SYNTHESIS OF DIHYDROFURANS BY METAL CATALYZED REACTION OF CYCLIC DIAZOCARBONYL COMPOUND

M.PHIL THSIS

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A DISSERTATION SUBMITTED TO THE PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER OF PHILOSOPHY (M.PHIL) IN CHEMISTRY

SUBMITTED BY

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THESIS ACCEPTANCE LETTER

The thesis entitled "Synthesis of dihydrofurans by metal catalyzed reaction of cyclic diazocarbonyl compound"submitted by Md. Abdul Bari, Roll No. 040303103F, Registration No. 0403033, Session April, 2003 has been accepted as satisfactory in partial fulfilment of the requirement for the degree of Master of Philosophy (M.Phil) in chemistry on June 25, 2008

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It is hereby declared that this thesis or any part of it has not been submitted elsewhere for the award of any degree or diploma.

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(Md Abdul Bari)

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Author 29.06.08
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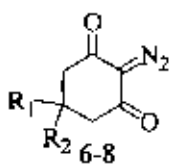
Title: "Synthesis of dihydrofurans by metal catalyzed reaction of cyclic diazocarbonyl compound"

Abstract

In view of the extensive natural occurrence and biological importance of dihydrobenzofuran and furan derivatives it was planned to develop a general and facile method for the synthesis of dihydrofurans through metal mediated catalyzed reactions of cyclic diazocarbonyl compounds. An efficient method for the synthesis of 4-oxo-2, 3,4,5,6,7-hexahydro-benzofuran-2-yl-acetate derivatives **10-12**, 2-chloromethyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-ones **28,29,30** through the rhodium pivalate catalyzed reaction of 2-diazo-cyclohexane-1,3-diones **6-8** with vinyl acetate and allyl chloride, respectively in mild coudition is reported.

Synthesis of 2-phenyl-6,7-dihydro-5*H*-benzofuran-4-ones **14,16,18** and 2-ethoxy methyl 3,5,6,7-tetrahydro-2*H*-benzofuran-4-ones **21,23,25** are also developed by rhodium catalyst reaction of 2-diazo-cyclohexane-1,3-diones with phenyl acetylene and allyl ethyl ether respectively under the same reaction coudition. In case of phenyl acetylene and allyl ethyl ether spiro compound 1-phenyl-spiro[2,5]oct-1-ene-4,8-diones **15,17,18** and 1-ethoxymethyl spiro[2,5]octane-4,8-diones **22,24,26** were obtained respectively as by products.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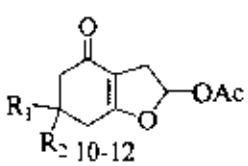
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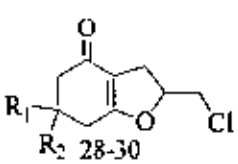
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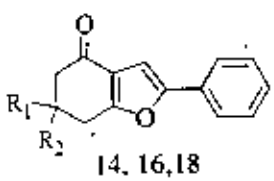
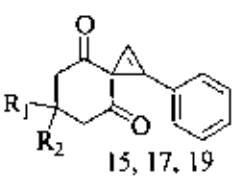

14, 16,18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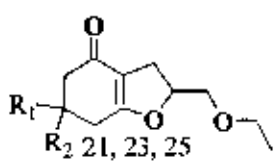
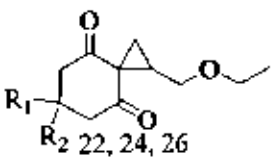

21, 23, 25


22, 24, 26

Where, R_1, R_2 = CH_3, H, $-CH(CH_3)_2$ etc.

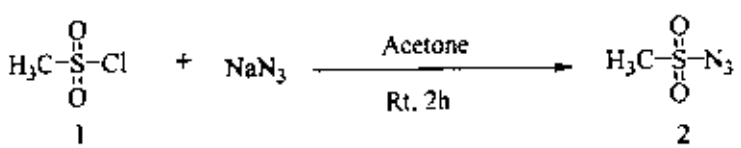
All the synthesized products were characterized by spectral data obtained from IR, UV and ^{1}HNMR. All synthesized compounds were tested antibacterial and antifungal activity, some of them demonstrated mild to moderate antimicrobial activity against most of the test organism.

SUMMARY

Investigations incorporated in this dissertation entitled "Synthesis of dihydrofurans by metal catalyzed reaction of cyclic diazo carbonyl compound" has been presented in four chapters. In the chapter 1, background of biological important and the important synthetic reactions involved in the synthesis are presented. Chapter 2 and chapter 3 deal with the detailed methodology and experimental procedure for the synthesis of dihydrofurans. Chapter 4 deals with the biological test of the synthesized products.

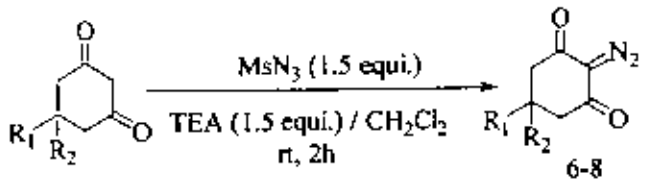
Chapter 1 represented the importance and synthesis of dihydrofuran and furan derivatives. Heterocyclic compounds containing furan or dihydrofuran moiety are of great interest, because of their occurrence in nature and their outstanding pharmaceutical and medicinal activities. Although various methods have been developed previously for the synthesis of dihydrofuran derivatives, only a few of them were mediated through rhodium or palladium catalysis.

In chapter 2, results and discussion of the synthesis of 4-oxo- 2,3,4,5,6,7-hexahydro-benzofuran-2-yl acetates **10-12,** 2-phenyl-6,7-dihydro-5*H*-benzofuran-4-ones **14,16,18** and 1-phenyl-spiro [2.5] oct-1-ene-4. 8-dione 15,17,19, 2-ethoxymethyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one **21,23,25** and 1-ethoxymethyl-spiro[2.5]octane-4, 8-diones **22, 24, 26** and also 2-chloromethyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-ones **28,29&30** are described as shown in the scheme 3-9. Reactions were carried out through rhodium pivalate catalyst under nitrogen atmosphere at room temperature for 2-4 hrs. The preparation of starting materials, methane sulfonyl azide and 2-diazo cyclohexane -1,3-diones **6-8** are described in this chapter as shown in the scheme 1 and 2. Structure of all of these synthesized dihydrofuran and spiro derivatives have been established on the basis of their UV, IR and NMR spectral evidences.



1 2

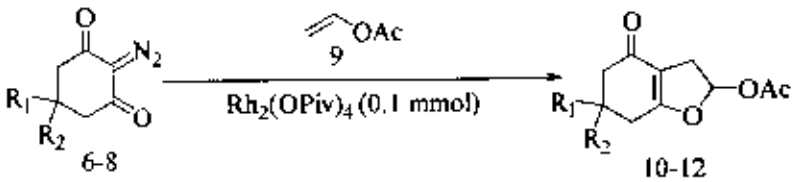
Scheme 1



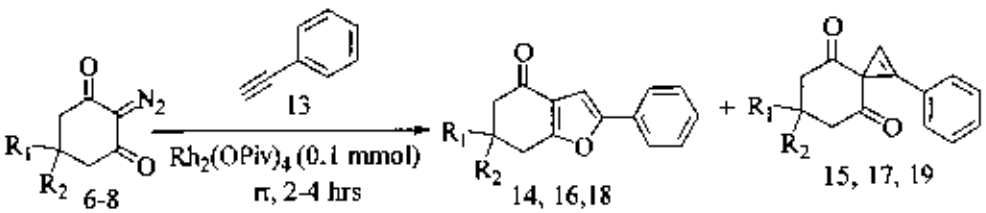
3-5 Where

3,6. $R_1 = R_2 = -CH_3$,
4,7. $R_1 = R_2 = -H$
5,8. $R_1 = H$, $R_2 = -CH(CH_3)_2$

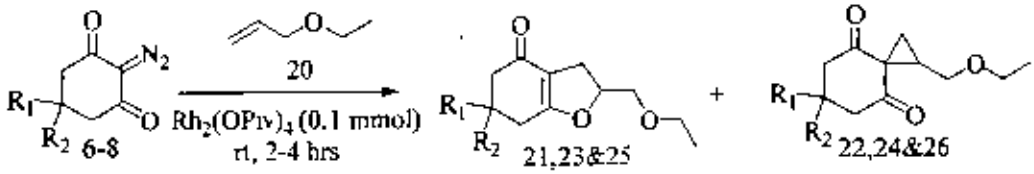
Scheme 2



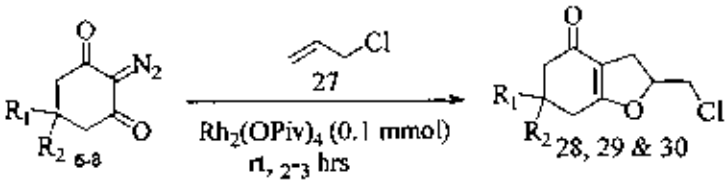
Scheme 3



Scheme 5



Scheme 8



Scheme 9

In chapter 3, all the experimental procedure and analytical data are reported. This chapter also contains references and important spectra of the synthesized compounds.

In chapter 4, introduction, methodology, results and discussion, reference and conclusion of the biological test of the synthesized compounds are presented. Eighteen synthesized heterocyclic compounds and three diazo compounds have been tested for antimicrobial activity against five gram-positive and eight gram- negative bacteria as well as three human fungal pathogens. Among tested compounds of furan and cyclopropane derivatives (10, 14, 21 and 28) exhibited relatively greater or moderate (10-12mm) inhibition of growth of the microorganism and compounds 15 and 22 showed mild (7-10mm) inhibitory activity against most of the tested organisms.

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Chapter-1

Introduction

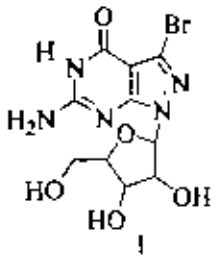
INTRODUCTION

1.1. Furans derivative and their importance

Heterocycles such as furan, pyrrole, indole and thiophene are versatile pharmacophores possessing a variety of biological activities[1]. A major challenge in organic synthesis today is to devise reactions that can form several carbon-carbon bonds in one operation leading to the construction of polycyclic structures with proper regio and stereochemical control[2]. Dihydrofurans and furans are two of the most important heterocycles with wide spread occurrence in nature[3]. The furan moiety is a core structure of many alkaloids such as kallolides and cembranolides[4], possessing a variety of biological activities. they are used as pharmaceutical, flavor. insecticidal, and fish antifeedant agents[5]. Their important biological activities and usefulness as synthetic intermediate of natural products have prompted a search for better methods of synthesis of dihydrofurans and furans. Although a number of synthetic methods for the preparation of dihydrofurans and furans have been reported, simple and efficient approaches still remain scare[6]. In recent years much effort has been devoted to study the effect of different transition metal catalysts on the decomposition of α-diazo carbonyl compounds[6]. The rhodium-catalyzed decomposition of diazocarbonyl compounds has become an important method in organic and natural product synthesis[7]. The rhodium (II) catalyzed reactions of acyclic and cyclic diazo dicarbonyl compounds with several substrates such as olefins, nitrate, isocyanates, carbondisulfides, furans, benzofurans, thiophenes and pyrroles have been extensively studied by many groups[8].

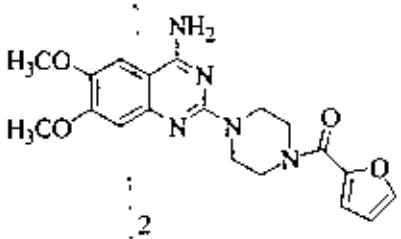
Isolation techniques and rapid structural elucidations of furan derivatives were developed by recent methods (UV, IR, NMR, Mass etc). A large number of furan derivatives have been discovered from the various sources. Many furan and dihydrofuran derivatives showed important biological activity.

Furan moiety containing Ribo nucleoside compounds showed in *vitro* activity against viruses and tumer cells. The guanosin analogous (**1**) showed significant activity in *vitro* L_{R10} and P_{388} Leukemia[9].



1

Varieties of antihypertensive agents contain pyrimidine and furan ring system. For example Prazosin(2)[10] a 2-substituted quinoline derivative has been used as a α-adrenocepter antagonist[10].



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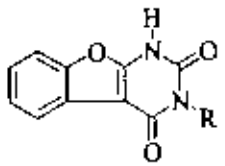
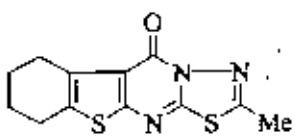
Patil, V. M. and co-workers[11] reported a new antialergic compound 3-amino-1, 2,3,4-tetrahydro-2, 4- dioxobenzofuro[3,2-d]pyrimidine (3).



3

The compound 6,7,8,9- tetrahydro-2- methyl -10*H*[1] benzothieno- [2,3-d] thiadiazolo [3,2-a] pyrimidine-10-one (4)[12] and dihydro-5*H*-[1,3,4] thiadiazolo [2,3-b] quinazolin-2,5-dione(5)[13] showed antiflammatory and analgesic activities.



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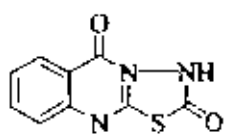
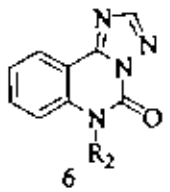


5

The pyrimidine[1,2,4]triazolo[1,5-c]quinazoline (**6**) exhibited the anticonvulsant, muscle relaxant, anxilytic and sedatives activity. Bezofuro[2,3-e]imidazo[1,2-c] pyrimidine (**7**) showed antidepressant activity and antihypertensive agents[14].



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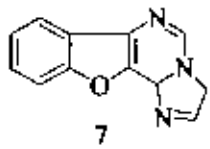

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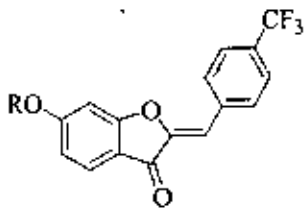
In 2003, Feng-Ling Qing and co-worker synthesized B-ring trifluoromethylated flavonoids derivatives demonstrated anticancer activities against human gastric adenocarcinoma cell line (SGC-7901).



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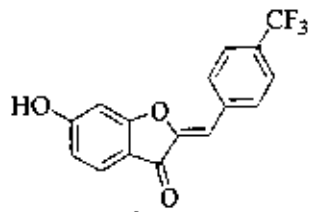
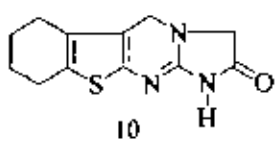


9

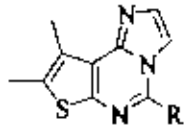
1.2. Some sulfur and nitrogen substituted furan derivatives and their importance. Heterocyclic compounds which contain five member ring such as furan, pyrrole, thiophene have become attractive target for organic synthesis because of their structural diversity and biological importance. Hetero aromatic and aliphatic compounds readily undergo cyclization, which allow convenient preparation for variety of furan derivatives.

In 1985, Ishikawa, F. et al[15] reported 1,2.3,5-tetrahydro-imidazol [1,2-a] thienopyrimidin -2-one **10** showed many biological activities.



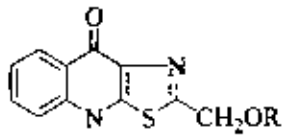
10

Rahman et al[16] reported 8,9- dimethyl imidazol [1,2-c]thieno[3,2-e] pyrimidine (**11a**) trimethyl imidazol[1,2-e]thieno[3,2-e]pyrimridine(**11b**), 8,9- dimethyl -5- phenyl imidazo [1,2-c]thieno[3,2-e]pyrimidine (**11c**) which showed antifungal and antibacterial activities.



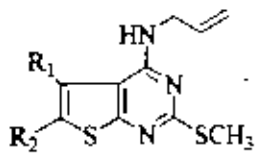
Where
11a. R = H
11b. R = CH_3
11c. R = Ph

In 1991, Nirupama Tiwari et al[17] reported that 2-aryloxymethyl-1, 2,4-thiadiazolo [2,2-b] quinazolin-4-one **12** demonstrated its fungicidal and herbicidal activities.



12

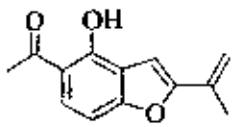
Rahman et al[18] reported that 4-allylamino-5, 6-dimethyl-2-methylthiothieno [2,3-d] pyrimidine **13** and 4-allylamino-2-methylthio-5,6,7-tetrahydrobenzothieno[2,3-d] pyrimidine **14** showed antifungal and antibacterial activities.



13. $R_1 = R_2 = H$
14. $R_1 = R_2 = -CH_3$

1.3. Natural Sources of Furans Moiety:

A furan moiety is found in a broad variety of natural products. The compounds containing the benzofuran moiety are widely distributed in nature[19]. They are used as versatile intermediates in organic and natural product synthesis[20]. They have also shown a range of biological activities[21]. Among these, isoeuparin (**15**) was isolated from the roots of Tagetes patula[22] and isotubaic acid (**16**) (rotenic acid) was obtained from the natural insecticide (rotenone) as a degradation product[23]. The synthetic approaches to isoeuparin[24] and isotubaic acid[25] had been reported.



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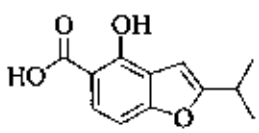
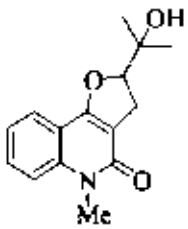
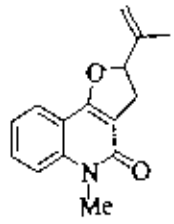


16

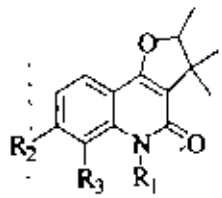
The dihydrofuroquinolinone and furoquinolinone alkaloids are widely distributed in nature[25]. They were primarily isolated from Rutaceae species as an angularly and linearly fused structure **17-29**. They are reported to have various biological activities such as antimicrobial, antimalarial, insecticidal, antineoplastic, antidiuretic, antiarrhythmic and sedative[26], and are also used as traditional medicines in China[27].



17
Araliopsine

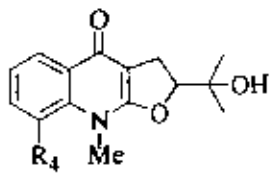


18
Almein

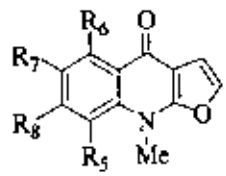


Where

19. R_1 = Me, R_2 = R_3 = H Oligophyline
20. R_1 = R_2 = R_3 = H, N-Dimethyloligophyline
21. R_1 = R_2 = H, R_3 = OCH_3, Oligophylbcine
22. R_1 = H, R_2 = R_3 = OCH_3, Oligophylacidine

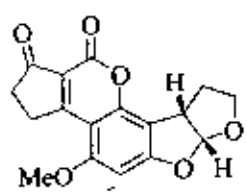


23. R_4 = H, Isoplatydesmine
24. R_4 = OCH_3, Balfourodine



25. R_5 = CH_3, R_6 = R_7 = R_8 = H Isodictamine
26. R_5 = CH_3, R_6 = OH, R_7 = R_8 = H Dictangustine-A
27. R_5 = CH_3, R_6 = R_7 = H, R_8 = OCH_3 Iso-r- fagarine
28. R_5 = CH_2CH_3, R_6 = R_7 = H, R_8 = OCH_3 Isotaifine
29. R_5 = $CH_2CHC(CH_3)_2$, R_6 = R_7 = OCH_3 Acrophylline

The complex polycyclic structures and their biological activities of the aflatoxins[29a] have made them important and challenging targets for total chemical synthesis.



Aflatoxin B2

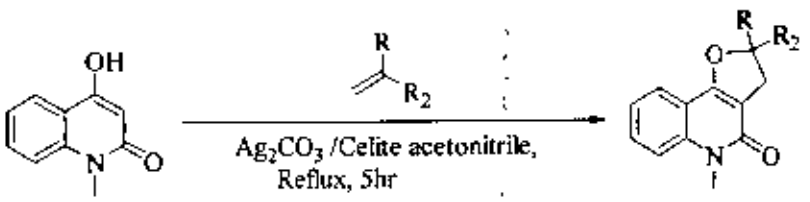
30

1.4. Synthesis of furan and dihydrofuran derivatives by various methods:

There are a lot of natural products containing furan or dihydrofuran derivatives which are more interesting in biologically active. For the synthesis of furans and dihydrofurans from different compounds many procedure are published, some of them are outline below.

1.4a. Synthesis of dihydrofurans by using Silver Catalyst:

In 2000, Lee, Y. R. et al reported that Ag_2CO_3/Celite (FeÂtizon reagent) is a simple and convenient reagent for synthesis of dihydrofuran formation[29b]. They described the efficient synthesis of dihydrofuroquinolinone and furoquinolinone derivatives starting from 4-hydroxy-2-quinolones and a variety of olefins in the presence of Ag_2CO_3/Celite.



1

Where
R = H, -CH_3 etc.
R_2 = Phenyl, -C_5H_{13}, -OEt, -OAc, -Ome, -OBu etc.

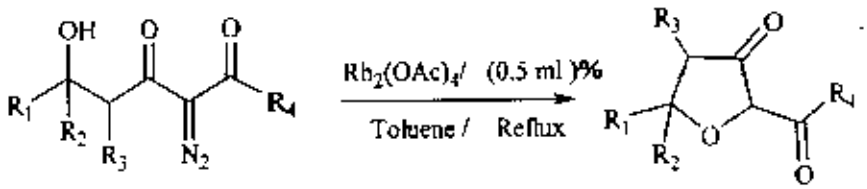
2

Scheme 1

While furans and dihydrofurans are initiatively a very attractive approach to make natural products, few general methodologies have been reported. Many new synthetic methodologies have been developed in recent years for the important of heterocyclic compounds. In particular, transition metal catalyzed transformations have been performed successfully. For example, platinum-catalyzed intramolecular hydroalkoxylation of λ-hydroxy olefins led to the formation of tetrahydrofuran derivatives[30].

1.4b. [2,3]-Rearrangement by Rhodium (II) Catalyst for Preparation of tetrahdrofurans derivatives:

In 2006, M. Liao et al. first investigated the diazo decomposition of the additional products in the presence of rhodium (II) acetate, with the expectation that Rh(II)-carbene intramolecular O–H insertion should occur to afford tetrahydrofuran derivatives (Scheme 2). ^{1}H NMR spectra of the crude products showed that only intramolecular O–H insertion products were formed in all cases.

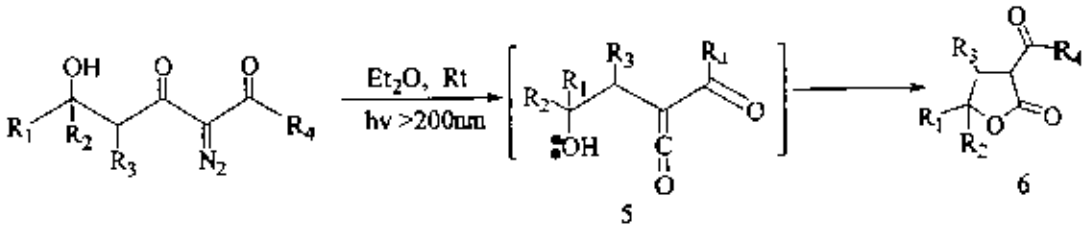


3 4

R_1 = Phenyl, -OEt , R_2 =H, -CH_3, etc. R_3 = Me, OMe
R_4 = Me, Phenyl etc.

Scheme 2

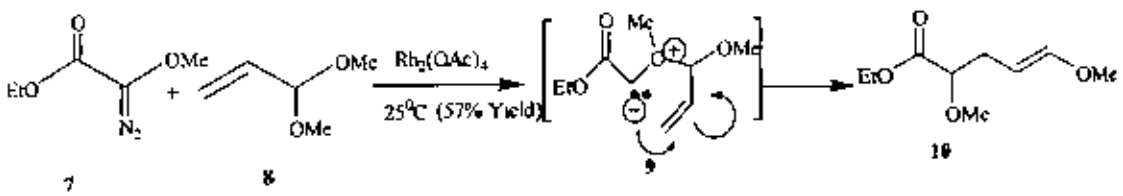
Next, photo-induced reaction of the diazo compounds 3 was examined, with the expectation that Wolff rearrangement should occur to generate the ketene intermediate **5**, which may be followed by an intramolecular nucleophilic attack by the hydroxy group. The reaction was carried out in the anhydrous ether solution under UV irradiation (150 W high-pressure Hg lamp, k > 200 nm) at room temperature. The starting diazo compound was completely consumed after 14–17 hrs, and ^{1}H NMR and ^{13}C NMR spectra indicated that the major product was the expected γ-butyrolactone derivative **6** (Scheme 3).



5 6

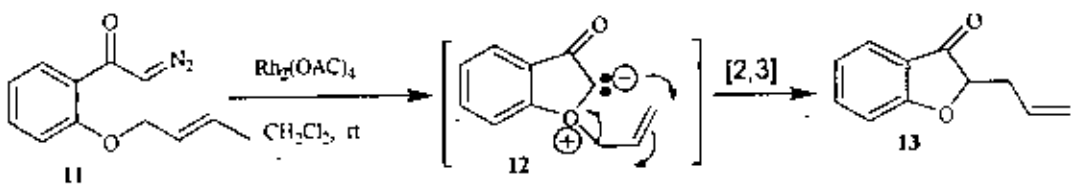
Scheme 3

[2,3]-Rearrangements of ylides derived from α-diazocarbonyl compounds with regard to the rhodium carbenoid. From literature survey, it was well established that Rh(II) carbenoids could interact with allylic ethers or acetals to furnish oxonium ylides which subsequently undergo [2,3]-rearrangement. Doyle had shown that Rh(II)-catalyzed decomposition of ethyl diazo acetate **7** in the presence of allylic acetals (e.g. **8**,) furnished allylic ethers[32] (e.g.,**10**).



Scheme 4

Pirrung later demonstrated that similar transformations could be achieved using α-diazoketones as well as α-diazoesters. For example, decomposition of α-diazoketone **11** with $Rh_2(OAc)_4$ in CH_2Cl_2 at room temperature furnished ether **13**[33].



Scheme 5

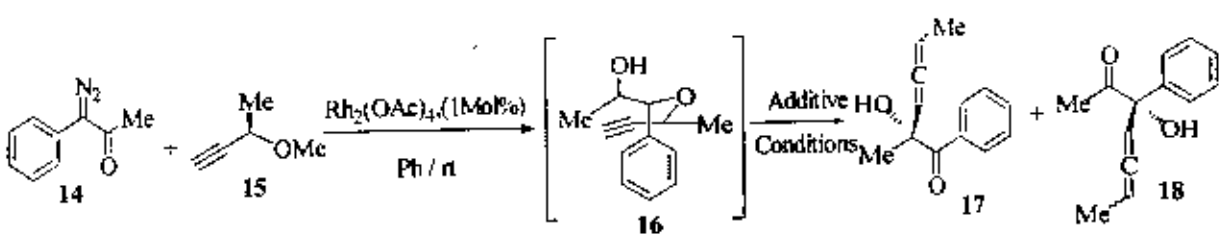
1.4c. Catalysis of [2,3]-rearrangement by other Lewis acids:

$Rh_2(tfa)_4$ acts as a Lewis acid catalyst to promote [2,3]-rearrangement of propargyloxy enol shown in the scheme 6. An investigation of other Lewis acid behaves similar activity. Numerously, Lewis acids were screened as shown in the table 1.

Table no 1: Lewis acids screened:

$MgBr_2{\cdot}OEt_2$	$BF_3{\cdot}OEt_2$	$EuCl_3$
$CuSO_4$	$Cu(OAc)_2$	$Cu(OTf)_2$
$CuCl_2$	$AgNO_3$	Ag_2PO_4
Ag_2O	$AgBF_4$	$AgSbF_6$
ZnI_2	$CdCl_2$	$SnCl_2$
SnI_2	$Sn(OAc)_4$	TiO_2
$Ti(OiPr)_4$	$TiCl_4$	$Zr(OiPr)_4{\cdot}OiPr$
$HgCl_2$	$Hg(OAc)_2$	$Hg(TFA)_2$
$Hg(NO_3)_2$	$LaCl_3$	$Fe(acac)_3$

Enol **16** was generated by treating of **14** and **15** (1.2 eqniv.) with $Rh_2(OAc)_4$. Conditions employed and selectivities observed with these additives are summarized in table **1a** as may be surmised from the data presented, most of these Lewis acids afforded only very modest catalysis of [2,3]-rearrangement when employed at stoichiometric loadings under refluxing benzene conditions. Two exceptions were obtained for the highly electrophilic silver (I) species $AgBF_4$ and $AgSbF_6$[34].

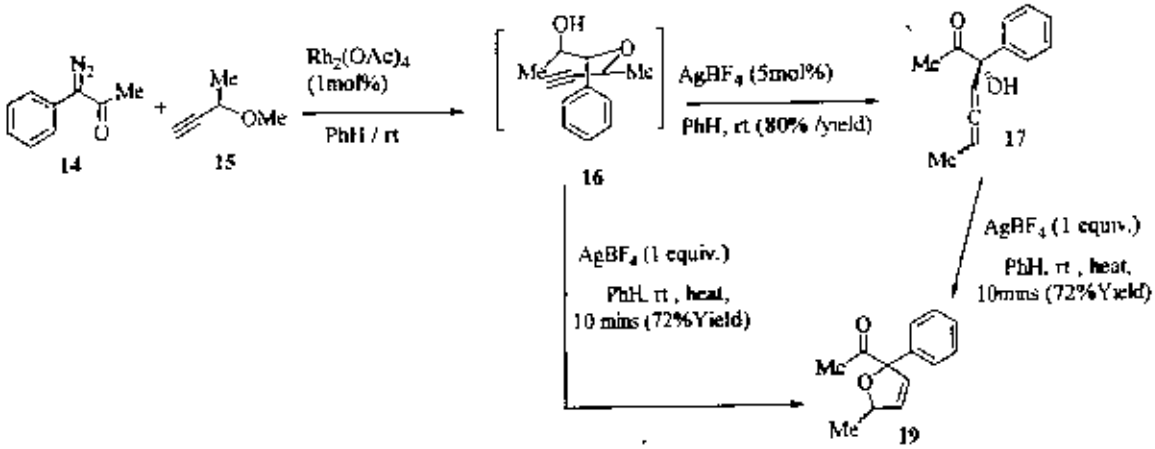


Scheme 6

Table 1a - Influence of non-Rh(II) Lewis acids on rearrangement of enol 16

Lewis acid additive	Conditions	17:18
no additive	PhH, Δ, 10 min	2.3 : 1
$AgNO_3$ (1.0 equiv)	PhH, Δ, 10 min	1 : 1.3
$AgNO_3$ (5.0 equiv)	PhH, Δ, 10 min	1 : 1.6
$AgNO_3$ (10.0 equiv)	PhH, Δ, 10 min	1 : 1.6
$CuSO_4$ (1.0 equiv)	PhH, Δ, 10 min	1 : 2.5
$SnCl_2$ (1.0 equiv)	PhH, Δ, 10 min	1 : 1.3
$SnCl_2$ (3.0 equiv)	PhH, Δ, 10 min	1 : 1.3
$AgBF_4$ (5 mol%)	PhH, rt, 2 min	1 : 60
$AgSbF_6$(5 mol%)	PhH, rt, 2 min	1 : 48

Ratios determined by ^1H NMR analysis of crude reaction mixtures. If the reaction employed in stoichiometric quantities at elevated temperature, $AgBF_4$ could also be used to promote cyclization of **17** to dihydrofuran **19** in very good yield (Scheme 7)[35]. Further studies demonstrated that this transformation could be accomplished *in situ* following [2,3]-rearrangement in the presence of stoichiometric loadings of $AgBF_4$.

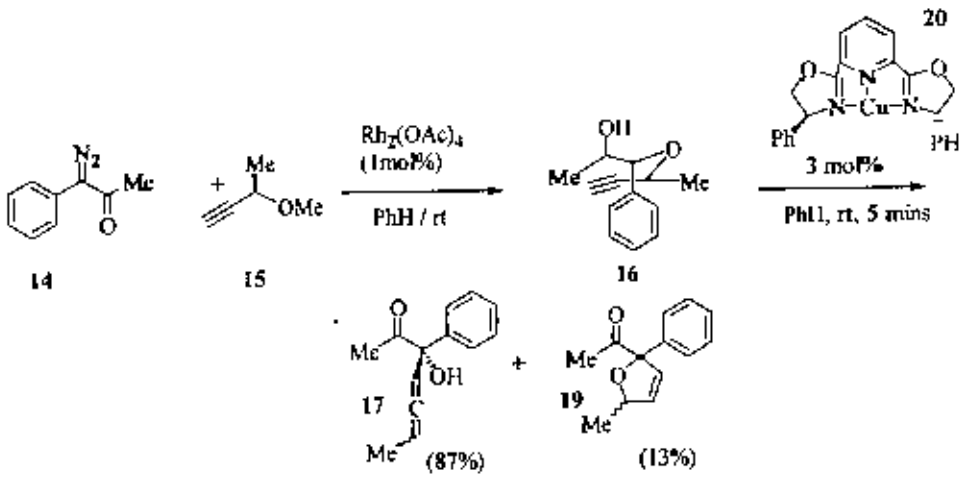


14 15 16 17 19

Scheme 7

It was felt that the poor catalytic activity observed with the remaining catalysts in table **1a** was attributable, in part, to poor solubility in the non-polar organic reaction medium as evidenced by the invariance in product ratio with increased loadings of both $AgNO_3$

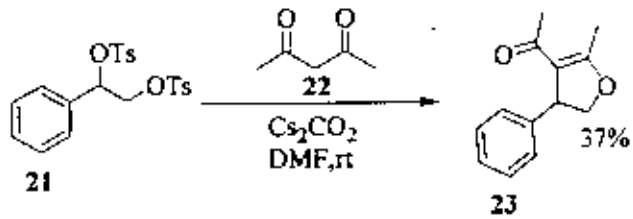
and $SnCl_2$. Consideration of ligand availability and ease of preparation led to the selection of bis(oxazolinyl)pyridine (pybox) Lewis acids [Cu-(*S,S*)-(**Phpybox**)](OTf)$_2$ and [Sn-(*S,S*)-(Ph-pybox)](OTf)$_2$ for investigation[38]. As may has been seen from scheme 8, both complexes displayed excellent catalytic activity, promoting [2,3]-rearrangement of enol **16** at room temperature and at low catalyst loadings. Curiously, use of the Cu(II) catalyst also resulted in the isolation of dihydrofuran in 19% yield. This species was not generated by Sn(II) catalysis. Suspecting that cyclization of **17** was occurring in the presence of Cu(II) in a manner analogous to that observed with Ag(I) (see Scheme 7), **17** was treated with both catalyst and $Rh_2(OAc)_4$ only to find that these conditions did not lead to formation of **19.**



Scheme 8

Seeking further certainty that **19** was not derived from 17 under Cu(II)-Catalyzed reaction conditions, the isotope labeling study depicted in Scheme 9 was performed. Diazoketone **14** was treated with $Rh_2(OAc)_4$ (**1** mol%) in the presence of both 3-butyn-2-ol **15** and deuterium labeled α-hydroxyketone **17**. Once enol formation was completed, catalyst 20 (5 mol %) was added, produced a resulting mixture of protic and deuterated [2,3]- rearrangement products **17** and **18**, but exclusively protic **19**. Thus, cyclization of **18** did not take place under the reaction conditions leading to the conclusion that dihydrofuran **19** must arise via a completing side-reaction in the presence of Cu(II) catalyst **20**.

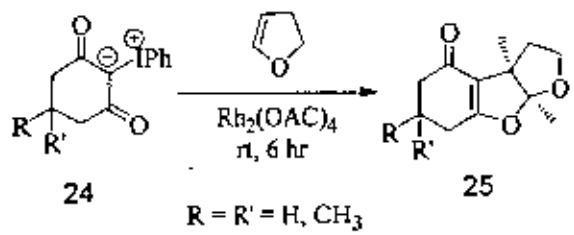
Thomas Wirth et al, in 2003, explored the possibility of adding bisnucleophiles to compound **21**. Addition of acetyl acetone (**22**), lead to the formation of a five-membered heterocycles that has been synthesized earlier by different routes[36]. After initial attack of the central carbon atom in **22** at the benzylic position, the enolate oxygen of the 1,3-dicarbonyl compound attacks as a second nucleophile to give the dihydrofuran derivative **23** in 37% yield[37].



Scheme 10

1.4d. Some different routes for synthesis of furans moiety:

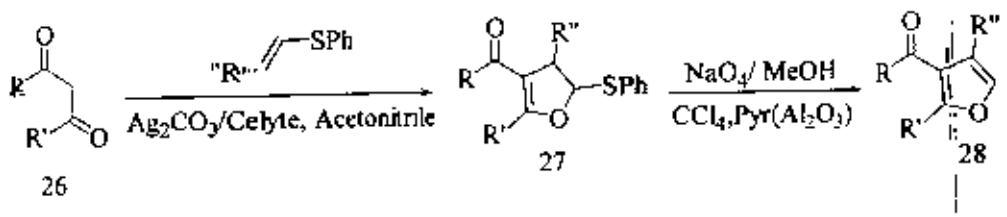
Reaction of iodonium ylides with dihydrofuran were examined by Korean scieutist[38]. When iodonium ylide **24**, was treated with 2,3-dihydrofuran as a solveut and a reactant at room temperature for 6 hr in the presence of 1 mol % of $Rh_2(OAc)_4$, cycloadduct **25** was obtained in an 81% yield (Scheme 11).



Scheme 11

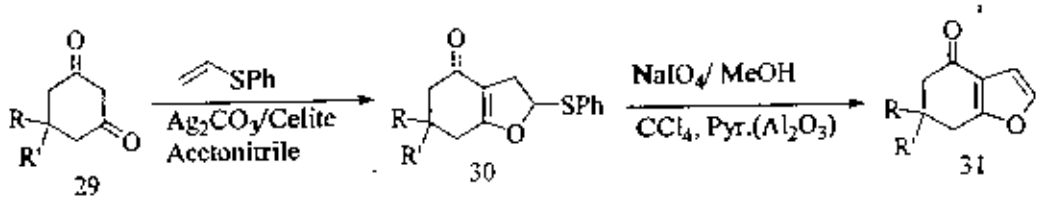
The structural assignment was analyzed from spectroscopic analysis. The *cis*-stereochemistry of **25** is supported by the coupling constant (J = 5.9 Hz) at δ = 6.19 due to acetal methane proton. The fused acetals are very important as a structural subunit of a variety of biologically active natural products such as aflatoxins[39-41], dendrillolide[42], clerodin[43], asteltoxin[44], hyacophiline45[49] and paraherquonin[50]. The application of the fused acetals to natural aflatoxin B2 and unnatural demethoxyaflatoxin B2 has been reported[51, 52].

In order to develop methodology of furan moiety, metal mediated salts Mn(III), Ce(1V), and Co(II)) have become an important method for the synthesis of heterocyclic frameworks[53]. Lee Y.R and his group reported that silver(I)/Celite is a simple and convenient reagent for dihydrofuran formation[55]. They described the efficient synthesis of 3-acylfurans by the oxidative cycloaddition of 1,3-dicarbonyl compounds to vinyl sulfides followed by $NaIO_4$ oxidation and syn-elimination under mild conditions. The sequence that they have developed begins with the reaction of 1,3-dicarbonyl compounds with vinyl sulfides (3-fold excess) in acetonitrile. Two equivalents of Ag_2CO_3/Celite are used for the formation of the dihydrofuran.



Scheme 12

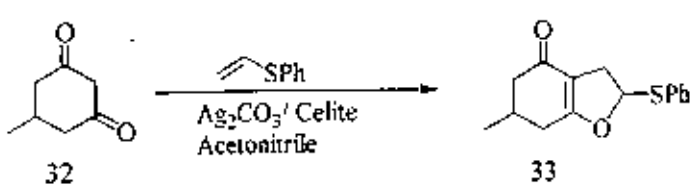
Synthesis of dihydrofurans and furans from the reaction of cychlohexane 1,3-dicarbonyl derivatives and vinyl sulfide [33] are shown in scheme 13.



Where R,R' = H, Me

Scheme 13

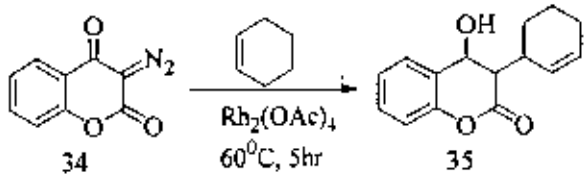
Yoshikoshi[56] had reported the transformations of 3-methylfuran annulation from 1,3-dicarbonyl compounds by using a phenylthionitroolefin. The data of the 3-acylfurans are also shown in scheme 14.



Scheme 14

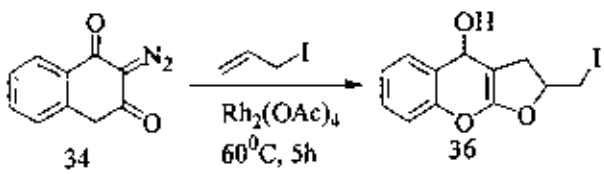
Forst[57-59] isolated furanomonoterpene (evodone) from *Evonia hortensis*. The spectroscopic properties of synthetic evodone agreed well with those reported in the literature. Another application of this technology to the total synthesis of furanoterpene, et-clausenan, was next examined, et-Clausenan has been isolated with rosethran as a mixture from leaves *of Clausenawilldenovii*, a large of shrub found in the Himalayas, Sri Lanka, and some elevated parts of southern and western India[60]. The structure of et-clausenan was established by spectroscopic analysis, but no synthetic methods are known.

Continuous process of synthesized dihydrofurans derivatives; additional reactions with several olefins were investigated, for preparation of the skeletons of naturally occurring coumarins and dihydrofurocoumarins[61]. Reaction of **34** with an excess of cyclohexene used as a solvent and a reagent, in the presence of 1 mol% of $Rh_2(OAc)_4$ at 60°C for 5 hr gave the unexpected rearranged product **35** in a 51% yield (Scheme 15). The two olefinic protons of **35** were observed at 6.29 and 6.04



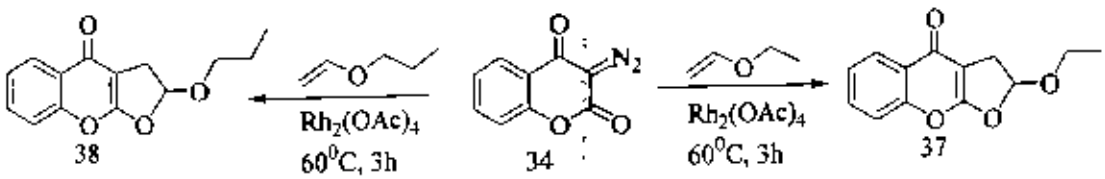
Scheme 15

When allyl iodide with electron-deficient olefin was used, the dihydrofurocoumarin **36** was obtained in 78% yield as a single compound. This result is also in clear contrast to that of Doyle, who reported that the rhodium(II)-catalyzed reactions of acyclic ethyl diazoacetate with allyl iodide afforded the [2,3]-rearranged product without forming the cycloaddition adduct as a single compound[62] (scheme 16).



Scheme 16

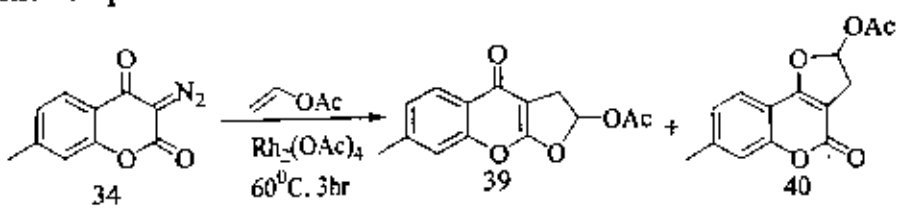
Another approach for dihydrofurocoumarin formation was obtained by using vinyl ethers[61]. On heating neat ethyl vinyl ether and isobutyl vinyl ether in the presence of 1 mol% of $Rh_2(OAc)_4$ for 3 hr, dihydrofurocoumarins **37** and **38** were produced in 69 and 64% yields, respectively. These results indicate that reactions with more electron-rich and electron-deficient olefins than simple alkenes such as cyclohexene provide an efficient route for synthesizing the dihydrofurocoumarin skeletons (scheme17).



38 34 37

Scheme 17

Next, reactions with vinyl acetates were also examined. Reaction of **34** with vinyl acetate at 60°C for 5 hr afforded the two regioisomeric cycloadducts **39** and **40** in 16 and 25% yields, respectively (Scheme 18). The two isomers were easily assigned from spectroscopic data. The ^1H NMR spectrum of angular dihydrofurocoumarin **39** showed methine peaks at 7.00 as a doublet associated with the dihydrofuran ring, whereas linear adduct **40** showed peaks at 6.87 as a doublet.



34 39 40

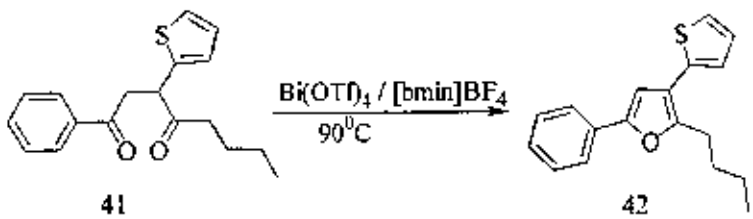
Scheme 18

In order to extend the utility of these reactions, one-step synthesis of a furocoumarin natural product was attempted. Pterophyllin 2 has been isolated from a small evergreen tree of *Ekebergia pterophylla*, found in South Africa[63]. The structure of pterophyllin 2 was established by spectroscopic analysis, but no synthetic methods are known.

Synthesis of these heterocycles is of great importance. Generally, furan, pyrrole and thiophene derivatives are prepared from 1,4-dicarbonyl compounds using acid catalysts. Strong acids such as concentrated H_2SO_4, P_2O_5, p-TSA and montmorillonite KSF and basic reagents including TsCl/ DBU, alumina, zirconium phosphate/zirconium sulfophenyl phosphate as well as microwave irradiation have been employed for their synthesis[64-65]. However, the synthesis of pyrroles and furans remains a challenge for synthetic chemists because of their sensitivity to acids.

Bismuth triflate has evolved as a remarkable Lewis acid catalyst for effecting various organic transformations[66]. Compared to lanthanide triflates, bismuth triflate is cheap and easy to prepare even on a multi-gram scale, from commercially available bismuth oxide and triflic acid[67].

In 2004,. Yadav, J. S. et al reported that this is the first published on the use of bismuth triflate as a catalyst for the synthesis of oxygen-, nitrogen- and sulfur-containing heterocycles[68]. In this article, they reported a mild and efficient method for the synthesis of furan, pyrrole and thiophene derivatives from 1,4-diketones using 5 mol% $Bi(OTf)_3$ immobilized in air and moisture stable $[bmim]BF_4$. Accordingly, treatment of 1-phenyl-3-(2-thienyl)-1,4-octanedione with 5 mol% of $Bi(OTf)_3$ in $[bmim]BF_4$ at 90 ^{0}C afforded 2-butyl-5-phenyl-3-(2-thienyl) furan in 85% yield (Scheme 19).

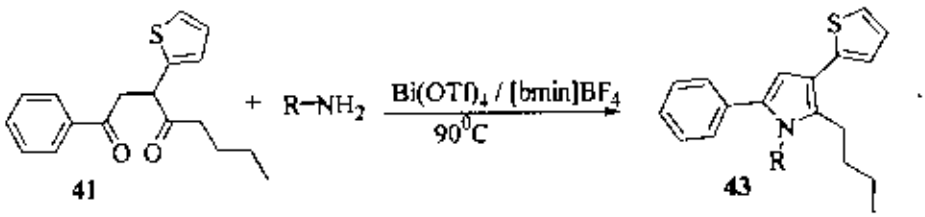


41 42

Scheme 19

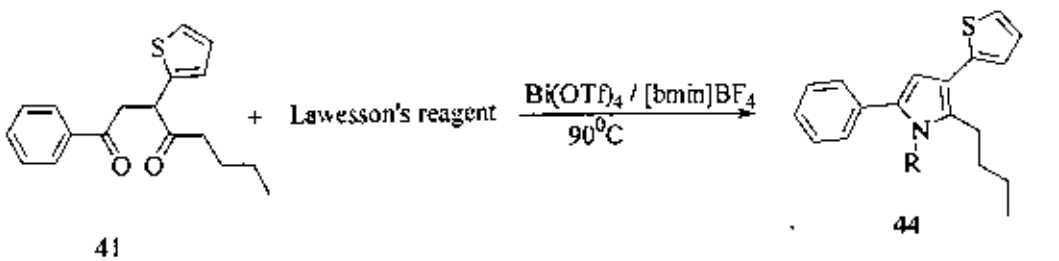
In a similar manner, various substituted 1,4-diketones underwent smooth cyclization to give the corresponding tri substituted furan derivatives[68]. In the absence of bismuth(III) triflate, no cyclization was observed in the ionic liquid alone. The starting 1,4- diketones were prepared according to procedures reported in literature[69]. Furthermore, treatment of 1,4-diketones with aryl amines under similar conditions resulted in the formation of the

corresponding pyrrole derivatives (Scheme 20). A variety of 1,4-diketones reacted smoothly with various aryl amines under identical conditions to give the respective tetrasubstituted pyrroles in good yield[68].



Scheme 20

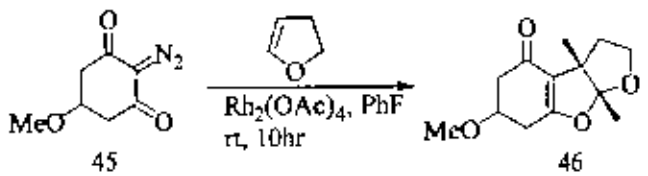
In addition, 1,4-diketones reacted efficiently with Lawesson's reagent under similar reaction conditions to give trisubstituted thiophene-pyrrole derivatives (Scheme 21).



Scheme 21

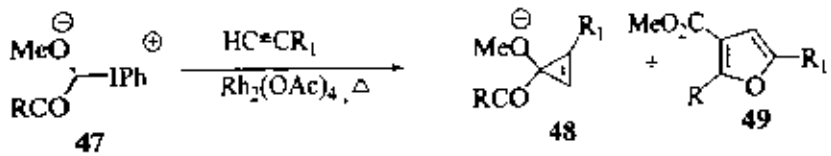
1,4-Diketones have been used as the common precursor for the synthesis of furan, pyrrole and thiophenes. This method is clean and free from side-products. The reactions were completed within 4–5.0 hr and the products were easily isolated by simple extraction with diethyl ether. The remaining ionic liquid containing the catalyst was recovered and recycled in subsequent reactions with only a gradual decrease in activity being observed.

Michael C. Pirrung has reported a number of advances in synthetic methodology and total synthesis based on the preparation of fused heterocyclic rings, such as the bis-tetrahydrofuran substructure contained within **46** (6-methoxy-2, 3,3a, 8a-tetrahydro-1, 8-dioxa-cyclopenta [a] inden-4-ol) using the formal dipolar cycloaddition of cyclic diazodicarbonyl compounds with vinyl ethers mediated by dirhodium catalysts[70]. Intermediate, in which a methoxycarbonyl group serves as a surrogate for the methoxy group, was consequently chosen as a product reasonably available from the dipolar cycloaddition of dihydrofuran with compound **46**[71] (Scheme 22).



Scheme 22

Barsila C. et al. reported that cycloadditions were observed upon reaction with terminal acetylenes. It is known. that copper(II) sulfate-catalyzed decomposition[82] of diethyl diazomalonate in the presence of phenylacetylene results in the formation of a mixture of a cyclopropene and a furan, while sensitized photolysis generates[83] furans as the primary products. The rhodium(II) acetate catalyzed decomposition[84] of diazo diketones **47**in the presence of terminal alkynes, results in cyclopropenes **48** and furans **49**, the isolation of which depends on the nature of the electron withdrawing group of the carbenoid In scheme 23.



Scheme 23

1.5.Rationale:

Heterocycles such as furan, pyrrole, indole and thiophene are versatile pharmacophores possessing a variety of biological activities[1]. Dihydrofurans and furans are two of the most important heterocycles with wide spread occurrence in nature[3]. Their important biological activities and usefulness as synthetic intermediate of natural products have prompted a search for better methods of synthesis of dihydrofurans and furans. Although a number of synthetic methods for the preparation of dihydrofurans and furans have been reported, simple and efficient approaches still remain scare[6]. In recent years much effort has been devoted to study of the effect of different transition metal catalysts on the decomposition of α-diazo carbonyl compounds[6]. The rhodium-catalyzed decomposition of diazocarbonyl compounds has become an important method in organic and natural product synthesis[7]. The rhodium (II) catalyzed reactions of acyclic and cyclic diazo dicarbonyl compounds with several substrates such as olefins, nitrate, isocyanates, carbondisulfides, furans, benzofurans, thiophenes and pyrroles have been extensively studied by many groups[8].

The use of diazo carbonyl compounds in transition metal-mediated insertion reactions has been extensively studied, particularly for the synthesis of theoretically interesting compounds as well as natural products[72-74]. However, only a few examples dealing with the preparation of oxygenated heterocycles reaction have been reported[74-78]. Over the past few years, several aspects of the Rh(II)-catalyzed reaction have been developed in order to increase the synthesis of furans moiety.

In view of the extensive natural occurrence and biological importance of dihydrofuran and furan derivatives, it was planned to develop a general and facile method for the synthesis of dihydrofurans through metal mediated catalyzed reaction of cyclic diazocarbonyl compound.

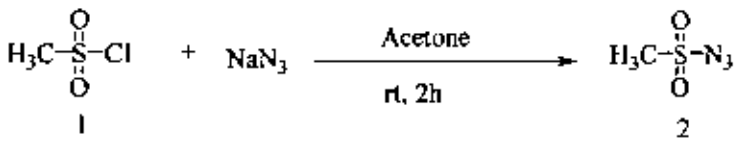
Chapter-2

Results and Discussion

RESULT AND DISCUSSIONS

2.1. Synthesis of methanesulfonyl azide 2:

Methanesulfonyl azide **2** was prepared by treating the solution of methanesulfonyl chloride **1**, acetone and sodium azide (1:1) equivalent at room temperature as shown in the scheme 1. After usual workup a low melting colourless solid **2** was obtained (yield 99%). The compound 2 was characterized by IR and literature report[54]

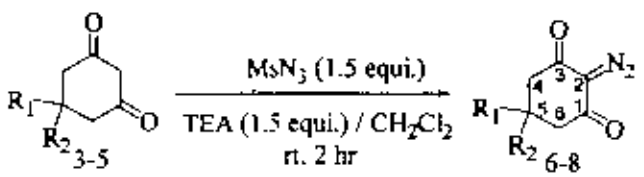


1 2

Scheme 1

2.2. Synthesis of 2-diazo-cyclohexane-1,3-dione derivatives 6-8:

2-Diazo-cyclohexane-1, 3-dione derivatives **6-8** were prepared by the diazo transfer reaction of the corresponding starting materials with mesyl azide according to Taber's method[79]. The preparation of 2-diazo-cyclohexane-1, 3-dione derivatives **6-8** using their corresponding cyclohexane-1,3-diones **3-5** and mesyl azide is shown in the scheme 2.



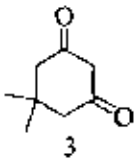
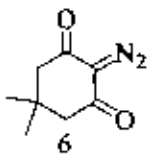
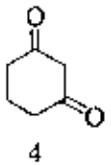
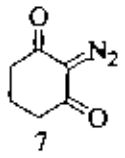
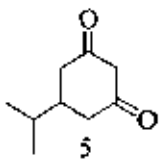
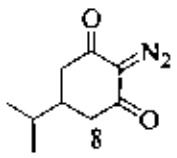
Where

3, 6. $R_1 = R_2 = -CH_3$
4, 7. $R_1 = R_2 = -H$
5, 8. $R_1 = H$, $R_2 = -CH(CH_3)$

Scheme 2

2-Diazo-cyclohexane-1, 3-dione derivatives **6-8** were synthesized by stirring a mixture of cyclohexane -1,3-diones **3-5**, mesyl azide and methylene chloride at room temperature. The reaction was stopped by adding 1N hydrochloric acid and water. After usual workup and purification by column chromatography on silica gel, 2-diazo cyclohexane-1,3-dione derivatives **6-8** were obtained (Table 1).

Table 1: Preparation of 2-diazo-cyclohexane-1,3-dione derivatives 6-8 in percentage

Entry	cyclohexane-1,3-dione	Condition	Product	Yield (%)
1.	 3	MsN_3	 6	96
2.	 4	MsN_3	 7	95
3.	 5	MsN_3	 8	90

2.2a. Characterization of 2- diazo-5,5- dimethyl cyclohexane-1,3-dione 6:

A light yellow solid was obtained (yield 96%), M.P. 67- 69 ^{0} C, which was highly moisture sensitive. The structure of compound **6** was established by spectral data. In UV (Fig. 6a) spectrum, the value was found in the range of λ_{max} 277.30 and 240.80 nm indicated diazo group.

The IR spectrum (CCl_4)(Fig. 6b) of this compound exhibited absorption bands at ν_{max} 2962.5 and 2889.2 cm^{-1} for stretching of methyl and methylene protons ($-CH_3$, $-CH_2$), 2189.1 and 2144.7 cm^{-1} for diazo group ($-C=N_2$), 1633.6 cm^{-1} for the presence of keto groups (- C=O).

The ^{1}H NMR spectrum (Fig. 6c) of the compound **6** explained the chemical shift position of δ 2.42 (s, 4H, C-4,6) for two methylene (–CH_2) groups, δ 1.02 (s, 6H) for the presence of two methyl (-CH_3) groups at C-5 position which are chemically equivalent that is assured structure of the compound **6**.

The structure of the compound **6** was further confirmed by its ^{13}C NMR data (Fig. 6d) at the chemical shift position of δ 201.79 and 201.61 due to the presence of (C=O) carbon, at δ 155.65 in favor of C=N_2, δ 52.61 and 52.38 designed for C-4 and C-6 respectively, δ 25.59 and 25.34 in support of -CH_3 carbon and δ 15.13 for C-5.

On the basis of complete analysis of the UV, IR, ^{1}H NMR and ^{13}C NMR spectra, the structure of this compound was accorded as 2- diazo-5,5- dimethyl cyclohexane-1,3-dione **6.**

2.2b. Characterization of 2-diazo-cyclohexane-1,3-dione 7:

The compound was obtained as a pale yellow solid which was very unstable in normal temperature. The yield was 95% and melting point was 44- 45^{0}C. The structure of compound **7** was characterized by spectral data. In UV spectrum (Fig. 7a) of the compound, the value was found in the range of 280.35 and 237.83 nm for diazo group.

The IR spectrum (Fig. 7b) of this compound showed absorption band at ν_{max} 2958.6 cm^{-1} and 2933.9 cm^{-1} for methylene protons (-CH_2-), at 2192.9 and 2129.3 cm^{-1} indicated for stretching of diazo group (C=N_2). at 1645.2 cm^{-1} designed for the presences of keto groups (- C=O).

The ^{1}H NMR spectrum (Fig. 7c) of the compound 7 demoastrated a two protons triplet at δ 2.97 (t, 2H, J=6.26 Hz) and 2.53(t, 2H, J =6.15 Hz) for two methylene (-CH_2-) group of C-4 and C-6, respectively and a two protons multiplet at δ 2.23 (m, 2H,) for the presence of methylene (-CH_2) group of C-5.

Its ^{13}C NMR spectrum (Fig. 7d) also exhibited the chemical shift at δ 197.89 and 197.07 for C=O, 156.6 for C=N_2, δ 38.63, 38.38 and 15.13 for C-4, C-6 and C-5. The presence of six carbon atoms was a good agreement with structure assign for **7.**

2.2c. **Characterization of 2-diazo-5-isopropyl-cyclohexane-1, 3-dione 8:**

The product **8** was a light white solid (yield 96%), M.P.: 58-59^{0}C. The structure of compound **8** was assigned by spectral data. In the UV spectrum (Fig. 8a) the value was found in the range of λ_{max} 276.53 and 235.85 nm.

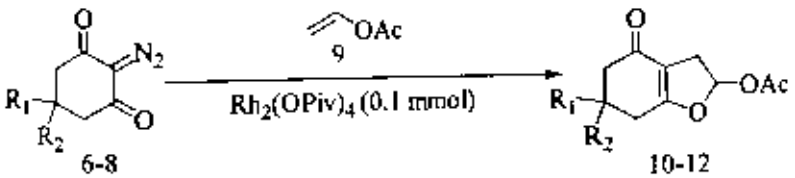
The IR spectrum (CCl_4) (Fig. 8b) of the compound **8** showed following characteristic bands: ν_{max} 2975.0 and 2958.0 cm^{-1} (str. -CH_3, and -CH_2), 2192.9 and 2129.3 cm^{-1} (C=N_2), 1641.3 cm^{-1} (str. - C=O).

The ^{1}H NMR spectrum (Fig. 8c) of this compound **8** illustrated a two protons double doublet at δ 2.83 (dd, 2H, J =8.26, 23.32 Hz) and 2.70 (dd, 2H, J = 8.26, 23.32 Hz) for methylene (-CH_2 -) group of C-4 and C-6, respectively, a one proton multiplet at δ 1.61 (m, 1H, C-5) and 1.20 (m, 1H, -CH(CH_3)$_2$) and a six protons doublet at δ 0.92 (d, 6H, J = 8.31 Hz) for indicating two methyl (2×-CH_3) groups.

The ^{13}C NMR spectrum (Fig. 8d) showed characteristic chemical shift at δ 201.49 (C=O), 201.31 (C=O), 155.35 (C=N_2), 40.61 and 40.38 designed for C-4 and C-6, 32.59 CH(CH_3) , 27.89 (C-5), 19.09, and 19.04 (2×CH_3). The ^{13}C NMR spectrum indicated the presence of nine carbons in the molecule corresponding to the molecular formula $C_9H_{12}N_2O_2$, thereby suggesting the formation of the compound **8**.

2.3. Synthesis of 4-oxo- 2,3,4,5,6,7-hexahydro-benzofuran-2-yl acetate derivatives 10-12:

The decomposition of 2-diazo-cyclohexane-1, 3-dione with vinyl ethyl ester using commercial metal mediated catalyst has been reported[80]. Several substituted of 4-oxo-2,3,4,5,6,7-hexahydro-benzofuran-2-yl acetate derivatives **10-12** were synthesized by the cyclization reaction of vinyl acetate with 2- diazo-cyclohexane-1, 3-dione **6-8** as shown in the scheme 3.

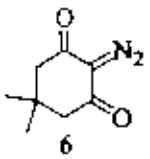
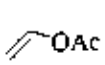
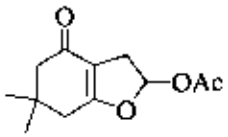
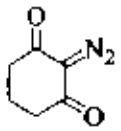
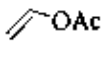
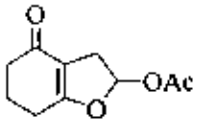
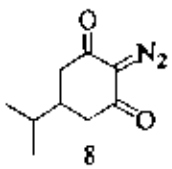
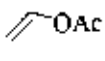
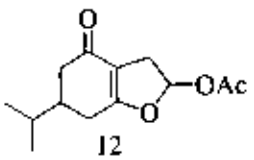


Where
6, 10. R_1=R_2 = $-CH_3$. $Rh_2(OPiv)_4$ = $Rh_2(OOCC(CH_3)_2CH_3)_4$
7, 11 R_1=R_2 = H
8, 12. R_1= H, R_2 = $-CH(CH_3)_2$

Scheme 3

Commercially available vinyl acetate 9 was selected as reaction material. Cyclization with 2-diazo-cyclohexane-1,3-dione derivatives **6-8** by $Rh_2(OPiv)_4$ catalyzed reaction at room temperature led to the desired products **10-12** as in the shown scheme 3. Reaction of entry 1 with 2-diazo-5, 5-dimethyl-cyclohexane-1, 3-dione gave product in the highest yield (66%) in the table 2.

Table 2: Synthesis of 4-oxo- 2,3,4,5,6,7-hexahydro-benzofuran-2-yl acetate 10-12:

Entry	2-Diazo-cyclohexane -1,3-dione derivatives	Vinyl acetate	Product	Yield (%)
1.	 6		 10	66
2.	 7		 11	42
3.	 8		 12	50

Catalyst: $Rh_2(OPiv)_4$ (1mol%), rt

Effect of catalyst, solvent and Temperature:

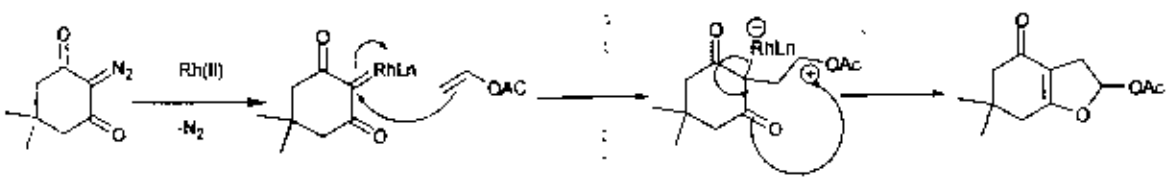
Effect of catalyst: There were used several common catalyst, such as; copper (I) iodide, bis-triphenyl Palladium **(II)** chloride and Rhodium pivalet in different portion to choose best catalyst, the best result obtained by using $Rh_2(OPiv)_4$ catalyst in vinyl acetate as a reaction material.

Effect of solvent: In order to get good yield for above reaction, several solvents were used, for example chloroform, methylene chloride. carbon tetrachloride, and without solvent, the good percentage of yield was obtained by neat reaction i.e. without solvent.

Temperature effect: For achieving highest percentage of product the reaction was carried out at several temperature such as, at room temperature, elevated temperature i.e. 40-50^{0}C and high temperature. At high temperature, the starting materials were decomposed and at an elevated temperature some unexpected products were appeared. So the suitable temperature was selected as room temperature.

Mechanism of the reactions for preparation of 4- oxo- 2,3,4,5,6,7-hexahydro-benzofuran-2-yl acetate:

Although the exact mechanism of the reaction is still not clear, it can be perceived that the reactions proceed on according to the scheme 4. From our observation it was clear that rhodium pivalet is a catalyst in the form of acid salt, so rhodium (II) cation is an acid catalyst. On the other hand diazo compound is a base. The initial step, the decomposition of diazo group is induced by the rhodium (II) catalyst. The corresponding compound is attacked by vinyl acetate to give cation intermediate. After leaving rhodium catalyst, cycloadduct is obtained by electro cyclic ring closure reaction. Ring closure of cycloadduct gives product **10.**



Scheme 4

2.3a. **Characterization of 6,6-dimethyl-4-oxo-2, 3,4,5,6,7-hexahydro-benzofuran-2-yl acetate 10:**

A colourless liquid product was obtained (yield 66%). The structure of compound **10** was assigned by spectral data. In the UV spectrum (Fig. 10a) of the compound **10** the value was found in the range of 253.70 and 239.15 nm.

The IR spectrum (Fig. 10b) showed absorption bands at ν_{max} 2962.5 and 2929.7 cm^{-1} (str. $-CH_3$, and $-CH_2$), 1768.6 cm^{-1} for ($O-COCH_3$) and 1645.2 cm^{-1} for the presences of ketone groups (-C=O), 1550.7 cm^{-1} for stretching of (-C=C-).

The ^1H NMR spectrum (Fig. 10c) exhibited a one proton double doublet at δ 6.72 (dd, 1H, J =7.51, 16.1 Hz.) for C-2, a three protons singlet at 3.95 (s, 3H) for (CH_3- CO-), a one proton double doublet at 3.06 (dd, 1H, J =7.51, 16.1 Hz) and δ 2.79 (dd, 1H, J =7.51, 16.1 Hz) in favor of $-CH_2-$ of C-3, a two hydrogens doublet at δ 2.35 (d, 2H, J = 11.24 Hz) and δ 2.25 (d, 2H, J = 7.08Hz) for the presence of ($-CH_2-$) of both C-5 and C-7, respectively and a chemical shift at δ 1.11 (s, 3H) and 1.07 (s, 3H) demonstrated Methyl groups ($-CH_3$) which attached to C-6.

The compound **10** also established by following characteristic ^{13}C NMR spectrum (Fig. 10d) : δ 197.89 (C=O), 171.34 (O-C=O), 162.82 (C-8), 105.62 (C-9), 92.24 (C-2), and δ 51.38, 41.13, 34.63, 27.89, 27.07, 17.61 and 16.17 designed for C-5, C-7, C-3, -$COCH_3$, 2×CH_3 and and C-6, correspondingly. So, the ^{13}C NMR spectrum indicated the presence of twelve carbons in the molecule corresponding to the molecular formula $C_{12}H_{16}O_4$, thereby suggesting the formation of compound **10.**

2.3b. **Characterization of 4-oxo-2, 3,4,5,6,7-hexahydro - benzofuran-2-yl acetate 11:** The colourless liquid was obtained (yield 42%). The structure of compound **11** was confirmed by UV, IR and NMR spectral data. The UV spectrum (Fig. 11a) indicated the absorption band at 260.75nm for keto groups.

The IR spectrum (CCl_4) (Fig. 11b) of this compound illustrated following characteristic absorption bands: ν_{max} 2999.7 and 2927.5 cm^{-1} (str. -CH_2), 1647.1 for (str. -C=O), 1558.7 cm^{-1} for stretching of (-C=C-).

The ^1H NMR spectrum (Fig. 11c) assigned the chemical shift for the determination of molecular structure of compound **11.** It is observed that a one proton multiplet at δ 6.50 (m, 1H) for -CH- of C-2, a three proton singlet at 3.85 (s, 3H) for methyl group of (CH_3-CO-), a one proton double doublet δ 2.95 (dd, 1H, J = 6.86, 14.69 Hz) and 2.72 (dd, 1H, J = 6.86, 14.69 Hz) in support of -CH- of C-3. a two protons triplet at 2.44 (t, 2H, J = 5.44 Hz) and 2.35 (t, 2H, J = 6.26 Hz) indicated methylene hydrogen of C- 5 and C-7 respectively and a two protons multiplet at δ 2.06 (m, 2H) pointed to the presence of methylene protons of (C-6).

Further the structure was confirmed by its ^{13}C NMR spectrum (Fig. 11d) which showed the chemical shift positions of δ 197.89 (C=O), 171.34 (-O-C=O). 163.89 (C-8), 106.65 (C-9), 92.34 (C-2) and 41.13, 34.63, 34.38, 17.61, and 16.17 for remaining carbon correspondingly. The displayed the presence of ten carbon atoms corresponding to its molecular formula $C_{10}H_{12}O_4$.

2.3c. Characterization of 6-isopropyl-4-oxo-2,3,4,5,6,7-hexahydro-benzofuran-2-yl acetate 12:

A colourless oily product was obtained (yield 50%). The structure of compound **12** was recognized from its spectral data. In UV spectrum (Fig. 12a) the value was found in the range of 261.75 nm.

The IR spectrum (CCl_4) (Fig. 12b) demonstrated following characteristic peaks: ν_{max} 2927.7 cm^{-1}(str.-CH_3 or -CH_2-), 1667.1 for (CH_3CO), 1646.6 cm^{-1} (str. C=O), 1548.7 cm^{-1} for stretching of (-C=C-).

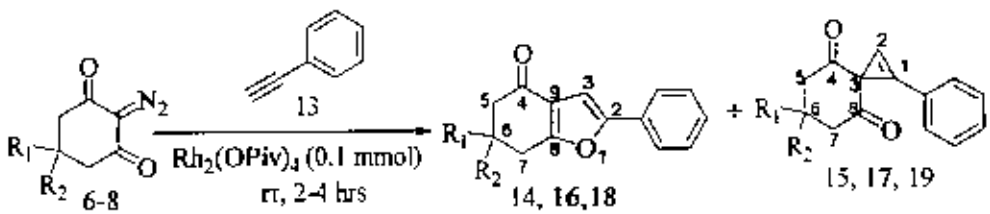
In the ^1H NMR spectrum (Fig. 12c) of this compound **12** the chemical shift was observed at δ 6.60 (m, 1H) for -CH- of C-2, 3.84 (s, 3H) for methyl group of (CH_3-CO-), δ 3.05 (dd, 1H, J = 6.68, 14.69 Hz) and 2.70 (dd, 1H, J = 6.68, 14.69 Hz) for -CH- of (C-3), δ 2.44 (d, 2H, J = 5.44 Hz) and δ 2.35 (d, 2H, J = 6.2 Hz) for two protons doublet of (C-5 & C-7), δ1.65 (m, 1H) and 1.21(m, 1H) for one hydrogen of C-6 and -$CH(CH_3)_2$, respectively and δ 0.99 (d, 6H, J=5.69 Hz) for six protons doublet of methyl (2×-CH_3) groups of Isopropyl.

The compound was further established from its ^{13}C NMR spectrum (Fig. 12d). The chemical shifts of this compound were showed following characteristic peak: δ 197.89 (C=O), 171.34 (-O-C=O), 162.82 (C-8), 105.62(C-9), 92.24 (C-2) and 48.38, 41.38, 37.94, 34.63, 33.89, 21.94, 21.89 and 16.17 for the remaining carbon atoms. The ^{13}C NMR spectrum indicated the presence of thirteen carbons in the molecule corresponding to the molecular formula $C_{13}H_{18}O_4$, thereby suggesting the formation of the compound **12**.

On the basis of complete analysis of the UV, IR, ^1H NMR and ^{13}C NMR spectra the structure of this compound was accorded as 6-isopropyl-4-oxo-2,3,4,5,6,7-hexahydro-benzofuran-2-yl acetate **12**:

2.4. Synthesis of 2-phenyl-6, 7- dihydro-5*H*-benzofuran-4-one 14,16,18 and 1-phenyl-spiro [2.5] oct-1-ene-4, 8-dione 15,17,19:

The decomposition of diazo compounds with terminal acetylene using commercial metal mediated catalyst has been reported[81]. During the preparation of 2-phenyl-6, 7- dihydro-5*H*-benzofuran-4-one, a by product was obtained unexpectedly. The second product 1-phenyl-spiro[2.5]oct-1-ene-4, 8-dione was obtained as major product when 2-diazo-cyclohexane-1,3-dione derivatives **6-8** were treated with phenyl acetylene at room temperature (Scheme 5).

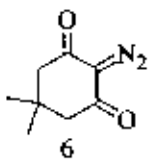
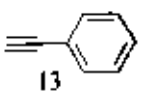
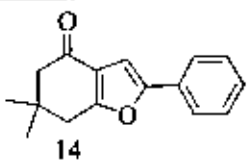
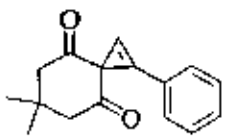
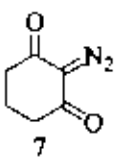
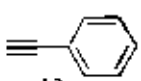
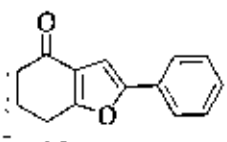
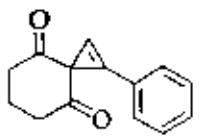
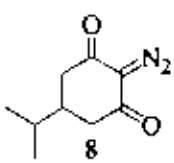
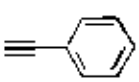
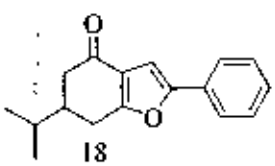
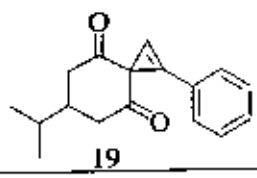


Where
6,14 & 15. R_1=R_2 = -CH_3,
7,16 & 17. R_1=R_2 = -H
8,18 & 19. R_1= H, R_2 = -$CH(CH_3)_2$

Scheme 5

Direct cyclization of 2-diazo -cyclohexane-1, 3-dione derivatives 6-8 with phenyl acetylene by metal mediated catalyzed reaction at room temperature led to the desired products (**14,16 18**) and by products (**15,17,19**). Several reactions of phenyl acetylene with a series of 2-diazo-cyclohexane-1,3-dione derivatives have been investigated to give corresponding 2-phenyl-6, 7- dihydro-5*H*-benzofuran-4-one and 1-phenyl-spiro[2.5]oct-1-ene-4, 8-dione derivatives are shown in table the table 3.

