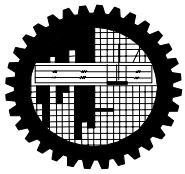
MICROWAVE ASSISTED SYNTHESIS OF BARBITURIC AND THIOBARBITURIC ACID DERIVATIVES

BY

DINA NASRIN

SUBMITTED IN THE PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER OF PHILOSOPHY (M. PHIL) IN CHEMISTRY



DEPARTMENT OF CHEMISTRY
BANGLADESH UNIVERSITY OF ENGINEERING AND TECHNOLOGY (BUET).
DHAKA-1000, BANGLADESH
JULY, 2011.

DEDICATED

TO

MY DAUGHTER

CANDIDATE'S DECLARATION

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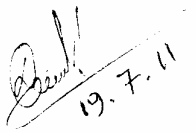

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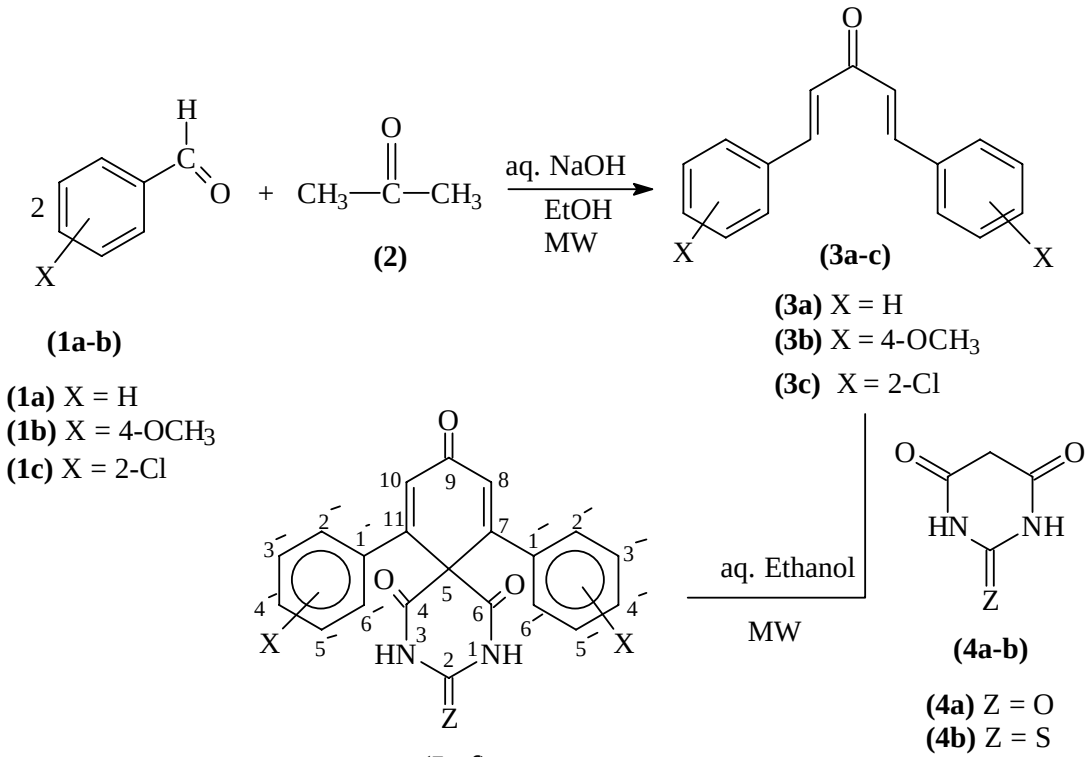
Contents

Chapter 3

Abstract

The parent barbituric acid and 2-thiobarbituric acid are convenient starting compounds for the preparation of different fused heterocycles and 5-substituted derivatives which are pharmacologically one of the most important classes of burbituric acid based compounds. 5-Substituted barbituric acid and thiobarbituric acid derivatives-(7,11-di-phenyl and substituteddi-phenyl-2-oxo/thioxo-1,3-diazaspiro[5,5]undecane-4,6,9-triones),**(5a-f)**, (Scheme -1) were synthesized in excellent yields by the condensation of diarylidene / substituted diarylidene acetones (3a-c) and barbituric or thiobarbituric acids in the presence of ethanol under microwave irradiation in solvent free condition. They are important class of hypnotic and sedative compounds.

Scheme-1



(1a-b)

(1a) X = H
(1b) X = 4-OCH_3
(1c) X = 2-Cl

(2)

(3a-c)

(3a) X = H
(3b) X = 4-OCH_3
(3c) X = 2-Cl

(4a-b)

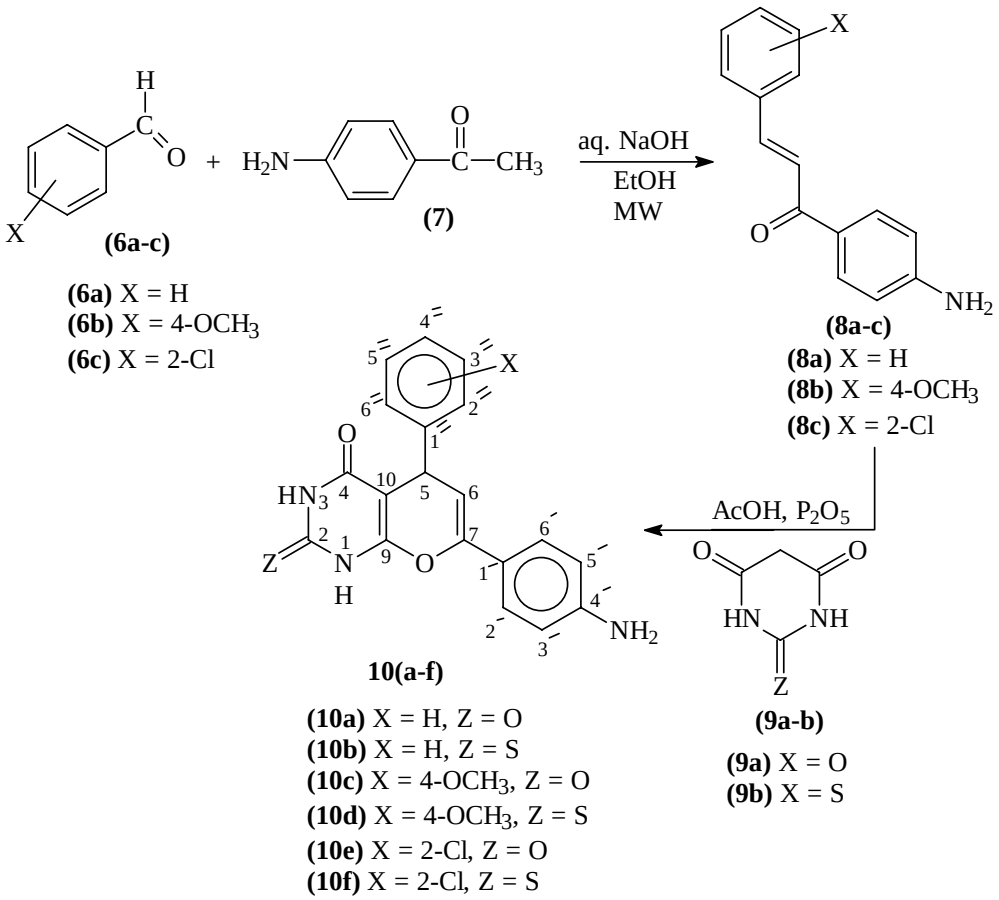
(4a) Z = O
(4b) Z = S

(5a-f)

(5a) X = H, Z = O
(5b) X = H, Z = S
(5c) X = 4-OCH_3, Z = O
(5d) X = 4-OCH_3, Z = S
(5e) X = 2-Cl, Z = O
(5f) X = 2-Cl, Z = S

(5-Aryl / substituted aryl-7-(4-aminoaryl)-1,2,3,4-tetrahydro-2-oxo/thioxo-4-oxo-5*H*-pyrano[2,3-d]pyrimidines),**(10a-f)** have been synthesized in a single step by the condensation of barbituric or thiobarbituric acids with arylidene/substituted arylidene acetophenone in glacial acetic acid in the presence of phosphorous pentoxide under microwave irradiation (Scheme-2). The solvent less synthesis apart from elimination of organic solvent from work-up, also gave improved yield as compared to the conventional heating, with reaction time reduced from hours to minutes.

Scheme-2



(6a-c)

(6a) X = H
(6b) X = 4-OCH_3
(6c) X = 2-Cl

(7)

(8a-c)

(8a) X = H
(8b) X = 4-OCH_3
(8c) X = 2-Cl

(9a-b)

(9a) X = O
(9b) X = S

10(a-f)

(10a) X = H, Z = O
(10b) X = H, Z = S
(10c) X = 4-OCH_3, Z = O
(10d) X = 4-OCH_3, Z = S
(10e) X = 2-Cl, Z = O
(10f) X = 2-Cl, Z = S

Investigation incorporated in this dissertation titled, “Microwave Assisted Synthesis of Barbituric and Thiobarbituric Acid Dderivatives” have been presented in three chapters. The first chapter is introductory section, in which the back ground, biological action, importance and microwave synthesis techniques are presented. The second chapter deals with rationale, results and discussion and conclusion for the synthesis of barbituric and thiobarbituric acid derivatives. The chapter three deals with the detailed methodologies and experimental procedure, spectra and references.

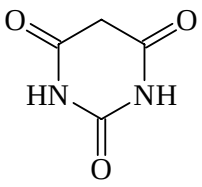
Chapter - 1

INTRODUCTION

Introduction

1.1 General Remarks

The diverse biological activity and coverage of a broad chemical space make barbituric acid derivatives excellent target compounds for organic and medicinal chemists[1]. Owing to their ready availability and various functionalization possibilities, the present barbituric acid **1** and 2-thiobarbiluric acid **2** are convenient starting compounds for the preparation of different fused heterocycles and 5-substituted derivatives which are pharmacologically the most important class of burbituric acid based compounds[1-10].



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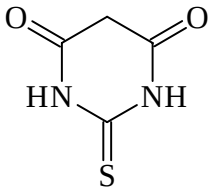

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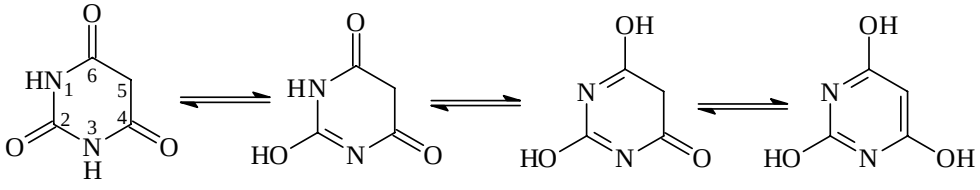
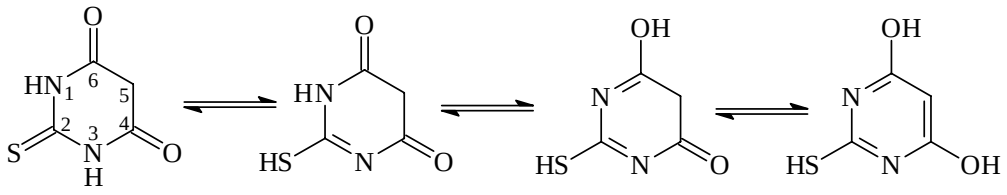
1.2 Structural Features of Barbituric Acid and Thiobarbituric acid

Barbituric Acid: Barbituric acid **1** may be regarded as 2,4,6(1*H*,3*H*,5*H*)-pyrimidinetrione or 2,4,6-trihydroxypyrimidine. This structure has been proposed because of the acidic nature of barbituric acid. On the other hand, barbituric acid contains an active methylene group, since it readily forms an oximino derivative with nitrous acid. On the basis of physical and chemical properties barbituric acid is believed to exist as the following tautomeric structures.



Barbituric acid **1** | Monohydroxy form (Monolactim) | Dithiolactim form (Dilactim) | Trihydroxy form (Trilactim)

Thiobarbituric Acid: When the carbonyl group in the 2-position of barbituric acid is replaced by a thiocarbonyl group, the compound is known as thiobarbituric acid or 2-thiobarbituric acid **2**. The tautomeric structures of **2** are shown below:



Thiobarbituric acid or 2-thiobarbituric acid **2** (Monothiolactim) (Dithiolactim) (Trithiolactim)

The active methylene group of thiobarbituric acid at 5-position behaves similarly as barbituric acid.

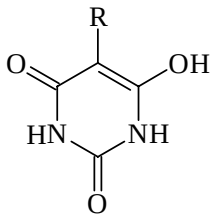
As the methylene in the 5-position of **1** and **2** is flanked by two carbonyl groups it may be regarded as an active methylene group and the methylene hydrogens can be replaced by suitable groups or structures.

It was shown by X-ray analysis[11, 12] that barbituric acid exists as the trioxo tautomer. The trihydroxy tautomer (trilactim) was ruled out in aqueous solution, because no ultraviolet bands which are characteristic of a trihydroxyhexahydropyrimidine structure were found[13]. Ultraviolet spectroscopy also revealed that barbituric acid, 1-methylbarbituric acid, and 1, 3-dimethylbarbituric acid display similar spectra, thereby providing further evidence against the existence of the trilactim[14]. Barbituric acid in aqueous solution, therefore, may be characterized by equilibrium among barbituric acid, monolactim and dilactim.

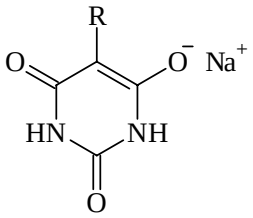
Ultraviolet spectroscopic studies were also conducted with monosubstituted and disubstituted barbituric acids[15-18]. It was shown that in aqueous solution these compounds predominate either in the dioxo tautomeric form (in alkaline medium) or in the trioxo tautomeric form (in acid medium).

The acidity of barbiturates in aqueous solution depends on the number of substiuents attached to barbituric acid. The dissociation contant (pK) of unsubstituted

barbituric acids ranges from 7.1 to 8.1[19]. Unsubstituted, 1-substituted, 5-substituted, 1,3-disubstituted and 1,5-disubstituted are strongly acidic because these compounds exist in the tautomeric form. The dissociation of one hydrogen (at 5-position) takes place readily; salts of barbituric acids are easily formed by treatment with bases.

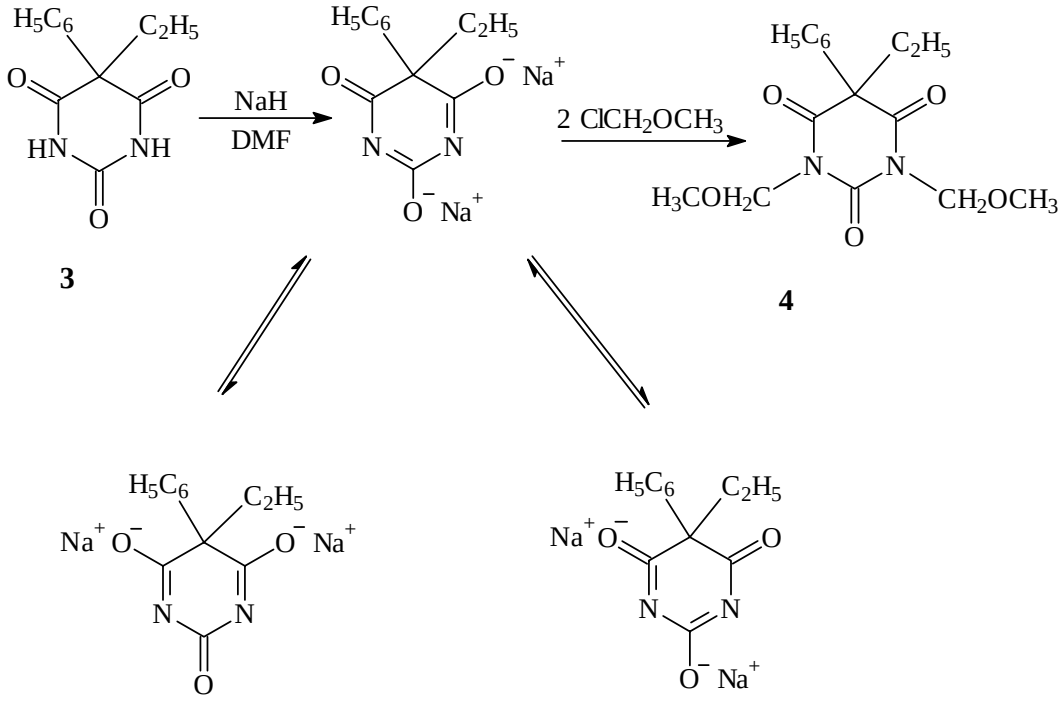


Tautomeric form
of barbituric acid



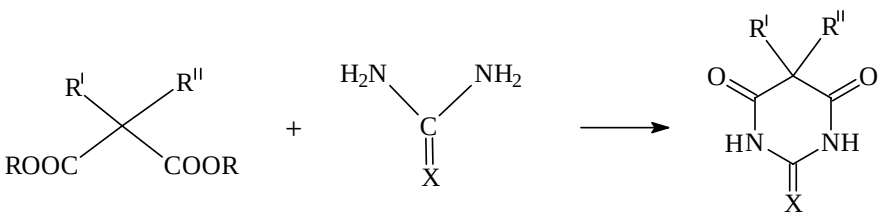
Na-Salt of barbituric acid

The 5,5-disubstituted barbituric acids; 5,5-disubstituted thiobarbituric acids; 1,5,5-trisubstituted barbituric acids are weakly acidic because these compounds exist predominantly in the trioxo tautomeric form. Although these substances are relatively weak acids, as shown by their dissociation constants in the range of 7.1 to 8.1, salts of these barbiturates are easily formed by treatment with bases. It has also been reported that 5,5-disubstituted barbituric acids undergo a second ionization as well[20]. The pK values are in the range of 11.7 to 12.7. It appears reasonable, therefore, to assume that dialkali metal salts of 5,5-disubstituted barbituric acid could be prepared, provided a strong enough base was used. Indeed, the preparation of dialkali salt of phenobarbital has been reported[21].



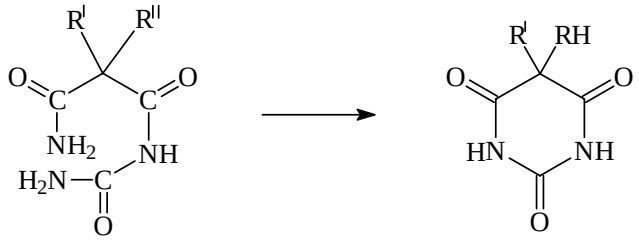
Preparation of C-5 substituted barbituric acids:

Condensation reactions are usually used in the preparation of barbituric acid derivatives. These reactions may take place in acidic, neutral or basic media. Condensation reactions in an alkaline medium involve malonic esters, [22] cyanoacetic esters and malonic amides on the one hand, and urea or thiourea on the other hand.



Where X=O or S

Cyclization of N-substituted ureas in an alkaline medium also produces barbiturates.



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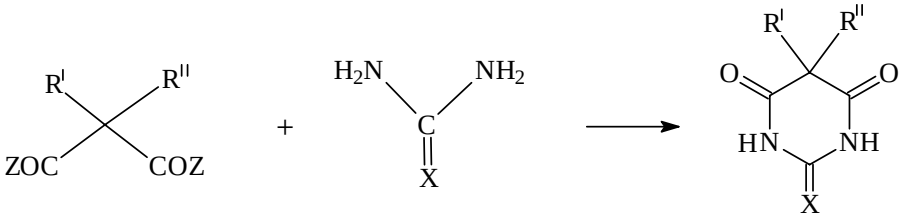
Condensation reactions in a neutral or acidic medium take place readily between malonyl chlorides or malonic acids and urea or thiourea.



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Where Z = OH or Cl and X = O or S

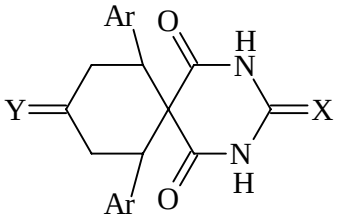
1.3 Importance of barbituric acid and thiobarbituric acid derivatives.

The barbituric acid and thiobarbituric acid have great pharmacological importance and several of its derivatives are used in the treatment of neurological disorders. Indeed thiobarbituric acid derivatives have more pharmacological activity due to the sulphur presence in the molecule. Because of the ample application and of the acid character, the barbiturates and thiobarbiturates are also used as reaction in synthesis of biological activity macro cycles. They have many fold uses. Some of them are mentioned bellow:

a) As anticonvulsant agents

A. N. Osman[23] and co-workers in 1996 performed synthesis and studied anti convulsant activity of some spiro compounds derived from barbituric and thiobarbituric acids. Divinyl ketones ArCH:CHOCH:CHAr (Ar=Ph, substituted phenyl), prepared by

the condensation of acetone with the appropriate aromatic aldehydes or Michael addition



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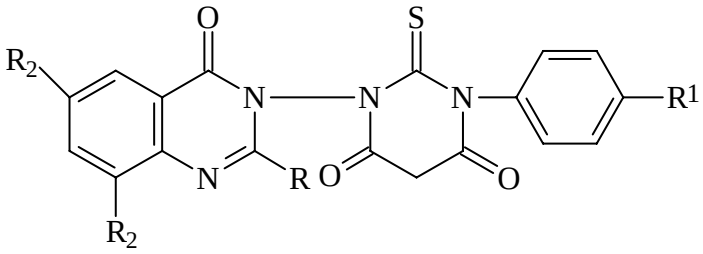
with barbituric acid or thiobarbituric acid gave the desired spiro compounds **12** (X=O, S). Preliminary pharmacological screenings of some of the new compounds reveal their anticonvulsant activity.

In 1999, G. V. S. R. Sarma[24] and co-workers synthesized twelve new 1-[2,6,8-trisubstituted-4(3*H*)-oxoquinazolin-3-yl]-3-(4-substitutedphenyl)thiobarbiturates**11** [R=Me, Ph; R^1=Br, Cl, H; R^2=Br, H] by treating 2,6,8-trisubstituted-3-[N^3-(4-substituted phenyl) thioureido] -4(3*H*)-quinazolones with malonic acid in presence of acetyl chloride.



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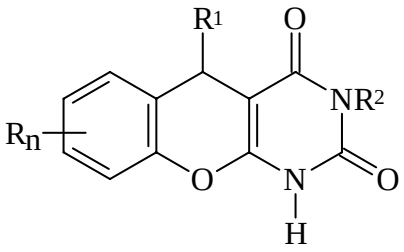
These thio-ureidoquinazolone intermediates were obtained by the condensation of 3-amino-2,6,8-trisubstituted-4(3*H*)-quinazolones with 4-substituted phenyl isothiocyanates.

b) Anti allergic agents

D. J. Blythin[25] in 1978, synthesized the compound **12** (n =1,2,3,4;R=H, alkyl, cycloalkyl, hydroxyalkyl, aminoalkyl, alkanoyloxy, CO_2H, carbaloxy, acyl, CHO, cyano, substituted carbonyl; R^1=H, alkyl; R^2=H, alkyl) which are useful as anti-allergic agents.



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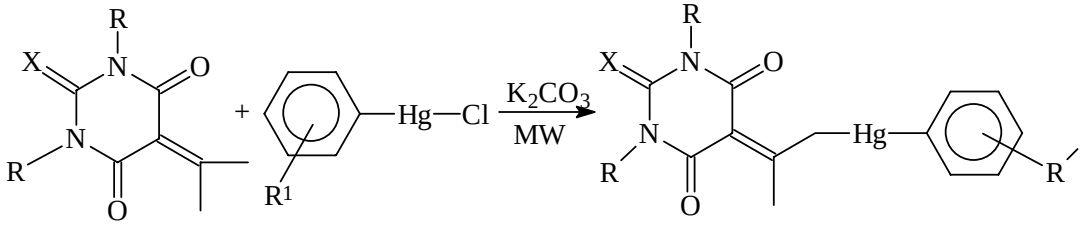
A mixture of 5, 2-NC-(OH)-C6H3CHO, barbituric acid and $MeSO_3H$ was refluxed to give the respective **12** (R_1=R_2=H, Rn=7-cyano).

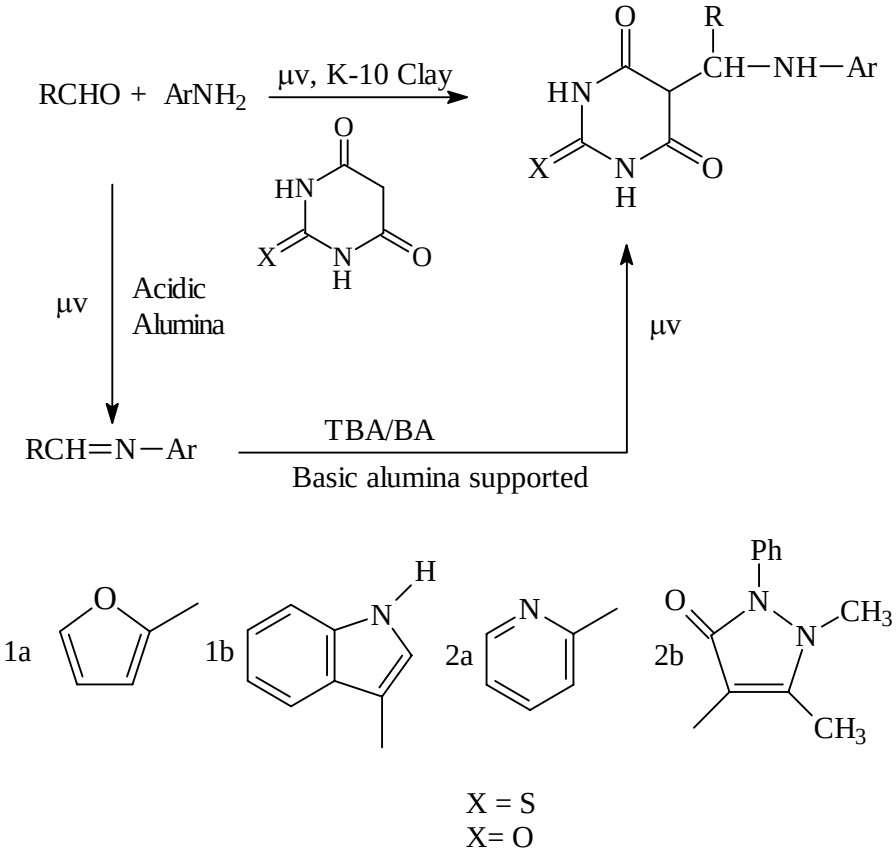
c) As antifungal agents

In 2002, M. Kidwai *et al.*[26] synthesized a series of new barbitural / thiobarbitural substituted organomercurial derivatives from pyrimidine derivatives and arylmercuric chloride over K_2CO_3 under microwave irradiations. The prepared compounds were tested against *A. niger* and *A. flavus* for their antifungal activity and were found to posses good activity.



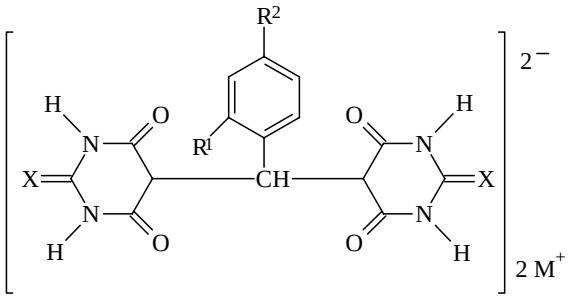
X = O, R =H R^1 = H, 4–OCl_3, 4–Br
X = S, R = H, C_6H_5

In 2005, an expeditious solventless synthesis of novel Mannich bases of thiobarbiturates and barbiturates using montmorillonite clay under microwave were synthesized by Mazaahir Kidwai *et al.*[27] All the compounds synthesized were screened for their antifungal activitiy against *A. niger* and *A. flavus* and found to possess good activity.



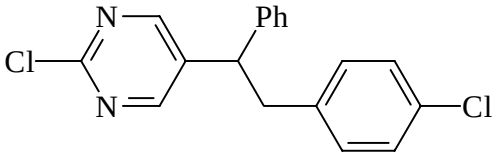
d) As antibacterial agents

In 1999, R. I. Ashkinazi[28] prepared compounds **13** [X=O, S; R^1=H, NO_2, alkoxy; R^2=H, NO_2, alkoxy, halo; M^+=H^+, pyridinium, (2-hydroxy ethyl) ammonium] having antibacterial, antichlamydial, antiviral and immunomodulating activity. Thus, 3 mmol of 2-thiobarbituric acid and 1.5 mmol of 4-chlorobenzaldehyde were refluxed 1-2 hours in 10-15 mL of pyridine to give **13** (X=S, R^1=H, R^2=Cl, M=$C_5H_5NH^+$) in 89% yield.



13

In 1996, Y. Fellahi[29] and co-workers prepared **14** by chlorination of the 5-substituted barbituric acid obtained by treatment of 5-benzylidene barbituric acid with an organozinc reagent in the preceding step. The trichloropyrimidines belong to a series of new pyrimidine derivatives which show antibacterial activity against the human bacterial flora of the axilla and foot. The characterization of this compound was done by spectroscopic data and X-ray analysis.



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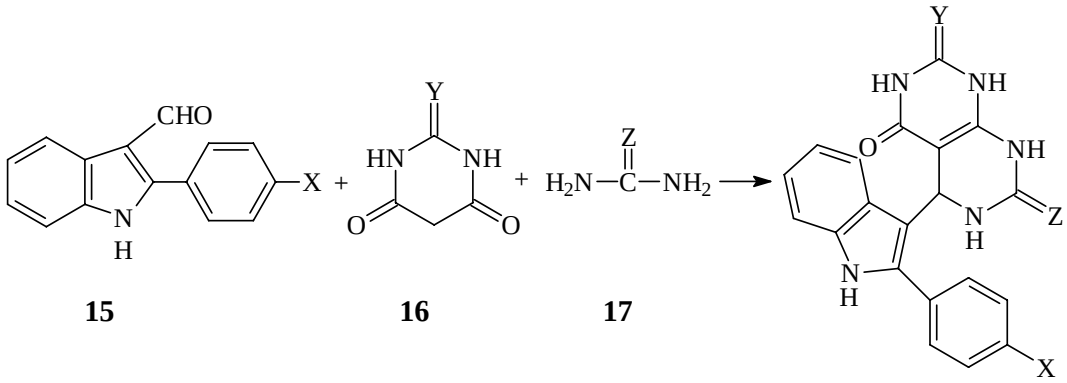
Ragini Gupta *et al.*[30] in 2011, synthesized the compound **18** by multi-component reaction of 3-formaldehyde **15** thiobarbituric acid/barbituric acid **16**and thiourea / urea **17**. Representative compounds were also evaluated for their antimicrobial activity against *Rhizopus stolonifer*, *Fusarium oxysporum*, *Escherichia coli* and *Pseudomonas aeruginosa* at different concentrations. Some of the compounds showed premising activity.

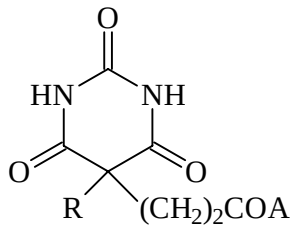


15 **16** **17** **18**

e) As antitumor agent

In 1998, A. Oliva[31] and co-workers prepared compounds **19**; [R=WV; A=R^1, $NR^2(CH_2)_m$ NR^9TR^{10}; R^1=OH, $C_{1\text{-}4}$ alkoxy, NH_2, mono- or di-($C_{1\text{-}4}$ alkyl)amino,

(un)substituted phenoxy, benzyloxy, etc.; R^9,R^{10}=H, (un)substituted C_{1-4} alkyl, Ph; R^9R^{10}NCO may form a 5- or 6- membered lactam ring; T=CO, SO_2; V=(un)substituted (un)saturated mono or bicyclic group optionaly containing 1-3 N, O, S; W=bond, C_{1-8} alkyl, C_{2-8} ; alkenyl; n=1-3] as enantiomers, racemates, diastereoisomers, tautomers or their mixtures, and their pharmaceutically acceptable salts, inhibitors of the metzincins useful for antimetastic and antitumor activity.



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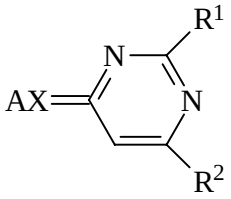
f) As herbicidal agent

In 1997, B. Li[32] and co-workers prepared 4-aryloxy (thio or amino) pyrimidine derivatives **22** (R^1, R^2= halo, alkyl, alkoxy, alkylamino, alkylthio, aryloxy; A=Ph, arom. Heterocycle contg. 1-3 O, S or N; X=O, S, sulfinyl, sulfonyl), useful as herbicides. Thus, reaction of barbituric acid with $POC1_3$ in $ClCH_2CH_2Cl$ in the presence of Et_3N gave 95% 2,4,6-trichloropyrimidine, reaction of which with NaOMe on MeOH followed by treatment with Me salicylate gave Me 2-(2,6-dimethoxy pyrimidine-l-4 oxy)-benzoate, **20**. Compound **20** showed herbicidal activity at 2250 g/ha.



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1.4 Microwave synthesis

1.4.1 Introduction

Microwave chemistry is the science of applying microwave irradiation to chemical reactions[33-35]. Microwaves act as high frequency electric fields and will generally heat anything with a mobile electric charge. Polar solvents are heated as their component molecules are forced to rotate with the field and lose energy in collisions. Semi conducting and conducting samples heat when ions or electrons within them form an electric current and energy is lost due to the electrical resistance of the material. Heating a reaction or chemical reactor by microwave radiation (as seen in a domestic microwave oven) has a number of advantages over conventional heating:

1. The heat is formed directly and rapidly in the sample,
2. Energy is not wasted in heating furnaces or oil baths,
3. The entire volume of the reactor can be heated (virtually) uniformly,
4. Selected volumes of the sample (including microscopic regions) can be selectively heated.

Conventional heating usually involves the use of a furnace or oil bath that heats the walls of the reactor by convection or conduction. The core of the sample takes much longer to achieve the target temperature (particularly when heating a large sample of ceramic bricks, for example). Rapid and homogeneous heating has the following benefits:

1. Reaction rate acceleration
2. Milder reaction conditions
3. Higher chemical yield
4. Lower energy usage

Some of these effects are derived from superheating or hot spots, well known effects in micro waving. Selective heating is particularly important in the microwave heating of supported metal catalysts. A specific application in synthetic chemistry is in the microwave heating of a binary system comprising a polar solvent and a polar solvent obtain different temperatures. Applied in a phase transfer reaction a water phase reaches a temperature of l00°C while a chloroform phase would retain a temperature of 50^{o}C. Microwave chemistry is particularly effective in dry media reactions.

In recent years, high-speed synthesis with microwave has attracted a considerable amount of attention[36]. More than 3500 articles have been published in the area of

microwave –assisted organic synthesis (MAOS) [37, 38] since the first reports on the use of microwave heating to accelerate organic chemical transformations by the group of Gedye and Giguers /Majetich[39] in 1986. In many of the published examples, microwave has been shown to dramatically reduce reaction times, increase product yield and enhance product purities by reducing unwanted side reactions compared to conventional heating methods. The advantages of these enabling technologies have more recently also been exploited in the context of multistep total synthesis[40] and medicinal chemistry /drug discovery[41] and have additionally penetrated related field such as polymer synthesis[42], material sciences[43] nanotechnologes[44] and biochemical processes[45]. The use of microwave irradiation in chemistry has become such a popular technique in the scientific community that it might be assumed in a few years most chemists will probably use microwave energy to heat chemical reactions on laboratory scale. The statement that, in principle, any chemical reaction that requires heat can be performed under microwave condition has today been generally accepted as a fact by the scientific community.

1.4.2 Microwave theory

Microwave irradiation is electromagnetic irradiation in the frequency range of 0.3 to 300 GHz. All domestic "kitchen" microwave ovens and all dedicated microwave reactors for chemical synthesis operate at a frequency of 2.45 GHz (which corresponds to a wavelength of 12.24 cm) to avoid interference with telecommunication and cellular phone frequencies The energy of the microwave photon in this frequency region (0.00 16 eV) is too low to break chemical bonds and is also lower than the energy of Brownian motion. It is therefore clear that microwaves cannot induce chemical reactions [46-48].

Microwave-enhanced chemistry is based on the efficient heating of materials by "microwave dielectric heating" effects. This phenomenon is dependent on the ability of a specific material (solvent or reagent) to absorb microwave energy and convert it into heat. The electric component[49] of an electromagnetic field causes heating by two main mechanisms: dipolar polarization and ionic conduction. Irradiation of the sample at microwave frequencies results in the dipoles or ions aligning in the applied electric

field. As the applied field oscillates, the dipole or ion field attempts to realign itself with the alternating electric field and, in the process, energy is lost in the form of heat through molecular friction and dielectric loss. The amount of heat generated by this process is directly related to the ability of the matrix to align itself with the frequency of the applied field. If the dipole does not have enough time to realign, or reorients too quickly with the applied field, no heating occurs. The allocated frequency of 2.45 GHz used in all commercial systems lies between these two extremes and gives the molecular dipole time to align in the field, but not to follow the alternating field precisely [47-48].

The heating characteristics of a particular material (for example, a solvent) under microwave irradiation conditions are dependent on its dielectric properties. The ability of a specific substance to convert electromagnetic energy into heat at a given frequency and temperature is determined by the so-called loss factor tanδ. This loss factor is expressed as the quotient tanδ=ε"/ε', where ε" is the dielectric loss, which is indicative of the efficiency with which electromagnetic radiation is converted into heat, and ε' is the dielectric constant describing the ability of molecules to be polarized by the electric field. A reaction medium with a high tanδ value is required for efficient absorption and, consequently, for rapid heating. The loss factors for some common organic solvents are summarized in Table 1. In general, solvents can be classified as high (tanδ.>0.5), medium (tanδ. 0.1-0.5), and low microwave absorbing (tanδ. <0.1).

Table 1. Loss factors (tanδ) of different solvents. [a]

Solvent	tanδ	Solvent	tanδ
ethylene glycol	1.350	DMF	0.161
ethanol	0.941	1,2-dichloroethane	0.127
DMSO	0.825	water	0.123
2-propanol	0.799	chlorobenzene	0.101
formic acid	0.722	chloroform	0.091
methanol	0.659	acetonitrile	0.062
nitrobenzene	0.589	ethyl acetate	0.059
1-butanol	0.571	acetone	0.054
2-butanol	0.447	tetrahydrofuran	0.047
1,2-dichlorobenzene	0.280	dichloromethane	0.042
NMP	0.275	toluene	0.040
acetic acid	0.174	hexane	0.020

[a] Data from ref. 15; 2.45 GHz, 20 ^{o}C

Other common solvents without a permanent dipole moment such as carbon tetrachloride, benzene, and dioxane are more or less microwave transparent. It has to be emphasized that a low tanδ value does not preclude a particular solvent from being used in a microwave-heated reaction. Since either the substrates or some of the reagents/catalysts are likely to be polared, the overall dielectric properties of the reaction medium will in most cases allow sufficient heating by microwaves. Furthermore, polar additives such as ionic liquids, for example, can be added to otherwise low-absorbing reaction mixtures to increase the absorbance level to the medium.

Traditionally, organic synthesis is carried out by conductive heating with an external heat source (for example, an oil bath). This is a comparatively slow and inefficient method for transferring energy into the system, since it depends on the thermal conductivity of the various materials that must be penetrated, and results in the temperature of the reaction vessel being higher than that of the reaction mixture. In contrast, microwave irradiation produces efficient internal heating (in-core volumetric heating) by direct coupling of microwave energy with the molecules (solvents, reagents, catalysts) that are present in the reaction mixture. Since the reaction vessels employed are typically made out of (nearly) microwave transparent materials, such as borosilicate glass, quartz, or Teflon, an inverted temperature gradient results compared to conventional thermal heating. The very efficient internal heat transfer results in minimized wall effects (no hot vessel surface) which may lead to the observation of so-called specific microwave effects for example, in the context of diminished catalyst deactivation.

1.4.3 Microwave Effects

Since the early days of microwave synthesis, the observed rate accelerations and sometimes altered product distributions compared to oil-bath experiments have led to speculation on the existence of socalled "specific" or "nonthermal" microwave effects[50-52] . Historically, such effects were claimed when the outcome of a synthesis performed under microwave conditions was different from the conventionally heated counterpart carried out at the same apparent temperature. Today most scientists agree that in the majority of cases the reason for the observed rate enhancements is a purely thermal/kinetic effect, that is, a consequence of the high reaction temperatures that can

rapidly be attained when irradiating polar materials in a microwave field. A high microwave absorbing solvent such as methanol (tanδ.=0.659) can be rapidly superheated to temperatures >100 °C above its boiling point when irradiated under microwave conditions in a sealed vessel. The rapid increase in temperature can be even more pronounced for media with extreme loss factors, such as ionic liquids where temperature jumps of 200 °C within a few seconds are not uncommon. Naturally, such temperature profiles are very difficult if not impossible to reproduce by standard thermal heating. Therefore, comparisons with conventionally heated processes are inherently troublesome.

Dramatic rate enhancements between reactions performed at room temperature or under standard oil bath conditions (heating under reflux) and high-temperature microwave-heated processes have frequently been observed. As Baghurst and Mingos have pointed out on the basis of simply applying the Arrhenius law [$k=A \exp(-E_a/RT)$], a transformation that requires 68 days to reach 90 % conversion at 27 °C, will show the same degree of conversion within 1.61 seconds (!) when performed at 227 °C (Table 2)[47] .The very rapid heating and extreme temperatures observable in microwave chemistry means that many of the reported rate enhancements can be rationalized by simple thermal/kinetic effects.

Table 2. Relationship between temperature and time for a typical first-order reaction.[a]

T [°C)	k [s^{-1}]	*t* (90 % conversion)
27	1.55×10^{-7}	68 days
77	4.76×10^{-5}	13.4 hours
127	3.49×10^{-3}	11.4 minutes
177	9.86×10^{-2}	23.4 seconds
227	1.43	1.61 seconds

[a] Data from ref 47; A= 4×10^{10} mol^{-1} s^{-1}, E_a = 100 kJ mol^{-1}.

In addition to the above mentioned thermal/kinetic effects, microwave effects that are caused by the uniqueness of the microwave dielectric heating mechanism must also be considered. These effects should be termed "specific microwave effects" and shall be defined as accelerations that can not be achieved or duplicated by conventional heating,

but essentially are still thermal effects. In this category fall the superheating effect of solvents at atmospheric pressure[53], the selective heating of, for example, strongly microwave absorbing heterogeneous catalysts or reagents in a less polar reaction medium[54-56] the formation of "molecular radiators" by direct coupling of microwave energy to specific reagents in homogeneous solution (microscopic hotspots) [55] the elimination of wall effects caused by inverted temperature gradients[57]. It should be emphasized that rate enhancements falling under this category are essentially still a result of a thermal effect (that is, a change in temperature compared to heating by standard convection methods), although it may be difficult to experimentally determine the exact reaction temperature.

Some authors have suggested the possibility of "nonthermal microwave effects" (also referred to as athermal effects). These should be classified as accelerations that can not be rationalized by either purely thermal/kinetic or specific microwave effects. Nonthermal effects essentially result from a direct interaction of the electric field with specific molecules in the reaction medium. It has been argued that the presence of an electric field leads to orientation effects of dipolar molecules and hence changes the pre-exponential factor *A* or the activation energy (entropy term) in the Arrhenius equation[50, 51.A] similar effect should be observed for polar reaction mechanisms, where the polarity is increased going from the ground state to the transition state, thus resulting in an enhancement of reactivity by lowering the activation energy [51]. Microwave effects are the subject of considerable current debate and controversy [50-52], and it is evident that extensive research efforts will be necessary to truly understand these and related phenomena[58]. Since the issue of microwave effects is not the primary focus of this Review, the interested reader is referred to more detailed surveys and essays covering this topic.

1.4.4 Processing Techniques

Frequently used processing techniques employed in microwave-assisted organic synthesis involve solvent less ("dry-media") procedures where the reagents are pre adsorbed on to either a more or less microwave transparent (silica, alumina, or clay)[59] or strongly absorbing (graphite)[60] inorganic support, which can additionally be doped with a catalyst or reagent. The solvent-free approach was very popular particularly in the early days of MAOS since it allowed the safe use of domestic household

microwave ovens and standard open-vessel technology. Although a large number of interesting transformations with "dry-media" reactions have been published in the literature[59], technical difficulties relating to non uniform heating, mixing, and the precise determination of the reaction temperature remain unsolved, in particular when scale-up issues need to be addressed. In addition, phase-transfer catalysis (PTC) has also been widely employed as a processing technique in MAOS[61].

Alternatively, microwave-assisted synthesis can be carried out in standard organic solvents either under open- or sealed-vessel conditions. If solvents are heated by microwave irradiation at atmospheric pressure in an open vessel, the boiling point of the solvent (as in an oil-bath experiment) typically limits the reaction temperature that can be achieved. In the absence of any specific or non thermal microwave effects (such as the superheating effect at atmospheric pressure which has been reported to be up to 40 °C)[53] the expected rate enhancements would be comparatively small. Nonetheless to achieve high reaction rates, high-boiling microwave-absorbing solvents such as DMSO, N-methyl-2-pyrrolidone (NMP), 1,2-dichlorobenzene (DCB), or ethylene glycol (see Table 1) have been frequently used in open vessel microwave synthesis[42]. However, the use of these solvents presents serious challenges during product isolation. The recent availability of modern microwave reactors with on-line monitoring of both temperature and pressure has meant that MAOS in sealed vessels, a technique pioneered by Strauss in the mid 1990s[62] has been celebrating a comeback in recent years. This is clearly evident from surveying the recently published literature in the area of MAOS, and it appears that the combination of rapid dielectric heating by microwaves with sealed-vessel technology (autoclaves) will most likely be the method of choice for performing MAOS in the future.

1.4.5 Equipment

Although many of the early pioneering experiments in microwave-assisted organic synthesis were carried out in domestic microwave ovens, the current trend is undoubtedly to use dedicated instruments for chemical synthesis. In a domestic microwave oven the irradiation power is generally controlled by on/off cycles of the magnetron (pulsed irradiation), and it is typically not possible to monitor the reaction

temperature in a reliable way. This disadvantage, combined with the unhomogeneous field produced by the low-cost magnetrons and the lack of safety controls, means that the use of such equipment can not be recommended. In contrast, all of today's commercially available dedicated microwave reactors for synthesis[63-65] feature built-in magnetic stirrers, direct temperature control of the reaction mixture with the aid of fiber-optic probes or IR sensors, and software that enables on-line temperature/pressure control by regulation of microwave power output.

1.4.6 Green advantages

While microwaves are both financially and energetically inexpensive to produce, the efficiency with which they can be used makes them an attractive 'green' alternative to other forms of heating. Moreover, in recent years there has been a drive within the chemical industry to reduce both the production of waste products and the use of solvents. Waste products equate with wasted resources, and solvents can be toxic, flammable, and expensive to dispose off Microwave chemistry provides a cleaner alternative, this time by exploiting the ability of microwaves to heat the reactants directly. Using only a minimum amount of solvent, the reactants are absorbed into a sponge-like support material (clays, aluminas, zeolites etc.). The reactants are then heated directly with microwaves to generate the products, which are then extracted, again with a minimum amount of solvent. Because microwave heating is essentially uniform throughout the material, there is no time lost waiting for thermal conduction to heat the sample and consequently, reaction times are often measured in minutes or even seconds.

A 'green' approach has been adopted by Chris Strauss, at the Commonwealth Scientific and Industrial Research Organization (CSIRO) in Australia. Strauss and his term carry out organic reactions in supercritical water - water at high pressures and elevated temperatures - instead of organic solvents. Under these conditions, the properties of water change markedly from those that we encounter under ambient conditions, and it acts as an excellent organic solvent. The advantage is that the solvent is non-flammable, and when the reaction is completed, the waste solvent may be disposed of down the laboratory drains.

The microwave chemistry is more than an academic interest has been demonstrated recently by the Dow Chemical Company in the US, faced with tighter regulation of

emission from an existing down or cleaning it up. By switching to a 60 kW microwave-based process, the plant has reduced its production of waste and unwanted by products, with increasing productivity and reducing energy costs.

1.4.7 The type of chemical reactions:

The effect of microwaves on chemical reactions is generally evaluated by comparing the time needed to obtain a given yield of the final products with respect to traditional heating. In most examples reported in the literature[66-68] the amount of reagents employed in these tests ranges from a few milligrams to a few grams. The reaction vessel is simply kept in the oven for a preset time, following most of the details described above.

One of the most interesting problems that technology should solve is the possibility of scaling-up the processes under microwaves. For this purpose flux reactors have been suggested. The reagents pass into the oven continuously through a serpentine at such a rate that each portion of the mass absorbs a fixed amount of microwave energy. Power levels can be modulated through the microwave Output: at a fixed power of the oven for varying times; or for a fixed time by varying patterns of on-off cycles[69].

Reactions which benefit more from the presence of microwaves are obviously those which have low rates under traditional conditions[70-72]. The reactions examined represent a large variety, ranging from hydrolysis of nitriles, amides and esters, to the formation of esters and ethers oxidation and hydrogenations; rearrangements and polymerizations, etc[73-74].

The Diels-Alder reaction represents a good model to study the effect of microwaves : the carbonyl group, besides being important in driving the reaction, acts as a antenna towards the radiation. The reaction is rapid when the starting diene is electron-rich and the dienophile is electron-poor; when dienophiles lack of activating groups the reactions requires a high temperature (>30^{o}C). The reaction between anthracene and maleic anhydride is a classical example of this[75].

Esters and nitriles are hydrolyzed very slowly either in basic or acidic medium under traditional conditions. Hydrolysis of these compounds offers a typical example of application of microwaves. A positive role is played in this case by the presence of strong acids or bases that increase the heating rate under microwave irradiation.

Etherification is a reaction largely studied under microwaves. The rate of etherification of benzoic acid was found to be increased under microwaves and the increase is a function of the length of the hydrocarbon chain of the alcohol. It must be pointed out that the boiling point of the alcohol also increases: higher temperature of the reaction can therefore also be used in the traditional method: as a consequence in this case the comparison between the two techniques is no longer homogeneous[73].

In the case of the Williamson reaction to form ethers between alkoxides and alkyl chlorides the ratio between substitution and elimination did not change[73].

On the contrary in the case of the sulphonation of naphthalene, the substitution in position-2 preferentially occurs under microwaves at temperature higher than 130 ^{o}C; while under traditional heating the filial product contains almost equimolar of 1 and 2 naphtalene-sulfonic acids at temperature lower than 130^{o}C[76].

Polymer chemistry will probably benefit greatly from the application of microwaves: in fact the presence of polar groups in the starting materials particularly favours the absorption of microwaves, allowing rapid and controlled synthesis, hardening and curing of the final products[38]. In these systems, different modes of energy supply can drive a reaction differently: e.g. in the case of epoxy resins, short impulses favour self-polymerization, whereas longer impulses of microwaves allow the reaction with amines.

The use of solid materials for the so-called dry-chemistry or without solvent appears very interesting and represents a new frontier for chemistry under microwaves [77-78].

Moreover the experimental conditions adopted in these cases simplify the chemical system, due to the absence of solvent and the problems related to it, such as loss for

evaporation or pressure increase in closed vessels. According to this methodology the reagents are dispersed on the surface of an inorganic and insoluble support, such as silica gel, alumina, commercial bentonitc and other oxides or silicates. Kept thus in close proximity on a large surface, the reagents are irradiated by microwaves in the absence of solvents and the reaction is very efficiently driven. At the end of the reaction the final products can simply be washed by a solvent and processed as usual. An acetylenic alcohol adsorbed on montmorillonite undergoes 92% rearrangement under microwaves, while, under conventional heating at the same temperature and for the same time, gives only a trace of the final producr[79-80].

In some cases the yield of the reaction is affected by the nature of the inorganic support. The influence of microwaves was demonstrated when the Pinacol/pinacolone rearrangement takes place in the presence of a charged phyllosilicate: moreover the conversion yield clearly depends on the nature of the inter layer cation of the solid support.

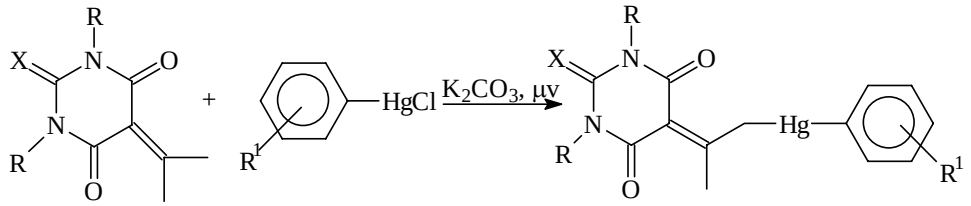
In addition to the benefit of saving solvents, a salient feature of this methodology is the selectivity of some reactions, such as those concerning protection and deprotection of functional groups. A neat selectivity was found in deacetylation of alkyl and aryl esters or among the different positions in the steroid nucleus of a bile acid methyl ester: in this last case, the different options are obtained simply by regulating the time of irradiation of the substrate dispersed on alumina[81].

Using clayfen, i.e. clay-iron (III) nitrate in the solid state, alcohols are readily oxidized in high yields to the corresponding carbonyl compounds. Sulphides can be oxidized to sulphoxides or to sulphones using sodium periodate on silica gel: under microwaves selectivity can be obtained by simply changing the ratio between regent to oxidant. Another example of reaction carded on a solid support is the condensation between 1-bromooctane and potassium acetate. These reactants do not display any property to absorb microwaves. On the contrary potassium acetate dispersed on alumina reaches 300^{o}C in 3 min under microwaves: this specific activation makes the reaction rapid; in this respect silica was found less efficient.

A very interesting field for the application of microwaves is the synthesis of radiopharmaceuticals or labeled drugs, especially when very short half-life positron emitters are employed. With isotopes such as 122 ^{o}C (3.6 min), 11^{o}C (20 min), 18^{o}C (110 min) the gain of even a few minutes in the reaction time could be of extreme importance for the final activity. The reactions of common radioisotopes are also improved in the presence of microwaves: reaction times as well as exposure to the radioactive emissions and the risks of possible contaminations are reduced[82-83].

1.5 Review on microwave assisted synthesis of barbituric acid and thiobarbituric acid derivatives.

M. Kidwai *et al.*[26], synthesized a series of new barbituryl /thiobarbituryl substituted organo-mercurial derivatives from pyridine derivatives and arylmercuric chloride over K_2CO_3 under microwave irradiations. This solvent less synthesis apart from eliminating organic solvent from workup step, also gave improved yield as compared to the conventional heating, with reacting time reduced from hours to minutes.

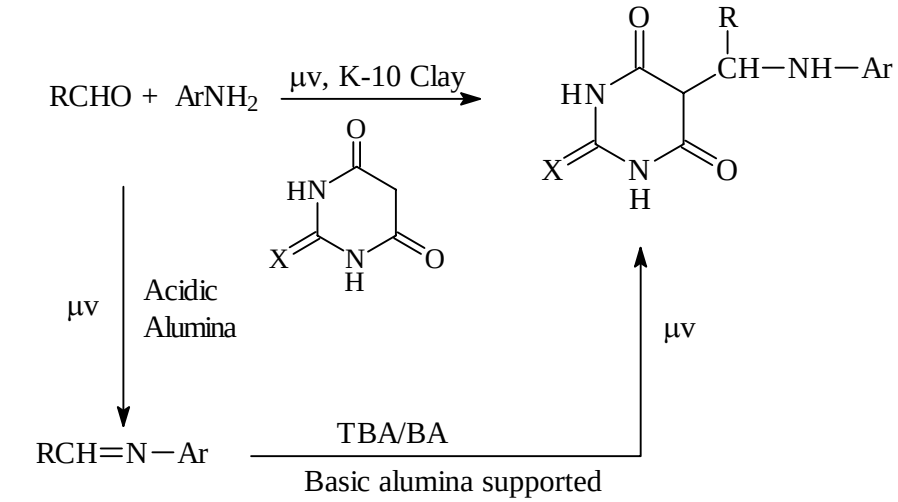


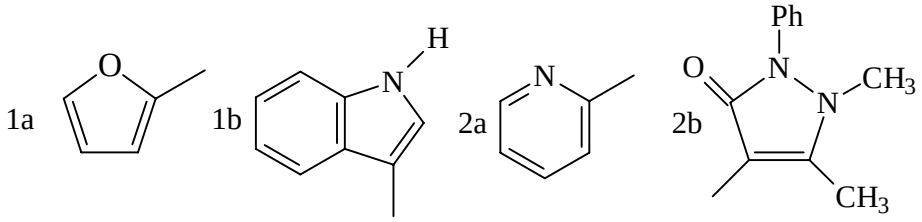
X = O ; R = H; R_1= H, 4-CH_3, 4-Br
X = S ; R = H, C_6H_5

A series of novel organotin compounds have been synthesized from reaction of tribenzyltin chloride with quinones/ barbiturates / triazoles on basic alumina in an open vessel under microwave irradiation by Bhanesh Dave *et al.*[84] The reaction time has been brought down from hours to seconds compared to conventional heating.

