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University of Karbala, College of Science
Department of Chemistry

Microwave Synthesis and Study of the Biological Activity for some New Imidazolidine Derivatives of Benzothiazole

A Thesis

Submitted to the Council of the College of Science, University of Karbala as a partial fulfillment of the requirements for M.Sc. degree in Chemistry

By

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1439 A.H *2017 A.D*

(يرفعِ اللهُ الَّذين آمنوا منكم والَّذين أوتوا العِلمَ درجاتٍ)

صَدَقَ اللهُ العَلِيُّ العَظِيم

(٥٨ المجادلة آية ١١)

Dedication

I dedicate this humble work to my father, who gave me everything

And to my mother, who gave me affection and love

I say to them: You and you gave me life and hope and the emergence of a passion for knowledge

My deary wife, my brothers and my family

And to every person taught me characters in my life of professors or parents

Acknowledgment

*Initially, I am most grateful to **Allah**, who gave me the strength and guidance throughout my life especially during this work.*

*I wish to express my deepest gratitude and sincere appreciation to my supervisor **Prof. Dr. Zeid Hassan Abood Al-a`arajy** for his immense guidance, kind support and Constant encouragement throughout the progress of the dissertation work, also I wish him a long life with best health.*

*I am deeply grateful to the Dean of the college of Science, University of Kerbala, **prof. Dr. Nawras aldahan** and also my gratitude to all the deanship staff in the College of Science.*

*I am grateful to **Asst. Prof. Dr. Baker Abid AL-Zahra Joda** the Head of Chemistry Department, for providing the facilities which helped in accomplishing my research and also great and special words of thanks are due to all the staff of Chemistry Department, College of Science, University of Karbala.*

My sincerest appreciation goes to my beloved family: dear parents, my brothers and my sisters for their endless love, patience, and the fortitude to stay by my side during these years.

Special thanks are also due to my colleagues and my close friends who kept on supporting me during all the hard times in my work and for their help and kindness.

Finally, I would like to express my thanks to all individuals who helped me in one way or another in the fulfillment of this work.

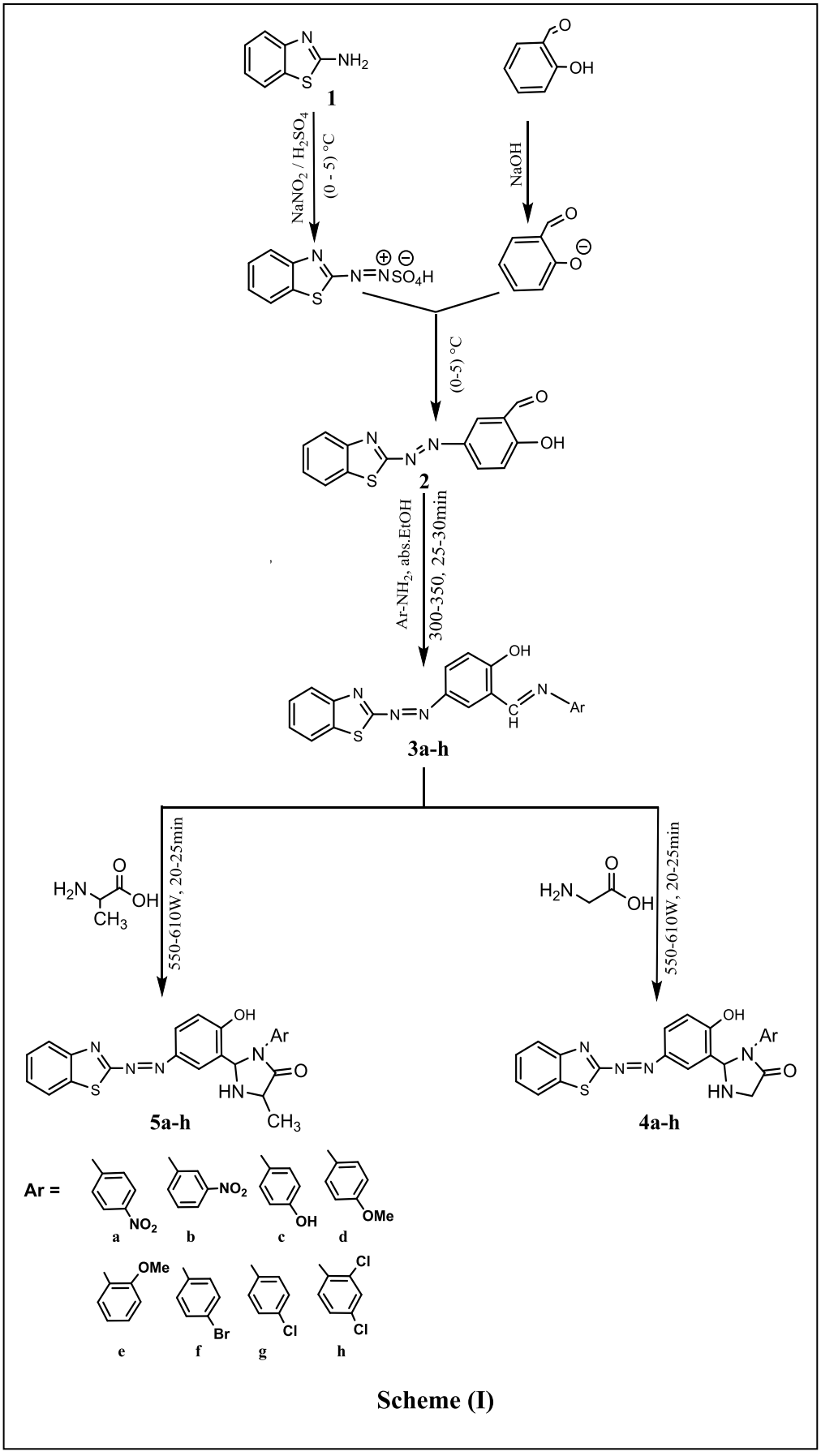
Hussein Ali Qabel alwaaly

Abstract

2-Aminobenzothiazole **1** was converted to the corresponding diazonium salt which was introduced in coupling reaction with alkaline solution of 2-hydroxybenzaldehyde as coupling reagent to give azo-benzothiazole derivative **2** bearing aldehyde group. The resulting aldehyde **2** was introduced in condensation reactions with the primary aromatic amines including (4-nitroaniline, 3-nitroaniline, 4-hydroxyaniline, 4-methoxyaniline, 2-methoxyaniline, 4-bromoaniline, 4-chloroaniline and 2,4-dichloroaniline) using microwave irradiation technique in absolute ethanol to produce eight imine derivatives of benzothiazole **3a**-**h**, respectively. The resulting imines **3a-h** were treated with both glycine and L-alanine using microwave irradiation in tetrahydrofuran afforded sixteen new imidazolidines **4a-h** and **5a-h** substituted with benzothiazole moiety, respectively, Scheme (I).

The chemical structures of the target compounds synthesized were deduced from (CHNS) elemental analysis and FT-IR, ^{1}H NMR spectral measurements. Preliminary *in vitro* antibacterial activity of the target compounds were investigated using two types of bacteria, *Staphylococcus aureus* (Gram-positive) and *Escherichia coli* (Gram-negative). The results indicated that the newly synthesized imidazolidines (compounds **4a**, **4b**, **4c**, **4d**, **4e**, **4g**, **4h**, **5c**, **5d**, **5f**, **5g**, and **5h**) exhibited greater activities than gentamycin against Gram-positive bacteria. On the other hand, compounds **4d**, **4h**, **5c**, and **5f** also showed better activities against Gram-negative bacteria when compared with that of the control drug (Gentamycin), Figures (3-43)-(3-47).

Abstract



Scheme (I)

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Abbreviations

Symbol	Definition
^{1}H NMR	Proton Nuclear Magnetic Resonance
FTIR	Fourier transform infrared spectroscopy
Abs.	Absolute
AcOH	Acetic acid
aq	aqua
br	Broad
Cat.	Catalyst
d	Doublet
MAOS	Microwave-assisted organic synthesis
TBAB	Tetrabutyl amounium bromide
Ref.	References
Com.	compound
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
No.	number
eq	equals
Et_2O	Diethyl ether
NMDA	N-methyl-D-aspartate
EtOAc	Ethyl acetate
P.T	Proton transition
EtOH	Ethanol
DCM	Data-constrained modelling
h.	Hour
m	Multiplet
M/ Z	Mass/charge
MeOH	Methanol
Min.	Minute
MW	Microwave
BAMMD	3-bis((2-aminopropyl)amino)methyl)-5-methylimidazolidine-2,4-dione
ppm	part per million
M.P.	Milting point
MHz	megahertz
r.t.	Room temperature
Rec.	Recrystallization
ref	Reflux

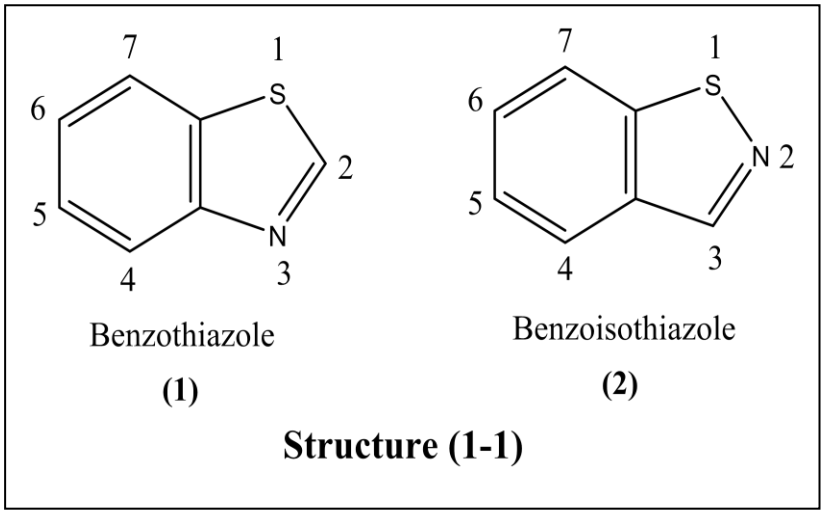
R_f	Retention factor
s	Singlet
Str.vib.(υ)	Stretching vibration
q	quartet
TBAB	Tetrabutylammonium bromide
BHI	Brain heart infusion
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
W	Watt
δ	Bending in IR and chemical shift in NMR

Chapter One

Introduction

1.1. Benzothiazoles

Benzothiazoles heterocyclic systems fused with benzene rings are now popular scaffolding for inclusion in drug design[1]. The most imperative is a bicyclic system where the benzene ring is fused to the 4,5 position of thiazole ring[1], Structure (1-1).



Structure (1-1)

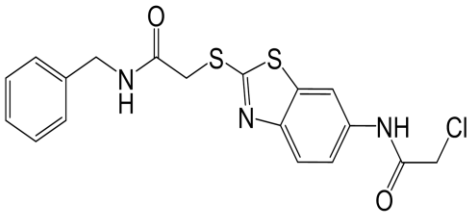
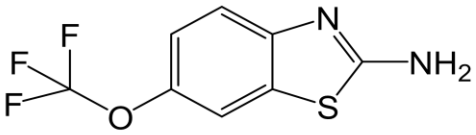
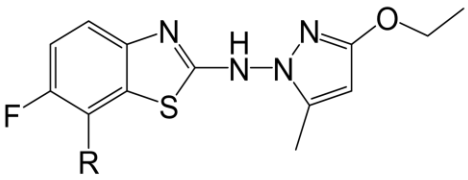
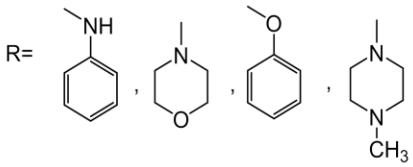
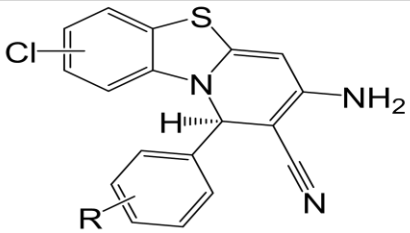
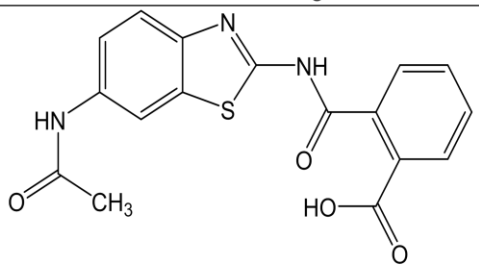
Benzothiazoles are the important pharmacophore and privileged sub-structures in medicinal chemistry owing to their involvement as a key component for various biological activities[2] such as antifungal[3] and antibacterial agents[4]. Benzothiazole nucleus containing molecules are also reported as antidiabetic[5], antitumor activity[6] and anti-inflammation[7].

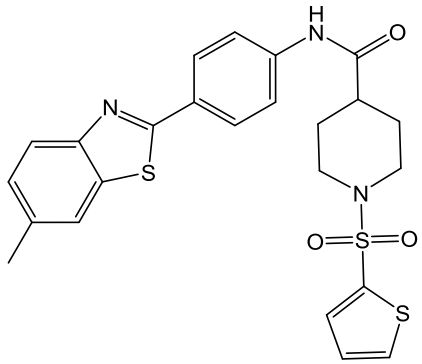
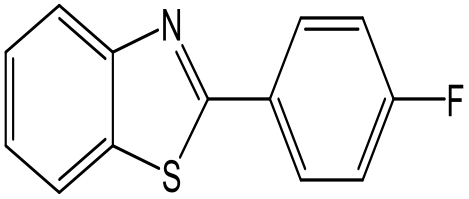
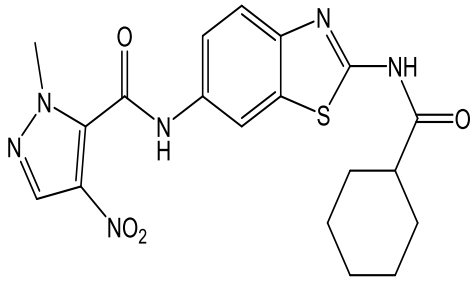
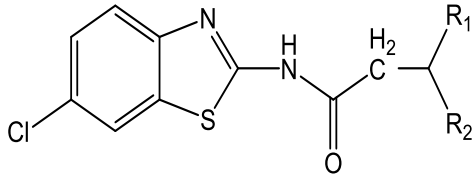
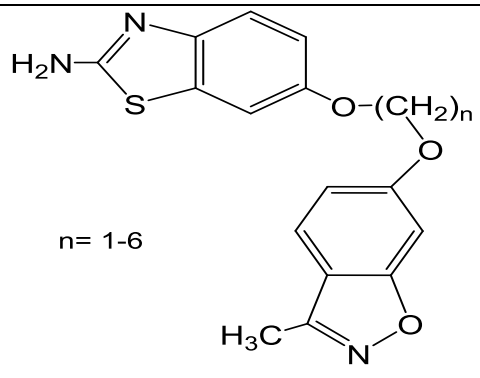
1.1.1. The biological activity of Benzothiazoles

Benzothiazoles compounds are further studied heterocyclic due to their wide spectrum of bioactivities. Among them, the benzothiazole derivatives are pharmacologically important because of their immunostimulant, anti-inflammatory, antifungal, antimicrobial, antitumor, and other activities[8]. Benzothiazole ring is a requirement for high schistosomicidal activity[9]. Benzothiazole derivatives of biological interest were synthesized and showed antimicrobial, anti-proliferative[10], antileishmanial[11], anticancer[12]

anthelmintic[13] and antiviral activities[14]. Table (1-1) shows biological activities for some benzothiazole derivatives.

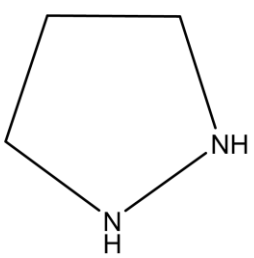
Table (1-1): The biological activities for some benzothiazole derivatives

Com. no.	Structure	Biological activity	Ref.
(3)		Antitumor activity.	15
(4)	 Riluzole	Anticonvulsant,anxiolytic effects and neuroprotective.	16
(5)	 	The synthesized compounds give anti-bacterial activities against *B.subtilis*, *S.aureus*and *E.coli* and for anti-fungal activities against *Candida albicans.*	17
(6)	 R= -Cl, 3,4,5-OCH_3	Anti-inflammatory activity.	18
(7)		Anti- inflammatory activity.	19

Com. no.	Structure	Biological activity	Refe.
(8)		Anti-inflammatory drugs, Fatty acid amide hydrolase (FAAH) inhibitor.	20
(9)		Anti-Alzheimer's activity.	21
(10)		Antitumor activity against anLLC xenograft model.	22
(11)		Antidiabetic activity.	23
(12)	 n= 1-6	Anti-bacterial activity and anti-fungal activity.	24

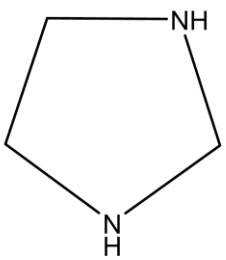
1.2. Imidazolidines

Imidazolidines (saturated imidazoles), also known as tetrahydroimidazoles are biologically active nitrogen containing heterocyclic moiety which have been reported to show wide array of significant bioactivities[25], Imidazolidine-2,4-diones (or hydantoins) are well known compounds since their discovery over a century ago. Hydantoins have found therapeutic applications in drugs such as the well established phenytoin[26], The derivatives of imidazolidine have an important role in medicinal chemistry owing to their wide application as drugs and drug-intermediates[27], Imidazolidines and their derivatives have shown anticonvulsive and antiarrhythmic pharmacological activities[28], Imidazolidine derivatives, or hydantoins, are synthetic compounds with different therapeutic applications. Many imidazolidine derivatives have psychopharmacological properties, such as phenytoin, famous for its anticonvulsant efficacy, but also effective in the treatment of neuropathic pain[29], Imidazolidine derivatives are found in many area of medicinal chemistry (serotonin and fibrinogen receptor antagonists, inhibitors of the glycine binding site of the NMDA receptor, antagonists of leukocyte cell adhesion, acting as allosteric inhibitors of the protein–protein interaction[30]. There are two structural isomers (1,2) and (1,3) imidazolidine, Structure (1-2).



(13)

1,2-pyrazolidine



(14)

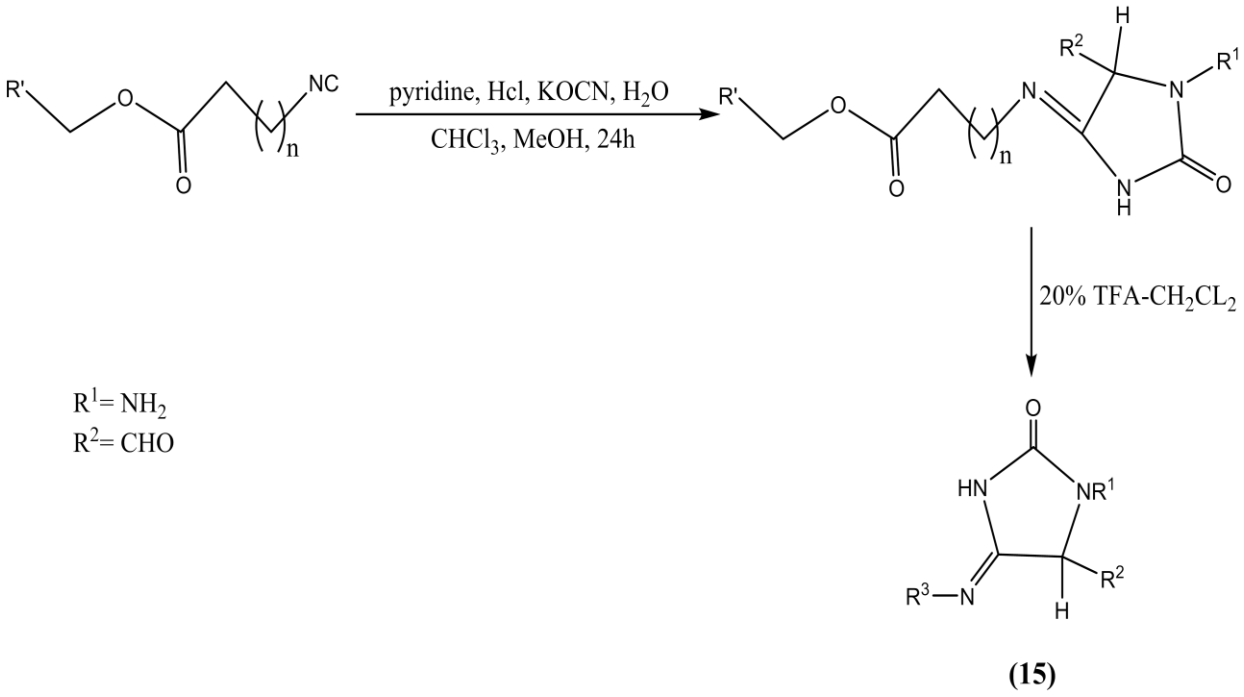
1,3-imidazolidine

Structure (1-2)

1.2.1 Synthesis of imidazolidines

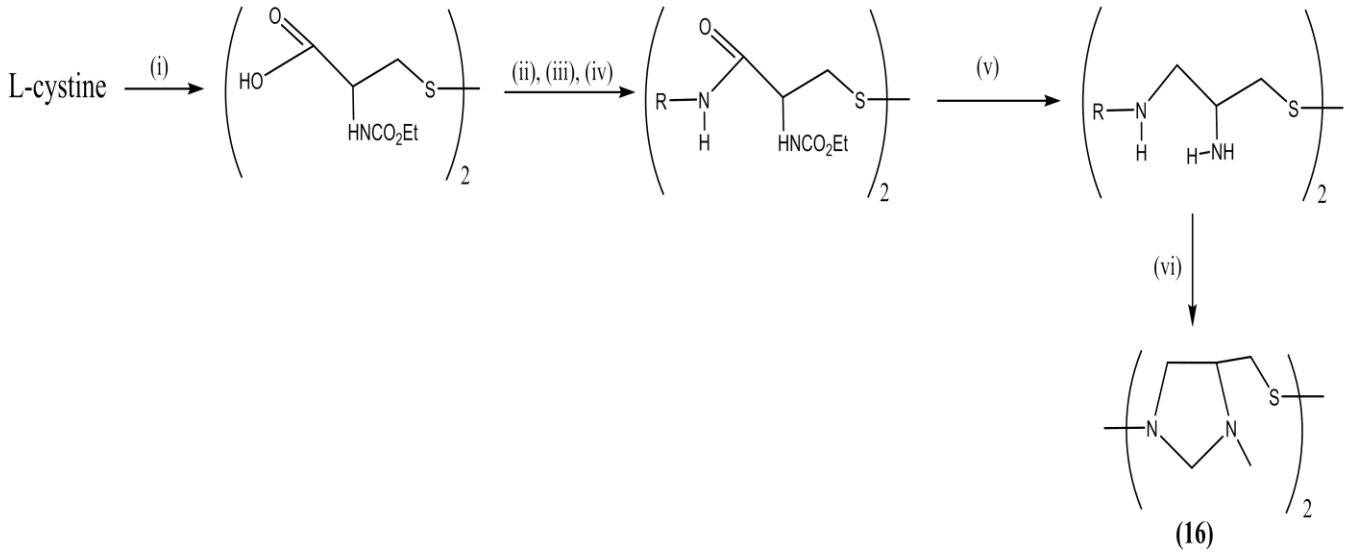
A considerable number of methods towards the formation of imidazolidine ring have been reported in recent years.

Short[31] et al. Synthesis of hydantoin 4-imides **(15)** , by immobilization of the isocyanide componen the desired product is then released from the support upon treatment with 20% trifluoroacetic acid-CH_2Cl_2, Scheme (1-1)



Scheme (1-1)

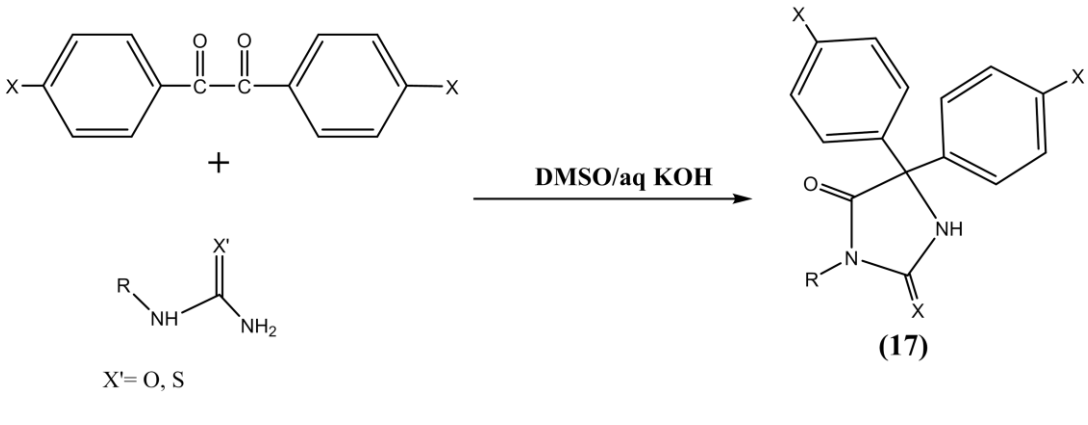
Several chiral imidazolidine disulfides **(16)** derived from L-cysteine have been synthesized[32], Scheme (1-2).



(i) 1 M aq. NaOH, ethyl chloroformate; (ii) N-methylmorpholine, $CHCl_3$; (iii) ethyl chloroformate; (iv) RNH_2 (a:R=(R)-methylbenzyl; b:R=(S)methylbenzyl; c:R=phenethyl; d:R=*n*-butyl); (v) $LiAlH_4$, reflux in THF; (vi) $(CH_2O)n$, reflux in benzene.

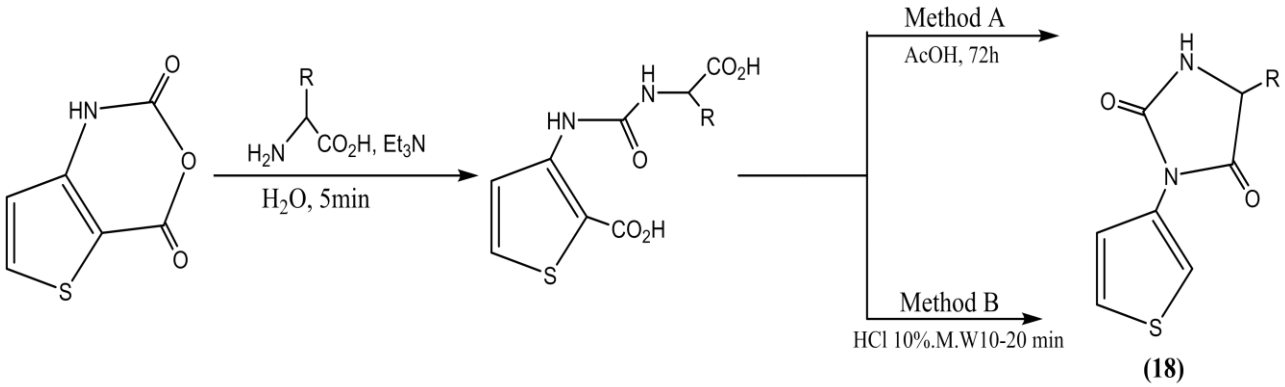
Scheme (1-2)

Muccioli[33] et al. Synthesized 5,5′-Diphenylimidazolidine-2,4-dione) and 5,5′-Diphenyl-2-thioxoimidazolidin-4-one derivatives **(17)**, using the microwave, Equation (1-1).



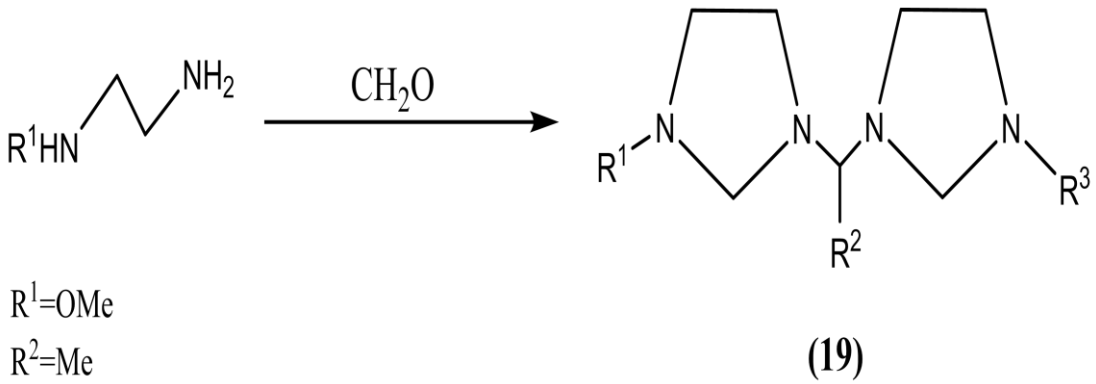
Equation (1-1)

Brouillette[26] et al. prepared series of twenty optically pure 3-(thien-3-yl)imidazolidine-2,4-dione **(18)** derivatives have been synthesized in 41–89% yield with all natural amino acids in a quick one-pot microwave-assisted, Scheme (1-3).



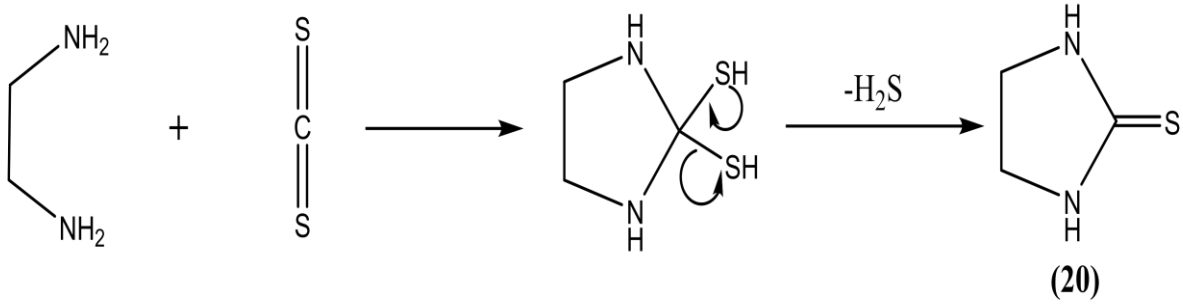
Scheme (1-3)

Caterina[34] et al. synthesized the (bis(3-arylimidazolidinyl-1) methanes) **(19)** by a condensation reaction between N-arylethylenediamines with an excess of formaldehyde, Equation (1-2).



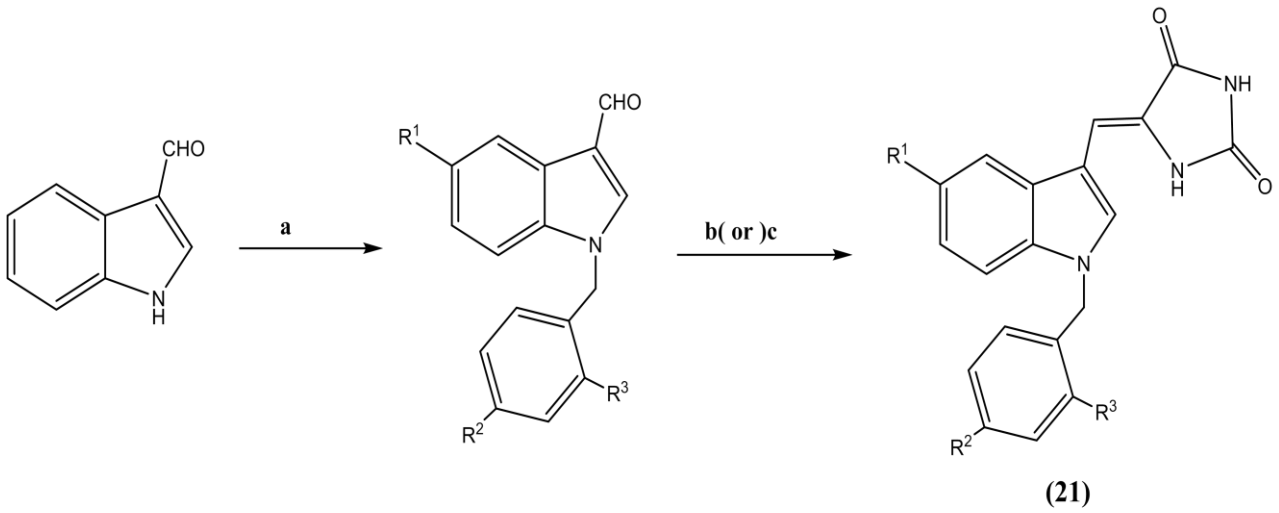
Equation (1-2)

Entezari[27] et al. synthesied imidazolidine-2-thione **(20)** as a in the presence of ultrasound (sono-synthesis) and in the absence of ultrasound (conventional method). Instead of reflux in the conventional method, Scheme (1-4).



Scheme (1-4)

Reddy[35] et al. Synthesized (Z)-5-(N-benzylindol-3-ylmethylene)imidazolidine-2,4-diones **(21)** under microwave irradiation and conventional heating methods. Scheme (1-5).

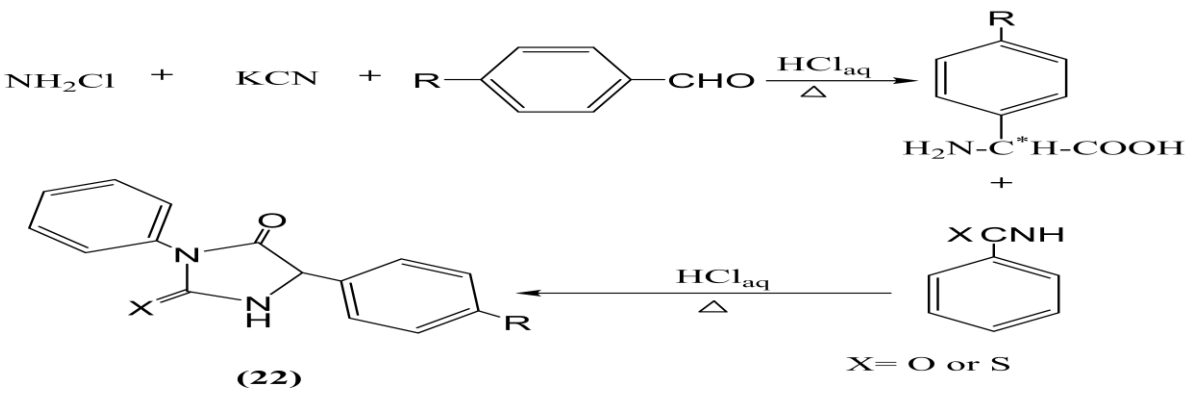


(21)

(a) appropriate benzyl halide, aqueous NaOH solution, triethylbenzylammonium chloride, DCM, rt; (b) Method-A: hydantoin, ammonium acetate in acetic acid, microwave irradiation, 40–60 s, 80–85% yield; (c) Method-B: hydantoin, ammonium acetate in acetic acid, 115–116 C, 8–12 h, 74–85% yield.

Scheme (1-5)

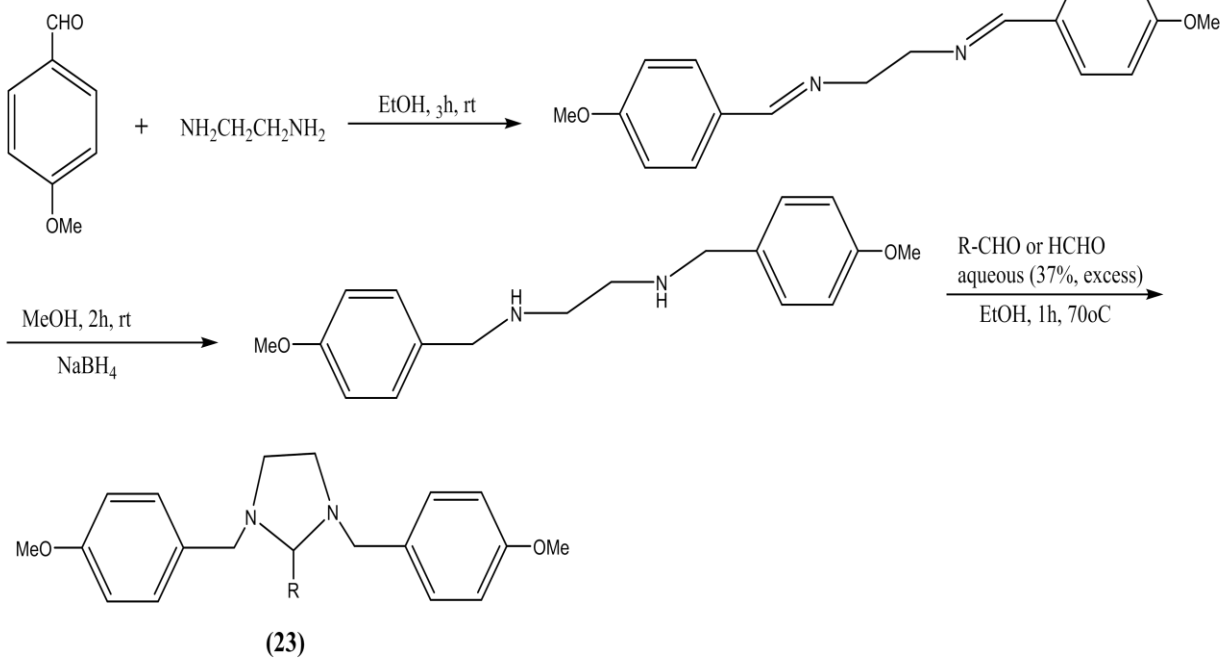
Luis[36] et al. synthesized 2,4-dione and 2-thioxo-4-one imidazolidinic derivatives **(22)** by reaction of amino acids with C-phenylglycine, phenyl isocyanate and phenyl isothiocyanate, Scheme (1-6).



(22)

Scheme (1-6)

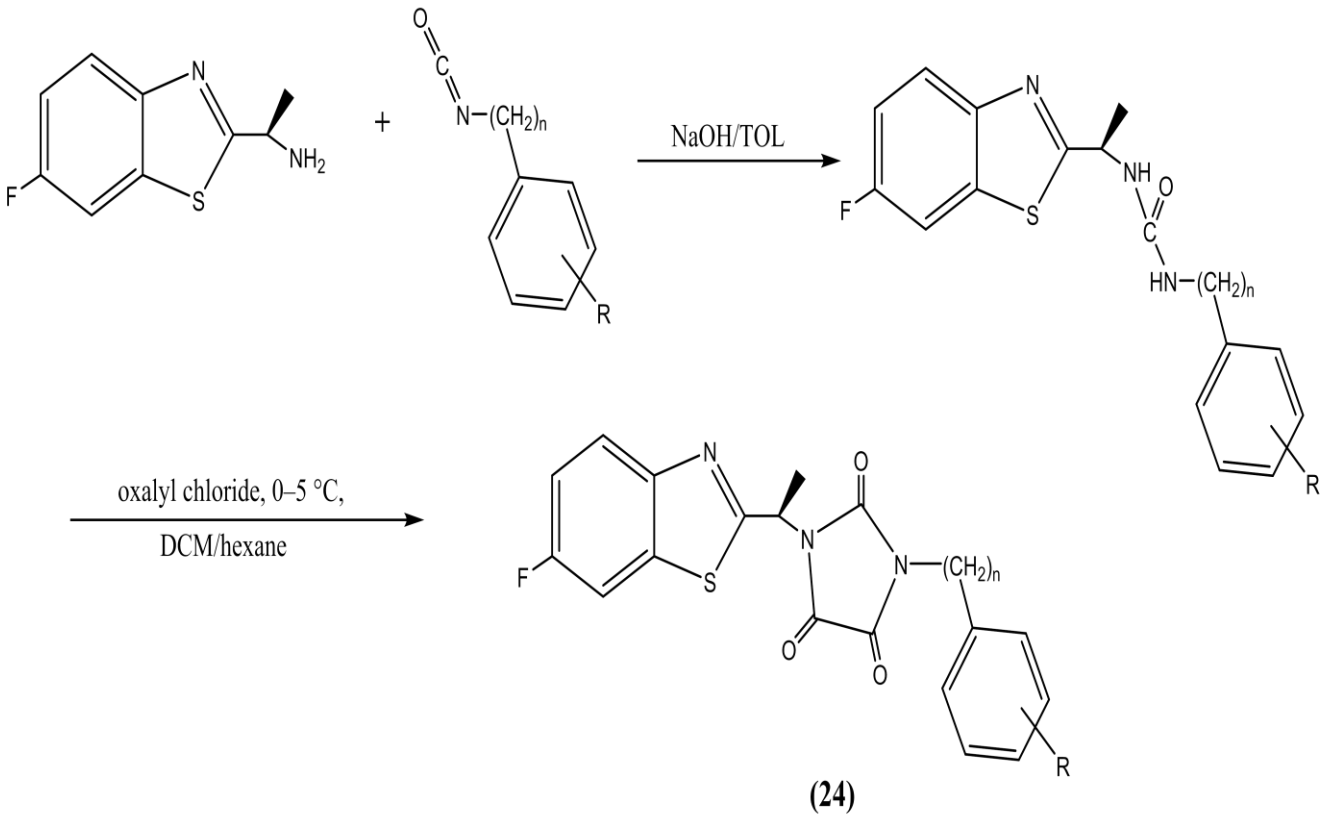
de Carvalho[37] et al. prepared N,N′-disubstituted ethylenediamine and imidazolidine derivatives **(23)** and their in vitro biological activities, Scheme (1-7).



(23)

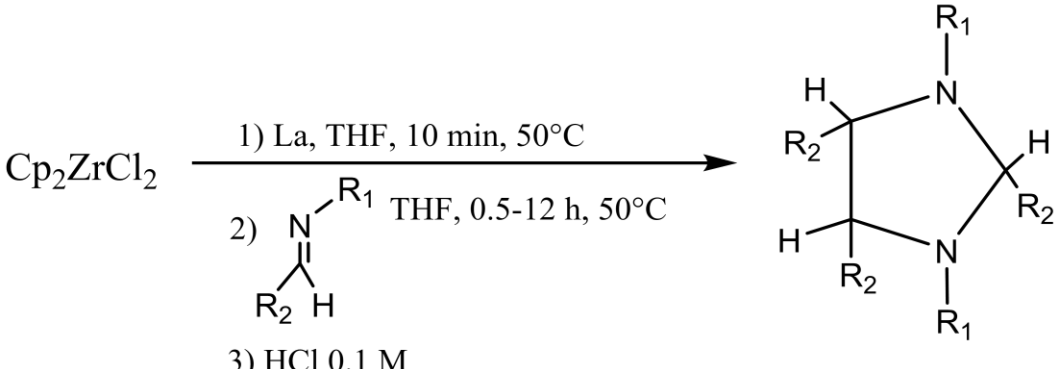
Scheme (1-7)

1-(aryl)-3-[(R)-1-(6-fluorobenzo[d]thiazol-2-yl)ethyl]imidazolidine-2,4,5-triones **(24)** were synthesized and determined by single-crystal X-ray diffraction was accomplished[38], Scheme (1-8).



Scheme (1-8)

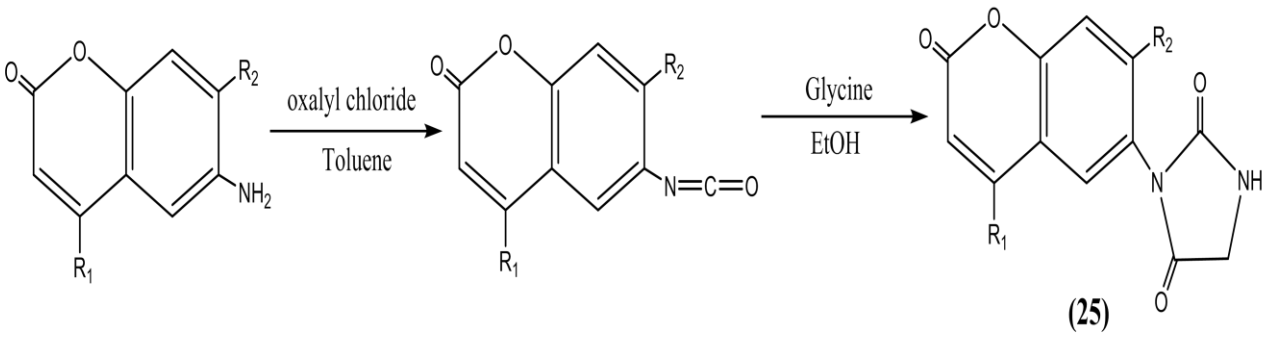
Soueidan[39] et al. synthesied vicinal diamines or imidazolidines **(25)** under mild conditions in good yields with high diastereoselectivity, Equation (1-3).



R_1=ph
R_2=C_5H_{11}

Equation (1-3)

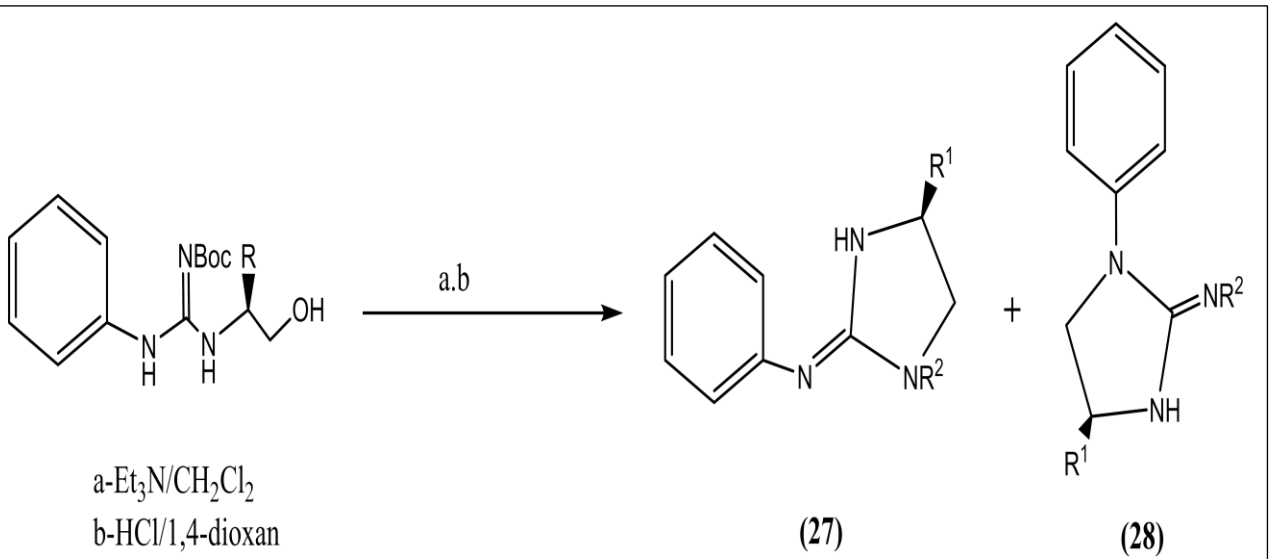
6-Aminocoumarin on treatment with oxalyl chloride gave coumarinyl-6-isocynate which was reacted with glycine to yield 1*H*-3-[2í-oxo-2í*H*-benzopyran-6í-yl]-5-imidazolidine-2,4-dione **(26)**[40], Scheme (1-9).



$R2=CH_3$ $R_1=H$

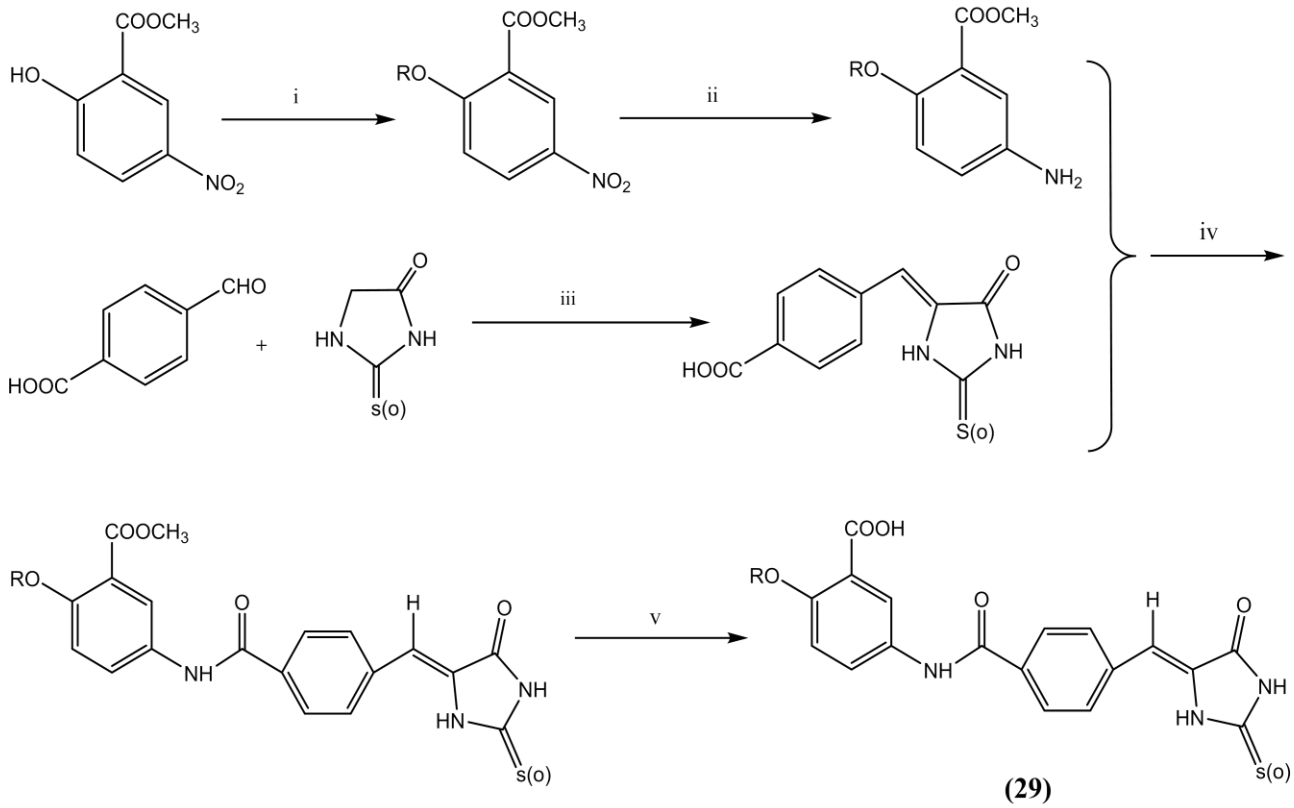
Scheme (1-9)

2-aryl iminoimidazolidines **(27)** and 1-aryl-2-iminoimidazolidines **(28)** were prepared in good yields via the cyclization of (2-hydroxyethyl)guanidines at 0 C[41], Equation (1-4).



