Ministry of High Education and Scientific Research
University of Babylon
College of Science
Chemistry Department

Synthesis , Characterization , Theoretical study and biological activity of New Organic Compounds based on Resorcinol

A Thesis

Submitted to the council of College of Science, University of Babylon in Partial Fulfillment of the Requirements for the Degree of Master in Chemistry Science

By

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2023 A.D **1444 A.H**

بسم الله الرحمن الرحيم

﴿ يَرْفَعِ اللَّهُ الَّذِينَ
آمَنُوا مِنكم والَّذِينَ أُوتُوا العِلْمَ
دَرَجاتٍ واللَّهُ بِما تَعْمَلُونَ خَبِيرٌ﴾

صدق الله العظيم

سورة المجادلة

الاية 11

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I Would like to express my thanks to Mr. Ayad Ali for his great help in all the steps of the work , also thank all my friends , colleagues who helped me in one way or another in the fulfillment of this work .

Tuqa Sattar

Dedication

To: Great teacher and Leader, Our messenger Mohammed and hisFamily.

To: My first love, my forever hero

My Dad

To: Whom that planted me in life as a seed and watered me from herblood drop by drop.

My mother

To: My support and my companions, to I see my joy in their eyes.

My brother and my sisters

To : My closest advisor, dedicated coparent, and the love of my life . who supported me every step of the way, as he always does, with patience, great insight, humor, and love.

My husband, Rakan Jamal

To: The my little prince and the joy of my life.

Taim

Tuga

List of Abbreviations

Symbol	Description
FTIR	Fourier Transform Infra-Red
TLC	Thin-layer chromatography
^1H-NMR	Proton Nuclear magnetic resonance
^{13}C-NMR	Carbon Nuclear magnetic resonance
TMS	Tetramethylsilane
ppm	Part per million
CHNS	elemental Analysis
g	Gram
mmol	Millimole
hr.	Hour
mL	Milliliter
DMSO	Dimethyl sulfoxide
GAA	Glacial Acetic Acid
Et_3N	Triethylamine
Str.	Stretch
Comp. symb.	Compounds symbol
M. formula	Molecular formula
M.Wt	Molecular weight
m.p	Melting point
^{o} C	Celsius degree
R_f	Retardation factor
DCM	Dichloromethane
Ar	Aromatic
IC_{50}	half maximal inhibitory concentration
PM3	Parameterization Model, Version 3
ESP	Electrostatic Potential
HOMO	Highest Occupied Molecular Orbital
LUMO	Lowest Unoccupied Molecular Orbital
E_b	Energy Barrier
ΔH	Enthalpy Reaction Chang
Ts	Transition State

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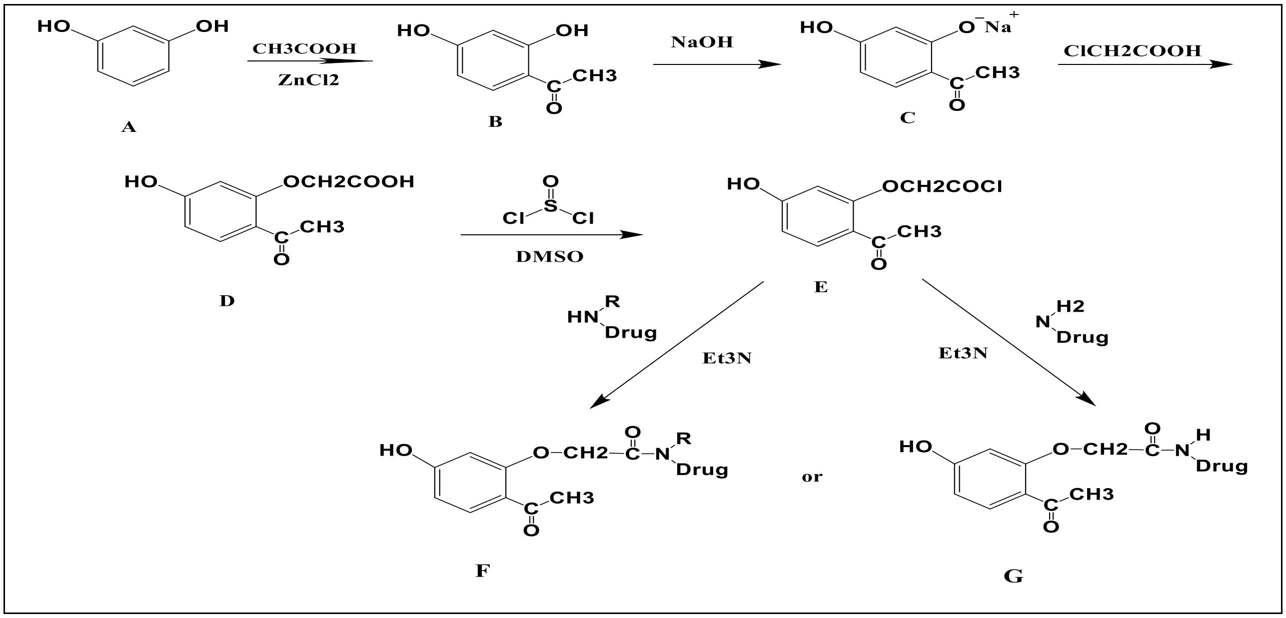
Summary

This work is related with preparation of new twenty-five derivatives for resorcinol as starting material. The characterization of derivatives structures is done by molecular spectroscopy instrumental technique as first stages. At second stage, theoretical simulation have been done to investigate the acylation reaction of resorcinol since the geometrical structures are calculated for all reaction component and their suggested transition states.

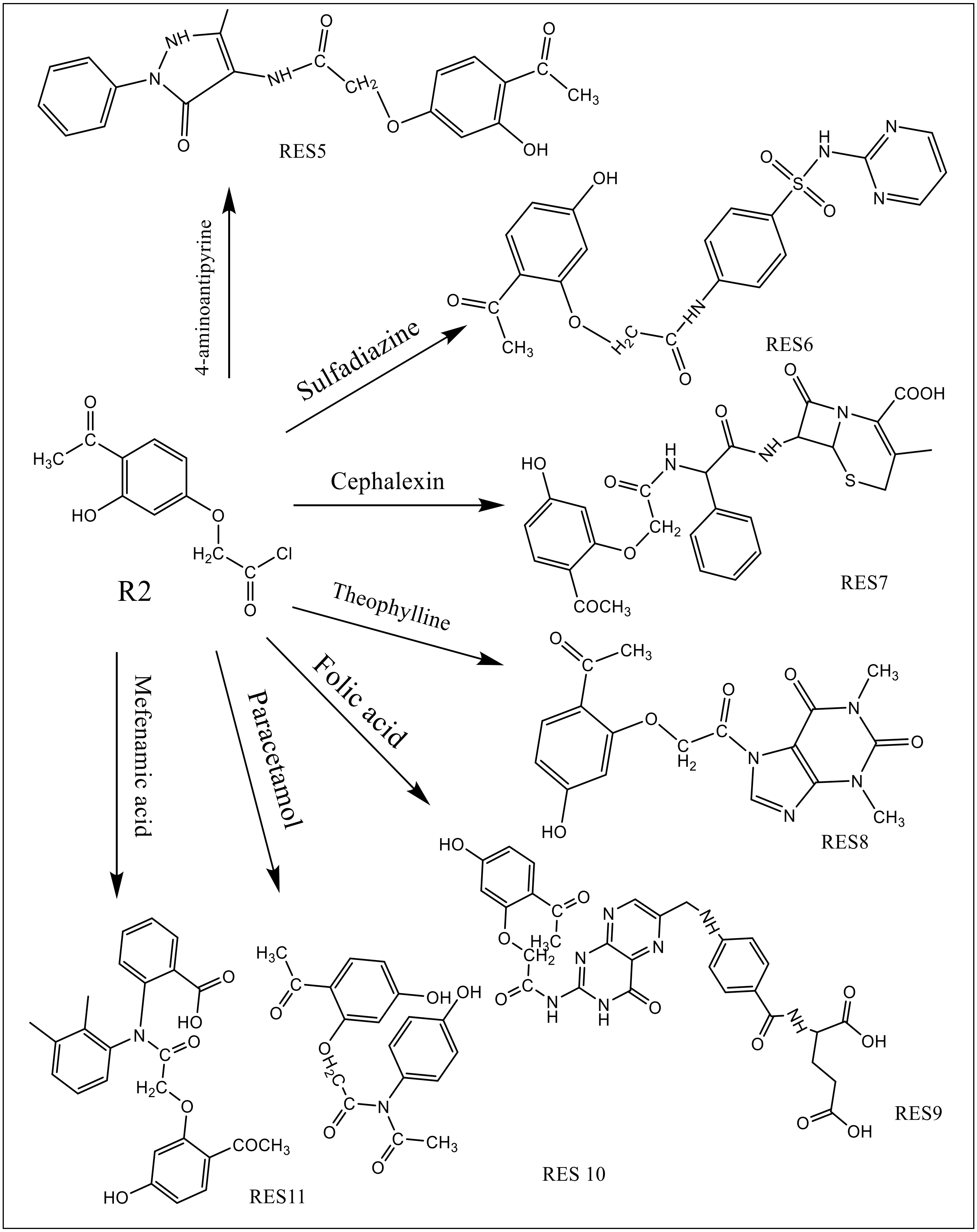
The most probable transitions states is investigated through the calculations of energetic and electronic properties to indicate the most likely pathway of the acylation reaction. The work included several paths. as follows: -

The first path:-

Direct interaction of seven amino drugs (Folic Acid, Mefenamic Acid, Sulfadiazine, Paracetamole, Theophylline , Cephalexin, 4-Aminoantipyrine) after converting the acid by using of $SOCI_2$ and DCM (dichloromethane) to form acid chloride ,after that add Et_3N to the resulting compounds (acid chloride).

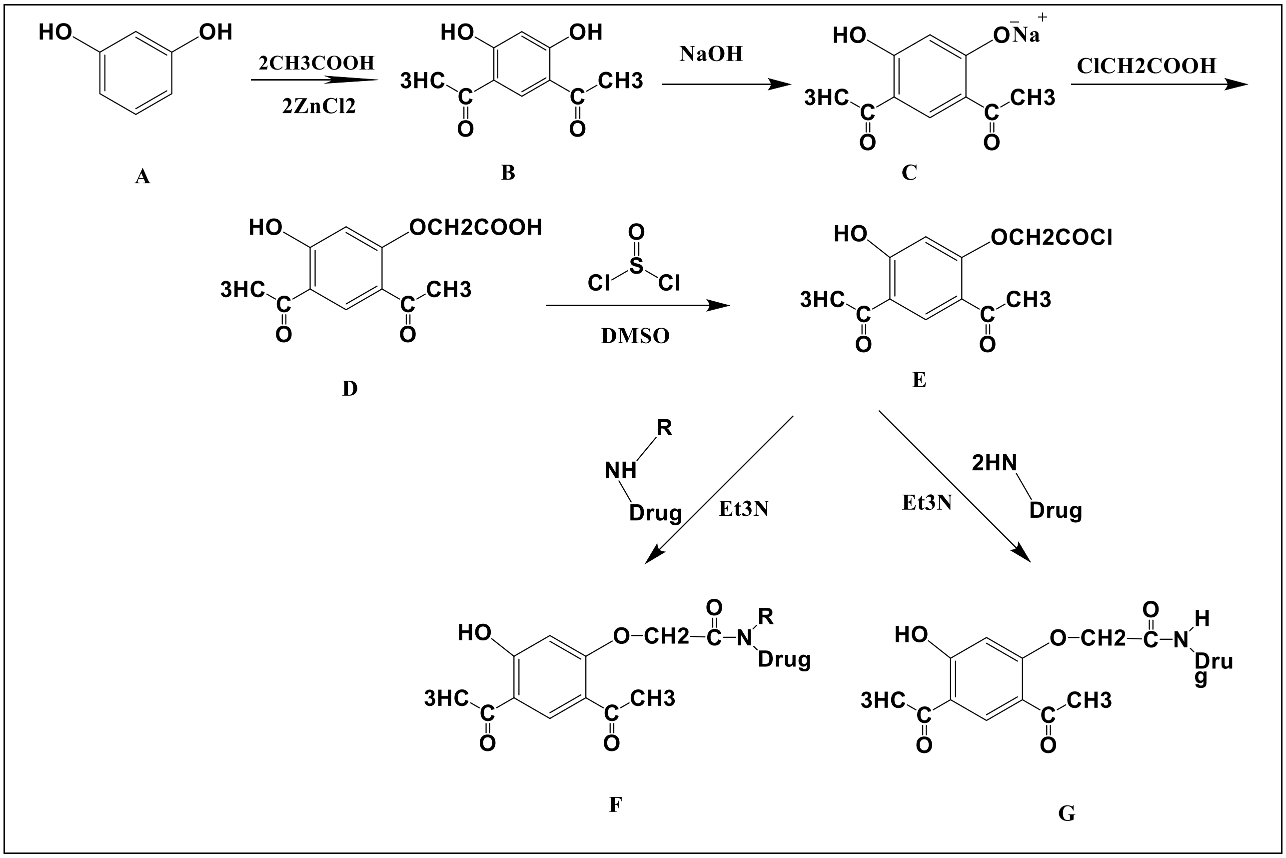


Scheme (1): Description for the synthesis of derivatives (RES5-RES11)

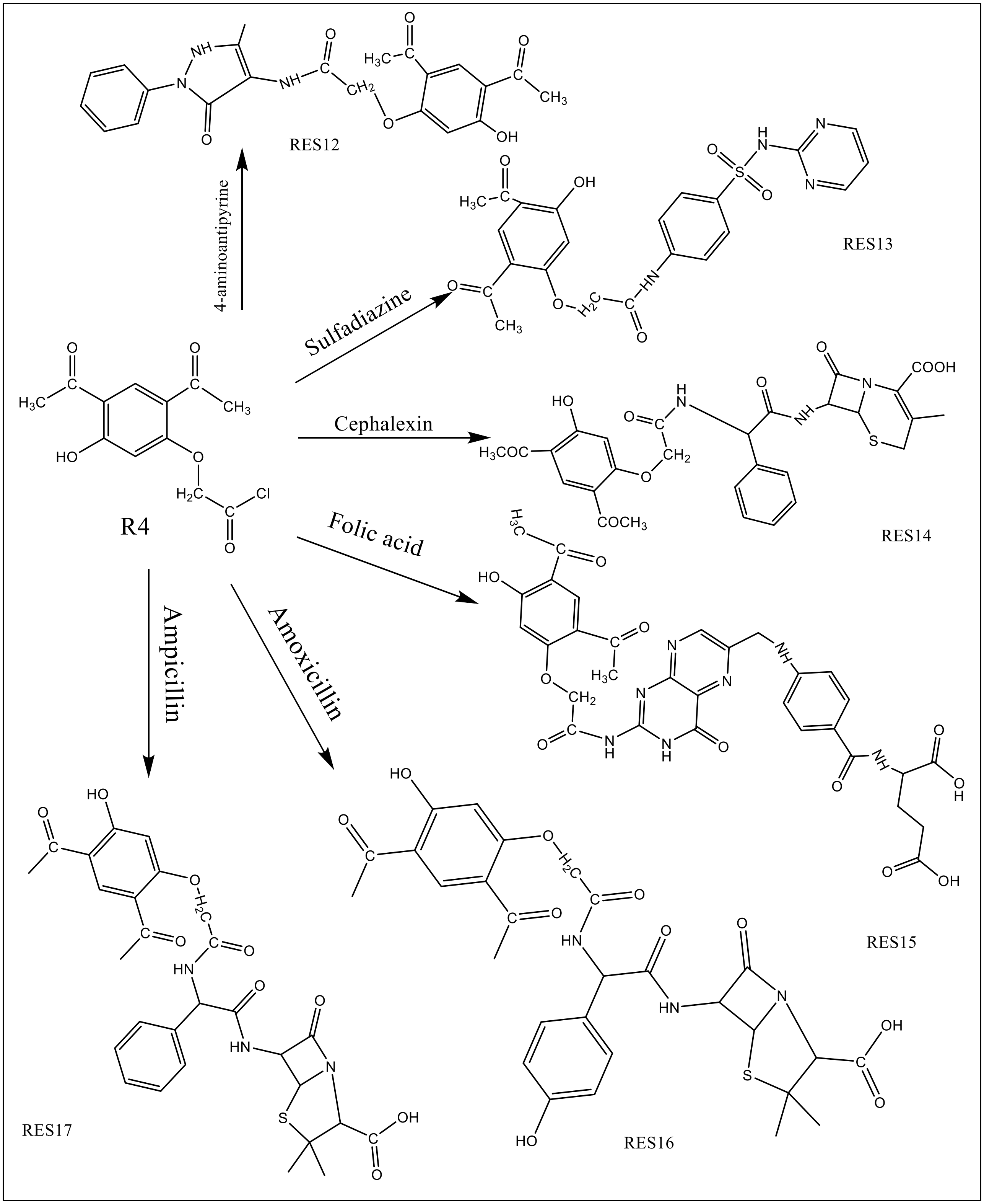

RES5
4-aminoantipyrine
Sulfadiazine
RES6
Cephalexin
RES7
R2
Theophylline
RES8
Folic acid
Paracetamol
Mefenamic acid
RES9
RES 10
RES11

The second Path:

The second path included the reaction of diacetyl resorcinol with chloro acetic acid and sodium hydroxide to replace the carboxyl group in site 2, as well as. its reaction with six different amino drugs to form new derivatives of resorcinol.

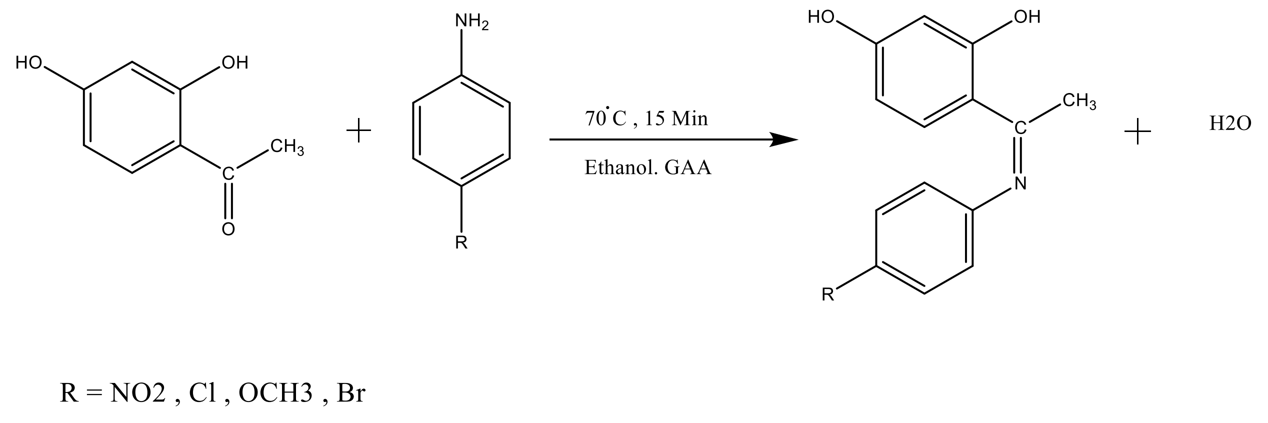


Scheme (2): Description for the synthesis of derivatives (RES12-RES17)


R4
4-aminoantipyrine
RES12
Sulfadiazine
RES13
Cephalexin
RES14
Folic acid
RES15
Amoxicillin
RES16
Ampicillin
RES17

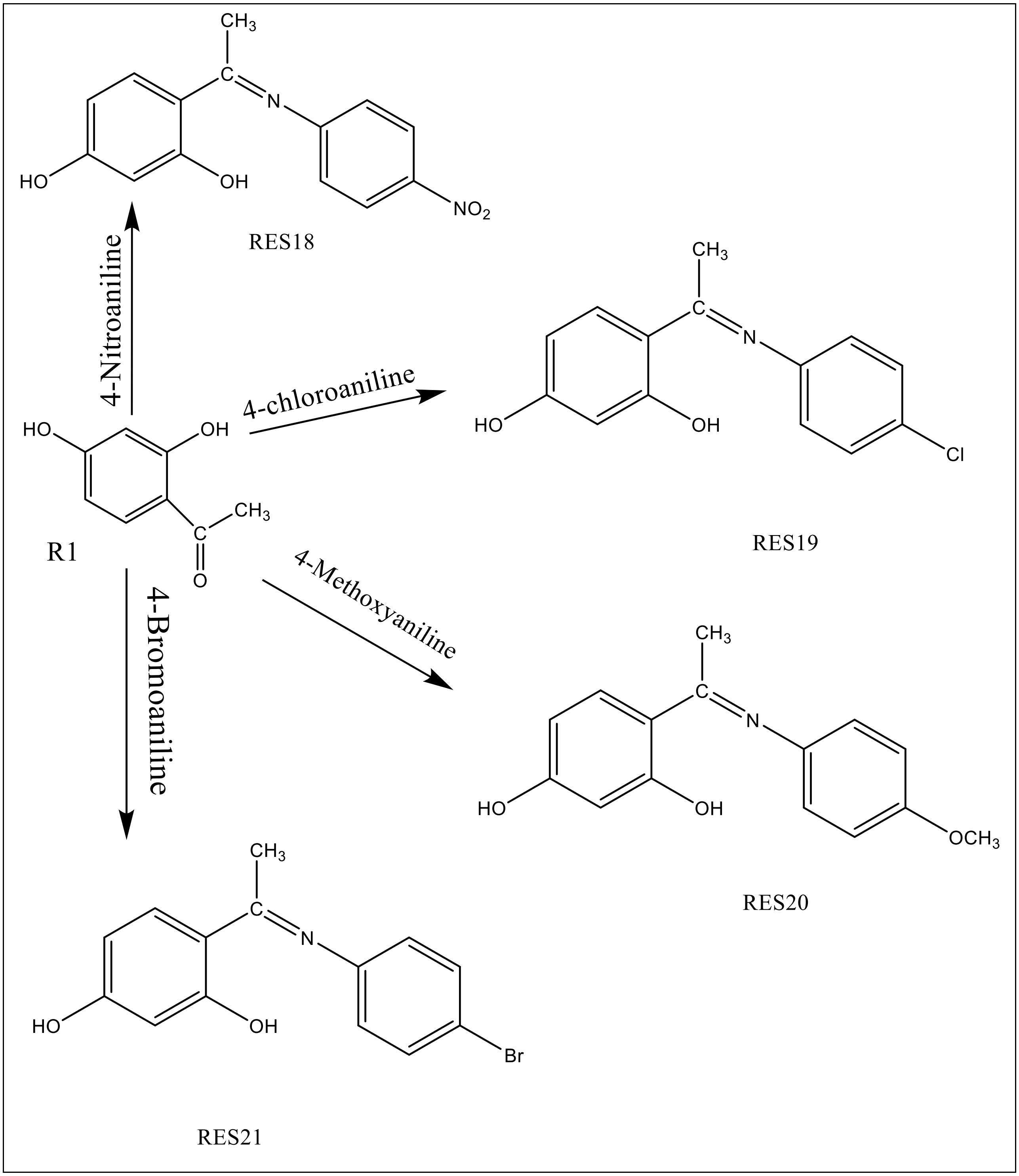
The Third Path :-

The Third path involves preparing and describing some phenolic Schiff basis (RES18-RES21) through the reaction of 2,4-dihydroxyacetophenone with four different derivatives of the aniline compound (4- nitro aniline , 4- chloro aniline , 4- methoxy aniline and 4-bromo aniline).



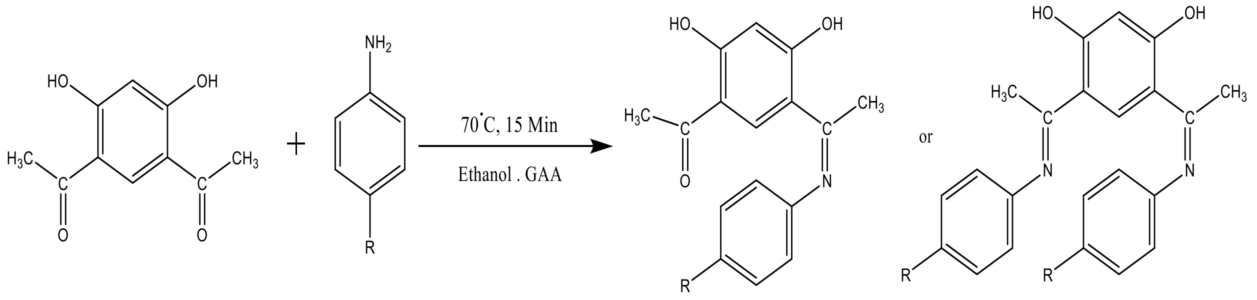
R = NO_2 , Cl , OCH_3 , Br

Scheme (3): Description for the synthesis of derivatives (RES18-RES21)


CH3
C
N
HO
OH
NO2
RES18
4-Nitroaniline
HO
OH
R1
CH3
C
O
4-chloroaniline
CH3
C
N
HO
OH
Cl
RES19
4-Methoxyaniline
CH3
C
N
HO
OH
OCH3
RES20
4-Bromoaniline
CH3
C
N
HO
OH
Br
RES21

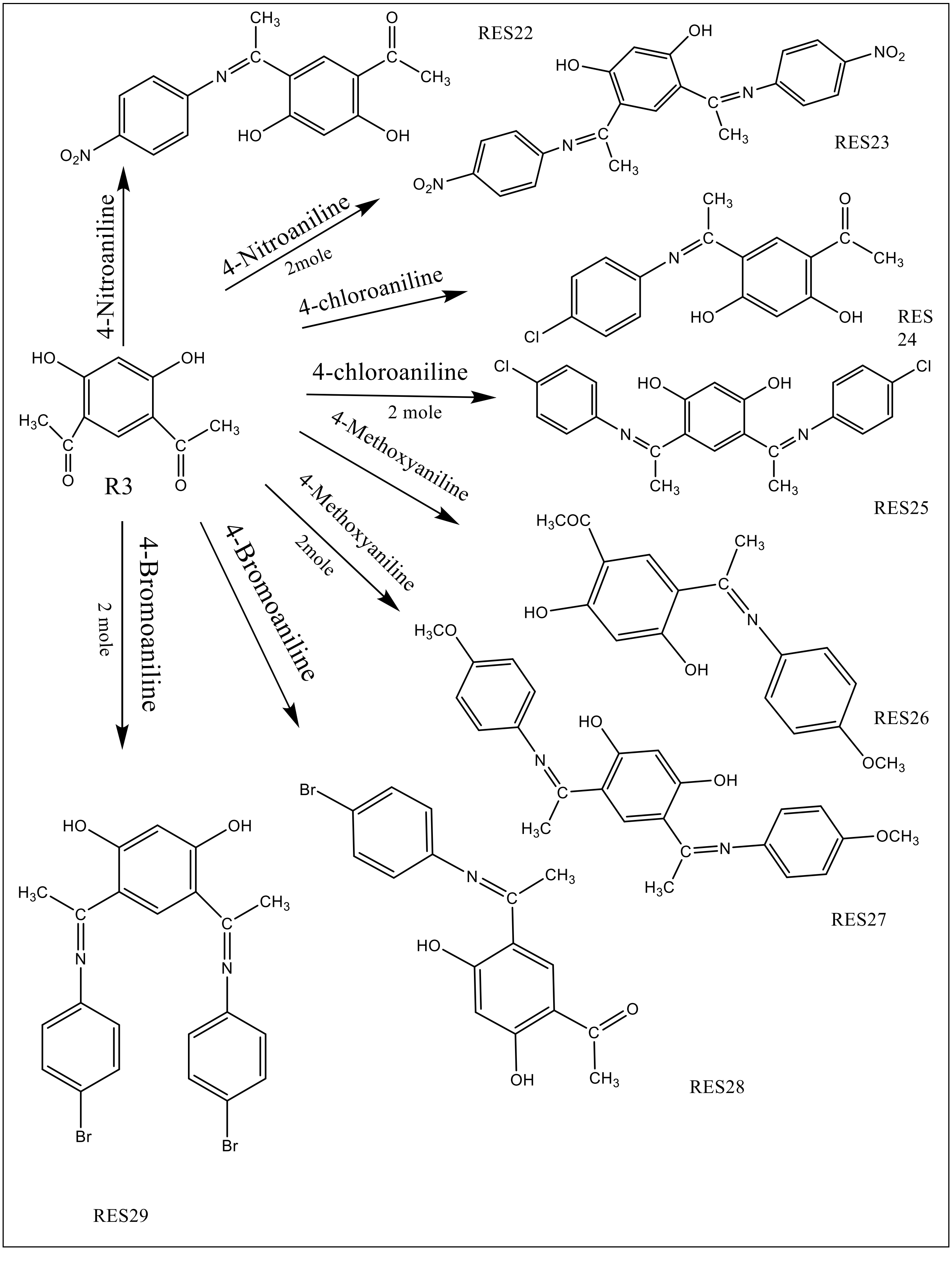
The Fourth path :

The Fourth path is included synthesis and characterization of some phenolic Schiff basis through the reaction of diacetyl resorcinol with four different derivatives of the aniline compound (4- nitro aniline , 4- chloro aniline , 4- methoxy aniline and 4-bromo aniline).



R = NO2 , Cl , OCH3 , Br

Scheme (4): Description for the synthesis of derivatives (RES22-RES29)


RES22
RES23
RES 24
RES25
RES26
RES27
RES28
RES29
R3
4-Nitroaniline
4-Nitroaniline
2mole
4-chloroaniline
4-chloroaniline
2 mole
4-Methoxyaniline
4-Methoxyaniline
2mole
4-Bromoaniline
2 mole
4-Bromoaniline
HO
OH
H3C
CH3
O
O2N
NO2
N
C
Cl
Br
H3COC
H3CO
OCH3

Theoretical study has been carried by using computation method Semi-empirical (PM_3). HyperChem 8.02 program have been used to achieve the required theoretical computations.

Theoretical simulations have been done to investigate the acylation reaction of resorcinol since the Geometrical structures are calculated for all reaction components and their suggested transition states. The most probable transition state is investigated through the calculations of energetic and electronic properties to indicate the most probable pathway of the acylation reaction. The calculation proves that the acylation reaction is done through the para position of aromatic ring with high yield present than other positions. At the same time the thermodynamic values and energy barrier value been calculated to employ Hess's law of thermochemistry for chemical reactions.

All synthesized derivatives were characterized by using FT-IR, 1H-NMR, 13C-NMR and CHNS and all the synthesized compounds were tested as antioxidant and all prepared derivatives were tested as antibacterial reagents versus *Staphylococcus aurous* and *(Klebsiella pneumonia)* and most of the tested compounds showed activity toward one or both classes of bacteria. The solubility of all synthesized compounds was studied in different solvents .

Chapter
ONE
Introduction

1. Introduction

1.1 Phenolic Compounds

Phenolic compounds are one of the classes of bioactive molecules most studied by the scientific community these molecules have well-reportedhealth benefits a daily diet enriched in these compounds is important to promote well-being. PC are considered antioxidants due to the donation of a hydrogen atom and/or an electron to free radicals, causing the break of chainreaction of oxidation. The antioxidant effect depends on the number and position of the hydroxyl groups [1].

In organisms , an oxidative process can be responsible for the generation of free radicals that attack the cells, leading to serious diseases, such as cancer, cardiovascular diseases , atherosclerosis , neurological disorders , hypertension , and diabetes mellitus , due to oxidative and nitrosative stress [1,2].

Other important bioactivities for maintaining good health have also been associated with these compounds, e.g. anti-inflammatory, antimicrobial, and anti-proliferative activities.[1,3]. These biological activities have aroused interest in the use of these molecules in the formulation of nutraceutical products[1,2]. However, although many bioactivities of phenolic compounds are proven in vitro, there is still a lack of information on their action in vivo; this is crucialinformation since several factors, such as bioavailability and absorption of these compounds, can interfere with their bioactive action [1,4].

In addition to the pharmacological interest in these compounds, their biological activities have also been explored in other industry sectors, such as in the food, [5,6] in the cosmetic [7] and in the packaging and textile industries [8,9].

Phenolic compounds are bioactive compounds that are normally associated with protective action for maintaining good health when consumed in the regular diet. These compounds have showed inhibitory action against the evolution of several serious diseases, such as cancer, Alzheimer's, and diabetes, among others.[1] These beneficial effects have been attributed mainly to the antioxidant and radical scavenging activities that can delay or inhibit the oxidation of DNA, proteins and lipids [2,6].

Phenols are found mainly in fruits, legumes, vegetables, tea, coffee, and accounts for the organoleptic characteristics of plant food. Likewise, phenolic compounds are responsible for the bitterness of fruits due to their interaction with salivary glycoprotein [10].

1.2 Resorcinol

In the last years, applications of new drug derivatives have been accelerated to increase the treatment effect towards a wide range of microbial organism that causes disease. One of the famous chemical compounds is resorcinol, a solid organic compound [11] , with less toxic than phenol [12].

Resorcinol is a 1,3-isomer (or meta-isomer) of benzenediol with the formula $C_6H_4(OH)_2$. White needle-like crystals with Faint, characteristic odor. Resorcinol is widely used in industry but is also used as a pharmaceutical agent for topically in dermatological remedies, pimples, associated pores and skin conditions[13]. It can also be utilized in aggregate with the opposite pimples remedy retailers, which include Sulfur [14,15] and used as a chemical intermediate for manufacturing of m-aminophenol, manufacturing of mild stabilizers for plastics [16], manufacturing of sunscreen arrangements for the pores and skin, manufacturing of dyes (fluorescein, eosin) [17], and anti-cancer agents [18,19].

Resorcinol (Figure 1-1) can also be used in many applications as floor coatings, silt, anti-corrosion coatings and adhesives when it interacts with formaldehyde and the formation of reso rcinol-formaldehyde (RF) resin as a product of the reaction [20].

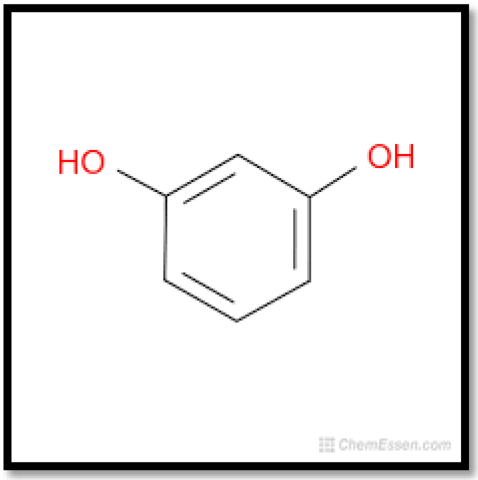


Figure (1-1) : Chemical structure of Resorcinol[21]

1.3 Organic, Medicinal and Pharmaceutical Compounds:

Organic chemistry is a sub discipline within chemistry involving the scientific study of the structure, properties, and reactions of organic compounds and organic materials, i.e., matter in its various forms that contain carbon atoms. It was one of the ultimate important chemical sciences in the medical and pharmaceutical studies, since it deals directly with the structure and medication nature including human bodies as well as structure and nature. That science has found mores application in the manufacture of compounds of commercial interest . In the structure of novel pharmacological active treatment medicines derived from original drugs structure, into synthesis complex compounds [22].

One of the main forces behind the search for therapeutic substances is still the function that this science has played in the pharmaceutical industry. The pharmaceutical industry are currently faced with the difficult and vital task of improving innovative medications. Due to their natural occurrence, the agricultural and pharmaceutical industries play a crucial role in the production of organic synthetic materials [23].

Recently works are still needed to minimize the attrition rate, expenditure, and time in the therapeutic agents discovery process concurrently addressing the enormous unmet medicinal needs.

Referencing the study report, preclinical toxicity and poor pharmacokinetic were the major reasons for the failure which happened in the treatment development, in addition to the lack of adverse effects and efficiency [24].

New drugs are required to cure new diseases , to novelty drugs less Hazardous and to treatment diseases ,whose drugs have become unproductive due to resistant of the microorganisms strains [25,26].

1.4 Pro-drugs

According to the International Union of Pure and Applied Chemistry (IUPAC), prodrugs are chemically processed active medicines that must undertake biological and chemical modifications before demonstrating medicinal responses. Prodrugs are compounds containing benign groups that are required for the removal of an undesired effect. In addition, improved and advanced pro-drug design can lead to superior pharmacokinetic properties, longer action, more selectivity, increased membrane permeability, and fewer adverse effects, among other advantages. Prodrugs currently account for (5-7) percent of all drugs approved. Prodrugs are typically discovered to be a basic chemical derivative that requires one or more chemical or enzymatic modifications to produce the active drug [27].

The concept of pro drug was first introduced in medicinal chemistry by Albert in 1951: “A pro drug is a molecule which does not have any intrinsicbiological activity but which is capable during the different phases of its metabolism to generate a biologically active drug” [28, 29].

The aim of employing prodrugs is to improve drug selectivity and optimize ADME (absorption, distribution, metabolism, and excretion) qualities. Several drug hurdles have been overcome using the pro-drug technique, and the drug's clinical -applicability has been optimized. Prodrug design has now succeeded in providing effective and selective drug delivery methods [30,31]**.**

1.5 Amoxicillin Drug:

Amoxicillin [D- [-]-a-amino-p hydroxybenzy] penicillin trihydrate] antibiotic is a p-hydroxy derivative of ampicillin. It is an antibiotic from the amino- penicillin group. The chemical formula is ($C_{16}H_{19}N_3O_5S$) which is one of the main -lactam antibiotics, higher bactericidal activity, active against different gram negative and gram positive bacteria. Class penicillin differs from one OH group situation. Amoxicillin (figure 1.3) is used as a therapeutic agent to treatment of some bacterial infections such as pneumonia, skin infections , and middle ear infections [32,33].

Amoxicillin actions inhibit the synthesis of cell walls of the bacteria. Bacterium such as Helicobacter pylori (gram negative) can infect the duodenum lining and stomach lining. Several antimicrobial agents (therapeutic agent) such as amoxicillin degrade quickly in an condition [34].

Amoxicillin has physical properties, such as high rate of absorption , high solubility, and high stability under acidic environmental. This drug allowing the administration orally, which can resistant the gastric acidity (pH) [35] . (Fig.1.2)

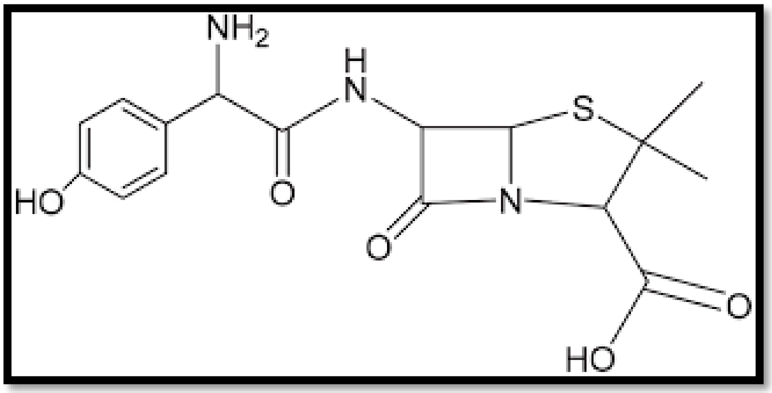


Figure 1.2 Chemical structure of Amoxicillin

1.6 Ampicillin Drug:

Ampicillin (AMP) is the most discovered pharmaceutical vigorous compounds, which has wide range of antimicrobial activity due to its structure which is B -lactam ring such as some antibiotic agents in this study. (AMP) is a semisynthetic penicillin used as a therapeutic agent for the prevention and treatment of numerous disease [36,37].

Ampicillin (Fig.1.3) is frequently used to treat various bacterial infections such as bronchitis, pneumonia, and skin, lung, ear, and urinary tract infections (UTI). Due to its importance as a wide- range antibiotic, pharmacodynamics and pharmacokinetics studies of ampicillin have been conducted in the past decades, ampicillin is widely prescribed for its broad-spectrum of low toxicity and antimicrobial properties [38,39].

Ampicillin can penetrate and prevent the growth of various sorts of bacteria, termed gram- negative bacteria(-Ve). Ampicillin is used typically to treat sinuses infections, middle ear infection, and bladder infection. Ampicillin has various properties such as , high solubility, broad range of activity, stability under acidic medium, and a higher rate of absorption [40] .

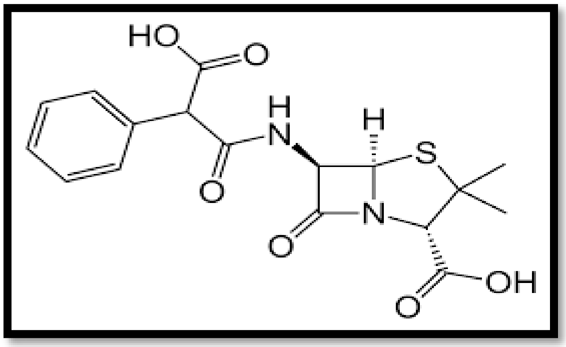


Figure 1.3: Chemical structure of Ampicillin

1.7 Theophylline Drug:

Theophylline [1, 3-dimethy1-3,7-dihydro-IH-purin-2,6-dion] drug methyl xanthine derivative. It is used to treatment COPD "chronic obstructive pulmonary disorder" in adults and asthma.

Theophylline found naturally in cocoa beans and tea in a trace amount. It is a weakly non-selective inhibitor of phosphodiesterase isoenzymes, but comparatively it is needed to high concentrations for maximum relaxation. Though the use of theophylline derivatives is still defined in the Global Initiative for Asthma in 2015 "GINA" report as supplementary therapeutic agent for the treatment [41-43] .

Doses of theophylline should not exceed 400 mg/d. Theophylline has a narrow therapy indicator; because of side effects problems of theophylline. Recently, studies have been rising the interest within selective (PDE) phosphodiesterase isoenzymes inhibitors .There have been efforts to improve on theophylline, by reducing the adversative effects of sensibility to toxic effects and it is risk of cytotoxicity due to age-related pharmacokinetic and pharmacodynamics changes [44] . (Fig.1.4)

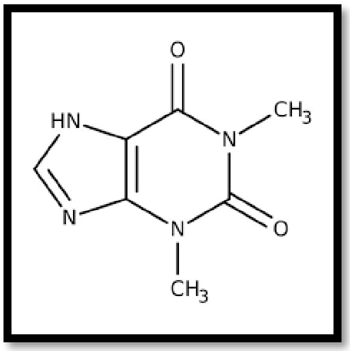


Figure 1.4: Chemical structure of Theophylline

1.8 Paracetamole Drug:

Paracetamole, (N-acetyl-para-aminophenol) also known as acetaminophen (PAPA), is the most frequently used as pain relieve and antipyretic, as well as to treat or fever in adults and children or mild-to-moderate pain. It is also used to treat pain in infants even in pregnant women, also used to treatment fever next to vaccination [45-48]

PAPA is a safe administration in patients who they have a history of asthma or peptic ulcers. Paracetamol (Fig.1.5), PAPA is available in various dosage which is frequently used to relieve pain caused by toothache, headaches, strains or sprain. The Paracetamol antipyretic effect is supposed to be caused by its capability to decrease synthesis of prostaglandin in the brain [49-51] .

PAPA obtainable from sixty years ago, it is better tolerated than the (NSAIDs) non-steroidal anti-inflammatory drugs it may be slightly less effective. Despite the fact there may be some action on COX-1 and COX-2 enzymes, this action is diverse from that show with another (NSAIDs) [52-53].

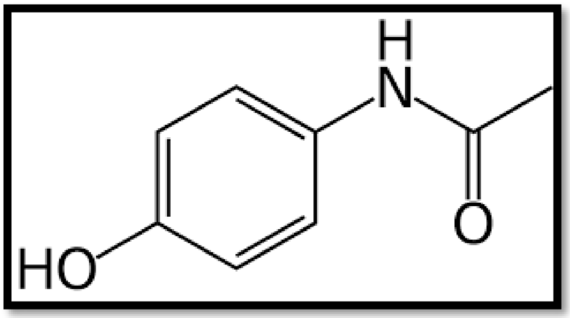


Figure 1.5: Chemical structure of Paracetamol

1.9 4-Amino Antipyrine Drug:

4-Amino antipyrine(4-AAP) or [4-amino-1,5-dimethyl-2-phenylpyrazole-3-one] (fig 1.6) is antipyrine derivative (pyrazolone derivative), it has revealed exceptional pharmacological properties ,for example antiviral, anti-inflammatory, analgesic (painkiller), anti-rheumatic, antipyretic, , and antimicrobial activities) . Moreover it is also used as originators in the synthesis of bio-active compounds i.e. B-lactams. 4-Aminoantipyrine also prophylactic of various diseases counting cancer , many antipyrine derivatives as well as assessed such as anti-inflammation , anticancer and analgesic action [55-57].

4-Aminoantipyrine diversities also have bio-activities action such as, anti-inflammatory, analgesic, anticancer activity, and antimicrobial. 4-Amino antipyrine derivatives have been extensively scrutinized because of their pharmacological, biological clinical, material and analytical applications and several chemotherapeutic agents [58,59] .

It is obvious from the conveyed literatures that pyrazole derivatives compounds showed antimicrobial activities as well as significant anthelmintic, structural variants produce new physic - chemical properties [60].

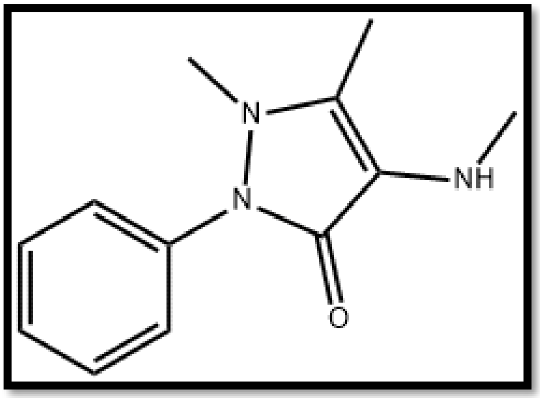


Figure 1.6: Chemical structure of 4-Aminoantipyrine

1.10 Cephalexin Drug:

Cephalexin (CFX) is an antibiotic that has a vast range of bactericidal activity, thus high inhibitory activities against a wide spectrum of gram-negative and gram-positive organisms. Cephalexin represented the first generation of cephalosporin antibiotics , it possesses better controlling over acute infections, with maximum utilization of drugs by enabling a reduction in the total dose amount of the administered and leads patient submission Cephalexin (CFX) [61-63] .

Cephalexin is one of the main ß-lactam group (Fig.1.4) [38]. It is an effective antibiotic used mainly as a therapeutic agent to treatment of respiratory tract and urinary tract infections and it is intentional for administration orally. However, it can also be given by intravenous, intramuscular. Cephalexin has several side effects such as skin irritation, stomachache, and diarrhea, cephalexin over dose is venomous and it needs for require medical care [64, 65].

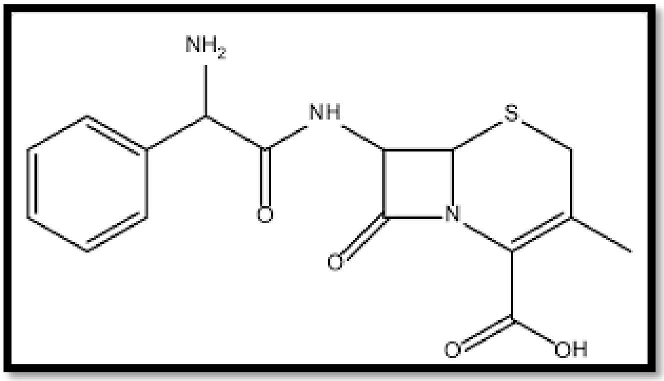


Figure 1.7: Chemical structure of Cephalexin

1.11 Folic Acid Drug:

Folic acid is a water-soluble vitamin, which is synthetically-produced and found in fortified foods and supplements. Folate is found naturally in plants, such as the dark green leafy vegetables. Folate is not synthesized de novo by humans, therefore the daily requirements are met from the dietary intake of folic acid supplements or food rich in this vitamin. Folate deficiency could lead to numerous common health problems. Hype homocysteinemia and the possibility of malignancy developments are the long termconsequences of this deficit albeit contradictory findings on these claims [66]

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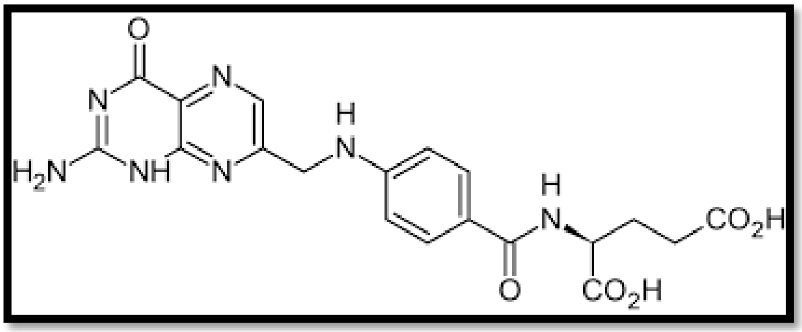


Figure 1.8: Chemical structure of Folic acid

1.12 Mefenamic Acid Drug:

Mefenamic acid (MA) [CisHisNO2] or Ponstan or 2-(2,3-Dimethyl phenyl) amino] benzoic acid is a non-steroidal anti-inflammatory drug (NSAID) used in acute conditions and chronic of inflammation and pain.

MA belongs to the aromatic amino acids group (Fig. 1.9) [67,68].

Mefenamic acid is a derivative of "anthranilic acid", is inhibitsproliferation and triggers apoptotic cell death of several human carcinoma cell lines. In addition to the analgesic and antipyretic properties predictable of NSAIDS, MA has been exposed to be effective as therapeutic agent in carcinoma cell lines and Alzheimer's disease [69] .

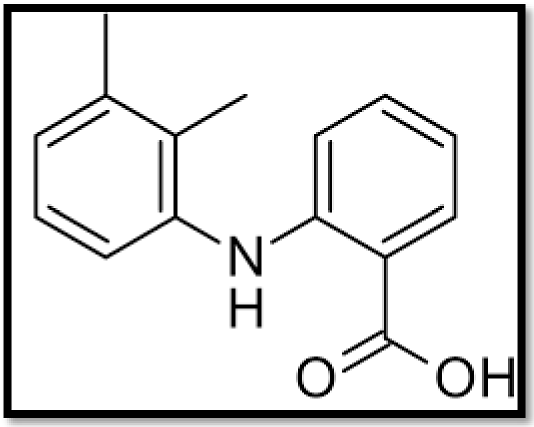


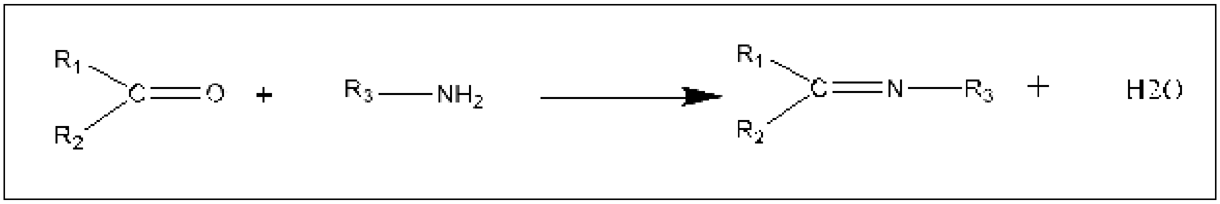
Fig 1.9 Chemical structure of Mefenamic acid

1.13 Schiff Bases

Schiff bases, which are organic compounds containing an imine group (- RCH=N-), which were prepared for the first time by the scientist Hogu Schiff1684 by condensation reaction between primary amines and carbonyl compounds (aliphatic or aromatic ketones or aldehydes) [70].

Under different conditions and in the presence of a catalyst. The general formula of the Schiff bases (R''R'C=NR), where each of the(R'' and R') aliphatic or aromatic groups or hydrogen atom, while R represents a substituted or unsubstituted benzene ring, then the Schiff bases are known as anils or benzanils [71].

Where the carbonyl group derived from aldehydes gives aldimines, while the derived ketones give ketoimines , as the amine group is responsible for giving these compounds high activity, as in the general reaction scheme(1-1) .



Scheme (1-1) General reaction to prepare Schiff bases

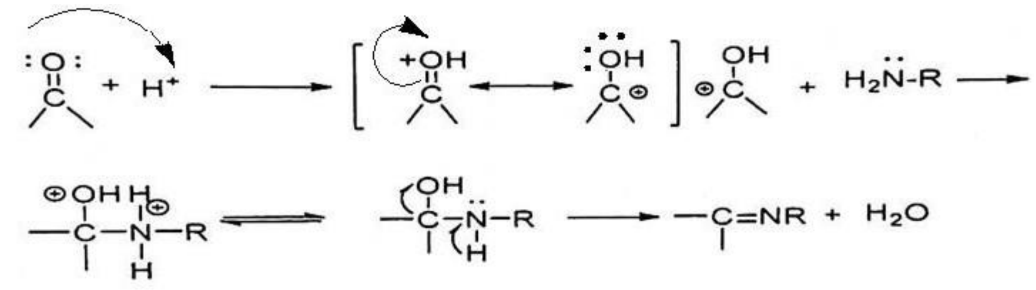
Schiff bases are characterized by many characteristics, and the most important of these characteristics is their relatively high stability. This stability is due to the starting materials necessary for the preparation of these bases (carbonyl and amine compounds). Aliphatic , which are often solid and have relative thermal stability [72] . As for the bases derived from aliphatic compounds, their characteristics are liquid [73].

1.13.1 Preparation of Schiff Base:

Schiff bases can be prepared in different ways, including:

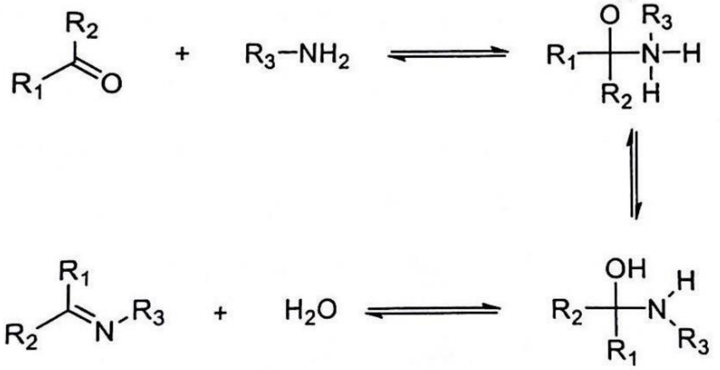
1.13.1.1 Condensation Reaction Method:

The condensation reaction method is one of the most popular methods for preparing Schiff bases. The reaction is catalyzed by the presence of dropsof glacial acetic acid or para toluene with sulfonic acid, hydrochloric acid, orpolypropylene glycol. The reaction often takes place by reflux of the carbonyl compounds with the amine. Where the reaction mechanism was studied by many researchers, which was explained that the acid gives the proton to the carbonyl group to configure the carbonium ion that is added to the amine group, as [74] in the scheme of the reaction mechanism (1-2) :



Scheme (1-2): Schiff bases mechanism

Sometimes the reaction does not require the presence of a catalyst for protonation, as aliphatic aldehydes and ketones quickly condense with primary amines to form corresponding Schiff bases, as there is no steric hindrance to aryl and phenyl groups. As for aromatic aldehydes and ketones, their reaction is slower with amines, so need to add acid as a catalyst.[75] as in the following diagram :



Scheme (1-3) Preparation of Schiff bases without the using catalyst

1.13.1.2 Microwave Irradiation Method

Microwaves are defined as electromagnetic waves located between radio frequencies and infrared radiation, as their wavelengths range between (0.1- 100 $cm^{-1)}$, and this corresponds to frequencies (0.3-300 kHz) [76].

Microwaves have insufficient energy to break bonds, as they are in the form of photons, not thermal energy, which is transformed during its interaction with the medium into heat, through which it can be reflected, transmitted, or absorbed, as there are some materials that have the ability to convert electromagnetic radiation into heat [76] .

1.13.2 Application of Schiff Base:

Schiff bases are important compounds used in organic compounds that have many applications in different fields, for example, biological , inorganic and analytical chemistry, where Schiff bases have important intermediates inmany enzymatic reactions through the reaction of an enzyme with the aminogroup or the carbonyl of the base material [77,78]

Schiff bases also have many effective biological applications, including anti-fungal, anti-bacterial, anti-malarial, anti-inflammatory, anti-viral, antipyretic, anti-cancer, anti-oxidant and also of great importance in industrial applications such as the food industry and the dye industry[79].

1.14 Computational Chemistry: -

Computational chemistry is located at the intersection of the chemistry, mathematics, physics and computer science, as well as can be used to describe the behavior of the atoms and the molecules. Theoretical studies have grown in importance in recent years, taking a leading role in science, especially in the fields of pharmaceutical research and chemistry. Computational chemistry is a branch of chemistry that merges theoretical chemistry and computer science to assist scientists in clearer grasping the problem at hand, as well as solving problems in the lab. The chief strength of computational chemistry that its results can be in close agreement with the experiment and can be predict the accurately and describe chemical phenomena and the molecules properties that have not yet been synthesized. There is a list of atomic and molecular properties that may be examined using basic modern computational chemistry programs such as HyperChem, Gaussian, GAMESS, and others. Programs are based on the computational framework, such as atomic and molecular energies, molecular geometries (bond lengths, bond angles, and torsions), absorption intensities, charge distributions and molecular orbital energies(HOMO and LUMO), reaction barriers, vibrational frequencies, energies and geometries of transition states [80,81] .

Solving the molecular Schrödinger equation is an essential goal of quantum computational chemistry projects. A fundamental premise of quantum mechanics, is fully defined by the mathematical function for coordinates and spins of many particles known as state or the wave function Ψ, which contains all information about the system that can be known. During the operation of the linear Hermitian operators, the information can be acquired from the wave function [82].

Computational chemistry includes a wide range of methods including: the molecular mechanics, the molecular dynamics and the electronic structure methods. The molecular mechanics is using classical mechanics for predicting the properties, whereas electronic structure calculations utilize quantum mechanics. Semi-empirical methods, ab initio, and the density functional theories. These theories are developed to describe ground-states and excited states properties for molecules, also stationary states or that develop with the time. Every theory has various levels of accuracy can be achievable and computational cost [83] .

1.14.1 Semi-empirical

Semi-empirical calculations are mainly based on neglecting the Hartree-Fock calculations and integrating with two electrons and replacing them with experimental values obtained from practical experiments, thus shortening thetime. Where this method came to improve the accuracy of the molecular mechanics method and to solve the problem of the long time taken by the complete calculations [84].

Semi-empirical methods describe molecules through of the clear interactions between the electrons and the nuclei. They are based on the following principles:

1-Electrons and nuclei are being distinguished from each other.

2-Electron-nuclear and electron-electron interaction are explicit.

3-Interactions determine the distribution of space of the nuclei, electrons and their energies.

One of the most important advantages of semi-experimental methods is that they give results of energy calculations from 100 to 1000 times faster than other computational methods, whether DFT or AB initio methods of similar predictive quality , and capability to describe the bond breaking and the bond forming reactions [85, 86].The semi=empirical methods that are most popular include MNDO, MINDO3, AM1, PM3, INDO, RM1 and CNDO [87].

1.14.1.1 Parameterization Model, version 3 (PM3)

It is one of the methods of semi-experimental calculations, and it is a correction of the AM1 method, and it is considered an appropriate method for treating organic systems, as it gives more accurate calculations of the heat of formation and gives accurate treatment of energies and bond lengths compared to the AM1 (Austin Method) and MNDO (Modified Neglect of Diatomic Overlap) methods. It is used to study compounds of transition elements. In general, the PM3 method is more common in use than other semi-experimental calculation methods [88,89] .

1.14.2 Ab –Initio Methods

A rigorous execution of the Hartree-Fock theory have been called ab-initio approach (from first principles), this name has been given to the computationswhich are obtain directly from theoretical principles of quantum mechanics, masses and charges of electrons, atomic nuclei and values of the fundamental physical constants, like the speed of light or Planck's constant, (C=2.998 x10®m/s), (h= 6.626x103* J.s) respectively, without the empirical data being included. These computations cover a semi- comprehensive mathematical treatment of the Hartree-Fock theory, which is inherent to the theoretical model .For complex algebraic formulae, exhaustive calculations of this sort can result in a potentially large number of integrations and differentiation [90,91].

Ab initio calculations are depended on solving Schrodinger equation. The ab-initio method has been used for calculating molecular geometries, spectra, vibrational frequencies, energies, electron affinities, ionization potentials and other properties like dipole moments that are connected with the electron distribution. Ab-initio ways should only be used on tiny systems. from among the disadvantage of ab-initio ways, The computational cost is high, and they always consume a massive amount of time, memory, and computer disk space [92,93].

1.14.3 Density Functional Theory

Density Functional Theory is the quantum mechanical modelling methodis the density functional theory (DFT) that has been used in chemistry and physics to investigate the electronic structure of a variety of body systems, including atoms and molecules and also condensed phases. The features of a many-electron system can be determined using functions that are spatially dependent on electron density in this theory .As a result, the term "density functional theory" was coined from the use of an electron density functional. Because of the nature of the DFT approach, it includes some of the electron correlation [90, 94,95].

DFT is one of the most popular methods which available in computational chemistry, condensed-matter physics and computational physics. DFT is an exceptionally successful approach for description the ground state properties of the metals, semiconductors and insulators. This success also materials like proteins and carbon nanotubes. The treatment of the excited states and the time-dependent processes within DFT method is much less developed [96] .

One significant advantage of DFT calculations is that they are faster and more accurate than ab initio approaches. With the same computing cost as HF techniques, DFT also contains components of electron correlation. This means that the DFT method is a particularly efficient approach to perform advanced computations on a system and can tackle systems more correctly and it is very big for post-HF approaches. The disadvantages of DFT methods include that they cannot be improved systematically like wave function-based approaches, making it impossible to quantify the error associated with the computation without using experimental data or other kinds of calculations. The use of the DFT method to characterize intermolecular interactions has its drawbacks, especially those involving dispersion forces or systems in which dispersion forces compete with other interactions (biomolecules) [97] .

A major problem in the DFT is that the required form of the functional which is map the electron density to electronic wave function is unknown from any system other than the free electron gas. Various approximations are be used to produce the functional required. In the LDA (local density approximation), the functional depends on value of the density in the coordinates where is evaluated the functional. The LDA is used widely and in successful in solid state physics however is an insufficient approximation for the molecular calculations [91] .

DFT has been used to predict structure of molecules, calculation and stability of structures (equilibrium, reaction intermediates and transition state),vibrational analysis, DFT underestimates band gap , charge distribution , the unpaired spin densities and characterization of the molecular orbitals-predictions of reactivity [98, 99].

1.14.4 Geometry optimization

Geometry optimization is a technique which is attempting to be find the configuration of the lowest energy or more relaxing conformation for the molecule. For all levels of calculation, the path is the same. Geometry optimization has to be the most necessary step in predicting the properties of a molecule using quantum mechanics calculations. A geometry optimized molecule represents the minimum structure of a potential energy surface, which is then used as a starting point for subsequent calculations such as single point, vibration, and so on. Geometry optimization can be used to findthe minima on the potential energy surface (PES), and therefore can predict equilibrium of the structure of molecular system. The initial state for the molecule is not given bond lengths naturally thus that the geometry optimization are used to be correct bond lengths. Researchers frequently are using the minimizations to create a structure at the stationary point for calculation a subsequent single point or to remove the excessive stress in a molecule, and preparing it for the molecular dynamics simulation [100,101].

1.14.5 Transition State (TS)

The transition state is used to calculate transition state energy and for theoptimization of reaction intermediate geometries[102]. The lower energy positions of the reactants and products on potential energy surface are separated by the higher energy region. The highest energy along a minimum energy pathway in going from the reactants to the products clarifies the transition state [103]. A transition structure (transition state) is the saddle point on the potential energy surface (PES) theoretically calculated, which is represent the highest point on a minimum energy path between the two min In classical quantum mechanics, the atoms or molecules collide with enough energy to form transition structure. In bimolecular, the transition state is performed when the two molecules, old bond is broken and a new bond is formed. The energy difference between the reactant and the potential energy maximum is referred to the activation energy. At a high temperature, the vibration energy is a higher than the transition energy to collision molecule leads to further prophesied transition state. Obtained the equilibrium geometry for reactant and product is requisite to calculate the transition state. A calculated transition structure may be sensitive to the level of theory employed [104, 105] .

1.15 Literature Survey

In 2010 Zheng X and Liao DF prepare A series of chrysin derivatives from 2-hydroxyacetophenone, 2,4-dihydroxyacetophenone, 2,4,6-trihydroxy-acetophenone, using modified Baker-Venkataraman transformation. Their anticancer activities in vitro were evaluated by the standard MTT method. The results of biological test showed that some of chrysin derivatives showed stronger anticancer activity than 5-fluorouracil [106].

Pulimamidi Saritha REDDY, P.V ananthalkashmi and V. jayatyagaraju in 2010 prepared Cr (III), Mn (II), Fe (III), Co (II), Ni (II), Cu (II) and Zn (II) complexes by template reaction of 5-acetyl 2,4-dihydroxyacetophenone and ethylenediamine in the presence of metal ions. The complexes have been characterized on the basis of elemental analyses, conductivity, magnetic moments, infrared and electronic spectral data. The Schiff base binds to metal ions in bis-multidentate ONNO mode leading to two dimensional Schiff base polymers [107].

