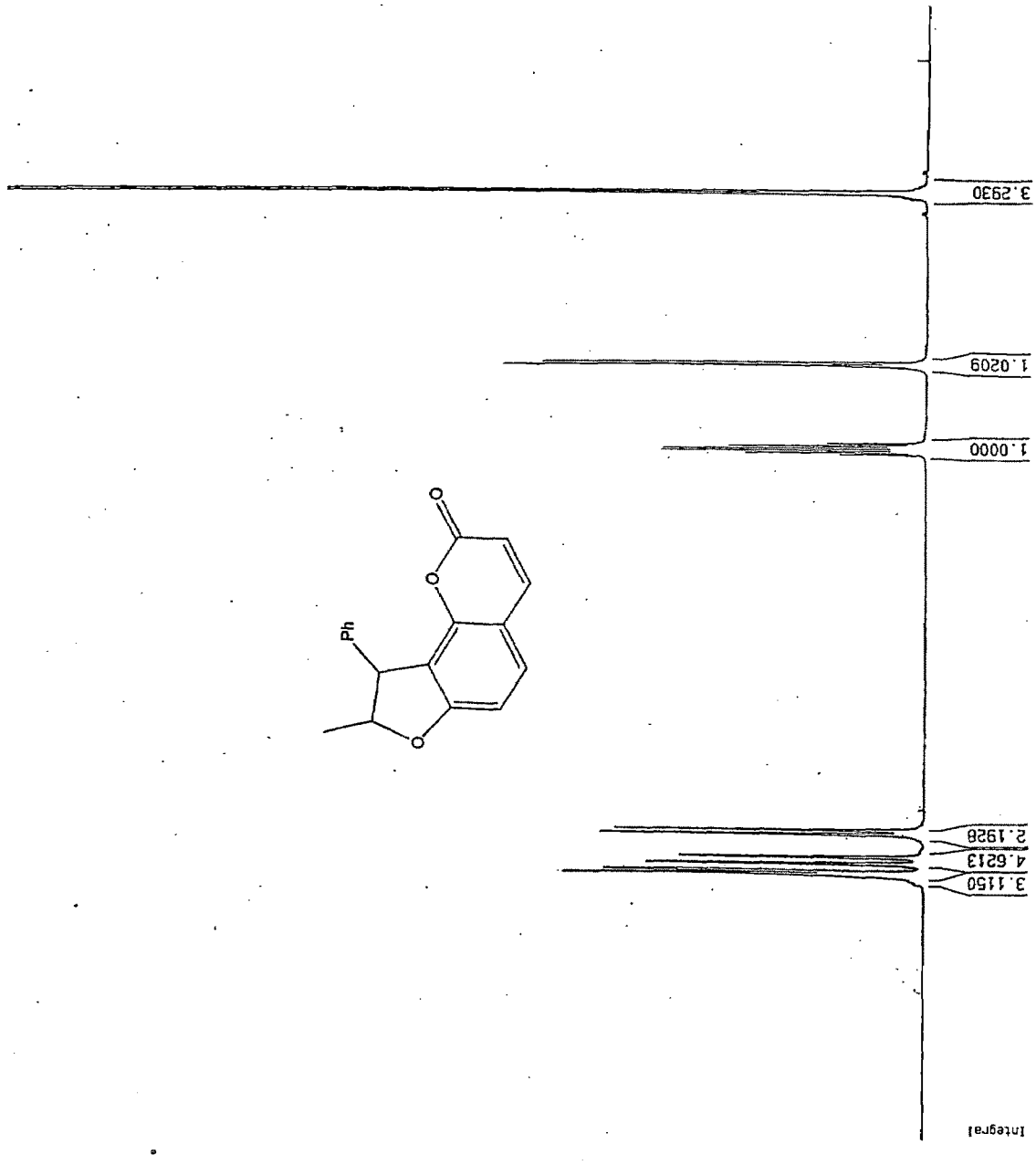
%C,H,N analysis (found) : C : 77.98 H : 5.31

PMR data (400MHz, $CDCl_3$) δ ppm: 1.31(d, J=8 Hz, 3H, -C<u>H</u>$_3$), 2.91(d, J=7.8 Hz, 1H, C-9), 3.63-3.81(m, 1H, C-8), 7.10(d, J=9.8 Hz, 2H, C-3 and C-4), 7.21-7.41(m, 5H, aromatic protons), 7.54(d, J=8.4 Hz, 2H, C-5 and C-6).

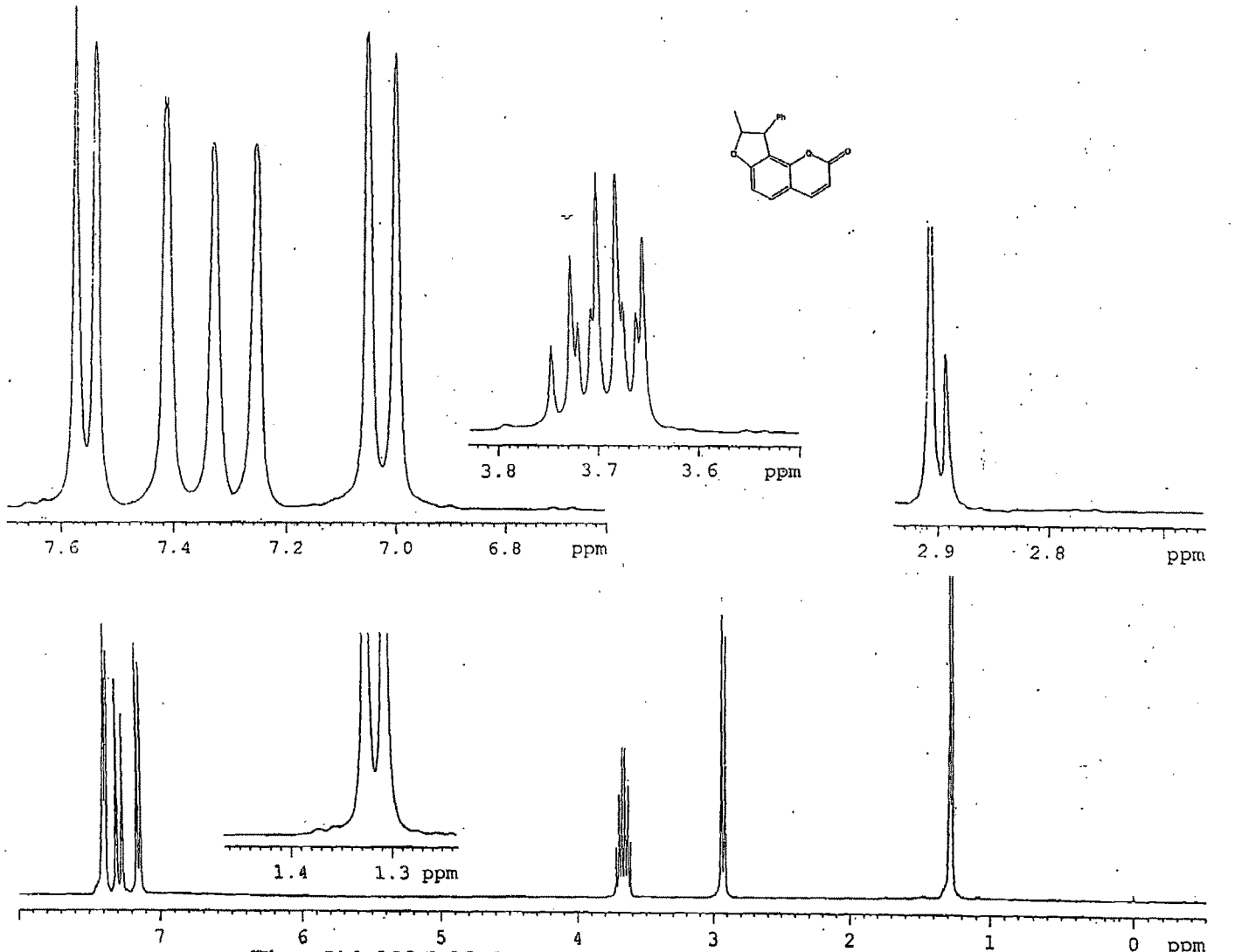


[Figure-53]: 8-Methyl-9-phenyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, 144



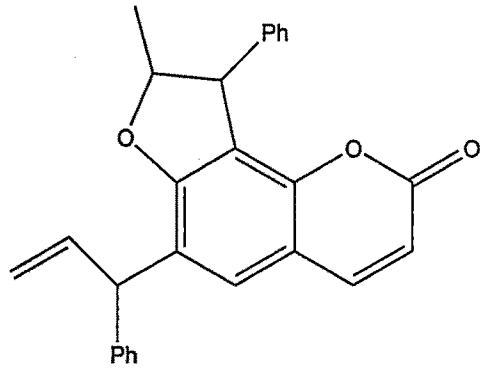


[Figure-54]: 8-Methyl-9-phenyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, 144



[Figure-54a]: 8-Methyl-9-phenyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, 144

8-Methyl-9-phenyl-6-(1-phenylprop-2-enyl)-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, **145:**



State : brownish crystalline solid

Molecular Formula : $C_{27}H_{22}O_3$

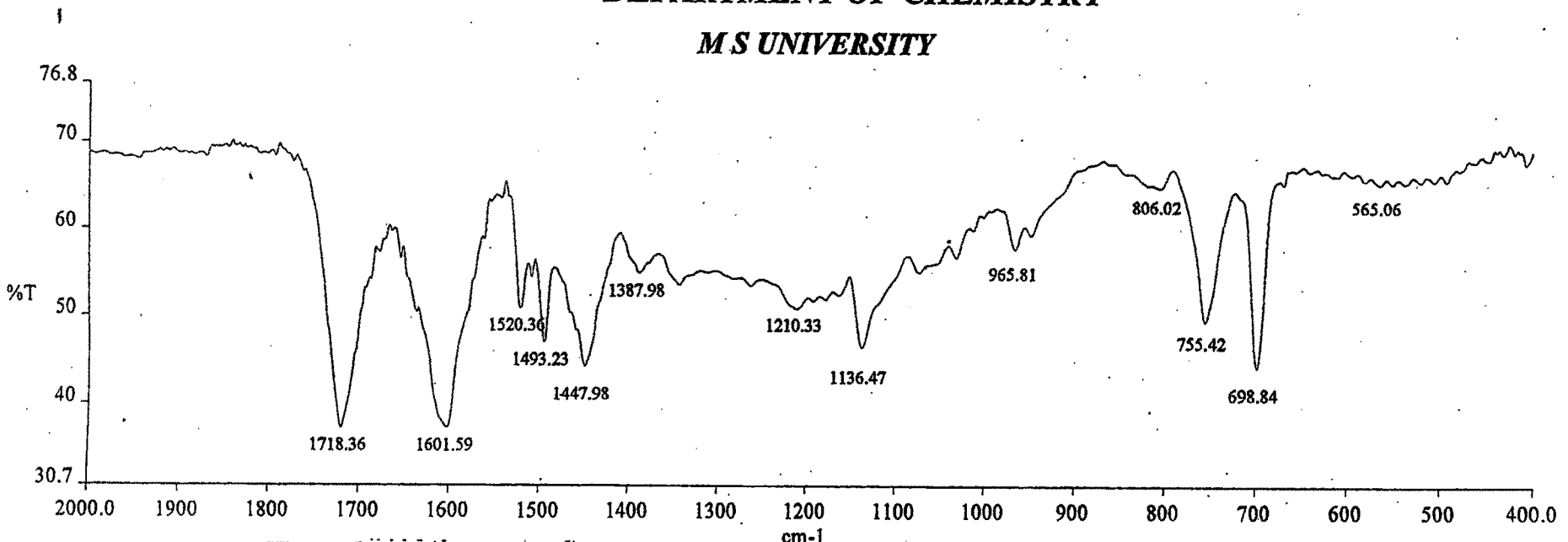
Melting Point : 148°C

% Yield : 21

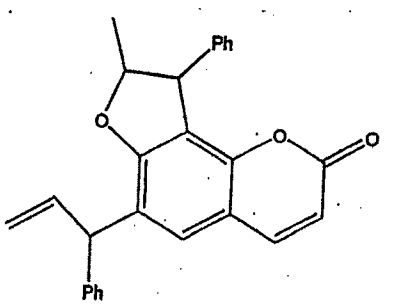
%C,H,N analysis (calculated) : C : 82.23 H : 5.58

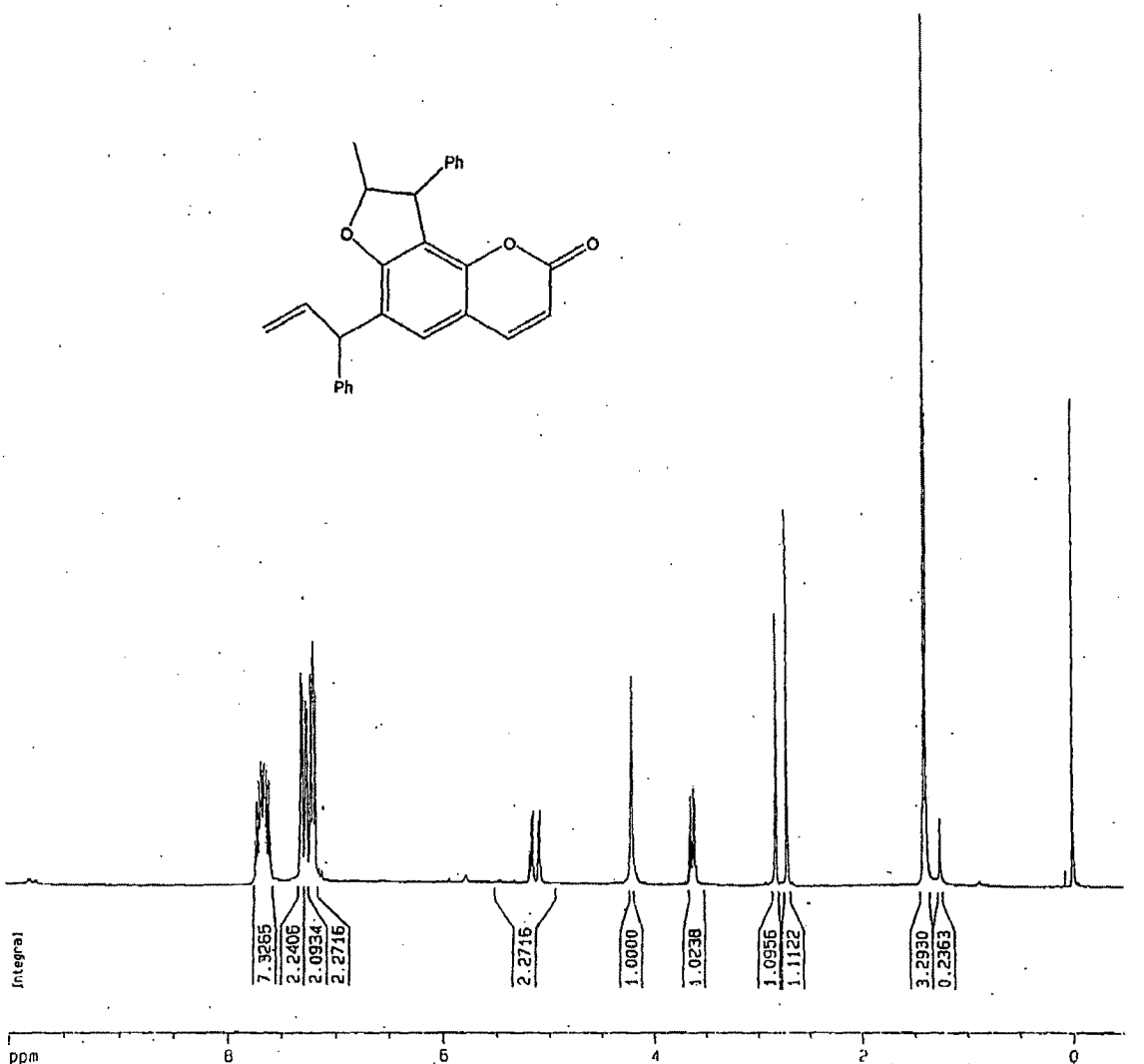
%C,H,N analysis (found) : C : 82.51 H : 5.78

PMR data (400MHz, $CDCl_3$) δ ppm: 1.35(d, J=8 Hz, 3H, -C<u>H</u>$_3$), 2.79(d, J=4.8 Hz, 1H, C-9), 2.94(d, J=4.8 Hz, 1H, Ar-C<u>H</u>-CH=), 3.84(m, 1H, -OC<u>H</u>-), 4.17(m, 1H, CH_2=C<u>H</u>- olefinic proton), 5.12(dd, J_1=J_2=0.9 Hz, 1H, olefinic proton), 5..21(dd, J_1=J_2=0.9 Hz, 1H, olefinic proton), 7.38-7.42(m, 2H, aromatic protons), 7.43(s, 1H, C-5), 7.48(d, J=9.3 Hz, 1H, C-3), 7.52(d, J=9.3 Hz, 1H, C-4), 7.73-7.92(m, 8H, aromatic protons).

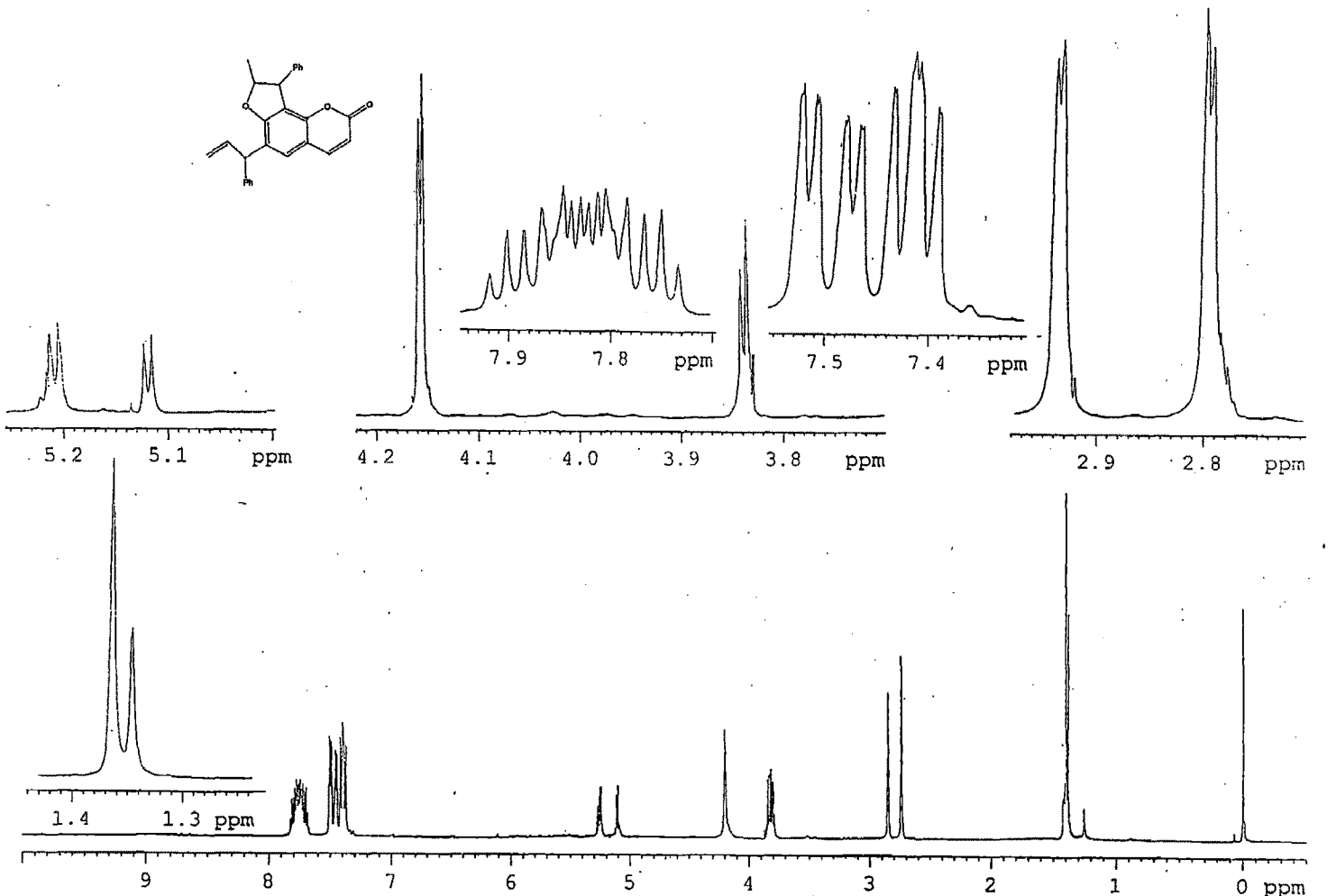


[Figure-55]: 8-Methyl-9-phenyl-6-(1-phenylprop-2-enyl)-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, 145





[Figure-56]: 8-Methyl-9-phenyl-6-(1-phenylprop-2-enyl)-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, 145



[Figure-56a]: 8-Methyl-9-phenyl-6-(1-phenylprop-2-enyl)-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, 145

CHAPTER-IV

Section-2

Knovaenegal and Claisen reactions of Allylated and Cinnamylated benzopyran-2H-ones

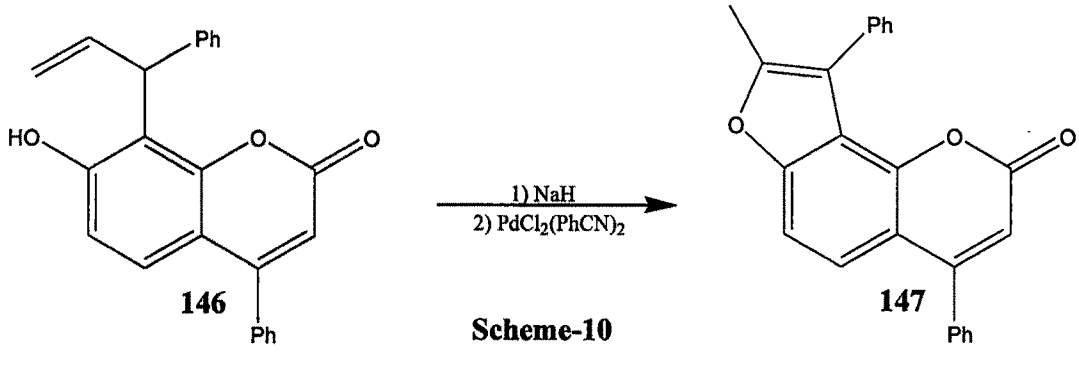
Section:2 Knovaenegal and Claisen reactions of Allylated and Cinnamylated 2H-1-benzopyran-2-ones

IV.4 Introduction

2H-1-benzopyran-2-one form an important class of naturally occurring oxygen heterocyclic compounds. The interest in these compounds has been enhanced due to their wide range of biological activity. A number of 2H-1-benzopyran-2-ones with 1,1-dimethyl allyl unit have been isolated from the natural sources and many of them have been found to possess hypotensive and spasmolytic activities[8].

During last few years various methods have been reported for the synthesis of allylated 2H-1-benzopyran-2-ones. In view of this it was considered interesting to develop a convenient synthesis of derivatives of 2H-1-benzopyran-2-one via allylation as well as cinnamylation of mono and diallyloxy 3-methyl benzaldehydes followed by Knoevenegal and Claisen reactions.

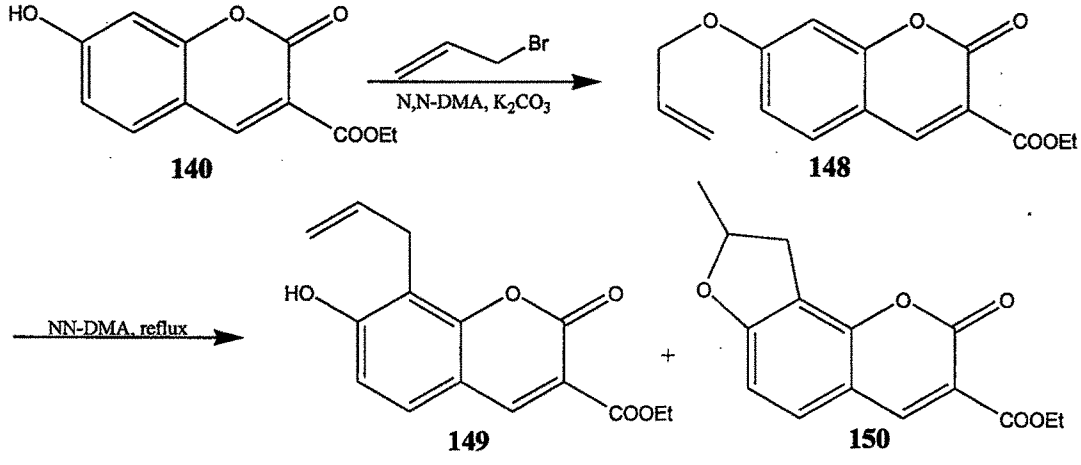
Rao[9] synthesized angularly fused furo benzopyrone **147** from 7-hydroxy-4-phenyl-8-(1-phenylprop-2-enyl)-2H-1-benzopyran-2-one **146** (Scheme-10).



Scheme-10

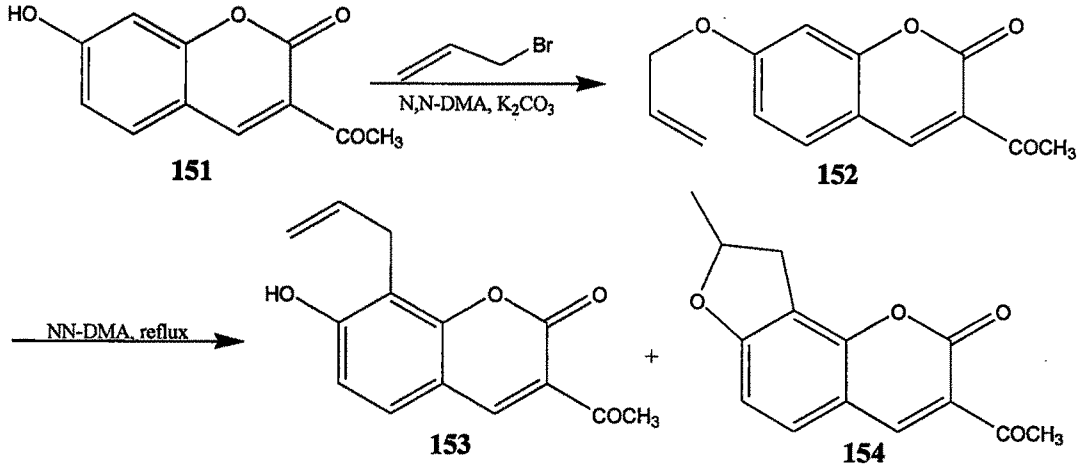
Synthesis of furo benzopyrones, ethyl-8-methyl-2,3-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one-3-carboxylate **150** and ethyl-3-acetyl-8-methyl-2,3-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one **154** was achieved by Knovaenegal reaction and Claisen rearrangement[1]. Allylated 7-hydroxy derivatives **148/152** were refluxed in dry DMF which underwent Claisen rearrangement to afford the cyclised products **150/154** along with rearranged products **149/153** respectively.

Bromination of **149** in acetic acid, followed by cyclisation with triethylamine in dry benzene afforded angularly fused bromomethyl furobenzopyrone **156** (Scheme-11, 12, 13).



