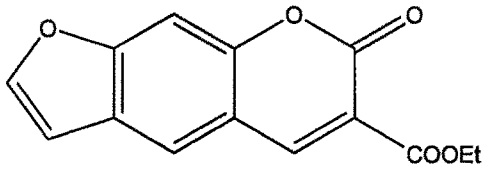
CHAPTER-II

Synthesis of Monofunctional Aminopsoralens

Synthesis of Monofunctional Aminopsoralens

II.1 Introduction

2H-1-Benzopyran-2-ones are naturally occurring compounds present, specially, in species of *umbeliferae*. Reppel[1], Spath[2] and Dean[3,4] have comprehensively reviewed the studies of 2H-1-benzopyran-2-ones, some are **9** to **12** represented below.



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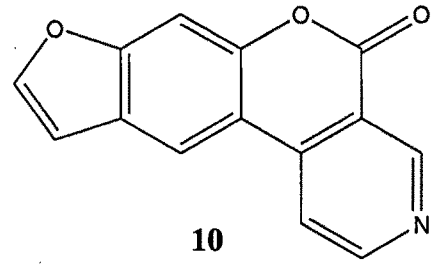

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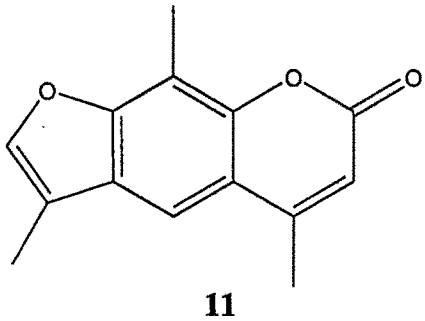

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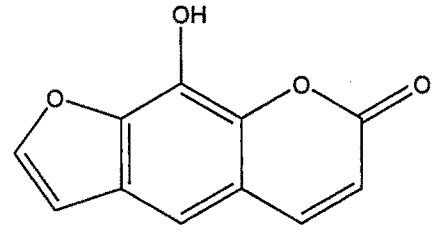

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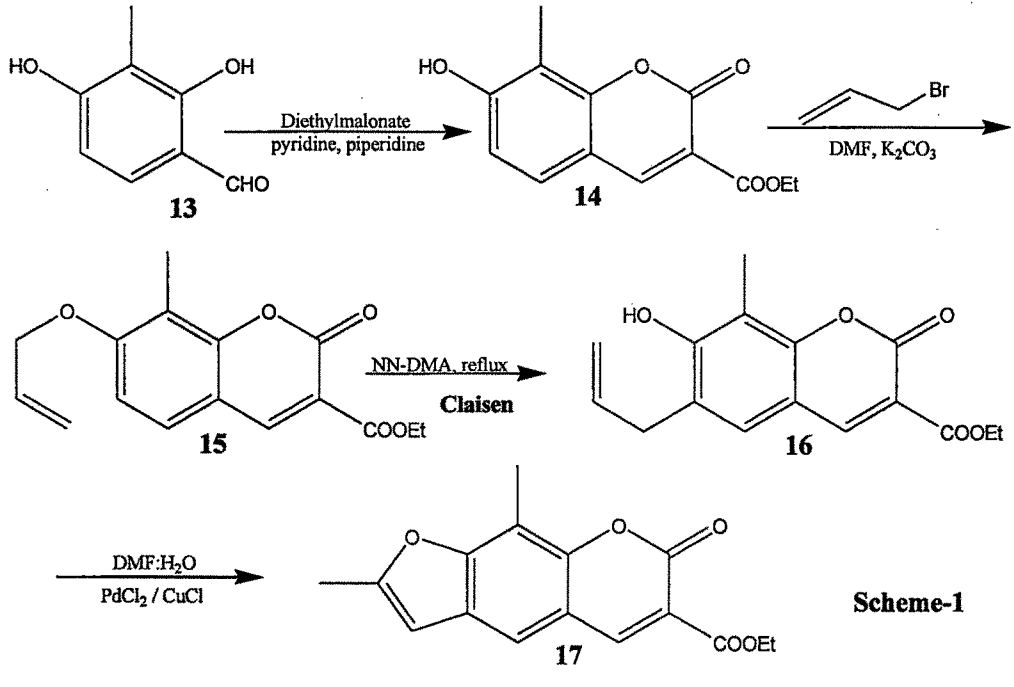
The studies of solubility and partition co-efficient in octanol-water system for suitable drug to be used in topical applications[5] have revealed that the trimethylpsoralen **11** could be most suitable for topical applications.

II.2 Strategies used for synthesis of fused furo-2H-1-benzopyran-2-ones:

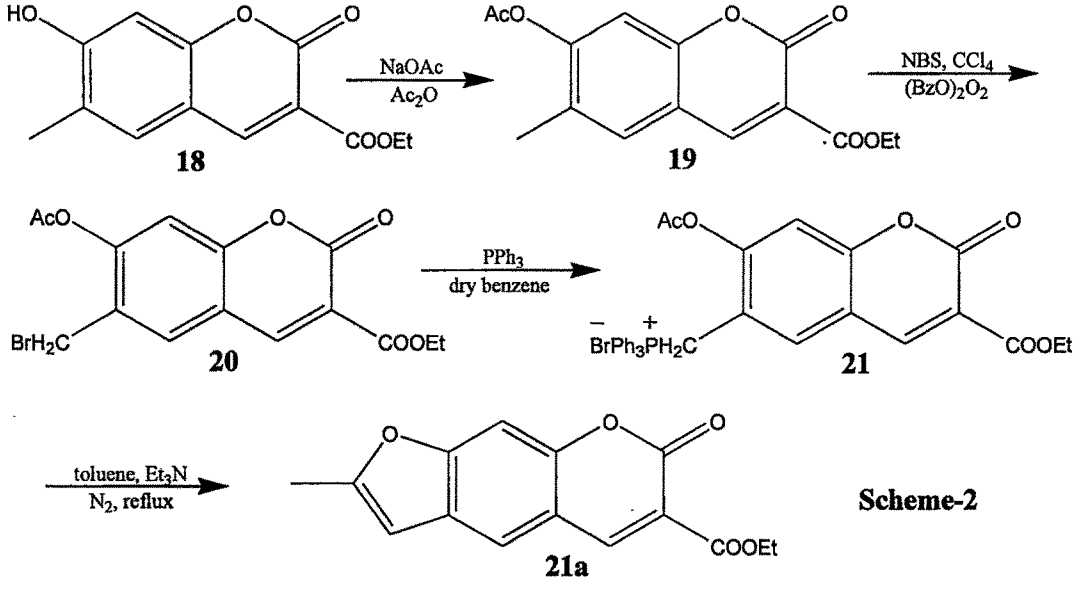
Various methods have been practiced for the synthesis of linearly fused furobenzopyrones. Recently, Knovaenegal condensation and Claisen rearrangement have been utilized[6] for the synthesis of ethyl 7,9-dimethyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-carboxylate **17**.

In this approach 2,4-dihydroxy-3-methylbenzaldehyde **13** was condensed with diethyl malonate in presence of piperidine and pyridine resulting in 2H-1-benzopyran-2-one derivative **14** which was then, allylated, followed by Claisen rearrangement in N,N-dimethylaniline to yield **16**. The oxy-palladation of **16** gave ethyl 7,9-dimethyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-carboxylate **17** (Scheme-1).



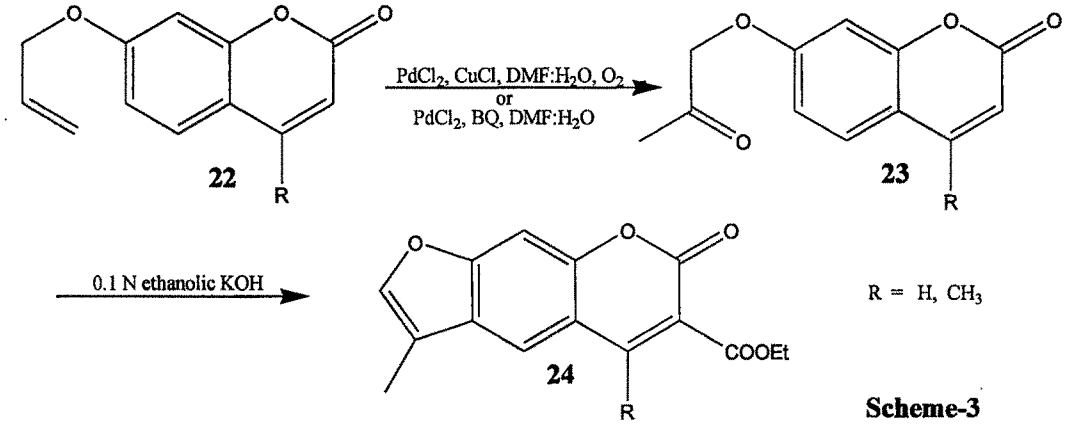
Scheme-1

In another approach, ethyl 7-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one-3-carboxylate **21a** was prepared using Wittig strategy.[7] For this **18** was first acetylated, followed by its bromination using NBS yielding bromomethyl derivative **20** which was, then, converted into ylide **21**, using triphenylphosphene. Ylide **21** in refluxing triethylamine gave **21a** (Scheme-2).



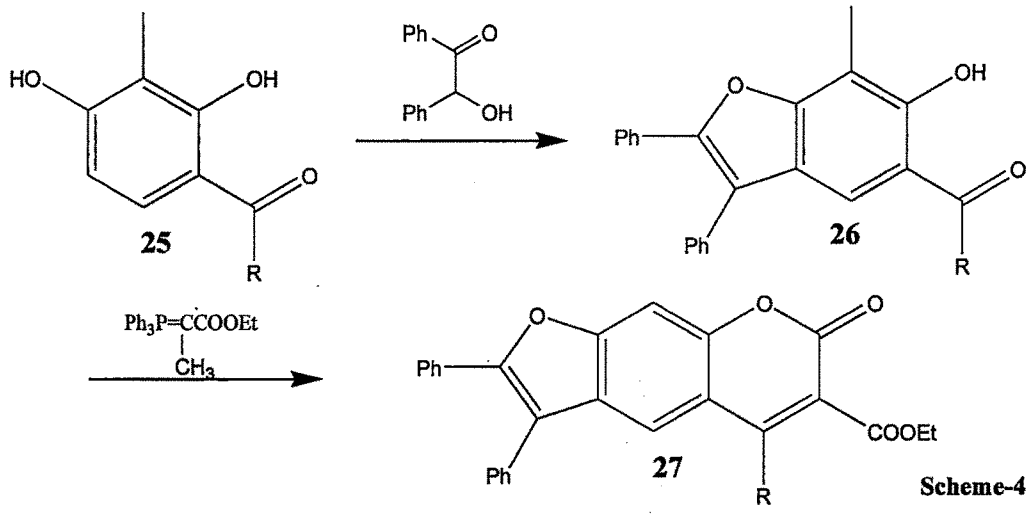
Scheme-2

The costlier oxy-palladation reaction has also been reported[8] (scheme-3) in which fused furobenzopyrones **24** were obtained from 7-allyloxy-2H-1-benzopyran-2-one **22**.



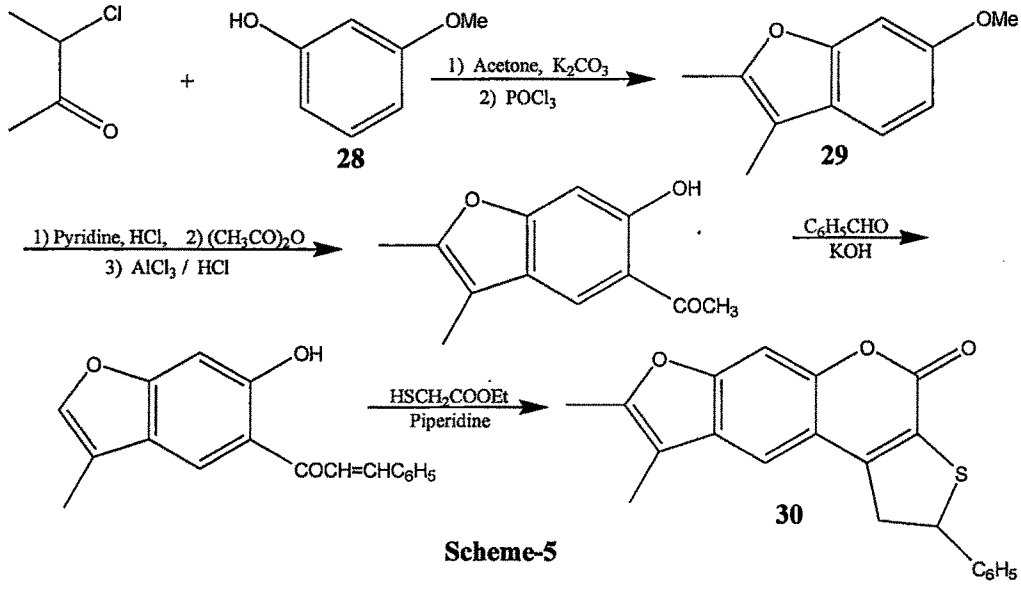
Scheme-3

Ahluwalia *et al*[9] used a strategy for formation of linearly fused furo benzopyrone in which first furan ring was developed, followed by treatment with Wittig ylide. For this, 2,4-dihydroxy-3-methylacetophenone **25** was condensed with benzoin in presence of *p*-toluene sulfonic acid, followed by Wittig reaction with ethoxy carbonyl methylene triphenylphosphorane which afforded furobenzopyrone **27** (scheme-4).



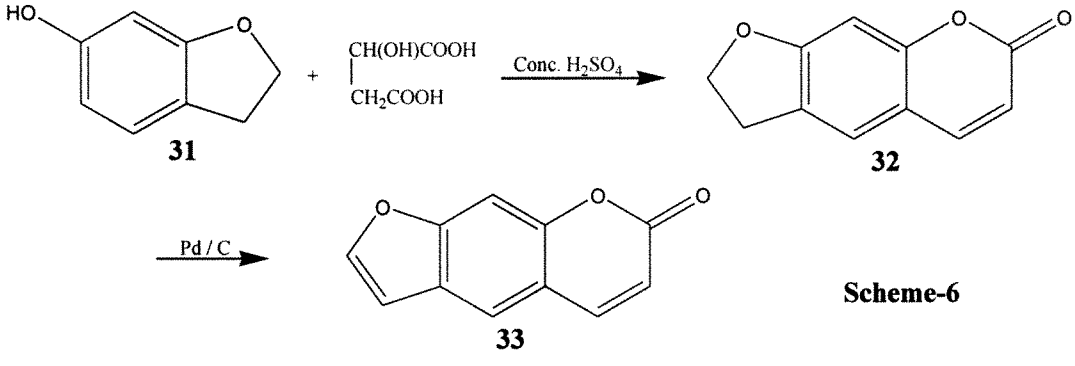
Scheme-4

Dihydrothieno fused furobenzopyrones **30** as well as their absorbance and fluorescence studies were reported by Zoubir *et al.*[10] They condensed 3-methoxyphenol **28** with 3-chlorobutan-2-one, followed by treatment with $POCl_3$ which gave **29**. Fries migration, condensation with benzaldehyde and mercapto ester treatment of **29** afforded furobenzopyrone **30** (schame-5).



Scheme-5

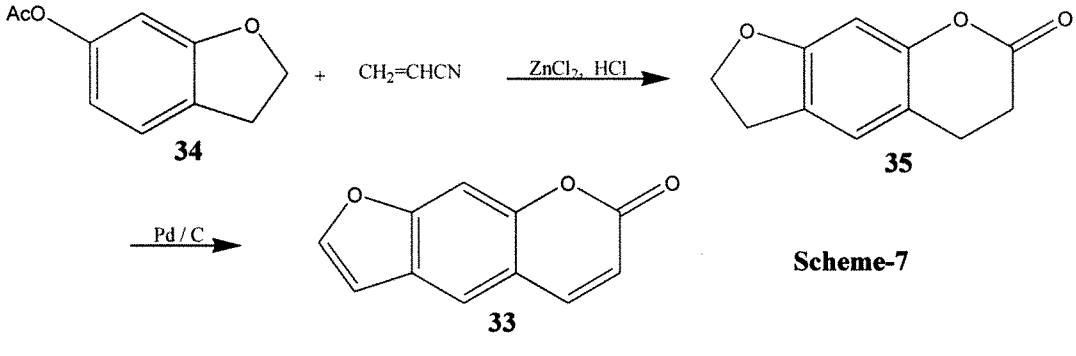
Spath and Pailer[11] used tetrahydro fused furobenzene directly to yield linear fused furobenzopyranone. Furo substituted hydoxybenzene **31**, was condensed with malic acid in presence of conc. sulphuric acid which furnished dihydrofurobenzopyrone **32** and on dehydrogenation with Pd/C, **32** afforded 2H-furo[3,2-*g*]-1-benzopyran-2-one **33** (scheme-6).



31 **32** **33**

Scheme-6

Acrylonitrile[12] was used to prepare 2H-furo[3,2-*g*]-1-benzopyran-2-one **33** in which 6-acetoxydihydrofurobenzene **34** was treated with acrylonitrile in presence of anhydrous $ZnCl_2$ and dry HCl affording 2,3,5,6-tetrahydrofuro[3,2-*g*]benzopyran-7H-one **35** and dehydrogenation of **35** with Pd/C yielded **33** (Scheme-7).

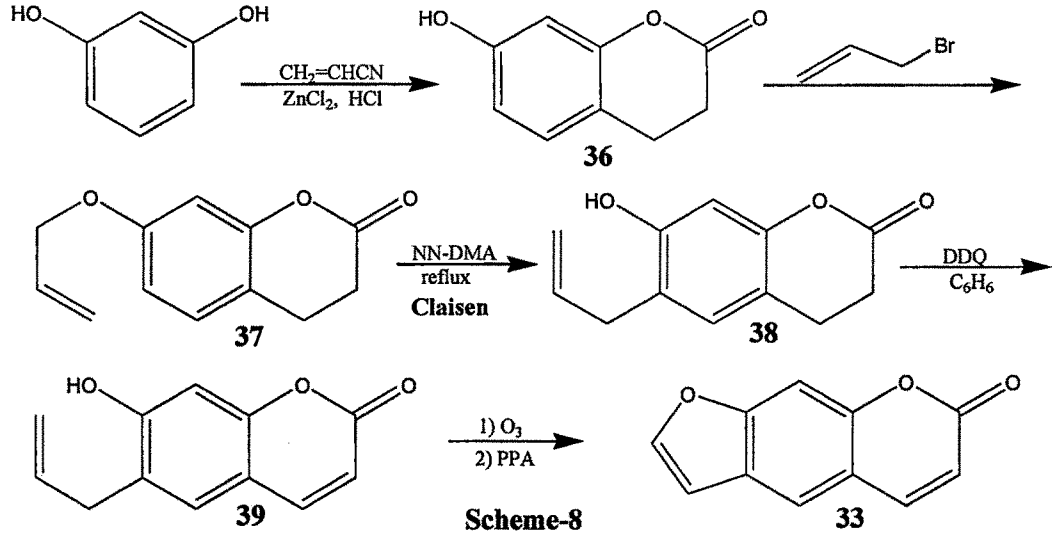


34 **35** **33**

Scheme-7

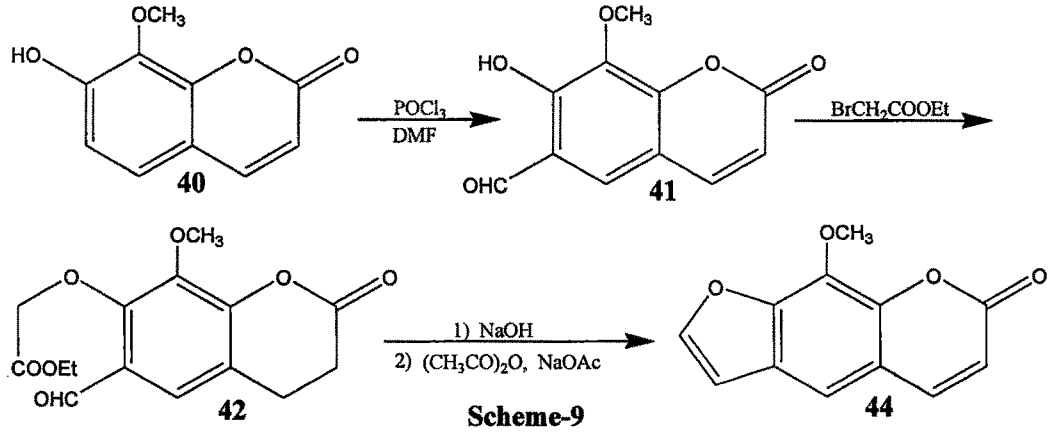
Use of ozonolysis to prepare linearly fused furo benzopyrones was achieved by Ray *et al.*[13] Condensation of resorcinol with acrylonitrile in presence of anhydrous $ZnCl_2$ and dry HCl furnished 7-hydroxy-dihydro-2H-1-benzopyran-2-one **36**, followed by allylation using allylbromide to give **37** and Claisen rearrangement in refluxing N, N-dimethylaniline giving **38**. Ozonolysis and subsequent cyclisation of **38** by

pyrophosphoric acid resulted in formation of 2H-furo[3,2-*g*]-1-benzopyran-2-one **33** (Scheme-8).



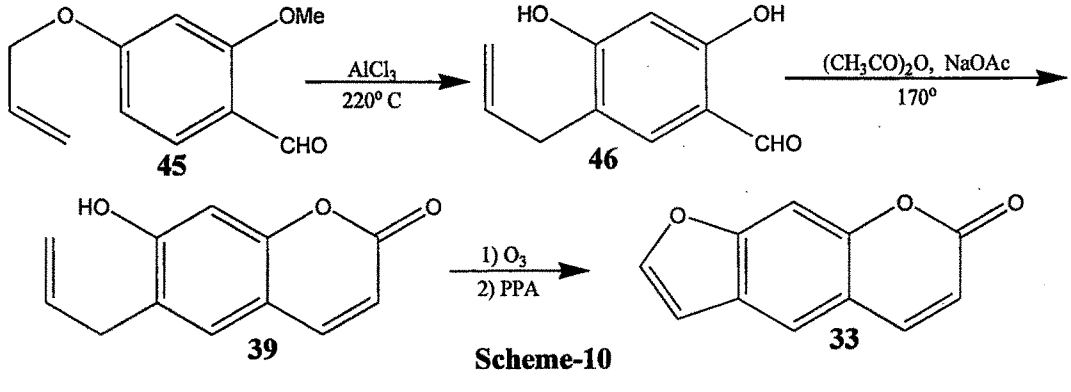
Scheme-8

Rodighiero and Antonello[14] used ethyl bromo acetate and cyclisation with acetic anhydride to synthesize fused furo benzopyrones (Scheme-9). In this synthesis, 7-hydroxy-8-mehtoxy-2H-1-benzopyran-2-one **40** was initially formylated to give **41** which was, then, treated with ethyl bromoacetate affording **42**. Hydrolysis of **42** by aq. NaOH and subsequent cyclisation with acetic anhydride gave 9-methoxy-2H-furo[3,2-*g*]-1-benzopyran-2-one **44**.



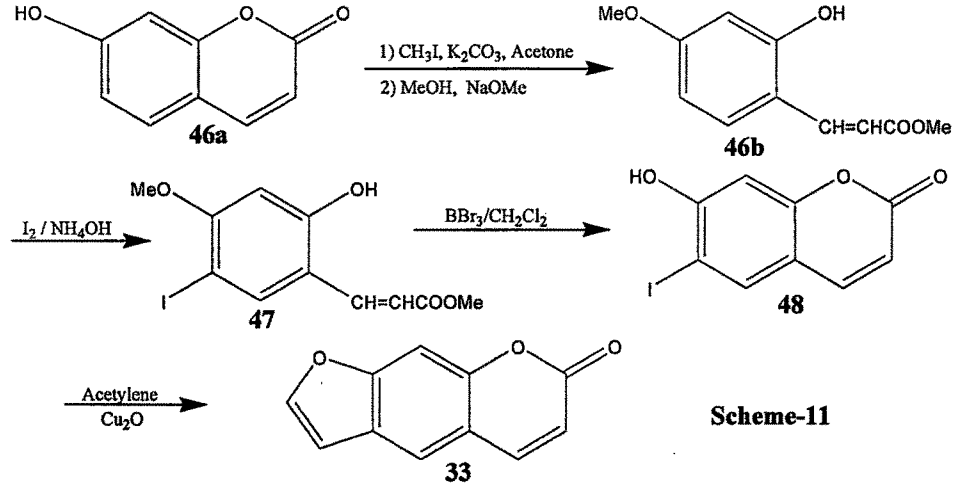
Scheme-9

In the similar way, Seshadri *et al*[15] used thermal rearrangement followed by cyclisation using pyrophosphoric acid. 4-Allyloxy-2-methoxytbenzaldehyde **45** was heated at 220 °C with anhydrous $AlCl_3$ affording 5-allyloxy-2,4-dihydroxybenzaldehyde **46** which on heating at 170 °C with acetic anhydride and sodium acetate furnished benzopyran-2H-one **39**. Ozonolysis and cyclisation with pyrophosphoric acid **39** gave 2H-furo[3,2-*g*]-1-benzopyran-2-one **33** (Scheme-10).



