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Ministry of Higher Education
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University of Baghdad
College of Education For Pure Science /Ibn Al-Haitham
Department of Chemistry

New Heterocyclic Compounds Containing Five- and Six-Membered Rings in The Same Molecule: Synthesis And Investigation Of Biological Activity

A thesis

Submitted to Council of College of Education For Pure Science ,Ibn-Al-Haitham , University of Baghdad , in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy in Chemistry

By

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1440AH *2018 AC*

بسم الله الرحمن الرحيم

فَأَمَّا الزَّبَدُ فَيَذْهَبُ جُفَاءً وَأَمَّا مَا يَنْفَعُ النَّاسَ

فَيَمْكُثُ فِي الْأَرْضِ

صدق الله العلي العظيم

سورة الرعد

«الآية ١٧»

Supervisor certification

I certify that this thesis was prepared under my supervision at Department of Chemistry, College of Education For Pure Science (Ibn Al Haitham), Baghdad University, as a partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry.

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Signature: Date:

Date: / / 2018
Prof. Dr. Jumbad H. Tomma

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We, the examining committee, certify that we have read this thesis and examined the student (**Sahar Fadhil Abbas**) in its contents and that, in our opinion , it is adequate with **" excellent "** standing as a thesis for the degree of Doctor of Philosophy in Science of Chemistry.

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I have certified upon the discussion of the examining committee.

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Date: / /
Address: Behalf/ The Dean of College of Education
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Dedication

To my father and mother…..

with my great love

Sahar

Acknowledgment

Praise be to God, and God's blessing and peace be upen our Prophet Mohammed who rescued mankind from darkness to light , It is with great pleasure that I place my deep sense of gratitude and heartfelt thanks to my supervisor **Prof. Dr. Jumbad H. Tomma** for suggesting the proposal , kind support and constant encouragement throughout the progress of the dissertation work .

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Sahar

Abstract

This work includes synthesis, characterization and study the biological activity of some new heterocyclic compounds containing five and six membered hetero rings in the same molecula as follows :

1) The compounds derived from 5,6-diphenyl-1,2,4-triazine-3-thiol, Scheme I and II.

The first synthetic route includes synthesis of new seven compounds of imidazole[VII]$_{a-g}$, starting with 5,6-diphenyl-1,2,4-triazine-3-thiol. Benzil reacted with thiosemecarbazide in 85% acetic acid to give 1,2,4-triazine compound [I], which was reacted with chloro ethyl acetate in fused sodium acetate and ethanol to obtain ester compound [II].The condensation of ester[II] with hydrazine hydrate in ethanol to produce new acid hydrazide [III]$_{a,b}$. The prouduct compound [III] $_{a,b}$ reacted with benzaldehyde or 4-substituted benzaldehyde to form Schiff bases[VI]$_{a-g}$. The reaction of Schiff bases with acetyl chloride in dry benzene led to formation N-acetyl compounds[V] $_{a-g}$. The thiourea derivatives[VI]$_{a-g}$ were formed by the reaction of N-acetyl with thiourea and anhydrouse sodium carbonat in acetone. The ring closur reaction of thiourea derivatives with benzion in DMF gives new imidazole compounds [VII]$_{a-g}$.

The second synthetic route includes the synthesis of imides and phthalazine compounds [VIII]$_{a-d}$ from fusion compound[III]$_{a,b}$ with phthalic or naphthalic acid anhydride .

The third synthetic route includes synthesis of hydrazone compounds [XI]$_{a,b}$ starting with acid hydrazide [III]$_{a,b}$, which reacted with ethyl aceto acetate in absolute ethanol to get 2-(2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)acetyl)-5-methyl-2,4-dihydro-3H-pyrazol-3-one[IX], the later product

was treated with acetyl chloride in the presence of calcium hydroxide in 1,4-Dioxane to give 4-acetyl-2-(2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)acetyl)-5-methyl-2,4-dihydro-3H-pyrazol-3-one[X]. Then acetyl pyrazol reacted with phenyl hydrazine or 2,4-dinitro phenyl hydrazine in ethanol and drops from glacial acetic acid (as a catalyst) under reflux conditions to produce the corresponding hydrazones$[XI]_{a,b}$.

2) The compounds derived from chalcones $[XII]_{a-c}$, Scheme III and IV.

The first synthetic route includes the synthesis of hydrazone compounds $[XVIII]_{a-f}$, starting with chalcones $[XII]_{a-c}$. 4- Hydroxy acetophenone reacted with benzaldehyde, anisaldehyde and 4-methyl benzaldehyde in basic medium to give three chalcones compounds$[XII]_{a-c}$ by Claisen-Schemidt reaction. The chalcones$[XII]_{a-c}$ reacted with ethylacetoacetate in basic medium to get new cyclohexenone derivatives $[XIII]_{a-c,}$ which reacted with ethylchloroacetate CH_3CO_2Na and ethanol to obtained ester compounds $[XIV]_{a-c}$. The condensation of esters$[XIV]_{a-c}$ with hydrazine hydrate led to obtain indazole derivatives $[XV]_{a-c}$. The reaction of indazole derivatives $[XV]_{a-c}$with ethyl acetoacetate led to formation new pyrazol derivatives $[XVI]_{a-c}$, which reacted with acetyl chloride in basic medium to get 4-acetyl pyrazoles $[XVII]_{a-c}$ .The later product reacted with phenyl hydrazine or 2,4 di nitrophenyl hydrazine to form hydrazone compounds $[XVIII]_{a-f}$.

The second synthetic route includes synthesis of Schiff base$[XIX]_{a-i}$ from reaction of indazole derivatives $[XV]_{a-c}$ with benzaldehyde or 4-substituted benzaldehyde to give new type of Schiff bases of indazole derivatives$[XIX]_{a-i}$

On the other hand, The third synthetic route includes the synthesis of isoxazole derivatives$[XX]_{\mathbf{a-c}}$, from the refluxed a mixture of cyclohexenones $[XII]_{a-c}$ and hydroxylamine hydrochloride and sodium hydroxide in ethanol to give isoxazole compounds $\mathbf{[}XX\mathbf{]}_{a-c}$, The OH group of compound $[XX]_{a-c}$

reacted with acid chloride in triethyl amine and (DMF , THF) at (0-4) ^{o} C to obtain new esters $[XXI]_{a-f}$.

The fourth synthetic route includes reaction of coumarin compounds with hydrazide compound$[XV]_{a-c}$ in glacial acetic under reflux to form quinolin-2-one derivatives $[XXII]_{a-f}$.

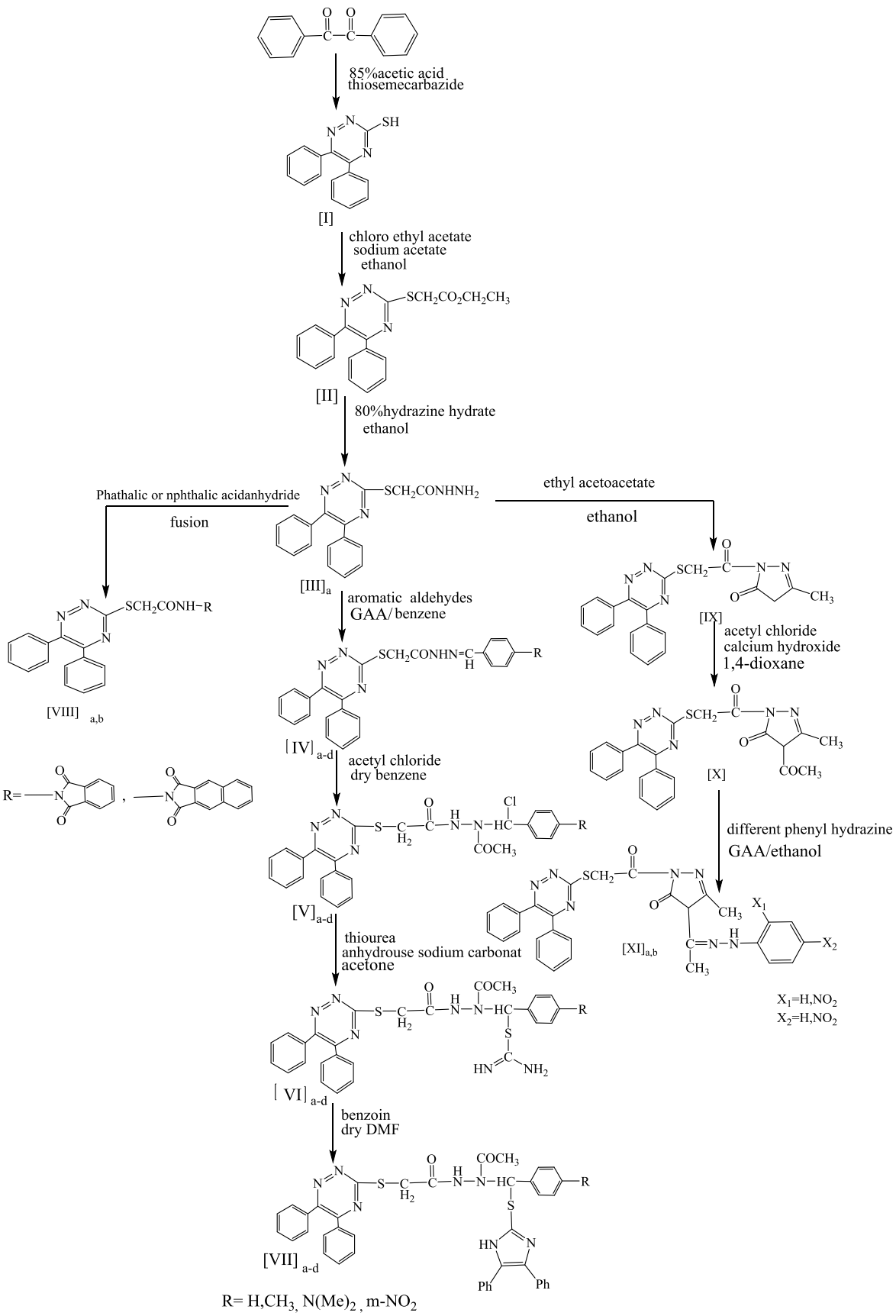
The fifth synthetic route includes synthesis of imides compounds of indazoles $[XXIII]_{a-f}$. These compounds were synthesized from the fusion of acid hydrazide$[XV]_{a-c}$ with acid anhydride.

3) The compounds derived from 4-(4-aminophenyl) oxazol-2-amine[XXIV], Scheme V .

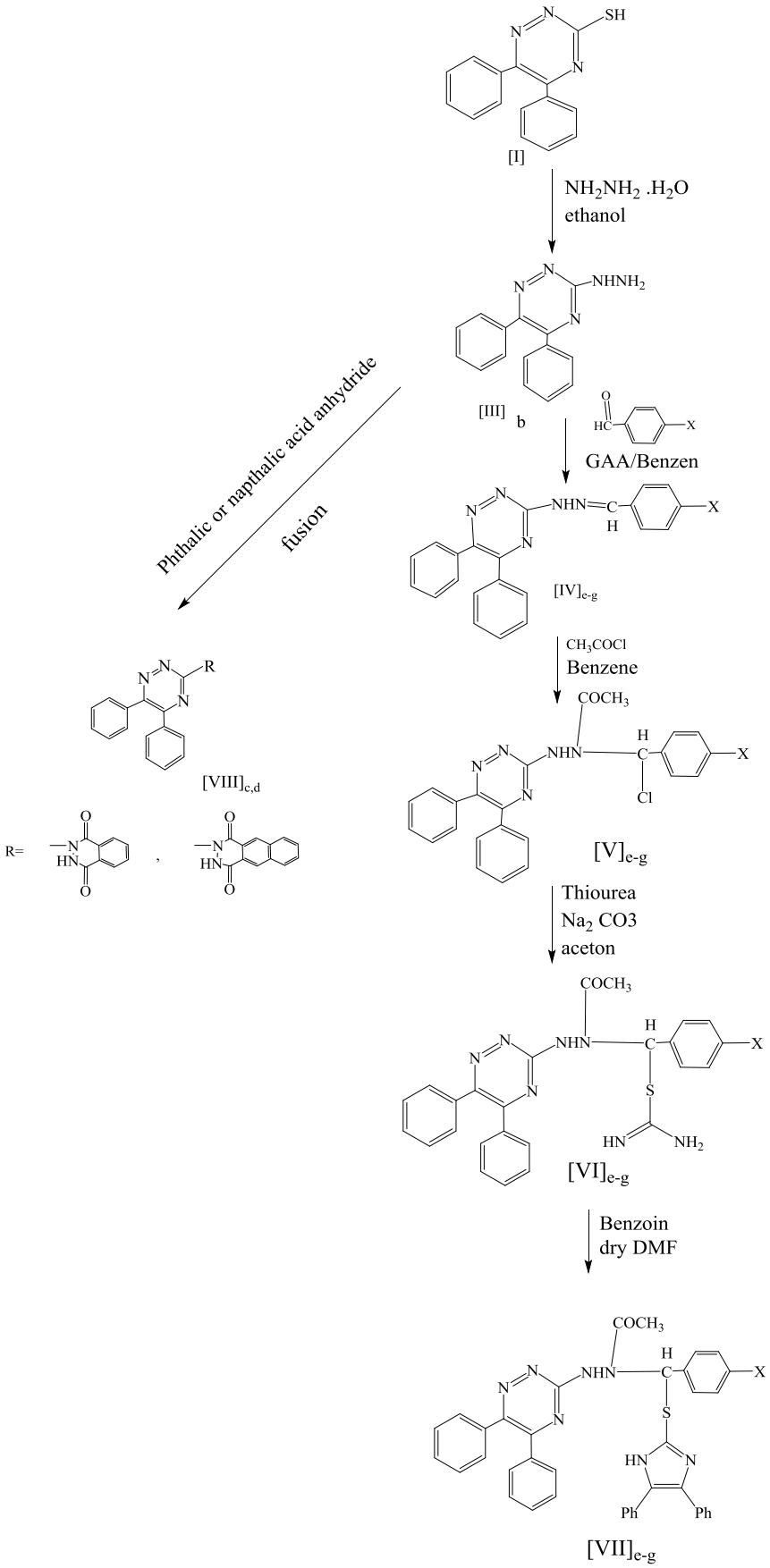
This route includes synthesis of 4-(4-aminophenyl)oxazol-2-amine [XXIV] by fusion of iodine with urea and 4- amino acetophenone. Then condensation of compound [XXIV] with benzaldehyde or 4-N,N-dimethyl benzaldehyde in benzene and glacial acetic acid to form new Schiff bases type $[XXV]_{a,b}$. The reaction of Schiff bases with acetyl chloride in dry benzene led to form N-acetyl compounds of oxazole type $[XXVI]_{a,b}$, thiourea derivatives$[XXVII]_{a,b}$, were obtaind from the reaction of N-acetyl with thiourea and anhydrous sodium carbonate in acetone. The ring closur reaction of thiourea compounds with diethyl malonate in dry benzene give pyrimidine dervitives $[XXVIII]_{a,b}$.

All the synthesized compounds were characterized by FTIR, ^{1}HNMR and mass spectroscopy (of some of them) .

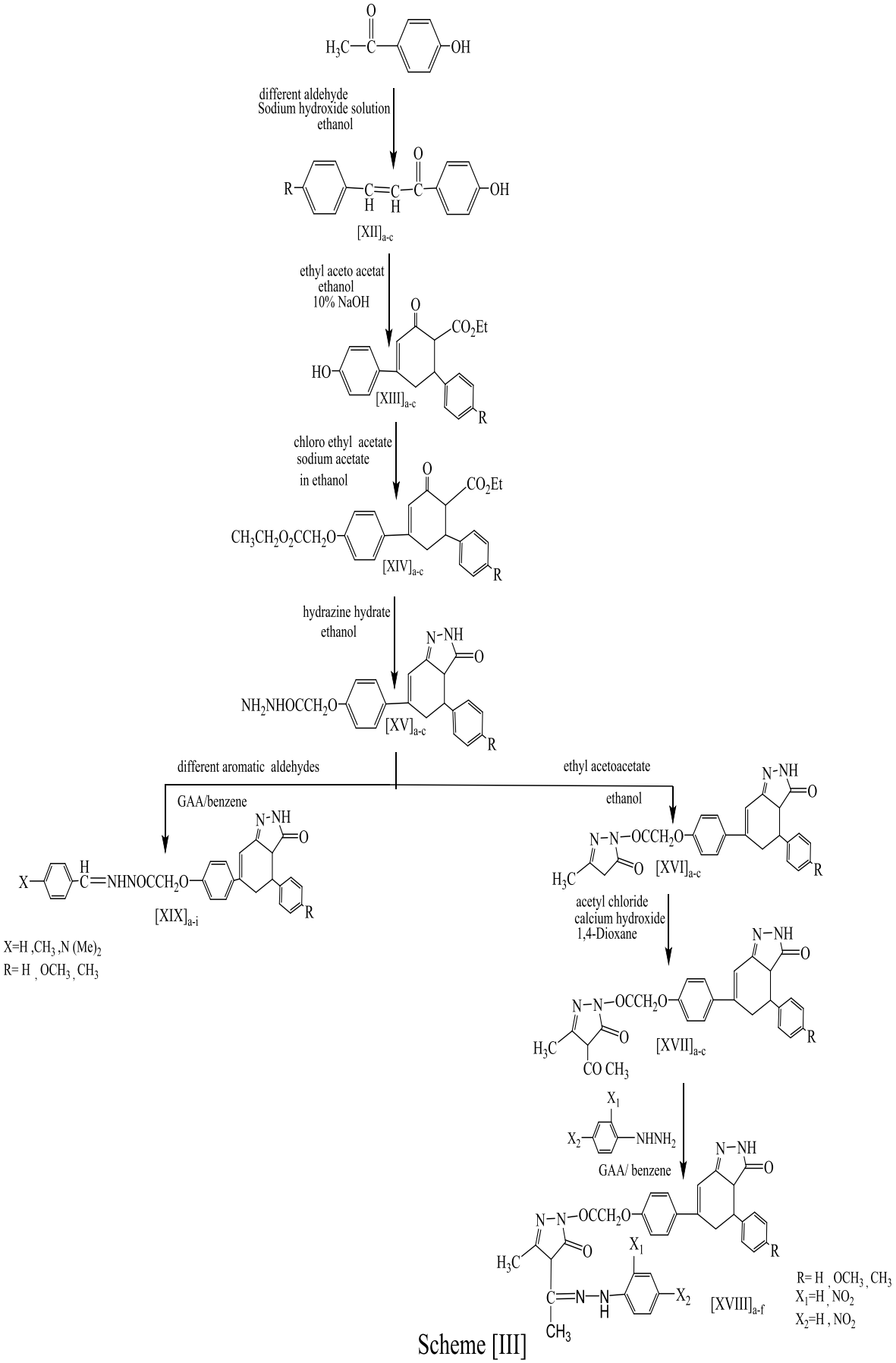
All newly synthesized compounds have been tested against antibacterial activity; *Bacillus subtitis* gram (+) and *E.coli* gram (-) bacteria and also on *candida albicans* fungal. Some compounds gave good biological activity and others did not show any biological activities.


85%acetic acid
thiosemecarbazide
[I]
chloro ethyl acetate
sodium acetate
ethanol
[II]
80%hydrazine hydrate
ethanol
Phathalic or nphthalic acidanhydride
fusion
ethyl acetoacetate
ethanol
[III]a
aromatic aldehydes
GAA/ benzene
[VIII] a,b
[IV] a-d
[IX]
acetyl chloride
calcium hydroxide
1,4-dioxane
[X]
acetyl chloride
dry benzene
different phenyl hydrazine
GAA/ethanol
[V]a-d
[XI]a,b
thiourea
anhydrouse sodium carbonat
acetone
[VI] a-d
benzoin
dry DMF
[VII] a-d
R= H,CH3, N(Me)2 , m-NO2
X1=H,NO2
X2=H,NO2

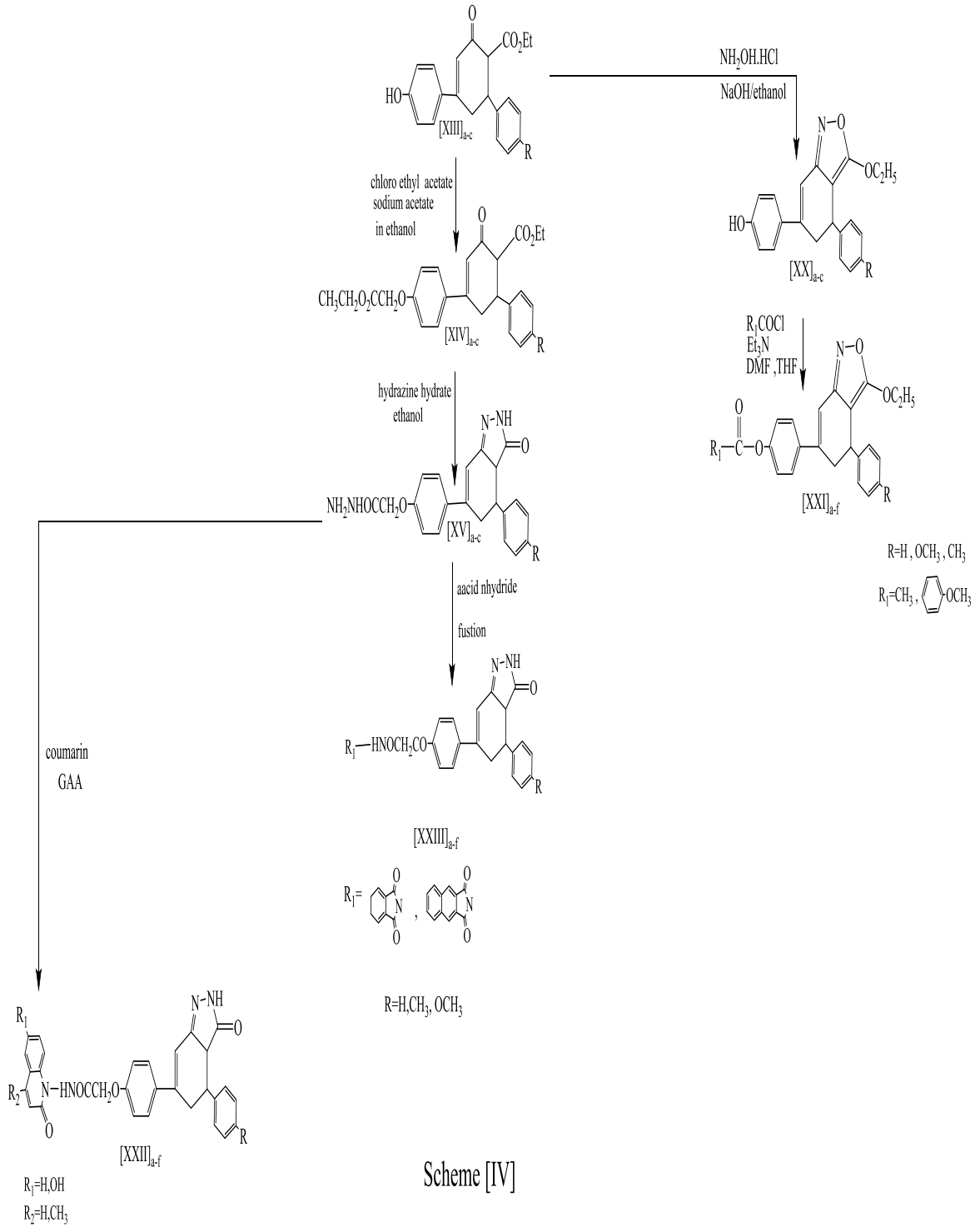
Scheme 1


[I]
NH2NH2 .H2O
ethanol
[III]
b
GAA/Benzen
Phthalic or napthalic acid anhydride
fusion
[IV]e-g
CH3COCl
Benzene
[V]e-g
[VIII]c,d
R=
Thiourea
Na2 CO3
aceton
[VI]e-g
Benzoin
dry DMF
[VII]e-g
X=H, CH3, N(Me) 2

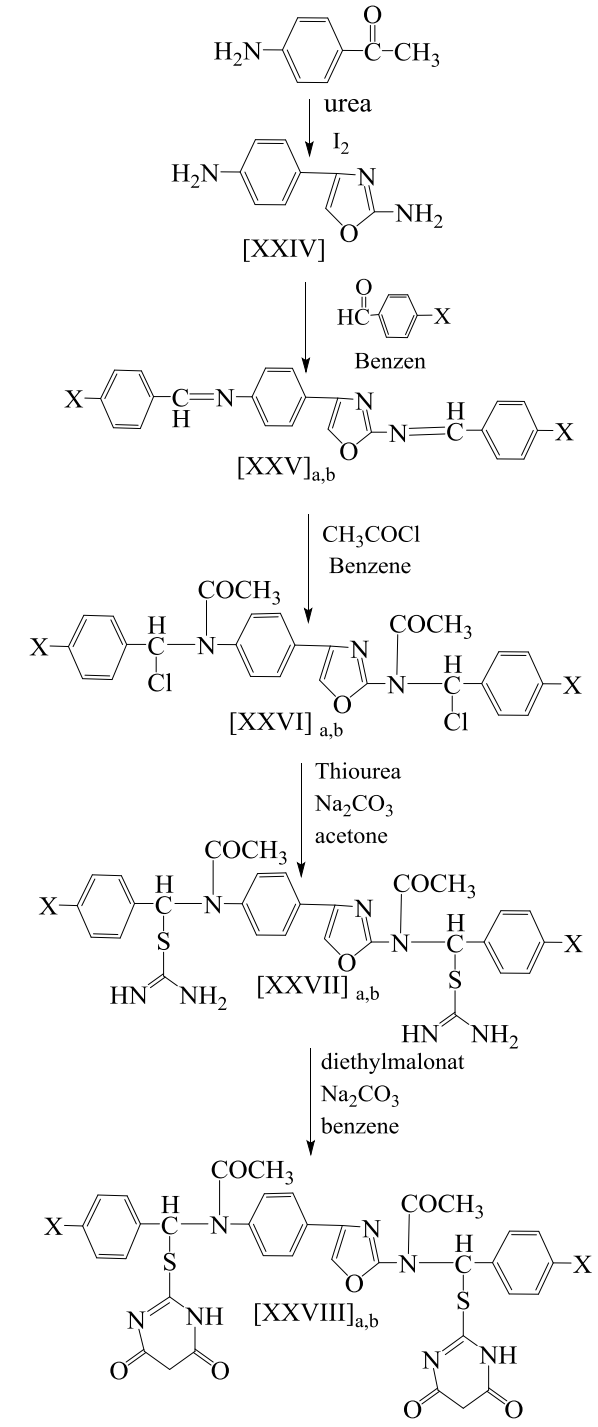
Scheme II


different aldehyde
Sodium hydroxide solution
ethanol
[XII]a-c
ethyl aceto acetat
ethanol
10% NaOH
[XIII]a-c
chloro ethyl acetate
sodium acetate
in ethanol
[XIV]a-c
hydrazine hydrate
ethanol
[XV]a-c
different aromatic aldehydes
GAA/benzene
[XIX]a-i
X=H ,CH3 ,N (Me)2
R= H , OCH3 , CH3
ethyl acetoacetate
ethanol
[XVI]a-c
acetyl chloride
calcium hydroxide
1,4-Dioxane
[XVII]a-c
GAA/ benzene
[XVIII]a-f
R= H , OCH3 , CH3
X1=H , NO2
X2=H , NO2

Scheme [III]


NH2OH.HCl
NaOH/ethanol
chloro ethyl acetate
sodium acetate
in ethanol
hydrazine hydrate
ethanol
aacid nhydride
fustion
coumarin
GAA
R1COCl
Et3N
DMF ,THF
[XIII]a-c
[XIV]a-c
[XV]a-c
[XX]a-c
[XXI]a-f
[XXII]a-f
[XXIII]a-f
R=H , OCH3 , CH3
R1=CH3 ,
OCH3
R=H,CH3, OCH3
R1=H,OH
R2=H,CH3

Scheme [IV]



X= H , $N(Me)_2$

Scheme [V]

List of abbreviations

DMF	N,N- dimethyl formamide
THF	Tetrahydrofuran
DEEM	diethylethoxymethylenemalonate
TBHP	tert-butyl hydroperoxide
TEBA	Triethylbenzylammonium chloride
TEA	triethylamine
GAA	Glacial acetic acid
PTC	phase transfer
py	pyridine
NMDA	N-methyl-D-aspartate receptor
hrs	hours
MWI	Microwave irradiation
DMSO-d_6	deuterated dimethyl sulfoxide
Conc.	concentration
abs.	absolute
gm	Gram
mL	Milliliter
m p	Melting point
^{o} C	Degree centigrade
^{1}HNMR	Proton Nuclear Magnetic Resonance
FTI R	Fourier Transform Infrared
cm^{-1}	Wave number
asym .	asymmetry
sym	symmetry
δ	Chemical shift
ppm	Part per million

s	singlet
d	doublet
t	triplet
q	quartet

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List of Schemes

1. Introduction

1.1. Heterocyclic Compounds

A cyclic compound containing all carbon atoms in ring formation is referred to as a carbocyclic compound. If at least one atom other than carbon, forms a part of the ring system then it is designated as a heterocyclic compound. Nitrogen, sulfur and oxygen are the most common hetero atoms. Heterocyclic rings may contain another hetero atoms. Extensive range of heterocyclic derivatives are known and the number is increasing rapidly. Heterocyclic ring may comprise of three or more atoms which may be saturated or unsaturated[(1)].

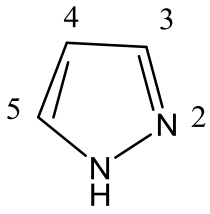
The cyclic part (from Greek kyklos, meaning "circle") of heterocyclic indicates that at least one ring structure is present in such a compound, while the prefix hetero- (from Greek heteros, meaning "other" or "different") refers to the noncarbon atoms, or heteroatoms .Heterocyclic compounds with three ,four , five, six and seven membered rings[(2-5)].

The heterocyclic ring may contain more than one hetero atom which may be similar or dissimilar. A large number of heterocyclic compounds are necessary to life. Various derivatives such as antibiotics, alkaloids, amino acids, vitamins, hormones and a large number of dyes and drugs contain heterocyclic moeity. Heterocycles play a vitals role in agricultural and pharmacological and synthetic fields. There is a large number of synthetic heterocyclic compounds with important applications are a valuable intermediates in synthesis [(6-9)] . In the past years, most heterocyclic systems have been used as a source to synthesis new compounds with varied biological potentials. Especially, nitrogen containing heterocyclic systems like pyrazoles, substituted oxazole play a vital role in discovering novel candidates having anti microbial potentials. The azoles exhibited anti-HIV antiviral activity [(10,11)].

1.2. Five member hetrocyclic ring

1.2.1. Pyrazoles

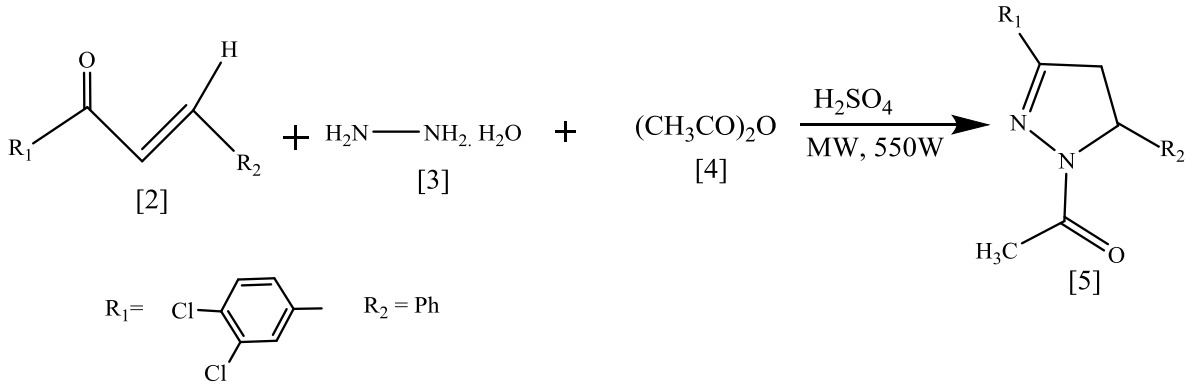
Pyrazoles [1] are important members of heterocyclic field with two adjacent nitrogens in a five-membered ring. Among the two nitrogen atoms; one is basic and the other is neutral in nature[12]. These are aromatic molecules due to their planar (SP^2) conjugated ring structures with six delocalized π-electrons. The aromaticity nature arises from the four π electrons and the unshared pair of electrons on the nitrogen of NH group, structure composed of three carbon atoms and two nitrogen atoms at 1and 2 positions[13].



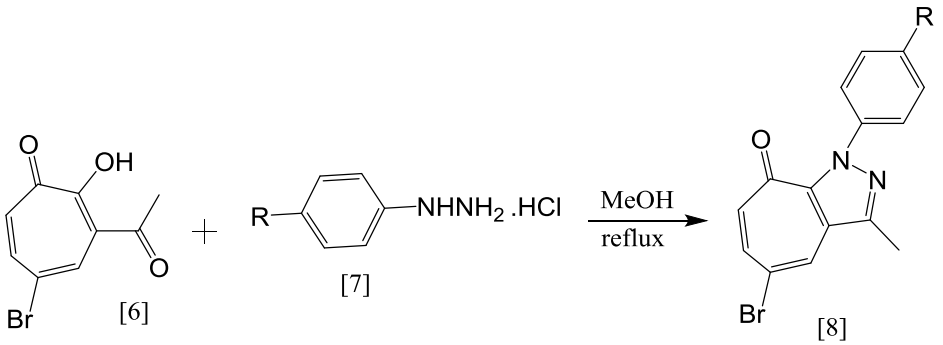
[1]

1.2.1.1.Synthesis of pyrazoles

1-acetyl pyrazoline derivatives[5] were synthesized by solvent-free cyclization cum acetylation of aryl chalcones [2] with hydrazine hydrate [3]and acetic anhydride[4] in the presence of H_2SO_4 as a catalyst under microwave irradiation[14].

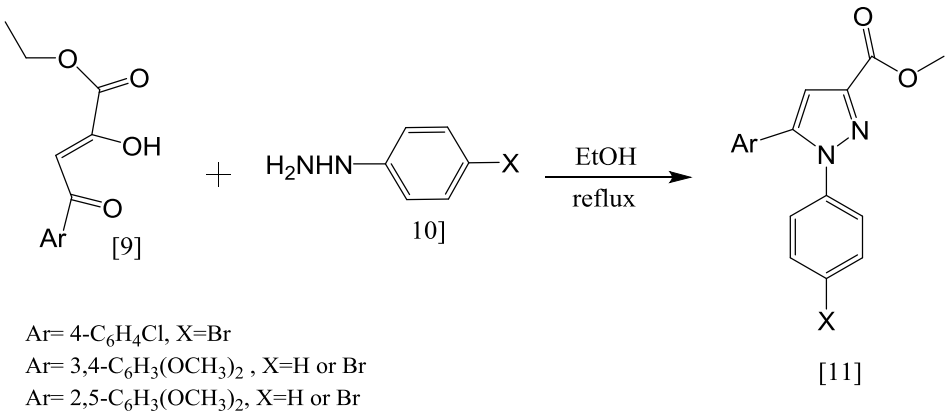


Also, 1-aryl-5-bromo-3-methyltropono[c] pyrazoles[8] were synthesized by reaction of compound [6] with arylhydrazine hydrochloride[7]in methanol [15] .



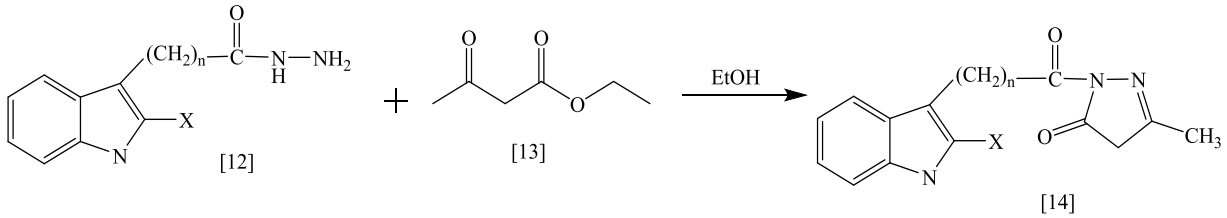
R=OCH_3, Cl, Br, CN

The synthesis of 1,5-diarylpyrazoles[11] were done by[16] regioselective cyclization reaction of β-diketones[9] with aryl hydrazine[10] in ethanol, the compound have antimicrobial activity .



Ar= 4-C_6H_4Cl, X=Br
Ar= 3,4-$C_6H_3(OCH_3)_2$, X=H or Br
Ar= 2,5-$C_6H_3(OCH_3)_2$, X=H or Br

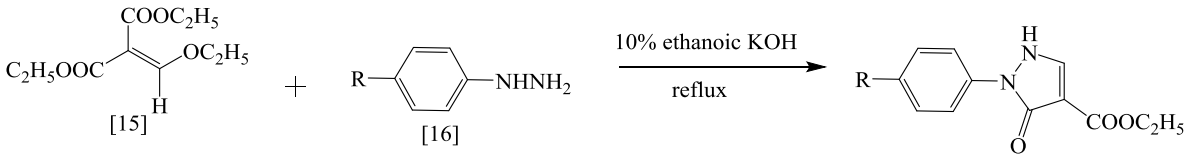
While, the pyrazolone derivatives [14], were synthesized by the reaction of equimolar from acid hydrazides [12] and ethylacetoacetate [13] in absolute ethanol [17].



[12] [13] [14]

X=H, Me ; n= 0,1,3

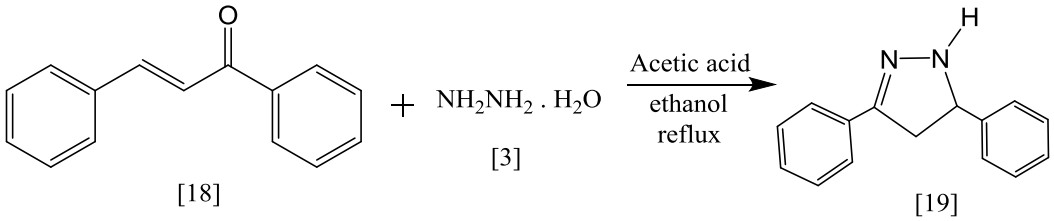
In addition[18], pyrazole-3-one-4-carboxylate derivatives[17] were generated by reacting diethylethoxymethylenemalonate(DEEM)[15] with substituted phenyl hydrazine[16] via base catalyzed cyclization reaction.



[15] [16] [17]

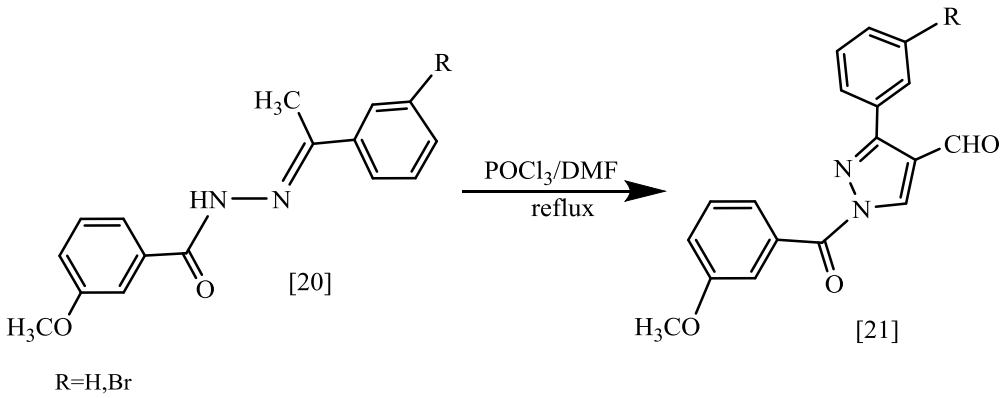
R= H, H_3CO , OH

Alam et al .,[19] reported the condensation reaction between chalcone[18] and hydrazine hydrate [3] in the presence of acetic acid in ethanol to give 3,5-diphenyl-4,5-dihydro-1H-pyrazole[19], this compound has antimicrobial activity .

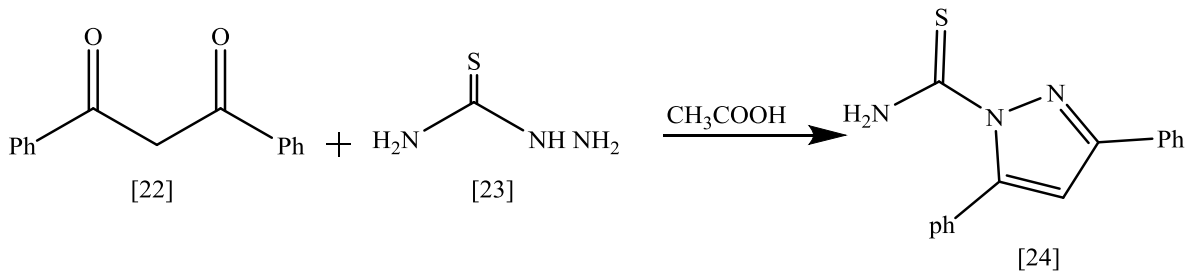


[18] [3] [19]

On the other hand[20], 3-(3-substituted phenyl)-1-(3-methoxybenzoyl)-1H-pyrazole-4-carbaldehyde [21] were synthesized by the reaction of N'-(3-substituted benzylidene)-3-methoxybenzohydrazid[20] with DMF and $POCl_3$, these compounds have antibacterial and antifungal activity.

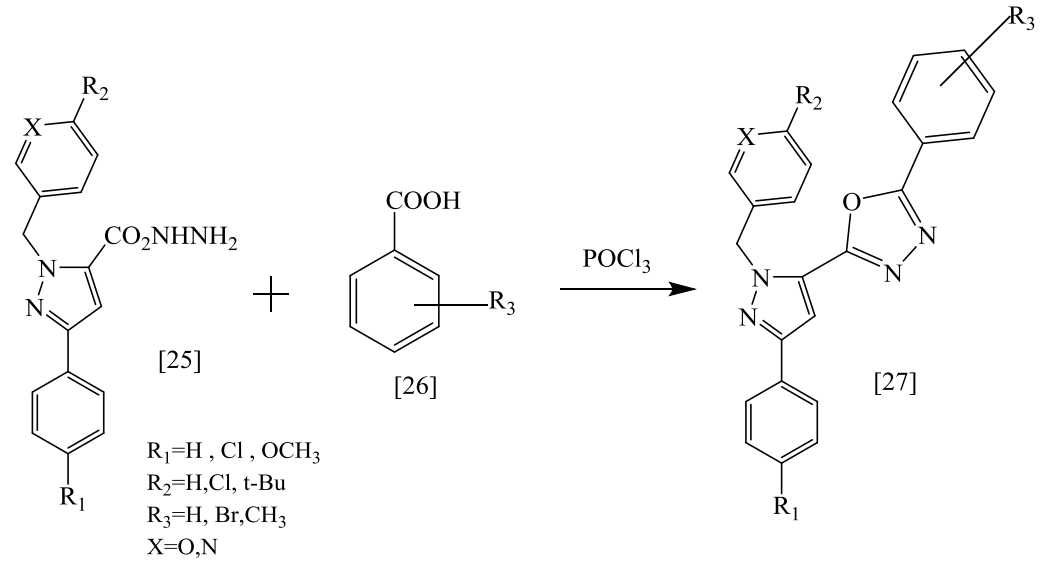


Finally[21],the 3,5-diphenyl-1*H*-pyrazole [24] was prepared according to the reaction of dibenzoylmethane[22] and thiosemicarbazide [23] in acetic acid.

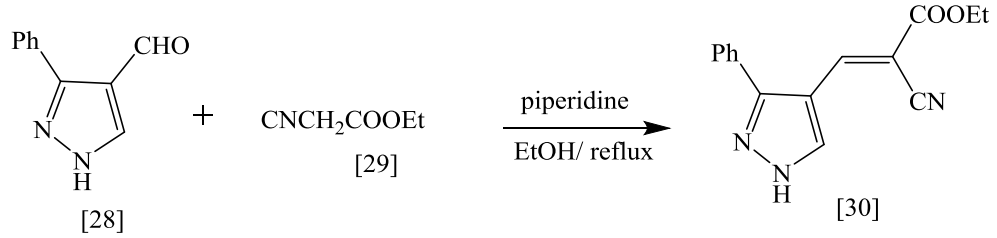


1.2.1.2 Reaction of pyrazoles and their derivatives

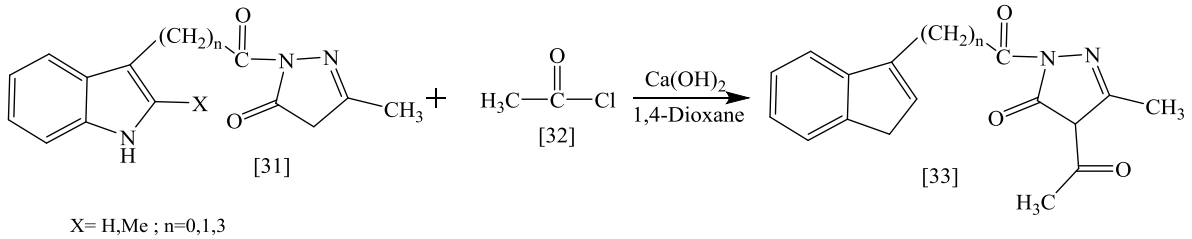
Mert .et al., [22] reacted pyrazole compounds [25] with substituted benzoic acid[26] in $POCl_3$to get 1,3,4-oxadiazole derivatives[27] .



While,[23] the reaction of 3-phenylpyrazole-4-carboxaldehyde[28]with ethylcyanoacetate [29] in ethanol and few drops of piperidine led to form 2-ethyl-2-cyano -3-(3-phenyl-1H-pyrazol-4-yl) acrylate [30].

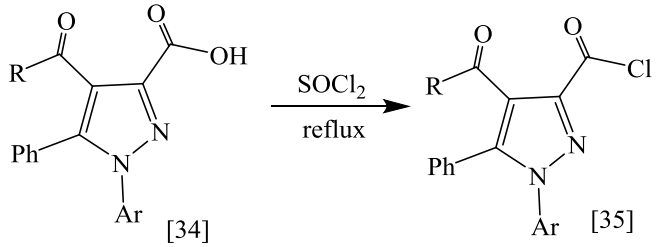


4-Acetyl pyrazolone compound [33]was synthesized by the reaction pyrazolone [31] and acetyl chloride[32] in 1,4-Dioxane in presence of calcium hydroxide[17].



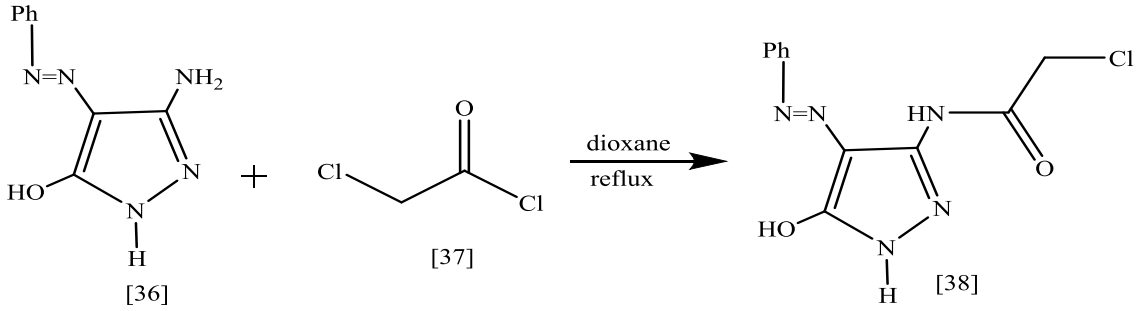
X= H,Me ; n=0,1,3

On the other hand, Kasimogullar et al., [24] converted pyrazole 3-carboxlyic acid[34] to accorsebonding acid chloride [35] using $SOCl_2$.

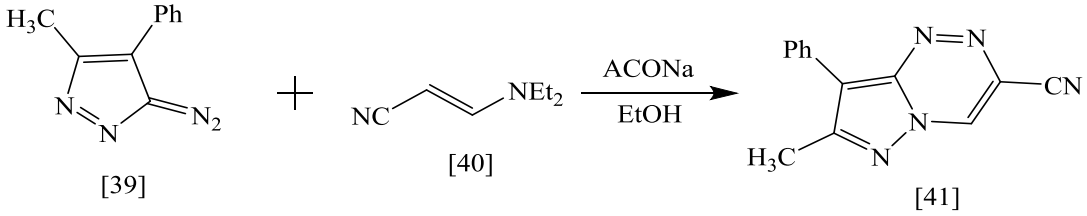


R=Ph, OEt
Ar=$Ph_3(-NO_2)$

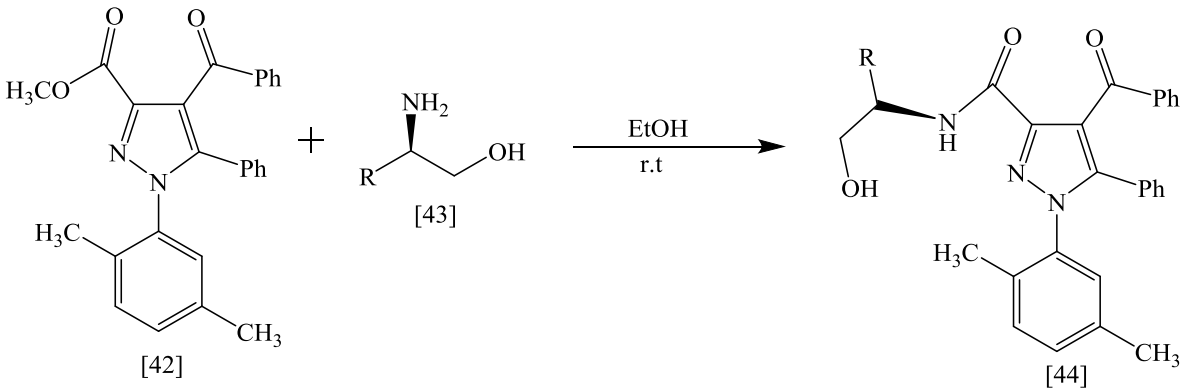
Furthermore[25], 3-Amino-5-hydroxy-4-phenylazo-1H-pyrazole [36] used as a material to synthesis of 2-chloro-N-(5-hydroxy-4-(phenyldiazenyl)-1H-pyrazol-3-yl)acetamide [38] as follows:



The fused pyrazole[26] ring with another hetrocyclic as in compound [41]were synthesized by cycloaddition reaction between 3-diazo-5-methyl-4-phenyl-3H-pyrazole[39] and 3-(diethylamino)acrylonitrile[40] in sodium acetat and ethanol .



Recently[27] , The chiral pyrazole-3-carboxamides [44] were synthesized via the reaction between pyrazole-3-carboxylate derivatives [42] and chiral amino alcohols [43] at room temperature.



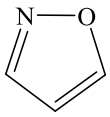
R=Ph, -CH(CH3)2 , -C2H5

1.2.1.3. Biological activity of Pyrazoles

Pyrazoles plays a crucial part in the development of theoretical studies and also useful to build blocks in organic field , with wide application as dyestuff, analytical reagents and agrochemicals . Pyrazole is a useful structural unit in the medicinal chemistry because its derivatives displayed various biological activities such as, analgesic , anti-inflammatory , antianxiety, antibacterial , antifungal , antitumour , antitubercular , and antiparasitic [28-32] .

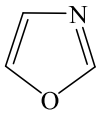
1.2.2 . Isoxazoles and oxazoles

Isoxazoles are unsaturated aromatic heterocyclic compounds containing a ring with three carbon atoms and two hetroatoms (oxygen and nitrogen) at 1,2-positiones[33] , respectively .



[45]

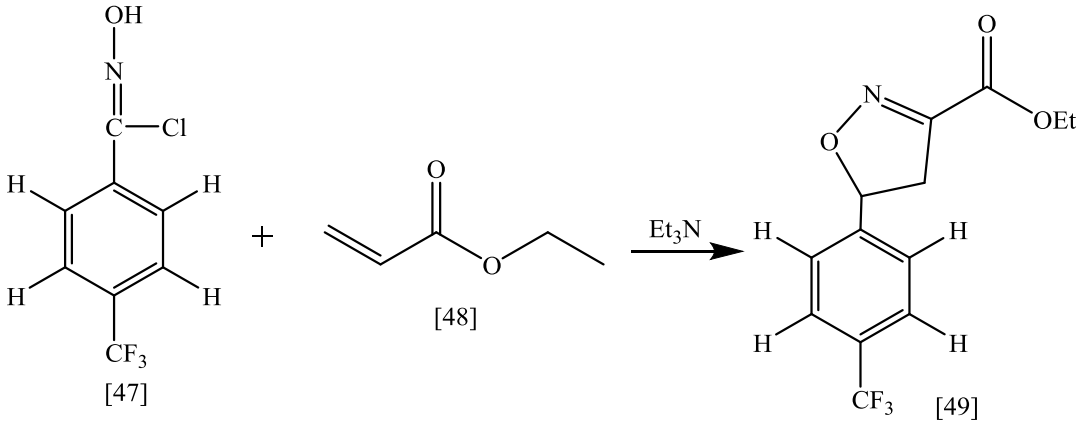
While the oxazoles are an important type of five-membered heterocyclic ring containing one oxygen and one nitrogen atom separated by one carbon in their structures[34]. The aromatic oxazole derivatives is relatively stable and is found widely in nature [1-3].



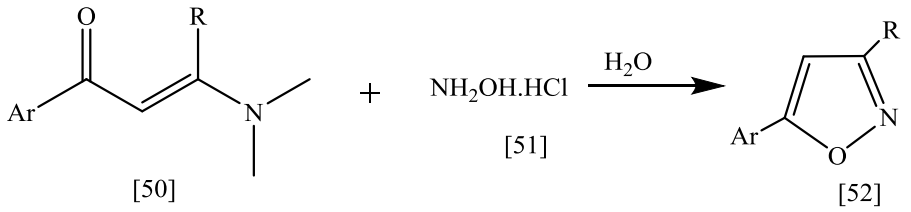
[46]

1.2.2.1. Synthesis of isoxazoles and oxazoles

In the presence of triethylamine[35], the reaction of ethyl acrylate[48] with compound [47] led to obtained 4,5-dihydroisoxazolinecarboxylates[49], the compound has antifungal activity.

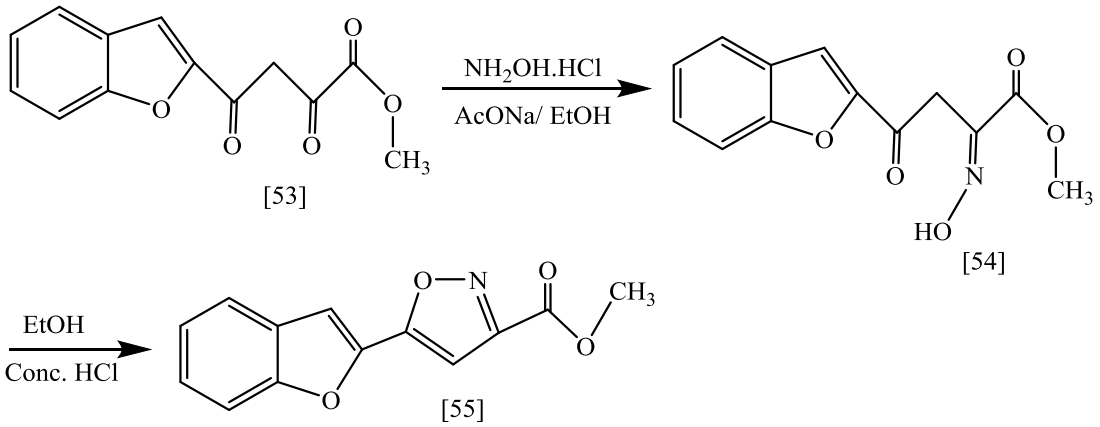


While, the reaction of 3-(dimethylamino)-1-arylprop-2-en-1-one derivative [50] and hydroxylamine hydrochloride[51] in aqueous media[36] led to give 5-arylisoxazole derivatives [52] .



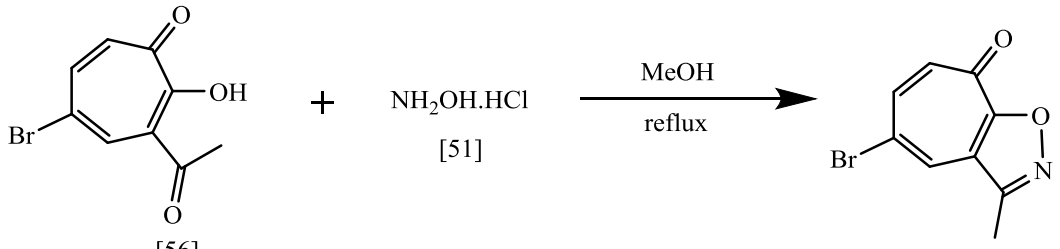
Ar=4-ClC_6H_4 , 4-$CH_3OC_6H_4$, C_6H_5 , 4-$CH_3OC_6H_4$
R=H, H, CH_3 , CH_3

On the other hand, the condensation of methyl 4-(benzofuran-2-yl)-2,4-dioxobutanoate [53] with hydroxyl amine hydrochloride [51]and sodium acetate in absolute ethanol formed methyl 4-(benzofuran-2-yl)-2-(hydroxyimino)- 4-oxobutanoate [54]. The later compound was heated in absolute ethanol and conc. HCl to get methyl 5(benzofuran-2-yl)-isoxazole-3-carboxylate [55], this compound has antimicrobial activity[37].



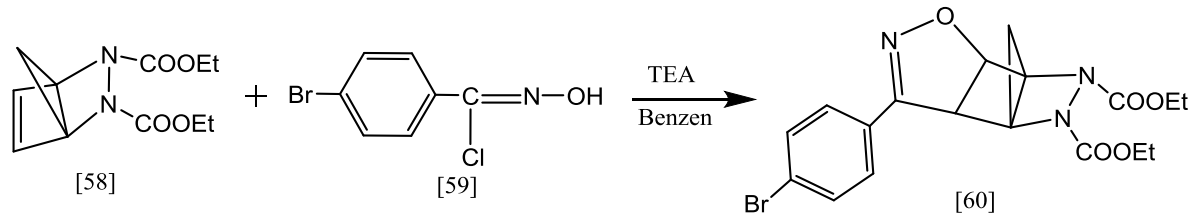
[53] [54] [55]

Also[38], the novel tropone –fused isoxazole [57] was synthesized from the reaction between hydroxyl amine hydrochlorid [51] and tropone[56] in methanol .



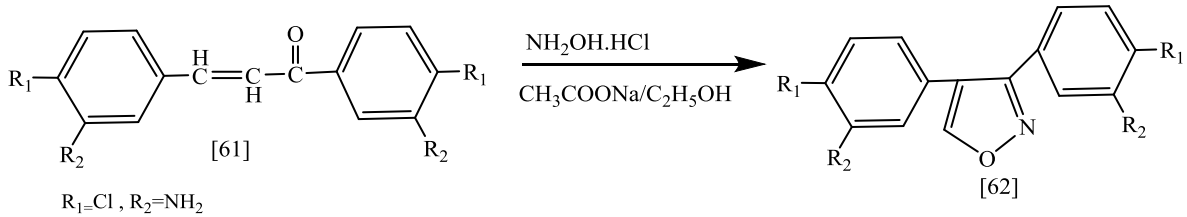
[56] [51] [57]

By using another reagents[39] and conditions a new isoxazole dervitive [60] was obtained as follows:



[58] [59] [60]

Joseph and George [40] were reported the synthesis of new isoxazoles [62] from cyclization reaction of chalcone[61] with hydroxyl amine hydrochloride [51] in basic medium .

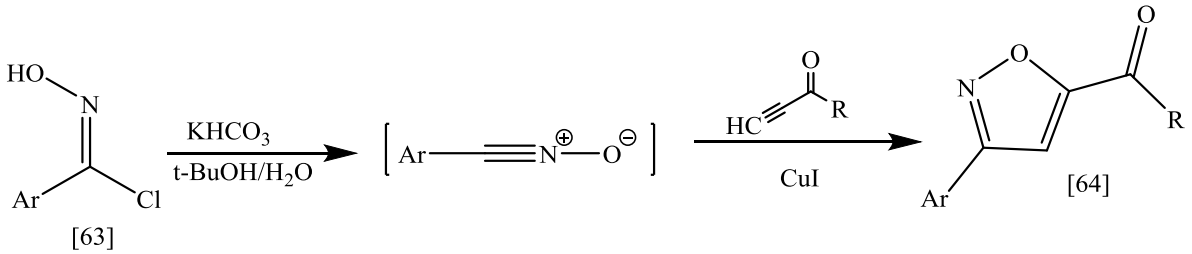


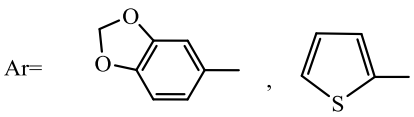
[61] [62]

R_1=Cl , R_2=NH_2

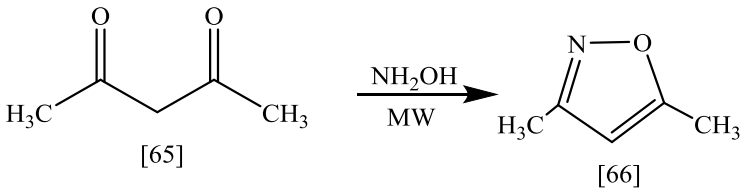
R_1=Br , R_2=NO_2

Furthermore, Oancea et al ., [41] used catalytic amounts of copper(I) iodide for preparation a new isoxazoles [64] from non-symmetrical activated alkynes [63] .



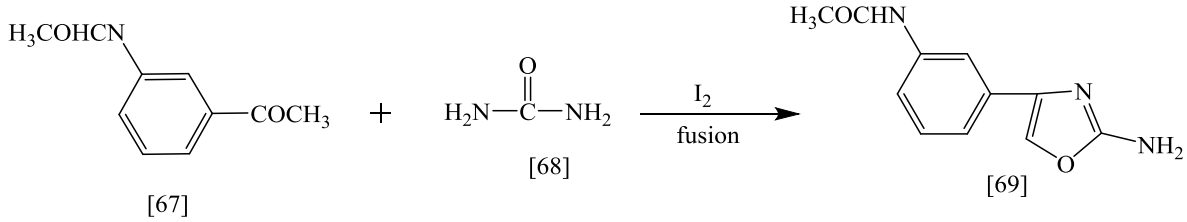


Finally, the cyclization reaction[42]of β-dicarbonyl compound[65]with hydroxylamine [51]under microwave irradiation (MW) led to form the 3,5-dimethyl isoxazole [66] .

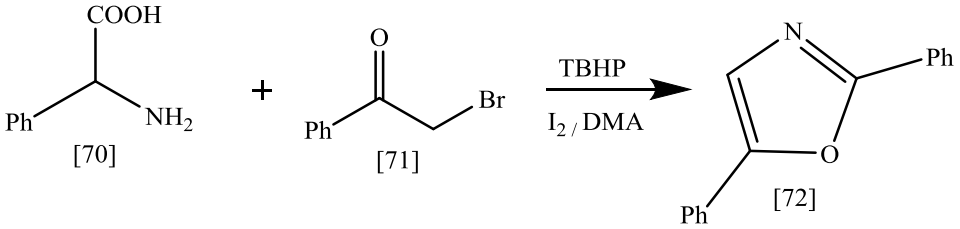


On the other hand, the synthesis of oxazoles include the following methods:

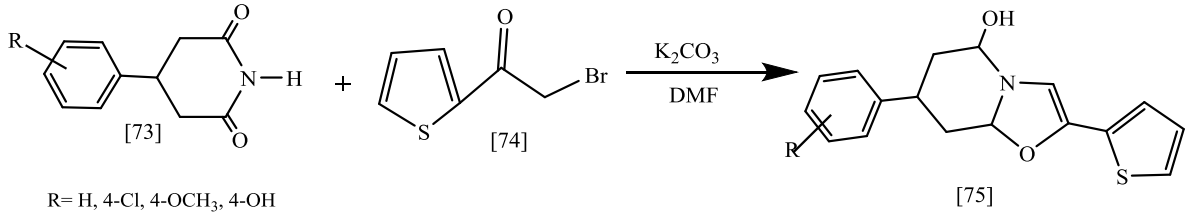
The 2-aminooxazole derivatives[69]was synthesized[43] by the reaction of 3-acetamidoacetphenone [67]with urea[68] using iodine (I_2) as a catalyst .



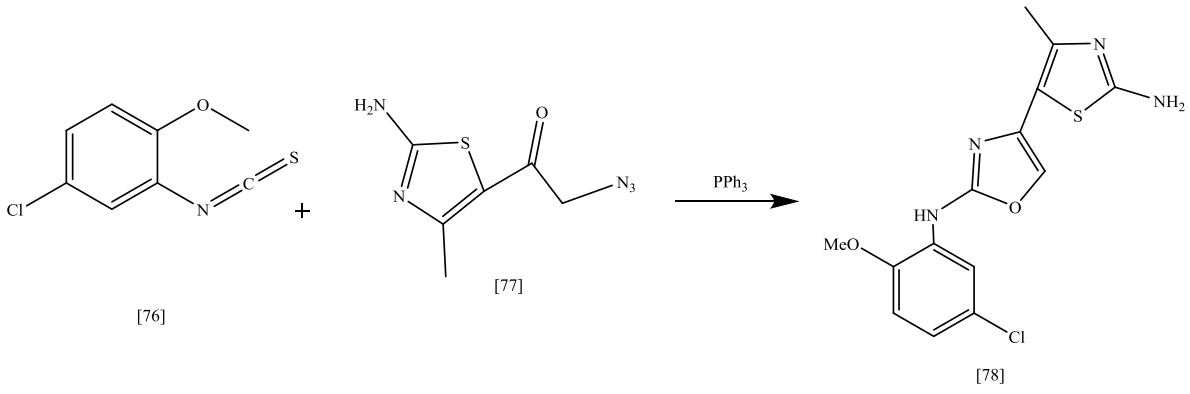
By using a primary α-amino acids phenylglycine[70]with 2-bromoacetophenone[71]in tert-butyl hydroperoxide (TBHP) as the oxidant and iodine as a catalyst, the 2,5-diphenyl oxazole [72]was synthesized [(44)].



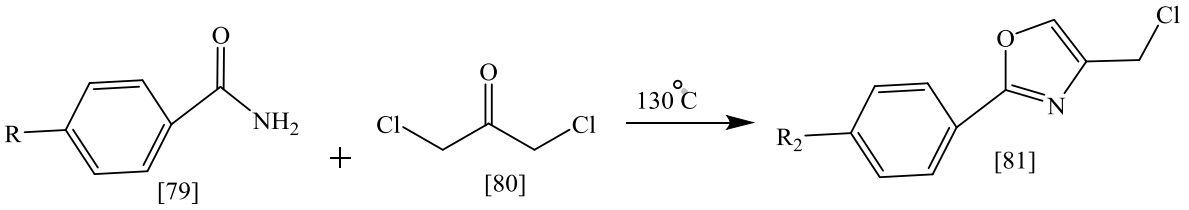
While, the heated a mixture of 4-subsutiuted -piperidine-4,6-dione[73], K_2CO_3, α- Bromoacetothiophenone[74]and DMF led to formation7-(4-Methoxy phenyl)-2-thiophene-2-yl-7H-oxazolo[3,2-a]pyridine-5-ol[75],these compounds have antibacterial and antifungal activities[(45)].



The condensation[(46)] of 4-chloro-2-isothiocyanato-1-methoxybenzene [76] with 1-(2-amino-4-methylthiazol-5-yl)-2-azidoethan-1-one [77] led to get new compounds containing oxazole ring adjacent to thiazole ring [78] .

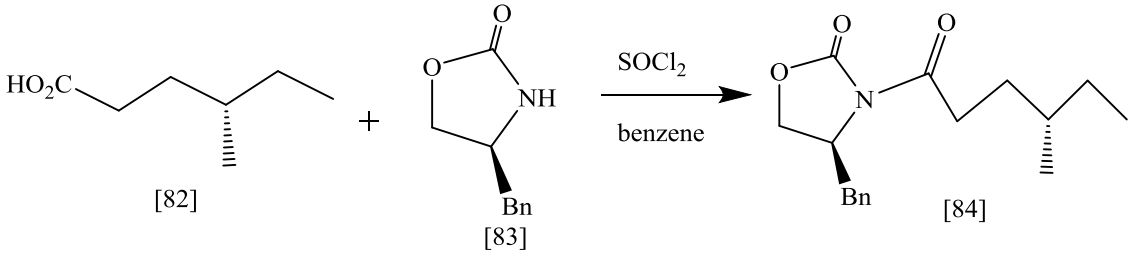


Wang et al., [(47)] were reported the treatment of 4-substituted benzamide [79] with 1,3-dichloropropanone [80] to produce 4-chloromethyl- 2-aryloxazole[81].

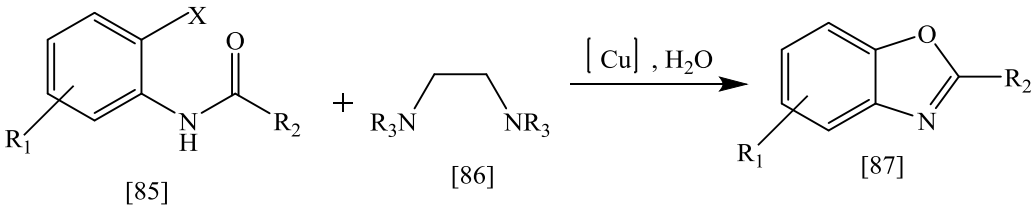


R=4-F, 4-Cl, 4-Cl_2

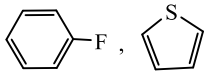
Tilvi and Singha[48], were condensed carboxylic acid [82] with (S)-4 benzyloxazolidin -2-one[83]to give (S)-4-benzyl-3-((S)-4-methylhexanoyl) oxazolidin-2-one[84] by using $SOCl_2$ in benzene.



In addition[49], the Copper catalyst was used to oxidative cycliztion of compound [85] with diamines [86] to form oxazole dervitives [87] .



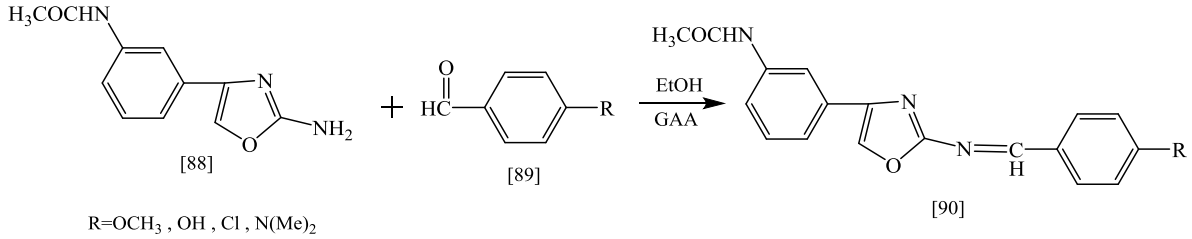
R_1= H, Me, F_3 CO

R_2= Ph ,  ,

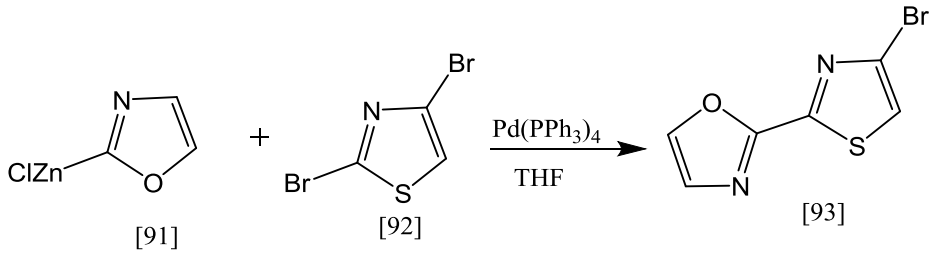
R_3=H, Me

1.2.2.2. Reaction of oxazoles and their derivatives

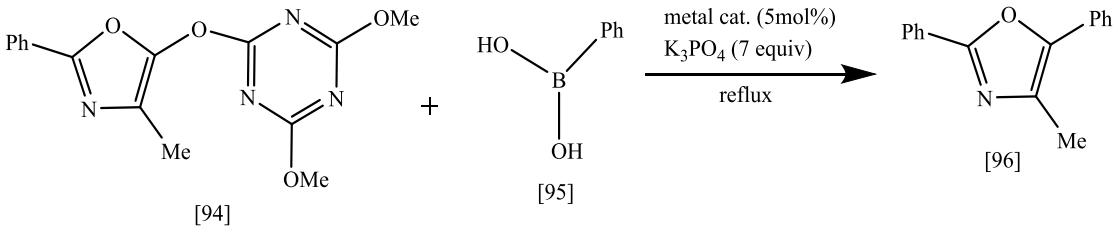
The reaction [43]of 2-aminoxazole derivatives [88] with aromatic aldehyde [89] in glacial acetic acid (GAA) and ethanol to give new Schiff bases [90] .



oxazol-2-ylzinc(II) chloride [91] was reacted in cross-coupling reaction [50] with 2,4-dibromothiazole [92] to yield 2-(4-bromothiazol-2-yl)oxazole[93]



By using the reaction[51] conditions of Suzuki–Miyaura coupling, 5-(triazinyloxy) oxazole [94]was reacted with phenylboronic acid [95] to produce oxazole derivative [96] .



1.2.2.3. Biological activity of isoxazoles and oxazoles

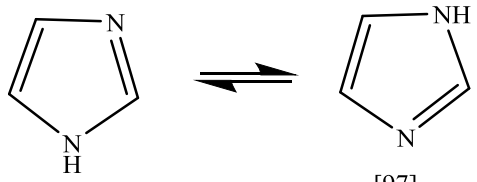
Isoxazole derivatives are an important class of heterocyclic pharmaceuticals and bioactive natural products because of their significant and wide spectrum of biological activities, including potent and selective antagonism of the NMDA receptor(N-methyl-D-aspartate receptor) [52] and anti-HIV activity [53-55]. Isoxazole compounds show antiviral

[56,57],antithrombotic [58,59], analgesic [60], COX-2 inhibitory [61],anti-inflamatory [62], antinociceptive [63] and anticancer [64]activities.

1,3-Oxazoles were found as a subunit of many biologically activity and synthetic intermediates which were leading to many other systems. A large number of oxazole compounds as candidates[65] or clinical drugs[66] or frequently employed for the treatment of various types of diseases[67], large development value and wide potential as medicinal agents[68].Oxazole compounds showed antibacterial [69],antifungal ,antiviral, antitubercular , anticancer, anti-inflammatory and analgesic, antidiabetic, antiparasitic, anti-obesitic, anti-neuropathic, anti oxidative as well as other biological activities[70-73].

1.2.3. Imidazoles

Imidazole (1,3-diaza-2,4-cyclopentadiene)[97]$_{a,b}$ with molecular formula $C_3H_4N_2$ is a planner five [74]. Five-membered ring system with three carbon and two nitrogen atoms at 1 and 3 positions. The systemic is aromatic and the name for the compound is 1,3-diazole, one of the annular N bear a H atom and can be regarded as a pyrole type N. It is, more basic than pyridine and less basic than ammonia[75].



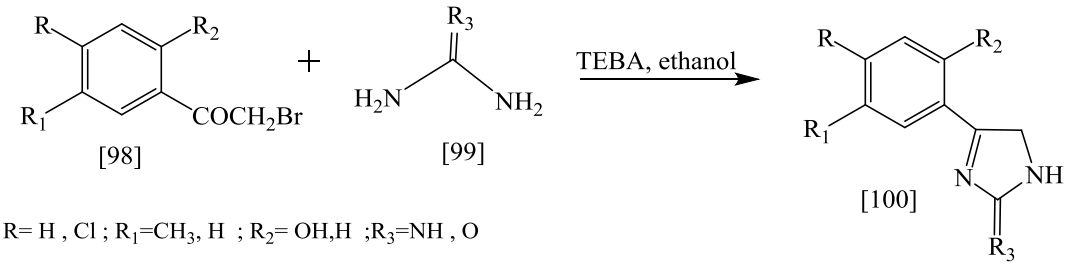
[97]$_a$ [97]$_b$

1.2.3.1. Synthesis of Imidazoles

There are many methods for synthesis imidazoles among of them :

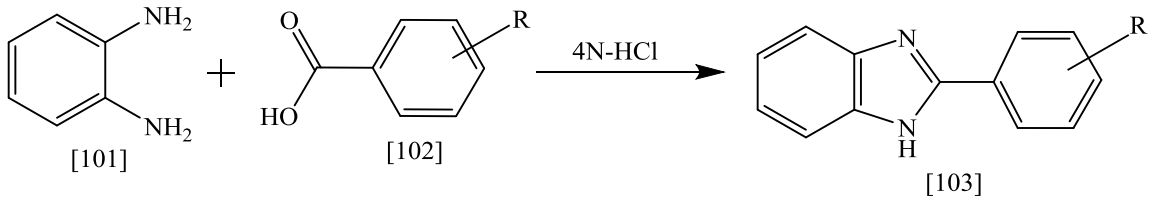
Dandale and Solanki[76], synthesized new 4-(substituted phenyl)-1H-imidazol-2(5H)-one[100] from the reaction of 2-bromo-1- (substituted phenyl)

ethanone[98] and compound [99] in triethylbenzylammonium chloride(TEBA) and ethanol .



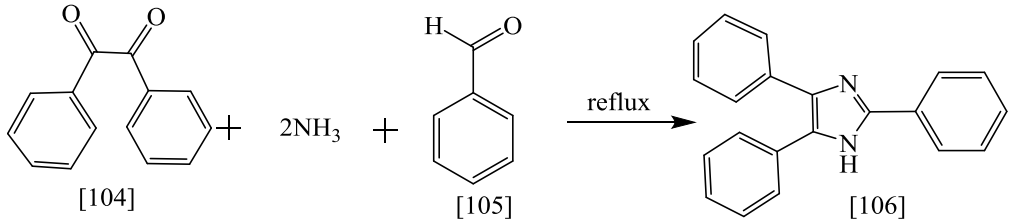
R= H , Cl ; R_1=CH_3, H ; R_2= OH,H ;R_3=NH , O

While[77], the refluxe of o-phenylenediamine [101]with derivatives of benzoic acids[102] in presence of 4N- HCl gave new imidazoles substituted 2-phenyl benzimidazoles[103]. These compound have antibacterial activity.

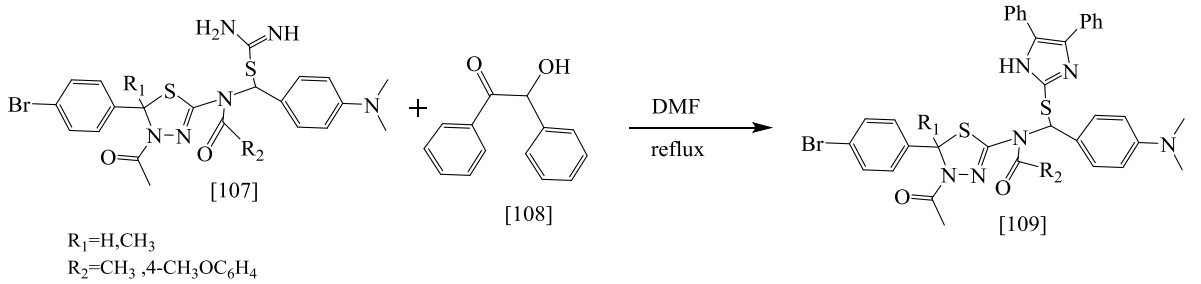


R=4-Cl, 4-NH_2 , 2-NO_2 , 3-OCH_3

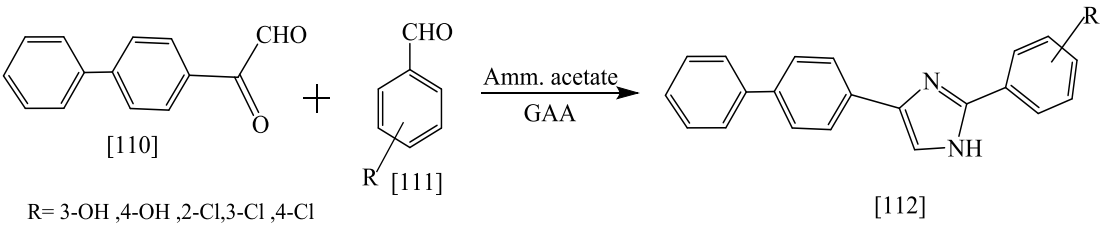
Furthermore, the condensation[78] of benzil [104]with benzaldehyde [105] in the presence of ammonia yielded 2, 4, 5- triphenylimidazole[106] .



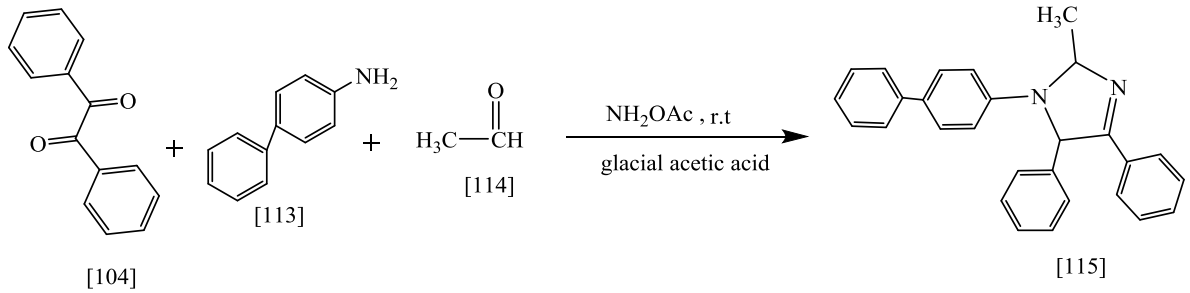
From the reaction[79] of N-thiourea compounds[107] with benzoin[108] in DMF gave imidazole dervatives [109].



When[80] Biphenyl-2-oxoacetaldehyde[110] reacted with different aromatic aldehyde[111] in presence of ammonium acetate and glacial acetic acid(GAA) led to obtained 4-(Biphenyl-4-yl)-2-(substituted phenyl)-1H-imidazole [112].These compound have antibacterial activity .



Furthermore[81], 1-([1,1'-biphenyl]-4-yl)-2-methyl-4,5-diphe-nyl-1H-imidazole[115] was synthesized from the reaction of benzil[104], α-naphthylamine[113] and actaldehyde[114] at room temperature in glacial acetic acid, and ammonium acetate .The compound have antibacterial activity.



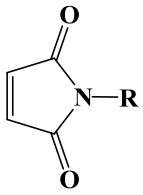
1.2.3.2. Biological activity imidazoles

Imidazoles play an important role in medicinal chemistry, because many of its derivatives have demonstrated significant biological activity[82-84].

1.2.4.Imides

In general imides are organic compounds containing the moiety (-CONHCO-) .They may be considered as N-mono acyl derivative of amides or as N,N′ -diacyl derivative of ammonia, and classified into two main types[85]:-

1- cyclic imides such as maleimide[116],phthalimide [117]and glutarimide[118] [86] .



[116]

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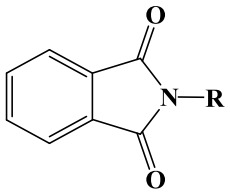

[117]

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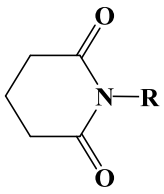
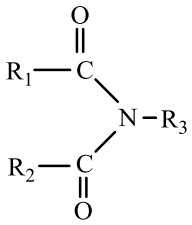


[118]

2-open chain imides, such as compound [119]

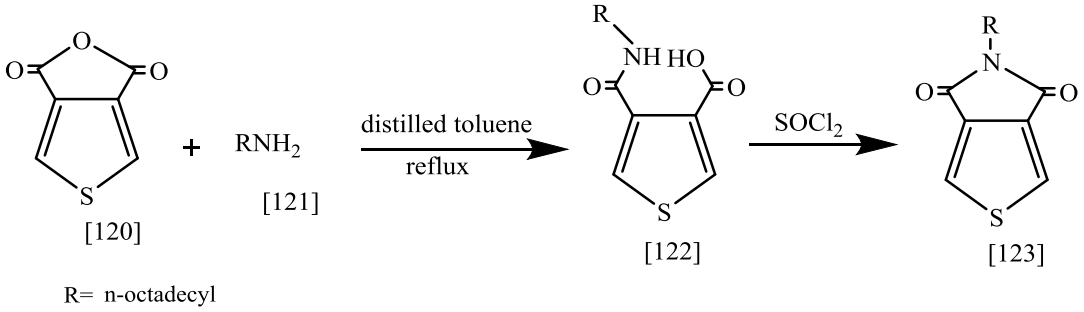


[119]

(R_1, R_2,R_3=Alkyl and aryl group)

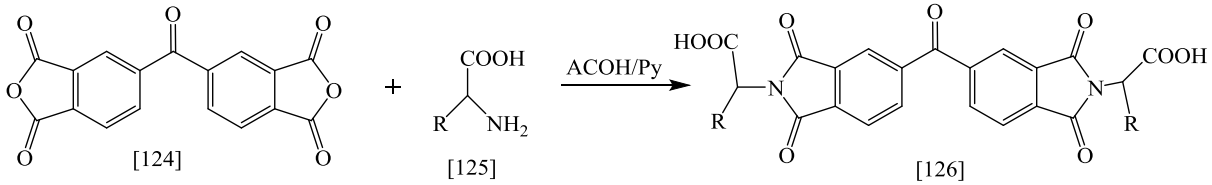
1.2.4.1. Synthesis of Imides

When[87] the thiophene-3,4-dicarboxylic anhydride[120] was refluxed by amine n-octadecylamine[121] in toluene obtain amic acid [122],which is converted to new imides [123] in $SOCl_2$.



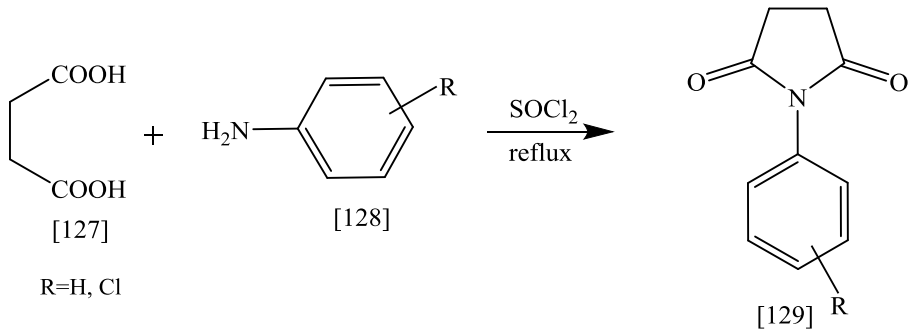
R= n-octadecyl

Almahy et al.,[88] were reacted 5,5'-carbonylbis (isobenzofuran-1,3-dione)[124]with amino acids[125] in acetic acid ,pyridine solution led to obtain new imides compounds [126].



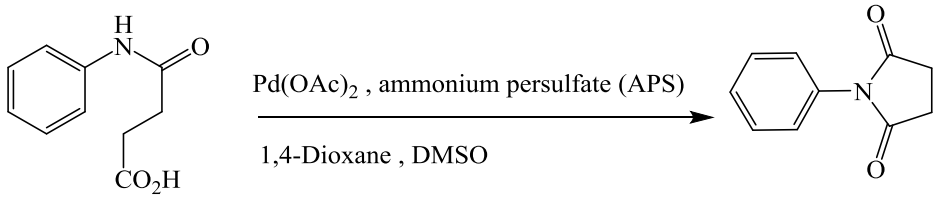
R= CH_3 ,$CH(CH_3)_2$, $CH_2CH(CH_3)_2$

The synthesis of 1-substituted phenyl pyrrolidine-2,5-dione[129]was reported by condensation[89] of succinic acid [127] with primary aromatic amine [128] using $SOCl_2$ under reflux.



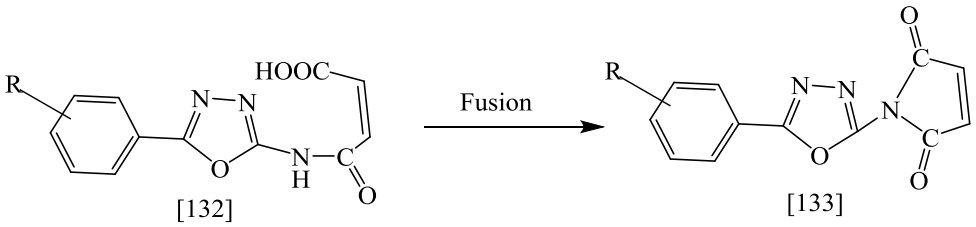
R=H, Cl

By using $Pd(OAc)_2$ and [90] ammonium persulfate (APS) in dioxane and DMSO, anew imide was synthesized [131] .



[130] [131]

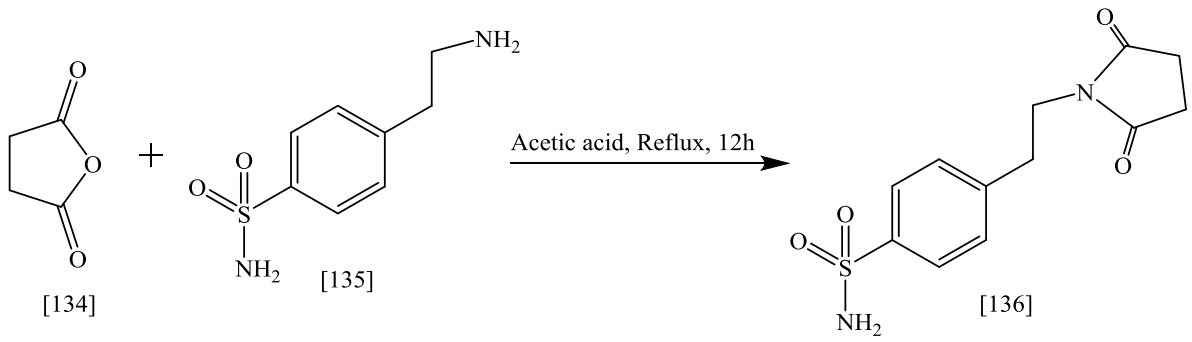
N-[5-substituted-1,3,4-oxadiazole-2-yl]maleimides[133] were prepared by applying fusion method, which involved fusion of the maleamic acids [132]in oil bath for one hour[91].



[132] [133]

R = 4-OH, 2-OH, H, 4-CH_3, 4-OCH_3

Also in the presence of acetic acid, the reaction[92]of dihydrofuran-2,5 dione [134] with 4-(2-aminoethyl) benzenesulfonamide [135] led to give 4-(2-(2,5-dioxopyrrolidin-1-yl)ethyl)benzenesulfonamide [136].



[134] [135] [136]

1.2.3.2.Biological activity of Imides

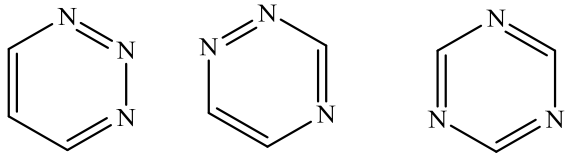
Imides possess an excellent mechanical properties , thermal stability and important class of bioactive molecules that show a wide range of pharmacological activities [93] .These derivatives are used as androgen receptor

antagonistic [94], anti-inflammatory[95] , anxiolytic [96], antiviral[97], antibacterial[98] and antitumor properties[99].

1.3. Six member hetrocyclic ring

1.3.1.Triazine

Triazines $[137]_{a,b,c}$ are the six membered heterocyclic compounds possessing three nitrogen in their structures[100] with general formula $C_3H_3N_3$.



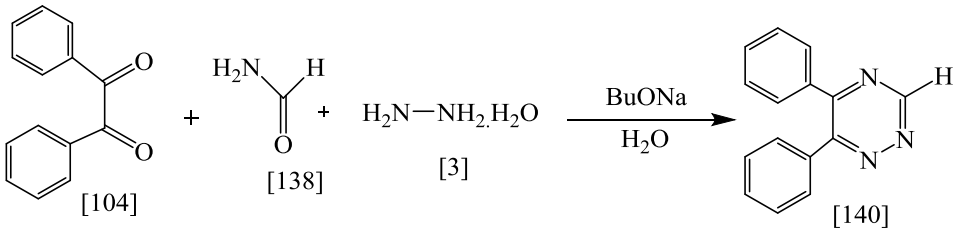
1,2,3-triazine $[137]_a$ 1,2,4-triazine $[137]_b$ 1,3,5-triazine $[137]_c$

The triazine structure is a heterocyclic ring, analogous to the six-membered benzene ring but with three carbons replaced by nitrogens. Triazine has three isomers related to the positions of their nitrogen atoms, and are referred to 1,2,3-triazine$[137]_a$, 1,2,4-triazine $[137]_b$ and 1,3,5-triazine$[137]_c$ [101-104].

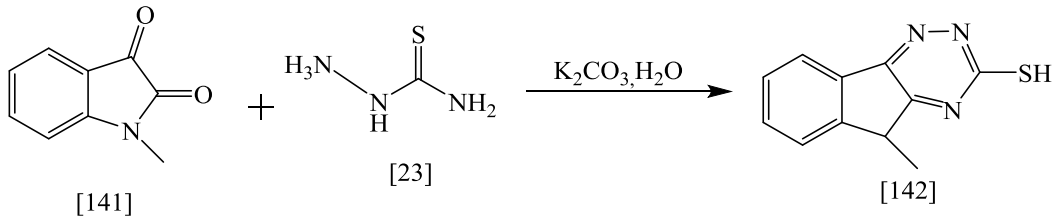
1.3.1.1.Synthesis of Triazine

The triazine derivatives were synthesized by many methods were mentioned in the literature as example in the following :

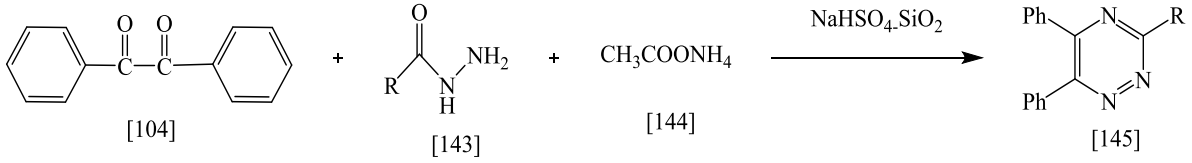
Phucho et al., [105] synthesized 5,6-diphenyl-1,2,4-triazine [140] from the reaction of 1,2-dicarbonyl compound [138] with amide [139] and hydrazine hydrate[3] in the presence of BuONa[139].



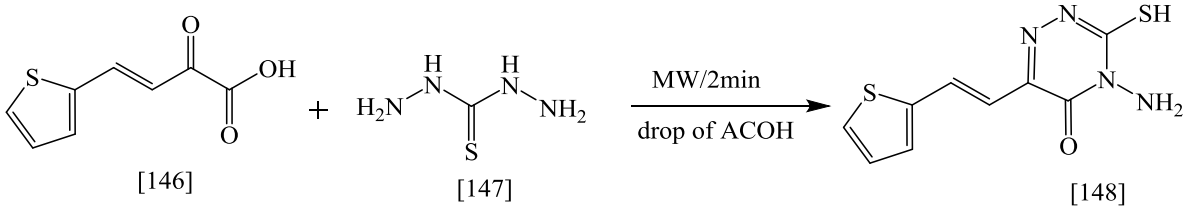
While, L.Gupta et al., [106] synthesized new fused triazines derivetive [142] by the reaction of 1-methyl istain[141] with thiosemicarbazide[23] using $K_2CO_3.H_2O$.



