CHAPTER-III

Section-1

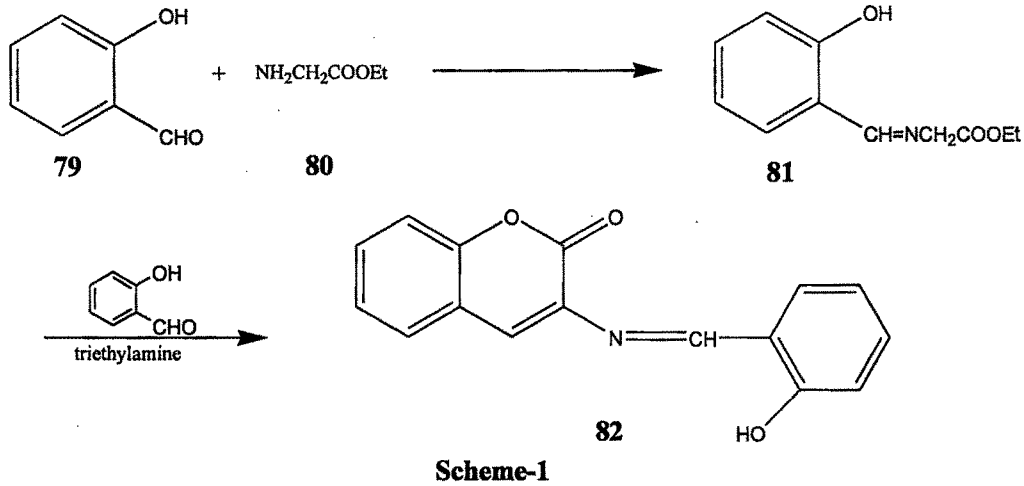
Synthesis of psora-Schiff bases

Section: 1 Synthesis of psora-Schiff bases

III.1 Introduction

2H-1-Benzopyran-2-ones, naturally occurring as well as synthetic, show antibiotic, antifungal, anthelmintic and anticoagulant properties[1-3].Analgesic and sedative properties of 3-amino-2H-1-benzopyran-2-ones have been reported in literature[4-5]. Schiff bases derived from 2H-1-benzopyran-2-one derivative have also been found to show moderate antibacterial activity[7].

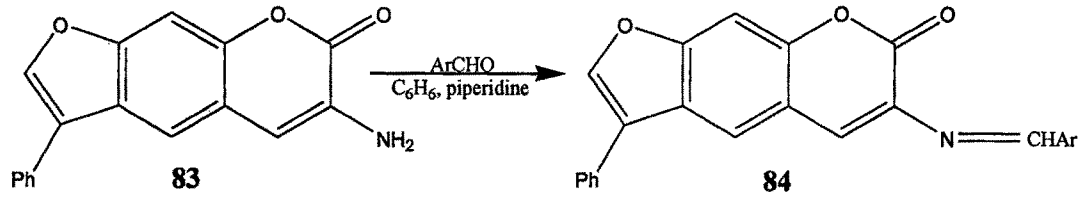
Kokotos *et al*[6] have reported formation of Schiff bases **82** of 2H-1-benzopyran-2-one in a single step by condensation of ethyl ester of glycine hydrochloride **80** and 2-hydroxybenzaldehyde **79** in presence of triethylamine (Scheme-1).



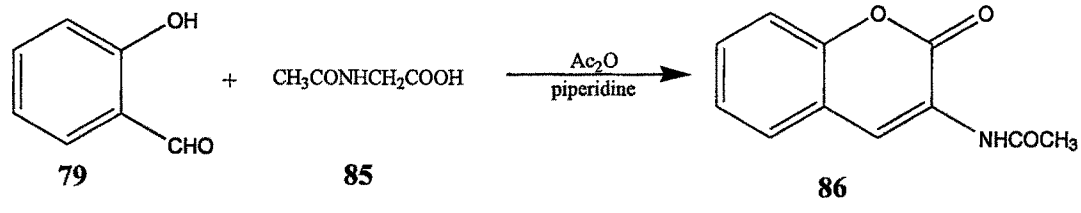
Scheme-1

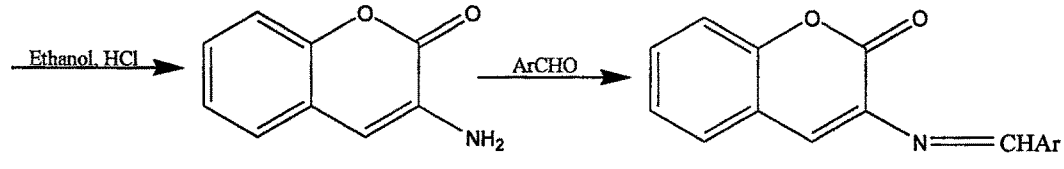
Various Schiff bases **84** from 6-phenyl-3-amino-2H-furo[3,2-g]-1-benzopyran-2-one **83** have been reported in the literature[8] (Scheme-2).

Schiff bases of 2H-1-benzopyran-2-one have also been reported by Kumar et al[4]. They condensed 2-hydroxybenzaldehyde **79** with acetyl glycine **80** in acetic anhydride, furnishing 3-acetamido-2H-1-benzopyran-2-one **86** which on hydrolysis with HCl afforded 3-amino-2H-1-benzopyran-2-one **87**. Condensation with benzaldehydes, compound **87** produced Schiff bases of 2H-1-benzopyran-2-ones **88** (Scheme-3).



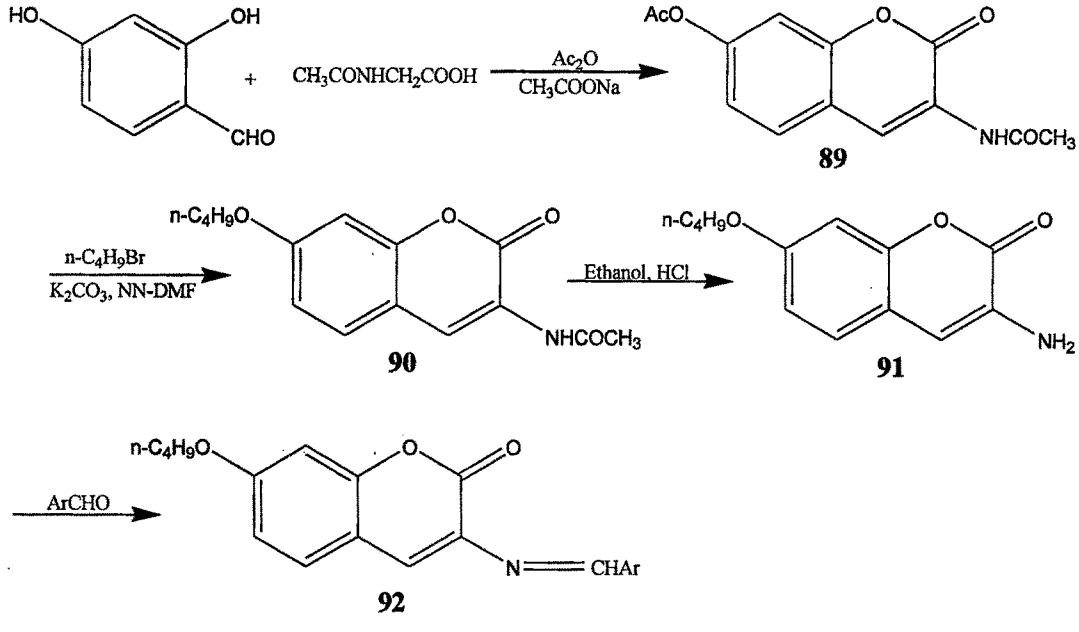
Scheme-2





Scheme-3

Schiff bases of the type **92** from 7-n-butoxy-3-amino-2H-1-benzopyran-2-one 13 have been prepared by Desai[7]. In this synthesis, 2,4-dihydroxybenzaldehyde was condensed with acetyl glycine **85** in presence of acetic anhydride and anhydrous sodium acetate to yield 3-acetamido-7-acetoxy-2H-1-benzopyran-2-one **89** which on treatment with n-butylbromide in dry DMF and anhydrous K_2CO_3 afforded 3-acetamido-7-n-butoxy-2H-1-benzopyran-2-one **90**. The compound **90** was, then, hydrolyzed by conc.H_2SO_4 in ethanol which gave 3-amino-7-n-butoxy-2H-1-benzopyran-2-one **91**. The condensation of the amino benzopyrone **91** with substituted benzaldehydes resulted in formation of corresponding Schiff bases of 2H-1-benzopyran-2-ones **92** (Scheme-4).



Scheme-4

III.2 Results and Discussion:

Some Schiff bases as well as some azetidinones from 3-acetamido-2H-1-benzopyran-2-one have been prepared. In present work, 3-acetamido-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one **65** was subjected to hydrolysis using aq. HCl in methanol to give 3-amino-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one **93** (Scheme-5). Condensation of this amino derivative **93** in benzene as well as N,N-dimethylformamide solvent, with various substituted benzaldehydes afforded corresponding Schiff bases **94-102.**

3-Amino-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one **93** exhibited IR bands at 3434 cm^{-1} and 3346 cm^{-1} for $-NH_2$ group and 1694 cm^{-1} for carbonyl of lactone ring [Figure-22].

Azomethine group of the Schiff bases was achieved by condensing amino product **93** with different substituted aromatic aldehydes. Higher yields were noticed in the condensation of aromatic aldehydes having electron withdrawing groups. In case of 2,3,4-trichloro benzaldehyde the yield was highest while in case of 2,4-dihydroxy benzaldehyde the yield was lowest. This can be attributed to the presence of chlorine

atoms which facilitates nucleophilic attack. Condensation did not take place with para vanillin.

PMR spectrum of 3-amino-6-methyl-2H-furo[3,2-g]-1-benzopyran-2-one,**93** exhibited a singlet at δ 2.25 for three protons of methyl group at C-6, a broad signal for two protons of amino group at δ 4.39-4.60, a singlet at δ 6.88 for proton at C-4, a singlet at δ 7.35 for a proton at C-9, a singlet at δ 7.39 for proton at C-5 and a singlet at δ 7.43 for proton at C-7 [Figure-23].

PMR of compound **94** exhibited a singlet at δ 2.40 for three methyl protons at C-6, another singlet at δ 2.82 for three methyl protons of benzal ring, a multiplet at 6.88-6.98 for two protons of benzal ring and two protons at C-4 as well as C-9, a doublet (J=6 Hz) at δ 7.39-7.88 for aromatic protons with o-coupling, a singlet at δ 7.88 for proton at C-5, a singlet at 8.31 for proton at C-7 and a singlet at 8.70 for –N=C<u>H</u> at C-3[Figure-25].

6-Methyl-3-(4-(N,N-di(2-chloroethyl)amino)benzalamino)-2H-furo[3,2-g]-1-benzopyran-2-one, **95** showed absorption band at 1715 cm^{-1} for carbonyl group of lactone. Its PMR exhibited a singlet at δ 2.10 for three methyl protons at C-6, a triplet at δ 3.10 for four protons of two methylene groups of 2 x -NC<u>H</u>$_2$CH$_2$Cl, another triplet at δ 4.10 for four protons of two mehtylene groups of 2 x -NCH$_2$C<u>H</u>$_2$Cl, a singlet at δ 6.99 for a proton at C-4, a multiplet at δ 7.04-7.15 for four protons of benzal ring, two singlets at 7.32-7.38 for two protons at C-9 and C-5, a singlet at 8.00 for a proton of C-7 and another singlet at 8.68 for proton of –N=C<u>H</u> at C-6 [Figure-26].

PMR spectrum of 6-methyl-3-(2,4-dihydroxybenzallimino)-2H-furo[3,2-g]-1-benzopyran-2-one, **96** exhibited a singlet at δ 2.50 for three methyl protons at C-6, a broad signal at δ 5.90-6.10 for -OH protons, a singlet at δ 6.90 for a proton at C-4, a multiplet at 7.44-7.68 for five protons three of benzal ring and two protons at C-9 as well as C-5, a singlet at δ 7.98 for proton at C-7 and a singlet at 8.52 for –N=C<u>H</u> at C-3 [Figure-27].

PMR spectrum of 6-methyl-3-(4-hydroxy-3-methoxybenzallimino)-2H-furo[3,2-g]-1-benzopyran-2-one, **97** exhibited a singlet at δ 2.19 for three methyl protons at C-6, another singlet at δ 3.83 for three methyl protons of –OCH$_3$ of benzal ring, a

doublet (J=7 Hz) at δ 6.87-6.89 for a proton of benzal ring, a singlet at δ 6.91 for proton at C-4, two singlets at δ 6.92 for benzal ring proton and proton at C-9, a singlet at δ 6.94 for a proton at C-5, a doublet (J=7 Hz) at δ 7.71-7.19 for a proton of benzal ring, a singlet at δ 7.25 for a proton at C-7, a broad signal at δ 7.28 for -OH proton and a singlet at δ 7.30-7.59 for –N=CH at C-3 [Figure-28].

PMR spectrum of 6-methyl-3-(2,4-dinitrobenzallimino)-2H-furo[3,2-g]-1-benzopyran-2-one, **98** exhibited a singlet at δ 2.24 for three methyl protons at C-6, a singlet at δ 6.78 for a proton at C-4, a doublet (J=6.3 Hz) at δ 6.82 for a proton of benzal ring, a singlet at δ 7.14 for a proton at C-9, a doublet (J=6.3 Hz) at δ 7.31 for a proton of benzal ring, a singlet at δ 7.53 for proton at C-5, a singlet at δ 8.58 for a benzal ring proton, a singlet at δ 8.70 for proton at C-7 and a singlet at 9.83 for –N=CH at C-3 [Figure-29].

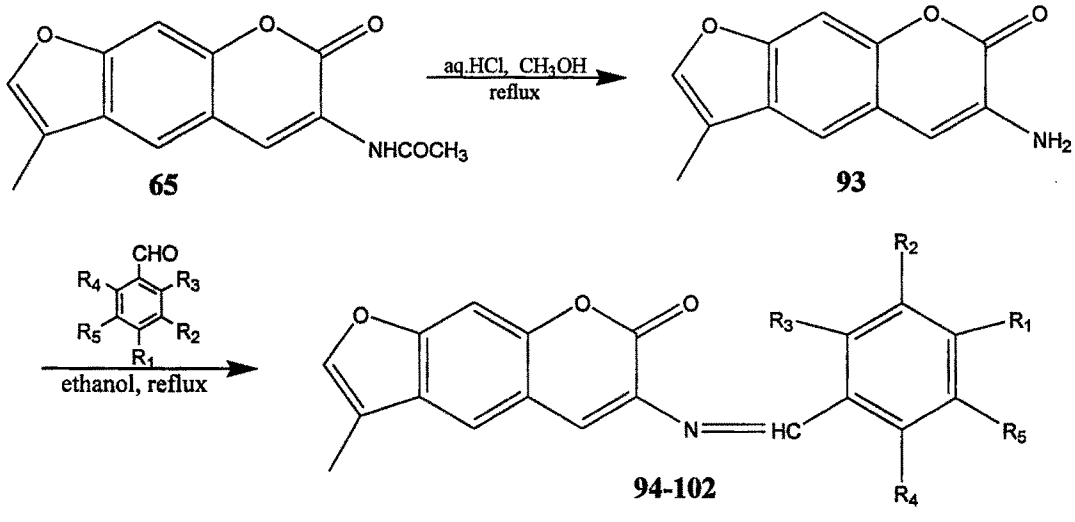
PMR spectrum of 6-methyl-3-(3,4-dichlorobenzallimino)-2H-furo[3,2-g]-1-benzopyran-2-one, **99** exhibited a singlet at δ 2.32 for three methyl protons at C-6, a singlet at δ 7.47 for a proton at C-4, two singlet at δ 7.56-7.59 for a proton at C-9 and an aromatic proton, a singlet at δ 7.77 for a proton at C-5, a singlet at δ 8.03 for a proton at C-7, a doublet (J=6.3 Hz) at δ 8.15 for a proton of benzal ring, another doublet (J=6.3 Hz) at δ 8.34 for a proton of benzal ring and a singlet at δ 9.46 for –N=CH at C-3 [Figure-31].

PMR spectrum of 6-methyl-3-(4-nitrobenzallimino)-2H-furo[3,2-g]-1-benzopyran-2-one, **100** exhibited a singlet at δ 2.30 for three methyl protons at C-6, a doublet (J=6.9 Hz) at δ 7.38 for two protons of phenyl ring, a singlet at δ 7.46 for a proton at C-4, a singlet at δ 7.49 for a proton of phenyl ring, a singlet at δ 7.54 for proton at C-9, a singlet at δ 7.66 for proton at C-5, a doublet at δ 7.74 for two aromatic protons, a singlet at δ 7.88 for proton at C-7 and a singlet at 9.34 for –N=CH at C-3 [Figure-35].

PMR spectrum of 6-methyl-3-(4-chlorobenzallimino)-2H-furo[3,2-g]-1-benzopyran-2-one, **101** exhibited a singlet at δ 2.31 for three methyl protons at C-6, a multiplet at 7.44-7.62 for four protons of benzal ring, a singlet at δ 7.74 for proton at C-4, a singlet at δ 8.00 for proton at C-9, a singlet at 8.31 for proton at C-5, a singlet at δ 8.82 for proton at C-7 and a singlet at 9.45 for –N=CH at C-3 [Figure-32].

PMR spectrum of 6-methyl-3-(2,3,4-trichlorobenzallimino)-2H-furo[3,2-g]-1-

benzopyran-2-one,**102** exhibited a singlet at δ 2.34 for three methyl protons at C-6, a doublet (J=7.7 Hz) at δ 7.08 for a proton of benzal ring, three singlets at δ 7.11-7.28 for the protons at C-4, C-9 and C-5, a doublet (J=7.7 Hz) at δ 7.52 for a proton of benzal ring, a singlet at δ 8.06 for proton at C-7 and a singlet at 8.68 for –N=CH at C-3 [Figure-37].



Scheme-5

Comp. No	R_1	R_2	R_3	R_4	R_5
94	CH_3	H	H	H	H
95	$N(CH_2CH_2Cl)_2$	H	H	H	H
96	OH	H	OH	H	H
97	OH	OCH_3	H	H	H
98	NO_2	H	NO_2	H	H
99	Cl	Cl	H	H	H
100	NO_2	H	H	H	H
101	Cl	H	H	H	H
102	Cl	Cl	Cl	H	H

III.3 Experimental:

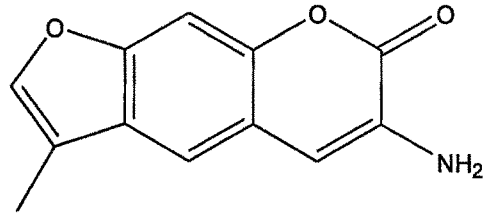
Procedure for the synthesis of 3-amino-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one 93

A suspension of 3-acetamido-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one **72** (1.00g, 0.00389mol) in methanolic solution of HCl (40ml of 36% aqueous HCl in 100ml CH_3OH) was refluxed for one hour, cooled followed by neutralization of the mixture with aqueous $NaHCO_3$ (150ml, 40% w/v). The solid thus obtained was filtered, dried and purified by column chromatography using petroleum ether-ethyl acetate mixture (80:20) and recrystallised from ethyl alcohol.

General Procedure for the synthesis of Schiff bases 94-102

A mixture of 3-amino-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one, **16** (0.5g, 0.0023 mol) and the substituted benzaldehydes (0.0021mol) in 20 ml of absolute ethanol with few drops of glacial acetic acid was refluxed for 24 hours. The completion of reaction was monitored by thin layer chromatography. The mixture was left over night. The separated suspention was filtered, dried and the solid thus obtained was purified by column chromatography using petroleum ether-ethyl acetate mixture (90:10) and recrystallised from ethyl alcohol.

3-Amino-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one, **93:**



State : pale yellow, crystalline

Molecular Formula : $C_{12}H_9O_3N$

Melting Point : 238 – 239 °C

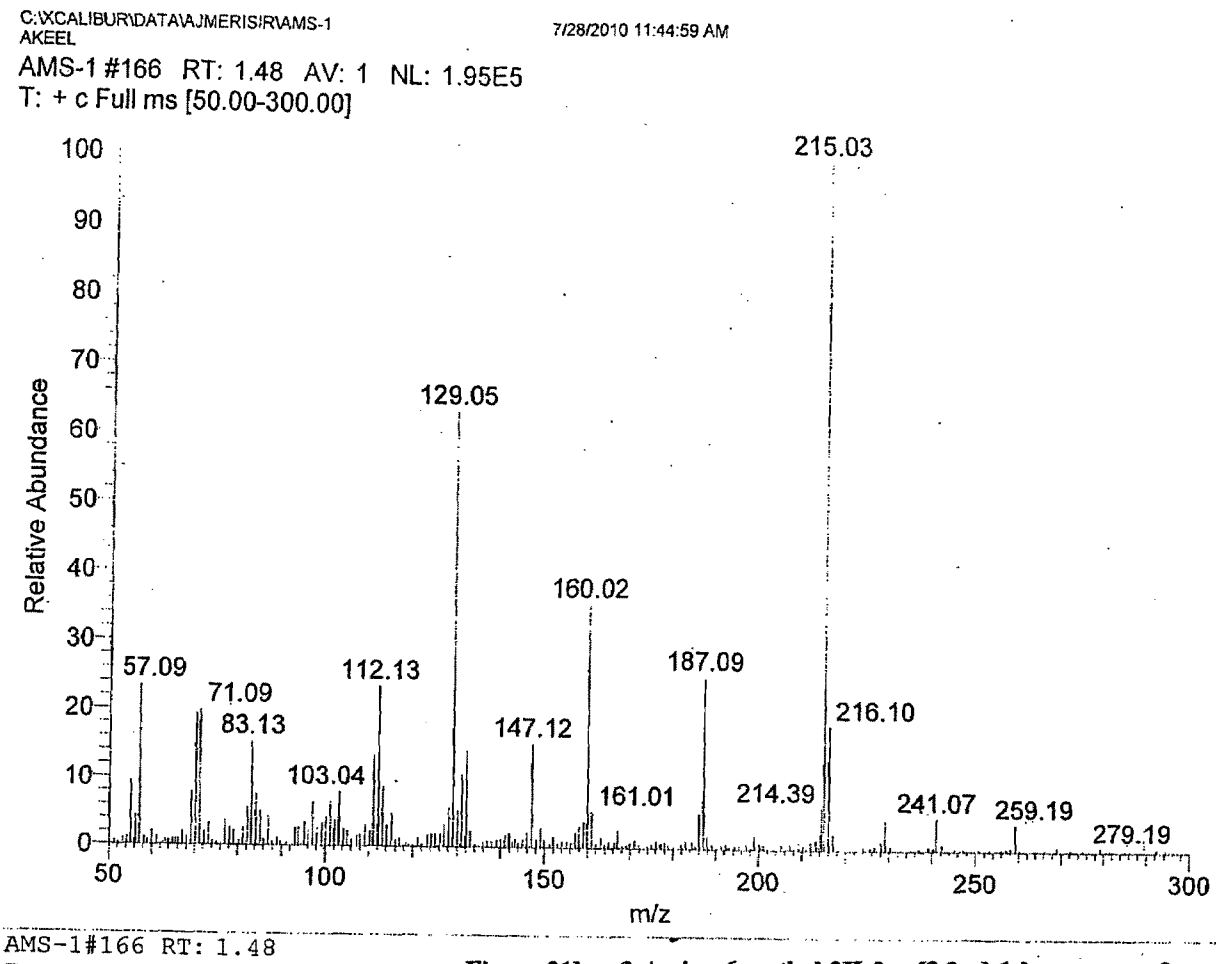
% Yield : 51

%C,H,N analysis (calculated) : C: 66.98 H: 4.21 N: 6.51

%C,H,N analysis (found) : C: 66.78 H: 4.19 N: 6.18

IR data (KBr) cm^{-1} : 3434, 3348, 2931, 1698, 1648, 1588, 1559, 1161, 1128.

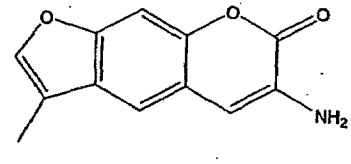
PMR data (400MHz, $CDCl_3$): δ 2.25(s, 3H, $C\underline{H}_3$), 4.39-4.60(br signal, 2H, -NH_2), 6.88(s, 1H, C-4), 7.35(s, 1H, C-9), 7.39(s, 1H, C-5), 7.43(s, 1H, C-7).