In 2020, Hala shkyair lihumis and Saadon Abdulla Aowda used 2,4-dihydroxychalcone to prepare (2,4-dihydroxychalcone) by the reaction of 2,4-dihydroxy acetophenone to condensation with aryl aldehyde by used of sodium hydroxide catalysts . These synthesized compounds had also been assessed by (DPPH) method, to test their antioxidant activity, and the results showed that the synthesized compound exhibit antioxidant activity [108].

Yoshihiro Tokudome and Tsuyoshi Hoshi in 2020 used resorcinol to prepare Twelve resorcinol derivatives synthesized by esterification with three functional groups (L-ascorb-6-yl, ethyl, and glyceryl) linked via four alkyl chains of varying lengths (n = 2–5) at the 4-position. The structures of the 12 resorcinol derivatives were confirmed by Nuclear Magnetic Resonance (NMR) [109].

Belaidi, *et al*., in 2013, used the Gaussian 09 and HyperChem programs at abinitio and DFT methods to study the geometries, bond angle, bond length,charge densities, the heat of formation, bandgap energy of HOMO and LUMOmolecular orbitals and Physico-chemical properties of thiazole and some of itsderivatives. as well as, they were found that the results of calculations agreewith experimental values [110].

Ebtihal K. K., *et al*., 2015, Theoretically, metal complexes of the new tridentate Schiff base are proposed and synthesized as ligand type (NNO) obtained from Isatine. New Schiff base ligand [(E)-3-[(Z)-3-(2-aminoethyl imino)-1, 5- dimethyl-2-phenyl-2, 3-dihydro-1H-pyrazol-4-ylimino] indolin-2-one]. Transition metal ions such as Co(II), Ni(II), and Cu have been used to prepare the chelate complexes of three ligands. The results suggest that the geometrical structures of Co(II), Ni(II), and Cu(II) complexes are octahedral. The spectrum method, conductivity, and magnetic behaver investigations are used to identify compounds [111].

Halla T. M., *et al*., 2016, Computational methods are utilized to study a new Parkinson's disease treatment. Using PM3 semi-empirical calculations and DFT based on STO-3G, nine chemical compounds have been proposed. Chemically changed derivatives of active drugs are used to make new medications, which ignore undesirable drug features such as low solubility, low selectivity, instability, and excessive toxicity. All of the suggestions are made to prevent adverse effects and improve absorption distribution in living tissues [112].

In 2016 H.. Mohammed, studied the synthesis of adrenaline in Sequence reactions from phenylalanine theoretically by using semi-empirical and DFT methods , calculated electronic properties for the probable prodrugs through five reactions, found E gap of phy, Tyr, DOPA,dopamine, noradrenaline and adrenaline are (0.870, 0.787, 0.101, 0.119,1.915 and 0.593 eV) respectively, also studied the energetic properties of the suggestion prodrugs, and found M-6-SPhe compound is favorite than other prodrugs due to its lowest value of energy -13229.816 kCal/mol and the highest value of energy gap 8.876eV[113].

Lekaa H. K., *et al.*, in 2018, studied the Chemical reactivity of a new suggested Chemotherapy agent. This study involved Our new suggested chemotherapy agent is diaminobis((methylthio)oxy) platinum (VI)chloride (DMOP) complex. The agent has been described to be an effective anticancer therapy. Suggested transition states formation of DMOP (II) complex (square planer) with purine bases (guanine and adenine) are studied by DFT/B3LYP method. They found an energy gap 0.02632 kCal.Mol^{-1} is a small value of indicators of high chemical reactivity for DMOP complex. The reaction is most probable of the complex with guanine bases than adenine bases by total energy value equal to -792.613 kcal mol^{-1} [114] .

1.16 Aim of This Study :

1- Synthesis and characterization of new organic compounds from Resorcinol as a starting material . The prepare compounds will be characterized by FTIR, 'HNMR, ''NMR andCHNS.

2- Investigate the geometrical structures of reaction chemical components and estimate the probable transition state of chemical reaction .

3- Applied biological activity to some of the prepared compounds like anti-oxidant and antibacterial.

Chapter TWO
Experimental part

2. Experimental part

2.1 Chemicals

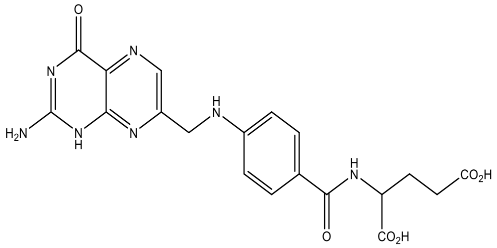
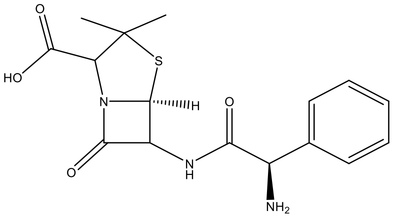
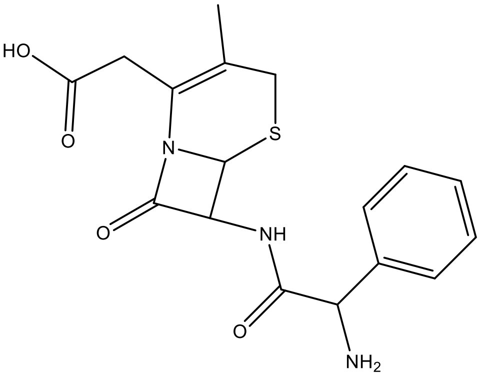
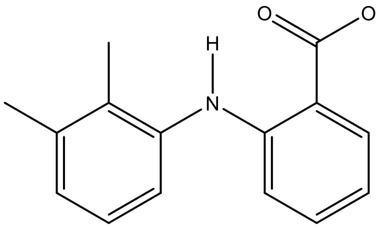
The chemical compounds used are of the highest purity available. The chemicals, supplier, and purity were recorded in table(2-1).

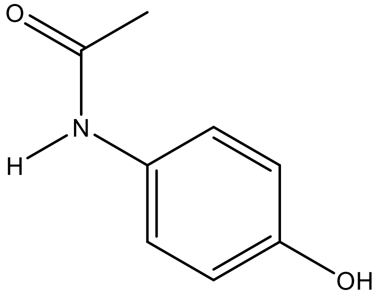
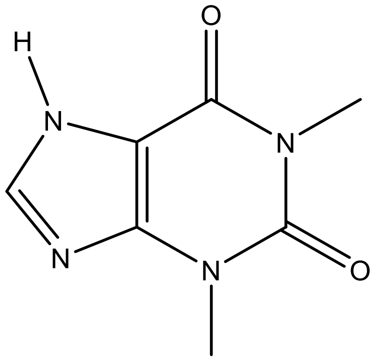
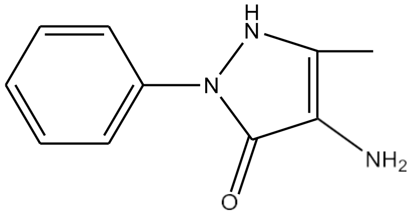
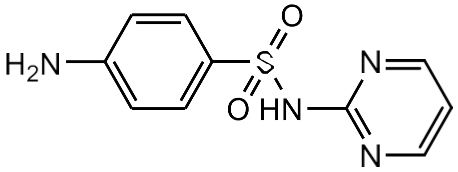
Table (2-1): supplier and purity for used chemicals

Chemicals	Supplier	Purity%
Acetone	Fluka	99.9
Chloroform	Fluka	99.9
Dichloromethane	Fluka	99.7
Diethyl ether	Fluka	99.9
Dimethylsulfoxide	Fluka	99.5
Di methyl formamide	Fluka	99.9
Hydrochloric acid	Fluka	36.5
Methanol	Fluka	99.9
n-Hexane	Fluka	99.9
Petroleum ether	Fluka	99.9
Sodium bicarbonate	Fluka	99.9
Sodium hydroxide	Fluka	99
Triethylamine (TEA)	Fluka	99.9
Thionyl dichloride	Fluka	99.9
1,4-Dioxane	Fluka	99.9

Glacial acetic acid	Baker	99
Acetic acid	CDH	99.9
Chloroacetic acid	CDH	99
4-Chloroaniline	CDH	99
Ethyl acetate	CDH	99
Ethanol absolute	CDH	99.9
Zinc chloride	CDH	99
4-Methoxyaniline	CDH	99
4-Nitroaniline	CDH	99
4-bromoaniline	CDH	99
Potassium hydroxide	GCC	99
4-aminoantipyrine	Samarra comp.	99.9
Sulfadiazine	Samarra comp.	99.9
Cephalexin	Samarra comp.	99.9
Theophylline	Samarra comp.	99.9
Mefenamic acid	Samarra comp.	99.9
Paracetamole	Samarra comp.	99.9
Folic acid	Samarra comp.	99.9
Ampicillin	Samarra comp.	99.9
Amoxicillin	Samarra comp.	99.9

Table (2-2): Name and chemical structure of drugs used in the preparation of co-drug

Comp. Sym.	Structural formula	Mwt	m .p °C
Folic acid		441.40	250
Ampicillin		349.4	199-201
Cephalexin		347.39	326-328
Mefenamic acid		241.8	230-232

Paracetamole		151.17	169-171
Theophylline		180-164	164-166
4-aminoantipyrine		203.24	209-211
Sulfadiazine		250.28	252-254

2.2 Instruments: -

2.2.1 Fourier Transformation Infrared spectrophotometerFTIR:

FT-IR spectra for prepared compounds were recorded on a Bruker, in the Chemistry Department, College of Science, Babylon University.

2.2.2 Melting point apparatus.

SMP30-Melting point apparatus, melting points for prepared derivatives were determined and are uncorrected; Chemistry Department, College of Science, Babylon University.

2.2.3 Nuclear magnetic resonance spectrophotometer:

^{1}HNMR and ^{13}C-NMR were recorded on an Innova, model Innova 5-oxford 500 Magnet NMR spectrophotometer, operating at (500MHz) for ^{1}HNMR and (125 MHz) for ^{13}CNMR. The chemical-shifts (δ) were measured in ppm in the University of Tehran's Central lab, with TMS as a standard (δ=0.0ppm).

2.2.4 Thin Layer Chromatography (TLC) :

TLC was performed on aluminum plates coated with 0.25mm layer of silica-gel (Fluka) , and the detection was followed by U.V.-Lamp at 254nm .or through coloring with iodine .

2.2.5 Micro elemental Analysis (CHNS):

Euro EA3000Elemental Analyzes in the central laboratory of the University of Tehran, the analysis of the microelements carbon, hydrogen,nitrogen, and sulfur was carried out.

2.3 Preparations:

The structures and physical data for prepared derivatives were recorded in the table (2-3), (2-4)

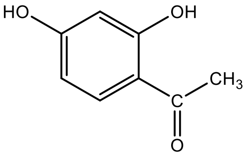
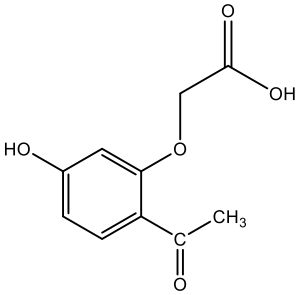
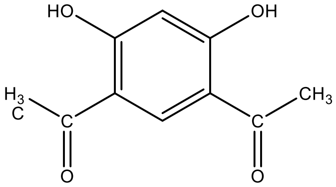
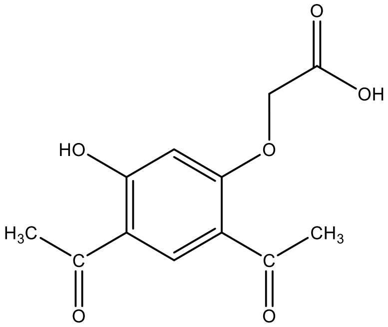
2.3.1 Synthesis of compounds (R1 and R3)

Anhydrous $ZnCl_2$ (15 g, 110 mmol) was added to 30 ml of CH_3COOH and heating at 140 °C. After all the $ZnCl_2$ has been dissolved, resorcinol (10 g, 90 mmol) has been stirred and heating for 3 hours at 150 °C in oil bath. The$ZnCl_2$ complex broke down by adding 50 % HCI (50 mL). In an ice bath, a bright yellow precipitate formed and cooled, then filtered. The product was washed with 5% HI and recrystallized with hot water, orange solid formed (7.99g, 80%), m.p.(144-146)°C.TLC was used to follow the reaction development [115] .

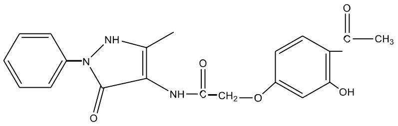
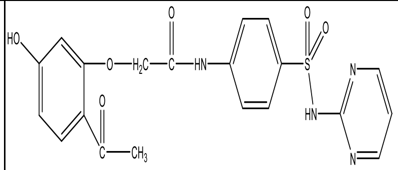
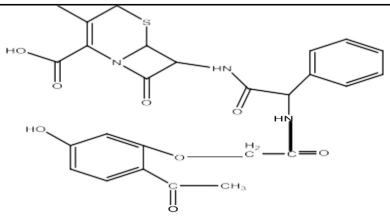
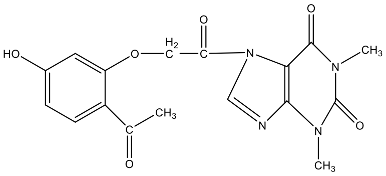
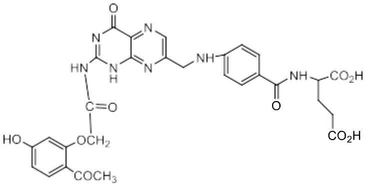
2.3.2 Synthesis of compounds (R2 and R4)

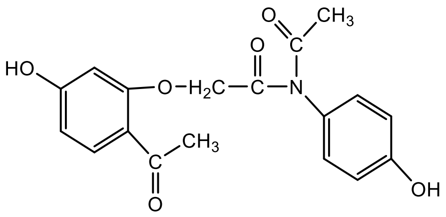
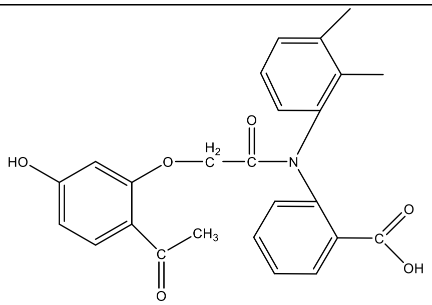
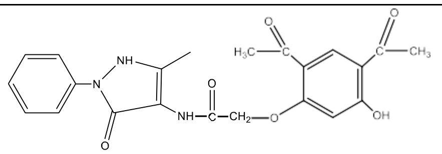
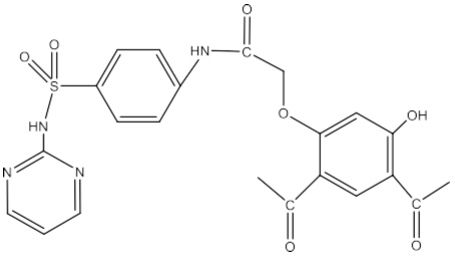
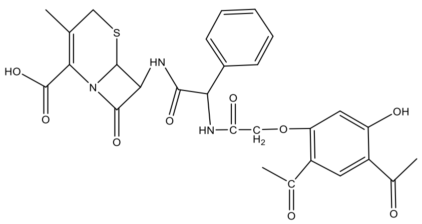
Dissolve 2 g of KOH in 40 mL of water in a 50 mL round bottom flask, 0.5 gm of (2,4-dihydroxyacetophenone , 2,6-diacetyl resorcinol) was added to the round bottom flask. The mixture was stirred until a homogeneous solution resulted. Fit the flask with a reflux condenser and heat to a gentle boil. Add 6 mL of a 50% aqueous solution (g/mL) of chloroacetic acid drop wise and boil the solution for 10 minutes. Cool the reaction mixture to room temperature and acidify the solution with dropwise addition of concentrated HI, monitor the pH with PH paper. Cool the mixture in ice bath and filter the precipitate by vacuum filtration. Recrystallize the crude solid from boiling water to afford compoundR2 and R4. The reaction was followed using TLC technique using (Ethyl acetate : acetone (1:1)) [116].

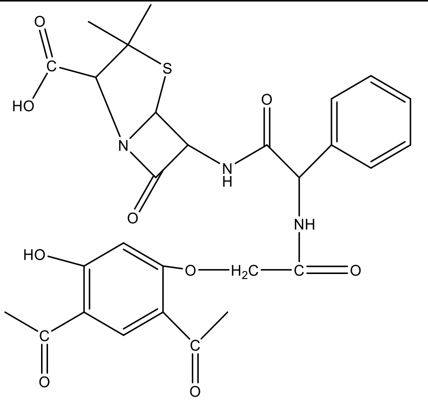
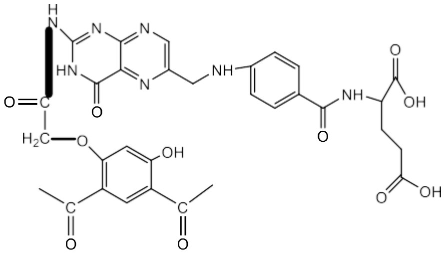
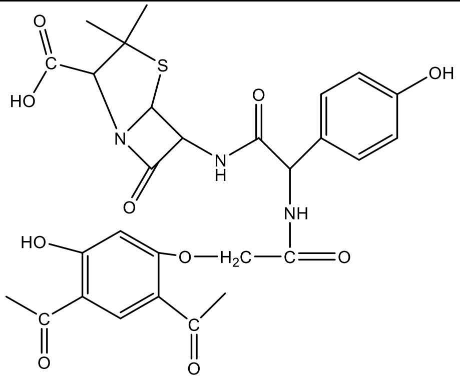
Table(2-3): Chemical structures of compounds (R1_R4)

Symbol	Chemical structure	Mwt gm/mol
R1		152.15
R2		210.19
R3		194.19
R4		252.22

Table(2-4): Some of physical properties of compound (RES 5_RES 17)

. Derivatives symbols	Structural formula	color	M. formula	M.Wt	m.p	Yield %	Rf
RES 5		Light brawn	$C_{20}H_{19}N_3O_5$	381.39	146-150	71%	0.73
RES 6		Dark brawn	$C_{20}H_{18}N_4O_6S$	442.45	92-94	97%	0.72
RES 7		Black	$C_{26}H_{25}N_3O_8S$	539.56	107-110	80%	0.79
RES 8		Dark green	$C_{17}H_{16}N_4O_6$	372.34	116-119	71%	0.76
RES 9		Dark Yellow	$C_{29}H_{27}N_7O_{10}$	633.57	98-100	90%	0.63

RES 10		Black	$C_{18}H_{17}NO_6$	343.34	108-111	80%	0.81
RES 11		Dark green	$C_{25}H_{23}N_1O_6$	433.46	123-125	82%	0.40
RES 12		Dark Brown	$C_{22}H_{21}N_3O_6$	423.43	110-112	88%	0.47
RES 13		Dark red	$C_{22}H_{20}N_4O_7S$	484.48	82-85	92%	0.73
RES 14		Dark brawn	$C_{28}H_{27}N_3O_9S$	581.6	107-111	92%	0.77

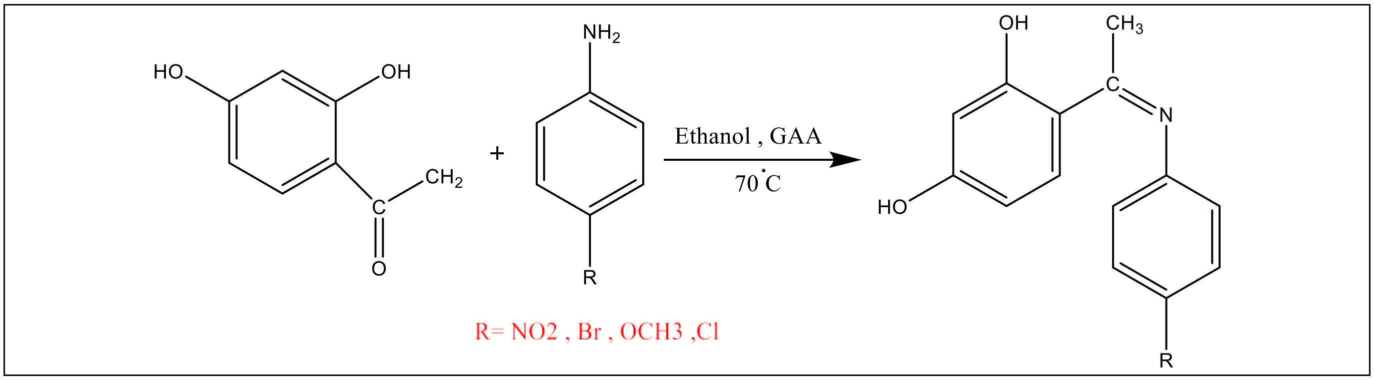
RES 15		Black	$C_{28}H_{29}N_3O_9S$	583.61	68-70	77%	0.52
RES 16		Yellow	**$C_{31}H_{29}N_7O_{11}$**	675.61	92-95	92%	0.54
RES 17		Dark brawn	$C_{28}H_{29}N_3O_{10}S$	599.61	82-85	70%	0.77

2.3.3 General procedure for one pot synthesis of amides (RES 5-RES 17)

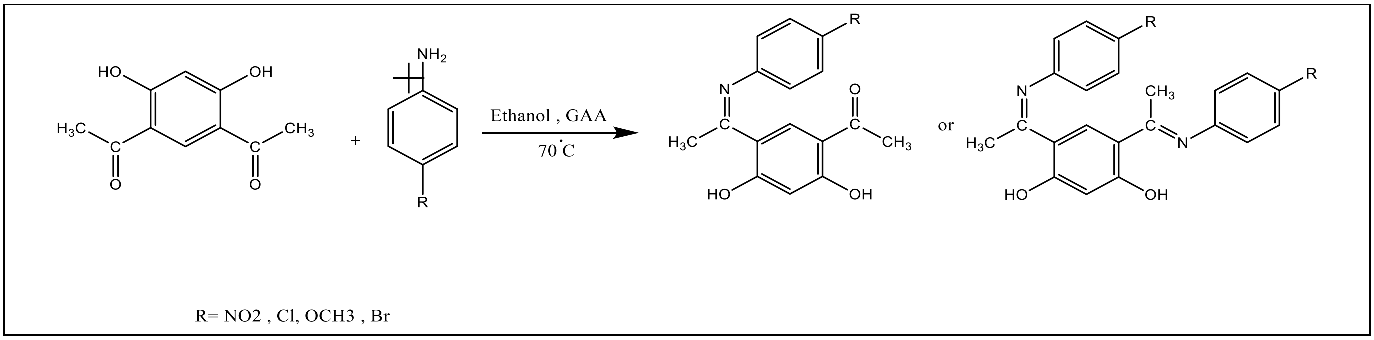
1 mmol of acetic acid is added to 1 mmol of amine and 3 mmol of triethylamine (Et3N) in dichloromethane, then 1 mmol of SOCl2 is added at room temperature. The mixture is stirred for 20 minutes at room temperature. The recovery of the reaction product is performed by evaporatingthe solvent under reduced pressure. The resulting residue is taken up in dichloromethane and washed first with 1 N HCl and then with 1 N NaOH. TLC was used to check the reaction development [117] .

2.3.4 General procedure of synthesis the Schiff bases (RES 18 – RES 29):

A reaction mixture of 2,4-dihydroxyacetophenone (Immole) and substituted anilines (1mmole) was dissolved in absolute ethanol (10-15ml) with 2-3 drops of glacial acetic acid and heated in a water bath at 70- 80 C for 60 min or by dean stark apparatusin presence of dry benzene. The process of the reaction completionwas followed by TLC. Filtration or evaporation of used solvent was done then the products were recrystallized from ethanol solvent[118].

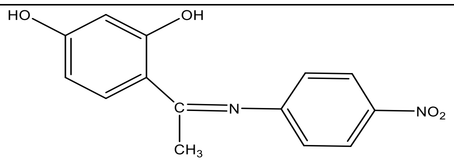
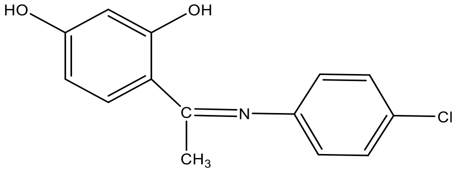
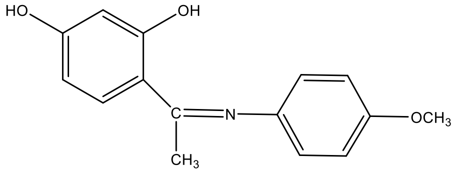
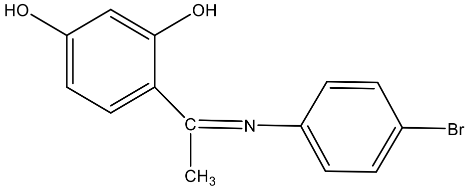
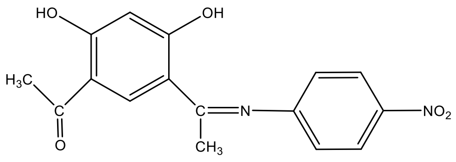
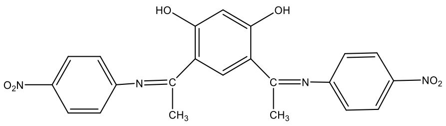


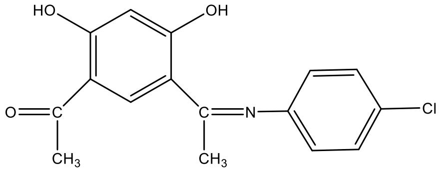
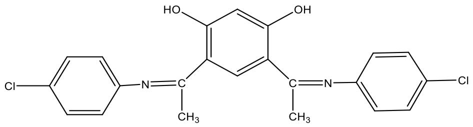
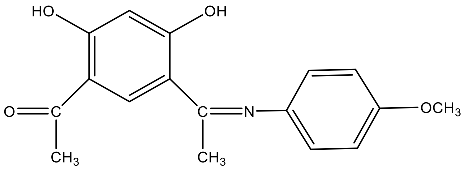
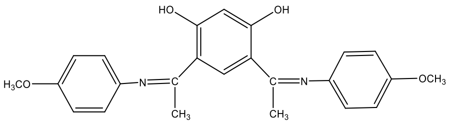
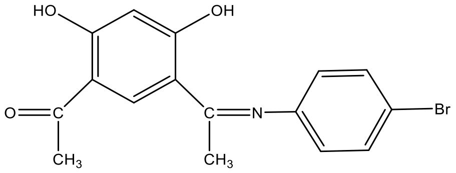
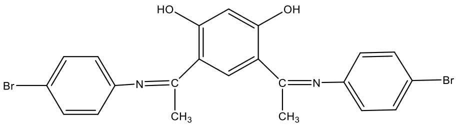
Scheme (2-1): Preparation of derivatives RES18-RES21



Scheme (2-2): Preparation of derivatives RES22-RES29

Table (2-5): The physical properties of compounds [RES 18-RES 29]

Derivatives symbol	Structural formula	color	M. formula	M.Wt	m.p	Yield %	Rf
RES18		Light yellow	$C_{14}H_{12}N_2O_4$	272.26	110-112	92%	0.71
RES19		Dark brawn	$C_{14}H_{12}ClNO_2$	261.71	265-267	97%	0.62
RES20		Black	**$C_{15}H_{15}NO_3$**	257.29	142-145	80%	0.74
RES21		Dark brown	$C_{14}H_{12}BrNO_2$	306.16	90-92	67%	0.52
RES22		Dark Yellow	**$C_{16}H_{14}N_2O_5$**	314.30	131-133	93%	0.67
RES23		Dark yellow	**$C_{22}H_{18}N_4O_6$**	434.41	115-118	94%	0.83

RES24		Light Brown	$C_{16}H_{14}ClNO_3$	303.74	130-132	80%	0.5
RES25		Dark Brown	$C_{22}H_{18}Cl_2N_2O_2$	413.30	123-126	88%	0.6
RES26		Brown	$C_{17}H_{17}NO_4$	299.33	124-126	78%	0.72
RES27		Dark brawn	$C_{24}H_{24}N_2O_4$	404.47	141-143	92%	0.57
RES28		Dark Brown	$C_{16}H_{14}BrNO_3$	348.20	136-138	66%	0.82
RES29		Dark Brown	$C_{22}H_{18}Br_2N_2O_2$	502.21	98-101	73%	0.52

2.4 Biological Activity:

2.4.1 Antibacterial Activity:

Antimicrobial susceptibility exams of a synthesized compounds have been accomplished in line with the “nicely diffusion technique ”. Synthesized compounds were evaluated on bacterial strains, one gram-fine bacteria (*staphylococcus aureus*) and one gram-terrible bacteria (*Klebsiella pneumonia*). Samples have been cultured on Muller Hinton agar medium at a temperature of 37 °C for a length of 24 hours, and the consequences have been precise for a few compounds, as proven in table [119].

2.4.2. Antioxidants Activity:

The solution changed into included from mild through overlaying the check tubes with aluminum foil. DPPH (four mg) turned into dissolved in onehundred mL of methanol. Some of the produced compounds have been used to make numerous concentrations of (25, 50, a hundred) ppm. It become madevia way of means of dissolving 1 milligram of the chemical in (10 mL) of methanol to make one hundred elements according to million, then diluting itto (50 and 25) components in keeping with million. The concentrations had been made withinside the equal way. 1 mL of the diluted or ordinary answer (25, 50, one hundred) ppm turned into brought to at least one mL of DPPH answer in a check tube. After 30 min. of incubation at 37 °C, the absorbance of every solution become measured the use of a spectrophotometer at 517 nm.The following equation turned into used to decide the capacity to scavenge DPPH radicals[120].

I % = (Absorption control – Absorption sample) /Absorption blank x 100

Absorption blank=0.003

2.5 The solubility:

The solubility for synthesized compounds was studied by using different polarity solvents, all prepared compounds are partially soluble in water due to relatively high molecular weight and they are completely solublein of DMSO, and ethanol. All synthesized compounds are insoluble in diethyl ether, petroleum ether, and ethyl acetate because the polarity forprepared compounds is higher than the polarity of these solvents.

2.6 Theoretical study

A theoretical investigation is done to prove the nature of the acylation reaction of resorcinol through the suggestion of three different transition states. Threesuggested transition states are examined for the most probable pathway of the acylation reaction.

2.5 Instruments and program

2.5.1 Computer

Computational studies were performed using Computer according to its specifications to increase efficiency reducing the time required to perform calculations.

Computer Discerption :

Computer type: HP – CORI i5

System type: 64-bit operating system, x64-based processor

Processor: 11th Gen Intel(R) Core (TM) i5-1135G7 @ 2.40GHz 2.42 GHz

Installed RAM: 8.00 GB (7.75 GB usable)

2.5.2 HyperChem

HyperChem version 8.0.2 is chemical computational program. It is the integrated graphic interface, computational a visualization package. It has seen a most use on the PCs. HyperChem includes ab initio, DFT, semi-empirical and molecular mechanics (MM) methods. These methods have been used for computing geometry optimization, transition states, vibrational frequencies, electronic excited states and MD, QM/MM and MC simulations. The program has the drawing mode, the backbone has been sketched and then hydrogen atoms have been added automatically. This sketcher does not set the lengths or angles bond, so has been used the MM optimization before doing time-consuming computations[121] . Various rendering modes are present in the graphic interface. It is used toshow molecular surfaces and vibrational mode animations. The electronic and vibrational spectra, as well as their intensities, are illustrated.

The calculation results are displayed on the screen by default, but they are not stored on the disk. The user can direct that all results from a particular sessionbe written to a log file. The MM force fields are included in the program, which includes MM^+, BIO^+, OPLS, and AMBER. The semi-empirical methods include (extended Huckel, CNDO, INDO, ZINDO, MINDO/3, MNDO, PM3, PM6 and AM1). As well as, the ab initio calculations. Several common basis sets are used [122] .

2.6 Theoretical Calculation Methods

2.6.1 Building and Displaying Molecules

Program tools have been used to build up the molecules. The molecules have been sketched by using a drawing tool after hyperchem window opened, a two-dimensional representation of a molecule has been drawn and then converted into three-dimensional structure by utilizing the model builder. Molecules have been displayed in different shapes (symbols,numbers) through using the list of display and selection of labels. The molecules have been displayed in the form of balls and cylinders, and tubes by using the display menu and then select Rendering.

Semi-empirical calculations were used to study the pathways of the reactions under study and to find the products most likely to appear during the reaction as well as to study the proposed transition states to find the most likely transition states that the reaction goes through to give the product. PM3 was chosen from the methods of semi-experimental calculations to perform theoretical calculations.

2.6.2 Geometry Optimization Calculations

Calculations were made for the geometry optimization of the particles to find the optimum Geometry Optimization. The Geometry Optimization calculations were performed after drawing the molecule in the program window and using the tools in the program toolbar. The required elements were also selected from the periodic table that was displayed by choosing Default Element from the Build menu. From the file menu, start log was chosen to open a file and give a unique name to save the calculations, then the setup menu, then select the semi-empirical calculations, and then choose the required calculation method after choosing the Geometry Optimization from the list Compute.

2.6.3 Transition State Calculations

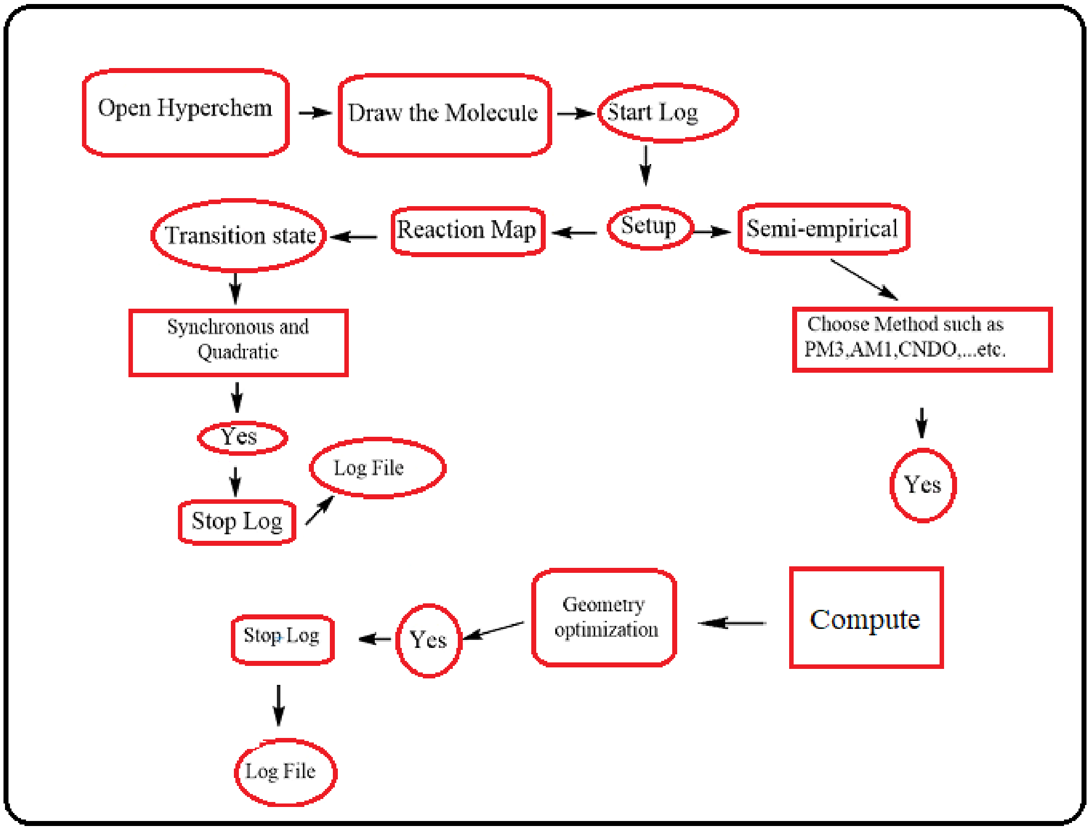
After the geometry optimization has been carried out for all structures reaction individually, At the beginning, the molecules and names of reactant and product have been chosen from the selected menu then the number has been selected from the labels menu, which is located in display menu. Then the reaction map in setup menu has been selected to merge the same transition state and product. After that transition state has been selected from compute menu and synchronous transit and quadratic have been chosen from options dialog box of transition state search. Before operation the transition state the start log in file menu has been chosen. Finally, stop log has been chosen and saving the results after the calculations had completed .

The transition state calculation should be done to find the energy barrier for the chemical reaction.

The activation energy (energy barrier) has been calculated
from the equation:

$$\mathbf{E_b = E_{TS} - \varepsilon\ E_r}$$

E_b represents the energy barrier , E_{TS} represents the total energy of transition state which has been taken from log file for the transition state . E_r represents summation of the total energy of reactants. Scheme (2-1) shows path of the computation into HyperChem program run the chemical system. At the same time the thermodynamic values and energy barrier value of each reaction step been calculated to employ Hess's law of thermochemistry for all chemical reactions.



Scheme (2-3). Flow chart run for Hyperchem Programme.

Chapter THREE

Results and discussion

The Results and Discussion

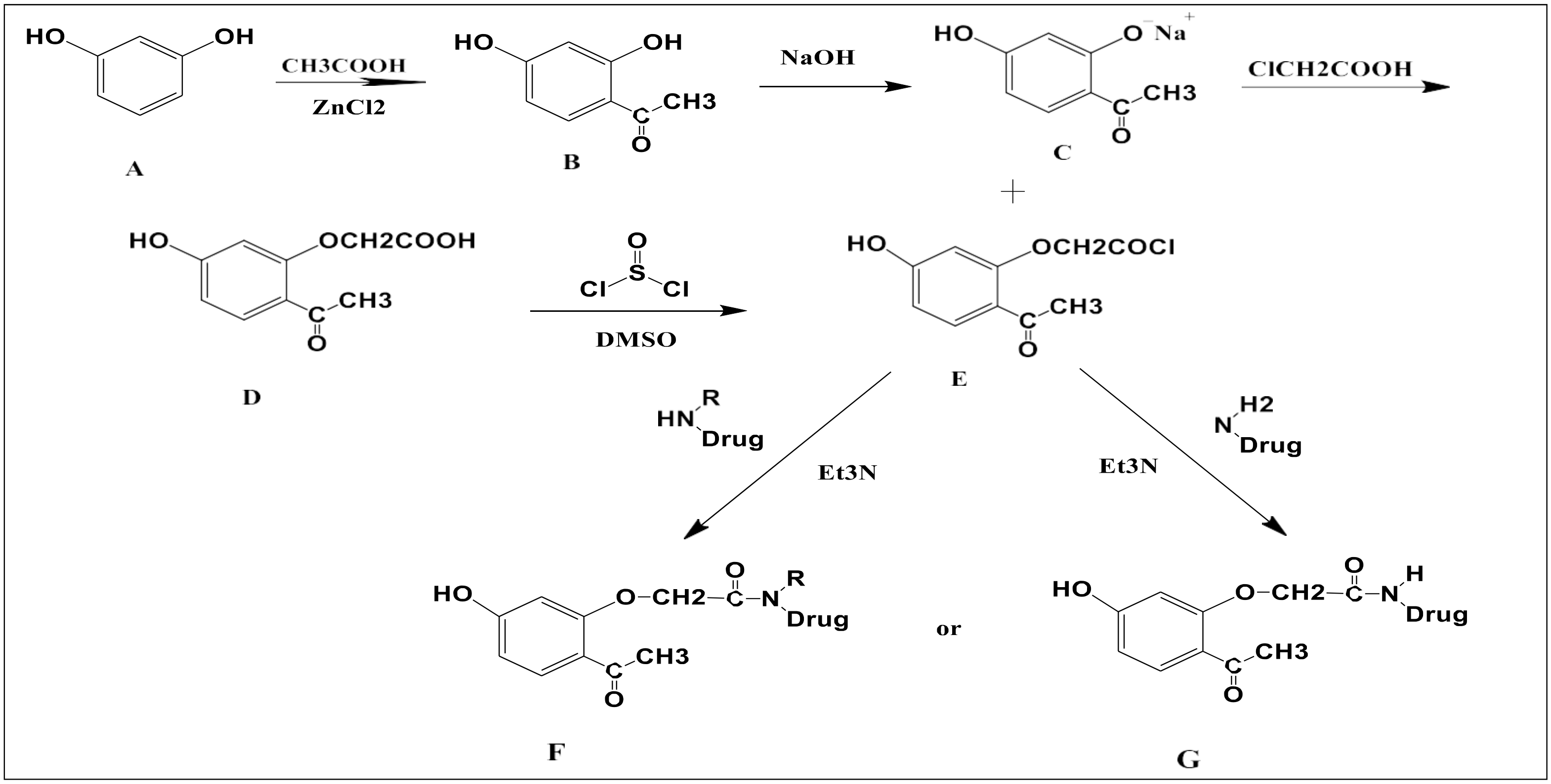
To enhance the properties of resorcinol and reduce its side effects, new derivatives based on resorcinol, and amino-containing drugs was synthesized by the formation of amide bonds. Resorcinol was used as starting material to synthesis the compounds (RES5 –RESS11) by reaction of (R2) with different amino-containing drugs (Sulfadiazine, Cephalexin, Mefenamic acid, Paracetamole, folic acid, Theophylline, and 4-Aminoantipyrine) respectively.

On another hand, resorcinol was used as starting material to form a new derivatives (RES12-RES17) which prepared by reaction of resorcinol with acetic acid to produce (4,6-Diacetylresorcinol) (R3). R3 compound , which reacted with Chloroaceticacid to produce compound R4 , This compound was reacted with different amino- containing drugs (Sulfadiazine, Cephalexin, Amoxicillin, Ampicillin, folic acid, and 4-Aminoantipyrine) respectively.

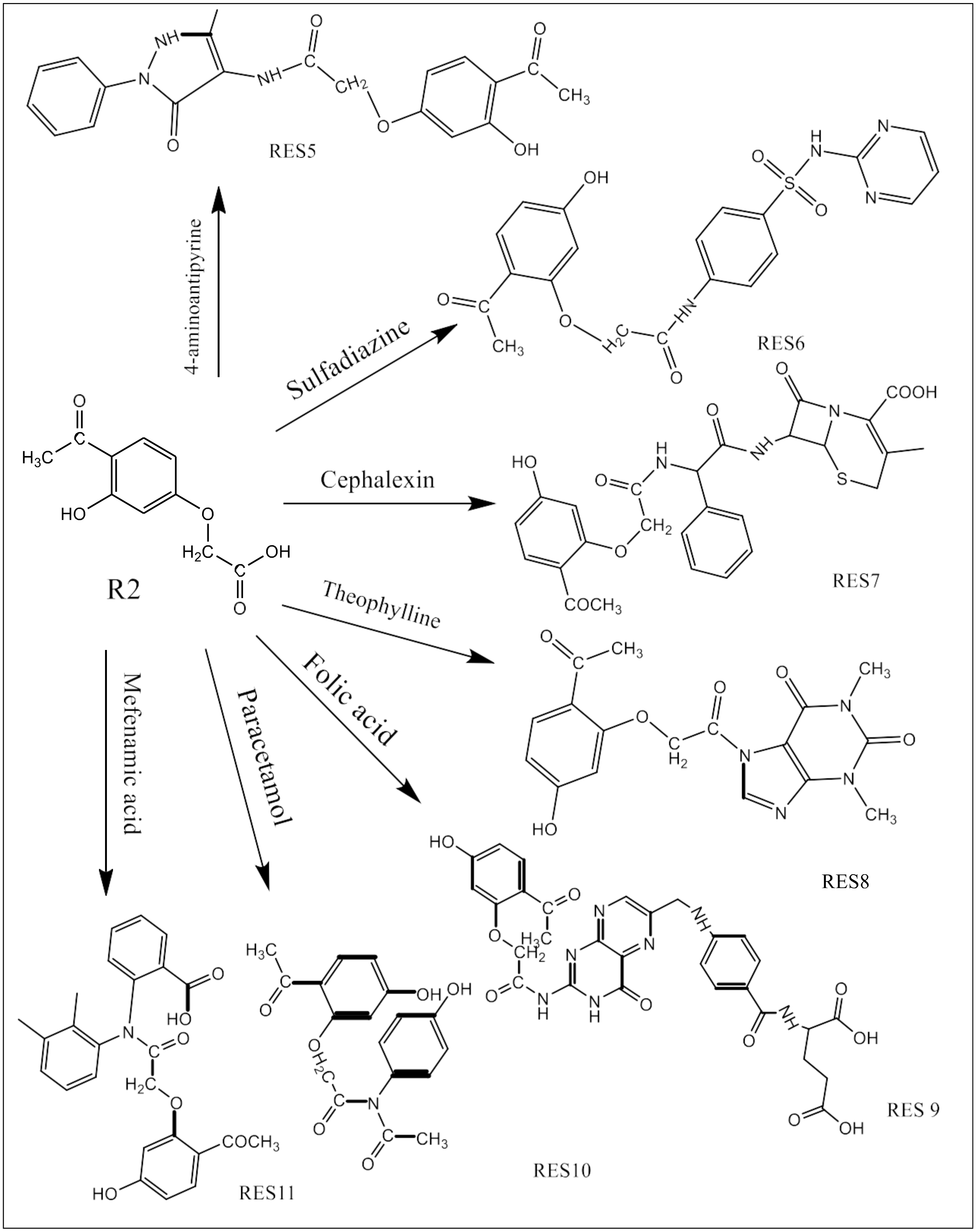
The synthesized derivatives were characterized and confirmed with FT-IR, ^{1}HNMR, ^{13}CNMR, and C.H.N techniques .

3.1. First path :

New amino-containing medications were created via the creation of amide bonds to improve the characteristics of resorcinol and lessen its negative effects. Resorcinol was used to react with seven amino medicines to create the compounds (RES5-RES11).

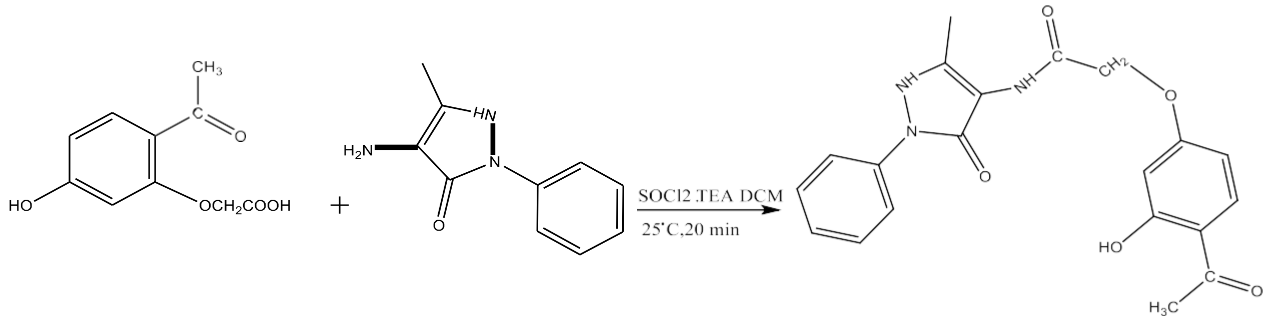


Scheme (3-1) : General scheme of Synthesis of compounds (RES 5- RES11)



Scheme (3-2): Synthesis of compounds RES5 – RES11

Compound (RES5) prepared from the reaction of R2 with 4-aminoantipyrine in existence DMSO , $SOCl_2$ and Triethylamine. Equation (3-1).



Equation (3-1): synthesis of RES5

The FT-IR spectrum of compound RES5 showed the following values (V_{max} cm^{-1}): 3394.83 (N-H str. groups) ,1566.25(N-H bend),1305.85 (C-N str. aryl), 1701.27 (C=O str.Ketones), 1680 (CO str. amide), 3560.01 (O-H phenol), 2895 (C-H str. Sp3), 1219 (C-O ether.), 1440(O-H bend) (Figure 3-1). ^{1}H-NMR (500 MHz,δ ppm): 10.6(O-H , phenol) 8.1(N-H ,sec. amide), 6.0-7.8 (C-H, aromatic), 4.6 (methylene),2.2 and 2. 4 (methyl), 2.51(DMSO) (Figure 3-2).^{13}C- NMR (125 MHz, δ ppm): 15.8-27.8 (C,CH_3), 67.5(C,CH_2), 160.1-165.4 (N-C=O),106.5-168.4 (C,Ar),104-134.4)(C,ethylene) 39.1 DMSO (Figure 3-3).

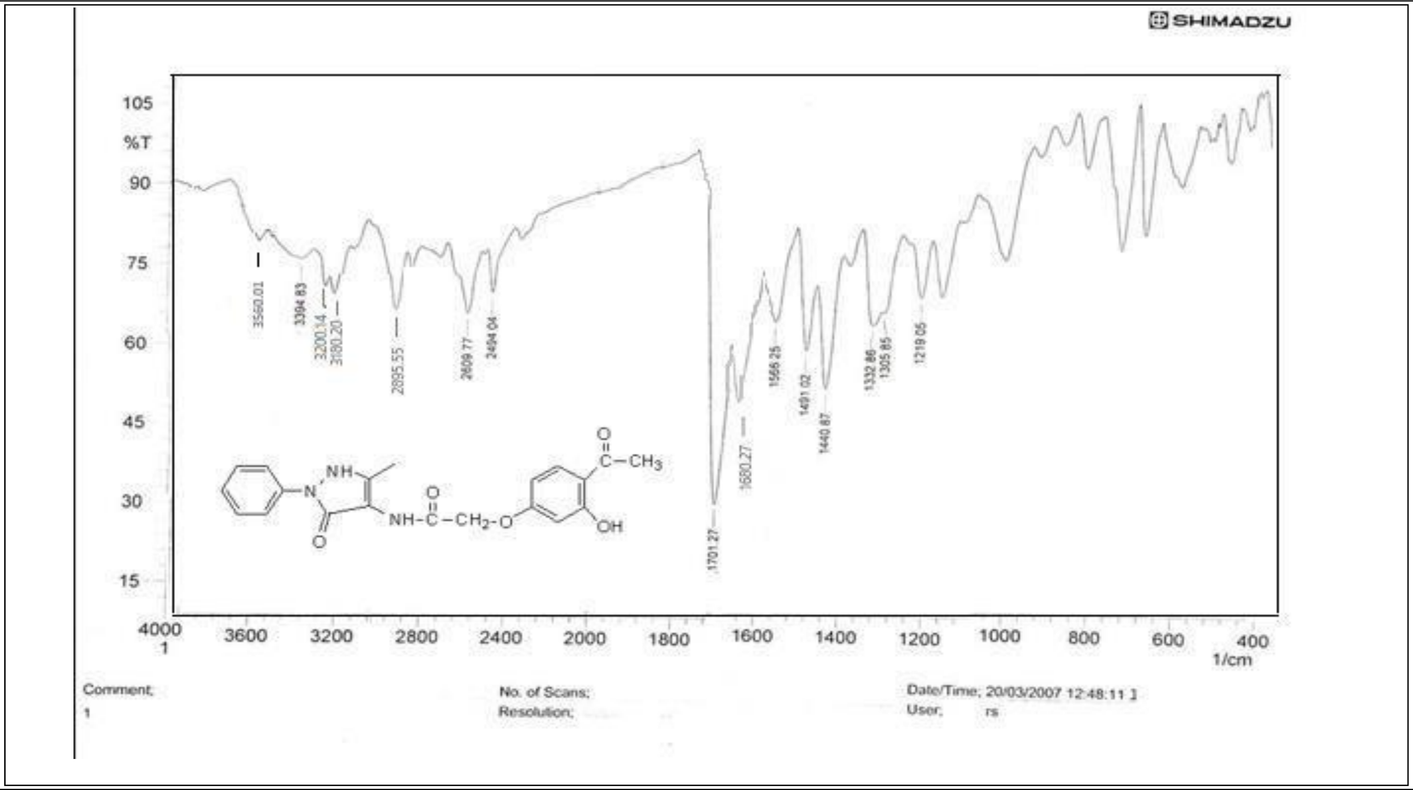
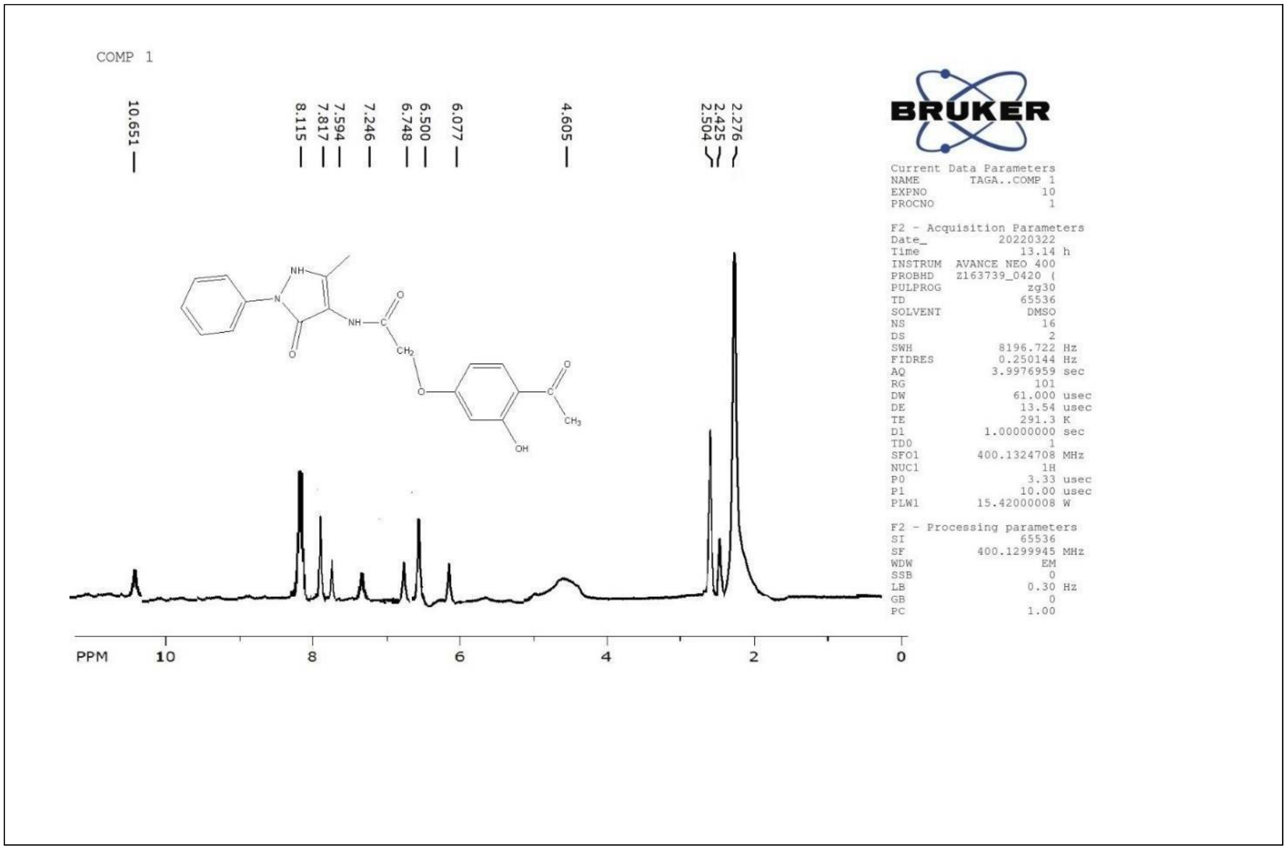


Figure (3-1) FTIR for compound RES5



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SOLVENT             DMSO
NS                    16
DS                     2
SWH             8196.722 Hz
FIDRES          0.250144 Hz
AQ             3.9976959 sec
RG                   101
DW                61.000 usec
DE                 13.54 usec
TE                 291.3 K
D1            1.00000000 sec
TD0                    1
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NUC1                  1H
P0                  3.33 usec
P1                 10.00 usec
PLW1         15.42000008 W

F2 - Processing parameters
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SSB                    0
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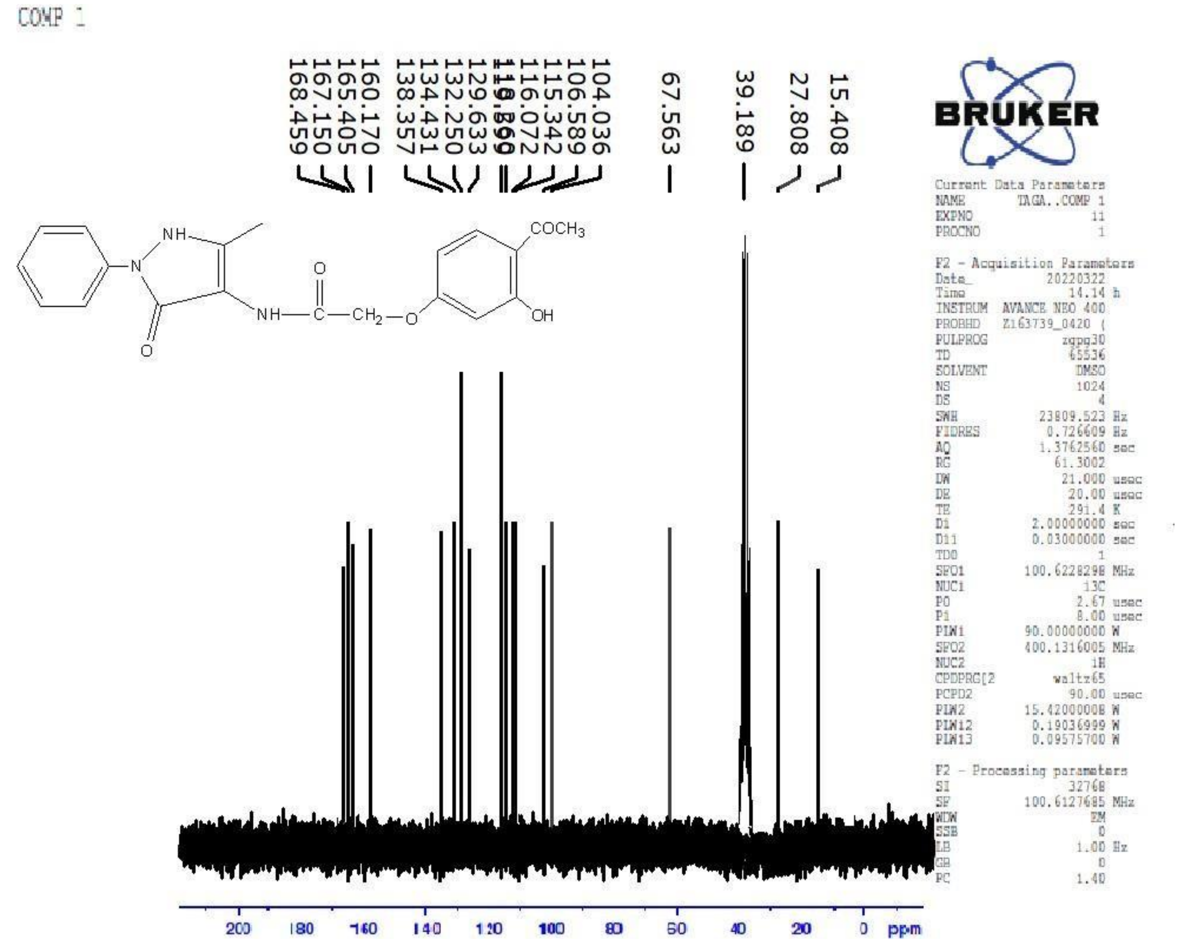
Figure (3-2) ^{1}HNMR for compound RES5



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PROCNO                  1

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TD                  65536
SOLVENT              DMSO
NS                   1024
DS                      4
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FIDRES           0.726609 Hz
AQ              1.3762560 sec
RG                61.3002
DW                 21.000 usec
DE                  20.00 usec
TE                  291.4 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1
SFO1          100.6228298 MHz
NUC1                  13C
P0                   2.67 usec
P1                   8.00 usec
PLW1          90.00000000 W
SFO2          400.1316005 MHz
NUC2                   1H
CPDPRG[2          waltz65
PCPD2               90.00 usec
PLW2          15.42000008 W
PLW12          0.19036999 W
PLW13          0.09575700 W

F2 - Processing parameters
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SF            100.6127685 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
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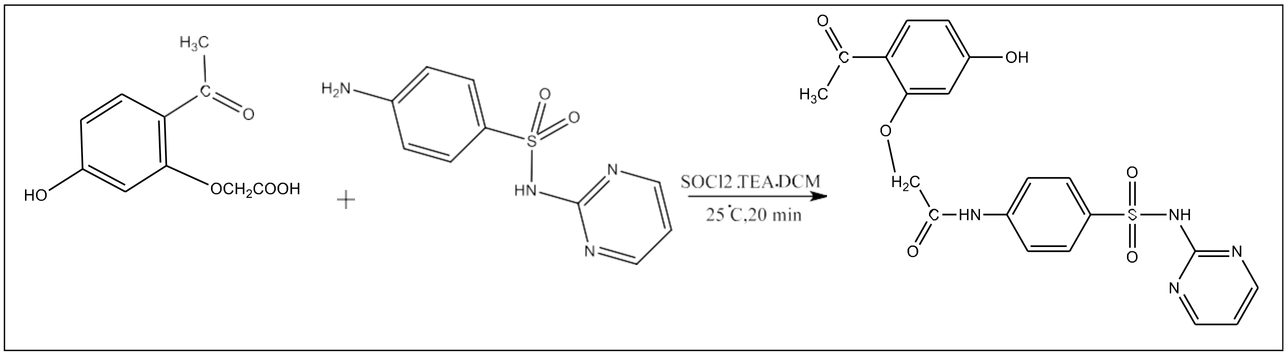
Figure (3-3) ^{13}CNMR for compound RES5

Compound (RES6) prepared from the reaction of R2 with Sulfadiazine in existence DMSO , $SOCl_2$ and triethylamine. Equation (3-2).



Equation (3-2): synthesis of RES6

FT-IR spectrum for RES6 showed the following values (*V*max cm-1): 3394.83 (N-H str. groups) ,1618(N-H bend),1710(C=O str.Ketones), 1680(CO str. amide), 3742.03 (O-H phenol), 3049.11(C-H str. Sp2 aromatic), 2939(C-H str. Sp3), 1313(C-O-C str. ether) and 1253(C-O str.), 1157(S=O) (Figure 3-4). ^{1}H-NMR (500 MHz, δ ppm): 9.98(O-H , alcohol) 9.96(N-H ,sec. amid), 11.3(Nsulfonamide), 6.4-7.6 (C-H, aromatic), 4.6 (methylene),2.6 (methyl) 7.7;8.4 (CH pyrimidine) , 2.5 (DMSO) (Figure 3-5). ^{13}C- NMR (125 MHz, δ ppm): 26.6 (C,CH_3), 66.6(C,CH_2), 157.9 -169.3 (C=N pyrimidine)167.6 (N-C=O),101.9-163.9 (C,Ar),198 (C, Carbonyl)40.3DMSO.(Figure3-6).