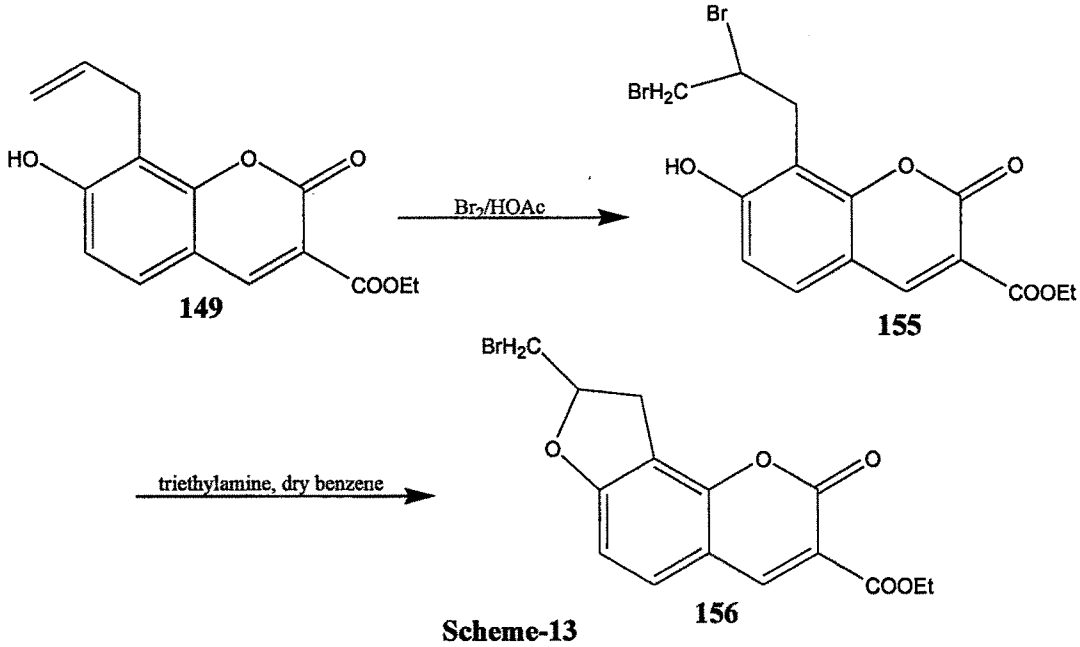
140 **148** **149** **150**

Scheme-11



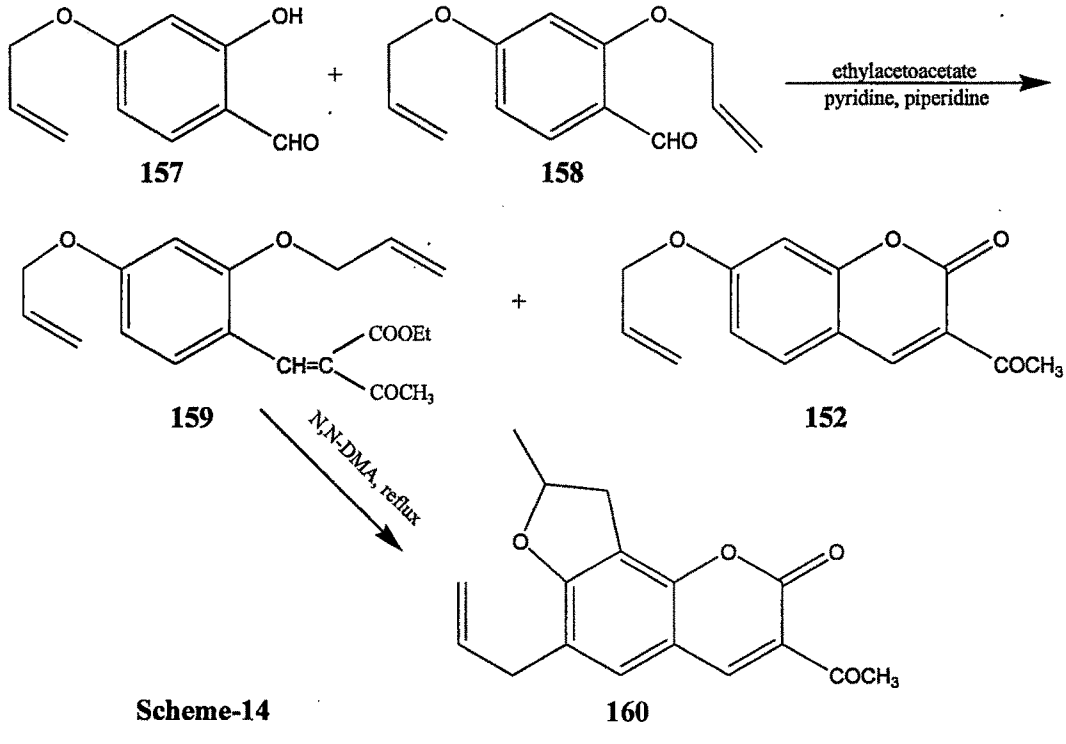
151 **152** **153** **154**

Scheme-12

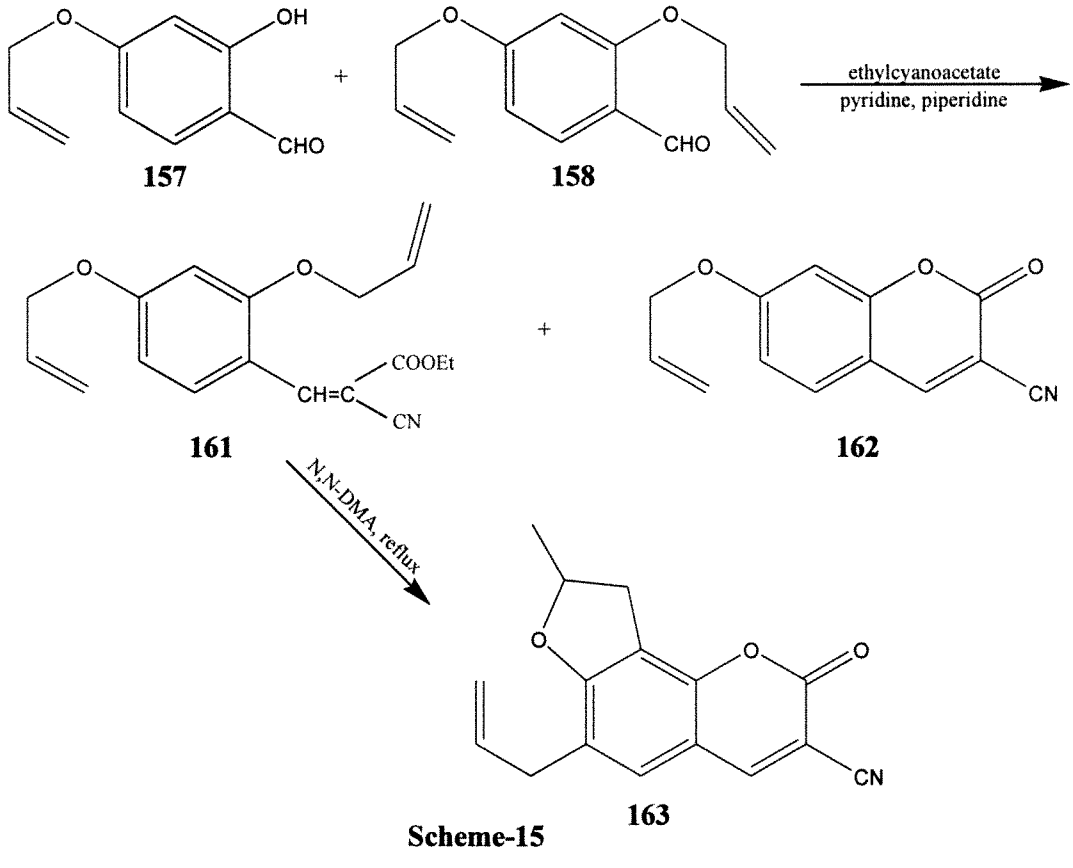


Scheme-13

Knovaenegal and Claisen reactions have been carried out on mixture of mono and diallyloxy derivatives of 2,4-dihydroxybenzaldehyde with ethylacetoacetate/ ethylcyanoacetate[1], afforded a mixture of an angularly fused allyl furobenzopyrone **160/163** along with an allyloxy benzopyrone **152/162** (Scheme-14, 15).



Scheme-14



Scheme-15

IV.5 Results and Discussion:

2,4-Dihydroxy-3-methylbenzaldehyde **164** on allylation gave monoallyloxy and diallyloxy products (**165** and **166**).

PMR spectrum of compound **165** exhibited a singlet at δ 2.46 for three protons of methyl group at aromatic ring, a multiplet at δ 4.31-4.40 for two -OC$\underline{H}_2$ protons, a double doublet at δ 4.44-4.59 for an olefinic -C$\underline{H}$=CH_2 proton, a double doublet at δ 5.03-5.15 for an olefinic -CH=C$\underline{H}_2$ proton, a double doublet at δ 5.76-5.94 for another olefinic -CH=C$\underline{H}_2$ proton, a doublet at δ 7.23 (J=9.3 Hz) for a C-5 proton, a doublet at δ 7.75 (J=9.3 Hz) for a C-6 proton, a singlet at δ9.90 for hydrogen bonded phenolic –OH and finally a singlet at δ 11.60 for an aldehyde proton[Figure- 57].

PMR spectrum of **166** exhibited a singlet at δ 2.70 for three protons of methyl group at aromatic ring, a multiplet at δ 4.61-4.71 for four protons of $OC\underline{H}_2$-, a multiplet at δ 4.91-5.10 for two olefinic -$C\underline{H}$=CH_2 protons, a multiplet at δ 5.40-5.61 for four olefinic -CH=$C\underline{H}_2$, protons, a doublet at δ 7.42 (J=8.4 Hz) for a C-5 proton, a doublet at δ 7.50 (J=8.4 Hz) for a C-6 proton and finally a singlet at δ10.11 for aldehyde proton [Figure-58].

2,4-Diallyloxy-3-methylbenzaldehyde **166** was condensed with ethyl cyano acetate in pyridine with catalytic amount of piperidine which afforded ethyl 2,4-diallyloxy-3-methyl-α-cyano cinnamate **167**. On Claisen rearrangement by refluxing in DMA for eight hours, compound **167** yielded 6-allyl-3-cyano-7-hydroxy-8-methyl-2H-1-benzopyran-2-one **168** (Scheme-16).

Diallyloxy compound **167** showed a strong IR band at 2228 cm^{-1} of cyanide group and 1711 cm^{-1} for –C=O of esters group [Figure- 59a].

PMR spectrum of compound **167** exhibited a triplet for three methyl protons of ethyl group of ester at δ 1.00, a singlet at δ 2.60 for three protons of methyl group at aromatic ring, a quartet at δ 4.08 for two methylene protons of ethyl group of ester, a multiplet at δ 4.31 for two -$C\underline{H}$=CH_2 olefinic protons, a multiplet at δ 4.60 for four protons of $OC\underline{H}_2$-, a multiplet at δ 5.12 for four olefinic protons of -CH=$C\underline{H}_2$, a singlet at δ 6.75 for a proton Ar-$C\underline{H}$=C, a doublet at δ 7.05 (J=8 Hz) for a C-5 proton and finally another doublet (J=8 Hz) at δ 7.31 for C-6 proton [Figure- 59].

Compound **168** showed IR absorption bands at 1701 cm^{-1}, 2228 cm^{-1} and 2228 cm^{-1} which confirmed carbonyl group of lactone, cyanide group and -OH phenolic group respectively [Figure-60].

PMR of compound **168** exhibited a singlet at δ 3.26 for three protons of methyl group at aromatic ring, a multiplet at δ 4.40-4.46 for two Ar-$C\underline{H}_2$- protons, a multiplet at δ 5.16 for a -$C\underline{H}$=CH_2 olefinic proton, a multiplet at δ 5.30-5.61 for two $C\underline{H}_2$=CH, olefinic protons, a singlet at δ 7.48 for a C-4 proton, a singlet at δ 7.62 for a C-5 proton and finally a broad signal at δ 8.80-9.30 for phenolic –OH proton [Figure- 61].

It should be noted that the formation of compound **168** indicates that one of the allyl group at C-2 got knocked off without going to C-3 which is blocked.

Similarly 2,4-dihydroxybenzaldehyde **54** on cinnamylation gave monocinnamylated **142** as well as dicinnamylated product **143**. The dicinnamyloxy compound **143** on Knoevenegal condensation with ethylcyanoacetate in presence of pyridine and catalytic amount of piperidine gave ethyl-2,4-dicinnamyloxy-α-cyanocinnamate **169** which in refluxing N,N-dimethylaniline underwent Claisen rearrangement furnishing 3-cyano-7-hydroxy-6-(1-phenylprop-2-enyl)-2H-1-benzopyran-2-one **170** (Scheme-17).

PMR of compound **169** exhibited a triplet at δ 1.20 for three methyl protons of ethyl group, a multiplet at 3.50 for two –OC<u>H</u>$_2$- protons, a quartet at δ 4.20 for two methylene protons of ethyl group, a multiplet at δ 5.25 for four olefinic protons, a multiplet at δ 6.75 for three Ar-C<u>H</u>=CH- protons and finally a multiplet at δ 7.18-7.98 accounts for thirteen aromatic protons [Figure- 62].

PMR of compound **170** exhibited a multiplet at δ 4.65 for a -C<u>H</u>=CH$_2$ olefinic proton, a multiplet at δ 4.77 for a Ar-C<u>H</u>-Ar proton, a multiplet at δ 5.03 for a C<u>H$_2$</u>=CH olefinic proton, another multiplet at δ 6.25 for a C<u>H$_2$</u>=CH olefinic proton, a singlet at δ 7.62 for a C-4 proton, a multiplet at δ 7.70-7.92 for five aromatic and one –OH protons, a singlet at δ 8.15 for a C-5 proton, a singlet at δ 8.31 for a C-9 proton and finally a multiplet at δ 8.55 for an aromatic proton [Figure- 63].

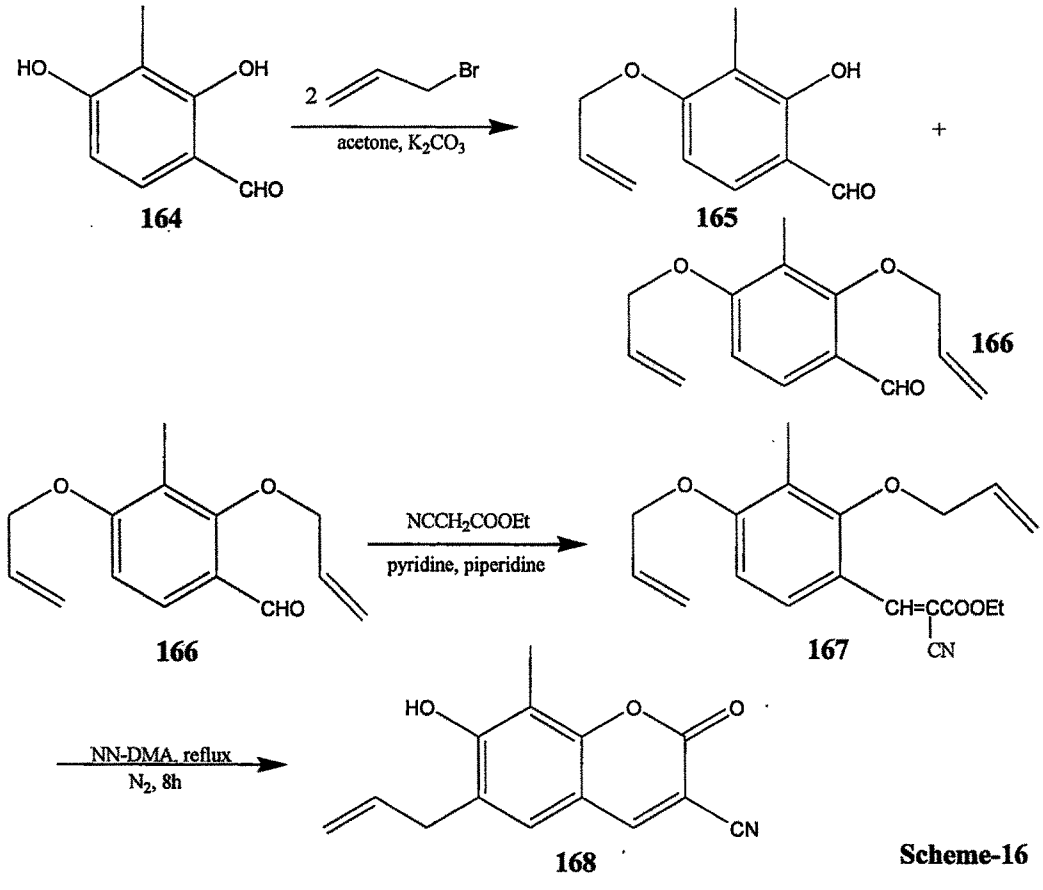
IV.6 Experimental:

Synthesis of 4-allyloxy-2-hydroxy-3-methylbenzaldehyde, 165 and 2,4-diallyloxy-3-methylbenzaldehyde, 166:

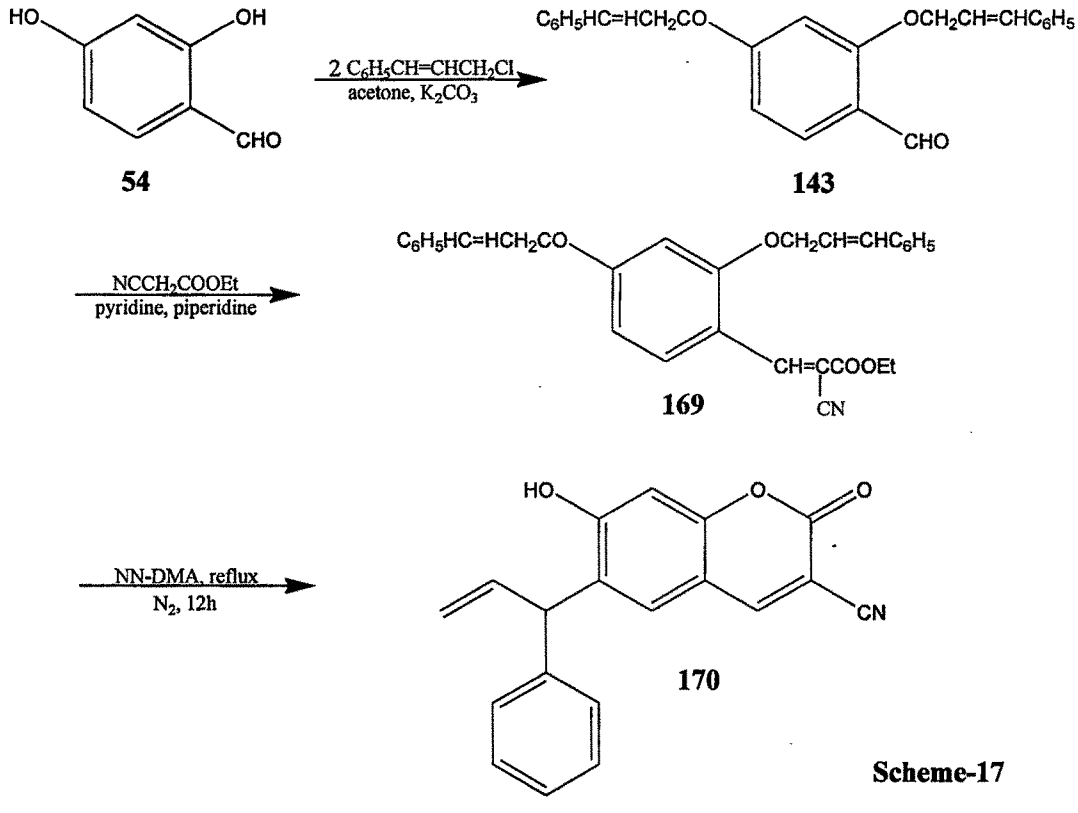
2,4-Dihydroxy-3-methyl benzaldehyde **52** (7.0g, 0.047mol) was refluxed with allyl bromide (12ml, 0.098mol) in presence of anhydrous K_2CO_3 (10g, 0.072mol) in dry acetone (180ml) for 5 hours. Monitoring with TLC showed two spots. Acetone was distilled off and the solid was subjected to column chromatography using pet.ether (40-60) as eluent. First five fractions of eluent (500ml) afforded a liquid compound **54** which was dried over anhydrous sodium sulphate. Then 1% benzene-pet.ether mixture was used as eluent which afforded compound **53**. On refluxing for 8 hours the yield of compound **54** was increased and on refluxing for >11 hours only one compound **54** was obtained.

Synthesis of ethyl 2,4-diallyloxy-3-methyl-α-cyanocinnamate, 167:

2,4-Diallyloxy-3-methyl benzaldehyde **54** (3.5g, 0.015mol) was heated in water bath with ethyl cyano acetate(1.7ml, 0.015mol) in presence of catalytic amount of piperidine(0.2ml) and solvent pyridine(8ml) for 28 hours. The reaction mixture was poured in cold aqueous (1:1) HCl(50ml). Separated solid was dried and subjected to column chromatography using 20% toluene-pet.ether mixture as eluent followed by recrystallization in ethanol.



Scheme-16



Scheme-17

Synthesis of 6-allyl-3-cyano-7-hydroxy-8-methyl-2H-1-benzopyran-2-one, 168:

Ethyl 2,4-diallyloxy-3-methyl-α-cyanocinnamate, **55** (4.0g) was refluxed in dry N,N-dimethylaniline (25ml) for eight hours under atmosphere of nitrogen. The reaction mixture was cooled and poured in cold aqueous (1:1) HCl (100ml). Separated solid was filterd, washed, dried and subjected to column chromatography and eluted out using 50% toluene-pet.ether mixture as eluent followed by recrystallization in ethanol.

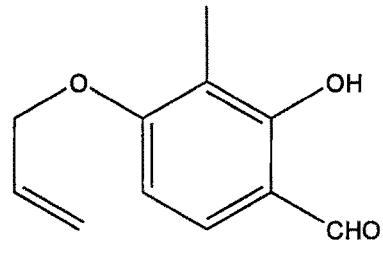
Synthesis of ethyl 2,4-dicinnamyloxy-α-cyanocinnamate, 169:

2,4-Dicinnamyloxy benzaldehyde **143** (7.0g, 0.015mol) was heated in water bath with ethyl cyano acetate(1.7ml, 0.015mol) in presence of catalytic amount of piperidine (0.2 ml) and solvent pyridine (15ml) for 30 hours. The reaction mixture was poured in cold aqueous (1:1) HCl (100ml). Separated solid was filtered, washed, dried and subjected to column chromatography and eluted out using 10% toluene-pet.ether mixture as eluent followed by recrystallization in ethanol.

Synthesis of 3-cyano -7-hydroxy- 6-(1-phenylprop-2-enyl)-2H-1-benzopyran-2-one, 170:

Ethyl 2,4-dicinnamyloxy-α-cyanocinnamate, **169** (4.0g) was refluxed in dry N,N-dimethylaniline (25ml) for eight hours under atmosphere of nitrogen. The reaction mixture was cooled and poured in cold aqueous (1:1) HCl (100ml). Separated solid was filtered, washed, dried and subjected to column chromatography and eluted out using 50% toluene-pet.ether mixture as eluent followed by recrystallization with ethanol.

4-Allyloxy-2-hydroxy-3-methylbenzaldehyde, **165:**



State : Oily

Molecular Formula : $C_{11}H_{12}O_3$

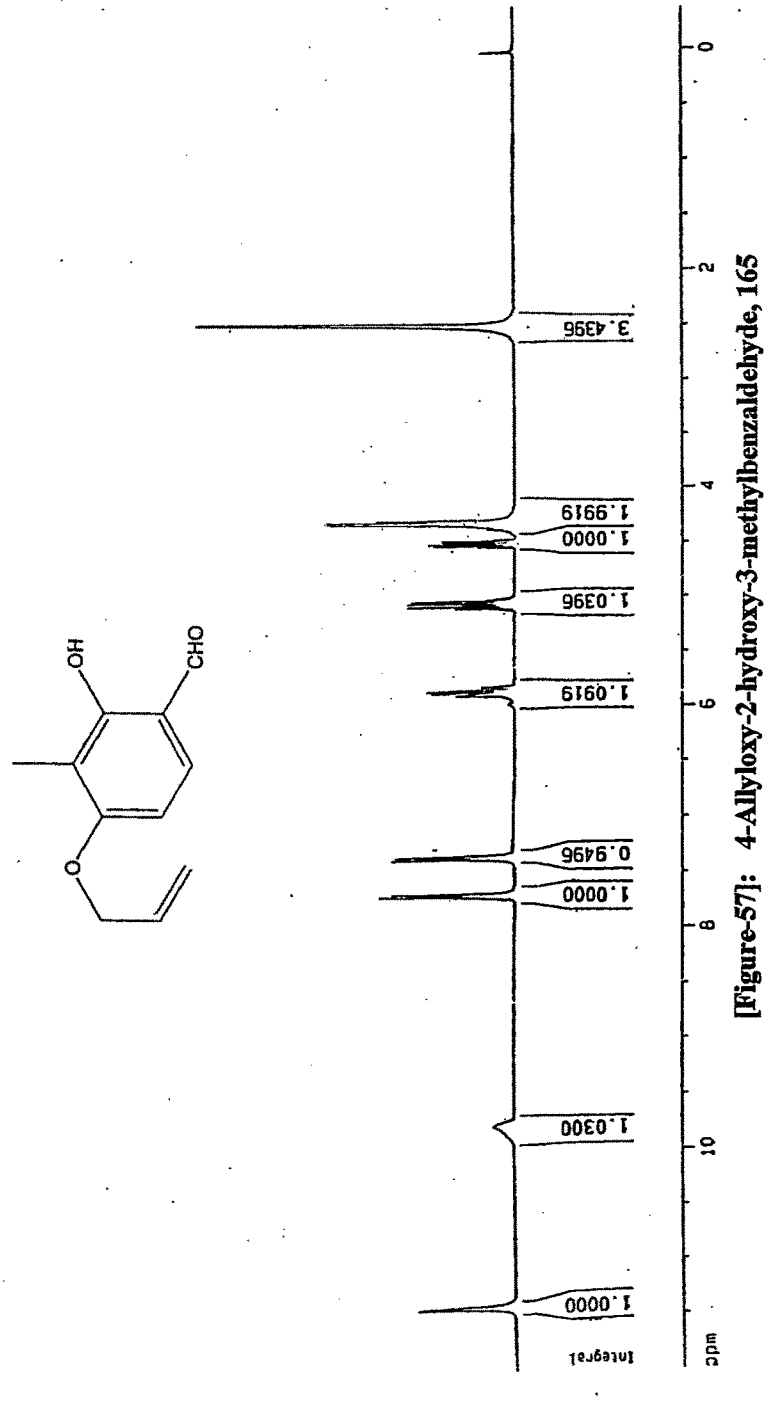
Boiling Point : 180-181°C

% Yield : 50

%C,H,N analysis (calculated) : C : 68.75 H : 6.25

%C,H,N analysis (found) : C : 68.61 H : 5.98

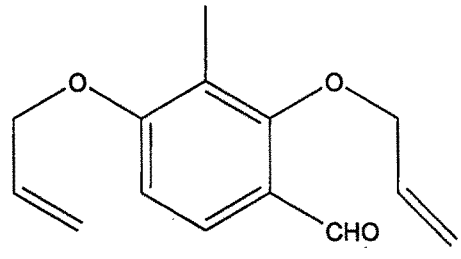
PMR data (400MHz, $CDCl_3$) δ ppm: 2.46(s, 3H, $-CH_3$), 4.31-4.40(m, 2H, $-OCH_2$), 4.44-4.59(dd, 1H, $-C\underline{H}=CH_2$ olefinic proton), 5.03-5.15(dd, 1H, $-CH=C\underline{H_2}$ olefinic proton), 5.76-5.94(dd, 1H, $-CH=C\underline{H_2}$ olefinic proton), 7.23(d, J=9.3 Hz, 1H, C-5), 7.75(d, J=9.3 Hz, 1H, C-6), 9.90(br signal, 1H, -OH), 11.60(s, 1H, -CHO).



[Figure-57]: 4-Allyloxy-2-hydroxy-3-methylbenzaldehyde, 165

[Figure-57a]: 4-Allyloxy-2-hydroxy-3-methylbenzaldehyde, 165

2,4-Diallyloxy-3-methylbenzaldehyde, **166:**



State : liquid

Molecular Formula : $C_{14}H_{16}O_3$

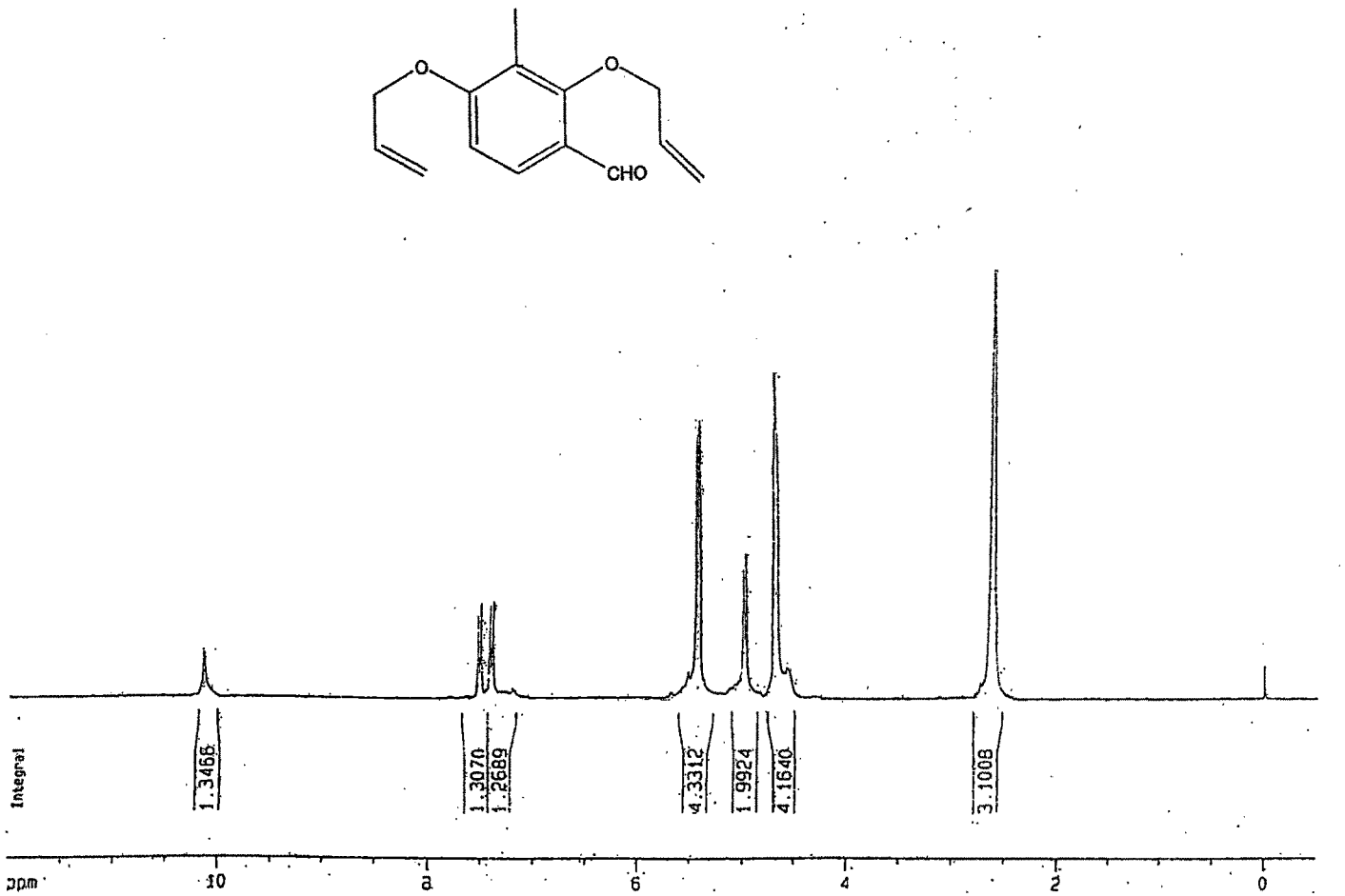
Boiling Point : 159-161°C

% Yield : 30

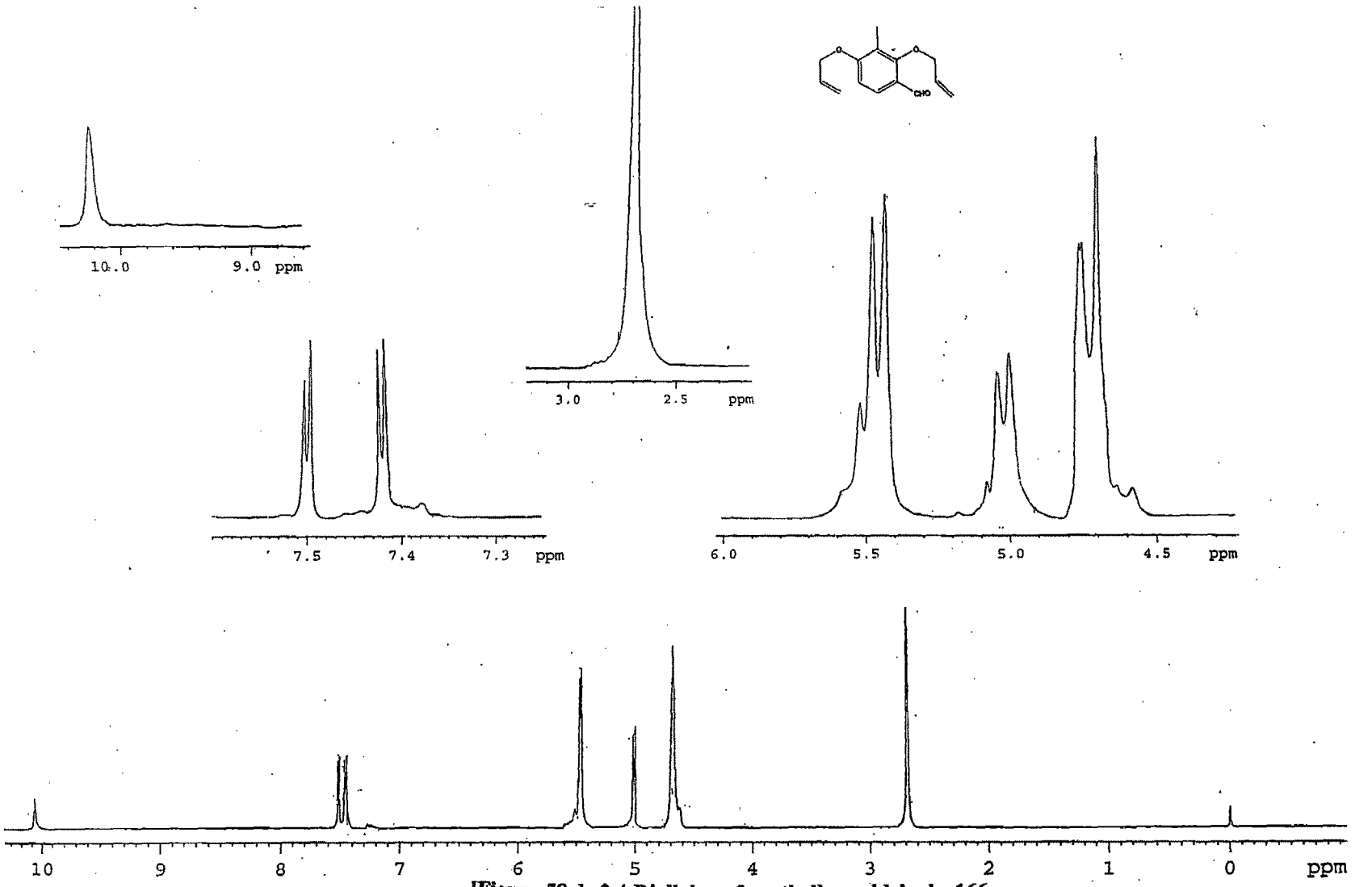
%C,H,N analysis (calculated) : C : 72.41 H : 6.90

%C,H,N analysis (found) : C : 72.21 H : 7.00

PMR data (400MHz, $CDCl_3$) δ ppm: 2.70(s, 3H, $-CH_3$), 4.61-4.71(m, 4H, $-OC\underline{H}_2$), 4.91-5.10(m, 2H, olefinic protons), 5.40-5.61(m, 4H, olefinic protons), 7.42(d, J=8.4 Hz, 1H, C-5), 7.50(d, J=8.4 Hz, 1H, C-6), 10.11(s, 1H, -CHO).