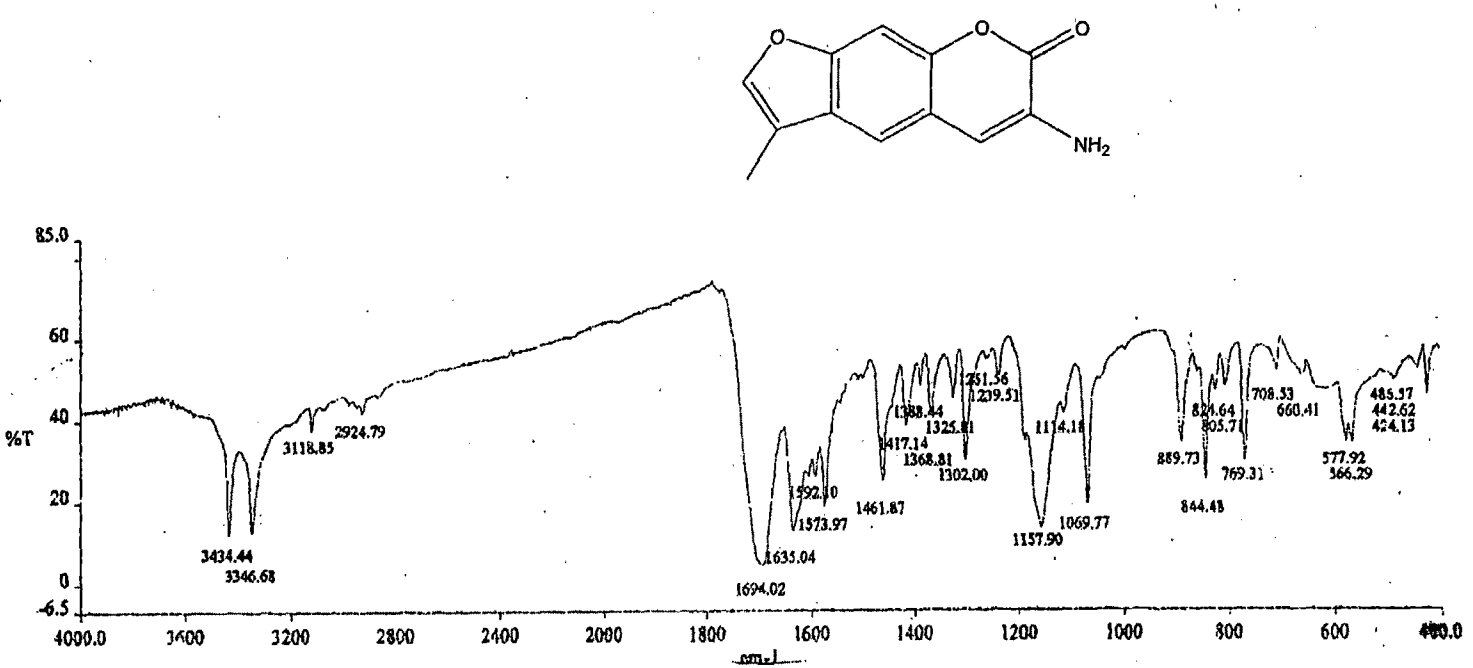


AMS-1#166 RT: 1.48
T: + c Full ms [50.00-300.00]

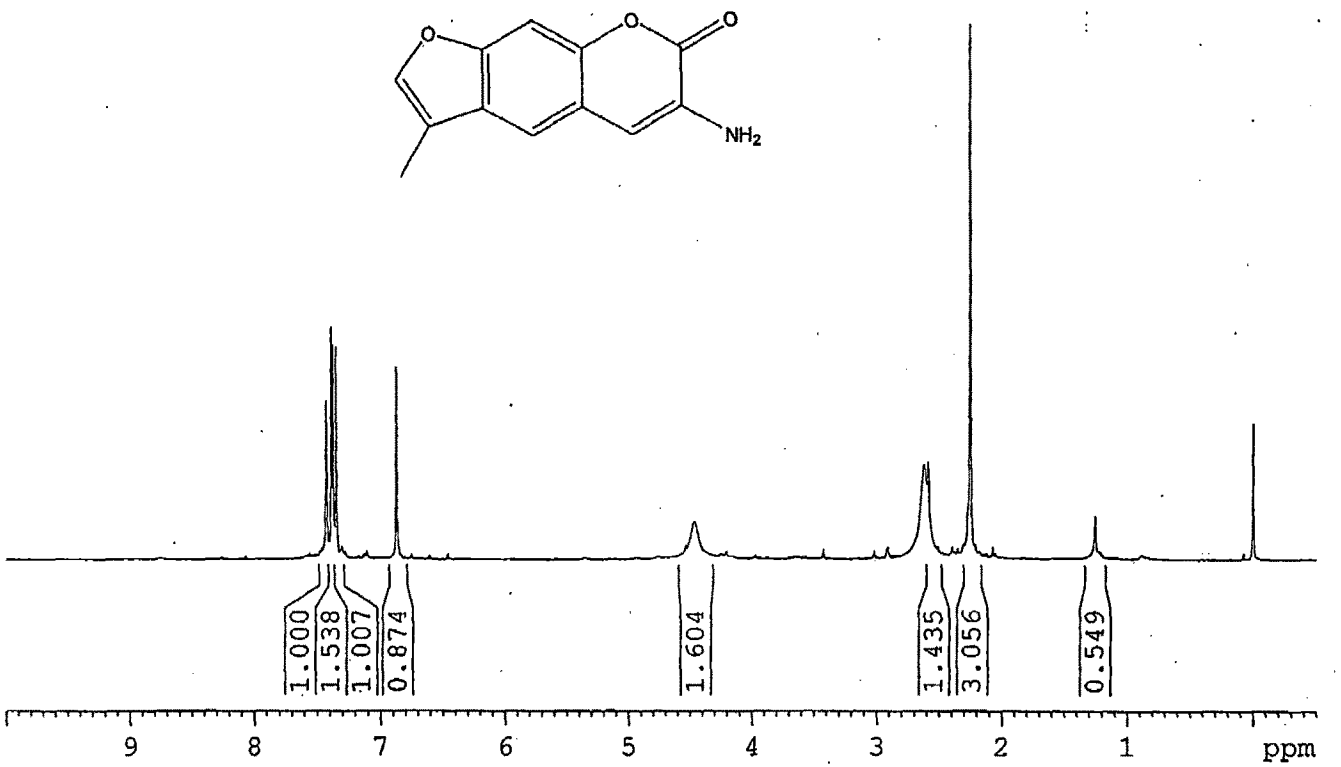
m/z	Intensity	Relative
69.08	15247.0	7.83
70.09	37439.0	19.23
71.09	38613.0	19.83
83.13	29771.0	15.29
84.12	14931.0	7.67
101.02	12729.0	6.54
103.04	15584.0	8.00
111.05	26059.0	13.38
112.13	45602.0	23.42
113.11	17092.0	8.78
129.05	123274.0	63.31
131.02	20805.0	10.68
132.04	27632.0	14.19
147.12	29711.0	15.26
160.02	69398.0	35.64
187.09	49328.0	25.33
215.03	194721.0	100.00
216.10	35655.0	18.31

Figure-21]: 3-Amino-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one 93





[Figure-22]: 3-Amino-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one 93



[Figure-23]: 3-Amino-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one 93

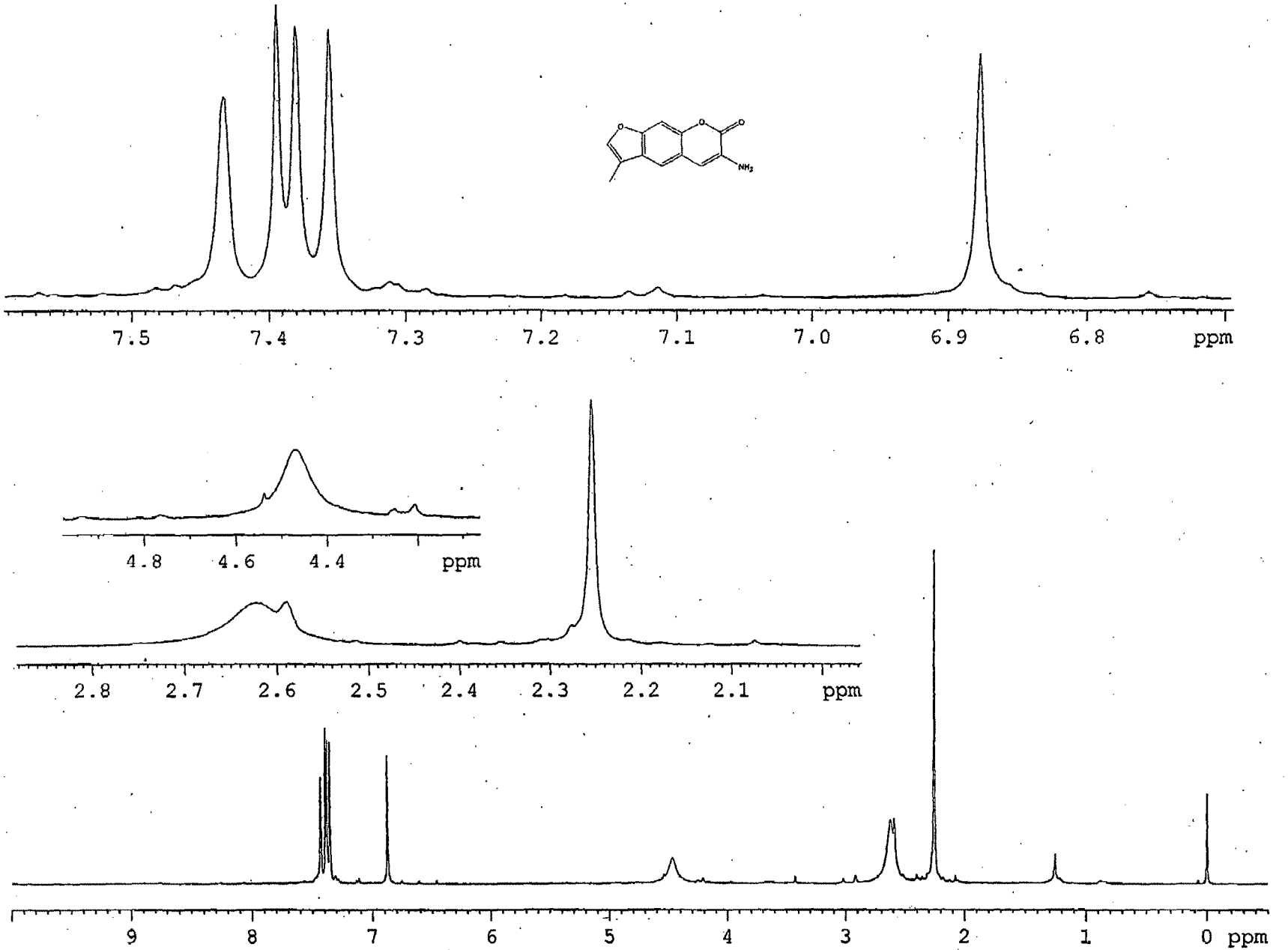
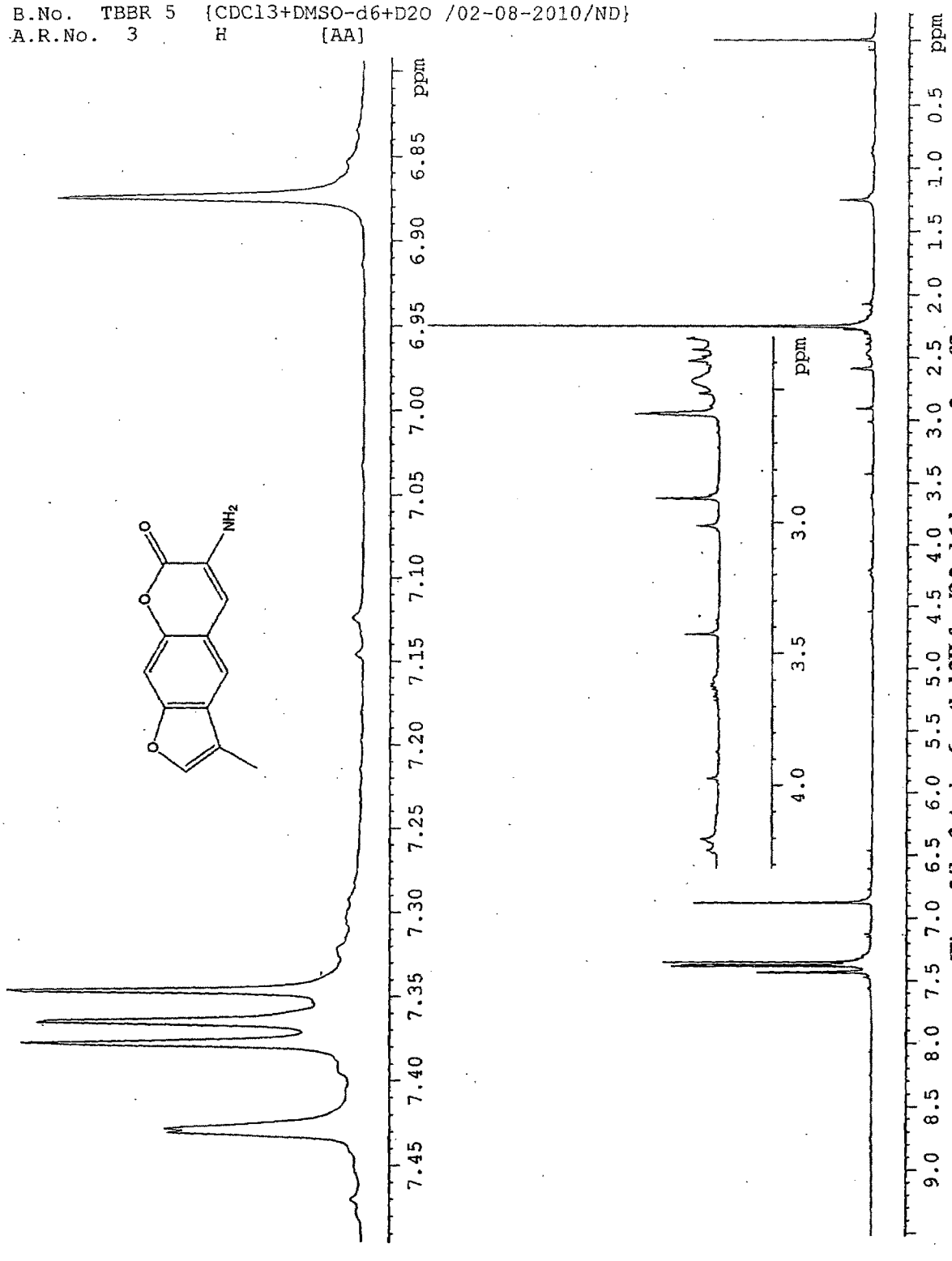
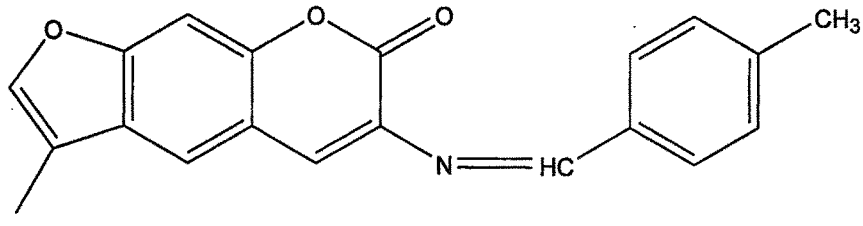


Figure-23a]: 3-Amino-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one 93



[Figure-24]: 3-Amino-6-methyl-2H-furo[3,2-g]-1-benzopyran-2-one 93

6-Methyl-3-(4-methylbenzalimino)-2H-furo[3,2-g]-1-benzopyran-2-one, **94:**



State : off white crystalline solid

Molecular Formula : $C_{20}H_{15}O_3N$

Melting Point : 180 - 181 °C

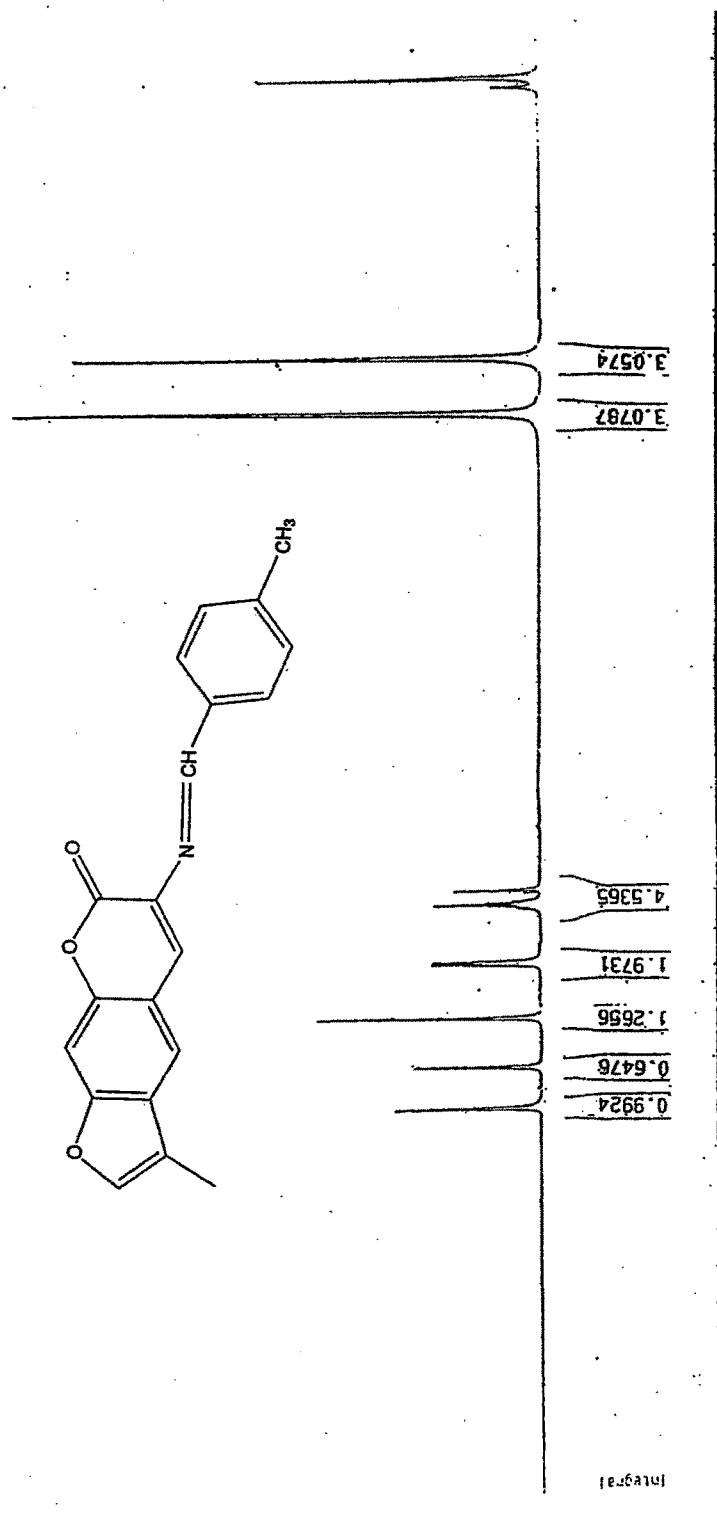
% Yield : 48

% C,H,N analysis (calculated) : C: 75.71 H: 4.73 N: 4.42

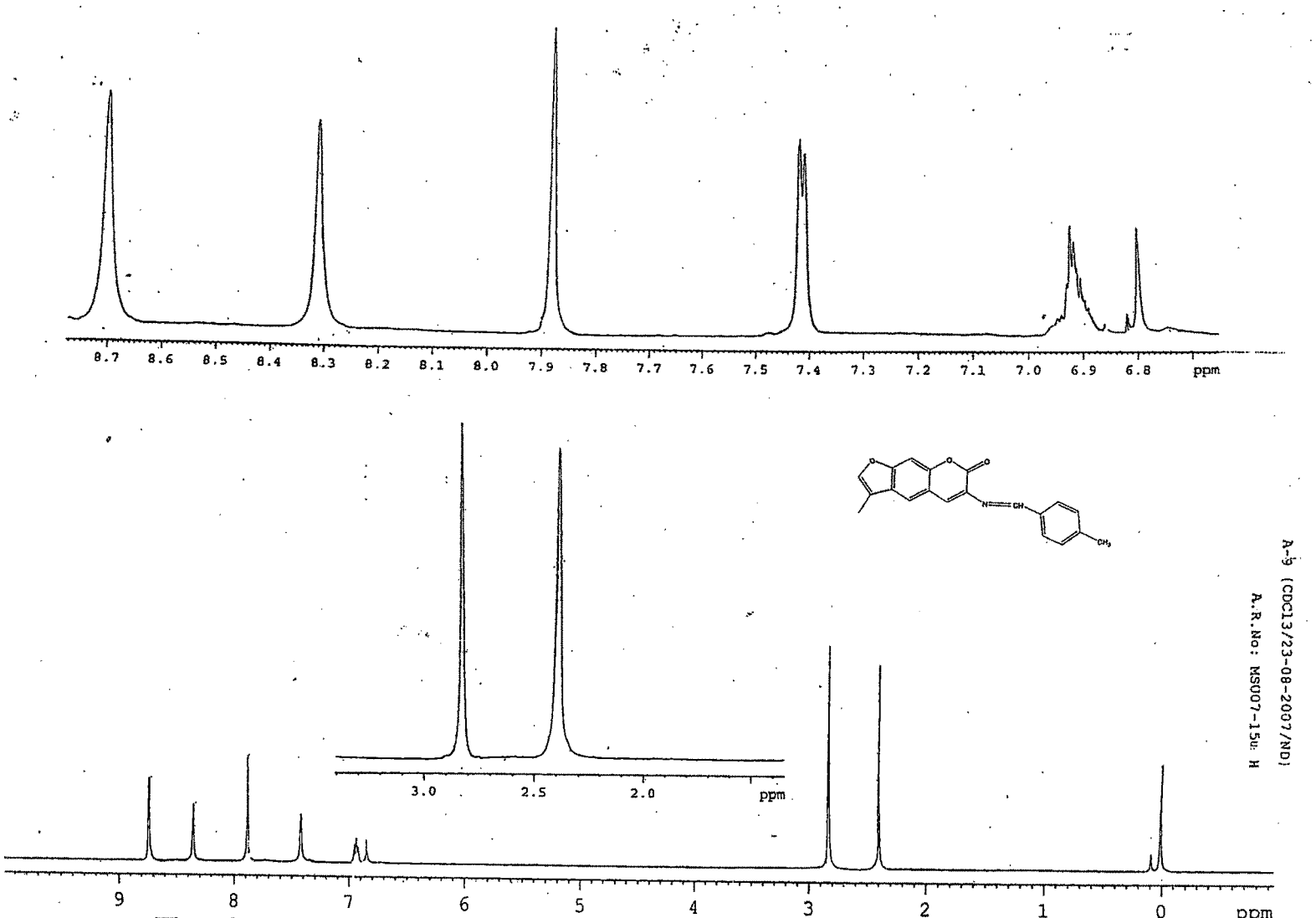
% C,H,N analysis (found) : C: 75.68 H: 4.60 N: 4.51

IR data (KBr) cm^{-1} : 2981, 1718, 1688, 1621, 1501, 1441, 1365, 1121, 841.

PMR data (400MHz, $CDCl_3$) : δ 2.40(s, 3H, $-C\underline{H}_3$), 2.82(s, 3H, Ar-$C\underline{H}_3$), 6.81-6.98(m, 4H, aromatic protons, C-4 and C-9 protons), 7.39-7.88(d, J=6 Hz, 2H, aromatic protons), 7.88(s, 1H, C-5), 8.31(s, 1H, C-7), 8.70(s, 1H, =C<u>H</u>Ar).

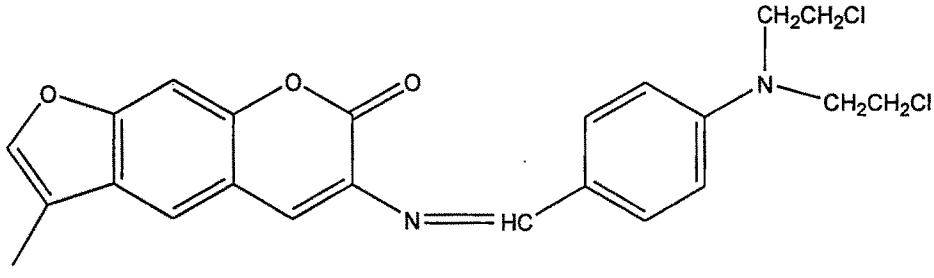


[Figure-25]: 6-Methyl-3-(4-methylbenzalimino)-2H-furo[3,2-g]-1-benzopyran-2-one, 94



[Figure-25a]: 6-Methyl-3-(4-methylbenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2- one, 94

6-Methyl-3-{4-[N,N-di(2-chloroethyl)amino]benzalimino}-2*H*-furo[3,2-*g*]-1-benzopyran-2-one, **95:**



State : pale brown amorphous solid

Molecular Formula : $C_{23}H_{20}O_3N_2Cl_2$

Melting Point : dec. >250°C

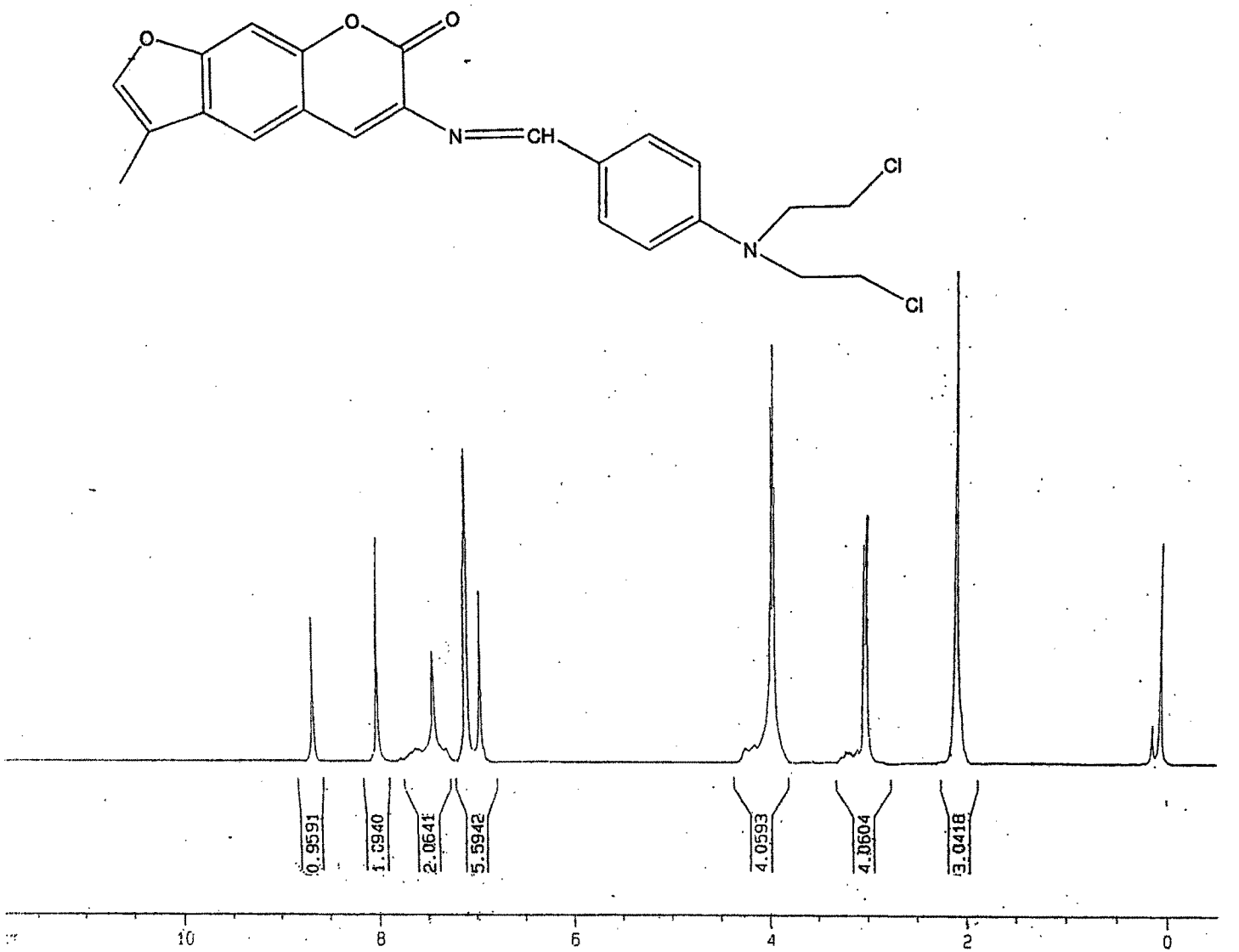
% Yield : 31

%C,H,N analysis (calculated) : C: 62.30 H: 4.51 N: 6.32

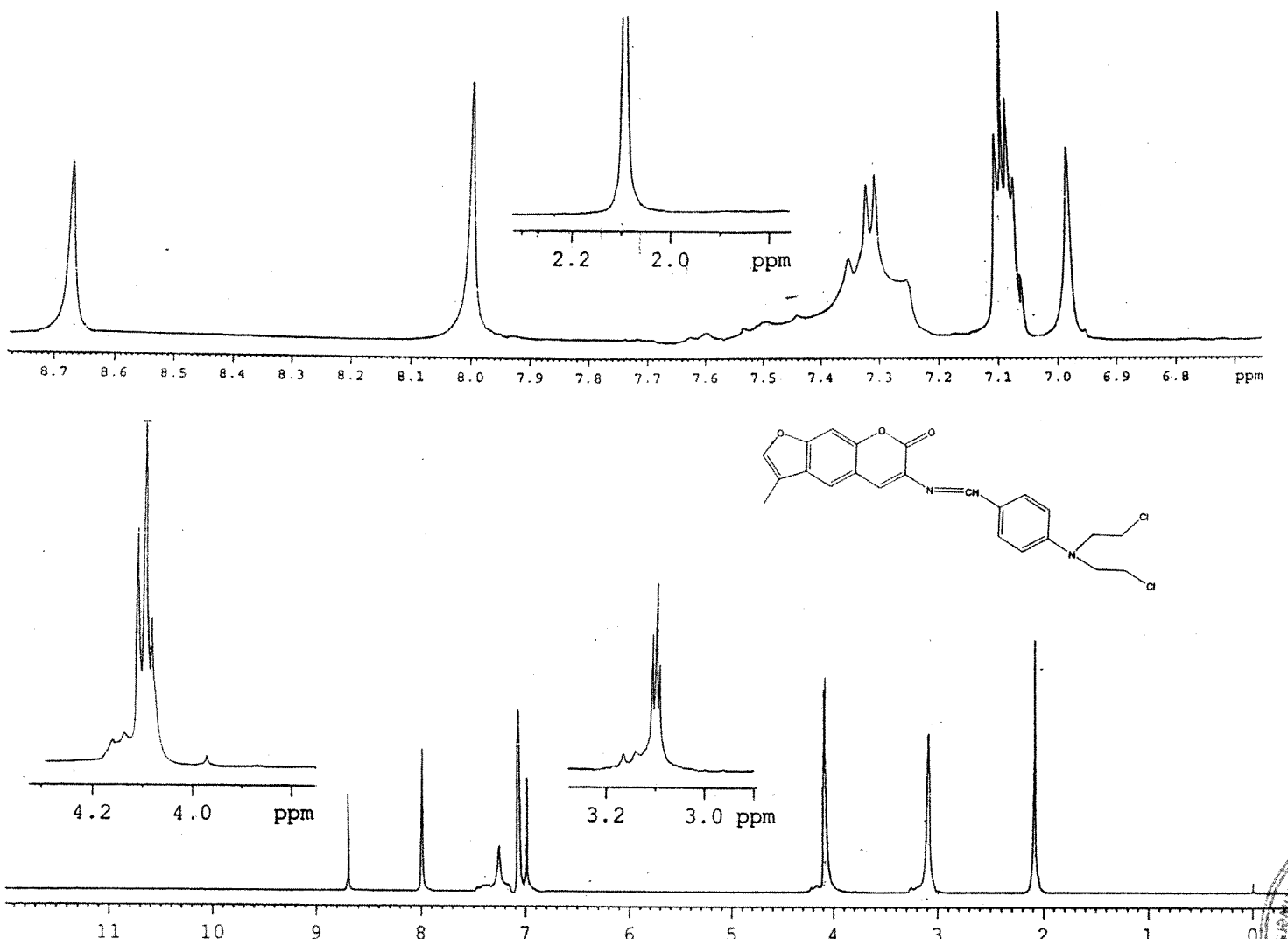
%C,H,N analysis (found) : C: 56.41 H: 2.61 N: 3.78

IR data (KBr) cm^{-1}: 3010, 2988, 2974, 1715, 1688, 1638, 1559, 1351, 1128, 820.