Equation (1-4)

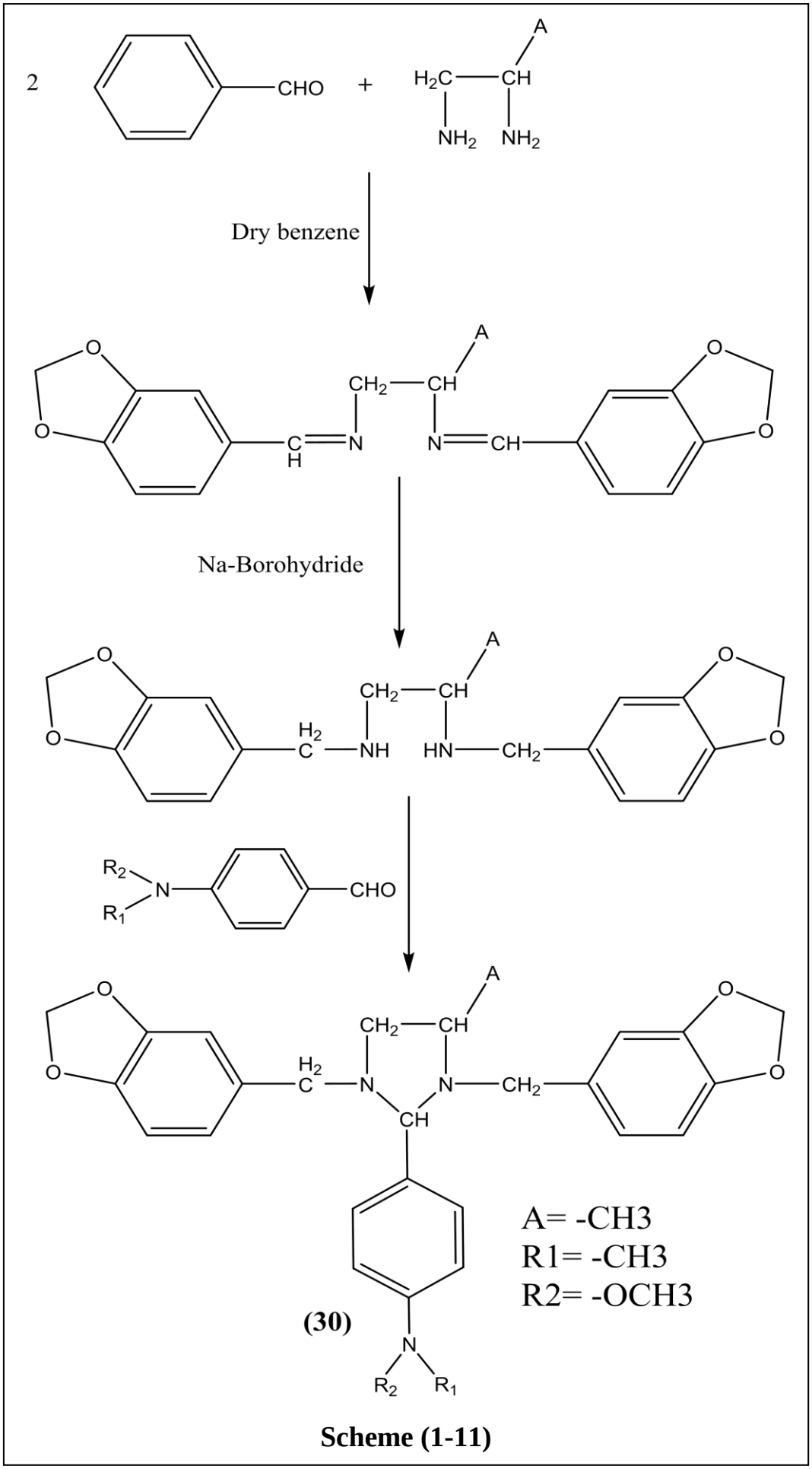
Liu[42] et al. synthesis of (Z)-2-substituted-5-(4-((2-substitued-5-oxoimidazolidin-4-ylidene)methyl)benzamido)benzoic acid derivatives**(29)**, Scheme (1-10).



(i) RBr, K_2CO_3, DMF; (ii) $SnCl_2$,H2O, C_2H_5OH; (iii) CH_3COOH, CH_3COONa; (iv) EDC HOBT, DIEA, DMF; (v) LiOH, CH_3OH, THF, H_2O.

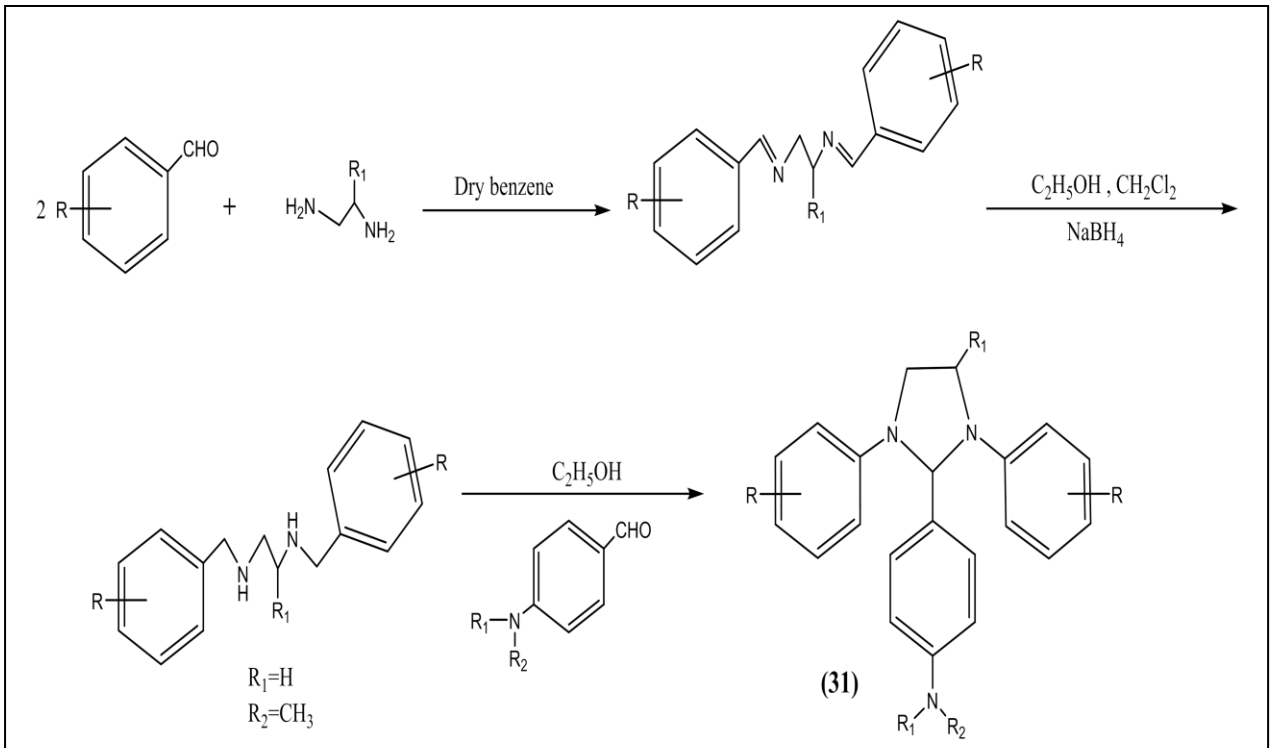
Scheme (1-10)

Khan[43] et al. synthesis of 4-(1,3-bis(benzo[d][1,3]dioxol-5- ylmethyl)-4-methylimidazolidin-2-yl)-N,N-diethyl aniline **(30)** by reacting different tetrahydro-di-Schiff bases with dimethylaminobenzaldehyde. Scheme (1-11).


2
CHO
+
A
H2C
CH
NH2
NH2
Dry benzene
A
CH2
CH
O
O
C
H
N
N
CH
O
O
Na-Borohydride
A
CH2
CH
O
O
H2
C
NH
HN
CH2
O
O
R2
N
R1
CHO
A
CH2
CH
O
O
H2
C
N
N
CH2
O
O
CH
A= -CH3
R1= -CH3
R2= -OCH3
(30)
N
R2
R1

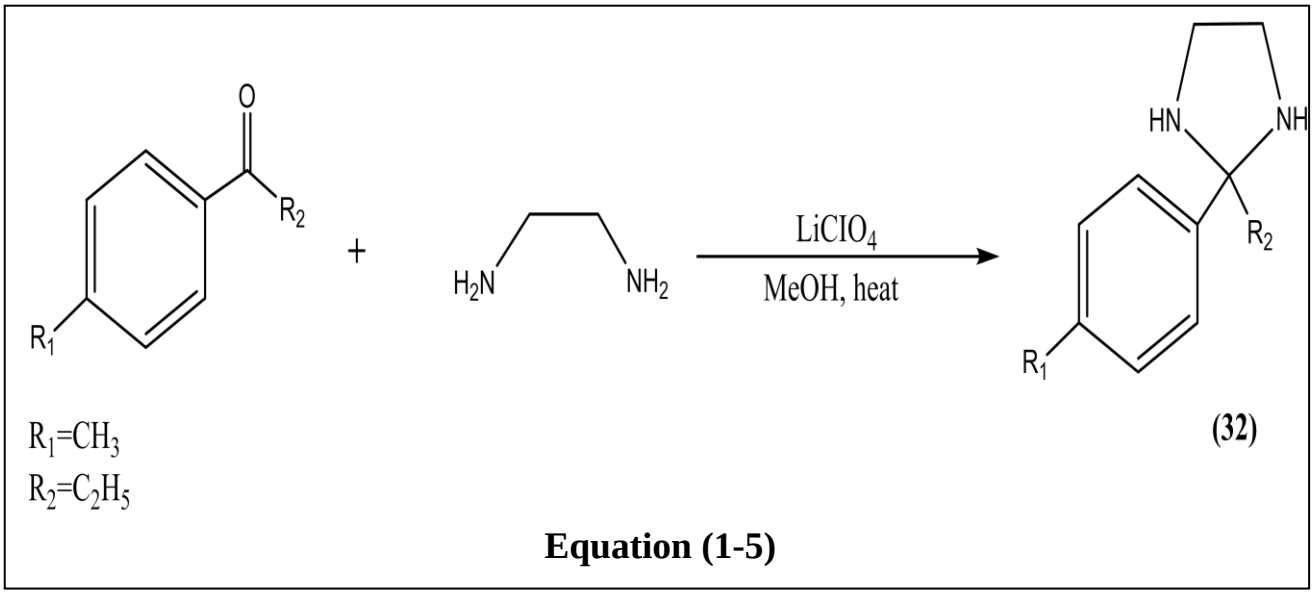
Scheme (1-11)

Substituted-imidazolidine derivatives **(31)** were synthesized and assayed in vivo to investigate their biological activity[44], Scheme (1-12).



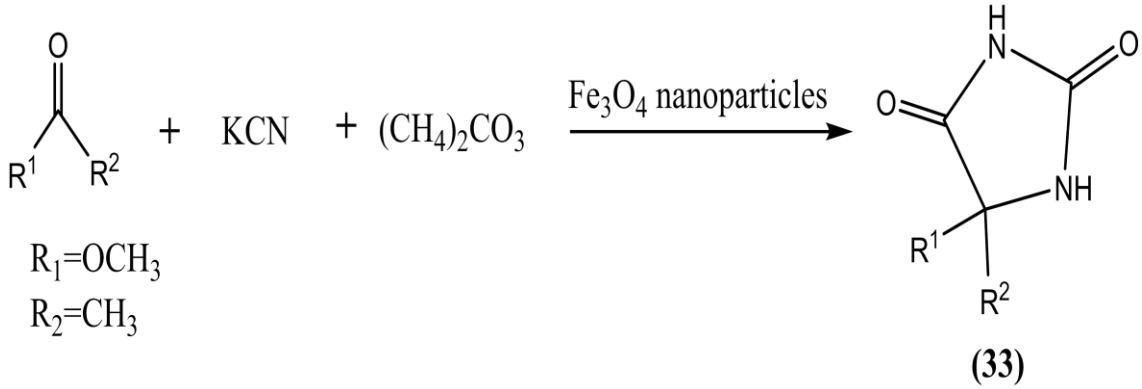
Scheme (1-12)

Naeimi[45] et al. prepared the imidazolidine derivatives **(32)** from reaction of different aromatic ketones with 1,2-ethanediamine in the presence of $LiClO_4$, Equation (1-5).



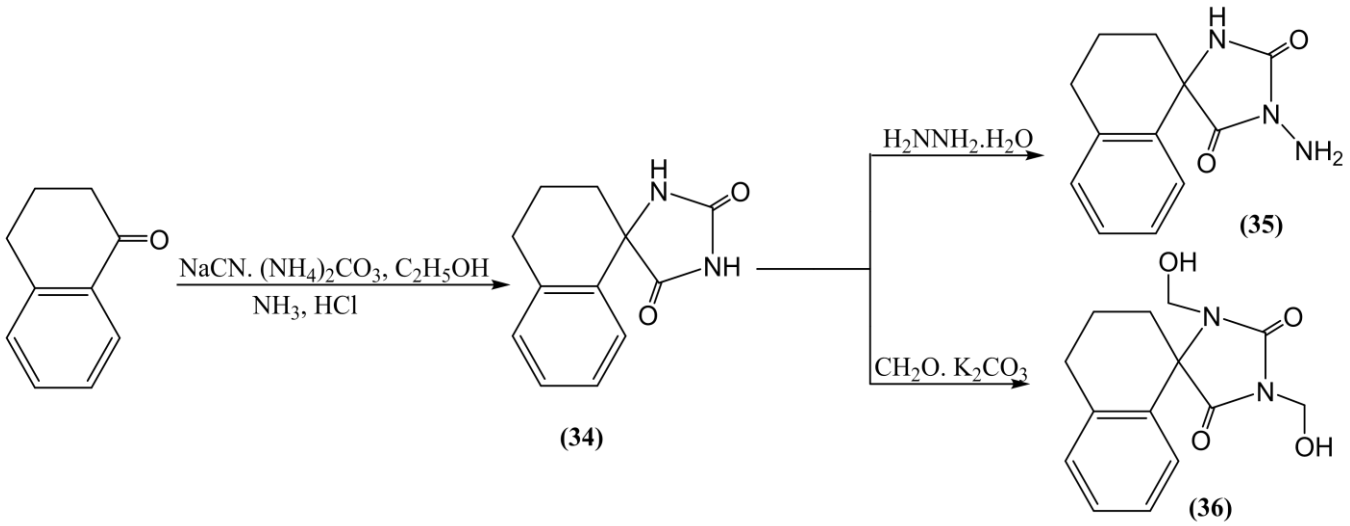
Equation (1-5)

Safari[46] et al. synthesis of 5,5-disubstituted hydantoins **(33)** by using magnetic Fe_3O_4 nanoparticles under solvent-free condition, Scheme (1-13).



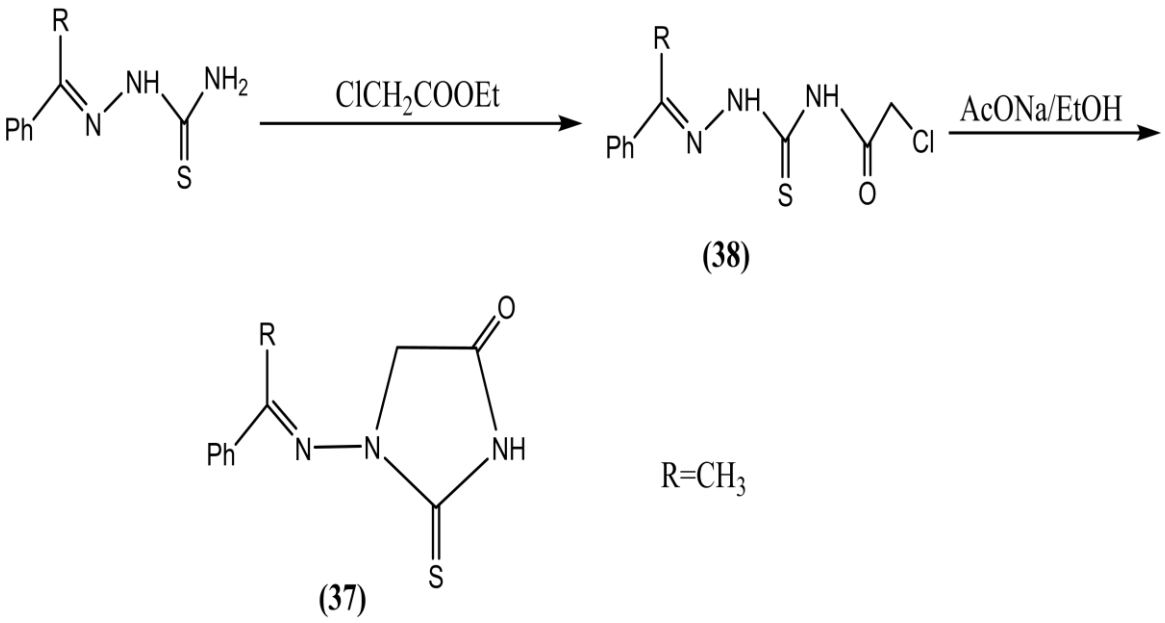
Scheme (1-13)

Marinov[47] et al. synthesized two imidazolidine compounds, 2,5- dione derivatives **(35)** and **(36)** from the imidazolidine compound **(34)**, Scheme (1-14).



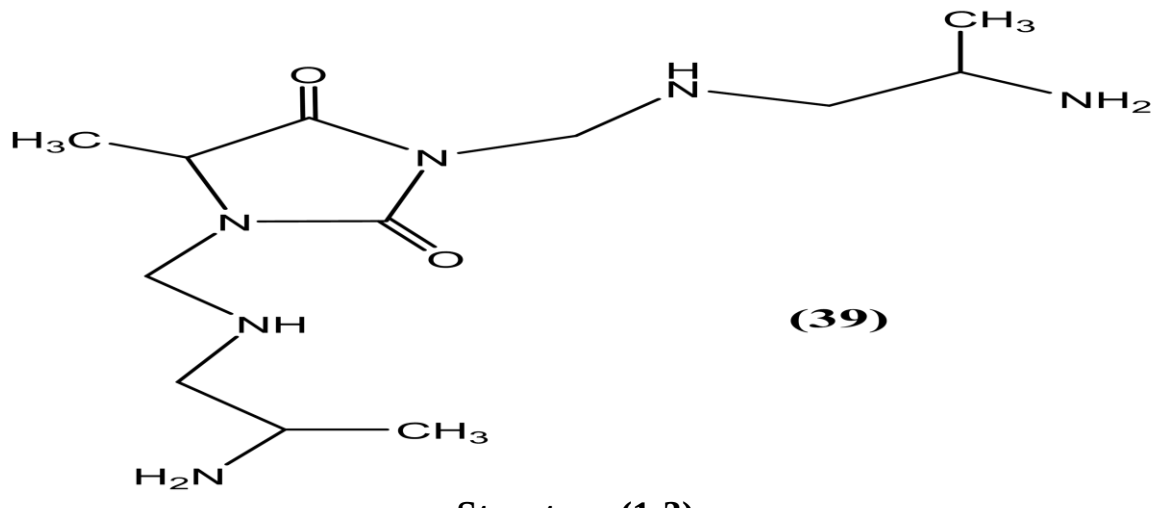
Scheme (1-14)

1-(Arylidene)amino-2-thioxo-imidazolidine-4-ones **(37)** have been synthesized via cyclization of 1-(arylidene)amino-3 (chloroacetyl)thiourea **(38)** in ethanol in presence of fused sodium acetate under heating[48], Scheme (1-15).



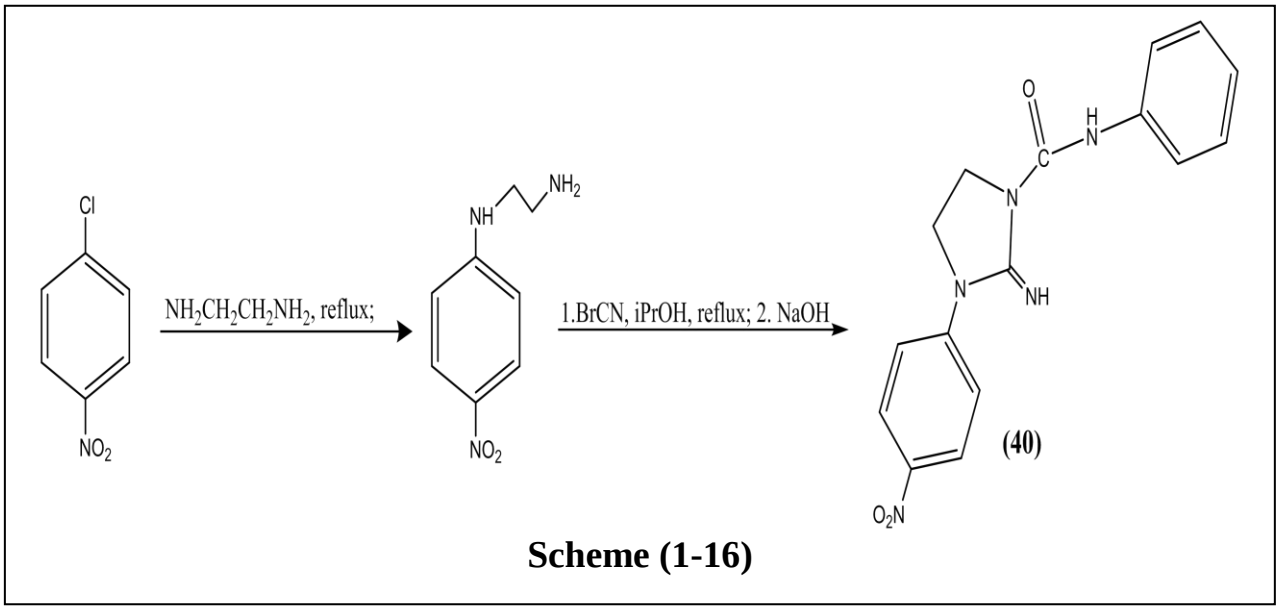
Scheme (1-15)

1,3-bis ((2-aminopropyl) amino) methyl)-5-methylimidazolidine-2,4-dione (BAMMD) **(39)** was synthesized as sand then studied as corrosion inhibitor for carbon steel and brass alloys at 0.2M sodium chloride. The optimal concentration of BAMMD is 50ppm[49], Structure (1-3).



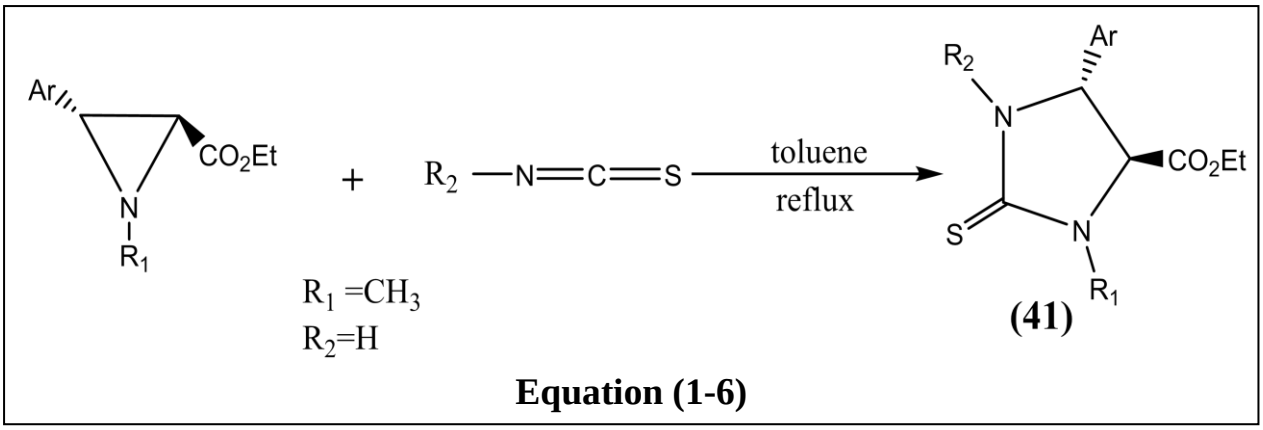
Structure (1-3)

Wróbel[50] et al. synthesized and tested the biological activity of Imidazoline derivative N-cyclohexyl-2-imino-3-(4-nitrophenyl)imidazolidine-1-carboxamide **(40)**, Scheme (1-16).



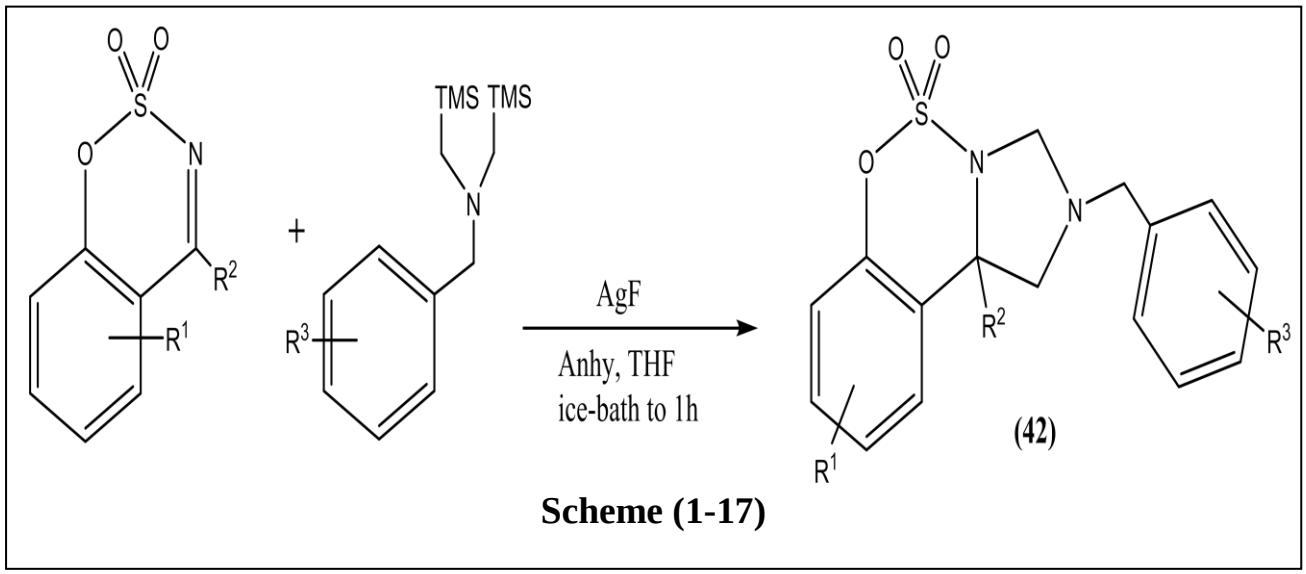
Scheme (1-16)

Tabarki[51] et al. used aziridine-2-carboxylates as starting materials In the reaction synthesis of imidazolidine-2 thiones **(41)**, Equation (1-6).



Equation (1-6)

Laha[52] et al. Synthesis of Imidazolidine Fused Sulfamidates **(42)** by [3+2]-Cycloaddition and benzosultams bearing a quaternary center, Scheme (1-17).

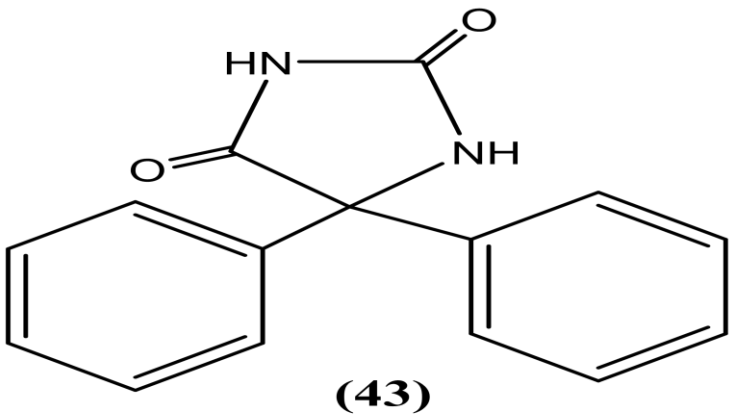


Scheme (1-17)

1-2-2.Biological Activity of Imidazolidines.

Tetrahydroimidazoles (imidazolidines) result interesting compounds due to their bioactivity, such as strogenic activity[53], anticancer[54], antifungal[55], antinociceptive activity[56], antiproliferative activity[57], antimicrobials[58], anti-tumor activity[59], anti- inflammatory[60], Anti-leishmanial[61], antiarrhythmic[62], anti-convulsant[63], angiotensin-antagonists, anticoagulants, and gastric proton-pump inhibitor[64], antidepressant[65], antiepileptic[66], antidiabetic[67], anti-hypertensive[68].

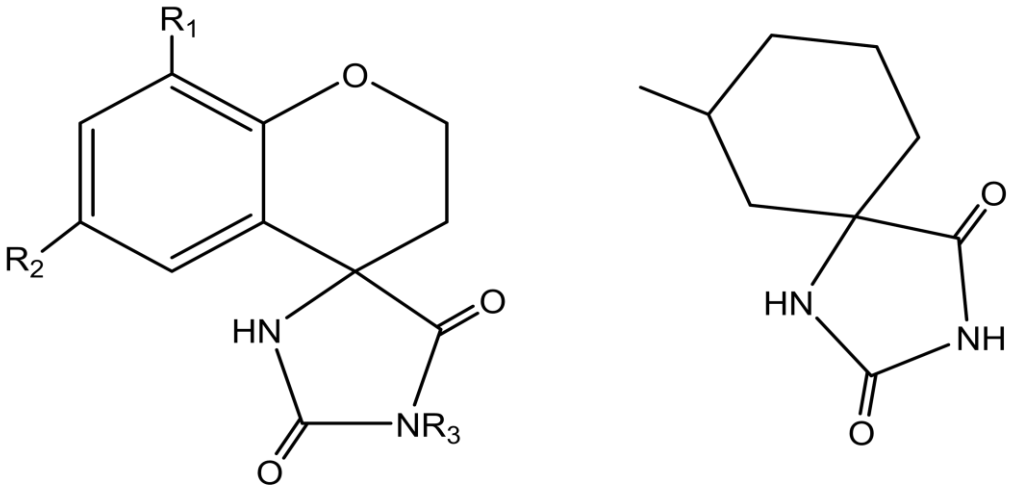
The phenytoin **(43)** used as a potential inhibitor of neuropathic pain[69], Structure (1-4).



(43)

Structure (1-4)

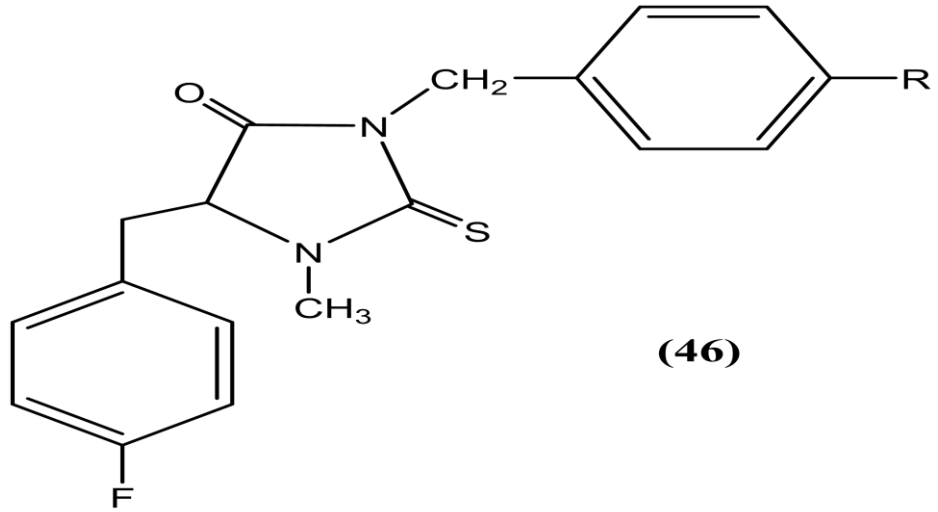
The imidazolidines **(44)** and **(45)** are high-effective compounds and used in antispasmodics and anti-epilepsy[70], Structure (1-5).



(44) **(45)**

Structure (1-5)

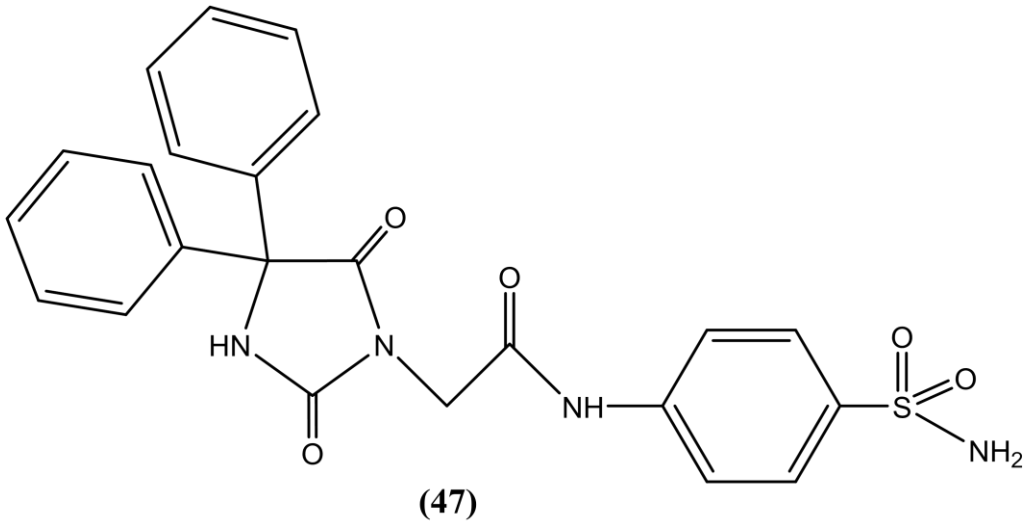
Albuquerque[71] et al. prepared and observed the biological activity of some imidazolidine compounds. They found that compound 3-benzyl-5-(4-fluoro-benzylidene)-1-methyl-2-thioxo-imidazolidin-4-one **(46)** has schistosomiasis effect, Structure (1-6).



(46)

Structure (1-6)

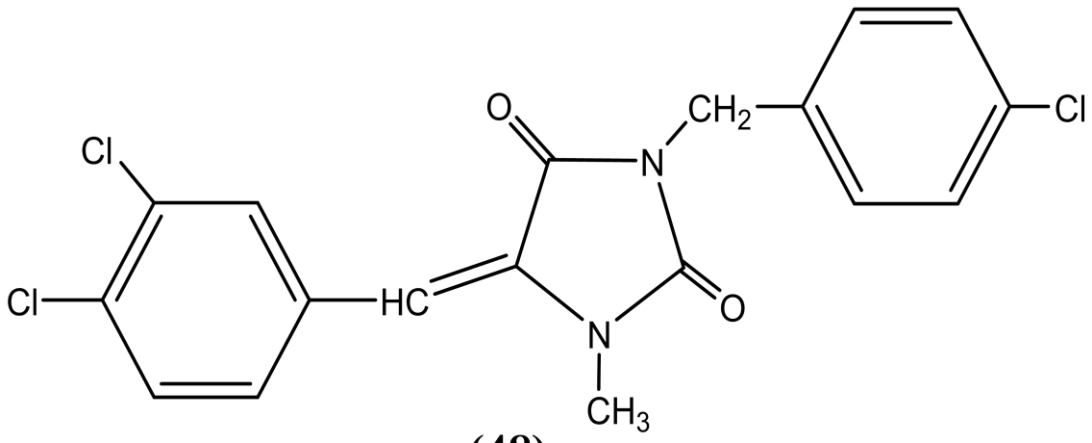
The imidazolidine derivative **(47)** 5,5-diphenylimidazolidine-2,4- dione possesses pharmacological activities such as anti-inflammatory and analgesic[72], Structure (1-7).



(47)

Structure (1-7)

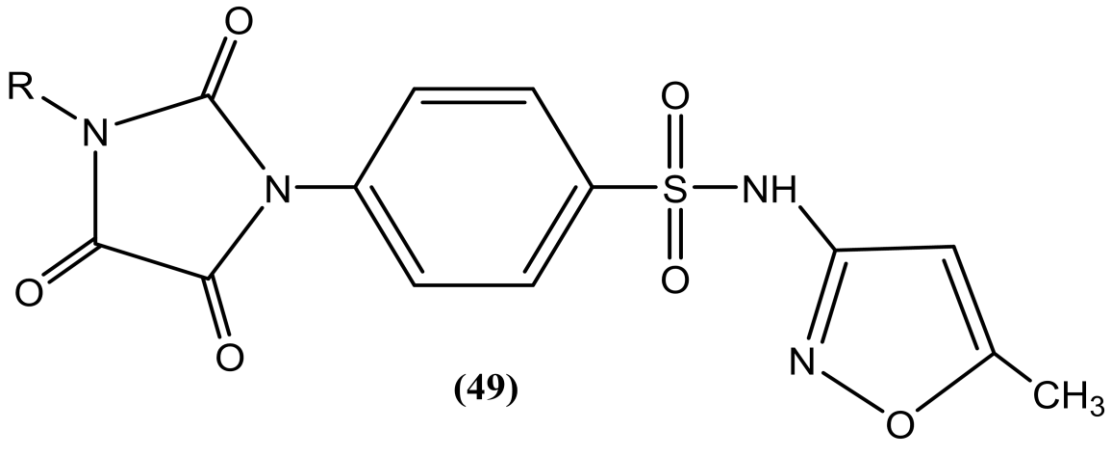
The imidazolidine derivative **(48)** 1-methyl-3-(4-chlorobenzyl)-5-(3,4-dichlorobenzylidene)imidazolidine-2,4-dione appeared antimicrobial activity[73], Structure (1-8).



(48)

Structure (1-8)

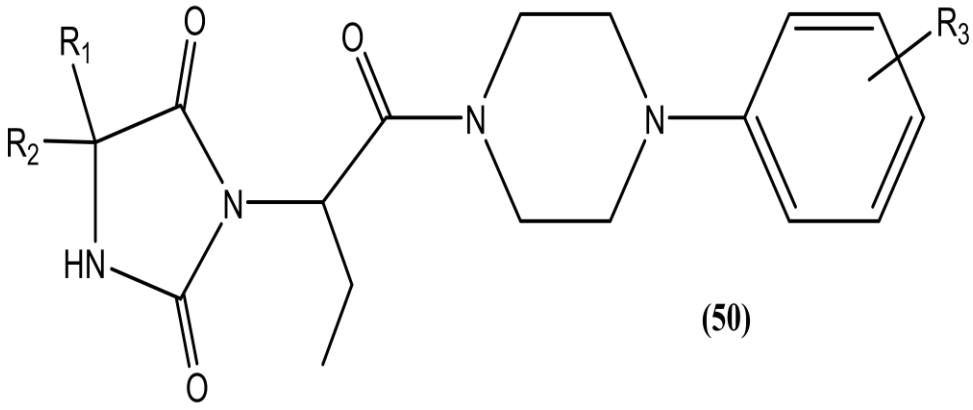
A series of novel sulphamethoxazole-based urea and imidazolidine-2,4,5-triones **(49)** have been designed and synthesised. The urea derivatives were obtained by the reaction of sulphamethoxazole and isocyanates, and their cyclisation to imidazolidine-2,4,5-triones was per-formed via oxalyl chloride. All synthesised derivatives were evaluated in vitro to determine their activity against gram-positive and gram-negative bacteria, fungi, mycobacterium tuberculosis[74], Structure (1-9).



(49)

Structure (1-9)

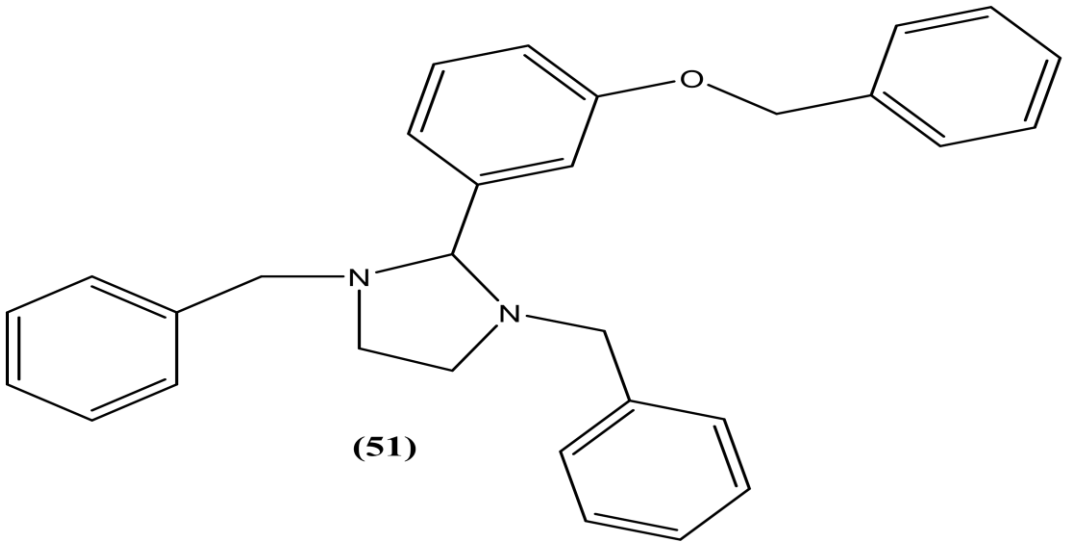
Methoxyphenylpiperazinpropyl derivatives of imidazolidine-2,4-dione **(50)** acted as antinociceptive agents in several rodent models of acute pain[75], Structure (1-10).



(50)

Structure(1-10)

The imidazolidine compound **(51)** 1,3-dibenzyl-2-(3-(benzyloxy)phenyl)imidazolidine showed biological activity as anti-aggregatory Alzheimer's disease[76]. Structure (1-11).



(51)

Structure (1-11)

1.3. Microwave assisted organic reactions

Microwaves have been used to speed up chemical reactions in the laboratory, which led scientists to investigate the mechanism of microwave dielectric heating and to identify the advantages of the technique for chemical synthesis.The first recorded application of microwave (MW) energy in organic synthesis is the aqueous emulsion polymerization of butyl acrylate, acrylic acid and methacrylic acid using pulsed

electromagnetic radiation. The start of the rapid growth of microwave-assisted procedures in organic synthesis was ignited in 1986 by pioneering papers by Gedye and co-workers and Giguere and co-workers[77].

The organic synthesis is one of the major role of research in chemistry, from plastics to medication it participates in the improvements of everyone life. Over the past few decades, many significant advances in practical aspects of organic chemistry have included novel synthetic strategies and methods as well as advent of a vast array of analytical techniques. In these environmentally conscious days, the developments in the technology are directed towards environmentally sound and cleaner procedures[78].

In the last decades the MW technique has been intensively used to carry out organic reactions of almost all kinds, and has become a useful non-conventional means of performing organic syntheses[79].

Microwave-assisted synthesis is green chemical method, the application of microwave-assisted is useful technology in organic synthesis because it is simple, sensitive, reducing the hazard, often possible to reduce reaction times to a few minutes under solvent free or lower solvent and increase the yields and easier work up as compared to conventional methods[80,81].

Microwave irradiation can be used instead of thermal heating. Furthermore, at the beginning of this century, green chemistry attracted considerable interest in the development of environmentally benign routes to numerous materials. Among these routes, microwave irradiation has effective tool in organic syntheses. Using metal catalysts in conjunction with microwaves may have significant advantages over classical heating methods since the inverted temperature gradient under microwave conditions may lead to increased lifetime of the catalyst[82].

1.3.1. Basic microwave equipment

The microwave equipment (also frequently called “ appli- cators ”) used in chemical processing can be divided into three basic categories: the multimode, the mono (or single)-mode, and the traveling-wave devices. The multimode applicators are the most widespread ones, with applications starting from domestic ovens up to large-scale industrial dryers. They usually have the form of a rectangular closed metal box a Faraday cage that has at least two dimensions longer than half of the wavelength. Inside the

cavity, a large number of resonance modes exist as the microwaves get reflected from the cavity walls. Owing to these reflections, wave interference occurs[83,84].

Microwave activation and solvent-free conditions in organic synthesis provides clean chemical processes characterized by enhanced reaction rates, higher yields and enhanced ease of manipulation[85], Figure (1-1).

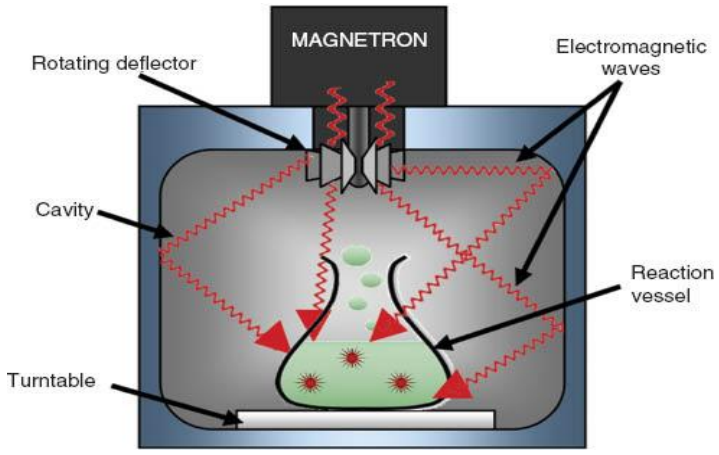


Fig. (1-1): Multimode microwave applicator

1.3.2. Microwave in organic Synthesis

Synthetic method has shown broad applications as a very efficient way to accelerate the course of many organic reactions, producing high yields and higher selectivity, lower quantities of side products and, consequently, easier work-up and purification of the products. Microwave-assisted organic synthesis (MAOS) is considered as an "green" technology, principally since many organic reactions can be carry out in solvent-free conditions[86].

(MAOS) has revolutionized organic synthesis. Small molecules can be built in a fraction of the time required by classical thermal methods. As a result, this technique has rapidly gained acceptance as a valuable tool for accelerating drug discovery and development processes[87].

(MAOS) is the study of chemical reactions under the effect of microwave radiation. Microwaves radiation have high energy electric fields and will generally heat any substance containing mobile electric charges. Microwave irradiation was found to increase the yields of the desired

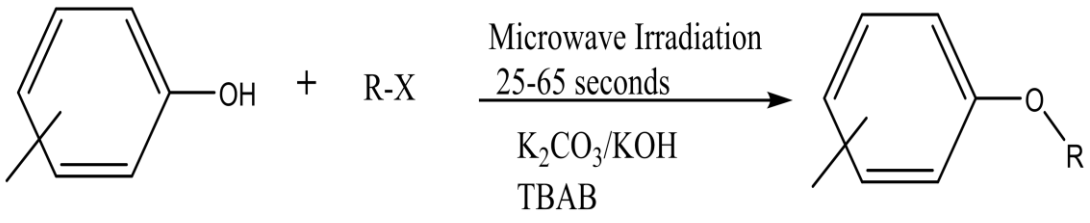
products and shorten the reaction times[88].

Microwave- assisted organic synthesis has been the one of the most researched applications of microwaves in chemical reactions.Chemists have successfully conducted a large range [89].

Organic reactions assisted with microwave irradiation such as Diels-Alder reactions between dienes and dienophiles, these reactions have been carried out with and without solid support and by both conventional and MW assisted techniques. Heck reaction, Suzuki reaction, Mannich reaction, hydrogenation of β-lactams, hydrolysis, dehydration, esterification, epoxidation, reductions, condensations and cycloaddition reactions[90].

1.3.2.1. Alkylation

Dariusz[91] et al. used microwave heating under solvent free PTC conditions for o-alkylation of phenols, Equation (1-7).



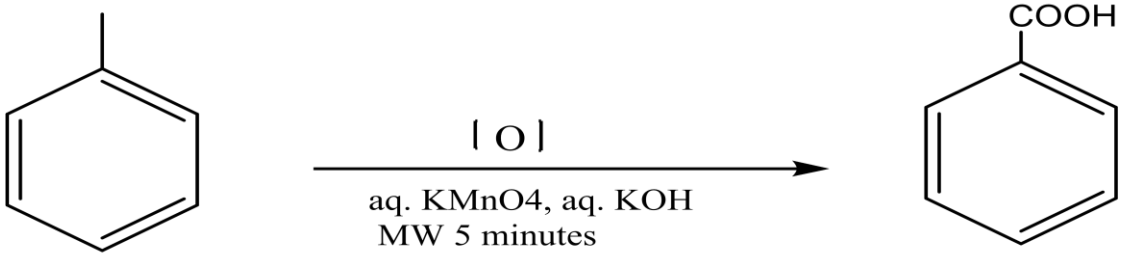
TBAB:tetrabutyl ammonium bromide

(52)

Equation (1-7)

1.3.2.2. Oxidation

Grewal[92] et al. Oxidized toluene to benzoic acid **(53)** with $KMnO_4$ by microwave radiation, Equation (1-8).