In 2005, Kidwei *et al.*[27] synthesized an expeditious solventless synthesis of novel Mannich bases of thiobarbiturates and barbiturates using montomorillonite clay under microwaves. This methodology eliminates the use of excess of solvent during the

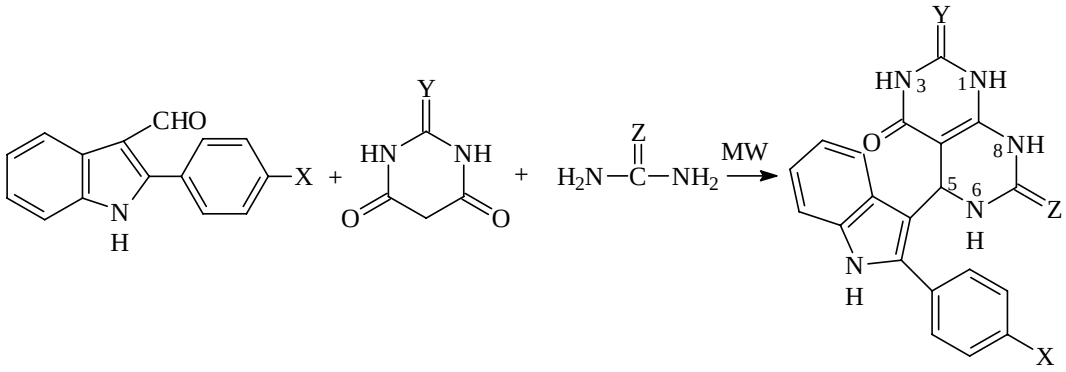
course of reaction. The reaction time is brought down from hours to minutes along with yield enhancement.





X = S
X= O

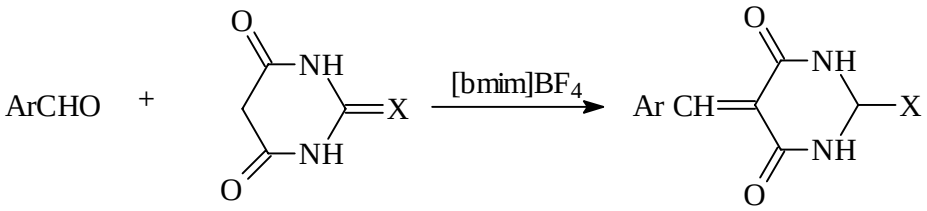
A series of 5-indolylpyrimido[4,5-d] pyrimidinones were obtained by multi comoponent reaction of 3-formyl indole thiobarbituric acid / barbituric acid and thiourea/ urea under microwave irradiation in dry by Ragini gupta *et al.*[30] in 2011.



4a: X = H, Y = O, Z = O; **4b:** X = H, Y = O, Z = S
4c: X = H, Y = O, Z = S; **4d:** X = H, Y = S, Z = S
4e: X = CH_3, Y = S, Z = O; **4f:** X = CH_3, Y = O, Z = S
4g: X = CH_3, Y = S, Z = S; **4h:** X = CH_3, Y = S, Z = S

A new microwave assisted synthesis of more 7-substituted 5-aryl-[Sup-1]*H*-pyrimido[4,5-d] pyrimidine -2,4-diones using mineral supports for their catalytic role and as energy transfer media is synthesized by Kidwei *et al.*[85] in 2007. The methodology eliminates the usage of solvent during the reaction. The rate enhancement and high yield is attributed to the coupling of solvent free conditions with microwaves.

In 2005, Chun Wang *et al*[86] used room temperature ionic liquid 1-n-butyl-3-methylimmidazolium terfluroborate ([bmim]BF_4) to promote the synthesis of 5-arylidene barbituric acids and thiobarbituric acid derivatives under the solid-state conditions of grinding or microwave irradiation without oranic solvent.



X = O, S

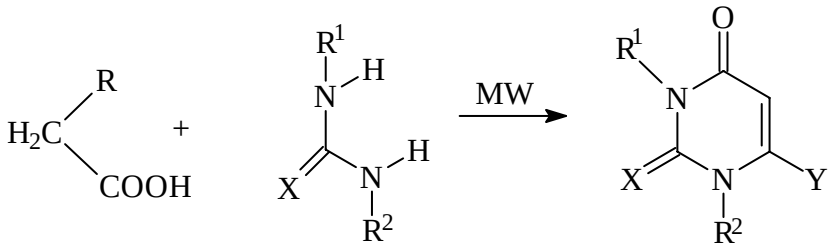
Reafatr M. Shaker *et al.*[87], in 2009, synthesized pyrido[3,2-d:6,5-d] dipyrimidine derivatives under microwave assisted conditions.

In 2003, Lu Jun *et al*[88], worked on the condensation reactions between aromatic aldehydes and thiobarbituric acid which were carried out under microwave irradiation, by grinding the reactants using NH_4OAc as a catalyst or with heating in water to give -arylidene thiobarbituric acid.

The reaction of aromatic aldehyde with 5,5-dimethyl-1,3-cyclohexandione under microwave irradiation has been carried out by the Shujiang *et al.*[89]

A series of 4,5-dihydro-3-hydroxy-1*H*-indazole derivatives have been prepared by Li Xiao-liu *et al.*[90] in 2008 from chalcones in good yield with assisted microwave irradiation, proving a facile method for the preparation of 4,5-dihydro-1*H*-indazole derivatives.

In 2005, Devi *et al.*[91] used an expedient method for the synthesis of 6-substituted uracils under microwave irradiation in a solvent free medium. In this method, condensation of malonic acid and ureas proceeds smoothly in the presence of acetic anhydride under microwave irradiation in solvent free conditions to give 6-hydroxy – uracils in excellent yields. Under identical conditions, the condensation of cyanoacetic acid and ureas in the presence of acetic anhydride, followed by cyclization in the presence of sodium hydroxide affords 6-amino-uracils in high yields. The work up procedures is simple and products need no purification.



R = COOH, CN

X = O, S
Y = OH, NH_2

Chapter - 2

RESULTS & DISCUSSION

2.0 Present work: Microwave Assisted Synthesis of Barbituric And Thiobarbituric Acid Derivatives.

2.1 Rationale

The diverse biological activity and coverage of a broad chemical space make barbituric acid derivatives excellent target compounds for organic and medicinal chemists. Owing to their ready availability and various fictionalization possibilities, the present barbituric acid and 2-thiobarbituric are convenient starting compounds for the preparation of different fused heterocycles and 5-substituted derivatives which are pharmacologically one of the most important classes of barbituric acid based compounds.

A huge literature has grown up in the field of synthesis and pharmaceutical activity of barbiturates and thiobarbiturates over the period of more than a century. Literature review[22, 92-96] shows that extensive works have been carried out on the multifarious synthesis, structure-reactivity relationship and pharmacological activity of barbituric and thiobarbaturic acid derivatives.

A large number of reports are available on the reaction of barbituric acid and thiobarbituric acid with carbonyl compounds-aldehydes, ketones and esters.[97-115] But it is observed that very little extent of work has been done on the reactions of barbituric acid and thiobarbiuturic acid with α,β – unsaturated carbonyl systems.[111,113,116,117] Having this in view, in continuation of our series of works [93-96,118] on barbituric acid and thiobarbituric acid derivative in the present work, we selected a number of diarylidene acetones[94-96,118,119] and arylidene-*p*-aminoacetophenones as the α,β – unsaturated carbonyl system having different substituents on the aromatic rings for reaction with barbituric acid and thiobarbituric acid as the active methylene component. Basically these fall under Michael and related reactions.

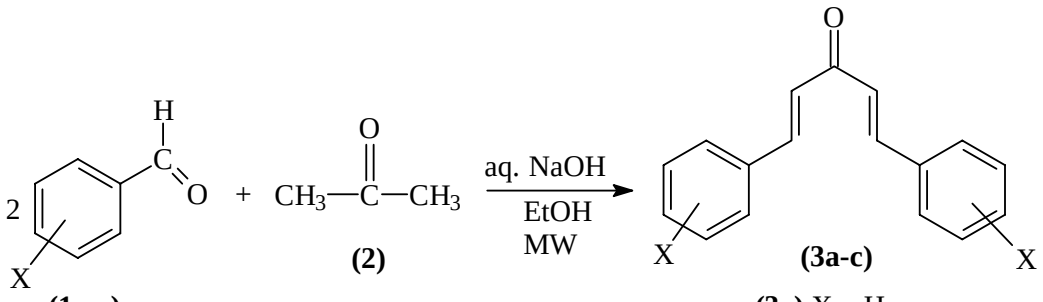
Although various routes for the synthesis of the compounds have been described, the majority of them involve a number of steps and the yields are poor[117]. Therefore, it is felt necessary to develop an efficient method. In the present work we report here a one step synthesis of barbituric and thiobarbituric acid derivatives under microwave

irradiation. This solvent less synthesis apart from eliminating organic solvent from work up step, also gave improved yield as compared to the conventional heating, with reaction time reduced from hours to minutes.

2.2 Results and discussion

Here a convenient approach for the synthesis of a series of 7,11–di–substituted phenyl–2–oxo/thioxo–1,3diazaspiro[5,5]undecane–4,6,9-triones and another series of 5, 7–disubstitutedphenyl–1,2,3,4–tetrahydro–2–oxo/thioxo–4–oxo–5*H*–pyrano[2,3–d] pyrimidines under microwave irradiation is reported.

The required starting materials diarylideneacetone and substituted diarylideneacetones, (**3a-c**) were prepared by carrying out reactions between acetone and the corresponding aromatic aldehyde using aqueous sodium hydroxide as catalyst under microwave irradiation(scheme-1). The solid product formed was filtered off under suction and washed with cold H_2O until neutral. Products were dried and recrystallized from aqueous EtOH.



(1a-c)

(1a) X = H
(1b) X = 4-OCH_3
(1c) X = 2-Cl

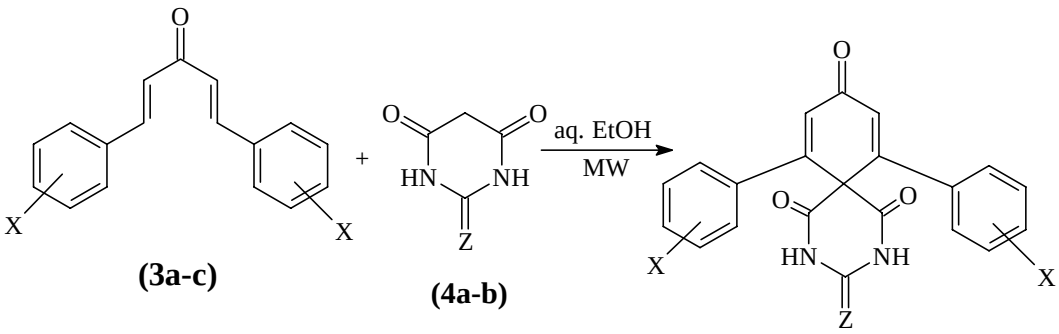
(2)

(3a-c)

(3a) X = H
(3b) X = 4-OCH_3
(3c) X = 2-Cl

Scheme-1

The products-(7,11-di-substituted phenyl-2-oxo/thioxo-1,3diazaspiro[5,5]undecane – 4,6,9triones),(**5a-f**) were synthesized by condensing the starting materials(**3a-c**) with barbituric and thiobarbituric acid in aqueous ethanol under microwave irradiation. The course of the reaction was followed by TLC on silica gel plates.



(3a-c)

(3a), X = H
(3b), X = 4–OCH_3
(3c), X = 2–Cl

(4a-b)

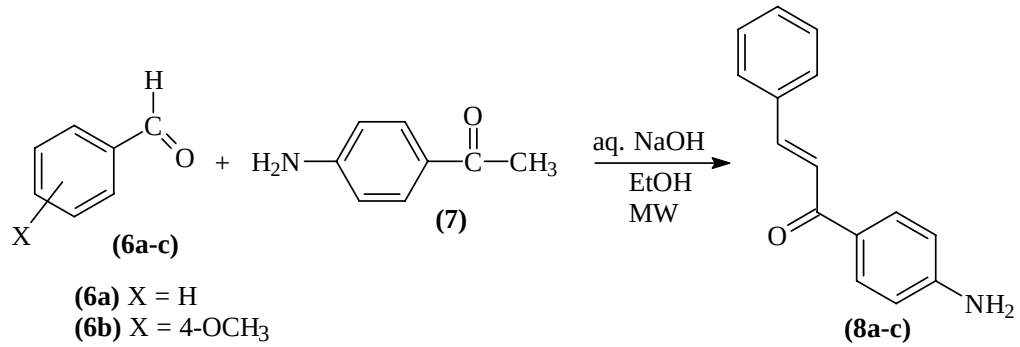
(4a), Z = O
(4b), Z = S

(5a-f)

(5a), X = H, Z = O
(5b), X = H, Z = S
(5c), X = 4–OCH_3, Z = O
(5d), X = 4–OCH_3, Z = S
(5e), X = 2–Cl, Z = O
(5f), X = 2–Cl, Z = S

Scheme-2

Another group of starting materials of arylidene–4–aminoacetophenones and substituted arylidene–4–aminoacetophenones), **(8a-c)** were prepared by the condensation of *p*-aminoacetophenone with benzaldehydesand substituted benzaldehydes(scheme-3) . The reactions were carried out in presence of alkali under microwave irradiation. After usual workup, the crude products were dried and recrystallized from aq. EtOH.



(6a-c)

(6a) X = H
(6b) X = 4-OCH_3
(6c) X = 2-Cl

(7)

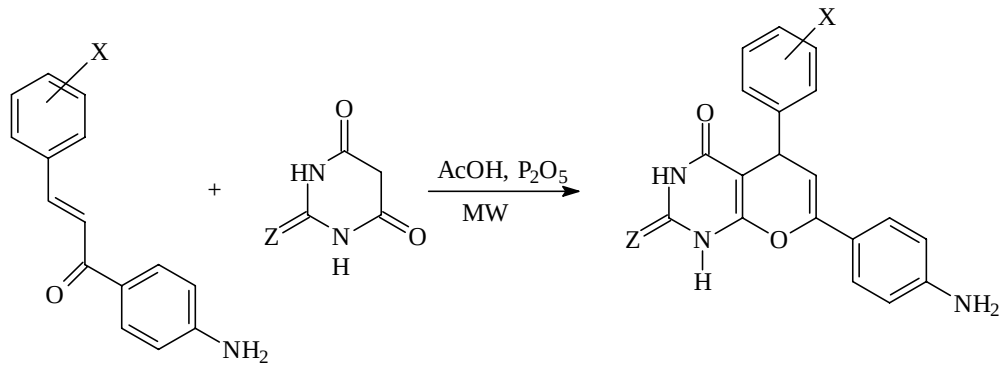
(8a-c)

(8a) X = H
(8b) X = 4-OCH_3
(8c) X = 2-Cl

Scheme-3

Compounds 5,7–disubstituted phenyl–1,2,3,4–tetrahydro–2–oxo/thiooxo–4–oxo–5*H*–pyrano[2,3–d] pyrimidines(**10a-f**) have been synthesized in single step by the condensation of barbituric and thiobarbituric acid with starting materials **(8a-c)** in glacial acetic acid in the presence of phosphorous pentoxide under microwave

irradiation (scheme-4). The course of the reaction was followed by TLC on silica gel plates.



(8a-c)

(8a), X = H
(8b), X = 4–OCH_3
(8c), X = 2–Cl

(9a-b)

(9a), Z = O
(9b), Z = S

(10a-f)

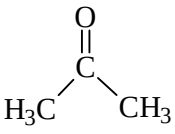
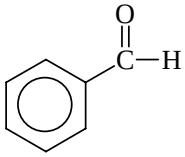
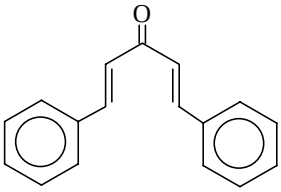
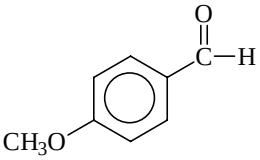
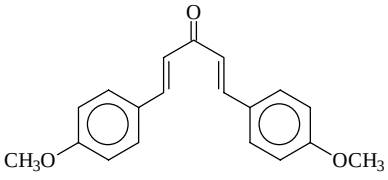
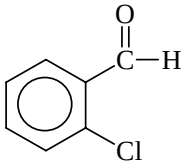
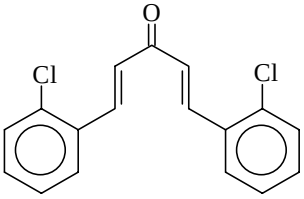
(10a), X = H, Z = O
(10b), X = H, Z = S
(10c), X = 4–OCH_3, Z = O
(10d), X = 4–OCH_3, Z = S
(10e), X = 2–Cl, Z = O
(10f), X = 2–Cl, Z = S

Scheme-4

2.3 Synthesis of starting materials (3a-c)

Three starting materials–dibenzylideneacetone, di-4-methoxybenzylidene acetone and di-2-chlorobenzylideneacetone were synthesized by the condensation reaction of acetone and corresponding aromatic aldehyde.

Table 1: Synthesis of starting materials dibenzylideneacetone and substituted dibenzylideneacetones, [3a-c].

Entry	Acetone	Benzyldehyde/ substituted benzyldehyde	Products	Yield %
I		 **(1a)**	 **(3a)**	85%
II		 **(1b)**	 **(3b)**	80%
III		 **(1c)**	 **(3c)**	83%

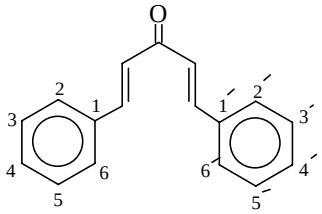
2.3.1 Characterization of starting materials

2.3.1.1 Characterization of dibenzylideneacetone,(3a):

The compound was yellow color; m.p.111-112^{0}C, yield 85%. The product was characterized by its UV, IR, and ^{1}H NMR and ^{13}C NMR spectral data.

The UV spectrum (fig-1) of the compound (**3a**) showed λ_{max} at 329 nm due to $\pi \rightarrow \pi^*$ of C=C-C=O and 229 nm due to $\pi \rightarrow \pi^*$ of C=C of phenyl group.

In the IR (KBr) spectrum (fig-2) of the compound (**3a**), the absorption band at 1651.0 cm^{-1} is due to the conjugation of the carbonyl group with double bond. The absorption at 1625.9 cm^{-1} was found for C=C double bond stretching, 1000-650 cm^{-1} absorption bands were obtained due to the =C-H out of plane of alkene. Aromatic stretching absorption band showed at 3051.2 $cm.^{-1}$ Aromatic C=C ring stretching absorption band was found at 1446.5 cm^{-1} region, 900-690 cm^{-1} absorption bands found for the aromatic =C-H out of plane bending vibration. Absorption at 694.3 cm^{-1} indicates the mono substituted benzene ring.



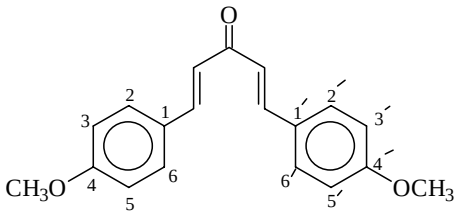
(3a)

2.3.1.2 Characterization of di-4-methoxybenzylideneacetone, (3b):

The compound was of brown color; m.p. 129-131^{0}C, yield 80%. The product was characterized by its UV, IR, ^{1}H NMR and ^{13}C NMR spectral data.

The UV spectrum (fig-3) of the compound showed λ_{max} at 366 nm due to $\pi \rightarrow \pi^*$ of C=C–C=O and at 240 nm due to $\pi \rightarrow \pi^*$ of C=C of phenyl group.

In the IR (KBr) spectrum (fig-4) of the compound **3b**, the absorption band at 1654.8 cm^{-1} is due to the conjugation of the carbonyl group with double bond. The absorption at 1629.7 cm^{-1} was found for C=C double bond stretching, 1029-750 cm^{-1} absorption bands were obtained due to the =C–H out of plane of alkene. Aromatic CH stretching absorption band CH showed at 2960.5 $cm.^{-1}$ Aromatic C=C ring stretching absorption band was found at 1596.9 cm^{-1} region. 900-690 cm^{-1} absorption bands found for the aromatic =C–H out of plane bending vibration. Absorption at 835.1 cm^{-1} indicates the para-disubstituted benzene ring.



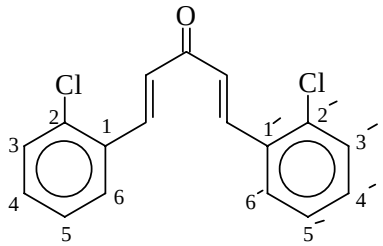
(3b)

2.3.1.3 Characterization of di-2-chlorobenzylideneacetone, (3c):

The compound was yellowish solid; m.p. 117-118^{0}C, yield 83%. The product was characterized by its UV, IR, ^{1}H NMR and ^{13}C NMR spectral data.

The UV spectrum (fig-5) of the compound showed absorption band at 233 nm due to $\pi \rightarrow \pi^*$ of C=C–C=O and at 209 nm due to $\pi \rightarrow \pi^*$ of C=C of phenyl group.

In the IR (KBr) spectrum (fig-6) of the compound **3c**, the absorption band at 1670.2 cm^{-1} due to the conjugation of the carbonyl group with double bond. The absorption at 1616.2 cm^{-1} was found for C=C double bond stretching, 1037-750 cm^{-1} absorption bands were obtained due to the =C–H out of plane of alkene. Aromatic stretching absorption band showed absorption at 3050.5 cm^{-1} .Aromatic C=C ring stretching absorption band was found at 1585.4 cm^{-1}, 900-690 cm^{-1} absorption bands found for the aromatic =C–H out of plane bending vibration. Absorption at 761.8 cm^{-1} indicates the ortho-disubstituted benzene ring.

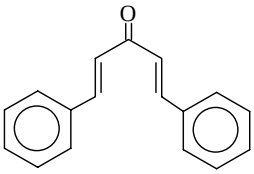
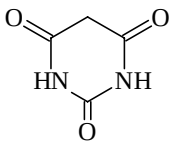
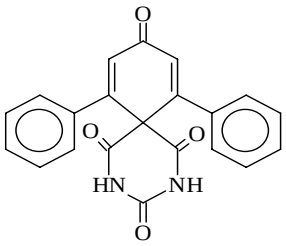
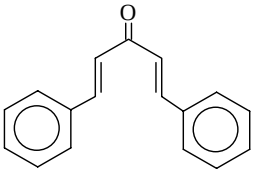
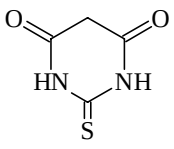
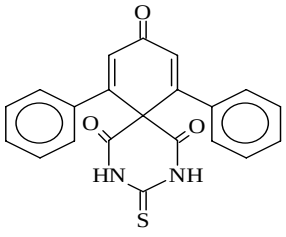
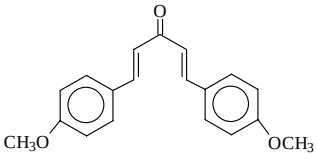
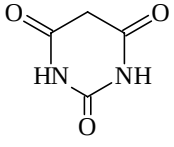
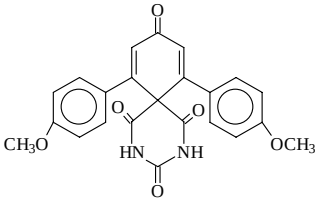
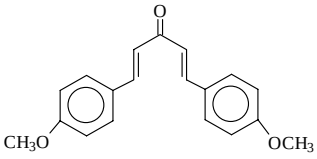
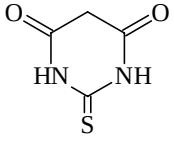
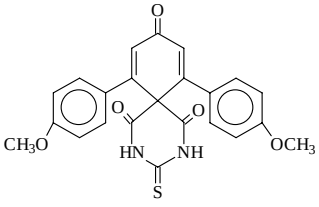


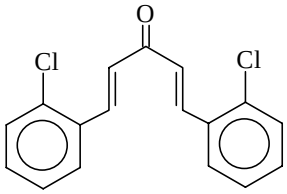
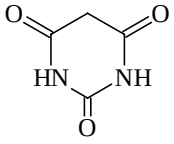
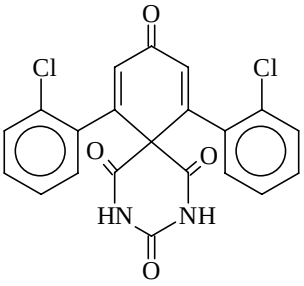
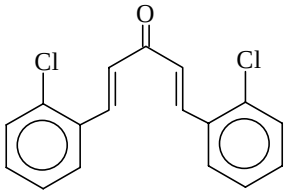
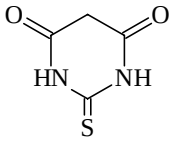
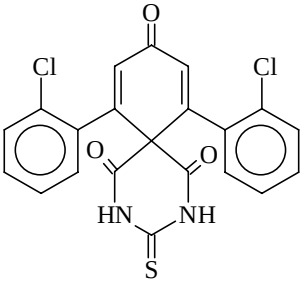
(3c)

2.4 Synthesis of 7,11-disubstituted phenyl-2-oxo/thioxo-1,3diazaspiro[5,5] undecane-4, 6, 9-triones, (5a-f)

Compounds **5a-f** were synthesized by the condensation reaction of starting materials **3a-f** with barbituric and thiobarbituric acids in aqueous ethanol under microwave irradiation.

Table 2: Synthesis of 7,11-disubstituted phenyl-2-oxo/thioxo-1,3diazaspiro[5,5] undecane-4,6,9-triones, **(5a-f)**

Entry	Reactant	Barbituric / Thiobarbituric acid	Products	Yield %
I	 **(3a)**	 **(4a)**	 **(5a)**	79%
II	 **(3a)**	 **(4b)**	 **(5b)**	74%
III	 **(3b)**	 **(4a)**	 **(5c)**	75%
IV	 **(3b)**	 **(4b)**	 **(5d)**	71%

Entry	Reactant	Barbituric/ Thiobarbituric acid	Products	Yield %
V	 **(3c)**	 **(4a)**	 **(5e)**	77%
VI	 **(3c)**	 **(4b)**	 **(5f)**	71%

2.4.1 Characterization of 7,11-di-phenyl and substituted di-phenyl 2-oxo/thioxo-1, 3-diazaspiro[5,5]undecane-4,6,9-triones compounds (5a-f):

2.4.1.1 Characterization of 7,11-di-phenyl-2-oxo-1, 3-diazaspiro[5,5]undecane-4, 6, 9-trione, 5a:

The compound was light yellow solid; m.p. 290-292^{0}C, yield 79%. The product was characterized by its UV, IR, ^{1}H NMR and ^{13}C NMR spectral data.

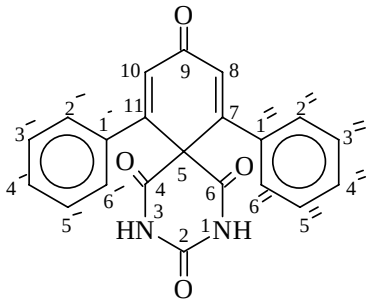
The UV spectrum (fig-7) of the compound showed absorption band, λ_{max}(nm) at 216 characteristic of such diazaspiro compounds.

In the IR(KBr) spectrum (fig-8) of the compound **5a**, the absorption band found at 3201.6 cm^{-1} shows the presence of N-H stretching absorption band, whereas a broad band at 1681.8 cm^{-1} represents the keto group (C=O) adjacent to N-H bond. The middle intensity vibration bands to the right (1640-1550) of the C=O absorption, is caused by the N-H bending vibration. A broad band of middle intensity in the 800-700 cm^{-1} region is responsible for the out of plane N–H wagging. Strong absorption bands in the 1342-1266 cm^{-1} region display strong C–N stretching absorption. The absorption band at 1705.0 cm^{-1} due to the conjugation of the carbonyl group with double bond. The absorption at 1625.8 cm^{-1} was found for the six membered cyclic double bond.1000-Absorption bands at 1000-650 cm^{-1} were obtained due to the =C–H out of plane of alkene. Aromatic stretching absorption band showed absorption at 3085.9 cm^{-1} .Aromatic C=C ring stretch absorption bands were found in pair at 1600 cm^{-1} region. Absorption bands at 900-690 cm^{-1} found for the aromatic =C–H out of plane bending vibration. Absorption band at 702.0 cm^{-1} indicates mono substitution of benzene ring.

The ^{1}H NMR spectrum (fig-9) of the compound showed the peak at δ_H 10.33 (s, 2H, -NH-) due to the N–H protons in the compound which were strongly deshielded and appeared as singlet in the ^{1}H NMR spectrum. The protons at the position C-8 & C-10 appeared as a doublet due to the meta coupling and the chemical shift was observed at δ_H 6.77 with J value 3.6 Hz. The chemical shift at δ_H 7.27 (d, 4H, Ar-H, J=7.69 Hz) was due to the similar CH protons of C-2′, C-6′ carbon of the both phenyl ring. The chemical shift position at δ_H 7.19 (t, 6H, Ar–H) showed as triplet due to the long rang coupling among the protons (C-3′, C-4′, C-5′) of the both ring.

The ^{13}C NMR spectrum (fig-10) of the compound showed the peak at δ_C 171.85 for C-9, at δ_C 170.60 for similar carbon of C-4 & C-6. The chemical shift at δ_C 148.55 represents the C-2 carbon. The chemical shift position at δ_C 136.68 showed C-8 & C-10 carbon. The chemical shafts at δ_C 128.37, δ_C 128.82, δ_C 127.72 and δ_C 125.52 represent the C-1′, C-3′ C-5′, C-2′ C-6′ C-4′ carbon of the both phenyl group respectively. The peak at δ_C 102.75 designated for similar carbon of C-7 C-11. The peak at δ_C 59.74 found due to the C-5 carbon.

On the basis of the UV, IR, ^{1}H NMR and ^{13}CNMR spectral data, the structure of this compound was assigned as-



(5a)

2.4.1.2 Characterization of 7,11-di-phenyl-2-thioxo-1,3-diazaspiro[5,5]undecane-4, 6,9-trione, 5b:

Light yellow solid was obtained with yield of 74%, m.p. 285-287^{o}C. By UV, IR, ^{1}H NMR and ^{13}C NMR spectral data, the structure of the compound was established.

The UV spectrum (fig-11) of the compound showed λ_{max} at 292nm due to $\pi \rightarrow \pi^{*}$ of C=C–C=O and at 241nm due to $\pi \rightarrow \pi^{*}$ of C=S group.

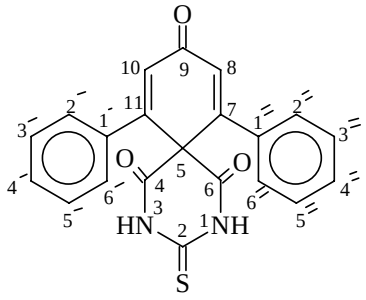
In the IR(KBr) spectrum (fig-12) of the compound **5b**, the absorption band found at 3138.0 cm^{-1}is due to the N-H stretching absorption, whereas a band at 1678.0 cm^{-1} represents the keto group (C=O) adjacent to N-H bond. Strong absorption bands in the 1377-1240 cm^{-1} region display strong C-N stretching absorption. The absorption band at 1708.8 cm^{-1} is due to the conjugation of the carbonyl group with double bond. Absorption of the internal double bond in the cyclohexene system is found at 1535.2 cm.$^{-1}$ Aromatic C-H stretching absorption band showed absorption at 2905.5 cm.$^{-1}$ Aromatic C=C ring stretch absorption band was found at 1433.0 cm.$^{-1}$ 705.9 cm^{-1} strong absorption band found for the aromatic mono substitution. A strong absorption band at 1149.5 cm^{-1} showed the presence of the thiocarbonyl (C=S) group.

The ^{1}H NMR spectrum (fig-13) of the compound showed , the peak at δ_{H} 11.26 (s, 2H,-NH-) due to the N-H protons in the compound which were strongly deshielded and appeared as singlet in the ^{1}H NMR spectrum. The similar protons at the position C-8 &

C-10 appeared as a doublet due to the meta coupling and the chemical shift was observed at δ_H 6.53 with J value 4.08 Hz. The chemical shift at δ_H 7.87 (dd, 4H, Ar-H, J=10.28 Hz) was due to the similar CH protons of C-2′,C-6′ carbon of the both phenyl ring. The chemical shift position at δ_H 7.62 (t, 6H, Ar-H) showed as triplet due to the long range coupling among the protons (C-3′,C-4′,C-5′) of the both ring.

The ^{13}C NMR spectrum (fig-14) of the compound showed the peak at δ_C 176.16 for C-9, at δ_C 169.69 for similar carbon of C-4 & C-6. The chemical shift at δ_C 168.22 represents the C-2 carbon. The chemical shift position at δ_C 136.51 showed C-8 & C-10 carbon. The chemical shifts at δ_C 129.96, δ_C 130.24, δ_C 127.69 and δ_C 126.01 represent the C-1′, C-3′ C-5′, C-2′ C-6′ C-4′ carbon of the both phenyl group respectively. The peak at δ_C 102.51 designated for similar carbon of C-7 C-11. The peak at δ_C 58.72 found due to the C-5 carbon.

On the basis of the UV, IR, ^{1}H NMR and ^{13}CNMR spectral data, the structure of this compound was assigned as-



(5b)

2.4.1.3 Characterization of 7, 11-di-*p*-methoxyphenyl-2-oxo-1,3-diazaspiro[5,5] undecane-4,6,9-trione, (5c):

The compound **5c** was light brown solid with m.p. 295-297^{0}C, yield 75%. The structure of the compound was assigned by spectral data.

The UV spectrum (fig-15) of the compound showed absorption bands, λ_{max}(nm) at 362.6

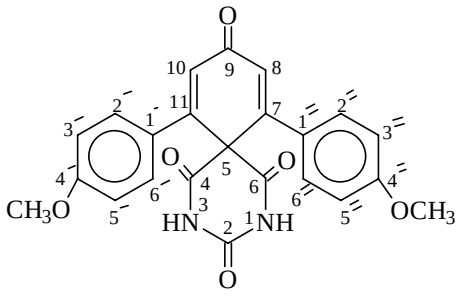
In the IR(KBr) spectrum (fig-16) of the compound **5c**, the absorption band found at 3425.3 cm^{-1}, due to the N-H stretching absorption, where as a broad band at 1689.5

cm^{-1} represents the keto group (C=O) adjacent to N-H bond. Strong absorption band at 1253.6 cm^{-1} display strong C-N stretching absorption. The absorption band at 1706.9 cm^{-1} is due to the conjugation of the carbonyl group with double bond. Absorption of the internal double bond in the cyclohexene system found at 1598.9 $cm.^{-1}$ Absorption at 1512.1 cm^{-1} found for the aromatic C=C ring stretch. Aromatic stretching absorption band showed absorption at 2947.0 $cm.^{-1}$ Aromatic C=C ring stretch absorption bands was found at 1446.5 $cm.^{-1}$ Strong absorption band found at 833.2cm^{-1} for the aromatic para-disubstituted ring. A strong absorption band at 1172.6 cm^{-1} found for the C-O stretch. The absorption at 2833 cm^{-1} indicates the aliphatic C-H bond present in the compound. The absorption at 1253.6 cm^{-1} found due to the C-H bond of $–OCH_3$ group.

The ^1H NMR spectrum (fig-17) of the compound showed , the peak at δ_H 10.40 (s,2H, -NH-) due to the N-H protons in the compound which were strongly deshielded and appeared as singlet in the ^1H NMR spectrum. The similar protons at the position C-8 & C-10 appeared as a doublet due to the meta coupling and the chemical shift was observed at δ_H 6.92 with J value 4.4 Hz. The chemical shift at δ_H 7.69(d, 4H, Ar-H, J=9.6 Hz) was due to the similar CH protons of C-3′, C-5′ carbon of the both phenyl ring. The chemical shift position at δ_H 7.55 (d, 4H, Ar-H, J=8.8 Hz) showed as doublet with J value 8.8 Hz, due to the protons of (C-2′ C-6′) of the both ring. The chemical shift position at δ_H 3.84(s, 6H,-OCH_3) was found in the form of singlet due to the two $–OCH_3$ groups.

The ^{13}C NMR spectrum (fig-18) of the compound showed the peak at δ_C 173.05 for C-9, at δ_C 168.25 for similar carbon of C-4 & C-6. The chemical shift at δ_C 167.10 represents the C-2 carbon. The peak at δ_C 159.59 was found due to the C-4′ carbon. The chemical shift position at δ_C 136.35 showed C-8 & C-10 carbon. The chemical shifts at δ_C 120.03, δ_C 114.51and δ_C 128.11 represent the C-1′, C-3′ C-5′and C-2′ C-6′ carbon of the both phenyl group respectively. The peak at δ_C 101.91 designated for similar carbon of C-7 C-11. The peak at δ_C 59.45 found due to the C-5 carbon and peak at δ_C 55.06 found for-OCH_3 group respectively.

On the basis of the UV, IR, ^1H NMR and ^{13}CNMR spectral data, the structure of this compound was assigned as-



(5c)

2.4.1.4 Characterization of 7,11-di-4-methoxyphenyl-2-thioxo-1,3-diazaspiro[5,5] undecane-4,6,9-trione, (5d):

A yellow color compound was obtained with 71% yield; m.p.282-284^{0}C. The structure of the compound was established by spectral data.

The UV spectrum (fig-19) of the compound showed absorption bands, λ_{max} (nm) at 231

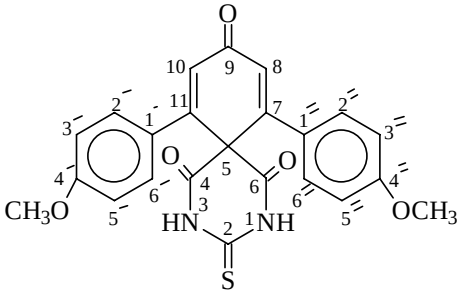
In the IR(KBr) spectrum (fig-20) of the compound **5d**, the absorption band found at 3190.0 cm^{-1}, due to the N-H stretching absorption, whereas a broad band at 1610.5 cm^{-1} represents the keto group (C=O) adjacent to N-H bond. Strong absorption band at 1251.7 cm^{-1} display strong C-N stretching absorption. The absorption band at 1699.2 cm^{-1} due to the conjugation of the carbonyl group with double bond. Absorption of the internal double bond in the cyclohexene system found at 1598.9cm.$^{-1}$ Absorption at 1512.1 cm^{-1} found for the aromatic C=C ring stretch. Aromatic stretching absorption band showed absorption at 2954.7 cm.$^{-1}$ Aromatic C=C ring stretch absorption bands was found at 1423.4 cm.$^{-1}$ Strong absorption band found at 835.1 cm^{-1} for the aromatic para-disubstituted ring. A strong absorption band at 1151.4 cm^{-1} for thiocarbonyl (C=S) group. The absorption at 2837.1 cm^{-1} indicates the aliphatic C-H bond (-OCH_3) present in the compound. The absorption at 1251.7 cm^{-1} found due to the C-O bond attached to aromatic ring and at 1180.4 cm^{-1} due to the C-O bond of –OCH_3 group.

The ^{1}H NMR spectrum (fig-21) of the compound showed , the peak at δ_H 11.33 (s,2H, -NH-) due to the N-H protons in the compound which were strongly deshielded and appeared as singlet in the ^{1}H NMR spectrum. The similar protons at the position C-8 & C-10 appeared as a doublet due to the long range coupling and the chemical shift was

observed at δ_H 6.89 with J value 4.0 Hz. The chemical shift at δ_H 7.77 (d, 4H, Ar-H, J=8.8 Hz) was due to the similar CH protons of C-3′, C-5′ carbon of the both phenyl ring. The chemical shift position at δ_H 7.31 showed as doublet with J value 8.8 Hz, due to the protons of (C-2′ C-6′) of the both ring. The chemical shift position at δ_H 3.956 was found in the form of singlet due to the two $-OCH_3$ group.

The ^{13}C NMR spectrum (fig-22) of the compound showed the peak at δ_C 177.75 for C-9, at δ_C 175.14 for similar carbon of C-4 & C-6. The chemical shift at δ_C 169.70 represents the C-2 carbon. The peak at δ_C 161.19 was found due to the C-4′ carbon. The chemical shift position at δ_C 137.05 showed C-8 & C-10 carbon. The chemical shifts at δ_C 119.41, δ_C 113.51and δ_C 128.31 represent the C-1′, C-3′ C-5′and C-2′ C-6′ carbon of the both phenyl group respectively. The peak at δ_C 102.01 designated for similar carbon of C-7 C-11. The peak at δ_C 60.25 found due to the C-5 carbon and peak at δ_C 55.35 found for-OCH_3 groups respectively.

On the basis of the UV, IR, ^1H NMR and ^{13}CNMR spectral data, the structure of this compound was assigned as-



(5d)

2.4.1.5 Characterization of 7,11-di-2-chlorophenyl-2-oxo-1,3-diazaspiro[5, 5]undecane-4, 6,9-trione, (5e):

The compound was yellow solid; yield 77%, m.p. 268-270^{0}C.

The UV spectrum (fig-23) of the compound showed absorption bands, λ_{max}(nm) at 235

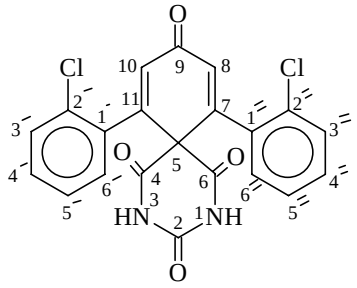
In the IR(KBr) spectrum (fig-24) of the compound **5e**, the absorption band found at 3350 cm^{-1}, due to the N-H stretching absorption, whereas a broad band at 1616.2 cm^{-1}

represents the keto group(C=O) adjacent to N-H bond. Strong absorption band at 1328.9 cm^{-1} display strong C-N stretching absorption the absorption band at 1665.5 cm^{-1} due to the conjugation of the carbonyl group with double bond. Absorption of the internal double bond in the cyclohexene system found at 1558.4$cm.^{-1}$ Absorption at 1587.3 cm^{-1} found for the aromatic C=C ring stretch. Aromatic stretching absorption band showed absorption at 3028.5 $cm.^{-1}$ Aromatic C=C ring stretch absorption bands was found at 1436.9 $cm.^{-1}$ 761.8 cm^{-1} strong absorption band found for the aromatic ortho-disubstituted ring. A strong absorption band at 1097.4 cm^{-1} found for aryl chloride(C-Cl) group.

The ^{1}H NMR spectrum (fig-25) of the compound showed , the peak at δ_H 10.79 (s,2H, -NH-) due to the N-H protons in the compound which were strongly deshielded and appeared as singlet in the ^{1}H NMR spectrum. The similar protons at the position C-8 C-10 appeared as a doublet due to the long range coupling and the chemical shift was observed at δ_H 7.17 with J value 4.4 Hz. The chemical shift at δ_H 7.71 (dd, 2H, Ar-H, J=8.0 Hz) was due to the similar CH protons of C-3′ carbon of the both phenyl ring. The chemical shift position at δ_H 7.44 (dd,2H,Ar-H,J=8.4) showed as double doublet with J value 8.4 Hz, due to the protons of C-6′ of the both ring. A peak at δ_H 7.35- 7.29 (m, 4H, Ar-H) was found for the protons of C-4′ and C-5′ of the both ring.

The ^{13}C NMR spectrum (fig-26) of the compound showed the peak at δ_C 176.01 for C-9, at δ_C 169.79 for similar carbon of C-4 C-6. The chemical shift at δ_C 168.22 represents the C-2 carbon. The chemical shift position at δ_C 136.38 showed C-8 & C-10 carbon. The chemical shifts at δ_C 134.94, δ_C 129.49, δ_C 129.05, δ_C 128.39, δ_C 126.11 and δ_C 117.93 represent the C-2′, C-6′, C-4′, C-3′, C-5′&C-1′ carbon of the both phenyl group respectively. The peak at δ_C 101.34 designated for similar carbon of C-7&C-11. The peak at δ_C 59.05 found due to the C-5 carbon.

On the basis of the UV, IR, ^{1}H NMR and ^{13}CNMR spectral data, the structure of this compound was assigned as-



(5e)

2.4.1.6 Characterization of 7,11-di-2-chlorophenyl-2-thioxo-1,3-diazaspiro[5,5] undecane-4,6,9-trione, (5f):

A light yellow solid was obtained with yield of 71%, M.P. 251-253^{o}C. By UV, IR, ^{1}H NMR and ^{13}C NMR spectral data, the structure of the compound was established.

The UV spectrum (fig-27) of the compound showed absorption band, λ_{max} (nm) at 294

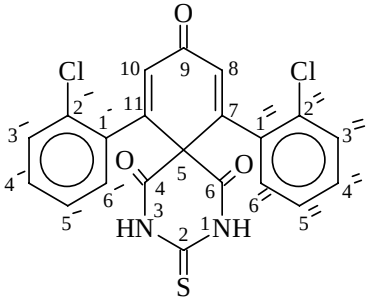
In the IR(KBr) spectrum (fig-28) of the compound **5f**, the absorption band found at 3236.3 cm^{-1}, due to the N-H stretching absorption, whereas a broad band at 1681.8 cm^{-1} represents the keto group(C=O) adjacent to N-H bond. Strong absorption band at 1238.2 cm^{-1} display strong C-N stretching absorption. The absorption band at 1701.1 cm^{-1} due to the conjugation of the carbonyl group with double bond. Absorption of the internal double bond in the cyclohexene system found at 1521.7cm.$^{-1}$ Absorption at 1541.0 cm^{-1} found for the aromatic C=C ring stretch. Aromatic stretching absorption band showed absorption at 3078.2 cm.$^{-1}$ Aromatic C=C ring stretch absorption bands was found at 1404.1 cm,$^{-1}$ 759.9 cm^{-1} strong absorption band found for the aromatic ortho-disubstituted ring. A strong absorption band at 1153.4 cm^{-1} found for thiocarbonyl group and at 1037.6 cm^{-1} for aryl chloride(C-Cl) group.

The ^{1}H NMR spectrum (fig-29) of the compound showed , the peak at δ_H 11.39 (s,2H , -NH-) due to the N-H protons in the compound which were strongly deshielded and appeared as singlet in the ^{1}H NMR spectrum. The similar protons at the position C-8 C-10 appeared as a doublet due to the long range coupling and the chemical shift was observed at δ_H 6.89 with J value 4.0 Hz. The chemical shift at δ_H 7.50 (d, 2H, Ar-H, J=8.4 Hz) was due to the similar CH protons of C-3′ carbon of the both phenyl ring. The chemical shift position at δ_H 7.44 showed as doublet with J value 8.8 Hz, due to the

protons of C-6′ of the both ring. A peak at δ_H 7.36-7.29 (m, 4H, Ar-H) was found for the protons of C-4′ & C-5′ of the both ring.

The ^{13}C NMR spectrum (fig-30) of the compound showed the peak at δC 176.39 for C-9, at δ_C 175.22 for similar carbon of C-4 & C-6. The chemical shift at δ_C 169.70 represents the C-2 carbon. The chemical shift position at δ_C 136.51 showed C-8 & C-10 carbon. The chemical shifts at δ_C 134.54, δ_C 129.99, δ_C 129.25, δ_C 128.01, δ_C 126.37 and δ_C 118.05 represent the C-2′, C-4′, C-6′, C-3′, C-5′& C-1′ carbon of the both phenyl group respectively. The peak at δ_C 101.01 designated for similar carbon of C-7&C-11. The peak at δ_C 60.03 found due to the C-5 carbon.

On the basis of the UV, IR, ^{1}H NMR and ^{13}CNMR spectral data, the structure of this compound was assigned as-

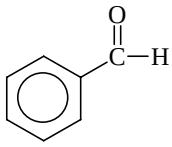
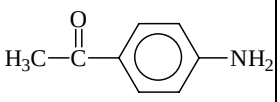
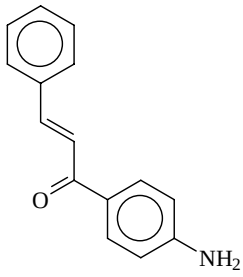
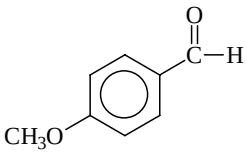
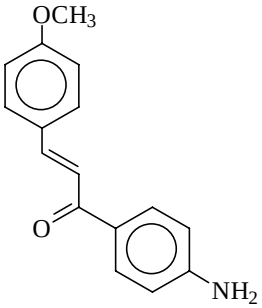
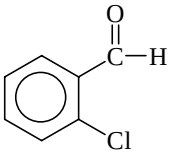
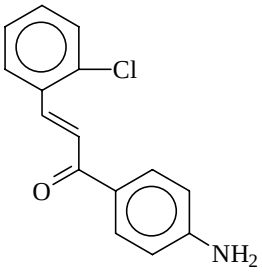


(5f)

2.5 Synthesis of starting materials, (8a-c)

By the condensation reaction of 4–aminoacetophenone and corresponding aromatic aldehyde three starting materials–benzylidene–4–aminoacetophenone, 4–methoxy benzylidene–4–aminoacetophenone and 2–chlorobenzylidene–4–aminoacetophenone were synthesized.

Table 3: Synthesis of starting materials (arylidine–4–aminoacetophenone) and substituted arylidene–4–aminoacetophenone **(8a-c)**.

Entry	Benzaldehyde and substituted benzaldehyde	4–amino acetophenone	Products	Yield %
I	 **(6a)**	 **(7)**	 **(8a)**	89%
II	 **(6b)**		 **(8b)**	80%
III	 **(6c)**		 **(8c)**	85%

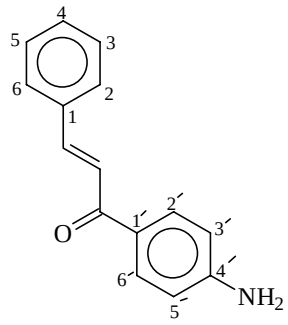
2.5.1 Characterization of starting materials

2.5.1.1 Characterization of bezylidene–4–aminoacetophenone (8a):

The compound was yellow solid; m.p.166-167^{0}C, yield 89%. The product was characterized by its UV, IR, ^{1}H NMR and ^{13}C NMR spectral data.

The UV spectrum (fig-31) of the compound showed absorption band at 226nm due to $\pi \rightarrow \pi^*$ of C=C-C=O and at 202nm due to $\pi \rightarrow \pi^*$ of C=C group.

In the IR (KBr) spectrum (fig-32) of the compound **8a**, two absorption bands found at 3460.1cm^{-1} and 3340.5 cm^{-1} indicate the presence of –NH_2 group. The middle intensity vibration bands to the right (1640-1550) of the C=O absorption, caused by the N-H bending vibration. A broad band of middle intensity in the 800-700 cm^{-1} region is responsible for the out of plane N-H wagging. Strong absorption bands in the 1342-1266 cm^{-1} region display strong C-N stretching absorption. The absorption band at 1654.8 cm^{-1} due to the conjugation of the carbonyl group with double bond. The absorption at 1629.7 cm^{-1} was found for acyclic double bond.1000-650 cm^{-1} absorption bands were obtained due to the =C-H out of plane of alkene. Aromatic stretching absorption band showed absorption at 3085.5 cm.$^{-1}$ Aromatic C=C ring stretch absorption bands was found at 1596.9 cm^{-1}. Absorption at 690.5 cm^{-1} indicates mono substitution of benzene ring and at 815.5 cm^{-1} indicates para substitution.



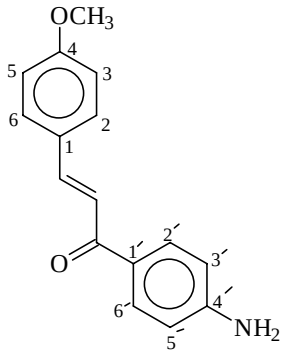
(8a)

2.5.1.2 Characterization of 4-methoxybezylidene–4–aminoacetophenone, (8b):

The compound was light brown solid; m.p. 175-176^{0}C yields 80%. The product was characterized by its UV, IR, ^{1}H NMR and ^{13}C NMR spectral data.

The UV spectrum (fig-33) of the compound showed absorption band at 231nm due to $\pi \rightarrow \pi^*$ of C=C-C=O and at 213nm due to $\pi \rightarrow \pi^*$ of C=C group.

In the IR (KBr) spectrum (fig-34) of the compound **8b**, two absorption bands found at 3448.5 cm^{-1} and 3361.7 cm^{-1} indicate the presence of –NH_2 group. The middle intensity vibration bands to the right (1640-1550) of the C=O absorption, caused by the N-H bending vibration. A broad band of middle intensity in the 800-700 cm^{-1} region is responsible for the out of plane N–H wagging. Strong absorption bands in the 1342-1266 cm^{-1} region display strong C–N stretching absorption. The absorption band at 1670.2 cm^{-1} due to the conjugation of the carbonyl group with double bond. The absorption at 1589.2 cm^{-1} was found for acyclic double bond.1000-650 cm^{-1} absorption bands were obtained due to the =C–H out of plane of alkene. Aromatic stretching absorption band showed absorption at 2950.5 cm.$^{-1}$ Aromatic C=C ring stretch absorption band was found at 1514.o cm^{-1}. Absorption at 840.5 cm^{-1} indicates para substitution of benzene ring.



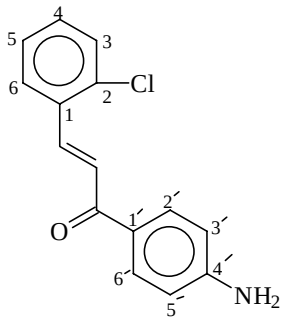
(8b)

2.5.1.3. Characterization of 2–chlorobezylidene–4–aminoacetophenone (8c):

The compound was light yellow solid; m.p.172-173^{0}C yields 85%. The product was characterized by its UV, IR, ^{1}H NMR and ^{13}C NMR spectral data.

The UV spectrum (fig-35) of the compound showed absorption band at 371nm due to $\pi \rightarrow \pi^*$ of C=C-C=O and at 231nm due to $\pi \rightarrow \pi^*$ of C=C group.

In the IR (KBr) spectrum (fig-36) of the compound **8c**, two absorption bands found at 3332.8 cm^{-1} and 3226.7 cm^{-1} indicate the presence of –NH_2 group. The middle intensity vibration bands to the right (1640-1550) of the C=O absorption, caused by the N-H bending vibration. A broad band of middle intensity in the 800-700 cm^{-1} region is responsible for the out of plane N-H wagging. Strong absorption bands in the 1342-1266 cm^{-1} region display strong C-N stretching absorption. The absorption band at 1649.0 cm^{-1} due to the conjugation of the carbonyl group with double bond. The absorption at 1606.6 cm^{-1} was found for acyclic double bond.1000-650 cm^{-1} absorption bands were obtained due to the =C–-H out of plane of alkene. Aromatic stretching absorption band showed absorption at 3050.5 cm.$^{-1}$ Aromatic C=C ring stretch absorption band was found at 1583.4 cm^{-1}. Absorption at 829.3 cm^{-1} indicates para substitution of benzene ring and 752.2 cm^{-1} indicates ortho substitution.

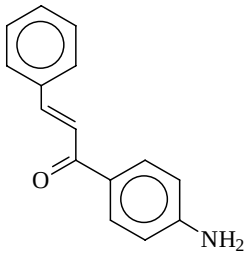
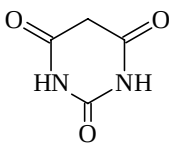
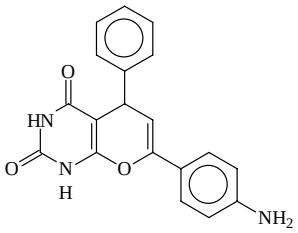
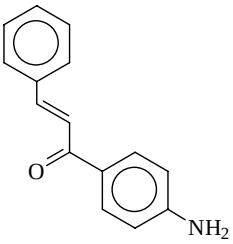
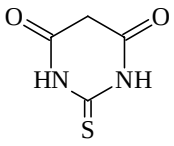
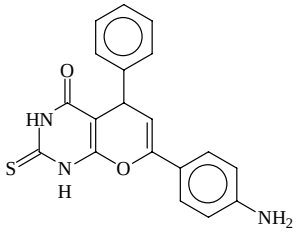
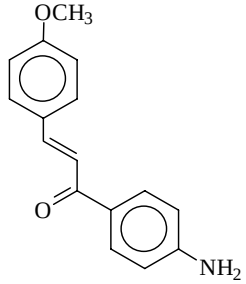
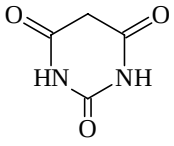
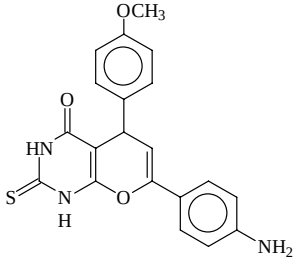


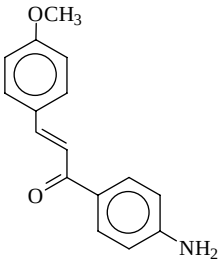
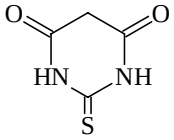
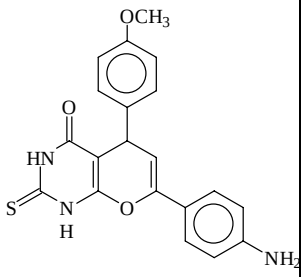
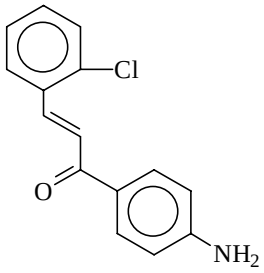
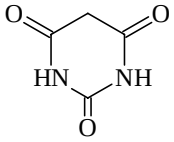
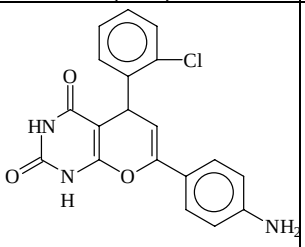
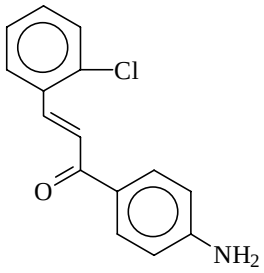
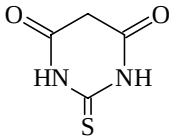
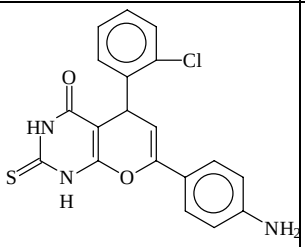
(8c)

2.6 Synthesis of 5,7–disubstitutedphenyl–1,2,3,4–tetrahydro–2–oxo/thioxo–4–oxo–5*H*–pyrano[2,3–d]pyrimidines, (10a-f):

By the condensation reaction of starting materials **(8a-c)** with barbituric or thiobarbituric acid in glacial acetic acid in the presence of phosphorous pentoxide compounds **(10a-f)** have been synthesized under microwave irradiation.