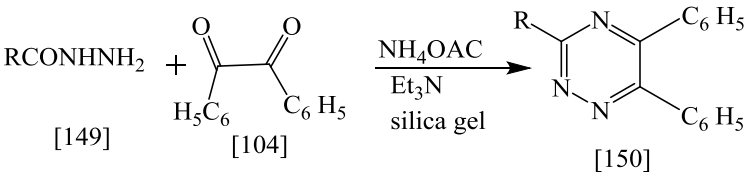
On the other hand , 5,6-diphenyl-1,2,4-triazines[145]was obtained from the coupling of benzil[104], with acid hydrazides [143] and ammonium acetate[144] using $NaHSO_4/SiO_2$ as a solid support [107].



By using microwave method, Saad et al .,[108] reported the synthesis of new trazine derivatives [148]by the ring closure reaction of 2-oxo-4-(thiophen-2-yl)but-3-enoic acid [146] with hydrazinecarbothiohydrazide [147] in acetic acid .This compound has activity against cancer cell.

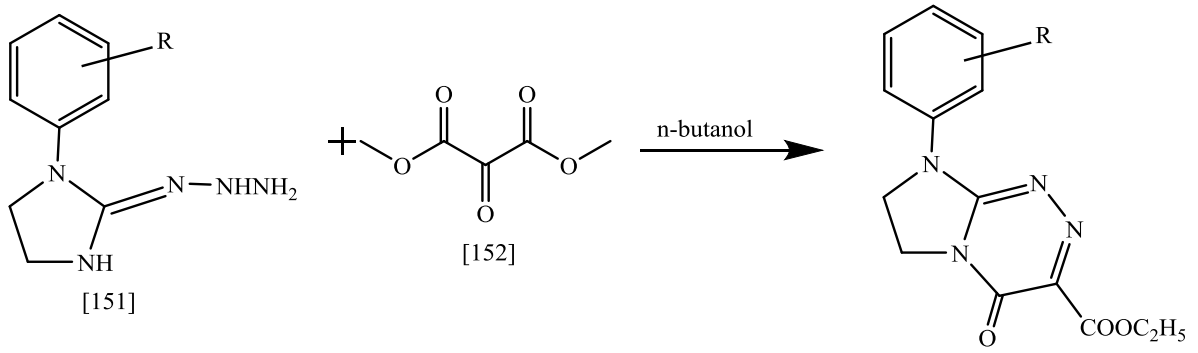


The traizines [150] derived from fatty[109] acid derivatives were synthesized as follows: These compounds have antibacterial activity .



R=Oleic ,Linoleic, Linolenic

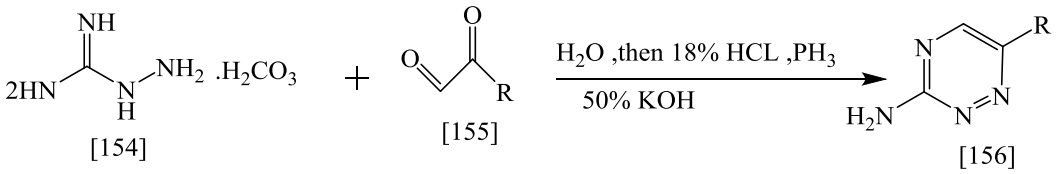
Arshad et al.,[110] synthesized ethyl 4-oxo-8-(substituted)-4,6,7,8-tetrahydroimidazo[2,1-c][1,2,4]triazine-3-carboxylate[153] from condensation reaction of 3-(1-(substuted)imidazolidin-2-ylidene)hydrazine [151] with dimethyl-2-oxomalonate [152] in n-butanol .



R= H, 4- Me, 4-MeO, 3-Cl, 3.4-Cl

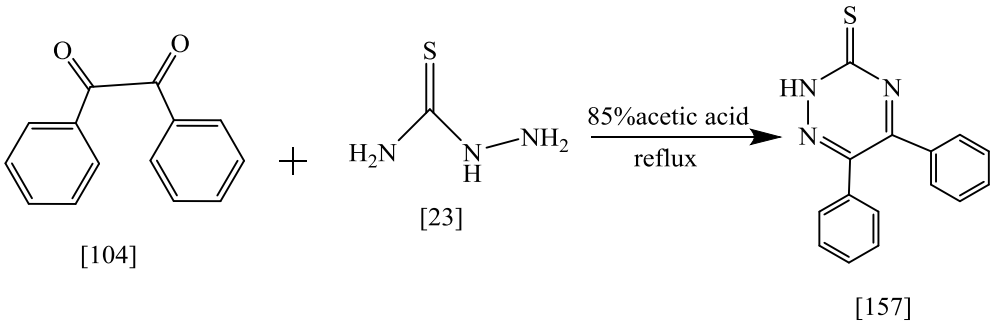
[153]

Horner et al., [111] were synthesized new 6-substituted 3-amino-1,2,4-triazines[156] by reaction between hydrazinecarboxymidamide[154]and compounds [155] in suitable conditions .



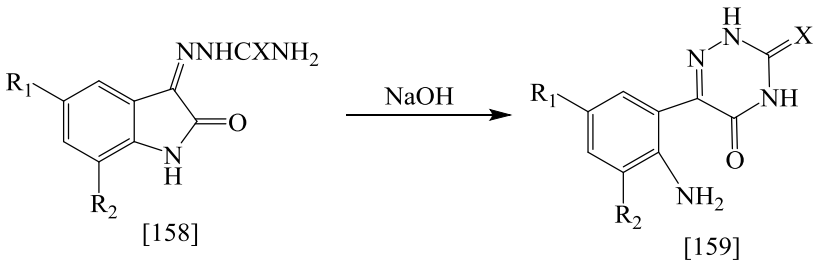
R=H ,Me ,Ph

Also, Arshad et al., [112] synthesized the triazines [157] from the reaction of benzil [104] and thiosemicrbazid [23] in 85% acetic acid .



[104] [23] [157]

A new type of triazines; 6-(2-amino-3,5-substituted phenyl)-1,2,4 triazine derivatives[159]were synthesized by kumar et al., [113] these compounds have anticancer activity and antimicrobial activity .



[158] [159]

X=O, S
R1=H, F, Cl, Br
R2=H, Br

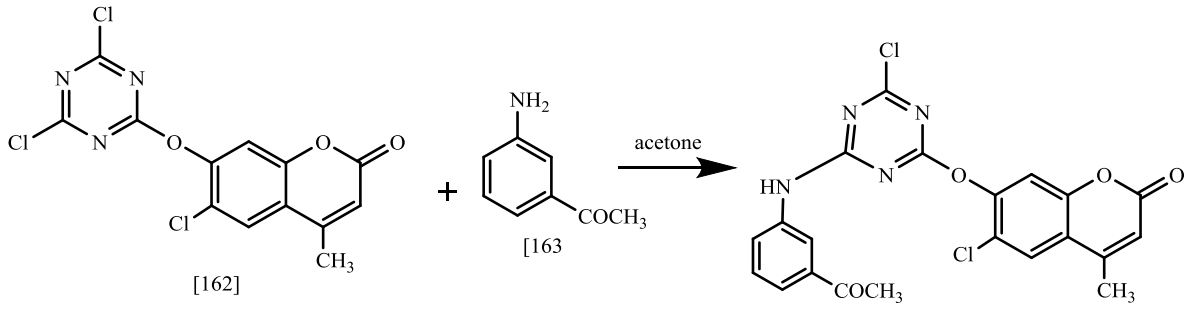
1.3.1.2. Reactions of 1,2 ,4-Triazines

4-amino-7-methyl-8-phenylpyrazolo[5,1-c][triazine-3-carbothio amide [160] was treated with α –haloketones[71] in hot DMF [114] gave the Hantzsch-type thiazoles[161].

[160] [71] [161]

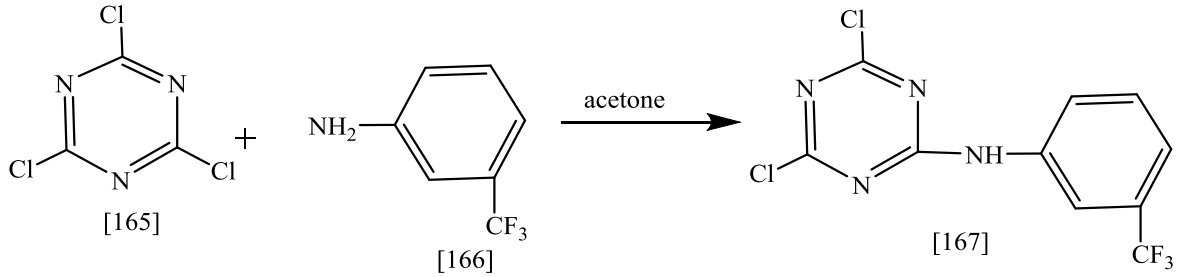
R=CH3
Ar= C6H5

While, the reaction of 2- [4'- methyl - 6' - chloro -2*H*- chromen -2' -one-7'-oxy] - 4,6 -dichloro -s - triazine [162] with 1-(3-aminophenyl)ethan-1-one [163] in acetone led to give 2- [4'- methyl - 6' - chloro-2*H*- chromen -2' -one-7'-oxy] - 4 - (3' - acetyl aminophenyl) - 6 - chloro -s – triazine[164] [115].



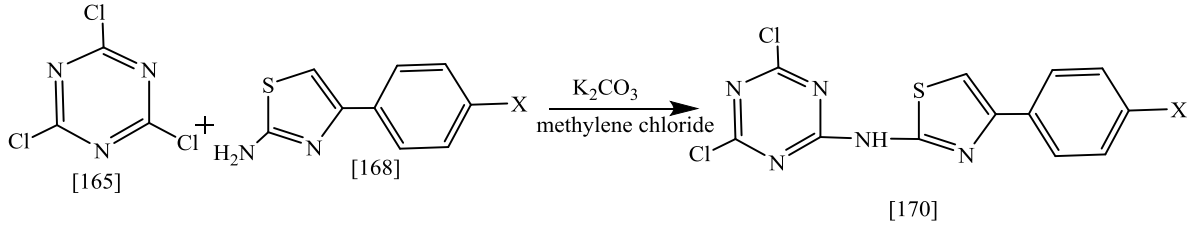
[162] [163] [164]

Solankee and Tailar[116] were reacted the 2,4,6-trichloro-1,3,5-triazine[165] with 3-trifluro- methyl anline [166] in acetone to get 2-(3-trifluromethylphenylamino)-4,6-dichloro- 1, 3, 5-triazine [167] .The compound has antitubercular activity .



[165] [166] [167]

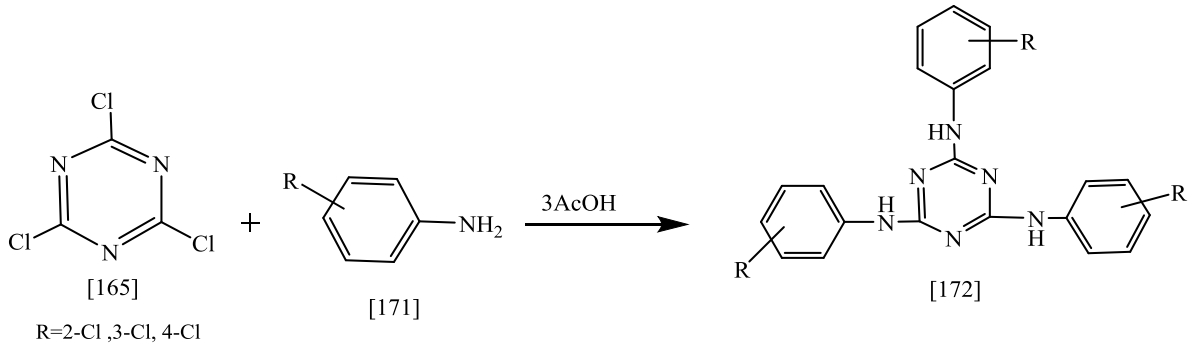
Also Balaha et al., [117] have been reacted the reaction of 2,4,6-trichloro-1,3,5-triazine [165] with 4-(4-substituted phenyl)thiazol-2-amine[168] in methyline chloride [169] gave N-(4,6-dichloro-1,3,5-triazin-2-yl)-4-(4 subsutituted phenyl) thiazol-2-amine[170].



[165] [168] [170]

X=H ,Cl, OCH_3, CH_3, NO_2

In addition[118], 2,4,6-trichloro-1,3,5-triazine[166] reacted with different substituted anilines[171]in acetic acid to give 2,4,6-tri substituted 1,3,5-triazine[172] .

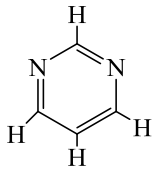


1.3.1.3.Biological activity of traizines

Triazines and its derivatives exhibited the variety of biological applications such as antifungal [119], anti-HIV[120], antiparasitic[121], anticancer[123] , anti-inflammatory[124], antiviral[125], antimicrobial[126], antimalarial[127] , besides this, triazines were used as herbicides, pesticides and dyes[128].

1.3.2.Pyrimidine

Pyrimidines [173] are six membered aromatic ring with one of the heterocyclic compounds, their structure composes of two nitrogen atoms at position 1 and 3



[173]

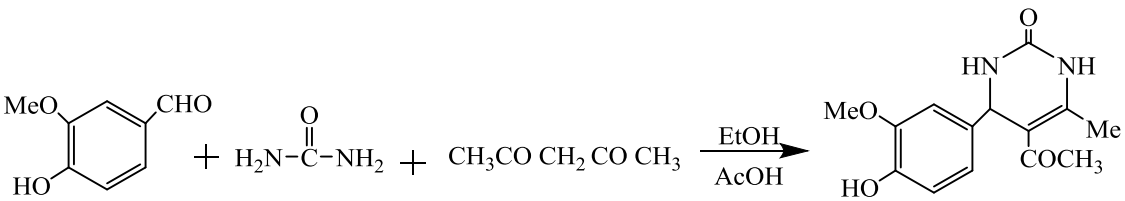
Pyrimidines were subjected as a large number of different modifications in order to obtain new derivatives having different biological properties. Many workers have studied the chemistry and pharmacological properties of pyrimidine derivatives .[129]

The origin of the pyrimidine term dates back to 1884 when Pinner coined the term from a combination of the words pyridine and amidine because of the structural similarity to compound [173].

Since these initial investigations hundreds of pyrimidine compounds have been found in biochemistry. The numerous modifications upon this scaffold and its relative importance in nature make it an interesting area of study.[130]

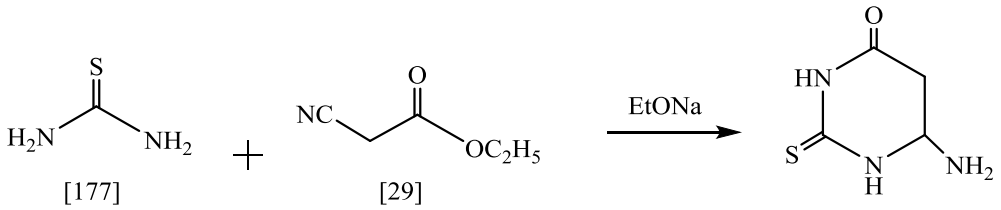
1.3.2.1.Synthesis of Pyrimidines

Tawfik et al., [131] prepared pyrimidine compound[176] by the reaction between 4-hydroxy -3-methoxy benzaldehyde[174],urea[68] and acetylacetone [175]in ethanol and acetic acid.

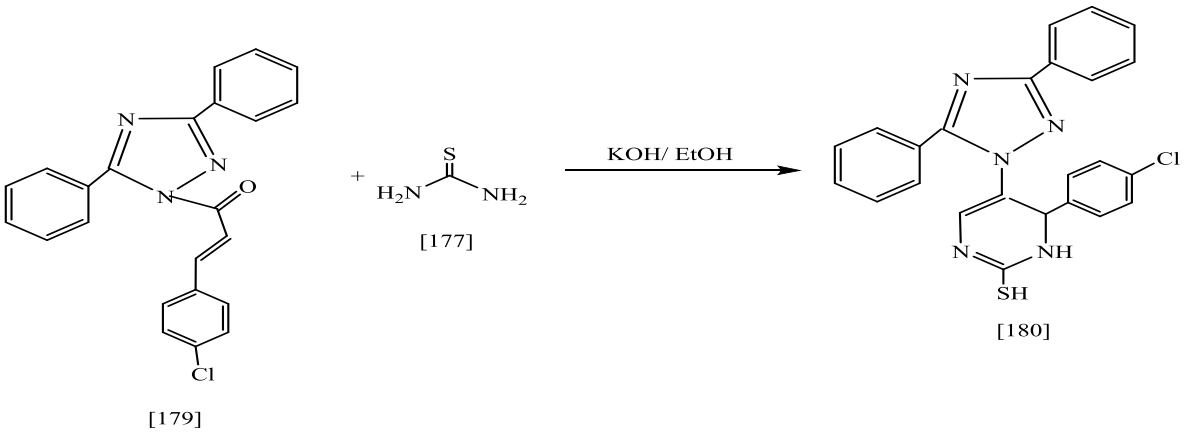


[174] [68] [175] [176]

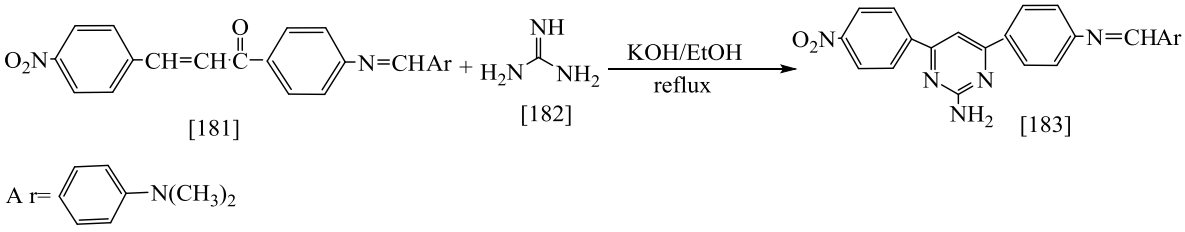
While, Mohamed et al.,[132] prepared pyrimidine [178] by the condensation of thiourea [177]with ethylcyanoacetate[29]in sodium ethoxide. The compound have antimicrobial activity .



Also, Khanage et al .,[133] synthesized 6-(4-chloro phenyl)-5-(3,5-diphenyl-1H-1,2,4-triazol-1-yl)-1,6-dihydropyrimidine-2-thiol [180] from the reaction of chalcones [179] with thiourea [177] in the presence of KOH and ethanol as a solvent. This compound has anticancer cell.

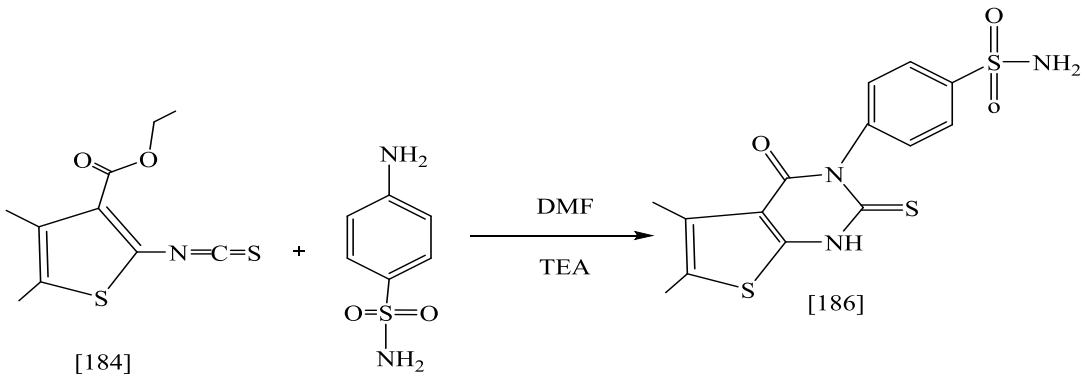


In addition, Mohsin [134] have been obtained new Pyrimidines [183] from refluxed of chalcones [181] with guanedin [182] in absolute ethanol and potassium hydroxide.



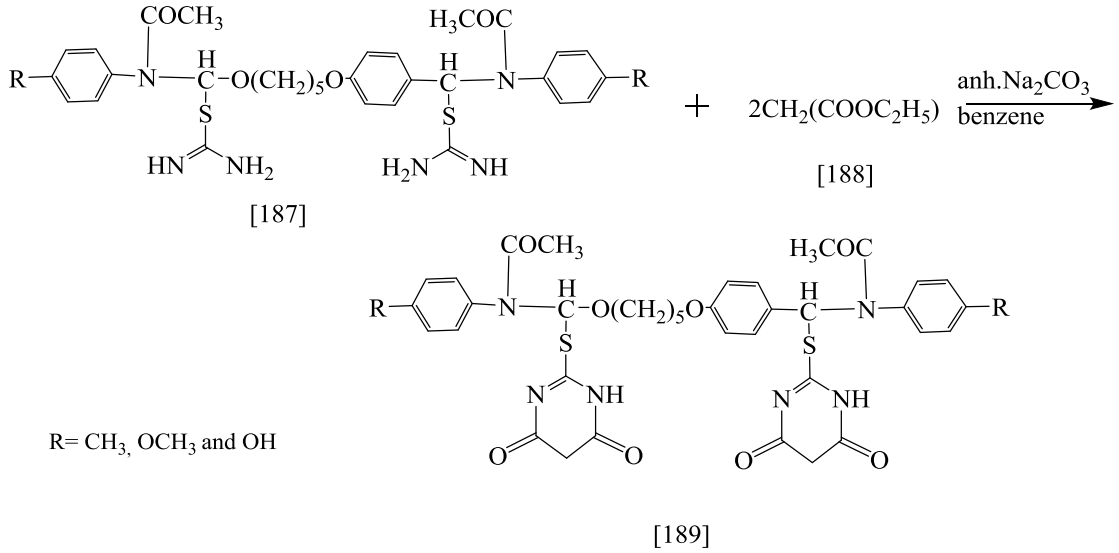
Ghorab et al., [135] were synthesized fused pyrimidine as ; 4-(5, 6-dimethyl-4-oxo-2-thioxo-1, 2-dihydrothieno[2, 3-d] pyrimidin-3(4H) yl) benzenesulfonamide [186], by the reaction of 2-isothiocyanato-4, 5-dimethyl thiophene-3- carboxylate [184] and 4-aminobenzenesulfonamide [185] in the

presence of triethylamine (TEA) and dimethyl formamide (DMF).This compound have anticancer activity .



[184] [185] [186]

Recently[136], new pyrimidine derivatives[189] were synthesized from reaction of N –thiourea compound [187] with diethylmalonate[188]in Na_2CO_3 benzene.



[187] [188] [189]

1.3.2.2. Biological activity of pyrimidine

Pyrimidine derivatives attract great interest due to the wide variety of biological activities observed for these compounds, such as anticancer, antiviral ,antitumor , anti-inflammatory and antimicrobial activities [137].

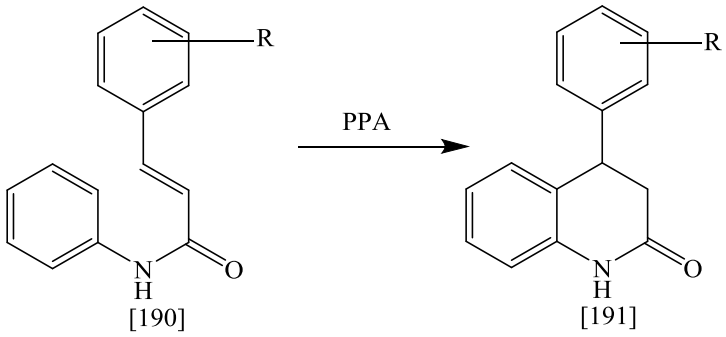
They are present throughout nature in various forms and are the building blocks of numerous natural[(138)] compounds from antibiotics to vitamins and liposacharides. The most commonly recognized pyrimidines are the bases of RNA and DNA [(139)], the most abundant being cytosine,thymine or uracil.

1.3.3. Quinoline

Quinoline or 1-aza-napthalene or benzo pyridine is one of the most nitrogen containing heterocyclic compound which have many of applications in medicinal, bioorganic, industrial as well as in the fields of synthetic organic chemistry . Quinoline ring structure is obtained by condensation of benzene ring with pyridine. Quinoline is aromatic compound and has a resonance energy of 47.3 K.cal/mol, and is weakly basic.[(140)]

1.3.3.1. Synthesis of quinoline

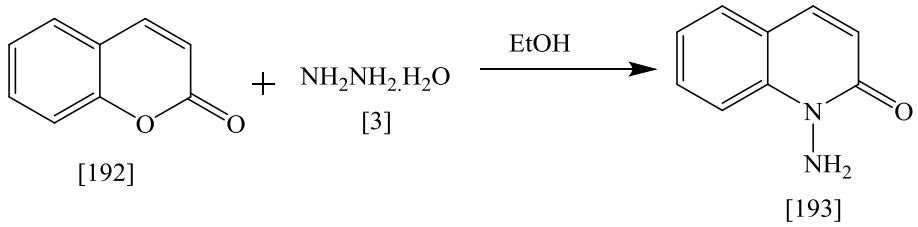
Guan et al., [(141)] were synthesized compounds [191] from a ring closure reaction of 3-substituted-phenyl-*N*-phenylacrylamide[190] by using polyphosphoric acid. These compounds have anticonvulsant activity.



[190] [191]

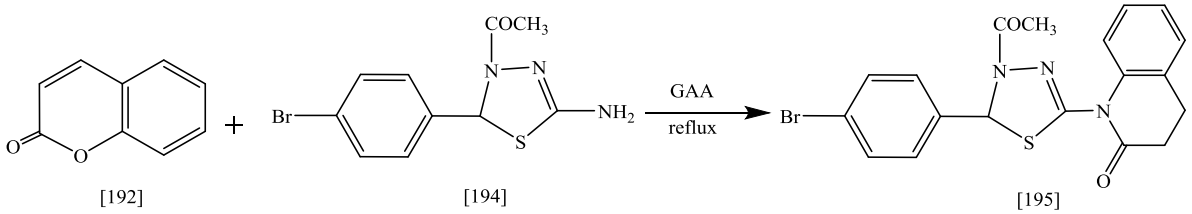
R=H , p-CH -, p-Cl ,p-F , p-OCH_3 , m-F

While,[(142)] N-amino quinoline-2-one[193] was obtained from coumarin[192] with excess of hydrazine hydrate (99%) [3] in absolute ethanol.



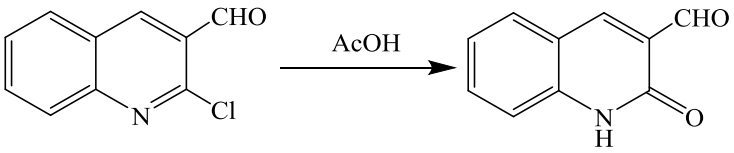
[192] [193]

Also, coumarin[192] was converted to the new quinoline compounds [195] by its condensation with amino derivatives in glacial acetic acid [(79)].



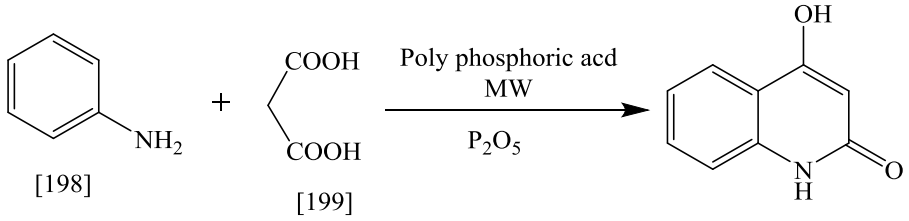
[192] [194] [195]

On the other hand, 2-Chloro-3-formylquinoline [196]was converted to 2-oxo-1,2-dihydroquinoline-3-carbaldehyde[197] by hydrolysis of the –Cl group in acetic acid [(143)].



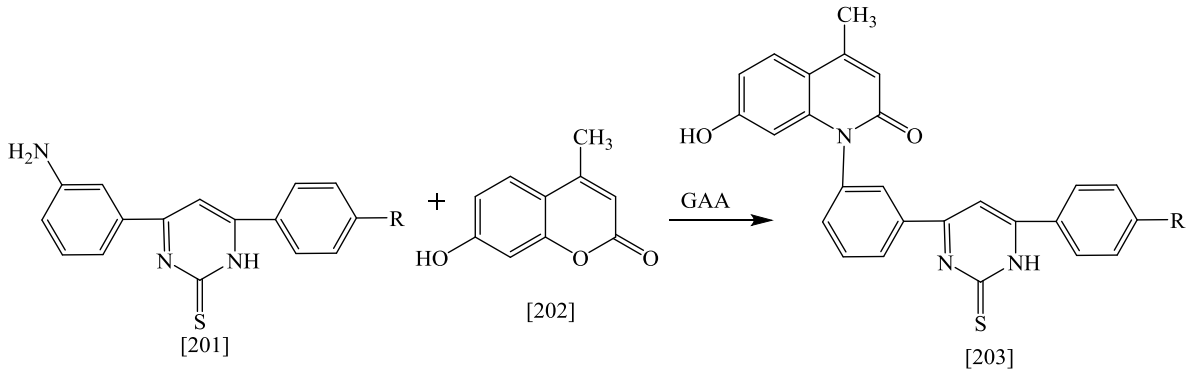
[196] [197]

By using[(144)] another method and reagents, 4-hydroxyquinolin-2(1H)-one [200] was synthesized from the reaction of aniline[198]with malonic acid[199] .These compounds have antibacterial activity and antifungal activity



[198] [199] [200]

Recently, Tomma et al., [145] were synthesized new quinolin -2-one dervitives [203] from condensation reaction of amino compounds [201] with coamarin[202] using glacial acetic as a catalyst and solvent.



R=4-Br , 4-NMe_2

1.3.3.2. Biological activitiey of quinoline

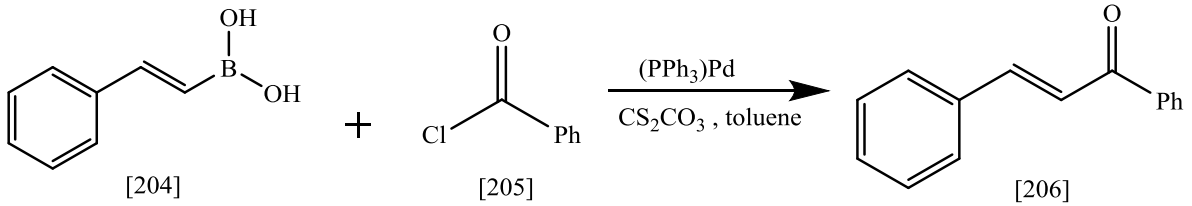
Quinoline and its derivatives are important due to their a wide range of biological activities as a drug analgesics,antiamoebic, tryphocidal, antiseptic and antiserotonin[146-149] . In addition to the quinolin , derivatives also exhibit good antimalarial, antitubercular, antibacterial, antihistaminic , antineurodegerative, anticonvulsant , antitumor , anticancers and antiallergics activitity[150-152].

1.3.4. Chalcones

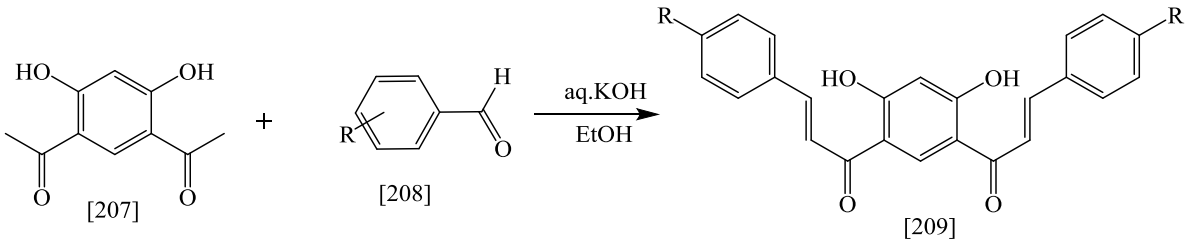
Chalcones(which were synthesized by Claisen-Schemidt condensation), they are well known[153] as intermediates for synthesizing various heterocyclic compounds. Chalcones are α,β- unsaturated ketones [154] and synthesized by many workers [155,156]. These flexible molecules appear in different conformations and their properties depend on a suitable ring substitution as well as on the presence of the α-β unsaturated ketone moiety [157] .

1.3.4.1. Synthesis of chalcones

The new chalcones [206] were synthesized by Suzuki coupling reaction[158] between benzoyl chlorides[205] and phenyl vinyl boronic acid [204] as in the following reaction .

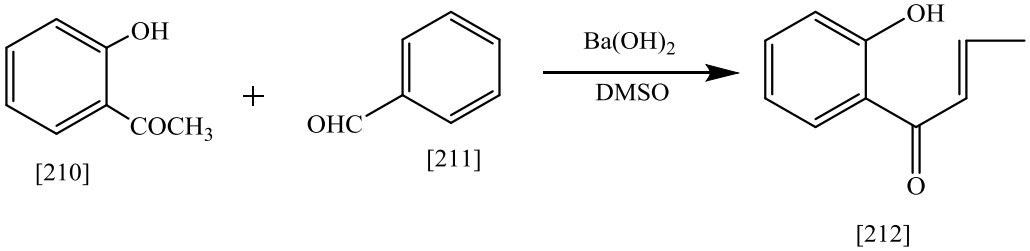


The reaction[159] of 1,1-(4,6-Dihydroxy-1,3-phenylene) diethanone [207]with arylaldehyde [208] in potassium hydroxide solution and ethanol led to give bis-chalcones[209].These compounds have antibacterial and antifungal activities .

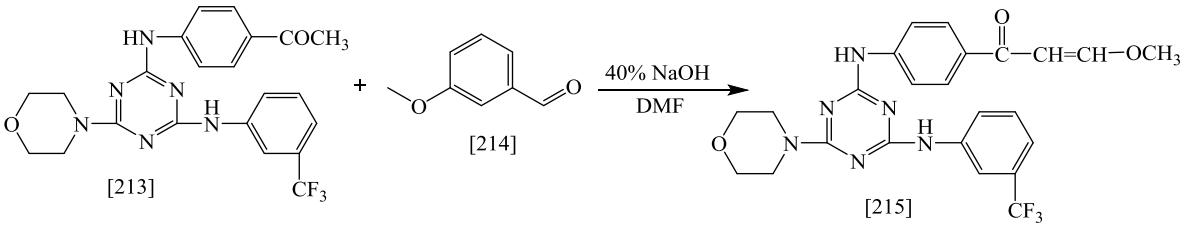


R= 4-Bromo , 3-Nitro

Padarthi et al., [160] reported a novel method for the synthesis of chalcone [212] in the presence of barium hydroxide in dry dimethyl sulphoxide (DMSO) medium.

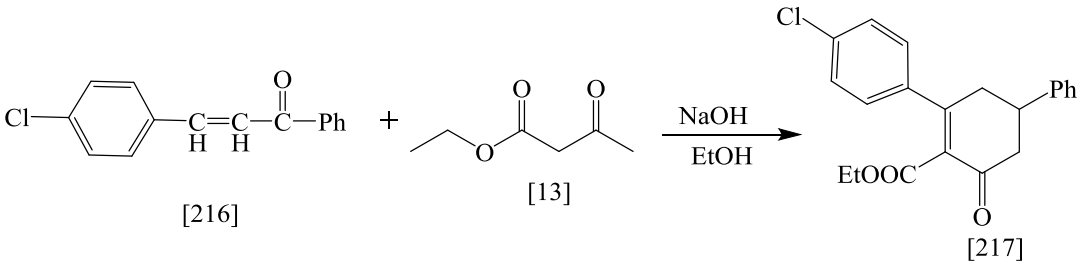


By reaction [161]of 1-(4-((4-morpholino-6-((3-(trifluoromethyl) phenyl) amino) -1,3,5-triazin-2-yl)amino)phenyl)ethan-1-one[213] with 3-methoxy benzaldehyde [214] in 40% NaOH and DMF, the compound 2-(3'-trifluromethylphenylamino)-4-(tetrahydro-1',4'-oxazine)-6-[4'-{3"-(3'"methoxy phenyl)- 2"- propenon-1"-yl} phenylamino]-1,3,5-triazine [215]was obtained. This compound has antitubercular and antibacterial activity .

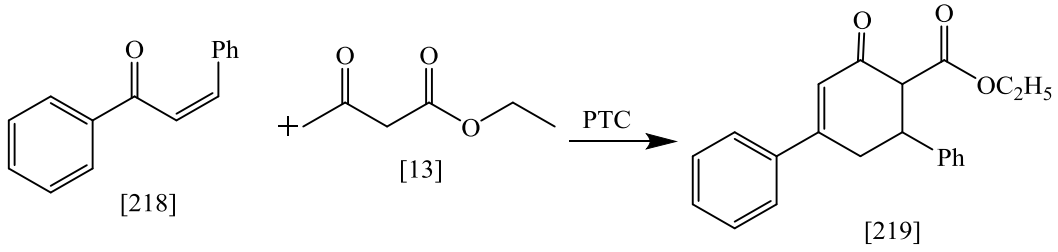


1.3.4.2.Reaction of chalcones

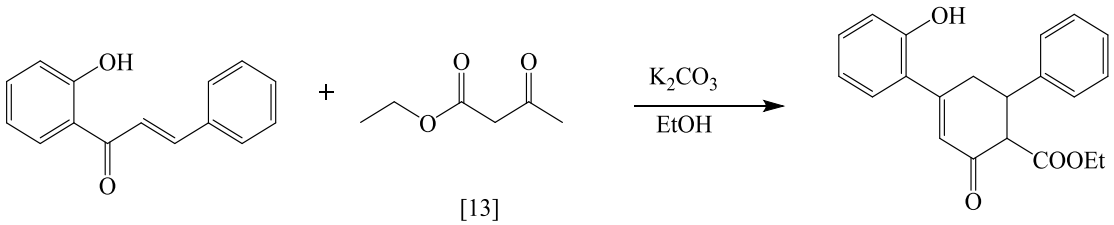
3-(4-chlorophenyl)-1-phenylprop-2-en-1-one[216] was reacted by ethyl aceto acetate [13]in NaOH and EtOH gave ethyl 4"-chloro-5'-oxo-1',2',5',6'-tetrahydro-[1,1':3',1"-terphenyl]-4'-carboxylate [217] [162].



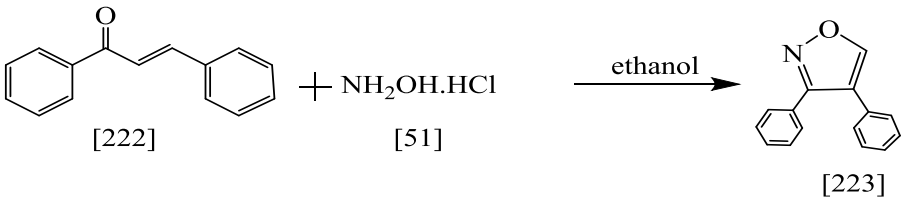
By using Tetra butyl ammonium iodide as phase transfer (PTC), Mohammed [163] was reacted the chalcones [218] with ethylaceto acetate ethyl gave 5'-oxo-2',3',4',5'-tetrahydro-[1,1':3',1"-terphenyl]-4'-carboxylate [219].



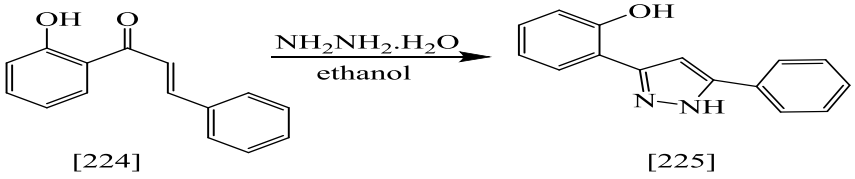
From reaction of 1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one[220] with ethyl aceto acetat [13]led in K_2CO_3 in ethanol to give ethyl 2-hydroxy-5'-oxo-2',3',4',5'-tetrahydro-[1,1':3',1''-terphenyl]-4carboxylate [221].The compound has antibacterial activity(164) .



While, the reaction of chalcone [222]with hydroxyl amine hydrochloride [51] in ethanol(165) led to formation a new isoaxazol [223] .

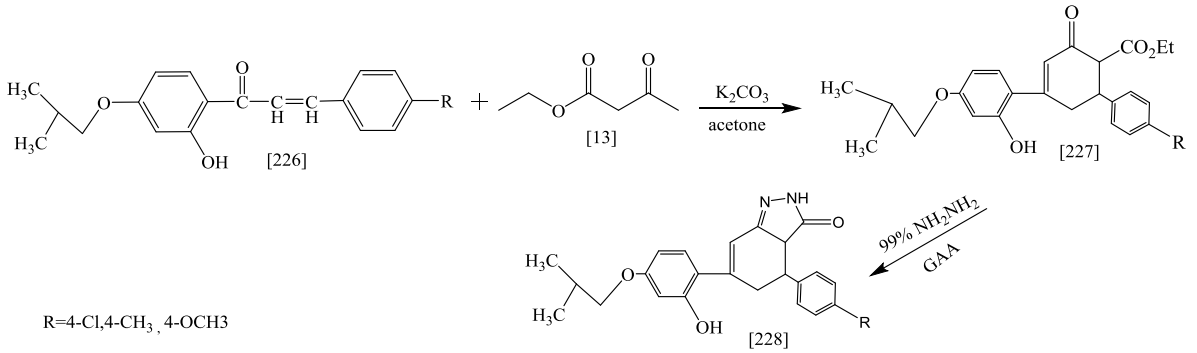


Ayyappa et al.,(166) used hydrazine hydrate 80% with ethanol as a solvent to synthesize 2-(5-phenyl-1H-pyrazol-3-yl)phenol[225] from 1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one [224] .

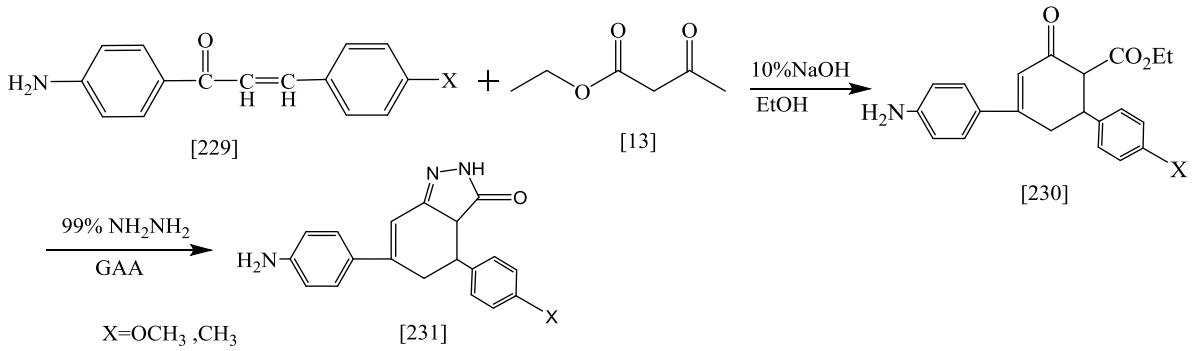


The refluxed a mixture of chalcone [226], ethyl acetoacetate[13] and anhydrous K_2CO_3 in dry acetone led to give compound [227]. Then the refluxed a mixture of the cyclohexenone [227] and hydrazine hydrate in glacial acetic acid (GAA) led to give 6-(2-hydroxy-4-isobutoxyphenyl)-4-(substituted

phenyl)-4,5-dihydro-2H-indazol-3(3aH)-one[228]. These compounds have antimicrobial activity [167].



Finally, Gali and Tomma[168] were synthesized new indazole derivatives [231] from chalcones [229] via two steps as fallows:

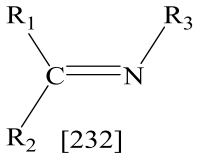


1.3.4.3.Biological activity of chalcones

Chalcones exhibited a number of biological activities. Such as antimicrobial [169], anti-inflammatory [170], analgesic [171], antiplatelet[172], antiulcerative[173], antimalarial[174], anticancer[175], antiviral[176], antileishmanial[177], antioxidant [178], antibacterial and antitubercular activities .

1.4. Hydrazones and Schiff Bases

Schiff bases are condensation products of primary amines and carbonyl compounds and they were discovered by a German chemist, Nobel Prize winner, Hugo Schiff in 1864[(179)]. Structurally, Schiff base (also known as imine or azomethine) is an analogue of a ketone or aldehyde in which the carbonyl group(C=O) was replaced by an imine group[(180)]



[232]

R_1,R_2 and R_3= alkyl or aryl

Schiff bases are used as a material in synthetic and medical fields. they also used as chelating ligands in the coordination chemistry and their metal complexes are a great interest for many years[(181)] . They are also used to prepare super-conducting polymers[(182)]. Hydrazones belongs to Schiff base compounds family with the structure

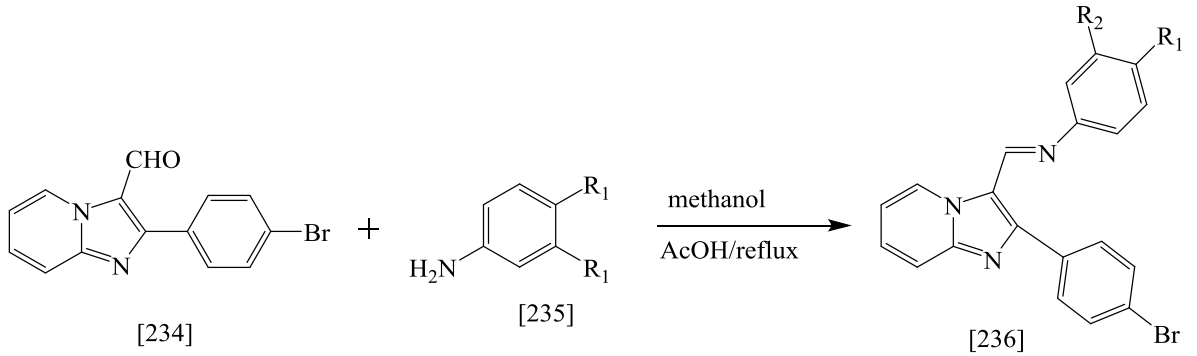
$R_2C=N-NHR_2$

[233]

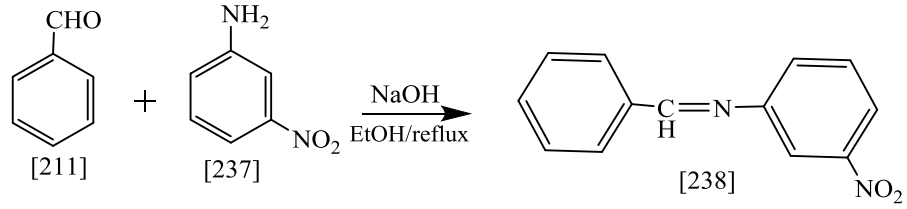
1.4.1. Synthesis of hydrazones and Schiff bases

The schiff base compounds were synthesized in acidic or basic medium. Also could be synthesized without catalyst as follows:-

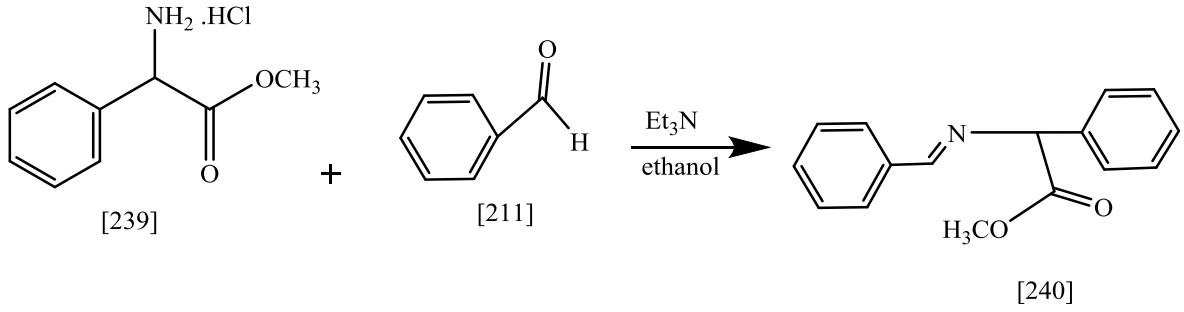
In the presence of glacial acetic acid (GAA), Bhale and Dongare [(183)] have been synthesized new Schiff bases by reaction of imidazo [1,2-a] pyridine 3-carboxyaldehyde[234] and substituted anilines[236]in methanol .These compounds have antifungal and antibacterial activity.



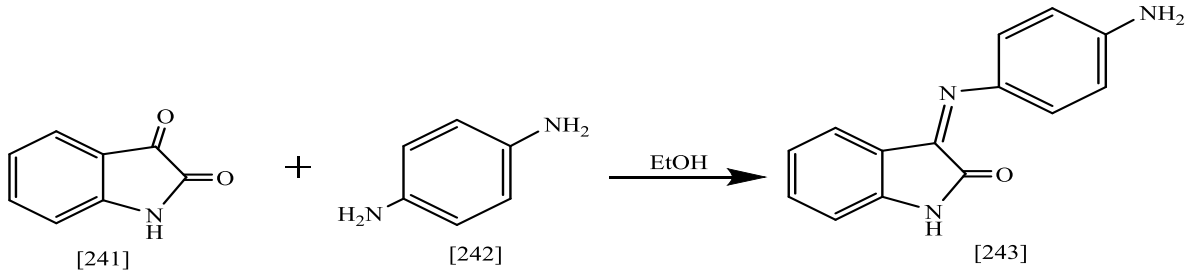
Also the Schiff base; [184] m-nitro aniline N-bezaldine[238]was synthesized by condensation of benzaldehyde[212], with m-nitro aniline[237] in ethanol with NaOH.



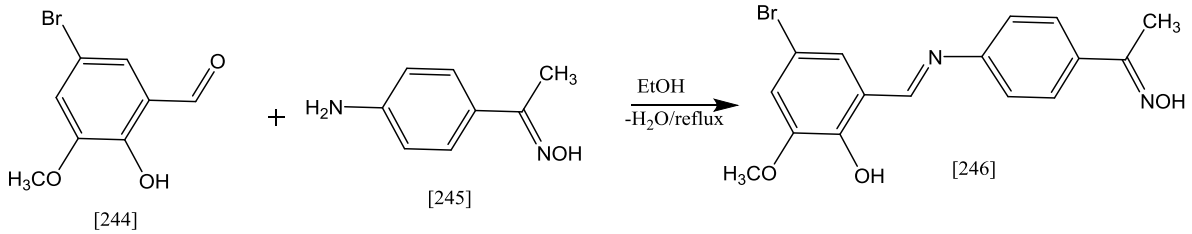
By using triethylamine (Et_3N), Goreci et al.,[185] were synthesized a new type of Schiff base[240] from the reaction of benzaldehyde[211] with compound [239] in ethanol .This compound has antioxidant activity.



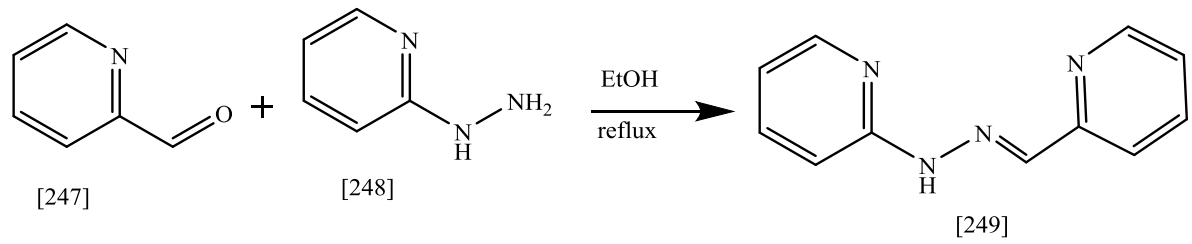
Without using acidic or basic medium , Oguntoye et al., [186] were obtained 3-((4-aminophenyl)imino) indolin-2-one[243] from the reaction of indoline-2,3-dione [241]with 1,4-phenylene diamine[242] in ethanol.



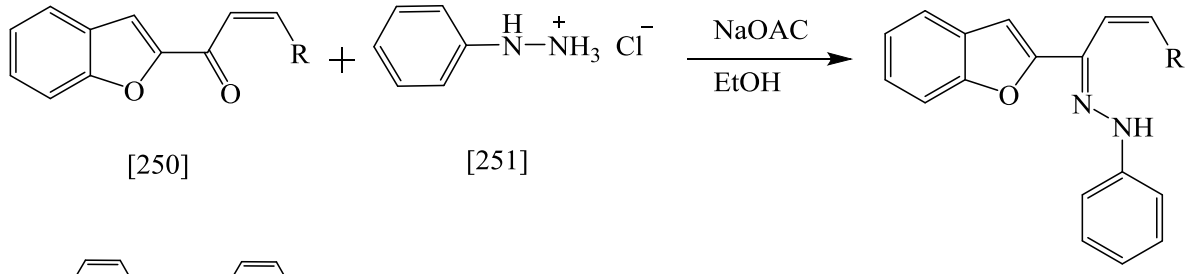
Also, the reaction of 4-aminoacetophenone oxime [245] with aldehyde [244] led to formation schiff bases[187] type [246] .



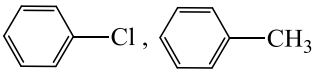
In addition[188], the new hydrazone :2(2-pyridine-2-yl)hydrazineylidene methyl)pyridine[249] was synthesized from the condensation reaction of -2-pyridine carbaldehyde [247] with 2-hydrazino pyridine [248] in ethanol.



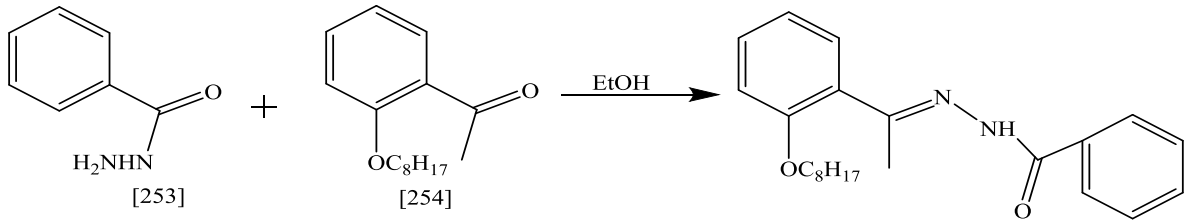
On the other hand,[189] the new type of hydrazone derivatives[252]was synthesized from the reaction of phenyl hydrazine hydrochloride[251]and 1-benzo[b] furan-2-yl-3-(substituded phenyl)prop-2-en1-one[250]using sodium acetate in ethanol .



[250] [251] [252]

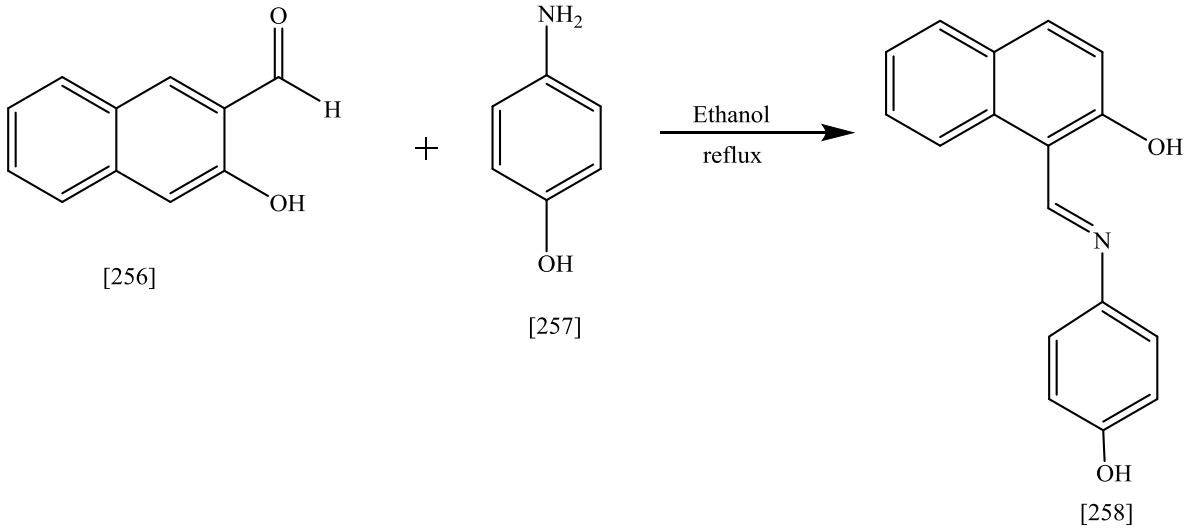
R= 

Abu Talip et al .,[190] reported the synthesis of Schiff bases type hydrazones [255] from reacted benzahydrazide [253] with aromatic ketone [254] in ethanol. This compound has antibacterial activity.



[253] [254] [255]

Finally, [191] The Schiff base[258] was synthesized by the condensation reaction of 2-hydroxy-1-naphthaldehyde [256]with 4-aminophenol[257] in ethanol .

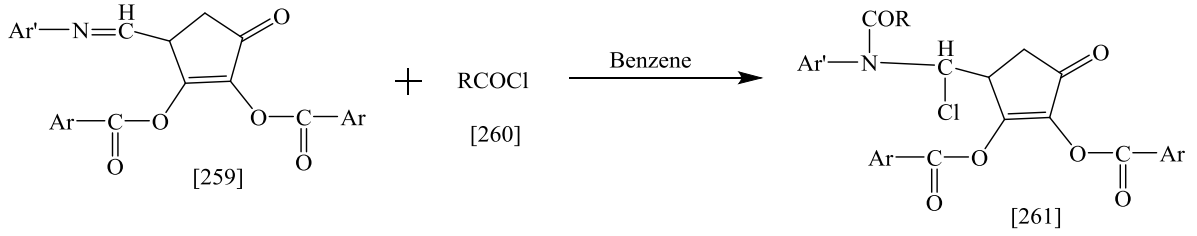


[256] [257] [258]

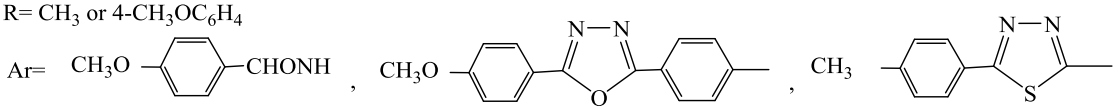
1.4.2. Reactions of hydrazones and Schiff bases

The imine group in the Schiff bases or hydrazones has been used for the synthesis of new hetrocyclic derivatives by many reactions under different condition as in the following:-

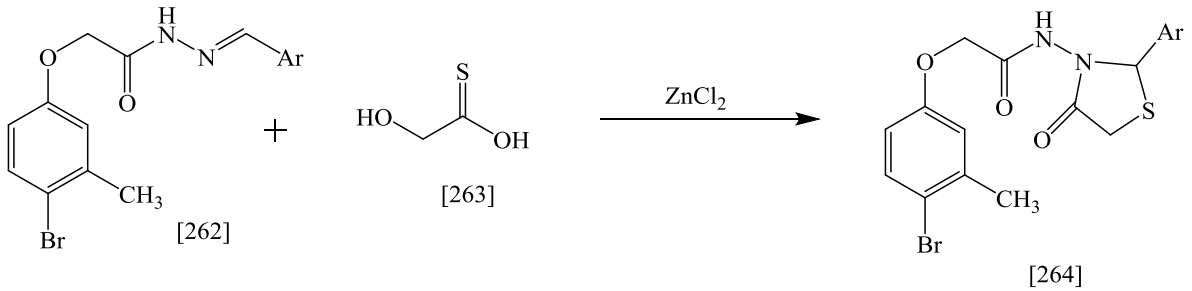
From reaction of Schiff bases[259]in dry benzene[192] with acetyl or anisoyl chloride[260] gave N-acyl compounds [261].

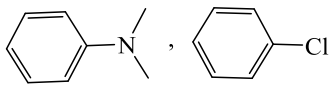


Ar=4-$CH_3COC_6H_4$
R= CH_3 or 4-$CH_3OC_6H_4$

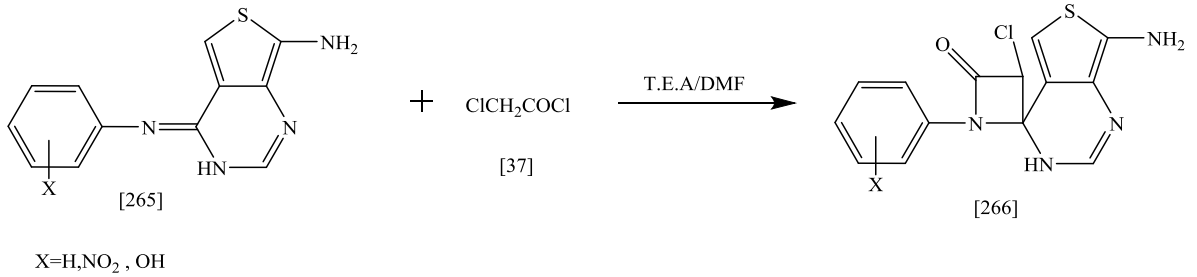


The cyclization[193] of the N- (substituted benzylidiene)-2-(4-bromo-3-methylphenoxy) acetamides[262] with thioglycolic acid[263]in the presence of zinc chloride gave 2-(4-bromo-3- methylphenoxy) -N-(4-oxo-2-arylthiazolidin-3-yl)acetamides[264]. These compounds have antimicrobial activity.



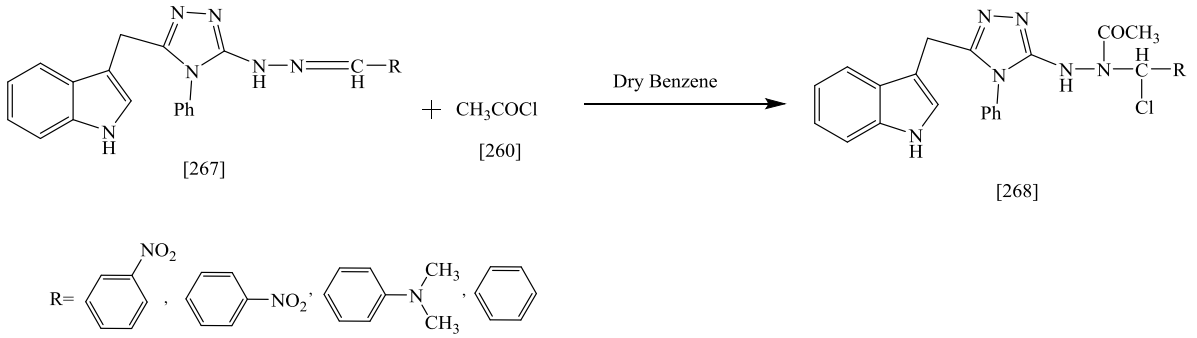
Ar= 

Elkanzi [194], was reacted the imine compound[265] with chloroacetyl chloride [37] in the presence of Et_3N/DMF to give spiro β lactam [266] .

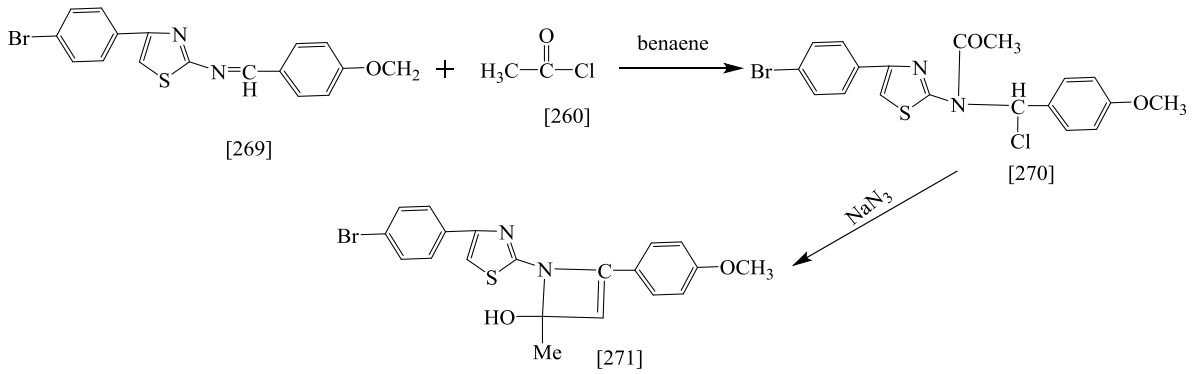


X=H,NO_2 , OH

Also, the synthesis of N-acyl derivatives[268] from reaction of Schiff bases[267] in dry benzene with acetyl chloride was mentioned by Aliawi et al., [195]. [260].



Another type of four hetrocyclic ring [196] was obtained via two steps firstly the refluxed of imino group of Schiff bases [269] with acetyl chloride[260] in dry benzene , secondly: reacted the N-acetyl compounds [270] with NaN_3 to get new four member hetrocyclic ring [271] .



1.4.3. Biological activity of hydrazones and Schiff bases

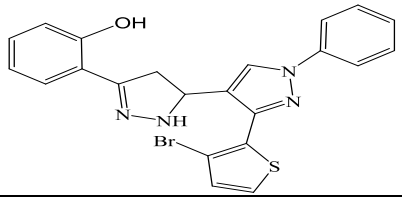
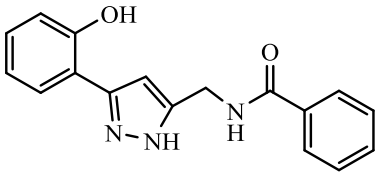
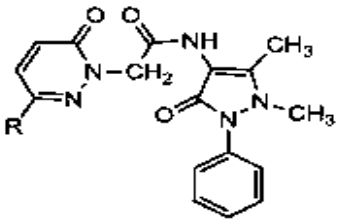
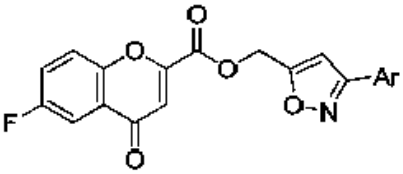
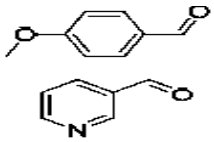
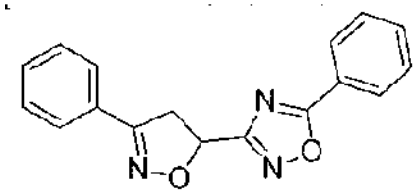
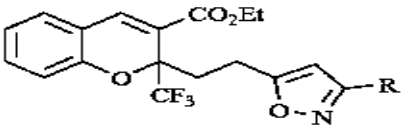
Schiff bases and hydrazones attract much interest both for synthetic and biological area[197] . Thus, they can be used as a material in the preparation of a

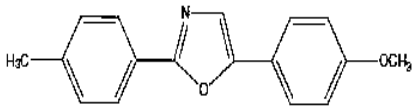
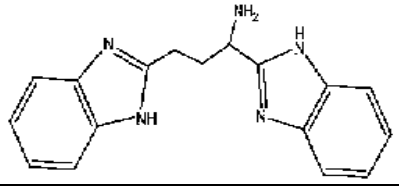
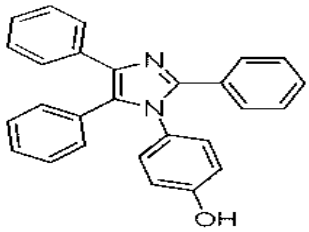
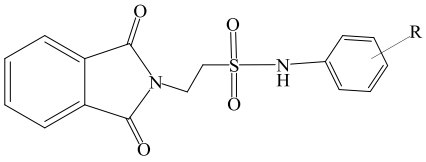
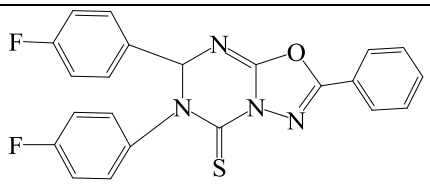
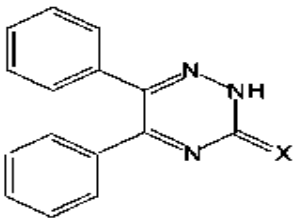
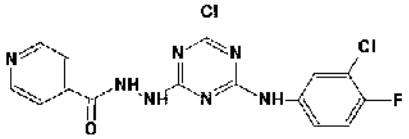
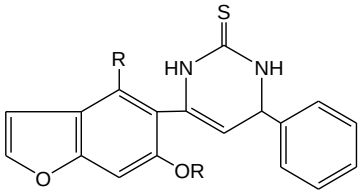
Comp No.	Structural Furmula	R	Biological activity	Ref.

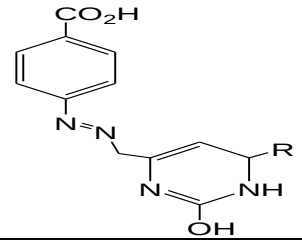
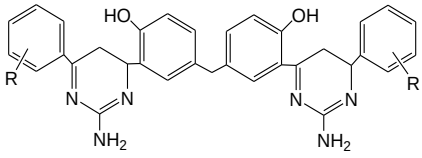
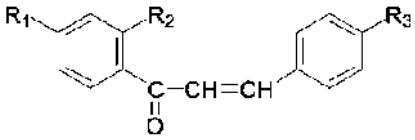
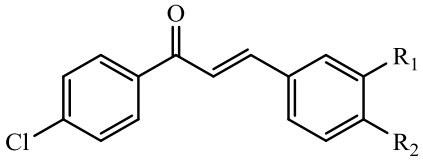
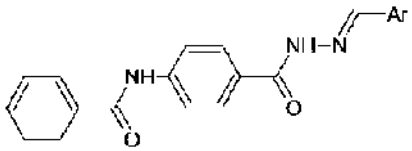
large number of industrial and biologically active compounds via ring closure, cycloaddition and replacement reactions[198] .

A literary survey reveals that Schiff bases derived from various heterocyclic possess cytotoxic [199] , anticonvulsant [200] , antiproliferative , antimicrobial [201] , anticancer [202] , and antifungal [203] activities. Table(1-1).

Table(1.1) : Biological activity of compounds

[272]			anti-Inflammatory	(204)
[273]			anti-Inflammatory	(205)
[274]		p-fluoro phenyl, piperazine, phenyl piperazine	anti-Inflammatory	(206)
[275]			antibacterial	(207)
[276]			antibacterial	(208)
[277]		4-FC_6H_4 , 4-$CH_3C_6H_4$, 4-$OCH_3C_6H_4$, 3-$CF_3C_6H_4$	anticancer	(209)
[278]		4-chloro phenyl, 2-pyridyl, 3- pyridyl, 2-furyl	anti-inflammatory	(210)

[279]			antibacterial and antifungal	(211)
[280]			antibacterial	(212)
[281]			antioxidant	(213)
[282]		2-OMe 3-OMe 4-OMe	antibacterial	(214)
[283]			antifungal	(215)
[284]		X=S,O	anti-inflammatory	(216)
[285]			antibacterial and antifungal	(217)
[286]		R= $COCH_3$, CH_3 , OCH_3	antimicrobial	(218)

[287]		R=Ph, 2-hydroxyphenyl ,4-hydroxyphenyl ,2-nitro phenyl ,2-chlorophenyl	antimicrobial	(219)
[288]		R=H, 4-OMe 4-Cl, 4-NO_2 4-Br, 2-Cl	antifungal and antibacterial	(220)
[289]		R_1=H,H R_2=2-OH,2-OH R_3=4-NO_2, 4-OCH_3	antibacterial anti-inflammatory	(221)
[290]		R1 = OCH_3 ,OCH_3,H R2 = O-Allyl ,OCH_3 ,OH	antimalarial	(222)
[291]		Ar=C6H5CO	antibacterial	(223)

The aim of the work

The aim of this work is synthesis and charctrazation of new heterocyclic compounds contain five and six membered ring and their derivatives in the same molecule

1. Synthesis and characterization of new heterocyclic compounds derived from 5,6-diphenyl-1,2,4-triazine-3-thiol as follows:

a) Synthesis and characterization of imadazole derived from Schiff bases
b) Synthesis and characterization of pyrazole (derived from acid hydrazide) then converting it to the corresponding hydrazones.
c) Synthesis and characterization of new imides

2. Synthesis and characterization of new heterocyclic compounds derived from 4-[3-(4`-substituted phenyl)-2-propene- 1-one]-hydroxide as follows:

a) Synthesis and characterization of new quinolin-2-one, imides, pyrazoles and hydrazones derived from indazol compounds

b) Synthesis and characterization of isoxazole derived from cyclohexenone compounds.

3. Synthesis and characterization of new N-acetyl thiourea and and pyrimidine compounds by many steps, derived from 4-(4-aminophenyl) -oxazol-2-amine

4. Study the biological activity towards antibacterial and antifungal of different type of heterocyclic compounds with a variety hetrocyclic rings.

Chemicals and techniques

2.1. Chemicals

The following chemicals in Table (2.1) were obtained from different companies. Some of these were purified to obtain better purity.

Table (2-1) listed Liquid and solid chemicals used in this work

Name of material	Name of company
Acetone99%	scharlau
Acetyl chloride99%	Aldrich
Anisaldehyde97%	Aldrich
Anisoyl chloride99.5%	Aldrich
4-aminoacetophenone 99%	Aldrich
Benzene 99.5%	Riedel-De Haen
Benzoin	Aldrich
Benzil	Aldrich
Chloroform 99.4%	Merck
Coumarin	Aldrich
4-dimethylaminobenzaldehyde 97%	Aldrich
Diethylether 99%	Aldrich
Dimethyl sulphoxide (DMSO)99%	BDH
Dimethyl formamide (DMF)99%	BDH
1,4-Dioxane99%	GCC
2,4-Dinitro Phenyl hydrazine99.5%	Merck
Di ethyl malonat	Aldrich
Ethanol absolute 99.8%	GCC
Ethylacetoacetate 99%	Aldrich
Ethylacetate 99%	Aldrich
Ethyl chloro acetate 99.8%	Aldrich
Hydrochloric acid 37%	Riedel-De Haen
Hydroxylamine hydrochloride	GPR
Hydrazine hydrate80%	Aldrich
Iodine 99.9%	Aldrich
3-nitrobenzaldehyde 98%	Aldrich
n-Hexane 99.5%	BDH
3-Nitrobenzaldehyde98%	Aldrich
Napthalic anhydride	Aldrich
Petroleum ether 60-80°C 96%	BDH

Phthalic anhydride	**Aldrich**
Resorcinol 99%	**Aldrich**
Sodium thiosulfate pentahydrate99%	**Riedal-deHaën**
Sodium acetate 99.9%	**Aldrich**
Benzaldehyde 98%	**Aldrich**
Sodium carbonateanhydrous98%	**AppliChem Gmbh**
Sodium hydroxide 97%	**Aldrich**
Thiourea 99%	**Merck**
Tolyl benzaldehyde99%	**Riedel –De Haen**
Thiosemicarbazide	**Merck**
THF	**Aldrich**
Tri ethyl amine	**Aldrich**
urea	**Fluka**

2.2. Techniques

2.2.1. Spectroscopy

a) Fourier transform infra-red spectrophotometer (FTIR)

FTIR spectra were recorded by using potassium bromide discs by a SHIMADZU (IR Affinity-1) FTIR spectroscopy. College of Education for Pure Science (Ibn-Al-Haitham), University of Baghdad, also some spectra were carried at (Ibn-Senaa) company (Baghdad-IRAQ).

b) Nuclear magnetic resonance spectrometer (^{1}HNMR)

^{1}HNMR spectra were carried out using Ultra Shield 300 MHz, Bruker, Switzerland, at University of Kasi , Turkey, also some spectra were carried out Ultra Shield 400 MHz and Ultra Shield 500 MHz, Bruker, University of Tehran , Center Lab. (in Iran) and Ultra Shield 300 MHz, Bruker ,Switzerland at University of Al-Bayt, College of Science (in Jordan), are reported in ppm(δ), DMSO-d6 was used as a solvent with TMS as an internal standard.

c) Mass spectroscopy

The mass spectra were recorded by MS model: 5975c VL MSD with Tripe-Axis Detector University of Tehran, Center Lab. (in Iran).

2.2.2. Melting points measurements

Uncorrected melting points were determined by using Hot-stage, Gallen Kamp melting point apparatus and they were uncorrected .

2.2.3. Thin layer chromatography (TLC)

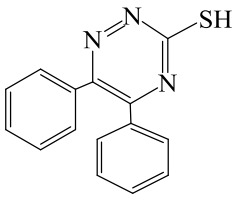
The TLC was performed on aluminum plates coated with layer of Silica gel, supplied by Merck. The spots were detected by iodine vapor. The purity and the compelet reaction of newly compounds was checked by using (n-hexane:ethyl acetate)(7:3)(v/v).

2.2.4. Biological activity screening

Biological activity screening were determined in center laboratory College of Education for Pure Science (Ibn-Al-Haitham), University of Baghdad

2.3. Synthetic procedures

2.3.1. prepration of 5,6-diphenyl-1,2,4-triazine-3-thiol [I].

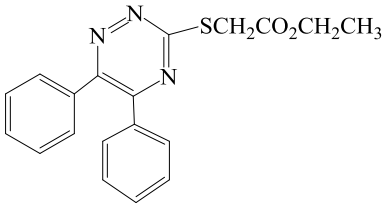


[1]

Benzil compound (1.05g ,0.005mol) was dissolved in 85% acetic acid with thiosemecarbazide (0.455g ,0.005 mol) in hot water (2mL), the mixture was refluxed for 4hrs[224]. The precipitate that appeared was filtered off and washed with water(for many times). The orange crystals obtained

were recrystallized from ethanol gave orange solid , yield 87 % , mp=218-220°C (lit mp 222–224 °C).

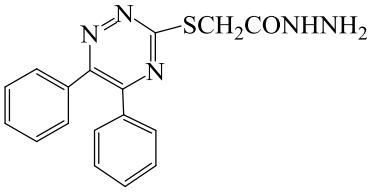
2.3.2. Synthesis of ethyl 2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio) acetate [II].



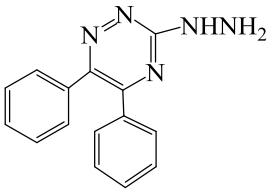
[II]

A mixture of compound [I] (0.266g ,0.001 mol), chloro ethyl acetate (0.122 mL, 0.001 mol) and fused sodium acetate (0.24g, 0.003mol) in ethanol was heated under reflux for 4hrs(225). Then cooled and poured onto water, the resulting yellow solid was filtered off ,washed with water, purification by using ether to produce compound [II], yield 80 %, mp 98 -100 ^{0}C.

2.3.3. Synthesis of 2-((5,6-diphenyl-1,2,4-triazin-3-yl) thio) acetohydrazide [III]$_a$ and 3-hydrazineyl-5,6-diphenyl-1,2,4-triazine [III]$_b$.



[III]$_a$



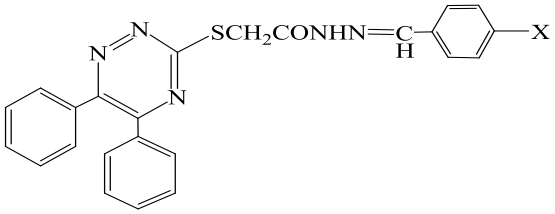
[III]$_b$

A solution of compound[II]$_a$ or compound [I] (0.06 mol) and hydrazine hydrate (5 mL) in (10 mL) of ethanol was heated under reflux during 2hrs(136). The mixture was then cooled to room temperature, and the solid obtained was filtered and recrystallized from ethanol.

Compound [III]$_a$: Yield 78% ; m.p = (75-76) ºC ; color : brown

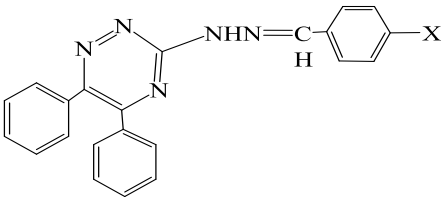
Compound [III]$_b$: Yield 80% ; m.p = (178-180)ºC lit.(175-178) ºC [112]; color :yellow

2.3.4. Synthesis of Schiff base compounds of triazines [IV]$_{a-g}$.



[IV]$_{a-d}$

X= H,CH_3, N(Me)$_2$, m-NO_2

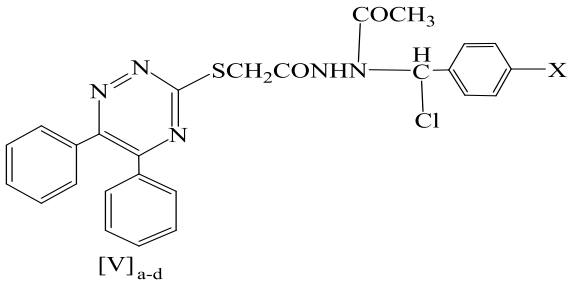


[IV]$_{e-g}$

X=H,CH_3, N(Me) $_2$

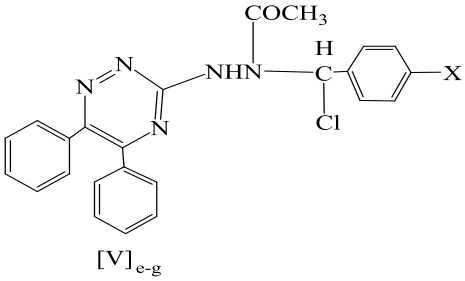
A mixture of acid hydrazides [III]$_a$ or compound [III]$_b$ (0.001 mole) with different aromatic aldehydes (0.001 mol), and three drops of glacil acetic acid in dry benzene(5mL) was refluxed for 4hrs[17]. The solvent was evaporated under vaccum and the solid recrystallized from acetone. The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds [IV] $_{a-g}$ were listed in Table (2-2).

2.3.5. Synthesis of N-acetyl dervitives [V] $_{a-g}$



[V]$_{a-d}$

X= H,CH_3, N(Me)$_2$, m-NO_2



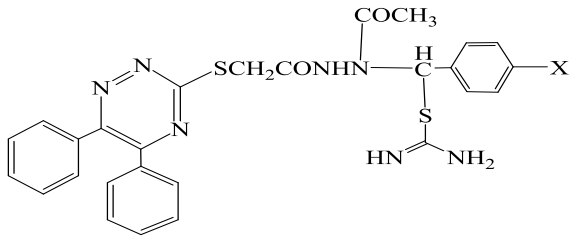
[V]$_{e-g}$

X=H,CH_3, N(Me) $_2$

To a stirred cooled solution of Schiff base [IV] $_{a-g}$ (0.01 mol) in 5mL of dry benzene, was added dropwise acetyl chloride (0.01 mol). The mixture was refluxed for 6hrs and the solvent was evaporated [195]. The residue was washed with water for many times. Recrystallization from ethanol. The

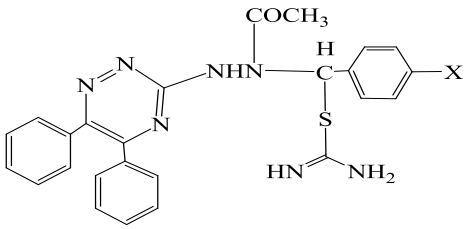
nomenclature, structural formula, molecular formula, yields and physical properties of these compounds [V] $_{a-g}$ were listed in Table (2-3).

2.3.6. Synthesis of thiourea dervitives [VI]$_{a-g}$.



[VI] $_{a-d}$

X= H,CH_3, N(Me)$_2$, m-NO_2

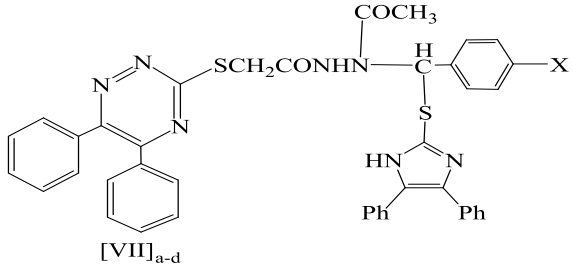


[VI] $_{e-g}$

X=H,CH_3, N(Me) $_2$

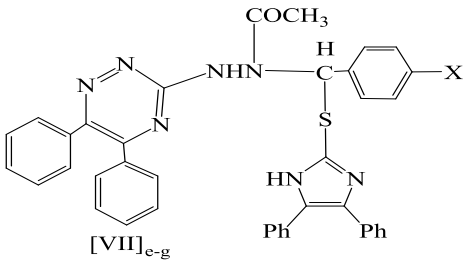
To a stirred solution of compound [VI]$_{a-g}$ (0.001mol) in dry DMF (5mL), the benzoin (0.035g, 0.001mol) was added .The reaction mixture was refluxed for 5hrs[(226)]. After cooling, drops of water was added with stirring

2.3.7. Synthesis of imidazol dervitives [VII] $_{a-g}$



[VII]$_{a-d}$

X= H,CH_3, N(Me)$_2$, m-NO_2

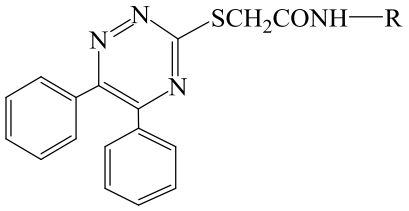


[VII]$_{e-g}$

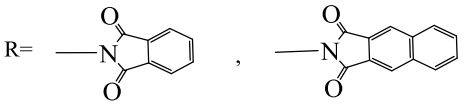
X=H,CH_3, N(Me) $_2$

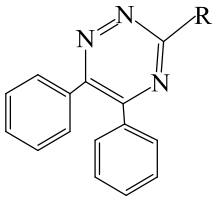
until precipitate separated out. The precipitate was filtererd, dried and recrystalized from ethyl acetat. The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds[VII] $_{a-g}$ were listed in Table (2-5).

2.3.8. Synthesis of imides compounds [VIII]$_{a-d}$

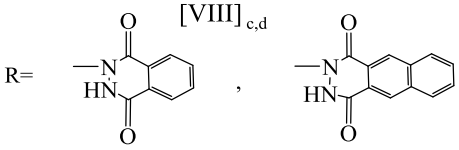


[VIII] $_{a,b}$



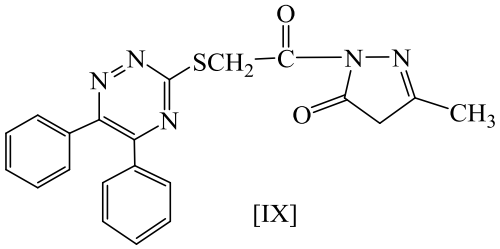


[VIII] $_{c,d}$



A mixture of hydrazide [III]$_{a,b}$ (0.323g, 0.001mol) and acid anhydride (0.001mol) was fusion for 1 hour[(91)]. The product was purified from wishing ether to give new imides. The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds [VIII]$_{a-d}$ were listed in Table (2-6).

2.3.9. Synthesis of 2-(2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)acetyl)-5-methyl-2,4-dihydro-3H-pyrazol-3-one[IX]

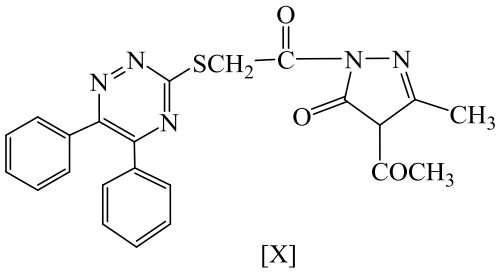


[IX]

A mixture containing acid hydrazide [III]$_a$ (0.45g, 0.0028 mole) and ethyl aceto acetate (0.4mL ,0.0028 mol) in absolute ethanol (4 mL) was

refluxed for 3 hrs[17]. The resulting pale brown was precipitate (on cooling), filtered and purified from ether to give a gammy the compound [IX], yield 70 %.

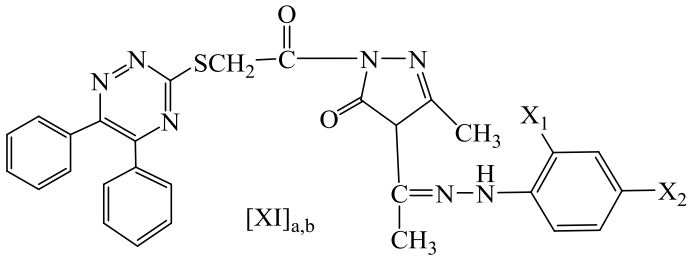
2.3.10. Synthesis of 4-acetyl-2-(2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)acetyl)-5-methyl-2,4-dihydro-3H-pyrazol-3-one [X].



[X]

1,4-Dioxane solution (5 mL) of compound [IX] (0.2g, 0.013 mol) and acetyl chloride (0.1mL, 0.013 mol) in the presence of (0.24g, 0.013 mol) calcium hydroxide was refluxed for 4 hrs in oil bath, after cooled the mixture to room temperature. The resulted solid was added to the dilute hydrochloric acid (0.5mL of conc. HCl in 2.5 mL water) [227]. The crude brown product was collected by filtrations, washed (several times with water), and recrystallized from acetone to give the compound [X], yield 68 % ,mp 130-132 ºC.

2.3.11. Synthesis 2-(2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)acetyl)-5-methyl-4-(1-(2-phenylhydrazineylidene)ethyl)-2,4-dihydro-3H-pyrazol-3-one[XI]$_a$ and 4-(1-(2-(2,4-dinitrophenyl) hydrazineylidene) ethyl)-2-(2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)acetyl)-5-methyl-2,4-dihydro-3H-pyrazol-3-one [XI]$_b$



$[XI]_{a,b}$

$[XI]_a$: X_1, X_2 =H

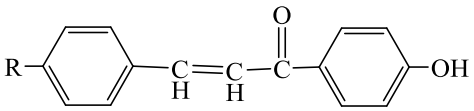
$[XI]_b$: X_1, X_2 =NO_2

A mixture of phenyl hydrazine or 2,4-dinitro phenyl hydrazine (0.001 mole), compound [X] (0.2g, 0.001 mole), ethanol 4 mL and drops from glacial acidic acid was refluxed for 4hrs. The solvent was evaporated under vaccum and the solid recrystallized from ethanol.

Compound $[XI]_a$: Yield 71% ; m.p = Gammy ; color : dark brown

Compound $[XI]_b$: Yield 72% ; m.p = (106-108) ºC; color : dark brown

2.3.12. Preparation of chalcones $[XII]_{a-c}$.

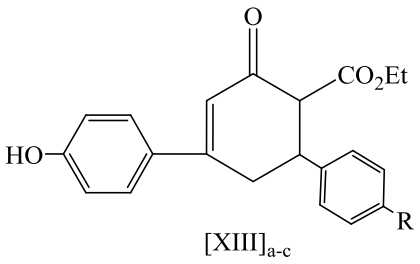


$[XII]_{a-c}$

R= H , CH_3, OCH_3

Equimolar quantities of 4-hydroxy acetophenone (1.36g, 0.01 mol) and benzaldehyde or 4-substituted benzaldehyde (0.01mol) were dissolved in a minimum amount of ethanol. Sodium hydroxide 40% (0.78g, 0.02 mol in 1.95 mL of water) was added slowly and the mixture was then cooled[(225)]. The product was poured slowly onto 200 mL of ice water with constant stirring. The precipitate obtained was filtered, washed and recrystallized from ethanol to yield chalcone $[XII]_{a-c}$. The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds were listed in Table (2-7).

2.3.13. Preparation of cyclohexenone derivatives $[XIII]_{a-c}$

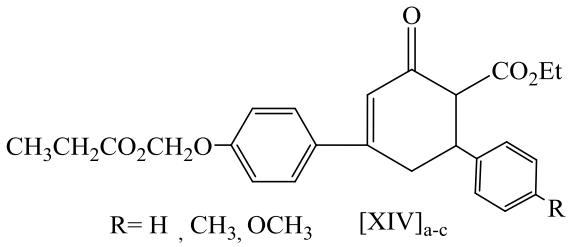


$[XIII]_{a-c}$

R= H , CH_3, OCH_3

A mixture of chalcone (0.003mol) and ethyl aceto acetat (0.7mL,0.003mol) in 10mL ethanol and the presence of 0.5mL (10% NaOH) was refluxed for 2hrs[228]. The reaction mixture was then poured with good stirring onto 200mL of ice-cold water and kept at room temperature until the reaction producte sparated as a solid .The sold was filtered off and purification from wishing ether. The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds were listed in Table (2-7).

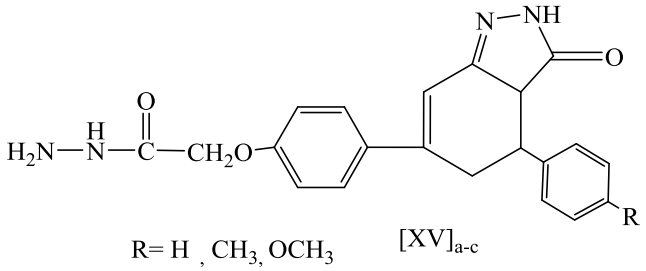
2.3.14. Synthesis of new ester derivatives of cyclohyxenone $[XIV]_{a-c}$



R= H , CH_3, OCH_3 $[XIV]_{a-c}$

These compounds were synthesized by using the same procedure given for the synthesis of compound [II] except using the compound $[XIII]_{a-c}$ instead of compound [I], the resulting solid was filtered off, washed with water, dried and recrystalization from ethanol to give compound $[XIV]_{a-c}$. The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds were listed in Table (2-8).

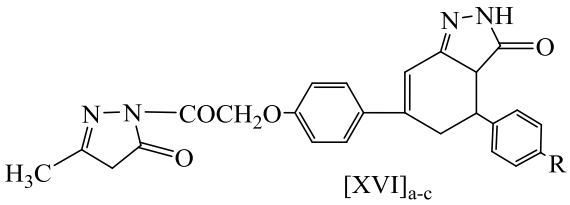
2.3.15. Synthesis of indazole derivative $[XV]_{a-c}$



R= H , CH_3, OCH_3 $[XV]_{a-c}$

These compounds were synthesized by using the same procedure given for the synthesis of compounds $[III]_{a,b}$ except using the compounds $[XIV]_{a-c}$ instead of compound [II], after cooling the solid formed was filtered off, air dried and recrystallized from chloroform. The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds were listed in Table (2-8).

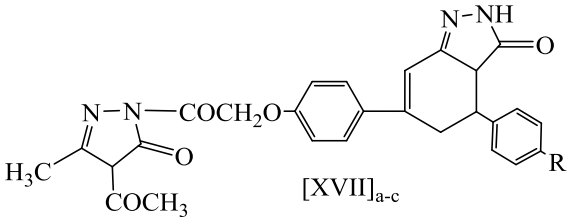
2.3.16. Synthesis of new pyrazol derivatives of of indazoles $[XVI]_{a-c}$



R= H , CH_3, OCH_3

These compounds were synthesized by using the same procedure given for the synthesis of compound [IX] except using the compounds$[XV]_{a-c}$ instead of compound $[III]_a$. The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds were listed in Table (2-9).

2.3.17. Synthesis of 6-(4-(2-(4-acetyl-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-2-oxoethoxy)phenyl)-4-phenyle[XVII]$_a$ and (4-substituted phenyl)-2,3a,4,5-tetrahydro-3H-indazol-3-one[XVII]$_{b,c}$

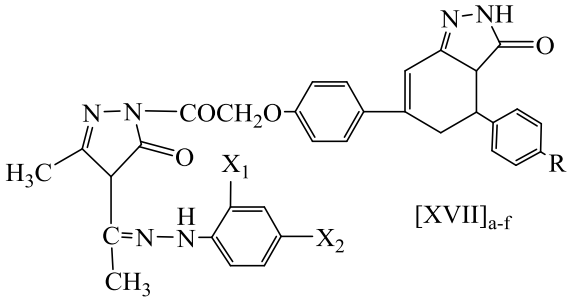


[XVII]$_{a-c}$

R= H , CH_3, OCH_3

These compounds were synthesized by using the same procedure given for the synthesis of compound [X] except using the compounds[XVI]$_{a-c}$ instead of compound [IX]. The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds were listed in Table (2-9).