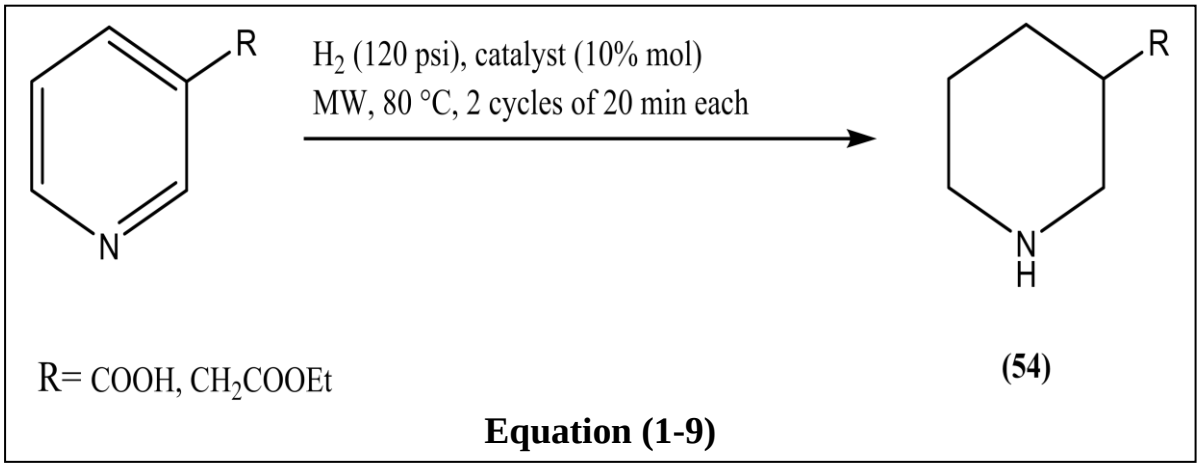


(53)

Equation (1-8)

1.3.2.3. Reductions

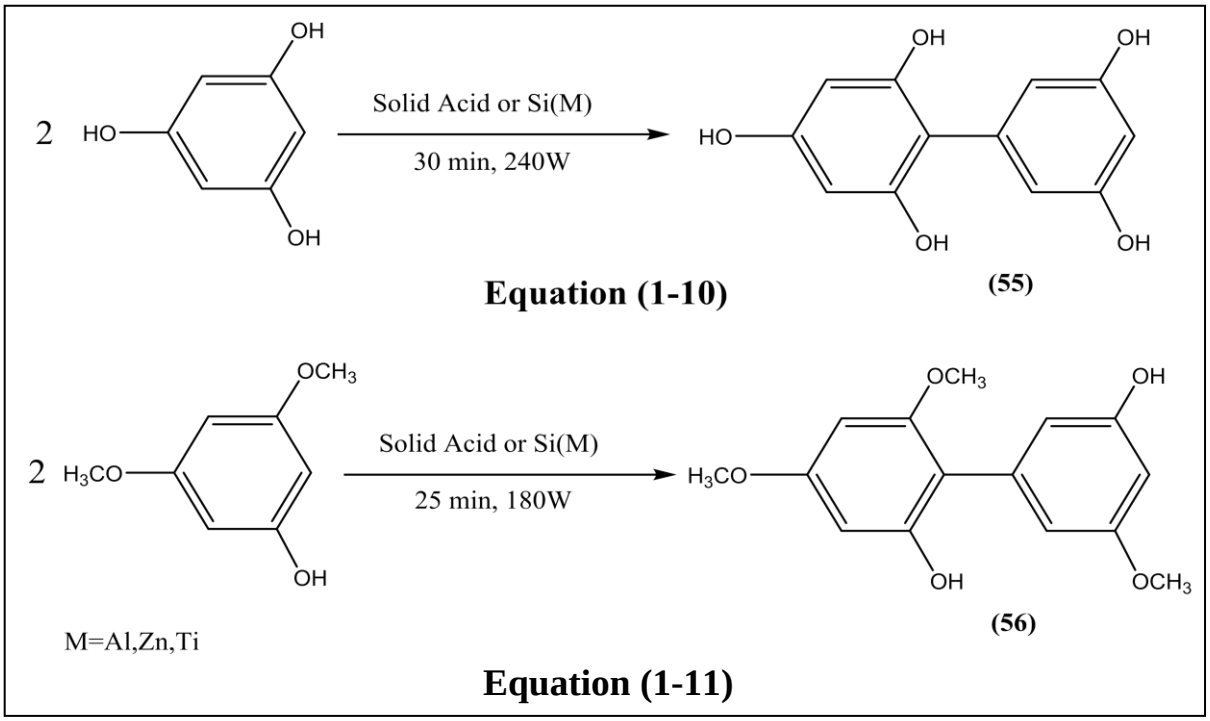
Piras[93] et al. converted the substituted pyridines into the corresponding piperidines **(54)** optimisation of the procedure for microwave-assisted hydrogenation, Equation (1-9).



Equation (1-9)

1.3.2.4. Condensations

Self-condensation of 1,3,5-trihydroxybenzene and 3,5-dimethoxyphenol using solid acid catalysts and microwave irradiation produces polyhydroxy-substituted biphenyl derivatives **(55)** and **(56)** in moderate to good yields[94], Equations (1-10) and (1-11).

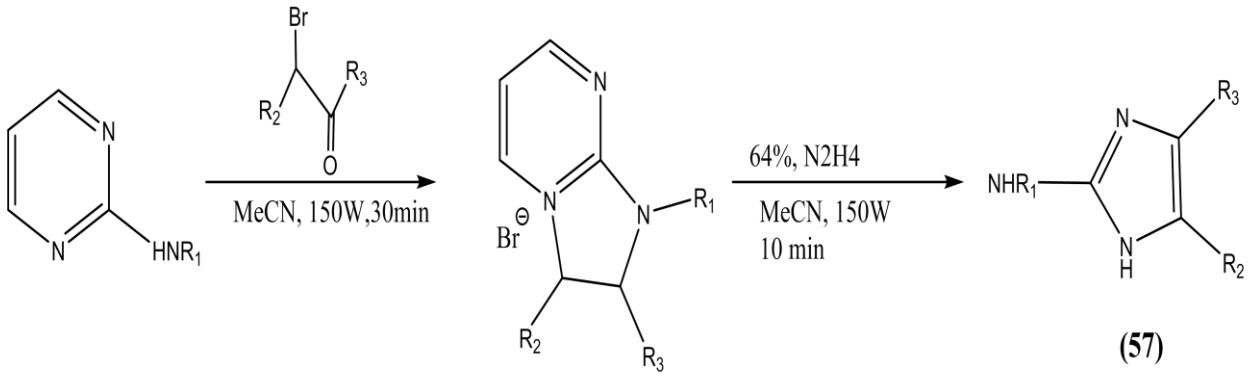


Equation (1-10)

Equation (1-11)

1.3.2.5. Cycloaddition

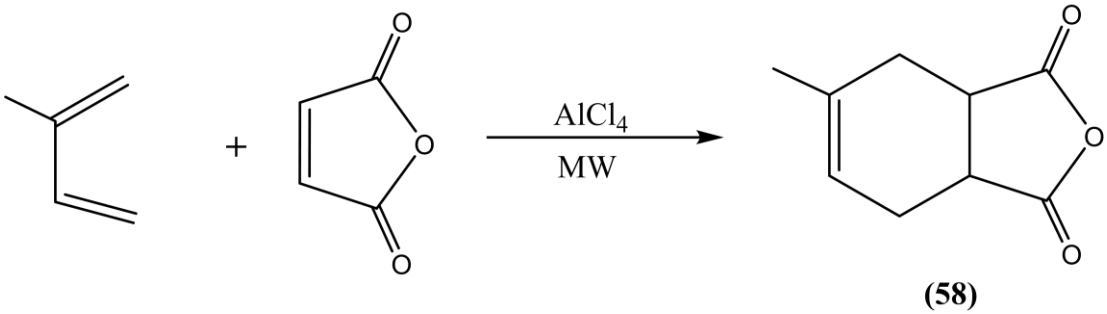
Ermolat[95] et al. synthesized 4,5-disubstituted-2-aminoimidazoles **(57)** has been developed starting from the readily available 2-aminopyrimidines and α-bromocarbonyl compounds using conventional heating or microwave irradiation, Scheme (1-18).



Scheme (1-18)

1.3.2.6. Diels-Alder reactions

The reactions between isoprene and a series of dienophiles have been carried out with and without solid support and by both conventional and MW assisted techniques produced Tetrahydro-2-benzofuran-1,3- dione[96] **(58)**. Equation (1-12).



Equation (1-12)

Aim of The Study

The present work aims to synthesize of two series of new imidazolidine derivatives containing benzothiazole moiety using microwave irradiation which might have some antibacterial activities.

Chapter Two

Experimental Part

2.1. Materials

All chemicals, reagents and solvents were provided from the commercial sources summarized in table (2-1**).**

Table (2-1): Chemicals and their commercial sources

Chemicals	Molecular formula	M.Wt. g/mol	Purity %	Supplied companies
2-Aminobenzothiazole	$C_7H_6N_2S$	150.20	97	Sigma Aldrich
Ethanol (absolute)	C_2H_6O	46.06	99.9	J.T.Baker, Netherlands
Sulfuric acid (Conc.)	H_2SO_4	98.08	99	Merck, Germany
Sodium nitrite	$NaNO_2$	68.99	99	BDH, England
2-Hydroxy benzaldehyde	$C_7H_6O_2$	122.12	98	S.D.Fine.india
Sodium hydroxide	NaOH	39.99	99	BDH, England
4-Bromoaniline	C_6H_6NBr	172.02	96	BDH, England
4-Chloroaniline	C_6H_6NCl	127.57	99	BDH, England
2,4-Dichloroaniline	$C_6H_5NCl_2$	162.01	95	BDH, England
4-Nitroaniline	$C_6H_6N_2O_2$	138.12	98	Fluka
3-Nitroaniline	$C_6H_6N_2O_2$	138.12	99	Fluka
4-Methoxyaniline	C_7H_9NO	123.16	98	BDH, England
2-Methoxyaniline	C_7H_9NO	123.16	98	BDH, England
4-Hydroxyaniline	C_6H_7NO	109.13	99	BDH, England
Glycine	$C_2H_5NO_2$	75.05	99	Fluka
Alanine	$C_3H_7NO_2$	88.99	99	Fluka
THF	C_4H_8O	72.10	99.7	J.T.Baker
Diethyl ether	$C_4H_{10}O$	74.12	99.5	Scharlau, Spain
n-Hexane	C_6H_{14}	86.17	99	Scharlau, Spain
Ethyl acetate	$C_4H_8O_2$	88.10	99	BDH, England

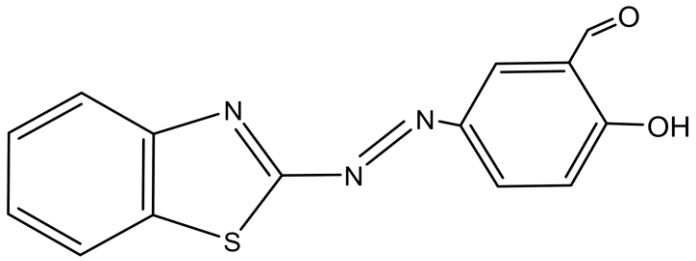
Iodine	I_2	253.80	99.5	GCC, Germany
Dimethyl sulfoxide	C_2H_6OS	78.13	99	BDH, England

2.2. Instrumentations

1. Silica TLC plates were used with an aluminum backing (0.2 mm, 60 F_{254}). The reactions were monitored by TLC and visualized by development of the TLC plates with Iodine vapor.
2. Melting points were recorded using an Electro thermal Stuart SMP 30 capillary melting point apparatus, UK.
3. Infrared spectra were recorded on SHIMADZU FTIR-8400S Infrared Spectrophotometer as potassium bromide discs in Kerbala University.
4. ^{1}H NMR spectra was collected on NMR spectrometer 500 MHz, Ascennd ^{TM} 500 Bruker, Germany at 500 MHz in DMSO-d_6 as solvent and TMS as an internal standard at a Faculty of Science, University of Tarbeat Modares, Iran.
5. Elemental Analysis (CHNS) was carried out with Perkin Elmer 300 A Elemental Analyzer at a Faculty of Science, University of Tarbeat Modares, Iran.
6. Microwave reactions were performed on Domestic microwave oven in Crucible.
7. Autoclave was used to sterilize agar media, supplied from Prestige Medical-England.
8. Incubator was used to maintain different temperature required for the growth of organism, supplied from Binder - Germany.

2.3. Preparation methods

2.3.1. Preparation of (E)-5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxybenzaldehyde 2 [97]



2

Fig. (2-1): Structure of compound **2**

A solution of 2-aminobenzothiazole (8.1 g, 0.054 mol) in H_2SO_4 (12mL) was cooled to 0°C.To this solution a cold solution of sodium nitrite (3.726 g, 0.054 mol) dissolved in distilled water (20 mL) was added drop wise with constant stirring. When the addition was completed, the resultant reaction mixture was left in ice-chest for 1h. The ice cold solution of diazonium bisulfate was then added drop wise to the cold solution of 2-hydroxy benzaldehyde (6.588 g, 0.054 mol) dissolved in (44 mL) of (10% w/v) sodium hydroxide with constant shaking. A dark dye resulted which darkened on adding more alkaline solution of phenol derivative. When the addition was completed, the resultant reaction mixture was vigorously stirred and filtered off. A saturated solution of the last compound in water was neutralized with concentrated hydrochloric acid. A solid separated out which was allowed to stand at room temperature for 30 min., then filtered off and washed well with distilled water. The precipitated substance was collected and recrystallized from ethanol to yield **2** as a dark brown solid (9.1692 g, 60%). The physical properties of compound **2** was given in table (2-2). [98]

2.3.2. General procedure for the preparation of imine derivatives 3a-h

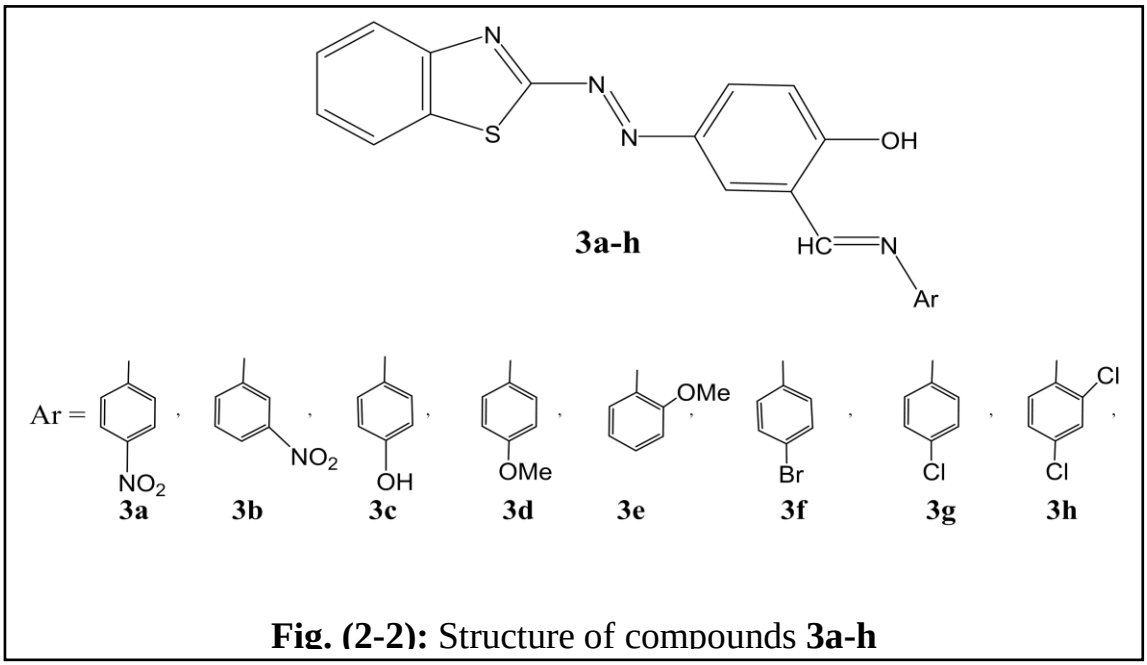
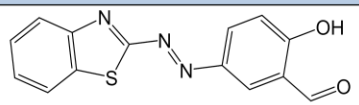
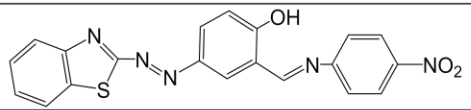
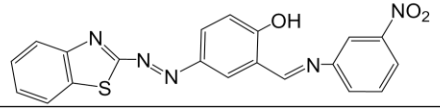
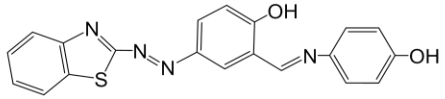
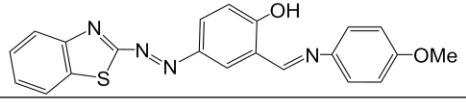
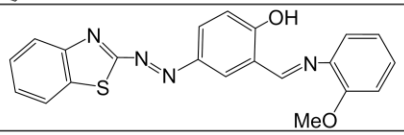
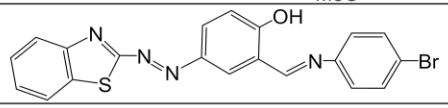
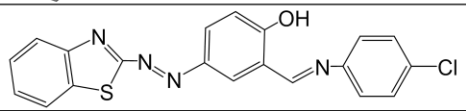
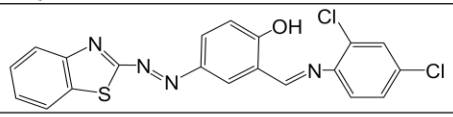


Fig. (2-2): Structure of compounds **3a-h**

All reactions were carried out on Domestic microwave oven in crucible. Reactions contained the azoaldehyde derivative **2** (0.283 g, 1 mmol), equimolar amount (1 mmol) of aniline derivatives (4-nitroaniline, 3-nitroaniline, 4-hydroxyaniline, 4-methoxyaniline, 2-methoxyaniline, 4-bromoaniline, 4-chloroaniline and 2,4-dichloroaniline respectively) and absolute ethanol (1 mL). The crucible was introduced to the center of a Domestic microwave oven and then heated (300-350W) for 25-30 minutes. TLC (*n*-hexane: EtOAc) showed that the reactions were completed. The products were washed with diethyl ether and recrystallized from ethanol. Table (2-2) shows physical properties and other characteristics for the synthesized compounds **3a-h**.

Table (2-2): Some physical properties and other characteristics for the synthesized imine derivatives 3a-h

Com. no.	Structure	Molecular formula	Color	M.Wt. g/mol	MW (W)	Reaction time (min)	Yield %	M.P. ºC	R_f
2		$C_{14}H_9N_3O_2S$	Dark brown	283.31	-	-	60	141-143	0.68 *n*-hexane : EtOAc 1 : 2
3a		$C_{20}H_{13}N_5O_3S$	Brown	403.42	350	30	78	221-223	0.78 *n*-hexane : EtOAc 1 : 2
3b		$C_{20}H_{13}N_5O_3S$	Dark brown	403.42	320	28	75	184-186	0.73 *n*-hexane : EtOAc 1 : 2
3c		$C_{20}H_{14}N_4O_2S$	Dark Brown	374.42	300	27	79	176-178	0.75 *n*-hexane : EtOAc 1 : 2
3d		$C_{21}H_{16}N_4O_2S$	Brown	388.45	300	26	73	195-197	0.88 *n*-hexane: EtOAc 1 : 2
3e		$C_{21}H_{16}N_4O_2S$	Dark brown	388.45	310	30	77	199.201	0.7 *n*-hexane : EtOAc 1 : 2
3f		$C_{20}H_{13}N_4OSBr$	Dark brown	437.32	320	30	69	173-175	0.83 *n*-hexane : EtOAc 1 : 2
3g		$C_{20}H_{13}N_4OSCl$	Brown	392.86	320	28	76	206-208	0.75 *n*-hexane : EtOAc 1 : 2
3h		$C_{20}H_{12}N_4OSCl_2$	Brown	427.30	310	30	77	163-165	0.7 *n*-hexane : EtOAc 1 : 2

2.3.3. General procedure for the synthesis of imidazolidine derivatives 4a-h

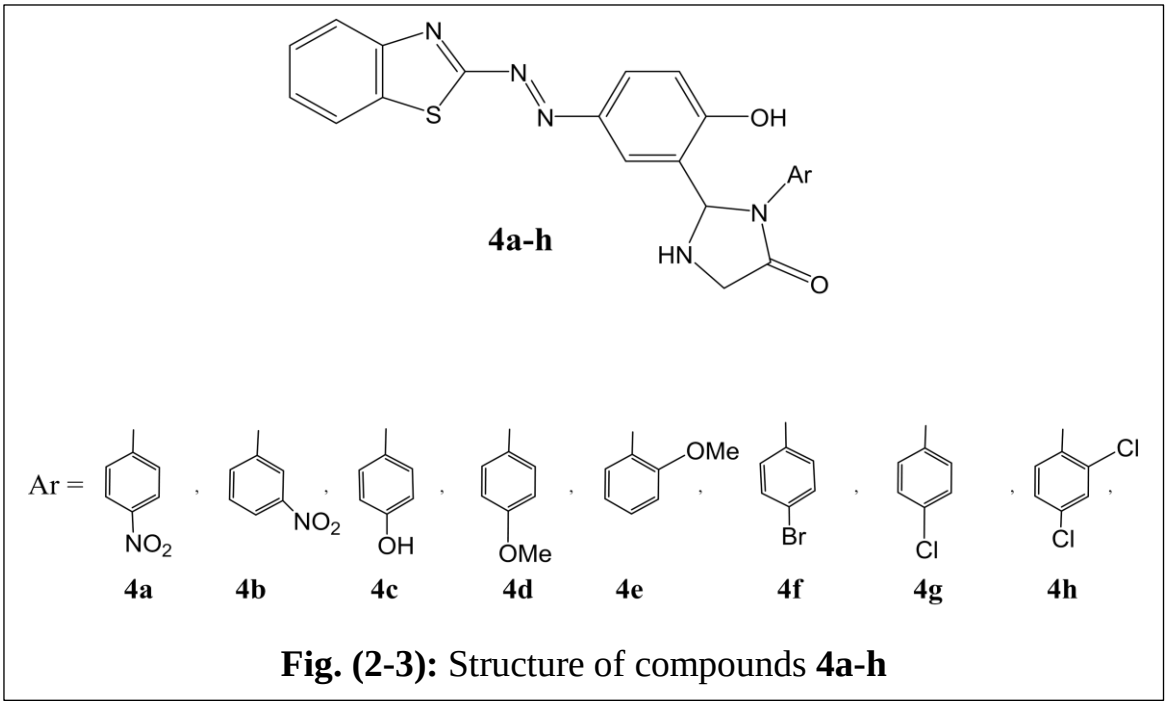
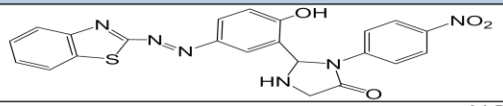
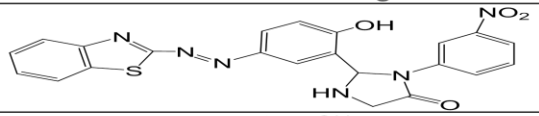
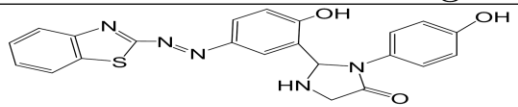
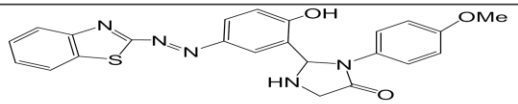
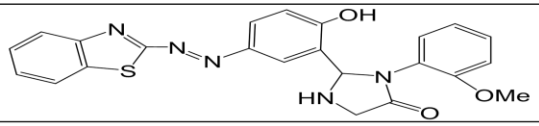
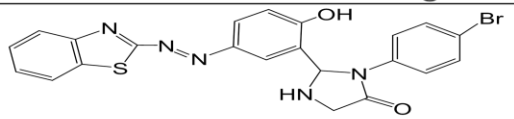
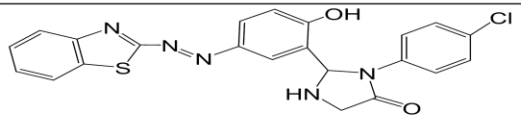
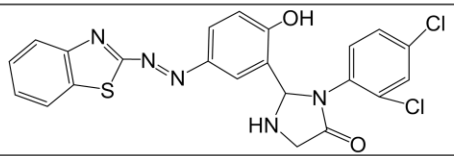


Fig. (2-3): Structure of compounds **4a-h**

A mixture of equimolar amounts of imine derivatives **3a-h** (1 mmol) and glycine (0.075 g, 1 mmol) in tetrahydrofuran (1 mL) was heated (550-610W) in microwave oven for 20-25 min. TLC (*n*-hexane: EtOAc) showed that the reactions were completed. The products were washed with diethyl ether and recrystallized from ethanol. Table (2-3) shows physical properties and other characteristics for the synthesized compounds **4a-h**.

Table (2-3): Some physical properties and other characteristics for the synthesized imidazolidine derivatives 4a-h

Com. no.	Structure	Molecular formula	Colour	M.Wt. g/mol	MW (W)	Reaction time (min)	Yield %	M.P. °C	R_f *n*-hexane: EtOAc 1 : 2
4a		$C_{22}H_{16}N_6O_4S$	Orange	460.47	600	24	75	281(dec.)	0.69
4b		$C_{22}H_{16}N_6O_4S$	Yellow	460.47	600	23	78	322-324	0.71
4c		$C_{22}H_{17}N_5O_3S$	Dark orange	431.47	550	23	75	219-221	0.71
4d		$C_{23}H_{19}N_5O_3S$	Dark Orange	445.50	550	22	78	134-136	0.69
4e		$C_{23}H_{19}N_5O_3S$	Yellow	445.50	570	24	74	198-200	0.68
4f		$C_{22}H_{16}N_5O_2SBr$	Orange	494.37	590	25	79	228-230	0.73
4g		$C_{22}H_{16}N_5O_2SCl$	Yellow	449.92	600	25	78	180-182	0.74
4h		$C_{22}H_{15}N_5O_2SCl_2$	Dark brown	484,36	610	23	76	233-235	0.72

2.3.4. General procedure for the synthesis of imidazolidine derivatives 5a-h

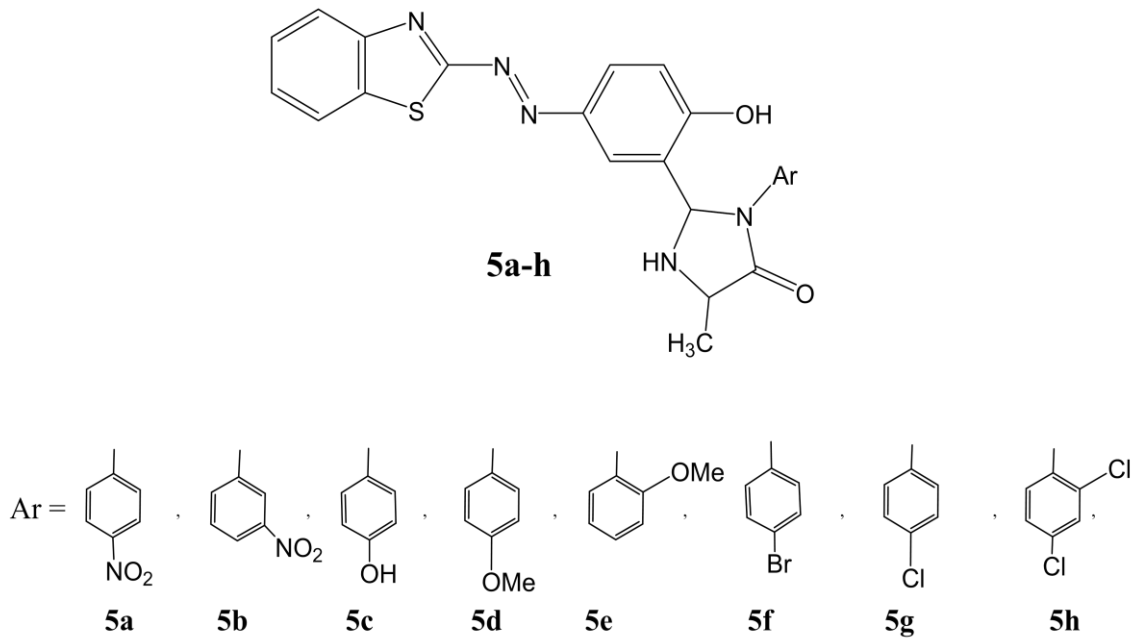
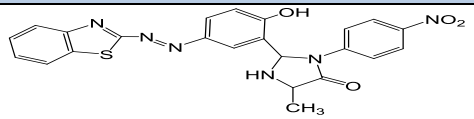
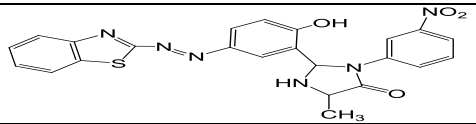
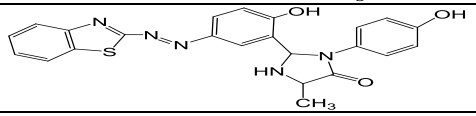
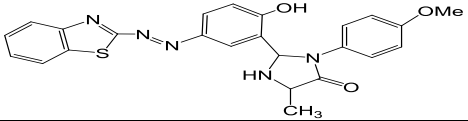
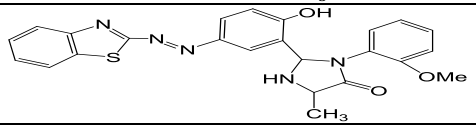
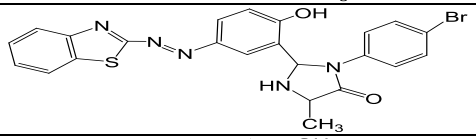
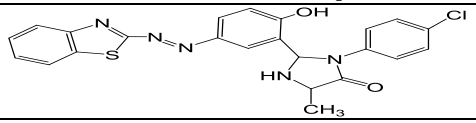
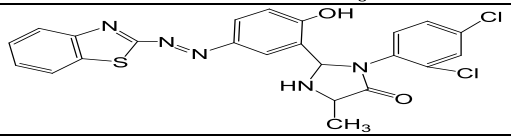


Fig. (2-4): Structure of compounds **5a-h**

A mixture of equimolar amounts of imine derivatives **3a-h** (1 mmol) and L-alanine (0.089 g, 1 mmol) in tetrahydrofuran (1 mL) was heated (550-610W) in microwave oven for 20-25 min. TLC (*n*- hexane: EtOAc) showed that the reactions were completed. The products were washed with diethyl ether and recrystallized from ethanol. Table (2-4) shows physical properties and other characteristics for the synthesized compounds **5a-h**.

Table (2-4): Some physical properties and other characteristics for the synthesized imidazolidine derivatives 5a-h

Com. no.	Structure	Molecular formula	Colour	M.Wt. g/mol	MW (W)	Reaction time (min)	Yield %	M.P. °C	R_f *n*-hexane: EtOAc 1 : 2
5a		$C_{23}H_{18}N_6O_4S$	Yellow	474.50	610	24	74	247-249	0.69
5b		$C_{23}H_{18}N_6O_4S$	Dark orange	474.50	600	23	73	241-243	0.71
5c		$C_{23}H_{19}N_5O_3S$	Dark orange	445.50	600	22	70	297-299	0.71
5d		$C_{24}H_{21}N_5O_3S$	Orange	459.53	560	21	74	232-234	0.69
5e		$C_{24}H_{21}N_5O_3S$	Orange	459.53	550	20	77	202-204	0.68
5f		$C_{23}H_{18}N_5O_2SBr$	Dark orange	508.40	570	24	76	279-281	0.73
5g		$C_{23}H_{18}N_5O_2SCl$	Yellow	463.94	600	22	78	318(dec)	0.74
5h		$C_{23}H_{17}N_5O_2SCl_2$	Dark brown	498.39	600	22	79	286-288	0.72

2.4. Antibacterial tests

2.4.1. Preparation of McFarland solution

McFarland solution (tube No. 0.5) consists of solution (A) which was prepared by dissolving 1.75g of Barium chloride $BaCl_2.H_2O$ in 100 ml of distilled water and solution (B) which was prepared by adding 1 ml of concentrated H_2SO_4 in 100 ml of distilled water. Immediately, 0.5 ml of solution (A) was added to 99.5 ml of solution (B).

This resulting solution was used for comparison to give the approximately number of germ cells (1.5×10^8 cell /ml) in bacterial cell suspension which is used in antibacterial activity[99].

2.4.2. Preparation of bacterial suspension

Brain heart infusion broth (BHI) broth were inoculated with tested bacterial isolates and incubated at 37 ^oC for 24h, then their turbidity was compared against standard McFarland solution No. (0.5).

Then an amount of 0.1 ml of isolates broth containing approximately (1.5×10^8 cell /ml), was spread it onto Muller Hinton agar plate by using a cotton swab and the plate approximately 60^o for each direction then plates were kept to stand upside down at room temperature for 15 min, the plat put in an incubation at 37 C for 24 h and by sterile rule the diameter of inhibition zone was determine[100].

2.4.3. Preparation of implant mediums (Agar)

The Muller Hinton agar medium was prepared by dissolving 38 g in 1000 ml of distilled water, boiled to dissolve the agar completely, sterilized by autoclave at 121 ^oC for 15 min and allowed to cool down to 45 ^oC. After that, the agar will pour into petridishes so it will be ready to be use[101].

2.4.4. Antibacterial tests method

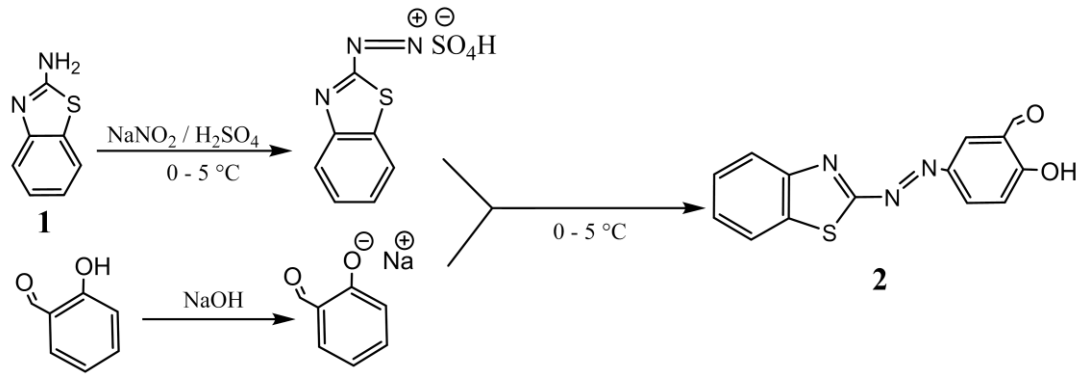
The antibacterial test has been carried out according to the disc diffusion method[102]. All synthesized imidazolidine **4a-h** and **5a-h** have been examined for their antibacterial activity *in vitro* against one type of Gram-positive bacteria (*Staphylococcus aurous*) and one type of Gram-negative bacteria (*Escherichia coli*). The agar plates have been surface- inoculated uniformly from both culture of the tested bacteria. In the solidified medium suitably spaced apart holes were made all 6 mm in diameter. These holes were filled with 40 µL of the prepared compounds (10 mg of the compound dissolved in 1ml of DMSO solvent). These plates have been incubated at 37 ^{o}C for 24 h. for both bacteria. The zones of bacterial growth inhibition around the discs have been measured in (mm).

Chapter Three

Results And Discussion

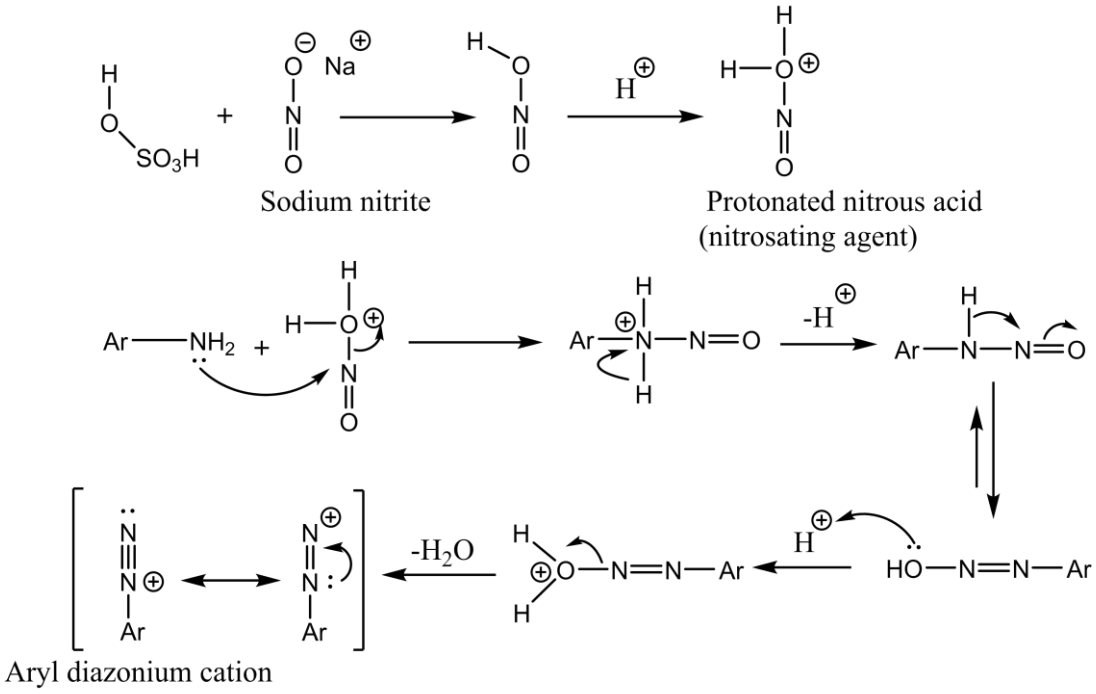
3.1. Synthesis of (E)-5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxybenzaldehyde 2

A coupling reaction between the diazonium salt of 2-aminobenzothiazole generated using H_2SO_4 and 2-hydroxybenzaldehyde dissolved in NaOH solution at (0-5) ^oC afforded azoaldehyde derivative **2**. Scheme (3-1).

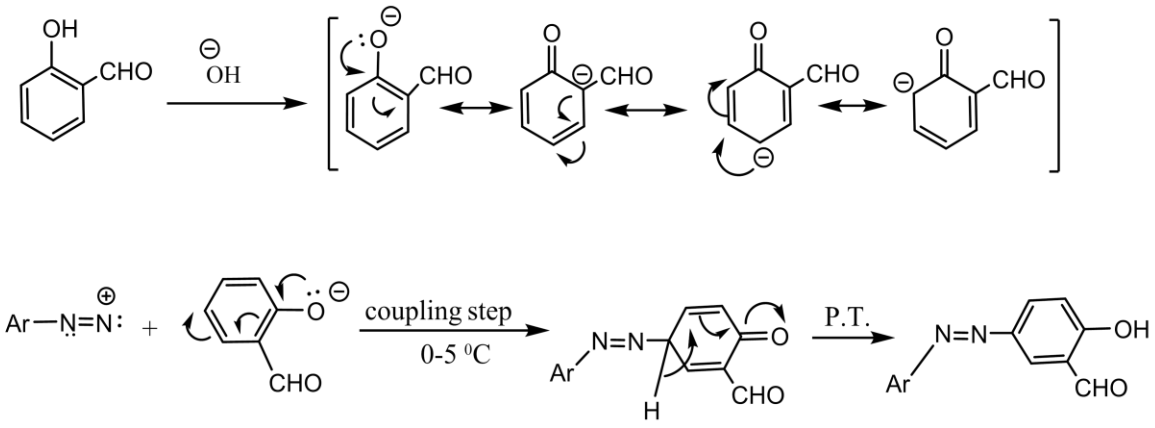


Scheme (3-1)

The coupling reaction is an electrophilic substitution reaction in aromatic systems proceeds according to the mechanism[103] described in Schemes (3-2 and 3-2a).



Scheme (3-2)

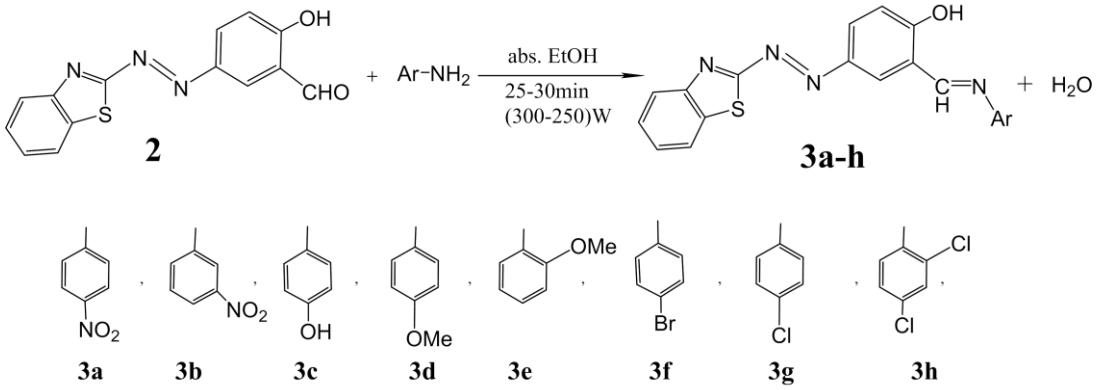


Scheme (3-2a)

FT-IR spectrum of azoaldehyde derivative **2**, fig. (3-2) showed disappearance of the sharp bands at 3375 cm^{-1} and 3306 cm^{-1} attributed to asymmetric and symmetric stretching vibrations of (NH_2) group in benzothiazole, fig. (3-1), and appearance of absorption band at 1375 cm^{-1} attributed to the stretching vibration of azo group (N=N). The band of (C=O) group stretching appeared at 1645 cm^{-1}. The (O-H) stretching appeared as a broad band at 3429 cm^{-1}. Other bands were listed in Table (3-1).

3.2. Synthesis of imine derivatives 3a-h

Aldehyde group in azoaldehyde derivative 2 was condensed with amino group of eight primary aromatic amines including (4-nitroaniline, 3-nitroaniline, 4-hydroxyaniline, 4-methoxyaniline, 2-methoxyaniline, 4-bromoaniline, 4-chloroaniline and 2,4-dichloroaniline, respectively) under microwave irradiation in absolute ethanol to produce eight imine derivatives 3a-h, respectively, in short reaction time and good yields as the platforms for this work, Scheme (3-3).



Scheme (3-3)

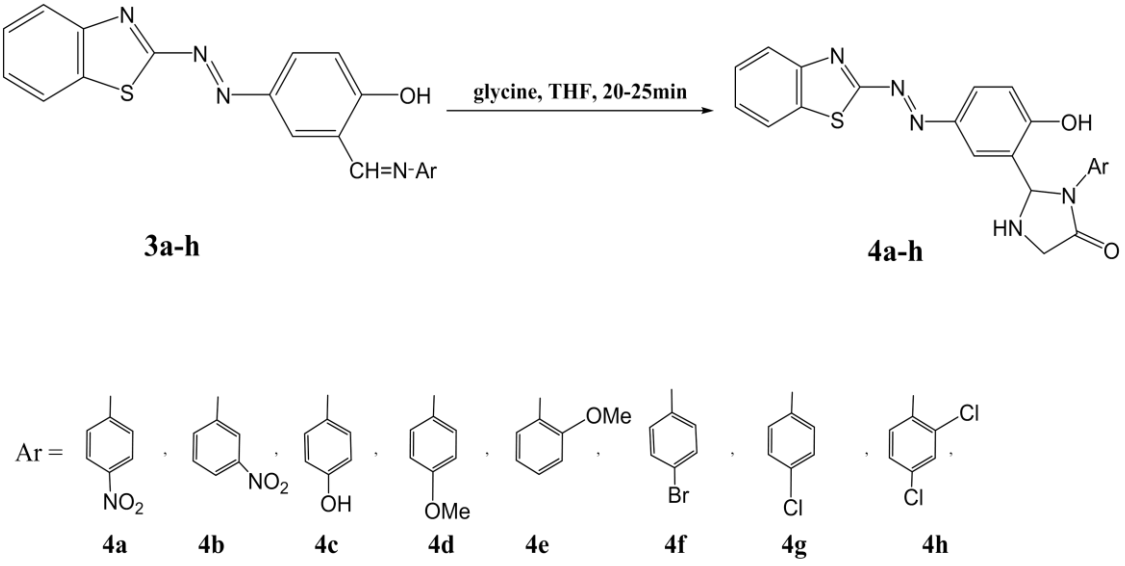
FT-IR spectra, figures (3-3)-(3-10) at ν (cm^{-1}) (KBr) of the synthesized imines **3a-h** illustrate good evidence that the reactions happened successfully by disappearing the strong band at 1645 cm^{-1} belong to the stretching vibration of (C=O) group and appearing medium-strong band at lower frequency at the range 1604-1633 cm^{-1} attributed to the stretching vibration of imine group (C=N). The benzothiazolic (C=N)str appeared at the range 1589-1610 cm^{-1}. Also, the spectra were devoid of the sharp bands for asymmetric and symmetric stretching vibrations of (NH_2) group at the general range 3400-3250 cm^{-1}. Other characteristic bands with their interpretation were summarized in Table (3-1).

Table (3-1): FT-IR data of imine derivatives 3a-h in cm^{-1}

Com. no.	FT-IR bands
2	3429_{br} (νO-H), 3068 (νC-H, benzene), 2856 and 2715 (νC-H, aldehyde), 1645 (νC=O, aldehyde), 1610 (νC=N, benzothiazole), 1502 and 1475 (νC=C, benzene), 1375 (νN=N), 759 (δo.o.p.C-H, benzene).
3a	3371 (νO-H), 3064 (νC-H, benzene), 1608 (νC=N, imine), 1589 (νC=N, benzothiazole), 1514 ($\nu as.NO_2$), 1448 (νC=C, benzene), 1404 (νN=N), 1336 ($\nu s.NO_2$), 758 (δo.o.p.C-H, benzene).
3b	3246 (νO-H), 3088 (νC-H, benzene), 1604 (νC=N, imine and νC=N, benzothiazole, vib. coupling), 1573 and 1502 and 1444 (νC=C, benzene), 1525 ($\nu as.NO_2$), 1396 (νN=N), 1354 ($\nu s.NO_2$), 758 (δo.o.p.C-H, benzene).
3c	3369 and 3298 (νO-H), 3032 (νC-H, benzene), 1610 (νC=N, imine and νC=N, benzothiazole, vib. coupling), 1514 and 1460 (νC=C, benzene), 1379 (νN=N), 827 (δo.o.p.C-H, benzene).
3d	3371 and 3298 (νO-H), 3037 (νC-H, benzene), 2949 ($\nu as.CH_3$), 1622 (νC=N, imine), 1595 (νC=N, benzothiazole), 1512 and 1456 (νC=C, benzene), 1392 (νN=N), 821 (δo.o.p.C-H, benzene).
3e	3462 and 3265 (νO-H), 3064 (νC-H, benzene), 2968 ($\nu as.CH_3$), 2870 ($\nu s.CH_3$), 1633 (νC=N, imine), 1608 (νC=N, benzothiazole), 1533, 1504 and 1444 (νC=C, benzene), 1363 (νN=N), 831 (δo.o.p.C-H, benzene).
3f	3369 and 3261 (νO-H), 3066 (νC-H, benzene), 1633 (νC=N, imine), 1608 (νC=N, benzothiazole), 1506 and 1489 (νC=C, benzene), 1363 (νN=N), 821 (δo.o.p.C-H, benzene).
3g	3369 and 3263 (νO-H), 3064 (νC-H, benzene), 1633 (νC=N, imine), 1606 (νC=N, benzothiazole), 1537, 1496 and 1442 (νC=C, benzene), 1367 (νN=N), 821 (δo.o.p.C-H, benzene).
3h	3470 and 3265 (νO-H), 3061 (νC-H, benzene), 1633 (νC=N, imine), 1608 (νC=N, benzothiazole), 1570, 1533, 1500 and 1444 (νC=C, benzene), 1363 (νN=N), 831 (δo.o.p.C-H, benzene).

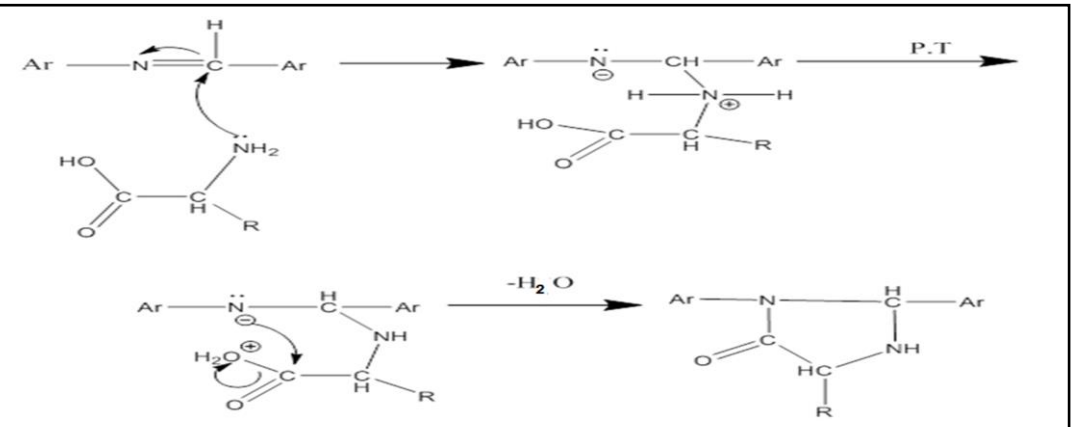
3.3. Synthesis of imidazolidines 4a-h

This series of imidazolidine derivatives was obtained in good yields and short reaction time via reaction of glycine with the synthesized imines **3a-h** using microwave irradiation in tetrahydrofuran, Scheme (3-4).



Scheme (3-4)

The reaction mechanism for formation of imidazolidine ring was described in Scheme (3-5)[104].



Scheme (3-5)

TLC technique showed that the rate of reaction is relatively increased in presence of electron-withdrawing groups substituted in benzene ring which is directly bonded with imine group nitrogen atom, the reason is due to the increasing the electrophilicity on the imine group carbon atom.