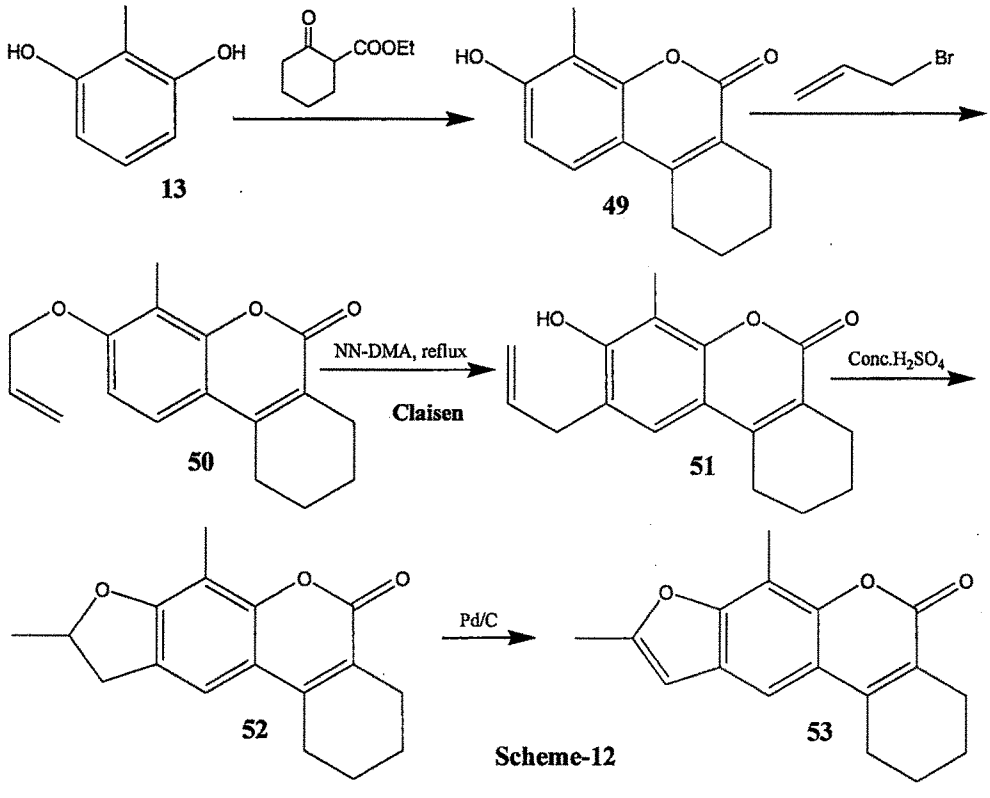
Scheme-10

Zubia *et al*[16] utilized iodination and acetylene for synthesis of fused furobenzopyrones in a different synthetic way (Scheme-11). 7-hydroxy-2H-1-benzopyran-2-one **46a,** was methylated, followed by opening of lactone ring and iodination using I_2 in aqueous ammonia which furnished **47**. The treatment of **47** with BBr_3/CH_2Cl_2 resulted in formation of 7-hydroxy-6-iodo-2H-1-benzopyran-2-one **48** which was coupled with an acetylenic reagent to furnish 2H-furo[3,2-g]-1-benzopyran-2-one **33**.



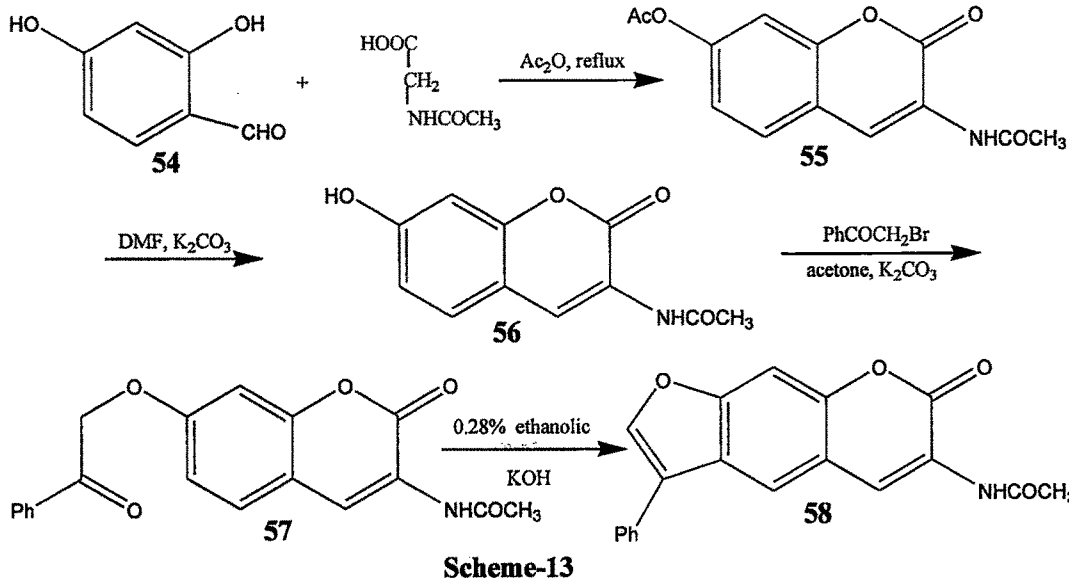
Scheme-11

Cyclohexyl substituted 2H-furo[3,2-*g*]-1-benzopyran-2-one was reported by Shaikh and Trivedi.[17] Condensation of 1,3-dihydroxy-2-methylbenzaldehyde **13** with ethyl cyclohexanone-2-carboxylate gave **49** which was allylated, followed by reflux in N,N-dimethylaniline affording 6-allyl-7-hydroxy-8-methyl-3,4-cyclohexanocoumarin **51**. On heating with conc. H_2SO_4 gave **51** which on and dehydrogenation using Pd/C, **51** gave cyclohexylfurobenzopyrone **53** (Scheme-12).



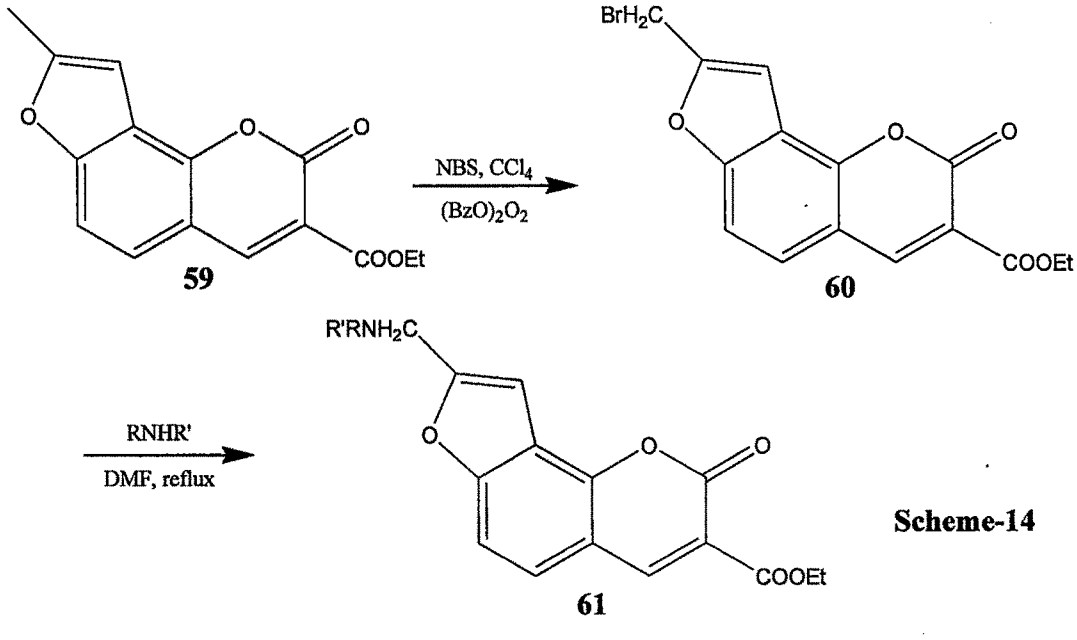
Scheme-12

Recently, synthesis of 3-acetamido-6-phenyl-2H-furo[3,2-*g*]-1-benzopyran-2-one **58** has been reported.[18] In this synthesis, 7-acetoxy-3-acetamido-2H-1-benzopyran-2-one **55**, prepared by condensation of acetylglycine with 2,4-dihydroxybenzaldehyde **54**, in refluxing N,N-dimethylformamide afforded deacetylated product **56** which on treatment with phenacylbromide gave 7-phenacyloxy-3-acetamido-2H-1-benzopyran-2-one **57**. Cyclization of **57** in ethanolic KOH furnished 3-acetamido-6-phenyl-2H-furo[3,2-*g*]-1-benzopyran-2-one **58** (Scheme-13).



Scheme-13

It has been reported[18] that the methyl group on furan ring of fused furobenzopyrones can be brominated by NBS in solvent like CCl_4 or $CHCl_3$ and subsequent treatment with amines results in substitution of bromine by corresponding amines **61** (Scheme-14).



Scheme-14

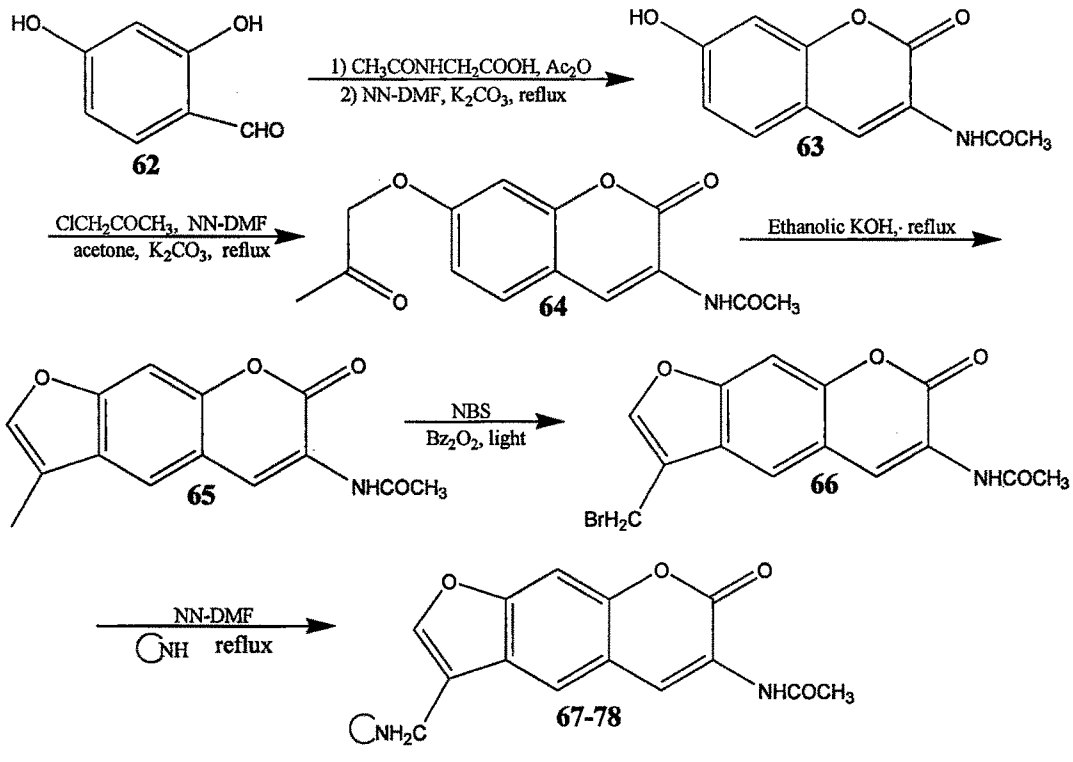
II.3 Results and Discussion

Linearly fused 2H-furo[3,2-*g*]-1-benzopyran-2-ones, i.e. psoralens, can engage furo as well as pyran sites during the intercalation between two pairs of DNA and show their biological function. This is referred to as bifunctional lesion. Whereas angularly fused 2H-furo[2,3-*h*]-1-benzopyran-2-ones, i.e. angelicins, can engage only pyran site for intercalation with DNA and show their biological function. This is referred to as monofunctional lesion.

With the aim of modifying monofunctional characters, 3-acetamido-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one **65** and some of its derivatives having substituted secondary aminomethyl groups at C-6 position have been prepared. In the present work initially 2, 4-dihydroxybenzaldehyde **62** was condensed with acetyl glycine resulting in formation of 3-acetamido-7-acetoxy-2H-1-benzopyran-2-one which in refluxing N,N-dimethylfomamide afforded 3-acetamido-7-hydroxy-2H-1-benzopyran-2-one **63.** Acetonylation with chloroacetone, compound **63** afforded 3-acetamido-7-acetonyloxy-2H-1-benzopyran-2-one **64** which on cyclization in alcoholic KOH yielded, exclusively, 3-acetamido-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one i.e. 3-acetamido-6-methylpsoralen **65** (Scheme-15).

It is worthwhile to mention here that the present approach eliminates use of costly Pd reagents employed previously for the synthesis of linearly fused furobenzopyran-2H-ones.[8]

Cyclisation of compound **64** was carried out by refluxing in ethanolic KOH (0.28%) which on work up afforded 3-acetamido-6-methyl-2H-furo[3,2-*g*]-1-benzopyran-2-one **65**. The compound **65** was, then, brominated using NBS in $CHCl_3$ under reflux to give 3-acetamido-6-bromomethyl-2H-furo[3,2-*g*]-1-benzopyran-2-one **66**. The brominated compound **65** was condensed with various acyclic and cyclic secondary amines to give corresponding 3-acetamido-6-substituted aminomethyl-2H-furo[3,2-*g*]-1-benzopyran-2-ones **67-78.**



Scheme-15

Compound **64** showed IR absorption bands at 3331 cm^{-1} for –NH- of amide group, 1728 cm^{-1} and 1709 cm^{-1} for carbonyl groups [Figure-1].

PMR Compound **64** exhibited a singlet at δ 1.83 for three protons of methyl of acetonyloxy substituent, a singlet at δ 2.49 for three protons of methyl group of acetamido substituent, a singlet at δ 4.53 for mehtylene protons of –$C\underline{H}_2$CO- at C-7, a broad signal at δ 6.88 for amide proton –N$\underline{H}$CO-, two doublets at δ 7.27-7.29 (J=8 Hz) for protons atC-5 and C-6, a singlet at δ 7.50 for proton at C-4 and a singlet at δ 7.75 for a proton at C-8 [Figure-2].

3-Acetamido-6-methyl-2H-1-benzopyran-2-one, **65** was confirmed by elemental analysis, IR, PMR and ^{13}CMR spectra. Compound **65** showed absorption bands at 3378 cm^{-1} for –NH- of amide group, 1738 cm^{-1} and 1711 cm^{-1} for carbonyl groups [Figure-3]. PMR exhibited singlet at δ 2.24 for mehtyl protons at C-6, another singlet at δ 2.51 for mehtyl protons of –NHCO$C\underline{H}_3$, a broad signal at δ 4.68 for amide proton –N$\underline{H}$CO-, a

singlet at δ 6.80 for a proton at C-4, a singlet at δ 7.23 for a proton at C-9, a singlet at δ 7.92 for a proton at C-5 and a singlet at δ 8.64 for a proton at C-5 [Figure-4].

3-Acetamido-6-(bromomethyl)-2H-1-benzopyran-2-one, **66** showed absorption bands at 3328 cm^{-1} for –NH- of amide group and 1741 cm^{-1} for carbonyl group [Figure-6]. PMR exhibited a singlet at δ 2.39 for three protons of methyl group of –NHCOC<u>H</u>$_3$ at C-3, a singlet for mehtylene protons of –C<u>H</u>$_2$Br at δ 4.64, a broad signal at δ 5.00 for –N<u>H</u>CO- proton, a singlet at δ 7.29 for a proton at C-4, a singlet at δ 7.49 for a proton at C-9, a singlet at δ 7.98 for a proton at C-5 and another singlet at 8.70 for a proton at C-7 [Figure-7].

3-Acetamido-6-(2,5-dihydropyrrolin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **67** showed absorption bands at 3348 cm^{-1} for –NH- of amide group and 1748 cm^{-1} and 1710 cm^{-1} for carbonyl groups. PMR exhibited a singlet at δ 2.33 for three protons of methyl group of –NHCOC<u>H</u>$_3$, a multiplet at δ 3.41 for four protons of two methylene groups of pyrroline ring, a singlet at δ 4.21 for two protons of –NC<u>H</u>$_2$Ar at C-6, a multiplet at δ 5.10 for two alkene protons of pyrroline ring, a singlet at δ 7.10 for a proton at C-4, a broad signal at δ 7.25 for –N<u>H</u>CO- proton, a singlet at δ 7.47 for a proton at C-9, a singlet at δ 7.92 for a proton at C-5 and a singlet at δ 7.83 for proton at C-7 [Figure-8].

3-Acetamido-6-(piperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **68,** showed absorption bands at 3389 cm^{-1} for –NH- of amide group, 3361cm^{-1} for NH of ring and 1751 cm^{-1} and 1701 cm^{-1} for carbonyl groups. PMR exhibited a singlet at δ 2.58 for three protons of methyl group of –NHCOC<u>H</u>$_3$, a multiplet at δ 3.45-3.65 for eight protons of four methylene groups of piperazine ring, a singlet at δ 4.16 for two protons of –NC<u>H</u>$_2$Ar at C-6, two singlets at δ 5.52 and δ 5.65 for -N<u>H</u> and -N<u>H</u>CO protons, a singlet at δ 6.72 for a proton at C-4, a singlet at δ 7.40 for a proton at C-9, a singlet at δ 7.96 for a proton at C-5 and a singlet at δ 8.53 for proton at C-7 [Figure-9].

3-Acetamido-6-(2-methylpiperidin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **69** showed absorption bands at 3310 cm^{-1} for –NH- of amide group and 1758 cm^{-1} and 1720 cm^{-1} for carbonyl groups. PMR exhibited a multiplet at δ 1.11-1.28 for two protons and a multiplet at δ 1.30-1.57 for four protons of ring C<u>H</u>$_2$, a doublet at δ 1.70 (J=8.1 Hz) for three protons of methyl group of ring, a singlet at δ 2.50 for three protons of methyl group of –NHCOC<u>H</u>$_3$, a multiplet at δ 3.35-3.50 for a proton C<u>H</u>N of ring, a

multiplet at δ 3.52-3.65 for two protons of ring $C\underline{H}_2N$, a singlet at δ 4.17 for two protons of $-NC\underline{H}_2Ar$ at C-6, a singlet at δ 7.18 for a proton at C-4, a singlet at δ 7.49 for a proton at C-9, a singlet at δ 7.80 for a proton at C-5 and a singlet at δ 8.29 for proton at C-7 [Figure-10].

3-Acetamido-6-(4-cyclohexylmethylpiperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **70** showed absorption bands at 3328 cm^{-1} for –NH- of amide group and 1730 cm^{-1} and 1710 cm^{-1} for carbonyl groups. PMR exhibited a multiplet at δ 1.38-1.51 for ten protons of cyclohexyl ring $C\underline{H}_2$, another multiplet at δ 1.61 for a cyclohexyl C<u>H</u> proton, a singlet at δ 2.43 for three protons of methyl group of $-NHCOC\underline{H}_3$, a multiplet at δ 3.42-3.56 for eight protons of $C\underline{H}_2$ of piperazine ring, a doublet (J=8 Hz) δ 3.62-3.68 for two protons of $-NC\underline{H}_2$, a singlet at δ 4.24 for two protons of $-NC\underline{H}_2Ar$ at C-6, a singlet at δ 6.84 for a proton at C-4, a broad signal at δ 7.01-7.05 for amide -N<u>H</u>CO proton, a singlet at δ 7.40 for a proton at C-9, a singlet at δ 7.83 for a proton at C-5 and a singlet at δ 8.40 for proton at C-7 [Figure-11].

3-Acetamido-6-(N,N-di(2-hydroxyethyl)aminomethyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **71** showed absorption bands at 3391 cm^{-1} for hydroxyl proton, a band at 3339 cm^{-1} for –NH- of amide group and 1729 cm^{-1} and 1700 cm^{-1} for carbonyl groups. PMR exhibited a singlet at δ 2.40 for three protons of methyl group of $-NHCOC\underline{H}_3$, a triplet (J=14 Hz) at δ 3.14-3.32 for four protons of $NC\underline{H}_2$ of piperazine ring, a broad signal with triplet (J=14 Hz) for four protons of $-OC\underline{H}_2$, a singlet at δ 4.15 for two protons of $-NC\underline{H}_2Ar$ at C-6, a broad signal for two hydroxyl at δ 4.60-5.00, a broad signal at δ 6.60 for amide -N<u>H</u>CO proton, a singlet at δ 6.80 for a proton at C-4, a singlet at δ 7.23 for a proton at C-9, a singlet at δ 7.59 for a proton at C-5 and a singlet at δ 8.10 for proton at C-7 [Figure-12].

3-Acetamido-6-(morpholin-4-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **72** showed absorption a band at 3321 cm^{-1} for –NH- of amide group and 1718 cm^{-1} and 1701 cm^{-1} for carbonyl groups [Figure-13]. PMR exhibited a singlet at δ 2.25 for three protons of methyl group of $-NHCOC\underline{H}_3$, a broad multiplet at δ 2.46-2.56 for four protons of $NC\underline{H}_2$ of morpholine ring, another broad multitiplet at δ 3.58-3.71 for four protons of $-OC\underline{H}_2$, a singlet at δ 3.72-3.90 for two protons of $-NC\underline{H}_2Ar$ at C-6, a broad signal at δ

4.46-5.30 for amide -NHCO proton, a singlet at δ 7.40 for a proton at C-4, a singlet at δ 7.88 for a proton at C-9, a singlet at δ 8.03 for a proton at C-5 and a singlet at δ 8.82 for proton at C-7 [Figure-14].

3-Acetamido-6-(pyrrolidin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one,**73** showed absorption bands at 3298 cm^{-1} for –NH- of amide group and 1757 cm^{-1} and 1701 cm^{-1} for carbonyl groups. PMR exhibited a multiplet at δ 1.51-1.65 for four ring protons β to N, a singlet at δ 2.30 for three protons of methyl group of –NHCOCH_3, a multiplet at δ 2.90-3.10 for four ring protons α to N, a singlet at δ 4.68 for two protons of –NCH_2Ar at C-6, a singlet at δ 7.33 for a proton at C-4, a singlet at δ 7.45 for a proton at C-9, a singlet at δ 7.72 for a proton at C-5, a broad signal at δ 8.00 for –NHCO- proton and a singlet at δ 8.68 for proton at C-7 [Figure-15].

3-Acetamido-6-(4-pyrrolidinylpiperidin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **74** showed absorption bands at 3341 cm^{-1} for –NH- of amide group and 1740 cm^{-1} and 1719 cm^{-1} for carbonyl groups. PMR exhibited a multiplet at δ 1.30-1.50 for eight ring protons β to N, a singlet at δ 2.30 for three protons of methyl group of –NHCOCH_3, a multiplet at δ 3.28-3.40 for a ring CHN proton, a multiplet at δ 3.45-3.55 for eight protons of ring CH_2 α to N and amide proton –NHCO, a singlet at δ 4.21 for two protons of –NCH_2Ar at C-6, a singlet at δ 6.83 for a proton at C-4, a singlet at δ 7.42 for a proton at C-9 and two singlets at δ 7.72 and δ 7.51 for protons at C-5 and C-7 respectively[Figure-16].

3-Acetamido-6-(4-methylpiperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one,**75** showed absorption bands at 3319 cm^{-1} for –NH- of amide group and 1721 cm^{-1} and 1703 cm^{-1} for carbonyl groups. PMR exhibited a singlet at δ 2.34 for three protons of methyl group of –NHCOCH_3, a multiplet at δ 2.40-2.45 for four protons of ring 2x -NCH_2, another multiplet at δ 3.58-3.62 for four protons of ring 2x -NCH_2 a singlet at δ 3.63 for three protons of NCH_3, a singlet at δ 3.67 for two protons of –NCH_2Ar at C-6, a singlet at δ 7.43 for a proton at C-4, a singlet at δ 7.47 for a proton at C-9, a singlet at δ 7.63 for a proton at C-5, a broad signal at δ 8.03 for amide proton NHCO and a singlet at δ 8.82 for proton at C-7 [Figure-17].

