CHAPTER III : SECTION 1

SYNTHESIS OF FUROBENZOPYRONES BY WITTIG REACTION

INTRODUCTION

There are several methods reported for the synthesis of furobenzopyrones in the literature and many of them were also discussed in the chapter II. In this section the emphasis is laid on intramolecular Wittig reaction which is a regiospecific synthetic method.

Wittig reaction, which was discovered by George Wittig[1], is a well-known method and is extensively being utilized to convert carbonyl compound to an olefin counterpart using either phosphorous ylide or sulphur ylide during the reaction.

Wittig reaction is easy to carry out and proceeds under milder conditions. The yield of olefin formed in this reaction is generally very high. An interesting feature of this reaction is that it gives olefins in which the position of the newly formed double bond is unambiguous. The stereochemistry of the olefin formed depends on the nature of the phosphorane, reactivity of carbonyl compound and the solvent used in the reaction.

Wittig reaction has also been attempted with arsenic[2], phosphocummulene and phophaallene[3] ylides and also been reported to use trialkylphosphites[4,5] in place of phosphorous ylides, which generates phosphorate anions for carbonyl olefination.

The method, Intramolecular Wittig reaction, which is going to be used in this section to synthesize angular and linear furobenzopyrones is only an extension to Wittig reaction developed by Le Corre and coworkers[6,7] for the synthesis of heterocyclic compounds. This method can also be utilized for the synthesis of macrolides[8] and naturally occurring 2-arylbenzofurans[9]. It was observed from the literature, the different approaches followed by various workers to prepare the angular and linear furobenzopyrones using Wittig reaction as key step and also could be noticed that some of the naturally occurring furobenzopyrone analogues are made more conveniently with higher yields rather than conventional methods.

Ahluwalia *et al.*[10] have reported the synthesis of different linear furobenzopyrones by the condensation of 2,4-dihydroxy-3-methylacetophenone (1a) or benzophenone **1b** with benzoin in the presence of p-toluenesulphonic acid followed by Wittig reaction of the resultant diphenylbenzofurans **2a,b** with ethoxycarbonylmethylene(triphenyl) phosphorane (3a) and 1-carboethoxy ethylidine(triphenyl) phosphorane (3b) furnished respective psoralen derivatives **4a-c**. **[Scheme III.1.1]**

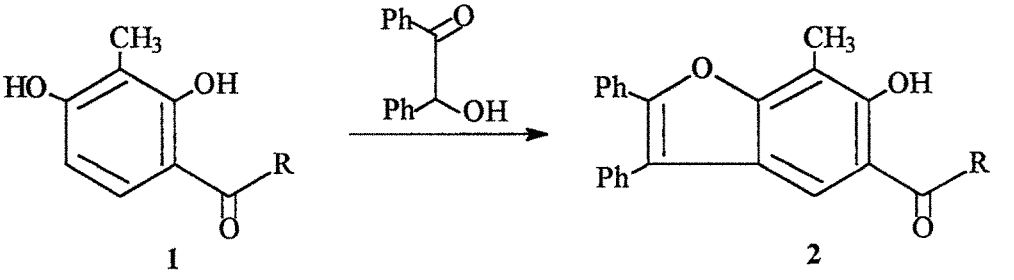
Nicolaides *et al.*[11] synthesized angular furocoumarins by treating o-quinone **5** with phosphorous ylide **6a,b** in refluxing dichloromethane to give o-quinomethane **7a,b**. Further, addition of triphenylphosphine or second ylide species **6a,b** yielded intermediates **8** and **10a,b** respectively, which on hydrolysis followed by internal hemiacetalization and dehydration afforded desired furobenzopyrones **9** and **11a,b** respectively. **[Scheme III.1.2]**

Lee[12] reported an efficient and different synthesis of angular furocoumarins from dihydrobenzofuran **12a-c**, which was obtained by reaction with diazoketone and vinylacetate followed by acid-catalyzed dehydration[13], and was formylated using excess of NaH in the presence of catalytic amount of KI and ethylformate in THF to give **13a-c**. Oxidation of **13a-c** with DDQ in refluxing benzene yielded aldehyde **14a-c**, when treated with (carboethoxymethylene)triphenylphosphorane in xylene[14], in order to get angelicin (15), oroselone (16) or oroselol (17). **[Scheme III.1.3]**

Mali and Sandhu[15] utilized the Wittig reaction method to synthesize naturally occurring furobenzopyrones conveniently in a single step in reasonably good yields, where other methods such as Claisen rearrangement produce relatively poor yields. 2-Hydroxy-4-prenyloxybenzaldehyde (18a) and 2-hydroxy-4-prenyloxyacetophenone (18b) when reacted with phosphoranes **19a,b** at 180-200°C for 3-23h produced on usual work up dihydroangelicin **20a,b** and dihydropsoralen **21a,b** derivatives. **[Scheme III.1.4]**

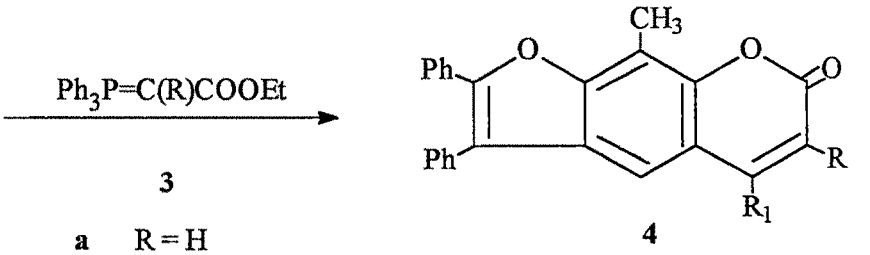
Soman and Trivedi[16] synthesized various substituted angelicin and psoralen derivatives using NBS followed by intramolecular Wittig reaction.

Scheme III.1.1



a $R = CH_3$
b $R = C_6H_5$

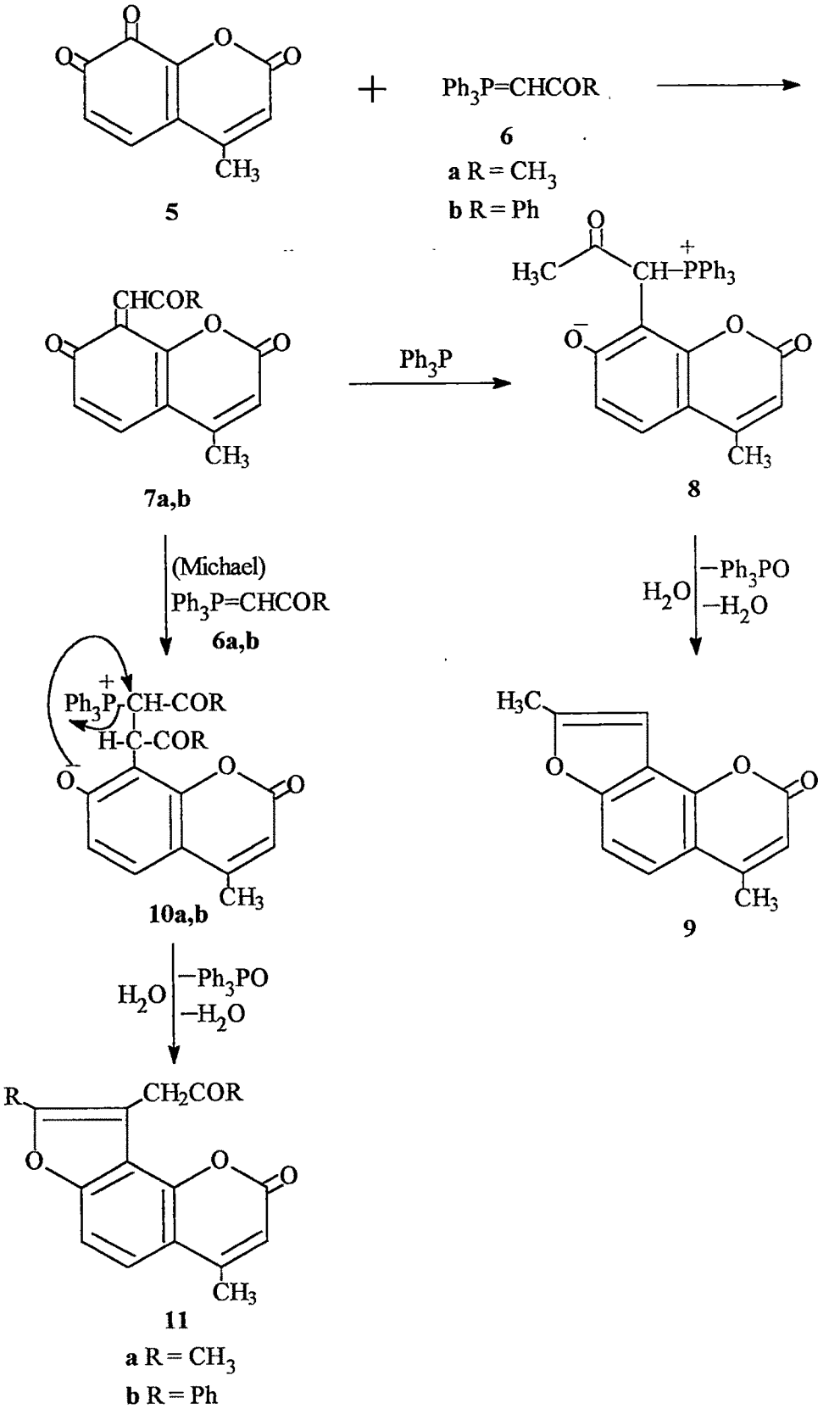
a $R = CH_3$
b $R = C_6H_5$



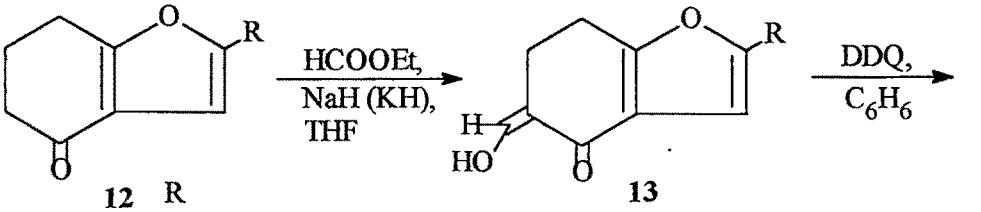
a $R = H$
b $R = CH_3$

	R	R_1
a	H	CH_3
b	CH_3	CH_3
c	H	C_6H_5

Scheme III.1.2

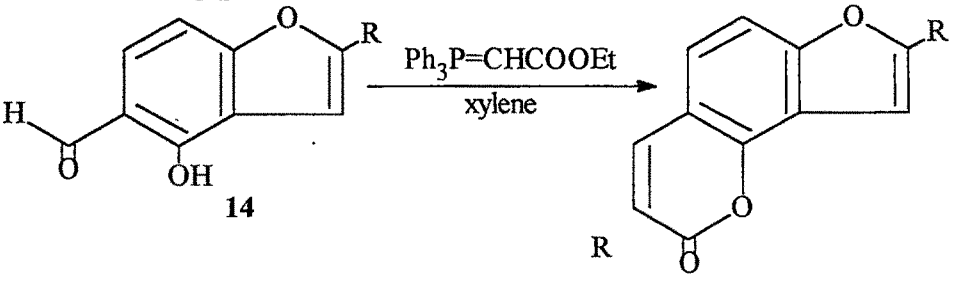


Scheme III.1.3



12 R
a H
b $CH_2=C(CH_3)$
c $(CH_3)_2(OH)C$

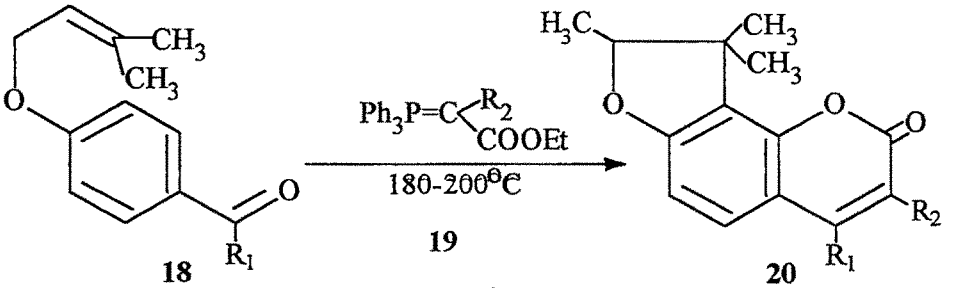
13



14

15 H ; Angelicin
16 $CH_2=C(CH_3)$; Oroselone
17 $(CH_3)_2(OH)C$; Oroselol

Scheme III.1.4



18

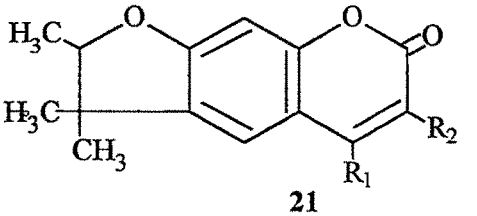
19

20

	R_1
a	H
b	CH_3

	R_2
a	H
b	CH_3

	R_1	R_2
a	H	H
b	H	CH_3

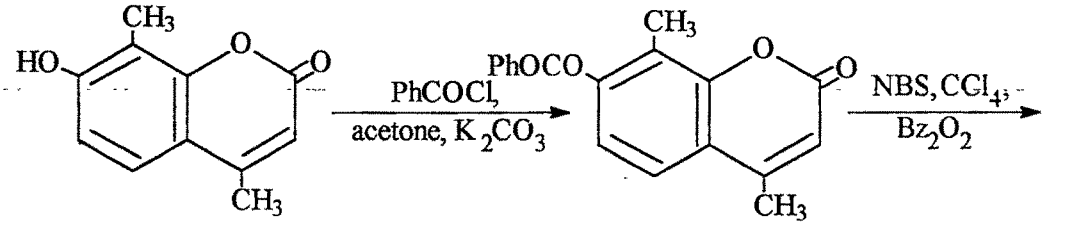


21

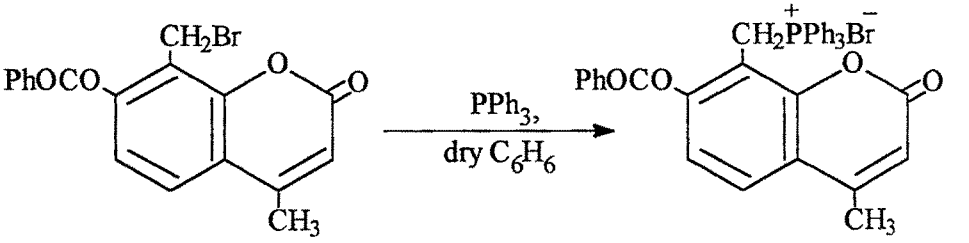
	R_1	R_2
a	H	H
b	H	CH_3

7-Hydroxy-4,8-dimethylcoumarin (22) was condensed with benzoylchloride in the presence of anhydrous K_2CO_3 resulted in the formation of 7-benzyloxy-4,8-dimethylcoumarin (23), which on bromination with N-bromosuccinimide yielded 7-benzyloxy-8-bromomethyl-4-methylcoumarin (24). Reaction of **24** with triphenylphosphine in dry benzene produced its corresponding phosphonium salt **25**, which insitu with triethylamine under nitrogen atmosphere afforded 7-methyl-2-phenylfuro(2,3-h)benzopyran-5H-one (26). **[Scheme III.1.5]**

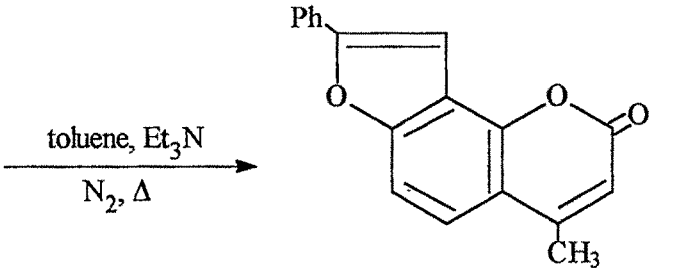
Scheme III.1.5



22 23



24 25



26

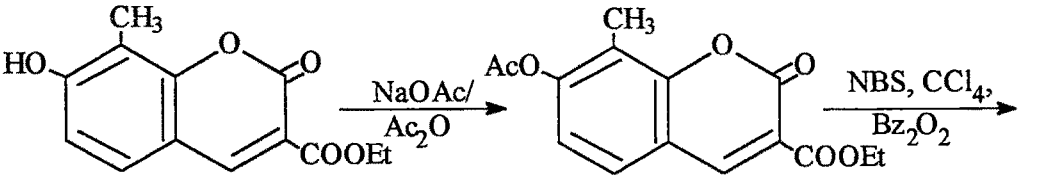
PRESENT WORK

In the chapter II we have reported the synthesis of both angular and linear furobenzopyrones having electron withdrawing groups such as -COOEt, -$COCH_3$ and -CN by subjecting 7-allyloxy derivatives to Claisen rearrangement in refluxing DMA. The results were promising in the synthesis of angular counterparts but were not good in the case of linear furobenzopyrones although it was well exploited by many workers using either -Br or -I as substituents in the 8^{th} position of benzopyrone and thus subjecting the 7-allyloxy derivatives to Claisen rearrangement.