PMR data (400MHz, $CDCl_3$) δ ppm : δ 2.10(s, 3H, -C<u>H</u>$_3$), 3.10(t, 4H, 2x-NC<u>H</u>$_2$), 4.10(t, 4H, 2x-C<u>H</u>$_2$Cl), 6.99(s, 1H, C-4), 7.04-7.15(m, 4H, aromatic protons), 7.23-7.38(s, 2H, C-9 and C-5), 8.00(s, 1H, C-7), 8.68(s, 1H, =C<u>H</u>Ar).

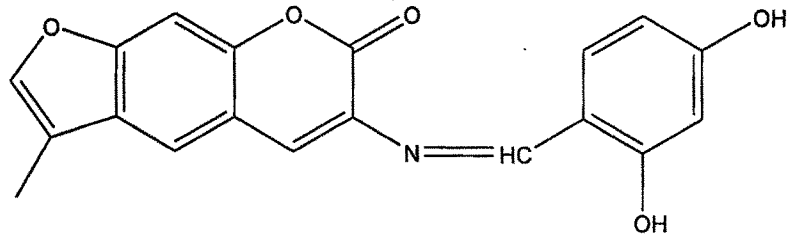


[Figure-26]: 6-Methyl-3-{4-[N,N-di(2-chloroethyl)amino]benzalimino}-2*H*-furo[3,2-g]-1-benzopyran-2-one, 95



[Figure-26a]: 6-Methyl-3-{4-[N,N-di(2-chloroethyl)amino]benzalimino}-2*H*-furo[3,2-*g*]-1-benzopyran-2-one, 95

6-Methyl-3-(2,4-dihydroxybenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **96:**



State : light brown crystalline solid

Molecular Formula : $C_{19}H_{13}O_5N$

Melting Point : >250°C

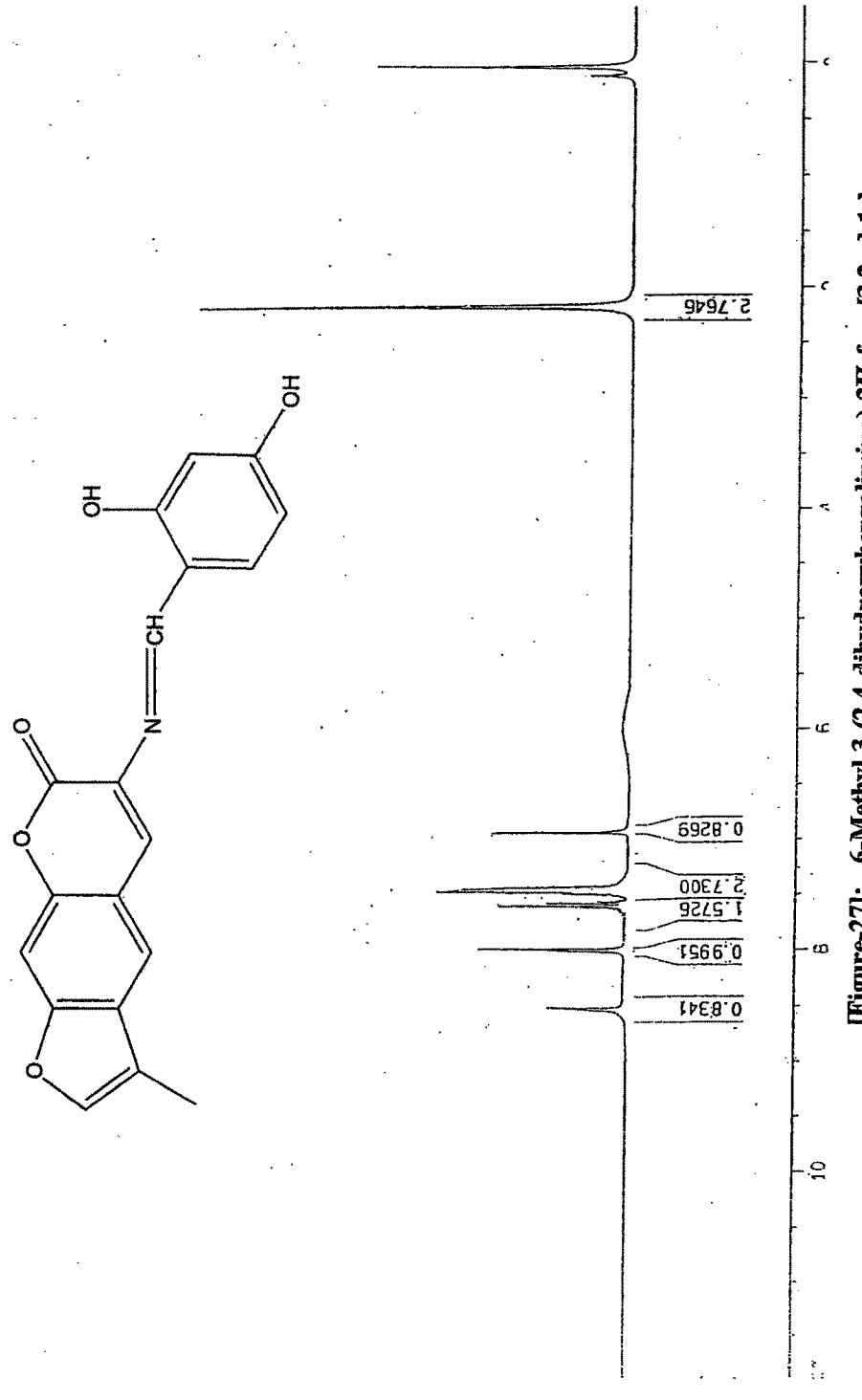
% Yield : 31

%C,H,N analysis (calculated) : C: 68.06 H: 3.88 N: 4.18

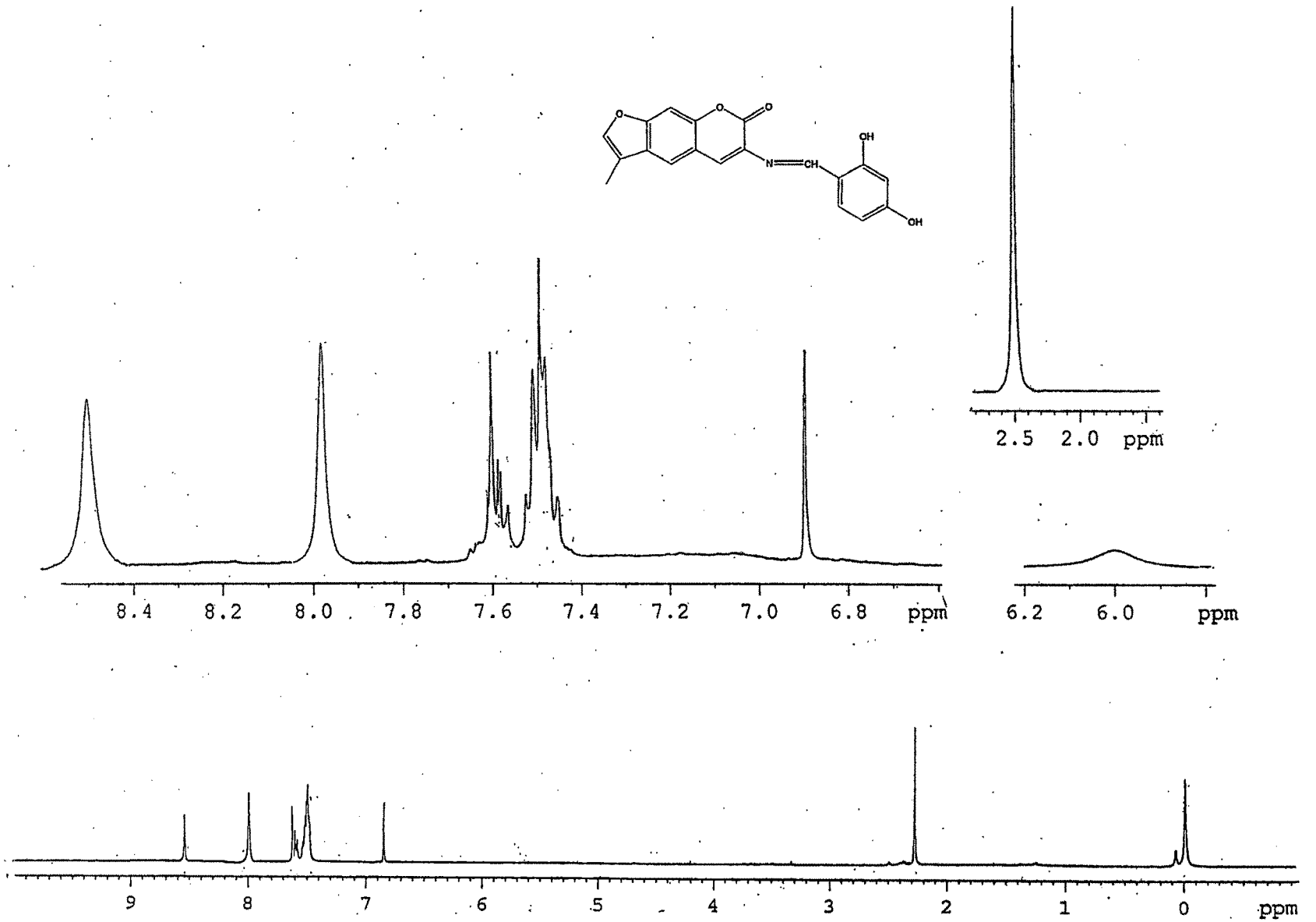
%C,H,N analysis (found) : C: 68.21 H: 3.78 N: 4.38

IR data (KBr) cm^{-1} : 3378, 2992, 2907, 1712, 1638, 1559, 1351, 1365, 1221, 1119, 721.

PMR data (400MHz, $CDCl_3$) : δ 2.50(s, 3H, -C<u>H</u>$_3$), 5.90-6.10(br hump, -O<u>H</u>), 6.90(s, 1H, C-4), 7.44-7.68(m, 5H, aromatic, C-9 and C-5 overlap), 7.98(s, 1H, C-7), 8.52(s, 1H, =C<u>H</u>Ar).

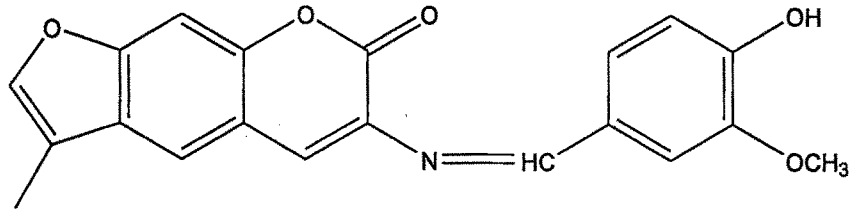


[Figure-27]: 6-Methyl-3-(2,4-dihydroxybenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one. 96



[Figure-27a]: 6-Methyl-3-(2,4-dihydroxybenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 96

6-Methyl-3-(4-hydroxy-3-methoxybenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **97:**



State : off white crystalline solid

Molecular Formula : $C_{20}H_{15}O_5N$

Melting Point : >250°C

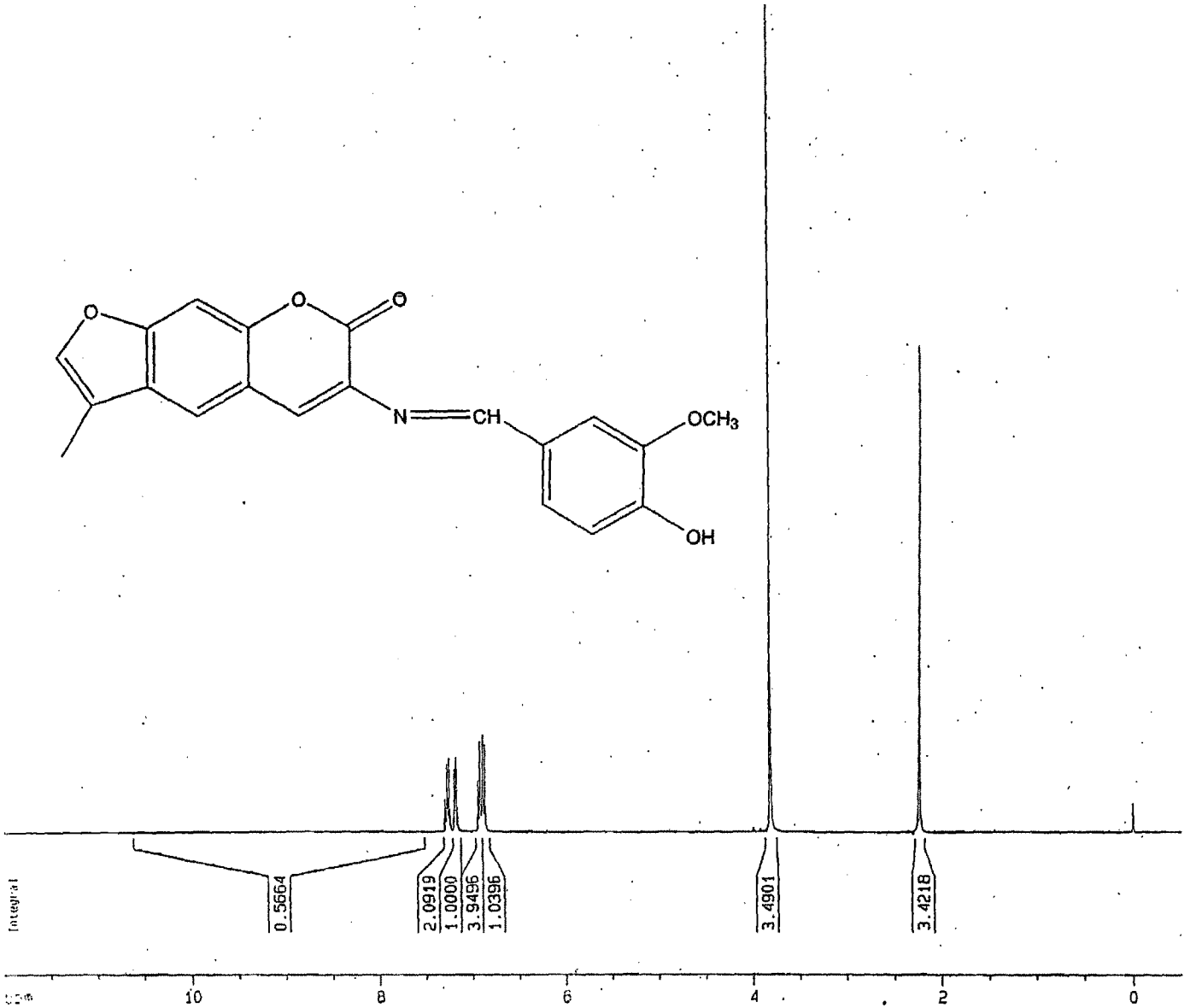
% Yield : 39

%C,H,N analysis (calculated) : C: 68.77 H: 4.30 N: 4.01

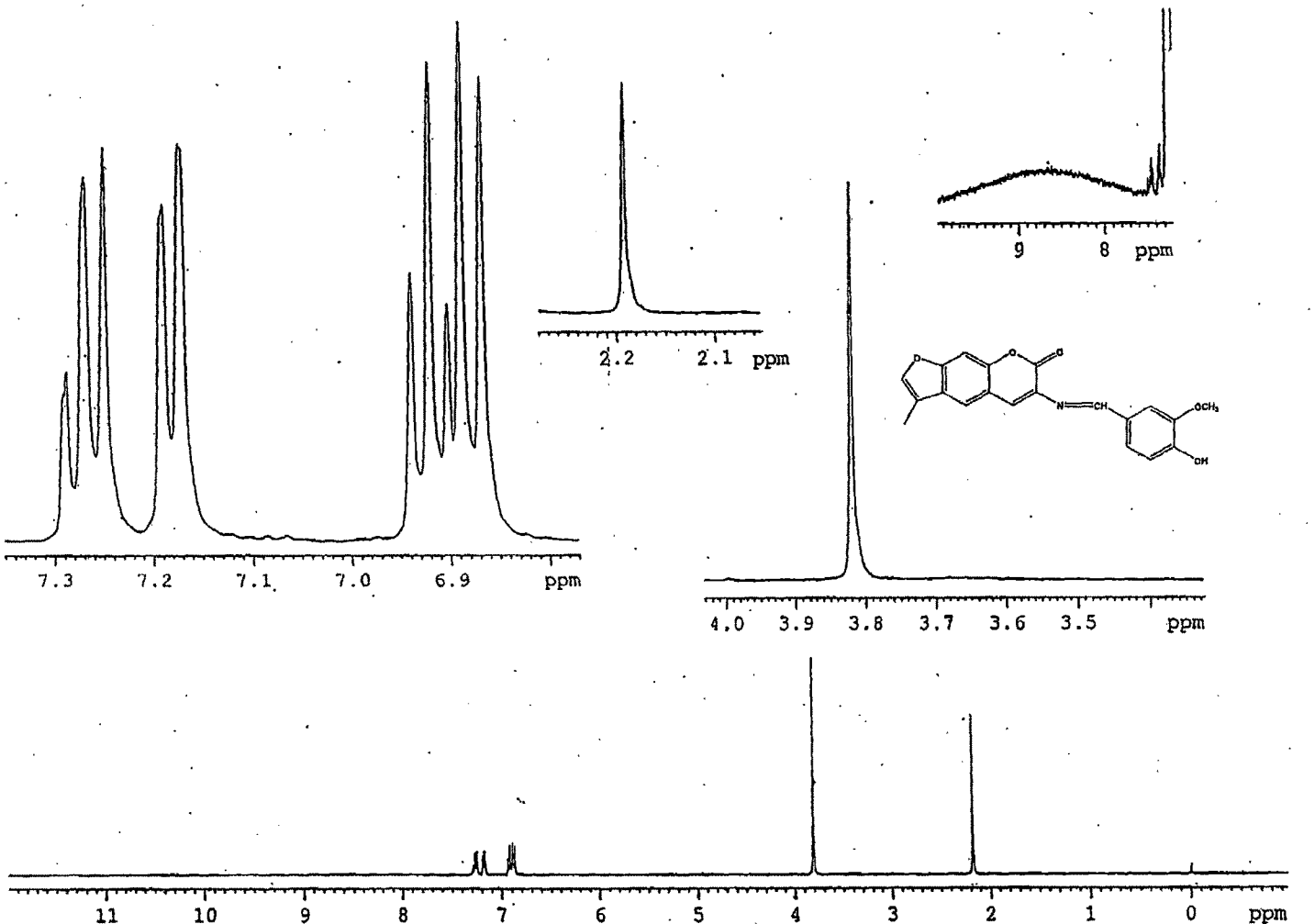
%C,H,N analysis (found) : C: 68.59 H: 4.50 N: 4.21

IR data (KBr) cm^{-1} : 3361(b), 2992, 2938, 1718, 1631, 1248, 1221, 1038, 798.

PMR data (400MHz, $CDCl_3$) δ ppm : δ 2.19(s, 3H, -C<u>H</u>$_3$), 3.83(s, 3H, -OC<u>H</u>$_3$), 6.87-6.89(d, J=7 Hz, 1H, aromatic proton), 6.91(s, 1H, C-4), 6.92(s, 2H, aromatic proton and C-9 overlap), 6.94(s, 1H, C-5), 7.17-7.19(d, J=7 Hz, 1H, aromatic proton), 7.25(s, 1H, C-7), 7.28(br s, 1H, -OH), 7.30-7.59(s, 1H, =C<u>H</u>Ar).

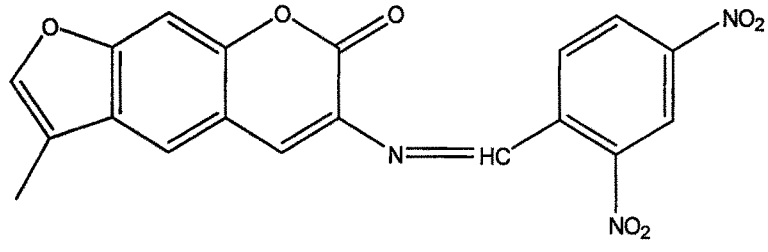


[Figure-28]: 6-Methyl-3-(4-hydroxy-3-methoxybenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 97



[Figure-28a]: 6-Methyl-3-(4-hydroxy-3-methoxybenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 97

6-Methyl-3-(2,4-dinitrobenzalimino)-2H-furo[3,2-g]-1-benzopyran-2-one, **98:**



State : yellow solid, crystalline

Molecular Formula : $C_{19}H_{11}O_7N_3$

Melting Point : >250°C

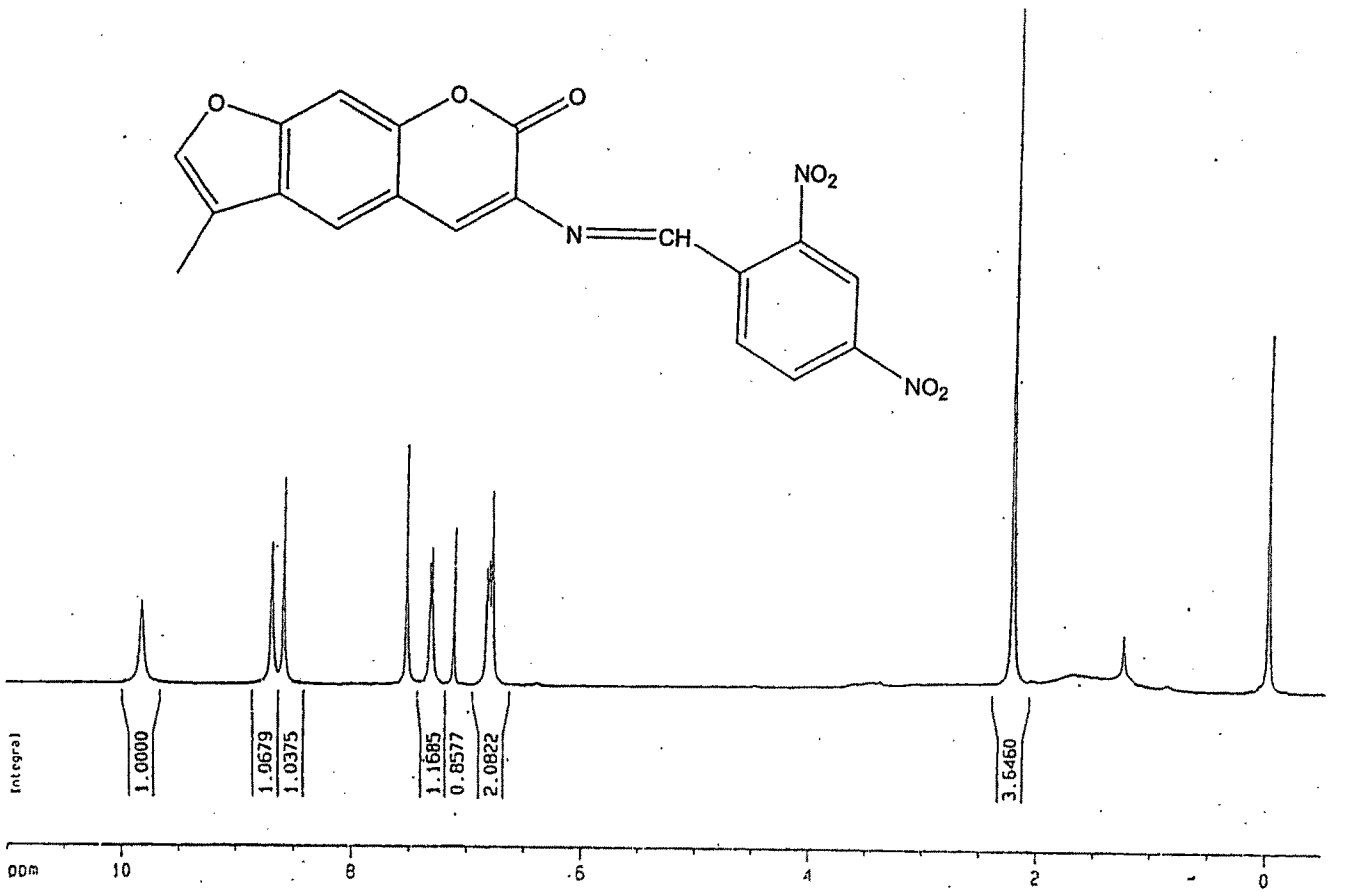
% Yield : 58

%C,H,N analysis (calculated) : C: 58.02 H: 2.79 N: 10.69

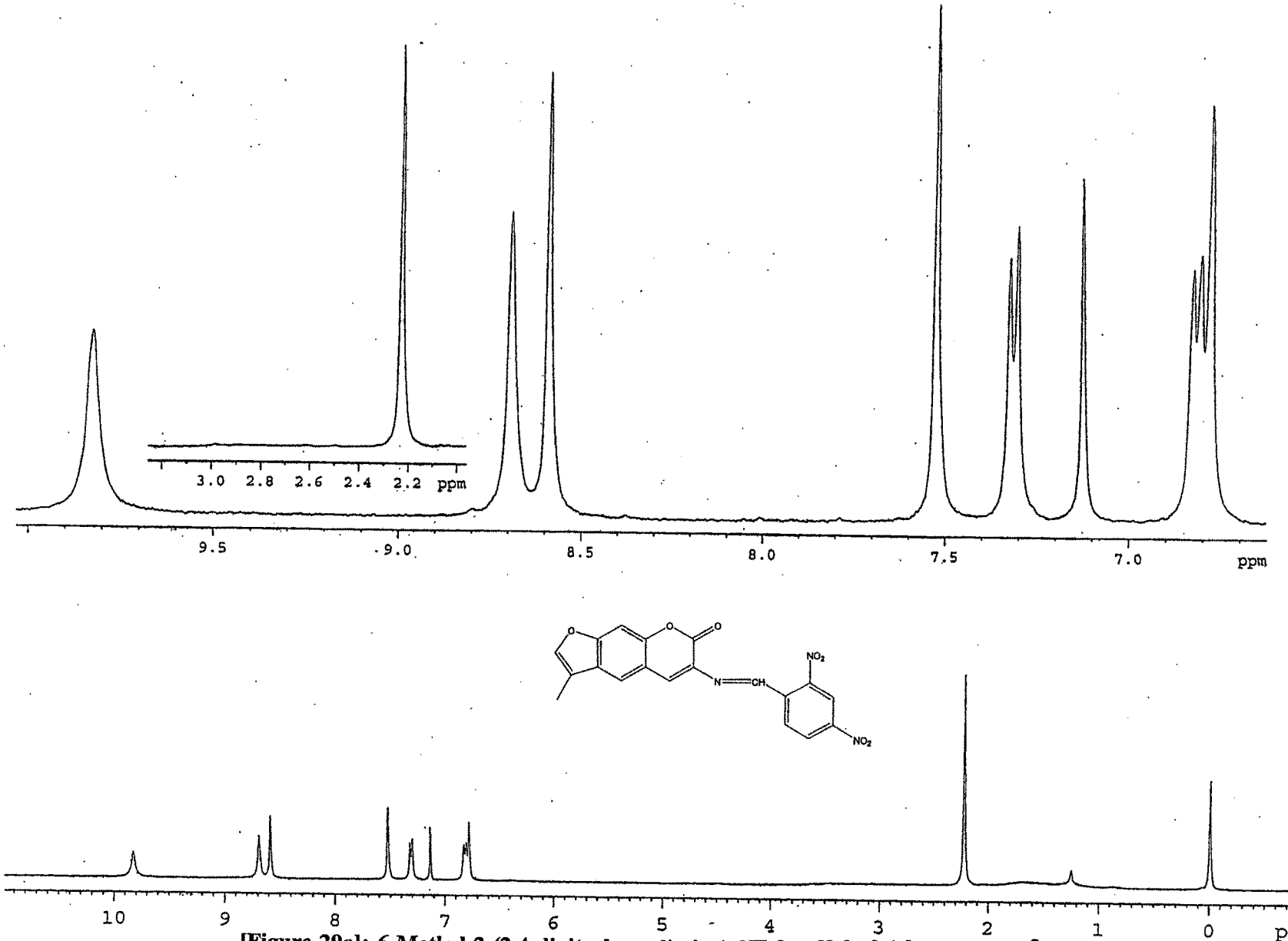
%C,H,N analysis (found) : C: 58.18 H: 3.08 N: 11.01

IR data (KBr) cm^{-1} : 3008, 2907 1712, 1631, 1561, 1359, 1121, 789.