3-Acetamido-6-(4-phenylpiperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **76** showed absorption bands at 3331 cm^{-1} for –NH- of amide group and 1731 cm^{-1} and 1710 cm^{-1} for carbonyl groups. PMR exhibited a singlet at δ 2.51 for three protons of methyl group of –NHCOC$\underline{H}_3$, a multiplet at δ 2.60-2.90 for four protons of ring NC$\underline{H}_2$, another multiplet at δ 3.50-3.80 for four protons of ring NC$\underline{H}_2$, a singlet at δ 4.25 for two protons of –NCH_2Ar at C-6, a multiplet at δ 6.75-7.10 for five aromatic protons, a broad signal at δ 7.32 for amide proton N$\underline{H}$CO, a singlet at δ 7.70 for a proton at C-4, a singlet at δ 7.90 for a proton at C-9, a singlet at δ 8.04 for a proton at C-5 and a singlet at δ 8.15 for proton at C-7 [Figure-18].

3-Acetamido-6-(4-allylpiperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **77** showed absorption bands at 3384 cm^{-1} for –NH- of amide group and 1722 cm^{-1} and 1704 cm^{-1} for carbonyl groups. PMR exhibited a singlet at δ 2.51 for three protons of methyl group of –NHCOC$\underline{H}_3$, a multiplet at δ 2.75-3.51 for eight protons of ring NC$\underline{H}_2$, a singlet at δ 4.04 for two protons of –NCH_2Ar at C-6, a multiplet at δ 4.90-5.60 for six protons of allylic, vinylic and amide N$\underline{H}$CO groups, a singlet at δ 7.20 for a proton at C-4, a singlet at δ 7.41 for a proton at C-9, a singlet at δ 8.00 for a proton at C-5 and a singlet at δ 8.42 for proton at C-7 [Figure-19].

3-Acetamido-6-(piperidin-1-yl-methyl)-2H-1-benzopyran-2-one, **78** showed absorption bands at 3318 cm^{-1} for –NH- of amide group and 1738 cm^{-1} and 1721 cm^{-1} for carbonyl groups. PMR exhibited a broad multiplet at δ 2.19-2.42 for six protons of three C$\underline{H}_2$ groups of piperidine ring, a singlet at δ 2.50 for three protons of methyl group of –NHCOC$\underline{H}_3$, a multiplet at δ 2.91-3.27 for four protons 2x -NC$\underline{H}_2$, a singlet at 4.44 for two protons of –NCH_2Ar at C-6, a broad signal at δ 7.34 for –N$\underline{H}$CO- proton, a singlet at δ 7.41 for a proton at C-4, a singlet at δ 7.80 for proton at C-9, a singlet at δ 8.04 for a proton at C-5 and a singlet at δ 8.73 for proton at C-7 [Figure-20].

II.4 Experimental:

Melting points were measured by capillary methods and are uncorrected. Purity of the compounds was checked by thin layer chromatography on silica gel using ultraviolet light and iodine vapour as visualizing agents.

Compounds were collected by column chromatography using mixture of light petroleum (60°-80°)/toluene or ethyl acetate. Elemental analysis was carried out on a Perkin-Elmer CHNS analyzer (Model-2400). Infrared spectra were recorded on a Perkin-Elmer-FTIR spectrophotometer (KBr discs). Proton nuclear magnetic resonance spectra were recorded on Bruker 400 MHz or Perkin-Elmer 90 MHz spectrophotometers.

Reagents were purified whenever necessary before use. Solvents were distilled and dried before use. Distilled acetone was stored over anhydrous K_2CO_3. 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.

Procedures for the synthesis of 64, 65 and 66.

3-Acetamido-7-acetonyloxy-2H-1-benzopyran-2-one, 64

The 3-acetamido-7-hydroxy-2H-1-benzopyran-2-one **63** (3.504g, 0.016mol) was dissolved in dry acetone (200ml) and N,N-dimethylformamide (25ml) in a round bottomed flask. This was followed by addition of anhydrous K_2CO_3 (10g), chloroacetone (1.932g, 0.021mol) and few crystals of KI were added to it. The mixture was refluxed for about two hours after which acetone was distilled off and the residue was poured in crushed ice (100g). The solid thus obtained was filtered and washed with aqueous NaOH solution (1%, 50ml) thoroughly and purified by column chromatography using petroleum ether (40°-60° C) as eluent and recrystallised from ethyl alcohol.

3-Acetamido-6-methyl-2H-1-benzopyran-2-one, 65

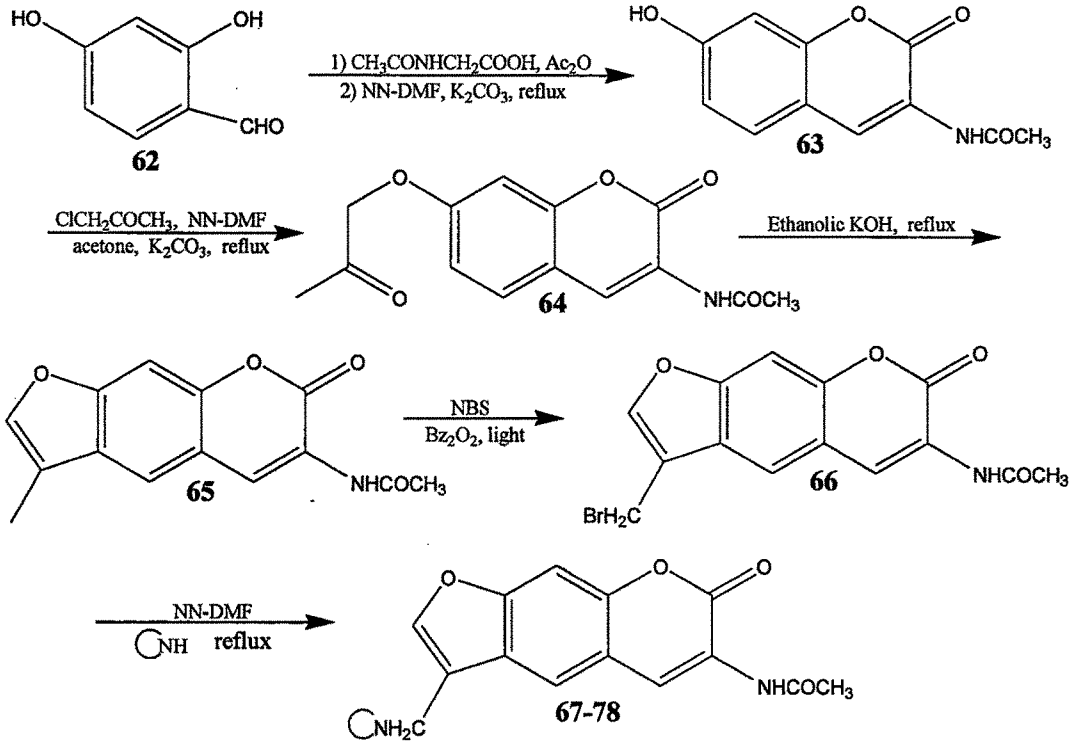
A solution of 3-acetamido-7-acetonyloxy-2H-1-benzopyran-2-one **64** (1.375g, 0.005 mol) in ethanolic KOH (0.29 %, 80ml) was refluxed for five hours after which ethanol was distilled off. To the residue cold aq. HCl (1N, 100ml) was added and it was then allowed to stand for about 10 hours. The solid obtained was filtered, dried and purified by column chromatography using petroleum ether (40°-60°C) as eluent and recrystallised from ethyl alcohol.

3-Acetamido-6-(bromomethyl)-2H-1-benzopyran-2-one, 66

3-Acetamido-6-methyl-2H-1-benzopyran-2-one **65** (2.570g, 0.01mol), freshly crystallized N-bromosuccinimide (1.780g, 0.01mol) and benzoyl peroxide (~10mg) was irradiated while heating under reflux in $CHCl_3$ (80ml) using tungsten lamp (ECE make, 200 W) for 24 hours. The hot reaction mixture was then filtered, followed by removal of chloroform by distillation. The solid thus obtained was dried and purified by column chromatography using petroleum ether (40°- 60°C) as eluent and recrystallised from ethyl alcohol.

General procedure for the synthesis of 67-78.

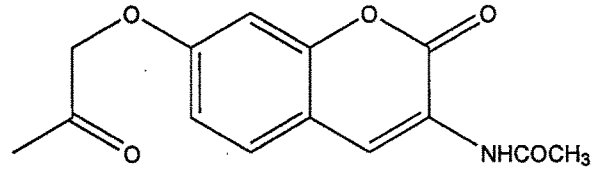
A solution of 3-acetamido-6-(bromomethyl)-2H-1-benzopyran-2-one **66** (0.672g, 0.002 mol) and the secondary amine (0.008mol) in N,N-dimethylformamide (50ml) was refluxed for one hour. The reaction mixture was then poured into water (100ml), the solid was filtered and purified by column chromatography using petroleum ether (40°-60° C) as eluent and recrystallised from ethyl alcohol.



Scheme-15

N—	= 2,5-dihydropyrrolinyl	**67**	= pyrrolidinyl	**73**
	= piperazinyl	**68**	= 4'-(1-pyrrolidinyl)piperidinyl	**74**
	= 2'-methylpiperidinyl	**69**	= N-methylpiperazinyl	**75**
	= N-(methylcyclohexyl)piperazinyl	**70**	= N-phenylpiperazinyl	**76**
	= N,N-diethanolamino	**71**	= N-allyllpiperazinyl	**77**
	= morpholinyl	**72**	= piperidinyl	**78**

3-Acetamido-7-acetonyloxy-2H-1-benzopyran-2-one, **64:**



State : White crystalline Solid

Molecular Formula : $C_{14}H_{13}O_5N$

Melting Point : 241-242 °C

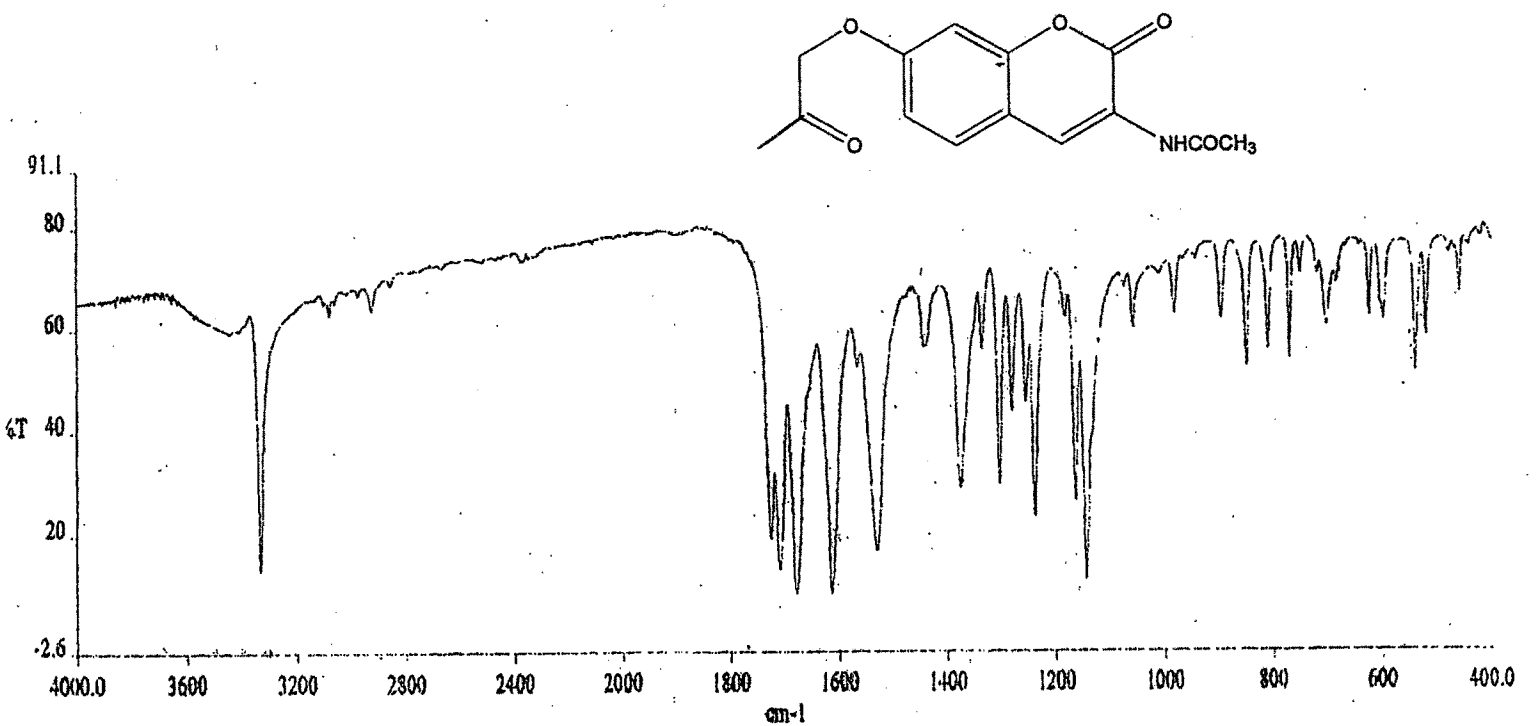
% Yield : 90

%C,H,N analysis (calculated) : C: 61.10 H: 4.73 N: 5.09

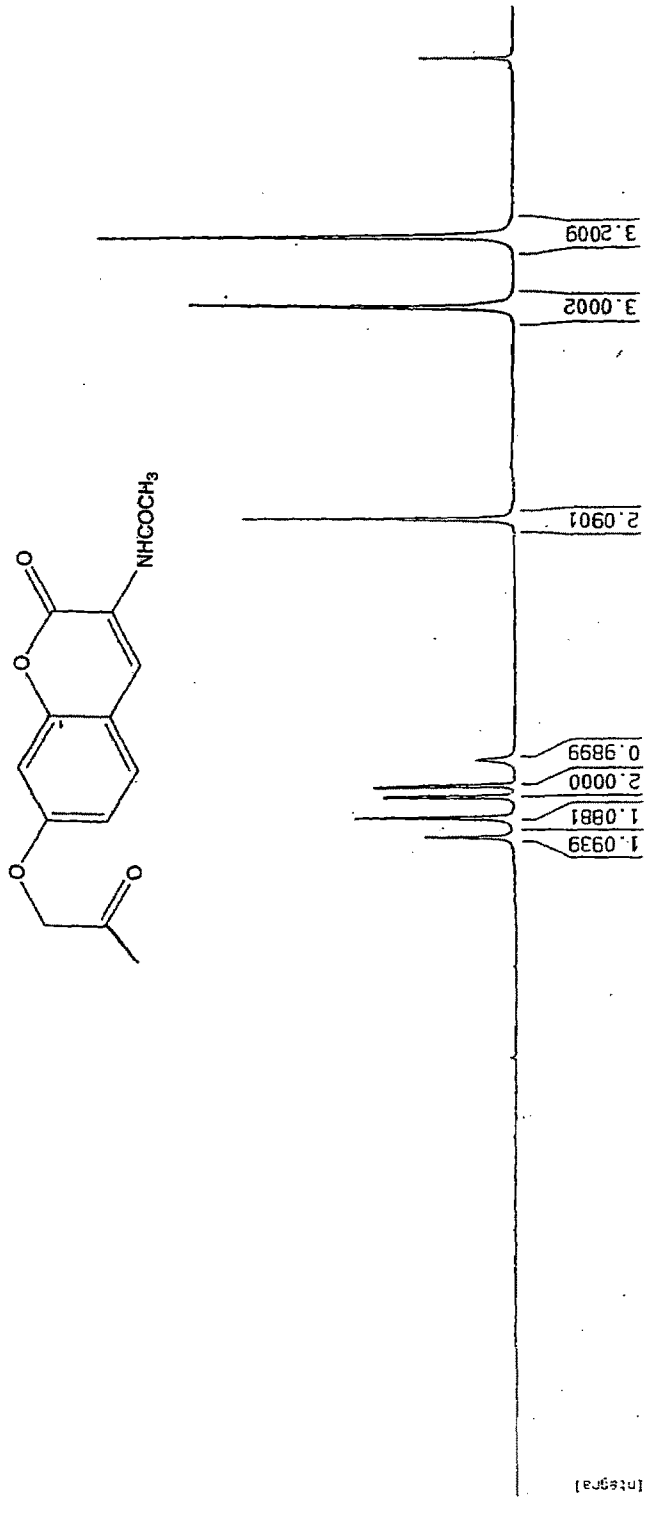
%C,H,N analysis (found) : C: 61.14 H: 4.60 N: 5.11

IR data (KBr) cm^{-1} : 3331, 3051, 2978, 1728, 1709, 1679, 1118.

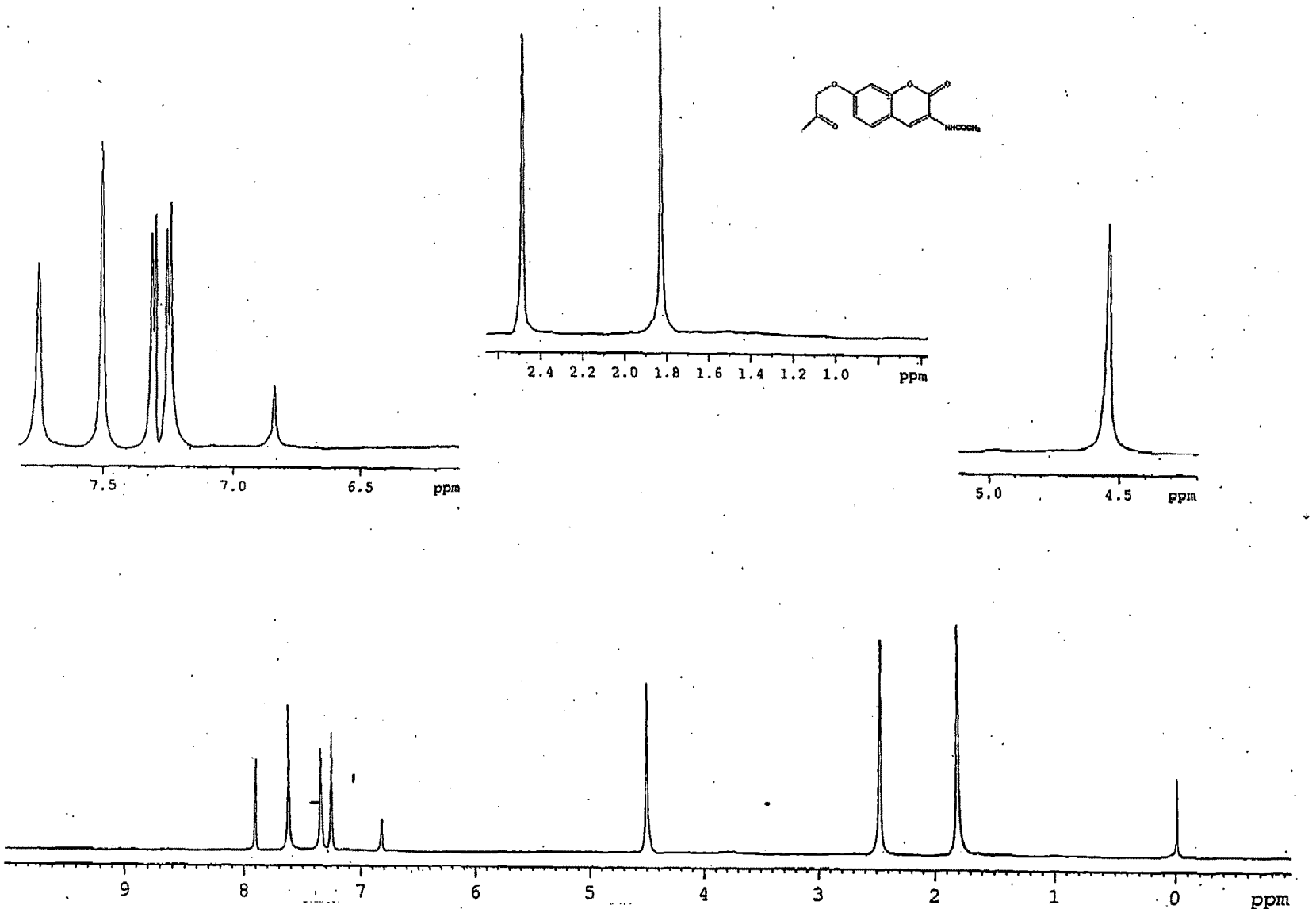
PMR data (400MHz, $CDCl_3$) δ ppm : 1.83(s, 3H, $C\underline{H}_3CO$-), 2.49(s, 3H, -NHCOC$\underline{H}_3$), 4.53(s, 2H, -C$\underline{H}_2$), 6.88(br s, 1H, -CO-N$\underline{H}$), 7.27- 7.29(two d, J= 8 Hz, 2H, C-5, C-6 protons), 7.50(s, 1H, C-4), 7.75(s, 1H, C-8).



[Figure-1]: 3-Acetamido-7-acetonyloxy-2H-1-benzopyran-2-one, 64

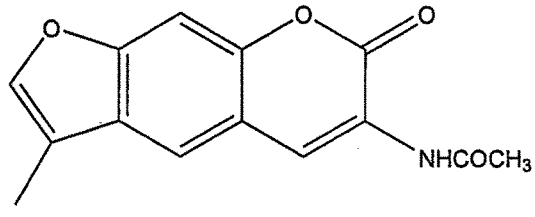


[Figure-2]: 3-Acetamido-7-acetonyloxy-2H-1-benzopyran-2-one, 64



[Figure-2a]: 3-Acetamido-7-acetonyloxy-2H-1-benzopyran-2-one, 64

3-Acetamido-6-methyl-2*H*-furo[3,2-*g*]-1-benzopyran-2-one, **65:**



State : White crystalline solid,

Molecular Formula : $C_{14}H_{11}O_4N$

Melting Point : 261-262 °C

% Yield : 50

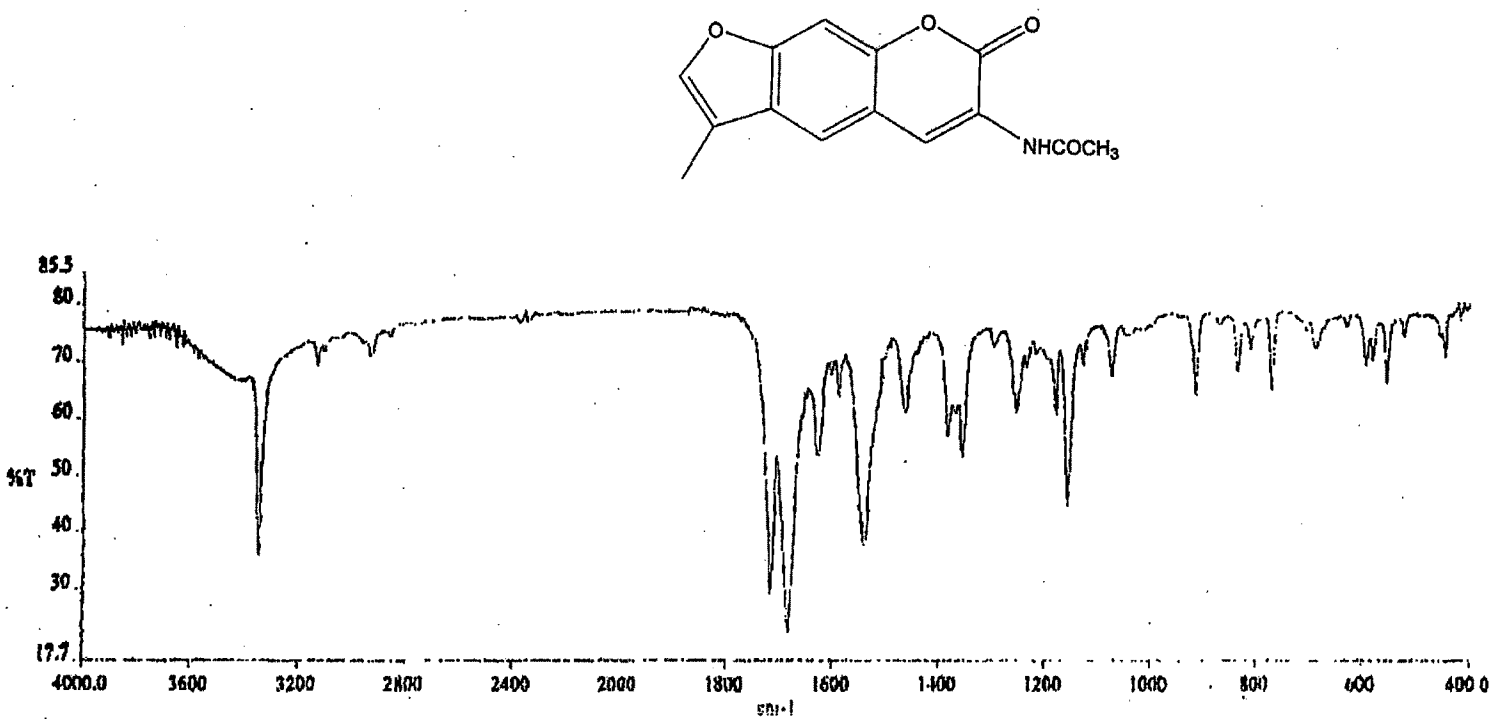
%C,H,N analysis (calculated) : C: 65.37 H: 4.28 N: 5.45