Table 3: Synthesis of 2-phenyl-6, 7- dihydro-5*H*-benzofuran-4-one 14,16,18 and 1-phenyl-spiro [2.5] oct-1-ene-4, 8-dione 15,17,18:

Entry	2-Diazo cyclo-hexane-1,3-dione	Phenyl acetylene	Product	Yield (%)	Product	Yield (%)
1.	 6	 13	 14	24.7	 15	62.5
2.	 7	 13	 16	23.36	 17	47.16
3.	 8	 13	 18	23.43	 19	59.05

$Rh_2(OPiv)_4$ (1Mol%)

To optimize product yields, several common solvents and metal mediated catalysts have been used as follows.

Effect of catalyst, solvent and Temperature:

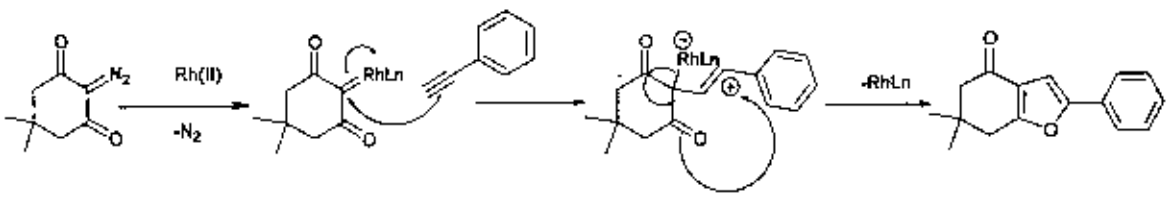
Effect of catalyst: There were used several common catalyst, such as; copper (I) iodide, bis-triphenyl palladium (II) chloride and rhodium pivalet in different portion to choose the best catalyst. The best result obtained by using $Rh_2(OPiv)_4$ catalyst in phenyl acetylene as a reaction material.

Effect of solvent: In order to get good yield for above reaction, several solvents were used, for example chloroform, methylene chloride, carbon tetrachloride, and without solvent. The good percentage of yield was obtained by neat reaction i.e. without solvent.

Temperature effect: For achieving highest percentage of product, the reaction was carried out at several temperature such as room temperature, elevated temperature i.e. 40-50^{0}C and high temperature. At high temperature, the starting materials were decompesed and at elevated temperature some unexpected products were appeared. So the best suitable temperature was selected as room temperature.

Mechanism of the reactions for preparation of 2-phenyl-6, 7- dihydro-5*H*-benzofuran-4-one 14,16,18:

The reaction proceeds smoothly in a short reaction time (2-3h) for terminal alkynes while alkenes were found to be comparatively low reactive than alkynes. The mechanism of this reaction is similar to synthesis of hexahydro-benzofuran-2-yl acetate reaction in the scheme 4. The loss of nitrogen is followed by the rhodium catalyst shift. It was described as shown in scheme 6. The corresponding compound is attacked by phenyl acetylene to give cation intermediate. The lost of rhodium cation is followed by the double bond shift to form expected electrocyclic ring close product[85].

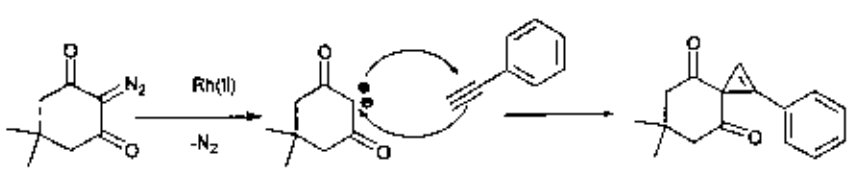


Scheme 6

Mechanism of the reactions for preparation of 1-phenyl-spiro [2.5] oct-1-ene-4, 8-dione 15,17,18:

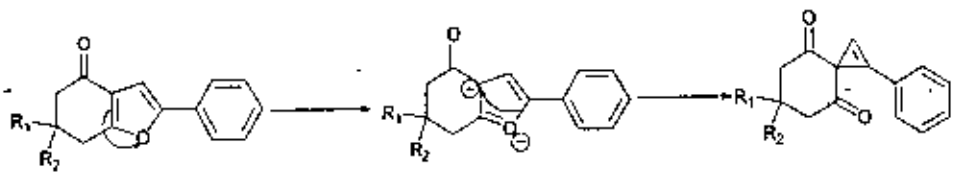
Although the exact mechanism of the reaction is still not clear, it is best described as shown in the Scheme 7a. We reasoned that placement of electron-withdrawing groups on the benzene ring of phenyl acetylene might decrease the nucleophilicity of the carbon-carbon double bond towards the intermediate electrophilic carbene. Using rhodium (II) catalyst selectivities did, in fact, increase the cyclopropene part.[82a]

The diazo compound first gives a carbene by expulsion of $Rh_2(OPiv)_4$. Intermediate is trapped by the double bond of alkylene group to give cyclopropene. Notable is the influence of the ligand ester group in the catalyst on enantiocontrol in cyclopropenation.



Scheme 7a

The other reporter explained the mechanism for the cyclopropenation in different way. It can be explained by the formation of cyclic product first and continued by the rearrangement of furan to form 3- member ring. The compound is stable as the by-product[82].



Scheme 7b

2.4a. **Characterization of 6,6-dimethyl-2-phenyl-6, 7-dihydro-5*H*-benzofuran-4-one 14:**

A yellow oily product was obtained (yield 24.7%). The structure of compound **14** was established by spectral data. In the UV spectrum (Fig. 14a) the λ_{max} value was found in the range of 257.15 nm for the absorption of phenyl and ketone group.

The IR spectrum (Fig. 14b) of the compound **14** has given an idea about the following characteristic picks: ν_{max} 3076.0 (str. Ar-H or C =CH), 2962.5 (str. -CH_3, and -CH_2), 1676.0(str.C=O), 1550.7 cm^{-1} for stretching of (-C=C-).

The ^1H NMR spectrum (Fig. 14c) exhibited the chemical shift for assigning the structure of compound **14.** It is observed that a two-proton doublet at δ 7.69 (d, 2H. J = 7.86 Hz) indicated of (Ar-H), 7.48 (t, 2H, J = 7.46 Hz) of (Ar-H), 7.30 (t, 1H. J = 7.26Hz) of (Ar-H), 5.38 (s, 1H) indicated one hydrogen of C-3, 2.76 (s, 2H, C-5) and δ 2.51(s, 2H, C-7) for C-5 & C-7 protons and the position of δ 0.99 (s, 6H) displayed methyl groups (2×-CH_3), which confirmed the structure of compound **14.**

2.4b. **Characterization of 6,6-dimethyl-1-phenyl-spiro[2.5]oct-1-ene-4,8-dione 15:**

Colourless crystal was collected (yield 62.5%). M.P.: 130-132^0 C. The structure of compound **15** was confirmed by spectral data. In the UV spectrum (Fig. 15a) the λ_{max} value was found in the range of 219.85, 270.45 and 283.55 nm which assigned the presence of benzene and ketone group.

The IR spectrum (Fig. 15b) revealed following characteristic absorption bands: ν_{max} 3099.4 (str. Ar-H or C =CH), 2958.6 (str. -CH_3, and -CH_2) and 1676.0 (str. - C=O).

The ^{1}H NMR spectrum (Fig. 15c) showed a two-protons doublet at δ 7.66(d, 2H, J = 7.86 Hz) for (Ar-H), a two protons triplet at δ 7.49(t, 2H, J = 7.88 Hz) for (Ar-H) and 7.29 (t, 1H, J = 7.48) for (Ar-H), a singlet spectrum at δ 6.88 (s, 1H) indicated one proton of C-2, a two protons singlet at 2.56 (s, 2H) and δ 2.55(s, 2H) in support of C-5 and C-7, respectively and the position of 0.99 (s, 6H) demonstrated methyl groups (2×-CH_3) which confirmed the formation of product **15**.

2.4c. **Characterization of 2-Phenyl-6, 7-dihydro-5*H*-benzofuran-4-one 16:**

A yellowish liquid product obtained (yield 23.36%).The structure of compound **16** was assigned by spectral data. In the UV spectrum (Fig. 16a) the λ_{max} value was found in the range of 258.45 and 275.85 nm.

The IR spectrum (CCl_4) (Fig. 16b) of this compound analyzed the absorption position of aromatic proton at ν_{max} 3099.4 (Ar-H or C =CH), stretching for methylene protons (-CH_2) at 2958.6 cm^{-1}, 1548.7 cm^{-1} for stretching of (-C=C-).

The ^{1}H NMR spectrum (Fig. 16c) showed the following characteristic chemical shift at δ 7.57 (d, 2H, J = 7.46 Hz), 7.36 (t, 2H, J = 7.82 Hz) and 7.29 (t, 1H, J = 7.37Hz) for (Ar-H), a singlet spectrum at δ 5.36 (s, 1H) indicated one hydrogen of C-2, a two proton triplet at the position of 2.99 (t, 2H, J = 6.26 Hz) and δ 2.43 (t, 2H, J = 6.8 Hz) for C-5 and C-7, respectively and the chemical shift position of δ 2.33 (m, 2H) for methylene (-CH_2-) protons of C-6. Complete analysis of the UV, IR, and ^{1}H NMR spectrum of this compound was agreement with the structure accorded to it as synthesis of 2-Phenyl-6, 7-dihydro-5*H*-benzofuran-4-one **16.**

2.4d. Characterization of 1-Phenyl-spiro [2.5] oct-1-ene-4, 8-dione 17:

Colourless solid compound was collected (yield 47.16%), M.P.: 120-122^{0}C. The structure of the compound **17** was justified by UV, IR and NMR spectral data. In the UV spectrum (Fig. 17a) of the compound showed the λ_{max} value in the range of 261nm for aromatic ring and keto group.

The IR spectrum (CCl_4) (Fig. 17b) of this product exhibited ν_{max} 3099.4 and 3053.1 cm^{-1} for aromatic protons (Ar-H or C =CH), 2945.1 cm^{-1} stretching for methylene protons (- CH_2) and 1651.0 cm^{-1} for ketone groups (- C=O).

The ^{1}H NMR spectrum(Fig. 17c) showed the chemical shift position of δ 7.77 (d, 2H, J = 7.51 Hz), δ 7.49 (t, 2H, J = 9.5 Hz) and δ 7.29 (t, 1H, J = 7.36 Hz) in favor of (Ar-H), 6.66 (s, 1H) informed only one hydrogen in cyclopropene ring (C-2). δ 2.95 (t, 2H, J = 6.26 Hz) and δ 2.53 (t, 2H, J = 6.15 Hz) indicated methylene protons of C-5H and C-7H respectively and δ 2.23 (m, 2H) for the presence of methylene (-CH_2-) protons that justified the structure of compound **17**.

2.4e. Characterization of 6-isopropyl-2-phenyl-6, 7-dihydro-5*H*-benzofuran-4-one 18:

A colourless liquid was obtained (yield 23.43%). The structure of compound **18** was assigned by spectroscopic data. In UV spectrum (Fig. 18a) the λ_{max} value was found in the range of 260.15 nm for keto group.

In the IR spectrum (CCl_4) (Fig. 18b) of the compound **18,** the absorption band of ν_{max} 30096.7 cm^{-1} indicated stretching of aromatic proton or double bond protons (Ar-H or C =CH), 2956.6 cm^{-1} for stretching of methylene protons (-CH_2). 1667.1 cm^{-1} stretching for the presences of ketone groups (- C=O).

It is observed by ^{1}H NMR spectrum (Fig. 18c) that a two-proton doublet at δ 7.88 (d, 2H, J = 7.51 Hz) of (Ar-H), δ 7.69 (t, 2H, J = 7.68 Hz) and δ 7.39 (t, 1H, J = 7.37 Hz) demonstrated 5 protons of the benzene ring, a singlet spectrum appeared at δ 5.28 (s, 1H, C-3H), δ 2.44 (d, 2H, J = 5.4 Hz) and δ 2.35 (d, 2H, J = 6.2 Hz) indicated methylene two hydrogen doublet of C-5 and C-7 respectively, a one hydrogen multiplet at δ 1.76 and

1.66 showed C-6 and –$CH(CH_3)_2$ and the peak of δ 1.07 (d, 6H, J = 8.72 Hz) demonstrated six protons doublet of methyl (2×-CH_3) groups which confirmed the structure of product **18**.

The structure of the compound further confirmed by its ^{13}C NMR spectrum (Fig. 18d) (100 MHz, $CDCl_3$). It was observed that the chemical shift at δ 192.89 (C=O), 167.82 (C-8), 165.82 (C-2), and 134.38, 130.79, 130.61, 130.38, 129.9 & 129.21 indicated for benzene protons, and 118.72 (C-9), 111.17 (C-3), 41.13 (C-5), 37.94 (C-6), 34.63 {$C(CH_3)_2$}, 33.89 (C-7), and 21.94 and 21.81 for 2×CH_3. So the ^{13}C NMR spectrum indicated the presence of seventeen carbon atoms in the molecule corresponding to the molecular formula $C_{17}H_{20}O_2$, thereby suggesting the formation of compound **18**.

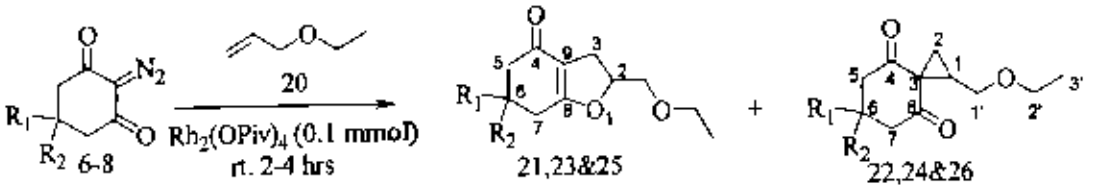
2.4f. Characterization of 6-Isopropyl-1-phenyl-spiro [2.5] oct-1-ene-4,8-dione 19:
White crystal was obtained (yield 59.05%), M. P.: 126-128^{0}C. The structure of compound **19** was interpreted by spectral data. In UV spectrum (Fig. 19a) the λ value was found in the range of 225.35and 299.55nm.

The IR spectrum (CCl_4) (Fig. 19b) of this compound assigned the following characteristic absorption peaks: ν_{max} 3099.4 cm^{-1} (str. Ar-H or C=CH), 2945.1 cm^{-1} for stretching of methylene protons (-CH_2), 1666.4 cm^{-1} informed the presences of ketone groups (- C=O) and there was no ester pick of carbon oxygen bond (-C-O).

The ^1H NMR spectrum (Fig. 19c) of this compound expressed following chemical shift at δ 7.66 (d, 2H, J = 7.86 Hz), δ 7.39 (t, 2H, J = 7.46 Hz) and δ 7.29 (t, 1H, J = 7.37) for (Ar-H) of the benzene ring, a singlet spectrum appeared at δ 7.10 indicated one hydrogen in cyclopropene ring of (C-2). δ 2.56 (d, 2H, J = 5.4 Hz) and 2.4 (d, 2H, J = 5.40Hz) indicated the presence of two protons doublet of C-5H and C-7H,respectively, a one hydrogen multiplet at the position of δ 1.81 (m, 1H) and 1.47(m, 1H) showed of chiral carbons of C-6H and –$CH(CH_3)_2$ and the peak at δ 1.23 (d, 6H, J = 8.72) revealed six protons doublet of methyl (-CH_3) groups. The spectra displayed the presence of eighteen hydrogens corresponding to its molecular formula $C_{17}H_{18}O_2$.

2.5. Synthesis of 2-ethoxymethyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-ones 21,23,25 and 1- ethoxymethyl-spiro[2.5]octane-4,8-dione 22,24,26 derivatives:

Decomposition of 3- diazo -chroman-4-one with vinyl ethyl ether using metal mediated catalyst has been reported[61]. In order to synthesis of furan derivatives, 2-diazo-cyclohexane-1,3-dione derivatives **6,7,8** were treated with allyl ethyl ether in presence of rhodium catalyst at room temperature to form desired products 2-ethoxymethyl-3.5,6,7-tetrahydro-2*H*-benzofuran-4-one **21,23,25**, but by products 1- ethoxymethyl-spiro[2.5]octane-4,8-dione **22,24,26** were produced as a major product as shown in the scheme 8 .

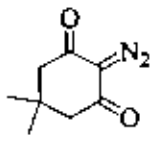
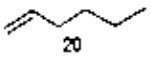
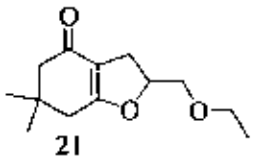
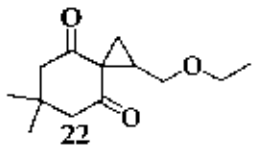
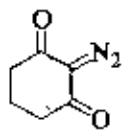
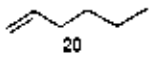
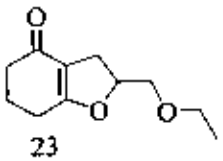
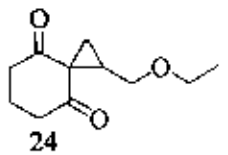
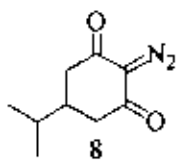
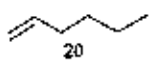
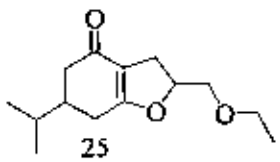
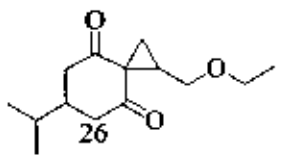


Where
6, 21 & 22. R_1=R_2 = CH_3,
7. 23 & 24. R_1=R_2 = H
8. 25 & 26. R_1= H, R_2 = -$CH(CH_3)_2$

Scheme 8

Several reactions of allyl ethyl ether with a series of 2-diazo-cyclohexane-1, 3-dione derivatives have been investigated to give corresponding 2-ethoxymethyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one **21,23,25** and by products 1- ethoxymethyl-spiro[2.5]octane-4,8-dione **22,24,26** derivatives as shown in the table 4.

Table 4: Synthesis of 2-ethoxymethyl-3,5,6,7-tetrahydro-2*H*- benzofuran-4-one 21,23,25 and 1- ethoxymethyl-spiro[2.5]octane-4,8-dione 22,24,26 derivatives:

Entry	2-Diazo cyclo-hexane-1,3-dione	Allyl ethyl ether	Product	Yield (%)	Product	Yield (%)
1.	 6	 20	 21	18	 22	78
2.	 7	 20	 23	18	 24	56
3.	 8	 20	 25	57	 26	37

$Rh_2(OPiv)_4$ (1Mol%)

To optimize product yields, several common solvents and metal mediated catalysts have been used as above. The rhodium (II) catalyzed decomposition of diazo diketones in the presence of terminal alkenes, the best results obtained for cyclopropanes and dihydrofurans. The isolation of which depends on the nature of the electron withdrawing group of the compounds. After estimation of yield percentage cyclopropanes were collected with highest yield (78%) which was more than three times of furans as shown in the table 4.

Effect of catalyst, solvent and temperature:

There were used several common catalyst, solvent and some different temperature to obtain the high yield, the best result obtained by using $Rh_2(OPiv)_4$ catalyst in allyl ethyl ether as reaction material and room temperature.

Reaction mechanism of 2-ethoxymethyl-3,5,6,7-tetrahydro-2H- benzofuran-4-one 21,23,25 and 22,24,26:

The mechanism of this reaction is similar to the synthesis of 2-phenyl-6. 7- dihydro-5*H*-benzofuran-4-one reaction form 2-diazo-cyclohexane-1,3-dione derivatives **6,7,8**. The loss of nitrogen is followed by the rhodium (II) catalyst shift and the following electrophilic addition by allyl ethyl ether lead to expected intermediate carbonyl compounds. The lost of rhodium cation is followed by the double bond shift to form expected electrocyclic ring closed product[85] as shown in the scheme 6. The cyclopropane can be explained by the formation of cyclic product first and continued by the rearrangement of furan to form 3- member ring. The compound is stable as the by-product[82] [82a] (scheme 7a and 7b).

2.5a. Characterization of 2-ethoxymethyl-6,6-dimethyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one 21:

Colourless liquid was yielded at 18%. The structure of compound **21** was assigned by spectral data. In UV spectrum (Fig.21a) the λ_{max} value was found in the range of 266.60 nm.

The IR spectrum (CCl_4) (Fig.21b) of the compound **21** exhibited following characteristic absorption bands at ν_{max} 2958.6 cm^{-1} (str. $-CH_3$, and $-CH_2$), 1676.0 cm^{-1} informed the presence of ketone groups (- C=O). 1550.7 cm^{-1} for stretching of (-C=C-).

The ^1H NMR spectrum (Fig. 21c) of this product showed that a one proton multiplet at δ 4.94(m, 1H, C-2H), a four protons multiplet at δ 3.56 -3.49 (m, 4H) identified ($-CH_2-$) which is attached to (-O-) of ether, a one proton triplet at δ 2.85 (t, 1H, J = 10.35 Hz) and 2.51 (m, 1H) for C-3H, a two protons singlet at δ 2.27 (s, 2H) and 2.19 (s. 2H) indicated for C-5H and C-7H respectively, δ 1.2 (t. 3H, J =7.02 Hz) informed the presence of three protons triplet of ($-CH_3$) which is attached to [$-CH_2$] and a six protons singlet at δ 1.06 (s, 6H) for two methyl groups ($2\times-CH_3$) which is attached to C-6. The ^1H NMR spectrum indicated the presence of twenty two hydrogen in the molecule corresponding to the molecular formula $C_{13}H_{22}O_3$, thereby suggesting the formation of the compound **21.**

2.5b.Characterization of 1-ethoxymethyl-6,6-dimethyl-spiro[2.5]octane-4,8-dione 22: A yellowish oily product was obtained (yield 78%).The structure of compound **22** was confirmed by UV, IR, and NMR data. In UV spectrum (Fig. 22a) the λ_{max} value was found in the range of 285.15, 255.20, 235.95 nm.

The IR spectrum (Fig. 22b) of the compound **22** showed the following identical absorption bands: ν_{max} 2962.5 cm^{-1} and 2929.7 cm^{-1} (str. -CH_3, and -CH_2). 1768.6 cm^{-1} and 1645.2 cm^{-1} informed the presences of ketone groups (- C=O).

The 1H NMR spectrum(Fig. 22c) of the compound **22** revealed that a one proton double doublet at δ 3.66 (dd, 1H, J = 4.52, 12.2 Hz) and multiplet at 3.43-3.18 (m. 1H) which is attached to C-1', a two protons multiplet at δ 3.25 (m, 2H, C-2') which attached to (-O-), a four protons multiplet at 2.67 (m, 4H) of (C-5 and C-7), a one proton multiplet at δ 2.29-2.19 (m, 1H) of C-1, a one proton double doublet at 1.96 (dd, 1H, J = 3.18. 8.91 Hz) and 1.87 (dd, 1H, J = 3.18, 8.91 Hz) contained -CH_2- of C-2, δ 1.09 (t, 3H, J = 7.0 Hz, C-3'H) indicated the presence of three protons triplet of terminal (-CH_3) and δ 1.15 and 1.02 (s, 3H) showed two methyl groups (2×-CH_3). On the basis of above spectral data, it was confirmed the formation of compound **22.**

2.5c. Characterization of 2-ethoxymethyl-3, 5, 6, 7-tetrahydro-2*H*-benzofuran-4-one 23: Colourless liquid compound was yielded at 18%. The structure of compound **23** was recognized by spectral data. The UV spectrum (Fig. 23a) of the compound was highlighted at absorption bands at 260.15. 238.20 nm.

The IR spectrum (CCl_4) (Fig. 23b) of this compound expressed following absorption band at ν_{max} 2958.6 cm^{-1}(str. -CH_2), 1647.1 cm^{-1} (str. - C=O), 1548.7 cm^{-1} for stretching of (-C=C-).

The ^{1}H NMR spectrum (Fig. 23c) of this compound explained a one proton multiplet at δ 4.98- 4.88 (m, 1H, C-2H), two protons multiplet at δ 3.59 – 3.45 (m, 2H) and 3.44 – 3.39 (m, 2H) for CH_2 which are attached to (-O-), a one proton multiplet at δ 2.89 – 2.80 (m,

1H) and 2.51 – 2.43 (m, 1H) for -CH_2- of C-3, δ 2.41- 2.39 (m, 2H), 2.34-2.29 (m, 2H) and 2.00 (t, 2H, J = 6.36 Hz) specified for methylene protons of (C-5, C-7 and C-6 H) in that order and δ 0.88 (t. 3H, J = 3.85Hz) indicated the presence of three protons triplet for terminal (-CH_3). The presence of sixteen hydrogen atoms was in good agreement with the molecular formula of $C_{11}H_{16}O_3$.

2.5d. Characterization of 1-ethoxymethyl-spiro [2.5] octane-4, 8-dione 24:

A reddish oily product was obtained 56% yield. The structure of compound **24** was interpreted by spectral data. In UV spectrum (Fig. 24a) the λ_{max} value was found in the range of 284.45, 258.55 nm.

The IR spectrum (CCl_4) (Fig. 24b) of the Compound **24** exhibited the absorption at ν_{max} 2962.5 and 2945.1 cm^{-1} for stretching of (-CH_3, and -CH_2), 1666.4 cm^{-1} for the presences of ketone groups stretching (- C=O).

The ^1H NMR spectrum (Fig. 24c) of this product **24** revealed that a one proton double doublet at δ 3.69 (dd, 1H, J = 4.54, 10.59 Hz, C-1') and multiplet at 3.43-3.33(m, 1H. C-1') for -CH_2- which is attached to (-O-), a one proton multiplet at 3.29-3.19 (m, 1H, C-2') and triplet at 3.13 (t, 1H, J = 10.36 Hz, C-2') indicated the presence of (-CH_2-) that attached to (-O-), a two proton multiplet at 2.89-2.65 (m, 2H) and 2.61-2.53 (m, 2H) and 2.21 (m, 2H) pointed toward (-CH_2-) for parent cyclohexane ring of (C-5 ,C-7 & C-6 respectively), 2.04-1.99 (m, 1H, C-1) demonstrated (-CH-) of C-1, a one proton double doublet at 1.97-1.94 (dd, 1H, J = 3.31, 8.85Hz) and 1.88 (dd, 1H, J = 3.31, 8.85Hz) point to (-CH_2-) of C-2, and a chemical shift of 1.07 (t, 3H, J = 7.0 Hz) triplet for methyl protons (-CH_3-).

Complete analysis of spectral data, the structure of this compound was accorded as 1-ethoxymethyl-spiro [2.5] octane-4, 8-dione **24**.

2.5e. Characterization of 2-ethoxymethyl-6-isopropyl-3, 5, 6, 7-tetrahydro-2*H*-benzofuran-4- one 25:

A liquid product was isolated at 57% yield. The structure of compound **25** was established by spectral data. In UV spectrum (Fig. 25a) the λ_{max} value was found in the range of 255.15 nm.

The IR spectrum (CCl_4) (Fig. 25b) of the compound **25** illustrated following characteristic band: ν_{max} 2958.6 cm^{-1} stretching of (-CH_2 and –CH_3). 1676.0 cm^{-1} strtching of keto groups (-C=O). 1550.7 cm^{-1} for stretching of (-C=C-).

The ^{1}H NMR spectrum (Fig. 25c) of this compound displayed following chemical shift at δ 5.0-4.9 (m, 1H) of C-2H. 3.58-3.49 (m, 4H) of -CH_2- which is attached to (-O-). δ 2.84(m, 1H) and 2.52 (m. 1H) for -CH_2- of C-3, δ 2.37(m, 2H) and 2.14(m, 2H) indicated methylene two hydrogen of C-5 & C-7 respectively, δ 2.04 (m, 1H) and 1.60 (m, 1H) showed tertiary hydrogen of C-6 and -$CH(CH_3)_2$, δ 1.20 (m, 3H) informed the presence of terminal three protons and u chemical shift at δ 0.91(d, 6H, J =5.44) carried out two methyl groups (2×-CH_3) of isopropyl.

2.5f. Characterization of 1-ethoxymethyl-6-isopropyl-spiro [2.5] octane-4,8-dione 26:

A yellowish oily product was obtained at 37% yield. The structure of compound **26** was interpreted by following spectral data. In UV spectrum (Fig. 26a), some different value was found in the range of λ_{max} 277.55 and 253.35nm.

The IR spectrum (CCl_4) (Fig. 26b) of the product **26** exhibited following characteristic band at ν_{max} 2962.5 and 2929.5 cm^{-1} (str. -CH_3, and -CH_2), 1764.1 and 1641.2 cm^{-1} (str.-C=O).

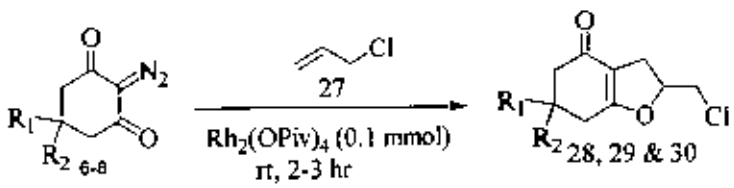
In the ^{1}H NMR spectrum (Fig. 26c) of this compound. a one proton double doublet at δ 3.66 (dd, 1H, J = 4.5, 8.4 Hz. C-1') and 3.25 (m, 1H, C-1') of CH_2 which is nearest of C-1. 3.15 (m, 1H, C-2') and 2.71 (m. 1H, C-2') of (-CH_2-) which is attached to (-O-), 2.30 (m, 2H) and 2.22 (m, 2H) of C-5 and C-7 respectively. 1.94 (m, 1H, C-2) for CH of C-2, 1.85

(m, 1H) and 1.62 (m, 1H) indicated -CH_2- of C-2, δ 1.50 (m, 1H, C-6) and 1.45(m, 1H, -$CH(CH_3)_2$) , δ 0.93 (d, 6H, J = 6.82 Hz) for two methyl groups (2×-CH_3) of isopropyl and 0.84 (t, 3H. J = 7.39 Hz) for terminal three protons (-CH_3).

On the basis of analysis of the UV, IR, ^{1}H NMR spectra, the structure of compound **26** was accorded as 1-ethoxymethyl-6-isopropyl-spiro [2.5] octane-4,8-dione.

2.6. Synthesis 2-chloromethyl-3, 5, 6, 7-tetrahydro-2*H*-benzofuran-4-one 28,29,30 derivatives:

Dihydrofurans prepared by treating diazo compound with electron-deficient olefin (allyl iodide) using metal mediated catalyst have been published[62]. To obtained 2-chloromethyl-3, 5, 6, 7-tetrahydro-2*H*-benzofuran-4-one **28,29,30** derivatives, 2-diazo-cyclohexane-1,3-dione derivatives **6,7,8** were treated with allyl chloride in presence of rhodium catalyst at room temperature shown in the scheme 9.

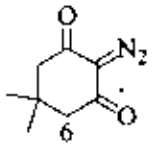
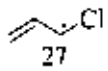
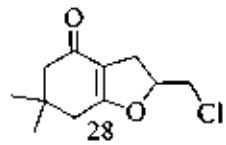
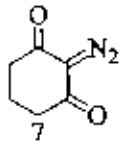
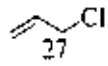
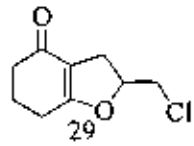
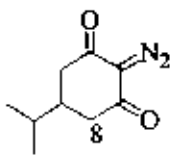
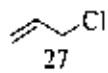
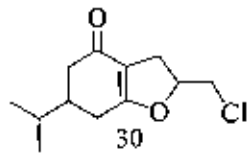


Where
6, 28. R_1=R_2 = -CH_3,
7, 29. R_1=R_2 = -H
8, 30. R_1= H, R_2 = -$CH(CH_3)_2$

Scheme 9

There were several reactions of allyl chloride with 2-diazo-cyclohexane-1, 3-dione derivatives **6-8** have been investigated to yield corresponding 2-chloromethyl-3, 5, 6, 7-tetrahydro-2*H*-benzofuran-4-one **28,29,30** derivatives are shown in the table 7. Reaction of eutry 1 with 2-diazo-5,5-dimethyl-cyclohexane-1,3-dione gave product **28** in the highest yield. 62.15%.

Table 7: Synthesis of 2-chloromethyl-3, 5, 6, 7-tetrahydro-2*H*-benzofuran-4-one 28,29,30 derivatives:

Entry	2-Diazo-cyclohexane-1,3-dione	Allyl chloride	Product	Yield (%)
1.	 6	 27	 28	62.16
2.	 7	 27	 29	33.67
3.	 8	 27	 30	37.0

Catalyst: $Rh_2(OPiv)_4$ (1mol%), Rt

To get highest percentage of product yield, several common solvents and metal mediated catalysts have been used as above. The rhodium (II) catalyzed decomposition of diazo diketones in the presence of allyl chloride, the best results carried out for dihydrofurans. The isolation of which depends on the nature of the electron withdrawing group of the compounds. After estimation of yield percentage dihydrofuran derivatives were collected highest yield percentage.

Effect of catalyst, solvent and temperature:

There were used several common catalyst. solvent and some different temperature to obtain the highest yield, the best result obtained by using $Rh_2(OPiv)_4$ catalyst in allyl chloride as a reaction material and room temperature.

Reaction mechanism of 2-chloromethyl-3, 5, 6, 7-tetrahydro-2*H*-benzofuran-4-one 28,29,30:

The mechanism of this reaction is similar to the synthesis of 2-phenyl-6, 7- dihydro-5*H*-benzofuran-4-one form 2-diazo-cyclohexane-1,3-dione derivatives **6,7,8**. The loss of nitrogen is followed by the rhodium (II) catalyst shift and the following electrofilic addition by allyl chloride lead to carbonyl compounds. The lost of rhodium cation is followed by the double bond shift to form furan ring closer product[85] scheme 6.

2.6a. Characterization of 2-chloromethyl-6,6-dimethyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one 28:

A yellowish liquid product **28** was yielded at 62.16%. The compound 28 was characterized the UV, IR and NMR spectra data. In UV spectrum (Fig. 28a) the λ_{max} value was found in the range of 276.30 nm.

In the IR spectrum (Fig. 28b) of the compound, the stretching of methyl protons at ν_{max} 2929.7 cm^{-1} and 2926.5 cm^{-1}, the stretching of ketone groups (- C=O) at 1645.2 cm^{-1}, 1550.7 cm^{-1} for stretching of (-C=C-).

The ^1H NMR spectrum (Fig. 28c) of this compound exhibited the following characteristic chemical shift at δ 5.02 (m,1H, C-2), δ 3.65 (m, 2H) for methylene two hydrogen multiplet of (-CH_2-Cl). δ 2.96 (m, 1H) and δ 2.72 (dd, J = 6.74, 13.0 Hz) contained -CH_2- of C-3, a two protons singlet at δ 2.29 (s, 2H) and 2.21 (s, 2H) of parent cyclohexane C-5 and C-7, respectively and δ 1.08 (s, 6H) six protons singlet of two methyl (2×-CH_3) groups. From the above spectra the structure of compound **28** was established as molecular formula of $C_{11}H_5ClO_2$.

2.6b. Characterization of 2-chloromethyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one 29:

A liquid product was obtained at 33.67% yield . The structure of compound **29** was highly regarded by spectral data. The UV spectrum (Fig.29a) of the compound showed following absorption band: λ_{max} 270.45 nm.

The IR spectrum (Fig. 29b) of this compound exhibited following characteristic peaks at ν_{max} 2927.7 and 2854.5 cm^{-1} for stretching of methyl protons. 1548.7 cm^{-1} for stretching of (-C=C-). .

The ^1H NMR spectrum (Fig. 29b) of the compound **29** showed a one proton multiplet at δ 5.00 (m, 1H) of (C-2H), δ 3.65 (m, 2H) for methylene two hydrogen of (-CH_2-Cl), a one proton double doublet at 2.95 (dd, 1H J = 6.86, 14.69 Hz) and 2.70 (dd, 1H, J = 6.86,

14.69 Hz) for -CH_2- of (C-3), a two protons multiplet at δ 2.45 (t, 2H, J = 6.26 Hz C-5) and triplet at 2.33 (t, 2H, J = 5.44 Hz) and two protons multiplet at 2.04 (m, 2H) for -CH_2- of parent cyclohexane of C-5, C-6, C-7, respectively. The ^{1}H NMR spectrums indicated the presence of eleven hydrogen atoms in the molecule corresponding to the molecular formula $C_9H_{11}ClO_2$.

2.6c. Characterization of 2-chloromethyl-6-isopropyl-3, 5, 6, 7-tetrahydro-2*H*-benzofuran-4-one 30:

A colourless liquid was produced at 37% yield. In UV spectrum (Fig. 30a) of the compound, the λ_{max} value was found in the range of 270.65 nm.

The IR spectrum (Fig.30b) showed following peaks: ν_{max} 2952.8 and 2929.7 cm^{-1} (str. -CH_3, and -CH_2), 1647.1 cm^{-1} (str. - C=O), 1548.7cm^{-1} for stretching of (-C=C-).

In the ^{1}H NMR spectrum (Fig.30c) of this compound, a one proton multiplet at the position of δ_H 5.0-4.9 (m, 1H, C-2). 3.58-3.49 (m, 2H) indicated methylene two hydrogen multiplet of (-CH_2-Cl), a proton double doublet at 2.96 (dd, 1H,J = 3.18, 8.91 Hz, C-3) and 2.84 (dd, 1H, J = 3.18. 8.91 Hz, C-3), a two protons doublet at δ 2.37 (d, 2H, J = 16.1 Hz, C-5) and 2.14 (d, 2H, J = 15.48 Hz, C-7) contained -CH_2- of parent cyclohexane, a one proton multiplet at 1.94 (m, 1H, C-6) and 1.60 (m, 1H, -$CH(CH_3)_2$) and a six protons doublet at δ 0.91 (d, 6H, J =5.44 Hz) indicated two methyl (2×-CH_3) groups.

On the basis of analysis of three spectral data, the compound was in complete agreement with the structure of accorded to it as 2-chloromethyl-6-isopropyl-3, 5, 6, 7-tetrahydro-2*H*-benzofuran-4-one **30.**

Discussions:

Table 8: Distinction among some diazo compounds:

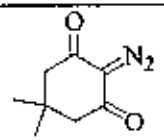
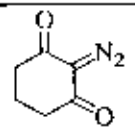
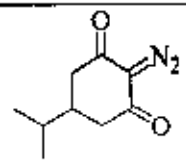
Comp. No.	Structure	UV(nm) λ_{max}	IR spectrum in ν_{max} cm^{-1}	1H NMR(δ_H)
6		277.30, 240.80	2189.1 (diazo, C=N_2), 2144.7(diazo, C=N_2), 1633.6 (C=O).	δ_H 2.42 (s, 4H, C-4 & C-6 H_2) & δ 1.02 (s, 6H, 2×-CH_3).
7		280.35, 237.83	2192.9(diazo, C=N_2), 2129.3 (diazo, C=N_2), 1645.2 (C=O).	δ_H 2.97 (t, 2H, J= 6.26, C-4H), 2.53 (t, 2H, J =6.15, C-6H) & 2.23 (m, 2H, C-5H)
8		276.53, 235.85	2192.9 (diazo, C=N_2), 2129.3 (diazo, C=N_2), 1641.3 (C=O).	δ_H 2.83, (dd, 2H, J =8.26, 23.32 Hz, C-4), δ 2.70 (dd, 2H, J = 8.26, 23.32 Hz, C-6), δ 1.61(m, 1H, C-5), δ 1.20 {m, 1H, -CH(CH_3)$_2$} & δ 0.92 (d, 6H, -CH_3, J = 8.31Hz, 2×-CH_3).

Table 9: Distinction among some spectral data of 4-oxo- 2,3,4,5,6,7-hexahydro-benzofuran-2-yl acetate derivatives 10-12:

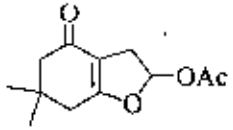
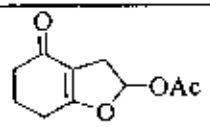
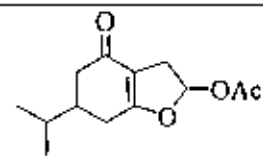
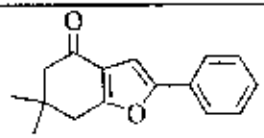
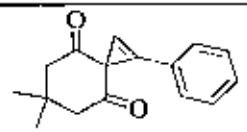
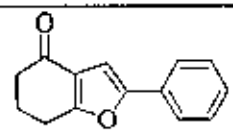
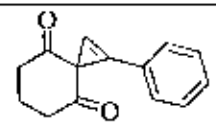
Comp. No.	Structure	UV(nm) λ_{max}	IR spectrum in ν_{max} cm^{-1}	1H NMR(δ_H)
10		253.70,	2962.5, 1768.6, 1645.2, 1550.7 (C=C) cm^{-1}	δ_H 6.72 (dd, 1H, J = 7.51, 16.1 Hz, C-2), 3.95 (s, 3H, $OCOCH_3$), 3.06 (dd, 1H, J = 7.51, 16.1 Hz, C-3), δ 2.79 (dd, 1H, J =7.51, 16.1 Hz, C-3), δ 2.35 (d, 2H, J = 11.24 Hz, C-5), δ 2.25 (d, 2H, J = 7.08, C-7), δ 1.11 (s, 3H, $-CH_3$) & 1.07 (s, 3H, $-CH_3$).
11		260.75	2957.8, 1646.4, 1650.5, 1558.7 (C=C) cm^{-1}	δ_H 6.50 (m, 1H, C-2), 3.85 (s, 3H, $-OCOCH_3$), 2.95(dd, 1H, J = 6.86, 14.69 Hz, C-3), 2.72 (dd, 1H, J = 6.86, 14.69 Hz, C-3), 2.44 (t, 2H, J = 5.44 Hz, C-5), 2.35 (t, 2H, J = 6.26 Hz, C-7) & 2.06 (m, 2H, C-6).
12		261.75,	2927.7, 1647.1, 1548.7 (C=C) cm^{-1}	δ_H 6.60 (m, 1H, C-2), 3.84 (s, 3H, $-OCOCH_3$), 2.95 (dd, 1H, J = 6.68, 14.69 Hz, C-3), 2.70 (dd, 1H, J = 6.68, 14.69 Hz, C-3), 2.44 (d, 2H, J = 5.44Hz, C-5), 2.35 (d, 2H, J = 6.20Hz, C-7), 1.65 (m, 1H, C-6), 1.21 {m, 1H, $CH(CH_3)_2$} and 0.99 (d, 6H, J=5.69Hz, $2\times CH_3$).

Table 10: Distinction among some spectral data of 2-phenyl-6,7-dihydro-5*H*-benzofuran-4-one derivatives 14,16,18 and 2-phenyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one derivatives 15,17,19:

Comp. No.	Structure	UV(nm) λ_{max}	IR spectrum in ν_{max} cm^{-1}	1H NMR(δ_H)
14		257.15, 220.65	3076.0, 2962.5, 1676.0 (C=O), 1550.7(C=C) cm^{-1}.	δ_H 7.69 (d, 2H, J = 7.86 Hz, ArH), 7.48 (t, 2H, J = 7.46Hz, ArH), 7.30 (t, 1H, J = 7.26, ArH), 5.38 (s, 1H, C-3), 2.76 (s, 2H, C-5), 2.51 (s, 2H, C-7) & 0.99 (s, 6H, 2×CH_3).
15		283.55, 270.4, 219.85	3099.4, 2958.6, 1676.0 cm^{-1}.	δ_H 7.76 (d, 2H, J = 7.86 Hz, ArH), 7.49 (t, 2H, J = 7.88 Hz, ArH), 7.29 (t, 1H, J = 7.26 Hz, ArH), 6.88 (s, 1H, C-3), 2.56 (s, 2H, C-5), 2.55 (s, 2H, C-7), and 0.99 (s, 6H, 2×CH_3).
16		275.85, 258.4, 220.85	3099.4, 2958.6, 1678.7 (C=O), 1548.7 (C=C) cm^{-1}.	δ_H 7.57 (d, 2H, J = 7.46 Hz, ArH), 7.36 (t, 2H, J =7.82 Hz, ArH), 7.29 (m. 1H, ArH), 5.36 (s, 1H, C-3), 2.99 (t, 2H, J = 6.26 Hz, C-5), 2.43 (t, 2H, J = 6.8 Hz, C-7) & 2.33(m, 2H, C-6).
17		296.55, 260.3, 223.45	3099.4, 3053.1, 2945.1, 1671.0 cm^{-1}	δ_H 7.77 (d, J = 5.63 Hz, ArH), 7.49 (t, 2H, J = 5.86 Hz, ArH), 7.29 (m, 1H, ArH), 6.66 (s, 1H, C-3H), 2.95 (t, 2H, J = 4.69 Hz, C-5H), 2.53 (t, 2H, J = 5.10 Hz, C-7H) & 2.23 (m, 2H, C-6H).

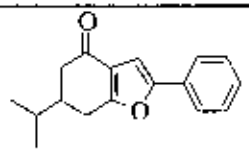
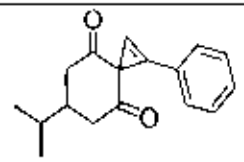
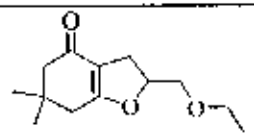
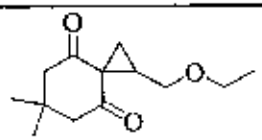
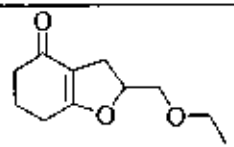
18		260.3, 223.45	30096.7, 2956.6. 1667.1, 1546.7 (C=C) cm^{-1}.	δ_H 7.88 (d. 2H, J = 7.51 Hz, C-ArH), 7.69 (t, 2H, J = 7.82 Hz, ArH), 7.39 (m, 1H, ArH), 5.28 (s, 1H, C-3H), 2.44 (d, 2H, J = 5.4 Hz, C-5H), 2.35 (d, 2H, J = 6.2Hz, C-7H), 1.76 (m, 1H, C-6H), 1.66 (m, 1 H, $-CH(CH_3)_2$) and 1.07 (d, 6H, J = 8.72Hz, $2\times CH_3$).
19		260.15, 220.95	3099.4, 2945.1, 1666.4 cm^{-1}	δ_H 7.66 (d, 2H, J = 7.51 Hz, ArH), 7.39 (t, 2H, J = 7.46 Hz, ArH), 7.29 (t, 1H, J = 7.37Hz, ArH), 7.10 (s, 1H, C-3H), δ 2.56 (d, 2H, J = 5.4Hz, C-5H), 2.4 (d, 2H, J = 5.4 Hz, C-7H), 1.81 (m, 1H, C-6H), 1.47 (m, 1 H, $-CH(CH_3)_2$) and 1.23 (d, 6H, J = 8.72Hz, $2\times CH_3$).

Table 11: Distinction among some spectral data of 2-ethoxymethyl-hexahydro-benzofuran-4-one derivatives 21, 23, 25 and 1-Ethoxymethyl-spiro [2.5] octane-4, 8-dione 22, 24, 26:

Comp. No.	Structure	UV(nm) λ_{max}	IR spectrum in ν_{max} cm^{-1}	1H NMR(δ_H)
21		266.60	1647.8, 1550.7 (C=C) cm^{-1}.	): δ_H 4.94 (m, 1H, C-2), 3.56 -3.49 (m, 4H, $-CH_2OCH_2-$), 2.85 (m, 1H, C-3), 2.51 (m, 1H, C-3), 2.27 (s, 2H, C-5), 2.19 (s, 2H, C-7), 1.2 (t, 3H, J = 7.02 Hz, $-CH_3$) & 1.06 (s, 6H, 2×$-CH_3$).
22		285.15	1768.6, 1645.2 cm^{-1}.	δ_H 3.68 (dd, 1H, J = 4.52, 12.2 Hz, -C-1'), 3.65(m, 1H, C-1'), 3.27 (m, 2H, C-2'), 2.67-2.43 (m, 4H, C-5 &C-7), 2.29-2.19 (m, 1H, C-1), 1.96 (dd, 1H, J = 3.18, 8.91 Hz, C-2), 1.87 (dd, 1H, J = 3.18, 8.91 Hz, C-2), 1.15 (s, 3H, C-3'), 1.09 (t, 3H, J = 7.0 Hz, $-CH_3$) & 1.02 (s, 3H, $-CH_3$).
23		260.15	1647.1, 1548.7 (C=C) cm^{-1}.	δ_H 4.98- 4.88 (m, 1H, C-2), 3.59 – 3.45 (m, 2H, $-CH_2O-$), 3.44- 3.39 (m, 2H, $-OCH_2-$), 2.89-2.80 (m, 1H, C-3), 2.51 – 2.43 (m, 1H, C-3), 2.41- 2.39 (m, 2H, C-5), 2.34-2.29 (m, 2H, C-7), 2.00 (t, 2H, J = 6.36 Hz, C-6), 0.88 (t, 3H, J = 3.85Hz, CH_3).

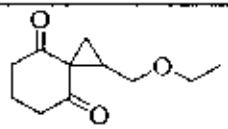
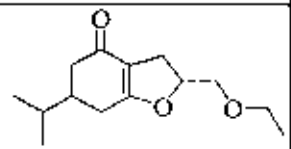
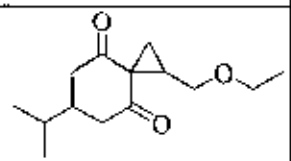
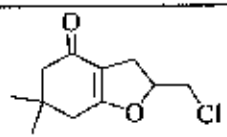
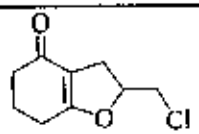
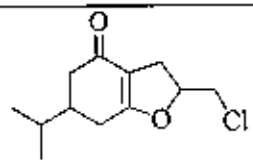
24		284.45	1666.4, 1655.5 cm^{-1}	δ_H 3.69 (dd, 1H, J = 4.54, 10.59 Hz, C-1'), 3.43-3.33 (m, 1H, C-1'), 3.29-3.19 (m, 1H, C-2'), 3.13 (t, 1H, J = 10.36 Hz, C-2'), 2.89-2.65 (m, 2H, C-5), 2.61-2.53 (m, 2H, C-7), 2.21 (m, 2H, C-6), 2.04-1.99 (m, 1H, C-1), 1.97-1.94 (dd, 1H, J = 3.31, 8.85 Hz, C-2), 1.88 (dd, 1H, J = 3.31, 8.85 Hz, C-2) & 1.07 (t, 3H, J = 7.0 Hz, C-3').
25		255.15,	1676.0, 1550.7 (C=C) cm^{-1}	δ_H 5.0-4.9 (m, 1H, C-2), 3.58-3.49 (m, 4H, $-CH_2OCH_2-$), 2.84 (m, 1H, C-3), 2.52 - 2.37 (m, 1H, C-3), 2.37 (m, 2H, C-5), 2.14 (m, 2H, C-7), 2.04 (m, 1H, C-6), 1.60 (m, 1H, $-CH(CH_3)_2$), 1.20 (m, 3H, $-CH_3$) & 0.91 (d, 6H, J =5.44 Hz, 2 ×$-CH_3$).
26		277.55,	1764.1, 1641.2 cm^{-1}.	δ_H 3.66 (dd, 1H, J = 4.5, 8.4 Hz, C-1'), 3.25 (m, 1H, C-1'), 3.15 (m, 1H, C-2'), 2.71 (m, 1H, C-2'), 2.30 (m, 2H, C-5), 2.22 (m, 2H, C-7), 1.94 (m, 1H, C-1), 1.85 (m, 1H, C-2), 1.62 (m, 1H, C-2),1.50 (m, 1H, C-6), 1.45 (m, 1H, $-CH(CH_3)_2$), 0.93 (d, 6H, J = 6.82 Hz, 2 ×$-CH_3$) & 0.84 (t, 3H, J = 7.39 Hz, C-3').

Table 12: Distinction among some spectral data of 2-chloromethyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one 28,29&30:

Comp. No.	Structure	UV(nm) λ_{max}	IR spectrum in ν_{max} cm^{-1}	1H NMR(δ_H)
28		276.30,	1645.2, 1550.7cm^{-1}.	δ_H 5.02 (m, 1H, C-2), 3.65 (m, 2H, -CH_2-Cl), 2.96 (m, 1H, C-3), 2.72 (dd, 1H, J = 6.74, 13.0 Hz, C-3), 2.29 (s, 2H, C-5), 2.21 (s, 2H, C-7) and 1.08 (s, 6H, 2 ×-CH_3).
29		270.45,	1648.6, 1548.7cm^{-1}.	δ_H 5.00 (m, 1H, C-2H), 3.65 (m, 2H, -CH_2-Cl), 2.90 (dd, 1H J = 6.86, 14.69 Hz, C-3), 2.70 (dd, 1H, J = 6.86, 14.69 Hz, C-3), 2.45 (t, 2H, J = 6.26 Hz C-5), 2.33 (t, 2H, J = 5.44Hz, C-7) & 2.04 (m, 2H, C-6).
30		270.65,	1647.1, 1548.7cm^{-1}.	δ_H 5.0-4.9 (m, 1H, C-2), 3.58-3.49 (m, 2H, -CH_2Cl), 2.96 (dd, 1H,J = 3.18, 8.91 Hz, C-3), 2.84 (dd, 1H, J = 3.18, 8.91 Hz, C-3), 2.37 (d, 2H, J = 16.1 Hz, C-5), 2.14 (d, 2H, J = 15.48 Hz, C-7), 1.94 (m, 1H, C-6), 1.60 (m, 1H, -$CH(CH_3)_2$), & 0.91 (d, 6H, J =5.44 Hz, 2 ×-CH_3)

Chapter-3

Experimental References and Spectra

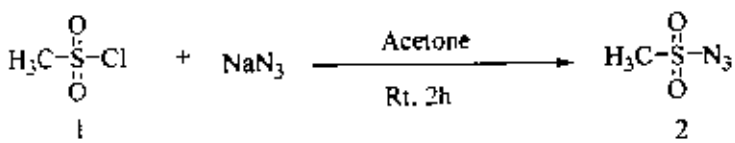
EXPERIMENTAL

3.1. Chemical reagents and experimental instruments:

All commercial reagents were purchased from E. Merck (Germany) and Fluka(Switzerland) and were used without further purification. Thin layer chromatography (TLC) plate made by Merck silica gel coated was used and visualized by UV lamp (254-365nm). Column chromatography was used for the separation by Merck Silica gel (60-120) mesh. Infrared (IR) spectra were obtained in cm^{-1} and recorded by SHIMADZU FTIR Spectrometer as KBr pellet or solution of CCl_4. UV spectra were recorded in dry EtOH with Shimatzu visible spectrophotometer and ^{1}H-NMR spectra were recorded by Bruker Model DPX 400 MHz and ARX 300 MHz spectrometer in $CDCl_3$ using 7.24 ppm as the solvent chemical shift.

3.2. Synthesis of methanesulfonyl azide 2:

The solution of methanesulfonyl chloride (100g. 11.45mmol) and acetone (100ml) in 250 ml two-neck round-bottomed flask was stirred at room temperature. Then equivalent ratio (1:1) of sodium azide (7.44g, 11.45mmol) was added gradually at 8 times (every 5 minutes break after putting sufficient ratio). After stirring for 1.30-2.0 hr. checking the white drops of bubble completely appeared. Then the reaction was stopped and filtered the solvent and the filtrate was collected. The solvent was removed properly by using under reduced pressure to obtain the crude product. Finally the crude product was washed with ether and dried under reduced pressnre to obtain a low melting colourless solid. The compound 2 was 120g (yield 99%).



Scheme 1

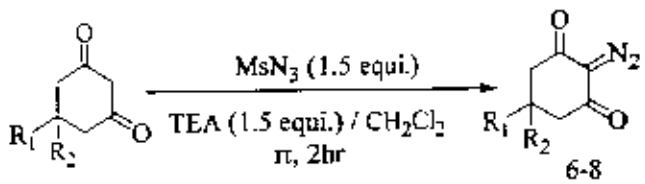
M.F.: $CH_3N_3O_2S$

Mol. Wt.: 121.12

IR Spectrum (CCl_4): ν_{max} 3315.4, 3014.5, 2931.6, 2304.8, 2088.8, 1708.8, 1508.2, 1095.5, 948.9 and 713.6 cm^{-1}.

3.3. General procedure for synthesis of 2-diazo- cyclohexane-1, 3-dione 6 -8:

2-Diazo-cyclohexane-1, 3-dione derivatives **6-8** were prepared by the diazo transfer reaction of the corresponding starting material with mesyl azide according to Taber's method[79]. A mixture of cyclohexane-1, 3-dione derivatives **3-5** (44.6mmol) and methylene chloride (30 ml) was taken in 250 ml two-neck round-bottom flask and was stirred at room temperature. Mesyl azide of 1.5 equivalent ratio (66.9 mmol) and equal molar of triethylamine (66.9 mmol) were added. After stirring for 1.30-2.0 hr, the reaction was monitored by TLC (n-hexane: ethyl acetate 1:1 v/v R_f = .5). Then the reaction was stopped by adding 1(N) hydrochloric acid and water and stirred for 30 minutes and the reaction mixture was washed with distilled water and $NaHCO_3$ solution and extracted by dichloromethane (3x100ml) and the combined organic layer was dried by magnesium sulphate and was filtered. Finally the solvent was removed properly under reduced pressure to obtain solid yellowish crude product **6-8.** The product was then purified by column chromatography on silica gel using hexane ethyl acetate (3:1) to give pure product. The solid product was dried by highly-reduced pressure then it was chilled. The product was yielded 90-99%, M.P. 44 - 69 ^{0}C. The formations of compounds 6-8 were confirmed by analysis of their UV, IR and ^{1}H NMR spectra.



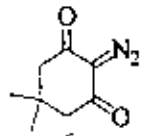
Where

3, 6. R_1 =R_2 = -CH_3
4, 7. R_1 =R_2 = H
5, 8. R_1 =H, R_2 = -CH(CH_3)

Scheme 2

3.3a. 2-Diazo- 5,5-dimethyl -cyclohexane-1, 3-dione 6:

A mixture of 5, 5-dimethyl cyclohexane-1, 3-dione **3** (5g, 44.6mmol), methylene chloride (30 ml) 1.5 equivalent ratio (7.1g, 66.9 mmol) and equal molar of triethyl amine (6.76g, 66.9 mmol) was stirred for 1.30-2.0 hrs to give product **6.** A yellowish solid was obtained 5.8g. (yield 99%), M.P: 68 - 69 ^{0}C.



6

M.F.: $C_8H_{10}N_2O_2$

UV (EtOH): λ_{max} 277.30, 240.80 nm.

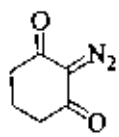
IR spectrum (CCl_4): ν_{max} 2962.5, 2889.2, 2189.1 (diazo, C=N_2), 2144.7 (diazo, C=N_2), 1633.6 (C=O), 1465.8, 1305.7, 1047.3, 1016.4 and 624.9 cm^{-1}.

^{1}H NMR spectrum: (400 MHz, $CDCl_3$):δ_H 2.42 (s, 4H, C-4 & C-6) & δ 1.02 (s, 6H, 2×-CH_3).

^{13}C NMR spectrum: (100 MHz, $CDCl_3$): δ 201.79 (C=O), 201.61 (C=O), 155.65(C-2), 52.61, 52.38, 25.59, 25.34 and 15.13(C-5).

3.3b. 2-Diazo-cyclohexane-1, 3-dione 7:

Reaction of cyclohexane-1, 3-dione (1.12g, 10.0 mmol), mesyl azide (1.59g, 15 mmol) and triethyl amine (1.51g, 15 mmol) in dichloromethane (10 ml) afforded **7** (1.31g, 95%) as a pale yellow solid, M.P. 44-45^0 C. The compound is very unstable in normal temperature. So it was preserved in deep fridge.



7

M. F.: $C_6H_6N_2O_2$

UV (EtOH): λ_{max} 280.35, 237.83 nm.

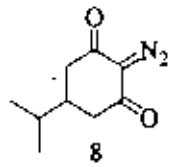
IR spectrum (CCl_4): ν_{max} 2958.6, 2933.9, 2192.9 (diazo, C=N_2), 2129.3 (diazo, C=N_2), 1645.2 (C=O), 1373.2, 1315.4, 1292.2, 1236.3, 1199.6, 1168.8, 997.1, 964.3, 725.2 and 570.0 cm^{-1}.

^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ_H 2.97 (t, 2H, J= 6.26, C-4), 2.53 (t, 2H, J =6.15, C-6) & 2.23 (m, 2H, C-5).

^{13}C NMR spectrum: (100 MHz, $CDCl_3$): δ 197.89 (C=O), 197.07 (C=O), 156.6 (C-2), 38.63, 38.38 and 15.13 (C-5).

3.3c. 2-Diazo-5-isopropyl-cyclohexane-1, 3-dione 8:

The formation of 2-diazo-5-isopropyl-cyclohexane-1, 3-dione **8** generated from the reaction of 5-isopropyl-cyclohexane-1,3-dione (1.54g. 10 mmol) with mesyl azide (1.59g, 15 mmol) and triethyl amine (1.515g, 15 mmol) in dichloromethane (10 ml). The yield was a light white solid 1.728g (yield 96%). M. P.: 57-59^0 C.



8

M. F.: $C_9H_{12}N_2O_2$

UV (EtOH): λ_{max} 276.53, 235.85 nm.

IR spectrum (CCl_4): ν_{max} 2975.0, 2958.0, 2935.5, 2895.0, 2192.9 (diazo, C=N_2), 2129.3 (diazo, C=N_2), 1641.3 (C=O), 1456.2, 1326.9, 997.1, 968.2, 721.3, 565.1 and 507.2 cm^{-1}.

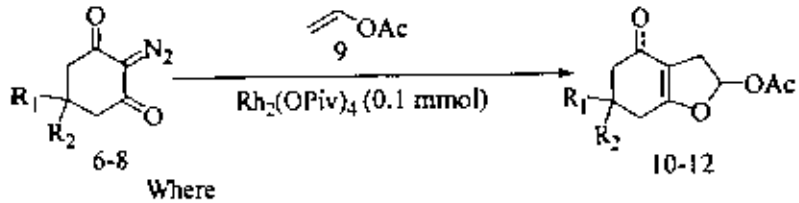
^{1}H NMR spectrum: (400 MHz, $CDCl_3$): δ_H 2.83, (dd, 2H, J =8.26, 23.32 Hz, C-4), δ 2.70 (dd, 2H, J = 8.26, 23.32 Hz, C-6), δ 1.61(m, 1H, C-5). δ 1.20 {m, 1H, -CH(CH_3)$_2$} & δ 0.92 (d, 6H, -CH_3, J = 8.31Hz. 2×-CH_3).

^{13}C NMR spectrum: (100 MHz, $CDCl_3$): 201.49 (C=O) and 201.31 (C=O), 155.35, 40.61, 40.38, 32.59, 27.89. 19.09, and 19.04.

3.4. General procedure for synthesis of 4-oxo- 2,3,4,5,6,7-hexahydro-benzofuran-2-yl acetate derivatives 10-12:

General Procedure

A mixture of 2-diazo-cyclohexane-1, 3-dione derivatives **6-8** (1 mmol) and vinyl acetate (10 mmol) was taken in the 100 ml two-neck round-bottom flask. Rhodium pivalate (0.1mmol) was added to the mixture and was stirred under nitrogen atmosphere for 2-3 hours at room temperature. The reaction was monitored by TLC, the solvent was removed under reduced pressure to obtain the crude product and then crude product was purified by column chromatography (n-Hexane-EtOAc) on silica gel to give corresponding substituted desired product and minor by product which was not isolated. Pure product was analyzed by IR and ^{1}H NMR.



Where

6, 10. R_1=R_2 = -CH_3, $Rh_2(OPiv)_4 = Rh_2(OOCC(CH_3)_2CH_3)_4$

7, 11. R_1=R_2 = H

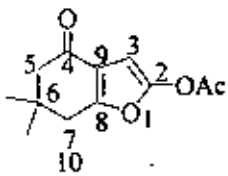
8, 12. R_1= H, R_2 = -$CH(CH_3)_2$

Scheme 3

The above reactions were carried out by several catalyst and solvents in different conditions.

3.4a. 6,6-Dimethyl-4-oxo-2, 3,4,5,6,7-hexahydro-benzofuran-2-yl acetate 10:

The reaction of vinyl acetate (3ml) with 2-diazo-5, 5-dimethyl-cyclohexane-1, 3-dione (166mg, 1.0mmol) by $Rh_2(OPiv)_4$ catalyst at room temperature led to the desired product 10. The compound was visible under UV lamp. A liquid product was collected in 148mg (yield 66%).



M. F.: $C_{12}H_{16}O_4$

UV (EtOH): λ_{max} 253.70 nm.

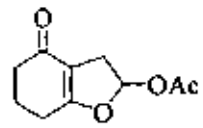
IR spectrum (CCl_4): 2962.5, 2929.7, 1768.6, 1645.2, 1550.7, 1404.1, 1203.5, 927.6 and 727.1 cm^{-1}.

^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ_H 6.72 (dd, 1H, J = 7.51, 16.1 Hz, C-2), 3.95 (s, 3H, $OCOCH_3$), 3.06 (dd, 1H, J = 7.51, 16.1 Hz, C-3), δ 2.79 (dd, 1H, J =7.51, 16.1 Hz, C-3), δ 2.35 (d, 2H, J = 11.24 Hz, C-5), δ 2.25 (d, 2H, J = 7.08, C-7), δ 1.11 (s, 3H, -CH_3) & 1.07 (s, 3H, -CH_3).

^{13}C NMR spectrum: (100 MHz, $CDCl_3$): δ 197.89, 171.34, 162.82, 105.62, 92.24, 51.38, 41.13, 34.63, 27.89, 27.07, 17.61 and 16.17.

3.4b. 4-Oxo-2, 3,4,5,6,7-hexahydro-benzofuran-2-yl acetate 11:

The reaction of cyclohexane-1, 3-dione (100 mg, 0.82 mol), vinyl acetate 1ml and $Rh_2(OPiv)_4$ (3 mg) to give product **11** (60 mg, 42. 24%) as a yellow oil .



11

M.F.: $C_{10}H_{12}O_4$

UV (EtOH): λ_{max} 260.75nm.

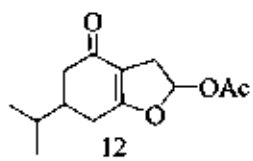
IR spectrum (CCl_4): 2999.7, 2927.5, 1647.1 (C=O), 1558.7, 1251.7, 1004.8, 908.4, 725.2 cm^{-1}.

^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ_H 6.50 (m, 1H, C-2), 3.85 (s, 3H, -$OCOCH_3$), 2.95(dd, 1H, J = 6.86, 14.69 Hz, C-3), 2.72 (dd, 1H, J = 6.86, 14.69 Hz, C-3), 2.44 (t, 2H, J = 5.44 Hz, C-5), 2.35 (t, 2H, J = 6.26 Hz, C-7) & 2.06 (m, 2H, C-6).

^{13}C NMR spectrum: (100 MHz, $CDCl_3$): 197.89 (C=O), 171.34, 163.89, 106.65, 92.34, 41.13, 34.63, 34.38, 17.61 and 16.17.

3.4c. 6-Isopropyl-4-oxo-2, 3,4,5,6,7-hexahydro-benzofuran-2-yl acetate 12:

A mixture of 2-diazo-5-isopropyl-cyclohexane-1, 3-dione 100 mg (0.55 mmol) and vinyl acetate 1 ml was taken in the 100 ml two-neck round-bottomed flask and was stirred at room temperature. $Rh_2(OPiv)_4$ 3 mg (0.1 mmol) was added under above method. A liquid product was collected in (67 mg 50.17%).



12

M. F. : $C_{13}H_{18}O_4$

UV (EtOH): λ_{max} 261.75 nm.

IR spectrum (CCl_4): 2927.7, 1646.6 (C=O), 1548.7, 1402.7, 1251.5, 1004.6, 970.1, 727.1 cm^{-1}.

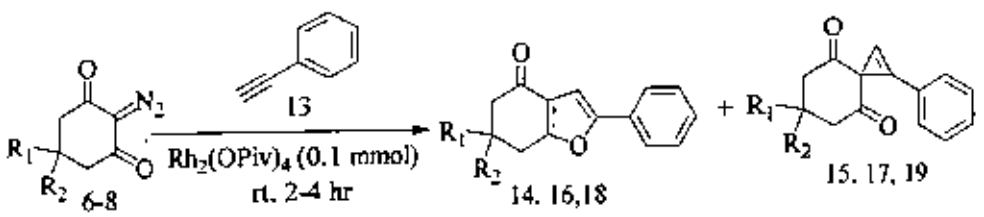
1H NMR spectrum (400 MHz, CDCl3): δ_H 6.60 (m, 1H, C-2), 3.84 (s, 3H, -OCOCH$_3$), 2.95 (dd, 1H, *J* = 6.68, 14.69 Hz, C-3), 2.70 (dd, 1H. J = 6.68, 14.69 Hz, C-3), 2.44 (d, 2H, J = 5.44Hz, C-5), 2.35 (d. 2H, J = 6.20Hz, C-7), 1.65 (m, 1H, C-6), 1.21 {m, 1H, CH(CH$_3$)$_2$} and 0.99 (d, 6H, J=5.69Hz, 2×CH$_3$).

^{13}C NMR spectrum: (100 MHz, CDCl$_3$): 197.89 (C=O), 171.34, 162.82, 105.62, 92.24, 48.38, 41.38, 37.94, 34.63, 33.89, 21.94, 21.89 and 16.17.

3.5. General Procedure for synthesis of 2-phenyl-6,7-dihydro-5*H*-benzofuran-4-one derivatives 14,16,18 and 2-phenyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one derivatives 15,17,19:

General procedure

A mixture of 2-diazo-cyclohexane-1, 3-dione derivatives **6-8** (1 mmol) and phenyl acetylene **13** (4 mmol) was taken in the 100 ml two-neck round-bottomed flask. Rhodium pivalate (0.1 mmol) was added to the mixture and was stirred under nitrogen atmosphere for 2-4 hrs at room temperature. After completion of the reaction (TLC-checked), the solvent was removed under reduced pressure to obtain the crude product. Then the crude product purified by column chromatography (hexane-EtOAc) on silica gel to give corresponding substituted two different products. Pure product was analyzed by UV, IR and 1H-NMR.



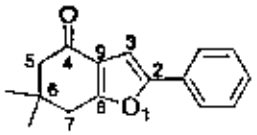
Where
6,14 & 15. R_1=R_2 = -CH$_3$,
7,16 & 17. R_1=R_2 = H
8,18 & 19. R_1= H, R_2 = -C(CH$_3$)$_2$

Scheme 5

3.5a. (I) 6,6-Dimethyl-2-phenyl-3, 5, 6, 7-tetrahydro-2*H*-benzofuran-4-one 14:

Rh$_2$(OPiv)$_4$ catalyzed reaction of 2-diazo-5, 5-dimethyl-cyclohexane-1, 3-dione **6** with phenyl acetylene **13** led to the desired product 6,6-dimethyl-2-phenyl-3. 5, 6, 7-

tetrahydro-2*H*-benzofuran-4-one **14** (60 mg, 24.7%) as oily product and a by-product 6,6-dimethyl-1-phenyl-spiro [2.5] oct-1-ene-4, 8-dione **15.**



14

M. F.: $C_{16}H_{16}O_2$

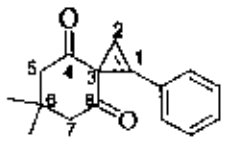
UV (EtOH): λ_{max} 257.15 nm.

IR spectrum (CCl_4): ν_{max} 3076.0, 2962.5, 1676.0 (C=O), 1550.7, 1357.8, 1091.6, 966.3, 723.3 and 572.8 cm^{-1}.

^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ_H 7.69 (d, 2H, J = 7.86 Hz, ArH), 7.48 (t, 2H, J = 7.46Hz, ArH), 7.30 (t, 1H, J = 7.26, ArH), 5.38 (s, 1H, C-3), 2.76 (s, 2H, C-5), 2.51 (s, 2H, C-7) & 0.99 (s, 6H, 2×CH_3).

(II) 6,6-Dimethyl-1-phenyl-spiro [2.5] oct-1-ene-4, 8-dione 15:

A white solid product **15** was obtained 150 mg (yield 62.5%), M.P. 130-132^0 C.



15

M.F.: $C_{16}H_{16}O_2$

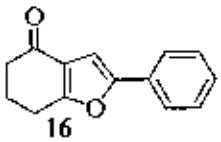
UV (EtOH): λ_{max}283.55, 270.45, 219.85 nm.

IR spectrum (KBr): ν_{max} 3099.4, 2958.6, 1676.0, 1456.2, 1436.9, 1224.7, 1014.5, 763.5 and 692.1 cm^{-1}.

^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ_H 7.76 (d, 2H, J = 7.86 Hz, ArH), 7.49 (t, 2H, J = 7.88 Hz, ArH), 7.29 (t, 1H, J = 7.26 Hz, ArH), 6.88 (s, 1H, C-3), 2.56 (s, 2H, C-5), 2.55 (s, 2H, C-7), and 0.99 (s, 6H, 2×CH_3).

3.5b(I). 2-Phenyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one 16:

Reaction of 2-diazo-cyclohexane-1, 3-dione **7** (138 mg, 1 mmol) with phenyl acetylene (1 mmol) was afforded an expected compound 2-phenyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one **16** (50 mg, 23.36%) as an oily product and a second product 1-phenyl-spiro [2.5] oct-1-ene-4, 8-dione **17**.



16

M. F.: $C_{14}H_{12}O_2$

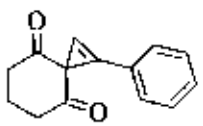
UV (EtOH): λ_{max} 275.85, 258.45 & 220.85 nm.

IR spectrum (CCl4): ν_{max} 3099.4, 2958.6, 1548.7, 1251.7, 1217.0, 1004.8, 979.8 and 727.1 cm^{-1}.

^{1}H NMR spectrum (400 MHz, CDCl3): δ_H 7.57 (d, 2H, J = 7.46 Hz, ArH), 7.36 (t, 2H, J =7.82 Hz, ArH), 7.28 (t, 1H, J = 7.6Hz, ArH), 5.36 (s, 1H, C-3), 2.99 (t, 2H, J = 6.26 Hz, C-5), 2.43 (t, 2H, J = 6.8 Hz, C-7) & 2.33(m, 2H, C-6).

(II). 1-Phenyl-spiro [2.5] oct-1-ene-4, 8-dione 17:

A colourless solid product **17** was afforded 100 mg (yield 47.16%), M. P.: 120-122^{0}C,



17

M.F.: $C_{14}H_{12}O_2$

Mol. Wt.: 212.24

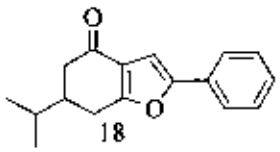
UV (EtOH): λ_{max} 296.55, 260.35 nm.

IR spectrum (KBr): ν_{max} 3099.4, 3053.1, 2945.1, 1651.0, 1450.4, 1359.7, 1238.2, 1136.0, 1001.0, 921.9, 765.7 and 694.3 cm^{-1}.