Table 4: (5,7–disubstitutedphenyl–1,2,3,4tetrahydro–2-oxo/thioxo–4–oxo–5H–pyrano[2,3–d] pyrimidines), **(10a-f).**

Entry	Arylidene 4-amino acetophenone	Barbituric/thiobarbituric acid	Products	Yield %
I	 **(8a)**	 **(9a)**	 **(10a)**	87%
II	 **(8a)**	 **(9b)**	 **(10b)**	84%
III	 **(8b)**	 **(9a)**	 **(10c)**	81%

Entry	Arylidene 4-amino acetophenone	Barbituric/thiobarbituric acid	Products	Yield %
IV	 **(8b)**	 **(9b)**	 **(10d)**	80%
V	 **(8c)**	 **(9a)**	 **(10e)**	85%
VI	 **(8c)**	 **(9b)**	 **(10f)**	82%

2.6.1 Characterization of 5,7–disubstitutedphenyl–1,2,3,4-tetrahydro–2–oxo/thioxo–4–oxo– 5*H*–pyrano[2,3–d]pyrimidines, (10a-f):

2.6.1.1 Characterization of 7-(4-aminophenyl)-5-phenyl-1,2,3,4-tetrahydro-pyrano [2,3-d]pyrimidine– 2,4(5*H)*-dione (10a)

The compound was yellow solid; m.p. 293-295^{0}C, yield 87%. The product was characterized by its UV, IR, ^{1}H NMR and ^{13}C NMR spectral data.

The UV spectrum (fig-37) of the compound showed absorption band at 322nm due to $\pi \rightarrow \pi^*$ of C=C-C=O and at 227nm due to $\pi \rightarrow \pi^*$ of C=C group.

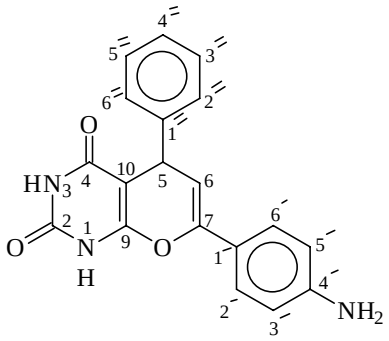
In the IR (KBr) spectrum (fig-38) of the compound **10a**, two absorption bands found at 3500.5cm^{-1} and 3410.5 cm^{-1} indicate the presence of –NH_2 group. A sharp and broad band at 3303.8 cm^{-1} indicates the presence of N-H group. The middle intensity vibration bands to the right (1640-1550) of the C=O absorption, caused by the N–H bending vibration. A broad band of middle intensity in the 800-700 cm^{-1} region is responsible for the out of plane N-H wagging. Strong absorption bands in the 1342-1266 cm^{-1} region display strong C-N stretching absorption. The absorption band at 1676.0 cm^{-1} due to the conjugation of the carbonyl group with double bond. The absorption at 1647.1 cm^{-1} was found for cyclic double bond.1000-650 cm^{-1} absorption bands were obtained due to the =C–H out of plane of alkene. Aromatic stretching absorption band showed absorption at 3085.5 cm.$^{-1}$ Aromatic C=C ring stretch absorption bands was found at 1595.0 cm^{-1}. Absorption at 695.5 cm^{-1} indicates mono substitution of benzene ring and at 825.5 cm^{-1}indicates para substitution. Absorption at 1176.5 cm^{-1} indicates the C–O bond of aliphatic system and 1220.9cm^{-1} indicates the aromatic C–O bond.

The ^{1}H NMR spectrum (fig-39) of the compound showed , the peak at δ_H 9.35 (s,2H, -NH-) due to the N–H protons in the compound which were strongly deshielded and appeared as singlet in the ^{1}H NMR spectrum. The protons at the position C-2″ C-6″ appeared as a doublet and the chemical shift was observed at δ_H 7.66 with J value 8.72 Hz. The chemical shift at δ_H 7.33(t, 3H, Ar-H) was due to the similar CH protons of C-3″ C-4″ C-5″ carbon. The chemical shift position at δ_H 7.14 (d,2H,Ar-H,J=7.8) showed as doublet due to the protons of C-2′ C-6′ carbon and at δ_H 6.78 showed doublet due to the protons of C-3′ C-5′ carbon. The proton at position 6 appeared as a doublet due to the vicinal coupling with the proton at position 5. The chemical shift was observed at δ_H 6.14 (d, 1H, CH, J=4.68).The 5-H in that compound gave signal at δ_H 4.27 (d, 1H, CH, J=4.68 Hz) as doublet due to the coupling of 5-H by 6-H with J value 4.68 Hz. The chemical shift at δ_H 3.50 (s, 2H,-NH_2) was obtained due to the –NH_2 group.

The ^{13}C NMR spectrum (fig-40) of the compound showed the peak at δ_C 164.03 for C-4, at δ_C 163.99 for C-2 and at 161.93 for C-9 carbon. The chemical shift at δ_C 140.88 represents the C-7 and at δ_C 137.75represents the C-6 carbon. The peaks at δ_C 133.35 and at δ_C 133.13 were found due to the C-1′&C-1″ carbon. The chemical shift position at δ_C 127.93 showed C-2′ & C-6′ carbon. The chemical shifts at δ_C 127.46, at δ_C 129.31

& at δ_C 129.06 represent the C-2″ &C-6″, C-3′&C-5′, C-3″ &C-5″ carbons respectively. The peaks at δ_C 127.35 and at δ_C 127.11 designated for carbons of C-4′&C-4″. The peak at δ_C 111.75 represents C-10. The peak at δ_C 31.87 found due to the C-5 carbon.

On the basis of the UV, IR, ^{1}H NMR and ^{13}CNMR spectral data, the structure of this compound was assigned as-



(10a)

2.6.1.2 Characterization of 7-(4-aminophenyl)-5-phenyl-2-thioxo-1, 2, 3, 4-tetrahydropyrano[2, 3-d]pyrimidine-4(5*H*)-one, **(10b)**

The compound was deep brown solid; m.p.275-276^{0}C yields 84%. The product was characterized by its UV, IR, ^{1}H NMR and ^{13}C NMR spectral data.

The UV spectrum (fig-41) of the compound showed absorption band at 299nm due to $\pi \rightarrow \pi^*$ of C=C-C=O

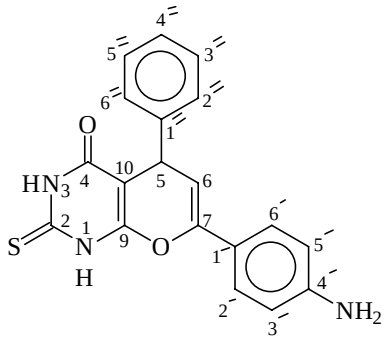
In the IR (KBr) spectrum (fig-42) of the compound **10b**, two absorption bands found at 3450.6 cm^{-1} and 3310.5 cm^{-1} indicate the presence of –NH_2 group. Absorption band at 3203.6 cm^{-1} indicates the presence of N-H group. The middle intensity vibration bands to the right (1640-1550) of the C=O absorption, caused by the N-H bending vibration. A broad band of middle intensity in the 800-700 cm^{-1} region is responsible for the out of plane N-H wagging. Strong absorption bands in the 1342-1266 cm^{-1} region display strong C-N stretching absorption. The absorption band at 1676.0 cm^{-1} due to the conjugation of the carbonyl group with double bond. The absorption at 1652.9 cm^{-1} was found for cyclic double bond.1000-650 cm^{-1} absorption bands were obtained due to the =C–H out of plane of alkene. Aromatic stretching absorption band showed absorption

at 3085.5 cm^{-1}. Aromatic C=C ring stretch absorption bands was found at 1596.9 cm^{-1}. Absorption at 685.5 cm^{-1}indicates mono substitution of benzene ring and at 835.6 cm^{-1} indicates para substitution. Absorption at1176.5 cm^{-1} indicates the C–O bond of aliphatic system and 1220.9cm^{-1} indicates the aromatic C–O bond.

The ^{1}H NMR spectrum (fig-43) of the compound showed , the peak at δ_H 10.31(s,2H,-NH-) due to the N-H protons in the compound which were strongly deshielded and appeared as singlet in the ^{1}H NMR spectrum. The protons at the position C-2″ & C-6″ appeared as a doublet and the chemical shift was observed at δ_H 7.91(d, 2H, Ar-H, J=8.49) with J value 8.49 Hz. The chemical shift at δ_H 7.74(m, 3H, Ar-H) was due to the similar CH protons of C-3″, C-4″&C-5″ carbon. The chemical shift position at δ_H 7.17 (d,2H,Ar-H,J=7.56) showed as doublet due to the protons of C-2′&C-6′ carbon and at δ_H 6.88 showed doublet due to the protons of C-3′&C-5′ carbon. The proton at position 6 appeared as a doublet due to the vicinal coupling with the proton at position 5. The chemical shift was observed at δ_H 6.24 (d, 1H, CH, J=4.60) with J value 4.60 Hz. The 5-H in that compound gave signal at δ_H 4.28 (d, 1H, CH, J=4.68) as doublet due to the coupling of 5-H by 6-H with J value 4.68 Hz. The chemical shift at δ_H 3.61 (s, 2H,-NH_2) was obtained due to the –NH_2 group.

The ^{13}C NMR spectrum (fig-44) of the compound showed the peak at δ_C 165.53 for C-4, at δ_C 163.99 for C-2 and at 162.13 for C-9 carbon. The chemical schift at δ_C 141.18 represents the C-7 and at δ_C 136.55 represents the C-6 carbon. The peaks at δ_C 132.35 and at δ_C 132.13 were found due to the C-1′&C-1″ carbon. The chemical schift position at δ_C 127.93 showed C-2′ & C-6′ carbon. The chemical schifts at δ_C 127.95, at δ_C 129.33& at δ_C 128.96 represent the C-2″ &C-6″, C-3′&C-5′, C-3″ &C-5″ carbons respectively. The peaks at δ_C 127.15 and at δ_C 126.91 designated for carbons of C-4′&C-4″. The peak at δ_C 32.07 found due to the C-5 carbon. The chemical shift at 112.15 was found for C-10 carbon.

On the basis of the UV, IR, ^{1}H NMR and ^{13}CNMR spectral data, the structure of this compound was assigned as-



(10b)

2.6.1.3 Characterization of 7-(4-aminophenyl)-5-(4-methoxyphenyl)-1,2,3,4-tetrahydro-pyrano[2,3-d]pyrimidine– 2,4(5*H)* -dione, (10c)

The compound was yellow solid; m.p. 297-298^{0}C, yield 81%. The product was characterized by its UV, IR, ^{1}H NMR and ^{13}C NMR spectral data.

The UV spectrum (fig-45) of the compound showed absorption band at 251nm due to π→ π * of C=C–C=O and at 222nm due to π→ π* of C=C group.

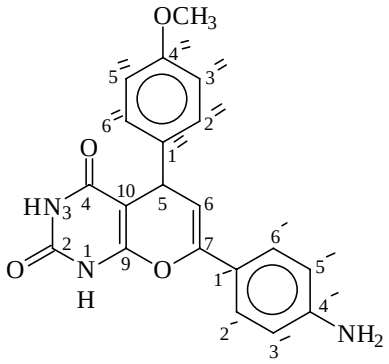
In the IR (KBr) spectrum (fig-46) of the compound **10c**, two absorption bands found at 3455.3 cm^{-1} and 3207.5 cm^{-1} indicate the presence of –NH_2 group. Absorption band at 3070.5 cm^{-1} indicates the presence of N-H group. The middle intensity vibration bands to the right (1640-1550) of the C=O absorption, caused by the N-H bending vibration. A broad band of middle intensity in the 800-700 cm^{-1} region is responsible for the out of plane N-H wagging. Strong absorption bands in the 1342-1266 cm^{-1} region display strong C-N stretching absorption. The absorption band at 1728.1 cm^{-1} due to the conjugation of the carbonyl group with double bond. The absorption at 1676.0 cm^{-1} was found for cyclic double bond.1000-650 cm^{-1} absorption bands were obtained due to the =C–H out of plane of alkene. Aromatic stretching absorption band showed absorption at 2885.5 cm.$^{-1}$ Aromatic C=C ring stretch absorption bands was found at 1550.7 cm^{-1}.Absorption at 805.5 cm^{-1}indicates para substitution of benzene ring. Absorption at1180.4 cm^{-1} indicates the C–O bond of aliphatic system and 1271.0 cm^{-1} indicates the aromatic C–O bond.

The ^{1}H NMR spectrum (fig-47) of the compound showed , the peak at δ_H 10.20 (s,2H,-NH-) due to the N–H protons in the compound which were strongly deshielded and

appeared as singlet in the ^{1}H NMR spectrum. The protons at the position C-2″ C-6″ appeared as a doublet and the chemical shift was observed at δ_H 7.40(d, 2H, Ar-H, J=8.84) with J value 8.84 Hz. The chemical shift at δ_H 7.29(d, 2H, Ar-H) was due to the similar CH protons of C-2′&C-6′ carbon with J value7.52 Hz. The chemical shift position at δ_H 6.97 (d,2H,Ar-H,J=8.0) showed as doublet due to the protons of C-3″&C-5″ carbon and at δ_H 6.75 showed doublet due to the protons of C-3′&C-5′ carbon. The proton at position 6 appeared as a doublet due to the vicinal coupling with the proton at position 5. The chemical shift was observed at δ_H 6.12 (d, 1H, CH, J=4.92) with J value 4.92 Hz. The 5-H in that compound gave signal at δ_H 4.35 (d, 1H, CH, J=4.6) as doublet due to the coupling of 5-H by 6-H with J value 4.6 Hz. The chemical shift at δ_H 3.81 (s, 3H,-OCH_3) was obtained due to the-OCH_3 group and at δ_H 3.55 (s, 2H,-NH_2) due to the –NH_2 group.

The ^{13}C NMR spectrum (fig-48) of the compound showed the peak at δ_C 164.01 for C-4, at δ_C 163.57 for C-2 and at 162.24 for C-9 carbon. The chemical shift at δ_C 141.36 represents the C-7 and at δ_C 137.55 represents the C-6 carbon. The peaks at δ_C 117.69 and at δ_C 119.07 were found due to the C-1′&C-1″ carbon. The chemical shift position at δ_C 130.35 showed C-2′ & C-6′ carbon. The chemical shifts at δ_C 130.79, at δ_C 115.60 & at δ_C 114.05 represent the C-2″ &C-6″, C-3′&C-5′, C-3″ &C-5″ carbons respectively. The peaks at δ_C 150.28 and at δ_C 155.13 designated for carbons of C-4′&C-4″. The chemical shift at δ_C 113.55 represents C-10 carbon. The peaks at δ_C 32.68 and at δ_C 55.79 found due to the C-5 and –OCH_3 group.

On the basis of the UV, IR, ^{1}H NMR and ^{13}CNMR spectral data, the structure of this compound was assigned as



(10c)

2.6.1.4 Characterization of 7-(4-aminophenyl)-5-(4-methoxyphenyl)-2-thioxo-1, 2, 3, 4-tetrahydropyrano[2, 3-d]pyrimidine-4(5*H*)-one, (10d)

The compound was light brown solid; m.p.281-283^{0}C, yield 80%. The product was characterized by its UV, IR, ^{1}H NMR and ^{13}C NMR spectral data.

The UV spectrum (49) of the compound showed absorption band at 284nm due to $\pi \rightarrow \pi^*$ of C=C-C=O

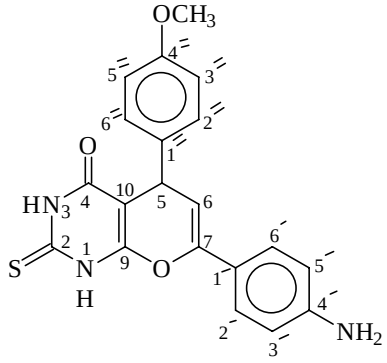
In the IR (KBr) spectrum (fig-50) of the compound **10d**, two absorption bands found at 3566.1cm^{-1} and 3544.9 cm^{-1} indicate the presence of –NH_2 group. Absorption band at 3446.6 cm^{-1} indicates the presence of N-H group. The middle intensity vibration bands to the right (1640-1550) of the C=O absorption, caused by the N-H bending vibration. A broad band of middle intensity in the 800-700 cm^{-1} region is responsible for the out of plane N-H wagging. Strong absorption bands in the 1342-1266 cm^{-1} region display strong C-N stretching absorption. The absorption band at 1662.5 cm^{-1} due to the conjugation of the carbonyl group with double bond. The absorption at 1654.8 cm^{-1} was found for cyclic double bond.1000-650 cm^{-1} absorption bands were obtained due to the =C-H out of plane of alkene. Aromatic stretching absorption band showed absorption at 2985.5 cm^{-1} .Aromatic C=C ring stretch absorption bands was found at 1512.1 cm^{-1}.Absorption at 835.4 cm^{-1}indicates para substitution of benzene ring. Absorption at1170.5 cm^{-1} indicates the C-O bond of aliphatic system and 1249.4cm^{-1} indicates the aromatic C-O bond.

The ^{1}H NMR spectrum (fig-51) of the compound showed , the peak at δ_H 10.87(s,2H,-NH-) due to the N–H protons in the compound which were strongly deshielded and appeared as singlet in the ^{1}H NMR spectrum. The protons at the position C-2″ & C-6″ appeared as a doublet and the chemical shift was observed at δ_H 7.49(d, 2H, Ar–H, J=8.48) with J value 8.48 Hz. The chemical shift at δ_H 7.30(d, 2H, Ar–H) was due to the similar CH protons of C-2′&C-6′ carbon with J value8.4 Hz. The chemical shift position at δ_H 6.98 (d,2H,Ar-H,J=8.12) showed as doublet due to the protons of C-3″&C-5″ carbon and at δ_H 6.86 showed doublet due to the protons of C-3′&C-5′ carbon. The proton at position 6 appeared as a doublet due to the vicinal coupling with

the proton at position 5. The chemical shift was observed at δ_H 6.18 (d, 1H, CH, J=4.68) with J value 4.68 Hz. The 5-H in that compound gave signal at δ_H 4.38 (d, 1H, CH, J=5.28) as doublet due to the coupling of 5-H by 6-H with J value 5.28 Hz. The chemical shift at δ_H 4.11sz (s, 3H,-OCH_3) was obtained due to the-OCH_3 group and at δ_H 3.57 (s, 2H,-NH_2) due to the –NH_2 group.

The ^{13}C NMR spectrum (fig-52) of the compound showed the peak at δ_C 166.41 for C-4, at δ_C 163.37 for C-2 and at 162.24 for C-9 carbon. The chemical shift at δ_C 143.31 represents the C-7 and at δ_C 135.59 represents the C-6 carbon. The peaks at δ_C117.35 and at δ_C 119.57 were found due to the C-1′&C-1″ carbon. The chemical shift position at δ_C 131.12 showed C-2′ & C-6′ carbon. The chemical shifts at δ_C 131.55, at δ_C 116.73 & at δ_C 114.50 represent the C-2″ &C-6″, C-3′&C-5′, C-3″ &C-5″ carbons respectively. The peaks at δ_C 149.28 and at δ_C 154.13 designated for carbons of C-4′&C-4″. The chemical shift at δ_C 112.49 represents C-10 carbon. The peaks at δ_C 31.96 and at δ_C 53.37 found due to the C-5 and –OCH_3 group.

On the basis of the UV, IR, ^{1}H NMR and ^{13}CNMR spectral data, the structure of this compound was assigned as



(10d)

2.6.1.5. Characterization of 7-(4-aminophenyl)-5-(2-chlorophenyl)-1,2,3,4-tetrahydro-pyrano[2,3-d]pyrimidine– 2,4(5*H)* -dione, (10e)

The compound was brown solid; m.p. 279-280^{0}C, yield 85%. The product was characterized by its UV, IR, ^{1}H NMR and ^{13}C NMR spectral data.

The UV spectrum (fig-53) of the compound showed absorption band at 324 nm due to $\pi \rightarrow \pi^*$ of C=C-C=O and at 234nm due to $\pi \rightarrow \pi^*$ of C=C group.

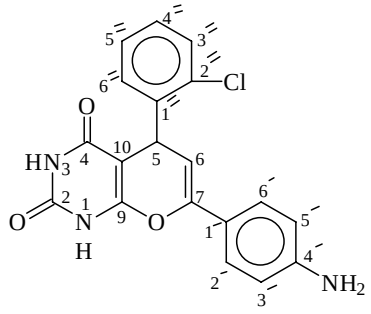
In the IR (KBr) spectrum (fig-54) of the compound **10e**, two absorption bands found at 3448.5cm^{-1} and 3433.1 cm^{-1} indicate the presence of $-NH_2$ group. Absorption band at 3413.8 cm^{-1} indicates the presence of N-H group. The middle intensity vibration bands to the right (1640-1550) of the C=O absorption, caused by the N-H bending vibration. A broad band of middle intensity in the 800-700 cm^{-1} region is responsible for the out of plane N-H wagging. Strong absorption bands in the 1342-1266 cm^{-1} region display strong C-N stretching absorption. The absorption band at 1720.4 cm^{-1} due to the conjugation of the carbonyl group with double bond. The absorption at 1684.5 cm^{-1} was found for cyclic double bond.1000-650 cm^{-1} absorption bands were obtained due to the =C–H out of plane of alkene. Aromatic stretching absorption band showed absorption at 2985.5 cm^{-1} .Aromatic C=C ring stretch absorption bands was found at 1595.0cm^{-1}. Absorption at 755.0 cm^{-1}indicates ortho substitution of benzene ring and at 845.5 cm^{-1} indicates para substitution. Absorption at1150.6 cm^{-1} indicates the C–O bond of aliphatic system and 1256.7cm^{-1} indicates the aromatic C–O bond.

The ^1H NMR spectrum (fig-55) of the compound showed , the peak at δ_H 10.31(s,2H,-NH-) due to the N-H protons in the compound which were strongly deshielded and appeared as singlet in the ^1H NMR spectrum. The proton at the position C-3″ appeared as a doublet and the chemical shift was observed at δ_H 7.36(d, 1H, Ar-H) with J value 2.32 Hz due to the long range coupling. The chemical shift at δ_H 7.33(m, 3H, Ar-H) was due to the CH protons of C-4″, C-5″&C-6″ carbons. The chemical shift position at δ_H 7.22 (m,4H,Ar-H) was found due to the protons of C-2′, C-3′,C-5′ &C-6′ carbons. The proton at position 6 appeared as a doublet due to the vicinal coupling with the proton at position 5. The chemical shift was observed at δ_H 6.36 (d, 1H, CH, J=3.80). The 5-H in that compound gave signal at δ_H 4.79 (d, 1H, CH, J=3.72) as doublet due to the coupling of 5-H by 6-H with J value 3.72 Hz. The chemical shift at δ_H 3.59 (s, 2H, $-NH_2$) was obtained due to the $-NH_2$ group.

The ^{13}C NMR spectrum (fig-56) of the compound showed the peak at δ_C 166.41 for C-4, at δ_C 164.17 for C-2 and at 162.54 for C-9 carbon. The chemical shift at δ_C 142.78 represents the C-7 and at δ_C 136.55 represents the C-6 carbon. The peaks at δ_C 117.32 and at δ_C 127.40 were found due to the C-1′&C-1″ carbon. The chemical shift position

at δ_C 128.37 showed C-2′ & C-6′ carbon. The chemical shifts at δ_C 134.98, at δ_C 129.09, at δ_C 125.32 and δ_C 129.96 represent the C-2″, C-3″, C-5″ &C-6″ carbons respectively. The chemical shift at δ_C 113.49 represents C-10 carbon. The peaks at δ_C 150.38 and at δ_C 130.65 designated for carbons of C-4′&C-4″ and the peak at δ_C 31.76 found due to the C-5 carbon.

On the basis of the UV, IR, ^{1}H NMR and ^{13}CNMR spectral data, the structure of this compound was assigned as-



(10e)

2.6.1.6 Characterization of 7-(4-aminophenyl)-5-(2-chloroyphenyl)-2-thioxo-1, 2, 3, 4-tetrahydropyrano[2, 3-d]pyrimidine-4(5*H*)-one, (10f)

The compound was deep yellow solid; m.p. 255-257^{0}C, yields 82%. The product was characterized by its UV, IR, ^{1}H NMR and ^{13}C NMR spectral data.

The UV spectrum (fig-57) of the compound showed absorption band at 322 nm due to $\pi \rightarrow \pi^*$ of C=C-C=O and at 233nm due to $\pi \rightarrow \pi^*$ of C=C group.

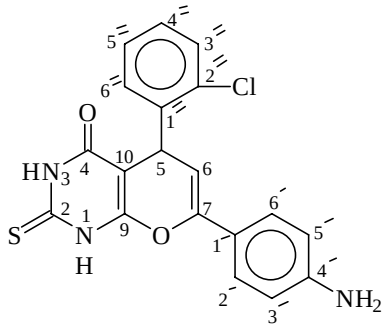
In the IR (KBr) spectrum (fig-58) of the compound **10f**, two absorption bands found at 3315.4cm^{-1} and 3184.3 cm^{-1} indicate the presence of –NH_2 group. Absorption band at 3107.1 cm^{-1} indicates the presence of N-H group. The middle intensity vibration bands to the right (1640-1550) of the C=O absorption, caused by the N-H bending vibration. A broad band of middle intensity in the 800-700 cm^{-1} region is responsible for the out of plane N-H wagging. Strong absorption bands in the 1342-1266 cm^{-1} region display

strong C-N stretching absorption. The absorption band at 1678.0 cm^{-1} due to the conjugation of the carbonyl group with double bond. The absorption at 1651.0 cm^{-1} was found for cyclic double bond.1000-650 cm^{-1} absorption bands were obtained due to the =C-H out of plane of alkene. Aromatic stretching absorption band showed absorption at 2985.5 cm^{-1} .Aromatic C=C ring stretch absorption bands was found at 1531.4 cm^{-1}. Absorption at 756.0 cm^{-1}indicates ortho substitution of benzene ring and at 833.2 cm^{-1} indicates para substitution. Absorption at 1178.0 cm^{-1} indicates the C-O bond of aliphatic system and 1220.9 cm^{-1} indicates the aromatic C-O bond.

The ^{1}H NMR spectrum (fig-59) of the compound showed , the peak at δ_H 10.99(s, 2H, -NH-) due to the N-H protons in the compound which were strongly deshielded and appeared as singlet in the ^{1}H NMR spectrum. The proton at the position C-3″ appeared as a doublet and the chemical shift was observed at δ_H 7.40(d, 1H, Ar-H, J=8.4) with J value 8.4 Hz. The chemical shift at δ_H 7.21(t, 3H, Ar-H) was due to the CH protons of C-4″, C-5″&C-6″ carbon. The chemical shift position at δ_H 7.13 (d,2H,Ar-H,J=8.12) showed as doublet due to the protons of C-2′&C-6′ carbon and at δ_H 6.72 showed doublet due to the protons of C-3′&C-5′ carbon. The proton at position 6 appeared as a doublet due to the vicinal coupling with the proton at position 5. The chemical shift was observed at δ_H 5.98 (d, 1H, CH, J=4.24) with J value 4.24 Hz. The 5-H in that compound gave signal at δ_H 4.42 (d, 1H, CH, J=4.4) as doublet due to the coupling of 5-H by 6-H with J value 4.4 Hz. The chemical shift at δ_H 3.61 (s, 2H,-NH_2) was obtained due to the –NH_2 group.

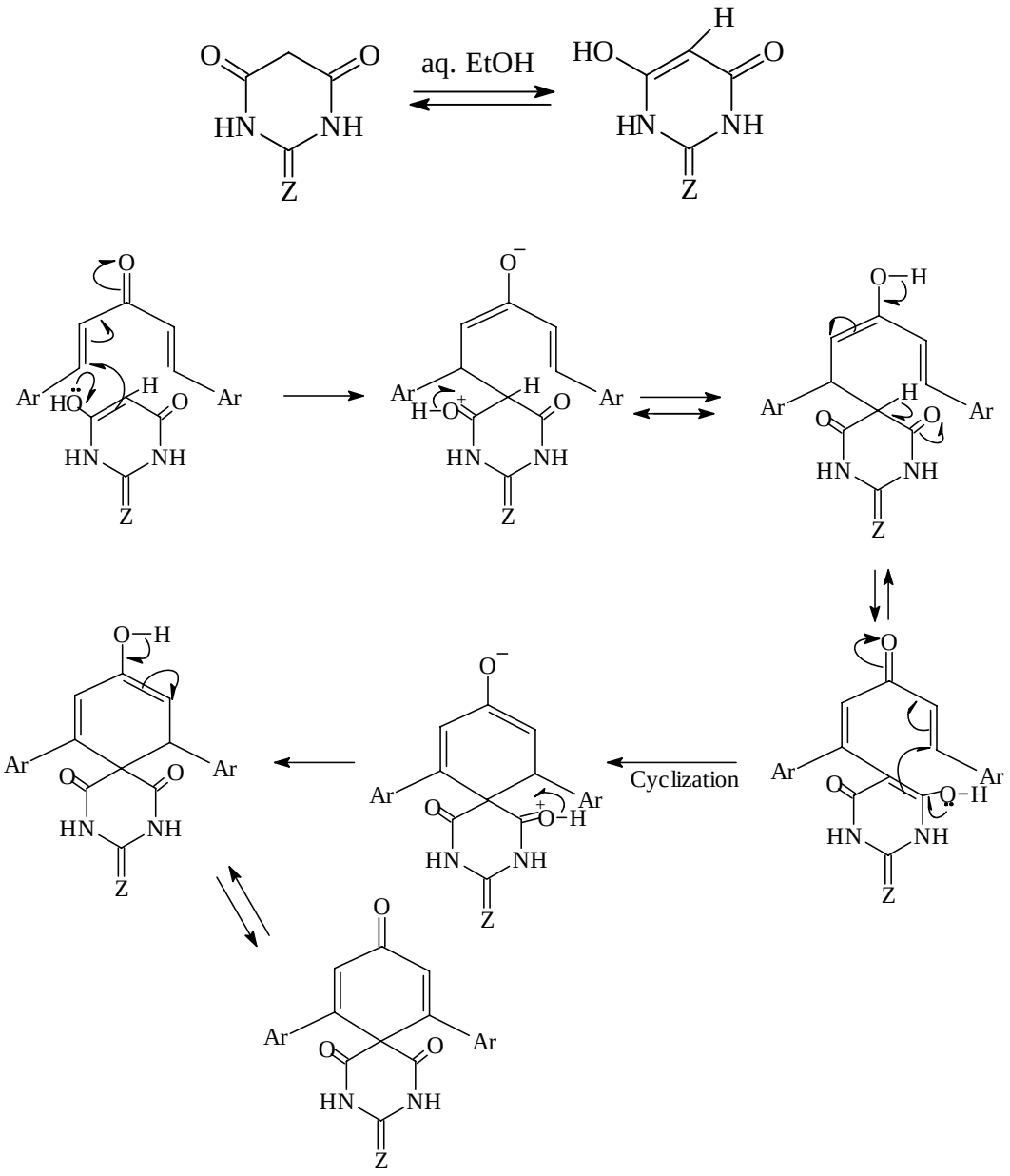
The ^{13}C NMR spectrum (fig-60) of the compound showed the peak at δ_C 167.77 for C-4, at δ_C 166.37 for C-2 and at 162.42 for C-9 carbon. The chemical shift at δ_C 141.45 represents the C-7 and at δ_C 136.99 represents the C-6 carbon. The peaks at δ_C 117.32 and at δ_C 127.15 were found due to the C-1′&C-1″ carbon. The chemical shift position at δ_C 128.94 showed C-2′ & C-6′ carbon. The chemical shifts at δ_C 135.74, at δ_C 129.88, at δ_C 126.71 and δ_C 130.12 represent the C-2″, C-3″, C-5″ &C-6″ carbons respectively. The chemical shift at δ_C 113.49 represents C-10 carbon. The peaks at δ_C 149.95 and at δ_C 130.36 designated for carbons of C-4′&C-4″ and the peak at δ_C 32.49 found due to the C-5 carbon.

On the basis of the UV, IR, ^{1}H NMR and ^{13}CNMR spectral data, the structure of this compound was assigned as-

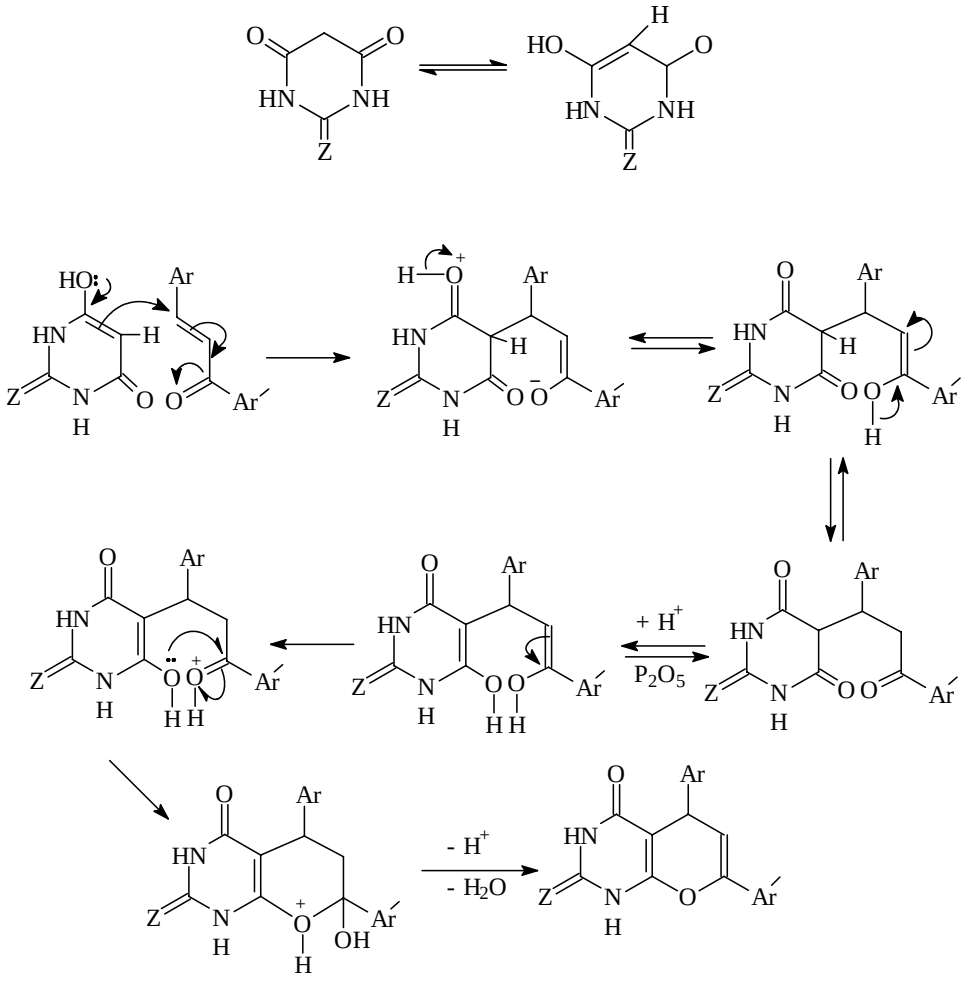


(10f)

2.7.1 A probable mechanism for the formation of 7, 11-disubstituted phenyl -2-oxo/thioxo-1, 3 diazaspiro[5, 5]undecane-4, 6, 9-trione, (5a-f)



2.7.2 A probable mechanism for the formation of 5, 7– Disubstitutedphenyl –1,2,3,4 tetrahydro–2-oxo/thioxo –4–oxo– 5*H*–pyrano[2,3–d]pyrimidine, (10a-f):



2.8 Conclusion

- A number of diarylideneacetones, **(3a-c)** and arylidene-*p*- aminoacetophenones, **(8a-c)** have been synthesized as the starting materials from the reactions of acetone and *p*-aminoacetophenones with benzaldehyde and substituted benzal-dehydes in presence of alkali.
- With the starting materials diarylideneacetones, **(3a-c)** a series of 5-substituted barbituric acid and thiobarbituric acid derivatives – (7,11-disubstituted –phenyl-2-oxo/thioxo-1,3-diazaspiro[5,5] undecane-4,6,9 triones), **(5a-f)** were synthesized in aqueous ethanol.
- Another series of compounnds (5,7-disubstituted phenyl-1,2,3,4-tetrahydro-2-oxo/thioxo-4-oxo-pyrano [2,3-d] pyrimidines), **(10a-f)** have been synthesized in single step by the condensation of barbituric acid and thiobarbituric acid with arylidene- *p*-aminoacetophenones, **(8a-c)** in glacial acetic acid in the presence of phosphorous pentoxide.
- All reactions were carried out in a domestic microwave oven [a common household appliance these days] with special fabricated glassware and optimum reaction conditions were determined.
- These synthesis apart from reducing the use of organic solvents from work up step, also gave improved yield as compared to the conventional heating with reaction time reduced from hours to minutes.
- Low amount of chemicals were used making the method of synthesis environmental friendly. In other words this modest thesis work was a part of ‘Green chemistry’ too.

Chapter - 3

EXPERIMENTAL

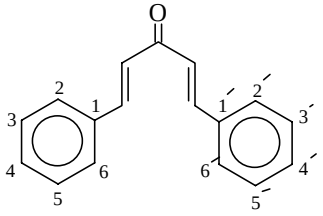
3.0 General Experimental

Melting points were determined in open capillary tubes in melting point apparatus. IR spectra were recorded on a Shimadzu FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrophotometer (400MHz) using tetramethylsilane as internal reference. Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60F-254(E. Merck), and the spots were visualized with UV light.

3.1 Synthesis of starting materials (dibenzylidene acetone and substituted dibenzylideneacetones, 3a-c)

3.1.1 Preparation of dibenzylideneacetone, 3a:

The mixture of acetone (1.1ml, 0.015mol), benzaldehyde (3.05ml, 0.03mol) and ethanol(10ml) were added drop wise in an aqueous solution of sodium hydroxide(5ml). The mixture appeared cloudy first but after sometimes it changed to a clear solution. The mixture was then put on the microwave oven and a separate beaker of ice was also put. After setting the microwave at 300 Watt, the reaction started gradually with 15seconds duration. The mixture turned to yellow color after 30 seconds and TLC was taken. After 60 seconds completion of the reaction was seen by TLC. Precipitation in the resulting solution started and the flask was allowed to stand overnight in refrigerator for complete precipitation. The mixture was filtered under suction on a Buchner funnel, washed with cold water to remove completely any remaining alkali and dried under vacuum pump. The crude product was recrystallized several times from ethanol to give pure dibenzylideneacetone.



(3a)

The compound **3a** was yellow solid, m.p.-111-112°C, R_f value 0.65 (chloroform: *n*-hexane) and yield 85%.

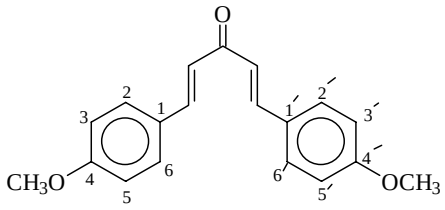
Spectral Data

UV (EtOH): λ_{max} 329,229nm.

IR (KBr): ν_{max} 3051.2, 1651.0, 1625.9, 1446.5, 694.3 cm^{-1}.

3.1.2 Preparation of di-4-methoxybenzylideneacetone, 3b:

Acetone (1.10ml, 0.015mol), 4-methoxybenzaldehyde (3.65ml, 0.03mol) and ethanol (10ml) were added drop wise in an aqueous solution of sodium hydroxide (5ml) in 50 ml flask. The mixture was then put on the microwave oven and a separate beaker of ice was put. After setting the microwave at 300 Wt, the reaction started gradually with 15 seconds duration. The mixture turned to brownish color after 45 seconds and TLC was taken. After 75 seconds completion of the reaction was seen by TLC. Precipitation in the resulting solution started and the flask was allowed to stand overnight in refrigerator for complete precipitation. The mixture was filtered under suction on a Buchner funnel, washed with cold water to remove completely any remaining alkali and dried under vacuum pump. The crude product was recrystallised several times from ethanol to give pure di-p-methoxybenzylideneacetone.



(3b)

The compound **3b** was brownish solid, m.p.-129-131°C, R_f value 0.76(chloroform) and yield 80%.

Spectral Data

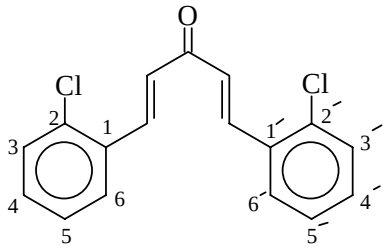
UV (EtOH): λ_{max} 366,240nm.

IR (KBr): ν_{max} 2960.5., 1654.8, 1629.7, 1596.9, 835.1 cm^{-1}

3.1.3 Preparation of di-2-chlorobenzylideneacetone, 3c:

In a 50 ml ground joint flask, an aqueous solution of sodium hydroxide (2.5ml) was taken and then a mixture of acetone (1.84ml, 0.025mol), 2-chlorobenzaldehyde (5.63ml, 0.05mol) and ethanol (10ml) were added drop wise in it.

The mixture appeared cloudy first but after sometimes it changed to a clear solution. The mixture was then put on the microwave oven and a separate beaker of ice was put. After setting the microwave at 300 Wt, the reaction started gradually with 15seconds duration. The mixture turned to yellow color after 30 seconds and TLC was taken. After 60 seconds completion of the reaction was seen by TLC. Precipitation in the resulting solution started and the flask was allowed to stand overnight in refrigerator for complete precipitation. The mixture was filtered under suction on a Buchner funnel, washed with cold water to remove completely any remaining alkali and dried under vacuum pump. The crude product was recrystallised several times from ethanol to give pure di-2-chlorobenzylideneacetone.



(3c)

The compound **3c** was yellow solid, m.p.-117-118°C, R_f value 0.82(chloroform) and yield 83%.

Spectral Data

UV (EtOH): λ_{max} 233, 209nm.

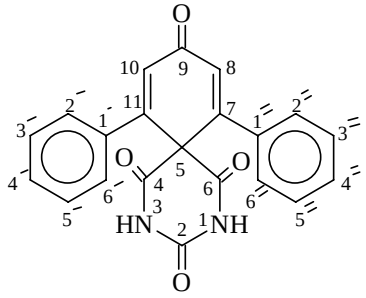
IR (KBr): ν_{max} 3050.5, 1670.2, 1616.2, 1585.4, 761.8 cm^{-1}

3.2 Synthesis of (7,11-di-phenyl & substituted di-phenyl 2-oxo/thioxo-1,3-diazaspiro [5,5 undecane-4,6,9 triones) compounds (5a-f):

3.2.1 Preparation of (7,11-di- phenyl 2-oxo-1,3-diazaspiro[5,5]undecane-4, 6, 9 trione), 5a:

Dibenzylideneacetone (0.29g, 1.25mmol) and barbituric acid (0.16 g, 1.25mmol) were dissolved in rectified spirit (10ml) and water (10) in a 50 ml ground joint flask. The reaction was carried out in a special microwave resistant glass ware. The mixture was kept in the microwave oven with another beaker of ice. The microwave was set at 300 Watt and the reaction was gradually started. The progress of the reaction was followed by TLC on silica gel plates (chloroform: n-hexane 4: 1). At the starting of the reaction in microwave the color of the reaction mixture was initially light yellow and at the end of 6.5 minutes it turned to brown color.

The product from the reaction mixture was put in refrigerator for complete precipitation. Precipitate from the fridge was of dark brown to light yellowish color. Yellow crystals were filtered under suction on a Buchner funnel and dried under vacuum pump. The crude product was recrystallized form ethanol and ethyl acetate to give pure (7, 11-dibenzyl- 2-oxo-1, 3-diazaspiro [5, 5] undecane-4, 6, 9 triones) compound. After recrystallization the color of the compound was found light yellow.



(5a)

The compound **5a** was light yellow solid, m.p.-290-292°C, R_f value 0.68(chloroform: *n*-hexane 4:1) and yield 79%.

Spectral Data

UV (EtOH): λ_{max} 216nm.

IR (KBr): ν_{max} 3201.6, 3085.9, 1681.8, 1625.8, 1705.0, 702.0 cm^{-1}

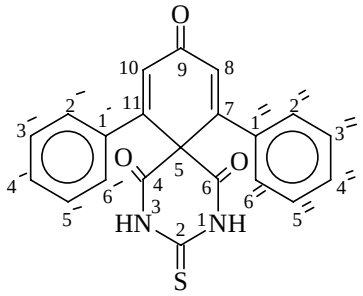
^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD): δ_H 10.33(s,2H,-NH-),6.77(d,2H, J=3.6Hz), 7.27(d,4H,Ar-H, J=7.69), 7.19(t,6H,Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ_C 171.85, 170.60, 148.55, 136.68, 128.37, 127.72, 125.52, 102.75, 59.74, 128.84

3.2.2 Synthesis of (7, 11-di- phenyl - 2-thioxo-1, 3-diazaspiro [5, 5] undecane-4, 6, 9 trione), 5b

In a 50 ml ground joint flask dibenzylideneacetone (0.29 g, 1.25mmol) and thiobarbituric acid (0.18 g, 1.25 mmol) were dissolved with rectified spirit (10) and water (10). The mixture was kept in the Microwave oven and with another beaker of ice. The microwave was set at 300 Watt and the reaction was gradually started. The progress of the reaction was followed by TLC on silica gel plates (chloroform: n-hexane 4:1). At the starting of the reaction in microwave the color of the reaction mixture was initially light yellow and at the end of 7.15 minutes it turned to deep brown. The product from the reaction mixture solution started to precipitate and was put to stand overnight in refrigerator for complete precipitation

Light yellowish crystals were filtered under suction on a Buckner funnel and dried under vacuum pump. The crude product was recrystallized form ethanol to give pure (7, 11-di-benzyl-2-thioxo-1, 3-diazaspiro [5, 5] undecane-4, 6,9triones) compound. After recrystallization the color of the compound was found light yellow.



(5b)

The compound **5b** was light yellow solid, m.p.-285-287°C, R_f value 0.83(chloroform: n-hexane 4:1) and yield 74%.

Spectral Data

UV (EtOH): λ_{max} 292, 241nm.

IR (KBr): ν_{max} 3138.0, 1678.0, 1708.8, 1535.2, 2905.5, 1433.0, 705.9, 1149.5 cm^{-1}

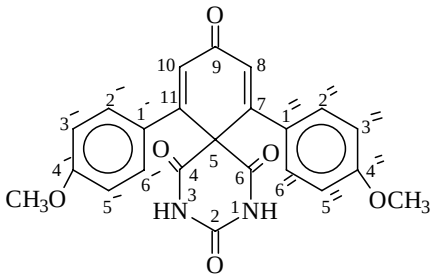
^{1}H NMR (400 MHz,$CDCl_3$+CD_3OD): δ_H 11.26(s,2H,-NH-),6.53(d,2H,CH, J=4.08Hz), 7.87(dd,4H,Ar-H, J=10.28), 7.62(t,6H,Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ_C 176.16, 168.22, 169.69, 136.51, 130.24, 129.96, 127.69, 126.01, 102.51, 58.72

3.2.3 Synthesis of (7,11-di-4-methoxy phenyl-2-oxo-1,3-diazaspiro[5, 5] undecane-4, 6,9 trione), 5c:

Di-p-methoxybenzylideneacetone (0.37 g, 1.25mmol) and barbituric acid (0.16 g, 1.25 mmol) were dissolved in rectified spirit (15) and water (10) in a 50 ml flask. The reaction was carried out in a special microwave glass ware. The progress of the reaction was followed by TLC on silica gel plates (ethanol: chloroform 1: 5). At the starting of the reaction in microwave the color of the reaction mixture was initially light yellow and gradually getting heat it turned to reddish color. At the end of 7 minutes 30 seconds it turned to deep brown. The product from the reaction mixture solution started to precipitate and was put to stand overnight in refrigerator for complete precipitation. Precipitate from the fridge was of deep brown color and were

filtered under suction on a Buchner funnel and dried under vacuum pump. The crude product was recrystallized form ethanol to give pure (7, 11-Di-p-methoxybenzyl-2-oxo-1, 3-diazaspiro [5, 5] undecane-4, 6,9 triones). The recrystallized product was light brown color.



(5c)

The compound **5c** was light brown solid, m.p.-295-297°C, R_f value 0.5 (ethanol: chloroform 1: 5) and yield 75%.

Spectral Data

UV (EtOH): λ_{max} 362.6nm.

IR (KBr): ν_{max} 3425.3, 1689.5, 833.2, 1706.9, 1598.9, 1512.1, 2947.0, 1446.5, 1172.6, 1253.6, 2823.6 cm^{-1}

^{1}H NMR (400 MHz,$CDCl_3$+CD_3OD): δ_H 10.40(s,2H,-NH-),6.92(d,2H,CH, J=4.4Hz), 7.69(d,4H,Ar-H, J=9.6), 7.55(d,4H,Ar-H,J=8.8), 3.84(s,6H,-OCH_3).

^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ_C 173.05, 167.10, 168.25, 159.59, 136.35, 120.03, 128.11, 114.51, 101.91, 59.45, 55.06.

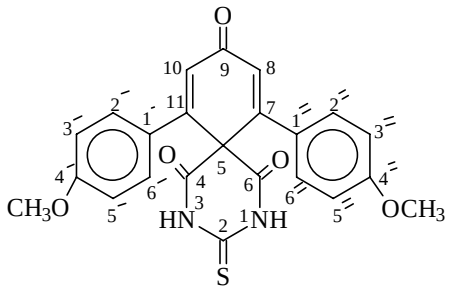
3.2.4 Synthesis of (7,11-di-4-methoxy phenyl-2-thioxo-1,3-diazaspiro[5,5] undecane-4, 6,9 trione), 5d:

In a 50 ml special microwave resistant glass ware di-*p*-methoxy benzylideneacetone (0.38 g, 1.25 mmole) and thiobarbituric acid (0.18 g, 1.25 mmol) were dissolved with rectified spirit (10ml) and water (10ml). The microwave was set at 300 Watt and the reaction was gradually started. The progress of the reaction

was followed by TLC on silica gel plates (chloroform). At the starting of the reaction in microwave the color of the reaction mixture was initially light yellow and gradually getting heat it turned to orange. At the end of 6.85 minutes it turned to deep yellow.

The product from the reaction mixture solution started to precipitate and was put to stand overnight in refrigerator for complete precipitation.

Deep yellow crystals were filtered under suction on a Buchner funnel and dried under vacuum pump. The crude product was recrystallized form ethanol to give pure (7, 11-di-*p*-methoxybenzyl-2-thioxo-1, 3-diazaspiro [5, 5] undecane-4, 6,9 triones).



(5d)

The compound **5d** was yellow solid, m.p.-282-284°C, R_f value 0.86 (chloroform) and yield 71%.

Spectral Data

UV (EtOH): λ_{max} 231nm.

IR (KBr): ν_{max} 3190.0, 1610.5, 1251.7, 835.1, 1699.2, 1598.9, 1512.1, 2954.7, 1423.4, 1180.4, 1151.4, 2837.1, 1251.7 cm^{-1}

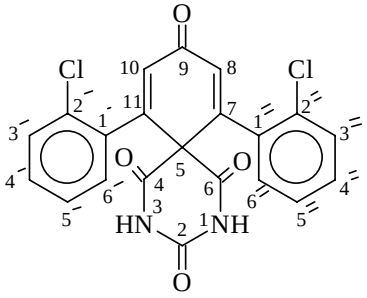
^{1}H NMR (400 MHz,$CDCl_3$+CD_3OD): δ_H 11.33(s,2H,-NH-),6.89(d,2H,CH, J=4.0Hz), 7.77(d,4H,Ar-H, J=8.8), 7.31(d,4H,Ar-H,J=8.4), 3.95(s,6H,-OCH_3).

^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ_C 177.75, 169.70, 175.15, 161.19, 137.05, 119.52, 113.51, 128.31, 102.01, 60.25, 55.35

3.2.5 Synthesis of (7, 11-di-2-chloro phenyl-2-oxo-1, 3-diazaspiro [5, 5] undecane-4, 6, 9 trione), 5e:

Di-2-chlorobenzylideneacetone (0.38g, 1.25 mmol) and barbituric acid (0.16g, 1.25 mmol) were dissolved in rectified spirit (10) and water (10) in a 50 ml ground joint flask. The reaction was carried out in a special microwave glass ware. The microwave was set at 300 Watt and the reaction was gradually started. The progress of the reaction was followed by TLC on silica gel plates (chloroform). At the starting of the reaction in microwave the color of the reaction mixture was initially light yellow and at the end of 6.75 minutes it turned to deep yellow color.

The product from the reaction mixture solution started to precipitate and was put to stand overnight in refrigerator for complete precipitation. Yellowish crystals were filtered under suction on a Buchner funnel and dried under vacuum pump. The crude product was recrystallized form methanol to give pure (7, 11-di-*o*-chlorobenzyl-2-oxo-1, 3-diazaspiro [5, 5] undecane-4, 6, 9 triones).



(5e)

The compound **5e** was deep yellow solid, m.p.-268-270°C, R_f value 0.77 (chloroform) and yield 77%.

Spectral Data

UV (EtOH): λ_{max} 235nm.

IR (KBr): ν_{max} 3350.5, 1616.2, 1328.9, 1665.5, 1558.4, 1587.3, 3028.5, 1436.9, 761.8, 1097.4 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD): δ_H 10.79(s,2H,-NH-),7.17(d,2H,CH, J=4.4Hz), 7.71(dd,2H,Ar-H, J=8.0),7.44(dd,4H,Ar-H,J=8.0),7.32-7.29(m,4H.) .

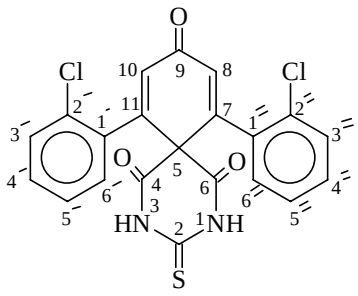
^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ_C 176.01, 168.22, 169.79, 101.34, 59.05, 136.38, 134.94, 129.49, 129.05, 128.39, 126.11, 117.93.

3.2.6 Synthesis of (7,11-di-2-chlorophenyl-2-thioxo-1,3-diazaspiro[5, 5] undecane-4, 6,9trione), 5f:

Di-2-chlorobenzylideneacetone (1.46 g, 0.01 mole) and thiobarbituric acid (0.18g, 1.25 mmol) were dissolved in rectified spirit (15ml) and water (10ml) in a 50 ml flask. The reaction was carried out in a special microwave glass ware. The microwave was set at 300 Watt and the reaction was gradually started. The progress of the reaction was followed by TLC on silica gel plates (chloroform). At the starting of the reaction in microwave the color of the reaction mixture was initially light brown and gradually getting heat it turned to reddish. At the end of 7.0 minutes it turned to deep brown.

The product from the reaction mixture solution started to precipitate and was put overnight in refrigerator for complete precipitation. Precipitate from the fridge was of dark brown to light yellowish color.

Light yellowish crystals were filtered under suction on a Buckner funnel and dried under vacuum pump. The crude product was recrystallized form ethanol to give pure (7, 11-di-benzyl-2-thioxo-1, 3-diazaspiro [5, 5] undecane-4, 6,9 triones).



(5f)

The compound **5f** was light yellow solid, m.p.-251-253°C, R_f value 0.69 (chloroform) and yield 71%.

Spectral Data

UV (EtOH): λ_{max} 294nm.

IR (KBr): ν_{max} 3236.3, 1681.8, 1238.2, 1701.1, 1521.7, 1541.0, 3078.2, 1404.1, 759.9, 1153.4, 1037.6 cm^{-1}

^{1}H NMR (400 MHz,$CDCl_3$+CD_3OD): δ_H 10.39(s,2H,-NH-),6.89(d,2H,CH, J=4.0Hz), 7.50(d,2H,Ar-H, J=8.4),7.44(d,2H,Ar-H,J=8.8),7.36-7.29(m,4H,Ar-H) .