FT-IR spectra, Figures (3-11)-(3-18) of compounds **4a-h** provide good evidence that the reactions happened successfully through appearing a strong band at the range 1666-1710 cm^{-1} attributed to the (C=O)str of the imidazolidine ring. The spectra also showed the appearance of absorption band at the range 1653-1683 cm^{-1} assigned to the (N-H)bend of the imidazolidine ring. The benzothiazolic (C=N)str appeared at the range 1602-1616 cm^{-1}. Other characteristic bands with their interpretation were summarized in table (3-2).

Table (3-2): FT-IR data of imidazolidine derivatives 4a-h in cm^{-1}

Com. no.	FT-IR bands
4a	3365_{br} (νO-H and νN-H, imidazolidine, vib. coupling), 3074 (νC-H, benzene), 1708 (νC=O, imidazolidine), 1680 (δN-H, imidazolidine), 1539 and 1456 (νC=C, benzene), 1516 (νas.NO_2), 1419 (νN=N), 1321 (νs.NO_2), 756 (δo.o.p.C-H, benzene).
4b	3402_{br} (νO-H and νN-H, imidazolidine, vib. coupling), 3074 (νC-H, benzene), 1710 (νC=O, imidazolidine), 1683 (δN-H, imidazolidine), 1604 (νC=N, benzothiazole), 1508 (νas.NO_2), 1456 and 1421 (νC=C, benzene), 1384 (νN=N), 1323 (νs.NO_2), 759 (δo.o.p.C-H, benzene).
4c	3200_{br} (νO-H and νN-H, imidazolidine, vib. coupling), 3080 (νC-H, benzene), 1670 (νC=O and δN-H, imidazolidine, vib. coupling), 1616 (νC=N, benzothiazole), 1539, 1514 and 1454 (νC=C, benzene), 1417 (νN=N), 893 (δo.o.p.C-H, benzene).
4d	3250_{br} (νO-H and νN-H, imidazolidine, vib. coupling), 3074 (νC-H, benzene), 2964 (νas.CH_3) 1670 (νC=O and δN-H, imidazolidine, vib. coupling), 1602 (νC=N, benzothiazole), 1514 and 1458 (νC=C, benzene), 1421 (νN=N), 829 (δo.o.p.C-H, benzene).

Com. no.	FT-IR bands
4e	3192_{br} (νO-H and νN-H, imidazolidine, vib. coupling), 3072 (νC-H, benzene), 1681 (νC=O, imidazolidine), 1653 (δN-H, imidazolidine), 1610 (νC=N, benzothiazole), 1558, 1541 and 1456 (νC=C, benzene), 1423 (νN=N), 823 (δo.o.p.C-H, benzene).
4f	3176_{br} (νO-H and νN-H, imidazolidine, vib. coupling), 3063 (νC-H, benzene), 1666 (νC=O and δN-H, imidazolidine, vib. coupling), 1610 (νC=N, benzothiazole), 1508 (νC=C, benzene), 1415 (νN=N), 823 (δo.o.p.C-H, benzene).
4g	3184_{br} (νO-H and νN-H, imidazolidine, vib. coupling), 3066 (νC-H, benzene), 1670 (νC=O and δN-H, imidazolidine, vib. coupling), 1610 (νC=N, benzothiazole), 1523 and 1508 (νC=C, benzene), 1417 (νN=N), 893 (δo.o.p.C-H, benzene).
4h	3232_{br} (νO-H and νN-H, imidazolidine, vib. coupling), 3082 (νC-H, benzene), 1681 (νC=O, imidazolidine), 1653 (δN-H, imidazolidine, vib. coupling), 1608 (νC=N, benzothiazole), 1554, 1541 and 1508 (νC=C, benzene), 1423 (νN=N), 819 (δo.o.p.C-H, benzene).

^{1}H NMR spectra of imidazolidines 4a-h

The structures of imidazolidine compounds **4a-h**, Figures (3-27)-(3-34) were proven by their ^{1}H NMR spectra (500 MHz, DMSO-d_6) which showed the peak for the methylene protons (CH_2) of imidazolidine ring as a doublet at δ 3.68–3.74 ppm. The (N-CH-N) proton of imidazolidine ring appeared as a doublet at 6.52–6.78 ppm. The (Ar-H) protons at δ 6.67–8.14 ppm, the (N-H) proton of imidazolidine ring as a singlet at 8.12–9.29 ppm. The (O-H) proton as a singlet at 9.17–9.64 ppm. The methoxy protons (O-CH_3) in compounds **4d** and **4e** appeared as a singlet at δ 3.94 and 3.83 ppm, respectively. The singlet signals around 2.49 ppm and 3.35–3.51 ppm

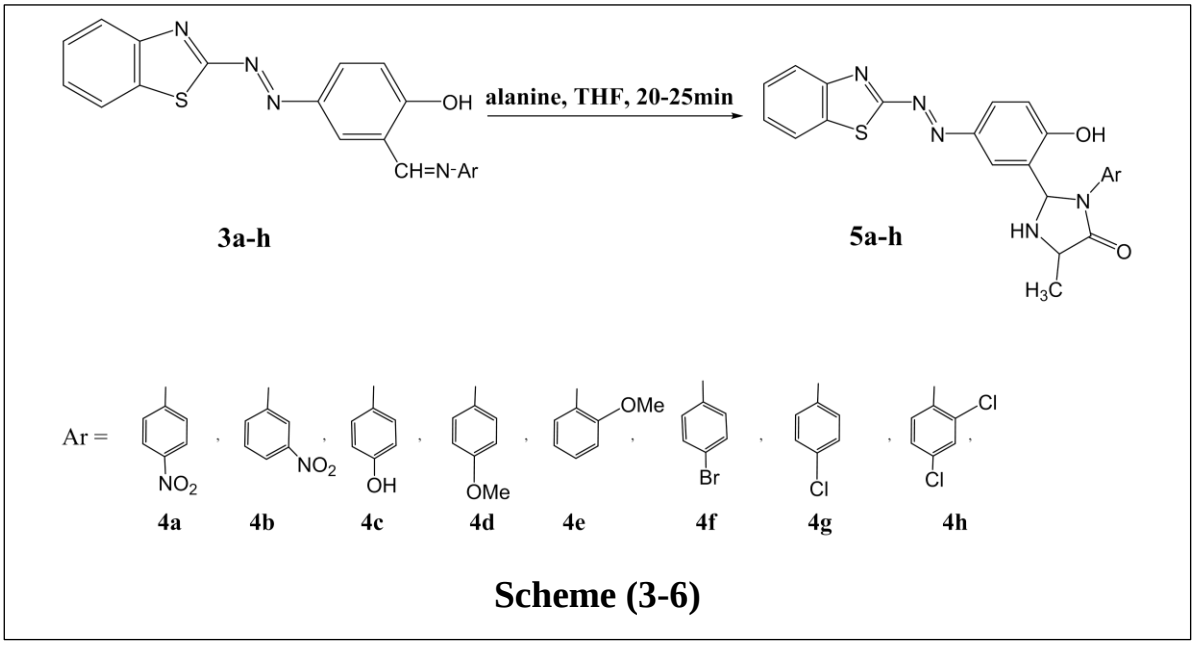
attributed to DMSO and absorbed H_2O in DMSO, respectively. The ^1H NMR data of compounds **4a-h** were summarized in table (3-3).

Table (3-3): ^1H NMR data of compounds 4a-h in ppm

Com. no.	^1H NMR δ (ppm)
4a	3.69 (d, J = 6.5 Hz, 2H, CH_2, imidazolidine), 6.63 (d, J = 8.1 Hz, 1H, CH, imidazolidine), 7.37–7.96 (11H, Ar–H), 8.14 (s, 1H, N–H, imidazolidine), 9.48 (s, 1H, O–H).
4b	3.69 (d, J = 20.0 Hz, 2H, CH_2, imidazolidine), 6.62 (s, 1H, CH, imidazolidine), 6.92–7.97 (11H, Ar–H), 8.12 (s, 1H, N–H, imidazolidine), 9.56 (s, 1H, O–H).
4c	3.69 (d, J = 11.3 Hz, 2H, CH_2, imidazolidine), 6.63 (d, J = 7.3 Hz, 1H, CH, imidazolidine), 6.89–7.99 (11H, Ar–H), 8.12 (s, 1H, N–H, imidazolidine), 9.53 (s, 2H, 2×O–H).
4d	3.69 (d, J = 12.8 Hz, 2H, CH_2, imidazolidine), 3.94 (s, 3H, O–CH3), 6.63 (d, J = 8.3 Hz, 1H, CH, imidazolidine), 6.79–7.98 (11H, Ar–H), 8.15 (s, 1H, N–H, imidazolidine), 9.52 (s, 1H, O–H).
4e	3.69 (d, J = 12.8 Hz, 2H, CH_2, imidazolidine), 3.83 (s, 3H, O–CH3), 6.77 (d, J = 8.3 Hz, 1H, CH, imidazolidine), 7.01–7.99 (11H, Ar–H), 8.15 (s, 1H, N–H, imidazolidine), 9.62 (s, 1H, O–H).
4f	3.69 (d, J = 23.8 Hz 2H, CH_2, imidazolidine), 6.54 (d, J = 8.0 Hz, 1H, CH, imidazolidine), 6.67–8.00 (11H, Ar–H), 8.15 (s, 1H, N–H, imidazolidine), 9.64 (s, 1H, O–H).
4g	3.69 (d, J = 23.8 Hz, 2H, CH_2, imidazolidine), 6.52 (d, J = 8.0 Hz, 1H, CH, imidazolidine), 6.67–7.99 (11H, Ar–H), 8.15 (s, 1H, N–H, imidazolidine), 9.17 (s, 1H, O–H).
4h	3.68 (d, J = 7.4 Hz, 2H, CH_2, imidazolidine), 6.74 (d, J = 8.3 Hz, 1H, CH, imidazolidine), 7.01–8.14 (10H, Ar–H), 9.29 (s, 1H, N–H, imidazolidine), 9.62 (s, 1H, O–H).

3.4. Synthesis of imidazolidines 5a-h

The reaction of imine group of imines **3a-h** with L-alanine using microwave irradiation in tetrahydrofuran produced the imidazolidine derivatives of benzothiazole **5a-h** in good yields and short reaction time. Scheme (3-6).



Scheme (3-6)

FT-IR spectra, Figures (3-19)-(3-26) of compounds **5a-h** afford good evidence that the reactions happened successfully through appearing a strong band at the range 1664-1710 cm^{-1} attributed to the (C=O)str of the imidazolidine ring. The spectra also showed the appearance of absorption band at the range 1651-1668 cm^{-1} belong to the (N-H) bend of the imidazolidine ring. The benzothiazolic (C=N)str. appeared at the range 1597-1618 cm^{-1}. Other characteristic bands with their interpretation were summarized in table (3-4).

Table (3-4): FT-IR data of imidazolidine derivatives 5a-h in cm^{-1}

Com. no.	FT-IR bands
5a	3234_{br} (νO-H and νN-H, imidazolidine, vib. coupling), 3057 (νC-H, benzene), 1664 (νC=O and δN-H, imidazolidine, vib. coupling), 1597 (νC=N, benzothiazole), 1510 ($\nu as.NO_2$), 1452 (νC=C, benzene), 1421 (νN=N), 1286 ($\nu s.NO_2$), 754 (δo.o.p.C-H, benzene).
5b	3203_{br} (νO-H and νN-H, imidazolidine, vib. coupling), 3064 (νC-H, benzene), 1668 (νC=O, imidazolidine), 1653 (δN-H, imidazolidine), 1604 (νC=N, benzothiazole), 1558 and 1454 (νC=C, benzene), 1510 ($\nu as.NO_2$), 1423 (νN=N), 1288 ($\nu s.NO_2$), 825 (δo.o.p.C-H, benzene).
5c	3209_{br} (νO-H and νN-H, imidazolidine, vib. coupling), 3093 (νC-H, benzene), 2987 ($\nu as.C\text{-}H_3$), 1668 (νC=O and δN-H, imidazolidine, vib. coupling), 1599 (νC=N, benzothiazole), 1514 and 1456 (νC=C, benzene), 1413 (νN=N), 823 (δo.o.p.C-H, benzene).
5d	3203 (νO-H), 3171 (νN-H, imidazolidine), 3070 (νC-H, benzene), 2943 ($\nu as.CH_3$) 1674 (νC=O, imidazolidine), 1658 (δN-H, imidazolidine), 1606 (νC=N, benzothiazole), 1516 and 1454 (νC=C, benzene), 1427 (νN=N), 827 (δo.o.p.C-H, benzene).
5e	3196_{br} (νO-H and νN-H, imidazolidine, vib. coupling), 3059 (νC-H, benzene), 1674 (νC=O, imidazolidine), 1660 (δN-H, imidazolidine), 1612 (νC=N, benzothiazole), 1548, 1512 and 1452 (νC=C, benzene), 1425 (νN=N), 821 (δo.o.p.C-H, benzene).
5f	3188_{br} (νO-H and νN-H, imidazolidine, vib. coupling), 3061 (νC-H, benzene), 2943 (νCH_3), 1668 (νC=O and δN-H, imidazolidine, vib. coupling), 1604 (νC=N, benzothiazole), 1504 and 1452 (νC=C, benzene), 1425 (νN=N), 823 (δo.o.p.C-H, benzene).
5g	3419_{br} (νO-H and νN-H, imidazolidine, vib. coupling), 3063 (νC-H, benzene), 1680 (νC=O, imidazolidine) 1651 (δN-H, imidazolidine), 1618 (νC=N, benzothiazole), 1558, 1539, 1512 and 1454 (νC=C, benzene), 1421 (νN=N), 817 (δo.o.p.C-H, benzene).
5h	3443_{br} (νO-H), 3213 (νN-H, imidazolidine), 3064 (νC-H, benzene), 1681 (νC=O, imidazolidine), 1651 (δN-H, imidazolidine, vib. coupling), 1610 (νC=N, benzothiazole), 1556, 1539, 1510 and 1456 (νC=C, benzene), 1423 (νN=N), 823 (δo.o.p.C-H, benzene).

^{1}H NMR spectra of imidazolidines 5a-h

The structures of imidazolidine compounds **5a-h**, Figures (3-35)-(3-42) were deduced by their ^{1}H NMR spectra which appeared doublet signal at δ 1.23–1.24 ppm, respectively belong to the methyl (CH_3) protons, the peak for the methine proton (C**H**-CH_3) of imidazolidine ring as a quartet at 3.78–3.85 ppm, respectively. The (N-CH-N) proton of imidazolidine appeared as a doublet at 6.51–6.64 ppm, respectively. The (Ar-H) protons at δ 6.66 –7.73 ppm, the (N-H) proton of imidazolidine ring as a singlet at 8.06–8.07 ppm, respectively. The (O-H) proton as a singlet at 9.49–10.12 ppm, respectively. The methoxy protons (O-CH_3) in compounds **5d** and **5e** appeared as a singlet at δ 3.61 and 4.16 ppm, respectively. The singlet signals around 2.49 ppm and 3.33–3.42 ppm attributed to DMSO and absorbed H_2O in DMSO, respectively. The ^{1}H NMR data of compounds **5a-h** were summarized in table (3-5).

Table (3-5): ^{1}H NMR data of compounds 5a-h in ppm

Com. no.	^{1}H NMR δ (ppm)
5a	1.24 (d, *J* = 6.7 Hz, 3H, CH_3), 3.84 (q, *J* = 6.7 Hz, 1H, CH–CH_3, imidazolidine), 6.52 (d, *J* = 7.8 Hz, 1H, N–CH–N, imidazolidine), 6.67–7.61 (11H, Ar–H), 8.07 (s, 1H, N–H, imidazolidine), 9.51 (s, 1H, O–H).
5b	1.24 (d, *J* = 6.7 Hz, 3H, CH_3), 3.78 (q, *J* = 7.0 Hz, 1H, CH–CH_3, imidazolidine), 6.52 (d, *J* = 8.1 Hz, 1H, N–CH–N, imidazolidine), 6.66–7.61 (11H, Ar–H), 8.06 (s, 1H, N–H, imidazolidine), 9.49 (s, 1H, O–H).
5c	1.24 (d, *J* = 6.9 Hz, 3H, CH_3), 3.84 (q, *J* = 7.0 Hz, 1H, CH–CH_3, imidazolidine), 6.51 (d, *J* = 8.1 Hz, 1H, N–CH–N, imidazolidine), 6.66–7.66 (11H, Ar–H), 8.07 (s, 1H, N–H, imidazolidine), 10.12 (s, 2H, 2×O–H).
5d	1.23 (d, *J* = 6.7 Hz, 3H, CH_3), 3.61 (s, 1H, O–CH_3), 3.85 (q, *J* = 6.6 Hz, 1H, CH–CH_3, imidazolidine), 6.52 (d, *J* = 8.0 Hz, 1H, N–CH–N, imidazolidine), 6.74–7.60 (11H, Ar–H), 8.06 (s, 1H, N–H, imidazolidine), 9.51 (s, 1H, O–H).
5e	1.24 (d, *J* = 6.7 Hz, 3H, CH_3), 3.84 (q, *J* = 6.8 Hz, 1H, CH–CH_3, imidazolidine), 4.16 (s, 1H, O–CH_3), 6.53 (d, *J* = 8.1 Hz, 1H, N–CH–N, imidazolidine), 6.70–7.73 (11H, Ar–H), 8.06 (s, 1H, N–H, imidazolidine), 9.64 (s, 1H, O–H).
5f	1.24 (d, *J* = 6.8 Hz, 3H, CH_3), 3.84 (q, *J* = 7.0 Hz, 1H, CH–CH_3, imidazolidine), 6.64 (d, *J* = 8.0 Hz, 1H, N–CH–N, imidazolidine), 7.00–7.61 (11H, Ar–H), 8.06 (s, 1H, N–H, imidazolidine), 9.50 (s, 1H, O–H).
5g	1.24 (d, *J* = 6.7 Hz, 3H, CH_3), 3.84 (q, *J* = 6.8 Hz, 1H, CH–CH_3, imidazolidine), 6.59 (d, *J* = 7.5 Hz, 1H, N–CH–N, imidazolidine), 7.02–7.61 (11H, Ar–H), 8.06 (s, 1H, N–H, imidazolidine), 9.53 (s, 1H, O–H).
5h	1.23 (d, *J* = 6.8 Hz, 3H, CH_3), 3.84 (q, *J* = 7.0 Hz, 1H, CH–CH_3, imidazolidine), 6.59 (d, *J* = 7.1 Hz, 1H, N–CH–N, imidazolidine), 6.81–7.73 (10H, Ar–H), 8.06 (s, 1H, N–H, imidazolidine), 9.65 (s, 1H, O–H).

(CHNS) Elemental analysis of compounds 4a-h and 5a-h

The (CHNS) elemental analysis results were all in good agreement with the proposed chemical structures for compounds **4a-h** and **5a-h** and given in Table (3-6).

Table (3-6): (CHNS) Elemental analysis of compounds 4a-h and 5a-h

Com. no.	Calculated %				Found %			
	C	**H**	**N**	**S**	**C**	**H**	**N**	**S**
4a	57.38	3.50	18.25	6.96	56.97	3.45	18.02	6.96
4b	57.38	3.50	18.25	6.96	57.01	3.45	18.12	6.37
4c	61.24	3.97	16.23	7.43	60.79	3.61	16.30	7.33
4d	62.01	4.30	15.72	7.20	61.88	4.26	15.51	7.01
4e	62.01	4.30	15.72	7.20	62.67	4.21	15.06	7.11
4f	53.45	3.62	14.17	6.49	52.69	3.59	13.99	6.45
4g	58.72	3.58	15.56	7.13	58.64	3.59	14.88	7.08
4h	54.54	3.12	14.46	6.61	53.98	3.05	14.30	6.54
5a	58.22	3.82	17.71	6.76	57.16	3.44	17.42	6.67
5b	58.22	3.82	17.71	6.76	58.88	3.52	17.35	6.62
5c	62.01	4.30	15.72	7.20	61.31	4.16	15.59	6.91
5d	62.73	4.61	15.24	6.98	62.44	4.32	15.21	6.75
5e	62.73	4.61	15.24	6.98	62.16	4.35	15.15	6.81
5f	54.33	3.57	13.77	6.03	53.66	3.33	13.43	6.10
5g	59.54	3.91	15.09	6.91	58.88	3.90	15.01	6.41
5h	55.41	3.43	14.09	6.43	54.96	3.29	13.94	6.43

3.5. Antibacterial activity

The antibacterial activity of all synthesized imidazolidines has been tested against Staphylococcus aurous (Gram-positive) and Escherichia coli (Gram-negative). The results of antibacterial action have been described in table (3-7) and photographs of growth inhibition zones have been illustrated in figures (3-43)-(3-47).

Table (3-7): The antibacterial activity of compounds 4a-h , 5a-h and Gentamycin as control drug

Bacteria	*Staphylococcus aurous* (Gram-positive)	*Escherichia coli* (Gram-negative)
Comp. no	**Diameter of inhibition zone in (mm)**	
4a	22	0
4b	18	15
4c	19	0
4d	16	16
4e	20	0
4f	0	10
4g	22	0
4h	21	17
5a	0	0
5b	11	0
5c	20	17
5d	19	0
5e	12	0
5f	20	16
5g	18	0
5h	22	0
DMSO	0	0
Gentamycin	15	15

Highly active (inhibition zone > 15 mm)

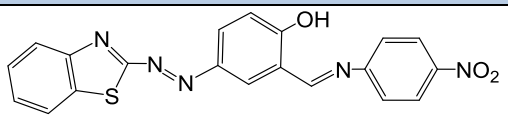
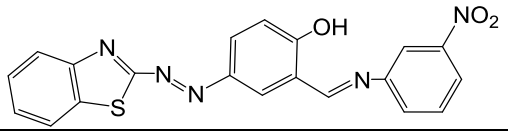
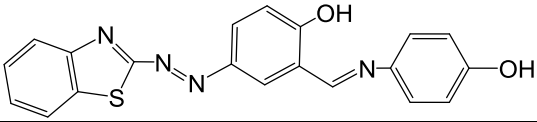
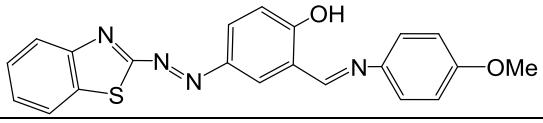
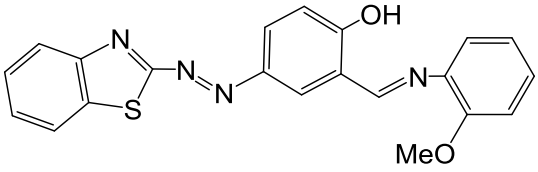
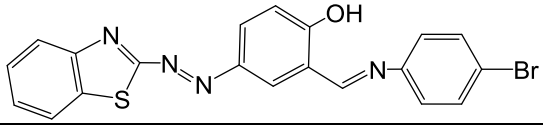
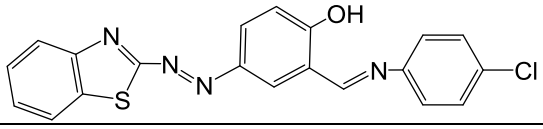
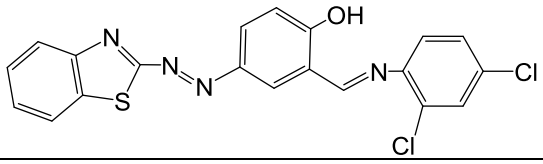
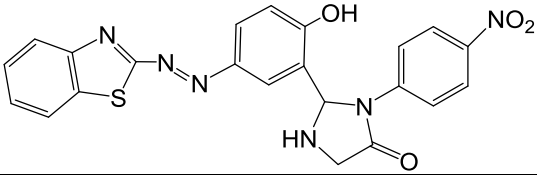
Moderately active (inhibition zone 11-15 mm)

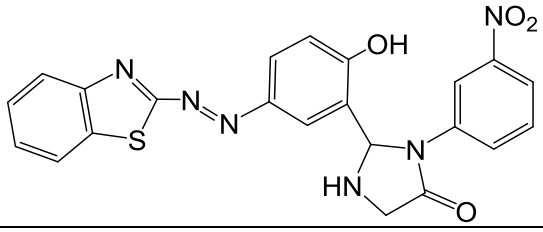
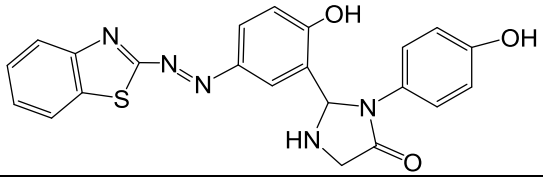
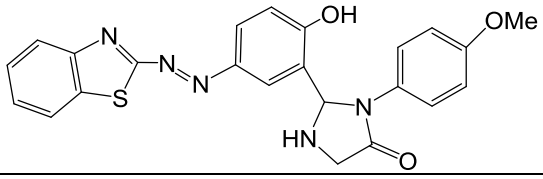
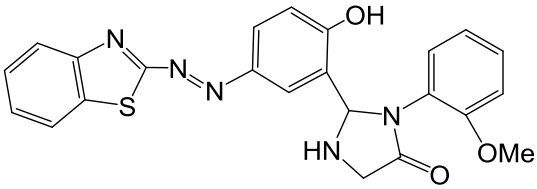
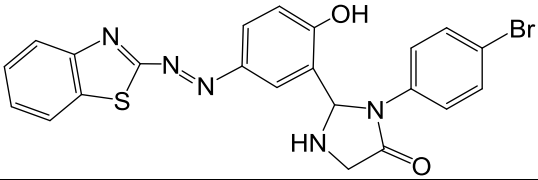
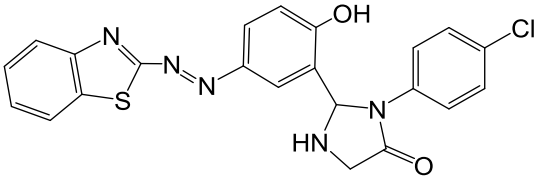
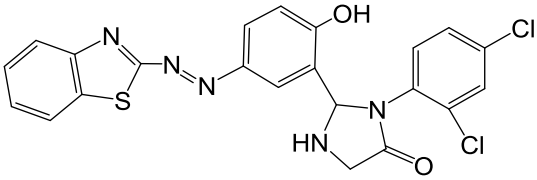
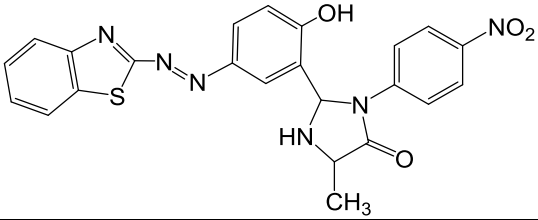
Slightly active (inhibition zone 5-10 mm)

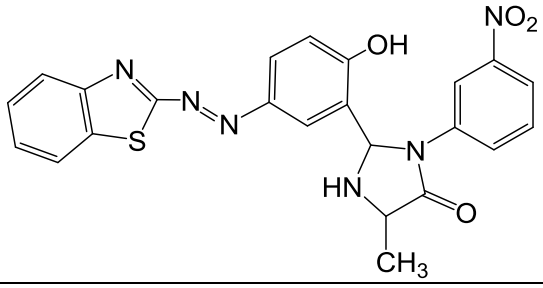
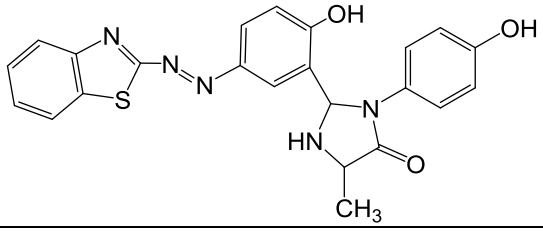
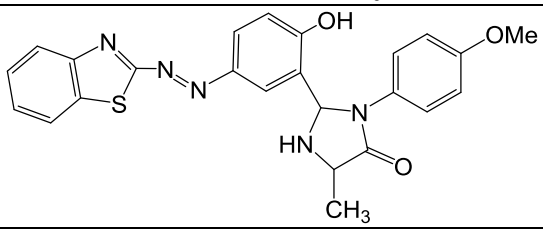
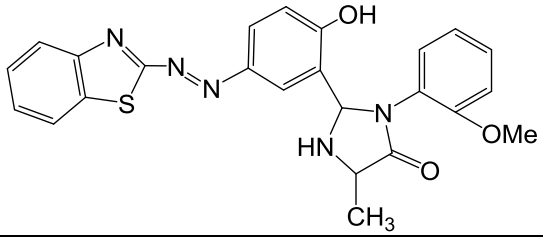
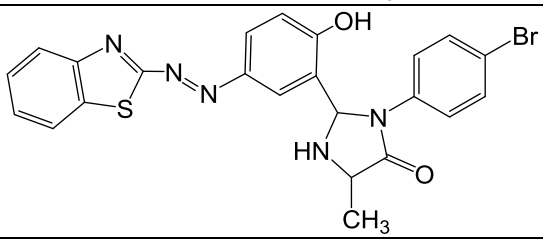
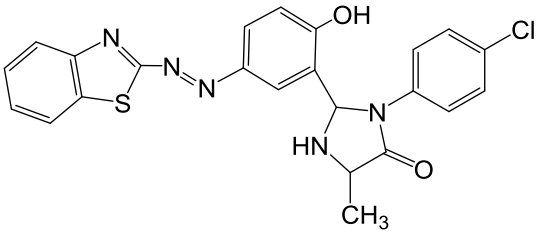
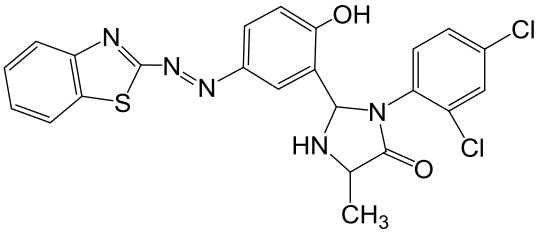
Inactive (inhibition zone < 5 mm)

From the data observed, it is found that Imidazolidine compounds 4a, 4b, 4c, 4d, 4e, 4g, 4h, 5c, 5d, 5f, 5g, and 5h were found to be of greater activity than gentamycin against Gram-positive bacteria. Moreover, compounds 4d, 4h, 5c, and 5f were also showed better activity to the control drug against Gram-negative bacteria.

Table (3-8): Names of the synthesized compounds

Comp. no	Structure	Name
3a		4-((E)-benzo[d]thiazol-2-yldiazenyl)-2-((E)-) ((4-nitrophenyl)imino)methyl)phenol.
3b		) 4-((E)-benzo[d]thiazol-2-yldiazenyl)-2-((E)-((3-nitrophenyl)imino)methyl)phenol.
3c		)4-((E)-benzo[d]thiazol-2-yldiazenyl)-2-((E)-((4-hydroxyphenyl)imino)methyl)phenol.
3d		)4-((E)-benzo[d]thiazol-2-yldiazenyl)-2-((E)-((4-methoxyphenyl)imino)methyl)phenol.
3e		) 4-((E)-benzo[d]thiazol-2-yldiazenyl)-2-((E)-((2-methoxyphenyl)imino)methyl)phenol.
3f		)4-((E)-benzo[d]thiazol-2-yldiazenyl)-2-((E)-((4-bromophenyl)imino)methyl)phenol.
3g		)4-((E)-benzo[d]thiazol-2-yldiazenyl)-2-((E)-((4-chlorophenyl)imino)methyl)phenol.
3h		) 4-((E)-benzo[d]thiazol-2-yldiazenyl)-2-((E)-((2,4-dichlorophenyl)imino)methyl)phenol.
4a		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(4-nitrophenyl)imidazolidin-4-one.

4b		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(3-nitrophenyl)imidazolidin-4-one.
4c		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(4-hydroxyphenyl)imidazolidin-4-one.
4d		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(4-methoxyphenyl)imidazolidin-4-one.
4e		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(2-methoxyphenyl)imidazolidin-4-one.
4f		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(4-bromophenyl)imidazolidin-4-one.
4g		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(4-chlorophenyl)imidazolidin-4-one.
4h		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(2,4-dichlorophenyl)imidazolidin-4-one.
5a		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-5-methyl-3-(4-nitrophenyl)imidazolidin-4-one.

5b		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-5-methyl-3-(3-nitrophenyl)imidazolidin-4-one.
5c		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(4-hydroxyphenyl)-5-methylimidazolidin-4-one.
5d		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(4-methoxyphenyl)-5-methylimidazolidin-4-one.
5e		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(2-methoxyphenyl)-5-methylimidazolidin-4-one.
5f		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(4-bromophenyl)-5-methylimidazolidin-4-one.
5g		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(4-chlorophenyl)-5-methylimidazolidin-4-one.
5h		(E)-2-(5-(benzo[d]thiazol-2-yldiazenyl)-2-hydroxyphenyl)-3-(2,4-dichlorophenyl)-5-methylimidazolidin-4-one.

Conclusions and Future work

Conclusions

1. The microwave irradiation is a efficient technique including short reaction time and high yield in comparison with the classical thermal method.
2. The rates of reactions of imines with glycine and alanine for formation of imidazolidines are approximately equal.
3. All synthesized imidazolidines could be converted to the corresponding phenol salts which are completely soluble in water.
4. The synthesized imidazolidines appeared higher biological action against Gram-positive bacteria than that of Gram-negative bacteria.
5. Imidazolidine compounds **4a**, **4b**, **4c**, **4d**, **4e**, **4g**, **4h**, **5c**, **5d**, **5f**, **5g**, and **5h** were found to be of greater activity than gentamycin against Gram-positive bacteria, while compounds **4d**, **4h**, **5c**, and **5f** showed better activity to the control drug against Gram-negative bacteria.

Future work

1. Synthesis of different azoimines via introducing the synthesized azoaldehyde in a condensation reactions with other primary amines which could be used as platforms for the synthesis of new imidazolidines.
2. Using the synthesized azoimines as precursors for the synthesis of β-Lactam derivatives via reaction with chloroacetyl chloride.
3. Treatment of the synthesized azoimines with cyclic anhydrides like maleic and succinic to obtained 1,3-oxazepines and 1,3-oxazepanes.
4. Evaluation the toxicity and minimum-influenced concentration for the synthesized imidazolidines.

5. Study the biological activity of the synthesized imidazolidines against other types of bacteria in addition to fungi, virus and some animal tissues diseases.