^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ_H 7.77 (d, J = 7.51 Hz, ArH), 7.49 (t, 2H, J = 9.5 Hz, ArH), 7.29 (t, 1H, J = 7.36Hz ArH), 6.66 (s, 1H, C-3H), 2.95 (t, 2H, J = 6.26 Hz, C-5H), 2.53 (t, 2H, J = 6.15Hz, C-7H) & 2.23 (m, 2H, C-6H).

3.5c(I). 6-Isopropyl-2-phenyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one 18:

$Rh_2(OPiv)_4$ catalyzed reaction of 2-diazo-5-isopropyl -cyclohexane-1, 3-dione **8** 100mg (0.55 mmol) with phenyl acetylene **13**(1 mmol) led to the desired product 6-isopropyl-2-phenyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one **18** (60 mg, 23.43%) as oily product and a bi-product 6-isopropyl-1-phenyl-spiro [2.5] oct-1-ene-4,8-dione **19.**



18

M.F.: $C_{17}H_{18}O_2$

Mol. Wt.: 254.32

UV (EtOH): λ_{max} 260.15 nm.

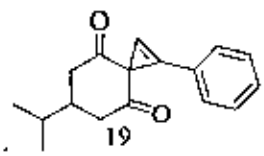
IR spectrum (CCl_4): ν_{max} 30096.7, 2956.6, 1667.1, 1546.7, 1256.7, 1224.6, 1004.6, 976.8, 908.6 and 725.6 cm^{-1}.

^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ_H 7.88 (d, 2H, J = 7.86 Hz, C-ArH), 7.69 (t, 2H, J = 7.86 Hz, ArH), 7.39 (t, 1H, J = 7.37 HzArH), 5.28 (s, 1H, C-3H), 2.44 (d, 2H, J = 5.4 Hz, C-5H), 2.35 (d, 2H, J = 6.2Hz, C-7H), 1.76 (m, 1H, C-6H), 1.66 (m, 1 H, $-CH(CH_3)_2$) and 1.07 (d, 6H, J = 8.72Hz, $2\times CH_3$).

^{13}C NMR spectrum: (100 MHz, $CDCl_3$): 192.89, 167.82, 165.82, 134.38, 130.79, 130.61, 130.38, 129.96, 129.21, 118.72, 111.17, 41.13, 37.94, 34.63, 33.89, 21.94 and 21.81.

(II) 6-Isopropyl-1-phenyl-spiro [2.5] oct-1-ene-4,8-dione 19:

A solid product was collected 150 mg (yield 59.05%), M. P.: 126-128^{0}C.



19

M. F.: $C_{17}H_{18}O_2$

Mol. Wt.: 254.32

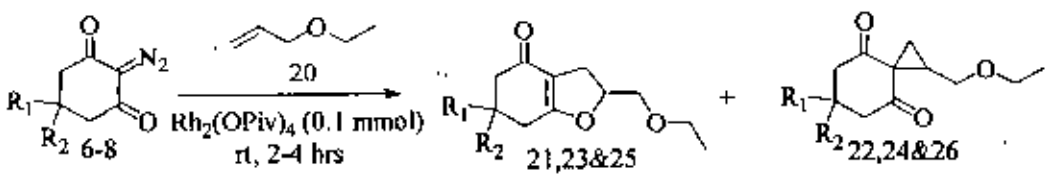
UV (EtOH): λ_{max} 299.55, 225.35 nm.

IR spectrum (KBr): ν_{max} 3099.4, 2945.1, 1666.4, 1458.1, 1436.3, 1136.0, 765.7 and 692.4 cm^{-1}.

^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ_H 7.66 (d, 2H, J = 7.86 Hz, ArH), 7.39 (t, 2H, J = 7.46 Hz, ArH), 7.29 (t, 1H, J = 7.37Hz, ArH), 7.10 (s, 1H, C-3H), δ 2.56 (d, 2H, J = 5.4Hz, C-5H), 2.4 (d, 2H, J = 5.4 Hz, C-7H), 1.81 (m, 1H, C-6H), 1.47 (m, 1 H, -CH$(CH_3)_2$) and 1.23 (d, 6H, J = 8.72Hz, 2×CH_3).

3.6. General procedure for synthesis of 2-ethoxymethyl-hexahydro-benzofuran-4-one derivatives 21, 23, 25 and 1-ethoxymethyl-spiro [2.5] octane-4, 8-dione 22, 24, 26: General Procedure

A mixture of 2-diazo-cyclohexane-1,3-dionederivatives **6-8** (1 mmol) and 3-ethoxy-propene (allyl ethyl ether) **20** (5 mmol) and rhodium pivalate (0.1mmol) was taken in air free R.B. flux and was stirred under nitrogen atmosphere for 2-4 hrs at room temperature. The progress of the reaction was monitored by TLC-checked. After completion of reaction, the solvent was removed under reduced pressure to obtain the crude product. Later the residue was purified by column chromatography (Hexane-EtOAc) on silica gel to give corresponding substituted two different products **21, 23, 25** and **22, 24, 26**. Pure products were analyzed by UV, IR and ^{1}H-NMR.

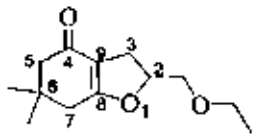


Where
6, 21 & 22. R_1=R_2 = -CH_3,
7, 23 & 24. R_1=R_2 = H
8, 25 & 26. R_1= H, R_2 = -C$(CH_3)_2$

Scheme 8

3.6a(I). 2-Ethoxymethyl-6, 6-dimethyl-hexahydro-benzofuran-4-one 21:

Reaction of 2-diazo-5, 5-dimethyl-cyclohexane-1, 3-dione **6** (1.66mg, 1.0 mmol) and 3-ethoxy-propene **20** (1mml) afforded desired product 2-ethoxymethyl-6, 6-dimethyl-hexahydro-benzofuran-4-one **21** (41mg, 18.14%) as a liquid and an unexpected product 1-ethoxymethyl-6, 6-dimethyl-spiro [2.5] octane-4, 8-dione **22**.



21

M.F.: $C_{13}H_{20}O_3$

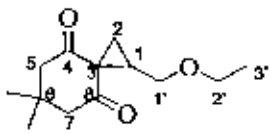
UV (EtOH): λ_{max} 266.60, 211.10 nm.

IR spectrum (CCl_4): ν_{max} 2962.5, 2929.7, 1768.6, 1645.2, 1550.7, 1427.2, 1404.1, 1203.5, 929.6 and 727.1 cm^{-1}.

^{1}H NMR spectrum (300 MHz, $CDCl_3$): δ_H 4.94 (m, 1H, C-2), 3.56 -3.49 (m, 4H, -CH_2OCH_2-), 2.85 (m, 1H, C-3), 2.51 (m, 1H, C-3), 2.27 (s, 2H, C-5), 2.19 (s, 2H, C-7), 1.2 (t, 3H, J = 7.02 Hz, -CH_3) & 1.06 (s, 6H, 2×-CH_3).

(II). **1-Ethoxymethyl-6, 6-dimethyl-spiro [2.5] octane-4, 8-dione 22:**

A liquid oily product was separated (176mg, 78.57%).



22

M. F.: $C_{13}H_{20}O_3$

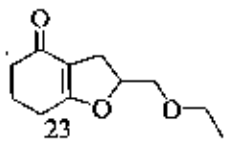
UV (EtOH): λ_{max} 285.15, 255.20, 235.95 and 211.95 nm.

IR spectrum (CCl_4): ν_{max} 2958.6, 1676.0, 1436.9, 1224.7, 1014.5, 763.8 and 692.4.

^{1}H NMR spectrum (300 MHz, $CDCl_3$): δ_H 3.68 (dd, 1H, J = 4.52, 12.2 Hz, -C-1'), 3.65(m, 1H, C-1'), 3.27 (m, 2H, C-2'), 2.67-2.43 (m, 4H, C-5 &C-7), 2.29-2.19 (m, 1H, C-1), 1.96 (dd, 1H, J = 3.18, 8.91 Hz, C-2), 1.87 (dd, 1H, J = 3.18, 8.91 Hz, C-2), 1.15 (s, 3H, C-3'), 1.09 (t, 3H, J = 7.0 Hz, -CH_3) & 1.02 (s, 3H, -CH_3).

3.6b(I). 2-Ethoxymethyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one 23:

2-Ethoxymethyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one **23** was prepared from the reaction of 2-diazo-cyclohexane-1, 3-dione **7** (138 mg, 1 mmol) with 3-ethoxy-propene **20** (1mml) by rhodium pivalet (.1mml) to yield 2-ethoxymethyl-3, 5,6,7-tetrahydro-2*H*-benzofurun-4-one **23** (36 mg, 18.36%) as liquid product and a dissimilar product 1-ethoxymethyl-spiro [2.5] octane-4, 8-dione 24.



23

M. F.: $C_{11}H_{16}O_3$

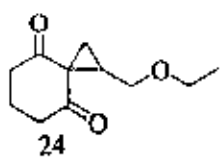
UV (EtOH): λ_{max} 260.15, 238.20 and 211.95 nm.

IR spectrum (CCl_4): ν_{max} 2958.6, 1647.1, 1548.7, 1251.7, 1224.7, 1004.8, 977.8, 908.4 and 725.2 cm^{-1}.

^{1}H NMR spectrum (300 MHz, $CDCl_3$): δ_H 4.98- 4.88 (m, 1H, C-2), 3.59 – 3.45 (m, 2H, $-CH_2O-$), 3.44- 3.39 (m, 2H, $-OCH_2-$), 2.89-2.80 (m, 1H, C-3), 2.51 – 2.43 (m, 1H, C-3), 2.41- 2.39 (m, 2H, C-5), 2.34-2.29 (m, 2H, C-7), 2.00 (t, 2H, J = 6.36 Hz, C-6), 0.88 (t, 3H, J = 3.85Hz, CH_3).

(II) 1-Ethoxymethyl-spiro [2.5] octane-4, 8-dione 24:

Colourless liquid product **24** was obtained (115 mg, 58.37%).



24

M. F.: $C_{11}H_{16}O_3$

UV (EtOH): λ_{max} 284.45, 258.55 and 212.70 nm.

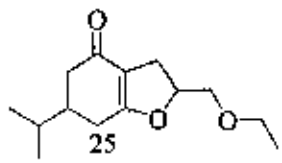
IR spectrum (CCl_4): ν_{max} 2945.1, 1666.4, 1610.5, 1458.1, 1136.0, 765.7 and 692.4 cm^{-1}.

^{1}H NMR spectrum (300 MHz, $CDCl_3$): δ_H 3.69 (dd, 1H, J = 4.54, 10.59 Hz, C-1'), 3.43-3.33 (m, 1H, C-1'), 3.29-3.19 (m, 1H, C-2'), 3.13 (t, 1H, J = 10.36 Hz, C-2'), 2.89-2.65 (m, 2H, C-5), 2.61-2.53 (m, 2H, C-7), 2.21 (m, 2H, C-6), 2.04-1.99 (m, 1H, C-1), 1.97-1.94 (dd, 1H, J =

3.31, 8.85 Hz, C-2), 1.88 (dd, 1H, J = 3.31, 8.85 Hz, C-2) & 1.07 (t, 3H, J = 7.0 Hz, C-3').

3.6c(I). 2-Ethoxymethyl-6-isopropyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one 25:

The mixture of 2-diazo-5-isopropyl-cyclohexane-1,3-dione **8** (180mg 1.0 mmol) and 3-ethoxy-propene (1 ml) and $Rh_2(OPiv)_4$ (3 mg 0.1 mmol) was stirred at room temperature to give 2-ethoxymethyl-6-isopropyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one **25** as a liquid product (138mg 57.17%) and 1-ethoxymethyl-6-isopropyl-spiro[2.5]octane-4,8-dione **26**.



25

M. F.: $C_{14}H_{22}O_3$

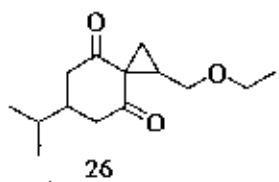
UV (EtOH): 255.15, 211.20 & 205.95 nm.

IR spectrum (CCl_4): ν_{max} 2962.7, 1674.1, 1641.2, 1550.7, 1404.1, 1053.1 and 727.7 cm^{-1}.

^{1}H NMR spectrum (300 MHz, $CDCl_3$): δ_H 5.0-4.9 (m, 1H, C-2), 3.58-3.49 (m, 4H, -CH_2OCH_2-), 2.84 (m, 1H, C-3), 2.52 -2.37 (m, 1H, C-3), 2.37 (m, 2H, C-5), 2.14 (m, 2H, C-7), 2.04 (m, 1H, C-6), 1.60 (m, 1H, -$CH(CH_3)_2$), 1.20 (m, 3H, -CH_3) & 0.91 (d, 6H, J =5.44 Hz, 2 ×-CH_3).

(II). 1-Ethoxymethyl-6-isopropyl-spiro[2.5]octane-4,8-dione 26:

A liquid product **26** was collected (90 mg 37.81%).



26

M. F.: $C_{14}H_{22}O_3$

UV (EtOH): λ_{max} 277.55, 253.35 & 211.45 nm.

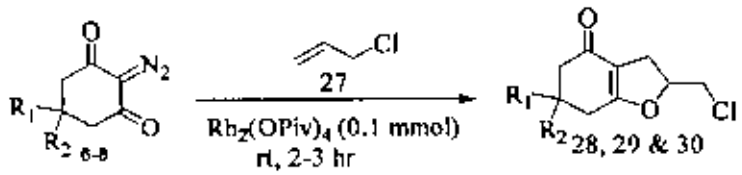
IR spectrum (CCl_4): ν_{max} 2958.6, 1600.8, 1371.3, 1245.9, 1028.0 and 731.0 cm^{-1}.

^{1}H NMR spectrum (300 MHz, $CDCl_3$): δ_H 3.66 (dd, 1H, J = 4.5, 8.4 Hz, C-1'), 3.25 (m, 1H, C-1'), 3.15 (m, 1H, C-2'), 2.71 (m, 1H, C-2'), 2.30 (m, 2H, C-5), 2.22 (m, 2H, C-7), 1.94 (m, 1H, C-1), 1.85 (m, 1H, C-2), 1.62 (m, 1H, C-2),1.50 (m, 1H, C-6), 1.45 (m, 1H, -$CH(CH_3)_2$), 0.93 (d, 6H, J = 6.82 Hz, 2 ×-CH_3) & 0.84 (t, 3H, J = 7.39 Hz, C-3').

3.7. General process of synthesis of 2-chloromethyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one 28,29&30:

General Procedure

A solution of 2-diazo-cyclohexane-1, 3-dione derivatives **6-8** (1 mmol) and allyl chloride (2 ml) and rhodium pivalate (0.1 mmol) was taken and stirred under nitrogen atmosphere for 2-3hrs at room temperature. The progress of the reaction was monitored by TLC-checked. After completion of reaction, the solvent was removed under reduced pressure to obtain the crude product. Later the residue was purified by column chromatography (Hexane-EtOAc) on silica gel to give corresponding substituted products 28, 29, 30 and small amount of by product. The product was analyzed by UV, IR and ^{1}H-NMR.

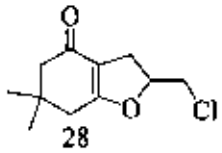


Where
6, 28. R_1=R_2 = -CH_3,
7, 29. R_1=R_2 = H
8, 30. R_1= H, R_2 = -$C(CH_3)_2$

Scheme 9

3.7a. 2-Chloromethyl-6, 6-dimethyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one 28:

A yellowish liquid product **28** was yielded (133 mg, 62.16%).



28

M. F.: $C_{11}H_{15}ClO_2$

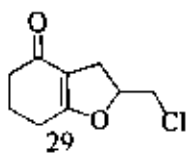
UV (EtOH): λ_{max} 276.30, 217.20 nm.

IR spectrum (CCl_4): ν_{max} 2962.5, 2929.7, 1645.2, 1550.7, 1404.1, 1369.4, 1203.5, 1053.1, 929.6 and 727.1 cm^{-1}.

^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ_H 5.02 (m, 1H, C-2), 3.65 (m, 2H, -CH_2-Cl), 2.96 (m, 1H, C-3), 2.72 (dd, 1H, J = 6.74, 13.0 Hz, C-3), 2.29 (s, 2H, C-5), 2.21 (s, 2H, C-7) and 1.08 (s, 6H, 2 ×-CH_3).

3.8b. 2-Chloromethyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one 29:

The reaction of 2-diazo-cyclohexane-1, 3-dione (138 mg, 1 mmol) with 3-chloro-propene (1 mml) by rhodium catalyst in afforded **29** (66 mg, 33.67%) as liquid product.



29

M.F.: $C_9H_{11}ClO_2$

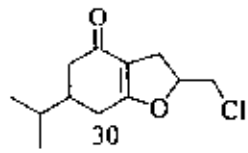
UV (EtOH): λ_{max} 270.45, 211.05 nm.

IR spectrum (CCl_4): ν_{max} 2927.7, 2854.5, 1548.7, 1253.6, 1004.8, 907.1, 727.1 and 628.8 cm^{-1}.

^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ_H 5.00 (m, 1H, C-2H), 3.65 (m, 2H, -CH_2-Cl), 2.90 (dd, 1H J = 6.86, 14.69 Hz, C-3), 2.70 (dd, 1H, J = 6.86, 14.69 Hz, C-3), 2.45 (t, 2H, J = 6.26 Hz C-5), 2.33 (t, 2H, J = 5.44Hz, C-7) & 2.04 (m, 2H, C-6).

3.8c. 2-Chloromethyl-6-isopropyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one 30:

2-Chloromethyl-6-isopropyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one **30** was prepared from the reaction of 2-diazo-5-isopropyl-cyclohexane-1, 3-dione **8** (180mg 1.0 mmol) with 3-chloro-propene (1 mml) in presence of $Rh_2(OPiv)_4$ (3 mg 0.1mmol) to obtain a liquid product **30** in 37% yield.



30

M.F.: $C_{12}H_{17}ClO_2$

UV (EtOH): λ_{max} 270.65, 211.10 nm.

IR spectrum (CCl_4): ν_{max} 2952.8, 2929.7, 1647.1, 1548.7, 1402.2, 1251.7, 1226.6, 1180.4, 1004.8, 970.1 and 727.1 cm^{-1}.

^1H NMR spectrum (300 MHz, $CDCl_3$): δ_H 5.0-4.9 (m, 1H, C-2), 3.58-3.49 (m, 2H, --CH_2Cl), 2.96 (dd, 1H, J = 3.18, 8.91 Hz, C-3), 2.84 (dd, 1H, J = 3.18, 8.91 Hz, C-3), 2.37 (d, 2H, J = 16.1 Hz, C-5), 2.14 (d, 2H, J = 15.48 Hz, C-7), 1.94 (m, 1H, C-6), 1.60 (m, 1H, -$CH(CH_3)_2$), & 0.91 (d, 6H, J =5.44 Hz, 2 ×-CH_3).

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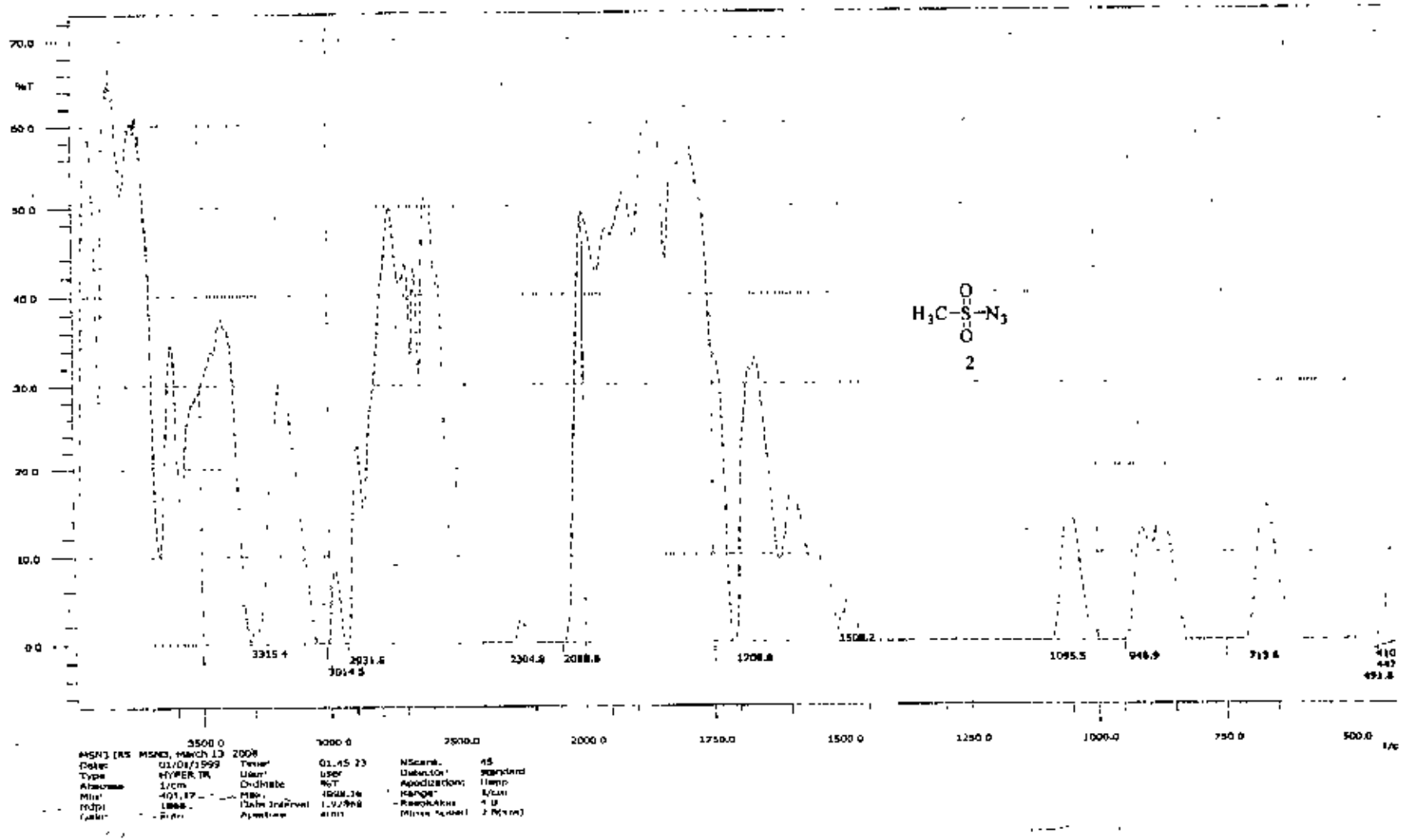
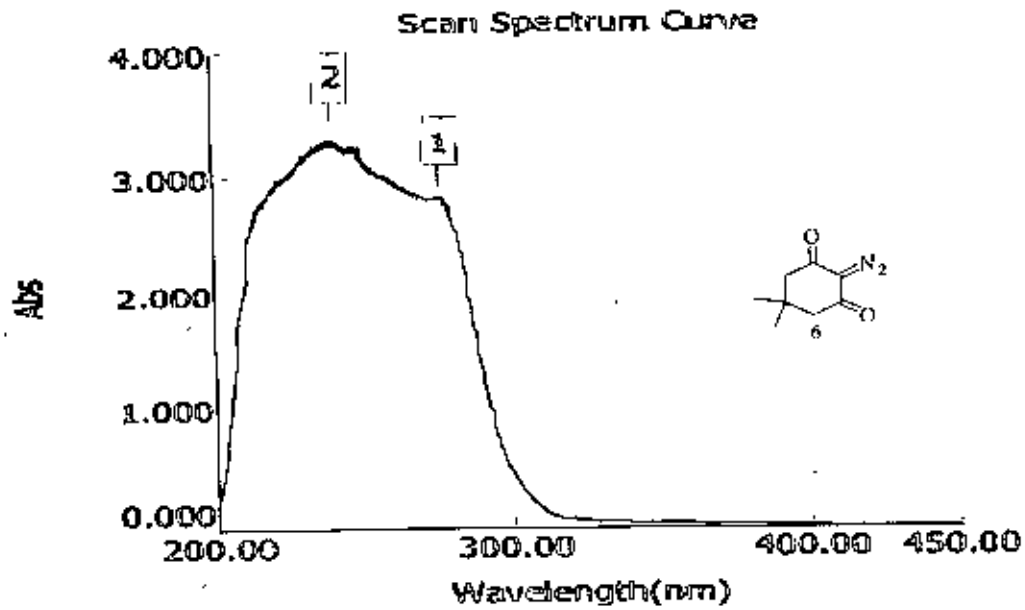


$$H_3C-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-N_3$$

2

Figure 1: IR spectrum of the compound **2**



1	Peak	277.30	2.790
2	Peak	240.80	3.386

○ Instrument Performance
Model : SPECTROPHOTOMETERS
Spectral BandWidth : 2.00 nm

○ Scan Spectrum Performance
Scan Range : 200.00 to 450.00 nm
Measure Mode : Abs
Interval : 0.05 nm
Speed : Fast
Data File : Untitled5.spd
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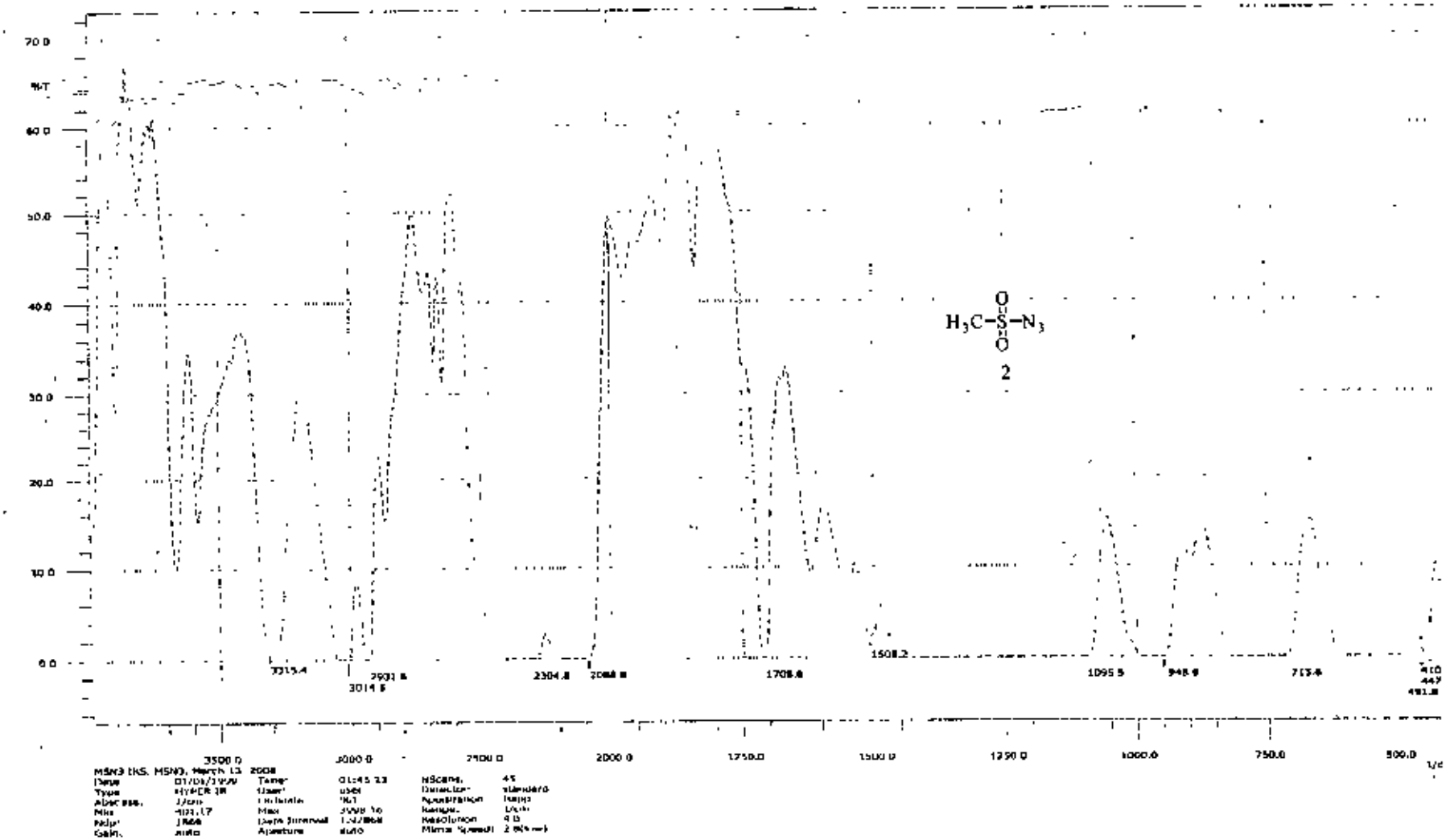
Method File:

○ Analysis Note
Analyser : Administrator
Sample Name : Sasi
Comment :

Figure 6a: UV spectrum of the compound 6



$$H_3C-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-N_3$$

2

Figure 1: IR spectrum of the compound 2

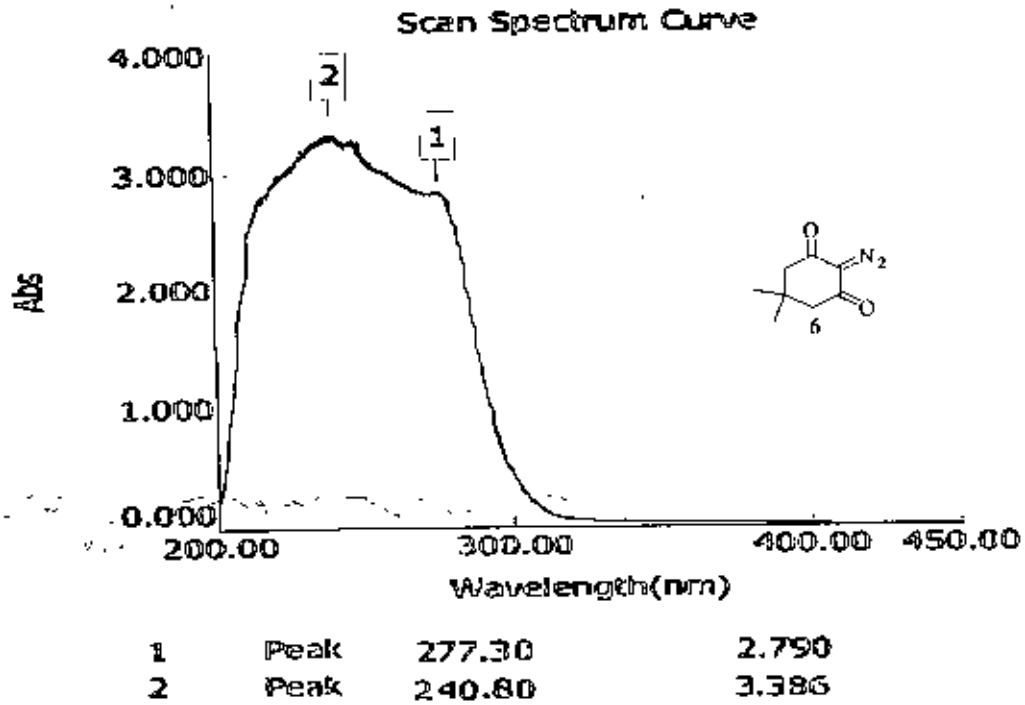


Figure 6a: UV spectrum of the compound **6**

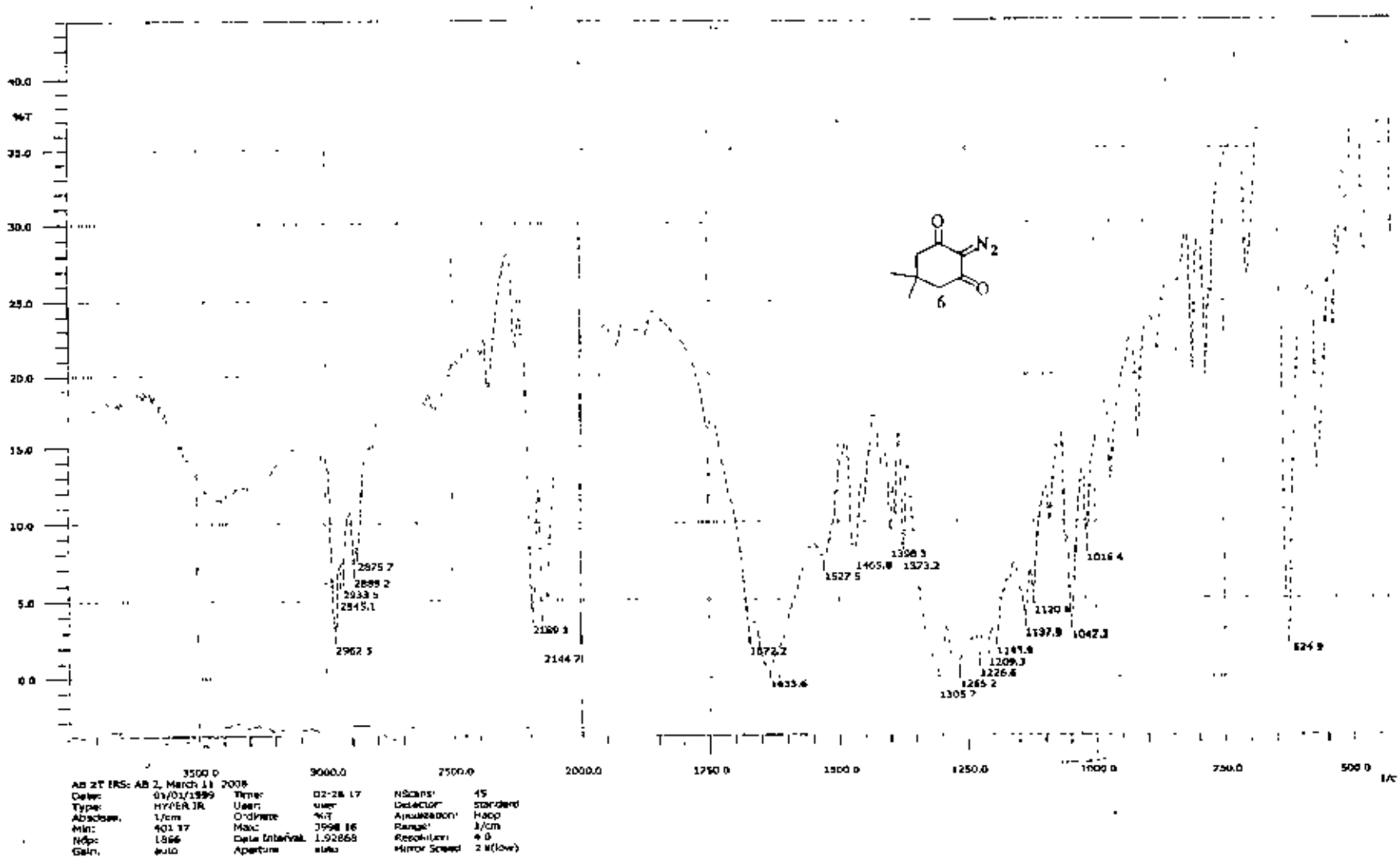
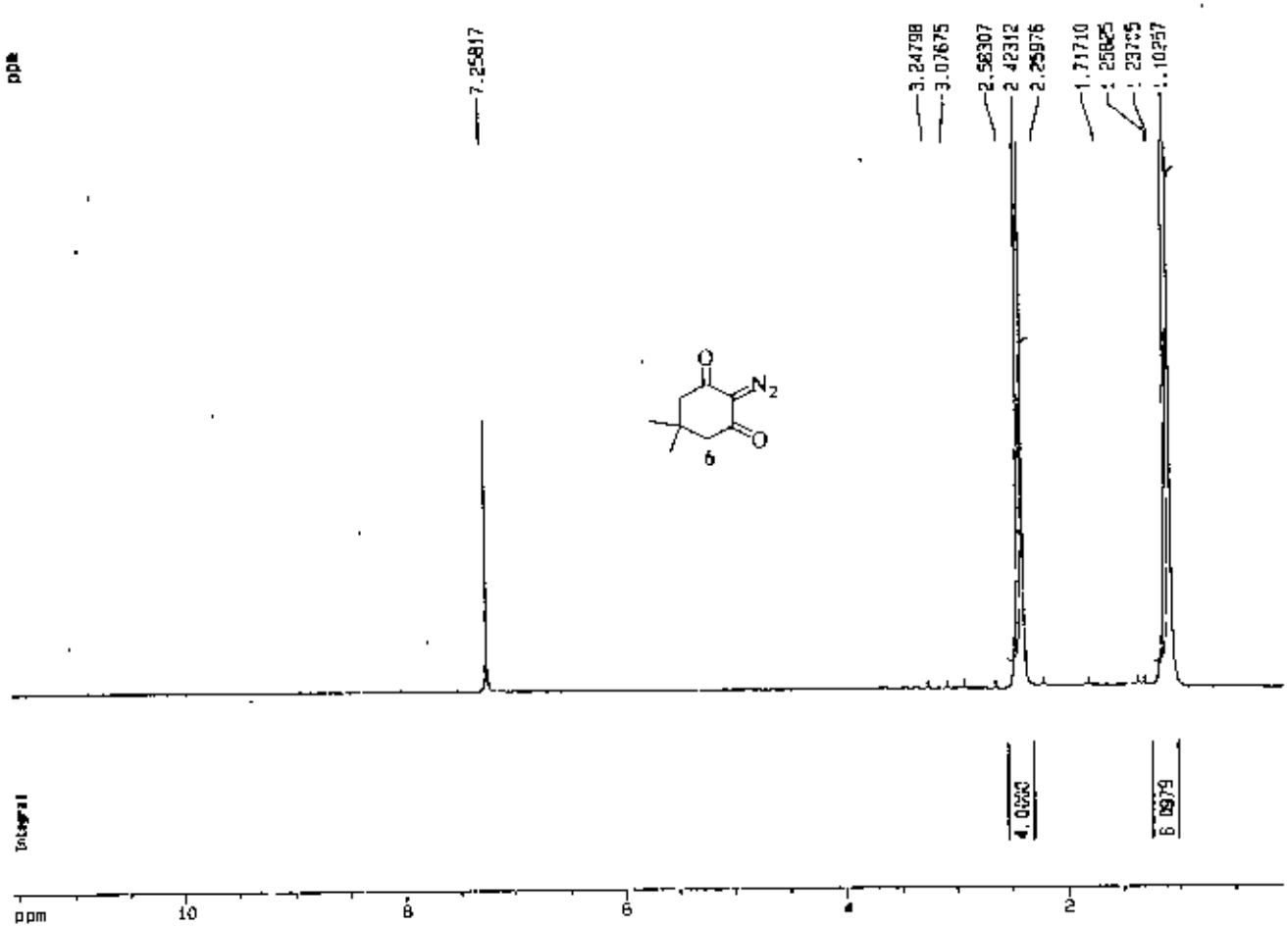


Figure 6b: IR spectrum of the compound **6**

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PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                      106
DS                        2
SWH                8410.255 Hz
FIDRES             0.195625 Hz
AQ                 2.5559040 sec
RG                     143.7
DW                  78.000 usec
DE                   6.00 usec
TE                   310.0 K
D1                1.00000000 sec

------------ CHANNEL f1 ------------
NUC1                     1H
P1                    8.30 usec
PL1                  -6.00 dB
SFO1           400.1428010 MHz

F2 - Processing parameters
SI                    32768
SF               400.1400090 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                    1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                 11.567 ppm
F1                 4624.43 Hz
F2P                 0.066 ppm
F2                   26.36 Hz
PPMCM              0.57456 ppm/cm
HZCM             229.90372 Hz/cm
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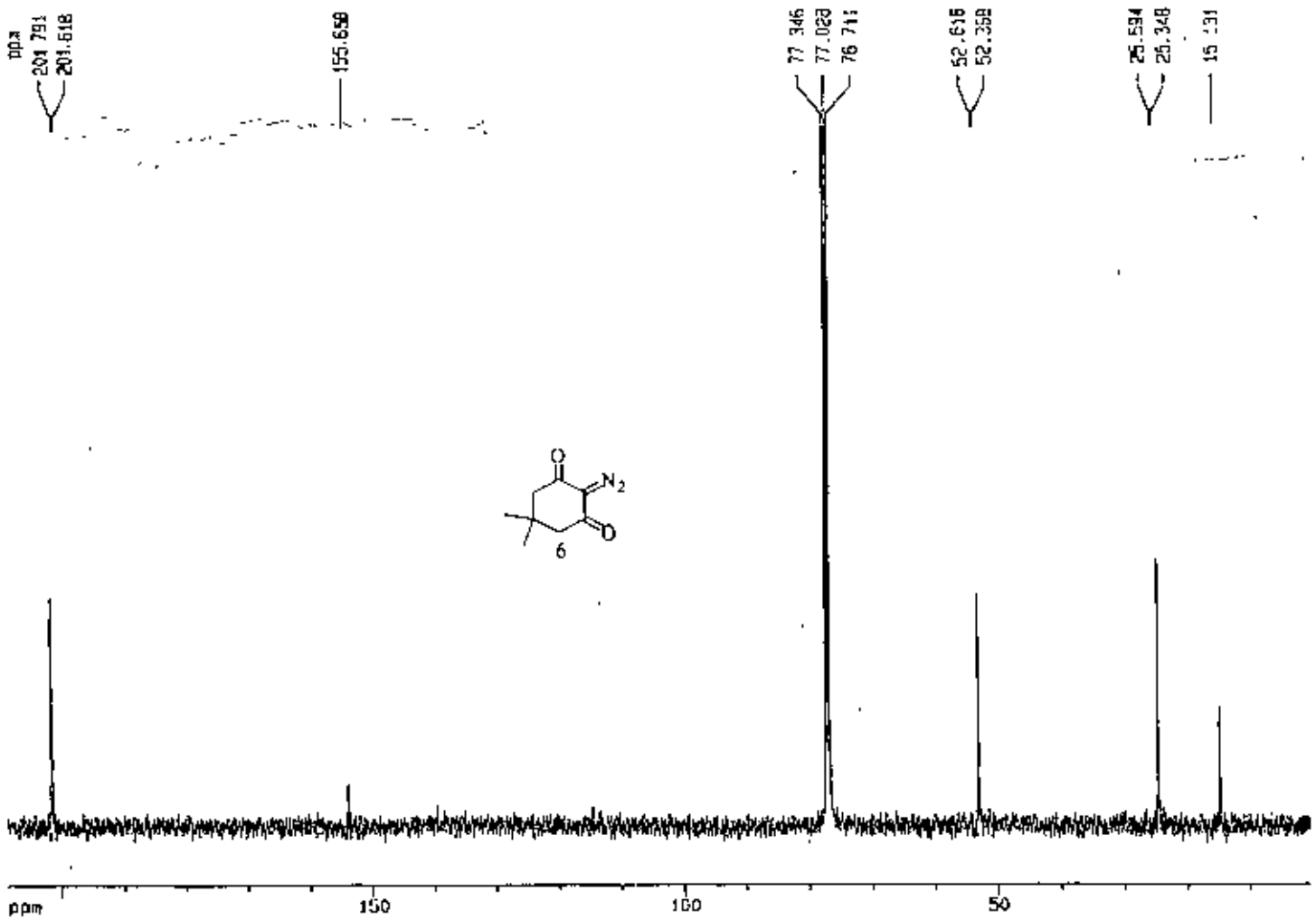
Figure 6c: ^{1}H NMR spectrum of the compound 6.

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PROCNO                    1

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PULPROG             zgpg30
TD                   32768
SOLVENT              CDCl3
NS                    3021
DS                       2
SWH              24154.590 Hz
FIDRES           0.737145 Hz
AQ               0.6783475 sec
RG                   16384
DW                  20.700 usec
DE                   6.00 usec
TE                  300.0 K
D1               1.50000000 sec
d11              0.03000000 sec
d12              0.00002000 sec

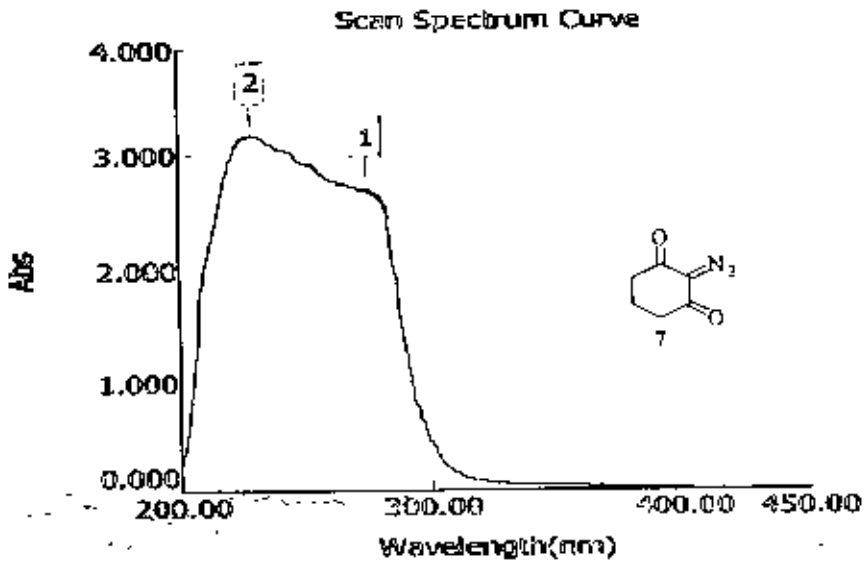
======== CHANNEL f1 ========
NUC1                  13C
P1                   8.30 usec
PL1                 -6.00 dB
SFO1          100.6253045 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                  1H
PCPD2                80.00 usec
PL2                  -4.00 dB
PL12                 16.00 dB
PL13                120.00 dB
SFO2          400.1400000 MHz

F2 - Processing parameters
SI                   32768
SF            100.6152808 MHz
WDW                  EM
SSB                   0
LB                    2.50 Hz
GB                    0
PC                    1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                 208.516 ppm
F1                20879.83 Hz
F2P                 0.608 ppm
F2                  61.24 Hz
PPMCM            10.39538 ppm/cm
HZCM             1045.93445 Hz/cm
```

Figure 6d : ^{13}H NMR spectrum of the compound **6**



1	Peak	280.35	2.690
2	Peak	237.83	3.306

○ Instrument Performance
Model : SPECTROPHOTOMETERS
Spectral Bandwidth : 2.00 nm

○ Scan Spectrum Performance
Scan Range : 200.00 to 450.00 nm
Measure Mode : Abs
Interval : 0.05 nm
Speed : Fast
Data File : Untitled5.spd
Create Date/Time : Thursday, March 18, 2008 8:23:27 PM
Data Type : Original
Method File:

○ Analyse Note
Analyser : Administrator
Sample Name : Blank
Comment :

Figure 7a: UV spectrum of the compound 7

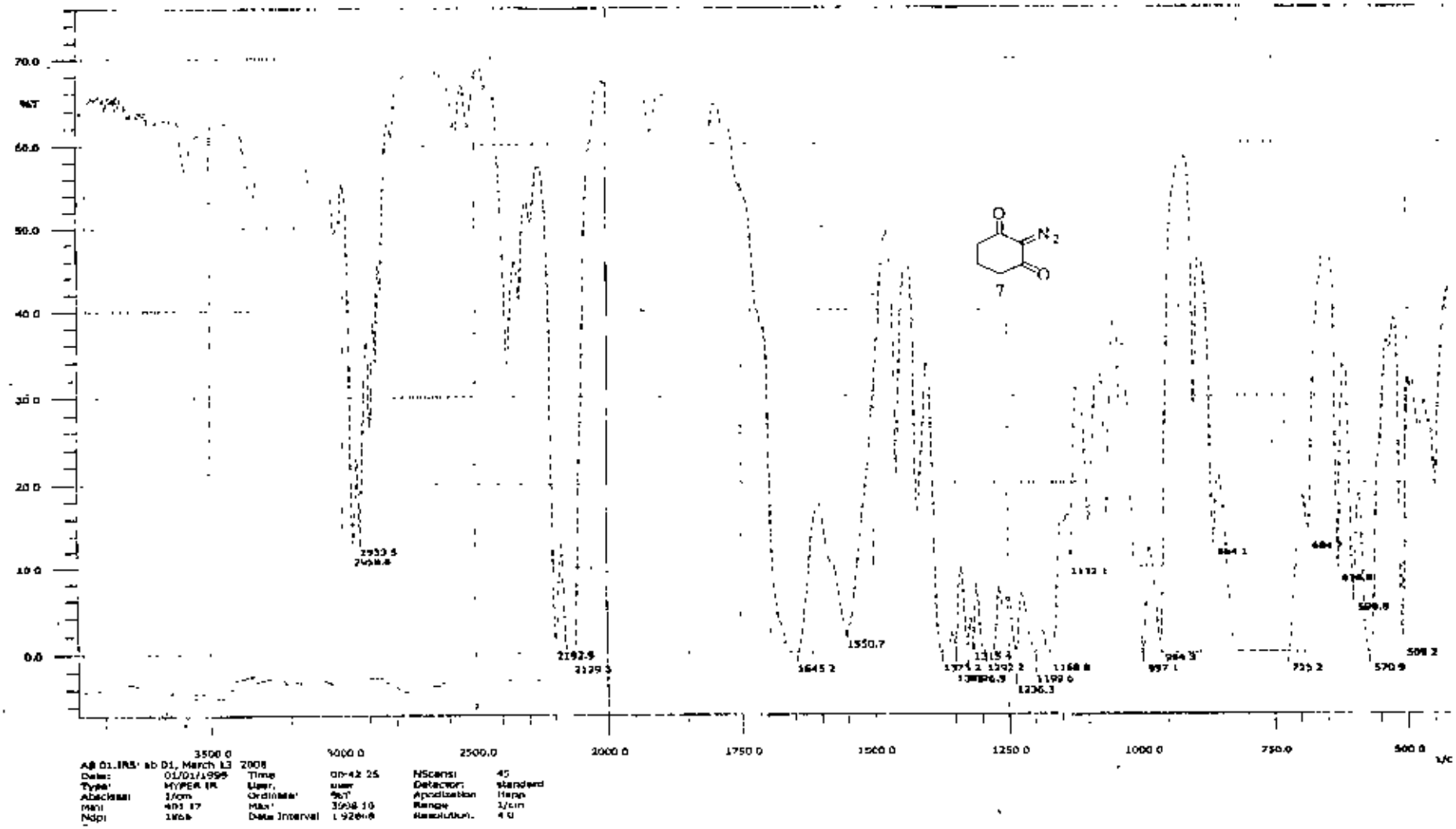
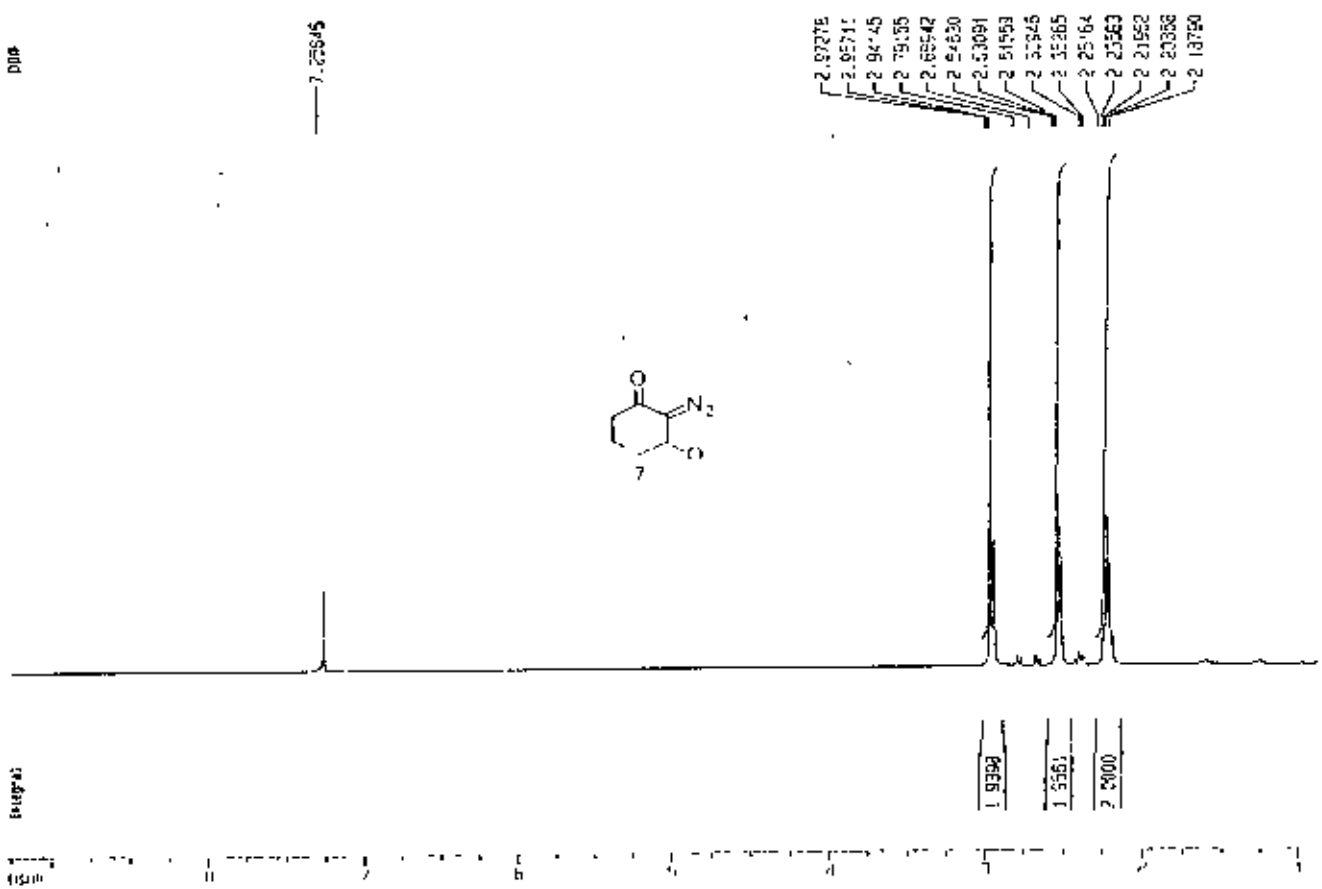


Figure 7b :IR spectrum of the compound 7

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PROCNO                    1

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PROBHD     5 mm Multinuc
PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                   128
DS                     2
SWH               6410.256 Hz
FIDRES            0.195629 Hz
AQ                2.5559540 sec
RG                   256
DW                78.000 usec
DE                 6.00 usec
TE                 310.0 K
D1                1.00000000 sec

------------ CHANNEL f1 ------------
NUC1                  1H
P1                 8.70 usec
PL1                0.00 dB
SFO1          400.1328010 MHz

F2 - Processing parameters
SI                 32768
SF            400.1400006 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.40

1D NMR plot parameters
CX                 20.00 cm
F1P                9.279 ppm
F1                3712.74 Hz
F2P                0.891 ppm
F2                356.74 Hz
PPMCM          0.41340 ppm/cm
HZCM          165.40001 Hz/cm
```

Figure 7b: ^{1}H NMR spectrum of the compound 7

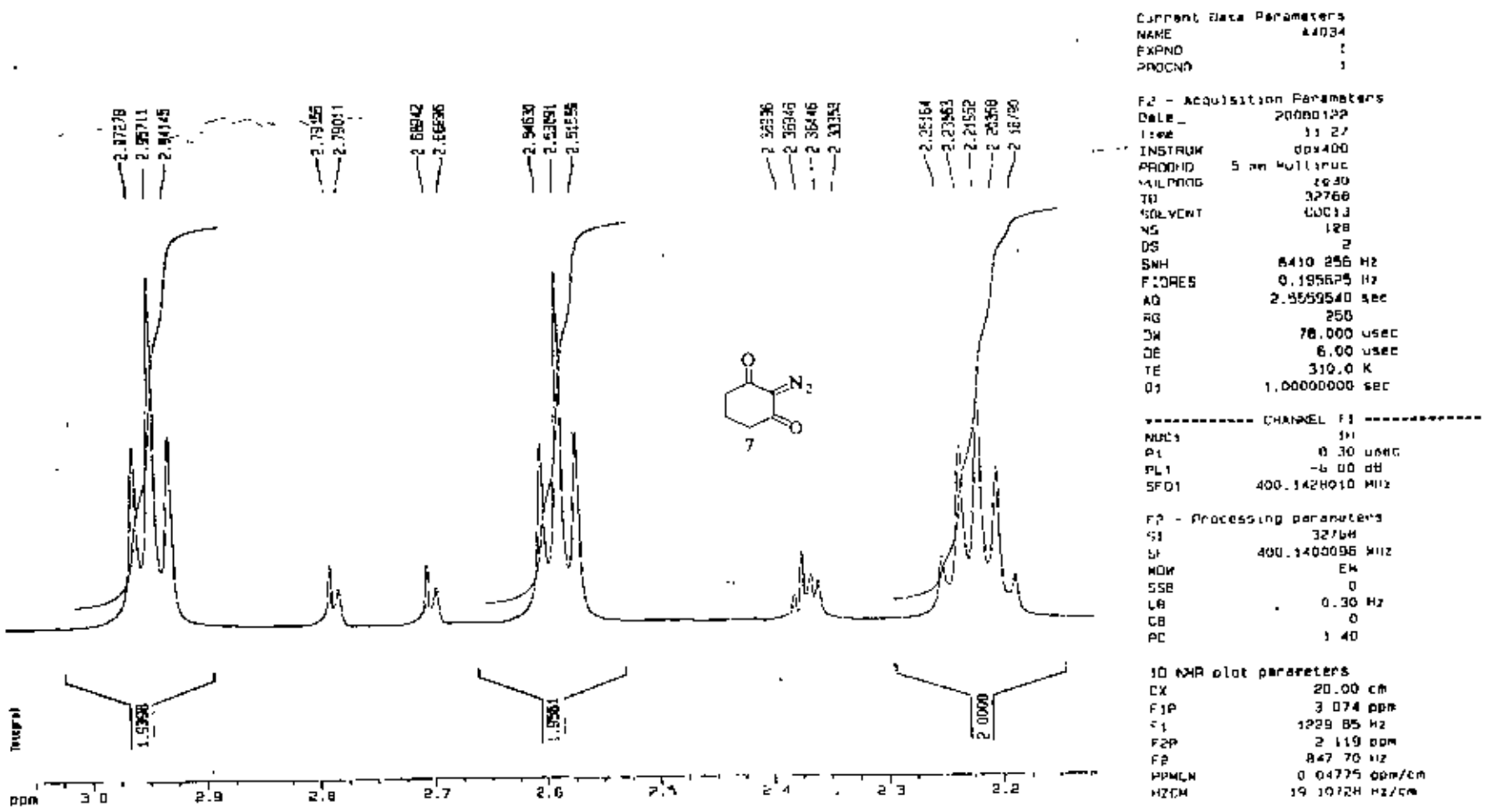
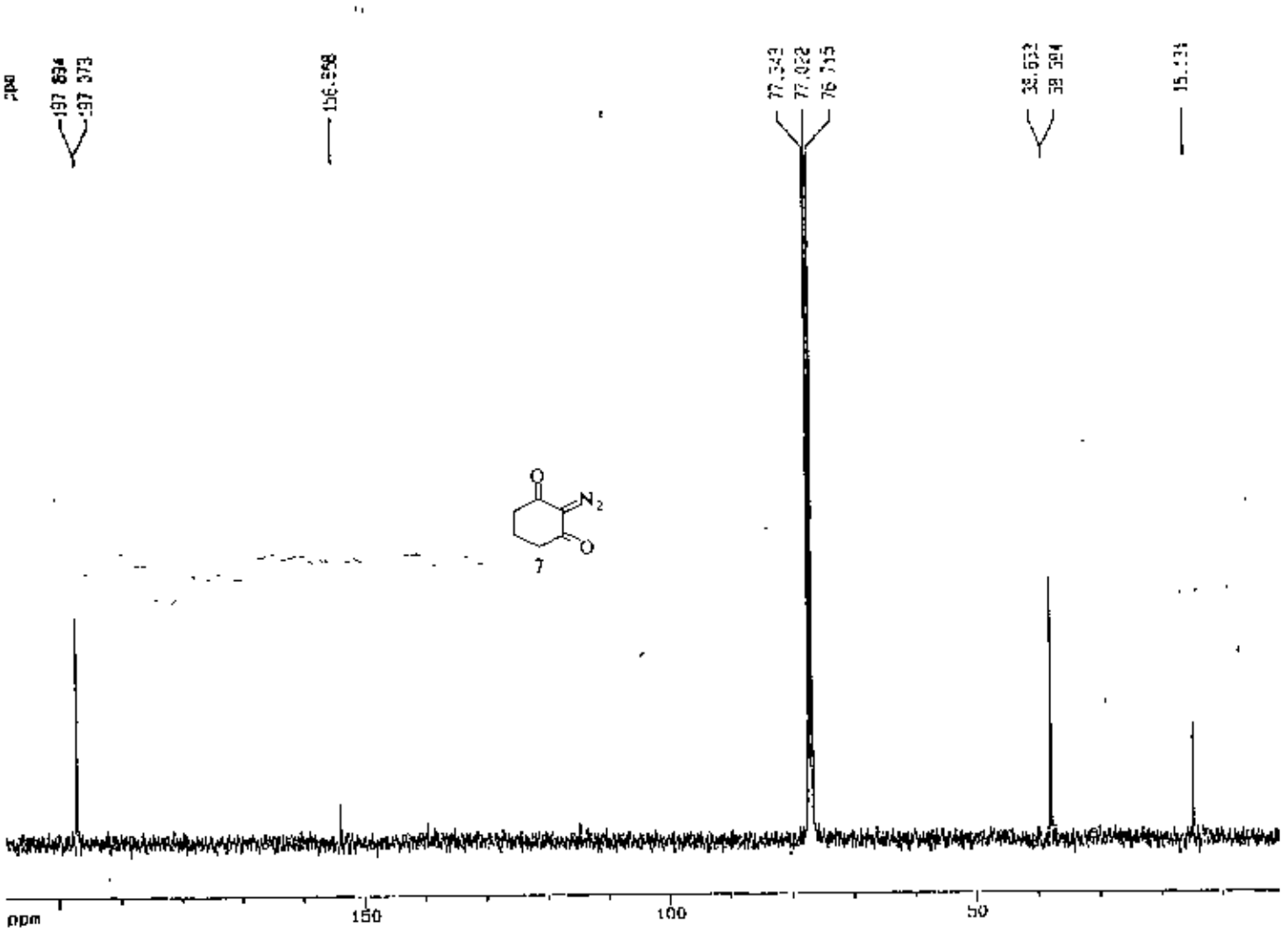


Figure 7b: ^{1}H NMR spectrum of the compound 7

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PROCNO                    1

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TD                    32768
SOLVENT               CDCl3
NS                     1021
DS                        2
SWH                24154.590 Hz
FIDRES             0.737140 Hz
AQ                 0.6783475 sec
RG                    16384
DW                   20.700 usec
DE                    6.00 usec
TE                  300.0 K
D1                  1.50000000 sec
D11                 0.03000000 sec
D12                 0.00002000 sec

---------- CHANNEL f1 ----------
NUC1                   13C
P1                    8.10 usec
PL1                  -6.00 dB
SFO1           100.6253045 MHz

---------- CHANNEL f2 ----------
CPDPRG2             waltz16
NUC2                   1H
PCPD2                80.00 usec
PL2                  -6.00 dB
PL12                 15.00 dB
PL13                120.00 dB
SFO2           400.1400000 MHz

F2 - Processing parameters
SI                    32768
SF             100.6152805 MHz
WDW                    EM
SSB                     0
LB                   2.50 Hz
GB                      0
PC                    1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                 206.316 ppm
F1                20978.91 Hz
F2P                   0.000 ppm
F2                  81.94 Hz
PPMCM             10.39538 ppm/cm
HZCM              1045.93445 Hz/cm
```

Figure 7d : ^{13}C NMR spectrum of the compound 7

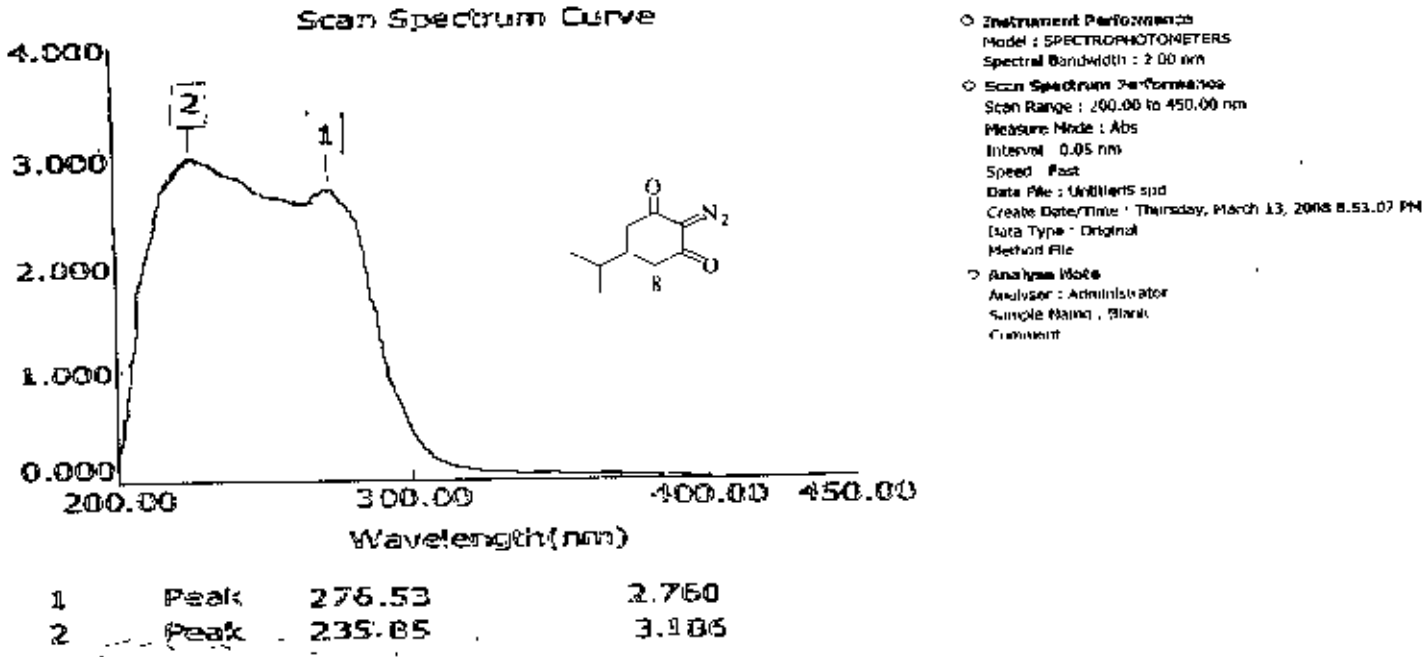


Figure 8a: UV spectrum of the compound **8**

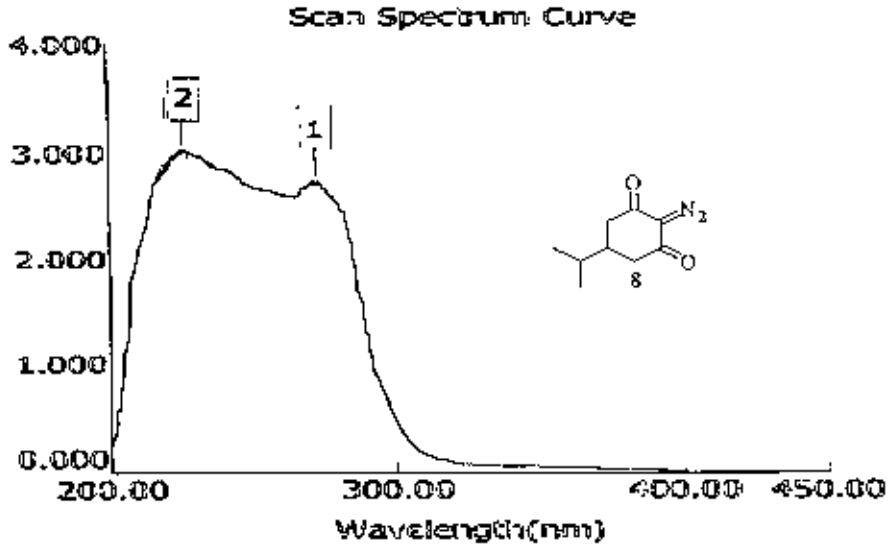


Figure 8a: UV spectrum of the compound **8**

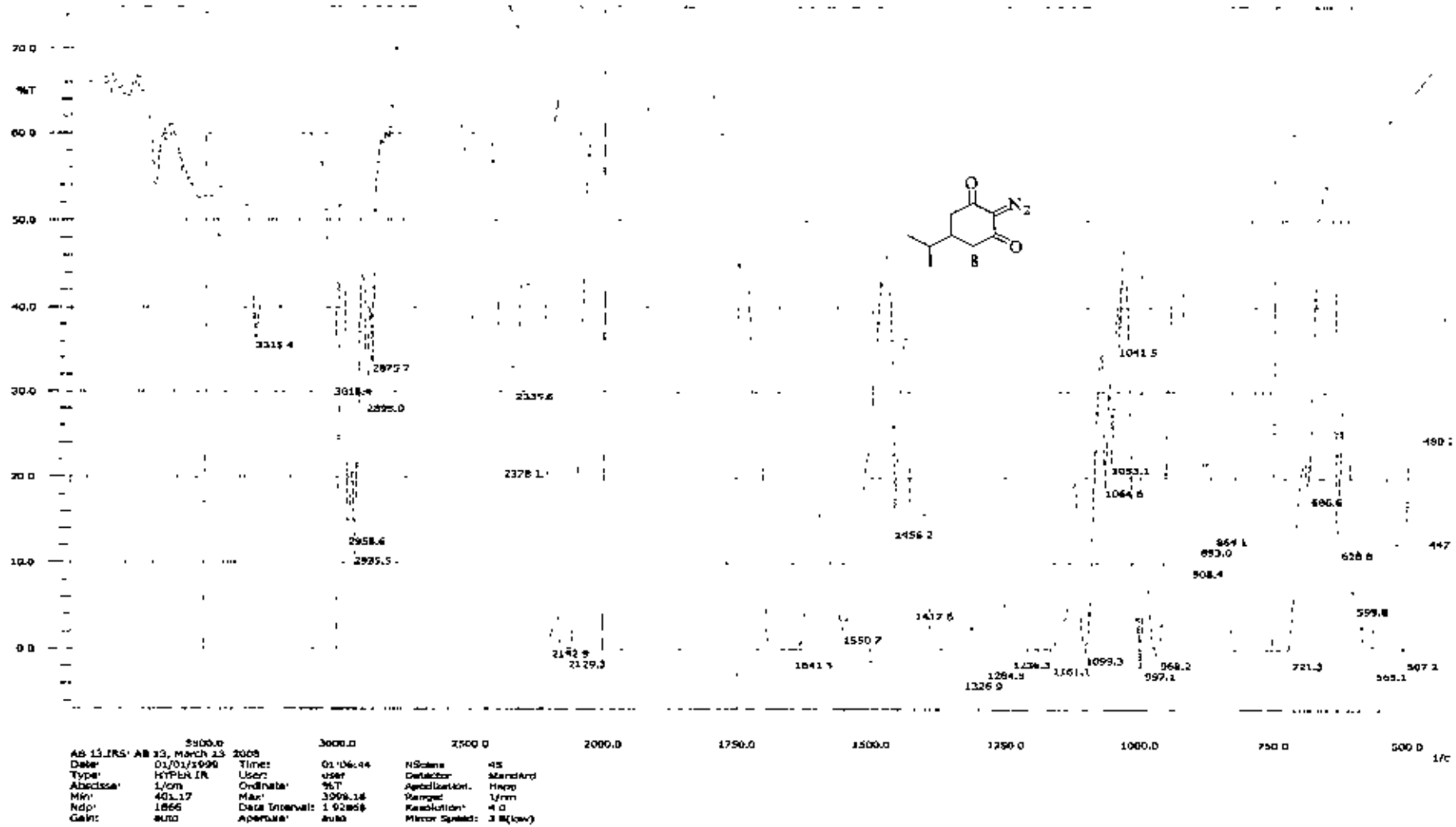
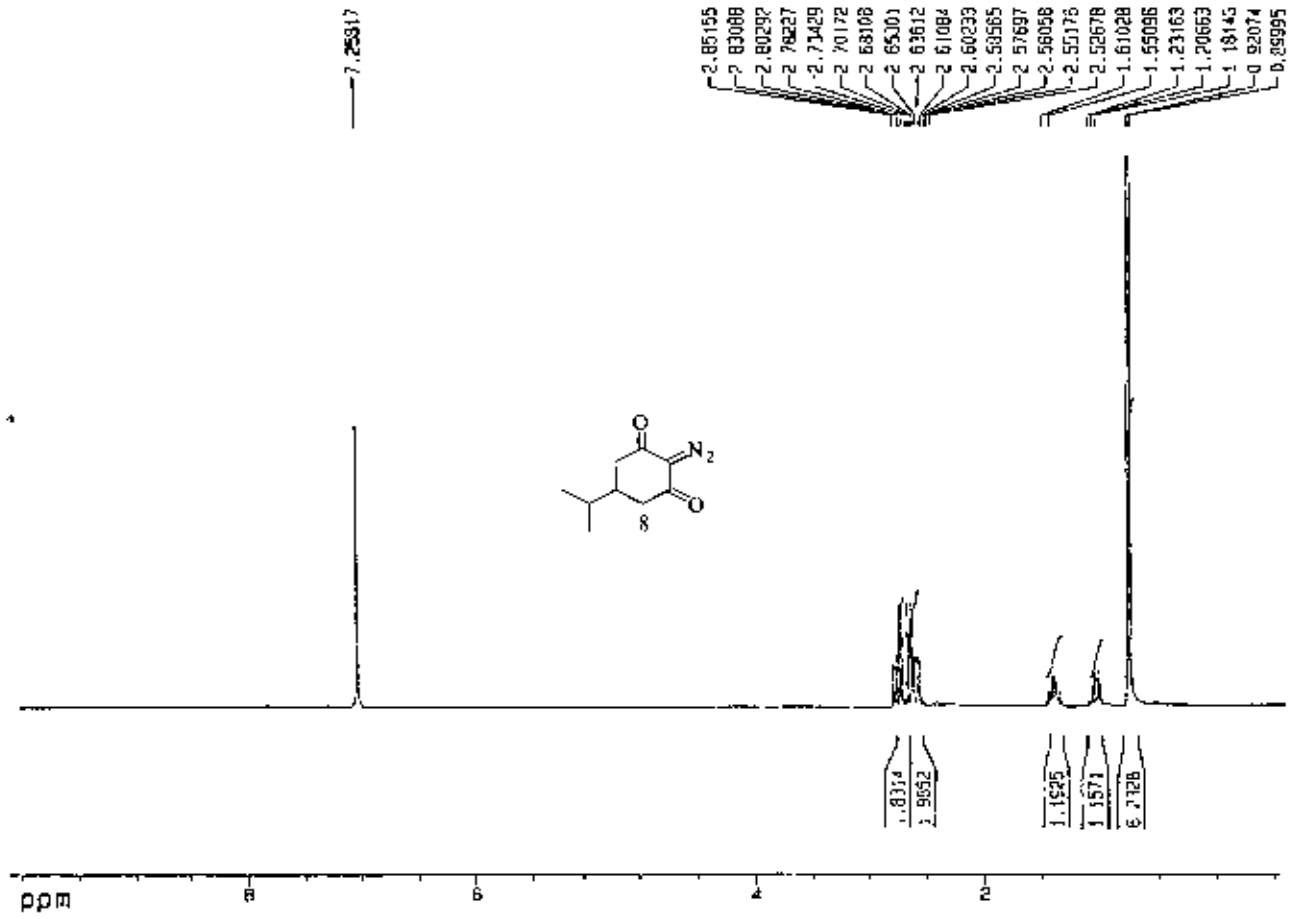


Figure 8b : IR spectrum of the compound **8**

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PROCNO                    1

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TD                    32768
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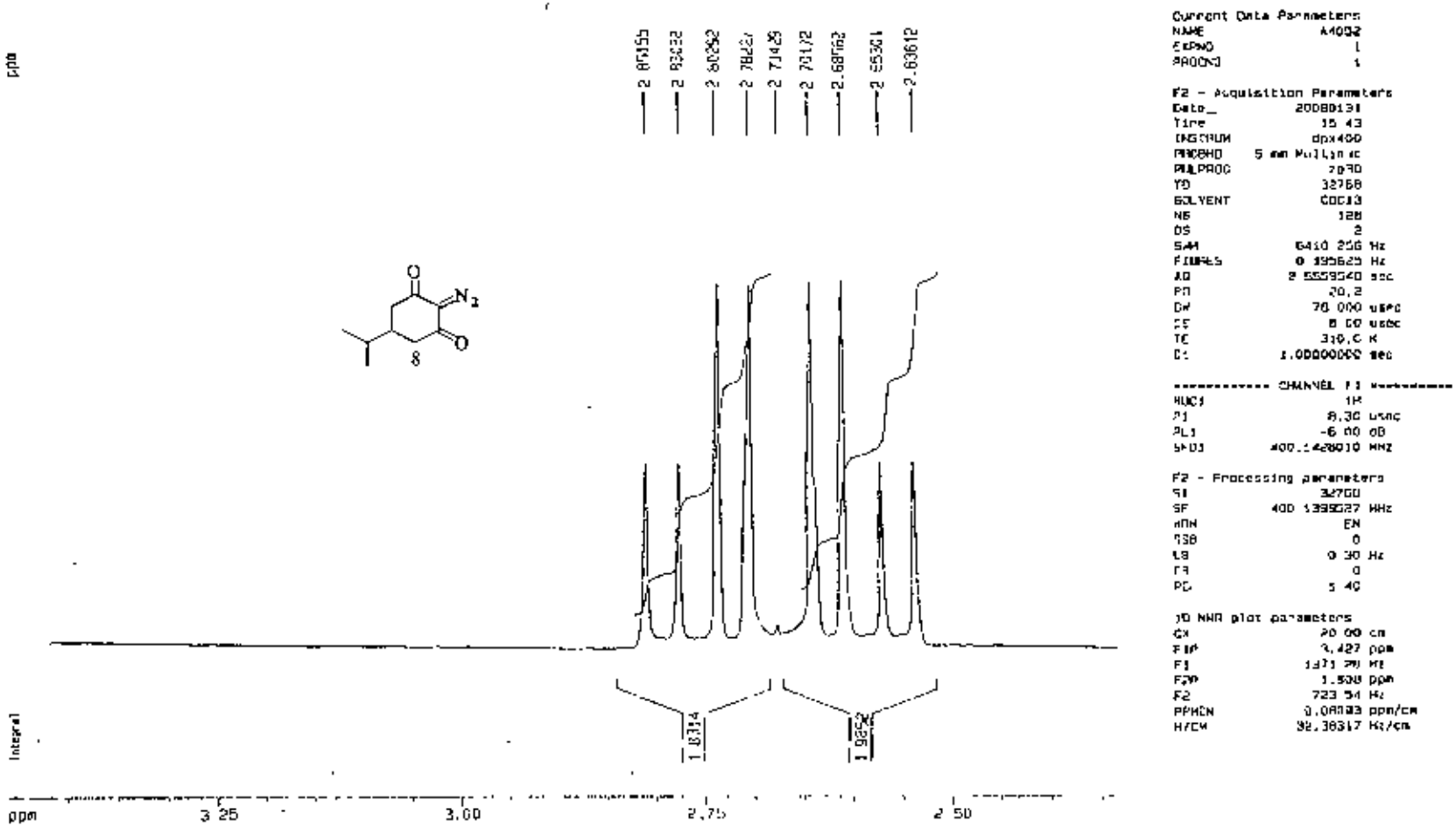
NS                      128
DS                        2
SWH               6410.256 Hz
FIDRES            0.195625 Hz
AQ                2.5559540 sec
RG                     20.2
DW                78.000 usec
DE                    6.00 usec
TE                   310.0 K
D1                1.00000000 sec

------------ CHANNEL f1 ------------
NUC1                      1H
P1                     8.30 usec
PL1                   -6.00 dB
SFO1            400.1428010 MHz

F2 - Processing parameters
SI                    32768
SF              400.1399527 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.40

1D NMR plot parameters
CX                    20.00 cm
F1P                   9.427 ppm
F1                 1371.20 Hz
F2P                   5.808 ppm
F2                  723.54 Hz
PPMCM              0.08093 ppm/cm
HZCM              32.38317 Hz/cm
```