PMR data (400MHz, $CDCl_3$) : δ 2.24(s, 3H $-C\underline{H}_3$), 6.78(s, 1H, C-4), 6.82(d, J=6.3 Hz, 1H, aromatic proton), 7.14(s, 1H, C-9), 7.31(d, J=6.3 Hz, 1H, aromatic proton), 7.53 (s, 1H, C-5), 8.58(s, 1H, aromatic proton), 8.70(s, 1H, C-7), 9.83(s, 1H, N=C$\underline{H}$Ar).

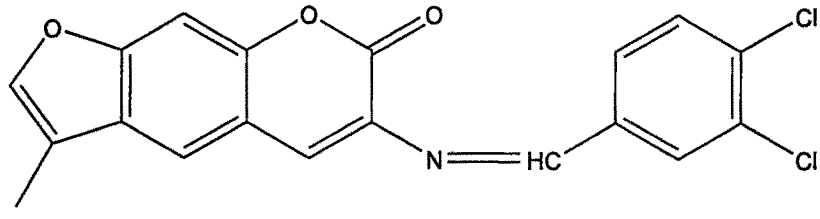


[Figure-29]: 6-Methyl-3-(2,4-dinitrobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 98



[Figure-29a]: 6-Methyl-3-(2,4-dinitrobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 98

6-Methyl-3-(3,4-dichlorobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **99**



State : light yellow solid, crystalline

Molecular Formula : $C_{19}H_{11}O_3NCl_2$

Melting Point : >250°C

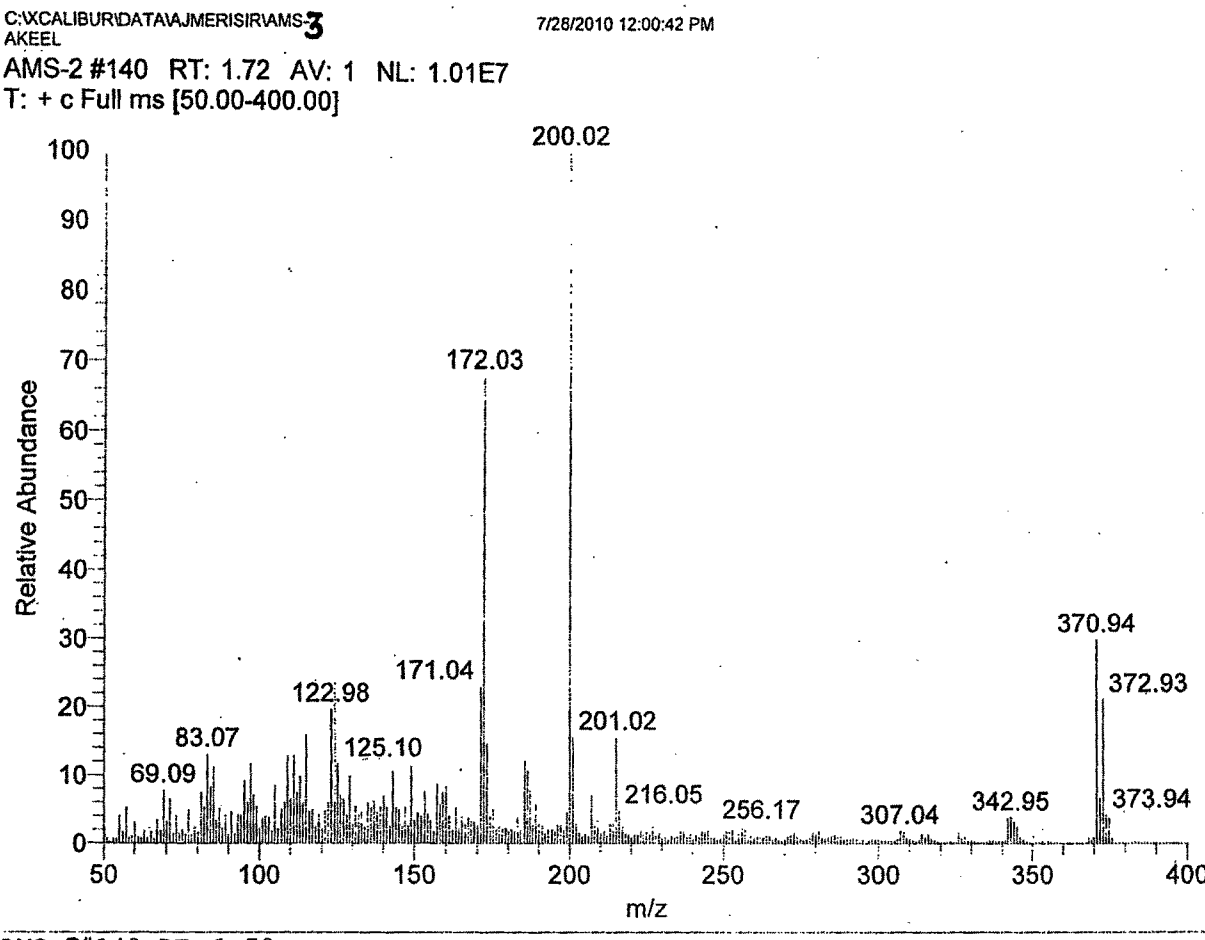
% Yield : 59

%C,H,N analysis (calculated): C: 61.29 H: 2.96 N: 3.76

%C,H,N analysis (found): C: 61.31 H: 3.01 N: 4.11

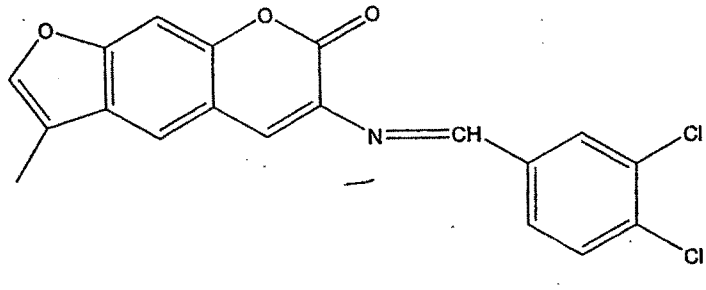
IR data (KBr) cm^{-1} : 3010, 2971, 1708, 1621, 1558, 1348, 1131, 781.

PMR data (400MHz, $CDCl_3$): δ 2.32(s, 3H $-C\underline{H}_3$), 7.47(s, 1H, C-4), 7.56-7.59(s, 2H, C-9 and an aromatic proton), 7.77(s, 1H, C-5), 8.03(s, 1H, C-7), 8.15(d, J=6.3 Hz, 1H, aromatic proton), 8.34 (d, J=6.3 Hz, 1H, aromatic proton), 9.46(s, 1H, =C<u>H</u>Ar).

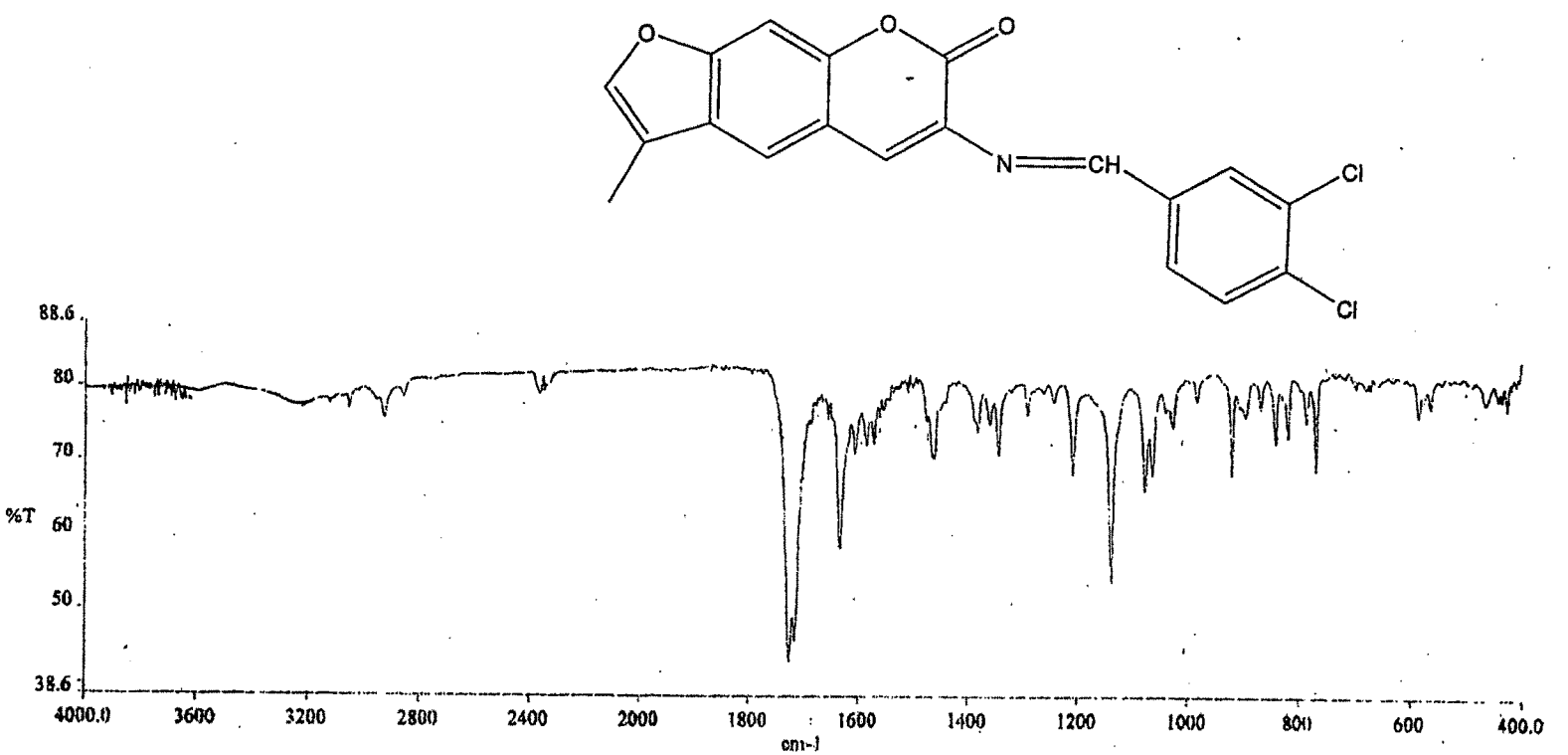


AMS-3#140 RT: 1.72
T: + c Full ms [50.00-400.00]

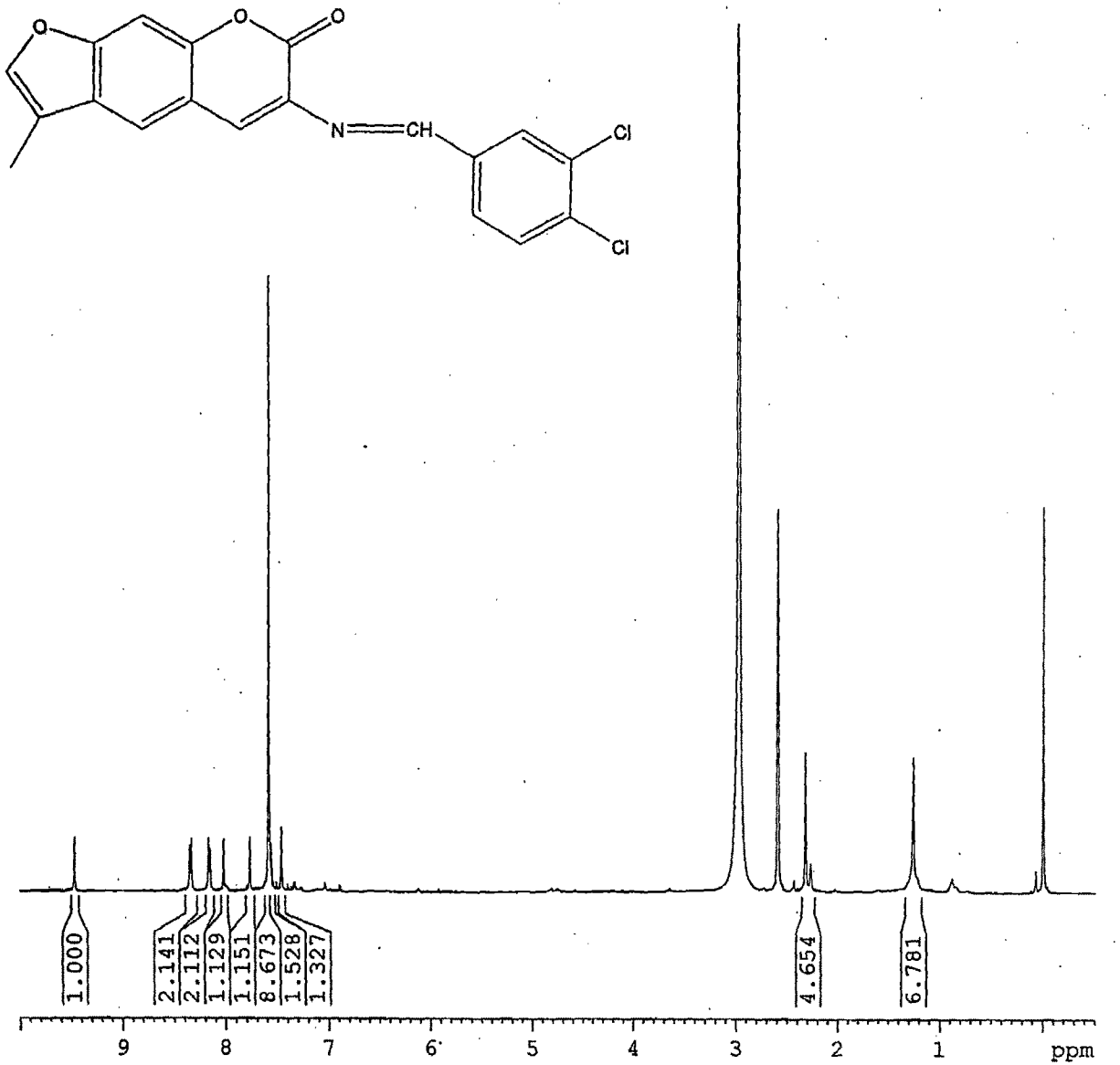
m/z	Intensity	Relative
97.08	1180883.0	11.65
109.00	1295810.0	12.78
111.10	1301106.0	12.83
115.05	1612114.0	15.90
122.98	1991577.0	19.64
125.10	1179651.0	11.63
143.05	1073564.0	10.59
149.04	1138314.0	11.23
171.04	2329959.0	22.98
172.03	6885220.0	67.90
173.01	1477760.0	14.57
185.36	1225725.0	12.09
186.27	1082423.0	10.67
200.02	10140138.0	100.00
201.02	1579933.0	15.58
215.04	1564759.0	15.43
370.94	3054215.0	30.12
372.93	2159361.0	21.30



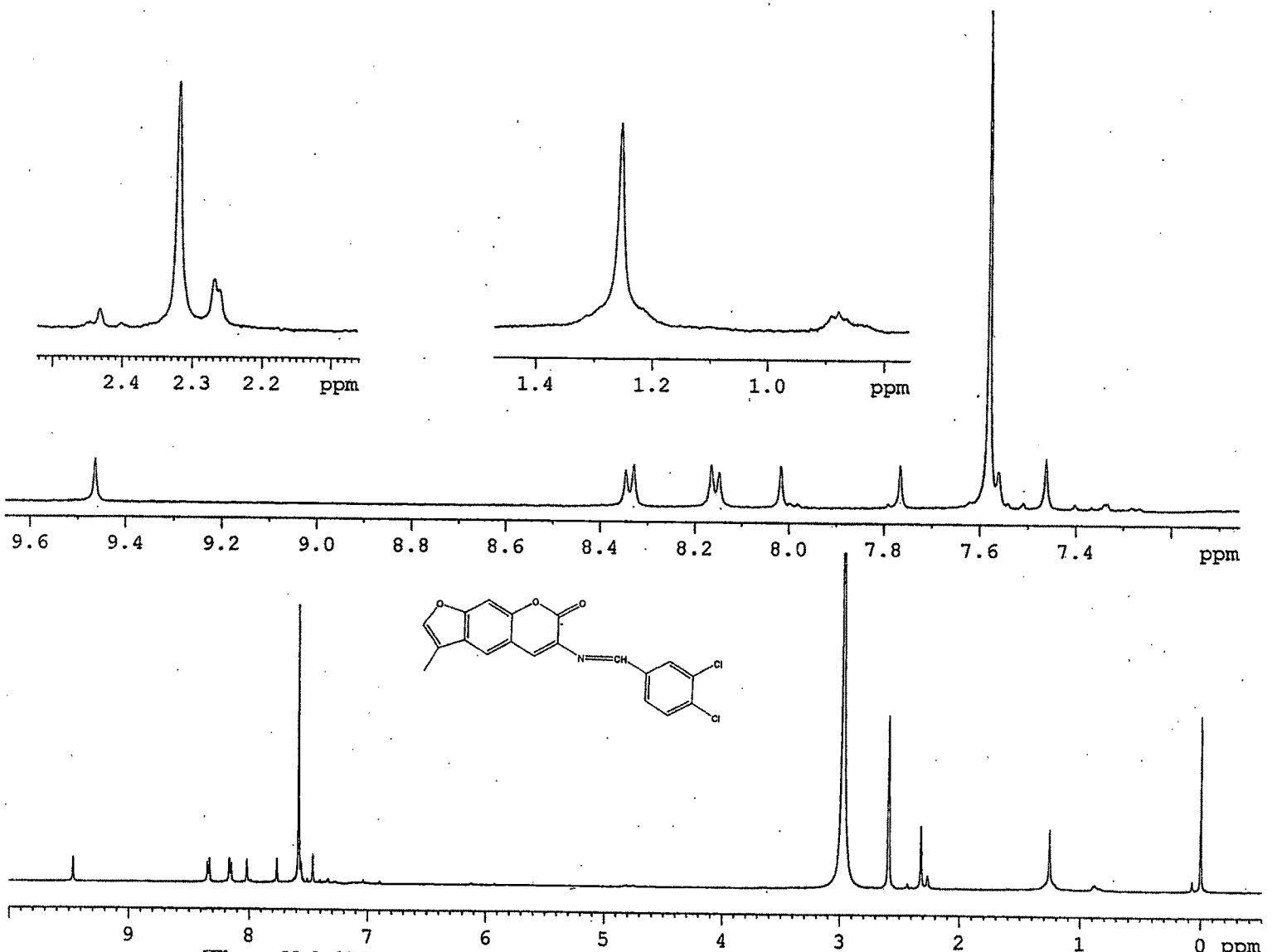
[Figure-30]: 6-Methyl-3-(3,4-dichlorobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 99



[Figure-31]: 6-Methyl-3-(3,4-dichlorobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 99

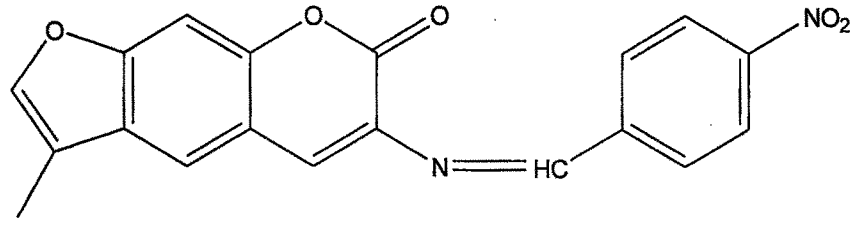


[Figure-32]: 6-Methyl-3-(3,4-dichlorobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 99



[Figure-32a]: 6-Methyl-3-(3,4-dichlorobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 99

6-Methyl-3-(4-nitrobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **100:**



State : yellow solid, crystalline

Molecular Formula : $C_{19}H_{12}O_5N_2$

Melting Point : 198 – 199 °C

% Yield : 59

%C,H,N analysis (calculated) : C: 65.52 H: 3.47 N: 8.05

%C,H,N analysis (found) : C: 65.59 H: 3.20 N: 7.78

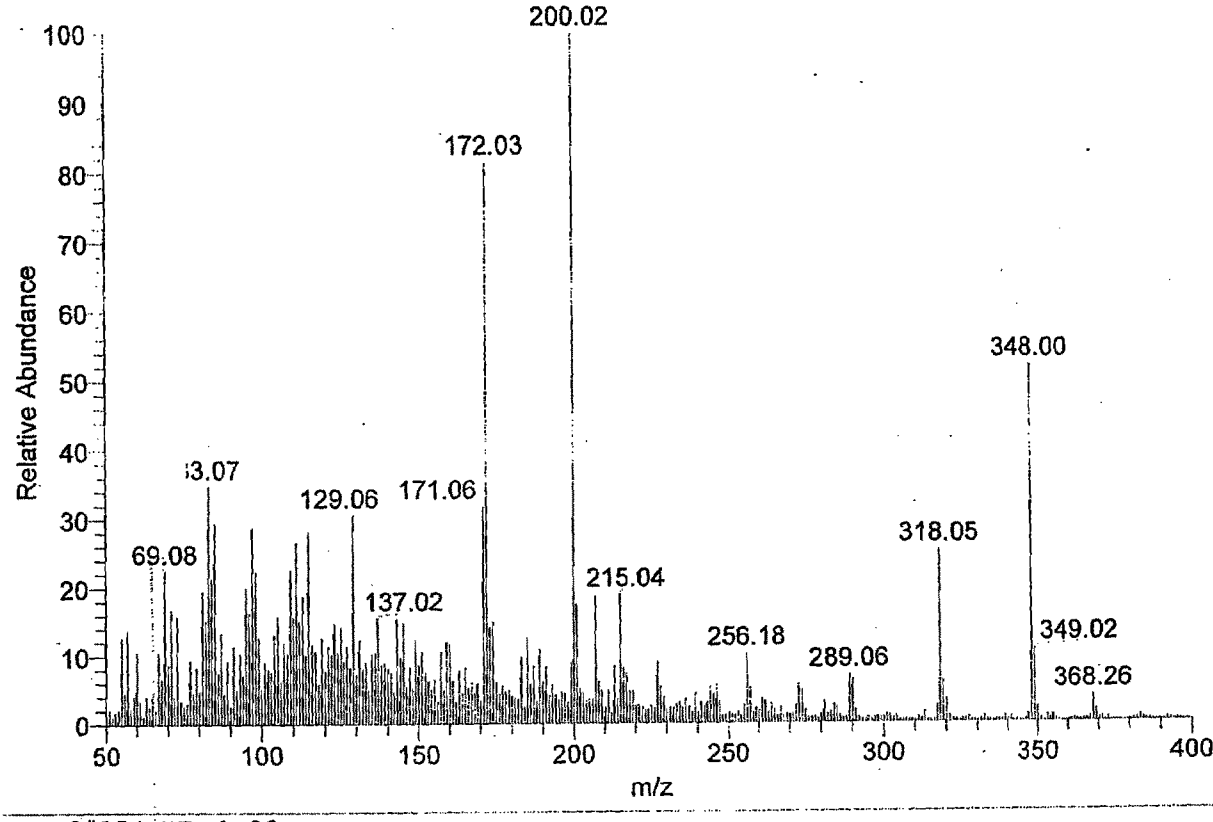
IR data (KBr) cm^{-1} : 2969, 1719, 1678, 1621, 1571, 1501, 1368, 1128, 779.

PMR data (400MHz, $CDCl_3$) : δ 2.30(s, 3H, C<u>H</u>$_3$), 7.38(d, J=6.9 Hz, 2H, aromatic proton), 7.46(s, 1H, C-4), 7.49(s,1H, aromatic proton), 7.54(s, 1H, C-9), 7.66(s, 1H, C-5), 7.74(d, 2H, aromatic proton), 7.88(s, 1H, C-7), 9.34(s, 1H, N=C<u>H</u>Ar).