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Appendix

A. Spectroscopic figures

A.1. FT-IR spectra

A.1.1. FT-IR spectra of 2-aminobenzothiazole 1 and azoaldehyde derivative 2

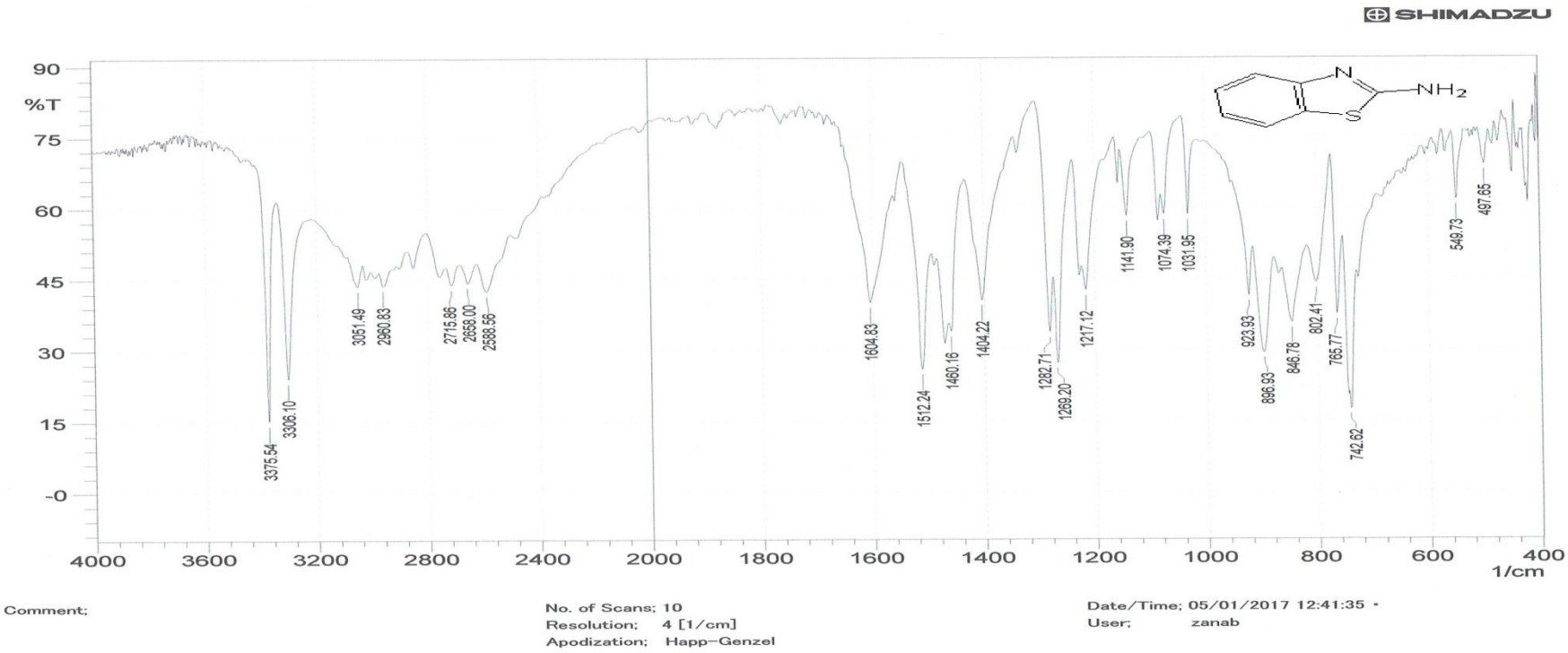


Fig. (3-1): FT-IR spectrum of **2-Aminobenzothiazole**

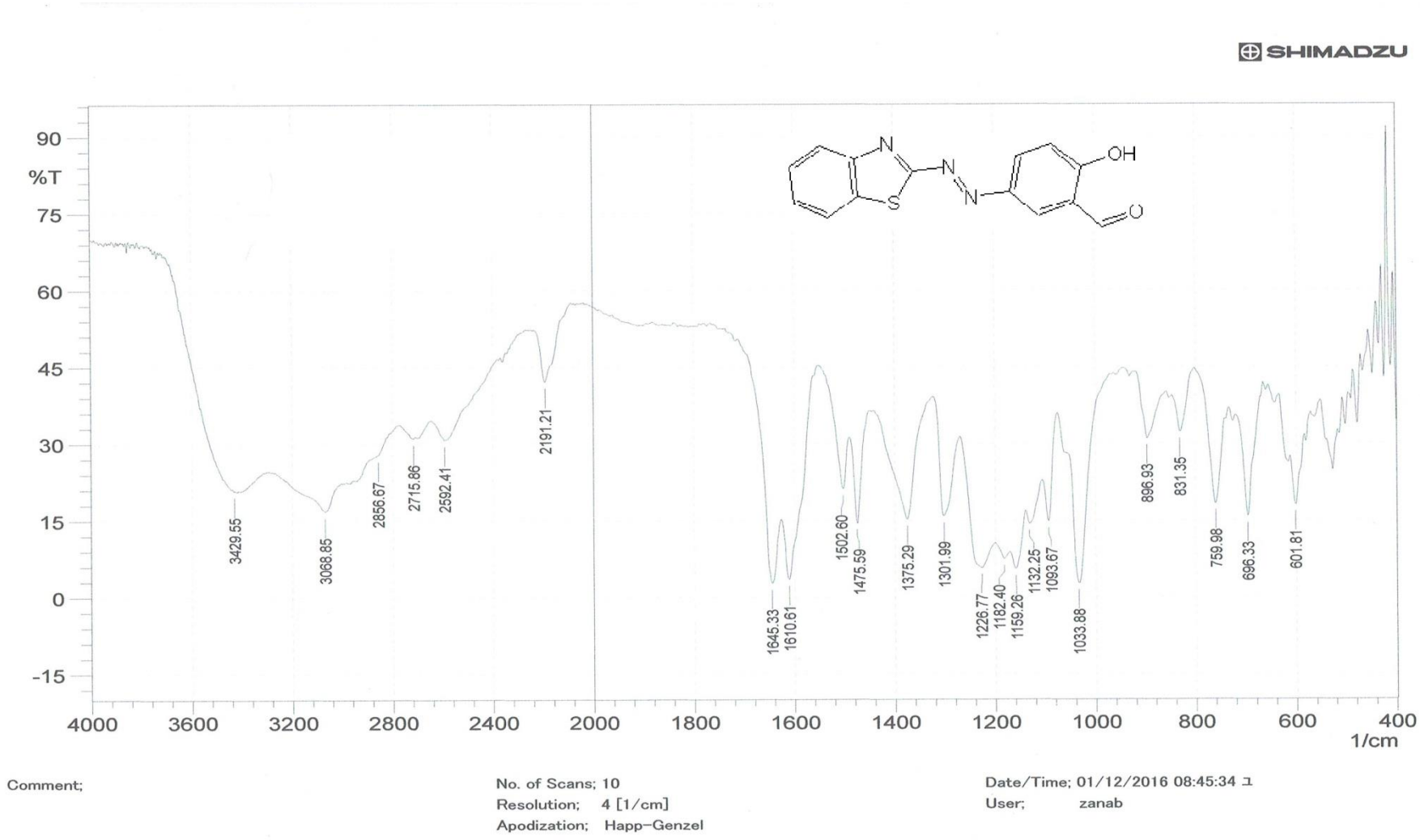


Fig. (3-2): FT-IR spectrum of **azoaldehyde** derivative **2**

A.1.2. FT-IR spectra of azoimine derivatives 3a-h

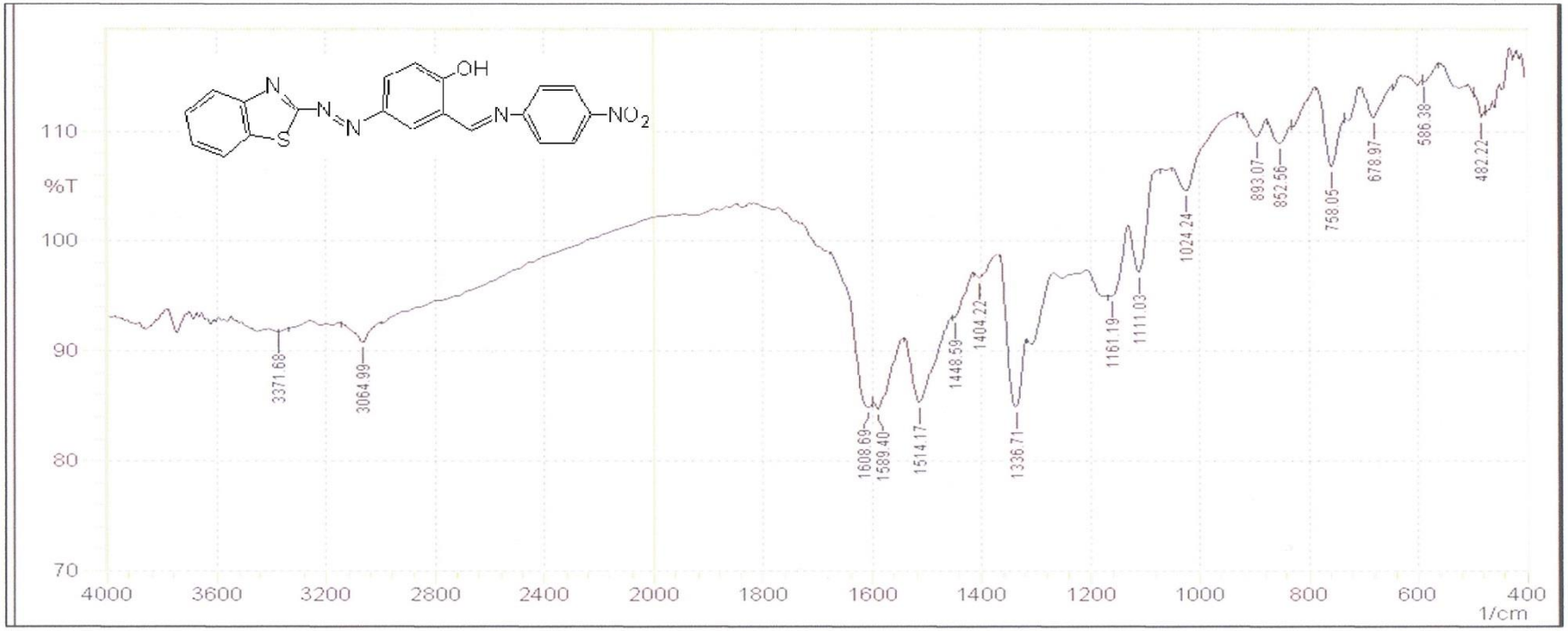


Fig. (3-3): FT-IR spectrum of compound **3a**

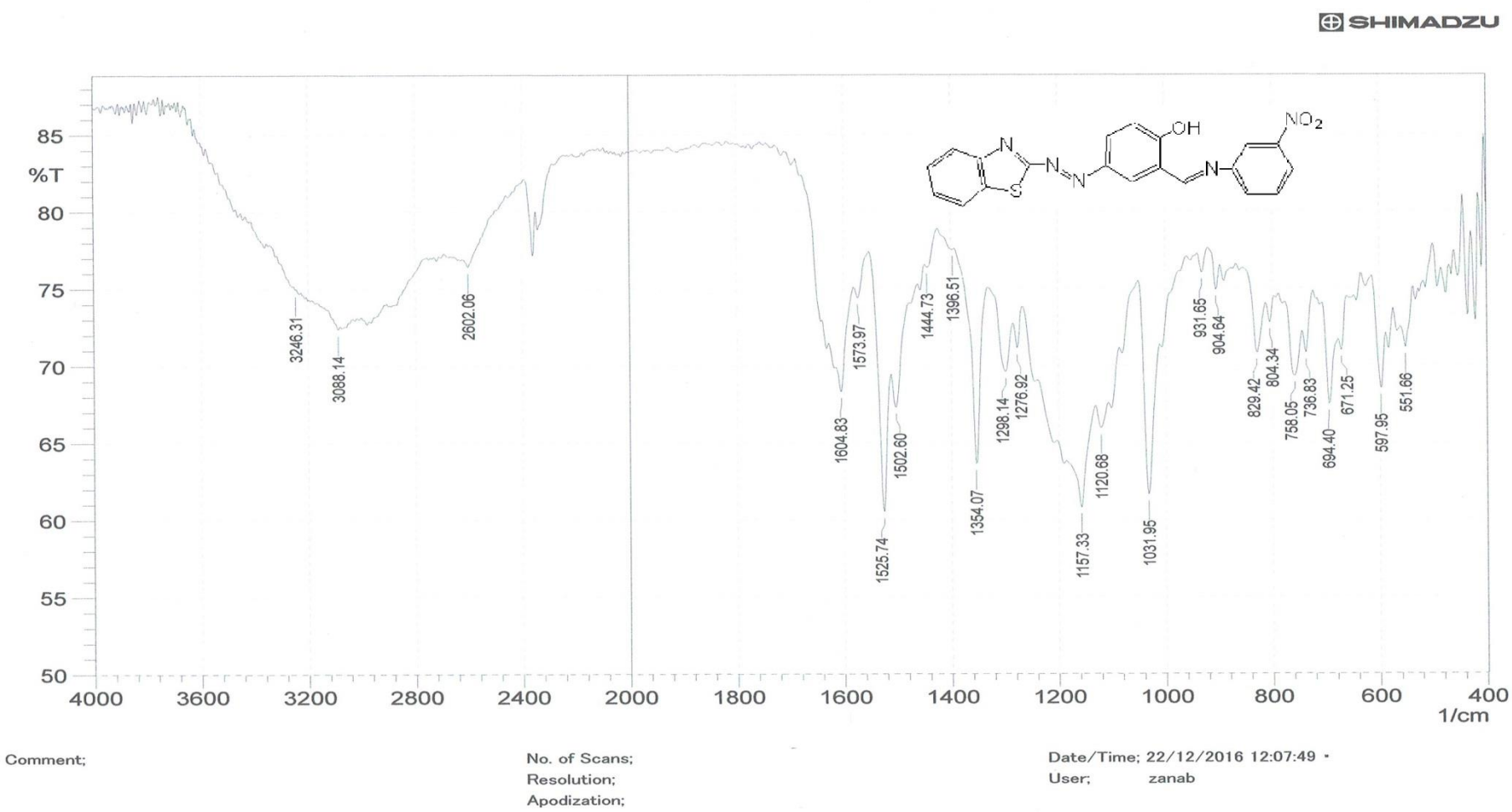


Fig. (3-4): FT-IR spectrum of compound **3b**

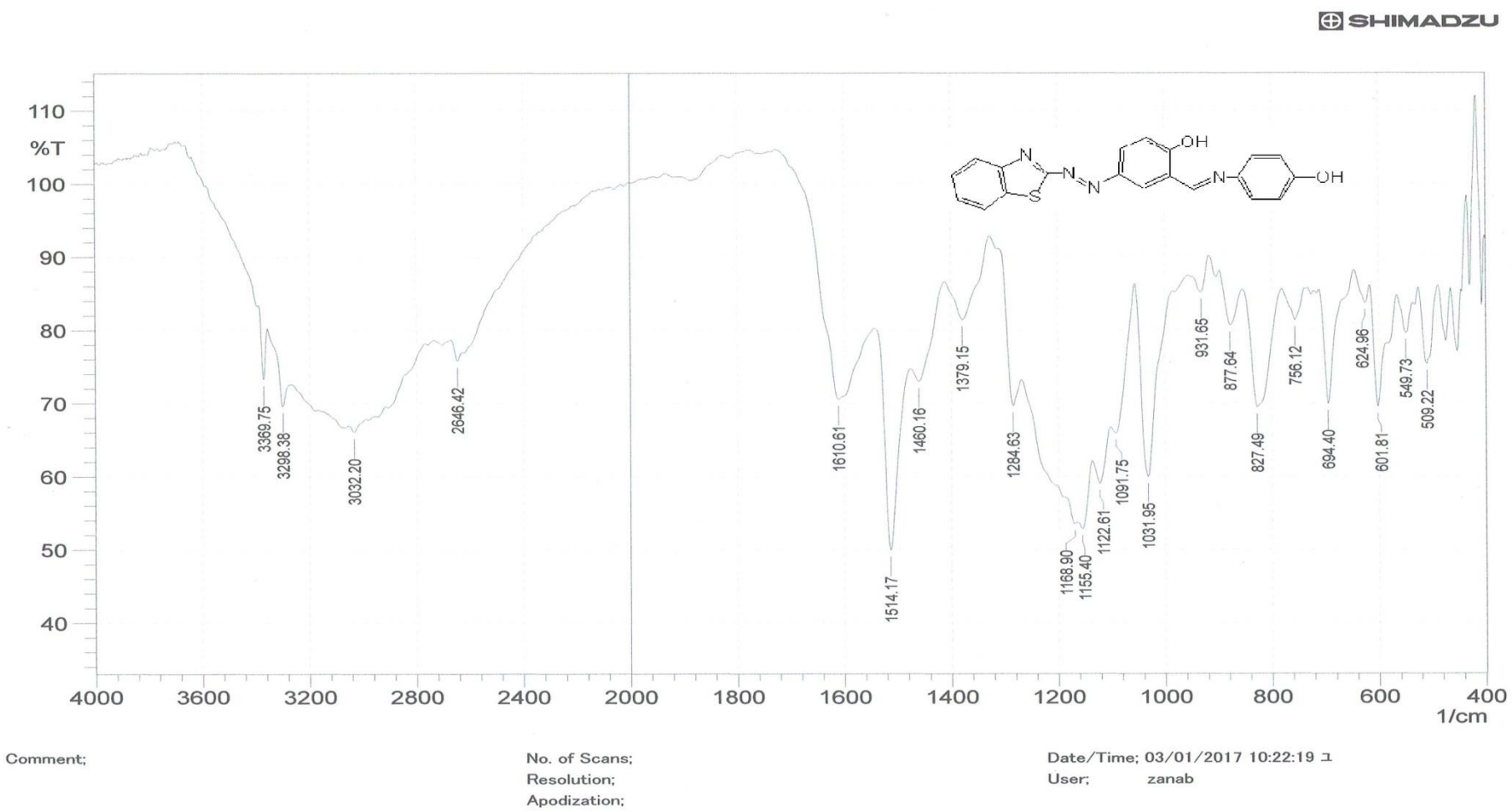


Fig. (3-5): FT-IR spectrum of compound **3c**

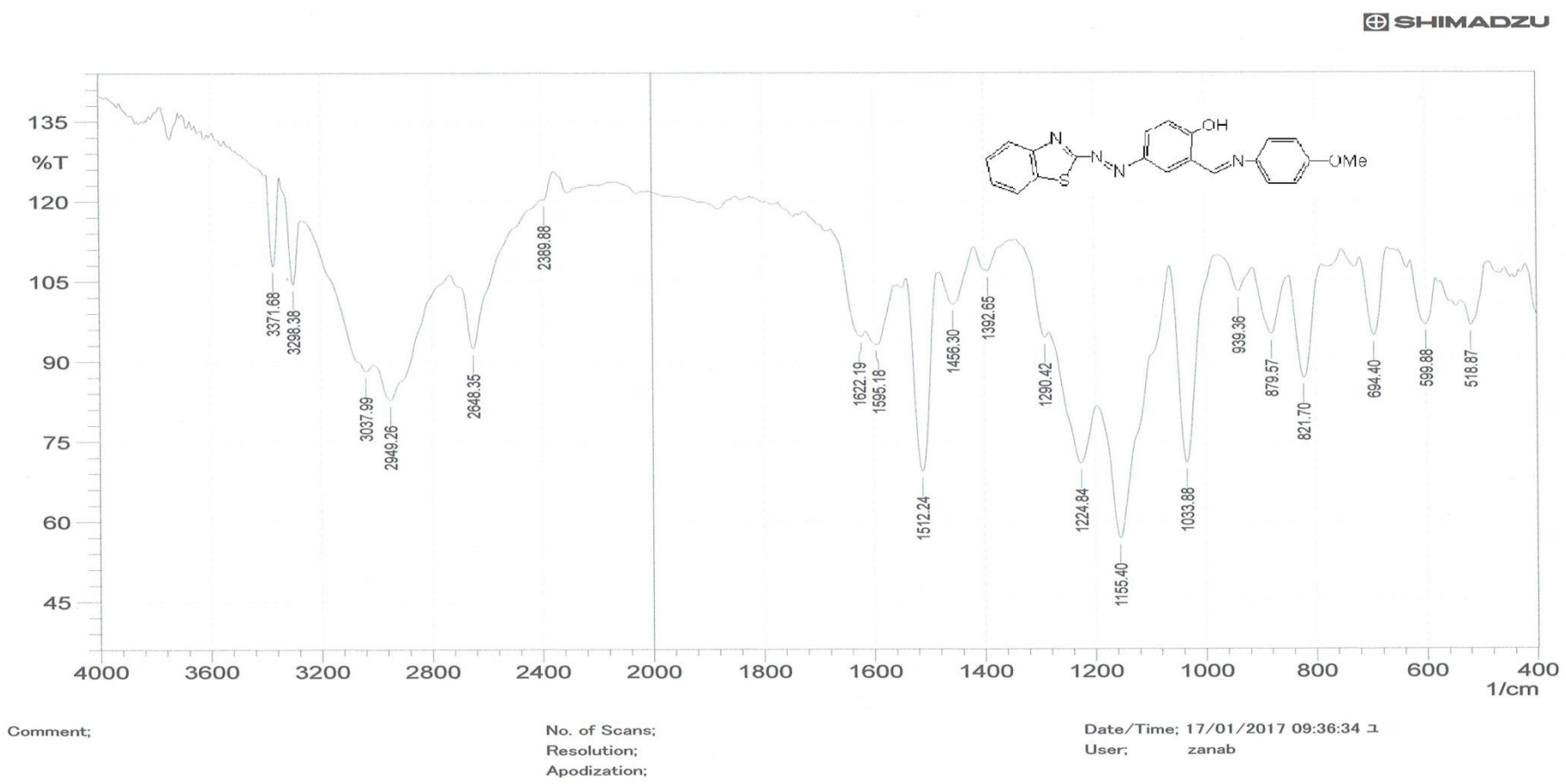


Fig. (3-6): FT-IR spectrum of compound **3d**

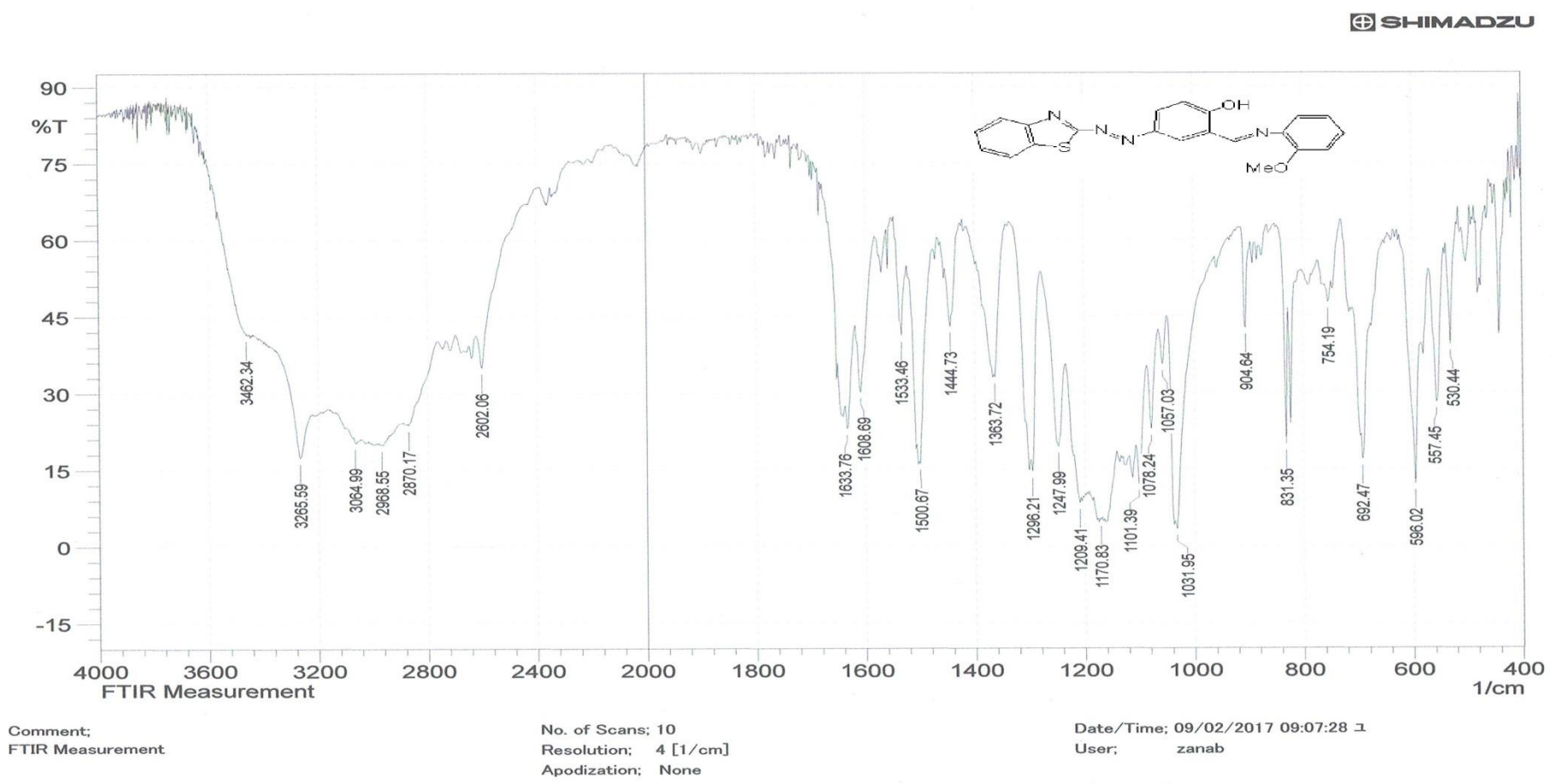


Fig. (3-7): FT-IR spectrum of compound **3e**

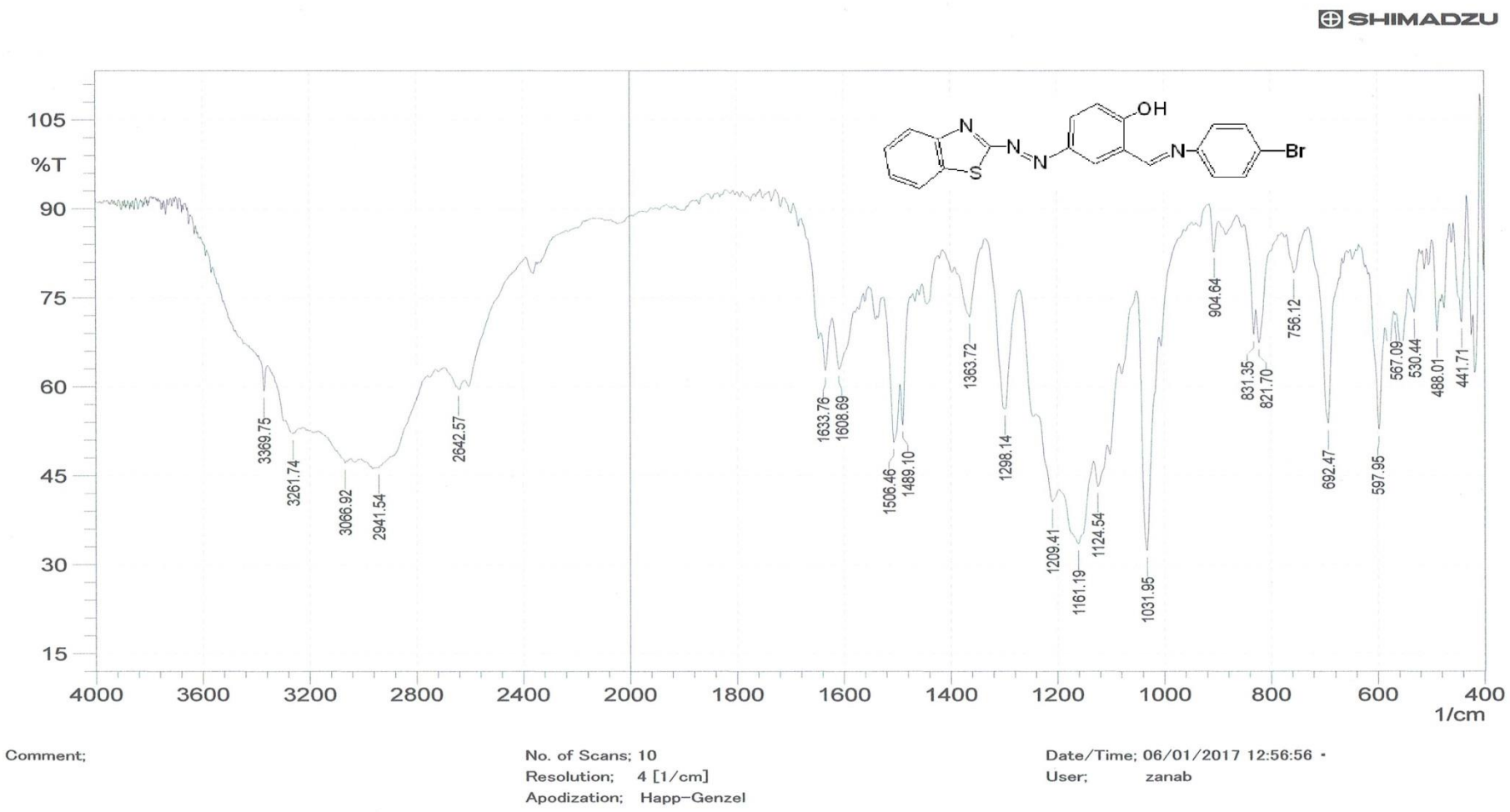


Fig. (3-8): FT-IR spectrum of compound **3f**

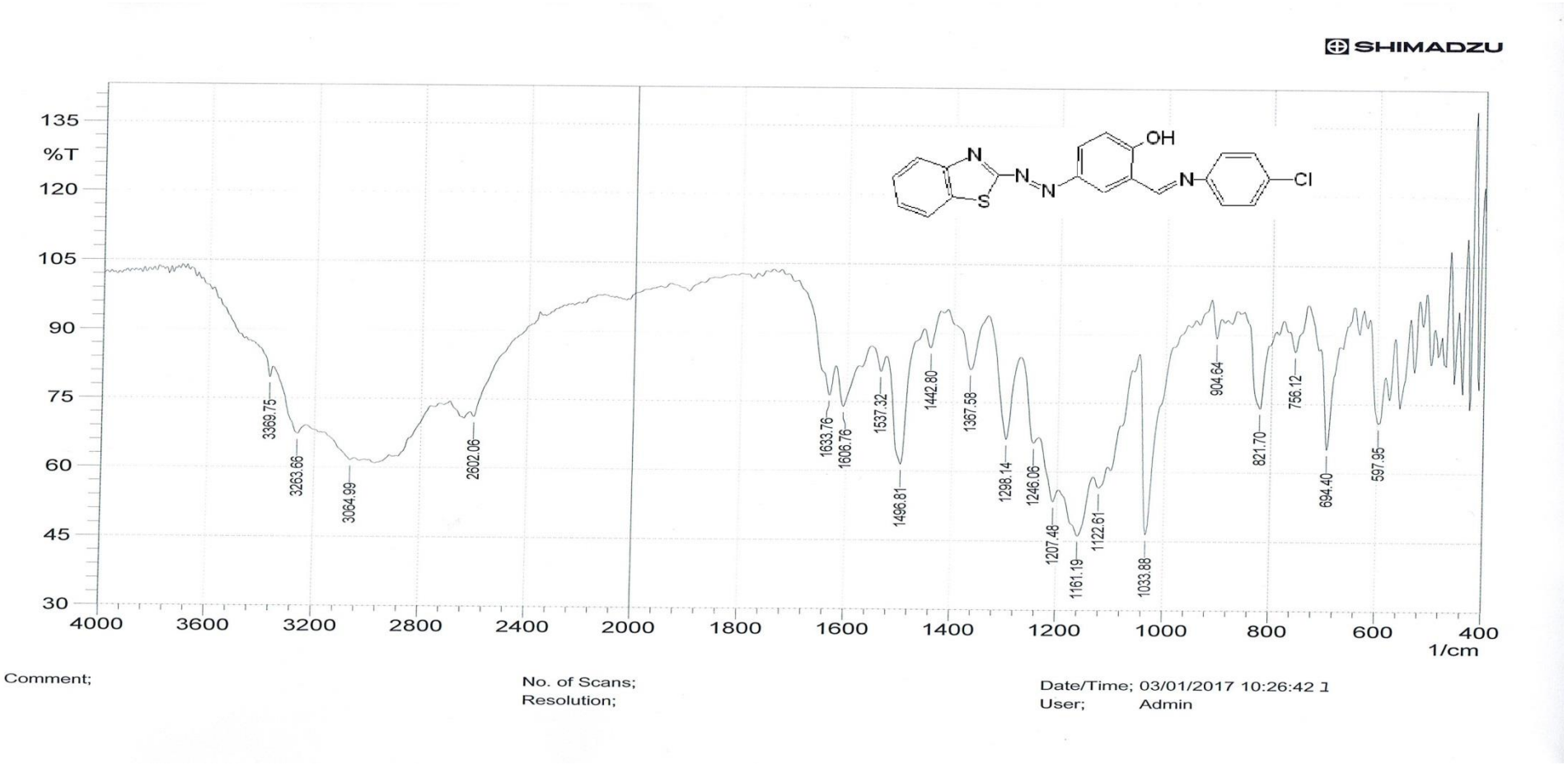


Fig. (3-9): FT-IR spectrum of compound **3g**

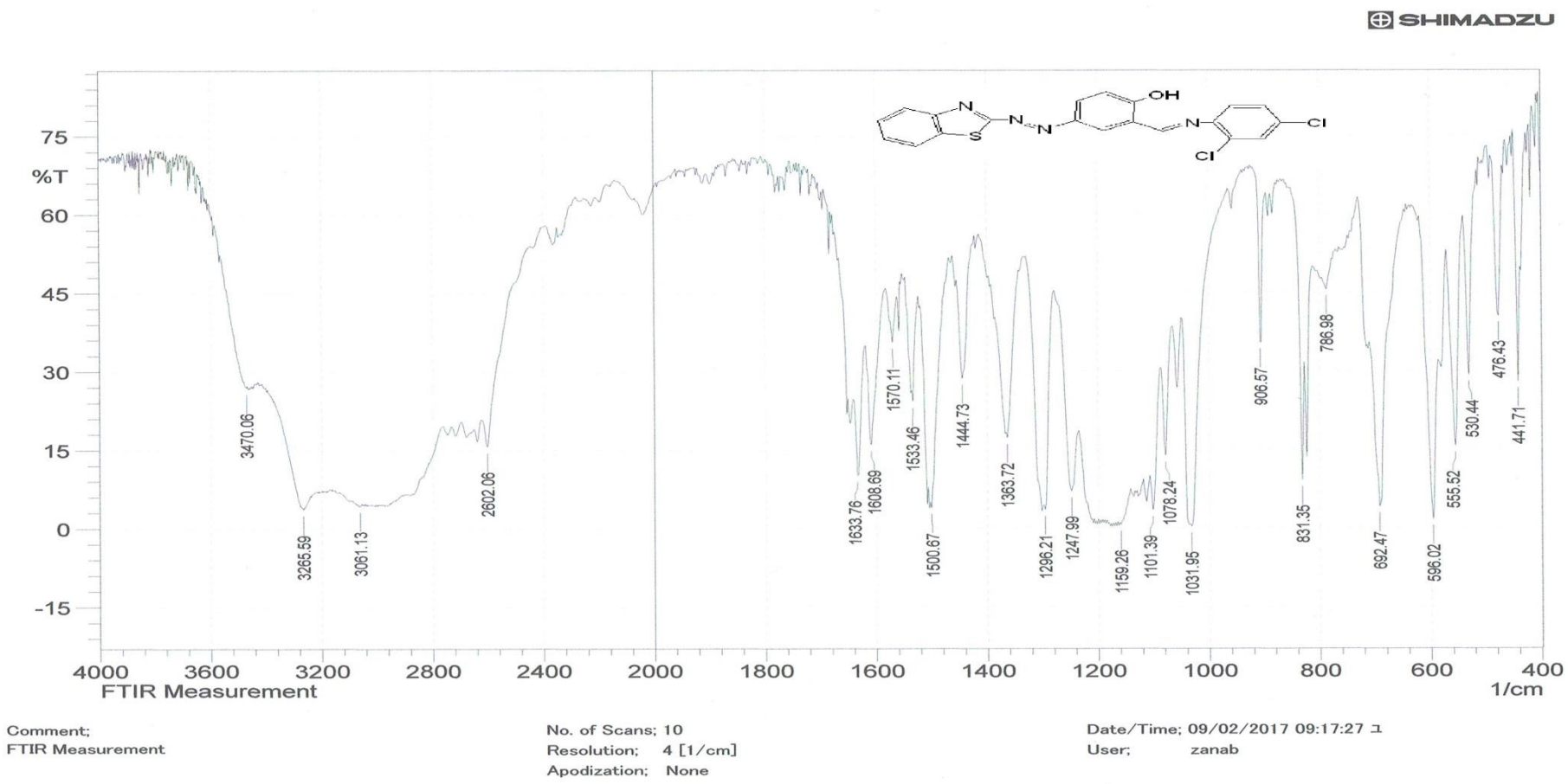


Fig. (3-10): FT-IR spectrum of compound **3h**

A.1.3. FT-IR spectra of imidazolidins 4a-h

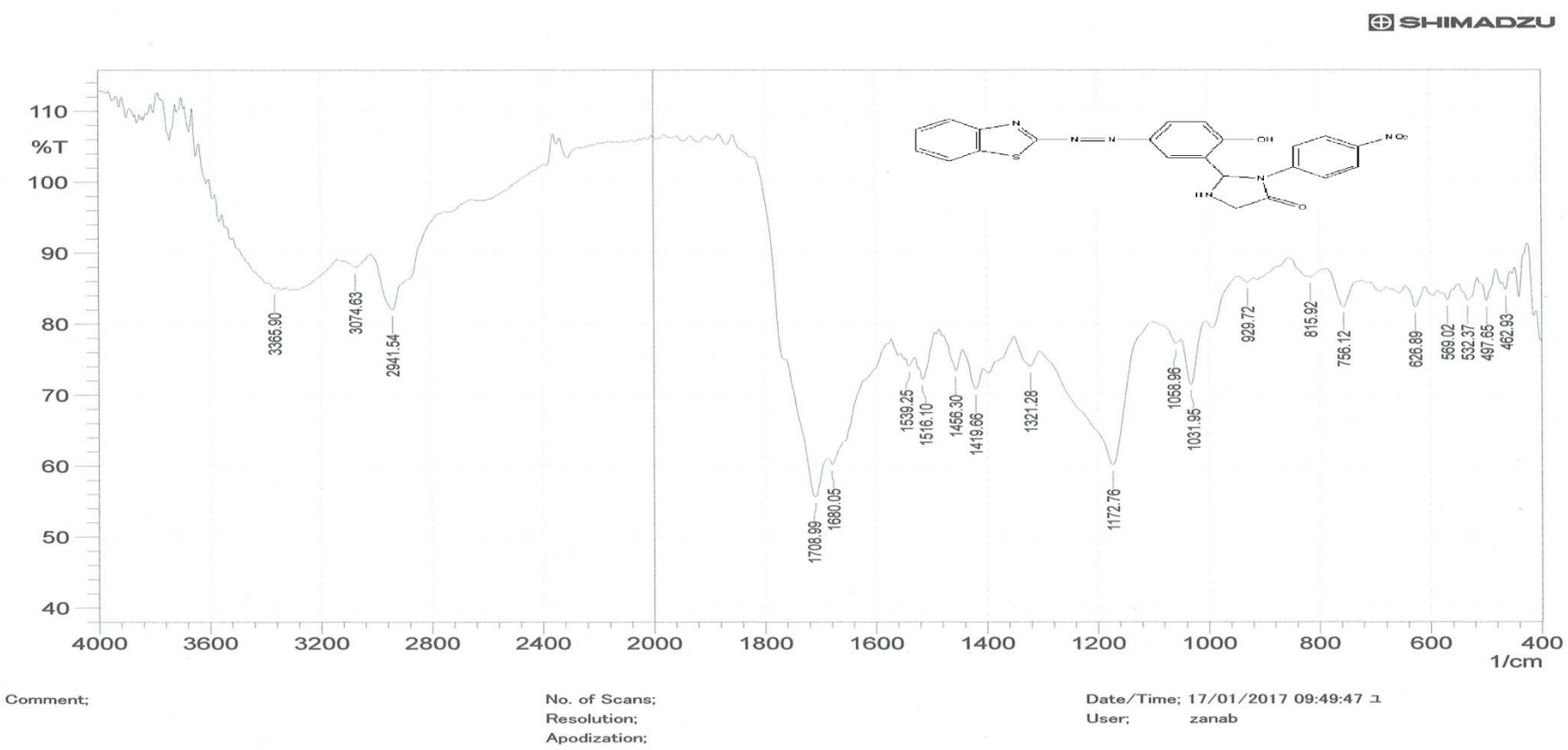


Fig. (3-11): FT-IR spectrum of compound **4a**

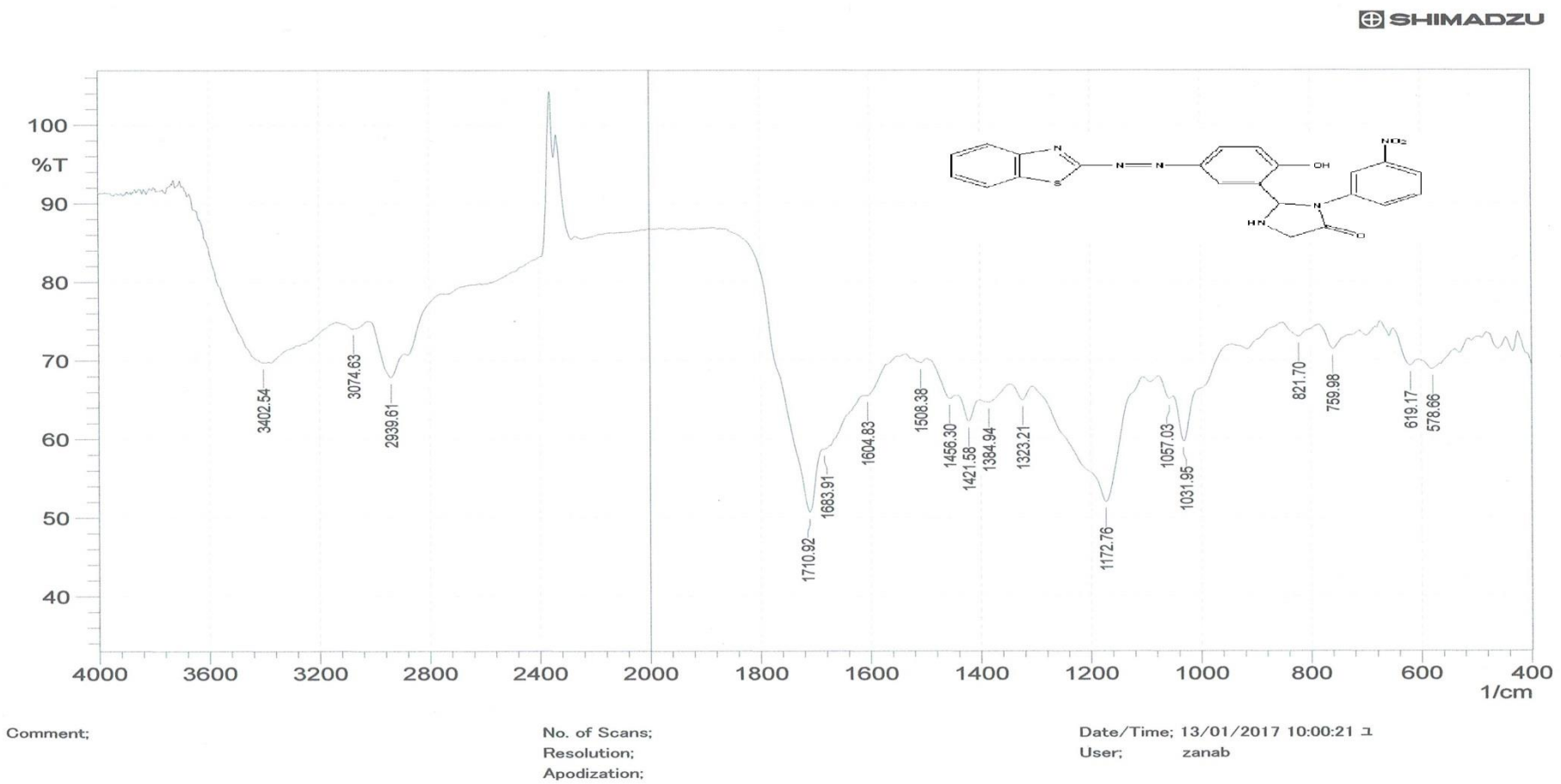


Fig. (3-12): FT-IR spectrum of compound **4b**

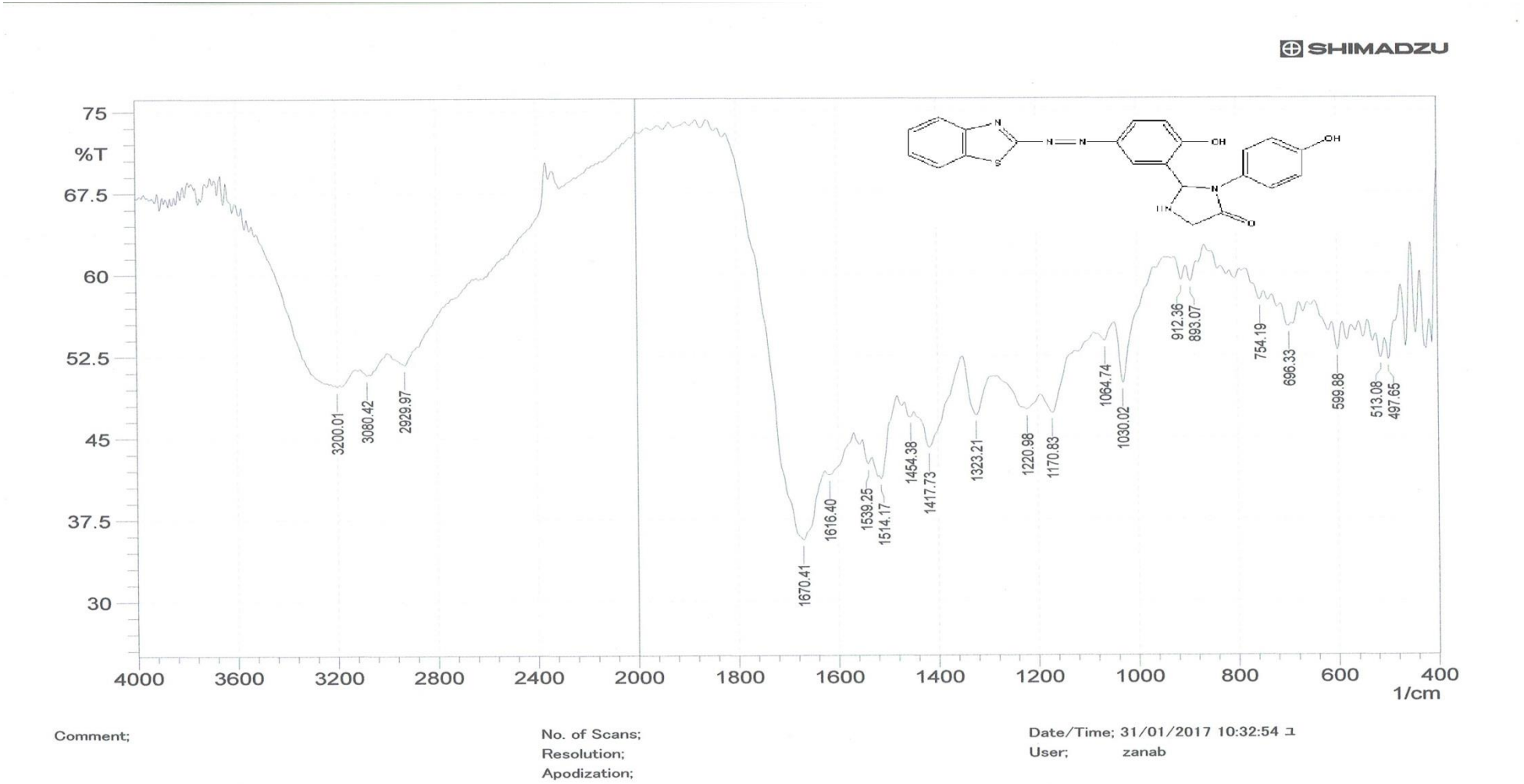


Fig. (3-13): FT-IR spectrum of compound **4c**

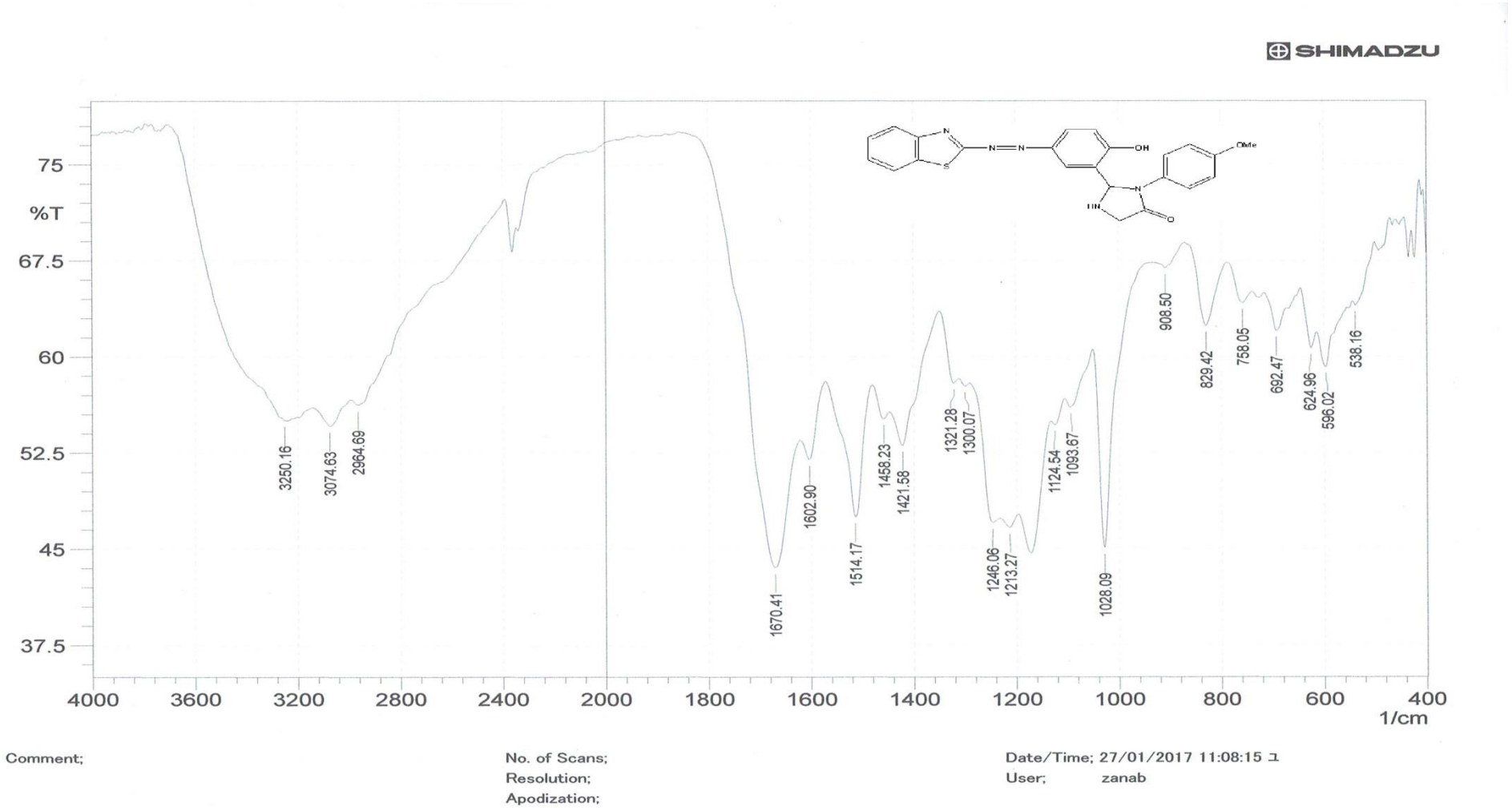


Fig. (3-14): FT-IR spectrum of compound **4d**

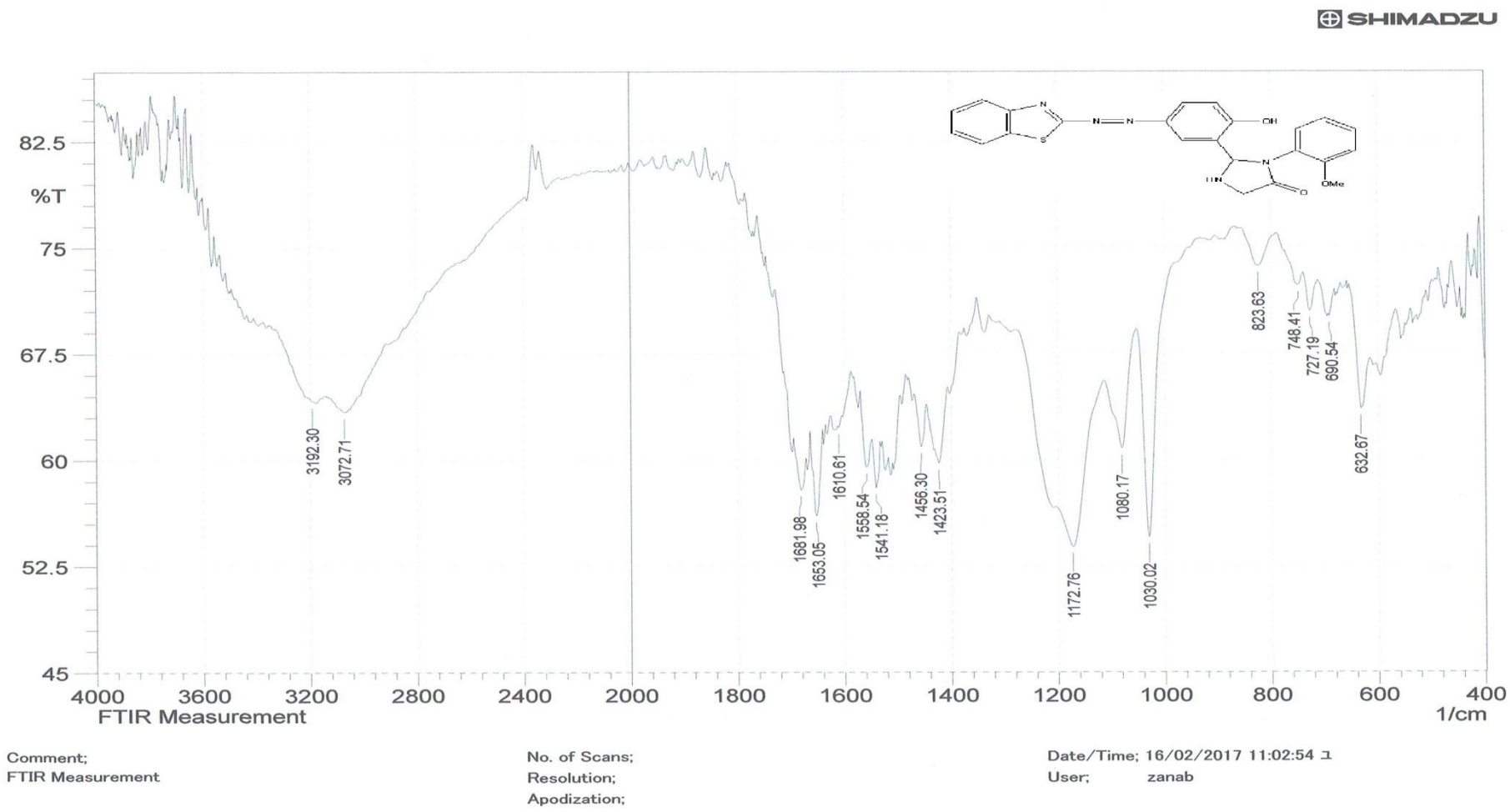


Fig. (3-15): FT-IR spectrum of compound **4e**

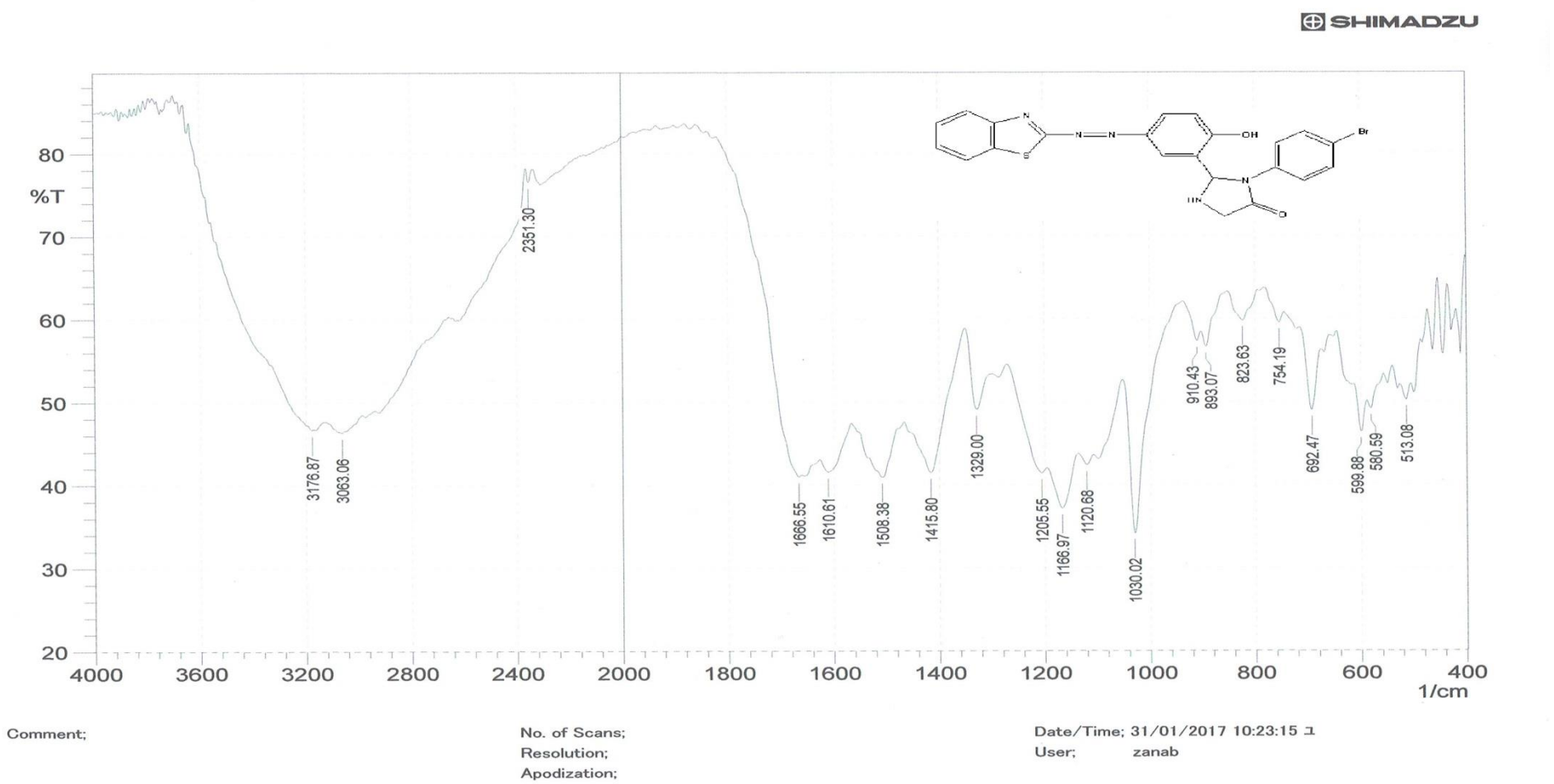


Fig. (3-16): FT-IR spectrum of compound **4f**

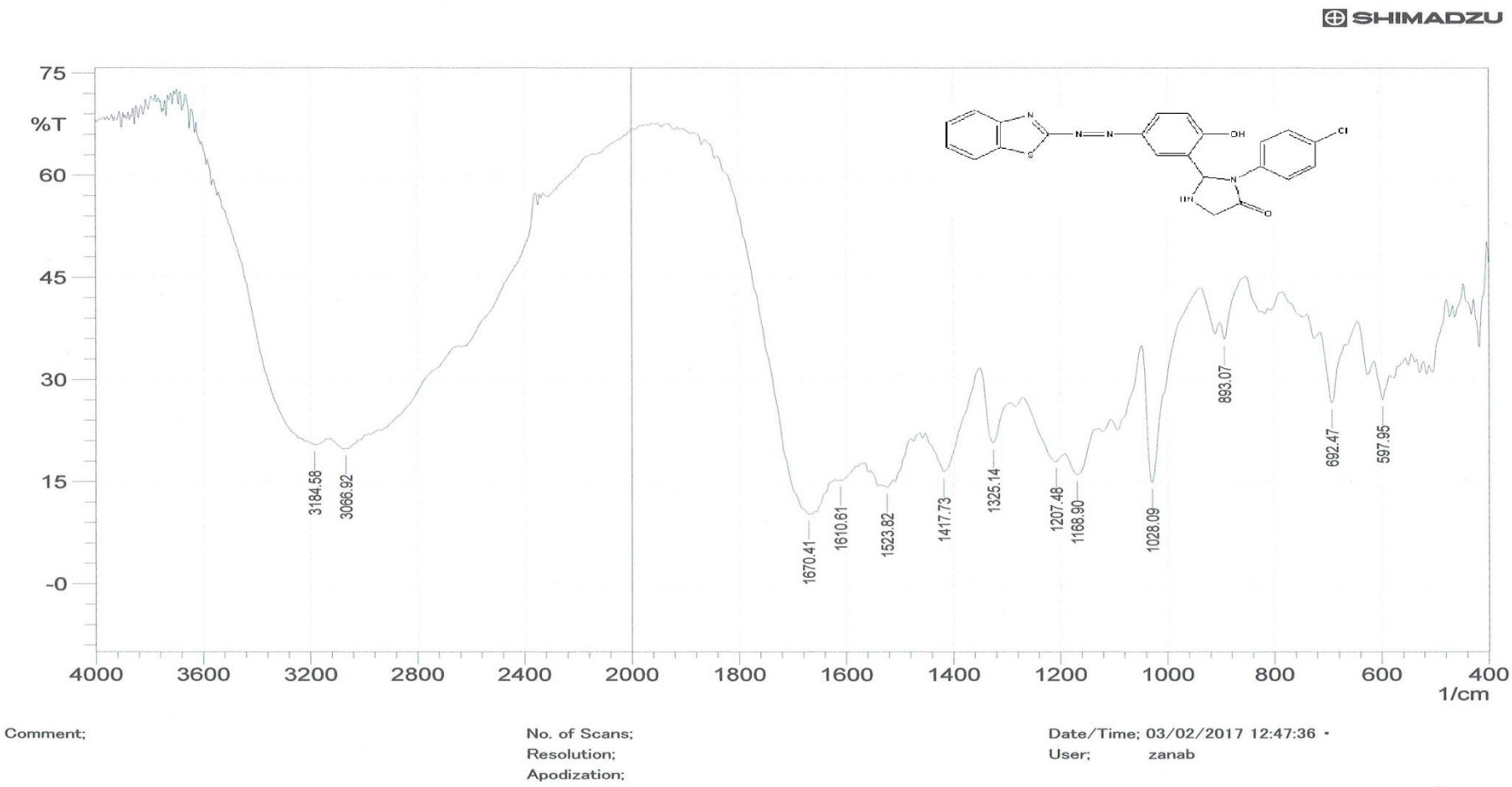


Fig. (3-17): FT-IR spectrum of compound **4g**

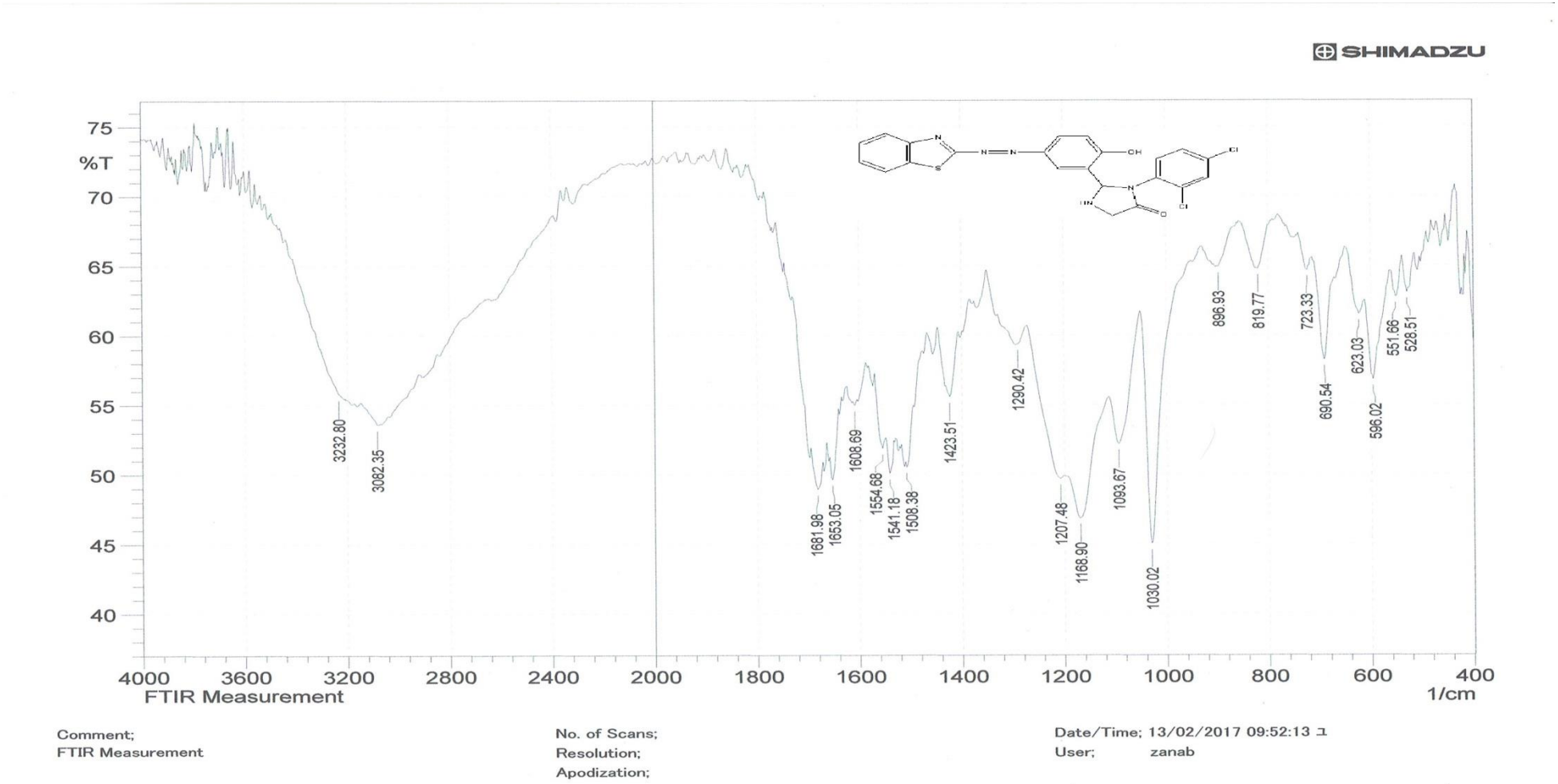


Fig. (3-18): FT-IR spectrum of compound **4h**

A.1.4. FT-IR spectra of imidazolidines 5a-h

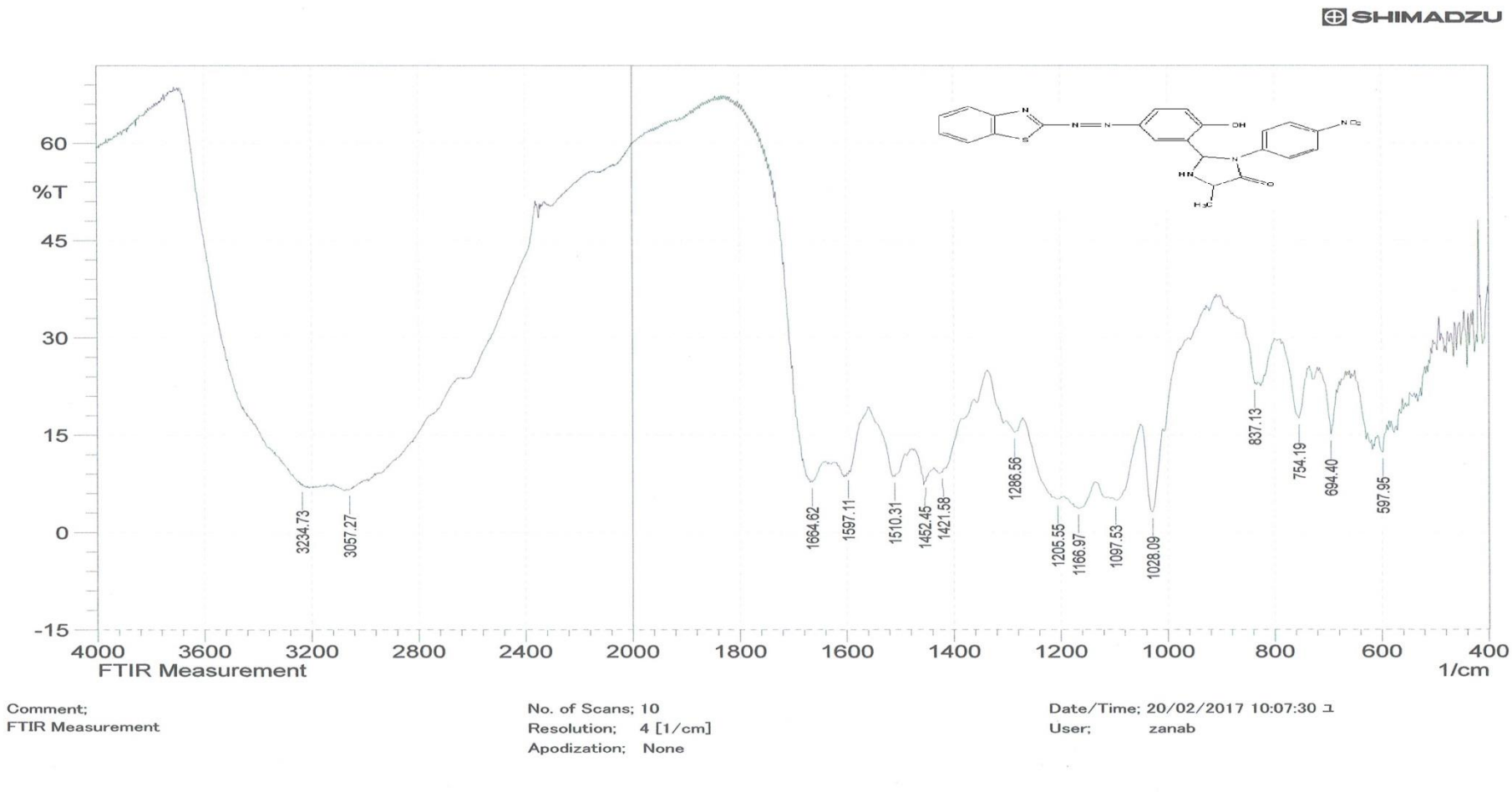


Fig. (3-19): FT-IR spectrum of compound **5a**

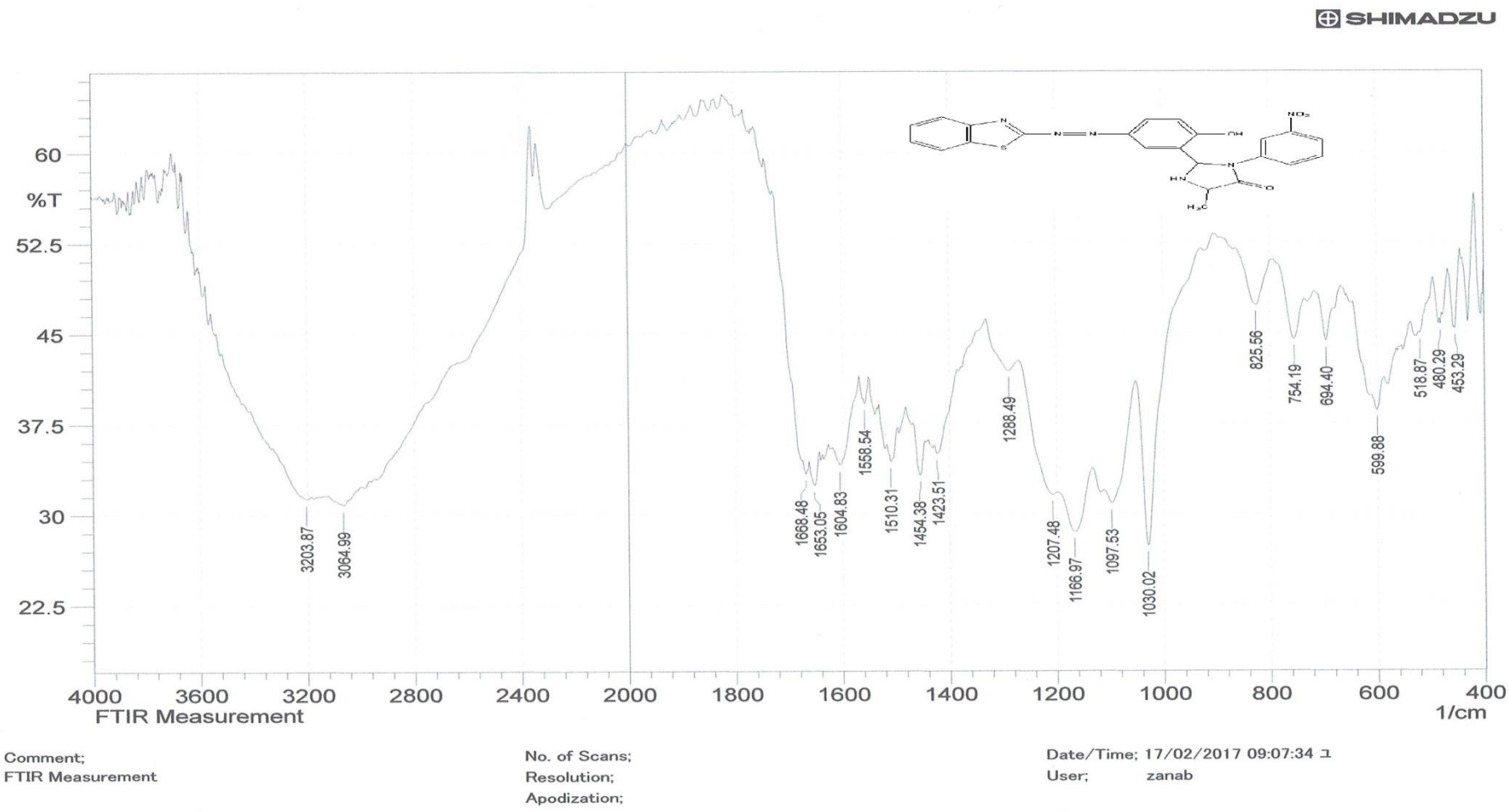


Fig. (3-20): FT-IR spectrum of compound **5b**

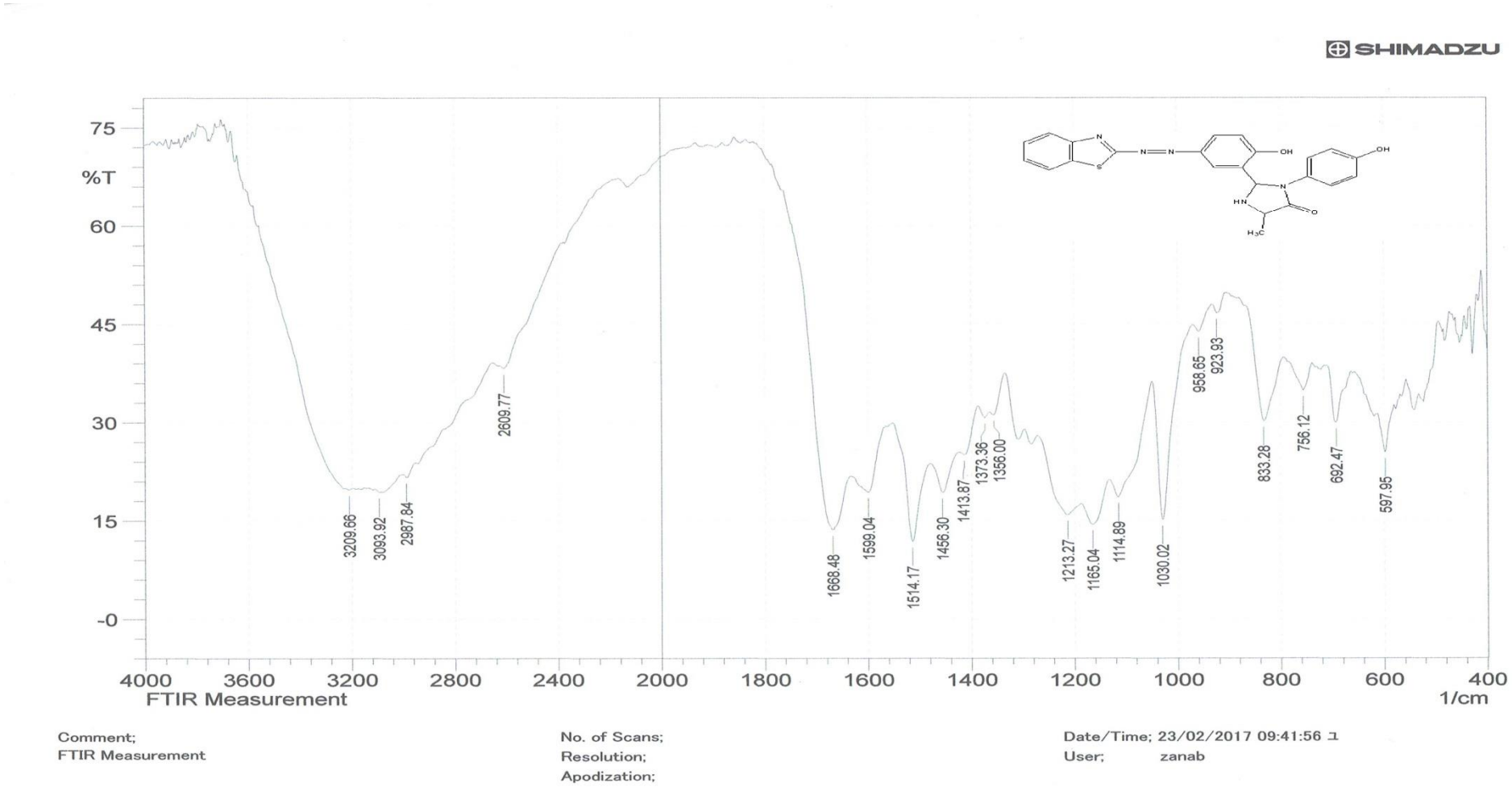


Fig. (3-21): FT-IR spectrum of compound **5c**

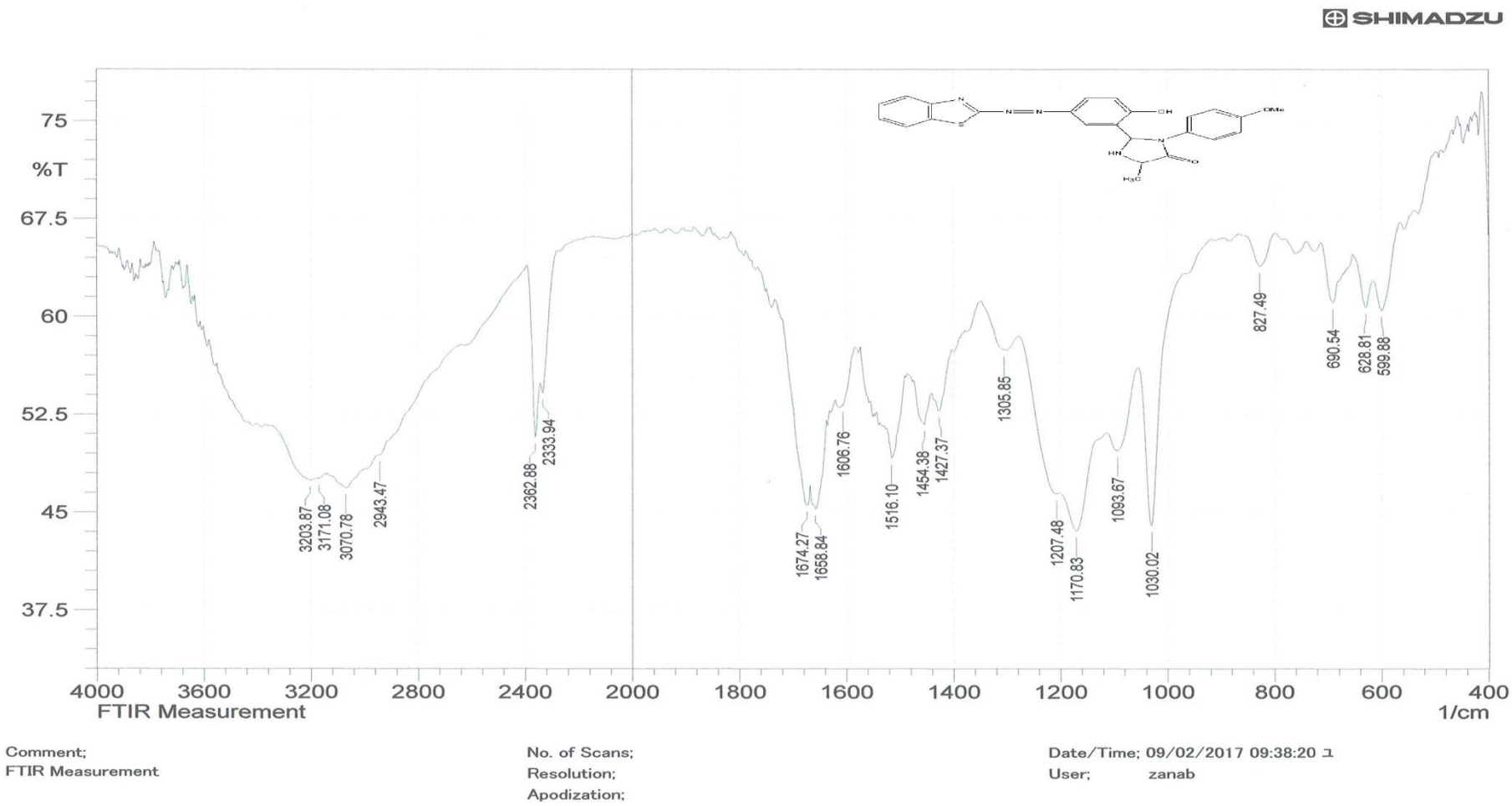