Figure 8c: ^{1}H NMR spectrum of the compound **8**



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EXPNO 1
PROCNO 1

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Time 15 43
INSTRUM dpx400
PROBHD 5 mm Multinuc
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 128
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 20.2
DW 78.000 usec
DE 6.00 usec
TE 310.0 K
D1 1.00000000 sec

------------ CHANNEL f1 ------------
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P1 8.30 usec
PL1 -6.00 dB
SFO1 400.1428010 MHz

F2 - Processing parameters
SI 32768
SF 400.1300527 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 5.40

1D NMR plot parameters
CX 20.00 cm
F1P 9.427 ppm
F1 1371.79 Hz
F2P 1.538 ppm
F2 723.54 Hz
PPMCM 0.08883 ppm/cm
HZCM 32.38317 Hz/cm

Figure 8c: ^{1}H NMR spectrum of the compound **8**

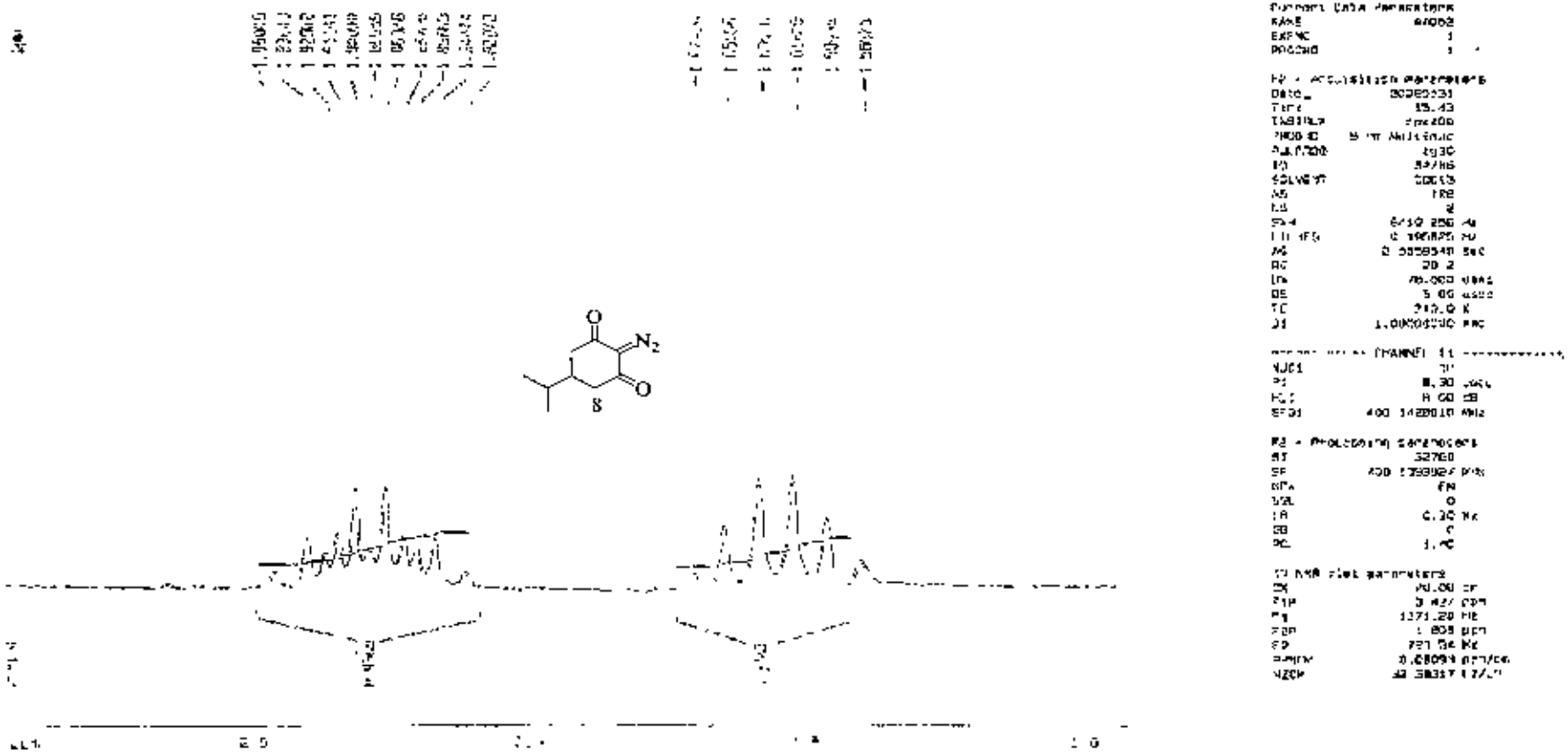


Figure 8c: 1H NMR spectrum of the compound **8**

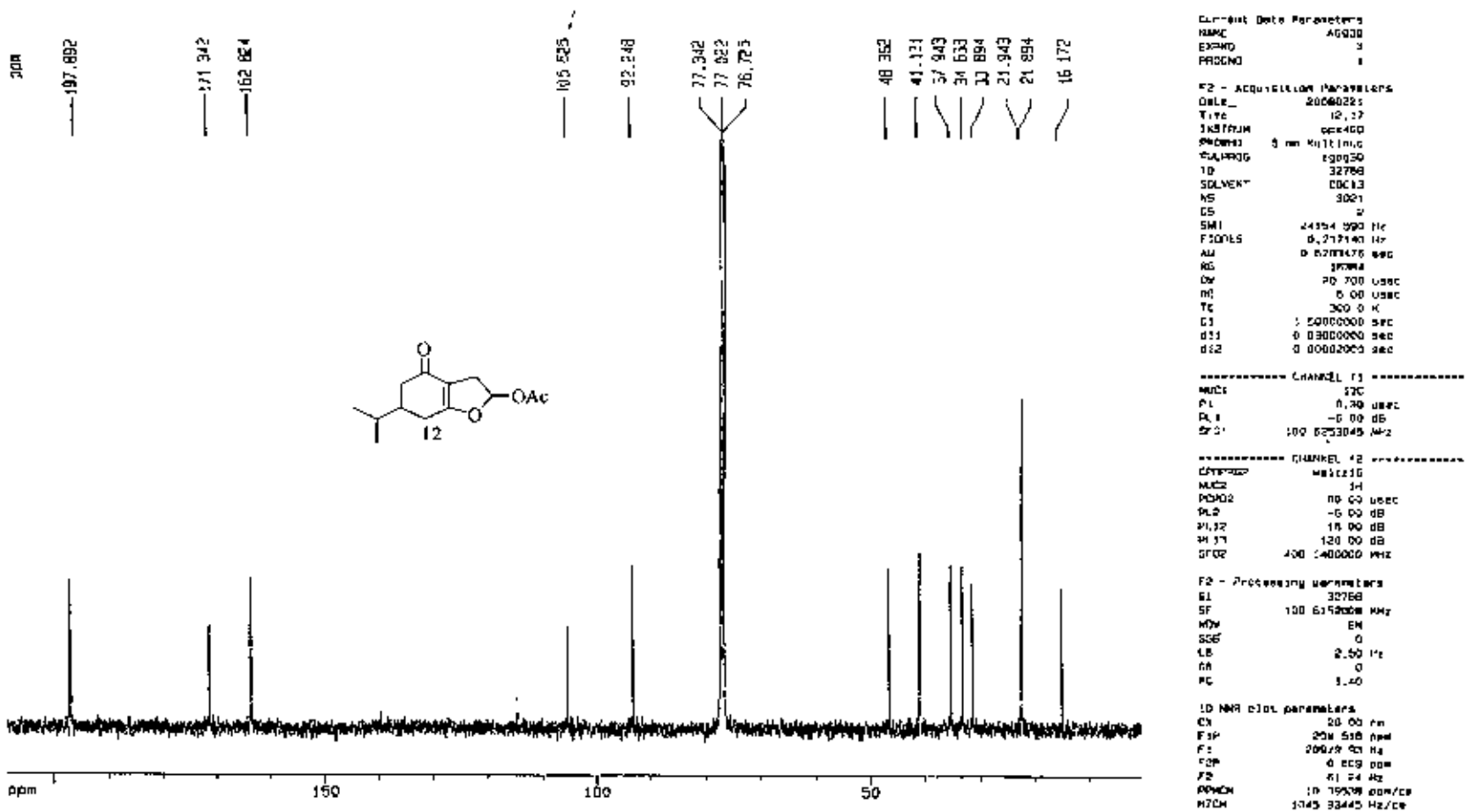
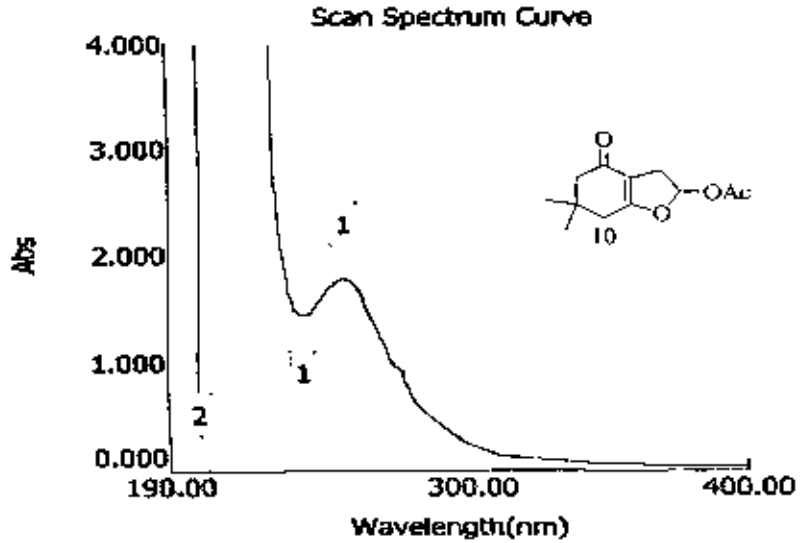


Figure 12d: ^{13}C NMR spectrum of the compound **12**



1	Peak	253.70	1.762
1	Valley	239.15	1.426
2	Valley	201.05	1.768

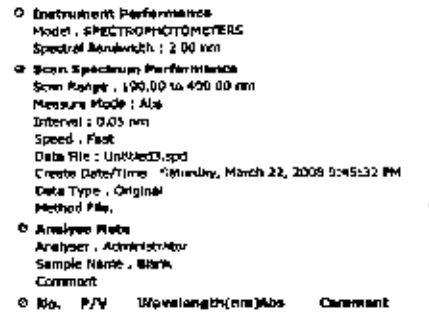


Figure 10a: UV spectrum of the compound **10**

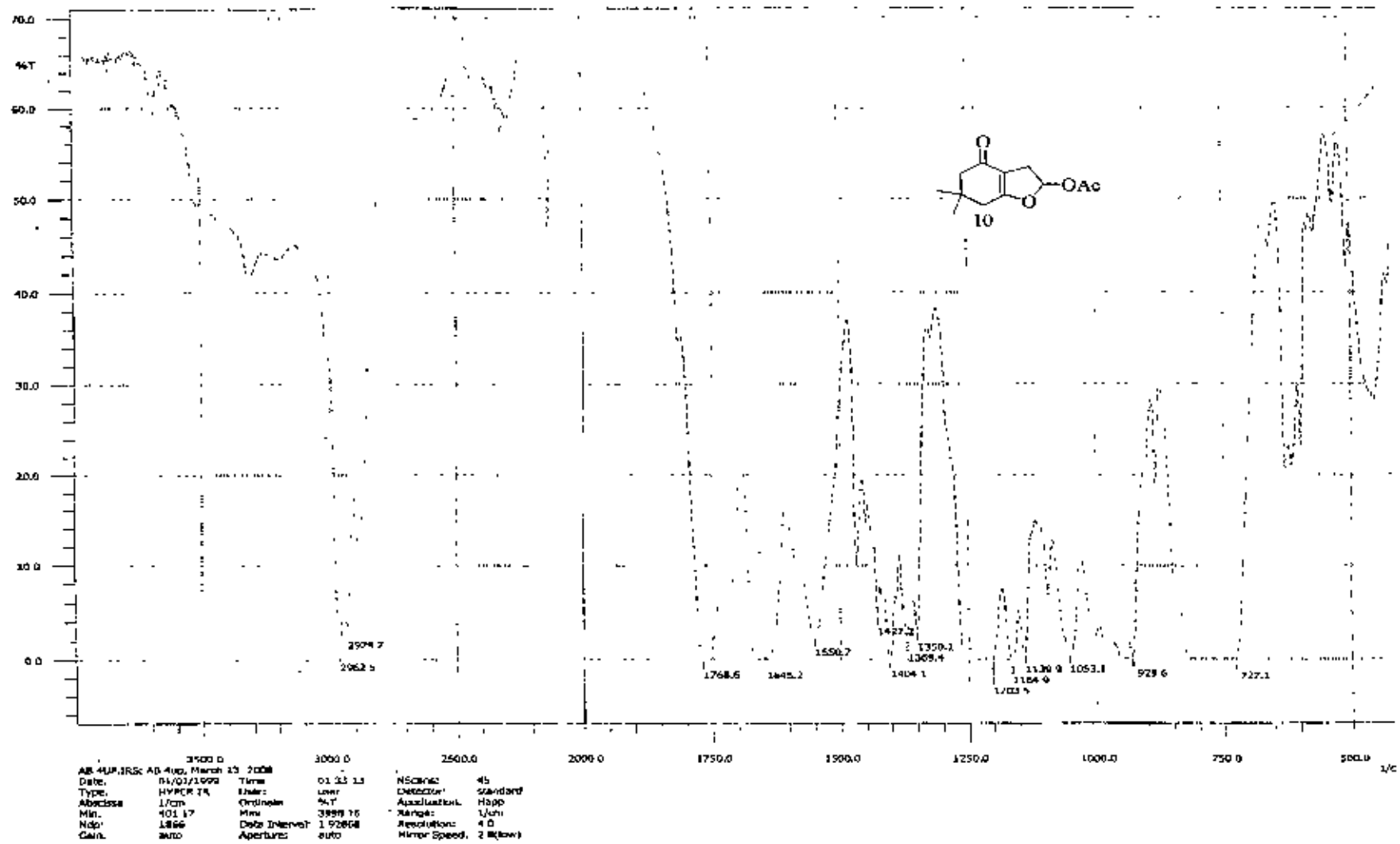
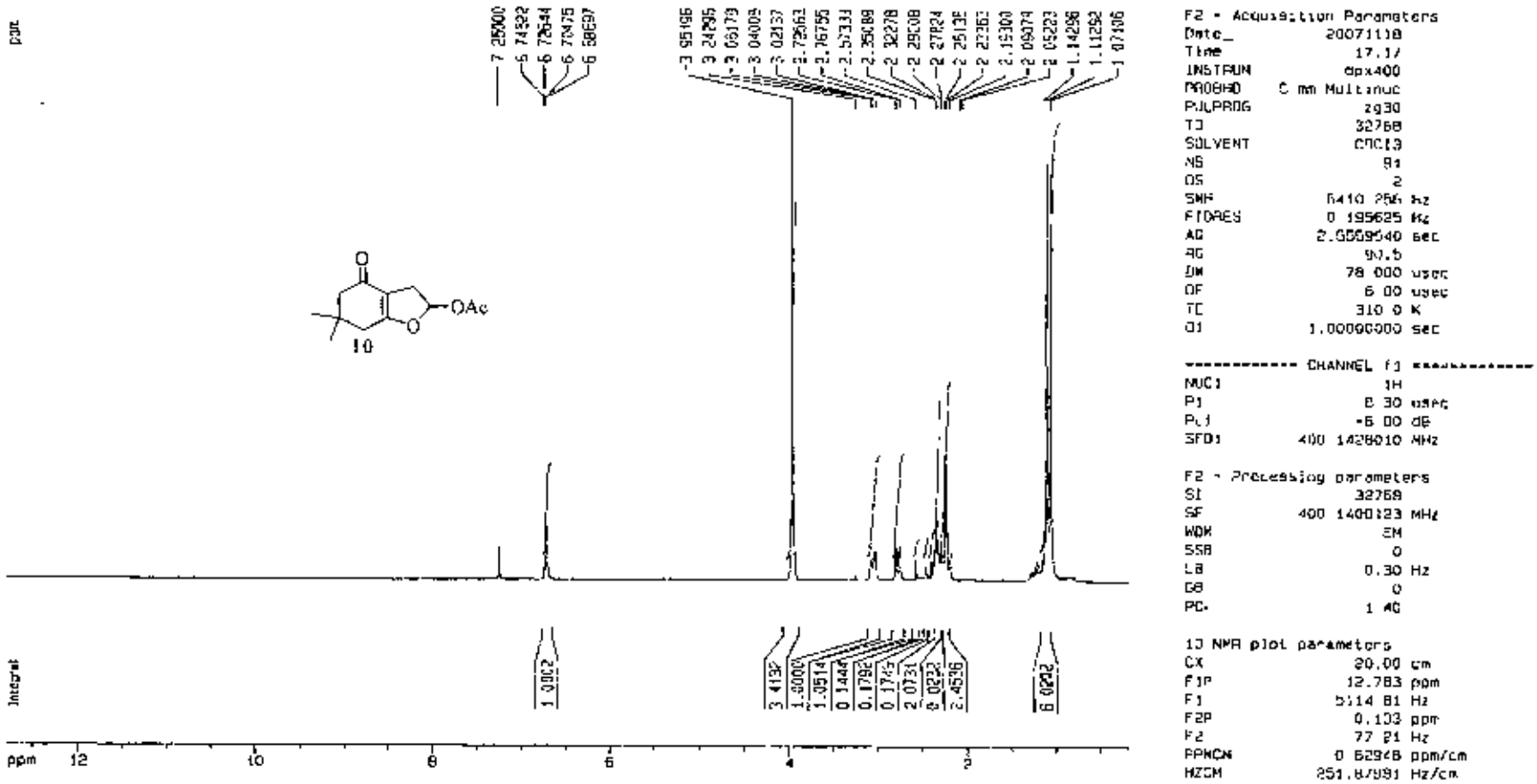


Figure 10b: IR spectrum of the compound **10**

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EXPNO                     1
PROCNO                    1

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PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                       64
DS                        2
SWH               8410.256 Hz
FIDRES            0.195625 Hz
AQ                2.0609540 sec
RG                     90.5
DW                  78.000 usec
DE                   6.00 usec
TE                  310.0 K
D1                1.00000000 sec

------------ CHANNEL f1 ============
NUC1                    1H
P1                   8.30 usec
PL1                 -6.00 dB
SFO1          400.1428010 MHz

F2 - Processing parameters
SI                    32768
SF          400.1400123 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                  12.783 ppm
F1                  5114.81 Hz
F2P                   0.103 ppm
F2                   77.21 Hz
PPMCM             0.62948 ppm/cm
HZCM              251.87981 Hz/cm
```

Figure 10c: ^{1}H NMR spectrum of the compound **10**

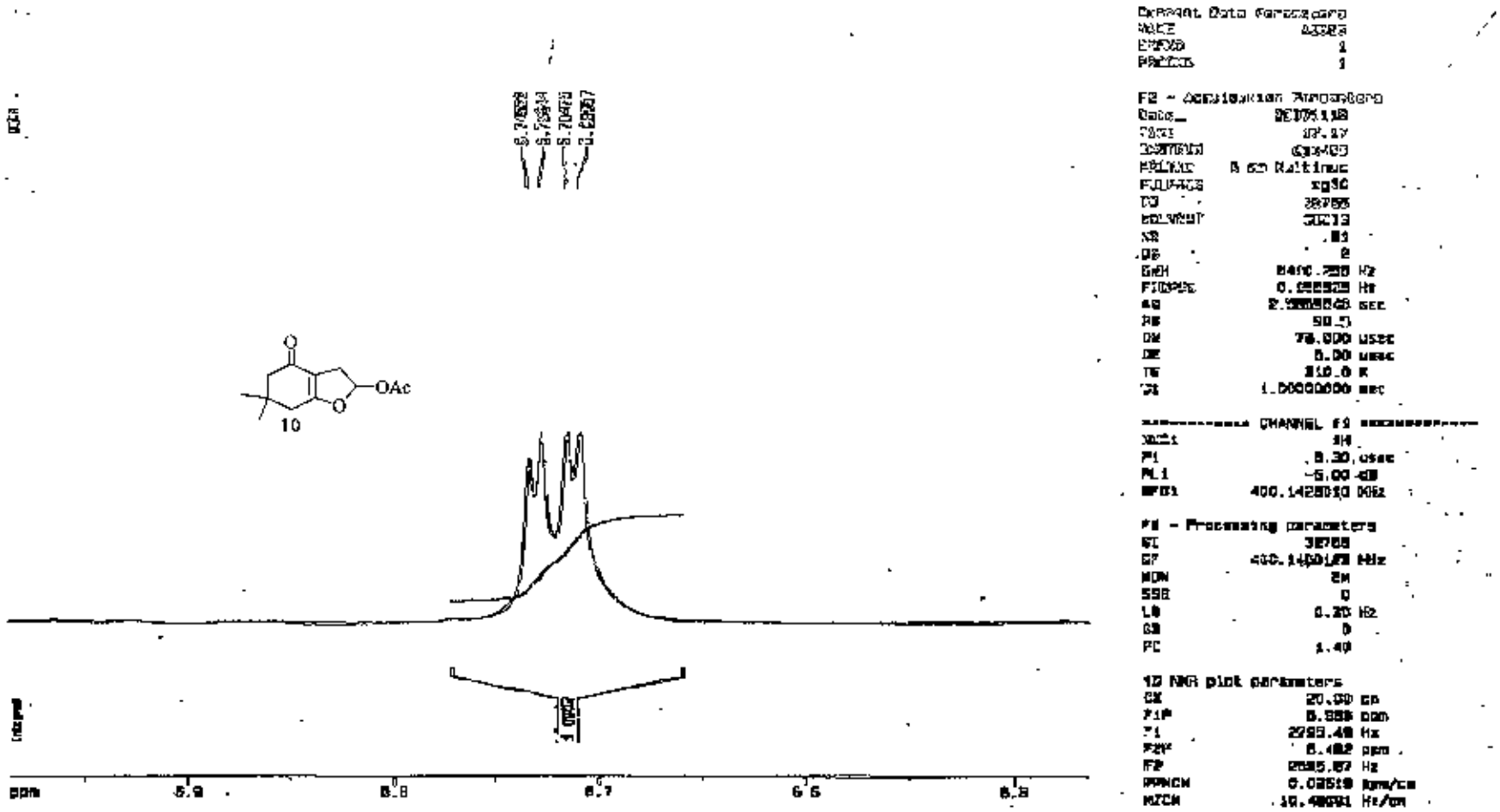


Figure 10c: ^{1}H NMR spectrum of the compound **10**

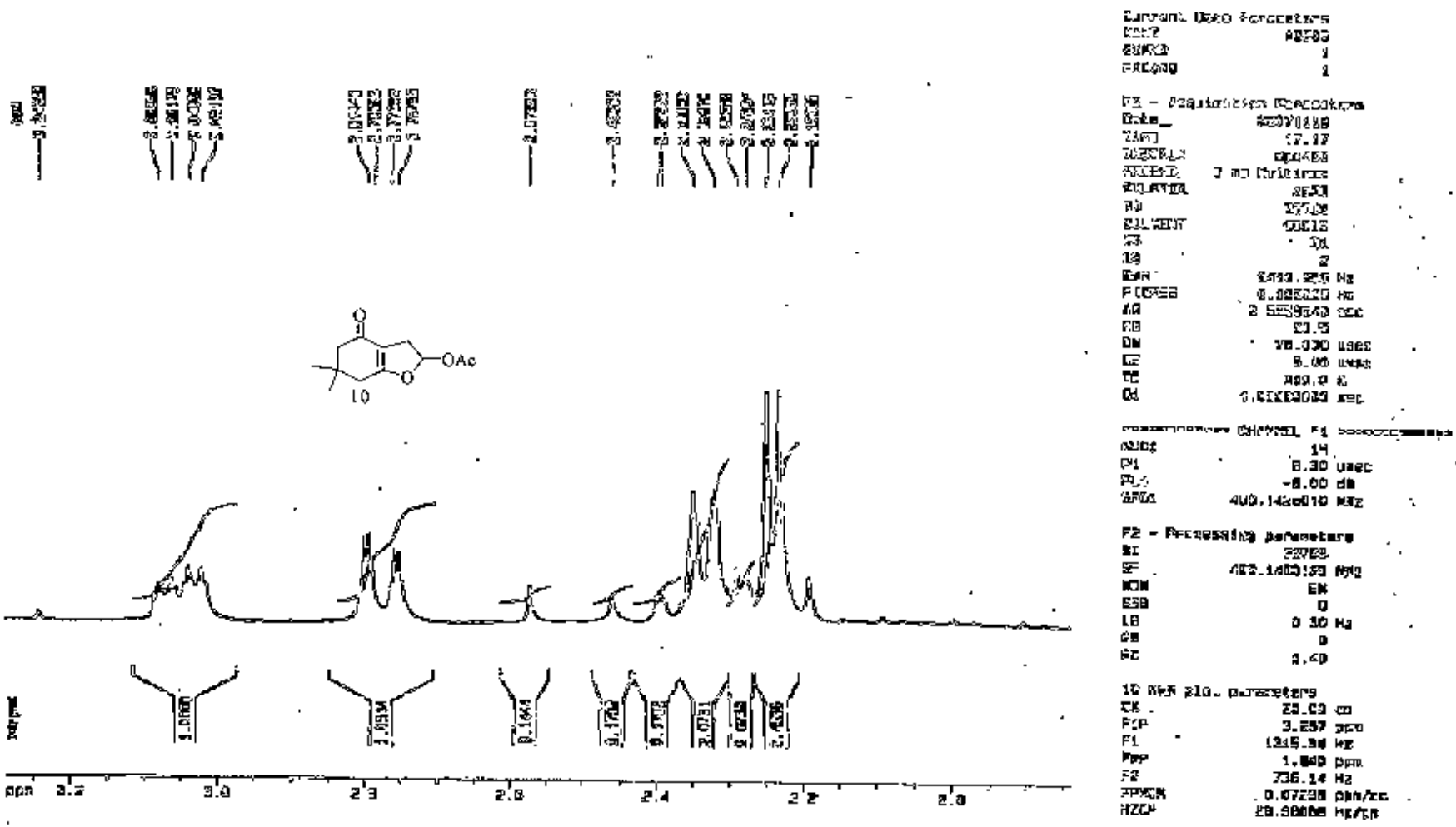


Figure 10c: ^{1}H NMR spectrum of the compound **10**

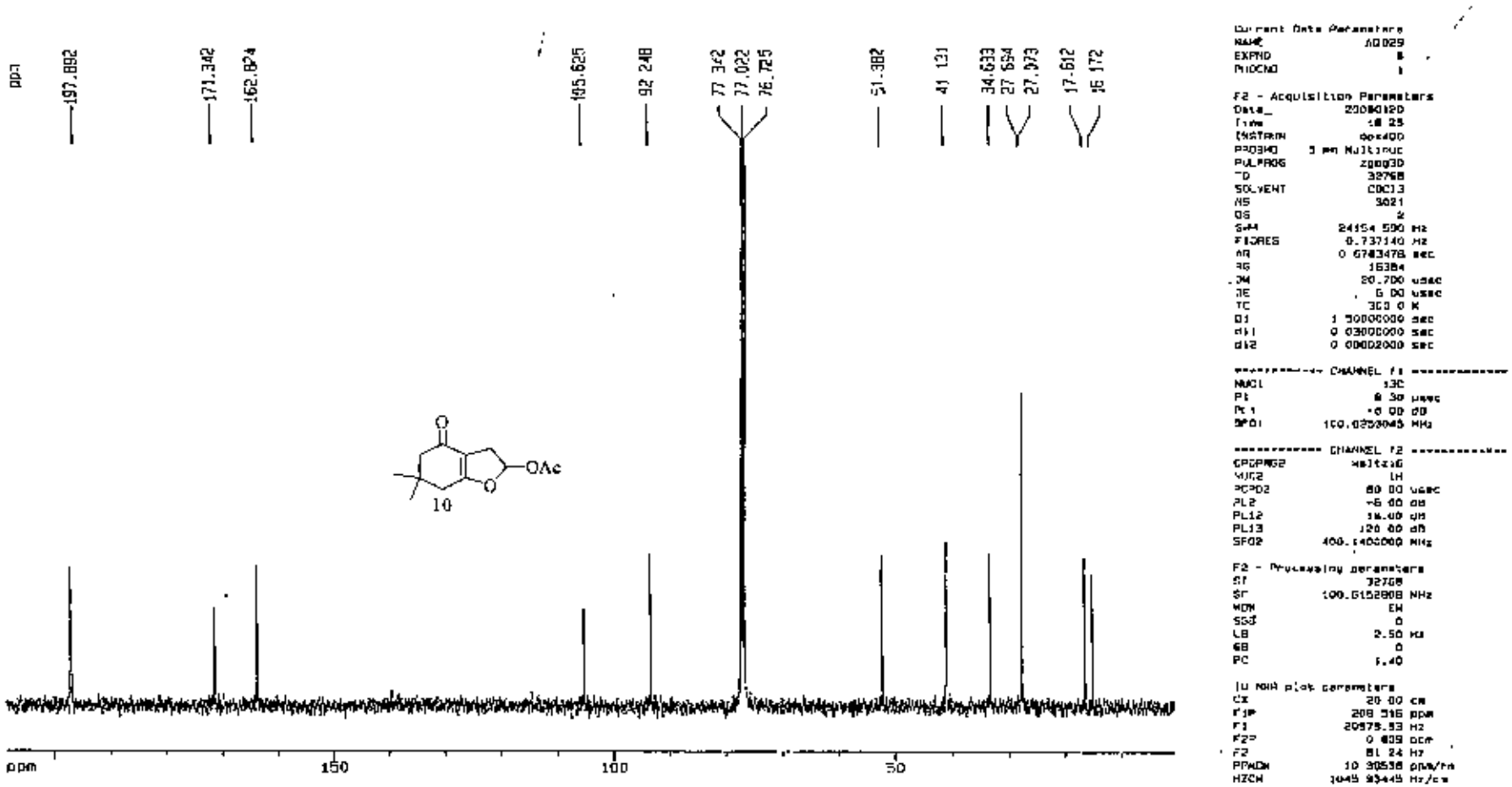
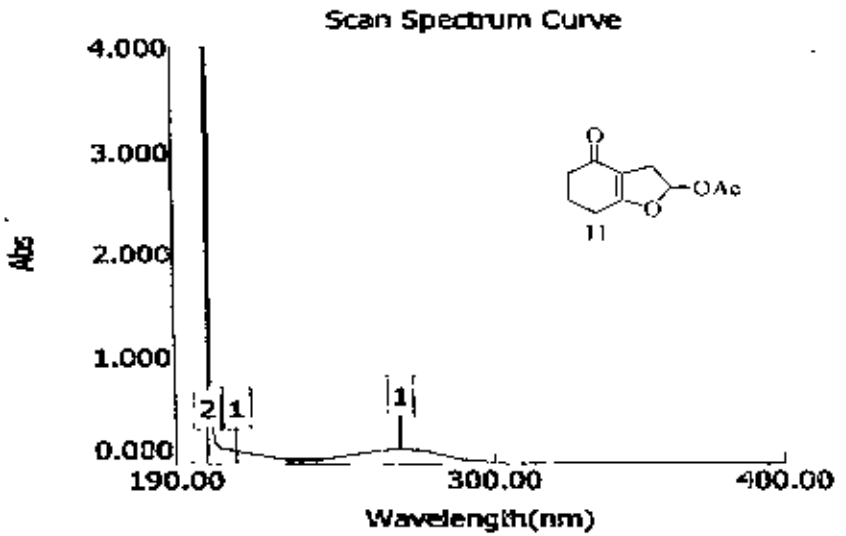


Figure 10d: ^{13}C NMR spectrum of the compound **10**



1	Peak	260.75	0.066
1	Valley	211.05	-0.229
2	Valley	201.05	-1.190

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Data Type : Original
Method File :

Analyse Note
Analyser : Administrator
Sample Name : Blank
Comment :

No.	P/V	Wavelength(nm)	Abs	Comment

Figure 11a :UV spectrum of the compound **11**

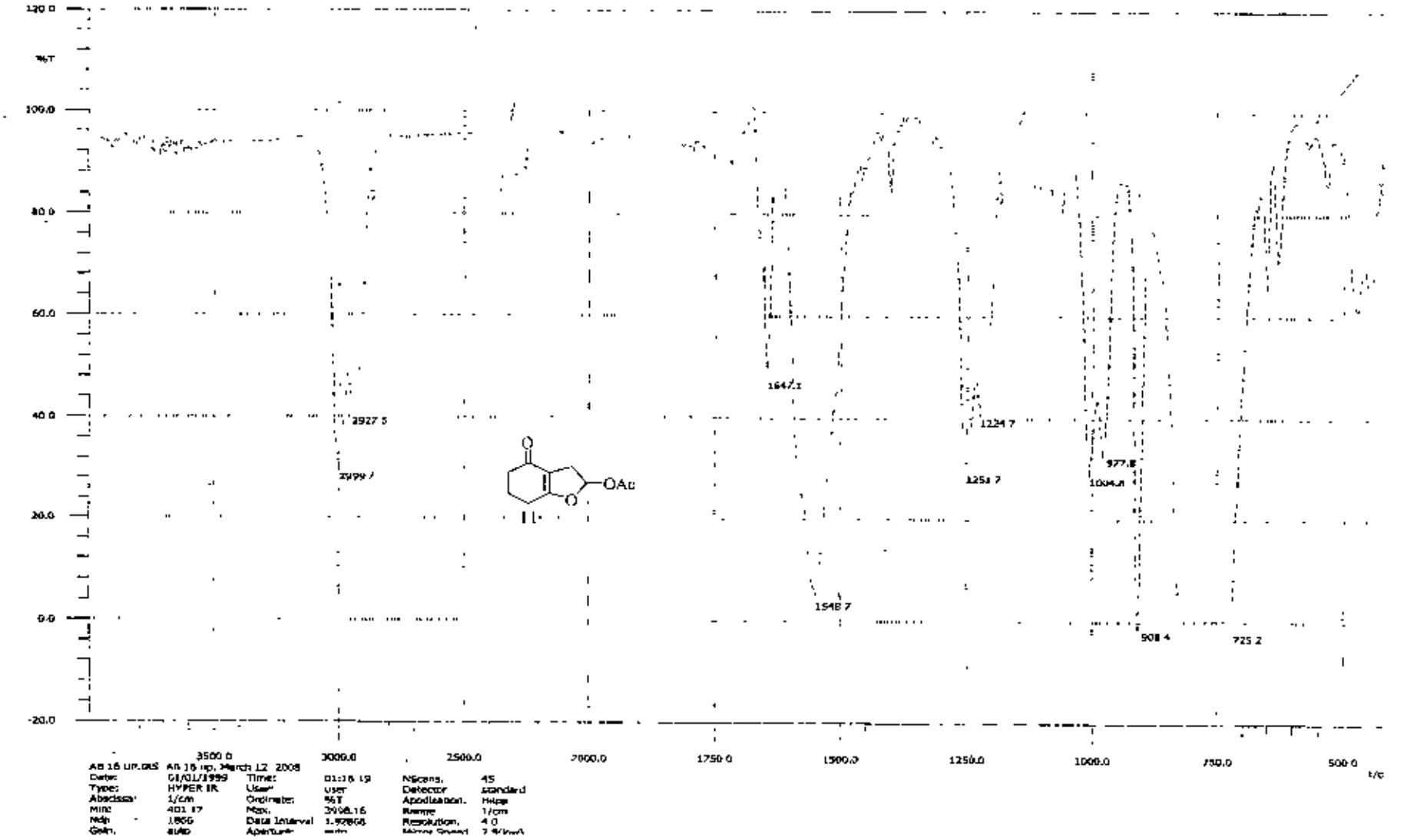
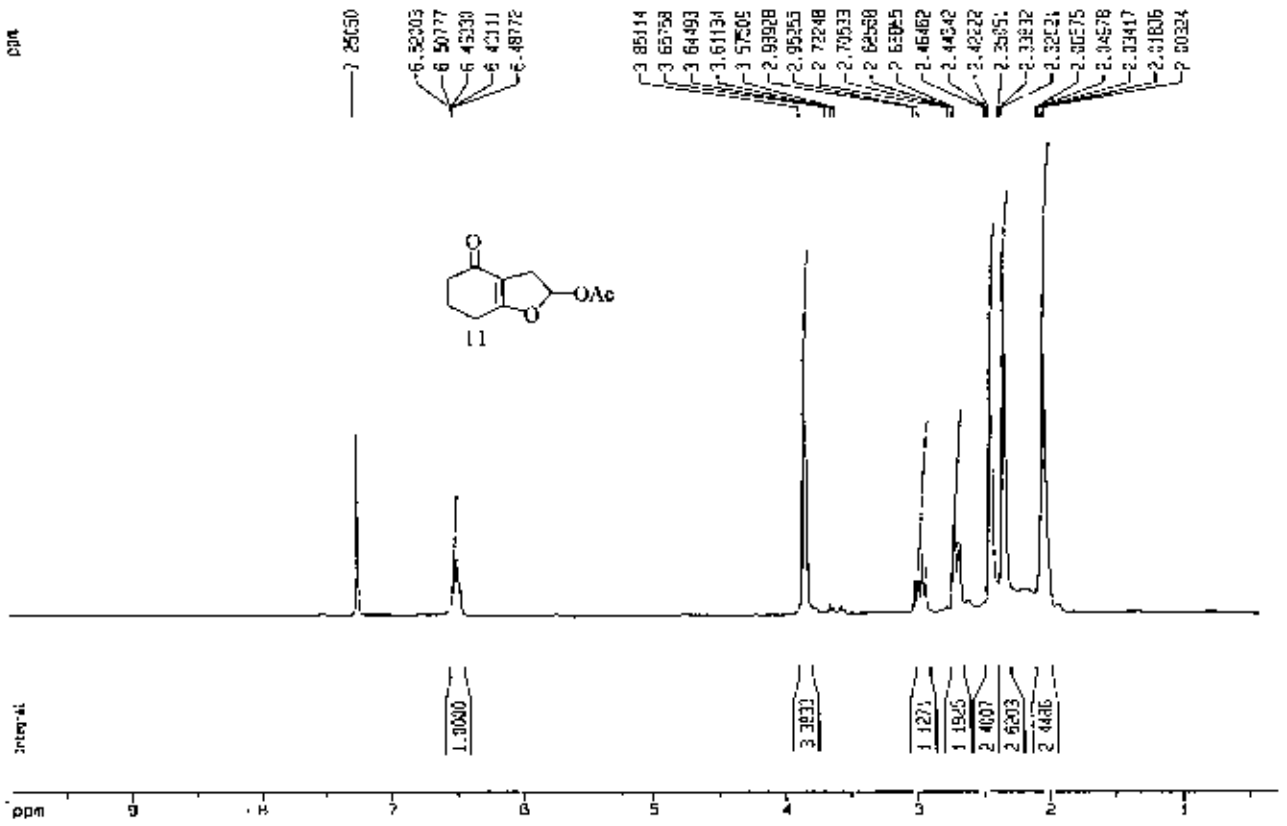


Figure 11b: IR spectrum of the compound **11**

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EXPNO                    1
PROCNO                   1

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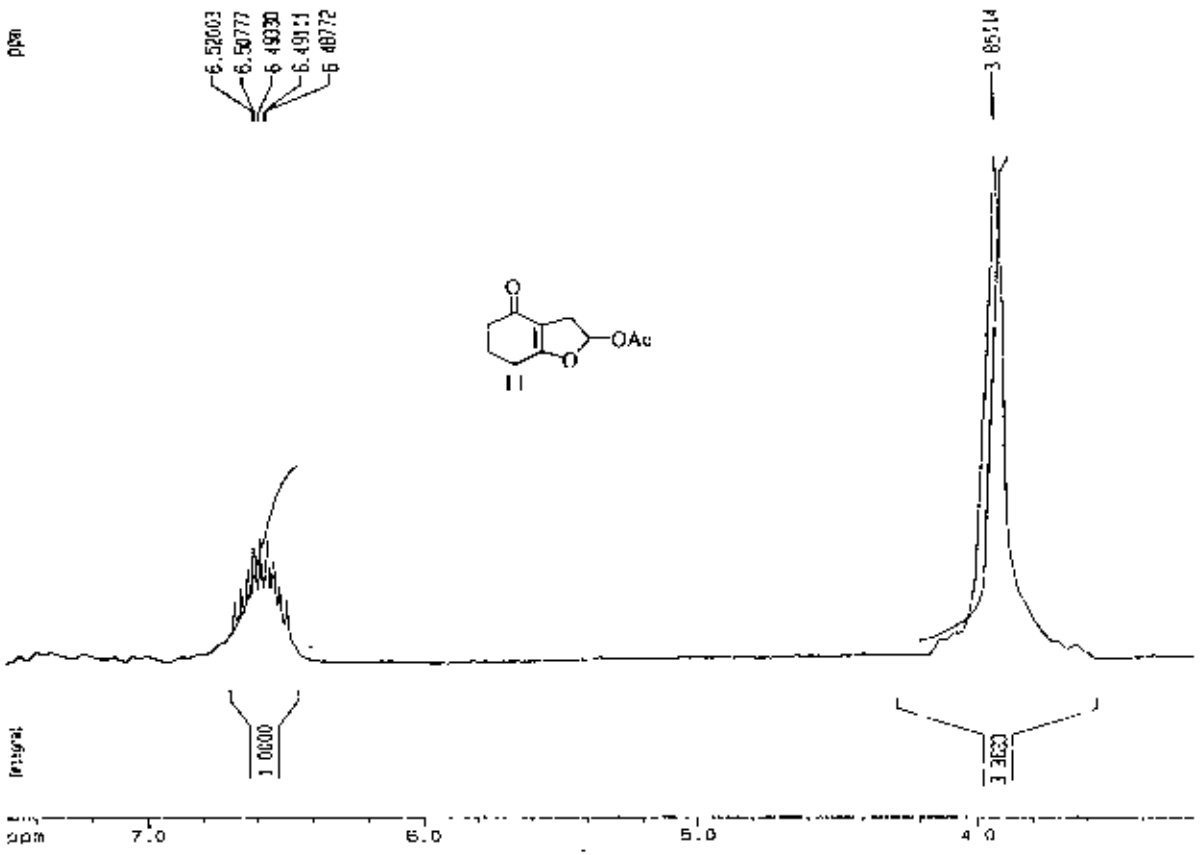
PROBHD     5 mm Multinuc
PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                    104
DS                      2
SWH              6410.256 Hz
FIDRES           0.195625 Hz
AQ               2.5559540 sec
RG                  203.2
DW                 78.000 usec
DE                  6.00 usec
TE                 310.0 K
D1              1.00000000 sec

------------- CHANNEL f1 -------------
NUC1                  1H
P1                 8.30 usec
PL1                -6.00 dB
SFO1         400.1428010 MHz

F2 - Processing parameters
SI                  32768
SF           400.1400126 MHz
WDW                    EM
SSB                     0
LB                  0.30 Hz
GB                      0
PC                   1.40

1D NMR plot parameters
CX                  20.00 cm
F1P                 9.926 ppm
F1                3971.61 Hz
F2P                 0.209 ppm
F2                 83.63 Hz
PPMCM              0.48183 ppm/cm
HZCM             192.79900 Hz/cm
```

Figure 11c: ^{1}H NMR spectrum of the compound **11**

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Current Data Parameters
NAME                  A4099
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
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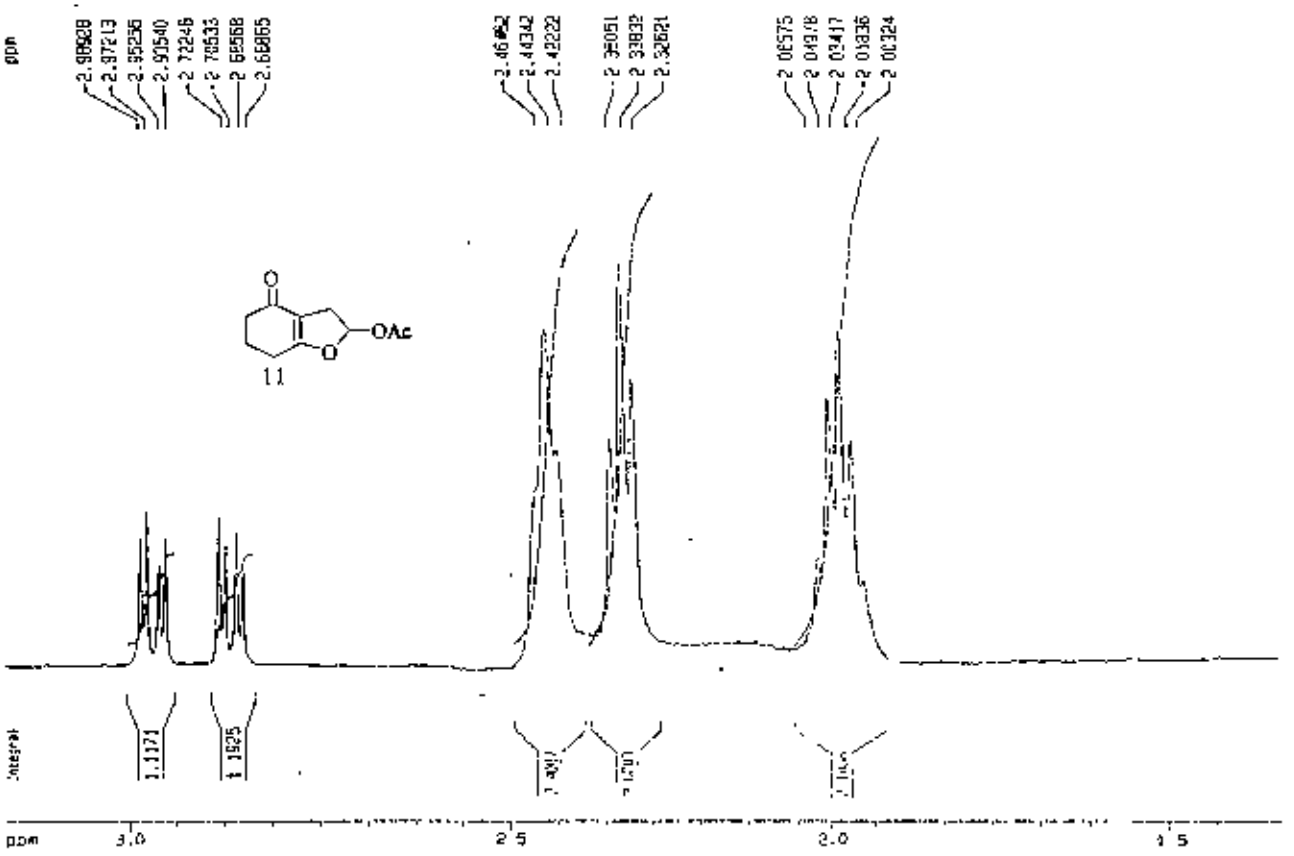
Time                 17.19
INSTRUM              dpx400
PROBHD     5 mm Multinuc
PULPROG              zg30
TD                  32768
SOLVENT              CDCl3
NS                     104
DS                       2
SWH              6410.256 Hz
FIDRES           0.195625 Hz
AQ               2.5559540 sec
RG                   203.2
DW                  78.000 usec
DE                   6.00 usec
TE                  310.0 K
D1               1.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                   8.30 usec
PL1                 -6.00 dB
SFO1          400.1420010 MHz

F2 - Processing parameters
SI                  32768
SF            400.1400126 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.40

1D NMR plot parameters
CX                  20.00 cm
F1P                 9.926 ppm
F1                3971.61 Hz
F2P                 0.289 ppm
F2                 115.63 Hz
PPMCM             0.49183 ppm/cm
HZCM            192.79900 Hz/cm
```

Figure 11c: ^{1}H NMR spectrum of the compound **11**

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EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
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Time                  17.19
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PROBHD     5 mm Multinuc
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                      104
DS                        2
SWH                6410.256 Hz
FIDRES             0.195625 Hz
AQ                 2.5559540 sec
RG                     203.2
DW                  78.000 usec
DE                   6.00 usec
TE                   310.0 K
D1                1.00000000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                     8.30 usec
PL1                   -6.00 dB
SFO1          400.1428010 MHz

F2 - Processing parameters
SI                    32768
SF            400.1400126 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.40

1D NMR plot parameters
CX                    20.00 cm
F1P                   9.926 ppm
F1                  3971.61 Hz
F2P                   0.289 ppm
F2                   115.89 Hz
PPMCM              0.48183 ppm/cm
HZCM             192.79900 Hz/cm
```

Figure 11e: ^{1}H NMR spectrum of the compound **11**

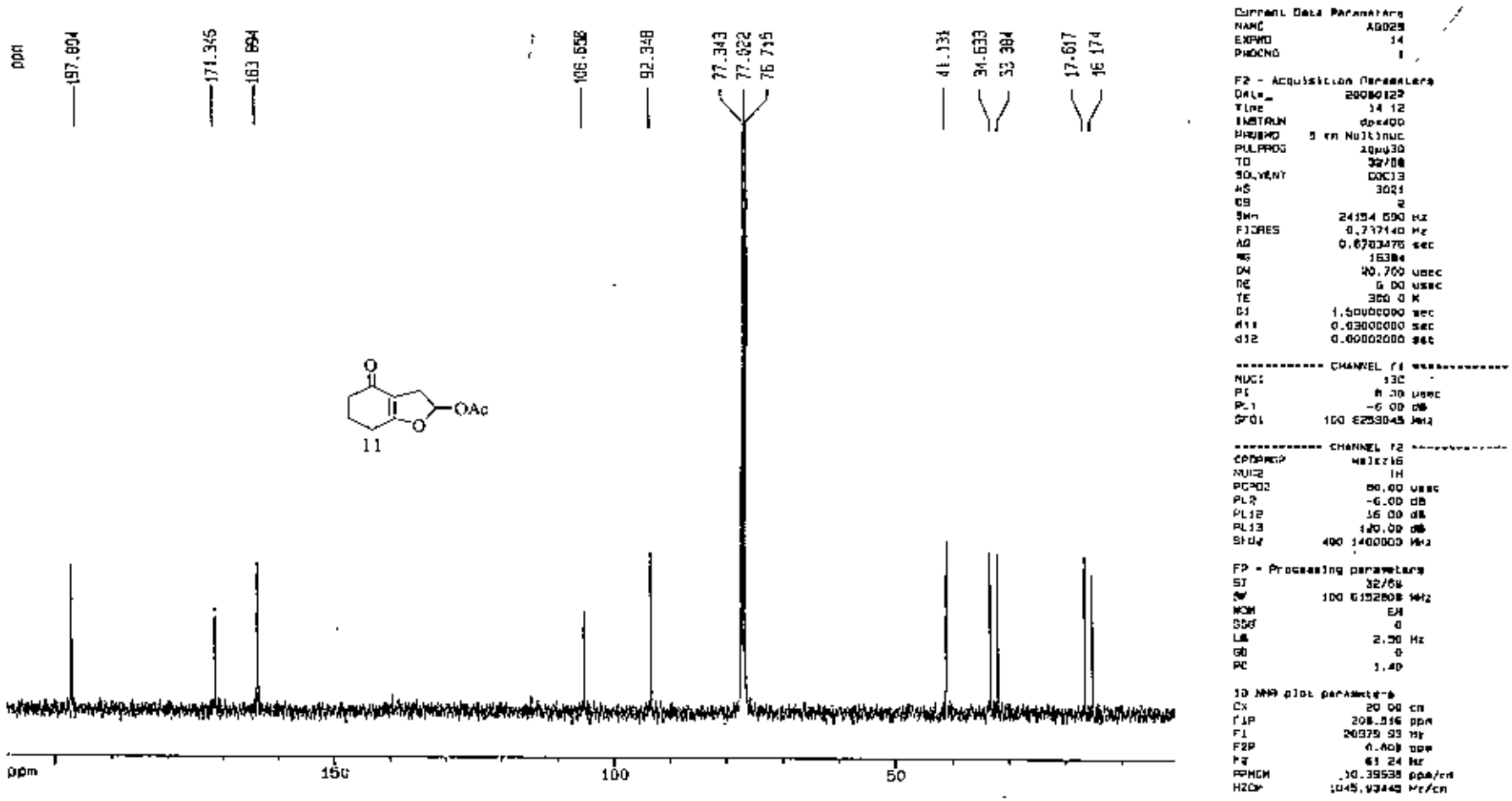
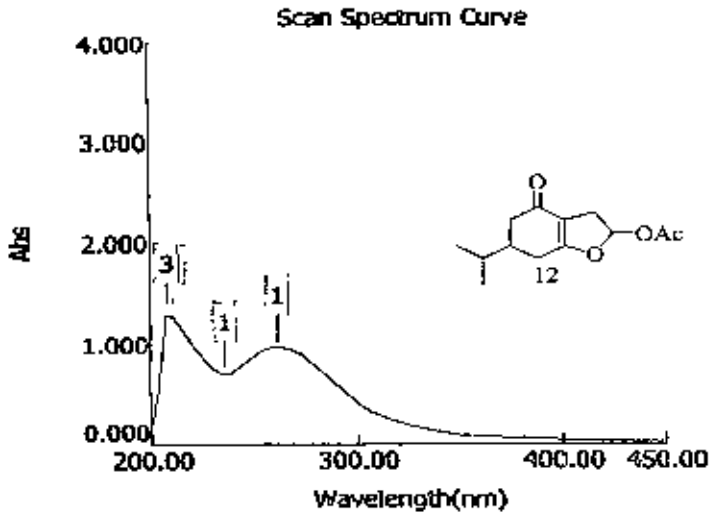


Figure 11d: ^{13}C NMR spectrum of the compound **11**



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  - Measure Mode : Abs
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  - Speed : Fast
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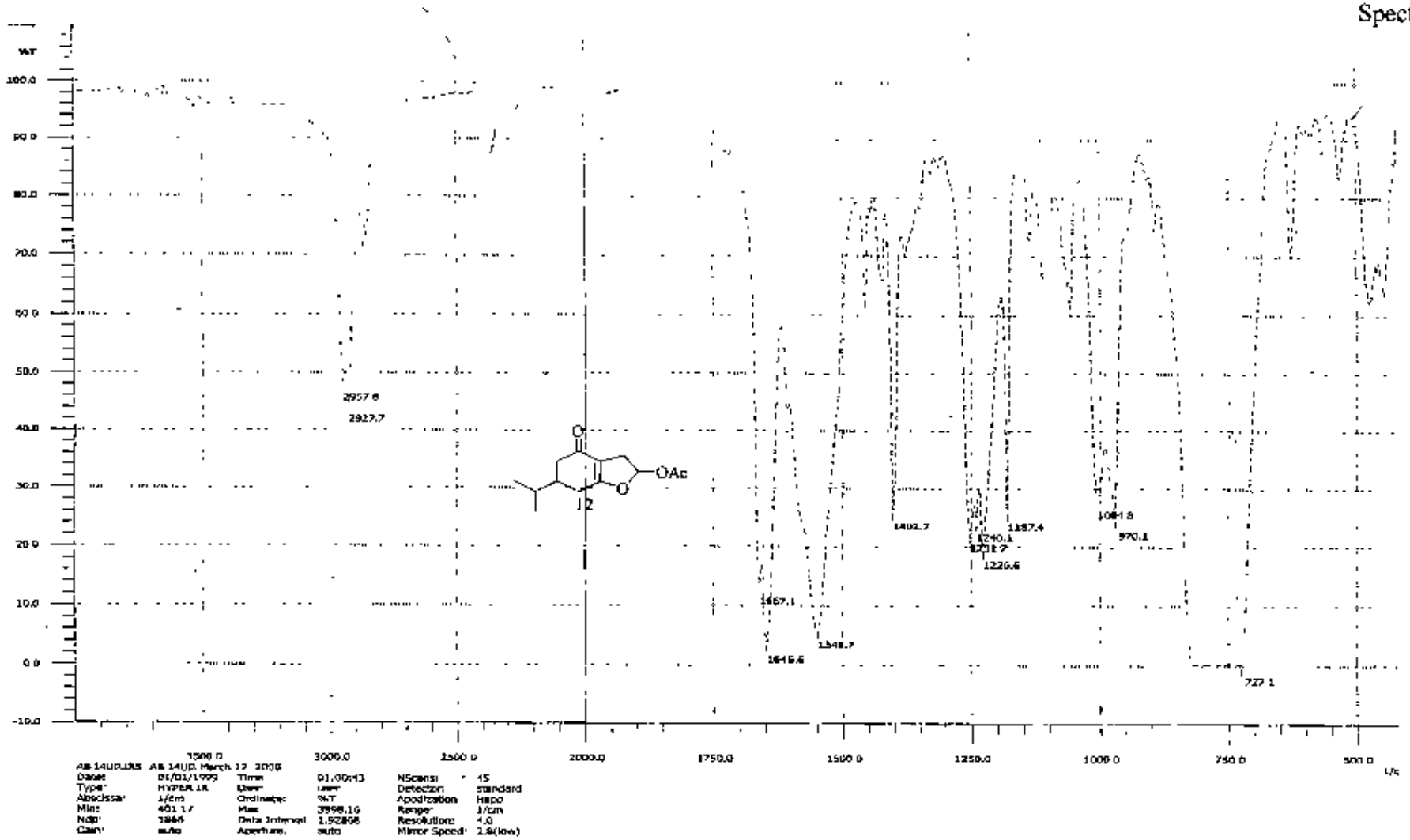
- Analyse Note
  - Analyser : Administrator
  - Sample Name : Blank
  - Comment :

No.	P/V	Wavelength(nm)	Abs	Comment
1	Peak	261.75	0.966	
2	Peak	211.10	1.265	
3	Peak	208.05	1.282	
1	Valley	236.10	0.706	

Figure 12a :UV spectrum of the compound **12**



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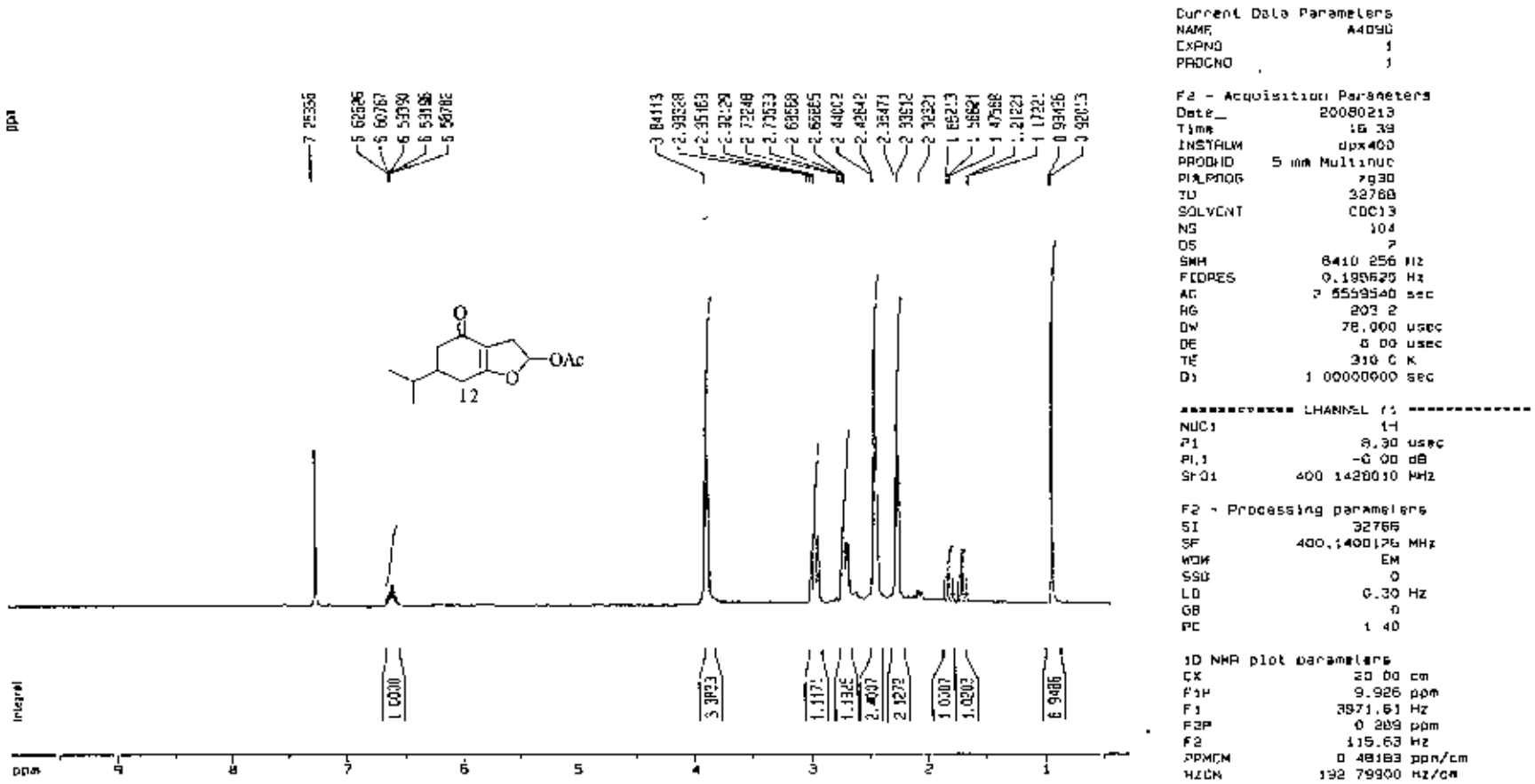
Abscissa:	1/cm	Ordinate:	%T	Apodization	Happ
Min:	401.17	Max:	3998.16	Range:	1/cm
Ndp:	1868	Data Interval	1.92868	Resolution:	4.0
Gain:	auto	Aperture:	auto	Mirror Speed:	2.8(low)

Figure 12b: IR spectrum of the compound **12**

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PROCNO                   1

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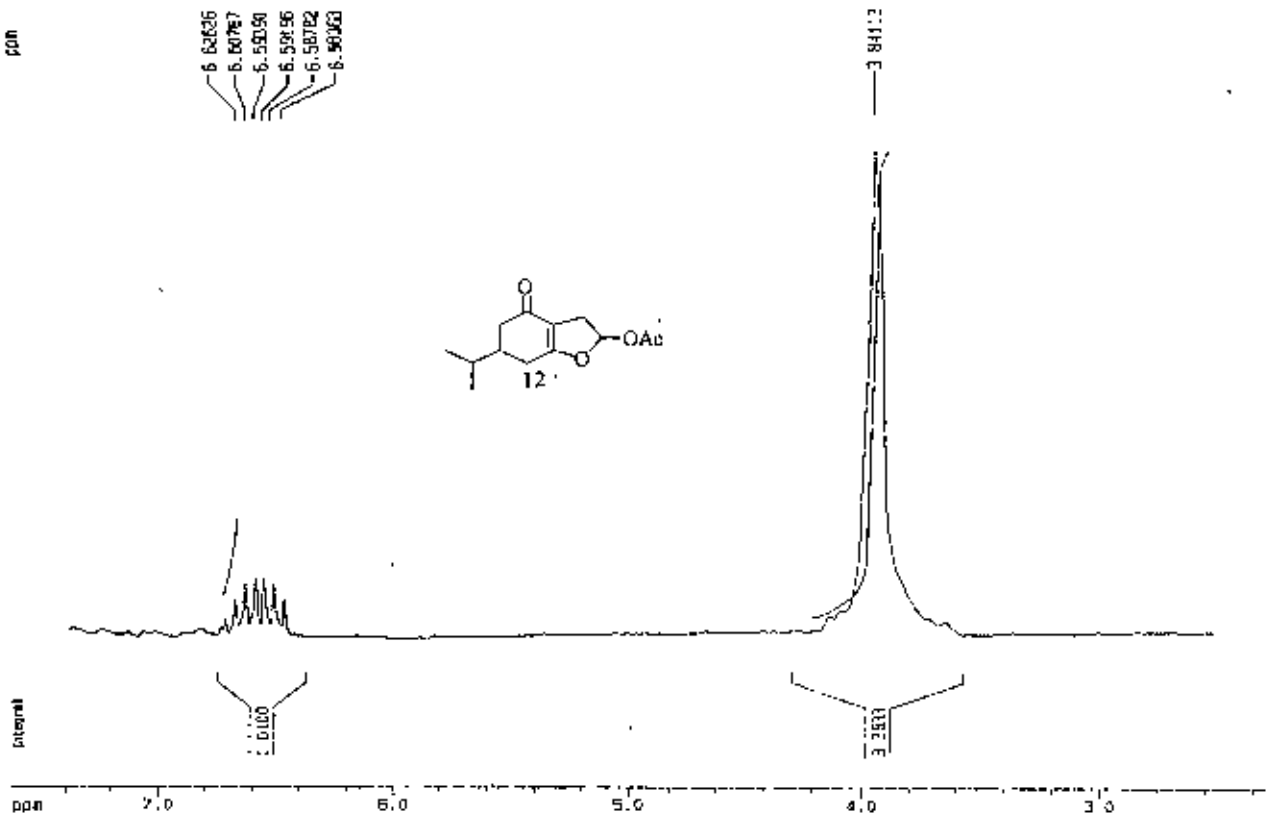
PROBHD     5 mm Multinuc
PULPROG            zg30
TD                 32768
SOLVENT            CDCl3
NS                 104
DS                 2
SWH              8410.256 Hz
FIDRES           0.195625 Hz
AQ               2.8559540 sec
RG                 203.2
DW                 78.000 usec
DE                 6.00 usec
TE                 310.0 K
D1               1.00000000 sec

========== CHANNEL f1 ============
NUC1                   1H
P1                   8.30 usec
PL1                 -0.00 dB
SFO1          400.1428010 MHz

F2 - Processing parameters
SI                 32768
SF            400.1400176 MHz
WDW                    EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.40

1D NMR plot parameters
CX                 20.00 cm
F1P                9.926 ppm
F1                3971.61 Hz
F2P                0.209 ppm
F2                 115.63 Hz
PPMCM              0.48183 ppm/cm
HZCM             192.79900 Hz/cm
```

Figure 12c: ^{1}H NMR spectrum of the compound **12**

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EXPNO                     1
PROCNO                    1

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PROBHD     5 mm Multinuc
PULPROG               zg30
TD                   32768
SOLVENT              CDCl3
NS                     104
DS                       2
SWH               6410.256 Hz
FIDRES            0.195625 Hz
AQ                2.5559540 sec
RG                    203.2
DW                   78.000 usec
DE                    6.00 usec
TE                   310.0 K
D1                1.00000000 sec

------------ CHANNEL f1 ------------
NUC1                    1H
P1                    8.30 usec
PL1                  -8.00 dB
SFO1           400.1428010 MHz

F2 - Processing parameters
SI                   32768
SF             400.1400126 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                   9.926 ppm
F1                 3971.61 Hz
F2P                   0.289 ppm
F2                  115.63 Hz
PPMCM                0.48183 ppm/cm
HZCM               192.79900 Hz/cm
```