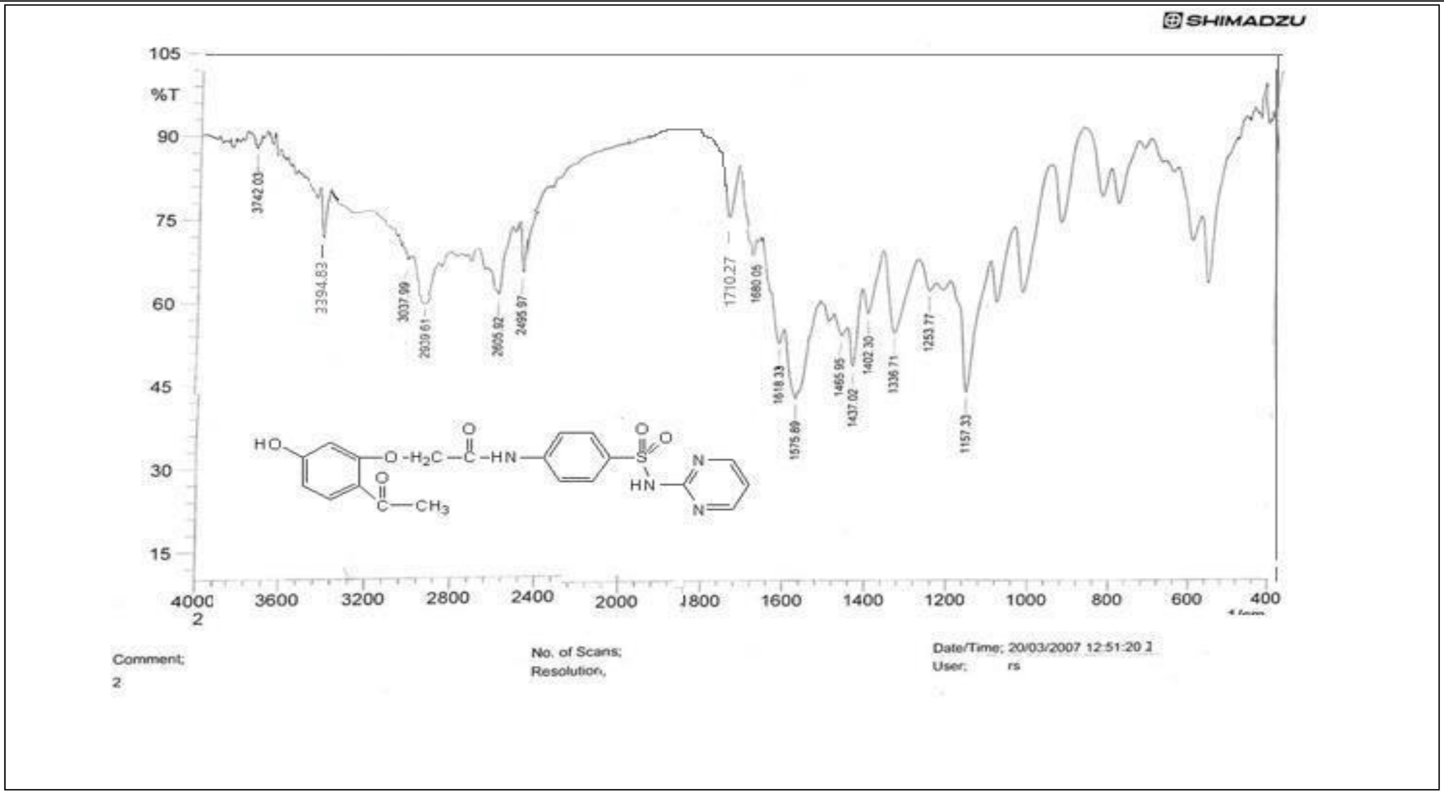
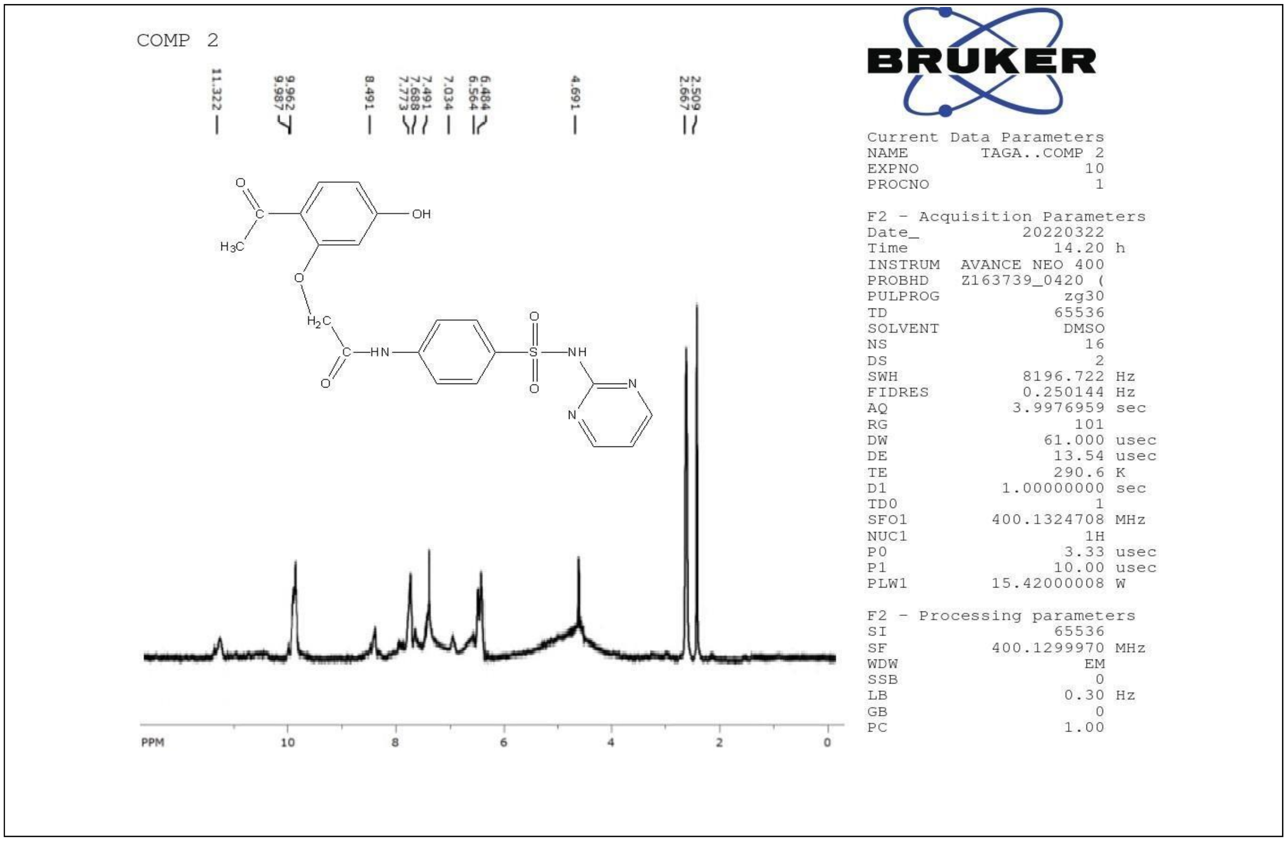


Figure (3-4) FTIR for compound RES6



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TD                65536
SOLVENT            DMSO
NS                   16
DS                    2
SWH            8196.722 Hz
FIDRES         0.250144 Hz
AQ            3.9976959 sec
RG                  101
DW               61.000 usec
DE                13.54 usec
TE                290.6 K
D1           1.00000000 sec
TD0                   1
SFO1        400.1324708 MHz
NUC1                 1H
P0                 3.33 usec
P1                10.00 usec
PLW1        15.42000008 W

F2 - Processing parameters
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SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
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Figure (3-5) ^{1}HNMR for compound RES6

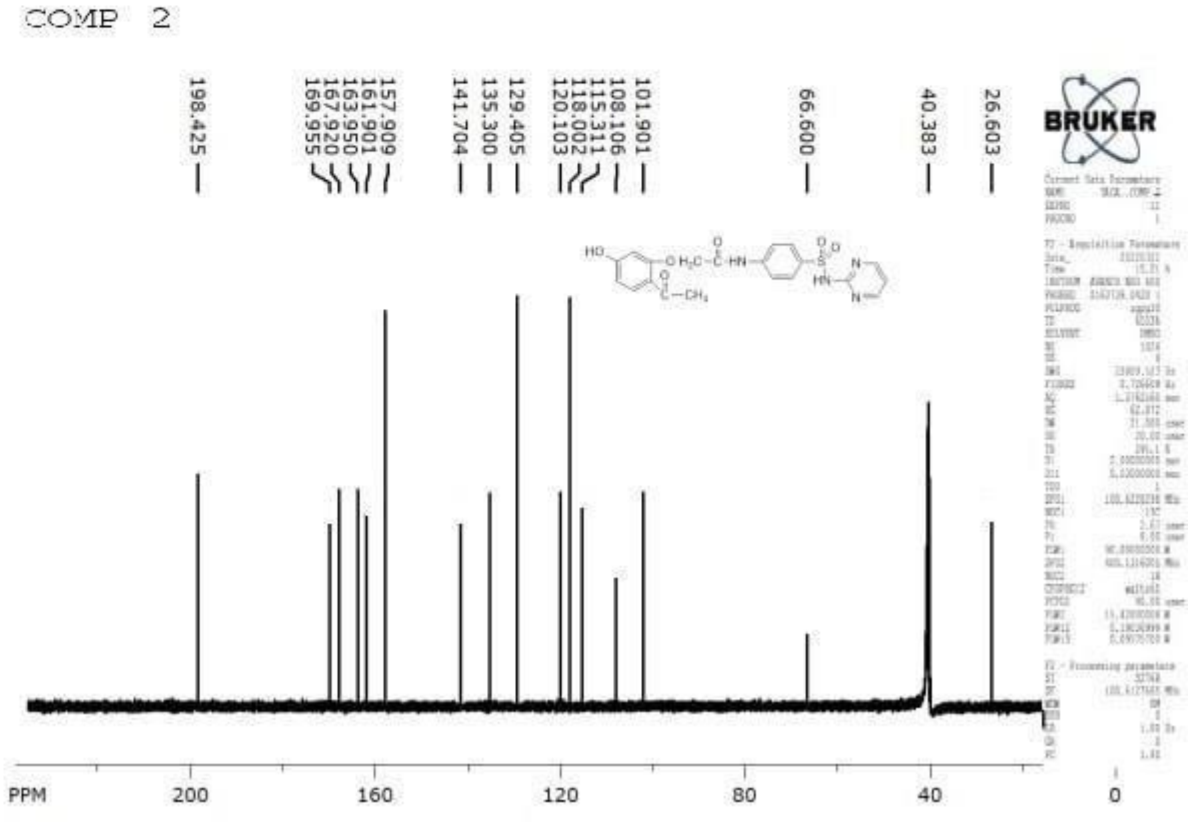
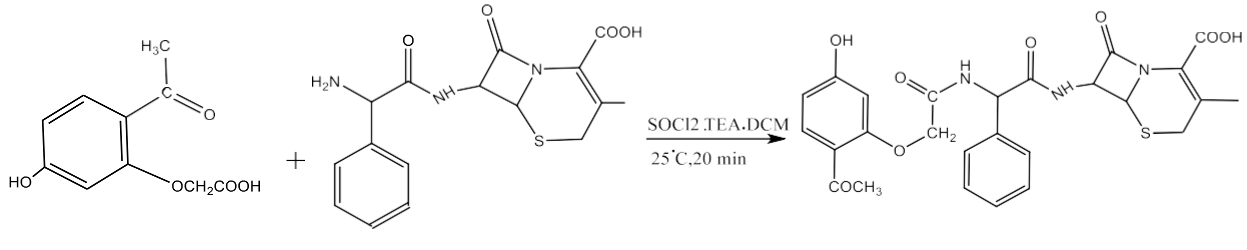


Figure (3-6) ^{13}CNMR for compound RES6

Compound (RES7) prepared from the reaction of R2 with Cephalexin in existence DMSO , $SOCl_2$ and triethylamine. Equation (3-3).



Equation (3-3): synthesis of RES7

FT-IR spectrum for RES7 showed the following values (Vmax cm-1): 3564 (N-H) ,1715(C=O Ketone), 1654(C=O amide), 3365 (O-H phenol), 3055 (C-H str. Sp2 aromatic),1504 (C=C arom.) , 1707 (C=O carb.) 2978 (OH carb) (Figure 3-7) . ^{1}H-NMR (500 MH, δ ppm): 12.5 (OH carb.) 10.6(O-H , phenol) , 8.1-8.8 (N-H ,sec. amid), , 6.4- 7.4 (C-H, aromatic), 3.16 (methylene),2.1-2.7 (methyl) , 2.5 (DMSO) (Figure 3-8). ^{13}C- NMR (125 MHz, δ ppm): 20.7-27.4 (C,CH_3), 30.9-68.1 (C,CH_2), 165.2-172.5 (N-C=O), 102.7-135.3 (C,Ar), - 161.9(C, Carboxyl), 198.8 (C,Carbonyl) 39.1 DMSO , (Figure 3-9).

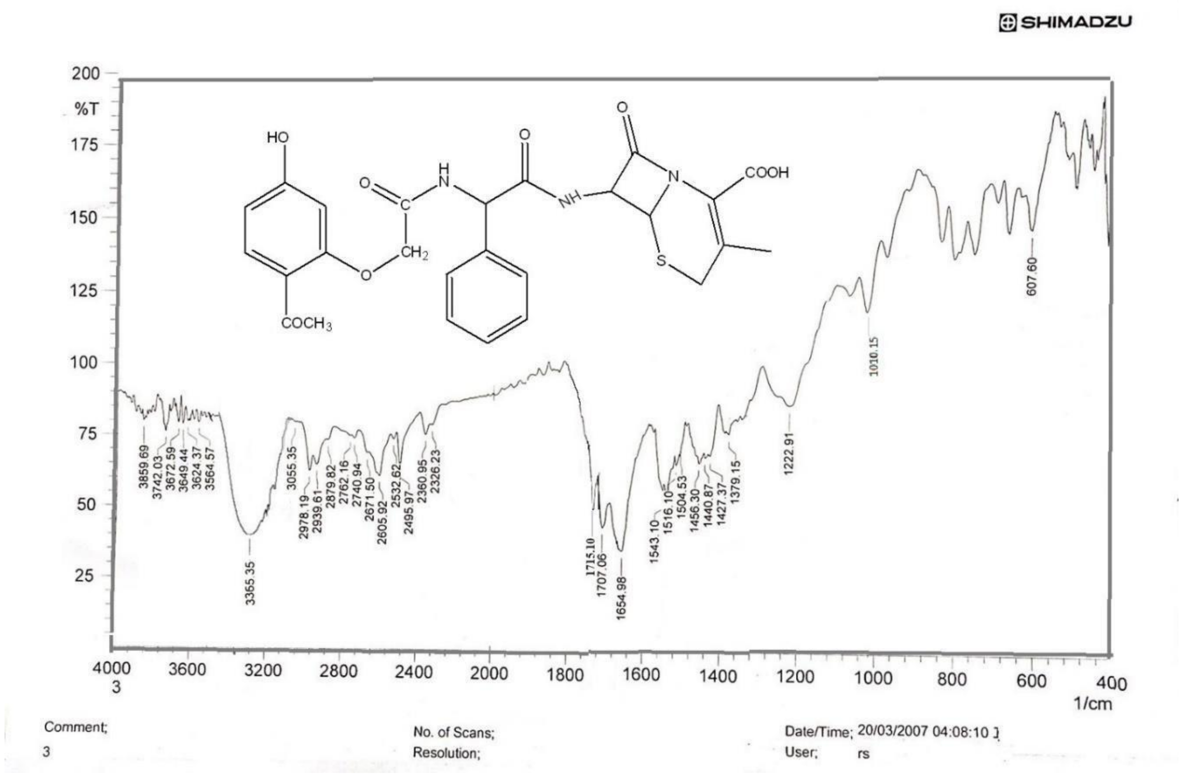
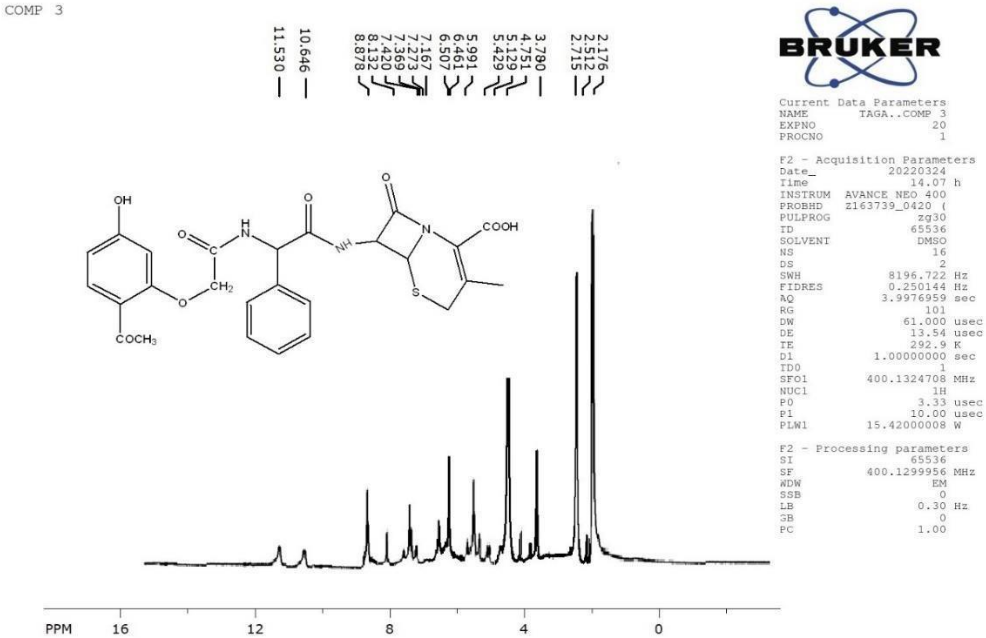


Figure (3-7) FTIR for compound RES7



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PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH             8196.722 Hz
FIDRES          0.250144 Hz
AQ             3.9976959 sec
RG                   101
DW                61.000 usec
DE                 13.54 usec
TE                 292.9 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  3.33 usec
P1                 10.00 usec
PLW1         15.42000008 W

F2 - Processing parameters
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WDW                   EM
SSB                    0
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GB                     0
PC                  1.00
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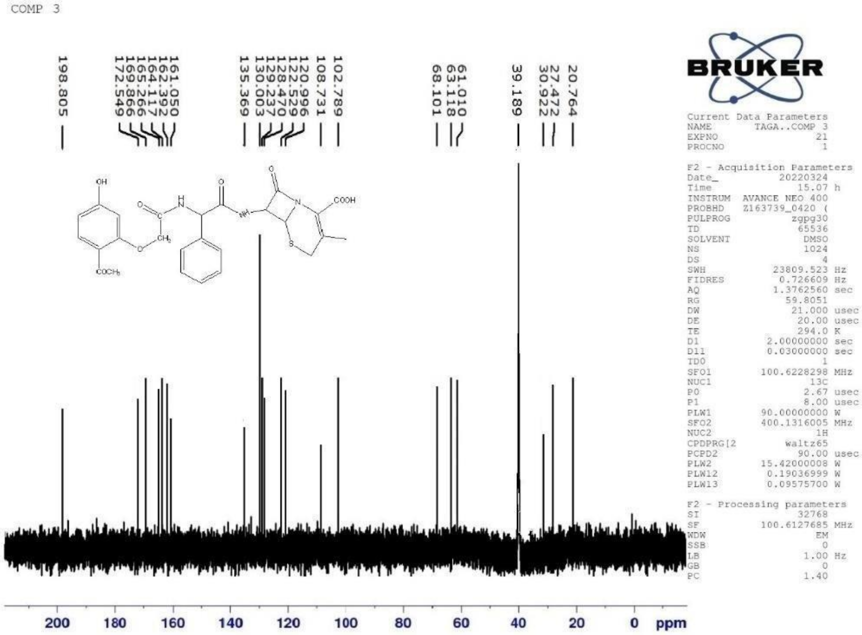
Figure (3-8) ^{1}HNMR for compound RES7



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TD                 65536
SOLVENT             DMSO
NS                  1024
DS                     4
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AQ             1.3762560 sec
RG               59.8051
DW                21.000 usec
DE                 20.00 usec
TE                 294.0 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1
SFO1         100.6228298 MHz
NUC1                 13C
P0                  2.67 usec
P1                  8.00 usec
PLW1         90.00000000 W
SFO2         400.1316005 MHz
NUC2                  1H
CPDPRG[2         waltz65
PCPD2              90.00 usec
PLW2         15.42000008 W
PLW12         0.19036999 W
PLW13         0.09575700 W

F2 - Processing parameters
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WDW                   EM
SSB                    0
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GB                     0
PC                  1.40
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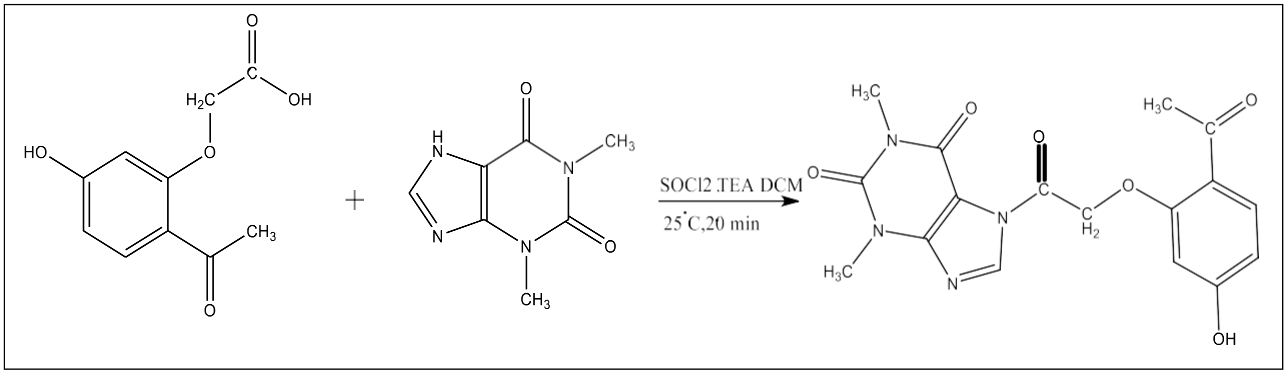
Figure (3-9) ^{13}CNMR for compound RES7

Compound (RES8) prepared from the reaction of R2 with Theophylline in existence DMSO , $SOCl_2$ and triethylamine. Equation (3-4).



Equation (3-4): synthesis of RES8

FT-IR spectrum for RES8 showed the following values (Vmax cm-1): 3375 (N-H) ,1720(C=O Ketone), 1689(C=O amide), 3650 (O-H phenol), 3020 (C-H str. Sp2 aromatic),1647 (C=C arom.) , 2976(CH str. Aliph.) (Figure 3-10)1H-NMR (500 MHz, δ ppm): 9. 8(O-H , phenol), 9.3 (imidazol) 6.4-7.5(C-H, aromatic), 1.19 (methylene),3.4-3.6 (methyl) , 2.5 (DMSO) (Figure 3-11). ^{13}C- NMR (125 MHz, δ ppm): 27.3(C,CH_3) , 29.8 (C,CH_3).31.5 (C,CH_3), 74.2 (C,CH_2), 156.3 (N-C=O), 120.9.7-164.8 (C,Ar), 169,2-198.8 (C,Carbonyl),41.2 DMSO,(Figure 3-12).

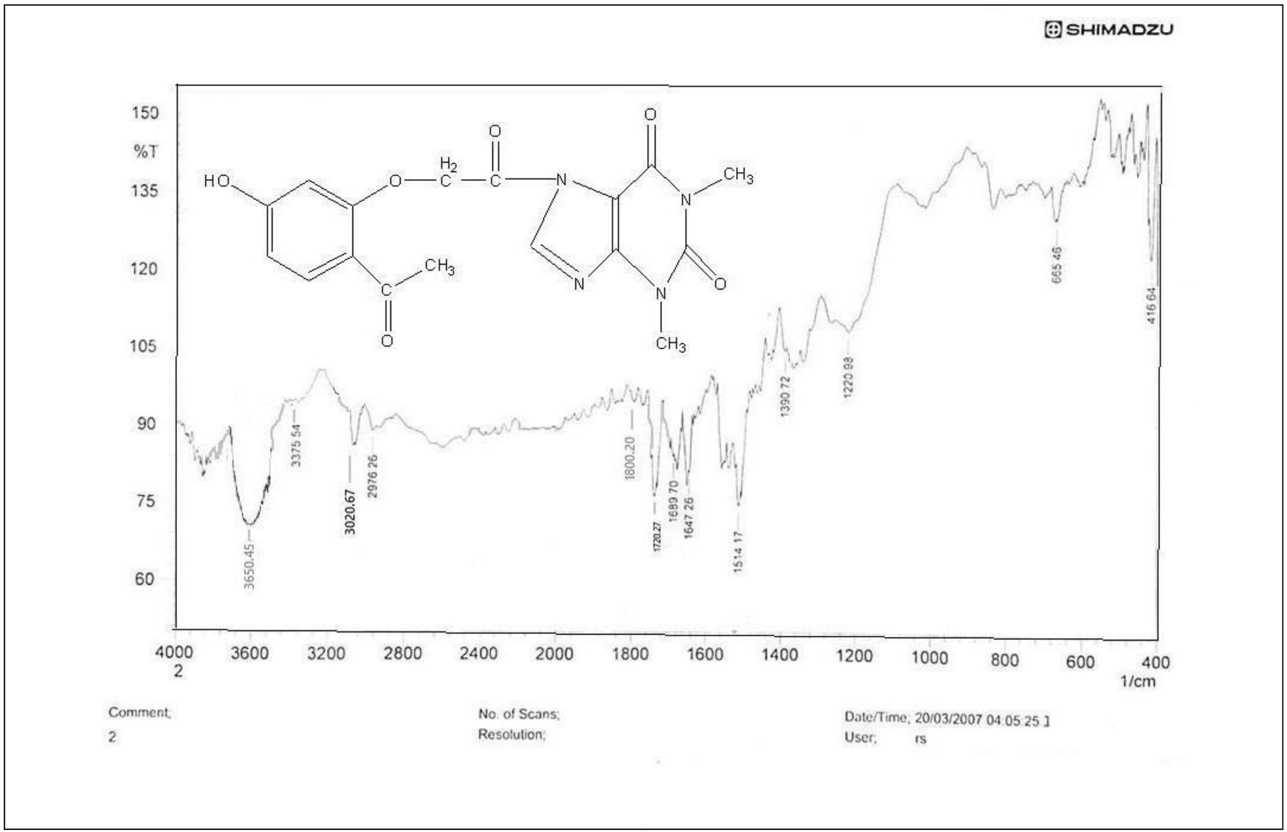


Figure (3-10) FTIR for compound RES8

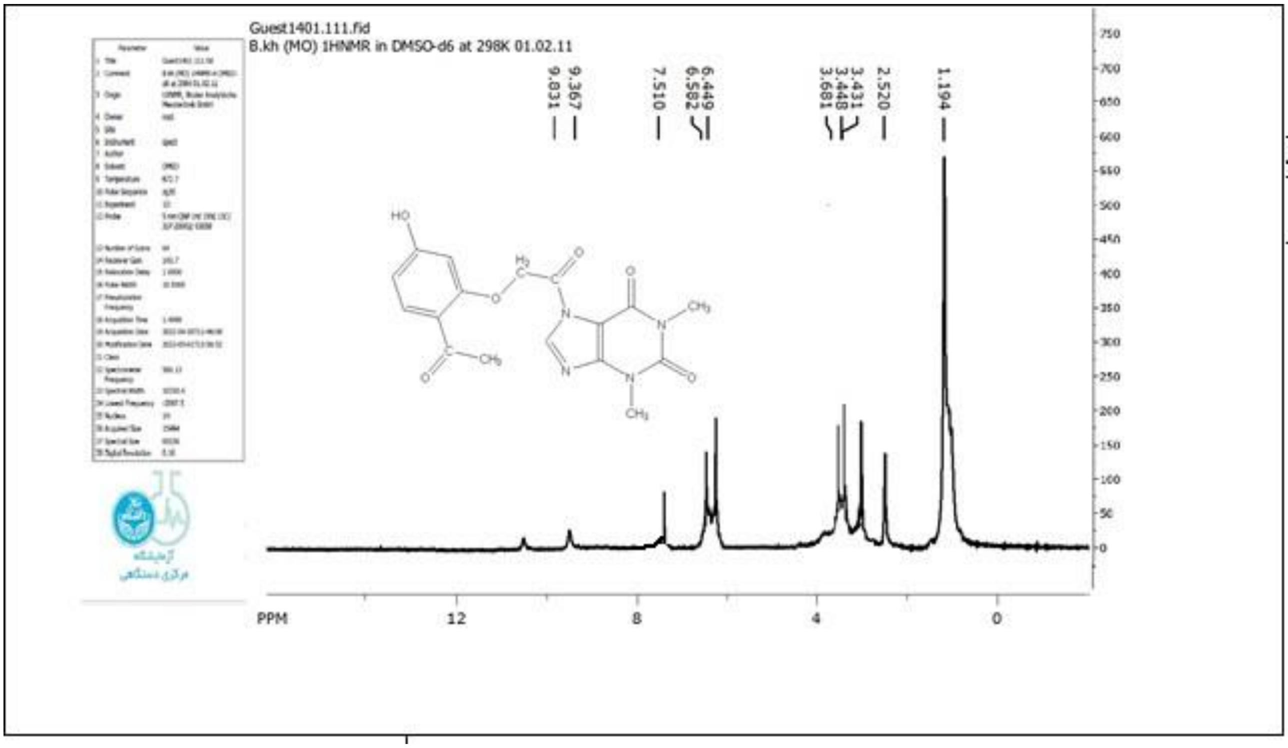
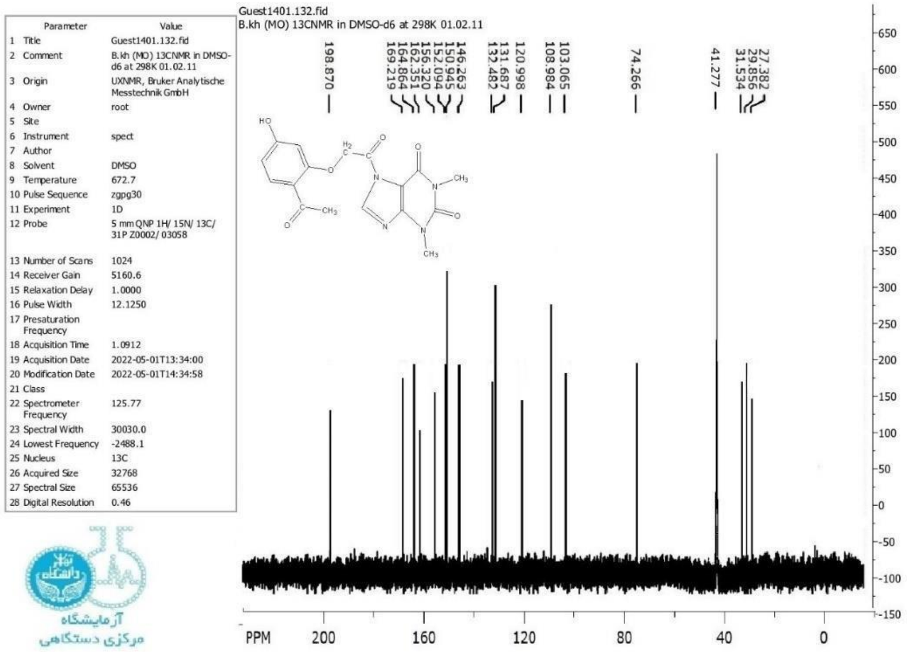


Figure (3-11) ^{1}HNMR for compound RES8



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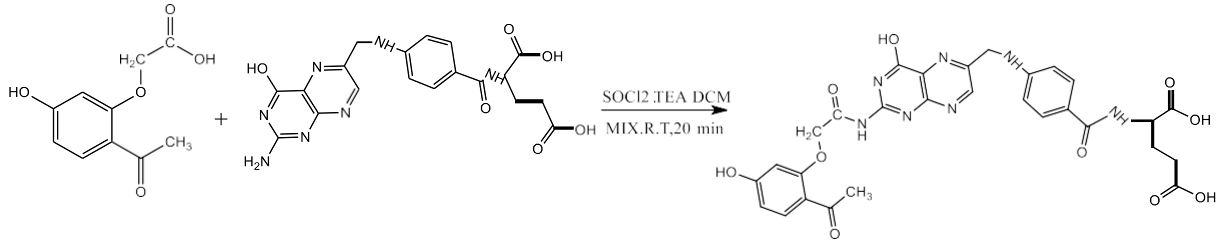
5 Site	
6 Instrument	spect
7 Author	
8 Solvent	DMSO
9 Temperature	672.7
10 Pulse Sequence	zgpg30
11 Experiment	1D
12 Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13 Number of Scans	1024
14 Receiver Gain	5160.6
15 Relaxation Delay	1.0000
16 Pulse Width	12.1250
17 Presaturation Frequency	
18 Acquisition Time	1.0912
19 Acquisition Date	2022-05-01T13:34:00
20 Modification Date	2022-05-01T14:34:58
21 Class	
22 Spectrometer Frequency	125.77
23 Spectral Width	30030.0
24 Lowest Frequency	-2488.1
25 Nucleus	13C
26 Acquired Size	32768
27 Spectral Size	65536
28 Digital Resolution	0.46

Guest1401.132.fid
B.kh (MO) 13CNMR in DMSO-d6 at 298K 01.02.11

Figure (3-12) ^{13}CNMR for compound RES8

Compound (RES9) prepared from the reaction of R2 with folic acid in existence DMSO , $SOCl_2$ and triethylamine. Equation (3-5).



Equation (3-5): synthesis of RES9

FT-IR spectrum for RES9 showed the following values (Vmax cm^{-1}): 1735(C=O Ketone), 1630(C=O amide), 3313 (O-H phenol), 3055 (C-H str. Sp2 aromatic),1533 (C=C arom.) , 1691 (C=O carb.), 1200 (C-O ether) (Figure 3-13) .

^{1}H-NMR (500 MHz, δ ppm): 11.5-11.9 (OH carb.) 9.8(O-H , phenol) , 6.5-8.5 (N-H ,sec. amid), , 6.2- 7.5 (C-H, aromatic), 4,3-4.4 (methylene),2.6 (methyl) , 2.5 (DMSO) (Figure 3-14). ^{13}C- NMR (125 MHz, δ ppm): 25.2 (C,CH$_3$),57.3 (C,CH alipha.),26.9-67.2 (C,CH$_2$ alipha.), 158.1-173.2 (N-C=O), 120.8-164.8(C,Ar), -174.7-179.2(C, Carboxyl), 102.7-132(CH.arom.) 198 (C,Carbonyl) , 41.2 DMSO ,(Figure 3-15).

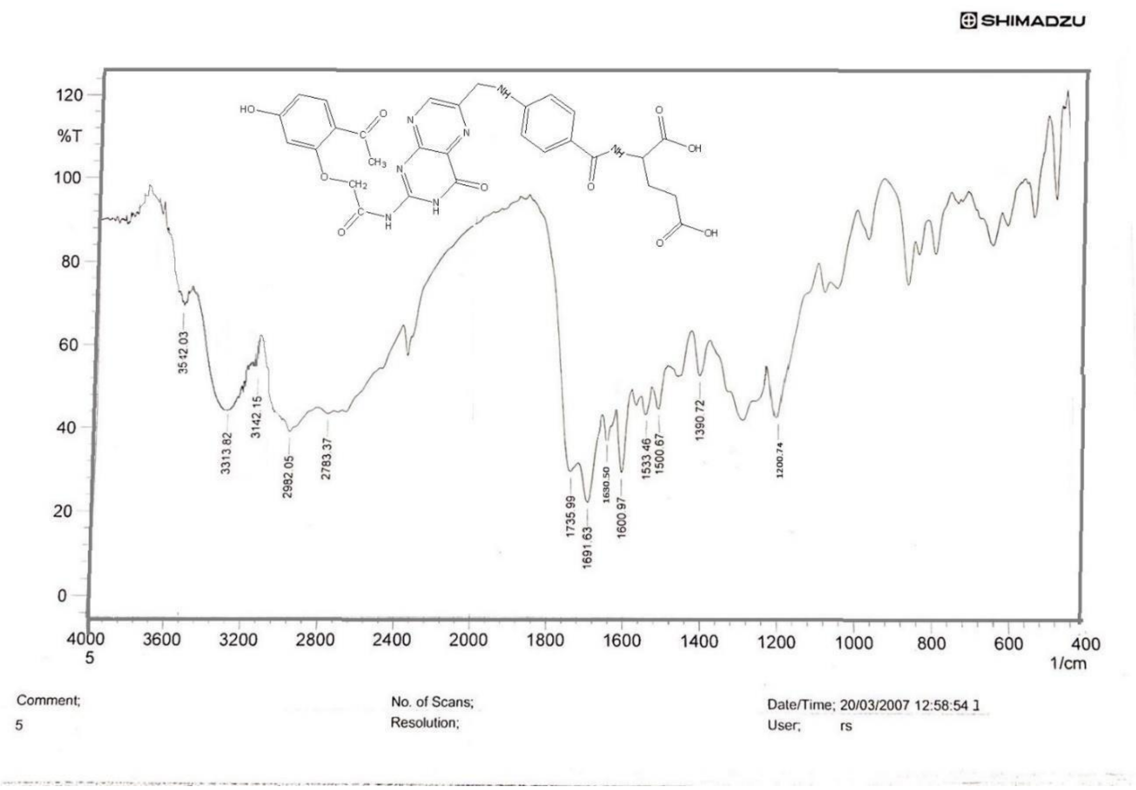
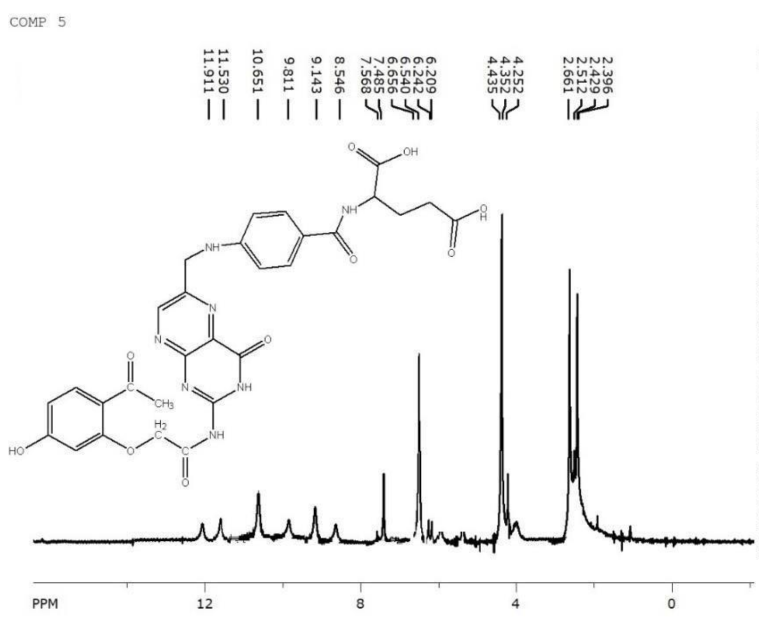


Figure (3-13) FTIR for compound RES9



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PROCNO                 1

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TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH             8196.722 Hz
FIDRES          0.250144 Hz
AQ             3.9976959 sec
RG                   101
DW                61.000 usec
DE                 13.54 usec
TE                 289.9 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  3.33 usec
P1                 10.00 usec
PLW1         15.42000008 W

F2 - Processing parameters
SI                 65536
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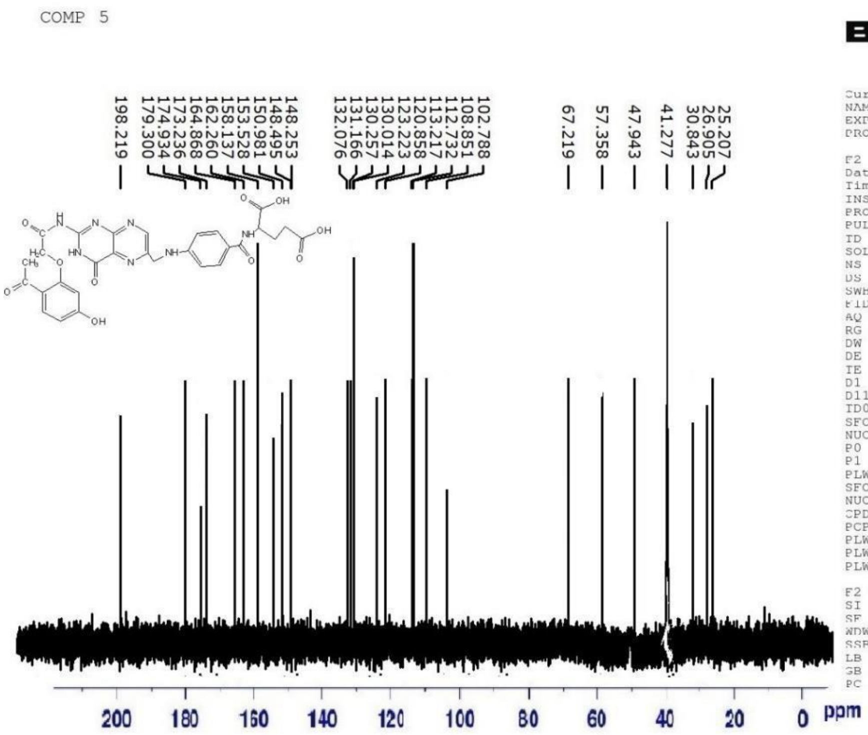
Figure (3-14) ^{1}HNMR for compound RES9



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PROCNO                 1

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PULPROG           zgpg30
TD                 65536
SOLVENT             DMSO
NS                  1024
DS                     4
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FIDRES          0.726609 Hz
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RG                60.704
DW                21.000 usec
DE                 20.00 usec
TE                 290.7 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1
SFO1         100.6228298 MHz
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P0                  2.67 usec
P1                  8.00 usec
PLW1         90.00000000 W
SFO2         400.1316005 MHz
NUC2                  1H
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PCPD2              90.00 usec
PLW2         15.42000008 W
PLW12         0.19036999 W
PLW13         0.09575700 W

F2 - Processing parameters
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WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
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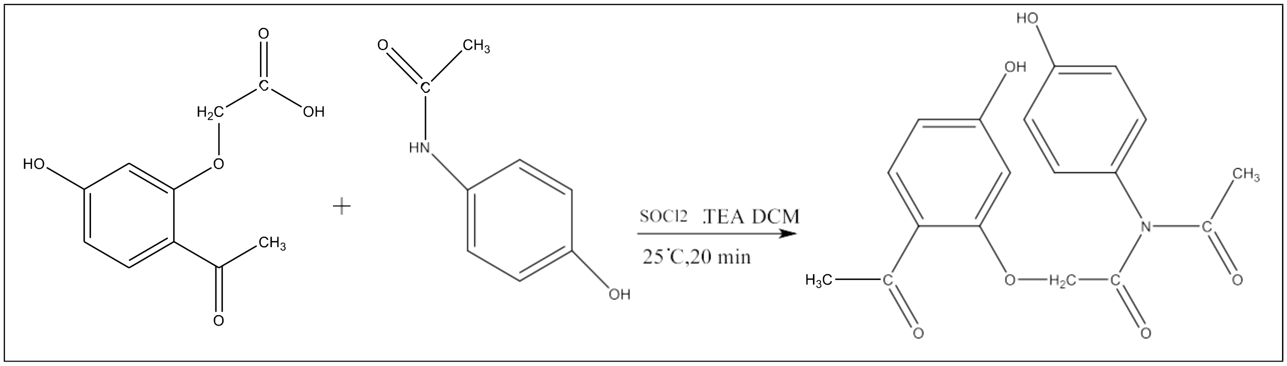
Figure (3-15) ^{13}CNMR for compound RES9

Compound (RES10) prepared from the reaction of R2 with paracetamol in existence DMSO , $SOCl_2$ and triethylamine. Equation (3-6).



Equation (3-6): synthesis of RES10

FT-IR spectrum for RES 10 showed the following values (vmax cm^{-1}): 1678 (C- N str.aryl), 1739 (C=O ketone), 1627 (C=O, amide), 3742 (O-H groups), 3100 (C- H aromatic), 2924 (C-H sp3), 1430 (O-H bend) (Figure 3-16) . ^{1}H-NMR (500 MHz,δ ppm): 9.5(O-H , alcohol) , 6.3- 7.4 (C-H, aromatic), 4.7(methylene) ,2.6-2.7 (methyl) , 2.5 (DMSO) (Figure 3-17). ^{13}C- NMR (125 MHz, δ ppm): 26.7 (C,CH_3), 27.2 (C,CH_3) , 63.9 (C,CH_2 alipha.), 166.8 (N-C=O), 121.2-164.4(C,Ar), - 174.7-179.2(C, Carboxyl), 103.3-130.4(CH.arom.) 198 (C,Carbonyl) (Figure 3-18).

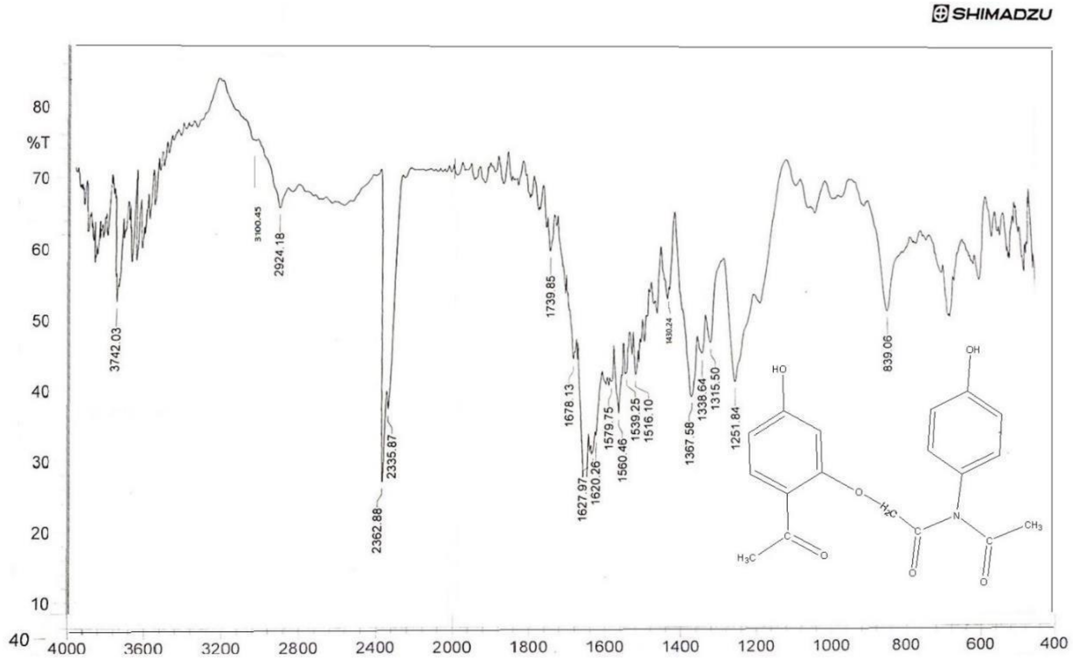
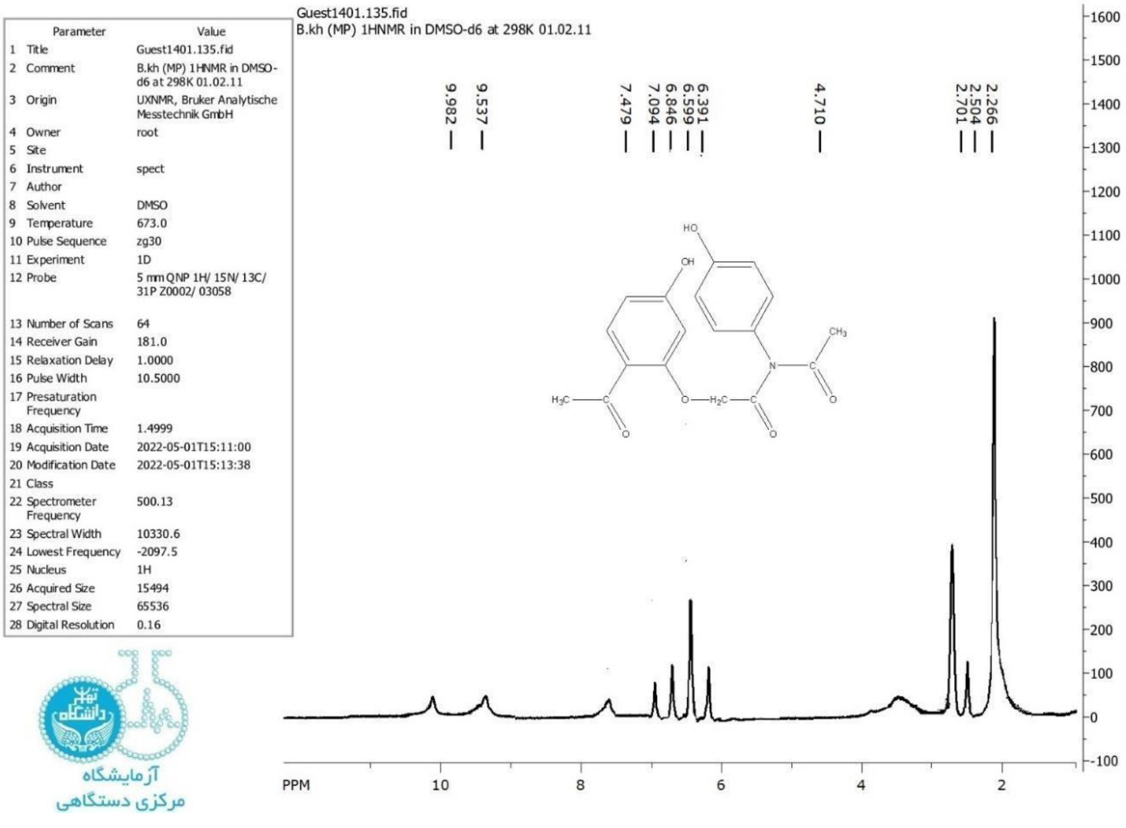


Figure (3-16) FTIR for compound RES10



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4 Owner	root
5 Site	
6 Instrument	spect
7 Author	
8 Solvent	DMSO
9 Temperature	673.0
10 Pulse Sequence	zg30
11 Experiment	1D
12 Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
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27 Spectral Size	65536
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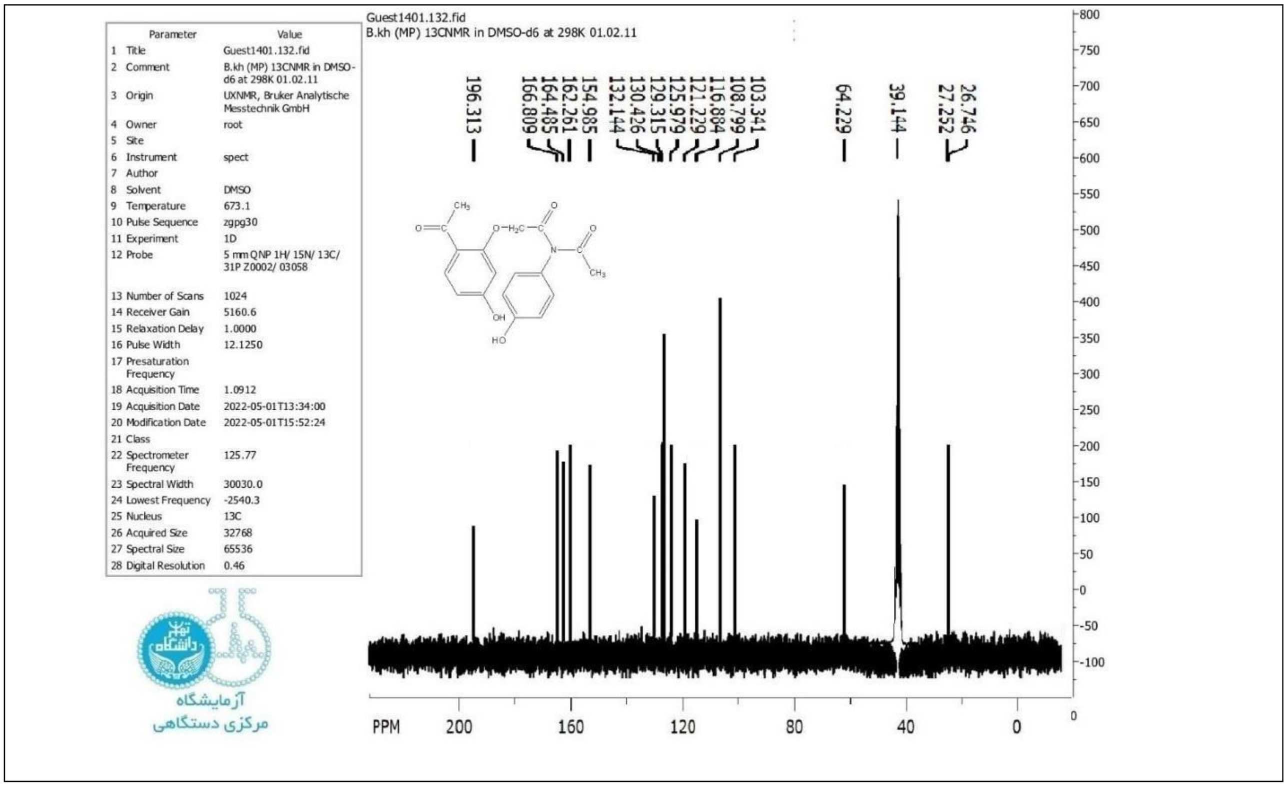
Guest1401.135.fid
B.kh (MP) 1HNMR in DMSO-d6 at 298K 01.02.11

Figure (3-17) ^{1}HNMR for compound RES10



	Parameter	Value
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5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	673.1
10	Pulse Sequence	zgpg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	1024
14	Receiver Gain	5160.6
15	Relaxation Delay	1.0000
16	Pulse Width	12.1250
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21	Class	
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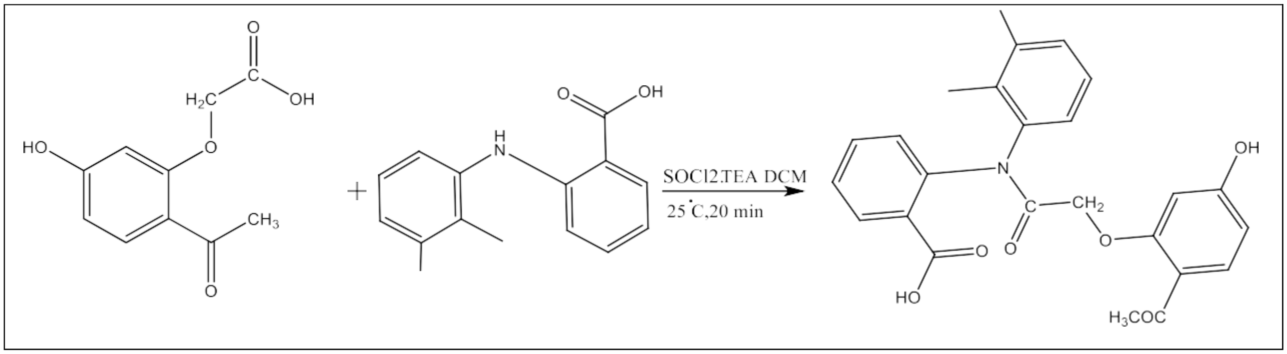
24	Lowest Frequency	-2540.3
25	Nucleus	13C
26	Acquired Size	32768
27	Spectral Size	65536
28	Digital Resolution	0.46

Figure (3-18) ^{13}CNMR for compound RES10

Compound (RES11) prepared from the reaction of R2 with Mefenamic acid in existence DMSO , $SOCl_2$ and triethylamine. Equation (3-7).



Equation (3-7): synthesis of RES11

FT-IR spectrum for RES11 showed the following values (Vmax cm-1): 1394 (C-N str.aryl), 1715 (C=O ketone), 1680 (C=O, amide), 3649 (O-H phenol), 3005 (C-H aromatic) , 1514 (C=C arom.) , 1729 (C=O carb.) (Figure 3-19) . 1H-NMR (500 MHz, δ ppm): 10.5(O-H , phenol) , 6.2- 8.2 (C-H, aromatic), 4.4(methylene) ,2.1-2.6 (methyl) , 2.5 (DMSO) (Figure 3-20). ^{13}C- NMR (125 MHz,δ ppm): 15.0 (C,CH_3), 18.8 (C,CH_3) , 27.3 (C,CH_3) , 66.8 (C,CH_2 alipha.), 163.8 (N-C=O), 112.9-164.2(C,Ar),169.9(C, Carboxyl), 103-135.5(CH arom.) ,198 (C,Carbonyl), 139.8 DMSO (Figure 3-21).

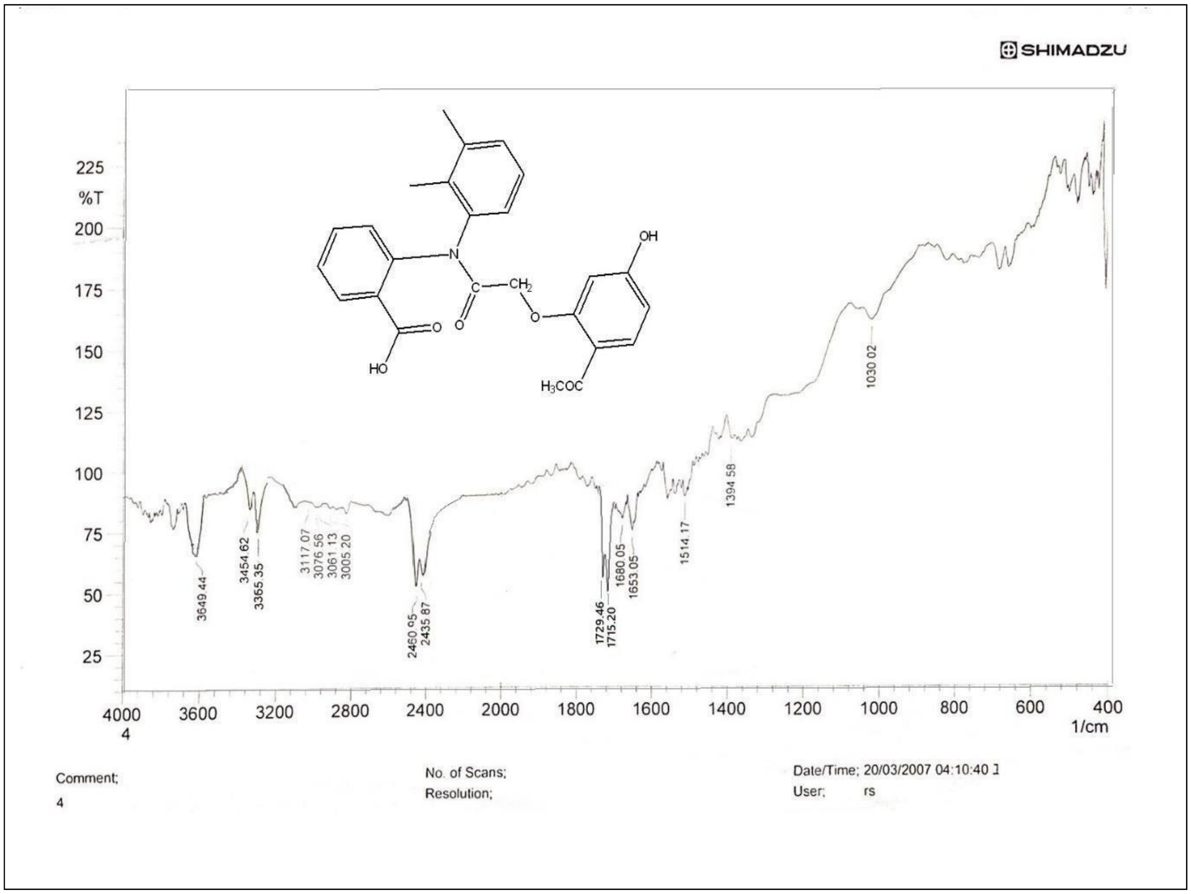
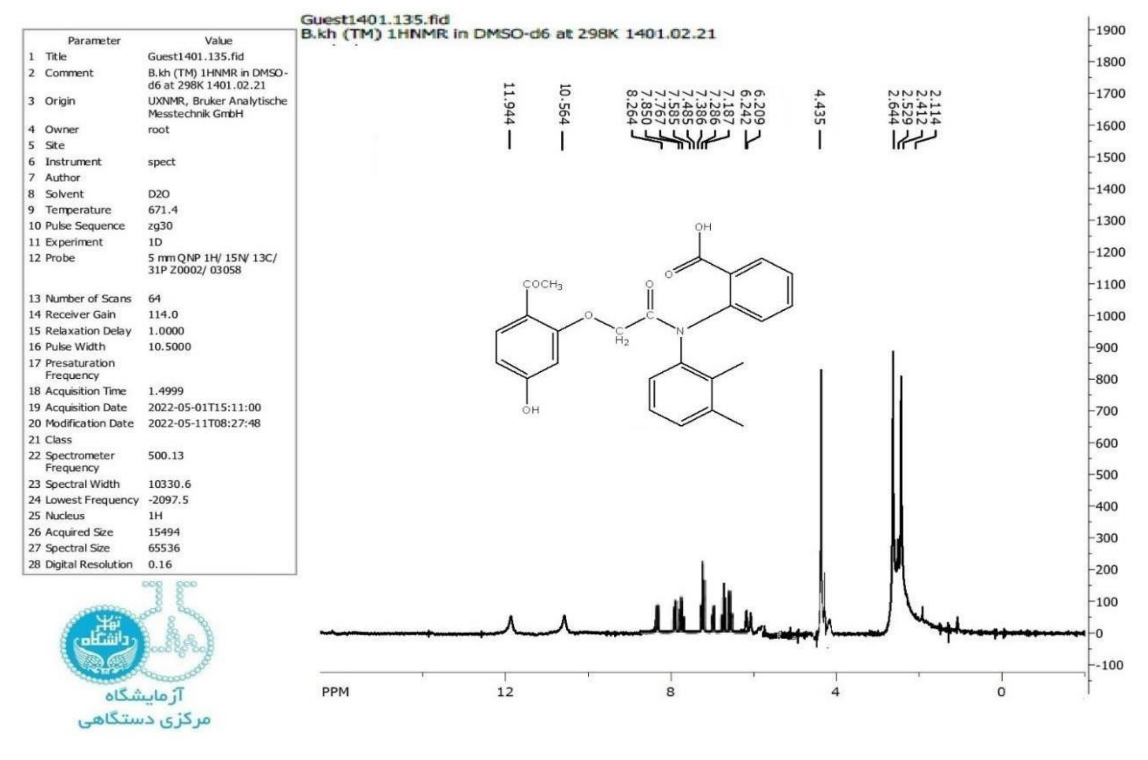


Figure (3-19) FTIR for compound RES11



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6 Instrument	spect
7 Author	
8 Solvent	D2O
9 Temperature	671.4
10 Pulse Sequence	zg30
11 Experiment	1D
12 Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13 Number of Scans	64
14 Receiver Gain	114.0
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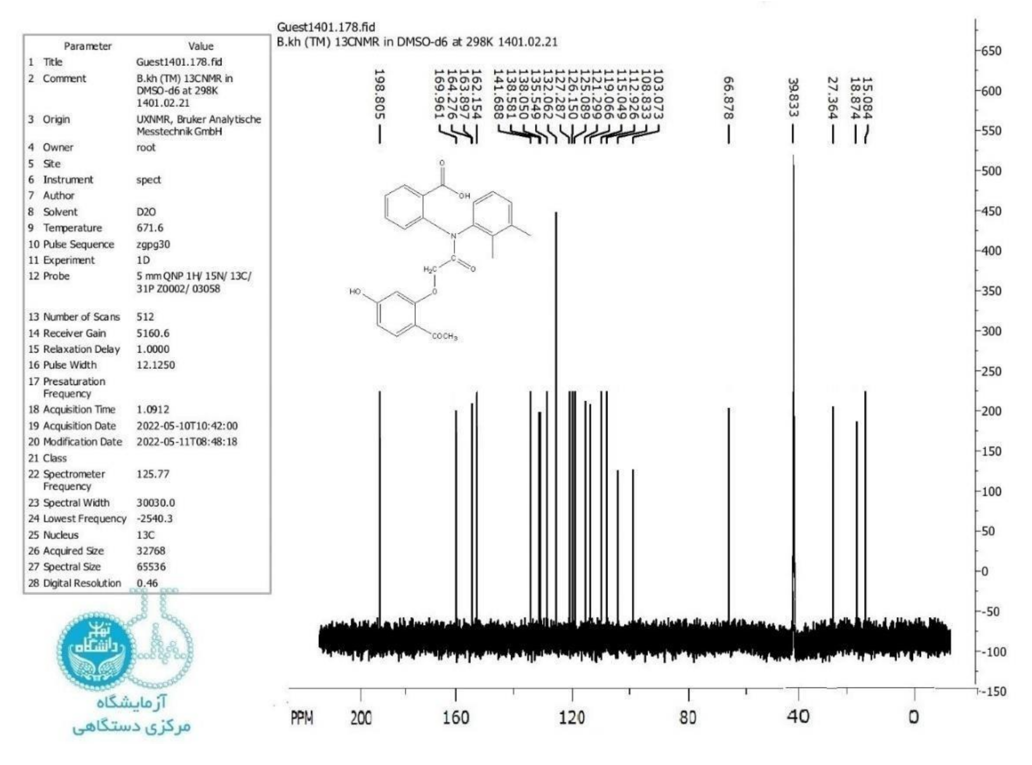
24 Lowest Frequency	-2097.5
25 Nucleus	1H
26 Acquired Size	15494
27 Spectral Size	65536
28 Digital Resolution	0.16

Guest1401.135.fid
B.kh (TM) 1HNMR in DMSO-d6 at 298K 1401.02.21

Figure (3-20) ^{1}HNMR for compound RES11



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6 Instrument	spect
7 Author	
8 Solvent	D2O
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10 Pulse Sequence	zgpg30
11 Experiment	1D
12 Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13 Number of Scans	512
14 Receiver Gain	5160.6
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16 Pulse Width	12.1250
17 Presaturation Frequency	
18 Acquisition Time	1.0912
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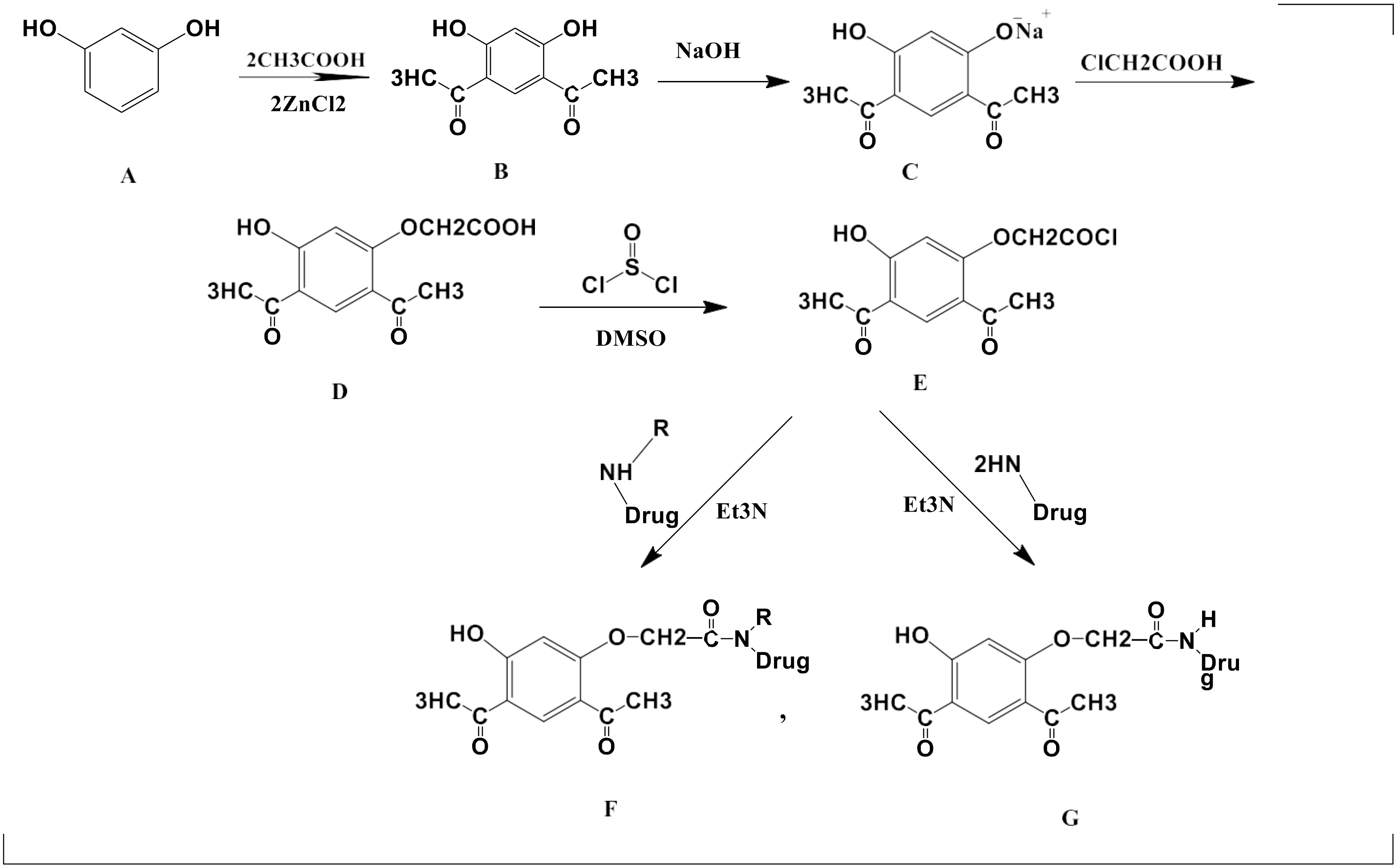
24 Lowest Frequency	-2540.3
25 Nucleus	13C
26 Acquired Size	32768
27 Spectral Size	65536
28 Digital Resolution	0.46

Guest1401.178.fid
B.kh (TM) 13CNMR in DMSO-d6 at 298K 1401.02.21

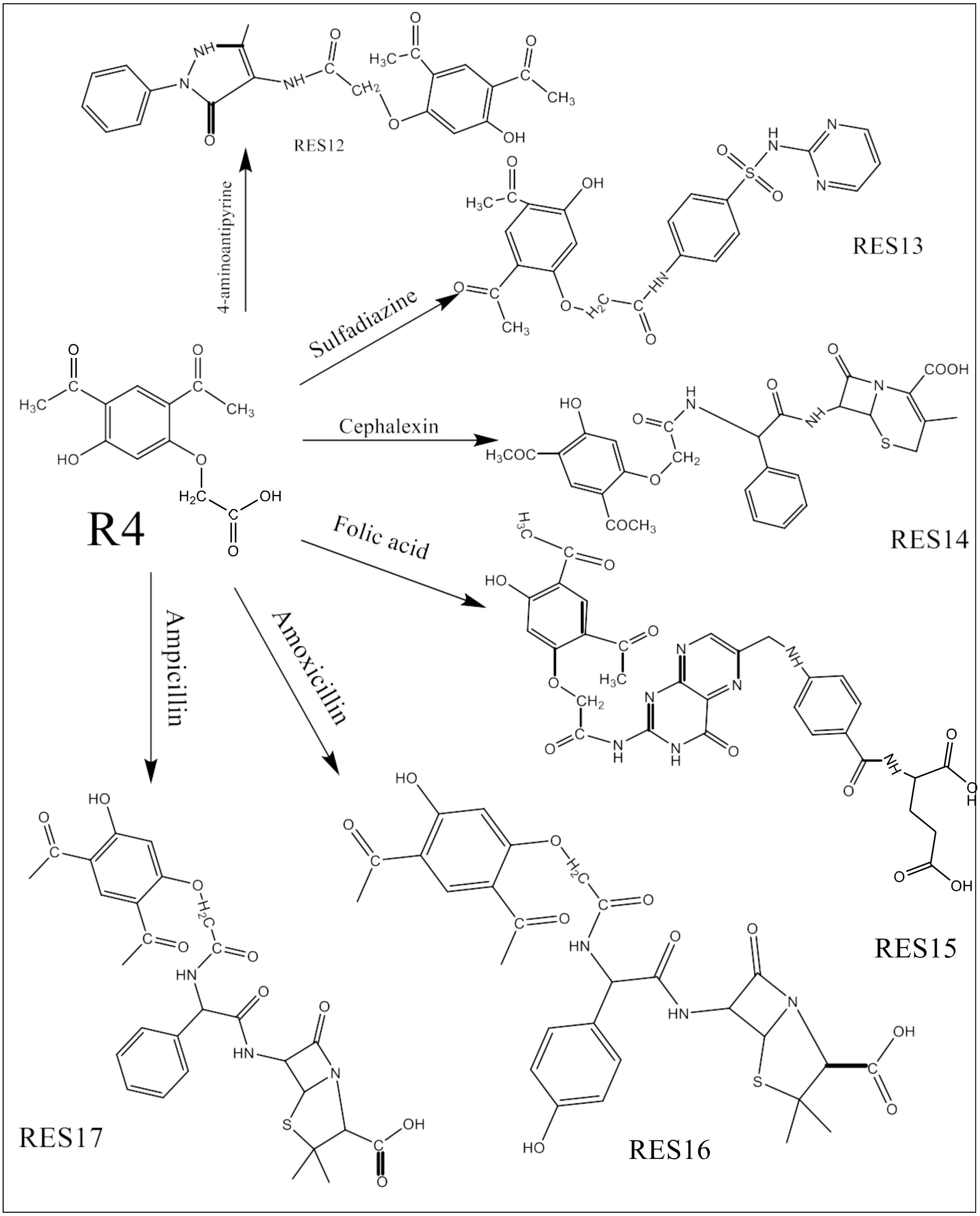
Figure (3-21) ^{13}CNMR for compound RES11

3.2. Second path

New amino-containing medications were created via the creation of amide bonds. Resorcinol was reacted with six amino medicines to create the compounds(RES12-RES17).