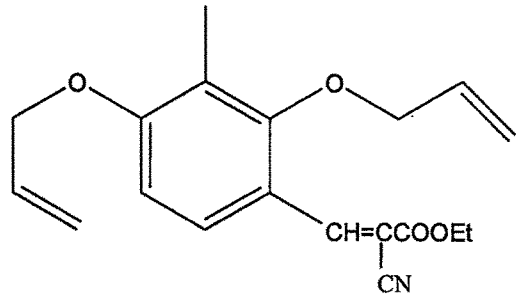


[Figure-58]: 2,4-Diallyloxy-3-methylbenzaldehyde, 166



[Figure-58a]: 2,4-Diallyloxy-3-methylbenzaldehyde, 166

Ethyl 2,4-diallyloxy-3-methyl-α-cyanocinnamate, **167:**



State : yellow solid

Molecular Formula : $C_{19}H_{21}O_4N$

Melting Point : 88-91°C

% Yield : 60

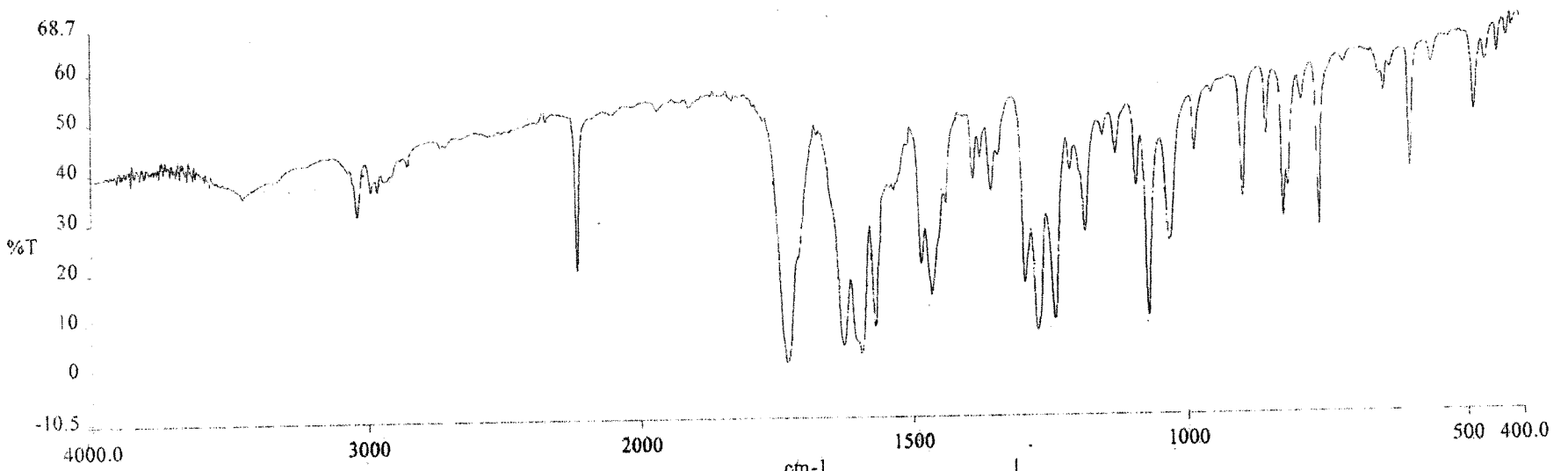
%C,H,N analysis (calculated) : C : 69.72 H : 6.42 N : 4.28

%C,H,N analysis (found) : C : 70.00 H : 6.11 N : 4.51

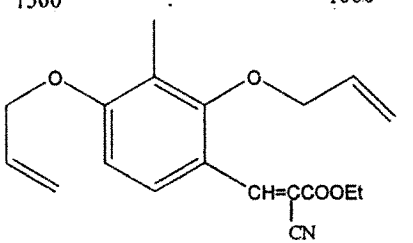
PMR data (400MHz, $CDCl_3$) δ ppm : 1.00(t, 3H, -$CH_2\underline{CH_3}$), 2.60(s, 3H, Ar-$C\underline{H_3}$), 4.08(q, 2H, -$C\underline{H_2}CH_3$), 4.31(m, 2H, -$C\underline{H}$=CH_2 olefinic), 4.60(m,4H, 2x-$OC\underline{H_2}$), 5.12(m, 4H, $C\underline{H_2}$=CH, olefinic protons), 6.75(s, 1H, Ar-$C\underline{H}$=C), 7.05(d, J=8 Hz, 1H, C-5), 7.31(d, J=8 Hz, 1H, C-6).

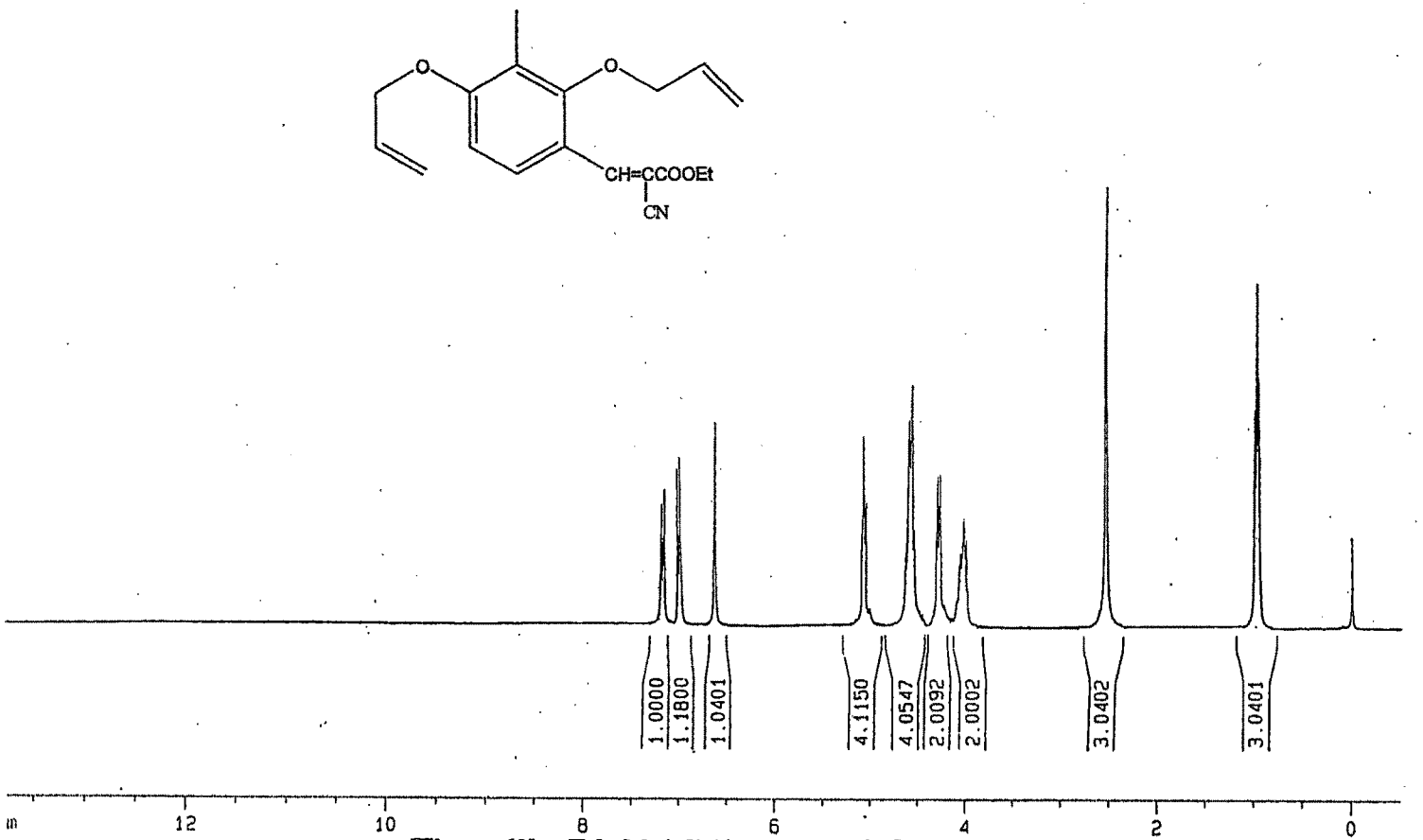
DEPARTMENT OF CHEMISTRY

M S UNIVERSITY



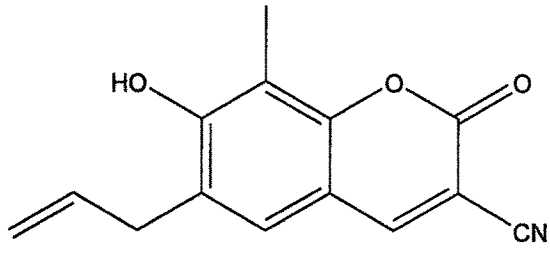
[Figure-59]: Ethyl 2,4-diallyloxy-3-methyl-α-cyanocinnamate, 167





[Figure-60]: Ethyl 2,4-diallyloxy-3-methyl-α-cyanocinnamate, 167

6-Allyl-3-cyano-7-hydroxy-8-methyl-2H-1-benzopyran-2-one, **168:**



State : orange yellow solid

Molecular Formula : $C_{14}H_{11}O_3N$

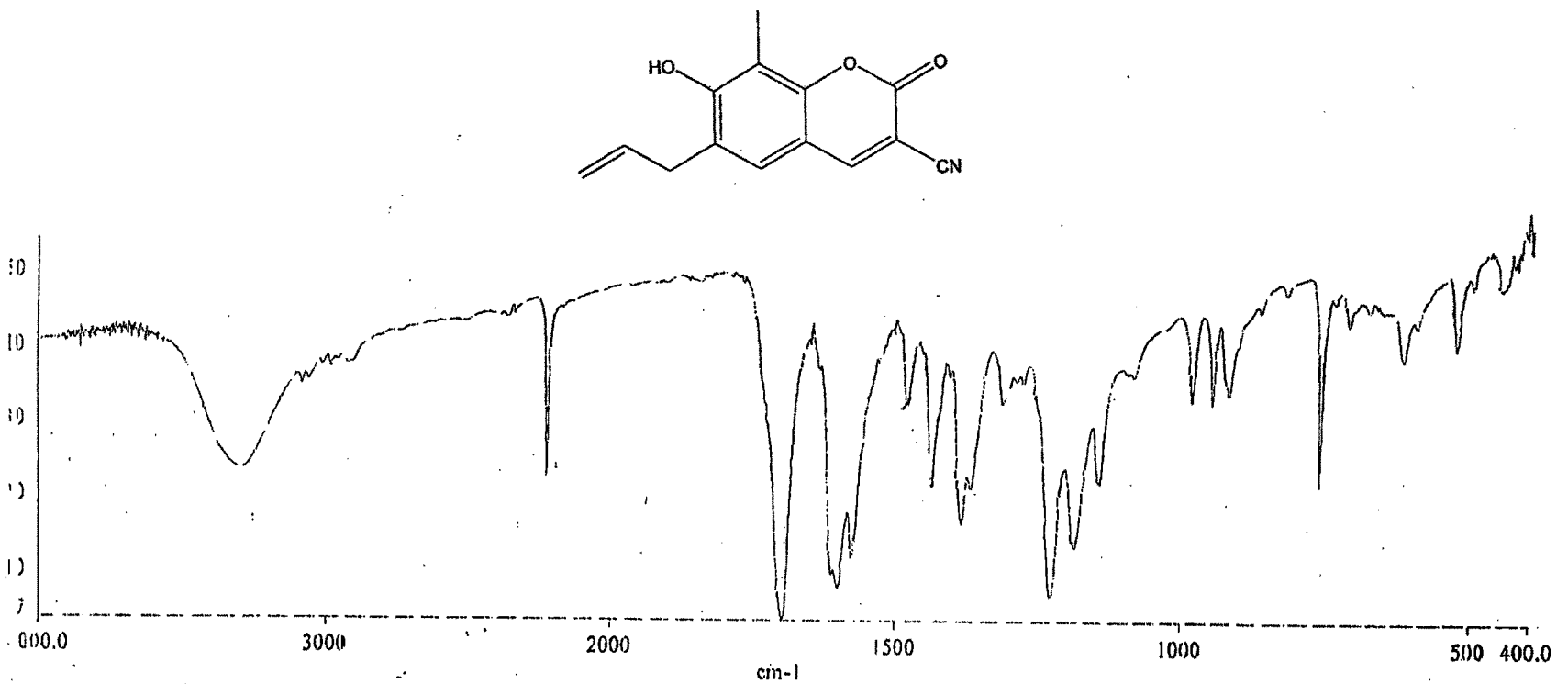
Melting Point : 205°C

% Yield : 50

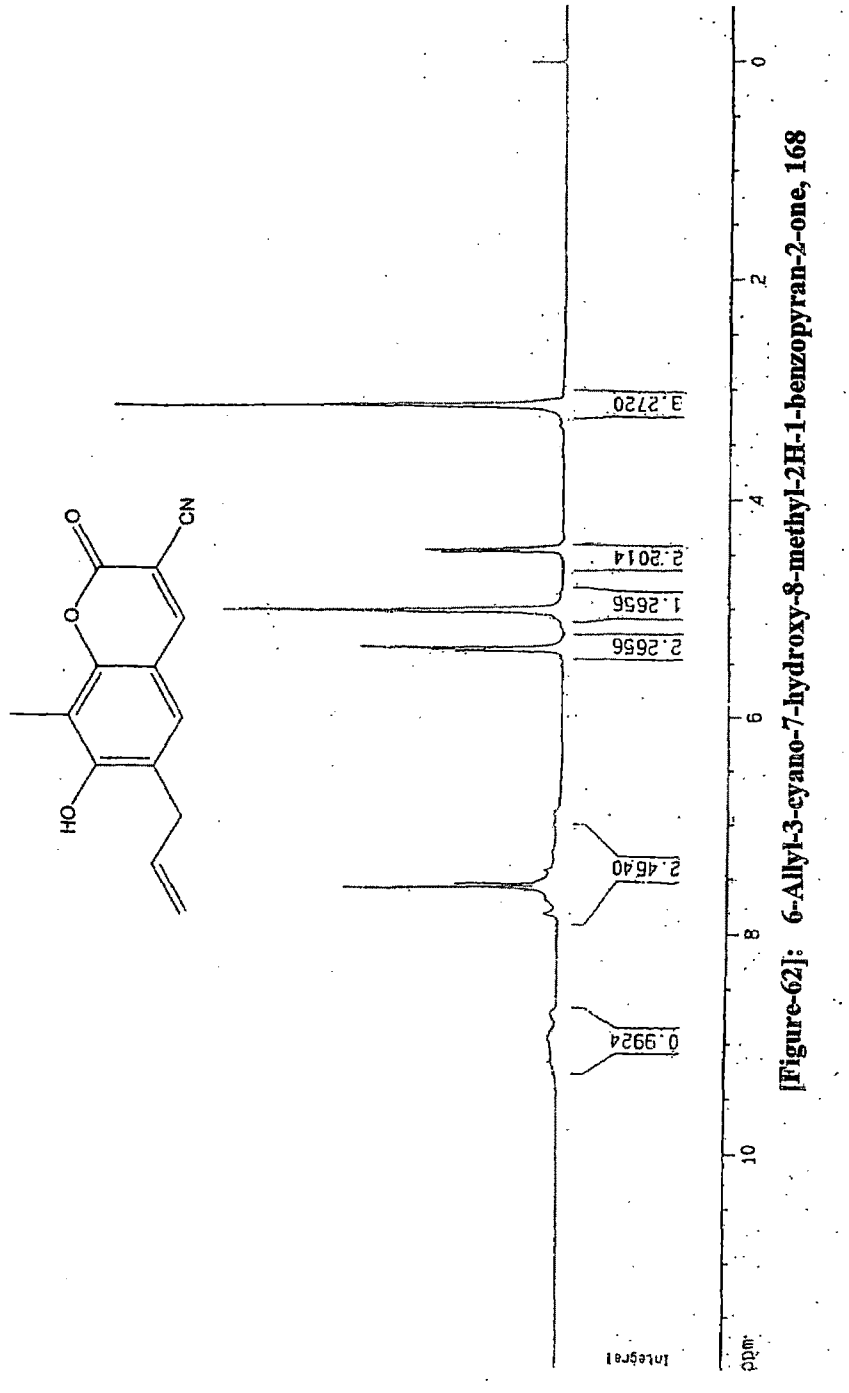
%C,H,N analysis (calculated) : C : 69.71 H : 4.56 N : 5.80

%C,H,N analysis (found) : C : 70.01 H : 4.78 N : 4.88

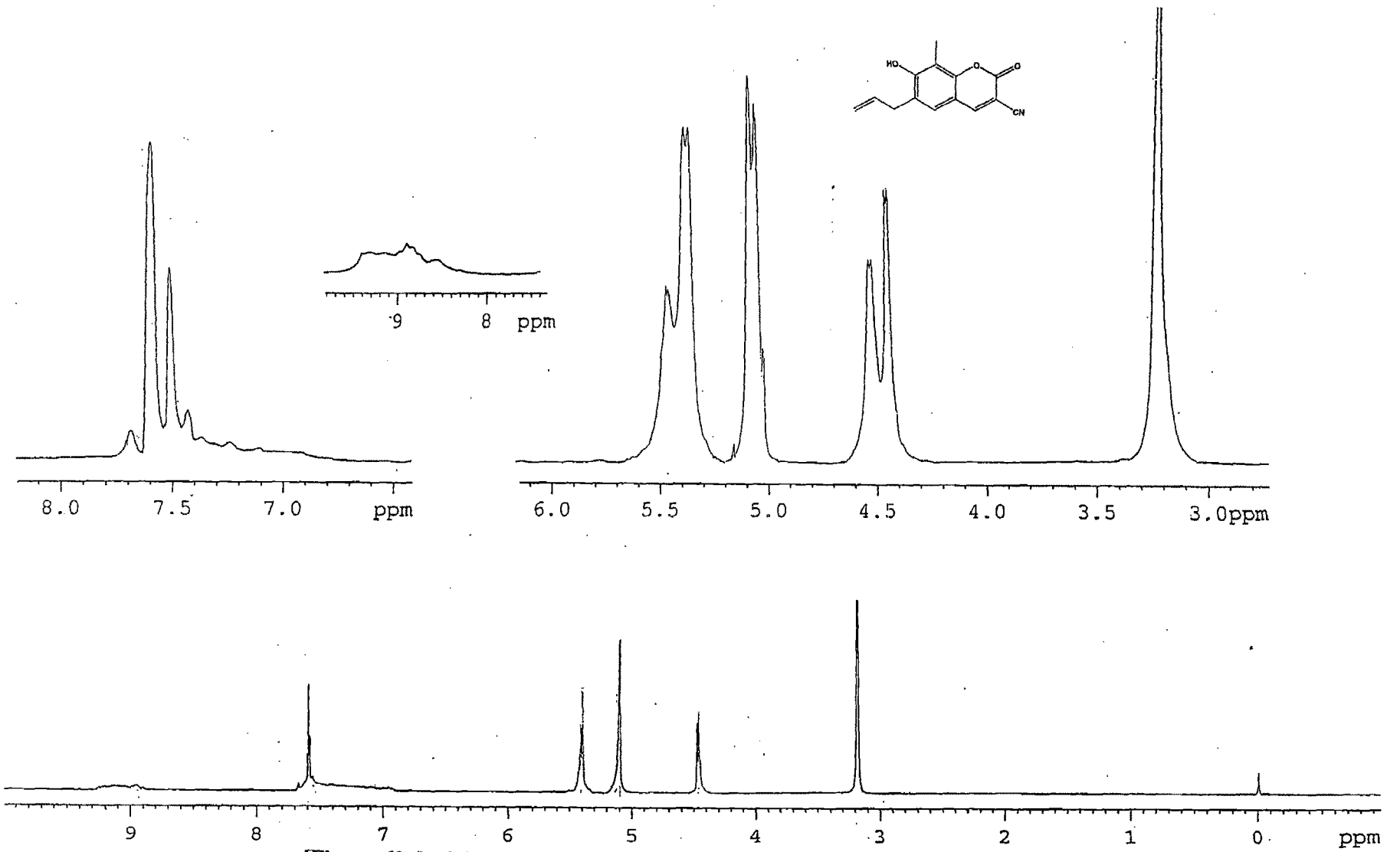
PMR data (400MHz, $CDCl_3$) δ ppm : 3.26(s, 3H, Ar-C<u>H</u>$_3$), 4.40-4.46(m, 2H, Ar-C<u>H</u>$_2$), 5.16(m, 1H, -C<u>H</u>=CH$_2$ olefinic), 5.30-5.61(m, 2H, C<u>H</u>$_2$=CH, olefinic protons), 7.48(s, 1H, C-4), 7.62(s, 1H, C-5), 8.80-9.30(br signal, phenolic –OH).



[Figure-61]: 6-Allyl-3-cyano-7-hydroxy-8-methyl-2H-1-benzopyran-2-one, 168

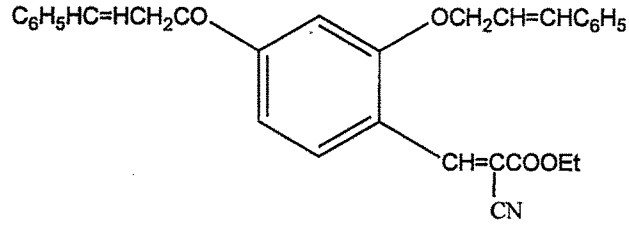


[Figure-62]: 6-Allyl-3-cyano-7-hydroxy-8-methyl-2H-1-benzopyran-2-one, 168



[Figure-62a]: 6-Allyl-3-cyano-7-hydroxy-8-methyl-2H-1-benzopyran-2-one, 168

Ethyl 2,4-dicinnamyloxy-α-cyanocinnamate, **169:**



State : yellow solid

Molecular Formula : $C_{30}H_{27}O_4N$

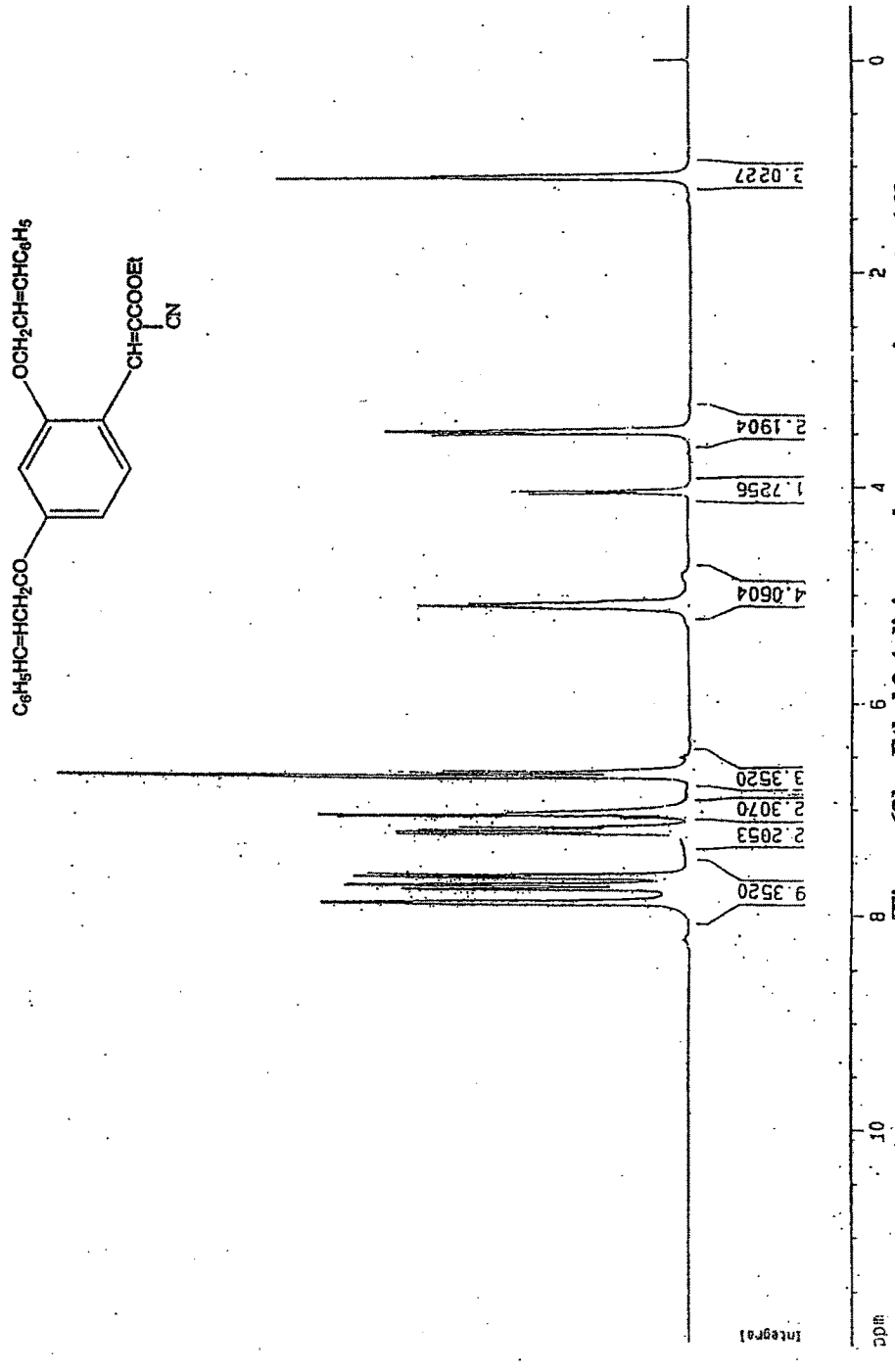
Melting Point : 128-131°C

% Yield : 30

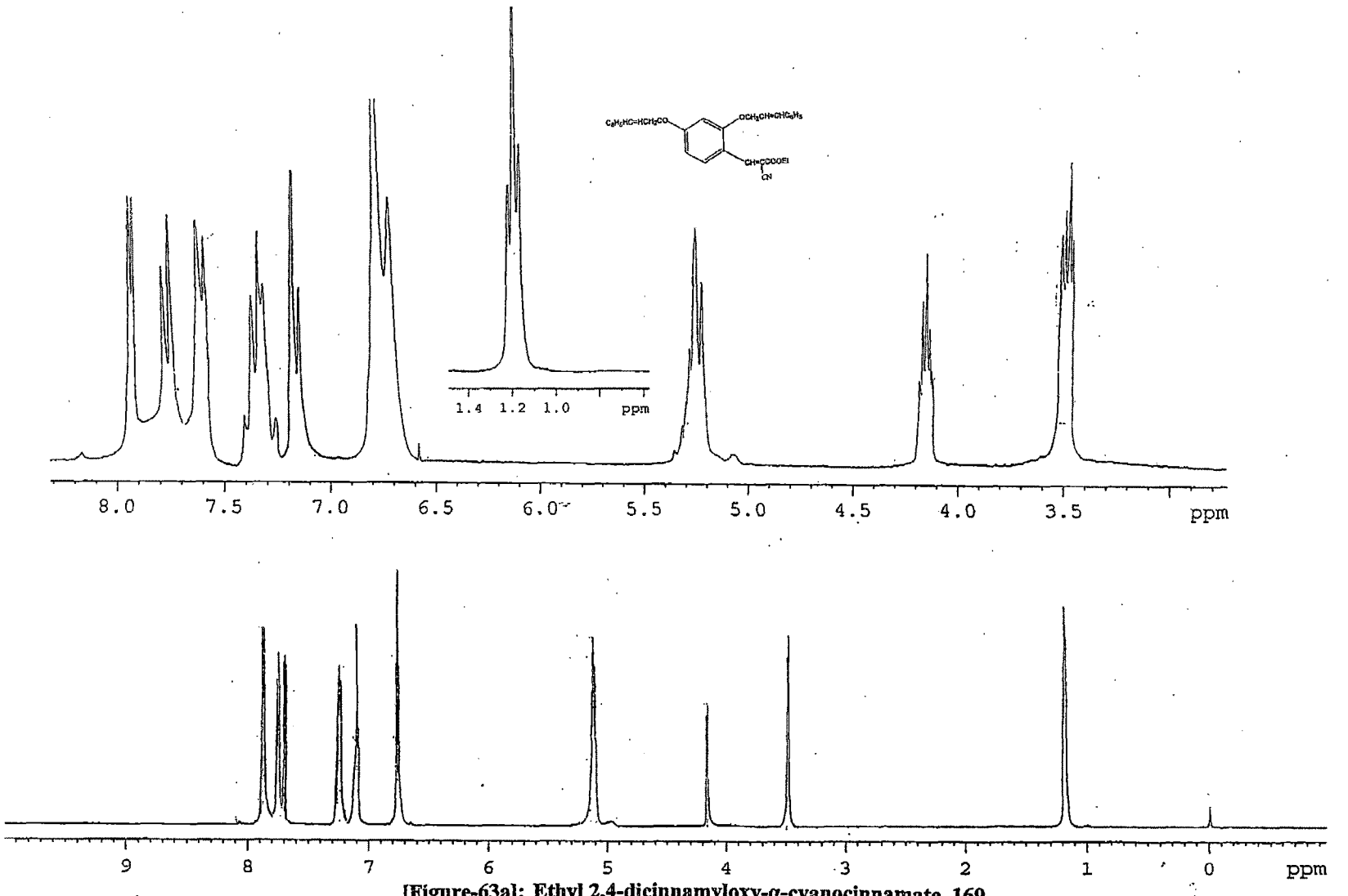
%C,H,N analysis (calculated) : C : 77.42 H : 5.80 N : 3.01

%C,H,N analysis (found) : C : 77.19 H : 5.68 N : 3.31

PMR data (400MHz, $CDCl_3$) δ ppm : 1.20 (t, 3H, -CH_2CH_3), 3.50(m, 2H, -OCH_2), 4.20(q, 2H, -CH_2CH_3), 5.25(m, 4H, olefinic protons), 6.75(m, 3H, 3xArCH=C-), 7.18-7.98(m, 13H, aromatic protons).

