



"Synthesis and Identification of (4, 5, 6 and 7) Membered Heterocyclic Derivatives from 5-nitrovanilline"

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Abstract

This work included synthesis new Schiff base (1-(3-((4-hydroxy-3-methoxy-5 nitrobenzylidene) amino) phenyl) ethan-1-one)(1) by reaction 5-nitrovanilline with 3-aminoacetophenone in acid medium, then (1) react with 2-amino-6-methoxybenzothiazole to get derivative (2). (2) React with (chloroacetyl chloride, thioglycolic acid, glycine, alanine, sodium azide, phthalic anhydride, maleic anhydride) to give (β -lactam, thiazolidine, imidazolidine, tetrazole, oxazepine) derivatives. In other side 5-nitrovanilline react with acetophenone derivative in alkaline medium to get 3-(4-hydroxy-3-methoxy-5-nitrophenyl)-1-(4-hydroxyphenyl)prop-2-en-1-one which react with (hydrazine, phenyl hydrazine, 2,4-dinitro phenyl hydrazine, hydroxyl amine hydrochloride, urea, thiourea, ethyl cyanoacetate, malononitrile, guanidine hydrochloride) to get (pyrazol, isoxazole, oxazine, thiazine, pyridine, pyrimidine) derivatives. The new synthesized compounds have been identified by their melting points, ^1H NMR, ^{13}C NMR and FT-IR spectra.

Keywords: Schiff bases, Chalcone, β -lactam, Thiazolidine, imidazolidine, Tetrazole, oxazepine, Pyrazol, Isoxazole, Oxazine, Thiazine, Pyridine, Pyrimidine.

Introduction

Schiff's bases are an important class of organic compounds, they were first reported by Hugo Schiff in 1864⁽¹⁾. Its compound has azomethine [-C=N-] group in their structure⁽²⁾, are formed by the condensation of a primary amine with a carbonyl compound⁽³⁾. Schiff bases are reported to show a variety of interesting biological activities, including antibacterial, antifungal, anticancer, and herbicidal activities⁽⁴⁾. Schiff bases are also administered as catalysts, intermediates in organic synthesis, pigments, dyes, polymeric stabilizers and corrosion inhibitors⁽⁵⁾.

Then Schiff bases react with sodium azide to give tetrazoles. They are aromatic five membered ring containing four nitrogen atoms⁽⁶⁾. The tetrazole heterocyclic was first discovered in 1985 by Bladin in Uppsala University upon formation of dicyan dimethyl hydrazine-a product of reaction dicyan with phenyl hydrazine⁽⁷⁾. The Tetrazole compound, however, is considered a quintet heterogeneous cyclical compounds which includes one Carbon atom and four Nitrogen atoms along with one Hydrogen atom, which

has the chemical formula $(\text{CN}_4\text{H})^{(8)}$. Imidazolidines, a saturated imidazole (tetrahydroimidazole), have been reported to have important biological activities including potential α -adrenergic receptor agonist, antimicrobial, antiparasitic, oral hypoglycaemic, antiarrhythmic, anticonvulsant, anti-inflammatory and analgesic⁽⁹⁾. 2-Azetidinones, commonly known as β -lactams, is a four membered cyclic amide, It is named as such, because the nitrogen atom is attached to the β - carbon relative to the carbonyl⁽¹⁰⁾. It is synthesized by Staudinger in 1907⁽¹¹⁾.

β -Lactams widely used as antibiotics, have occupied a basic position in medicinal chemistry for almost a century now⁽¹²⁾. Thiazolidinones are classified as doubly unsaturated five membered heterocyclic compounds contain one nitrogen, one sulphur and three carbon atoms including a carbonyl group⁽¹³⁾. The chemistry of thiazolidin-4-one ring systems is of considerable interest as it is a core structure in various synthetic pharmaceuticals displaying a broad spectrum

of biological activities such as anti-inflammatory, antitubercular, antibacterial, antihistaminic, antifungal, anti HIV, anticonvulsant and cardiovascular etc⁽¹⁴⁾. Oxazepine is non-homologous seven member ring that contains two heteroatom (Oxygen and Nitrogen)⁽¹⁵⁾. Schiff base reacts with phthalic anhydride, Maleic anhydride and substituted phthalic anhydride to give and test its biological activity Oxazepine derivative introduced in 1965 for use in relief of the psychoneuroses characterized by anxiety and tension⁽¹⁶⁾. Oxazepine derivatives are found to be effective against anxiety and associated with schizophrenia, also found that (7-hydroxyamoxapine) is a pharmaceutical composite affecting the nervous center (CNS).

A send (as example) is an antidepressant with a mild sedative component to its action in animals (omoxazepine) reduced the uptake of noradrenalin and serotonin and block⁽¹⁷⁾. The chalcones are the convenient intermediates for the synthesis five, six and seven members heterocycles, often have exhibited diverse biological activity⁽¹⁸⁾. α,β -Unsaturated ketones display a wide range of pharmacological properties, including cytotoxicity towards different cancer cell lines, antimitotic, antimutagenic, antibacterial, antiviral, anti-inflammatory and hepatoprotective activities⁽¹⁹⁾. Pyrazole belongs to the family of azoles i.e. five-membered ring containing nitrogen and carbon atom. The dihydropyrazoles are called pyrazolines.

Some substituted pyrazolines and their derivatives have been reported to possess some interesting biological activities such as anticancer, insecticidal, antibacterial etc⁽²⁰⁾. Isoxazoles possess interesting medicinal properties and have some industrial utility. Many biologically active isoxazoles and reduced isoxazole derivatives have been reported, viz., the naturally occurring antituberculosis, antibiotic cycloserine, the mono amine oxidase inhibitor: isocarboxazid, useful in psychotherapy and Isoxazole steroids show anabolic activity, eg., Denazole⁽²¹⁾.

1,3thiazines-nitrogen and sulfur and 1,3 oxazine contains- nitrogen and oxygen in their six membered heterocyclic ring (N-C-S, N-C-O linkage). The heterocyclic compounds which contain nitrogen, sulphur and oxygen

possess an enormous significance in the field of medicinal chemistry. Thiazine and oxazine derivatives possess various biological activities such as anti-tubercular, antifungal, anti-bacterial, analgesic, anti-inflammatory, anti-cancer etc. Different chalcone derivatives are used as the starting material for the synthesis of thiazines and oxazines⁽²²⁾. Pyridine and related pyrimidines are classes of fused heterocycles that are of considerable interest because of the diverse range of their biological properties. These are among a wide variety of nitrogen heterocycles that have been explored for developing pharmaceutically important molecules⁽²³⁾.

Pyrimidine is a six-member heterocyclic compound that contains two nitrogen atoms at positions 1 and 3. The structure of the pyrimidine ring is similar to benzene and pyridine. The key role pyrimidines play in cellular processes has made them valuable leads for drug discovery. Pyrimidine derivatives are known to be biologically active compounds and substituted pyrimidines have shown wide range of biological activities like anti tubercular, antibacterial, antioxidant, anti-inflammatory activity⁽²⁴⁾.

Experimental

(FTIR) Spectra (4000-400cm⁻¹) in KBr disk were recorded on a SHIMADZU FTIR-8400S Fourier Transform. Melting point was measured using Stuart, UK. ¹H NMR and ¹³C-NMR were recorded on Fourier transformation Bruker spectrometer, operating at (400MHz) with (DMSO-d₆) measurements were made at Department of chemistry, university of Tehran Iran.

Synthesis of (1-(3-((4-hydroxy-3-methoxy-5-nitrobenzylidene) amino) phenyl) ethan-1-one) [1]

A mixture of equimolar quantities (0.005mol) of 5-nitro vaniline and (0.005) of 3-aminoacetophenone and (3 drops) of glacial acetic acid was refluxed for (6) h in 30 ml of ethanol. The reaction mixture was cooled and kept for (24 hs). The crystals found were filtered, dried and recrystallized from ethanol⁽¹⁻⁵⁾.

Synthesis of (2-methoxy-4-(((3-(1-((6-methoxybenzo[d]thiazol-2-yl) imino) ethyl) phenyl) imino) methyl)-6-nitrophenol)[2].