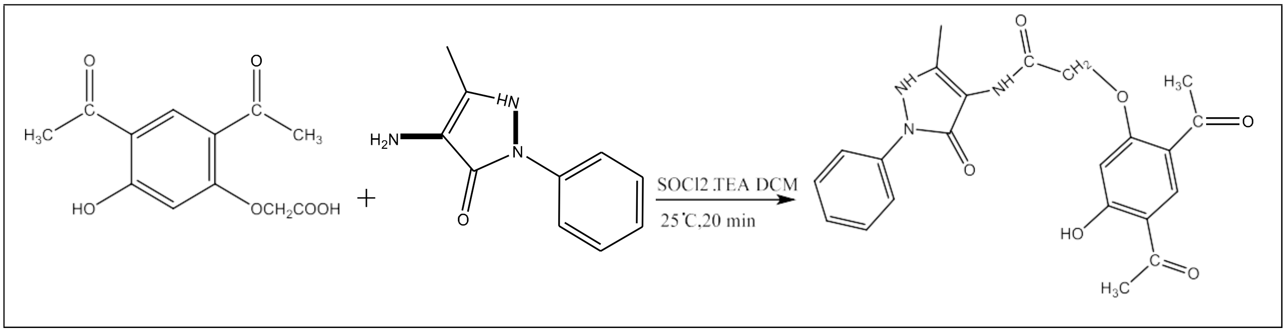


Scheme (3-3): General scheme for Synthesis of compounds (RES12-RES17)



Scheme (3-4): Synthesis of compounds RES12 – RES17

Compound (RES12) prepared from the reaction of R4 with 4-aminoantipyrine in existence DMSO, $SOCl_2$ and Triethylamine. Equation (3-8).



Equation (3.8): synthesis of RES12

The FT-IR spectrum of compound RES12 showed the following values (V_{max} cm^{-1}): 3385(N-H str. groups) , 1725.26 (C=O str.Ketones), 1699.34 (CO str. amide), 3550.63 (O-H phenol), 2877 (C-H str. Sp3), 1161 (C-O ether.) , 1491.02 (C=C, arom.) , 3010.67 (C-H str. arom.)(Figure 3-22). ^{1}H-NMR (500 MHz, δ ppm): 9.8(O-H , phenol) , 9.2 (N-H ,sec. amide), 3.9 (N-H ,sec. amine), 6.2-7.56 (C-H, aromatic), 4.4 (methylene),2.1 - 2.6 (methyl), 2.51(DMSO) (Figure 3-23).^{13}C- NMR (125 MHz,δ ppm): 15.8 - 26.7 (C,CH_3), 68.3(C,CH_2), 161.5-168.3 (N-C=O),120.4-170.3(C,arom.),103.9-134.4 (C,ethylene) , 196.4-198.9 (C-carbonyl) , 41.2 DMSO .(Figure 3-24).

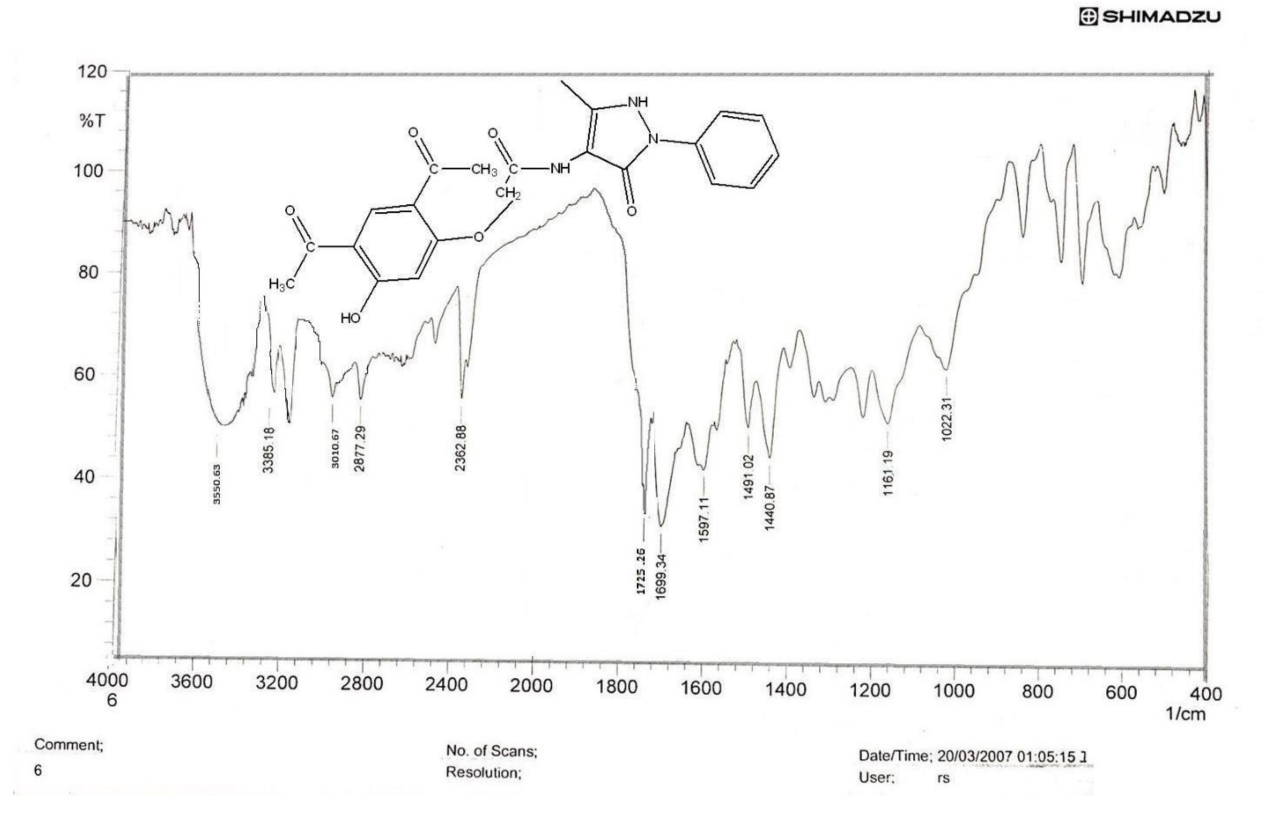


Figure (3-22) FTIR for compound RES12

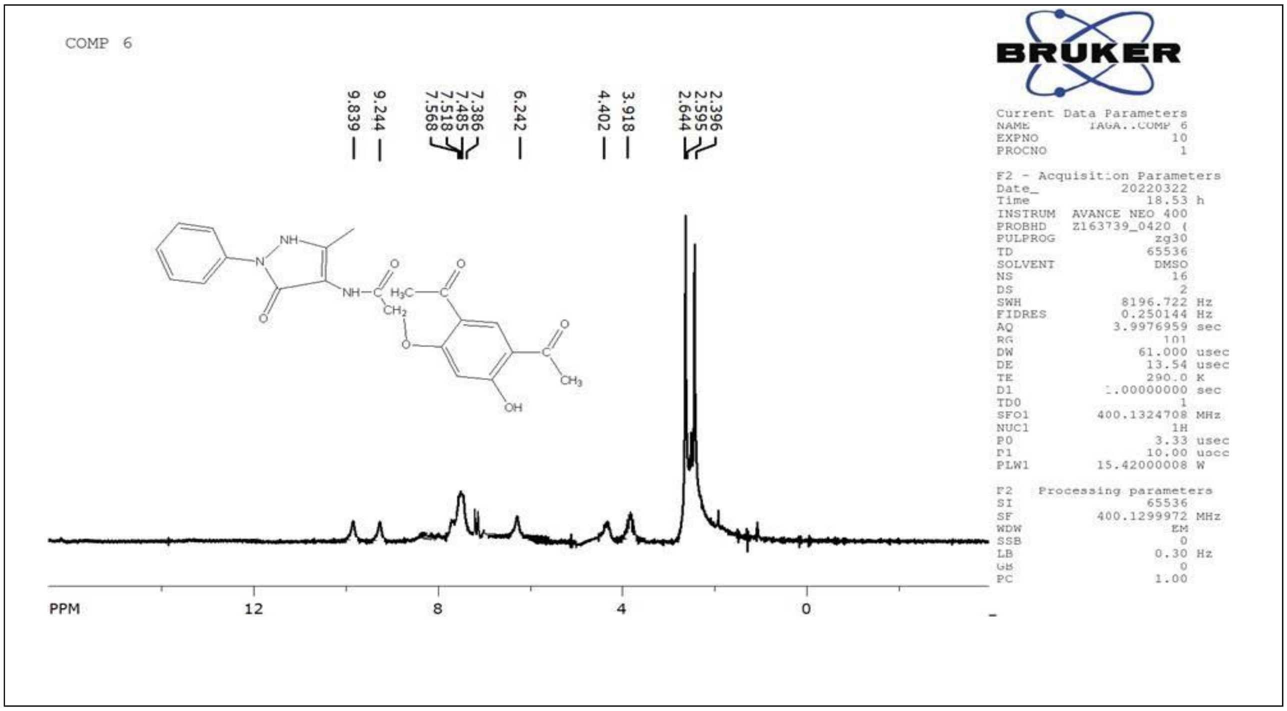
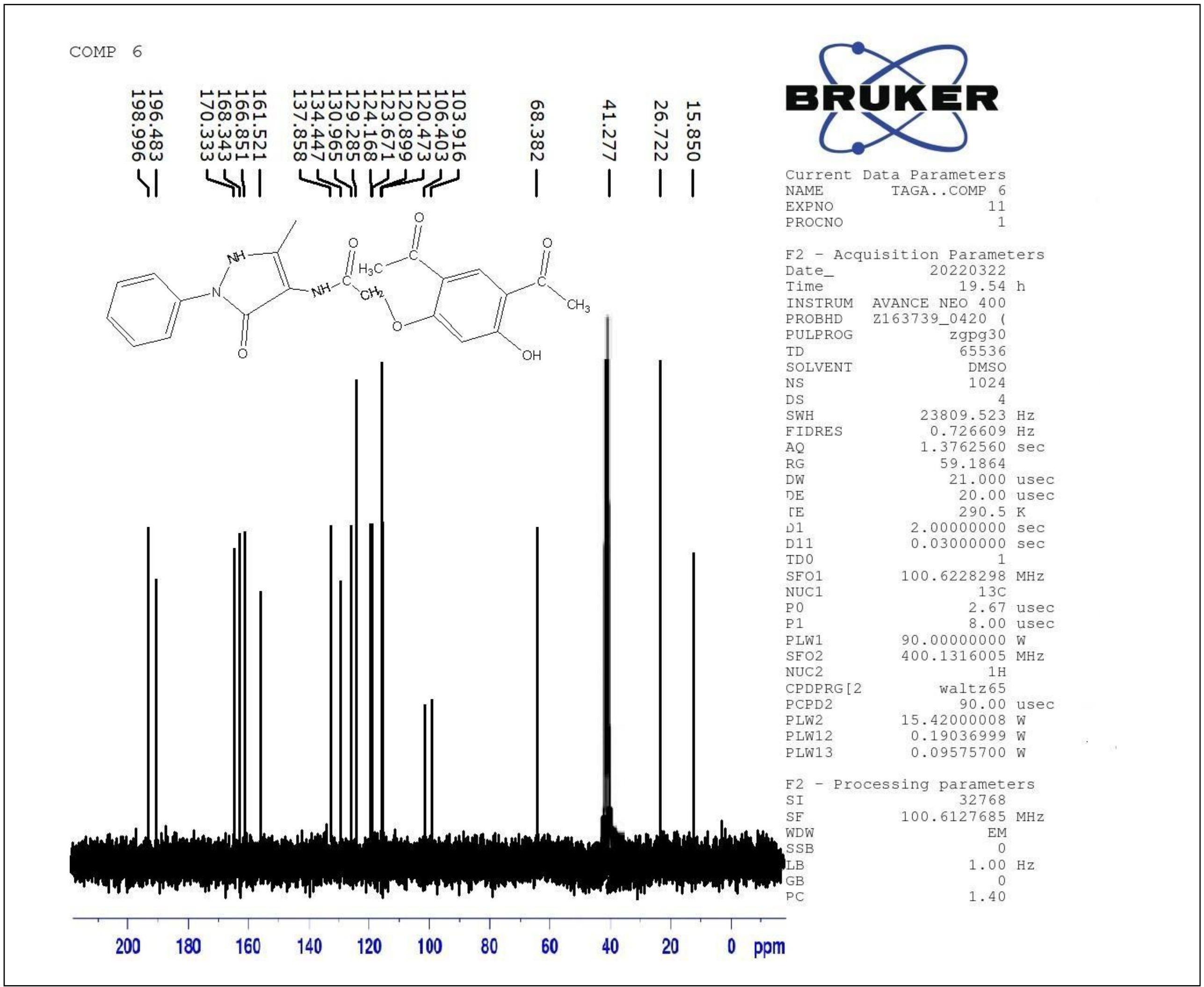


Figure (3-23) ^{1}HNMR for compound RES12



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Current Data Parameters
NAME          TAGA..COMP 6
EXPNO                   11
PROCNO                   1

F2 - Acquisition Parameters
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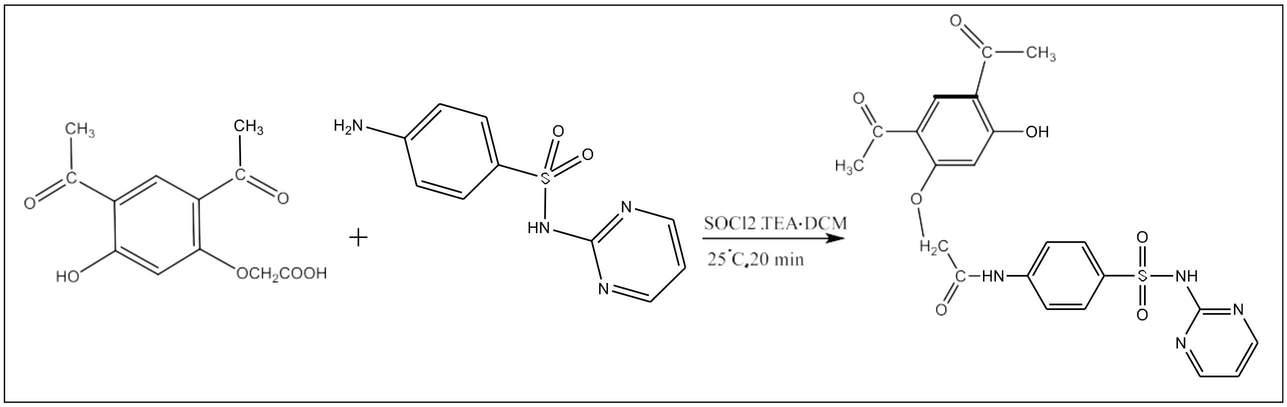
Time                 19.54 h
INSTRUM   AVANCE NEO 400
PROBHD    Z163739_0420 (
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                   1024
DS                      4
SWH             23809.523 Hz
FIDRES           0.726609 Hz
AQ              1.3762560 sec
RG                59.1864
DW                 21.000 usec
DE                  20.00 usec
TE                  290.5 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1
SFO1          100.6228298 MHz
NUC1                  13C
P0                   2.67 usec
P1                   8.00 usec
PLW1          90.00000000 W
SFO2          400.1316005 MHz
NUC2                   1H
CPDPRG[2          waltz65
PCPD2               90.00 usec
PLW2          15.42000008 W
PLW12          0.19036999 W
PLW13          0.09575700 W

F2 - Processing parameters
SI                  32768
SF            100.6127685 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

Figure (3-24) ^{13}CNMR for compound RES12

Compound (RES13) prepared from the reaction of R4 with sulfadiazine in existence DMSO, $SOCl_2$ and Triethylamine. Equation (3-9).



Equation (3-9): synthesis of RES13

FT-IR spectrum for RES13 showed the following values (Vmax cm-1): 3358.18 (N-H amide) ,1618(N-H bend),1720(C=O str.Ketones), 1640(CO str. amide), 3540.18 (O-H phenol), 3008 (C-H str. Sp2 aromatic), 1435.09 (C=C arom.), 1161(C-O-C str. ether)(Figure 3-25). ^{1}H-NMR (500 MHz, δ ppm): 9.9 (O-H , phenol) 10.5(N-H ,sec. amid), 11.5(Nsulfonamide), 7.5- 7.7 (C-H, aromatic), 4.5 (methylene),2.6 (methyl), 8.2 (CH pyrimidine) , 2.5 (DMSO) (Figure 3-26). ^{13}C-NMR (125 MH, δ ppm): 27.3 (C,CH_3), 64.6(C,CH_2), 116.5 -158.2 -168.2 (C=N pyrimidine) ,167 (N-C=O),120.2-142.4 (C=C arom.),196.2-198.4 (C, Carbonyl) , 104.8-130,2 (CH arom.) 39.1 DMSO. (Figure 3-27).

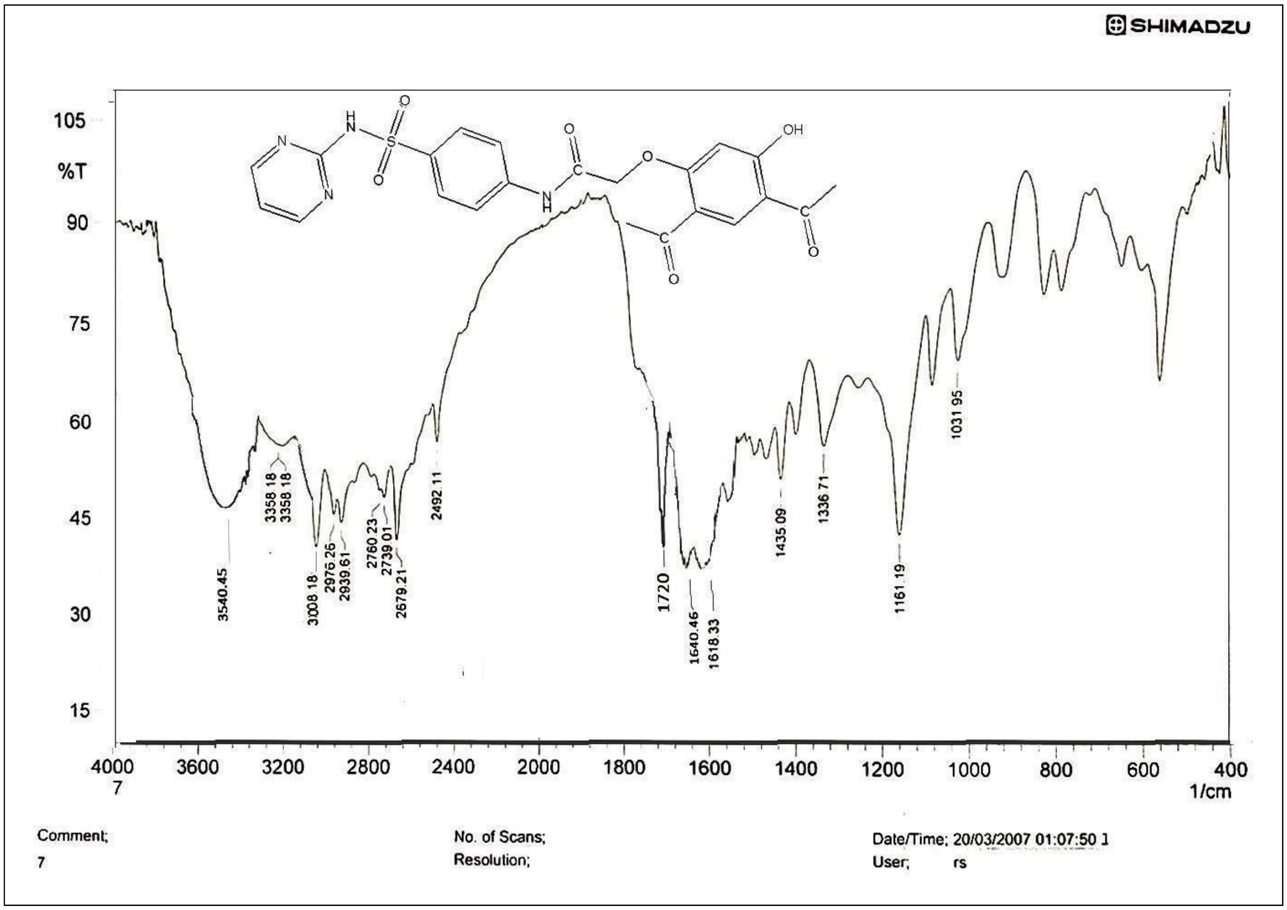
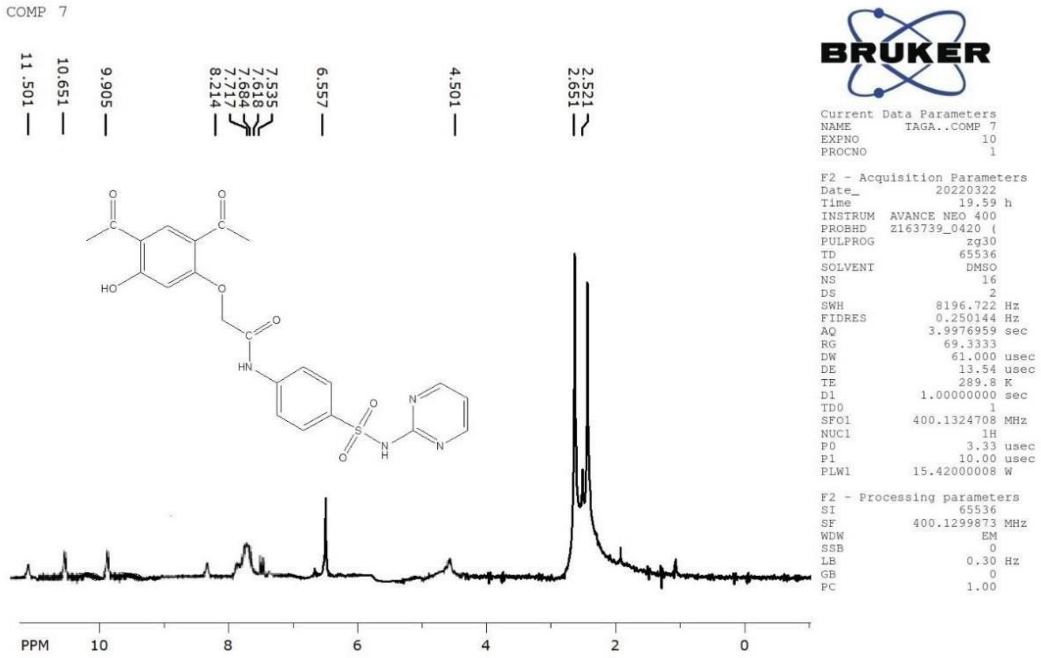


Figure (3-25) FTIR for compound RES13



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Current Data Parameters
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EXPNO                10
PROCNO                1

F2 - Acquisition Parameters
Date_          20220322
Time              19.59 h
INSTRUM  AVANCE NEO 400
PROBHD   Z163739_0420 (
PULPROG            zg30
TD                65536
SOLVENT            DMSO
NS                   16
DS                    2
SWH            8196.722 Hz
FIDRES         0.250144 Hz
AQ            3.9976959 sec
RG              69.3333
DW               61.000 usec
DE                13.54 usec
TE                289.8 K
D1           1.00000000 sec
TD0                   1
SFO1        400.1324708 MHz
NUC1                 1H
P0                 3.33 usec
P1                10.00 usec
PLW1        15.42000008 W

F2 - Processing parameters
SI                65536
SF          400.1299873 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```
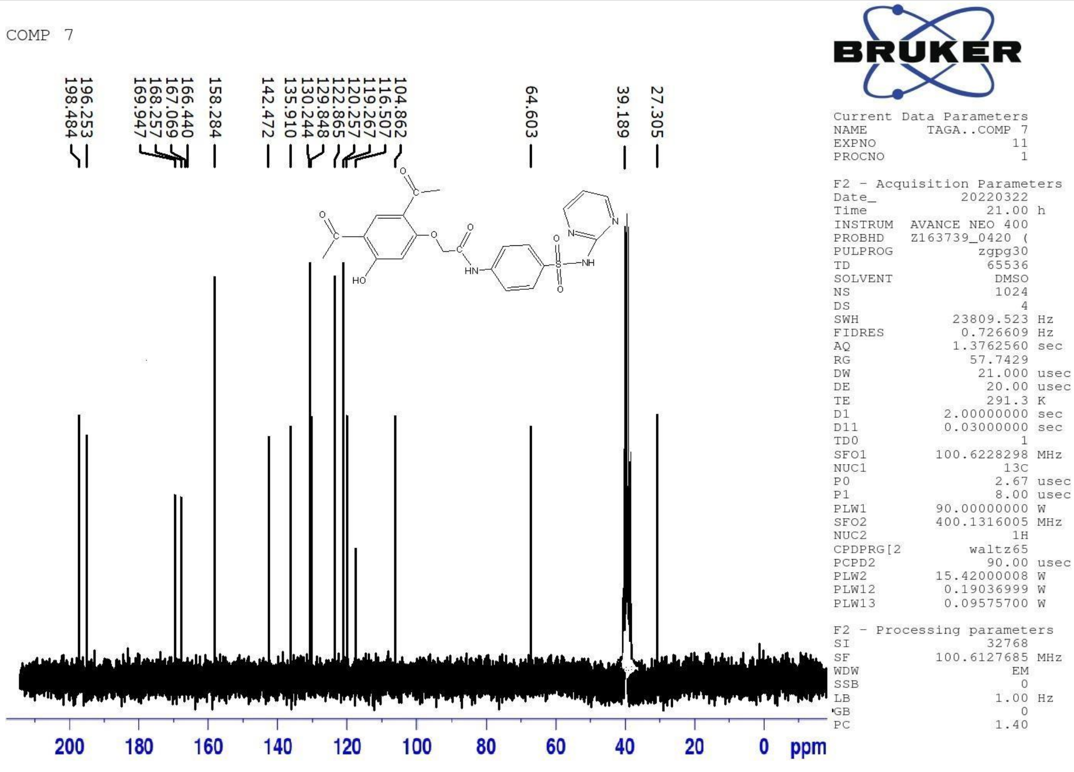

Figure (3-26) ^{1}HNMR for compound RES13



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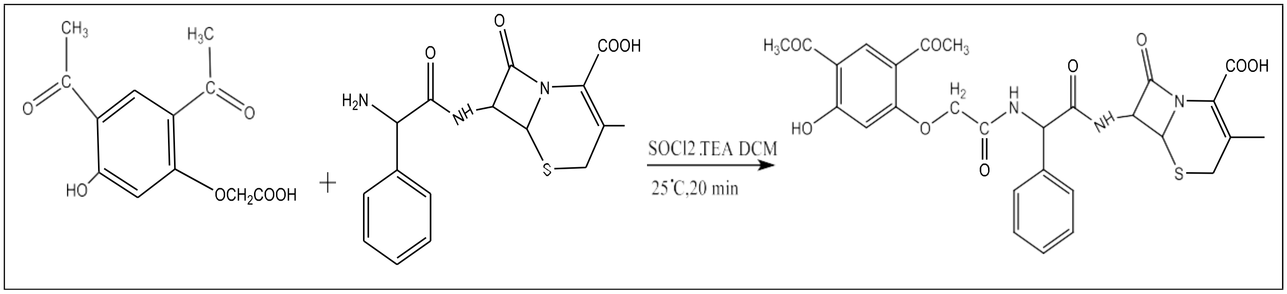
Current Data Parameters
NAME       TAGA..COMP 7
EXPNO                11
PROCNO                1

F2 - Acquisition Parameters
Date_          20220322
Time              21.00 h
INSTRUM  AVANCE NEO 400
PROBHD   Z163739_0420 (
PULPROG         zgpg30
TD                65536
SOLVENT            DMSO
NS                 1024
DS                    4
SWH           23809.523 Hz
FIDRES         0.726609 Hz
AQ            1.3762560 sec
RG              57.7429
DW               21.000 usec
DE                20.00 usec
TE                291.3 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        100.6228298 MHz
NUC1                13C
P0                 2.67 usec
P1                 8.00 usec
PLW1        90.00000000 W
SFO2        400.1316005 MHz
NUC2                 1H
CPDPRG[2        waltz65
PCPD2             90.00 usec
PLW2        15.42000008 W
PLW12        0.19036999 W
PLW13        0.09575700 W

F2 - Processing parameters
SI                32768
SF          100.6127685 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

Figure (3-27) ^{13}CNMR for compound RES13

Compound (RES14) prepared from the reaction of R4 with Cephalexin in existence DMSO , $SOCl_2$ and triethylamine. Equation (3-10).



Equation (3-10): synthesis of RES14

FT-IR spectrum for RES14 showed the following values (vmax cm^{-1}): 3301 (N-H amide) ,1715(C=O Ketone), 1670(C=O amide), 3553 (O-H phenol), 3005 (C-H str. Sp2 aromatic),1510 (C=C arom.) , 1707 (C=O carb.) , 2978.19 (OH carb) , 1217 (C-O ether)(Figure 3-28) . ^{1}H-NMR (500 MHz, δ ppm): 12.7 (OH carb.) 16.2(O-H , phenol) , 7.9-8.3 (N-H ,sec. amid), , 6.4- 7.3 (C-H, aromatic), 3.0-4.6(methylene),2.59-2.6 (methyl), 5.9 (CH,methine) ,5.4-5.1 (CH , propiolactam) 2.5 (DMSO) (Figure 3-29). ^{13}C- NMR (125 MH, δ ppm): 19.8-26.6 (C,CH_3), 30.7-66.7 (C,CH_2), 164.6-168.3-171.7 (N-C=O), 119.7-169.3 (C,arom.), 161.3(C, Carboxyl), 197.4 -202.1 (C,Carbonyl) , 62.2-60.2 (CH alipha.)39.9 DMSO , (Figure 3-30).

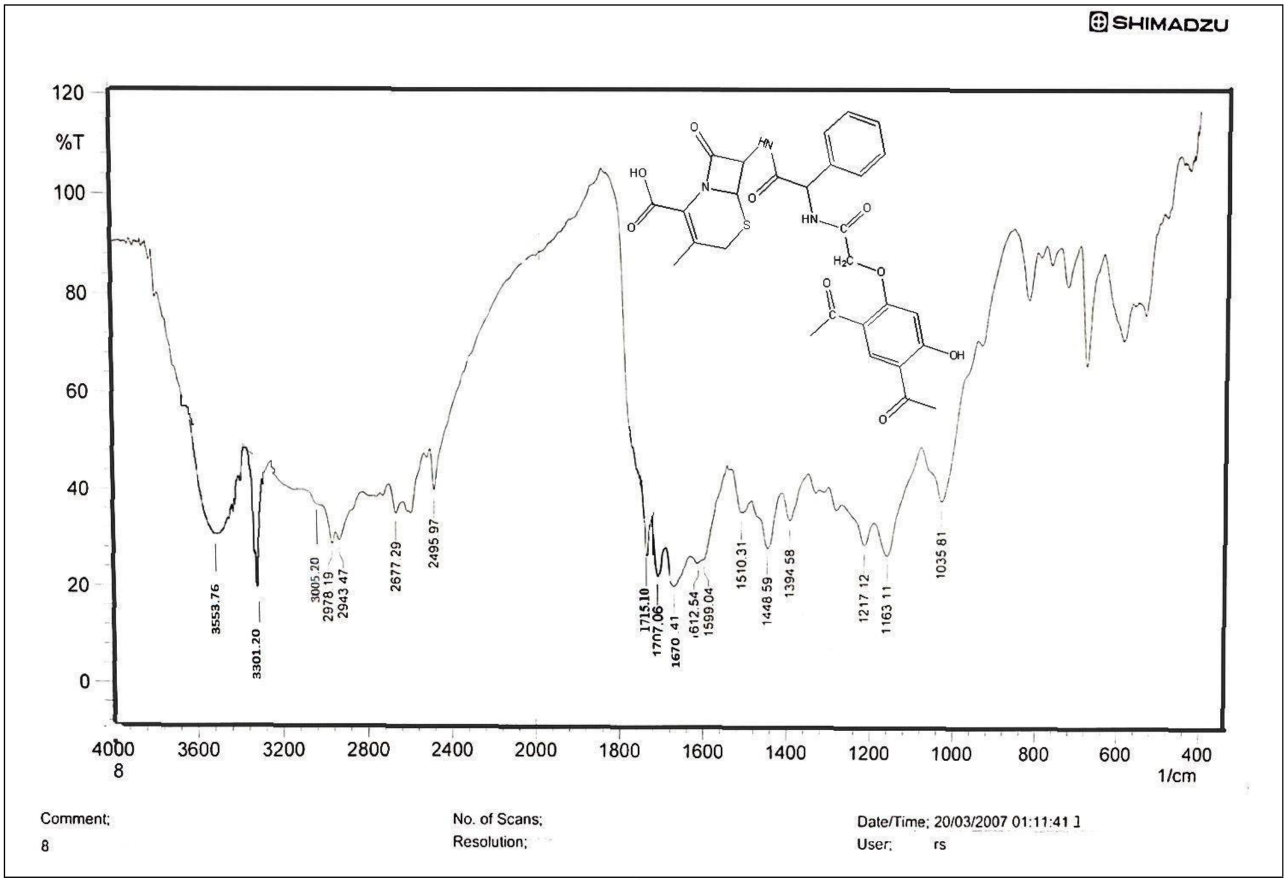
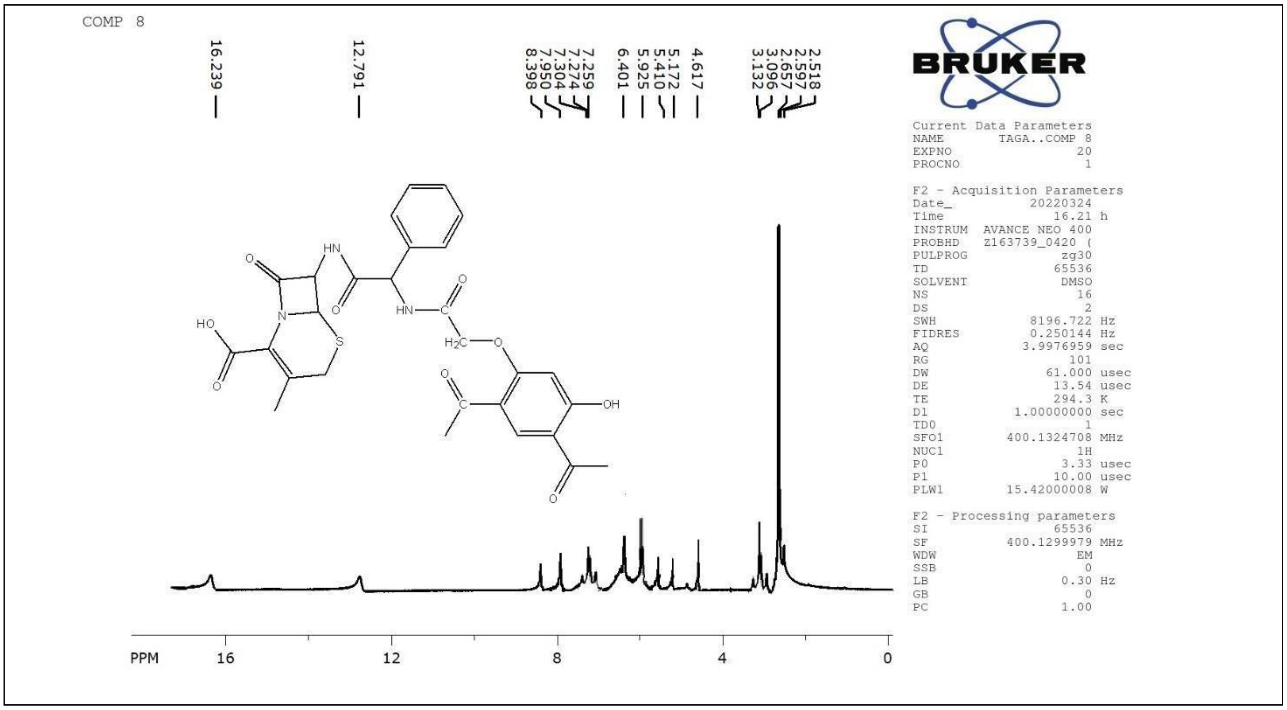


Figure (3-28) FTIR for compound RES14



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Current Data Parameters
NAME          TAGA..COMP 8
EXPNO                   20
PROCNO                   1

F2 - Acquisition Parameters
Date_             20220324
Time                 16.21 h
INSTRUM   AVANCE NEO 400
PROBHD    Z163739_0420 (
PULPROG               zg30
TD                   65536
SOLVENT               DMSO
NS                      16
DS                       2
SWH               8196.722 Hz
FIDRES            0.250144 Hz
AQ               3.9976959 sec
RG                     101
DW                  61.000 usec
DE                   13.54 usec
TE                   294.3 K
D1              1.00000000 sec
TD0                      1
SFO1           400.1324708 MHz
NUC1                    1H
P0                    3.33 usec
P1                   10.00 usec
PLW1           15.42000008 W

F2 - Processing parameters
SI                   65536
SF             400.1299979 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```
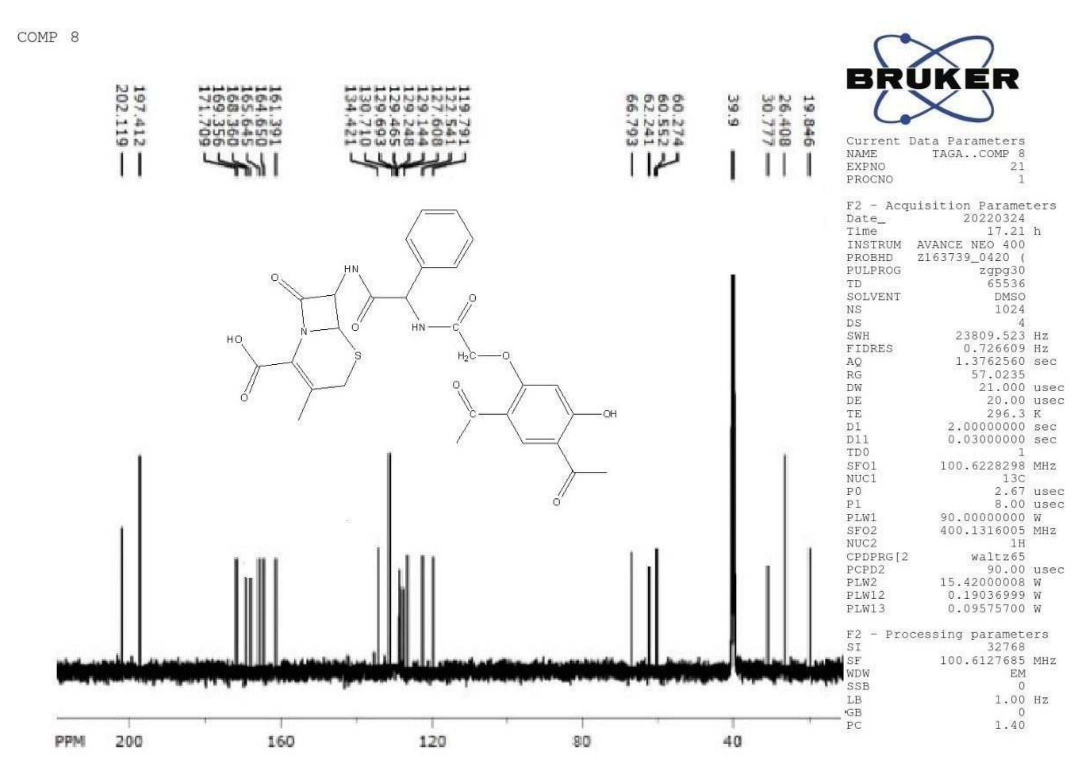

Figure (3-29) ^{1}HNMR for compound RES14



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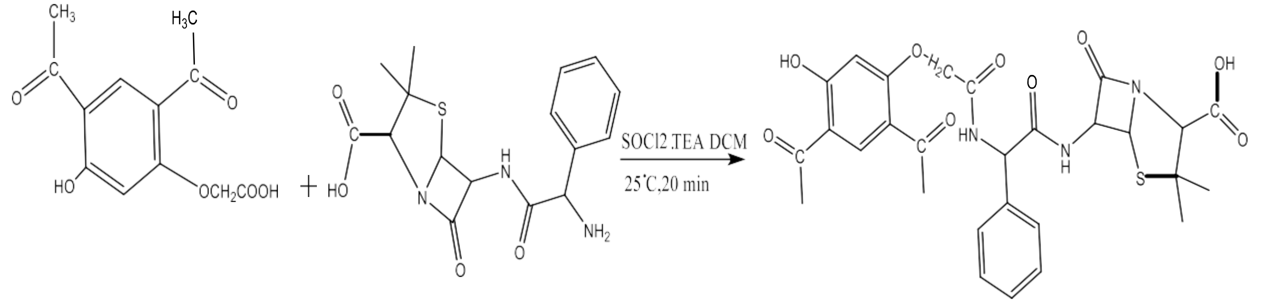
Current Data Parameters
NAME         TAGA..COMP 8
EXPNO                  21
PROCNO                  1

F2 - Acquisition Parameters
Date_            20220324
Time                17.21 h
INSTRUM  AVANCE NEO 400
PROBHD   Z163739_0420 (
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                   1024
DS                      4
SWH             23809.523 Hz
FIDRES           0.726609 Hz
AQ              1.3762560 sec
RG                57.0235
DW                 21.000 usec
DE                  20.00 usec
TE                  296.3 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1
SFO1          100.6228298 MHz
NUC1                  13C
P0                   2.67 usec
P1                   8.00 usec
PLW1          90.00000000 W
SFO2          400.1316005 MHz
NUC2                   1H
CPDPRG[2          waltz65
PCPD2               90.00 usec
PLW2          15.42000008 W
PLW12          0.19036999 W
PLW13          0.09575700 W

F2 - Processing parameters
SI                  32768
SF            100.6127685 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

Figure (3-30) ^{13}CNMR for compound RES14

Compound (RES15) prepared from the reaction of R4 with ampicillin in existence DMSO , $SOCl_2$ and triethylamine. Equation (3-11).



Equation (3-11): synthesis of RES15

FT-IR spectrum for RES15 showed the following values (Vmax cm-1): 3180 (N-H amide) ,1705(C=O Ketone), 1680(C=O amide), 3620 (O-H phenol), 3002 (C-H str. Sp2 aromatic),1471 (C=C arom.) , 1734 (C=O carb.) , 2976(OH carb) , 1396 (C-O ether)(Figure 3-31) . ^{1}H-NMR (500 MHz, δ ppm): 11.3 (OH carb.) 10.2(O-H , phenol) , 8.3-8.4 (N-H ,sec. amid), , 6.8- 7.6 (C-H, aromatic), 4.8(methylene),2.1-2.7 (methyl), 5.9 (CH,methine) , 2.5 (DMSO) (Figure 3-32). ^{13}C-NMR (125 MHz, δ ppm): 26.2-27.8 (C,CH_3), 66.1 (C,CH_2), 170.1-172.2-175.2 (N-C=O), 123.1-169.2 (C,arom.),106.3-130.8(CH arom.) 169.7(C, Carboxyl), 198.8 - 196.2 (C,Carbonyl) , 60.2 (CH alipha.)39.1 DMSO , (Figure 3-33).

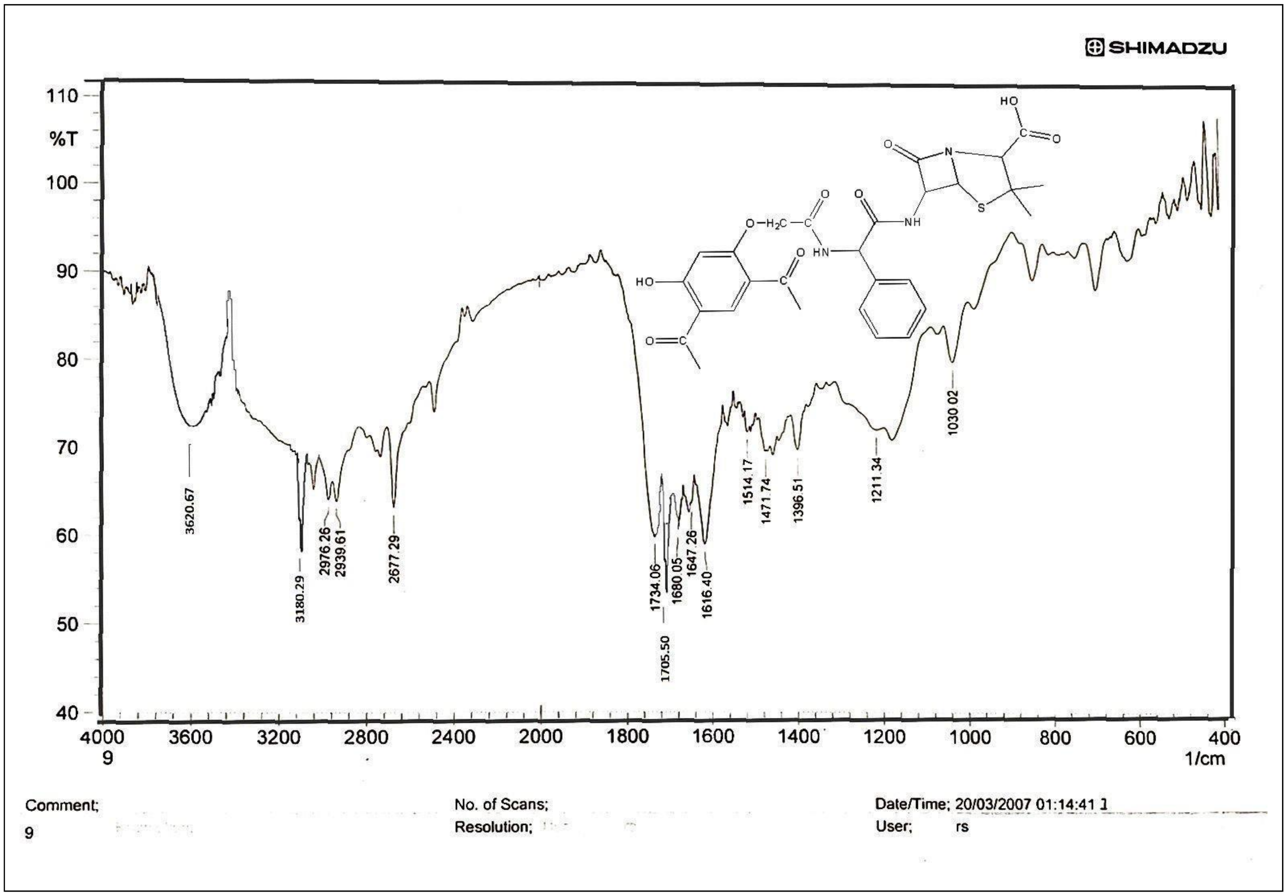
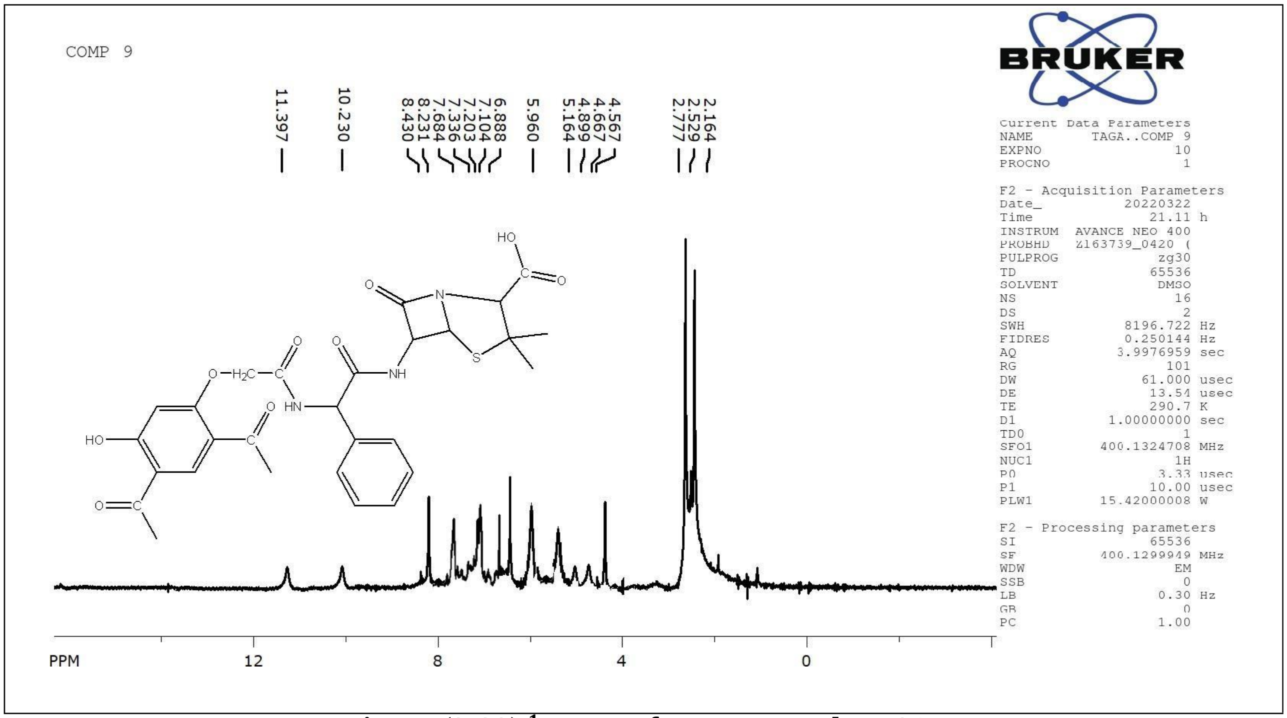


Figure (3-31) FTIR for compound RES15



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Current Data Parameters
NAME        TAGA..COMP 9
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220322
Time               21.11 h
INSTRUM  AVANCE NEO 400
PROBHD   Z163739_0420 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH             8196.722 Hz
FIDRES          0.250144 Hz
AQ             3.9976959 sec
RG                   101
DW                61.000 usec
DE                 13.54 usec
TE                 290.7 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  3.33 usec
P1                 10.00 usec
PLW1         15.42000008 W

F2 - Processing parameters
SI                 65536
SF           400.1299949 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```
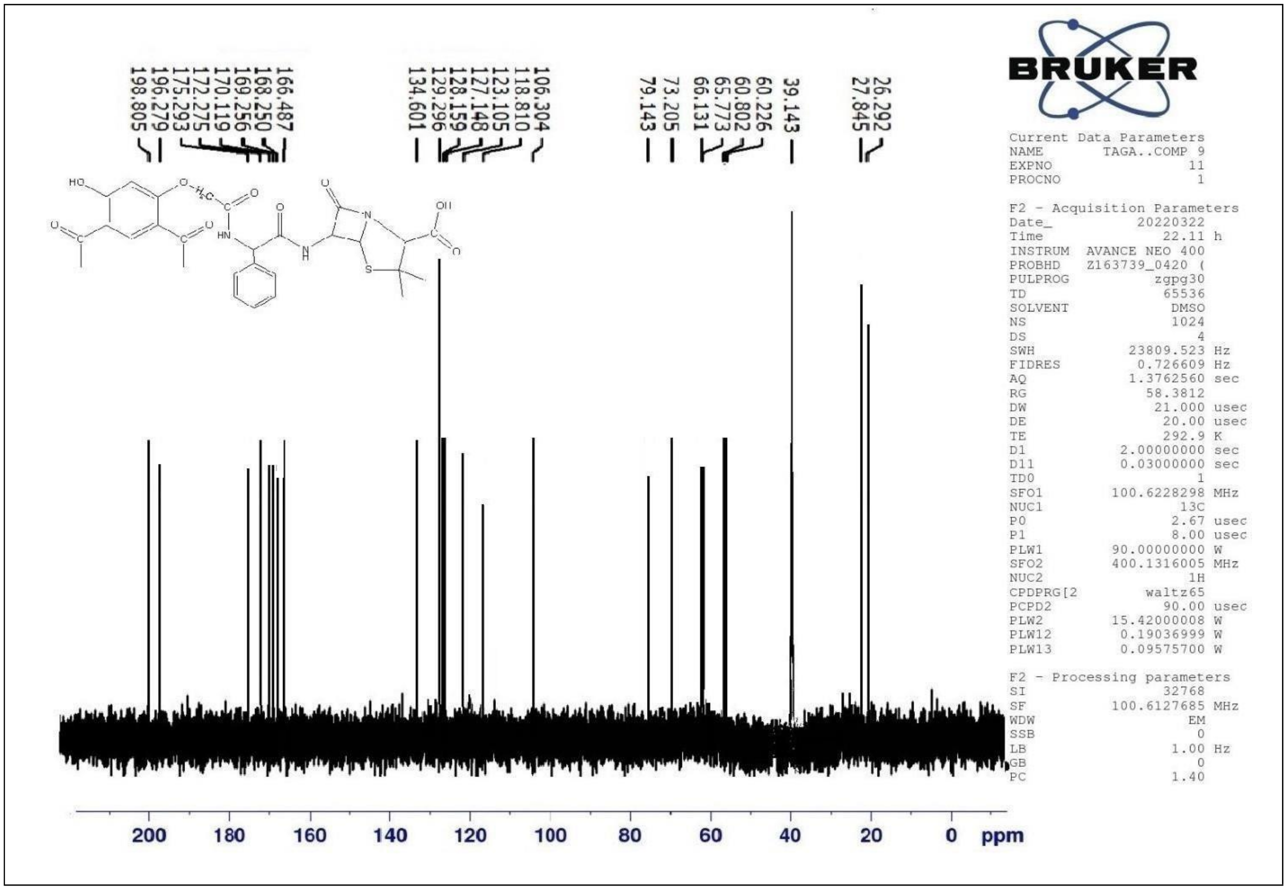

Figure (3-32) ^{1}HNMR for compound RES15



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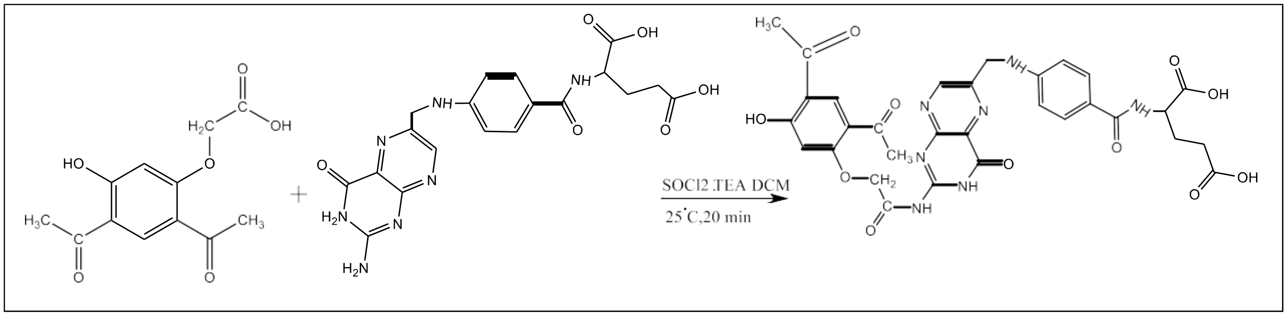
Current Data Parameters
NAME        TAGA..COMP 9
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20220322
Time               22.11 h
INSTRUM  AVANCE NEO 400
PROBHD   Z163739_0420 (
PULPROG           zgpg30
TD                 65536
SOLVENT             DMSO
NS                  1024
DS                     4
SWH            23809.523 Hz
FIDRES          0.726609 Hz
AQ             1.3762560 sec
RG               58.3812
DW                21.000 usec
DE                 20.00 usec
TE                 292.9 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1
SFO1         100.6228298 MHz
NUC1                 13C
P0                  2.67 usec
P1                  8.00 usec
PLW1         90.00000000 W
SFO2         400.1316005 MHz
NUC2                  1H
CPDPRG[2         waltz65
PCPD2              90.00 usec
PLW2         15.42000008 W
PLW12         0.19036999 W
PLW13         0.09575700 W

F2 - Processing parameters
SI                 32768
SF           100.6127685 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

Figure (3-33) ^{13}CNMR for compound RES15

Compound (RES16) prepared from the reaction of R4 with folic acid in existence DMSO , $SOCl_2$ and triethylamine. Equation (3-12).



Equation (3-12): synthesis of RES16

FT-IR spectrum for RES16 showed the following values (Vmax cm-1): 1705(C=O Ketone), 1654 (C=O amide) , 3643 (O-H phenol), 3020 (C-H str. Sp2 aromatic),1600 (C=C arom.) , 1770 (C=O carb.) 2978 (OH carb.), 1176 (C-O ether) (Figure 3-34) . ^{1}H-NMR (500 MHz, δ ppm): 11.8 (OH carb.) 9.8(O-H , phenol) , 6.4-8.6 (N-H ,sec. amid), 10.2 (NH guanidine) , 6.5- 7.5 (C-H, aromatic), 2.1`-4.4 (methylene),2.6 (methyl) , 2.5 (DMSO) (Figure 3-35). ^{13}C- NMR (125 MHz, δ ppm): 27.3 (C,CH_3),57.2 (C,CH alipha.),28-68.6 (C,CH_2 alipha.), 157.8-171.6 (N-C=O), 118.8-154.1(C,arom.), 173.1-176.2(C, Carboxyl), 108-132.4(CH.arom.) , 196.6-198.8 (C,Carbonyl) , 39.1 DMSO ,(Figure 3-36).