^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ_C 176.39, 169.70, 175.22, 136.51, 134.54, 129.99, 129.25, 128.01, 126.37, 118.05, 101.01, 60.03

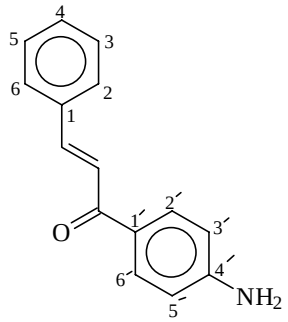
3.3 Synthesis of starting materials (arylidene & substitutedarylidene-4-aminoacetophenone), (8a-c):

3.3.1 Preparation of benzylidene-4-aminoacetophenone), 8a:

p-aminoacetophenone (0.76ml, 1.25mmol) and benzaldehyde (1.01g, 1.25mmol) were dissolved in ethanol (10ml) in two separate conical flasks. The two solutions were allowed to mix quickly and then freshly prepared sodium hydroxide solution (5ml) were added drop wise to it. The reaction was carried out in a special microwave glass ware. Then the mixture was kept on the microwave oven with separate beaker of ice. The microwave was set at 300 Watt and the reaction was started in 15 seconds duration. The color of the mixture turned yellow within 15 seconds.

Irradiation was continued for 75 seconds in total with intervals for monitoring the reaction by TLC. When the reaction was complete as shown in TLC, the appearance of precipitate was observed in the reaction mixture and the flask was allowed to stand overnight in refrigerator for complete precipitation.

The mixture was filtered under suction on a Buchner funnel and the crude product was recrystallized from ethanol to give pure benzylidene-*p*-aminoacetophenone.



(8a)

The compound **8a** was yellow solid, m.p.-166-167°C, R_f value 0.69 (chloroform) and yield 89%.

Spectral Analysis

UV spectrum

Its UV spectrum (fig-10) in methanol showed absorption bands at 226 nm and at 202 nm.

IR spectrum

The IR spectrum (fig-9) of the product run as KBr pellet, showed characteristic absorption bands (ν_{max} in cm^{-1}) at 3460.1, 3340.5, 1654.8, 1629.7, 3085.5, 1596.9, 815.5, and 690.5.

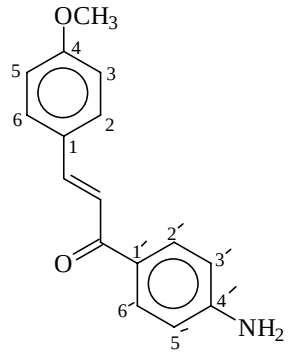
3.3.2 Preparation of 4-methoxybezylidene-4-aminoacetophenone), 8b:

In two separate conical flask, 4-aminoacetophenone (1.76 ml, 0.015 ml) and 4-methoxybenzaldehyde (1.82 ml, 0.015 mol) were dissolved in 10 ml ethanol. The two solutions were allowed to mix quickly and then freshly prepared sodium hydroxide solution (5ml) were added drop wise to it. The reaction was carried out in a special microwave assisted glass ware. The microwave was set at 300 Watt and the reaction was started in 15 seconds duration. The color of the mixture turned light brown within 30 seconds.

Irradiation was continued for 1.45 minutes in total with intervals for monitoring the reaction by TLC. When the reaction was complete as shown in TLC, the appearance of

precipitate was observed in the reaction mixture and the flask was allowed to stand overnight in refrigerator for complete precipitation.

The mixture was filtered under suction on a Buchner funnel and the crude product was recrystallized from ethanol to give pure 4-methoxy benzylidene-*p*-aminoacetophenone **(8b)**.



(8b)

The compound **8b** was light brown solid, m.p.-175-176°C, R_f value 0.69 (chloroform) and yield 80%.

Spectral Analysis

UV **spectrum**

Its UV spectrum (fig-10) in methanol showed absorption bands at 213nm and 231nm

IR spectrum

The IR spectrum (fig-9) of the product run as KBr pellet, showed characteristic absorption bands (ν_{max} in cm^{-1}) at 3448.5, 3361.7, 1670.2, 1589.2, 2950.5, 1514.4, 840.5.

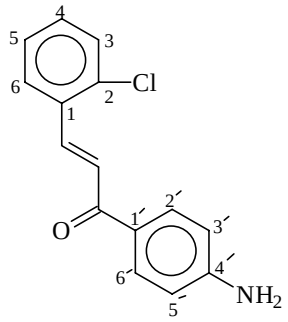
3.3.3 Preparation of 2-chlorobezylidene-4-aminoacetophenone, 8c:

p-aminoacetophenone (1.76 ml, 0.015 mol) and 2-chlorobenzaldehyde (1.69 ml, 0.015 mol) were dissolved in ethanol (10ml) in two separate conical flasks and then the two solutions were allowed to mix quickly. 5 ml freshly prepared sodium hydroxide

solution (5ml) was added drop wise to it and then the reaction was carried out in a special microwave glass ware. The microwave was set at 300 Watt and the reaction was started in 15 seconds duration. The color of the mixture turned light yellow within 15 seconds.

Irradiation was continued for 1.15 minutes in total with intervals for monitoring the reaction by TLC. When the reaction was complete as shown in TLC, the appearance of precipitate was observed in the reaction mixture and the flask was allowed to stand overnight in refrigerator for complete precipitation.

The mixture was filtered under suction on a Buckner funnel and the crude product was recrystallized from ethanol to give pure 2-chlorobenzylidene-4-aminoacetophenone **(8c)**.



(8c)

The compound **8c** was light yellow solid, m.p.-172-173°C, R_f value 0.69 (chloroform) and yield 85%.

Spectral Analysis

UV spectrum

Its UV spectrum (fig-10) in methanol showed absorption bands at 371 nm and at 231 nm.

IR spectrum

The IR spectrum (fig-9) of the product run as KBr pellet, showed characteristic absorption bands (ν_{max} in cm^{-1}) at 3332.8, 3226.7, 1649.2, 1606.6, 3050.5, 1583.4, 829.3, and 752.2.

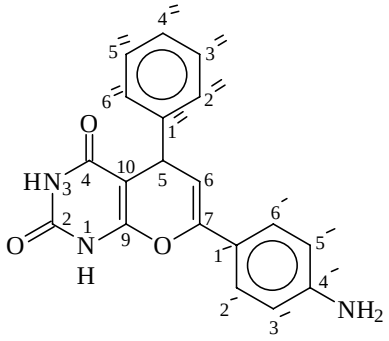
3.4 Synthesis of 5,7–disubstitutedphenyl–1,2,3,4 tetrahydro–2– oxo/thioxo–4–oxo–5*H*–pyrano[2,3–d]pyrimidine, (10a-f)

3.4.1 Preparation of 7-(4-aminophenyl)-5-phenyl-1,2,3,4-tetrahydro-pyrano[2,3-d]pyrimidine– 2,4(5*H)* -dione (10a)

A mixture of benzyliden-*p*-aminoacetophenone (0.28 g, 1.25 mmol) and barbituric acid (0.16 g, 1.25 mmol) were dissolved in acetic acid (10ml) and P_2O_5 (0.5g) in a 50 ml flask. The reaction was carried out in a special glass ware. The microwave was set at 300 Watt and the reaction was gradually started. The progress of the reaction was followed by TLC on silica gel plates (chloroform: ethyl acetate 3: 2). At the starting of the reaction in microwave the color of the reaction mixture was initially light brown and gradually getting heat it turned to yellow. The time required for the reaction was 5.5 minutes.

The product from the reaction mixture solution started to precipitate and was put to stand overnight in refrigerator for complete precipitation.

Yellowish crystals were filtered under suction on a Buchner funnel and dried under vacuum pump. The crude product was recrystallized form ethanol.



(10a)

The compound **10a** was yellow solid, m.p.-293-295°C, R_f value 0.67 (chloroform: ethylacetate 3:2) and yield 87%.

Spectral Analysis

UV (EtOH): λ_{max} 322 nm and 227 nm.

IR (KBr): ν_{max} 3500.5, 3410.5, 3303.8, 1676.0, 1647.1, 3085.5, 1595.0, 1176.5, 1220.9, 695.5, 825.5.

^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD): δ_H 9.35(s,2H,-NH-), 6.14(d,1H,CH, J=4.68Hz), 7.66(d,2H,Ar-H, J=8.72),7.33(t,3H), 7.14(d,2H,Ar-H), 6.78(d,2H), 4.27(d,1H), 3.50(s,2H,NH_2).

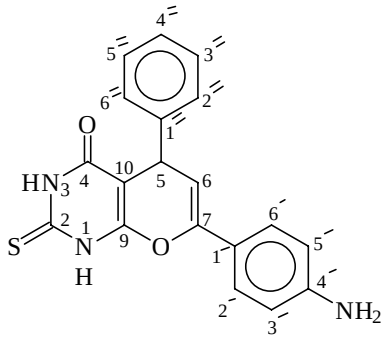
^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ_C 164.03, 163.99, 161.93, 140.88, 137.75, 111.75, 31.87, 133.35, 133.13, 129.31, 129.06, 127.93, 127.46, 127.35, 127.11

3.4.2 Synthesis of 7-(4-aminophenyl)-5-phenyl-2-thioxo-1, 2, 3, 4-tetrahydropyrano[2, 3-d]pyrimidine-4(5*H*)-one, (10b)

In a 50 ml ground joint flask, benzylidene-4-aminoacetophenone (0.28 g, 1.25 mmol) and thiobarbituric acid (0.18 g, 1.25m mol) were dissolved with acetic acid (15ml) and P_2O_5 (0.5g). The mixture was kept in the microwave oven with another beaker of ice. The microwave was set at 300 Watt and the reaction was gradually started. The progress of the reaction was followed by TLC on silica gel plates (chloroform: ethyl acetate 2:1). At the starting of the reaction in microwave the color of the reaction mixture was initially light yellow and gradually getting heat it turned to orange. At the end of 6.5 minutes it turned to deep brown.

The product from the reaction mixture solution started to precipitate and was put to stand overnight in refrigerator for complete precipitation.

The crude product was recrystallized form ethanol.



(10b)

The compound **10b** was deep brown solid, m.p.-275-276°C, R_f value 0.79 (chloroform: ethyl acetate 2:1) and yield 84%.

Spectral Analysis

UV (EtOH): λ_{max} 299 nm.

IR (KBr): ν_{max} 3450.6, 3310.5, 3203.6, 1676.9, 1652.9, 3085.5, 1596.9, 1176.5, 1220.9, 685.5, 835.6 cm^{-1}.

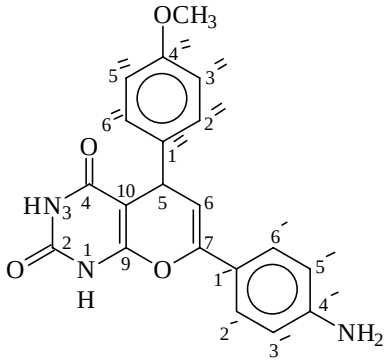
^{1}H NMR (400 MHz,$CDCl_3$+CD_3OD): δ_H 10.31(s,2H,-NH-),6.88(d,2H), 7.91(d,2H),7.74(m,3H), 7.17(d,2H), 6.24(d,1H), 4.28(d,1H), 3.61(s,2H).

^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ_C 165.53, 163.91, 162.13, 141.18, 136.55, 32.07, 112.15, 132.35, 132.13, 129.33, 128.96, 127.95, 127.56, 127.15, 126.91

3.4.3 Synthesis of 7-(4-aminophenyl)-5-(4-methoxyphenyl)-1,2,3,4-tetrahydro-pyrano[2,3-d]pyrimidine– 2,4(5*H)* -dione, (10c)

A mixture of 4-methoxybenzylidene-4-aminoacetophenone (0.31 g, 1.25 mmol) and barbituric acid (0.16 g, 1.25 mmol) were dissolved in acetic acid (10ml) and P_2O_5 (0.5g) in a 50 ml flask. The reaction was carried out in a special microwave assisted glass ware. The microwave was set at 300 Watt and the reaction was gradually started. The progress of the reaction was followed by TLC on silica gel plates (chloroform: ethanol 5:1). At the starting of the reaction in microwave the color of the reaction mixture was initially light brown. At the end of 7.15 minutes it turned to yellow.

The product from the reaction mixture solution started to precipitate and was put stand overnight in refrigerator for complete precipitation. Yellow crystals were filtered under suction on a Buckner funnel and dried under vacuum pump. The crude product was recrystallized form methanol.



(10c)

The compound **10c** was yellow solid, m.p.-297-298°C, R_f value 0.58 (chloroform: ethanol 5:1) and yield 81%.

Spectral Analysis

UV (EtOH): λ_{max} 294 nm and 222 nm.

IR (KBr): ν_{max} 3455.3, 3207.5, 3070.5, 1728.1, 1676.0 2885.5, 1550.7, 1180.4, 1271.0, 805.5cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD): δ_H 10.20(s,2H,-NH-),6.75(d,2H), 7.40(d,2H), 7.29(d,2H), 6.97(d,2H), 6.12(d,1H), 4,35(d,1H), 3.81(s,3H), 3.55(s,2H).

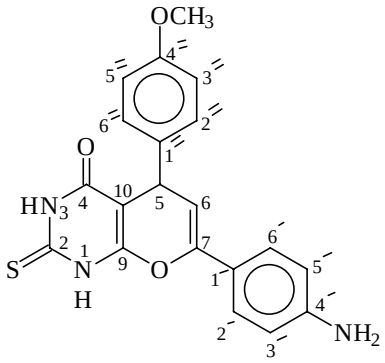
^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ_C 164.01, 163.57, 162.24, 141.36, 155.13, 150.28, 137.55, 113.55, 32.68, 55.79, 130.79, 130.35, 119.07, 117.69, 115.60, 114.05

3.4.4 Synthesis of 7-(4-aminophenyl)-5-(4-methoxyphenyl)-2-thioxo-1, 2, 3, 4-tetrahydropyrano[2, 3-d]pyrimidine-4(5*H*)-one, (10d)

4-methoxybenzylidene-*p*-aminoacetophenone (0.31 g, 1.25 mmol) and thiobarbituric acid (0.18 g, 1.25 mmol) were dissolved with acetic acid (15 ml) and then P_2O_5 (0.5g) was added to it. The mixture was kept in the microwave oven. The microwave was set at 300 Watt and the reaction was gradually started. The progress of the reaction was followed by TLC on silica gel plates (ethyl acetate: *n*- hexane 1:2). At the starting of the reaction the color of the reaction mixture was initially light yellow and gradually getting heat it turned to orange. At the end of 7.30 minutes it turned to deep brown.

The product from the reaction mixture solution started to precipitate and was put to stand overnight in refrigerator for complete precipitation.

Deep brown crystals were filtered under suction on a Buchner funnel and dried under vacuum pump. The crude product was recrystallized form ethanol.



(10d)

The compound **10d** was yellow solid, m.p.-281-283°C, R_f value 0.86 (ethyl acetate: *n*-hexane 1:2) and yield 80%.

Spectral Analysis

UV (EtOH): λ_{max} 284 nm.

IR (KBr): ν_{max} 3566.1, 3544.9, 3446.6, 1662.5, 1654.8, 2985.5, 1512.1, 1170.5, 1249.4, 835.4cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD): δ_H 10.87(s,2H,-NH-),7.49(d,2H) 7.30(d,2H), 6.98(d,2H), 6.86(d,2H), 6.18(d,1H), 4.38(d,1H), 4.11(s,3H), 3.57(s,2H).

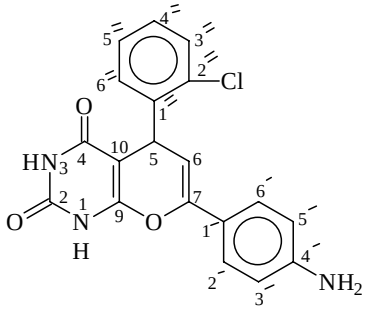
^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ_C 166.41, 163.37, 162.24, 143.31, 154.13, 149.28, 135.59, 112.49, 131.55, 131.12, 119.57, 117.35, 114.50. 31.96, 53.37.

3.4.5 Synthesis of 7-(4-aminophenyl)-5-(2-chlorophenyl)-1,2,3,4-tetrahydro-pyrano[2,3-d]pyrimidine– 2,4(5*H)* -dione, (10e)

In a special ground joint flask, 2-chlorobenzylidene-*p*-aminoacetophenone (0.32 g, 1.25 mmol) and barbituric acid (0.16 g, 1.25 mmol) were taken and dissolved these with acetic acid (10ml). After that P_2O_5 (0.5g) was added and the mixture was kept in the microwave oven with another beaker of ice. The microwave was set at 300 Watt and the reaction was gradually started. The progress of the reaction was followed by TLC on silica gel plates (chloroform: ethyl acetate 1: 1). At the end of 6.5 minutes it turned to brown color.

The product from the reaction mixture solution started to precipitate and was put in refrigerator for complete precipitation.

The products were filtered under suction on a Buckner funnel and dried under vacuum pump. The crude product was recrystallized form methanol.



(10e)

The compound **10e** was brown solid, m.p.-279-280°C, R_f value 0.45 (chloroform: ethyl acetate 1:1) and yield 85%.

Spectral Analysis

UV (EtOH): λ_{max} 324 nm and 234 nm.

IR (KBr): ν_{max} 3448.5, 3433.1, 3413.8, 1720.4, 1684.5, 2985.5, 1595.5, 1150.6, 1256.7, 755.0, 895.5cm^{-1}.

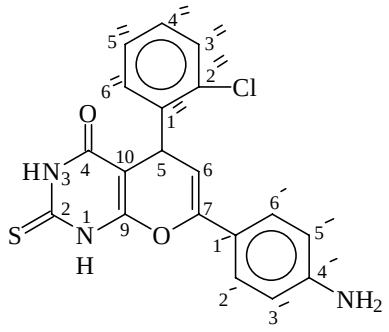
^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD): δ_H 10.31(s,2H,-NH-),7.36(d,1H), 7.33(m,3H), 7.24-7.19(m,4H), 6.36(d,1H), 4.79(d,1H), 3.59(s,2H).

^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ_C 166.41, 164.17, 162.54, 142.78, 150.38, 136.55, 134.98, 130.65, 129.95, 129.09, 128.37, 127.40, 125.32,117.32, 116.93, 113.49, 31.76.

3.4.6 Synthesis of 7-(4-aminophenyl)-5-(2-chloroyphenyl)-2-thioxo-1, 2, 3, 4-tetrahydropyrano[2, 3-d]pyrimidine-4(5*H*)-one, (10f)

A mixture of 2-chlorobenzylidene-*p*-aminoacetophenone (0.32 g, 1.25 mmol) and thiobarbituric acid (0.18 g, 1.25 mmol) were dissolved in acetic acid (10 ml) and P_2O_5 (0.5g) in a 50 ml flask. The microwave was set at 300 Watt and the reaction was gradually started. The progress of the reaction was followed by TLC on silica gel plates (chloroform: ethyl acetate 4: 1). At first the color of the reaction mixture was initially light yellow. At the end of 6.85 minutes it turned to deep yellow color. The product from the reaction mixture solution started to precipitate and was put stand overnight in refrigerator for complete precipitation.

Brown products were filtered under suction on a Buchner funnel and dried under vacuum pump. The crude product was recrystallized form ethanol.



(10f)

The compound **10f** was deep yellow solid, m.p.-255-257°C, R_f value 0.45 (chloroform: ethyl acetate 4:1) and yield 82%.

Spectral Analysis

UV (EtOH): λ_{max} 233 and 322 nm.

IR (KBr): ν_{max} 3315.4, 3184.3, 3107.1, 1678.0, 1651.0, 2985.5, 1531.4, 1178.0, 1220.9, 756.0, 833.2cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD): δ_H 10.99(s,2H,-NH-),7.40(d,1H), 7.21(t,3H), 7.13(d,2H), 5.98(d,1H), 4,42(d,1H), 3.61(s,2H).

^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD): δ_C 167.77, 166.37, 162.42, 141.45, 149.95, 136.99, 135.74, 130.36, 130.12, 129.88, 128.94, 127.15, 126.71, 117.32, 116.93, 113.49, 32.49.

SPECTRA

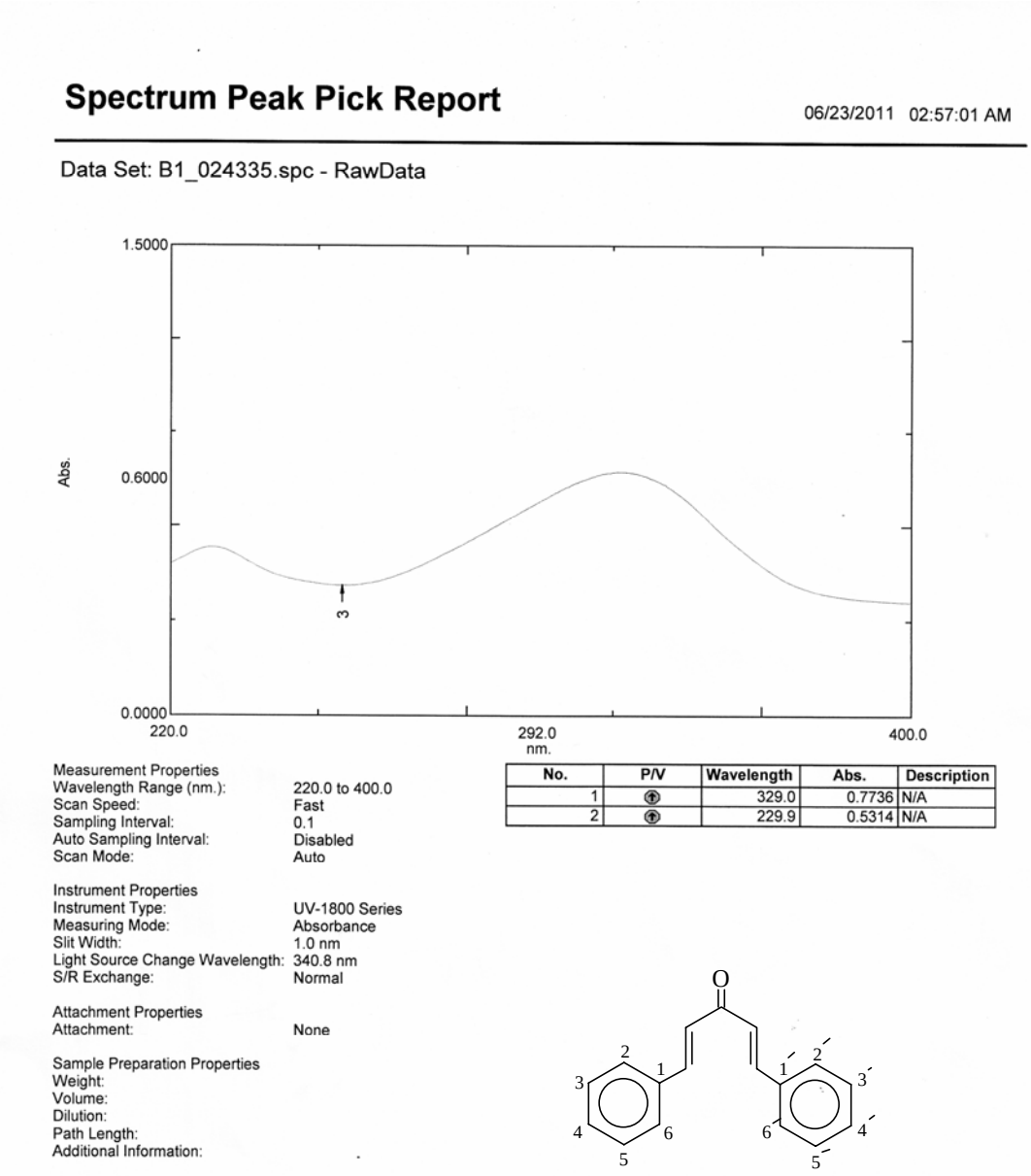


Fig-1: UV spectrum of compound **3a**.

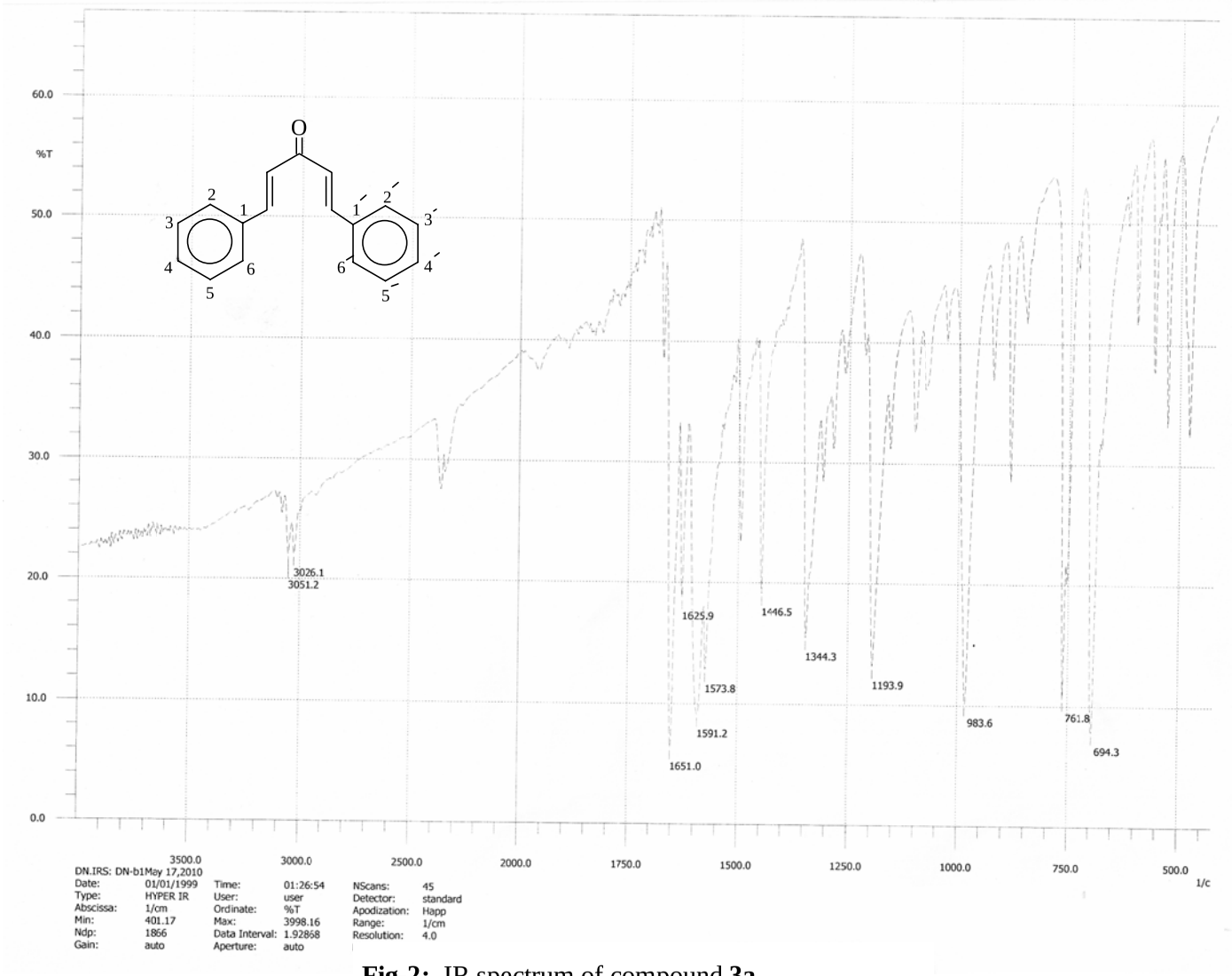


Fig-2: IR spectrum of compound **3a**.

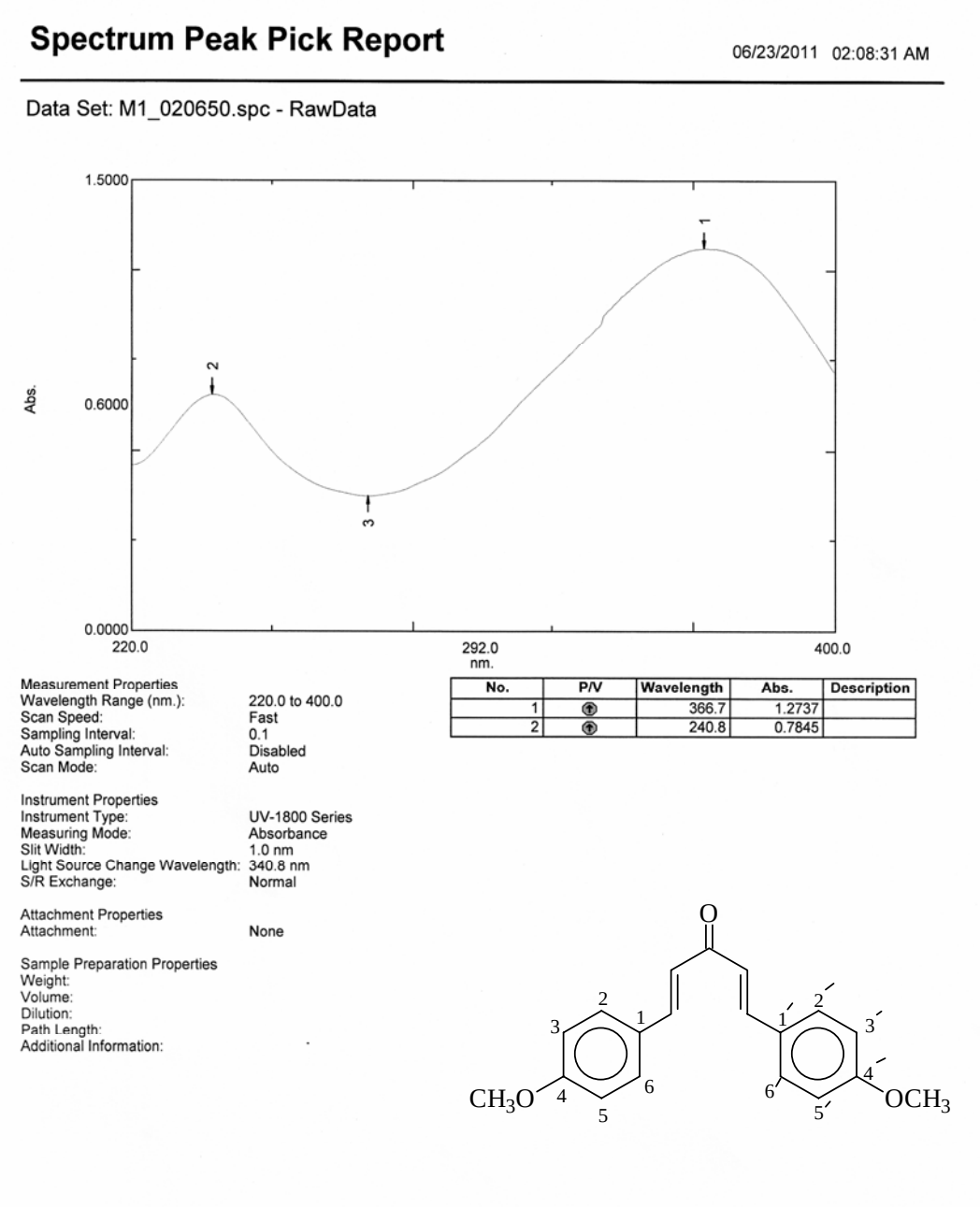


Fig-3: UV spectrum of compound **3b**.

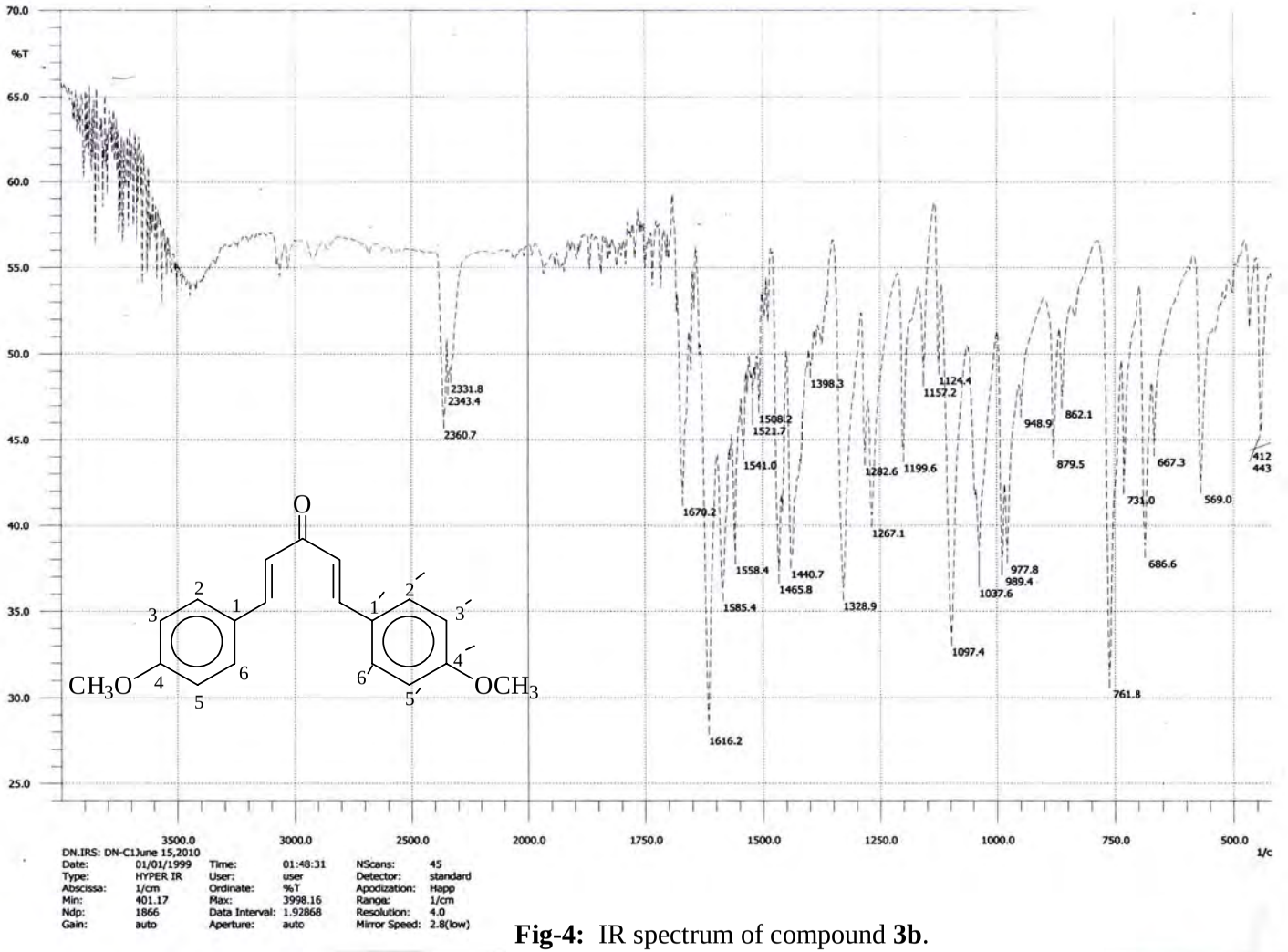
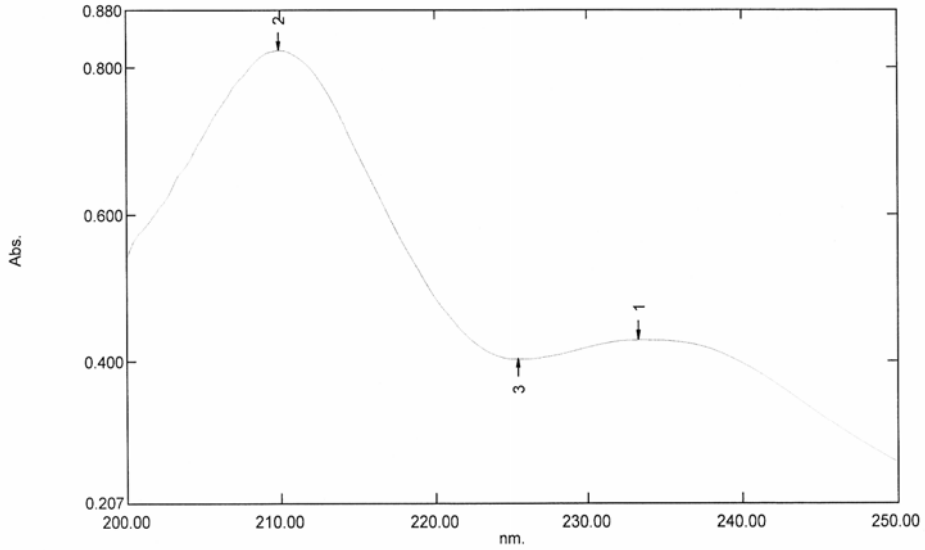


Fig-4: IR spectrum of compound **3b**.

Spectrum Peak Pick Report

09/21/2010 01:57:28 PM

Data Set: Storage 135526 - RawData - C:\Documents and Settings\Super\Desktop\Samina\Sample-C1R..spc



Measurement Properties	
Wavelength Range (nm.):	200.00 to 250.00
Scan Speed:	Fast
Sampling Interval:	0.1
Auto Sampling Interval:	Enabled
Scan Mode:	Single

Sample Preparation Properties	
Weight:	100mg
Volume:	10ml
Dilution:	100ml
Path Length:	1cm
Additional Information:	

Instrument Properties	
Instrument Type:	UV-1600 Series
Measuring Mode:	Absorbance
Slit Width:	2.0 nm
Light Source Change Wavelength:	340.8 nm
S/R Exchange:	Normal

Attachment Properties	
Attachment:	None-

No.	P/V	Wavelength	Abs.	Description
1	↑	233.30	0.429	
2	↑	209.90	0.824	
3	↓	225.40	0.403	

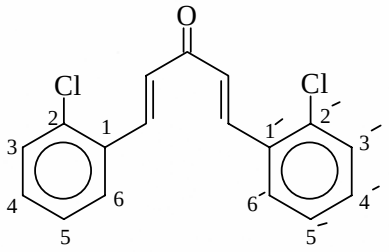


Fig-5: UV spectrum of compound **3c**.

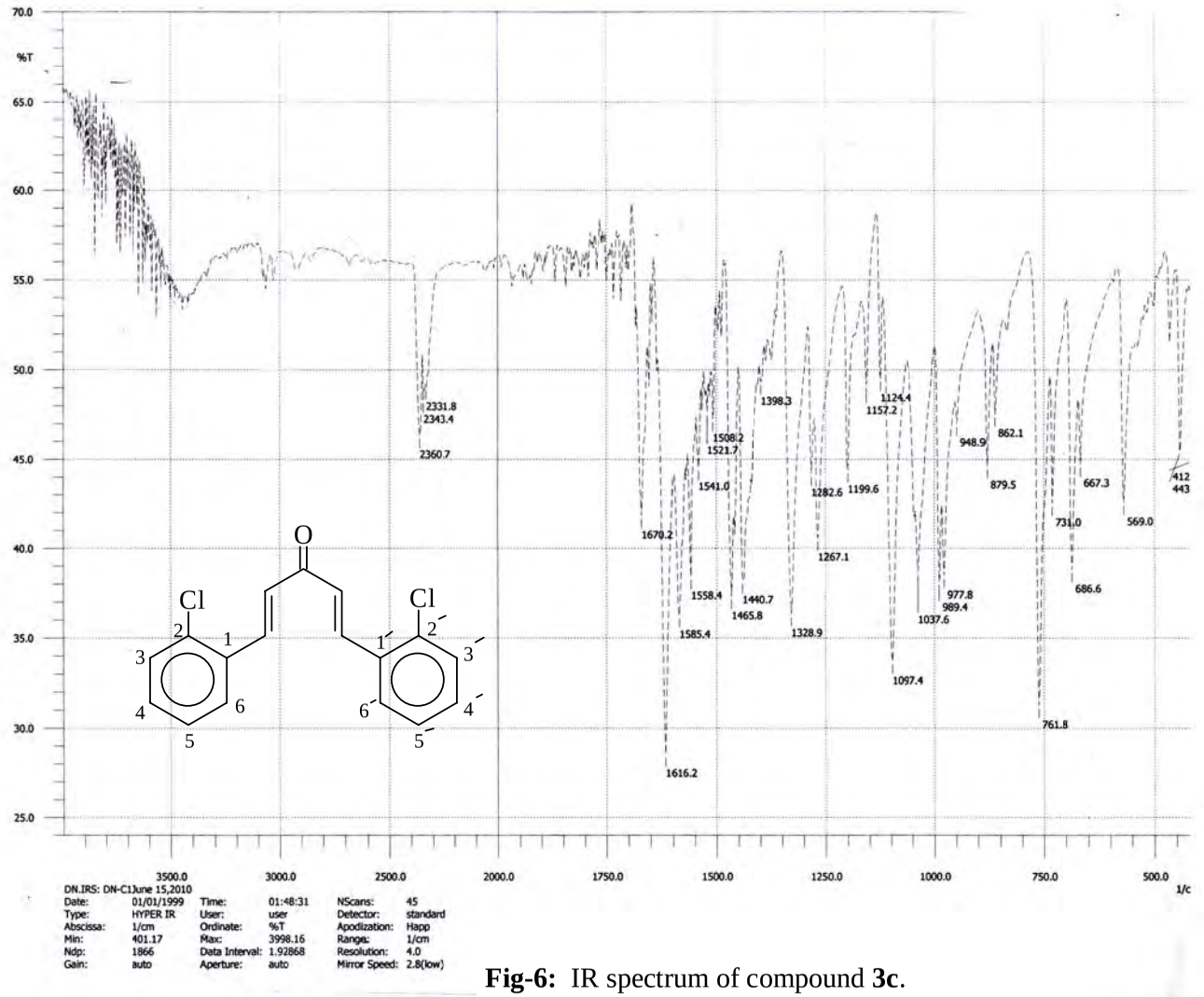


Fig-6: IR spectrum of compound **3c**.

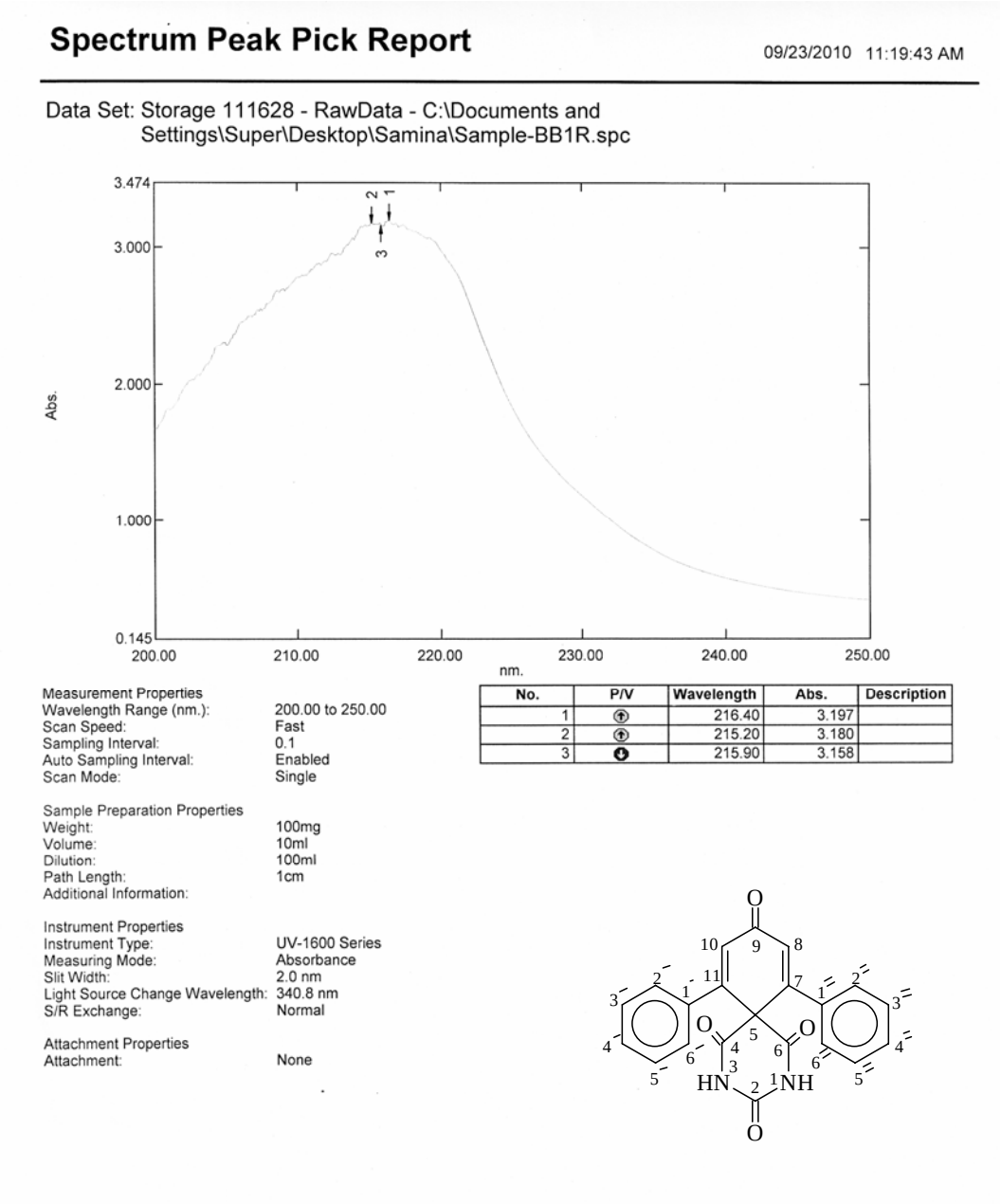


Fig-7: UV spectrum of compound **5a**.

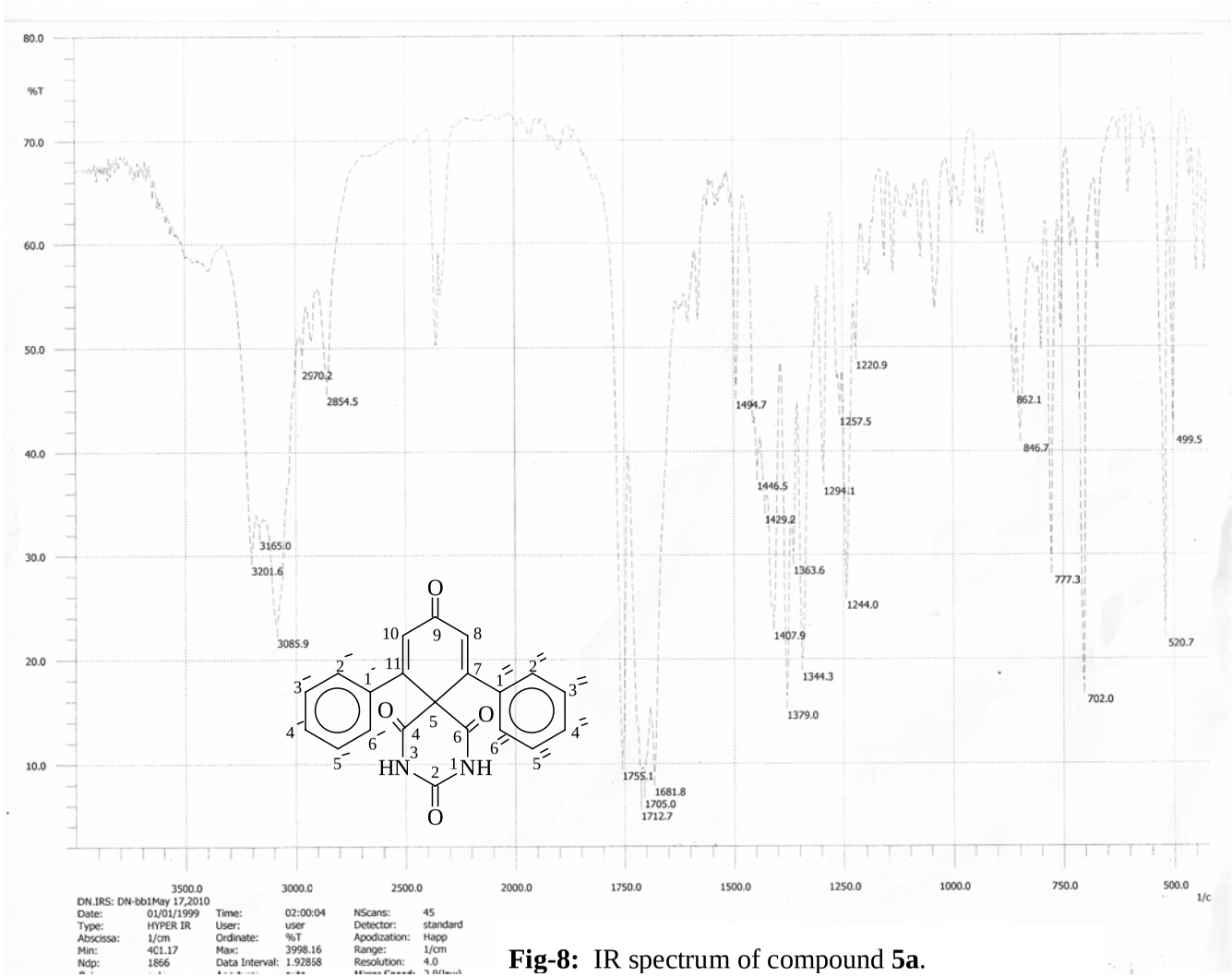


Fig-8: IR spectrum of compound **5a**.

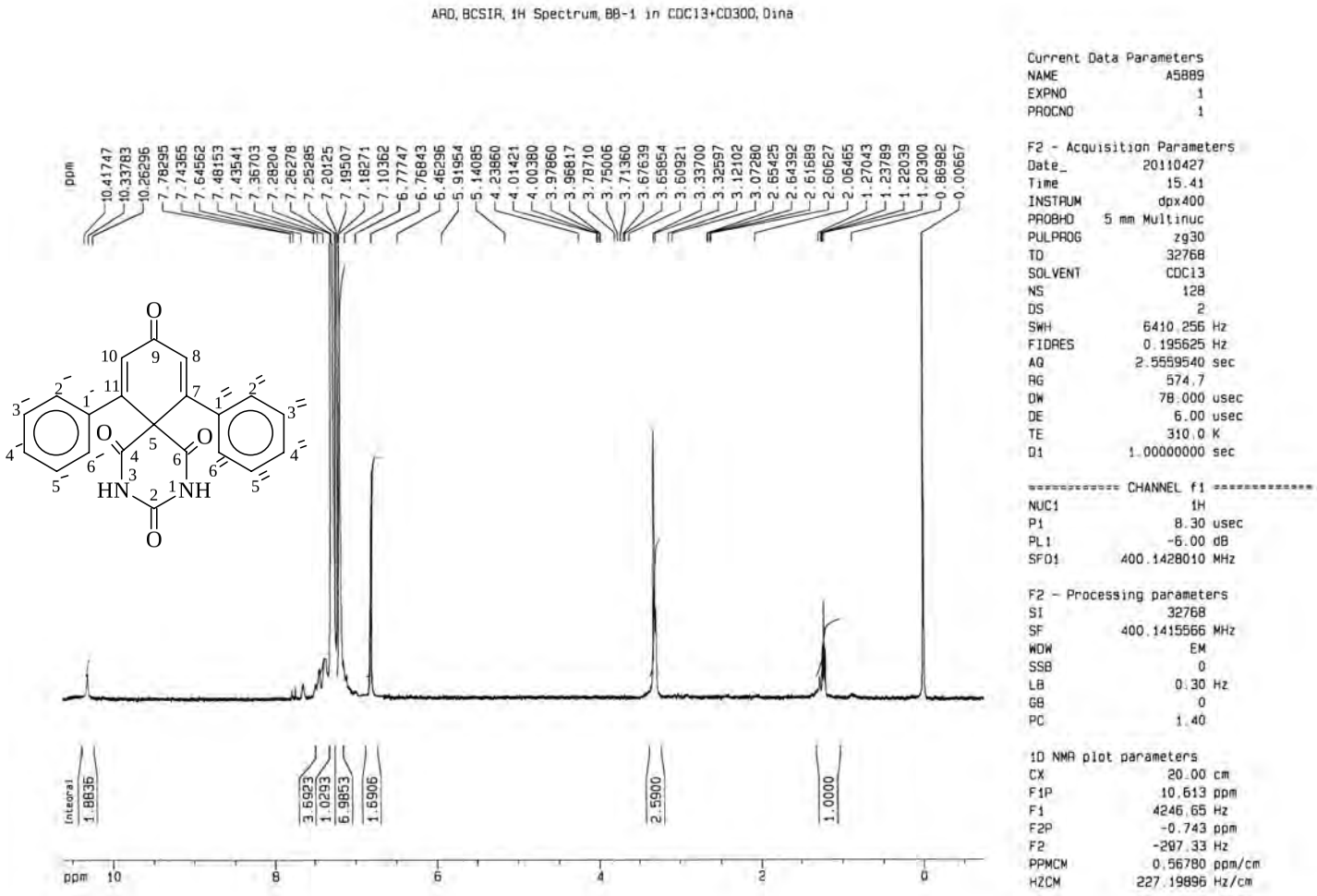


Fig-9: ^{1}H NMR spectrum of compound **5a**.

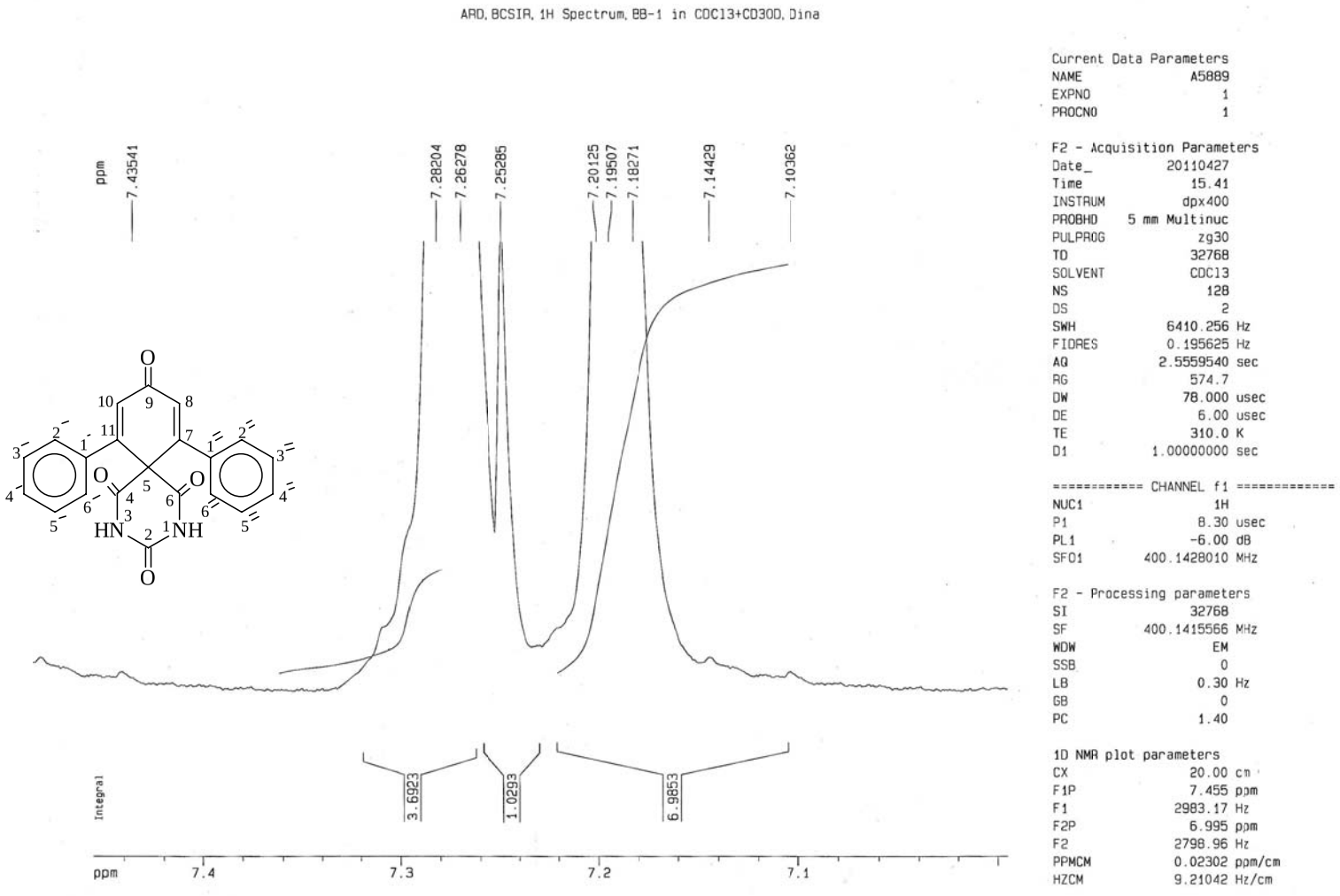


Fig-9: ^{1}H NMR spectrum of compound **5a** (expanded).