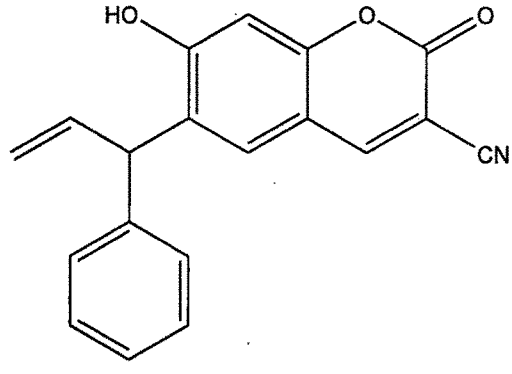


[Figure-63]: Ethyl 2,4-dicinnamyloxy-α-cyanocinnamate, 169



[Figure-63a]: Ethyl 2,4-dicinnamyloxy-α-cyanocinnamate, 169

3-Cyano-7-hydroxy-6-(1-phenylprop-2-enyl)-2H-1-benzopyran-2-one, **170:**



State : orange yellow solid

Molecular Formula : $C_{19}H_{13}O_3N$

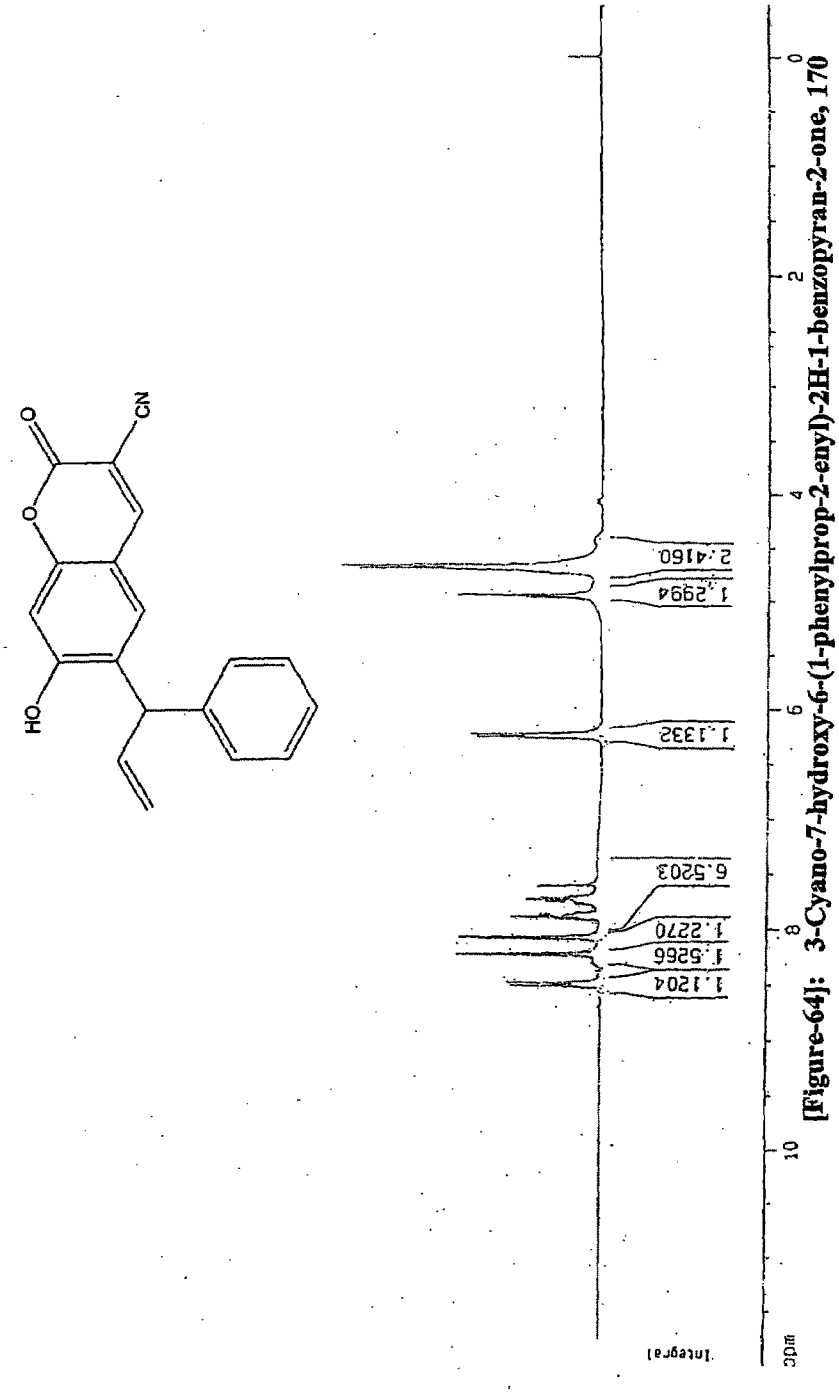
Melting Point : 219-221°C

% Yield : 40

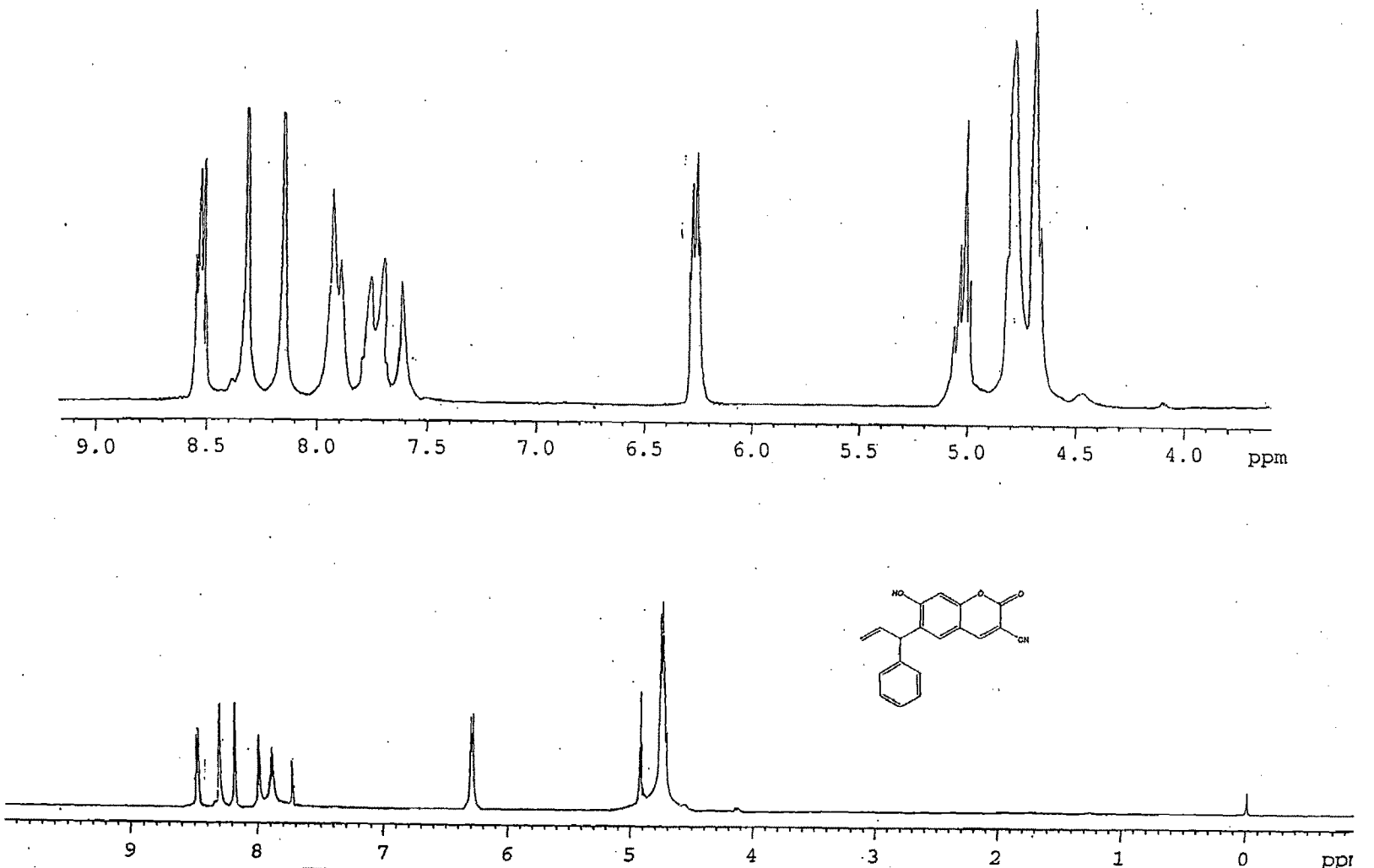
%C,H,N analysis (calculated) : C : 75.24 H : 4.29 N : 4.62

%C,H,N analysis (found) : C : 75.01 H : 4.10 N : 4.81

PMR data (400MHz, $CDCl_3$) δ ppm : 4.65(m, 1H, -C<u>H</u>=CH_2 olefinc proton), 4.77(m, 1H, Ar-C<u>H</u>-Ar), 5.03(m, 1H, $C\underline{H_2}$=CH- olefinic proton), 6.25(m, 1H, $C\underline{H_2}$=CH, olefinic proton), 7.62(s, 1H, C-4), 7.70-7.92(m, 5H, aromatic and –OH proton), 8.15(s, 1H, C-5), 8.31(s, 1H, C-9), 8.55(m, 1H, aromatic proton).



[Figure-64]: 3-Cyano-7-hydroxy-6-(1-phenylprop-2-enyl)-2H-1-benzopyran-2-one, 170



[Figure-64a]: 3-Cyano-7-hydroxy-6-(1-phenylprop-2-enyl)-2H-1-benzopyran-2-one, 170

CHAPTER-IV

Section-3

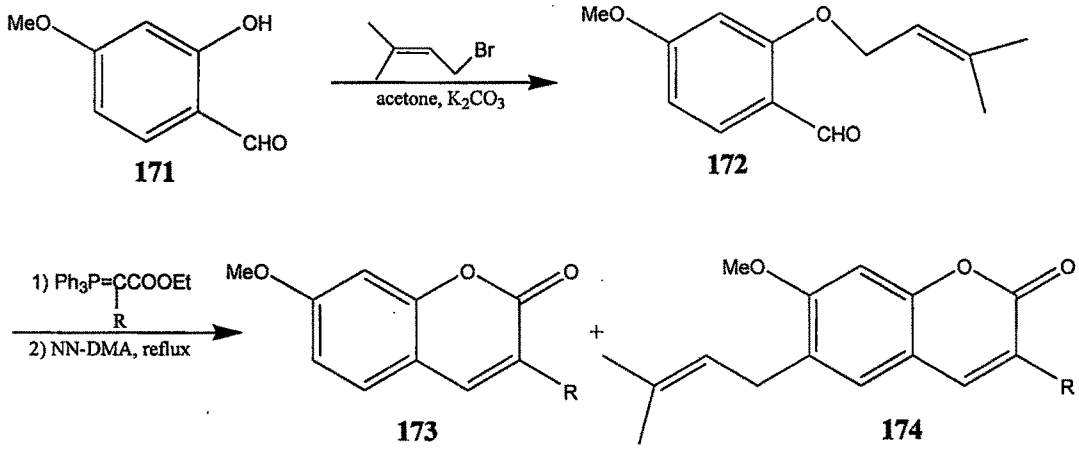
Claisen rearrangement and Wittig reactions of Prenylated benzopyran-2H-ones

Section:3 Claisen rearrangement and Wittig reaction of prenylated 2H-1-benzopyran-2-ones

IV.7 Introduction

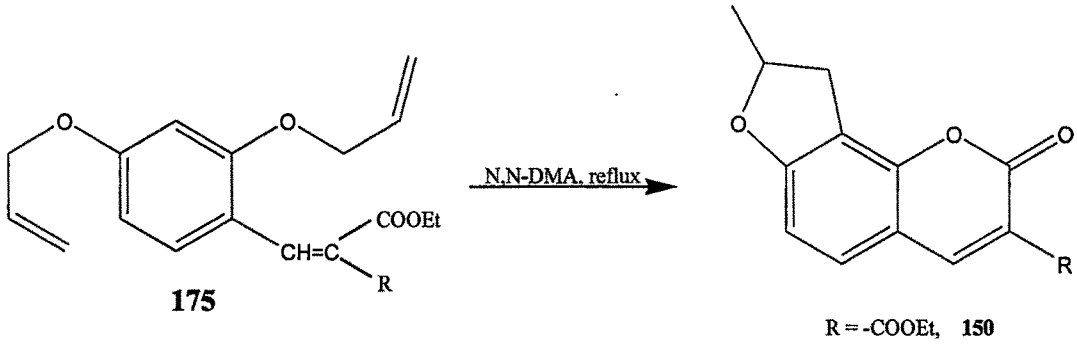
Claisen and Wittig strategies have been employed extensively for the preparations of 2H-1-benzopyan-2-ones.

Mali *et al*[10] reported the synthesis of 7-methoxy-3-prenyloxybenzopyran-2H-one **173** and 7-methoxy-6-prenyloxybenzopyran-2H-one **174** utilizing combination of Claisen rearrangement and Wittig reaction. They also synthesized related compounds by treating prenyloxybenzaldehyde with different phosphoranes in DMA under nitrogen atmosphere (Scheme-18).



Scheme-18

A facile one step synthesis of angularly furofused benzopyrones has been reported[1] in which diallyloxy cinnamate **175** containing electron withdrawing group at α-position was subjected to Claisen rearrangement in DMA (Scheme-19). It was reported that ethyl 2,4-diallyloxy cinnamates produce furobenzopyrones derivatives in a single step if the cinnamyl chain contains electron withdrawing group at α-position.



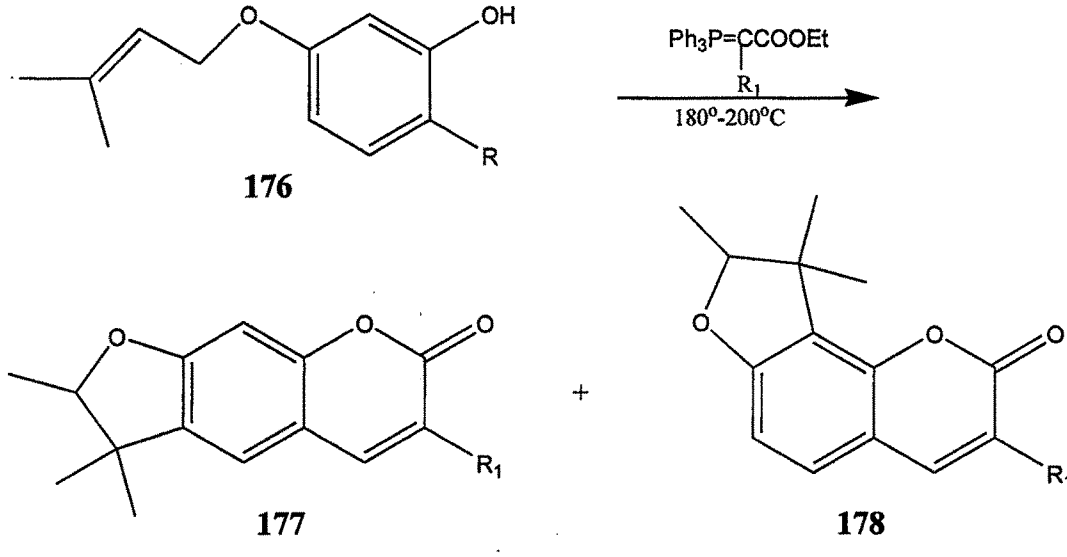
175

R = -COOEt, **150**

R = -$COCH_3$, **154**

Scheme-19

Wittig method was utilized to synthesize naturally occurring furobenzopyrones conveniently in a single step and reasonably good yields by Sandhu and Mali[11]. 2-Hydroxy-4-prenyloxy benzaldehydes **176** when treated with ethyl 2-substituted phosphorane carboxylate at 180°C-200°C for 24 hours, gave angular dihydrofurobenzopyrones **178** along with little linear furobenzopyrones **177** (Scheme-20).



176

177

178

R= CHO, $COCH_3$

R_1 = H, CH_3

Scheme-20

IV.8 Results and Discussion:

For the present work, in view of understanding Claisen and Wittig reactions, prenylated 2,4-dihydroxy benzaldehyde was subjected to Wittig reaction followed by Claisen rearrangement in N,N-dimethyl aniline.

Resorcylaldehyde **54** was condensed initially with prenylbromide and the subsequent monoprenylated compound **179** as well as diprenylated compound **180** were, then, subjected to Wittig reaction with carboethoxy methylene triphenyl phosphorane in THF affording ethyl-2-hydroxy-4--(1,1-dimethylprop-2-enyloxy)cinnamate **181** and ethyl 2,4-di(1,1-dimethylprop-2-enyloxy)cinnamate, **182** both as E / Z mixtures. In refluxing N,N-dimethylaniline, this mixture underwent Claisen rearrangement giving an unidentified liquid compound and one alkali insoluble liquid compound **183** (Scheme-21). The compound **183** showed an IR band at 1730 cm^{-1} indicating lactone ring formation.

PMR spectrum of compound **179** exhibited a singlet at δ 1.05 for six protons of two methyl groups of prenyl chain, a multiplet at δ 3.90 for an olefinic -C<u>H</u>=CH_2 protons, a multiplet at δ 4.92-5.10 for two olefinic -CH=C<u>H_2</u> protons, a doublet at δ 7.10 (J=8.3 Hz) for a C-6 proton, a doublet at δ 7.20 (J=8.3 Hz) for a C-5 proton, a singlet at δ 7.30 for a C-3 proton and finally a singlet at δ11.30 for aldehyde proton [Figure-64].

Low melting compound **179** when treated with ethyl carboethoxy methylene triphenyl phosphorane in dry THF, gave only ethyl-2-hydroxy-4--(1,1-dimethylprop-2-enyloxy)cinnamate **181**. On further prenylation with prenyl bromide, compound **181** yielded desired ethyl 2,4-di(1,1-dimethylprop-2-enyloxy)cinnamate, **182**.

Compound **182** was also obtained directly by condensing **180** with phosphorane in dry THF. The comparison of the products was done by elemental analysis and IR spectrum superposition [Figure-69].

PMR spectrum compound **180** exhibited a singlet at 1.34-1.38 for twelve protons of four methyl groups of prenyl chain, two multiplets at 4.95 and 5.21 for two –C<u>H</u>=CH_2 protons, a multiplet at δ 5.52 for two olefinic -CH=C<u>H_2</u> protons, another multiplet at δ 5.70 for two olefinic -CH=C<u>H_2</u> protons, a doublet at δ 7.41 (J=8.2 Hz) for C-5 and C-6

protons, a singlet at δ 7.80 for a C-3 proton and finally a singlet at δ10.50 for aldehyde proton [Figure-65].

PMR spectrum of compound **181** exhibited a triplet at δ 1.16 for three protons of methyl group of $-OCH_2C\underline{H}_3$, two singlets one at δ 1.50 and another at δ 1.78 for six protons of two methyl groups of prenyl chain, a quartet at δ 4.73 for two methylene protons of $-OC\underline{H}_2CH_3$ group, a multiplet at δ 4.95-5.12 for three olefinic protons, a multiplet at δ 5.52 for an olefinic $-C\underline{H}=CH_2$ proton, a doublet at δ 6.66 (J=7.5 Hz) for Ar-$C\underline{H}$=C- proton, a doublet at δ 7.12 (J=8.3 Hz) for a C-3 proton, a doublet at δ 7.20 (J=8.3 Hz) for a C-4 proton and finally a singlet at δ 7.29 for a C-6 proton [Figure-66].

PMR spectrum of compound **182** exhibited a singlet at δ 1.31-1.38 for twelve protons of four methyl groups of prenyl chain, a triplet at δ 1.40 for three protons of methyl group of $-OCH_2C\underline{H}_3$, a quartet at δ 4.40 for two methylene protons of $-OC\underline{H}_2CH_3$ group, a doublet at δ 4.89 (J=9.1 Hz) for a =C$\underline{H}$COOEt proton, a multiplet at δ 5.03 for an olefinic-$C\underline{H}=CH_2$ proton, a multiplet at δ 5.34-5.42 for four olefinic $-CH=C\underline{H}_2$ protons, a multiplet at δ 5.52 for an olefinic-$C\underline{H}=CH_2$ proton, a doublet at δ 6.36 (J=3.8 Hz) for Ar-$C\underline{H}$=C- proton, a doublet at δ 7.66 (J=8.4 Hz) for a C-5 proton, a doublet at δ 7.71 (J=8.4 Hz) for a C-6 proton and finally a singlet at δ 7.50 for a C-3 proton [Figure-68].

PMR spectrum of compound **183** exhibited a singlet at δ 1.16 for six protons of two methyl groups on the ring, two singlets one at δ 1.50 and another at δ 1.58 for six protons of two methyl groups on alkene chain, a triplet at δ 1.74 for two Ar-CH_2-$C\underline{H}_2$-$C(CH_3)_2$- protons, a triplet at δ 3.00 for two Ar-$C\underline{H}_2$-CH_2-$C(CH_3)_2$- protons, a multiplet at δ 5.16-5.50 for three olefinic protons, a doublet at δ 6.80 (J=7.5 Hz) for a C-3 proton, a singlet at δ 7.29 for a C-5 proton and finally a doublet at δ 7.41 (J=7.5 Hz) for a C-4 proton [Figure-71].

Diprenyloxy derivative **180** on Knoevenegal condensation with ethyl cyano acetate in the presence of pyridine and catalytic amount of piperidine afforded an unexpected alkali insoluble product **184** (Scheme-22).

PMR spectrum of compound **184** exhibited a singlet at δ 1.10-1.16 for six protons of two methyl groups of prenyl chain, a multiplet at δ 4.20 for an olefinic -C<u>H</u>=CH_2 proton, a multiplet at δ 4.93 for an olefinic -CH=C<u>H_2</u>, proton, a multiplet at δ 5.21 for another olefinic -CH=C<u>H_2</u> proton, a doublet at δ 7.14 (J=8.4Hz) for a C-5 proton, a singlet at δ 7.25 (J=8.4Hz) for a C-4 proton, a doublet at δ 7.38 (J=8.4Hz) for a C-6 proton and finally a singlet at δ 7.47 for a C-8 proton [Figure-64].

Formation of compound **184** suggests that during Knovaenegal condensation the prenyl group at C-2 in **180** got knocked off to facilitate the formation of pyrone ring.

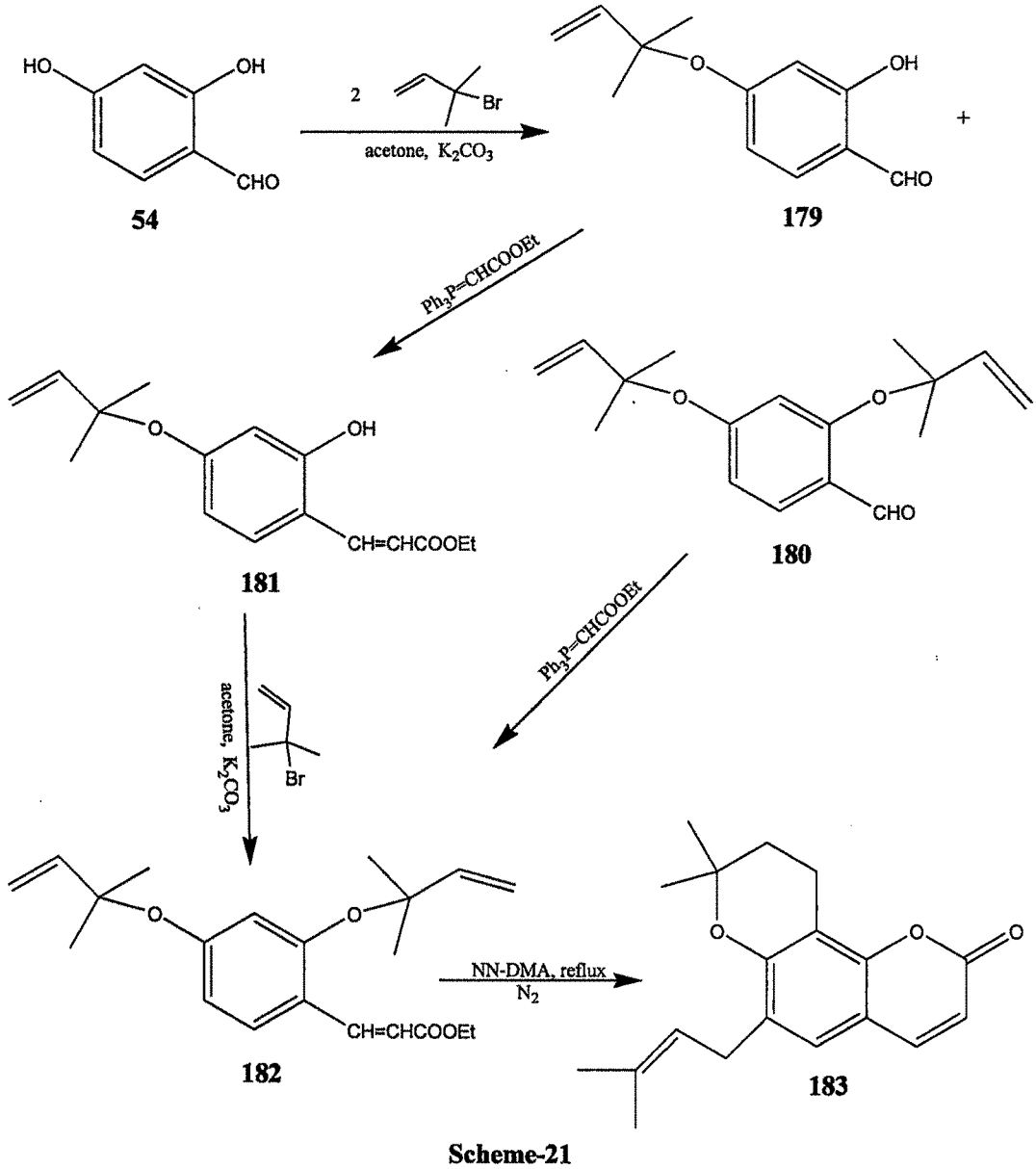
IV.9 Experimental:

Synthesis of 2-hydroxy-4-(1,1-dimethylprop-2enyloxy)benzaldehyde, 179 and 2,4-di(1,1-dimethylprop-2enyloxy)benzaldehyde, 180

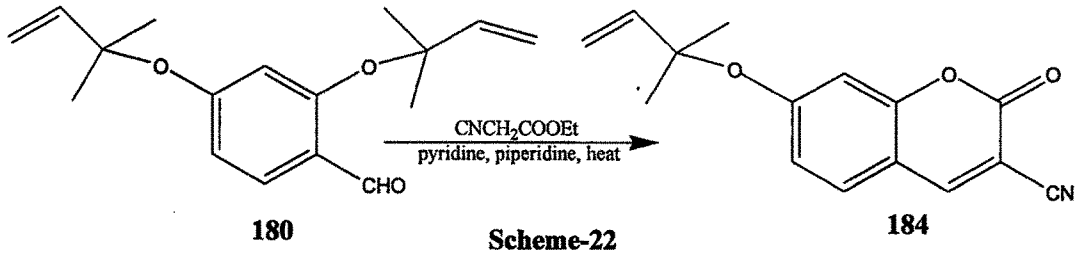
2,4-Dihydroxybenzaldehyde **54** (7.0g, 0.047mol) was refluxed with prenyl bromide (14.6ml, 0.098mol) in presence of anhydrous K_2CO_3 (10g, 0.072mol) in dry acetone (180ml) for 8 hours. Monitoring with TLC showed two spots. Acetone was distilled off and the residue was subjected to column chromatography using pet.ether(40-60) as eluent. First five fractions of eluent(500ml) afforded a liquid compound **180** which was dried over anhydrous sodium sulphate. Then elution with 10% toluene-pet.ether mixture afforded compound **179** which was recrystallised by ethanol.