2.3.18. Synthesis of hydrazone compounds type [XVIII] $_{a-f}$

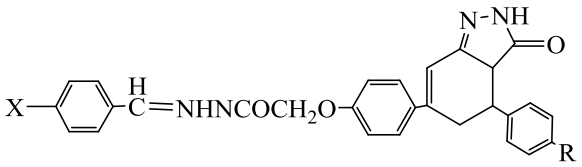


[XVII]$_{a-f}$

R= H , CH_3, OCH_3
X_1,X_2=H
or X_1 ,X_2=NO_2

These compounds were synthesized by using the same procedure given for the synthesis of compound [XI] except using the compounds[XVII]$_{a-c}$ instead of compound [X]. The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds were listed in Table (2-10).

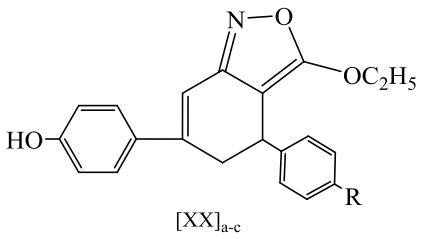
2.3.19. Synthesis of Schiff base of indazole derivatives $[XIX]_{a-i}$



X=H ,CH_3 ,N $(Me)_2$ $[XIX]_{a-i}$
R= H , CH_3, OCH_3

These Schiff bases were synthesized by using the same procedure given for the synthesis of compounds $[IV]_{a-g}$ except using the compounds $[XV]_{a-c}$ instead of compounds $[III]_{a,b}$. The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds were listed in Table (2-11).

2.3.20. Synthesis of fused isoxazole derivatives$[XX]_{a-c}$.

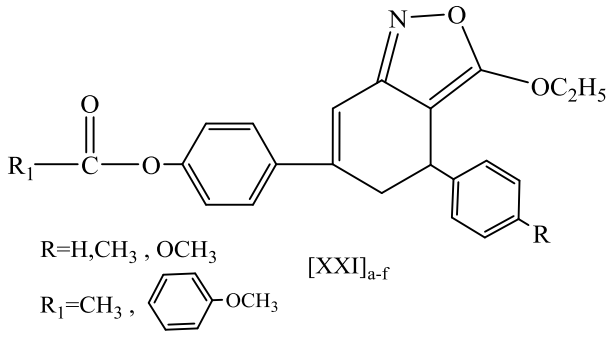


$[XX]_{a-c}$

R= H , OCH_3 , CH_3

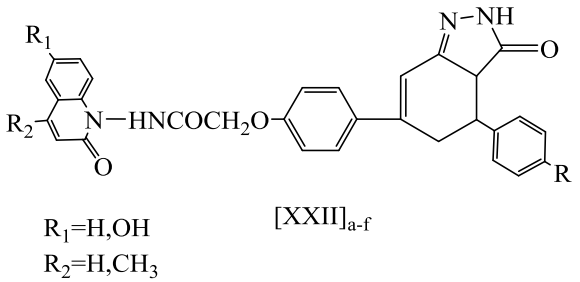
Cyclohexenone compounds $[XIII]_{a-c}$ (0.01 mol), hydroxylamine hydrochlorid (0.07g, 0.01 mole) and sodium hydroxide (0.13g, 0.03 mol) in ethanol (3mL) was heated under reflux for 16-18 hrs[229]. The reaction mixture is cooling and poured onto crushed ice , the solid separated was filtered and the purification from wishing ether . The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds were listed in Table (2-12).

2.3.21. Synthesis of ester compounds of isoxazole derivatives $[XXI]_{a-f}$



To a stirred solution of compound $[XX]_{a-c}$ (0.001 mol), triethyl amine (0.2mL, 0.002mol) in dried mixture of (1mL DMF and 2.5 mL THF), was added dropwise carboxylic acid chloride (0.001 mol) at (0-4) ºC. After the addition had been completed the resulting suspension was stirred at the same temperature for 3hrs[230]. The triethyl amine hydrochloride salt was precipitate, it was filtered and the filtrate was poured with stirring onto 50 mL ice –water. then the mixture was extracted by adding 20mL of diethyl ether .The ether solution was evaporated to give a residue which was recrystallized from ethanol /water. The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds were listed in Table (2-12).

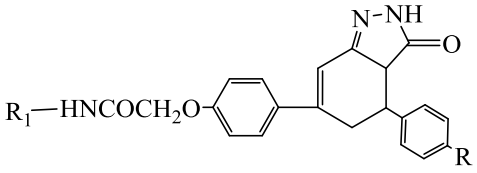
2.3.22. Synthesis of quinolin-2-one derivatives $[XXII]_{a-f}$.



Equivalent moles of coumarin compounds (0.01 mol) and amine compounds$[XV]_{a-c}$ (0.35g,0.01 mol) were dissolved in glacial acetic acid (3mL) and refluxed for 6hrs[231] and the residue poured onto ice water to get a

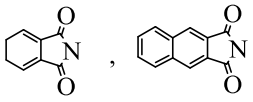
solid product. The obtained product was filtered, dried at room temperature and recrytalized from acetone . The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds were listed in Table (2-13).

2.3.23.Synthesis of imides compounds of indazole $[XXIII]_{a-f}$



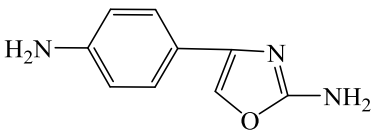
$[XXIII]_{a-f}$

R=H,CH_3, OCH_3

R_1=  ,

These compounds were synthesized by using the same procedure given for the synthesis of compound $[VIII]_{a,b}$ except using the compounds $[XV]_{a-c}$ instead of compound [III] . The nomenclature, structural formula, molecular formula, yields and physical properties of these compounds were listed in Table (2-14).

2.3.24. Preparation of 4-(4-aminophenyl)oxazol-2-amine [XXIV].

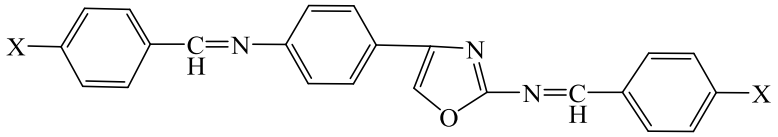


[XXIV]

In flask 250 mL, the mixture iodine (3.78g , 0.03mol), urea (1.81g , 0.06mol) and 4- amino acetophenone (2.3 g , 0.03mol), was fusion for 8 hrs[43].then cooled , washed with diethyl ether and solution of sodium

thiosulfate , the brown precipitated was filtered and purified wish from ether to give the brown solid , yield 60 % , mp=180-182 ºC

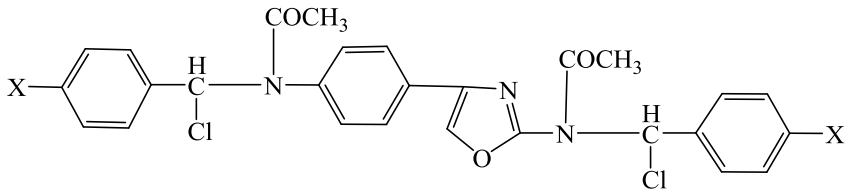
2.3.25. Synthesis of Schiff bases [XXV] $_{a,b}$



X= H , $N(Me)_2$ $[XXV]_{a,b}$

These compounds were synthesized by using the same procedure given for the synthesis of compounds $[IV]_{a-g}$ except using (0.002 mol) from different aldehyde and using the compound [XXIV] instead of compound $[III]_{a,b}$ and the reaction mixture refluxed for 10 hrs. The solid recrystallized from ethanol. The nomenclature, structural formula, molecular formula, yields and physical properties were listed in Table (2-15).

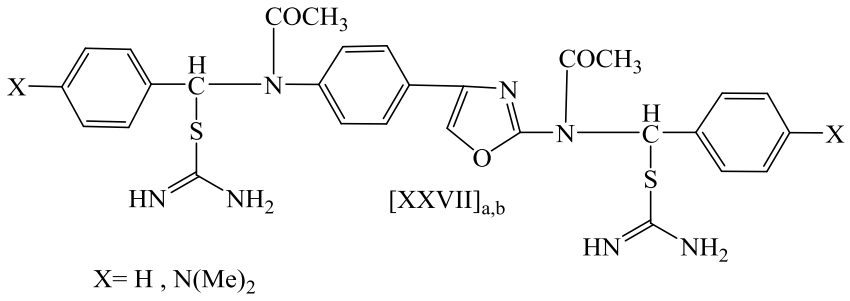
2.3.26. Synthesis of N-acyl dervitives of oxazole [XXVI] $_{a,b}$



X= H , $N(Me)_2$ $[XXVI]_{a,b}$

This compounds were synthesized by using the same procedure given for the synthesis of compounds $[V]_{a-g}$ except using (0.02mol) from acetyl chloride and using the compounds **[**XXV] $_{a,b}$ instead of compounds $[IV]_{a-g}$.and refluxed the reaction mixture for 24 hrs. The nomenclature, structural formula, molecular formula, yields and physical properties were listed in Table (2-15).

2.3.27. Synthesis of thiourea dervitives of oxazole [XXVII] a,b

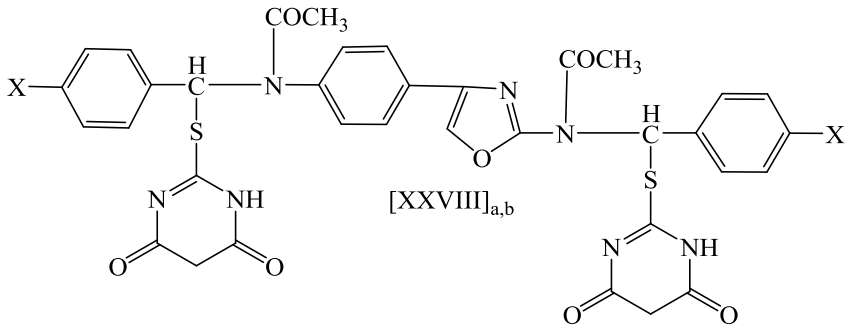


[XXVII]a,b

X= H , N(Me)2

This compounds were synthesized by using the same procedure given for the synthesis of compounds [VI]a-g except using(0.02mol) from thiourea and using the compounds **[**XXVI] a,d instead of compounds [V]a-g. and refluxed the reaction mixture for 10 hrs. The nomenclature, structural formula, molecular formula, yields and physical properties were listed in Table (2-15).

2.3.28. Synthesis of Pyrimidine derivatives [XXVIII] a,b



[XXVIII]a,b

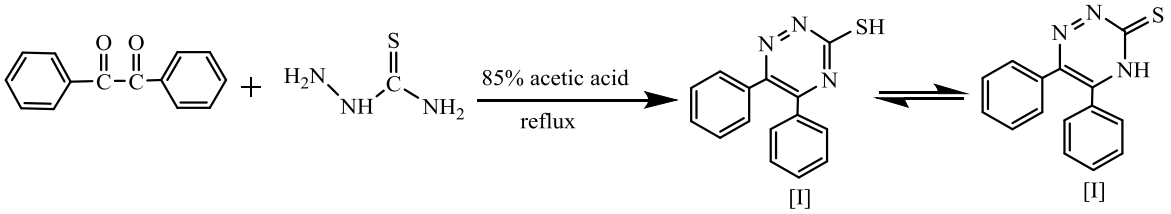
X= H , N(Me)2

A mixture of thiourea derivatives [XXIX] a,d, (0.001mol), diethyl malonate (0.0064g, 0.002 mol) and anhydrouse sodium carbonate (0.05g , 0.0024 mol) in dry benzene 5mL was refluxed for 10 hrs[(136)]. The reaction mixture was cooled and poured on to ice water and filtered off, dried and purified from wishing ether. The nomenclature, structural formula, molecular formula, yields and physical properties were listed in Table (2-15).

3.1. Results and Discussion

3.1.1.preparation and characterization of 5,6-diphenyl-1,2,4-triazine-3-thiol [I].

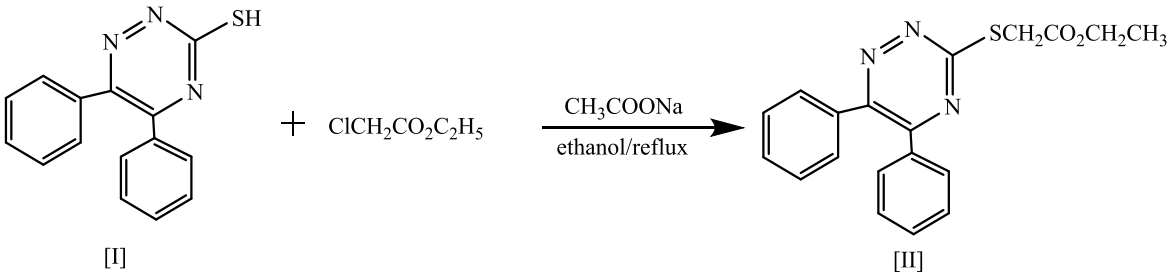
The triazine compound [I] was prepared from the reaction of equimolar of benzil and thiosmecarbazid in 85% acetic acid by the ring closure reaction (225)



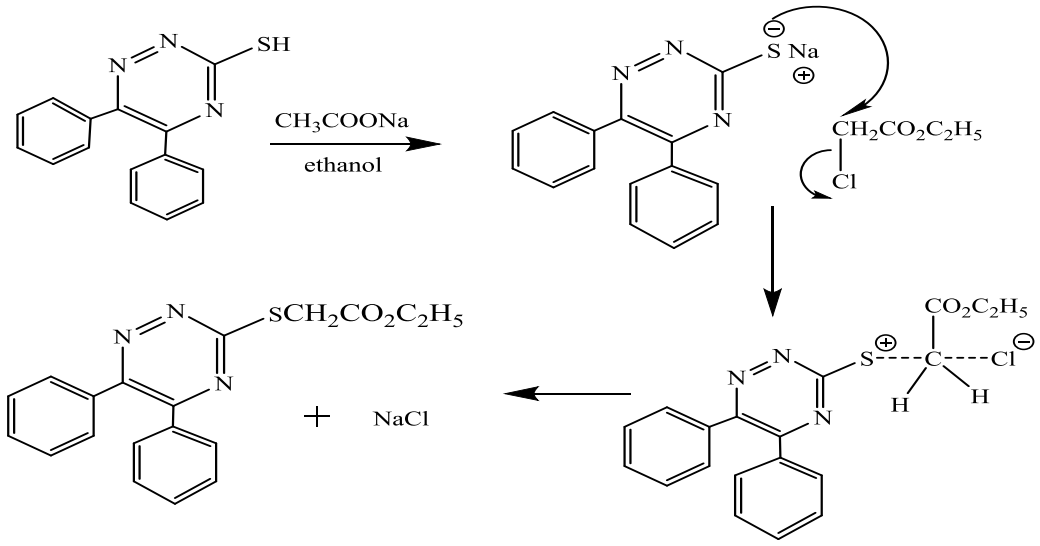
The structure of triazine was characterized by melting point and FTIR spectrum, Figure (3-1) . This Figure showed the disappearance of absorption bands of (C=O) and (OH) groups and other peaks such as NH_2 groups of the starting materials together with the appearance of new absorption stretching bands due to C=S at (1190) cm^{-1}, N=N appeared at 1554cm^{-1}, and the C=N stretching appeared at 1662 cm^{-1}.

3.1.2. Synthesis and characterization of ethyl 2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio) acetate [II].

The ester compound [II] was synthesized by refluxed a mixture of compound[I], [225] chloro ethyl acetate and fused sodium acetate in ethanol.



This compound was synthesized according to the SN_2 mechanism as in Scheme (3-1).



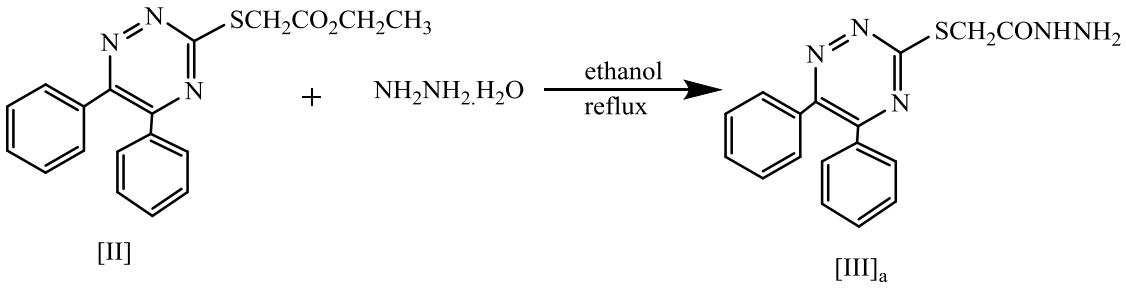
Scheme (3-1)

The ester compound [II] was charecteized by FTIR and ^{1}HNMR spectroscopy. The FTIR spectrum, showed absorption stretching bands at 1732 cm^{-1} due to stretching vibration band of the (C=O) for ester group, besides to the disappearance stretching band of (C=S) group with appearance of stretching band for C-S at 717 cm^{-1}, Figure (3-2)

^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of ester compound [II], Figure (3-3) showed many signals in the region δ(7.35-7.95) ppm that could be attributed to the ten aromatic protons, besides to a singlet signal at δ 4.23 ppm for two protons SCH_2 group. A quartet signal at δ (4.09-4.13) ppm due to two protons of $CO\underline{CH_2}CH_3$. Finally a triplet signal at δ 1.13-1.18 ppm could be attributed to the three protons of CH_3 group.

3.1.3. Synthesis and characterization of 2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio) acetohydrazide[III]$_a$ and 3-hydrazineyl-5,6-diphenyl-1,2,4-triazine [III]$_b$.

The condensation of ester[II] with hydrazine hydrate in ethanol led to formation acorresponding acid hydrazide [III]$_a$.

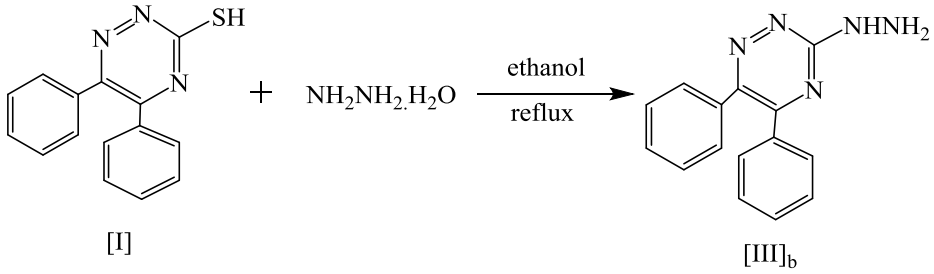


[II] [III]$_a$

The compound [III]$_a$ was characterized by FTIR and ^{1}HNMR spectroscopy. The FTIR spectrum of compound[III]$_a$, showed new absorption bands at(3321 -3215) cm^{-1} due to stretching (asym. and sym.) of NH_2 and NH groups and a good stretching vibration band for (C=O) of amide group at 1629 cm^{-1}, Figure (3-4).

^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of acid hydrazide [III]$_a$, showed a signal at δ8.7 ppm due to NH protons of hydrazide moiety, Figure (3- 5) The spectrum also showed a multiple signal in the region δ(7.21-7.45) ppm that could be attributed to the ten aromatic protons. A singlet signal appeared at δ 5.3ppm for two protons of NH_2 group besides to a singlet signal at δ4.0 ppm for two protons of SCH_2 group.

While, The compound $[III]_b$ was synthesized by the reaction of compound[I], in ethanol with 80% hydrazine hydrate.



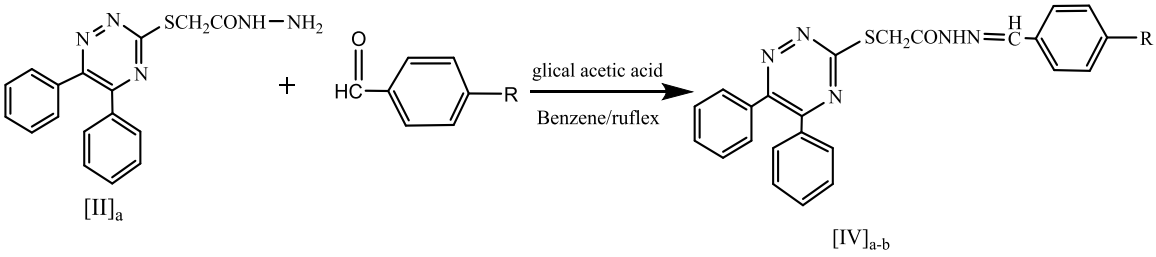
[I] $[III]_b$

The structure of the compound $[III]_b$ was studied by FTIR and ^{1}HNMR spectroscopy. The FTIR spectrum, showed the disappearance of absorption band of the C=S with appearance new absorption stretching bands in the region (3325-3142) of NH_2 and NH groups(asym. and sym.), Figure(3-6).

The ^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of compound $[II]_b$, showed a singlet signal at δ10.21 ppm could be attributed to a proton of NH group, many signals in the region δ(7.20-7.46) ppm for ten aromatic protons**,** Figure (3-7) .Also the spectrum showed a good signal at δ 6.15ppm for two protons of NH_2 group.

3.1.4. Synthesis and characterization of Schiff base compounds of triazines $[IV]_{a-g}$.

Schiff bases$[IV]_{a-d}$ were obtained from the reaction of one mole of acid hydrazide $[III]_a$ with one mole of different aromatic aldehyde in glacial acetic acid and benzene.



$[II]_a$ $[IV]_{a-b}$

R= H,CH_3, $N(Me)_2$, m-NO_2

The Schiff bases , were identified by FTIR and ^{1}HNMR spectra (of some of them) .

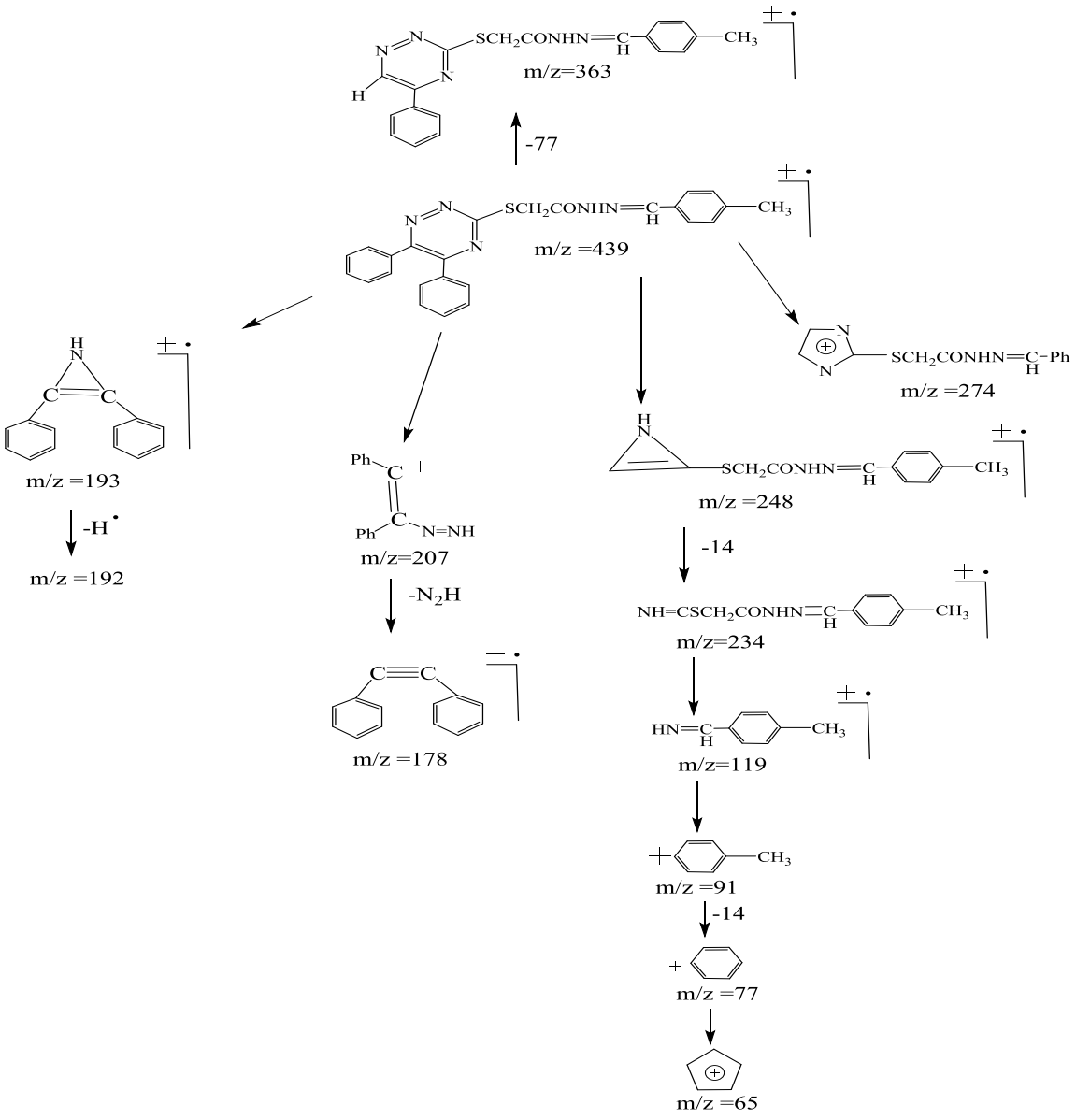
FTIR spectrum of compound $[IV]_a$, showed the disappearance of absorption bands due to NH_2 group together with the appearance of new absorption band at 1612 cm^{-1} which is assigned to imine group (C=N) stretching, Figure(3-8). The other FTIR data of functional groups which are characteristic of these compounds were given in Table (3-1) .

The ^{1}HNMR spectrum(in DMSO-d_6 as a solvent) of compound $[IV]_a$, showed a sharp signal at δ 11. 96 ppm could be attributed to one proton of NH group of (NHN=C-) moiety, a sharp signal at δ 8.72 ppm due to a proton of azomethine groups (CH=N), Figure (3-9). Many signals in the region δ(7.37-7.90)ppm for fifteen aromatic protons . The spectrum did not showed any signal for SCH_2 protons that may be related to the toutomer state between ($SCH_2CO \rightleftharpoons SCH=COH$), that indicated by appearance a good singlet signal at δ 8.30ppm and a singlet at δ 7.16ppm and gave good evidence to the presence OH and CH= group of toutomers .

The ^{1}HNMR spectrum(in DMSO-d_6 as a solvent) of compound $[IV]_b$, showed a sharp signal at δ 11.89 ppm could be attributed to one proton of NH group of (NHN=C-) moiety, a sharp signal at δ 8.26 ppm due to a proton of azomethine groups (CH=N), Figure (3-10). Many signals in the region δ(7.25-7.75)ppm for fourteen aromatic protons. The spectrum did not showed any signal for SCH_2 protons that may be related to the toutomer state between ($SCH_2CO \rightleftharpoons SCH=COH$) and that indicated by appearance a

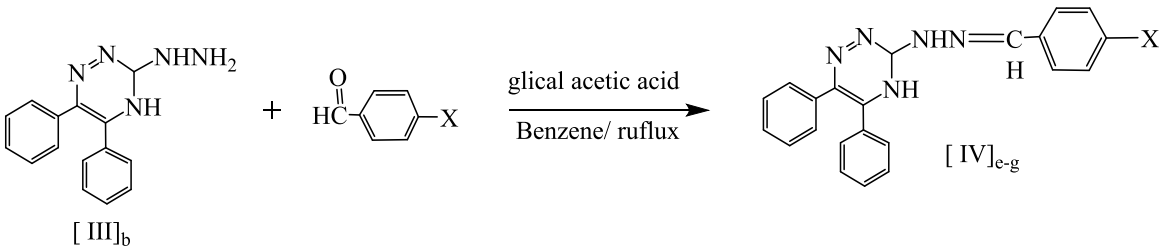
good singlet signal at δ 8.67ppm and a singlet at δ7.12ppm which are give good evidence to the presence OH and CH= group of toutomers .Finally a sharp singlet signal appeared δ 2.35ppm for three protons of CH_3 group.

The mass spectrum of compound $[IV]_b$, showed the base peak at m/z = 178 and the peaks at (m/z =274,248, 207, 193,178) were give good evidence to presence the 1,2,4 triazine ring, Figure (3-11) . In addition the two peaks at (77, 65) refers to presence the benzene ring[232]. The most characteristic fragments of this compound were illustrated in Scheme(3-2).



Scheme (3-2) fragmentation pattern of compound $[IV]_b$

While the Schiff bases$[III]_{e-g}$ were obtained from the reaction of one mole of compound $[III]_b$ with one mole of different aromatic aldehyde in benzene and glacial acetic acid.



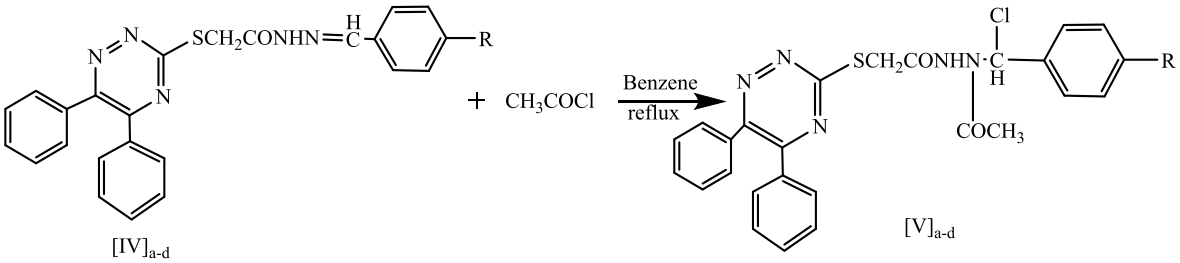
[III]b

X=H,CH_3, N(Me) 2

These compounds were characterization by FTIR spectroscopy .FTIR spectrum, Figure (3-12) of compounds $[IV]_f$, showed the disappearance of absorption bands due to NH_2 group together with the appearance of new absorption band at (1625) cm^{-1} which is assigned to imine (C=N) stretching. The other FTIR data of functional groups which are characteristic of these compounds were given in Table (3-1) .

3.1.5. Synthesis and characterization of N-actyl dervitives$[V]_{a-g}$

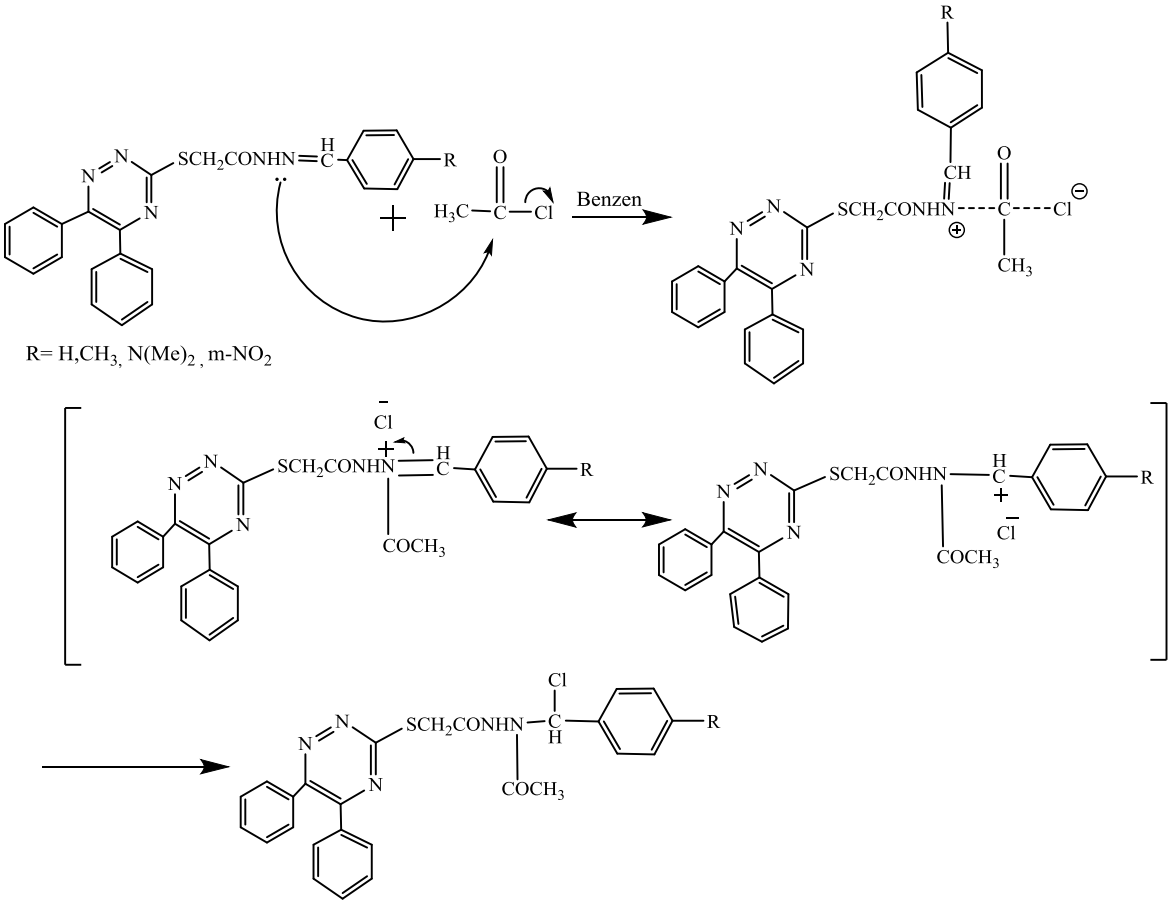
The reaction of one mole of Schiff base $[IV]_{a-d}$ in dry benzene, with one mole of acetyl chloride led to get N-actyl compounds$[V]_{a-d}$.



[IV]a-d [V]a-d

R= H,CH_3, $N(Me)_2$, m-NO_2

The mechanism [17] of this reaction may be outlined in scheme (3-3)



Scheme (3-3)

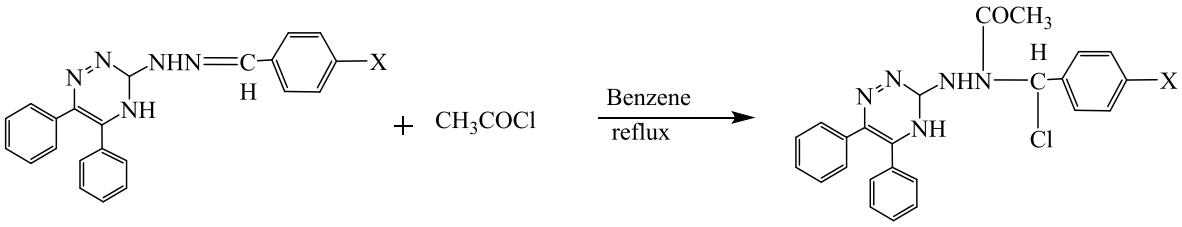
These compounds were identified by FTIR and ^{1}HNMR spectroscopy, the characteristic FTIR absorption bands of these compounds were listed in Table (3-2). The FTIR spectrum of compound $[V]_a$, was confirmed from the disappearance of stretching band due to C=N of Schiff bases and other peaks characterized of the starting materials with the appearance of stretching bands due to C=O and C-Cl at 1681 $cm^{-1}$and 744 cm^{-1} ,respectively , Figure (3-13).

The ^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of compound$[V]_a$, showed a singlet signal at δ 12.13 ppm could be attributed to a proton of (CONH) group, many signals in the region δ(7.39-7.78) ppm due to fifteen aromatic protons and CH-Cl proton, two singlet signal at δ8.31ppm

andδ7.18ppm for ($SCH_2CO \rightleftharpoons SCH=COH$) toutomers protons, a singlet signal at δ1.83ppm due to three protons of $CO\underline{CH_3}$ group, Figure (3-14).

The ^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of compound$[V]_b$, showed a singlet signal at δ 12.34 ppm could be attributed to a proton of (CONH) group, many signals in the region δ(7.65-7.78) ppm due to fourteen aromatic protons and CH-Cl proton, Figure (3-15).Three singlet signal at δ8.67ppm, δ7.08ppm and δ4.13 ppm for ($SCH_2CO \rightleftharpoons SCH=COH$) toutomers protons. Two singlet signals at δ2.37 ppm and δ2.18 ppm due to three protons of $PhCH_3$ and three protons of $COCH_3$, respectively.

While the N-acetyl compounds type$[V]_{e-g}$ were synthesized from the reaction of one mole of Schiff base $[IV]_{\mathbf{e-g}}$ with one mole acetyl chloride in dry benzene.



X=H,CH_3, $N(Me)_2$

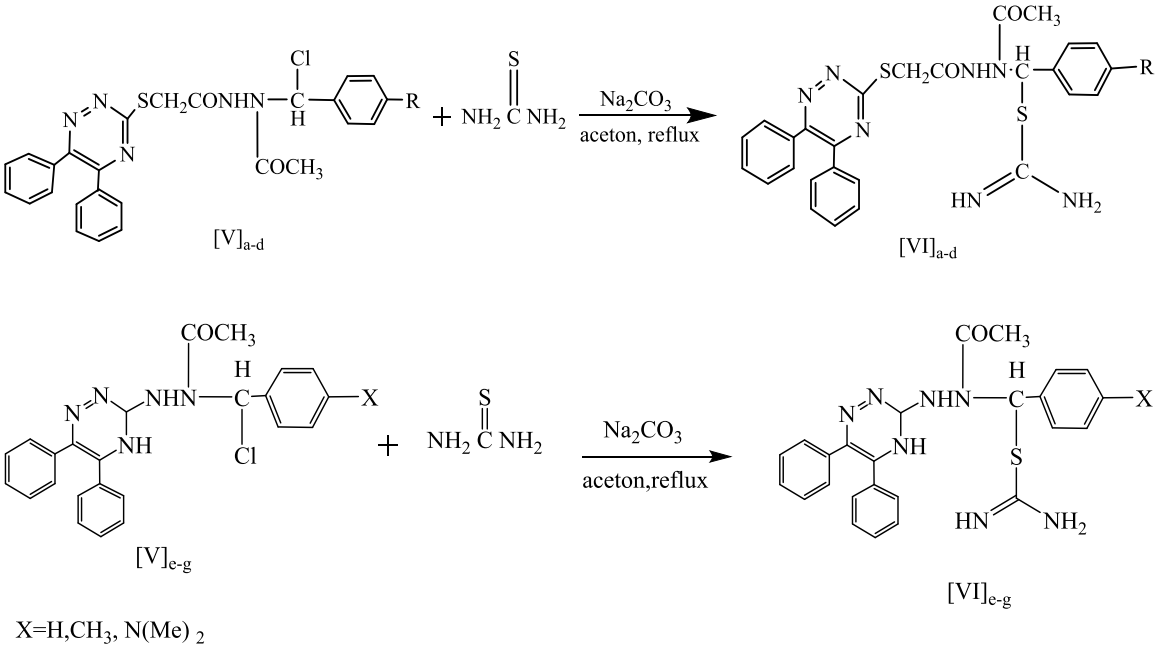
The characteristic FTIR absorption bands of these compounds were listed in Table (3-2), the FTIR spectrum of compound $[V]_g$, confirmed from the disappearance of stretching band due to C=N of Schiff bases and other peaks characterized of the starting materials with the appearance of new stretching band at 1645 cm^{-1} and 785 cm^{-1}due to C=O and C-Cl group, respectively, Figure(3-16).

The ^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of compound $[V]_f$, showed a singlet signal at δ 9.68 ppm could be attributed to a proton of (NH) group, many signals in the region δ(7.31-7.78) ppm duo to fourteen aromatic

protons and CH-Cl proton, Figure (3-17). Two singlet signals at δ2.38 ppm and δ1. 83 ppm due to three protons of $PhCH_3$ and three proton of $COCH_3$, respectively.

3.1.6. Synthesis and characterization of thiourea dervitives $[VI]_{a-g}$

When reacted one mole of N-actyl compounds$[V]_{a-g}$ with one mole of thiourea in Na_2CO_3 and acetone led to get thiourea compounds $[VI]_{a-g}$,as follows :-



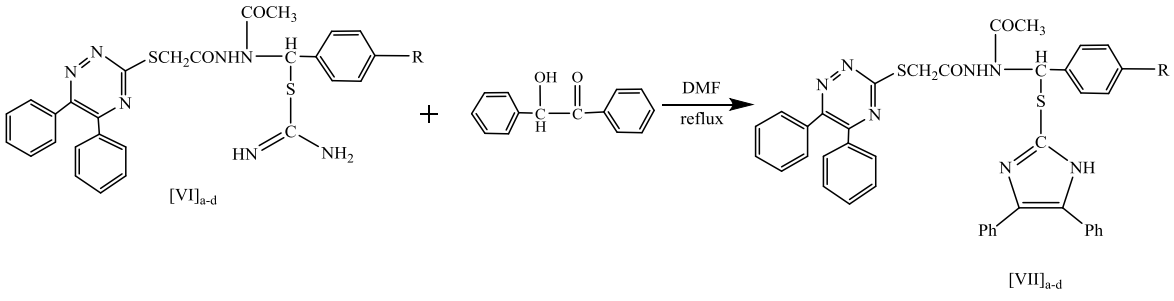
These compounds were identified by FTIR and ¹HNMR spectroscopy and these data give good evidence to formation the N-thiourea derivatives $[VI]_{a-g}$, the FTIR spectrum of compounds$[VI]_c$ and $[VI]_e$, Figure (3-18) and (3-19) respectively , showed the disappearance of stretching band due to of C-Cl of N-actyl compounds and other peaks characterized of the starting materials with the appearance of three bands in the region (3375-3159) and (3234-3205)cm^{-1} stretching band due to asym, sym of NH_2, NH groups respectively. The FTIR absorption bands data of these compounds $[VI]_{a-g}$ were listed in Table(3-3).

The ^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of compound $[VI]_a$, showed a singlet signal at δ12.05 ppm due to a proton of CONH, also showed a singlet signal at δ8.28 ppm, Figure (3-20).This could be attributed to one proton of (=NH)group, many signals appeared in the region δ (7.36-7.72) ppm due to fifteen aromatic protons and (CH-N) proton, three singlet signals at δ 4.88 ppm, δ 4.63ppm and δ 2.08 ppm could be attributed for protons of NH_2 ,SCH_2 and $COCH_3$, respectively.

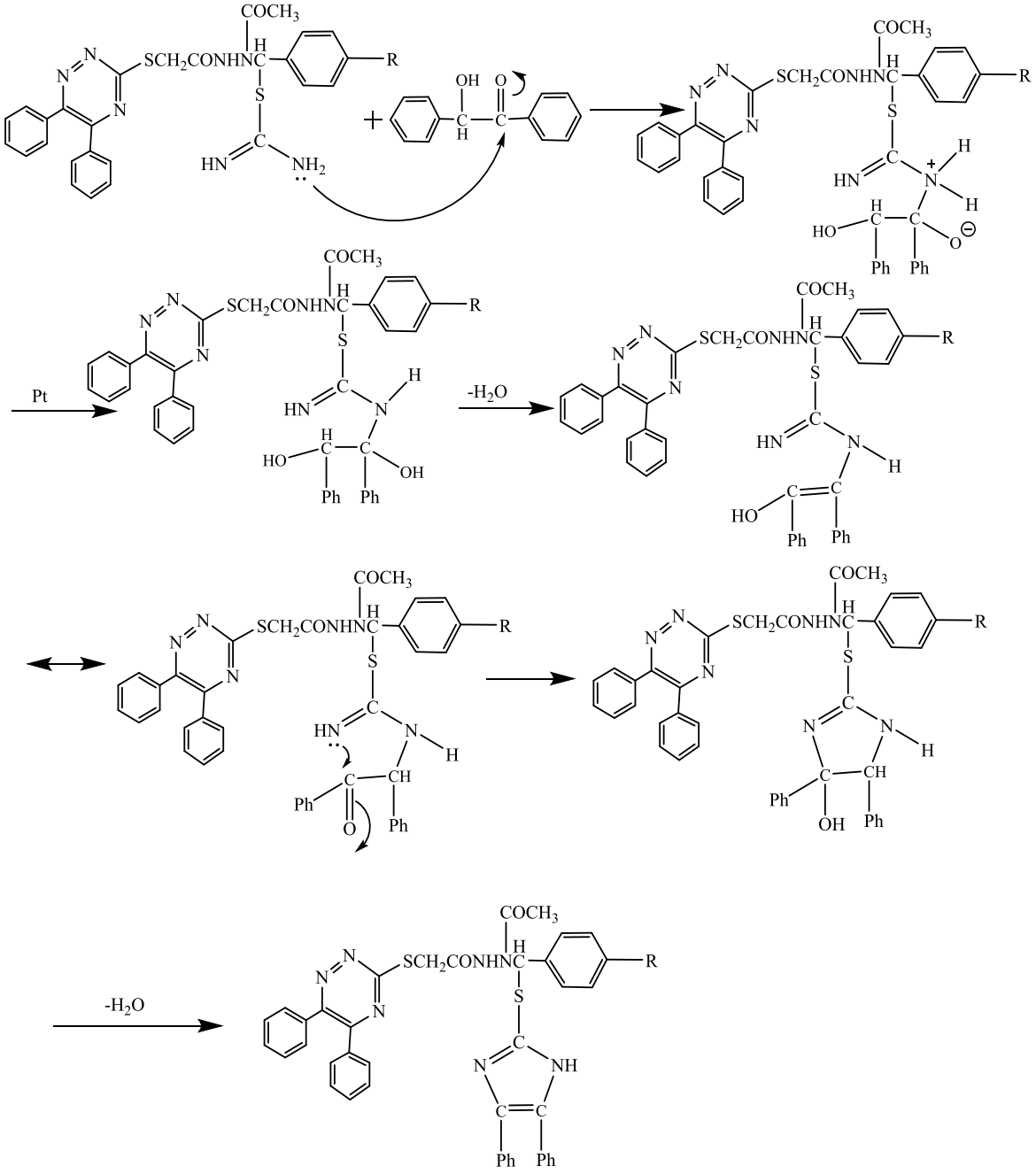
While, the ^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of compound $[V]_e$, showed a singlet signal at δ11.97 ppm due to a proton of NH, also showed a singlet signal at δ8.29 ppm, Figure (3-21).This could be attributed to proton of (=NH), many signals appeared in the region δ (7.39-7.75) ppm due to aromatic protons and(CH-N) proton, two singlet signals at δ 2.72 ppm and δ 2.20 ppm due to protons of NH_2 and $COCH_3$, respectively.

3.1.7. Synthesis and characterization of imidazol compounds $[VII]_{a-g}$

The imidazol compound $[VII]_{a-d}$ were synthesized by ring closure reaction of one mole of compound $[VI]_{a-d}$ with one mole of benzoin in DMF .



The suggested mechanism of this reaction [226] was outlined in Scheme (3-4).



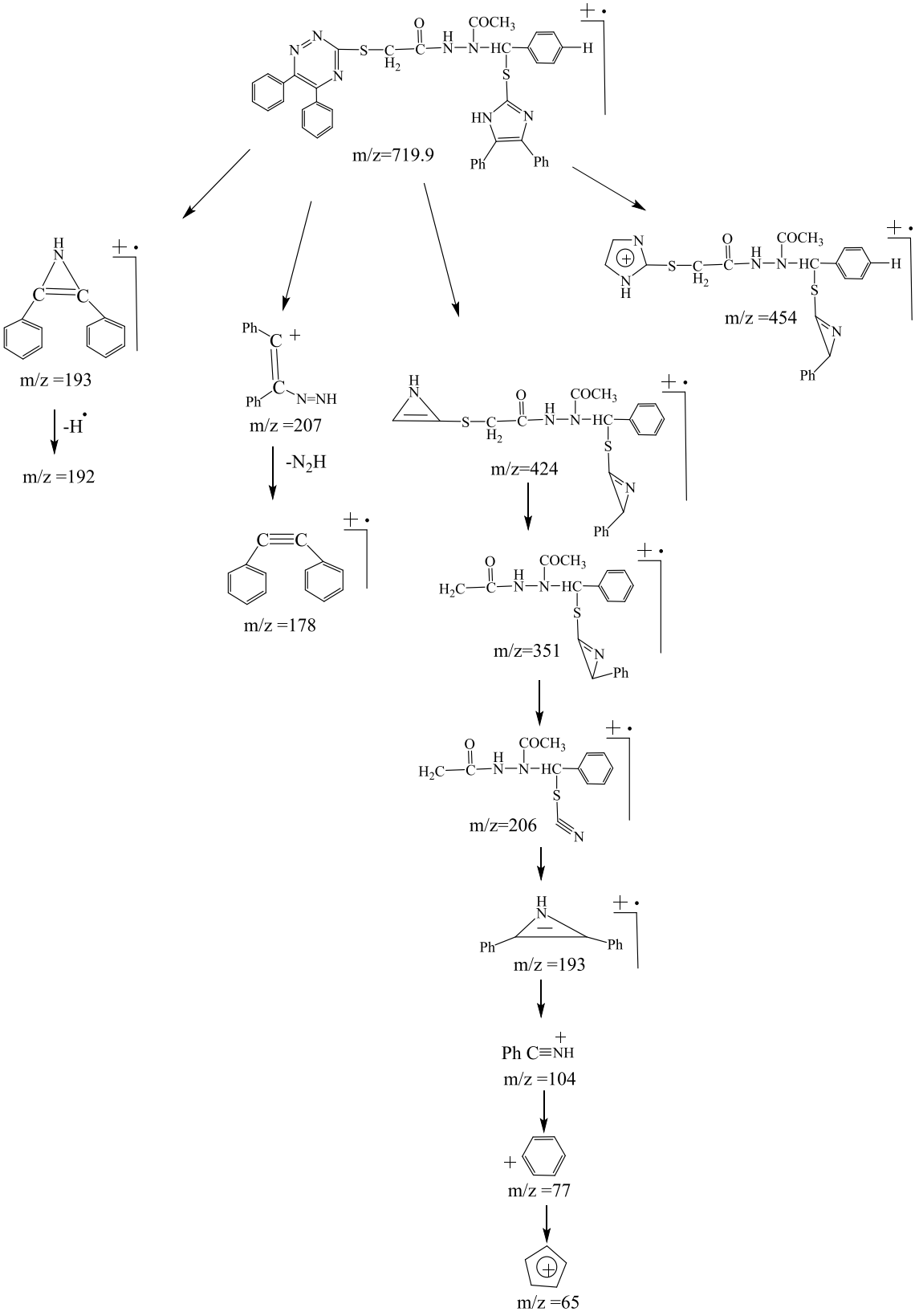
Scheme (3-4)

These compounds were identified from FTIR,¹HNMR and mass spectroscopy of some of them. The characteristic FTIR absorption bands of compound $[VII]_b$, confirmed from the appearance new band C=N at 1612 cm^{-1} and disappearance the band for NH_2 stretching, Figure (3-22). The FTIR absorption bands data of these compounds $[VII]_{a-d}$ were listed in Table (3-4).

The ^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of compound $[VII]_a$, showed a singlet signal at δ 11.97 ppm, Figure (3-23). This could be attributed to a proton of CONH group , also showed a singlet signal at δ8.00 ppm due to a proton of NH group in imidazol ring. Many signals in the region δ(7.23-7. 57) ppm for twenty five aromatic protons, the two signals at δ8.29 ppm and δ7.21ppm could be attributed to the two protons of OH and CH= groups (toutomer). The proton of CH-N group appeared at δ 6.03ppm , a singlet signals at δ 2.20 for three protons of $COCH_3$ group.

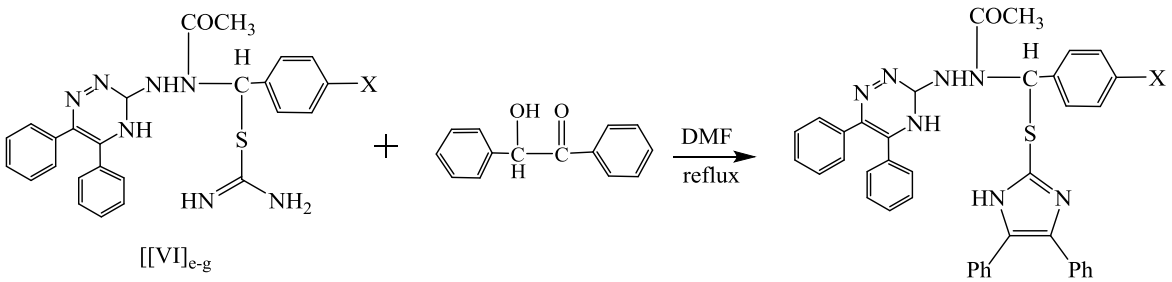
The ^{1}HNMR spectrum(in DMSO-d_6 as a solvent) of compound $[VII]_b$, showed a singlet signal at δ 11.90 ppm, Figure (3-24). This could be attributed to one proton of CONH group, also showed a singlet signal at δ8.00ppm due to a proton of NH group in imidazol ring. Many signals in the region δ(7.25-7.57)ppm for twenty four aromatic protons, the two singlet signals at δ8.67ppm and δ7.23ppm could be attributed to the two protons of OH and CH= groups (toutomer). The one proton of CH- N group appeared at δ 6.03ppm, also showed a singlet a signal at δ 2.25 ppm due to three proton of $PhCH_3$, a singlet signal at δ 2.03 ppm due to three protons of $COCH_3$ group,

The mass spectrum of compound $[VII]_a$, showed apparent ion at m/z =719.9 and a base peak at m/z =105, Figure (3-25). The characteristic fragmentation at (m/z = 207, 193,178) and m/z =(454,351,206,104) were related to the triazine and imidazole rings[232,233] , respectively, Scheme (3-5).



Scheme (3-5) fragmentation pattern of compound $[VII]_a$

The imidazol compound $[VII]_{e-g}$ were synthesized by the reaction of one mole of compound $[VI]_{e-g}$ with one mole of benzoin in DMF .



[[VI]e-g

X=H,CH3, N(Me) 2

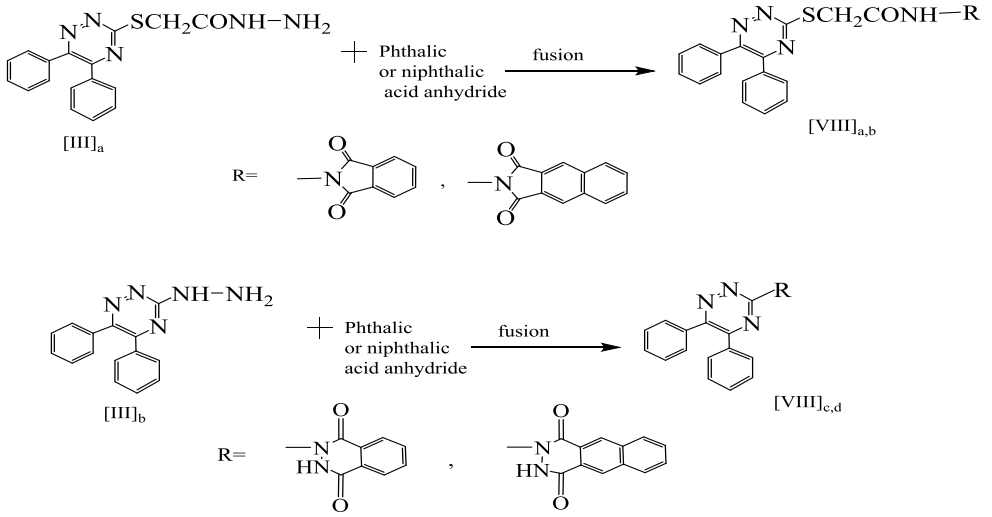
[VII]e-g

The characteristic FTIR absorption bands of compound $[VII]_e$, exhibited appearance new band stretching due to C=N at 1612 cm^{-1} and disappearance band of NH_2 stretching, Figure(3-26). The FTIR absorption bands data of these compounds $[VII]_{e-g}$ were listed in Table (3-4).

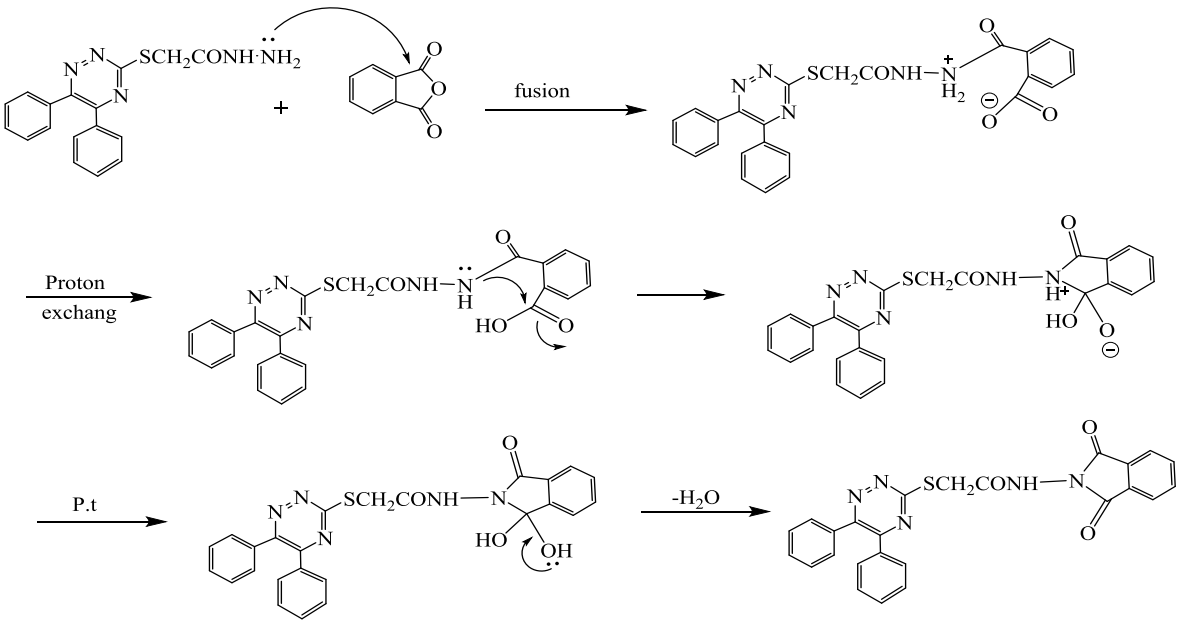
The ^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of compound $[VII]_e$, showed a singlet signal at δ11.95ppm, Figure (3-27). This could be attributed to a proton of NH group. Many signals in the region δ(7.24-7.73) ppm for twenty five aromatic protons. The two singlet signals at δ7.99ppm and δ7.97ppm could be attributed to the two protons of NH (exchange of imidazole ring), the one proton of CH-N group appeared at δ 6.02ppm, Also a singlet signals appeared at δ 2.18 ppm for three protons of $COCH_3$ group.

3.1.8. Synthesis and characterization the imides and phthalazine of triazine compounds $[VIII]_{a-d}$

The reaction of one mole of compound $[III]_{a,b}$ with one mole of phthalic or naphthalic acid anhydride under fusion give new cyclic imides $[VIII]_{a-d}$



The reaction was carried out through nucleophilic attack of amino group on carbon atom of one carbonyl group in phthalic or naphthalic acid anhydride, the mechanism [234] of this reaction may be outlined as follows in , Scheme (3-6).



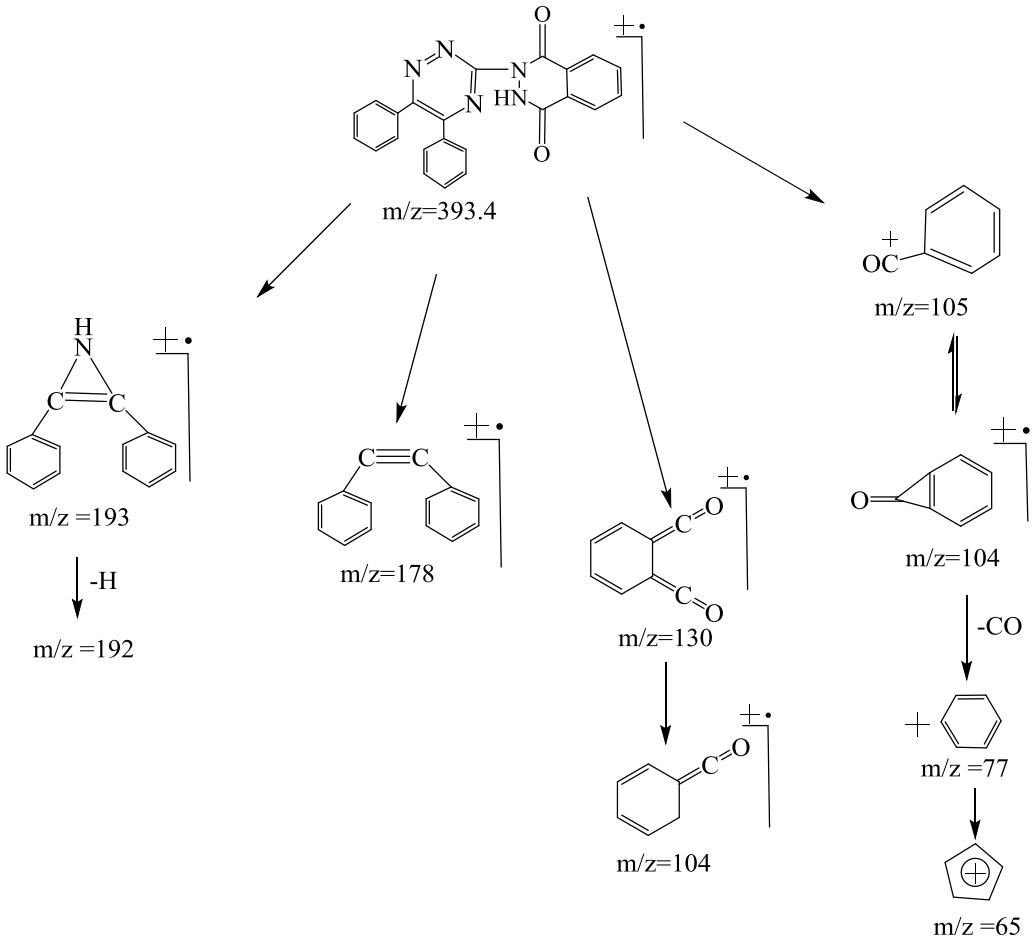
Scheme (3-6)

The structure of imides $[VIII]_{a-d}$ were studied by FTIR, ^{1}HNMR and mass spcetoscopy (of some of them), the FTIR spectrum of compound $[VIII]_a$, showed appearance new stretching bands around (1735- 1662) cm^{-1} which could be attributed to asymmetry and symmetry stretching vibration of the carbonyl group (cyclic imide) [235], Figure(3-28)

The ^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of imide compound $[VIII]_a$, Figure (3-29) showed a singlet signal at δ10.14ppm could be attributed to a proton of (CONH) group, many signals in the region δ(7.36-7.93) ppm for fourteen aromatic protons, a singlet signal at δ4.25ppm could be attributed for two protons of (SCH_2) group.

While, the FTIR spectrum of compound $[VIII]_c$, showed appearance new stretching bands at 1718 cm^{-1} and 1693 cm^{-1}, Figure (3-30). which could be attributed to asymmetry and symmetry stretching vibration of the carbonyl group (cyclic). The FTIR absorption bands data of these compounds $[VIII]_{a-d}$ were listed in Table (3-5).

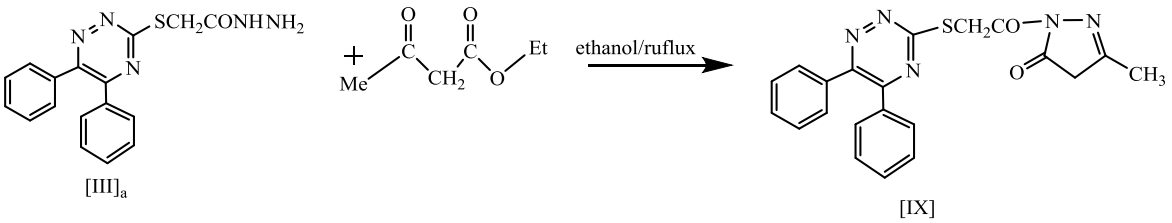
The mass spectrum of compound $[VIII]_c$. showed apparent ion at m/z=393.4 and a base peak at m/z = 178, Figure (3-31). The characteristic fragmentation [236] at (m/z = 193,178,104) were related to the triazine and phthalazine moiety, Scheme (3-7).



Scheme (3-7) fragmentation pattern of compound $[VIII]_c$

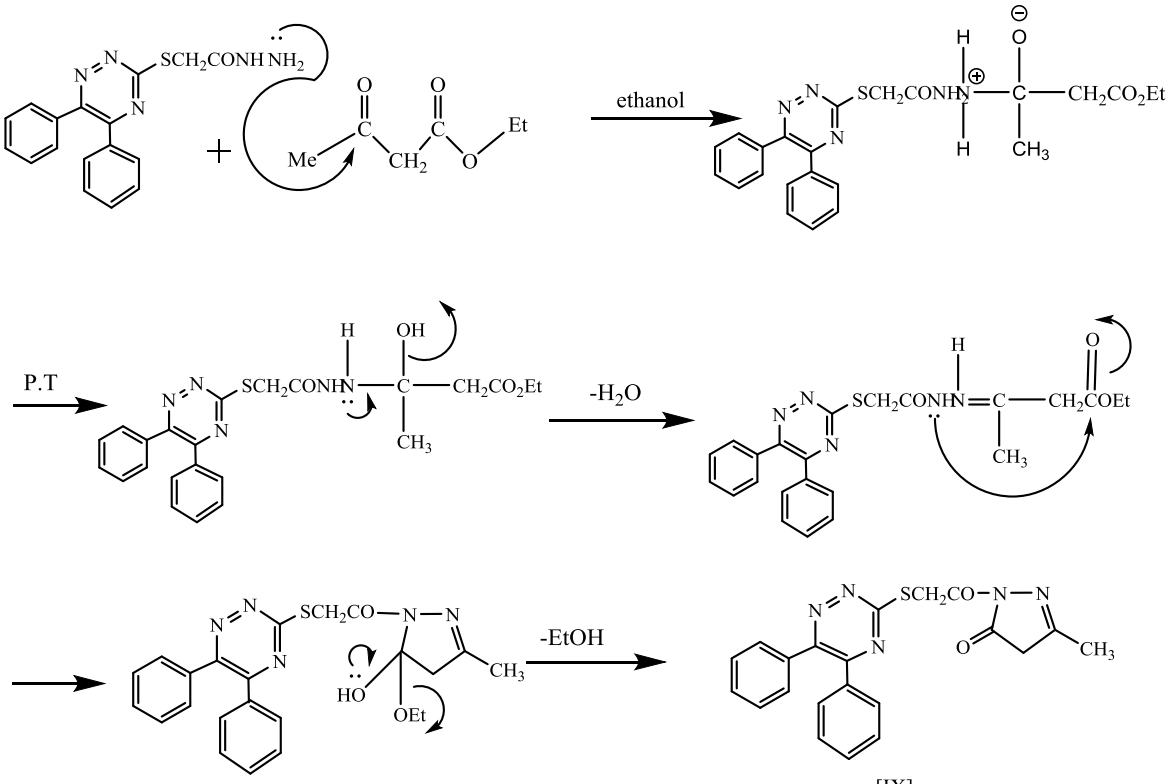
3.1.9. Synthesis and characterization of 2-(2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)acetyl)-5-methyl-2,4-dihydro-3H-pyrazol-3-one[IX].

The reflux of a mixture from one mole of acid hydrazide type $[III]_a$ and one mole of ethyl aceto acetate in absolute ethanol gave the new pyrazole compounds [IX].



$[III]_a$ [IX]

The path way mechanism[17] of this reaction may be outline in Scheme (3-8).



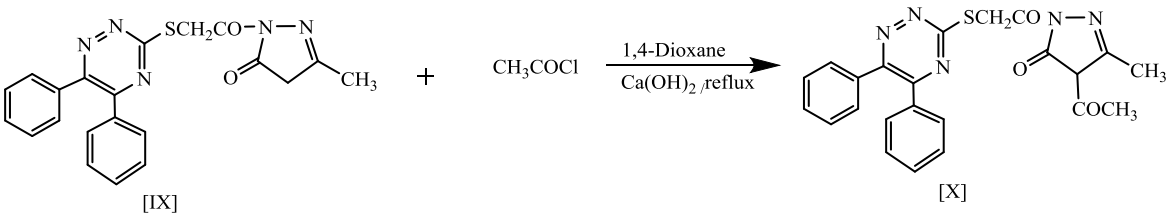
Scheme(3-8)

These compounds were identified by FTIR and ^{1}HNMR spectroscopy. FTIR spectrum of pyrazole compound showed a stretching band due to C=O group at1710 cm^{-1}, Figure (3-32). Also appearance new stretching absorption band at 1614 are due to C=N group of pyrazole ring.

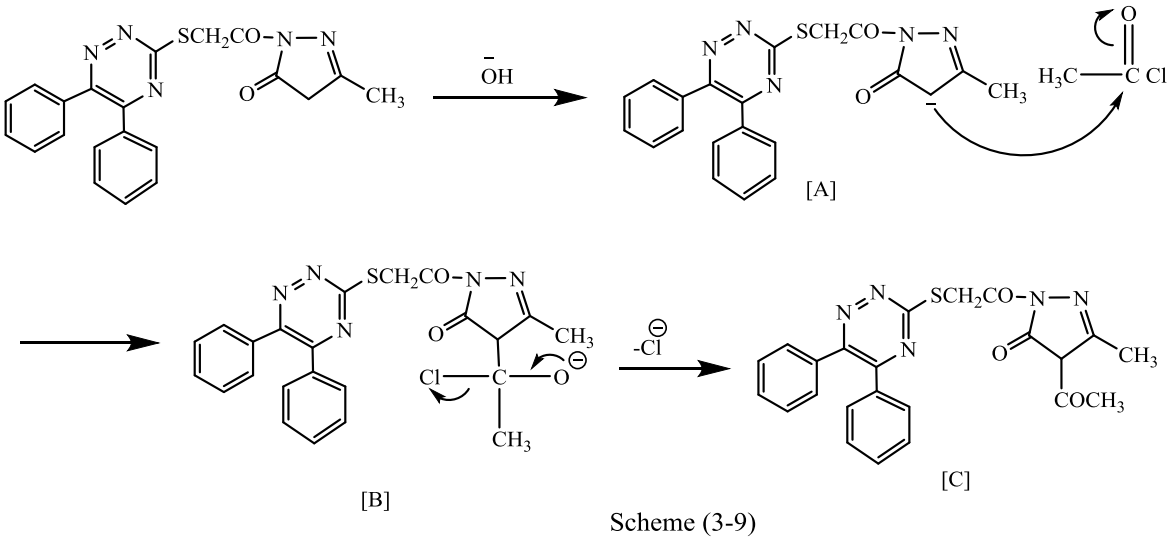
The ^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of pyrazole compound [IX], showed many signals in the region δ (7.44-7.54) ppm for ten aromatic protons, a singlet signal at δ4.21ppm, Figure (3-33).This could be attributed for two protons of (SCH_2) group, a singlet signal at δ 2.15 ppm due to two protons of CH_2 for pyrazole ring[237]. A singlet signal at δ1.3ppm may be related to three protons of CH_3 group at C_5 from pyrazole ring.

3.1.10. Synthesis and characterization of 4-acetyl-2-(((5,6-diphenyl-1,2,4-triazin-3-yl)thio)methyl)-5-methyl-2,4-dihydro-3H-pyrazol-3-one [X].

The compound [X] was synthesized by the reaction of one mole from pyrazole compound [IX] and one mole of acetyl chloride in the presence of one mole from calcium hydroxide in 1,4-dioxane.



The mechanism [17]of this reaction include carbanion intermediate [A] formation in the first step, followed by addition reaction of this carbanion to the carbon of carbonyl group to led intermediate [B] in second step, (Scheme 3-9). Finlly, elimination the Cl anion (as a good leaving group) to formation compound [C] .



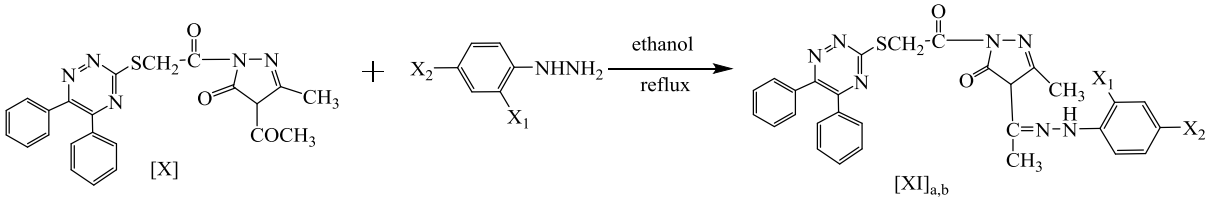
Scheme (3-9)

The synthesized compound is characterized by FTIR and ^{1}HNMR spectroscopy. The FTIR spectrum of 4-acetyl pyrazole[X], showed new stretching band for C=O (acetyl) at 1693 cm^{-1}, Figure(3-34).

The ^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of compound[X], showed many signals in the region δ(7.13-7. 43)ppm for ten aromatic protons, a singlet signal at δ 4.07ppm, Figure (3-35) .This could be attributed for two protons of (SCH_2) group. Three protons of $COCH_3$ group appeared at δ2.28ppm , a singlet signal at δ1.23ppm due to three protons of CH_3 group at C_5 from of pyrazole ring.

3.1.11. Synthesis and characterization of hydrazone compounds type $[XI]_{a,b}$

Aryl hydrazone derivatives $[XI]_{a,b}$ were synthesized by the reaction of one mole of compound [X] with one mole of phenyl hydrazine or 2,4- dinitro phenyl hydrazine in ethanol.



[X] $[XI]_{a,b}$

$[XI]_a$: X_1 ,X_2=H
$[XI]_b$:X_1, X_2=NO_2

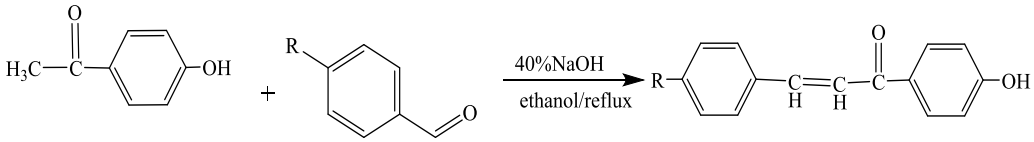
The structure of these compounds were studied by FTIR and ^{1}HNMR spectroscopy. The FTIR spectra of these two compounds, showed the disappearance of absorption band of the C=O(acetyl) with appearance a new absorption stretching bands a round 1614 cm^{-1} and 3319 cm^{-1} of C=N group and NH group, as in Figure(3-36) of compound$[XI]_b$.

^{1}HNMR (in DMSO-d_6 as a solvent) of compound $[XI]_b$, showed a singlet signal at δ10.83ppm, Figure (3-37).This could be attributed to a proton of NH group. Many signals in the region δ(7.18-7.70)ppm for thirteen aromatic protons, a singlet signal at δ5.05ppm could be attributed for two protons of (SCH_2) group, three protons of N=C-CH_3 group appeared at

δ2.13ppm, Finally a singlet signal at δ1.24ppm due to three protons of CH_3 group at C_5 from pyrazole ring .

3.1.12. Preparation and characterization of chalcones $[XII]_{a-c}$

Chalcones $[XII]_{a-c}$ are synthesized by Claisen-Schmidt condensation of one mole of 4 - hydroxy acetophenone and one mole of 4- substituted benzaldehyde in two mole of base catalyzed (NaOH) medium to yield the desire chalcones.

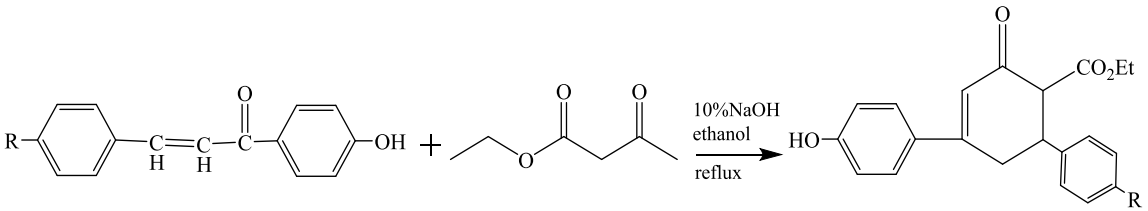


R= H , OCH_3 , CH_3 $[XII]_{a-c}$

The structural assignments of the chalcones $[XII]_{a-c}$ was studied by their FTIR spectroscopy. The FTIR spectrum of compound$[XII]_a$, indicated the appearance of a broad band for νO-H at (3296) cm^{-1}, with absorption sharp stretching bands at (1660)cm^{-1} and 1645 cm^{-1} due to C=O and C=C of chalcone, respectively, Figure(3-38). FTIR absorption bands data of these compounds $[XII]_{a-c}$ were listed in Table(3-6).

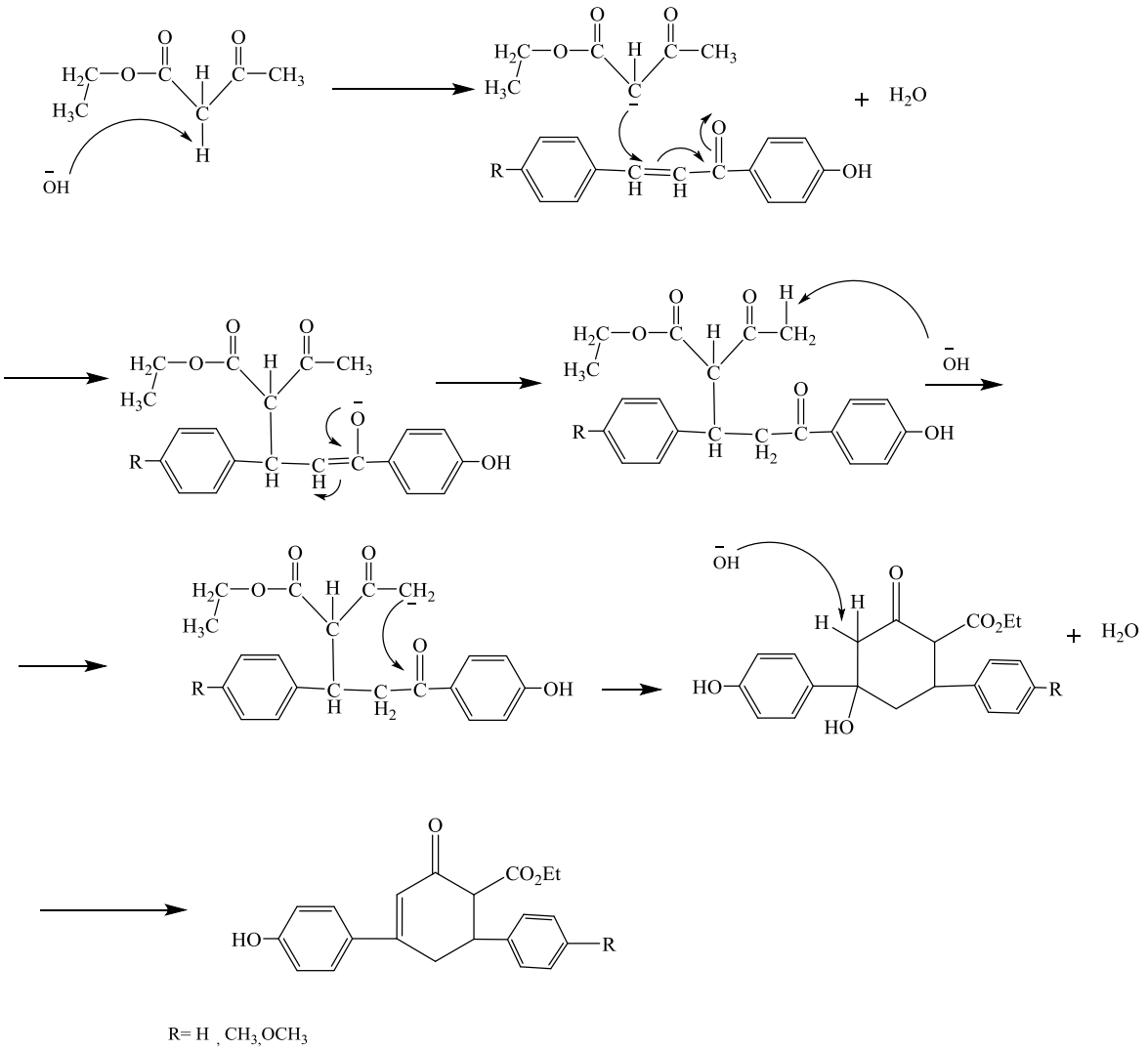
3.1.13. Preparation and characterization of cyclohexenone derivatives $[XIII]_{a-c}$

The compounds $[XIII]_{a-c}$ synthesized from the reaction of one mole from chalcone and one mole from ethyl acetoacetat in ethanol in the presence of 10% NaOH .



R= H , CH_3, OCH_3

The mechanism [229] of this reaction may be outlined as follows in Scheme (3-10)



Scheme(3-10)

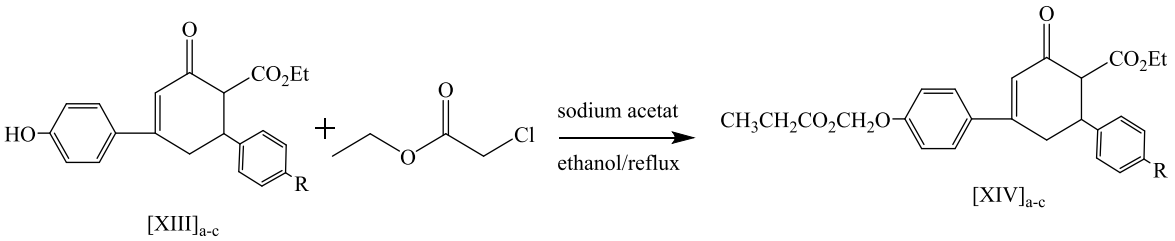
The structural assignments of the compound $[XIII]_{a-c}$ were identified by their FTIR and ^{1}HNMR spectral data. The FTIR spectrum of compound $[XIII]_a$, indicated a shifting of OH group and appearance two absorption stretching bands at (1714) $cm^{-1}$and (1645) cm^{-1} due to C=O stretching for ester and ketones, respectively, Figure (3-39). The FTIR absorption bands data of these compounds $[XIII]_{a-c}$ were listed in Table (3-6).

^{1}HNMR spectrum of compound $[XIII]_a$, showed the following characteristic chemical shift (DMSO-d_6 as a solvent), a broad signal at δ

10.10 ppm for a proton of OH group, Figure(3-40). Many signals appeared in the region δ (6.79-7.81) ppm for nine aromatic a protons, while appearance a singlet signal at δ 6.46 ppm could be attributed to a proton of C=CH of cyclohexenone. A doublet good signal at δ4.07 ppm due to one proton of cyclohexenone ring for $CHCO_2Et$, a quartet signal at δ (3.86-3.91) ppm due to two protons of $O\underline{CH_2}CH_3$. Also a quarteted at δ3.61 ppm could be related to one proton of <u>CH</u>Ph group, and a doublet signal at δ (3.59-3.64) ppm for two protons of $\underline{CH_2}$ of cyclohexenone ring. Finally a triplet signal at δ 0.94-0.97 ppm could be attributed to the three protons of CH_3 group.

3.1.14. Synthesis and characterization of new ester derivatives of cyclohexenone $[XIV]_{a-c}$

The reaction of one mole of compound$[XIII]_{a-c}$ with one mole of ethyl chloro acetate and three mole from fused sodium acetat in ethanol to give ester derivatives$[XIV]_{a-c}$



$[XIII]_{a-c}$ $[XIV]_{a-c}$

The new ester compounds $[XIV]_{a-c}$ were charecteized by FTIR and ^{1}HNMR spectroscopy. The FTIR spectrum of compound $[XIV]_a$ showed absorption band at 1737cm^{-1} due to a stretching vibration of the (C=O) for ester, a new stretching bands at 1240 cm^{-1} for C-O of ester group, Figure (3-41). Besides to the disappearance the bands of O-H. The FTIR absorption bands data of these compounds $[XIV]_{a-c}$ were listed in Table (3-7).

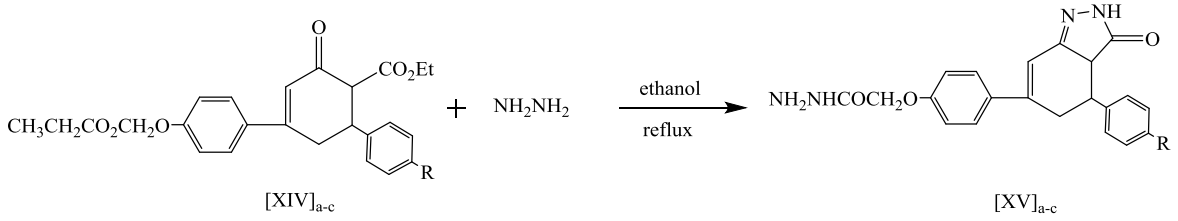
^{1}HNMR spectrum of compound$[XIV]_a$, showed the following characteristic chemical shift (DMSO-d_6 as a solvent), Figure (3-42). Many

signals appeared in the region δ (6.77-8.07) ppm for nine aromatic protons, while appearance singlet signal at δ 6.46 ppm could be attributed to a proton of C=CH of cyclohexenone. Also showed a doublet signal at δ 4.0 ppm due to one proton of $CHCO_2Et$ and a singlet signal at δ 3.78 ppm for two protons of $O\underline{CH_2}CO$ group, a quartet signal at δ (3.82-3.93) ppm due to four protons of two $O\underline{CH_2}CH_3$ groups. A quartet signal at δ3.54 ppm could be related to one proton of <u>CH</u>Ph group. A doublet signal δ (2.94-2.98) ppm for two protons for $\underline{CH_2}$ of cyclohexenone ring. Finally a triplet at δ 0.94-0.97 ppm could be attributed to the three protons of two CH_3 groups .

^{1}HNMR spectrum of compound $[XIV]_c$, showed the following characteristic chemical shift (DMSO-d_6 as a solvent), δ ppm: 6.86-8.07 (m,8H ,of eight aromatic protons); 6.45 (s,1H, C=CH); 4.0 (s, 1H,$CHCO_2Et$); 3.85 -3.70 (m, 9H , $2O\underline{CH_2}$, OCH_2CO and OCH_3); 3.7 (d,1H,<u>CH</u>CO_2); 3.60 (q, 1H, , <u>CH</u>Ph); 2.9 (d,2H, $\underline{CH_2}$ of cyclohexenone ring); 0.94-0.97 (t,3H,CH_3), Figure (3-43).

3.1.15. Synthesis and characterization of indazol derivative $[XV]_{a-c}$.

The indazol derivatives $[XV]_{a-c}$were synthesized by the reaction of one mole of compounds $[XV]_{a-c}$ with excess of 98% hydrazine hydrate in ethanol.



$[XIV]_{a-c}$ $[XV]_{a-c}$

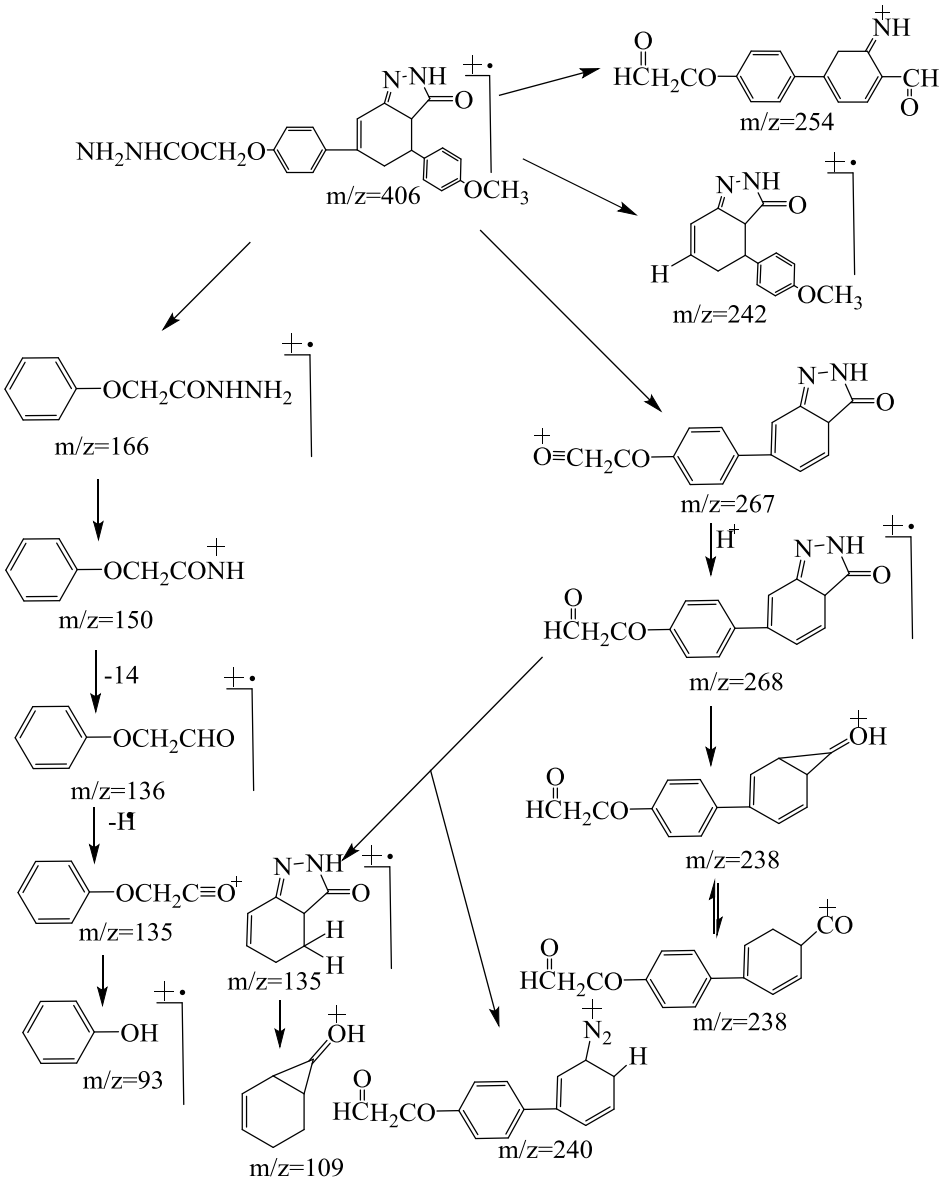
The compounds $[XV]_{a-c}$ were characterized using FTIR, ^{1}HNMR and mass spectroscopy, the FTIR of compound $[XV]_b$, showed new absorption stretching bands in the region (3331- 3184) cm^{-1} due to (NH and NH_2) groups and at1662 cm^{-1} for (C=O) of amide group for hydrazide moiety, Figure(3-44). Also the spectrum showed a stretching band at 1640 cm^{-1} for C=N of

indazole ring. The FTIR absorption bands data of these compounds $[XV]_{a-c}$ were listed in Table (3-7).

^{1}HNMR spectrum of compound $[XV]_a$, showed the following characteristic chemical shift (DMSO-d_6 as a solvent), a singlet signal at δ 9.70 ppm due to one proton of NH for indazole ring), Figure(3-45). Many signals appeared in the region δ (6.78-7.38) ppm for nine aromatic protons and CONH proton, while appearance singlet signal at δ 6.66 ppm could be attributed to a proton of C=CH of cyclohexenone ring. Also showed a singlet signal at δ 4.2 ppm for two protons of O$\underline{CH_2}$CO group , signal at δ 3.57 ppm due to of NH_2 and CH at fused ring , a quartet signal at δ3.2 ppm could be related to one proton of $\underline{CH}$Ph group. A doublet signal δ2.9ppm for two protons of $\underline{CH_2}$ for cyclohexenone ring.

^{1}HNMR spectrum of compound $[XVII]_c$, showed the following characteristic chemical shift (DMSO-d_6 as a solvent) , δ ppm: 9.54 (s,1H, NH of indazole ring); 9.19(s,1H, CONH); 6.67-7.74(m, 8H, aromatic protons); 6.59 (s,1H, C=CH); 4.0(s, 2H, O$\underline{CH_2}$CO); 3.67-3.73 (signals of 3H for NH_2 and CH at fused ring); 3.2 (q, 1H, $\underline{CH}$Ph) ; 2.85 (d,2H, $\underline{CH_2}$ of ring), Figure(3-46).

The mass spectrum of compound $[XVII]_c$, exhibited a molecular ion at m/z=405.5,also showed a characteristic fragmentation of indazole moiety at m/z =(254,238,242,240 and 109), Figure(3-47). Besides to appeared many peaks at m/z=(268,166,150,135 and 94) to give a good evidence for the formation this compound .



Scheme (3-11) fragmentation pattern of compound $[XVII]_c$

3.1.16. Synthesis and characterization the new pyrazol derivatives of indazoles[XVI] $_{a-c}$.

The new pyrazole derivatives $[XVI]_{a-c}$ were synthesized from heating under reflux a mixture of one mole of acid hydrazides $[XV]_{a-c}$ and one mole of ethyl aceto acetate in absolute ethanol.

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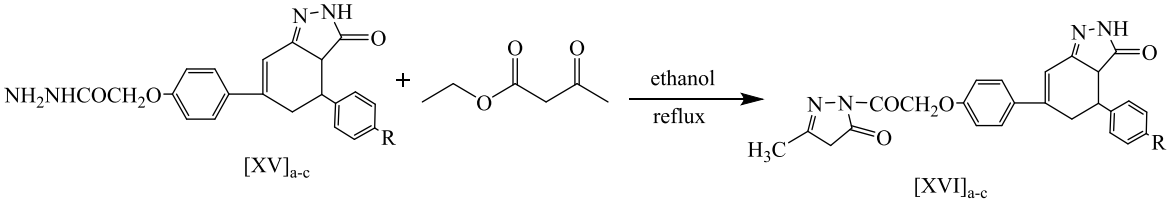


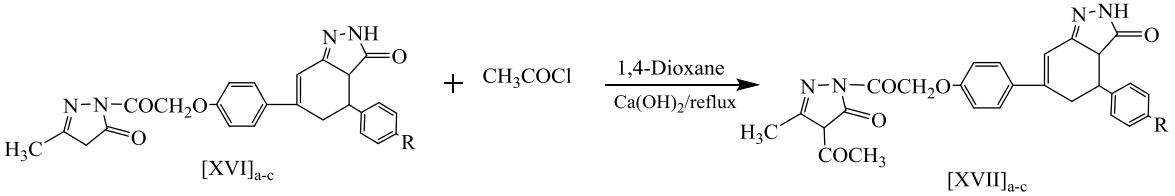
R= H , CH_3 ,OCH_3

These compounds were identified by FTIR and ^{1}HNMR spectroscopy. FTIR spectrum of compound $[XVI]_a$, showed new stretching band due to C=O group (which is connected with pyrazole ring) at 1720cm^{-1}, Figure(3-48). It also appearance of new absorption stretching band due to C=N group (endocyclic) of pyrazole ring at (1645) cm^{-1}. The FTIR absorption bands data of these compounds $[XV]_{a-c}$ were listed in Table (3-8).