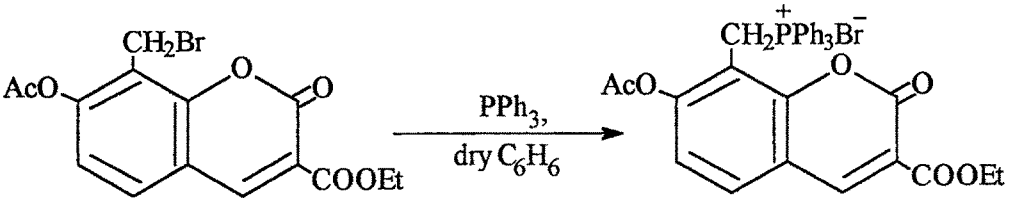
In the present work a different approach was planned to synthesize both angular and linear furobenzopyrones. 7-Hydroxy-8-methyl/6-methyl benzopyrone is first acetylated followed by bromination with NBS to convert methyl to bromomethyl group and subsequently a furan ring is built up using intramolecular Wittig method. This method being regiospecific will not only give pure products but also reasonably good yields of the product.

Synthesis of ethyl-2-methylfuro(2,3-h)benzopyran-5H-one-6-carboxylate (109) was achieved by condensing 2,4-dihydroxy-3-methyl benzaldehyde with diethylmalonate to obtain ethyl-7-hydroxy-8-methyl benzopyran-2H-one-3-carboxylate (27), which on acetylation afforded ethyl-7-acetoxy-8-methylbenzopyran-2H-one-3-carboxylate (28). **28** on reaction with N-bromosuccinimide and a pinch of benzoyl peroxide, an initiator in CCl_4 solvent under 200W-tungsten bulb gave ethyl-7-acetoxy-8-bromomethyl benzopyran-2H-one-3-carboxylate (29). **[Scheme III.1.6]** The structure of **29** was confirmed from its elemental analysis and IR spectrum as it showed bands in KBr at 1758 and 1711cm^{-1} for >CO of -OAc overlapped with >CO of lactone, while the absorption band for >CO of ester appeared at 1692cm^{-1}. **[Fig. III.1.1]** Its PMR spectrum exhibited signals in $CDCl_3$ as δ 1.41, a triplet for three methyl group protons of ester at C-3; a singlet at 2.44 for three methyl

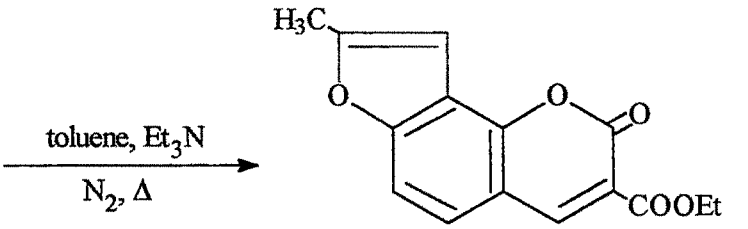
Scheme III.1.6



27 28



29 30



109

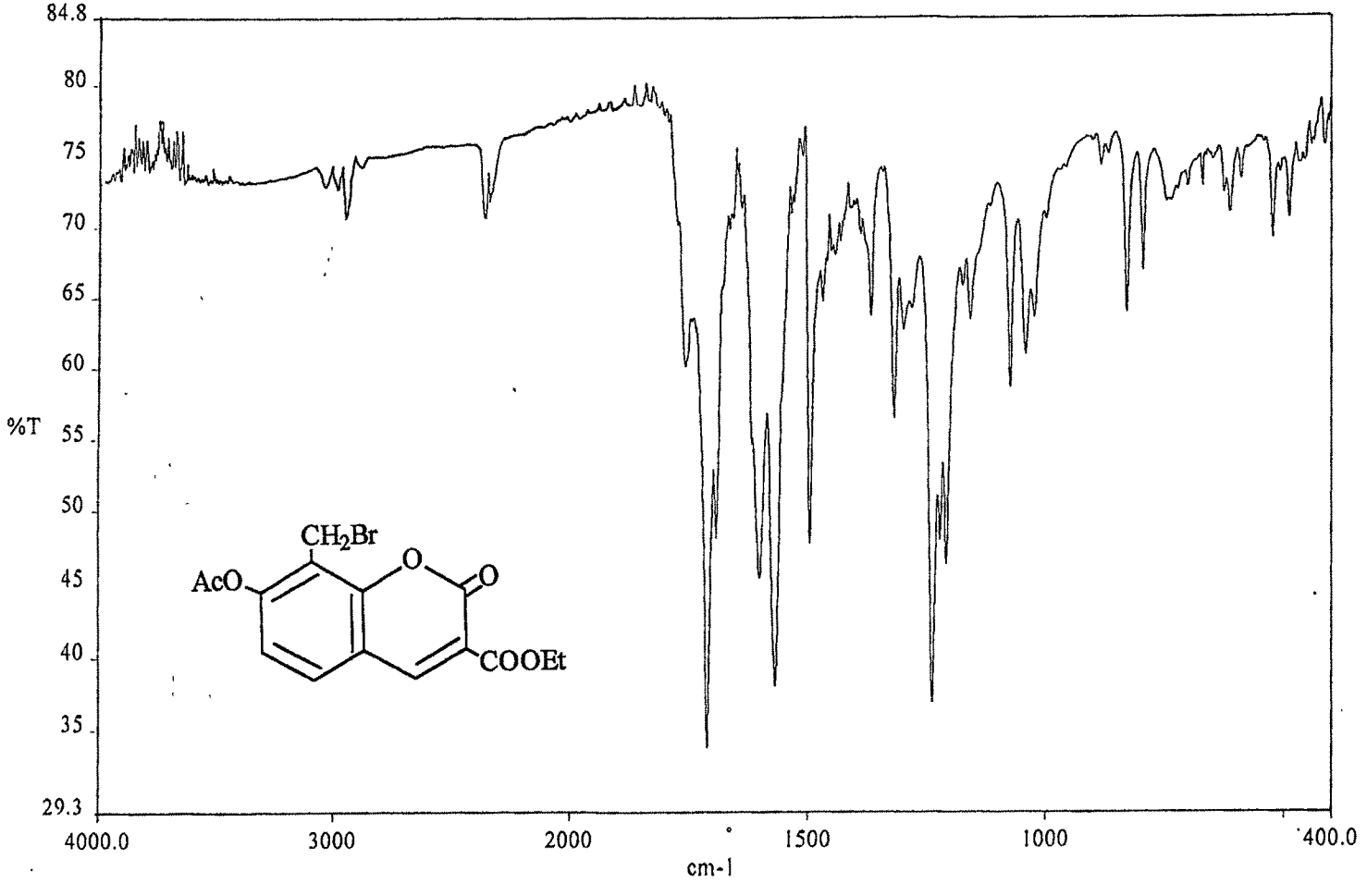

84.8
80
75
70
65
60
%T
55
50
45
40
35
29.3
4000.0
3000
2000
1500
1000
400.0
cm-1
CH2Br
AcO
O
O
COOEt

Fig. III.1.1

group protons of -$COCH_3$ at C-7; a quartet appeared at 4.45 for two methylene protons of ester at C-3; a singlet at 4.65 for two methylene protons of -CH_2Br at C-8; two doublets appeared at 7.20, J = 8Hz and 7.55, J = 8Hz for protons at C-6 and C-5 and a singlet for proton C-4 at 8.50. **[Fig. III.1.2]** **29** when allowed to react with triphenylphosphine in dry benzene afforded Wittig salt ethyl-7-acetoxy-8-bromotriphenylphosphonium benzopyran-2H-one-3-carboxylate (30). The solid, thus obtained after distillation of benzene was used insitu for further reaction, suspended in boiling dry toluene with triethylamine as a base under the nitrogen atmosphere. Working up of the reaction mixture gave angular furocoumarin **109**. Its structure was confirmed from its elemental analysis, mmp and by matching with PMR signals as ethyl-2-methylfuro(2,3-h)benzopyran-5H-one-6-carboxylate.

Ethyl-2-methylfuro(3,2-g)benzopyran-7H-one-6-carboxylate (35) was prepared by condensing 2,4-dihydroxy-5-methylbenzaldehyde with diethylmalonate to give ethyl-7-hydroxy-6-methylbenzopyran-2H-one-3-carboxylate (31), which on acetylation with anhydrous sodium acetate and acetic anhydride produced ethyl-7-acetoxy-6-methylbenzopyran-2H-one-3-carboxylate (32). **[Scheme III.1.7]** **32** on bromination with NBS in CCl_4 yielded ethyl-7-acetoxy-6-bromomethylbenzopyran-2H-one-3-carboxylate (33), which was confirmed by elemental analysis, IR and PMR spectra. Its IR spectrum exhibited absorption bands in KBr at 1764 and 1751cm^{-1} for >CO of -OAc and lactone, while the band at 1695cm^{-1} is due to >CO of ester. **[Fig. III.1.3]** PMR in $CDCl_3$ showed signals at δ 1.40, a triplet for three methyl group protons of ester at C-3; a singlet at 2.45 for three methyl group protons of -$COCH_3$ at C-7; a quartet appeared at 4.40 for two methylene protons of ester at C-3; a singlet at 4.45 for two methylene protons of -CH_2Br at C-6; two singlets at 7.30 and 7.70 for protons at C-8, C-5 and a singlet for proton C-4 at 8.50. **[Fig. III.1.4]**. **33** when reacted with triphenylphosphine in dry benzene gave its corresponding phosphonium salt **34**. The reaction of **34** with triethylamine under the atmosphere

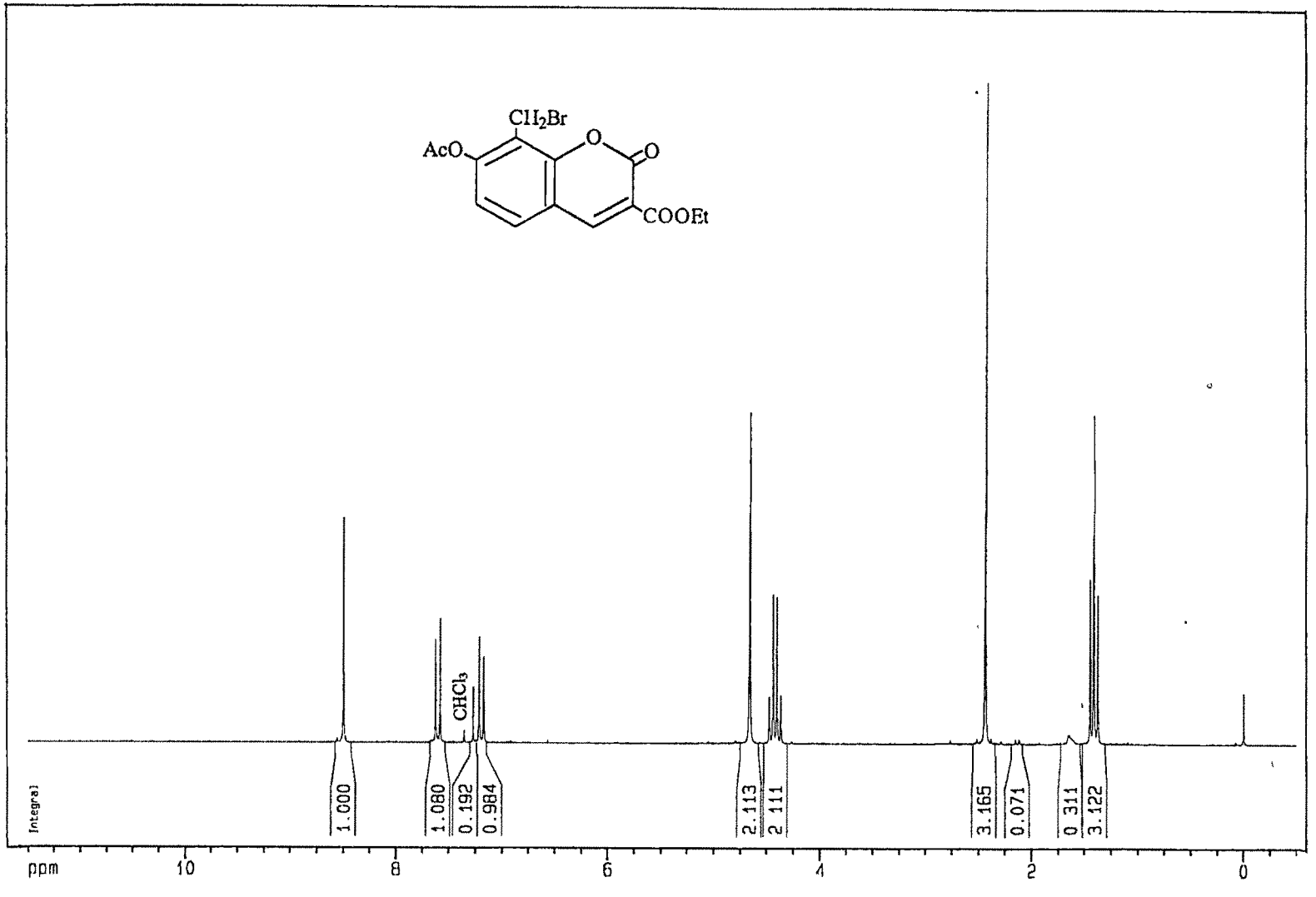
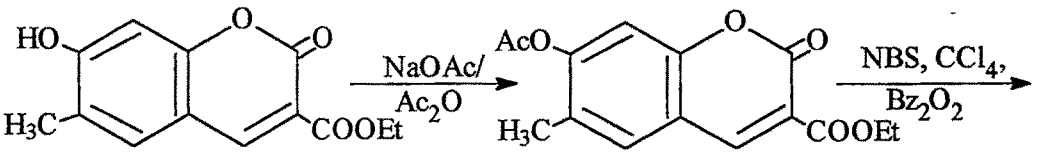
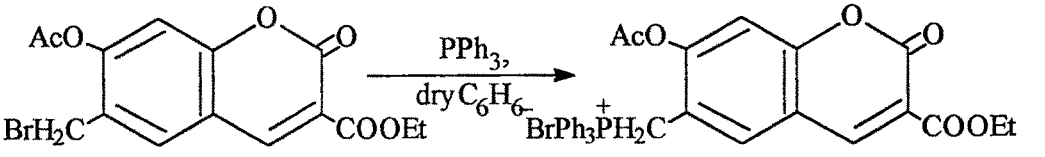

ClI2Br
AcO
O
O
COOEt
CHCl3
Integral
1.000
1.080
0.192
0.984
2.113
2.111
3.165
0.071
0.311
3.122
ppm
10
8
6
4
2
0