C:\XCALIBUR\DATA\AJMERISIR\AMS-2
AKEEL

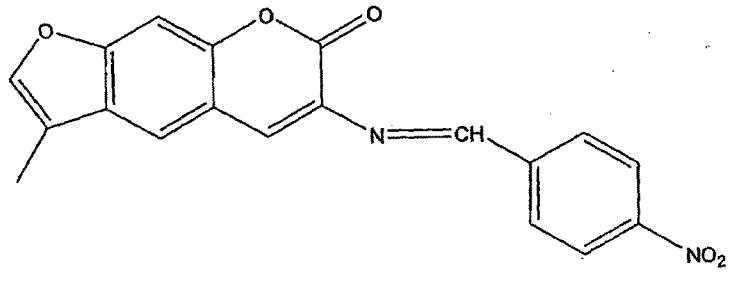
7/28/2010 12:17:17 PM

AMS-3 #154 RT: 1.89 AV: 1 NL: 2.81E6
T: + c Full ms [50.00-400.00]

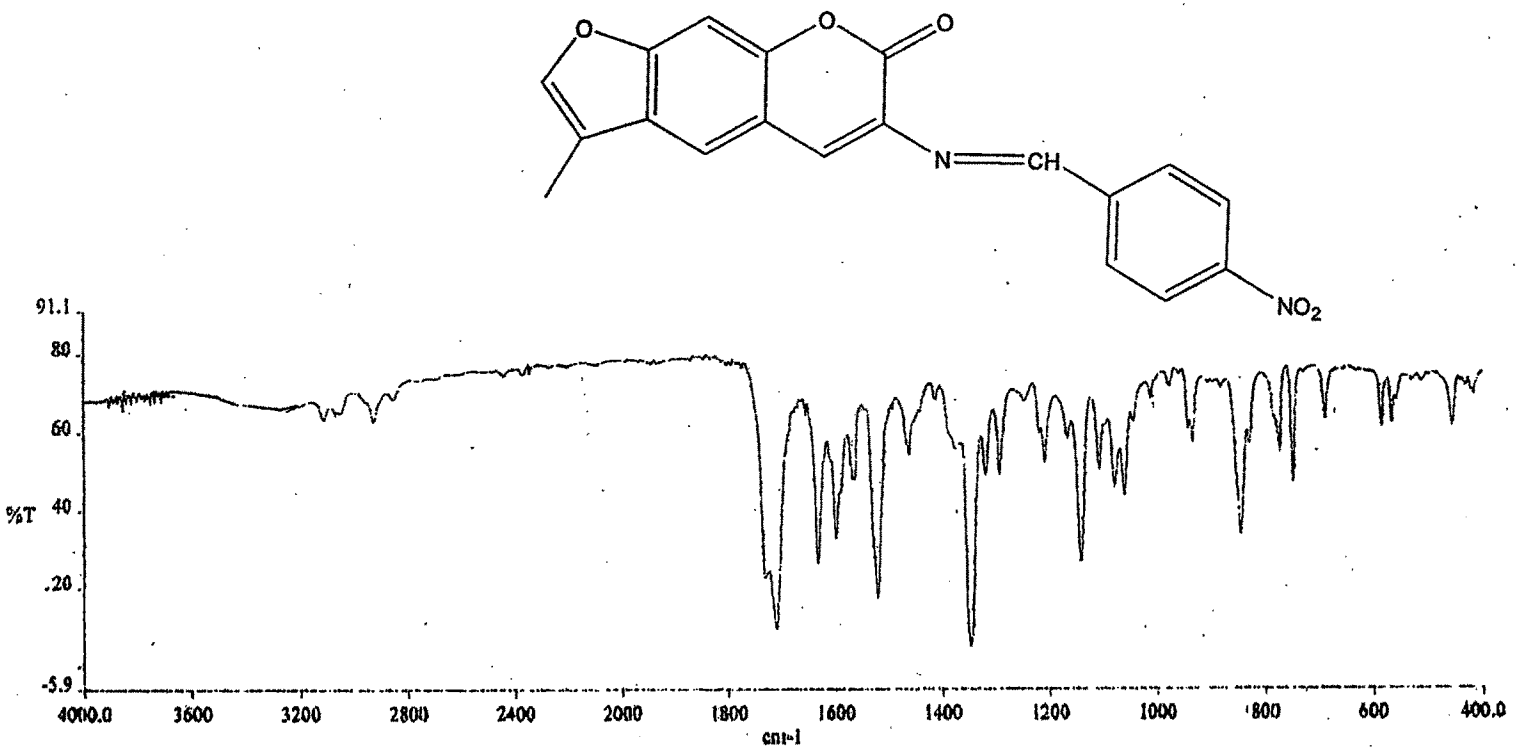


AMS-2#154 RT: 1.89
T: + c Full ms [50.00-400.00]

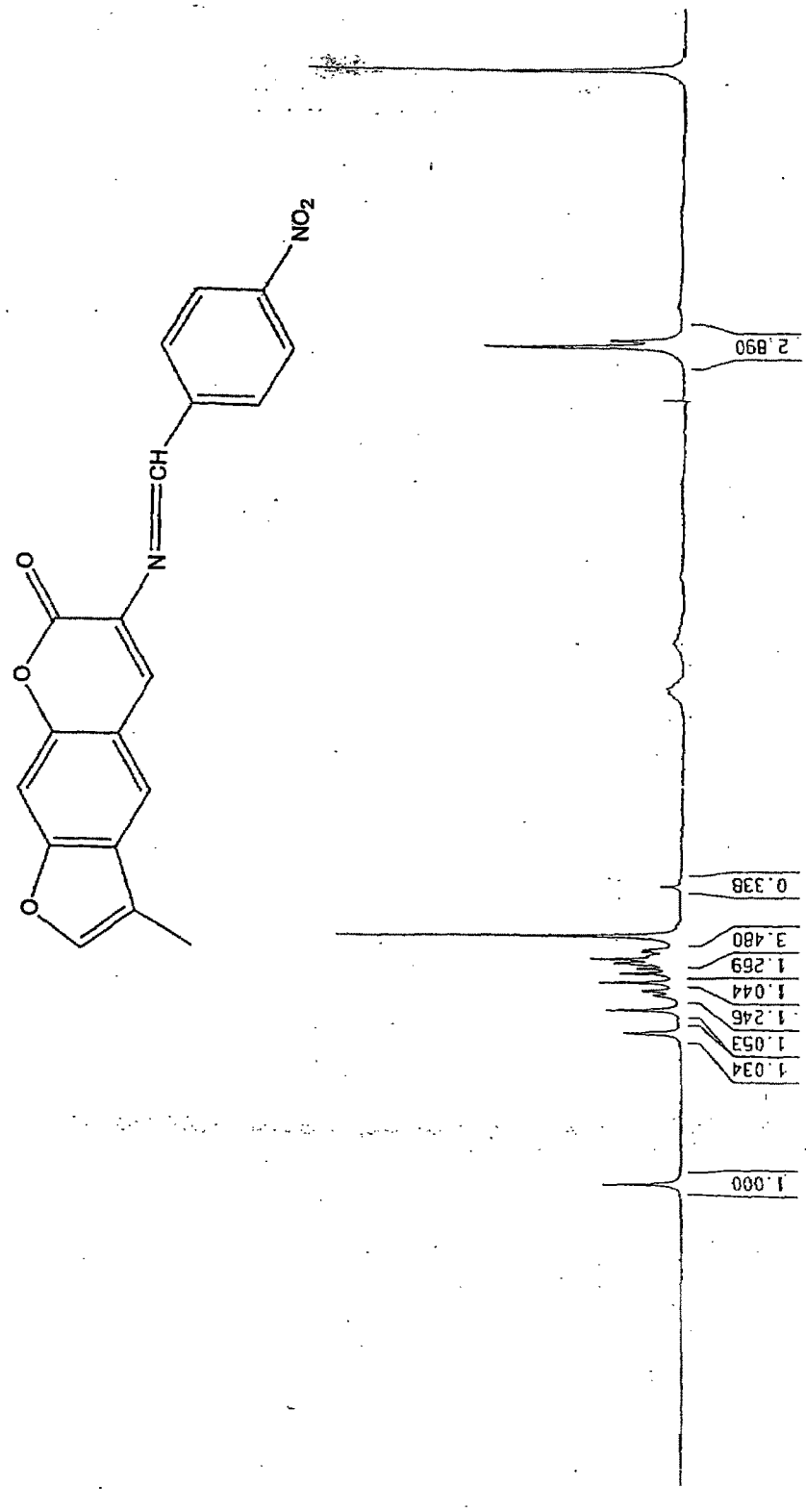
m/z	Intensity	Relative
83.07	979180.0	34.81
84.08	603092.0	21.44
85.08	827431.0	29.41
95.08	563208.0	20.02
97.09	808550.0	28.74
98.08	628322.0	22.34
109.10	635926.0	22.61
111.12	748537.0	26.61
113.09	525780.0	18.69
115.05	794764.0	28.25
129.06	861321.0	30.62
171.06	896194.0	31.86
172.03	2296298.0	81.63
200.02	2812994.0	100.00
207.02	525885.0	18.69
215.04	532832.0	18.94
318.05	712902.0	25.34
348.00	1467640.0	52.17



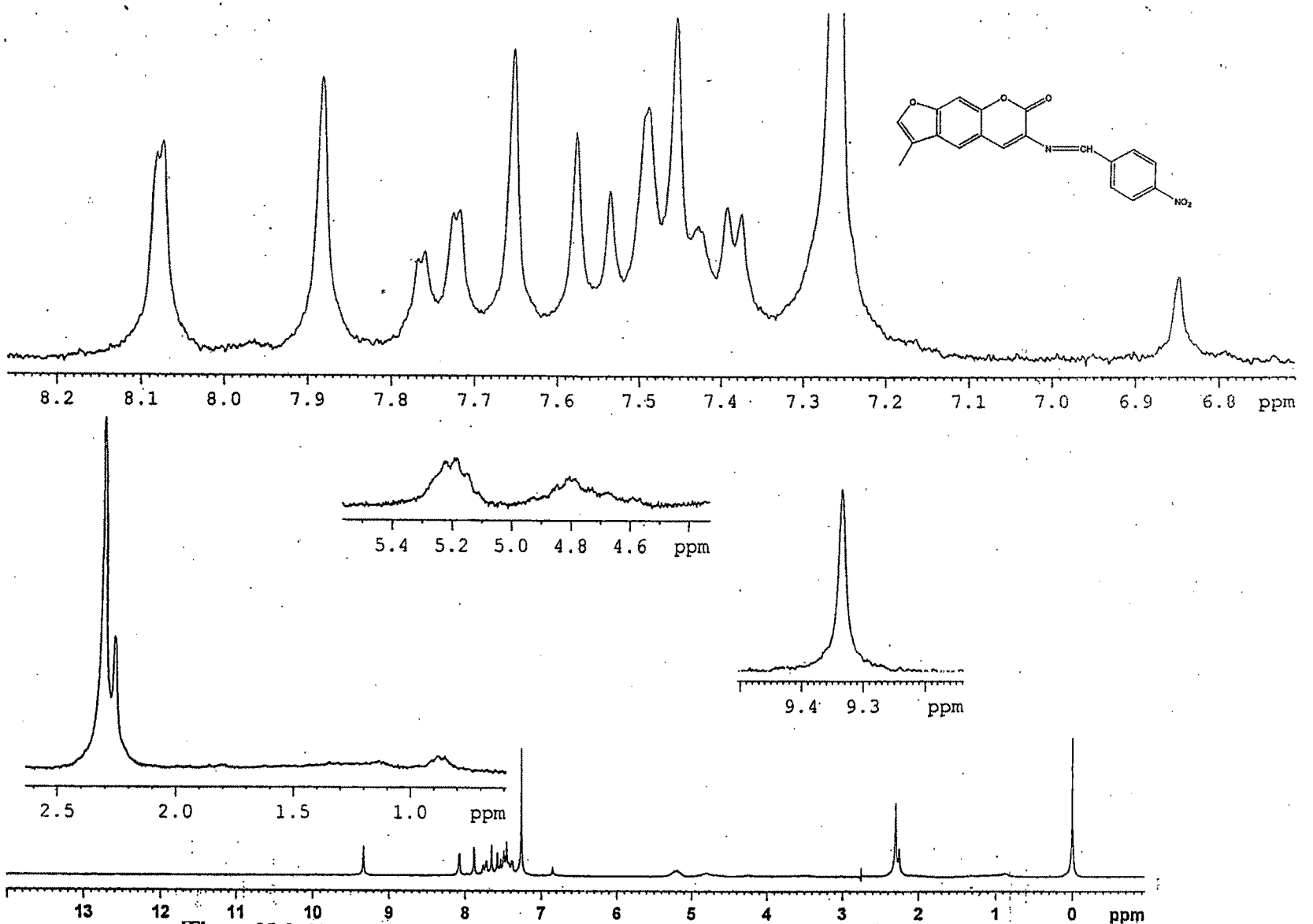
[Figure-33]: 6-Methyl-3-(4-nitrobenzalimino)-2H-furo[3,2-g]-1-benzopyran-2-one, 100



[Figure-34]: 6-Methyl-3-(4-nitrobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 100

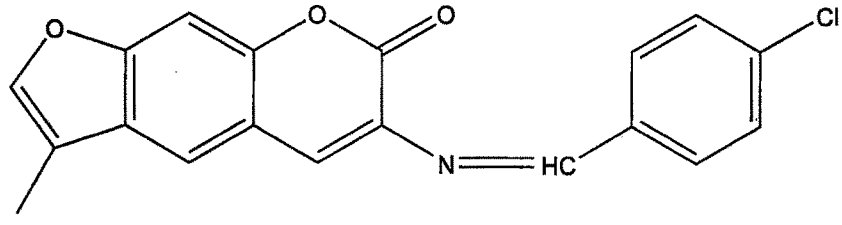


[Figure-35]: 6-Methyl-3-(4-nitrobenzalimino)-2H-furo[3,2-g]-1-benzopyran-2-one, 100



[Figure-35a]: 6-Methyl-3-(4-nitrobenzalimino)-2H-furo[3,2-g]-1-benzopyran-2-one, 100

6-Methyl-3-(4-chlorobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **101:**



State : light yellow, crystalline

Molecular Formula : $C_{19}H_{12}O_3NCl$

Melting Point : 218 – 221 °C

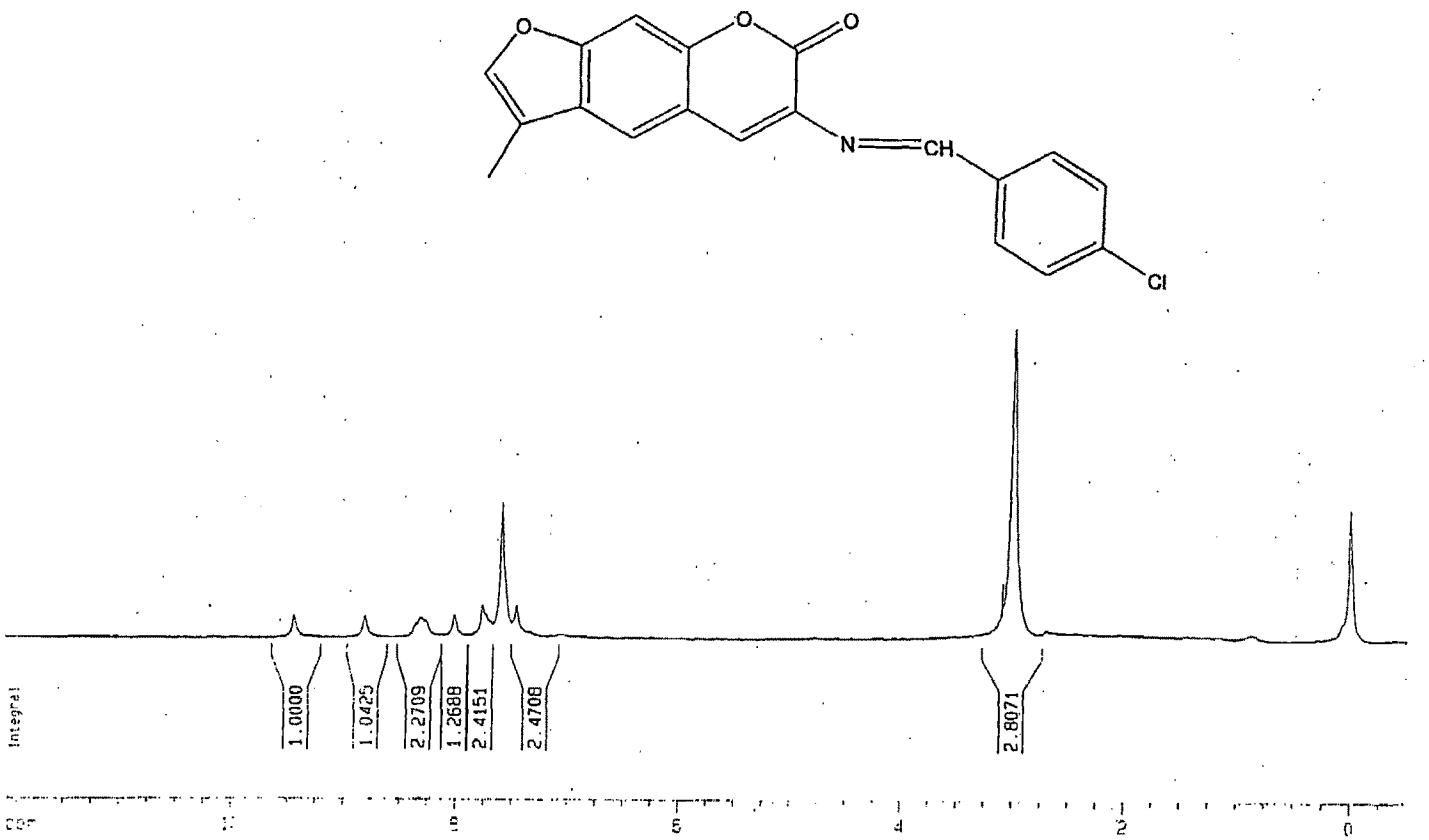
% Yield : 51

%C,H,N analysis (calculated) : C: 67.56 H: 3.56 N: 4.15

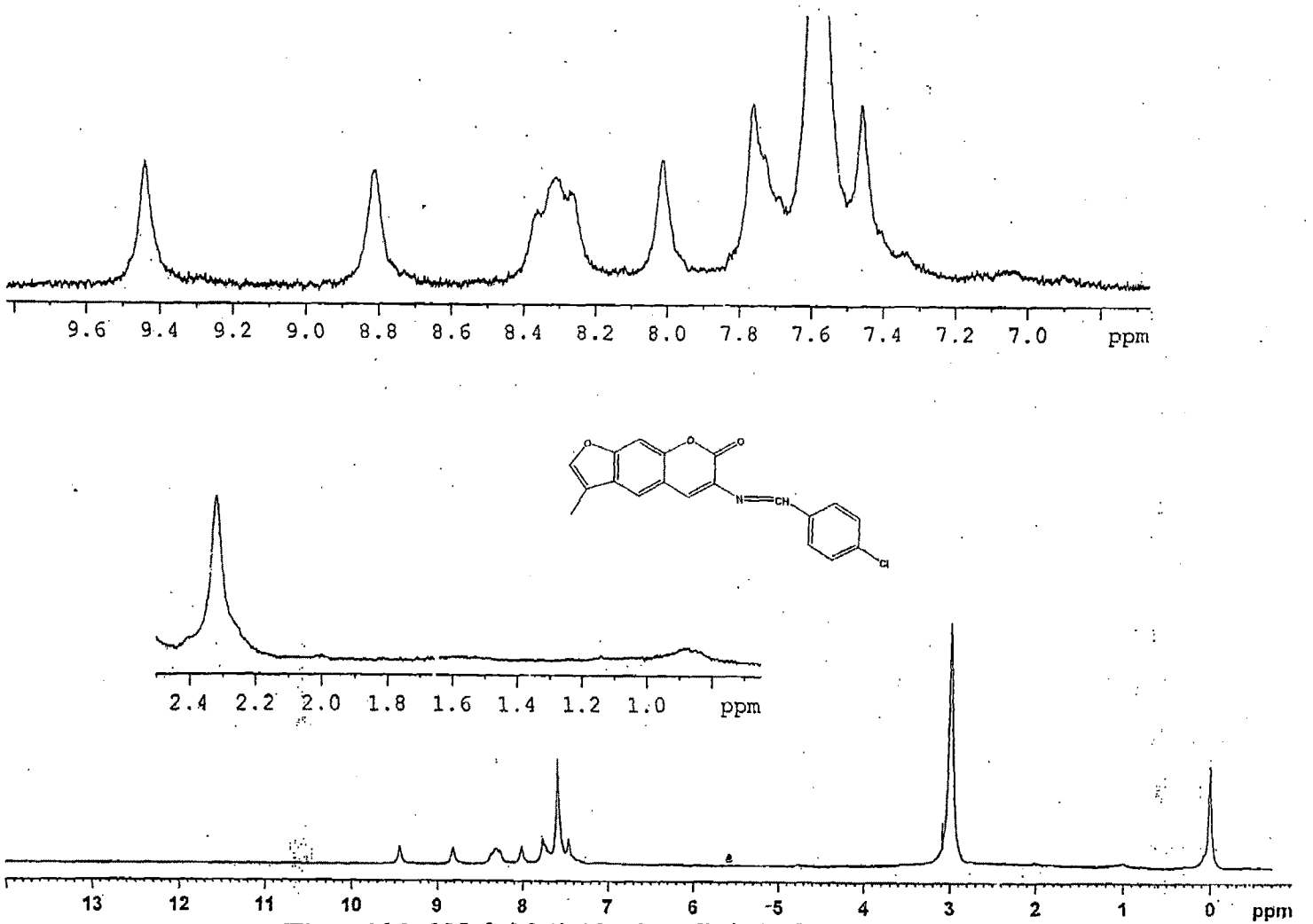
%C,H,N analysis (found) : C: 67.51 H: 3.71 N: 4.38

IR data (KBr) cm^{-1} : 2991, 1721, 1638, 1558, 1128, 801, 791.

PMR data (400MHz, $CDCl_3$) : δ 2.31(s, 3H -C<u>H</u>$_3$), 7.44-7.62(m, 4H, aromatic protons), 7.74(s, 1H, C-4), 8.00(s, 1H, C-9), 8.31(s, 1H, C-5), 8.82(s, 1H, C-7), 9.45(s, 1H, N=C<u>H</u>Ar).

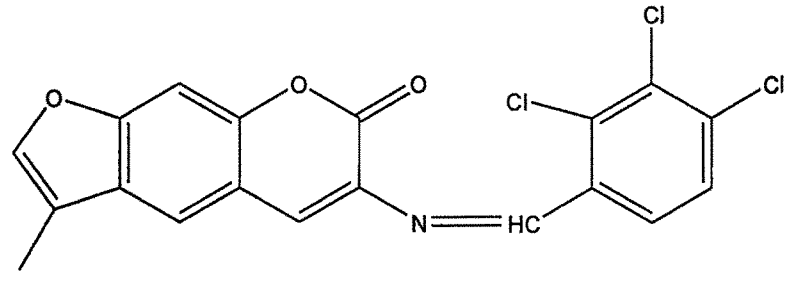


[Figure-36]: 6-Methyl-3-(4-chlorobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 101



[Figure-36a]: 6-Methyl-3-(4-chlorobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 101

6-Methyl-3-(2,3,4,-trichlorobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **102:**



State : pale yellow crystalline solid

Molecular Formula : $C_{19}H_{10}O_3NCl_3$

Melting Point : >250 °C

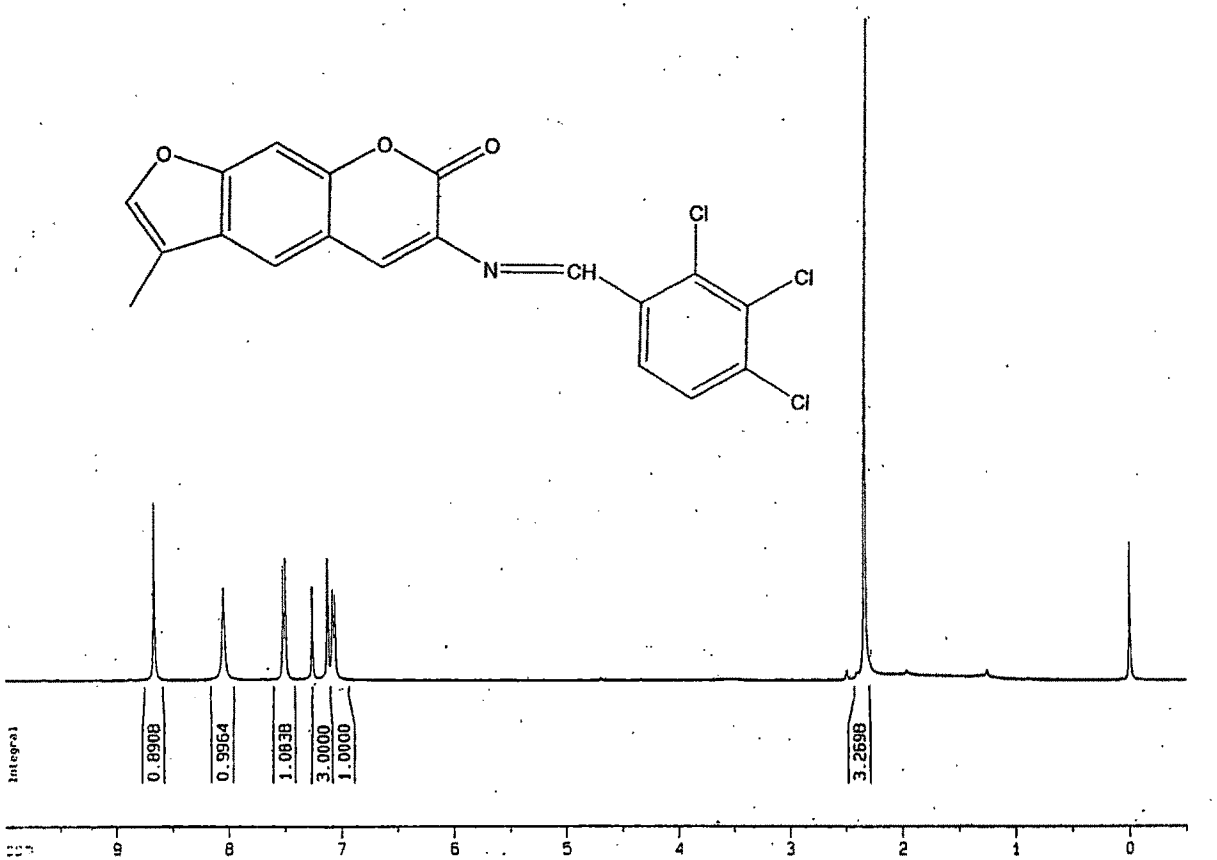
% Yield : 51

%C,H,N analysis (calculated) : C: 56.08 H: 2.46 N: 3.44

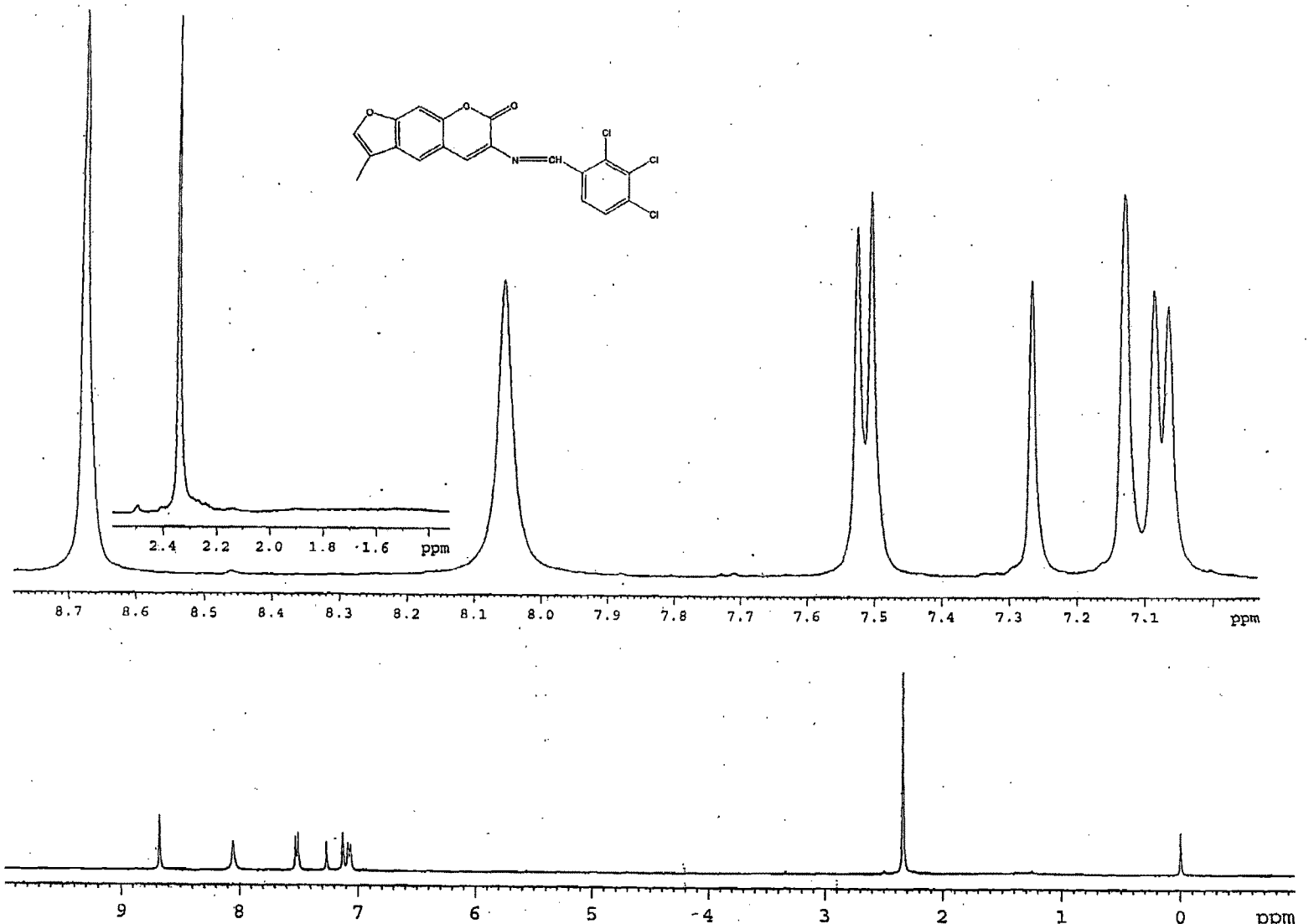
%C,H,N analysis (found) : C: 55.81 H: 2.33 N: 3.74

IR data (KBr) cm^{-1} : 2971, 2949, 1728, 1681, 1198, 1128, 785.