^{1}HNMR spectrum of compound $[XVI]_a$, showed the following characteristic chemical shift (DMSO-d_6 as a solvent) : a singlet signal at δ 10.79 ppm due to one proton for NH of indazole ring, Figure(3-49). Many signals appeared in the region δ 6.68-7.57 ppm for nine aromatic protons, while appearance a singlet signal at δ 6.60 ppm could be attributed to a proton of C=CH of cyclohexenone. Also showed a singlet signal at δ 4.16 ppm due to two protons of O$\underline{CH_2}$CO group, a doublet signal at δ 3.98 ppm due to of CH at fused ring, a quartet signal at δ3.06-3.10 ppm could be related to proton of $\underline{CH}$Ph group. Also a singlet signal at δ 2.89ppm may be attributed for two proton of CH_2 of pyrazole ring, and a doublet signal at δ 2.15 ppm for two protons of $\underline{CH_2}$ of cyclohexenone ring. A singlet signal at δ 1.74 ppm for three protons of CH_3 group at C_3 of pyrazole ring.

3.1.17. Synthesis and characterization of 6-(4-(2-(4-acetyl-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-2-oxoethoxy)phenyl)-4-(4-substituted phenyl)-2,3a,4,5-tetrahydro-3H-indazol-3-one[XVII]$_{a-c}$

The compounds [XVII]$_{a-c}$ were synthesized by the reaction of one mole from pyrazole derivatives [XVII]$_{a-c}$ and one mole of acetyl chloride in 1,4-dioxane in presence of one mole calcium hydroxide.



R= H , CH_3, OCH_3

The synthesized compounds are characterized by FTIR and ^{1}HNMR spectroscopy. The FTIR spectrum of 4- acetyl pyrazoles [XVII]$_a$, showed new stretching band due to C=O (acetyl) besides to other carbonyl, Figure(3-50). The FTIR absorption bands data of these compounds [XVII]$_{a-c}$ were listed in Table (3-8).

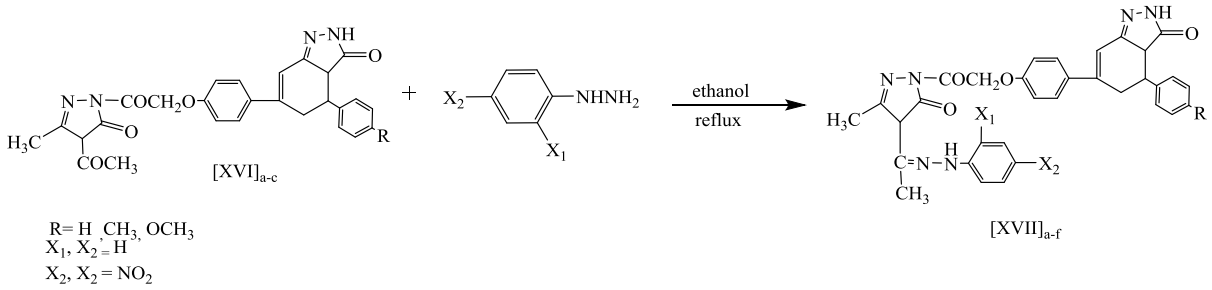
^{1}HNMR spectrum of compound [XVII]$_a$, showed the following characteristic chemical shift (DMSO-d_6 as a solvent), a singlet signal at δ 10. 94 ppm due to a proton of NH of indazole ring, Figure(3-51). Multiplet signals appeared in the region δ 6.75-7.63 ppm for nine aromatic protons, while a singlet signal at δ 6.58 ppm could be attributed to a proton of C=CH of cyclohexenone. Also showed a singlet signal at δ 4.15 ppm due to two protons of O$\underline{CH_2}$CO group, a doublet signal at δ 3.99 ppm due to one protons of CH at fused ring,. A quartet signal at δ3.57-3.59 ppm could be related to one proton of $\underline{CH}$Ph group. A doublet signal δ2.73ppm for two protons of $\underline{CH_2}$ of cyclohexenone ring. Finally, two singlet signals at δ 2.27ppm and δ 1.23ppm could be attributed to three protons of CO$\underline{CH_3}$ and

three protons of CH_3 group at C_3 of pyrazole ring, respectively. While the proton of pyrazole ring appeared at δ 2.14ppm as asinglet signal

Also the ^{1}HNMR spectrum of compound $[XVII]_b$, showed the following characteristic chemical shift (DMSO-d_6 as a solvent) δ ppm: 9.97 (s,1H , NH of indazole ring); (6.81-7.40) (m,8H ,for eight aromatic protons); 6.84 (s,1H, C=CH) ; 4.15 (s, 2H, O$\underline{CH_2}$CO); 3.85 (d,1H of fused ring) ;3.77-3.82 (q, 1H, $\underline{CH}$Ph); 3.0 (d,2H, $\underline{CH_2}$ of pyrazole ring) ; 2.29 (d, 3H, $COCH_3$) ; 2.26(s,3H, Ph CH_3), 2.17 (s,1H,CH of pyrazol ring), 1.29(s,3H,CH_3 at C_3 of pyrazole ring), Figure(3-52) .

3.1.18. Synthesis and characterization the hydrazone compounds of indazoles $[XVIII]_{a-f}$

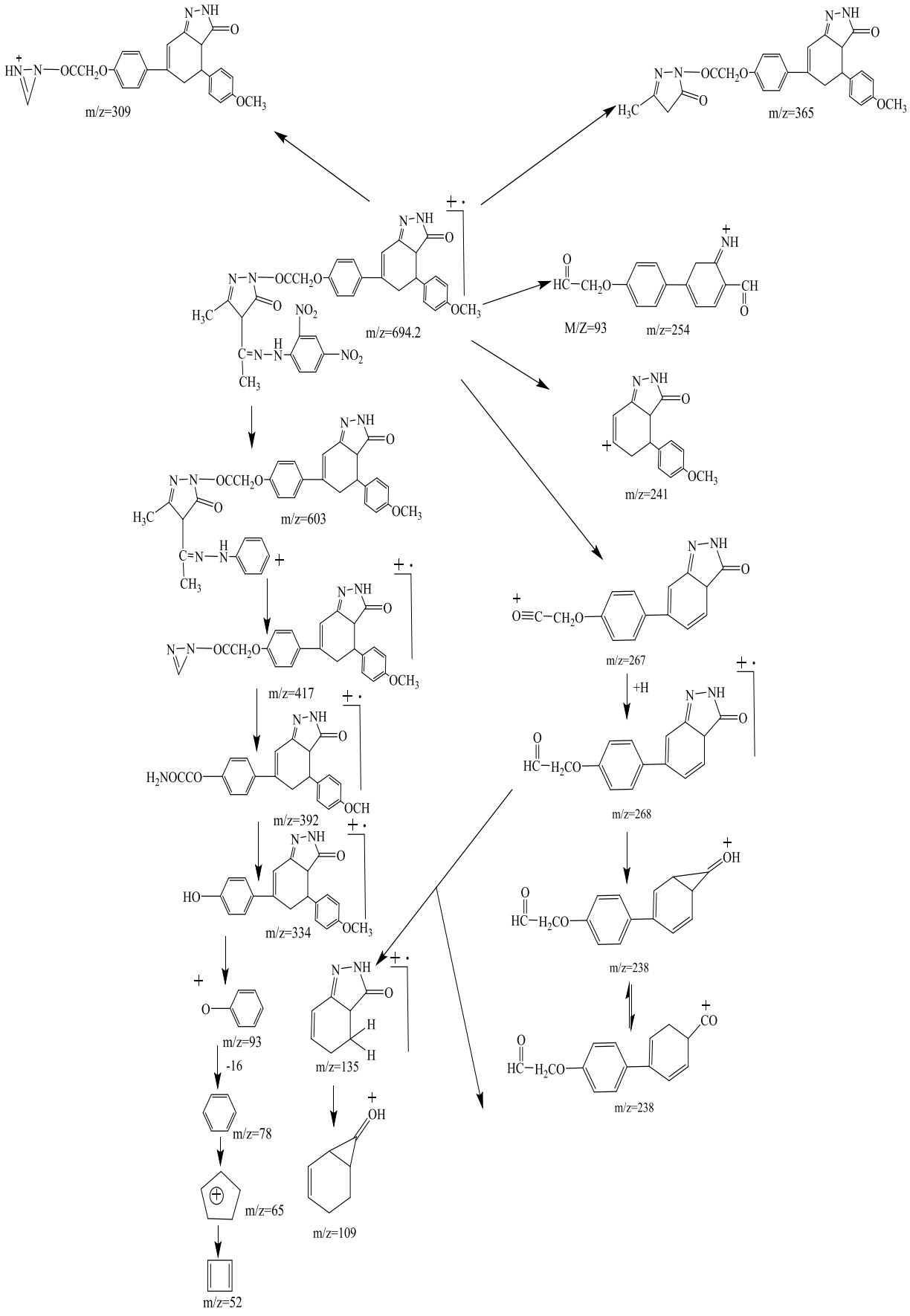
Aryl hydrazone derivatives type $[XVIII]_{a-f}$ were synthesized by the reaction of one mole of acetyl compounds$[XVII]_{a-c}$ with one mole of phenyl hydrazine or 2,4-dinitro phenyl hydrazine in ethanol.



The structure of these compounds were studied by FTIR , ^{1}HNMR and mass spectroscopy. The FTIR spectrum of compound$[XVII]_f$, showed the disappearance of absorption band of the C=O(acetyl group) with appearance a new absorption stretching bands of C=N group and NH group, Figure(3-53). The FTIR absorption bands data of these compounds $[XVII]_{a-f}$ were listed in Table (3-9).

^{1}HNMR spectrum of compound $[XVII]_d$, showed the following characteristic chemical shift (DMSO-d_6 as a solvent) :a singlet signal at δ 9.59 ppm and δ 9.25 ppm due to proton of NH of indazole ring and NH-N group, respectively, Figure(3-54). Many signals appeared in the region δ (6.74-7. 97) ppm for nine aromatic protons, while appearance a singlet signal at δ 6.70 ppm could be attributed to a proton of C=CH of cyclohexenone ring. Also showed a singlet signal at δ 4.16 ppm for two protons of O$\underline{CH_2}$CO group and a singlet signal at δ 1.91 ppm due to one proton of pyrazole ring. A doublet signal at δ 3.51ppm due to one proton of CH at fused ring, a quartet signal at δ2.98-3.04 ppm could be related to proton of $\underline{CH}$Ph group. Also showed a doublet signal δ2.68ppm for two protons $\underline{CH_2}$ of cyclohexenone ring, Finally two singlet signal at δ 2.26 ppm , and δ 1.23 ppm could be related to three protons of $CH_3C=N$ and three protons of CH_3 at C_3 of pyrazole ring, respectively.

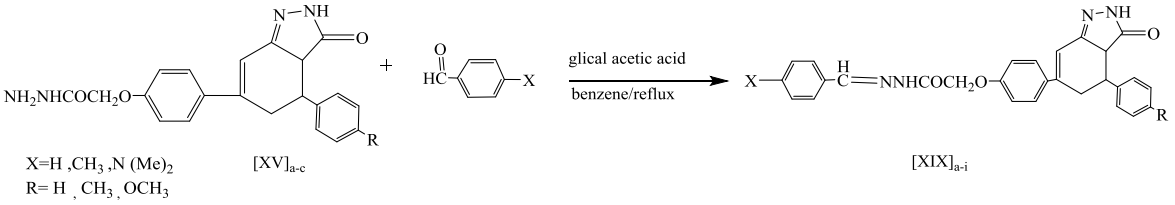
The mass spectrum of compound $[XVII]_f$, Figure(3-55) showed good characteristic fragmentation of this compound at (m/z=603, 417, 392, 334,309 268, 238, 254, 241, 198, 135 ,109, 93, 78 , 69and 52), as in Scheme (3-12).



Scheme (3-12) fragmentation pattern of compound $[XVIII]_f$

3.1.19. Synthesis and characterization the Schiff base compounds of indazoles $[XIX]_{a-i}$

The new Schiff bases type$[XIX]_{a-i}$ were synthesized from condensation of one mole from acid hydrazide$[XV]_{a-c}$ with one mole from different aromatic aldehydes in benzene and glacial acetic acid .

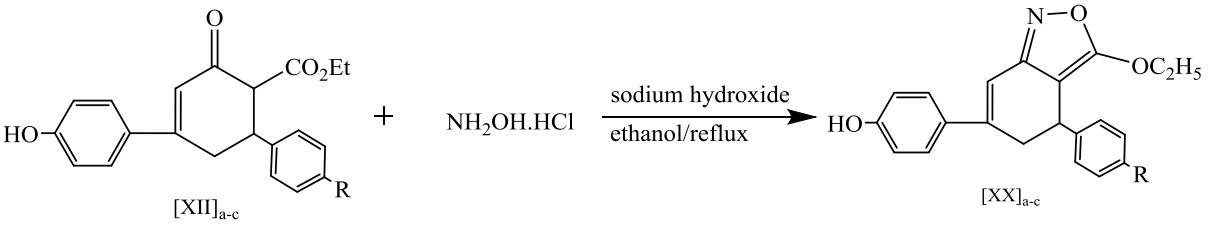


The Schiff bases $[XIX]_{a-i}$ were identified by FTIR and ^{1}HNMR spectroscopy, the FTIR absorption-spectrum of compound$[XIX]_f$, showed disappearance of absorption bands for NH_2 group together with appearance a new absorption band which is assigned to imine group (C=N) stretching, Figure(3-56). The FTIR absorption bands data of these compounds $[XIX]_{a-i}$ were listed in Table (3-10).

^{1}HNMR spectrum of compound$[XIX]_a$, showed the following characteristic chemical shift (DMSO-d_6 as a solvent): a singlet signal at δ 10.75ppm, δ 10.02ppm, Figure(3-57) . This could be attributed to NH of indazole ring and NH of hydrazone moiety, also a singlet signal at 8.72 ppm due to a proton of CH=N. Many signals appeared in the region δ (6.82-7.98)ppm for nine aromatic protons, while appearance singlet signal at δ 6.80 ppm could be attributed to a proton of C=CH of cyclohexenone. Also showed a singlet signal at δ 3.79 ppm for two protons of O$\underline{CH_2}$CO group, a doublet signal at δ 3.71ppm due to one proton of CH at fused ring, signal at δ3.66 ppm could be related to a proton of $\underline{CH}$Ph group. A doublet signal appeared at δ 2.26ppm for two protons of $\underline{CH_2}$ for cyclohexenone ring.

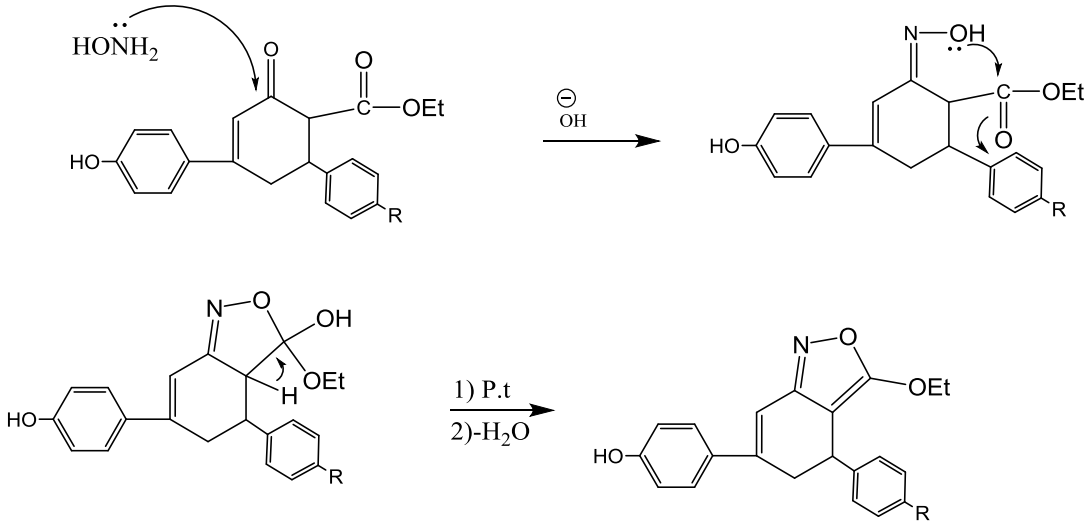
3.1.20. Synthesis and characterization of fused isoxazole derivatives[XX]$_{a-c}$

The refluxed a mixture of one mole of cyclohexenones[XII]$_{a-c}$ and one mole of hydroxylamine hydrochlorid and sodium hydroxide in ethanol led to give compounds [XX]$_{a-c}$.



R= H , OCH_3 , CH_3

The mechanism [229] of this raction as outlined in Scheme(3-13)



Scheme (3-13)

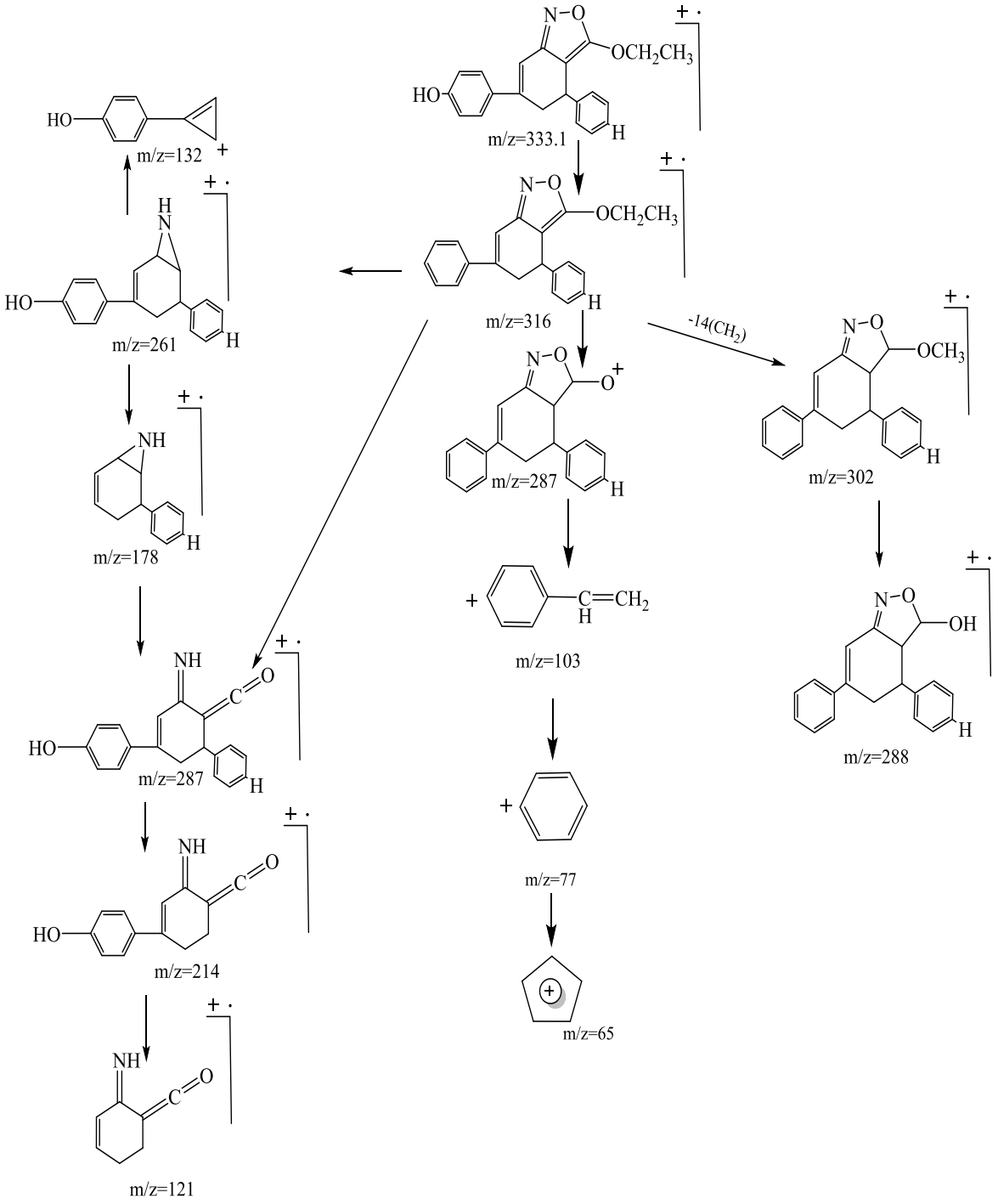
The structure of the isoxazoles **[**XX**]**$_{a-c}$ have been characterized by FTIR, ^{1}HNMR and mass spectroscop. The FTIR spectrum of isoxazole[XX]$_a$, showed the disappearance bands characterisitic of ester moiety and appearance a stretching band at 1635cm^{-1} due to νC=N of isoxazole ring (endocyclic) and νC-O of isoexole ring at 1263 cm^{-1}, Figure(3-58). The

characteristics FTIR absorption bands of isoxazoles $[XX]_{a-c}$ were listed in Table (3-11) .

^{1}HNMR (in DMSO-d_6 as a solvent) of isoxazole compound $[XX]_b$, showed many signals in the region δ (6.84-8.08) ppm for eight aromatic protons of benzene rings, Figure(3-59). a singlet signal at δ 10.33 ppm could be attributed to a proton of OH group, while appearance a singlet signal at δ6.81ppm could be attributed to one proton of C=CH of cyclohexenone ring, a quartet signal appeared at δ 4.19-4.21 ppm for two protons of $O\underline{CH_2}CH_3$ groups. A triplet signal at δ3.86-3.95 ppm could be related to one proton of $\underline{CH}$Ph group. A doublet signal δ2.24 ppm for two protons of $\underline{CH_2}$ of cyclohexenone ring. Also a singlet signal at δ 2.35 ppm due to three protons of $PhCH_3$ group, and a signal at δ 1.23ppm for three protons of terminal CH_3 group.

^{1}HNMR (in DMSO-d_6 as a solvent) of isoxazole compound $[XX]_c$, showed many signals in the region δ (6.89-8.06) ppm for eight aromatic protons of benzene rings. a singlet signal at δ 10.39ppm, Figure (3-60). could be attributed to a proton of OH groups, while appearance a singlet signal at δ6.82ppm could be attributed to one proton of C=CH of cyclohexenone ring. A signal at δ3.82 ppm could be related to one proton of $\underline{CH}$Ph groups and to three protons of OCH_3. Also a quartet signal appeared at δ 3.69-3.74 ppm for two protons of $O\underline{CH_2}CH_3$ groups , a doublet signal at δ2.07ppm could be related to two protons of CH_2 group, and finally a signal at δ 1.24 ppm due to three protons of CH_3 group.

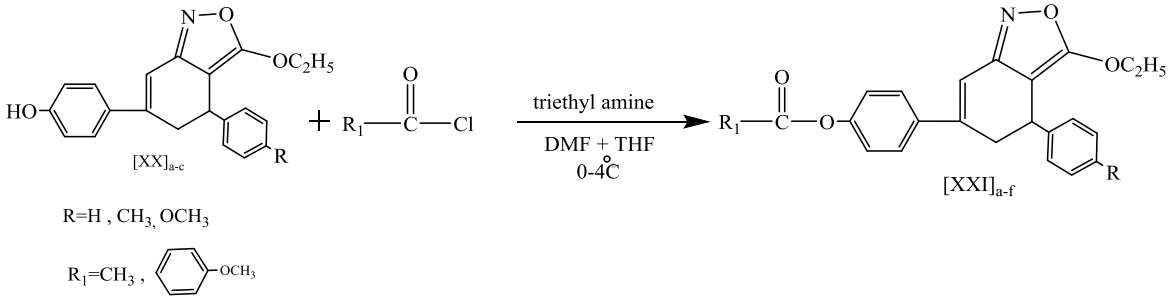
The mass spectrum of compound[XX]$_a$, exhibited a molecular ion at m/z=333,also showed a characteristic fragmentation of isoxazol moiety at m/z =(287,261, 214,178,132 and121), Figure(3-61). Besides to appeared many peaks at m/z=(316,302,288,103) to give a good evidence for the formation this compound .



Scheme (3-14) fragmentation pattern of compound [XX]$_a$

3.1.21. Synthesis and characterization the new ester compounds of isoxazoles $[XXI]_{a-f}$

The new esters $[XXI]_{a-f}$ were synthesized from the reaction of one mole of compound $[XX]_{a-c}$ and one mole of acid chloride in triethyl amine and (DMF , THF) at (0-4)°C.

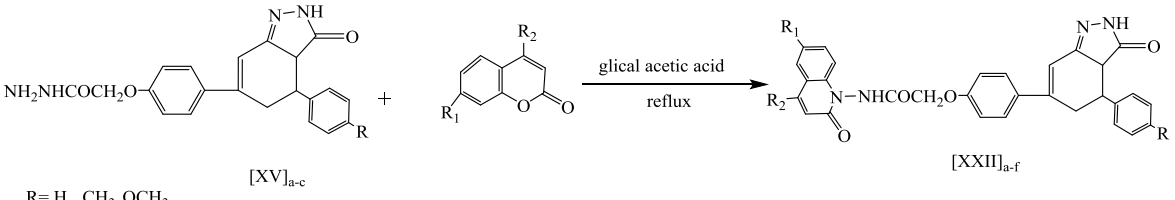


The ester compounds $[XXI]_{a-f}$ were charecteized by FTIR and ^{1}HNMR spectroscopy . The FTIR spectrum of compound $[XXI]_c$, showed new bands at 1757 cm^{-1} due to a stretching vibration of the (C=O) for ester, stretching band at 1251$cm^{-1}$for C-O of ester and C-O ether, Figure(3-62). Besides to the disappearance stretching bands of O-H. The FTIR absorption bands data of these compounds $[XXI]_{a-f}$ were listed in Table (3-11).

^{1}HNMR spectrum of compound $[XXI]_a$, showed the following characteristic chemical shift (DMSO-d_6 as a solvent), Figure(3-63). Multiplet signals appeared in the region δ (7.22-7.99) ppm for nine aromatic protons, while appearance a singlet signal at δ7.19ppm could be attributed to one proton of C=CH of cyclohexenone ring, a quartet signal appeared at δ (3.83-3.90) ppm for two protons of O$\underline{CH_2}CH_3$. A triplet signal at δ3.03-3.07 ppm could be related to one proton of $\underline{CH}$Ph group. A doublet signal δ 2.89ppm for two protons of $\underline{CH_2}$ of cyclohexenone ring. Finally a singlet signal appeared at δ2. 28 ppm for $COCH_3$ and a triplet signal at δ 1.18 ppm could be attributed to the three protons of CH_3 groups.

3.1. 22. Synthesis and characterization of quinolin-2-one derivatives $[XXII]_{a-f}$

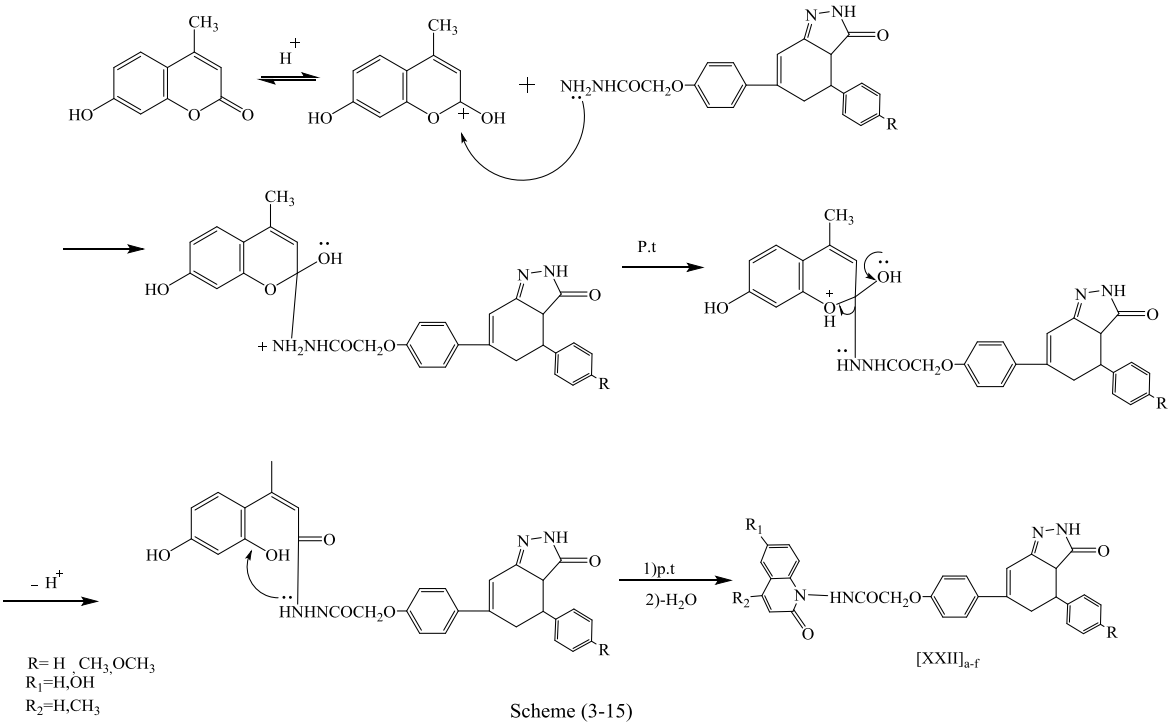
Equivalent moles of coumarin compounds and hydrazide compound $[XV]_{a-c}$ were dissolved in glacial acetic and heating under reflux led to formation compounds$[XXII]_{a-f}$.



$[XV]_{a-c}$ $[XXII]_{a-f}$

R= H, CH_3, OCH_3
R_1=H,OH
R_2=H,CH_3

The mechanism [231] of this reaction may be outlined as follows in Scheme (3-15).



R= H, CH_3, OCH_3
R_1=H,OH
R_2=H,CH_3

$[XXII]_{a-f}$

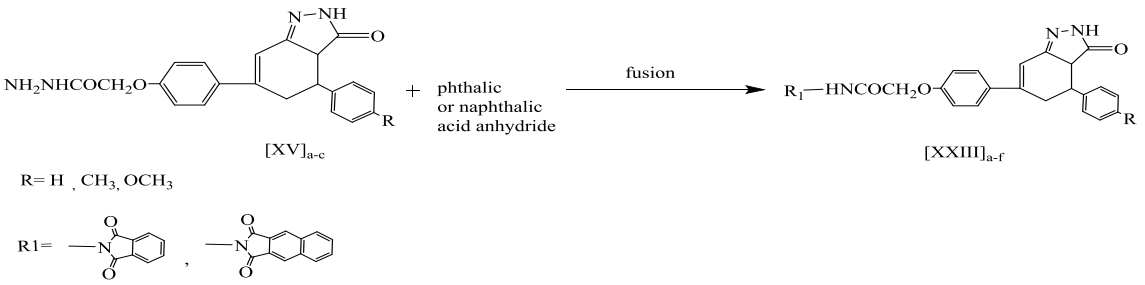
Scheme (3-15)

The structure of quinoline derivatives $[XXII]_{a-f}$ have been characterized by, FTIR and^{1}HNMR spectroscopy .Characteristic FTIR absorption bands of quinoline derivatives $[XXI]_e$ showed a shifting data of in carbonyl stretching band C=O of lactam [238]group of quinoline-2-one then C=O of coumarin, and disappearance the two bands of NH_2 group of acid hydrazide, Figure(3-64). The FTIR absorption bands data of these compounds$[XXII]_{a-f}$ were listed in Table (3-12).

^{1}HNMR spectrum of compound $[XXII]_b$,showed the following characteristic chemical shift (DMSO-d_6 as a solvent) :a singlet signal at δ 10.6 ppm, Figure(3-65). This could be attributed for two proton of NH indazole ring and NHCO group, many signals appeared in the region δ (6.70-7.81) ppm for twelve aromatic protons. While appearance a singlet signal at δ6.26 ppm could be attributed to three protons of C=CH of cyclohexenone and quinoline. Also, showed three signals between δ (3.76-4.09) ppm for aproton of CH at fused ring, two proton of O$\underline{CH_2}$ group and proton of CHPh proton. A doublet signal at δ 2.94ppm for two protons of $\underline{CH_2}$ of cyclohexenone ring. Finally a good signal appeared at δ 2.30 ppm due to three protons of Ph$\underline{CH_3}$, and two protons of CH_2 of cyclohexenone ring.

3.1.23. Synthesis and characterization the imides compounds of indazoles $[XXIII]_{a-f}$

These compounds were synthesized from the fusion of one mole of acid hydrazide$[XV]_{a-c}$ with one mole of acid anhydride.

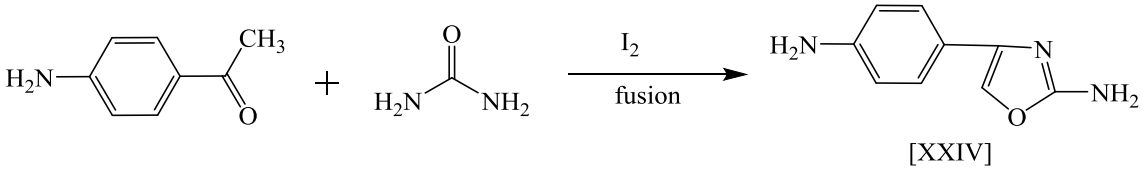


The structure of imides $[XXIII]_{a-f}$ were studied by FTIR and ^{1} HNMR spectrascopy . The FTIR spectrum of compound $[XXIII]_c$ exhibited significant two stretching bands at1743cm^{-1} and 1710 cm^{-1}which could be attributed to the (asym and sym) carbonyl group (cyclic imide), Figure(3-66).The FTIR absorption bands data of these compounds $[XXIII]_{a-f}$ were listed in Table (3-13).

^{1}HNMR spectrum of compound$[XXIII]_a$, showed the following characteristic chemical shift (DMSO-d_6 as a solvent) : a singlet signal at δ11.34ppm could be attributed to a proton of NH of indazole ring and a singlet signal at δ 9.53 ppm to a proton of NHCO group, Figure(3-67). Many signals appeared in the region δ (6.71-7.59) ppm for twenty aromatic protons, while appearance a singlet signal at δ 6.58 ppm could be attributed to one proton of C=CH for cyclohexenone ring. Also showed a singlet signal at δ 4.12 ppm for two protons of O$\underline{CH_2}$CO group, a doublet signal appeared at δ 3.66 ppm for CH at fused ring . A signal at δ3.08 ppm could be related to proton of $\underline{CH}$Ph group. A doublet signal at δ 2.88 ppm for two protons of $\underline{CH_2}$ of cyclohexenone ring.

3.1.24. Synthesis and characterization 4-(4-aminophenyl)-oxazol-2 amine [XXIV]

4-(4-aminophenyl)-oxazol-2-amine[XXIV] was prepared by fusion of iodine with urea and 4- amino acetophenone



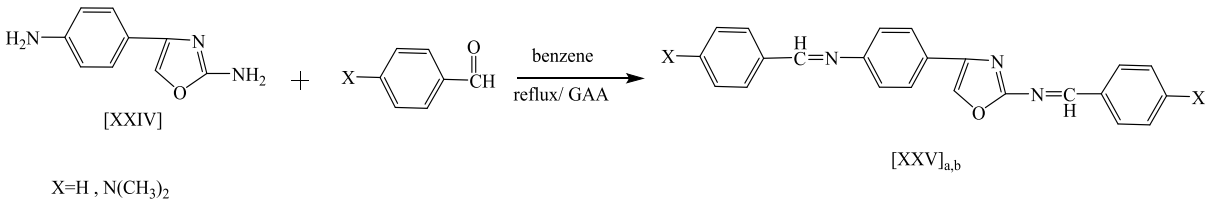
[XXIV]

This compounds was characterized by melting point and FTIR spectroscopy, the FTIR spectrum, showed disappearance absorption band due to C=O stretching of 4- amino acetophenone, with appearance of

stretching band for C=N and C-O at 1647 cm^{-1} and (1278,1174) cm^{-1}, respectively, Figure(3-68). Also showed the stretching bends due to asym. and sym. Of NH_2 group between (3431-3211) cm^{-1} .

3.1.25. Synthesis and characterization the Schiff bases of oxazole [XXV] a,b

The new Schiff bases type $[XXV]_{a,b}$ were synthesized from condensation of one mole from compound [XXIV] with two mole from different aromatic aldehydes in benzene and glacial acetic acid.



[XXIV]

X=H , $N(CH_3)_2$

$[XXV]_{a,b}$

These compounds were characterized by FT-IR and by ^{1}HNMR spectroscopy. The characteristic FT-IR spectrum of compound $[XXV]_b$, showed the disappearance of stretching vibration bands for NH_2 of 4-(4-aminophenyl)-oxazol-2-amine and υC=O group (for aldehyde), Figure(3-69). Also appearance of new absorption stretching bands at 1656 for imine group. The characteristic FT-IR absorption bands of these compounds $[XXVII]_{a,b}$ were listed in the Table (3-14).

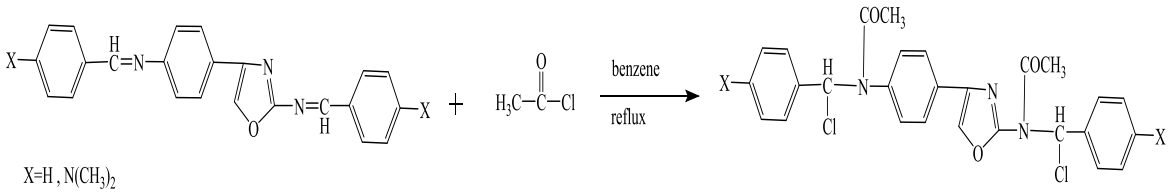
The ^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of compound $[XXV]_a$ in showed a singlet signal at δ 8.97 ppm assigned of one proton of CH=N[(239)] group that is good evidence to the formation Schiff base $[XXV]_a$, Figure(3-70) . In addition multiplet signal at δ 7.19-8.14 ppm attributed for fourteen protons due to aromatic benzene rings and the one proton of oxazole ring appeared at δ 6.55 ppm.

While, the ^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of compound $[XXV]_b$ showed a singlet signal at δ 9.66ppm assigned of one proton of CH=N group, Figure(3-71) . In addition multiplet signal at δ 6.77-7.86 ppm

that attributed for twelve protons of aromatic benzene rings, and a proton for oxazole ring appeared at δ 6.55 ppm, a singlet signal appeared at δ 3.04 ppm for six protons of two CH_3 groups.

3.1.26. Synthesis and characterization the N-acetyl compounds [XXVI] $_{a,b}$

The reaction of one mole of Schiff base $[XXV]_{a,b}$ in dry benzene, with two mole of acetyl chloride led to get N-acetyl compounds[XXVI] $_{a,b}$.

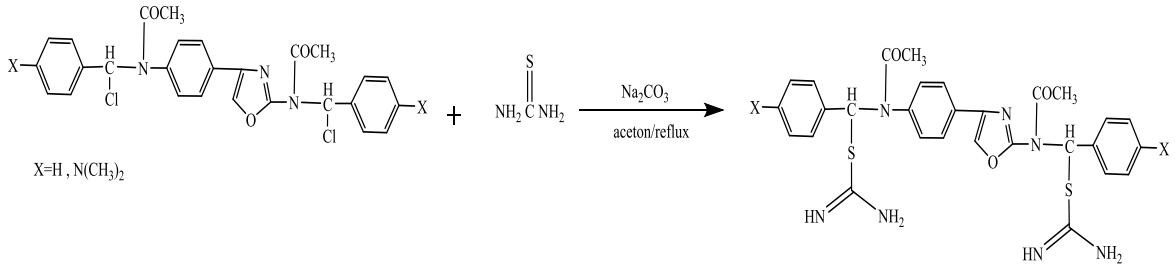


These compounds were characterized by FT-IR and by ^{1}HNMR spectroscopy. The characteristic FT-IR spectrum of compound $[XXVI]_a$ as in Figure(3-72) showed the disappearance of stretching band due to C=N of Schiff base and other peaks characterized of the starting materials with the appearance of new stretching bands due to C=O and C-Cl at 1691cm^{-1}and 767cm^{-1}, respectively. The FTIR absorption bands data of these compounds $[XXVI]_{a,b}$ were listed in Table (3-14).

The ^{1}HNMR spectrum(in DMSO-d_6 as a solvent) of N-acetyl $[XXVI]_b$ in showed a singlet signal at δ 6.80 ppm could be attributed for one proton of CH-Cl, Figure(3-73). Also the spectrum showed a singlet signal at δ 2.81 ppm due to three protons of acetyl ($COCH_3$) group, besides to a singlet signal at δ3.04ppm for six protons of two CH_3 groups.

3.1.27. Synthesis and characterization the Thiourea compounds of oxazoles [XXVII] $_{a,b}$

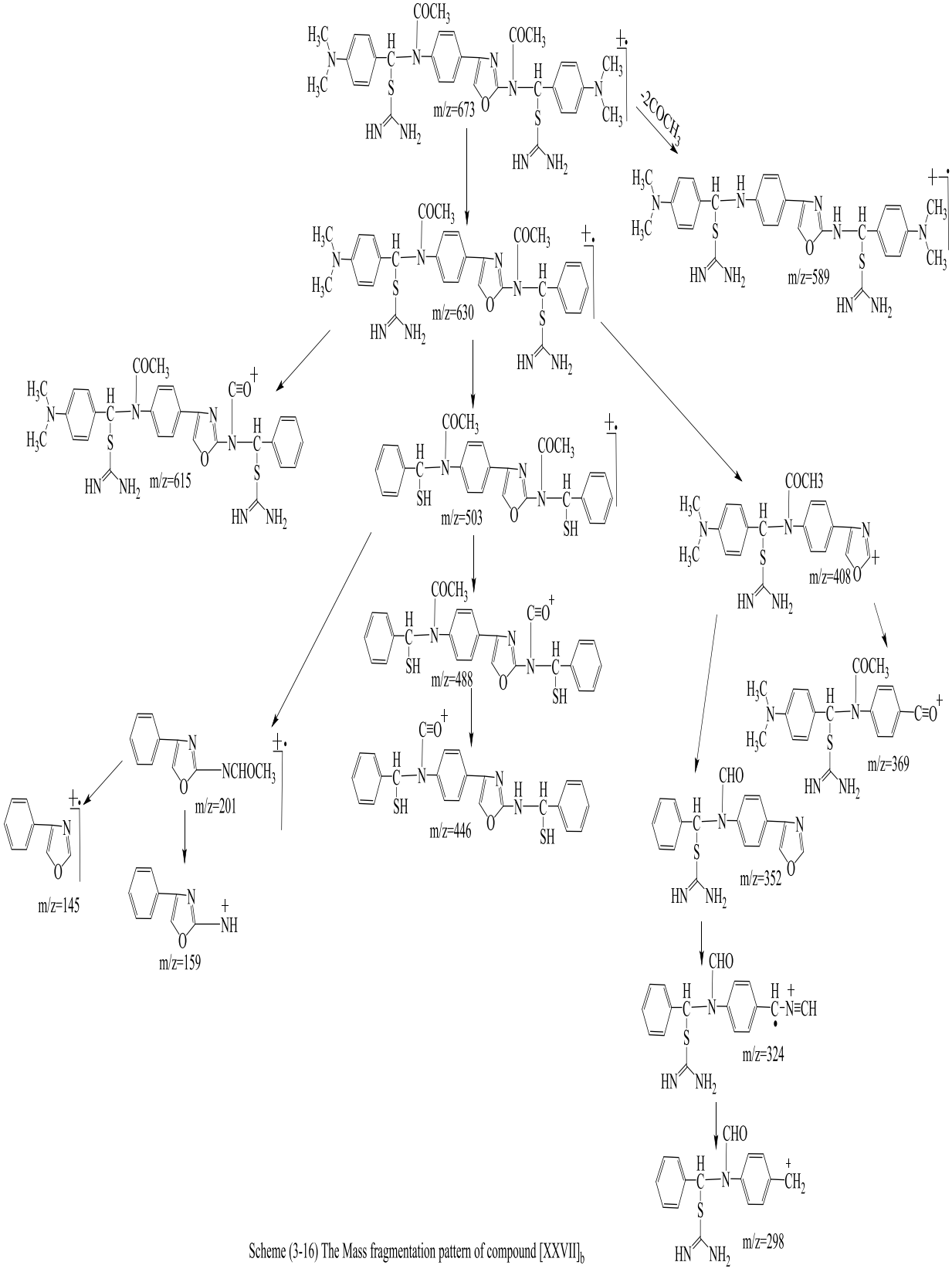
When reacted the one mole of N-actyl compounds with two mole of thiourea in Na_2CO_3 and acetone led to get thiourea compounds [XXVII] $_{a,b}$



The synthesized compounds are characterized by FTIR and ^{1}HNMR spectroscopy. The FTIR spectrum of compounds $[XXVII]_a$, gave a good evidence to formation of thiourea derivatives from disappearance of stretching band due to of C-Cl of N-actyl compounds with the appearance a new stretching in the region bands at (3433-3199) cm^{-1} stretching band due to asym, sym of NH_2, NH groups, Figure(3-74). The FTIR absorption bands data of these compounds $[XXVII]_{a,b}$ were listed in Table (3-14).

The ^{1}HNMR spectrum (in DMSO-d_6 as a solvent) of compound $[XXVII]_b$ showed a singlet signal at δ7.6 ppm could be attributed to one proton of (=NH) group[240], Figure (3-75).It also showed a multiplet signal at δ(6.59-7.4)ppm that attributed for twelve protons of aromatic benzene rings and a proton for oxazole ring, in addition showed a signal at δ 3.97ppm for two protons of NH_2 group. Also showed a singlet signal at δ3.05ppm for six protons of two NMe_2 groups, besides to a singlet signal appeared at δ 2.86ppm due to six protons of two acetyl ($COCH_3$) groups.

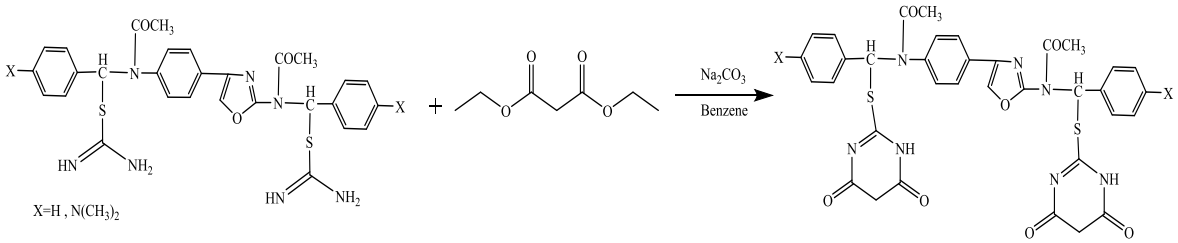
The mass spectrum of compound $[XXVII]_b$, exhibited a characteristic fragmentations formation at m/z= (630, 615,589, 503, 488, 446,408, 370, 352, 324, 298, 201,159 and 145) and that gave indicated to the formation of this compound, Figure(3-76).



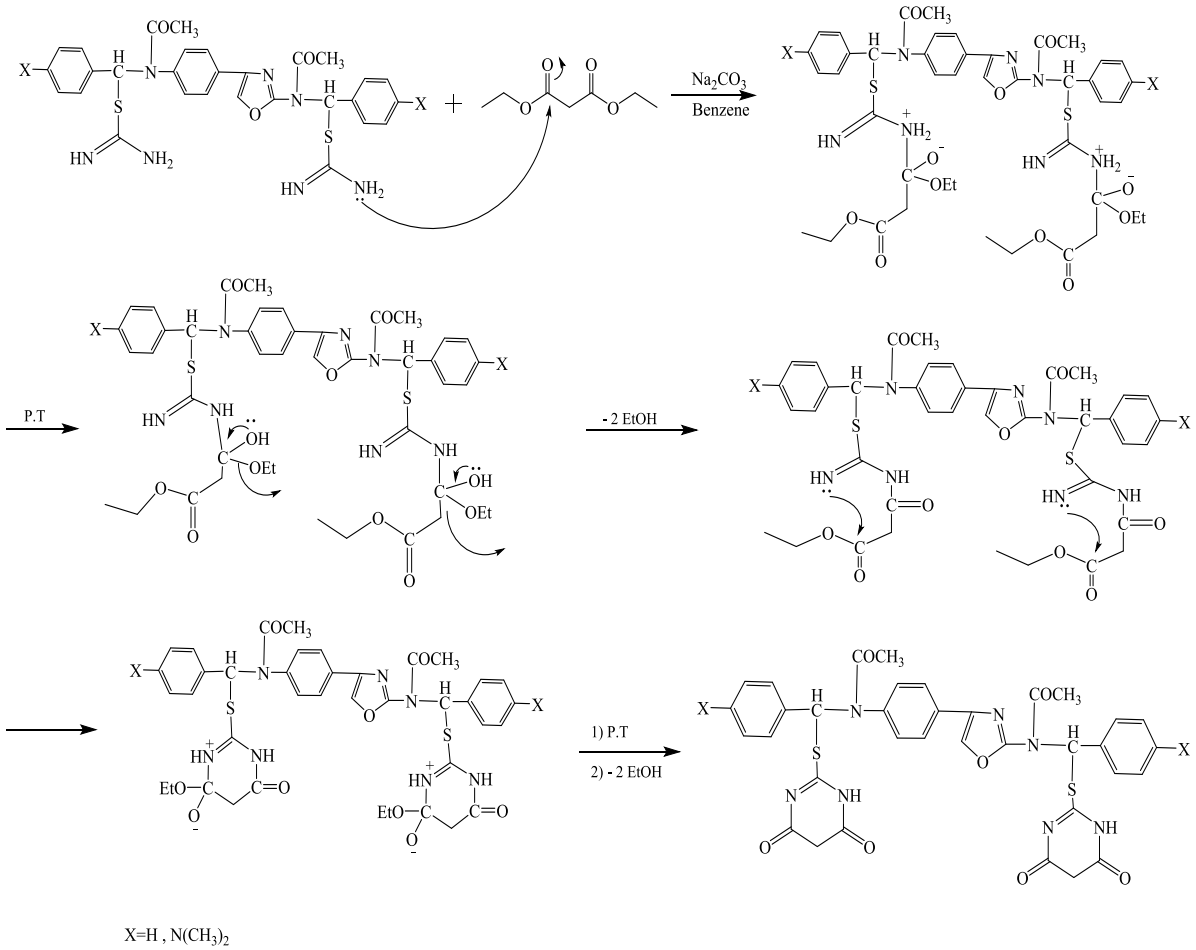
Scheme (3-16) The Mass fragmentation pattern of compound [XXVII]$_b$

3.1.28. Synthesis and characterization of Pyrimidine derivatives [XXVIII] a,b

The pyrimidine compound $[XXVIII]_{a,b}$ were synthesized by ring closure reaction of one mole of compounds $[XXVII]_{a,b}$ with two mole of diethyl malonat in dry benzene.



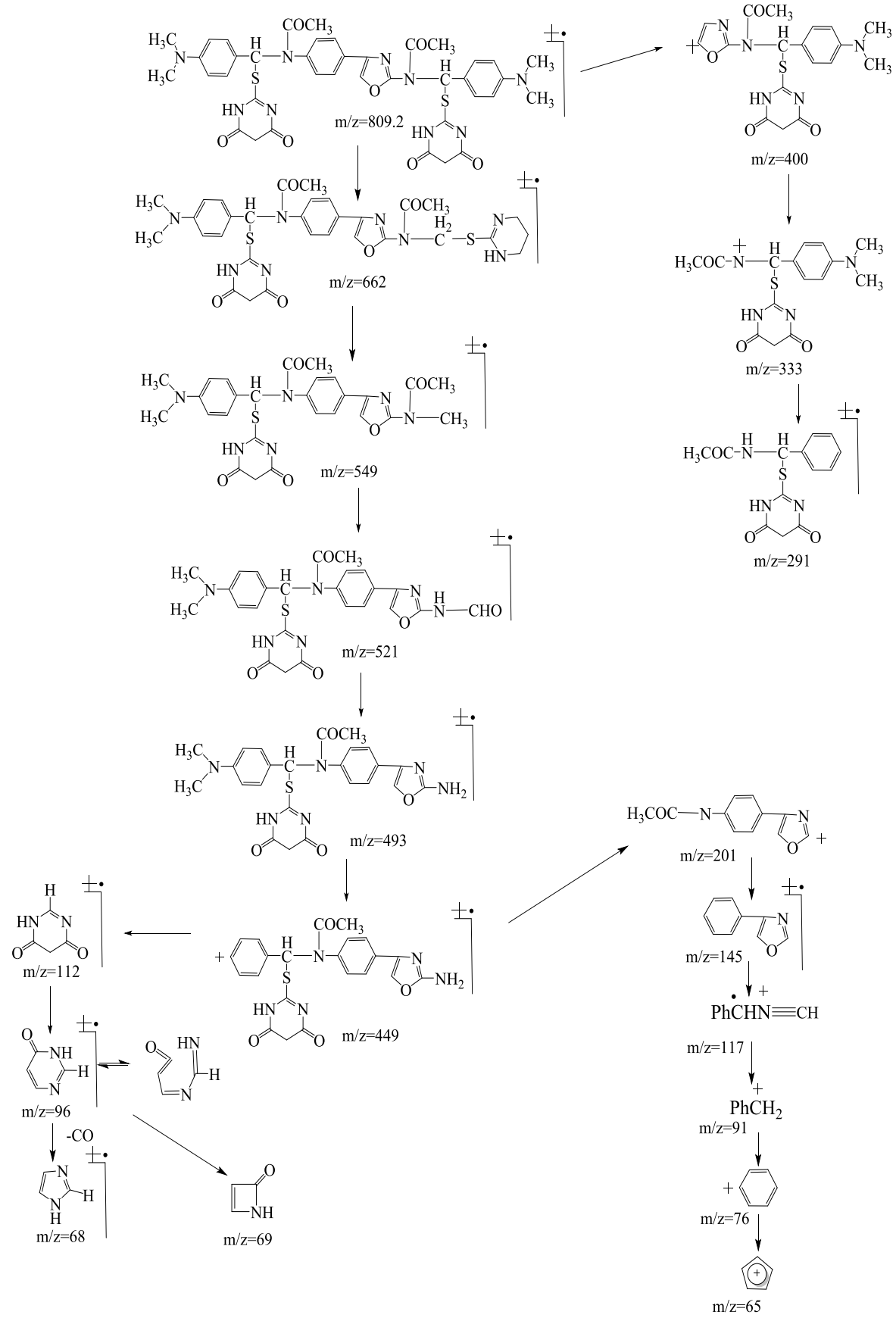
The mechanism of this reaction may be outlined as follows in Scheme (3-17)



Scheme (3-17)

These compounds were identified by FTIR and Mass spectroscopy . FTIR spectrum of compound $[XXVIII]_a$, showed appearance of new stretching bands due to C=N at 1665 cm^{-1} and C=O at1710 cm^{-1}, Figure(3-77). It also showed disappearance the two stretching bands of NH_2 group. The FTIR absorption bands data of these compounds $[XXVIII]_{a,b}$ were listed in Table (3-14).

The mass spectrum of compound $[XXVII]_b$, showed a characteristic fragmentations to the presence of pyrimidine moiety at m/z =(662, 112, 96, 69 and 68), Figure(3-78). Besides to appeared many fragmentations at m/z=(200, 145,117 and 91) that give a good evidence for the presence of the oxazole ring



Scheme (3-18) The Mass fragmentation pattern of compound $[XXVIII]_b$

3.2.Biological Activity

Heterocyclic rings considered an important class of compounds having a wide spectrum of biological activity, the heterocyclic compounds are well known for antibacterial activity. The antibacterial activity and anti fungal of the synthesized compounds was performed according to the agar diffusion method [241], using two types of bacteria; *Escherichia coli* (G-) and *Bacillus subtitis* (G+), and one type of fungal *Candida albicans*. The prepared agar and petri dishes were sterilized by autoclaving for 20 min at 37^{o}C. The agar was surface inoculated uniformly from the both cultures of the tested microorganisms, the two types of bacteria and fungal were activated in nutrient agar medium and dextrose agar medium, respectively at 37^{o}C for 24 hrs. Each of tested compounds was dissolved in DMSO (which was used as a solvent and as control) to give concentration 10^{-2}M. The zones of inhibition formed were measured in millimeter.

The biological activity of all synthesized compounds were studied by using antibacterial activity against *Bacillus subtitis* gram(+)and *E.coli* gram(-) bacteria and some of them against *Staphlocococs aureus* .Also against *candida albicans* fungal and the results were compared with metronidazole drug and discuss as follows:

1)The first line (triazine derivatives) showed:-

a) All the Schiff basses type$[IV]_{a-g}$, showed good biological activity against *E.coli* and *bacillus subtitis*. While the schiff bases$[IV]_{a,b,g}$ did not show any antifungal activity (*candida albicans*), the Schiff bases$[IV]_{c,d,e,f}$ showed good antifungal activity agnaist *candida albicans* fungal.

b) N-aceyl compounds$[V]_{a-g}$ exhibited good activity against bacterial and antifungal activity, except the compounds $[V]_{e,g}$ did not showed any antifungal activity, in addition compound$[V]_{d}$ did not showed any

biological activity against bacteria and fungal.

c) On the other hand, the thiourea derivatives[VI]$_{a-g}$ showed different activity between negative and good activities against bacteria and fungal activity. The compound[VI]$_f$ show very high activity towards two type of bacteria.

d) the imidazole derivatives[VII]$_{a-d,f}$ did not showed any biological activity (antibacterial and antifungal), Although the presence of the imidazole moiety, except compound[VII]$_{a,b,f}$ showed antifungal activity. The only compound [VII]$_g$ exhibited good biological activity, towards bacteria and fungal types, also the compound [VII]$_e$ showed only antibacterial activity, Finally the imidazoles type[VII]$_{a-d}$ also examined against *Staphlocococs aureus* and did not showed any inhibition zone.

e) Imide compounds [VIII]$_{a-d}$ exhibited good data against bacterial and antifungal activity, but the compounds [VIII]$_c$ showed only antifungal activaty.

f) The pyrazole derivatives [IX]-[X] showed good antibacterial activity towards type(gram+) and only compounds[XI]$_{a,b}$ did not showed any antibacterial against type(gram-), the pyrazole[IX] showed antifungal activity, while the other pyrazoles type[X],[XI]$_{a,b}$ did not showed antifungal activity.

The antibacterial and antifungal data of the compounds [IV]$_{a-g}$-[XI]$_{a-g}$ were listed in Table(3-15) and (3-16).

2)The second line (indazole derivatives) showed:-

a) indazole compounds [XV]$_{a-c}$, showed good biological activity against *E.coli* gram (-) and *bacillus subtitis* gram (+). While the compound [XV]$_a$ did not showed any antibacterial activity against gram (+), indazol compounds [IV]$_{a-c}$ did not showed any antifungal activity .Table(3-17).

b)Pyrazole compound of indazole $[XVI]_{a-c}$ were showed different biological activity between good to no biological activity as in Table (3-17).

c) On the other hand, the 4-acetyl pyrazole type $[XVII]_{a-c}$ did not showed any biological activity against bacterial and antifungal activity excepted compound $[XVII]_c$ have good antifungal activity,as in Table(3-17).

d) The aryl hydrazone derivatives type $[XVIII]_{a-f}$ and the Schiff bases type $[XIX]_{a-i}$ showed antibacterial activity and some of them showed antifungal activity. The aryl hydrazone showed antibacterial activity a higher them Schiff bases $[XIX]_{a-i}$, Table (3-17).

e) Isoxazole$[XX]_{a-c}$ and their esters $[XXI]_{a-f}$ showed different good inhibition zones against bacterial and antifungal activity excepted compounds $[XXI]_{c,f}$ did not showed any antifungal activity, Table(3-18)

f) Quinolin-2-one derivatives $[XXII]_{a-f}$ showed good biological activity against bacterial and antifungal activity excepted compound $[XXII]_e$ did not show any antifungal activity, as in Table(3-19).

g) Imides compounds of indazoles$[XXIII]_{a-f}$ showed different data between (good to high) activity against fungal activity and a good activity against bacterial excepted compounds $[XXIII]_{a,c}$ did not showed antifungal activity, as in Table(3-20).

3)The third line (oxazole derivatives) showed:-

n) Schiff bases type $[XXV]_{a,b}$ showed good biological activity against *E.coli* (gram-) and *bacillus subtitis* gram (+) and good antifungal activity, N-acetyl compounds $[XXVI]_{a,b}$, exhibited good data against bacterial and antifungal activity, but the compounds $[XXVI]_b$ did not showed any antifungal activity, while, the thiourea derivatives$[XXVII]_{a,b}$ showed antifungal activity and the compound$[XXVII]_a$ showed good antibacterial

against gram (+) but compounds $[XXVII]_b$ did not showed antibacterial Pyramidine dervitives $[XXVIII]_{a,b}$ did not exhibted any biological activity except compound $[XXVIII]_b$ have good antibacterial against gram(-) .

The results in general showed that most of the tested compounds possess biological activity against the two types of the bacteria and one type of antifungal. The biological activity of the synthesized compounds, which were exhibited high, moderate or no inhibition zones couled be related to the type of hetrocyclic unit and active groups. Figures(3-80)-(3-82) showed the effect of these compounds on two types of bacteria and one type of antifungal.

Conclusions

In this work new derivatives (esters , hydrazide and their heterocyclic compounds) derived from 5,6-diphenyl-1,2,4-triazine-3-thiol and 4-[3-(4`-phenyl or substituted phenyl)-2-propene-1-one]-phenol besides to new derivatives derived from and 4-(4-aminophenyl)-oxazol-2-amine were synthesized and characterized, and the following conclusions could be drawn.

1-New Schiff bases $[IV]_{a-g}$ and $[XXV]_{\mathbf{a,b}}$ were synthesized in benzene in good yield , these Schiff bases were using as starting material for synthesized new N-acetyl then, their thiourea and imidazole derivatives$[VII]_{a-g}$ and primidine $[XXVIII]_{a,b,}$ in moderate yield by simple method.

2- New indazoles $[XV]_{a-c}$ with hydrazide moiety were synthesized in one step reaction to give moderate yield, these indazoles were using as a starting material for synthesized new pyrazole and fused isoxazole derivatives . Many of These compounds synthesized by using simple method and short time .

3- The 4-acetyl pyrazole derivatives have been synthesiszed by using a simple method and these new compounds reacted with phenyl hydrazones to give new type of hydrazones at position 4-from pyrazole ring in good yield .

4-The oxazole derivatives have been synthesized by refluxed for a long time between (10-24) hrs. with low yields.

5-The physical properties and spectral data give good information and indicate of the suggested structure for the new synthesized compounds.

6- Many synthesized compounds give good biological activity and other did not showed any biological activities. That may be related to the functional groups and the chemical structure for the examined compounds.

Suggestion of future work

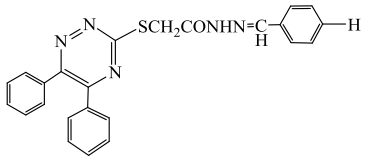
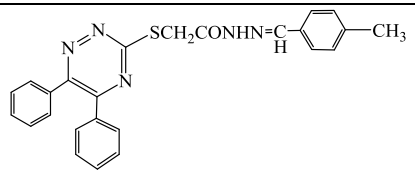
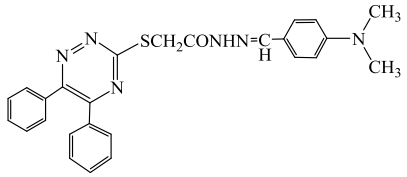
1-Converted the amino group in 4(4-amino phenyl)-oxazole-2-amine) to azo compound .

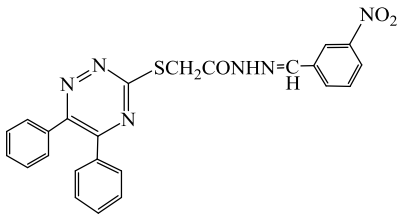
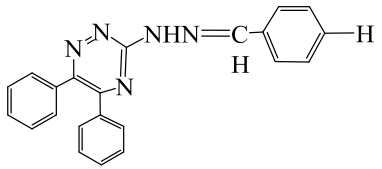
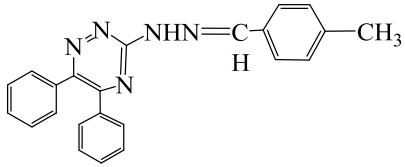
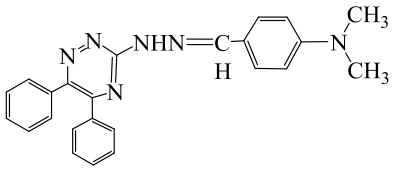
2-Synthhesis new tetrazole and thiazolidinone from the new Schiff base (were synthesized in this work).

3-Study the liquid crystalline properties of the synthesized compounds.

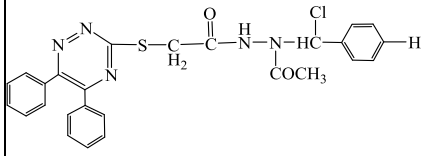
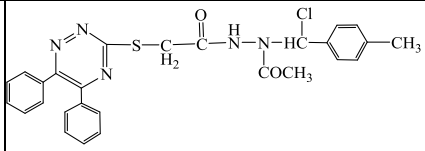
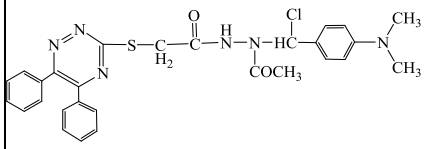
4-Study the anticancer cell of the synthesized compounds

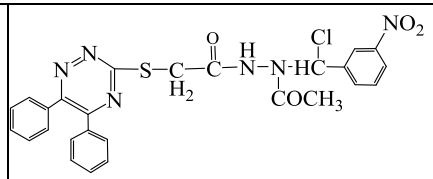
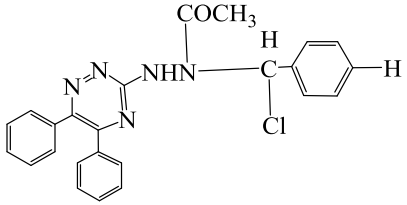
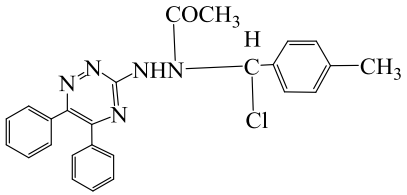
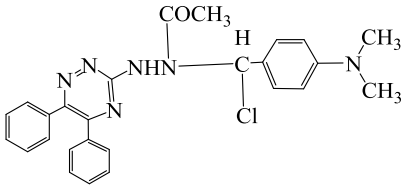
Table(2-2):The Nomenclature, yields, Structural formula, chemical formula and physical properties of Schiff bases [IV]$_{a-g}$

Comp. No.	Nomenclature	Structural formula	Molecuar formula	M. P ^{0}C	Yield %	Color
[IV]$_a$	N'-benzylidene-2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)acetohy-drazide		$C_{24}H_{19}N_5OS$	80-82	80	Pale yellow
[IV]$_b$	2-((5,6-diphenyl-1,2,4-triazin-3-yl) thio)-N'-(4-methylbenzylidene) acetohydrazide		$C_{25}H_{21}N_5OS$	224-226	82	Pale yellow
[IV]$_c$	N'-(4(dimethylamino) benzyl idene) -2-((5,6-diphenyl-1,2,4-triazin-3-yl) thio) acetohydrazide		$C_{26}H_{24}N_6OS$	230-232	87	Pale orang

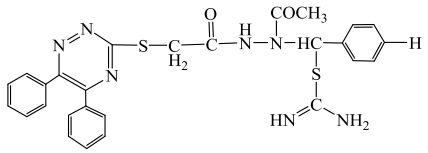
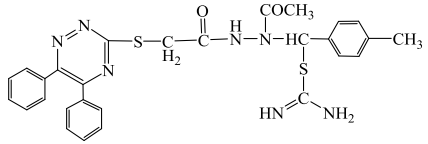
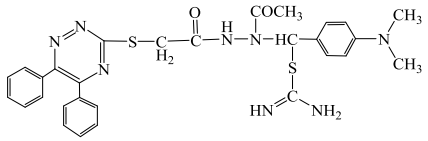
$[IV]_d$	2-((5,6-diphenyl-1,2,4-triazin-3-yl) thio)-N'-(3-nitrobenzylidene) acetohydrazide		$C_{24}H_{18}N_6O_3S$	84-85	77	Yellow
$[IV]_e$	3-(2-benzylidenehydrazineyl)-5,6-diphenyl-1,2,4-triazine		$C_{22}H_{17}N_5$	156-158	81	Pale yellow
$[IV]_f$	3-(2-(4-methylbenzyl idene)) hydrazineyl)-5,6-diphenyl-1,2,4-triazine		$C_{23}H_{19}N_5$	196-198	80	Orange
$[IV]_g$	3-(2-(4di-methyl amino benzyl idene) hydrazineyl)-5,6-diphenyl-1,2,4-triazine		$C_{24}H_{22}N_6$	214-216	83	Pale yellow

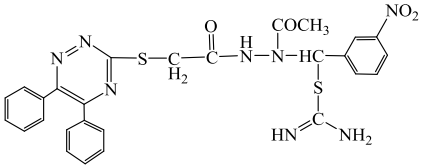
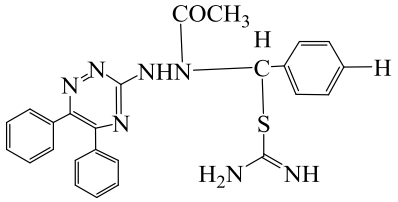
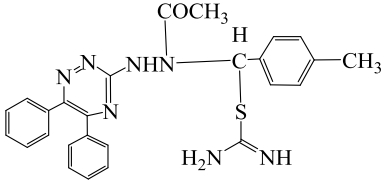
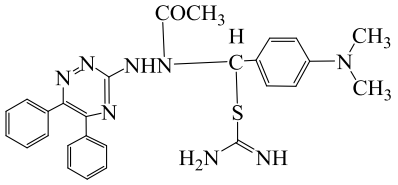
Table(2-3): The Nomenclature, Structural formula, chemical formula and physical properties of N-acetyl compounds [V]$_{a-g}$

Comp. No.	Nomenclature	Structural formula	Molecuar formula	M. P ^{0}C	Yield %	Color
[V]$_a$	N'-acetyl-N'-(chloro(phenyl) methyl) -2-((5,6-diphenyl-1,2,4-triazin-3-yl) thio) acetohydrazide		$C_{26}H_{22}ClN_5O_2S$	230-232	62	Yellow
[V]$_b$	N'-acetyl-N'-(chloro(4-tolyl) methyl)-2-((5,6-diphenyl-1,2,4-triazin-3-yl) thio)acetohydrazide		$C_{27}H_{24}ClN_5O_2S$	82-84	65	Green
[V]$_c$	N'-acetyl-N'-(chloro(4-(dimethyl amino)phenyl)methyl)-2-((5,6-dipenyl-1,2,4-triazin-3-yl)thio)acetohydrazide		$C_{28}H_{27}ClN_6S$	220-222	67	Dark brown

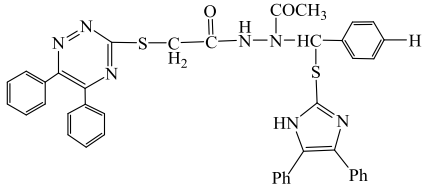
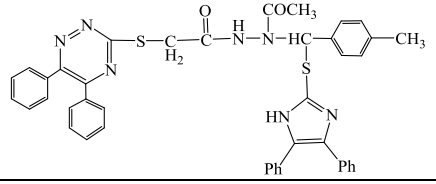
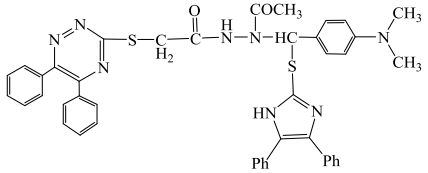
$[V]_d$	N'-acetyl-N'-(chloro(3-nitro phenyl) methyl)-2-((5,6-diphenyl-1,2,4-triazin -3-yl)thio) acetohydrazide		$C_{26}H_{21}ClN_6O_4S$	208-210	60	Yellow
$[V]_e$	N'-(chloro(phenyl)methyl)-N-(5,6 diphenyl-1,2,4-triazin-3-yl)acetohydrazide		$C_{24}H_{20}ClN_5O$	192-194	70	Green
$[V]_f$	N'-(chloro(4-tolyl)methyl)-N-(5,6-diphenyl-1,2,4-triazin-3-yl)acetohydrazide		$C_{25}H_{22}ClN_5O$	60-62	70	Brown
$[V]_g$	N'-(chloro(4-(dimethylamino) phenyl) methyl)-N-(5,6-diphenyl-1,2,4 triazin -3-yl)acetohydrazide		$C_{26}H_{25}ClN_6O$	80-82	73	Pale brown

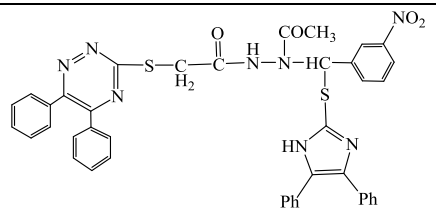
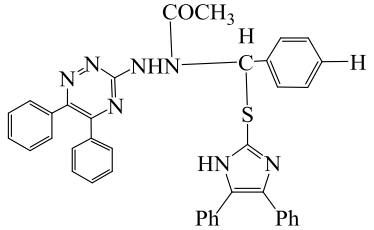
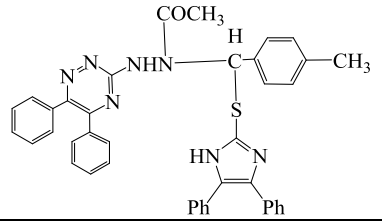
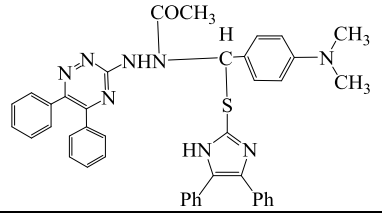
Table(2-4): The Nomenclature , Structural formula, chemical formula and physical properties of N-thiourea compounds [VI]$_{a-g}$

Comp. No.	Nomenclature	Structural formula	Molecuar formula	M. P ^{0}C	Yield %	Color
[VI]$_a$	(N-acetyl-N'-(2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)acetyl) hydrazineyl) (phenyl)methyl carbamimidothioate		$C_{27}H_{25}N_7O_2S_2$	76-78	62	Green
[VI]$_b$	(N-acetyl-N'-(2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)acetyl) hydrazineyl) (4-tolyl)methyl carbamimidothioate		$C_{28}H_{27}N_7O_2S_2$	240-242	65	Dark brown
[VI]$_c$	(N-acetyl-N'-(2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)acetyl) hydrazineyl) (4-(dimethyl amino) phenyl)methyl carbamimidothioate		$C_{29}H_{30}N_8O_2S_2$	208-210	67	Green

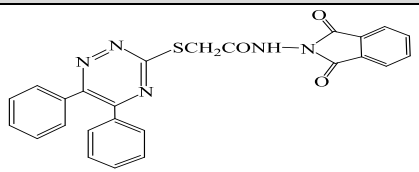
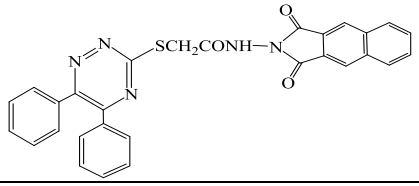
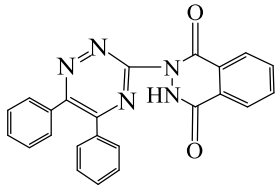
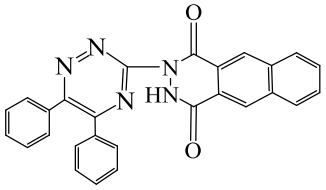
$[VI]_d$	(N-acetyl-N'-(2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)acetyl) hydrazineyl) (3-nitrophenyl) methyl carbamimi dothioate		$C_{27}H_{24}N_8O_4S_2$	222-224	60	Pale yellow
$[VI]_e$	(N-acetyl-N'-(5,6-diphenyl-1,2,4-triazin-3-yl) hydrazineyl) (phenyl) methyl carbamimidothioate		$C_{25}H_{23}N_7OS$	228-230	65	Yellow
$[VI]_f$	(N-acetyl-N'-(5,6-diphenyl-1,2,4-triazin-3-yl)hydrazineyl)(4-tolyl) methyl carbamimidothioate		$C_{26}H_{25}N_7OS$	80-82	60	Brown
$[VI]_g$	(N-acetyl-N'-(5,6-diphenyl-1,2,4-triazin-3-yl)hydrazineyl)(4-(dimethylamino)phenyl)methyl carbamimidothioate		$C_{27}H_{28}N_8OS$	160-162	67	Pale brown

Table(2-5): The Nomenclature , Structural formula, chemical formula and physical properties of imidazol compounds [VII]$_{a-g}$

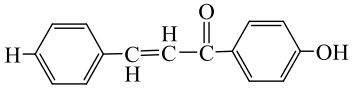
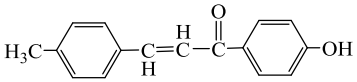
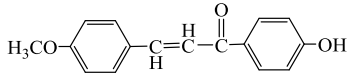
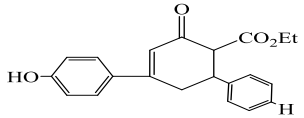
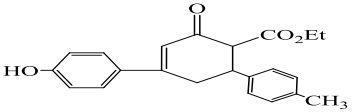
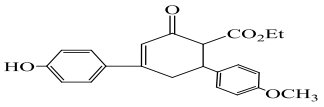
Comp. No.	Nomenclature	Structural formula	Molecuar formula	M. P ^{0}C	Yield %	Color
[VII]$_a$	N'-acetyl-2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)-N'-(((4,5-diphenyl-1H-imidazol-2-yl)thio) (phenyl) methyl) acetohydrazide		$C_{41}H_{33}N_7O_2S_2$	114-116	55	Green
[VII]$_b$	N'-acetyl-2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)-N'(((4,5-diphenyl-1H-imidazol -2-yl)thio) (4-tolyl) methyl) acetohydrazide		$C_{42}H_{35}N_7O_2S_2$	118-120	57	Pale yellow
[VII]$_c$	N'-acetyl-N'-((4-(dimethylamino) phenyl) ((4,5-diphenyl-1H-imidazol-2-yl)thio)methyl)-2-((5,6-diphenyl-1,2,4-triazin-3-yl) thio)acetohydrazide		$C_{43}H_{38}N_8O_2S_2$	120-122	60	Yellow

$[VII]_d$	N'-acetyl-2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)-N'-(((4,5-diphenyl-1H-imidazol-2-yl)thio)(3-nitrophenyl) methyl)acetohydrazide		$C_{41}H_{32}N_8O_4S_2$	209-210	52	Pale yellow
$[VII]_e$	N-(5,6-diphenyl-1,2,4-triazin-3-yl)-N'-(((4,5-diphenyl-1H-imidazol-2-yl)thio)(phenyl)methyl)acetohydrazide		$C_{39}H_{31}N_7OS$	130-130	65	Pale yellow
$[VII]_f$	N-(5,6-diphenyl-1,2,4-triazin-3-yl)-N'-(((4,5-diphenyl-1H-imidazol-2-yl)thio)(p-tolyl)methyl)acetohydrazide		$C_{40}H_{33}N_7OS$	95-97	60	Yellow
$[VII]_g$	N'-((4-(dimethylamino)phenyl)((4,5-diphenyl-1H-imidazol-2-yl)thio) methyl)-N-(5,6-diphenyl-1,2,4-triazin-3-yl)acetohydrazide		$C_{41}H_{36}N_8OS$	120-122	67	Brown

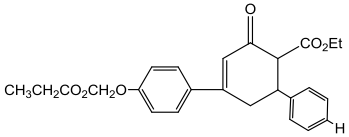
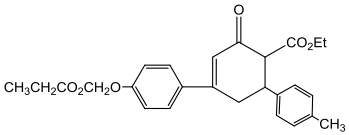
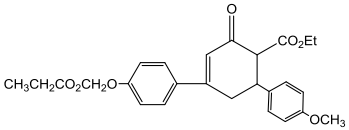
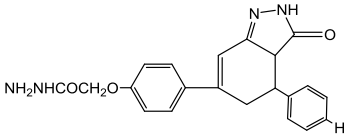
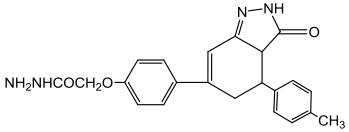
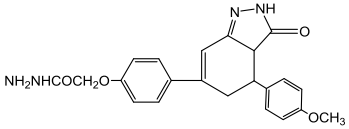
Table(2-6):The Nomenclature, Structural formula, chemical formula and physical properties of compounds [VIII]$_{a-d}$

Comp. No.	Nomenclature	Structural formula	Molecuar formula	M. P ^{0}C	Yield %	Color
[VIII]$_a$	N-(1,3-dioxoisoindolin-2-yl)-2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio)acetamide		$C_{25}H_{17}N_5O_3$ S	200-202	70	Pale yellow
[VIII]$_b$	N-(1,3-dioxo-1,3-dihydro-2H-benzo[f]isoindol-2-yl)-2-((5,6-diphenyl-1,2,4-triazin-3-yl)thio) acetamide		$C_{29}H_{19}N_5O_3$ S	158-160	71	Pale yellow
[VIII]$_c$	2-(5,6-diphenyl-1,2,4-triazin-3-yl)-2,3-dihydrophthalazine-1,4-dione		$C_{23}H_{15}N_5O_2$ S	222-224	80	Pale yellow
[VIII]$_d$	2-(5,6-diphenyl-1,2,4-triazin-3-yl)-2,3-dihydrobenzo[g]phthalazine-1,4-dione		$C_{27}H_{17}N_5O_2$	258-260	82	Pale brown

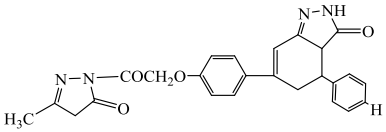
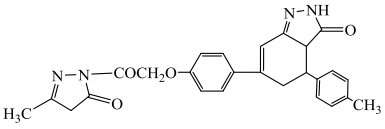
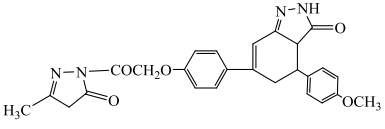
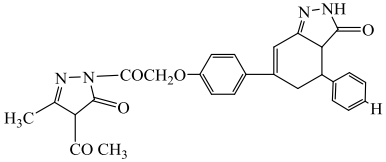
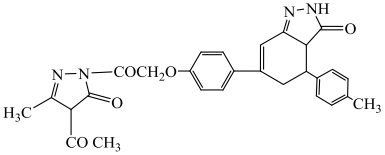
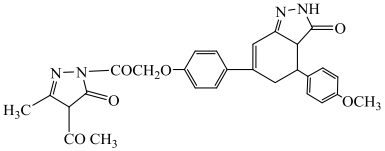
Table(2-7):The Nomenclature, Structural formula, chemical formula and physical properties of compounds [XII]$_{a-c}$ and [XIII]$_{a-c}$

Comp. No.	Nomenclature	Structural formula	Molecuar formula	M. P ^{0}C	Yield %	Color
[XII]$_a$	1-(4-hydroxyphenyl)-3-phen-yl prop-2-en-1-one		$C_{15}H_{12}O_2$	160-162	80	Pale yellow
[XII]$_b$	1-(4-hydroxyphenyl)-3-(4-tol-yl) prop-2-en-1-one		$C_{16}H_{14}O_2$	172-174	77	Off white
[XII]$_c$	1-(4-hydroxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one		$C_{16}H_{14}O_3$	180-182	82	Yellow
[XIII]$_a$	ethyl 4-hydroxy-5'-oxo-2',3',4',5'-tetrahydro-[1,1 ':3 ',1"-terphenyl]-4'-carboxylate		$C_{21}H_{20}O_4$	140-142	70	Orange
[XIII]$_b$	ethyl 4-hydroxy-4"-methyl-5'-oxo-2',3',4',5'-tetrahydro-[1,1':3',1"-terphenyl]-4'-carboxylate		$C_{22}H_{22}O_4$	124-125	70	Yellow
[XIII]$_c$	ethyl 4-hydroxy-4"-methoxy-5'-oxo-2',3',4',5 '-tetrahydro-[1,1':3',1"-terphenyl]-4'-carboxylate		$C_{22}H_{22}O_5$	120-122	73	Pale yellow

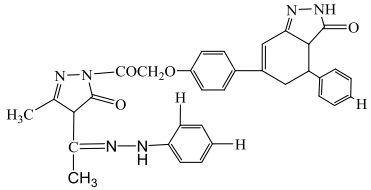
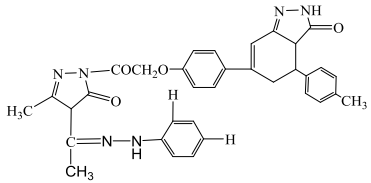
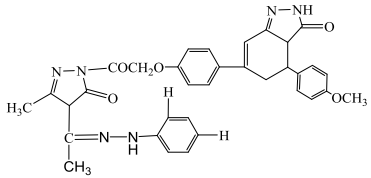
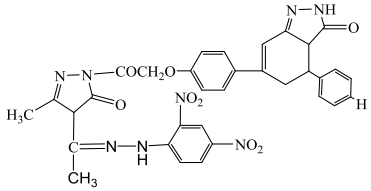
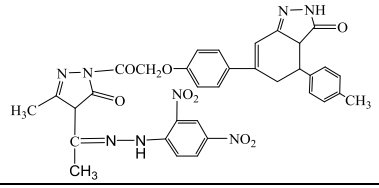
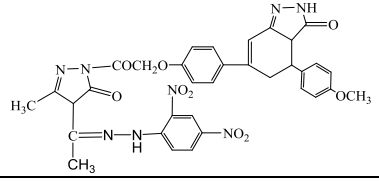
Table(2-8):The Nomenclature , Structural formula, chemical formula and physical properties of compounds $[XIV]_{a-c}$ and$[XV]_{a-c}$

Comp. No.	Nomenclature	Structural formula	Molecuar formula	M. P ^0C	Yield %	Color
$[XIV]_a$	ethyl 4-(2-ethoxy-2-oxoethoxy)-5'-oxo-2',3',4',5'-tetrahydro-[1,1':3',1" -terphenyl]-4'-carboxylate		$C_{25}H_{26}O_6$	130-132	65	Pale yellow
$[XIV]_b$	ethyl 4-(2-ethoxy-2-oxoethoxy)-4"-methyl-5'-oxo-2',3',4',5'-tetrahydro-[1,1':3',1"-terphenyl]-4'-carboxylate		$C_{26}H_{28}O_6$	138-140	62	Yellow
$[XIV]_c$	ethyl 4-(2-ethoxy-2-oxoethoxy)-4"-methoxy-5'-oxo-2',3',4',5'-tetrahydro-[1,1':3',1"-terphenyl]-4'-carboxylate		$C_{26}H_{28}O_7$	176-178	67	Pale orange
$[XV]_a$	2-(4-(3-oxo-4-phenyl-3,3a,4,5-tetra hydro-2H-indazol-6-yl) phenoxy) acetohydrazide		$C_{21}H_{20}N_4O_3$	112-114	67	Brown
$[XV]_b$	2-(4-(3-oxo-4-(4-tolyl)-3,3a,4,5-tetrahydro-2H-indazol-6-yl) phenoxy) acetohydrazide		$C_{22}H_{22}N_4O_3$	58-60	66	Off white
$[XV]_c$	2-(4-(4-methoxyphenyl) -3-oxo-3,3a,4,5-tetrahydro-2H-indazol-6-yl)phenoxy) acetohydrazide		$C_{22}H_{22}N_4O_4$	76-78	68	Orange

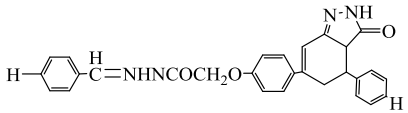
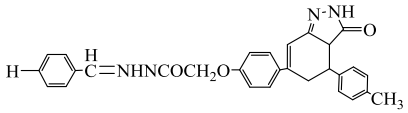
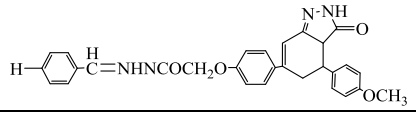
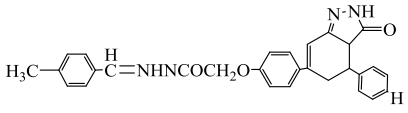
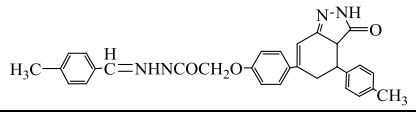
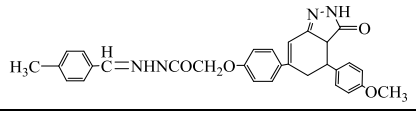
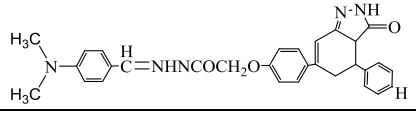
Table(2-9):The Nomenclature, Structural formula, chemical formula and physical properties of compounds $[XVI]_{a-c}$ and $[XVII]_{a-c}$

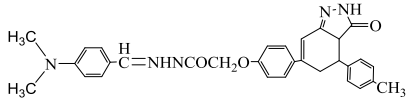
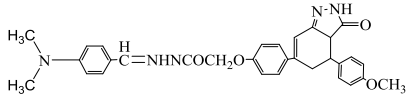
Comp. No.	Nomenclature	Structural formula	Molecuar formula	M. P ^0C	Yield %	Color
$[XVI]_a$	6-(4-(2-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-2-oxoethoxy) phenyl)-4-phenyl-2,3a,4,5-tetrahydro-3H-indazol-3-one		$C_{25}H_{22}N_4O_4$	Gammy	65	Yellow
$[XVI]_b$	6-(4-(2-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-2-oxoethoxy) phenyl)-4-(4-tolyl)-2,3a,4,5-tetrahydro-3H-indazol-3-one		$C_{26}H_{24}N_4O_4$	50-52	62	Brown
$[XVI]_c$	4-(4-methoxyphenyl)-6-(4-(2-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-2-oxoethoxy) phenyl)-2,3a,4,5-tetrahydro-3H-indazol-3-one		$C_{26}H_{24}N_4O_5$	98-100	66	Brown
$[XVII]_a$	6-(4-(2-(4-acetyl-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-2-oxo ethoxy) phenyl)-4-phenyl-2,3a,4,5-tetrahydro-3H-indazol-3-one		$C_{27}H_{24}N_4O_5$	138-140	58	Pale yellow
$[XVII]_b$	6-(4-(2-(4-acetyl-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-2-oxo ethoxy)phenyl)-4-(4-tolyl)-2,3a,4,5-tetrahydro-3H-indazol-3-one		$C_{28}H_{26}N_4O_5$	Gammy	57	Brown
$[XVII]_c$	6-(4-(2-(4-acetyl-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-2-oxoethoxy) phenyl) -4-(4-methoxy phenyl)-2,3a,4,5-tetrahydro-3H-indazol-3-one		$C_{28}H_{26}N_4O_6$	82-84	60	Brown

Table(2-10):The Nomenclature, Structural formula, chemical formula and physical properties of hydrazone compounds [XVIII] a-

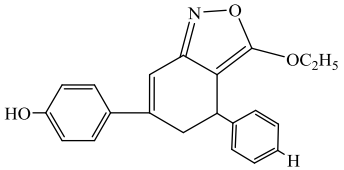
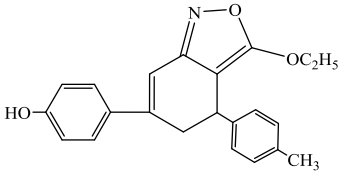
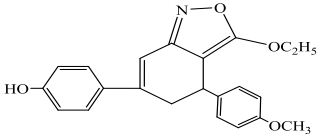
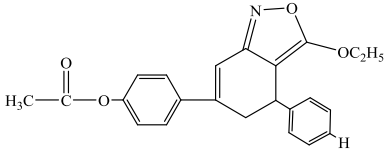
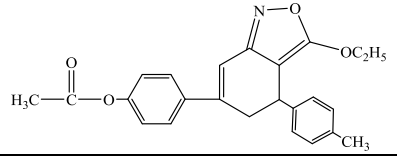
Comp. No.	Nomenclature	Structural formula	Molecuar formula	M. P ^0C	Yield %	Color
[XVIII] a	6-(4-(2-(3-methyl-5-oxo-4-(1-(2-phenylhydrazineyl idene)ethyl)-4,5-dihydro-1H-pyrazol-1-yl)-2-oxo ethoxy)phenyl)-4-phenyl-2,3a,4,5-tetrahydro-3H-indazol-3-one		$C_{33}H_{30}N_6O_4$	58-60	60	Brown
[XVIII] b	6-(4-(2-(3-methyl-5-oxo-4-(1-(2-phenylhydrazineyl idene)ethyl)-4,5-dihydro-1H-pyrazol-1-yl)-2-oxo ethoxy) phenyl)-4-(4-tolyl)-2,3a,4,5-tetrahydro-3H-indazol-3-one		$C_{34}H_{32}N_6O_4$	64-66	60	Brown
[XVIII] c	4-(4-methoxyphenyl)-6-(4-(2-(3-methyl-5-oxo-4-(1-(2-phenylhydrazineylidene)ethyl) -4,5-dihydro-1H-pyrazol-1-yl)-2-oxoethoxy)phenyl)-2,3a,4,5-tetrahydro-3H-indazol-3-one		$C_{34}H_{32}N_6O_5$	102-104	62	Pale brown
[XVIII] d	6-(4-(2-(4-(1-(2-(2,4-dinitrophenyl)hydrazineyl idene)ethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-2-oxoethoxy)phenyl)-4-phenyl -2,3a,4,5-tetra hydro-3H-indazol-3-one		$C_{33}H_28N_8O_8$	110-112	60	Pale orange
[XVIII] e	6-(4-(2-(4-(1-(2-(2,4-dinitrophenyl) hydrazineyl idene) ethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-2-oxoethoxy)phenyl)-4-(4-tolyl)-2,3a ,4,5-tetrahydro-3H-indazol-3-one		$C_{34}H_{30}N_8O_8$	70-72	61	Orang
[XVIII] f	6-(4-(2-(4-(1-(2-(2,4-dinitrophenyl) hydrazineyl idene)ethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-2-oxoethoxy) phenyl)-4-(4-methoxy phenyl)-2,3a,4,5-tetrahydro-3H-indazol-3-one		$C_{34}H_{30}N_8O_9$	142-144	62	Brown

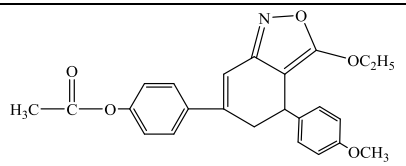
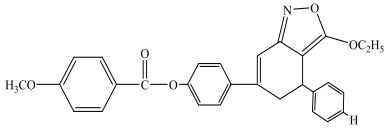
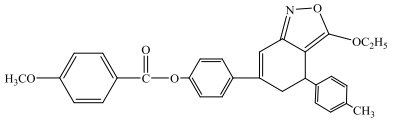
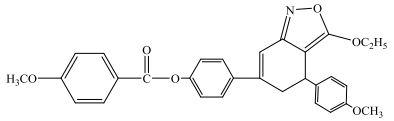
Table(2-11):The Nomenclature, Structural formula, chemical formul and physical properties of Schiff bases indazol derivatives[XIX]$_{a-i}$