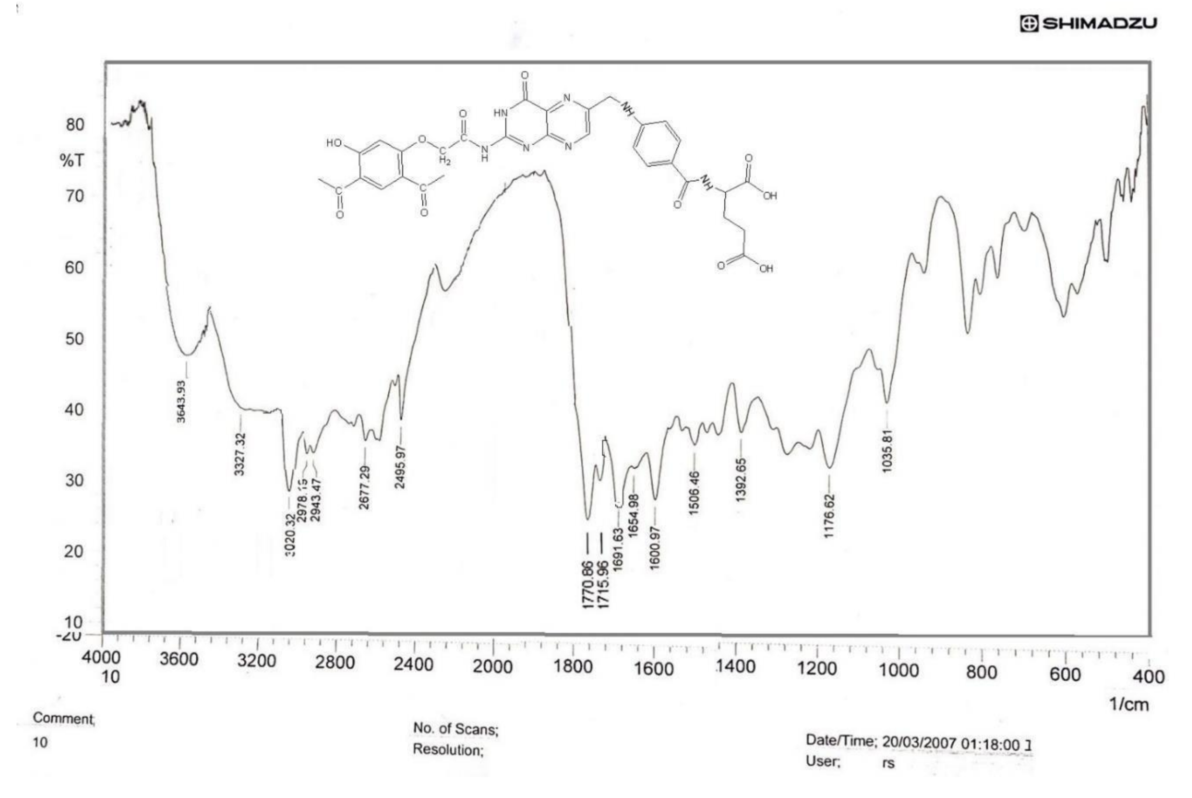
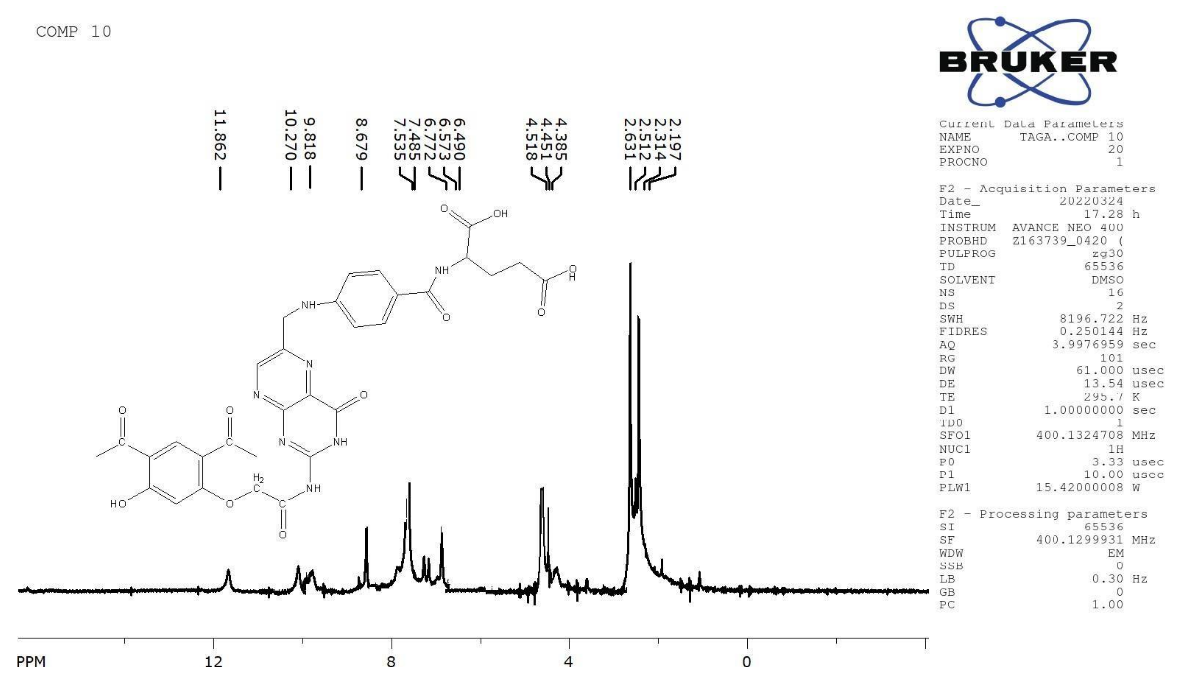


Figure (3-34) FTIR for compound RES16



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EXPNO                 20
PROCNO                 1

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PROBHD    Z163739_0420 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH             8196.722 Hz
FIDRES          0.250144 Hz
AQ             3.9976959 sec
RG                   101
DW                61.000 usec
DE                 13.54 usec
TE                 295.7 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  3.33 usec
P1                 10.00 usec
PLW1         15.42000008 W

F2 - Processing parameters
SI                 65536
SF           400.1299931 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

Figure (3-35) ^{1}HNMR for compound RES16

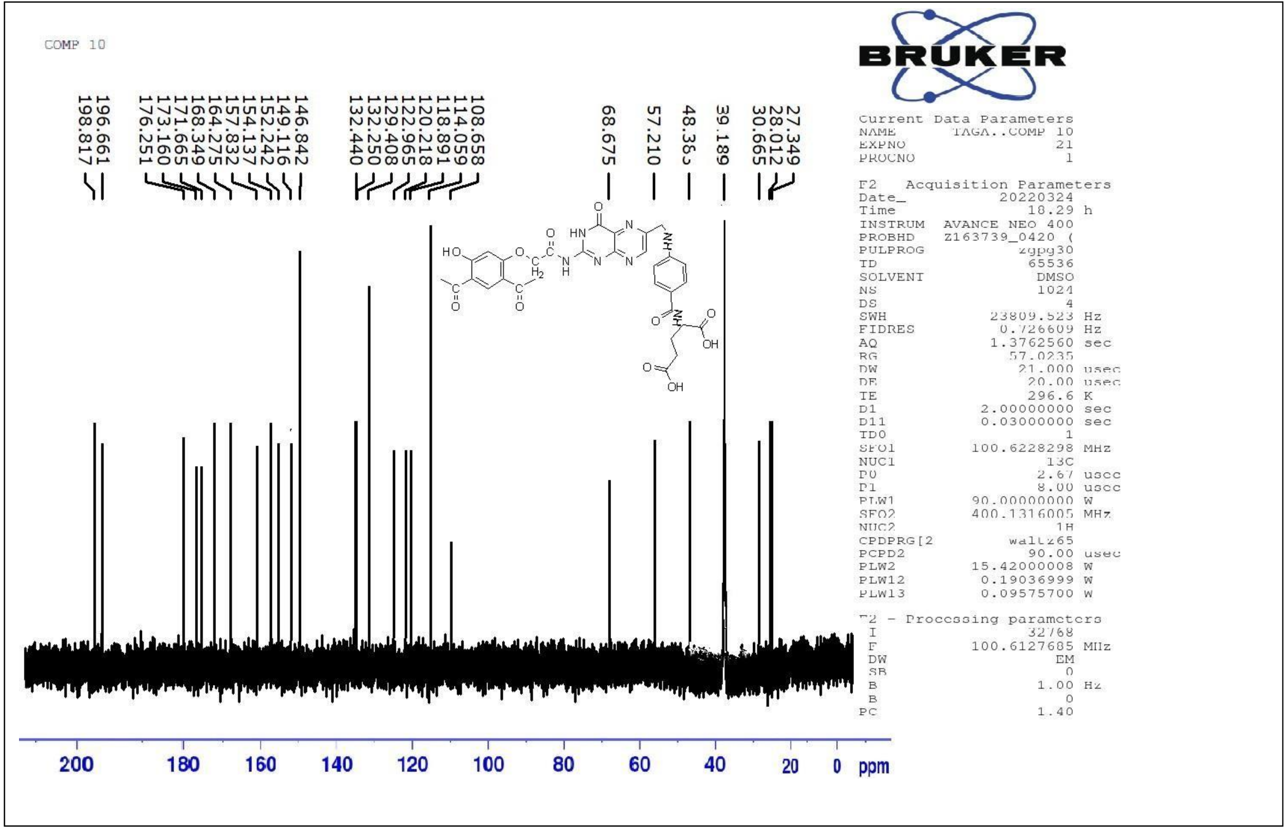
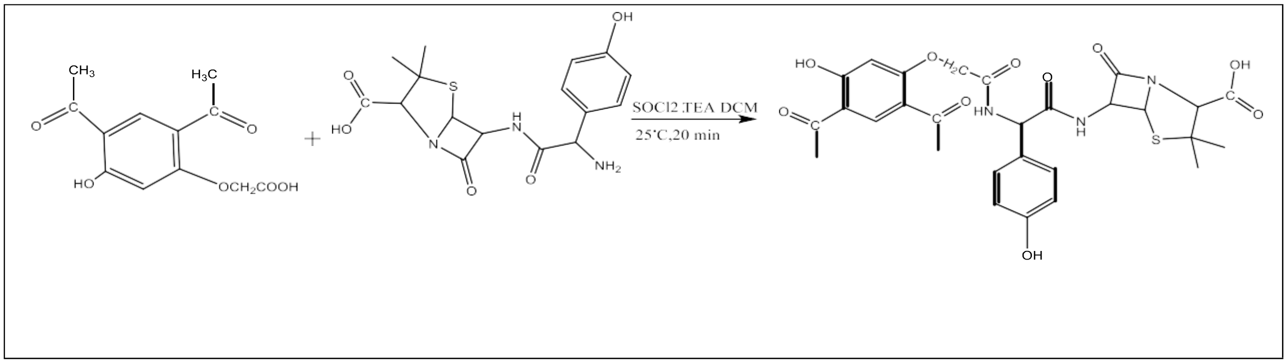


Figure (3-36) ^{13}CNMR for compound RES16

Compound (RES17) prepared from the reaction of R4 with amoxicillin in existence DMSO, $SOCl_2$ and Triethylamine. Equation (3-13).



Equation (3-13): synthesis of RES17

FT-IR spectrum for RES17 showed the following values (Vmax cm-1): 3180 (N-H amide) ,1705(C=O Ketone), 1680(C=O amide), 3677 (O-H phenol),1465(C=C arom.) , 1740 (C=O carb.) , 2787(OH carb) , (Figure 3-37) . ^{1}H-NMR (500 MHz,δ ppm): 11.4 (OH carb.) 9.8-16.2(O-H , phenol) , 8.5-8.4 (N-H ,sec. amid) ,6.9- 7.5 (C-H, aromatic), 4.9 (methylene), 2.2-2.6 (methyl), 5.7 (CH,methine) , 2.5 (DMSO) (Figure 3-38). ^{13}C- NMR (125 MH, δ ppm): 27.3-29.8 (C,CH_3), 64.6 (C,CH_2), 172-176.2 (N-C=O), 122.2-169.9(C,arom.),108-130.2(CH arom.) 168(C, Carboxyl), 198.8 -196.8 (C,Carbonyl) , 60.2 (CH alipha.)39.1 DMSO , (Figure 3-39).

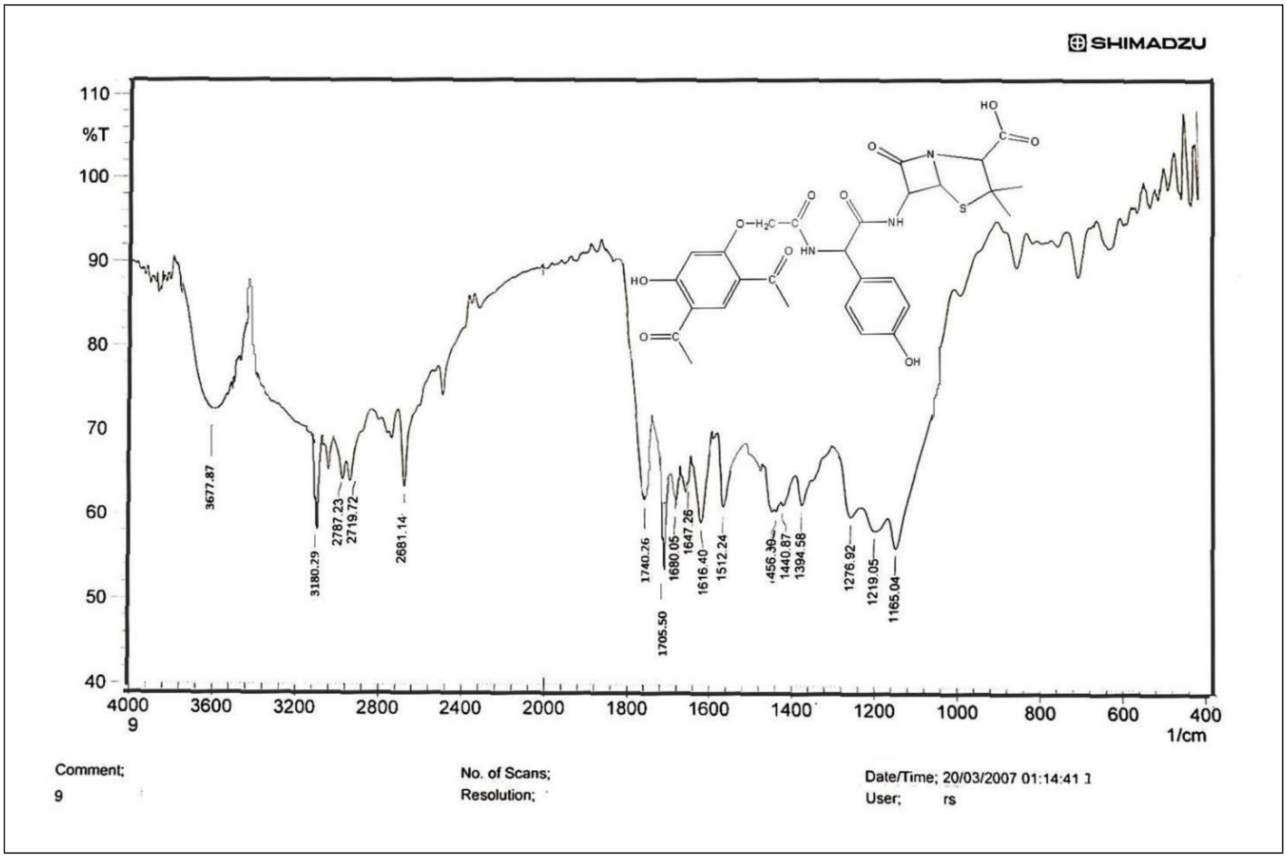
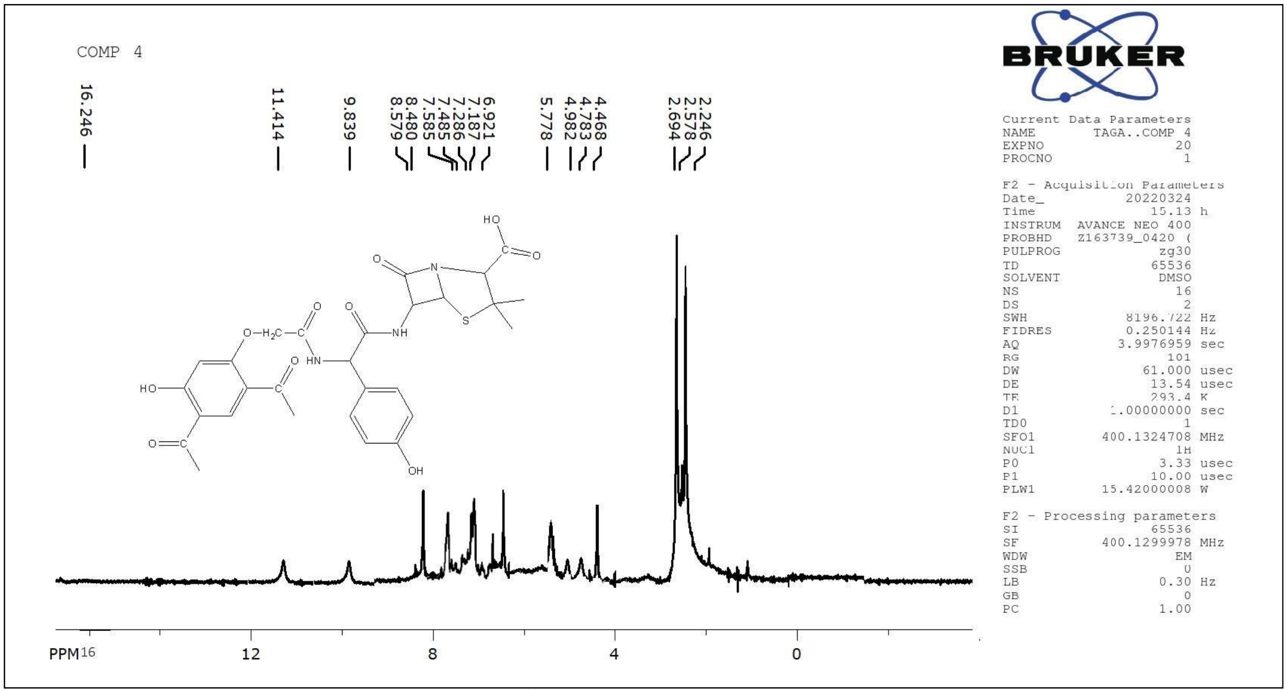


Figure (3-37) FTIR for compound RES17



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PROCNO                 1

F2 - Acquisition Parameters
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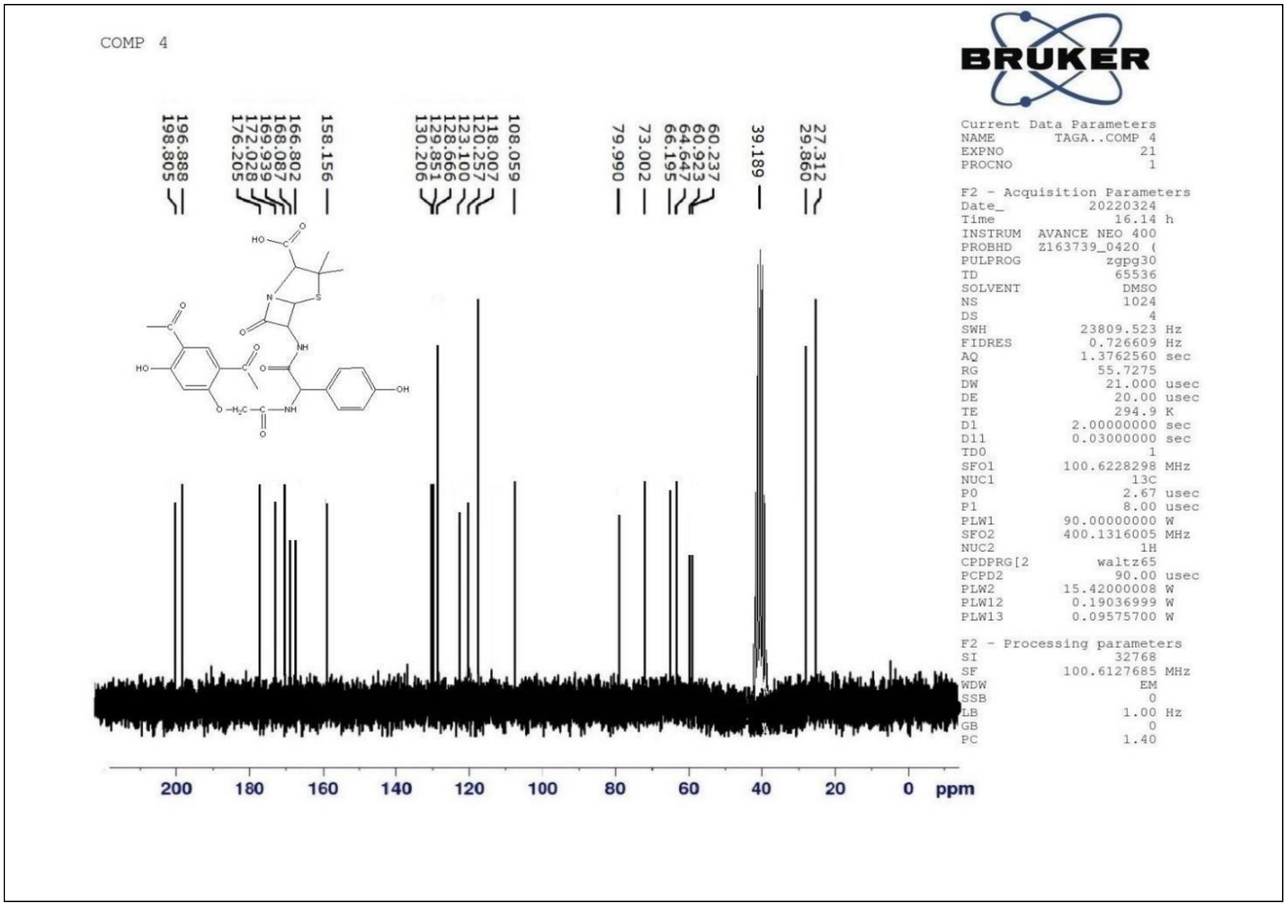
PROBHD    Z163739_0420 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH             8196.722 Hz
FIDRES          0.250144 Hz
AQ             3.9976959 sec
RG                   101
DW                61.000 usec
DE                 13.54 usec
TE                 293.4 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                  3.33 usec
P1                 10.00 usec
PLW1         15.42000008 W

F2 - Processing parameters
SI                 65536
SF           400.1299978 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

Figure (3-38) ^{1}HNMR for compound RES17



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Current Data Parameters
NAME        TAGA..COMP 4
EXPNO                 21
PROCNO                 1

F2 - Acquisition Parameters
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Time               16.14 h
INSTRUM   AVANCE NEO 400
PROBHD    Z163739_0420 (
PULPROG           zgpg30
TD                 65536
SOLVENT             DMSO
NS                  1024
DS                     4
SWH            23809.523 Hz
FIDRES          0.726609 Hz
AQ             1.3762560 sec
RG               55.7275
DW                21.000 usec
DE                 20.00 usec
TE                 294.9 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1
SFO1         100.6228298 MHz
NUC1                 13C
P0                  2.67 usec
P1                  8.00 usec
PLW1         90.00000000 W
SFO2         400.1316005 MHz
NUC2                  1H
CPDPRG[2         waltz65
PCPD2              90.00 usec
PLW2         15.42000008 W
PLW12         0.19036999 W
PLW13         0.09575700 W

F2 - Processing parameters
SI                 32768
SF           100.6127685 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```
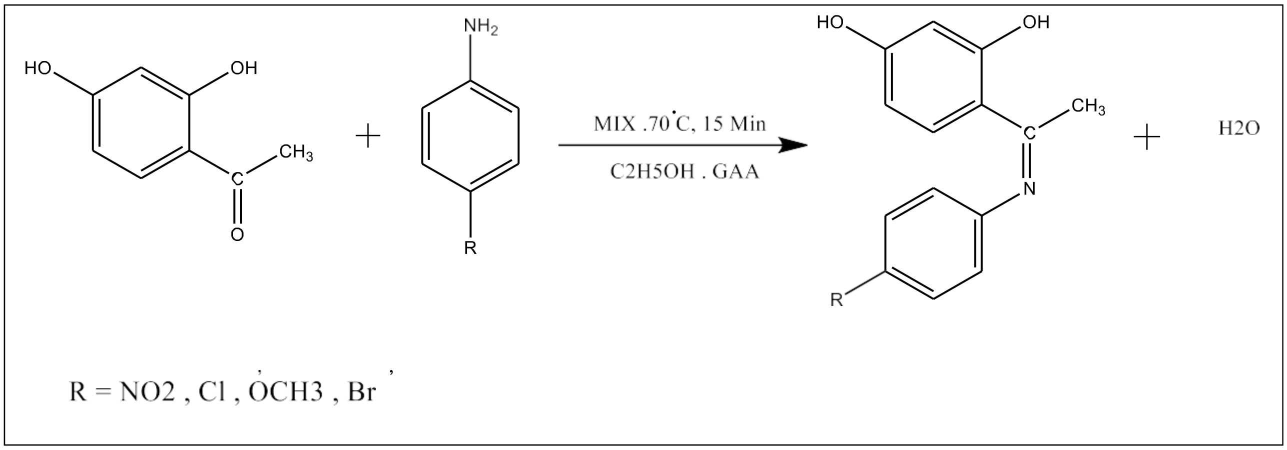
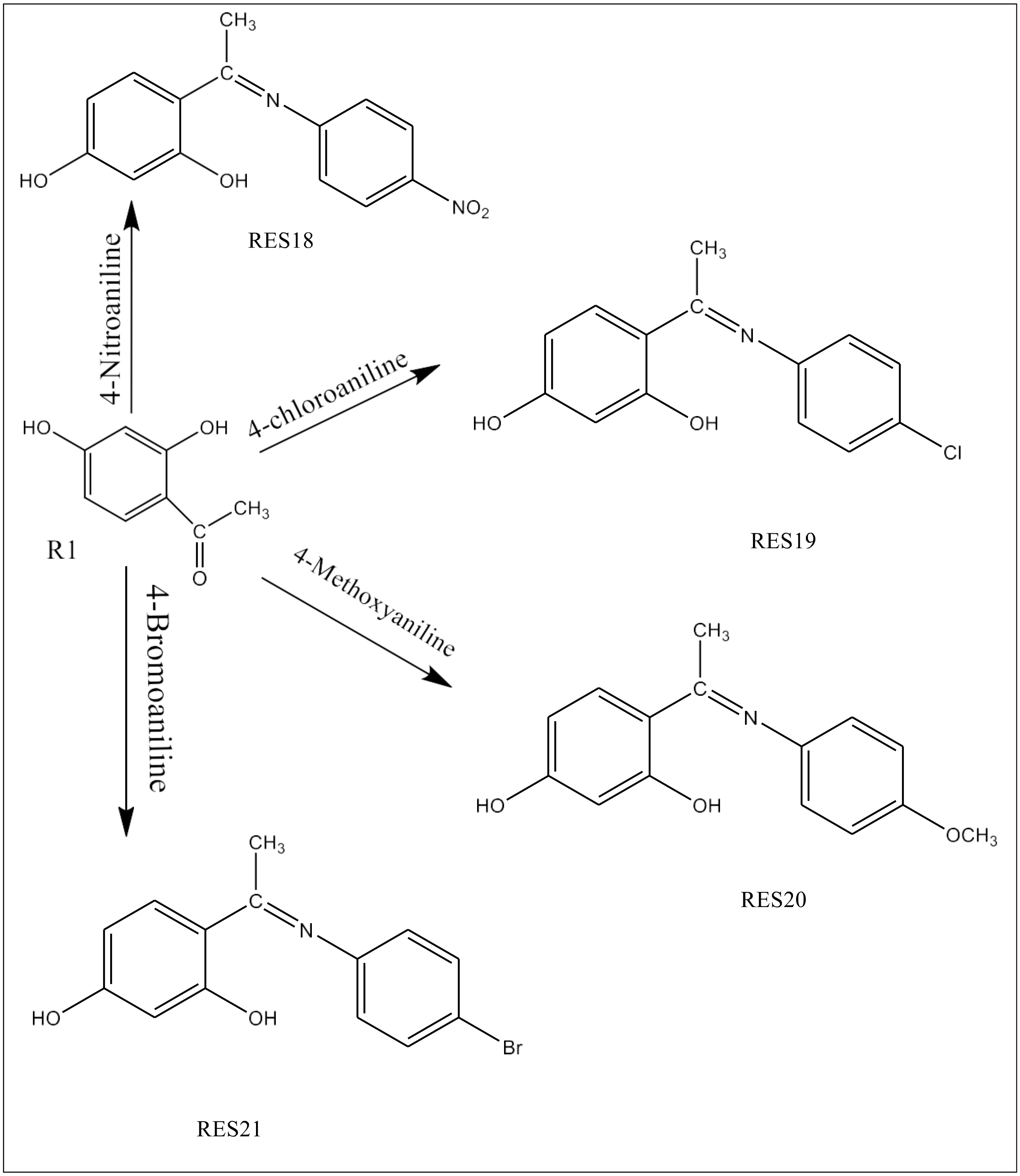

Figure (3-39) ^{13}CNMR for compound RES17

3-3. Third Path Synthesis of Compounds RES18-RES21 (Schiff bases)

These compounds were synthesized from the reaction 2,4-dihydroxyacetophenone (R1) with different four aniline derivatives.

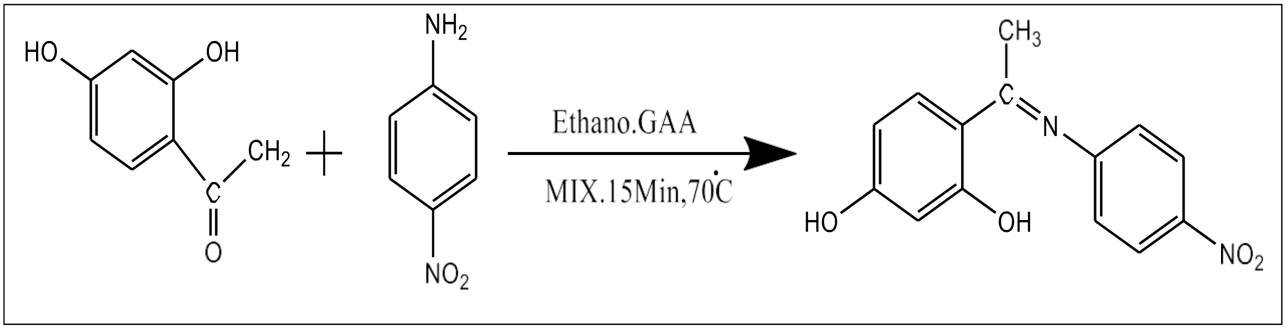


Scheme (3-5): General scheme of Synthesis of compounds (RES18-RES 21) .



Scheme (3-6): Synthesis of Schiff bsses RES18 – RES21

Schiff base (RES18) prepared from the reaction of R1 with 4-Nitroaniline in existence ethanol , and Glacial acetic acid. Equation (3-14).



Equation (3-14): synthesis of RES18

FT-IR spectrum for RES18 showed the following values (vmax cm^{-1}): 1635.69(C=N imine), 3360-3479 (O-H phenol),1475(C=C arom.) , 3080 (CH arom.) , 2800 (CH SP3) , 1300.07 (NO_2 arom.)(Figure 3-40) . ^{1}H-NMR (500 MHz,δ ppm): 9.5-10.1(O-H , plenol) , 6.8 - 8.1 (C-H, aromatic), 2.2 (methyl), 6.3-7.5 (CH benzylidenimin), 2.5 (DMSO) (Figure 3-41). ^{13}C- NMR (125 MHz, δ ppm): 18.2 (C,CH_3), 165.3 (C-N imine) , 104.3-130.2(CH arom.) , 112.2 -162.8 (C arom.) , 39.9 DMSO , (Figure 3-42).

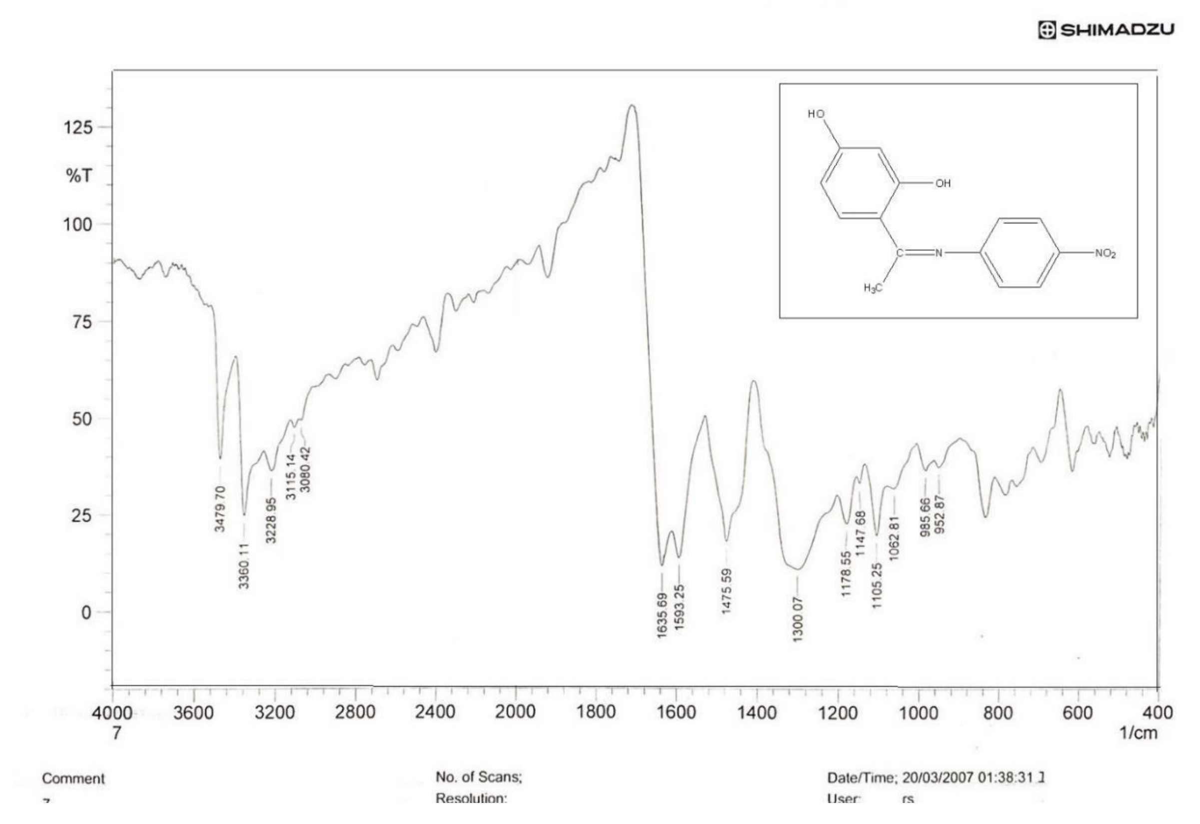
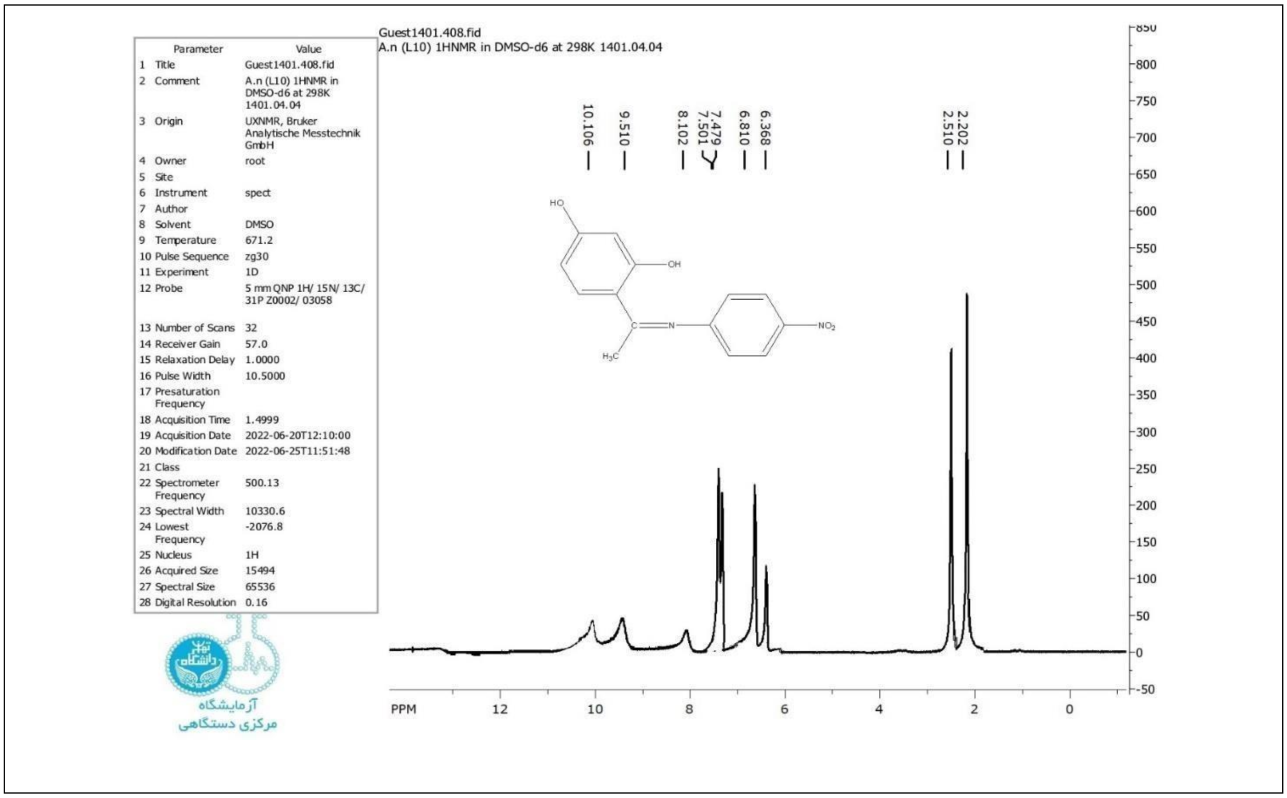


Figure (3-40) FTIR for compound RES18



	Parameter	Value
1	Title	Guest1401.408.fid
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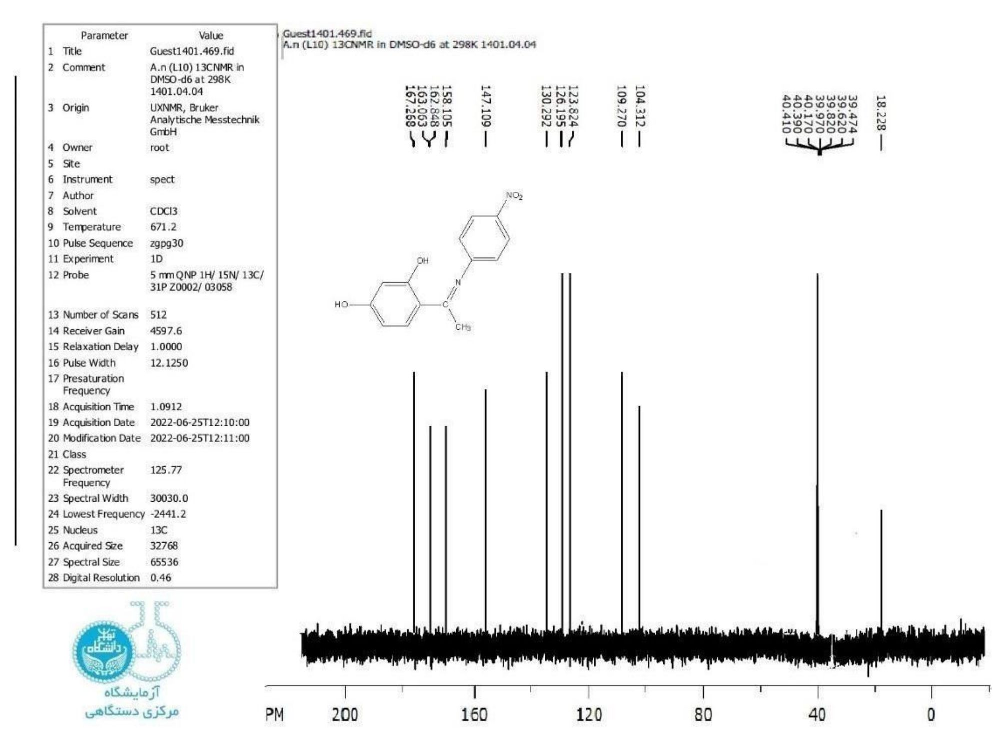
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	671.2
10	Pulse Sequence	zg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	32
14	Receiver Gain	57.0
15	Relaxation Delay	1.0000
16	Pulse Width	10.5000
17	Presaturation Frequency	
18	Acquisition Time	1.4999
19	Acquisition Date	2022-06-20T12:10:00
20	Modification Date	2022-06-25T11:51:48
21	Class	
22	Spectrometer Frequency	500.13
23	Spectral Width	10330.6
24	Lowest Frequency	-2076.8
25	Nucleus	1H
26	Acquired Size	15494
27	Spectral Size	65536
28	Digital Resolution	0.16

Figure (3-41) ^{1}HNMR for compound RES18

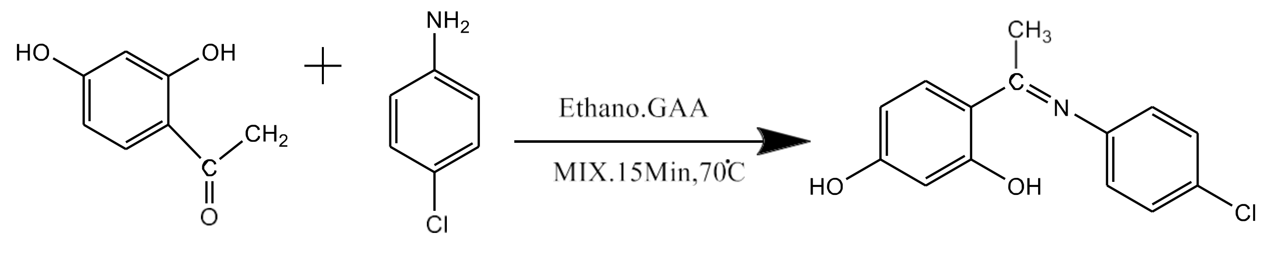


	Parameter	Value
1	Title	Guest1401.469.fid
2	Comment	A.n (L10) 13CNMR in DMSO-d6 at 298K 1401.04.04
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	CDCl3
9	Temperature	671.2
10	Pulse Sequence	zgpg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	512
14	Receiver Gain	4597.6
15	Relaxation Delay	1.0000
16	Pulse Width	12.1250
17	Presaturation Frequency	
18	Acquisition Time	1.0912
19	Acquisition Date	2022-06-25T12:10:00
20	Modification Date	2022-06-25T12:11:00
21	Class	
22	Spectrometer Frequency	125.77
23	Spectral Width	30030.0
24	Lowest Frequency	-2441.2
25	Nucleus	13C
26	Acquired Size	32768
27	Spectral Size	65536
28	Digital Resolution	0.46

Guest1401.469.fid
A.n (L10) 13CNMR in DMSO-d6 at 298K 1401.04.04

Figure (3-42) ^{13}CNMR for compound RES18

Schiff base (RES19) prepared from the reaction of R1 with 4-Chloroaniline in existence ethanol , and Glacial acetic acid. Equation (3-15).



Equation (3-15): synthesis of RES19

FT-IR spectrum for RES19 showed the following values (Vmax cm-1): 1635 (C=N imine), 3477 (O-H phenol),1475(C=C arom.) , 3020 (CH arom.) , 2850 (CH SP3) , 758 (C-Cl)(Figure 3-43) . ^{1}H-NMR (500 MH, δ ppm): 9.8-10.6 (O-H , alcohol) , 6.9

- 7.9 (C-H, aromatic), 2.2 (methyl), 6.2-7.4 (CH benzylidenimin), 2.5 (DMSO) (Figure 3-44). ^{13}C- NMR (125 MH, δ ppm): 18.2 (C,CH_3), 167.2 (C-N imine) , 104.3-131(C-H arom.) , 112.2 -162.8 (C- arom.) , 39.9 DMSO , (Figure 3-45).

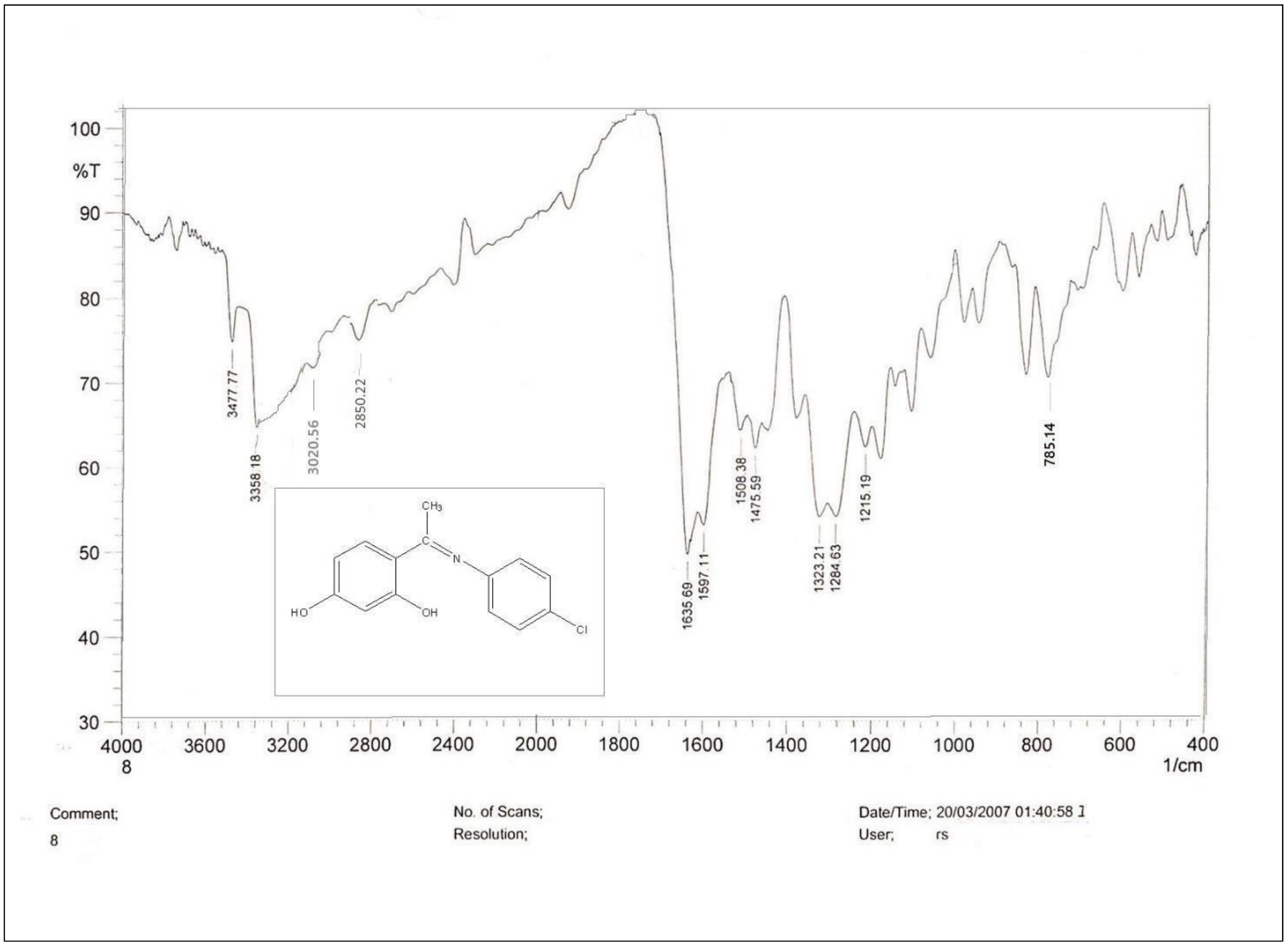
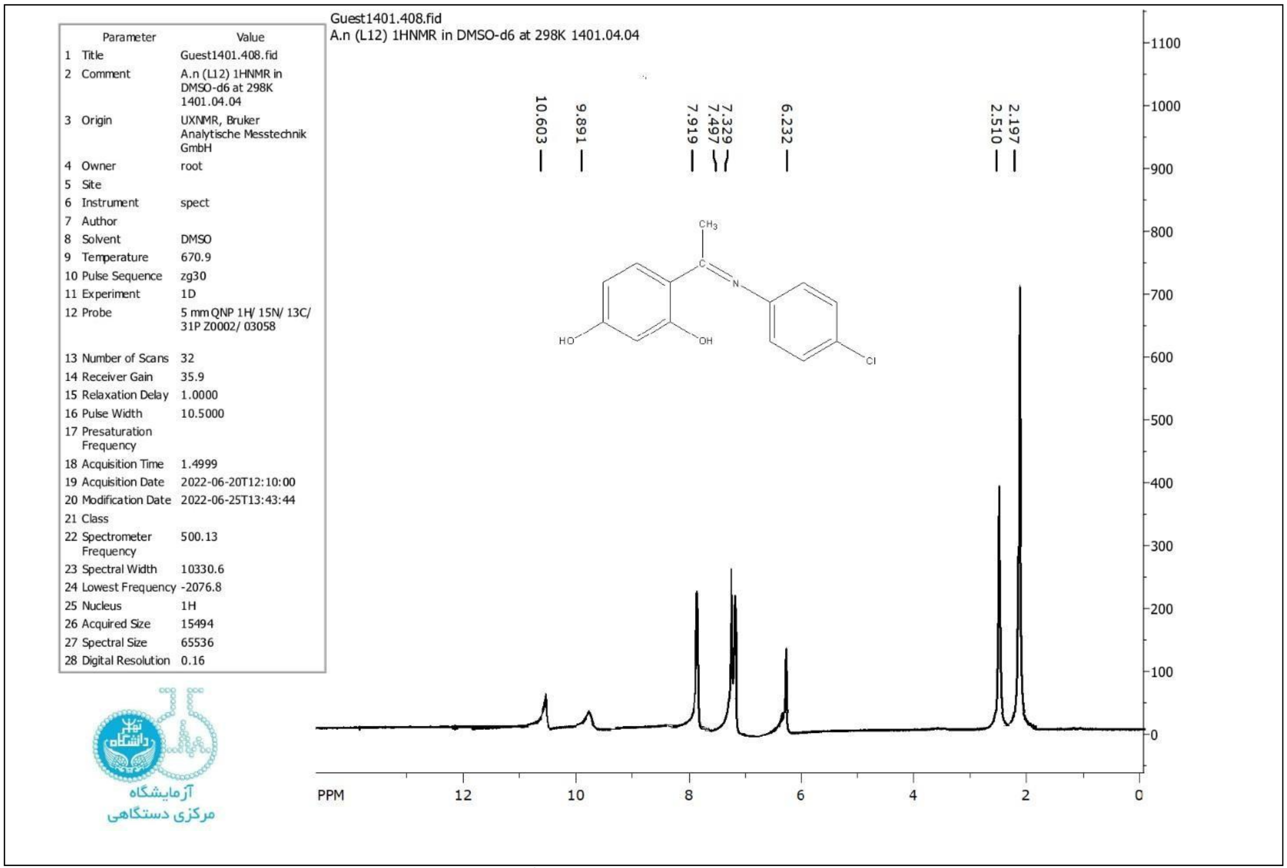


Figure (3-43) FTIR for compound RES19



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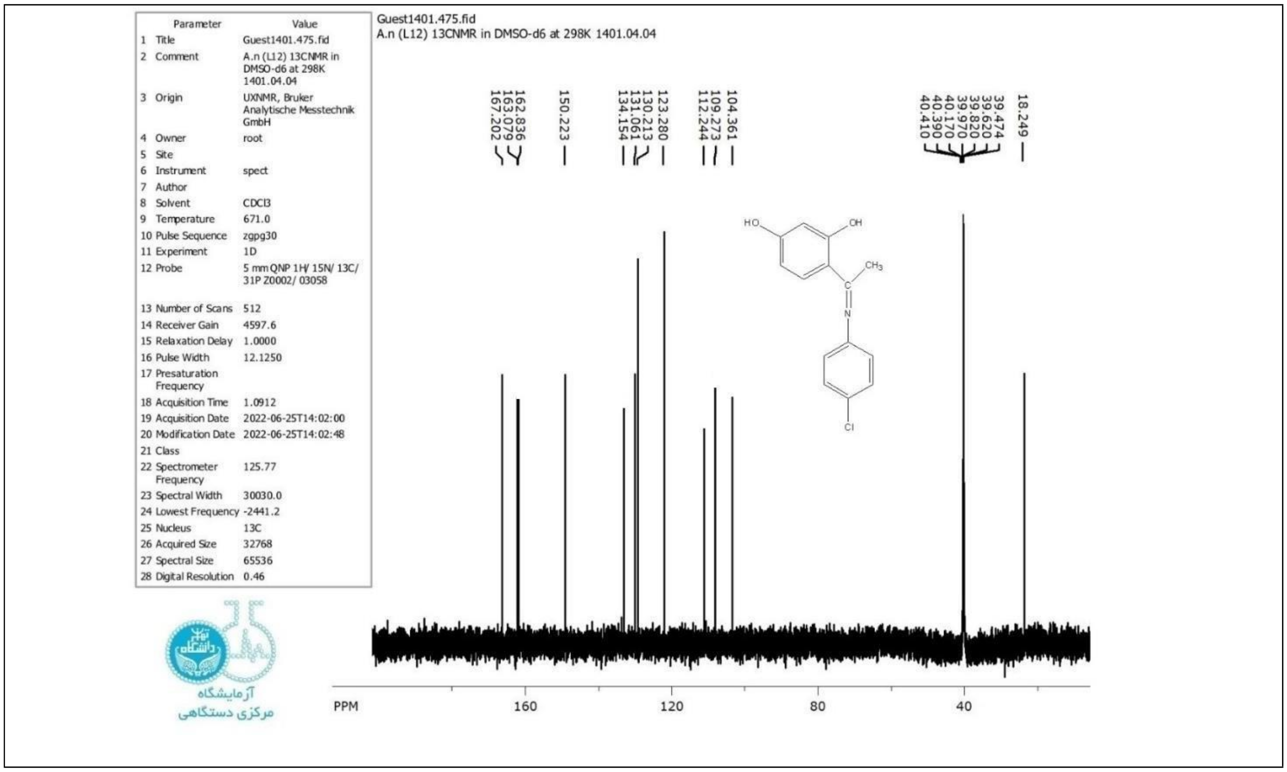
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	670.9
10	Pulse Sequence	zg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	32
14	Receiver Gain	35.9
15	Relaxation Delay	1.0000
16	Pulse Width	10.5000
17	Presaturation Frequency	
18	Acquisition Time	1.4999
19	Acquisition Date	2022-06-20T12:10:00
20	Modification Date	2022-06-25T13:43:44
21	Class	
22	Spectrometer Frequency	500.13
23	Spectral Width	10330.6
24	Lowest Frequency	-2076.8
25	Nucleus	1H
26	Acquired Size	15494
27	Spectral Size	65536
28	Digital Resolution	0.16

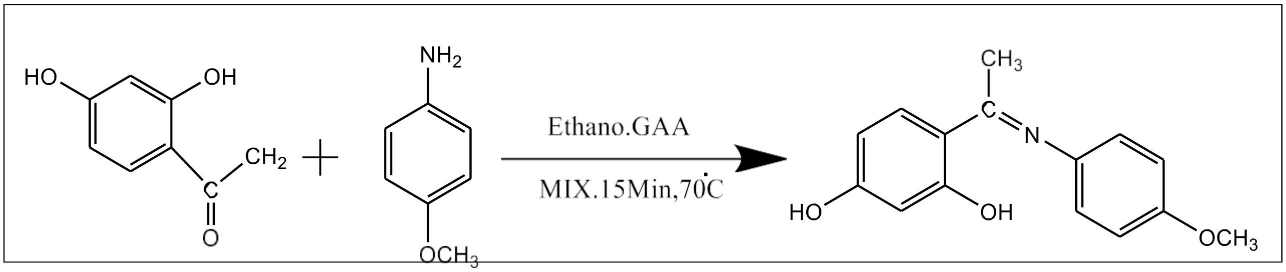
Figure (3-44) ^{1}HNMR for compound RES19



	Parameter	Value
1	Title	Guest1401.475.fid
2	Comment	A.n (L12) 13CNMR in DMSO-d6 at 298K 1401.04.04
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	CDCl3
9	Temperature	671.0
10	Pulse Sequence	zgpg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	512
14	Receiver Gain	4597.6
15	Relaxation Delay	1.0000
16	Pulse Width	12.1250
17	Presaturation Frequency	
18	Acquisition Time	1.0912
19	Acquisition Date	2022-06-25T14:02:00
20	Modification Date	2022-06-25T14:02:48
21	Class	
22	Spectrometer Frequency	125.77
23	Spectral Width	30030.0
24	Lowest Frequency	-2441.2
25	Nucleus	13C
26	Acquired Size	32768
27	Spectral Size	65536
28	Digital Resolution	0.46

Figure (3-45) ^{13}CNMR for compound RES19

Schiff base (RES20) prepared from the reaction of R1 with 4-Methoxyaniline in existence ethanol , and Glacial acetic acid. Equation (3-16).



Equation (3-16): synthesis of RES20

FT-IR spectrum for RES20 showed the following values (Vmax cm-1): 1678 (C=N imine), 3446-3552 (O-H phenol),1455(C=C arom.) , 3020 (CH arom.) , 2885 (CH SP3) , 1265 (C-O-C) (Figure 3-46) . ^{1}H-NMR (500 MHz,δ ppm): 10.3-10.1 (O-H , alcohol) , 7.1 - 7.8 (C-H, aromatic), 1.8-3.8 (methyl), 6.1-7.4 (CH benzylidenimin), 2.5 (DMSO) (Figure 3-47). ^{13}C- NMR (125 MH, δ ppm): 55.8-18.2 (C,CH_3), 167.2 (C-N imine) , 102.8-130.2 (C-H arom.) , 112 -162.8 (C- arom.) , 40.1 DMSO , (Figure 3-48).

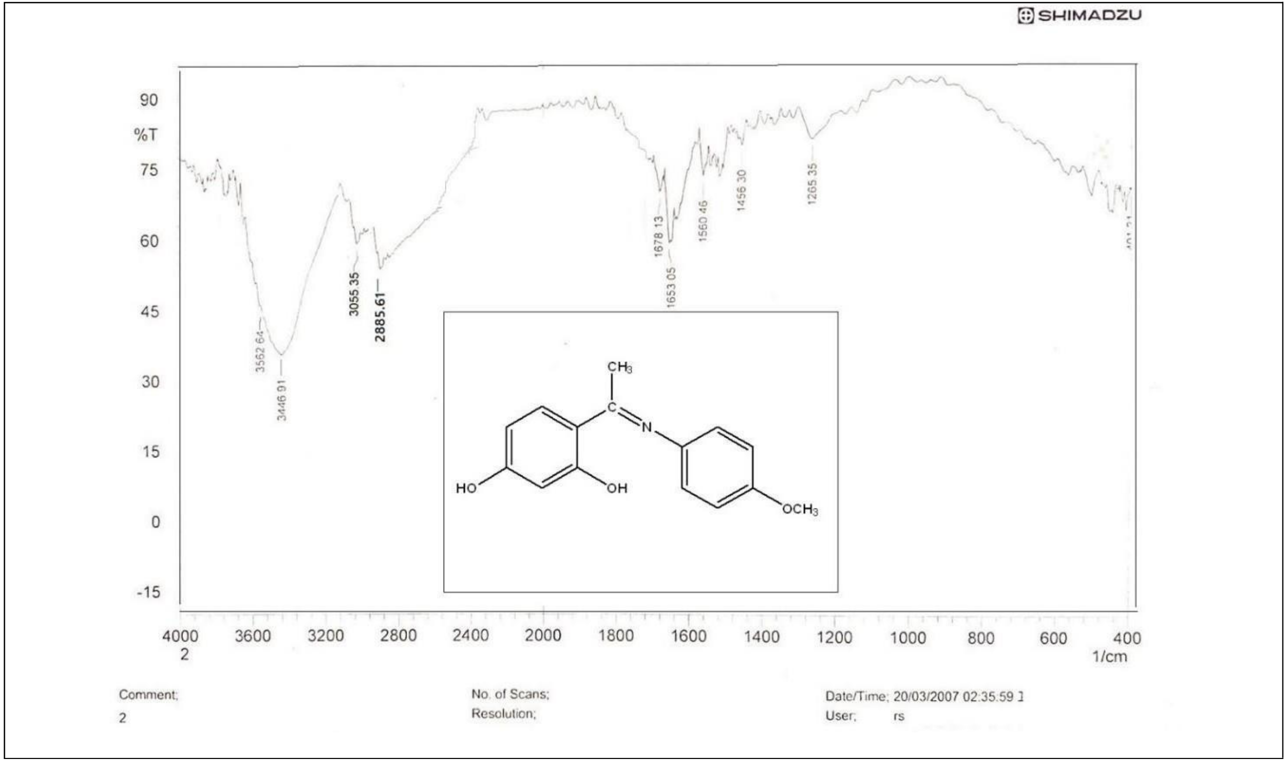
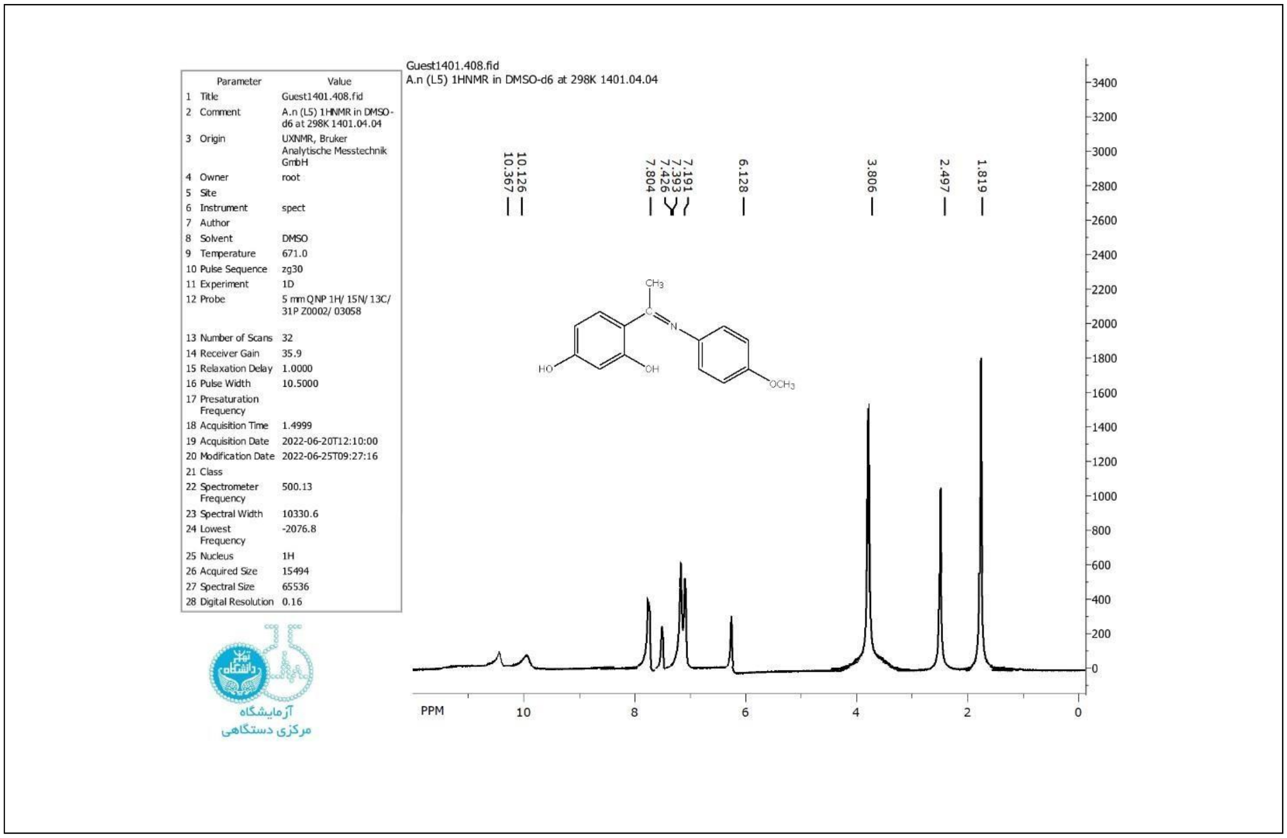


Figure (3-46) FTIR for compound RES20



Guest1401.408.fid
A.n (L5) 1HNMR in DMSO-d6 at 298K 1401.04.04

	Parameter	Value
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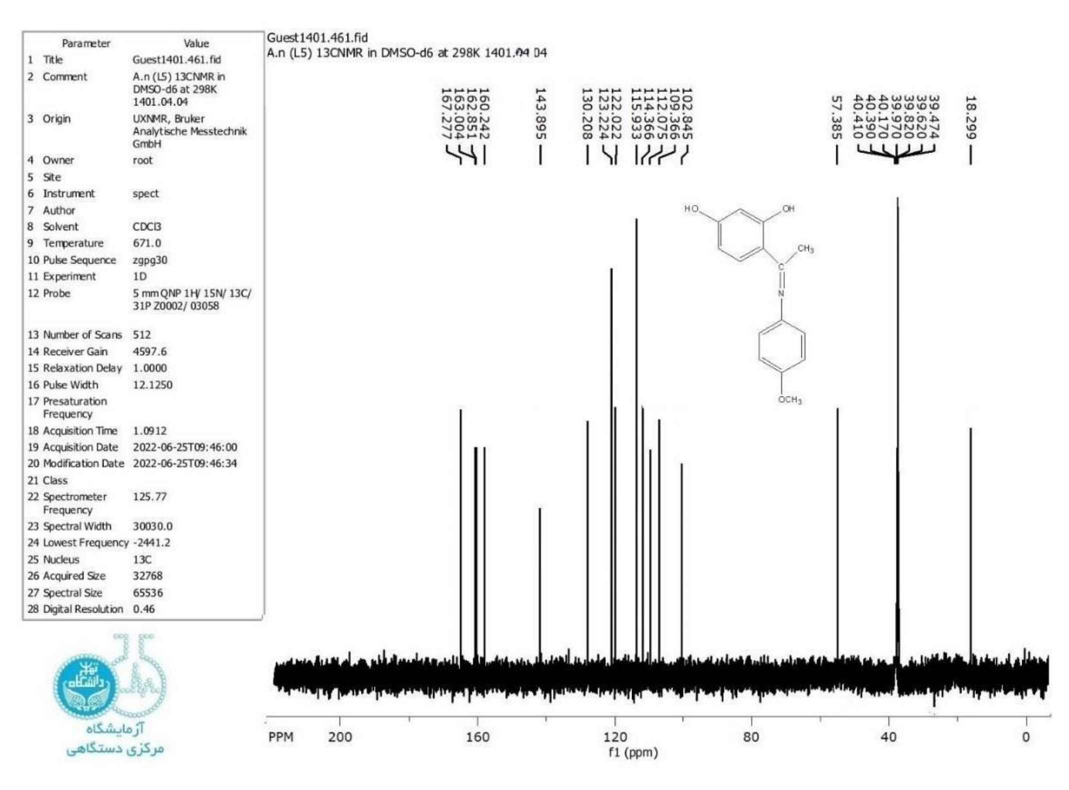
2	Comment	A.n (L5) 1HNMR in DMSO-d6 at 298K 1401.04.04
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	671.0
10	Pulse Sequence	zg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	32
14	Receiver Gain	35.9
15	Relaxation Delay	1.0000
16	Pulse Width	10.5000
17	Presaturation Frequency	
18	Acquisition Time	1.4999
19	Acquisition Date	2022-06-20T12:10:00
20	Modification Date	2022-06-25T09:27:16
21	Class	
22	Spectrometer Frequency	500.13
23	Spectral Width	10330.6
24	Lowest Frequency	-2076.8
25	Nucleus	1H
26	Acquired Size	15494
27	Spectral Size	65536
28	Digital Resolution	0.16

Figure (3-47) ^{1}HNMR for compound RES20



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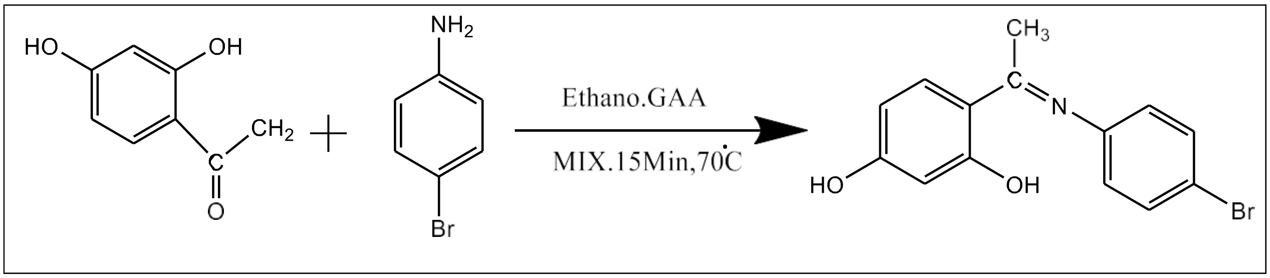
1 Title	Guest1401.461.fid
2 Comment	A.n (L5) 13CNMR in DMSO-d6 at 298K 1401.04.04
3 Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4 Owner	root
5 Site	
6 Instrument	spect
7 Author	
8 Solvent	CDCl3
9 Temperature	671.0
10 Pulse Sequence	zgpg30
11 Experiment	1D
12 Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13 Number of Scans	512
14 Receiver Gain	4597.6
15 Relaxation Delay	1.0000
16 Pulse Width	12.1250
17 Presaturation Frequency	
18 Acquisition Time	1.0912
19 Acquisition Date	2022-06-25T09:46:00
20 Modification Date	2022-06-25T09:46:34
21 Class	
22 Spectrometer Frequency	125.77
23 Spectral Width	30030.0
24 Lowest Frequency	-2441.2
25 Nucleus	13C
26 Acquired Size	32768
27 Spectral Size	65536
28 Digital Resolution	0.46

Guest1401.461.fid
A.n (L5) 13CNMR in DMSO-d6 at 298K 1401.04 04

Figure (3-48) ^{13}CNMR for compound RES20

Schiff base (RES21) prepared from the reaction of R3 with 4-Bromoaniline in existence ethanol , and Glacial acetic acid. Equation (3-17).