Figure 12c: 1H NMR spectrum of the compound **12**

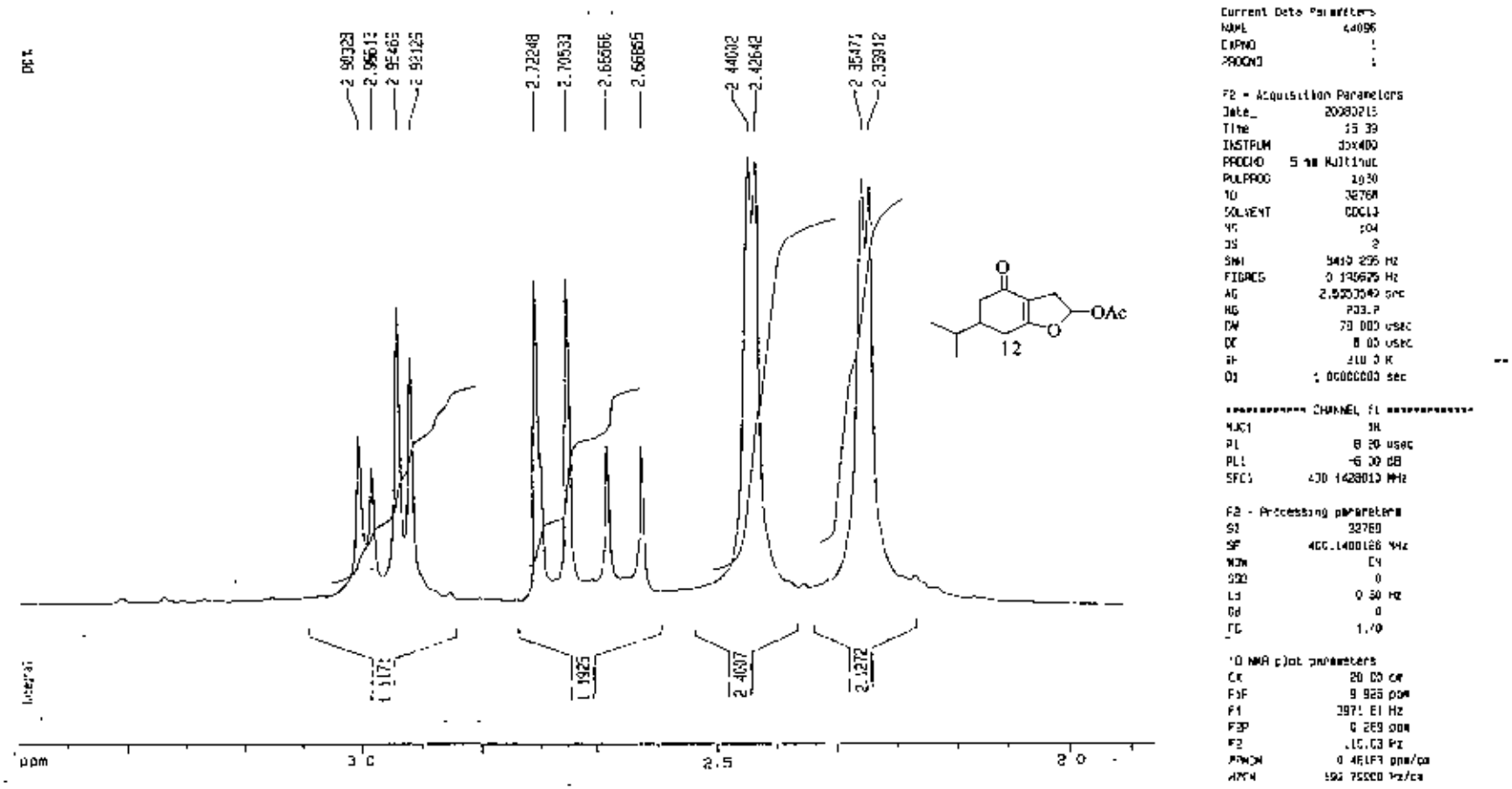


Figure 12c: 1H NMR spectrum of the compound **12**

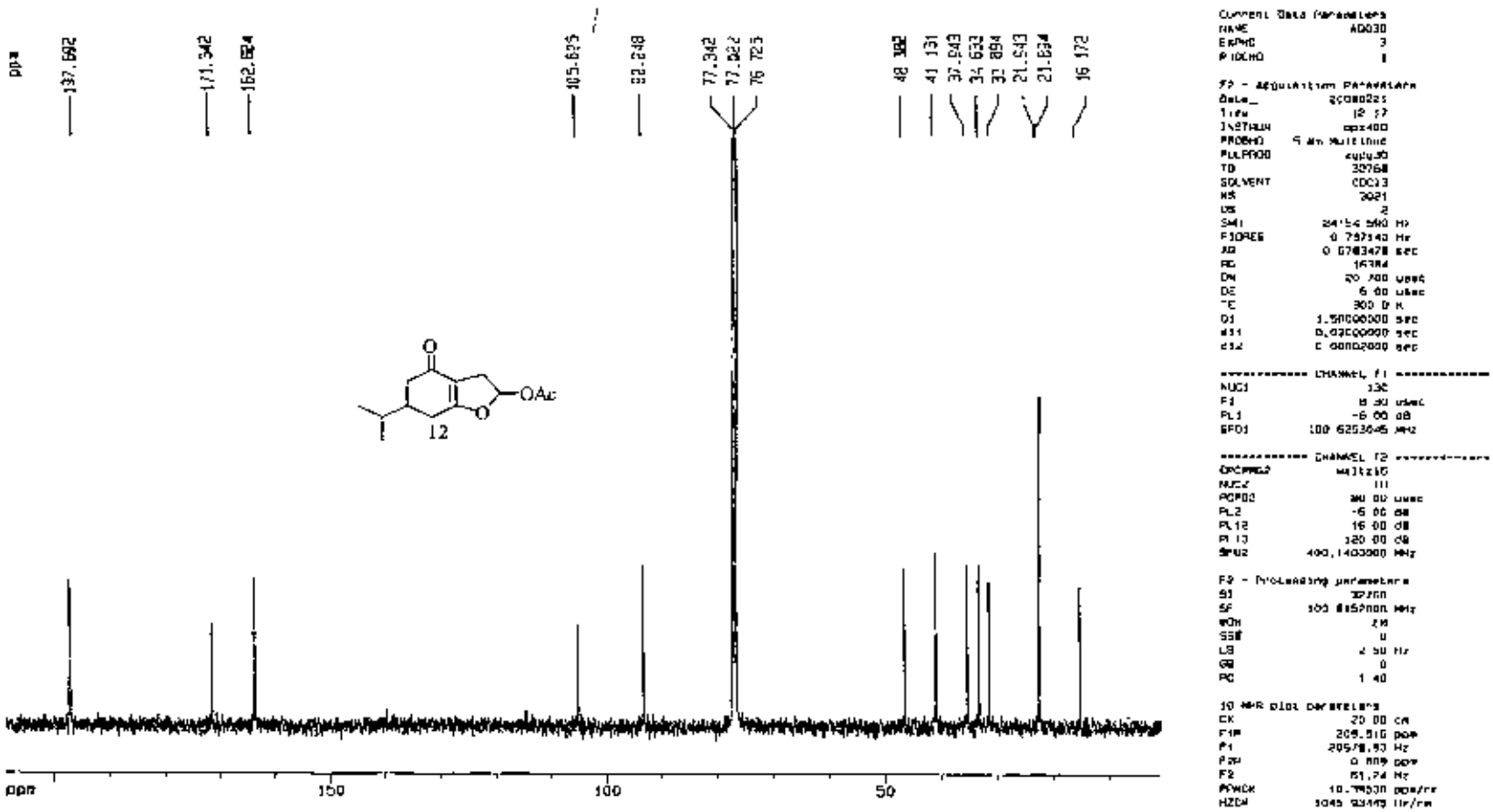
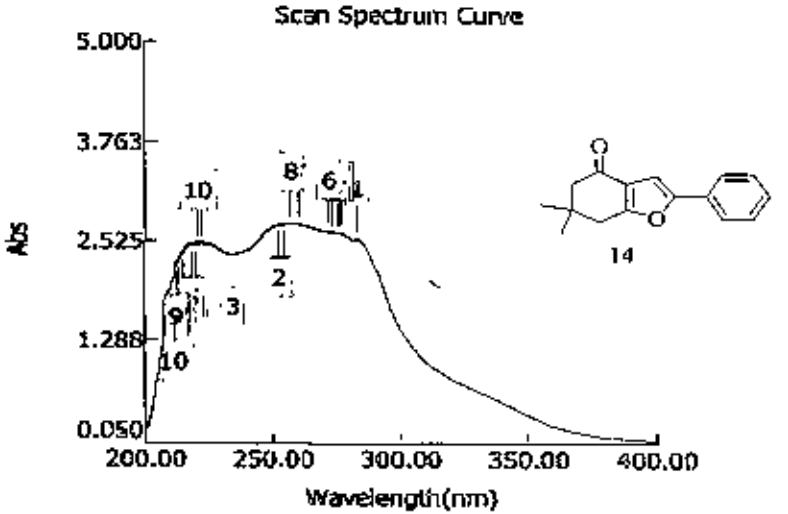


Figure 12d: ^{13}C NMR spectrum of the compound **12**



14

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Scan Range : 200.00 to 400.00 nm
Measure Mode : Abs
Interval : 0.05 nm
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Data File : Untitled.spd
Create Date/Time : Wednesday, March 12, 2008 9:25:36 PM
Data Type : Original
Method File:

Analyse Mode
Analyser : Administrator
Sample Name : Blank
Comment :

No.	P/V	Wavelength(nm)	Abs	Comment

8	Peak	257.15	2.759
9	Peak	222.15	2.510
10	Peak	220.65	2.513
3	Valley	234.40	2.347

Figure 14a :UV spectrum of the compound **14**

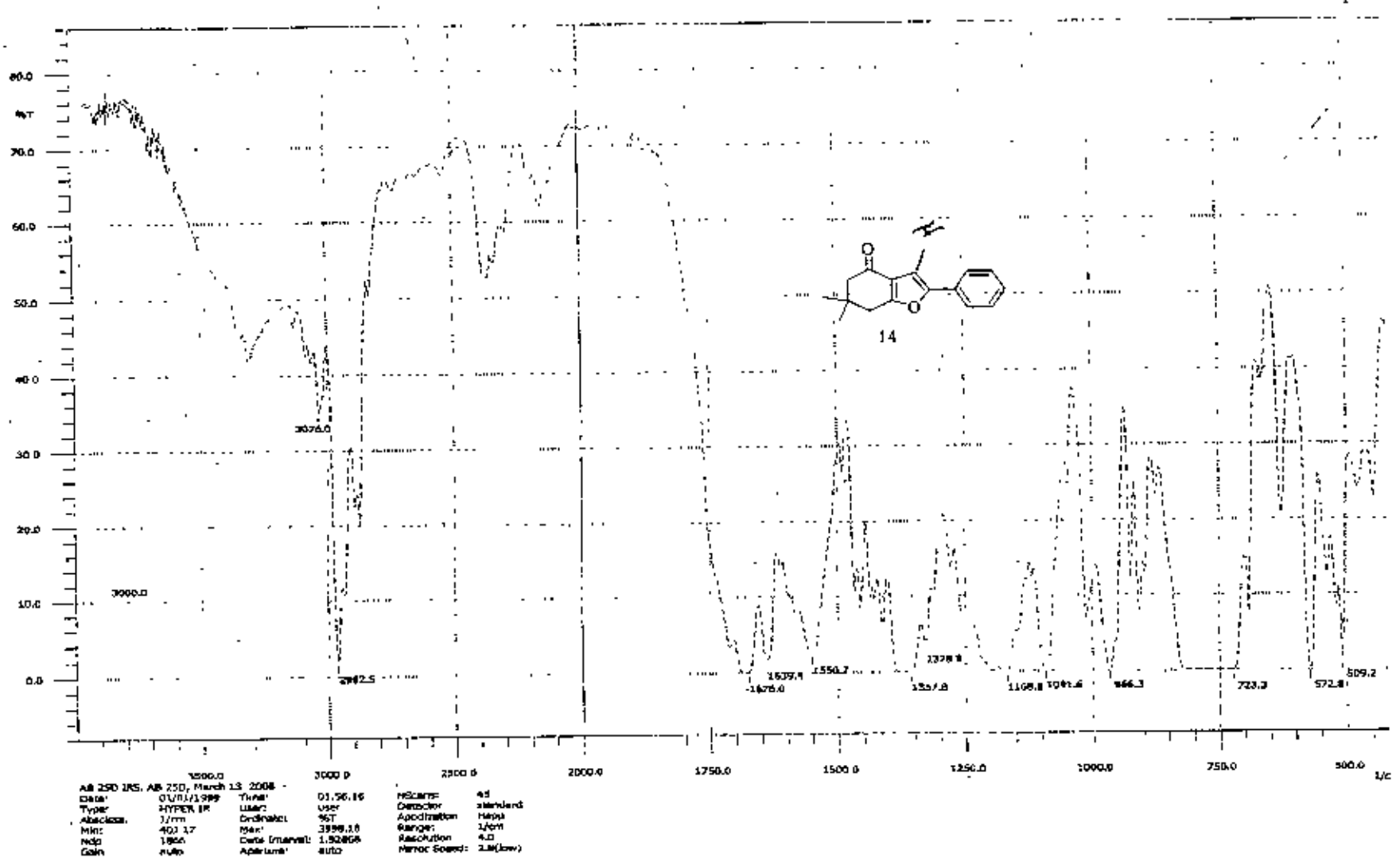


Figure 14b: IR spectrum of the compound **14**

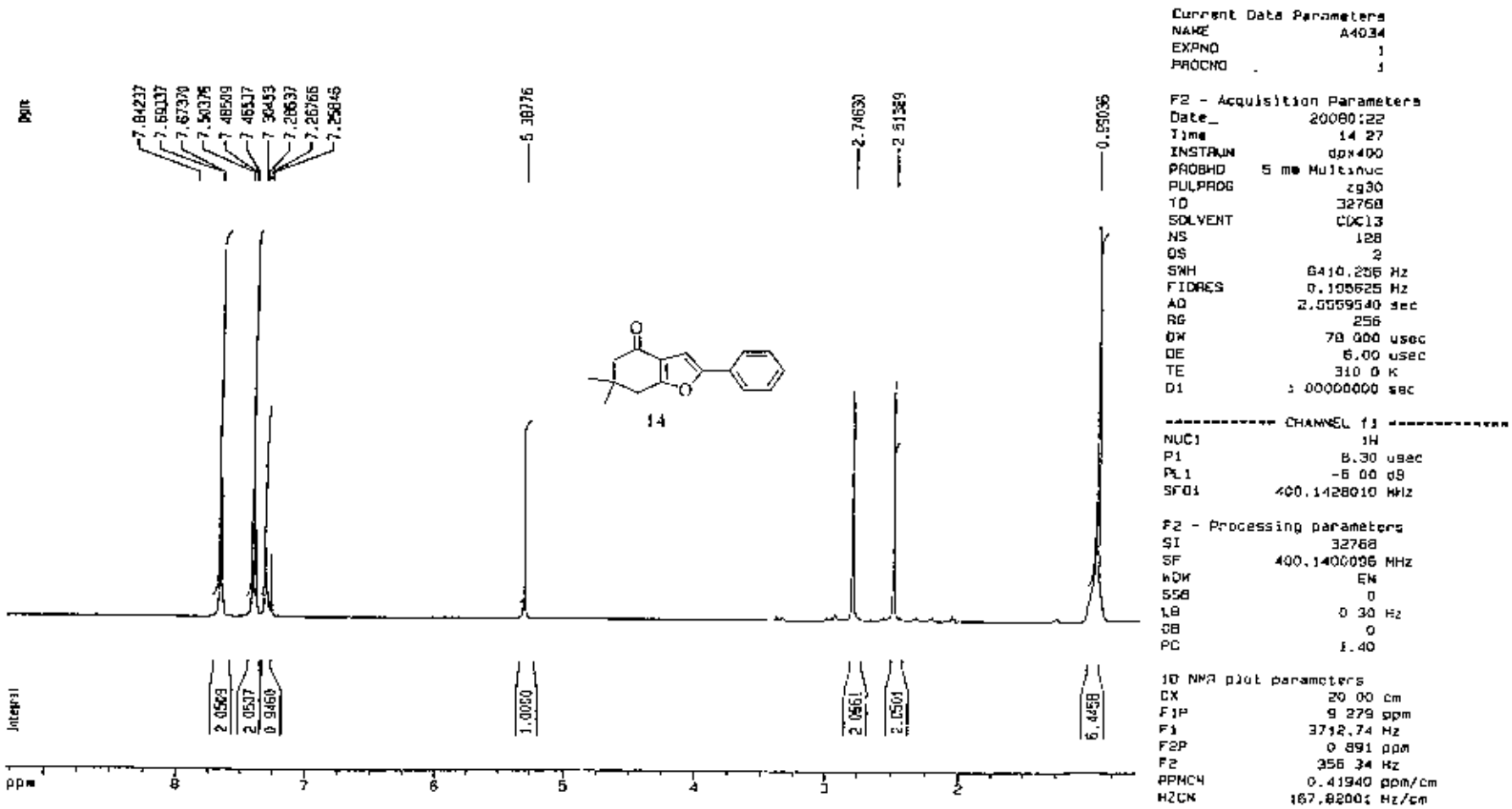
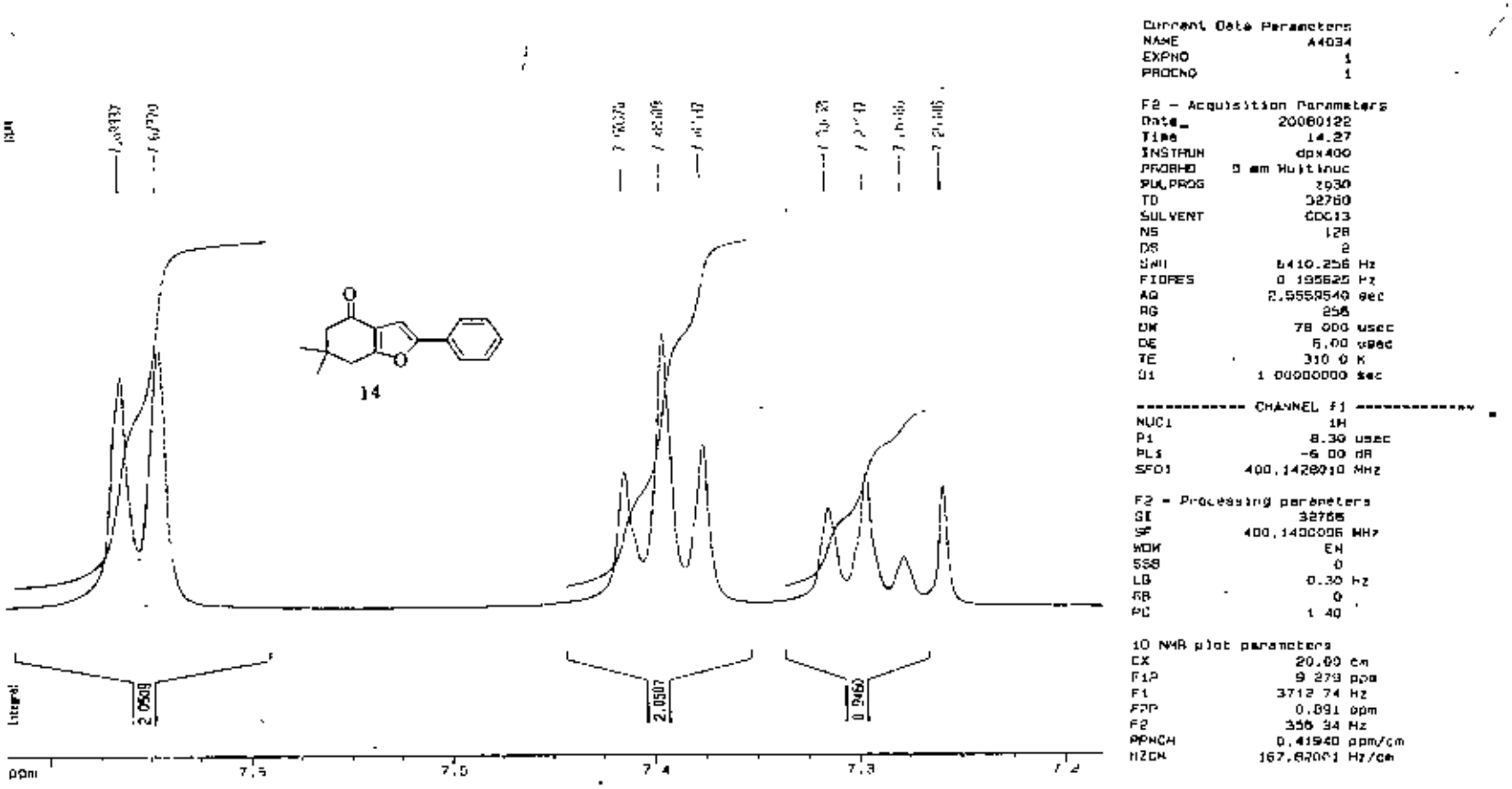


Figure 14c: ^{1}H NMR spectrum of the compound **14**

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EXPNO                     1
PROCNO                    1

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Time                  14.27
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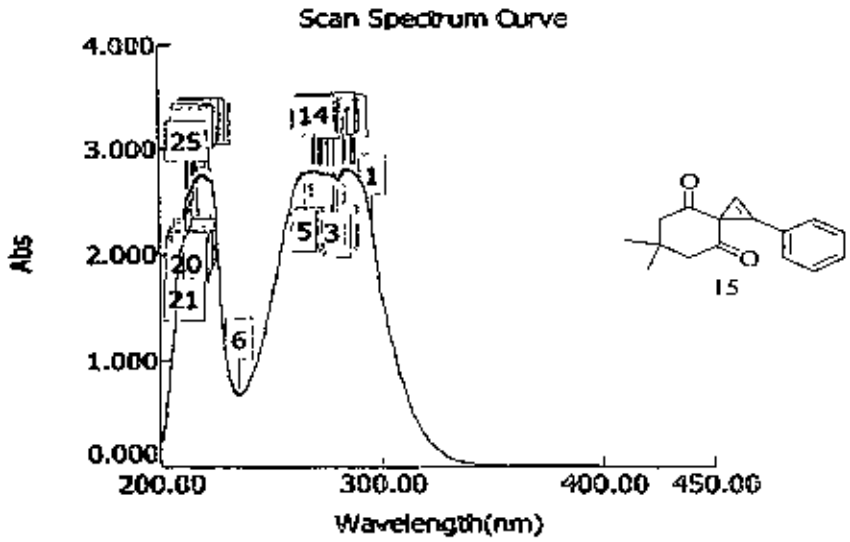
PROBHD     5 mm Multinuc
PULPROG                2930
TD                    32760
SOLVENT               CDCl3
NS                      128
DS                        2
SWH                6410.256 Hz
FIDRES            0.195625 Hz
AQ                2.5558540 sec
RG                      256
DW                  78.000 usec
DE                   6.00 usec
TE                  310.0 K
D1                1.00000000 sec

------------ CHANNEL f1 ------------
NUC1                      1H
P1                     8.30 usec
PL1                   -6.00 dB
SFO1           400.1428010 MHz

F2 - Processing parameters
SI                      32768
SF             400.1400006 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.40

1D NMR plot parameters
CX                     20.00 cm
F1P                  9.279 ppm
F1                3712.74 Hz
F2P                  0.891 ppm
F2                 356.94 Hz
PPMCM              0.41940 ppm/cm
HZCM             167.82061 Hz/cm
```

Figure 14c: ^{1}H NMR spectrum of the compound **14**



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Measure Mode : Abs
Interval : 0.05 nm
Speed : Fast
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Create Date/Time : Thursday, March 13, 2008 8:35:23 PM
Data Type : Original
Method File:

Analyse Note
Analyser : Administrator
Sample Name : Blank
Comment :

No.	P/V	Wavelength(nm)	Abs	Comment
6	Peak	283.55	2.824	
14	Peak	270.45	2.800	
18	Peak	219.85	2.797	
6	Valley	234.40	0.647	

Figure 15a :UV spectrum of the compound **15**

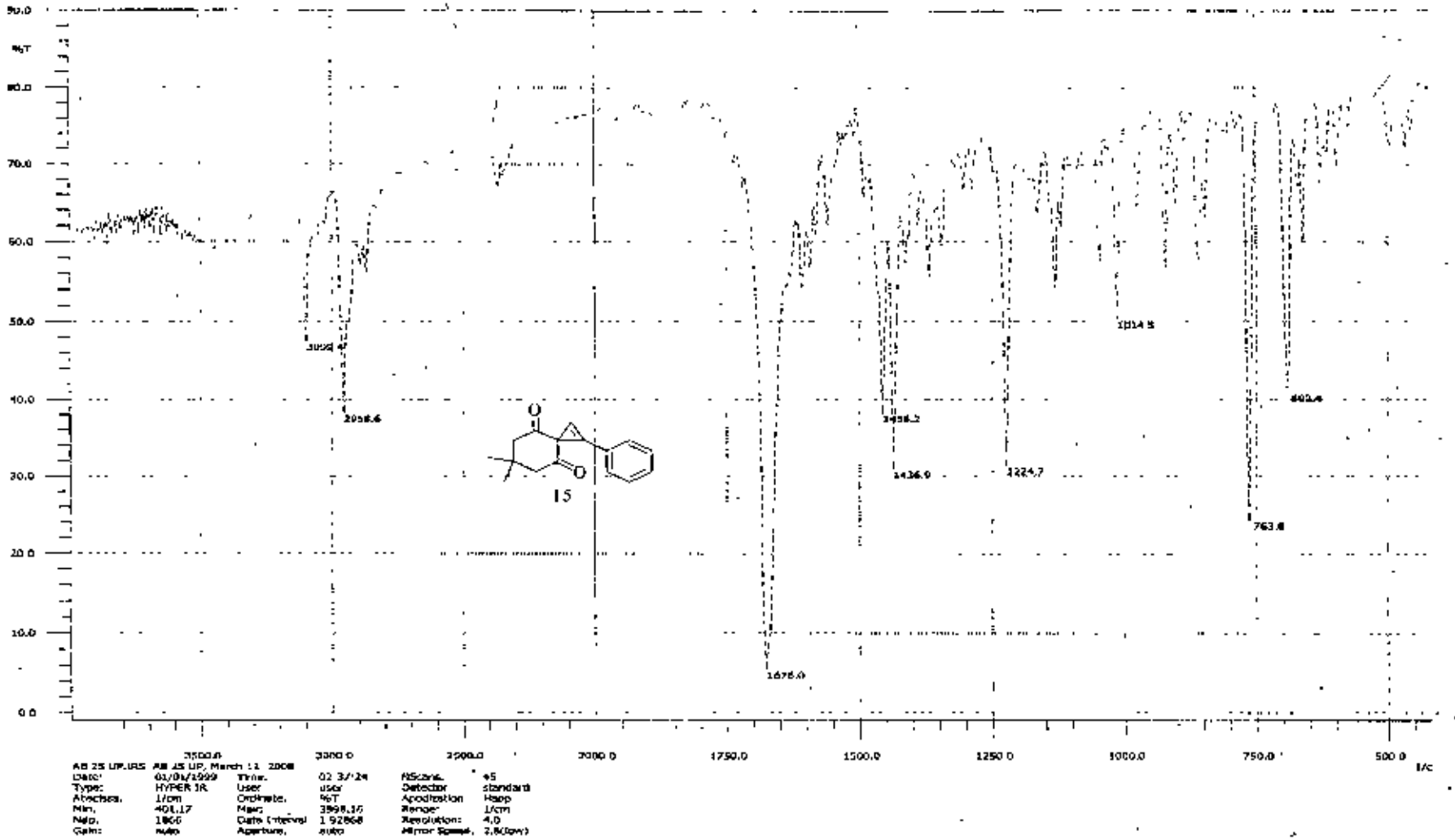
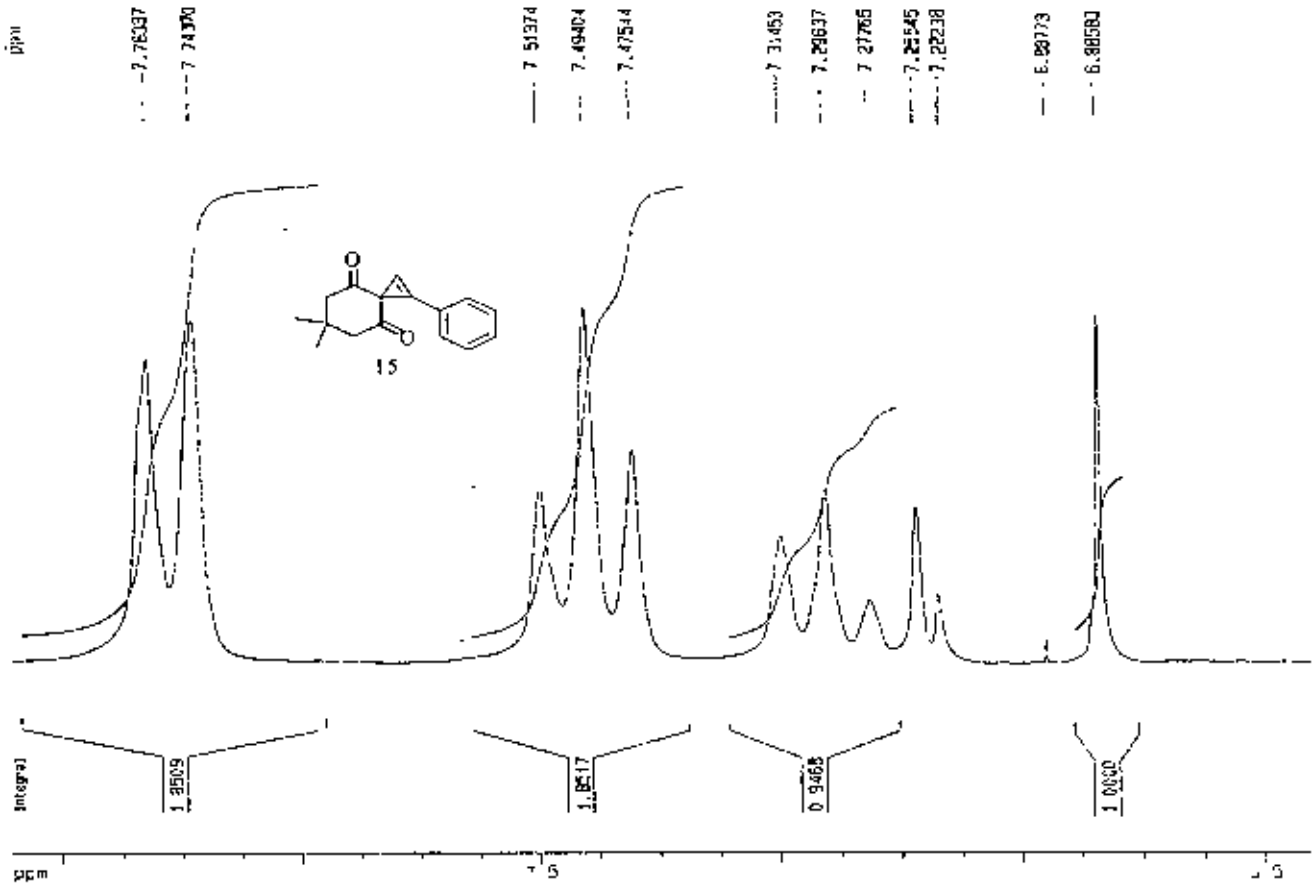


Figure 15b: IR spectrum of the compound **15**

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NAME                  A4054
EXPNO                     1
PROCNO                    1

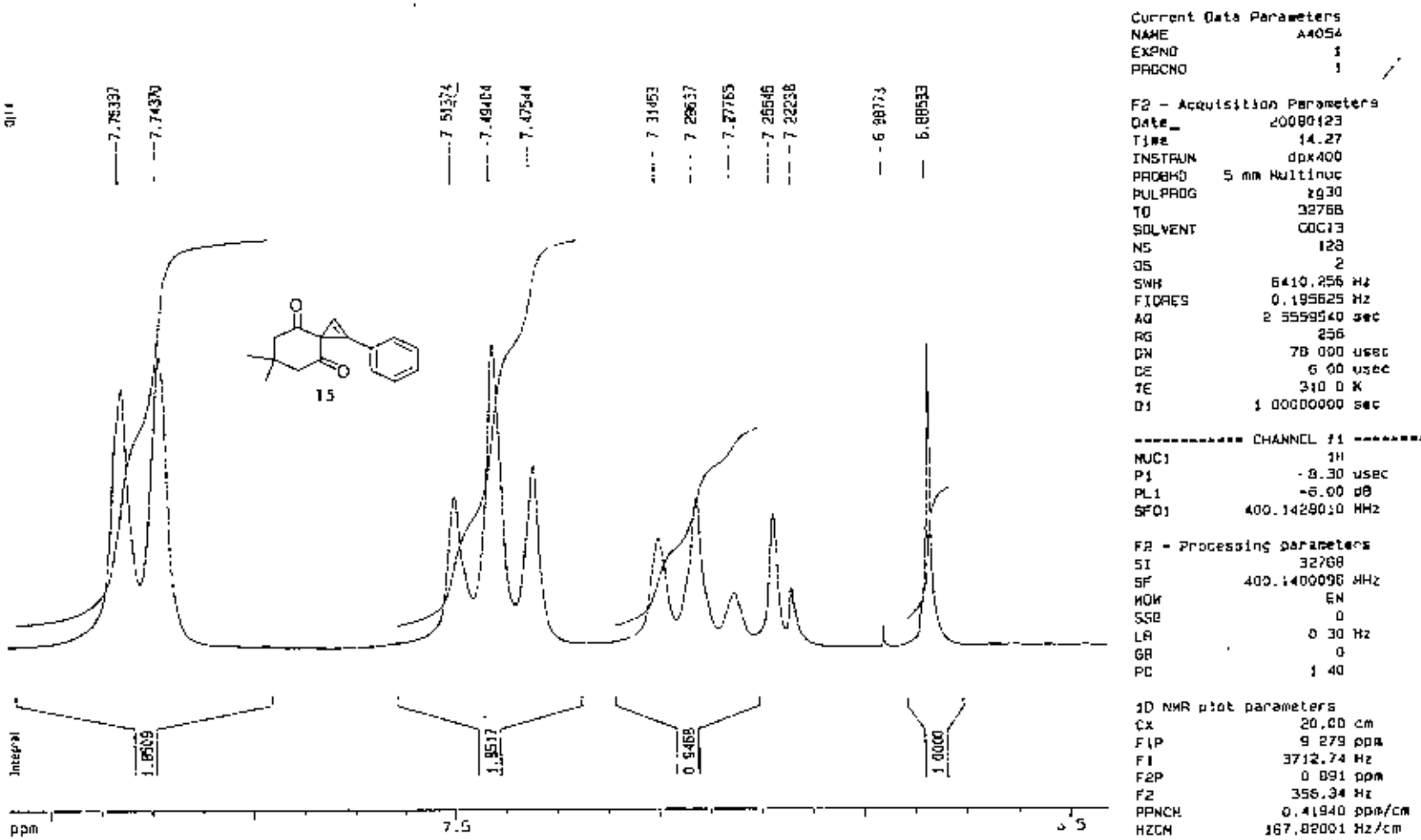
F2 - Acquisition Parameters
Date_              20080123
Time                  14.27
INSTRUM               dpx400
PROBHD     5 mm Multinuc
PULPROG               zg30
TD                   32768
SOLVENT              CDCl3
NS                     128
DS                       2
SWH               6410.256 Hz
FIDRES            0.195625 Hz
AQ                2.5559540 sec
RG                     256
DW                  78.000 usec
DE                   6.00 usec
TE                  310.0 K
D1                1.00000000 sec

------------ CHANNEL f1 --------
NUC1                   1H
P1                  8.30 usec
PL1                -6.00 dB
SFO1          400.1428010 MHz

F2 - Processing parameters
SI                   32768
SF              400.1400096 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.40

1D NMR plot parameters
CX                  20.00 cm
F1P                 9.279 ppm
F1                3712.74 Hz
F2P                 0.891 ppm
F2                 356.34 Hz
PPMCM           0.41940 ppm/cm
HZCM          167.82601 Hz/cm
```

Figure 15c: ^{1}H NMR spectrum of the compound **15**



Current Data Parameters
NAME A4054
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20080123
Time 14.27
INSTRUM dpx400
PROBHD 5 mm Multinuc
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 128
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 256
DW 78.000 usec
DE 6.00 usec
TE 310.0 K
D1 1.00000000 sec

---------- CHANNEL f1 --------
NUC1 1H
P1 9.30 usec
PL1 -6.00 dB
SFO1 400.1429010 MHz

F2 - Processing parameters
SI 32768
SF 400.1400098 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
F1P 9.279 ppm
F1 3712.74 Hz
F2P 0.891 ppm
F2 356.34 Hz
PPMCM 0.41940 ppm/cm
HZCM 167.82001 Hz/cm

Figure 15c: ^{1}H NMR spectrum of the compound **15**

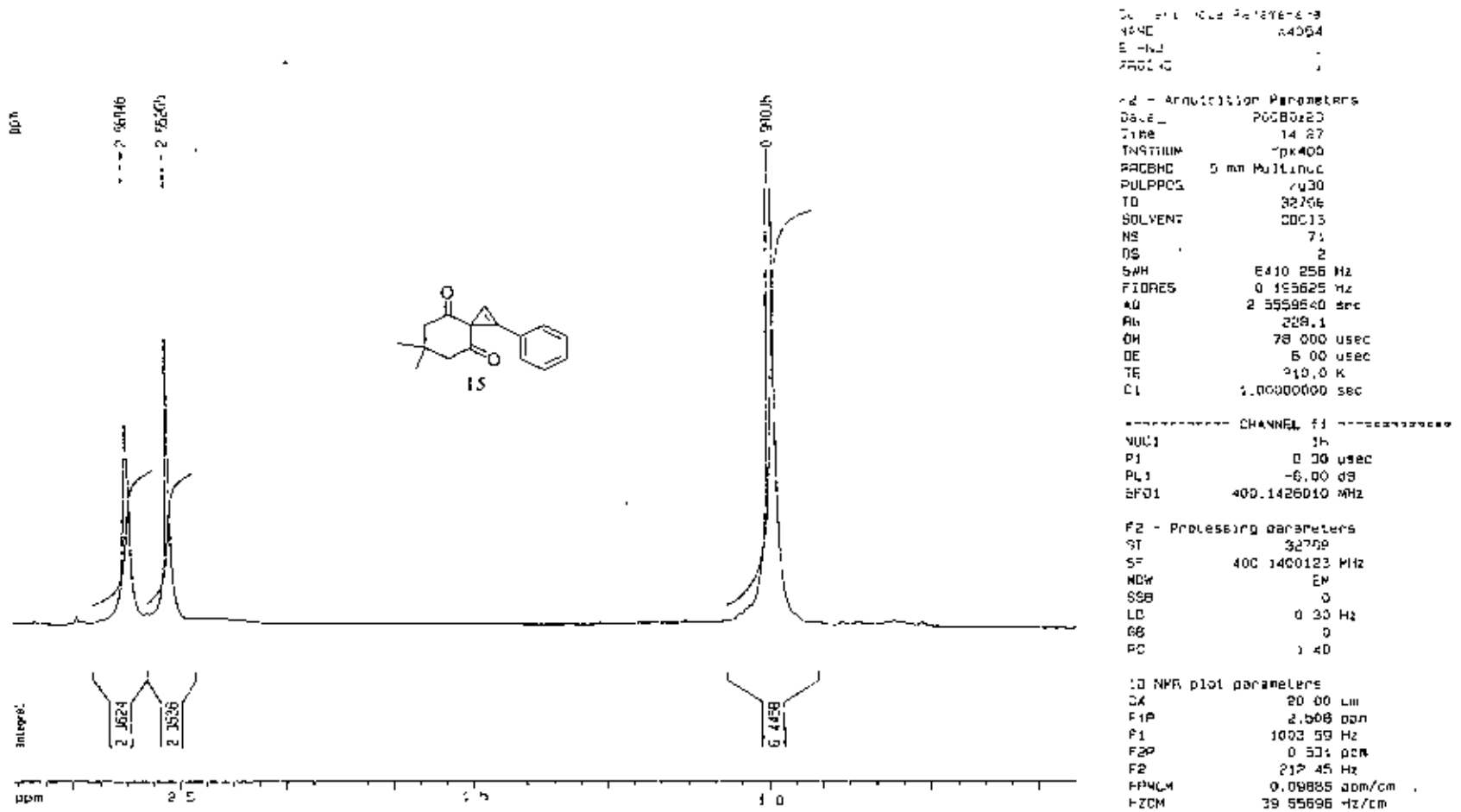
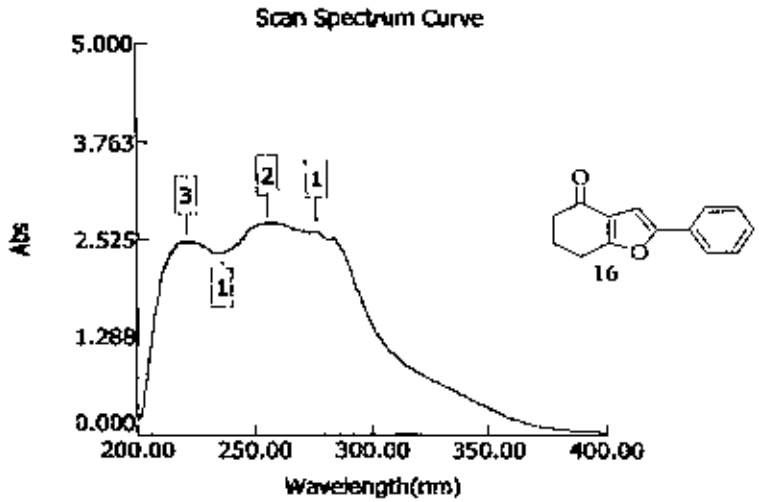


Figure 15c: ^{1}H NMR spectrum of the compound **15**



1	Peak	275.85	2.571
2	Peak	258.45	2.680
3	Peak	220.85	2.517
3	Valley	234.40	2.500

Instrument Performance
Model : SPECTROPHOTOMETERS
Spectral Bandwidth : 2.00 nm
Scan Spectrum Performance
Scan Range : 200.00 to 400.00 nm
Measure Mode : Abs
Interval : 0.05 nm
Speed : Fast
Data File : Untitled4.spd
Create Date/Time : Wednesday, March 12, 2008 5:21:24 PM
Data Type : Original
Method File:
Analyse Note
Analyser : Administrator
Sample Name : Blank
Comment :
No. P/V Wavelength(nm) Abs Comment

Figure 16a :UV spectrum of the compound **16**

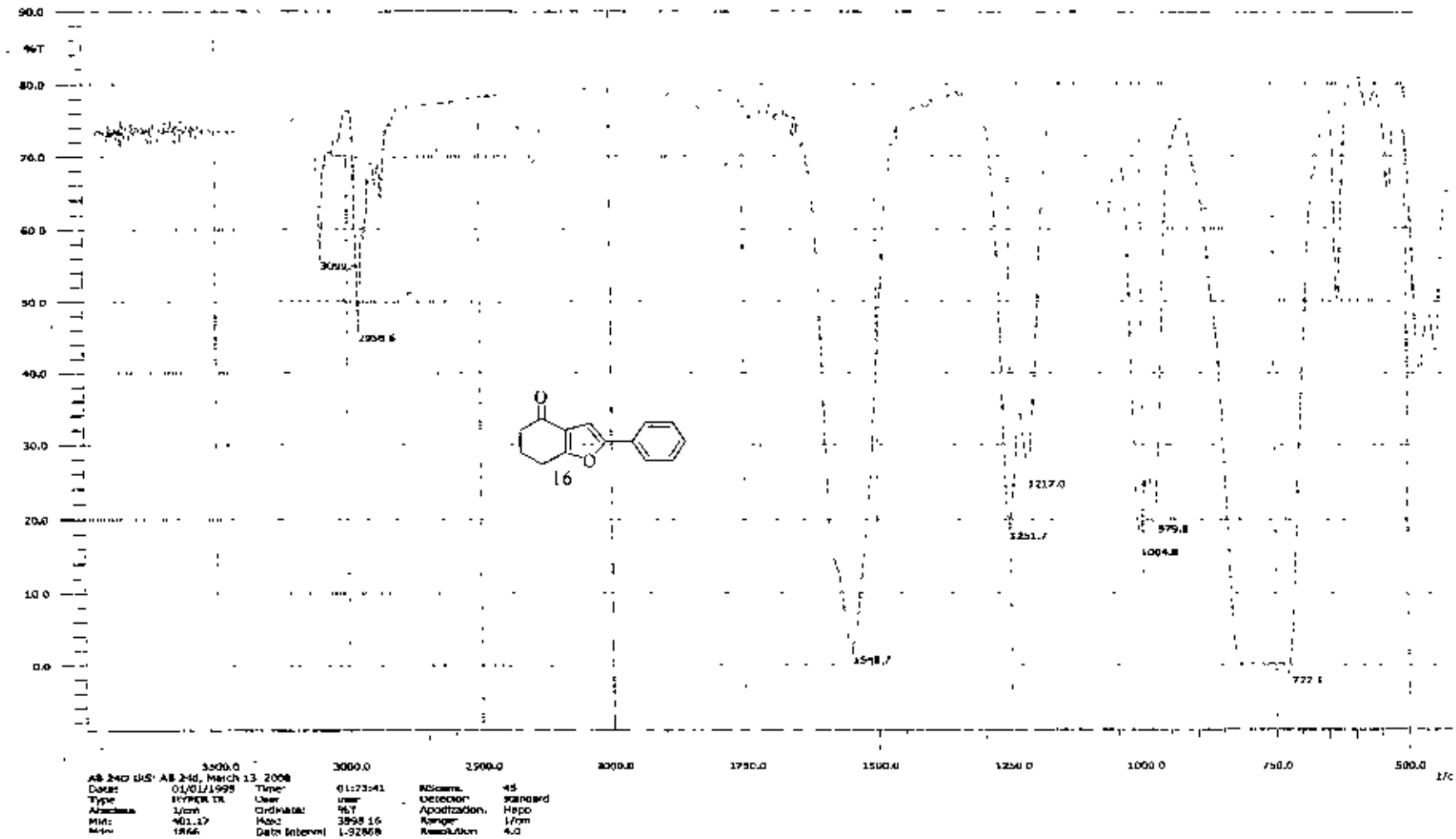
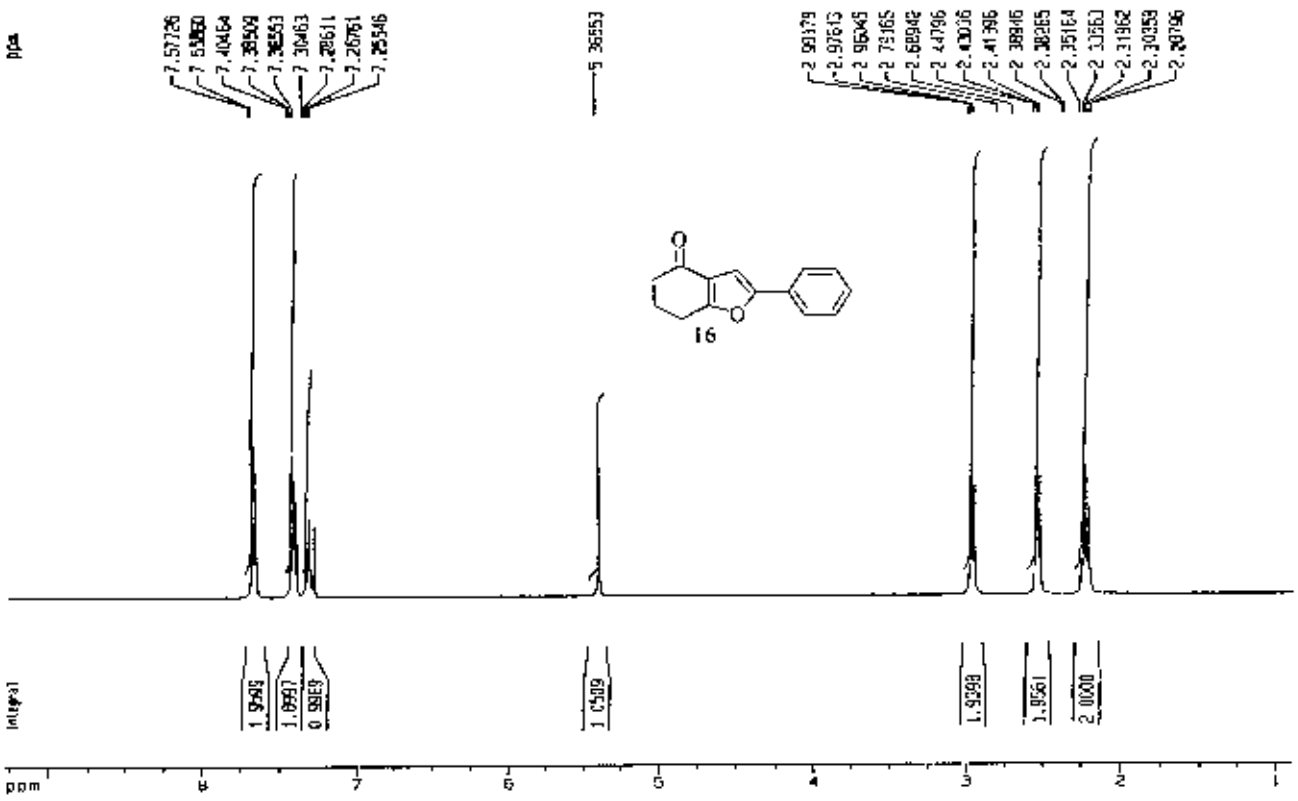


Figure 16b: IR spectrum of the compound **16**




```
Current Data Parameters
NAME                  A4037
EXPNO                     1
PROCNO                    1

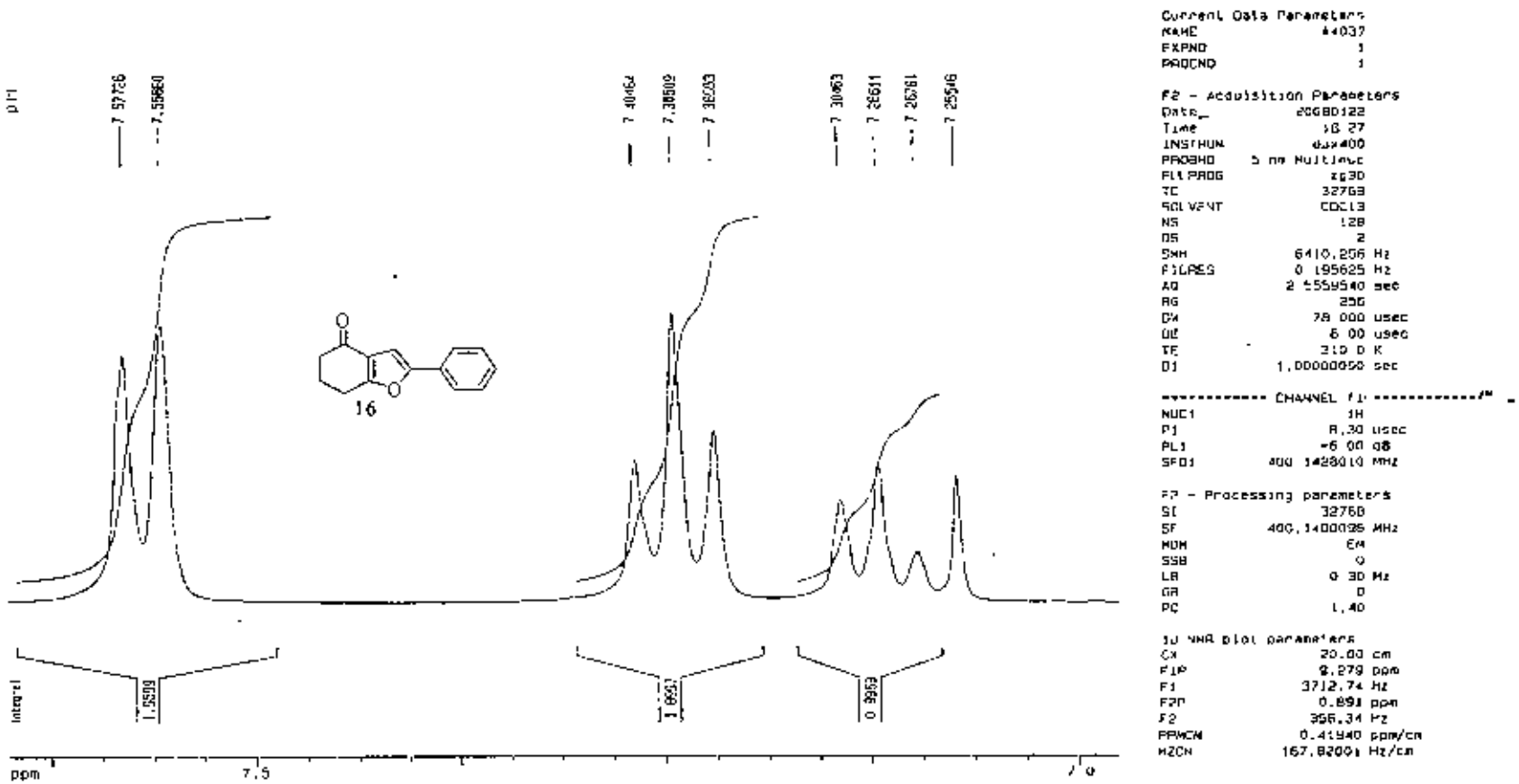
F2 - Acquisition Parameters
Date_              20080122
Time                 16 27
INSTRUM              dpx400
PROBHD     5 mm Multinuc
PULPROG               zg30
TD                   32768
SOLVENT              CDCl3
NS                     128
DS                       2
SWH               6410.256 Hz
FIDRES            0.195625 Hz
AQ                2.5559540 sec
RG                     256
DW                78.000 usec
DE                 6.00 usec
TE                 310.0 K
D1                1.00000000 sec

------------ CHANNEL f1 ------------
NUC1                   1H
P1                  8.30 usec
PL1                -6.00 dB
SFO1          400.1420010 MHz

F2 - Processing parameters
SI                   32768
SF            400.1400096 MHz
WDW                    EM
SSB                     0
LB                  0.30 Hz
GB                      0
PC                   1.40

1D NMR plot parameters
CX                  20.00 cm
F1P                 9.279 ppm
F1                3712.74 Hz
F2P                 0.891 ppm
F2                 356.34 Hz
PPMCM             0.41940 ppm/cm
HZCM            167.82001 Hz/cm
```

Figure 16c: ^{1}H NMR spectrum of the compound **16**




```
Current Data Parameters
NAME                  44037
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_              20080122
Time                  16 27
INSTRUM             dpx400
PROBHD     5 mm Multinuc
PULPROG               zg30
TD                   32768
SOLVENT              CDCl3
NS                     128
DS                       2
SWH               6410.256 Hz
FIDRES            0.195625 Hz
AQ                2.5559540 sec
RG                     256
DW                  78.000 usec
DE                   6.00 usec
TE                  310.0 K
D1                1.00000000 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                   8.30 usec
PL1                 -6.00 dB
SFO1          400.1428010 MHz

F2 - Processing parameters
SI                   32768
SF              400.1400025 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.40

1D NMR plot parameters
CX                  20.00 cm
F1P                 8.279 ppm
F1                3312.74 Hz
F2P                 0.891 ppm
F2                356.34 Hz
PPMCM             0.41940 ppm/cm
HZCM            167.82001 Hz/cm
```

Figure 16c: ^{1}H NMR spectrum of the compound **16**

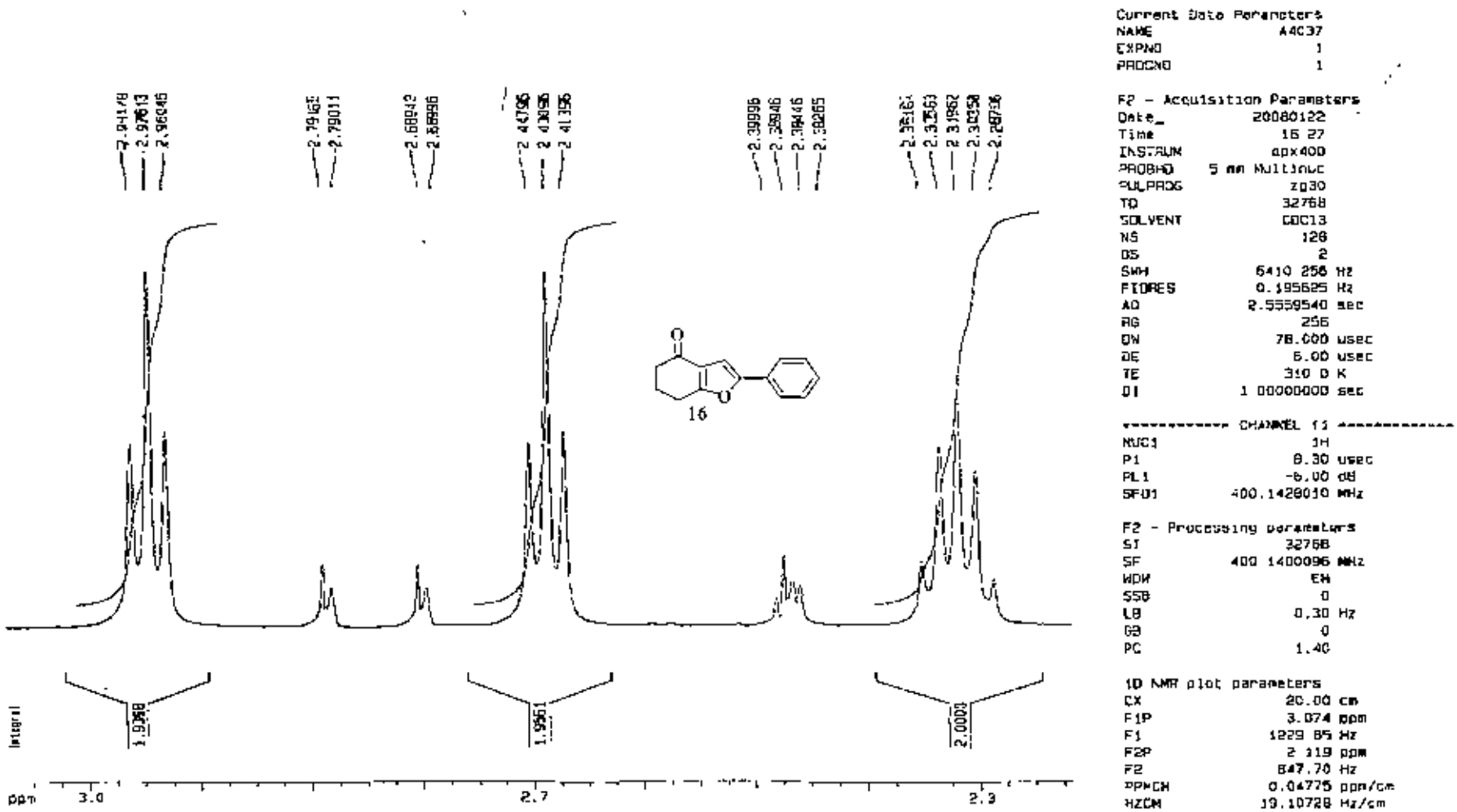
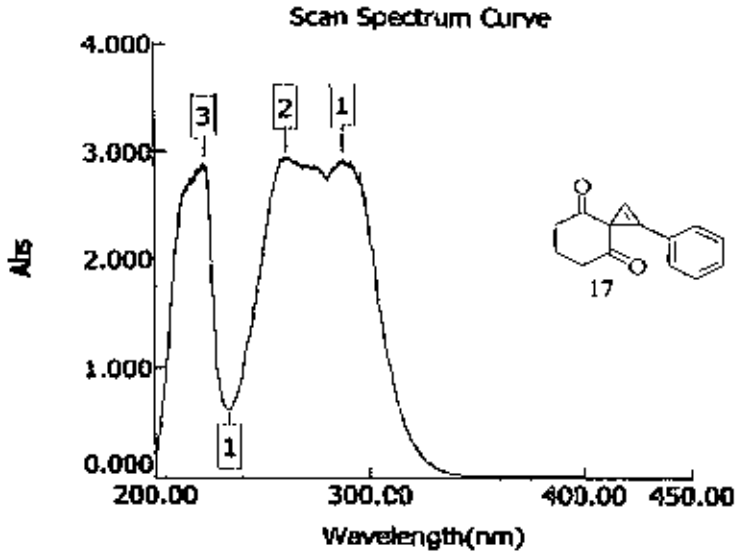


Figure 16c: ^{1}H NMR spectrum of the compound **16**



- Instrument Performance
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- Scan Spectrum Performance
  Scan Range : 200.00 to 450.00 nm
  Measure Mode : Abs
  Interval : 0.05 nm
  Speed : Fast
  Data File : Untitled3.spd
  Create Date/Time : Thursday, March 13, 2008 8:15:22 PM
  Data Type : Original
  Method File:
- Analyse Note
  Analyser : Administrator
  Sample Name : Blank
  Comment :
- No. P/V Wavelength

1	Peak	296.55	2.760
2	Peak	260.35	2.903
3	Peak	223.45	2.865
1	Valley	234.80	0.745

Figure 17a :UV spectrum of the compound 17

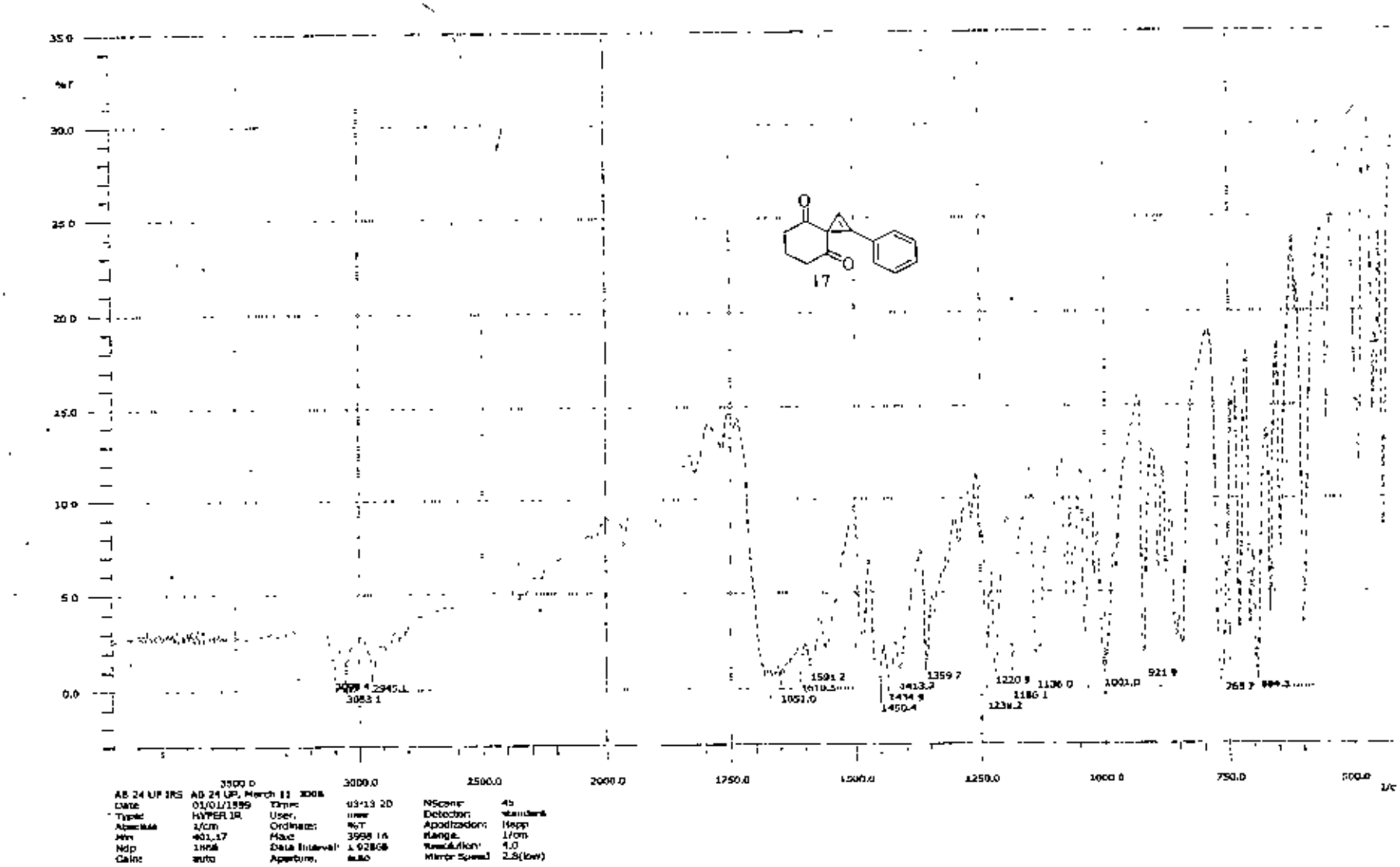
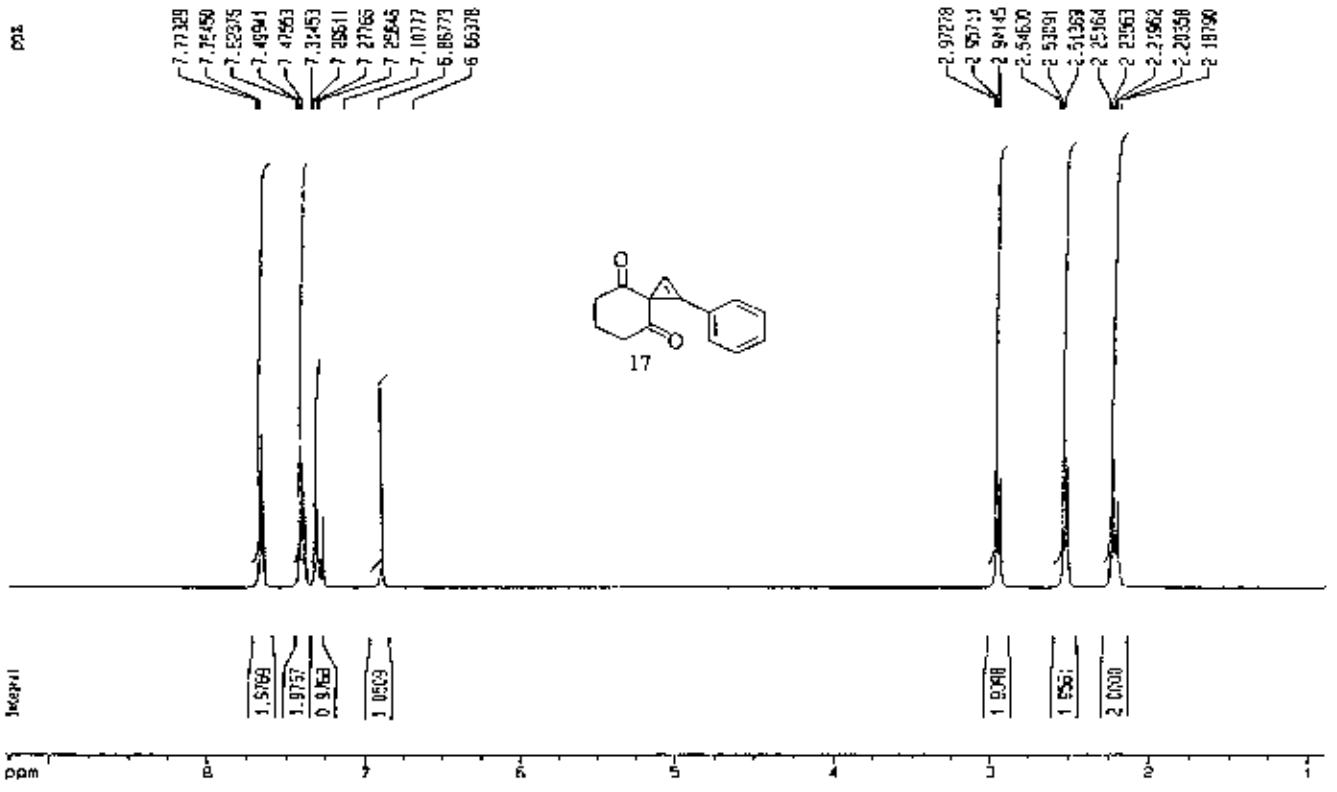


Figure 17b: IR spectrum of the compound **17**




```
Current Data Parameters
NAME                  A4055
EXPNO                     1
PROCNO                    1

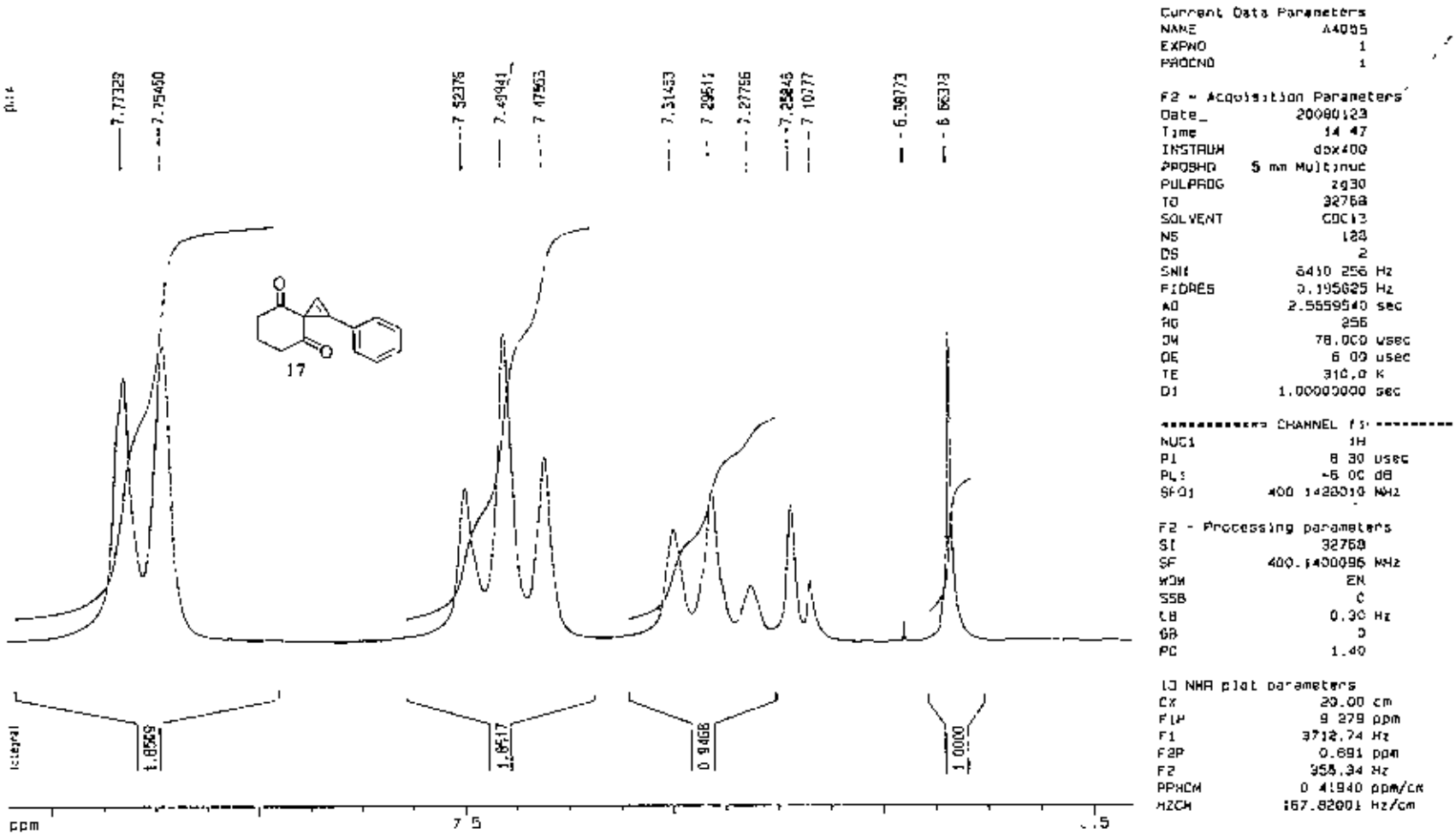
F2 - Acquisition Parameters
Date_              20090123
Time                  14 47
INSTRUM             dpx400
PROBHD     5 mm Multinuc
PULPROG               zg30
TD                   32768
SOLVENT              CDCl3
NS                     128
DS                       2
SWH              6410.256 Hz
FIDRES           0.195625 Hz
AQ               2.7559540 sec
RG                     258
DW                78.000 usec
DE                 6.00 usec
TE                310.0 K
D1             1.00000000 sec

------------ CHANNEL f1 ------------
NUC1                  1H
P1                 8.30 usec
PL1               -6.00 dB
SFO1         400.1428010 MHz

F2 - Processing parameters
SI                   32768
SF           400.1400098 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                   1.40

1D NMR plot parameters
CX                  20.00 cm
F1P                 8.279 ppm
F1                 3312.74 Hz
F2P                 0.891 ppm
F2                  358.34 Hz
PPMCM          0.41940 ppm/cm
HZCM           167.82001 Hz/cm
```

Figure 17c: ^{1}H NMR spectrum of the compound **17**




```
Current Data Parameters
NAME                  A4055
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_              20080123
Time                  14 47
INSTRUM               dpx400
PROBHD     5 mm Multinuc
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                      128
DS                        2
SWH               6410.256 Hz
FIDRES            0.195625 Hz
AQ                2.5559540 sec
RG                      256
DW                 78.000 usec
DE                  6.00 usec
TE                  310.0 K
D1                1.00000000 sec

========== CHANNEL f1 =========
NUC1                      1H
P1                     8.30 usec
PL1                   -6.00 dB
SFO1            400.1428010 MHz

F2 - Processing parameters
SI                    32768
SF              400.1400096 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.40

1D NMR plot parameters
CX                    20.00 cm
F1P                 9.279 ppm
F1                 3712.74 Hz
F2P                 0.691 ppm
F2                  958.34 Hz
PPMCM             0.41940 ppm/cm
HZCM              167.82001 Hz/cm
```

Figure 17c: ^{1}H NMR spectrum of the compound 17

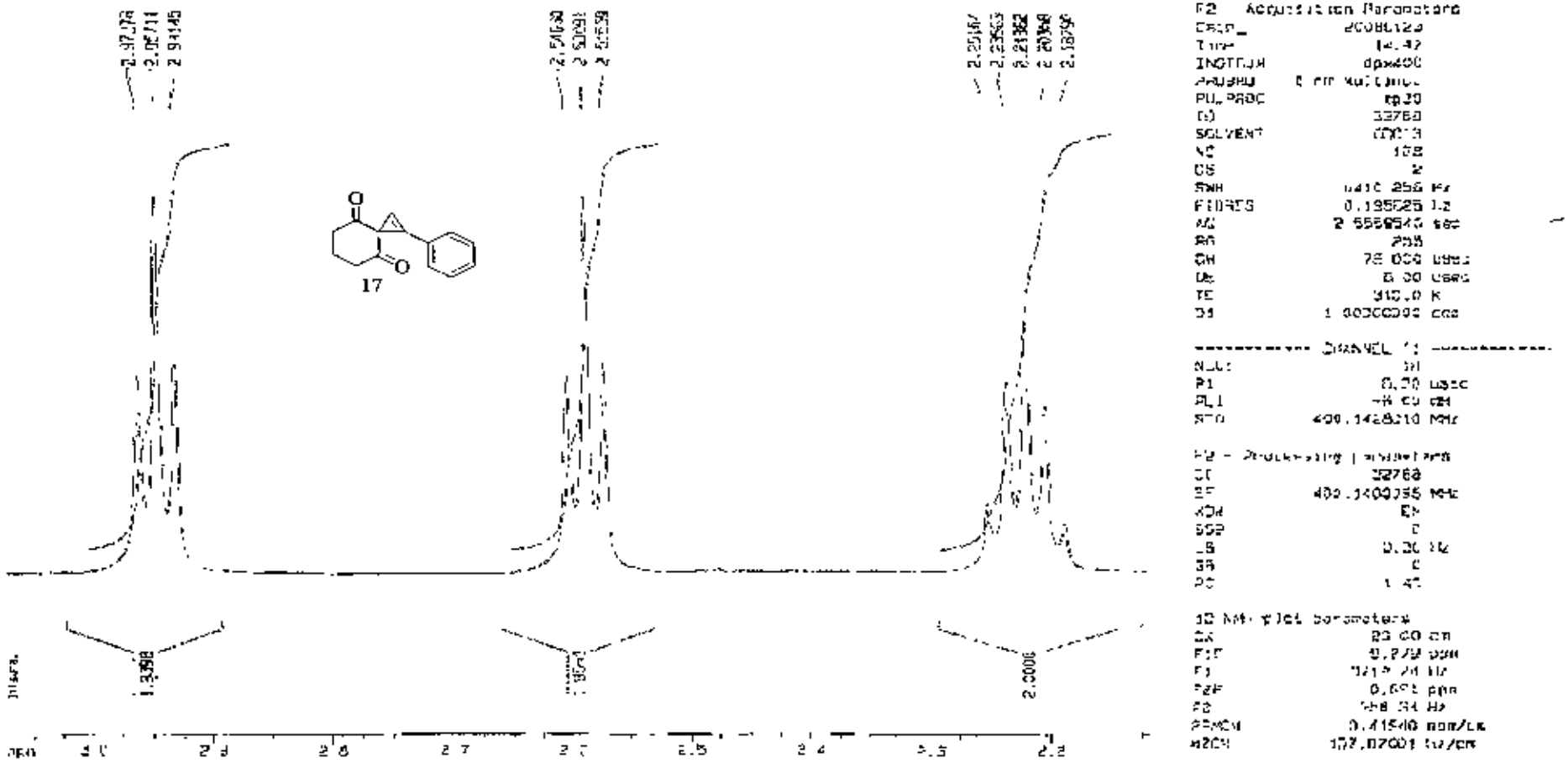
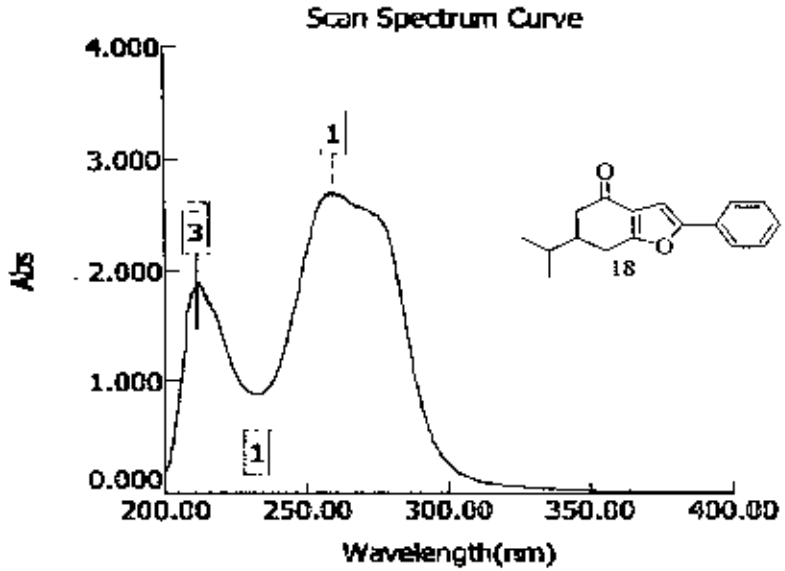