PMR data (400 MHz, $CDCl_3$) : δ 2.34(s, 3H $-C\underline{H}_3$), 7.08(d, J=7.7 Hz, 1H, aromatic proton), 7.11-7.28(s, 3H, C-4, C-9 and C-5 protons), 7.52(d, J=7.7 Hz, 1H, aromatic proton), 8.06(s, 1H, C-7), 8.68(s, 1H, =C<u>H</u>Ar).



[Figure-37]: 6-Methyl-3-(2,3,4,-trichlorobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 102



[Figure-37a]: 6-Methyl-3-(2,3,4,-trichlorobenzalimino)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 102

CHAPTER-III

Section-2

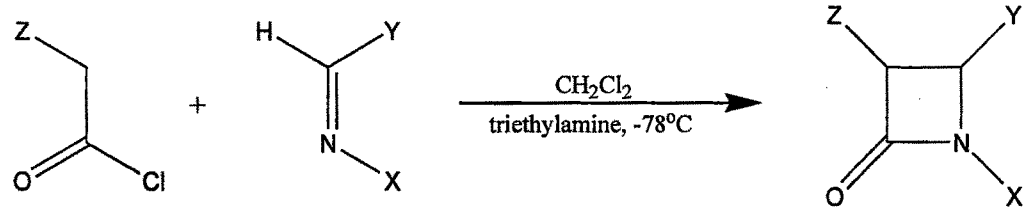
Synthesis of psora-azetidinones

Section:2 Synthesis of psora-azetidinones

III.4 Introduction:

Utility of azetidinones as synthones for various biologically active compounds as well as their recognition as cholesterol absorption inhibitor[9-13] and enzyme inhibitor[15-16] has been reported.

Azetidinones were reported by Banick and Backer involving the reaction of aromatic imines with acid chloride[14]. Aromatic imine **104** was treated with acid chloride **103** in the presence of triethylamine at -78°C affording azetidinones **105** (Scheme-6).

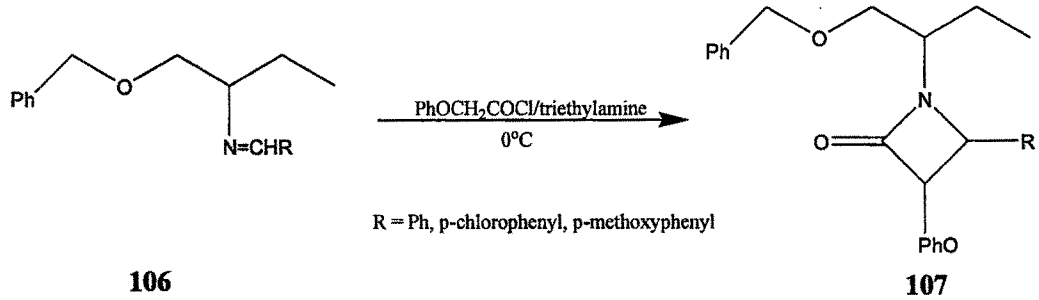


103 **104** **105**

X = Ph, naphthyl Y = Ph Z = OAc, OPh

Scheme-6

Synthesis of 4-phenyl-3-phenoxy-1-(1-phenoxymethylpropyl) azetidin-2-one **107** from the imine **106** has been reported recently[15]. In this synthesis, imine **106** was treated with phenoxy acetylchloride in presence of triethylamine in solvent dichloromethane which gave the azetidinone**107** (Scheme-7).



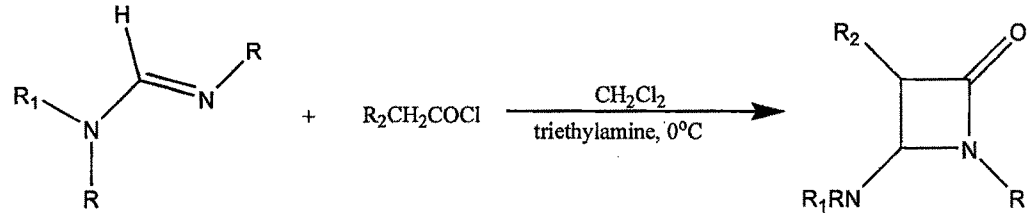
106 **107**

R = Ph, p-chlorophenyl, p-methoxyphenyl

Scheme-7

Bhawal *et al*[16] reported synthesis of 4-acylamino-2-azetidinones **110**. In this synthesis, the imine **108** was treated with acyl chloride **109** in presence of triethylamine

at 0°C yielding azetidinones **110** (Scheme-8). An azetidinone derivative, useful for synthesis of antibiotic, loracarbef has also been reported by Lee *et al* [18].

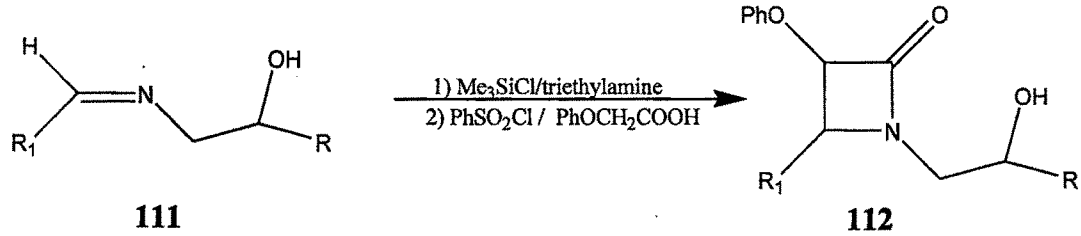


108 **109** **110**

R = phenyl, p-chlorophenyl, m-methylphenyl $R_1 = C_6H_5CO$, 4-$NO_2C_6H_5CO$ $R_2 = C_6H_5O$

Scheme-8

Synthesis of N-2-hydroxyethyl-2-azetidinones **112** has been reported by Sharma and Bhaduri[17]. The imine **111** was silylated using trimethylsilyl chloride in triethylamine, followed by treatment with phenoxy acetic acid in the presence of benzene sulphonyl chloride affording azetidinone **112** (Scheme-9).



111 **112**

R = phenyl, p-chlorophenyl R_1 = phenyl

Scheme-9

III.5 Results and Discussion:

In present study, several novel psora-azetidinones have been prepared with a view to examining their probable pharmacological activity. A strategy was applied for synthesis of azetidinones in which an active -C=N center of Schiff bases of linearly furo fused 2H-1-benzopyran-2-one derivatives i.e. psoralens **98-102**, is treated with chloro acetyl chloride / phenoxy acetyl chloride in triethyl amine (Scheme-10).

3-Acetamido-6-methyl-2H-1-benzopyran-2-one **65** was hydrolysed by 36% aq. HCl in methanol. The condensation of the resulting 3-amino-6-methyl-2H-1-benzopyran-

2-one **93** with substituted benzaldehydes afforded corresponding psora-Schiff bases **98-102**. Formation of the azetidinones was carried out at ice temperature. It is found that the formation of psora-azetidinones is facilitated by benzalimino ring. Also the sharp melting points were not obtained as psora-azetidinones got decomposed beyond 250°C.

IR bands in the range of 3018-2998 cm^{-1}, 1778-1701 cm^{-1}, 1691-1678 cm^{-1} confirmed aromatic ring and carbonyl groups of respective azetidinones. Bands in the range of 1500-1520 cm^{-1} confirmed –C-N linkages and bands in the range of 1238-1188 cm^{-1} confirmed –C-O linkages. PMR of each azetidinones showed doublets for –N–CH– and –CH–CO– protons.

1-(6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(4-chlorophenyl)-3-phenoxyazetidin-2-one,**113** showed IR absorption bands at 1752 cm^{-1} and 1721 cm^{-1} which confirmed the presence of carbonyl groups of four membered ring and lactone respectively [Figure-38].

PMR specrum of compound **113** exhibited a singlet at δ 2.45 for three protons of methyl group at C-6, two doublets one at δ 3.17 (J=10 Hz) for one proton of –N-CH– linkage and another doublet at δ 5.29(J=10 Hz) for one proton of –CH–CO– linkage of four membered ring, a multiplet at δ 7.29-7.59 for nine protons which account for five phenoxy aromatic nucleus, two phenyl ring and two for C-4, C-9 protons, two singlets at δ 7.78 for C-5 and C-7 protons and a doublet (J=8 Hz) at δ 7.86 for aromatic protons of benzal ring[Figure-39].

1-(6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(4-nitrophenyl)-3-phenoxyazetidin-2-one, **114** showed IR absorption band at 1729 cm^{-1} which confirmed the presence of carbonyl groups of four membered ring[Figure-40].

PMR specrum of compound **114** exhibited a singlet at δ 2.40 for three protons of methyl group at C-6, two doublets one at δ 3.70 (J=10 Hz) for one proton of –N-CH– linkage and another doublet at δ 5.21(J=10 Hz) for one proton of –CH–CO– linkage of four membered ring, a multiplet at δ 6.88-7.00 for three aromatic protons, another multiplet at δ 7.21-7.58 for nine protons which account for five phenoxy aromatic nucleus and four for C-4, C-9, C-5 and C-7 protons. Finally two doublets (J=8.6 Hz) one at δ 7.62 and another at δ 8.00 account for four aromatic protons of phenyl ring [Figure-41].

1-(6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(2,4-dinitrophenyl)-3-phenoxyazetidin-2-one,**115** showed IR absorption bands at 1749 cm^{-1} and 1728 cm^{-1} which confirmed the presence of carbonyl groups of four membered ring and lactone [Figure-42].

PMR specrum of compound **115** exhibited a singlet at δ 2.49 for three protons of methyl group at C-6, two doublets one at δ 3.88 (J=7.5 Hz) for one proton of –N-CH– linkage and another doublet at δ 5.19(J=7.5 Hz) for one proton of –CH–CO– linkage of four membered ring, a multiplet at δ 6.78-7.30 for nine protons which account for five phenoxy aromatic nucleus and four for C-4, C-9, C-5 and C-7 protons, two doublets (J=8 Hz) one at δ 7.41 and another at δ 7.62 for two aromatic protons of phenyl ring and finally a singlet at δ 8.40 for a proton of phenyl ring [Figure-43].

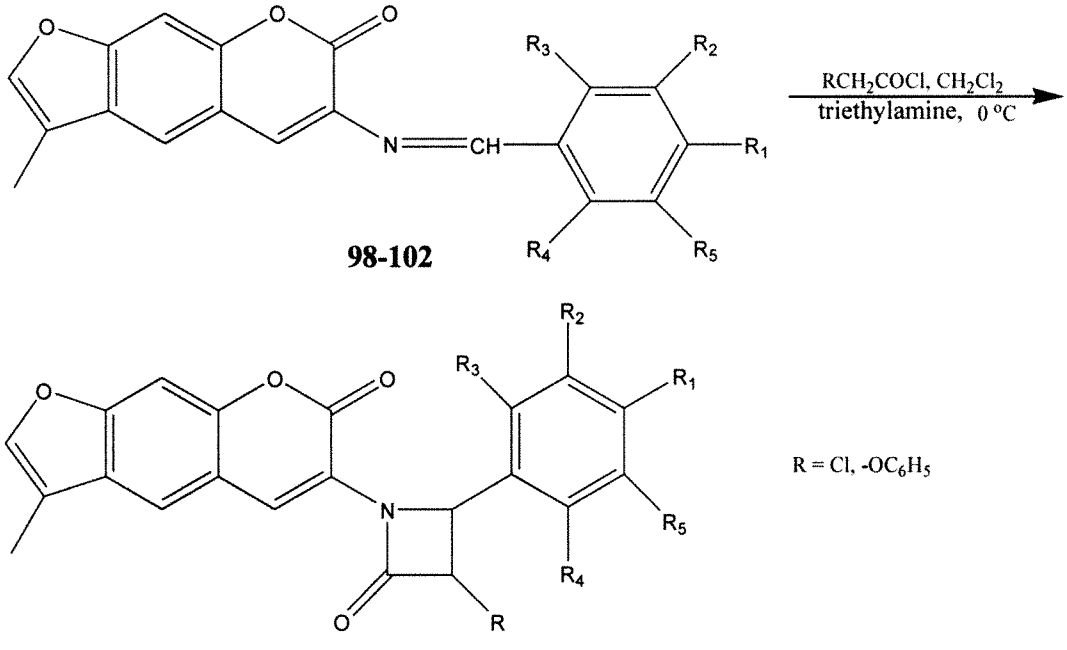
1-(6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(3,4-dichlorophenyl)-3-phenoxyazetidin-2-one,**116** showed IR absorption bands at 1747 cm^{-1} and 1720 cm^{-1} which confirmed the presence of carbonyl groups of four membered ring and lactone [Figure-44].

PMR specrum of compound **116** exhibited a singlet at δ 2.54 for three protons of methyl group at C-6, two doublets one at δ 3.81 (J=5.5 Hz) for one proton of –N-CH– linkage and another doublet at δ 5.21(J=5.5 Hz) for one proton of –CH–CO– linkage of four membered ring, a multiplet at δ 6.86-6.97 for seven protons which account for five phenoxy aromatic nucleus and two for C-4, C-9 protons, two doublets (J=7.7 Hz) one at δ 7.31-7.33 and another at δ 7.36-7.39 account for two aromatic protons of phenyl ring, a singlet at δ 7.53 for a proton at C-5, a singlet at δ 7.92 for a proton at C-7 and finally a singlet at δ 8.38 for a proton of phenyl ring [Figure-45].

1-(6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(2,3,4-trichlorophenyl)-3-chloroazetidin-2-one,**117** showed IR absorption bands at 1743 cm^{-1} and 1725 cm^{-1} which confirmed the presence of carbonyl groups of four membered ring and lactone [Figure-46].

PMR specrum of compound **117** exhibited a singlet at δ 2.30 for three protons of methyl group at C-6, two doublets one at δ 4.61 (J=8.8 Hz) for one proton of –N-CH– linkage and another doublet at δ 5.52(J=8.8 Hz) for one proton of –CH–CO– linkage of

four membered ring, a singlet at δ 6.78 for a proton at C-4, a doublet (J=7.3 Hz) at δ 6.91 for a proton of phenyl ring, a singlet at δ 7.26 for a proton at C-9, a doublet (J=7.6 Hz) at δ 7.45 for a proton of phenyl ring, a singlet at δ 7.98 for a proton at C-5 and a singlet at δ 8.64 for a proton at C-7 [Figure-47].



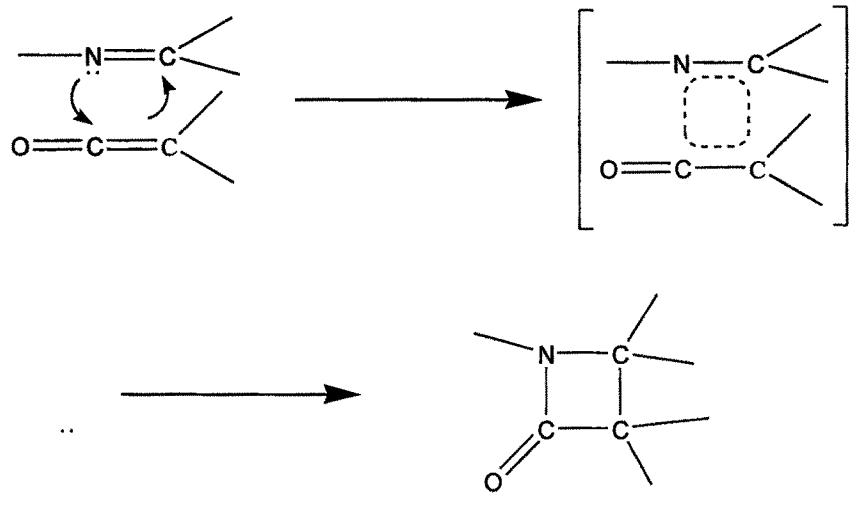
98-102

113-117

Scheme-10

Comp. no	R	R_1	R_2	R_3	R_4	R_5
113	C_6H_5O	Cl	H	H	H	H
114	C_6H_5O	NO_2	H	H	H	H
115	C_6H_5O	NO_2	H	NO_2	H	H
116	C_6H_5O	Cl	Cl	H	H	H
117	Cl	Cl	Cl	Cl	H	H

Psora-azetidinones formation can be generalized by the following proposed mechanism. This mechanism involves initially formation of ketene from the acid chloride in presence of triethylamine and then cycloaddition reaction between imine linkage and ketene generates a cyclic transition state which is facilitated by benzalimino aromatic nucleus.



III.6 Experimental:

Reagents were purified whenever necessary before use. Solvents were distilled and dried before use. Dichloromethane was dried, distilled and stored over 4A° molecular sieves before use. Column chromatography was carried out using silica gel (60-120 mesh). Thin layer chromatography was carried out using silica gel (75μ). Yields are quoted for isolated, purified and dried products.

General procedure for synthesis of psora-azetidinones 113-116:

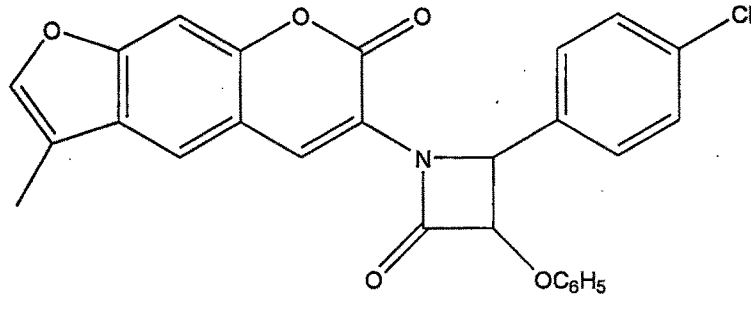
A solution of appropriate Schiff base **98-101** (0.001mol) in dichloromethane (0.005mol) and triethylamine (0.001mol) was prepared and chilled to 0 °C. To it was added a solution of phenoxyacetylchloride (0.0011mol) in dichloromethane (0.0024mol) drop wise with constant stirring while maintaining the temperature at 0 °C. This was followed by stirring the reaction mixture at room temperature for five hours. The progress of the reaction was monitored by TLC. The reaction mixture was then poured into crushed ice (100g) and stirred further for 10 min. followed by removal of dichloromethane under reduced

pressure. Filtration of the solid and purification by column chromatography using benzene furnished the psora-azetidinones which were recrystallised from ethanol.

Procedure for synthesis of psora-azetidinone 117:

A solution of Schiff base **102** (0.001mol) in dichloromethane (0.005mol) and triethylamine (0.001mol) was prepared and chilled to 0 °C. To it was added a solution of chloroacetylchloride (0.0011mol) in dichloromethane (0.0024mol) drop wise with constant stirring while maintaining the temperature at 0 °C. This was followed by stirring the reaction mixture at room temperature for five hours. The progress of the reaction was monitored by TLC. The reaction mixture was then poured into crushed ice (100g) and stirred further for 10 min. followed by removal of dichloromethane under reduced pressure. Filtration of the solid and purification by column chromatography using benzene furnished the psora-azetidinone which was recrystallised from ethanol.

1-(6-Methyl-2H-furo[3,2-g]-1-benzopyran-2-one -3-yl)-4-(4-chlorophenyl)-3-phenoxyazetidin-2-one, **113:**



State : light yellow amorphous solid

Molecular Formula : $C_{27}H_{18}O_5NCl$

Melting Point : dec. >250°C

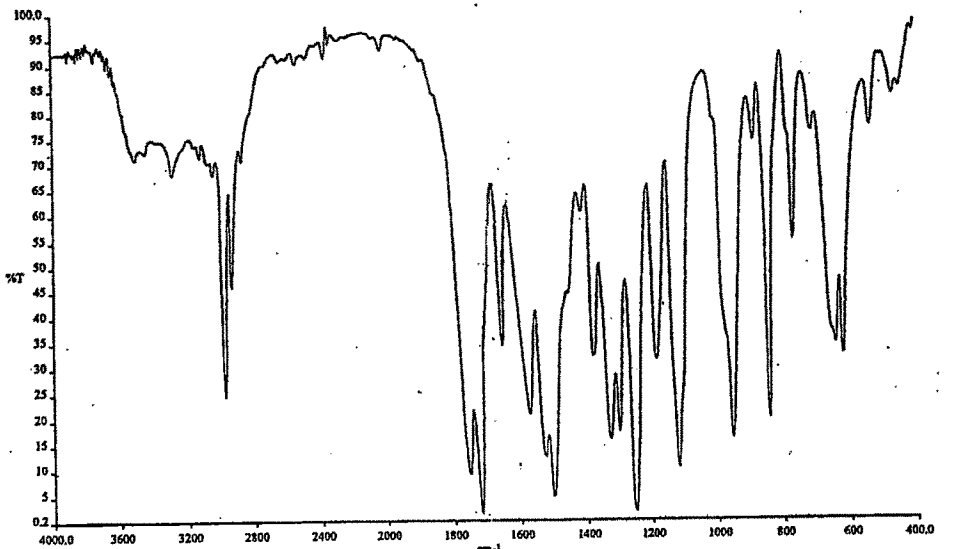
% Yield : 35

%C,H,N analysis (calculated) : C: 68.72 H: 3.82 N: 2.97

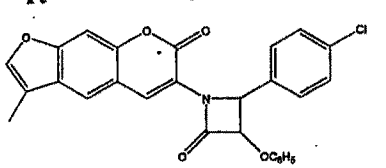
%C,H,N analysis (found) : C: 68.49 H: 3.68 N: 3.08

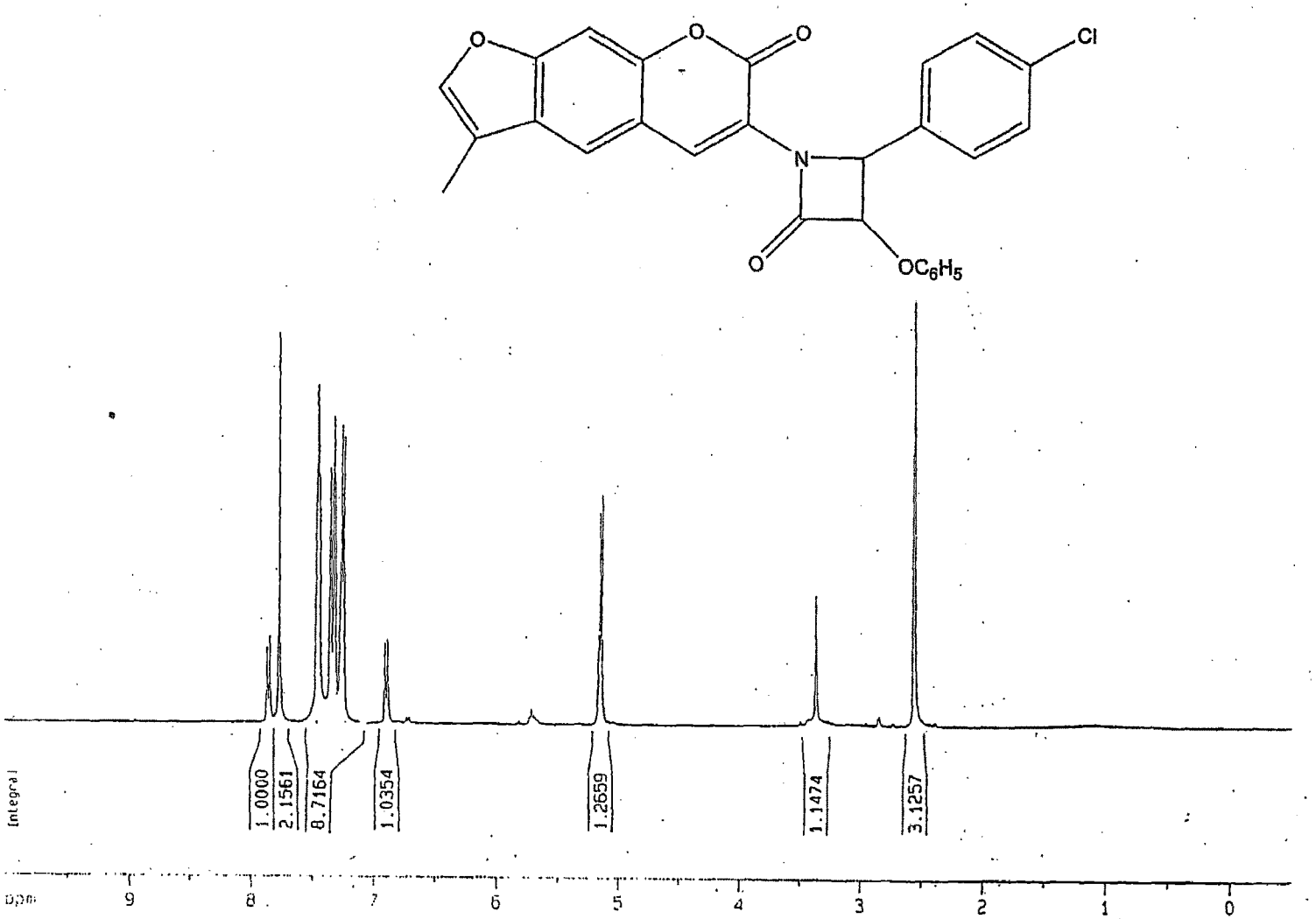
IR data (KBr) cm^{-1} : 3045, 2977, 1752, 1721, 1650, 1572, 1253, 843, 769.

PMR data (400MHz, $CDCl_3$): δ 2.45(s 3H, $-CH_3$), 3.17(d, 1H, N-C<u>H</u>-), 5.29(d, J=10 Hz, 1H, -CO-C<u>H</u>-OC_6H_5), 6.90(d, J=8 Hz, 1H), 7.29-7.59(m, 9H, aromatic, C-4 and C-9 protons overlap), 7.78(s, 2H, C-5 and C-7 protons overlap), 7.86(d, J=8 Hz, 1H).