Equation (3-17): synthesis of RES21

FT-IR spectrum for RES21 showed the following values (Vmax cm-1): 1653 (C=N imine), 3743-3550 (O-H phenol),1473(C=C arom.) , 3059 (C-H arom.) , 2943 (CH

SP3) , 647 (C-Br) (Figure 3-49) . 1H-NMR (500 MH, δ ppm): 10.6-9.2 (O-H , alcohol) , 7.1 - 7.9 (C-H, aromatic), 2.0 (methyl), 6.2-7.7 (C-H benzylidenimin), 2.5 (DMSO) (Figure 3-50). ^{13}C- NMR (125 MH, δ ppm): 18.2 (C,CH_3), 167.2 (C-N imine) , 104.2-133.4 (C-H arom.) , 112.2 -162.7 (C- arom.) , 39.9 DMSO , (Figure 3-51).

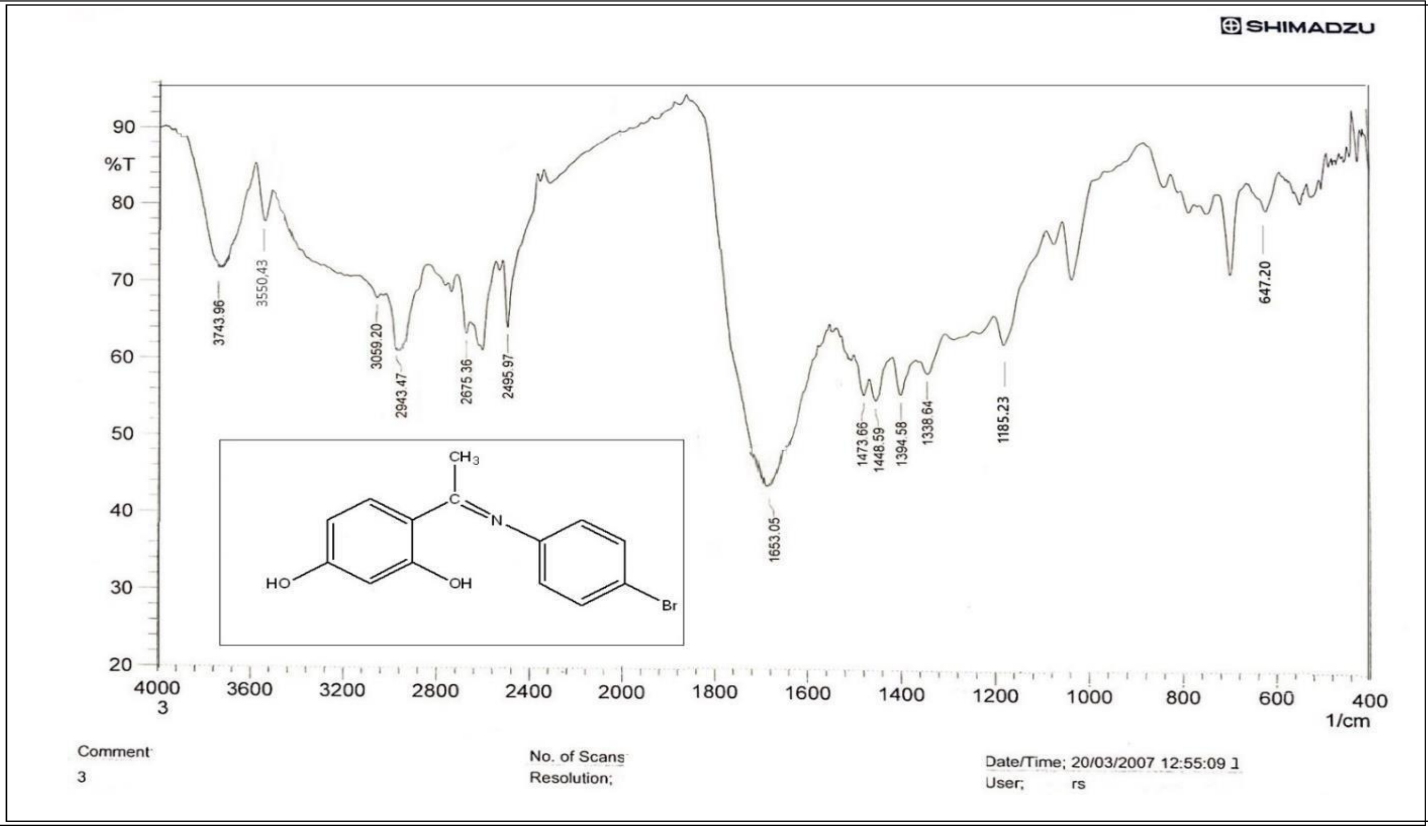
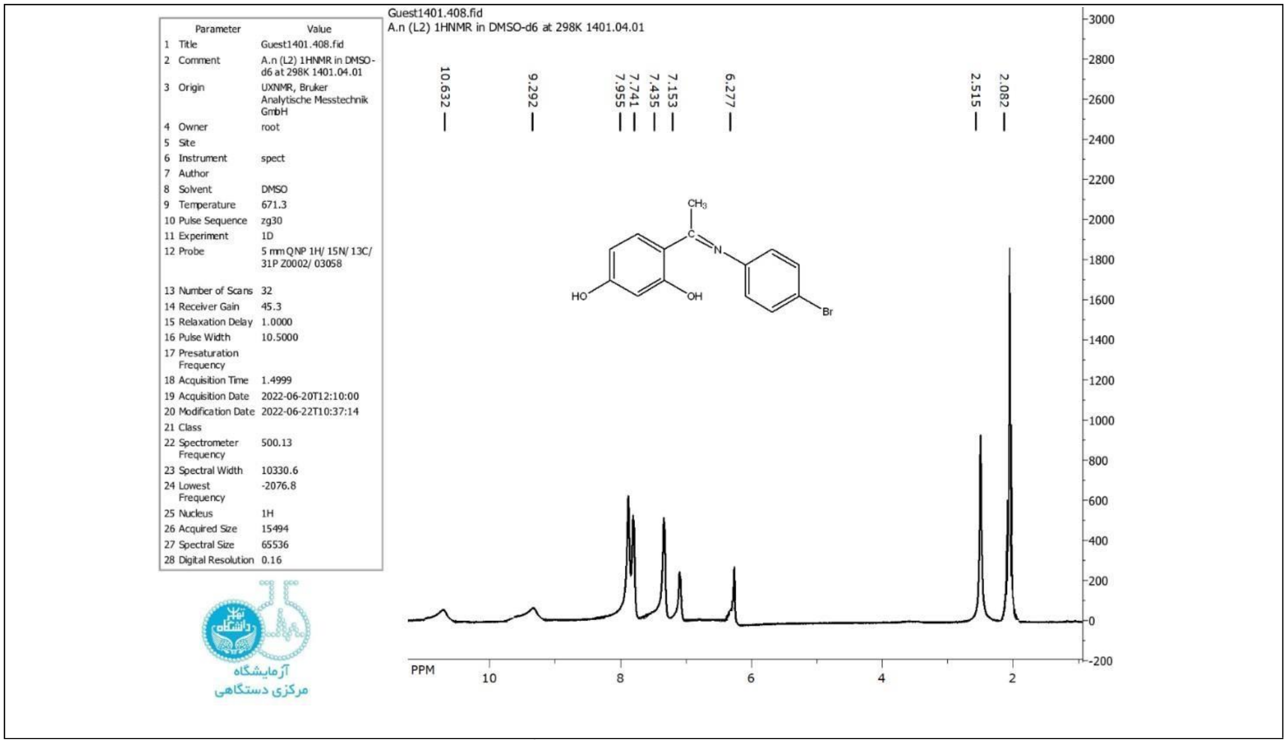


Figure (3-49) FTIR for compound RES21



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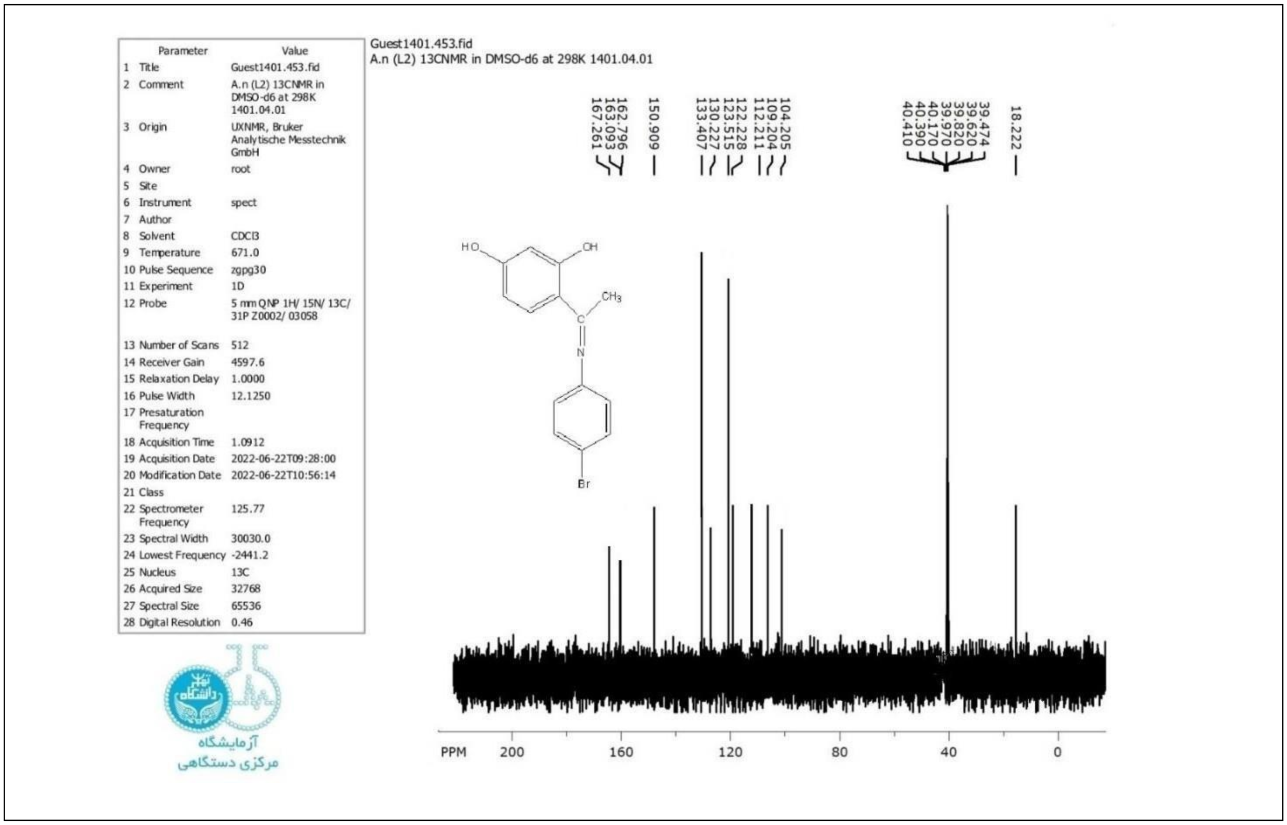
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	671.3
10	Pulse Sequence	zg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	32
14	Receiver Gain	45.3
15	Relaxation Delay	1.0000
16	Pulse Width	10.5000
17	Presaturation Frequency	
18	Acquisition Time	1.4999
19	Acquisition Date	2022-06-20T12:10:00
20	Modification Date	2022-06-22T10:37:14
21	Class	
22	Spectrometer Frequency	500.13
23	Spectral Width	10330.6
24	Lowest Frequency	-2076.8
25	Nucleus	1H
26	Acquired Size	15494
27	Spectral Size	65536
28	Digital Resolution	0.16

Figure (3-50) ^{1}HNMR for compound RES21

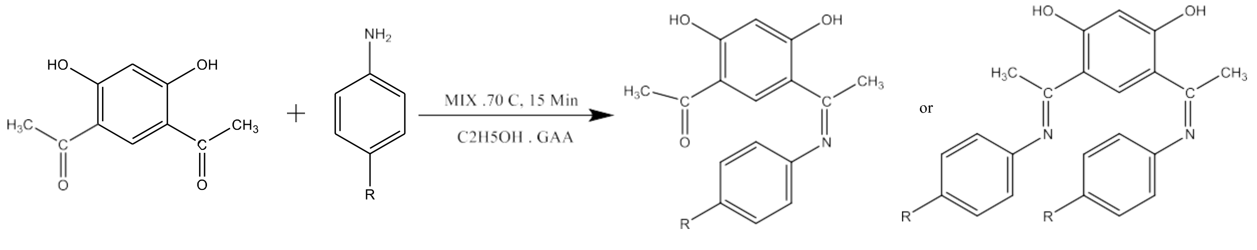


	Parameter	Value
1	Title	Guest1401.453.fid
2	Comment	A.n (L2) 13CNMR in DMSO-d6 at 298K 1401.04.01
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	CDCl3
9	Temperature	671.0
10	Pulse Sequence	zgpg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	512
14	Receiver Gain	4597.6
15	Relaxation Delay	1.0000
16	Pulse Width	12.1250
17	Presaturation Frequency	
18	Acquisition Time	1.0912
19	Acquisition Date	2022-06-22T09:28:00
20	Modification Date	2022-06-22T10:56:14
21	Class	
22	Spectrometer Frequency	125.77
23	Spectral Width	30030.0
24	Lowest Frequency	-2441.2
25	Nucleus	13C
26	Acquired Size	32768
27	Spectral Size	65536
28	Digital Resolution	0.46

Figure (3-51) ^{13}CNMR for compound RES21

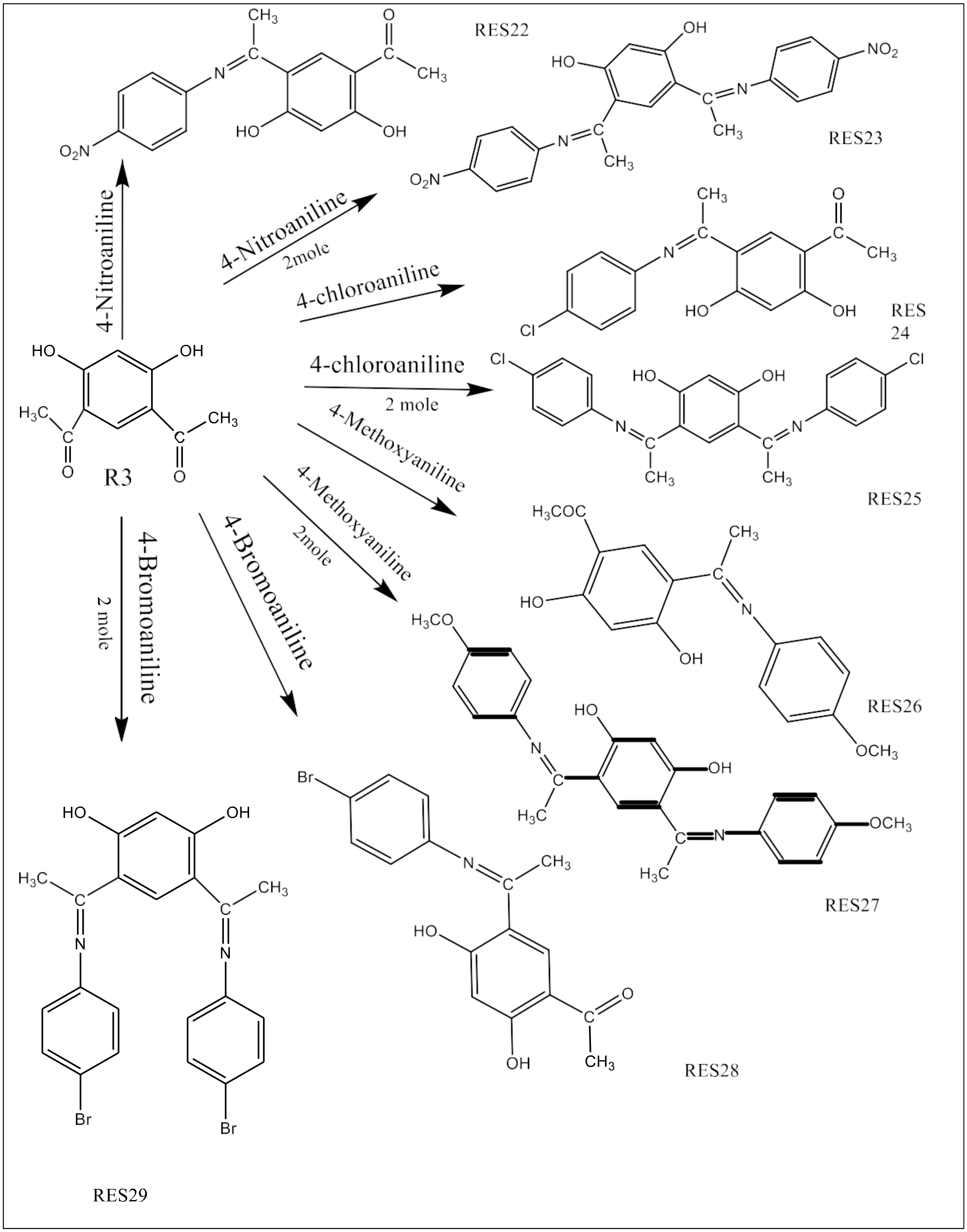
3-4. Fourth line Synthesis of Compounds RES22-RES29 (Schiff base)

These compounds were synthesized from the reaction diacetylresorcinol (R3) with different four aniline derivatives.



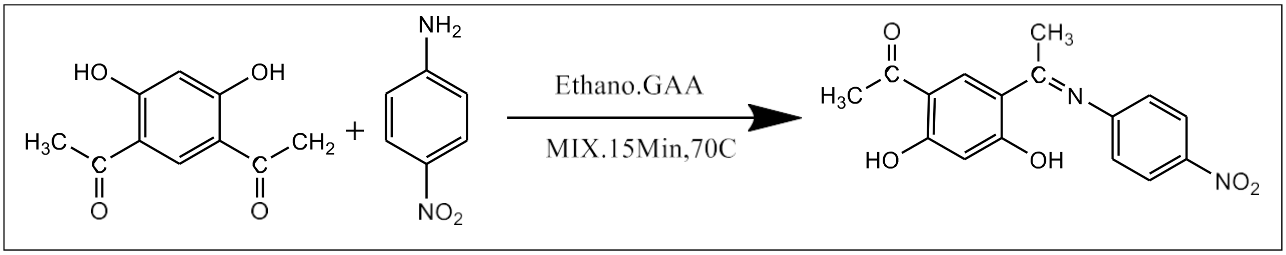
R = NO2 , Cl , OCH3 , Br

Scheme (3-7): General scheme of Synthesis of compounds (RES22-RES29)



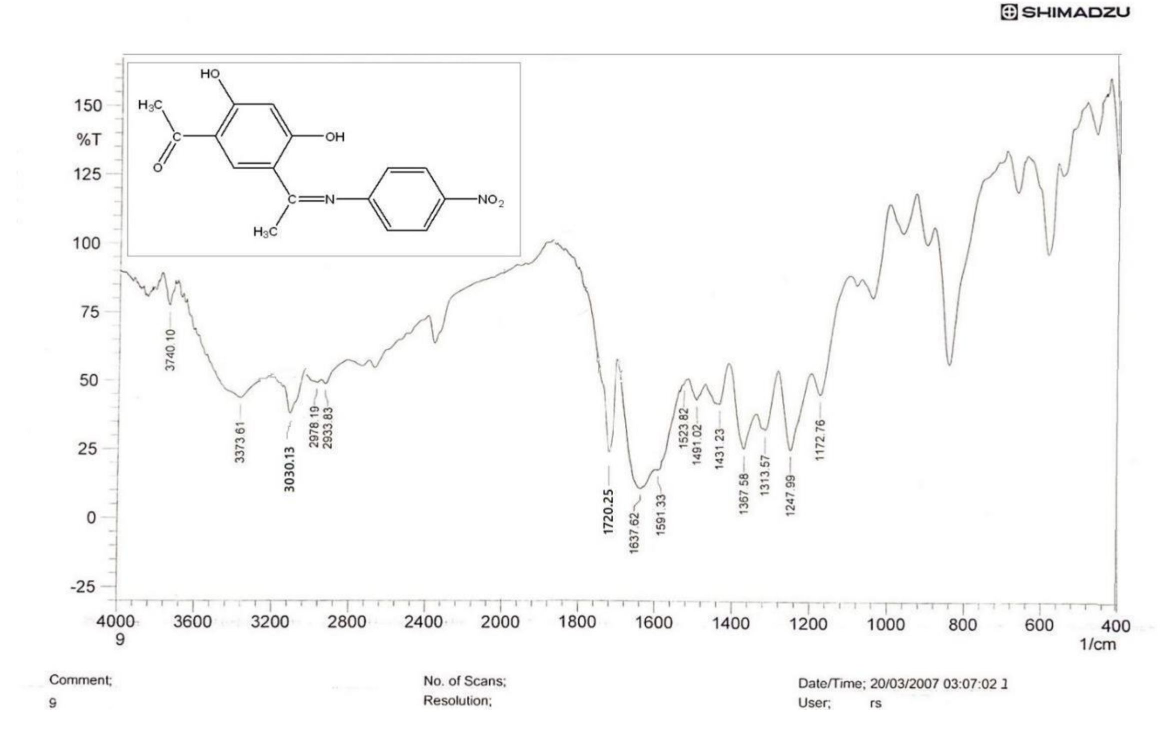
Scheme (3-8): Synthesis of Schiff basses RES22 – RES29

Schiff base (RES22) prepared from the reaction of R3 with 4-Nitroaniline in existence ethanol , and Glacial acetic acid. Equation (3-18).



Equation (3-18): synthesis of RES22

FT-IR spectrum for RES22 showed the following values (Vmax cm-1): 1637.62(C=N imine), 3373-3740 (O-H alcohol),1491(C=C arom.) , 3030 (C-H arom.) , 2933-2978 (CH SP3) , 1715 (C=O ketone)1313.57 (NO_2 arom.)(Figure 3-52) . 1H-NMR (500 MH, δ ppm): 10.6-12.6(O-H , alcohol) , 6.7- 8.3 (C-H, aromatic), 2.4-2.6 (methyl), 6.4-7.9 (C-H benzylidenimin), 2.5 (DMSO) (Figure 3-53). ^{13}C- NMR (125 MH, δ ppm): 18.7-26.6 (C,CH_3), 165.3 (C-N imine) , 108.9-132.2(C-H arom.) , 111.3 -167.8 (C arom.) ,198.8 (C - carbonyl) , 39.9 DMSO , (Figure 3-54).

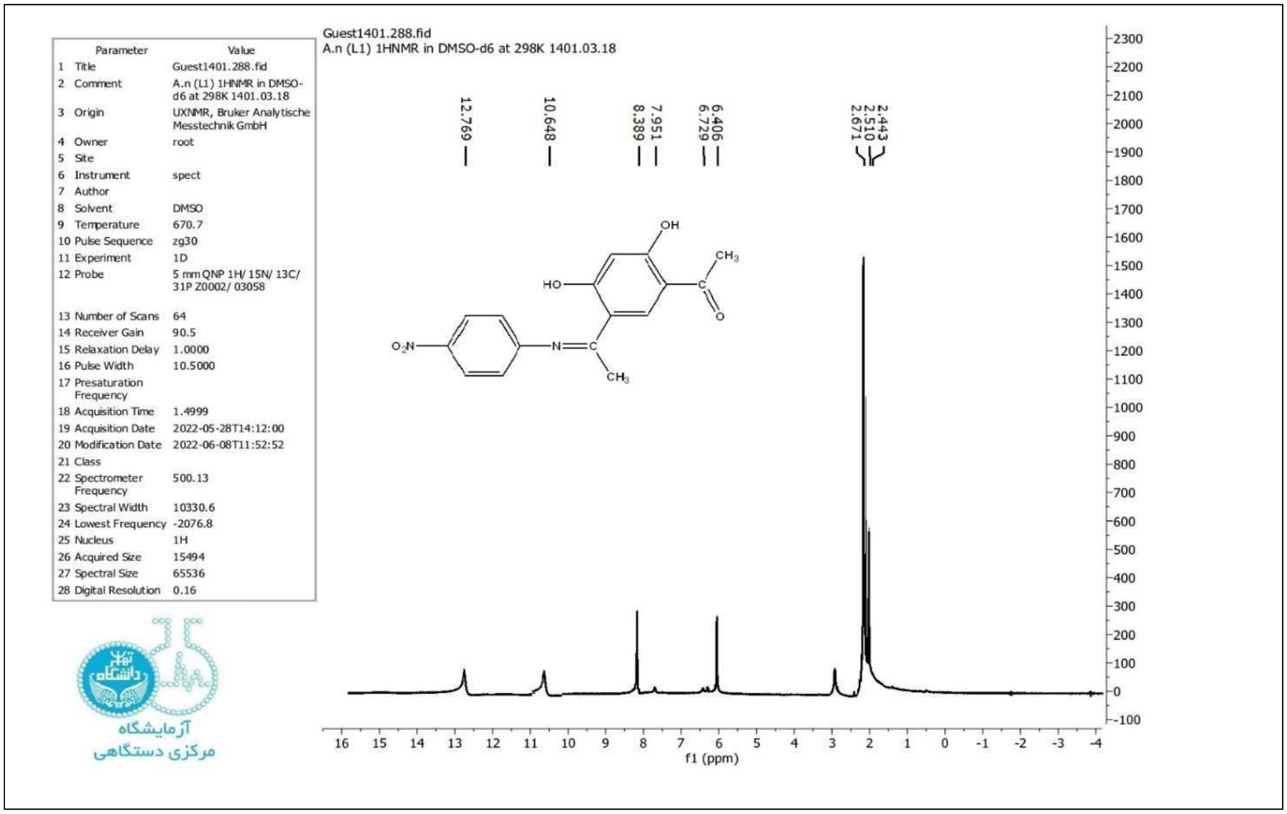


Comment;
9

No. of Scans;
Resolution;

Date/Time; 20/03/2007 03:07:02 1
User; rs

Figure (3-52) FTIR for compound RES22



Guest1401.288.fid
A.n (L1) 1HNMR in DMSO-d6 at 298K 1401.03.18

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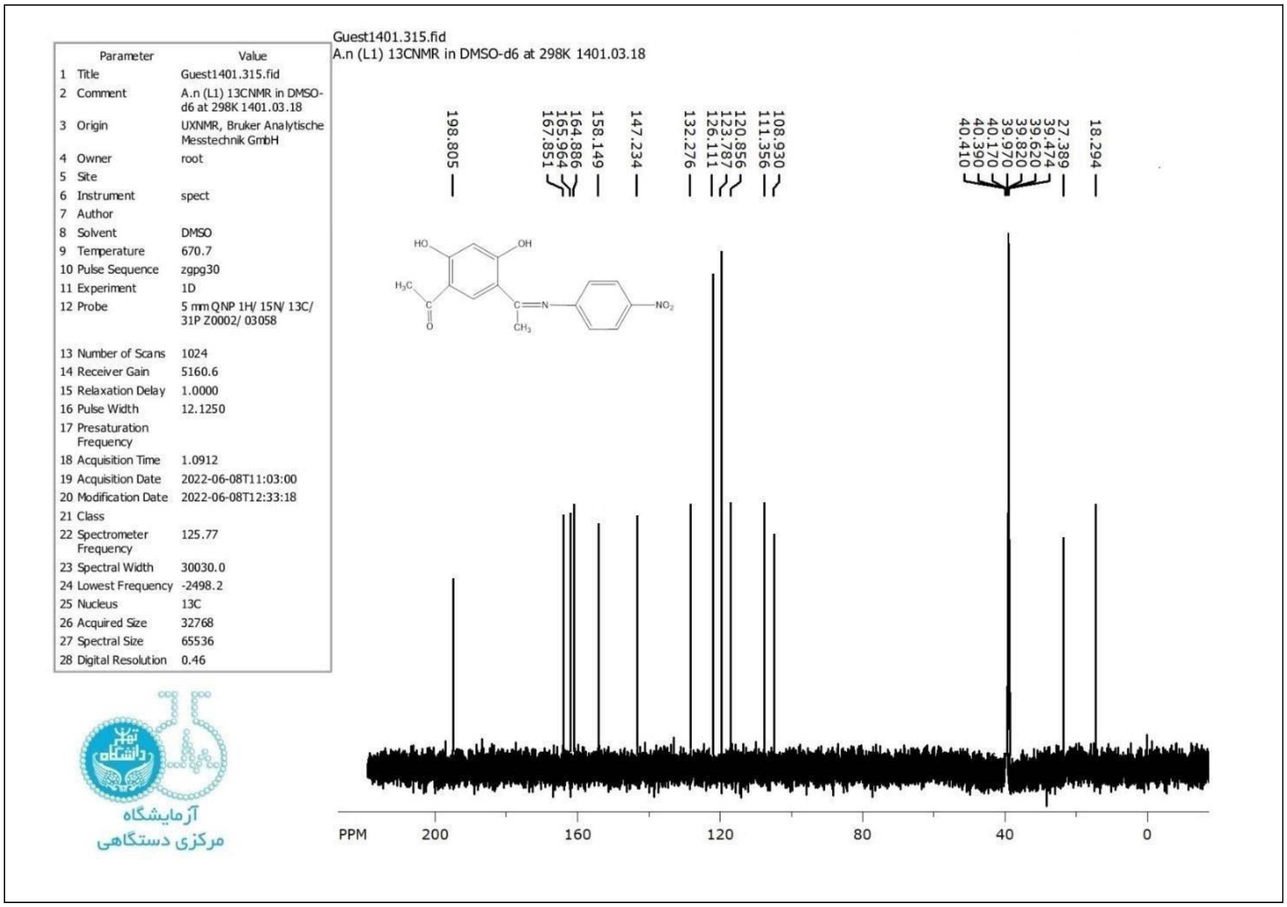
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	670.7
10	Pulse Sequence	zg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	64
14	Receiver Gain	90.5
15	Relaxation Delay	1.0000
16	Pulse Width	10.5000
17	Presaturation Frequency	
18	Acquisition Time	1.4999
19	Acquisition Date	2022-05-28T14:12:00
20	Modification Date	2022-06-08T11:52:52
21	Class	
22	Spectrometer Frequency	500.13
23	Spectral Width	10330.6
24	Lowest Frequency	-2076.8
25	Nucleus	1H
26	Acquired Size	15494
27	Spectral Size	65536
28	Digital Resolution	0.16

Figure (3-53) ^{1}HNMR for compound RES22



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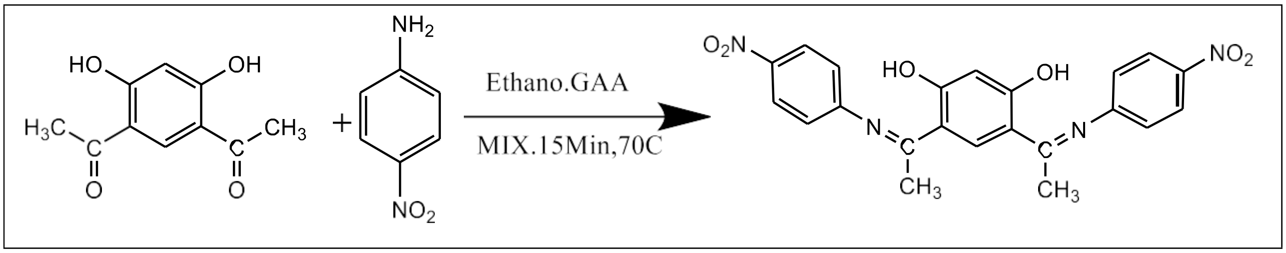
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	670.7
10	Pulse Sequence	zgpg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	1024
14	Receiver Gain	5160.6
15	Relaxation Delay	1.0000
16	Pulse Width	12.1250
17	Presaturation Frequency	
18	Acquisition Time	1.0912
19	Acquisition Date	2022-06-08T11:03:00
20	Modification Date	2022-06-08T12:33:18
21	Class	
22	Spectrometer Frequency	125.77
23	Spectral Width	30030.0
24	Lowest Frequency	-2498.2
25	Nucleus	13C
26	Acquired Size	32768
27	Spectral Size	65536
28	Digital Resolution	0.46

Figure (3-54) ^{13}CNMR for compound RES22

Schiff base (RES23) prepared from the reaction 1 mole of R4 with 2 mole of 4-Nitroaniline in existence ethanol , and Glacial acetic acid. Equation (3-19).



Equation (3-19): synthesis of RES23

FT-IR spectrum for RES23 showed the following values (Vmax cm-1): 1635.69(C=N imine), 3477-3360 (O-H phenol),1477(C=C arom.) , 3040 (C-H arom.) , 2850(C-H SP3) , 1301.99 (NO_2 arom.)(Figure 3-55) . ^{1}H-NMR (500 MHz,δ ppm): 12.7 (O-H , phenol) , 6.9- 8.1 (C-H, aromatic), 2.6 (methyl), 6.5-7.9 (C-Hbenzylidenimin), 2.5 (DMSO) (Figure 3-56). ^{13}C- NMR (125 MHz,δ ppm): 18.2-27.3 (C,CH_3), 167.2 (C=N imine) , 108.1-132.3 (C-H arom.) , 111.4 -164.4 (C arom.) ,39.9 DMSO , (Figure 3-57).

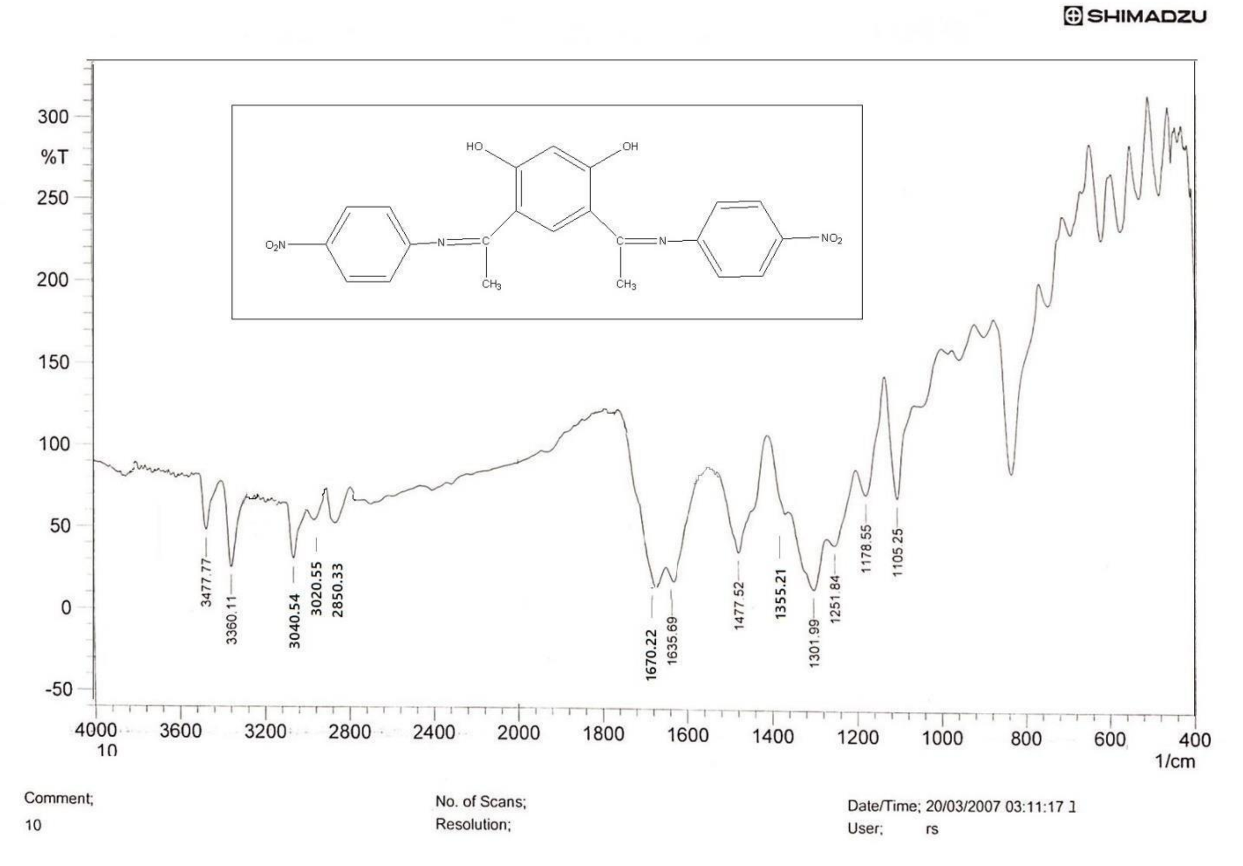
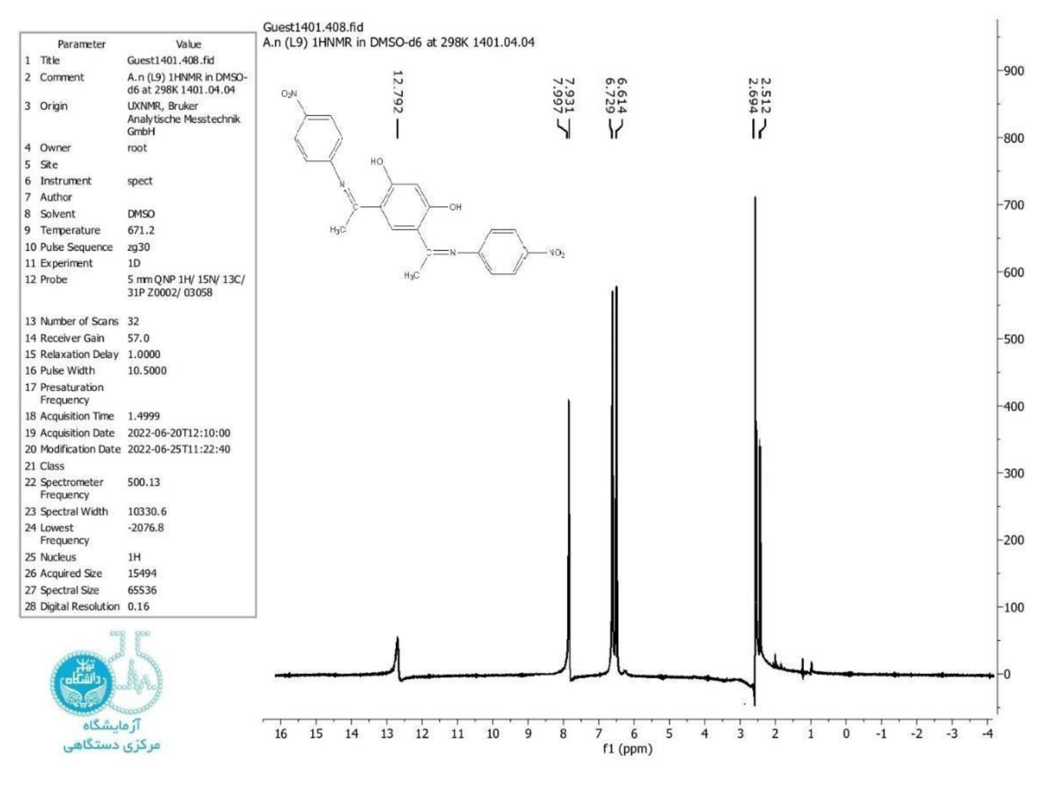


Figure (3-55) FTIR for compound RES23



Parameter		Value
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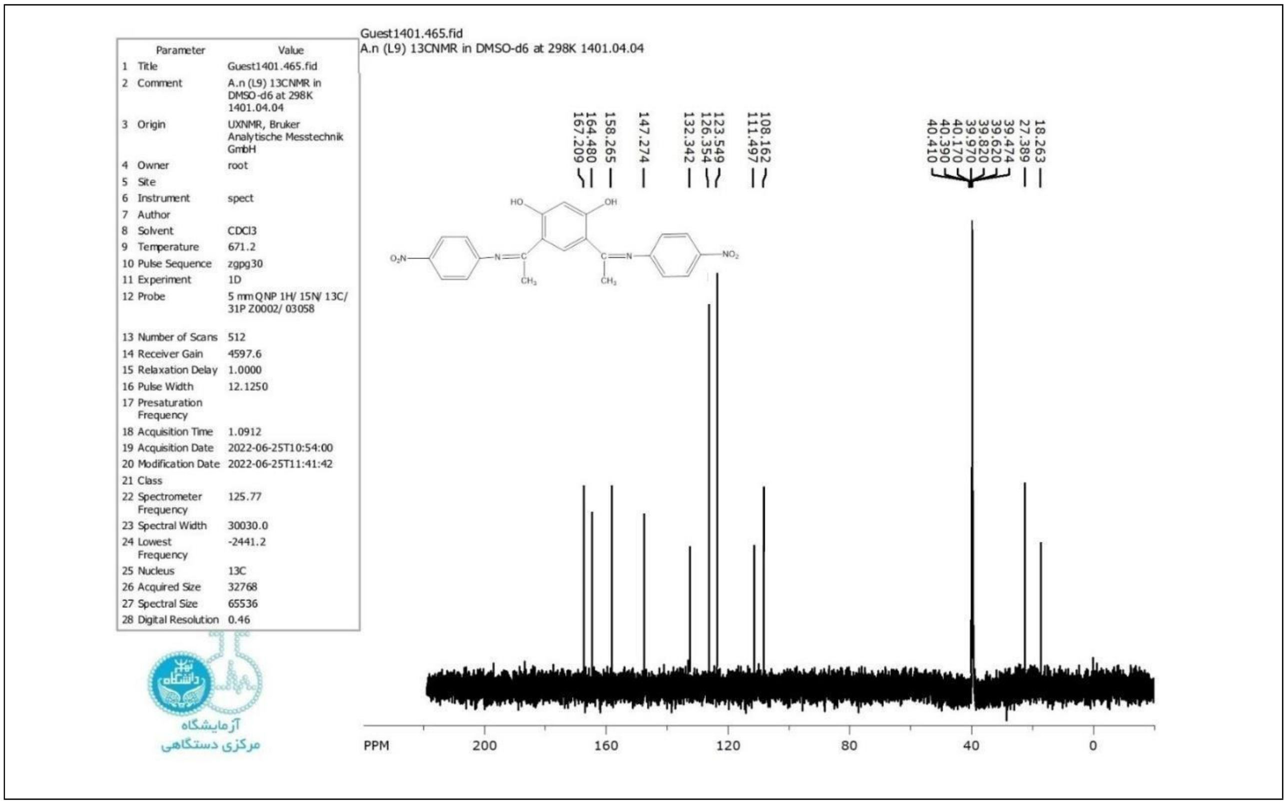
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	671.2
10	Pulse Sequence	zg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	32
14	Receiver Gain	57.0
15	Relaxation Delay	1.0000
16	Pulse Width	10.5000
17	Presaturation Frequency	
18	Acquisition Time	1.4999
19	Acquisition Date	2022-06-20T12:10:00
20	Modification Date	2022-06-25T11:22:40
21	Class	
22	Spectrometer Frequency	500.13
23	Spectral Width	10330.6
24	Lowest Frequency	-2076.8
25	Nucleus	1H
26	Acquired Size	15494
27	Spectral Size	65536
28	Digital Resolution	0.16

Guest1401.408.fid
A.n (L9) 1HNMR in DMSO-d6 at 298K 1401.04.04

Figure (3-56) ^{1}HNMR for compound RES23

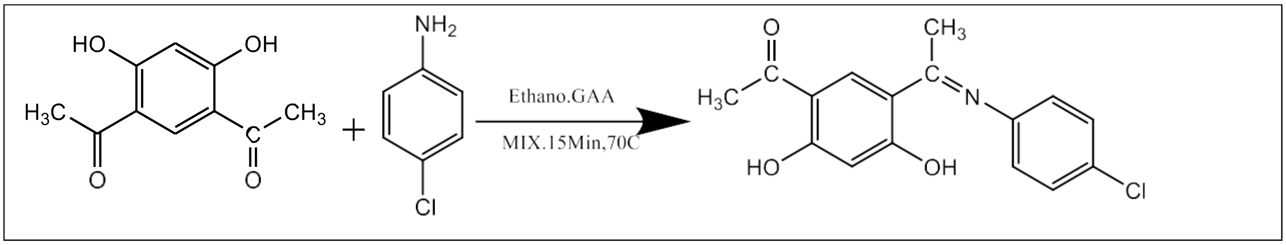


Parameter		Value
1	Title	Guest1401.465.fid
2	Comment	A.n (L9) 13CNMR in DMSO-d6 at 298K 1401.04.04
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	CDCl3
9	Temperature	671.2
10	Pulse Sequence	zgpg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	512
14	Receiver Gain	4597.6
15	Relaxation Delay	1.0000
16	Pulse Width	12.1250
17	Presaturation Frequency	
18	Acquisition Time	1.0912
19	Acquisition Date	2022-06-25T10:54:00
20	Modification Date	2022-06-25T11:41:42
21	Class	
22	Spectrometer Frequency	125.77
23	Spectral Width	30030.0
24	Lowest Frequency	-2441.2
25	Nucleus	13C
26	Acquired Size	32768
27	Spectral Size	65536
28	Digital Resolution	0.46

Guest1401.465.fid
A.n (L9) 13CNMR in DMSO-d6 at 298K 1401.04.04

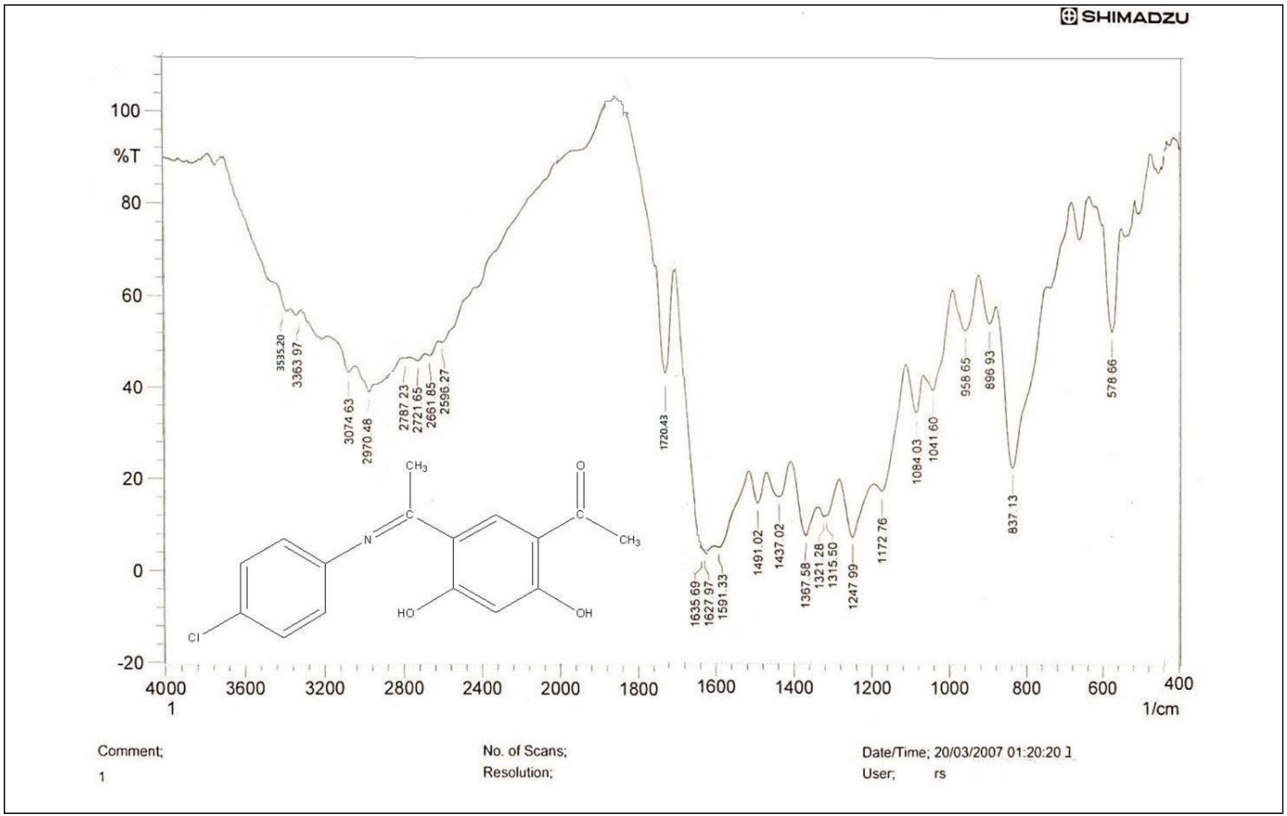
Figure (3-57) ^{13}CNMR for compound RES23

Schiff base (RES24) prepared from the reaction of R3 with 4-Chloroaniline in existence ethanol , and Glacial acetic acid. Equation (3-20).



Equation (3-20): synthesis of RES24

FT-IR spectrum for RES24 showed the following values (vmax cm^{-1}): 1627 (C=N imine), 3363-3535 (O-H phenol), 1491 (C=C arom.) , 3074 (CH arom.) , 2787-2924 (C-H SP3) , 1720 (C=O ketone) 578.60 (C-Cl) (Figure 3-58) . ^{1}H-NMR (500 MHz,δppm): 12.7-15.8 (O-H , phenol) , 6.9 - 7.4 (C-H, aromatic), 1.8-2.6 (methyl), 6.5-8.2 (CH benzylidenimin), 2.5 (DMSO) (Figure 3-59). ^{13}C- NMR (125MHz, δ ppm): 18.2-27.3 (C,CH_3), 165.1 (C-N imine) , 109-130.9(C-H arom.) , 111.3 - 167.7 (C- arom.) , 198.8(C-carbonyl) , 39.9 DMSO , (Figure 3-60).



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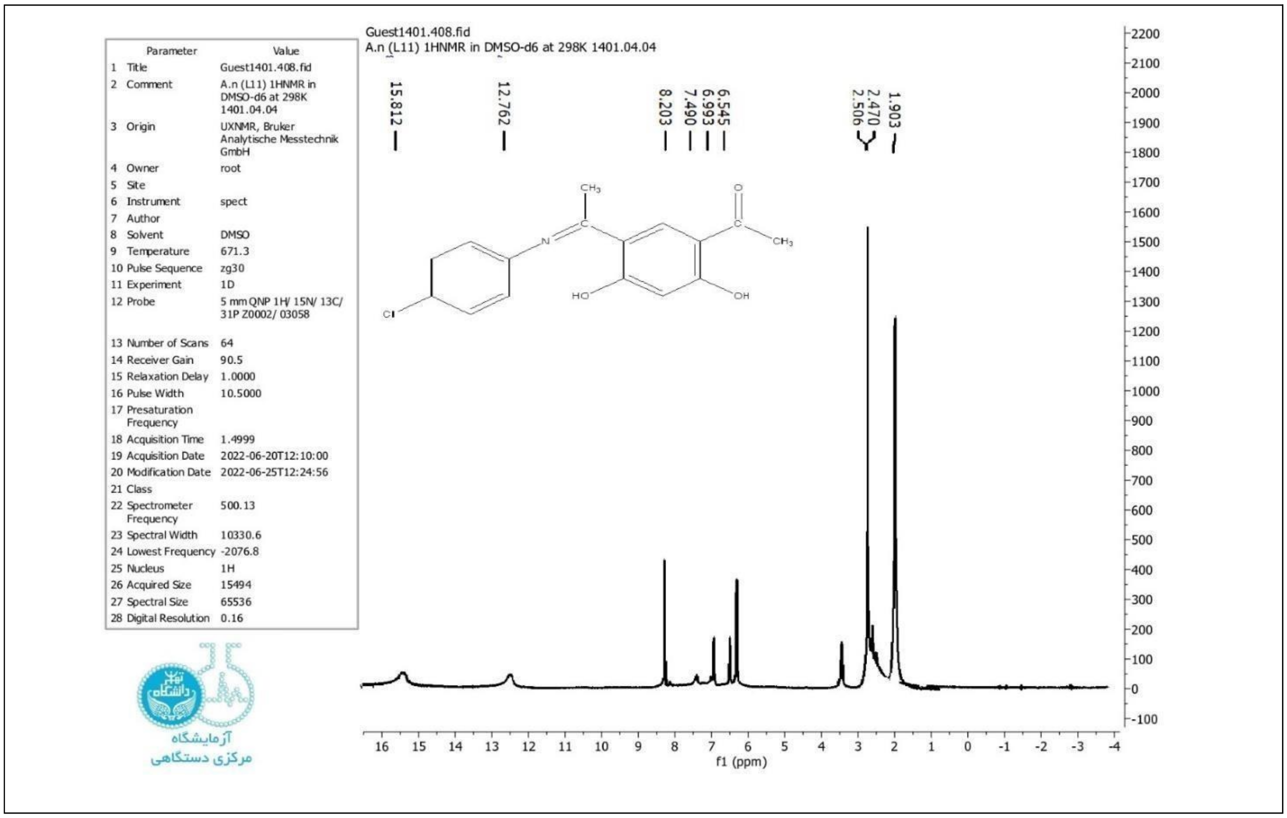
No. of Scans;
Resolution;

Date/Time; 20/03/2007 01:20:20 1
User; rs

Figure (3-58) FTIR for compound RES24



Parameter		Value
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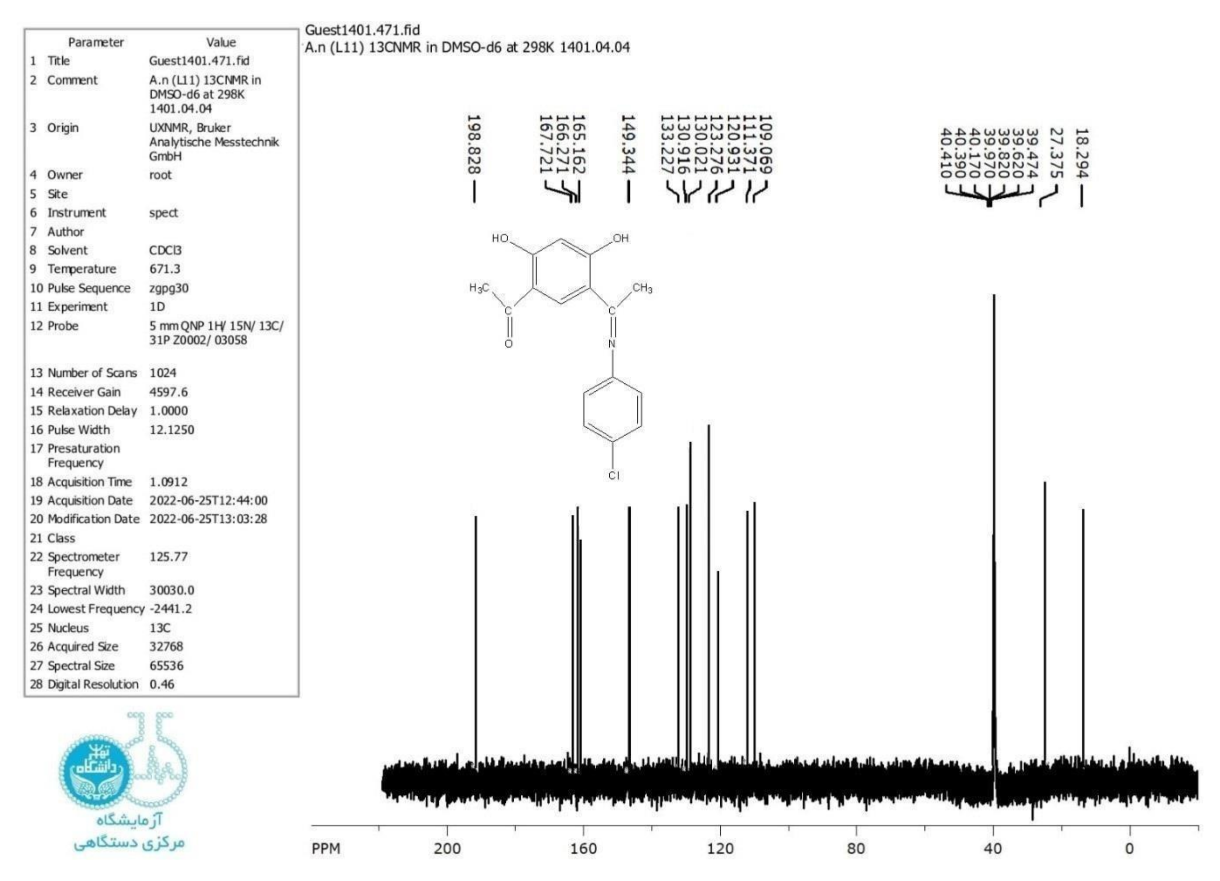
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	671.3
10	Pulse Sequence	zg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	64
14	Receiver Gain	90.5
15	Relaxation Delay	1.0000
16	Pulse Width	10.5000
17	Presaturation Frequency	
18	Acquisition Time	1.4999
19	Acquisition Date	2022-06-20T12:10:00
20	Modification Date	2022-06-25T12:24:56
21	Class	
22	Spectrometer Frequency	500.13
23	Spectral Width	10330.6
24	Lowest Frequency	-2076.8
25	Nucleus	1H
26	Acquired Size	15494
27	Spectral Size	65536
28	Digital Resolution	0.16

Guest1401.408.fid
A.n (L11) 1HNMR in DMSO-d6 at 298K 1401.04.04

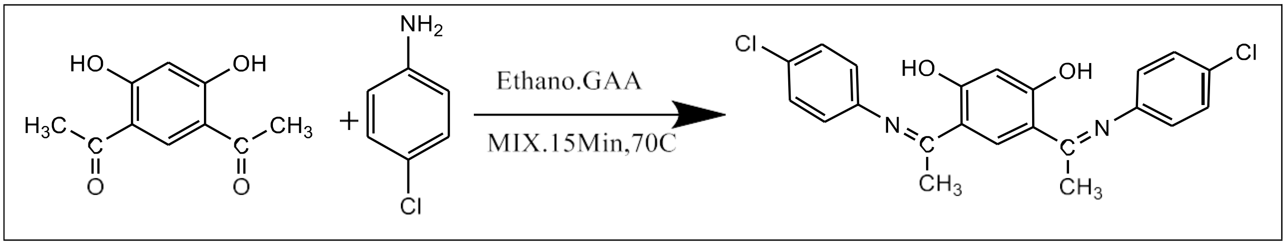
Figure (3-59) ^{1}HNMR for compound RES24


Guest1401.471.fid
A.n (L11) 13CNMR in DMSO-d6 at 298K 1401.04.04

Parameter	Value
1 Title	Guest1401.471.fid
2 Comment	A.n (L11) 13CNMR in DMSO-d6 at 298K 1401.04.04
3 Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4 Owner	root
5 Site	
6 Instrument	spect
7 Author	
8 Solvent	CDCl3
9 Temperature	671.3
10 Pulse Sequence	zgpg30
11 Experiment	1D
12 Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13 Number of Scans	1024
14 Receiver Gain	4597.6
15 Relaxation Delay	1.0000
16 Pulse Width	12.1250
17 Presaturation Frequency	
18 Acquisition Time	1.0912
19 Acquisition Date	2022-06-25T12:44:00
20 Modification Date	2022-06-25T13:03:28
21 Class	
22 Spectrometer Frequency	125.77
23 Spectral Width	30030.0
24 Lowest Frequency	-2441.2
25 Nucleus	13C
26 Acquired Size	32768
27 Spectral Size	65536
28 Digital Resolution	0.46

Figure (3-60) ^{13}CNMR for compound RES24

Schiff base (RES25) prepared from the reaction 1 mole of R3 with 2 mole 4-Chloroaniline in existence ethanol , and Glacial acetic acid. Equation (3-21).



Equation (3-21): synthesis of RES25

FT-IR spectrum for RES25 showed the following values (vmax cm^{-1}): 1650 (C=N imine), 3371-3550 (O-H phenol), 1496 (C=C arom.) , 3070 (CH arom.) , 2924 (C-H SP3) , 585.20 (C-Cl) (Figure 3-61) . ^{1}H-NMR (500 MHz,δ ppm): 10.1 (O-H , phenol) , 7.01 - 7.4 (C-H, aromatic), 1.9 (methyl), 6.5-8.3 (CH benzylidenimin), 2.5 (DMSO) (Figure 3-62). ^{13}C- NMR (125MHz, δ ppm): 18.2 (C,CH$_3$), 167.2 (C=N imine) , 109.2-132(C-H arom.) , 111.4 -164.1 (C- arom.) , 40 DMSO , (Figure 3-63).