Fig. III.1.2

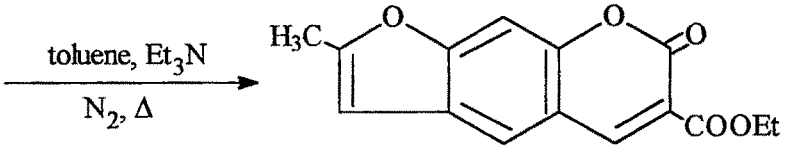
Scheme III.1.7



31 32



33 34



35

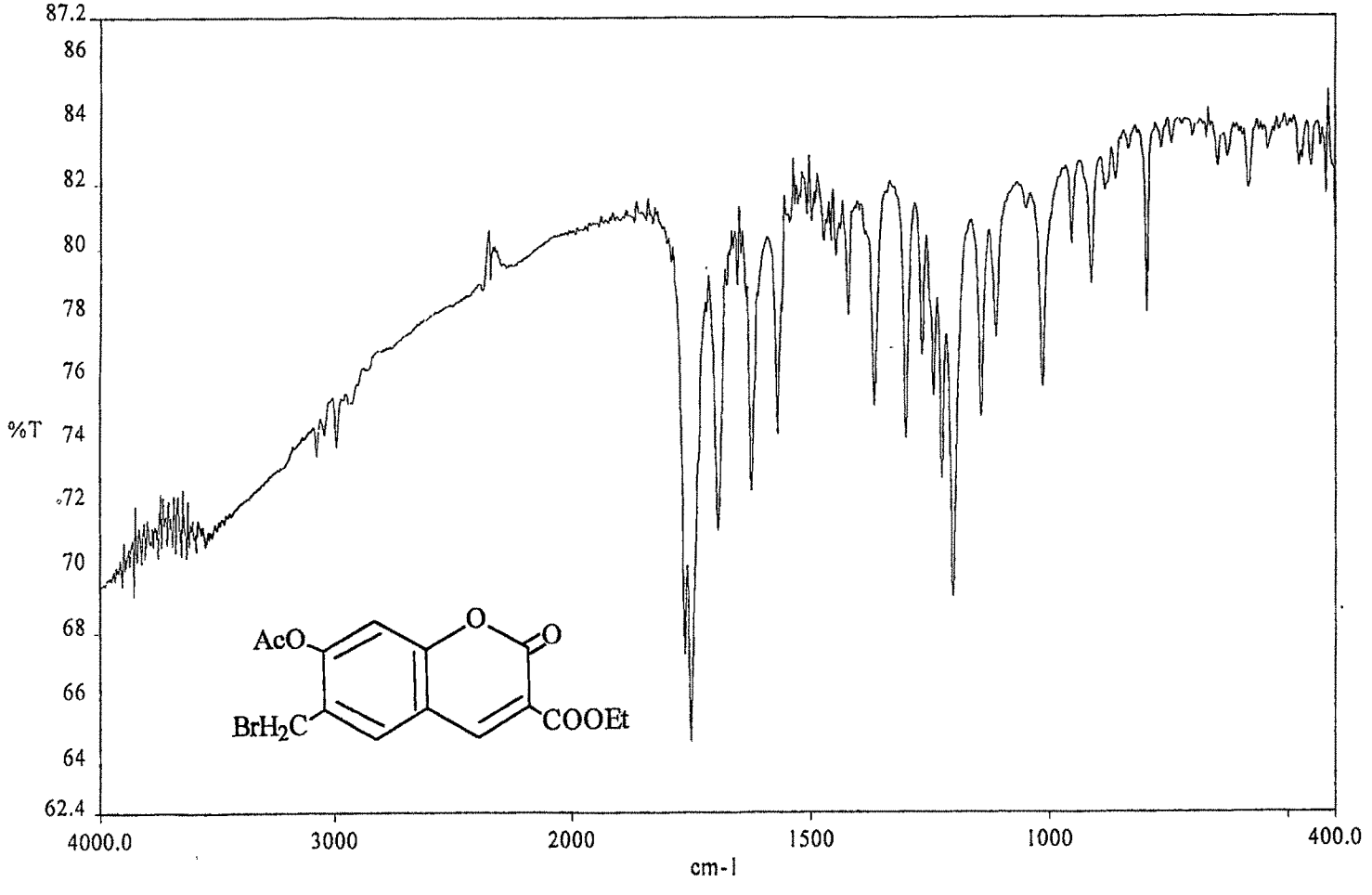

87.2
86
84
82
80
78
76
%T 74
72
70
68
66
64
62.4
4000.0
3000
2000
1500
1000
400.0
cm-1
AcO
O
O
BrH2C
COOEt

Fig. III.1.3

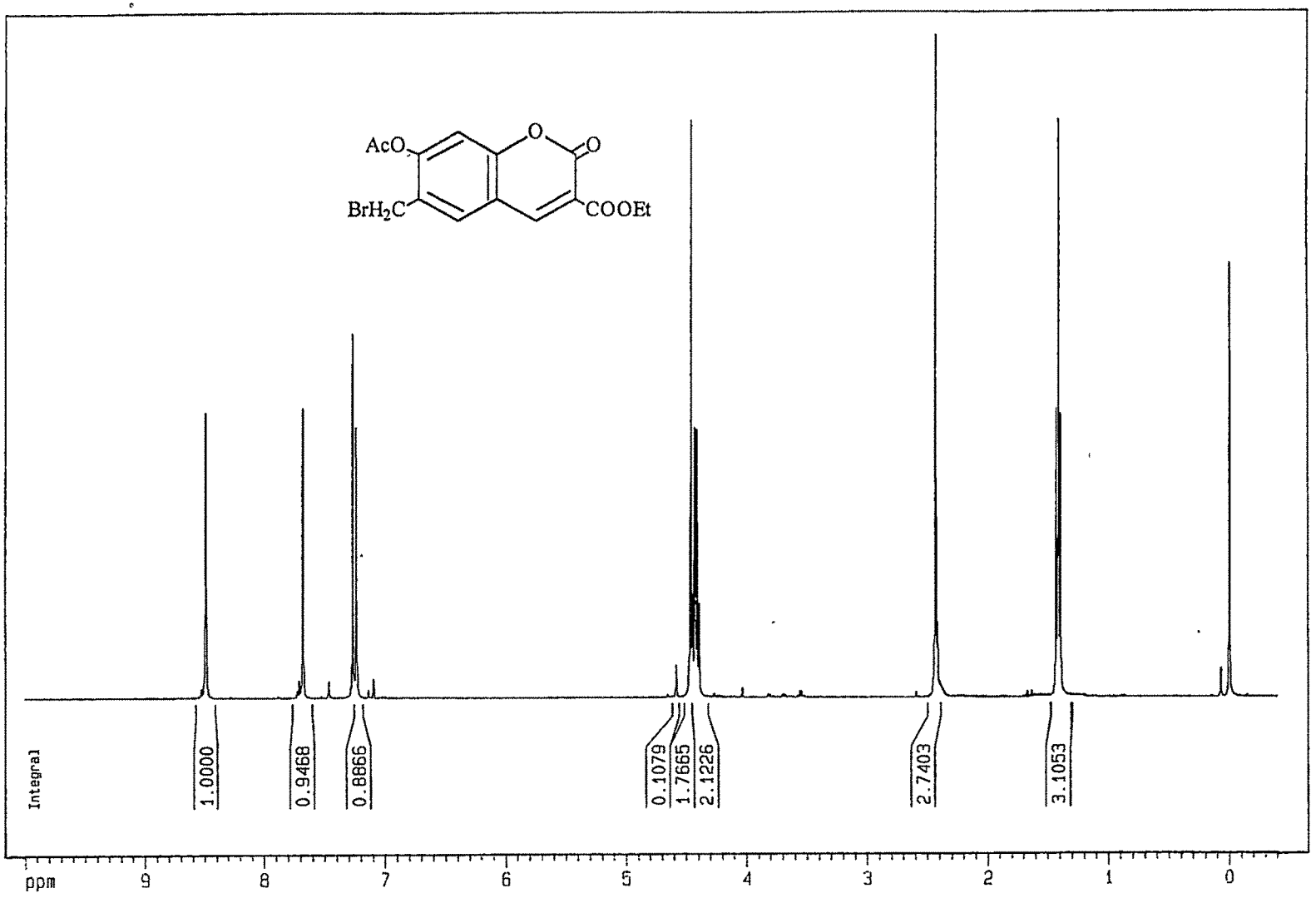

AcO
O
O
BrH2C
COOEt
Integral
1.0000
0.9468
0.8866
0.1079
1.7665
2.1226
2.7403
3.1053
ppm
9
8
7
6
5
4
3
2
1
0

Fig. III.1.4

of N_2 gave ethyl-2-methylfuro (3,2-g)benzopyran-7H-one-6-carboxylate (35). Its IR spectrum in KBr exhibited two bands at 1751 and 1700cm^{-1} for >CO of lactone and ester respectively **[Fig. III.1.5]** while the PMR in $CDCl_3$ showed signals at δ 1.45, a triplet for three methyl group protons of ester at C-6; a singlet at 2.45 for three methyl group protons at C-2; a quartet appeared at 4.40 for two methylene protons of ester at C-6; a singlet at 6.45 for proton at C-3; two singlets obtained at 7.35 and δ 7.65 for protons at C-4 and C-9 and a singlet for proton C-5 at 8.50. **[Fig. III.1.6]**

Synthesis of 2-methyl-6-acetylfuro(2,3-h)benzopyran-5H-one (120) was achieved by condensing 2,4-dihydroxy-3-methylbenzaldehyde with ethylacetoacetate in pyridine using piperidine to afford 7-hydroxy-3-acetyl-8-methylbenzopyran-2H-one (36), which on acetylation furnished 7-acetoxy-3-acetyl-8-methylbenzopyran-2H-one (37). **37** on bromination with NBS using a pinch of benzoyl peroxide as an initiator in chloroform under tungsten lamp yielded 7-acetoxy-3-acetyl-8-bromomethylbenzopyran-2H-one (38). **[Scheme III.1.8]** Its structure was established on the basis of elemental analysis, IR and PMR. The IR band at 1700cm^{-1} is for >CO of lactone overlapped with >CO of -OAc and the band at 1666cm^{-1} is due to >CO of acetyl group. **[Fig. III.1.7]** while the PMR spectrum showed signals in $CDCl_3$ at δ 2.30, a singlet for three methyl group protons of -$COCH_3$ at C-3; a singlet at 2.40 for three methyl group protons of -$OCOCH_3$ at C-7; another singlet at 4.65 for two methylene protons of -CH_2Br at C-8; two doublets appeared at 7.20 and 7.55 for protons at C-6 and C-5 and a singlet for proton C-4 at 8.50. **[Fig. III.1.8]** **38** on reaction with triphenylphosphine in dry benzene gave 7-acetoxy-3-acetyl-8-bromotriphenyl-phosphoniumbenzopyran-2H-one (39), which insitu refluxed with dry toluene and triethylamine under the atmosphere of nitrogen yielded 2-methyl-6-acetylfuro(2,3-h)benzopyran-5H-one (120). Its structure was confirmed by TLC comparison and mmp.

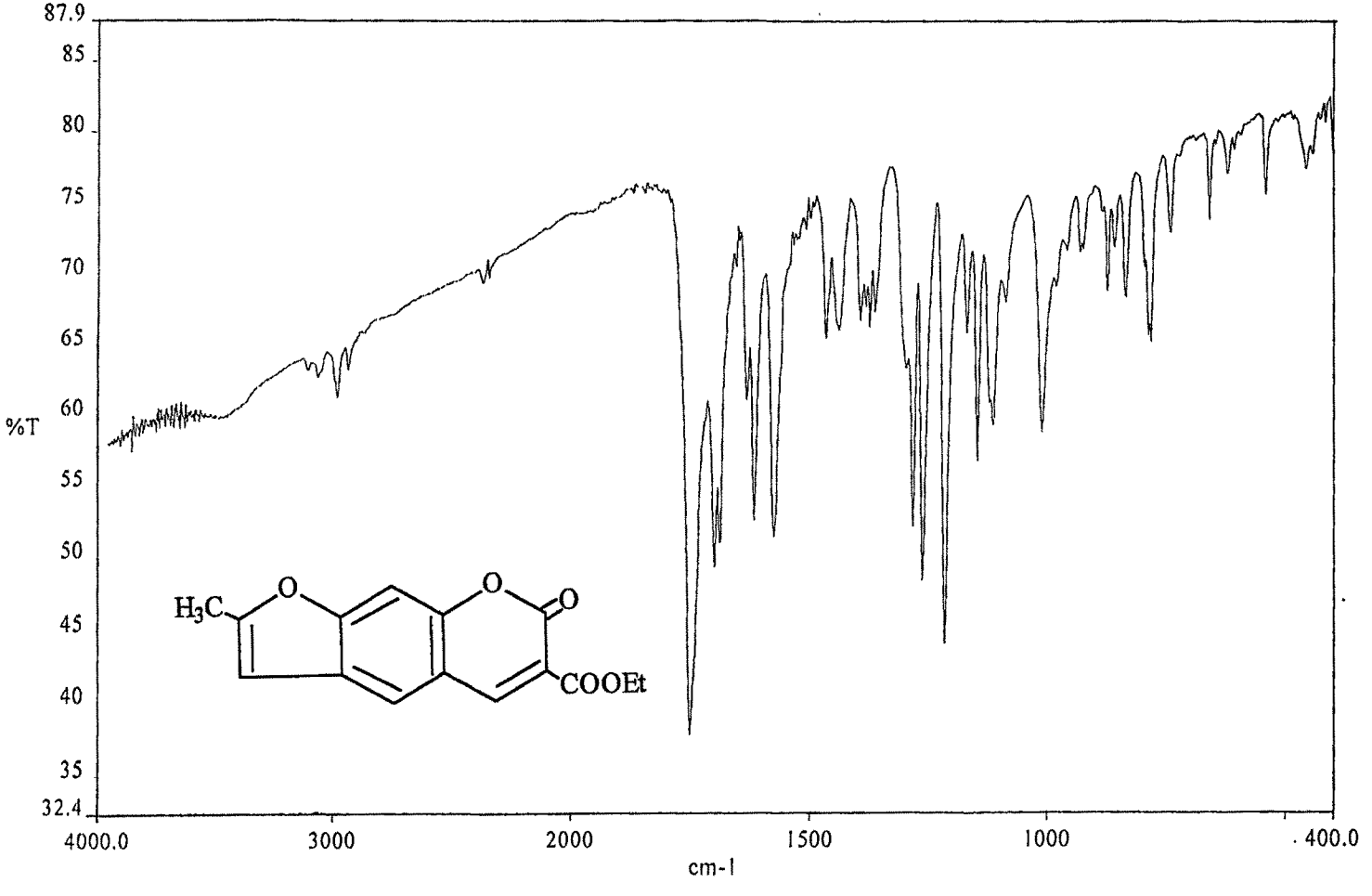

87.9
85
80
75
70
65
60
55
50
45
40
35
32.4
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
H3C
O
O
O
COOEt