%C,H,N analysis (found) : C: 64.89 H: 4.18 N: 5.12

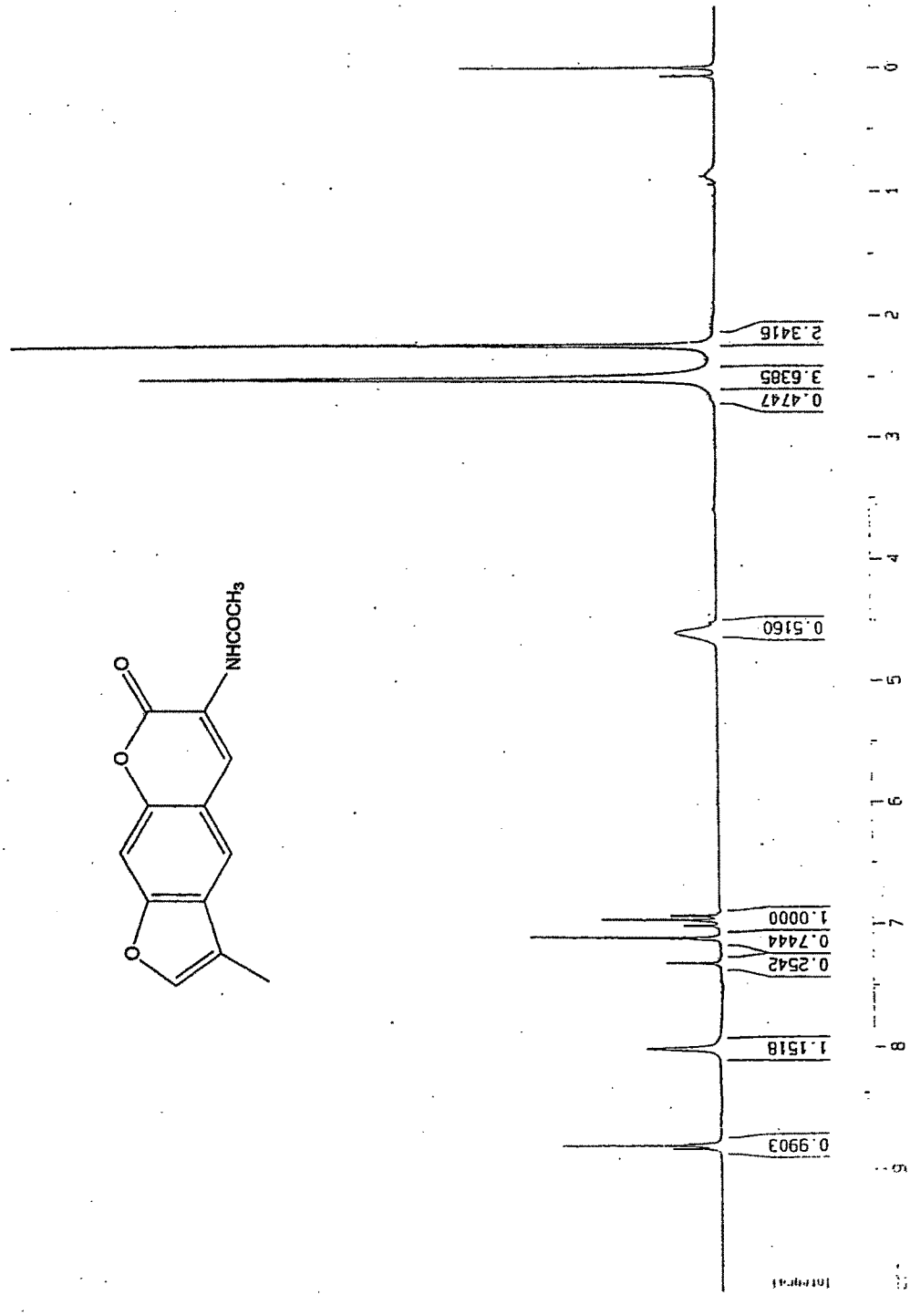
IR data (KBr) cm^{-1} : 3378, 3011, 2969, 1738, 1711, 1680, 1124

PMR data (400MHz, $CDCl_3$): δ 2.24(s, 3H, $C\underline{H}_3$- at C-6), 2.51(s, 3H, -NHCO$C\underline{H}_3$), 4.68(br s, 1H, -N$\underline{H}$CO), 6.80(s, 1H, C-4), 7.23(s, 1H, C-9), 7.92(s, 1H, C-5), 8.64(s, 1H, C-7).

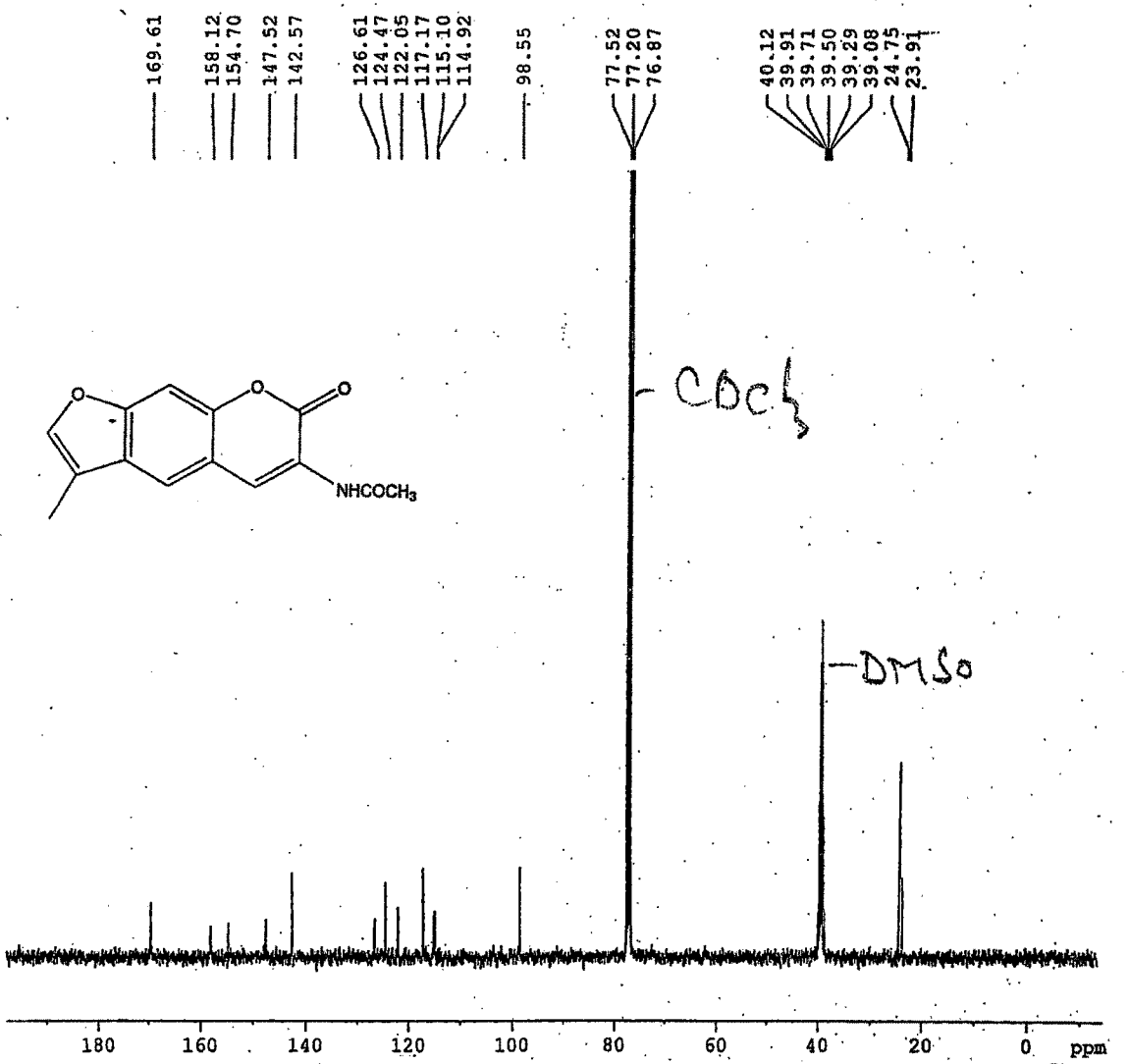
^{13}CMR: 169.61, 158.12, 154.70, 147.52, 142.57, 126.61, 124.47, 122.05, 117.17, 115.10, 114.92, 98.55, 24.75, 23.91.



[Figure-3]: 3-Acetamido-6-methyl-2H-1-benzopyran-2-one, 65

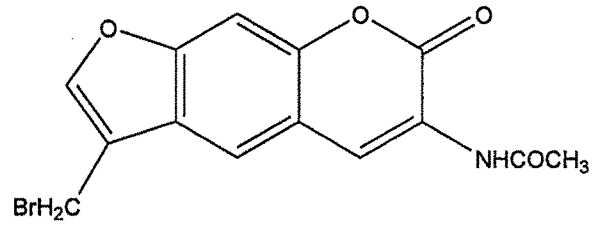


[Figure-4]: 3-Acetamido-6-methyl-2H-1-benzopyran-2-one, 65



[Figure-5]: 3-Acetamido-6-methyl-2H-1-benzopyran-2-one, 65

3-Acetamido-6-(bromomethyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **66:**



State : off white amorphous solid

Molecular Formula : $C_{14}H_{10}O_4NBr$

Melting Point : 289 - 291°C

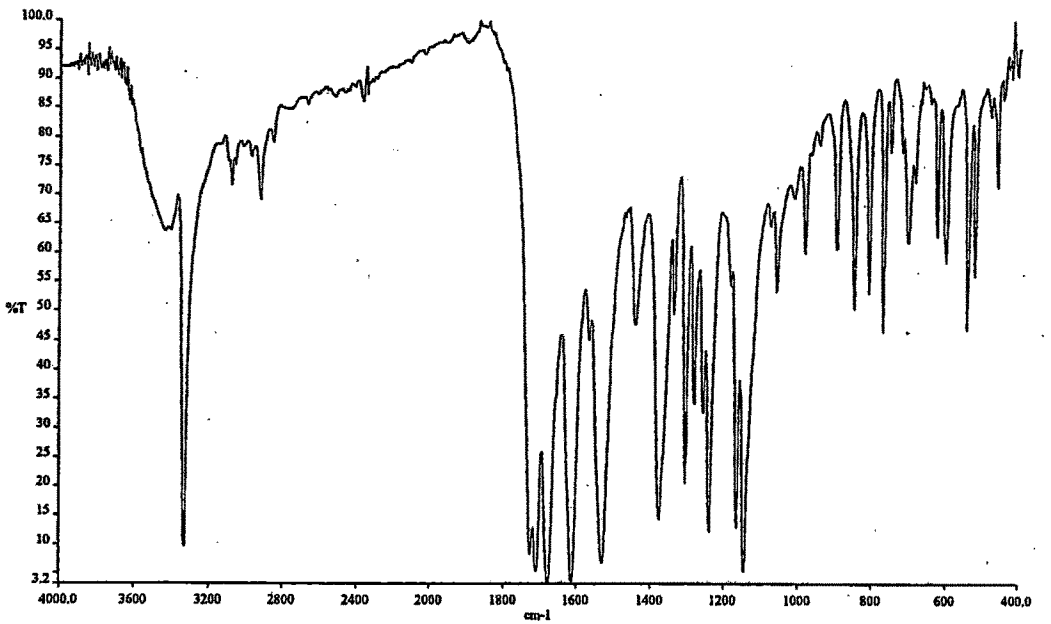
% Yield : 68

%C,H,N analysis (calculated) : C: 50.01 H: 2.97 N: 4.17

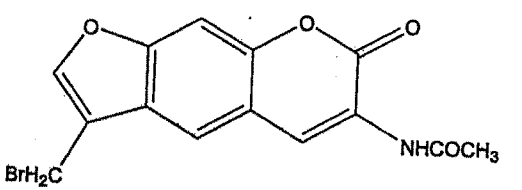
%C,H,N analysis (found) : C: 49.91 H: 2.91 N: 4.28

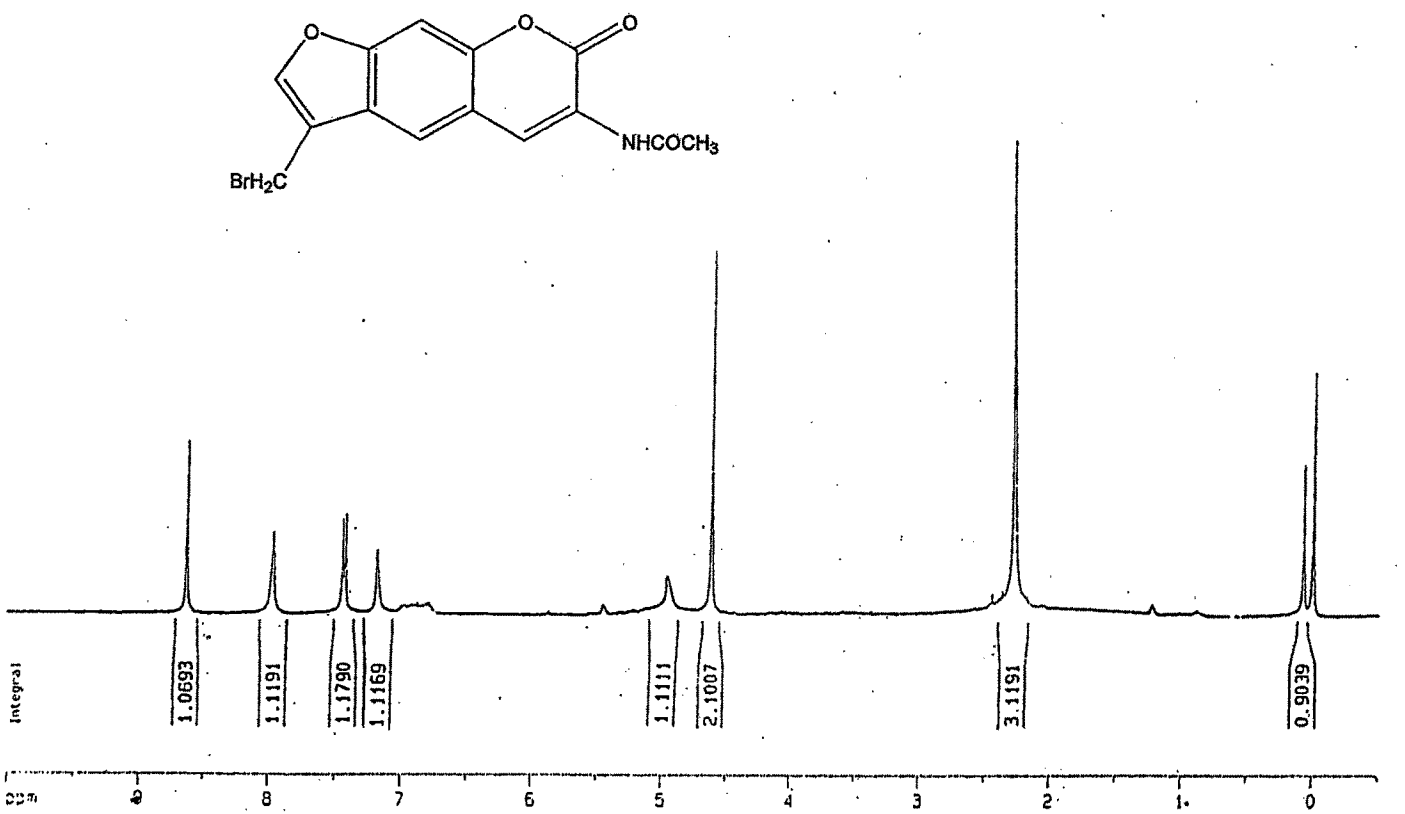
IR data (KBr) cm^{-1}: 3328, 3068, 2998, 2961, 1741, 1708, 1638, 1128, 738.

PMR data (400MHz, $CDCl_3$): δ 2.39(s, 3H, -NHCOC<u>H</u>$_3$), 4.64(s, 2H, -C<u>H</u>$_2$Br), 5.00(br s, 1H, -N<u>H</u>CO), 7.29(s, 1H, C-4), 7.49(s, 1H, C-9), 7.98(s, 1H, C-5), 8.70(s, 1H, C-7).



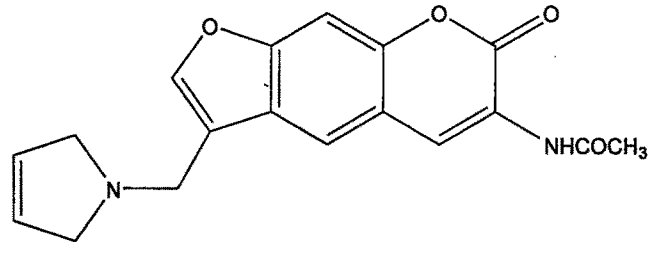
[Figure-6]: 3-Acetamido-6-(bromomethyl)-2H-1-benzopyran-2-one, 66





[Figure-7]: 3-Acetamido-6-(bromomethyl)-2H-1-benzopyran-2-one, 66

3-Acetamido-6-(2,5-dihydropyrrolin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **67:**



State : yellow amorphous solid

Molecular Formula : $C_{18}H_{16}N_2O_4$

Melting Point : 258 - 260 °C

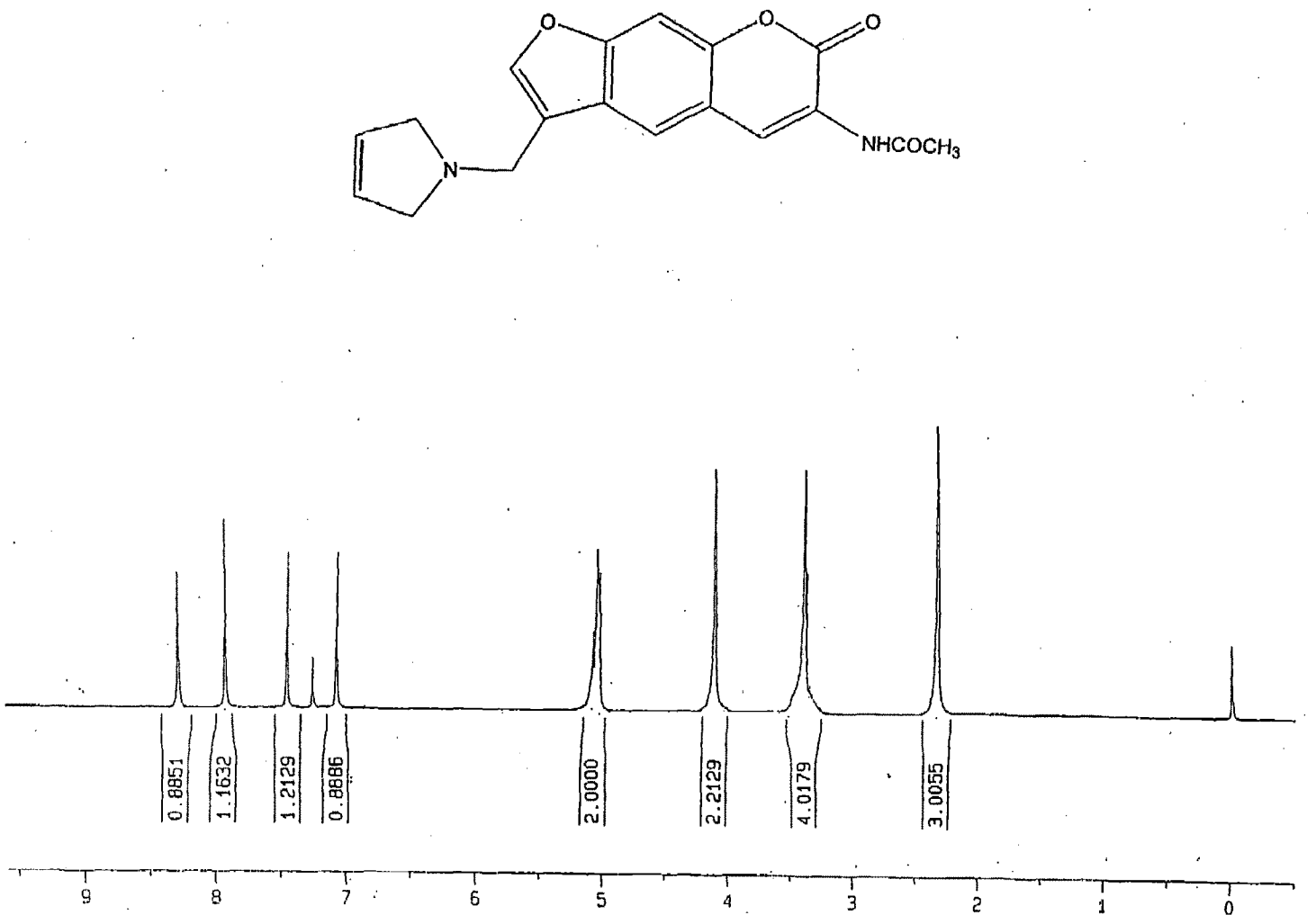
% Yield : 51

%C,H,N analysis (calculated) : C: 66.67 H: 4.94 N: 8.64

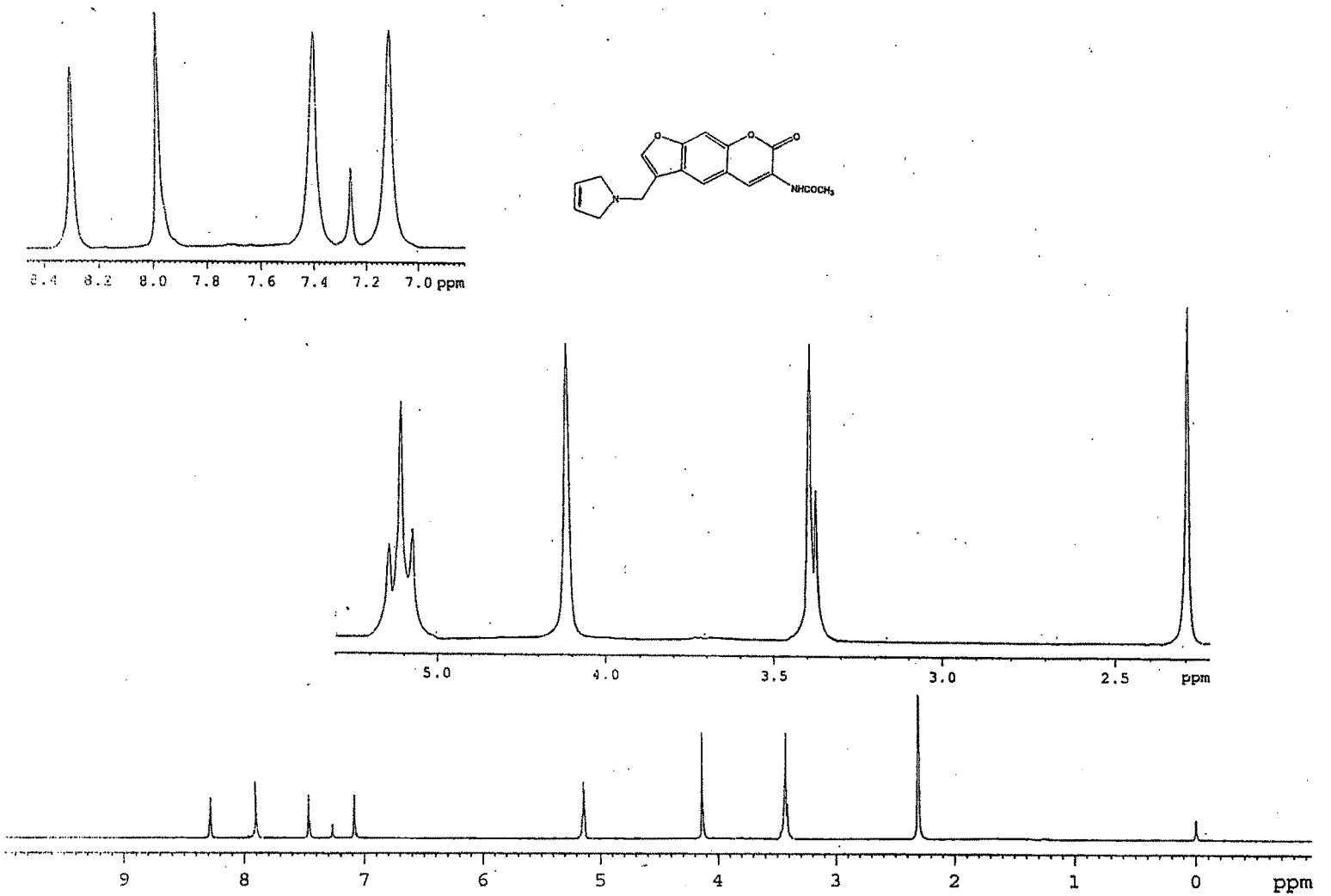
%C,H,N analysis (found) : C: 66.61 H: 4.98 N: 8.91

IR data (KBr) cm^{-1} : 3348, 3008, 2993, 2968, 1748, 1710, 1641, 1131.