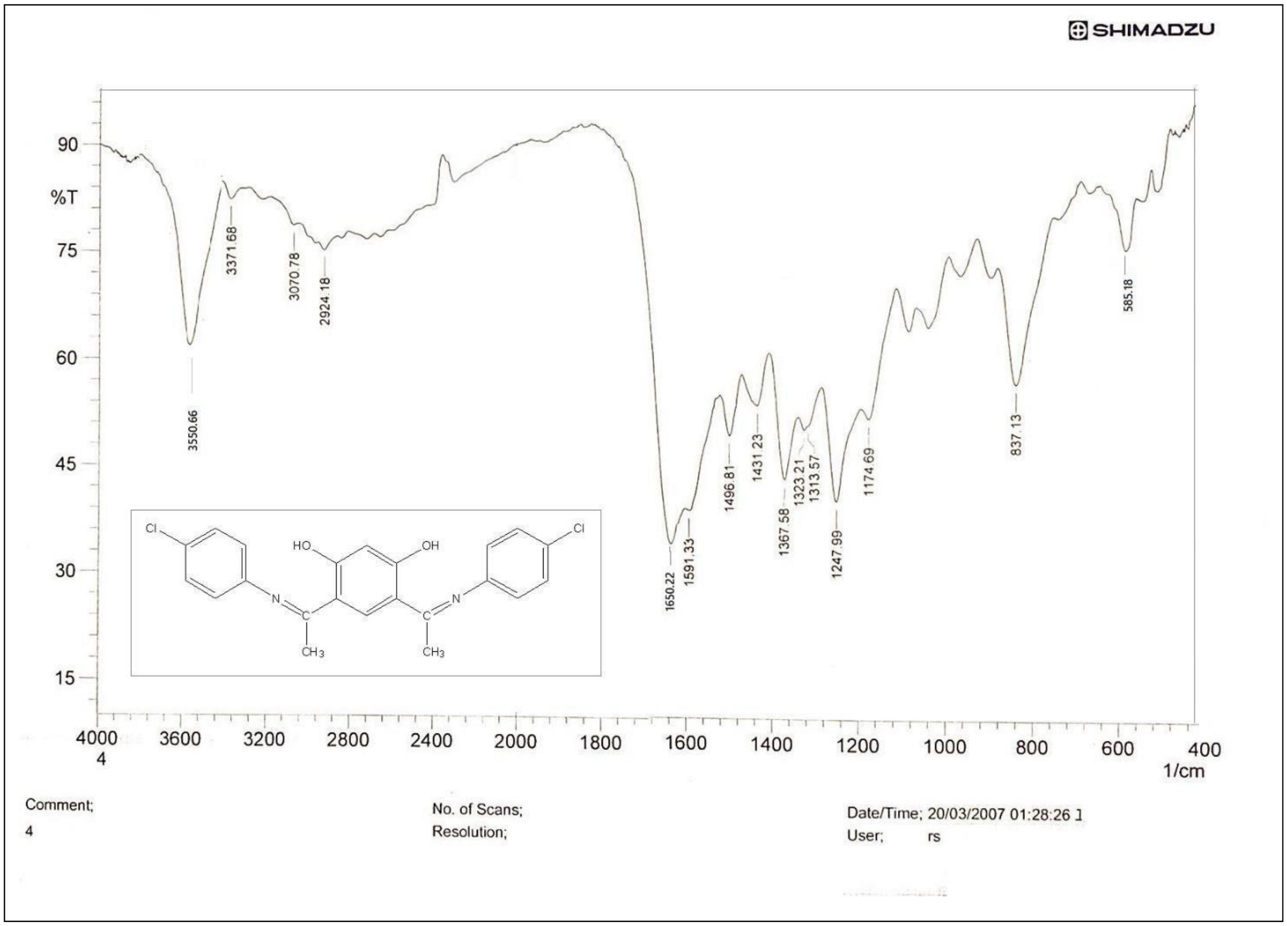
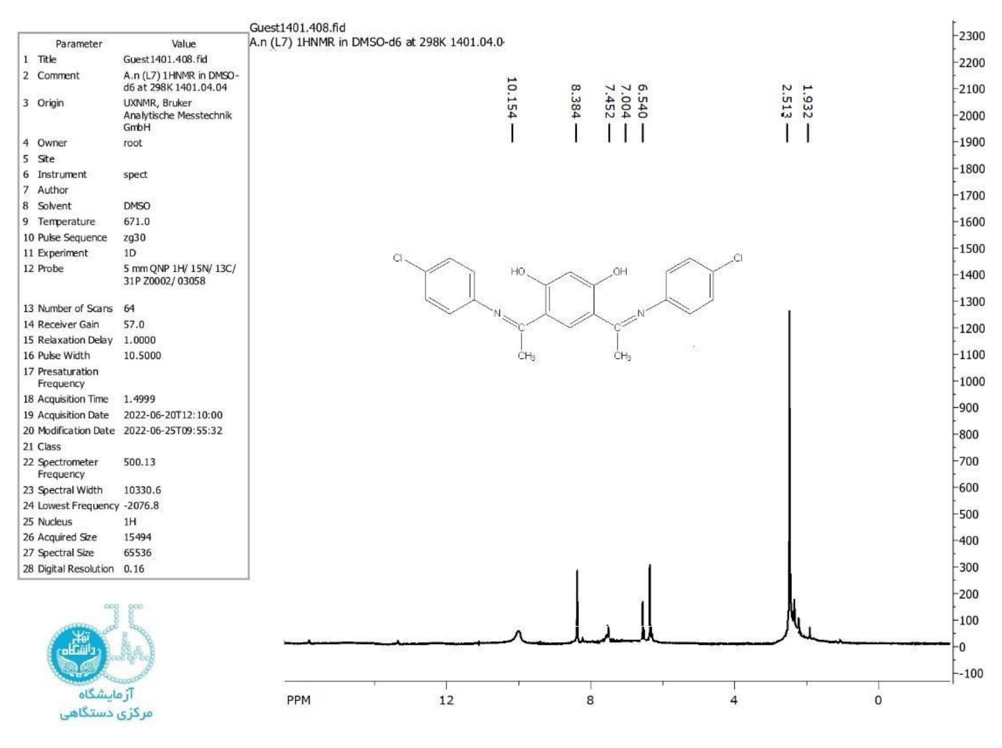


Figure (3-61) FTIR for compound RES25



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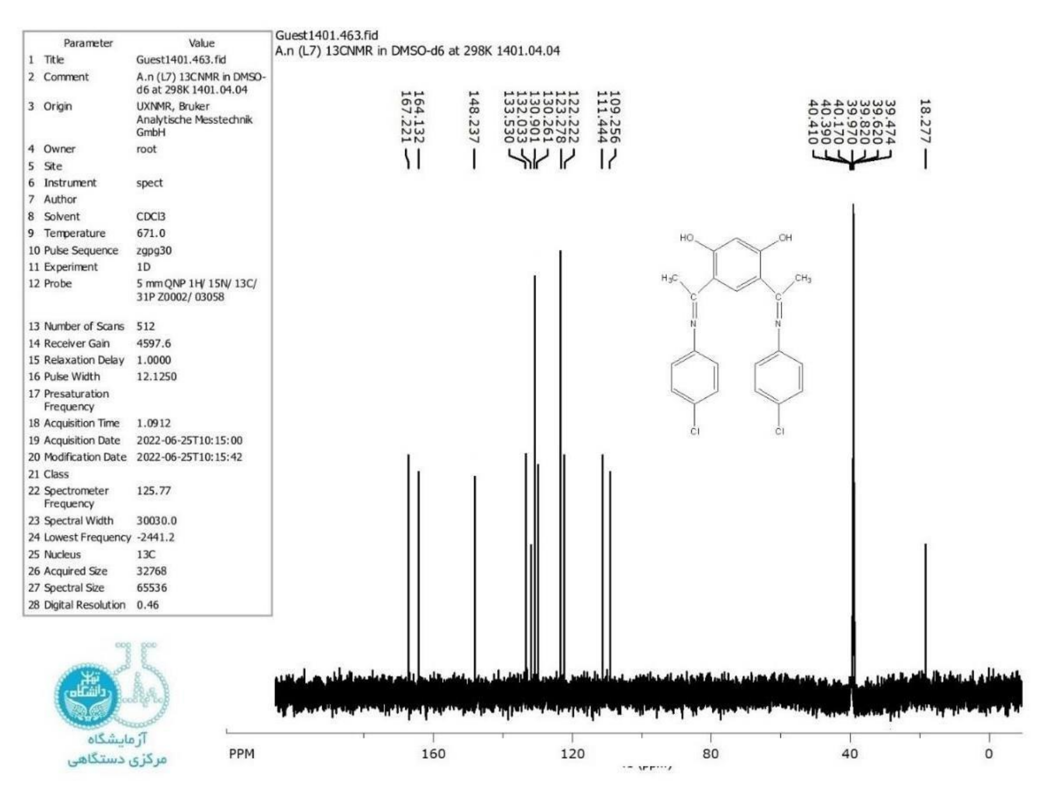
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	671.0
10	Pulse Sequence	zg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	64
14	Receiver Gain	57.0
15	Relaxation Delay	1.0000
16	Pulse Width	10.5000
17	Presaturation Frequency	
18	Acquisition Time	1.4999
19	Acquisition Date	2022-06-20T12:10:00
20	Modification Date	2022-06-25T09:55:32
21	Class	
22	Spectrometer Frequency	500.13
23	Spectral Width	10330.6
24	Lowest Frequency	-2076.8
25	Nucleus	1H
26	Acquired Size	15494
27	Spectral Size	65536
28	Digital Resolution	0.16

Figure (3-62) ^{1}HNMR for compound RES25



	Parameter	Value
1	Title	Guest1401.463.fid
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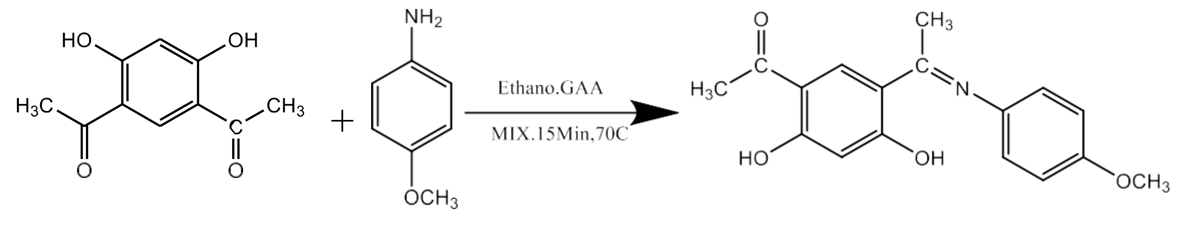
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	CDCl3
9	Temperature	671.0
10	Pulse Sequence	zgpg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	512
14	Receiver Gain	4597.6
15	Relaxation Delay	1.0000
16	Pulse Width	12.1250
17	Presaturation Frequency	
18	Acquisition Time	1.0912
19	Acquisition Date	2022-06-25T10:15:00
20	Modification Date	2022-06-25T10:15:42
21	Class	
22	Spectrometer Frequency	125.77
23	Spectral Width	30030.0
24	Lowest Frequency	-2441.2
25	Nucleus	13C
26	Acquired Size	32768
27	Spectral Size	65536
28	Digital Resolution	0.46

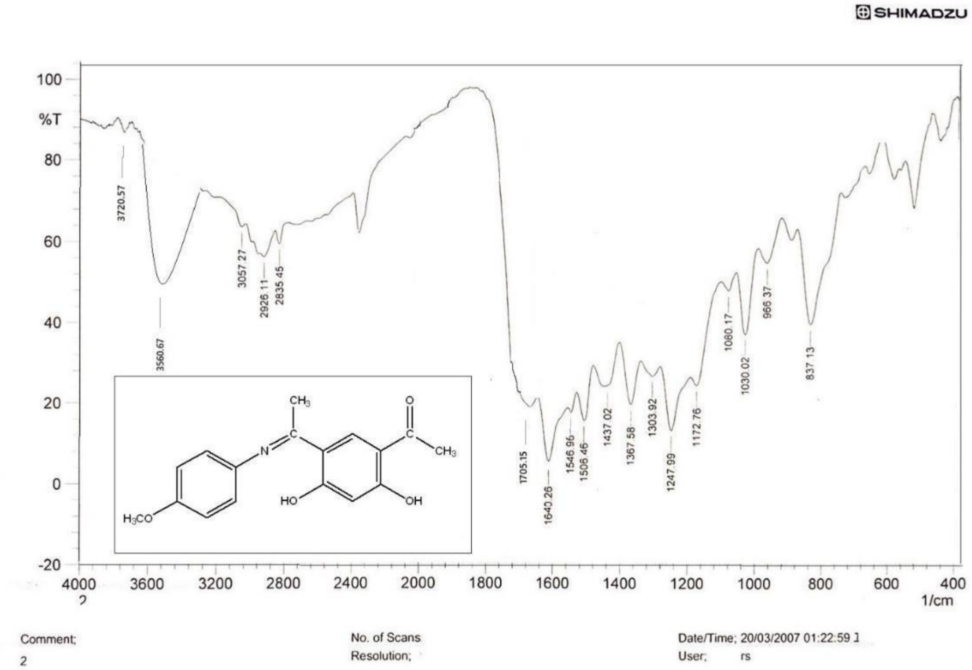
Figure (3-63) ^{13}CNMR for compound RES25

Schiff base (RES26) prepared from the reaction of R3 with 4-Methoxyaniline in existence ethanol , and Glacial acetic acid. Equation (3-22).



Equation (3-22): synthesis of RES26

FT-IR spectrum for RES26 showed the following values (vmax cm-1): 1646 (C=N imine), 3560-3720 (O-H phenol),1437 (C=C arom.) , 3057 (C-H arom.) , 2835-2926 (C-H SP3) , 1030 (C-O-C) , 1705 (C=O ketone) (Figure 3-64) . ^{1}H-NMR(500 MHz, δ ppm): 12.7-10.07 (O-H , phenol) , 6.7 - 7.8 (C-H, aromatic), 2.4-2.6-3.3 (methyl), 6.27 (C-H benzylidenimin), 2.5 (DMSO) (Figure 3-65). ^{13}C- NMR (125MHz, δ ppm): 56.6-27.3-18.4 (C,CH_3), 166.5 (C-N imine) , 109.3-130.6 (C-H arom.) , 111.3 -169.2 (C- arom.) , 40 DMSO , (Figure 3-66).



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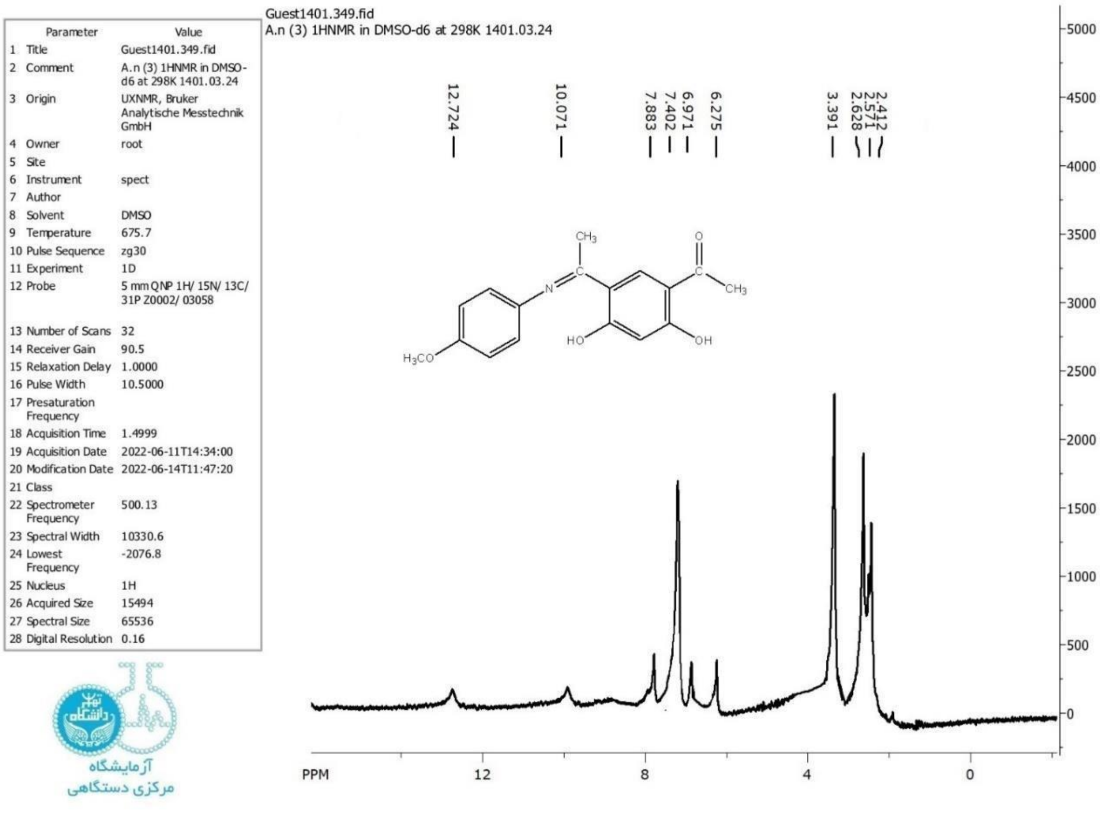
Resolution;

Date/Time; 20/03/2007 01:22:59 1
User; rs

Figure (3-64) FTIR for compound RES26



Guest1401.349.fid
A.n (3) 1HNMR in DMSO-d6 at 298K 1401.03.24

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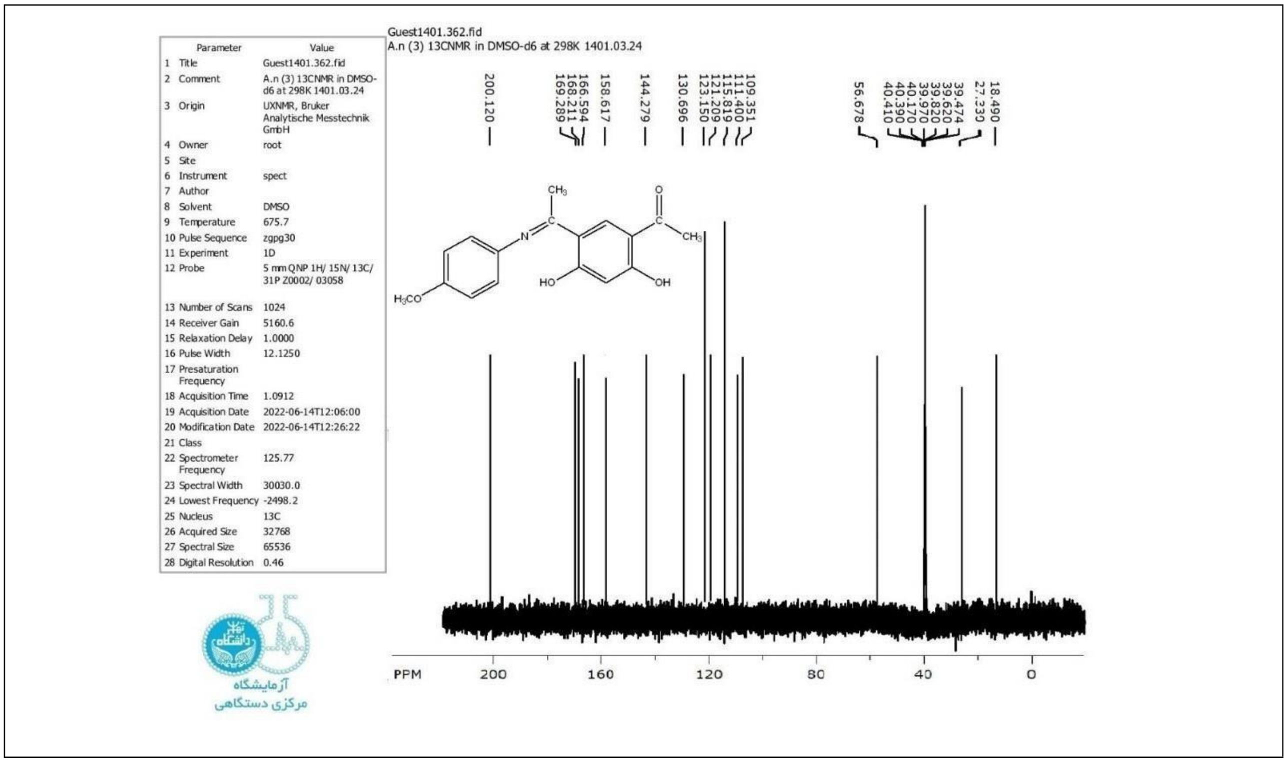
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	675.7
10	Pulse Sequence	zg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	32
14	Receiver Gain	90.5
15	Relaxation Delay	1.0000
16	Pulse Width	10.5000
17	Presaturation Frequency	
18	Acquisition Time	1.4999
19	Acquisition Date	2022-06-11T14:34:00
20	Modification Date	2022-06-14T11:47:20
21	Class	
22	Spectrometer Frequency	500.13
23	Spectral Width	10330.6
24	Lowest Frequency	-2076.8
25	Nucleus	1H
26	Acquired Size	15494
27	Spectral Size	65536
28	Digital Resolution	0.16

Figure (3-65) ^{1}HNMR for compound RES26



	Parameter	Value
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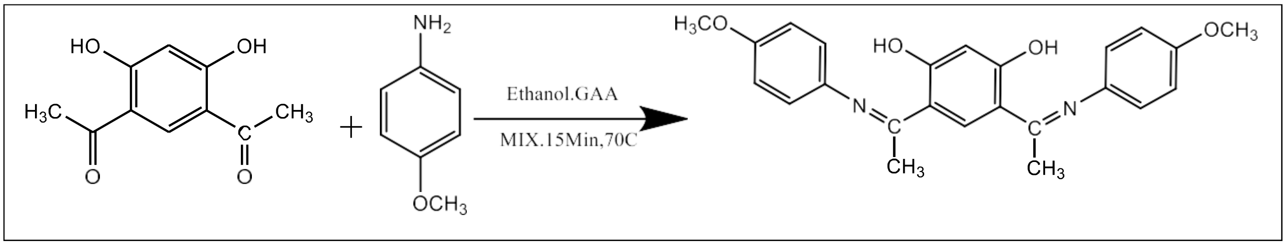
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	675.7
10	Pulse Sequence	zgpg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	1024
14	Receiver Gain	5160.6
15	Relaxation Delay	1.0000
16	Pulse Width	12.1250
17	Presaturation Frequency	
18	Acquisition Time	1.0912
19	Acquisition Date	2022-06-14T12:06:00
20	Modification Date	2022-06-14T12:26:22
21	Class	
22	Spectrometer Frequency	125.77
23	Spectral Width	30030.0
24	Lowest Frequency	-2498.2
25	Nucleus	13C
26	Acquired Size	32768
27	Spectral Size	65536
28	Digital Resolution	0.46

Figure (3-66) ^{13}CNMR for compound RES26

Schiff base (RES27) prepared from the reaction 1mole of R3 with 2mole of 4-methoxyaniline in existence ethanol , and Glacial acetic acid. Equation (3-23).



Equation (3-23): synthesis of RES27

FT-IR spectrum for RES27 showed the following values (vmax cm-1): 1648 (C=N imine), 3590.20 (O-H phenol),1454 (C=C arom.) , 3001 (C-H arom.) , 2941.54 (C-H SP3) , 1247.99 (C-O-C) , (Figure 3-67) . 1H-NMR (500MHz,δ ppm): 9.8 (O-H , phenol) , 7.0 - 7.5 (C-H, aromatic), 2.4-3.6 (methyl), 6.64-7.03 (C-H benzylidenimin), 2.5 (DMSO) (Figure 3-68). ^{13}C- NMR (125MHz, δ ppm): 56.1-18.3 (C,CH$_3$), 167.7(C-N imine) , 109.2-131.9 (C-H arom.) , 111.4 -164.4 (C-arom.) , 39.9 DMSO , (Figure 3-69).

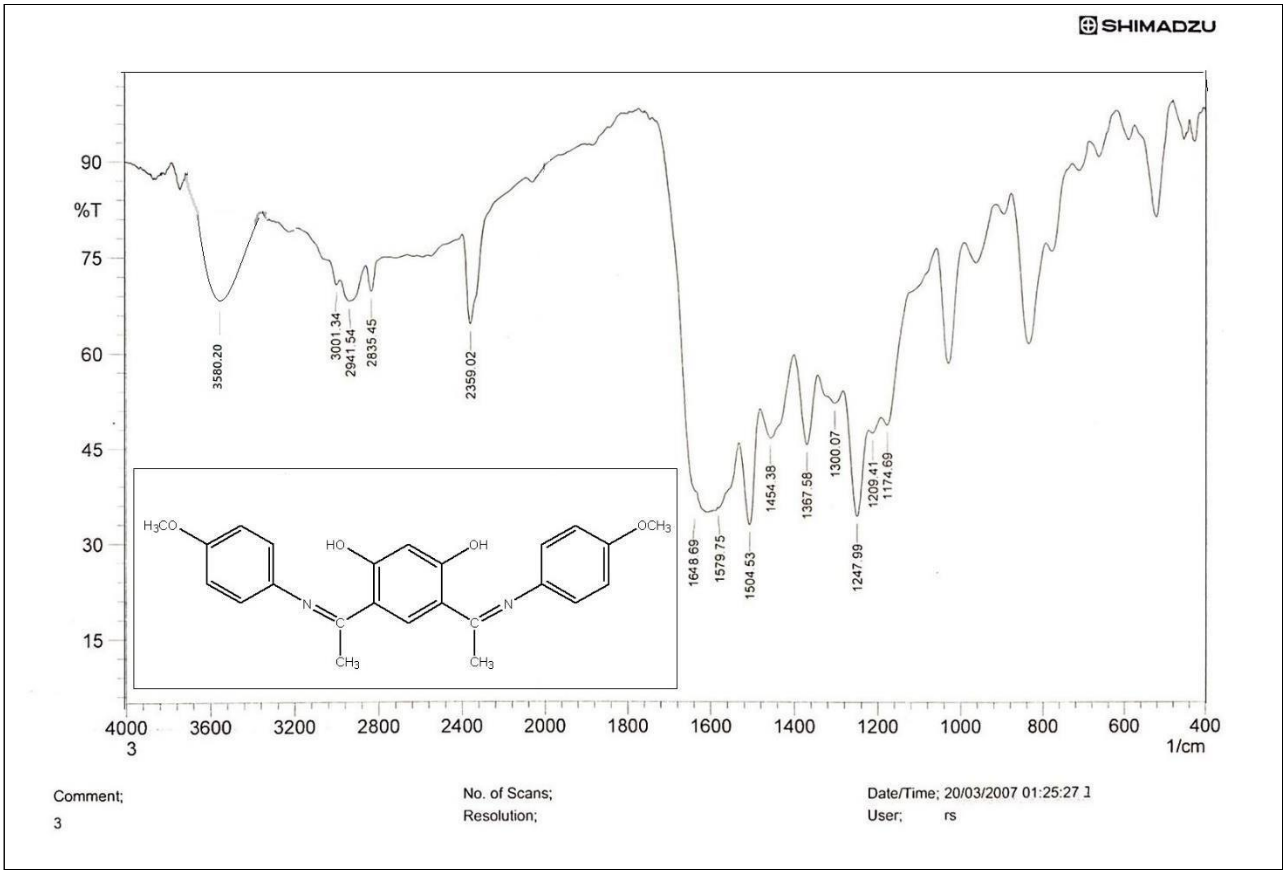
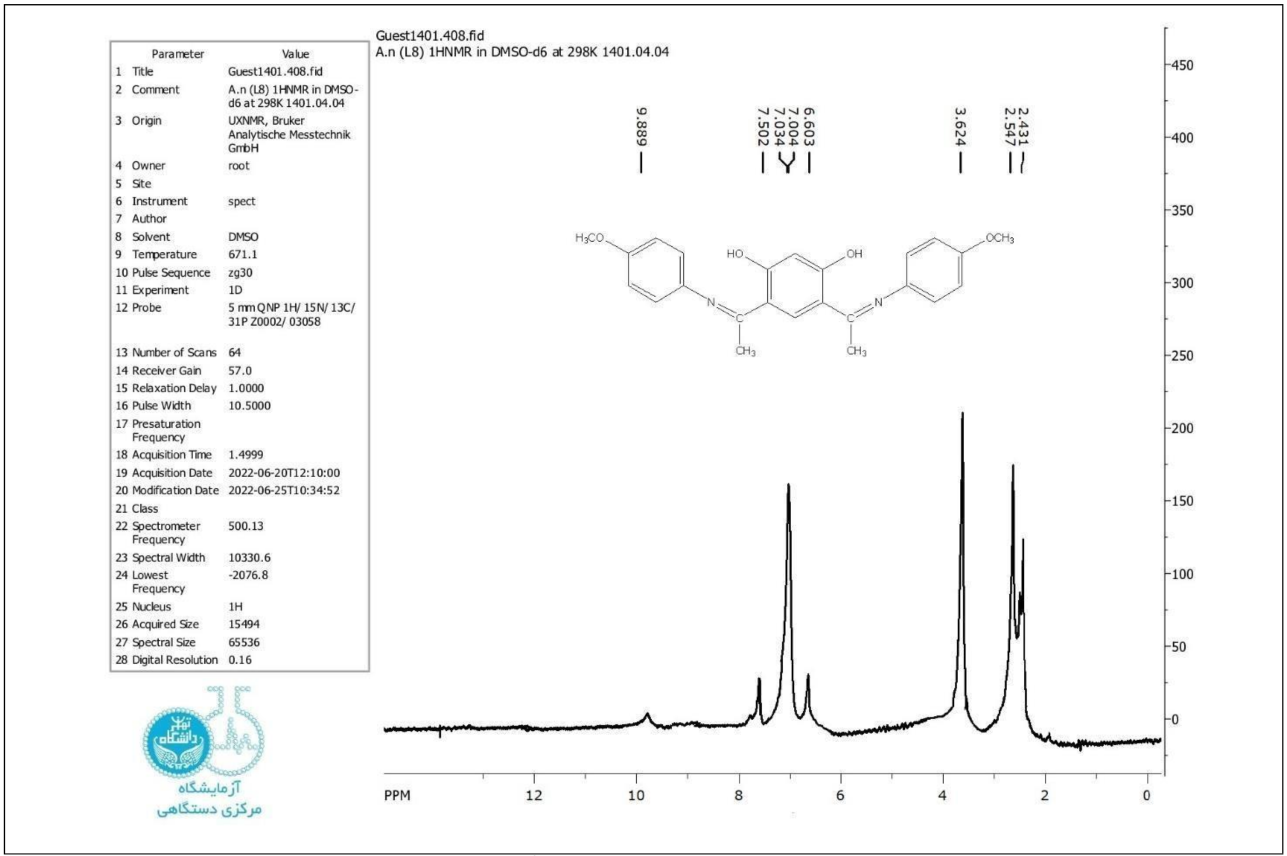


Figure (3-67) FTIR for compound RES27



Guest1401.408.fid
A.n (L8) 1HNMR in DMSO-d6 at 298K 1401.04.04

	Parameter	Value
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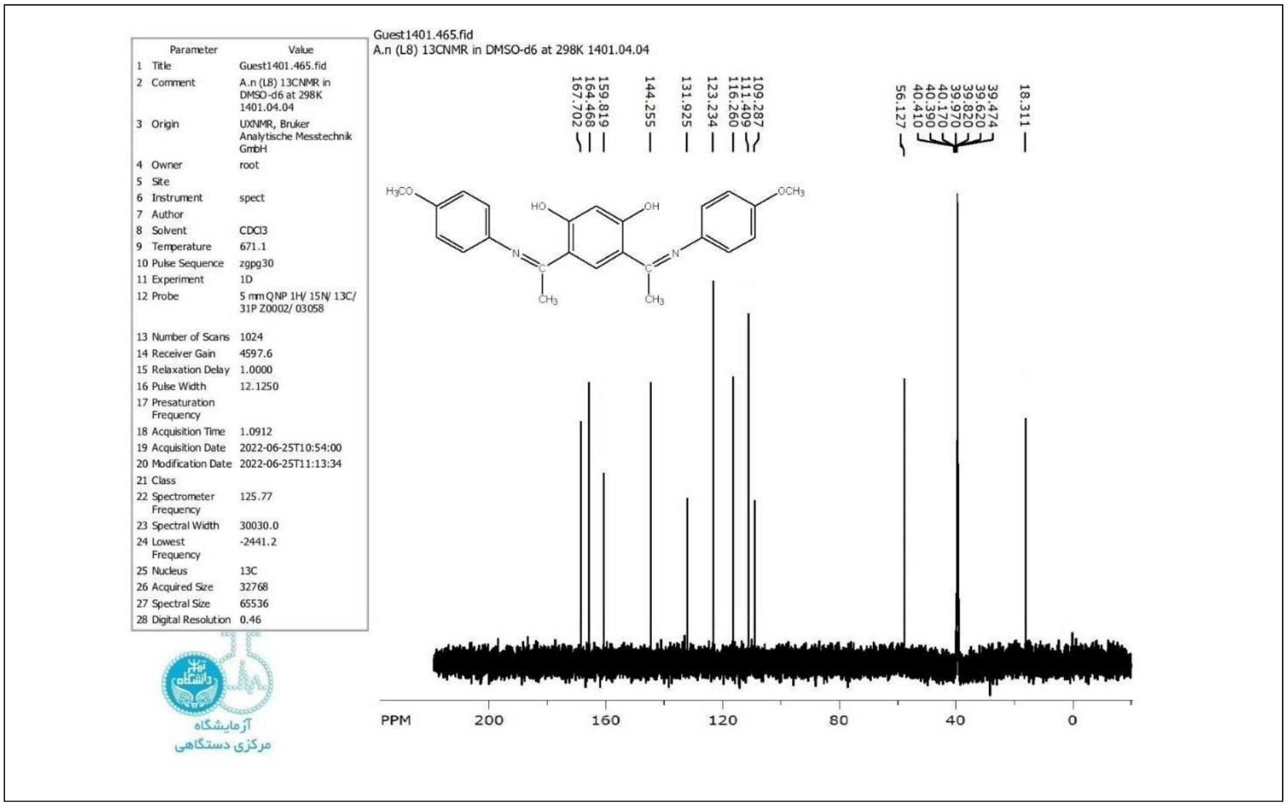
2	Comment	A.n (L8) 1HNMR in DMSO-d6 at 298K 1401.04.04
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	671.1
10	Pulse Sequence	zg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	64
14	Receiver Gain	57.0
15	Relaxation Delay	1.0000
16	Pulse Width	10.5000
17	Presaturation Frequency	
18	Acquisition Time	1.4999
19	Acquisition Date	2022-06-20T12:10:00
20	Modification Date	2022-06-25T10:34:52
21	Class	
22	Spectrometer Frequency	500.13
23	Spectral Width	10330.6
24	Lowest Frequency	-2076.8
25	Nucleus	1H
26	Acquired Size	15494
27	Spectral Size	65536
28	Digital Resolution	0.16

Figure (3-68) ^{1}HNMR for compound RES27

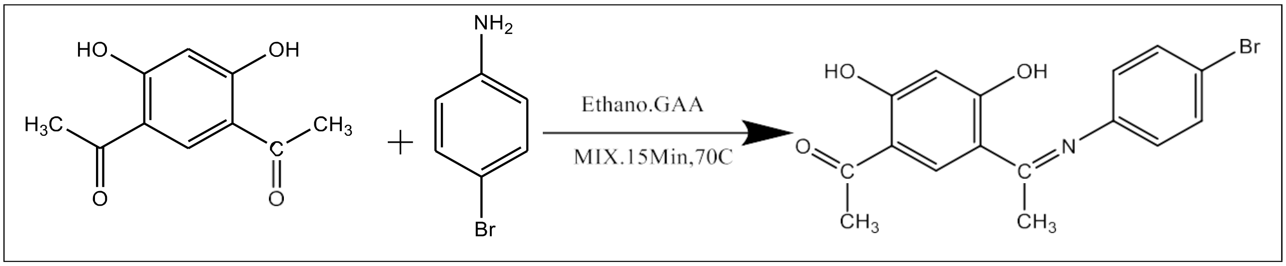


Guest1401.465.fid
A.n (L8) 13CNMR in DMSO-d6 at 298K 1401.04.04

	Parameter	Value
1	Title	Guest1401.465.fid
2	Comment	A.n (L8) 13CNMR in DMSO-d6 at 298K 1401.04.04
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	CDCl3
9	Temperature	671.1
10	Pulse Sequence	zgpg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	1024
14	Receiver Gain	4597.6
15	Relaxation Delay	1.0000
16	Pulse Width	12.1250
17	Presaturation Frequency	
18	Acquisition Time	1.0912
19	Acquisition Date	2022-06-25T10:54:00
20	Modification Date	2022-06-25T11:13:34
21	Class	
22	Spectrometer Frequency	125.77
23	Spectral Width	30030.0
24	Lowest Frequency	-2441.2
25	Nucleus	13C
26	Acquired Size	32768
27	Spectral Size	65536
28	Digital Resolution	0.46

Figure (3-69) ^{13}CNMR for compound RES27

Schiff base (RES28) prepared from the reaction R3 with 4-Bromoaniline in existence ethanol , and Glacial acetic acid. Equation (3-24).



Equation (3-24): synthesis of RES29

FT-IR spectrum for RES28 showed the following values (Vmax cm-1): 1637.62 (C=N imine), 3602-3367 (O-H alcohol),1491(C=C arom.) , 3074 (C-H arom.) , 2924.18 (C-H SP3), 1715 (C=O ketone) , 558 (C-Br) (Figure 3-70) . ^{1}H-NMR (500 MHz,δ ppm): 12.7-10.2 (O-H , phenol) , 7.03 - 7.25 (C-H, aromatic), 2.6-1.9 (methyl), 6.2-8.1 (C-H benzylidenimin), 2.5 (DMSO) (Figure 3-71). ^{13}C- NMR (125 MHz,δ ppm): 18.4-27.4 (C,CH_3), 165.9 (C-N imine) , 109.2-133.2 (C-H arom.) , 111.2 -168.2 (C- arom.) , 199.6 (C - Carbonyl) 39.9 DMSO , (Figure 3-72).

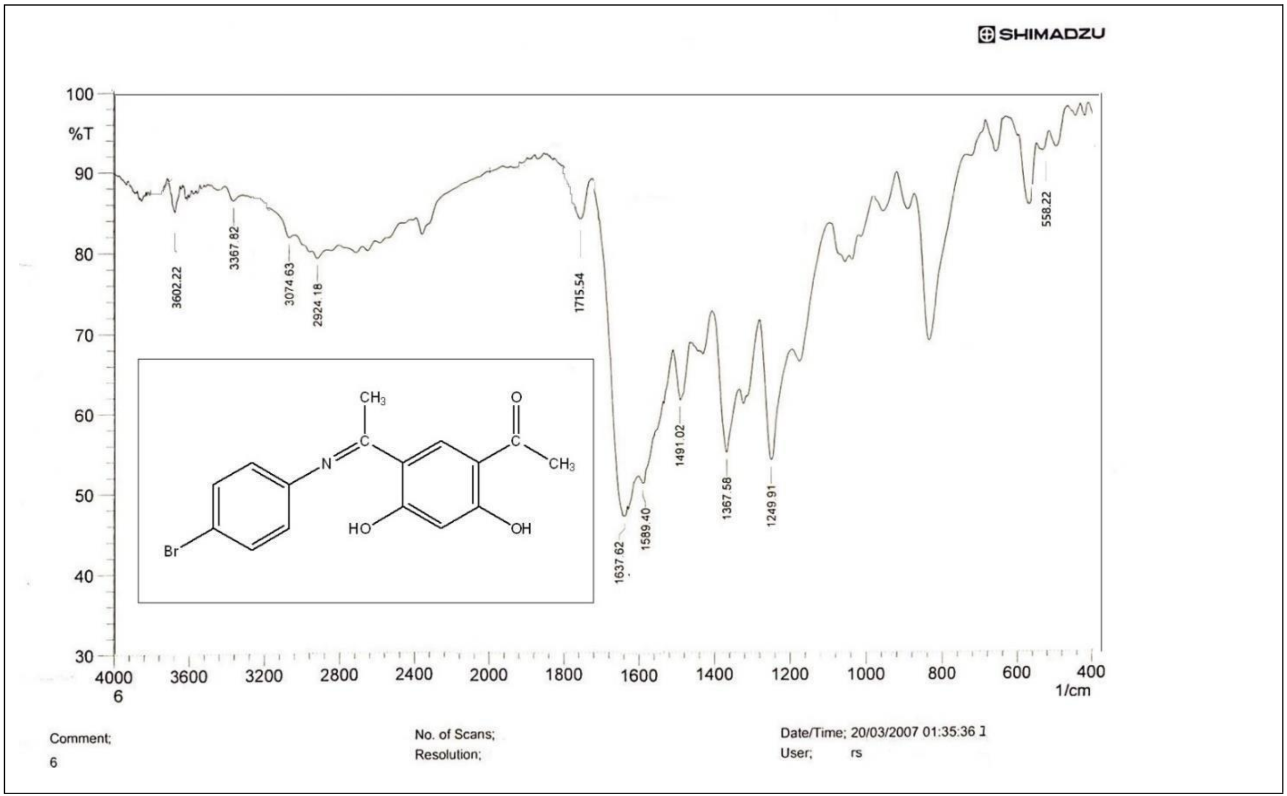
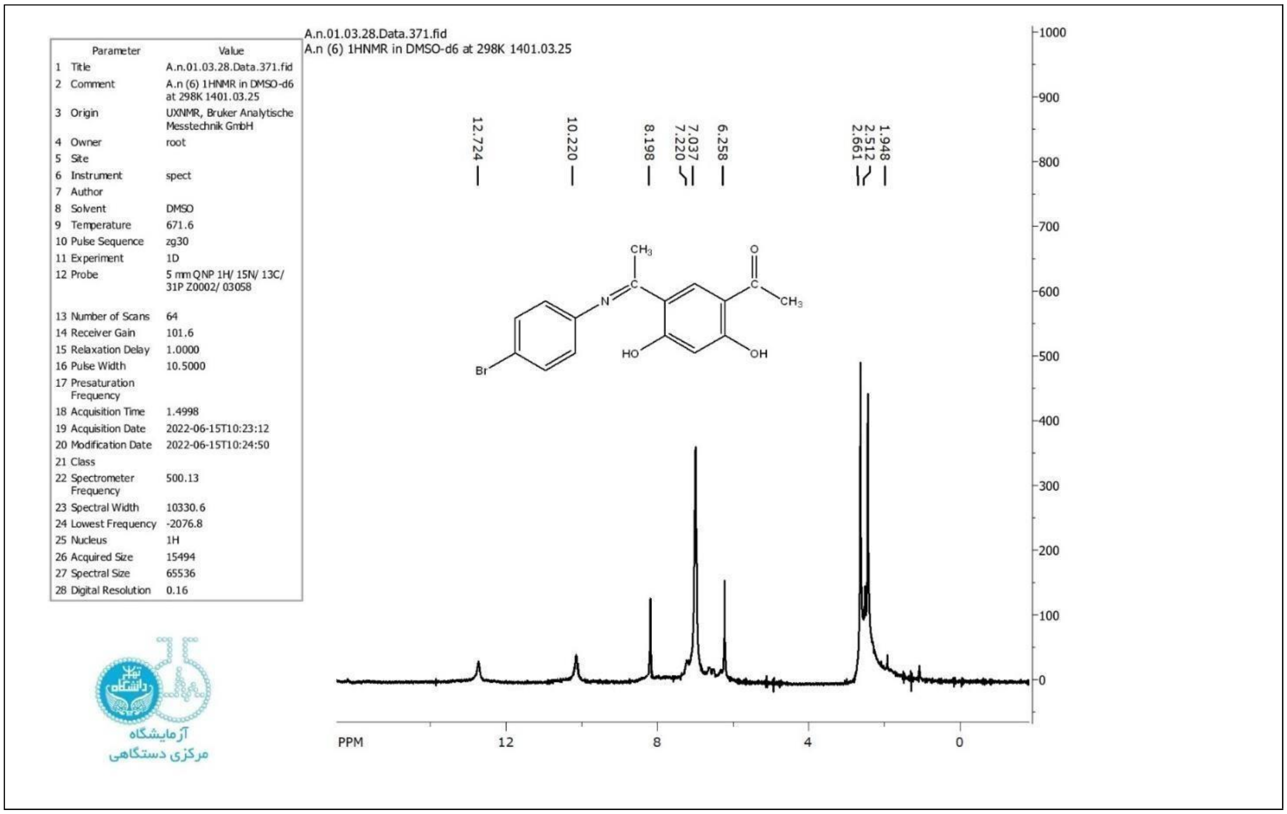
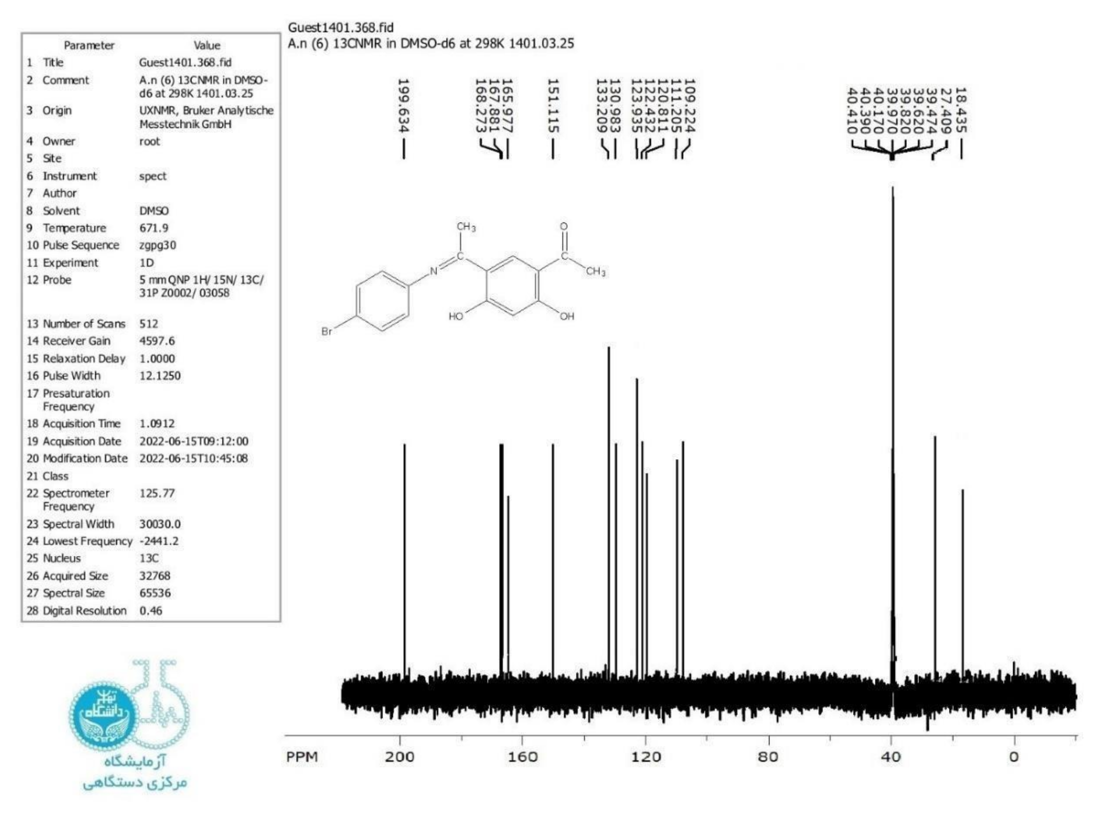


Figure (3-70) FTIR for compound RES28



Parameter	Value
1 Title	A.n.01.03.28.Data.371.fid
2 Comment	A.n (6) 1HNMR in DMSO-d6 at 298K 1401.03.25
3 Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4 Owner	root
5 Site	
6 Instrument	spect
7 Author	
8 Solvent	DMSO
9 Temperature	671.6
10 Pulse Sequence	zg30
11 Experiment	1D
12 Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13 Number of Scans	64
14 Receiver Gain	101.6
15 Relaxation Delay	1.0000
16 Pulse Width	10.5000
17 Presaturation Frequency	
18 Acquisition Time	1.4998
19 Acquisition Date	2022-06-15T10:23:12
20 Modification Date	2022-06-15T10:24:50
21 Class	
22 Spectrometer Frequency	500.13
23 Spectral Width	10330.6
24 Lowest Frequency	-2076.8
25 Nucleus	1H
26 Acquired Size	15494
27 Spectral Size	65536
28 Digital Resolution	0.16

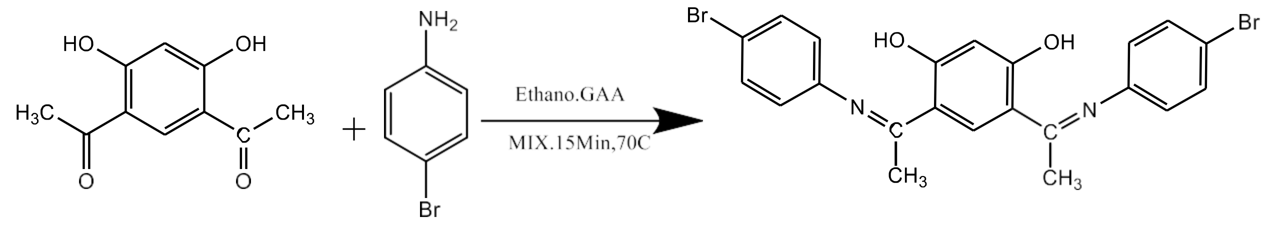
Figure (3-71) ^{1}HNMR for compound RES28



	Parameter	Value
1	Title	Guest1401.368.fid
2	Comment	A.n (6) 13CNMR in DMSO-d6 at 298K 1401.03.25
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	671.9
10	Pulse Sequence	zgpg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	512
14	Receiver Gain	4597.6
15	Relaxation Delay	1.0000
16	Pulse Width	12.1250
17	Presaturation Frequency	
18	Acquisition Time	1.0912
19	Acquisition Date	2022-06-15T09:12:00
20	Modification Date	2022-06-15T10:45:08
21	Class	
22	Spectrometer Frequency	125.77
23	Spectral Width	30030.0
24	Lowest Frequency	-2441.2
25	Nucleus	13C
26	Acquired Size	32768
27	Spectral Size	65536
28	Digital Resolution	0.46

Figure (3-72) ^{13}CNMR for compound RES28

Schiff base (RES29) prepared from the reaction 1mole of R3 with 2mole of 4-bromoaniline in existence ethanol , and Glacial acetic acid. Equation (3-25).



Equation (3-25): synthesis of RES29

FT-IR spectrum for RES29 showed the following values (vmax cm^{-1}): 1637.62

(C=N imine), 3365.90 (O-H phenol),1489.20(C=C arom.) , 3072.71 (C-H arom.) , 2926.11 (C-H SP3) , 578.66 (C-Br) (Figure 3-73) . ^{1}H-NMR (500MHz, δ ppm): 11.3 (O-H , phenol) , 7.03 - 7.9 (C-H, aromatic), 2.4 (methyl), 6.99-8.19 (C-H benzylidenimin), 2.5 (DMSO) (Figure 3-74). ^{13}C- NMR (125MHz, δ ppm): 18.3 (C,CH_3), 167.2 (C-N imine) , 109.2-133.3 (C-H arom.) , 111.8 -163.7 (C- arom.) , 39.9 DMSO , (Figure 3-75).

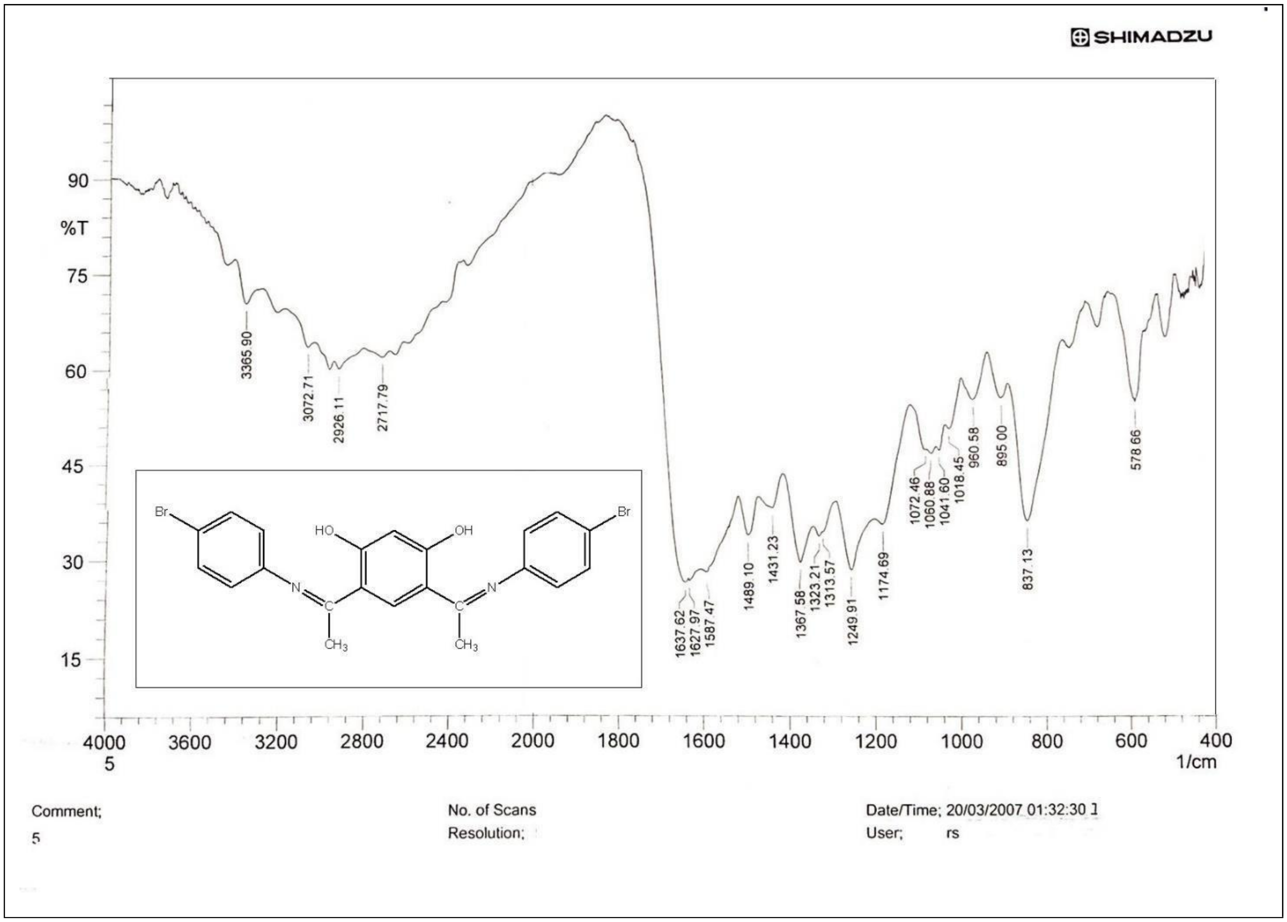
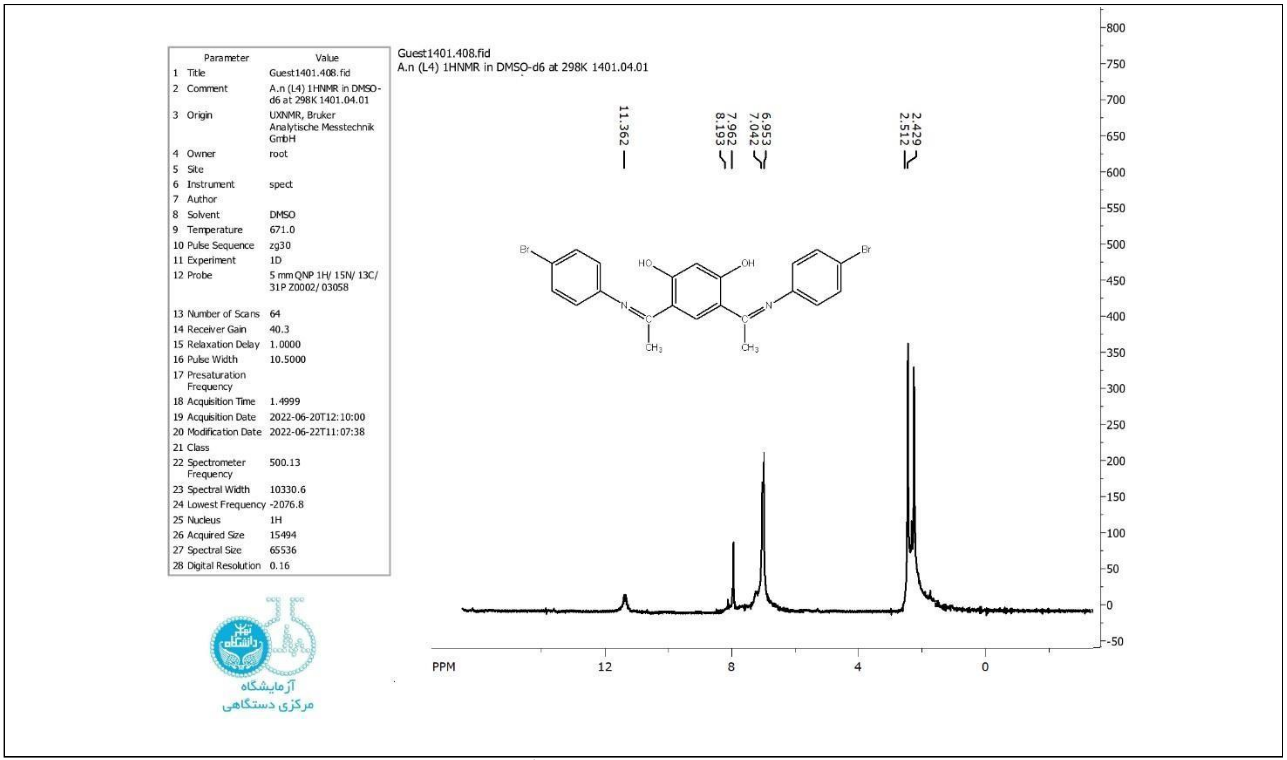


Figure (3-73) FTIR for compound RES29



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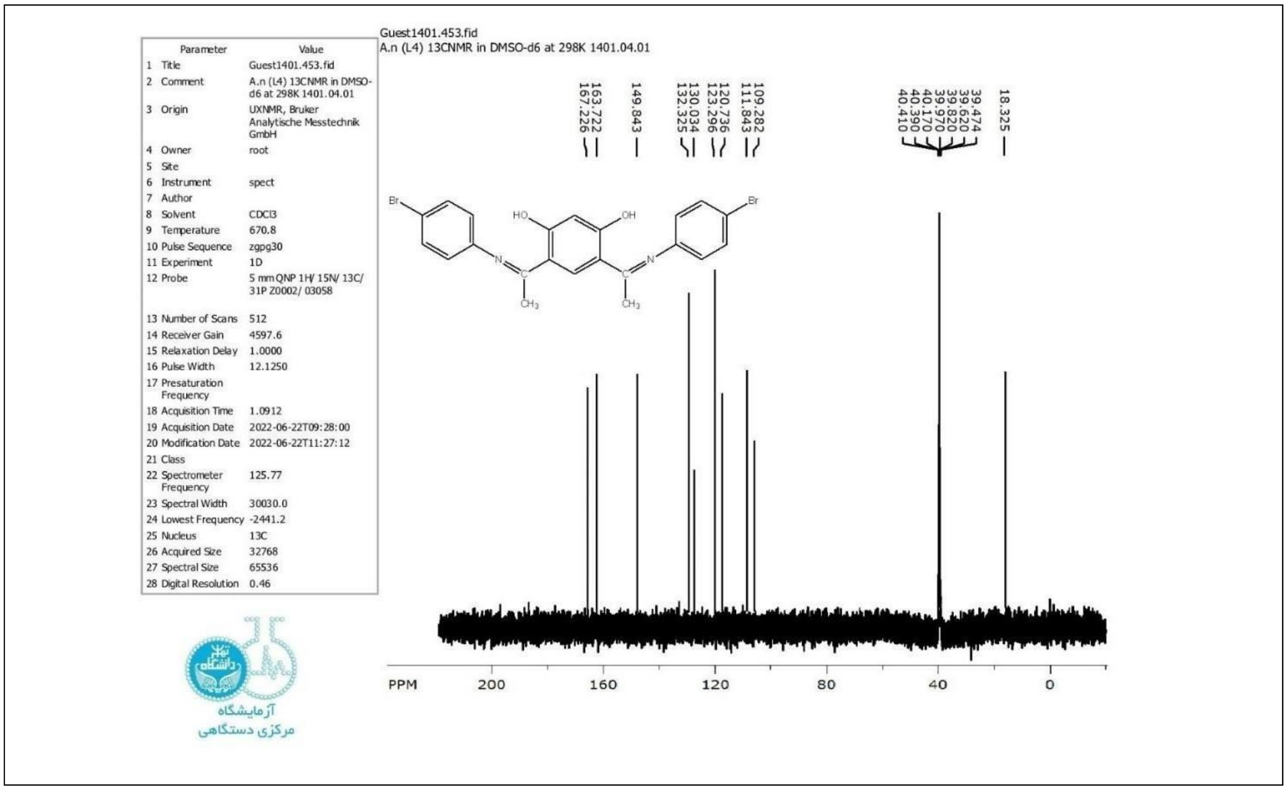
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	DMSO
9	Temperature	671.0
10	Pulse Sequence	zg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	64
14	Receiver Gain	40.3
15	Relaxation Delay	1.0000
16	Pulse Width	10.5000
17	Presaturation Frequency	
18	Acquisition Time	1.4999
19	Acquisition Date	2022-06-20T12:10:00
20	Modification Date	2022-06-22T11:07:38
21	Class	
22	Spectrometer Frequency	500.13
23	Spectral Width	10330.6
24	Lowest Frequency	-2076.8
25	Nucleus	1H
26	Acquired Size	15494
27	Spectral Size	65536
28	Digital Resolution	0.16

Guest1401.408.fid
A.n (L4) 1HNMR in DMSO-d6 at 298K 1401.04.01

Figure (3-74) ^{1}HNMR for compound RES29



Parameter		Value
1	Title	Guest1401.453.fid
2	Comment	A.n (L4) 13CNMR in DMSO-d6 at 298K 1401.04.01
3	Origin	UXNMR, Bruker Analytische Messtechnik GmbH
4	Owner	root
5	Site	
6	Instrument	spect
7	Author	
8	Solvent	CDCl3
9	Temperature	670.8
10	Pulse Sequence	zgpg30
11	Experiment	1D
12	Probe	5 mm QNP 1H/ 15N/ 13C/ 31P Z0002/ 03058
13	Number of Scans	512
14	Receiver Gain	4597.6
15	Relaxation Delay	1.0000
16	Pulse Width	12.1250
17	Presaturation Frequency	
18	Acquisition Time	1.0912
19	Acquisition Date	2022-06-22T09:28:00
20	Modification Date	2022-06-22T11:27:12
21	Class	
22	Spectrometer Frequency	125.77
23	Spectral Width	30030.0
24	Lowest Frequency	-2441.2
25	Nucleus	13C
26	Acquired Size	32768
27	Spectral Size	65536
28	Digital Resolution	0.46

Guest1401.453.fid
A.n (L4) 13CNMR in DMSO-d6 at 298K 1401.04.01

Figure (3-75) ^{13}CNMR for compound RES29

Table (3-1): C.H.N.S Elementary analysis for some prepared derivatives

		C%		H%		N%		S%	
Comp.	Molecular formula	Calculated	Found	Calculated	Found	Calculated	Found	Calculated	Found
RES19	$C_{14}H_{12}NO_2Cl$	64.1	64.4	4.5	4.41	5.3	5.28		
RES24	$C_{16}H_{14}NO_3Cl$	63.2	63.3	4.65	4.7	4.61	4.95		
RES23	$C_{22}H_{18}N_4O_6$	60.8	60.92	4.14	4.21	12.8	12.79		
RES18	$C_{14}H_{12}N_2O_4$	61.7	61.34	4.4	4.39	10.2	10.3		
RES14	$C_{28}H_{27}N_3O_9S$	57.7	57.8	4.6	4.62	7.2	7.09	5.502	5.43
RES16	$C_{31}H_{29}N_7O_{11}$	55.06	54.91	4.2	4.08	14.5	14.35		
RES9	$C_{29}H_{27}N_7O_{10}$	54.9	55.2	4.26	4.3	15.4	15.51		
RES7	$C_{26}H_{25}N_3O_8S$	57.8	58.01	4.63	4.68	7.78	7.8	5.93	5.89

3-5. The solubility:

All generated compounds are moderately soluble in water due to their relatively high molecular weight, while they are entirely soluble in DMSO and ethanol. The solubility of synthesized compounds was examined using various polarity solvents. Because the polarity of created compounds is higher than the polarity of these solvents.