A mixture of equimolar quantities (0.005mol) of compound [1] and (0.005) of 3-2-amino-6-methoxybenzothiazole and (3 drops) of glacial acetic acid was refluxed for (6) h in 30 ml of ethanol. The reaction mixture was cooled and kept for (24 hs). The crystals found was filtered, dried and recrystallized from ethanol (1-5).

Synthesis of 2-methoxy-4-(1-(3-(1-(6-methoxybenzo[d]thiazol-2-yl)-5-methyl-4,5-dihydro-1H-tetrazol-5-yl)phenyl)-4,5-dihydro-1H-tetrazol-5-yl)-6-nitrophenol [3].

Compounds of (2) (0.001mole) was dissolved in (20mL) dioxane and mixed with (0.002mole) sodium azide. These mixtures were refluxed for (48) h at T=55°C. The crystals found was filtered, dried and recrystallized from ethanol (6-8).

Synthesis Imidazolidine derivatives [4, 5]

A mixture of Schiff bases (2) (0.001mol) dissolved in THF (15mL) and (alanine, glycine) (0.002mol) was dissolved in THF (15mL) and refluxed for 48 hs. The reaction was then cooled and recrystallized from absolute ethanol (9).

Synthesis of 2-(3-(2-(4-hydroxy-3-methoxy-5-nitrophenyl)-4-oxothiazolidin-3-yl)phenyl)-3-(6-methoxybenzo[d]thiazol-2-yl)-2-methylthiazolidin-4-one [6].

Mercator acetic acid (0.002 mol) in 1,4-dioxane (20 ml) was added to (0.001 mol) of Schiff bases (2). Then added to mixture (0.5 gm) anhydrous zinc chloride with stirring then the mixture was refluxed for 16 hours. The reaction mixture was cooled and kept for (24 hs). The crystals found was filtered, dried and recrystallized from ethanol (13,14).

Synthesis of 3-chloro-4-(3-(3-chloro-2-(4-hydroxy-3-methoxy-5-nitrophenyl)-4-oxoazetidin-1-yl)phenyl)-1-(6-methoxybenzo[d]thiazol-2-yl)-4-methylazetidin-2-one [7].

To Triethylamine (0.006 mol) in 1, 4-dioxane, chloroacetyl chloride (0.002 mol) was added drop wise to a solution of the compounds (2) (0.001 mol) and at 10 temperature. The reaction mixture was stirred for 12h. The solid obtained was recrystallized from ethanol (10-12).

Synthesis of Oxazepine Derivatives [8, 9].

A mixture of Schiff base (2) (0.001mole) and (phthalic anhydride, maleic anhydride) (0.002mole) was dissolved in (20mL) 1,4-dioxane. The mixture was refluxed for 28hrs in water bath at (70°C), the precipitate was filtered and recrystallized from ethanol (15-17).

Synthesis of 3-(4-hydroxy-3-methoxy-5-nitrophenyl)-1-(4-hydroxyphenyl) prop-2-en-1-one [10].

Chalcones are synthesized by reacting equimolar amounts of (0.01 mol) 5-nitrovanillin and (0.01 mol) 4-hydroxyacetophenon in the presence of (10%) sodium hydroxide (10ml) and (50ml) ethanol. Shake it thoroughly and kept it in the shaker for 6 hour. Neutralized with hydrochloric acid (5%), After that it taken from the shaker and keep it for 12 hours in the refrigerator, filter it using whatmann filter paper and dried (18,19).

Synthesis of 4-(3-(4-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-5-yl)-2-methoxy-6-nitrophenol (11)

To a solution of (10) (0.0015 mol) in ethanol (30 ml), a 99% hydrazine hydrate (0.0015 mol) was added and the reaction mixture was refluxed on water bath at 78°C gently for about 10 hours. After the completion of reaction, the reaction mixture was concentrated and cooled, the resulting solid so obtained was filtered, washed several times with distilled water, dried and crystallised from ethanol (20).

Synthesis of 4-(1-(2, 4-dinitrophenyl)-3-(4-hydroxyphenyl)- 4, 5- dihydro- 1H pyrazol-5-yl)-2-methoxy-6-nitrophenol (12)

To a solution of (10) (0.0015 mol) in ethanol (30 ml), a 2,4-dinitrophenylhydrazine (0.0015 mol) was added with (3drops) glacial acetic acid and the reaction mixture was refluxed on water bath at 78°C gently for about 15 hours. After the completion of reaction, the reaction mixture was concentrated and cooled, the resulting solid so obtained was filtered, washed several times with distilled water, dried and crystallised from ethanol (20).

Synthesis of 4-(3-(4-hydroxyphenyl)-4,5-dihydroisoxazol-5-yl)-2-methoxy-6-nitrophenol [13].

The derivative (10) and hydroxylamine hydrochloride in presence of Na OH /absolute ethanol was refluxed on a water bath for 14

hours. The reaction was then cooled and recrystallized from absolute ethanol⁽²¹⁾.

Synthesis of 4-(2-amino-6-(4-hydroxyphenyl)-6H-1,3-oxazin-4-yl)-2-methoxy-6-nitrophenol [14].

Chalcone (0.0015mol) was added to a solution of urea (0.0015mol) in ethanol (25ml) at room temperature. The reaction mixture was stirred for 16 hr. After the completion of reaction, the reaction was then cooled and the final resulting (14), recrystallized from absolute ethanol⁽²²⁾.

Synthesis of 4-(2-amino-6-(4-hydroxyphenyl)-4H-1,3-thiazin-4-yl)-2-methoxy-6-nitrophenol [15].

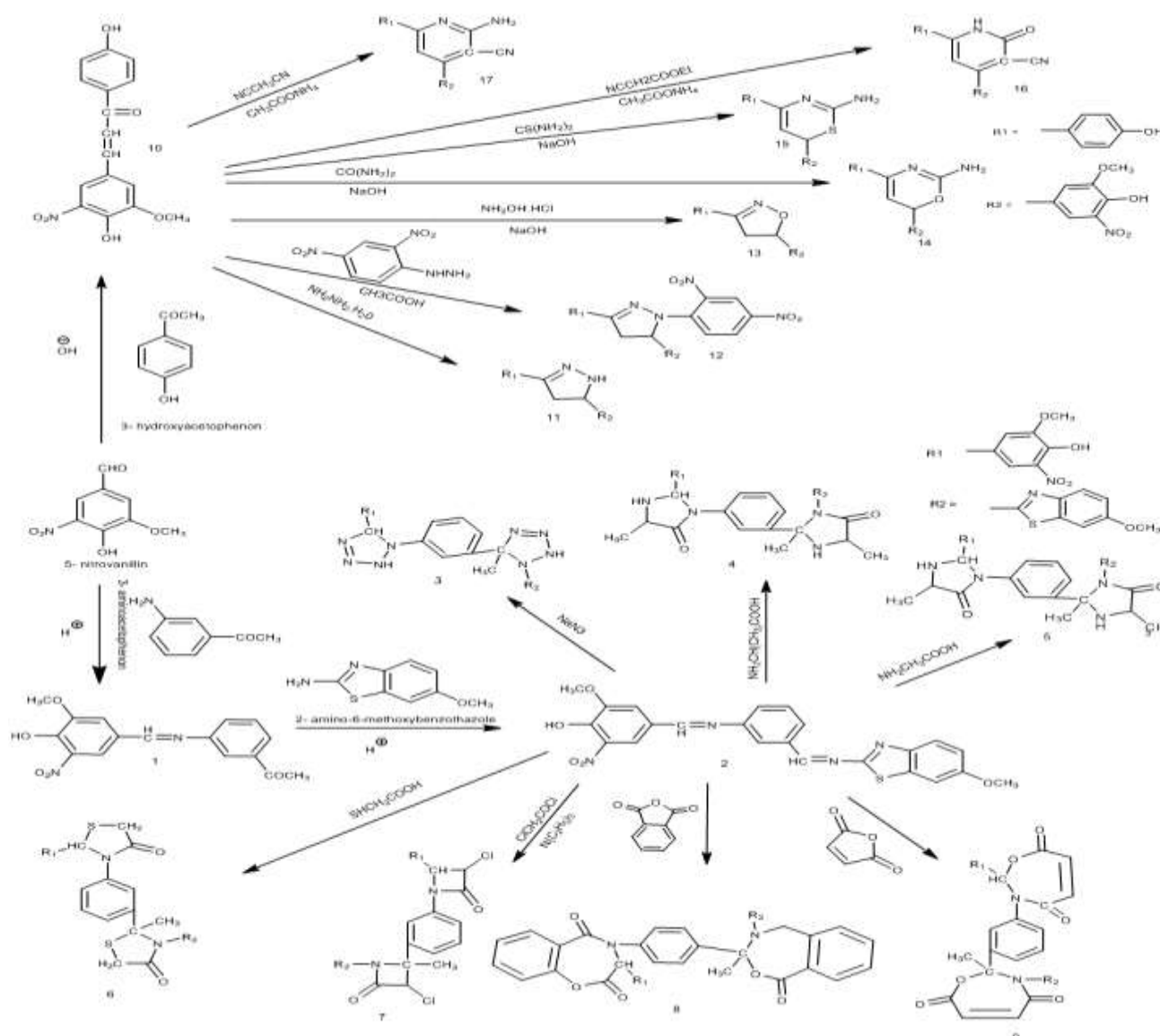
Chalcone (0.0015mol) was added to a solution of theorem (0.0015mol) in ethanol (25ml) at room temperature. The reaction mixture was stirred for 16 hr. After the completion of reaction, the reaction was then cooled and the final resulting (15), recrystallized from absolute ethanol⁽²²⁾.