Fig. III.1.5

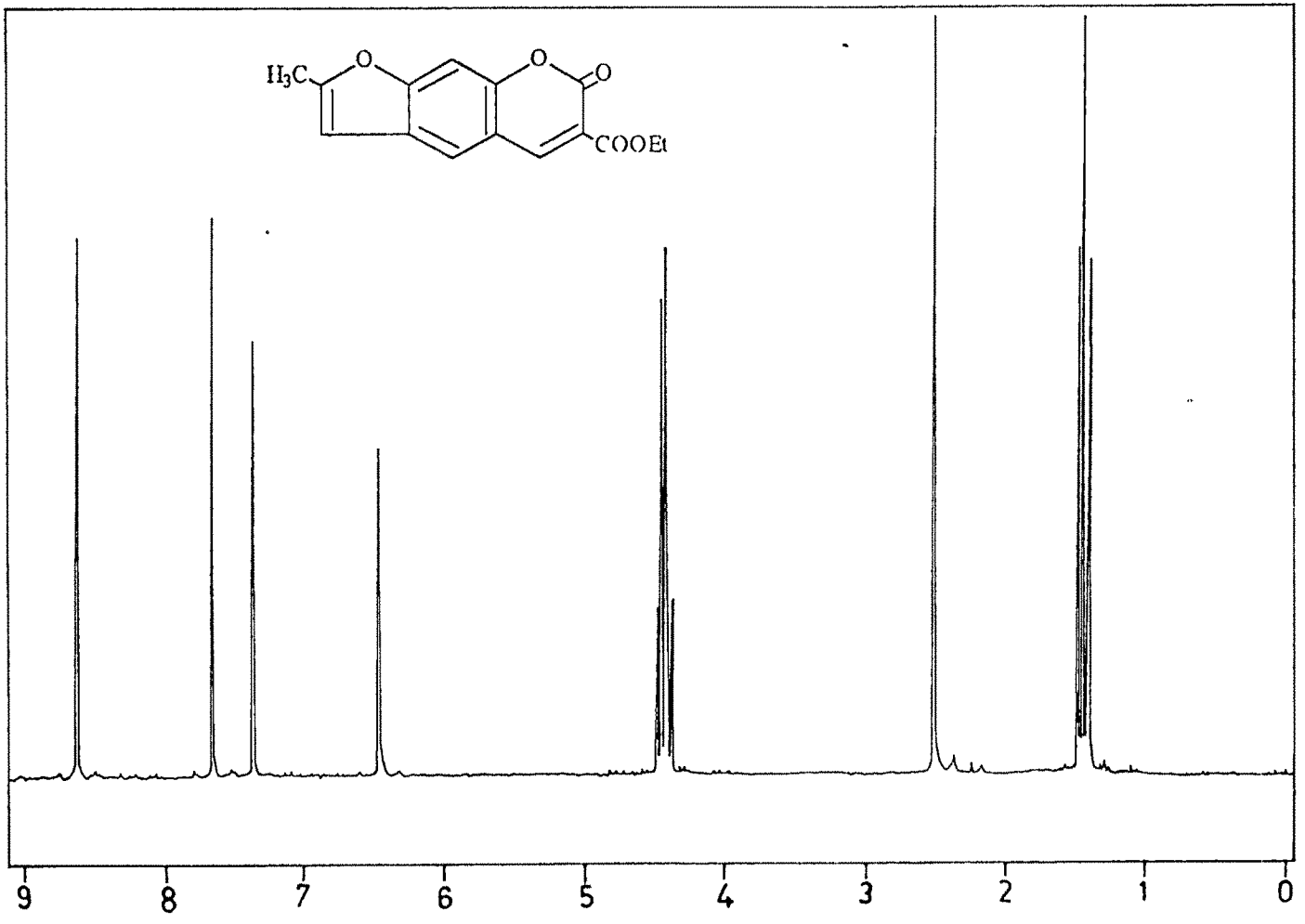


Fig. III.1.6

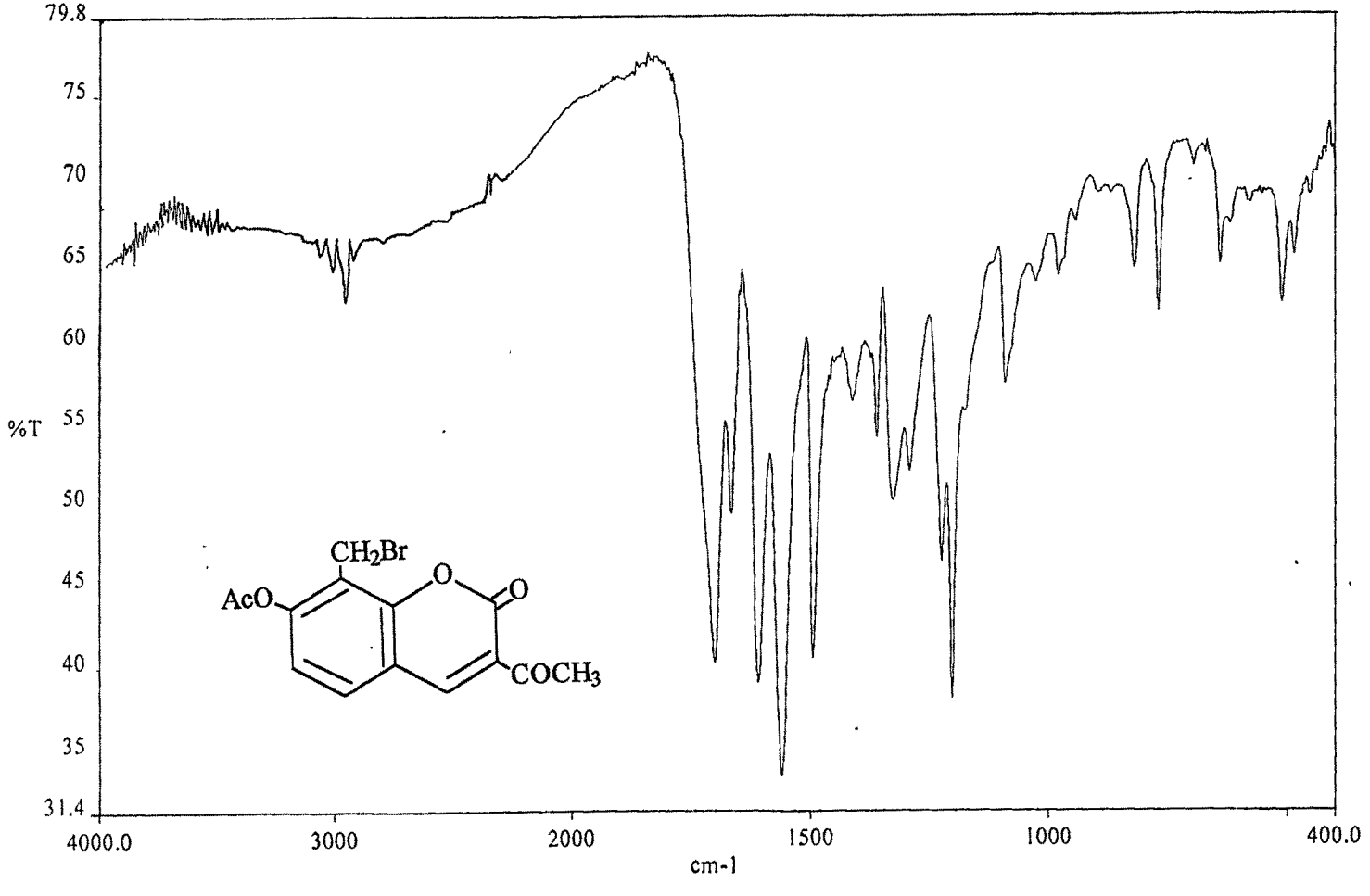

79.8
75
70
65
60
55
50
45
40
35
31.4
%T
4000.0
3000
2000
1500
1000
400.0
cm-1
CH2Br
O
O
AcO
COCH3

Fig. III.1.7

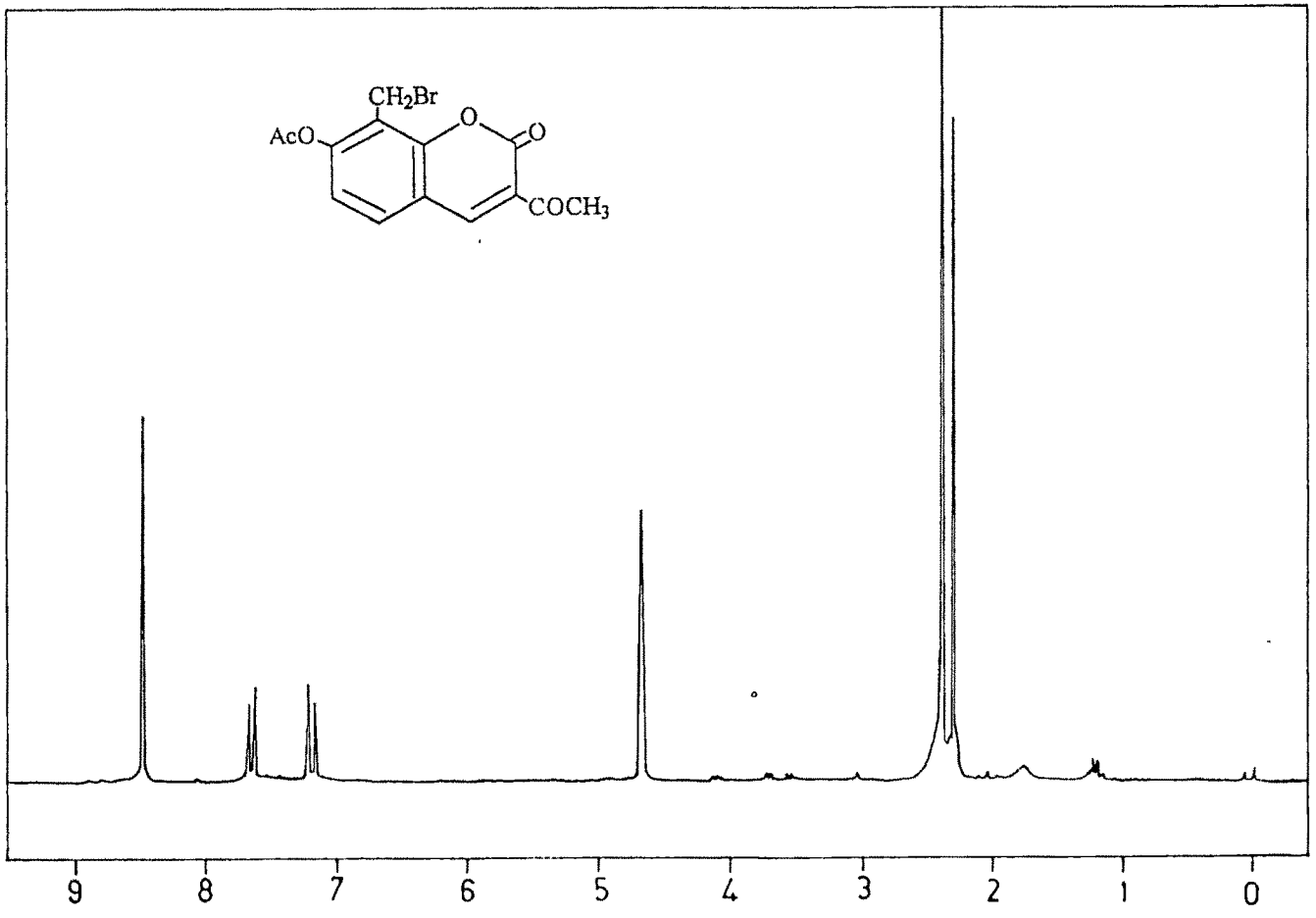
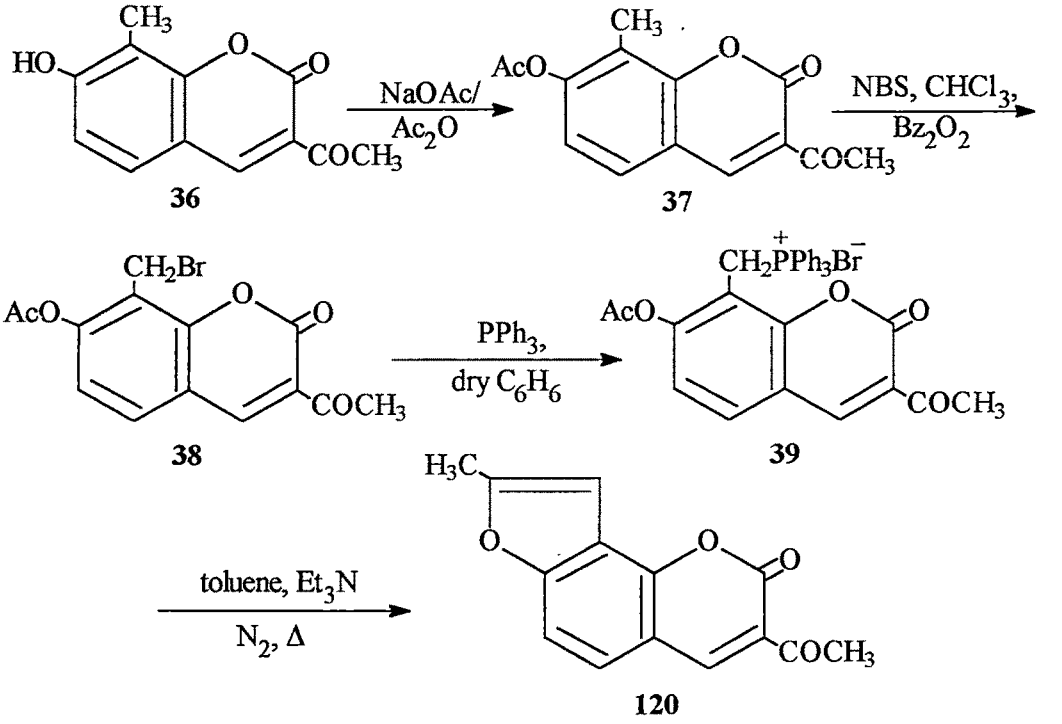


Fig. III.1.8

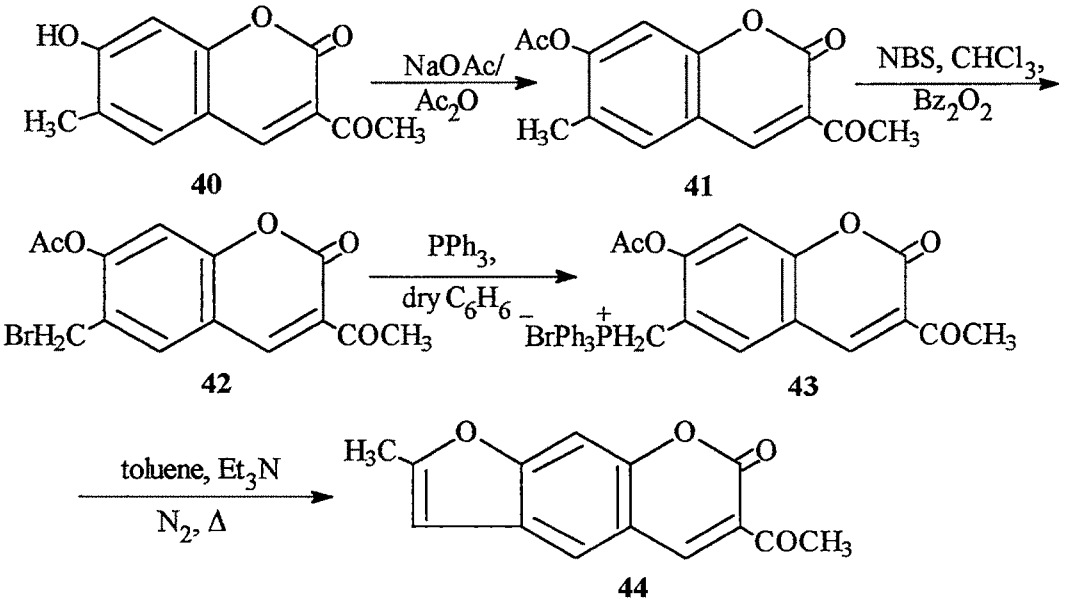
2-Methyl-6-acetylfuro(3,2-g)benzopyran-7H-one (44) was prepared by first condensing 2,4-dihydroxy-5-methylbenzaldehyde with ethylacetoacetate in dry pyridine and piperidine to get 7-hydroxy-3-acetyl-6-methylbenzopyran-2H-one (40), which was acetylated with acetic anhydride and anhydrous sodium acetate to afford 7-acetoxy-3-acetyl-6-methylbezopyran-2H-one (41). **41** when reacted with NBS and benzoyl peroxide in chloroform under 200W-tungsten bulb yielded 7-acetoxy-3-acetyl-6-bromomethylbezopyran-2H-one (42). **42** on reaction with triphenylphosphine in dry benzene gave the corresponding phosphonium salt **43**, which was suspended in dry toluene and triethylamine base under nitrogen atmosphere to give linear furocoumarin **44**. **[Scheme III.1.9]** Its structure was established by elemental analysis, IR spectrum which showed two absorption bands in KBr at 1727 and 1674cm^{-1} due to >CO of lactone and acetyl group **[Fig. III.1.9]** and PMR signals in $CDCl_3$ appeared at δ 2.50, a singlet for three methyl group protons at C-2; a singlet at 2.75 for three methyl group protons of -$COCH_3$ at C-6; a singlet at 6.45 for proton at C-3; two singlets appeared at 7.40 and 7.65 for protons at C-4 and C-9 and singlet at 8.55 for proton C-5. **[Fig. III.1.10]**