Table (3- 2): The solubility of prepared derivatives in different solvents.

Solv. Comp.	DMSO	water	Etha.	Ace.	Meth.	Haxe.	1,4-dioxan	DCM	DMF	Diet. ether	P. ether	Ethyl ace.
RES5	+	-	+	-	+	-	+	partial	+	-	-	-
RES6	+	partial	+	-	+	-	+	+	+	-	-	partial
RES7	+	-	+	-	partial	+	-	-	+	partial	-	-
RES8	+	-	+	-	+	-	+	+	+	-	-	+
RES9	+	partial	+	+	+	-	partial	partial	+	-	-	partial
RES10	+	+	-	-	-	+	+	-	+	-	-	-
RES11	+	partial	-	partial	-	-	-	+	-	+	-	-
RES12	+	partial	-	-	-	partial	-	partial	+	+	-	+
RES13	+	partial	-	-	-	-	+	partial	+	partial	-	-
RES14	+	partial	-	+	partial	+	-	+	+	-	-	-
RES15	+	partial	+	-	+	partial	partial	-	+	+	-	partial
RES16	+	partial	+	-	partial	-	+	-	-	-	-	-
RES17	+	partial	+	-	partial	-	-	-	+	partial	-	-
RES18	+	-	-	Partial	-	-	partial	+	+	-	-	+
RES19	+	-	Partial	-	+	+	-	-	+	-	-	-
RES20	+	partial	+	+	+	-	partial	-	-	partial	-	-
RES21	+	-	-	partial	-	Partial	+	-	+	-	-	+
RES22	+	partial	+	+	partial	-	-	partial	-	-	-	-
RES23	+	partial	+	+	+	Partial	-	+	+	partial	-	partial
RES24	+	partial	+	+	+	-	Partial	-	+	partial	-	-
RES25	+	partial	+	+	partial	Partial		-	+	+	-	-
RES26	+	partial	+	+	-	partial	partial	-	-	-	-	-
RES27	+	partial	+	+	-	-	-	-	+	+	-	-
RES28	+	partial	+	+	partial	partial	-	-	+	-	-	-
RES29	+	partial	+	+	-	+	+	-	+	-	-	-

3.6 Biological Activity:

3.6.1. Antibacterial activity

The results showed that most of the investigated chemicals have good antibacterial activity. These bacteria were selected due to their vast clinical value and the fact that they are resistant to a wide range of antibiotics and chemical drugs in addition to causing a number of ailments. According to Table 3, the synthesized chemicals can suppress the bacteria by changing their concentrations, proving that they have biological action against them.

figure (3-76,3-77). illustrates the variation in toxicity caused by changes to functional groups or structures.

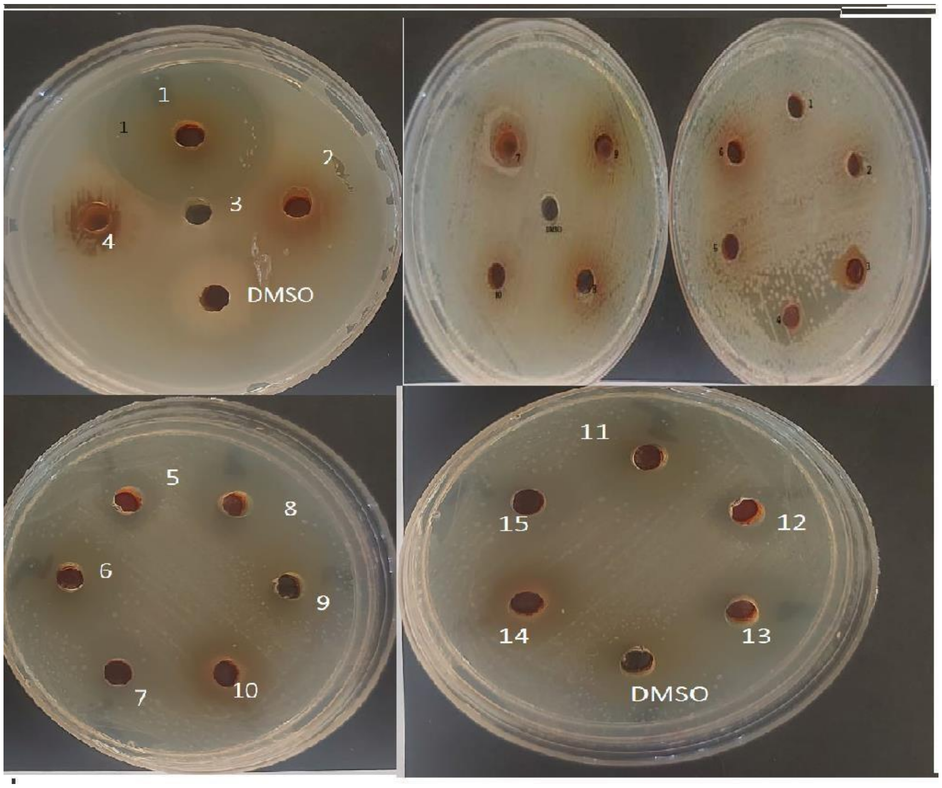


Figure (3-76). Staphylococcus aureus activity test

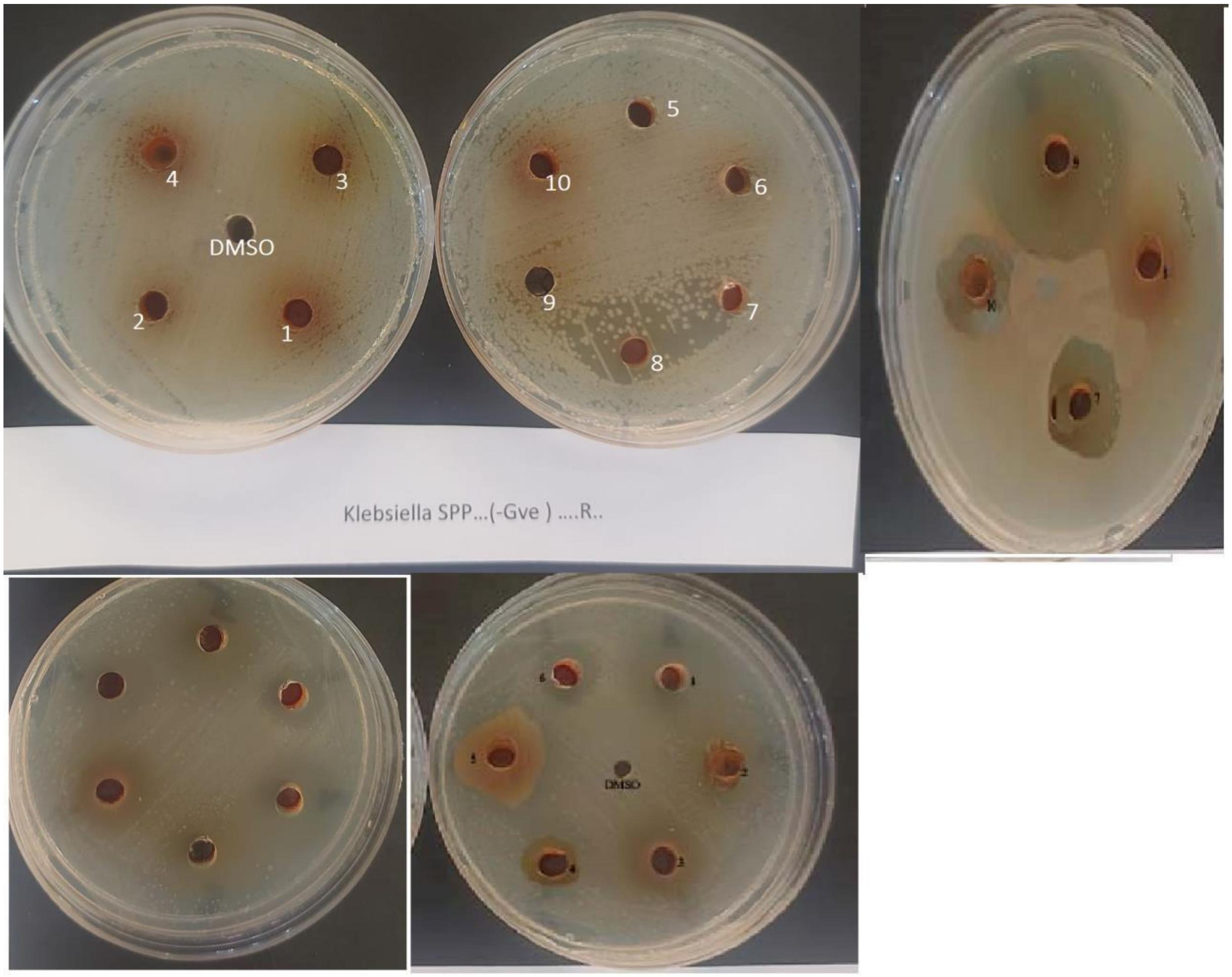


Figure (3-77) Klebsiella pneumonia activity test

Table (3-3): Antibacterial activity for compounds (RES5-RES29)

No. of Comp.	Antibacterial activity test	
	Staphylococcus aureus (Gram-positive bacteria)	*klebsiella pneumonia* (Gram-negative bacteria)
Control	**23**	**16**
RES5	**30**	**-**
RES6	**17**	**-**
RES7	**20**	**-**
RES8	**30**	**-**
RES9	**11**	**-**
RES10	**20**	**-**
RES11	**25**	**-**
RES12	**35**	**-**
RES13	**-**	**-**
RES14	**-**	**-**
RES15	**26**	**14**
RES16	**18**	**0**
RES17	**20**	**15**
RES18	**17**	**10**
RES19	**8**	**10**
RES20	**10**	**15**
RES21	**17**	**10**
RES22	**23**	**10**
RES23	**0**	**8**
RES24	**14**	**0**
RES25	**20**	**15**
RES26	**24**	**17**

RES27	**26**	**19**
RES28	**38**	**28**
RES29	**29**	**18**

3-6-2. Antioxidants activity

The conventional DPPH method was used to perform the compounds' antiradical action .Table (3-4) Fig: (3-78) The majority of the substances had moderate to high antioxidant activity when compared to normal (ascorbic acid) activity (IC50=4.02 mg/mL).

Table (3-4): Antioxidants activity for compounds (RES5- RES29)

Sample No.	Scaving %			
	25 mg/mL	50 mg/mL	100 mg/mL	IC50
RES5	36.15	55.83	68.03	1.79
RES6	37.45	50.28	60.28	1.79
RES7	85.43	37.05	46.88	2.33
RES8	43	69.08	91.28	1.26
RES9	38.25	55.53	62.03	1.83
RES10	35.87	60.11	83.13	1.59
RES11	45.5	62.05	86.62	1.28
RES12	40.95	59.25	73.24	1.51
RES13	48.25	58.03	65.23	1.15
RES14	45.87	64.31	80.13	1.21
RES16	39.25	58.83	64.83	1.66

RES17	34.25	52.25	58.58	2.13
RES18	25.25	33.25	44.58	3.62
RES19	24.32	31.09	45.87	2.88
RES20	45	72.08	91.08	1.15
RES21	35.5	54.33	60.83	1.98
RES22	39.5	65	91	1.41
RES23	38.12	56.07	69..	1.8
RES24	44.5	67.25	89.42	1.24
RES25	42	68.04	90.8	1.1
RES26	23.09	30.02	46.67	3.01
RES27	41.5	66.08	48.61	2.5
RES28	37	53.43	59.9	1.67
(Ascorbic acid)	80.95	89.25	93.54	4.02

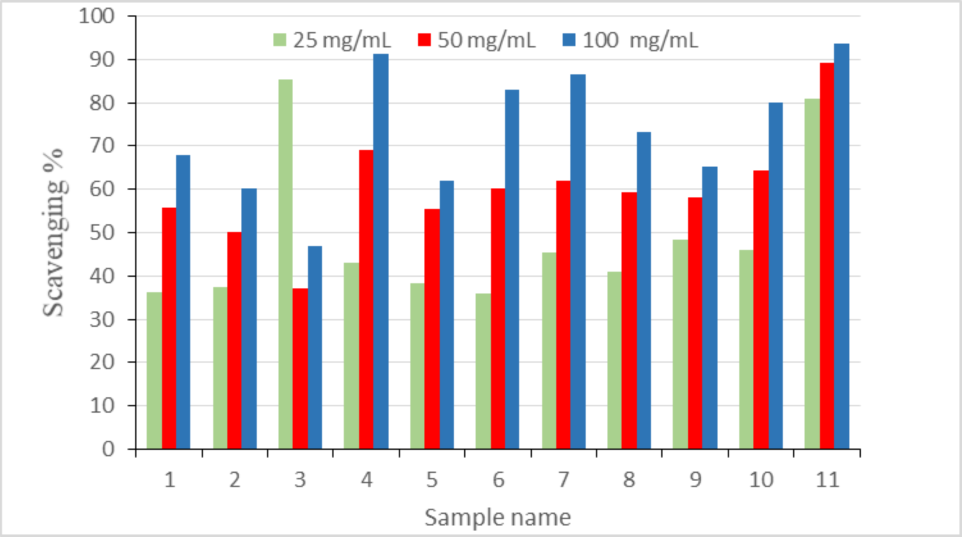


Figure (3-79): standard DPPH method for compound (RES5-RES14)

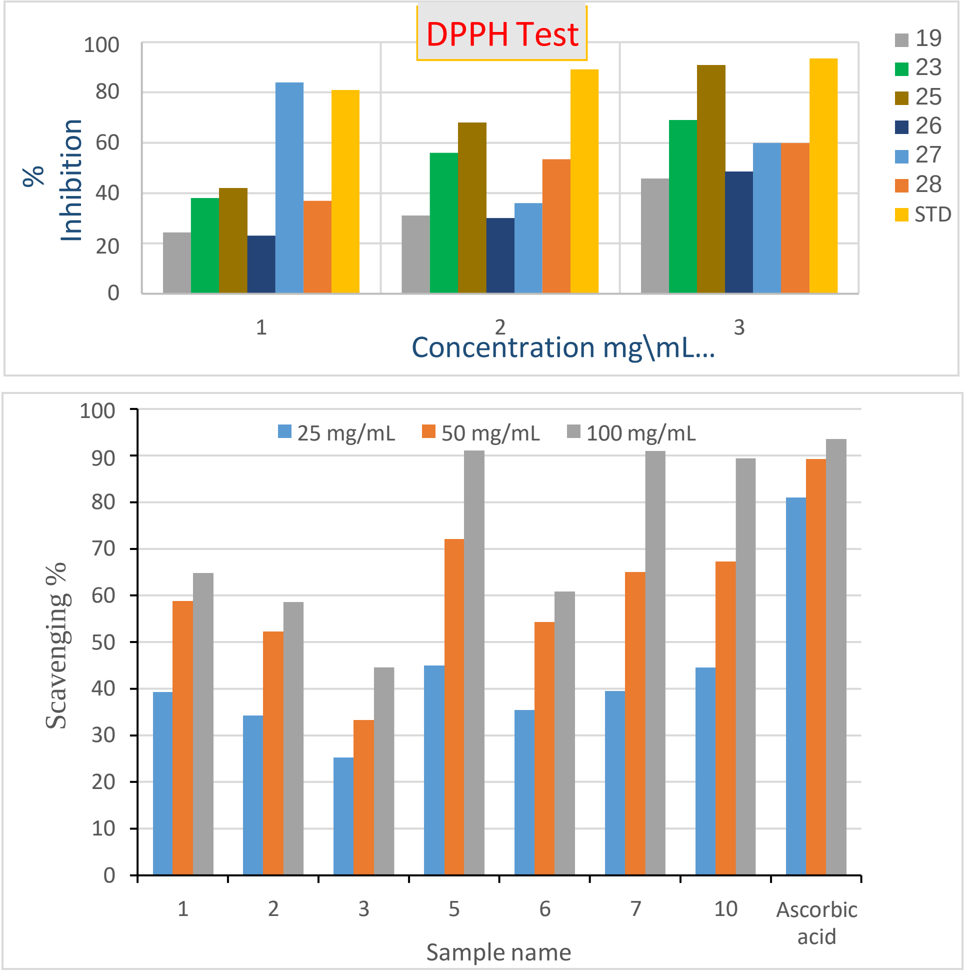


Figure (3-80): standard DPPH method for compound (RES16-RES28)

3.7 Theoretical Study

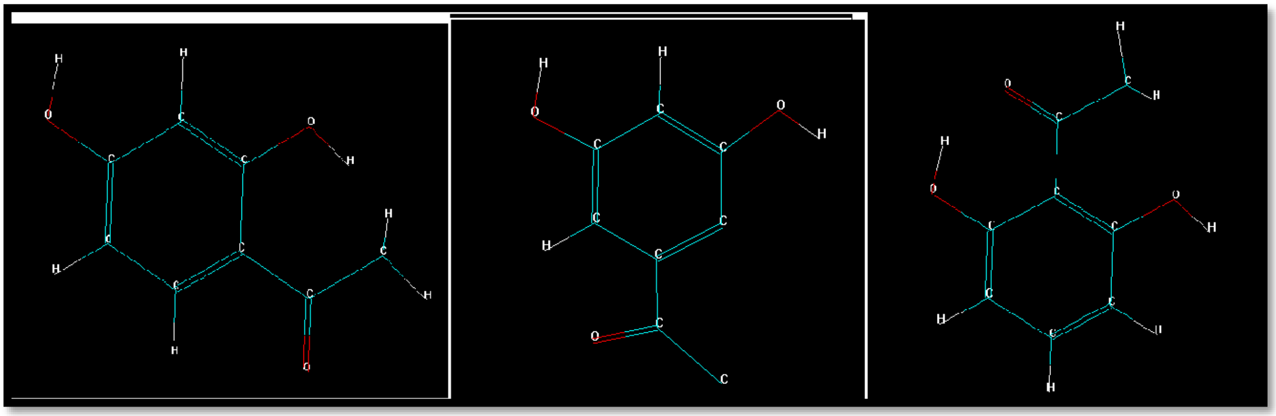
3-7-1 Geometry optimization structure

Molecular structural properties of resorcinol drug were estimated using semi- empirical method (PM3). The geometry-optimized structure of resorsinol is released a total energy equal to -32068.8667524 (kcal/mol). Heat of Formation equal to - 67.4561304 (kcal/mol) .

3.7.2 Theoretical Study For the acylation reaction of Resorcinol by using acetic acid .

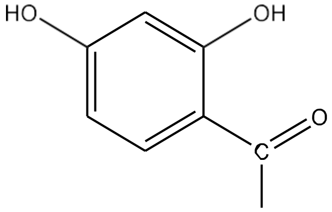
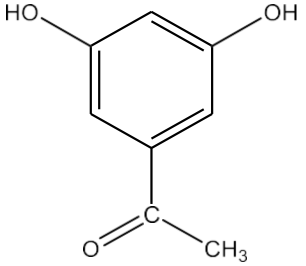
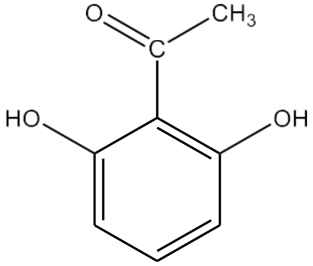
In theoretical study the acylation reaction of resorcinol has been carried out using semi-empirical methods (PM3), where the Geometrical properties have been calculated.

Three different transition states have been suggested and the most probable transition state been investigated depending upon the electronic properties to suggest the most probable pathway of the reaction. The calculations prove that the first transition state is the most probable than other state due its energetic values of total energy, binding energy, heat of formation and energy barrier that’s equal to -52484.354, -2258.926 , -132.550 , 36.907 respectively by Kcal mol-1 units .The pathway of reaction is spontaneous and exothermic .



Figure(3-80)The geometrical suggested transition state for acylation reaction calculated by PM3 semi-empirical method.

Table (3-5) Calculations of transition states, energy barrier and ƐΔH for the acylation reaction

No.	Transition states Kcal/mol	Energy barrier Kcal/mol	ƐΔH Kcal/mol
	-52484.354	36.907	51.32
	-52418.483	102.778	48.6
	-52452.764	68.497	47.653

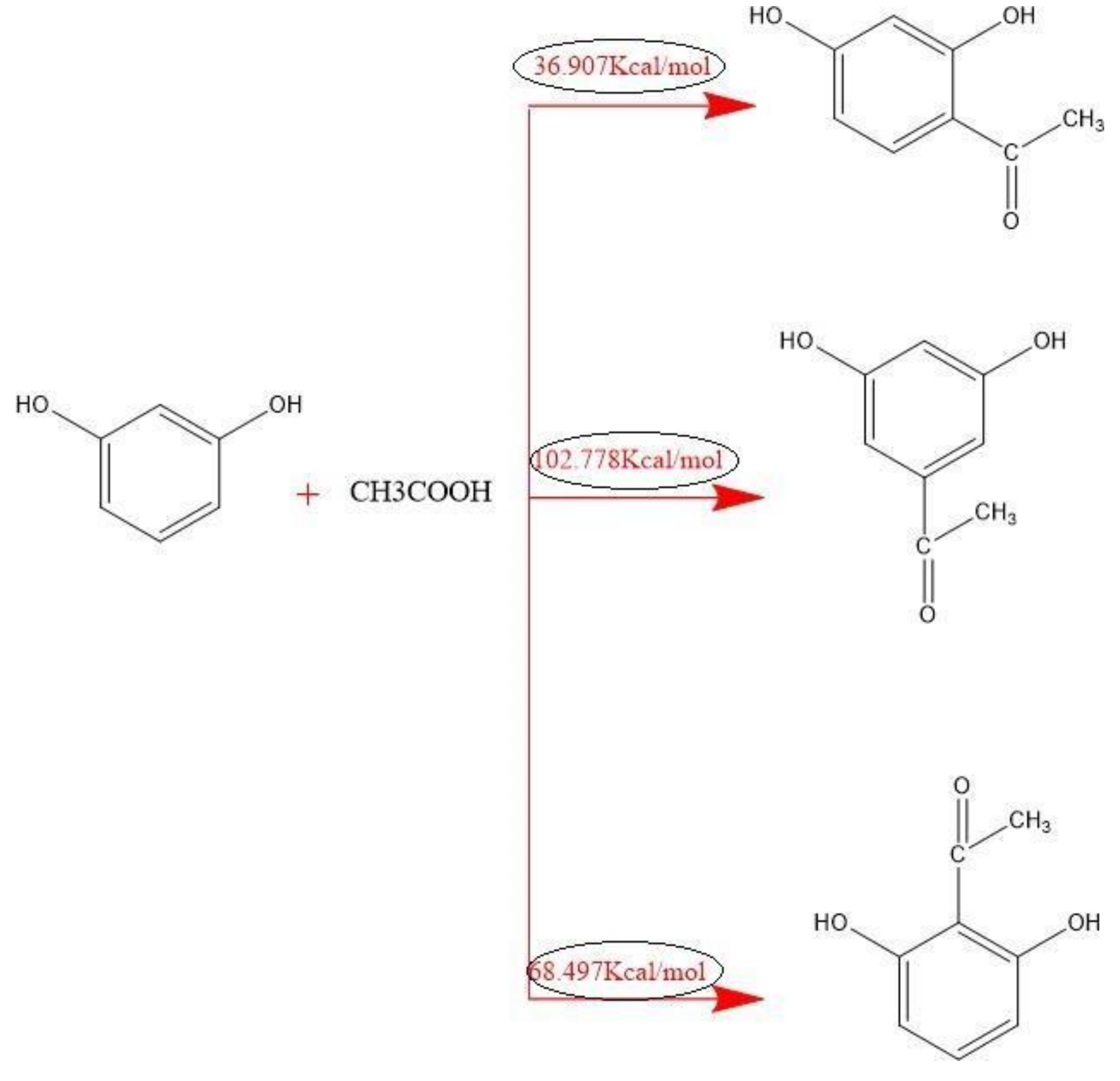


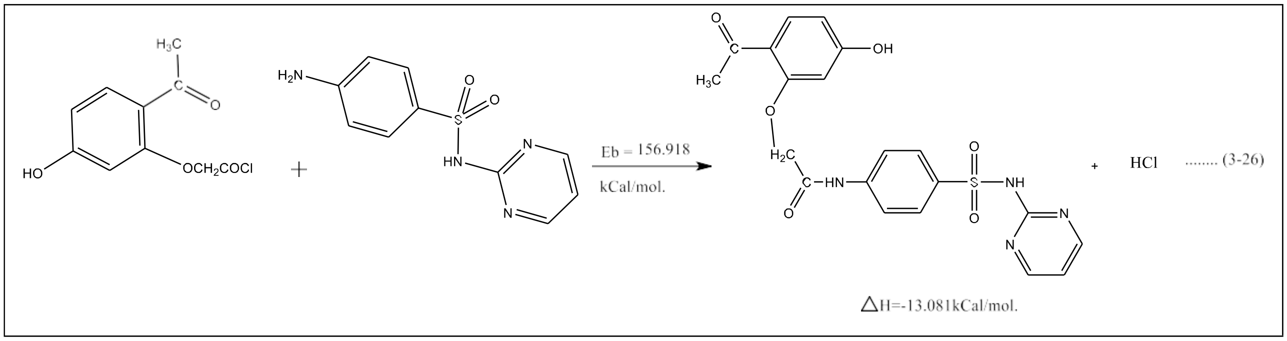
Figure (3-81) Calculations of transition states of acylation reaction

3.7.3 Transition State

The transitional state of the interaction of four types of drugs was studied with each of the possible products formed from the reaction of acylation of resorcinol in order to find out the most likely transition state to occur during the scientific interaction, which was studied by semi-empirical calculations.

When conducting the semi-empirical calculations, it was found that the proposed first transition state is the most likely transition state to occur because it has the lowest value of total energy, bonding energy, and heat of formation.

When comparing the energy properties of the drugs interacting with 2,4-dihydroxyacetophenone in each of the cases, we find that the interaction of the drugs in the first case is the most likely to occur, as the interaction of the drug sulfadiazine with R1 in the first case is the most likely to occur because it has the lowest value of the total energy and bonding energy and the heat of formation compared to its interaction with the other two proposed cases, where the total energy for it in the first case was equal to -129836.039 and the energy barrier was 156.918 kcal/mol, while in the second case the value of the total energy-128345.901kcal/mol for it and the interaction barrier was 211.102 .In the third case, it has a total energy equal -127815.833 to and an energy barrier equal to 740.667 . (Equation 3-26) (Table 3-6)

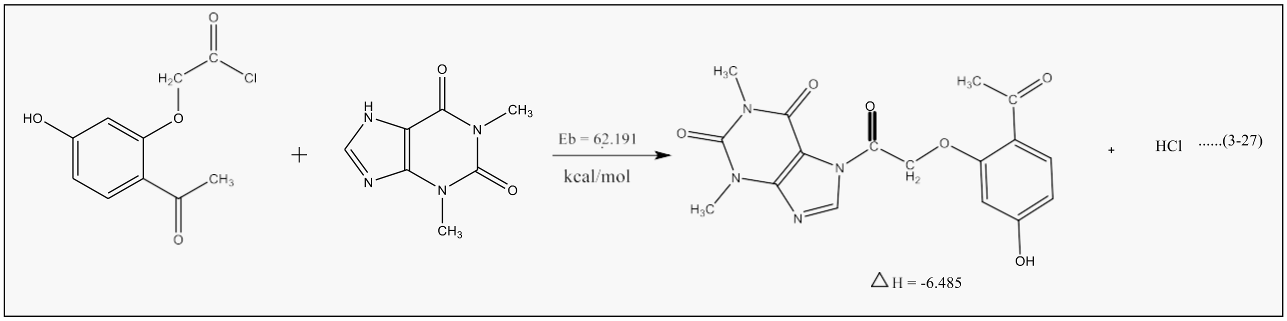


Equation (3-26) : Synthesis of compound RES6

Table (3.6) : Energetic properties of Transition states for the resorcinol derivatives RES 6 .

The derivative RES 6	The first transitional state	The second transitional state	The third transition state
Total Energy of R1	-64899.190	-876.90264	-64902.373
Total Energy of R2	-65093.767	-63654.127	-63654.127
Total Energy of P1	-122334.280	-120893.545	-120905.781
Total Energy of P2	-7671.757	-7671.757	-7671.757
Transition State	-129836.039	-128345.901	-127815.833
Energy barrier	156.918	211.102	740.667
ƐΔH Kcal/mol	-13.081	-8.3	-20.037

In the interaction of theophylline with 2,4-dihydroxyacetophenone, also from the comparison of properties, it was found that the first case is the most likely case to occur, as it has a total energy value equal to -115320.468 and an energy barrier of value 62.191In the second transitional state, the total energy value was equal -115211.335 to and energy barrier175.01, and in the third transitional state, it was equal to-115107.388 and energy barrier equal to 278.454. (Equation 3-27) (Table 3-7)



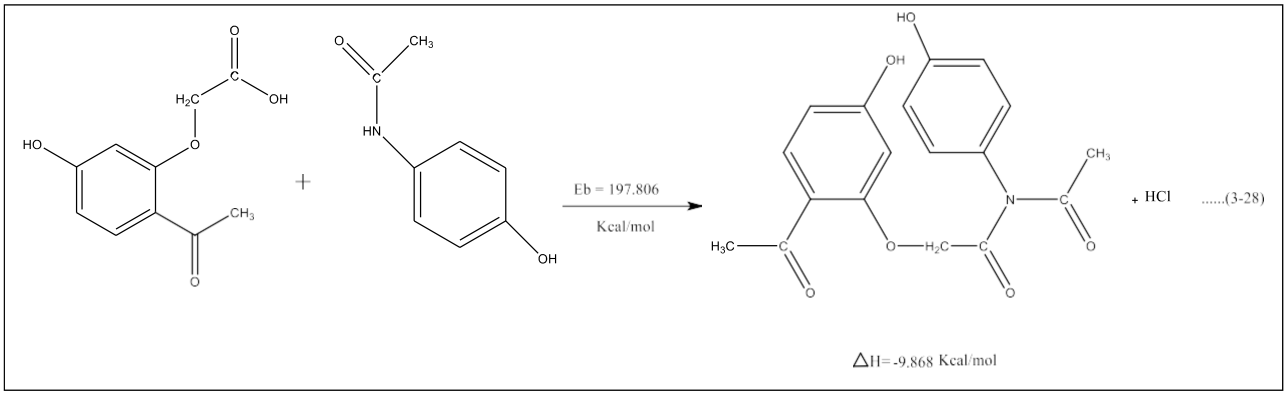
......(3-27)

Equation (3-27) : Synthesis of compound RES8

Table (3-7) : Energetic properties of Transition states for the resorcinol derivatives RES 8.

The derivative RES 8	The first transition state	The second transition state	The third transition state
Total Energy of R1	-64899.190	-64902.876	-64902.373
Total Energy of R2	-50483.469	-50483.469	-50483.469
Total Energy of P1	-107717.387	-107715.920	-107715.881
Total Energy of P2	-7671.757	-7671.757	-7671.757
Transition State	-115320.468	-115211.335	-115107.388
Energy barrier	62.191	175.01	278.454
ƐΔH Kcal/mol	-6.485	-1.332	-1.795

In the interaction of Paracetamole with 2,4-dihydroxyacetophenone , also from the comparison of properties , it was found that the first case is the most likely case to occur, as it has a total energy value equal to -107047.767 and an energy barrier of value 197.806 In the second transitional state, the total energy value was equal -107023.683to and energy barrier 225.576 , and in the third transitional state, it was equal to-106975.953 and energy barrier equal to 272.803 . (Equation 3-28) (Table 3-8)

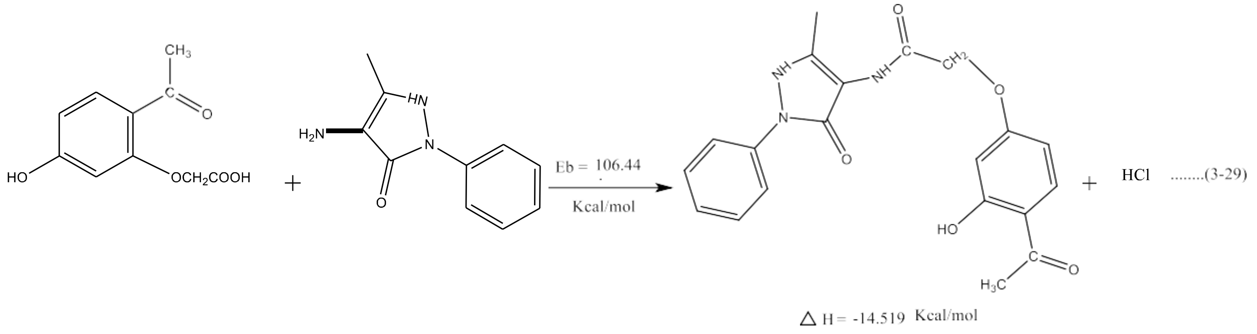


Equation (3-28) : Synthesis of compound RES10

The derivative RES 10	The first transitional state	The second transitional state	The third transition state
Total Energy of R1	-64899.190	-64902.876	-64902.373
Total Energy of R2	-423466.383	-42346.383	-42346.383
Total Energy of P1	-99583.684	-99584.704	-99585.040
Total Energy of P2	-7671.757	-7671.757	-7671.757
Transition State	-107047.767	-107023.683	-106975.953
Energy barrier	197.806	225.576	272.803
ƐΔH Kcal/mol	-9.868	-7.538	-7.128

Table (3-8) : Energetic properties of Transition states for the resorcinol derivative RES 10.

In the interaction of the drug 4-aminoantypyrine with 2,4-dihydroxyacetophenone in the first case is the most likely to occur because it has the lowest value of the total energy and bonding energy And the heat of formation compared to its interaction with the other two proposed cases, where the total energy for it in the first case was equal to -113994.386 and the energy barrier was 106.44, while in the second case the value of the total energy-113943.907kcal/mol for it and the interaction barrier was 160.609.In the third case, it has a total energy equal -114070.303 to and an energy barrier equal to 33.71. (Equation 3-29) (Table 3-9)



Equation (3-29) : Synthesis of compound RES5

Table (3-9) : Energetic properties of Transition states for the resorcinol derivative RES 5.

The derivative RES 5	The first transitional state	The second transitional state	The third transition state
Total Energy of R1	-64899.190	-64902.876	-64902.373
Total Energy of R2	-49201.640	-49201.640	-49201.640
Total Energy of P1	-106443.587	-106442.729	-106442.432
Total Energy of P2	-7671.757	-7671.757	-7671.757
Transition State	-113994.386	-113943.907	-114070.303
Energy barrier	106.44	160.609	33.71
ƐΔH Kcal/mol	-14.519	35.343	-1.795

3.8 Conclusions:

1. Successfully synthesized new Resorcinol derivatives via binding to other drugs containing amino group.

2. Confirmed all new derivatives structures via characterization with different techniques including FT-IR, ^{1}HNMR, ^{13}CNMR, and CHNS.

3. Most of the synthesized derivatives give good antibacterial and antioxidant activity.
4. All synthesized compounds are stable in different conditions

5. The use of theoretical calculations in calculating the optimal spatial position, finding the reaction pathways, and deducing the transition states during the reaction .

6. A study of the transition states of the acylation reaction of resorcinol showed that the proposed first transition state is the most likely transition state to occur with an energy barrier equal to 36.907 kcal/mol .

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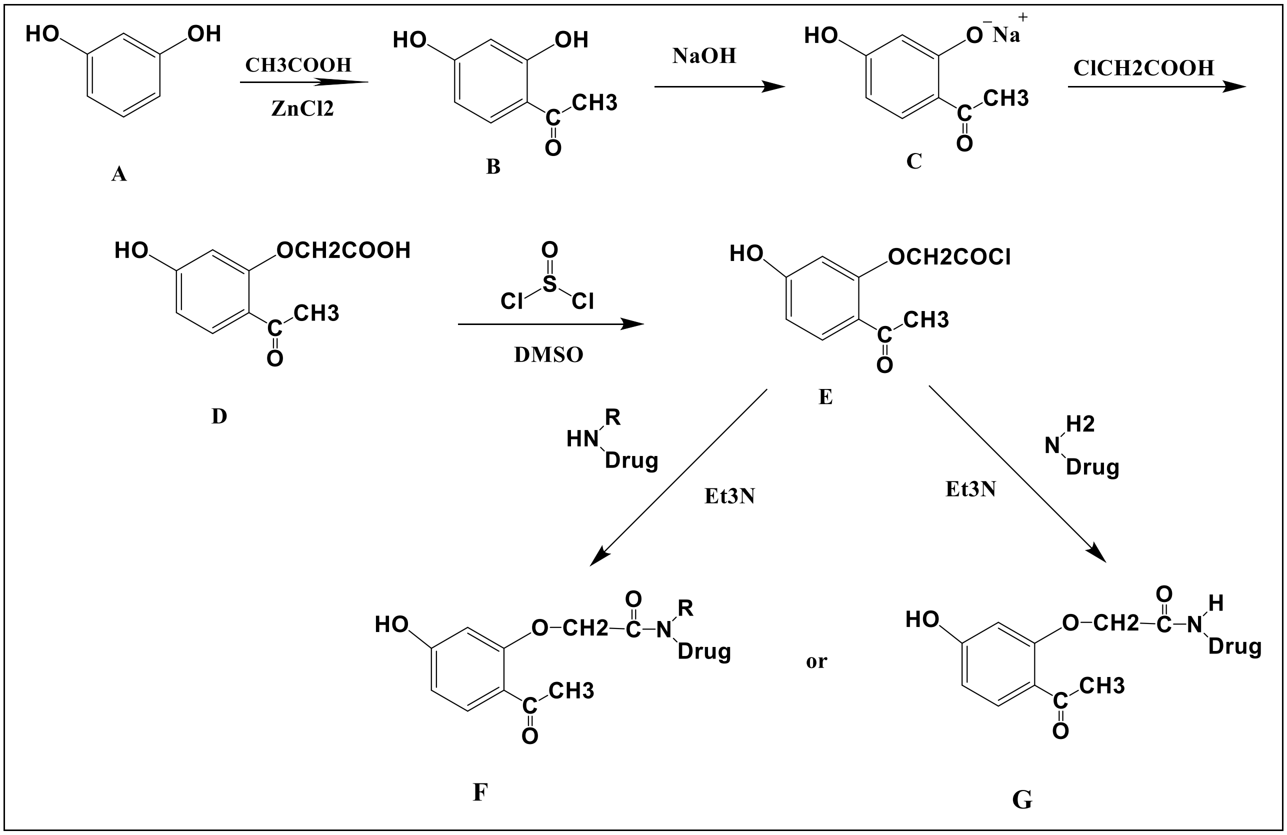
الخلاصة:-

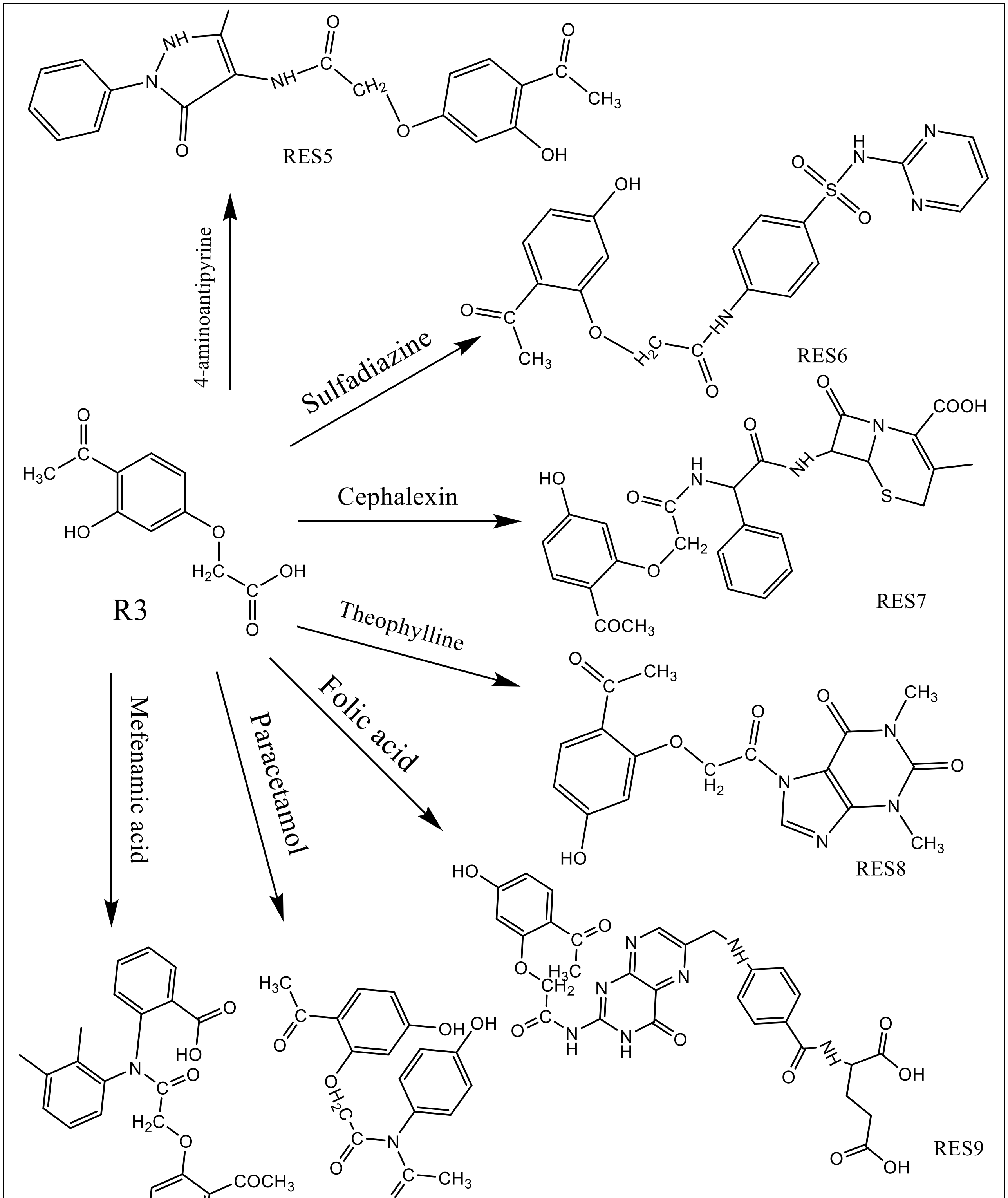
تتضمن هذه الدراسة استخدام الريسورسينول كمادة اساسية لتحضير خمسة وعشرون مشتقا جديدا له . تم تشخيص هذه المشتقات المحضرة بواسطة تقنية التحليل الطيفي الجزيئي كمرحلة اولى, في المرحلة الثانية ، تم إجراء عمليات محاكاة نظرية للتحقيق في تفاعل الأسيلة للريسورسينول حيث تم حساب الهياكل الهندسية لجميع مكونات التفاعل وحالات الانتقال المقترحة الخاصة بهم. تم التحقق من الحالات الانتقالية الأكثر احتمالية للحدوث من خلال حسابات الخصائص الطاقية والإلكترونية .

المسار الاول: -

تم تحضير المسار الأول عن طريق تحويل مجموعة الكربوكسيل إلى كلوريد الحامض بواسطة استخدام كلوريد الثيونيل ثم يذوب في ثنائي كلورو الميثان ثم يتفاعل مع بعض الأدوية المحتوية على المجموعة الأمينية (حمض الفوليك ، سيفاليكسين ، 4-أمينو أنتيبيرين ، ، باراسيتومول ، ثيوفينيل ، حامض الميفيناميك ، وسلفاديازين) لإنتاج أنظمة عقاقير ثنائية الجزيئات عن طريق تكوين اصرة امايدية .

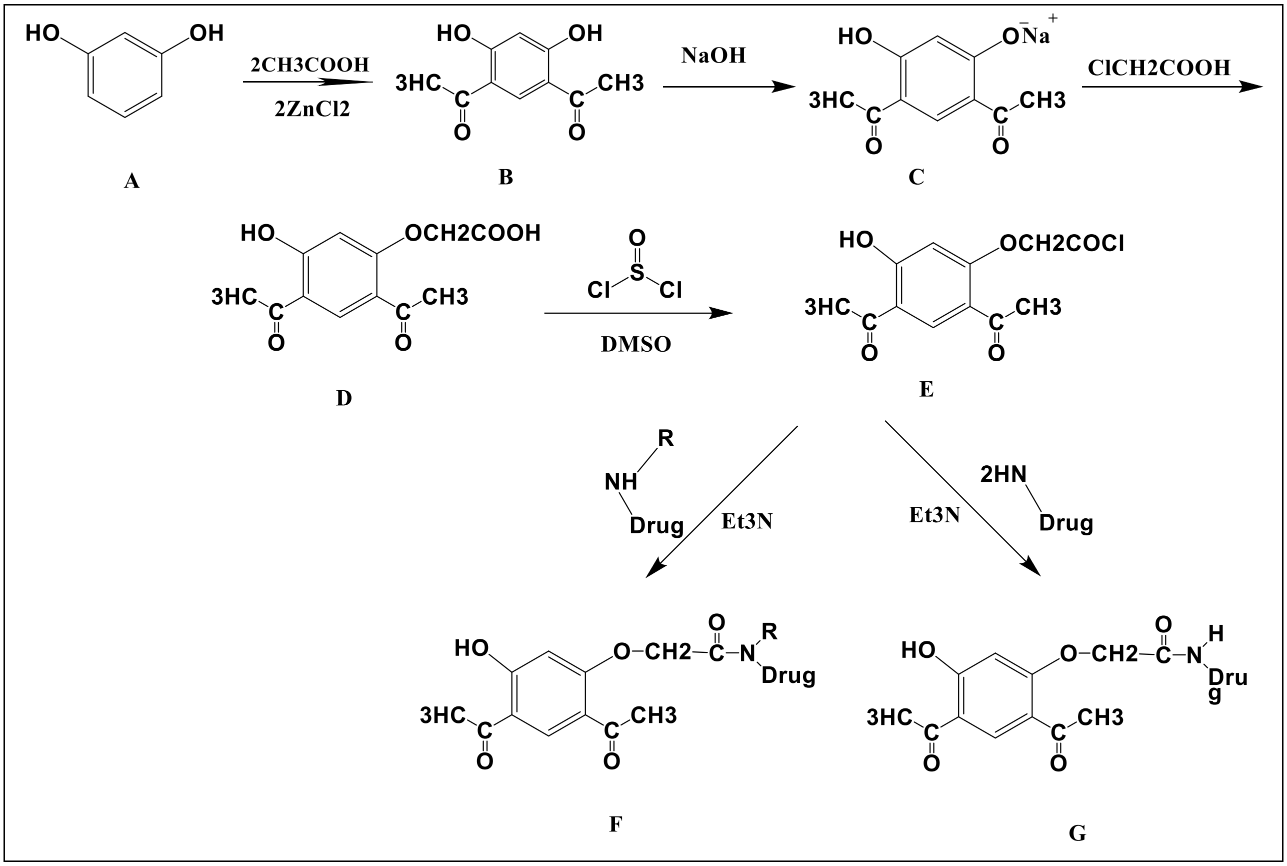


مخطط 1 : تحضير الانظمة الدوائية (RES 5- RES 11)

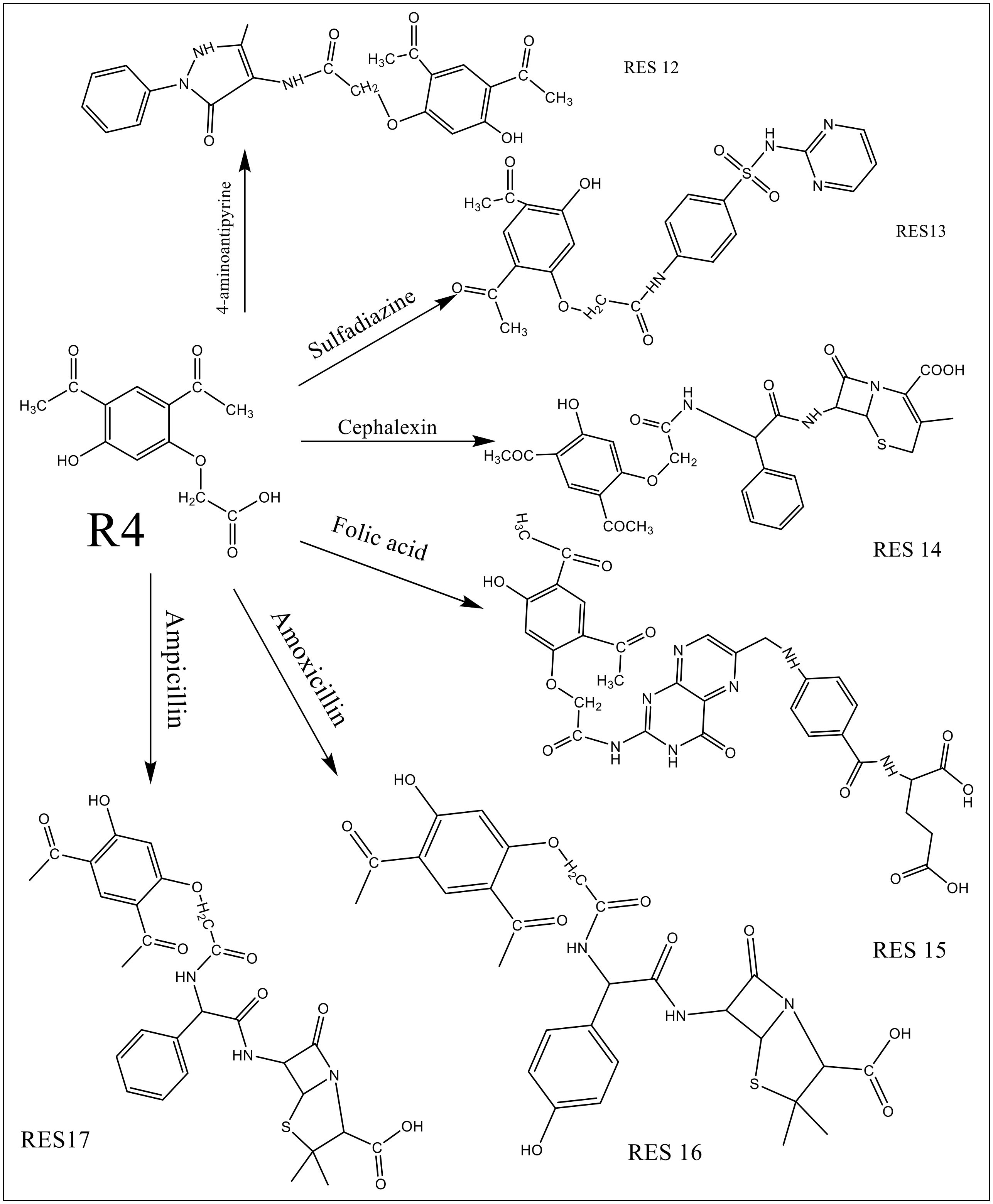


المسار الثاني :-

تضمن المسار الثاني تفاعل ثنائي اسيل ريسورسينول مع كلوريد حامض الخليك و هيدروكسيد الصوديوم أيضًا ليحل محل مجموعة الكربوكسيل في الموقع 2 ، وكذلك تفاعله مع ستة عقاقير أمينية مختلفة لتكوين مشتقات جديدة من الريسورسينول .

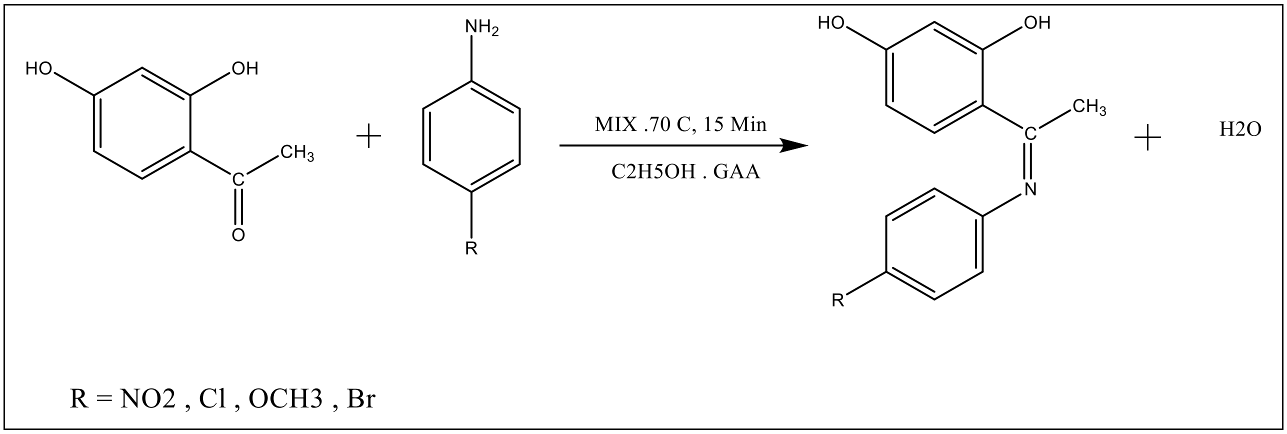


مخطط 2 : تحضير الانظمة الدوائية (RES 12 - RES 17)

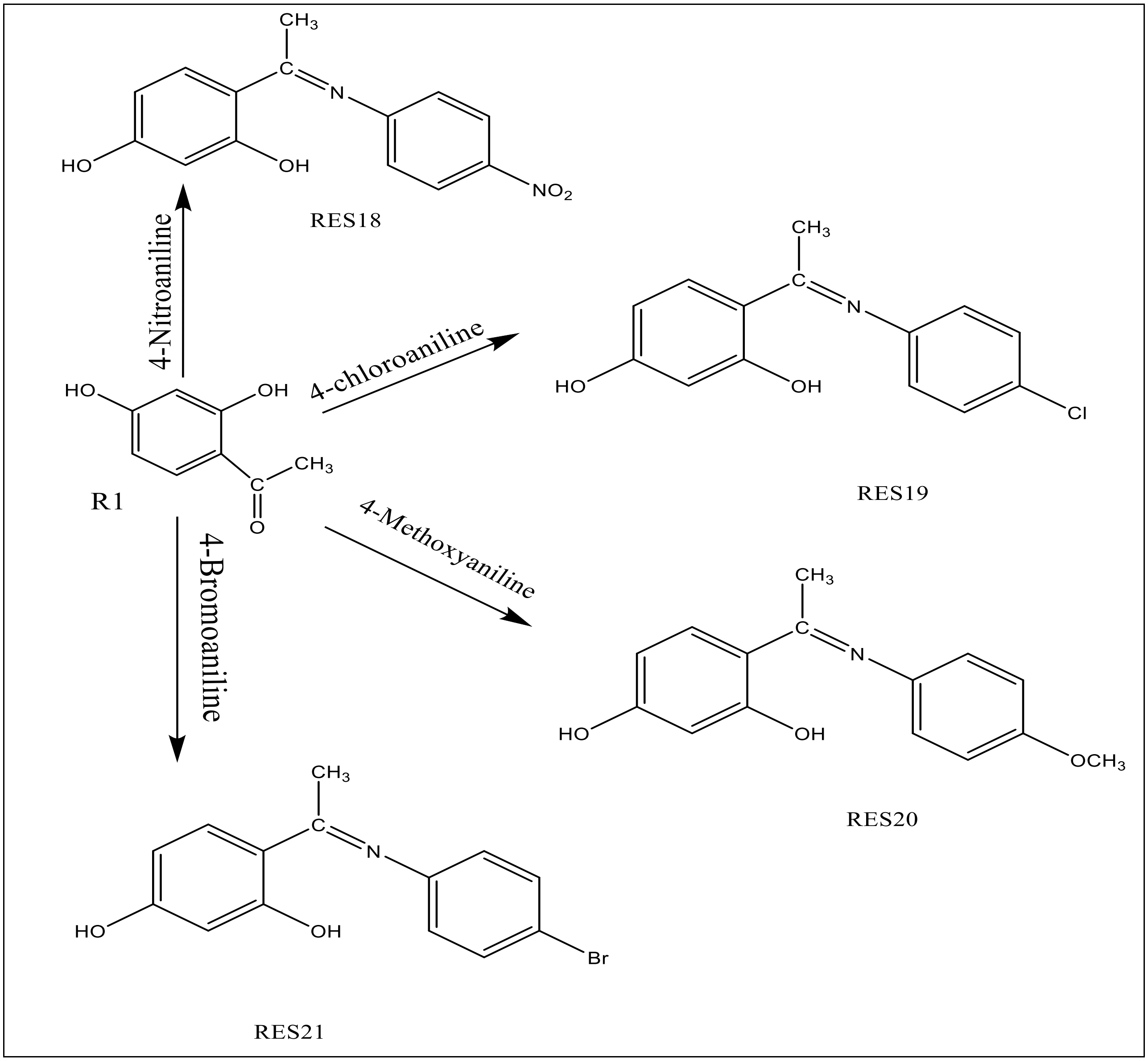

RES 12
4-aminoantipyrine
RES13
Sulfadiazine
Cephalexin
RES 14
R4
Folic acid
Ampicillin
Amoxicillin
RES 15
RES17
RES 16

المسار الثالث :-

تتضمن المرحلة الثالثة تحضير وتشخيص بعض قواعد شيف الفينولية (RES18-RES21) من خلال تفاعل 2،4-ثنائي هيدروكسي أسيتوفينون مع أربعة مشتقات مختلفة من مركب الأنيلين (4-نيترو أنيلين ، 4- كلورو أنيلين ، 4- ميثوكسي أنيلين و 4 -برومو انيلين).

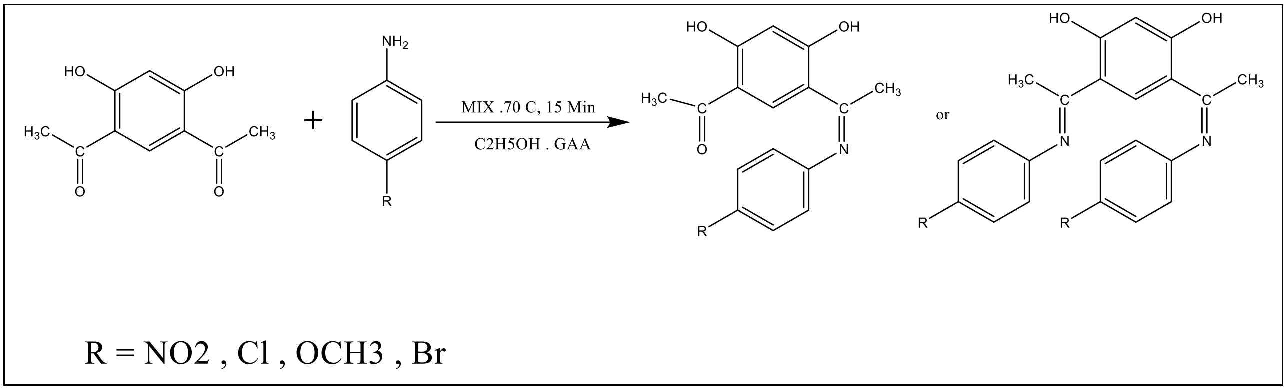


مخطط 3 : تحضيرقواعد شف (RES 18- RES21)



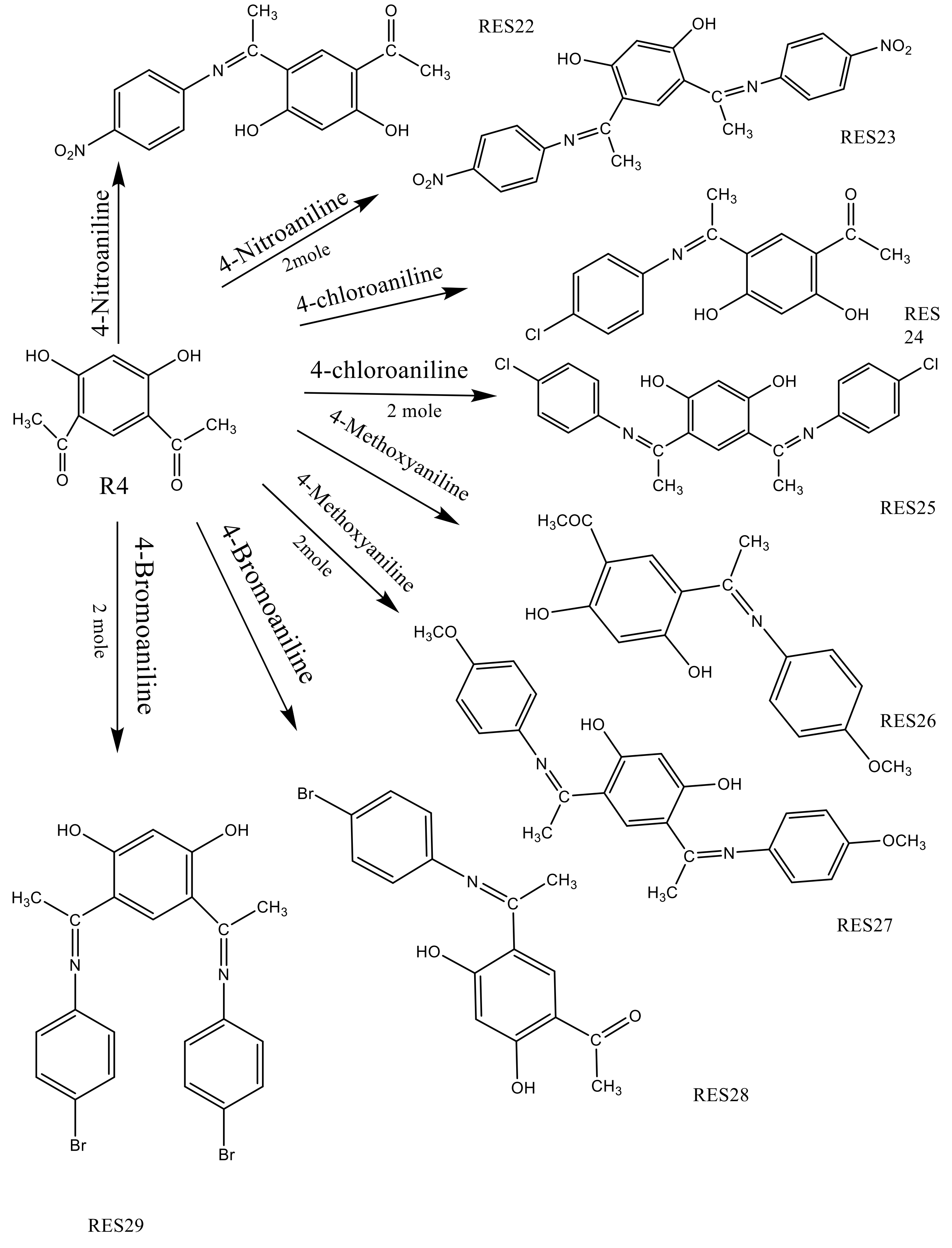
المسار الرابع :-

يتضمن المسار الرابع تحضير وتشخيص بعض قواعد شيف الفينولية من خلال تفاعل ثنائي اسيل ريسورسينول مع أربعة مشتقات مختلفة من مركب الأنيلين (4- نيترو أنيلين ، 4- كلورو أنيلين ، 4- ميثوكسي أنيلين و 4-برومو أنيلين). تم استخدام تقنية كروماتوغافيا الطبقة الرقيقة لتتبع جميع خطوات التفاعل الكيميائي.



R = NO2 , Cl , OCH3 , Br

مخطط 4 : تحضيرقواعد شف (RES 22- RES29)


R4
4-Nitroaniline
4-Nitroaniline
2mole
4-chloroaniline
4-chloroaniline
2 mole
4-Methoxyaniline
4-Methoxyaniline
2mole
4-Bromoaniline
4-Bromoaniline
2 mole
RES22
RES23
RES 24
RES25
RES26
RES27
RES28
RES29

جميع المركبات الجديدة المحضرة تم تشخيصها باستخدام طيف الاشعة تحت الحمراء, (FT-IR) طيف الرنين النووي المغناطيسي للبروتون (^{1}H-NMR) , طيف الرنين النووي المغناطيسي لنظير الكاربون والتحليل الدقيق للعناصر CHNS إضافة الى التقنيات أعلاه تم دراسة الفعالية للمشتقات كمضادات اكسدة وكذلك فعاليتها ضد البكتريا لجميع المركبات المحضرة باستخدام بكتريا الغرام السالب (*Klebsiella pneumonia*) وبكتريا الغرام الموجب (*Staphylococcus aureus*) وان اغلب المركبات قيد الاختبار أظهرت فعالية تجاه احد او كلا الصنفين البكتيريين .كذلك تم دراسة الذوبانية للمركبات المحضرة في مذيبات مختلفة.

وزارة التعليم العالي و البحث العلمي

جامعة بابل

كلية العلوم

قسم الكيمياء

تحضير وتشخيص ودراسة نظرية وفعالية بايولوجية لمركبات عضوية جديدة من الريسورسينول

رسالة

مقدمة الى مجلس كلية العلوم – جامعة بابل كجزء من متطلبات نيل درجة الماجستير

في العلوم / الكيمياء

من قبل

تقى ستار عبد دخيل

بكالوريوس علوم كيمياء / جامعة بغداد (٢٠١٣)

بإشراف

أ.د. سعدون عبدالله عودة   أ.د.عباس عبد علي دريع الصالحي

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