Fig. (3-22): FT-IR spectrum of compound **5d**

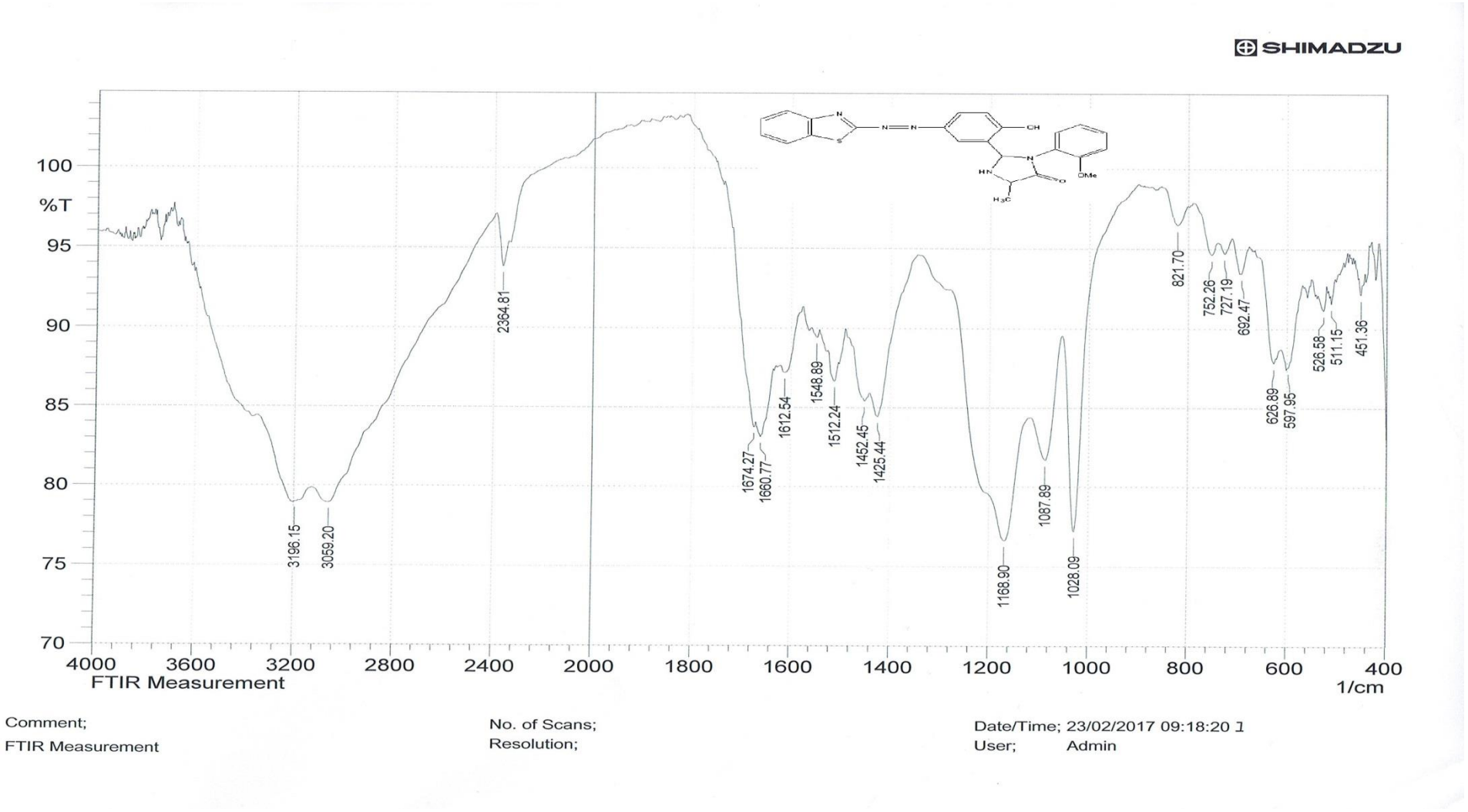


Fig. (3-23): FT-IR spectrum of compound **5e**

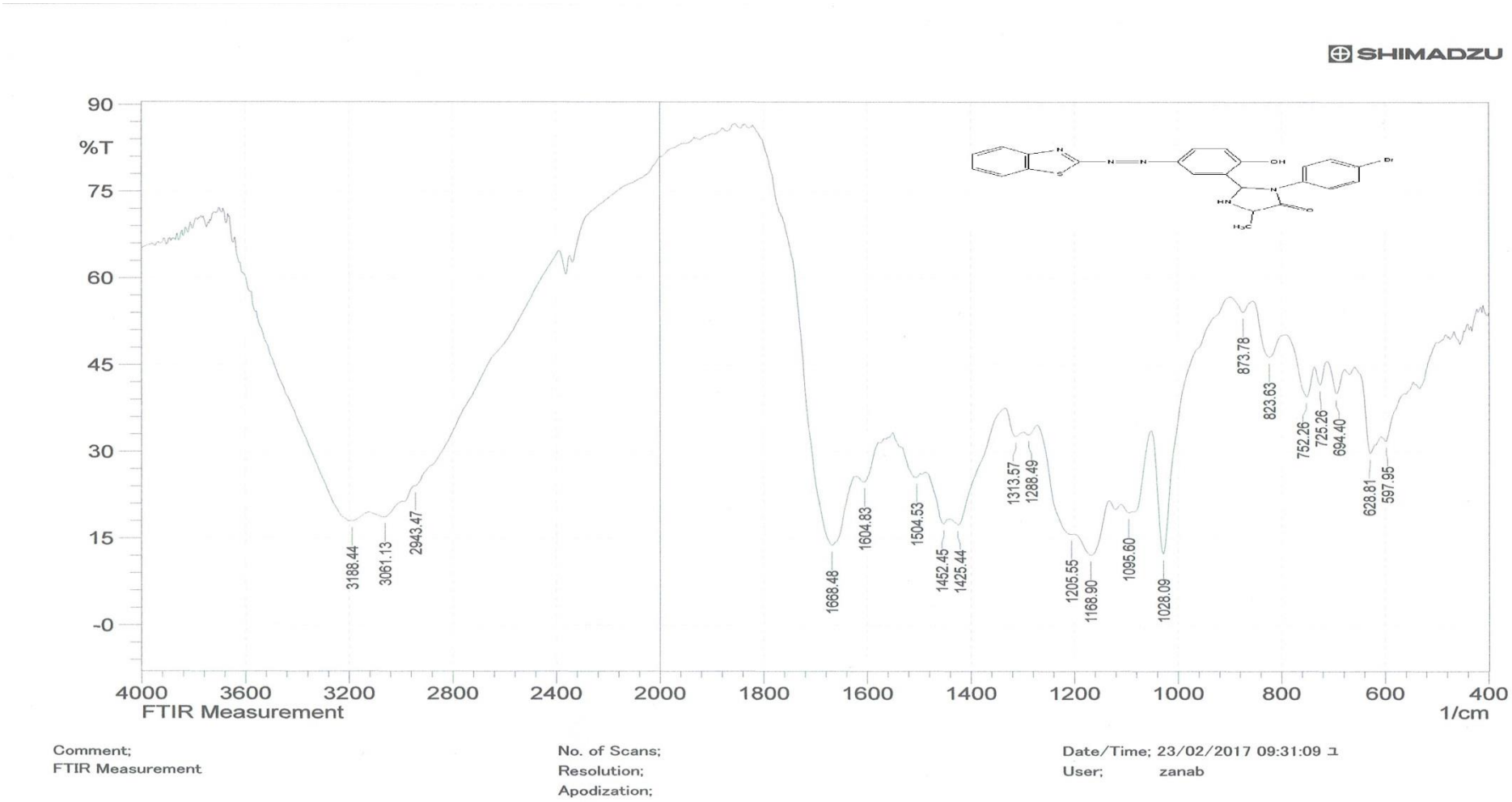


Fig. (3-24): FT-IR spectrum of compound **5f**

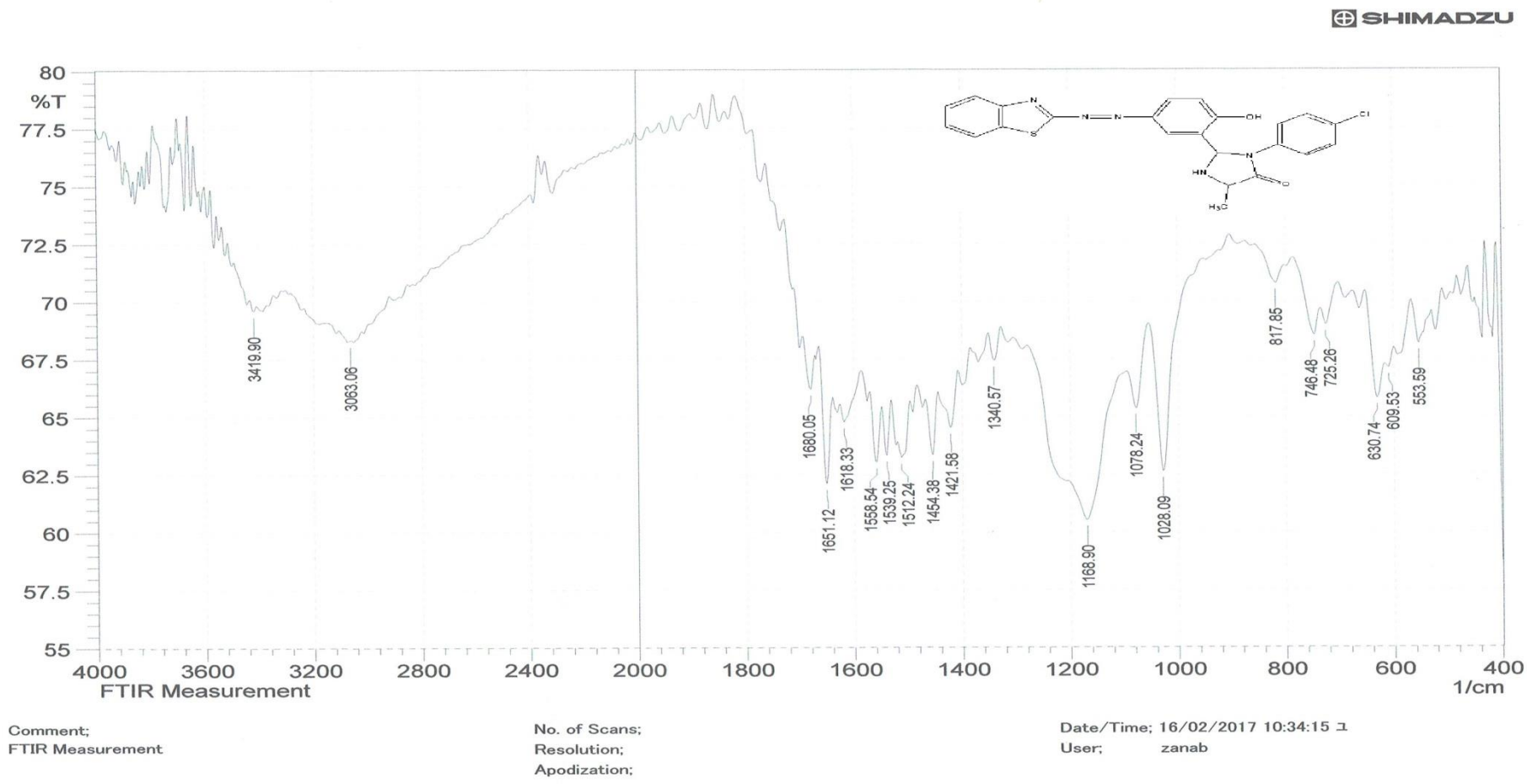


Fig. (3-25): FT-IR spectrum of compound **5g**

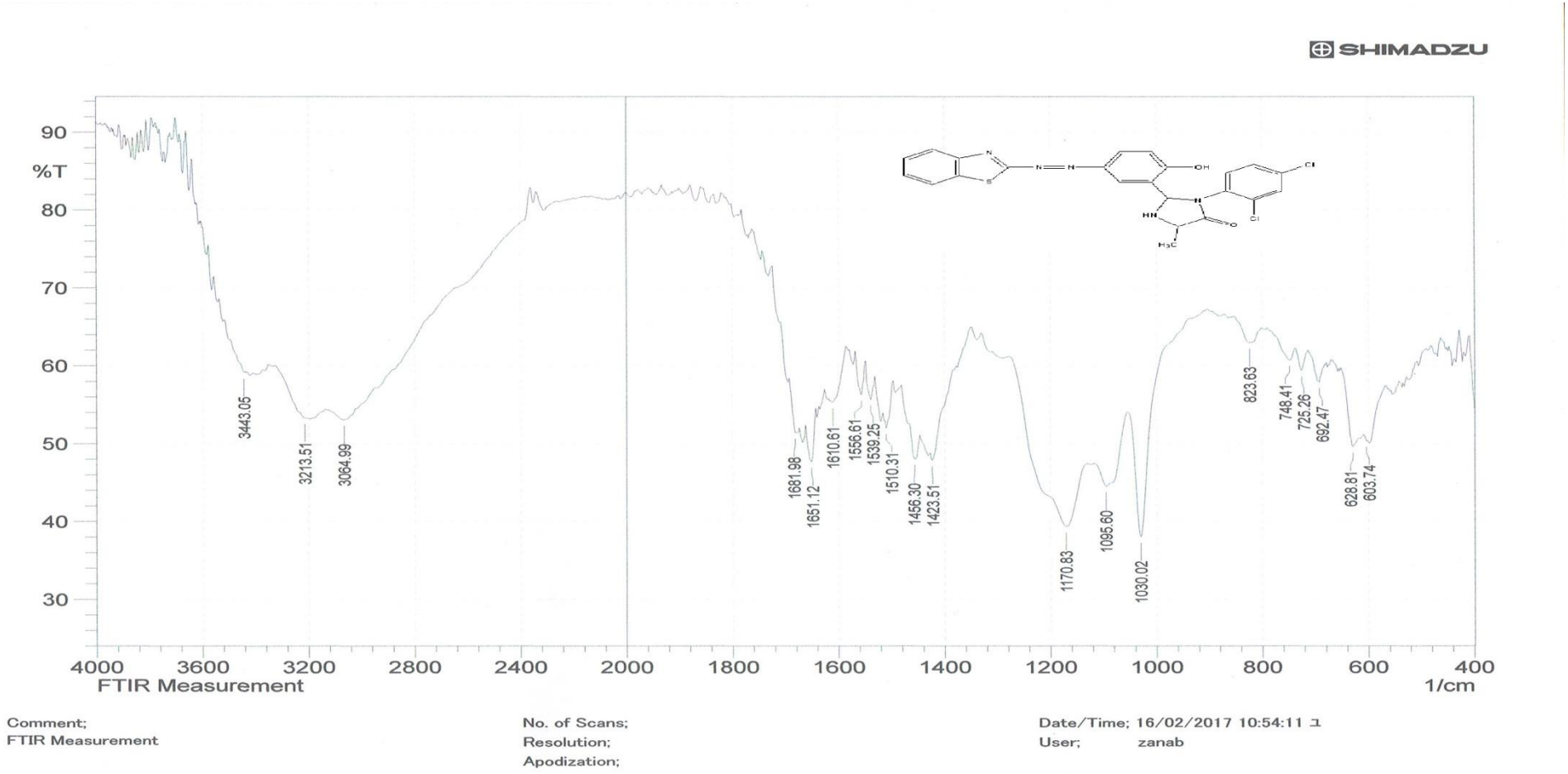


Fig. (3-26): FT-IR spectrum of compound **5h**

A.2. ^{1}H NMR spectra

A.2.1. ^{1}H NMR spectra of imidazolidins 4a-h

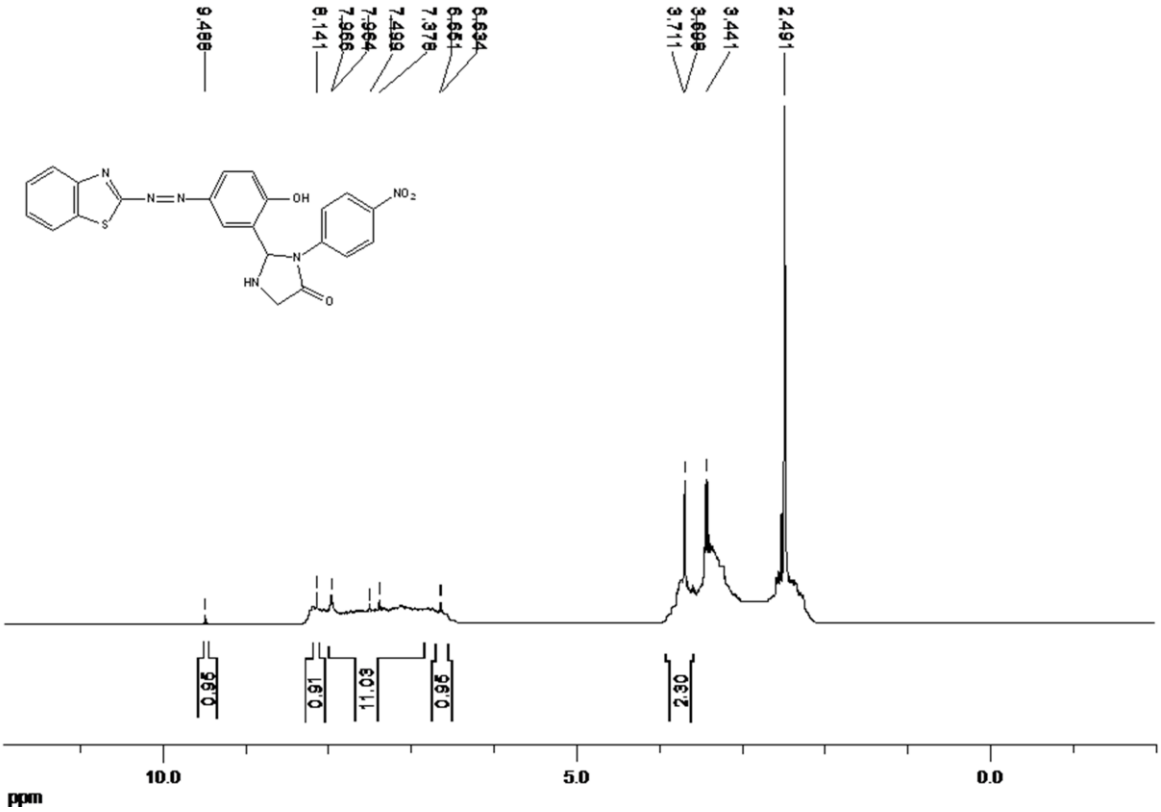


Fig. (3-27): ^{1}H NMR spectrum of compound **4a** in ppm

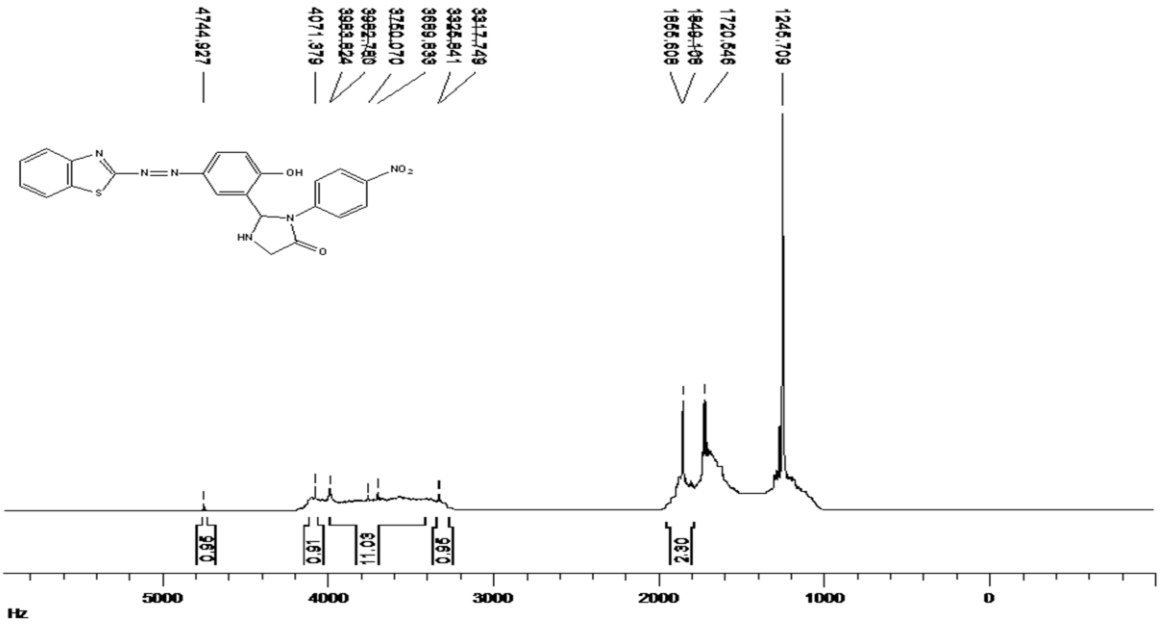


Fig. (3-27): ^{1}H NMR spectrum of compound **4a** in Hz

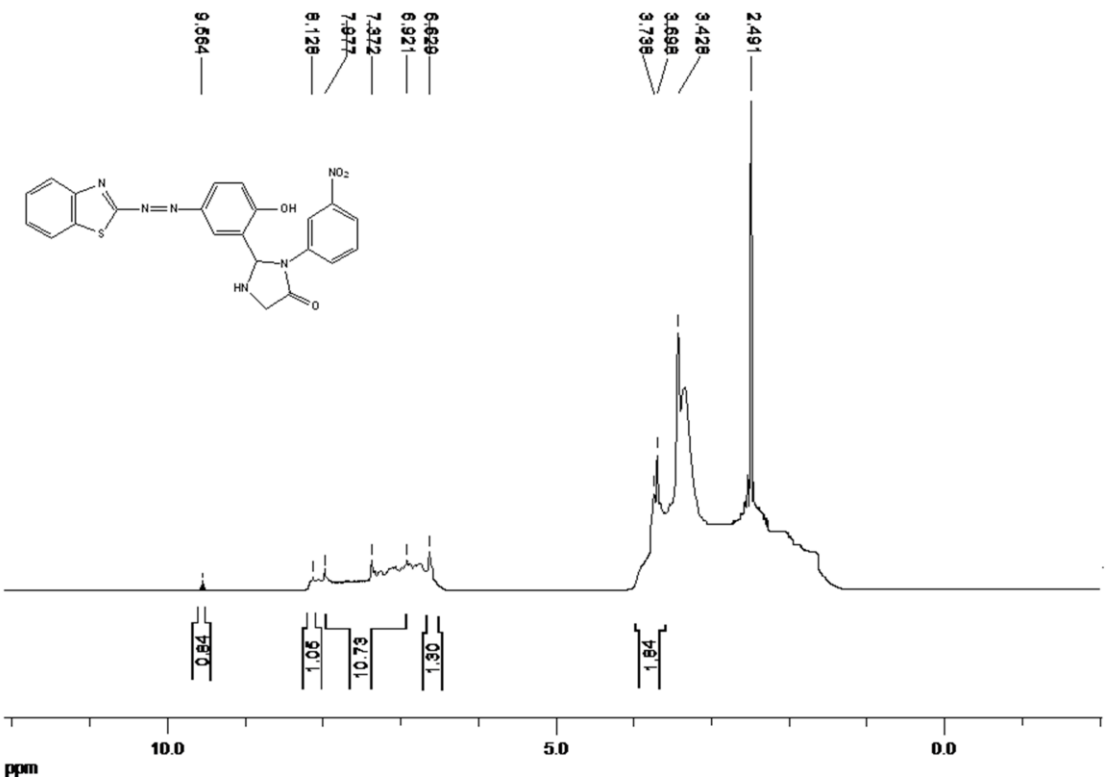


Fig. (3-28): ^{1}H NMR spectrum of compound **4b** in ppm

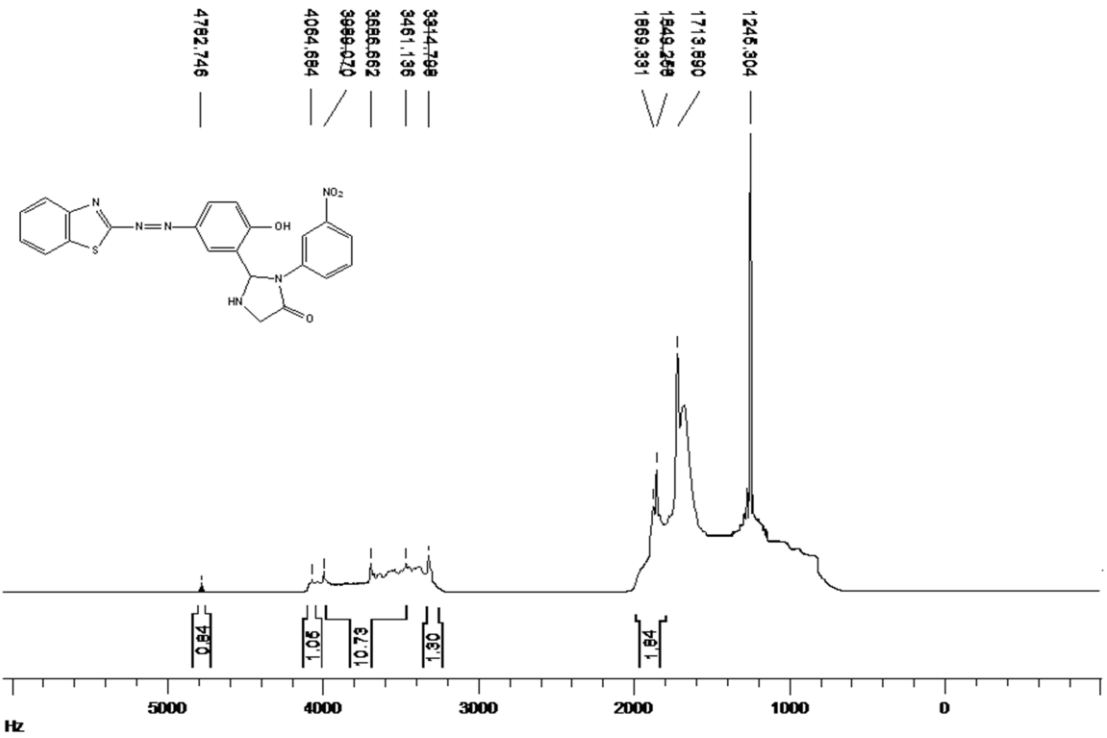


Fig. (3-28): ^{1}H NMR spectrum of compound **4b** in Hz

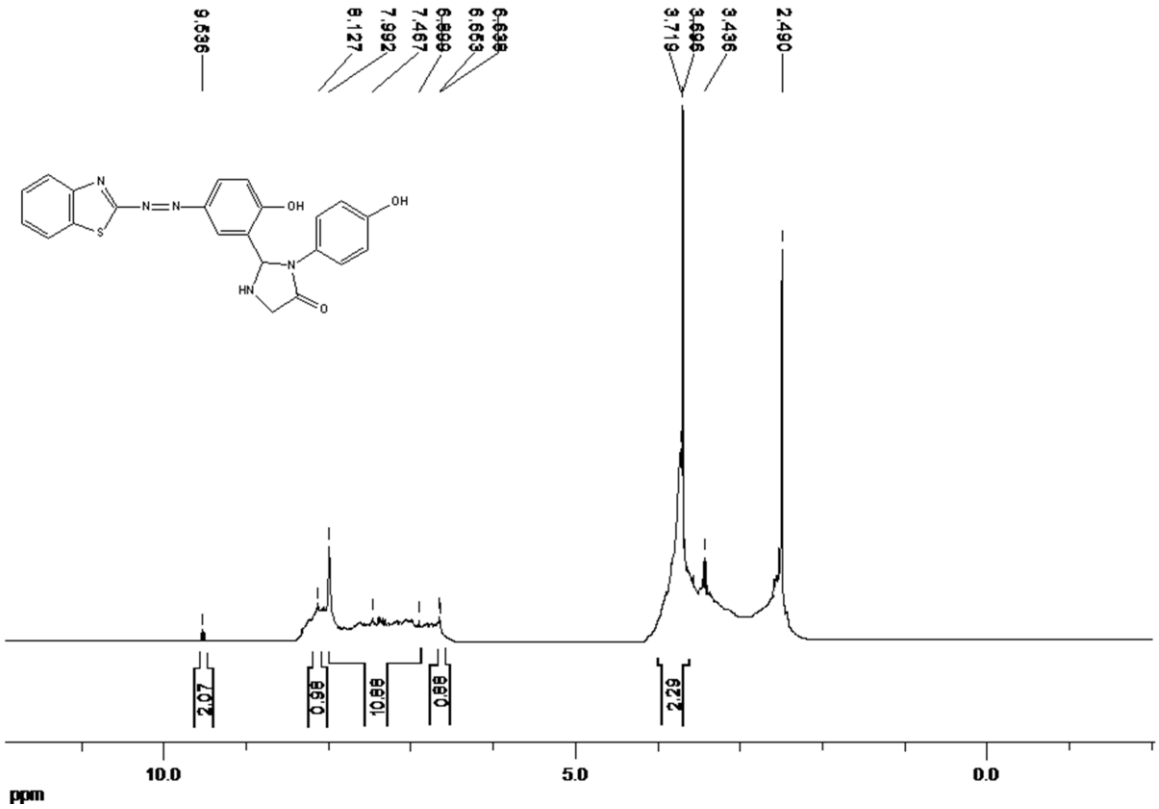


Fig. (3-29): ^{1}H NMR spectrum of compound **4c** in ppm

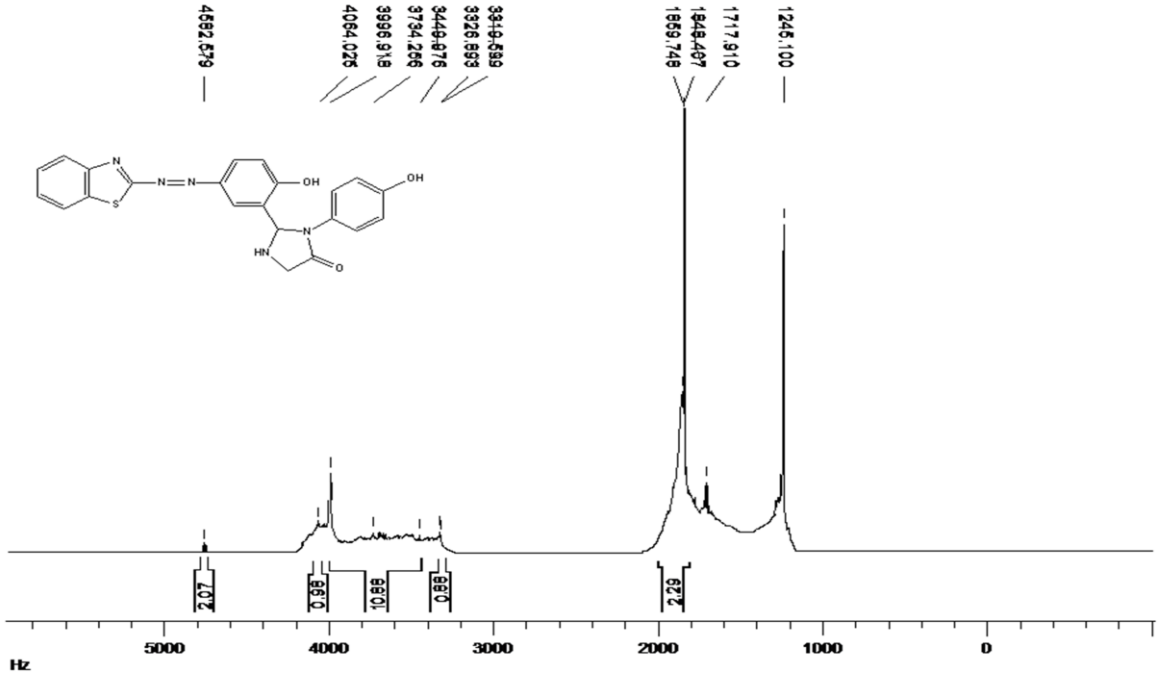


Fig. (3-29): ^{1}H NMR spectrum of compound **4c** in Hz

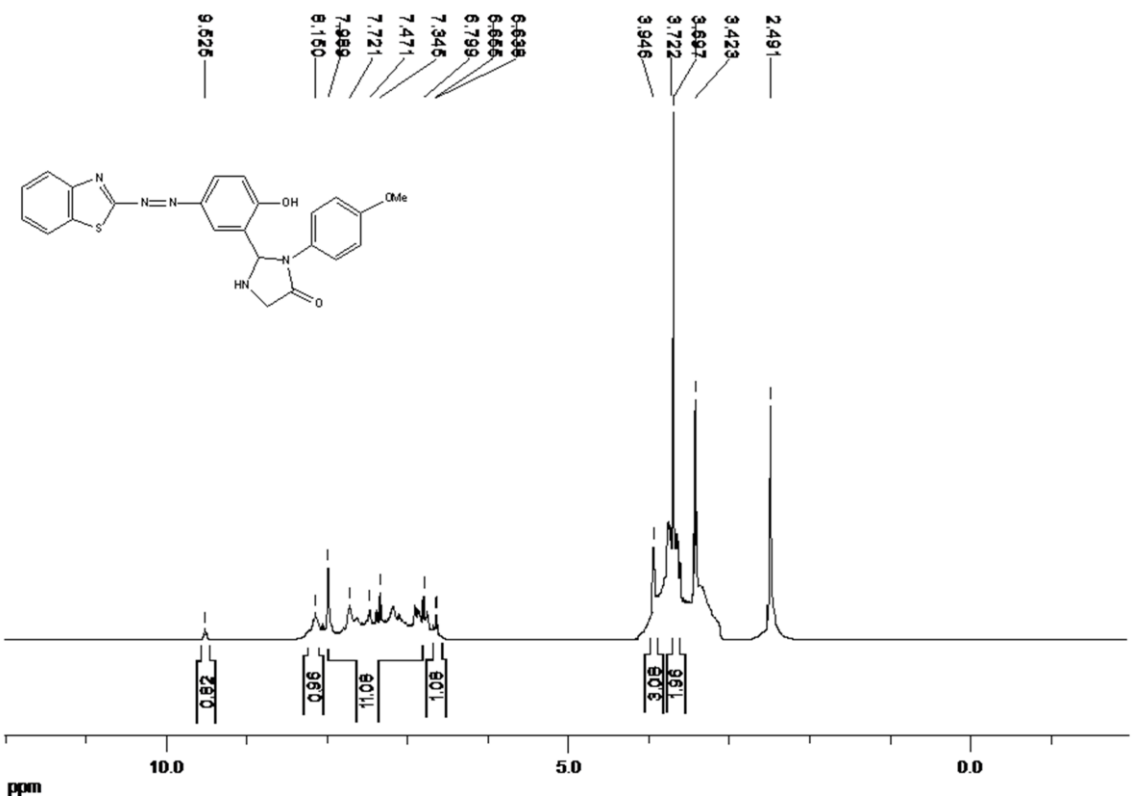


Fig. (3-30): ^{1}H NMR spectrum of compound **4d** in ppm

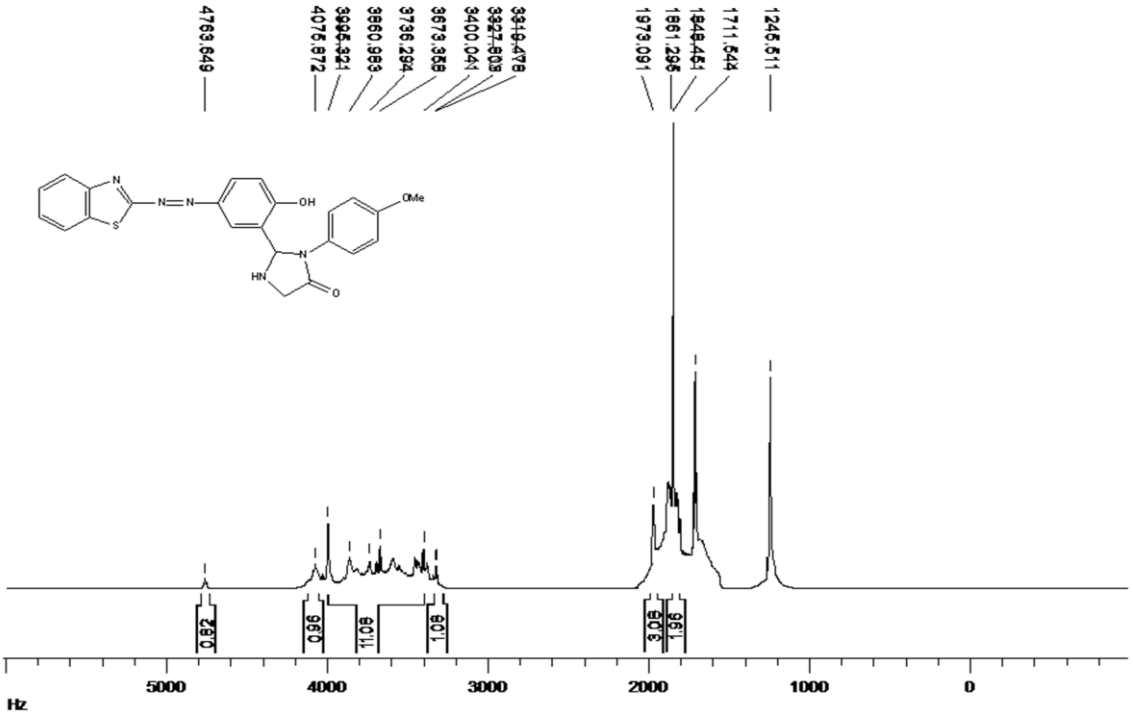


Fig. (3-30): ^{1}H NMR spectrum of compound **4d** in Hz

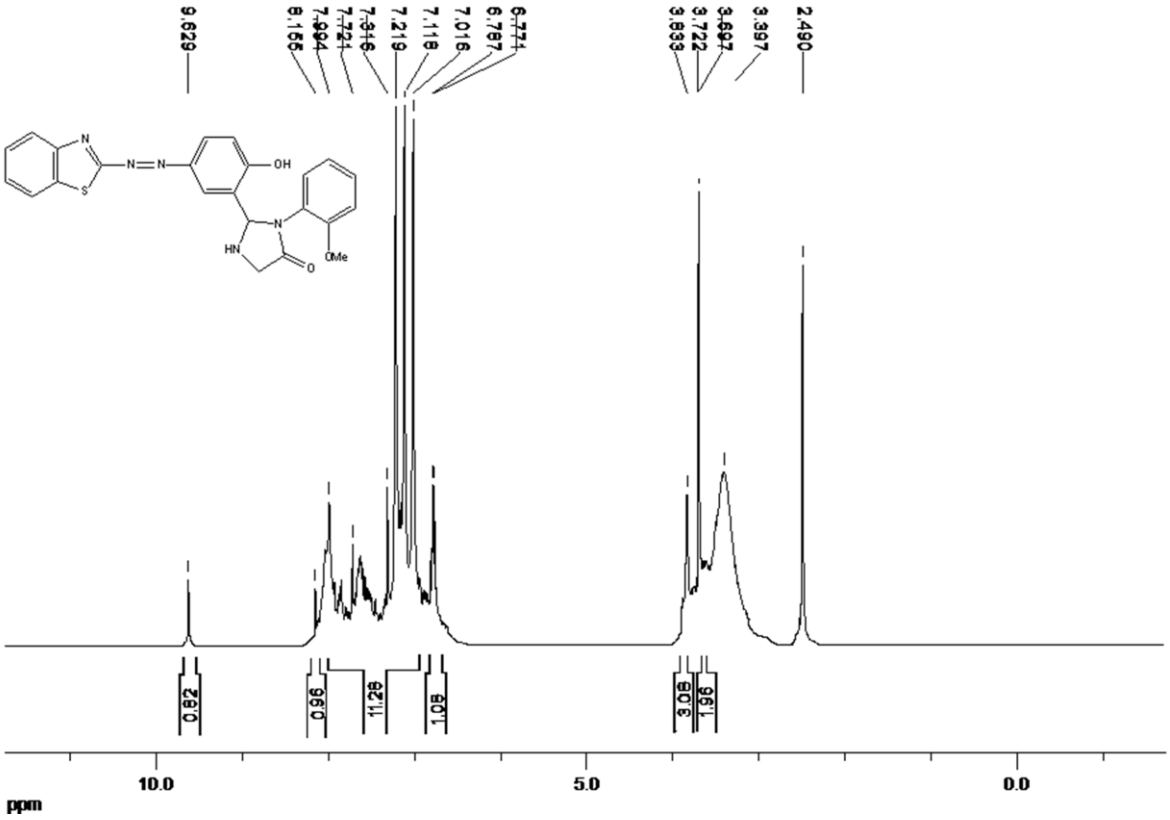


Fig. (3-31): ^{1}H NMR spectrum of compound **4e** in ppm

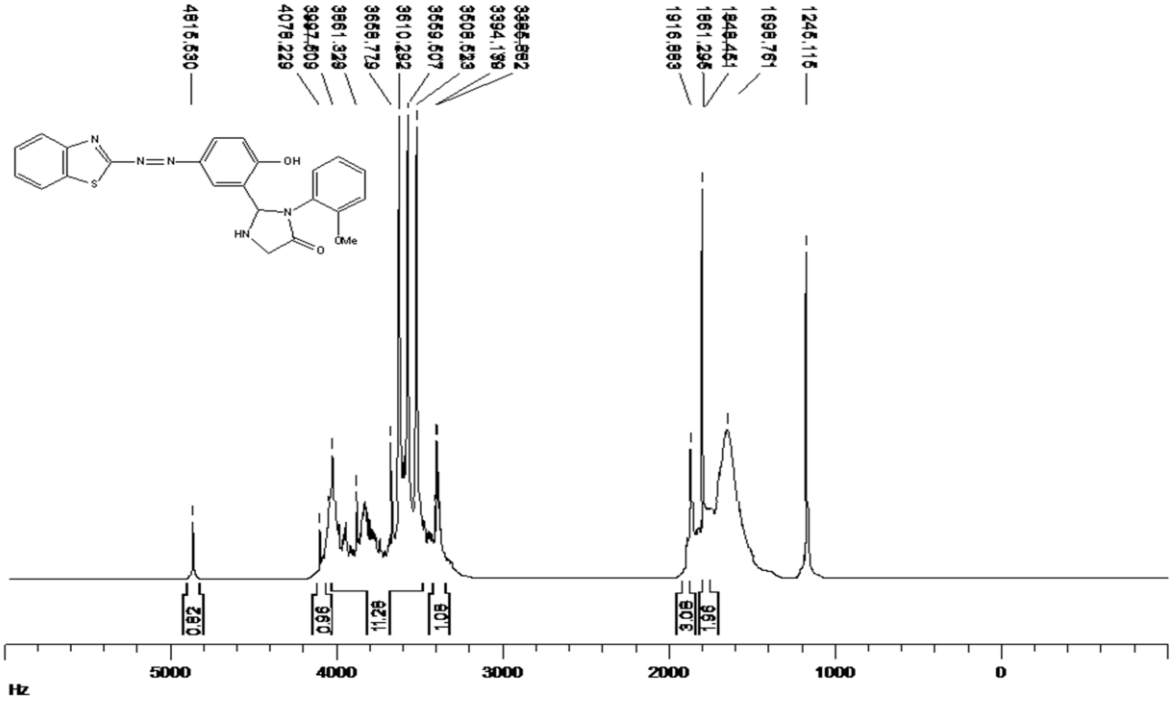


Fig. (3-31): ^{1}H NMR spectrum of compound **4e** in Hz

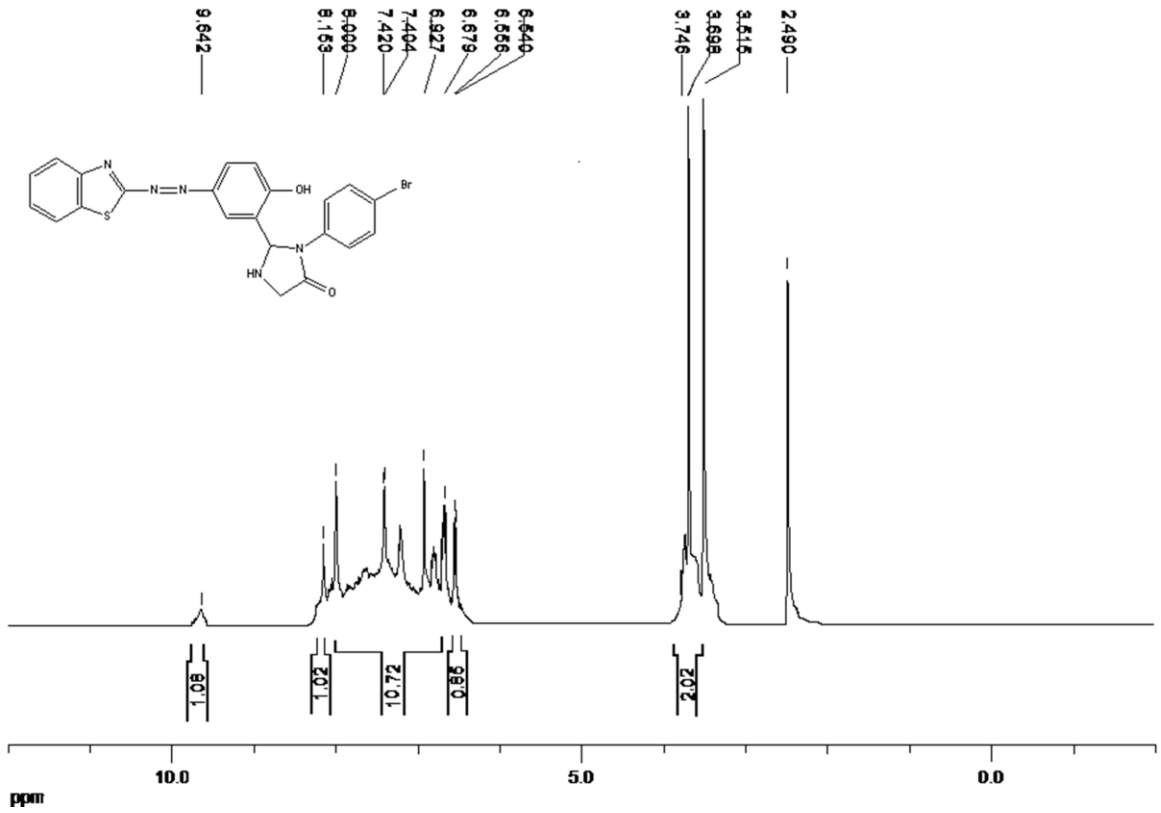


Fig. (3-32): ^{1}H NMR spectrum of compound **4f** in ppm

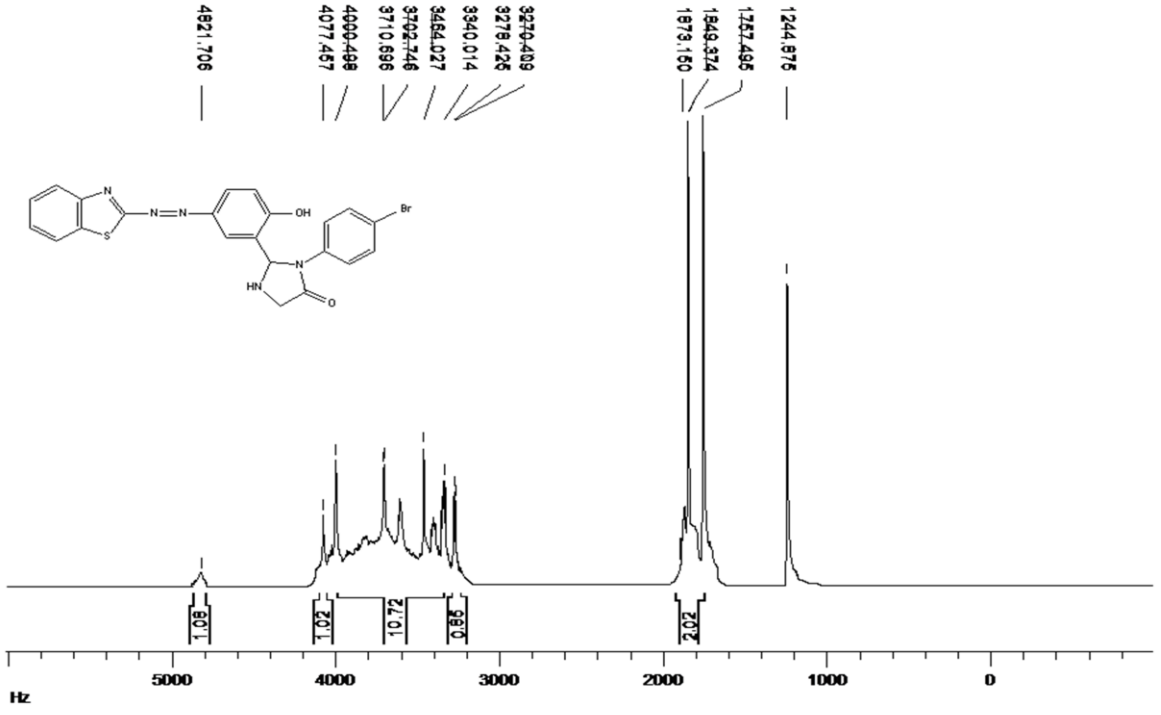


Fig. (3-32): ^{1}H NMR spectrum of compound **4f** in Hz

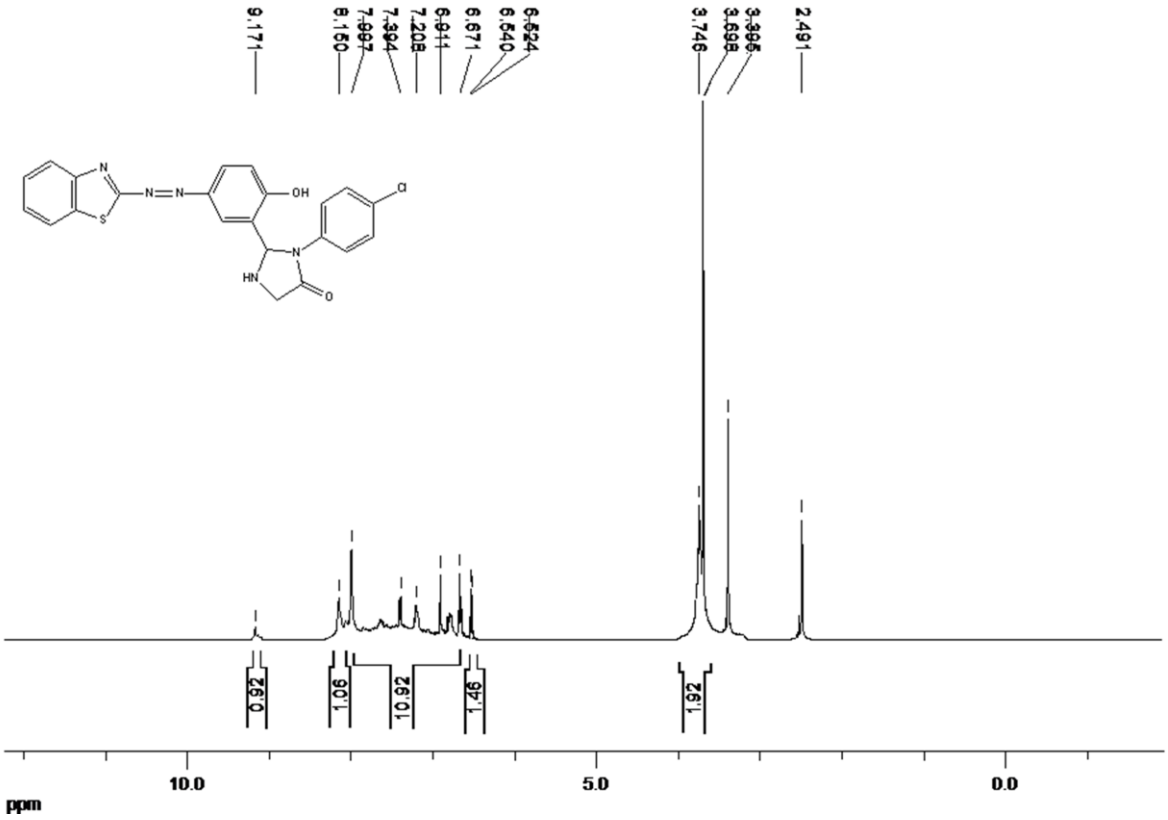


Fig. (3-33): ^{1}H NMR spectrum of compound **4g** in ppm

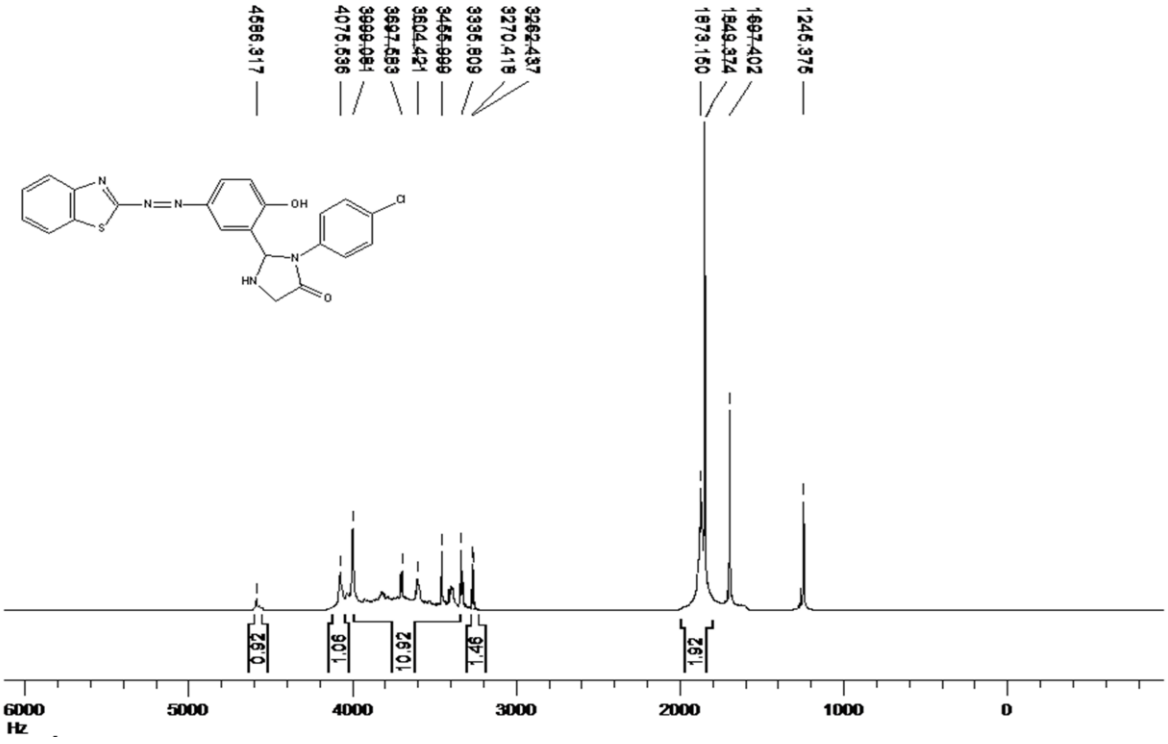


Fig. (3-33): ^{1}H NMR spectrum of compound **4g** in Hz

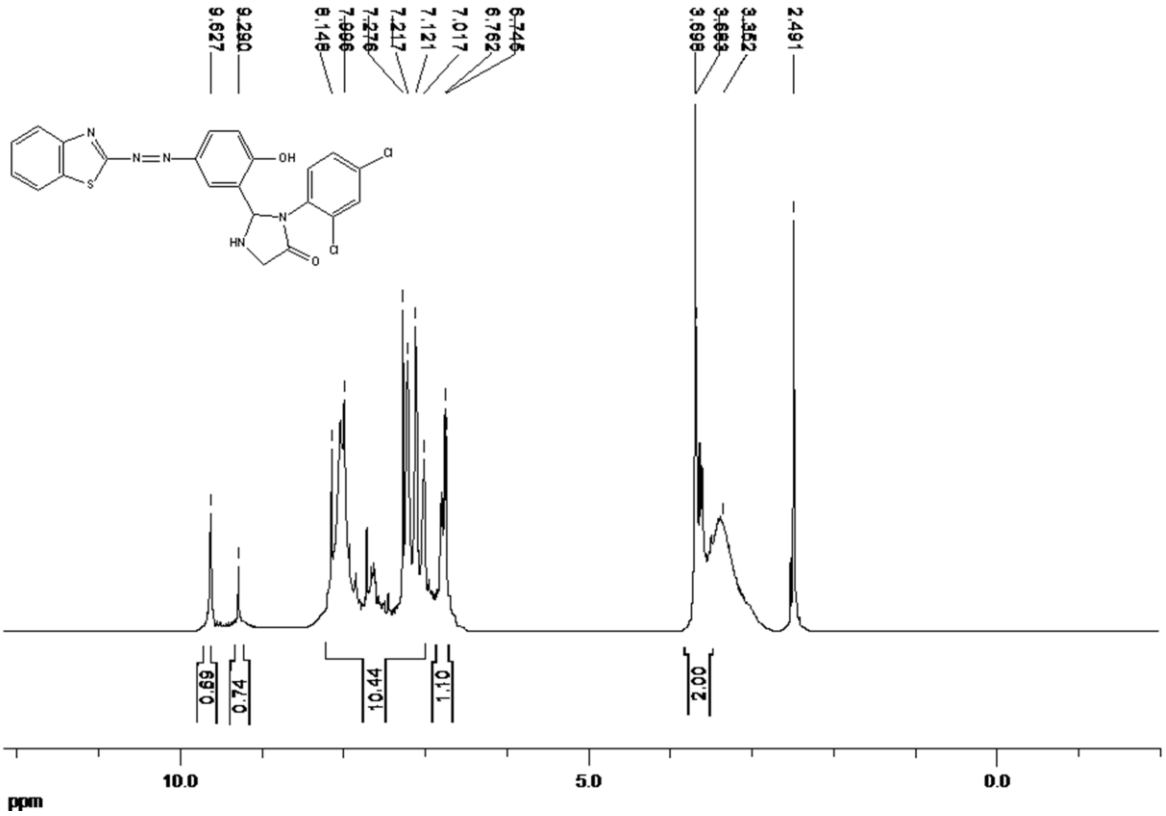


Fig. (3-34): ^{1}H NMR spectrum of compound **4h** in ppm

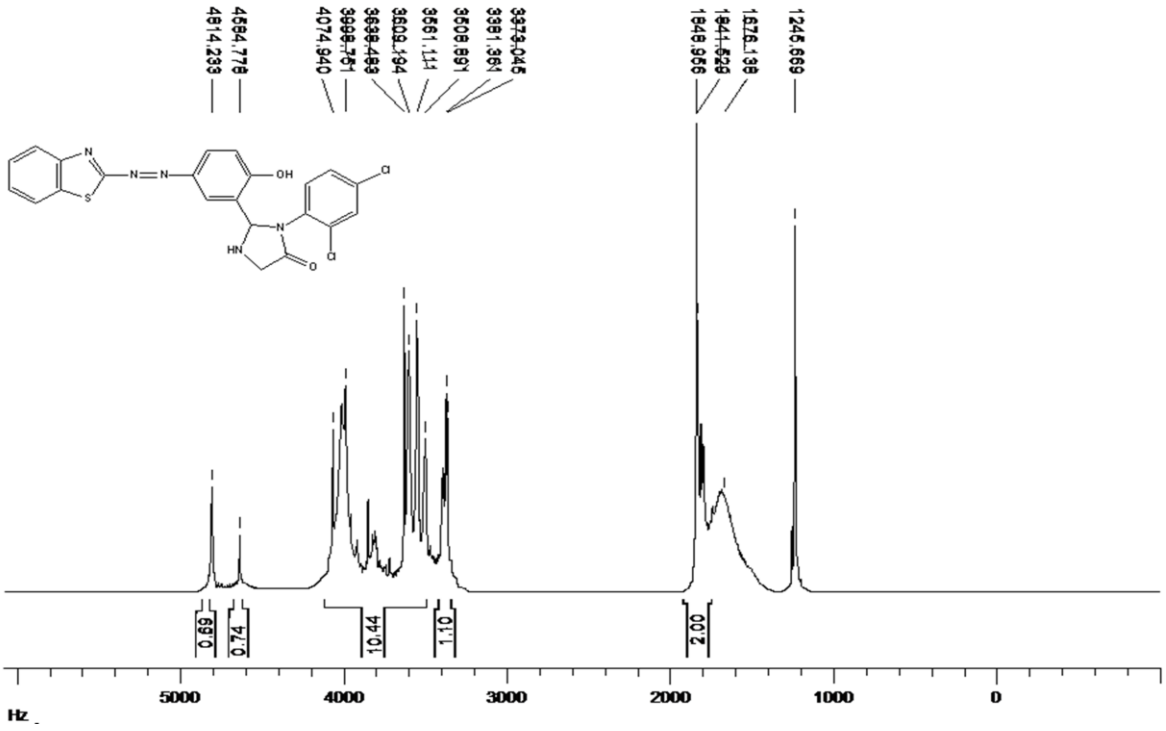


Fig. (3-34): ^{1}H NMR spectrum of compound **4h** in Hz

A.2.2. ^{1}H NMR spectra of imidazolidins 5a-h

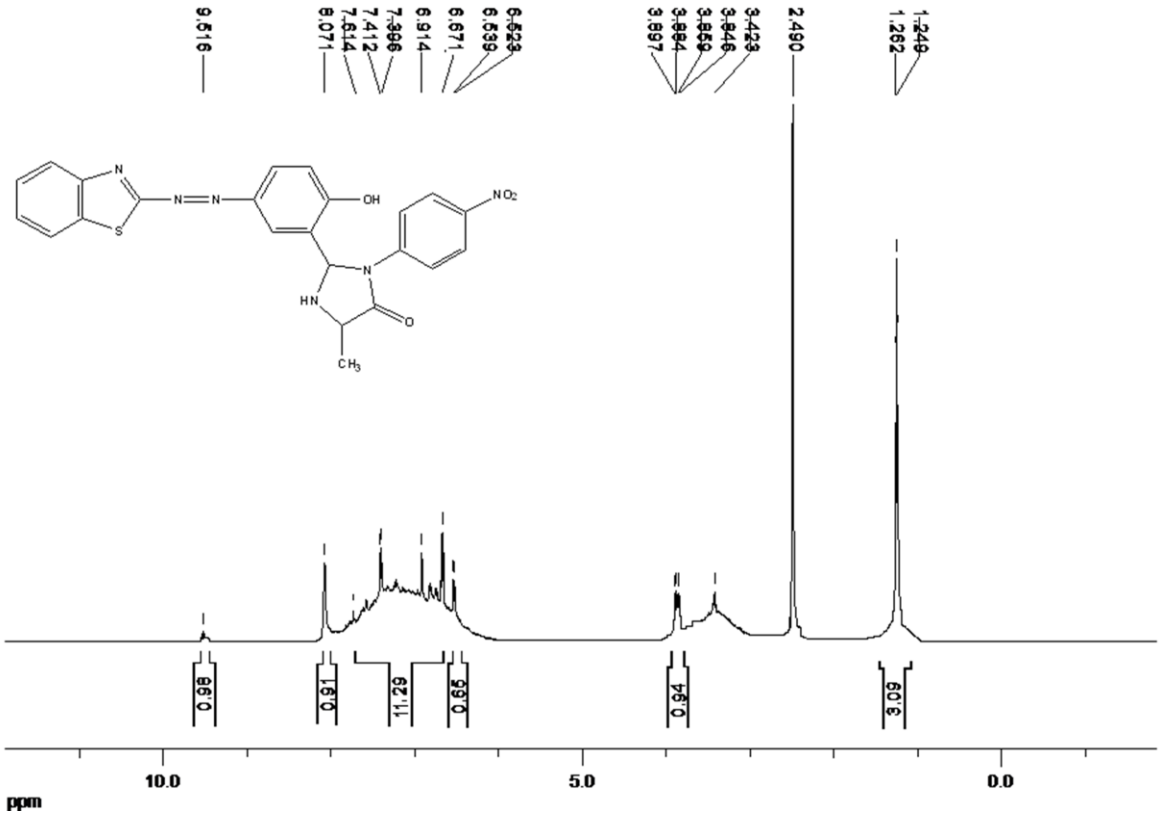


Fig. (3-35): ^{1}H NMR spectrum of compound **5a** in ppm

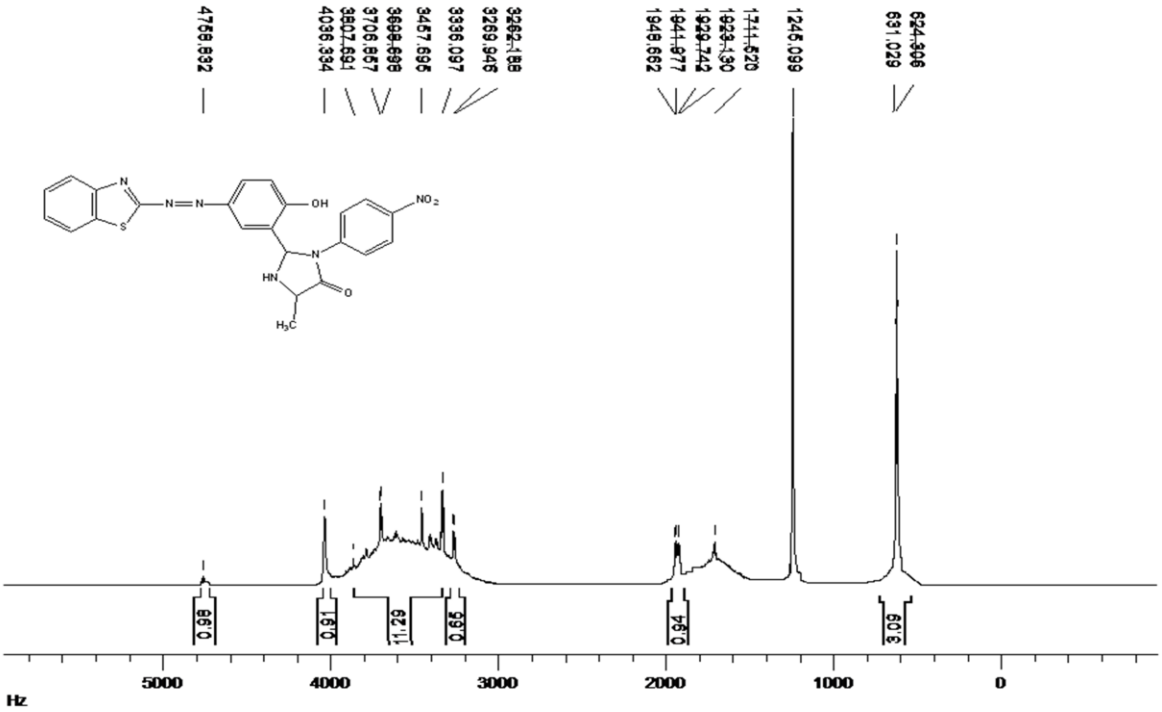