Comp. No.	Nomenclature	Structural formula	Molecuar formula	M. P ^{0}C	Yield %	Color
[XIX]$_a$	N'-benzylidene-2-(4-(3-oxo-4-phenyl-3,3a,4,5-tetrahydro-2H-indazol-6-yl)phenoxy) acetohydrazide		$C_{28}H_{24}N_4O_3$	56-58	81	Brown
[XIX]$_b$	N'-benzylidene-2-(4-(3-oxo-4-(p-tolyl)-3,3a,4,5-tetrahydro-2H-indazol -6-yl)phenoxy) acetohydrazide		$C_{29}H_{26}N_4O_3$	68-70	83	Brown
[XIX]$_c$	N'-benzylidene-2-(4-(4-(4-methoxy phenyl)-3-oxo-3,3a,4,5-tetrahydro-2H-indazol-6-yl)phenoxy) acetohydrazide		$C_{29}H_{26}N_4O_4$	66-68	85	Brown
[XIX]$_d$	N'-(4-methylbenzylidene)-2-(4-(3-oxo-4-phenyl-3,3a,4,5-tetrahydro-2H-indazol-6-yl)phenoxy) acetohydrazide		$C_{29}H_{26}N_4O_3$	104-106	79	brown
[XIX]$_e$	N'-(4-methylbenzylidene)-2-(4-(3-oxo-4-(p-tolyl)-3,3a,4,5-tetrahydro-2H-indazol-6-yl)phenoxy) acetohydrazide		$C_{30}H_{28}N_4O_3$	140-142	81	Yellow
[XIX]$_f$	2-(4-(4-(4-methoxyphenyl)-3-oxo-3,3a,4,5-tetrahydro-2H-indazol-6-yl)phenoxy)-N'-(4-methyl benzylidene) acetohydrazide		$C_{30}H_{28}N_4O_4$	90-92	82	Brown
[XIX]$_g$	N'-(4-(dimethylamino) benzylidene)-2-(4-(3-oxo-4-phenyl-3,3a,4,5-tetrahydro-2H-indazol-6-yl) phenoxy) acetohydrazide		$C_{30}H_{29}N_5O_3$	120-122	80	Orange

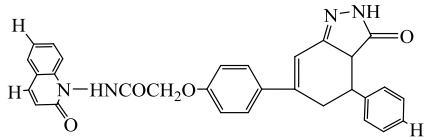
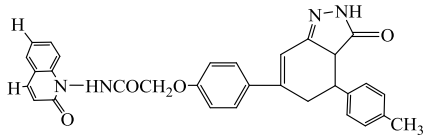
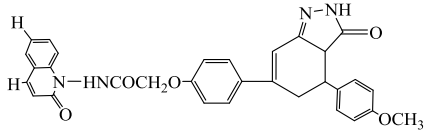
$[XIX]_h$	N'-(4-(dimethylamino) benzylidene)-2-(4-(3-oxo-4-(p-tolyl)-3,3a,4,5-tetrahydro-2H-indazol-6-yl) phenoxy)acetohydrazide		$C_{31}H_{31}N_5O_3$	250-252	82	Brown
$[XIX]_i$	N'-(4-(dimethylamino) benzylidene)-2-(4-(4-(4-methoxyphenyl)-3-oxo-3,3a,4,5-tetrahydro-2H-indazol-6-yl)phenoxy)acetohydrazide		$C_{30}H_{31}N_5O_4$	134-136	84	Brown

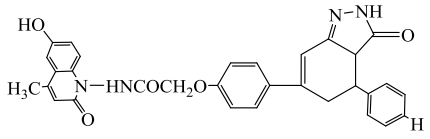
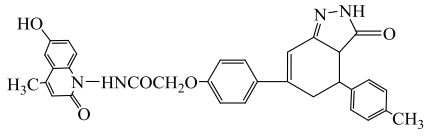
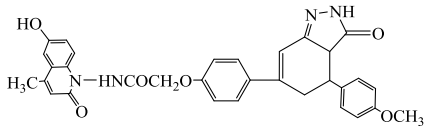
Table(2-12):The Nomenclature , Structural formula, chemical formula and physical properties of compounds [XX]$_{a-c}$ and [XXI]$_{a-f}$

Comp. No.	Nomenclature	Structural formula	Molecuar formula	M. P ^{0}C	Yield %	Color
[XX]$_a$	4-(3-ethoxy-4-phenyl-4,5-dihydrobenzo[c]isoxazol-6-yl) phenol		$C_{21}H_{19}NO_3$	126-128	65	Pale brown
[XX]$_b$	4-(3-ethoxy-4-(4-tolyl)-4,5-dihydrobenzo[c]isoxazol-6-yl) phenol		$C_{22}H_{21}NO_3$	78-80	66	Pale brown
[XX]$_c$	4-(3-ethoxy-4-(4-methoxy phenyl)-4,5-dihydrobenzo [c]isoxazol-6-yl) phenol		$C_{22}H_{21}NO_4$	112-114	67	brown
[XXI]$_a$	4-(3-ethoxy-4-phenyl-4,5-dihydrobenzo[c]isoxazol-6-yl)phenyl acetate		$C_{23}H_{21}NO_4$	80-82	60	yellow
[XXI]$_b$	4-(3-ethoxy-4-(4-tolyl)-4,5-dihydrobenzo[c]isoxazol-6-yl) phenyl acetate		$C_{24}H_{23}NO_4$	Gammy	65	brown

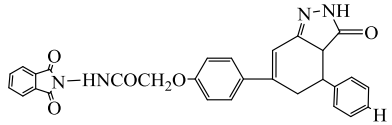
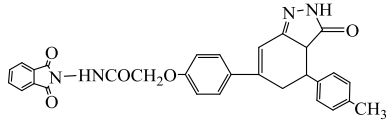
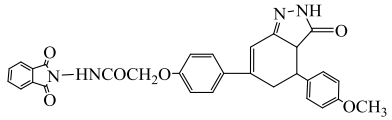
$[XXI]_c$	4-(3-ethoxy-4-(4-methoxy phenyl)-4,5-dihydrobenzo [c]isoxazol-6-yl)phenyl acetate		C_{24} $H_{23}NO_5$	Gammy	62	Brown
$[XXI]_d$	4-(3-ethoxy-4-phenyl-4,5-dihydrobenzo[c]isoxazol-6-yl)phenyl 4-methoxy benzoate		C_{29} $H_{25}NO_5$	Gammy	60	Dark brown
$[XXI]_e$	4-(3-ethoxy-4-(4-tolyl)-4,5-dihydrobenzo [c] isoxazol-6-yl)phenyl 4-methoxybenzoate		C_{30} $H_{27}NO_5$	174-176	65	Yellow
$[XXI]_f$	4-(3-ethoxy-4-(4-methoxy phenyl)-4,5-dihydrobenzo [c]isoxazol-6-yl)phenyl 4-methoxybenzoate		C_{30} $H_{27}NO_6$	128-130	62	Brown

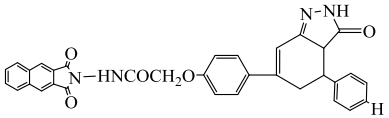
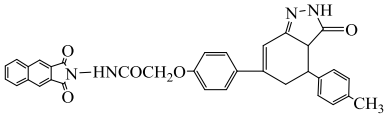
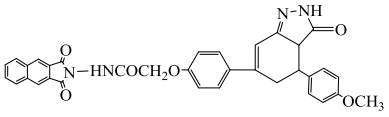
Table(2-13):The Nomenclature, Structural formula, chemical formula and physical properties of quinline derivatives [XXII]$_{a-f}$

Comp. No.	Nomenclature	Structural formula	Molecuar formula	M. P ^{0}C	Yield %	Color
[XXII]$_a$	N-(4-(3-oxo-4-phenyl-3,3a,4,5-tetrahydro-2H-indazol-6-yl) phenyl)-2-((2-oxoquinolin-1(2H)-yl)oxy) acetamide		$C_{30}H_{24}N_4O_4$	130-132	75	Orang
[XXII]$_b$	N-(4-(3-oxo-4-(4-tolyl)-3,3a,4,5-tetrahydro-2H-indazol-6-yl) phenyl)-2-((2-oxoquinolin-1(2H)-yl)oxy) acetamide		$C_{31}H_{26}N_4O_4$	104-106	74	Pale yellow
[XXII]$_c$	N-(4-(4-(4-methoxyphenyl)-3-oxo-3,3a,4,5-tetrahydro-2H-indazol-6-yl)phenyl)-2-((2- oxo quinolin-1(2H)-yl)oxy)acetamide		$C_{31}H_{26}N_4O_5$	50-52	76	Brown

$[XXII]_d$	2-((6-hydroxy-4-methyl-2-oxo quinolin-1(2H)-yl)oxy)-N-(4-(3-oxo-4-phenyl-3,3a,4,5-tetra hydro-2H-indazol-6-yl)phenyl) acetamide		$C_{31}H_{26}N_4O_5$	168-170	70	Pale orange
$[XXII]_e$	2-((6-hydroxy-4-methyl-2-oxo quinolin-1(2H)-yl)oxy)-N-(4-(3-oxo-4-(4-tolyl)-3,3a,4,5-tetra hydro-2H-indazol-6-yl)phenyl) acetamide		$C_{32}H_{28}N_4O_5$	110-112	72	Pale brown
$[XXII]_f$	2-((6-hydroxy-4-methyl-2-oxo quinolin-1(2H)-yl)oxy)-N-(4-(4-(4-methoxyphenyl)-3-oxo-3,3a ,4,5-tetrahydro-2H-indazol-6-yl)phenyl) acetamide		$C_{32}H_{28}N_4O_6$	143-145	70	Yellow

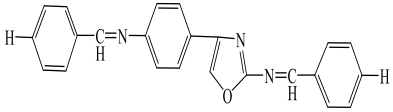
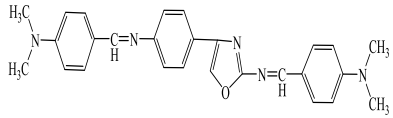
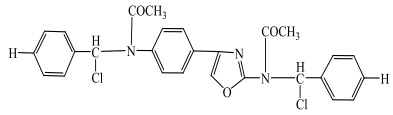
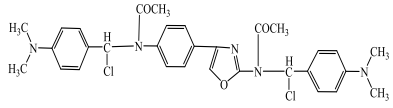
Table(2-14):The Nomenclature, Structural formula, chemical formula and physical properties of imide compounds $[XXIII]_{a-f}$

Comp. No.	Nomenclature	Structural formula	Molecuar formula	M. P ^0C	Yield %	Color
$[XXIII]_a$	N-(1,3-dioxoisoindolin-2-yl)-2-(4-(3-oxo-4-phenyl-3,3a,4,5-tetra hydro-2H-indazol-6-yl)phenoxy) acetamide		$C_{29}H_{22}N_4O_5$	198-200	80	Yellow
$[XXIII]_b$	N-(1,3-dioxoisoindolin-2-yl)-2-(4-(3-oxo-4-(4-tolyl)-3,3a,4,5-tetra hydro-2H-indazol-6-yl)phenoxy) acetamide		$C_{30}H_{24}N_4O_5$	168-170	79	Brown
$[XXIII]_c$	N-(1,3-dioxoisoindolin-2-yl)-2-(4-(4-(4-methoxyphenyl)-3-oxo-3,3a ,4,5-tetrahydro-2H-indazol-6-yl) phenoxy) acetamide		$C_{30}H_{24}N_4O_6$	130-132	82	Brown

$[XXIII]_d$	N-(1,3-dioxo-1,3-dihydro-2H-benzo[f]isoindol-2-yl)-2-(4-(3-oxo-4-phenyl-3,3a,4,5-tetrahydro-2H-indazol-6-yl)phenoxy) acetamide		$C_{33}H_{24}N_4O_5$	138-140	70	Brown
$[XXIII]_e$	N-(1,3-dioxo-1,3-dihydro-2H-benzo[f]isoindol-2-yl)-2-(4-(3-oxo-4-(4-tolyl)-3,3a,4,5-tetrahydro-2H-indazol-6-yl)phenoxy) acetamide		$C_{34}H_{26}N_4O_5$	178-180	70	Yellow
$[XXIII]_f$	N-(1,3-dioxo-1,3-dihydro-2H-benzo[f]isoindol-2-yl)-2-(4-(4-(4-methoxyphenyl)-3-oxo-3,3a,4,5-tetrahydro-2H-indazol-6-yl) phenoxy) acetamide		$C_{34}H_{26}N_4O_6$	148-150	72	Brown

Table(2-15):The Nomenclature, Structural formula, chemical formula and physical properties of oxazole derivatives

[XXV] $_{a,b}$ - [XXVIII] $_{a,b}$

Comp. No.	Nomenclature	Structural formula	Molecuar formula	M. P ^{0}C	Yield %	Color
[XXV]$_a$	N-(4-(2-(benzylidene amino) oxazol-4-yl) phenyl) -1-phenyl methanimine		$C_{23}H_{17}N_3O$	80-82	65	Dark brown
[XXV]$_b$	4-(((4-(2-((4-(dimethyl amino) benzyl idene)amino)oxazol-4-yl)phenyl) imino) methyl)-N,N-dimethyl aniline		$C_{27}H_{27}N_5O$	118-120	68	Pale brown
[XXVI]$_a$	N-(chloro(phenyl)methyl)-N-(4-(2-(N (chloro(phenyl) methyl) acetamido) oxazol-4-yl) phenyl)acetamide		$C_{27}H_{23}Cl_2N_3O_3$	60-62	58	yellow
[XXVI]$_b$	N-(chloro(4-(dimethyl amino) phenyl) methyl)-N-(4-(2-(N-(chloro(4-(dimethyl amino) phenyl)methyl) acetamido)oxazol-4-yl)phenyl) acetamide		$C_{31}H_{33}Cl_2N_5O_3$	248-250	59	brown

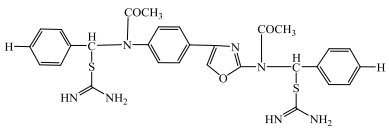
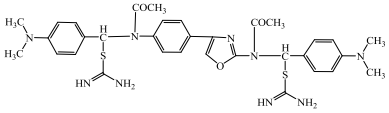
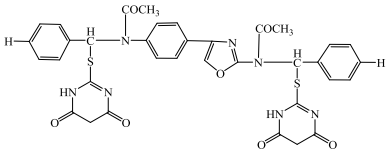
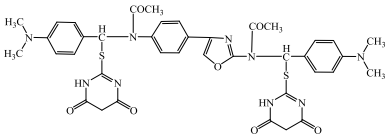
$[XXVII]_a$	(N-(4-(4-(N-((carbamimidoylthio)(phenyl) methyl)acetamido)phenyl)oxazol-2-yl) acetamido)(phenyl)methylcarbamimido thioate		$C_{29}H_{29}N_7O_3S_2$	180-182	55	Pale yellow
$[XXVII]_b$	(N-(4-(4-(N-((carbamimidoylthio)(4-(dimethylamino)phenyl)methyl) acetamido) phenyl)oxazol-2-yl)acetamido)(4(dimethyl amino)phenyl)methyl carbamimidothioate		$C_{33}H_{39}N9O_3S_2$	140-142	56	Pale brown
$[XXVIII]_a$	N-(((4,6-dioxo-1,4,5,6-tetrahydro pyrimidin-2-yl)thio)(phenyl)methyl)-N-(4-(2-(N-(((4,6-dioxo-1,4,5,6-tetrahydropyrimidin-2-yl)thio) (phenyl)methyl)acetamido)oxazol-4-yl) phenyl) acetamide		$C_{35}H_{29}N_7O_7S_2$	Gammy	51	yellow
$[XXVIII]_b$	N-((4(dimethylamino)phenyl)((4,6-dioxo-1,4,5,6-tetrahydropyrimidin-2-yl)thio) methyl)-N-(4-(2-(N-((4(dimethylamino) phenyl)((4,6-dioxo-1,4,5,6-tetrahydro pyrimidin-2yl)thio)methyl)acetamido) oxazol-4-yl) phenyl) acetamide		$C_{39}H_{39}N_9O_7S_2$	>300	53	Brown

Table (3-1):Characteristic FTIR absorption bands of Schiff bases compounds[IV]$_{a-g}$

Comp. No.	υNH	υC-H arom.	υC-H Aliph.	υC=O	υC=N	υC=C arom.	υC-N	Others
[IV]$_a$	3234	3051	2983-2885	1664	1612	1589	1344	
[IV]$_b$	3230	3055	2995-2927	1647	1614	1589	1348	
[IV]$_c$	3215	3039	2981-2845	1665	1616	1597	1361	
[IV]$_d$	3230	3060	2922-2855	1649	1616	1593	1348	υNO_2 asym,sym 1514,1319
[IV]$_e$	3209	3055	--	--	1639	1589	1346	
[IV]$_f$	3161	3030	2991-2866	--	1625	1604	1321	
[IV]$_g$	3205	3026	2974-2875	--	1625	1600	1359	

Table (3-2):Characteristic FTIR absorption band of N-acetyl compounds[V]$_{a-g}$

Comp. No.	υNH	υC-H arom.	υC-H Aliph.	υC=O	υC=C arom.	υC-N	Others
[V]$_a$	3336	3057	2916-2850	1681	1600	1375	υC-Cl 744
[V]$_b$	3221	3041	2953-2852	1662	1591	1373	υC-Cl 796
[V]$_c$	3259	3040	2924-2860	1666	1600	1377	υC-Cl 740
[V]$_d$	3200	3088	2974-2856	1680	1600	1348	υC-Cl 760 υNO_2asym,sym 1521,1320
[V]$_e$	3220	3061	2989-2840	1664	1589	1370	υC-Cl758
[V]$_f$	3170	3049	2931-2868	1681	1580	1365	υC-Cl754
[V]$_g$	3200	3043	2927-2864	1645	1593	1365	υC-Cl 785

Table (3-3):Characteristic FTIR absorption band of N-thiourea compounds [VI]$_{a-g}$

Comp. No.	υNH$_2$,NH	υC-H arom.	υC-H Aliph.	υC=O	υC=C arom.	υC-N	Others
[VI]$_a$	3360-3190	3089	2922-2852	1651	1598	1342	υC-S 767
[VI]$_b$	3380-3219	3059	2956-2858	1662	1589	1377	υC-S 752
[VI]$_c$	3275-3159	3041	2924-2866	1662	1587	1377	υC-S 746
[VI]$_d$	3172	3086	2966-2850	1676	1604	1348	υC-S 767 υNO$_2$ asym,sym 1525,1330
[VI]$_e$	3234-3205	3050	2991-2887	1662	1589	1348	υC-S 758
[VI]$_f$	3340-3108	3057	2927-2868	1674	1590	1378	υC-S 767
[VI]$_g$	3425-3209	3055	2935-2812	1658	--	1370	υC-S 752

Table (3-4):Characteristic FTIR absorption band of imidazol compounds[VII]$_{a-g}$

Comp. No.	υNH	υC-H arom.	υC-H Aliph.	υC=O	υC=N	υC=C arom.	υC-N	Others
[VII]$_a$	3414, 3379	3061	2950-2933	1678	1620	1595	1340	
[VII]$_b$	3412, 3377	3059	2929-2854	1676	1612	1593	1386	
[VII]$_c$	3408, 3375	3059	2945-2855	1678	1610	1595	1388	
[VII]$_d$	3412, 3375	3028	2931-2835	1678	1635	1595	1348	υNO_2 asym,sym 1525,1311
[VII]$_e$	3412-3379	3059	2931-2850	1678	1612	1593		
[VII]$_f$	3414-3385	3059	2935-2840	1678	1640	1590		
[VII]$_g$	3408-3380	3057	2980-2841	1678	1639, 1616	1598		

Table (3-5): Characteristic FTIR absorption bands data of imide and phthalazine compounds[VIII]$_{a-d}$

Comp. No.	Characteristic bands FTIR spectra(cm^{-1})					
	υ (NH)	υ (C-H) aromatic	υ (C-H) aliphatic	υ (C=O)	υ (C=C) aromatic	C-N
$[VIII]_a$	3183	3020	2900-2854	1766,1735, 1662	1600	1377
$[VIII]_b$	3182	3053	2970-2850	1793,1768, 1662	1583	1381
$[VIII]_c$	3228	3062	--	1718,1693	1587	1355
$[VIII]_d$	3220	3050	--	1730,1710	1598	1363

Table (3-6): Characteristic FTIR absorption bands data of Chalcone compounds[XII]$_{a-c}$ and cyclohexenone derivatives[XIII]$_{a-c}$

Comp. No.			Characteristic bands FTIR spectra(cm^{-1})				
	υ OH	υ(C-H) aromatic	υ(C-H) aliphatic	υ(C=O)	υ C=C of chalcone	υ(C=C) aromatic	Other
[XII]$_a$	3296	3064	--	1660	1645	1600	
[XII]$_b$	3207	3066	2947-2891	1658	1643	1587	
[XII]$_c$	3220	3049	2976-2838	1650	1640	1597	υC-O ether 1251
[XIII]$_a$	3358	3062	2980-2935	1714, 1645		1591	
[XIII]$_b$	3371	3024	2980- 2922	1726, 1645		1604, 1587	
[XIII]$_c$	3404	3039	2931-2835	1714, 1693		1604, 1587	υC-O ether 1230

Table (3- 7): Characteristic FTIR absorption bands data of new ester derivatives[XIV]$_{a-c}$ and indazol compounds [XV]$_{a-c}$

Comp. No.				Characteristic bands FTIR spectra(cm^{-1})				
	υ NH,NH_2	υ(C-H) aromatic	υ(C-H) aliphatic	υ(C=O)	υC=N	υC=C	υC-O	υC-N
[XIV]$_a$	--	3062	2951-2823	1737, 1645	--	1627, 1590	1240	--
[XIV]$_b$	--	3026	2970-2814	1732, 1645	--	1604, 1587	1222	--
[XIV]$_c$	--	3045	2974-2835	1735, 1647	--	1600	1253	--
[XV]$_a$	3315-3169	3055	2970-2852	1656	1610	1600	1230	1330
[XV]$_b$	3331, 3184	3030	2987- 2823	1662	1640	1606	1242	1342
[XV]$_c$	3329-3169	3026	2995-2837	1664	1647	1606	1242	1340

Table (3-8): Characteristic FTIR absorption bands data of pyrazol compounds[XVI] $_{a-c}$ and acetyl pyrazol compounds[XVII] $_{a-c}$

Comp. No.		Characteristic bands FTIR spectra(cm^{-1})					
	υNH	υ(C-H) aromatic	υ(C-H) aliphatic	υ(C=O)	υ(C=N)	υ(C=C) aromatic	υC-O
$[XVI]_a$	3246	3062	2924-2872	1720,1670	1645	1604	1226
$[XVI]_b$	3197	3020	2980-2823	1720,1664	1645	1606	1222
$[XVI]_c$	3238	3060	2987-2833	1732,1699	1635	1606	1244
$[XVII]_a$	--	3028	2954-2852	1730,1710, 1699	1650	1606	1222
$[XVII]_b$	--	3028	2954-2852	1730,1710, 1699	1655	1606	1222
$[XVII]_c$	--	3040	2940-2852	1730,1710, 1695	1645	1606	1246

Table (3-9): Characteristic FTIR absorption bands data of hydrazone compounds[XVIII] a-f

Comp. No.		Characteristic bands FTIR spectra(cm^{-1})						
	υ NH	υ(C-H) aromatic	υ(C-H) aliphatic	υ(C=O)	υ(C=N)	υ(C=C) aromatic	υC-O	Others
[XVIII] a	3270	3057	2924-2854	1730, 1700	1665, 1645	1598	1232	
[XVIII] b	3240	3051	2922-2854	1726, 1697	1665, 1637	1597	1249	
[XVIII] c	3284	3040	2927-2840	1730, 1690	1655	1598	1246	
[XVIII] d	3232	3030	2929-2835	1730, 1695	1640	1612	1240	υ NO_2 asym, sym 1512 , 1334
[XVIII] e	3290	3040	2924-2868	1730, 1698	1665, 1635	1612	1274	υ NO_2 asym, sym 1502, 1309
[XVIII] f	3319	3088	2929-2852	1728, 1710	1635	1608	1246	υ NO_2 asym, sym 1508, 1309

Table (3-10): Characteristic FTIR absorption bands data for Schiff bases of indazol dervatives[XIX]$_{a-i}$

Comp. No.		Characteristic bands FTIR spectra(cm^{-1})						
	υ NH	υ(C-H) aromatic	υ(C-H) aliphatic	υ(C=O)	υ(C=N)	υ(C=C)	υC-N	υC-O
[XIX]$_a$	3200	3059	2920-2840	1685	1645, 1622	1598	1323	1246
[XIX]$_b$	3213	3059	2930-2850	1695,1681	1655, 1625	1600	1317	1226
[XIX]$_c$	3215	3062	2920-2850	1687	1645, 1620	1604	1310	1271
[XIX]$_d$	3210	3030	2976-2860	1695,1681	1625	1606	1321	1271
[XIX]$_e$	3223	3030	2920-2834	1695,1680	1638, 1620	1608	1310	1232
[XIX]$_f$	3230	3030	2972-2835	1688,1680	1645	1606	1323	1246
[XIX]$_g$	3200	3060	2910-2818	1700,1675	1651	1593	1367	1228
[XIX]$_h$	3210	3050	2940-2802	1690,1680	1645	1595	1361	1271
[XIX]$_i$	3200	3010	2910-2800	1700, 1664	1640	1587	1365	1226

Table (3-11): Characteristic FTIR absorption bands data of Isoxazol compounds[XX]$_{a-c}$ and their ester compounds of isoxazole derivatives [XXI]$_{a-f}$

Comp. No.			Characteristic bands FTIR spectra(cm^{-1})				
	υ (OH)	υ (C-H) aromatic	υ (C-H) aliphatic	υ (C=O)	υ (C=N)	υ (C=C) aromatic	υ C-O
[XX]$_a$	3302	3030	2940-2825	--	1635	1595	1263,1226
[XX]$_b$	3240	3026	2940-2845	--	1651	1600	1276,1222,
[XX]$_c$	3265	3010	2935-2850	--	1647	1602	1244
[XXI]$_a$	--	3028	2935-2852	1755	1649	1600	1250
[XXI]$_b$	--	3045	2924-2870	1757	1664	1598	1230
[XXI]$_c$	--	3066	2933-2841	1757	1660	1595	1251
[XXI]$_d$	--	3026	2980-2841	1730	1680	1600	1255, 1219
[XXI]$_e$	--	3074	2962-2883	1732	1685	1604	1265, 1215
[XXI]$_f$	--	3030	2980-2841	1732	1680	1600	1259, 1220

Table (3-12): Characteristic FTIR absorption bands data of quinline-2-one compounds[XXII]$_{a-f}$

Comp. No.		Characteristic bands FTIR spectra(cm^{-1})						
	υ NH	υ(C-H) aromatic	υ(C-H) aliphatic	υ(C=O)	υ(C=N)	υ(C=C) aromatic	υC-N	Others
[XXII]$_a$	3242, 3182	3016	2927-2830	1726, 1710, 1697	1647	1602	1369	
[XXII]$_b$	3200, 3134	3022	2924-2823	1726, 1700	1620	1600	1363	
[XXII]$_c$	3209	3020	2953-2850	1726, 1701	1640	1602	1363	
[XXII]$_d$	3169	3060	2924-2810	1710, 1695, 1678	1640	1598	1363	υ OH 3103
[XXII]$_e$	3201	3050	2940-2830	1730, 1693, 1680	1640	1600	1368	υ OH over lap with υNH at 3201
[XXII]$_f$	3200	3084	2927-2850	1708, 1700, 1695	1647	1598	1360	υ OH 3220

Table (3-13): Characteristic FTIR absorption bands data of Imide compounds type[XXIII]$_{a-f}$

Comp. No.			Characteristic bands FTIR spectra(cm^{-1})				
	υ NH	υ(C-H) aromatic	υ(C-H) aliphatic	υ(C=O)	υ(C=N)	υ(C=C) aromatic	υ C-O
[XXIII]$_a$	3161	3024	2930-2870	1708, 1693, 1662	1645	1597	1259
[XXIII]$_b$	3167	3016	2940-2897	1735, 1707, 1660	1620	1598	1261
[XXIII]$_c$	3234	3020	2954-2852	1743, 1720, 1710, 1699	1640	1606	1247
[XXIII]$_d$	3230	3061	2922-2850	1770, 1740, 1693, 1662	1647	1602	1269
[XXIII]$_e$	3238	3026	2920-2880	1772, 1734, 1699, 1665	1647	1612	1260
[XXIII]$_f$	3250	3024	2956-2899	1776, 1728, 1708, 1662	1645	1585	1232

Table (3-14): Characteristic FTIR absorption bands data of oxazole derivetives [XXV]$_{a,b}$, [XXVI] $_{a,b}$, [XXVII] $_{a,b}$, [XXVIII] $_{a,b}$

Comp. No.			Characteristic bands FTIR spectra(cm^{-1})						
	υNH_2, NH	υ(C-H) aromatic	υ(C-H) aliphatic	υ(C=O)	υ(C=N)	υ(C=C) aromatic	υC-N	υC-O	Others
$[XXV]_a$	--	3066	--	--	1681	1600	1323	1288-1176	--
$[XXV]_b$	--	3060	2906-2815	--	1656	1591	1338	1230, 1165	υ C-N$(Me)_2$ 1367
[XXVI] $_a$	--	3057	2929-2862	1691	1640	1591	1309	1261, 1174	υ C-Cl ,767
[XXVI] $_b$	--	3043	2926-2864	1705	1658	1591	1336	1230, 1163	υ C-Cl ,700
[XXVII] $_a$	3433-3199	3057	2966-2922	1678	1664	1595	1332	1265, 1174	υ C-S , 869
[XXVII] $_b$	3429-3167	3086	2947-2816	1705	1658	1593	1315	1230, 1165	υ C-S , 875 υ C-N$(Me)_2$ 1365
[XXVIII] $_a$	3340	3049	2933, 2868	1710, 1674	1665	1597	1336	1243, 1170	υ C-S , 871
$[XXVIII]_b$	3336	3040	2929-2868	1728, 1700	1670	1597	1338	1228	υ C-S , 871

Table (3-15): Inhibition Zones of Schiff bases $[IV]_{a-g}$ -imidazoles $[VII]_{a-g}$

Compound No.	Inhibition Zone (mm.)			
	Bacillius Subtilis	***Staphylococcus aureus***	***E. Coli***	***Candida albicans***
	Gram Positive(+)	**Gram Positive(+)**	**Gram negative(-)**	
$[IV]_a$	20		20	––
$[IV]_b$	26		20	––
$[IV]_c$	23		20	21
$[IV]_d$	25		20	20
$[IV]_e$	18		19	23
$[IV]_f$	19		19	24
$[IV]_g$	20		21	––
$[V]_a$	24		19	23
$[V]_b$	29		19	21
$[V]_c$	26		24	26
$[V]_d$	––		––	––
$[V]_e$	23		19	––
$[V]_f$	23		21	18
$[V]_g$	23		19	––
$[VI]_a$	––		19	27
$[VI]_b$	21		20	––
$[VI]_c$	21		––	––
$[VI]_d$	19		––	24
$[VI]_e$	22		22	30
$[VI]_f$	40		38	––
$[VI]_g$	19		19	––
$[VII]_a$	––	––	––	20

$[VII]_b$	––	––	––	23
$[VII]_c$	––	––	––	––
$[VII]_d$	––	––	––	––
$[VII]_e$	19		19	––
$[VII]_f$	––		––	24
$[VII]_g$	23		19	24
Metronidazole	34		18	25
Control (DMSO)	––		––	––

Table (3-16): Inhibition Zones of imide and pyrazole derivatives[VIII]$_{a-d}$ - [XI]$_{a,b}$

Compound No.	Inhibition Zone (mm.)		
	Bacillius Subtilis	***E. Coli***	***Candida albicans***
	Gram Positive(+)	**Gram negative(-)**	
[VIII]$_a$	22	24	16
[VIII]$_b$	28	28	25
[VIII]$_c$	-	-	27
[VIII]$_d$	23	23	20
[IX]	22	26	18
[X]	23	22	--
[XI]$_a$	23	--	--
[XI]$_b$	22	--	--
Metronidazole	34	18	25
Control (DMSO)	––	––	––

Table (3-17): Inhibition Zones of indazoles $[XV]_{a-c}$ - Schiff bases type $[XIX]_{a-i}$

Compound No.	Inhibition Zone (mm.)		
	Bacillius Subtilis	*E. Coli*	*Candida albicans*
	Gram Positive (+)	Gram negative (-)	
$[XV]_a$	–	19	–
$[XV]_b$	21	32	–
$[XV]_c$	19	19	–
$[XVI]_a$	19	19	–
$[XVI]_b$	–	19	21
$[XVI]_c$	–	–	–
$[XVII]_a$	–	–	–
$[XVII]_b$	–	–	–
$[XVII]_c$	–	–	25
$[XVIII]_a$	24	26	24
$[XVIII]_b$	24	26	–
$[XVIII]_c$	24	25	–
$[XVIII]_d$	24	24	–
$[XVIII]_e$	23	19	–
$[XVIII]_f$	22	19	–
$[XIX]_a$	23	20	25
$[\ XIX\ ]_b$	–	24	24
$[\ XIX\ ]_c$	19	22	23
$[\ XIX\ ]_d$	23	22	23
$[\ XIX\ ]_e$	20	22	21
$[\ XIX\ ]_f$	20	22	–
$[\ XIX\ ]_g$	22	20	–
$[\ XIX\ ]_h$	20	19	–
$[\ XIX\ ]_i$	20	24	–
Metronidazole	34	18	25
Control (DMSO)	–	–	–

Table (3-18): Inhibition Zones of isoxazole derivatives[XX]$_{a-c}$and their new esters [XXI]$_{a-f}$.

Compound No.	Inhibition Zone (mm.)		
	Bacillius Subtilis	***E. Coli***	***Candida albicans***
	Gram Positive(+)	**Gram negative(-)**	
[XX]$_a$	26	23	26
[XX]$_b$	24	24	34
[XX]$_c$	23	21	19
[XXI]$_a$	23	20	20
[XXI]$_b$	24	23	24
[XXI]$_c$	19	20	--
[XXI]$_d$	20	20	25
[XXI]$_e$	20	19	43
[XXI]$_f$	20	18	--
Metronidazole	34	18	25
Control (DMSO)	––	––	––

Table (3-19): Inhibition Zones of quinline-2-one derivatives $[XXII]_{a-f}$

Compound No.	Inhibition Zone (mm.)		
	Bacillius Subtilis	***E. Coli***	***Candida albicans***
	Gram Positive(+)	**Gram negative(-)**	
$[XXII]_a$	25	24	28
$[XXII]_b$	21	24	20
$[XXII]_c$	24	24	26
$[XXII]_d$	25	25	24
$[XXII]_e$	22	20	--
$[XXII]_f$	29	24	25
Metronidazole	34	18	25
Control (DMSO)	––	––	––

Table (3-20): Inhibition Zones of imides compounds of indazoles $[XXIII]_{a-f}$

Compound No.	Inhibition Zone (mm.)		
	Bacillius Subtilis	***E. Coli***	***Candida albicans***
	Gram Positive(+)	**Gram negative(-)**	
$[XXIII]_a$	24	25	--
$[XXIII]_b$	25	24	21
$[XXIII]_c$	20	19	-
$[XXIII]_d$	25	26	41
$[XXIII]_e$	19	20	41
$[XXIII]_f$	20	28	36
Metronidazole	34	18	25
Control (DMSO)	––	––	––

Table (3-21): Inhibition Zones of Schiff bases $[XXV]_{a,b}$- Pyrimidine dervitives $[XXVIII]_{a,b}$.

Compound No.	Inhibition Zone (mm.)		
	Bacillius Subtilis	***E. Coli***	***Candida albicans***
	Gram Positive(+)	**Gram negative(-)**	
$[XXV]_a$	23	24	25
$[XXV]_b$	24	26	28
$[XXVI]_a$	26	26	18
$[XXVI]_b$	21	24	--
$[XXVII]_a$	24	--	18
$[XXVII]_b$	--	--	17
$[XXVIII]_a$	--	--	--
$[XXVIII]_b$	--	23	--
Metronidazole	34	18	25
Control (DMSO)	––	––	––

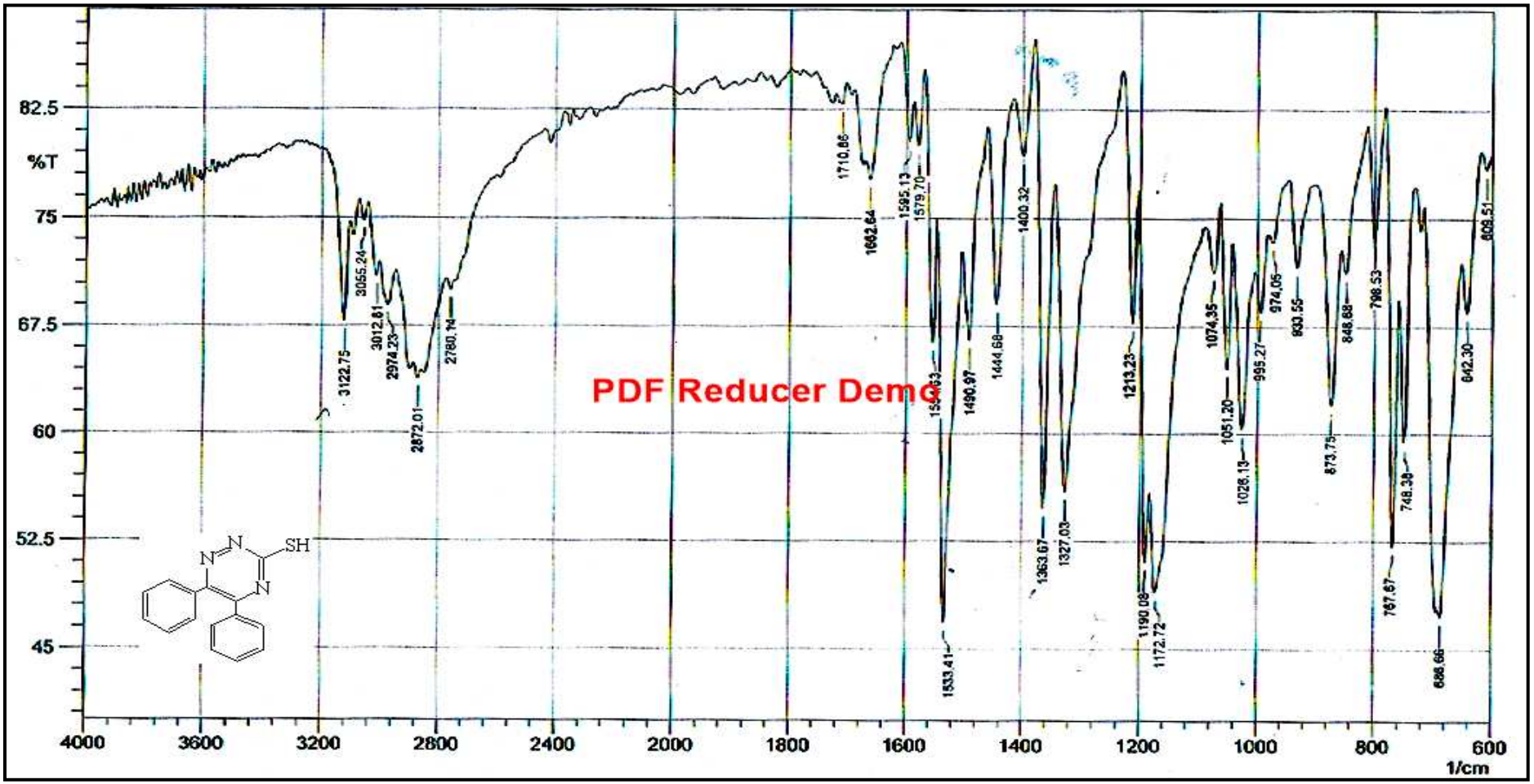


Figure (3-1) FTIR –spectrum of compound [I]

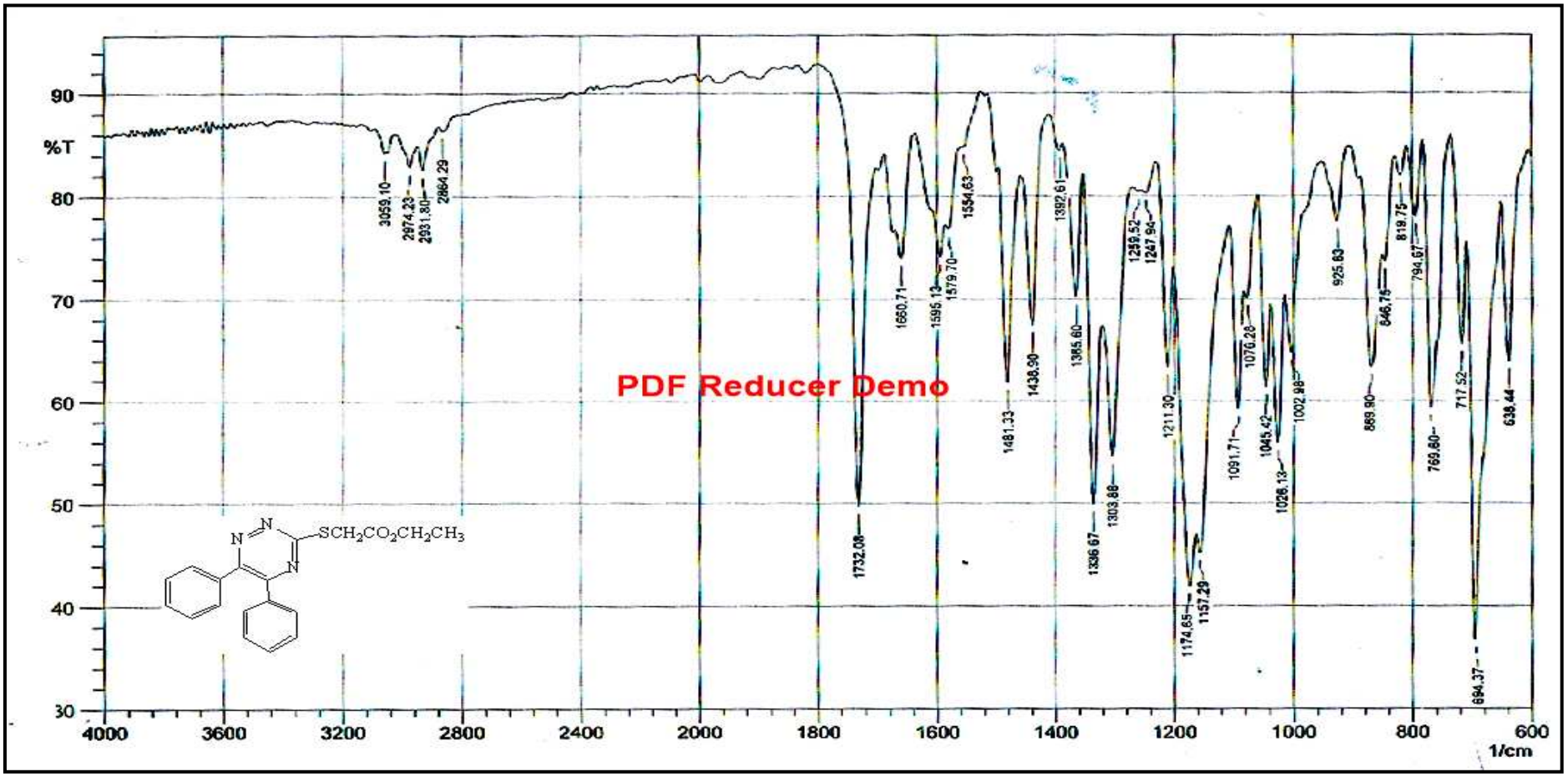


Figure (3-2) FTIR –spectrum of compound [II]

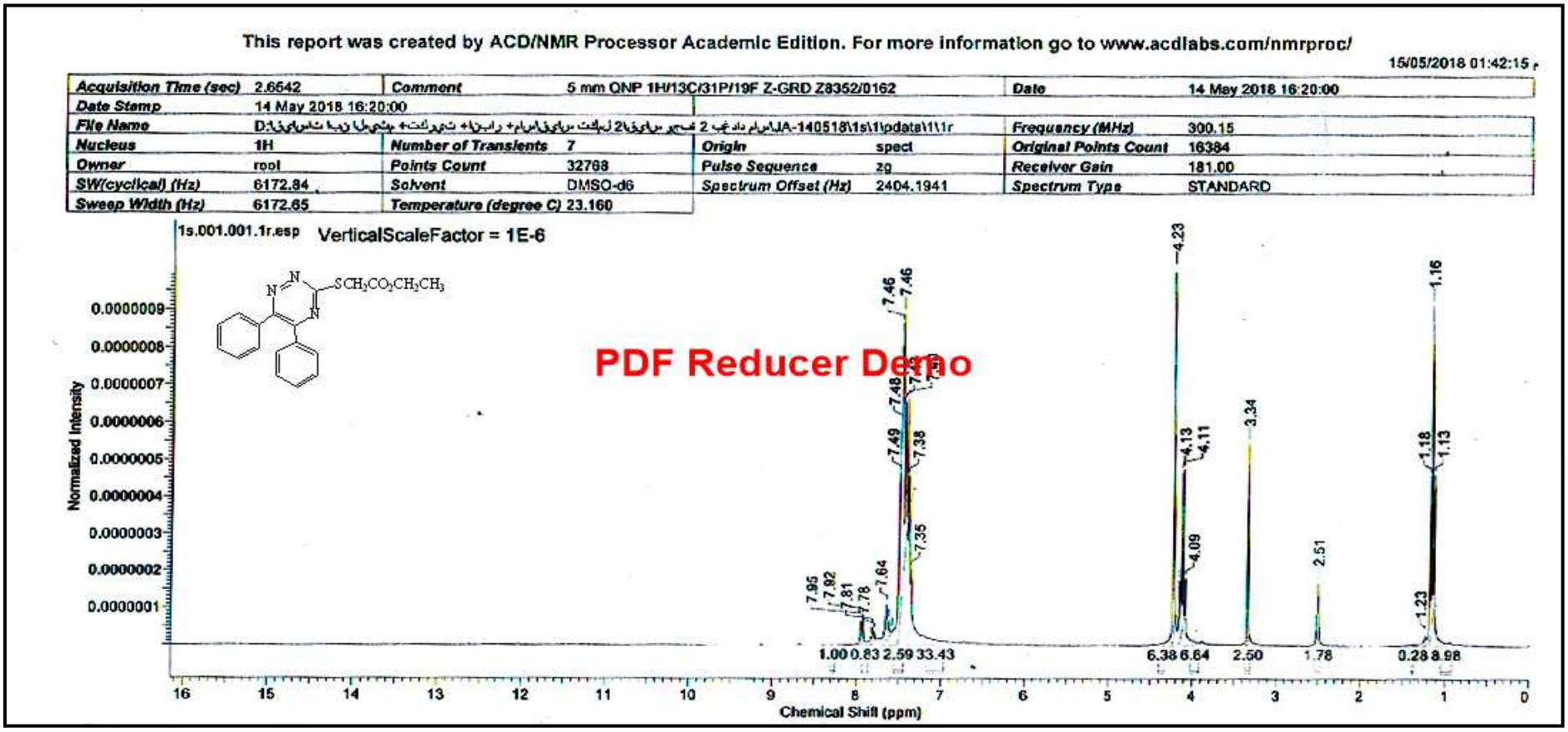


Figure (3-3) ^{1}HNMR –spectrum of compound [II]