Synthesis of 4-(4-hydroxy-3-methoxy-5-nitrophenyl)-6-(4-hydroxyphenyl)-2-oxo-1,2-dihydropyridine-3-carbonitrile [16]

A mixture of compounds (10) (0.0015mol), ethylcyanoacetata (0.0015mol) and ammonium acetate (0.002mol) in absolute ethanol (30ml) was refluxed for 12 hr's. After cooling, the formed product was collected by filtration, washed with ethanol, dried and crystallized from the proper solvent to give the title compounds⁽²³⁾.

Synthesis of 2-amino-6-(4-hydroxy-3-methoxy-5-nitrophenyl) - 4-(4-hydroxyphenyl) nicotinonitrile [17]

A mixture of compounds (10) (0.0015mol), malononitrile (0.0015mol) and ammonium acetate (0.002mol) in absolute ethanol (30ml) was refluxed for 12 hr's. After cooling, the formed product was collected by filtration, washed with ethanol, dried and crystallized from the proper solvent to give the title compounds⁽²⁴⁾.



Scheme 1: Preparation of Compounds (1-17)

Results and Discussion

The Compound (1) (1-(3-((4-hydroxy-3-methoxy-5-nitrobenzylidene) amino) phenyl) ethan-1-one)

Was obtained as yellow solid yield 66% , m.p155⁰C.The infrared spectrum data of compound (1) showed band at (1681) cm⁻¹ for (C=O), (1620) cm⁻¹ for (C=N), (1203.50) cm⁻¹ for (C-O), (2877.69 , 2947.03) cm⁻¹ for (C-H) aliphatic , (3078.18) cm⁻¹ for (C-H) aromatic, (3325.05) cm⁻¹ for (OH), (1530,1350) cm⁻¹ for (NO₂).The ¹H-NMR (DMSO-d₆) spectrum data of compound (1) show δ : 3.9 (s, 3H , COCH₃) , 9.8 (s, 1H , OH) , 6.7 (s, 1H , CH=N) , 7 – 8.6 (m , 6H , Ar) , 2.6 (s, 3H , OCH₃).The ¹³C-NMR (DMSO-d₆) spectrum data of compound (1) show δ : 197 (C₁₅) , 26 (C₁₄) , 56 (C₁₆) , 137.9 (C₇) , (137.7 – 105) C_{arom.}

The Compound (2) (2-methoxy-4-(((3-(1-((6-methoxybenzo [d] thiazol-2 yl) imino)ethyl) phenyl) imino)methyl)-6-nitrophenol)

Was obtained as orange solid yield 85% , m.p(78 – 81)⁰C.The infrared spectrum data of compound (2) showed band at, (1604) cm⁻¹ for (C=N), , (2839.02 , 2939.31) cm⁻¹ for (C-H) aliphatic , (3085.89) cm⁻¹ for (C-H) aromatic. The ¹H-NMR (DMSO-d₆) spectrum data of compound (2) show δ : 1.9 (s, 3H , CH₃) , 9.7 (s, 1H , OH) , 6.7 (s, 1H , CH=N) , 6.8 – 8.7 (m , 9H , Ar-H) , 3.7 – 3.9 (s, 6H , OCH₃).

The ¹³C-NMR (DMSO-d₆) spectrum data of compound (1) show δ : 165 (C₁₅) , 159 (C₁₄) , 130 (C₁₆) , 154 (C₇) , 138 (C₁₉) , 137 (C₃) , 132 (C₈) , 129 (C₄) , 27 (C₂₃) , 56 (C₂₉) , 55 (C₂₄) , (105 – 126) C_{arom.}

The Compound (3)2-methoxy-4-(1-(3-(1-(6-methoxybenzo [d] thiazol-2-yl) - 5-methyl-4, 5-dihydro-1H-tetrazol-5-yl) phenyl)-4,5-dihydro-1H-tetrazol-5-yl)-6-nitrophenol

was obtained as red solid yield 79% , m.p(125 – 130)⁰C.The infrared spectrum data of compound (3) showed band at (1643.24 – 1674.1) cm⁻¹ for (N=N), , (2839.02 , 2954.74) cm⁻¹ for (C-H) aliphatic , (3093.61) cm⁻¹ for (C-H) aromatic , (3294.19) cm⁻¹ for (NH) imidazolidine , (3386.77) cm⁻¹ for (OH) , (1612.38) cm⁻¹ for (C=C) aromatic , (1535.23) cm⁻¹ for (C-N).The ¹H-NMR (DMSO-d₆) spectrum data of compound (3) show δ : 2.6 (s, 3H , CH₃) , 9.4 (s, 1H , OH) , 6.7 – 7.9 (m , 5H , Ar-H) , 3.5 – 3.7 (s, 6H , OCH₃) , 5.3 (s, 1H , N-CH-N) , 8.4 (d , 1H , NH-CH) imidazolidine , 8.05 (s, 1H , NH-C) imidazolidine. The ¹³C-NMR (DMSO-d₆) spectrum data of compound (3) show δ : 164 (C₁₅) , 160 (C₁₉) , 155 (C₃) , 154 (C₁₆) , 149 (C₅) , 146 (C₄) , 26 (C₂₃) , 55.4 (C₂₂) , 55.5 (C₂₄) , 55.6 (C₁₇) , 66.4 (C₁₈) , (105 – 118) C_{arom.}

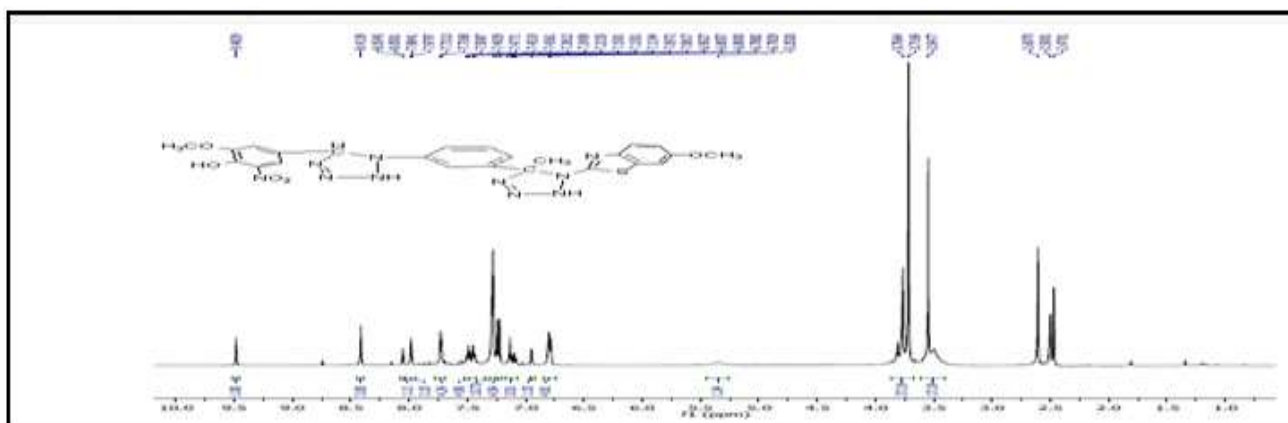


Figure 1: ¹H-NMRfor Compound (3)