Synthesis of ethyl-2-hydroxy-4--(1,1-dimethylprop-2-enyloxy)cinnamate,181

2-Hydroxy-4-prenyloxy benzaldehyde **179**(5.0g, 0.024mol) was refluxed in dry tetrahydrofuran (80ml) with carboethoxy methylene triphenyl phosphorane(8.5g, 0.024mol) under atmosphere of nitrogen for 8 hours. Completion of reaction was checked by TLC. Tetrahydrofuran was distilled off and residue was dried and subjected to column chromatography using 1% toluene-pet.ether eluent followed by drying of liquid product with sodium sulphate and purification by distillation.



Scheme-21



Scheme-22

Synthesis of ethyl 2,4-di(1,1-dimethylprop-2-enyloxy)cinnamate, 182

2,4-Diprenyloxy benzaldehyde **180**(2.5g, 0.0092mol) was refluxed in dry tetrahydrofuran (80ml) with carboethoxy methylene triphenyl phosphorane(3.2g, 0.0092mol) under atmosphere of nitrogen for 8 hours. Tetrahydrofuran was distilled off and residue was dried and subjected to column chromatography using 10% toluene-pet.ether mixture as eluent followed by drying of liquid product with sodium sulphate and purification by distillation.

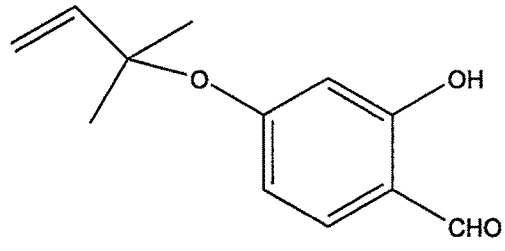
Synthesis of 6-(3-methylbutan-2-enyl)-8,8-dimethyl-9,10-dihydro-2H-pyrano[2,3-*h*]-1-benzopyran-2-one, 183

Ethyl 2,4-diprenyloxy-α-cinnamate, **182**(1.5g) was refluxed in dry N,N-dimethylaniline (18ml) under atmosphere of nitrogen for four hours. Mixture was poured in cold aqueous (1:1) HCl(100ml) and organic part was extracted with diethyl ether. Residue obtained, after evaporation of ether, was subjected to column chromatography using 30% benzene-petroleum ether(60-80) eluent affording a liquid compound **183** which was dried with sodium sulphate and purified by distillation.

Synthesis of 3-cyano-7-(1,1-dimethylprop-2-enyloxy)-2H-benzopyran-2-one 184

2,4-Diprenyloxybenzaldehyde **180** (4.1g, 0.015mol) was heated in water bath with ethyl cyano acetate(1.7ml, 0.015mol) in presence of catalytic amount of piperidine(0.2ml) and solvent pyridine(8ml) for 30 hours. The reaction mixture was poured in cold aqueous (1:1) HCl(50ml). Separated solid was dried and subjected to column chromatography using 50% toluene-pet.ether mixture as eluent. The solid thus obtained was recrystallized in ethanol.

2-Hydroxy-4-(1,1-dimethylprop-2-enyloxy)benzaldehyde, **179**



State : brownish solid

Molecular Formula : $C_{12}H_{14}O_3$

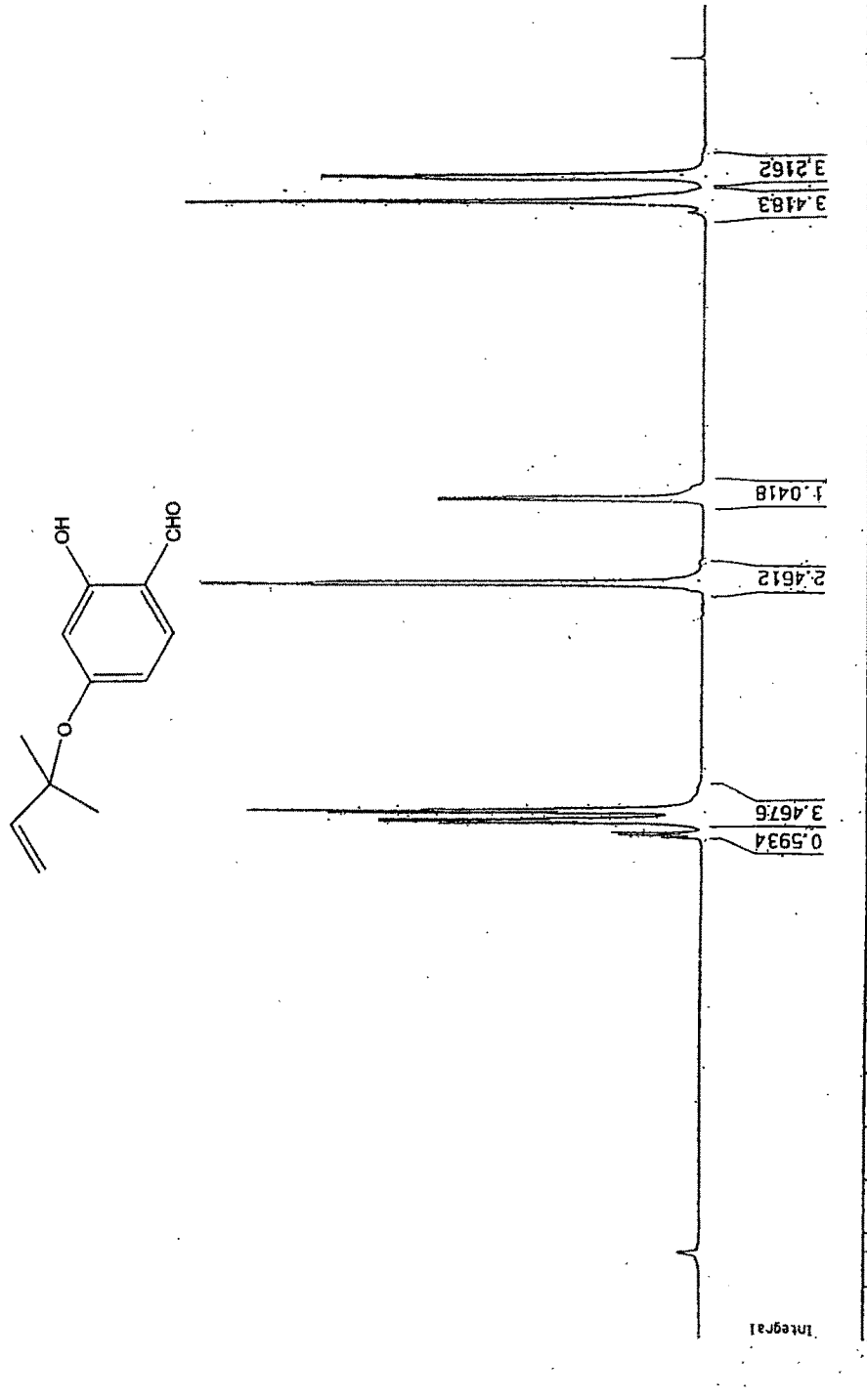
Melting Point : 65°C

% Yield : 50

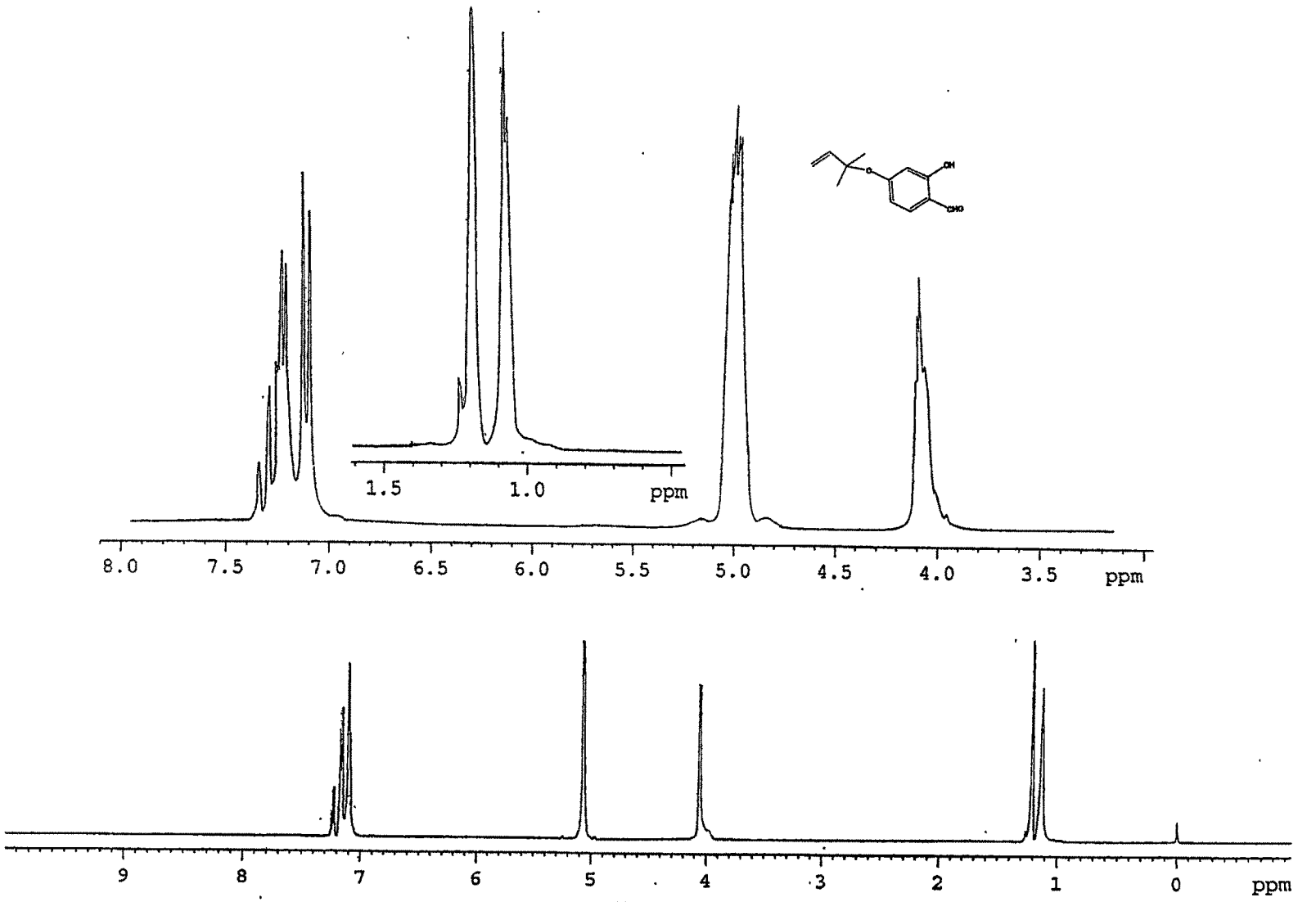
%C,H,N analysis (calculated) : C : 69.90 H : 6.79

%C,H,N analysis (found) : C : 69.90 H : 6.90

PMR data (400MHz, $CDCl_3$) δ ppm: 1.05—1.29(s, 6H, 2xC<u>H</u>3), 3.90-4.17(m, 1H, -C<u>H</u>=CH2 olefinic proton), 4.92-5.10(m, 2H, C<u>H</u>2=CH- olefinic proton), 7.10(d, J=8.3 Hz, 1H, C-6), 7.20(d, J=8.3 Hz, 1H, C-5), 7.30(s, 1H, C-3), 11.30(s, 1H, -C<u>H</u>O).

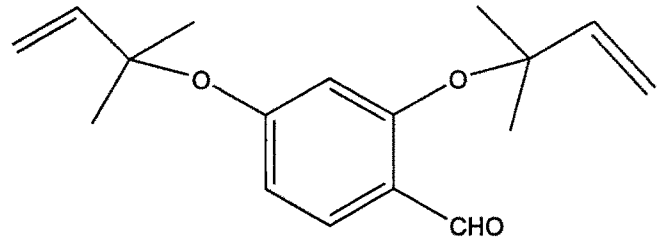


[Figure-65]: 2-Hydroxy-4-(1,1-dimethylprop-2enyloxy)benzaldehyde, 179



[Figure-65a]: 2-Hydroxy-4-(1,1-dimethylprop-2enyloxy)benzaldehyde, 179

2,4-Di(1,1-dimethylprop-2-enyloxy)benzaldehyde, **180**



State : liquid

Molecular Formula : $C_{17}H_{22}O_3$

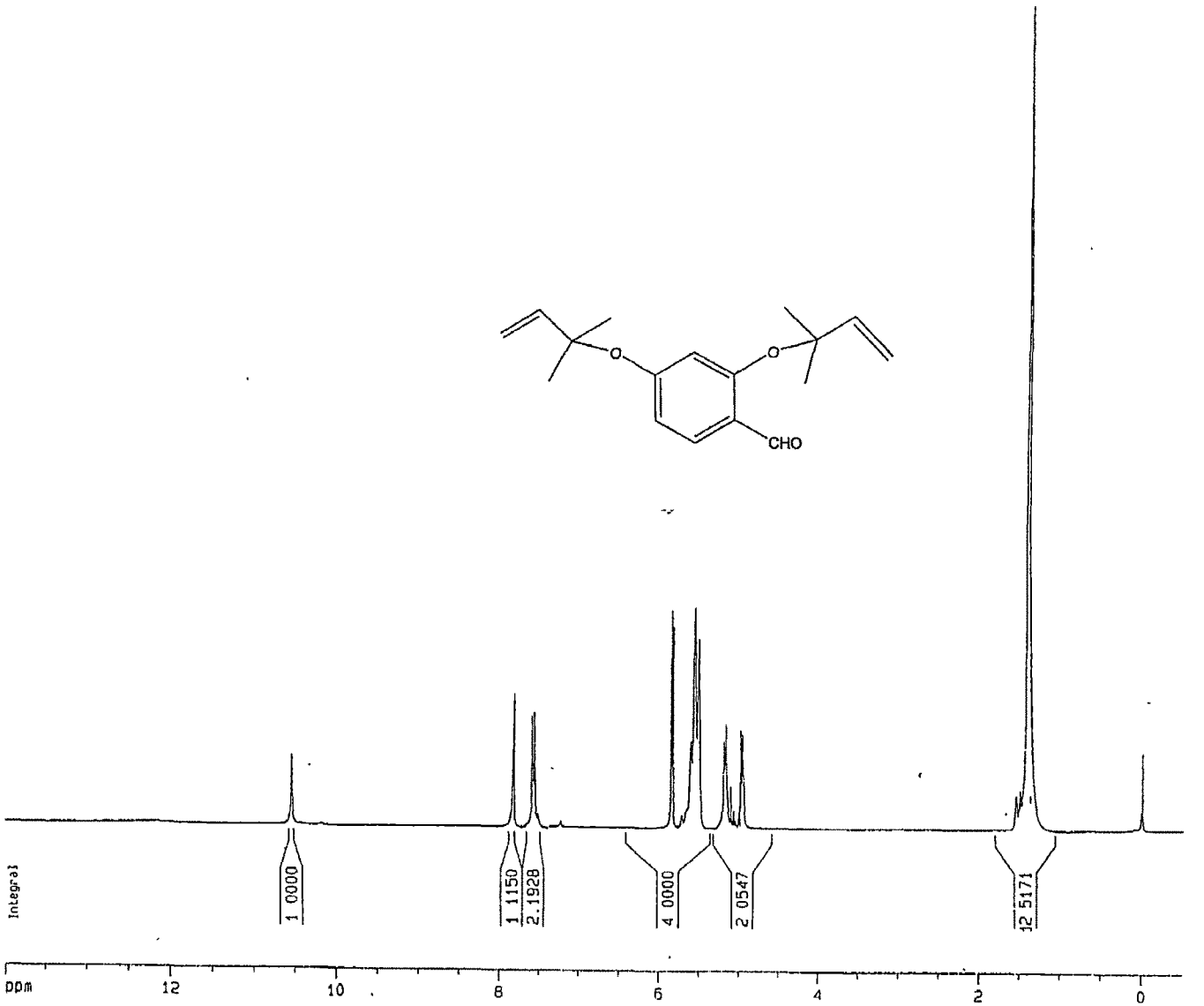
Boiling Point : 171°C

% Yield : 40

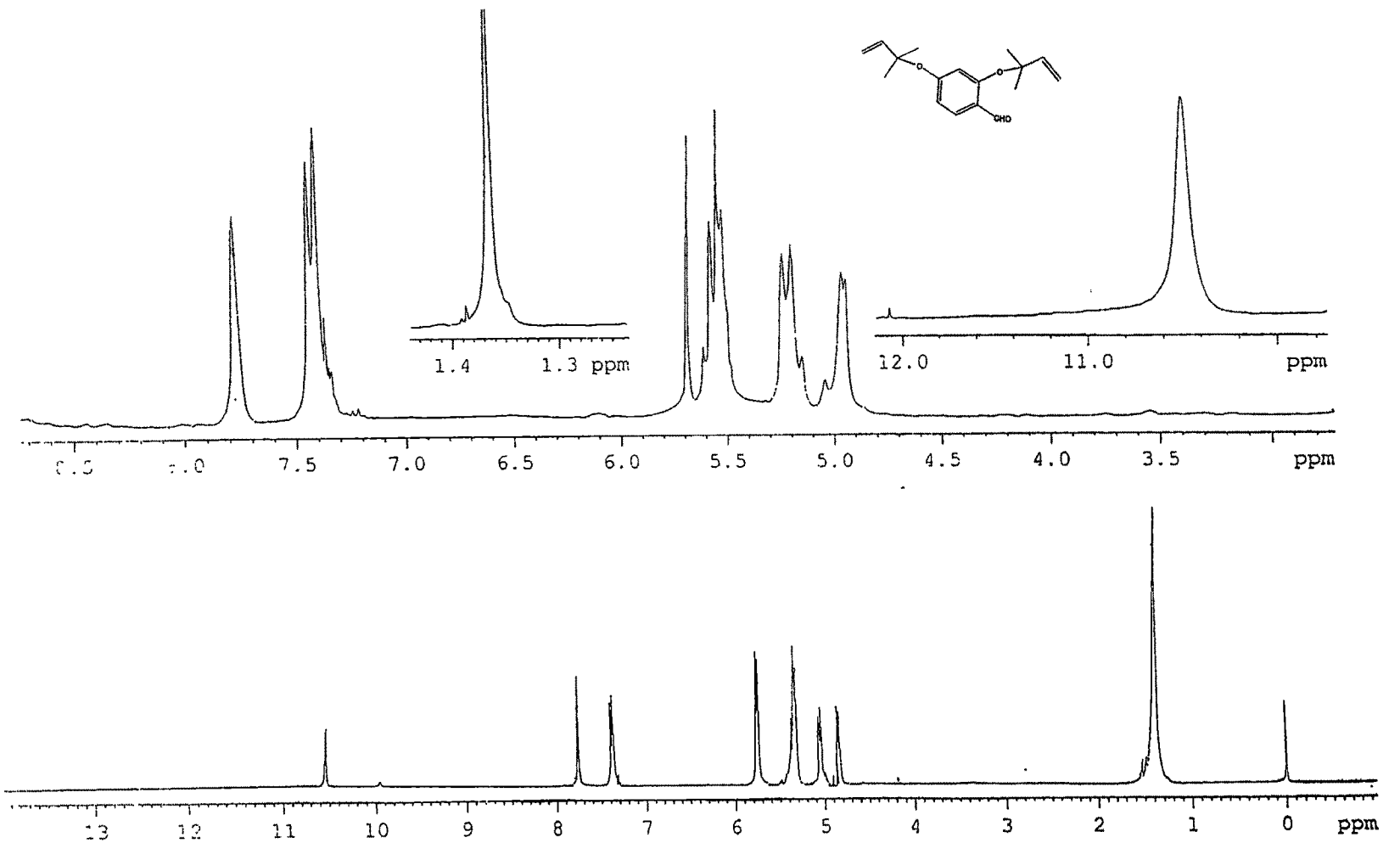
%C,H,N analysis (calculated) : C : 74.45 H : 8.03

%C,H,N analysis (found) : C : 74.00 H : 8.18

PMR data (400MHz, $CDCl_3$) δ ppm: 1.34-1.38(s, 12H, 4xC<u>H</u>3), 4.95(m, 1H, -C<u>H</u>=CH2 olefinic proton), 5.21(m, 1H, -C<u>H</u>=CH2 olefinic proton), 5.52(m, 2H, C<u>H</u>2=CH- olefinic proton), 5.70(m, 2H, C<u>H</u>2=CH- olefinic proton), 7.41(d, J=8.2 Hz, 2H, C-5 and C-6), 7.80(s, 1H, C-3), 10.50(s, 1H, -C<u>H</u>O).

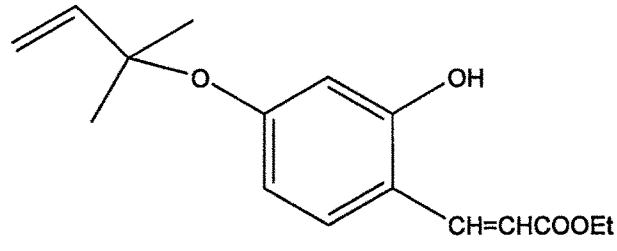


[Figure-66]: 2,4-Di(1,1-dimethylprop-2enyloxy)benzaldehyde, 180



[Figure-66a]: 2,4-Di(1,1-dimethylprop-2enyloxy)benzaldehyde, 180

Ethyl-2-hydroxy-4--(1,1-dimethylprop-2-enyloxy)cinnamate,**181**



State : liquid

Molecular Formula : $C_{16}H_{20}O_4$

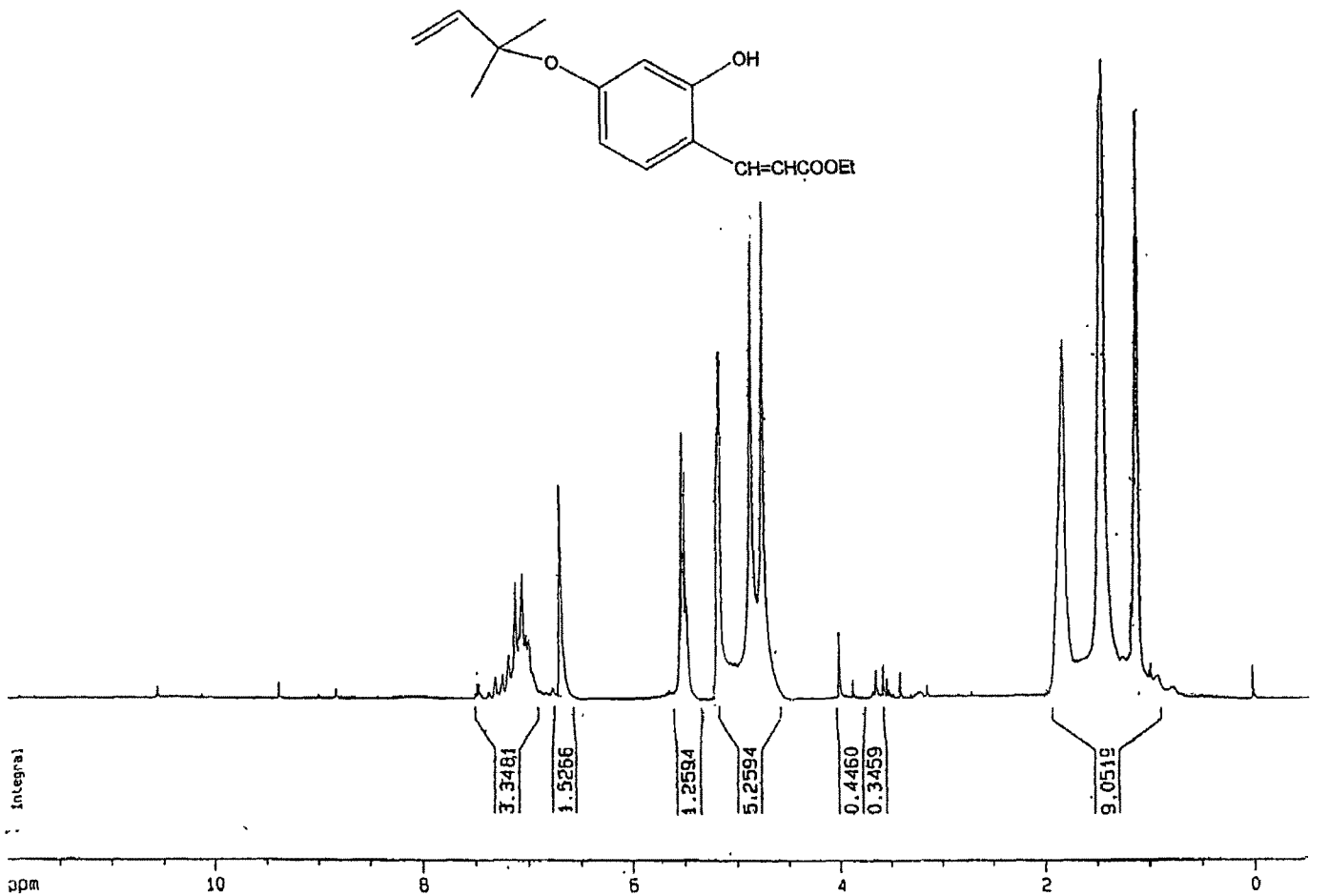
Boiling Point : 201-203°C

% Yield : 48

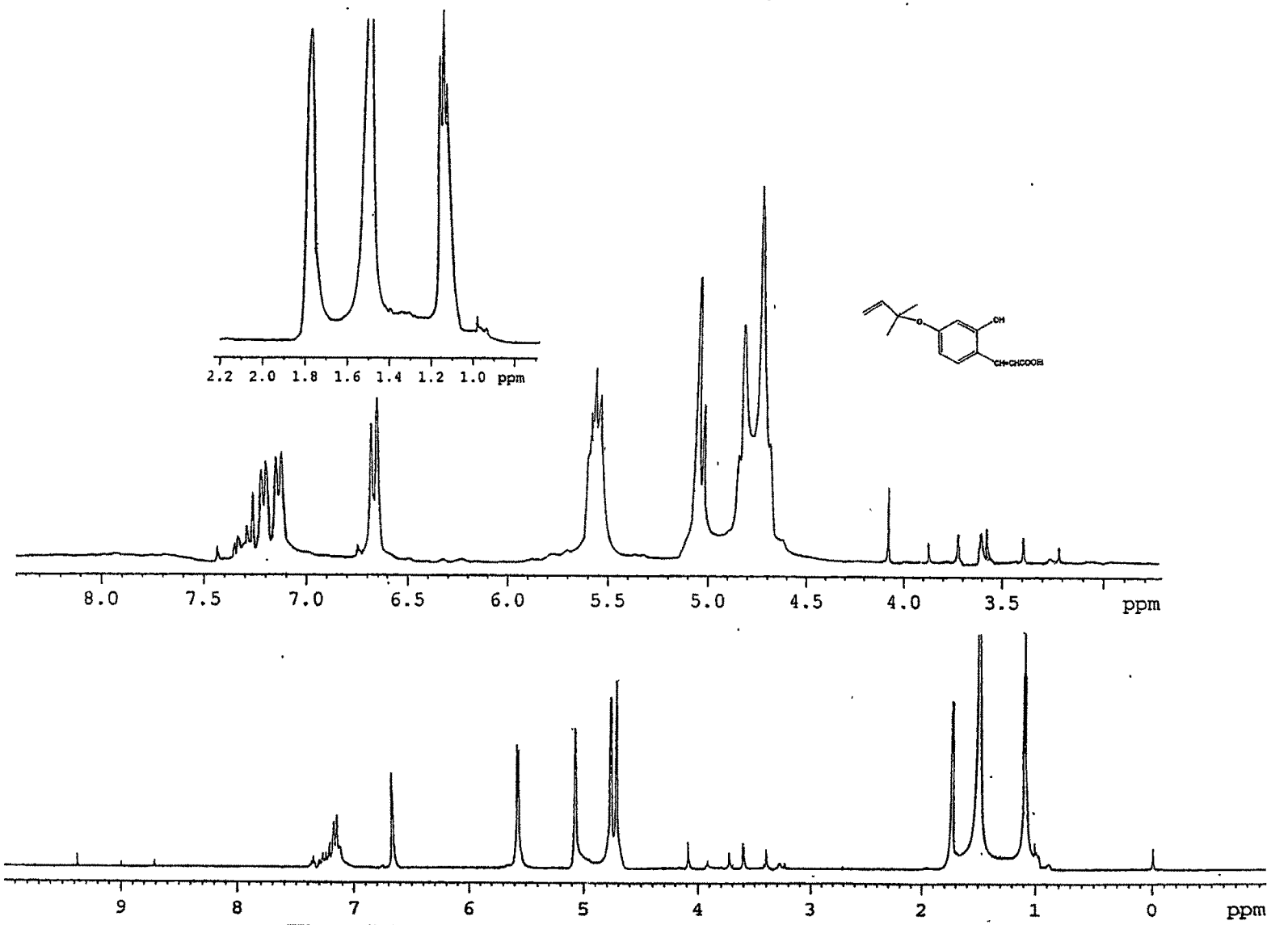
%C,H,N analysis (calculated) : C : 69.56 H : 7.24

%C,H,N analysis (found) : C : 70.00 H : 7.35

PMR data (400MHz, $CDCl_3$) δ ppm: 1.16(t, 3H, -CH2CH3), 1.50(s, 3H, -CH3), 1.78(s, 3H, -CH3), 4.73(q, 2H, -OCH2CH3), 4.95-5.12(m, 3H, olefinic protons), 5.52(m, 1H, -CH=CH2 olefinic proton), 6.66(d, J=7.5 Hz, 1H, ArCH=C-), 7.12(d, J=8.3 Hz, 1H, C-3), 7.20(d, J=8.3 Hz, 1H, C-4), 7.29(s, 1H, C-6).