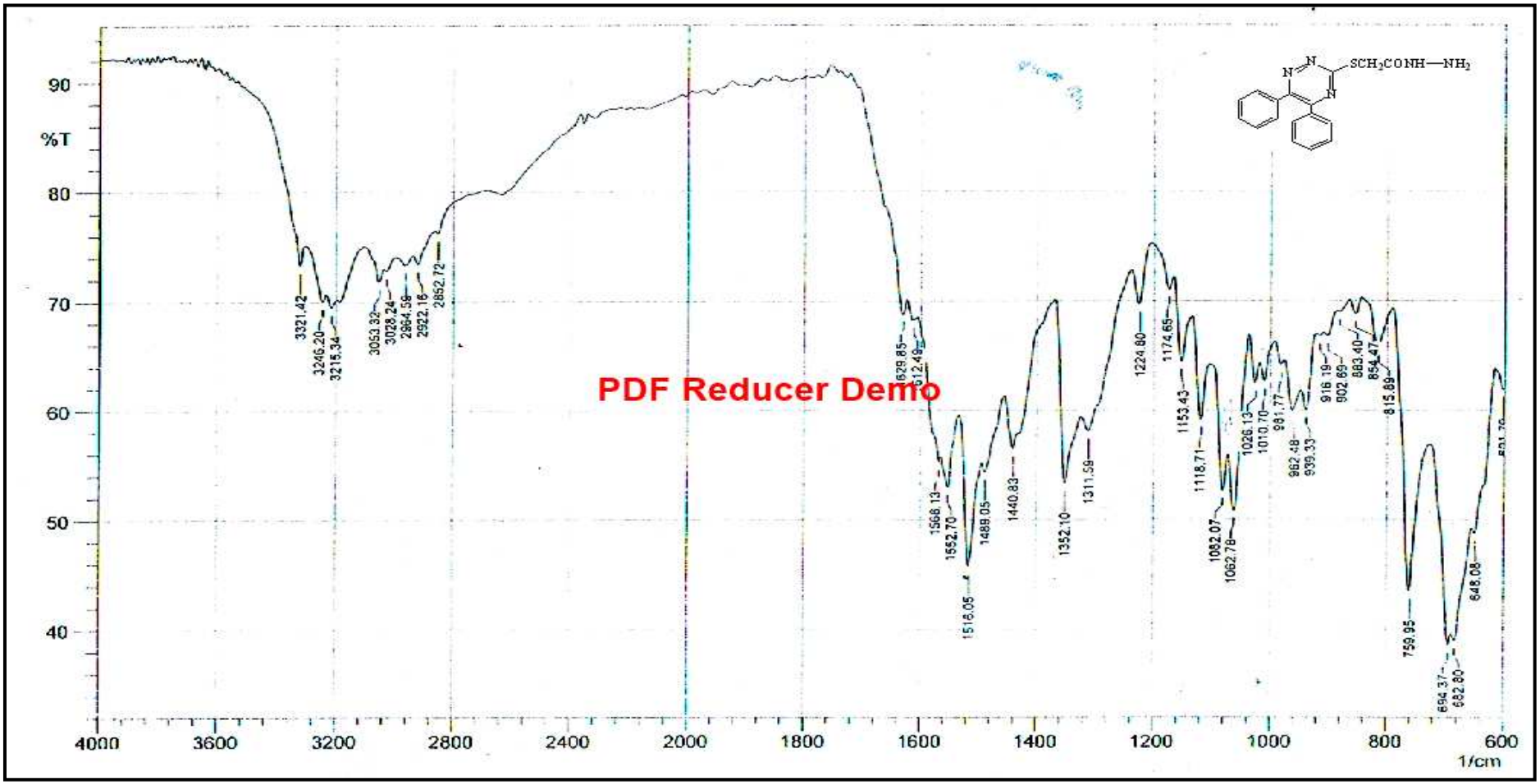


Figure (3-4) FTIR –spectrum of compound $[III]_a$

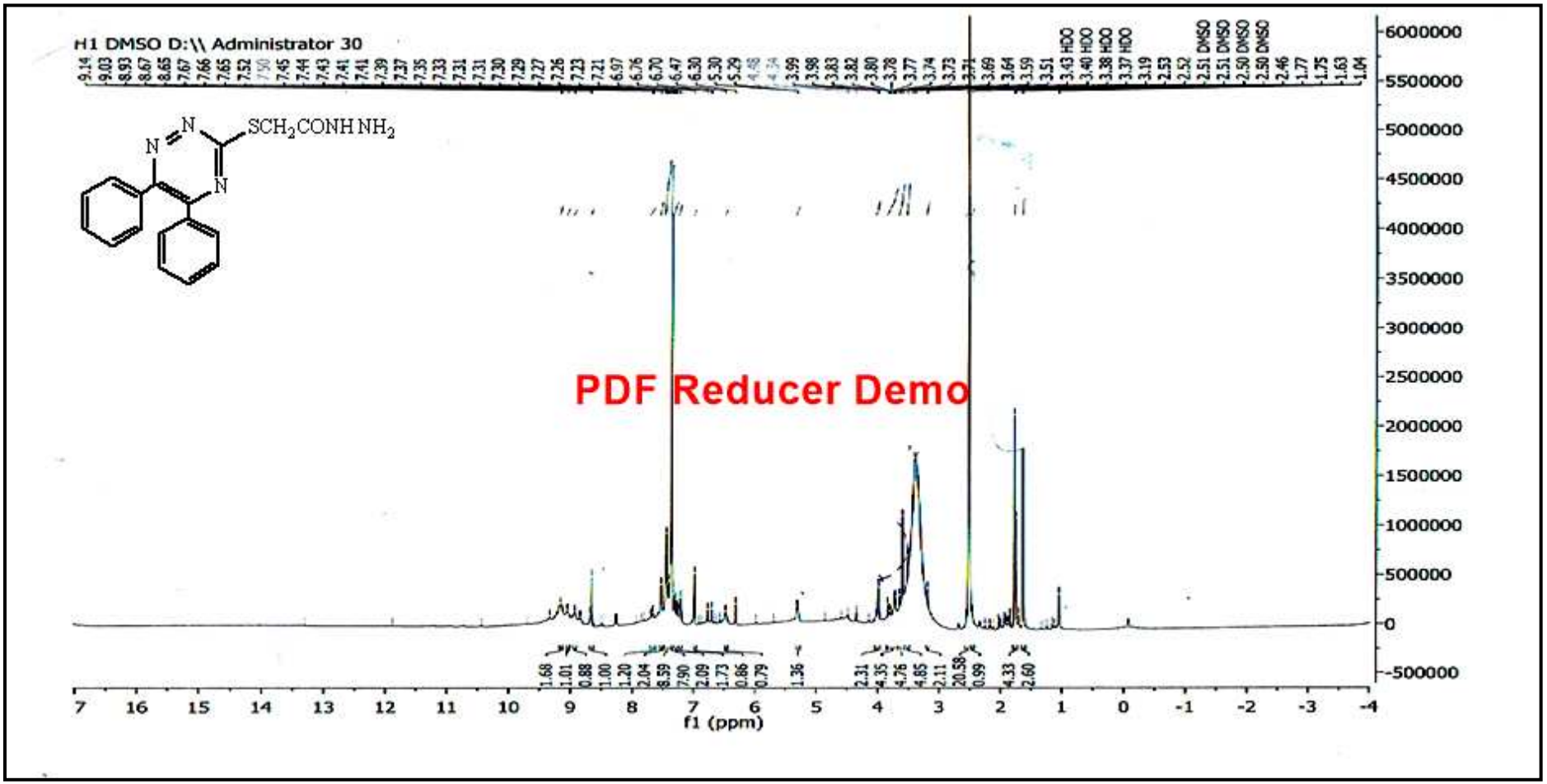


Figure (3-5) ^{1}HNMR –spectrum of compound $[III]_a$

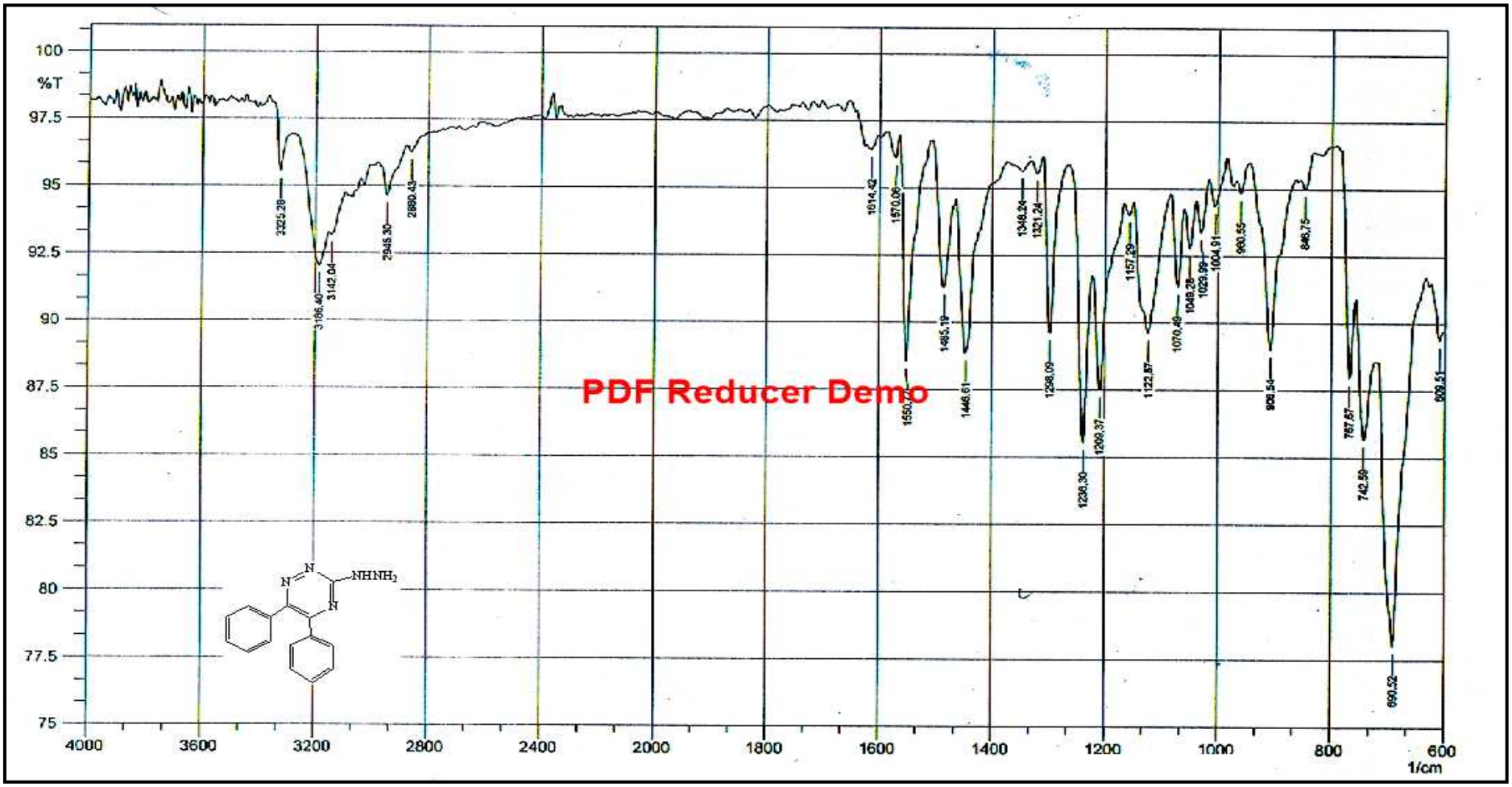


Figure (3-6) FTIR –spectrum of compound $[III]_b$

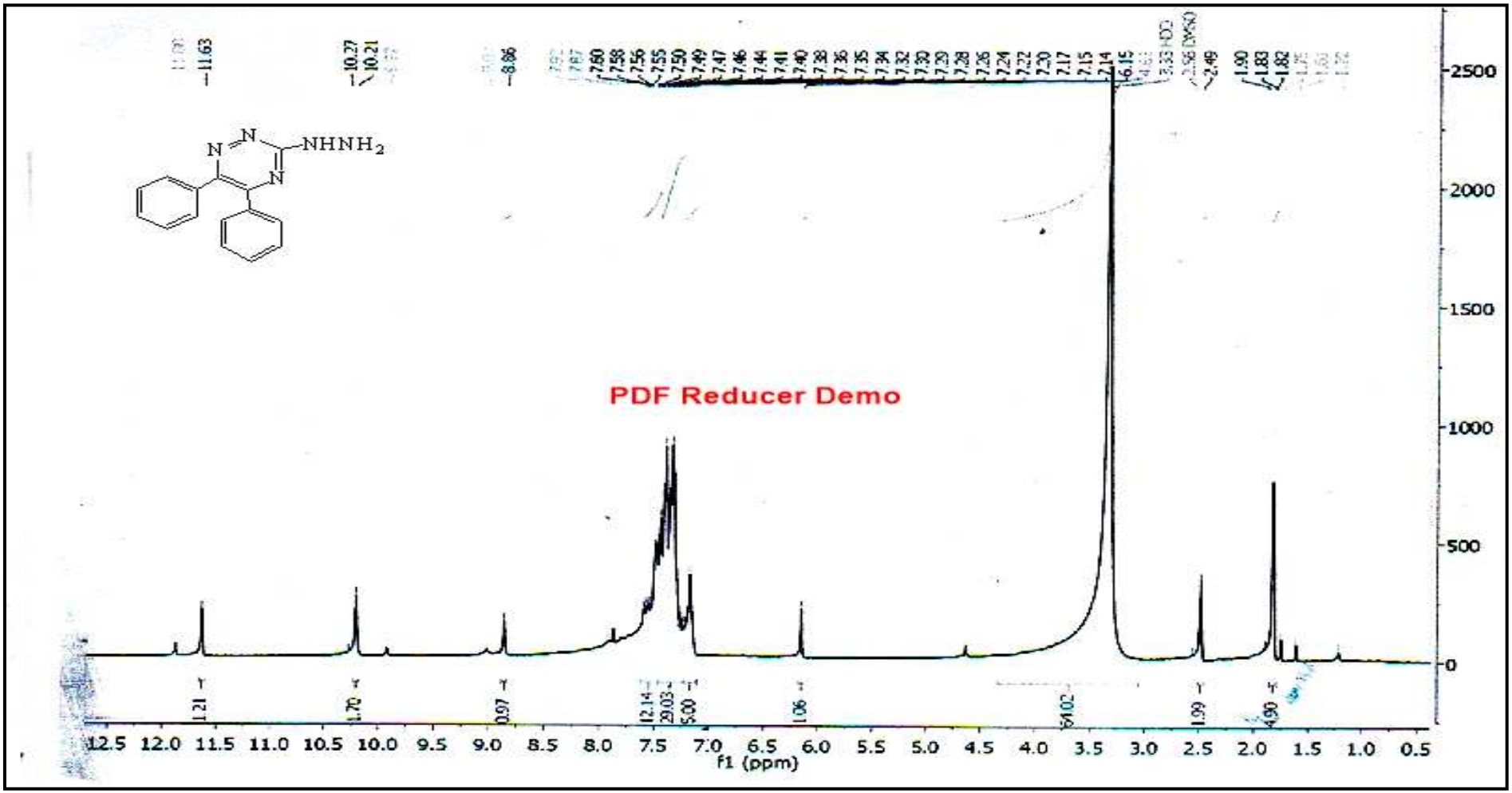


Figure (3-7) ^{1}HNMR –spectrum of compound $[III]_a$

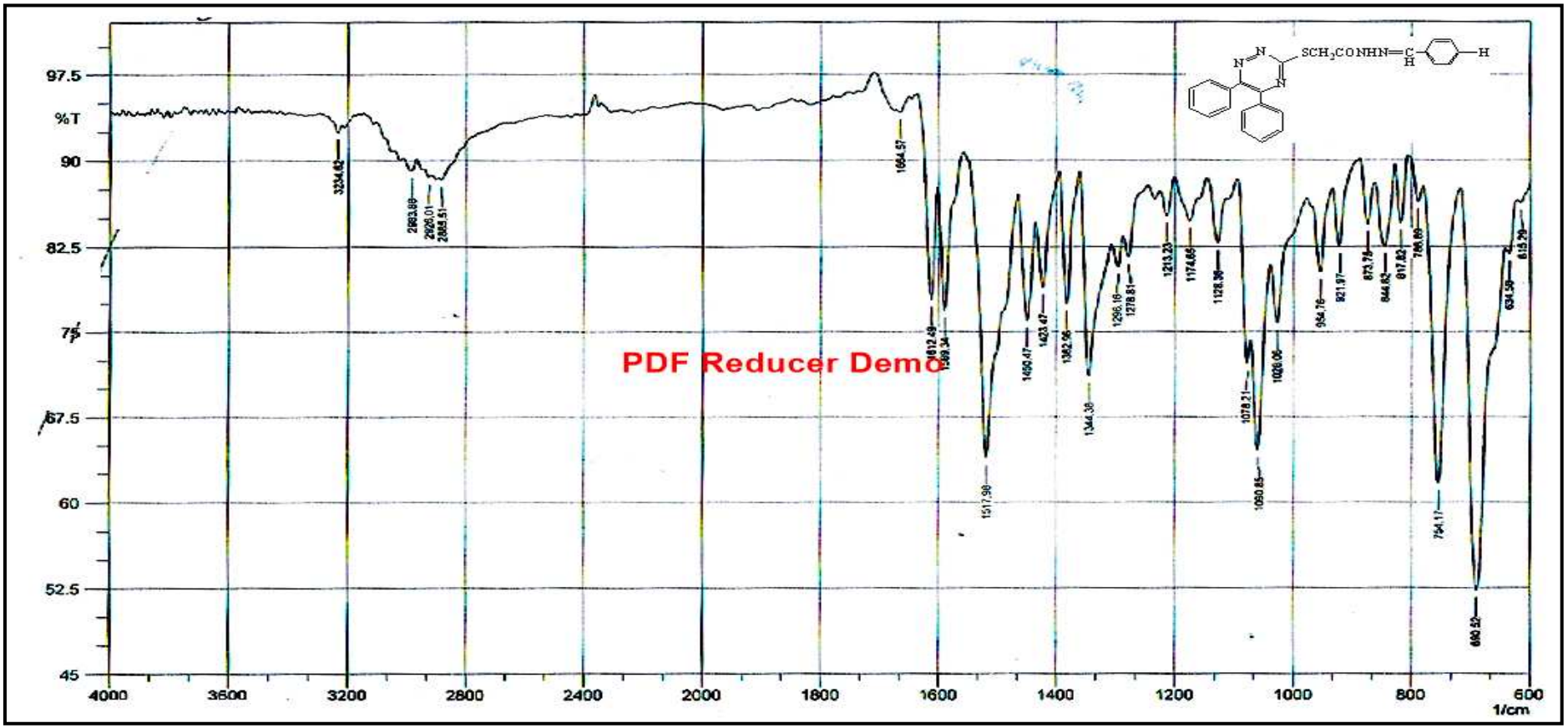


Figure (3-8) FTIR –spectrum of compound $[IV]_a$

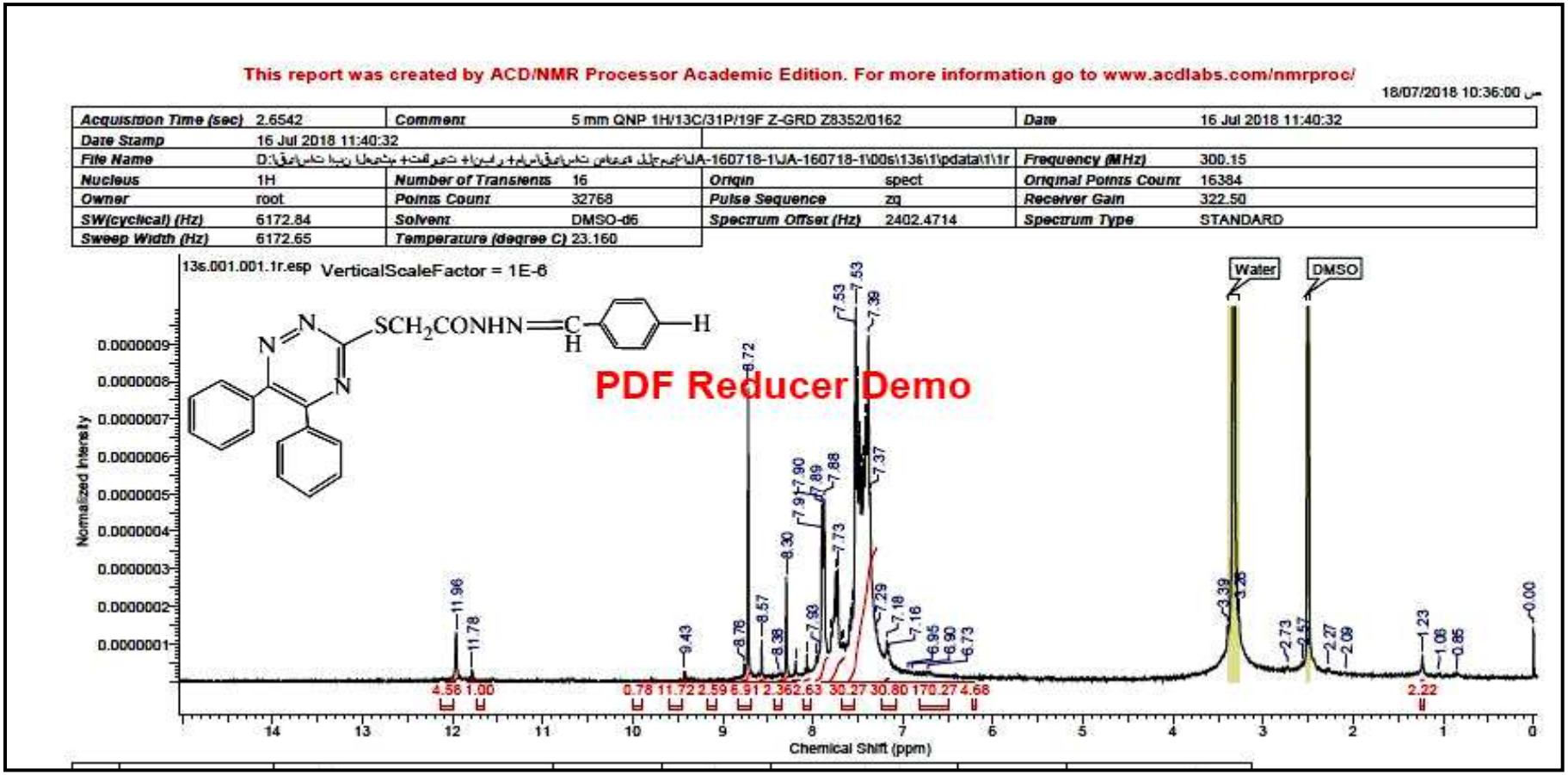


Figure (3-9) ^{1}HNMR –spectrum of compound $[IV]_a$

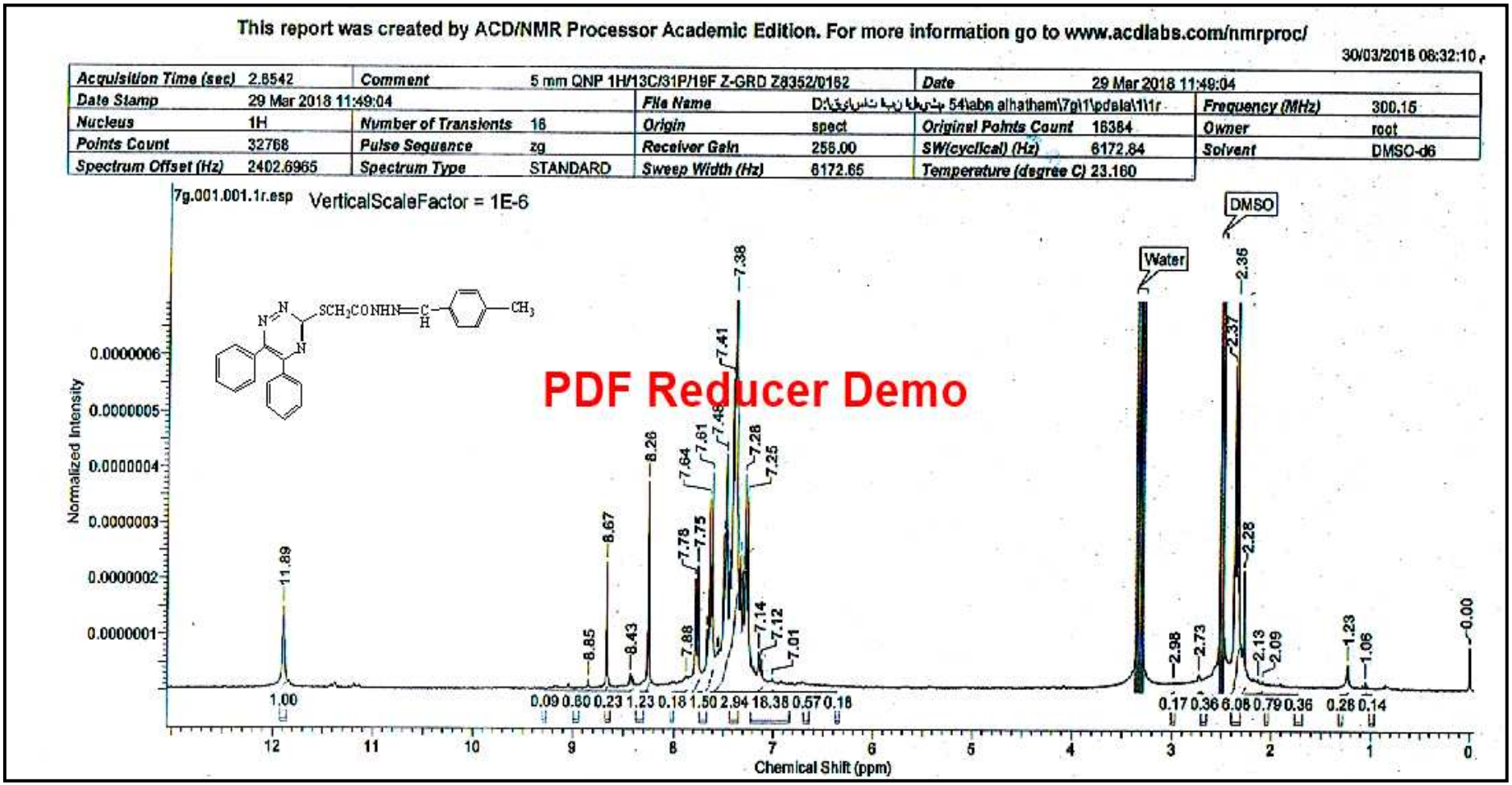


Figure (3-10) ^{1}HNMR –spectrum of compound $[IV]_b$

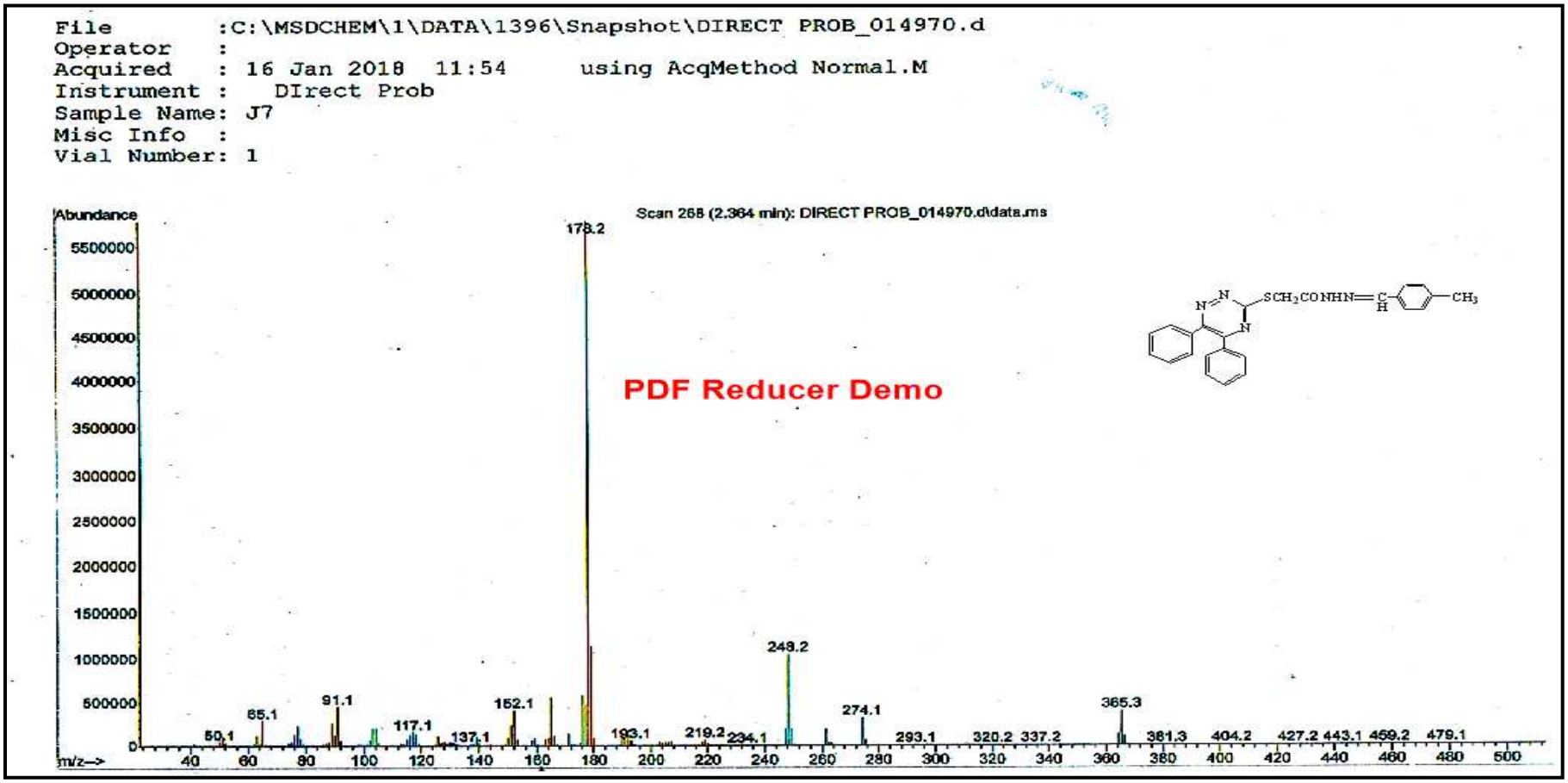


Figure (3-11)The mass spectrum of compound[IV]$_b$

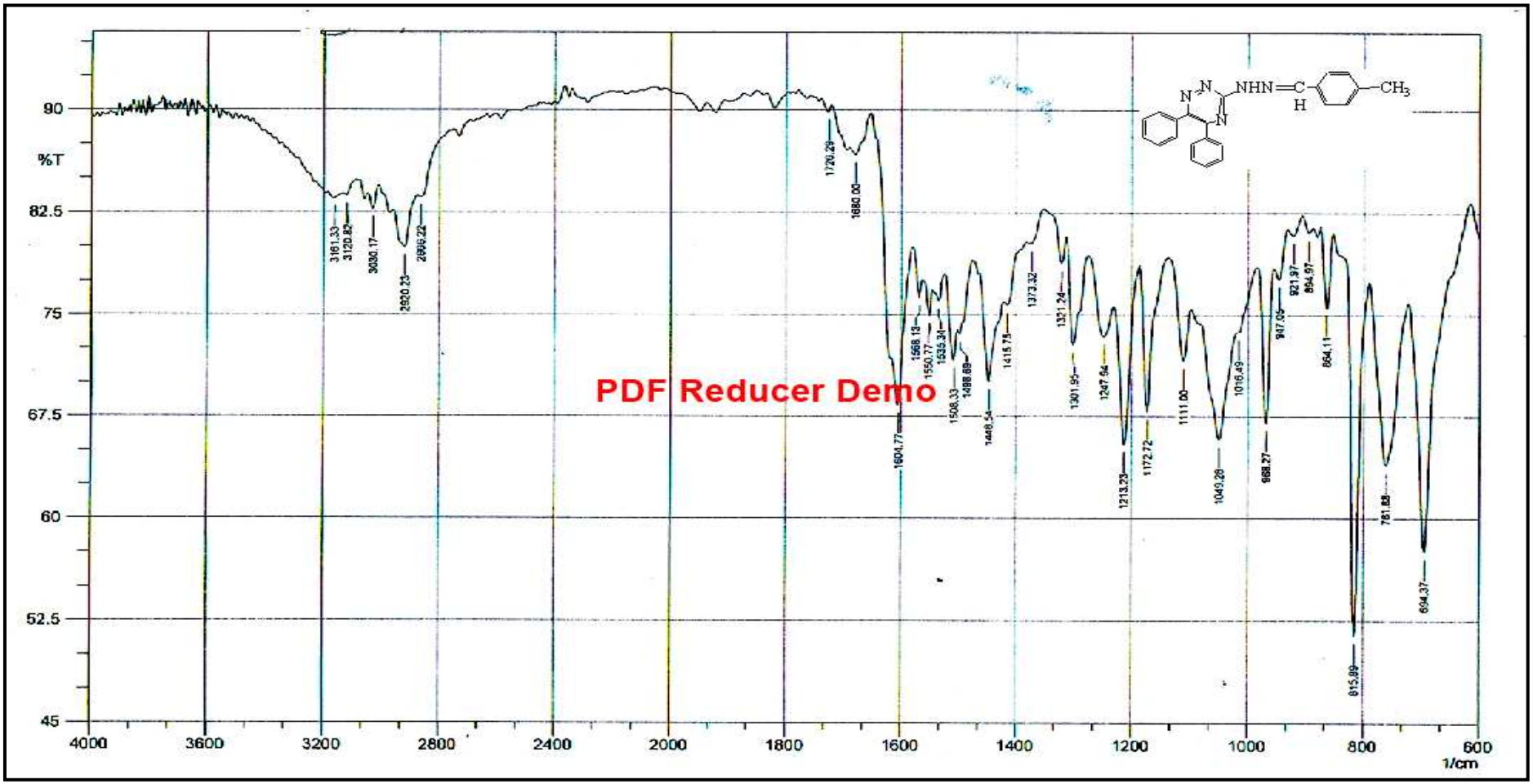


Figure (3-12) FTIR –spectrum of compound $[IV]_f$

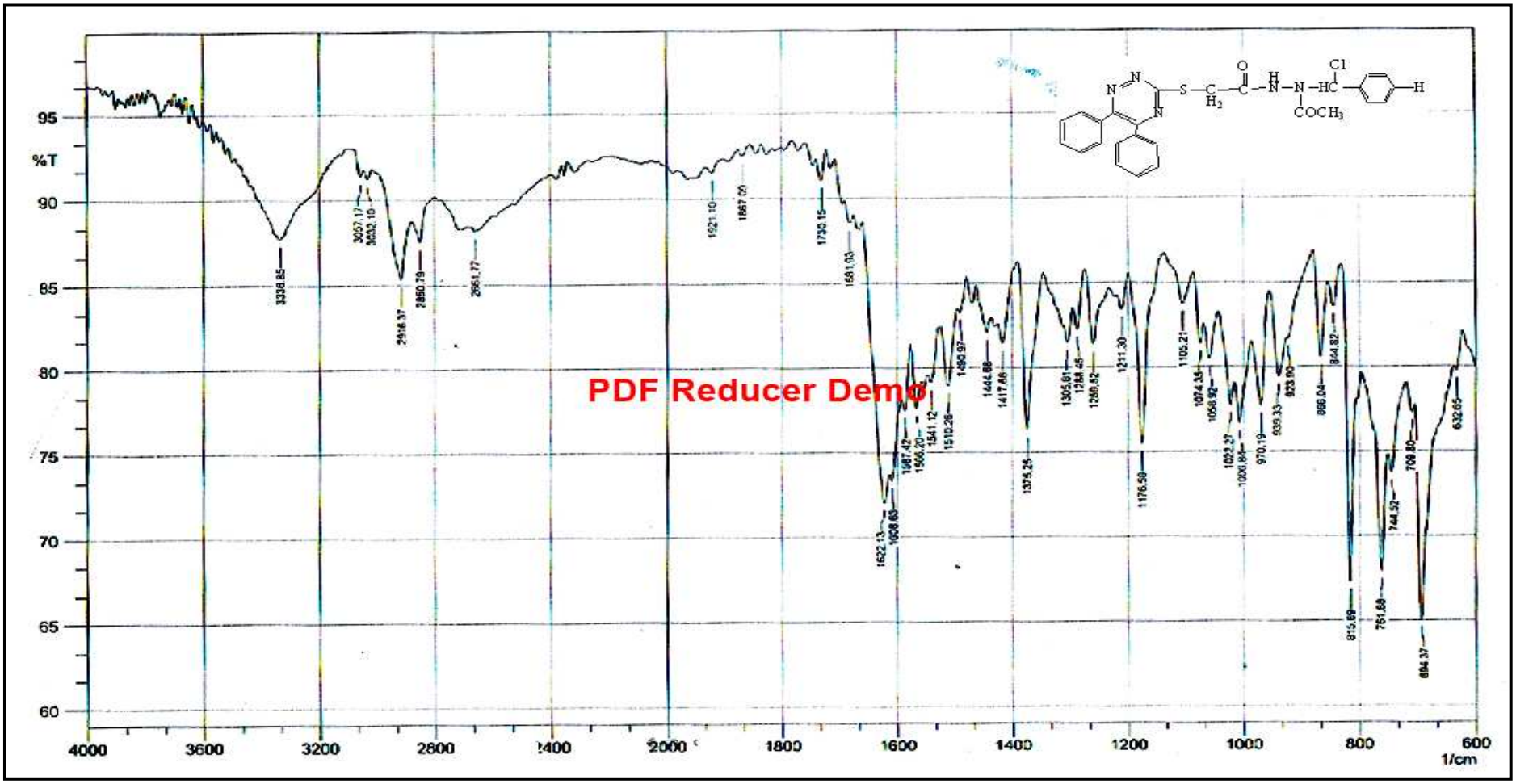


Figure (3-13) FTIR –spectrum of compound $[V]_a$

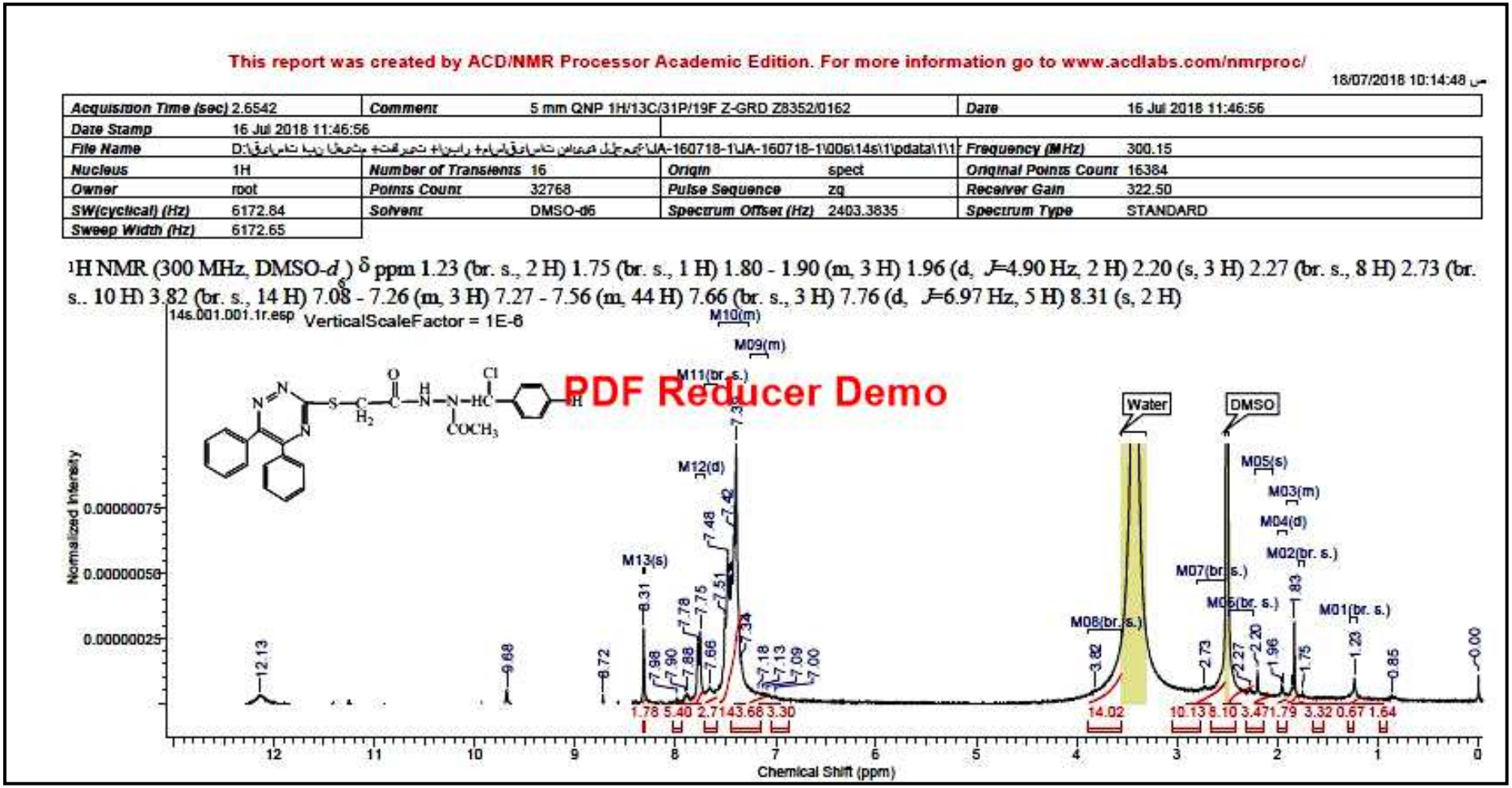


Figure (3-14) ^{1}HNMR –spectrum of compound $[V]_a$

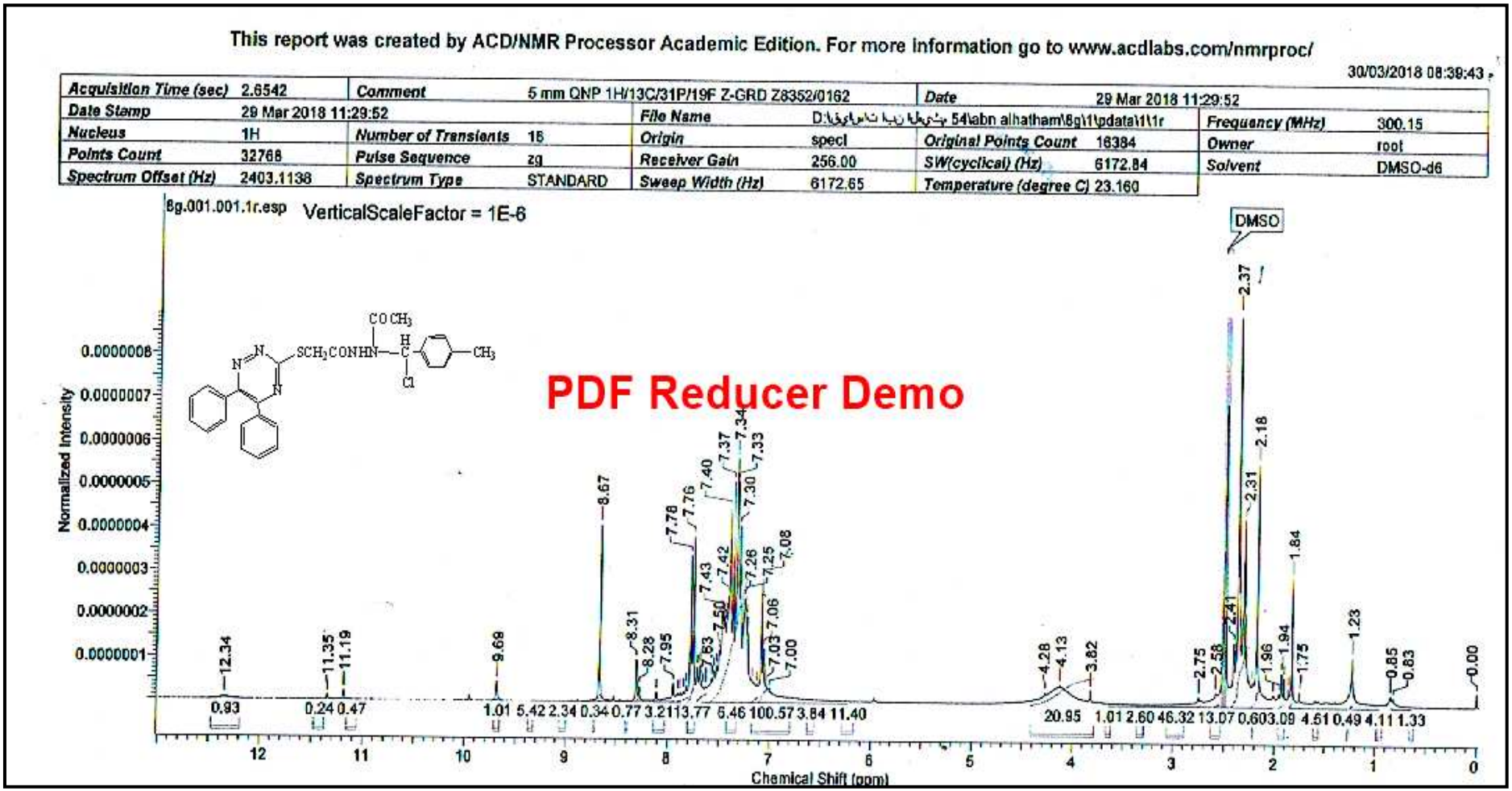


Figure (3-15) ^{1}HNMR –spectrum of compound [V] $_{b}$

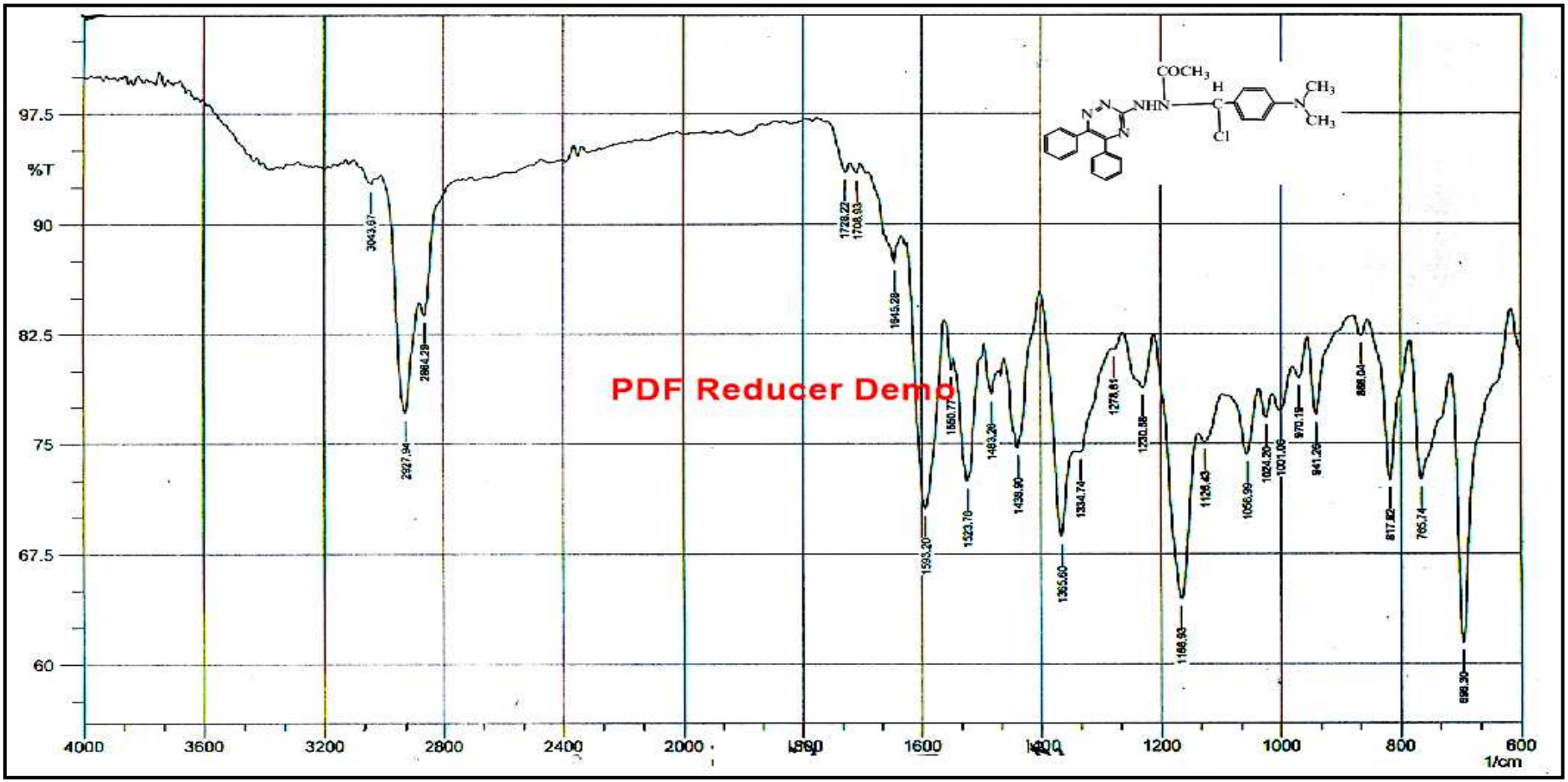


Figure (3-16) FTIR –spectrum of compound $[V]_g$

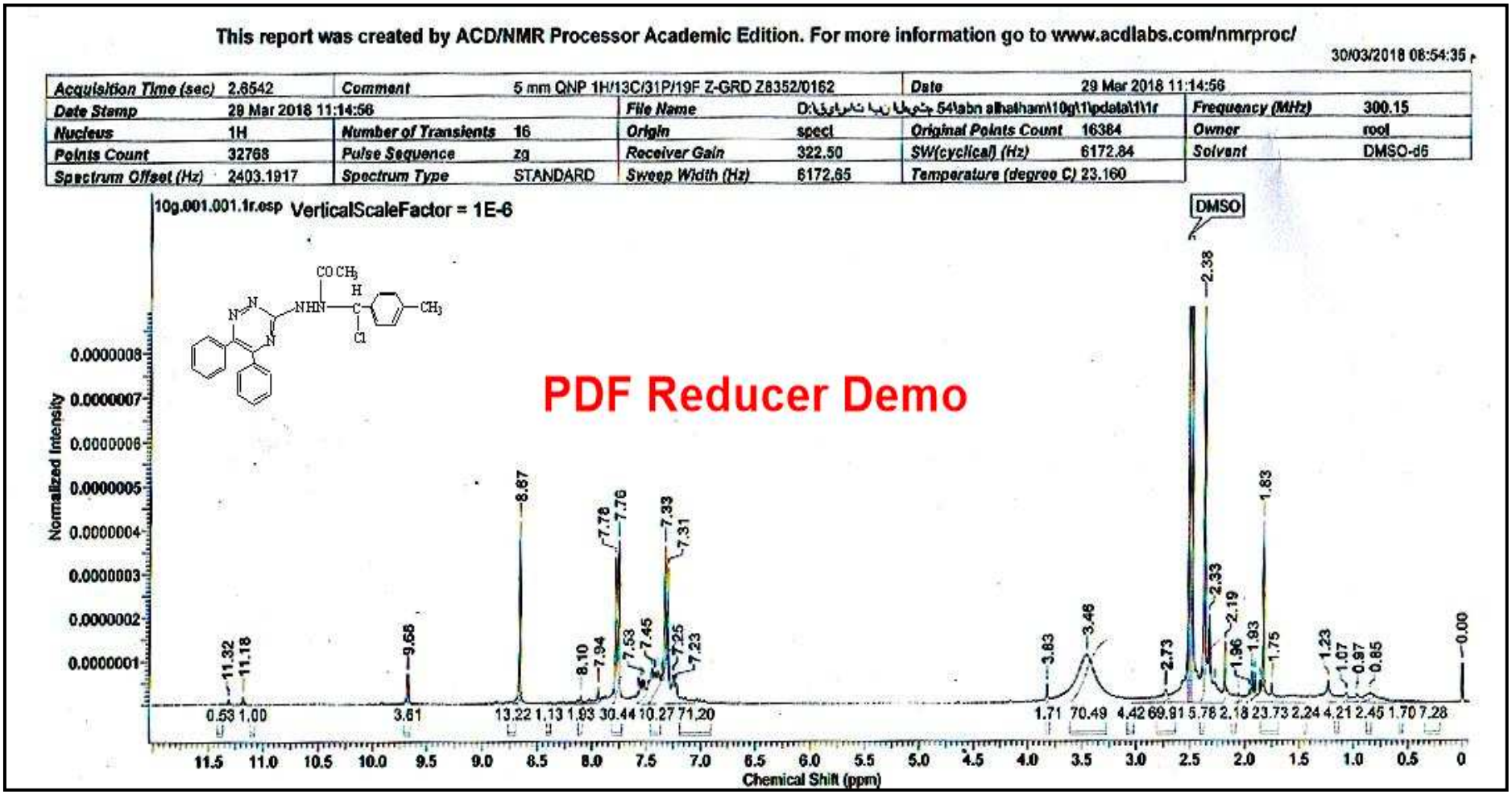


Figure (3-17) ^{1}HNMR –spectrum of compound $[V]_f$

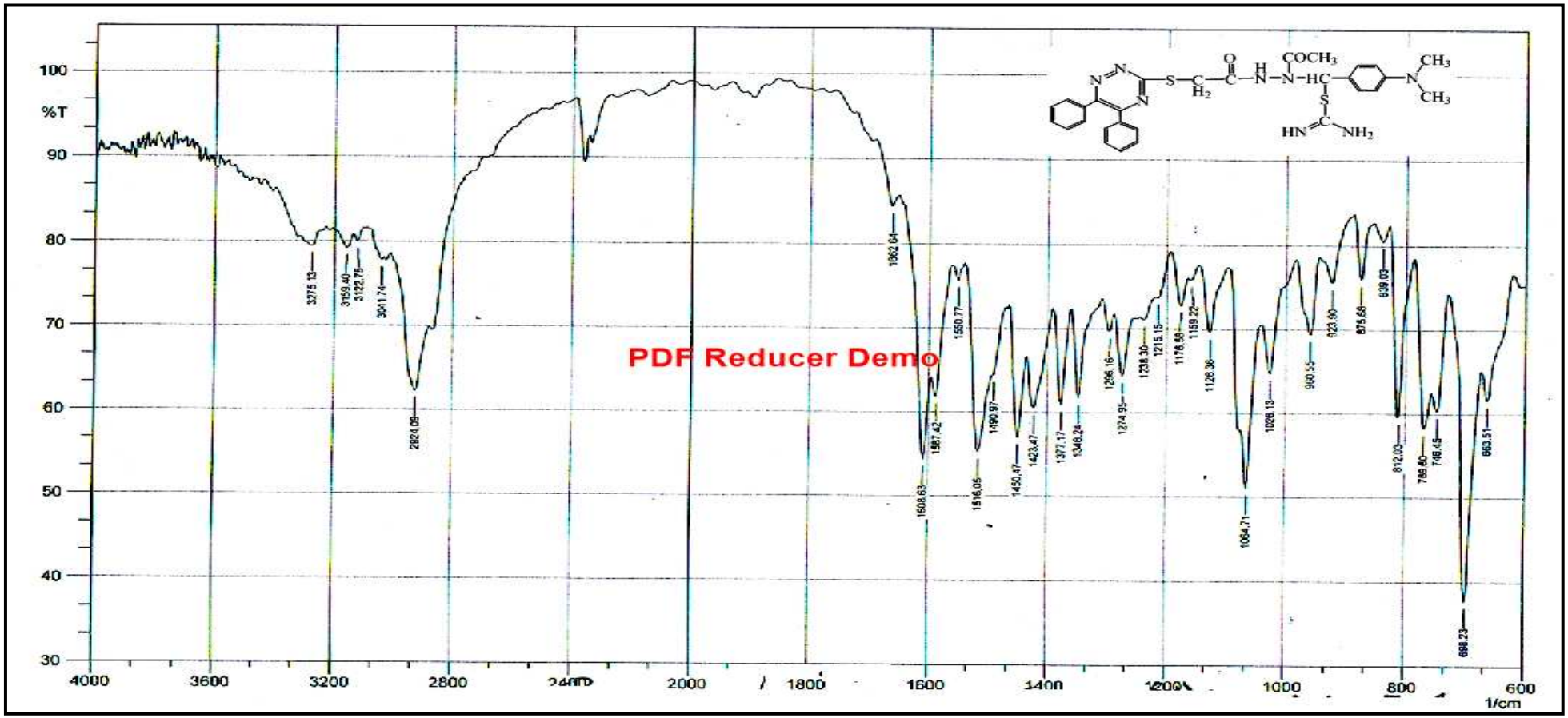


Figure (3-18) FTIR –spectrum of compound $[VI]_c$

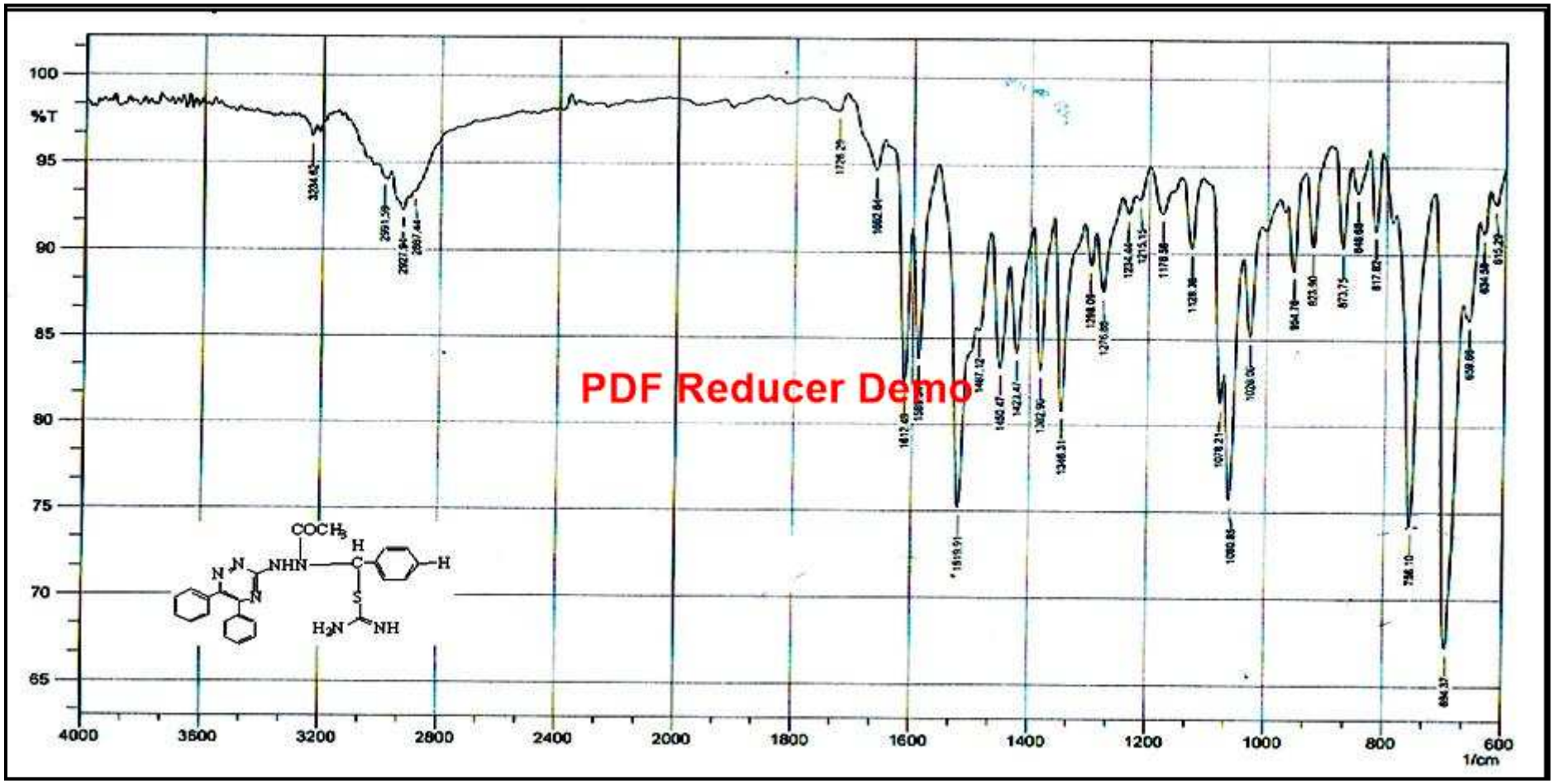


Figure (3-19) FTIR –spectrum of compound $[VI]_e$

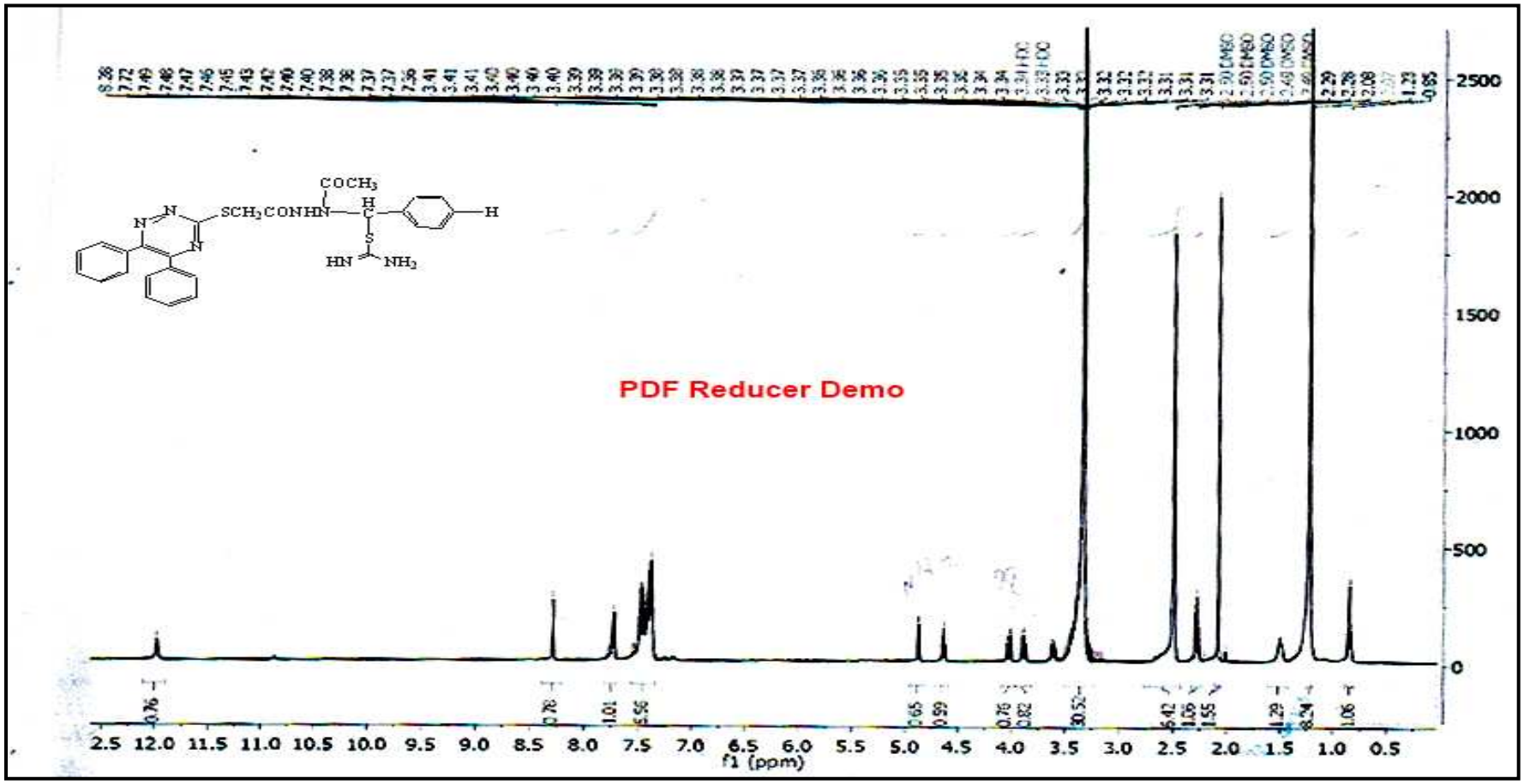


Figure (3-20) ^{1}HNMR –spectrum of compound $[VI]_a$

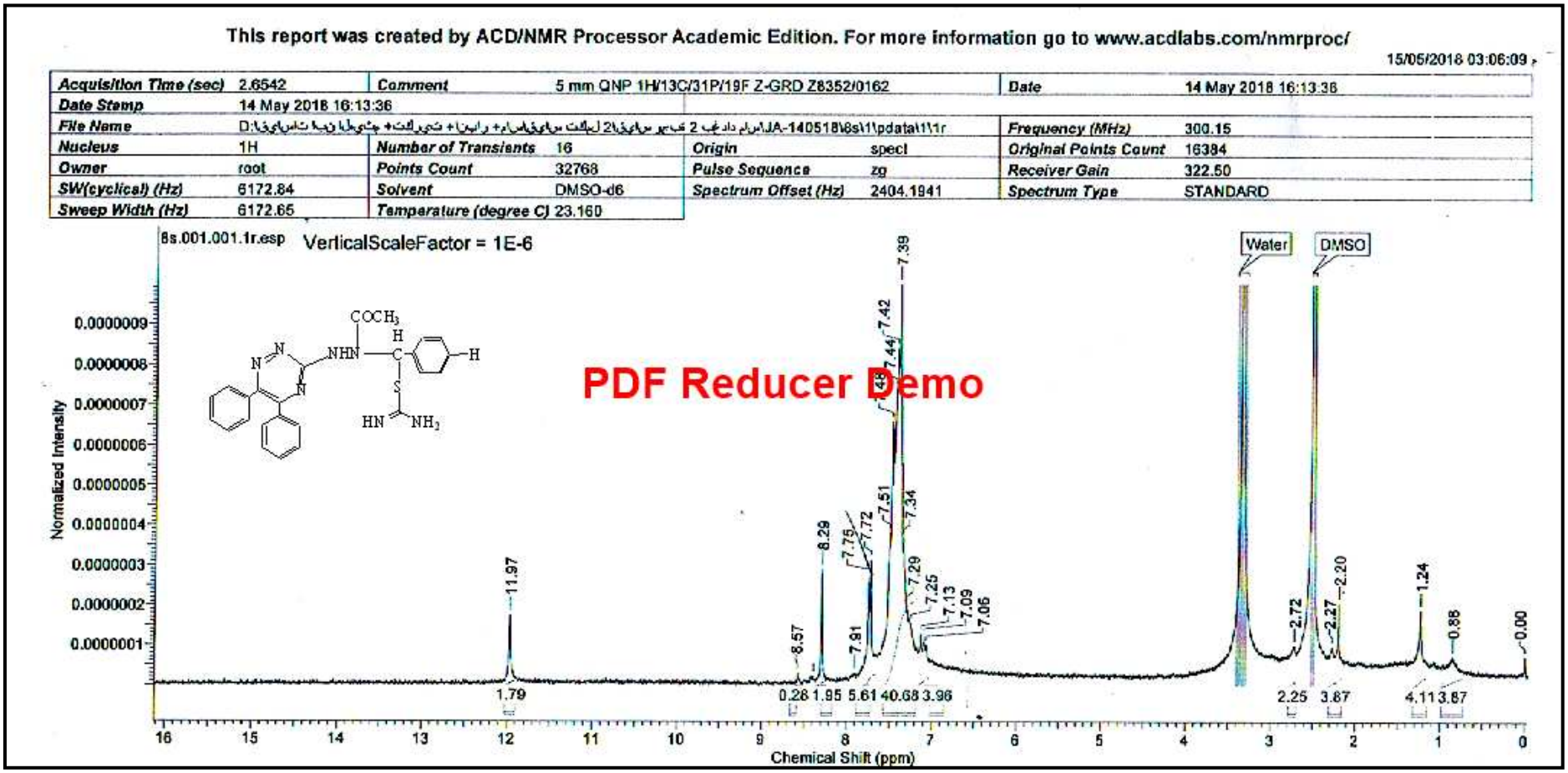


Figure (3-21) ^{1}HNMR –spectrum of compound $[V]_e$

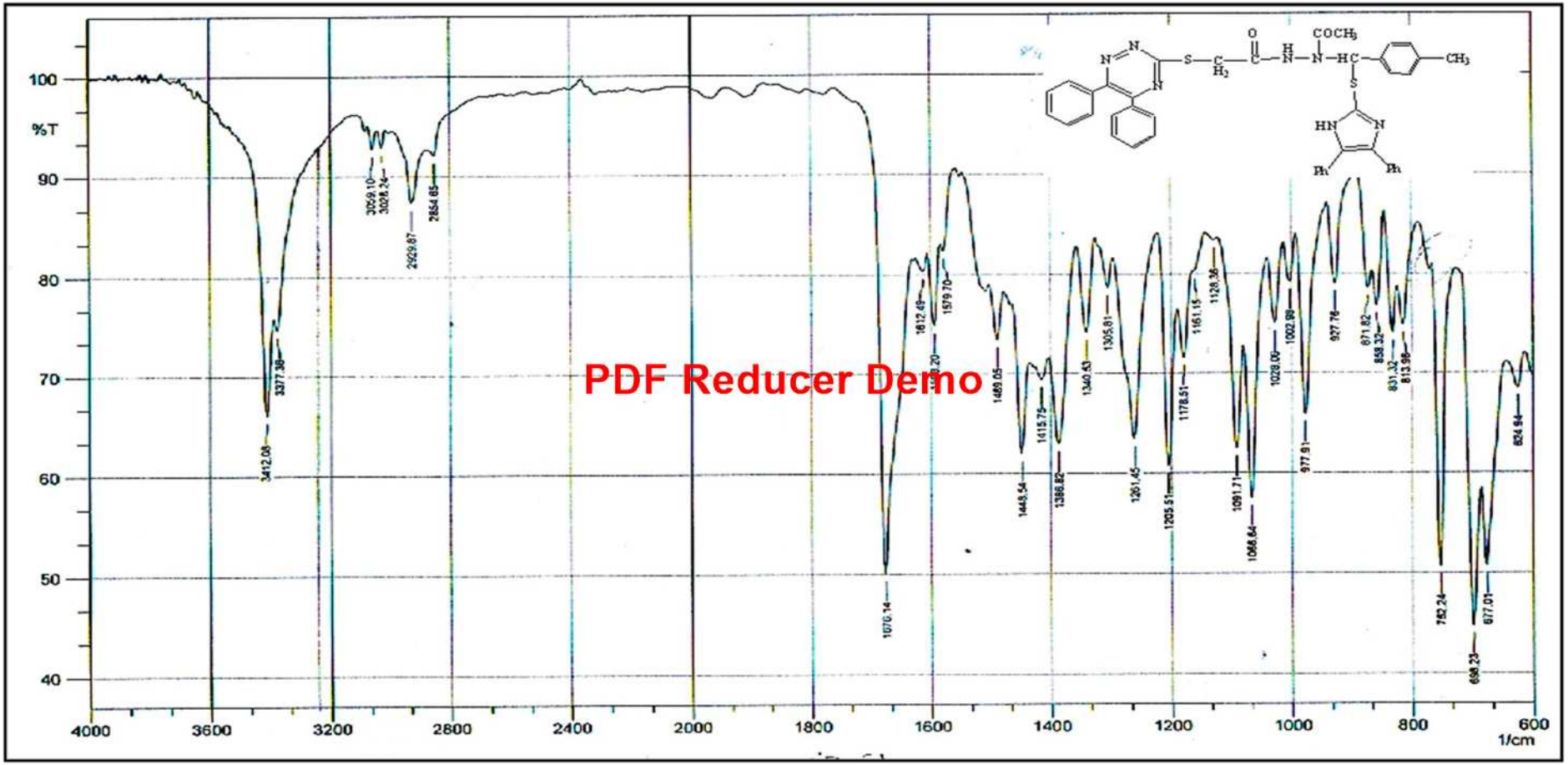


Figure (3-22) FTIR –spectrum of compound $[VII]_b$

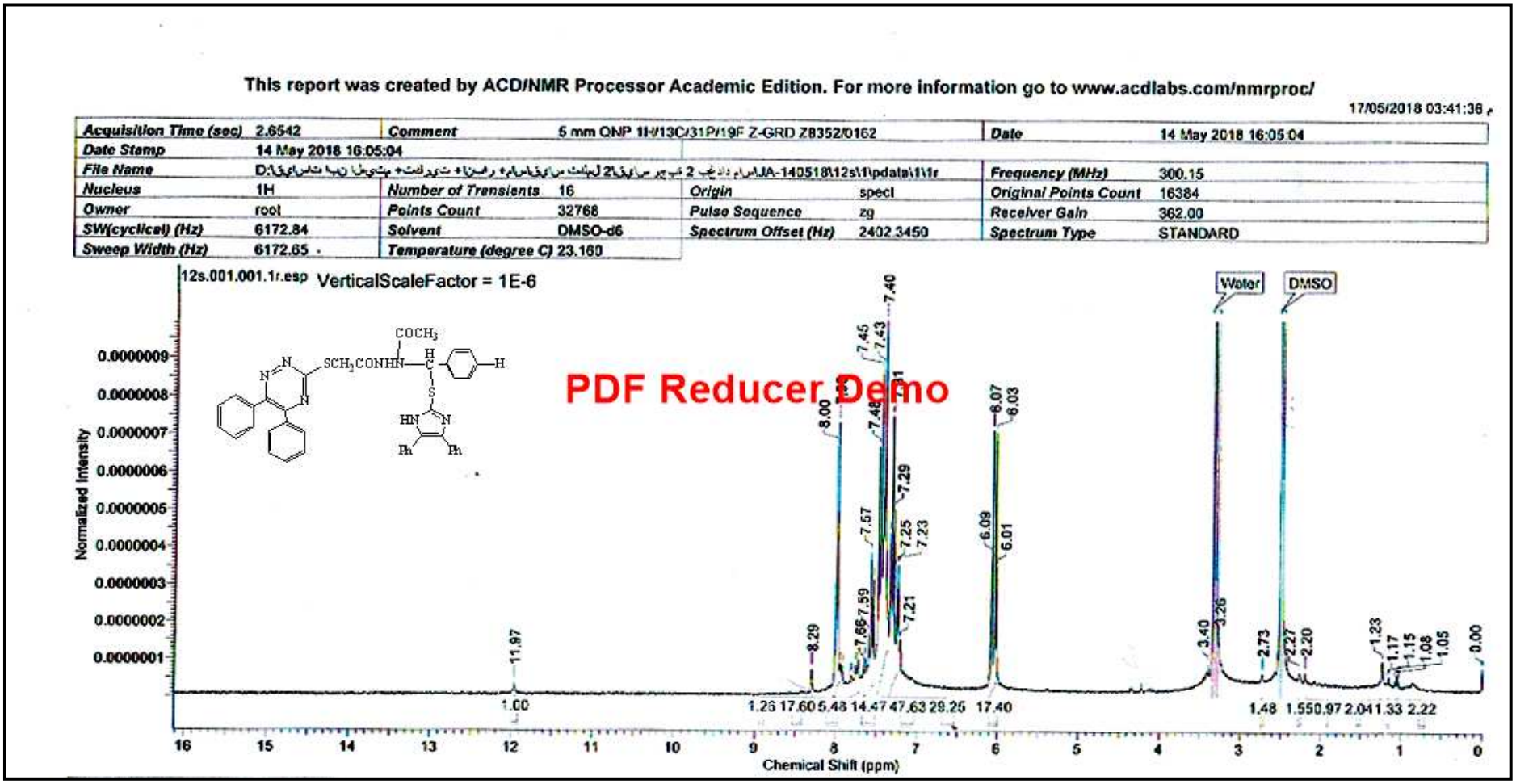


Figure (3-23) ^{1}HNMR –spectrum of compound [VII]$_a$

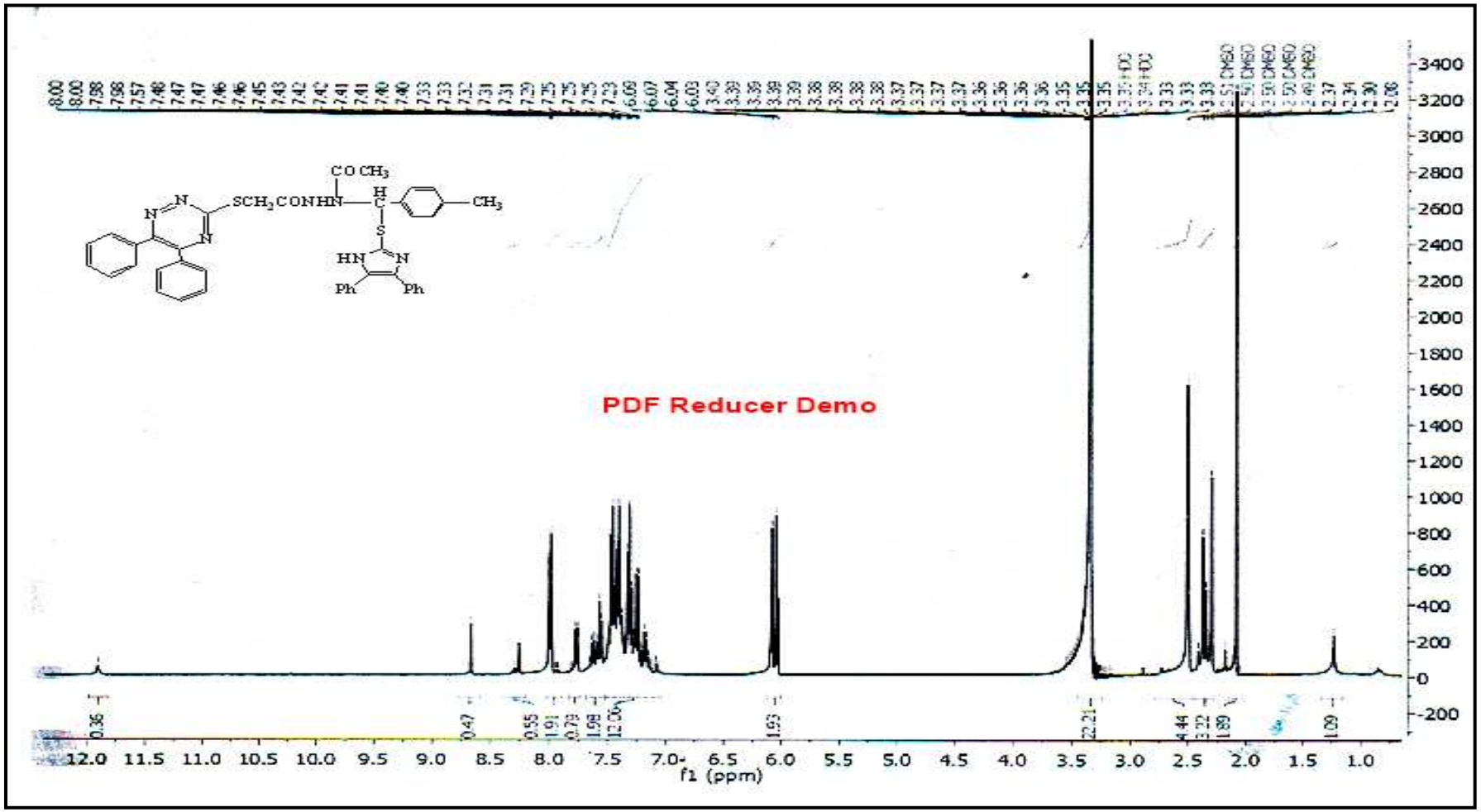


Figure (3-24) ^{1}HNMR –spectrum of compound[VII]$_b$

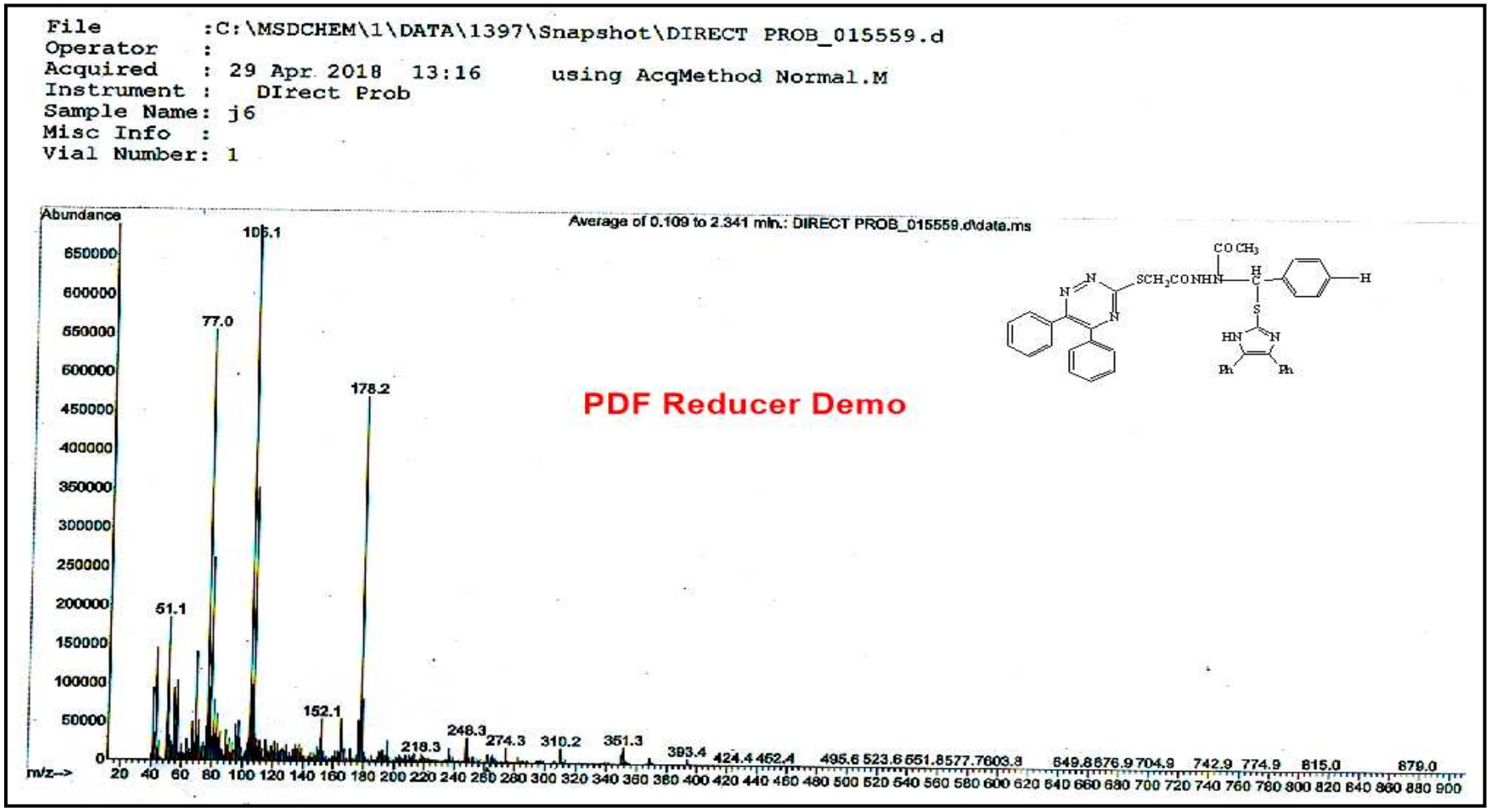


Figure (3-25)The mass spectrum of compound[VII]$_a$

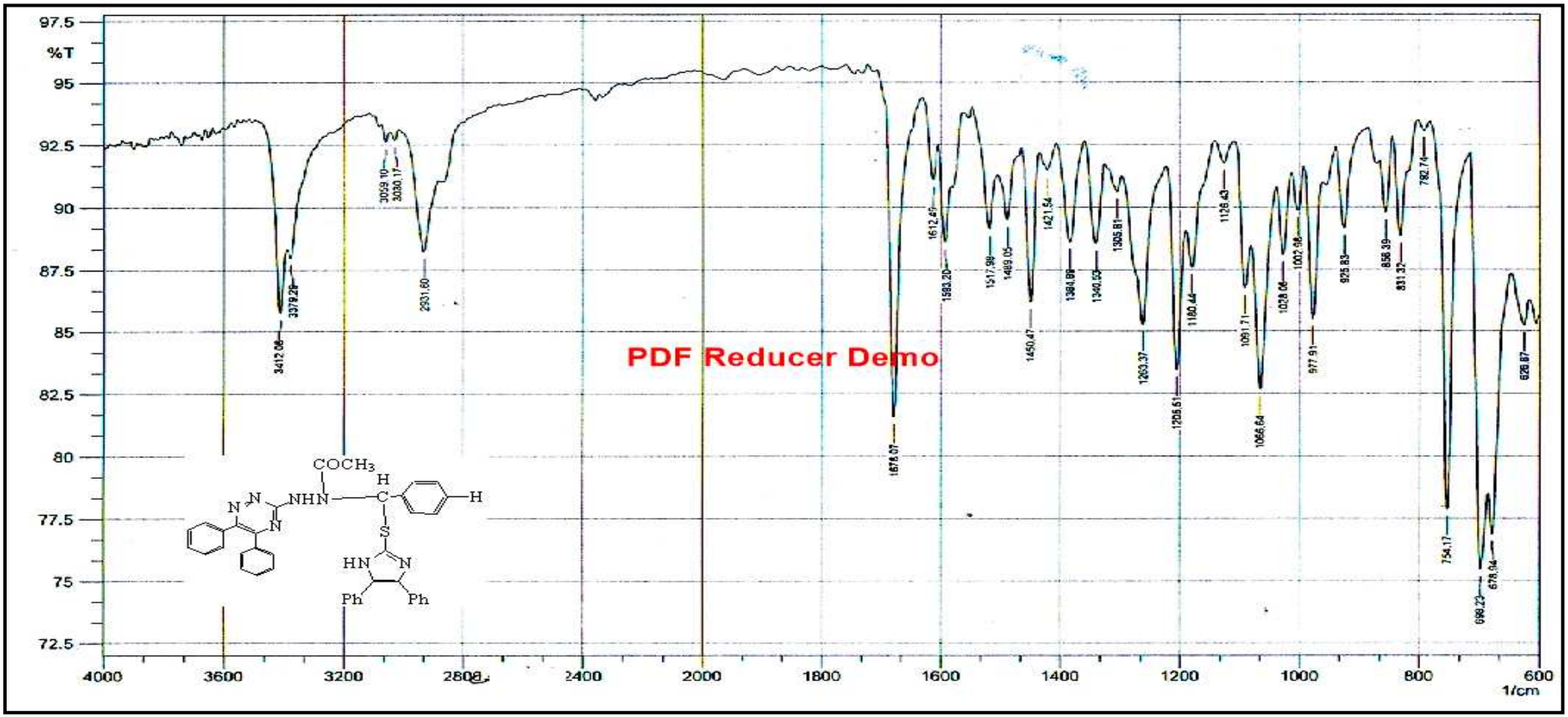


Figure (3-26) FTIR –spectrum of compound $[VII]_e$

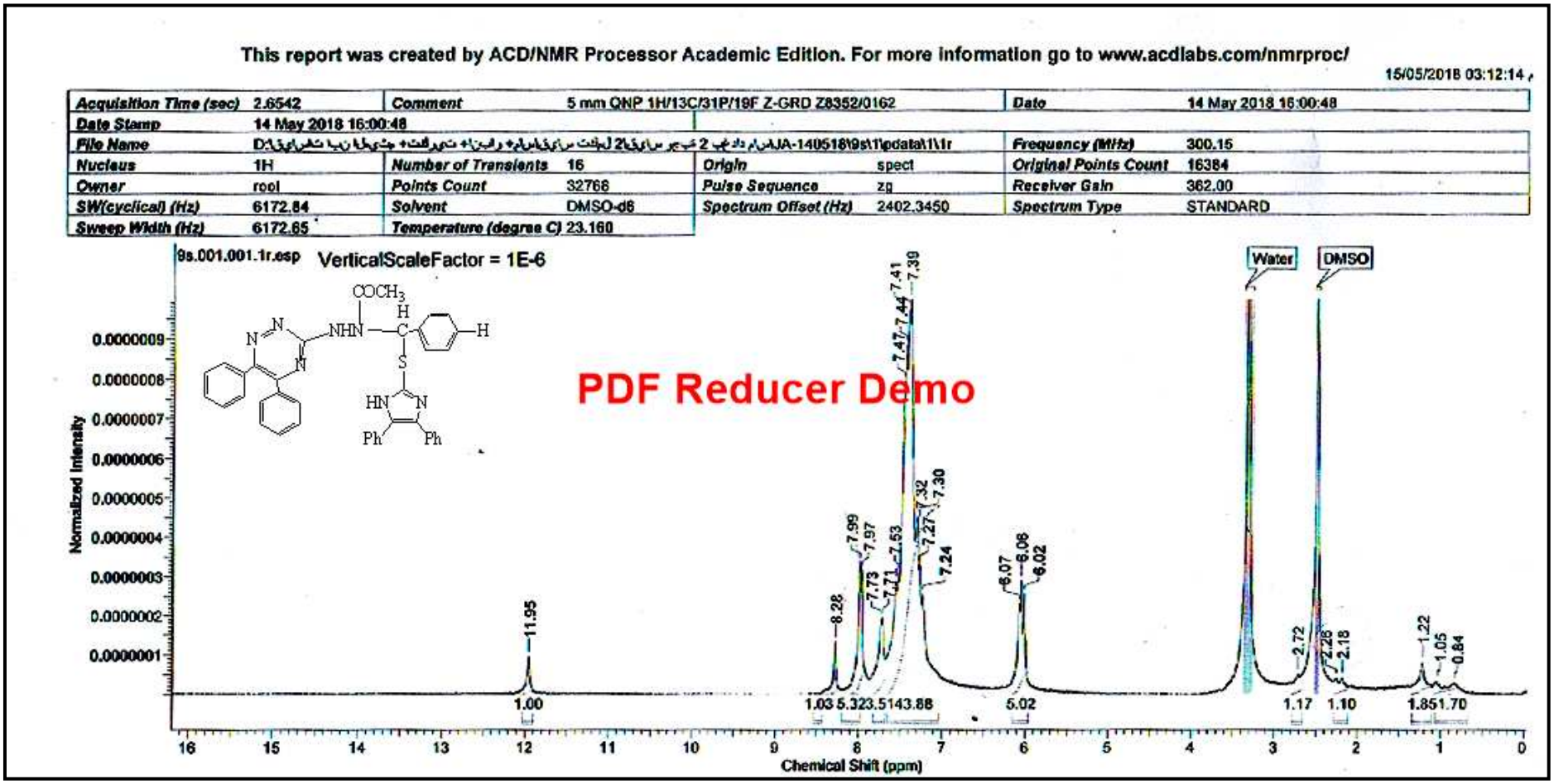


Figure (3-27) ^{1}HNMR –spectrum of compound $[VII]_e$

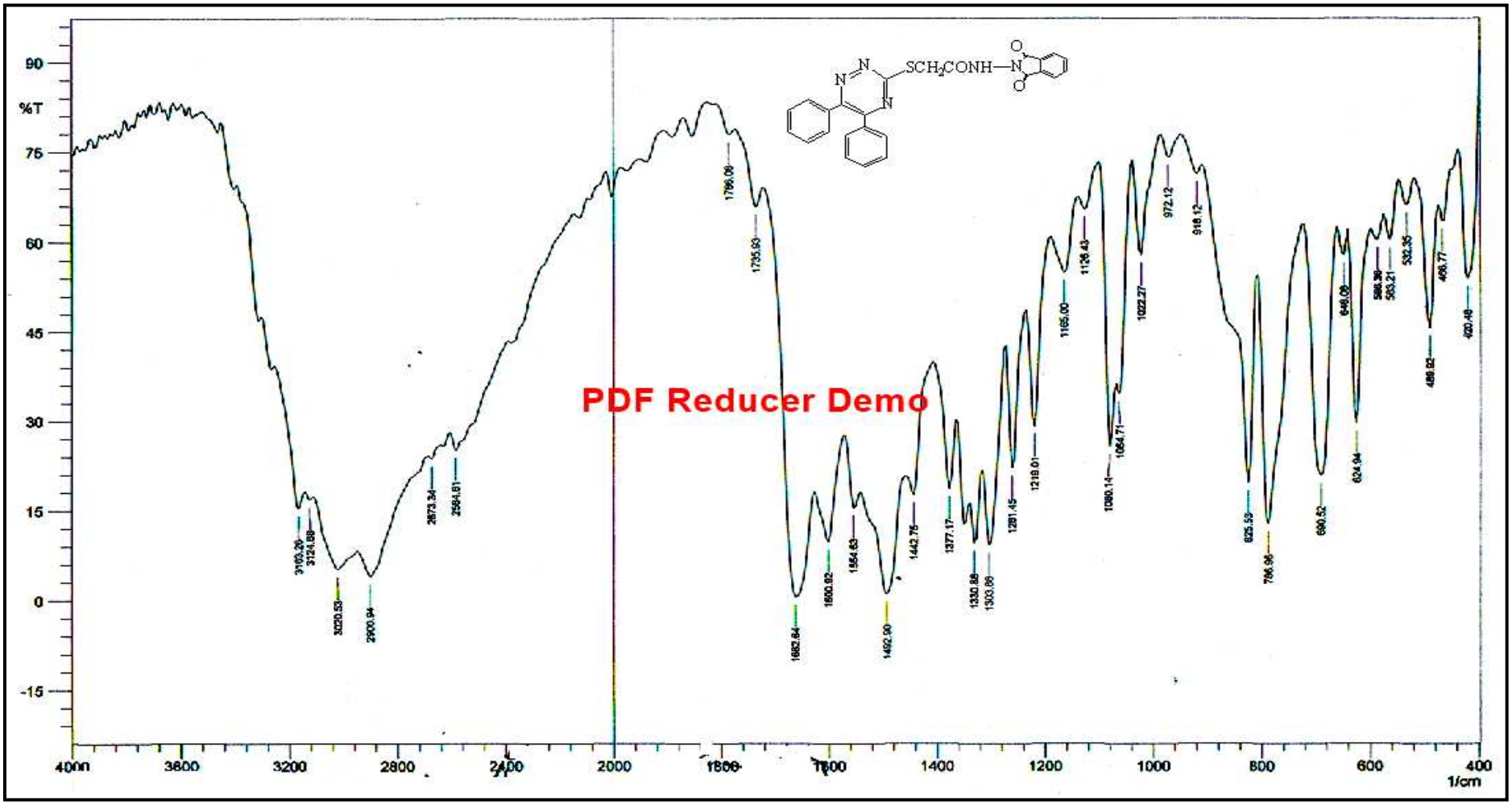


Figure (3-28) FTIR –spectrum of compound $[VIII]_a$

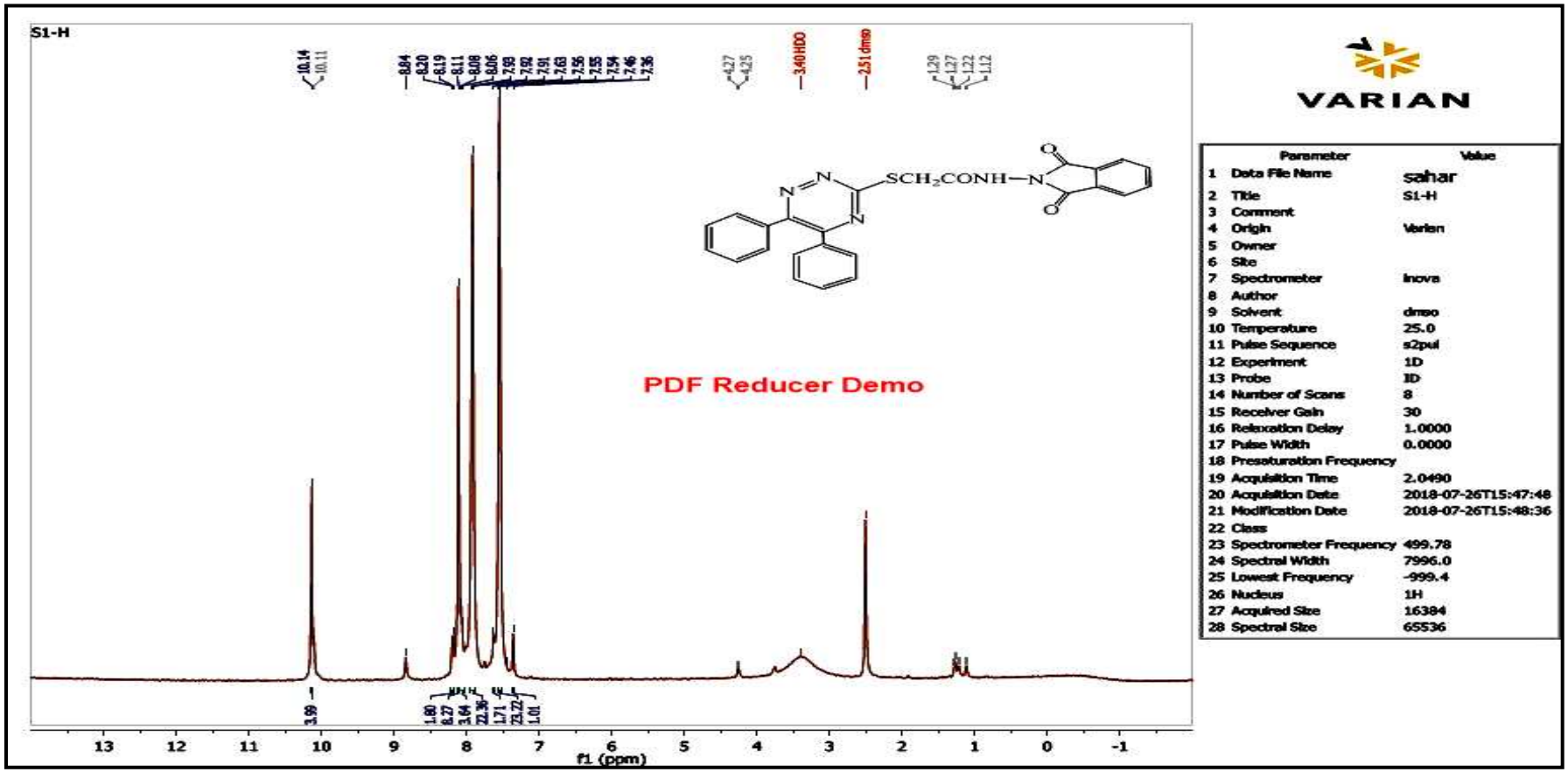


Figure (3-29) ^{1}HNMR –spectrum of compound $[VII]_a$

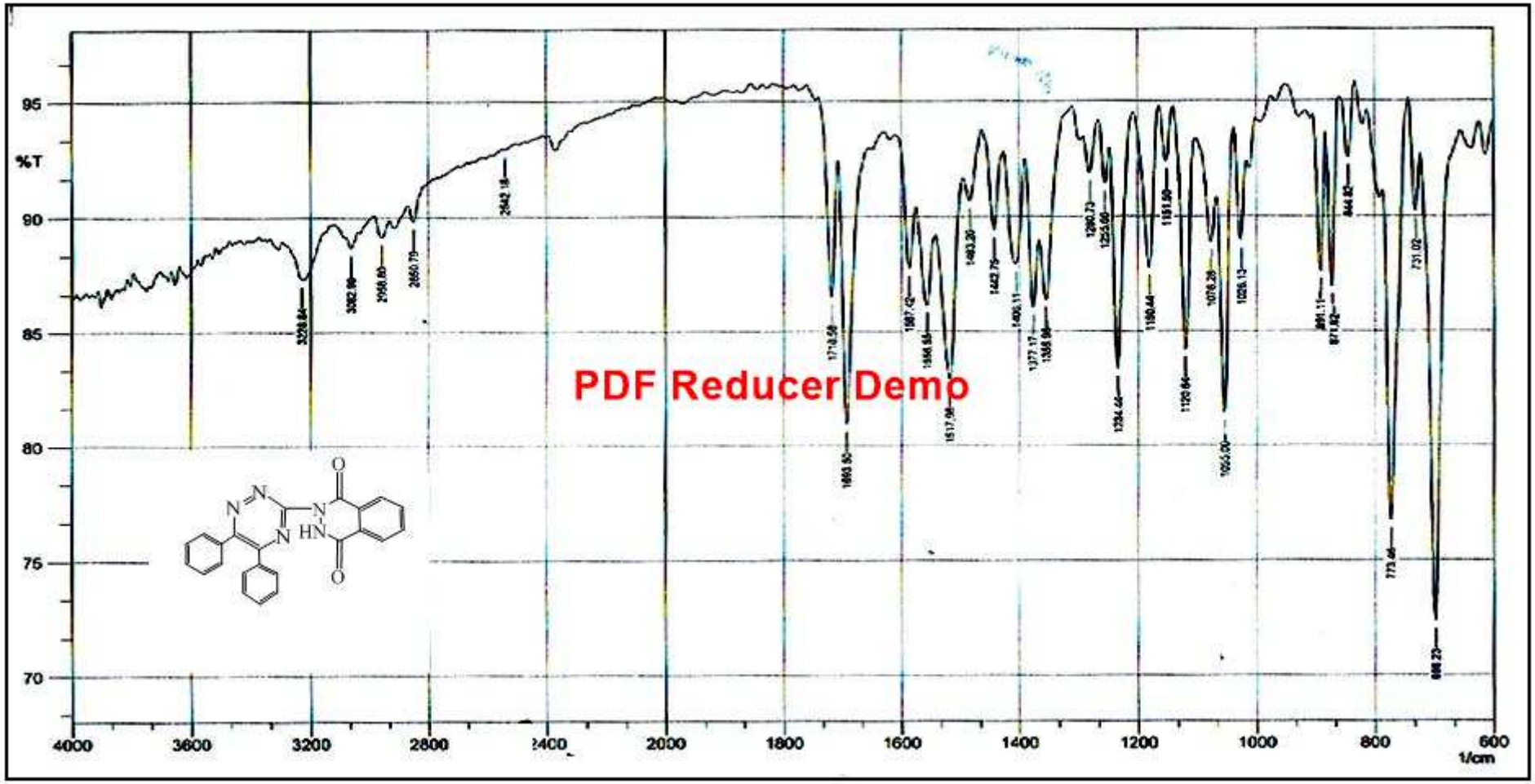
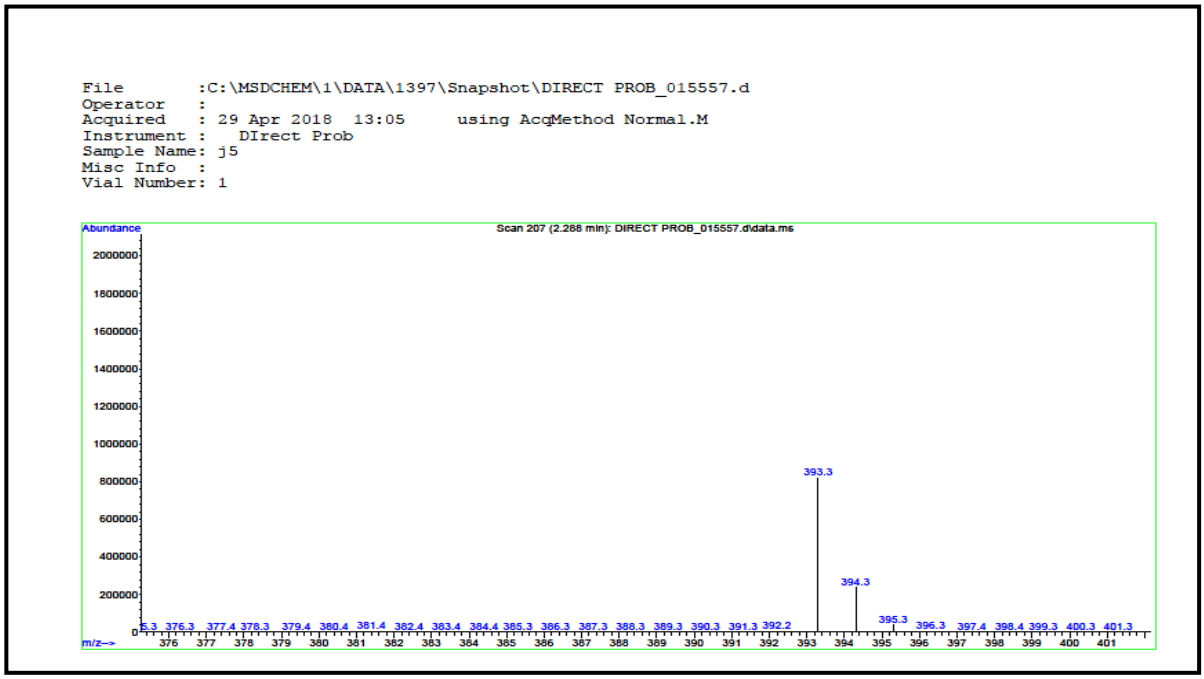


Figure (3-30) FTIR –spectrum of compound $[VIII]_c$



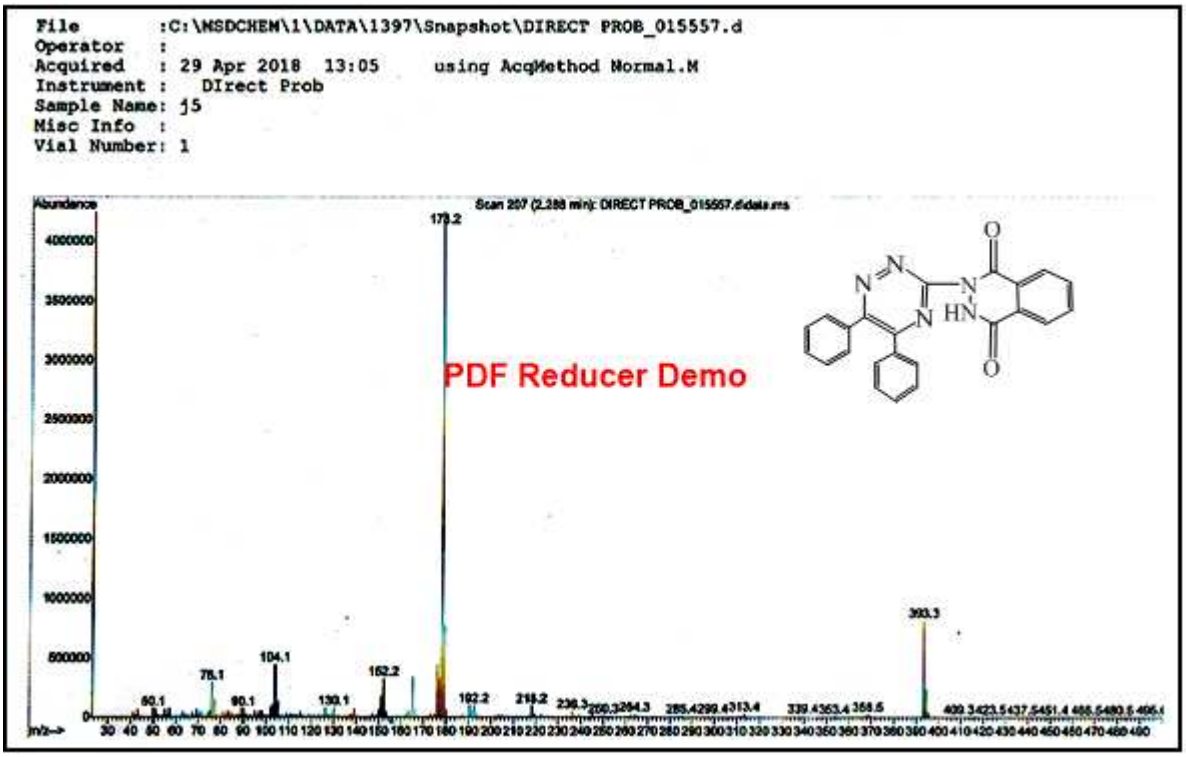


Figure (3-31)The mass spectrum of compound[VIII]$_c$

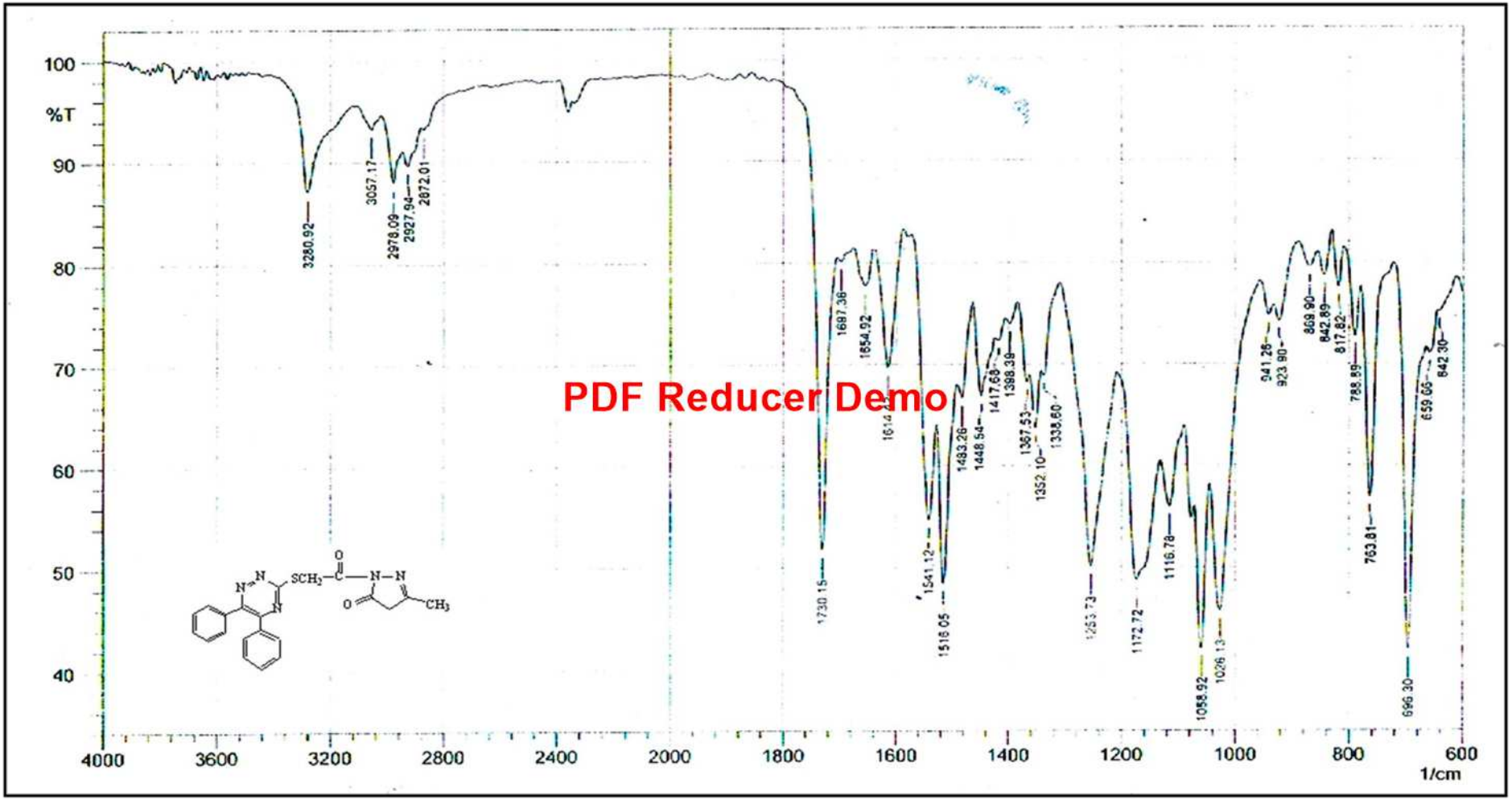


Figure (3-32) FTIR –spectrum of compound [IX]

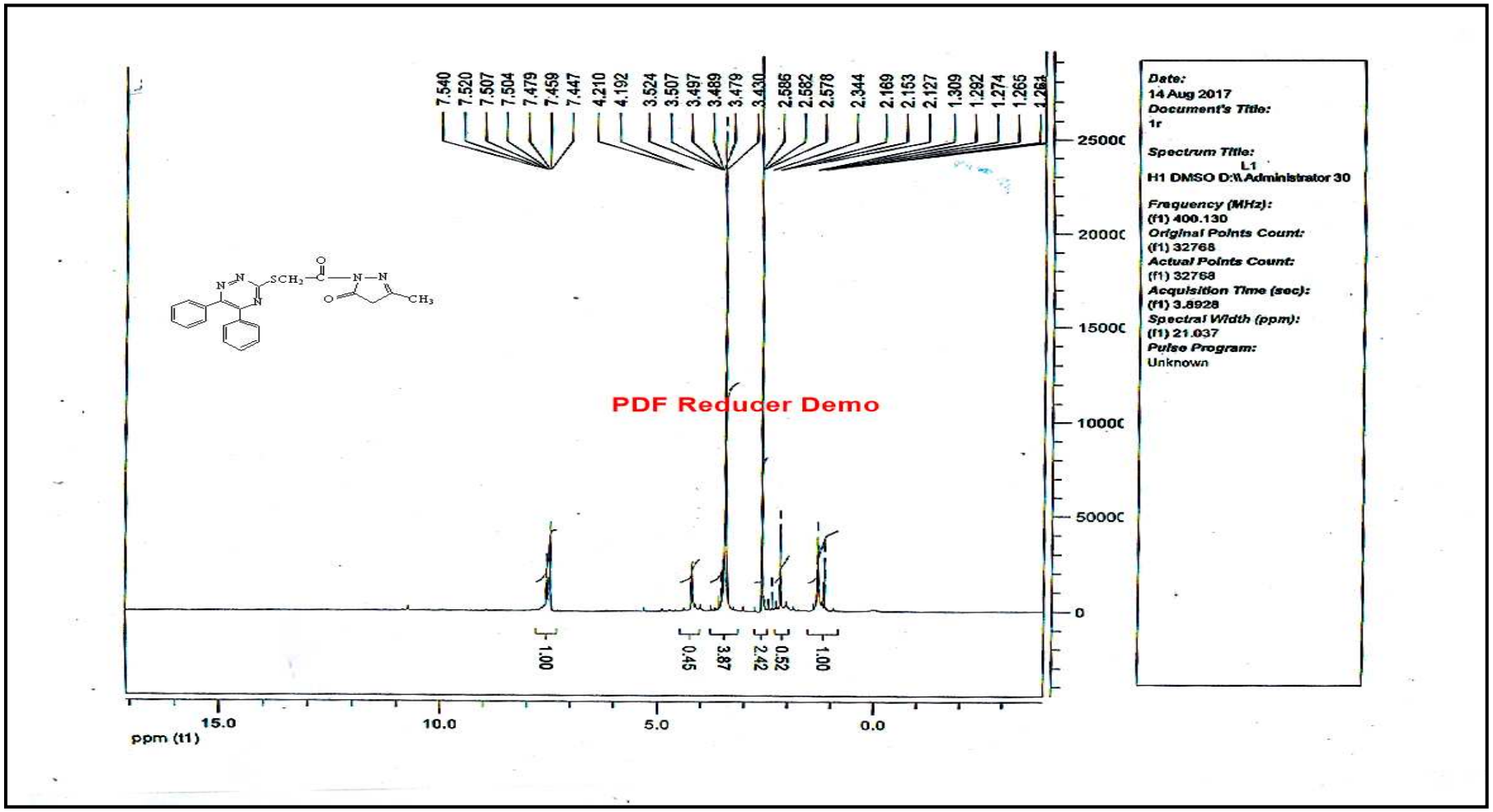


Figure (3-33) ^{1}HNMR –spectrum of compound [IX]

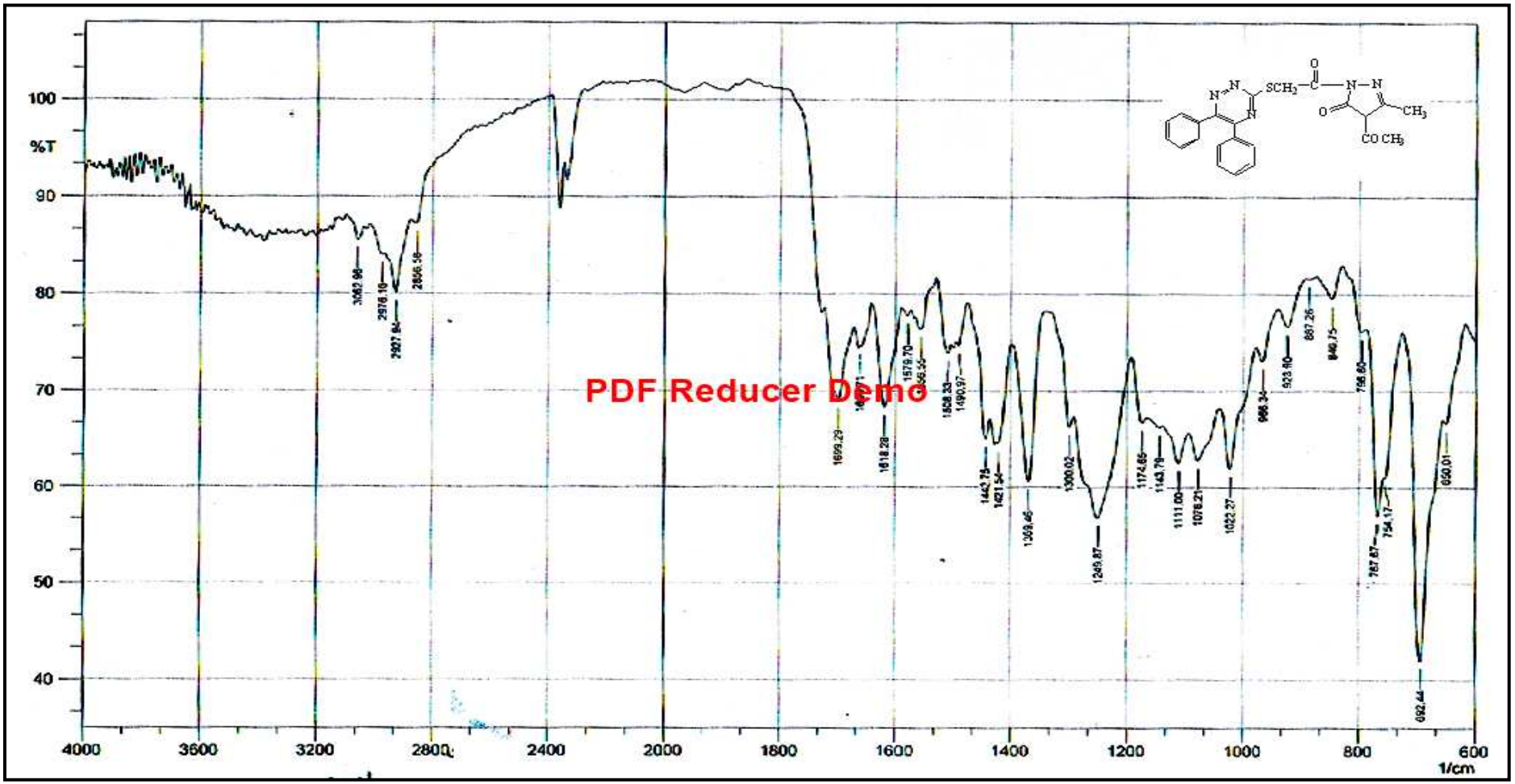


Figure (3-34) FTIR –spectrum of compound [X]

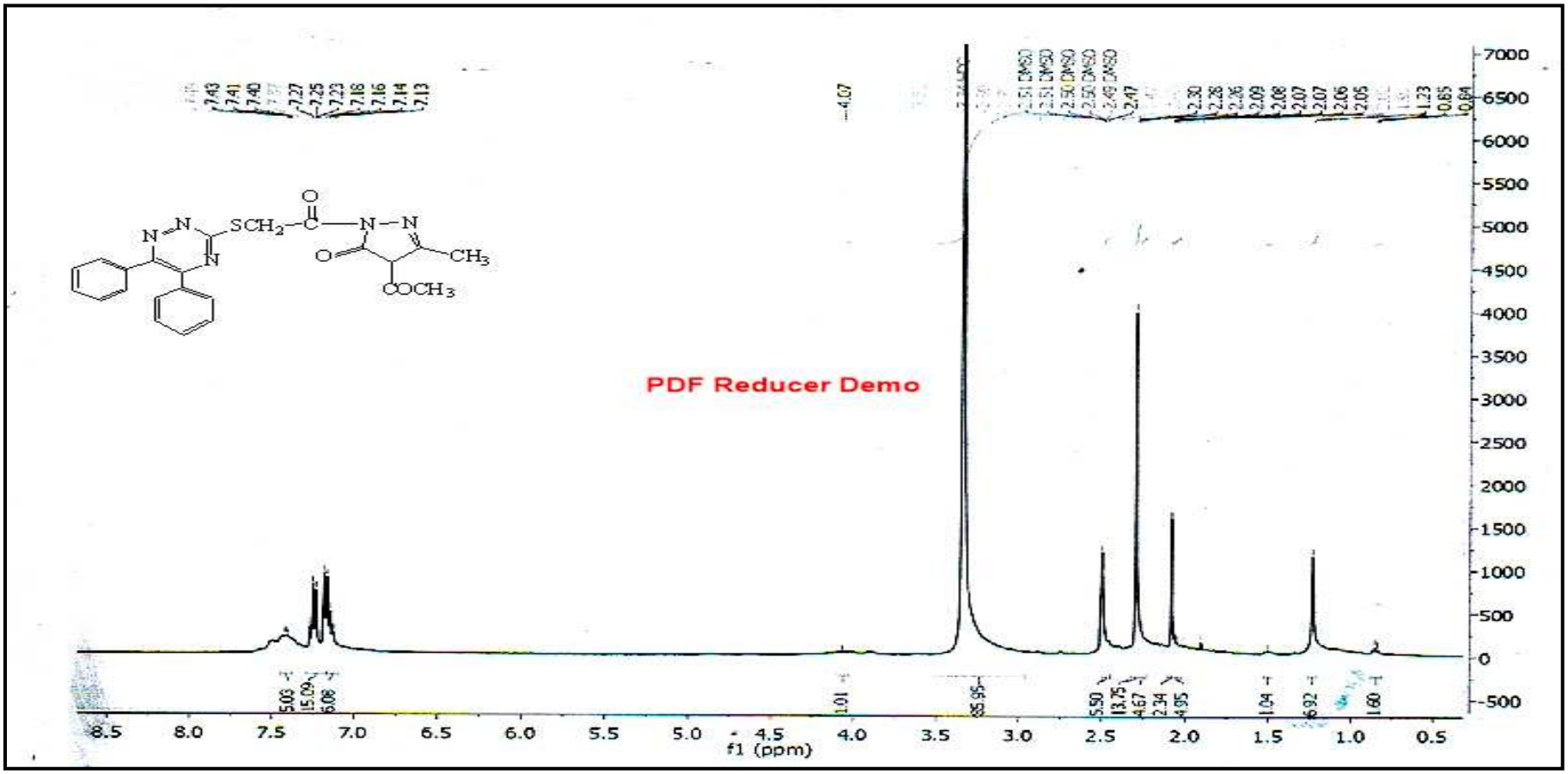


Figure (3-35) ^{1}HNMR –spectrum of compound [X]

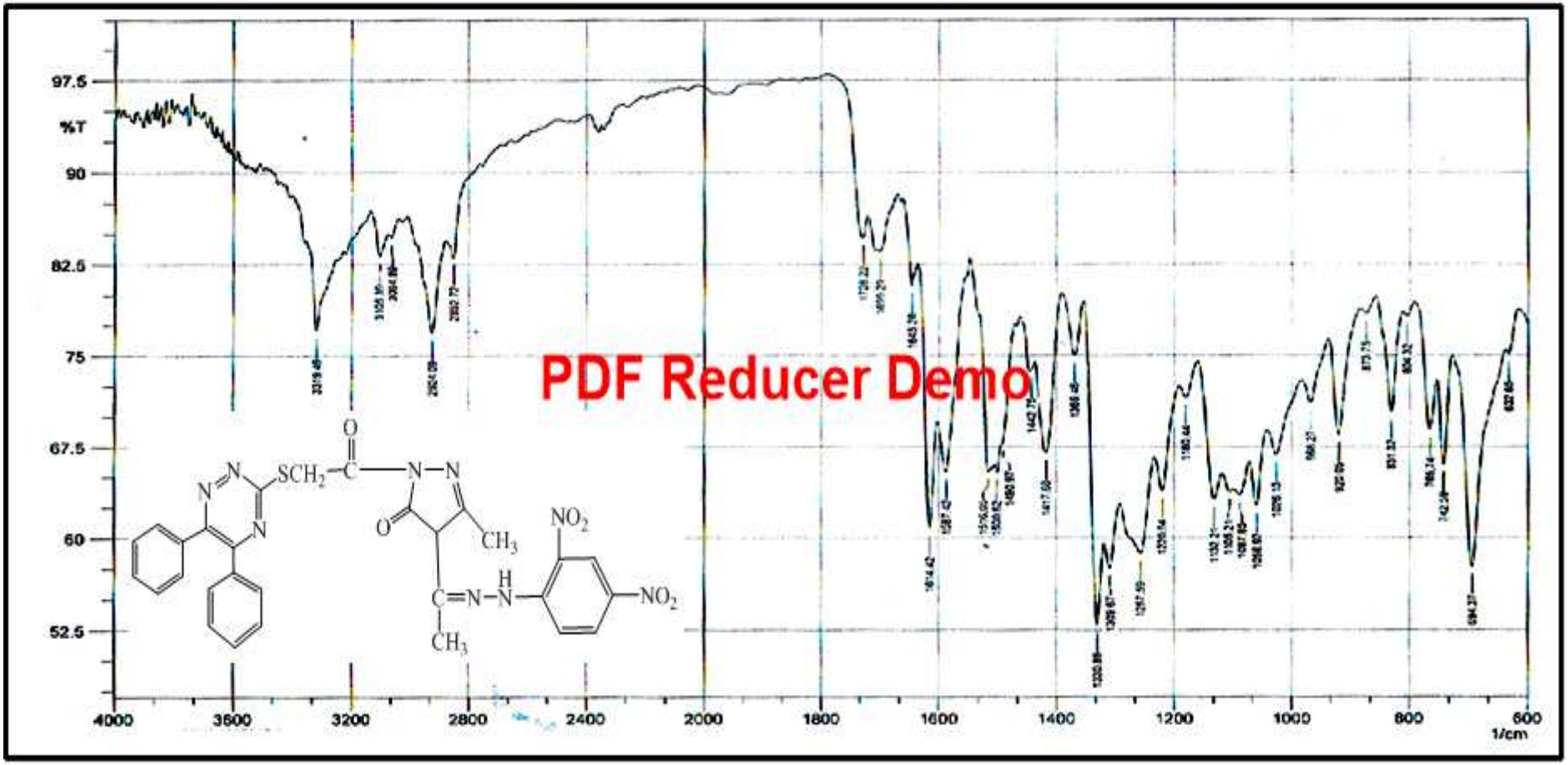


Figure (3-36) FTIR –spectrum of compound $[XI]_b$

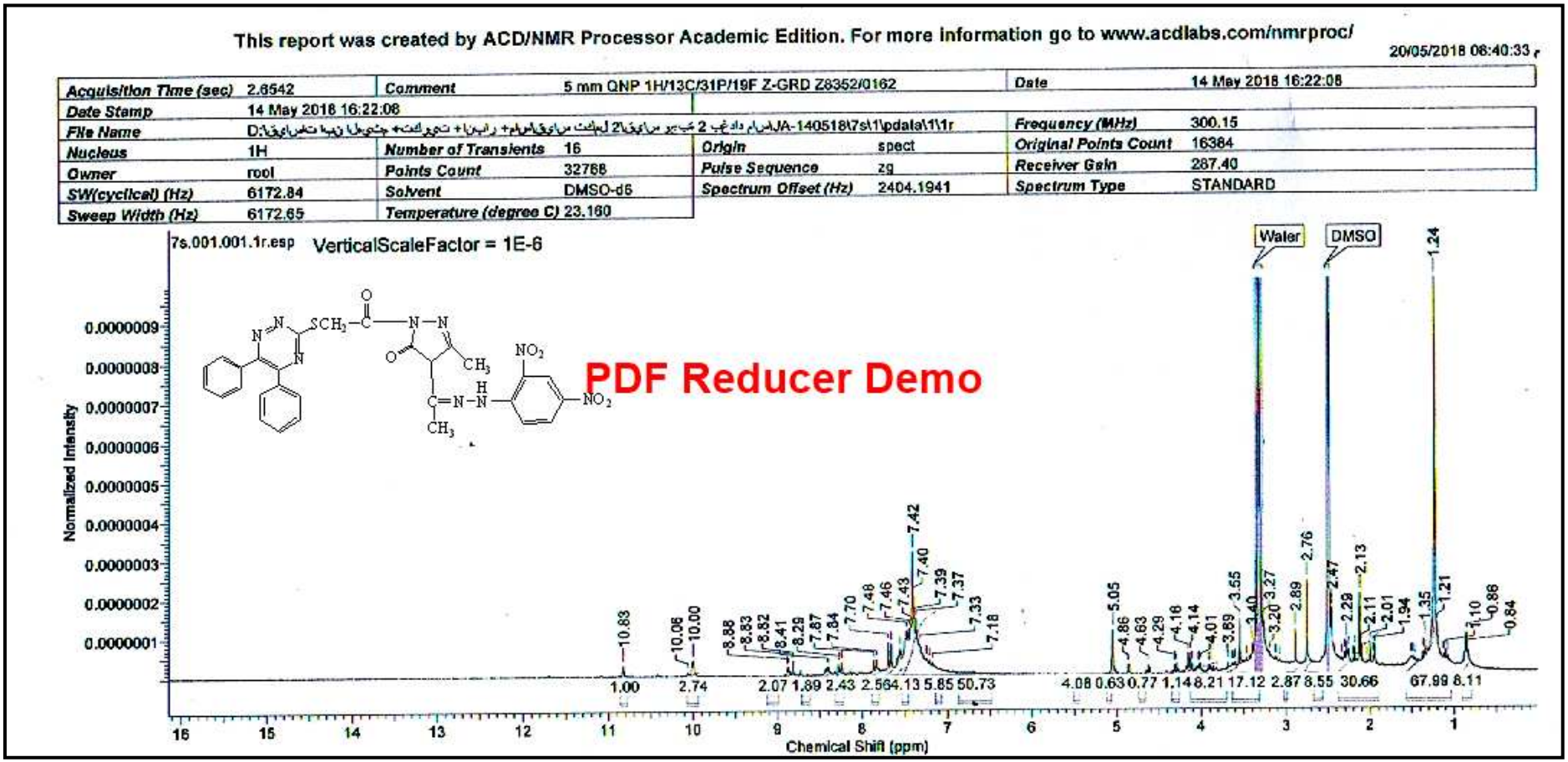


Figure (3-37) ^{1}HNMR –spectrum of compound [XI]

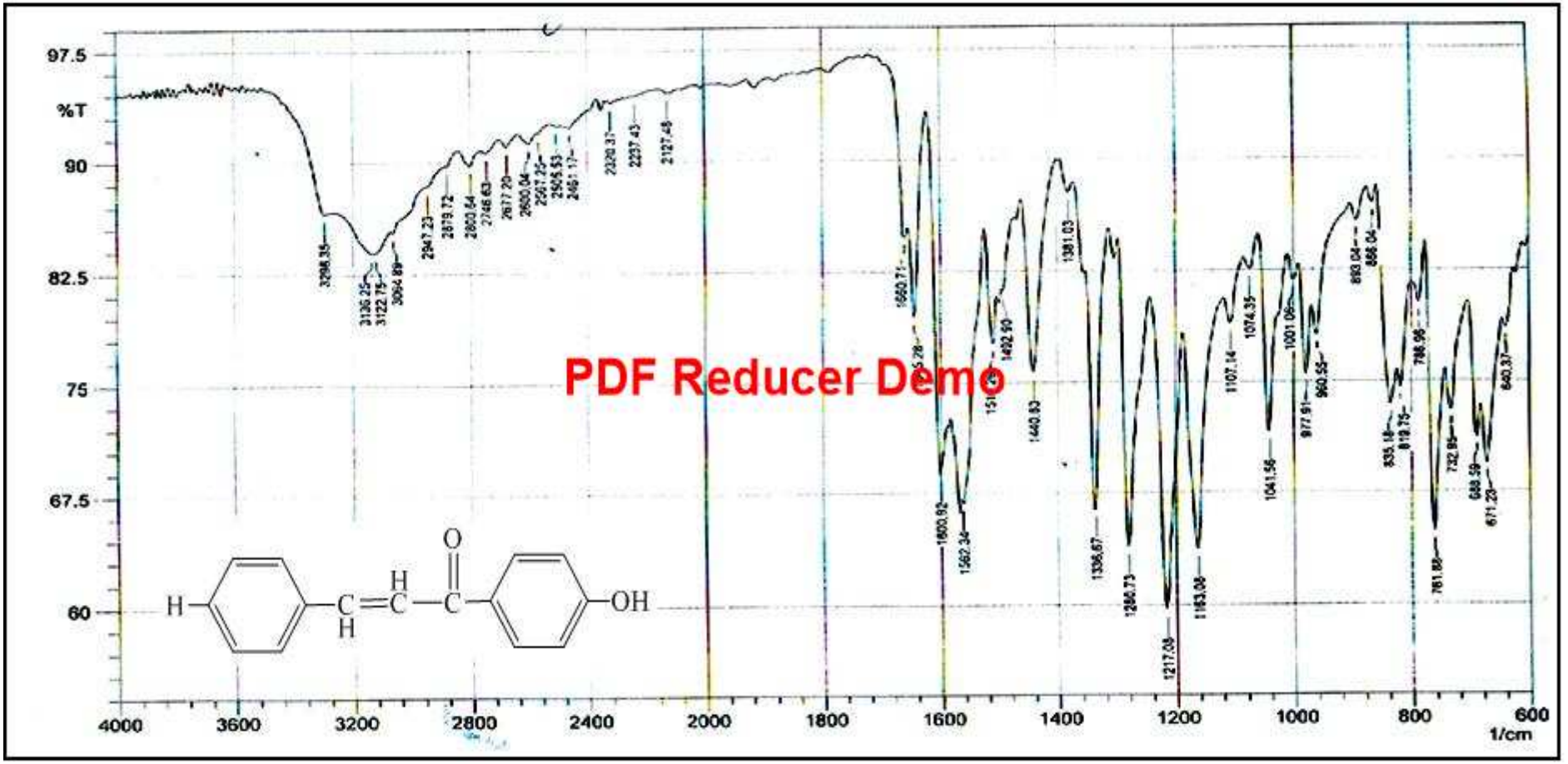


Figure (3-38) FTIR –spectrum of compound $[XII]_a$

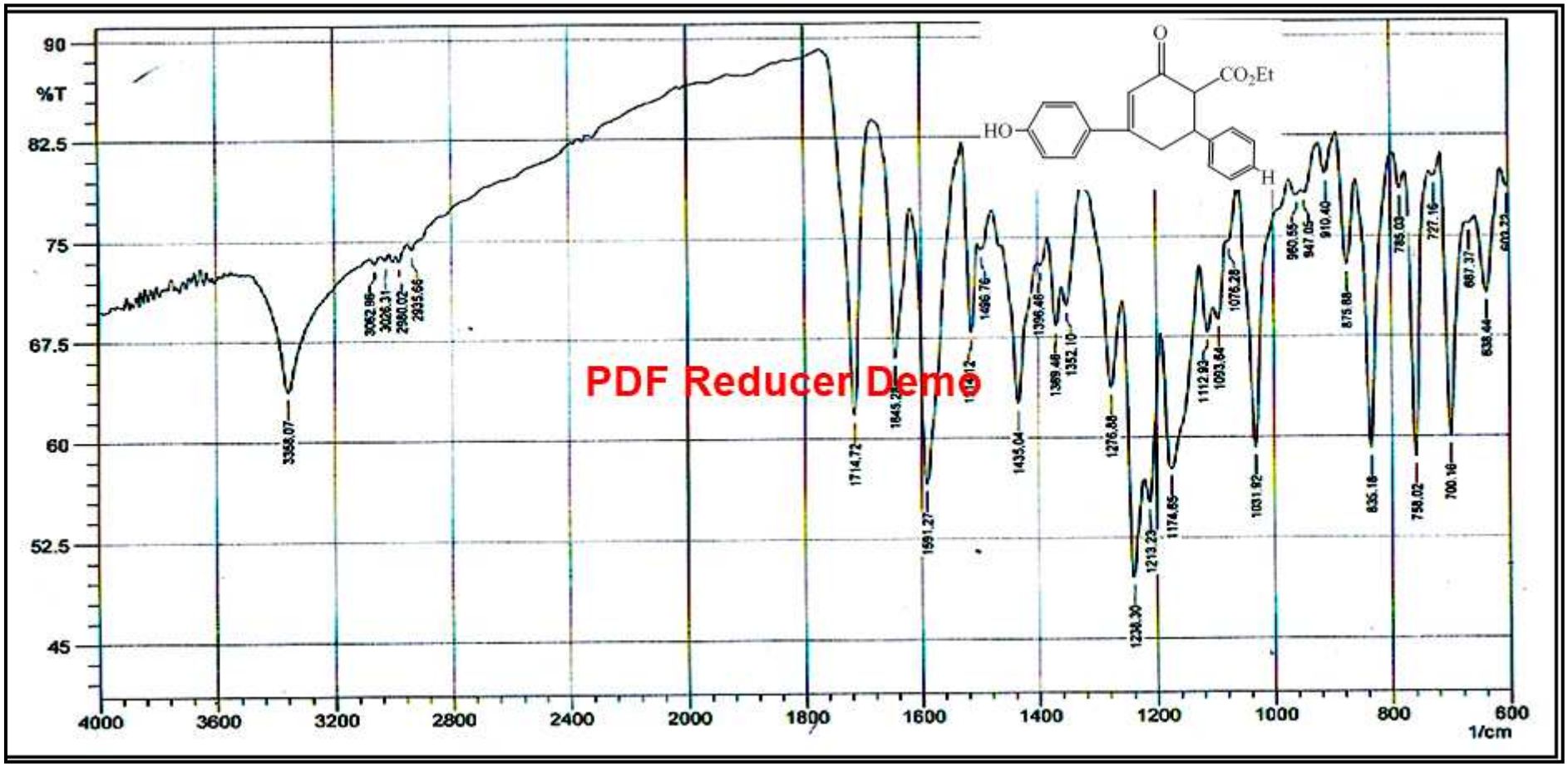
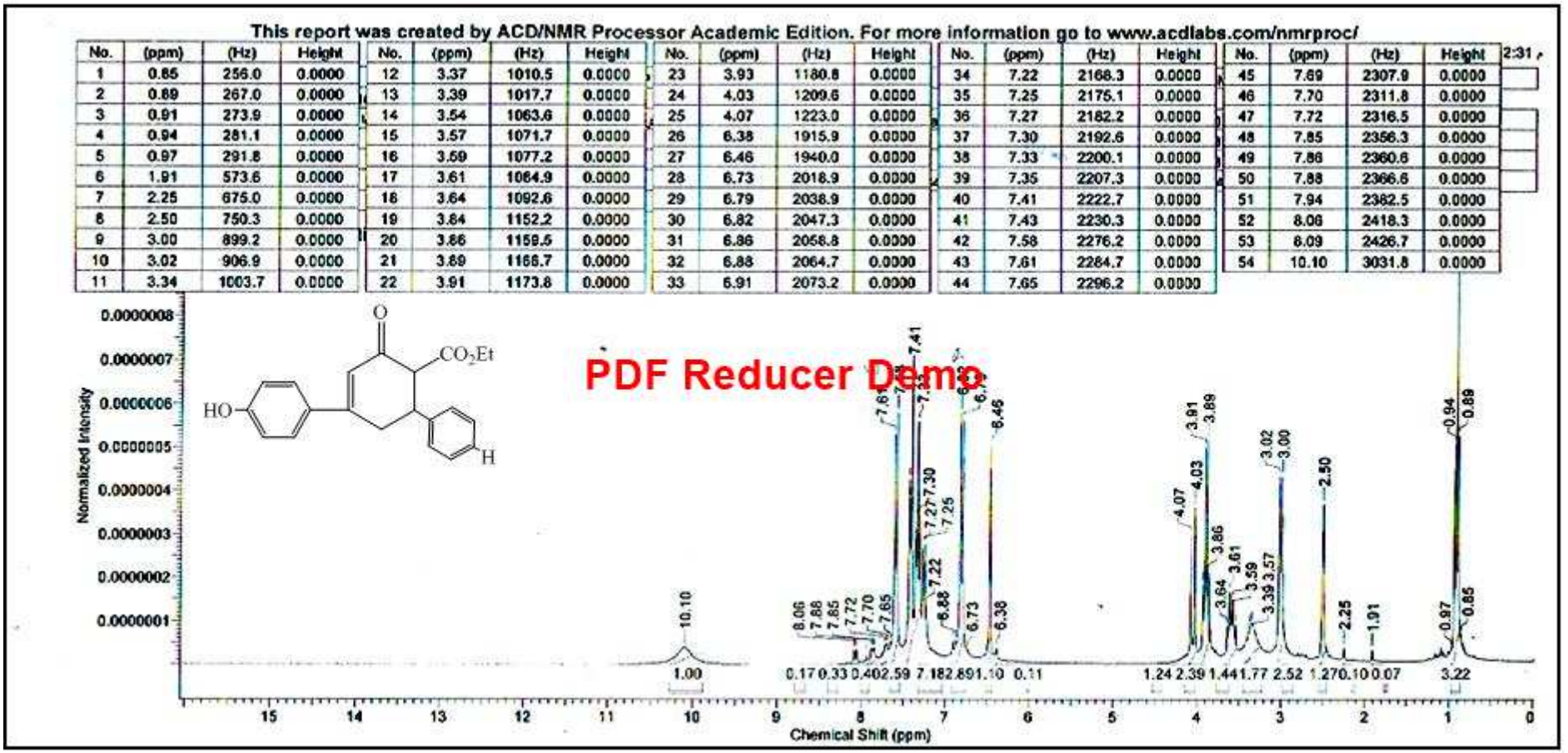


Figure (3-39) FTIR –spectrum of compound $[XIII]_a$



No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height	No.	(ppm)	(Hz)	Height
1	0.85	256.0	0.0000	12	3.37	1010.5	0.0000	23	3.93	1180.8	0.0000	34	7.22	2168.3	0.0000	45	7.69	2307.9	0.0000
2	0.89	267.0	0.0000	13	3.39	1017.7	0.0000	24	4.03	1209.6	0.0000	35	7.25	2175.1	0.0000	46	7.70	2311.8	0.0000
3	0.91	273.9	0.0000	14	3.54	1063.6	0.0000	25	4.07	1223.0	0.0000	36	7.27	2182.2	0.0000	47	7.72	2316.5	0.0000
4	0.94	281.1	0.0000	15	3.57	1071.7	0.0000	26	6.38	1915.9	0.0000	37	7.30	2192.6	0.0000	48	7.85	2356.3	0.0000
5	0.97	291.8	0.0000	16	3.59	1077.2	0.0000	27	6.46	1940.0	0.0000	38	7.33	2200.1	0.0000	49	7.86	2360.6	0.0000
6	1.91	573.6	0.0000	17	3.61	1084.9	0.0000	28	6.73	2018.9	0.0000	39	7.35	2207.3	0.0000	50	7.88	2366.6	0.0000
7	2.25	675.0	0.0000	18	3.64	1092.6	0.0000	29	6.79	2038.9	0.0000	40	7.41	2222.7	0.0000	51	7.94	2382.5	0.0000
8	2.50	750.3	0.0000	19	3.84	1152.2	0.0000	30	6.82	2047.3	0.0000	41	7.43	2230.3	0.0000	52	8.06	2418.3	0.0000
9	3.00	899.2	0.0000	20	3.86	1159.5	0.0000	31	6.86	2058.8	0.0000	42	7.58	2276.2	0.0000	53	8.09	2426.7	0.0000
10	3.02	906.9	0.0000	21	3.89	1166.7	0.0000	32	6.88	2064.7	0.0000	43	7.61	2284.7	0.0000	54	10.10	3031.8	0.0000
11	3.34	1003.7	0.0000	22	3.91	1173.8	0.0000	33	6.91	2073.2	0.0000	44	7.65	2296.2	0.0000				