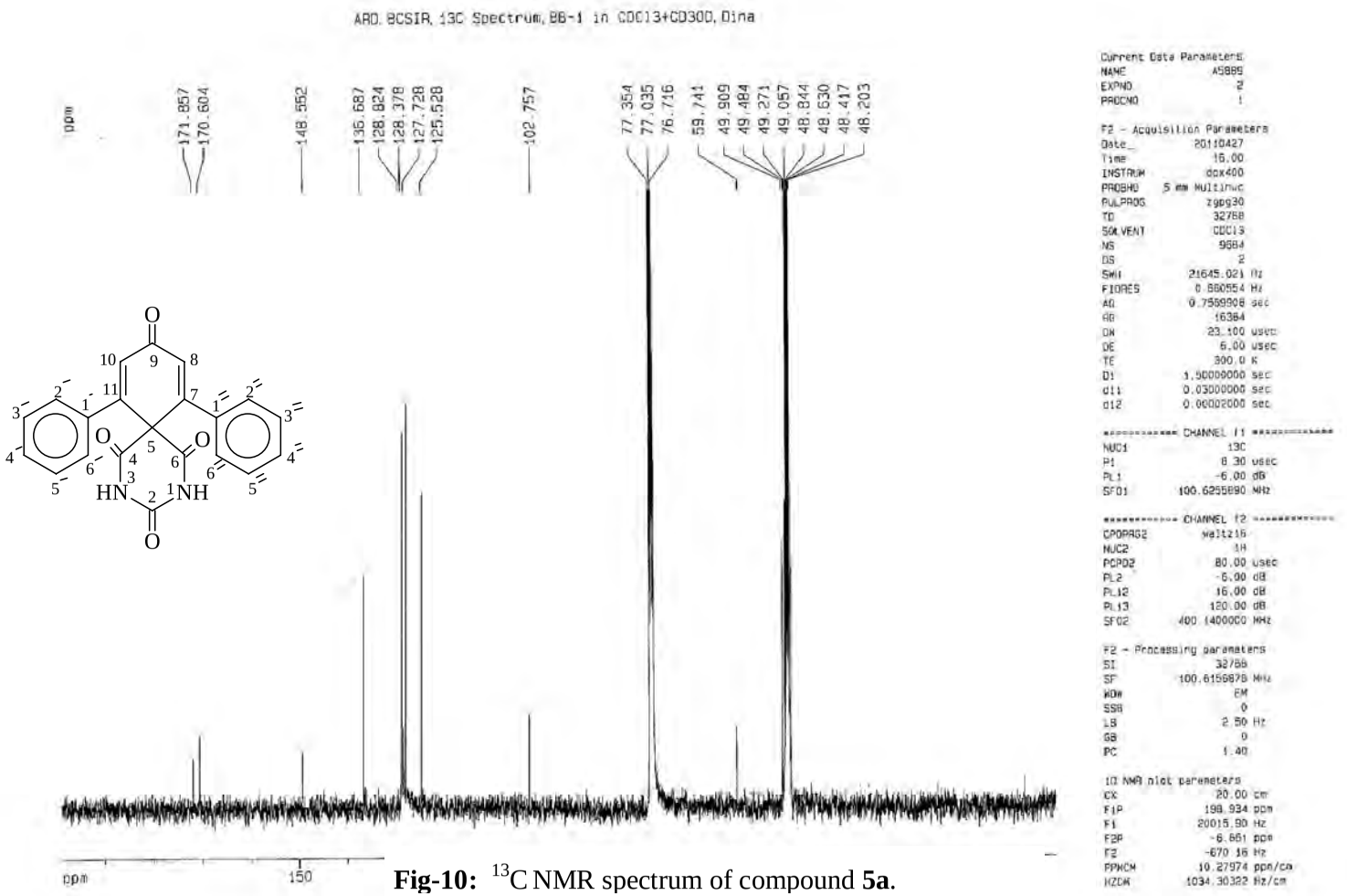


Fig-10: ^{13}C NMR spectrum of compound **5a**.

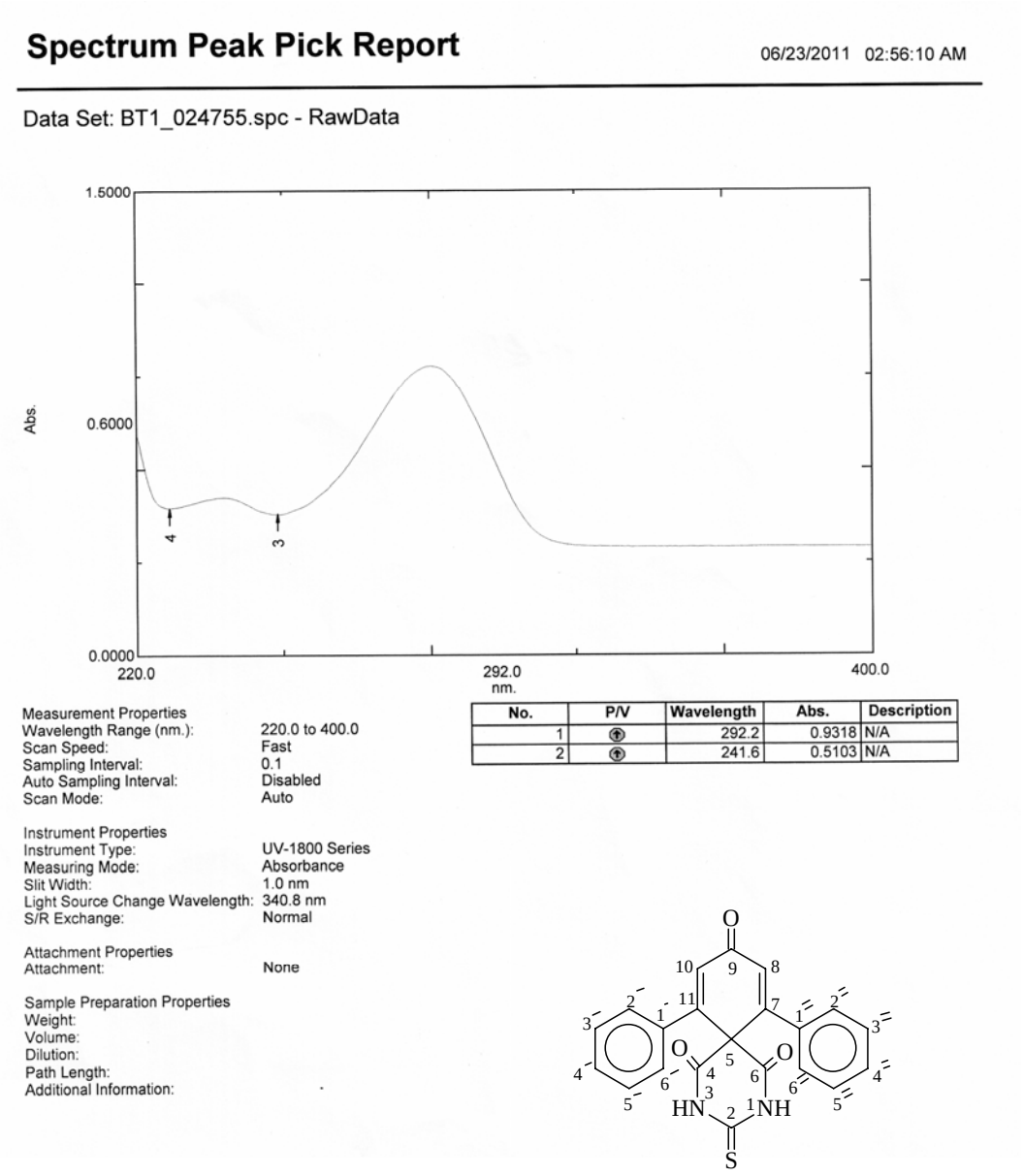


Fig-11: UV spectrum of compound **5b**.

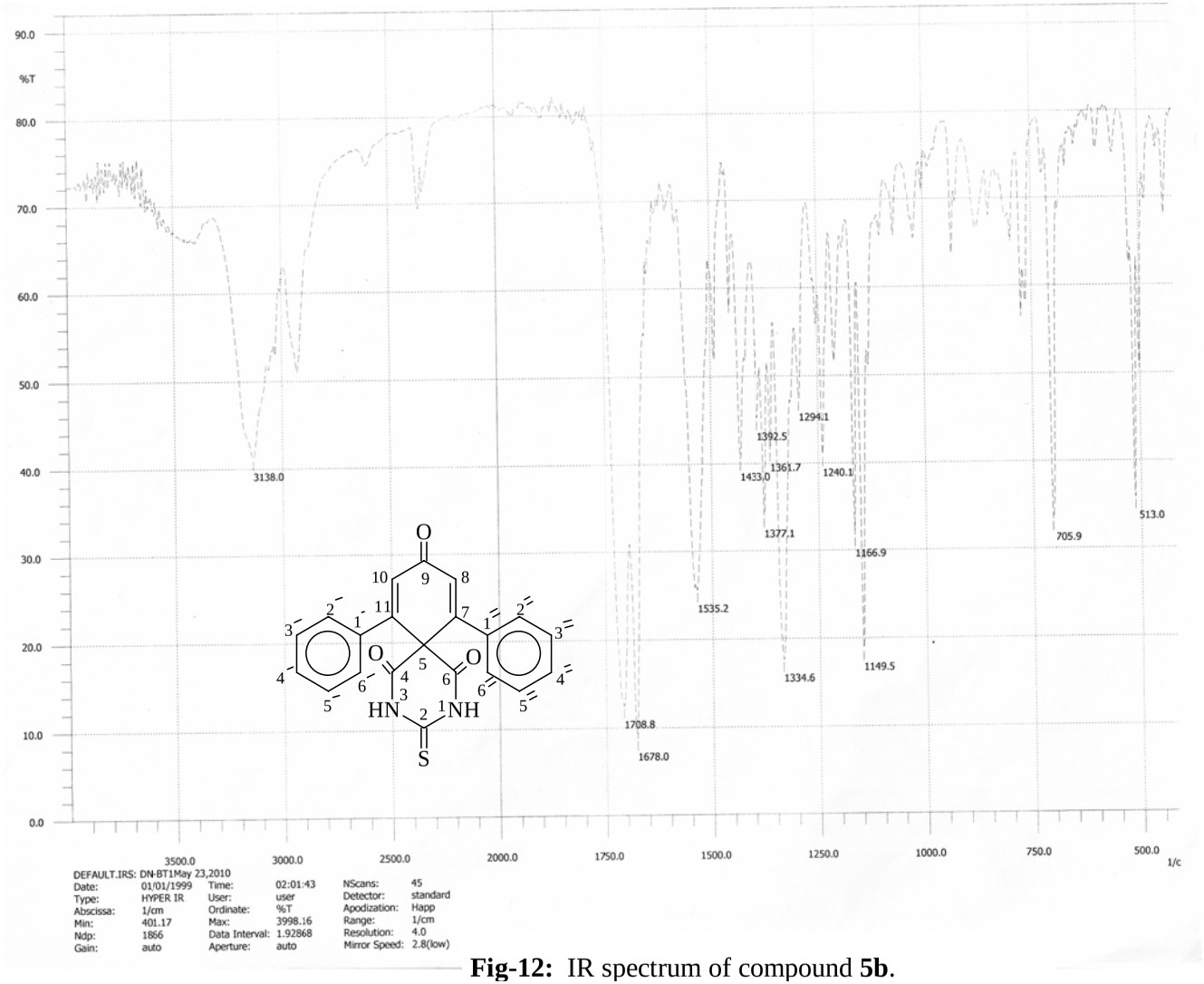


Fig-12: IR spectrum of compound **5b**.

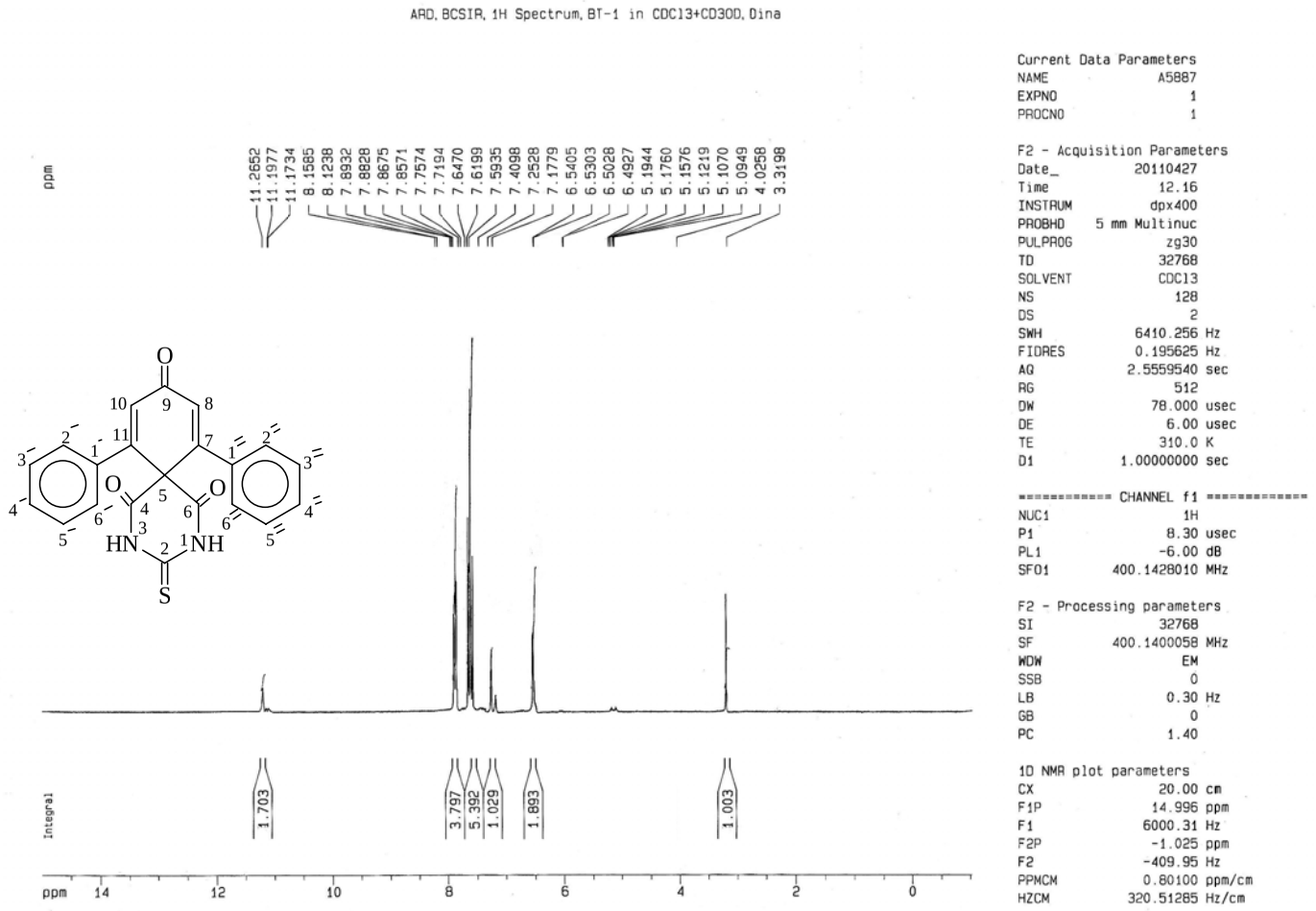


Fig-13: ^{1}H NMR spectrum of compound **5b**.

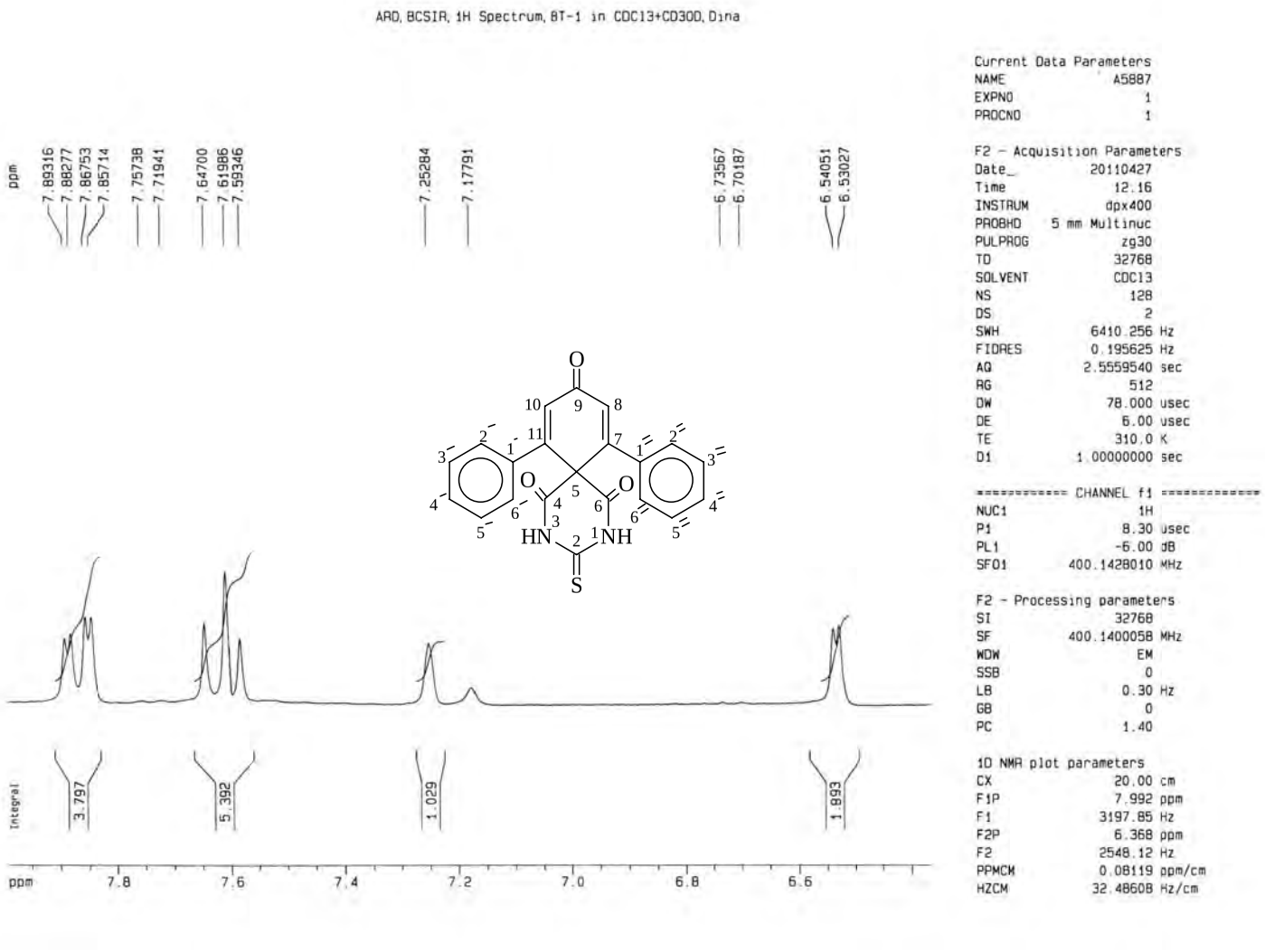


Fig-13: ^{1}H NMR spectrum of compound **5b** (expanded).

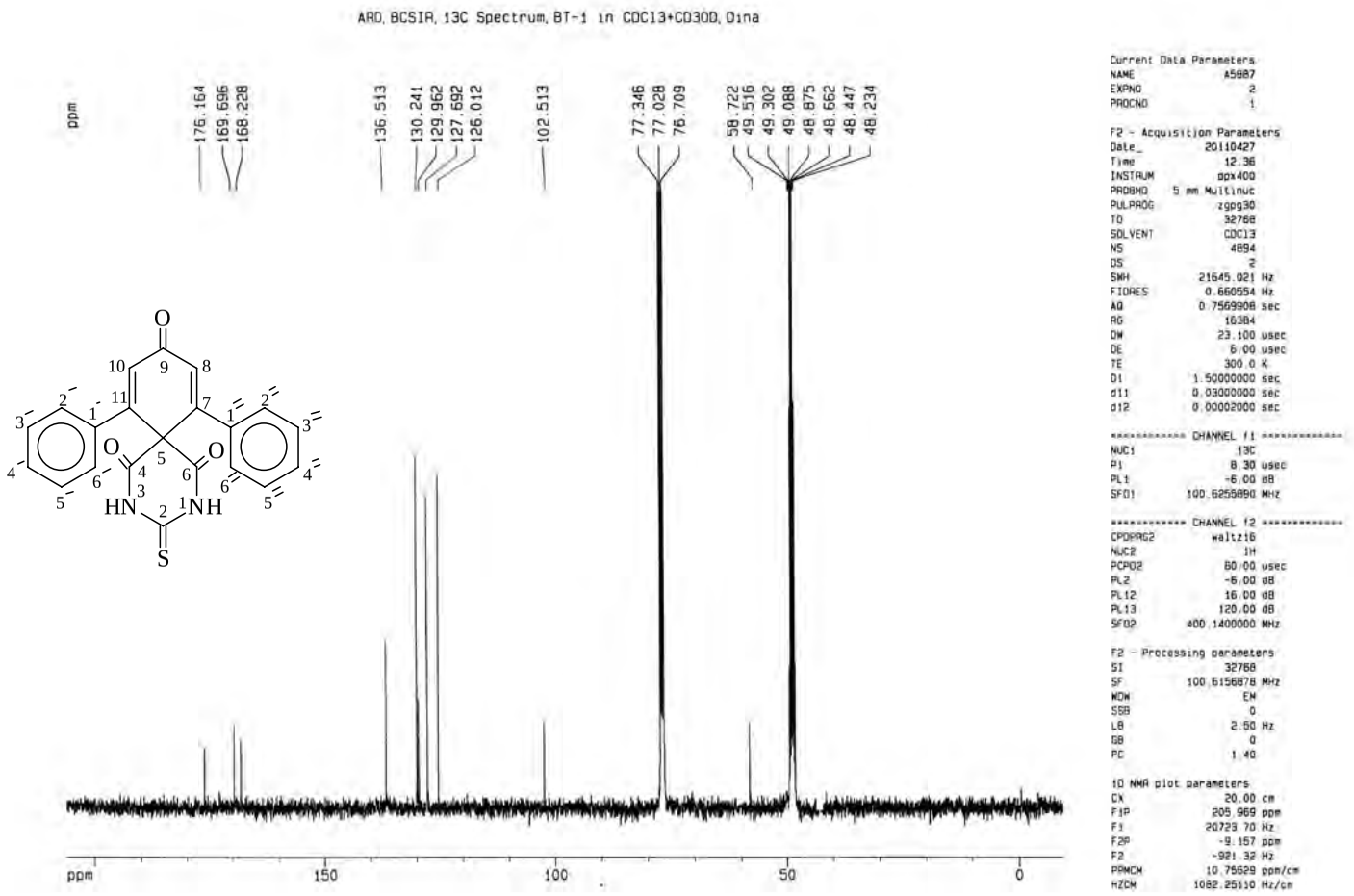


Fig-14: ^{13}C NMR spectrum of compound **5b**.

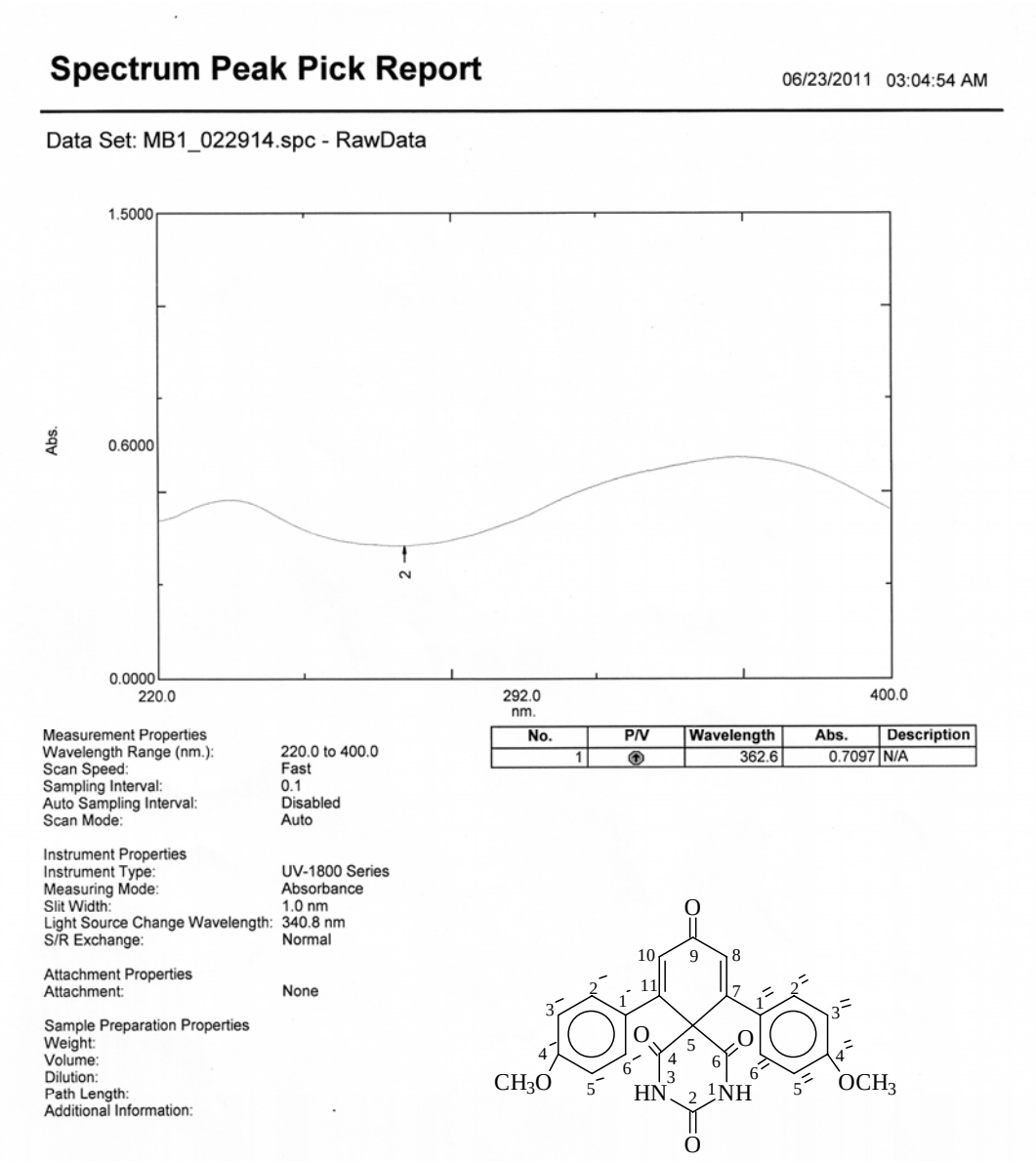


Fig-15: UV spectrum of compound **5c**.

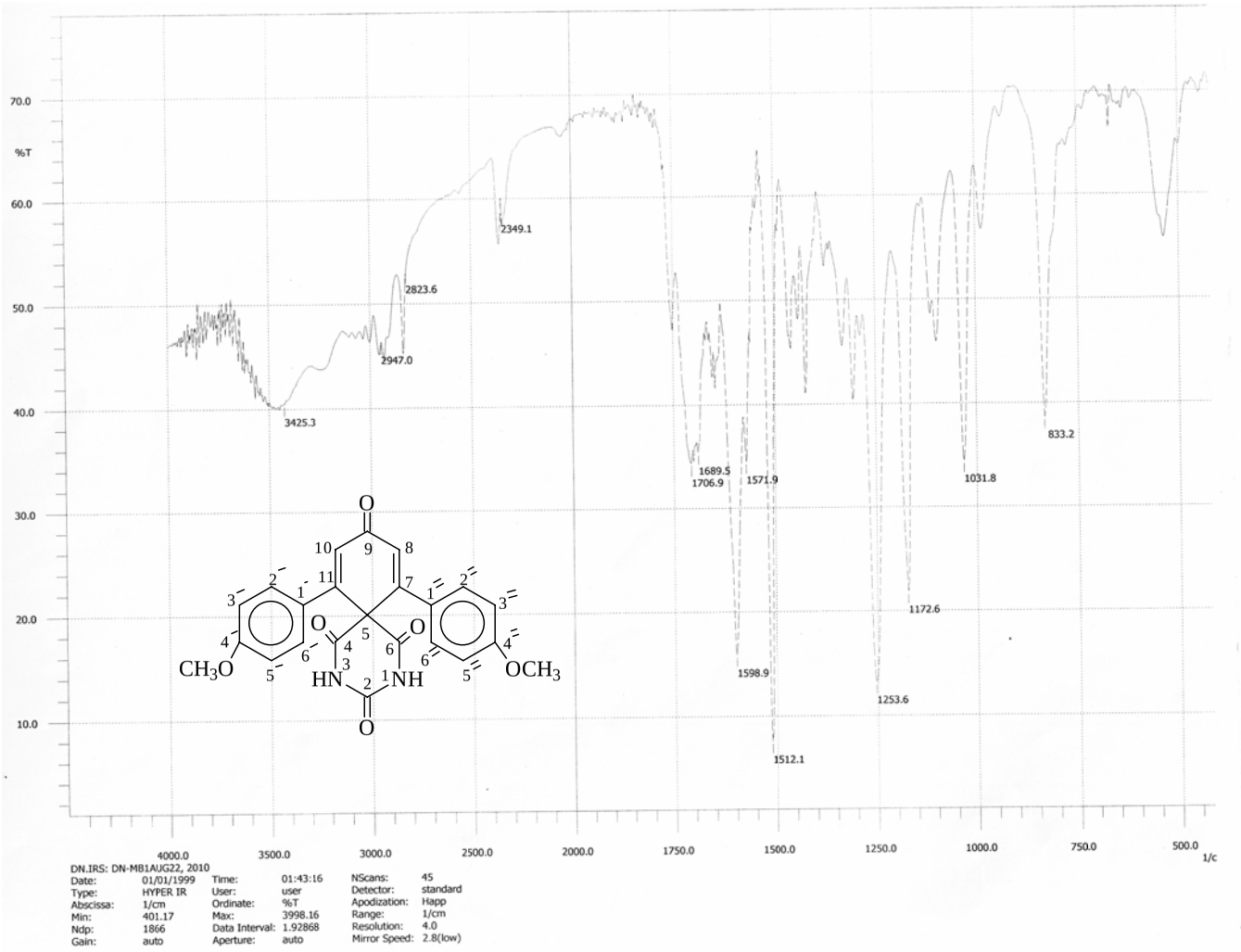


Fig-16: IR spectrum of compound **5c**.

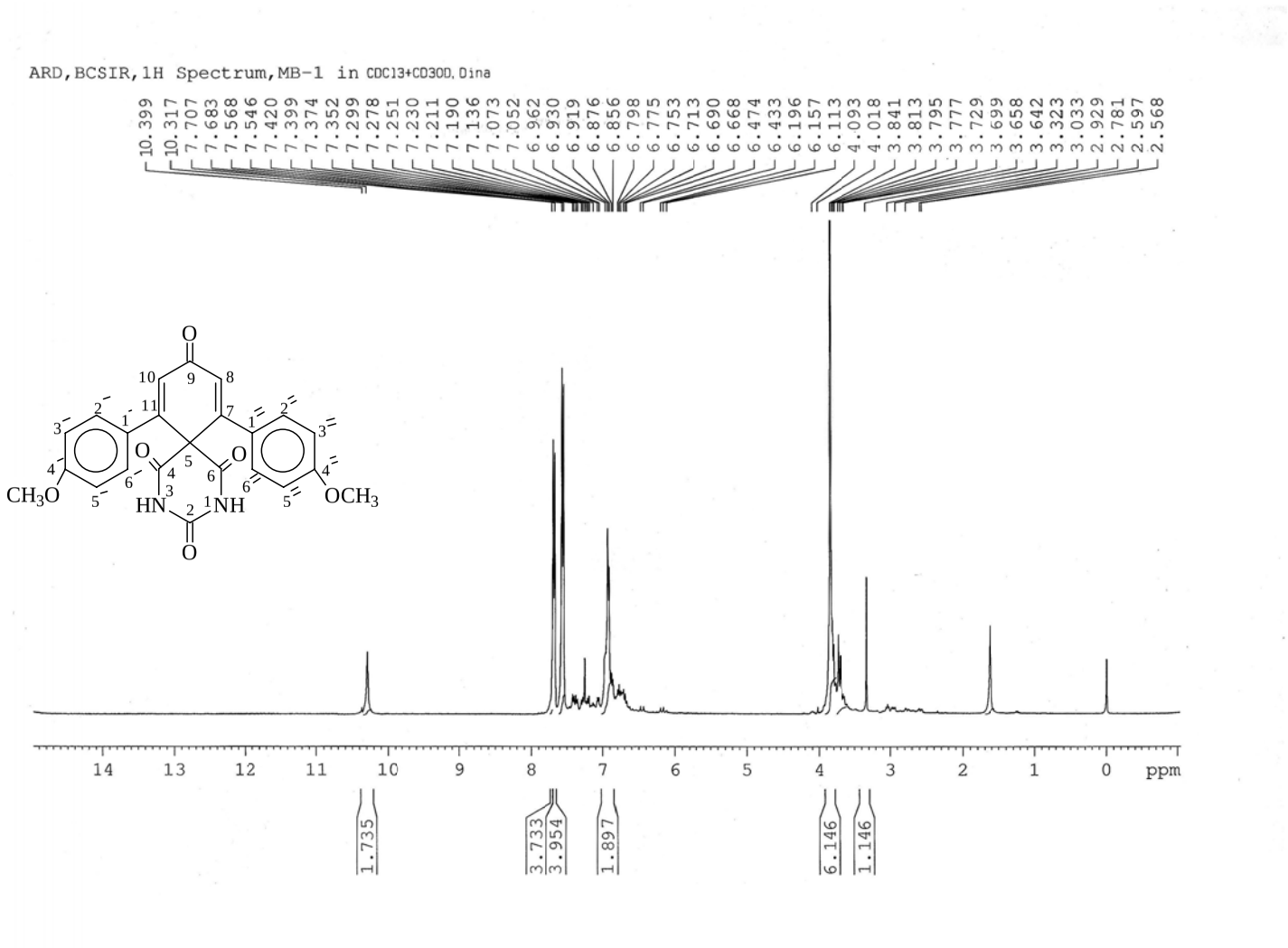


Fig-17: ^{1}H NMR spectrum of compound **5c.**

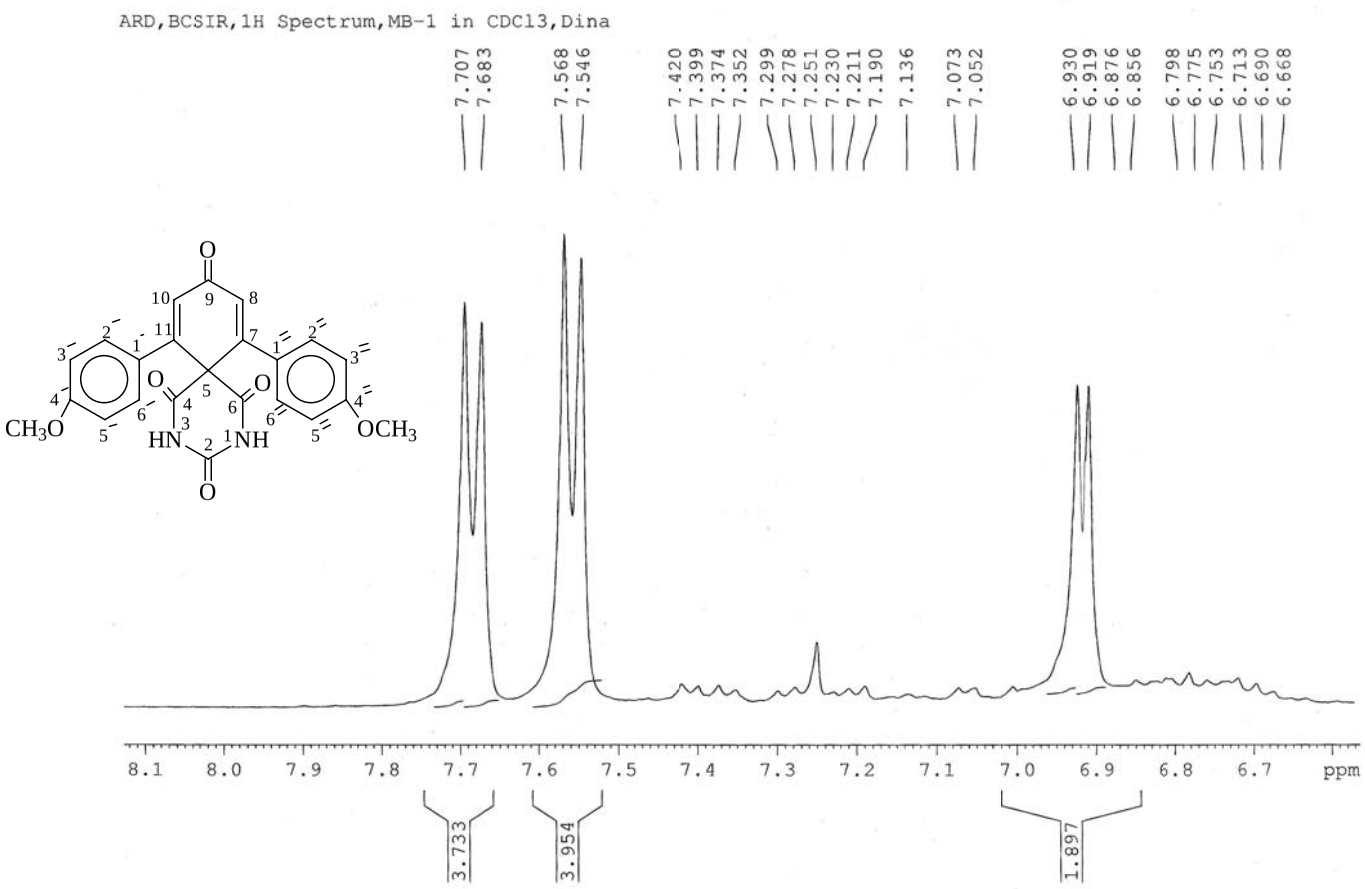


Fig-17: ^{1}H NMR spectrum of compound **5c** (expanded).

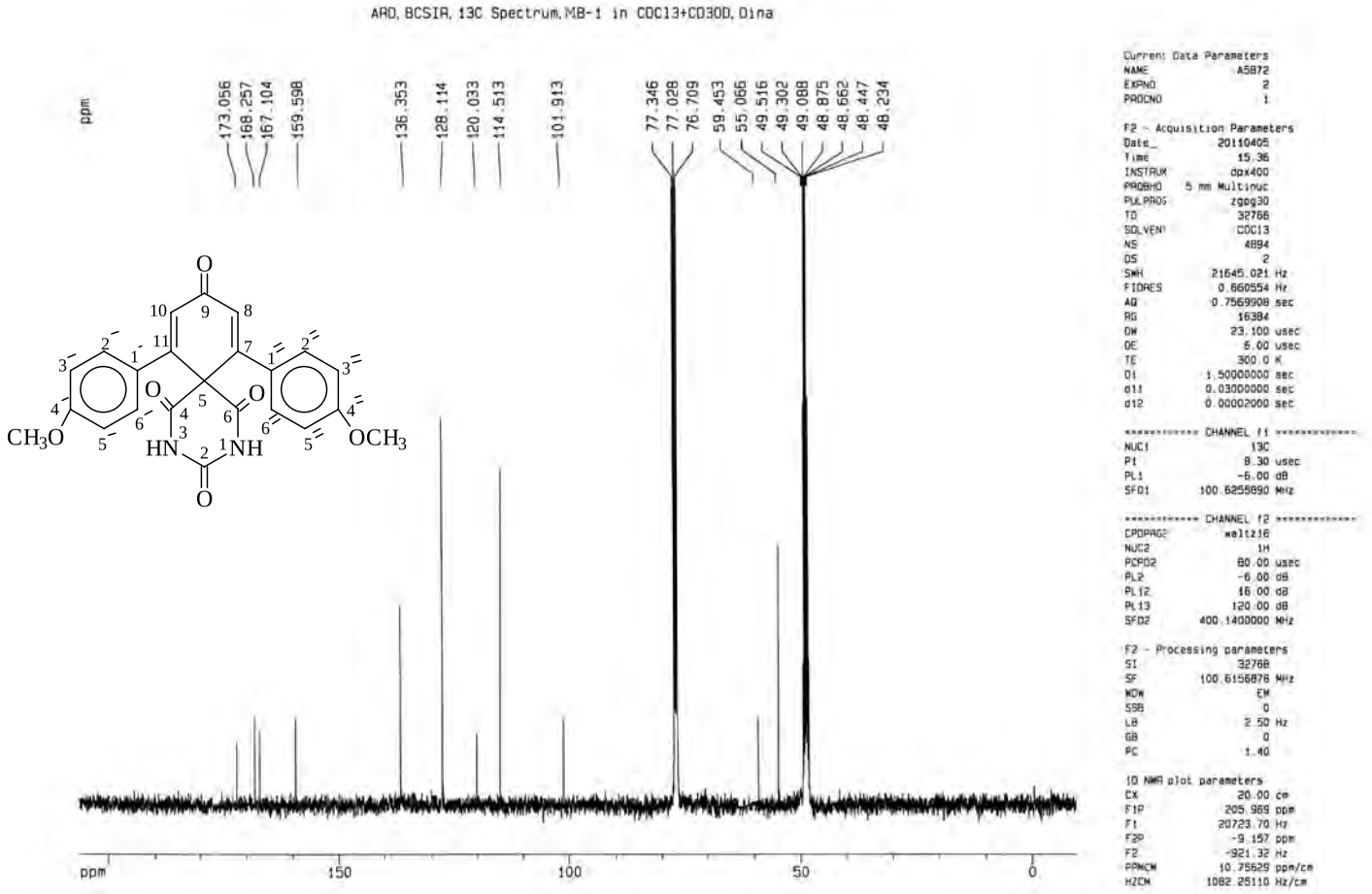


Fig-18: ^{13}C NMR spectrum of compound **5c**.

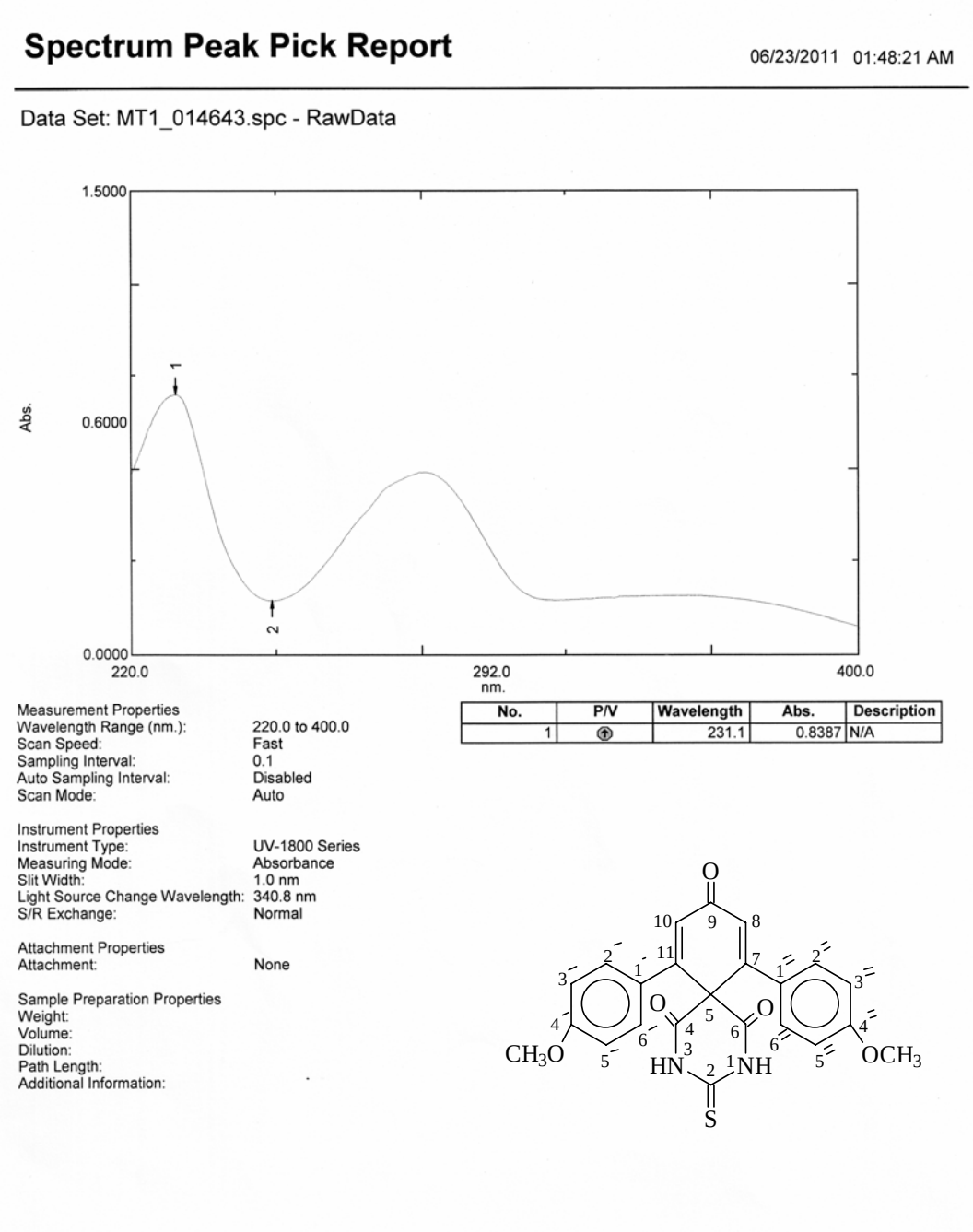


Fig-19: UV spectrum of compound **5d**.

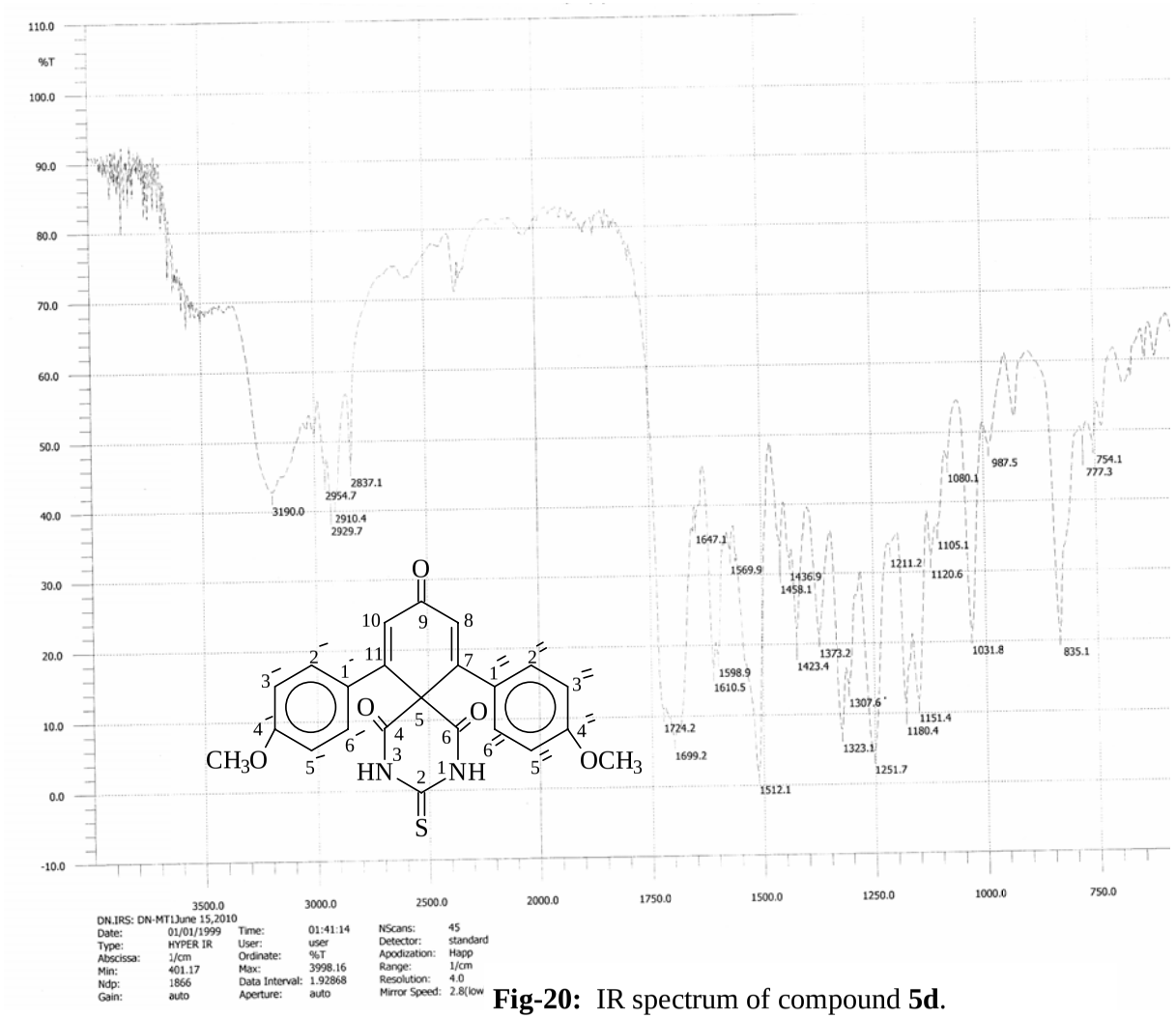


Fig-20: IR spectrum of compound **5d**.

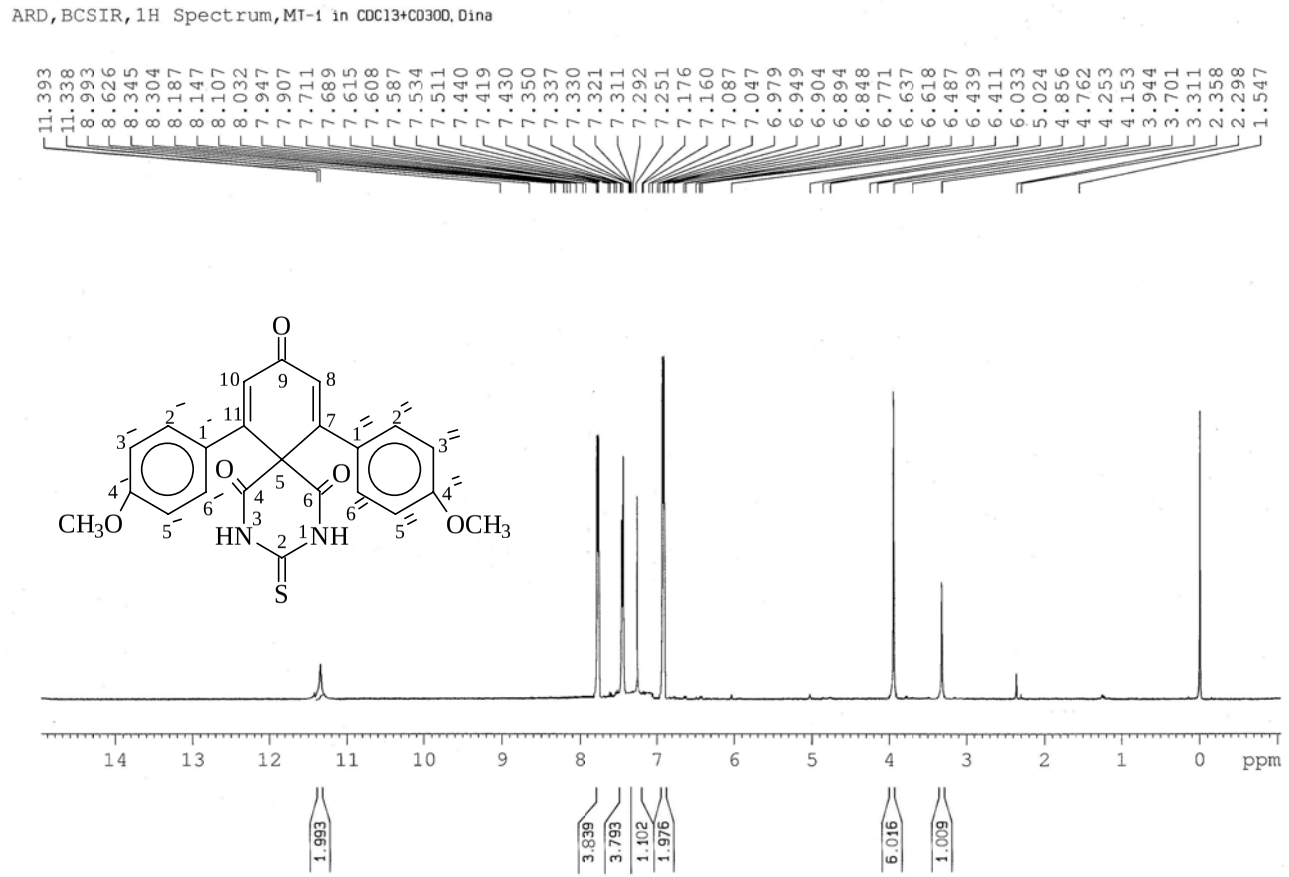


Fig-21: ^{1}H NMR spectrum of compound **5d**.

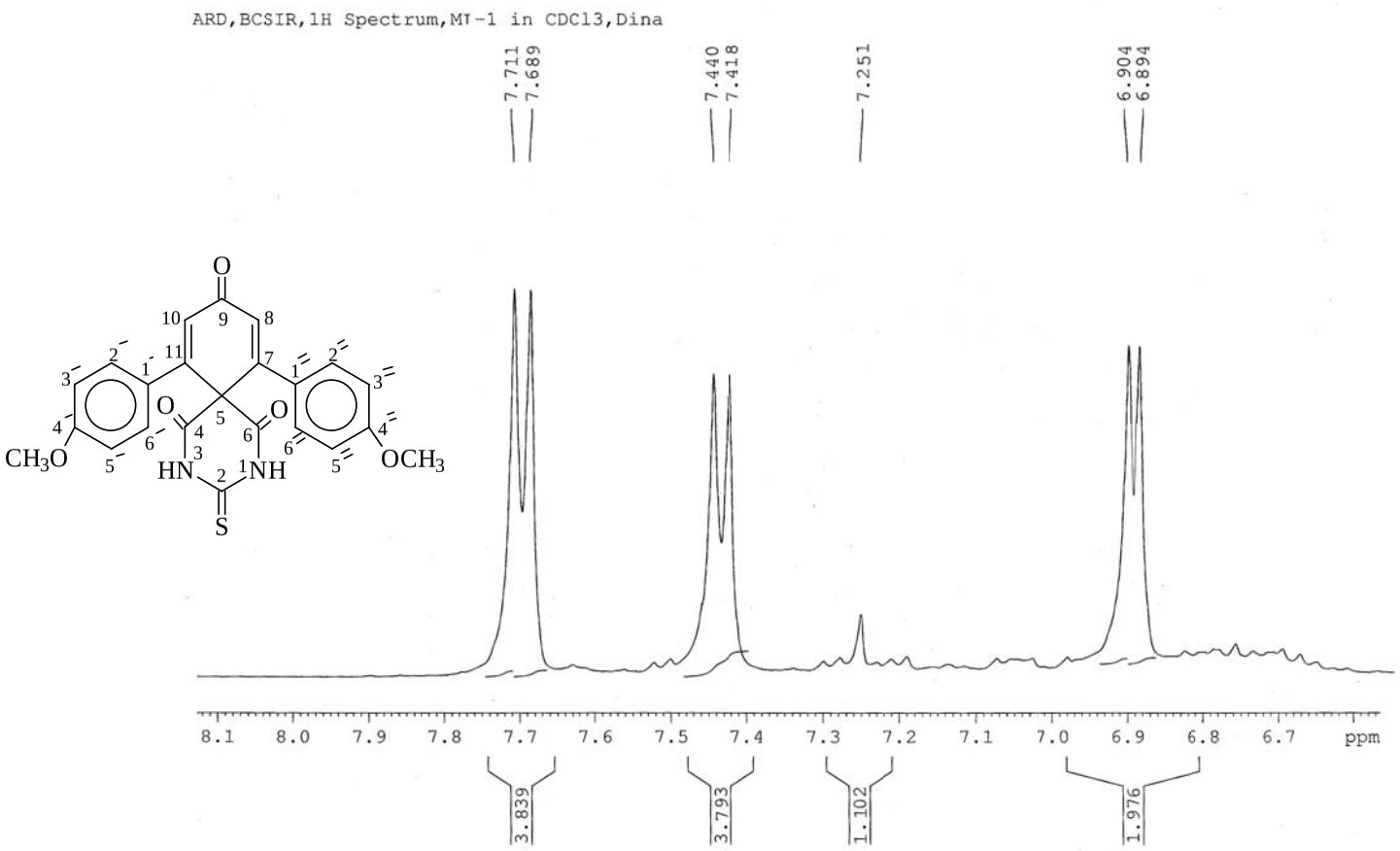


Fig-21: ^{1}H NMR spectrum of compound **5d** (expanded).