The compound (4) Imidazolidine derivatives

Was obtained as brown yield 75% The infrared spectrum data of compound (4) showed band at, (1674) cm⁻¹ for (C=O), , (2877 , 2939) cm⁻¹ for (C-H) aliphatic , (3078) cm⁻¹ for (C-H) aromatic , (3340) cm⁻¹ for (OH) , (3118) cm⁻¹ for (N-H) imidazolidine, (1604) cm⁻¹ for (C=C) aromatic , (1542) cm⁻¹ for (C-

N).The ¹H-NMR (DMSO-d₆) spectrum data of compound (4) show δ : 1.03, 1.7 (s, 9H , CH₃) , 9.46 (s, 1H , OH) , 6.7 – 7.3 (s, 7H , Ar-H) , 3.3 (s, 6H , OCH₃) , 3.5 (t, 2H , -CH) , 3.8 (s, 1H , CH) , 9.42 (s, 2H , NH) imidazolidine. The ¹³C-NMR (DMSO-d₆) spectrum data of compound (4) show δ : 188 (C₁₇, C₉) , 164 (C₁₉) , 163 (C₃) , 154 (C₂₃) ,

(105 – 131) $C_{aromatic}$, 149 (C_{10}) , 146 (C_{20}) , 99.9 (C_8 , C_{18}) , 65 (C_7) , 56.4 (C_{30}) , 55.5 (C_{26}) , 15.2 (C_{27} , C_{29}) , 16.3 (C_{28}) , 84 (C_{16}) .

The Compound (5) Imidazolidine derivatives

Was obtained as brown yield 79% The infrared spectrum data of compound (5) showed band at, (1735.81) cm^{-1} for (C=O), , (2877.6 , 2939.31) cm^{-1} for (C-H) aliphatic , (3078.18) cm^{-1} for (C-H) aromatic , (3217.04 , 3217.05) cm^{-1} for (NH) , (3317.65) cm^{-1} for (OH) , (1604.66) cm^{-1} for(C=C) , (1542.95) cm^{-1} for (C-N) .The ^1H -NMR (DMSO- d_6)

spectrum data of compound (5) show δ : 1.03 (S, 3H , CH_3) , 9.3 (S , 1H , OH) , 6.7 – 7.2 (M , 9H , Ar-H) , 3.2 (S , 6H , OCH_3) , 1.05 (S , 3H , CH_3) , 3.4 (S , 4H , CH_2) , 3.8 (S , 1H , CH) , 8.1 , 7.9 (S , 2H , NH) .

The ^{13}C -NMR (DMSO- d_6) spectrum data of compound (5) show δ : 186 (C_{17} , C_9) , 164 (C_{18}) , 154 (C_3) , 146 (C_{22}) , 131 (C_{10}) , 95 (C_{15}) , 80 (C_7) , 18.6 (C_{26}) , 55.5 (C_{25}) , 55.6 (C_{27}) , 15.2 (C_{27} , C_{29}) , 65 (C_8 , C_{16}) , (105 – 118) C_{arom} .

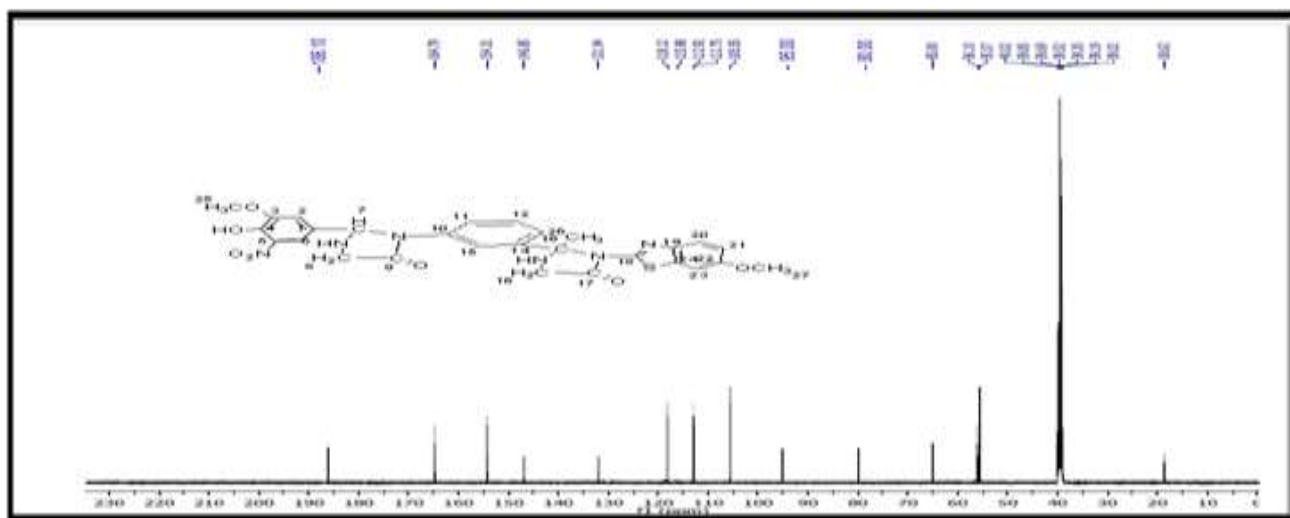


Figure 2: ^{13}C -NMRfor Compound (5)

The compound (6) 2-(3-(2-(4-hydroxy-3-methoxy-5-nitrophenyl)-4-oxothiazolidin-3-yl)phenyl)-3-(6-methoxybenzo[d]thiazol-2-yl)-2-methylthiazolidin-4-one

Was obtained as brown yield 92%.The infrared spectrum data of compound (6) showed band at, (1681.81) cm^{-1} for (C=O), (2885.31 , 2977.89) cm^{-1} for (C-H) aliphatic , (3100) cm^{-1} for (C-H) aromatic , (3314) cm^{-1} for (OH) , (1612.38) cm^{-1} for (C=N) , (

1550.66) cm^{-1} for (C=C).The ^1H -NMR (DMSO- d_6) spectrum data of compound (6) show δ : 1.07 (S, 3H , CH_3) , 9.2 (S , 1H , OH) , 6.7 – 7.6 (M , 9H , Ar-H) , 3.37 , 3.4 (S , 6H , OCH_3) , 3.8 (S , 1H , CH) , 3.5 (S , 4H , CH_2) .The ^{13}C -NMR (DMSO- d_6) spectrum data of compound (6) show δ : 197 (C_{18} , C_9) , 166 (C_{19}) , 154 (C_3) , 148 (C_{23}) , 130 (C_9) , 129 (C_{20}) , 26 (C_{27}) , 55 (C_{26} , C_{28}) , 62 (C_8) , 64 (C_7) , 66 (C_{16}) , (105 – 118) C_{arom} .

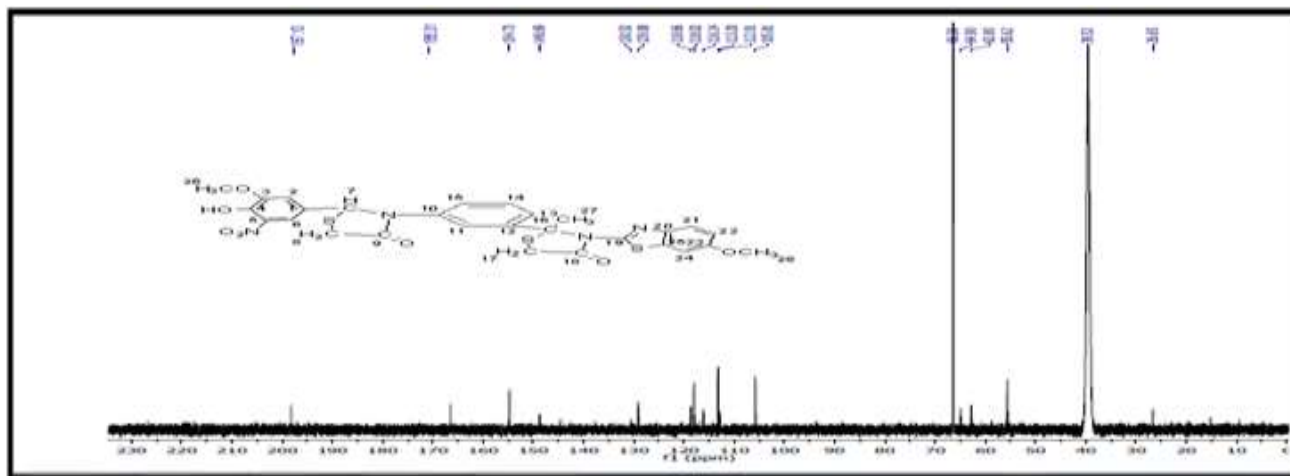


Figure 3: ^{13}C -NMRfor Compound (6)