Scheme III.1.8



36 37 38 39 120

Scheme III.1.9



40 41 42 43 44

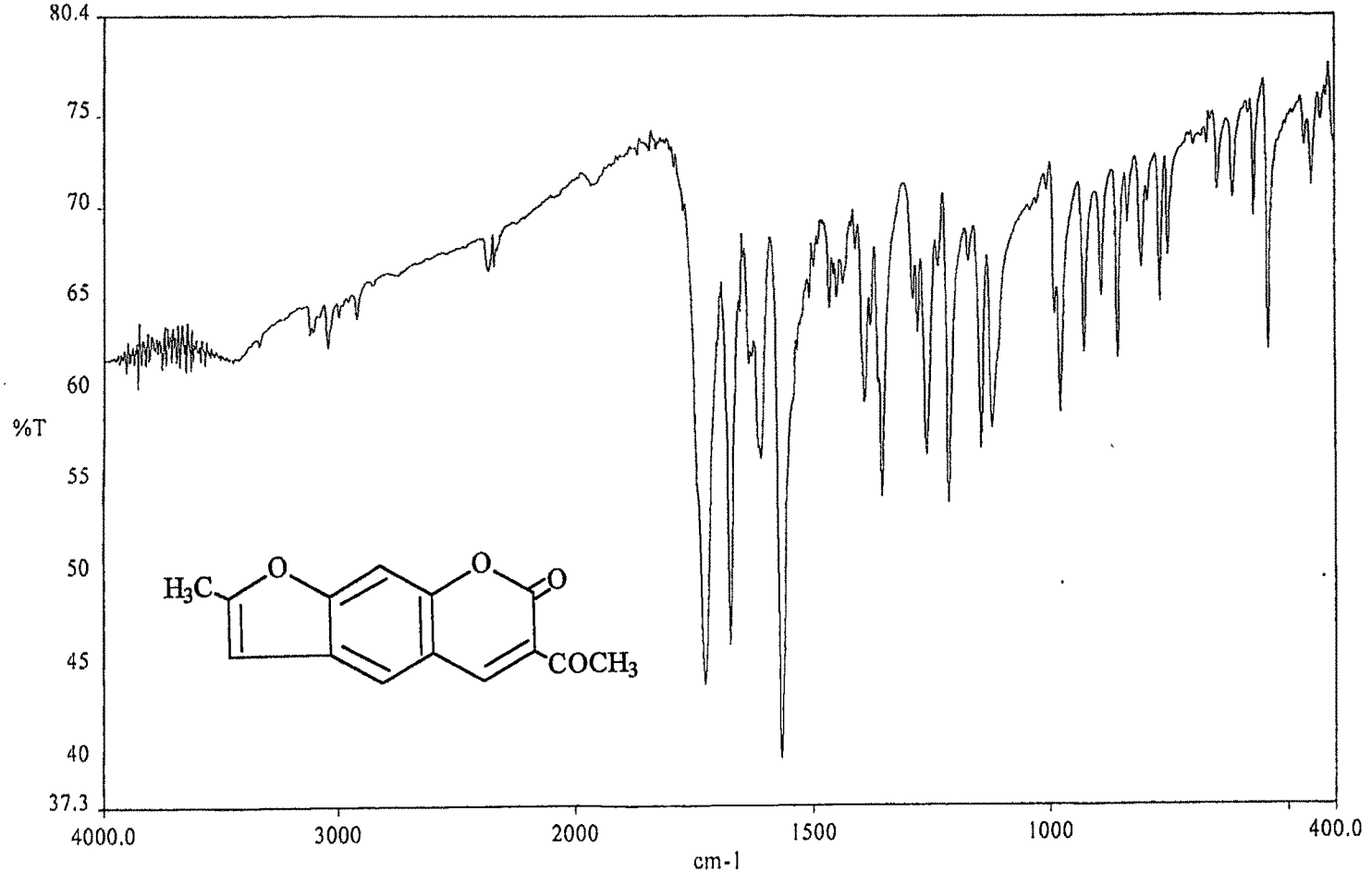

80.4
75
70
65
60
%T
55
50
45
40
37.3
4000.0
3000
2000
1500
1000
400.0
cm-1
H3C
O
O
O
COCH3

Fig. III.1.9

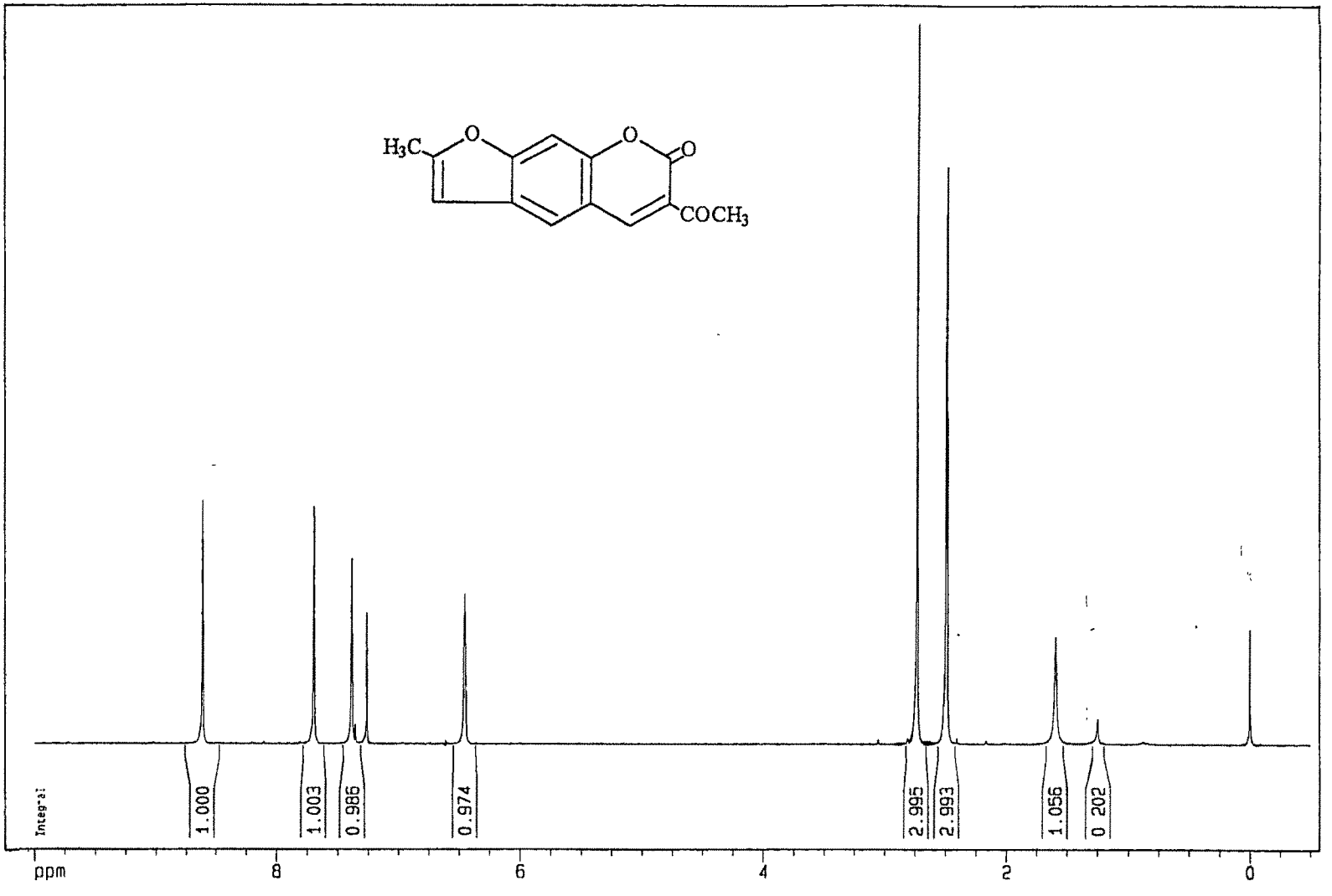

H3C
O
O
O
COCH3
Integral
1.000
1.003
0.986
0.974
2.995
2.993
1.056
0.202
ppm
8
6
4
2
0

Fig. III.1.10

EXPERIMENTAL

^{1}H-NMR spectra were recorded on Bruker 200MHz or Perkin-Elmer 90MHz spectrophotometer. Chemical shifts are relative to tetramethylsilane. Infrared spectra were recorded on Perkin-Elmer FT-IR spectrometer (Spectrum RX 1). Melting points were obtained by open capillary method and are uncorrected. Elemental analyses were carried out on Perkin-Elmer C,H,N,S analyzer (Model 2400).

Ethyl-7-hydroxy-8-methylbenzopyran-2H-one-3-carboxylate (27):

A mixture of 2,4-dihydroxy-3-methylbenzaldehyde (5g, 32.9mmol) in dry pyridine (5ml), piperidine (0.3ml, 3.5mmol) and diethylmalonate (5.3ml, 32.9mmol) was reacted at 50-60°C for 24h. The reaction mixture then poured into cold dilute HCl to obtain solid, which was recrystallized from ethanol as pale yellow needles (6.5g, 79.7%), m.p. 251°C.

Analysis	:	Found	:	C, 62.81%; H, 4.72%
$C_{13}H_{12}O_5$	:	Requires	:	C, 62.90%; H, 4.84%

Ethyl-7-acetoxy-8-methylbenzopyran-2H-one-3-carboxylate (28):

A homogeneous mixture of ethyl-7-hydroxy-8-methylbenzopyran-2H-one-3-carboxylate (5g, 20.1mmol) and anhydrous sodium acetate (15g, 0.18mole) in acetic anhydride (8ml, 78.4mmol) was heated at 100°C on a steambath for 6h. The reaction contents were added in to cold water to get solid, which was filtered off, dried and recrystallized from ethanol as colourless needles (4.8g, 82%), m.p. 126°C.

Analysis	:	Found	:	C, 61.97%; H, 4.71%
$C_{15}H_{14}O_6$	:	Requires	:	C, 62.06%; H, 4.83%

Ethyl-7-acetoxy-8-bromomethylbenzopyran-2H-one-3-carboxylate (29):

Ethyl-7-acetoxy-8-methylbenzopyran-2H-one-3-carboxylate (2.4g, 8.3mmol) in carbontetrachloride (100ml) was added to freshly prepared N-bromosuccinimide (1.5g, 8.3mmol) and a pinch of benzoyl peroxide as an initiator. The contents were refluxed under 200W-tungsten lamp for 16h. The separated succinimide was filtered hot and excess of CCl_4 distilled off to obtain product, which was recrystallized from ethanol as pale yellow needles (2.3g, 75.4%), m.p. 154°C.

Analysis : Found : C, 48.62%; H, 3.43%

$C_{15}H_{13}O_6Br$: Requires : C, 48.78%; H, 3.52%

IR(KBr) cm^{-1} : 3070, 2991, 2952, 1758, 1711, 1692, 1601, 1495, 1240

Ethyl-2-methylfuro(2,3-h)benzopyran-5H-one-6-carboxylate (109):

A mixture of ethyl-7-acetoxy-8-bromomethylbenzopyran-2H-one-3-carboxylate (1.5g, 4.1mmol) and triphenylphosphine (1.1g, 4.1mmol) was dissolved in dry benzene (80ml) and kept in refluxing for 6h. Excess benzene was distilled out, which left a yellow solid triphenylphosphonium salt of coumarin **30**. It was suspended in dry toluene (100ml), triethylamine (2.0ml, 19.8mmol) was added and refluxed under the atmosphere of N_2 for 17h. The reaction mixture was filtered hot and toluene was distilled out. The solid obtained was purified by column chromatography using benzene as an eluent to give **109**, which recrystallized from ethanol as yellow crystals (0.95g, 86.3%), m.p. 143°C.

Analysis : Found : C, 66.02%; H, 4.38%

$C_{15}H_{12}O_5$: Requires : C, 66.17%; H, 4.41%

Ethyl-7-hydroxy-6-methylbenzopyran-2H-one-3-carboxylate (31):

2,4-Dihydroxy-5-methylbenzaldehyde (5g, 32.9mmol) in dry pyridine (5ml) was left at 50-60°C for 24h with diethylmalonate (5.3ml, 32.9mmol) and piperidine (0.3ml, 3.5mmol). The mixture was poured into cold dilute HCl to

get solid, which recrystallized finally from ethanol as yellow needles (6.4g, 78.5%), m.p. 150-1°C.

Analysis : Found : C, 63.11%; H, 4.70%

$C_{13}H_{12}O_5$: Requires : C, 62.90%; H, 4.84%

Ethyl-7-acetoxy-6-methylbenzopyran-2H-one-3-carboxylate (32):

A mixture of ethyl-7-hydroxy-6-methylbenzopyran-2H-one-3-carboxylate (5g, 20.1mmol) in acetic anhydride (8ml, 78.4mmol) and anhydrous sodium acetate (15g, 0.18mole) was heated at 100°C for 6h. It was then poured into ice cold water. The product was filtered, dried and recrystallized from ethanol as colourless needles (4.7g, 80.3%), m.p. 159°C.

Analysis : Found : C, 62.35%; H, 4.97%

$C_{15}H_{14}O_6$: Requires : C, 62.06%; H, 4.83%

Ethyl-7-acetoxy-6-bromomethylbenzopyran-2H-one-3-carboxylate (33):

Ethyl-7-acetoxy-6-methylbenzopyran-2H-one-3-carboxylate (2.0g, 6.9mmol) in distilled CCl_4 (90ml) was added to N-bromosuccinimide (1.2g, 6.9mmol) and a pinch of benzoyl peroxide. The mixture was refluxed for 16h under irradiation with 200W-tungsten lamp, which was then filtered hot to remove unwanted succinimide and CCl_4 was distilled off. The product obtained was recrystallized from ethanol (1.9g, 74.8%), m.p. 217°C.

Analysis : Found : C, 48.47%; H, 3.39%

$C_{15}H_{13}O_6Br$: Requires : C, 48.78%; H, 3.52%

IR(KBr) cm^{-1} : 3076, 2989, 2948, 1764, 1751, 1695, 1620, 1243

Ethyl-2-methylfuro(3,2-g)benzopyran-7H-one-6-carboxylate (35):

A solution of ethyl-7-acetoxy-6-bromomethylbenzopyran-2H-one-3-carboxylate (1.2g, 3.2mmol) in dry benzene (80ml) and triphenylphosphine (0.85g, 3.2mmol) was refluxed for 6h. Excess of benzene was distilled out to get triphenylphosphonium salt of coumarin **34**, which was suspended as such in

boiling dry toluene (100ml) and triethylamine (2.0ml, 19.8mmol) under the stream of nitrogen for 17h. It was filtered hot and excess of toluene was distilled to yield solid, which was purified by column chromatography using benzene and recrystallized the product **35** with ethanol as yellow needles (0.8g, 90.9%), m.p. 164°C.

Analysis : Found : C, 66.03%; H, 4.36%

$C_{15}H_{12}O_5$: Requires : C, 66.17%; H, 4.41%

IR(KBr) cm^{-1} : 3068, 2981, 2942, 1751, 1700, 1616, 1575, 1230, 1148

7-Hydroxy-3-acetyl-8-methylbenzopyran-2H-one (36):

A mixture of 2,4-dihydroxy-3-methylbenzaldehyde (5g, 32.9mmol) in dry pyridine (5ml), piperidine (0.3ml, 3.5mmol) and ethylacetoacetate (4.3ml, 33.0mmol) was left at 50-60°C. The product, which obtained on usual workup, was recrystallized from ethanol as yellow needles. (5.5g, 76.7%), m.p. 265°C.

Analysis : Found : C, 66.38%; H, 4.86%

$C_{12}H_{10}O_4$: Requires : C, 66.05%; H, 4.59%

7-Acetoxy-3-acetyl-8-methylbenzopyran-2H-one (37):

A homogeneous mixture of 7-hydroxy-3-acetyl-8-methylbenzopyran-2H-one (5g, 22.9mmol) and fused sodium acetate (15g, 0.18mole) was heated in acetic anhydride (8ml, 78.4mmol) on steambath for 6h. The mixture was then dropped into cold water and separated solid was filtered, dried to obtain **37** and recrystallized from ethanol as colourless needles (5.0g, 83.3%), m.p. 176-77°C.

Analysis : Found : C, 64.33%; H, 4.51%

$C_{14}H_{12}O_5$: Requires : C, 64.61%; H, 4.62%

7-Acetoxy-3-acetyl-8-bromomethylbenzopyran-2H-one (38):

To a solution of 7-acetoxy-3-acetyl-8-methylbenzopyran-2H-one (2.0g, 7.7mmol) in distilled chloroform (70ml), NBS (1.4g, 7.7mmol) and a pinch of benzoyl peroxide were added and refluxed under tungsten lamp for 17h. Excess

$CHCl_3$ was distilled out after the reaction and obtained solid was boiled with water to remove succinimide. The product **38** was filtered, dried and recrystallized from excess of ethanol as yellow needles (1.9g, 73.0%), m.p. 185°C.

Analysis : Found : C, 49.78%; H, 3.14%

$C_{14}H_{11}O_5Br$: Requires : C, 49.56%; H, 3.24%

IR(KBr) cm^{-1} : 3075, 2988, 2946, 1700, 1666, 1608, 1495, 1230

2-Methyl-6-acetylfuro(2,3-h)benzopyran-5H-one (120):

A mixture of 7-acetoxy-3-acetyl-8-bromomethylbenzopyran-2H-one (1.0g, 2.9mmol) in dry benzene (100ml) and triphenylphosphine (0.8g, 2.9mmol) was refluxed for 6h. Excess of benzene was distilled out and phosphonium salt **39**, thus obtained was suspended in dry toluene (110ml), triethylamine (2.0ml, 19.8mmol) was added and refluxed under the atmosphere of N_2 for 17h. The product, which obtained on usual work up was purified by column chromatography using benzene as eluent and recrystallized from ethanol as yellow needles (0.62g, 87.3%), m.p. 201°C.

Analysis : Found : C, 69.29%; H, 4.02%

$C_{14}H_{10}O_4$: Requires : C, 69.42%; H, 4.13%

7-Hydroxy-3-acetyl-6-methylbenzopyran-2H-one (40):

A mixture of 2,4-dihydroxy-5-methylbenzaldehyde (5g, 33mmol) in dry pyridine (5ml) was kept with ethylacetoacetate (4.3ml, 33mmol) and piperidine (0.3ml, 3.5mmol) at 50-60°C for 24h. The product, which obtained on usual work up was recrystallized from ethanol as yellow needles (5.3g, 73.9%), m.p. 209°C.

Analysis : Found : C, 66.42%; H, 4.35%

$C_{12}H_{10}O_4$: Requires : C, 66.05%; H, 4.59%

7-Acetoxy-3-acetyl-6-methylbenzopyran-2H-one (41):

A homogenous mixture of 7-hydroxy-3-acetyl-6-methylbenzopyran-2H-one (5g, 25.8mmol) and anhydrous sodium acetate (15g, 0.18mole) in acetic anhydride (8ml, 78.4mmol) was heated at 100°C for 6h. The contents were added into cold water to get solid, which was filtered off, dried and recrystallized from ethanol as colourless needles (4.8g, 80.5%), m.p. 209°C.