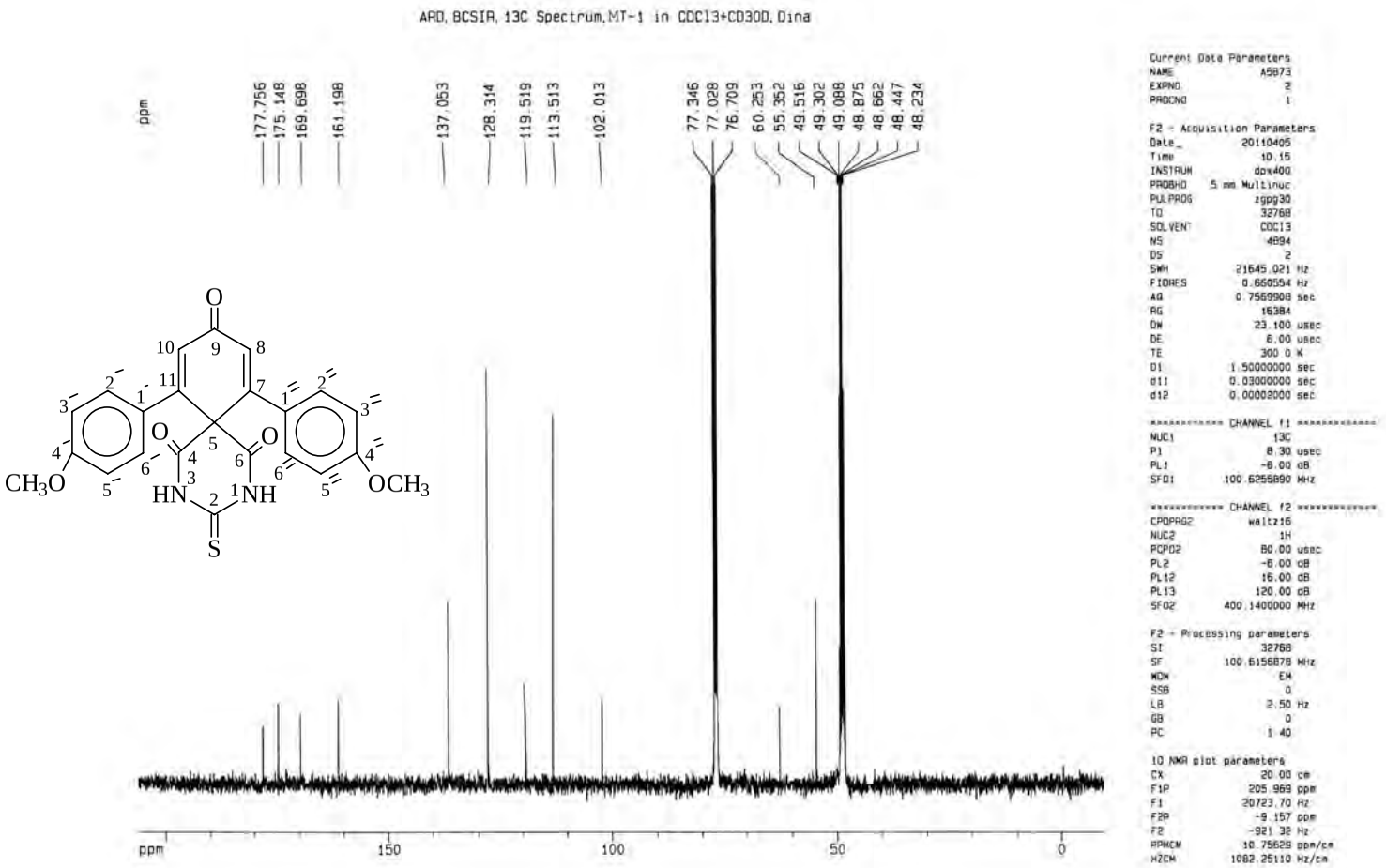


Fig-22: ^{13}C NMR spectrum of compound **5d**.

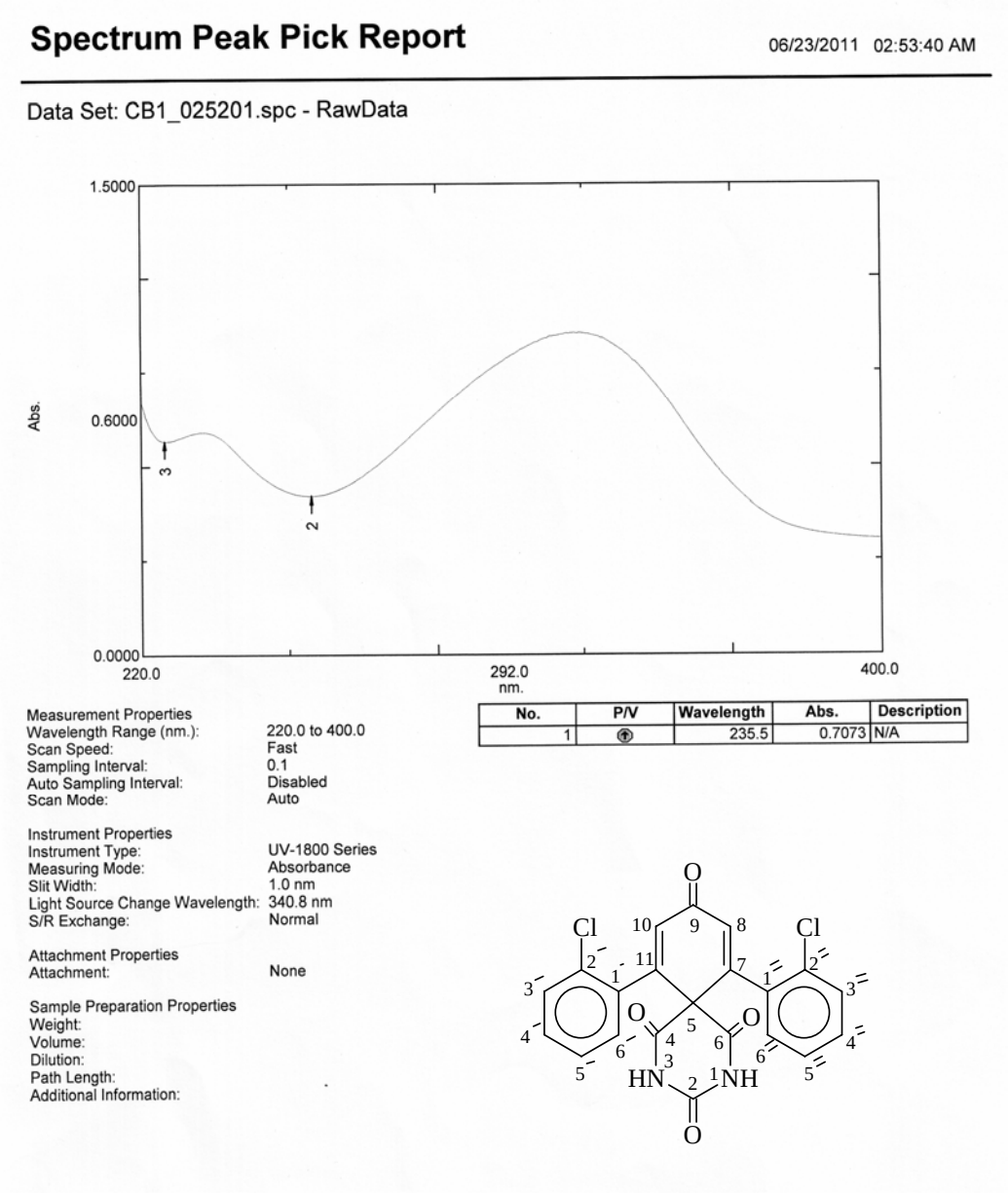


Fig-23: UV spectrum of compound **5e**.

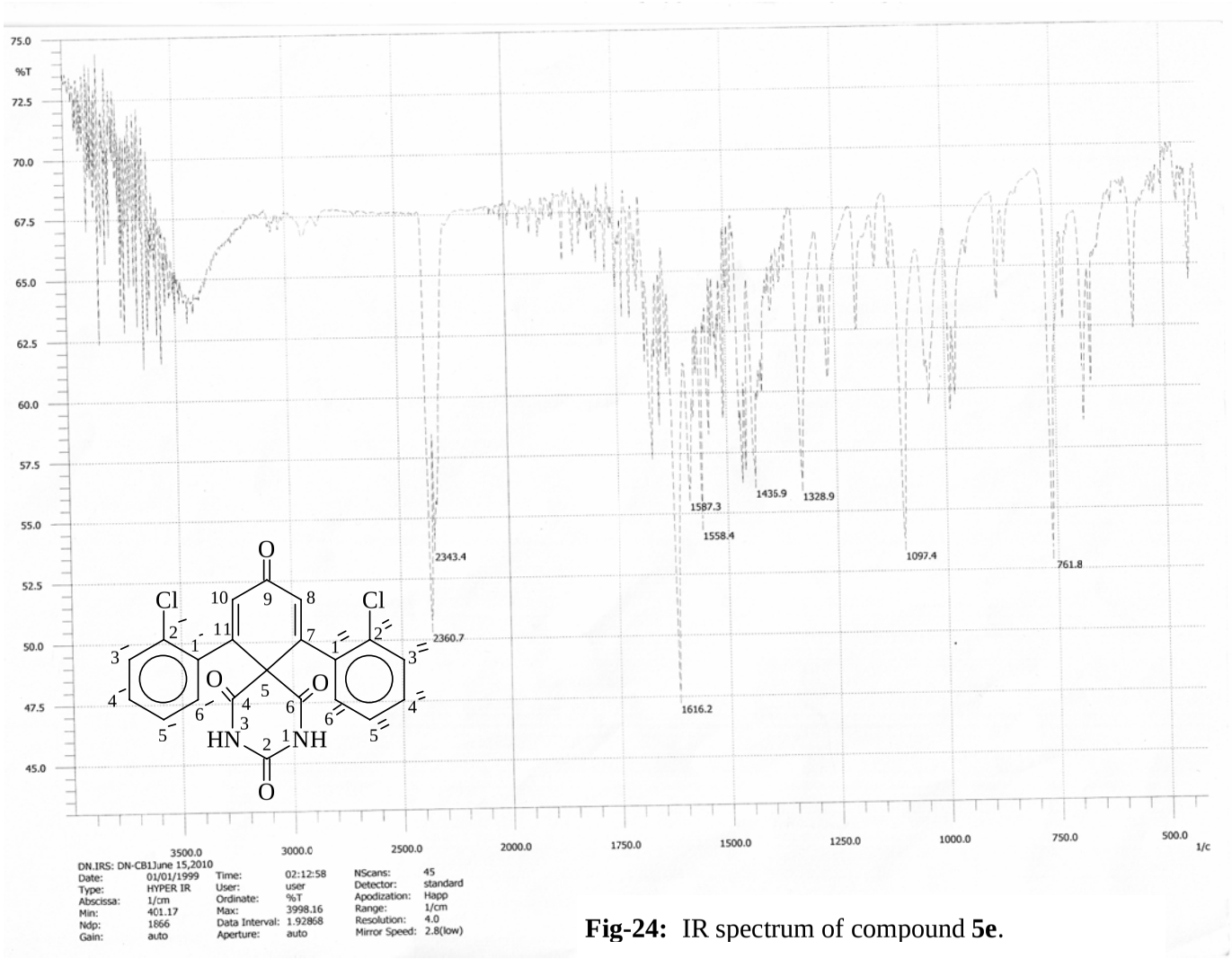


Fig-24: IR spectrum of compound **5e**.

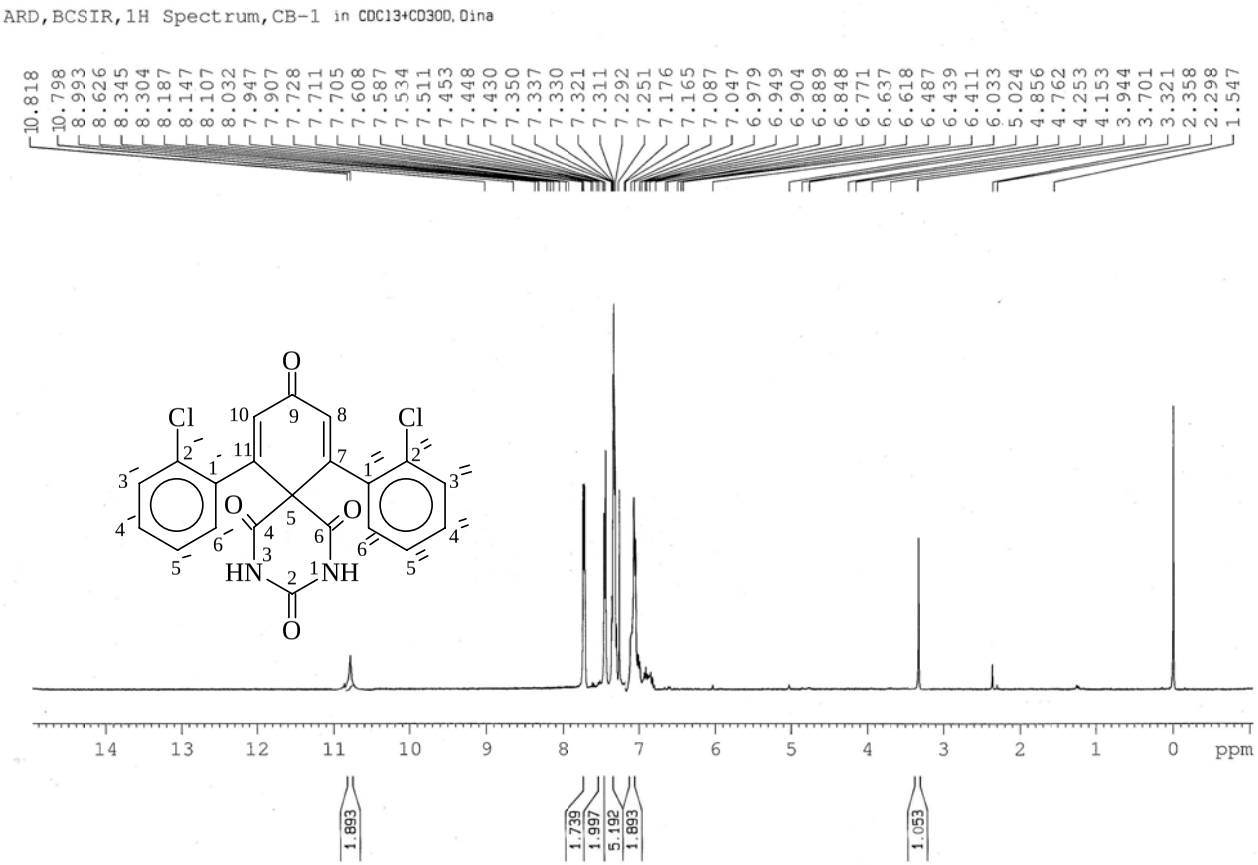


Fig-25: ^{1}H NMR spectrum of compound **5e**.

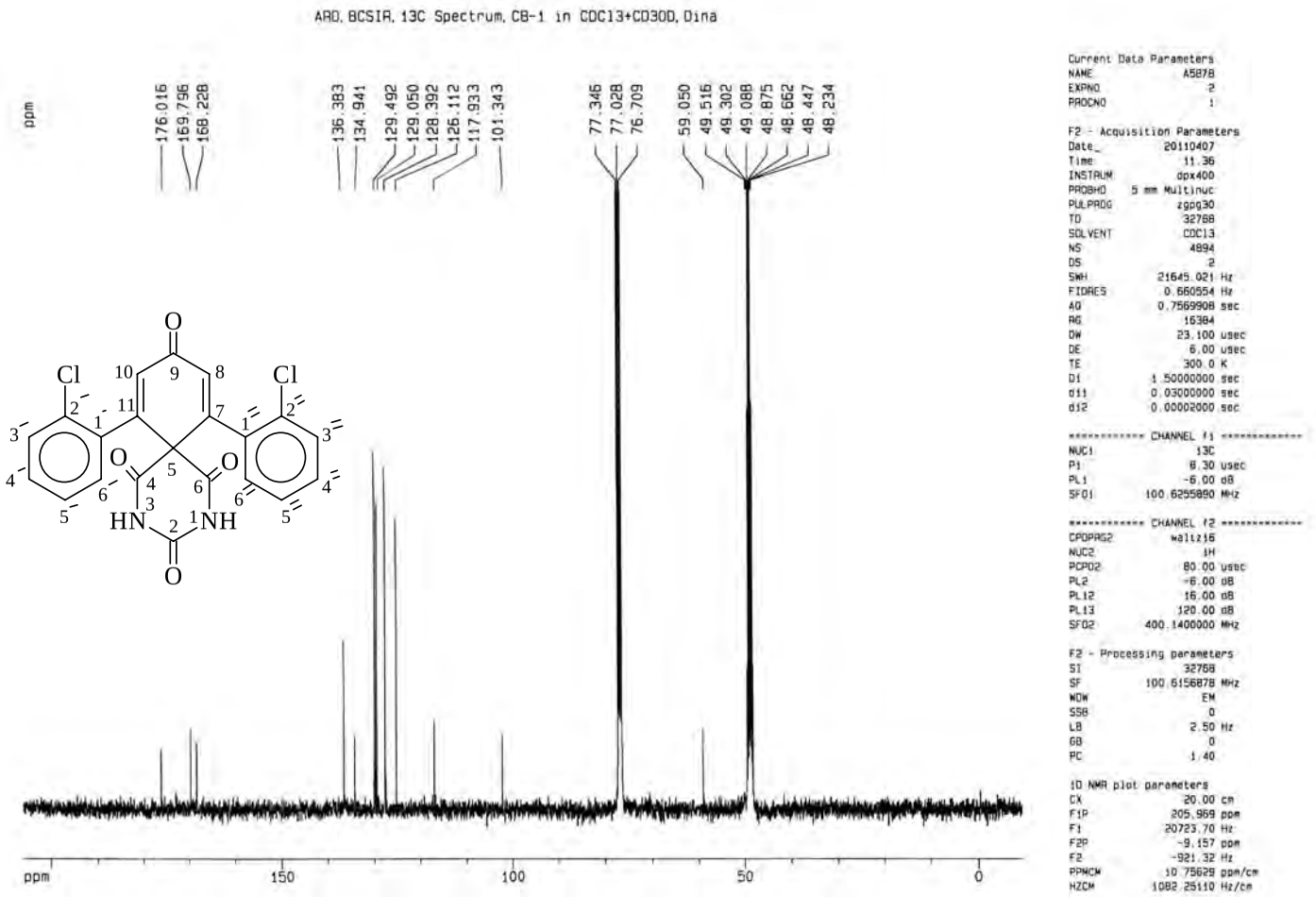


Fig-26: ^{13}C NMR spectrum of compound **5e**.

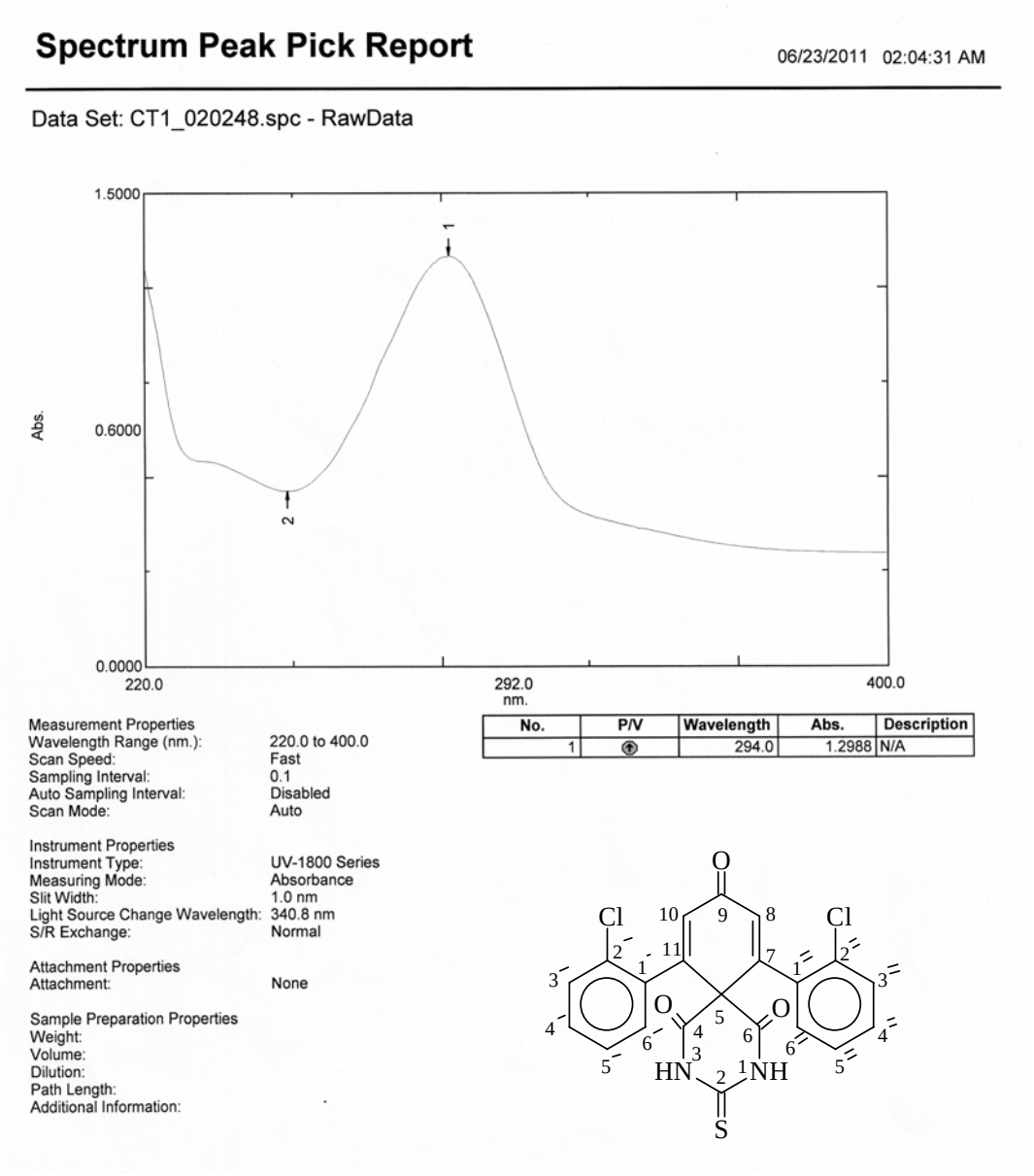


Fig-27: UV spectrum of compound **5f**.

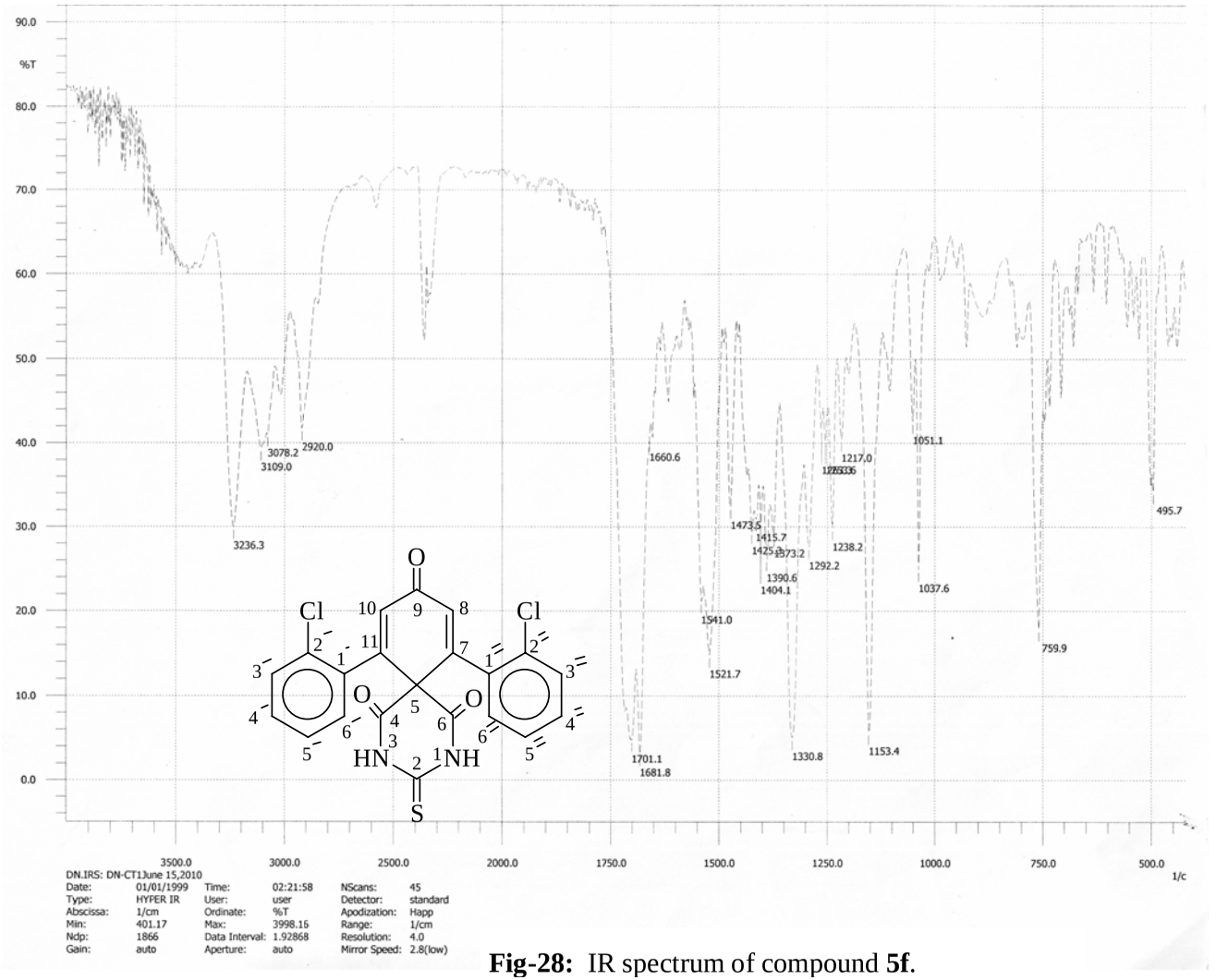


Fig-28: IR spectrum of compound **5f**.

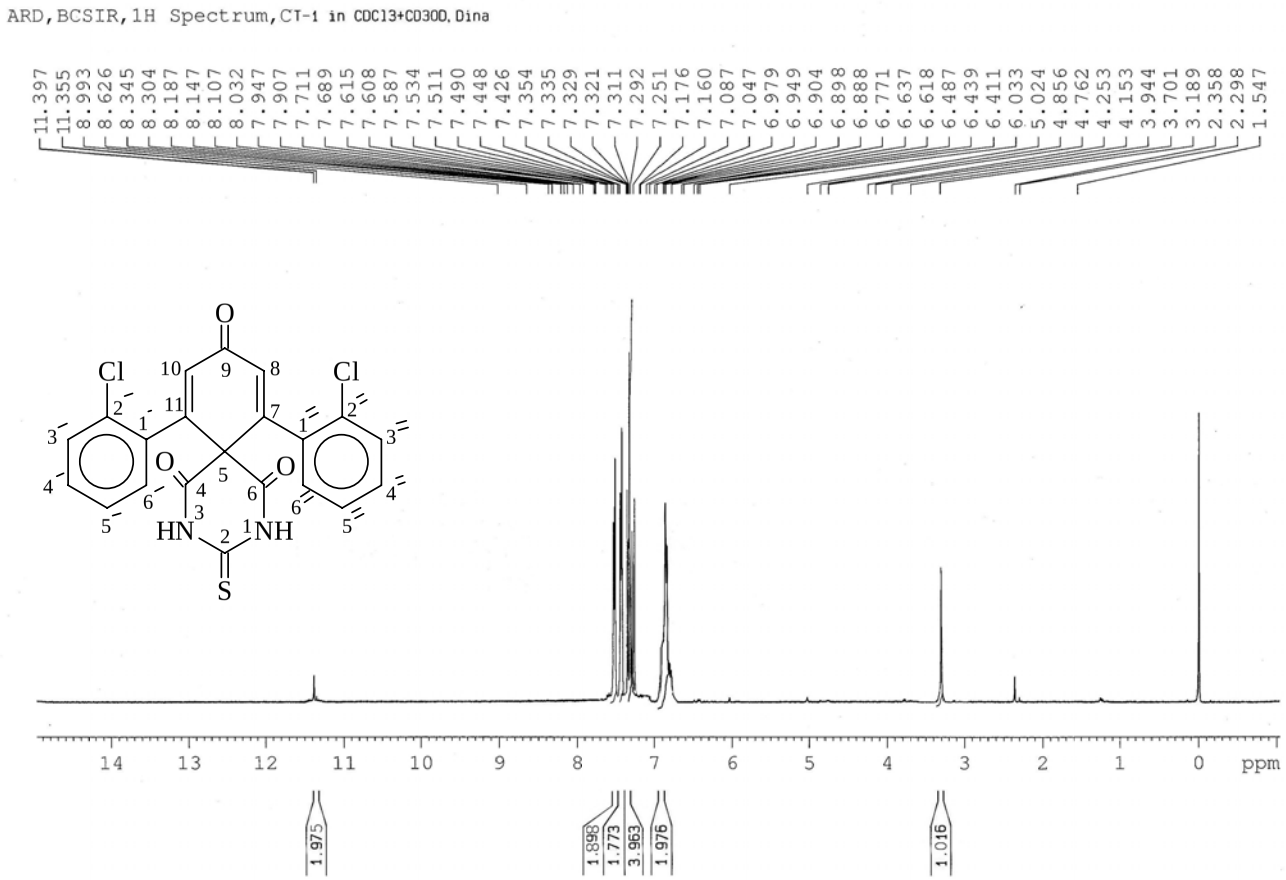


Fig-29: ^{1}H NMR spectrum of compound **5f**.

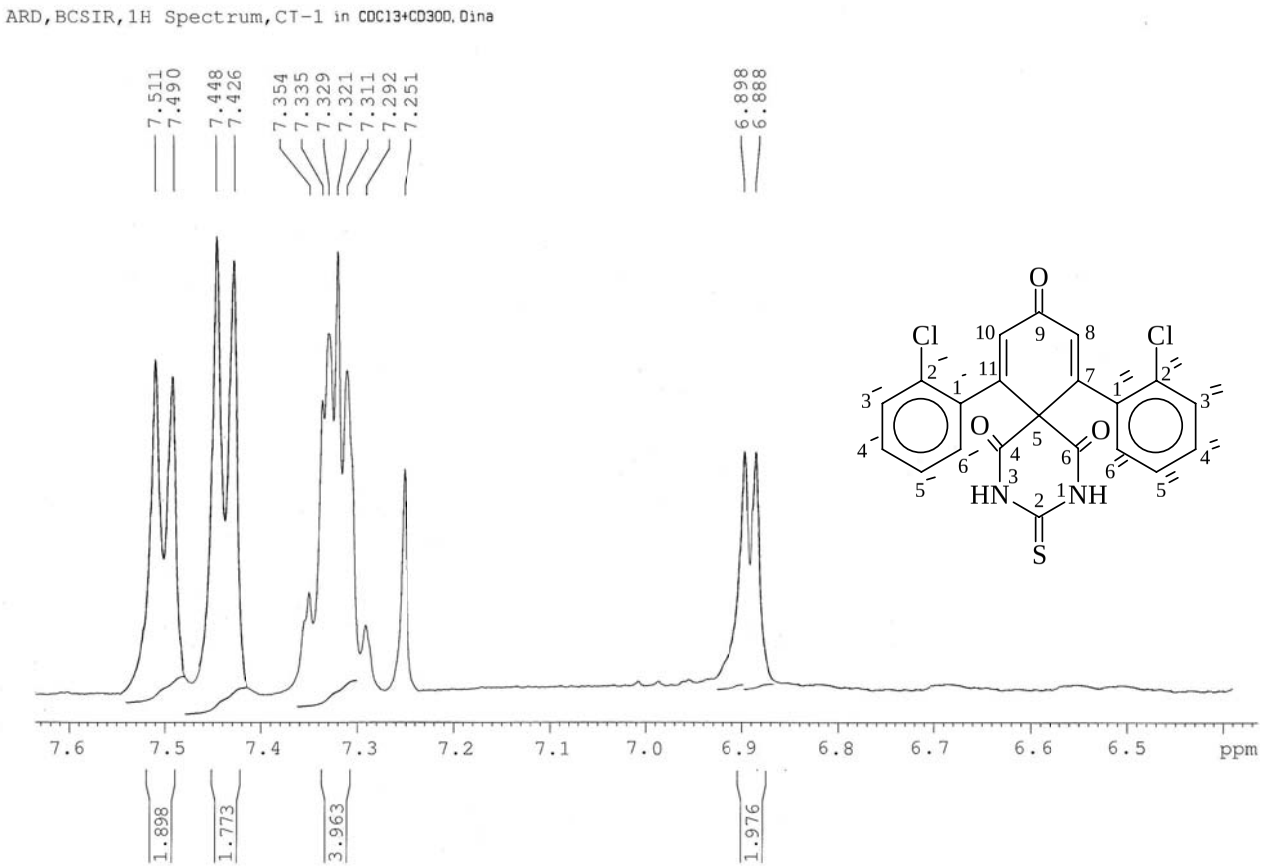


Fig-29: ^{1}H NMR spectrum of compound **5f** (expanded).

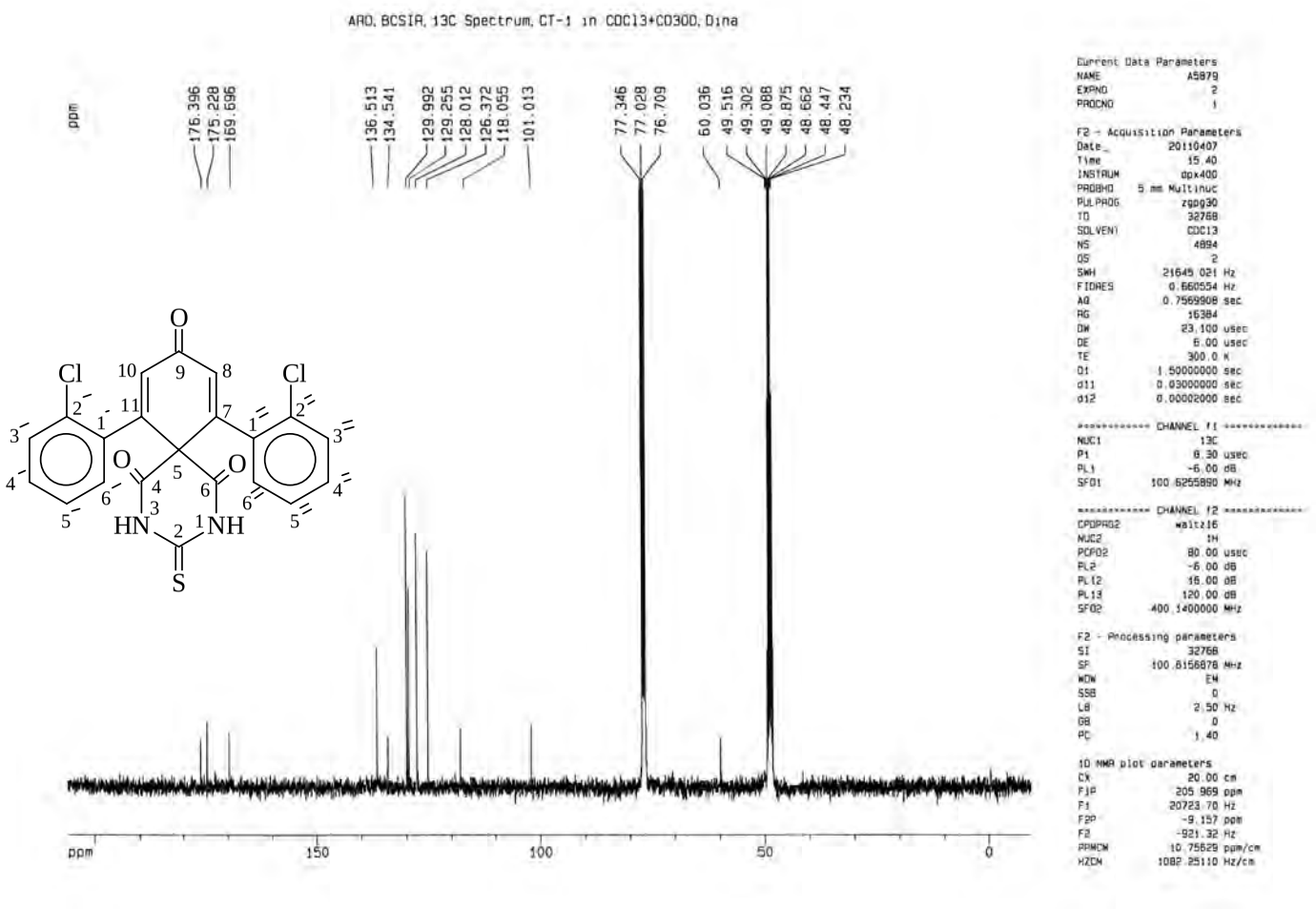


Fig-30: ^{13}C NMR spectrum of compound **5f**.

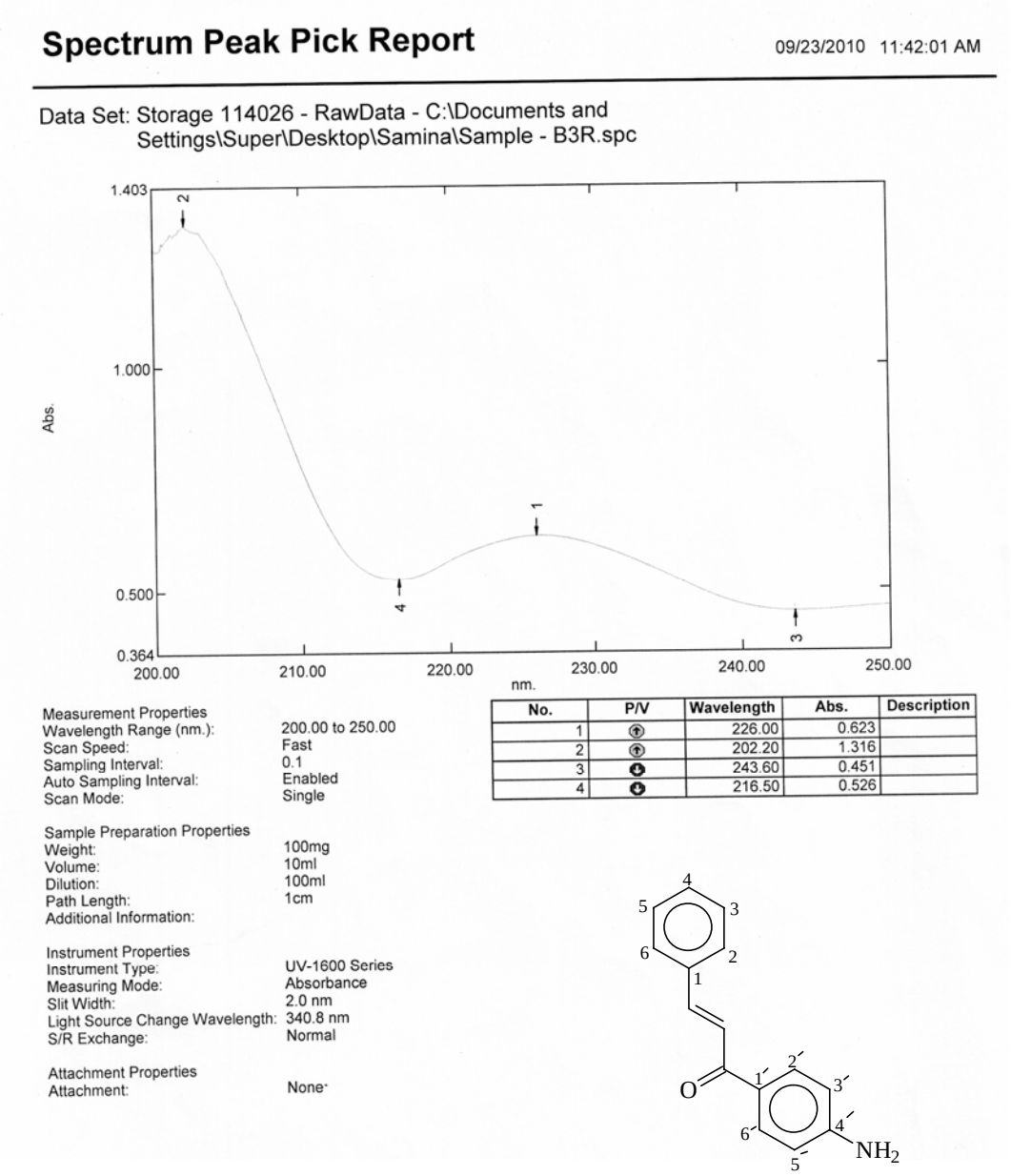


Fig-31: UV spectrum of compound **8a**.

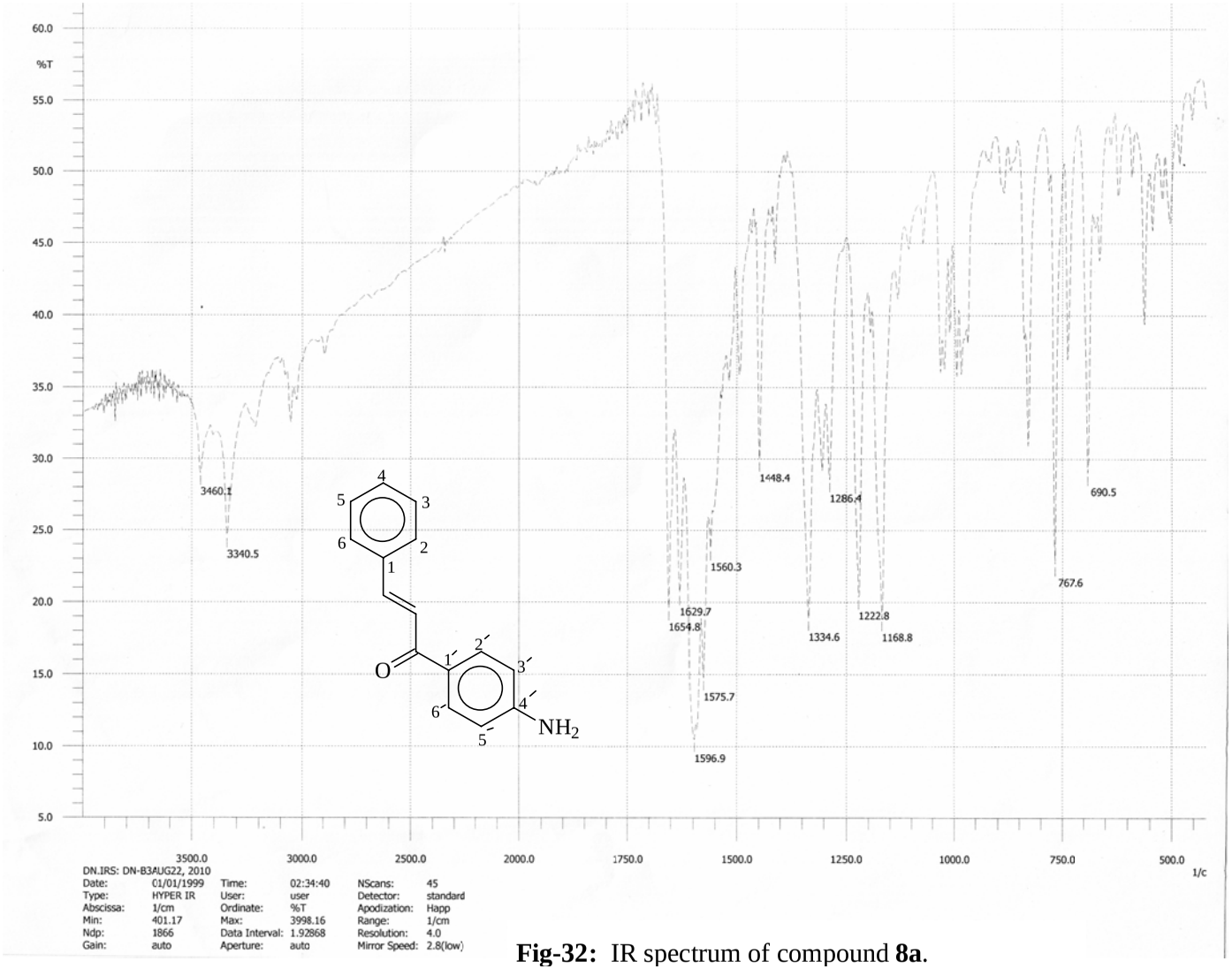
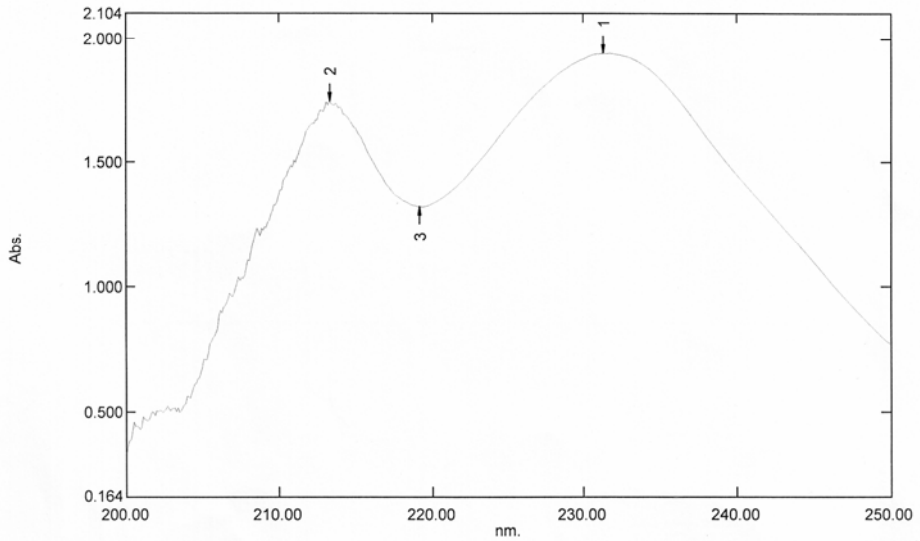


Fig-32: IR spectrum of compound **8a**.

Spectrum Peak Pick Report

09/22/2010 01:55:32 PM

Data Set: Storage 135342 - RawData - C:\Documents and Settings\Super\Desktop\Samina\Sample-M3R.spc



No.	P/V	Wavelength	Abs.	Description
1	↑	231.30	1.942	
2	↑	213.30	1.749	
3	↓	219.20	1.321	

Measurement Properties
Wavelength Range (nm.): 200.00 to 250.00
Scan Speed: Fast
Sampling Interval: 0.1
Auto Sampling Interval: Enabled
Scan Mode: Single

Sample Preparation Properties
Weight: 100mg
Volume: 10ml
Dilution: 100ml
Path Length: 1cm
Additional Information:

Instrument Properties
Instrument Type: UV-1600 Series
Measuring Mode: Absorbance
Slit Width: 2.0 nm
Light Source Change Wavelength: 340.8 nm
S/R Exchange: Normal

Attachment Properties
Attachment: None

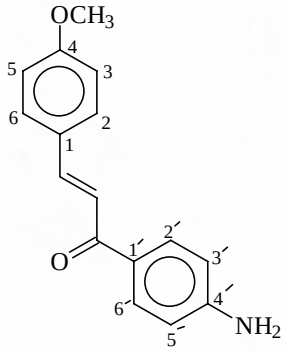


Fig-33: UV spectrum of compound **8b**.

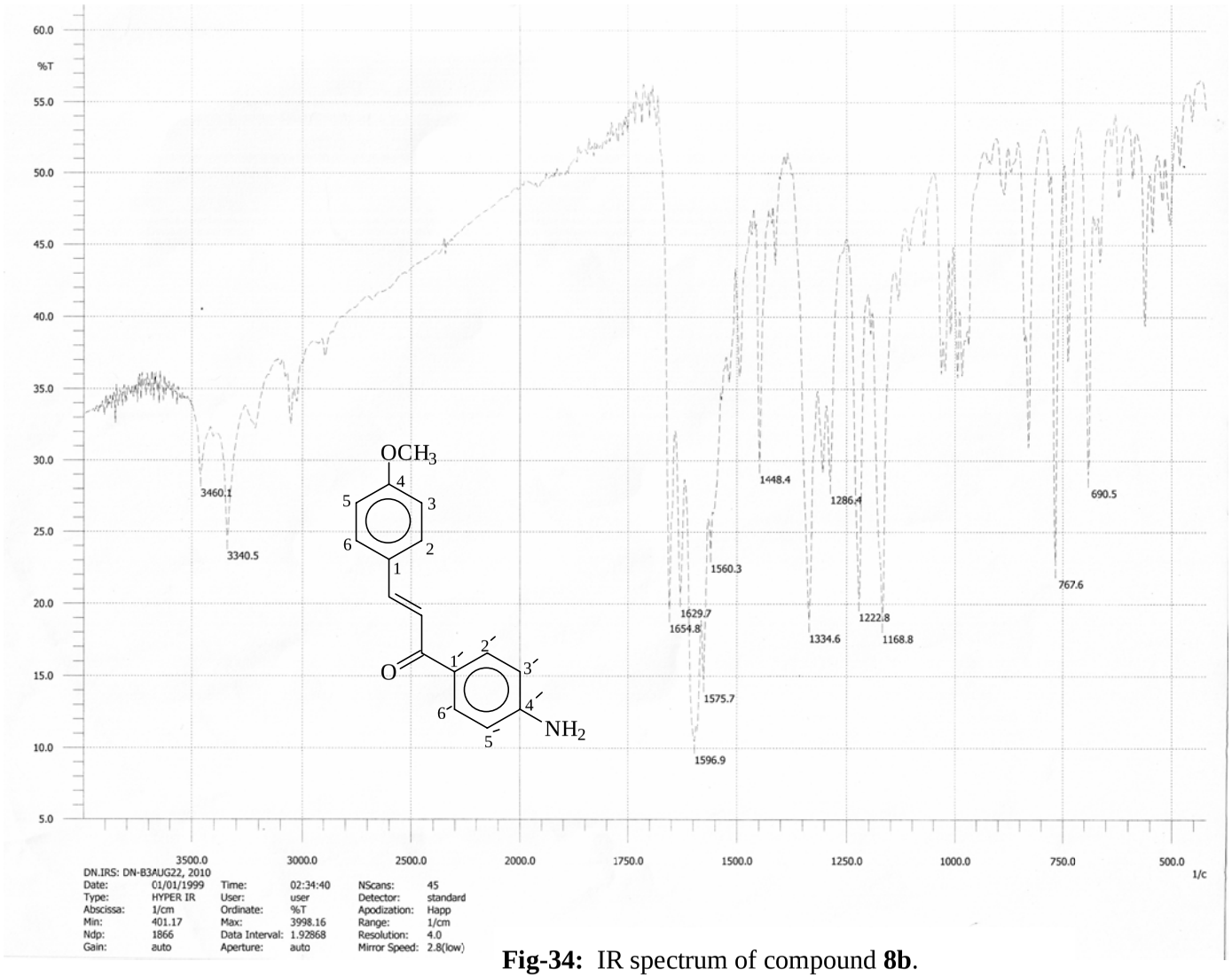


Fig-34: IR spectrum of compound **8b**.

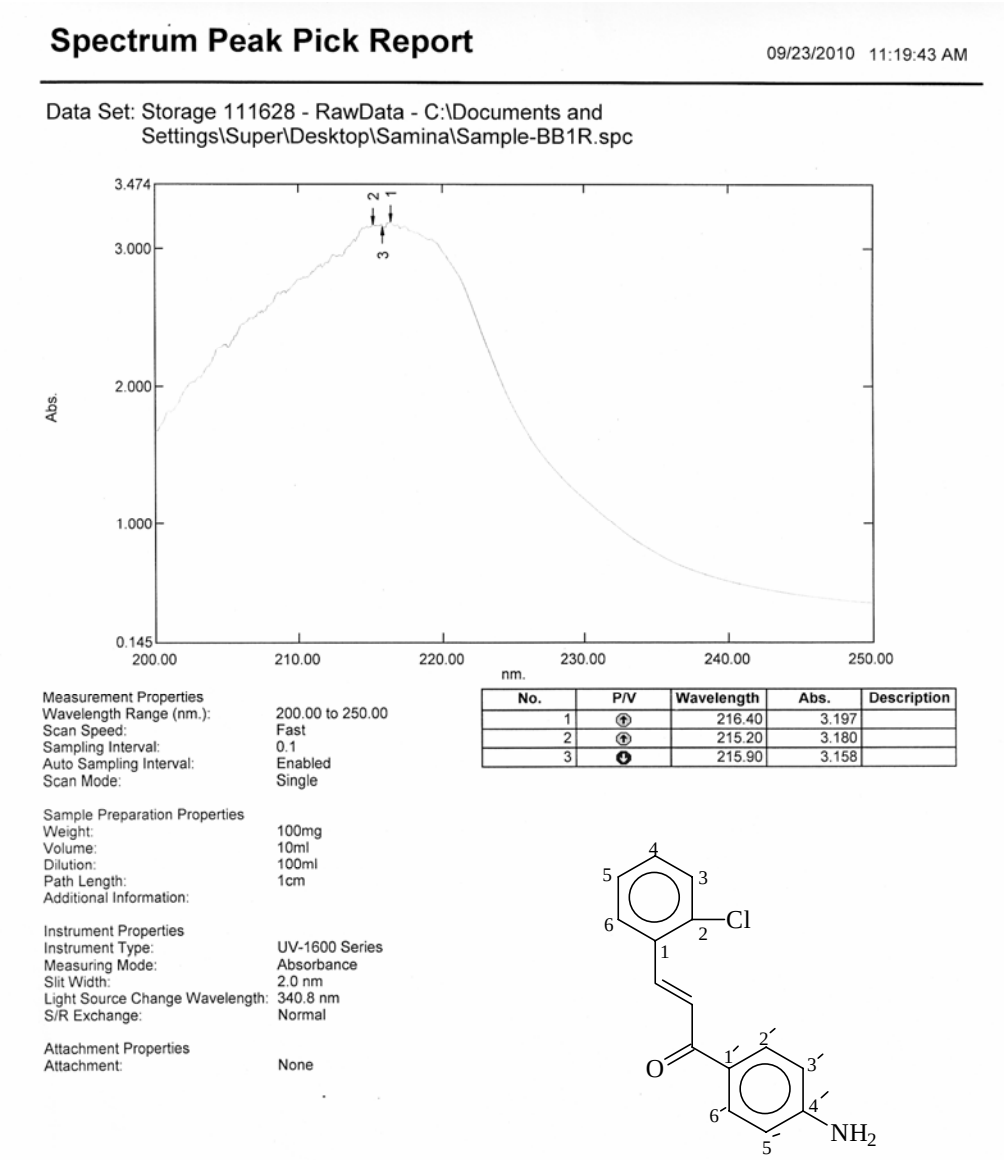


Fig-35: UV spectrum of compound **8c**.

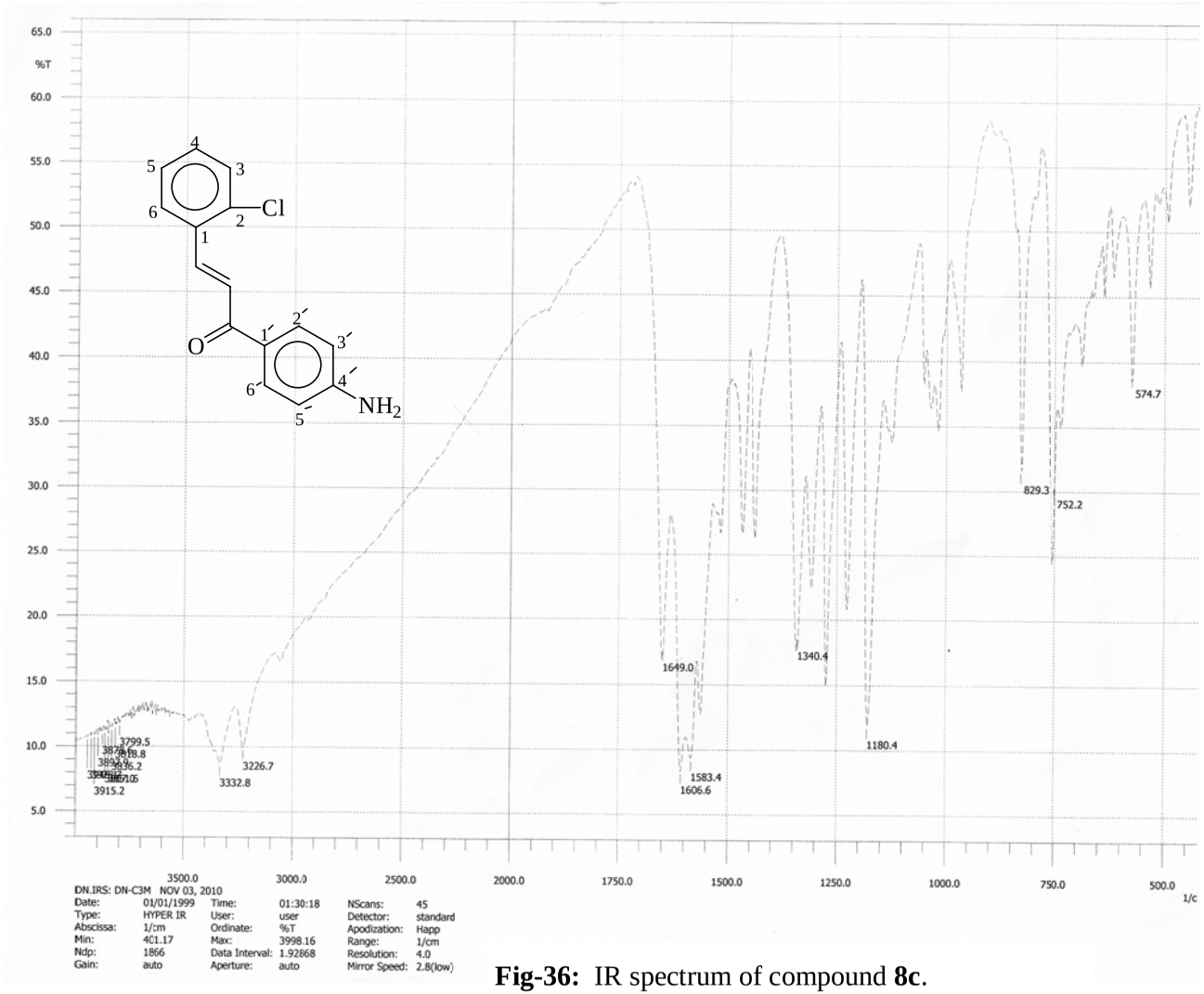


Fig-36: IR spectrum of compound **8c**.