PMR data (400MHz, $CDCl_3$) : δ 2.33(s, 3H, -NHCOC<u>H</u>$_3$), 3.41(m, 4H, -NC<u>H</u>$_2$), 4.21(s, 2H, -NC<u>H</u>$_2$Ar), 5.10(m, 2H, alkene protons), 7.10(s, 1H, C-4), 7.25(br s, 1H, -N<u>H</u>CO), 7.47(s, 1H, C-9), 7.93(s, 1H, C-5), 7.83(s, 1H, C-7).

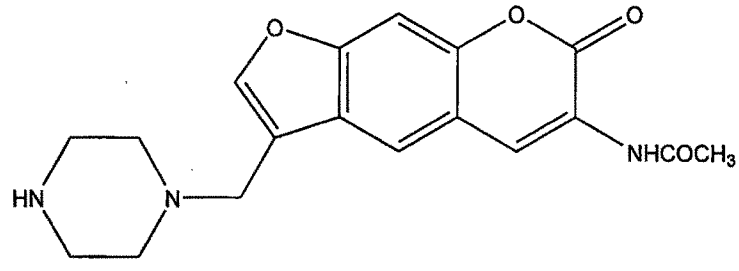


[Figure-8]: 3-Acetamido-6-(2,5-dihydropyrrolin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 67



[Figure-8a]: 3-Acetamido-6-(2,5-dihydropyrrolin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 67

3-Acetamido-6-(piperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **68:**



State : brownish yellow amorphous solid

Molecular Formula : $C_{18}H_{19}N_3O_4$

Melting Point : 271 - 273 °C

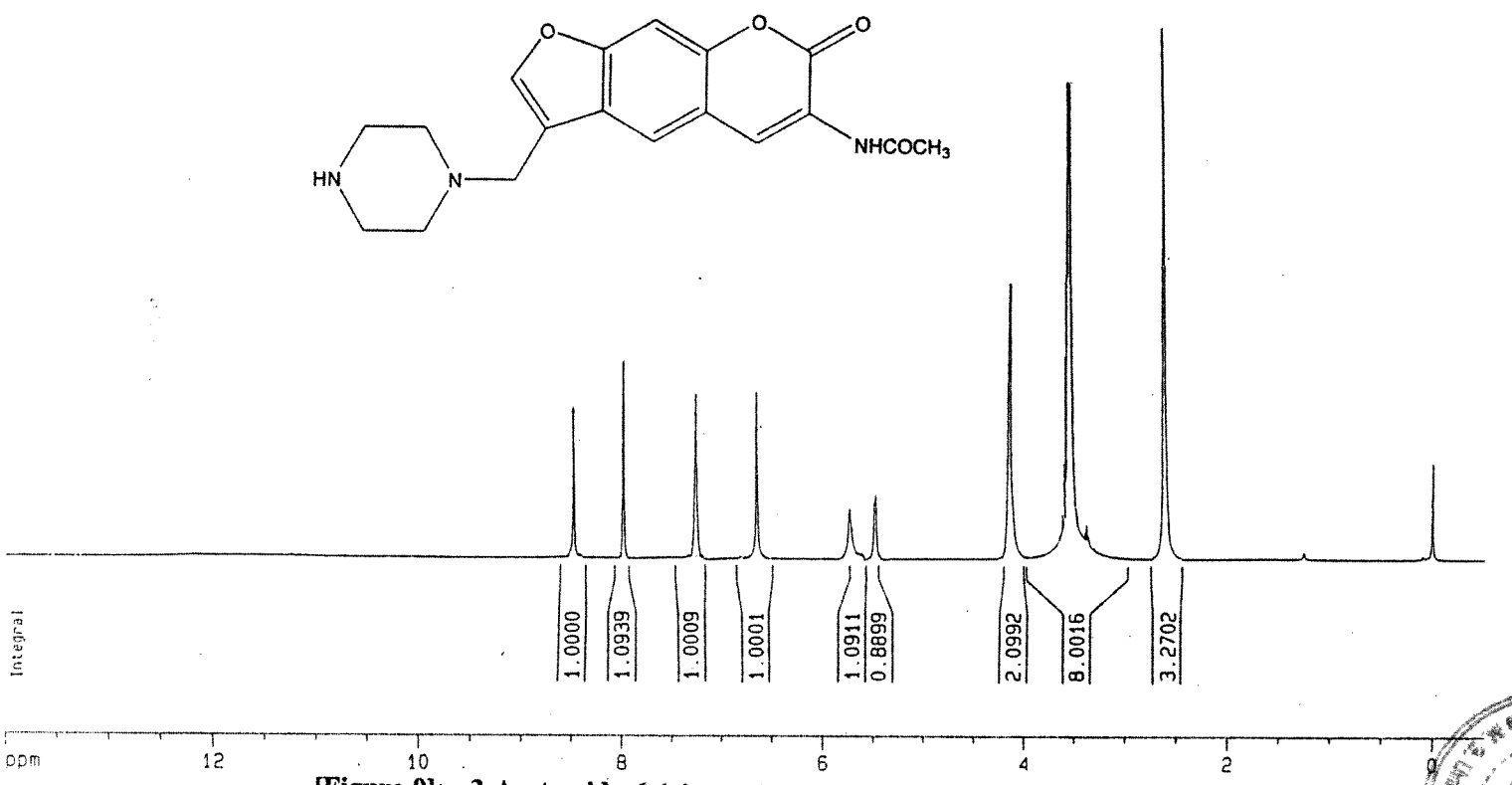
% Yield : 48

%C,H,N analysis (calculated) : C: 63.34 H: 5.57 N: 12.32

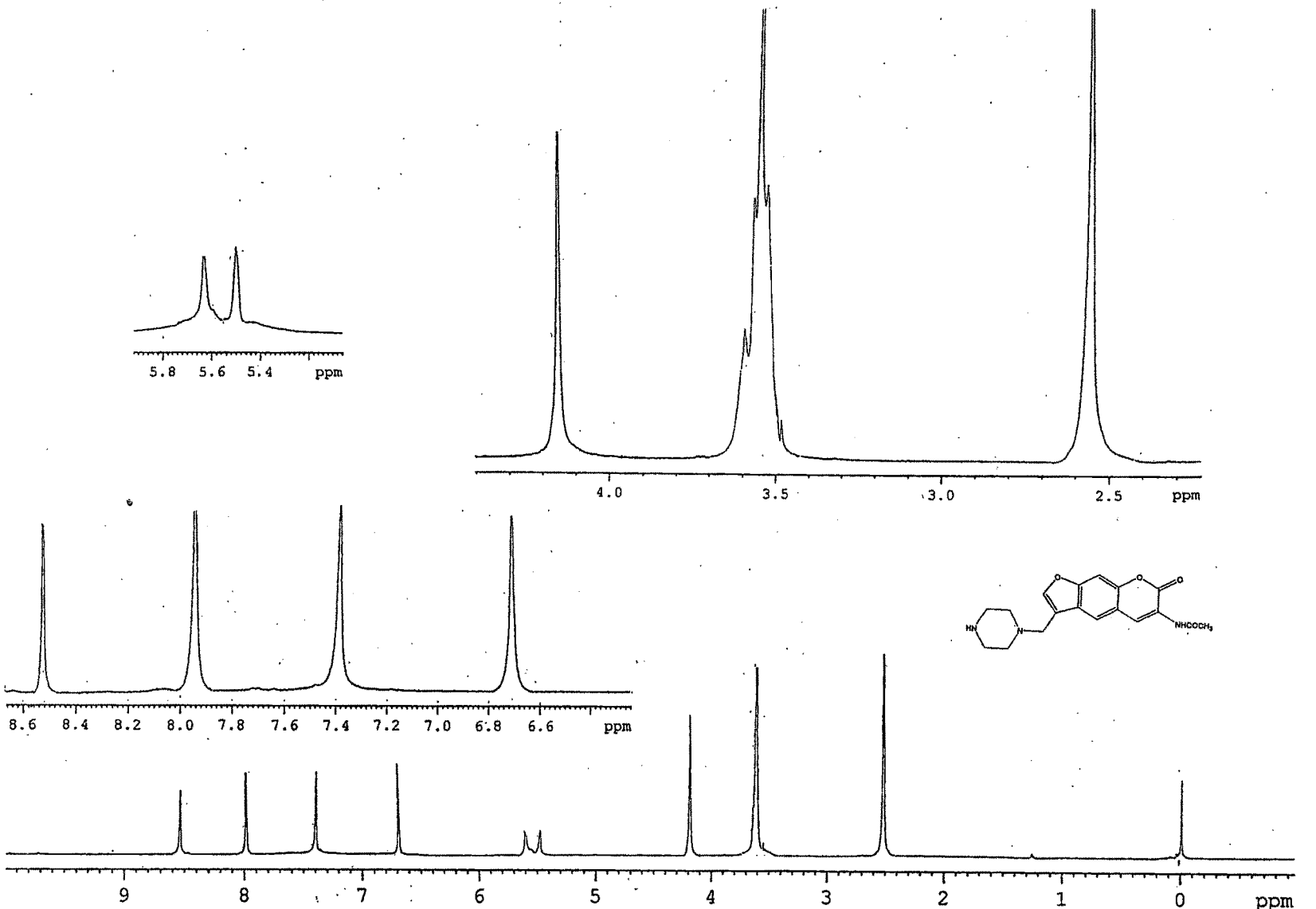
%C,H,N analysis (found) : C: 63.19 H: 5.21 N: 12.51

IR data (KBr) cm^{-1}: 3389, 3361, 3078, 2982, 2940, 1751, 1701, 1658, 1128, 730.

PMR data (400MHz, $CDCl_3$) : δ 2.58(s, 3H, -NHCOC$\underline{H}_3$), 3.45-3.65(m, 8H, ring C$\underline{H}_2$), 4.16(s, 2H, -NC$\underline{H}_2$Ar), 5.52 and 5.65(two s, 2H, -N$\underline{H}$ and -N$\underline{H}$CO), 6.72(s, 1H, C-4), 7.40(s, 1H, C-9), 7.96(s, 1H, C-5), 8.53(s, 1H, C-7).

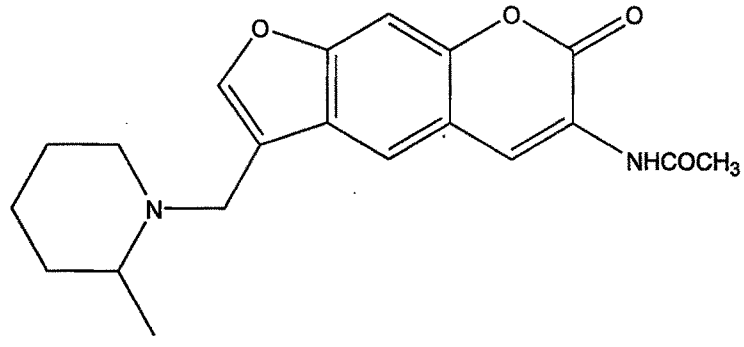


[Figure-9]: 3-Acetamido-6-(piperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 68



[Figure-9a]: 3-Acetamido-6-(piperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 68

3-Acetamido-6-(2-methylpiperidin-1-yl-methyl)-2H-furo[3,2-g]-1-benzopyran-2-one, **69:**



State : yellow amorphous solid

Molecular Formula : $C_{20}H_{22}N_2O_4$

Melting Point : 265 - 267 °C

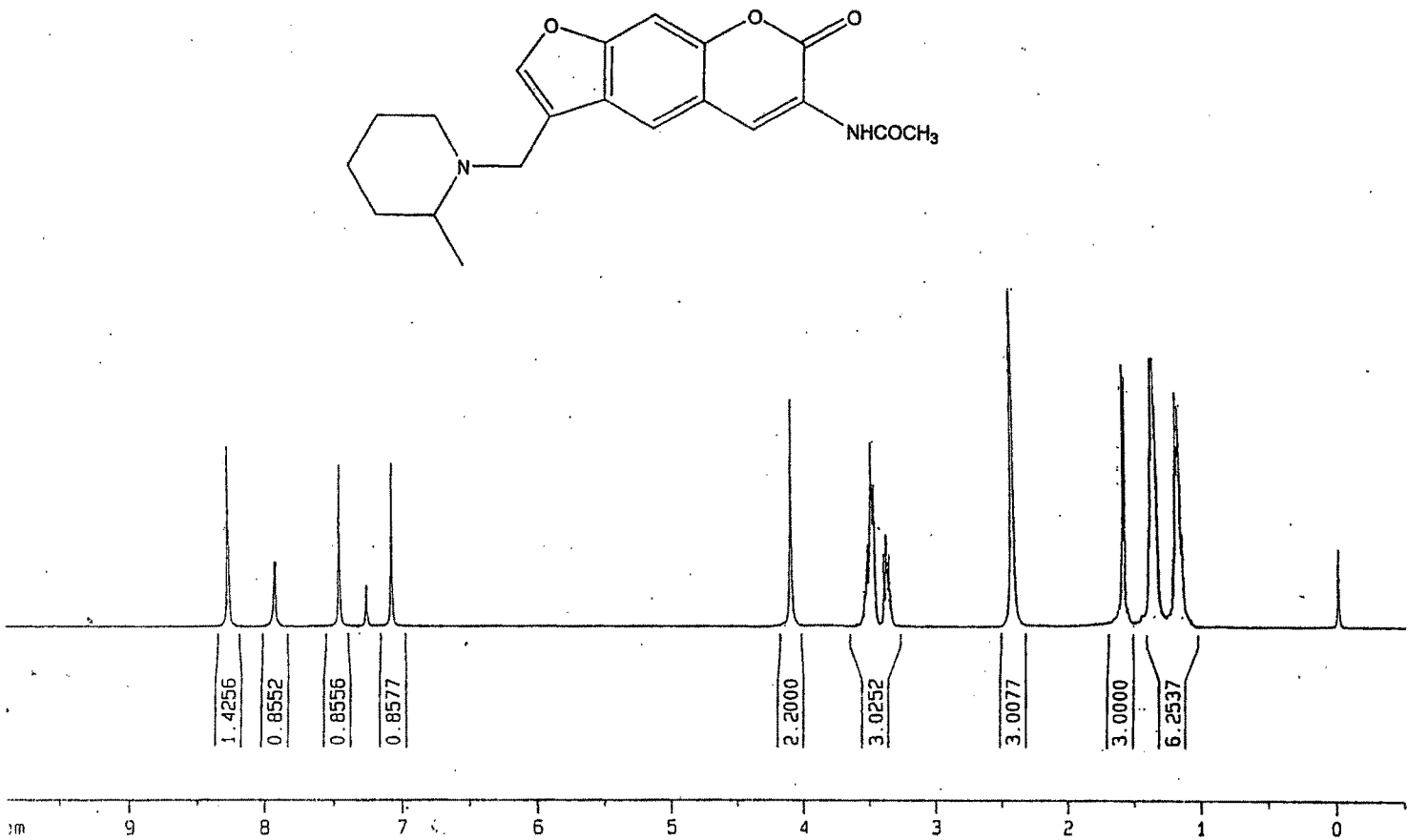
% Yield : 51

%C,H,N analysis (calculated) : C: 67.79 H: 6.21 N: 7.91

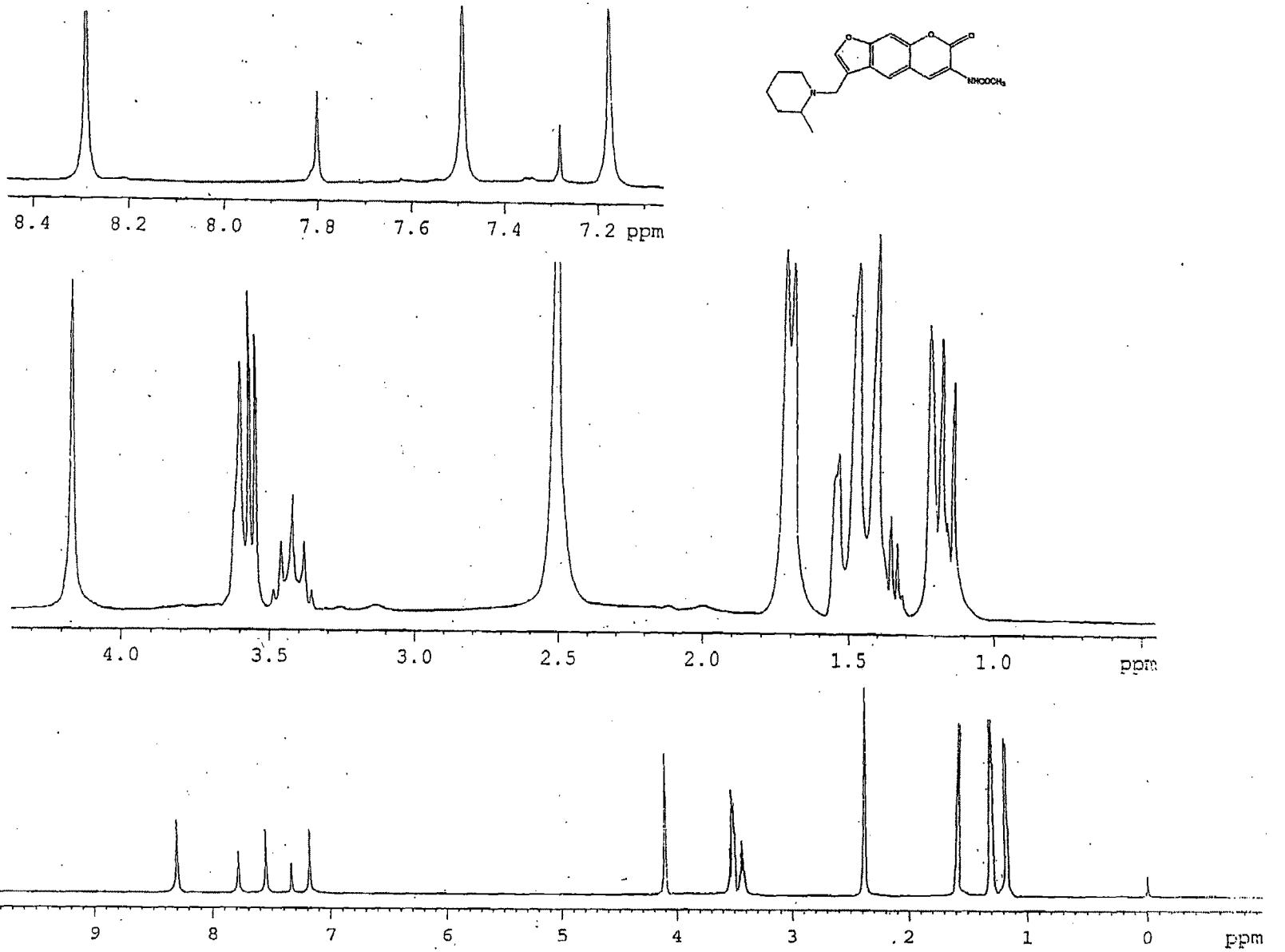
%C,H,N analysis (found) : C: 67.58 H: 6.11 N: 8.01

IR data (KBr) cm^{-1} : 3310, 3008, 2991, 2968, 1758, 1720, 1651, 1140, 728.

PMR data (400MHz, $CDCl_3$) : δ 1.11-1.28(m, 2H, ring –CH_2), 1.57-1.30(m, 4H, ring -$C\underline{H}_2$), 1.70(d, J=8.1Hz, 3H, ring -$C\underline{H}_3$), 2.50(s, 3H, -NHCO$C\underline{H}_3$), 3.35-3.50(m, 1H, C$\underline{H}$N), 3.52-3.65(m, 2H, ring -$C\underline{H}_2$N), 4.17(s, 2H, -N$C\underline{H}_2$Ar), 7.18(s, 1H, C-4), 7.28(br s, 1H, -N$\underline{H}$CO), 7.49(s, 1H, C-9), 7.80(s, 1H, C-5), 8.29(s, 1H, C-7).

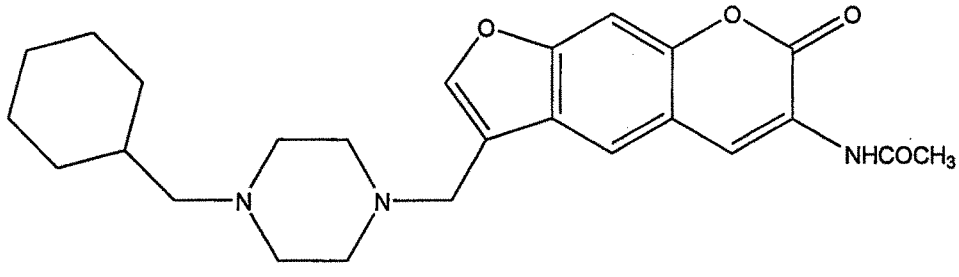


[Figure-10]: 3-Acetamido-6-(2-methylpiperidin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 69



[Figure-10a]: 3-Acetamido-6-(2-methylpiperidin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 69

3-Acetamido-6-(4-cyclohexylmethylpiperazin-1-yl-methyl)-2H-furo[3,2-g]-1-benzopyran-2-one, **70:**