Analysis : Found : C, 64.41%; H, 4.49%

$C_{14}H_{12}O_5$: Requires : C, 64.61%; H, 4.62%

7-Acetoxy-3-acetyl-6-bromomethylbenzopyran-2H-one (42):

7-Acetoxy-3-acetyl-6-methylbenzopyran-2H-one (2.0g, 7.7mmol) and freshly prepared NBS (1.4g, 7.9mmol) were dissolved in chloroform (80ml) using benzoyl peroxide and refluxed under tungsten bulb for 17h. The product, which obtained on usual work up was recrystallized from excess of ethanol as yellow crystalline solid (1.7g, 65.4%), m.p. 194°C.

Analysis : Found : C, 49.81%; H, 3.47%

$C_{14}H_{11}O_5Br$: Requires : C, 49.56%; H, 3.24%

2-Methyl-6-acetylfuro(3,2-g)benzopyran-7H-one (44):

A mixture of 7-acetoxy-3-acetyl-6-bromomethylbenzopyran-2H-one (1.0g, 2.9mmol) and triphenylphosphine (0.8g, 2.9mmol) was dissolved in dry benzene (90ml) and refluxed for 6h. Then benzene was distilled out to obtain Wittig salt **43**, which was suspended in dry toluene (100ml), triethylamine (2.0ml, 19.8mmol) was added and refluxed under the atmosphere of N_2 for 17h. After usual work up, product was purified by column chromatography using benzene and recrystallized from ethanol as yellow needles (0.6g, 84.5%), m.p. 247°C.

Analysis : Found : C, 69.23%; H, 4.21%

$C_{14}H_{10}O_4$: Requires : C, 69.42%; H, 4.13%

IR(KBr) cm^{-1} : 3051, 2986, 2941, 1727, 1624, 1610, 1220, 1146

REFERENCES

1. G. Wittig and G. Geissler, Ann., **44**, 580 (1953); Chem. Abstr., **48**, 7566h (1954).
2. R. S. Tewari and K. C. Gupta, Ind. J. Chem., **14B**, 419 (1976); R. S. Tewari and S. C. Chaturvedi, Synthesis, 616 (1978).
3. H. Bestmann, G. Schmid and D. Sandmeier, Angew. Chem., **88**, 92 (1976); Chem. Abstr., **84**, 89946t (1976).
4. H. O. House, Modern synthetic Reactions, 2nd Ed., W. A. Benjamin Inc., London (1972).
5. Maercker, Organic Reactions, John Wiley and Sons Inc., New York, **14**, 270 (1965).
6. Hercouet and M. Le Corre, Tetrahedron, **37**, 2861 (1981).
7. Hercouet, M. Le Corre and Y. Le Floch, Synthesis, 597 (1982).
8. W. Clark-Sill, C. Gennari, J. Nogueg and D. Pearson, J. Am. Chem. Soc., **106**, 260 (1984).
9. A. McKittrick, R. Scannell and R. Stevenson, J. Chem. Soc.: Perkin Trans. I, 3017 (1982).
10. V. Ahluwalia, R. Gupta, M. Grover, I. Mukherjee and C. H. Khanduri, Ind. J. Chem., **27B**, 1138 (1988).
11. D. N. Nicolaides, C. Bezergiannidou-Balouctsi, K. E. Litinas, E. Malamidou-Xenikaki, D. Mentzafos and A. Terzis, J. Chem. Res.(S), 108 (1993).
12. Y. R. Lee, Tetrahedron, **51**, 3087 (1995).
13. M. C. Pirrung and Y. R. Lee, Tetrahedron Lett., **35**, 6231 (1994).
14. R. S. Kondedeshmukah and M. V. Paradkar, Ind. J. Chem., **32B**, 1159 (1993).
15. R. S. Mali and P. K. Sandhu, J. Chem. Res.(S), 148 (1996).
16. S. P. Chandratre, Ph. D. Thesis, M. S. Univ. of Baroda, Baroda, 122 (1989).

Chapter III : Section 2

Synthesis of Furobenzopyrones by Oxypalladation

INTRODUCTION

This section mainly comprises the synthesis of furobenzopyrones using oxypalladation as the key step. In the literature, metal complexes were often found to be utilized in the synthesis of heterocycles under mild conditions. Among those, palladium complexes undoubtedly lie in a unique position due to their versatility and reactivity[1-4]. The reactivity of palladium complexes basically depends on their valency. Fundamentally palladium(II) acts as a Lewis acid and due to its inherent oxidizing ability it is generally reduced to Pd(0) during the reaction.

The discovery of Wacker process using $PdCl_2$ catalyst with $CuCl_2$ and O_2 to produce acetaldehyde from ethylene has opened up the area of functionalization of ethylene through palladium catalyzed oxidation[3-6]. Modern organic chemistry of palladium has made rapid progress since the invention of the Wacker process. At present a variety of organic reactions induced or catalyzed by palladium compounds offer useful synthetic approaches for organic compounds[1,2]. The important reactions among them are vinylacetate from ethylene in acetic acid[7] and 1,4-diacetoxy-2-butene from butadiene[8].

The sequential oxidation and reduction reaction in the Wacker process constitutes a catalytic cycle is given below.

$$CH_2{=}CH_2 + H_2O + PdCl_2 \longrightarrow CH_3\text{-}CH{=}O + Pd(0) + 2HCl$$

$$Pd(0) + 2CuCl_2 \longrightarrow PdCl_2 + 2CuCl$$

$$2CuCl + 2HCl + 0.5O_2 \longrightarrow 2CuCl_2 + H_2O$$

$$CH_2{=}CH_2 + 0.5O_2 \longrightarrow CH_3\text{-}CH{=}O$$

The above Wacker process is carried out in aqueous medium containing HCl. Later Smidt and coworkers[5,6] reported that in general terminal olefins are

converted to methyl ketones rather than aldehydes and also observed it as a unique one step method for the synthesis of ketones from olefins. However, further studies revealed that the oxidation of higher terminal olefins under the same conditions is slow and sometime accompanied by undesired byproducts formed by the chlorination of carbonyl compounds by Copper(II) chloride and isomerization of double bonds[9]. The slow rate of the reaction is partly solved by the addition of suitable organic reagents, which can mix with olefins. The use of acetonitrile, DMSO retarded oxidation due to complex formation. Thus DMF is found to be good for the oxidation, where as the use of acetic acid or higher temperature facilitates isomerization. Best yields are observed with solvent system containing 12-17% water (by volume) in DMF[10] and the rate of cyclization is faster and reaches maximum when Cu/Pd ratio is 1.

In the Wacker process reoxidants are used along with Pd(II) to convert Pd(0) back to Pd(II). Generally Copper(II) chloride or copper(II) salts are employed, as they are good oxidants. But copper(II) chloride produce chlorinated carbonyl compounds along with desired ones. Thus a number of reoxidants have been tried to overcome the problem. Some of the reoxidants are copper(I) chloride, copper(II) nitrate and copper acetate[11]. Moiseer *et al.*[12] introduced benzoquinone for the first time as reoxidant.

INTRAMOLECULAR OXYPALLADATION OF ALKENES

In simple Wacker process of oxidation of olefins, the nucleophile such as -Cl or -OAc in PdX_2 attack olefins coordinated to the metal forming a σ bonded Pd(II) intermediate which on subsequent β-elimination of Pd-H species leads to the products. The intramolecular version of this reaction is useful for the synthesis of heterocyclic compounds in which the nucleophilic attack by a hetero atom leads to intermediate, followed by β-elimination of Pd-H finally results heterocyclic compound which bears a double bond in a stable position via equilibriation. In general $PdCl_2$ appears to afford six membered products

predominantly where as five membered heterocycles are preferred products with $Pd(OAc)_2$[13].

Pd(II) catalyzed oxidations and intramolecular version for various heterocycles have also been studied and reviewed on dienes and as well as on alkynes[14].

Currently Pd salts, complexes are extensively being used for making different heterocyclic compounds. Some of the approaches and mechanism are discussed here.

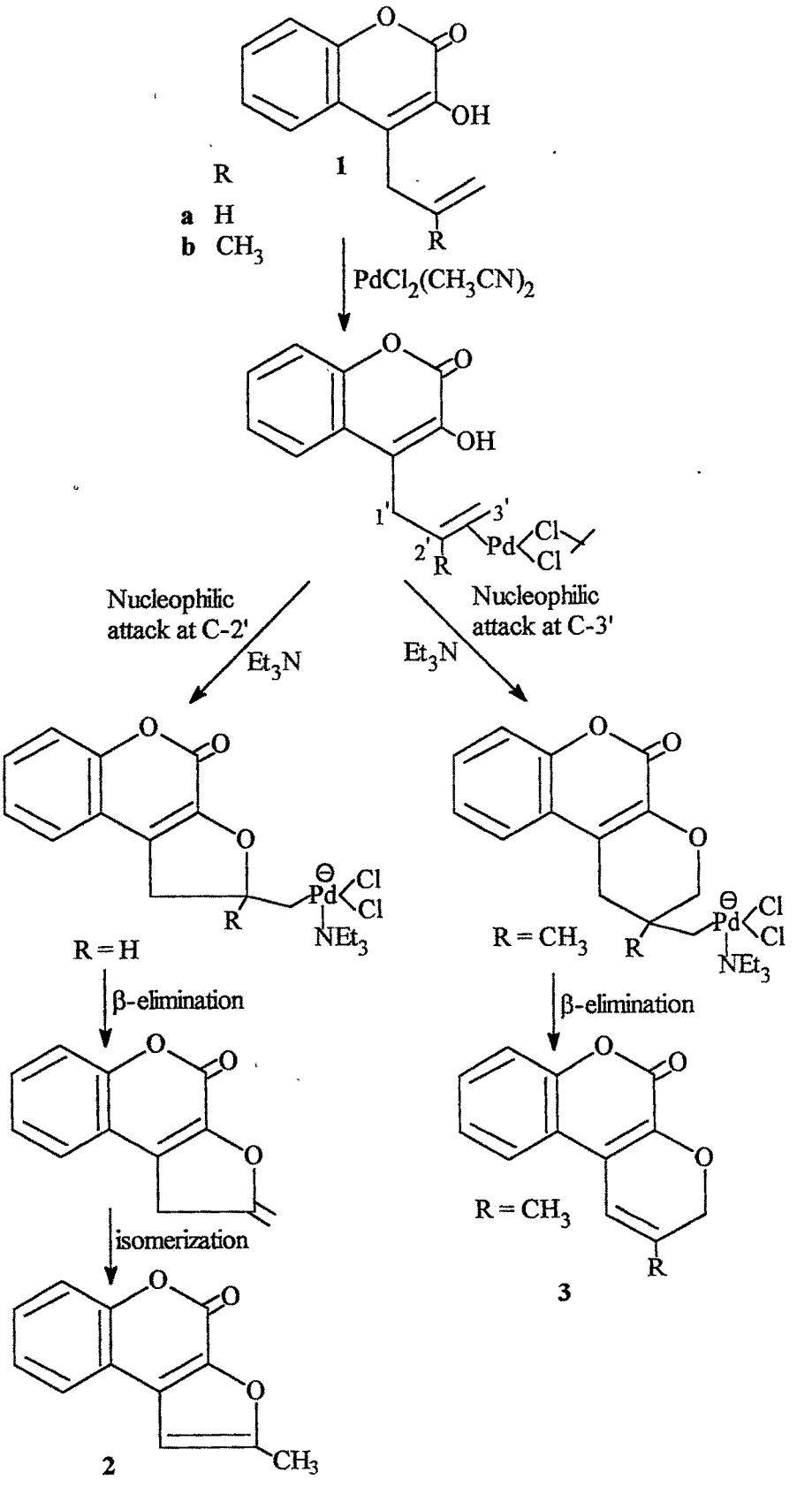
Mitra *et al.*[25] synthesized furo and pyrano coumarins in one step by Pd(II) assisted cyclization of hydroxyallylcoumarins. 4-Allyl-3-hydroxy coumarin (1a) on treatment with stoichiometric amount of $PdCl_2(CH_3CN)_2$ afforded exclusively 2-methyl-4(H)-oxofuro[2,3-c][1]benzopyran (2), while in the case of 3-hydroxy-4-(2-methylallyl)coumarin (1b), it afforded more stable pyranocoumarin 2-methyl-3H-5(H)-oxopyrano[2,3-c][1]benzo- pyran (3) due to lack of a hydrogen atom at C-2′ which is necessary for β-elimination. **[Scheme III.2.1]**

Rao *et al.*[16] achieved the synthesis of 2-methyl-3,7-diphenylfuro (2,3-h) benzopyran-5H-one (6) from 7-hydroxy-4-phenyl-8-(1′-phenylprop-2′-ene) benzopyran-2H-one (4), making sodium salt **5** using dichloro bis(benzonitrile)palladium complex $PdCl_2(PhCN)_2$. **[Scheme III.2.2]**

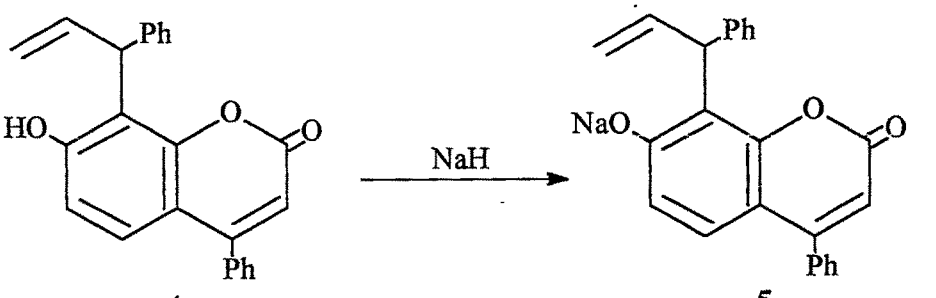
Iyer *et al.*[17] synthesized antijuvenile hormones Precocene-I **8a**, Precocene-II **8b** and other bioactive 2,2-dimethyl-2H-chromenes **8c** by intramolecular oxidative cyclization of 2-isoprenylphenols **7a-c** catalyzed by a palladium(II) salt. **[Scheme III.2.3]**

Mitra *et al.*[18] converted few substituted allyl and allyloxy coumarins in to their carbonyl derivatives using Wacker process in the presence of catalytic amount of Palladium(II) chloride in oxygen atmosphere. Cyclization occurred when a free hydroxyl group is present in adjacent position. **[Scheme III.2.4]**