The compound (7) 3-chloro-4-(3-(3-chloro-2-(4-hydroxy-3-methoxy-5-nitrophenyl)-4-oxoazetidin-1-yl) phenyl)-1-(6-methoxybenzo [d] thiazol-2-yl) - 4-methylazetidin-2-one

Was obtained as yellow yield 77%.The infrared spectrum data of compound (7) showed band at, (1689.53) cm^{-1} for (C=O), (2877.60 , 2939.31) cm^{-1} for (C-H) aliphatic , (3070.46) cm^{-1} for (C-H) aromatic , (3217.04) cm^{-1} for (OH) , (1604.66) cm^{-1} for (C=N) , (

1550.66) cm^{-1} for (C=C), (1481.23) cm^{-1} for (C- N) ,(802.33) cm^{-1} for (C-Cl) .The ^1H -NMR (DMSO- d_6) spectrum data of compound (7) show δ : 1.8 (S, 3H , CH_3) , 9.7 (S , 1H , OH) , 6.9 – 8.2 (M , 10H , Ar-H) , 3.03 (S , 3H , OCH_3) , 3.9 (d , 1H , CH-N) , 4.4 (d , 2H , CH-Cl) .The ^{13}C -NMR (DMSO- d_6) spectrum data of compound (7) show δ : 190 , 197 (C_{18} , C_9) , 186 (C_{19}) , 156 (C_5) , 155 (C_{23}) , (104 – 137) $\text{C}_{\text{aromatic}}$, 142 (C_{20}) , 139 (C_{10}) , 8 (C_{26}) , 26 (C_{27}) , 42(C_{15}) , 56 , 55 ($\text{C}_8, \text{C}_{17}$) .

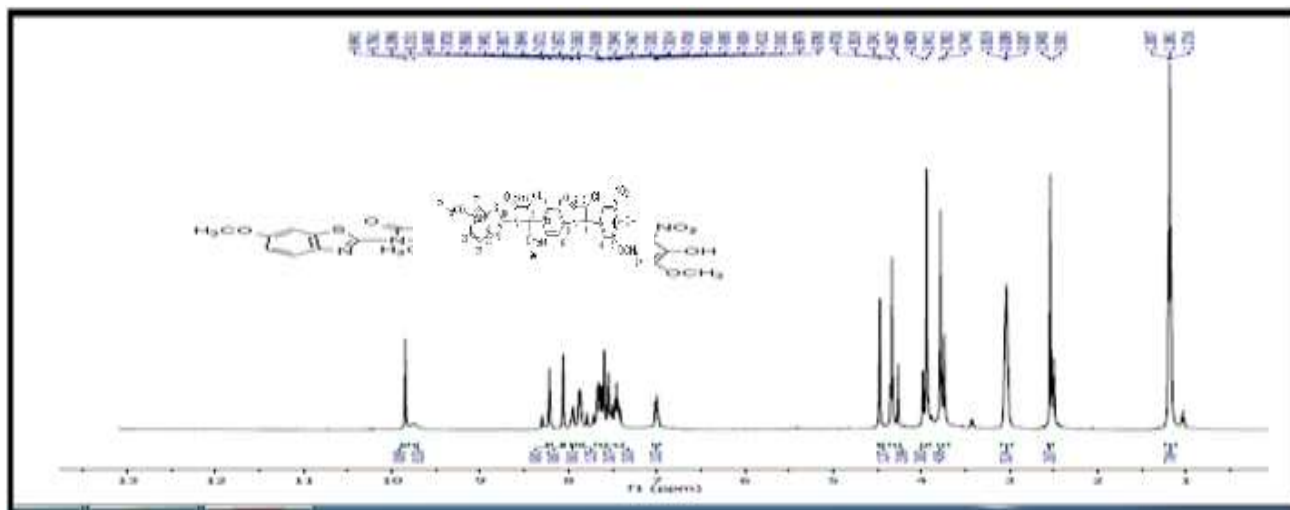


Figure 4: ^1H -NMR for Compound (7)

The Compound (8) Oxazepine Derivatives

was obtained as yellow solid yield 70%,m.p(105) $^{\circ}\text{C}$ The infrared spectrum data of compound (8) showed band at, (1681.81) cm^{-1} for (C=O), (2862.17 , 2970.17) cm^{-1} for (C-H) aliphatic , (3078.18) cm^{-1} for (C-H) aromatic , (3209.33) cm^{-1} for (OH) , (1650) cm^{-1} for (C=N) , (1550.66) cm^{-1} for (C=C), (1481.23) cm^{-1} for (C- N) .The ^1H -NMR (DMSO- d_6) spectrum data of compound (8)

show δ : 1.9 (S, 3H , CH_3) , 9.8 (S , 1H , OH) , 7 – 8.2 (M , 9H , Ar-H) , 3.5 (S , 6H , OCH_3) , 3.9 (s , 1H , CH-N) , 6.2 – 6.5 (d , 4H , CH=CH) .The ^{13}C -NMR (DMSO- d_6) spectrum data of compound (8) show δ : 190 , 197 (C_8 , C_{11} , C_{19} , C_{22}) , 167 (C_{23}) , 163 (C_3 , C_{27}) , 155 (C_{24}) , (104 – 139) $\text{C}_{\text{aromatic}}$, 148 (C_{12}) , 142 (C_5) , 26 (C_{30}) , 55.61 (C_{29}) , 55.68 (C_{31}) , 56 (C_7) , 66 (C_{18}) .

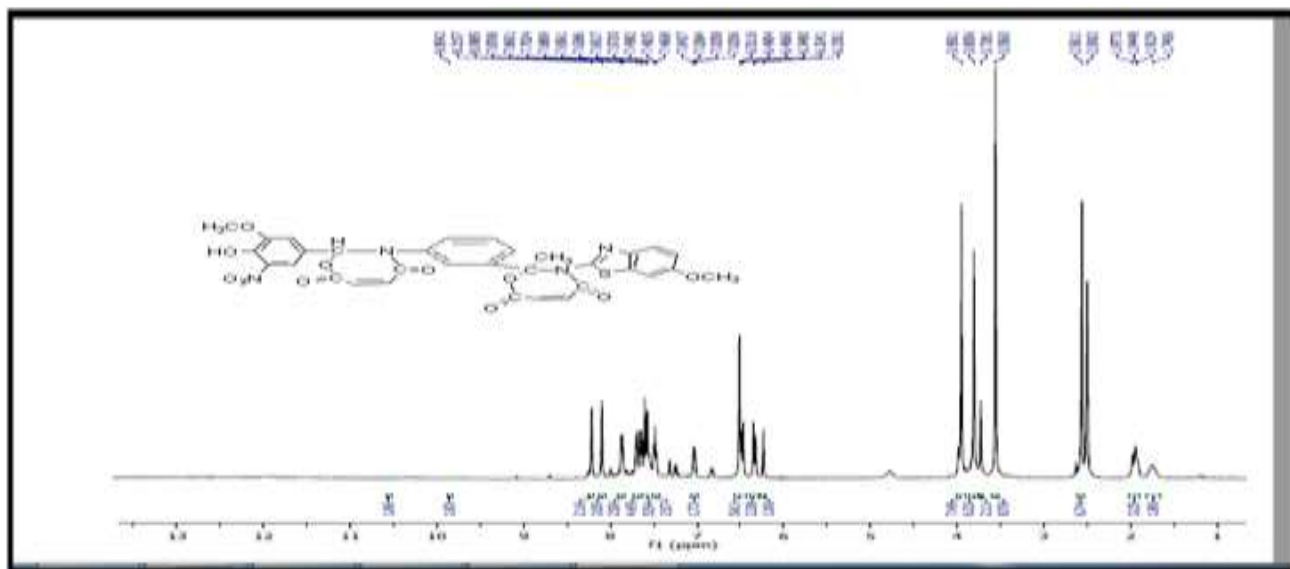


Figure 5: ^1H -NMR for Compound (8)