State : yellow amorphous solid

Molecular Formula : $C_{25}H_{31}N_3O_4$

Melting Point : >280 °C

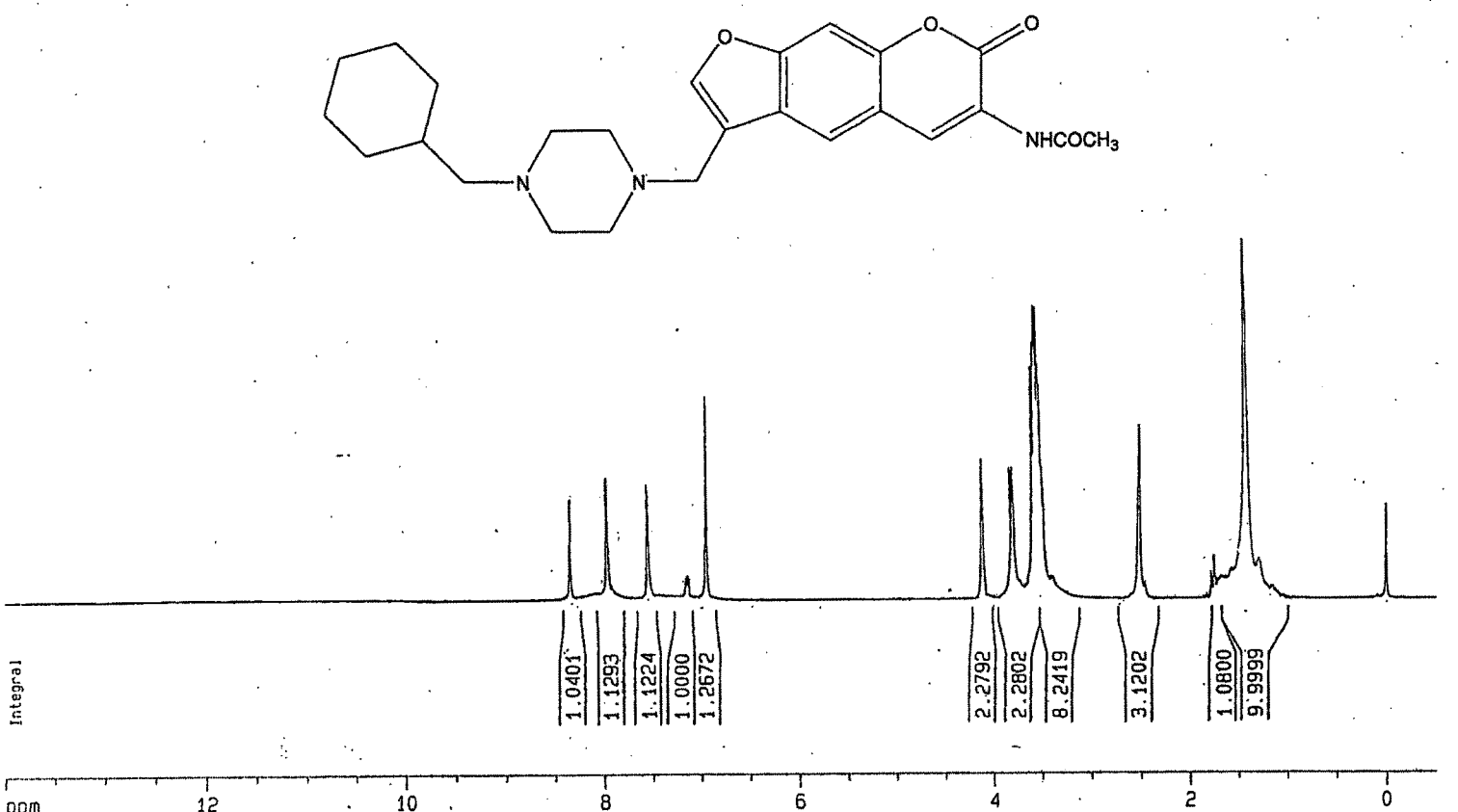
% Yield : 48

%C,H,N analysis (calculated) : C: 68.65 H: 7.09 N: 9.61

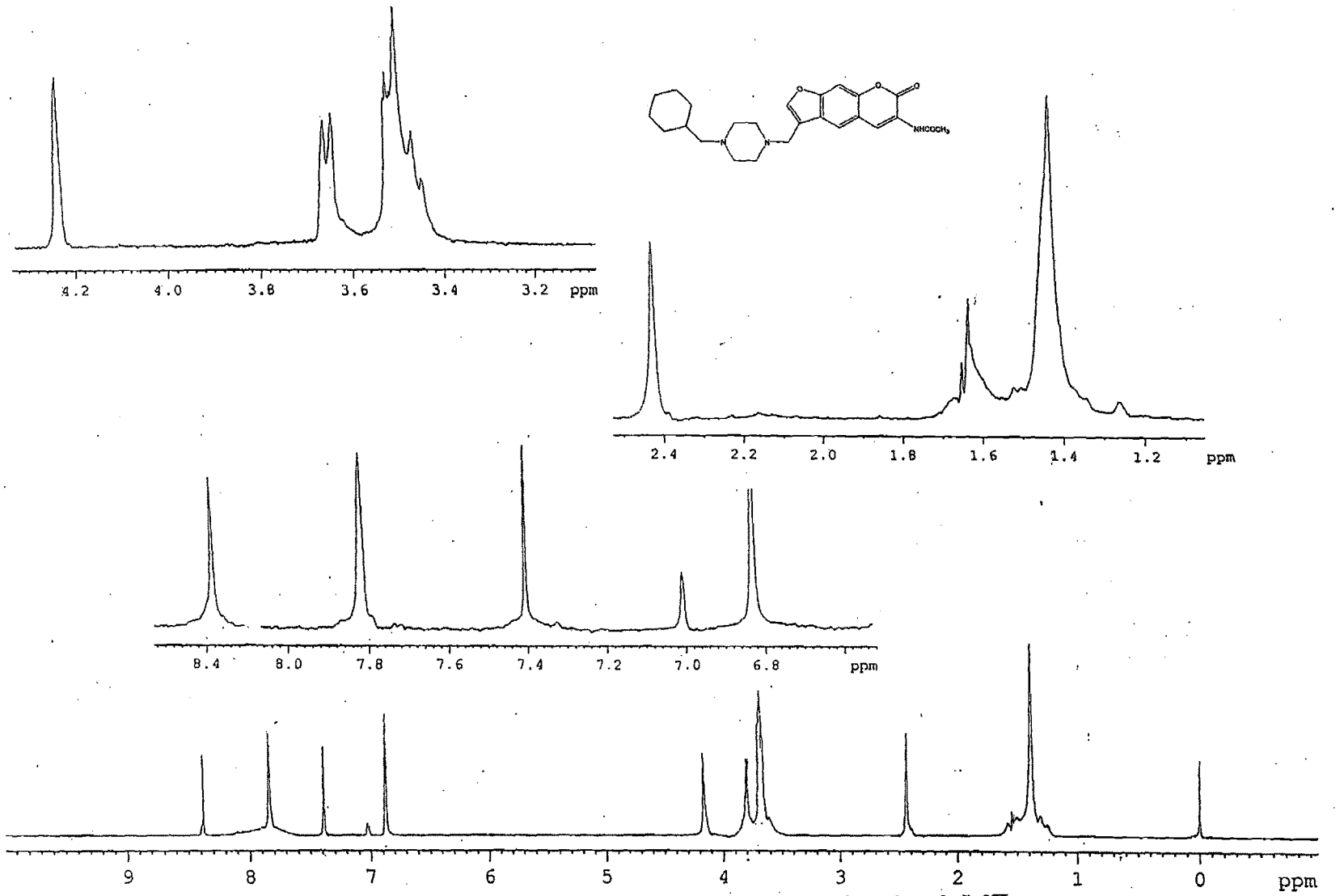
%C,H,N analysis (found) : C: 68.50 H: 8.01 N: 9.81

IR data (KBr) cm^{-1} : 3328, 3050, 2980, 1730, 1710, 1630, 1110, 728.

PMR data (400MHz, $CDCl_3$) : δ 1.38-1.51(m, 10H, 5× $C\underline{H}_2$ of cyclohexyl ring), 1.61(m, 1H,cyclohexyl CH proton), 2.43(s, 3H, -NHCOC$\underline{H}_3$), 3.56-3.42(m, 8H, 4 × $C\underline{H}_2$ of piperazine ring), 3.62-3.68(d, J=8 Hz, 2H, -NC$\underline{H}_2$), 4.24(s, 2H, -NC$\underline{H}_2$Ar), 6.84 (s, 1H, C-4), 7.03-7.01(br s, 1H, -CON$\underline{H}$), 7.40(s, 1H, C-9), 7.83(s, 1H, C-5), 8.40(s, 1H, C-7).

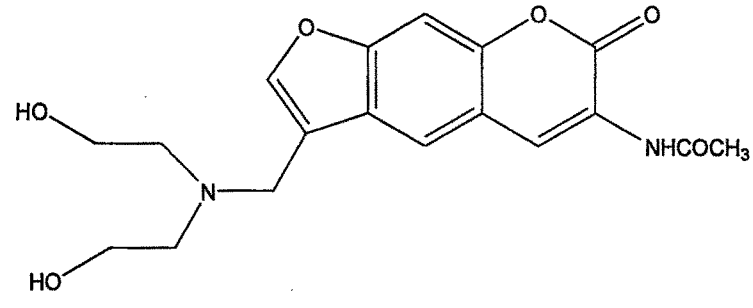


[Figure-11]: 3-Acetamido-6-(4-cyclohexylmethylpiperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 70



[Figure-11a]: 3-Acetamido-6-(4-cyclohexylmethylpiperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 70

3-Acetamido-6-(N,N-di(2-hydroxyethyl)aminomethyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **71:**



State : brownish yellow amorphous solid,

Molecular Formula : $C_{18}H_{20}O_6N_2$

Melting Point : 269 - 271°

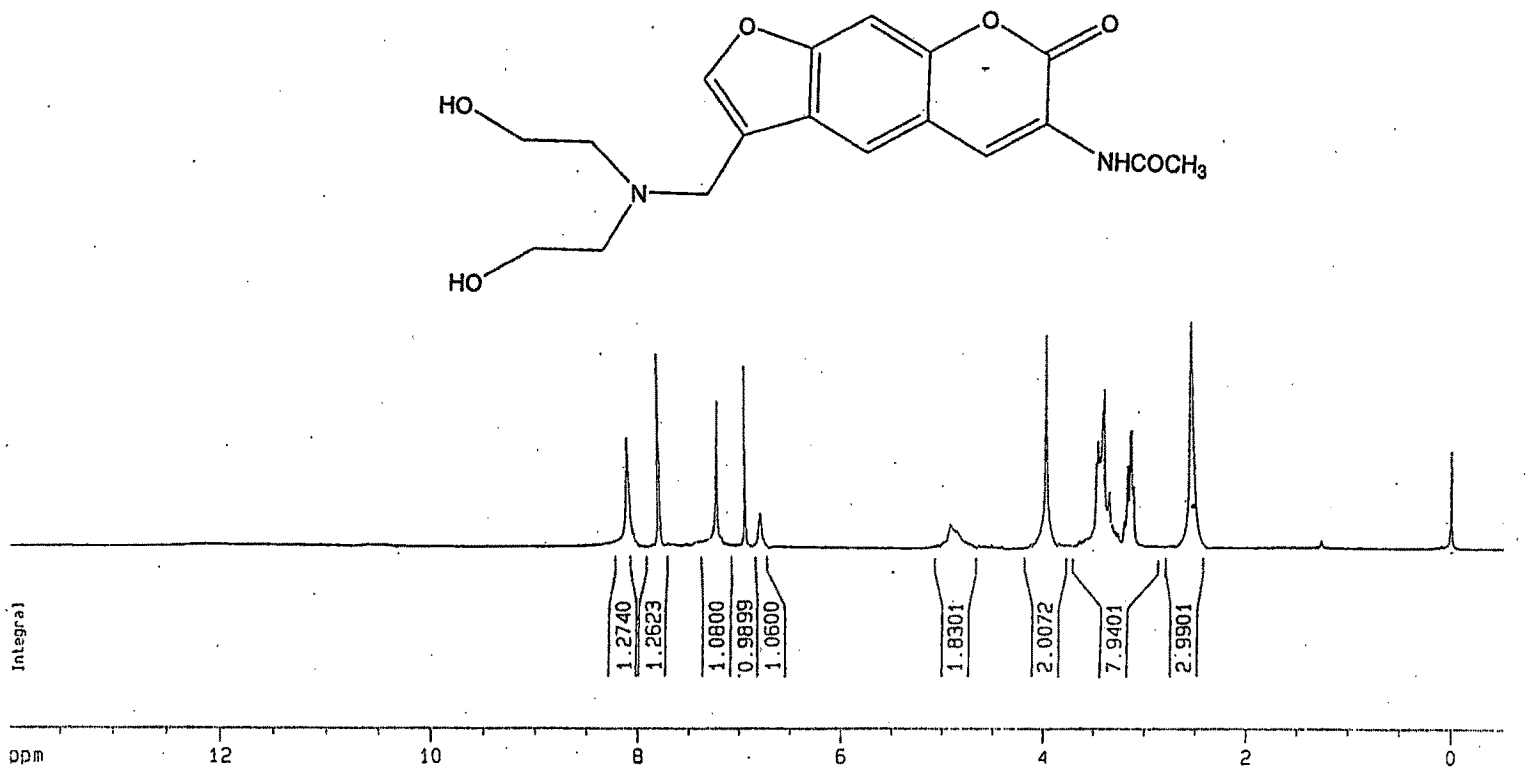
% Yield : 51

%C,H,N analysis (calculated) : C: 60.00 H: 5.55 N: 7.80

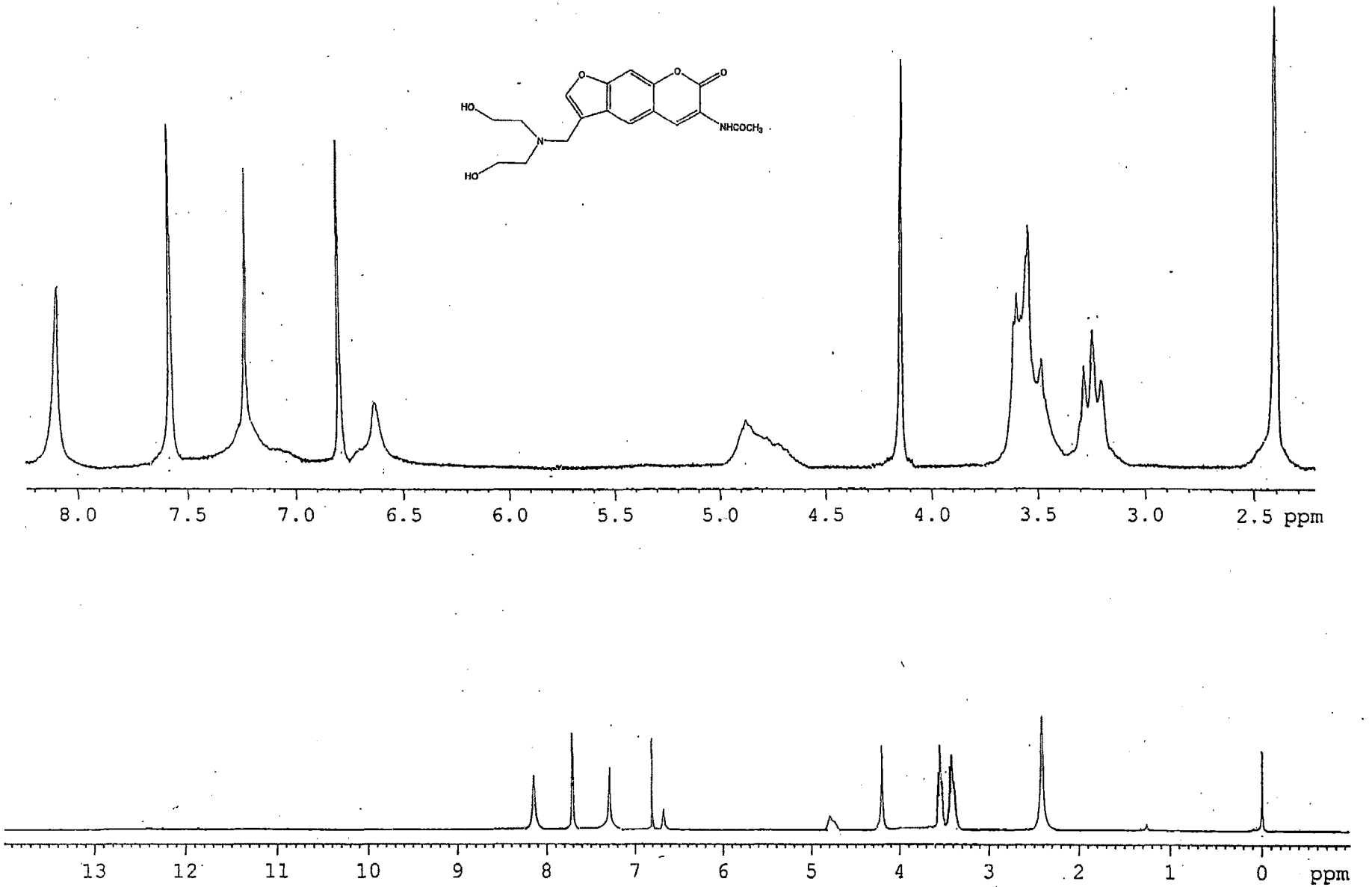
%C,H,N analysis (found) : C: 60.10 H: 5.41 N: 7.91

IR data (KBr) cm^{-1} : 3391, 3339, 2991, 2939, 1729, 1700, 1629, 1131.

PMR data (400MHz, $CDCl_3$) : δ 2.40(s, 3H, -NHCOC<u>H</u>$_3$), 3.14-3.32(t, J=14 Hz, 4H, 2x-NC<u>H</u>$_2$), 3.41-3.70(br signal with t, J=14 Hz, 4H, 2x-OC<u>H</u>$_2$), 4.15(s, 2H, -NC<u>H</u>$_2$Ar), 4.60-5.00(br signal, 2H, hydroxyl protons), 6.60(br s, 1H, -CONH), 6.80(s, 1H, C-4), 7.23(s, 1H, C-9), 7.59(s, 1H, C-5), 8.10(s, 1H, C-7).

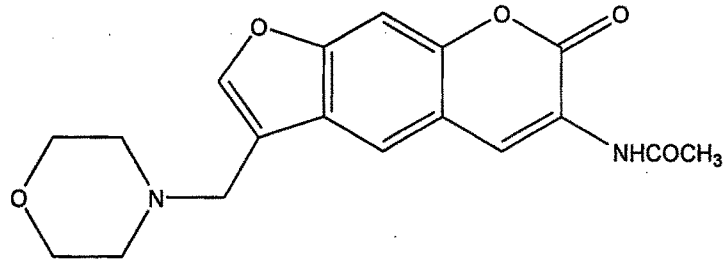


[Figure-12]: 3-Acetamido-6-(N,N-di(2-hydroxyethyl)aminomethyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 71



[Figure-12a]: 3-Acetamido-6-(N,N-di(2-hydroxyethyl)aminomethyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 71

3-Acetamido-6-(morpholin-4-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **72:**



State : pale yellow amorphous solid

Molecular Formula : $C_{18}H_{18}O_5N_2$

Melting Point : 280 - 281°C

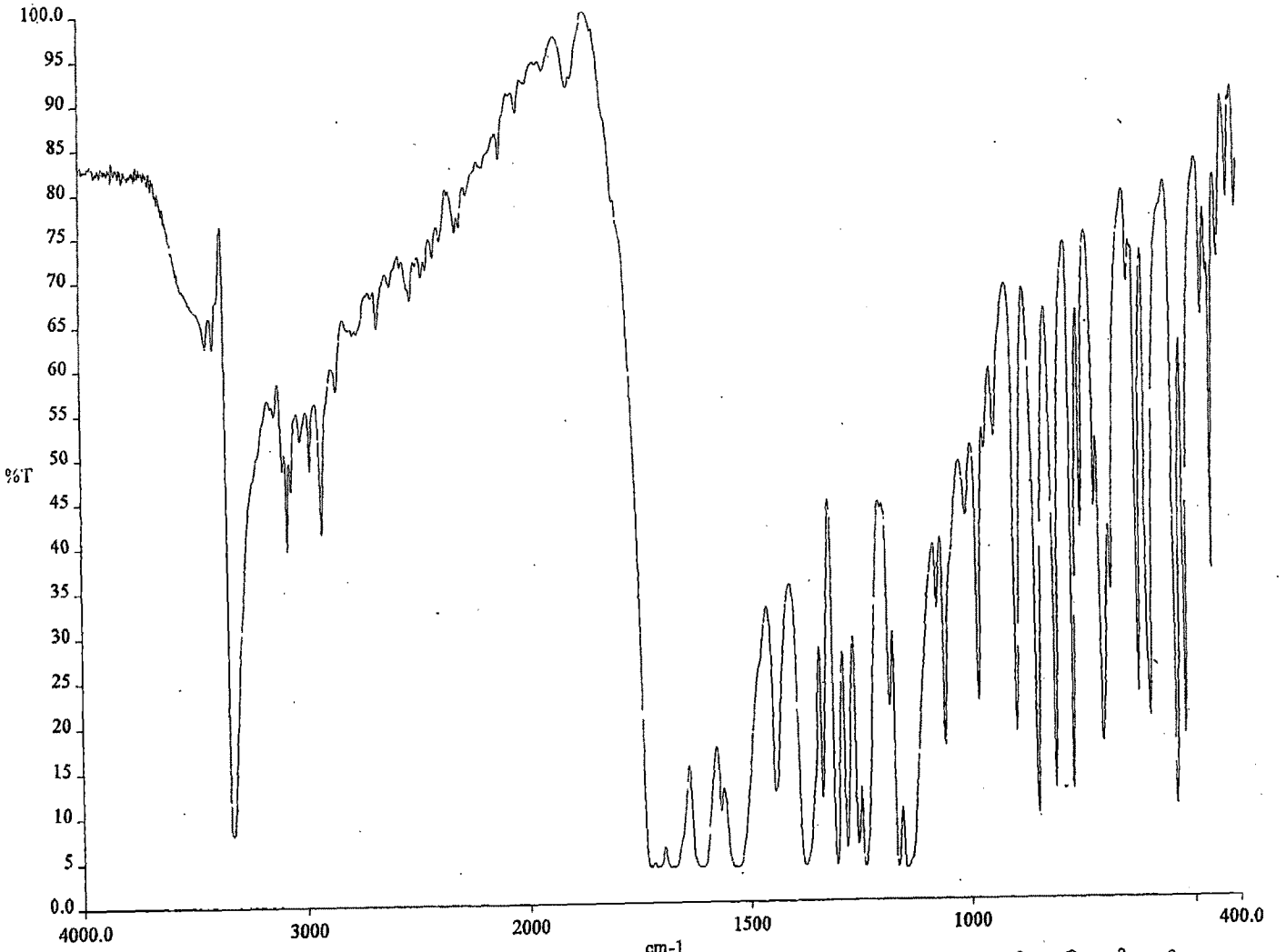
% Yield : 79

%C,H,N analysis (calculated) : C: 63.15 H: 5.26 N: 8.19

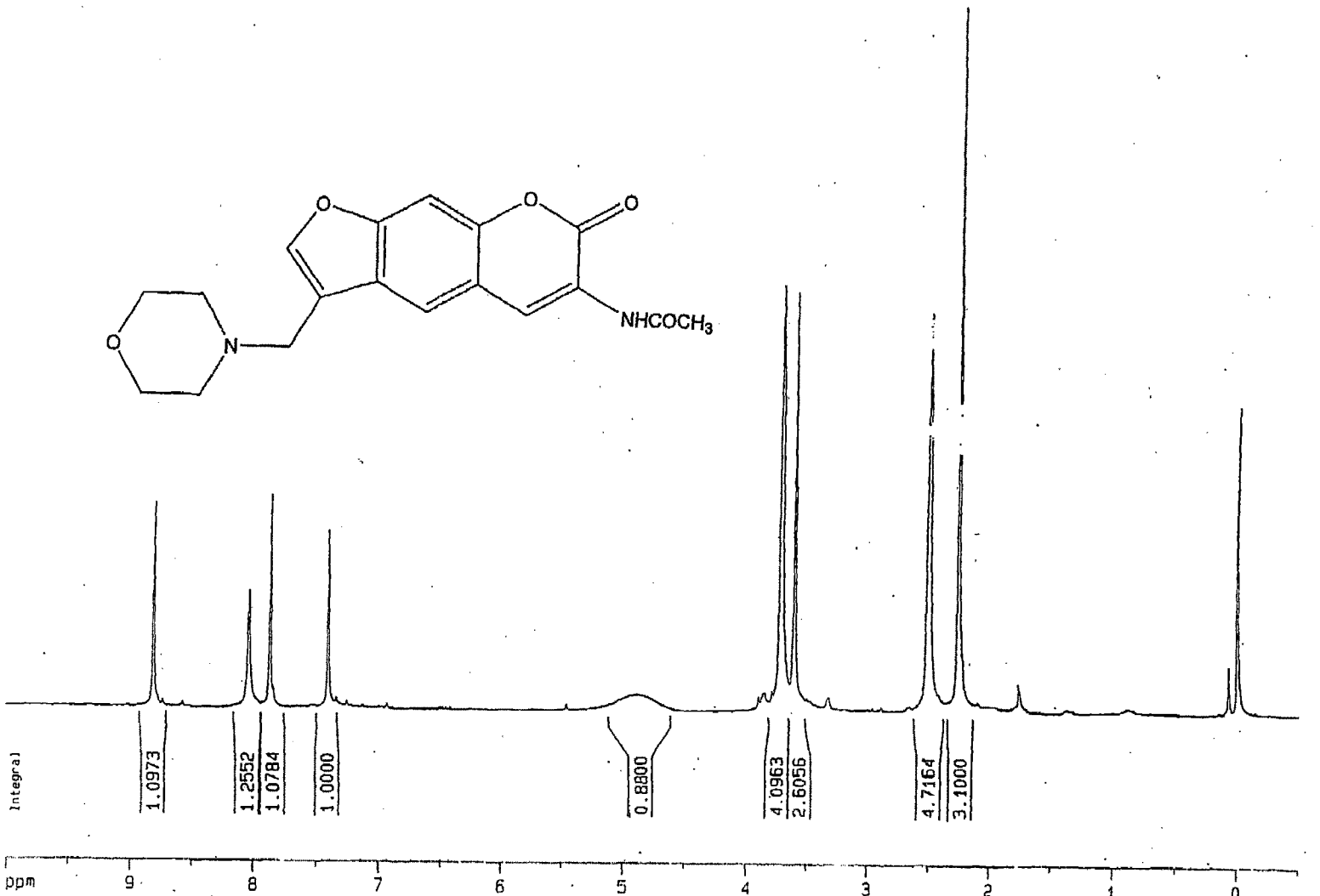
%C,H,N analysis (found) : C: 63.01 H: 5.18 N: 8.39

IR data (KBr) cm^{-1} : 3321, 3071, 2983, 2940, 1718, 1701, 1629, 1118.