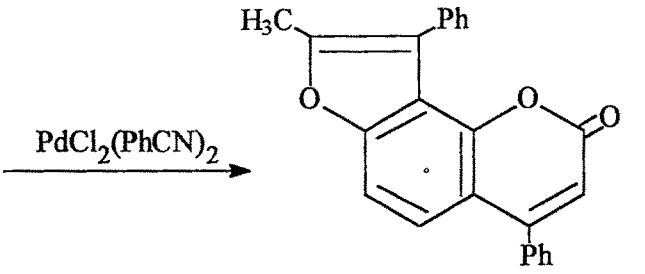
Scheme III.2.1



Scheme III.2.2

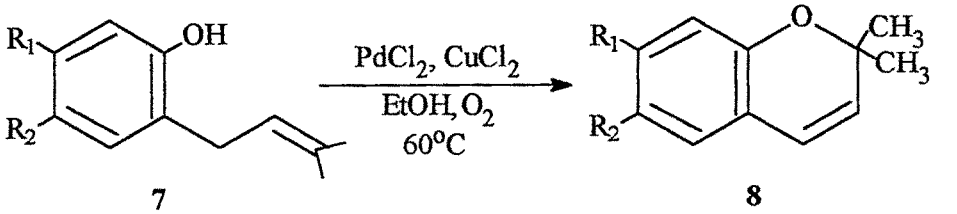


4 5



6

Scheme III.2.3

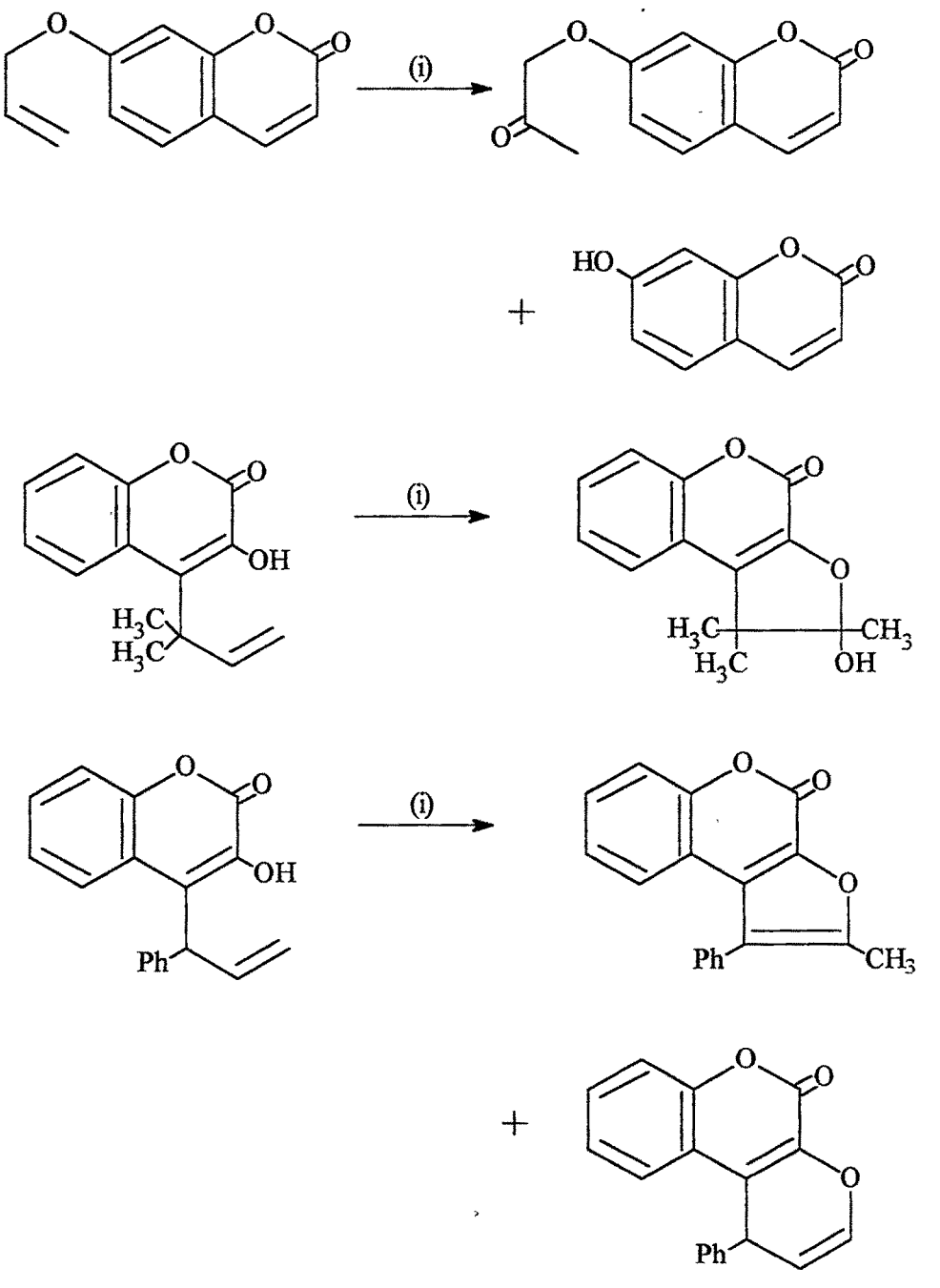


7 8

	R_1	R_2
a	OCH_3	H
b	OCH_3	OCH_3
c	H	OH

	R_1	R_2
a	OCH_3	H
b	OCH_3	OCH_3
c	H	OH

Scheme III.2.4



(i) = $PdCl_2$, $CuCl_2$, O_2, DMF:H_2O, 25^oC, 8h

PRESENT WORK

The present work in this section mainly deals with the oxidation of terminal double bond of allylic function using Wacker technique to synthesize target furobenzopyrones. Two different approaches were followed to effect the double bond to yield desired ones. In the first method palladium chloride in combination with cuprous chloride in the atmosphere of oxygen as used in the Wacker method, was employed. Here cuprous chloride was used in place of cupric chloride to avoid possible nuclear halogenation which helps to convert back the reduced Pd(0) to Pd(II). While in the second method, a freshly prepared p-benzoquinone was used in place of cuprous chloride to oxidize Pd(0) to Pd(II), which is a simple modification, though it was reported[10] earlier but seldom exploited.

The main endeavour of the present work is to study the Wacker oxidation on different benzopyrones and to compare the yields as well as feasibility of the reaction.

3-Methylfurobenzopyrones **3a-c** were prepared by two methods:

(A) *Oxidation by cuprous chloride:*

7-Allyloxybenzopyrone derivatives **9a-c** were subjected to catalytic oxidation in the presence of $PdCl_2$, cuprous chloride and molecular oxygen in aqueous dimethylformamide solution at room temperature with stirring. Mixture of two products was observed to form from TLC, were isolated and confirmed as oxidized 7-acetonyloxybenzopyrone **10a-c** derivatives and second as deallylated starting compound from their elemental analysis and spectral information.

(B) *Oxidation by benzoquinone:*

The oxidation was also carried out with freshly prepared benzoquinone in place of CuCl and O_2. After the reaction was completed, the products **10a-c**

were identified from their TLC, mmp, elemental analysis and spectral information.

Despite the formation of deallylated product it could be observed that the yields of the oxidized products were more pronounced in the case of benzoquinone oxidation rather than with $PdCl_2$ and CuCl oxidation.

The above obtained oxidized 7-acetonyloxybenzopyrone derivatives **10a-c** were subjected to ring closure by refluxing them in ethanolic KOH to give 3-methylfurobenzopyrones **11a-c**. Structures of the products were established on the basis of their elemental analysis and spectral data. **[Scheme III.2.5]**

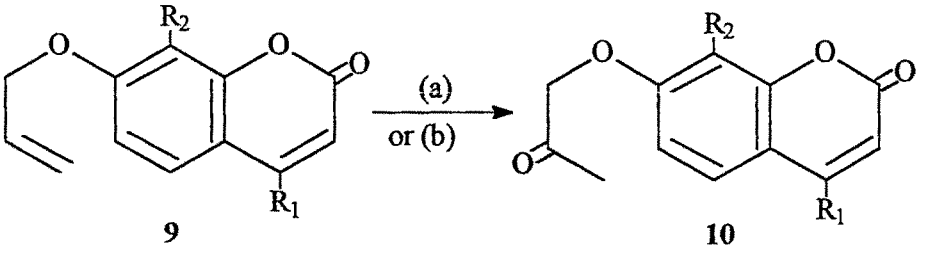
Similarly 2-methylfurobenzopyrones **14a-c** were prepared by two methods:

7-Acetoxy/hydroxy-8-/6-allylbenzopyrone derivatives **12a-c, 15a-c** were subjected to catalytic oxidation in the presence of $PdCl_2/CuCl/O_2$ or $PdCl_2$/BQ as described above. In the case of 7-acetoxy-8-/6-allylbenzopyrones **12a-c**, it was anticipated to give better yields of furobenzopyrone as acetyl group happened to be a good leaving group and facilitates in an enhanced way for intramolecular cyclization. Contrary to the above, a mixture of 7-acetoxy- and 7-hydroxy acetonylbenzopyrone derivatives **13a-c** were observed after working out of the reaction. Elemental analysis and spectral information confirmed the formation of the products.

While 7-hydroxy-8-/6-allylbenzopyrone derivatives **15a-c** yielded only cyclized furobenzopyrones **14a-c**. The most interesting part here was that the yields were far better in $PdCl_2$/CuCl oxidation rather than in the other case.

7-Acetoxy/hydroxy-8-/6-acetonylbenzopyrone derivatives **13a-c** when subjected to ring closure by refluxing with ethanolic HCl gave 2-methylfurobenzopyrones **14a-c**. Formation of products was confirmed from their elemental analysis and spectral data. **[Scheme III.2.6 & III.2.7]**

Scheme III.2.5

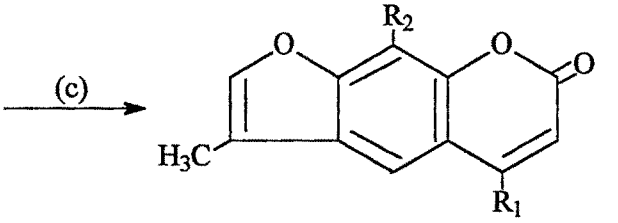


9

	R_1	R_2
a	H	H
b	CH_3	H
c	CH_3	H

10

	R_1	R_2
a	H	H
b	CH_3	H
c	CH_3	H

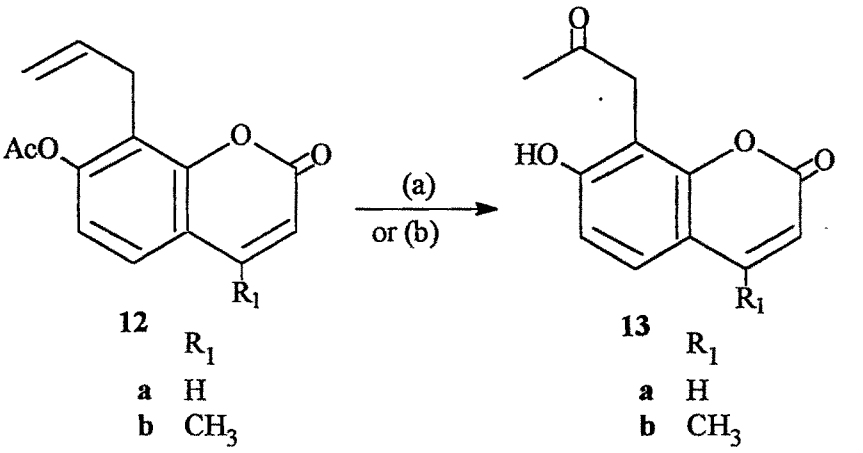


11

	R_1	R_2
a	H	H
b	CH_3	H
c	CH_3	H

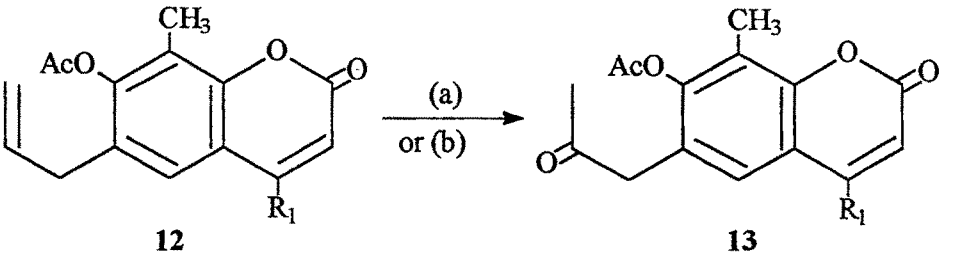
(a) $PdCl_2$, CuCl, DMF:H_2O,O_2 (b) $PdCl_2$, BQ, DMF:H_2O
(c) 0.1N ethanolic KOH

Scheme III.2.6



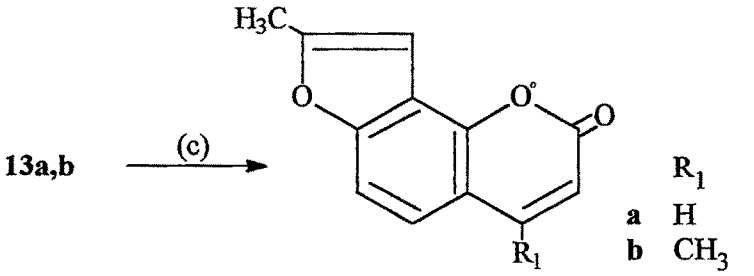
12 **13**

	R_1
a	H
b	CH_3



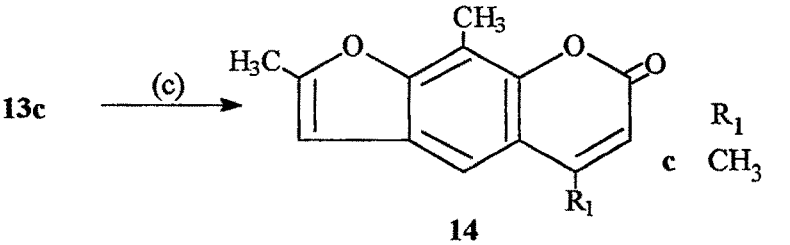
12 **13**

	R_1
c	CH_3



	R_1
a	H
b	CH_3

14



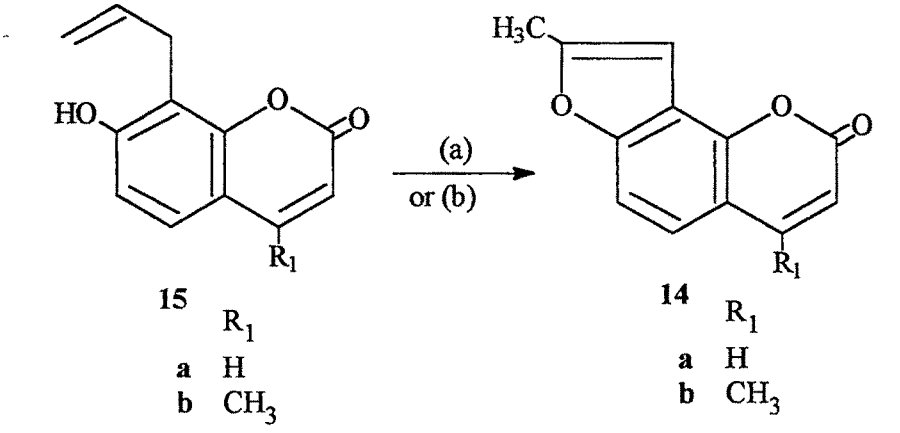
	R_1
c	CH_3

14

(a) $PdCl_2$, CuCl, DMF:H_2O, O_2 (b) $PdCl_2$, BQ, DMF:H_2O

(c) ethanol/HCl (50%)

Scheme III.2.7

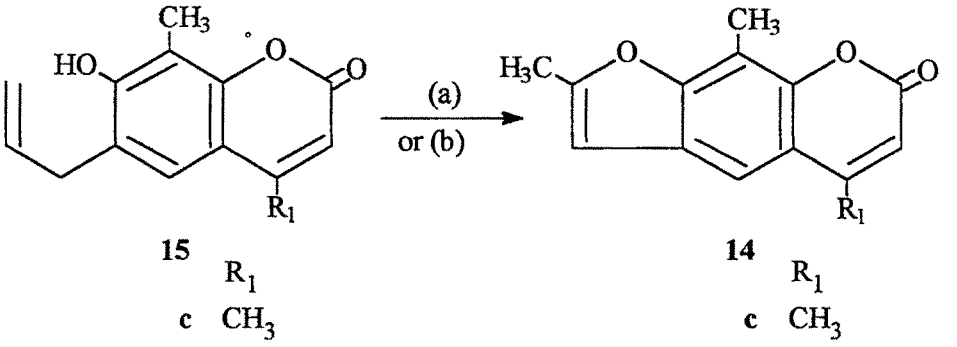


15

	R_1
a	H
b	CH_3

14

	R_1
a	H
b	CH_3



15

	R_1
c	CH_3

14

	R_1
c	CH_3

(a) $PdCl_2$,CuCl, DMF:H_2O,O_2 (b) $PdCl_2$,BQ, DMF:H_2O

From all the above observations it could be concluded that though the oxidation with benzoquinone is easy and economical as it requires nominal quantities of $PdCl_2$, it gives better yields with allyl ethers only. $CuCl/PdCl_2$ will be more useful as far as yields are concerned when o-hydroxyallyl compounds are to be oxidized catalytically.

EXPERIMENTAL

^{1}H-NMR spectra were recorded on Bruker 200MHz or Perkin-Elmer 90MHz spectrophotometer. Chemical shifts are relative to tetramethylsilane. Infrared spectra were recorded on Shimadzu IR-408 or Perkin-Elmer FT-IR spectrometer (Spectrum RX 1). Melting points were taken by capillary method and are uncorrected. Elemental analyses were performed on Colemen C,H-analyzer or Perkin-Elmer C,H,N,S analyzer (Model 2400).

General procedure for oxidation of 7-allyloxybenzopyrones by CuCl (10a-c):

To a solution of 7-allyloxybenzopyrones **9a-c** (5mmol) in DMF:H_2O (7:1ml), freshly prepared cuprous chloride (5mmol) and palladium chloride (0.5mmol) were added. The mixture was stirred at room temperature under the atmosphere of oxygen monitoring with TLC. After 9h, the contents were poured into cold 3N HCl to obtain a solid, which was then treated with dilute alkali to remove deallylated benzopyrone. Products **10a-c** were finally purified by recrystallization. The percentage yields of different reactions are tabulated for comparison in **Table III.2.1.1**. M.p., elemental analysis, spectral data and solvent of crystallization of individual product are given below separately.