Figure 17c: ^{1}H NMR spectrum of the compound **17**



Instrument Performance
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Measure Mode : Abs
Interval : 0.05 nm
Speed : Fast
Data File : Untitled2.spd
Create Date/Time : Wednesday, March 12, 2008 8:53:43 PM
Data Type : Original
Method File:

Analyse Meta
Analyser : Administrator
Sample Name : Blank
Comment

No.	P/V	Wavelength(nm)	Abs	Comment
1	Peak	260.15	2.722	
2	Peak	211.20	1.912	
3	Peak	210.95	1.835	
1	Valley	232.20	0.885	

Figure 18a :UV spectrum of the compound **18**

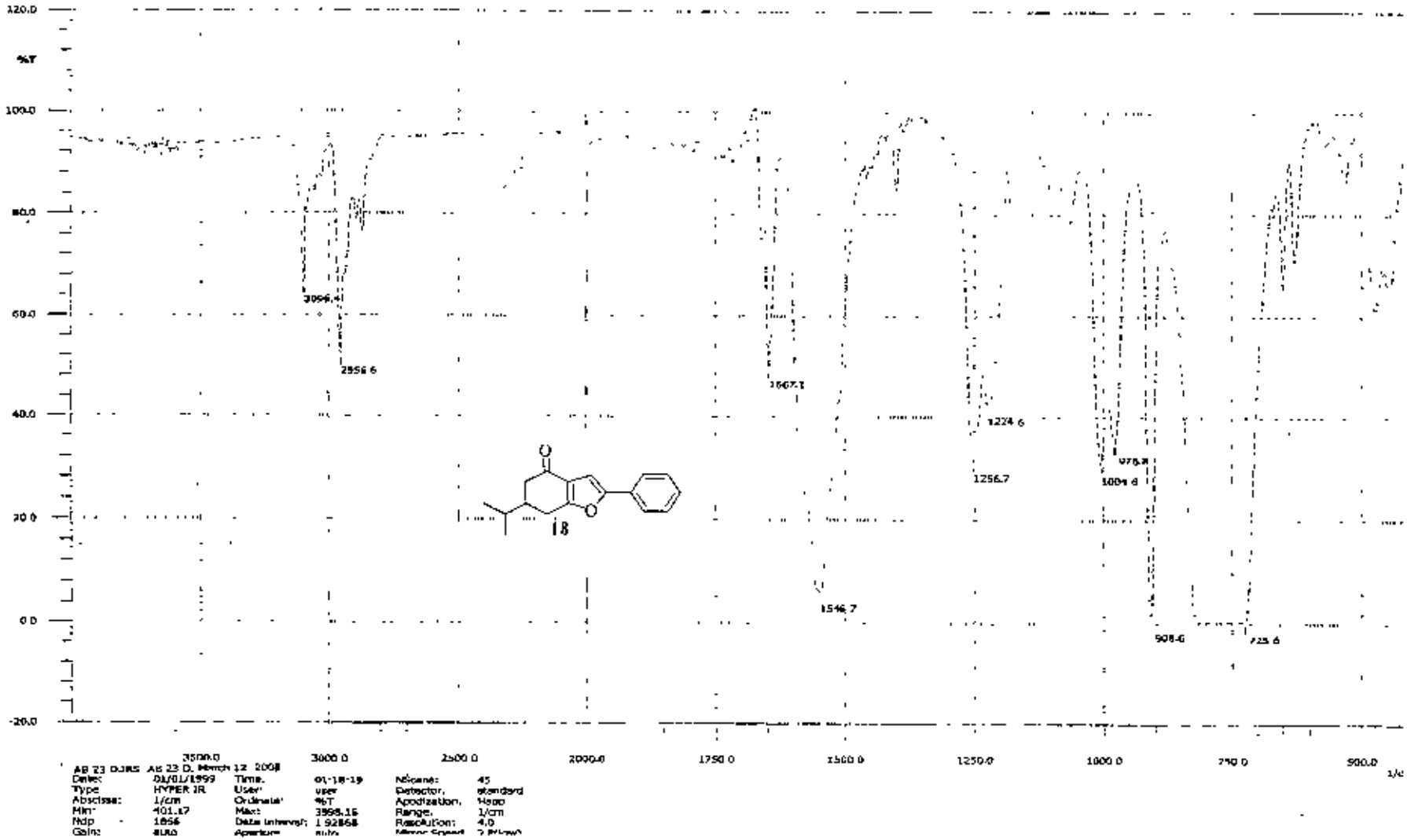
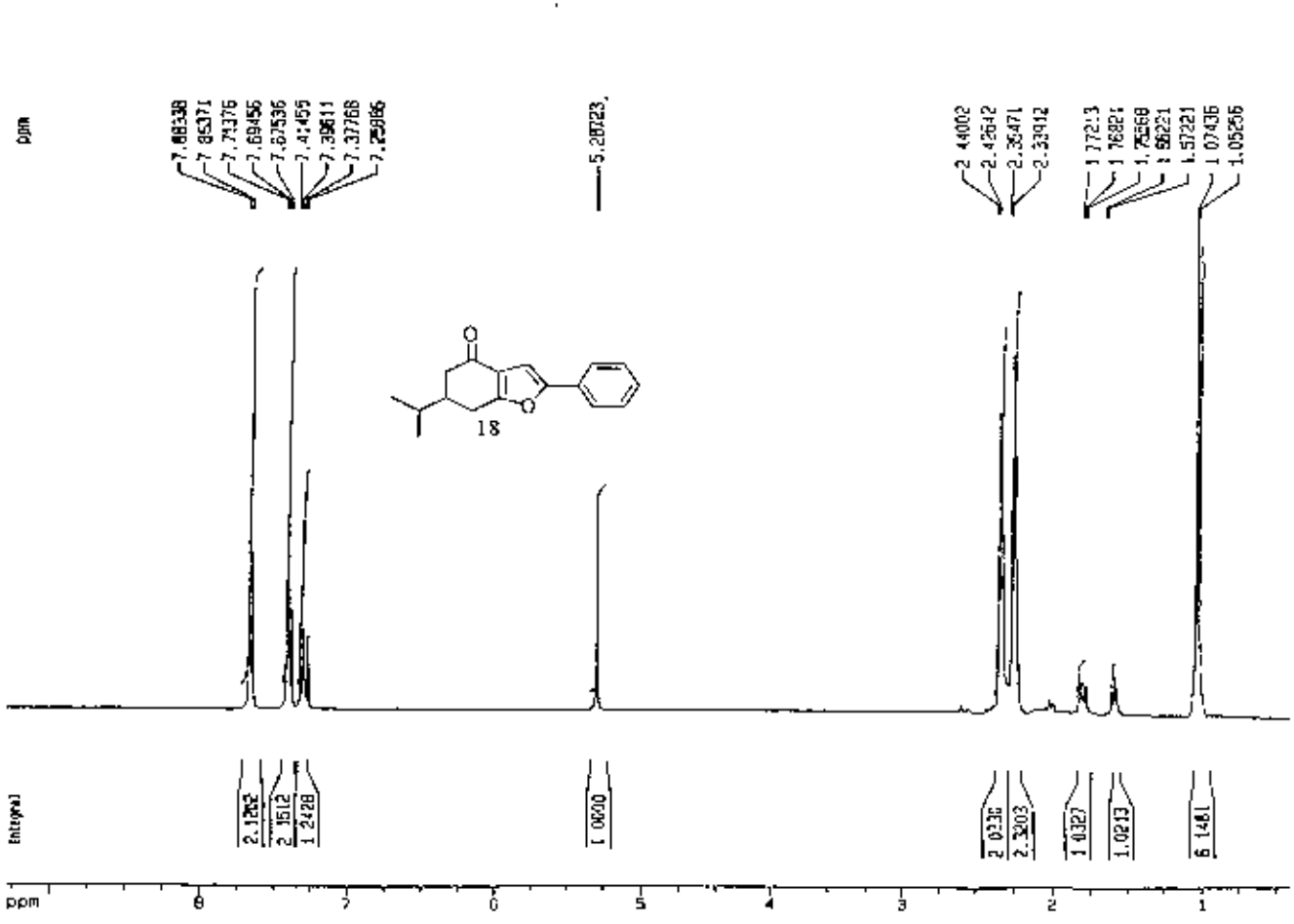


Figure 18b: IR spectrum of the compound **18**




```
Current Data Parameters
NAME                  A4024
EXPNO                     1
PROCNO                    1

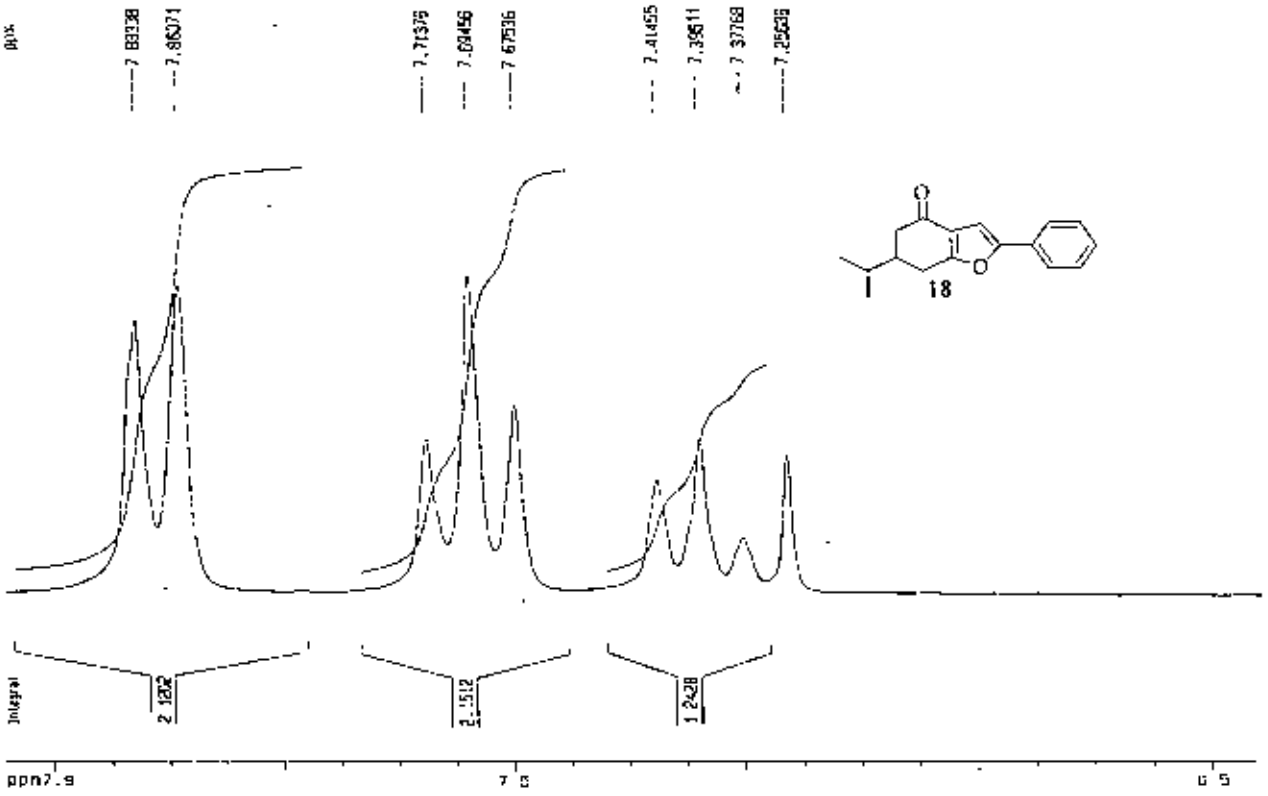
F2 - Acquisition Parameters
Date_              20080120
Time                  11.27
INSTRUM               dpx400
PROBHD     5 mm Multinuc
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                      128
DS                        2
SWH               6410.256 Hz
FIDRES            0.195625 Hz
AQ                2.5559540 sec
RG                      256
DW                 78.000 usec
DE                  6.00 usec
TE                 310.0 K
D1                1.00000000 sec

------------ CHANNEL f1 ------------
NUC1                      1H
P1                     8.30 usec
PL1                   -6.00 dB
SFO1            400.1428010 MHz

F2 - Processing parameters
SI                    32768
SF              400.1400096 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.40

1D NMR plot parameters
CX                    20.00 cm
F1P                   8.279 ppm
F1                 3312.74 Hz
F2P                   0.891 ppm
F2                  356.34 Hz
PPMCM              0.41940 ppm/cm
HZCM             167.82001 Hz/cm
```

Figure 18c: ^{1}H NMR spectrum of the compound **18**

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Current Data Parameters
NAME                  A4024
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_              20080120
Time                  11.27
INSTRUM              dpx400
PROBHD     5 mm Multinuc
PULPROG               zg30
TD                   32768
SOLVENT              CDCl3
NS                     128
DS                       2
SWH              8410.256 Hz
FIDRES           0.128625 Hz
AQ               2.5559540 sec
RG                     256
DW                78.000 usec
DE                 6.00 usec
TE                 310.0 K
D1              1.00000000 sec

------------- CHANNEL f1 -------------
NUC1                   1H
P1                 8.30 usec
PL1                -6.00 dB
SFO1          400.1420016 MHz

F2 - Processing parameters
SI                   32768
SF          400.1400086 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                   1.40

1D NMR plot parameters
CX                 20.00 cm
F1P                9.279 ppm
F1                3712.74 Hz
F2P                0.851 ppm
F2                 356.34 Hz
PPMCM              0.41940 ppm/cm
HZCM             167.82001 Hz/cm
```

Figure 18c: ^{1}H NMR spectrum of the compound **18**

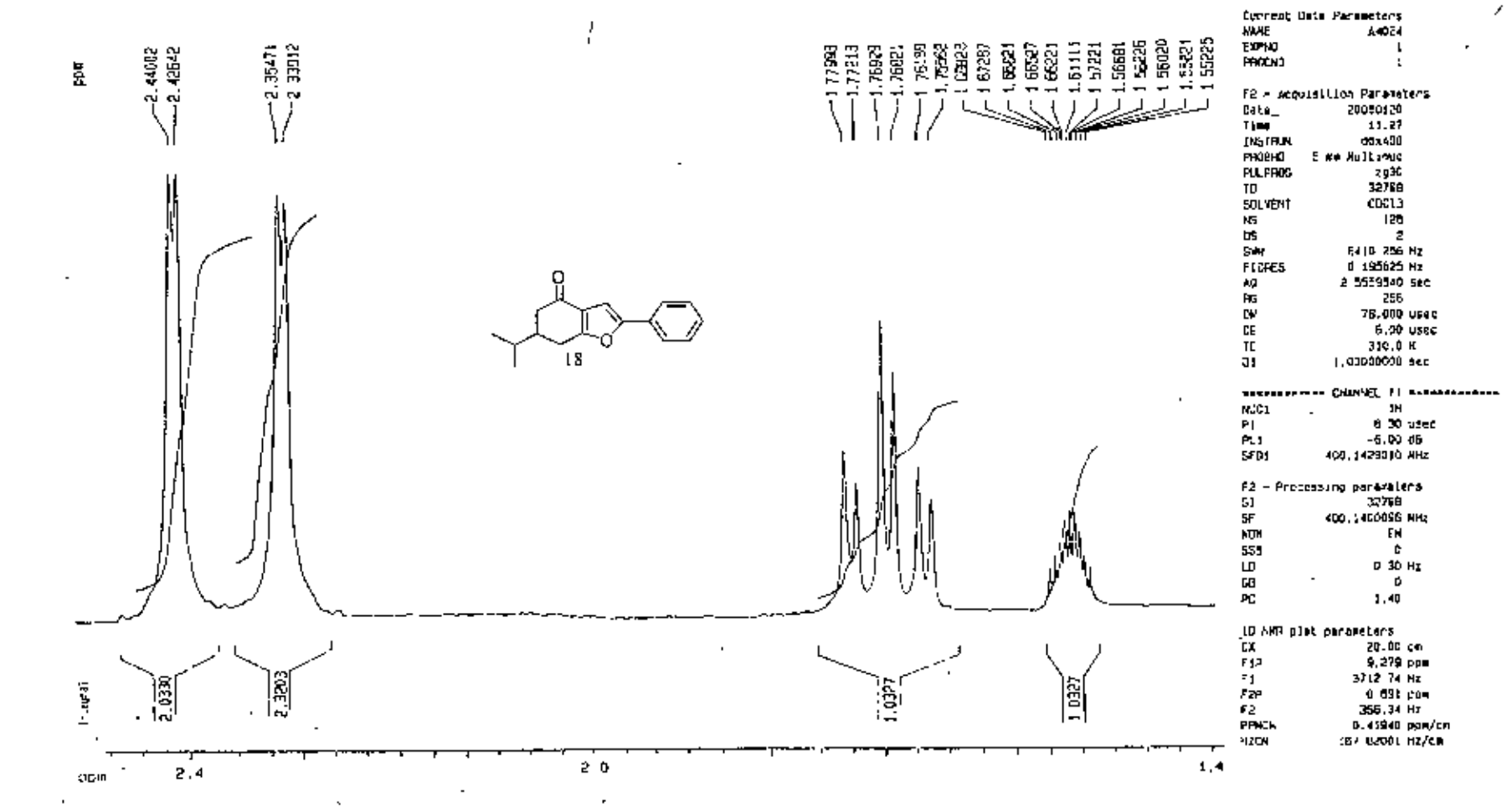


Figure 18c: ^{1}H NMR spectrum of the compound **18**

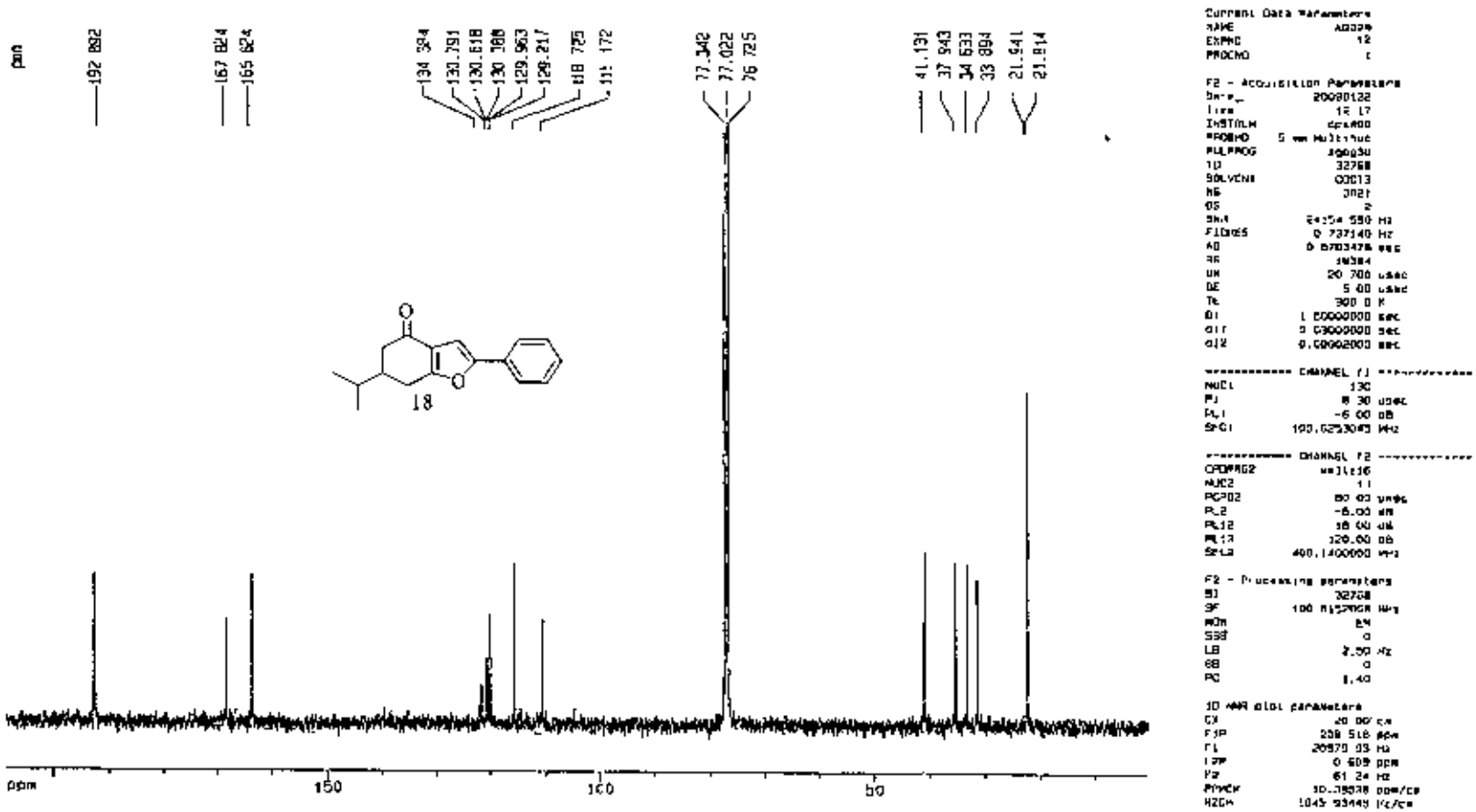
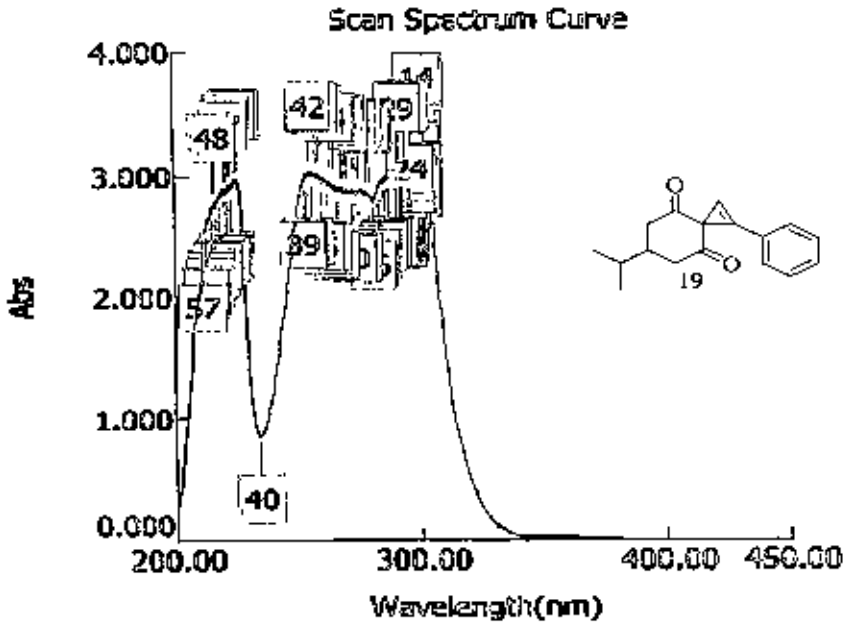


Figure 18d: ^{13}C NMR spectrum of the compound **18**



Instrument Performance
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Spectral Bandwidth : 2.00 nm

Scan Spectrum Performance
Scan Range : 200.00 to 450.00 nm
Measure Mode : Abs
Interval : 0.05 nm
Speed : Fast
Data File : Untitled1.spd
Create Date/Time : Thursday, March 13, 2008 7:37:15 PM
Data Type : Original
Method File:

Analysis Note
Analyser : Administrator
Sample Name : Blank
Comment :

No.	P/V	Wavelength(nm)	Abs	Comment
14	Peak	295.55	3.077	
42	Peak	255.35	3.035	
43	Peak	225.35	2.947	

Figure 19a :UV spectrum of the compound **19**

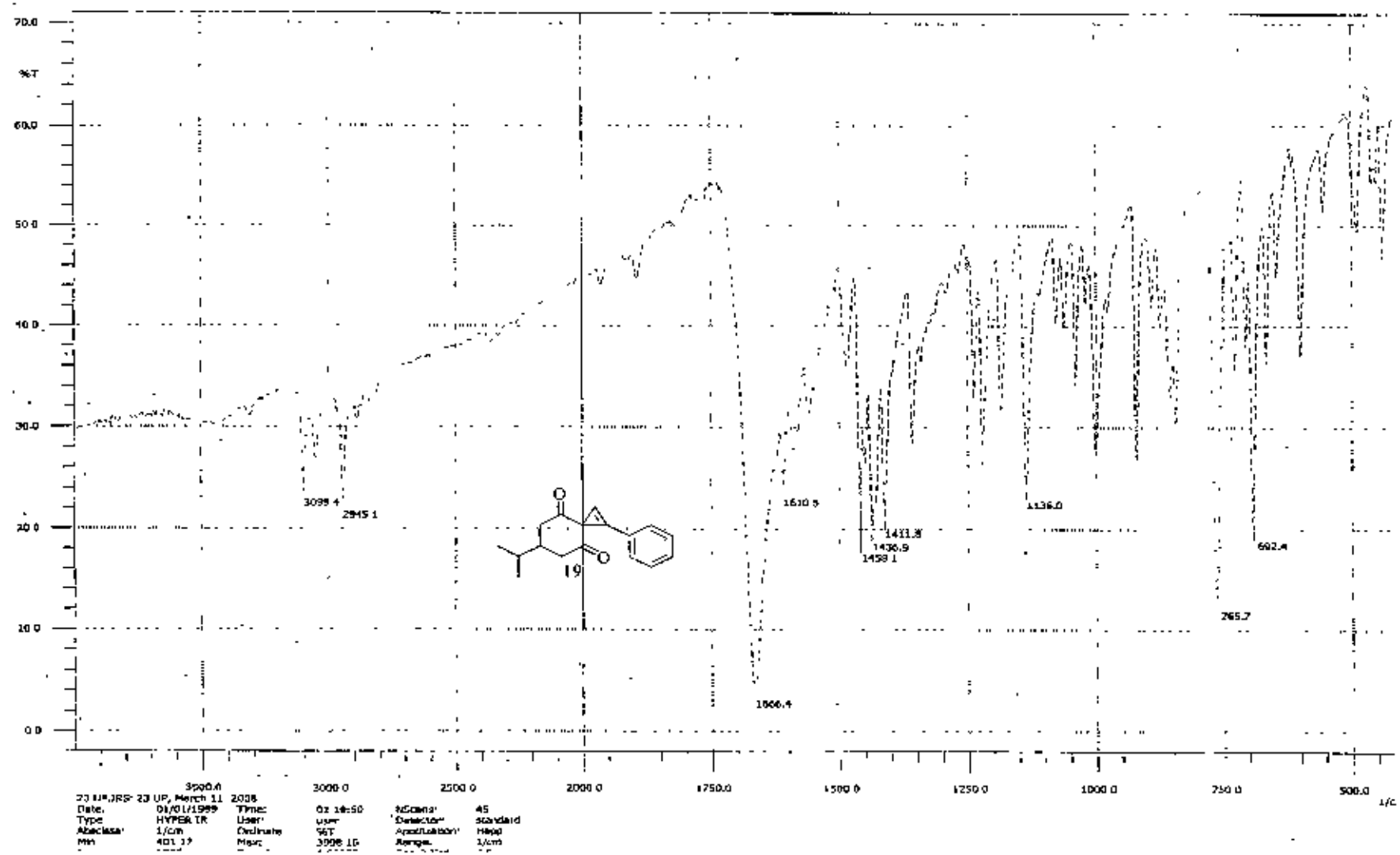
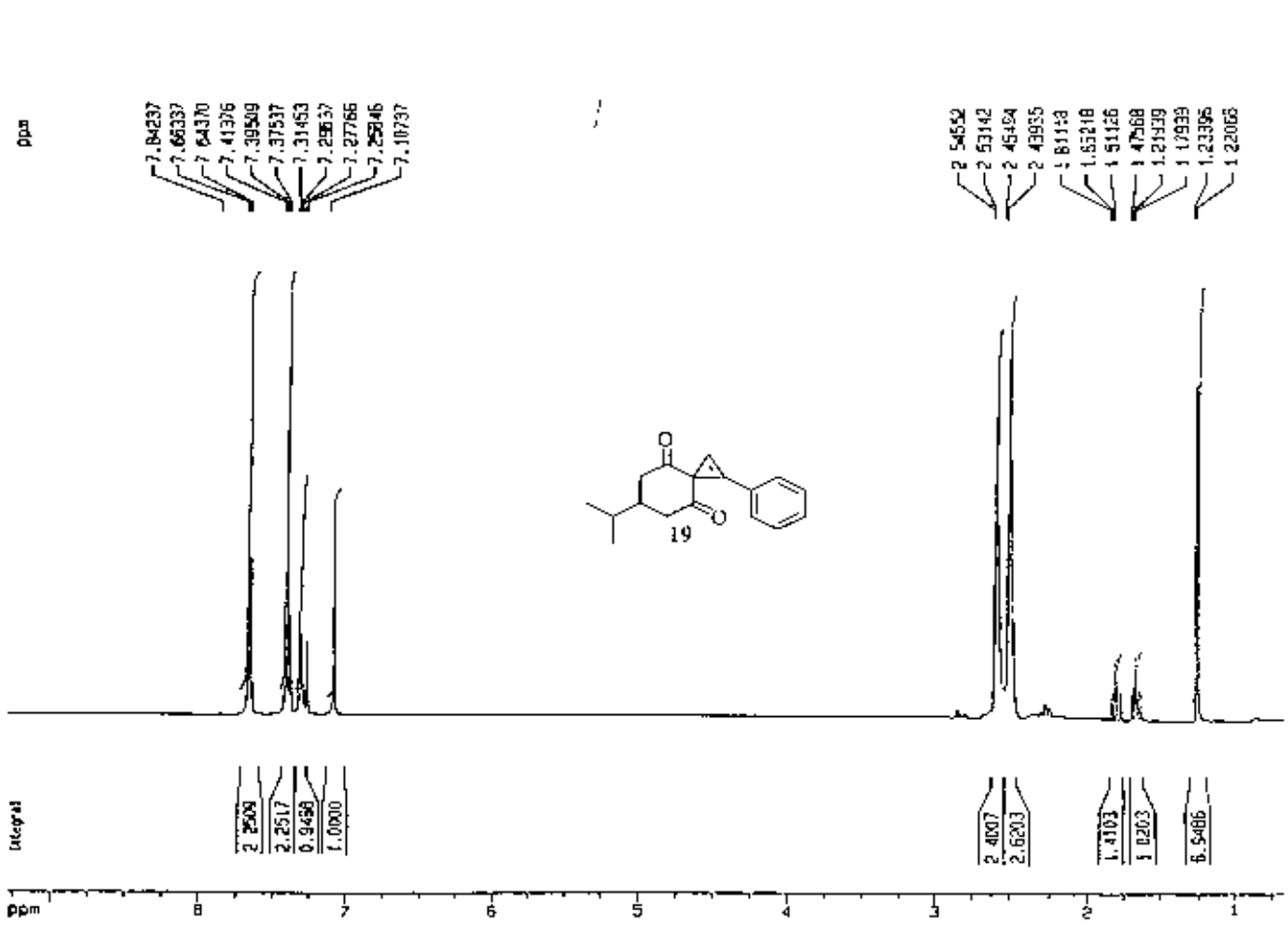


Figure 19b: IR spectrum of the compound **19**




```
Current Data Parameters
NAME                  A4144
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_              20080222
Time                  11.27
INSTRUM               dpx400
PROBHD     5 mm Multinuc
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                      128
DS                        2
SWH               6410.256 Hz
FIDRES            0.195625 Hz
AQ                2.5559040 sec
RG                      256
DW                 78.000 usec
DE                  6.00 usec
TE                  310.0 K
D1                1.00000000 sec

------------ CHANNEL f1 ------------
NUC1                    1H
P1                  8.30 usec
PL1                 -6.00 dB
SFO1          400.1428010 MHz

F2 - Processing parameters
SI                    32768
SF          400.1400098 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                9.279 ppm
F1                 3712.74 Hz
F2P                0.891 ppm
F2                 350.34 Hz
PPMCM             0.41940 ppm/cm
HZCM             167.82001 Hz/cm
```

Figure 19c: ^{1}H NMR spectrum of the compound **19**

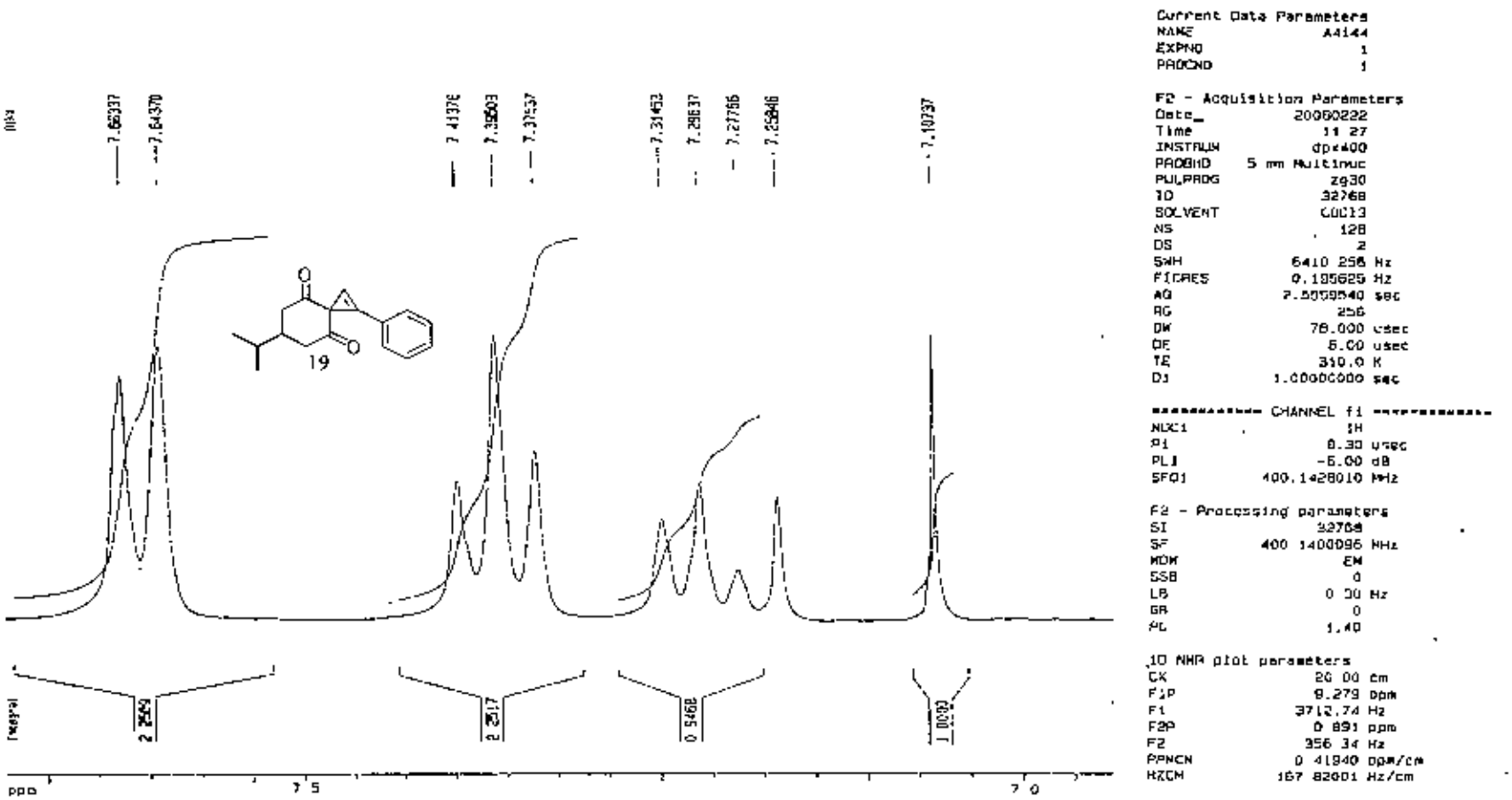


Figure 19c: ^{1}H NMR spectrum of the compound **19**

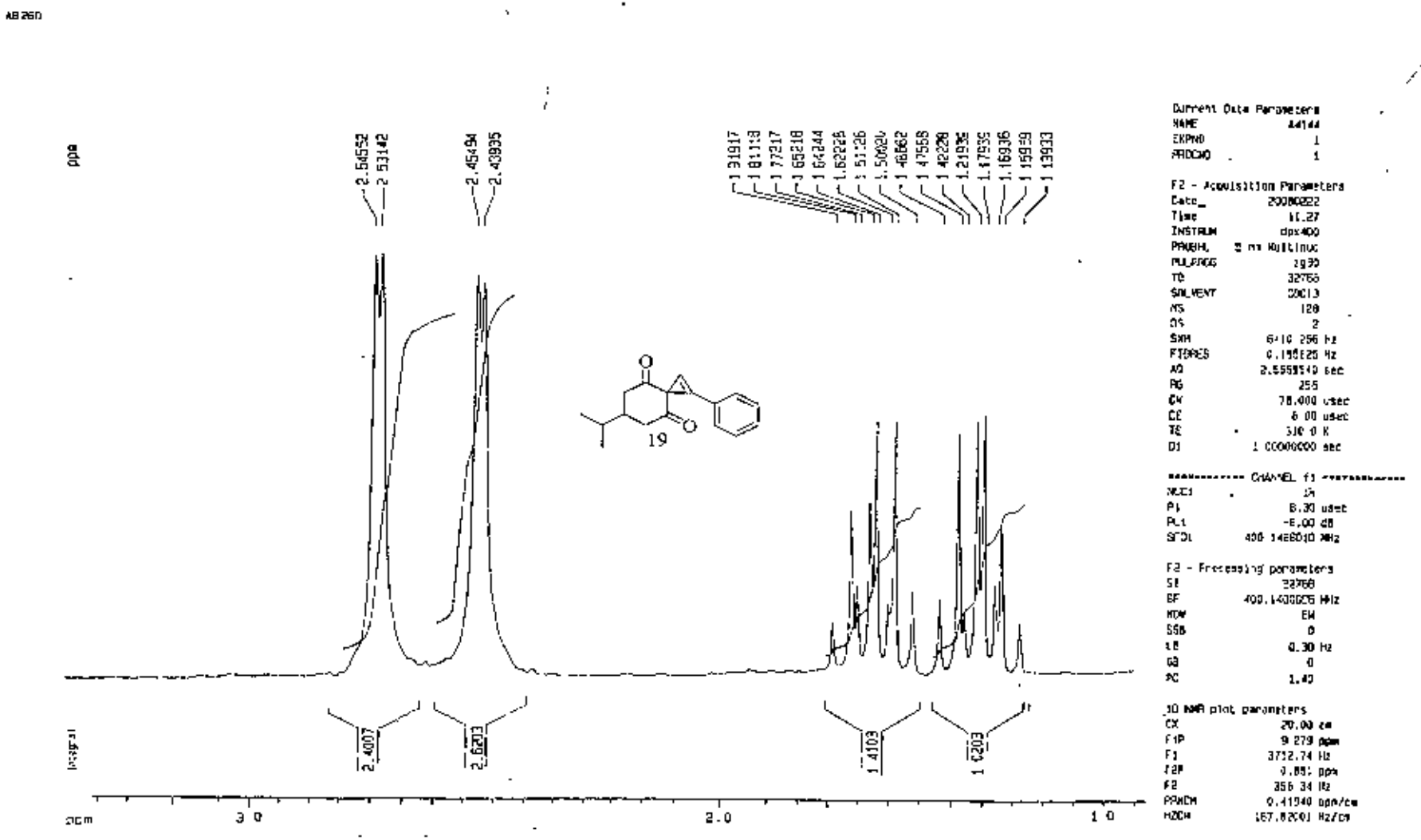
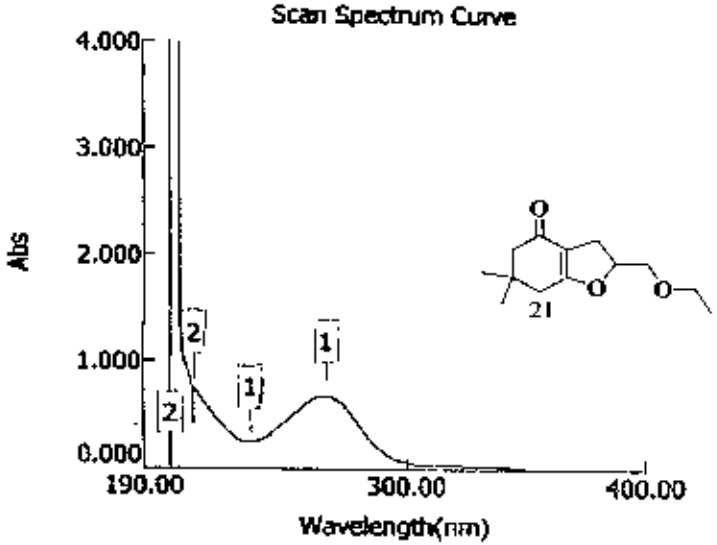


Figure 19c: ^{1}H NMR spectrum of the compound **19**



1	Peak	266.60	0.676
2	Peak	211.10	0.751
1	Valley	234.80	0.245
2	Valley	201.05	-1.558

- **Instrument Performance**
  Model : SPECTROPHOTOMETERS
  Spectral Bandwidth : 2.00 nm
- **Scan Spectrum Performance**
  Scan Range : 190.00 to 400.00 nm
  Measure Mode : Abs
  Interval : 0.05 nm
  Speed : Fast
  Data File : Untitled2.spd
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  Data Type : Original
  Method File:
- **Analyse Note**
  Analyser : Administrator
  Sample Name : Blank
  Comment :
- No. P/V Wavelength(nm) Abs Comment

Figure 21a :UV spectrum of the compound **21**

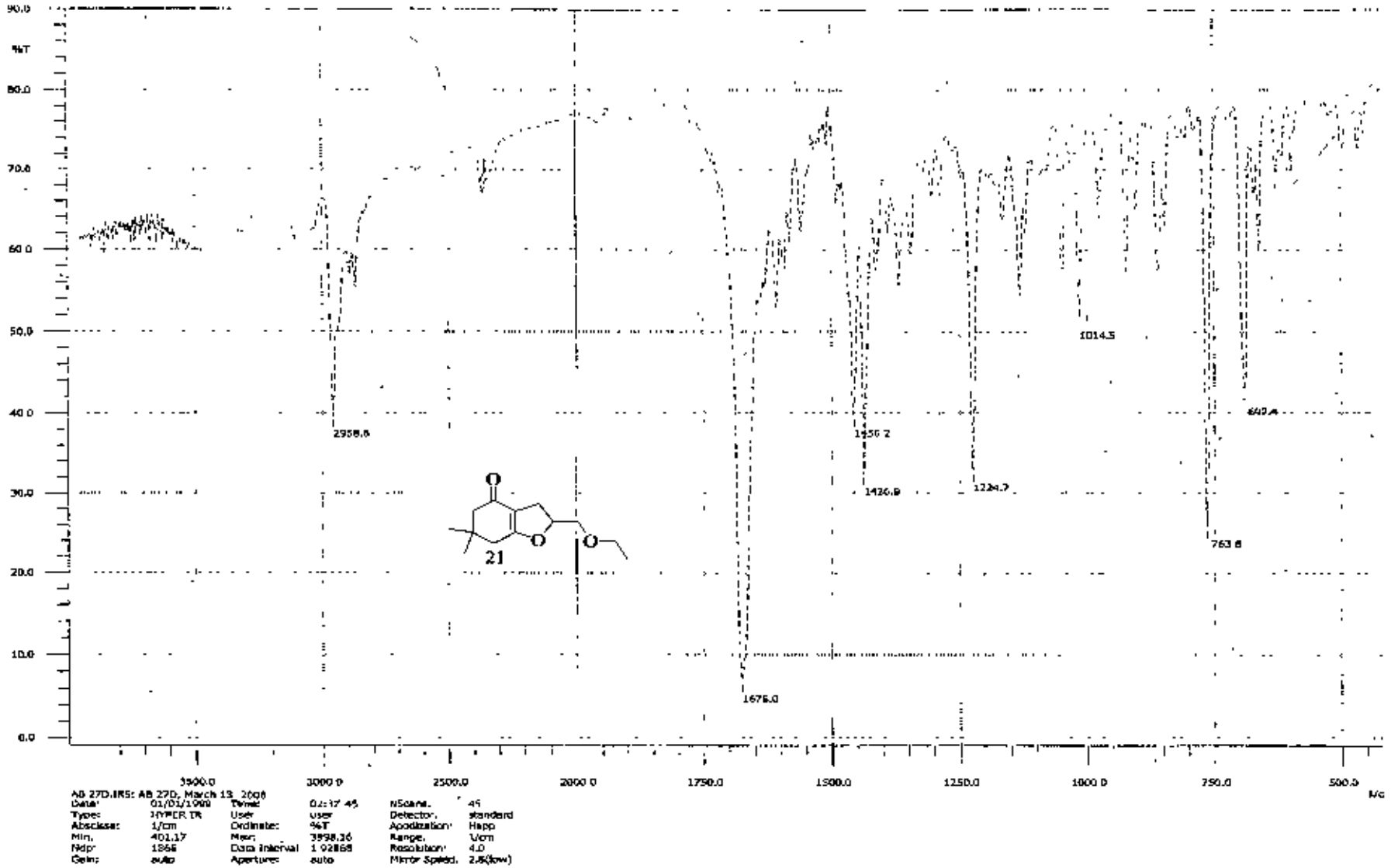
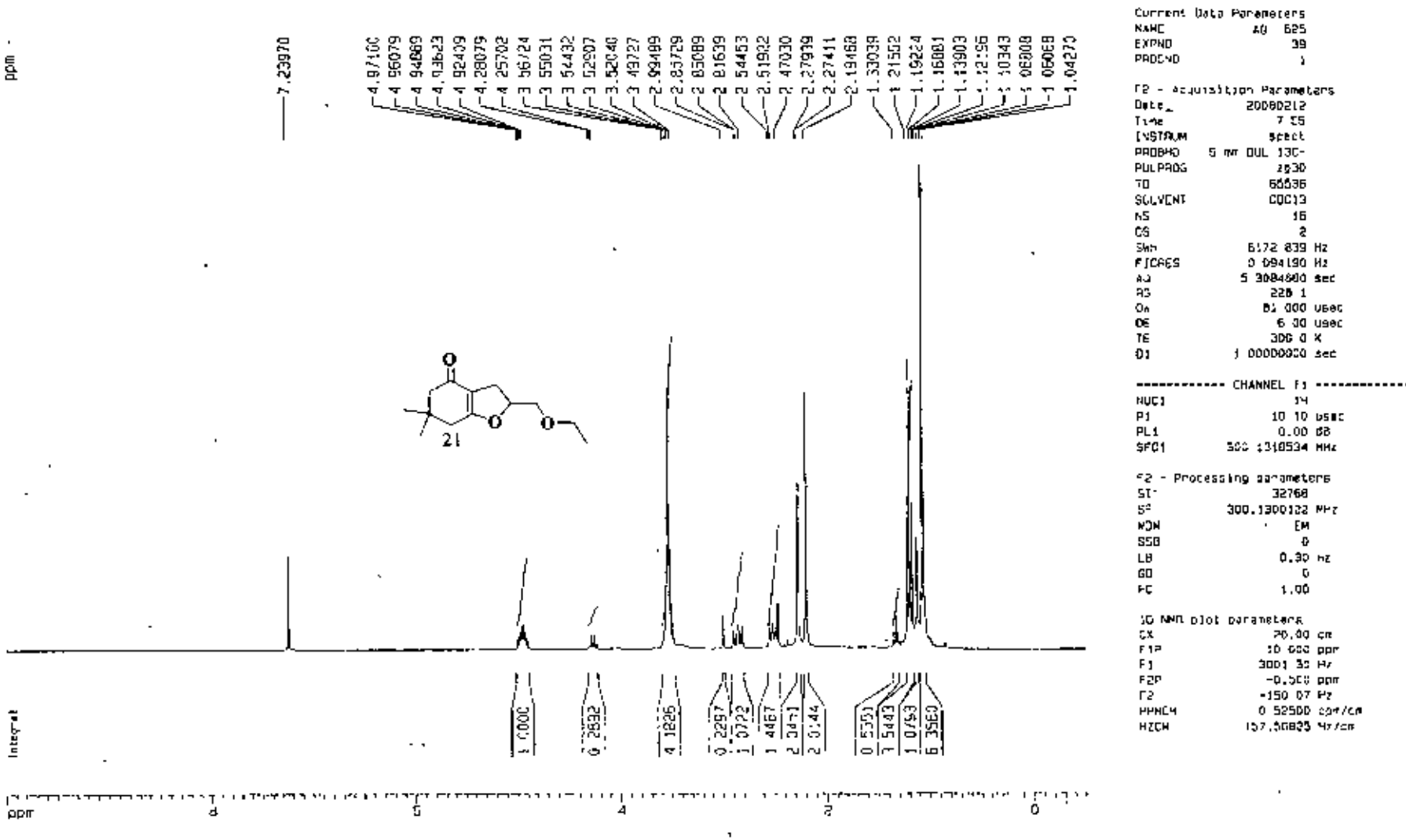


Figure 21b: IR spectrum of the compound **21**




```
Current Data Parameters
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EXPNO                     39
PROCNO                     1

F2 - Acquisition Parameters
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Time                   7 55
INSTRUM                spect
PROBHD     5 mm DUL 13C-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               6172.839 Hz
FIDRES            0.094190 Hz
AQ                5.3084800 sec
RG                    228.1
DW                   81.000 usec
DE                    6.00 usec
TE                   300.0 K
D1                1.00000000 sec

------------ CHANNEL f1 ------------
NUC1                     1H
P1                    10.10 usec
PL1                    0.00 dB
SFO1          500.1310534 MHz

F2 - Processing parameters
SI                    32768
SF            300.1300122 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00

1D NMR plot parameters
CX                    20.00 cm
F1P                   10.000 ppm
F1                 3001.35 Hz
F2P                  -0.508 ppm
F2                 -150.07 Hz
PPMCM              0.52500 ppm/cm
HZCM              157.50825 Hz/cm
```

Figure 21c: ^{1}H NMR spectrum of the compound 21

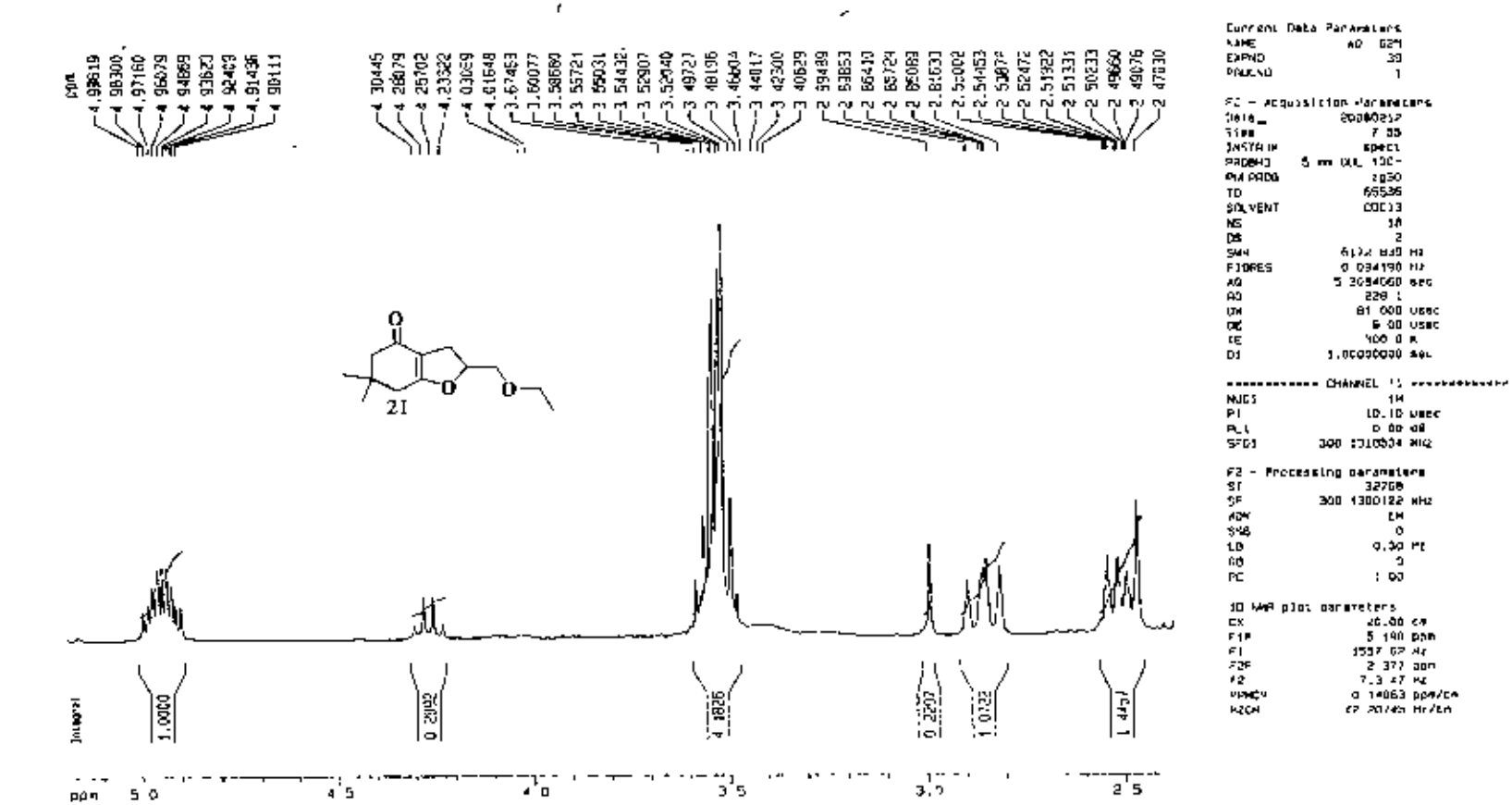
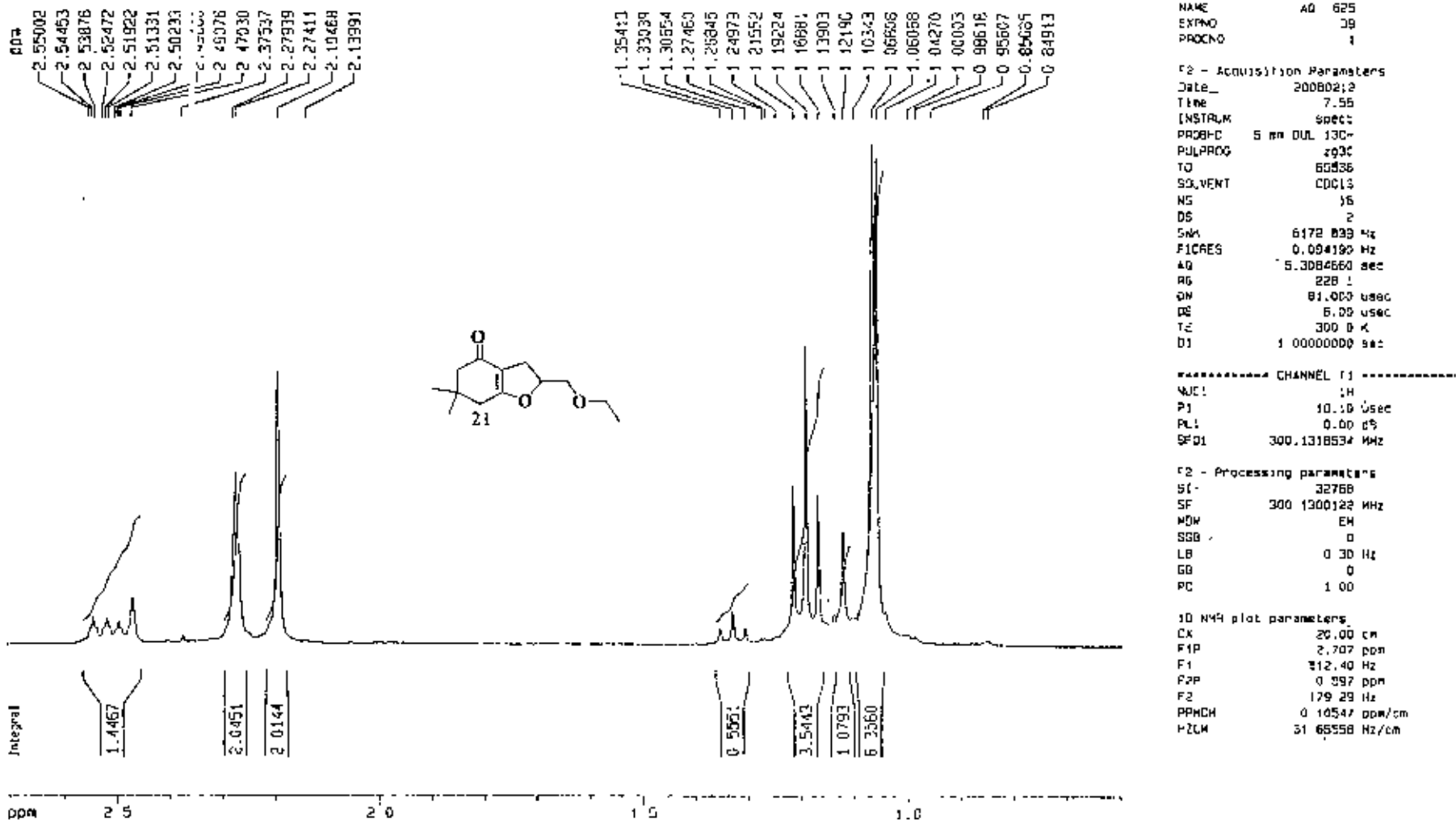


Figure 21c: ^{1}H NMR spectrum of the compound **21**




```
Current Data Parameters
NAME                  AQ  625
EXPNO                     39
PROCNO                     1

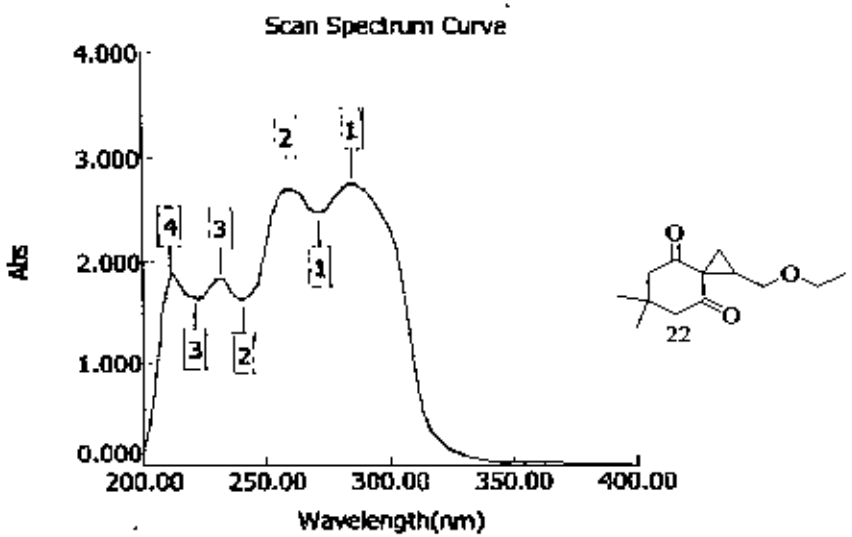
F2 - Acquisition Parameters
Date_              20080212
Time                   7.55
INSTRUM                spect
PROBHD     5 mm DUL 13C-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               6172.839 Hz
FIDRES            0.094190 Hz
AQ                5.3084660 sec
RG                    228.1
DW                   81.000 usec
DE                    6.00 usec
TE                   300.0 K
D1                1.00000000 sec

================ CHANNEL f1 =============
NUC1                     1H
P1                   10.10 usec
PL1                   0.00 dB
SFO1           300.1318534 MHz

F2 - Processing parameters
SI                    32768
SF           300.1300122 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                    1.00

1D NMR plot parameters
CX                   20.00 cm
F1P                   2.707 ppm
F1                  812.40 Hz
F2P                   0.597 ppm
F2                  179.29 Hz
PPMCM             0.10547 ppm/cm
HZCM             31.65558 Hz/cm
```

Figure 21c: ^{1}H NMR spectrum of the compound **21**



1	Peak	285.15	2.722
2	Peak	255.20	2.702
3	Peak	235.95	1.805
4	Peak	211.95	1.835
1	Valley	272.10	2.579
2	Valley	242.50	1.735
3	Valley	221.05	1.799

Instrument Performance
Model : SPECTROPHOTOMETERS
Spectral Bandwidth : 2.00 nm

Scan Spectrum Performance
Scan Range : 200.00 to 400.00 nm
Measure Mode : Abs
Interval : 0.05 nm
Speed : Fast
Data File : Untitled2.spd
Create Date/Time : Wednesday, March 16, 2008 8:53:46 PM
Data Type : Original
Method File:

Analyse Note
Analyser : Administrator
Sample Name : Blank
Comment :

No.	P/V	Wavelength(nm)	Abs	Comment

Figure 22a :UV spectrum of the compound **22**

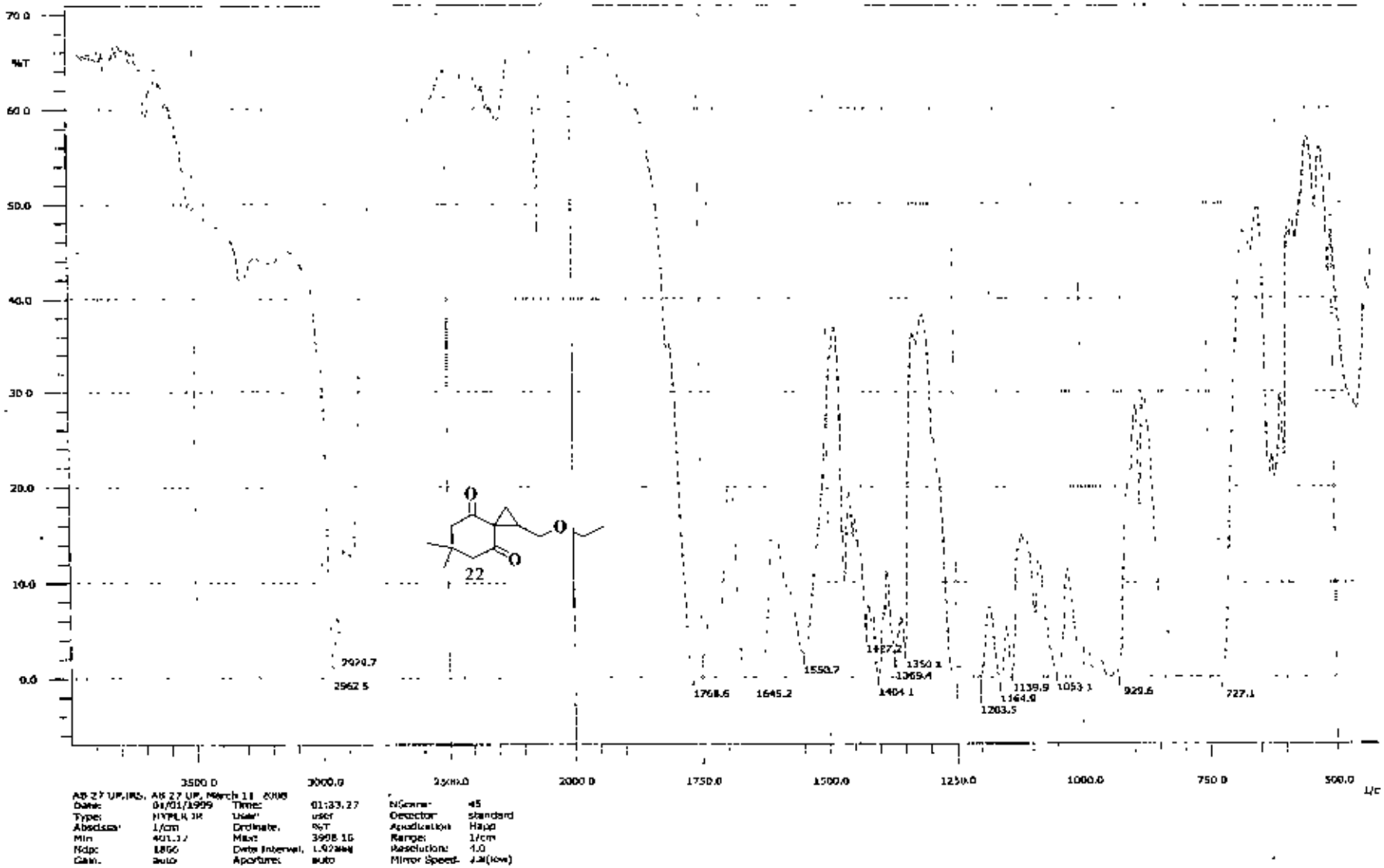


Figure 22b: IR spectrum of the compound **22**

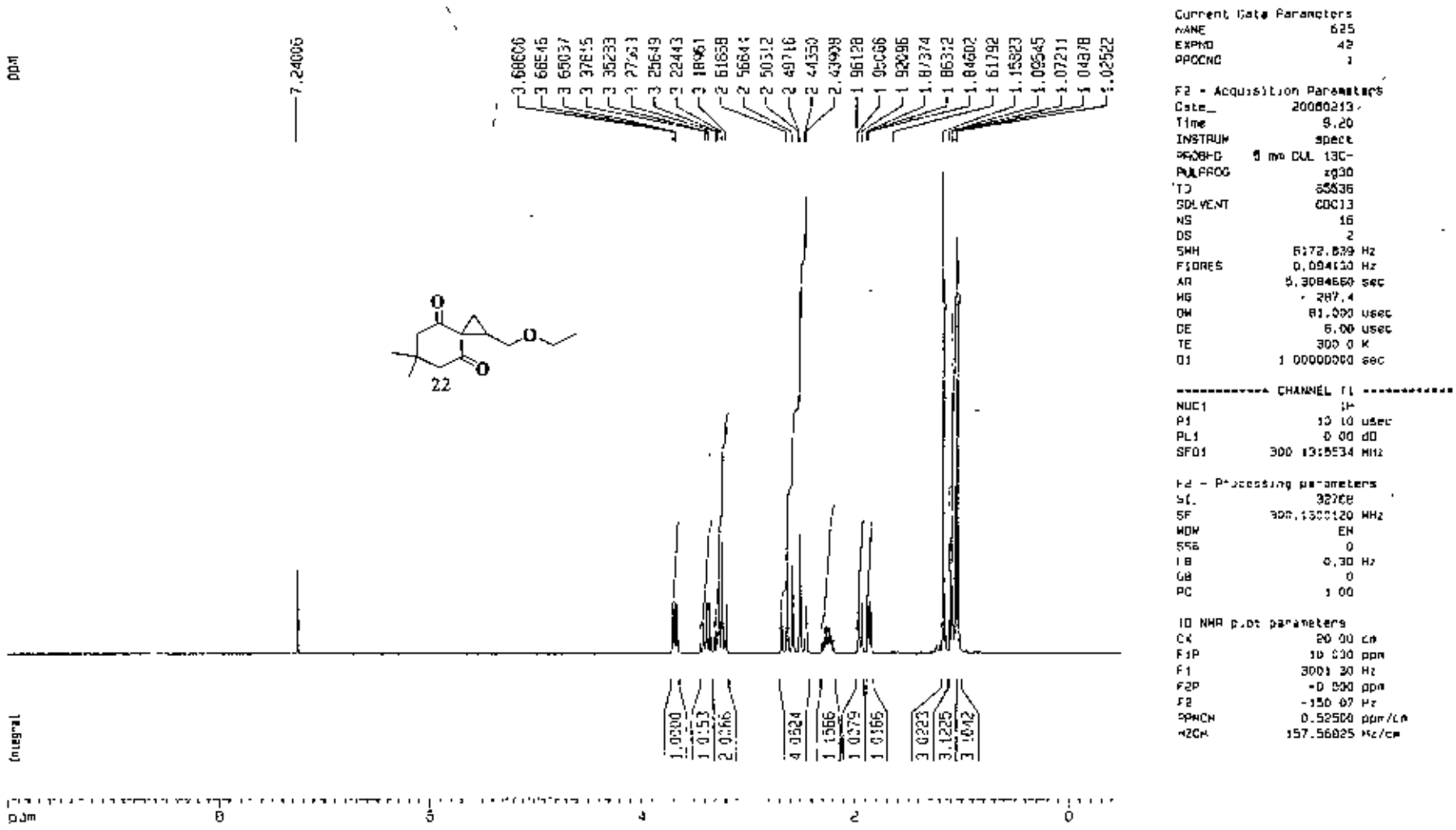
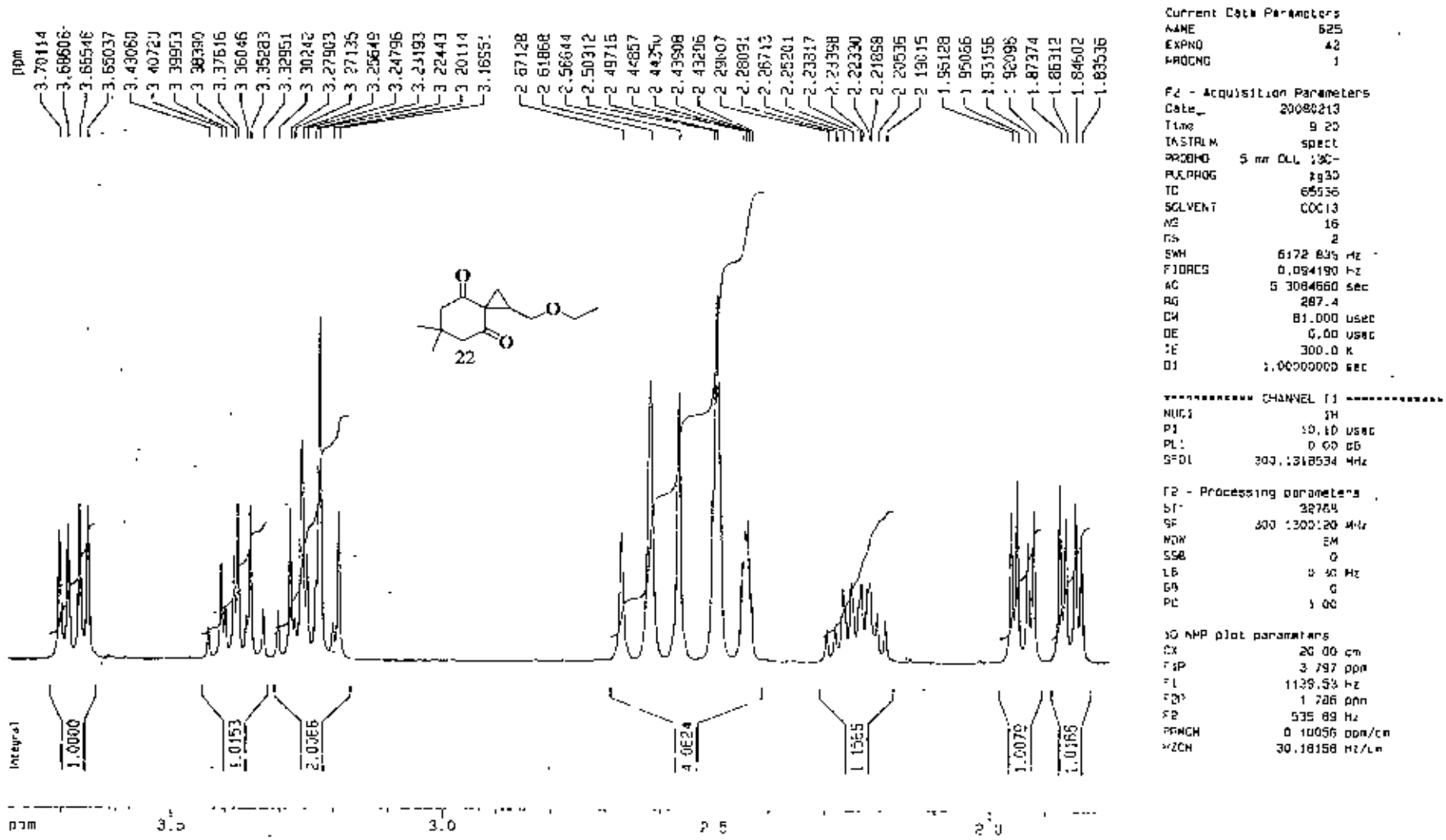


Figure 22c: ^{1}H NMR spectrum of the compound **22**




```
Current Data Parameters
NAME                  625
EXPNO                  42
PROCNO                  1

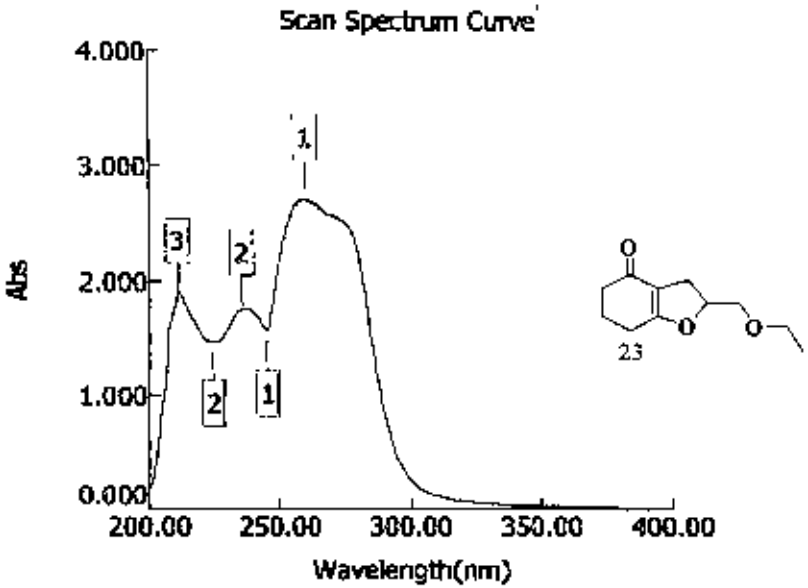
F2 - Acquisition Parameters
Date_          20080213
Time                9 25
INSTRUM             spect
PROBHD     5 mm DUL 13C-
PULPROG             zg30
TD                 65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH           6172.839 Hz
FIDRES        0.094190 Hz
AQ            5.3084660 sec
RG                  287.4
DW             81.000 usec
DE              6.00 usec
TE              300.0 K
D1             1.00000000 sec

========== CHANNEL f1 ==========
NUC1                   1H
P1                  10.10 usec
PL1                 0.00 dB
SFO1          300.1318534 MHz

F2 - Processing parameters
SI                  32754
SF          300.1300120 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00