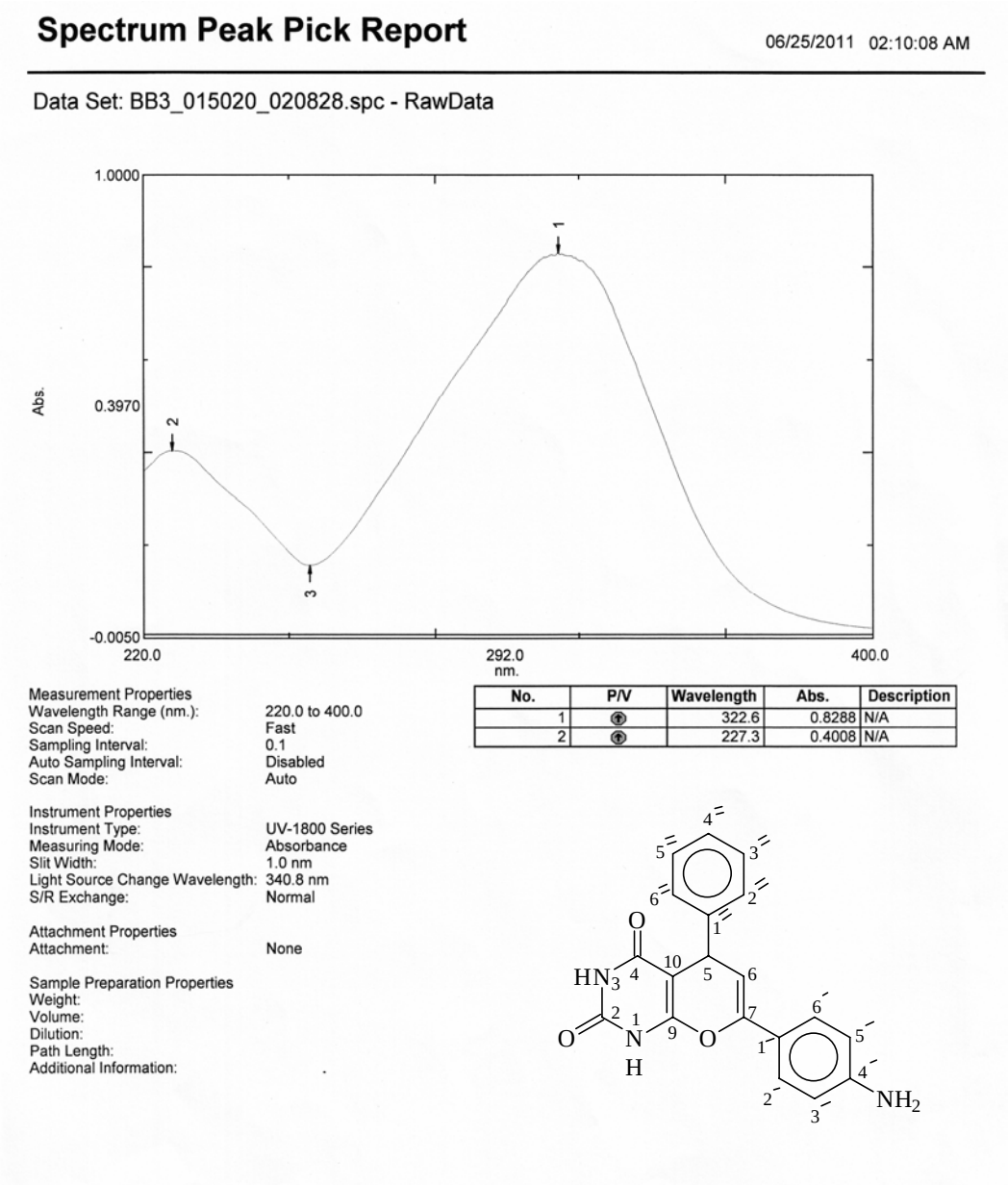


Fig-37: UV spectrum of compound **10a**.

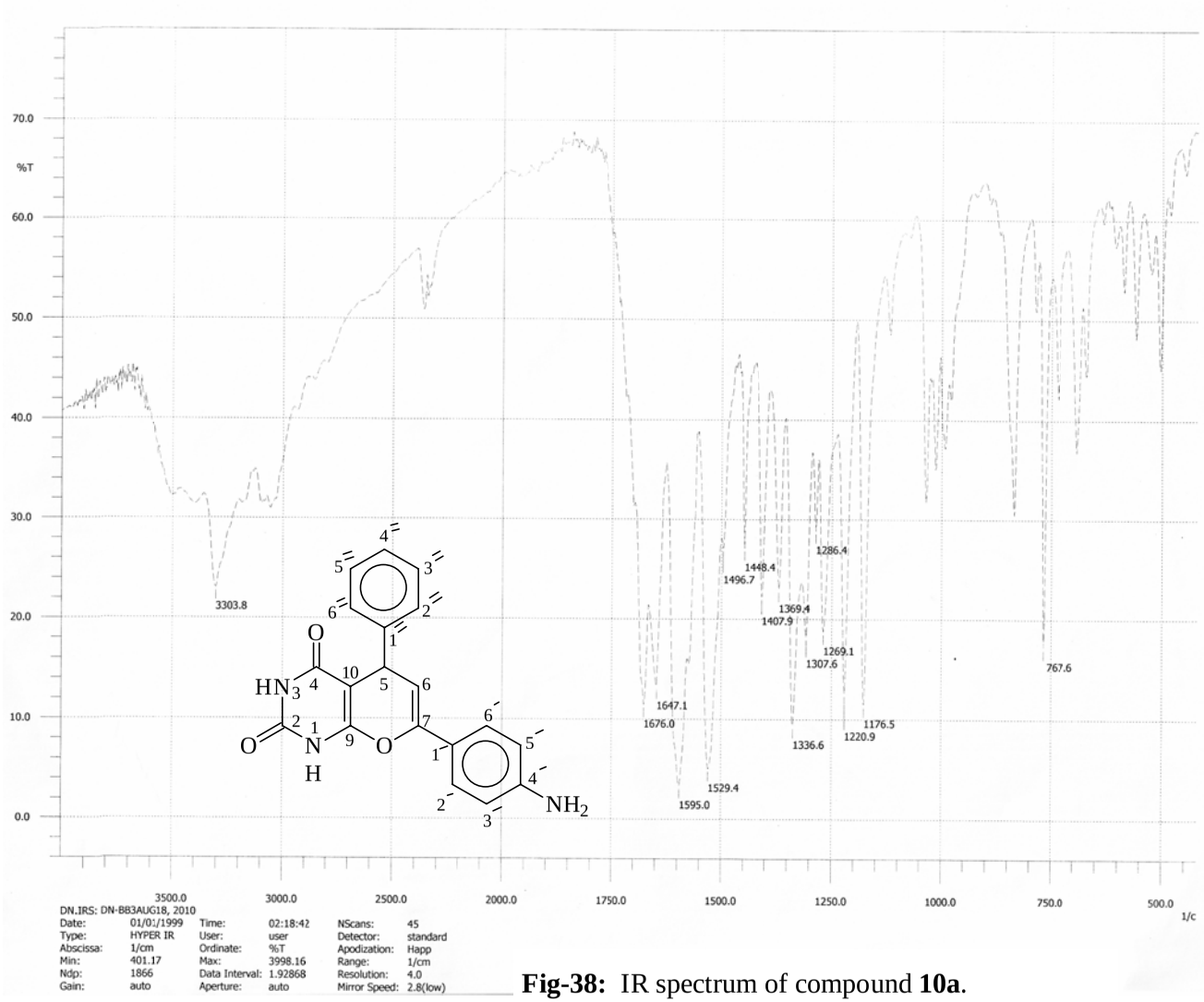


Fig-38: IR spectrum of compound **10a**.

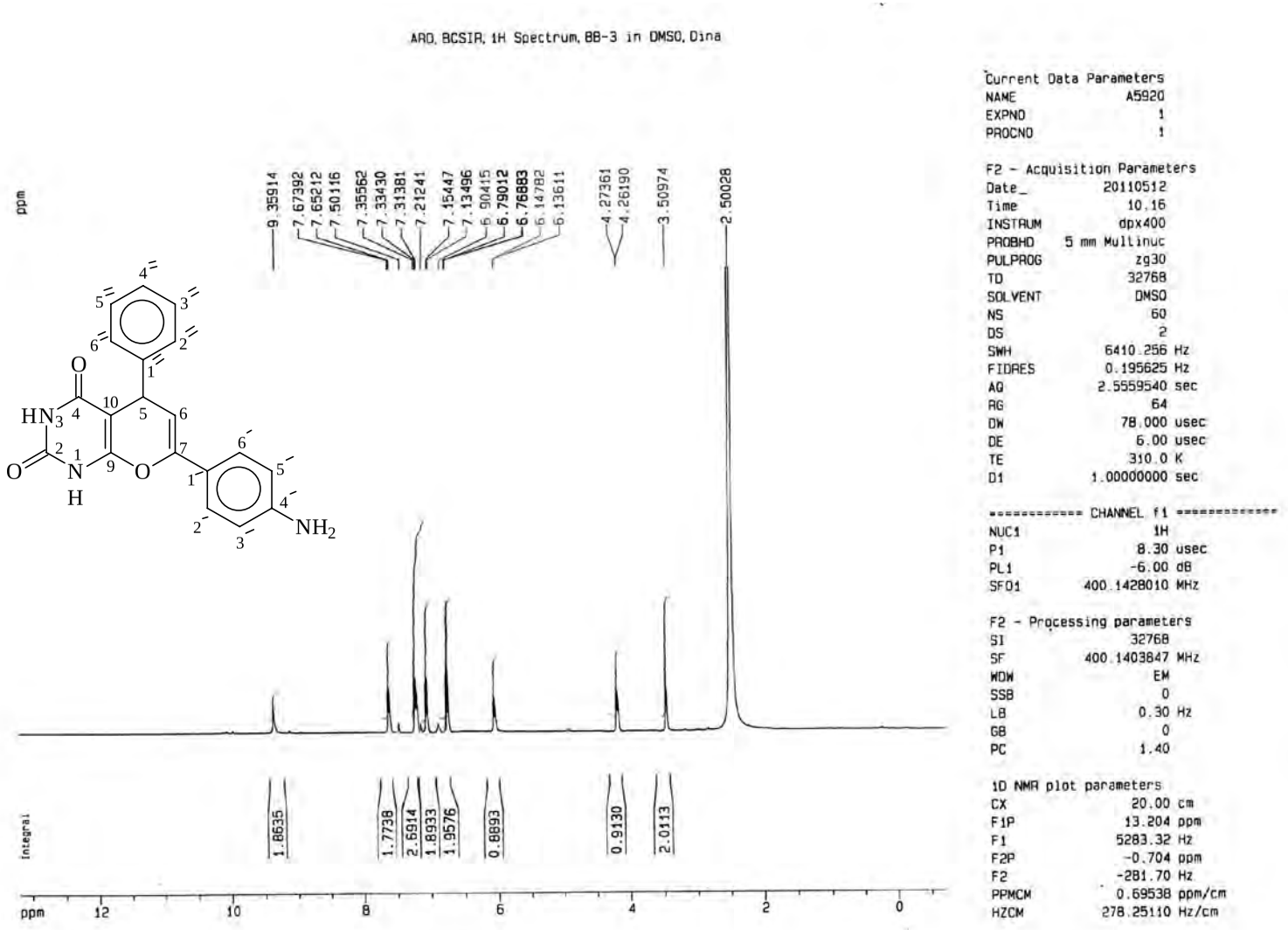


Fig-39: ^{1}H NMR spectrum of compound **10a**.

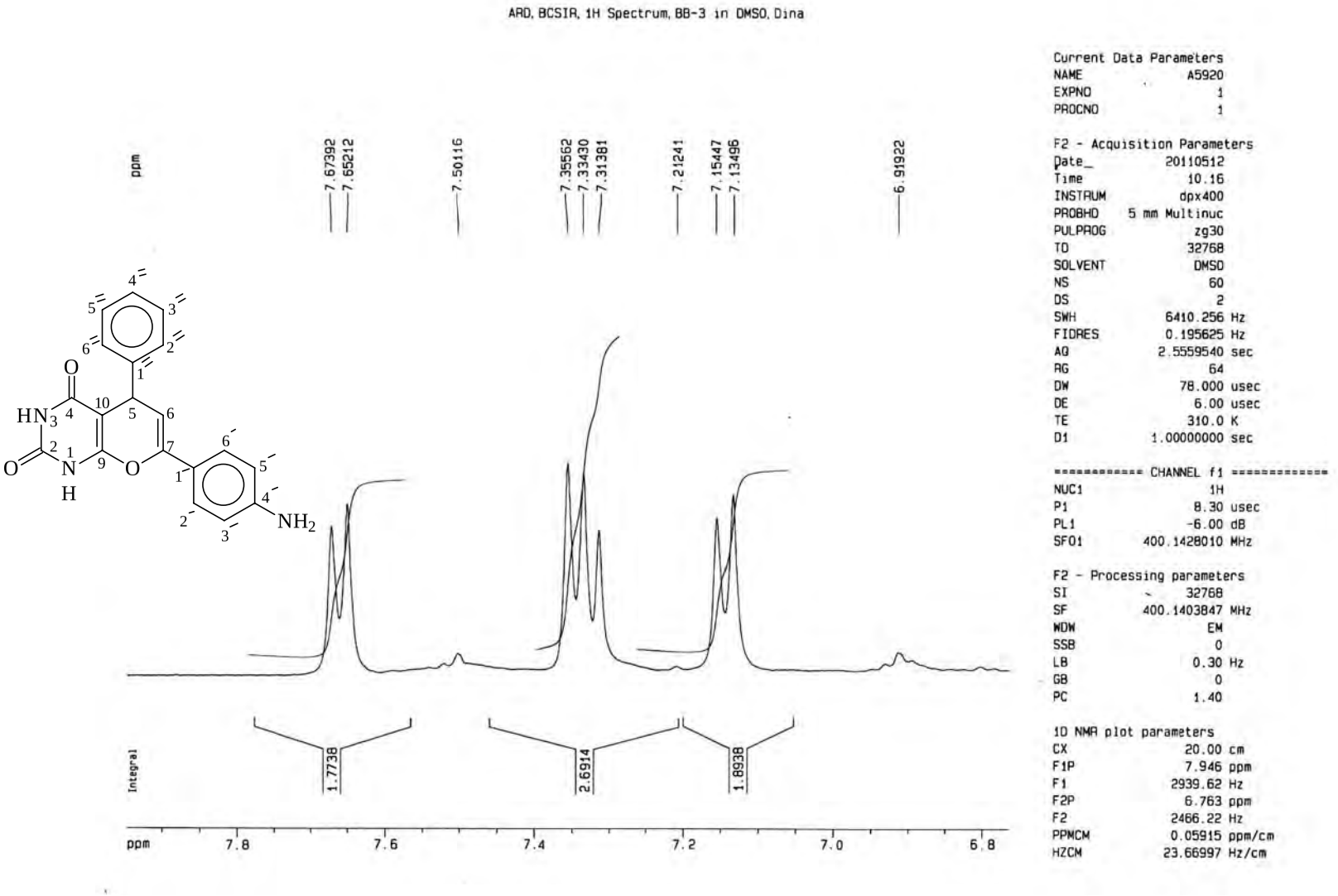


Fig-39: ^{1}H NMR spectrum of compound **10a** (expanded).

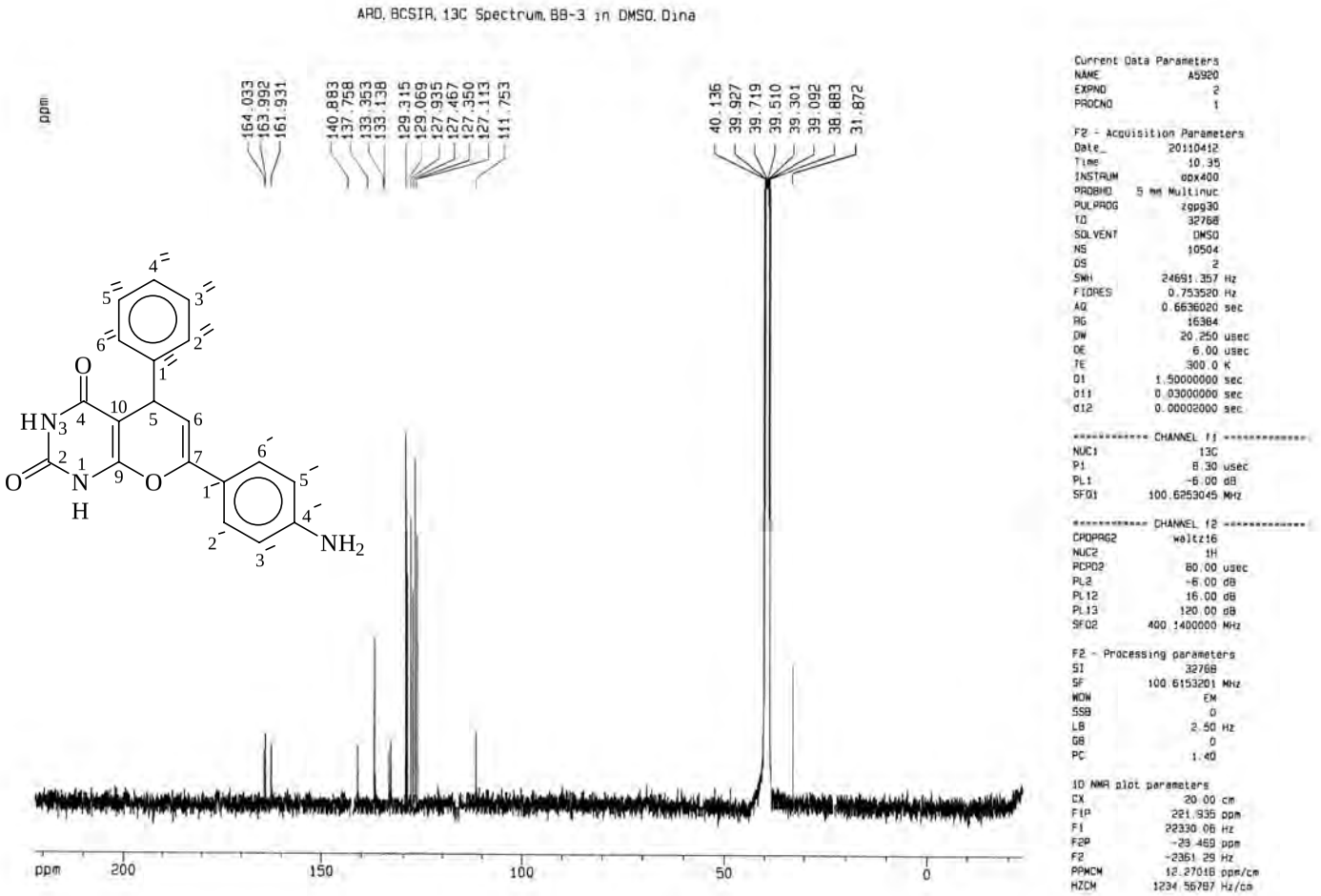


Fig-40: ^{13}C NMR spectrum of compound **10a**

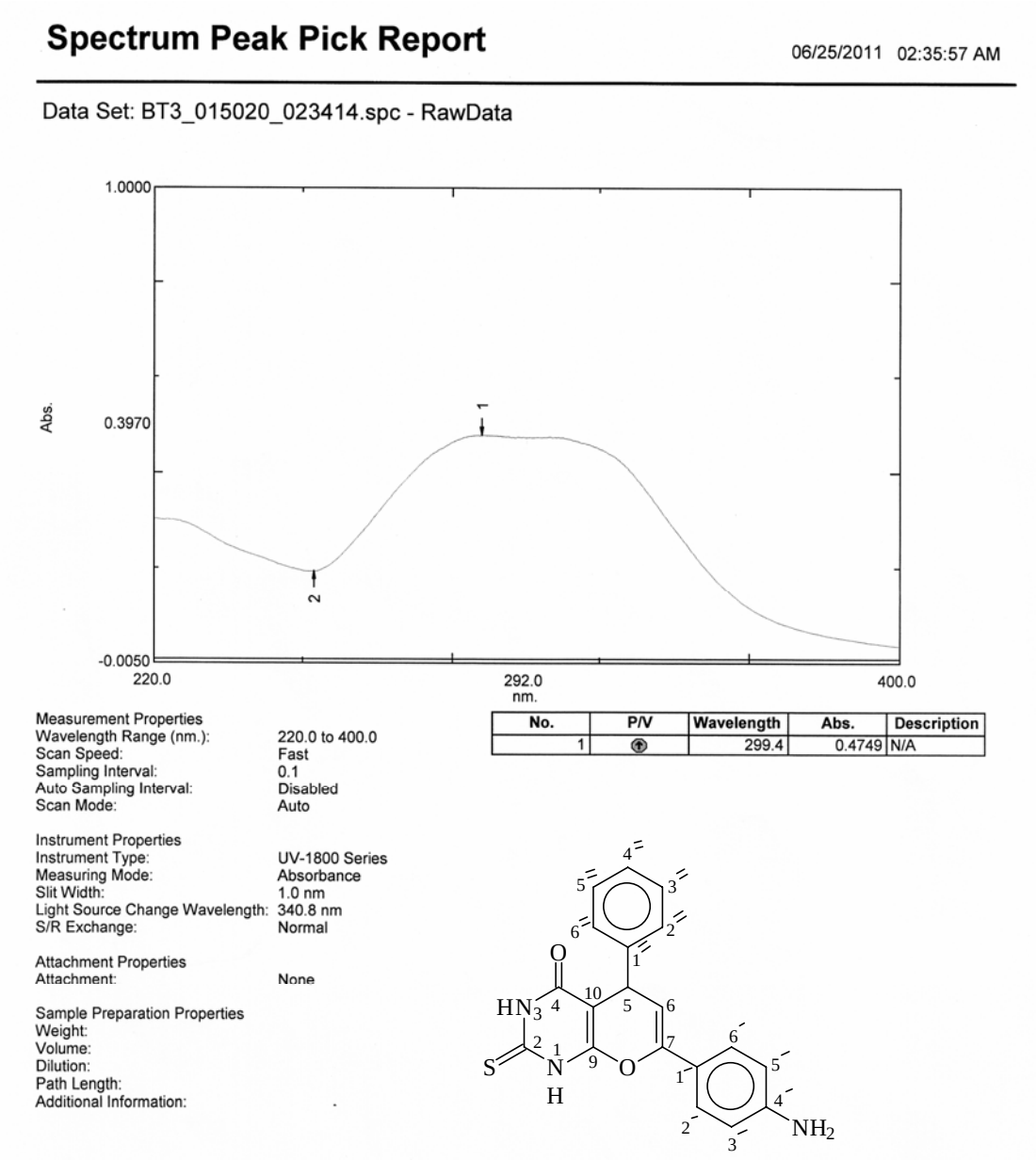


Fig-41: UV spectrum of compound **10b**.

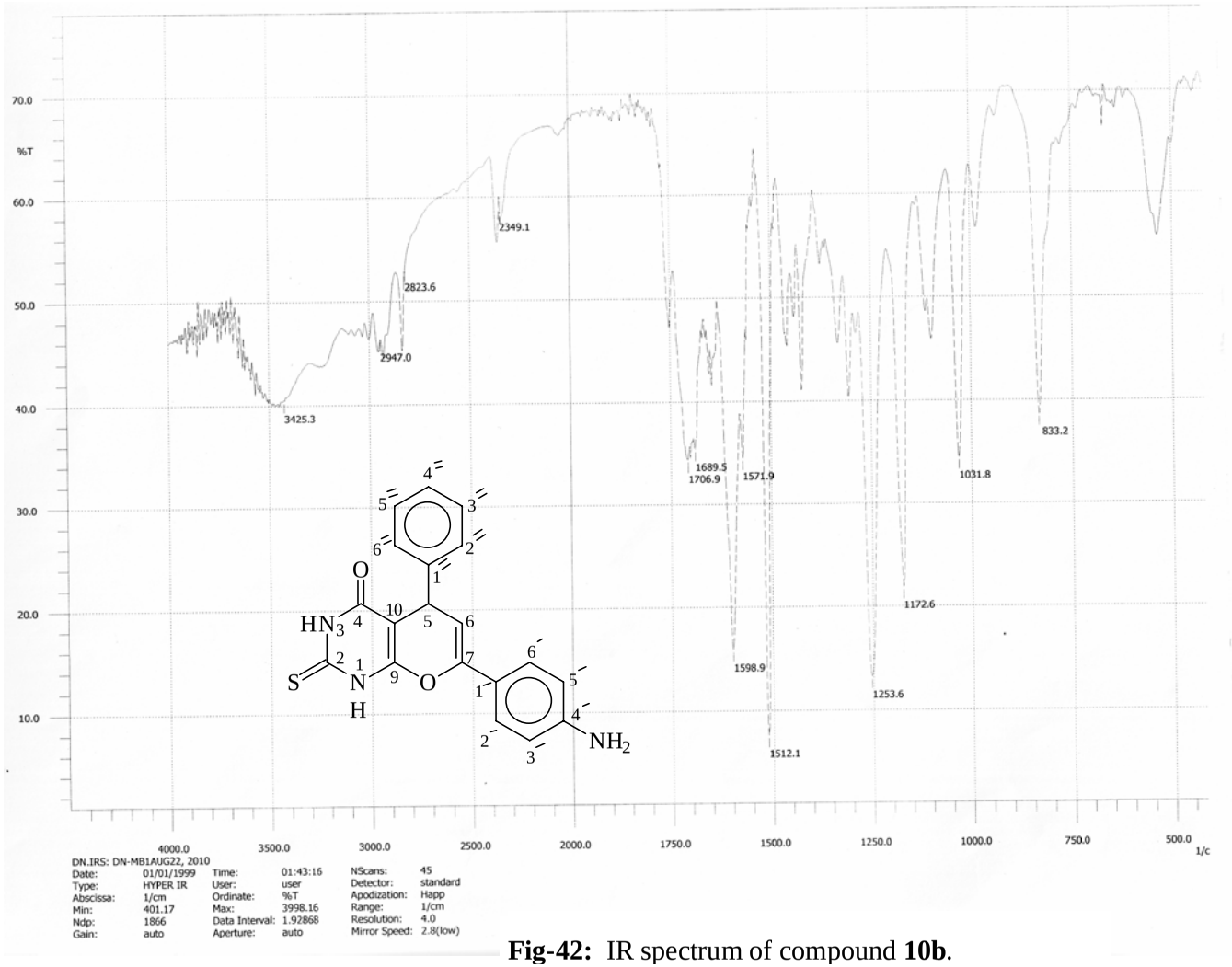


Fig-42: IR spectrum of compound **10b**.

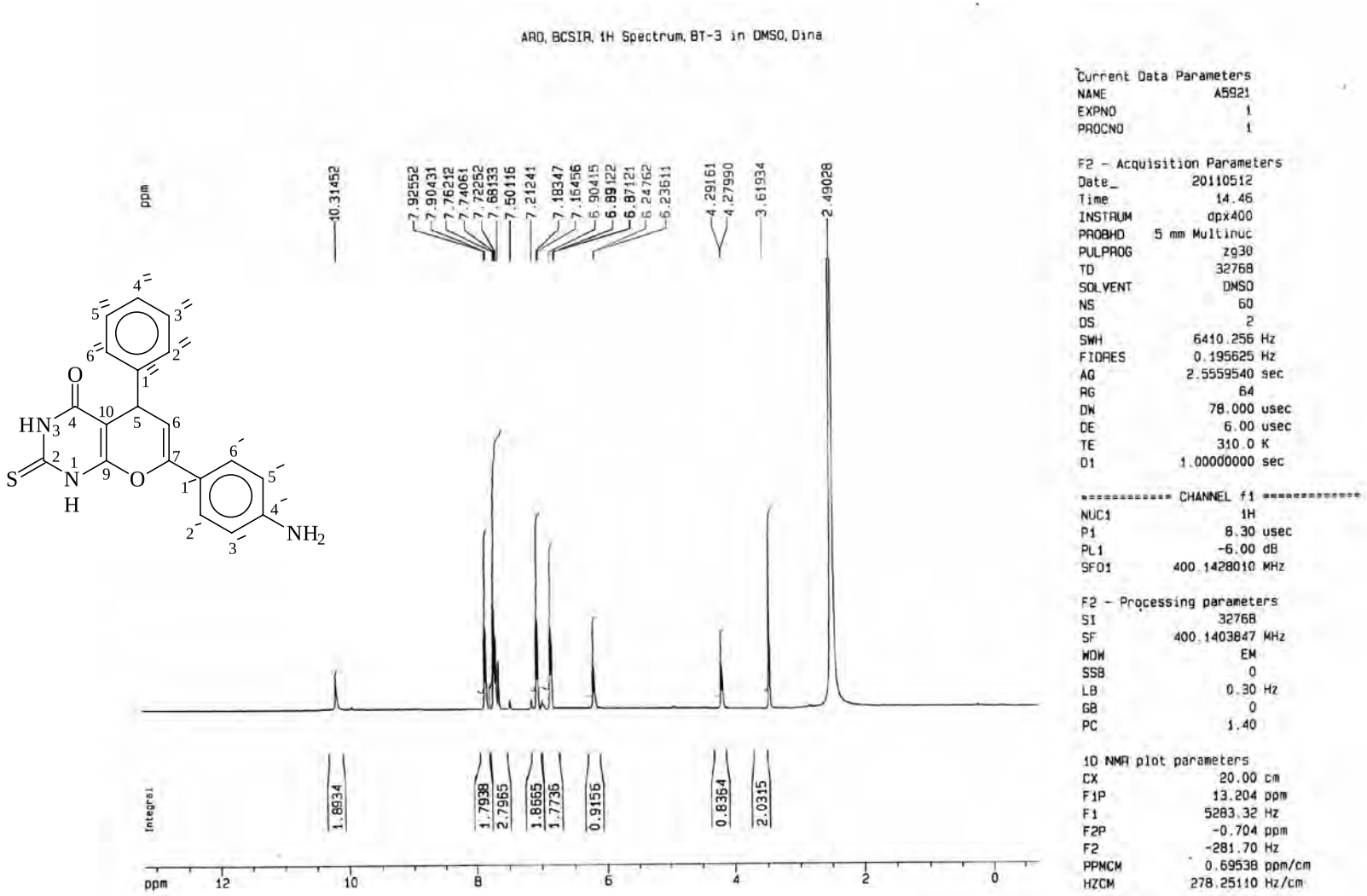


Fig-43: ^{1}H NMR spectrum of compound **10b**.

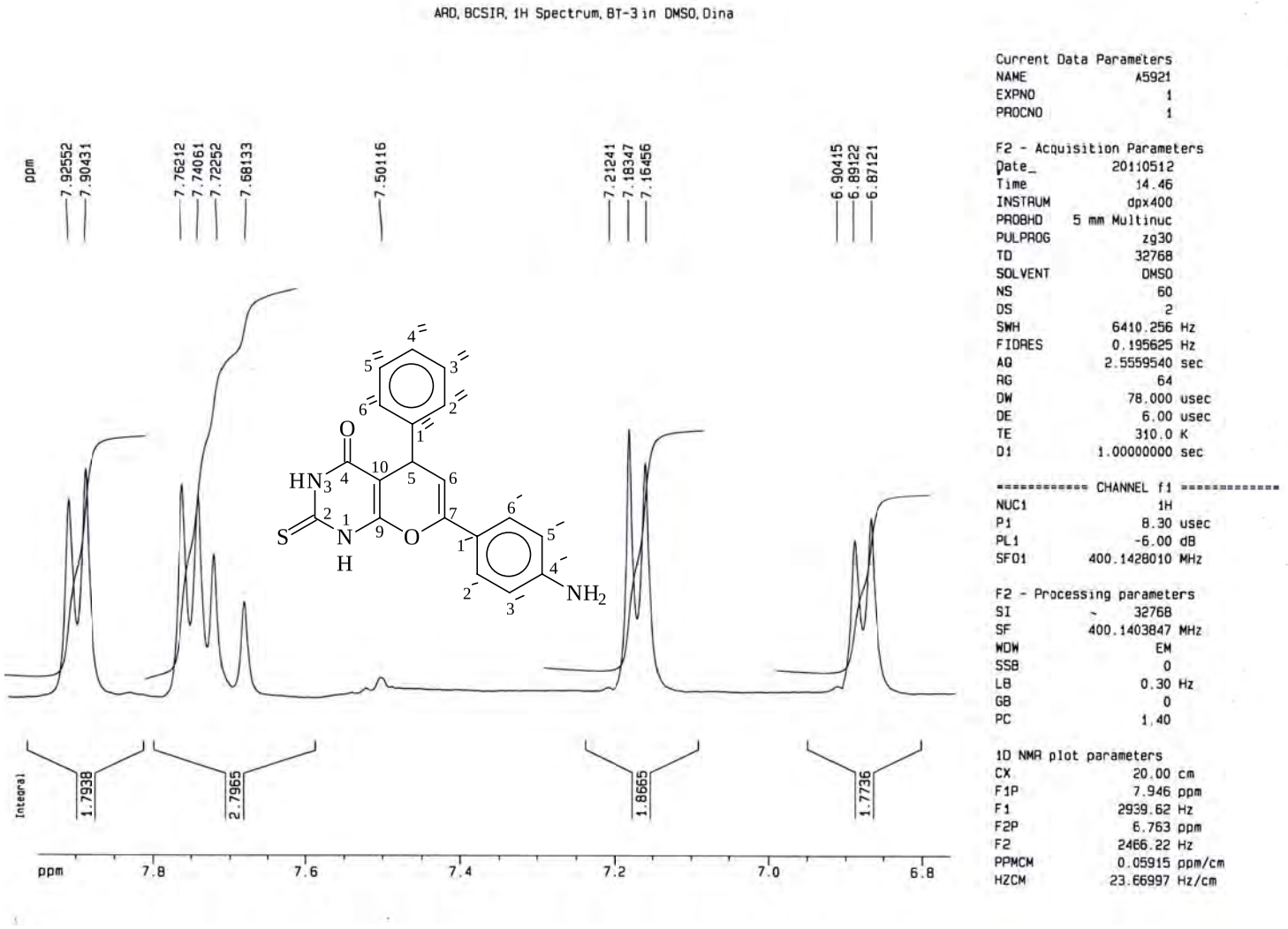


Fig-43: ^{1}H NMR spectrum of compound **10b** (expanded).

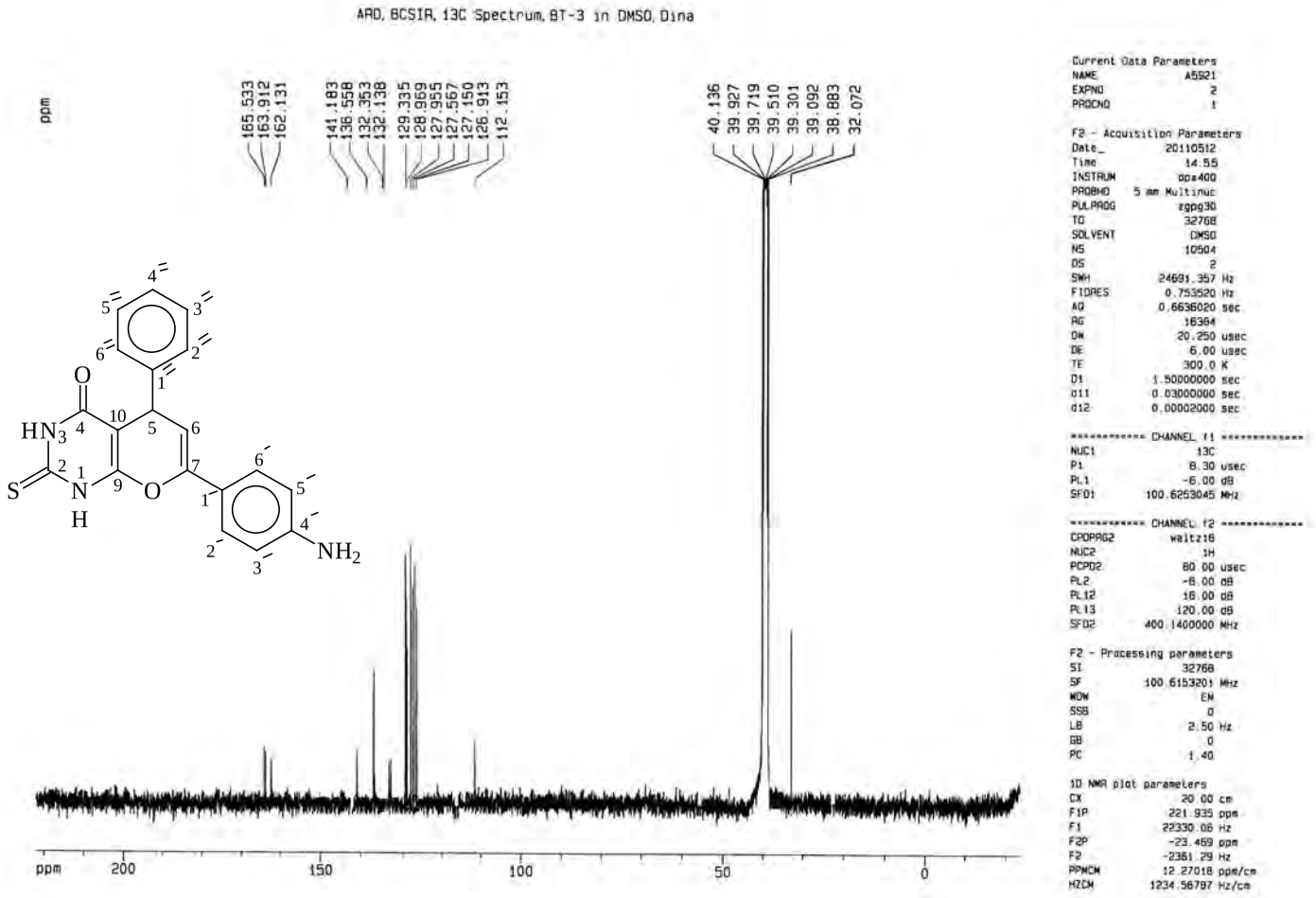


Fig-44: ^{13}C NMR spectrum of compound **10b**.

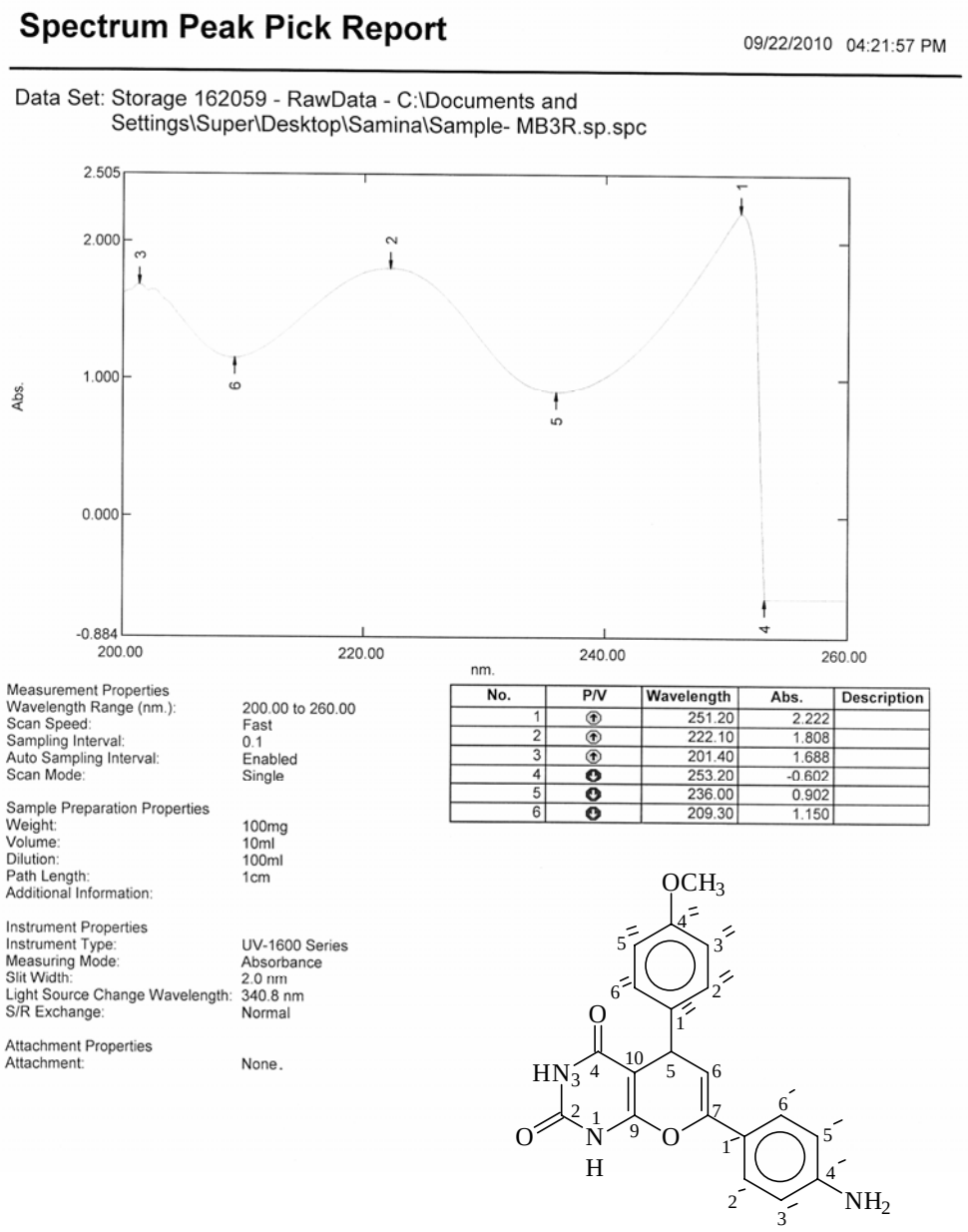


Fig-45: UV spectrum of compound **10c**.

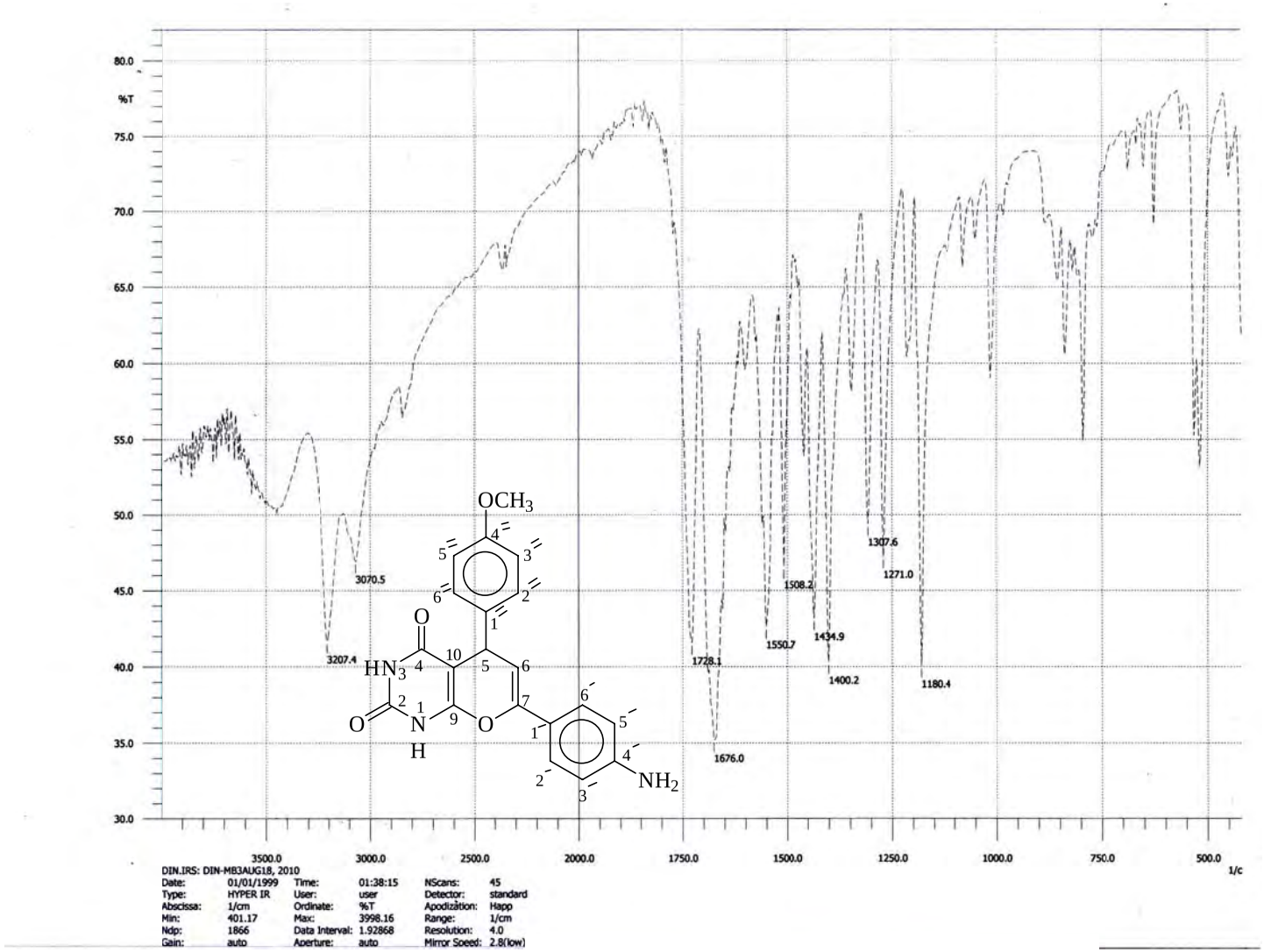


Fig-46: IR spectrum of compound **10c**.

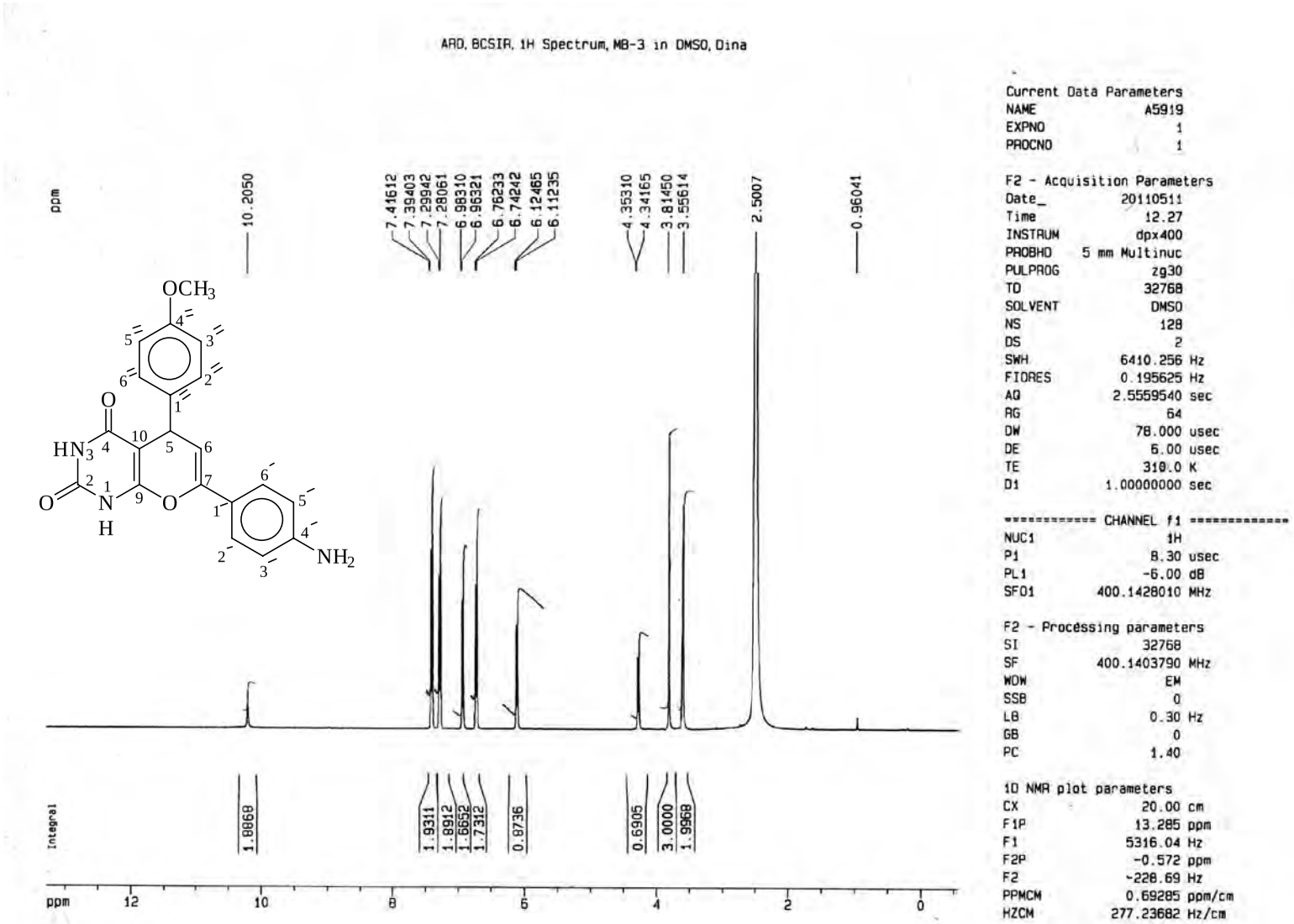


Fig-47: ^{1}H NMR spectrum of compound **10c**.

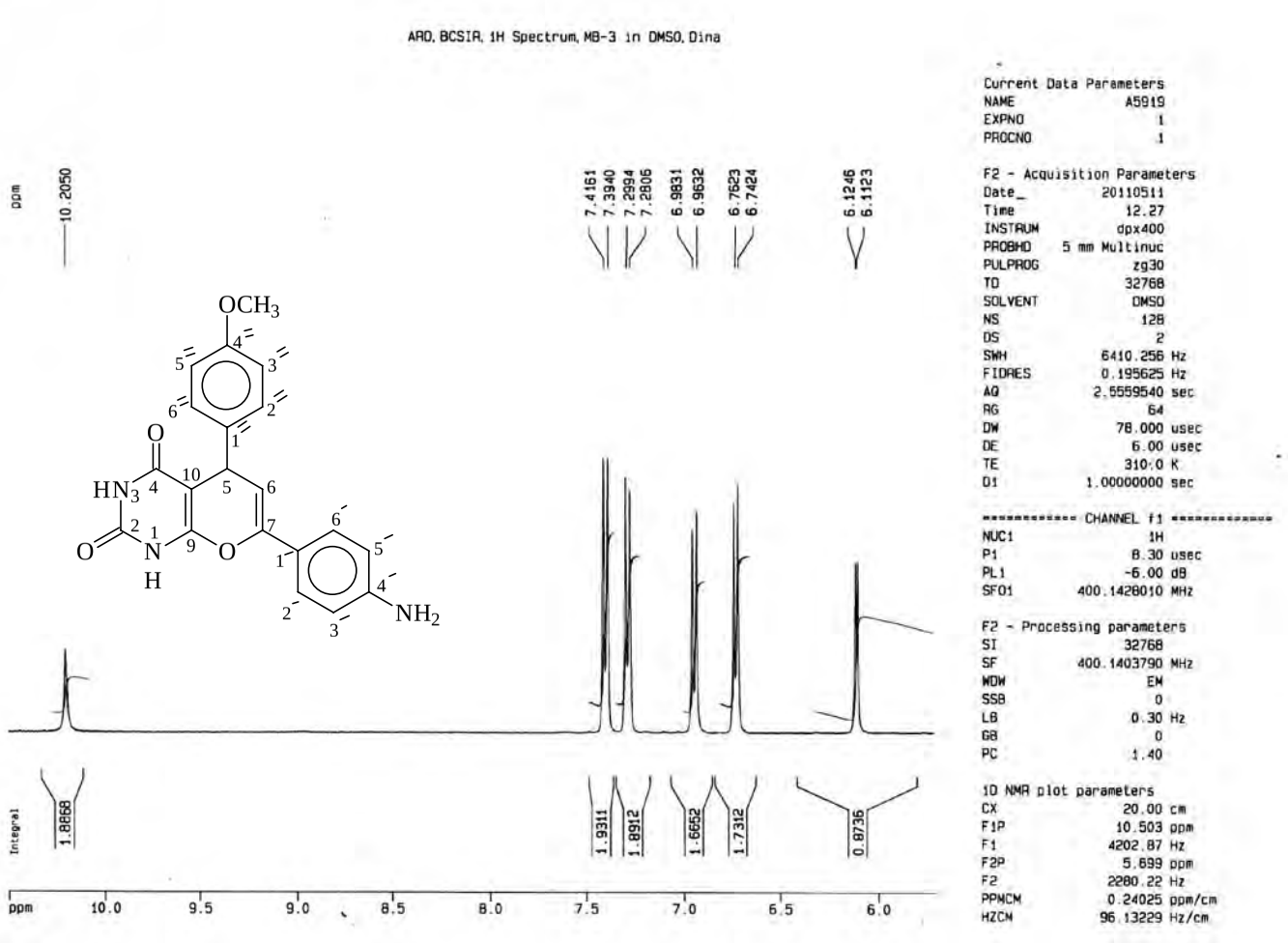


Fig-47: ^{1}H NMR spectrum of compound (expanded) **10c**.

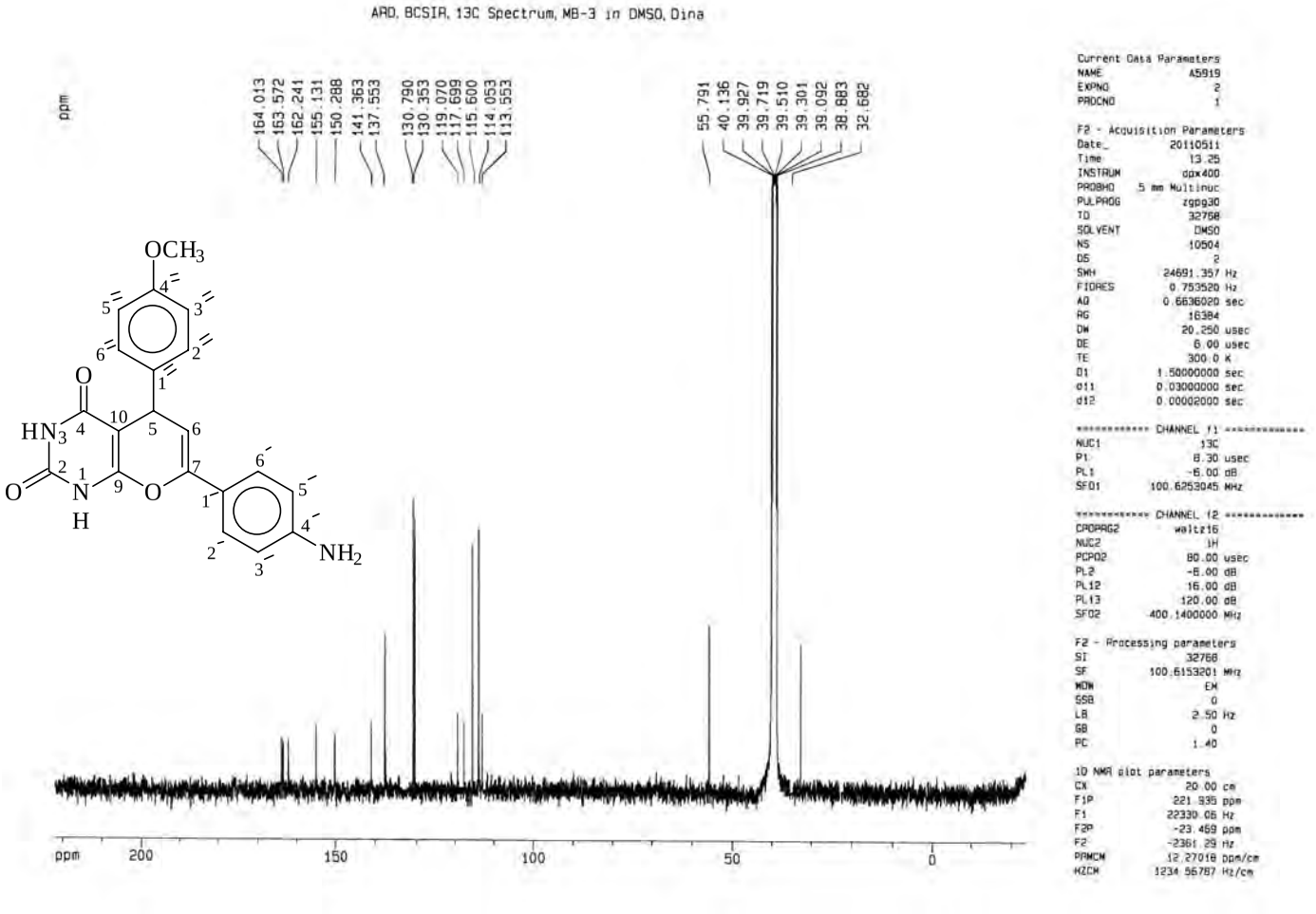


Fig-48: ^{13}C NMR spectrum of compound **10c**.