Fig. (3-35): ^{1}H NMR spectrum of compound **5a** in Hz

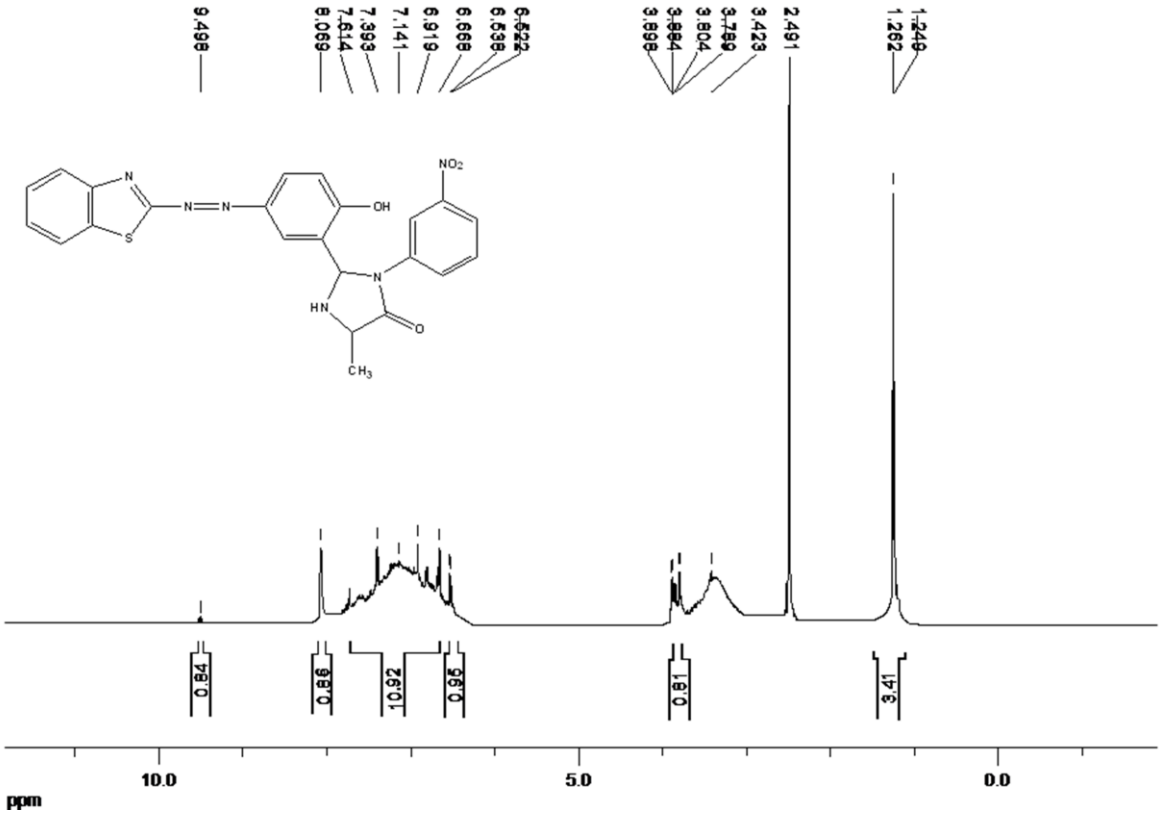


Fig. (3-36): ^{1}H NMR spectrum of compound **5b** in ppm

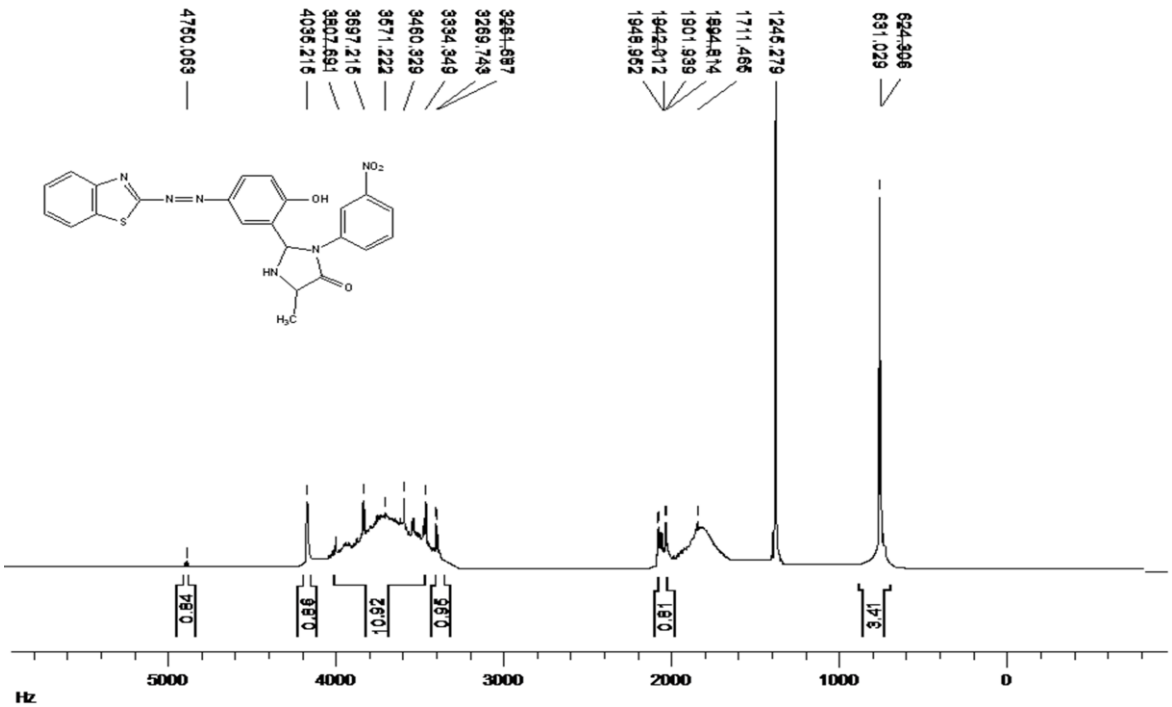


Fig. (3-36): ^{1}H NMR spectrum of compound **5b** in Hz

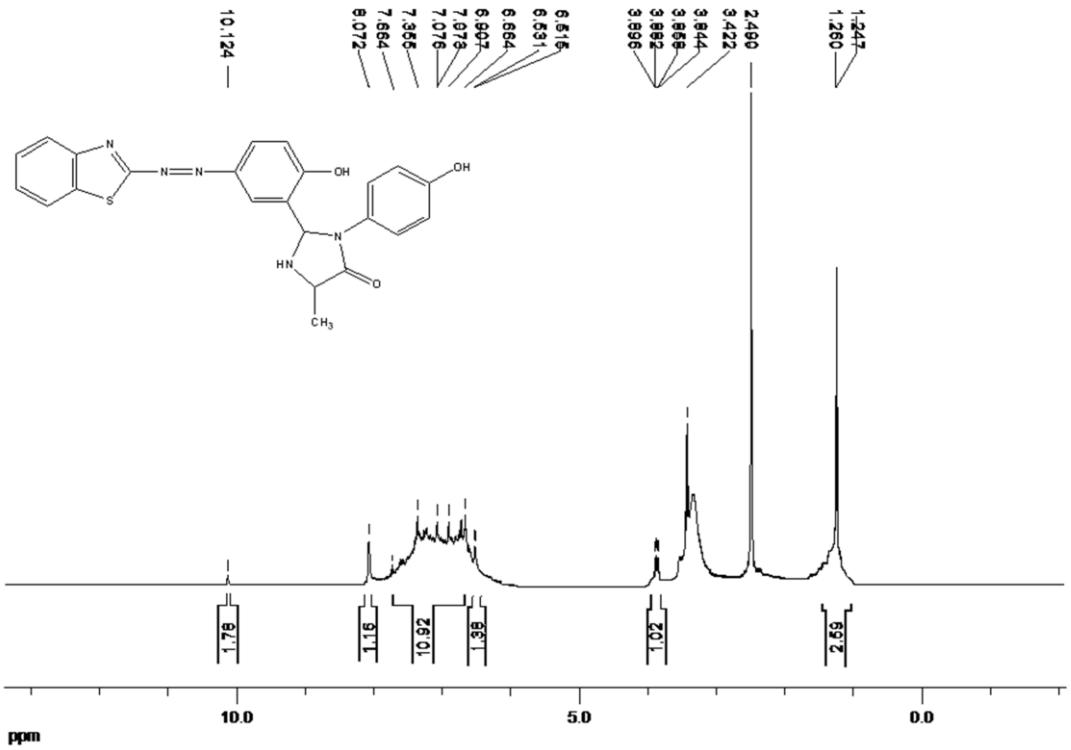


Fig. (3-37): ^{1}H NMR spectrum of compound **5c** in ppm

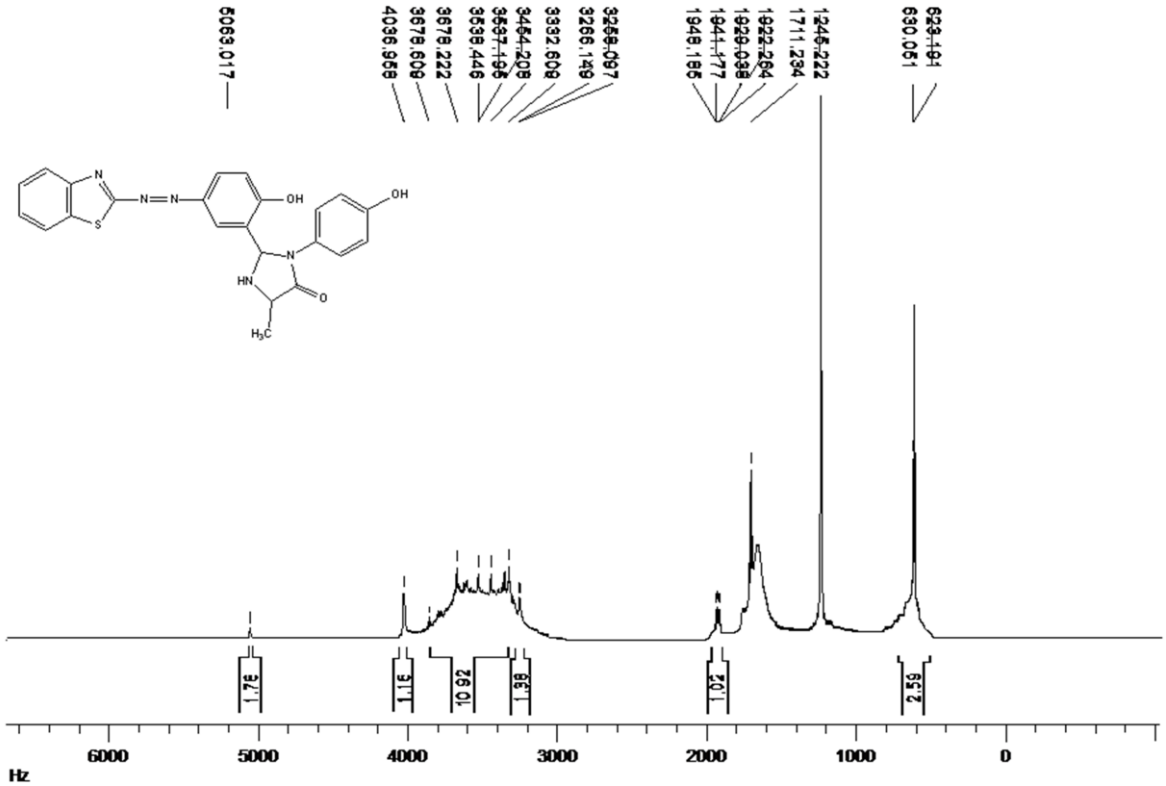


Fig. (3-37): ^{1}H NMR spectrum of compound **5c** in Hz

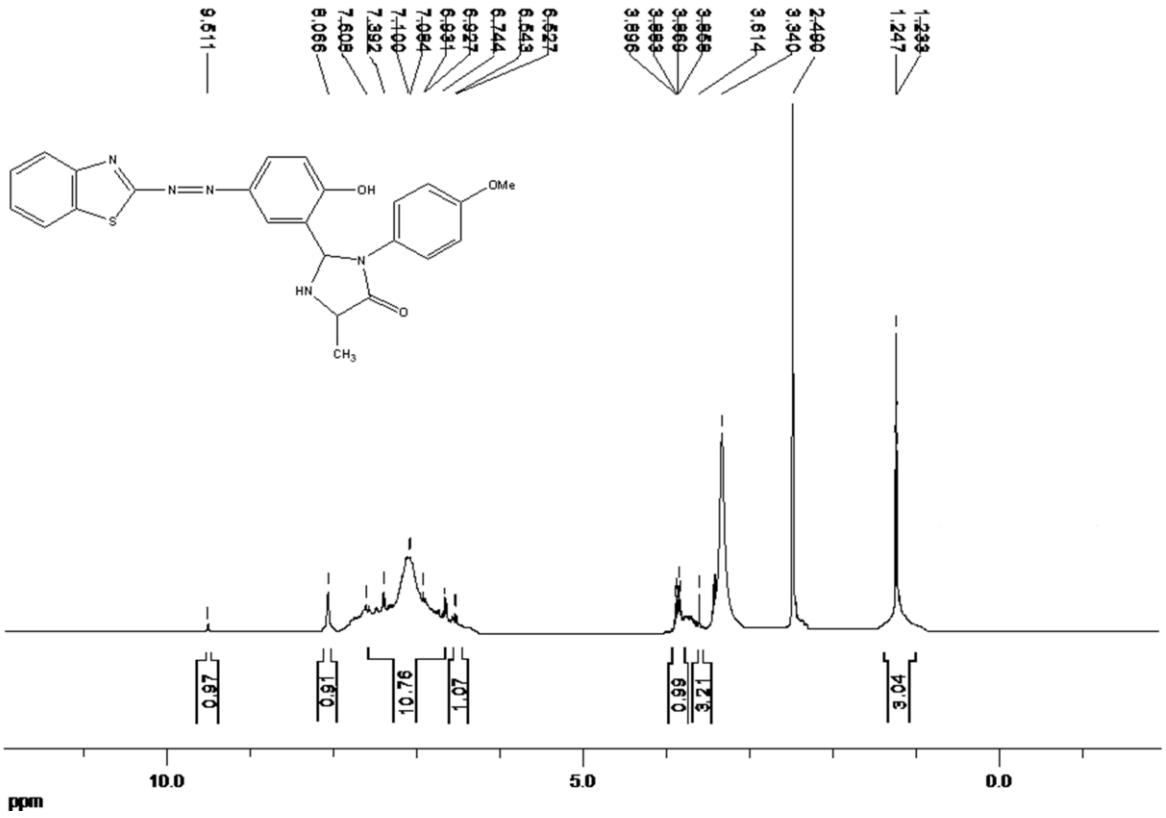


Fig. (3-38): ^{1}H NMR spectrum of compound **5d** in ppm

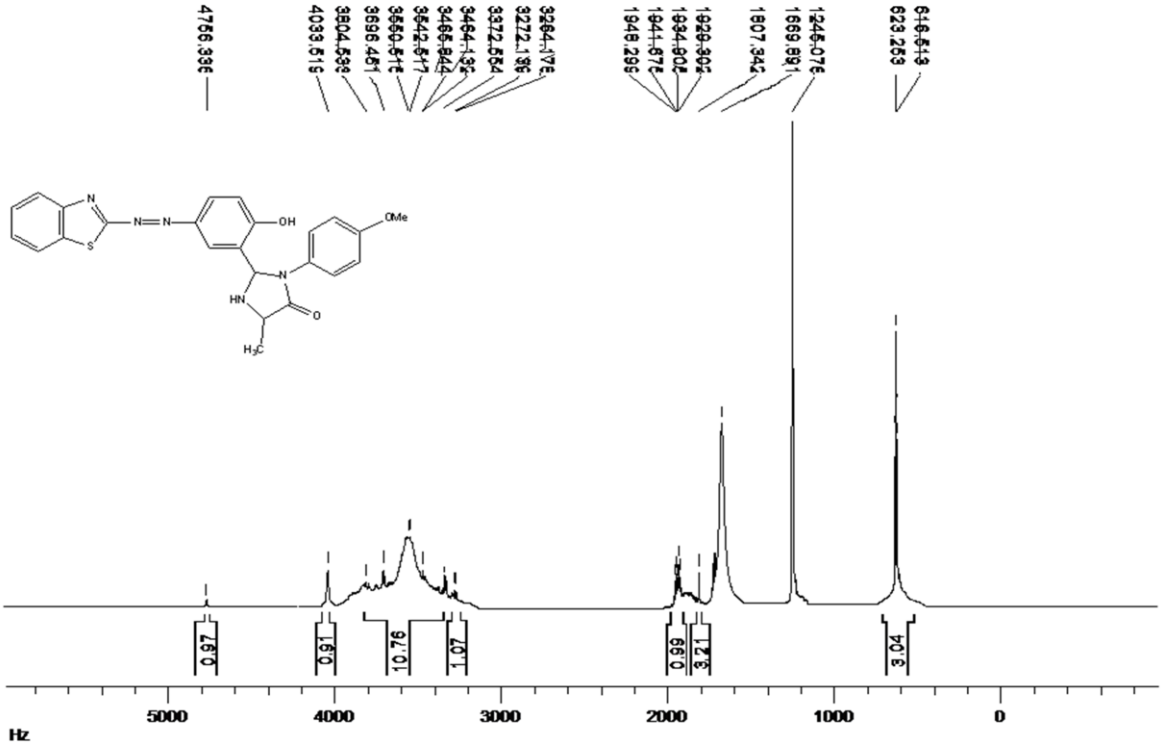


Fig. (3-38): ^{1}H NMR spectrum of compound **5d** in Hz

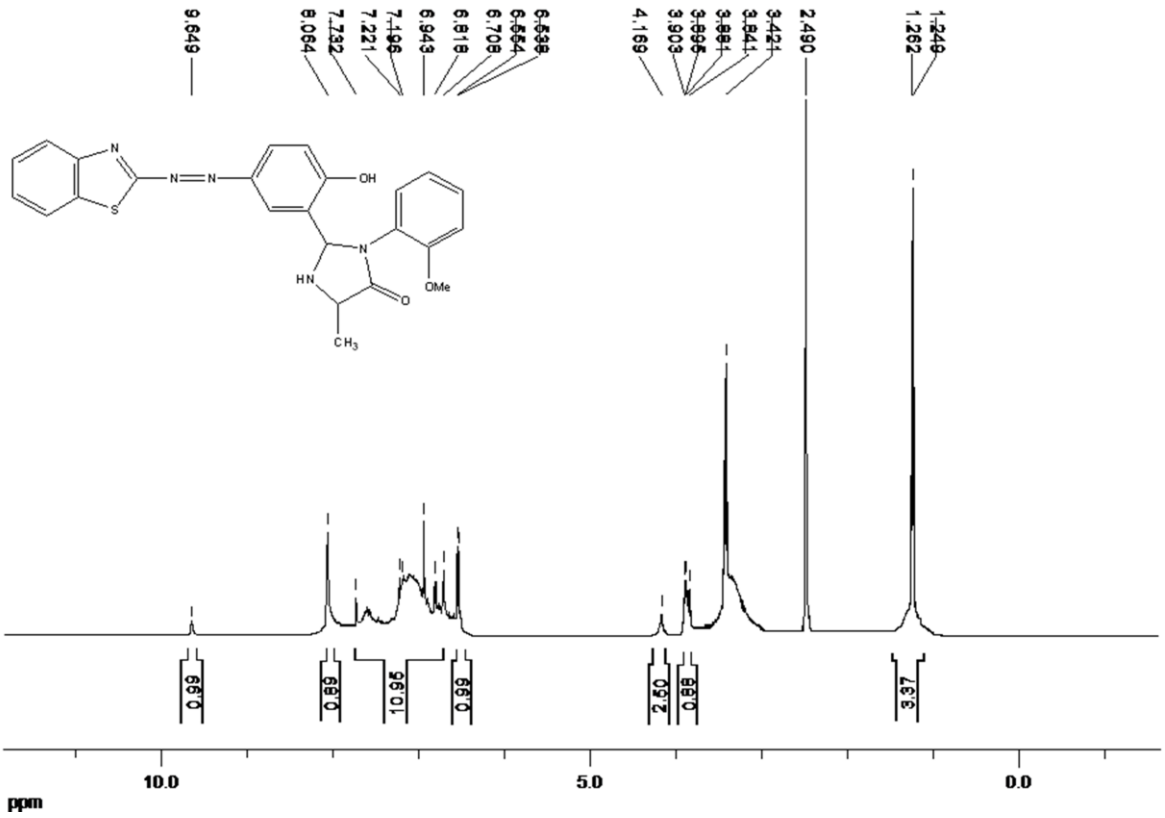


Fig. (3-39): ^{1}H NMR spectrum of compound **5e** in ppm

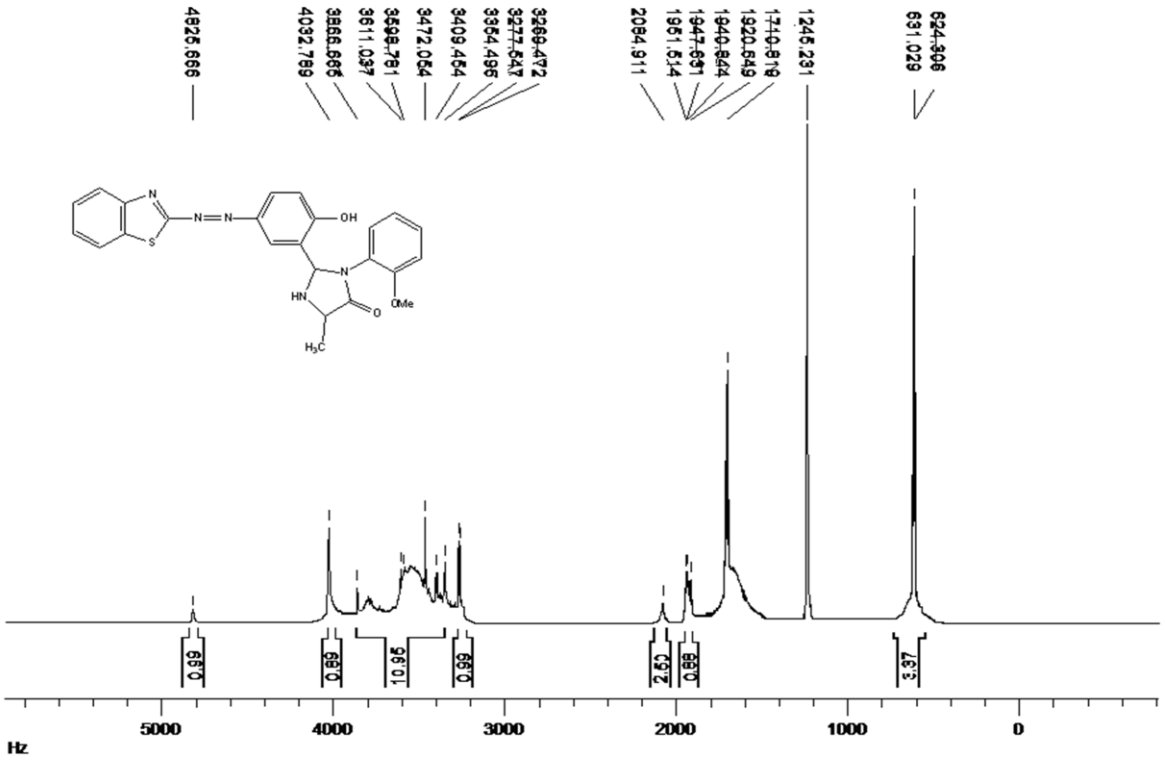


Fig. (3-39): ^{1}H NMR spectrum of compound **5e** in Hz

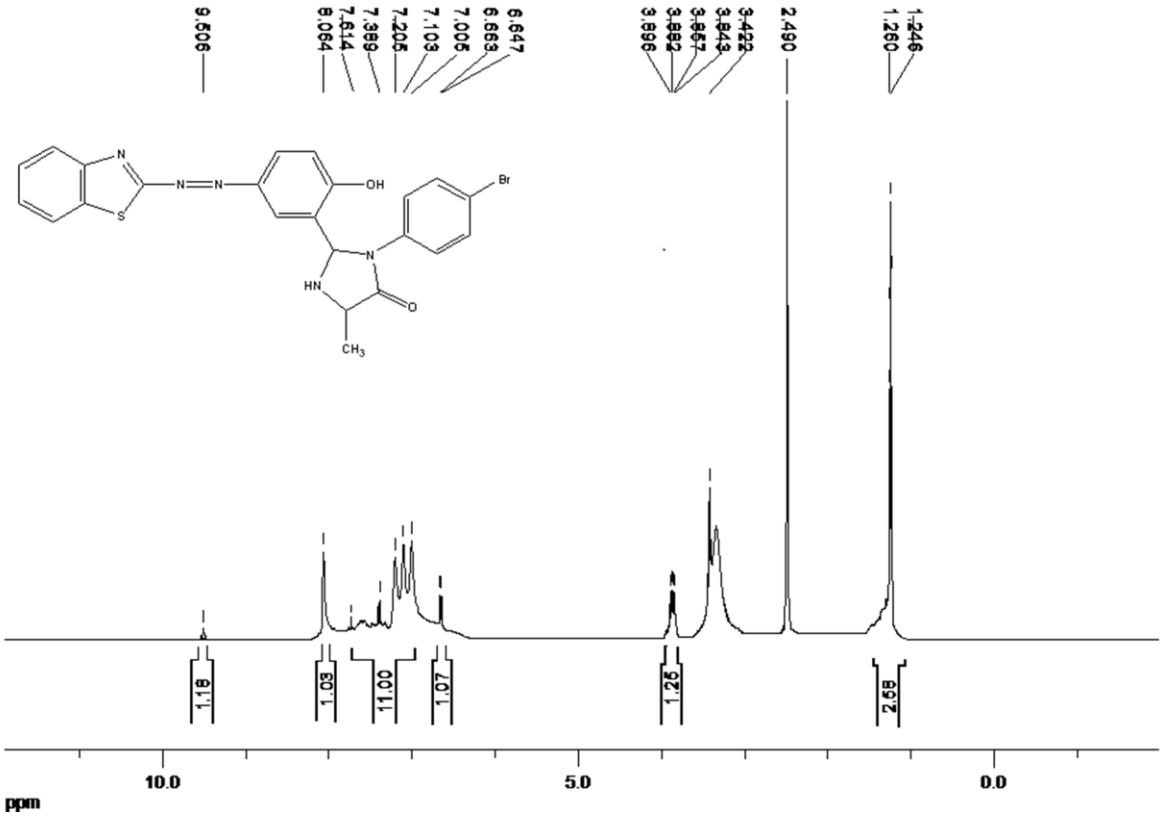


Fig. (3-40): ^{1}H NMR spectrum of compound **5f** in ppm

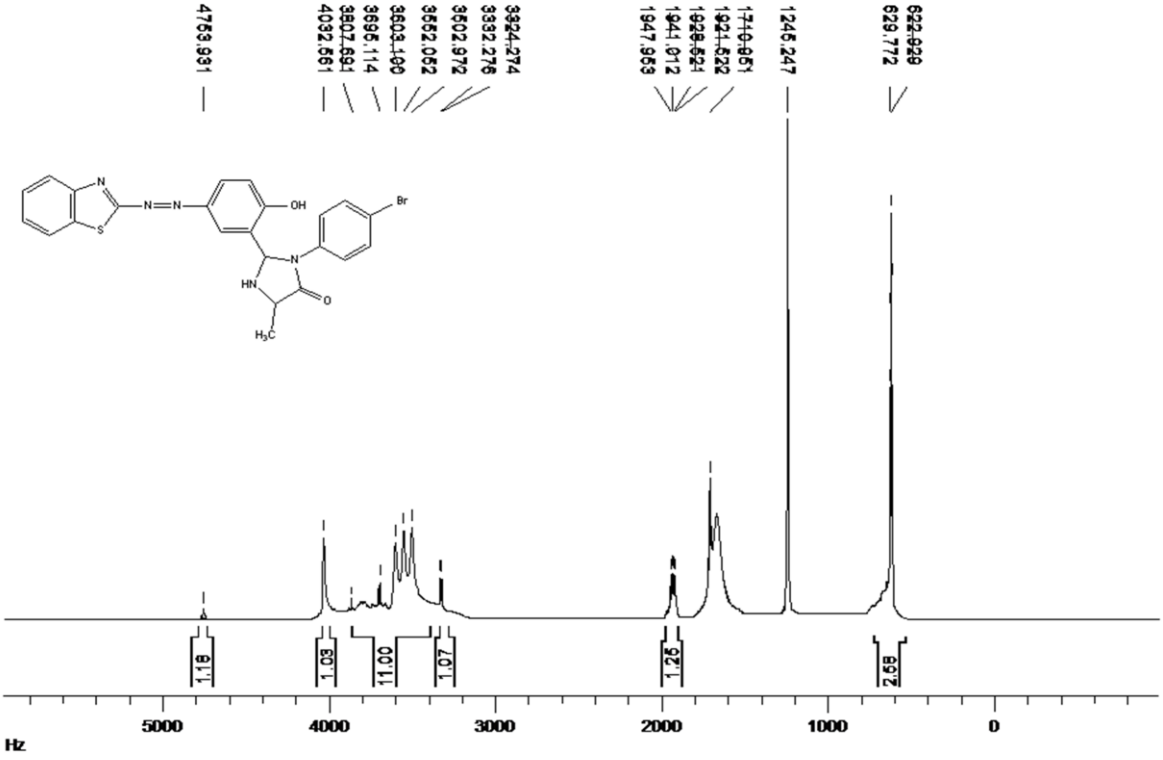


Fig. (3-40): ^{1}H NMR spectrum of compound **5f** in Hz

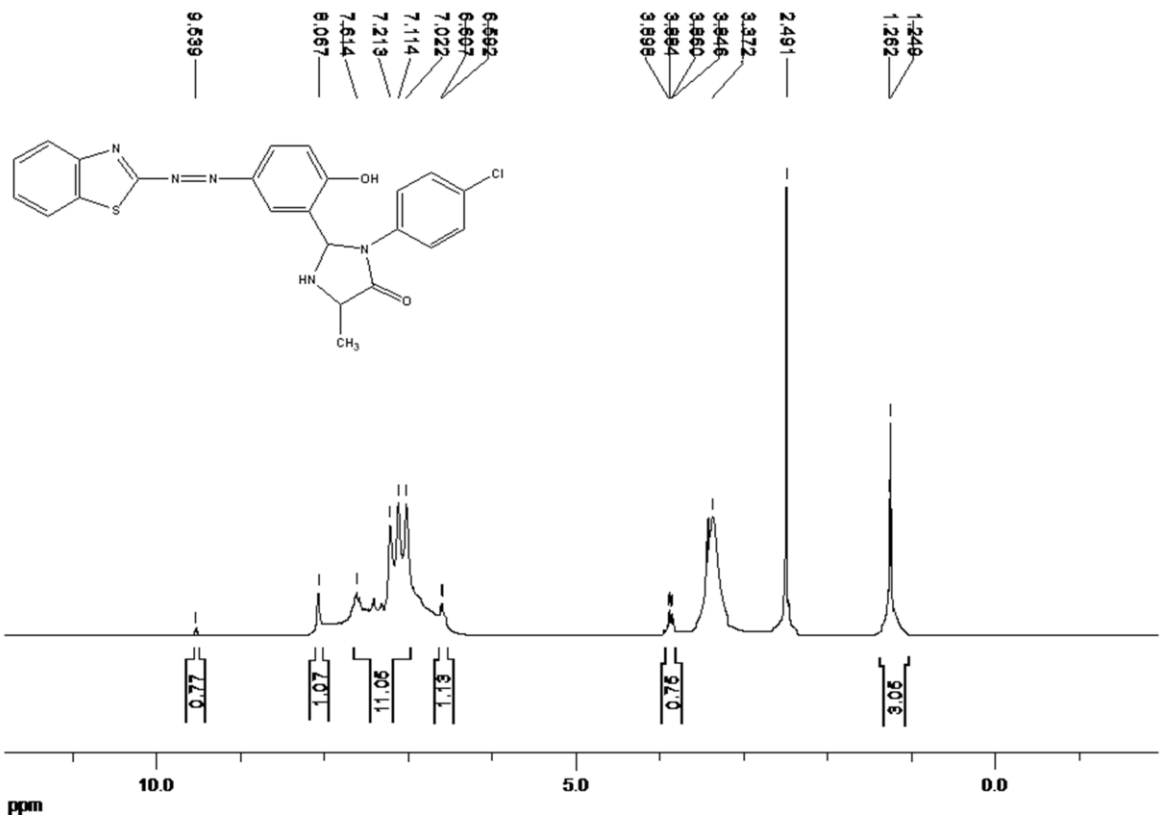


Fig. (3-41): ^{1}H NMR spectrum of compound **5g** in ppm

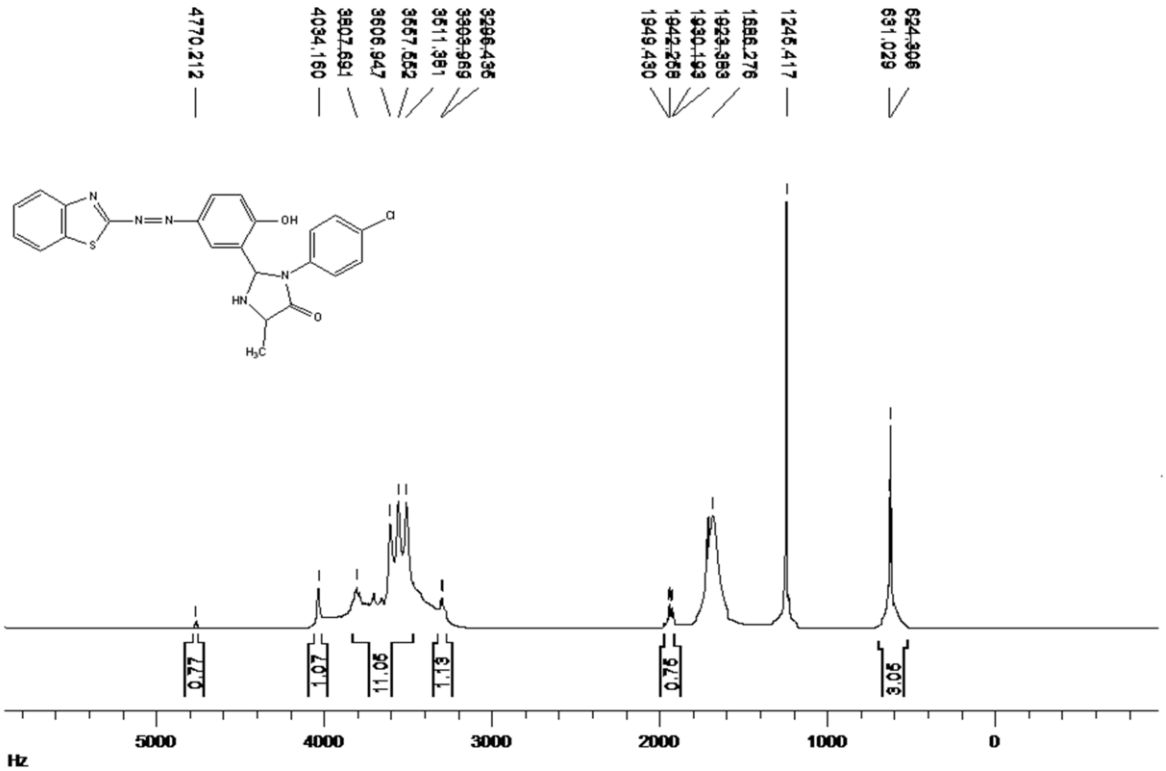


Fig. (3-41): ^{1}H NMR spectrum of compound **5g** in Hz

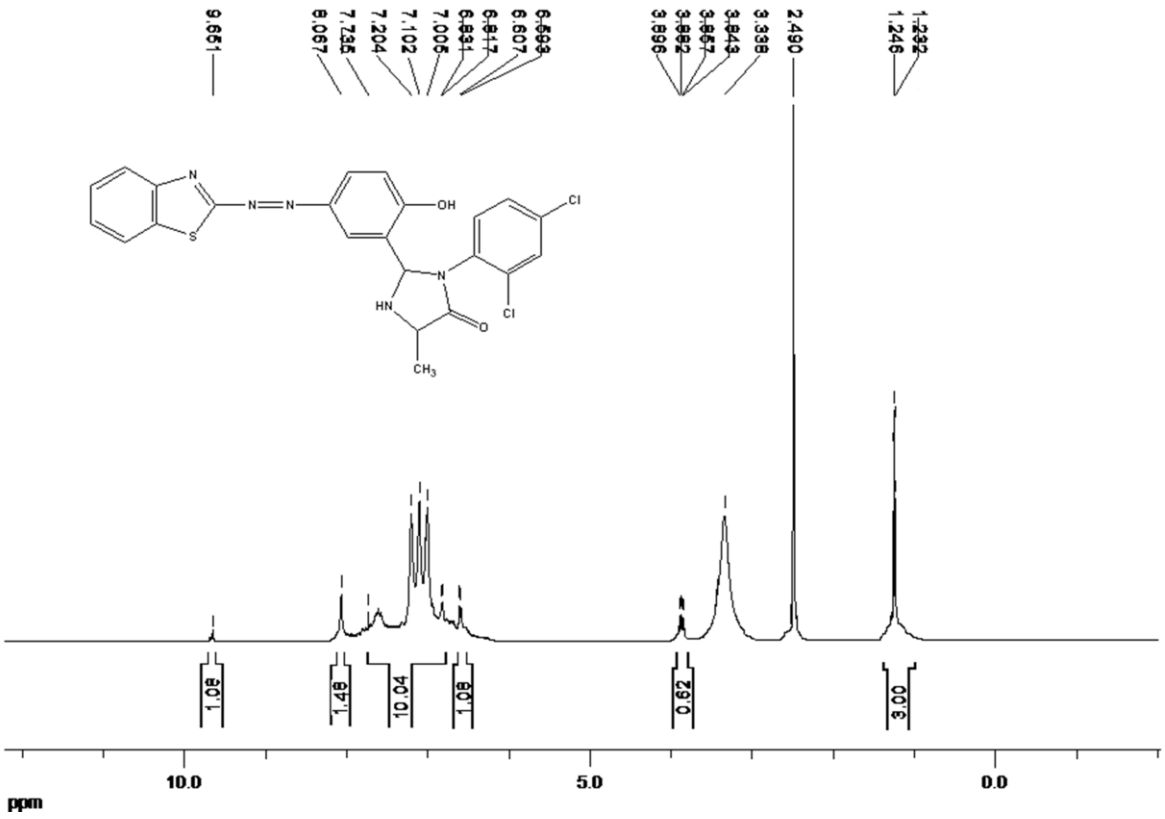


Fig. (3-42): ^{1}H NMR spectrum of compound **5h** in ppm

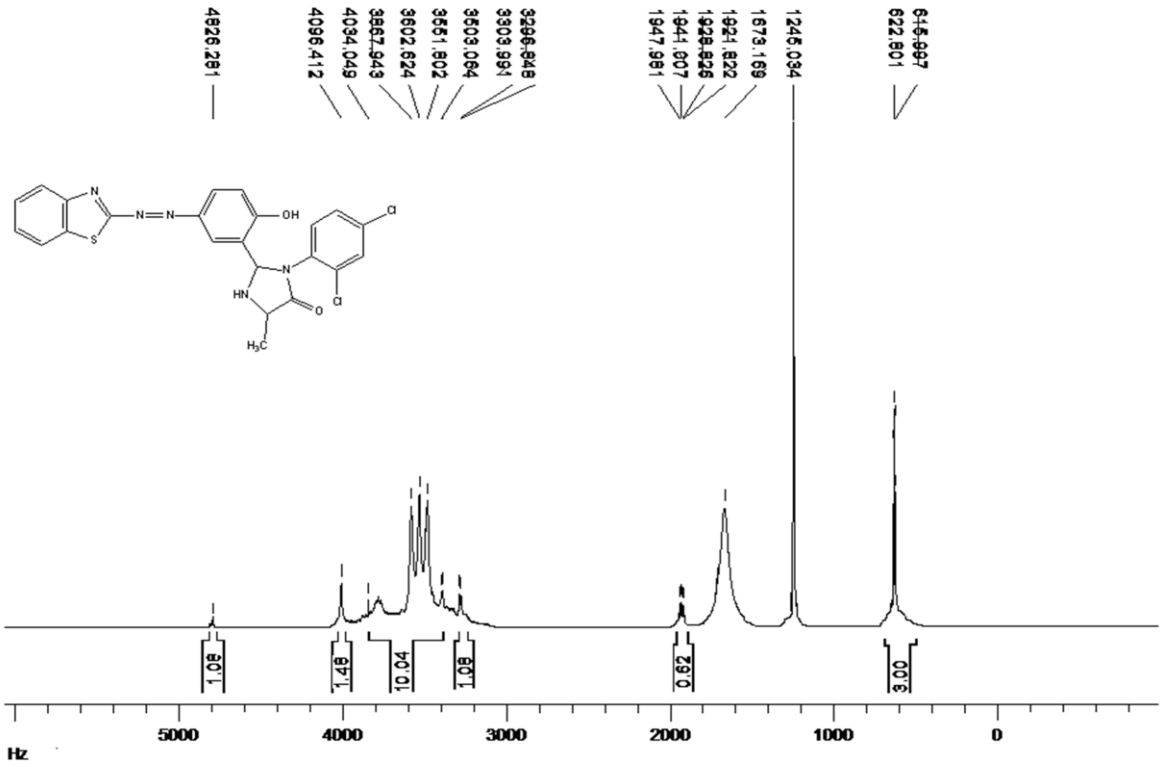


Fig. (3-42): ^{1}H NMR spectrum of compound **5h** in Hz

B. Antibacterial photographs

B.1. Antibacterial photographs of imidazolidine 4a-h against *Staphylococcus aurous*

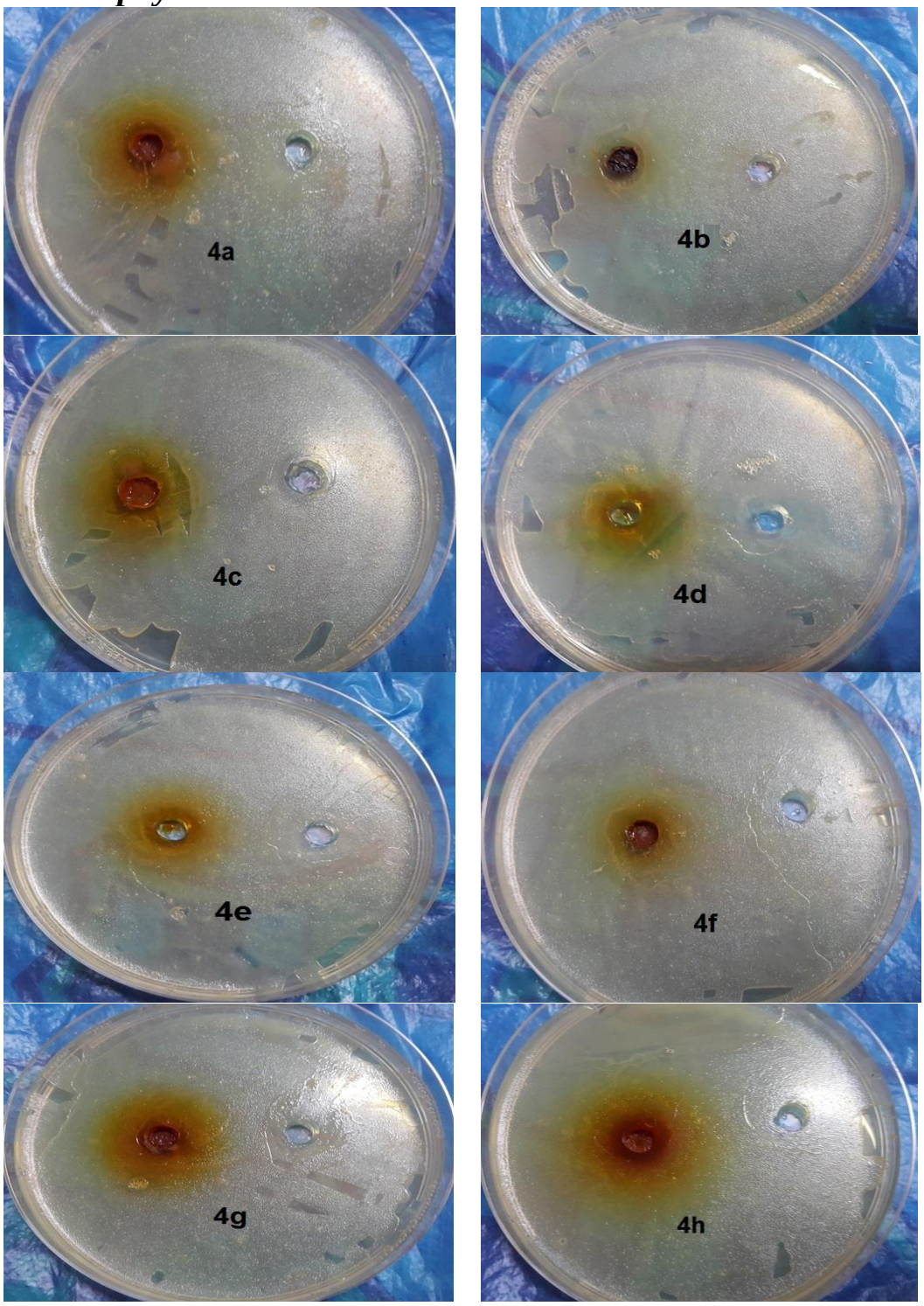


Fig.(3-43): Antibacterial activity of imidazolidine **4a-h** against *Staphylococcus aurous*

B.2. Antibacterial photographs of imidazolidine 5a-h against *Staphylococcus aurous*

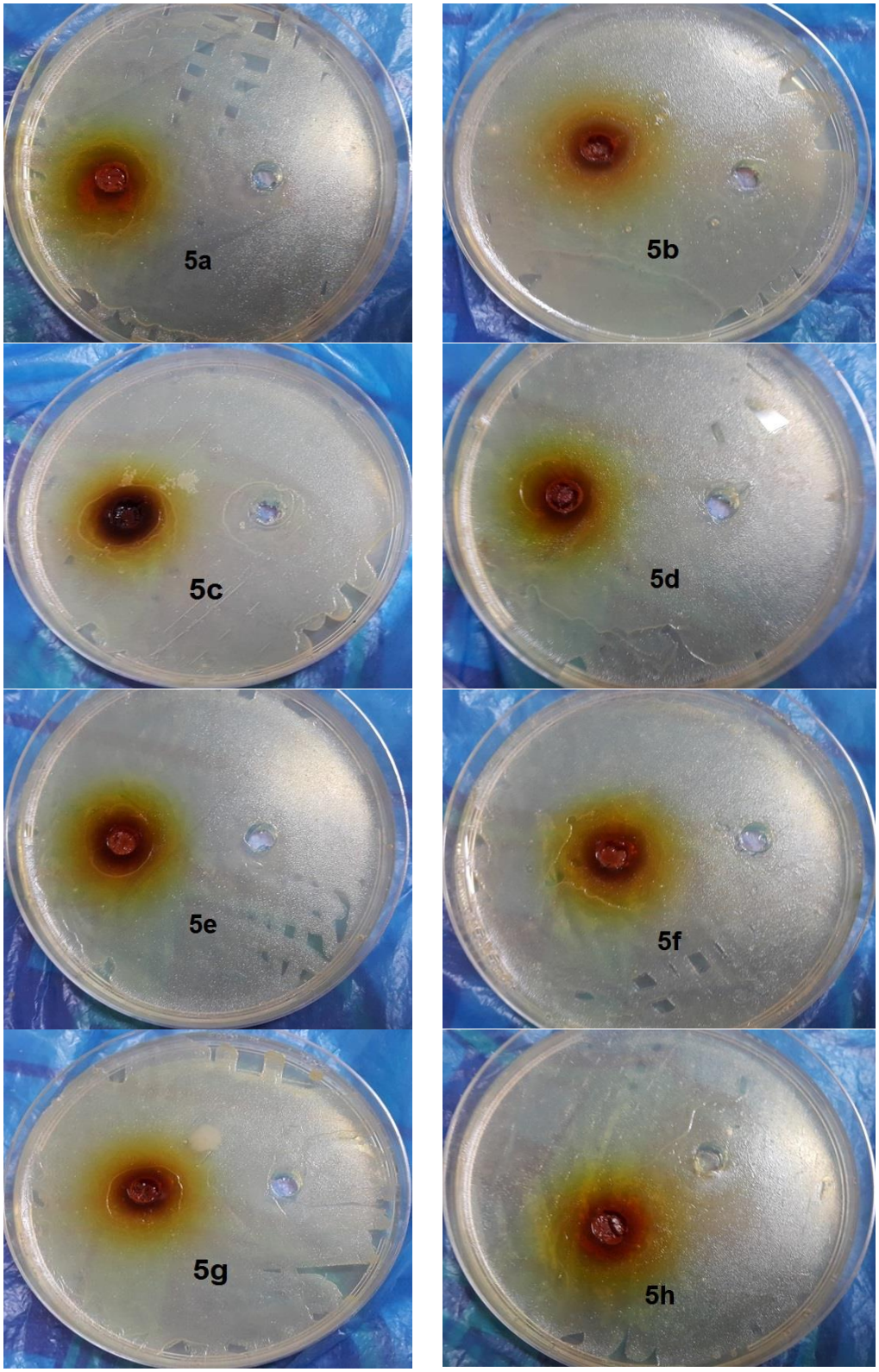


Fig. (3-44): Antibacterial activity of imidazolidine **5a-h** against *Staphylococcus aurous*

B.3 Antibacterial photographs of imidazolidine 4a-h against *Escherichia coli*

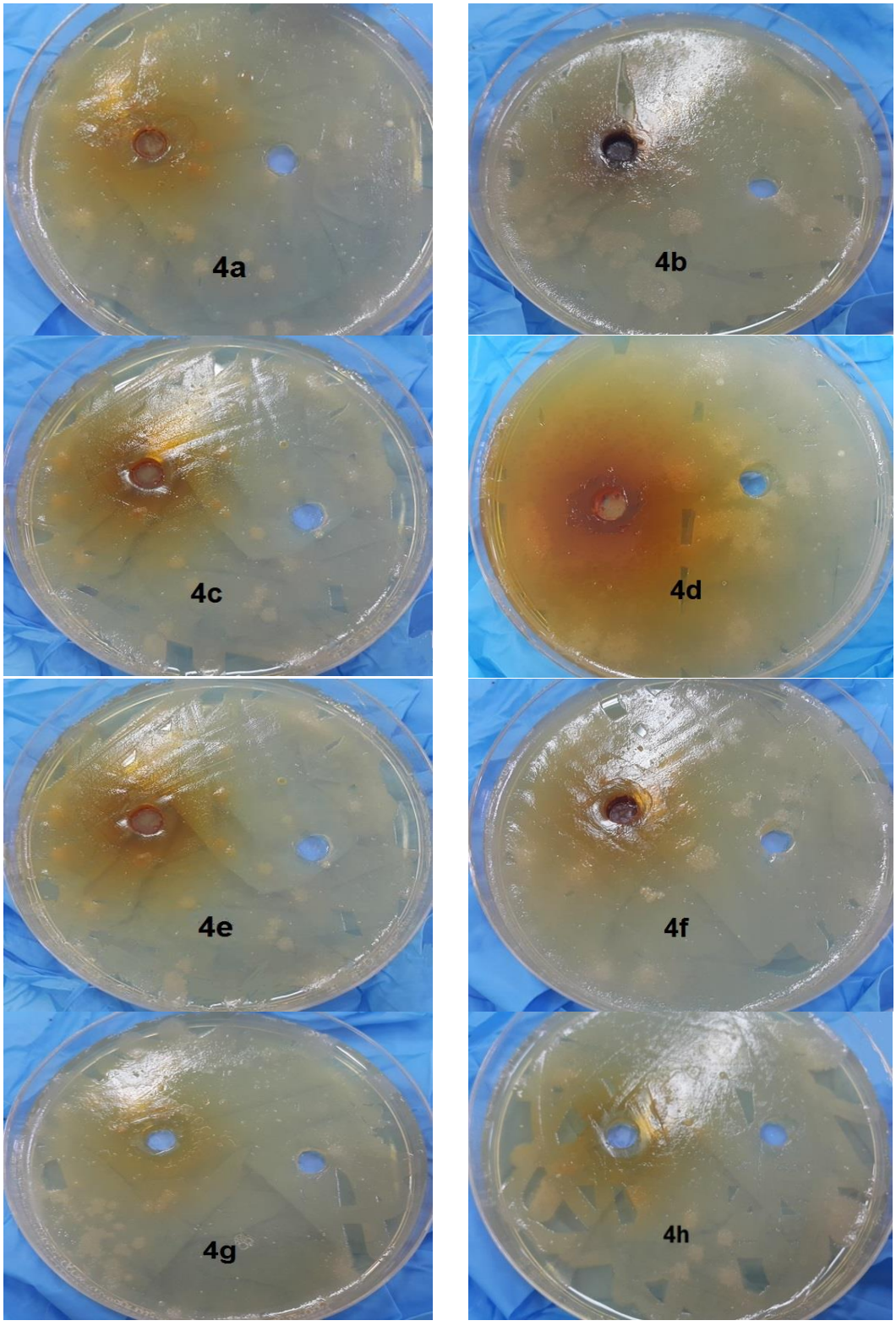


Fig. (3-45): Antibacterial activity of imidazolidine **4a-h** against *Escherichia coli*

B.4. Antibacterial photographs of imidazolidine 5a-h against *Escherichia coli*

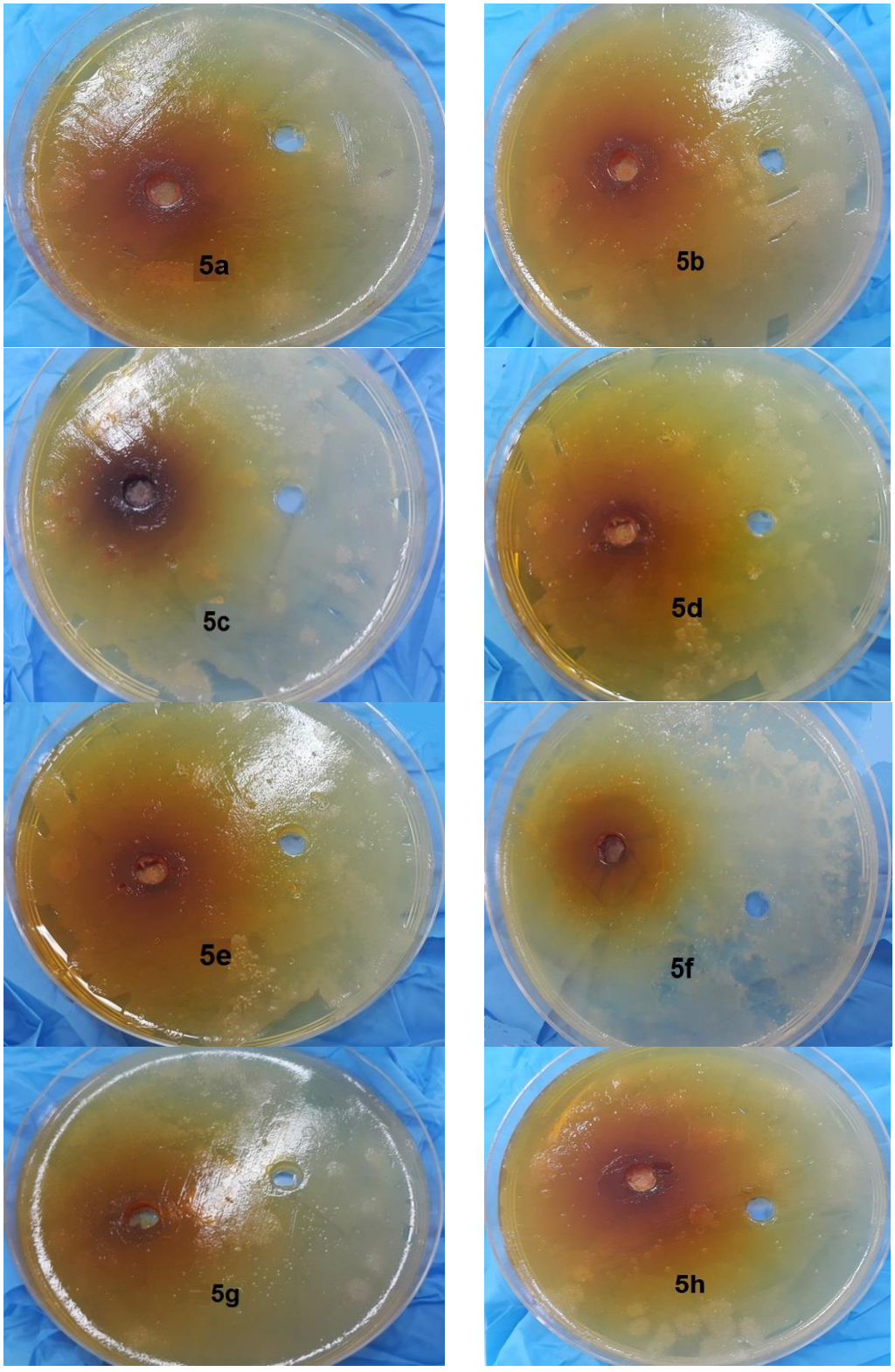