The Compound (9) Oxazepine Derivatives

Was obtained as yellow solid yield 71%, m.p(168 – 172) °C. The infrared spectrum data of compound (9) showed band at, (1689.53) cm^{-1} for (C=O), (2864.74 , 2977.89) cm^{-1} for (C-H) aliphatic , (3078.18) cm^{-1} for (C-H) aromatic , (3201.61) cm^{-1} for (OH) , (1650) cm^{-1} for (C=N) , (1550.66) cm^{-1} for (C=C), (1473.51) cm^{-1} for (C- N).The ^1H -NMR (DMSO- d_6) spectrum data of compound (9) show δ : 2.5 (S, 3H , CH_3) , 9.8 (S , 1H , OH) , 7 – 8.3 (M , 17H , Ar-H) , 3.5 (S , 6H , OCH_3) .The ^{13}C -NMR (DMSO- d_6) spectrum data of compound (9) show δ : 190 ,197 (C_8 , C_{14} , C_{22} , C_{29}) , 168 (C_{30}) , 167 (C_4 , C_{27}) , 150 (C_{24}) , (104 – 139) $\text{C}_{\text{aromatic}}$, 148 (C_{23}) , 142 (C_{15}) , 26 (C_{38}) , 55.61 (C_{37} , C_{39}) , 56.7(C_7) , 66.3 (C_{21}) .

The compound (10) 3-(4-hydroxy-3-methoxy-5-nitrophenyl)-1-(4-hydroxyphenyl)prop-2-en-1-one

Was obtained as yellow solid yield 85% , m.p(284) °C.The infrared spectrum data of compound (10) showed band at (2839.02, 2947.03) cm^{-1} for (C-H) aliphatic , (3001.03, 3062.75) cm^{-1} for (C-H) aromatic , (3448.49, 3517.92) cm^{-1} for (OH) , (1596.95) cm^{-1} for

(C=C) , (1550.66) cm^{-1} for (N=O) , (1658.67) cm^{-1} for (C=O).The ^1H -NMR (DMSO- d_6) spectrum data of compound (10) show δ : 3.4 (S, 3H , OCH_3) , 6.862 , 6.866 (d , 2H , $\text{CH}=\text{CH}$) , 9.4 (S , 2H , OH) , 7.983-7.987 (M , 6H) .The ^{13}C -NMR (DMSO- d_6) spectrum data of compound (10) show δ : 55.3 (C_{16}) , 188 (C_7) , 165 (C_4) , 155 (C_{14}) , (104 – 134) C_{arom} .

The compound (11) 4-(3-(4-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-5-yl)-2-methoxy-6-nitrophenol

Was obtained as red solid yield 90% , m.p(312) °C.The infrared spectrum data of compound (11) showed band at (2846.74 , 2923.88) cm^{-1} for (C-H) aliphatic , (3078.18) cm^{-1} for (C-H) aromatic , (3448.49) cm^{-1} for (OH) , (1612.38) cm^{-1} for (C=N) , (1542.95) cm^{-1} for (C=C).The ^1H -NMR (DMSO- d_6) spectrum data of compound (11) show δ : 9.3 (S, 2H , OH) , 3.69 (T , 1H , CH) , 3.3 (S , 3H , CH_3) , 3.65(d,2H, CH_2),8.3 (S , 1H , NH) , (6.8 – 7.9) (M , 6H , Ar-H).The ^{13}C -NMR (DMSO- d_6) spectrum data of compound (11) show δ : 55.3 (C_{16}) , 159 (C_4) , 155 (C_{12}) , 134 (C_7) , (105 – 123) C_{arom} .

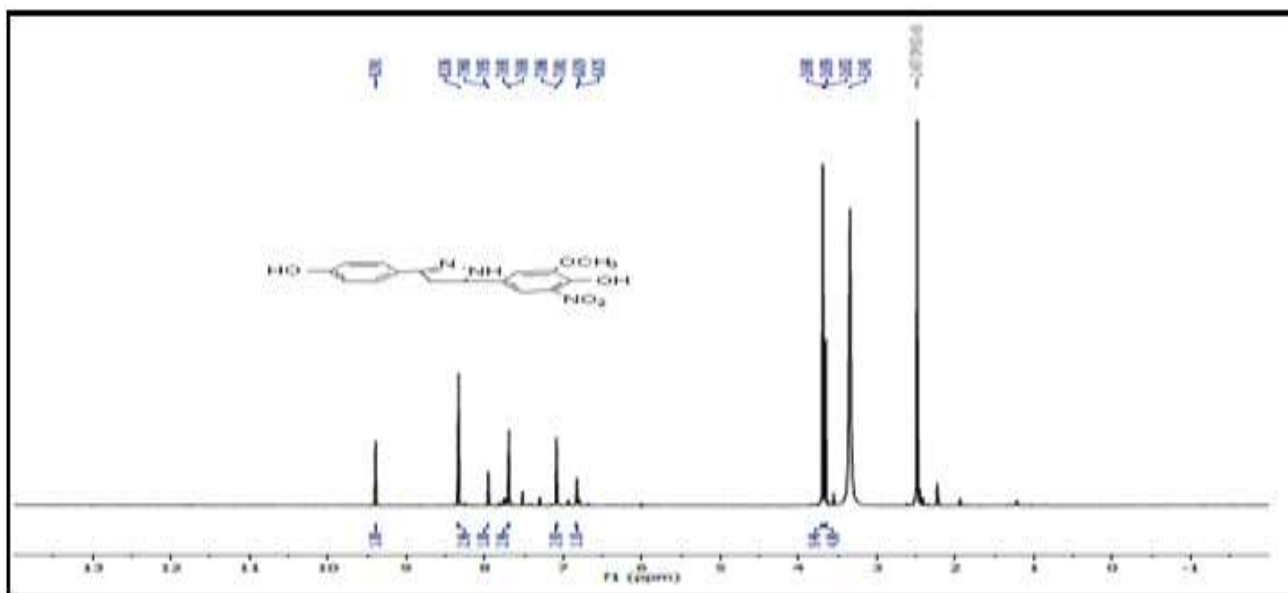
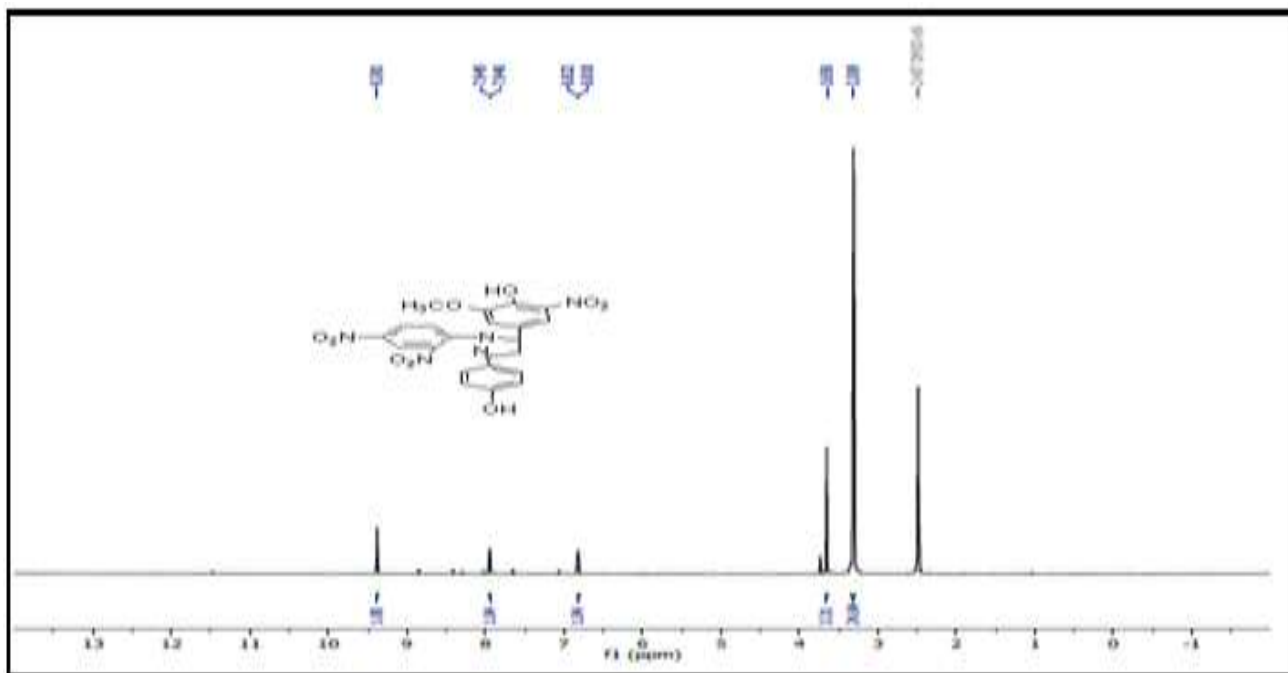