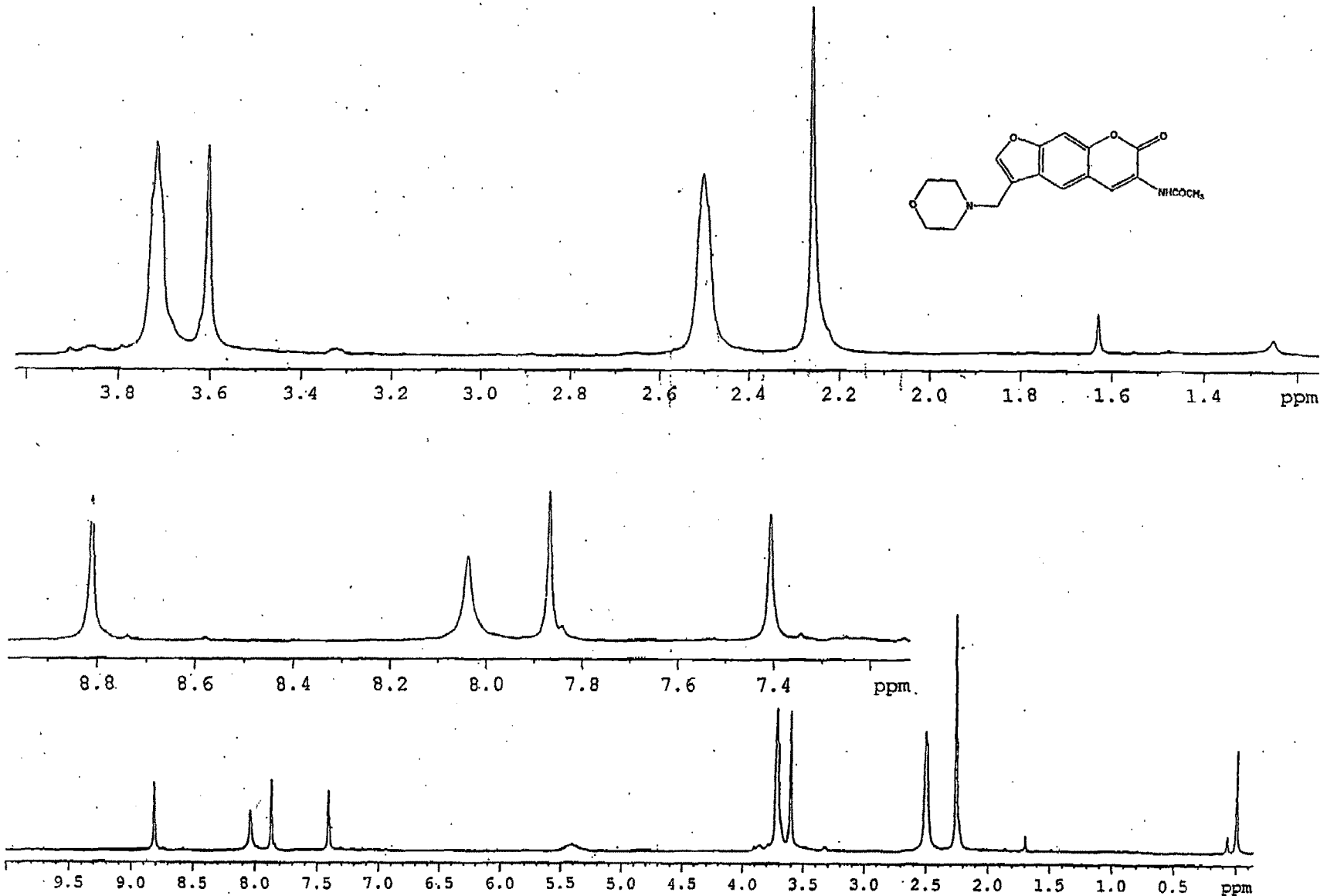
PMR data (400MHz, $CDCl_3$) : δ 2.25(s, 3H, -NHCOC<u>H</u>$_3$), 2.50(br m, 4H, ring -2xNC<u>H</u>$_2$), 3.58-3.71(br m, 4H, ring 2x-OC<u>H</u>$_2$), 3.72-3.90(s, 2H, -NC<u>H</u>$_2$Ar), 4.46-5.30(br s, 1H, -CONH), 7.40(s, 1H, C-4), 7.88(s, 1H, C-9), 8.03(s, 1H, C-5), 8.82(s, 1H, C-7).



[Figure-13]: 3-Acetamido-6-(morpholin-4-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 72

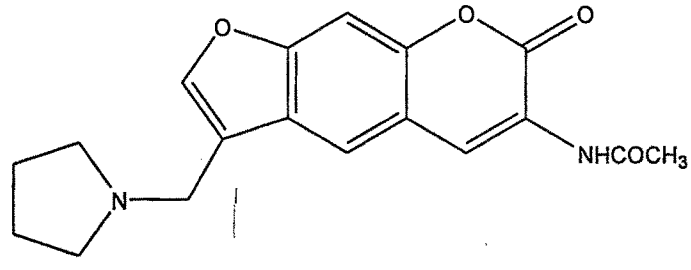


[Figure-14]: 3-Acetamido-6-(morpholin-4-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 72



[Figure-14a]: 3-Acetamido-6-(morpholin-4-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 72

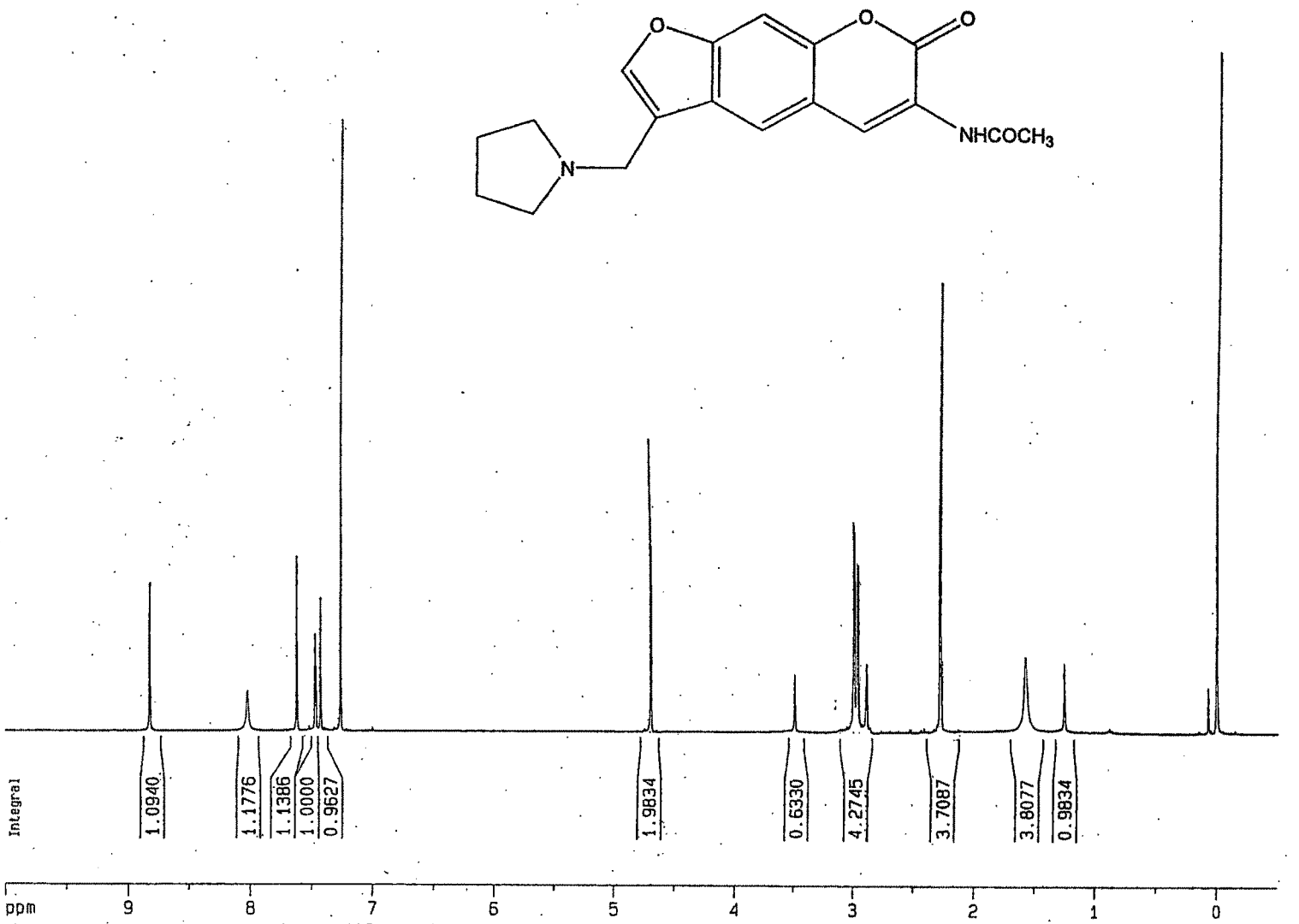
3-Acetamido-6-(pyrrolidin-1-yl-methyl)-2H-furo[3,2-g]-1-benzopyran-2-one,**73:**



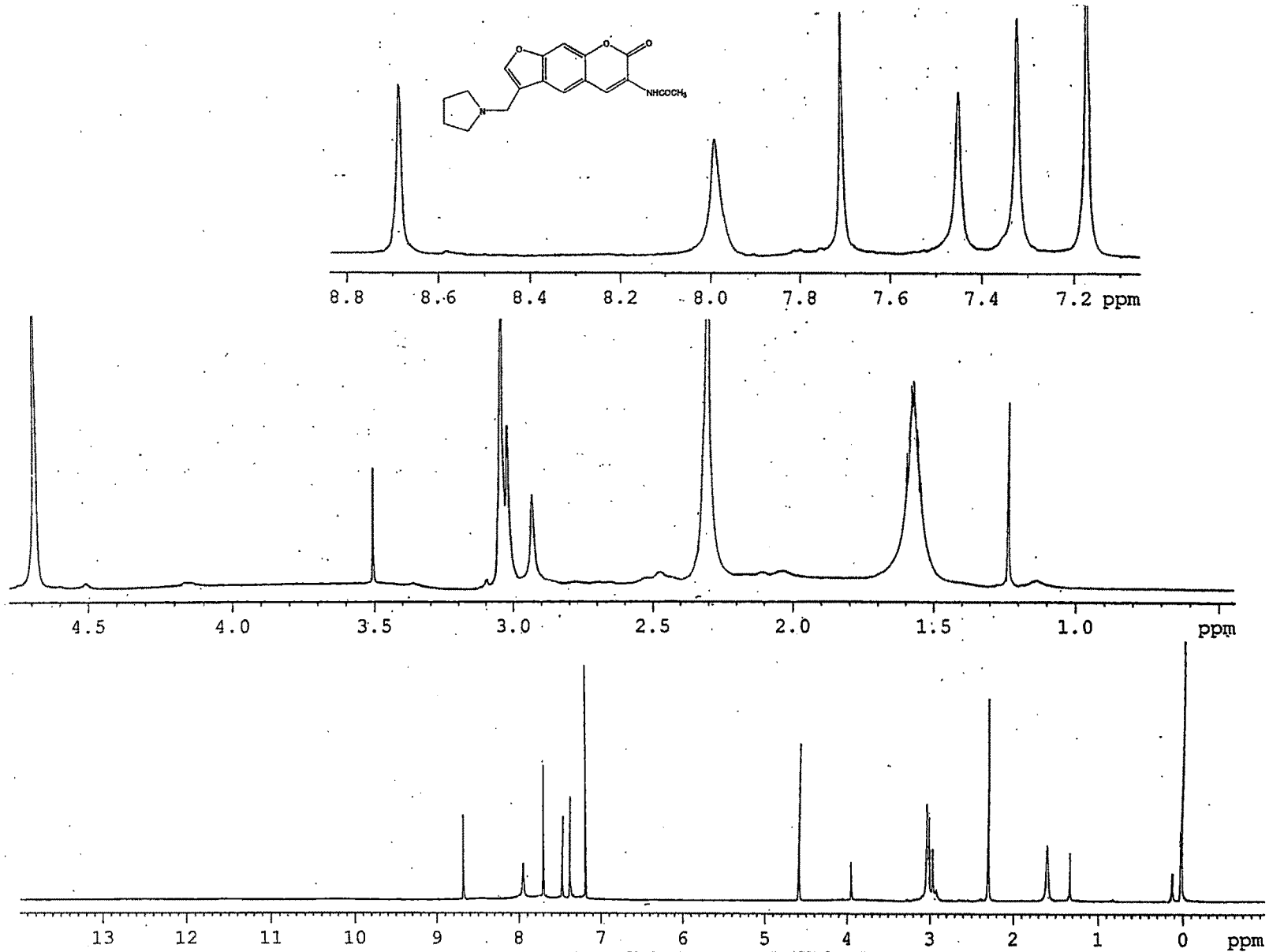
State :	yellow amorphous solid
Molecular Formula :	$C_{18}H_{18}N_2O_4$
Melting Point :	251 - 253 °C
% Yield :	58
%C,H,N analysis (calculated) :	C: 66.26 H: 5.52 N: 8.59
%C,H,N analysis (found) :	C: 66.00 H: 5.41 N: 8.78

IR data (KBr) cm^{-1} : 3298, 2999, 2949, 1757, 1701, 1668, 1098, 724.

PMR data (400MHz, $CDCl_3$) : δ 1.51-1.65 (m, 4H, ring H β to N, 2× -C<u>H</u>$_2$-), 2.30(s, 3H, -NHCOC<u>H</u>$_3$), 2.90-3.10(m, 4H, ring H α to N, 2× -C<u>H</u>$_2$), 4.68(s, 2H, -NC<u>H</u>$_2$Ar), 7.33(s, 1H, C-4), 7.45(s, 1H, C-9), 7.72(s, 1H, C-5), 8.00(br s, 1H, -CON<u>H</u>), 8.68(s, 1H C-7).

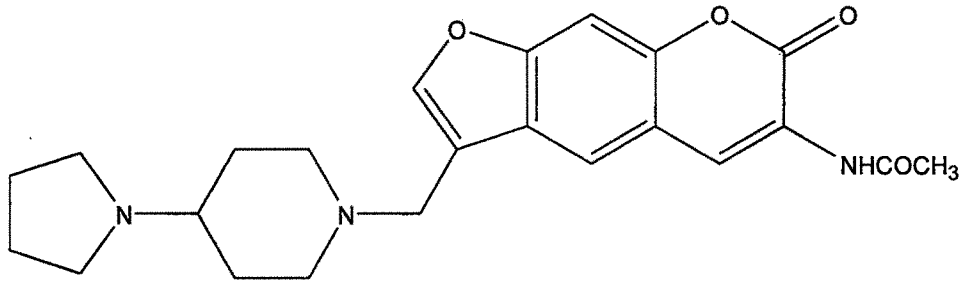


[Figure-15]: 3-Acetamido-6-(pyrrolidin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one,73



[Figure-15a]: 3-Acetamido-6-(pyrrolidin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one,73

3-Acetamido-6-(4-pyrrolidinylpiperidin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **74:**



State : orange yellow amorphous solid

Molecular Formula : $C_{23}H_{27}N_3O_4$

Melting Point : >280 °C

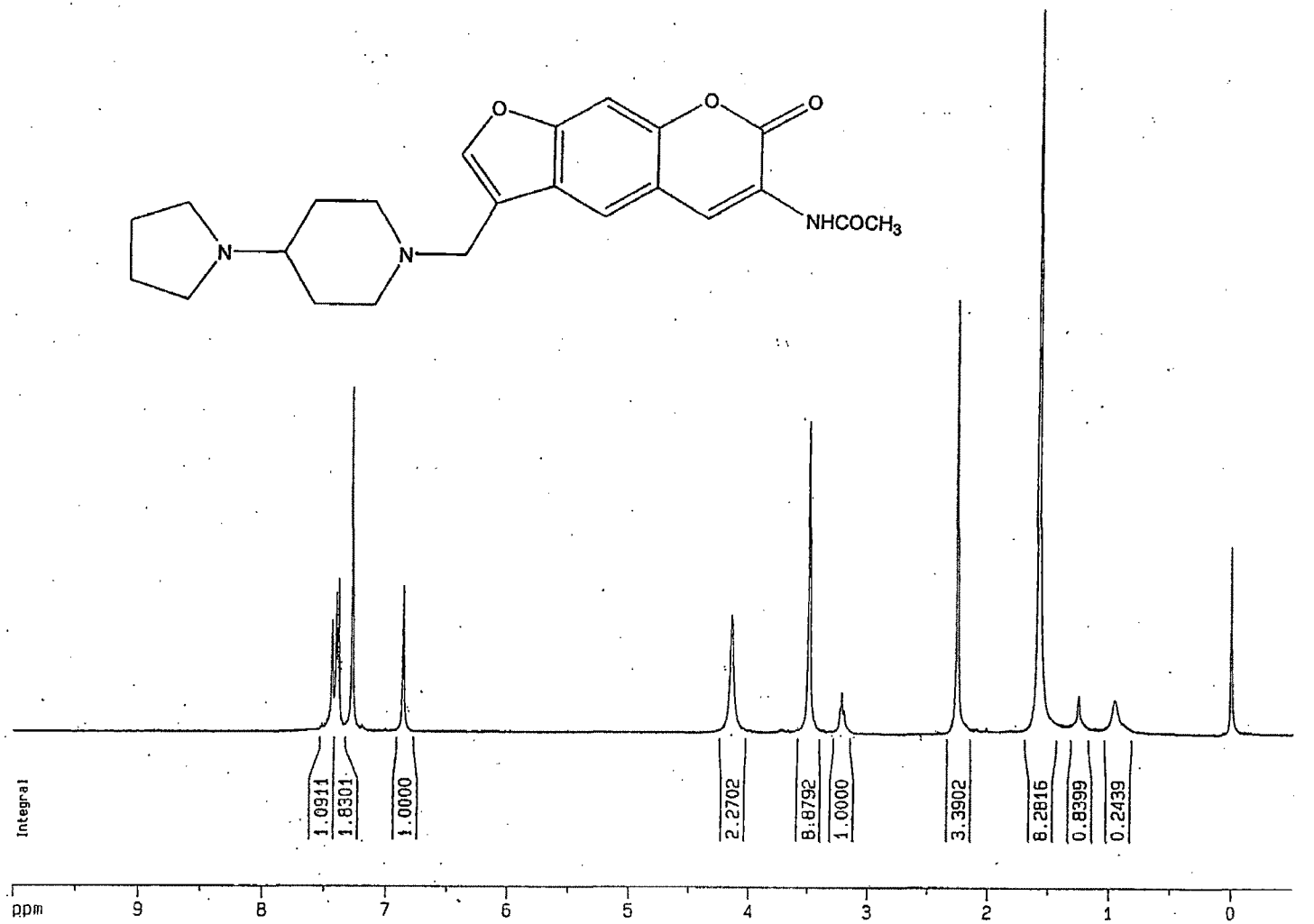
% Yield : 49

% C,H,N analysis (calculated) : C: 67.48 H: 6.60 N: 10.27

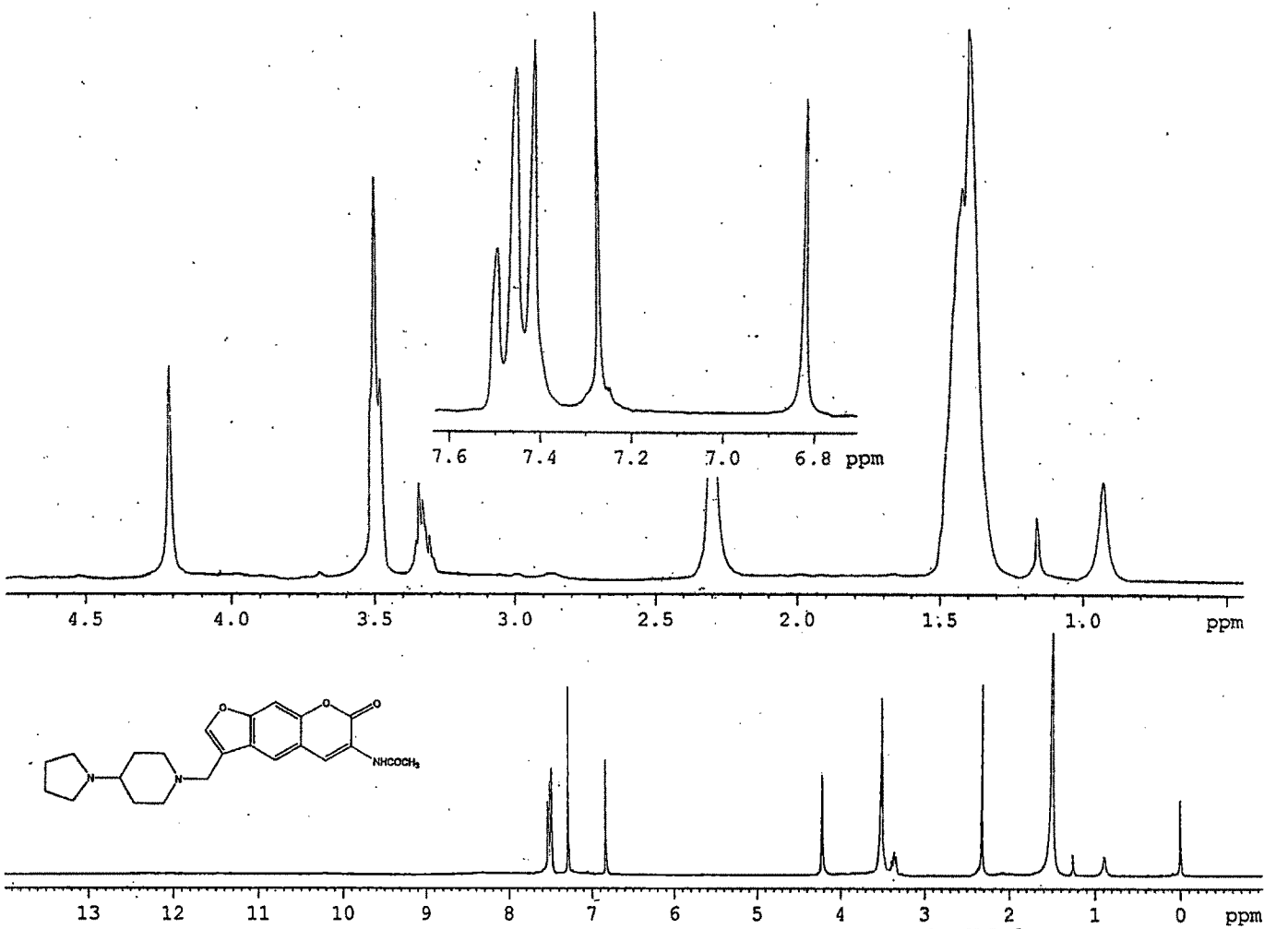
%C,H,N analysis (found) : C: 67.31 H: 6.41 N: 10.38

IR data (KBr) cm^{-1} : 3341, 3008, 2969, 1740, 1719, 1678, 1091, 731.

PMR data (400MHz, $CDCl_3$) : δ 1.30-1.50(m, 8H, ring C<u>H</u>$_2$ β to N), 2.30(s, 3H, -NHCOC<u>H</u>$_3$), 3.28-3.40(m, 1H, ring C<u>H</u>-N), 3.45-3.55(m, 9H, ring C<u>H</u>$_2$ α to N and -CON<u>H</u>), 4.21(s, 2H, -NC<u>H</u>$_2$Ar), 6.83(s, 1H, C-4), 7.42(s, 1H, C-9), 7.47-7.51(two s, 2H, C-5, C-7).