Figure (3-40) ^{1}HNMR –spectrum of compound [XIII]$_a$

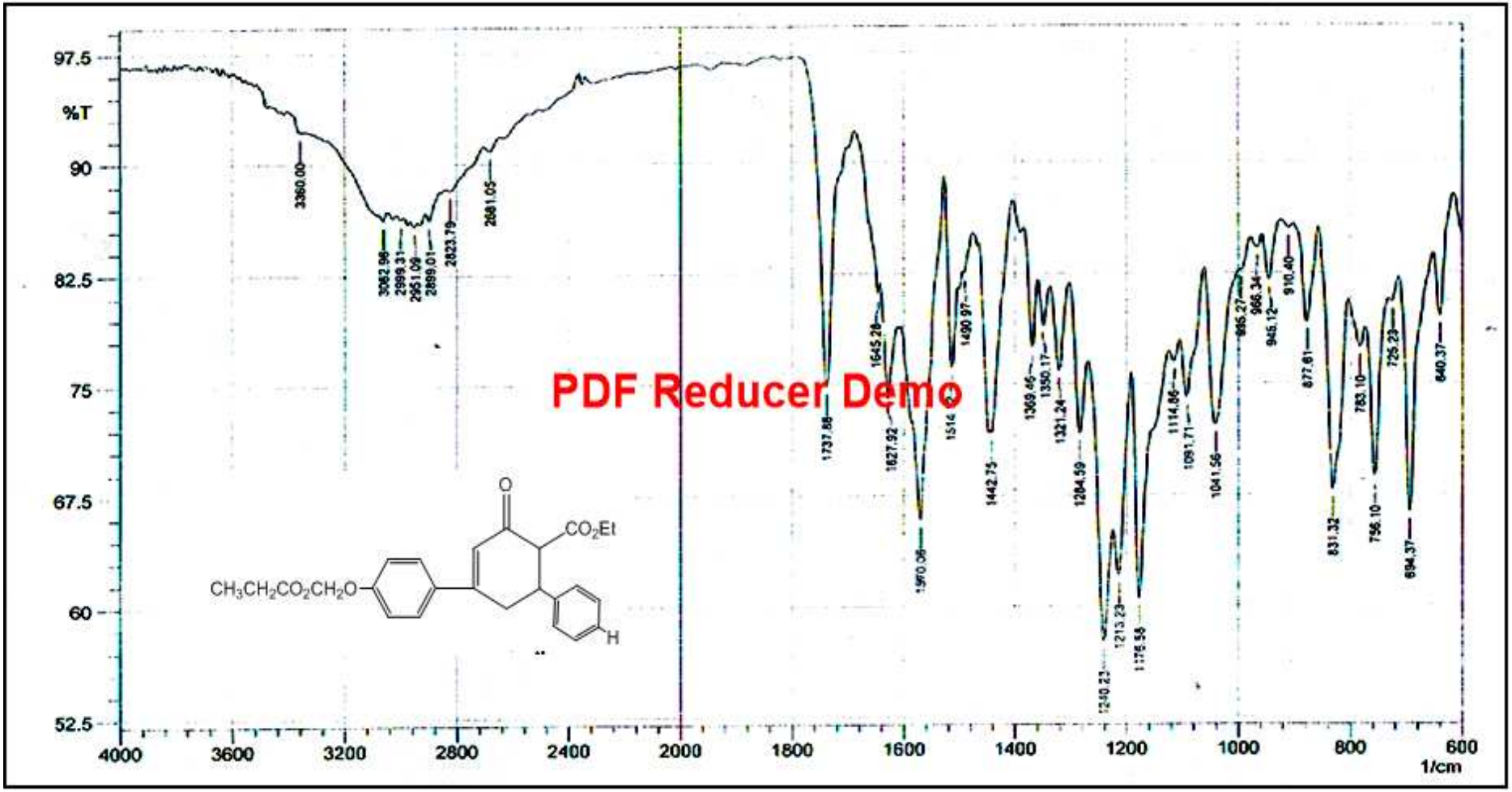


Figure (3-41) FTIR –spectrum of compound $[XIV]_a$

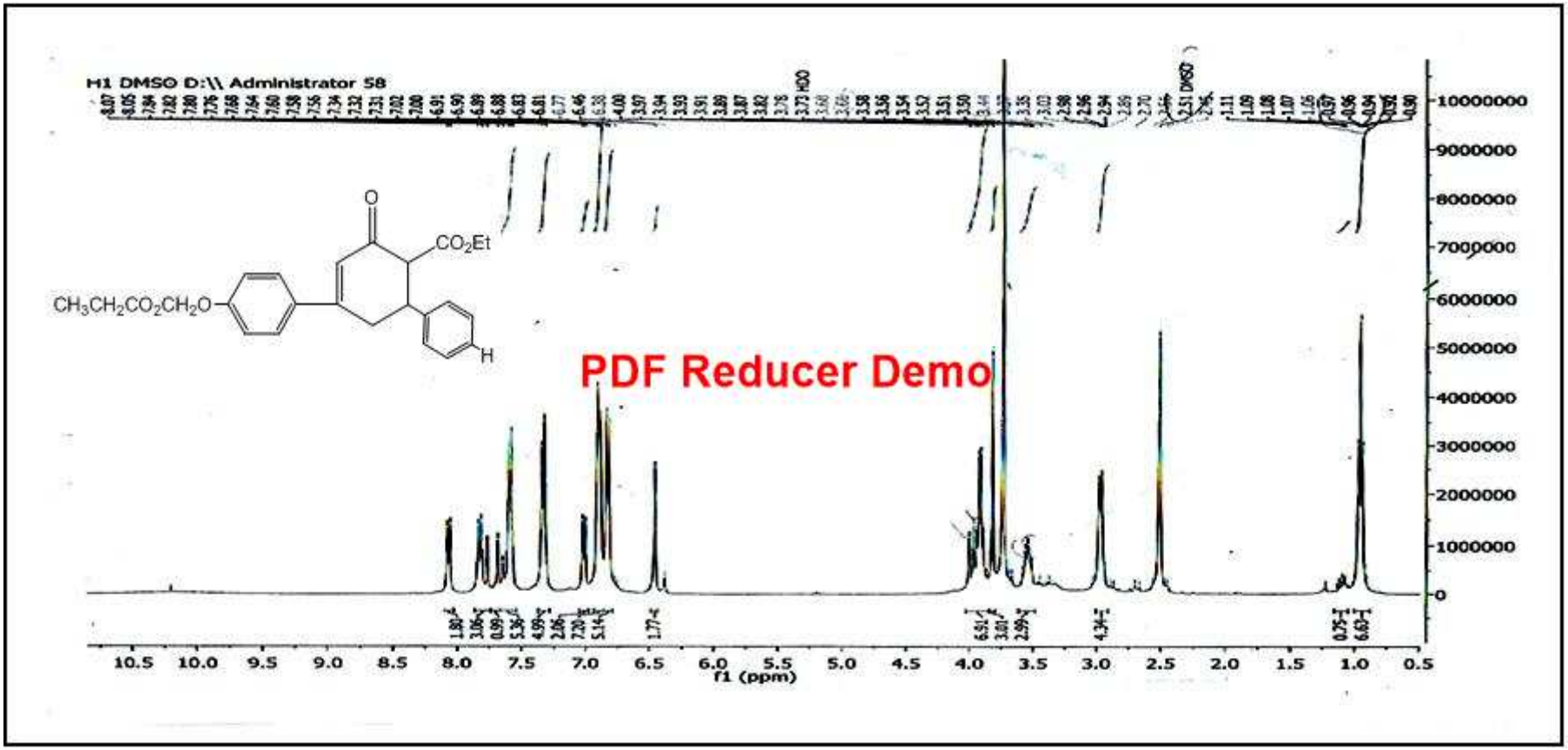


Figure (3-42) ^{1}HNMR –spectrum of compound $[XIV]_a$

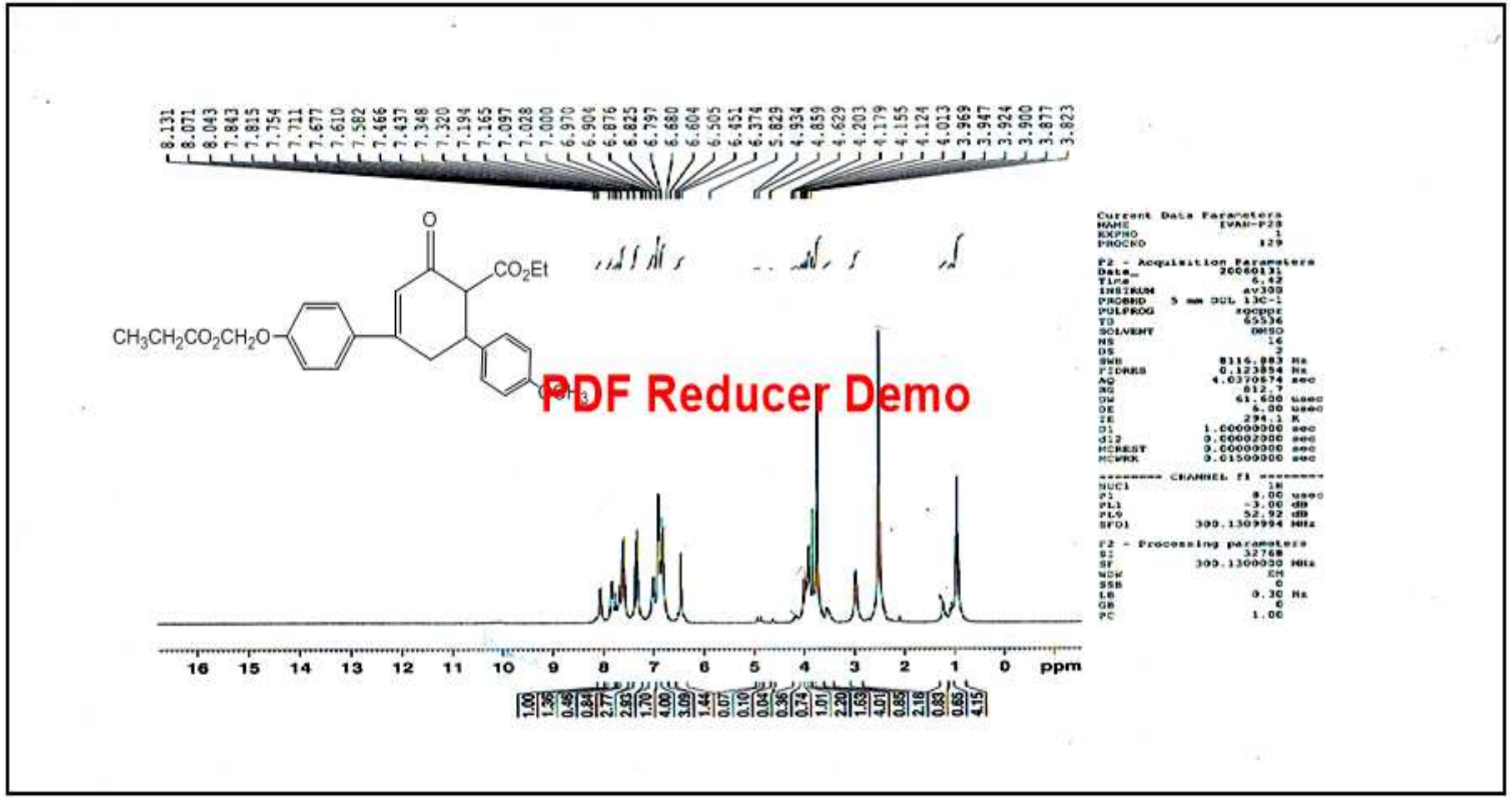


Figure (3-43) ^{1}HNMR –spectrum of compound $[XIV]_c$

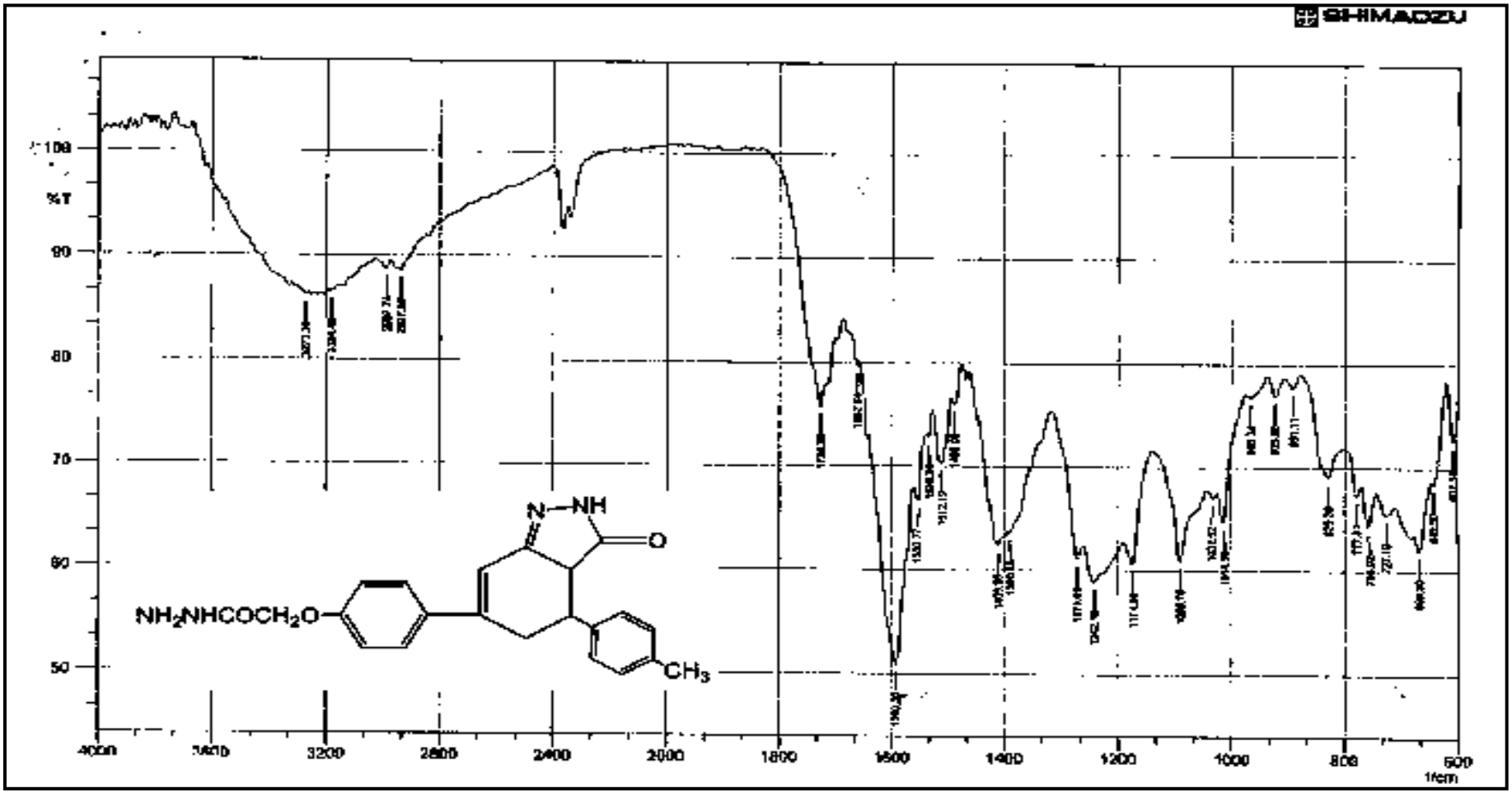


Figure (3-44) FTIR –spectrum of compound $[XV]_b$

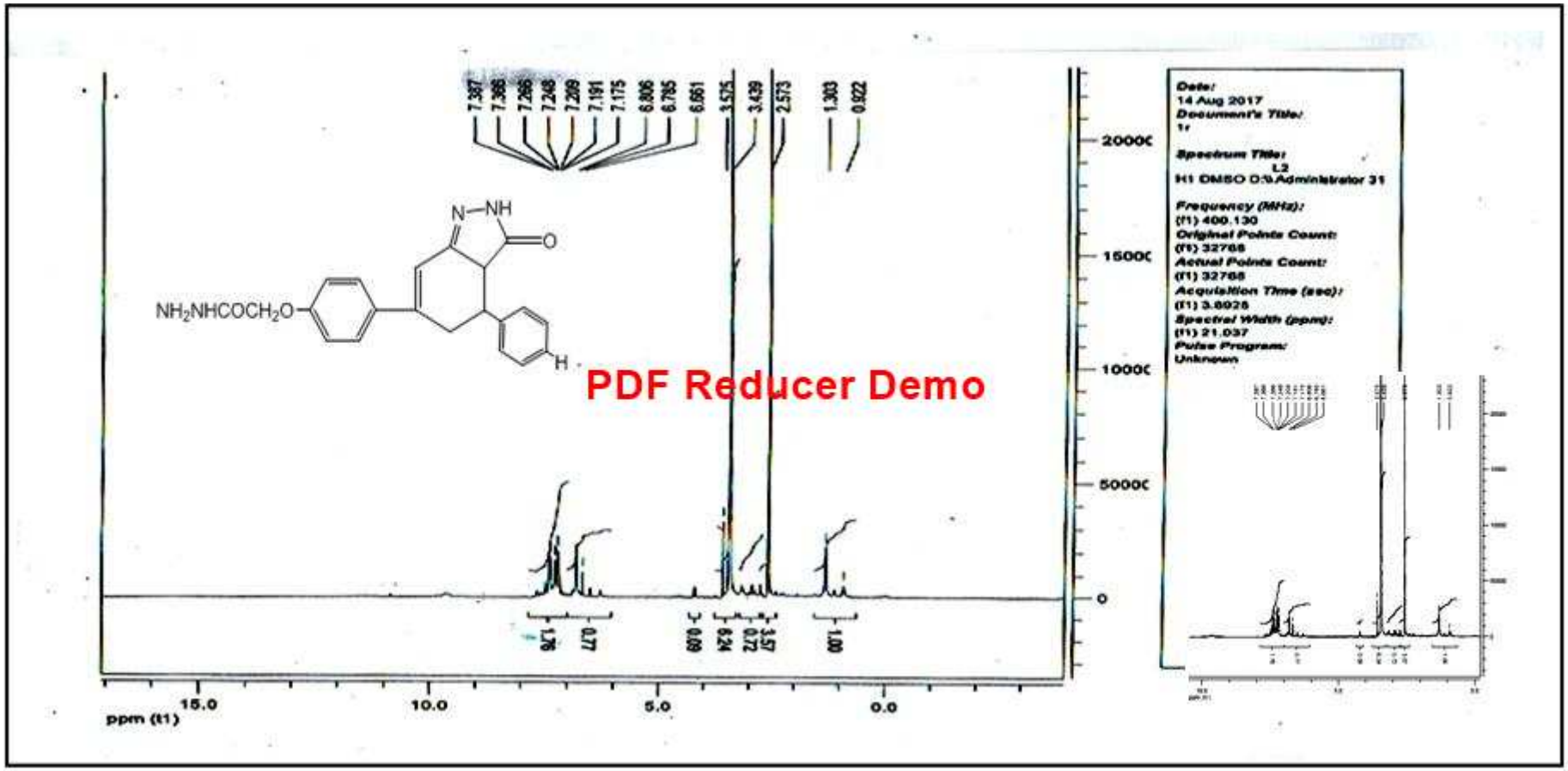


Figure (3-45) ^{1}HNMR –spectrum of compound $[XV]_a$

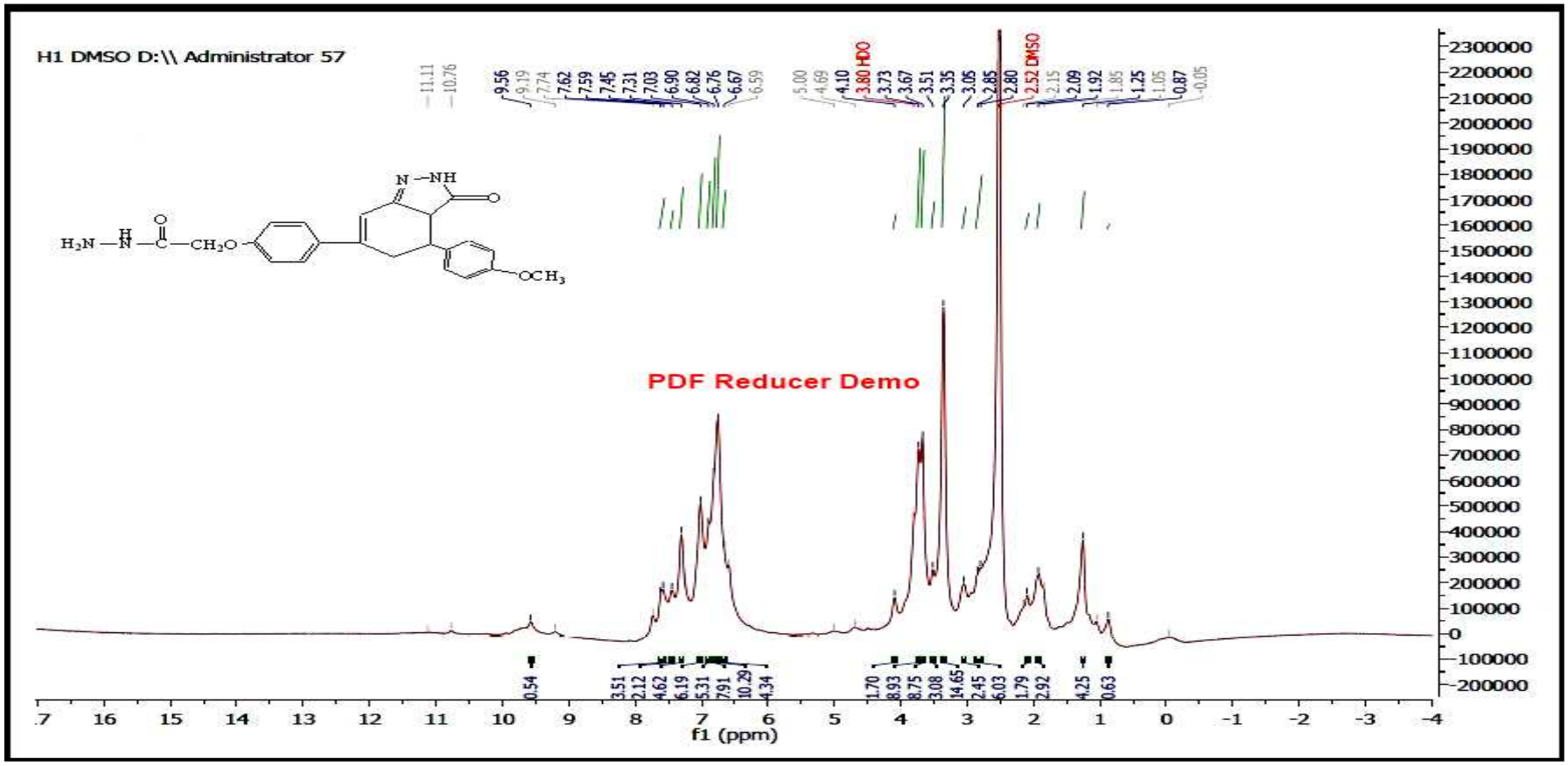
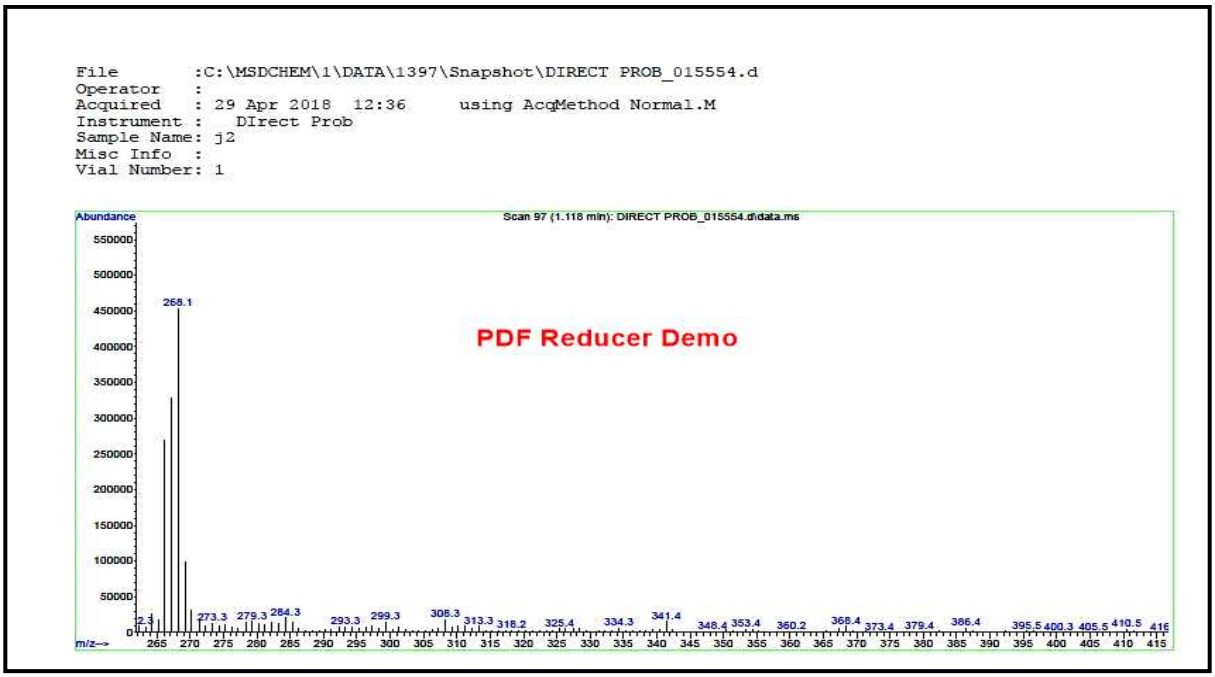


Figure (3-46) ^{1}HNMR –spectrum of compound $[XVII]_c$



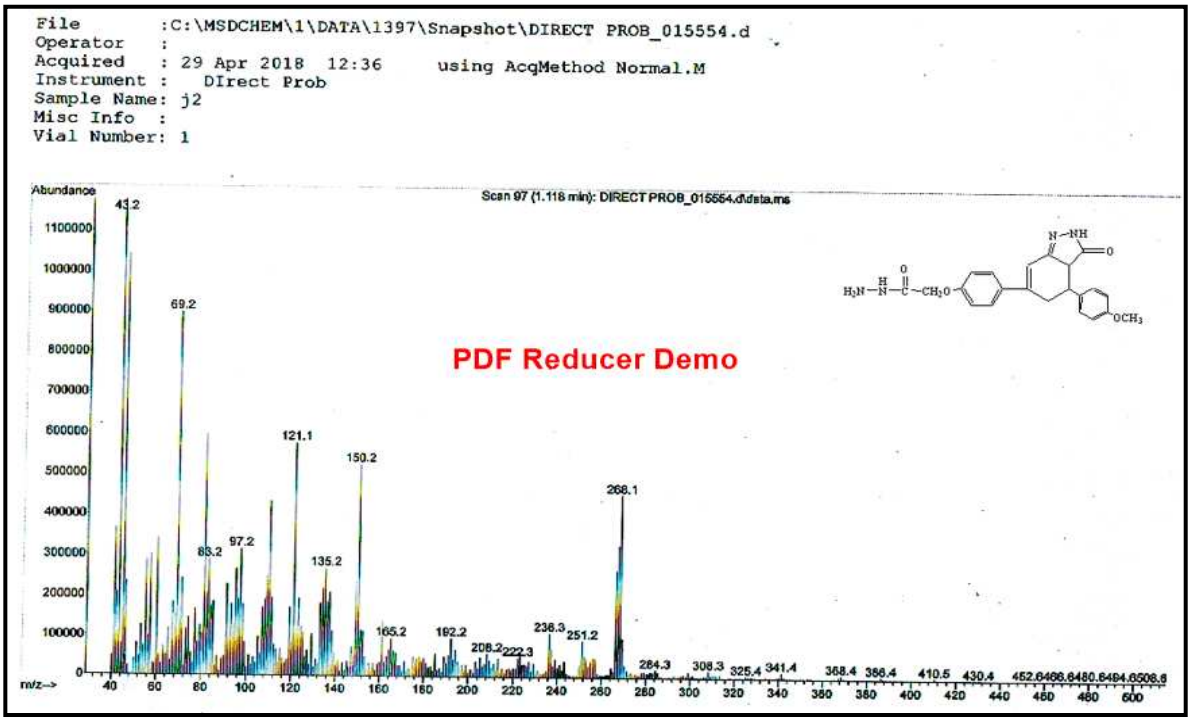


Figure (3-47)The mass spectrum of compound[XVII]$_c$

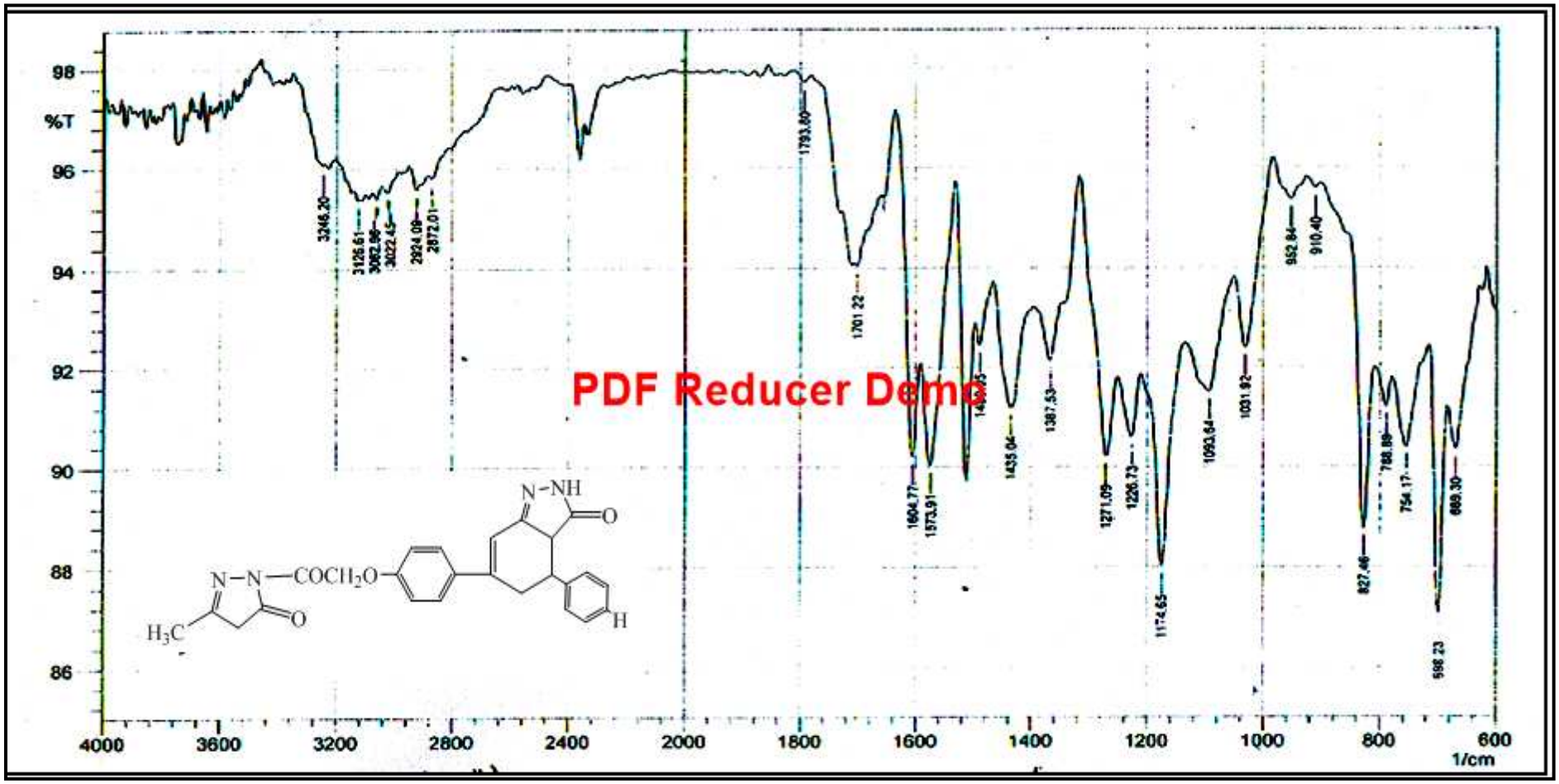


Figure (3-48) FTIR –spectrum of compound $[XVI]_a$

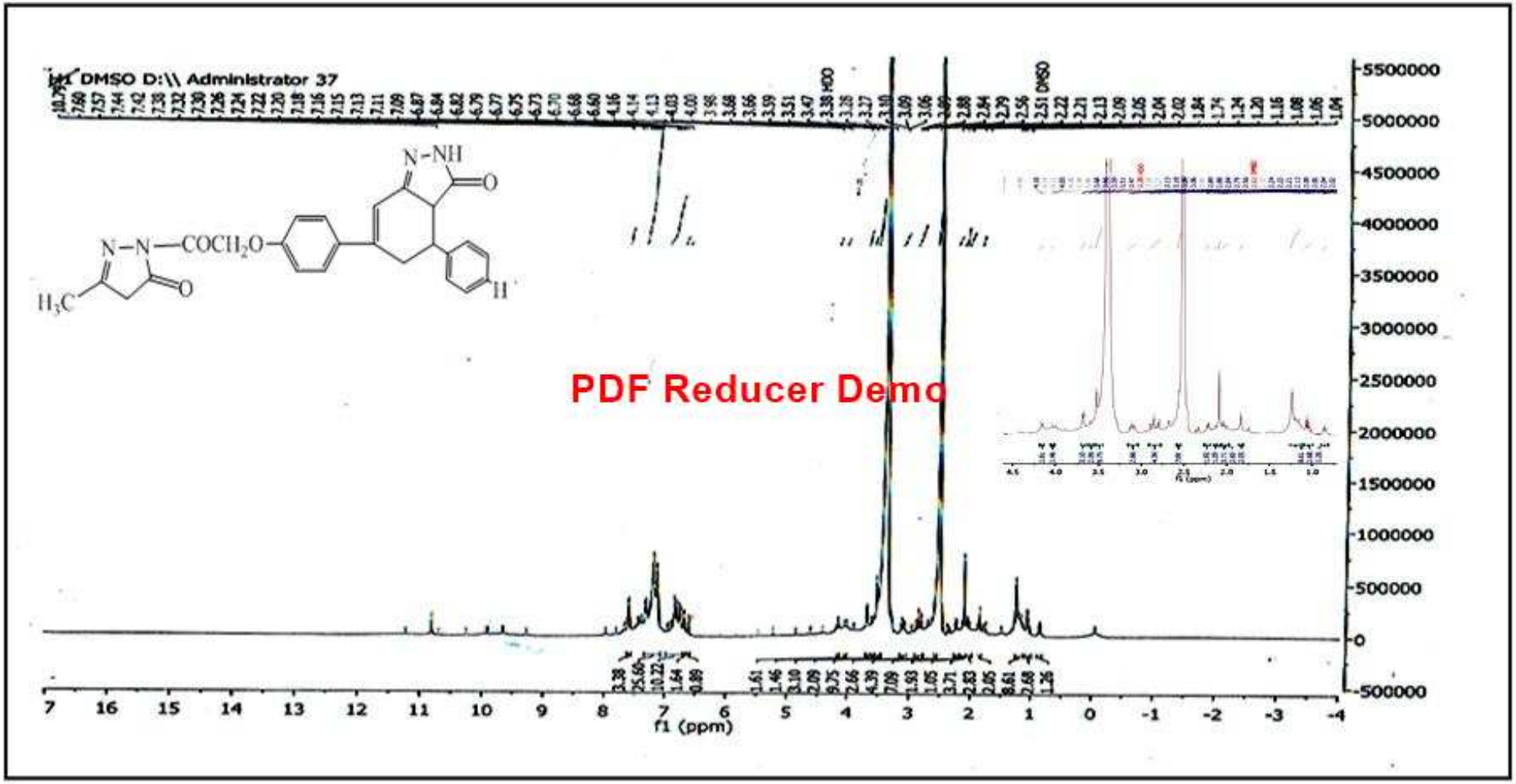


Figure (3-49) ^{1}HNMR –spectrum of compound $[XVI]_a$

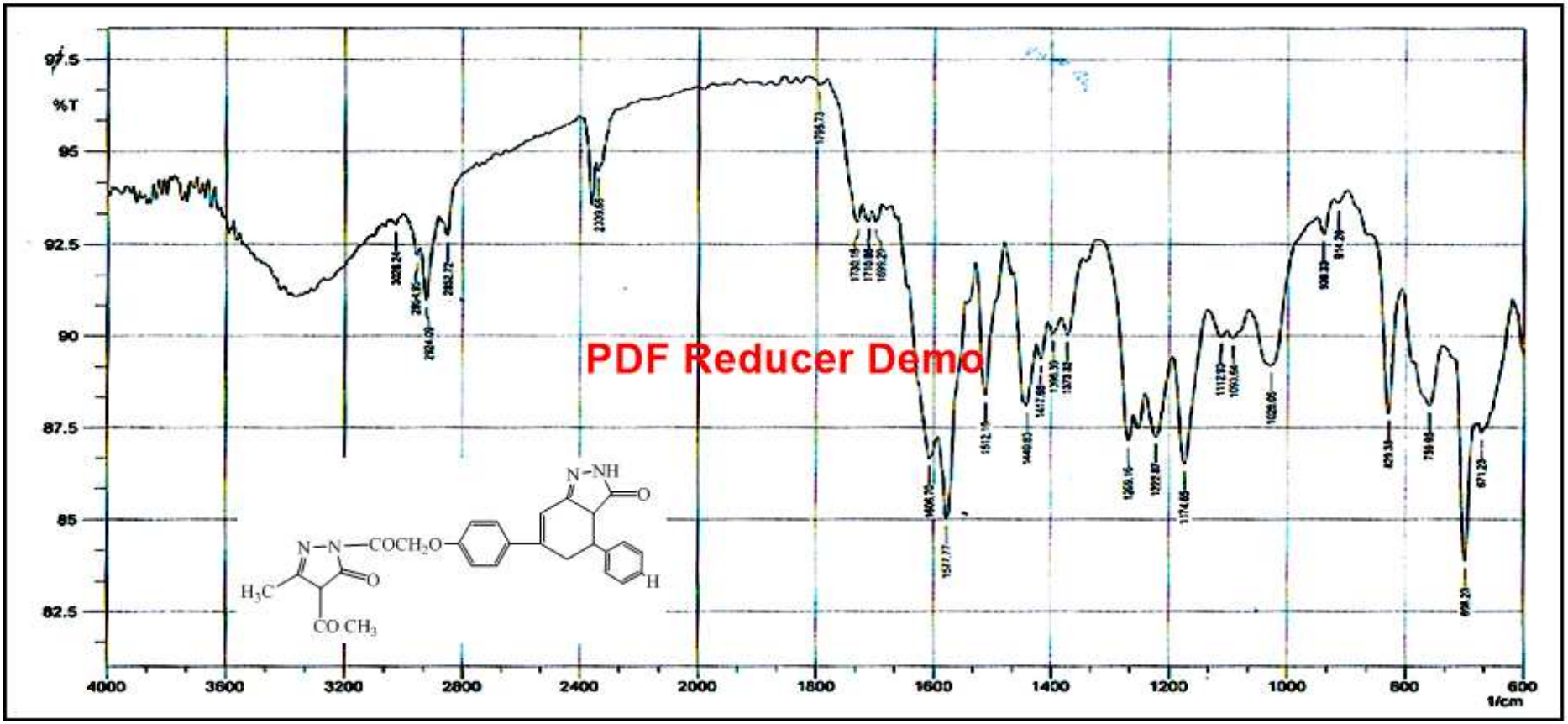


Figure (3-50) FTIR –spectrum of compound $[XVII]_a$

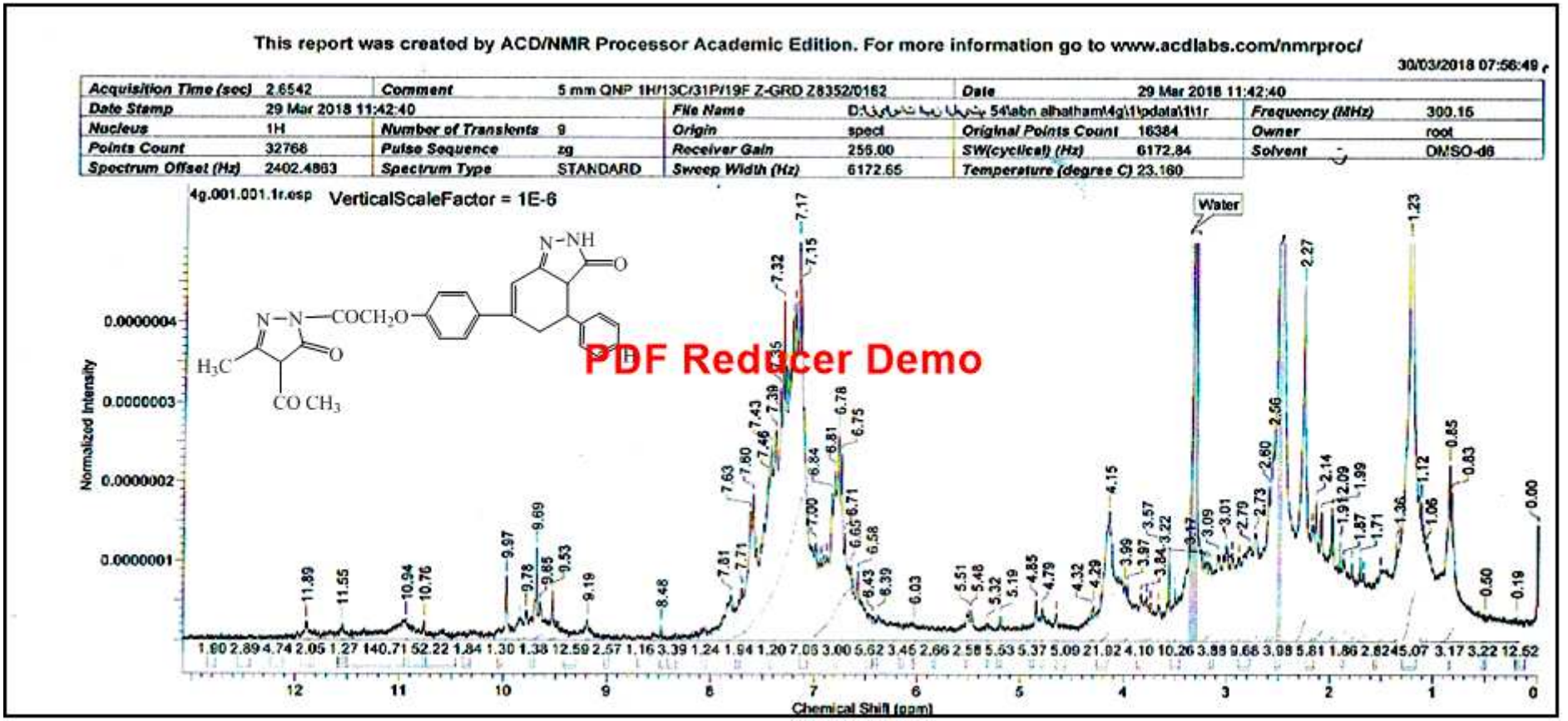


Figure (3-51) ^{1}HNMR –spectrum of compound [XVII]$_a$

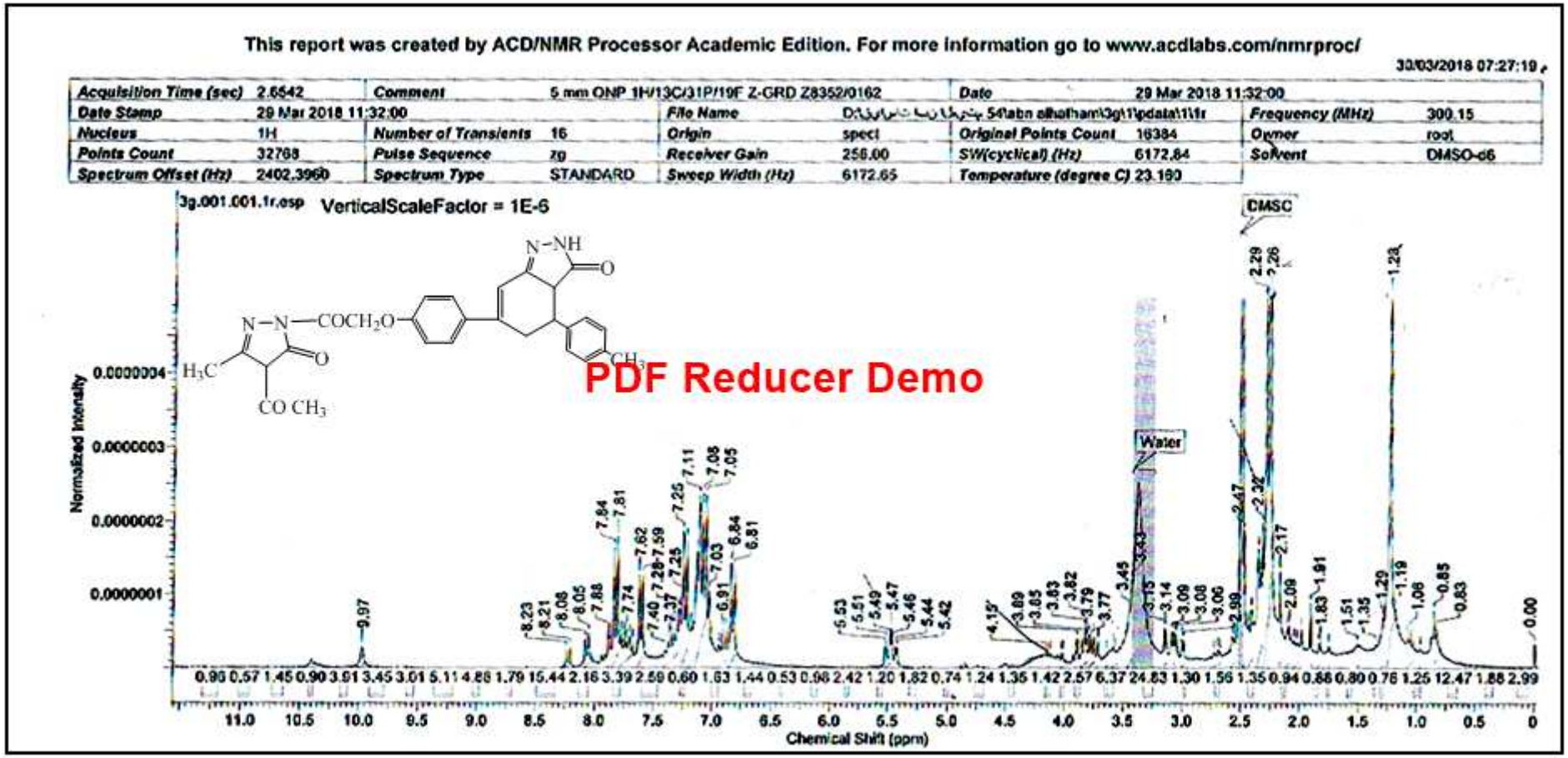


Figure (3-52) ^{1}HNMR –spectrum of compound $[XVII]_b$

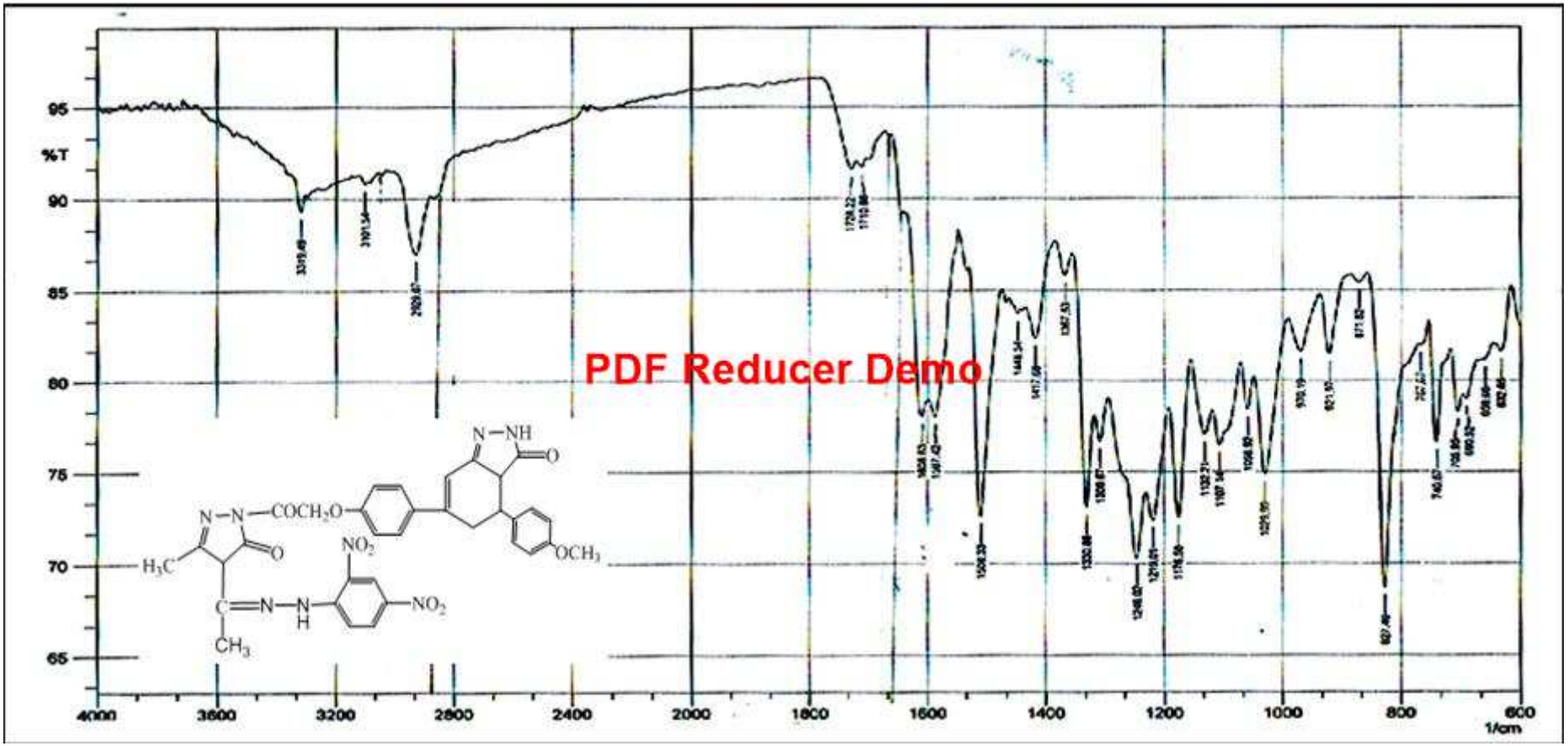


Figure (3-53) FTIR –spectrum of compound $[XVII]_f$

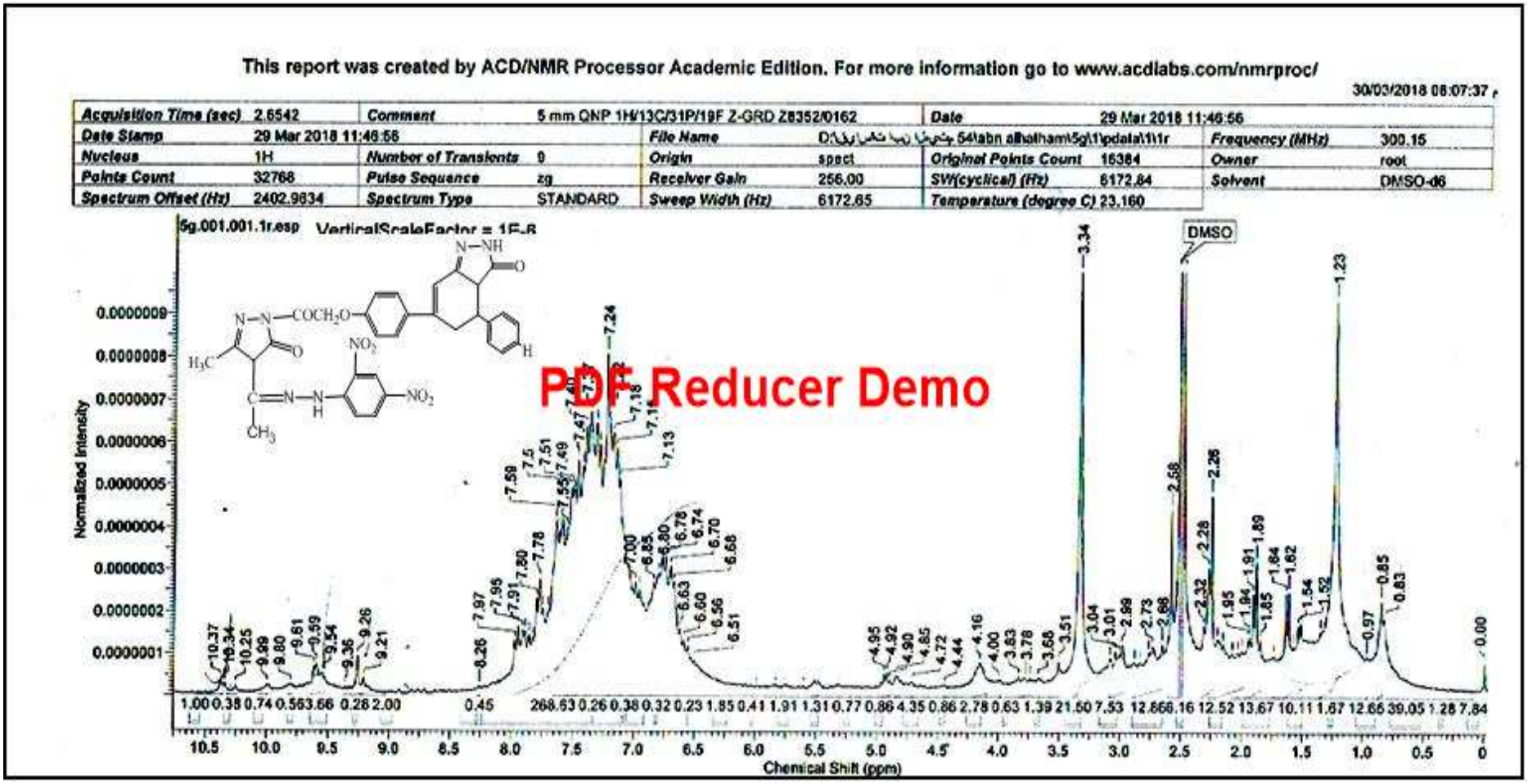
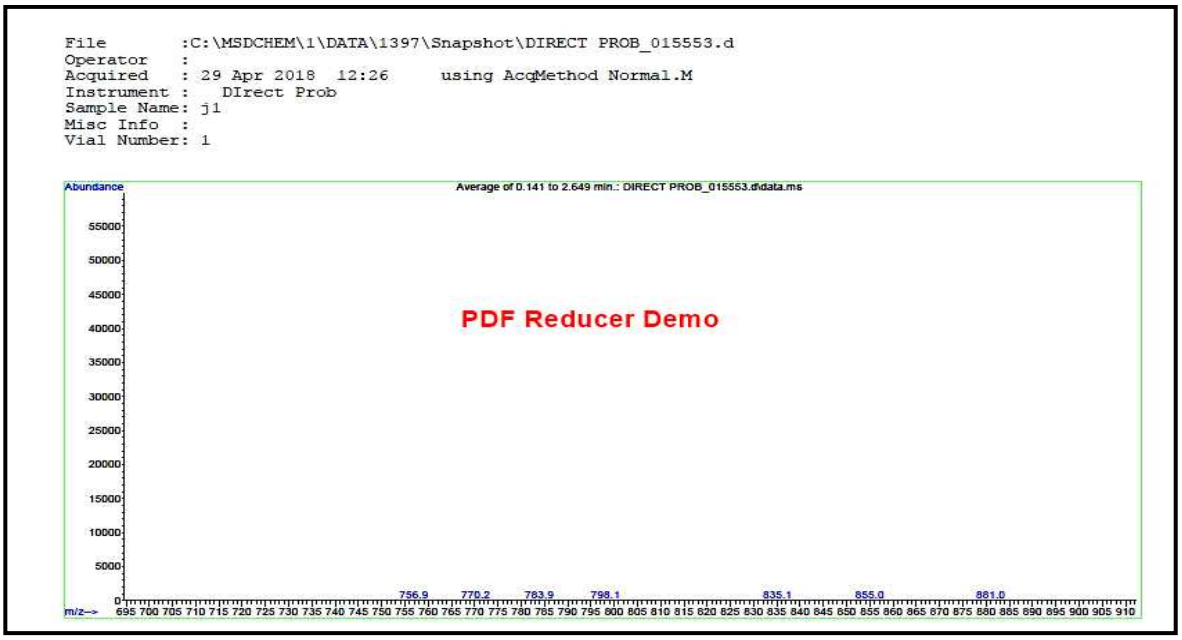


Figure (3-54) ^{1}HNMR –spectrum of compound $[XVII]_d$



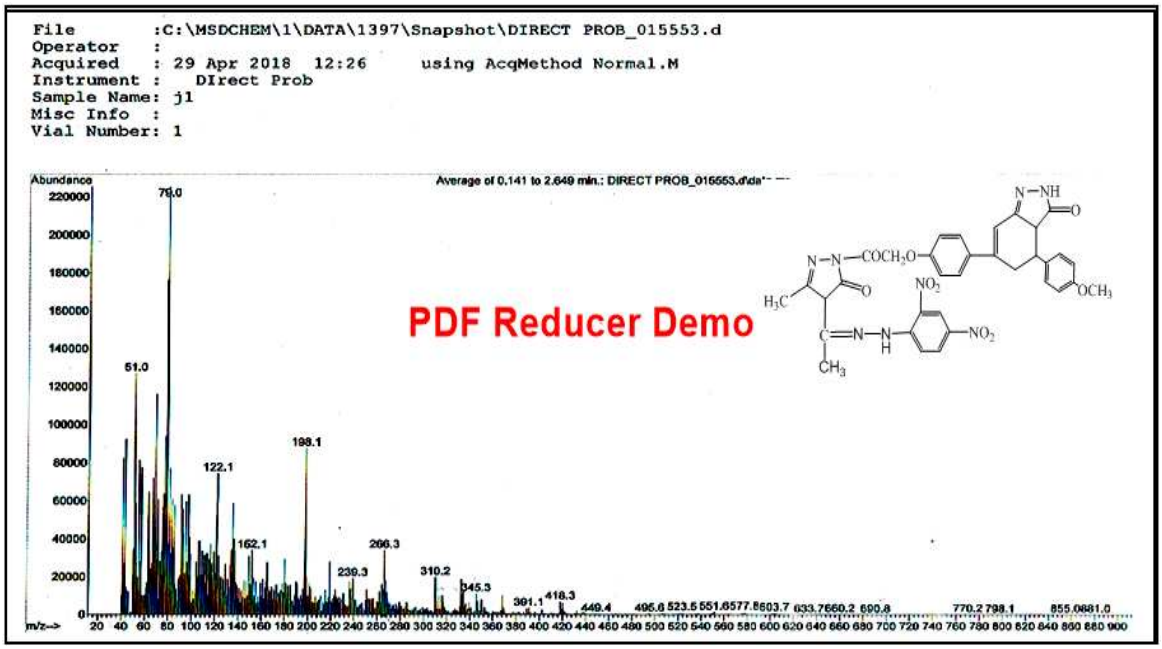


Figure (3-55)The mass spectrum of compound[XVII]$_f$

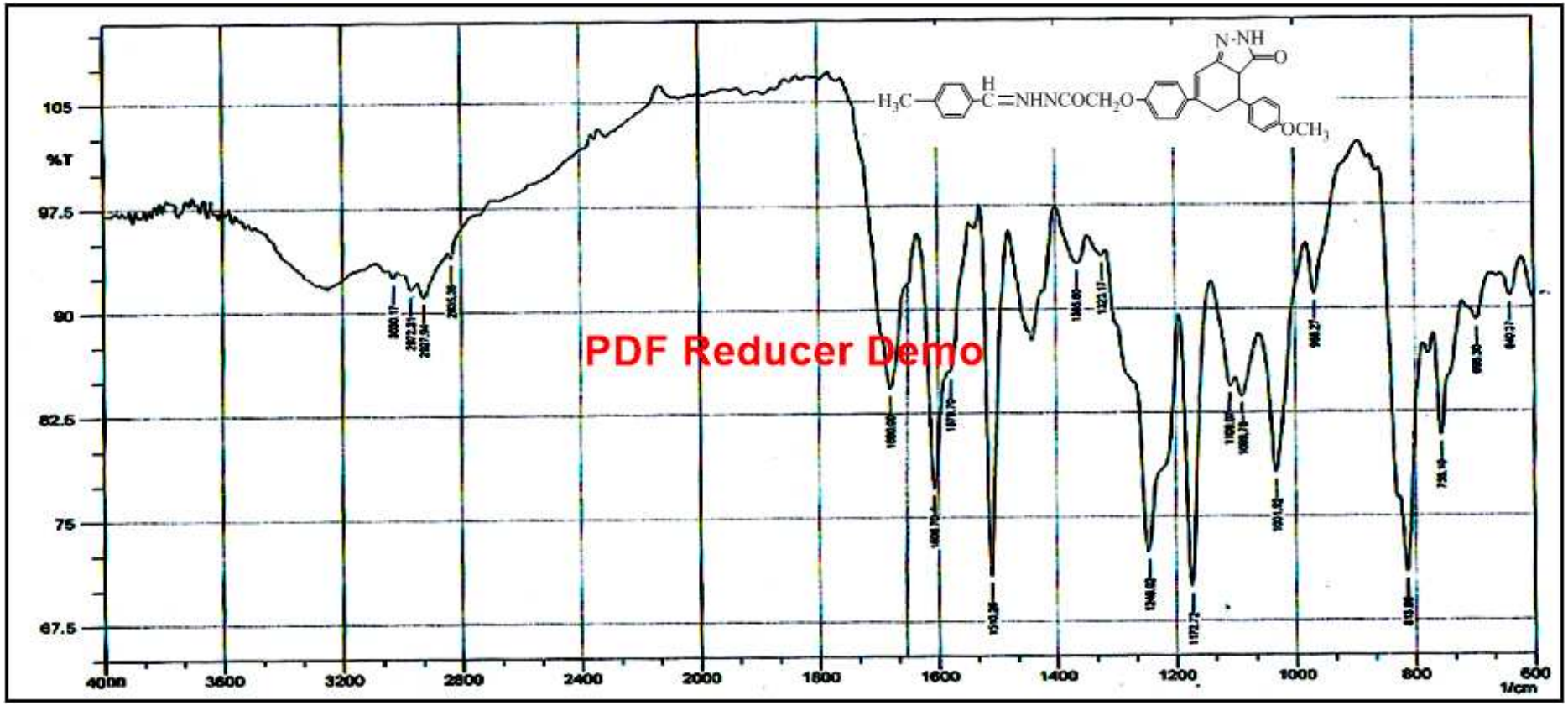


Figure (3-56) FTIR –spectrum of compound $[XIX]_f$

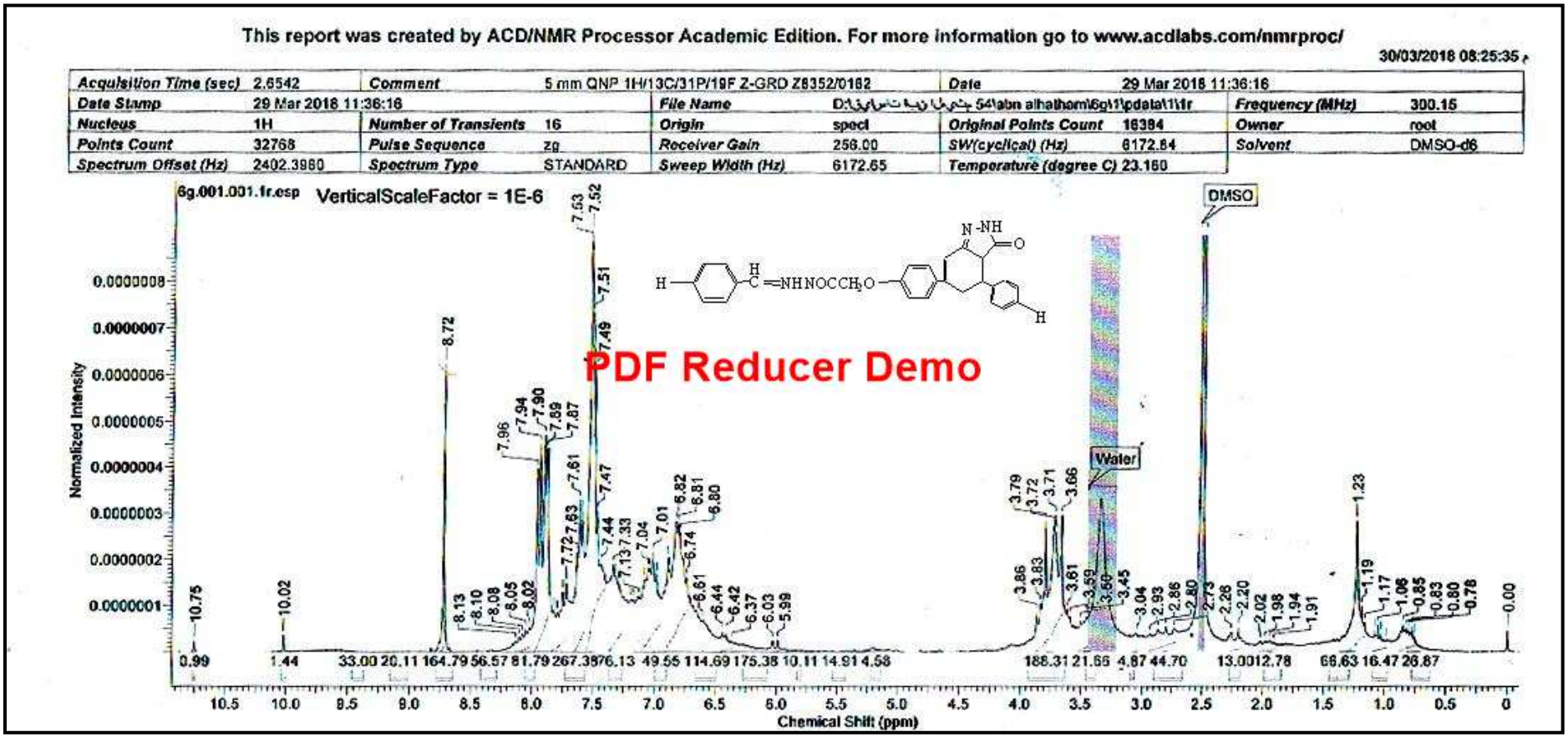


Figure (3-57) ^{1}HNMR –spectrum of compound $[XIX]_a$

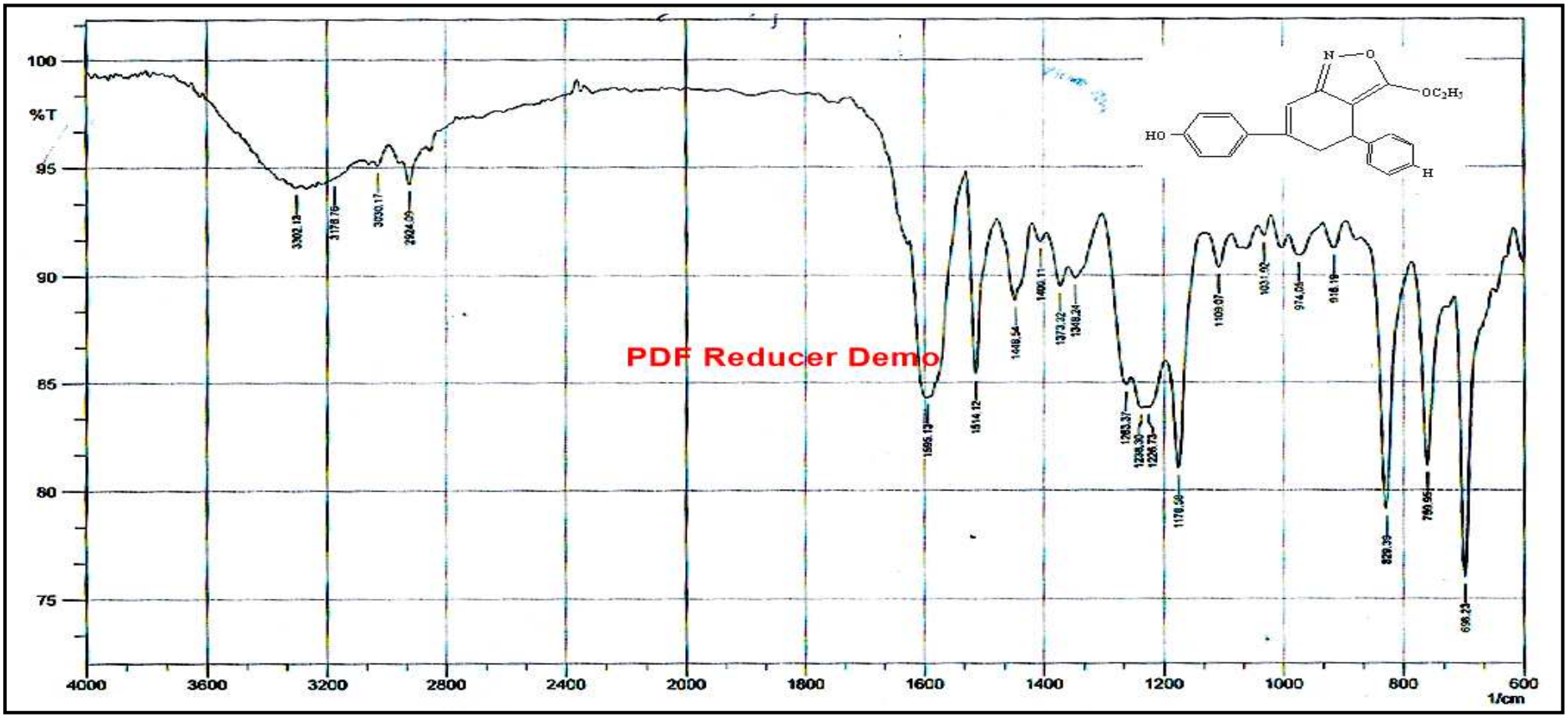


Figure (3-58) FTIR –spectrum of compound $[XX]_a$

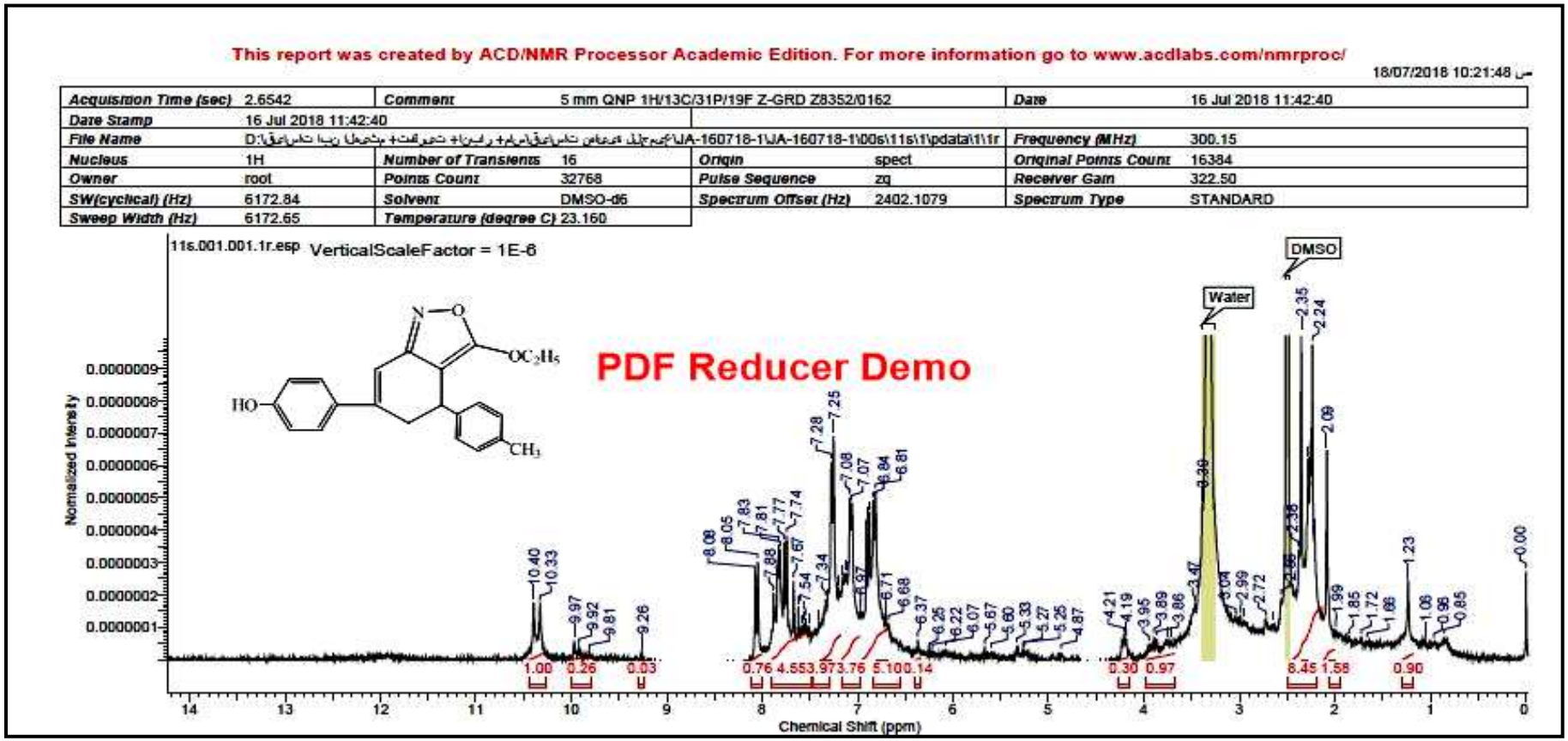


Figure (3-59) ^{1}HNMR –spectrum of compound $[XX]_b$

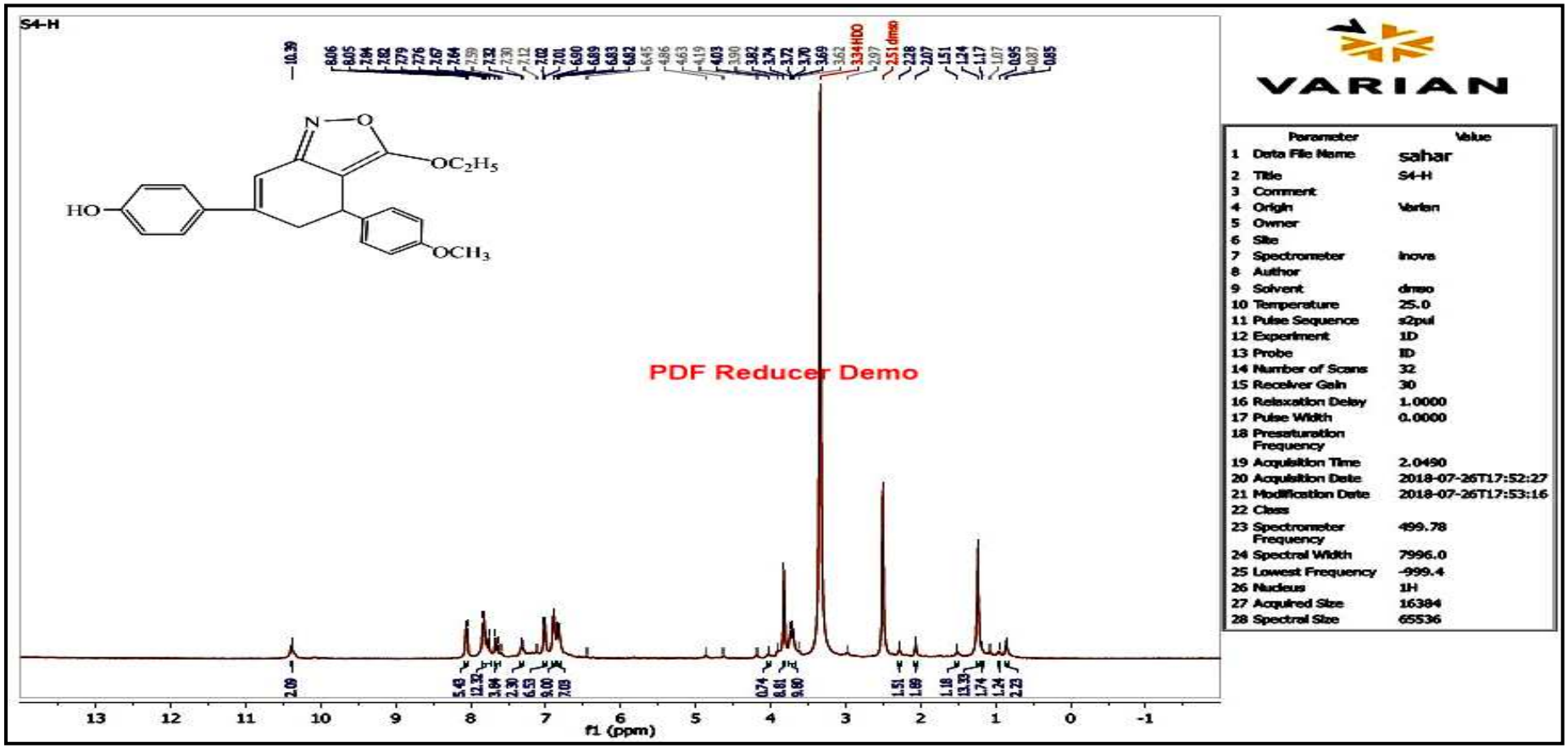
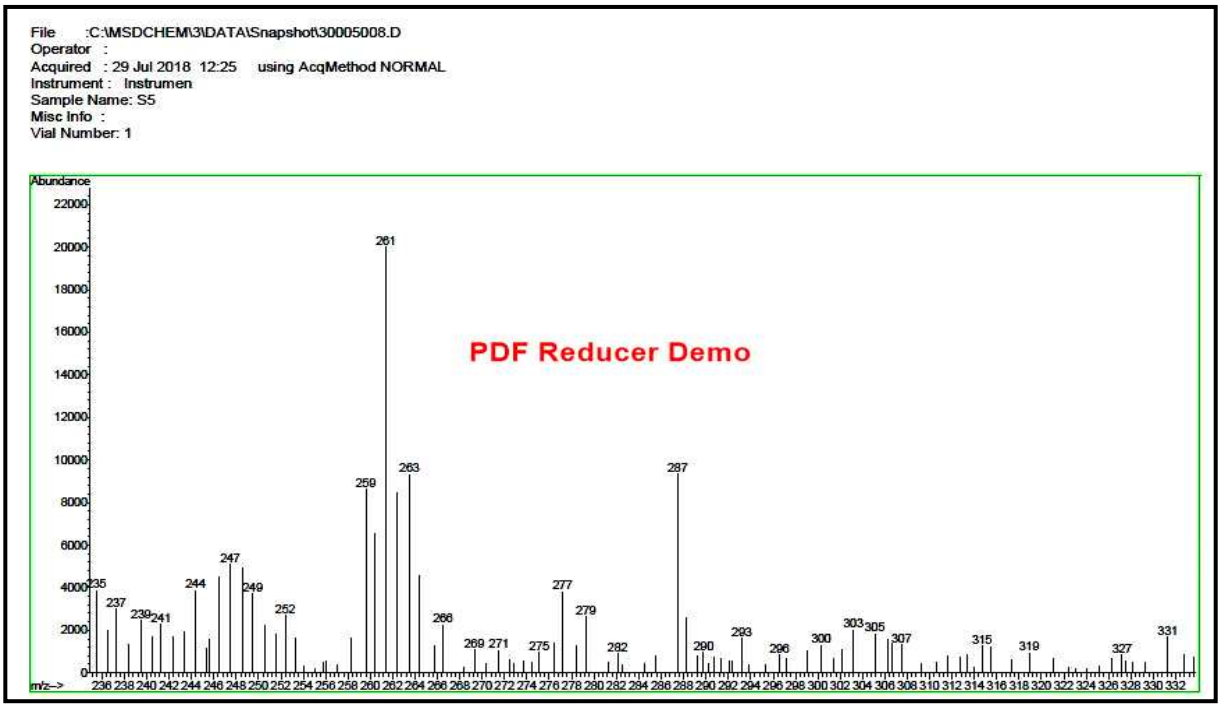