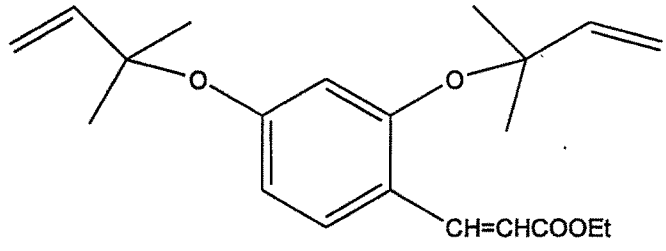


[Figure-67]: Ethyl-2-hydroxy-4--(1,1-dimethylprop-2-enyloxy)cinnamate,181



[Figure-67a]: Ethyl-2-hydroxy-4--(1,1-dimethylprop-2-enyloxy)cinnamate,181

Ethyl 2,4-di(1,1-dimethylprop-2-enyloxy)cinnamate, **182**



State : liquid

Molecular Formula : $C_{21}H_{28}O_4$

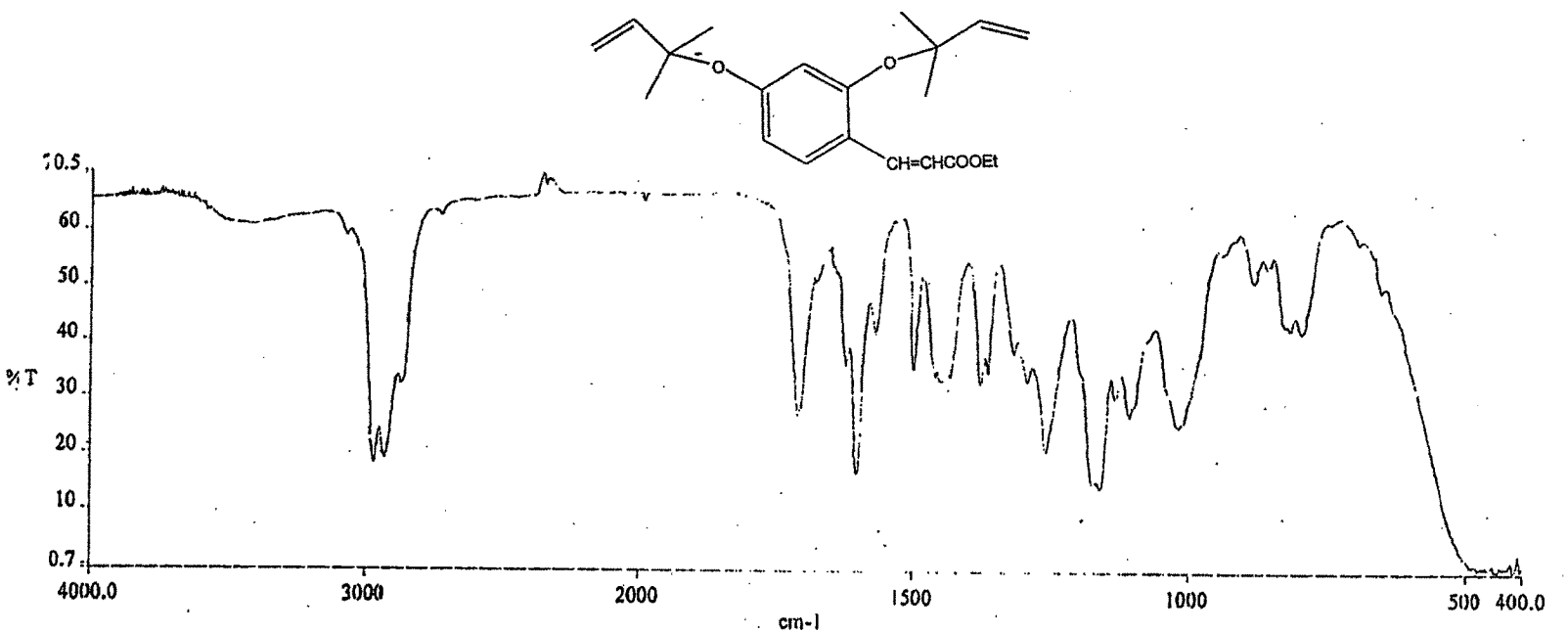
Boiling Point : 181-184°C

% Yield : 30

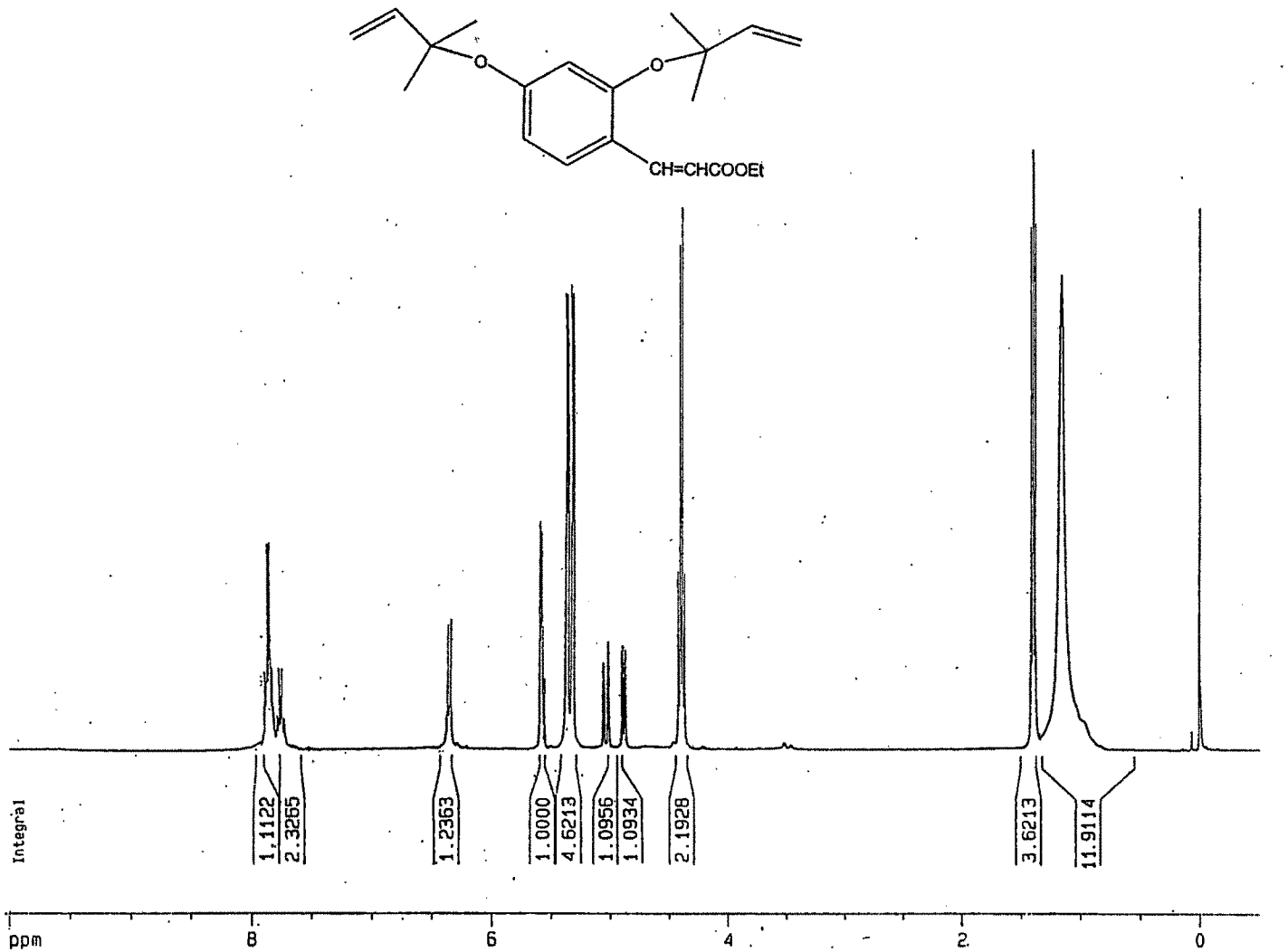
%C,H,N analysis (calculated) : C : 73.25 H : 8.14

%C,H,N analysis (found) : C : 73.11 H : 8.41

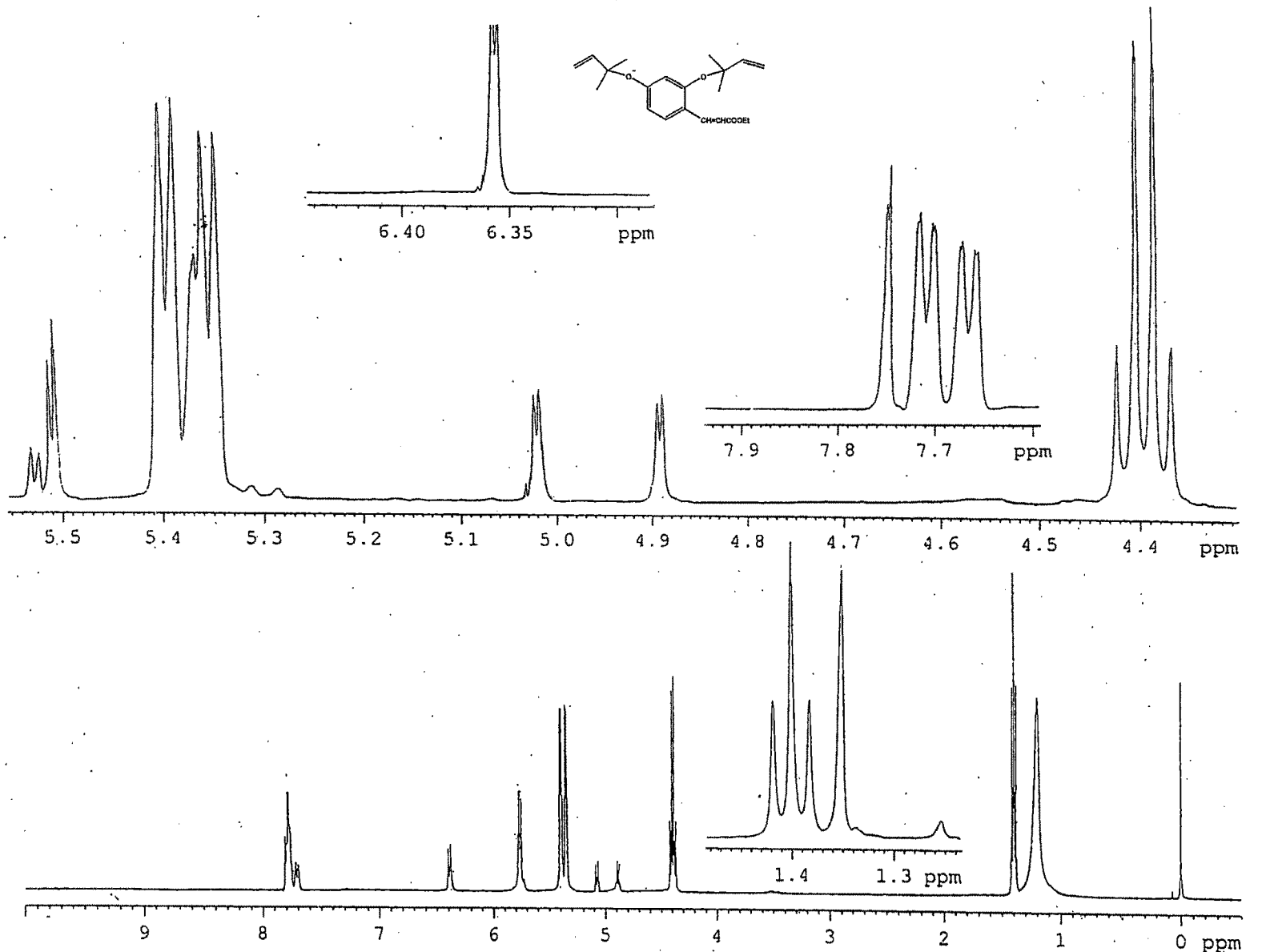
PMR data (400MHz, $CDCl_3$) δ ppm: 1.31-1.38(s, 12H, 4x-CH_3), 1.40(t, 3H, -$CH_2\underline{C}H_3$), 4.40(q, 2H, -$O\underline{C}H_2CH_3$), 4.89(d, J=9.1 Hz, 1H, =$C\underline{H}$COOEt), 5.03(m, 1H, -$C\underline{H}$=CH_2 olefinic proton), 5.34-5.42(m, 4H, $C\underline{H}_2$=CH- olefinic protons), 5.52(m, 1H, -$C\underline{H}$=CH_2 olefinc proton), 6.36(d, J=3.8 Hz, 1H, Ar$C\underline{H}$=C-), 7.66(d, J=8.4 Hz, 1H, C-5), 7.71(d, J=8.4 Hz, 1H, C-6), 7.50(s, 1H, C-3).



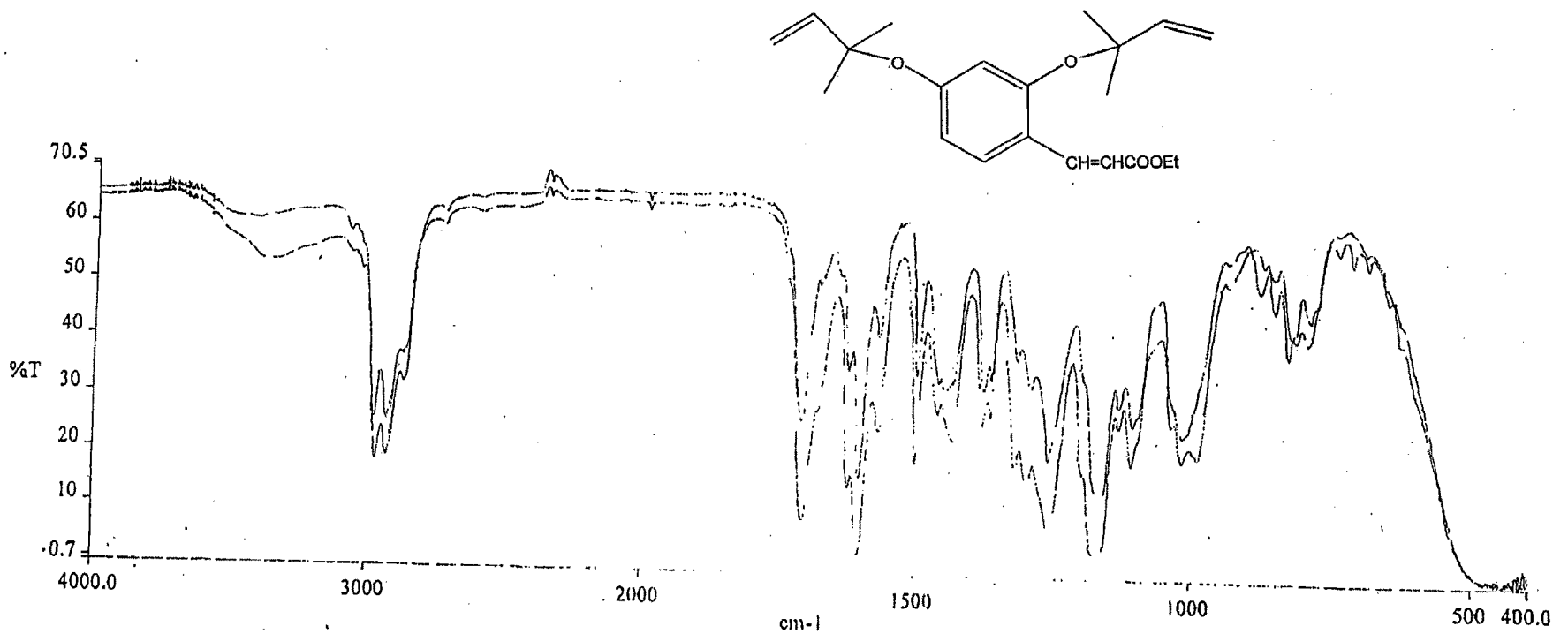
[Figure-68]: Ethyl 2,4-di(1,1-dimethylprop-2-enyloxy)cinnamate, 182



[Figure-69]: Ethyl 2,4-di(1,1-dimethylprop-2-enyloxy)cinnamate, 182

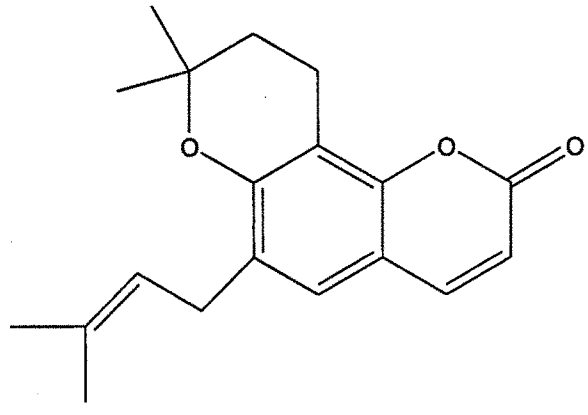


[Figure-69a]:Ethyl 2,4-di(1,1-dimethylprop-2-enyloxy)cinnamate, 182



[Figure-70]: Ethyl 2,4-di(1,1-dimethylprop-2-enyloxy)cinnamate, 182

6-(3-Methylbutan-2-enyl)-8,8-dimethyl-9,10-dihydro-2H-pyrano[2,3-*h*]-1-benzopyran-2-one, **183**



State : liquid

Molecular Formula : $C_{19}H_{22}O_3$

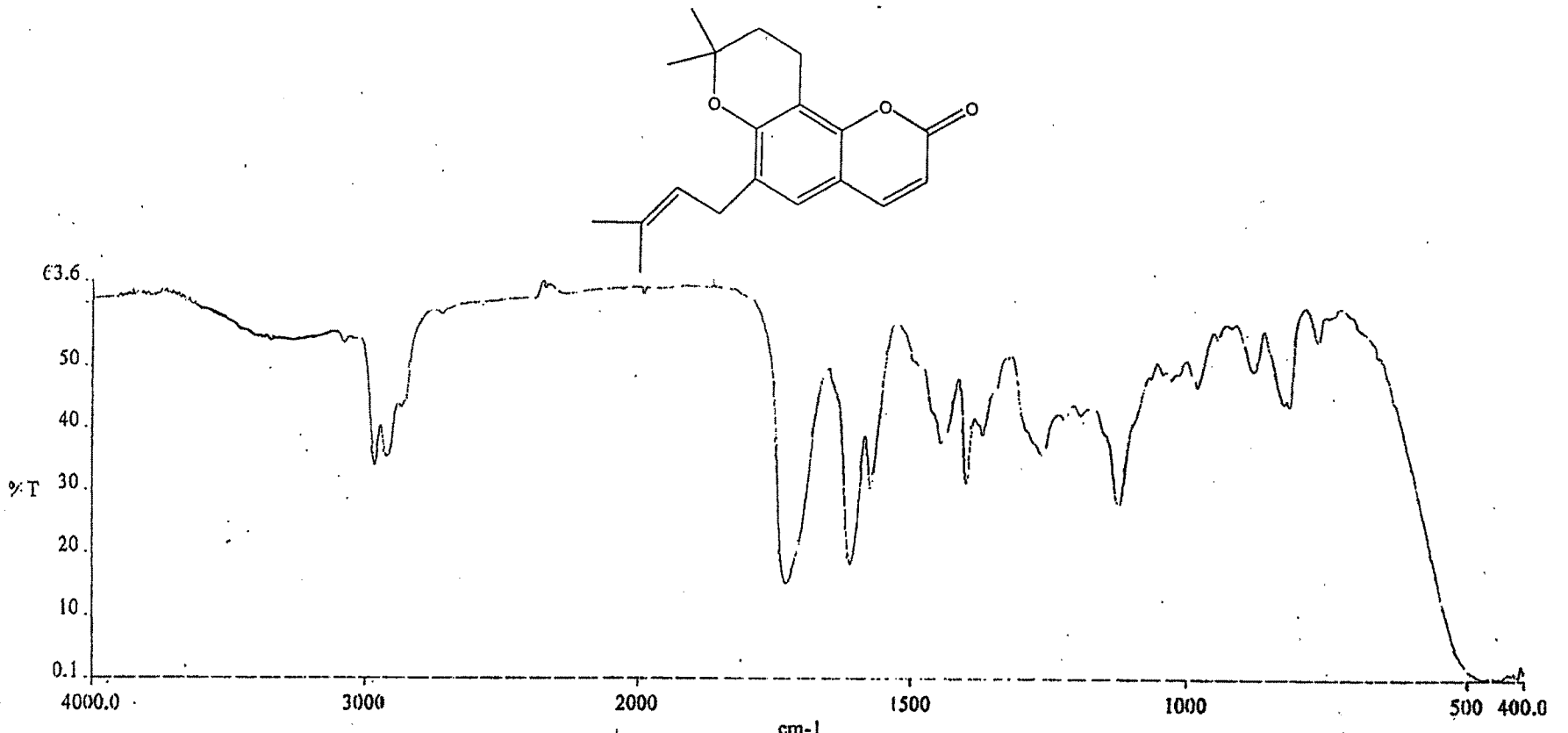
Boiling Point : 221°C

% Yield : 38

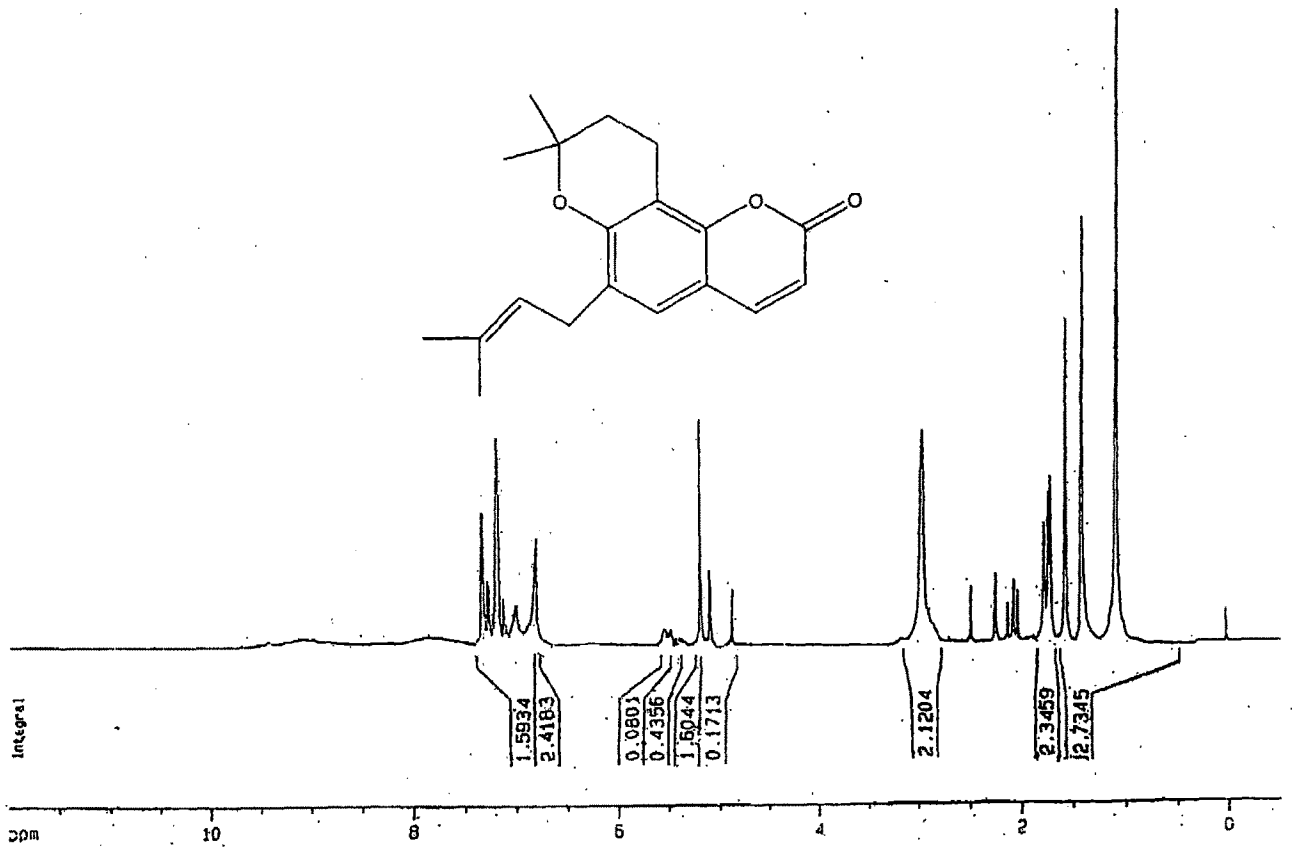
%C,H,N analysis (calculated) : C : 76.51 H : 3.38

%C,H,N analysis (found) : C : 76.81 H : 3.48

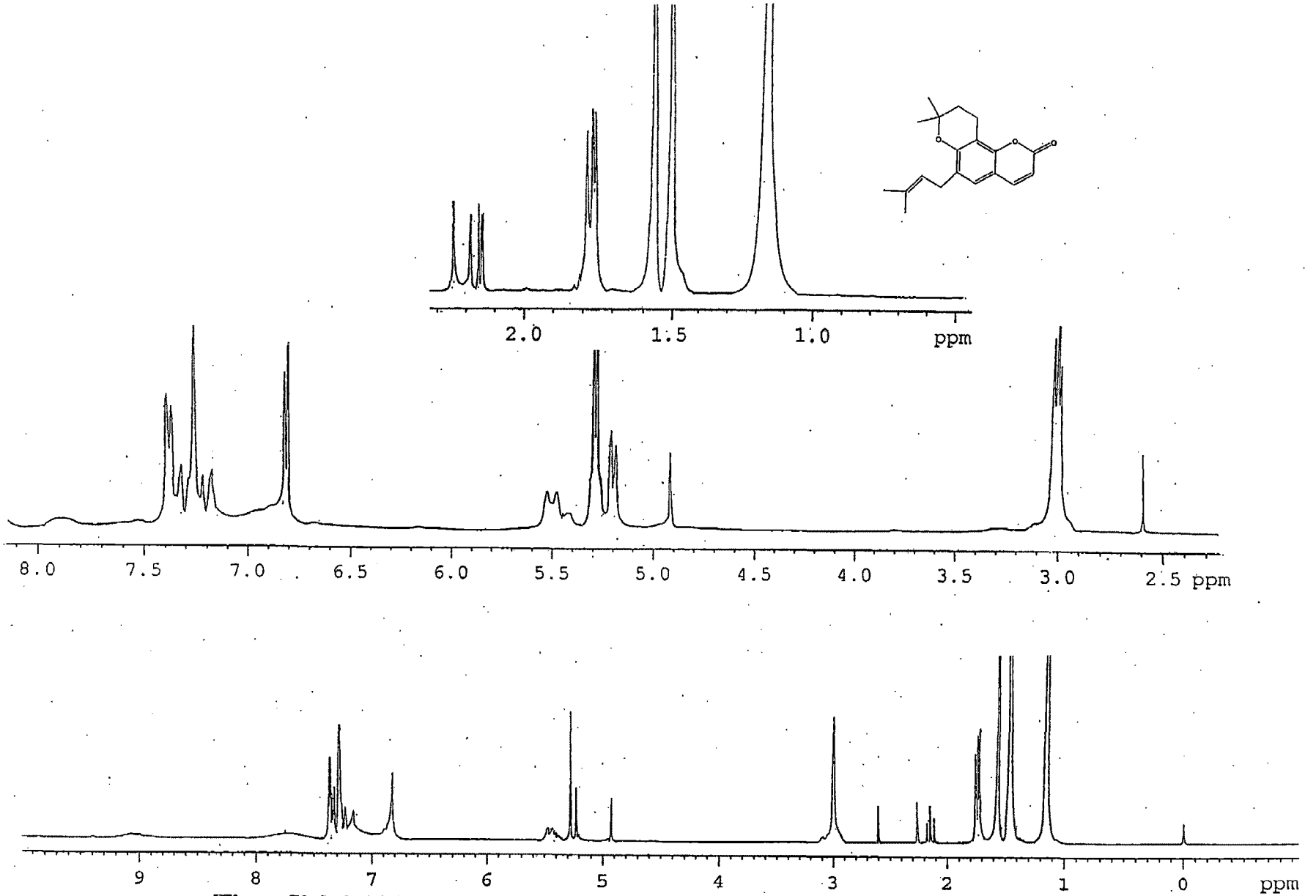
PMR data (400MHz, $CDCl_3$) δ ppm : 1.16(s, 6H, 2x-CH_3), 1.50(s, 3H, -CH_3), 1.58(s, 3H, -CH_3), 1.74(t, 2H, Ar-CH_2-C$\underline{H}_2$-C(CH_3)2-), 3.00(t, 2H, Ar-C$\underline{H}_2$-CH_2-C(CH_3)2-), 5.16-5.56(m, 3H, Olefinic protons), 6.80(d, J=7.5 Hz, 1H, C-3), 7.29(s, 1H, C-5), 7.41(d, J=7.5 Hz, 1H, C-4).