1D NMR plot parameters
CX                 20.00 cm
F1P                3.797 ppm
F1                 1139.53 Hz
F2P                1.726 ppm
F2                 535.89 Hz
PPMCM              0.10056 ppm/cm
HZCM              30.18156 Hz/cm
```

Figure 22c: ^{1}H NMR spectrum of the compound **22**



Instrument Performance
Model : SPECTROPHOTOMETERS
Spectral Bandwidth : 2.00 nm

Scan Spectrum Performance
Scan Range : 200.00 to 400.00 nm
Measure Mode : Abs
Interval : 0.05 nm
Speed : Fast
Data File : Untitled2.spd
Create Date/Time : Wednesday, March 15, 2006 8:55:45 PM
Data Type : Original
Method File:

Analyze Mode
Analyser : Administrator
Sample Name : Blank
Comment :

No.	P/V	Wavelength(nm)	Abs	Comment
1	Peak	260.15	2.722	
2	Peak	238.20	1.712	
3	Peak	210.95	1.835	
1	Valley	245.20	1.612	
2	Valley	222.25	1.482	

Figure 23a :UV spectrum of the compound 23

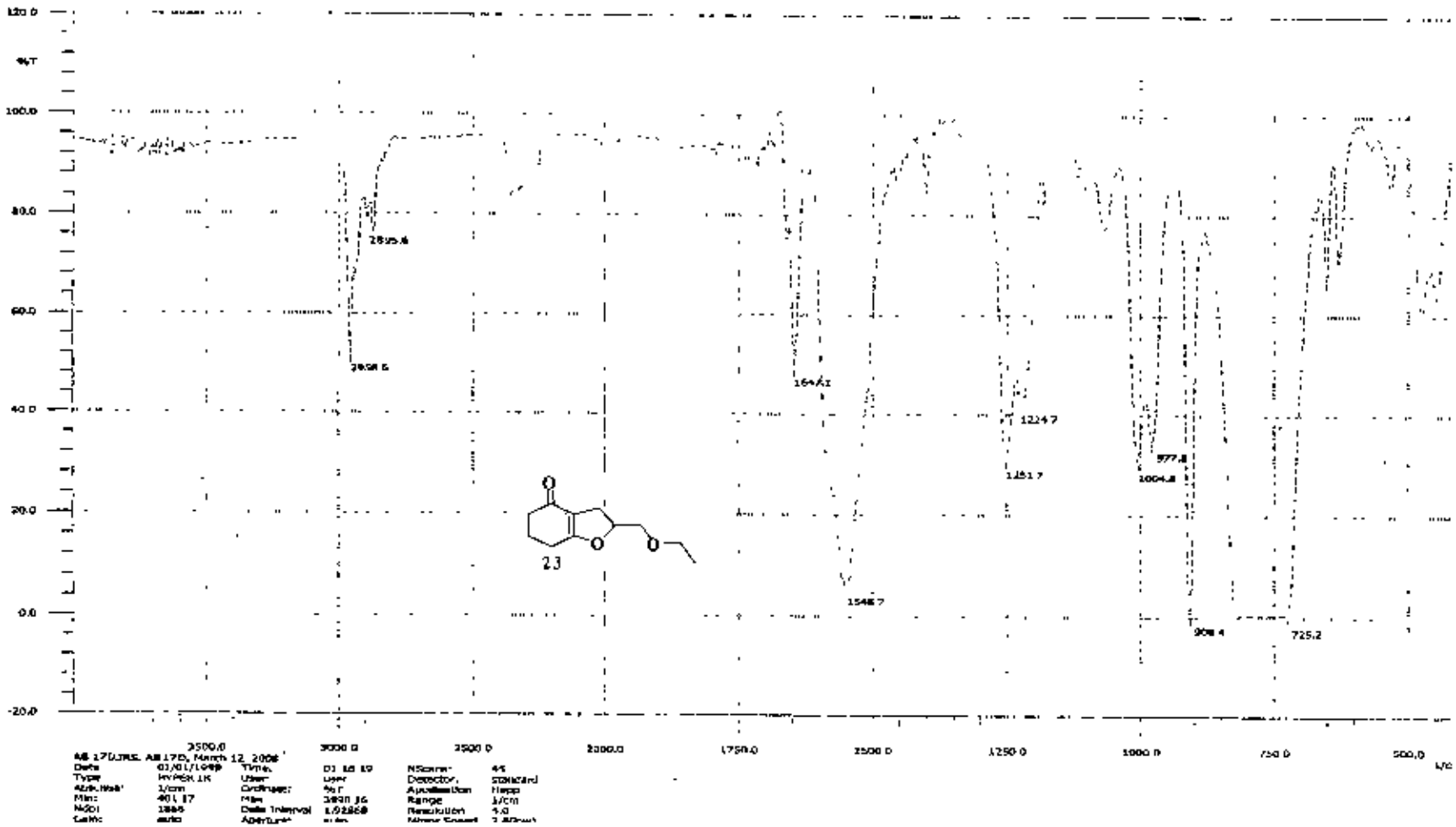
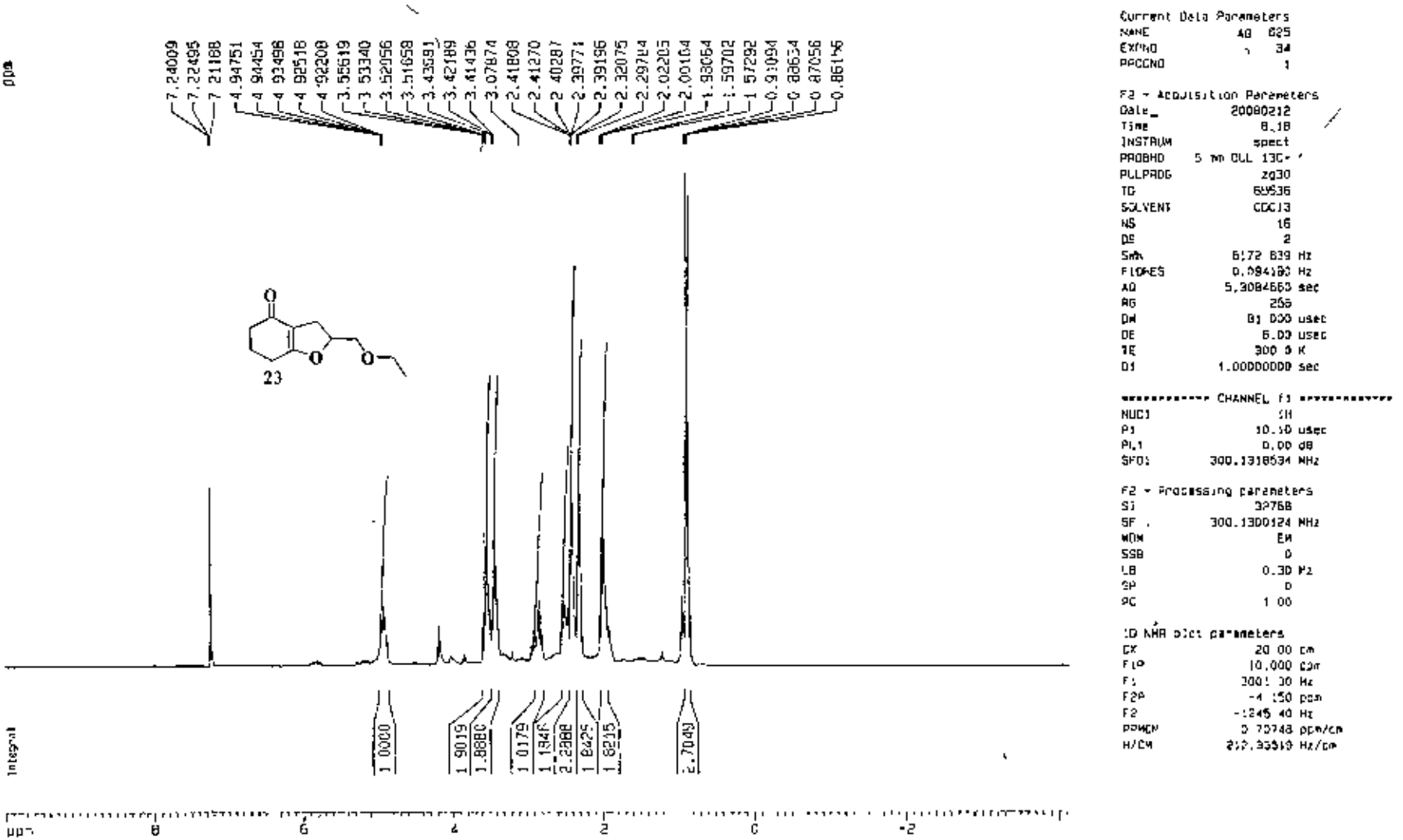


Figure 23b: IR spectrum of the compound **23**




```
Current Data Parameters
NAME                  AB  625
EXPNO                  ,   34
PROCNO                     1

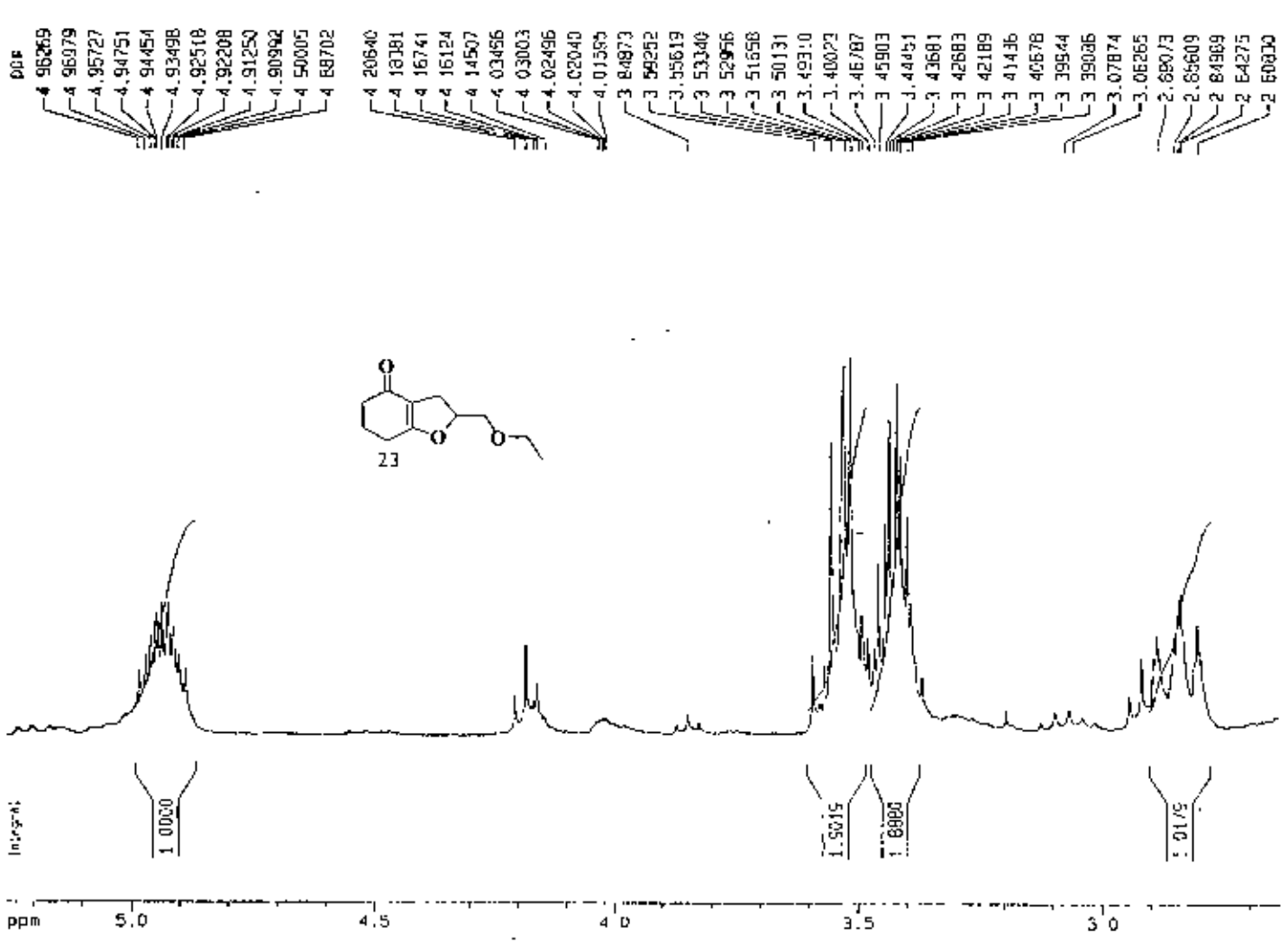
F2 - Acquisition Parameters
Date_              20080212
Time                   8.18
INSTRUM               spect
PROBHD     5 mm DUL 13C- '
PULPROG                zg30
TD                   65536
SOLVENT              CDCl3
NS                       16
DS                        2
SWH               6172.839 Hz
FIDRES            0.094183 Hz
AQ                5.3084663 sec
RG                      256
DW                 81.000 usec
DE                  6.00 usec
TE                 300.0 K
D1                1.00000000 sec

========== CHANNEL f1 ==========
NUC1                      1H
P1                     10.10 usec
PL1                     0.00 dB
SFO1           300.1318634 MHz

F2 - Processing parameters
SI                       32768
SF                300.1300124 MHz
WDW                         EM
SSB                          0
LB                      0.30 Hz
GB                           0
PC                      1.00

1D NMR plot parameters
CX                     20.00 cm
F1P                   10.000 ppm
F1                  3001.30 Hz
F2P                  -4.150 ppm
F2                  -1245.40 Hz
PPMCM                0.70748 ppm/cm
HZCM                212.93519 Hz/cm
```

Figure 23c: ^{1}H NMR spectrum of the compound **23**




```
Current Data Parameters
NAME                  AQ  625
EXPNO                 34
PROCNO                1

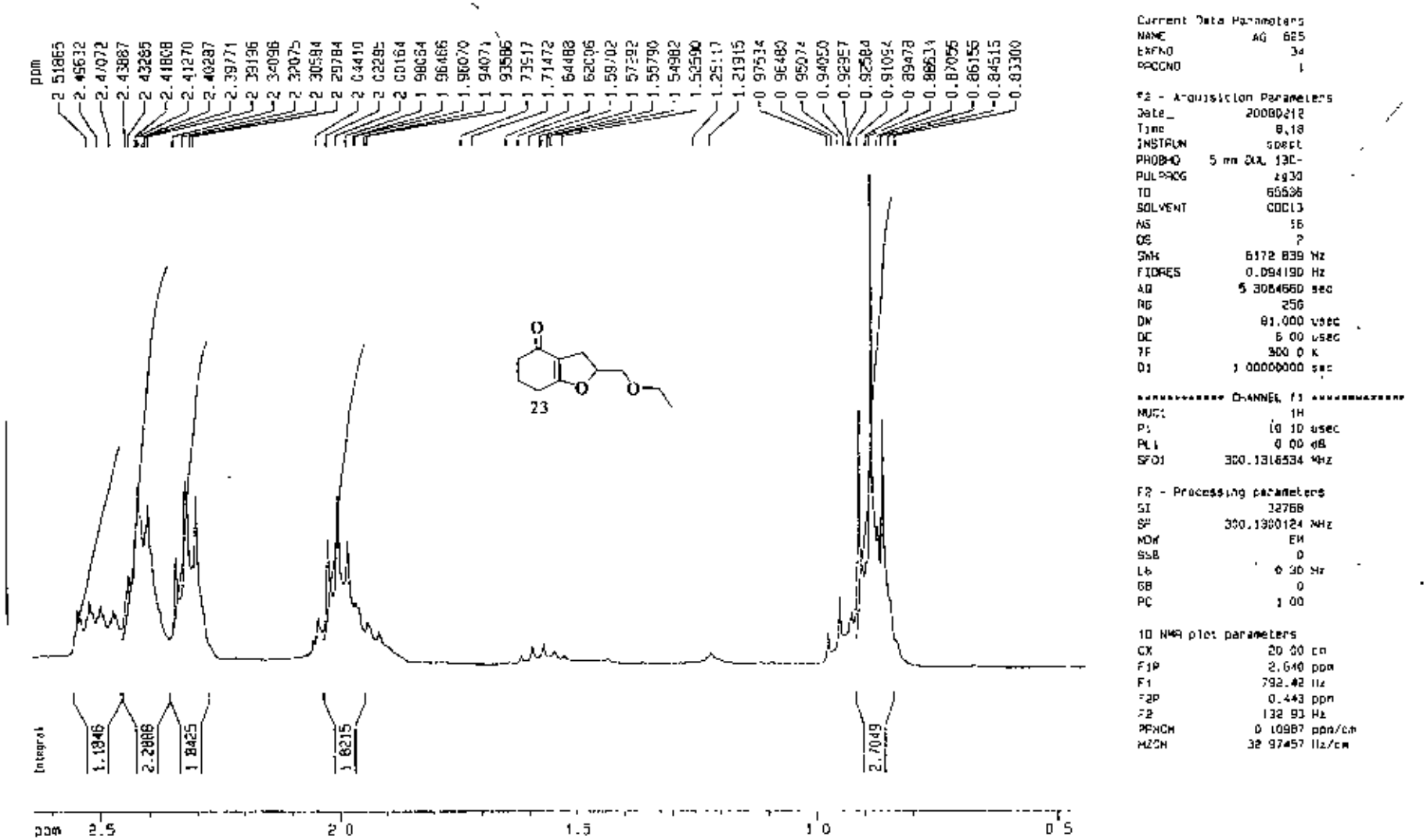
F2 - Acquisition Parameters
Date_              20080212
Time                  8.18
INSTRUM               spect
PROBHD     5 mm QXL 13C-
PULPROG               zg30
TD                    65536
SOLVENT               CDCl3
NS                    16
DS                    2
SWH                6172.839 Hz
FIDRES             0.094190 Hz
AQ                 5.3084660 sec
RG                    256
DW                   81.000 usec
DE                    6.00 usec
TE                  300.0 K
D1                  1.00000000 sec

------------ CHANNEL f1 ------------
NUC1                  1H
P1                   10.10 usec
PL1                   0.00 dB
SFO1          300.1318534 MHz

F2 - Processing parameters
SI                    32768
SF          300.1300124 MHz
WDW                   EM
SSB                   0
LB                    0.30 Hz
GB                    0
PC                    1.00

1D NMR plot parameters
CX                   20.00 cm
F1P                   5.253 ppm
F1                 1576.66 Hz
F2P                   2.638 ppm
F2                  791.74 Hz
PPMCM              0.13076 ppm/cm
HZCM              39.24572 Hz/cm
```

Figure 23c: ^{1}H NMR spectrum of the compound **23**



Current Data Parameters
NAME AG 685
EXPNO 34
PROCNO 1

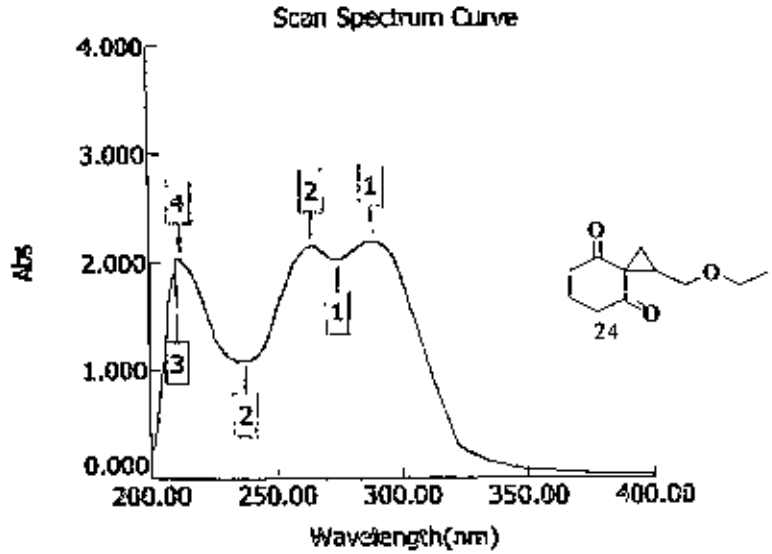
F2 - Acquisition Parameters
Date_ 20080218
Time 8.18
INSTRUM spect
PROBHD 5 mm DUL 13C-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 56
DS 2
SWH 6172.839 Hz
FIDRES 0.094190 Hz
AQ 5.3084660 sec
RG 256
DW 81.000 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

CHANNEL f1
NUC1 1H
P1 10.10 usec
PL1 0.00 dB
SFO1 300.1316534 MHz

F2 - Processing parameters
SI 32768
SF 300.1300124 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 2.640 ppm
F1 792.42 Hz
F2P 0.443 ppm
F2 132.93 Hz
PPMCM 0.10987 ppm/cm
HZCM 32.97457 Hz/cm

Figure 23c: ^{1}H NMR spectrum of the compound **23**



Instrument Performance
Model : SPECTROPHOTOMETERS
Spectral Bandwidth : 2.00 nm

Scan Spectrum Performance
Scan Range : 200.00 to 400.00 nm
Measure Mode : Abs
Interval : 0.05 nm
Speed : Fast
Data File : Untitled1.spd
Create Date/Time : Wednesday, March 12, 2008 8:26:36 PM
Data Type : Original
Method File:

Analyse Note
Analyser : Administrator
Sample Name : Blank
Comment :

No.	P/V	Wavelength(nm)	Abs	Comment
1	Peak	284.45	2.229	
2	Peak	258.55	2.151	
3	Peak	212.70	2.031	
4	Peak	211.95	2.041	
1	Valley	273.10	2.040	
2	Valley	234.50	0.997	
3	Valley	211.05	1.579	

Figure 24a :UV spectrum of the compound **24**

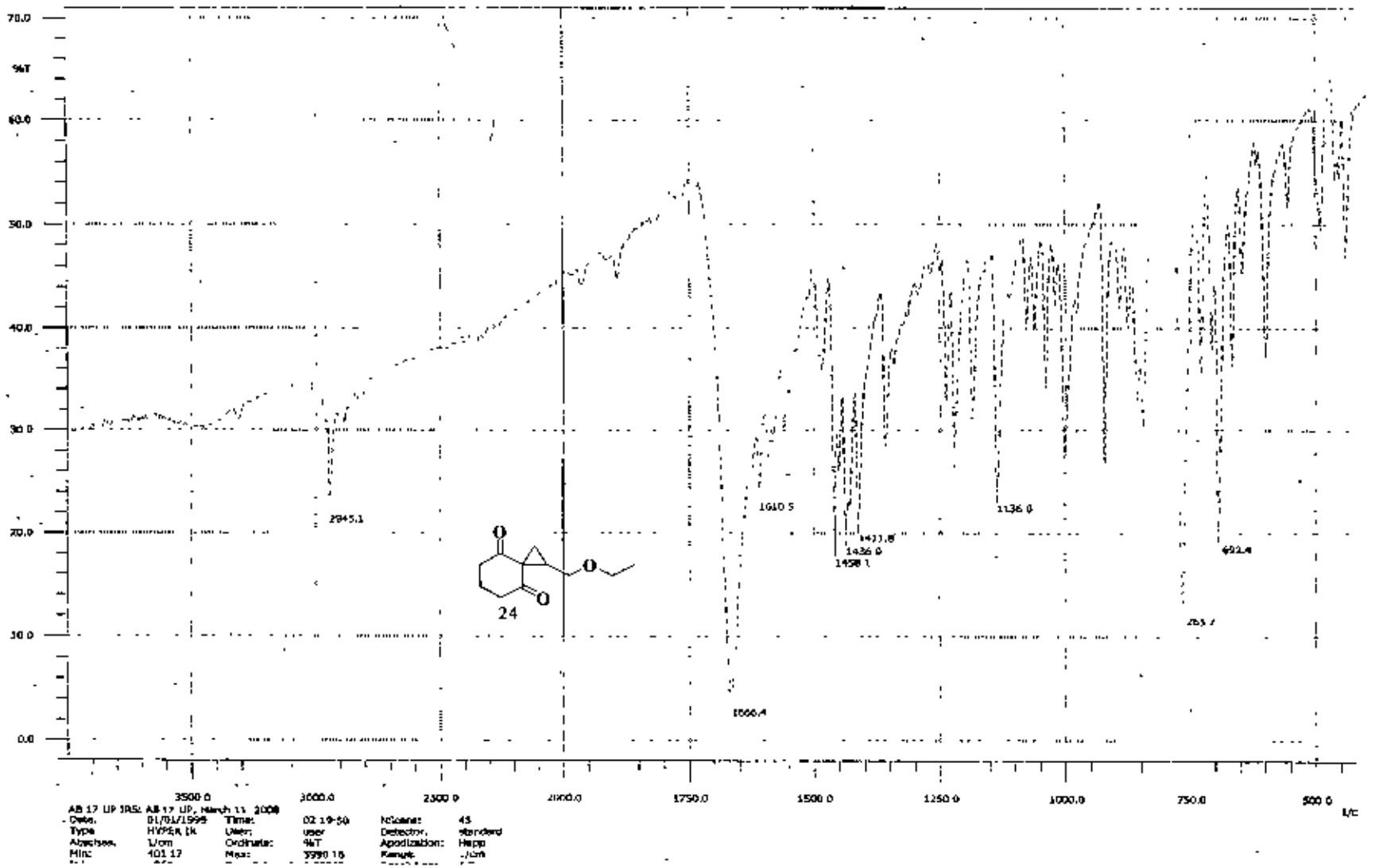
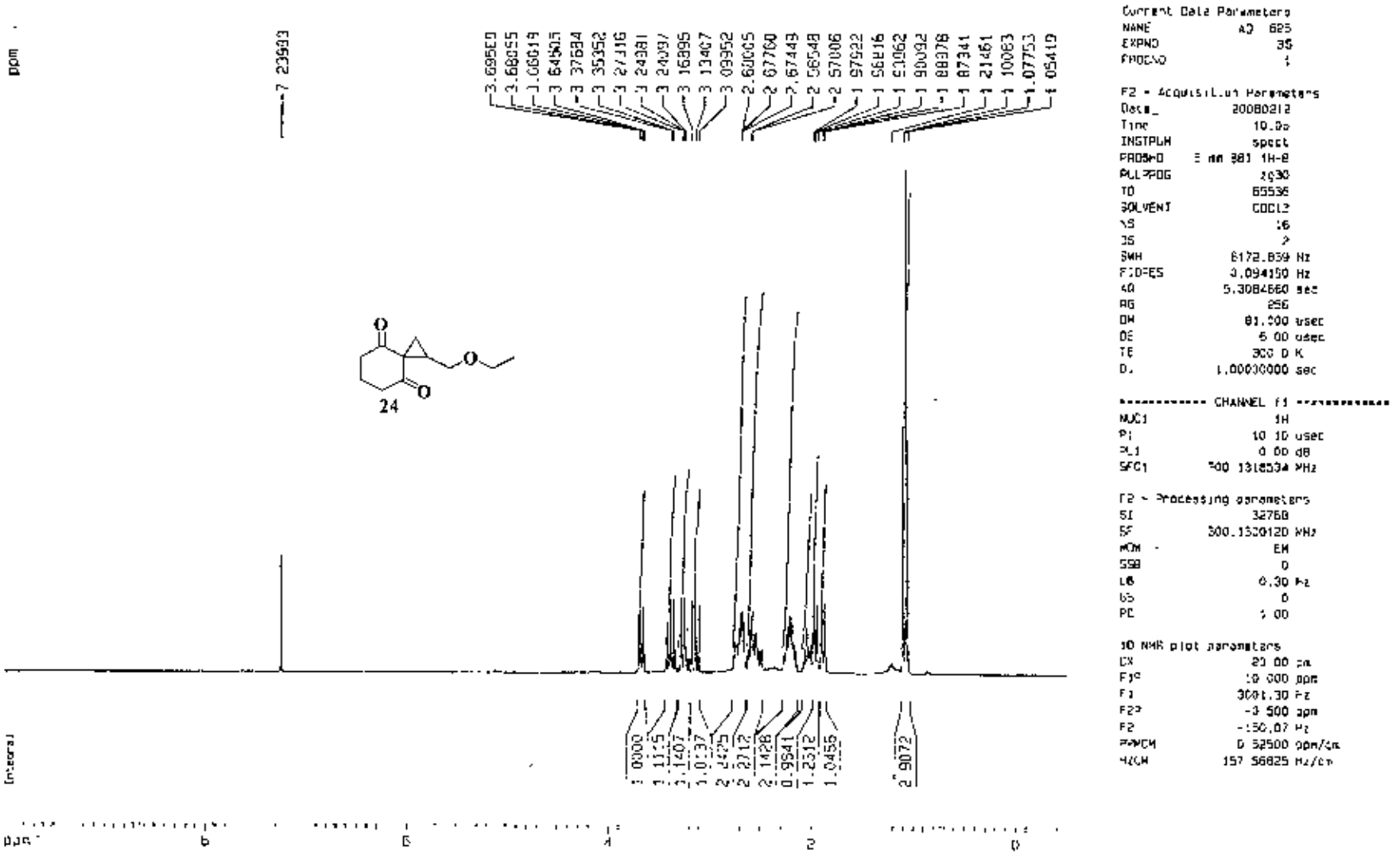


Figure 24b: IR spectrum of the compound 24




```
Current Data Parameters
NAME                  AD  625
EXPNO                     35
PROCNO                     1

F2 - Acquisition Parameters
Date_              20080212
Time                   10.0o
INSTRUM                spect
PROBHD     5 mm 3B1 1H-B
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH               6172.839 Hz
FIDRES            0.094150 Hz
AQ                5.3084660 sec
RG                      256
DW                 81.000 usec
DE                  6.00 usec
TE                  300.0 K
D1                1.00000000 sec

========== CHANNEL f1 ============
NUC1                      1H
P1                   10.10 usec
PL1                   0.00 dB
SFO1           500.1316534 MHz

F2 - Processing parameters
SI                        32768
SF              500.1320012 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00

1D NMR plot parameters
CX                      20.00 cm
F1P                   10.000 ppm
F1                  5001.30 Hz
F2P                  -3.500 ppm
F2                  -150.07 Hz
PPMCM                0.52500 ppm/cm
HZCM                157.56825 Hz/cm
```

Figure 24c: ^{1}H NMR spectrum of the compound **24**

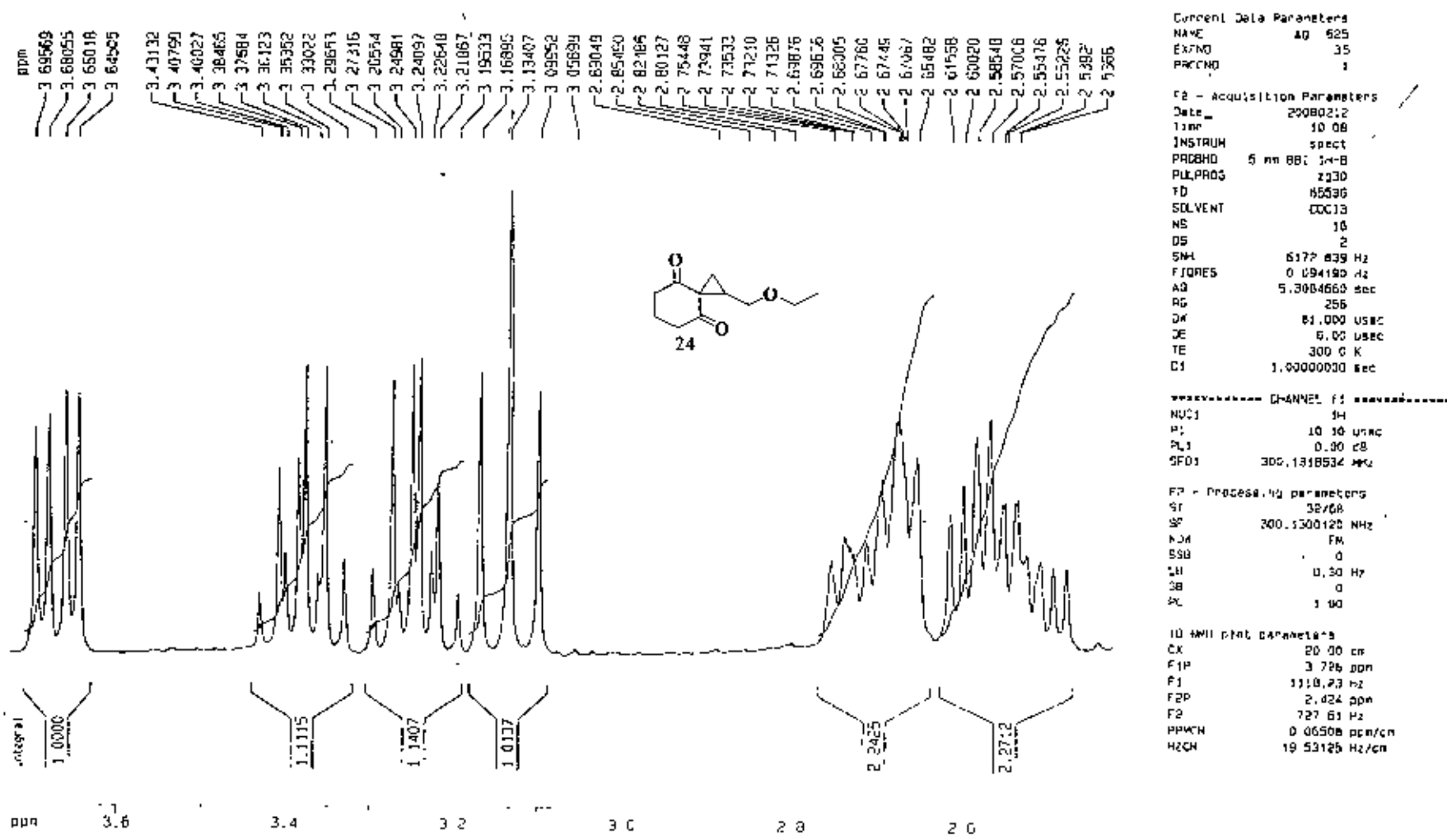
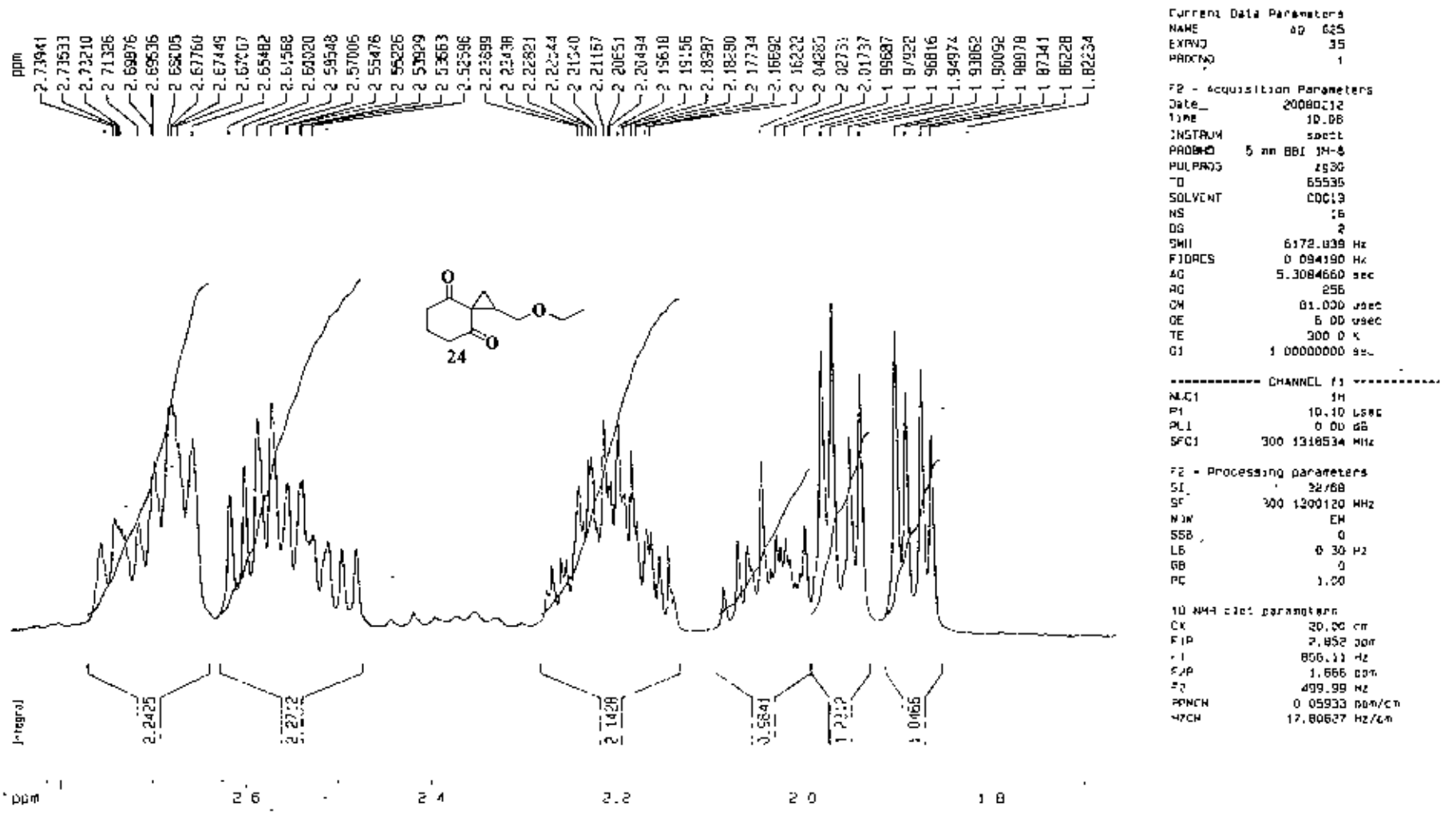


Figure 24c: ^{1}H NMR spectrum of the compound **24**




```
Current Data Parameters
NAME                  AD  025
EXPNO                     35
PROCNO                     1

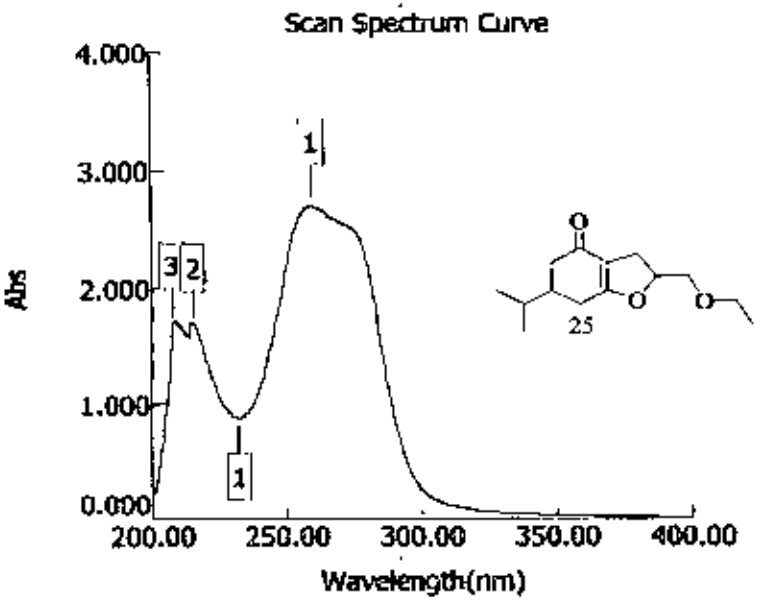
F2 - Acquisition Parameters
Date_              20080212
Time                   10.08
INSTRUM                spect
PROBHD     5 mm BBI 1H-&
PULPROG                zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                6172.839 Hz
FIDRES             0.094190 Hz
AQ                 5.3084660 sec
RG                       256
DW                  81.000 usec
DE                   6.00 usec
TE                  300.0 K
D1                 1.00000000 sec

------------ CHANNEL f1 ------------
NUC1                      1H
P1                     10.10 usec
PL1                     0.00 dB
SFO1             300.1318534 MHz

F2 - Processing parameters
SI                       32768
SF               300.1300120 MHz
WDW                        EM
SSB                         0
LB                     0.30 Hz
GB                          0
PC                      1.00

1D NMR plot parameters
CX                     20.00 cm
F1P                    2.852 ppm
F1                   856.11 Hz
F2P                    1.666 ppm
F2                   499.99 Hz
PPMCM              0.05933 ppm/cm
HZCM              17.80627 Hz/cm
```

Figure 24c: ^{1}H NMR spectrum of the compound **24**



1	Peak	255.15	2.727
2	Peak	211.20	1.712
3	Peak	205.95	1.735
1	Valley	232.20	0.885

Instrument Performance
Model : SPECTROPHOTOMETERS
Spectral Bandwidth : 2.00 nm

Scan Spectrum Performance
Scan Range : 200.00 to 400.00 nm
Measure Mode : Abs
Interval : 0.05 nm
Speed : Fast
Data File : Untitled2.spd
Create Date/Time : Wednesday, March 14, 2008 8:54:44 PM
Data Type : Original
Method File:

Analysis Note
Analyser : Administrator
Sample Name : Blank
Comment :

No. P/V Wavelength(nm) Abs Comment

Figure 25a :UV spectrum of the compound **25**

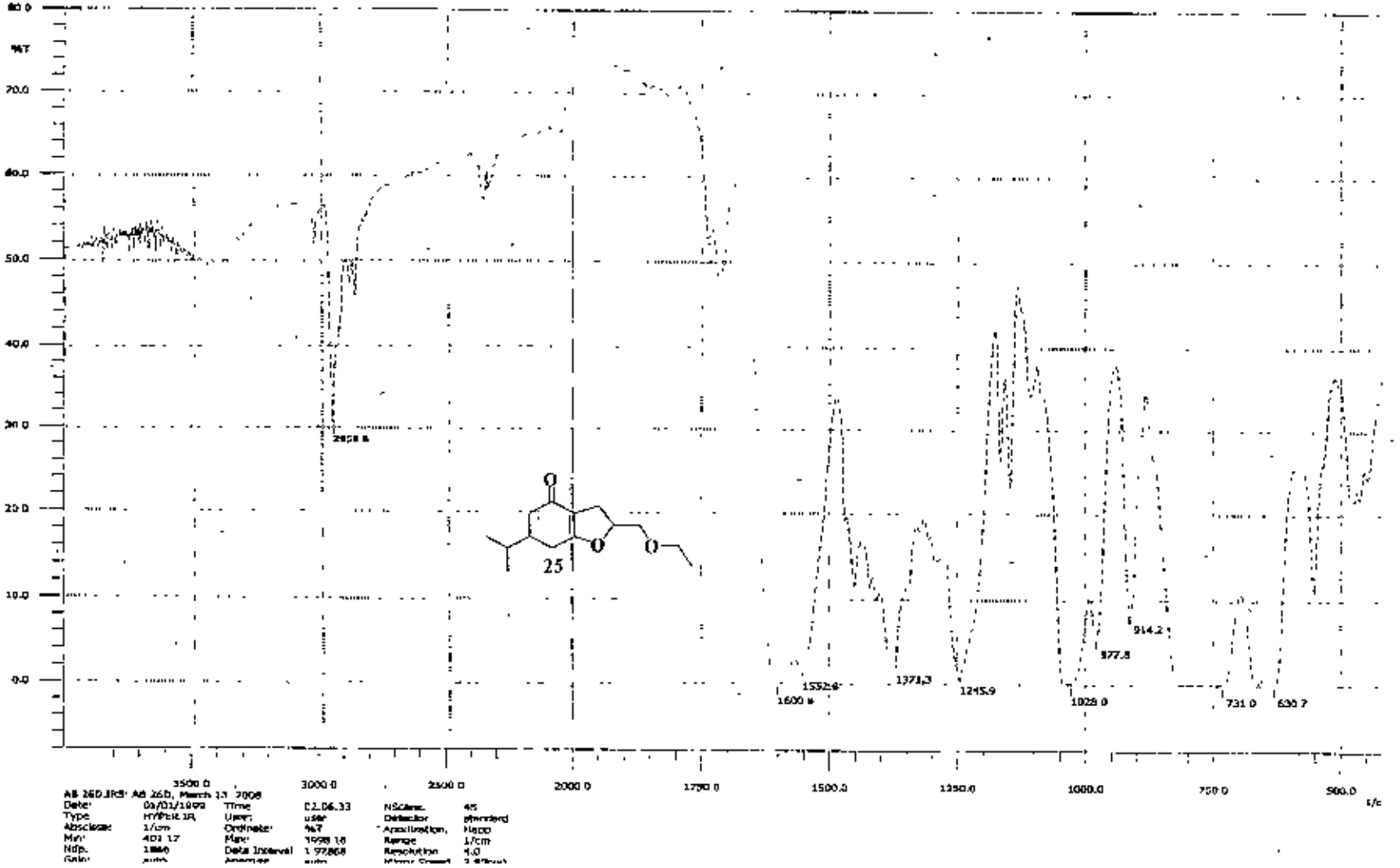


Figure 25b: IR spectrum of the compound **25**

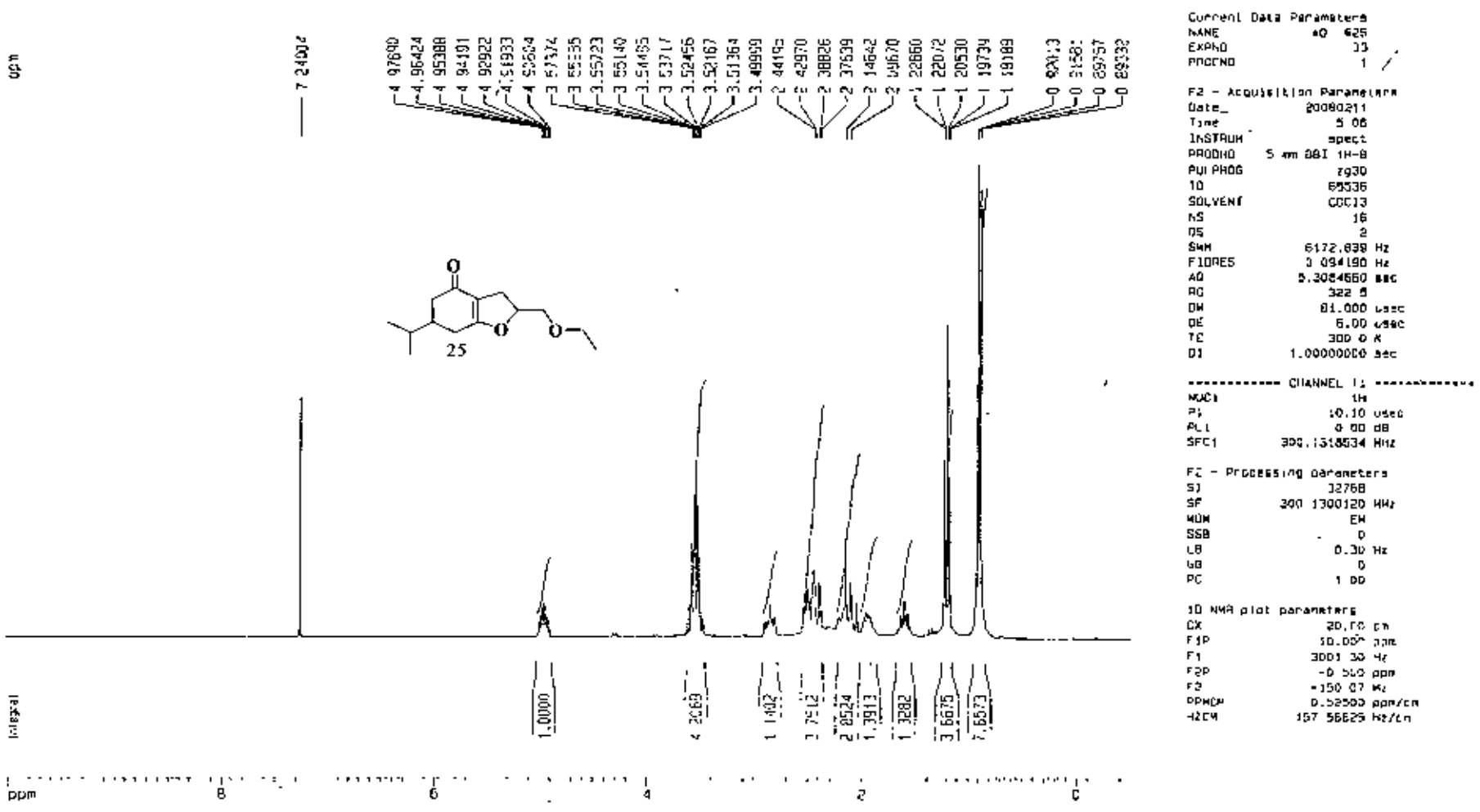


Figure 25c: ^{1}H NMR spectrum of the compound **25**

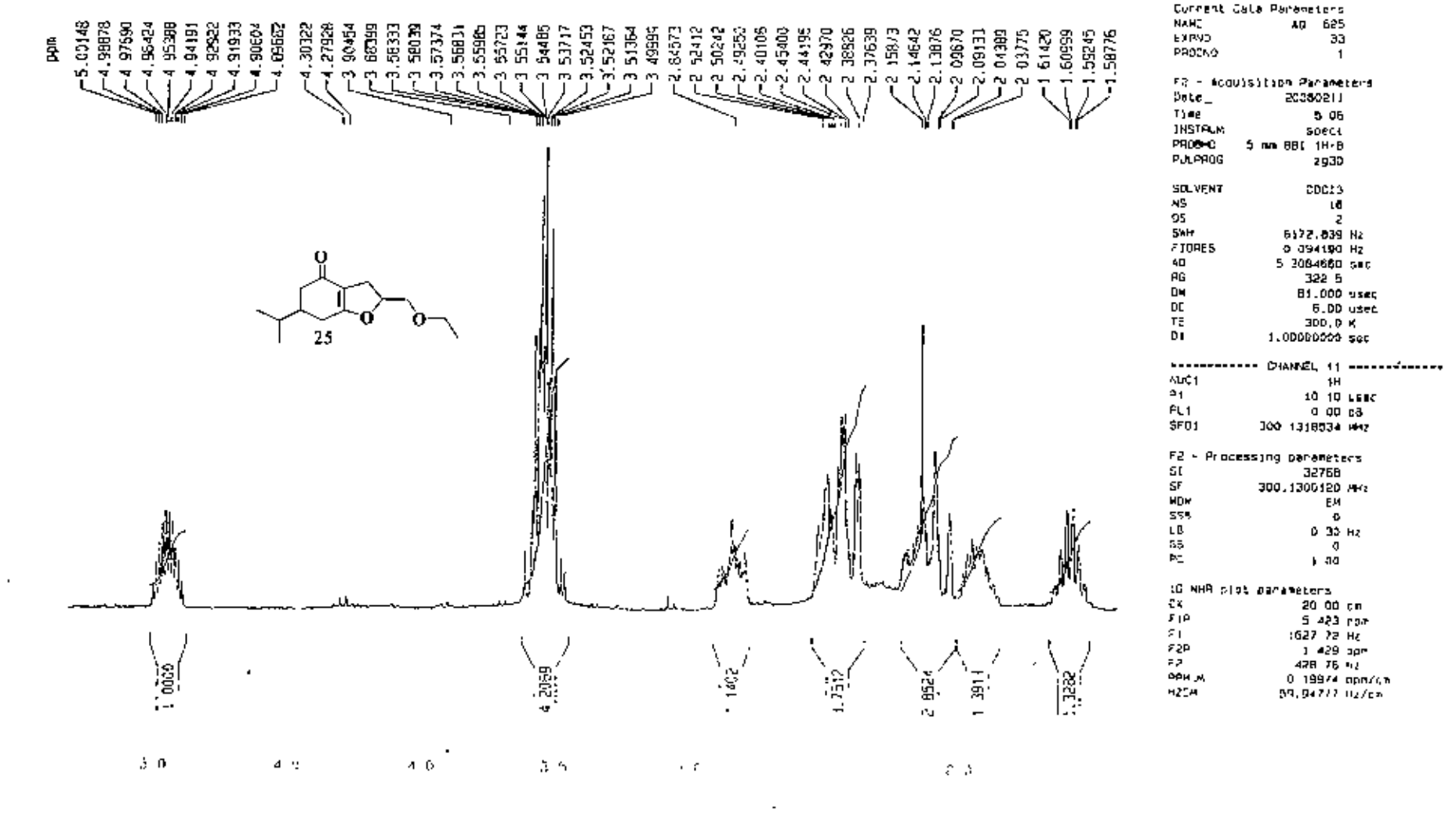


Figure 25c: ^{1}H NMR spectrum of the compound **25**

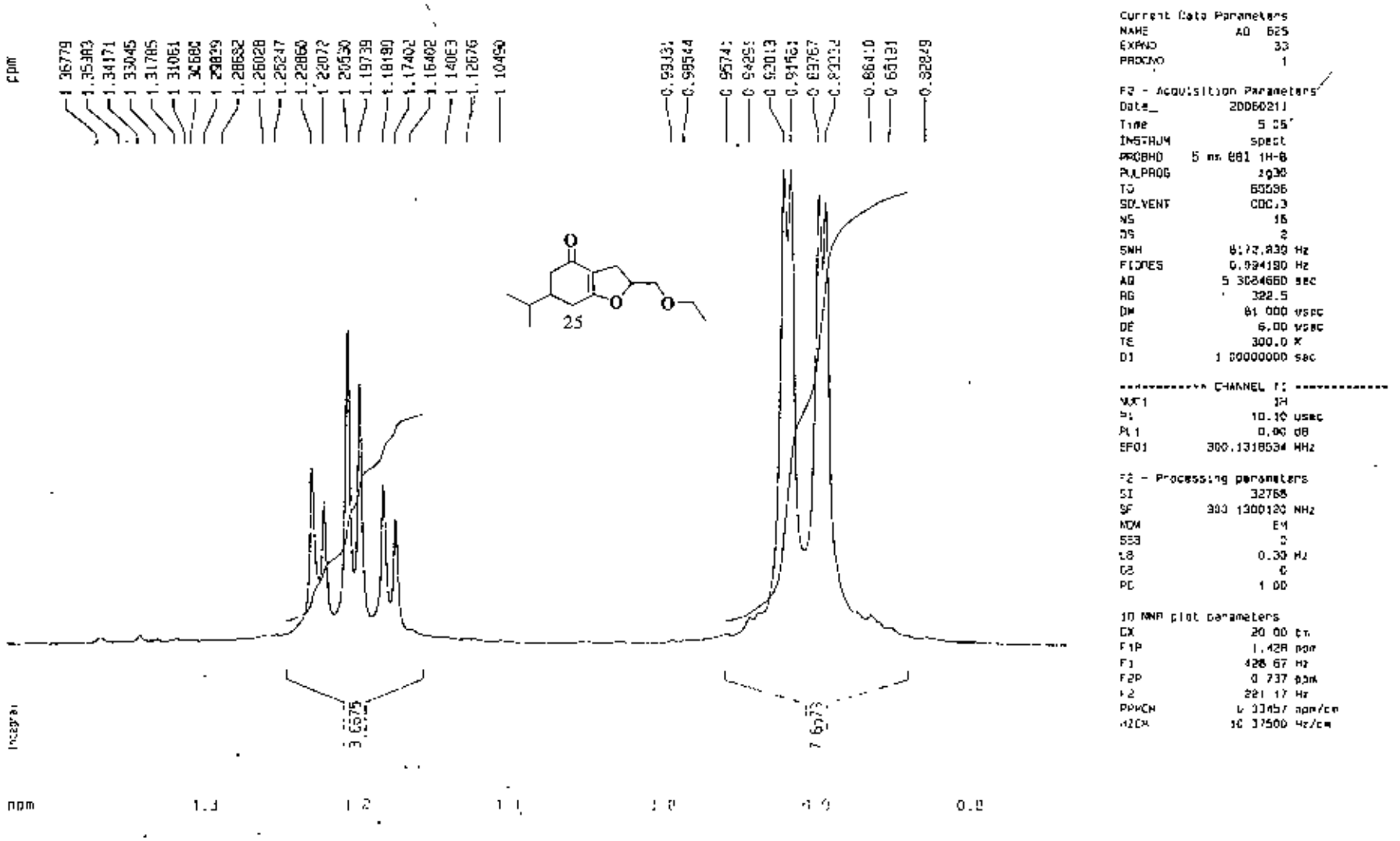
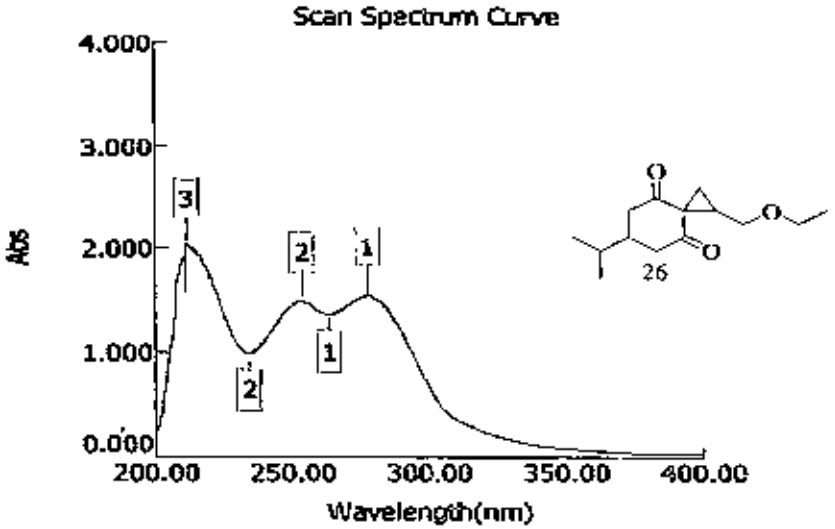


Figure 25c: ^{1}H NMR spectrum of the compound **25**



Instrument Performance
Model : SPECTROPHOTOMETERS
Spectral Bandwidth : 2.00 nm

Scan Spectrum Performance
Scan Range : 200.00 to 400.00 nm
Measure Mode : Abs
Interval : 0.05 nm
Speed : Fast
Data File : Untitled1.spd
Create Date/Time : Wednesday, March 12, 2008 6:26:36 PM
Data Type : Original
Method File:

Analyse Mode
Analyst : Administrator
Sample Name : Blank
Comment :

1	Peak	277.55	1.530
2	Peak	253.35	1.483
3	Peak	211.45	2.065
1	Valley	265.80	1.383
2	Valley	265.80	0.983

Figure 26a :UV spectrum of the compound **26**

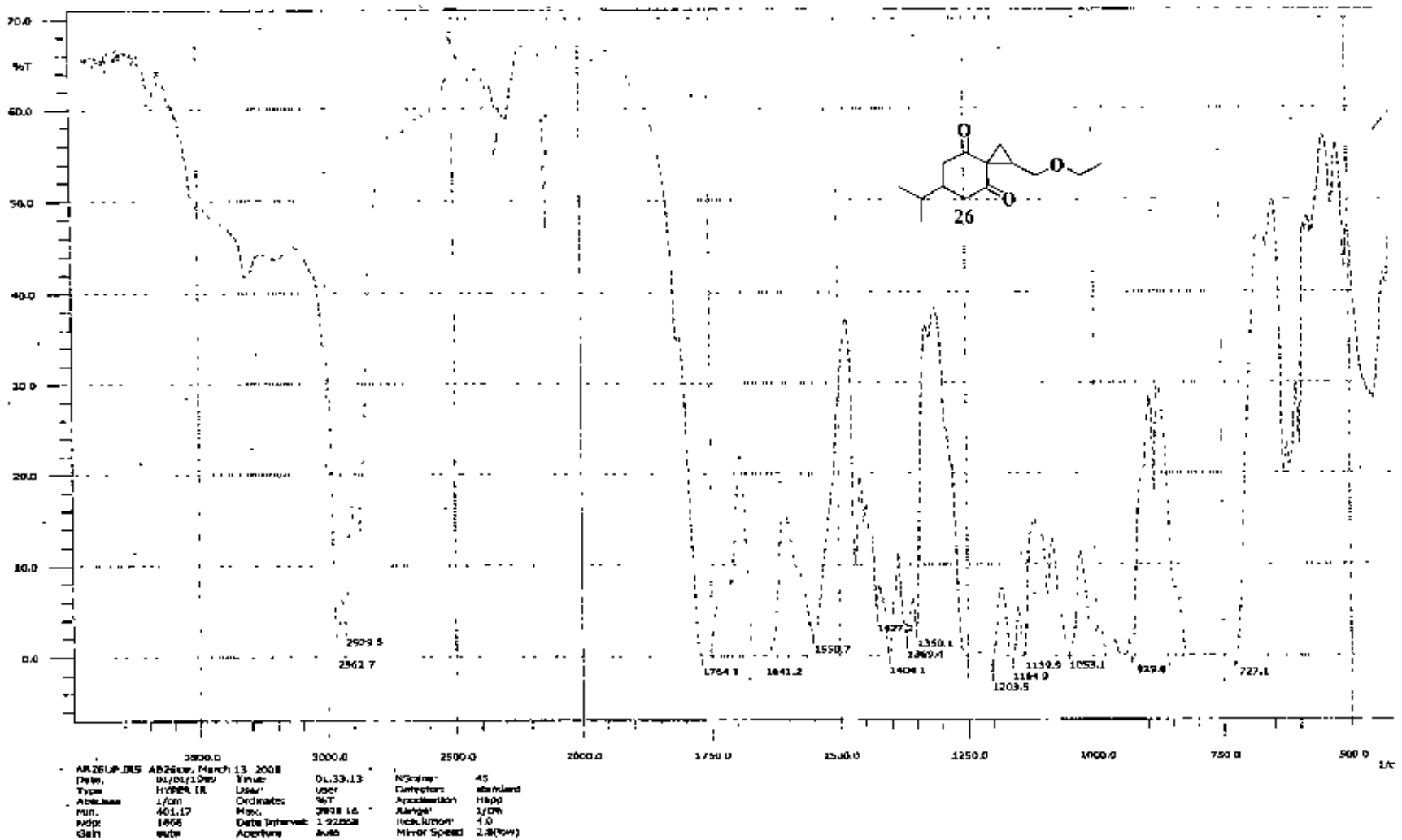
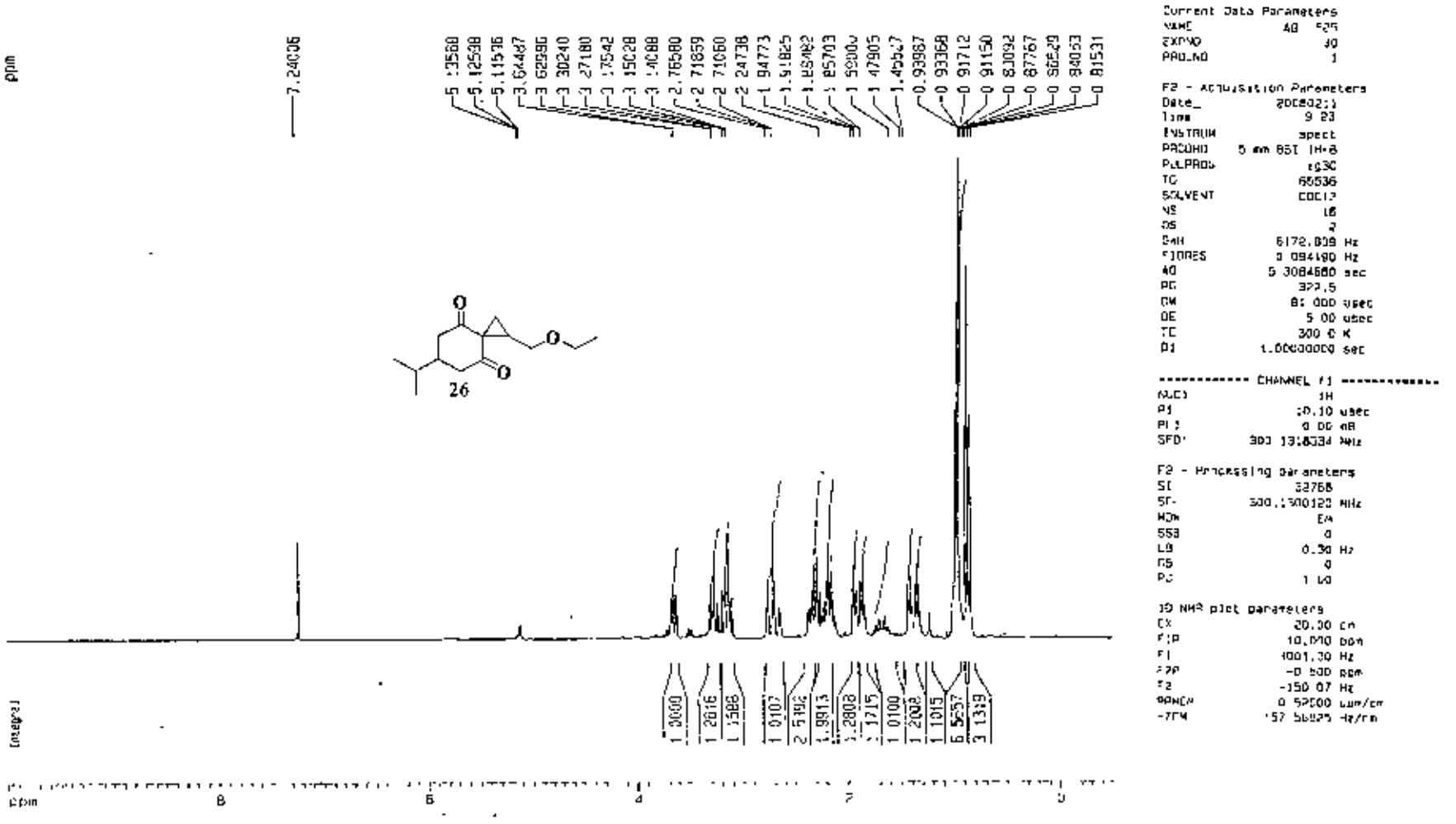


Figure 26b: IR spectrum of the compound **26**




```
Current Data Parameters
NAME                  AB  525
EXPNO                 10
PROCNO                1

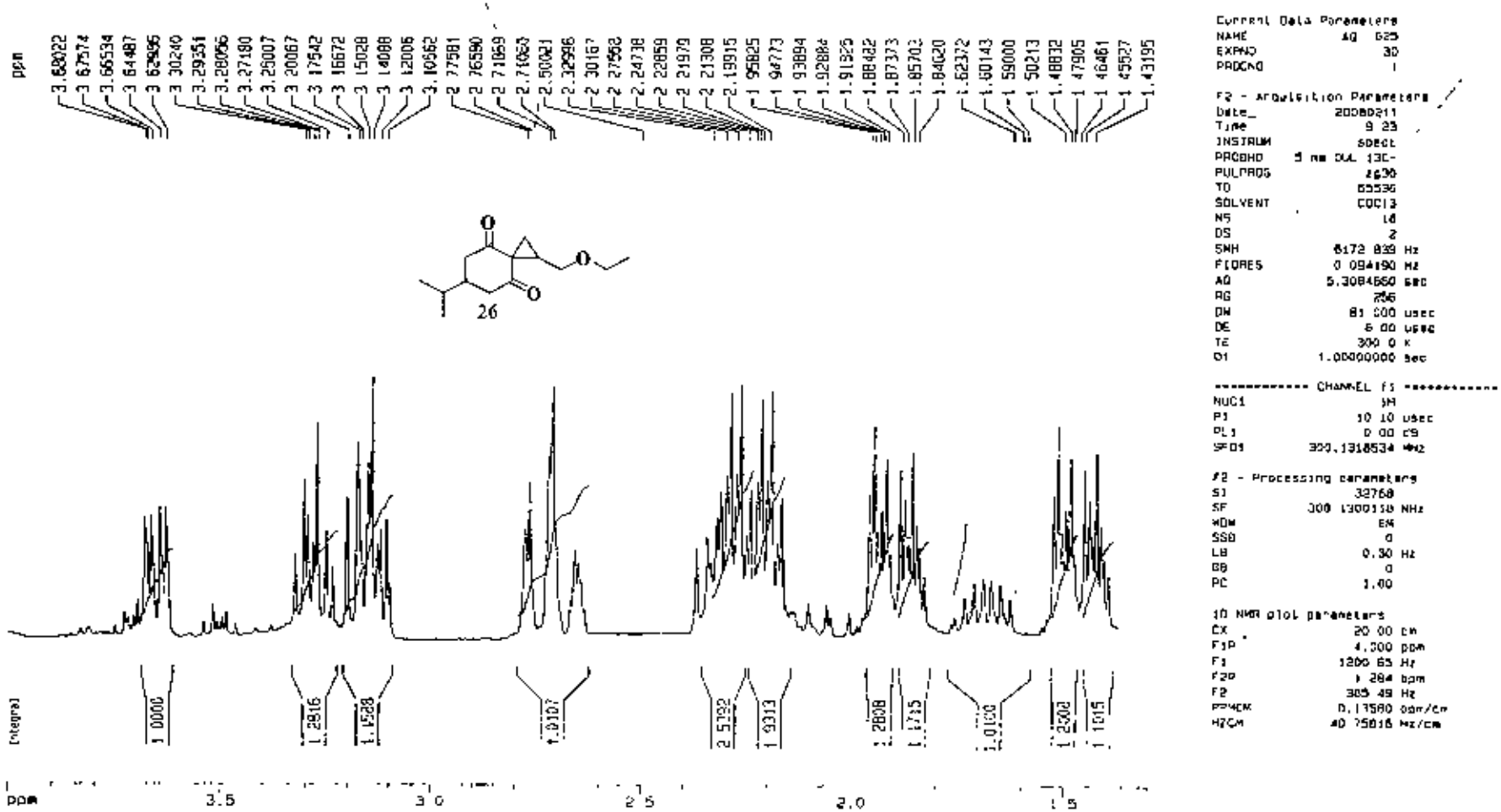
F2 - Acquisition Parameters
Date_              20080211
Time                  9 23
INSTRUM               spect
PROBHD     5 mm BBI 1H-B
PULPROG               zg30
TD                    65536
SOLVENT               CDCl3
NS                    16
DS                    2
SWH               6172.839 Hz
FIDRES            0.094180 Hz
AQ                5.3084680 sec
RG                    322.5
DW                   81.000 usec
DE                    5.00 usec
TE                  300.0 K
D1                1.00000000 sec

------------ CHANNEL f1 ------------
NUC1                  1H
P1                  10.10 usec
PL1                   0.00 dB
SFO1            300.1318334 MHz

F2 - Processing parameters
SI                    32768
SF                300.1300123 MHz
WDW                   EM
SSB                   0
LB                    0.30 Hz
GB                    0
PC                    1.00

1D NMR plot parameters
CX                   20.00 cm
F1P                  10.000 ppm
F1                 1001.30 Hz
F2P                  -0.500 ppm
F2                 -150.07 Hz
PPMCM                0.50000 ppm/cm
HZCM               -75.04625 Hz/cm
```

Figure 26c: ^{1}H NMR spectrum of the compound **26**




```
Current Data Parameters
NAME                  AQ  625
EXPNO                 30
PROCNO                1

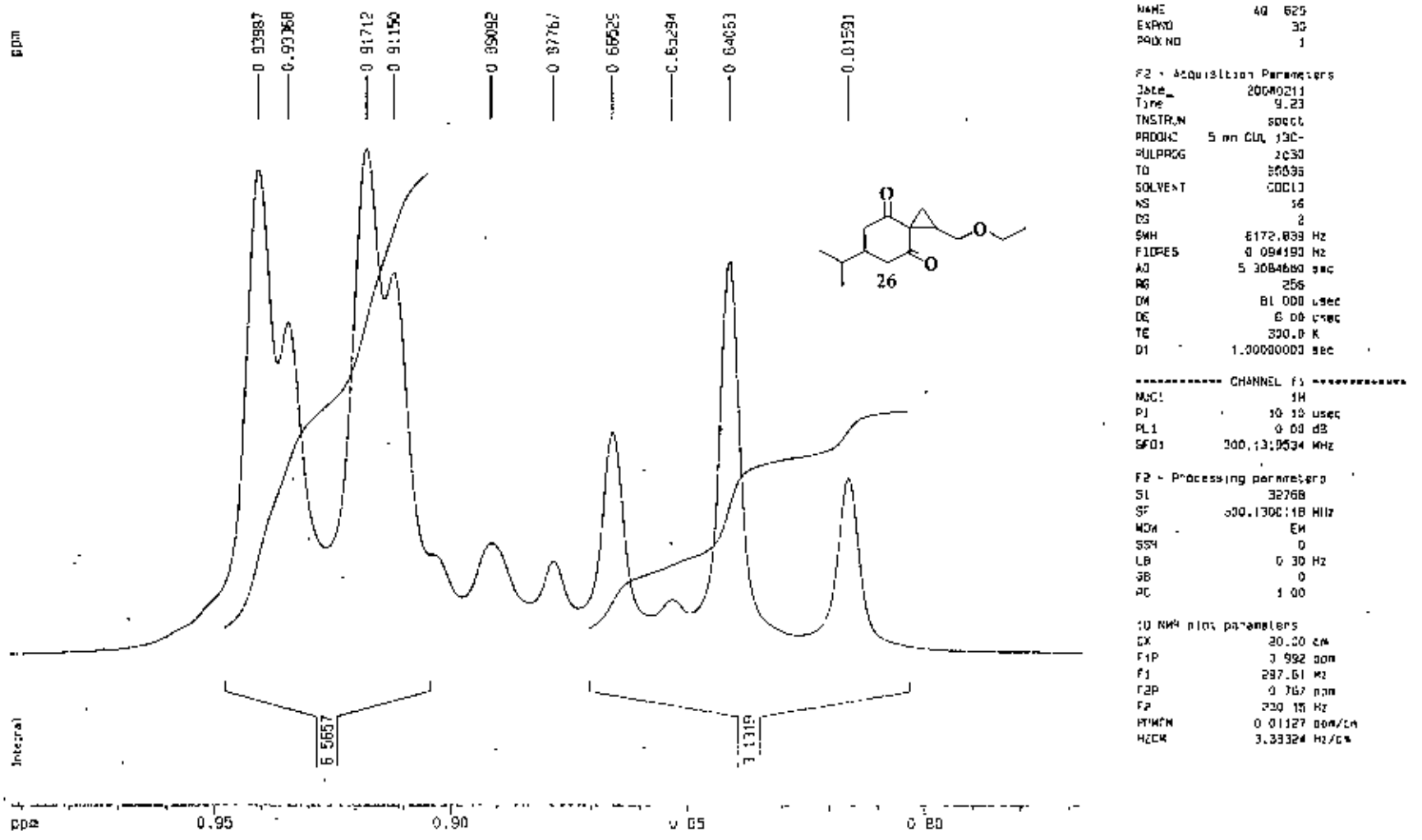
F2 - Acquisition Parameters
Date_              20080211
Time                  9 25
INSTRUM               spect
PROBHD     5 mm DUL 13C-
PULPROG               zg30
TD                    65536
SOLVENT               CDCl3
NS                    16
DS                    2
SWH               6172.839 Hz
FIDRES            0.094190 Hz
AQ                5.3084860 sec
RG                    256
DW                  81.000 usec
DE                  6.00 usec
TE                  300.0 K
D1                1.00000000 sec

------------ CHANNEL f1 ------------
NUC1                  1H
P1                  10.10 usec
PL1                 0.00 dB
SFO1            300.1318534 MHz

F2 - Processing parameters
SI                    32768
SF              300.1300138 MHz
WDW                   EM
SSB                   0
LB                  0.30 Hz
GB                    0
PC                  1.00