Figure 6: ^1H -NMR for Compound (11)

The Compound (12)4-(1-(2,4-dinitrophenyl)-3-(4-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-5-yl)-2-methoxy-6-nitrophenol

Was obtained as brown solid yield 98% , m.p(289) °C.The infrared spectrum data of compound (11) showed band at (2839.02 , 2947.03) cm^{-1} for (C-H) aliphatic , (3070.46) cm^{-1} for (C-H) aromatic , (3433.06) cm^{-1} for

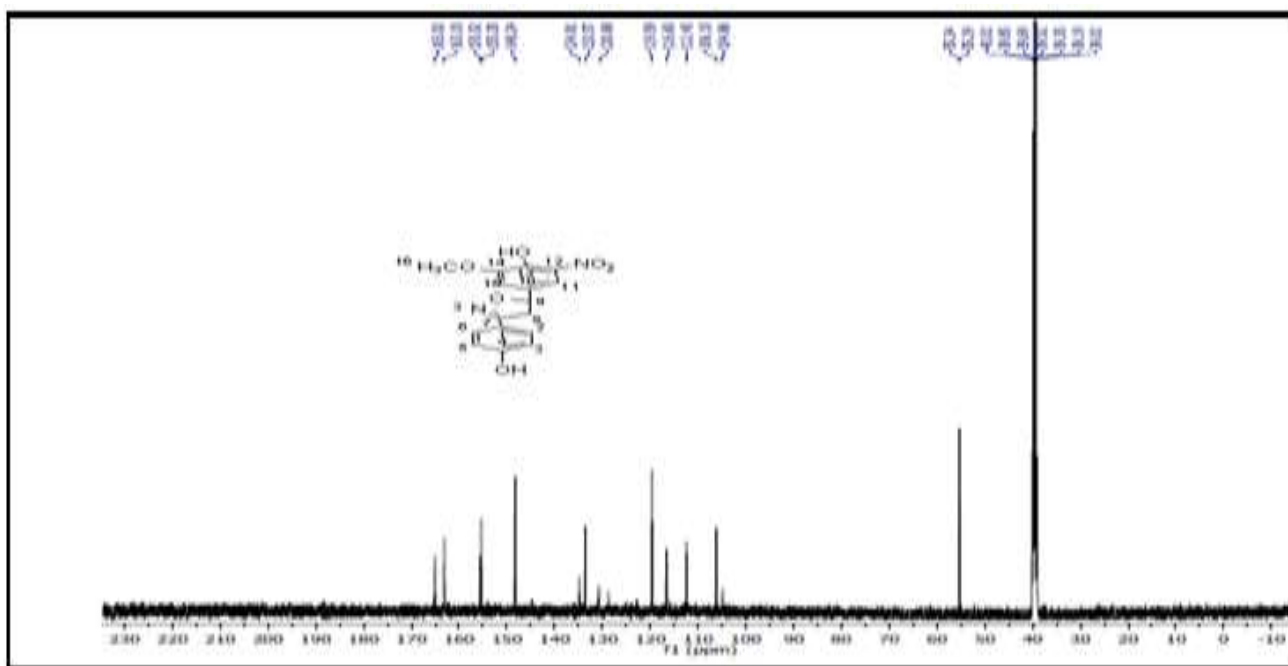
(OH) , (1596.95) cm^{-1} for (C=N) , (1550.66,1350) cm^{-1} for (NO_2).The ^1H -NMR (DMSO- d_6) spectrum data of compound (12) show δ : 9.3 (S, 2H , OH) , (3.3) (S , 3H , OCH_3) , 3.6 (d , 3H , CH_2) , 3.8 (T , 1H , CH) , (6.8 – 7.9) (M , 6H , Ar-H).The ^{13}C -NMR (DMSO- d_6) spectrum data of compound (12) show δ : 55.2 (C_{20}) , 164 (C_4) , 155 (C_8) , (104 – 134) cm^{-1} for C_{arom} .

Figure 7: ¹H-NMR for Compound (12)

The Compound (13) 4-(3-(4-hydroxyphenyl)-4,5-dihydroisoxazol-5-yl)-2-methoxy-6-Nitrophenol

Was obtained as red solid yield 98% , m.p(191)°c.The infrared spectrum data of compound (13) showed band at (2839.02 , 2923.88) cm⁻¹ for (C-H) aliphatic , (3085.89) cm⁻¹ for (C-H) aromatic , (3433.06) cm⁻¹ for (OH) , (1612.38) cm⁻¹ for (C=N-O) , (

1535.23, 1350) cm⁻¹ for (NO₂).The ¹H-NMR (DMSO-d₆) spectrum data of compound (13) show δ: 9.4 (S, 2H , OH) , (3.66) cm⁻¹ for (S , 3H ,OCH₃) , 3.68 cm⁻¹ for (T , 1H , CH) , 3.66(d,2H,CH₂),(6.9 – 8) cm⁻¹ for (M , 6H, Ar-H).The ¹³C-NMR (DMSO-d₆) spectrum data of compound (13) show δ: 55.3 (C₁₆) , 165 (C₇) , 163 (C₄) , 155 (C₉) ,55.2(C₈), (104 – 148) cm⁻¹ for C_{arom}.

Figure 8: ¹³C-NMR for Compound (13)

The compound (14) 4-(2-amino-6-(4-hydroxyphenyl)-6H-1,3-oxazin-4-yl)-2-methoxy-6-nitrophenol

Was obtained as yellow solid yield 80% , m.p(225)°c.The infrared spectrum data of compound (14) showed band at (3371.34 , 3456.20) cm⁻¹ for (NH₂) , (1674.10) cm⁻¹ for

(C=N-O) , (1604.66) cm^{-1} for (C=C) . (1550.66) cm^{-1} for (C-N) , (3458) cm^{-1} for(OH). The ^1H -NMR (DMSO- d_6) spectrum data of compound (14) show δ : 9.43 (S, 2H , OH) , (5.5) (S, 2H ,NH₂) , 3.5 (S, 3H , OCH₃) , 3.6

(S, 1H , CH) , (6.67 – 8) cm^{-1} for (M, 6H, Ar-H). The ^{13}C -NMR (DMSO- d_6) spectrum data of compound (14) show δ : 55.3 (C₁₇) , 165 (C₁₀) , 160 (C₁₄) , 156 (C₃) , 92 (C₇) , (116 – 135) C_{arom.}

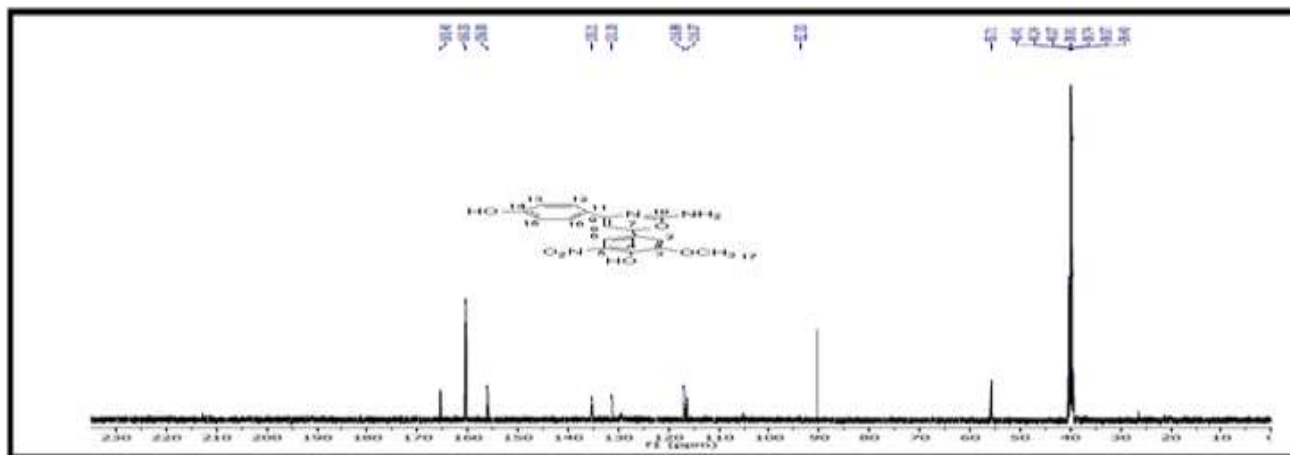


Figure 9: ^{13}C -NMR for Compound (14)