[Figure-71]: 6-(3-Methylbutan-2-enyl)-8,8-dimethyl-9,10-dihydro-2H-pyrano[2,3-*h*]-1-benzopyran-2-one, 183

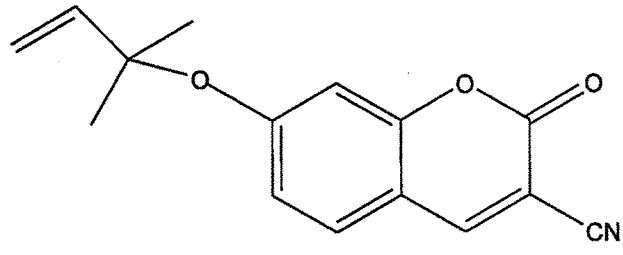


[Figure-72]: 6-(3-Methylbutan-2-enyl)-8,8-dimethyl-9,10-dihydro-2H-pyrano[2,3-*h*]-1-benzopyran-2-one, 183



[Figure-72a]: 6-(3-Methylbutan-2-enyl)-8,8-dimethyl-9,10-dihydro-2H-pyrano[2,3-*h*]-1-benzopyran-2-one, 183

3-Cyano-7-(1,1-dimethylprop-2-enyloxy)-2H-benzopyran-2-one, **184**



State : light orange solid

Molecular Formula : $C_{15}H_{13}O_3N$

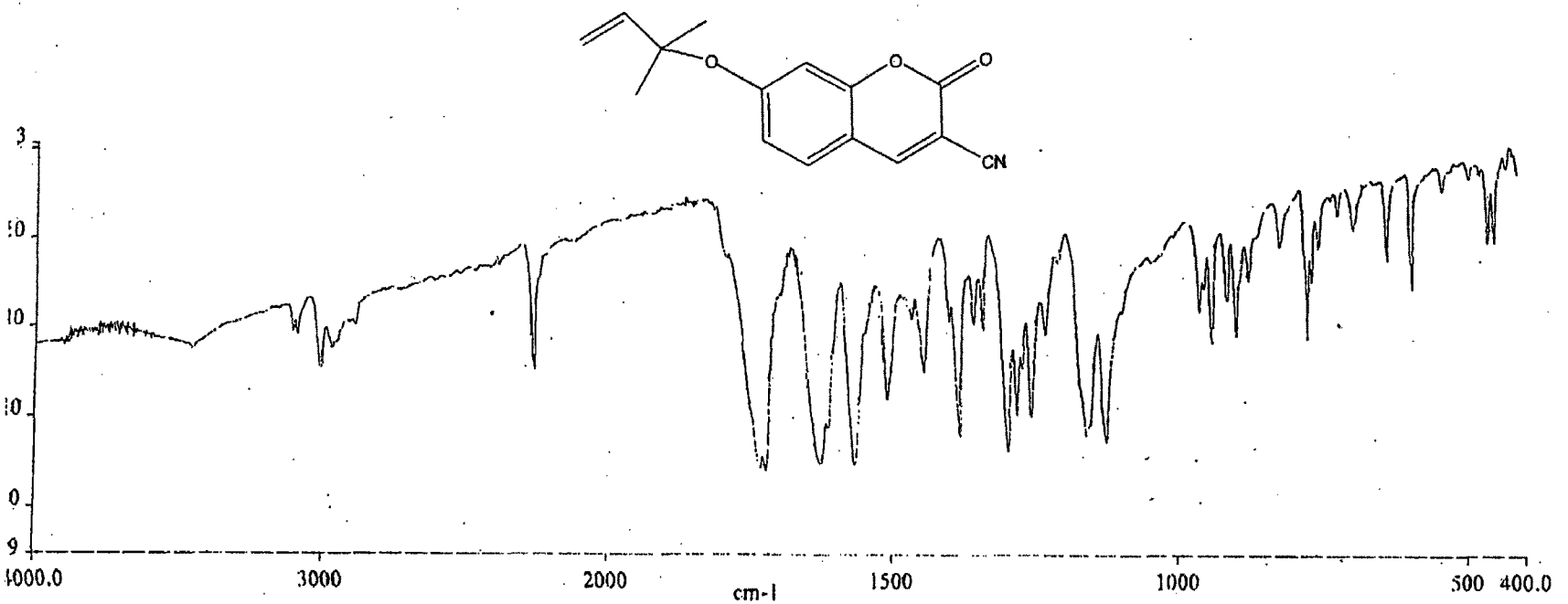
Melting Point : 188-190°C

% Yield : 50

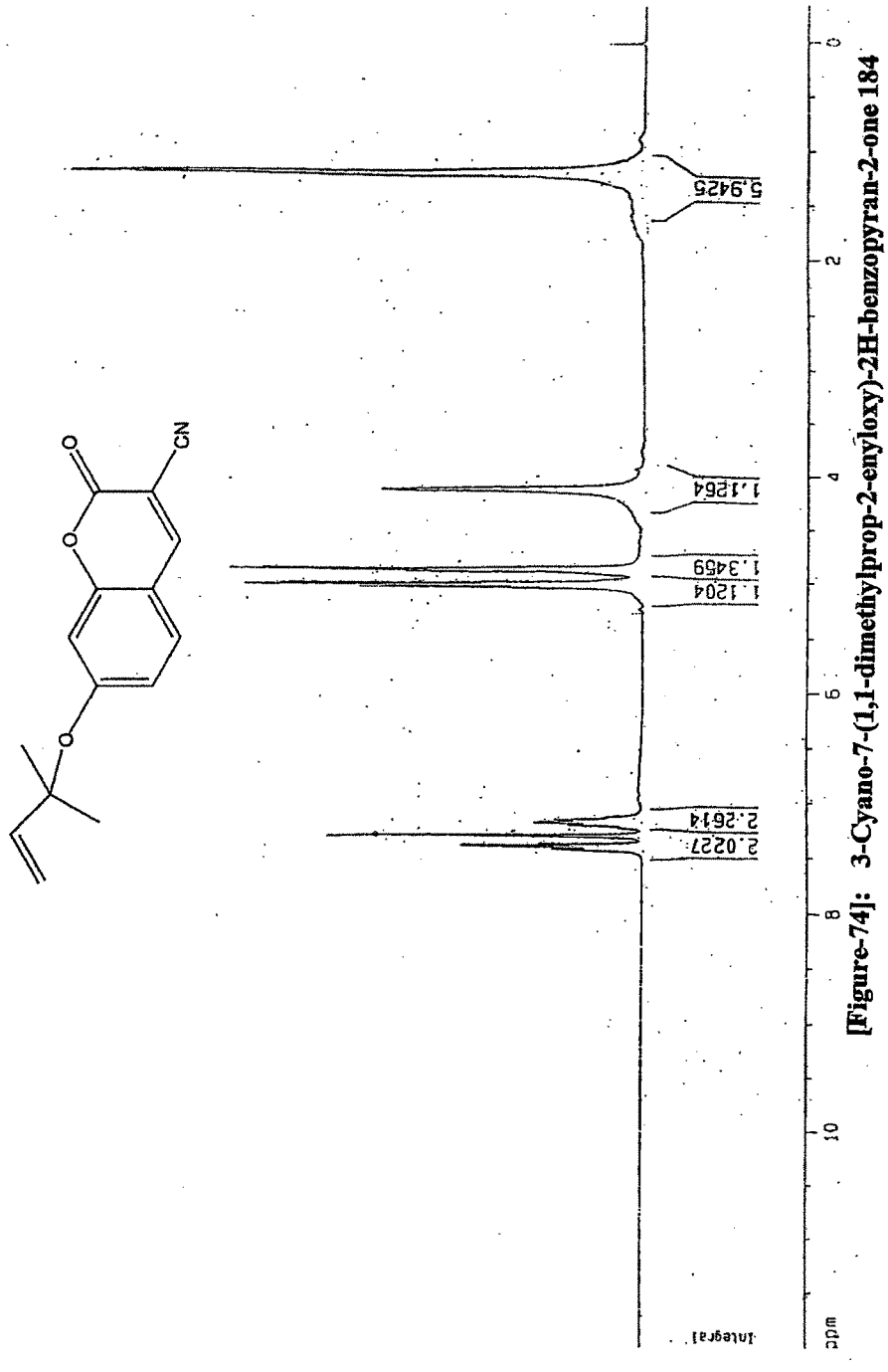
%C,H,N analysis (calculated) : C : 70.59 H : 5.09 N : 5.49

%C,H,N analysis (found) : C : 70.23 H : 5.28 N : 5.81

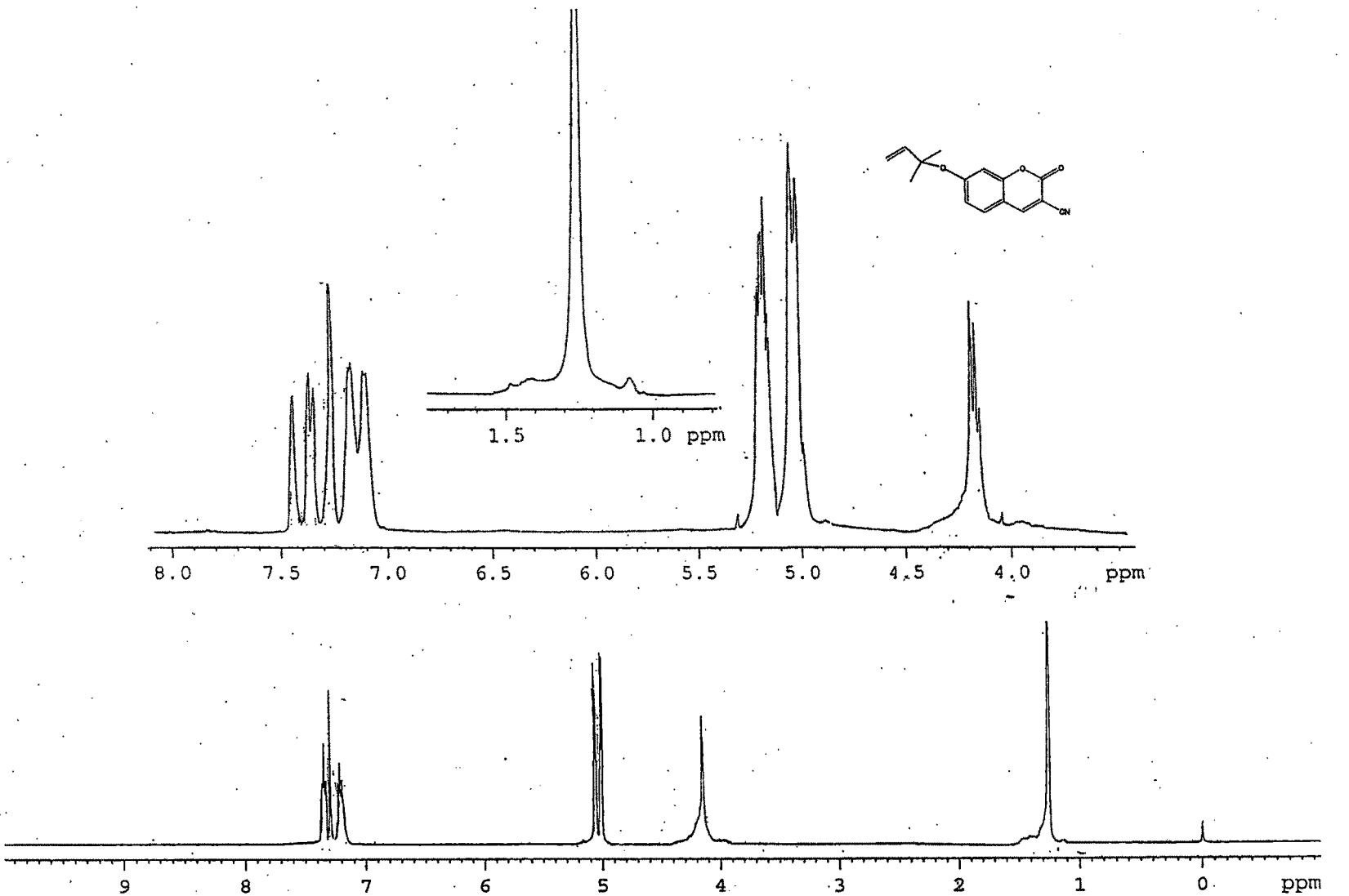
PMR data (400MHz, $CDCl_3$) δ ppm : 1.10-1.16(s, 6H, 2x-CH_3), 4.20(m, 1H, -C<u>H</u>=CH_2 olefinic proton), 4.93(m, 1H, C<u>H</u>2=CH- olefinic proton), 5.21(m, 1H, C<u>H</u>2=CH- olefinic proton), 7.14(d, J=8.4 Hz, 1H, C-5), 7.25(s, 1H, C-4), 7.38(d, J=8.4 Hz, 1H, C-6), 7.47(s, 1H, C-8).



[Figure-73]: 3-Cyano-7-(1,1-dimethylprop-2-enyloxy)-2H-benzopyran-2-one 184



[Figure-74]: 3-Cyano-7-(1,1-dimethylprop-2-enyloxy)-2H-benzopyran-2-one 184



[Figure-74a]:3-Cyano-7-(1,1-dimethylprop-2-enyloxy)-2H-benzopyran-2-one 184

CHAPTER-IV

Section-4

Synthesis of novel benzopyran-2H-ones using l-2-amino-1-butanol

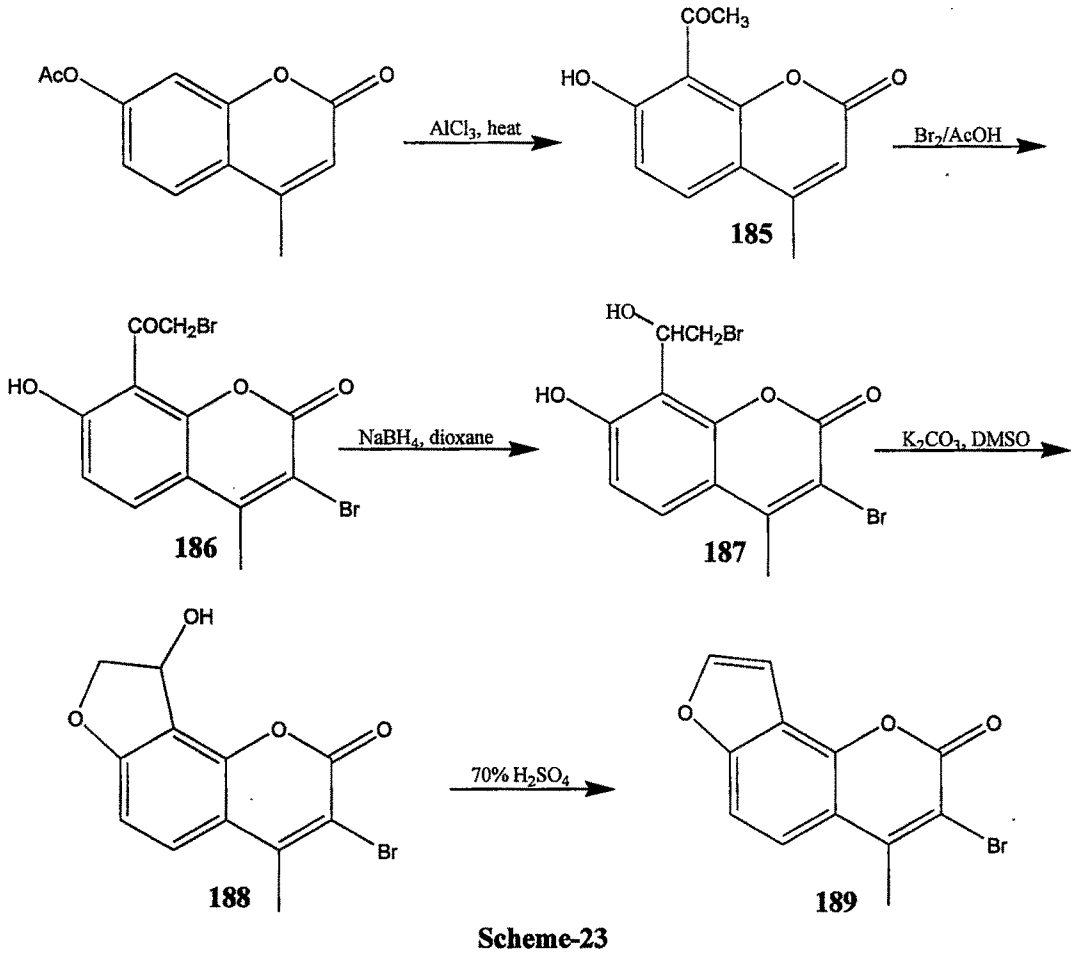
Section:4 Synthesis of novel benzopyran-2H-ones using l-2-amino-1-butanol

IV.10 Introduction

The construction of linearly and angularly fused 2H-furo-1-benzopyran-2-one has been a subject of interest chiefly on account of the synthesis of a range of natural product with established biological activity. Pursuance of synthesis of angularly as well as linearly furo fused 2H-1-benzopyran-2-ones created interest in further building up of a heterocycle frame in them so that their biological activity may be enhanced or modified.

A method of synthesis of angularly fused furobenzopyrone **189** via formation of 7-hydroxy-8-halogenoacetyl-4-methylbenzopyran-2H-one **187** was reported by Traven *et al*[12] in reasonably good yield. The method involved reduction of keto group by $NaBH_4$ and cyclisation by H_2SO_4 (Scheme-23). In this method halide functionality at 3-position was achieved.

In the present work it was considered to introduce an amide linkage to the previously synthesized angularly fused 2H-furo-1-benzopyran-2-one-3-carboxylate and 7-cinnamyloxy-2H-1-benzopyran-2-one-3-carboxylate using an optically active reagent l-2-aminobutanol and to study cyclization of these amide derivatives by heating with N,N-dimethyl aniline or $POCl_3$.



Scheme-23

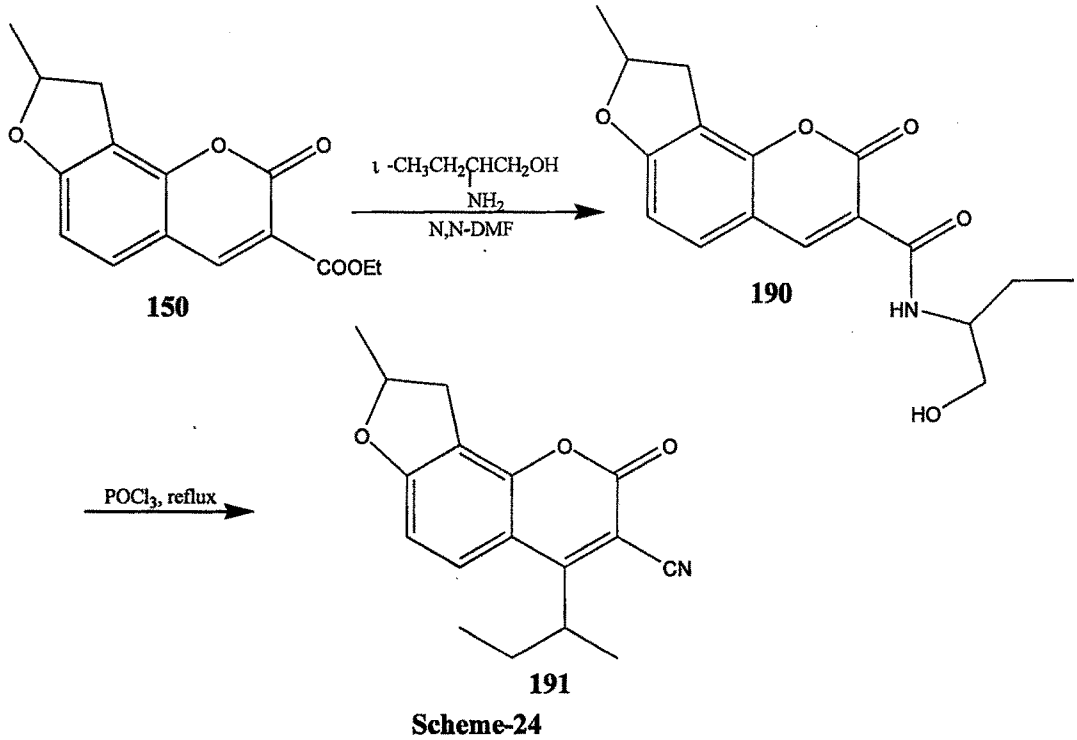
IV.11 Results and Discussion:

Synthesis of ethyl 8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one-3-carboxylate **150** was achieved from diethylmalonate and 2,4-dihydroxybenzaldehyde by following a reported procedure[1]. Ethyl 7-hydroxy-2H-1-benzopyran-2-one-3-carboxylate on allylation in DMF and anhydrous K_2CO_3, followed by Claisen rearrangement in N,N-dimethylaniline gave a mixture of two isomers, one alkali soluble and another alkali insoluble. The alkali insoluble compound **150** was separated, purified and used.

With the aim of constructing an active lactam ring, a strategy was used in which the fused furobenzopyran-2H-ones were treated with active L-2-amino-1-butanol and

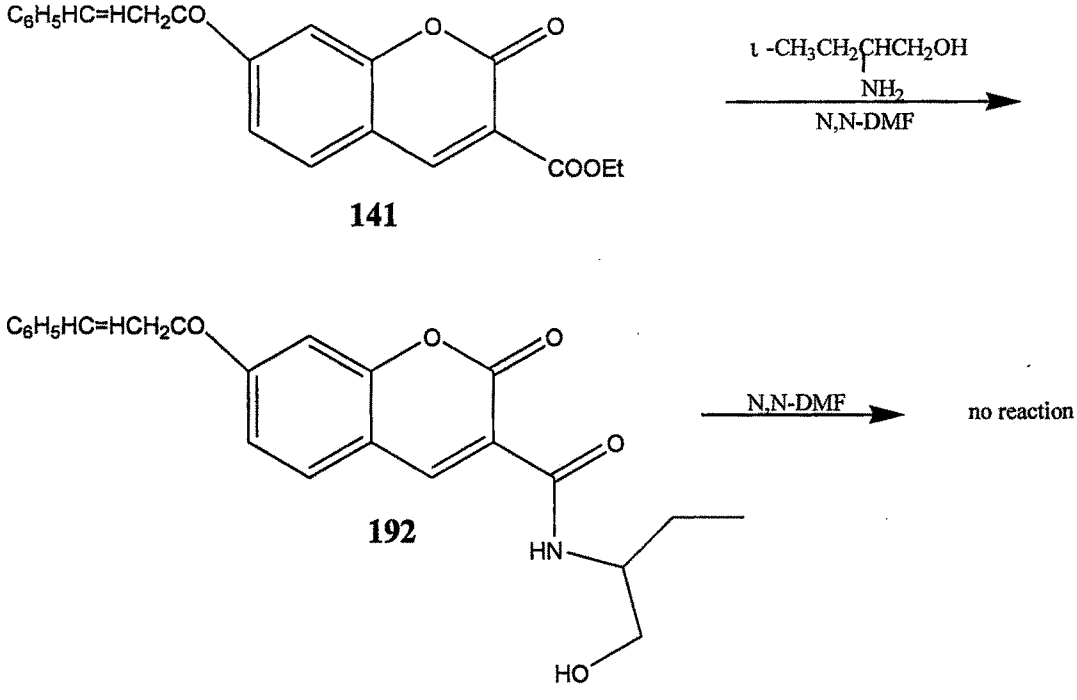
subsequent cyclization to yield cyclic analogue. For this, ethyl 8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one-3-carboxylate **150** (i.e. 8-methyl-3-carboethoxy-8,9-dihydroangelicin) was treated with ι-2-amino-1-butanol in DMF, which gave an amide derivative 3-{N-(1-hydroxybutan-2-yl)methanamido}-8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, **190**. On refluxing compound **190** in N,N-dimethylaniline, as per our anticipation, seven membered lactam ring was not formed and starting material was recovered. However on refluxing compound **190** with $POCl_3$, a cyano derivative 3-cyano-8-methyl-4-(1-methylpropanyl)-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one,**191** was obtained (Scheme-24).

Similarly, ethyl 7-cinnamyloxy-2H-1-benzopyran-2-one-3-carboxylate **141** on treatment with ι-2-amino-1-butanol afforded corresponding amide derivative **192** which did not undergo Claisen rearrangement in refluxing N,N-dimethylaniline and was recovered unchanged (Scheme-25).



150 **190** **191**

Scheme-24



Scheme-25

PMR spectrum of compound **190** exhibited a triplet at δ 1.10 for three methyl protons of ethyl group -$CH_2C\underline{H}_3$, a doublet at δ 1.60 for three methyl protons $C\underline{H}_3CH$-O on furan ring, a quadrate at δ 1.70 for two –$C\underline{H}_2CH_3$ protons of ethyl group, a doublet at δ 1.92 for two Ar-$C\underline{H}_2$-CH protons of ring, a multiplet at δ 2.91 for a proton –NH-C<u>H</u>, a multiplet at δ 3.50-3.75 for two HO-$C\underline{H}_2$-CH protons, a multiplet at δ 3.80 for a -OC<u>H</u>- of ring, a broad singlet at δ 4.20 for -N<u>H</u>- proton, a broad multiplet at δ 5.21-5.42 for –OH proton, a doublet at δ 6.71 (J=8Hz) for a C-5 proton, another doublet at 7.47 (J=8Hz) for a C-6 proton and finally a singlet at δ 8.30 for proton at C-4[Figure-75].

PMR spectrum of compound **191** exhibited a triplet at δ 1.07 for three methyl protons of ethyl group -$CH_2C\underline{H}_3$, a doublet at δ 1.25 for three methyl protons $C\underline{H}_3CH$- of alkyl chain, a multiplet at δ 1.34 for two methylene $CH_3C\underline{H}_2CH$- protons, a doublet at δ 1.50 for three –$OCHC\underline{H}_3$ protons on the ring, a multiplet at δ 2.10 for a Ar-C<u>H</u> proton, a doublet at δ 2.30 for two Ar-$C\underline{H}_2$-CH protons of ring, a multiplet at δ 3.63 for a -OC<u>H</u>-

proton of ring, a doublet at δ 7.41 (J=8.1 Hz) for a C-5 proton and finally another doublet at δ 7.71 (J=8.1 Hz) for a C-6 proton[Figure-76].

PMR spectrum of compound **192** exhibited a triplet at δ 1.10 for three methyl protons of ethyl group -$CH_2\underline{CH_3}$, a quartet at δ 1.25 for two methylene protons $\underline{CH_2}CH_3$ of ethyl group, a multiplet at δ 2.21 for a proton –NH-C<u>H</u>, a multiplet at δ 3.63 for two HO-$\underline{CH_2}$-CH protons, a multiplet at δ 4.00 for two -CH=$\underline{CH_2}$O- protons, a broad singlet at δ 5.10 for -N<u>H</u>- proton, a broad multiplet at δ 5.12-5.52 for –OH proton, a multiplet at δ 6.27 for an ArCH=C<u>H</u> proton, another multiplet at δ 7.10 for an ArCH=C<u>H</u> proton, a broad multiplet at δ 7.14-7.50 for seven aromatic protons, a singlet at δ 7.80 for a C-4 proton and finally a singlet at δ 8.30 for proton at C-8[Figure-77].

IV.12 Experimental:

Synthesis of 3-{N-(1-hydroxybutan-2-yl)methanamido}-8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, 190

2-Amino-1-butanol (2.5ml, 0.028mol) and ethyl 8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one-3-carboxylate **150** (7.6g, 0.028mol) were refluxed in dry N,N-dimethylformamide (30ml) for one hour. The reaction mixture was cooled and added to crushed ice (200g). Very light yellow product was collected by subjecting separated solid to chromatography using a 50:50 mixture of petroleum ether(60-80)-ethylacetate followed by recrystallization in ethanol.

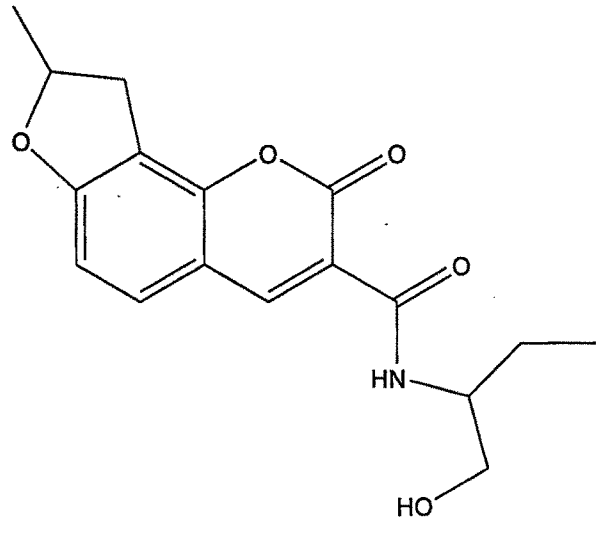
Synthesis of 3-cyano-8-methyl-4-(1-methylpropanyl)-8,9-dihydro-2H-furo [2,3-*h*]-1-benzopyran-2-one, 191

3-{N-(1-hydroxybutan-2-yl)methanamido}-8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, **190** (1.0g) was refluxed for eight hours in phosphorous oxychloride (10ml). The reaction mixture was cooled and poured into ice cold water(150ml) and left over night. The solid separated was filtered, dried and purified by column chromatography using eluent 10% ethyl acetate-petroleum ether(60-80) mixture followed by recrystallization in ethanol.

Synthesis of 7-cinnamyloxy-3-{N-(1-hydroxybutan-2-yl)methanamido}-2H-1-benzopyran-2-one, 192

2-Amino-1-butanol (2.5ml, 0.028mol) and ethyl 7-cinnamyloxy-2H-1-benzopyran-2-one-3-carboxylate **141** (9.8g, 0.028mol) were refluxed in dry N,N-dimethylformamide (30ml) for one hour. The reaction mixture was cooled and added to crushed ice (200g). Product was collected by subjecting separated solid to chromatography using a 50:50 mixture of petroleum ether(60-80)-ethylacetate followed by recrystallization in ethanol.