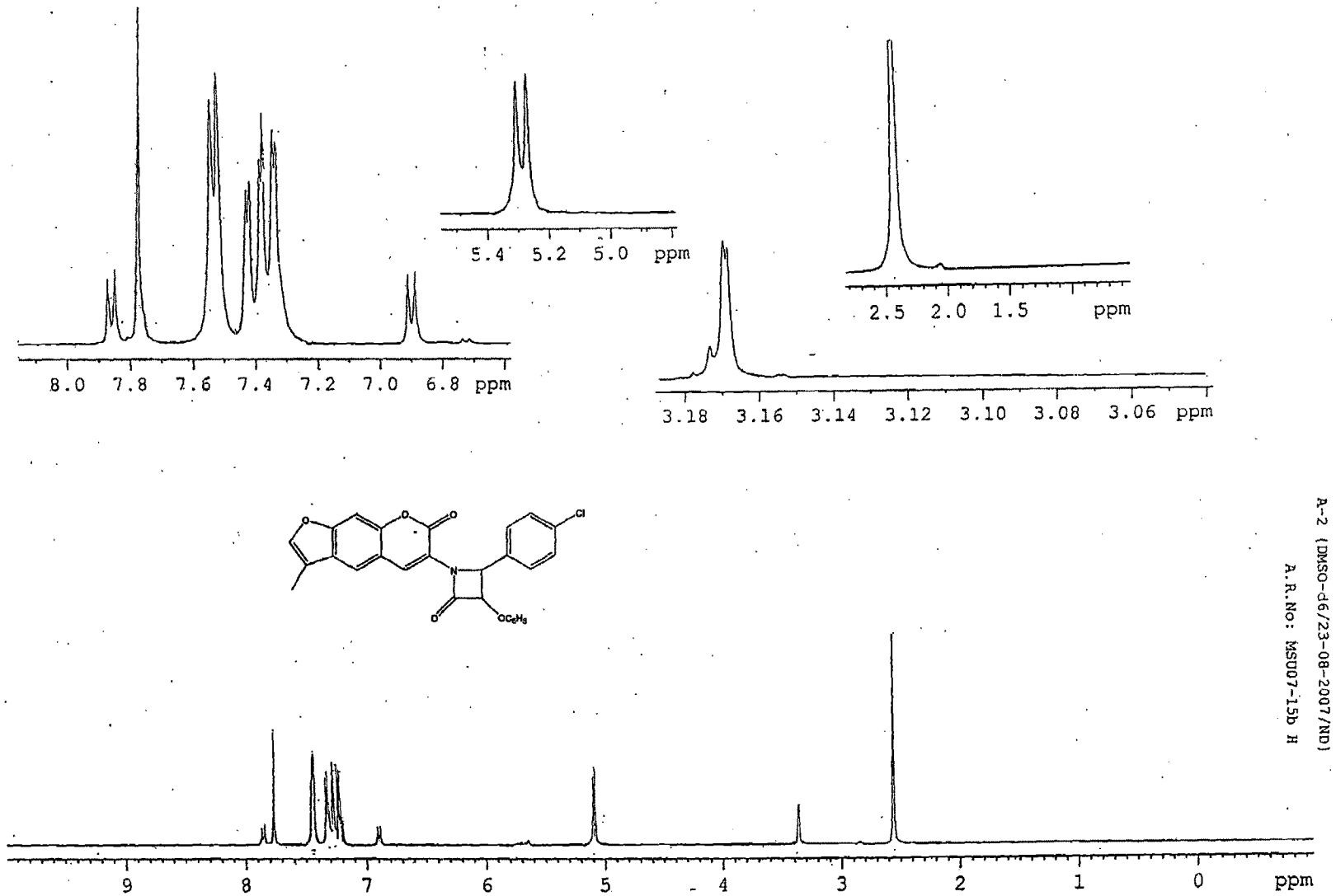


[Figure-38]: 1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(4-chlorophenyl)-3-phenoxyazetidin-2-one, 113



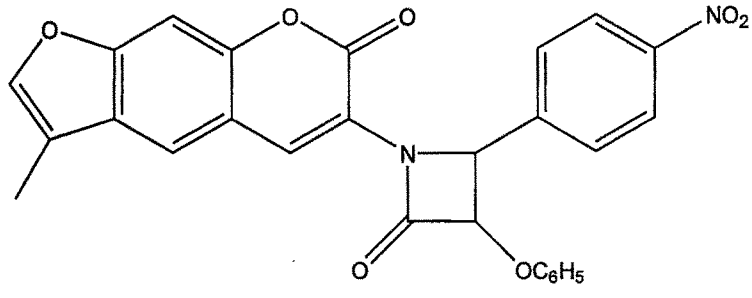


[Figure-39]: 1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(4-chlorophenyl)-3-phenoxyazetidin-2-one, 113



[Figure-39a]: 1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(4-chlorophenyl)-3-phenoxyazetidin-2-one, 113

1-(6-Methyl-2H-furo[3,2-g]-1-benzopyran-2-one -3-yl)-4-(4-nitrophenyl)-3-phenoxyazetidin-2-one, **114:**



State : yellow amorphous solid

Molecular Formula : $C_{27}H_{18}O_7N_2$

Melting Point : dec. >250°C

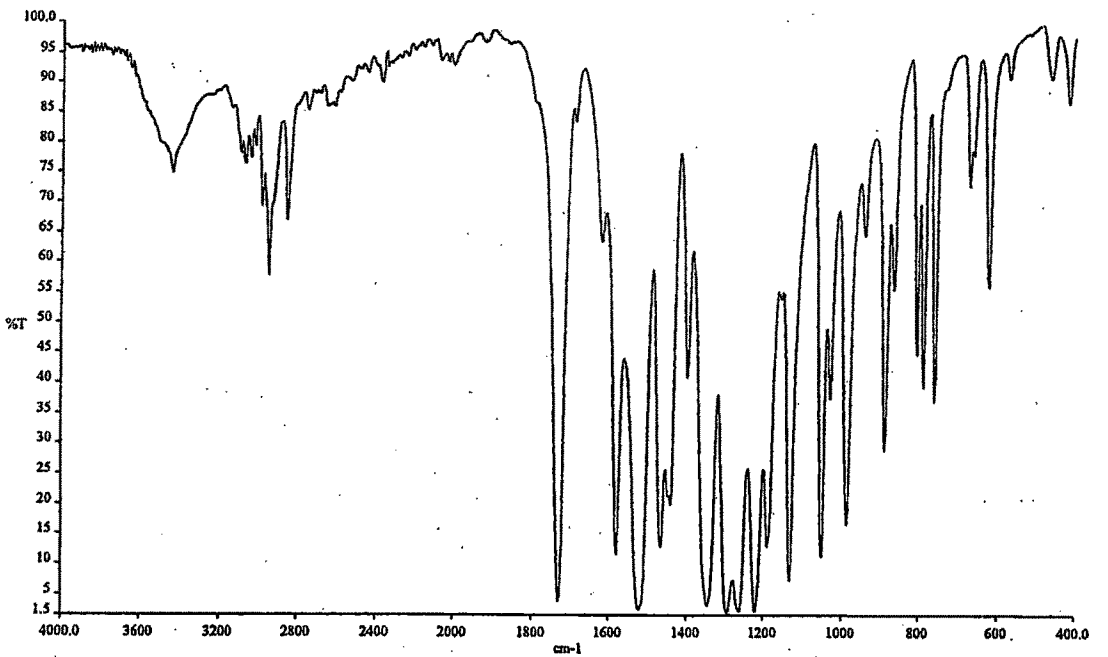
% Yield : 38

%C,H,N analysis (calculated) : C: 67.22 H: 3.73 N: 5.81

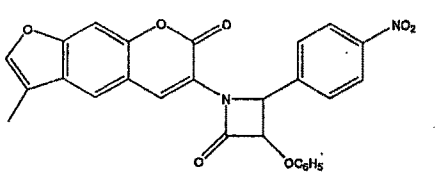
%C,H,N analysis (found) : C: 67.00 H: 3.86 N: 5.98

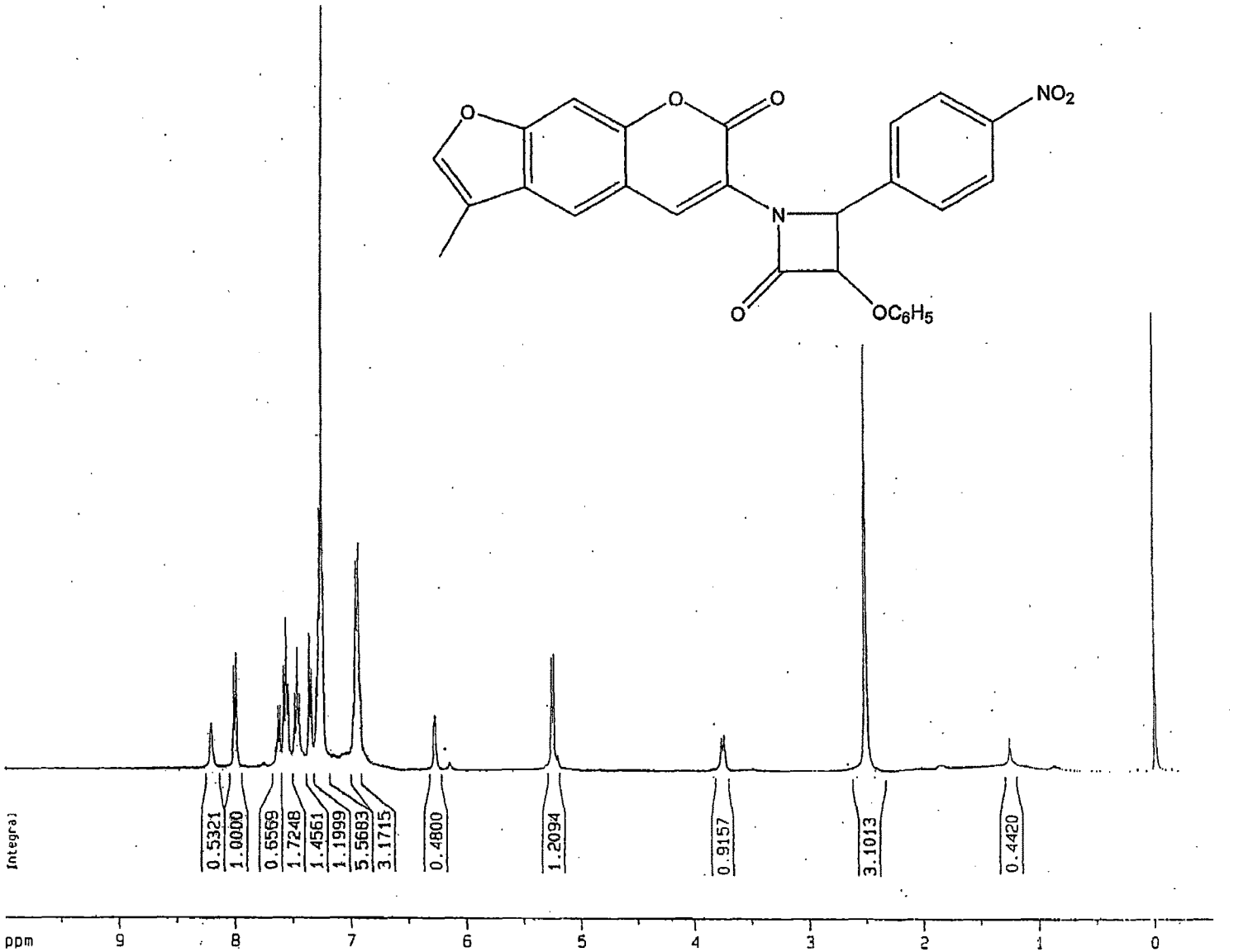
IR data (KBr) cm^{-1} : 3018, 2981, 1729, 1687, 1619, 1521, 1344, 1220, 864.

PMR data (400MHz, $CDCl_3$) δ ppm : 2.40(s, 3H, $C\underline{H}_3$), 3.70(d, J=10 Hz, 1H, N-C<u>H</u>-), 5.21(d, J=10 Hz, 1H, -CO-C<u>H</u>-OC_6H_5), 6.88-7.00(m, 3H, aromatic protons), 7.21-7.58(m, 9H, aromatic, C-4, C-9, C-5 and C-7 protons overlap), 7.62(d, J=8.6 Hz, 2H, aromatic protons), 8.00(d, J=8.6 Hz, 2H, aromatic protons ortho to -NO_2).

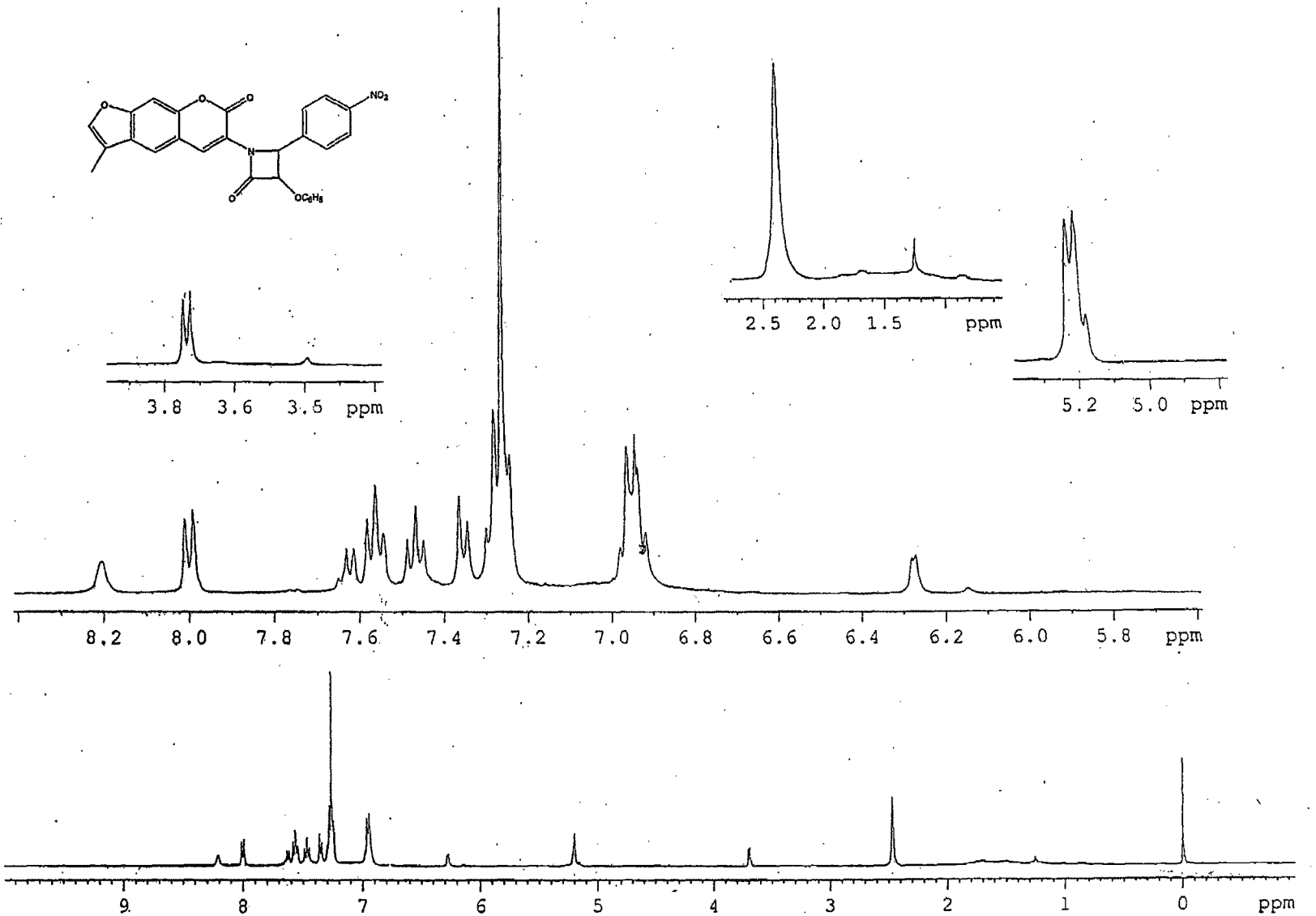


[Figure-40]:1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(4-nitrophenyl)-3-phenoxyazetidin-2-one, 114



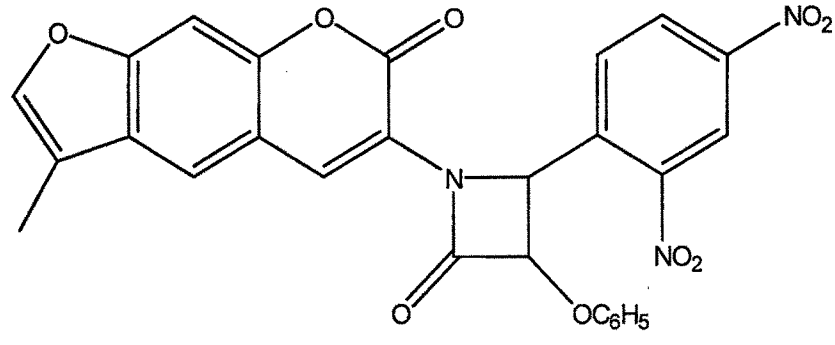


[Figure-41]:1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(4-nitrophenyl)-3-phenoxyazetidin-2-one, 114



[Figure-41a]:1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(4-nitrophenyl)-3-phenoxyazetidin-2-one, 114

1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one -3-yl)-4-(2,4-dinitrophenyl)-3-phenoxyazetidin-2-one, **115:**



State : yellow crystalline solid

Molecular Formula : $C_{27}H_{17}O_9N_3$

Melting Point : dec. >250°C

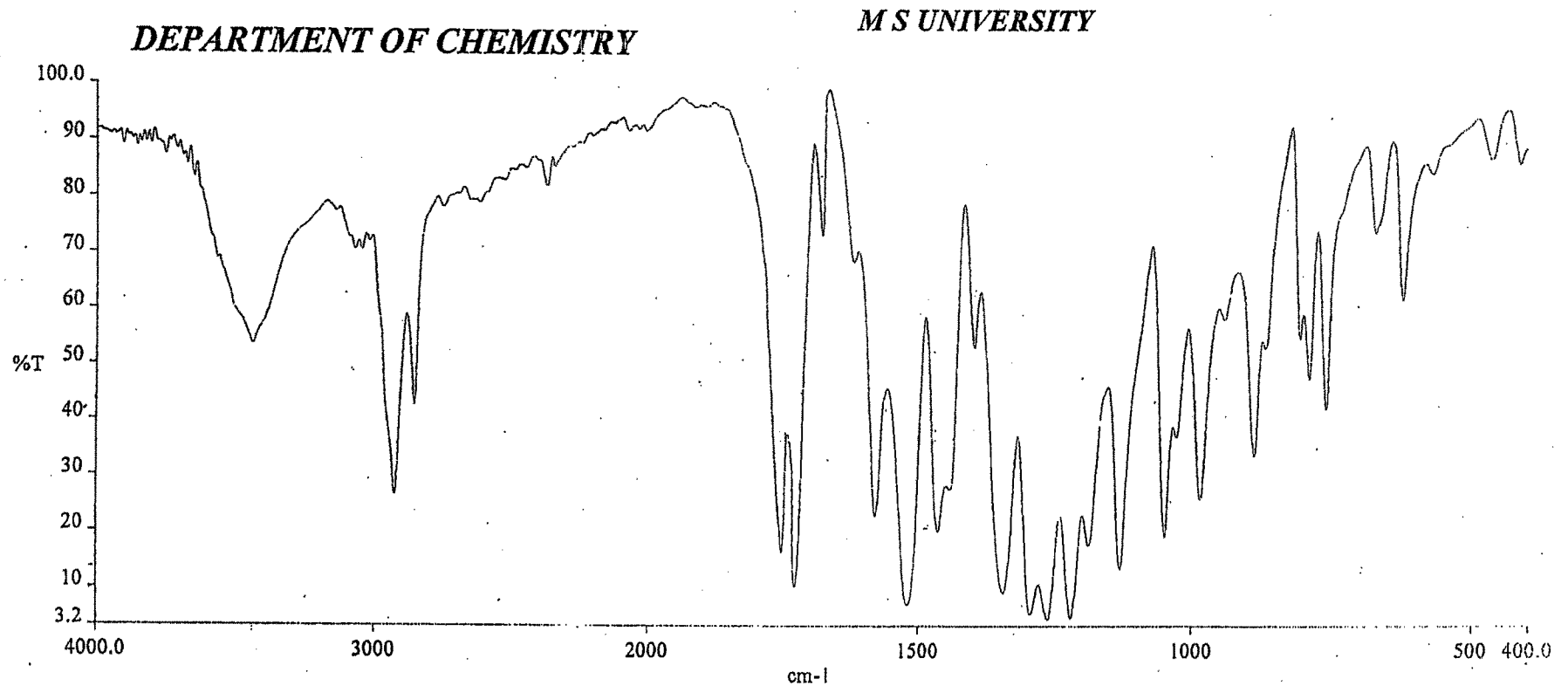
% Yield : 41

%C,H,N analysis (calculated) : C: 61.48 H: 3.22 N: 7.97

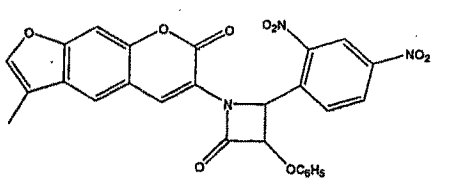
%C,H,N analysis (found) : C: 61.11 H: 3.48 N: 8.11

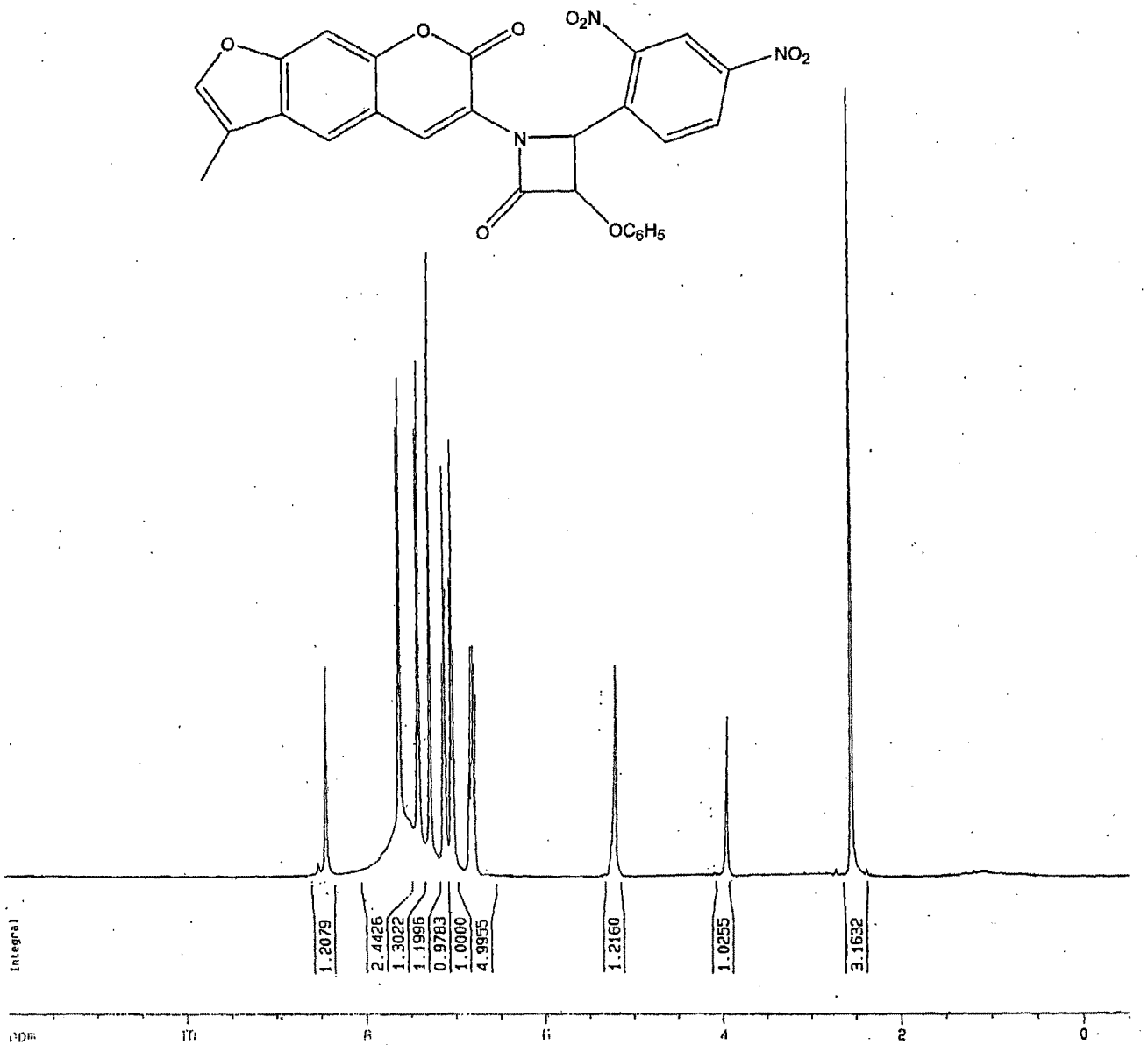
IR data (KBr) cm^{-1} : 3043, 2925, 1749, 1728, 1679, 1520, 1343, 1220, 887.

PMR data (400MHz, $CDCl_3$) δ ppm : 2.49(s 3H,-C<u>H</u>$_3$), 3.88(d, J=7.5 Hz, 1H, N-C<u>H</u>-), 5.19(d, J=7.5 Hz 1H, -CO-C<u>H</u>-OC_6H_5), 6.78-7.30(m, 9H, aromatic, C-4, C-9, C-5 and C-7 protons overlap), 7.41(d, J=8 Hz, 1H), 7.62(d, J=8 Hz, 1H), 8.40(s, 1H, aromatic proton).