Figure (3-60) ^{1}HNMR –spectrum of compound $[XX]_c$



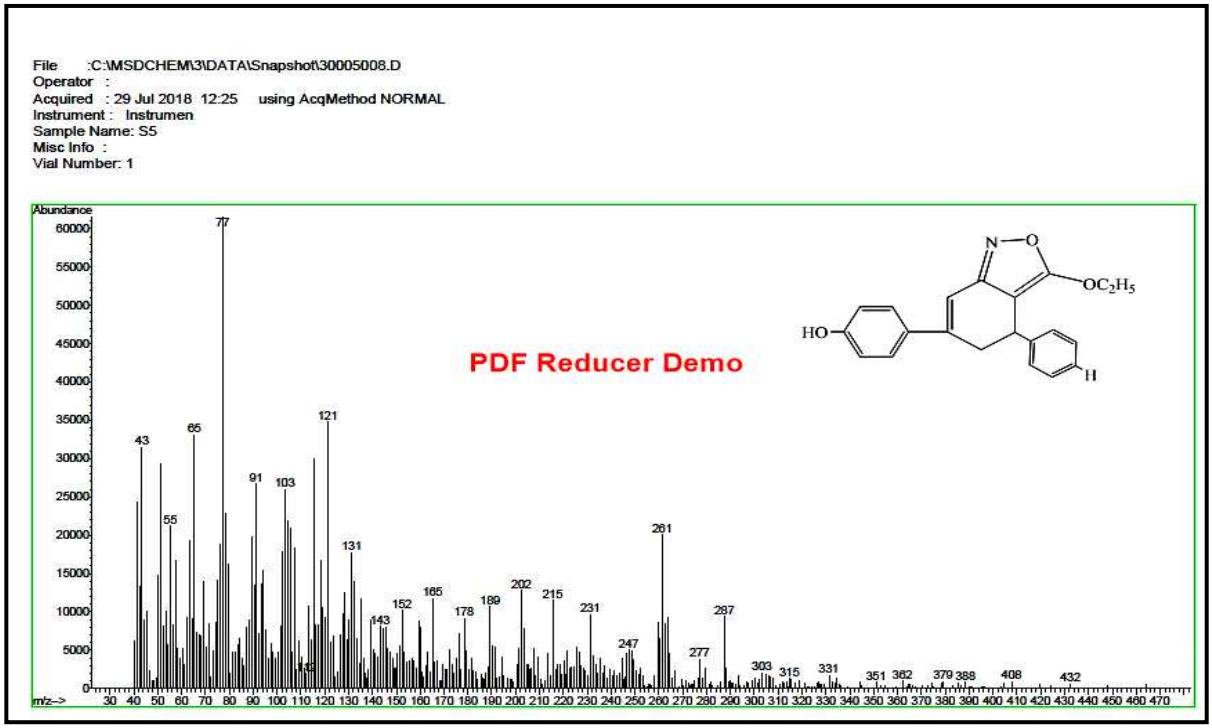


Figure (3-61)The mass spectrum of compound[XX]$_a$

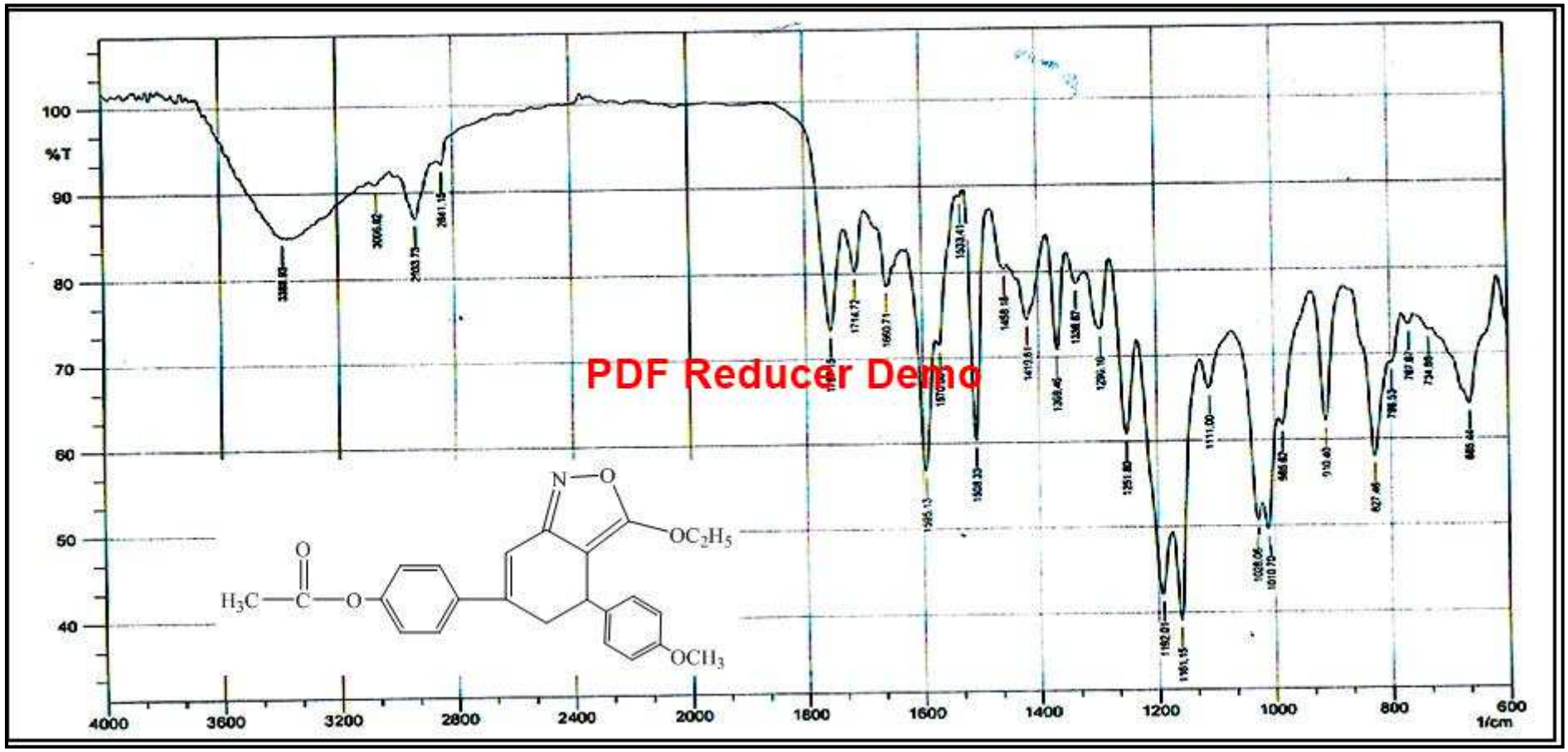


Figure (3-62) FTIR –spectrum of compound[XXI]$_c$

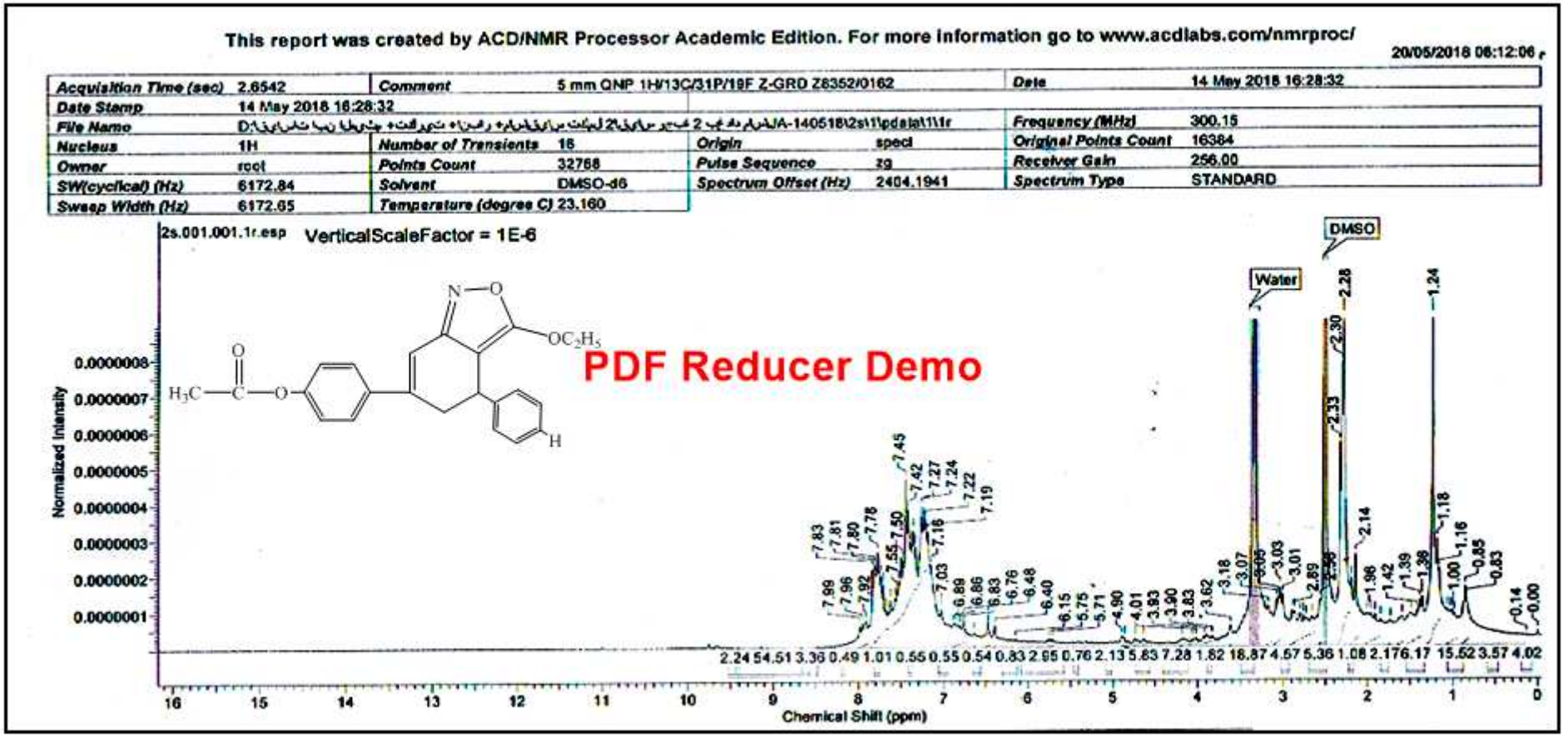


Figure (3-63) ^{1}HNMR –spectrum of compound $[XXI]_a$

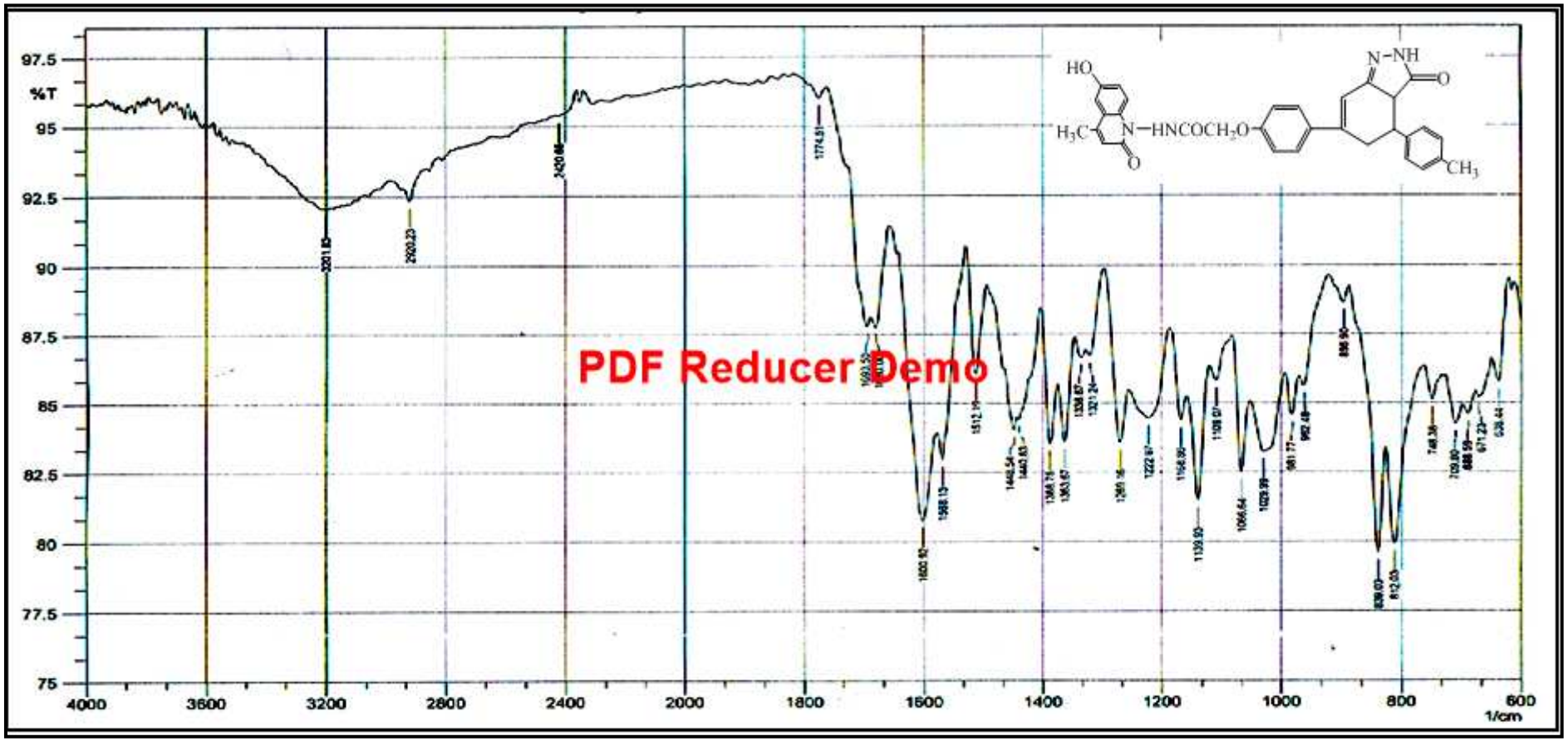


Figure (3-64) FTIR –spectrum of compound[XXII]$_e$

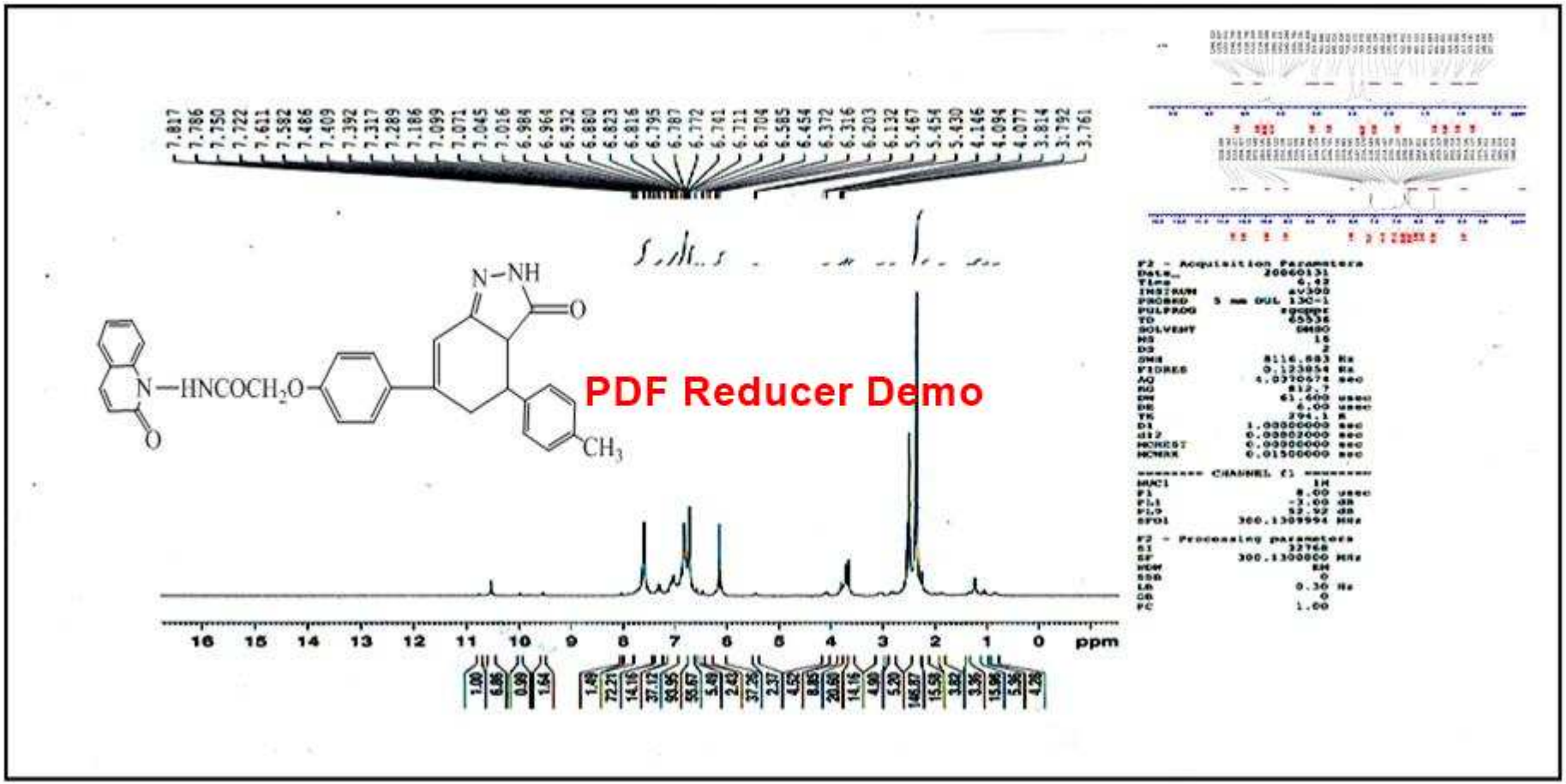


Figure (3-65) ^{1}HNMR –spectrum of compound $[XXII]_b$

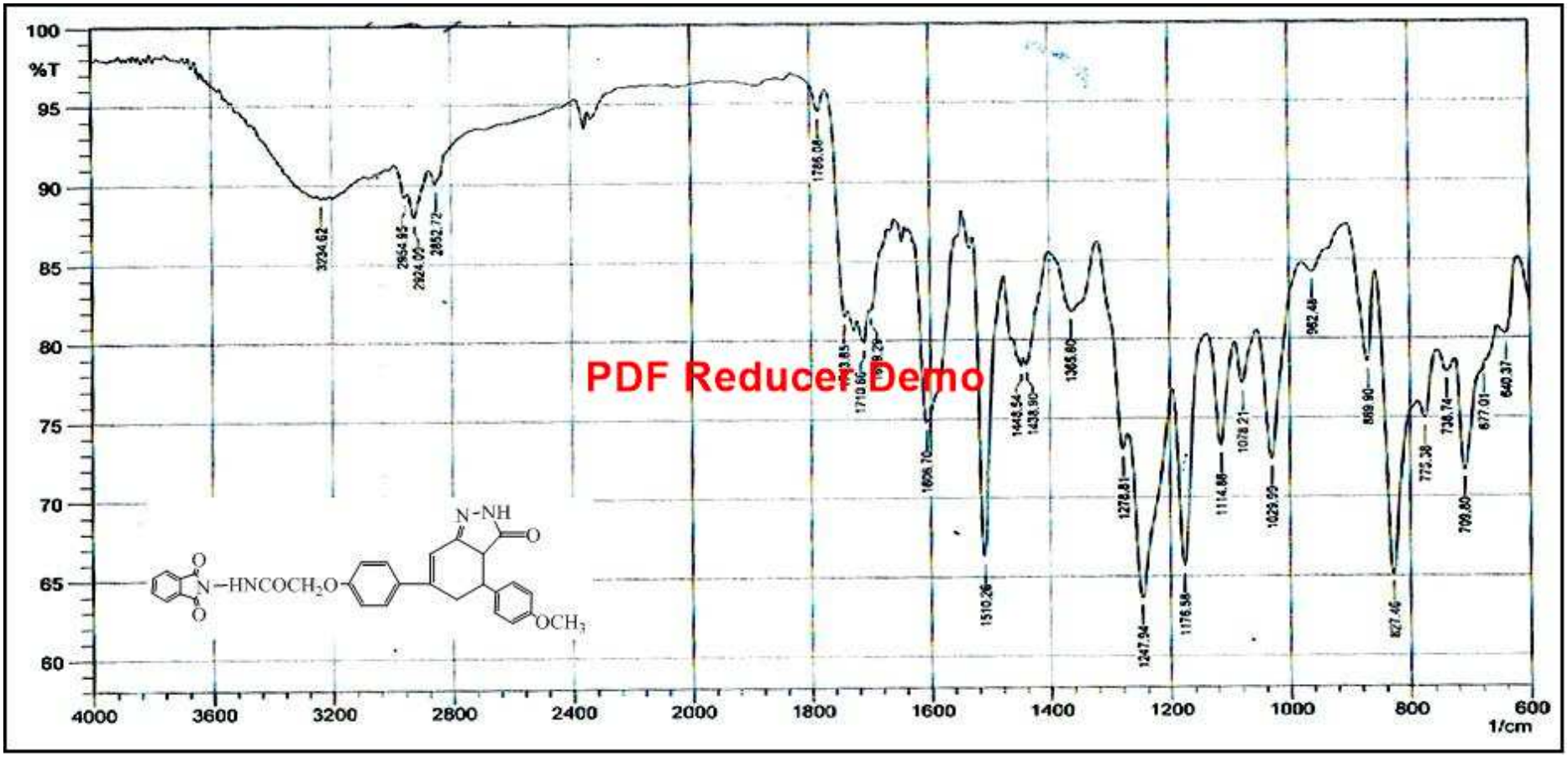


Figure (3-66) FTIR –spectrum of compound $[XXIII]_c$

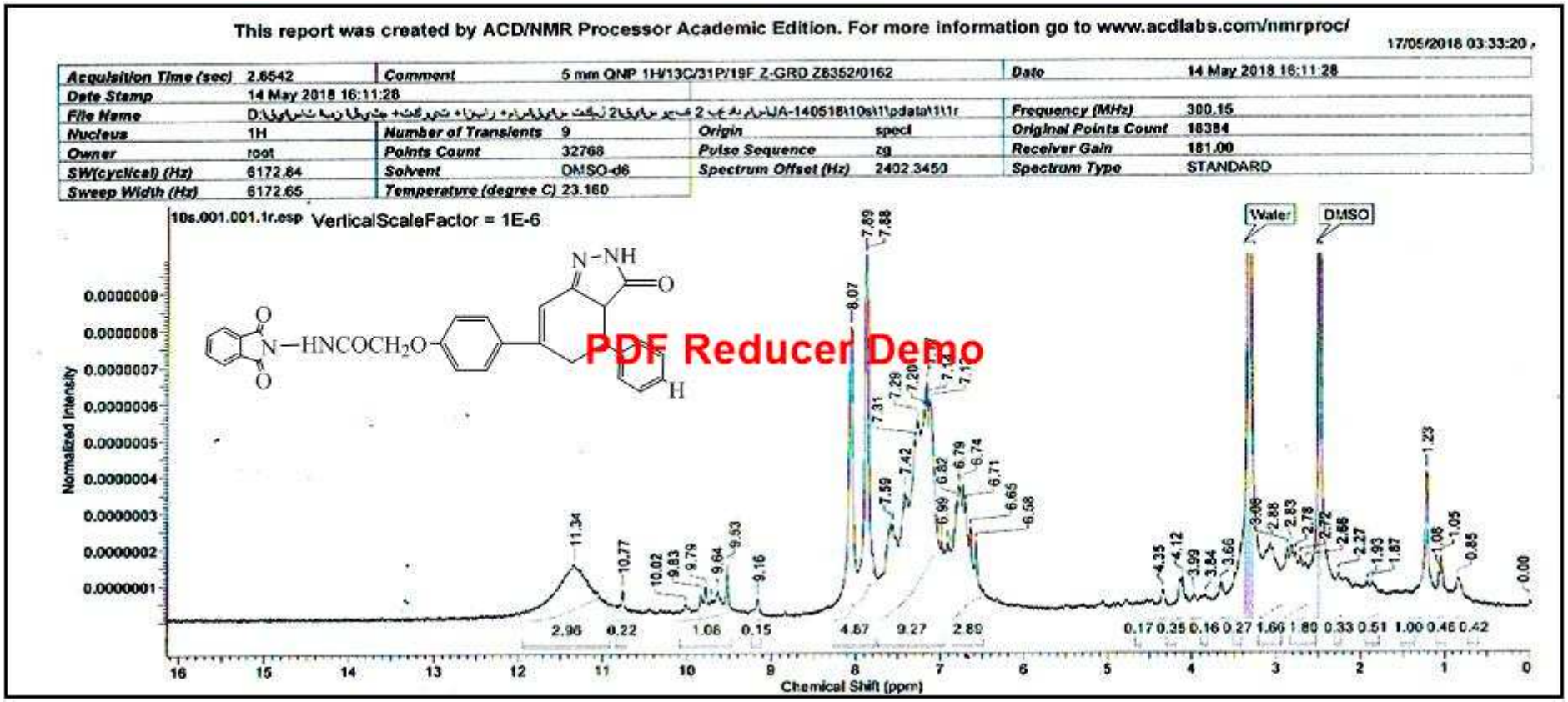


Figure (3-67) ^{1}HNMR –spectrum of compound $[XXIII]_a$

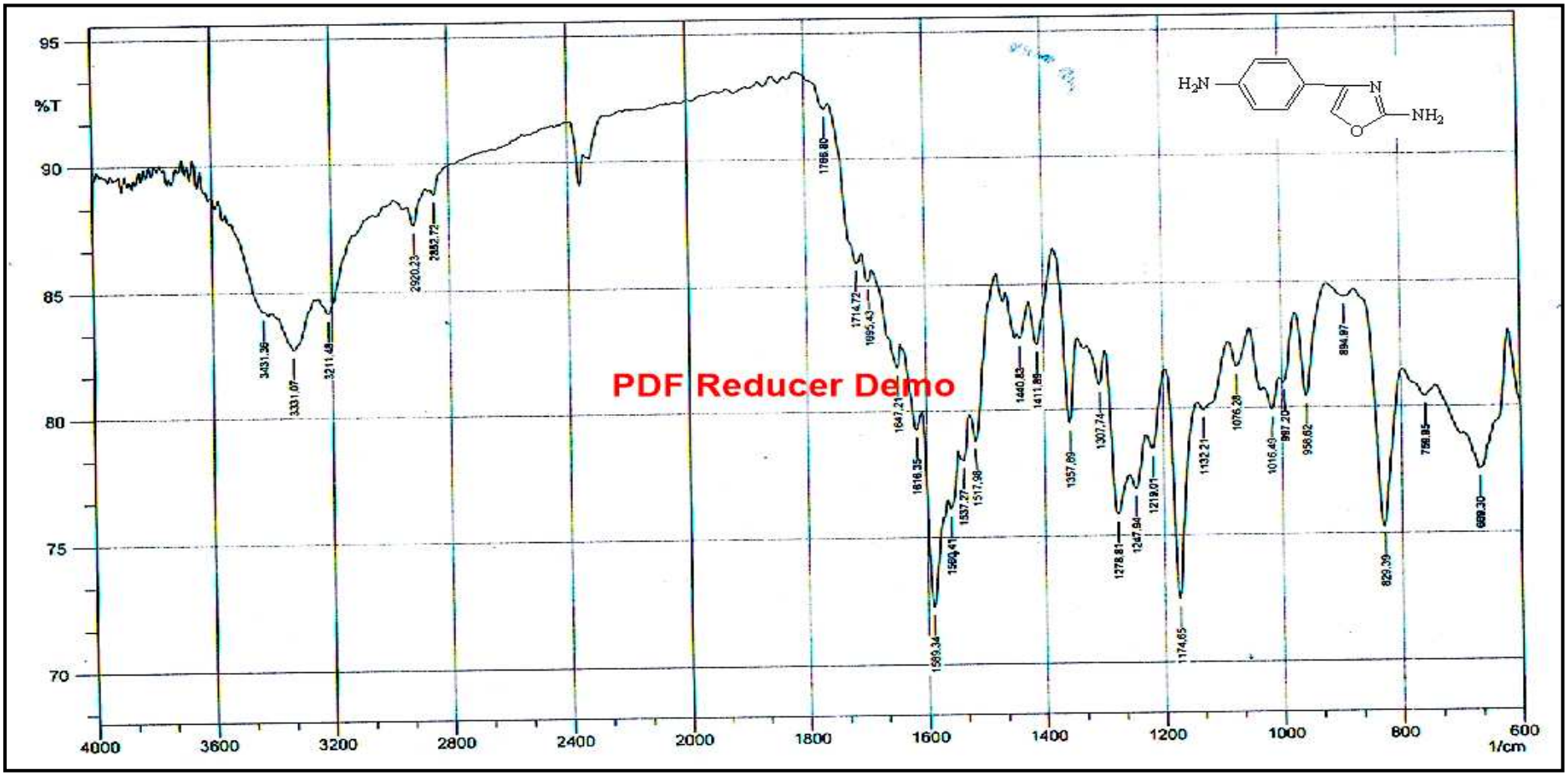


Figure (3-68) FTIR –spectrum of compound [XXIV]

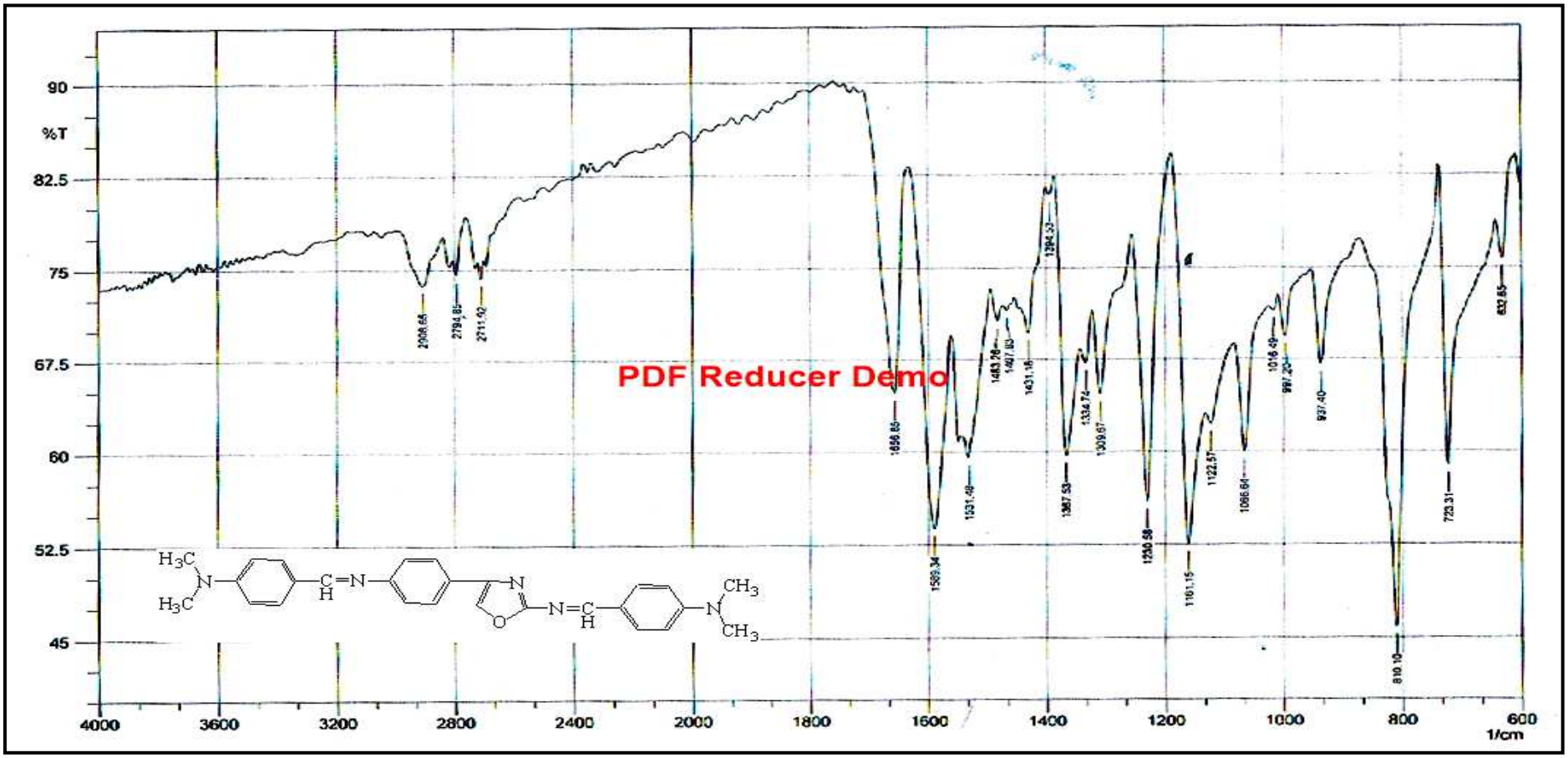


Figure (3-69) FTIR –spectrum of compound $[XXV]_b$

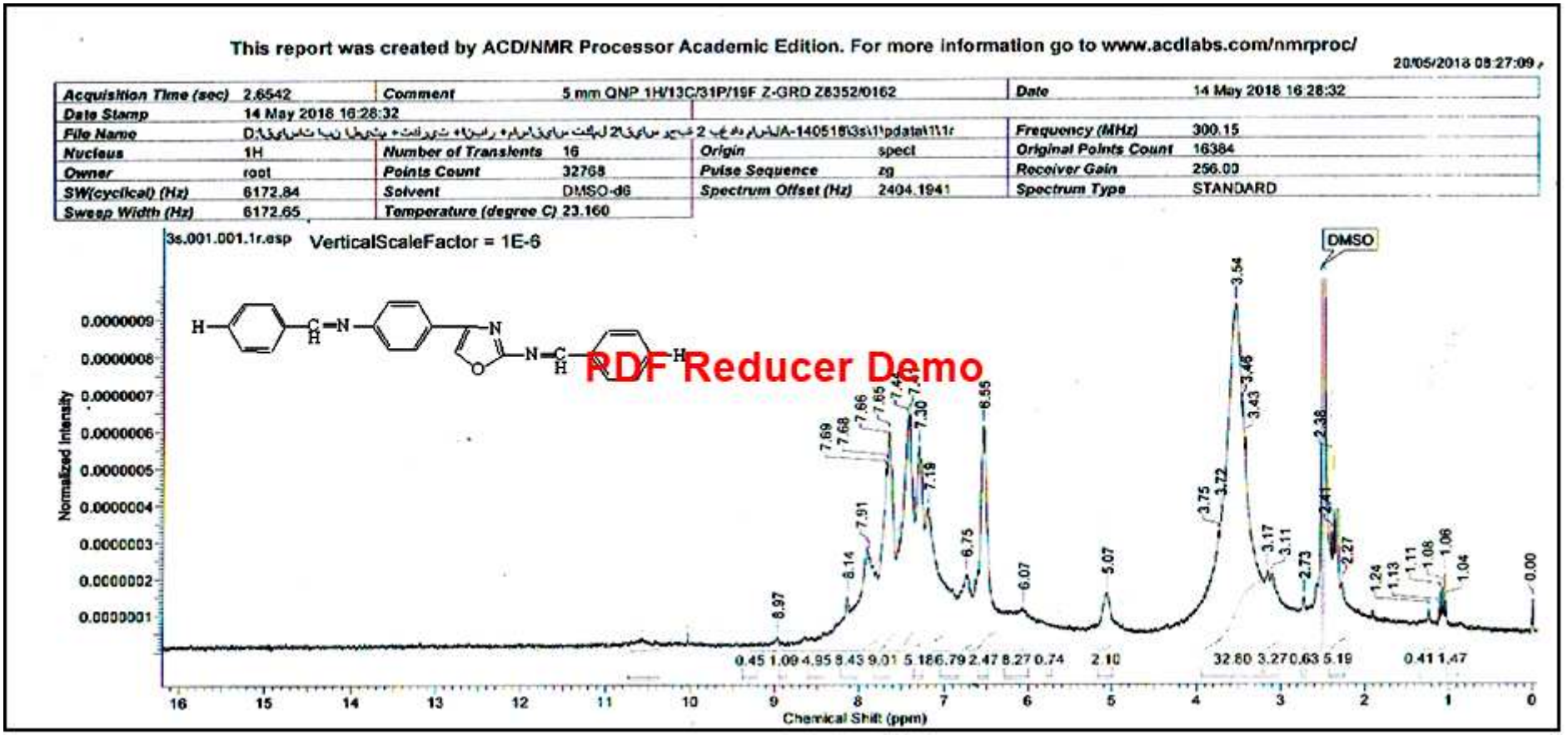


Figure (3-70) ^{1}HNMR –spectrum of compound [XXV]$_a$

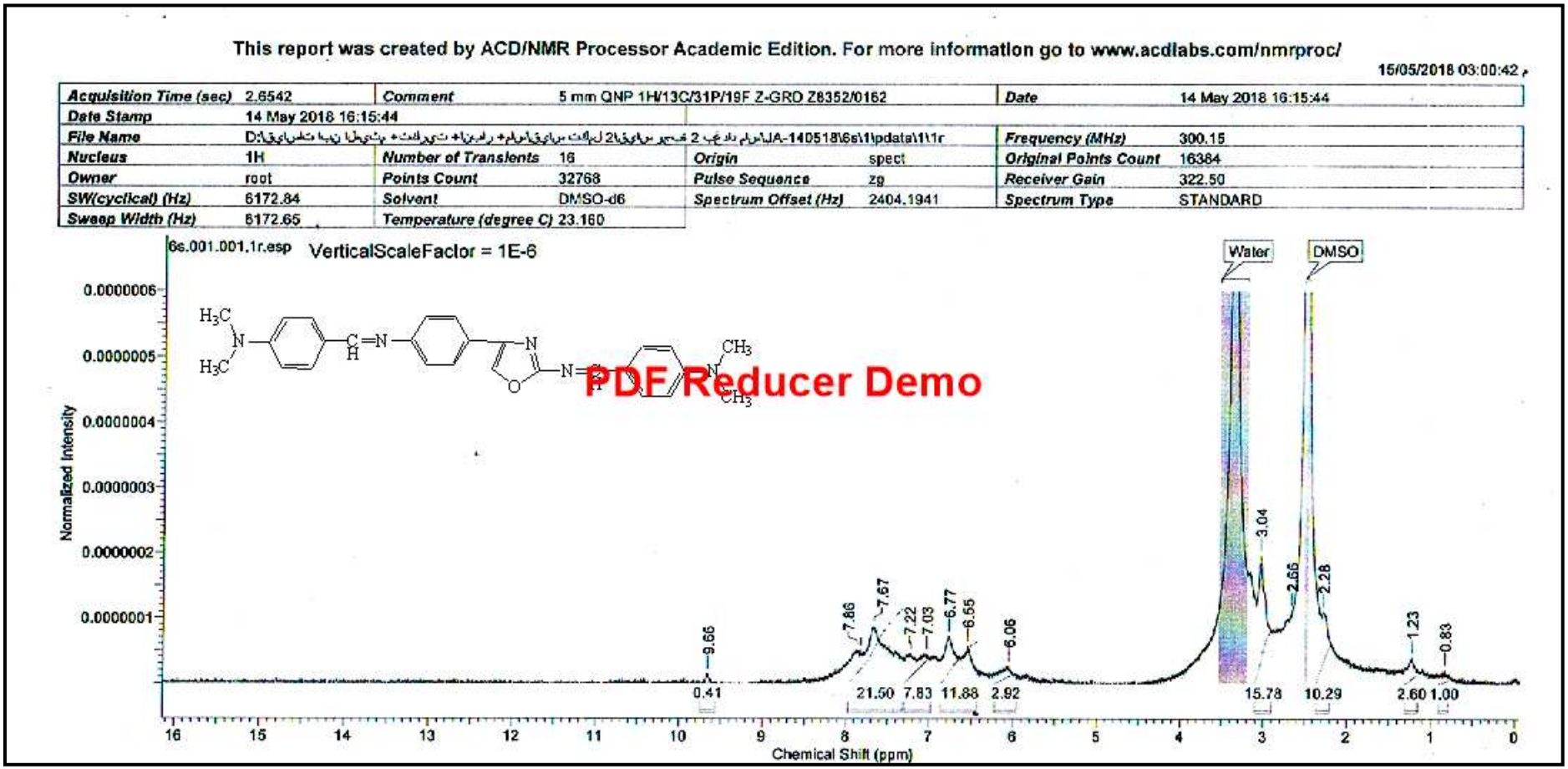


Figure (3-71) ^{1}HNMR –spectrum of compound [XXV]$_b$

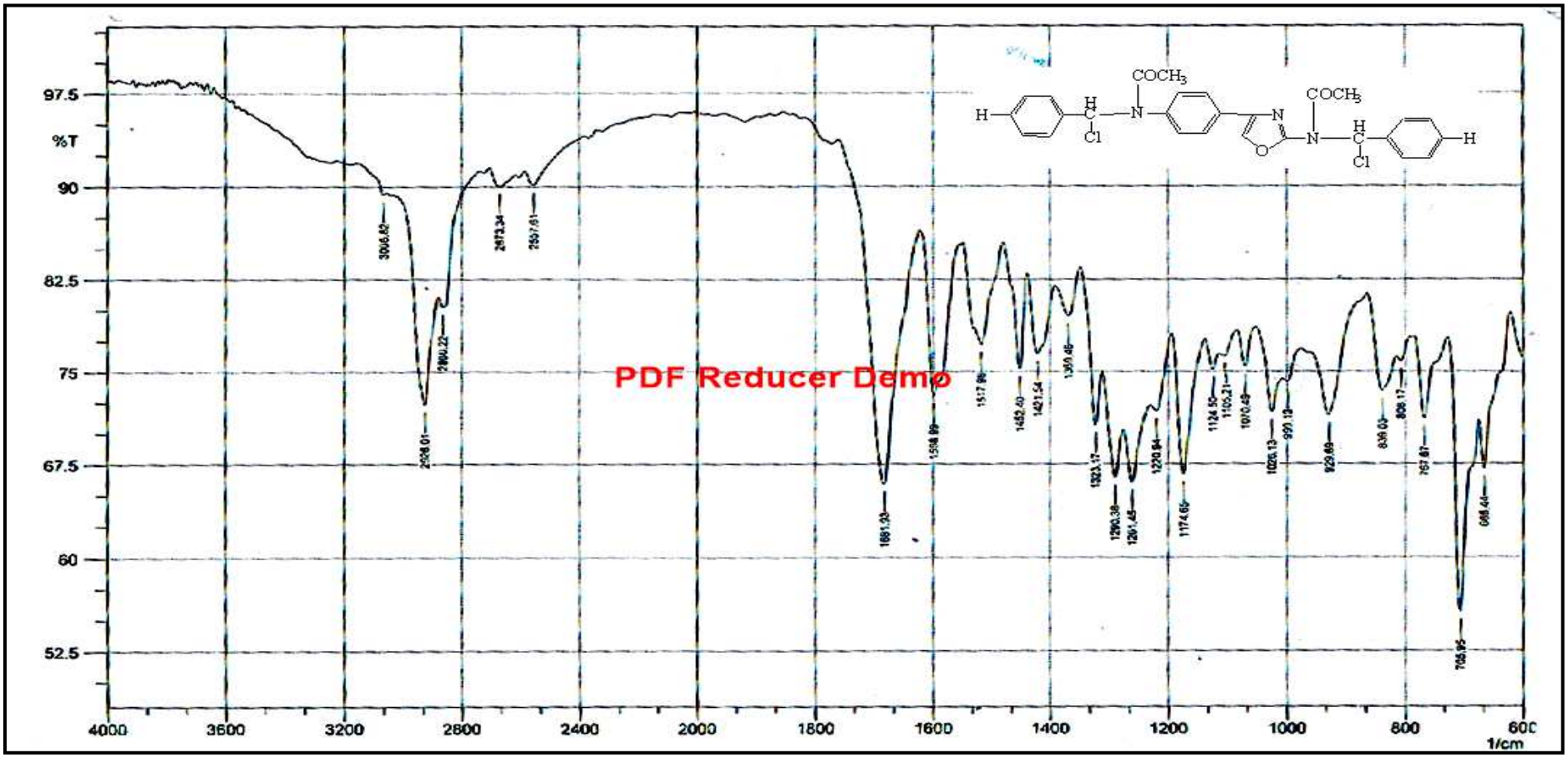


Figure (3-72) FTIR –spectrum of compound [XXVI]$_a$

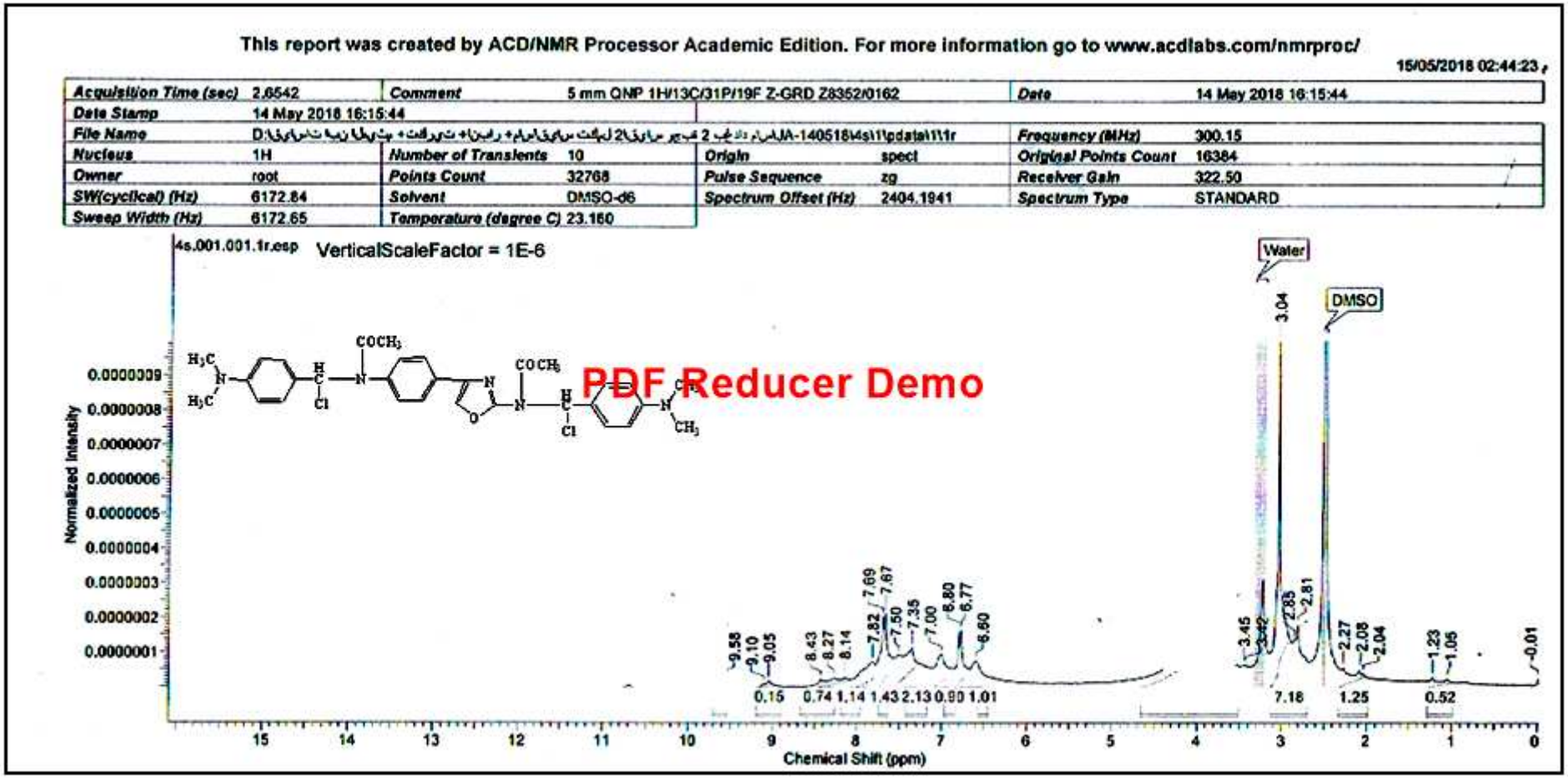


Figure (3-73) ^{1}HNMR –spectrum of compound $[XXVI]_b$

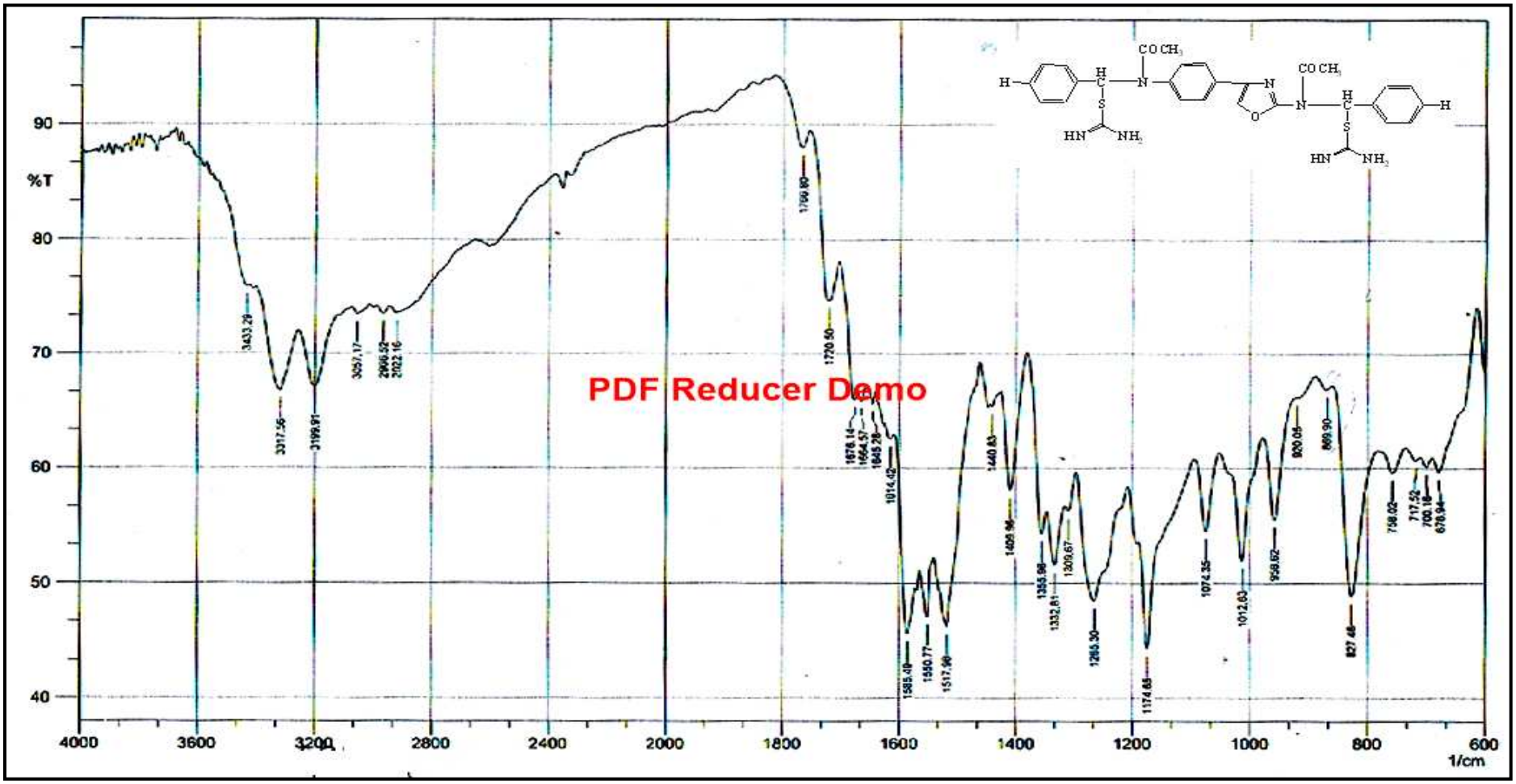


Figure (3-74) FTIR –spectrum of compound $[XXVII]_a$

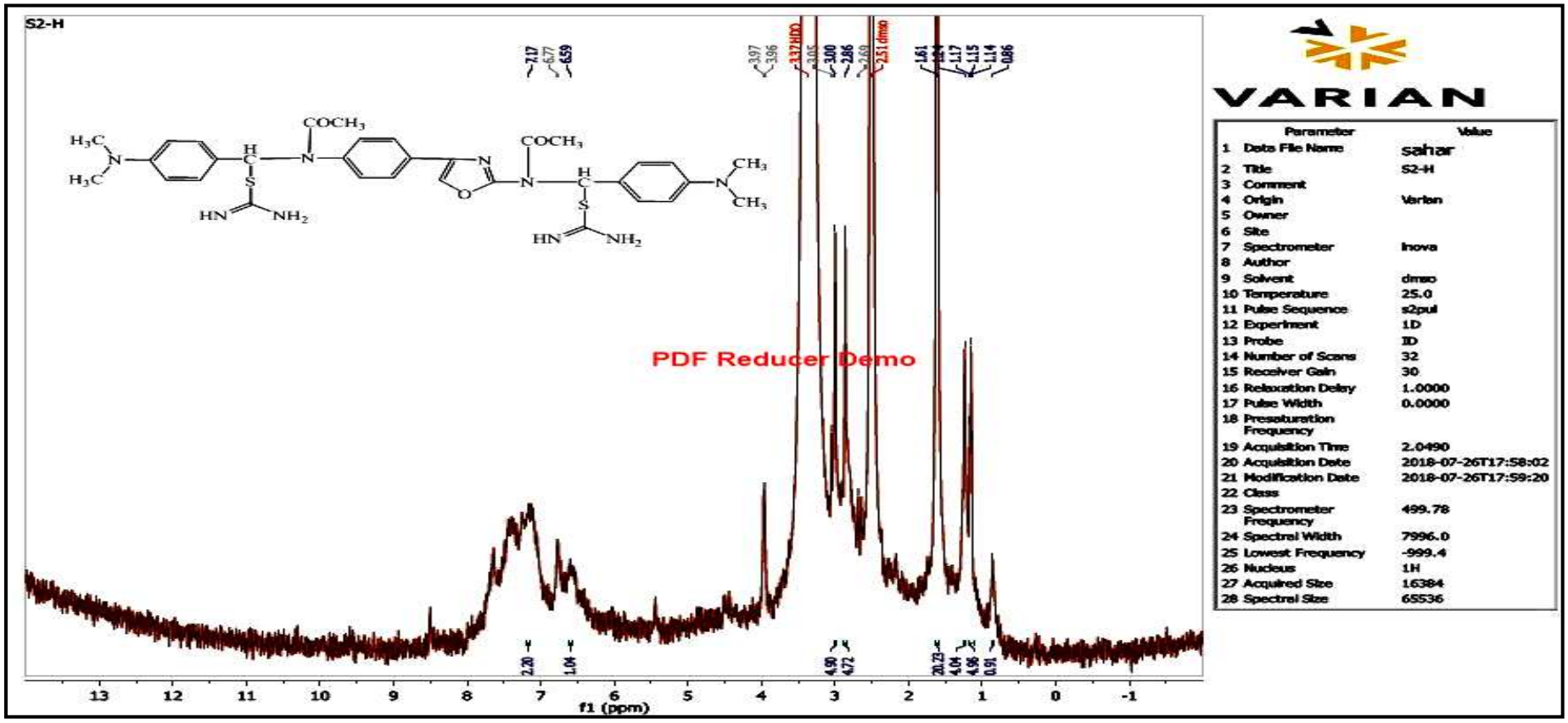
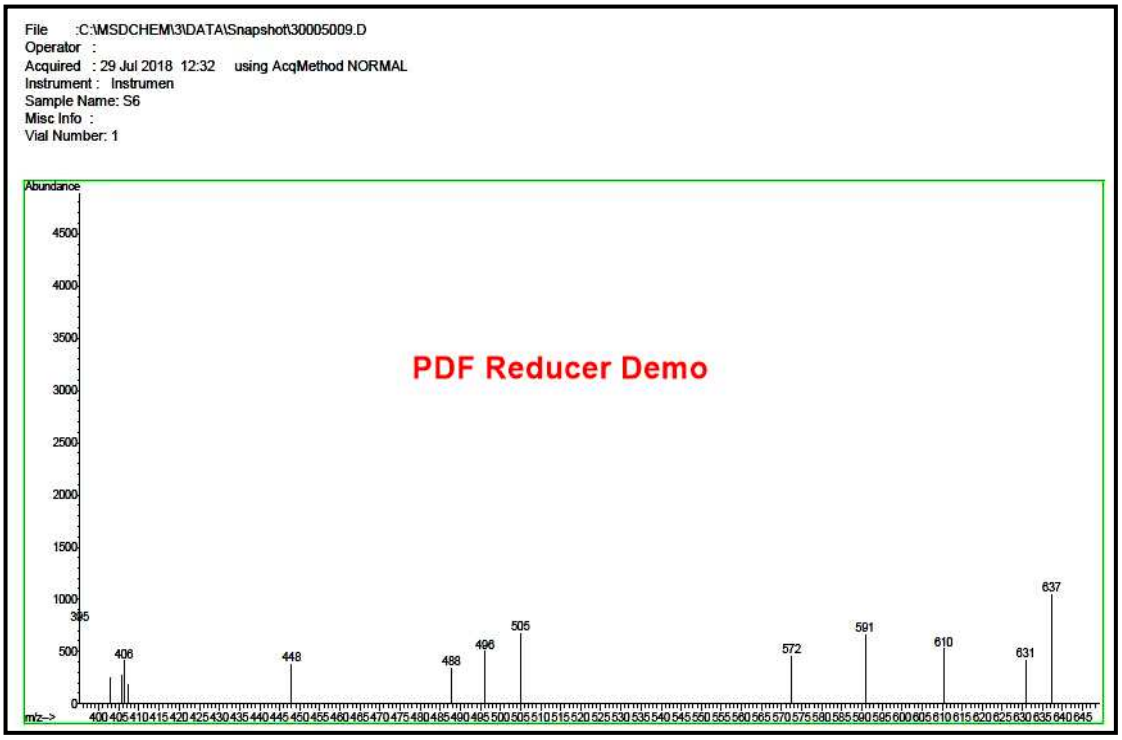


Figure (3-75) ^{1}HNMR –spectrum of compound [XXVII]$_{\mathbf{b}}$



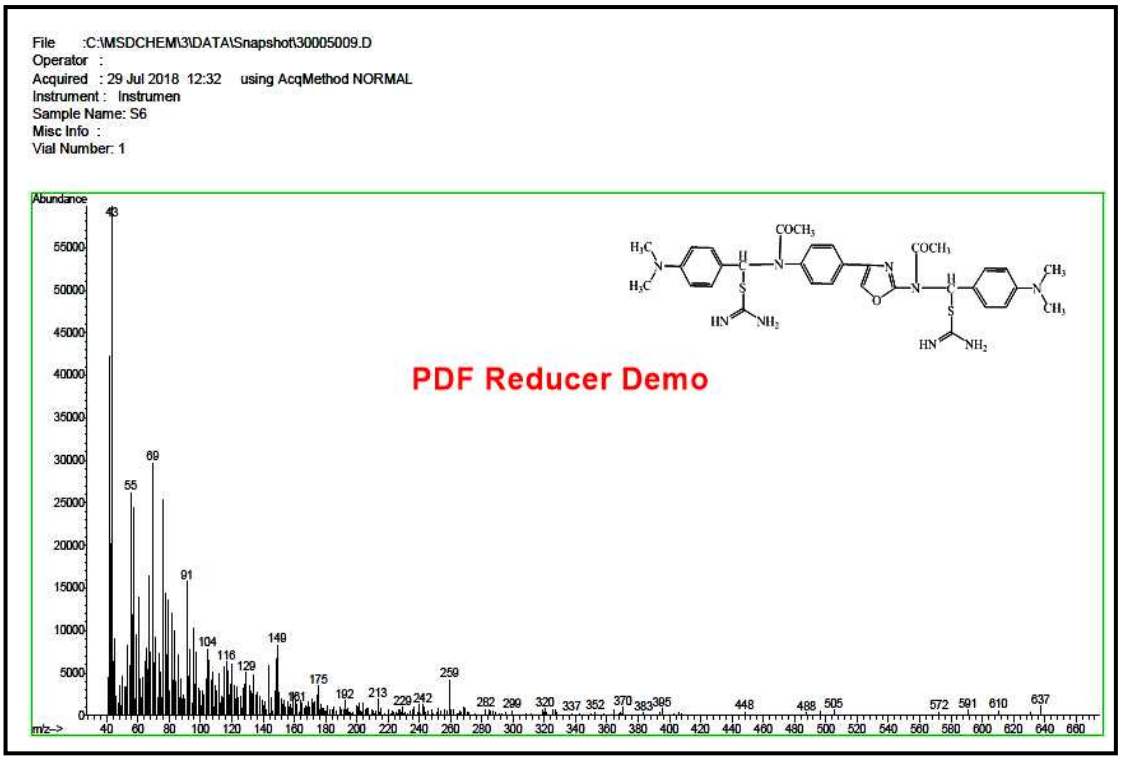


Figure (3-76)The mass spectrum of compound[XXVII]$_b$

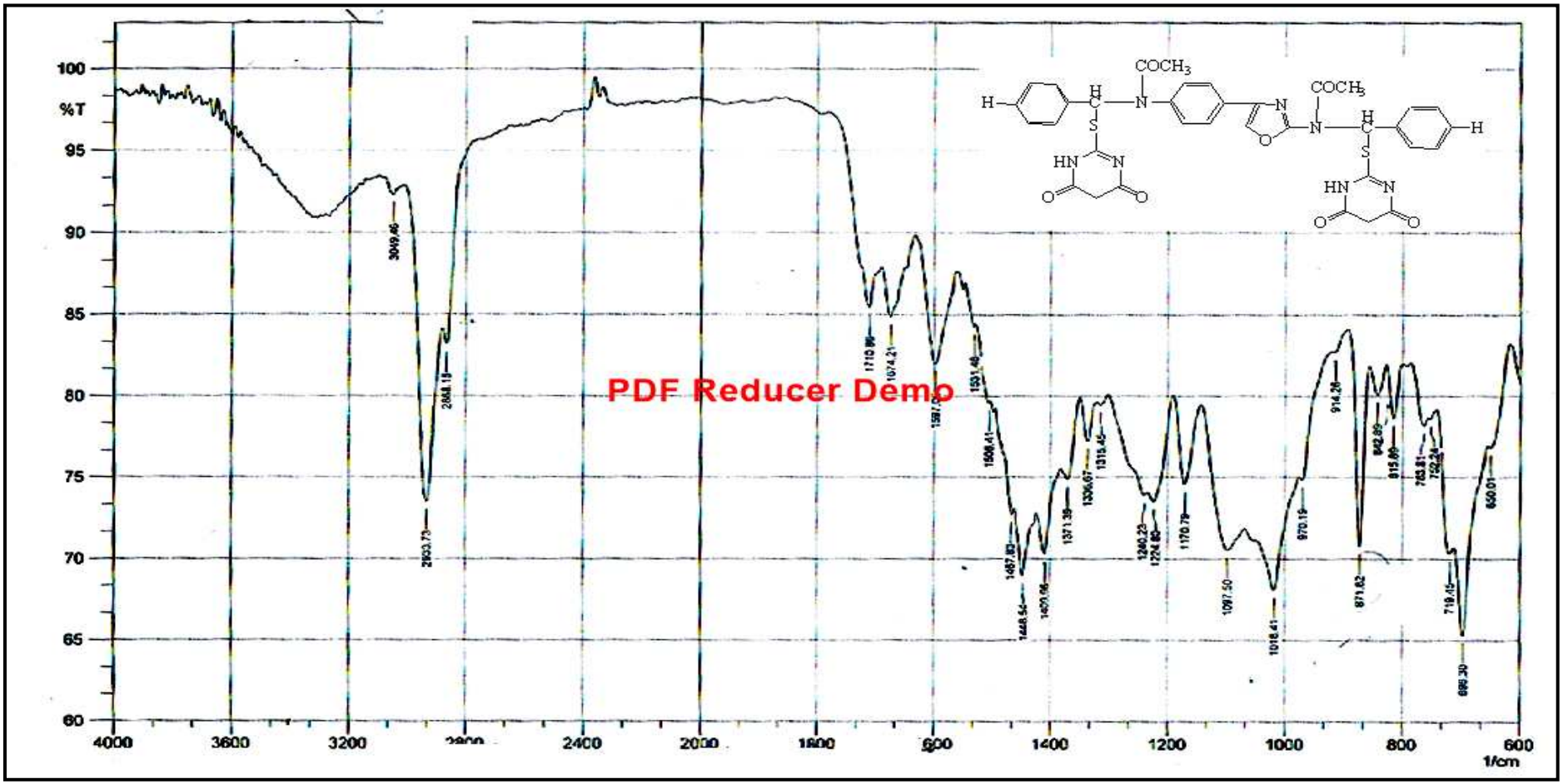
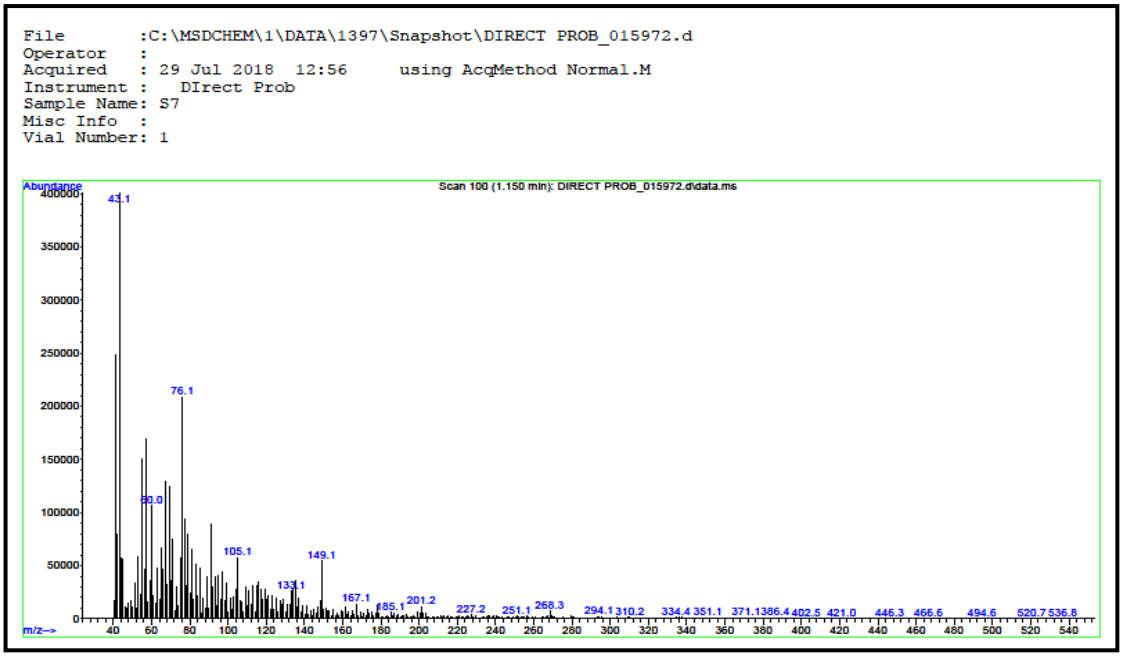


Figure (3-77) FTIR –spectrum of compound [XXVIII]$_a$



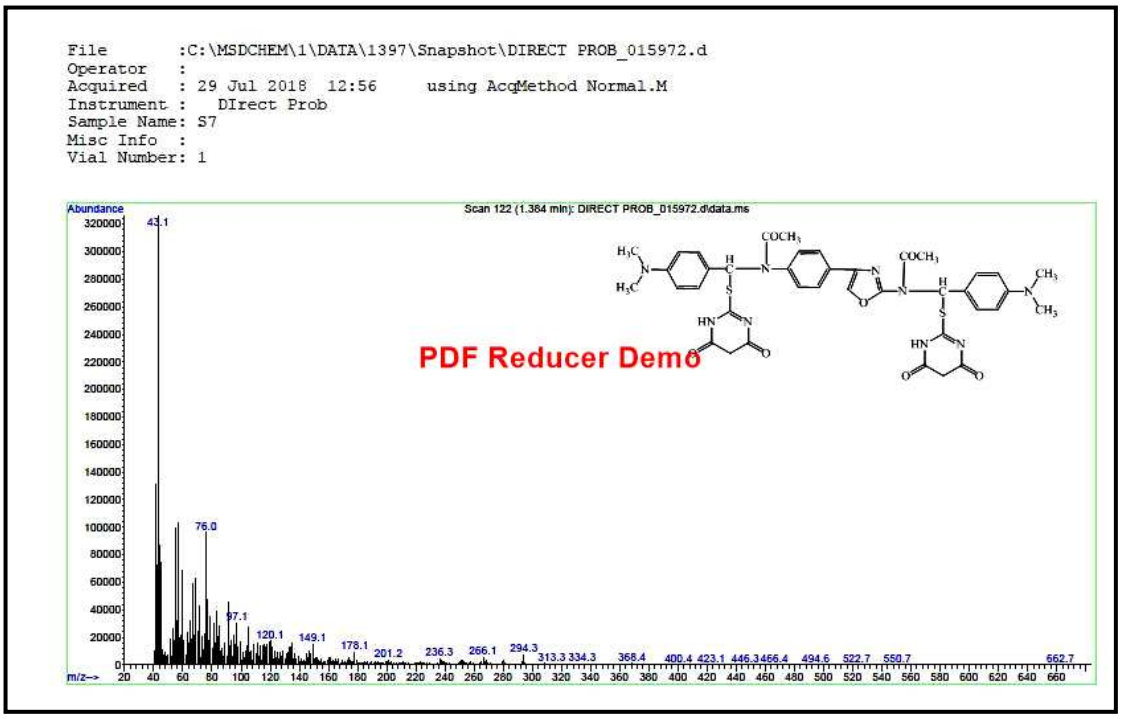
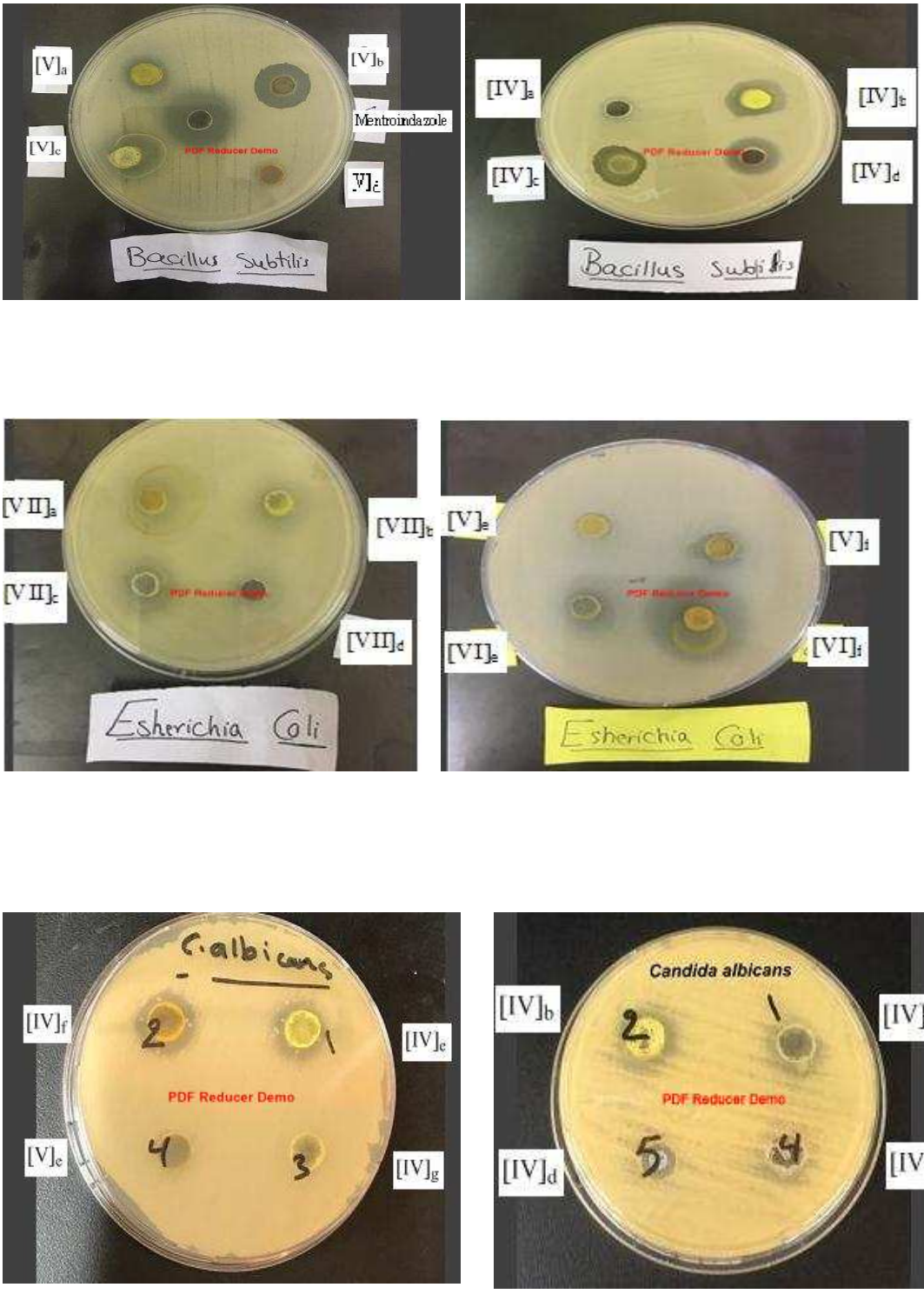
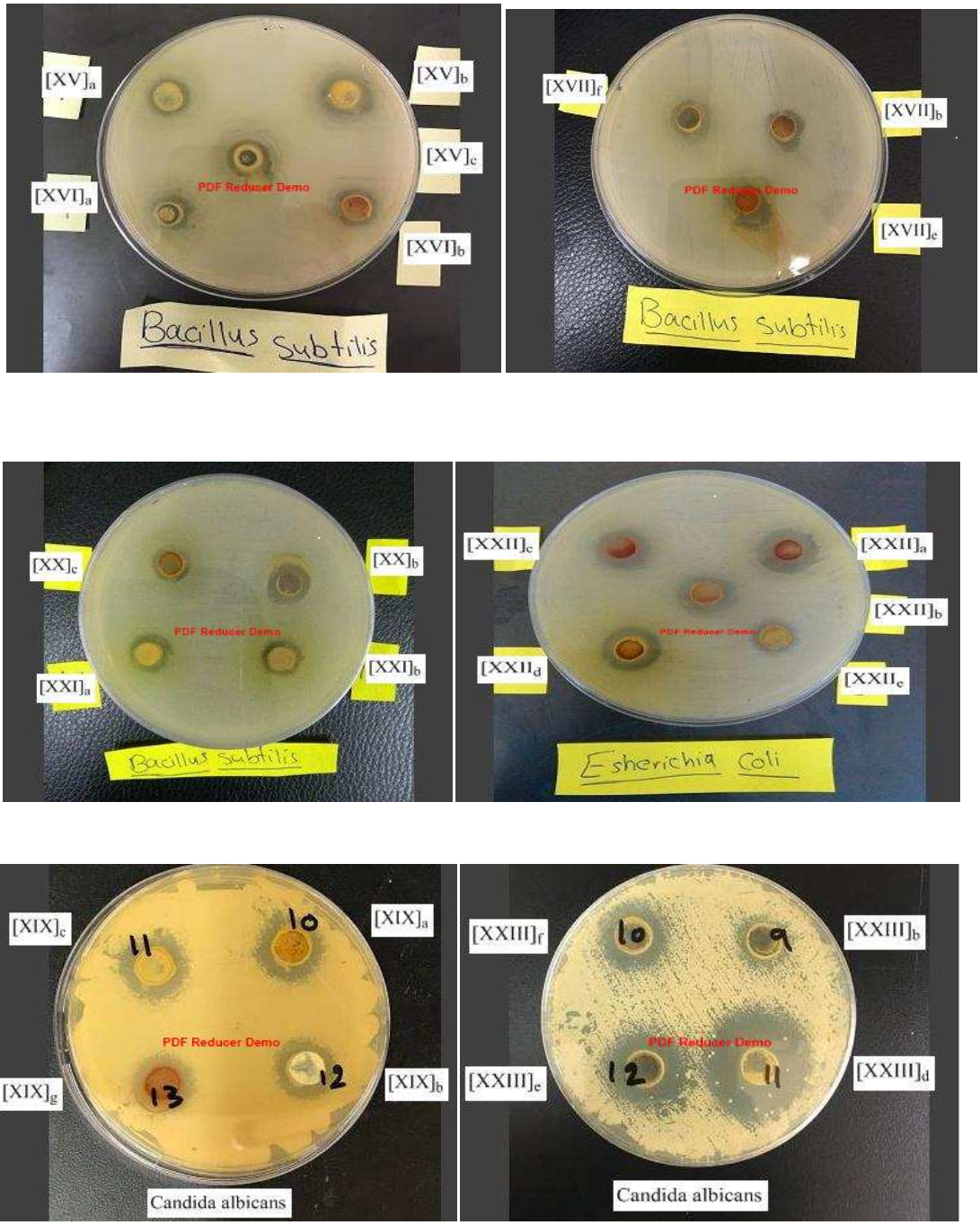


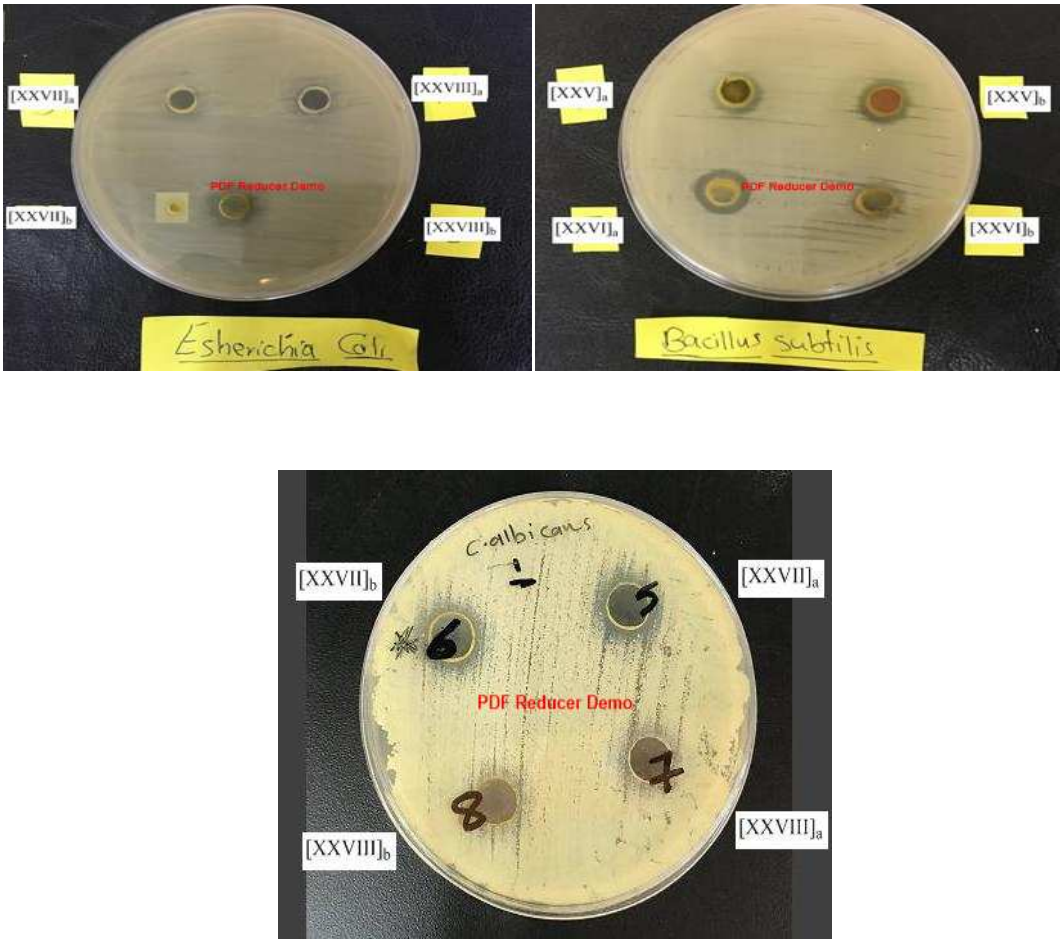
Figure (3-78)The mass spectrum of compound[XXVIII]$_b$



Figure(3-79): Antibacterial activity of compounds[IV]$_{a-g}$ -[VII]$_{a-g}$ against, *E.coli* , *Bacillius Subtilis* and antifungal *candida albicans*



Figure(3-80): Antibacterial activity of compounds[XV]$_{a-c}$,[XVI]$_{a,b}$,[XVII]$_{b,e,f}$,[XX]$_{b,c}$, [XXI]$_{a,b}$, [XXII] a$_{,b,c,d,e,}$ against, *E.coli* , *Bacillius Subtilis* and antifungal activity of compounds[XIX]$_{a,b,c,g}$,[XXIII]$_{b,d,e,f}$ against *candida albicans*



Figure(3-81): Antibacterial activity of compounds$[XXV]_{a,b}$ -$[XXVIII]_{a,b}$ against, *E.coli* , *Bacillius Subtilis* and antifungal *candida albicans*

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الخلاصة

يتضمن بحثنا تحضير وتشخيص مركبات حلقية غير متجانسة تحتوي حلقة خماسية وسداسية في نفس الجزيئة ودراسة الفعالية البيولوجية لها كما يلي:-

١-المركبات المشتقة من 6،5-ثنائي فنيل- 4،2،1 ترايازين، مخطط رقم II,I

يتضمن الخط الاول تحضير مركبات الايمدازول ،مبتدأ بالمركب 6،5 ثنائي فنيل- 4،2،1- ترايازين حيث تم تحضيره من تفاعل البنزل مع ثايوسيميكاربازايد بوجود 85% من حامض الخليك ليتم الحصول على 4،2،1- ترايازين [I] ، ومن ثم مفاعلته مع كلورو اثيل اسيتيت بوجود خلات الصوديوم المنصهرة والايثانول وذلك لتكوين مركب الاستر [II]، ومن تكاثف المركب الاخير مع الهيدرازين المائي في الايثانول ينتج حامض الهيدرازايد $[III]_{a,b}$، ومن مفاعلة حامض الهيدرازايد مع الديهايدات متنوعة في مذيب البنزين وبضع قطرات من حامض الخليك الثلجي ينتج مركبات قواعد الشف $[VI]_{a-g}$.

ومن مفاعلة المركبات الناتجة مع كلوريد الاستيل بوجود البنزين ليعطي مركبات N-acetyle $[V]_{a-g}$ ،ومن تفاعل N-acetyle مع ثايويوريا وكاربونات الصوديوم اللامائية في مذيب الاسيتون لينتج مشتقات الثايويوريا $[VI]_{a-g}$ thiourea، وبواسطة تفاعل الغلق الحلقي لمركبات thiourea $[VI]_{a-g}$ مع البنزوين في مذيب DMF نحصل علىمركبات الايمدازول $[VII]_{a-g}$ الجديدة.

من جهة اخرى يتم صهر المركب $[III]_{a,b}$ مع انهدريد حامض الفثالك او النفثالك ليتم الحصول على مركبات الايميد والفثالازين $[VIII]_{a-d}$.

يتم الحصول على الهيدرازونات $[XI]_{a,b}$ ،مبتدأ بحامض الهيدرازايد الذي يتفاعل مع اثيل اسيتو اسيتيت في الايثانول لينتج مركب البايرزول [IX]،ومن ثم يفاعل المركب الجديد مع كلوريد الاسيتل بوجود هيدروكسيد الكالسيوم في 4،1- دايوكسان ليعطي 4-اسيتل بايرزول [X]،ومن ثم يتم التصعيد عكسيا مع فنيل هيدرازين او 4،2 - ثنائي ناترو فنيل هيدرازين في الايثانول وبضع قطرات من حامض الخليك الثلجي لينتج مركبات الهيدرازون $[XI]_{a,b}$ الجديدة.

٢-المركبات الجديدة والمشتقة من الجالكون المعوض $[XII]_{a-c}$ ،مخطط رقم IV.III

يتضمن الخط الاول تكوين مركبات الهيدرازون $[XVIII]_{a-f}$،مبتدأ بالجالكون المعوض-$[XII]_{a-c}$ ،4- هيدروكسي اسيتوفينون يتم مفاعلته مع الديهايدات متنوعة بوجود وسط قاعدي(NaOH) لتكوين ثلاثة جالكونات متنوعة $[XII]_{a-c}$،ومن ثم يتم مفاعلتها مع اثيل اسيتو اسيتت بوسط قاعدي لينتج مركبات السايكلوهيكسينون $[XIII]_{a-c}$، ومن ثم يتم تصعيد الناتج مع اثيل كلورو اسيتيت بوجود خلات الصوديوم في الايثانول المطلق لتكوين مركبات الاستر $[XIV]_{a-c}$، من تكاثف الاستر الناتج مع الهيدرازين في الايثانول كمذيب لينتج مركبات الاندازول الجديدة $[XV]_{a-c}$ ، ومن ثم تصعيد الاندازول الناتج مع اثيل اسيتو اسيتيت لتكوين مركبات البيرازول$[XVI]_{a-c}$.يحول الناتج الى4-اسيتل بايرزول من مفاعلة البايرزول $[XVI]_{a-c}$ مع كلوريد الاسيتل في البنزين الجاف ومن ثم يتم التصعيد العكسي مع فنيل هيدرازين او4,2 - ثنائي ناترو فنيل هيدرازين بوجود الايثانول وبضع قطرات من حامض الخليك الثلجي لينتج مركبات الهيدرازون $[XVIII]_{a-f}$.

من جهة اخرى تم تحضير مركبات قواعد الشف نوع $[XIX]_{a-i}$ من مفاعلة مشتق الانداوزل $[XV]_{a-c}$ مع الديهايدات متنوعة في الايثانول وبضع قطرات من حامض الخليك الثلجي.

بينما تم تحضير مركبات الايزوكزازول $[XX]_{a-c}$ من التصعيد العكسي لمركبات السايكلوهكسينون $[XII]_{a-c}$ مع هيدروكسيل امين هيدروكلورايد بوجود هيدروكسيد الصوديوم في الايثانول كمذيب لتكوين مركبات الايزوكزازول $[XX]_{a-c}$ ، ومن ثم مفاعلة الناتج مع كلوريد الحامض مع ثلاثي اثيل امين بوجود مزيج من (DMF , THF) بدرجة (0-4) درجة مئوية لتكوين مركبات الاستر نوع $[XXI]_{a-f}$.

في حين يتم تحضير مركبات الكوينولين-2-اون $[XXII]_{a-f}$ من تصعيد الكيومارين مع مركبات الاندازول$[XV]_{a-c}$ في حامض الخليك الثلجي.

من جهة اخرى تم تحضير مركبات الايميد نوع $[XXIII]_{a-f}$ من صهر مركبات الاندازول$[XV]_{a-c}$ مع انهدريد حامض الفثالك او النفثالك لينتج مركبات الايميد $[XXIII]_{a-f}$.

٣- المركبات المشتقة من 4-(4-امينو فنيل) - اوكسازول -2- امين). مخطط رقم V

تم تحضير مركبات البريميدين باستخدام 4-(4-امينو فنيل)- اوكسازول -2- امين)

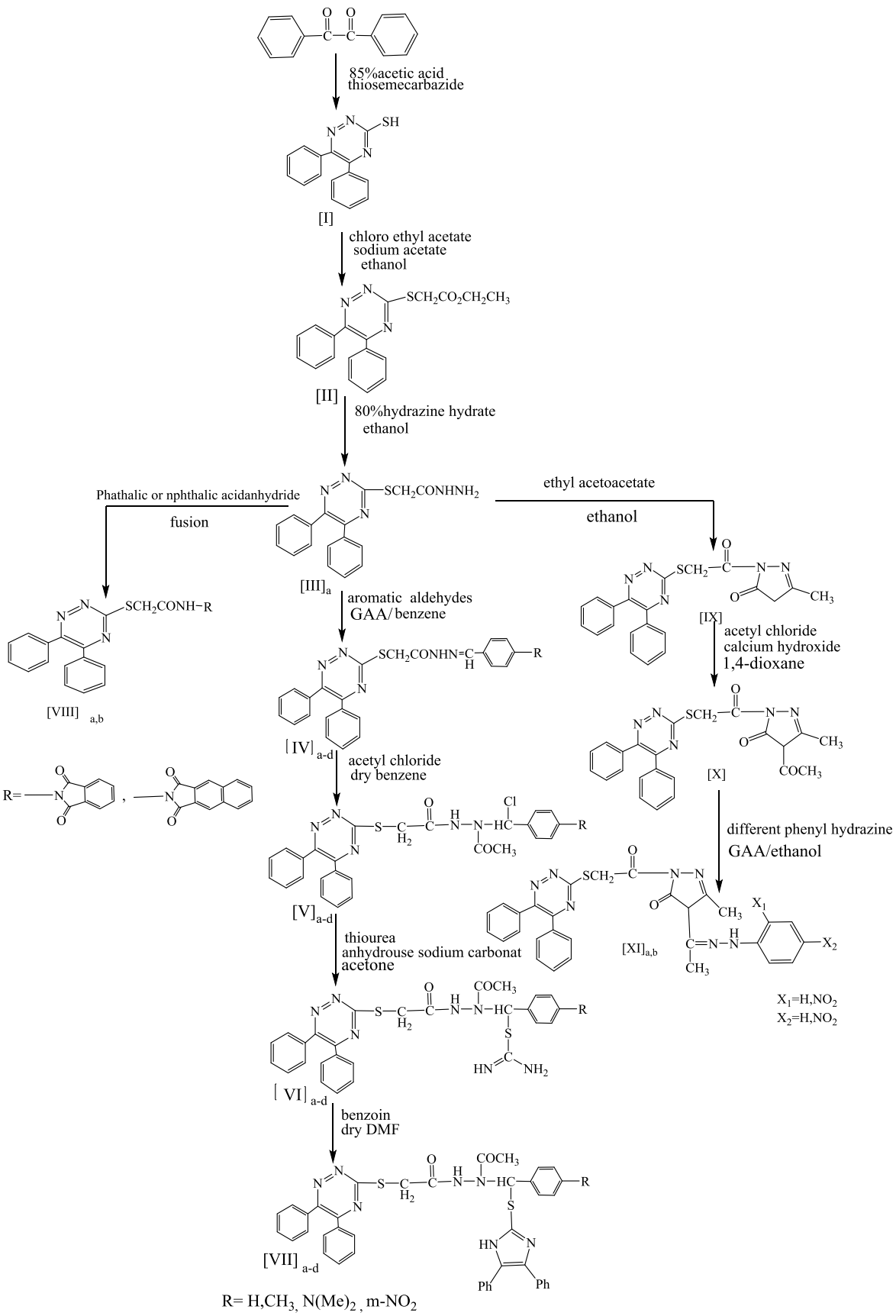
وذلك من صهر 4-امينو اسيتوفينون مع اليوريا بوجود اليود ليتم الحصول على4-(4-امينو فنيل) - اوكسازول -2- امين) [XXIV]،ومن مفاعلة المركب الاخيرة مع البنزالديهايد او4- ثنائي مثيل بنزالديهايد في البنزين الجاف وبضع قطرات من حامض الخليك الثلجي حصلنا على مركبات الشف الجديدة نوع $[XXV]_{a,b}$

كذلك من مفاعلة الناتج الاخير مع كلوريد الاستيل بوجود البنزين ليعطي مركبات N- acetyle[XXVI] $_{a,b}$ ،ومن تفاعل N-acetyleمع الثايويوريا وكاربونات الصوديوم اللامائية في مذيب الاسيتون ينتج مشتقات اليوريا نوع $_{a,b}$ [XXVII]، ان تفاعل الغلق الحلقي لمركبات الثايويوريا مع ثنائي ايثل مالونيت في البنزين يعطي مركبات البريميدين $_{a,b}$ [XXVIII].

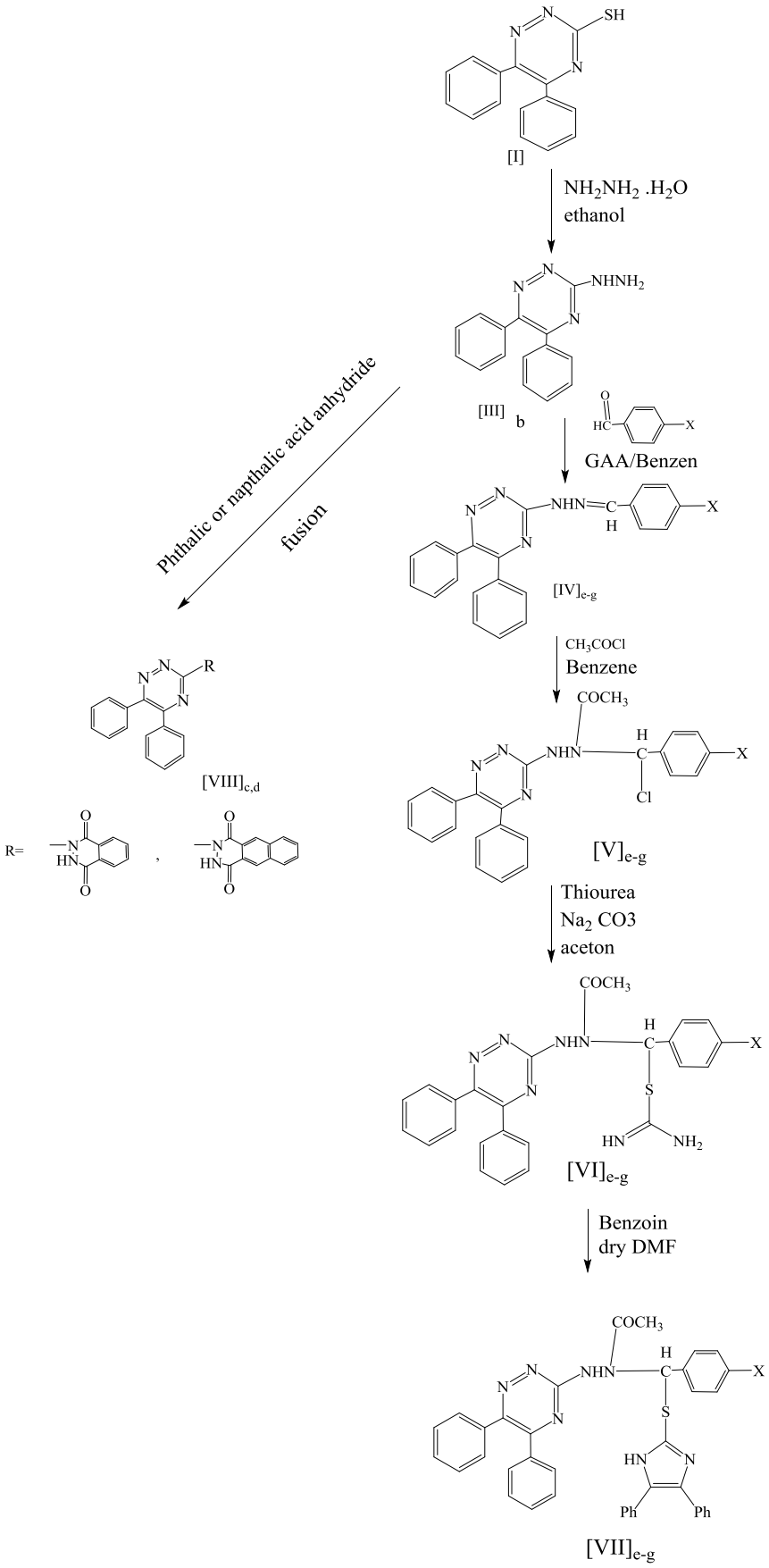
شخصت جميع المركبات المحضرة اعلاه بواسطة اطياف الاشعة تحت الحمراء وطيف الرنين النووي المغناطيسي ^{1}HNMR وطيف الكتلة (للبعض منها) .

درست الفعالية البيولوجية للمركبات المحضرة باستخدام نوعين من البكتريا (+gram) *Bacillus subtitis* و (-gram) *E.coli* ونوع واحد من الفطريات *candida albicans*.

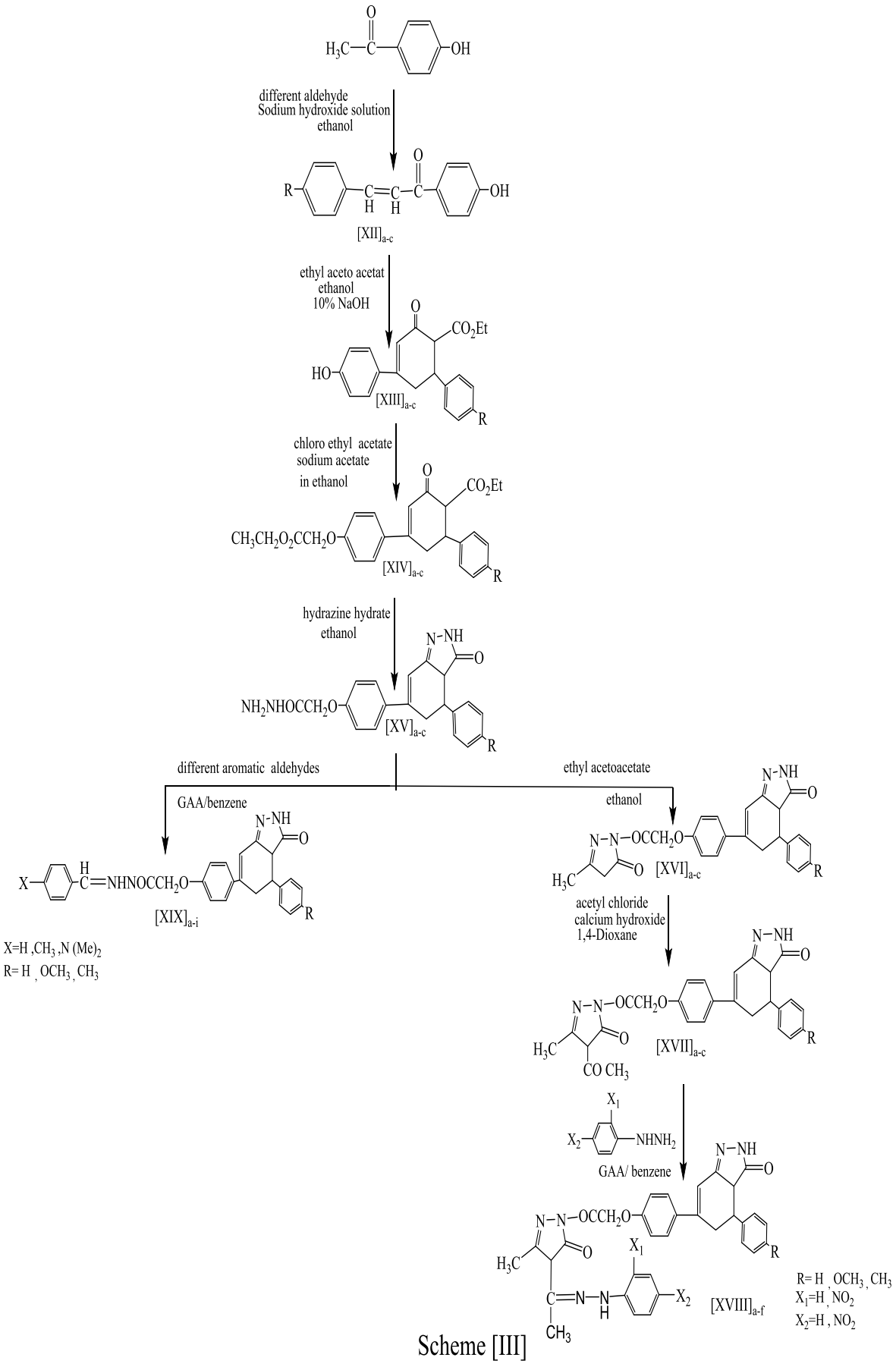
بعض المركبات اعطت فعالية جيدة والبعض الاخر لم يعطي اي فعالية بيولوجية تجاه البكتريا والفطريات.


85%acetic acid
thiosemecarbazide
[I]
chloro ethyl acetate
sodium acetate
ethanol
[II]
80%hydrazine hydrate
ethanol
Phathalic or nphthalic acidanhydride
fusion
ethyl acetoacetate
ethanol
[III]a
aromatic aldehydes
GAA/ benzene
[VIII] a,b
[IV] a-d
[IX]
acetyl chloride
calcium hydroxide
1,4-dioxane
[X]
acetyl chloride
dry benzene
different phenyl hydrazine
GAA/ethanol
[V]a-d
[XI]a,b
thiourea
anhydrouse sodium carbonat
acetone
[VI] a-d
benzoin
dry DMF
[VII] a-d
R= H,CH3, N(Me)2 , m-NO2
X1=H,NO2
X2=H,NO2

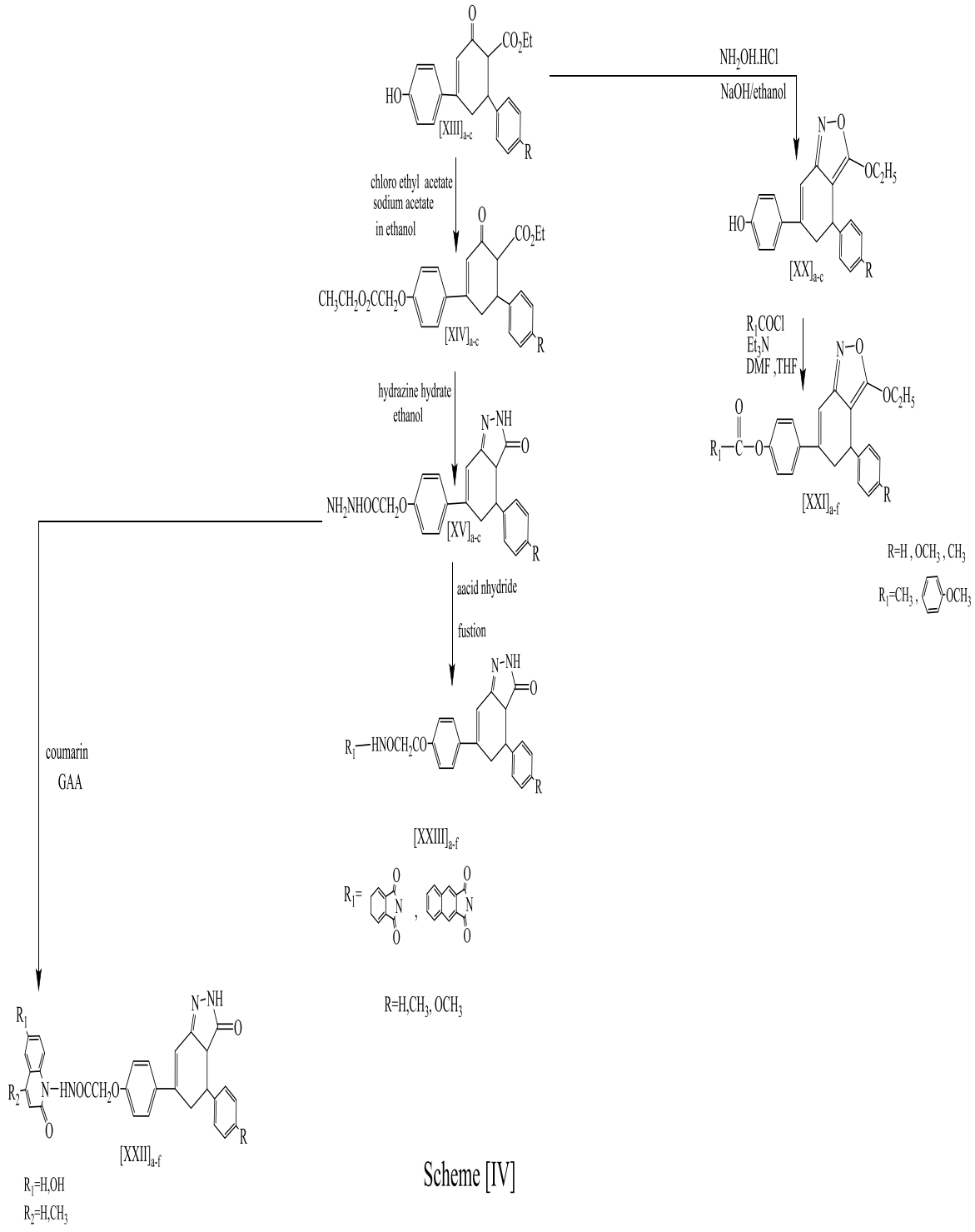
Scheme 1


[I]
NH2NH2 .H2O
ethanol
[III]
b
GAA/Benzen
Phthalic or napthalic acid anhydride
fusion
[IV]e-g
CH3COCl
Benzene
[V]e-g
[VIII]c,d
R=
Thiourea
Na2 CO3
aceton
[VI]e-g
Benzoin
dry DMF
[VII]e-g
X=H, CH3, N(Me) 2

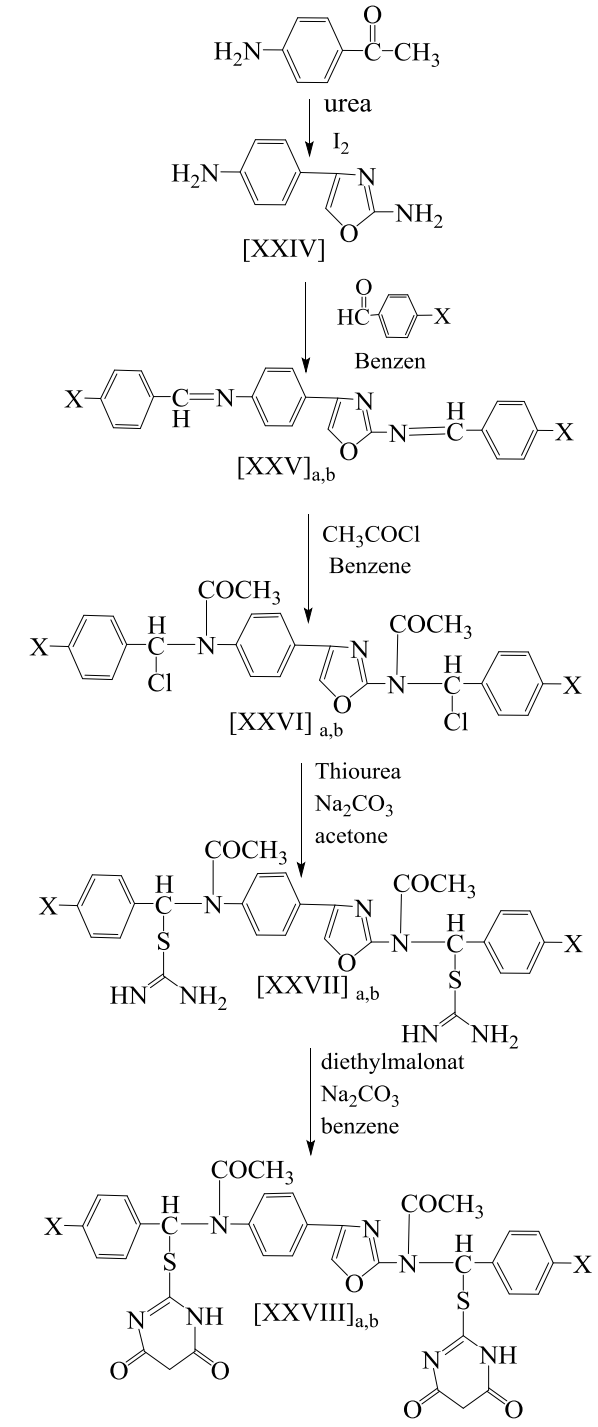
Scheme II


different aldehyde
Sodium hydroxide solution
ethanol
[XII]a-c
ethyl aceto acetat
ethanol
10% NaOH
[XIII]a-c
chloro ethyl acetate
sodium acetate
in ethanol
[XIV]a-c
hydrazine hydrate
ethanol
[XV]a-c
different aromatic aldehydes
GAA/benzene
[XIX]a-i
X=H ,CH3 ,N (Me)2
R= H , OCH3 , CH3
ethyl acetoacetate
ethanol
[XVI]a-c
acetyl chloride
calcium hydroxide
1,4-Dioxane
[XVII]a-c
GAA/ benzene
[XVIII]a-f
R= H , OCH3 , CH3
X1=H , NO2
X2=H , NO2

Scheme [III]


NH2OH.HCl
NaOH/ethanol
chloro ethyl acetate
sodium acetate
in ethanol
hydrazine hydrate
ethanol
aacid nhydride
fustion
coumarin
GAA
R1COCl
Et3N
DMF ,THF
[XIII]a-c
[XIV]a-c
[XV]a-c
[XX]a-c
[XXI]a-f
[XXII]a-f
[XXIII]a-f
R=H , OCH3 , CH3
R1=CH3 ,
OCH3
R=H,CH3, OCH3
R1=H,OH
R2=H,CH3

Scheme [IV]



X= H , $N(Me)_2$

Scheme [V]

جمهورية العراق
وزارة التعليم العالي والبحث العلمي
جامعة بغداد
كلية التربية للعلوم الصرفة/ إبن الهيثم
قسم الكيمياء

مركبات حلقية غير متجانسة جديدة تحتوي على حلقات خماسية وسداسية في نفس الجزيئة :تحضيرها وفحص فعاليتها البايولوجية

رسالة مقدمة إلى

مجلس كلية التربية للعلوم الصرفة - إبن الهيثم/ جامعة بغداد كجزء من متطلبات نيل درجة فلسفة دكتوراه في الكيمياء

من قبل

سحر فاضل عباس

بكلوريوس علوم في الكيمياء-٢٠٠٥

ماجستير علوم في الكيمياء-٢٠١٤

باشراف

أ.د. جمبد هرمز توما

١٤٤٠ هـ **٢٠١٨ م**