Fig. (3-46): Antibacterial activity of imidazolidine **5a-h** against *Escherichia coli*

B.5. Antibacterial photographs of Gentamycin against *Staphylococcus aurous* and *Escherichia coli*

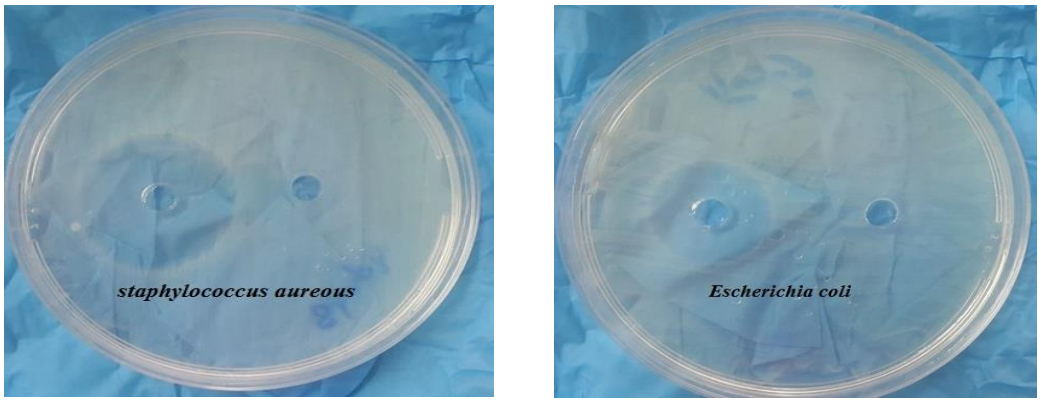


Fig. (3-47): Antibacterial activity of Gentamycin against *Staphylococcus aurous* and *Escherichia coli.*

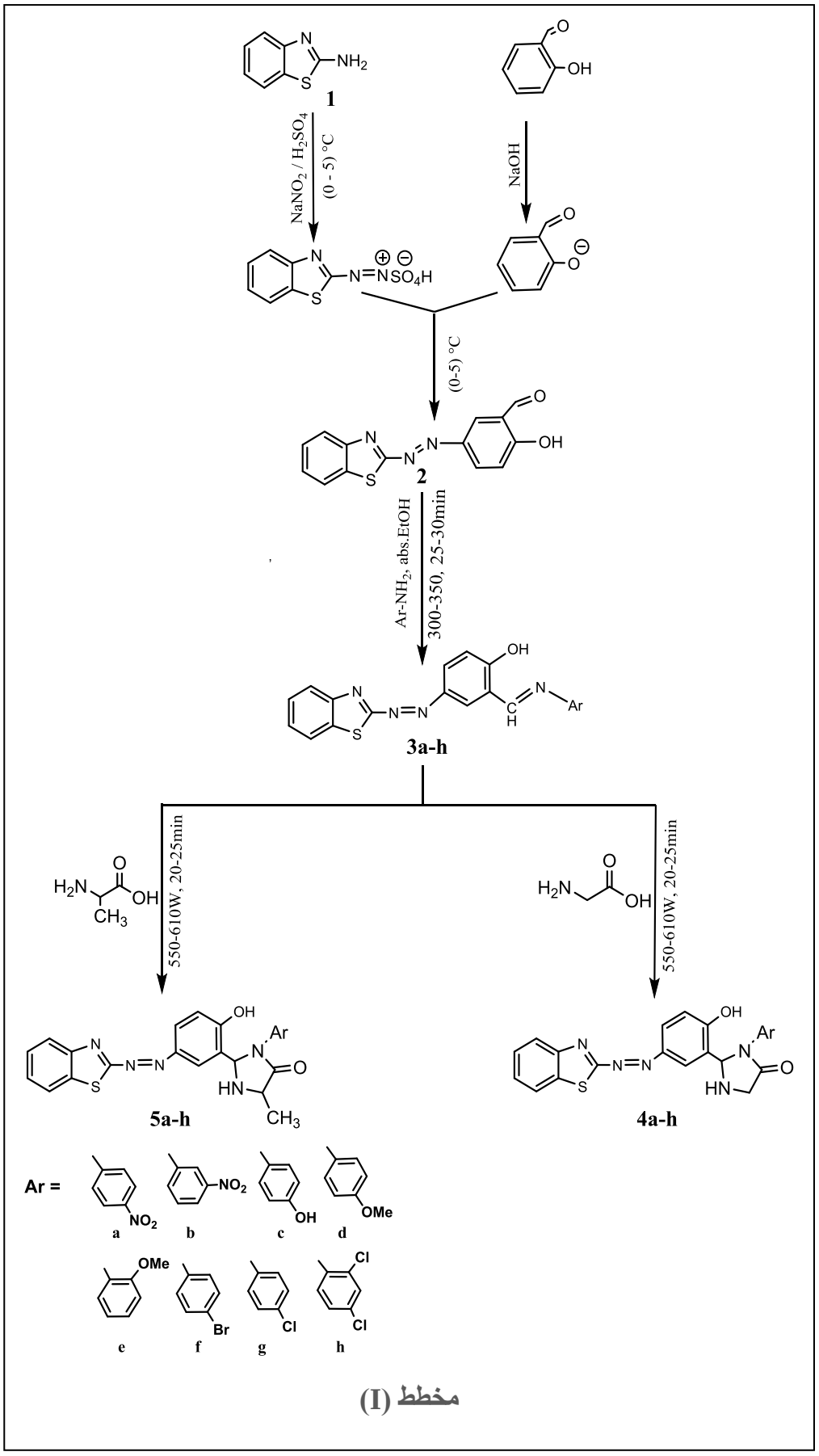
الخلاصة

الخلاصة

تم تحويل مركب 2-امينوبنزوثيازول **1** الى ملح الدايازونيوم المقابل والذي ادخل في تفاعل ازدواج مع محلول قاعدي لمركب 2-هيدروكسي بنزالديهايد ككاشف ازدواج للحصول على مشتق الازوبنزوثيازول **2** الحاوي على مجموعة الديهايد. ادخل الالديهايد الناتج **2** في تفاعلات تكثيفية مع الامينات الاولية الاروماتية المتضمنة (4-نايتروانيلين، 3-نايتروانيلين، 4-هيدروكسي انيلين، 4-ميثوكسي انيلين، 2-ميثوكسي انيلين، 4-برومو انيلين ، 4-كلورو انيلين و 4,2-ثنائي كلورو انيلين) باستعمال تقنية المايكروويف في الايثانول المطلق للحصول على ثمان مشتقات ايمين لحلقة البنزوثيازول **3a-h** على التوالي. عوملت الايمينات الناتجة **3a-h** مع كل من الكلايسين والالانين باستعمال تقنية المايكروويف في التيتراهايدروفيوران فأعطت ستة عشر من مشتقات الايميدازوليدين الجديدة **4a-h** و **5a-h** الحاوية على وحدة البنزوثيازول ، مخطط (I).

شخصت تراكيب جميع المركبات الجديدة المحضرة بوساطة التحليل الكمي للعناصر (CHNS) والطرائق الطيفية المتضمنة مطيافية الأشعة تحت الحمراء والرنين النووي المغناطسي للبروتون. تم فحص الفعالية البايولوجية لكافة المركبات الجديدة المحضرة ضد نوعين من البكتريا هما (*Staphylococcus aurous*) الموجبة لصبغة كرام و (*Escherichia coli*) السالبة لصبغة كرام، وقد بينت نتائج الاختبار الاولي بان مركبات الايميدازوليدين المحضرة (**4a**، **4b** **4c**، **4d**، **4e**، **4g**، **4h**، **5c**، **5d**، **5f**، **5g**، **5h**) تمتلك تاثيرا أعظم من الجنتامايسين تجاه البكتريا الموجبة لصبغة كرام، كما اظهرت مركبات (**4d**، **4h**، **5c**، **5f**) تاثيرا اعظم من الجنتامايسين تجاه البكتريا السالبة لصبغة كرام، الاشكال (3-43)-(3-47).

الخلاصة



مخطط (I)

جمهورية العراق
وزارة التعليم العالي والبحث العلمي
جامعة كربلاء/كلية العلوم
قسم الكيمياء

تحضيرمايكروي ودراسة الفعالية البيولوجية لبعض مشتقات الايميدازوليدين الجديدة للبنزوثيازول

رسالة مقدمة إلى
مجلس كلية العلوم- جامعة كربلاء
وهي جزء من متطلبات نيل درجة الماجستير في الكيمياء

من قبل
حسين علي قابل
بكالوريوس علوم كيمياء (٢٠١٢)
جامعة كربلاء/ كلية العلوم

بإشراف

أ. د. زيد حسن عبود الأعرجي

١٤٣٩ هـ ٢٠١٧ م