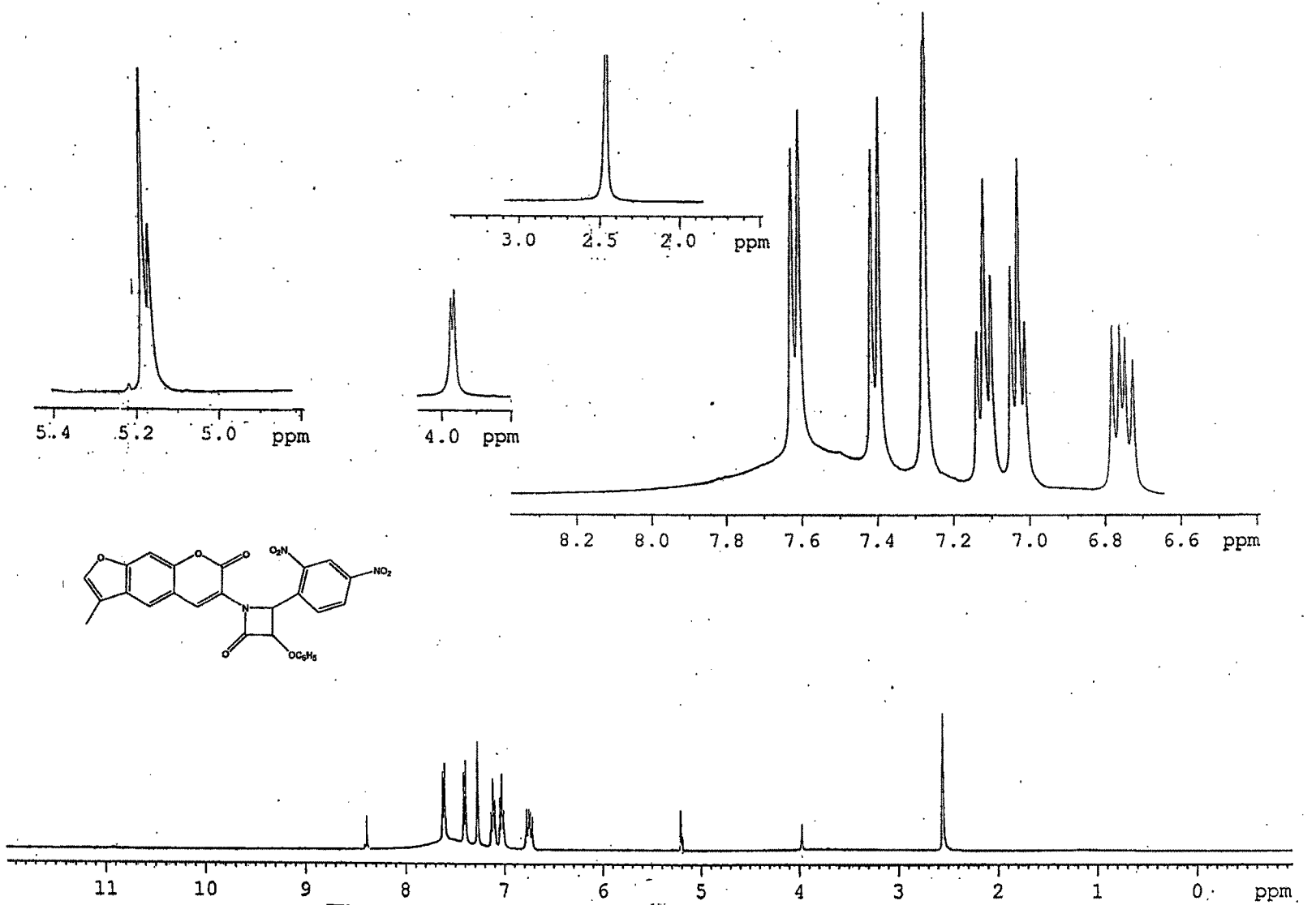


[Figure-42]: 1-(6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(2,4-dinitrophenyl)-3-phenoxyazetidin-2-one, 115



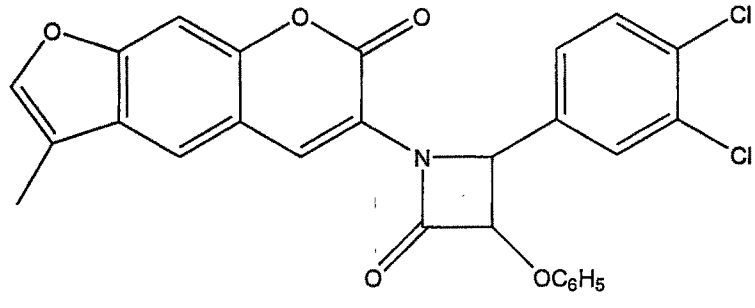


[Figure-43]: 1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(2,4-dinitrophenyl)-3-phenoxyazetidin-2-one, 115



[Figure-43a]: 1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(2,4-dinitrophenyl)-3-phenoxyazetidin-2-one, 115

1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one -3-yl)-4-(3,4-dichlorophenyl)-3-phenoxyazetidin-2-one, **116:**



State : light yellow amorphous solid

Molecular Formula : $C_{27}H_{17}O_5NCl_2$

Melting Point : dec. >250°C

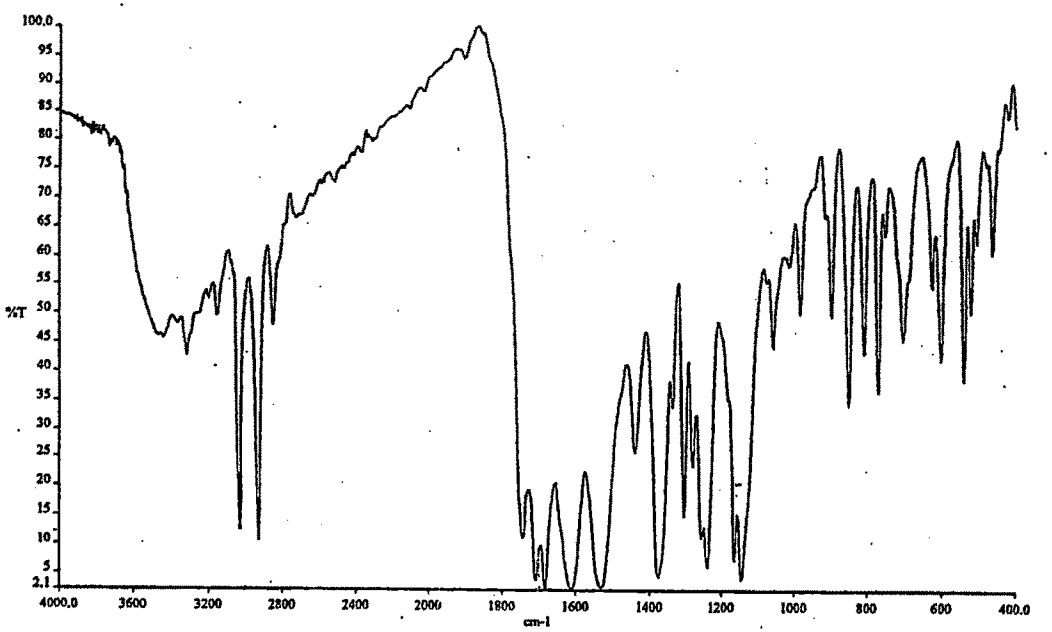
% Yield : 41

%C,H,N analysis (calculated) : C: 64.03 H: 3.36 N: 2.77

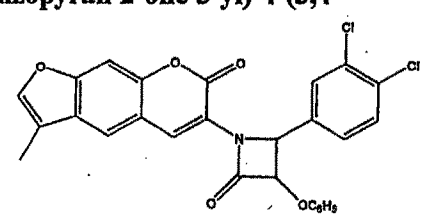
%C,H,N analysis (found) : C: 64.31 H: 3.56 N: 2.98

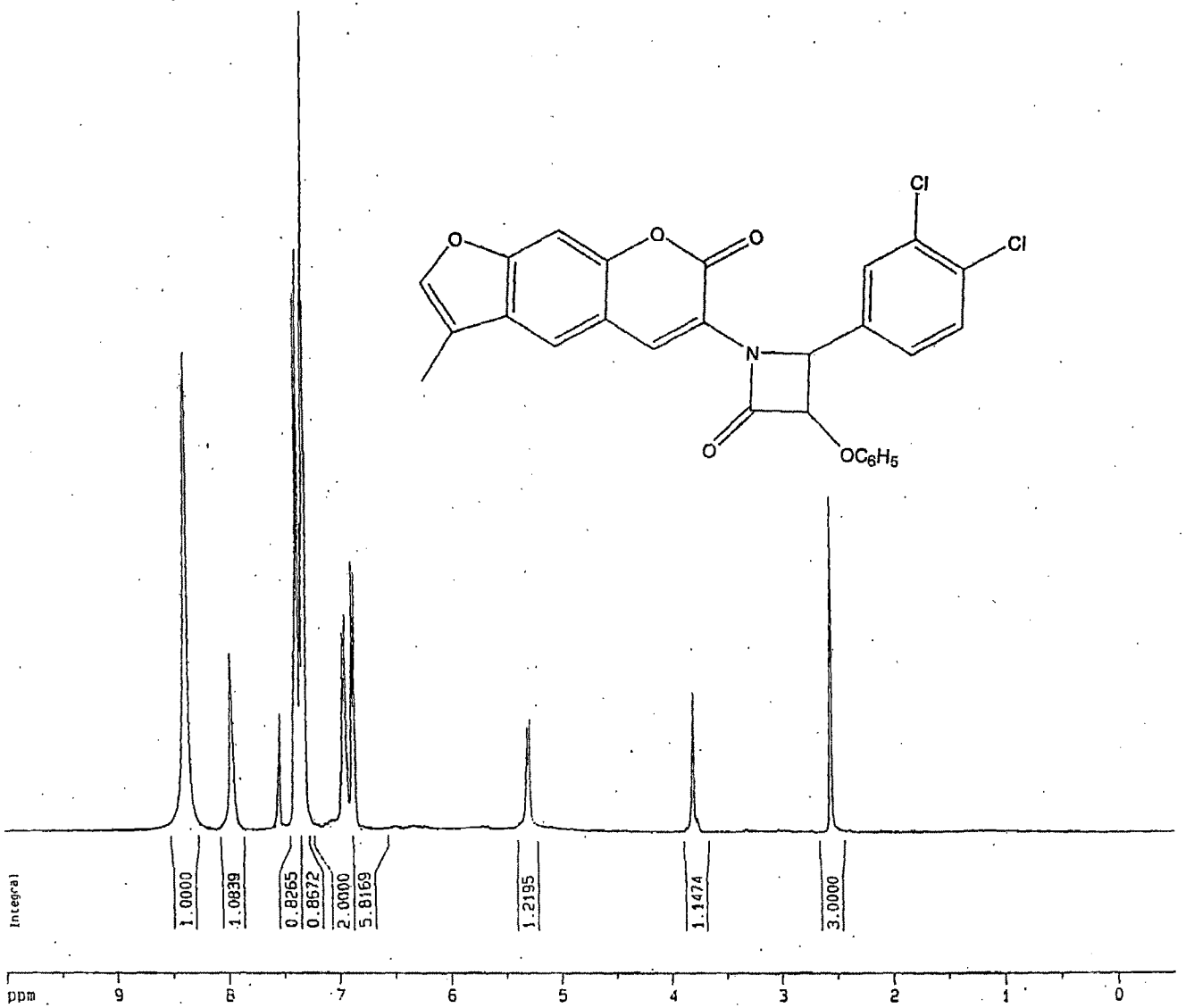
IR data (KBr) cm^{-1} : 3040, 2925, 1747, 1720, 1678, 1612, 1239, 809, 771.

PMR data (400MHz, $CDCl_3$) δ ppm: 2.54(s 3H,-C<u>H</u>$_3$), 3.81(d, J=5.5 Hz, 1H, N-C<u>H</u>-), 5.21(d, J=5.5 Hz, 1H, -CO-C<u>H</u>- OC_6H_5), 6.86-6.97(m, 7H, aromatic, C-4 and C-9 protons overlap), 7.31-7.33(d, J=7.7 Hz, 1H), 7.36-7.39(d, J=7.7 Hz, 1H), 7.53(s, 1H, C-5), 7.92(s, 1H, C-7), 8.38(s, 1H, aromatic protons).

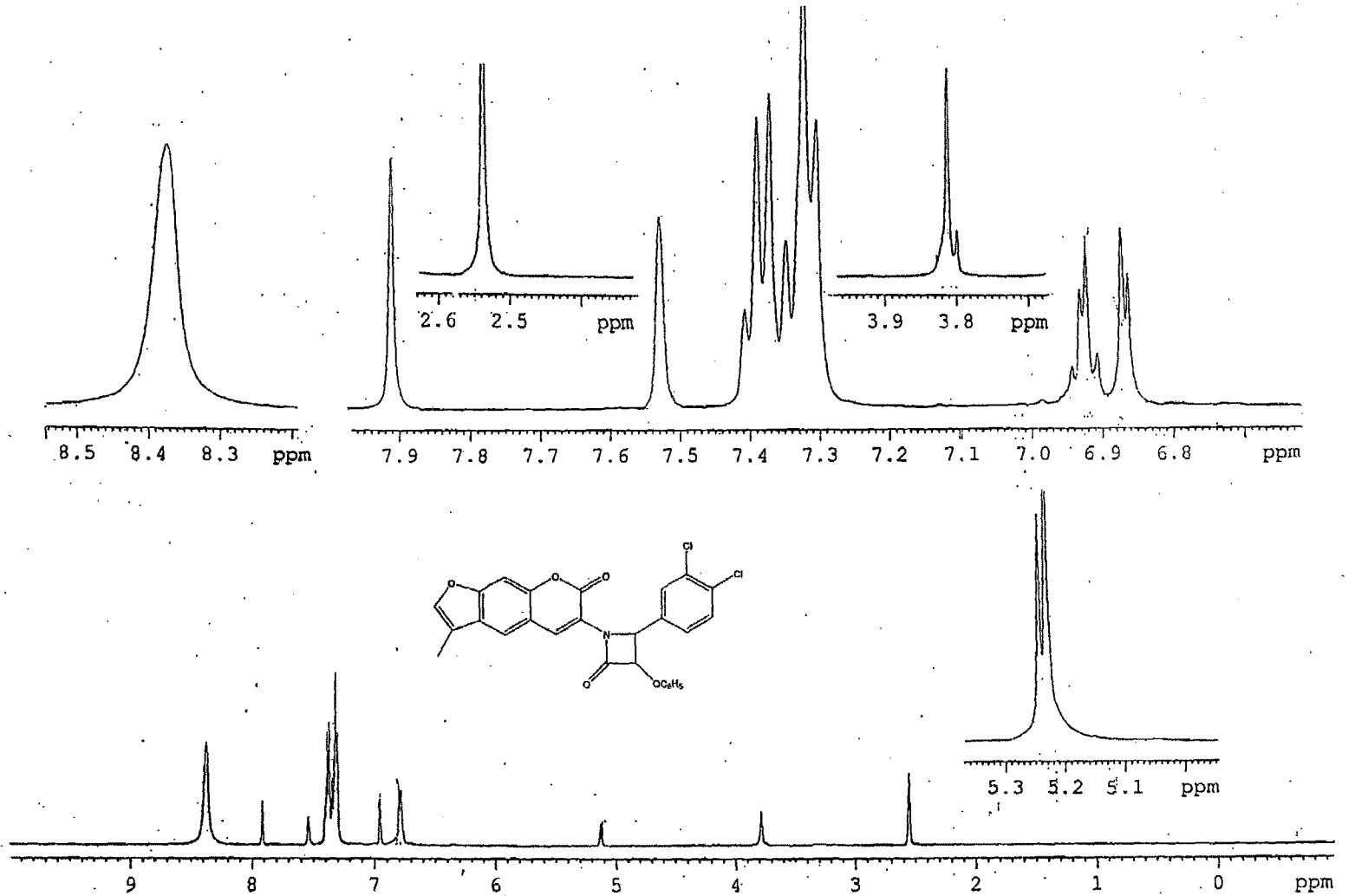


[Figure-44]: 1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(3,4-dichlorophenyl)-3-phenoxyazetidin-2-one, 116



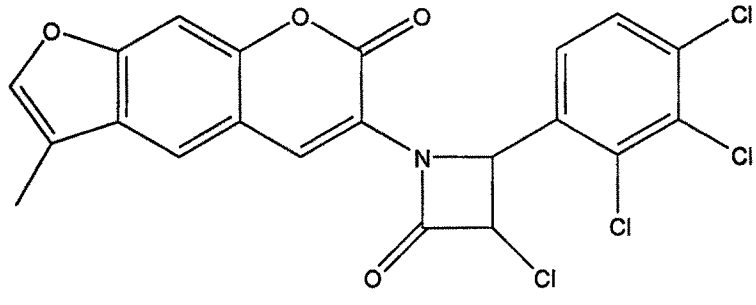


[Figure-45]: 1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(3,4-dichlorophenyl)-3-phenoxyazetidin-2-one, 116



[Figure-45a]: 1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(3,4-dichlorophenyl)-3-phenoxyazetidin-2-one, 116

1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one -3-yl)-4-(2,3,4,-trichlorophenyl)-3-chloroazetidin-2-one, **117:**



State : brownish yellow amorphous solid

Molecular Formula : $C_{21}H_{11}O_4NCl_4$

Melting Point : dec. >250°C

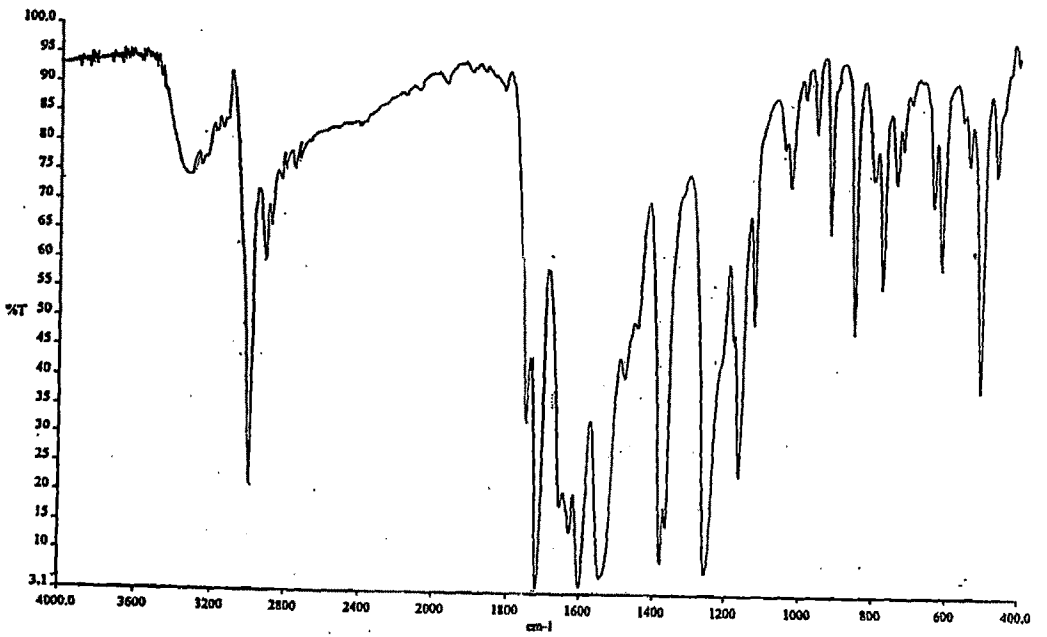
% Yield : 51

%C,H,N analysis (calculated) : C: 52.17 H: 2.28 N: 2.90

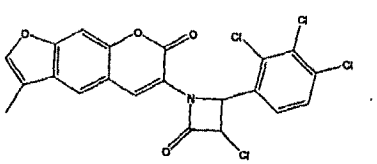
%C,H,N analysis (found) : C: 52.11 H: 2.48 N: 3.01

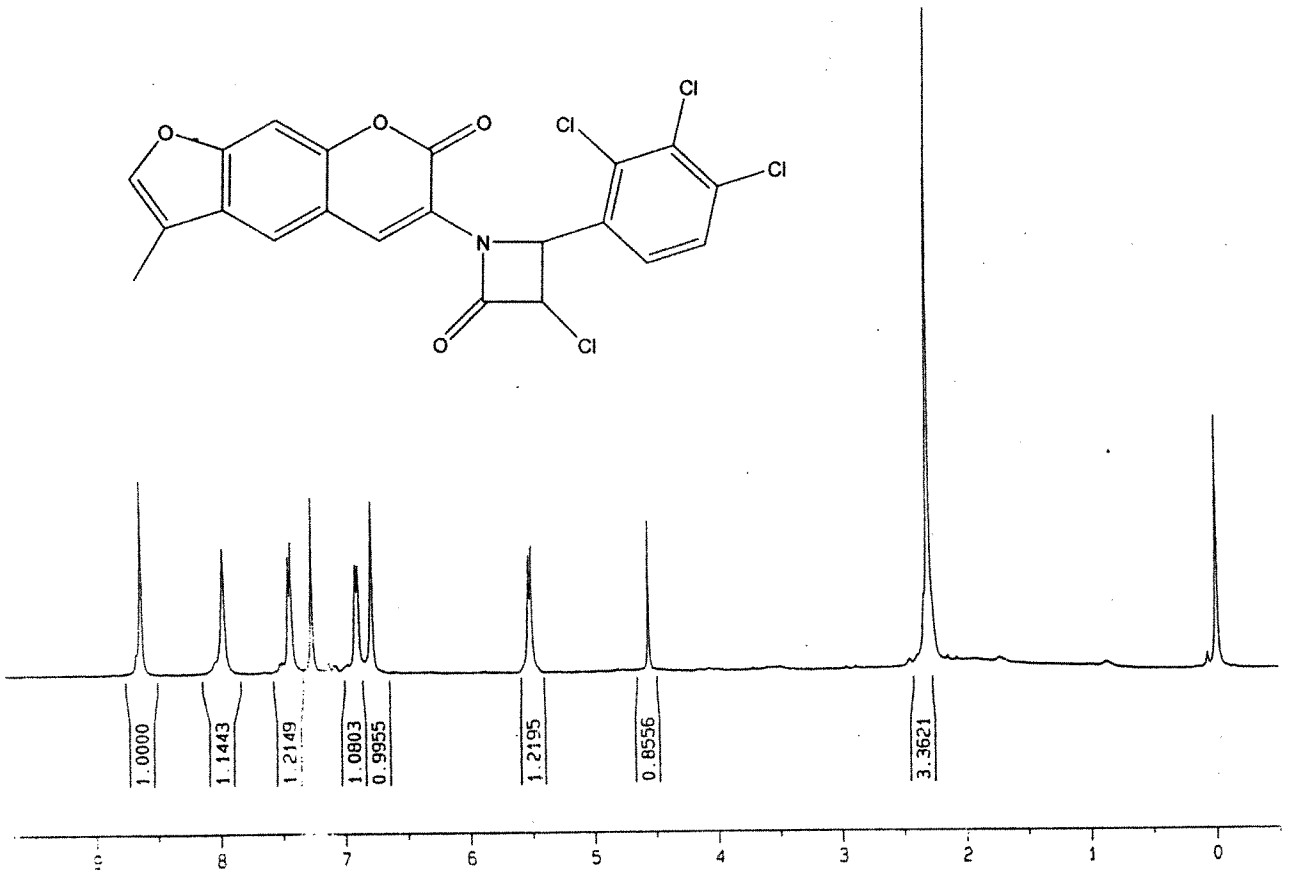
IR data (KBr) cm^{-1} : 3001, 2922, 1743, 1725, 1655, 1600, 1256, 798.

PMR data (400MHz, $CDCl_3$): δ 2.30(s 3H,-C<u>H</u>$_3$), 4.61(d, J=8.8 Hz, 1H, N-C<u>H</u>-), 5.52(d, J=8.8 Hz, 1H, -CO-C<u>H</u>-Cl), 6.78(s,1H, C-4), 6.91(d, J=7.3 Hz, 1H), 7.26(s, 1H, C-9), 7.45(d, J=7.6 Hz, 1H), 7.98(s, 1H, C-5), 8.64(s, 1H, C-7).

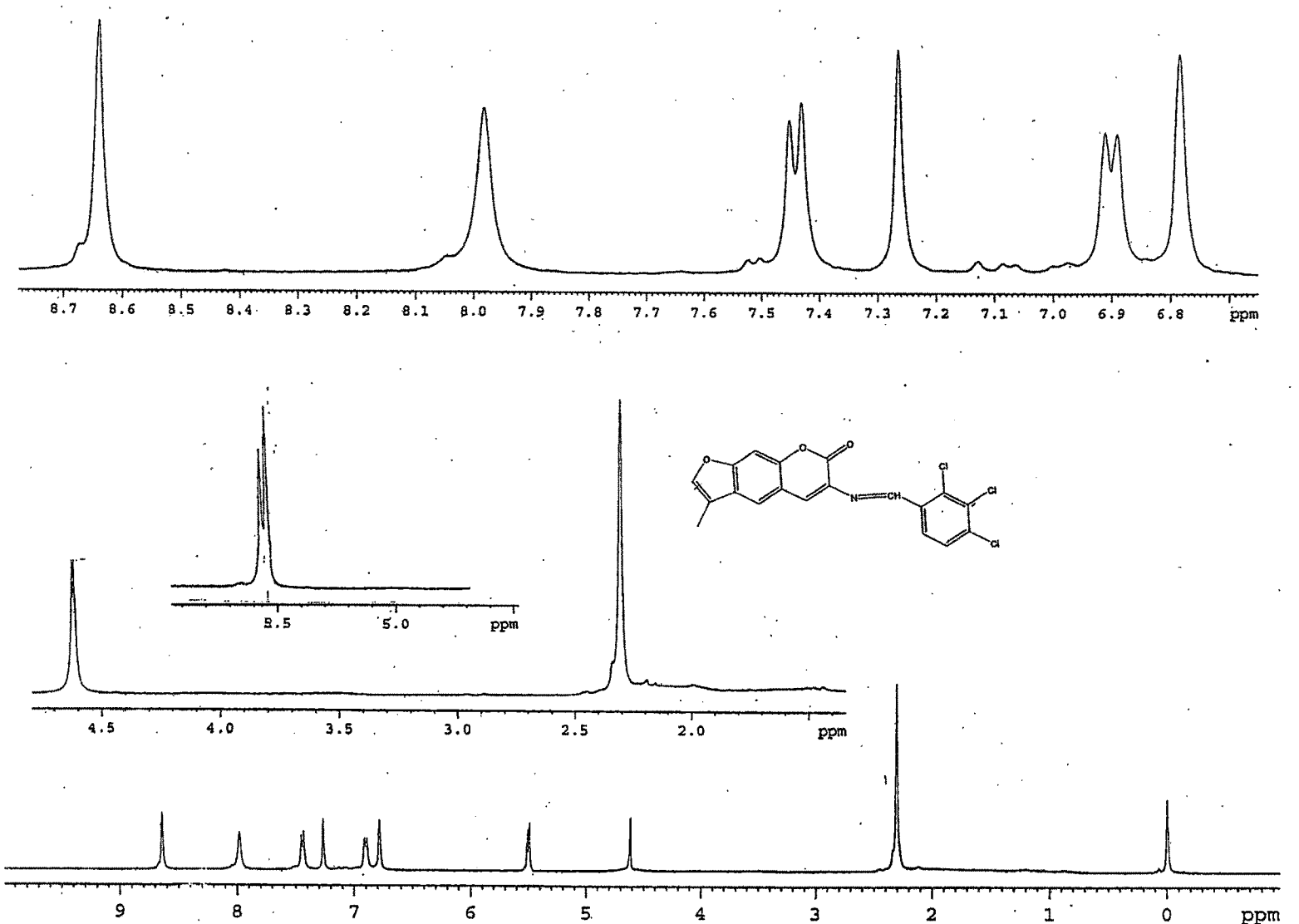


[Figure-46]: 1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(2,3,4,-trichlorophenyl)-3-chloroazetidin-2-one, 117





[Figure-47]: 1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(2,3,4,-trichlorophenyl)-3-chloroazetidin-2-one, 117



[Figure-47a]: 1-(6-Methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-yl)-4-(2,3,4,-trichlorophenyl)-3-chloroazetidin-2-one, 117

III.7 Conclusion:

A convenient synthesis of important chemotherapeutic agents such as psora-Schiff bases and psora-azetidin-2-ones have been achieved which does not involve use of costlier reagents like Pt or Pd compounds. It is to be noted that "Psora-azetidin-2-ones formation is facilitated by the benzalimino ring.

III.8 References:

1 M. A. Stahmann, C. F. Huebner and K. P. Link, J. Biol. Chem., **1941**, 138, 513.

2 R. B. Arora and C. N. Mathur, Brit. J. Pharmacol., **1963**, 20, 29.

3 E. Grunberg and M. Bennett, Antimicrobiol. Agents Chemother, **1965**, 786.

4 A. Kumar, M. Verma, A. Saxena and K. Shanker, Ind. J. Chem., **1987**, 26B, 378.

5 S. Pandya, Ph. D. Thesis, Univ. Bombay, India, **1939**, 173.

6 G. Kokotos and C. Tzougraki, J. Heterocyclic Chem., **1986**, 23, 87.

7 Devki Desai, Ph. D. Thesis, M. S. Univ. of Baroda, India, **1999**, 162.

8 Samir Mistry, Ph.D. Thesis, The M.S.University of Baroda, India, **2002,** 89.

9 D. A. Burnett, M. A. Caplen, M. A. Davis Jr., R. E. Burrier, J. W. Clader, J. Med. Chem., **1994**, 37, 7332.

10 D. A. Burnett, Tetrahedron Lett., **1994**, 35, 7339.

11 W. D. Vaccaro, H. R. Davis, Bioorg. Med. Chem. Lett., **1998**, 8, 313.

12 A. Zarks, S. Chackalamamil, S. Dugar, J. org. Chem.,**1996**, 16, 8341.

13 R. Annunziata, M. Bengalia, M. Cinquini, Tetrahedron:Asymmetry, **1999**, 10, 4841.

14 B. K. Banik, F. F. Backer, Tetrahedron Lett., **2000**, 41, 6551

15 D. Nair, Ph.D. Thesis, The M.S.University of Baroda, India, **2004,** 89.

16 K. J. Thiagrajan, V. G. Puranik, A. R. A. S. Deshmukh, B. M. Bhawal, Tetrahedron Lett., **2000**, 56, 7811.

17 S. D. Sharma, S. Bhaduri, J. Chem. Res.(S), **2001**, 321

18 J. C. Lee, G. T. Kim, Y. K. Shim, S. H. Kang, Tetrahedron Lett., **2001**, 42, 4519.

19 H. Staudinger, Liebigs. Ann. Chem., **1907**, 51, 356.

20 A. K. Mukerjee, A. K. Singh, Synthesis, **1975**, 547.

21 A. K. Mukerjee, A. K. Singh, Tetrahedron, **1978**, 34, 1731

22 A. Greeberg, C. M. Breneman, J. F. Liebman, β-lactems: Cyclic Amides of Distinction Ed: Wiley: New York, **2000**, 157.

23 W. D. Vaccaro, R. Sher, H. R. Davis, Bioorg. Med. Chem. Lett., **1998,** 8, 35.

24 A. D. Brothwick, G. Weingarte, T. M. Haley, M. Tomaszewski, W. Wang, Z. Hu, J. Berard, H. Jin, L. Yuen, T. S. Mansour, Bioorg. Med. Chem. Lett., **1998,** 8, 365.

25 H. Hassan, R. Soliman, Synth. Commun., **2000**, 30, 246.

26 A. G. Griesbeck, H. Heckroth, Synlett., **2002**, 131.

27 D. A. Evans, E. B. Sjogren, Tetrahedron Lett., **1985**, 26, 3783.

28 C. Palomo, J. M. Aizpurua, I. Ganboa, M. Oiarbide, Eur. J. Org. Chem., **1999,** 3223.

29 W. D. Vaccaro, R. Sher, H. R. Davis, Bioorg. Med. Chem. Lett., **1998**, 8, 35.