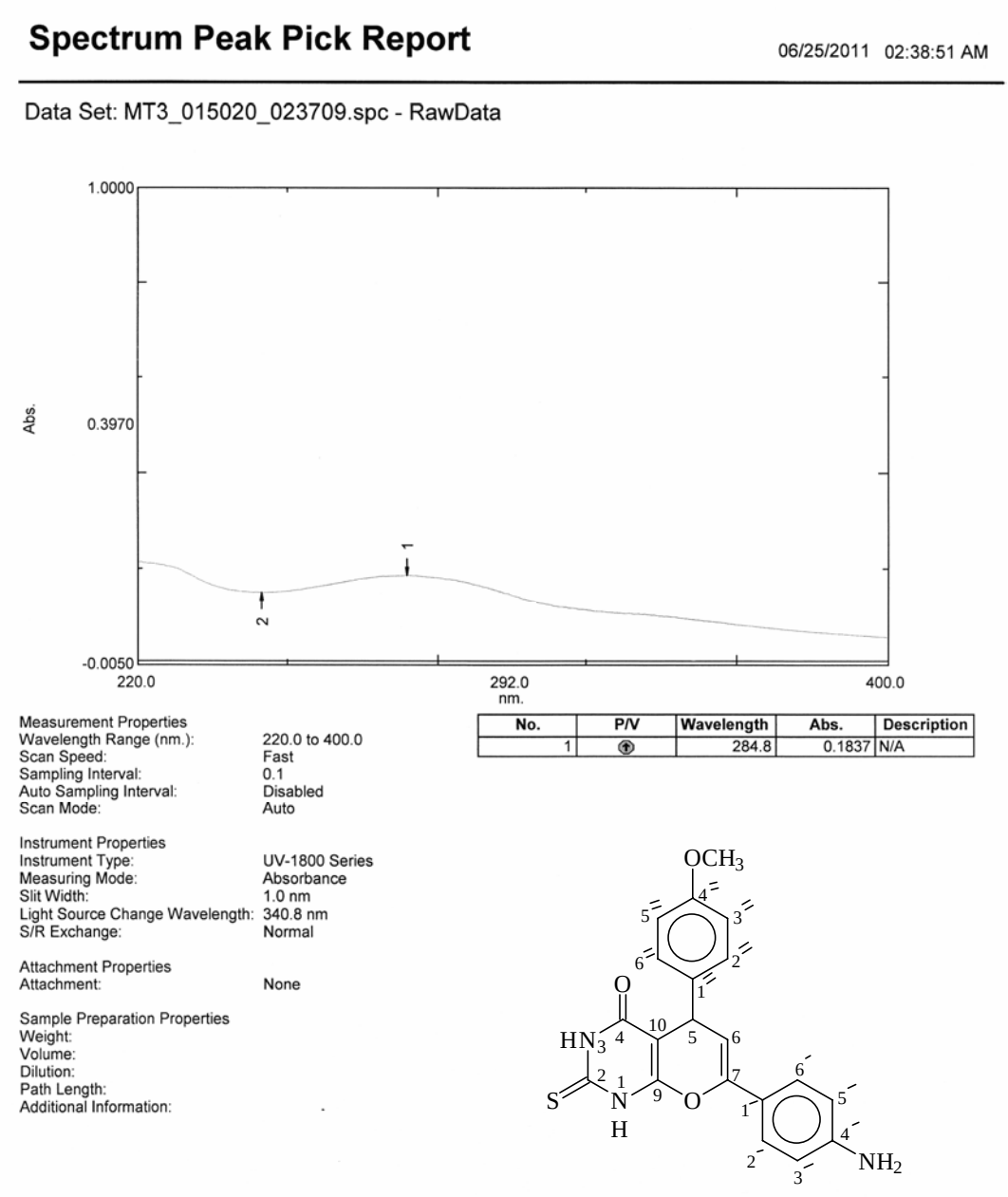


Fig-49: UV spectrum of compound **10d**.

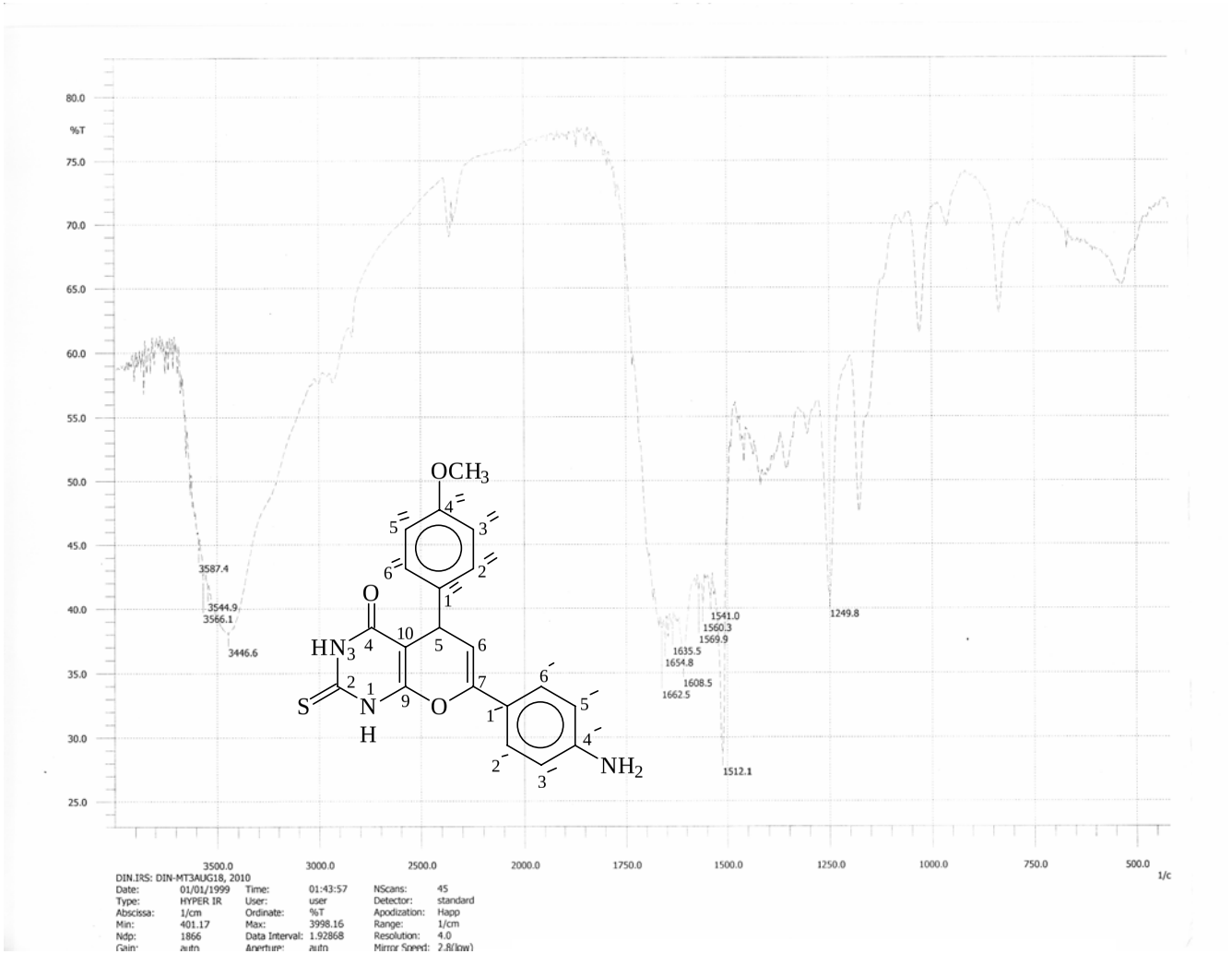


Fig-50: IR spectrum of compound **10d**.

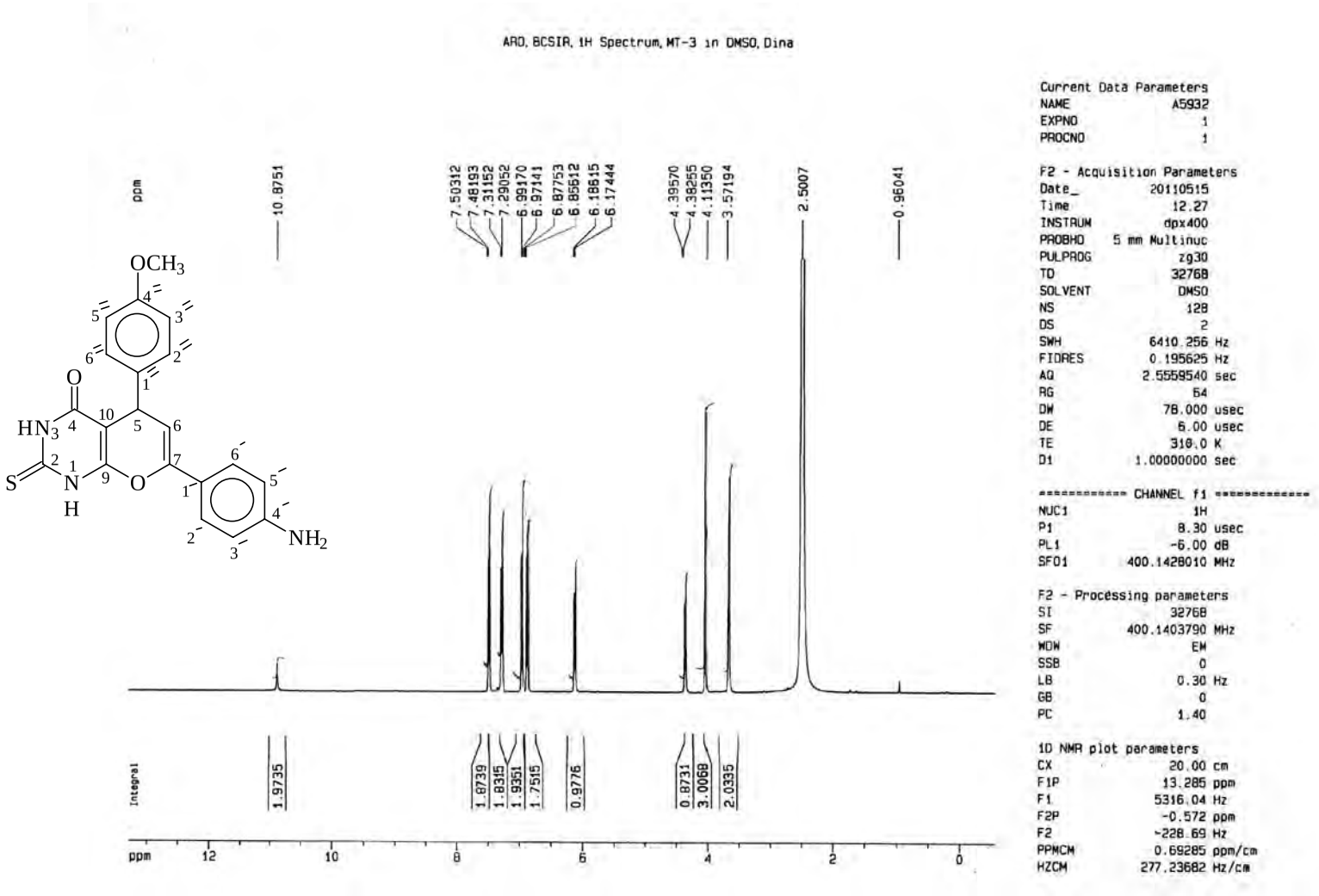


Fig-51: ^{1}H NMR spectrum of compound **10d** .

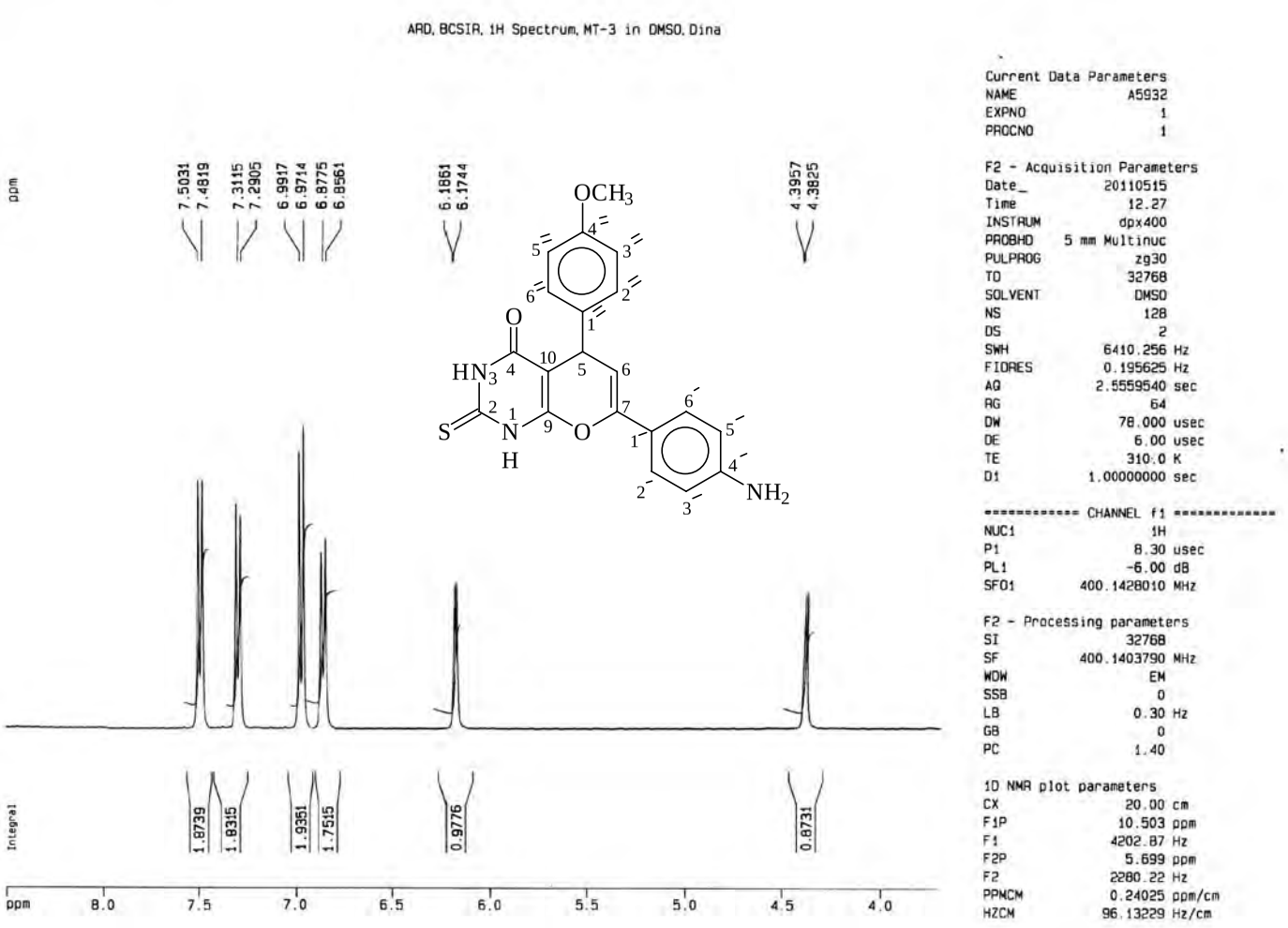


Fig-51: ^{1}H NMR spectrum of compound **10d** (expanded).

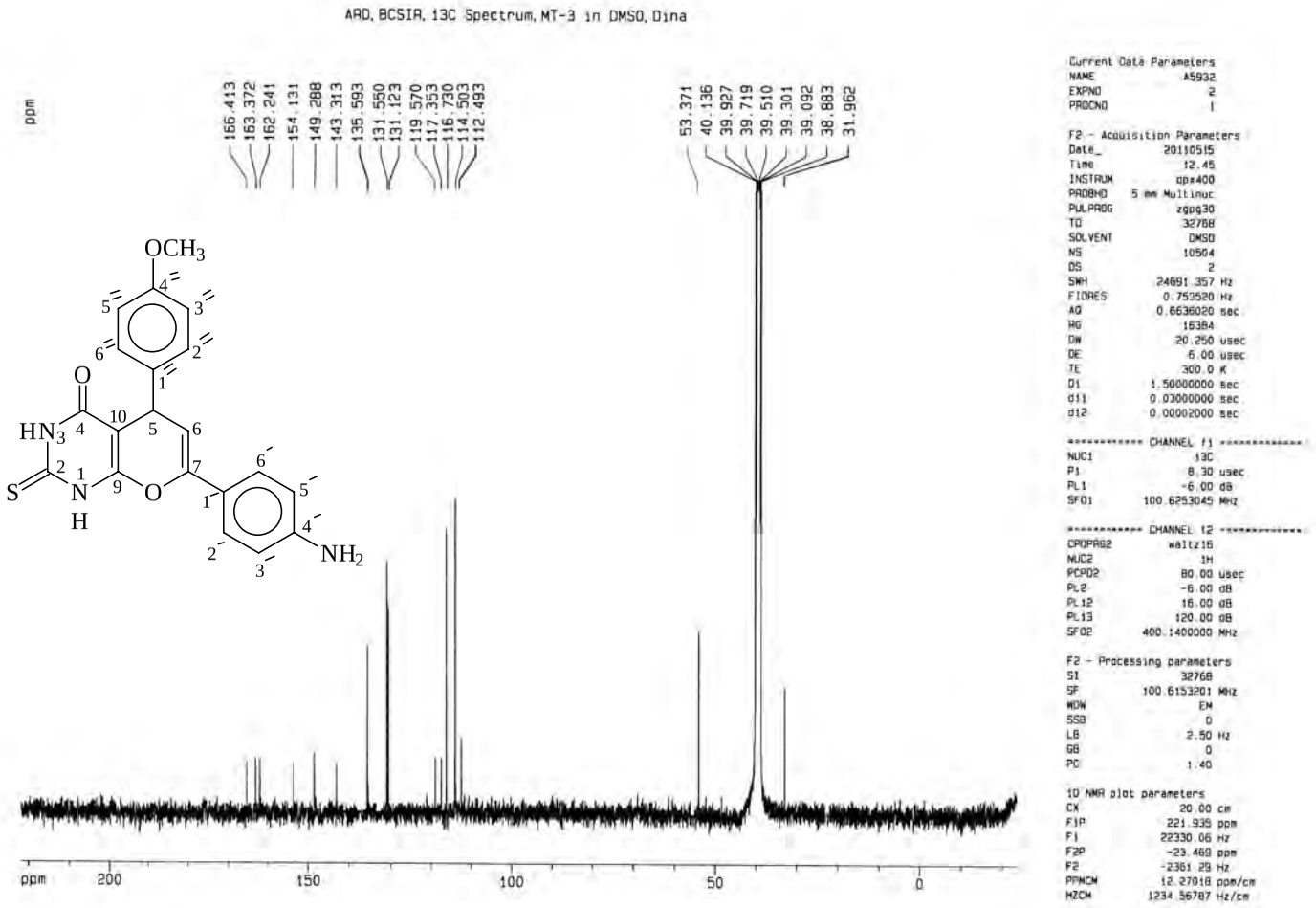
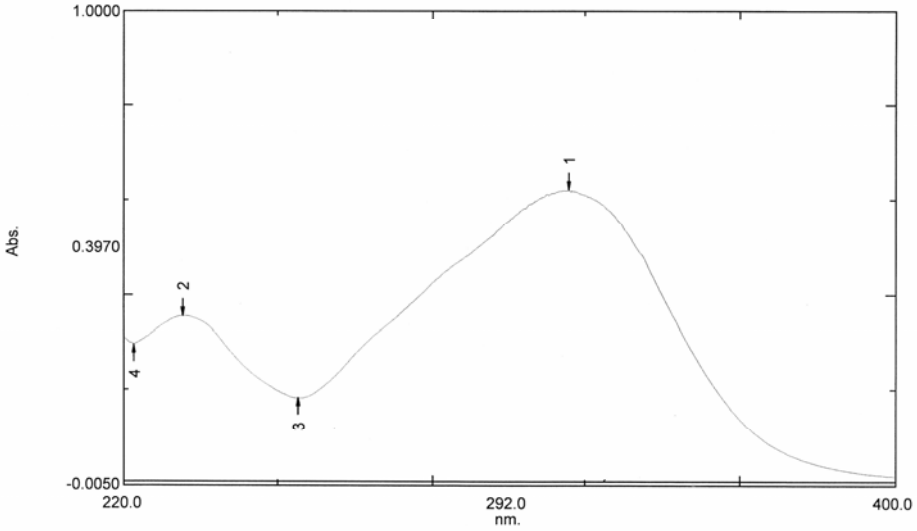


Fig-52: ^{13}C NMR spectrum of compound **10d**.

Spectrum Peak Pick Report

06/25/2011 02:00:24 AM

Data Set: DN-CB3_015815.spc - RawData



No.	P/V	Wavelength	Abs.	Description
1	↑	324.1	0.6187	N/A
2	↑	234.1	0.3528	N/A

Measurement Properties
Wavelength Range (nm.): 200.0 to 400.0
Scan Speed: Fast
Sampling Interval: 0.1
Auto Sampling Interval: Disabled
Scan Mode: Auto

Instrument Properties
Instrument Type: UV-1800 Series
Measuring Mode: Absorbance
Slit Width: 1.0 nm
Light Source Change Wavelength: 340.8 nm
S/R Exchange: Normal

Attachment Properties
Attachment: None

Sample Preparation Properties
Weight:
Volume:
Dilution:
Path Length:
Additional Information:

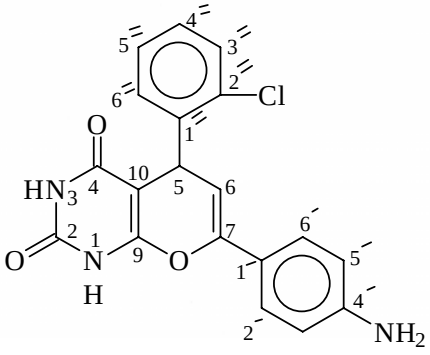


Fig-53: UV spectrum of compound **10e**.

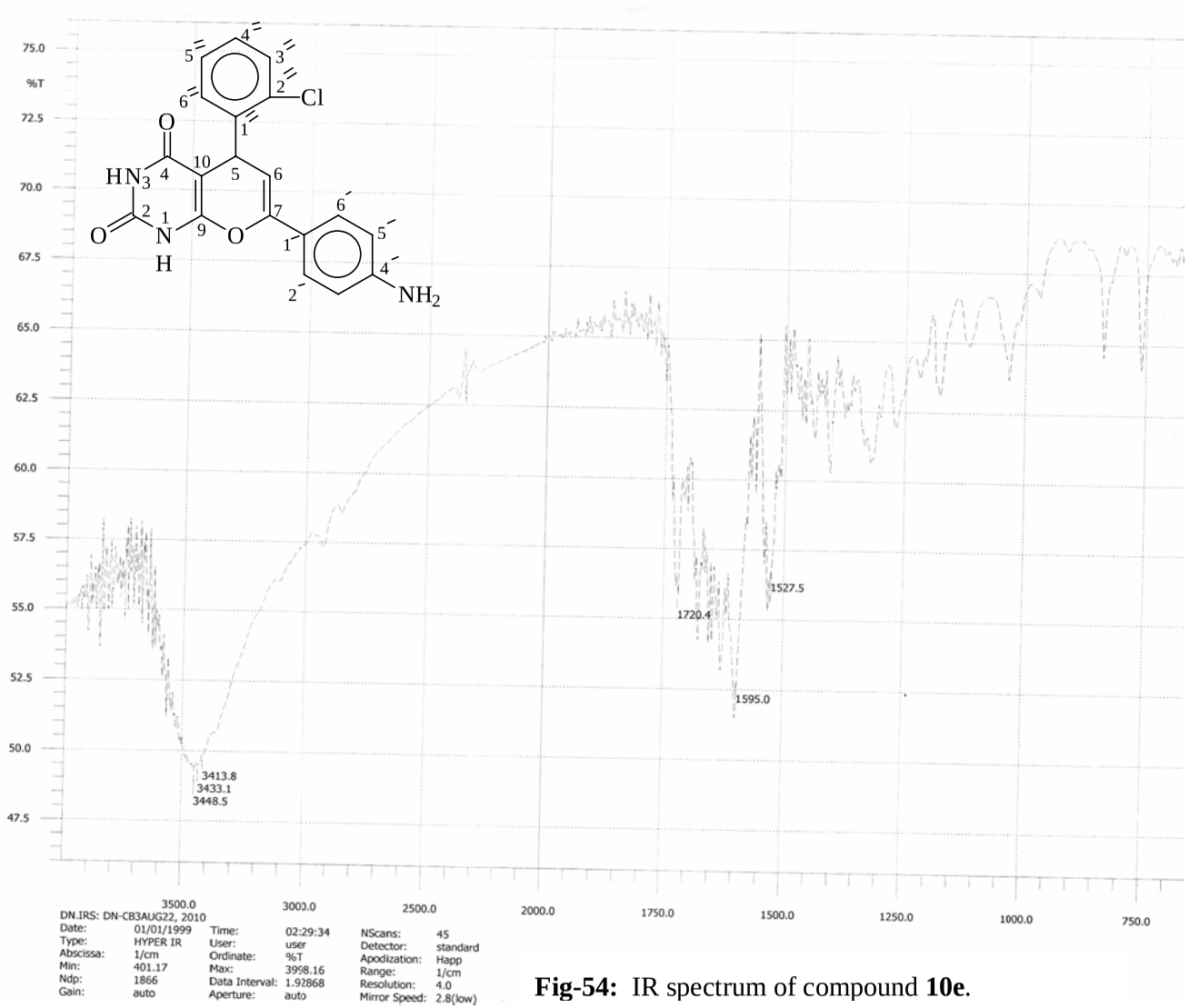


Fig-54: IR spectrum of compound **10e**.

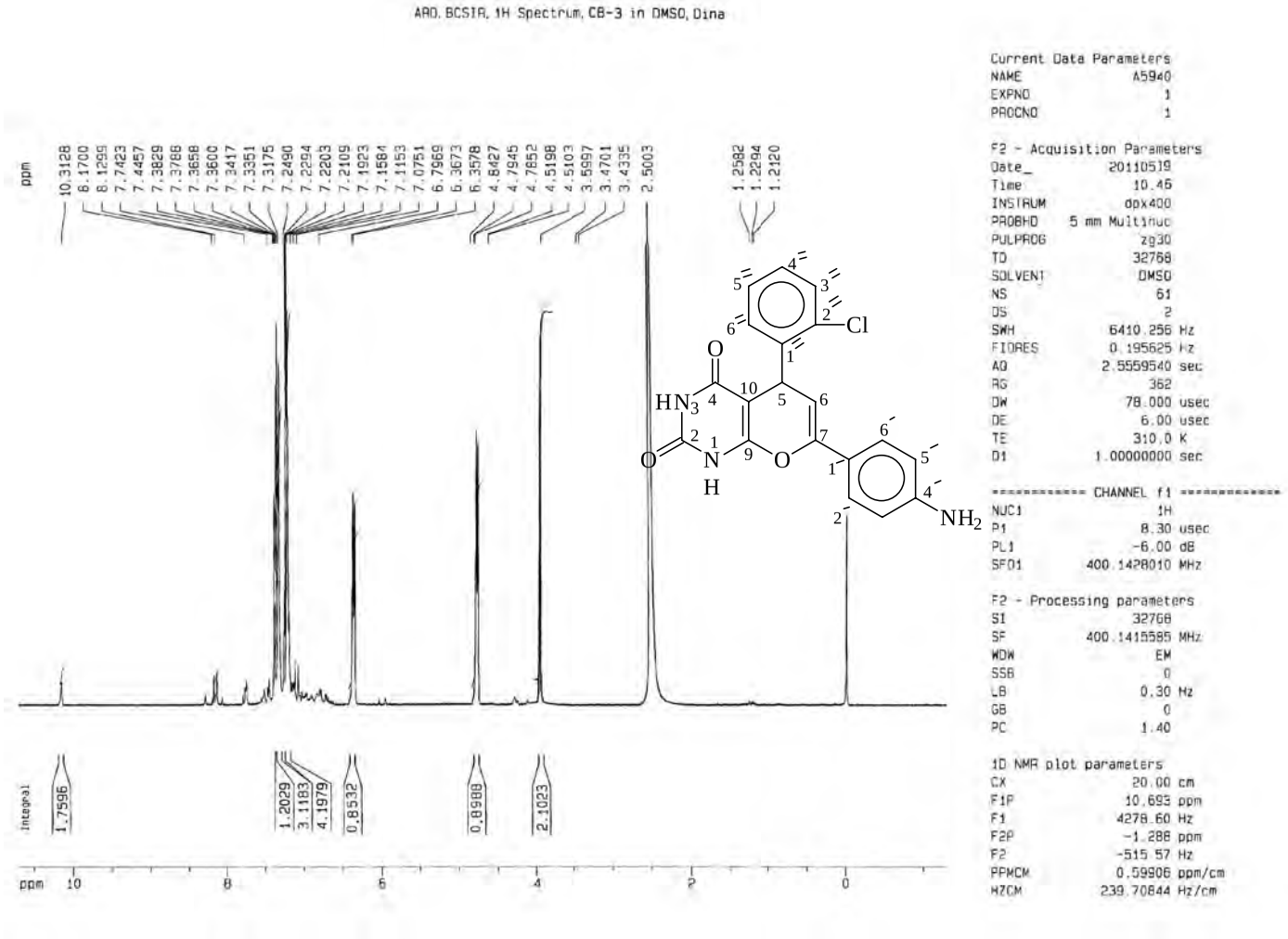


Fig-55: ^{1}H NMR spectrum of compound **10e**.

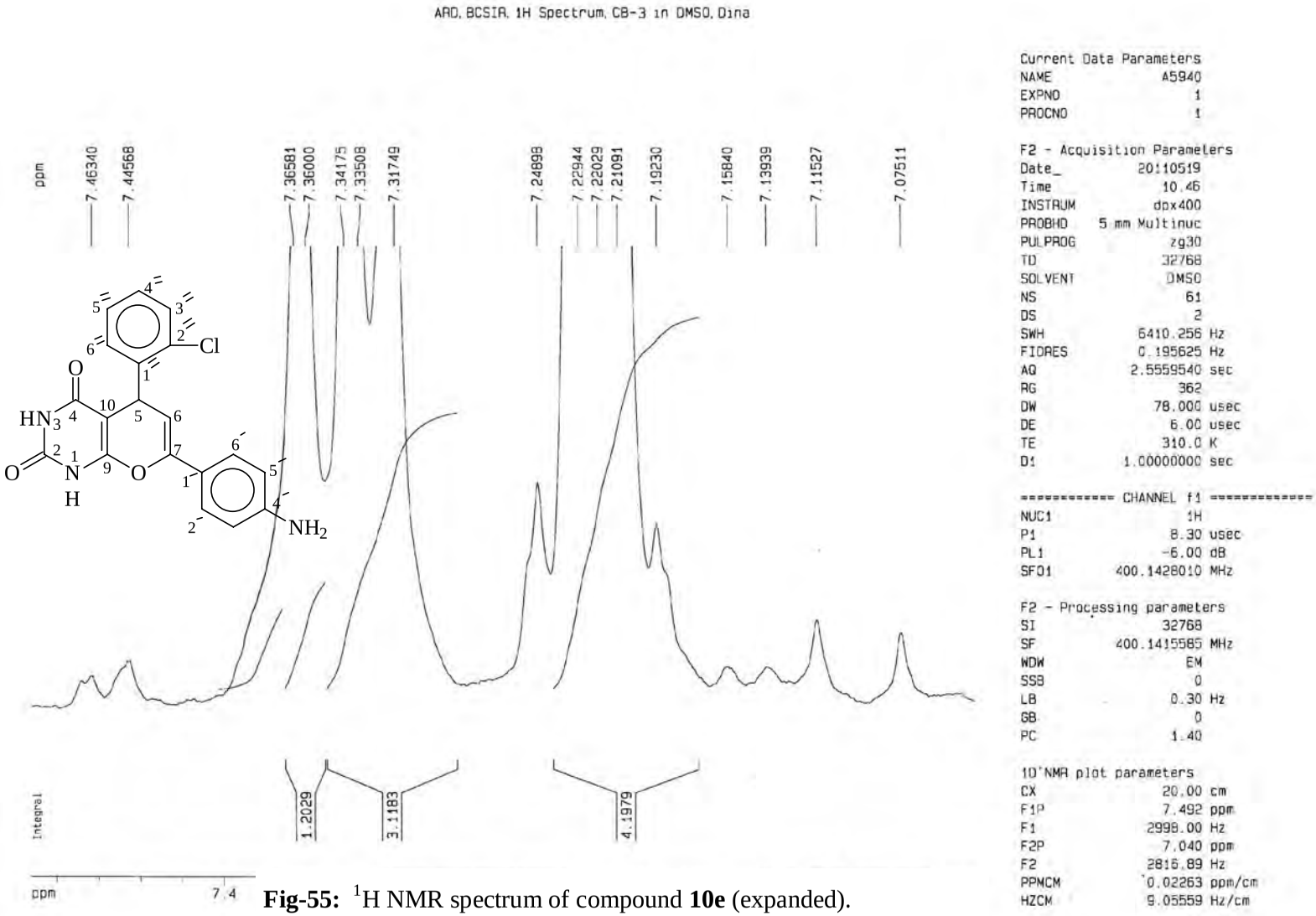


Fig-55: ^{1}H NMR spectrum of compound **10e** (expanded).

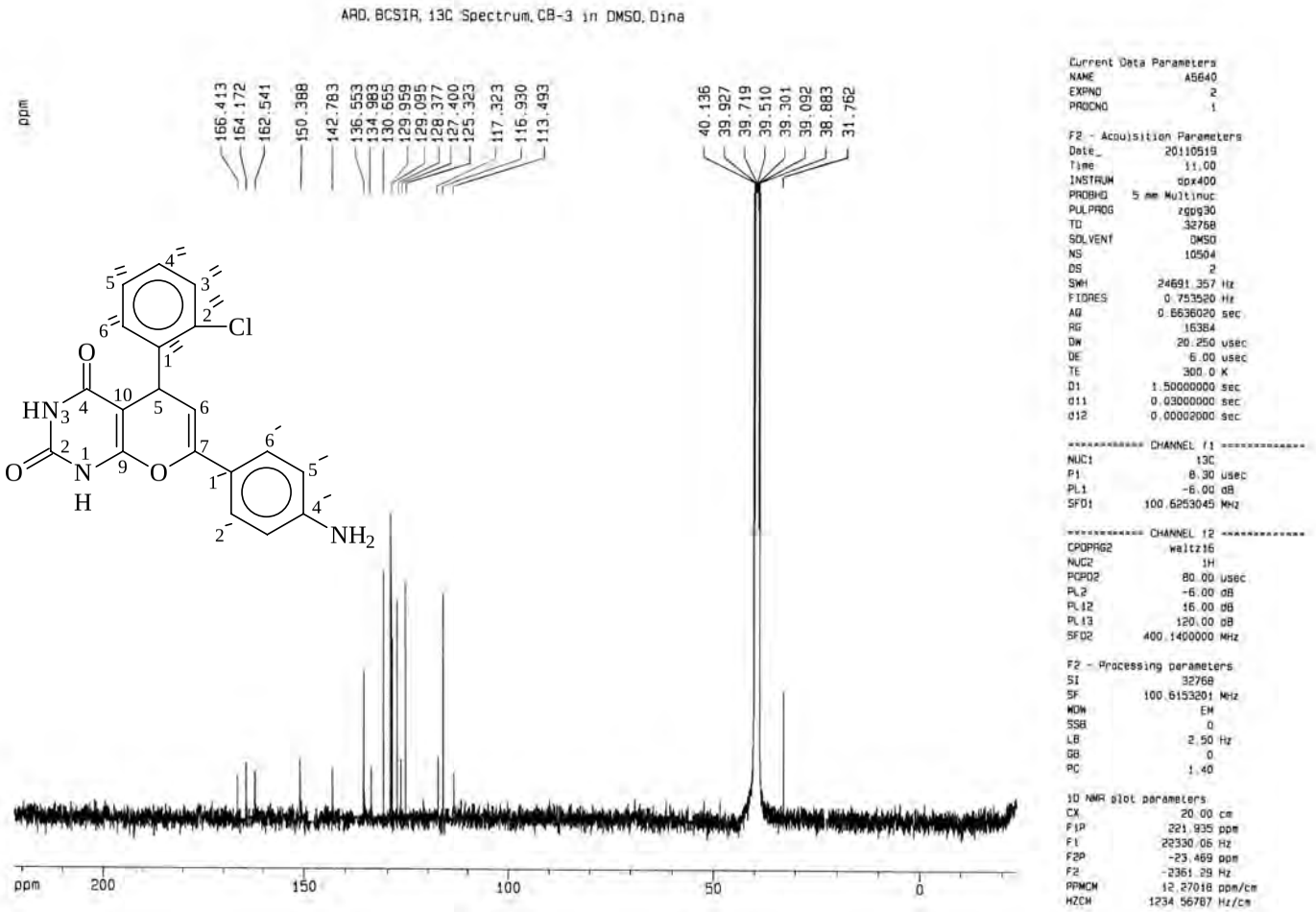


Fig-56: ^{13}C NMR spectrum of compound **10e**.

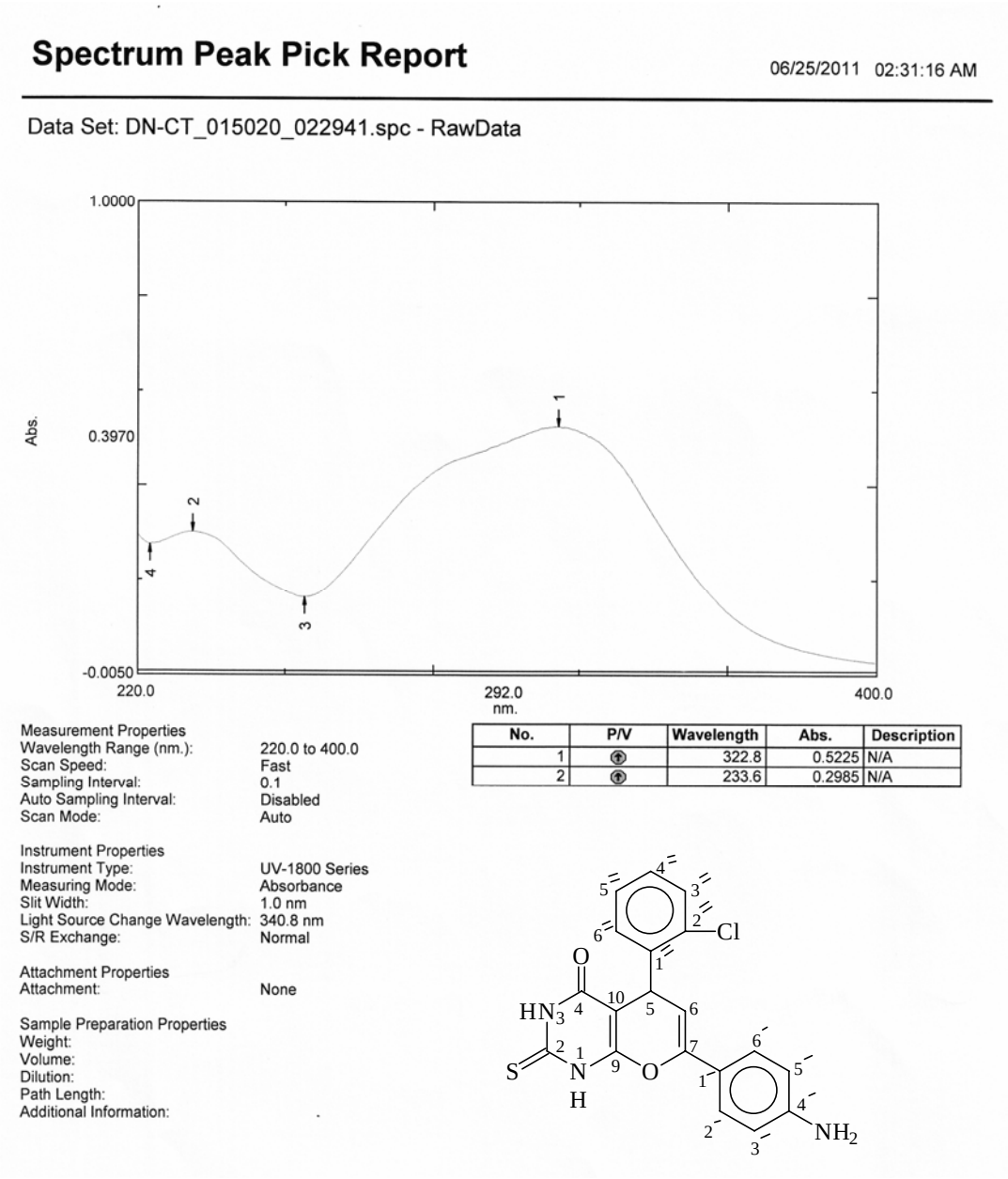


Fig-57: UV spectrum of compound **10f**.

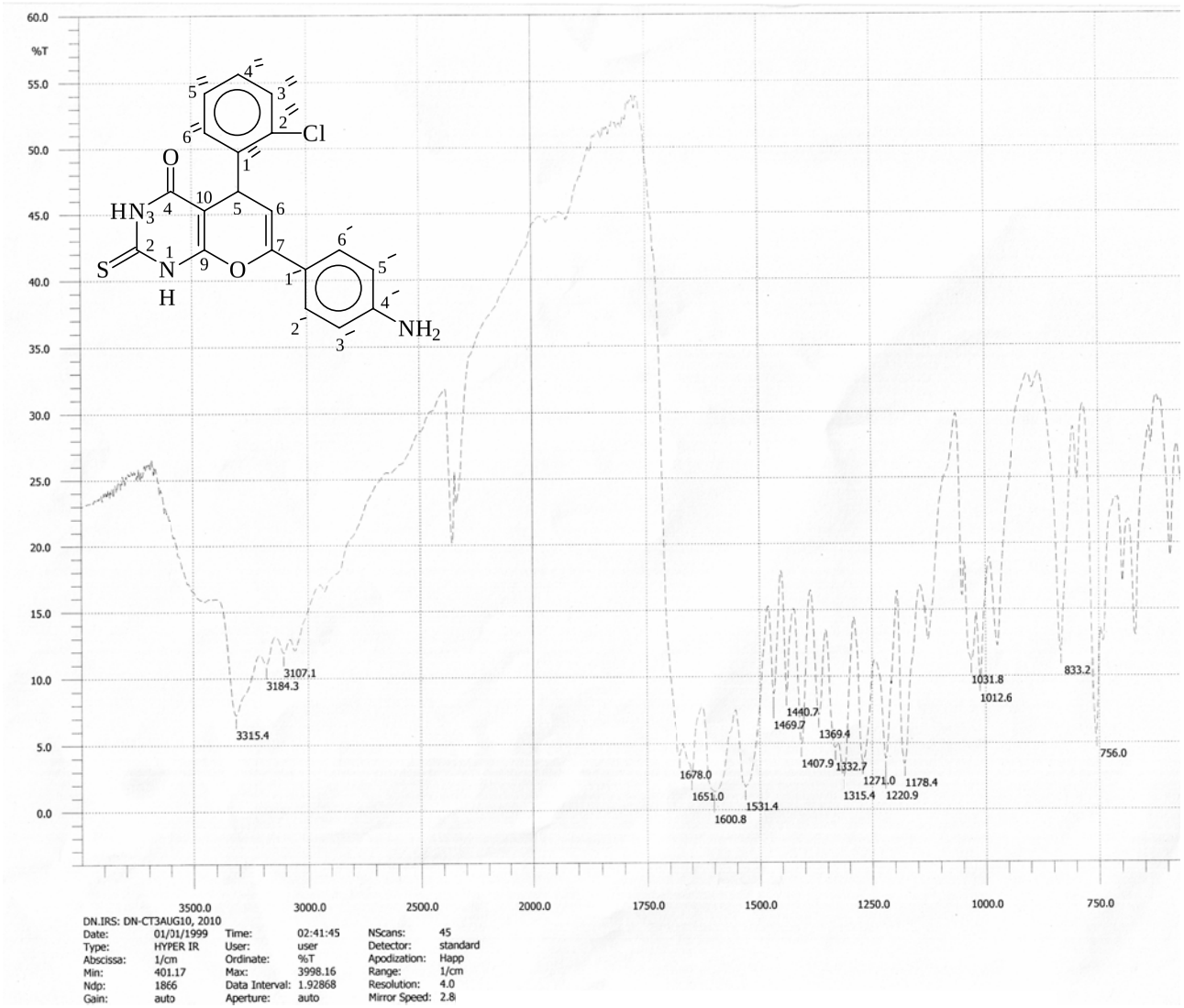


Fig-58: IR spectrum of compound **10f**.

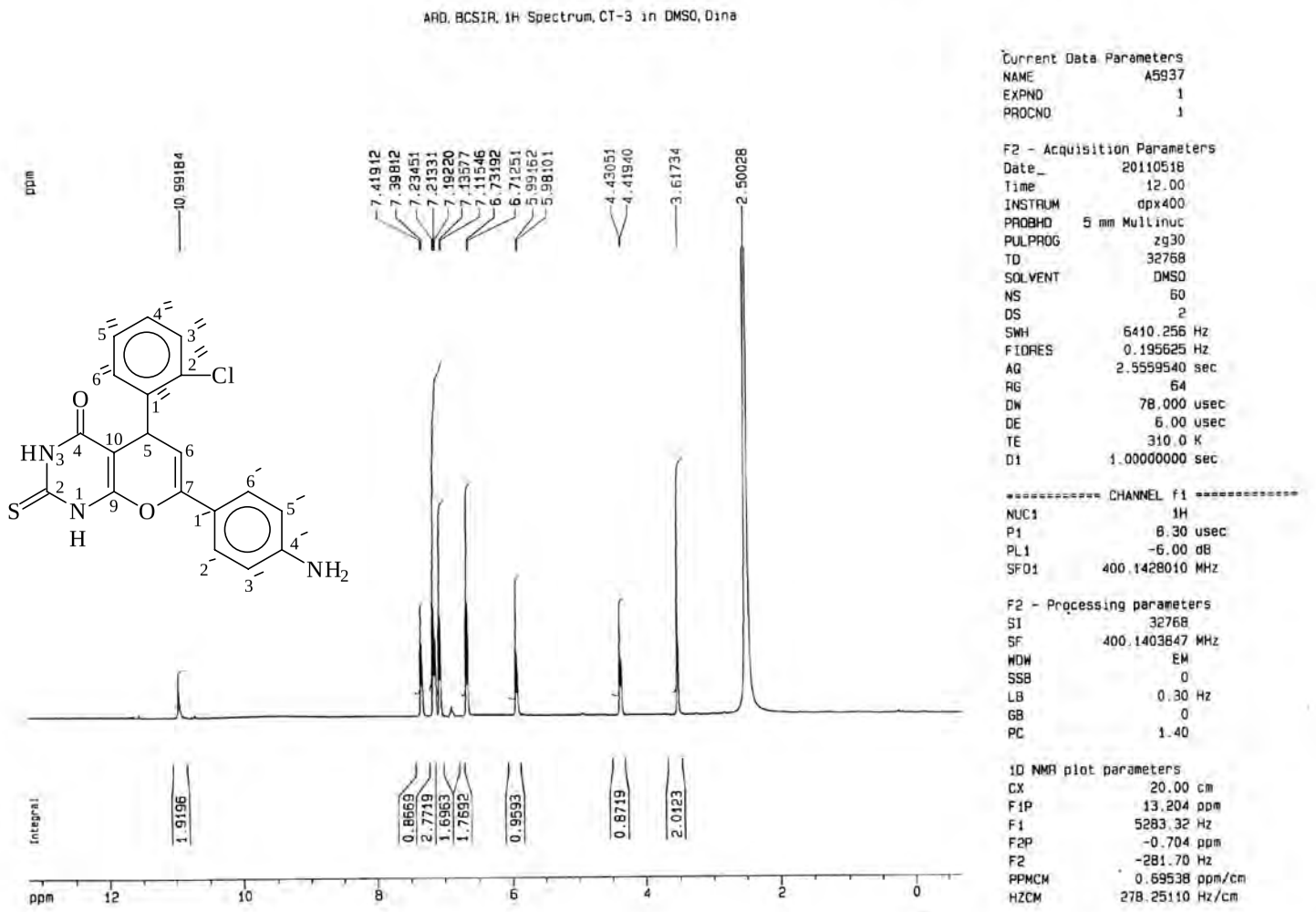


Fig-59: ^{1}H NMR spectrum of compound **10f**

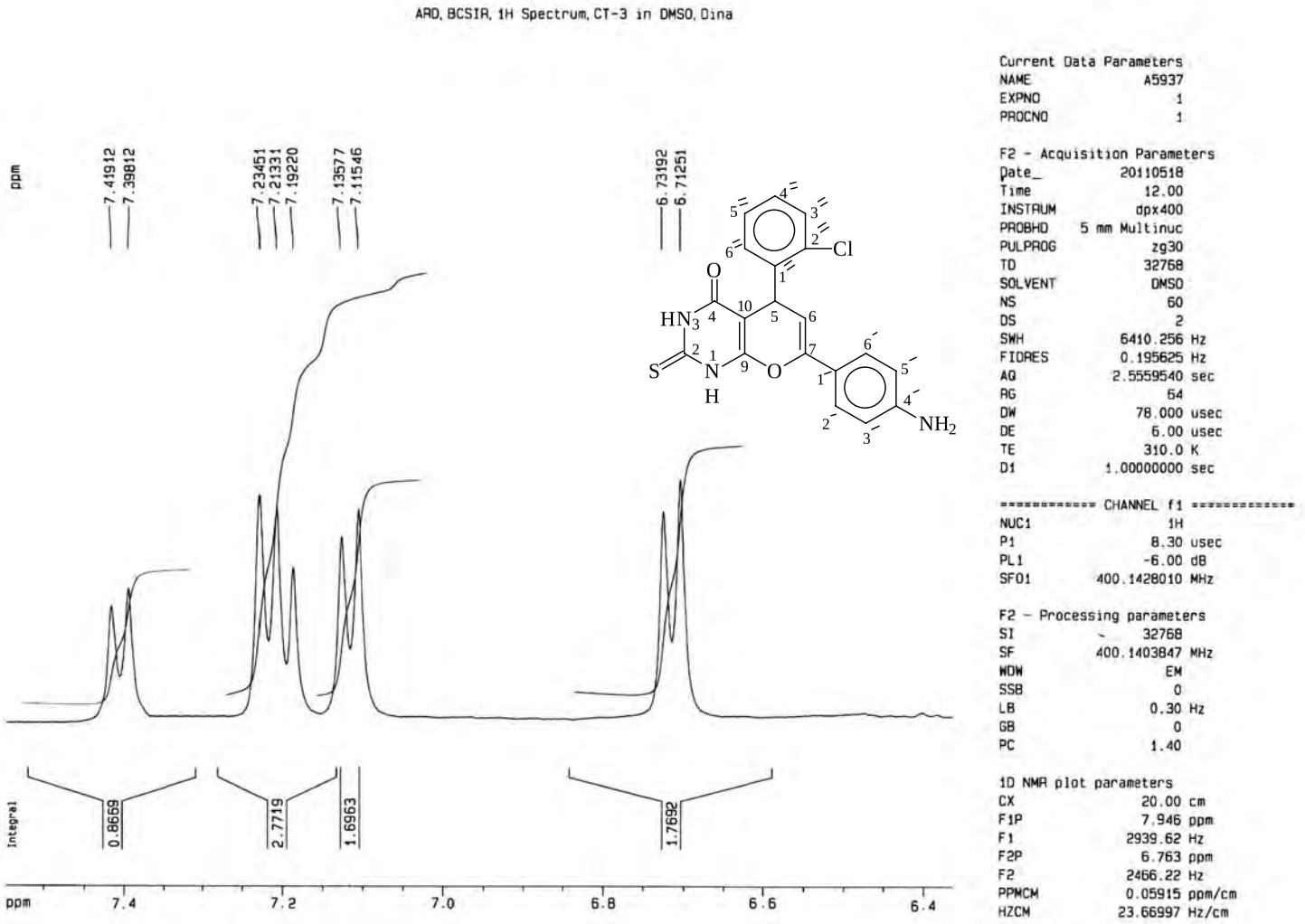


Fig-59: ^{1}H NMR spectrum of compound **10f** (expanded).

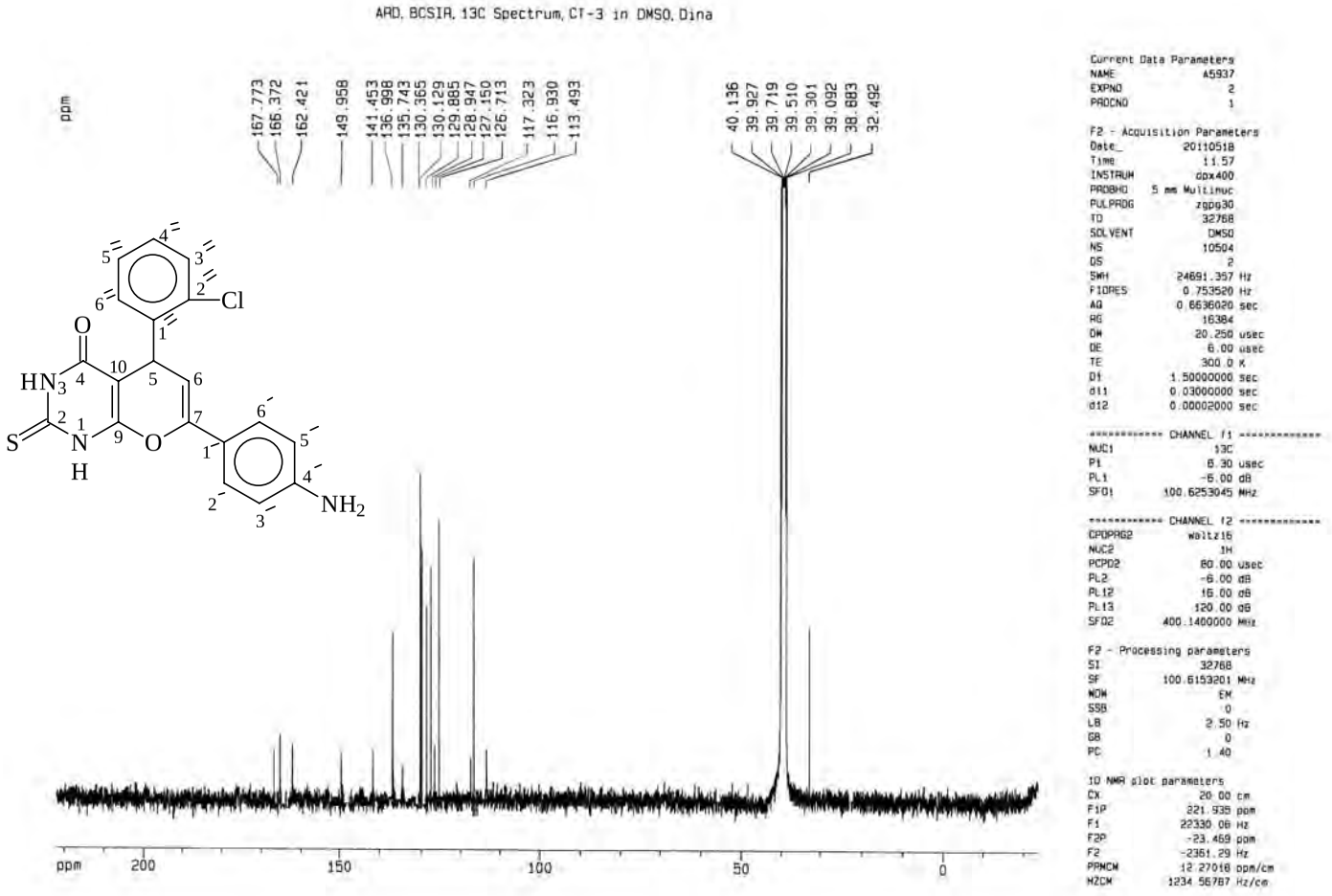


Fig-60: ^{13}C NMR spectrum of compound **10f**.

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