General procedure for oxidation of 7-allyloxybenzopyrones by BQ (10a-c):

A mixture of **9a-c** (10mmol) in DMF:H_2O (7:1ml), freshly prepared p-benzoquinone (10mmol) and palladium chloride (0.1mmol) was stirred at room temperature monitoring with TLC. The reaction was worked out in the same way as described above resulted in the formation of **10a-c**, which finally recrystallized. The results are shown in **Table III.2.1.1**.

7-Acetonyloxybenzopyran-2H-one (10a):

m.p. 174°C (ethanol)

Analysis : Found : C, 66.50%; H, 4.54%

$C_{12}H_{10}O_4$: Requires : C, 66.05%; H, 4.59%

IR(KBr) cm^{-1} : 1710, 1610, 1405, 1285, 1240, 1130

PMR($CDCl_3$+DMSO): δ 2.25 (s, 3H of $-CH_3$ in acetonyloxy group at C-7); 4.65 (s, 2H of $-CH_2-$ of acetonyloxy group at C-7); 6.15 (d, J = 9Hz, 1H at C-3); 6.60-6.85 (m, 2H at C-6 and C-8); 7.40 (d, J = 9Hz, 1H at C-5); 7.60 (d, J = 9Hz, 1H at C-4)

7-Acetonyloxy-4-methylbenzopyran-2H-one (10b):

m.p. 157°C (ethanol)

Analysis : Found : C, 67.70%; H, 5.55%

$C_{13}H_{12}O_4$: Requires : C, 67.23%; H, 5.17%

IR(KBr) cm^{-1} : 1715, 1615, 1375, 1285, 1140

PMR($CDCl_3$): δ 2.25 (s, 3H of $-CH_3$ at C-4); 2.35 (s, 3H of $-CH_3$ in acetonyloxy group at C-7); 4.55 (s, 2H of $-CH_2-$ of acetonyloxy group at C-7); 6.10 (s, 1H at C-3); 6.50-6.85 (m, 2H at C-6 and C-8); 7.45 (d, J = 9Hz, 1H at C-5)

7-Acetonyloxy-4,8-dimethylbenzopyran-2H-one (10c):

m.p. 174°C (ethanol)

Analysis : Found : C, 68.12%; H, 5.57%

$C_{14}H_{14}O_4$: Requires : C, 68.29%; H, 5.69%

IR(KBr) cm^{-1} : 1720, 1610, 1390, 1290, 1120

PMR($CDCl_3$): δ 2.30 (s, 3H of $-CH_3$ at C-4); 2.35 (s, 3H of $-CH_3$ at C-8); 2.45 (s, 3H of $-CH_3$ in acetonyloxy group at C-7); 4.60 (s, 2H of $-CH_2-$ of acetonyloxy group at C-7); 6.15 (s, 1H at C-3); 6.65 (d, J = 8Hz, 1H at C-6); 7.40 (d, J = 8Hz, 1H at C-5)

General procedure for cyclization of 7-acetonyloxybenzopyrones (11a-c):

7-Acetonyloxybenzopyrones **10a-c** (2mmol) in ethanolic KOH (0.1N, 50ml) were refluxed for 7h. Excess of ethanol was distilled off and resultant solution dropped into cold dilute HCl. The obtained products **11a-c** were filtered, dried and purified by column chromatography using benzene as eluent, were finally recrystallized. **Table III.2.1.2** shows the yield of each product after cyclization.

3-Methylfuro(3,2-g)benzopyran-7H-one (11a):

m.p. 188°C (benzene)

Analysis : Found : C, 71.68%; H, 4.21%

$C_{12}H_8O_3$: Requires : C, 72.00%; H, 4.00%

IR(KBr) cm^{-1} : 1715, 1580, 1390, 1210, 1130, 1105

PMR($CDCl_3$): δ 2.25 (s, 3H of $-CH_3$ at C-3); 6.30 (d, J = 9Hz, 1H at C-6); 7.30 (s, 1H at C-4); 7.40 (s, 1H at C-2); 7.45 (s, 1H at C-9); 7.70 (d, J = 9Hz, 1H at C-5)

3,5-Dimethylfuro(3,2-g)benzopyran-7H-one (11b):

m.p. 220°C (ethanol)

Analysis : Found : C, 73.21%; H, 4.95%

$C_{13}H_{10}O_3$: Requires : C, 72.90%; H, 4.67%

IR(KBr) cm^{-1} : 1710, 1580, 1390, 1140

PMR($CDCl_3$): δ 2.25 (s, 3H of $-CH_3$ at C-3); 2.50 (s, 3H of $-CH_3$ at C-5); 6.20 (s, 1H at C-6); 7.35 (s, 1H at C-4); 7.45 (s, 1H at C-2); 7.65 (s, 1H at C-9)

3,5,9-Trimethylfuro(3,2-g)benzopyran-7H-one (11c):

m.p. 185-86°C (ethanol)

Analysis : Found : C, 73.48%; H, 5.30%

$C_{14}H_{12}O_3$: Requires : C, 73.68%; H, 5.26%

IR(KBr) cm^{-1} : 1710, 1596, 1395, 1110

PMR($CDCl_3$): δ 2.30 (s, 3H of -CH_3 at C-3); 2.55 (s, 3H of -CH_3 at C-5); 2.60 (s, 3H of -CH_3 at C-9); 6.25 (s, 1H at C-6); 7.45 (s, 1H at C-4); 7.55 (s, 1H at C-2)

General procedure for oxidation of 7-acetoxy/hydroxy-8-/6-allyl benzopyrones by CuCl (13a-c, 14a-c):

To a solution of 7-acetoxy/hydroxy-8-/6-allylbenzopyrones **12a-c, 15a-c** (5mmol) in DMF:H_2O (7:1ml), freshly prepared cuprous chloride (5mmol) and palladium chloride (0.5mmol) were added. The reaction mixture was stirred under oxygen atmosphere at room temperature monitoring with TLC. After the completion of reaction, the contents were dropped into cold 3N HCl to give solid, which were then treated with dilute alkali to separate alkali soluble and insoluble products. Alkali soluble fraction was acidified by HCl and the obtained products **13a-c, 14a-c** were recrystallized. **Table III.2.2.1** and **Table III.2.3** display the percentage yield of individual product. M.p., elemental analysis, spectral data and solvent of crystallization of each product are given below separately.

General procedure for oxidation of 7-acetoxy/hydroxy-8-/6-allyl benzopyrones by benzoquinone (13a-c, 14a-c):

An intimate mixture of **12a-c, 15a-c** (5mmol) in DMF:H_2O (7:1ml), freshly prepared p-benzoquinone (10mmol) and palladium chloride (0.05mmol) was stirred at room temperature monitoring with TLC. The reaction was then worked out as described above and products **13a-c, 14a-c** were purified by recrystallization. The results are depicted in **Table III.2.2.1** and **Table III.2.3** separately.

7-Hydroxy-8-acetonylbenzopyran-2H-one (13a):

m.p. 178°C (ethanol)

Analysis : Found : C, 65.92%; H, 4.56%

$C_{12}H_{10}O_4$: Requires : C, 66.05%; H, 4.59%

IR(KBr) cm^{-1} : 3475, 1700, 1610, 1580, 1385, 1370, 1075

7-Hydroxy-8-acetonyl-4-methylbenzopyran-2H-one (13b):

m.p. 185°C (ethanol)

Analysis : Found : C, 67.21%; H, 5.09%

$C_{13}H_{12}O_4$: Requires : C, 67.23%; H, 5.17%

IR(KBr) cm^{-1} : 3465, 1720, 1620, 1580, 1390, 1370, 1080

PMR($CDCl_3$+DMSO): δ 2.25 (s, 3H of $-CH_3$ at C-4); 2.40 (s, 3H of $-CH_3$ in acetonyl group at C-8); 3.95 (s, 2H of $-CH_2-$ of acetonyl group at C-8); 6.05 (s, 1H at C-3); 6.90 (d, J = 9Hz, 1H at C-6); 7.40 (d, J = 9Hz, 1H at C-5)

7-Acetoxy-6-acetonyl-4,8-dimethylbenzopyran-2H-one (13c):

m.p. 207-8°C (ethanol)

Analysis : Found : C, 66.45%; H, 5.59%

$C_{16}H_{16}O_5$: Requires : C, 66.67%; H, 5.55%

IR(KBr) cm^{-1} : 1760, 1735, 1700, 1620, 1580, 1395, 1370, 1200, 1090

PMR($CDCl_3$): δ 2.15 (s, 3H of $-CH_3$ at C-4); 2.25 (s, 3H of $-CH_3$ at C-8); 2.35 (s, 3H of $-CH_3$ in $-OCOCH_3$ at C-7); 2.45 (s, 3H of $-CH_3$ of acetonyl group at C-6); 3.65 (s, 2H of $-CH_2-$ of acetonyl group at C-6); 6.30 (s, 1H at C-3); 7.35 (s, 1H at C-5)

2-Methylfuro(2,3-h)benzopyran-5H-one (14a):

m.p. 156°C (benzene)

Analysis : Found : C, 71.83%; H, 4.07%

$C_{12}H_8O_3$: Requires : C, 72.00%; H, 4.00%

IR(KBr) cm^{-1} : 1730, 1600, 1400, 1116

PMR($CDCl_3$): δ 2.60 (s, 3H of -CH_3 at C-2); 6.50 (d, 1H at C-6); 6.80 (s, 1H at C-3); 7.45 (d (overlapped), 2H at C-9 and C-8); 7.90 (d, 1H at C-4)

2,7-Dimethylfuro(2,3-h)benzopyran-5H-one (14b):

m.p. 182°C (benzene)

Analysis : Found : C, 72.87%; H, 4.56%

$C_{13}H_{10}O_3$: Requires : C, 72.90%; H, 4.67%

IR(KBr) cm^{-1} : 1730, 1605, 1395, 1090

PMR($CDCl_3$): δ 2.40 (s, 3H of -CH_3 at C-2); 2.45 (s, 3H of -CH_3 at C-7); 6.15 (s, 1H at C-6); 6.60 (s, 1H at C-3); 7.20 (d, J = 9Hz, 1H at C-9); 7.35 (d, J = 9Hz, 1H at C-8)

2,5,9-Trimethylfuro(3,2-g)benzopyran-7H-one (14c):

m.p. 235°C (ethanol)

Analysis : Found : C, 73.46%; H, 5.21%

$C_{14}H_{12}O_3$: Requires : C, 73.68%; H, 5.26%

IR(KBr) cm^{-1} : 1720, 1610, 1590, 1400, 1100

PMR($CDCl_3$): δ 2.44 (s, 3H of -CH_3 at C-5); 2.47 (s, 3H of -CH_3 at C-9); 2.55 (s, 3H of -CH_3 at C-2); 6.20 (s, 1H at C-6); 6.34 (s, 1H at C-3); 7.20 (s, 1H at C-4)

General procedure for cyclization of 7-acetoxy/hydroxy-8-/6-acetonyl benzopyrones (14a-c):

7-Acetoxy/hydroxy-8-/6-acetonylbenzopyrones **13a-c** (2mmol) were refluxed in ethanolic HCl (50%, 50ml) for 6h. The reaction mixture was cooled and poured over crushed ice. Separated solid was filtered and purified by column chromatography using benzene as eluent. Finally they were recrystallized and confirmed as **14a-c** from their elemental analysis and spectral data. The percentage yield of each product is given in **Table III.2.2.2**.

TABLE III.2.1.1

	OXYPALLADATION BY CuCl						OXYPALLADATION BY BQ					
Comp. No.	Sub. (gm)	CuCl (gm)	$PdCl_2$ (gm)	Yield (gm)	Yield (%)	Prod. No.	Sub. (gm)	BQ (gm)	$PdCl_2$ (gm)	Yield (gm)	Yield (%)	Prod. No.
9a	1.00	0.50	0.09	0.47 + 0.30 sol	43.9	**10a**	2.02	1.10	0.018	1.26 + 0.10 sol	57.8	**10a**
9b	1.08	0.50	0.09	0.52	44.8	**10b**	2.16	1.10	0.018	1.40	60.3	**10b**
9c	1.15	0.50	0.09	0.58 + 0.05 sol	47.1	**10c**	2.30	1.10	0.018	1.54 + 0.50 sol	62.6	**10c**

TABLE III.2.1.2

CYCLIZATION BY ETHANOL/KOH				
Comp. No.	Sub. (gm)	Yield (gm)	Yield (%)	Prod. No.
10a	0.44	0.25	62.5	**11a**
10b	0.46	0.26	61.9	**11b**
10c	0.49	0.30	66.6	**11c**

TABLE III.2.2.1

	OXYPALLADATION BY CuCl						OXYPALLADATION BY BQ					
Comp. No.	Sub. (gm)	CuCl (gm)	$PdCl_2$ (gm)	Yield (gm)	Yield (%)	Prod. No.	Sub. (gm)	BQ (gm)	$PdCl_2$ (gm)	Yield (gm)	Yield (%)	Prod. No.
12a	1.22	0.50	0.09	0.72 -OH oxi	66.0	**13a**	1.22	0.50	0.009	0.51 -OH oxi	46.8	**13a**
12b	1.30	0.50	0.09	0.87 -OH oxi	74.5	**13b**	1.30	0.50	0.009	0.60 -OH oxi + 0.26 unreact	51.4	**13b**
12c	1.36	0.50	0.09	1.10 -OAc oxi	76.4	**13c**	1.36	0.50	0.009	0.75 -OAc oxi	52.1	**13c**

TABLE III.2.2.2

	CYCLIZATION BY ETHANOL/HCl			
Comp. No.	Sub. (gm)	Yield (gm)	Yield (%)	Prod. No.
13a	0.44	0.26	65.0	**14a**
13b	0.46	0.29	69.0	**14b**
13c	0.58	0.33	71.7	**14c**

TABLE III.2.3

	OXYPALLADATION BY CuCl						OXYPALLADATION BY BQ					
Comp. No.	Sub. (gm)	CuCl (gm)	$PdCl_2$ (gm)	Yield (gm)	Yield (%)	Prod. No.	Sub. (gm)	BQ (gm)	$PdCl_2$ (gm)	Yield (gm)	Yield (%)	Prod. No.
15a	1.00	0.50	0.09	0.60	60.6	**14a**	1.00	0.55	0.009	0.45	45.4	**14a**
15b	1.08	0.50	0.09	0.75	70.1	**14b**	1.08	0.55	0.009	0.58	54.2	**14b**
15c	1.15	0.50	0.09	0.85	74.6	**14c**	1.15	0.55	0.009	0.65	57.0	**14c**

REFERENCES

1. J. Tsuji, Organic Synthesis with Palladium Compounds, Springer-Verlag, Berlin (1980).
2. B. Trost and T. Verhoeven, Comprehensive Organometallic Chemistry, Ed. by G. Wilkinson, Oxford, **8**, 854 (1982).
3. P. M. Henry, Palladium Catalyzed Oxidation of Hydrocarbons, Reidel, Dordrecht, 41 (1980).
4. P. M. Maitlis, The Organic Chemistry of Palladium, Academic, New York, **2**, 77 (1971).
5. J. Smidt, W. Hafner, R. Jira, J. Sedlmeier, R. Sieber, R. Ruttinger and H. Kojer, Angew. Chem., **71**, 176 (1959); Chem. Abstr., **53**, 16940e (1959).
6. J. Smidt, W. Hafner, R. Jira, R. Sieber, J. Sedlmeier and A. Sabel, Angew. Chem., **74**, 93 (1962); Chem. Abstr., **57**, 11903f (1962).
7. S. Nakamura and A. Yasui, J. Catal., **17**, 366 (1970).
8. T. Onoda, J. Ger. Offen., 2217452 (1972); Chem. Abstr., 78, 57786.
9. R. Jira and W. Freieslehen, Organometal React., 3 (1972).
10. W. H. Clement and C. M. Selwitz, J. Org. Chem., **29**, 241 (1964).
11. M. Hrusovsky, J. Vajtko and M. Hung, J. Ind. Chem., **2**, 137 (1974).
12. I. Moiseev, M. Vargaftik and Ya. Syrkin, Doklady Akad. Nauk SSSR, **133**, 377 (1960); Chem. Abstr., **54**, 24350g (1960).
13. T. Hosokawa, S. Yamashita and S.-I. Murahashi, Bull. Chem. Soc. Jpn., **49**, 3662 (1976).
14. T. Hosokawa and S.-I. Murahashi, Heterocycles, **33**, 1079 (1992).
15. Jayati Mitra and Alok Kumar Mitra, Ind. J. Chem., **33B**, 276 (1994).
16. S. S. Madhava Rao, Ph. D. Thesis, M. S. Univ. of Baroda, Baroda, 138 (1990).
17. M. Iyer and G. Trivedi, Syn. Comm., **20**, 1347 (1990).
18. Jayati Mitra and Alok Kumar Mitra, Ind. J. Chem., **31B**, 693 (1992).