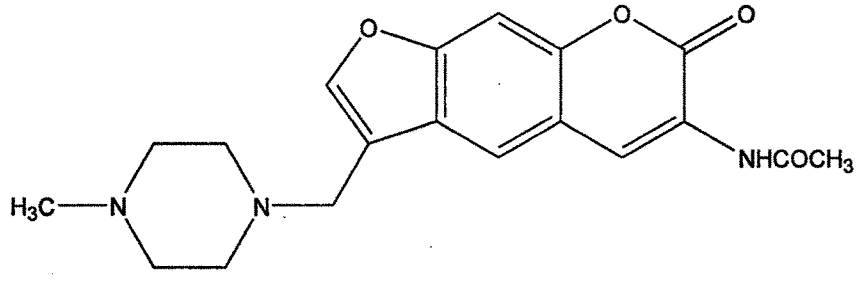


[Figure-16]: 3-Acetamido-6-(4-pyrrolidinylpiperidin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 74



[Figure-16a]: 3-Acetamido-6-(4-pyrrolidinylpiperidin-1-yl-methyl)-2H-furo[3,2-g]-1-benzopyran-2-one, 74

3-Acetamido-6-(4-methylpiperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **75:**



State : pale yellow amorphous solid,

Molecular Formula : $C_{19}H_{12}O_4N_3$

Melting Point : 268-269°C

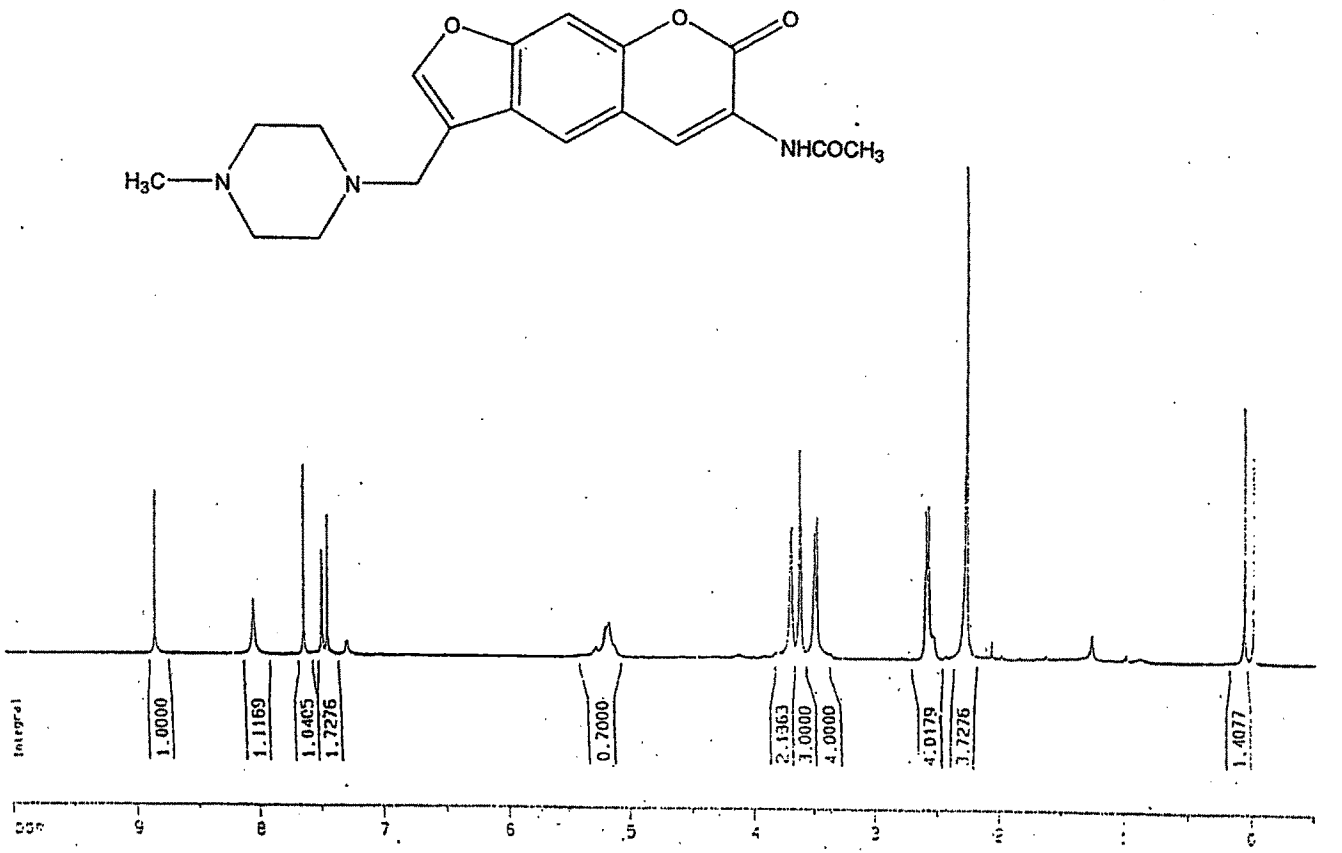
% Yield : 69

%C,H,N analysis (calculated) : C: 64.23 H: 5.91 N: 11.83

%C,H,N analysis (found) : C: 64.11 H: 5.88 N: 11.98

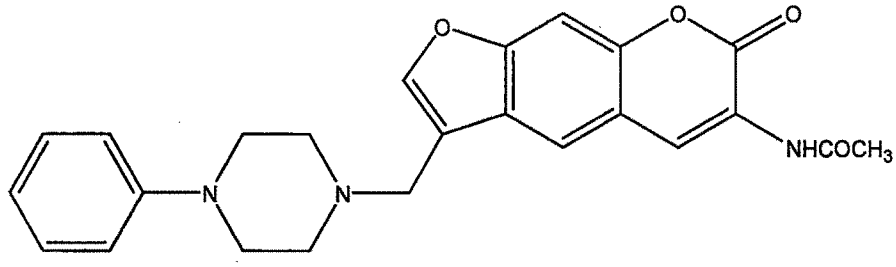
IR data (KBr) cm^{-1} : 3319, 3069, 2979, 2939, 1721, 1703, 1628, 1561, 1138

PMR data (400MHz, $CDCl_3$) : δ 2.34(s, 3H, NHCOC<u>H</u>$_3$), 2.40-2.45(m, 4H, 2×C<u>H</u>$_2$), 3.58-3.62(m, 4H, 2×C<u>H</u>$_2$), 3.63(s, 3H, -NC<u>H</u>$_3$), 3.67(s, 2H, -NC<u>H</u>$_2$Ar), 7.43(s, 1H, C-4), 7.47(s, 1H, C-9), 7.63(s, 1H, C-5), 8.03(br signal, 1H, -CON<u>H</u>), 8.82(s, 1H, C-7).



[Figure-17]: 3-Acetamido-6-(4-methylpiperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 75

3-Acetamido-6-(4-phenylpiperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **76:**



State : light yellow amorphous solid,

Molecular Formula : $C_{24}H_{23}O_4N_3$

Melting Point : 287-289 °C

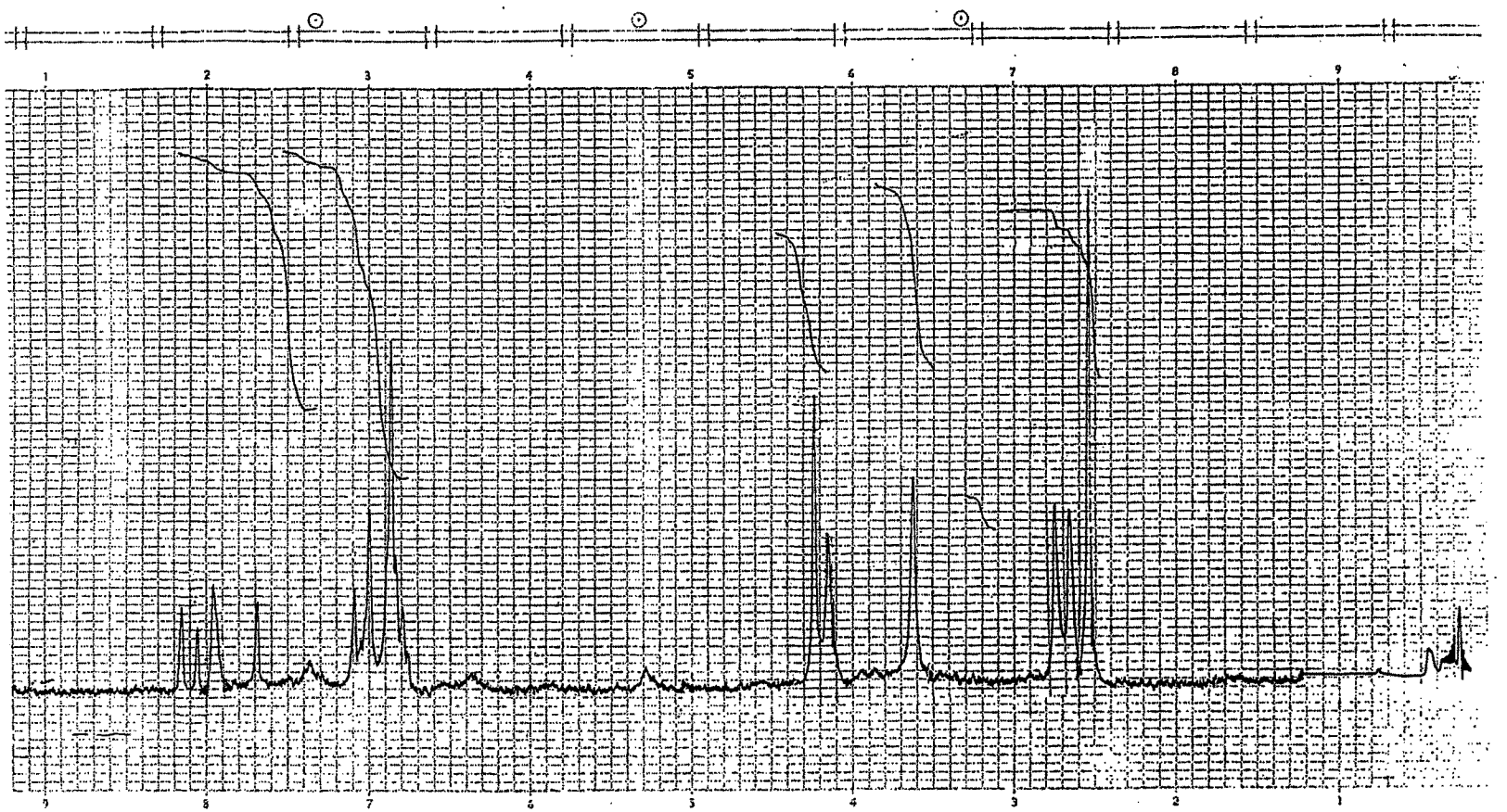
% Yield : 61

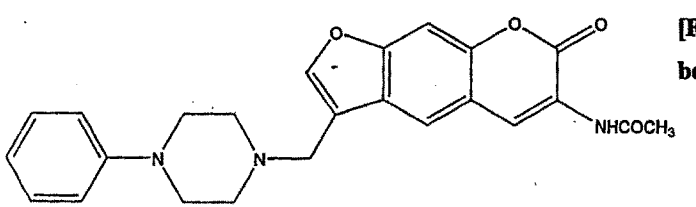
%C,H,N analysis (calculated) : C: 69.06 H: 5.52 N: 10.07

%C,H,N analysis (found) : C: 68.88 H: 5.61 N: 10.28

IR data (KBr) cm^{-1} : 3331, 3088, 2988, 2941, 1731, 1710, 1631, 1598, 1141

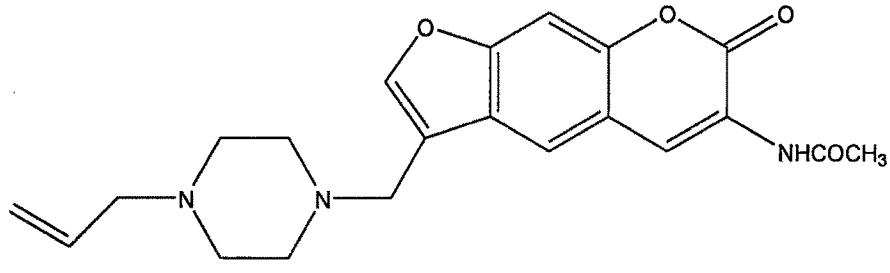
PMR data (90MHz, $CDCl_3$) : δ 2.51(s, 3H, -NHCOC<u>H</u>$_3$), 2.60-2.90(m, 4H, ring C<u>H</u>$_2$), 3.50-3.80(m, 4H, ring C<u>H</u>$_2$), 4.25(s, 2H, -NC<u>H</u>$_2$Ar), 6.75-7.10(m, 5H, aromatic protons), 7.32(br s, 1H, -CON<u>H</u>), 7.70(s, 1H, C-4), 7.90(s, 1H, C-9), 8.04(s, 1H, C-5), 8.15(s, 1H, C-7).





[Figure-18]: 3-Acetamido-6-(4-phenylpiperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 76

3-Acetamido-6-(4-allylpiperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **77:**



State : light brown amorphous solid,

Molecular Formula : $C_{21}H_{23}O_4N_3$

Melting Point : 270°

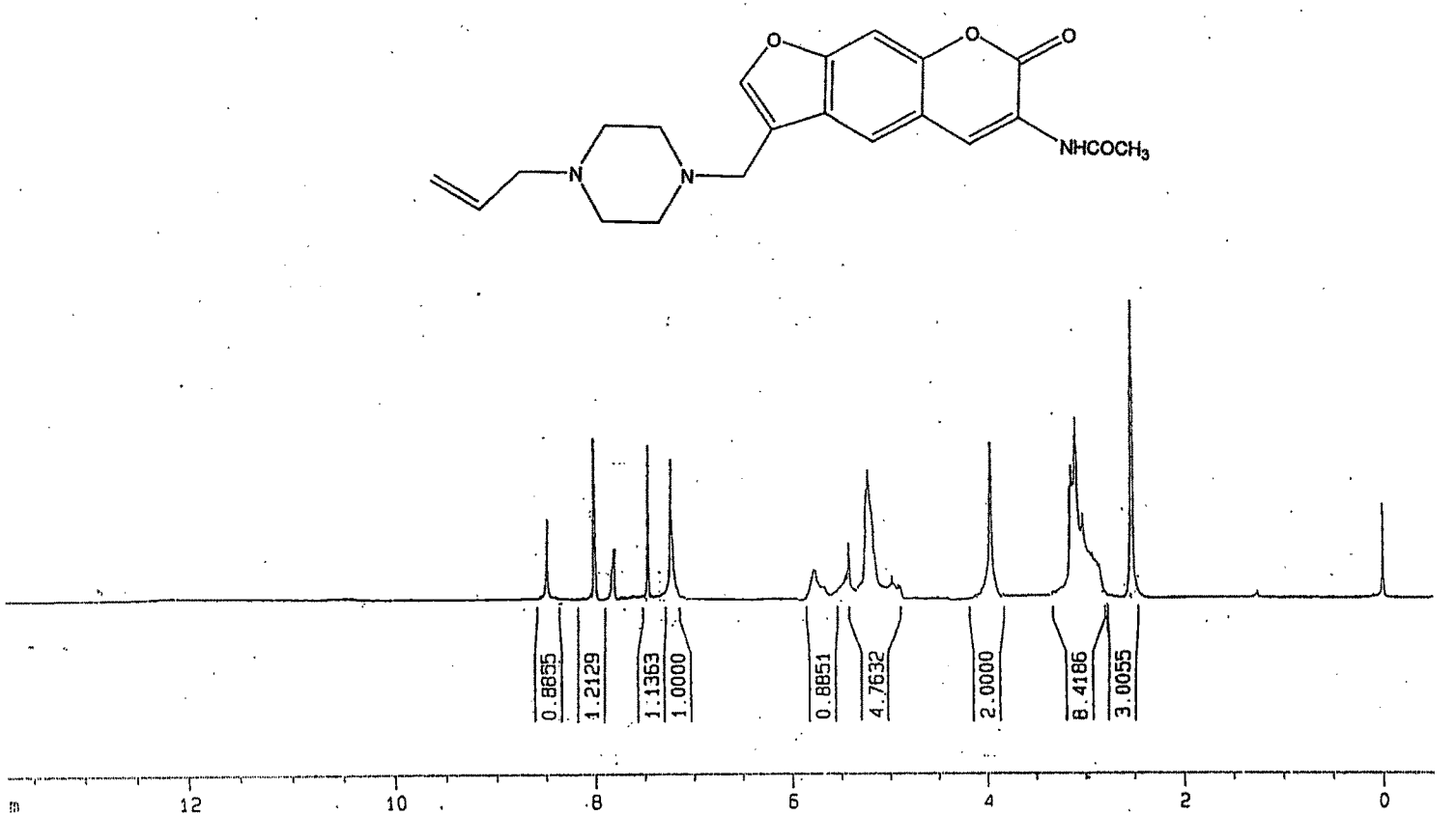
% Yield : 49

%C,H,N analysis (calculated) : C: 66.14 H: 6.07 N: 11.04

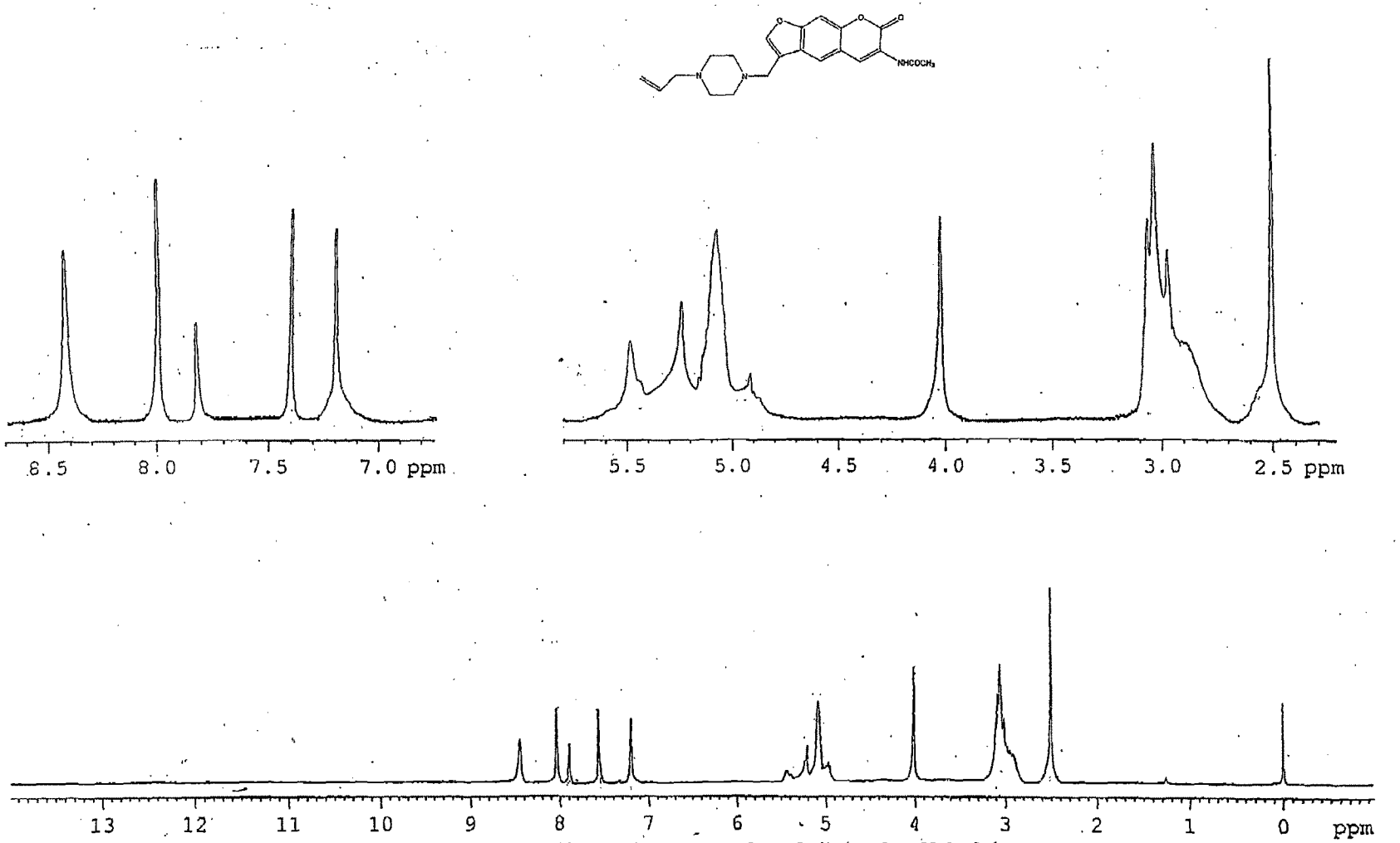
%C,H,N analysis (found) : C: 66.72 H: 5.94 N: 11.81

IR data (KBr) cm^{-1} : 3384, 3081, 2979, 2929, 1722, 1704, 1619, 1142.

PMR data (400MHz, $CDCl_3$) : δ 2.51(s, 3H, NHCOC<u>H</u>$_3$), 2.75-3.15(m, 8H, -NC<u>H</u>$_2$ of pyrazine ring), 4.04(s, 2H, -NC<u>H</u>$_2$Ar), 4.90-5.60(m, 6H, allylic, vinylic, -CON<u>H</u> protons), 7.20(s, 1H, C-4), 7.41(s, 1H, C-9), 8.00(s, 1H, C-5), 8.42(s, 1H, C-7).

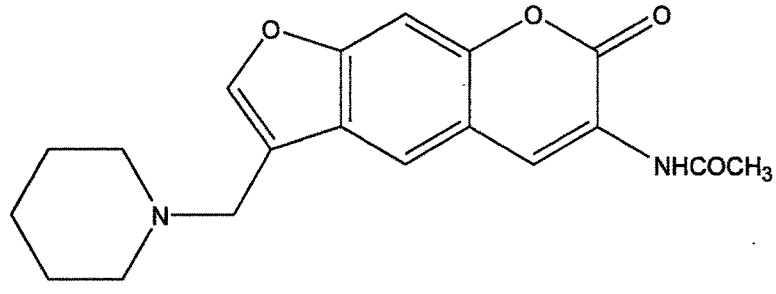


[Figure-19]: 3-Acetamido-6-(4-allylpiperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 77



[Figure-19a]: 3-Acetamido-6-(4-allylpiperazin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 77

3-Acetamido-6-(piperidin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, **78:**



State : pale yellow amorphous solid

Molecular Formula : $C_{19}H_{20}O_4N_2$

Melting Point : 258 – 259 °C

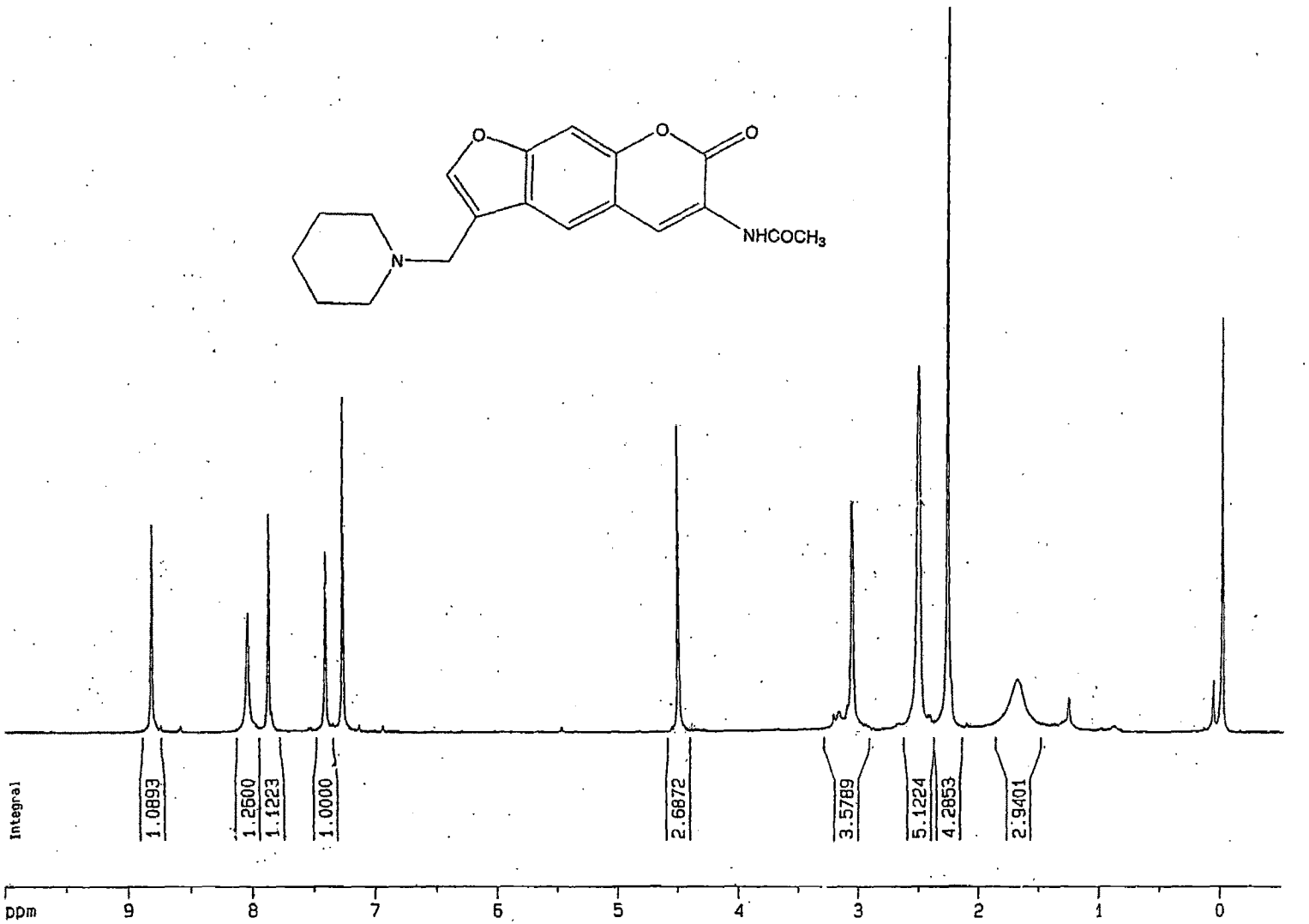
% Yield : 71

%C,H,N analysis (calculated) : C: 69.06 H: 5.91 N: 8.24

%C,H,N analysis (found) : C: 69.11 H: 5.79 N: 8.38

IR data (KBr) cm^{-1}: 3318, 3078, 2981, 2958, 1738, 1711, 1631, 1121, 730.

PMR data (400MHz, $CDCl_3$) : δ 2.19-2.42(br m 6H, ring C<u>H</u>$_2$), 2.50(s, 3H, -NHCOC<u>H</u>$_3$), 2.91-3.27(m, 4H, ring 2x-NC<u>H</u>$_2$), 4.44(s, 2H, -NC<u>H</u>$_2$Ar), 7.34(br s, 1H, -N<u>H</u>CO), 7.41(s, 1H, C-4), 7.80(s, 1H, C-9), 8.04(s, 1H, C-5), 8.73(s, 1H, C-7).



[Figure-20]: 3-Acetamido-6-(piperidin-1-yl-methyl)-2H-furo[3,2-*g*]-1-benzopyran-2-one, 78

II.5 Conclusion:

Several novel amino psoralens have been synthesized using cyclic as well as acyclic secondary amines by simple and convenient methods which do not involve costlier reagents as well as drastic conditions. These aminopsoralens may fulfill the monofunctional lesion for their chemotharapeutic applications.

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