3-{N-(1-hydroxybutan-2-yl)methanamido}-8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, **190**



State : yellowish solid

Molecular Formula : $C_{17}H_{19}O_5N$

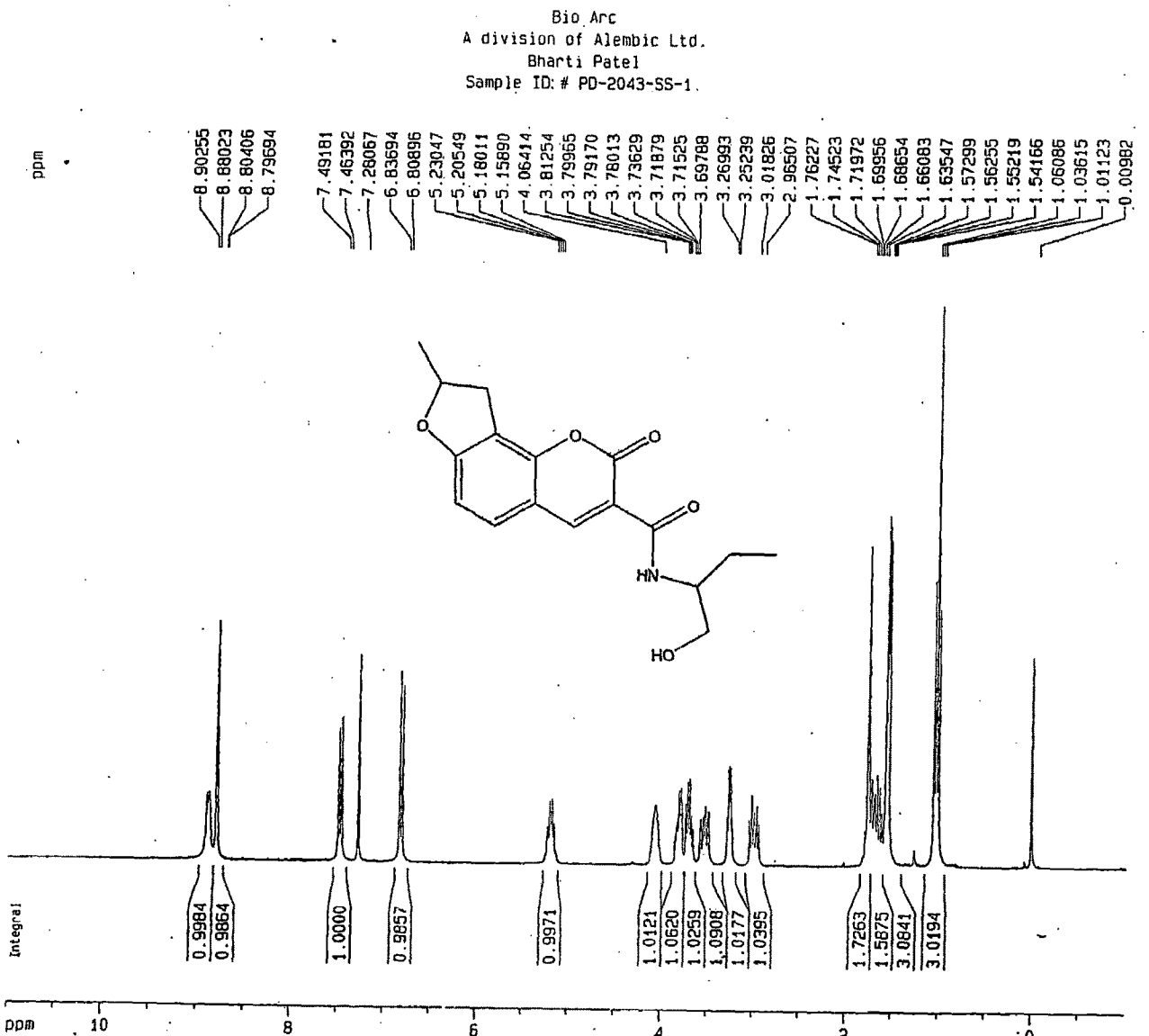
Melting Point : 180°C

% Yield : 80

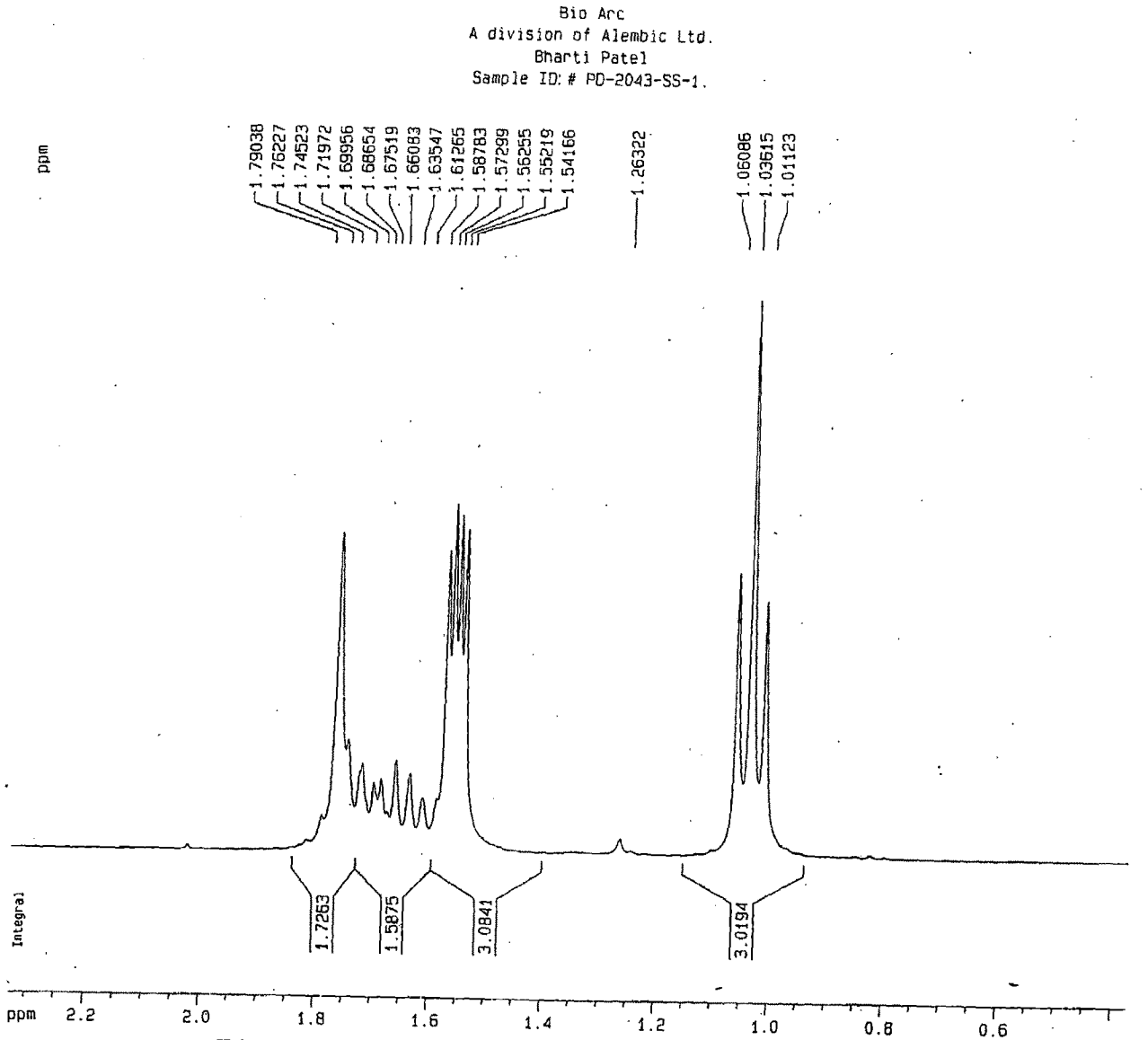
%C,H,N analysis (calculated) : C : 70.23 H : 5.85 N : 3.56

%C,H,N analysis (found) : C : 69.98 H : 5.68 N : 4.01

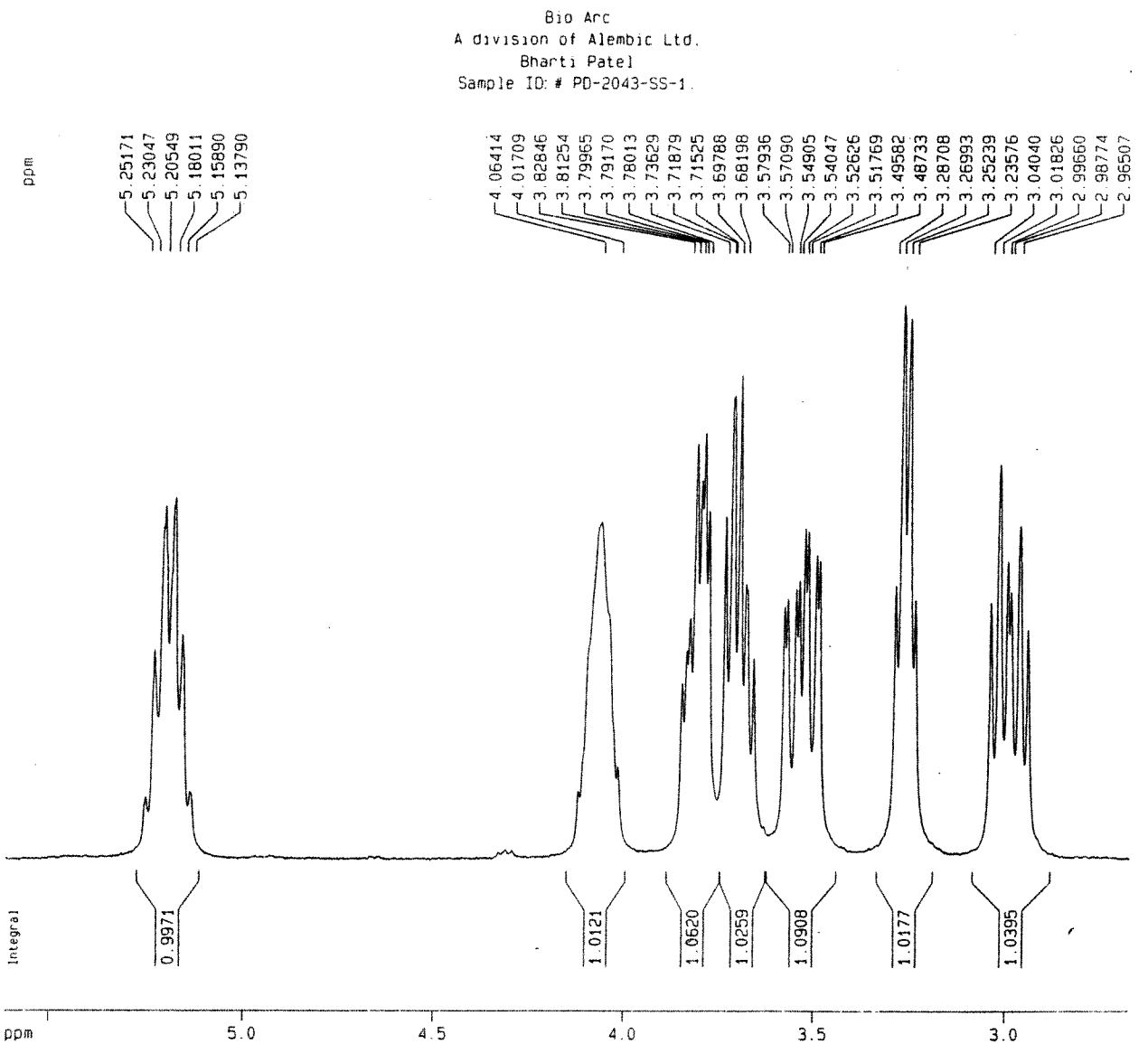
PMR data (400MHz, $CDCl_3$) δ ppm : 1.10(t, 3H, -CH2CH3), 1.60(d, 3H, CH3CH-O on ring), 1.70(q, 2H, CH3CH2-), 1.92(d, 2H, Ar-CH2-CH of ring), 2.91(m, 1H, -NH-CH-), 3.50-3.75(m, 2H, HO-CH2-CH), 3.80(m, 1H, -OCH- of ring), 4.20(br signal, 1H, -NH-), 5.21-5.42(br m, 1H, -OH), 6.71(d, J=8 Hz, 1H, C-5), 7.47(d, J=8 Hz, 1H, C-6), 8.30(s, 1H, C-4).



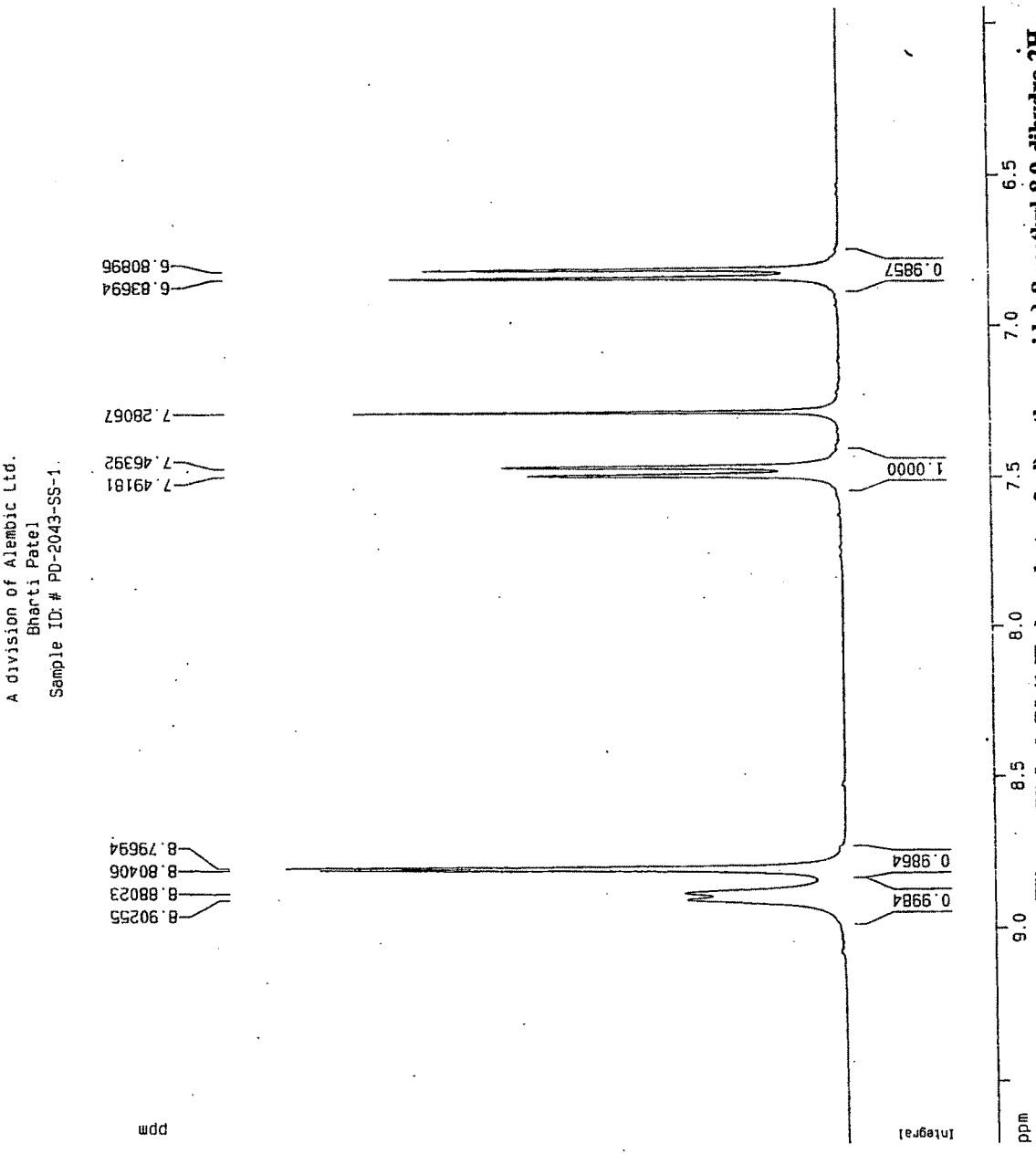
[Figure-75]: 3-{N-(1-Hydroxybutan-2-yl)methanamido}-8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, 190



[Figure-75a]:3-{N-(1-Hydroxybutan-2-yl)methanamido}-8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, 190

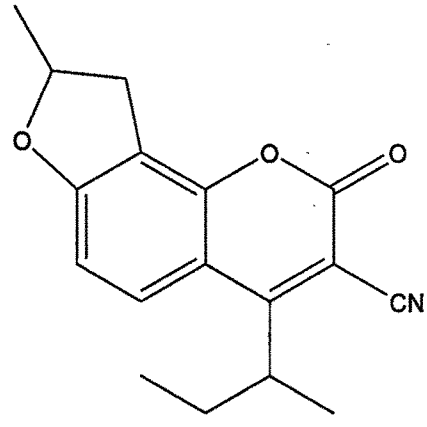


[Figure-75b]: 3-{N-(1-Hydroxybutan-2-yl)methanamido}-8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, 190



[Figure-75c]: 3-{N-(1-Hydroxybutan-2-yl)methanamido}-8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, 190

3-Cyano-8-methyl-4-(1-methylpropanyl)-8,9-dihydro-2H-furo [2,3-*h*]-1-benzopyran-2-one, **191**



State : yellowish solid

Molecular Formula : $C_{17}H_{17}O_3N$

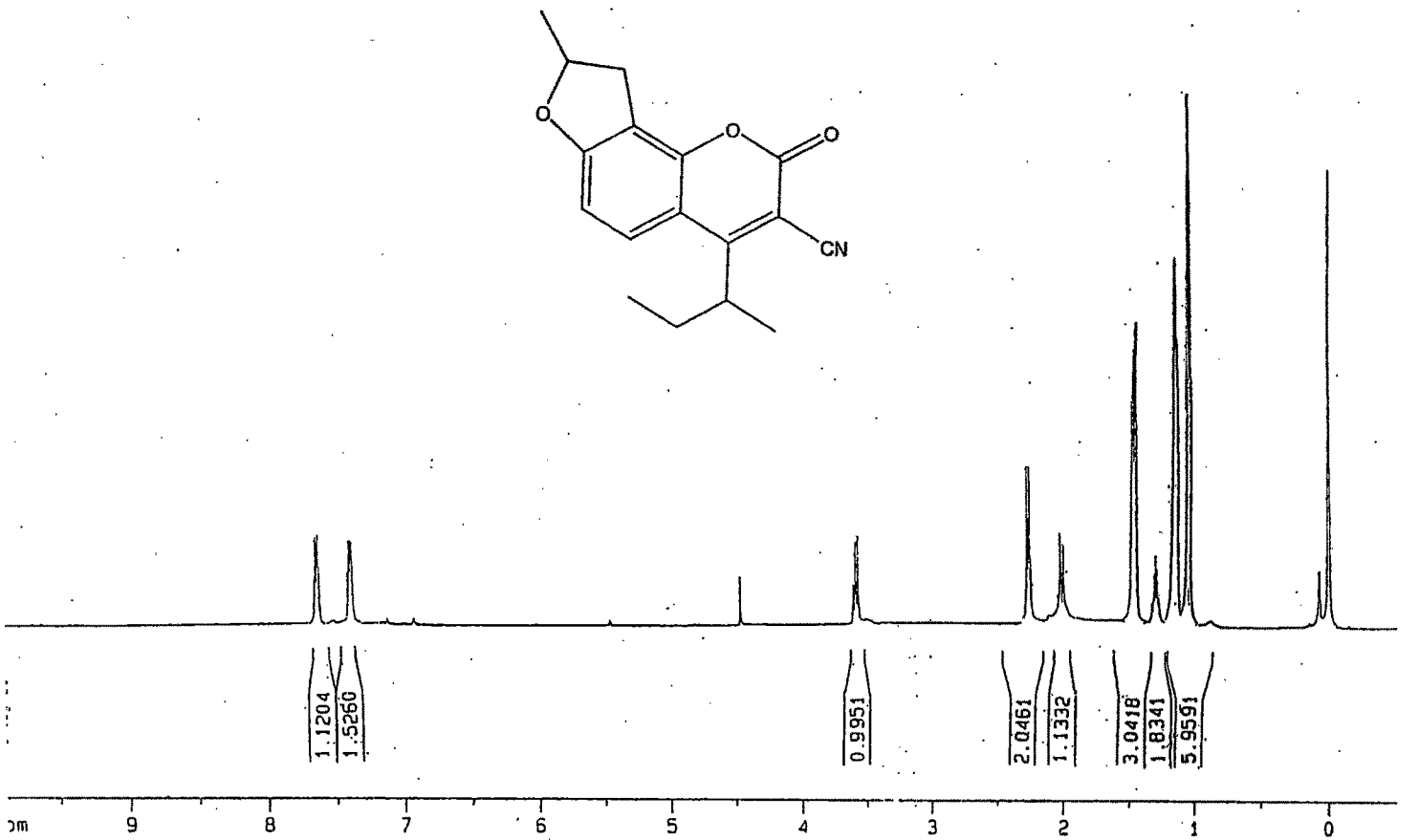
Melting Point : 131°C

% Yield : 50

%C,H,N analysis (calculated) : C : 72.08 H : 6.00 N : 4.94

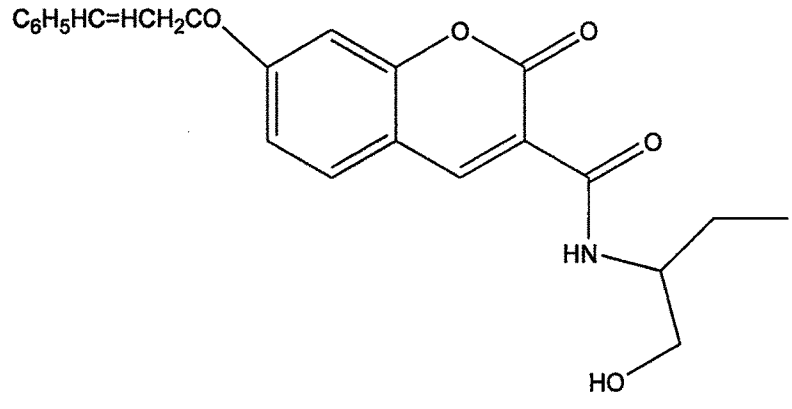
%C,H,N analysis (found) : C : 71.98 H : 5.98 N : 4.90

PMR data (400MHz, $CDCl_3$) δ ppm : 1.07(t, 3H, -CH2C<u>H</u>3), 1.25(d, 3H, -CHC<u>H</u>3), 1.34(m, 2H, CH3C<u>H</u>2CH-), 1.50(d, 3H, C<u>H</u>3CH-O on ring), 2.10(m, 1H, Ar-C<u>H</u>), 2.30(d, 2H, Ar-C<u>H</u>2-CH of ring), 3.63(m, 1H, -OCH- of ring), 7.41(d, J=8.1 Hz, 1H, C-5), 7.71(d, J=8.1 Hz, 1H, C-6).



[Figure-76]: 3-Cyano-8-methyl-4-(1-methylpropanyl)-8,9-dihydro-2H-furo [2,3-*h*]-1-benzopyran-2-one, 191

7-Cinnamyloxy-3-{N-(1-hydroxybutan-2-yl)methanamido}-2H-1-benzopyran-2-one, **192**



State : yellow solid

Molecular Formula : $C_{23}H_{23}O_5N$

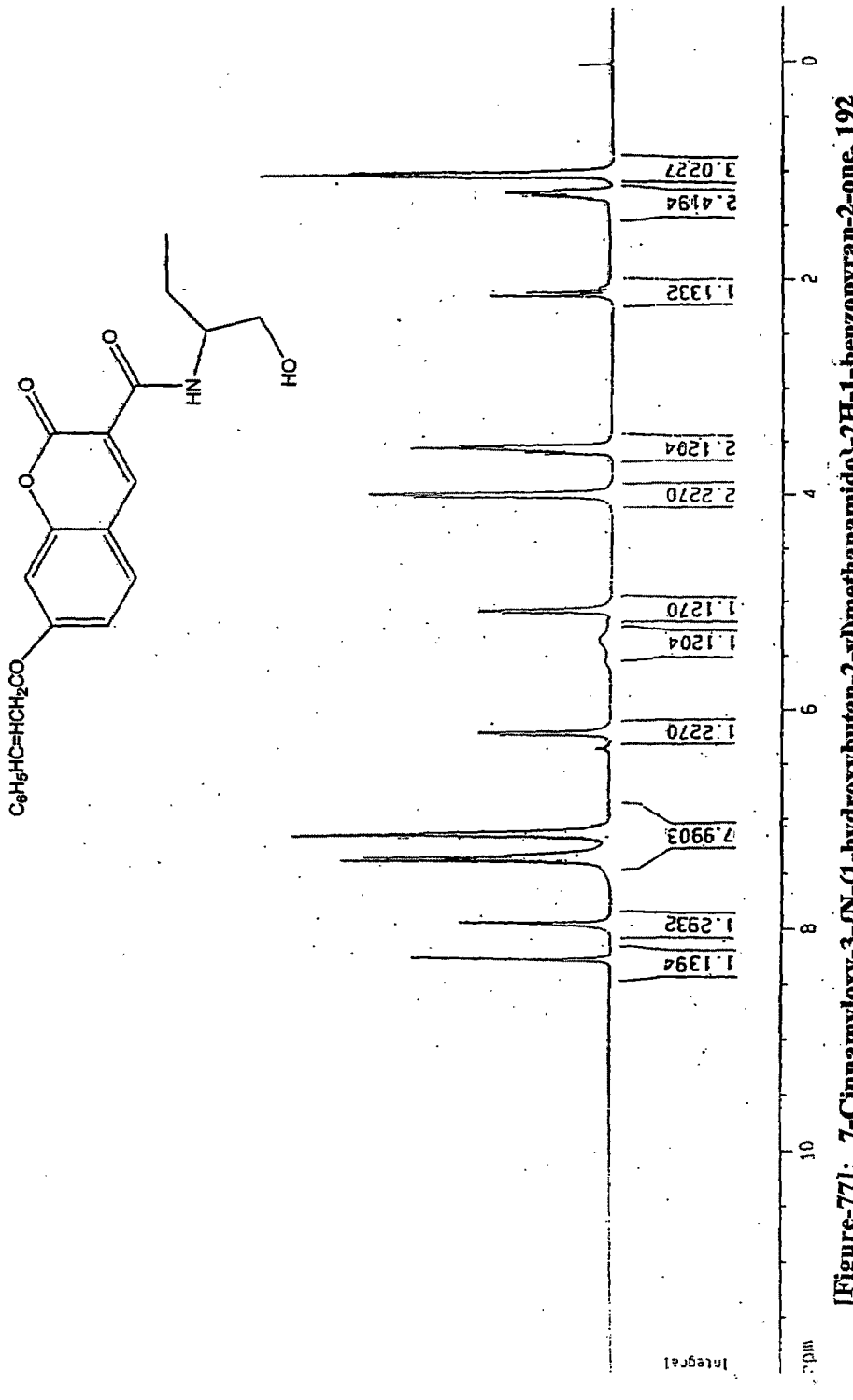
Melting Point : 128°C

% Yield : 40%

C,H,N analysis (calculated) : C : 70.23 H : 5.85 N : 3.56

C,H,N analysis (found) : C : 70.14 H : 5.70 N : 3.69

PMR data (400MHz, $CDCl_3$) δ ppm : 1.10(t, 3H, -CH2CH3), 1.25(q, 2H, CH3CH2- of alkyl chain), 2.21(m, 1H, -NH-CH-), 3.63(m, 2H, HO-CH2-CH), 4.00(m, 2H, -CH=CH2O-), 5.10(br signal, 1H, -NH-), 5.12-5.52(br m, 1H, -OH), 6.27(m, 1H, ArCH=CH), 7.10(m, 1H, Ar-CH=CH-), 7.14-7.50(m, 7H, aromatic protons), 7.80(s, 1H, C-4), 8.30(s, 1H, C-8).



[Figure-77]: 7-Cinnamyloxy-3-{N-(1-hydroxybutan-2-yl)methanamido}-2H-1-benzopyran-2-one, 192

Thu Jan 24, 2008
14:02:35
SPARC* BARODA*
AUTOPOL IV
Serial No. 2422

Meas. Type : Sp. Rot.
Wavelength : 589 nm
Concentration : 0.074%
Cell Length : 100.000 mm
Response Time : 2 sec
Sample Name : ML2

Sample ID #	Count	Meas.
	1	2.704
	2	0.000
	3	1.352
	4	-1.352
	5	-5.407

counts: 5
average: -0.541
std. dev.: 3.112
max: 2.704
min: -5.407

counts: 5
average: -0.541
std. dev.: 3.112
max: 2.704
min: -5.407

Optical activity of **3-{N-(1-hydroxybutan-2-yl)methanamido}-8-methyl-8,9-dihydro-2H-furo[2,3-*h*]-1-benzopyran-2-one, 190 [Figure-78]**

Thu Jan 24, 2008
14:00:00
SPARC* BARODA*
AUTOPOL IV
Serial No. 2422

Meas. Type : Sp. Rot.
Wavelength : 589 nm
Concentration : 0.086%
Cell Length : 100.000 mm
Response Time : 2 sec
Sample Name : ML1

Sample ID #	Count	Meas.
	1	17.448
	2	31.406
	3	19.774
	4	25.590
	5	25.590

counts:	5
average:	23.962
std. dev.:	5.493
max:	31.406
min:	17.448

counts:	5
average:	23.962
std. dev.:	5.493
max:	31.406
min:	17.448

Optical activity of **3-cyano-8-methyl-4-(1-methylpropanyl)-8,9-dihydro-2H-furo [2,3-*h*]-1-benzopyran-2-one, 191 [Figure-79]**

IV.13 Conclusion:

With the aim of synthesizing benzopyran-2H-ones having similarity to naturally occurring biologically active benzopyrone derivatives, we have prepared a large number of useful novel benzopyran-2H-ones. Moreover, some novel angelicins containing amide linkage have been synthesized. One of the objectives of research was to study relative ease of Claisen and Wittig reaction of allyloxy, cinnamyloxy and prenyloxy benzopyrones. From all above observations it is found that the rearrangements proceed more easily with allyloxy derivatives whereas they are difficult with cinnamyloxy derivatives.

It was expected that intra-molecular Michael type addition would take place in acrylamide moety of **190** resulting in formation of novel seven membered lactam ring. However, in contrast to our anticipation, heating compound **190** under reflux in phosphorous oxychloride furnished cyanoangelicin **191.**

IV.14 References:

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