1D NMR plot parameters
CX                  20.00 cm
F1P                 4.000 ppm
F1                1200.65 Hz
F2P                 1.284 ppm
F2                  385.49 Hz
PPMCM             0.13580 ppm/cm
HZCM             40.75016 Hz/cm
```

Figure 26c: ^{1}H NMR spectrum of the compound **26**



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EXPNO 30
PROCNO 1

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Time 9.23
INSTRUM spect
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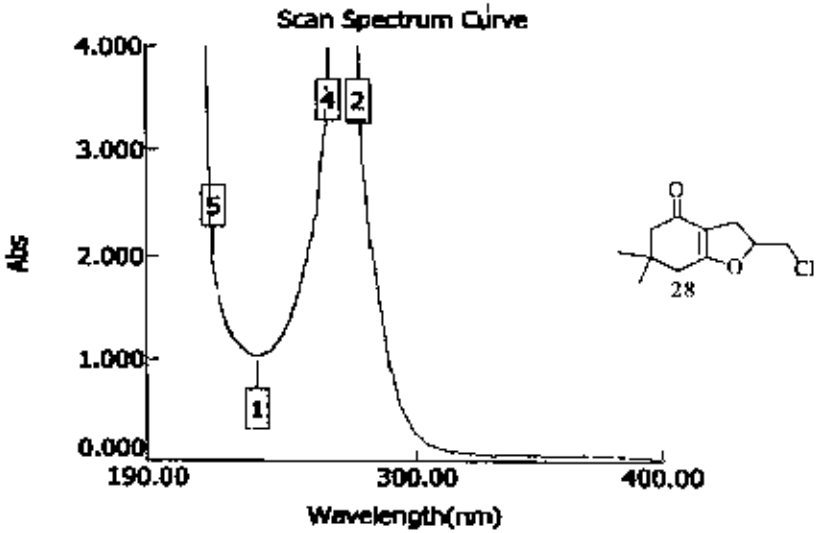
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6172.839 Hz
FIDRES 0.094193 Hz
AQ 5.3084480 sec
RG 256
DW 81.000 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

------------ CHANNEL f1 ------------
NUC1 1H
P1 10.10 usec
PL1 0.00 dB
SFO1 300.1319534 MHz

F2 - Processing parameters
SI 32768
SF 300.1300118 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 3.992 ppm
F1 297.61 Hz
F2P 0.767 ppm
F2 230.15 Hz
PPMCM 0.01127 ppm/cm
HZCM 3.38324 Hz/cm

Figure 26c: ^{1}H NMR spectrum of the compound **26**



- **Instrument Performance**
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  Spectral Bandwidth : 2.00 nm
- **Scan Spectrum Performance**
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  Measure Mode : Abs
  Interval : 0.05 nm
  Speed : Fast
  Data File : Untitled1.spd
  Create Date/Time : Sunday, March 25, 2008 6:39:55 PM
  Data Type : Original
  Method File:
- **Analyse Note**
  Analyser : Administrator
  Sample Name : Blank
  Comment :

No.	P/V	Wavelength(nm)	Abs	Comment
1	Peak	276.30	3.969	
2	Peak	276.10	9.999	
3	Peak	264.05	9.999	
4	Peak	263.80	9.999	
5	Peak	217.20	1.948	
1	Valley	234.85	1.033	

Figure 28a :UV spectrum of the compound **28**

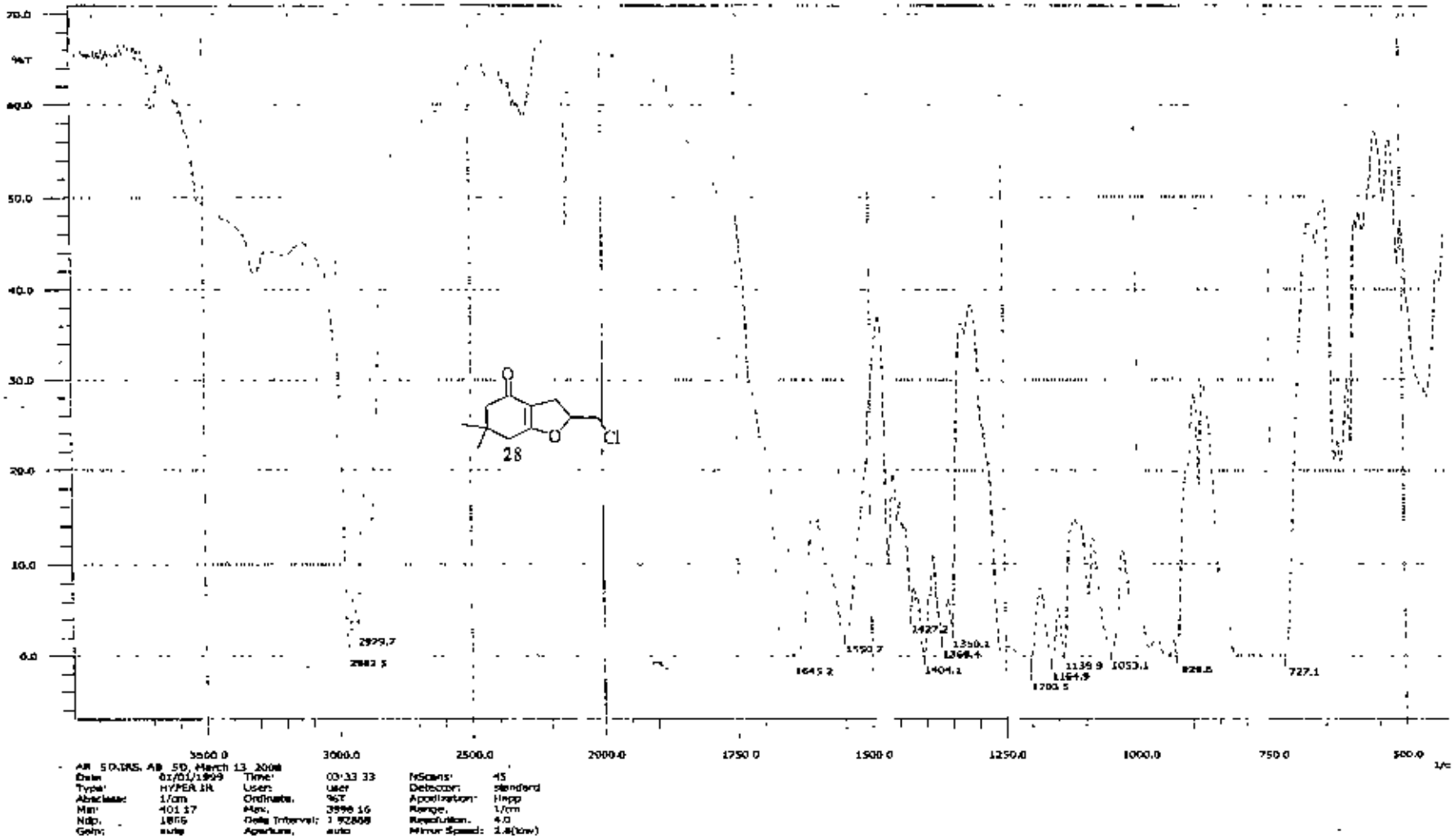


Figure 28b: IR spectrum of the compound **28**

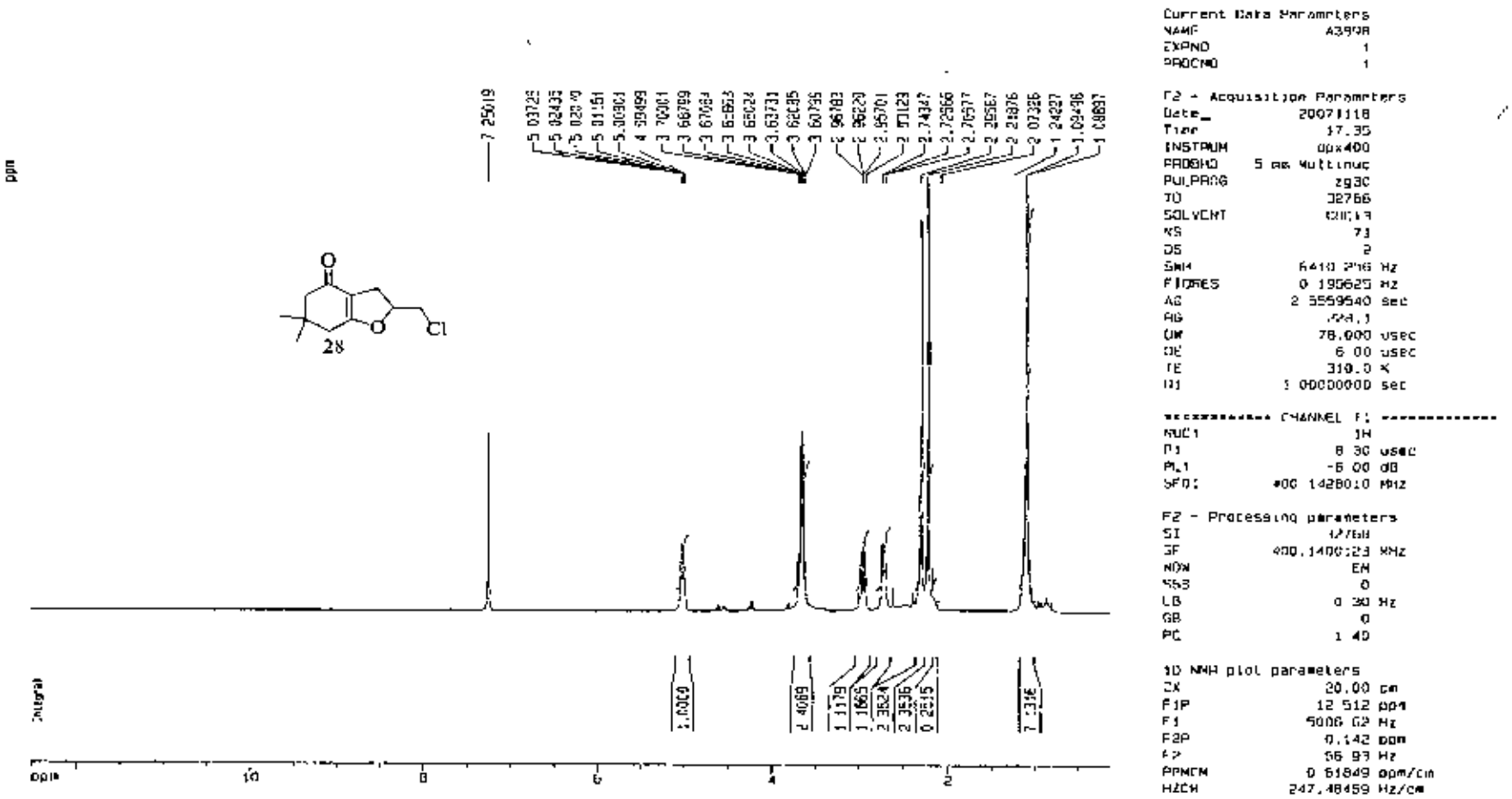


Figure 28c: ^{1}H NMR spectrum of the compound **28**

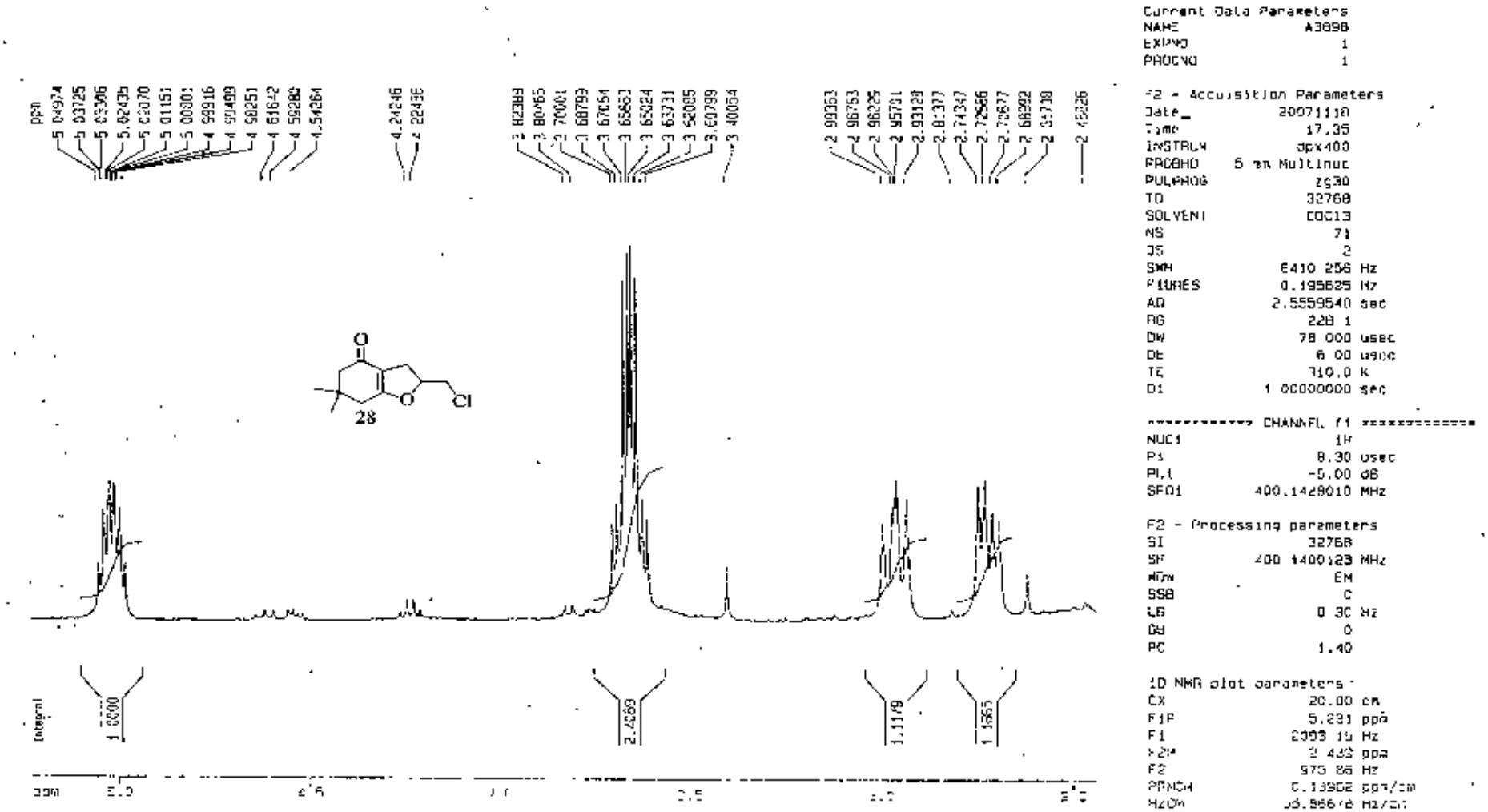
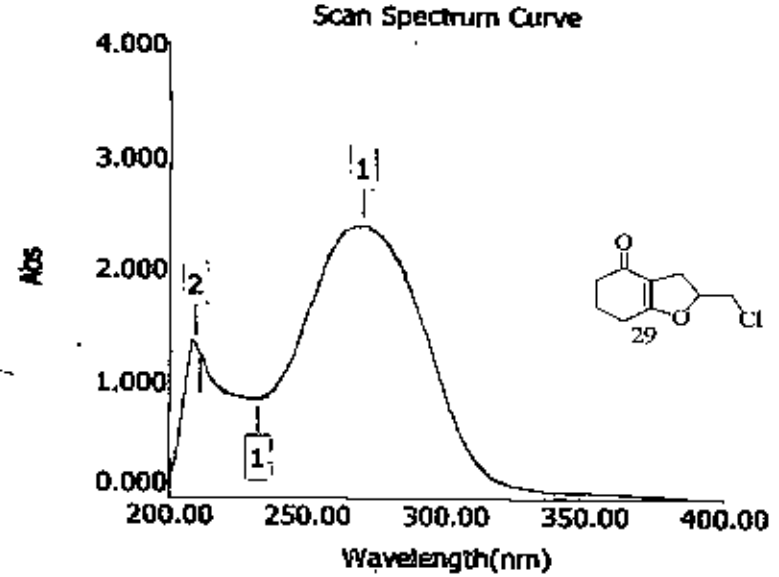


Figure 28c: ^{1}H NMR spectrum of the compound **28**



1	Peak	270.45	2.529
2	Peak	211.05	1.481
1	Valley	234.50	0.897

- **Instrument Performance**
  Model : SPECTROPHOTOMETERS
  Spectral Bandwidth : 2.00 nm
- **Scan Spectrum Performance**
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  Interval : 0.05 nm
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  Data Type : Original
  Method File: `
- **Analyse Note**
  Analyser : Administrator
  Sample Name : Blank
  Comment :

Figure 29a :UV spectrum of the compound **29**

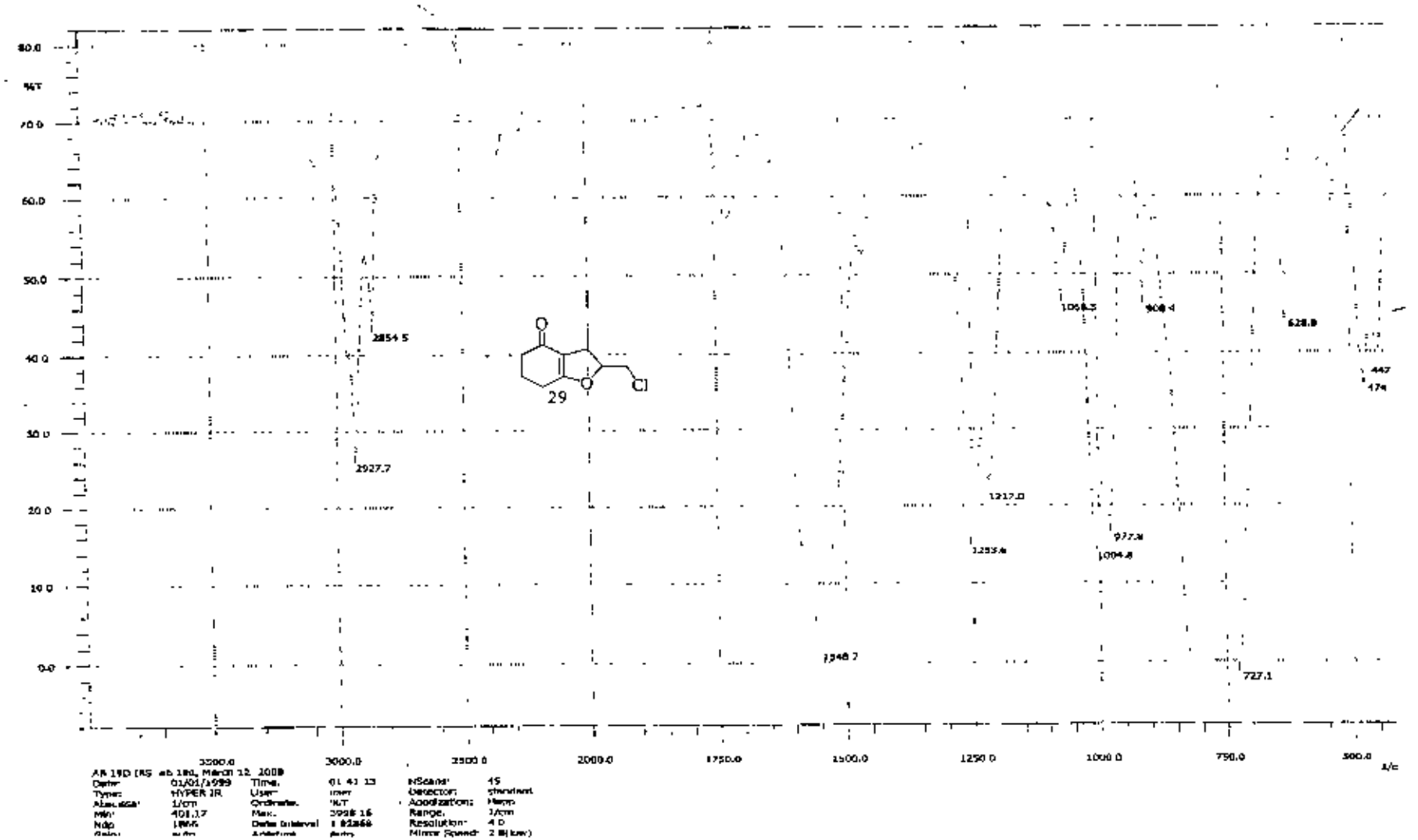
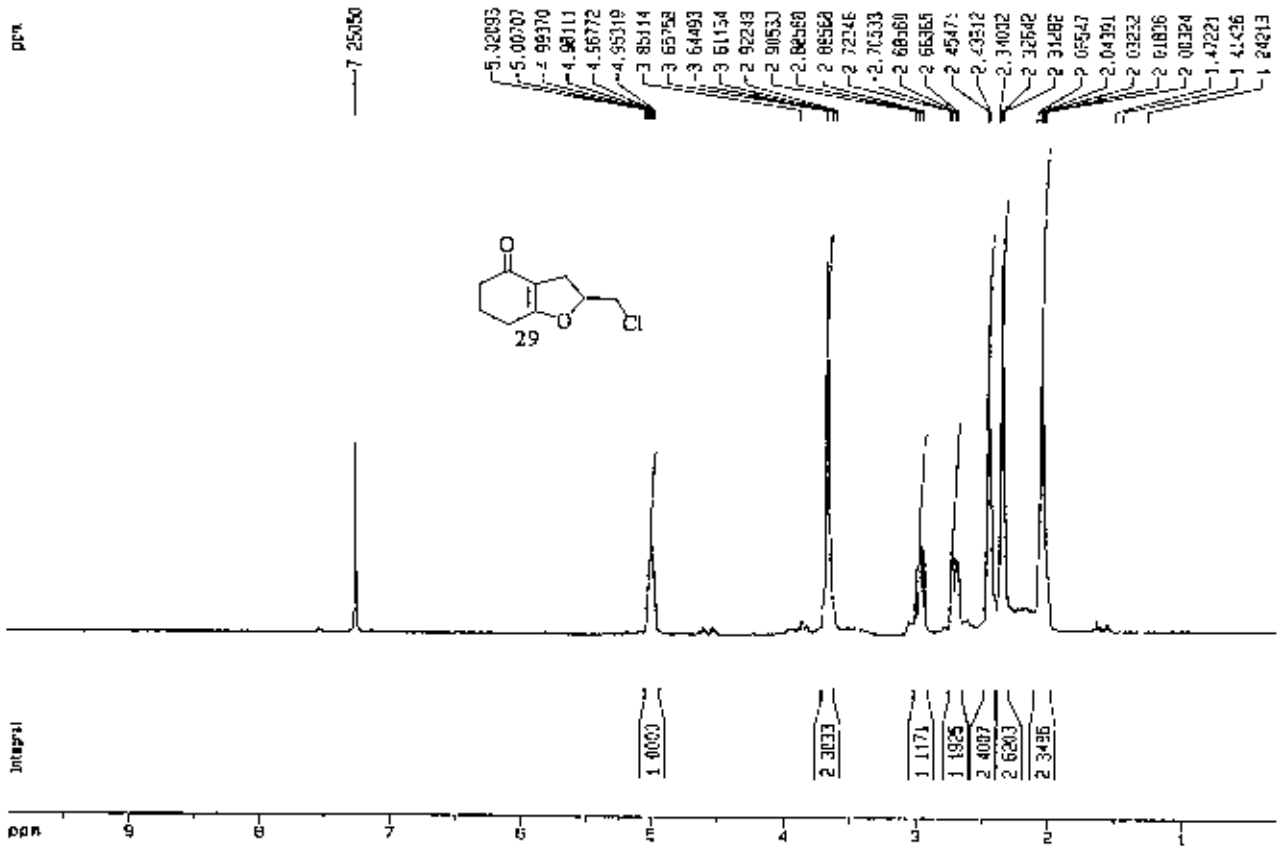


Figure 29b: IR spectrum of the compound **29**

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PROCNO                    1

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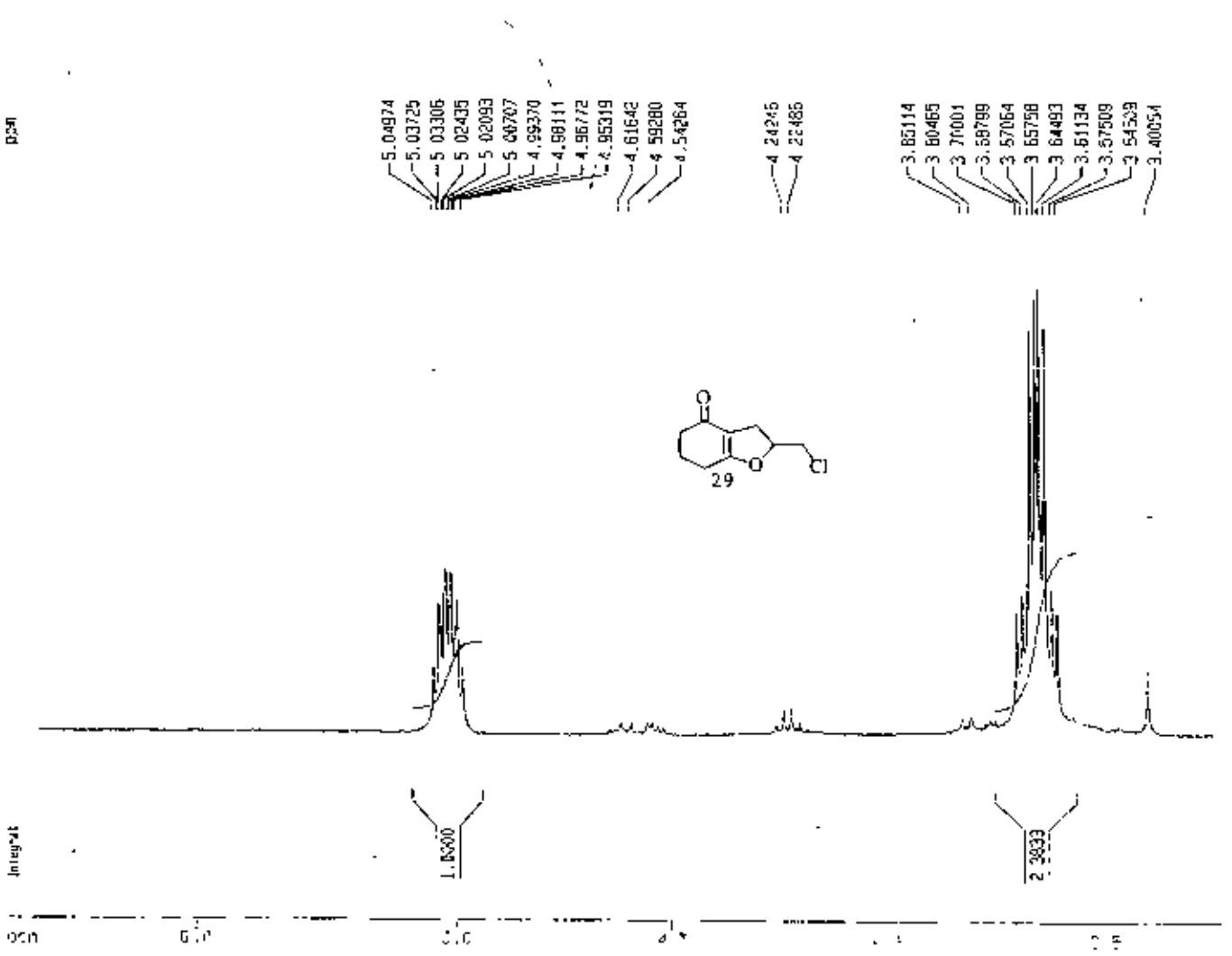
PULPROG               zg30
TD                   32768
SOLVENT              CDCl3
NS                     104
DS                       2
SWH                6410.256 Hz
FIDRES             0.195625 Hz
AQ                 2.5559640 sec
RG                     203.2
DW                    78.000 usec
DE                     6.00 usec
TE                    310.0 K
D1                 1.00000000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                      8.30 usec
PL1                    -6.00 dB
SFO1              400.1428010 MHz

F2 - Processing parameters
SI                       32768
SF                400.1400126 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.40

1D NMR plot parameters
CX                      20.00 cm
F1P                      9.926 ppm
F1                    3971.61 Hz
F2P                      0.289 ppm
F2                     115.63 Hz
PPMCM                 0.48183 ppm/cm
HZCM                192.78900 Hz/cm
```

Figure 29c: ^{1}H NMR spectrum of the compound **29**




```
Current Data Parameters
NAME                  A4096
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_              20060213
Time                  16.19
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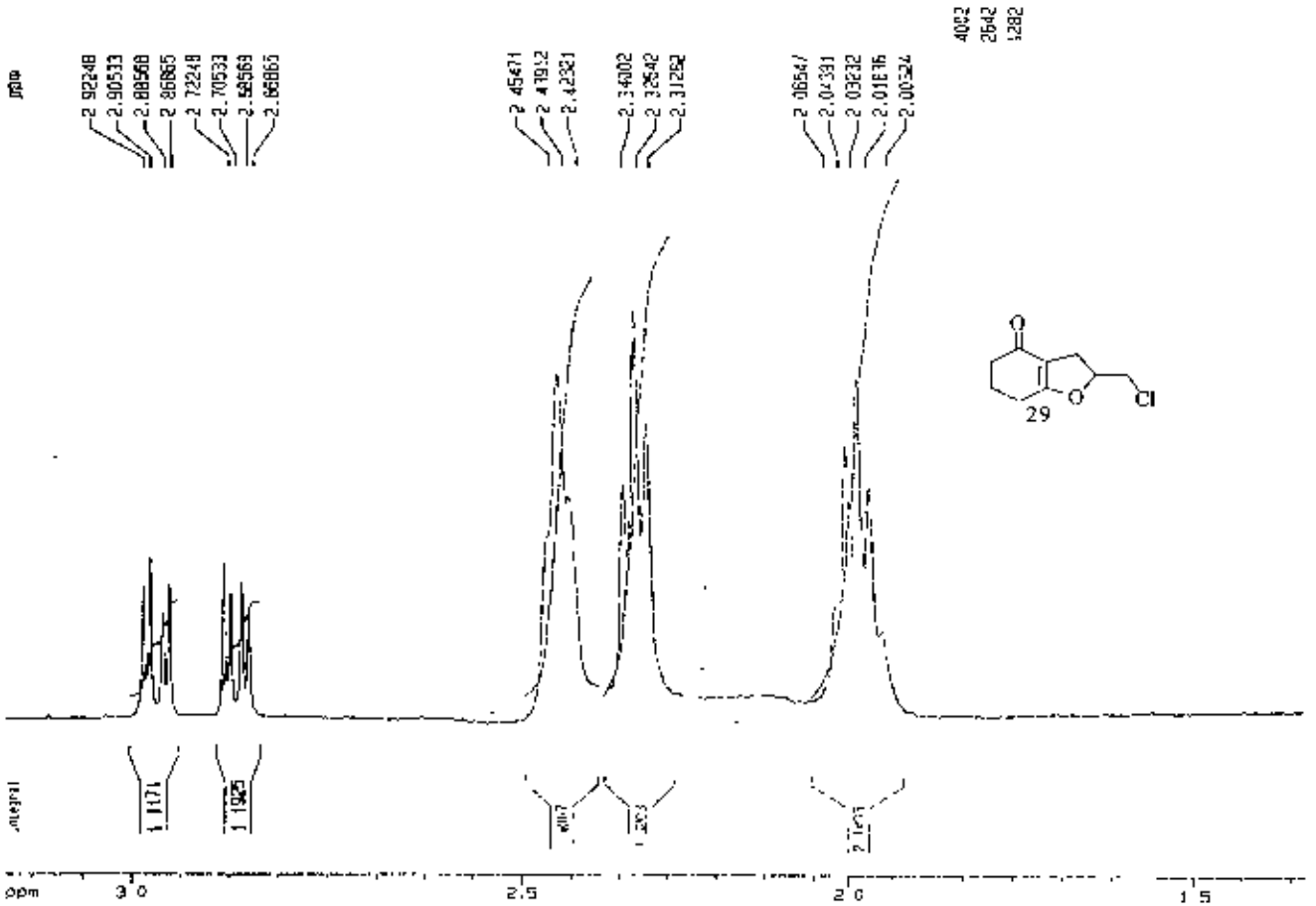
PROBHD     5 mm Multinuc
PULPROG               zg30
TD                   32768
SOLVENT               CDCl3
NS                      104
DS                        2
SWH               6410.256 Hz
FIDRES            0.195625 Hz
AQ                2.5559540 sec
RG                    203.2
DW                   78.000 usec
DE                    6.00 usec
TE                   310.0 K
D1                1.00000000 sec

========== CHANNEL f1 ============
NUC1                    1H
P1                    8.30 usec
PL1                  -6.00 dB
SFO1           400.1420010 MHz

F2 - Processing parameters
SI                    32768
SF              400.1400126 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                    1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                   9.926 ppm
F1                 3971.61 Hz
F2P                   0.289 ppm
F2                  115.63 Hz
PPMCM             0.48183 ppm/cm
HZCM            192.79900 Hz/cm
```

Figure 29c: ^{1}H NMR spectrum of the compound **29**

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Current Data Parameters
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EXPNO                    1
PROCNO                   1

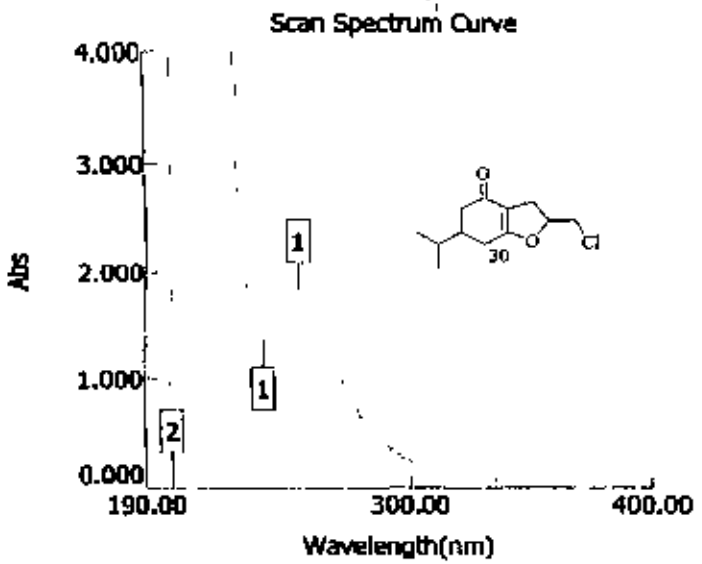
F2 - Acquisition Parameters
Date_              20080213
Time                  16 19
INSTRUM             dpx400
PROBHD     5 mm Multinuc
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                      104
DS                        2
SWH                6410.258 Hz
FIDRES             0.195625 Hz
AQ                 2.5555540 sec
RG                    203.2
DW                   78.000 usec
DE                    6.00 usec
TE                   310.0 K
D1                1.00000000 sec

========== CHANNEL f1 ==========
NUC1                     1H
P1                    8.30 usec
PL1                  -6.00 dB
SFO1           400.1400010 MHz

F2 - Processing parameters
SI                    32768
SF              400.1400126 MHz
WDW                      EM
SSB                       0
LB                    0.30 Hz
GB                        0
PC                    1.40

1D NMR plot parameters
CX                   20.00 cm
F1P                   9.926 ppm
F1                 3971.61 Hz
F2P                   0.209 ppm
F2                   115.63 Hz
PPMCM                0.40183 ppm/cm
HZCM               192.70900 Hz/cm
```

Figure 29c: ^{1}H NMR spectrum of the compound **29**



1	Peak	253.70	1.762
1	Valley	239.15	1.426
2	Valley	201.05	-1.768

- **Instrument Performance**
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  Spectral Bandwidth : 2.00 nm
- **Scan Spectrum Performance**
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  Data Type : Original
  Method File:
- **Analyse Note**
  Analyser : Administrator
  Sample Name : Blank
  Comment :
- **No. P/V Wavelength(nm)Abs Comment**

Figure 30a :UV spectrum of the compound 30

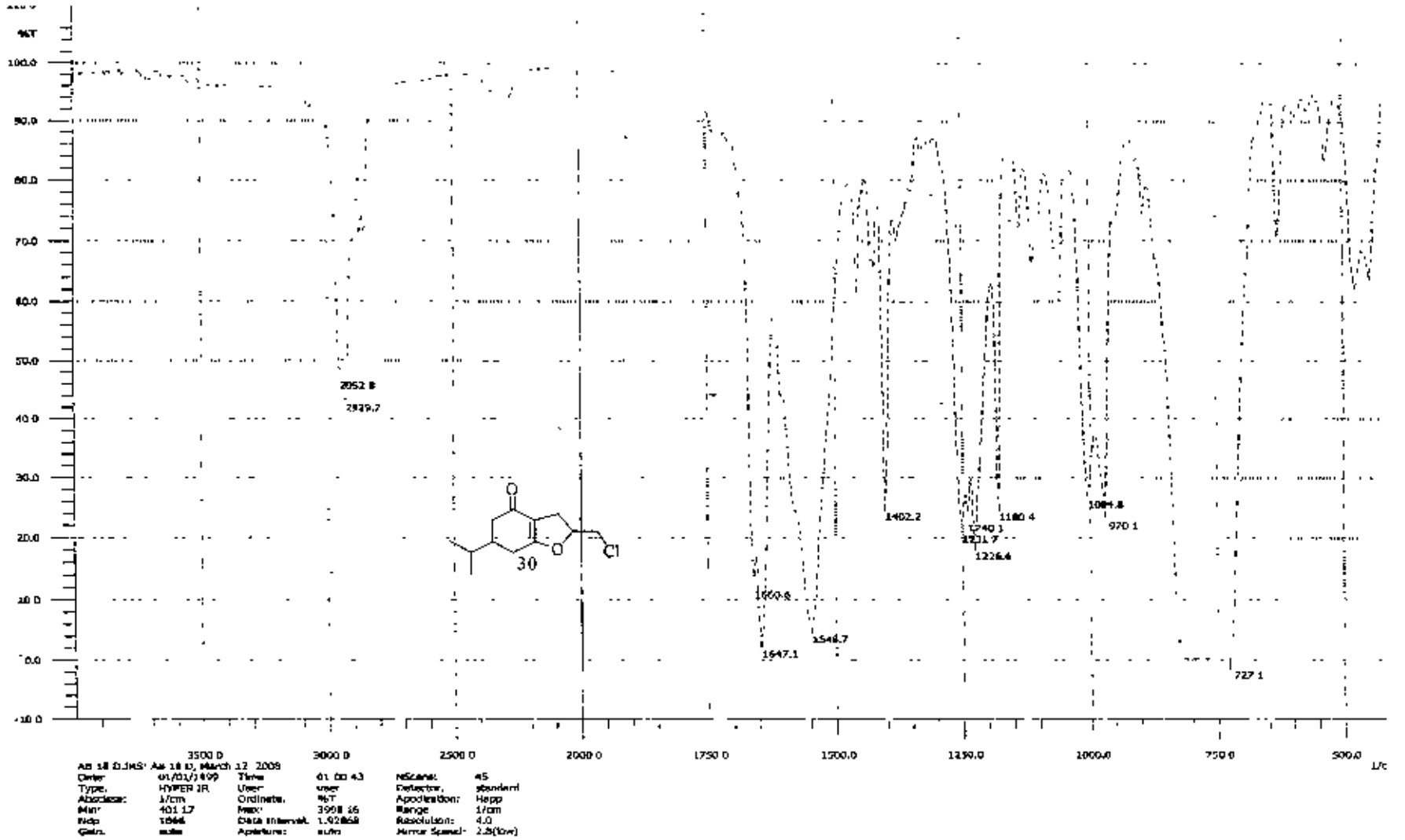
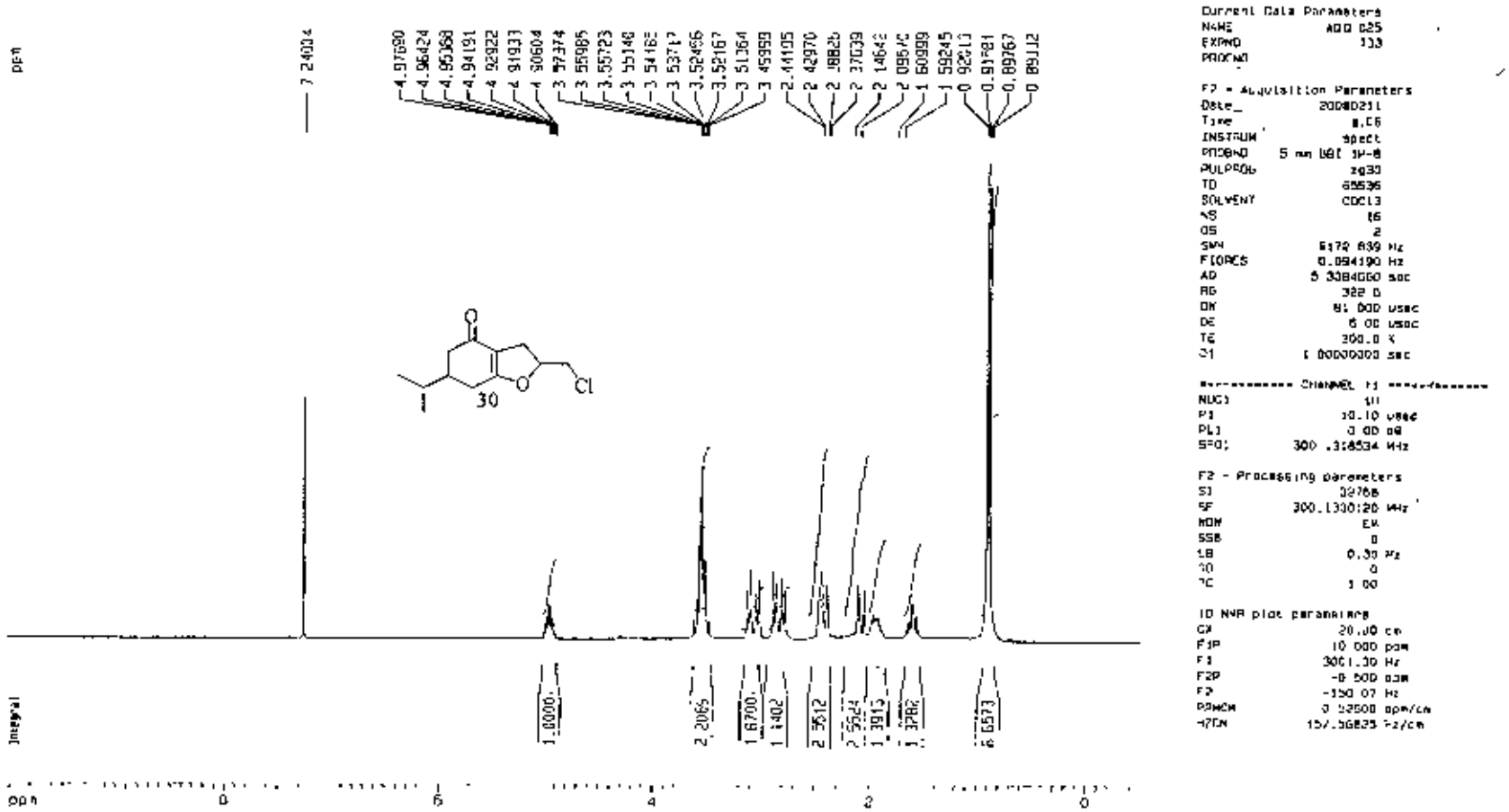


Figure 30b: IR spectrum of the compound **30**

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Current Data Parameters
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EXPNO                     133
PROCNO

F2 - Acquisition Parameters
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Time                    8.06
INSTRUM                 spect
PROBHD     5 mm QBI 1H-B
PULPROG                 zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                9172.839 Hz
FIDRES             0.139990 Hz
AQ                 3.5684000 sec
RG                    322.0
DW                   81.000 usec
DE                    6.00 usec
TE                   300.0 K
D1                 1.00000000 sec

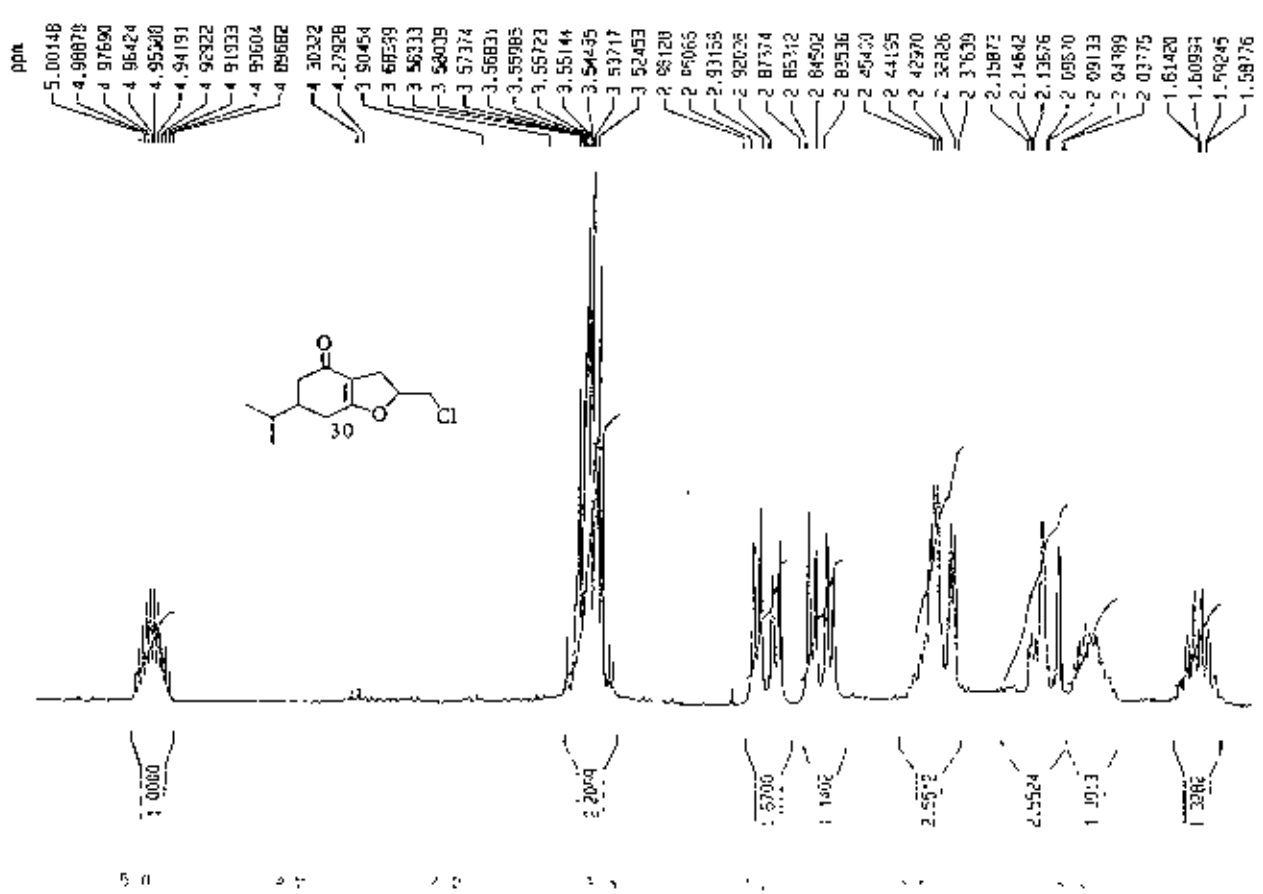
========== CHANNEL f1 ==========
NUC1                     1H
P1                    10.10 usec
PL1                    0.00 dB
SFO1          300.1318534 MHz

F2 - Processing parameters
SI                       32768
SF                300.1300120 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00

1D NMR plot parameters
CX                      20.00 cm
F1P                    10.000 ppm
F1                   3001.30 Hz
F2P                   -0.500 ppm
F2                    -150.07 Hz
PPMCM                 0.50000 ppm/cm
HZCM                 150.06825 Hz/cm
```

Figure30c: ^{1}H NMR spectrum of the compound **30**

AB 250

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EXPNO                 133
PROCNO                  1

F2 - Acquisition Parameters
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Time                6 05
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PULPROG             ag30

SOLVENT             CDCl3
NS                     16
DS                      2
SWH              6172,839 Hz
FIDRES           0 094190 Hz
AQ               5 3084660 sec
RG                   322 5
DW                 81 000 usec
DE                  6 00 usec
TE                  300 0 K
D1               1 00000000 sec

========== CHANNEL f1 ============
NUC1                  1H
P1                 10 ,0 usec
PL1                 0 00 dB
SFO1          300 1318534 MHz

F2 - Processing parameters
SI                  32768
SF          300,1300120 MHz
WDW                    EM
SSB                     0
LB                 0 30 Hz
GB                      0
PC                  1 00

1D NMR plot parameters
CX                 20 00 cm
F1P                ,5 423 ppm
F1                 1627 72 Hz
F2P                1 629 ppm
F2                 488 76 Hz
PPMCM              0 13974 ppm/cm
HZCM               39 0477? Hz/cm
```

Figure30c: ^{1}H NMR spectrum of the compound **30**

Chapter-4

Antimicrobial Screening

INTRODUCTION

Bacteria and fungi are responsible for many infectious diseases. The increasing clinical implications of drug resistant fungal and bacterial pathogens have lent additional urgency to antimicrobial drug research. The deterioration of human population due to enhance of prevalence of infections diseases is becoming a global problem[1]. It was found from the literature that nitrogen and sulfur containing compounds showed marked microbial activities[2-6]. When heterocyclic part of the compounds,such as; imidazole, nitroimidazole etc. become attached to carbohydrates[7], their efficiency to inhibit bacteria of fungus sharply increased. It was also found that a large number of biologically active compounds possesses aromatic and heteroaromatic nucleus. If an active nucleus is linked to another nucleus, the resulting molecule may possess greater potential for biological activity[8]. In *vitro* antimicrobial activities of fused pyrimidines were successfully evaluated in our laboratory[9].

M. shaheb[10] a post graduate student carried out in *vitro* antimicrobial activates of fused pyrimidine derivatives. M. S. Rahman[11] showed that antimicrobial activities of alkaloids plant leaves. The alkaloids were screened against several pathogenic bacteria.

S. M. Shahed[12, 13] a former research student of organic laboratory carries out antifungal activities of a series of acylated D- Mannose derivatives.

M. fakruddin[14] also a research student of organic laboratory carries out antifungal activities of a series of fused pyrimidine derivatives. He used five human pathogenic bacteria *viz. Bacillus cereus, Bacillus megaterium, Bacillus subtilis, Staphylococcus aureusand* and four pathogenic fungi, *viz. Vibrio mimicus, Vibrio parahemolyticus, Aspergillus niger and panicillum sp.* S. M. Abe Kawsar [15, 16] also a former research student of organic laboratory carried out in *vitro* antibacterial activities of a series of acylated uridine derivatives.

Recently, our groups synthesized 2-substituted benzofurans[17], isoindonone and isoquinolinone[18] and tested their antibacterial and antifungal activities. Plants are the

natural reservoir of many antimicrobial agents. In recent times, traditional medicine as an alternative form of health care and to overcome microbial resistance has led the researchers to investigate the antimicrobial activity of medicinal plants (Austin *et al.,* 1999).

4.1. Materials and methods:

The anti bacterial activities of furan derivatives were studied against twelve bacteria and the activities of the same compounds were also studied against four fungi. For the detection of antibacterial activities the disc diffusion method[19] was followed.

The antimicrobial screening which is the first stage of antimicrobial drug research is performed to ascertain the susceptibility of various fungi and bacteria to any agent. This test measures the ability of each test sample to inhibit the *in vitro* fungal and bacterial growth. This ability may be estimated by any of the following three methods.

a) Disc diffusion method

b) Serial dilution method

c) Bioautographic method

Bnt there is no standardized method for expressing the results of antimicrobial screening (Ayafor *et. al*; 1982). Some investigators use the diameter of zone of inhibition and/or the minimum weight of extract to inhibit the growth of microorganisms. However, a great number of factors viz., the extraction methods (Nadir *et al.,* 1986), inoculum volume, culture medium composition (Bayer *et al.*, 1966), p^H (Leven *et al.,* 1979), and incubation temperature (Lorian, 1991) can influence the results.

Among the above mentioned techniques the disc diffusion (Bauer et al[19]., 1966) is a widely accepted in vitro investigation for preliminary screening of test agents which may possess antimicrobial activity. It is essentially a quantitative or qualitative test indicating the sensitivity or resistance of the microorganisms to the test materials. However, no distinction between bacteriostatic and bactericidal activity can be made by this method (Roland, R[20]., 1982).

4.1a. Principle of disc diffusion method:

In this classical method, antibiotics diffuse from a confined source through the nutrient agar gel and create a concentration gradient. Dried and sterilized filter paper discs (6 mm diameter) containing the test samples of known amounts are placed on nutrient agar medium uniformly seeded with the test microorganisms. Standard antibiotic (kanamycin) discs and blank discs are used as positive and negative control. These plates are kept at low temperature (4°C) for 24 hours to allow maximum diffusion of the test materials to the surrounding media (Barry, 1976). The plates are then inverted and incubated at 37°C for 24 hours for optimum growth of the organisms. The test materials having antimicrobial property inhibit microbial growth in the media surrounding the discs and thereby yield a clear, distinct area defined as zone of inhibition. The antimicrobial activity of the test agent is then determined by measuring the diameter of zone of inhibition expressed in millimetre (Bary, 1976; Bauer *et al,* 1966; Lester, 1972).

In the present study the crude extracts, fractions as well as some pure compounds were tested for antimicrobial activity by disc diffusion method. The experiment is carried out more than once and the mean of the readings is required (Bayer *et al.,* 1966).

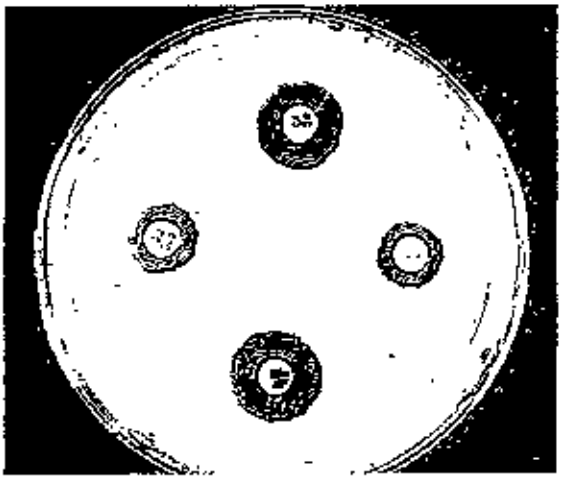


Fig.2: Disc diffusion method

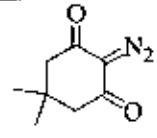
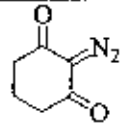
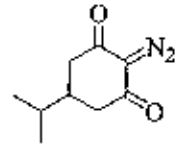
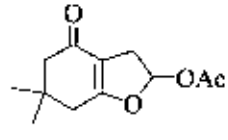
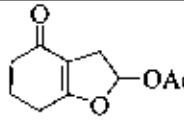
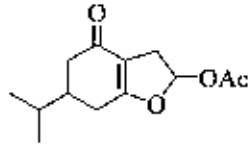
4.2. Experimental:

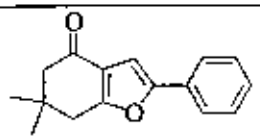
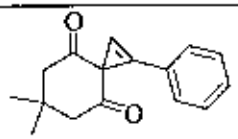
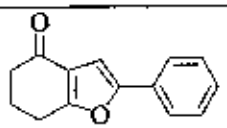
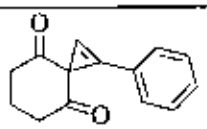
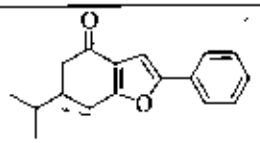
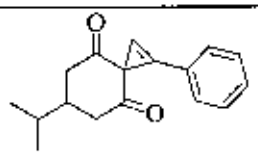
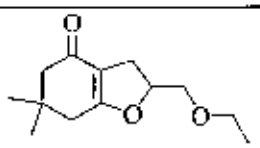
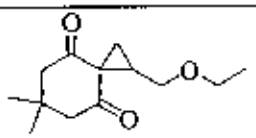
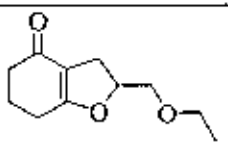
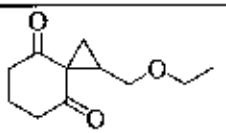
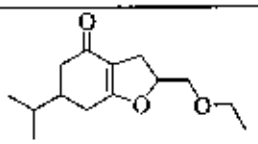
4.2a. Apparatus and reagents:

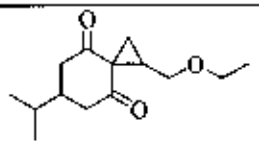
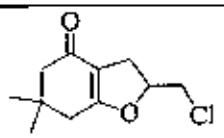
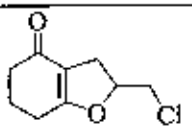
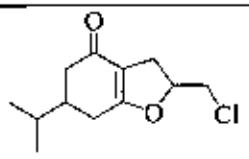
Filter paper discs	Petri dishes	Inoculating loop
Sterile cotton	Sterile forceps	Spirit burner
Micropipette	Screw cap test tubes	Nose mask and Hand gloves
Laminar air flow hood	Autoclave	Incubator
Refrigerator	Nutrient agar medium	Ethanol
Chloroform		

4.2b. Test materials:

Table 4.1a: List of compounds used for antibacteral activities:

Comp. no.	Name of the test chemicals	Molecular formula
6	2-Diazo- 55-dimethyl -cyclohexane-1, 3-dione	
7	2-Diazo-cyclohexane-1, 3-dione	
8	2-Diazo-5-isopropyl-cyclohexane-1, 3-dione	
10	6,6-Dimethyl-4-oxo-2,3,4,5,6.7-hexahydro-benzofuran- 2-yl acetate	
11	4-Oxo-2, 3,4,5,6,7-hexahydro-benzofuran-2-yl acetate	
12	6-Isopropyl-4-oxo-2, 3,4,5.6,7-hexahydro-benzofuran-2-yl acetate	

14	6,6-Dimethyl-2-phenyl-3, 5, 6, 7-tetrahydro-2*H*-benzofuran-4-one	
15	6,6-Dimethyl-1-phenyl-spiro [2.5] oct-1-ene-4, 8-dione	
16	2-Phenyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one	
17	1-Phenyl-spiro [2.5] oct-1-ene-4, 8-dione	
18	6-Isopropyl-2-phenyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one	
19	6-Isopropyl-1-phenyl-spiro [2.5] oct-1-ene-4,8-dione	
21	2-Ethoxymethyl-6, 6-dimethyl-hexahydro-benzofuran-4-one	
22	1-Ethoxymethyl-6, 6-dimethyl-spiro [2.5] octane-4, 8-dione	
23	2-Ethoxymethyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one	
24	1-Ethoxymethyl-spiro [2.5] octane-4, 8-dione	
25	2-Ethoxymethyl-6-isopropyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one	

26	1-Ethoxymethyl-6-isopropyl-spiro[2.5]octane-4,8-dione	
28	2-Chloromethyl-6, 6-dimethyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one	
29	2-Chloromethyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one	
30	2-Chloromethyl-6-isopropyl-3, 5,6,7-tetrahydro-2*H*-benzofuran-4-one	

4.2c. Test organisms:

The microbial strains used for the experiment were collected as pure cultures from the Institute of Nutrition and Food Science (INFS), University of Dhaka. Both gram positive and gram-negative organisms were taken for the test and they are listed in the Table 7.1.

Table 4.1b: List of test microorganisms:

Gram positive Bacteria	Gram negative bacteria	Fungi
Bacillus cereus	*Escherichia coli*	*Candida albicans*
Bacillus megaterium	*Pseudomonas aeruginosa*	*Aspergillus niger*
Bacillus subtilis	*Salmonella paratyphi*	*Sacharomyces cerevaceae*
Staphylococcus aureus	*Salmonella typhi*	
Sarcina lutea	*Shigella boydii*	
	Shigella dysenteriae	
	Vibrio mimicus	
	Vibrio parahemolyticus	

The bacterial and fungal strains used for the experiment were collected as pure cultures from the Institute of Nutrition and Food Science (INFS), University of Dhaka. Both gram positive and gram-negative organisms were taken for the test and they are listed in the Table 5.1.

4.2d. Composition of culture medium:

Nutrient agar medium (DIFCO) was used in the present study for testing the sensitivity of the organisms to the test materials and to prepare fresh cultures.

Table 4.2: Composition of nutrient agar medium:

a. Nutrient agar medium

Ingredients	Amounts
Bacto peptone	0.5 gm
Sodium chloride	0.5 gm
Bacto yeast extract	1.0 gm
Bacto agar	2.0 gm
Distilled water q.s.	100 ml
pH	7.2-7.6 at 25°C

a. Nutrient broth medium :

Ingredients	Amounts
Bacto beef extract	0.3 gm
Bacto peptone	0.5 gm
Distilled water q.s.	100 ml
pH	7.2 ±0.1 at 250C

b. Muller – Hunton medium:

Ingredients	Amounts
Beef infusion	30 gm
Casamino acid	1.75 gm
Starch	0.15 gm
Bacto agar	1.70 gm
Distilled water q.s.	100 ml
pH	7.3 ±0.2 at 250 C

d. Tryptic soya broth medium (TSB):

Ingredients	Amounts
Bacto tryptone	1.7 gm
Bacto soytone	0.3 gm
Bacto dextrose	0.25 gm
Sodium chloride	0.5 gm
Di potassium hydrogen Phosphate	0.25 gm
Distilled water q.s.	100 ml
pH	7.3 ± 0.2 at 250c

Nutrient agar medium (DIFCO) is the most frequently used and also used in the present study for testing the sensitivity of the organisms to the test materials and to prepare fresh cultures.

4.2e. Preparation of medium:

Calculated amount of each of the constituents was taken in a conical flask and distilled water was added to it to make the required volume. The contents were heated in a water bath to make a clear solution. The pH (at 25°C) was adjusted at 7.2-7.6 using NaOH or HCl 10 ml and 5 ml of the medium was then transferred in screw cap test tubes to prepare plates and slants respectively. The test tubes were then capped and sterilized by autoclaving at 15-lbs pressure at 121°C for 20 minutes. The slants were used for making fresh culture of microorganisms that were in turn used for sensitivity study.

4.2f. Sterilization procedures:

To avoid any type of contamination and cross contamination by the test organisms the antimicrobial screening was done in Laminar Hood and all types of precautions were strictly maintained. UV light was switched on an hour before working in the Laminar Hood. Petridishes and other glassware were sterilized by autoclaving at a temperature of 121°C and a pressure of 15-lbs./sq. inch for 20 minutes. Micropipette tips, cotton, forceps, blank discs etc. were also sterilized by UV light.

4.2g. Preparation of subculture:

In an aseptic condition under laminar air cabinet, the test organisms were transferred from the pure cultures to the agar slants with the help of a transfer loop to have fresh pure cultures. The inoculated strains were then incubated for 24 hours at 37°C for their optimum growth. These fresh cultures were used for the sensitivity test.

4.2h. Preparation of the test plates

The test organisms were transferred from the subculture to the test tubes containing about 10 ml of melted and sterilized agar medium with the help of a sterilized transfer loop in an aseptic area. The test tubes were shaken by rotation to get a uniform suspension of the organisms. The microbial suspension was immediately transferred to the sterilized petridishes. The petridishes were rotated several times clockwise and anticlockwise to assure homogenous distribution of the test organisms in the media.

4.2i. Preparation of discs

Measured amount of each test sample (specified in table 7.4) was dissolved in specific volume of solvent (chloroform or methanol) to obtain the desired concentrations in an aseptic condition. Sterilized metrical (BBL, Cocksville, USA) filter paper discs were taken in a blank Petri dish under the laminar hood. Then discs were soaked with solutions of test samples and dried.

Standard Kanamycin (30 µg/disc) discs were used as positive control to ensure the activity of standard antibiotic against the test organisms as well as for comparison of the response produced by the known antimicrobial agent with that of produced by the test sample. Blank discs were used as negative controls which ensure that the residual solvents (left over the discs even after air-drying) and the filter paper were not active themselves.

4.2j. Diffusion and incubation

The sample discs, the standard antibiotic discs and the control discs were placed gently on the previously marked zones in the agar plates pre-inoculated with test

microorganisms. The plates were then kept in a refrigerator at 4°C for about 24 hours upside down to allow sufficient diffusion of the materials from the discs to the surrounding agar medium. The plates were then inverted and kept in an incubator at 37°C for 24 hours.

4.2k. Determination of the zone of inhibition

The antimicrobial potency of the test agents are measured by their activity to prevent the growth of the microorganisms surrounding the discs which gives clear zone of inhibition.

After incubation, the antimicrobial activity of the test materials was determined by measuring the diameter of the zones of inhibition in millimetre with transparent scale.

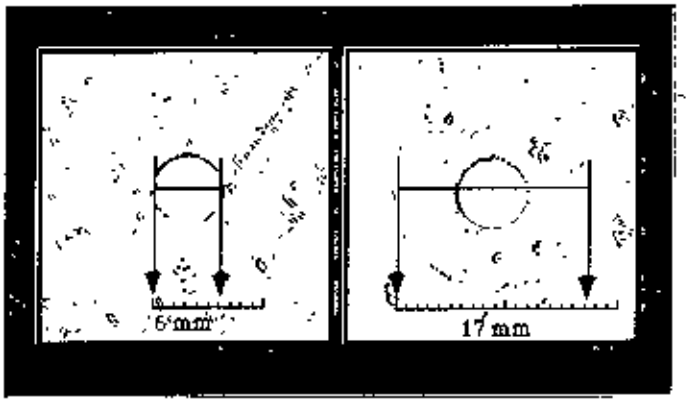


Fig 3: Determination of the zone of inhibition

4.3 RESULTS AND DISCUSSION OF THE TEST SAMPLES:

The antimicrobial activities of new furan derivatives were examined in the present study. The antibacterial activities of furan and propane derivatives were studied against thirteen bacteria such as *Bacillus cereus, Bacillus megaterium, Bacillus subtilis, Staphylococcus aureus, Sarcina lutea, Escherichia coli, Pseudomonas aeruginosa, Salmonella paratyphi, Salmonella typhi, Shigella boydii, Shigella dysenteriae, Vibrio mimicus, Vibrio parahemolyticus* and the activities of the same compounds were also studied against three fungi such as *Candida albicans, Aspergillus niger, Sacharomyces cerevaceae*

. The chloroform soluble of compounds (10, 14, 15, 21, 22, and 28) showed mild to moderate inhibitory activity against microbial growth & the average zone of inhibition produced by them 7-12 mm.

The result of the diameter of inhibition zone and % of inhibition of microbial growth due to the effect of chemicals, are presented in table 6.3 to table 6.6.

The antibacterial activities were measured in terms of diameters of zone of inhibition in (mm). All experiments were performed thrice to minimize the experimental plus individual errors. The mean value of the diameters of zone inhibition (M.DIZ) was taken as in disc for determining antimicrobial spectra. Sensitivity test results are in table 6.3 to 6.6 and were compared with a standard antibiotic kanamycin (30 µm/disc).

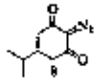
The gram positive and gram negative as well as pathogenic fungi used in the present investigation, were found to be comparatively resistant against six synthesized compounds (10, 14, 21, and 28), at a dose of 200 µm/disc in (table 6.4, 6.5 and 6.6) and compounds 15, 22 showed mild inhibitory activity against most of the tested organisms.

On the other hand, chloroform soluble of starting materials showed mild inhibitory (M.DIZ 7-9 mm) activity against three G(+), *Bacillus cereus, Bacillus subtilis, Staphylococcus aureus and* three G(-),*Pseudomonas aeruginosa, Salmonella paratyphi, Vibrio mimicus* and a fungi, *Candida albicans* of the tested organisms in table 6.3.

Compounds no.**10** showed moderate inhibitory (M.DIZ 10-12) activity was noticed against *Bacillus cereus, Shigella boydii, Shigella dysenteriae, Vibrio mimicus, Vibrio parahemolyticus Candida albicans, Aspergillus niger, Sacharomyces cerevacae.* Similarly comp.**15** demonstrated moderate inhibitory (M.DIZ 10-12) activity against all of the microbial organism and compound **22** showed moderate sensitivity (M.DIZ 10-12) against most of all organism except Escherichia *coli, Pseudomonas, aeruginosa and Aspergillus niger.* Compound **28** also effected of the range of 10 -12 mm of *Sacharomyces cerevacae, Bacillus megaterium and Shigella boydii* shown in **table 4.4-4.6.**

The mild inhibition was found against most of the organism for synthesized compounds 10, 14, 21, 22 and 28 in the range of (M.DIZ 7-9 mm). Therefore, it is not possible to determine the essential structure feature for antimicriobial action of this series of compound properly.

Table 4.3: Antimicrobial activity of test samples of starting materils:

Test microorganisms	Diameter of zone of inhibition(mm)			
	6 	7 	8 	KAN
Gram positive bact.				
Bacillus cereus	7	-	8	32
Bacillus megaterium	-	-	-	30
Bacillus subtilis	7	-	-	33
Staphylococcus aureus	7	-	-	35
Sarcina lutea	-	-	-	34
Gram negative bact.				
Escherichia coli	-	-	-	32
Pseudomonas aeruginosa	7	-	-	30
Salmonella paratyphi	-	7	7	35
Salmonella typhi	-	-	-	30
Shigella boydii	-	-	-	20
Shigella dysenteriae	-	-	-	25
Vibrio mimicus	-	7	-	28
Vibrio parahemolyticus	-	-	-	32
Fungi				
Candida albicans	8	-	-	32
Aspergillus niger	-	-	-	32
Sacharomyces cerevacae	-	-	-	30

Interpretation of sensitivity test results:

Gram (+) Bacteria:		**Gram (-) bacteria**	
18mm (M.DIZ)	= Sensitive	>16mm (M.DIZ)	= Sensitive
14-18 mm (M.DIZ)	= Intermediate	13-16 mm (M.DIZ)	= Intermediate
>14 mm (M.DIZ)	= resistant	>13 mm (M.DIZ)	= resistant

KAN : Standard kanamycin disc

"-" indicated no sensitivity or zone of inhibition lower than 6 mm.

Table 4.4: Antimicrobial activity of test samples of 10 -12 and 28- 30:

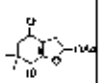
Name of microorganisms	Diameter of zone of inhibition(mm)						
Done	200µg/ disc	200µg/ disc	200µg/ disc	200µg/ disc	200µg/ disc	200µ/ disc	Stand 30
	Number of test samle						
	10 	**11** 	**12** 	**28** 	**29** 	**30** 	Kan.
Gram positive bact.							
Bacillus cereus	10	-	-	8	-	-	32
Bacillus megaterium	8	-	-	10	-	-	33
Bacillus subtilis	8	-	-	8	-	-	34
Staphylococcus aureus	8	-	-	9	-	-	31
Sarcina lutea	9	-	-	9	-	-	30
Gram negative bact.							
Escherichia coli	9	-	-	7	-	-	29
Pseudomonas aeruginosa	9	-	-	8	-	-	32
Salmonella paratyphi	8	-	-	9	-	-	31
Salmonella typhi	8	-	-	9	-	-	32
Shigella boydii	10	-	-	10	-	-	33
Shigella dysenteriae	11	9	-	7	-	-	34
Vibrio mimicus	10	-	-	8	-	-	35
Vibrio parahemolyticus	12	-	-	9	-	-	34
Fungi							
Candida albicans	12	-	-	9	-	-	33
Aspergillus niger	-	9	-	9	-	-	30
Sacharomyces cerevacae	11	7	-	11	-	-	30

Table 4.5: Antimicrobial activity of test samples of 14 -19:

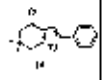
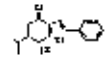
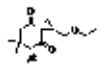
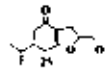
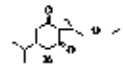
Name of microorganisms	**Diameter of zone of inhibition(mm)**						
Done	200µg/ disc	200µg/ disc	200µg/ disc	200µg/ disc	200µg/ disc	200µ/ disc	Stand 30
	Number of test samle						
	14 	**15** 	**16** 	**17** 	**18** 	**19** 	Kan.
Gram positive bact.							
Bacillus cereus	-	10	-	-	-	-	36
Bacillus megaterium	-	11	-	-	-	-	40
Bacillus subtilis	-	11	-	-	-	-	40
Staphylococcus aureus	-	12	-	-	-	-	36
Sarcina lutea	-	10	-	-	-	-	36
Gram negative bact.							
Escherichia coli	8	10	-	-	-	-	39
Pseudomonas aeruginosa	7	12	-	-	-	-	35
Salmonella paratyphi	8	11	-	-	-	-	35
Salmonella typhi	8	10	-	-	-	-	37
Shigella boydii	7	10	-	-	-	-	33
Shigella dysenteriae	9	11	-	-	-	-	34
Vibrio mimicus	7	10	-	-	-	-	37
Vibrio parahemolyticus	8	12	-	-	-	-	38
Fungi							
Candida albicans	8	12	-	-	-	-	33
Aspergillus niger	9	10	-	-	-	-	38
Sacharomyces cerevacae	7	11	-	-	-	-	34

Table 4.6: Antimicrobial activity of test samples of 21 -26:

Name of microorganisms	Diameter of zone of inhibition(mm)						
Done	200µg/ disc	200µg/ disc	200µg/ disc	200µg/ disc	200µg/ disc	200µ/ disc	Stand 30
	Number of test samle						
	21 	22 	23 	24 	25 	26 	K a n
Gram positive bact.							
Bacillus cereus	-	10	-	-	-	-	33
Bacillus megaterium	9	10	-	-	-	-	36
Bacillus subtilis	-	11	-	-	-	-	35
Staphylococcus aureus	-	10	-	-	-	-	35
Sarcina lutea	-	10	-	-	-	-	31
Gram negative bact.							
Escherichia coli	8	9	-	-	-	-	32
Pseudomonas aeruginosa	-	9	-	-	-	-	33
Salmonella paratyphi	7	10	-	-	-	-	31
Salmonella typhi	-	10	-	-	-	-	32
Shigella boydii	-	10	-	-	-	-	33
Shigella dysenteriae	9	11	-	-	-	-	34
Vibrio mimicus	-	10	-	-	-	-	35
Vibrio parahemolyticus	-	12	-	-	-	-	34
Fungi							
Candida albicans	-	12	-	-	-	-	33
Aspergillus niger	9	-	-	-	-	-	32
Sacharomyces cerevacae	7	11	-	-	-	-	34

The obtained result clearly indicated the presence of potent antimicrobial agents in the extractives. Bioactivity guided isolation can be carried out to separate bioactive metabolites.

4.4. Conclusion:

Eighteen synthesized heterocyclic compounds and three diazo compounds have been tested for in antimicrobial activity against five gram-positive and eight gram – negative bacteria as well as three human fungal pathogens. Some of this compound demonstrated mild to moderate antimicrobial activity against most of the test organism. From these structures we found that the cyclopropane ring causes relatively microbial growth inhibition.

Among tested compounds of furan and cyclopropane derivatives (10, 14, 15, 21, 22, and 28) exhibited relatively greater inhibition of growth of the microorganism. The higher activity of the compounds (10, 14, 21 and 28) could probably bed due to their dimethyl substitution of C-6 position of cyclohexane ring. Which subsequently facilitated the diffusion of the chemical entities through the microbial call wall?

Substitution of ispropyl of the ring carbon, with bulkier terminal alkane group decrease in the antimicrobial activity of the remaining compounds, while cyclohexane without substitution at the same place produce weakly active compounds.

4.5. References:

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CONCLUSIONS:

In conclusions, an efficient synthetic route for the synthesis of dihydrofuran derivatives is established successfully.

► Firstly, the synthesis of 2-diazo-1,3-dione derivatives from cyclic diketone with several substitutes is reported.

The one pot synthesis of 4-oxo- 2,3,4,5,6,7-hexahydro-benzofuran-2-yl acetate by the rhodium catalyzed reaction of 2-diazoketone derivatives and vinyl acetate is developed in mild condition.

►The one pot synthesis of 2-phenyl-6, 7- dihydro-5*H*-benzofuran-4-ones and 1-phenyl-spiro [2.5] oct-1-ene-4, 8-diones by using rhodium catalyzed reactions of 2-diazo cyclohexane 1,3-dione derivatives and phenyl acetylene is established successfully.

►The one pot reaction of allyl etbyl ether by the rhodium catalysis afforded 2-alkyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-ones and 1-alkyl-spiro[2.5]octane-4,8-dione derivatives is developed in mild condition.

► The preparation of a variety of dihydrofurans by using rhodium catalyzed reactions of 2-diazo cyclohexane 1,3- dione derivatives and allyl chloride to afford 2-chloromethyl-3,5,6,7-tetrahydro-2*H*-benzofuran-4-one derivatives is also established successfully.

These reactions provide a rapid entry to synthesis of dihydrofurans and spiro compounds in mild condition. This methodology is also expected to be widely used in synthesis of furan skeleton containing natural products and spiro compounds.

►Finally, all synthesized compounds were tested antibacterial and antifungal activity, some of them demonstrated mild to moderate antimicrobial activity against most of the test organism.

►Therefore, rhodium (II) mediated synthesis may provide a new entry into the naturally occurring biologically active dihydrofuran skeletons and spiro derivatives.