The Compound (15) 4-(2-amino-6-(4-hydroxyphenyl)-4H-1, 3-thiazin-4-yl)-2-methoxy-6-Nitrophenol

Was obtained as yellow solid yield 90% , m.p(200) $^{\circ}\text{C}$. The infrared spectrum data of compound (15) showed band at (3278.76 , 3379.05) cm^{-1} for (NH₂) , (1612.38) cm^{-1} for (C=N) , (1550.66) cm^{-1} for (C=C) , (2854.45 , 2923.88) cm^{-1} for (C-H) aliphatic,(3550) cm^{-1} for(OH), (3101.32 , 3178.47) cm^{-1} for (C-H) aromatic. The ^1H -NMR (DMSO- d_6) spectrum data of compound (15) show δ : 9.4 (S, 2H , OH) , (4.7) (S, 2H ,NH) , 3.4 (S, 3H , OCH₃) , 3.6 (S, 1H , CH) , (6.8 – 8.3) (M, 6H, Ar-H). The ^{13}C -NMR (DMSO- d_6) spectrum data of compound (15) show δ : 55 (C₁₇) , 164 (C₁₀) , 155 (C₁₄) , 134 (C₃) , 92 (C₇) , (116 – 131) C_{arom.}

The compound (16) 4-(4-hydroxy-3-methoxy-5-nitrophenyl)-6-(4-

hydroxyphenyl) - 2- oxo- 1,2-dihydropyridine- 3- carbonitrile

Was obtained as orange solid yield 96% , m.p(182) $^{\circ}\text{C}$. The infrared spectrum data of compound (16) showed band at (2846.74 , 2985.60) cm^{-1} for (C-H) aliphatic , (3078.18) cm^{-1} for (C-H) aromatic, (3240.19) cm^{-1} for (NH) , (3433.06 , 3479.34) cm^{-1} for (OH) , (1735) cm^{-1} for (C=O) , (1681.81) cm^{-1} for (C=C) , (1604) cm^{-1} for (C-N) , (1550.66) cm^{-1} for (N=O) , (2214.13) cm^{-1} for (CN group) . The ^1H -NMR (DMSO- d_6) spectrum data of compound (16) show δ : 9.4 (S, 2H , OH) , 3.6 (S, 3H , OCH₃) , 8.1 (S, 1H , NH) , (6.9 – 7.9) (M, 7H, Ar-H). The ^{13}C -NMR (DMSO- d_6) spectrum data of compound (16) show δ : 188 (C₉) , 55 (C₁₈) , 89 (C₈) , 61 (C₁₁) , 164 (C₁₀) , 163 (C₄) , 154 (C₅) , (106 – 137) C_{arom.}

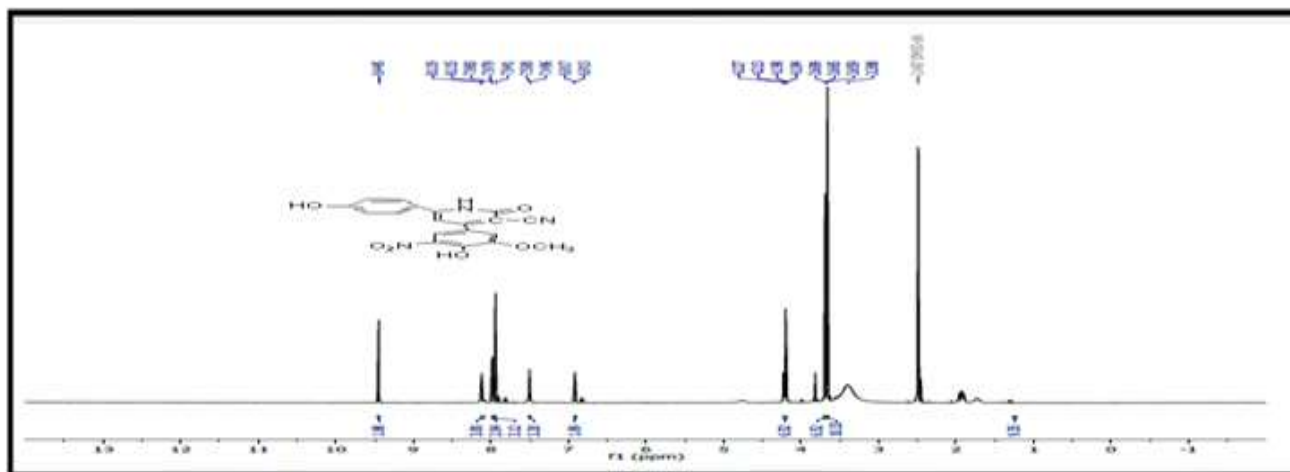


Figure 10: ^1H -NMR for Compound (16)

The compound (17)2-amino-6-(4-hydroxy-3-methoxy-5-nitrophenyl)-4-(4-hydroxyphenyl) nicotinonitrile

Was obtained as brown solid yield 97% , m.p(228)^oC.The infrared spectrum data of compound (17) showed band at (2839.02 , 2939.31) cm⁻¹ for (C-H) aliphatic , (3016.46) cm⁻¹ for (C-H) aromatic, (3240.19) cm⁻¹ for (NH₂) , (3456.20) cm⁻¹ for (OH) , (1604.66)

cm⁻¹ for (C=N) , (1542.95) cm⁻¹ for (C=C) , (2221.84) cm⁻¹ for (CN group). The ¹H-NMR (DMSO-d₆) spectrum data of compound (17) show δ: 9.4 (S , 2H , OH) , (4.3) (S , 2H ,NH₂) , 3.6 (S , 3H , OCH₃) , (6.8 – 8) (M , 7H, Ar-H).The ¹³C-NMR (DMSO-d₆) spectrum data of compound (17) show δ: 55.2 (C₁₈) , 111 (C₁₉) , 164 (C₁₀) , 157 (C₉) , 155 (C₁₅) , 154 (C₅) , (111 - 106 - 137) C_{arom.}

Table1: Analytical and physical data of compounds

No.	Molecular formula	Color	M.P °C	Rf	Yield%
1	C ₁₆ H ₁₄ N ₂ O ₅ (314.09)	Yellow	155	0.58	66
2	C ₂₄ H ₂₀ N ₄ O ₅ S (476.12)	Orange	78 – 81	0.6	85
3	C ₂₄ H ₂₂ N ₁₀ O ₅ S (562.57)	Red	125	0.3	79
4	C ₃₀ H ₃₀ N ₆ O ₇ S (618.67)	Brown	Serum	0.5	75
5	C ₂₈ H ₂₆ N ₆ O ₇ S (590.61)	Brown	Serum	0.4	79
6	C ₂₈ H ₂₄ N ₄ O ₇ S ₃ (624.70)	Brown	Serum	0.6	92
7	C ₂₈ H ₂₂ Cl ₂ N ₄ O ₇ S (629.47)	Yellow	Serum	0.8	77
8	C ₃₂ H ₂₄ N ₄ O ₁₁ S (672.62)	Yellow	105 – 110	0.5	70
9	C ₄₀ H ₂₈ N ₄ O ₁₁ S (772.15)	Yellow	168 – 172	0.37	71
10	C ₁₆ H ₁₃ NO ₆ (315.28)	yellow	284	0.87	85
11	C ₁₆ H ₁₃ N ₃ O ₅ (327.30)	red	312	0.73	90
12	C ₂₂ H ₁₅ N ₅ O ₉ (493.39)	brown	289	0.9	98
13	C ₁₆ H ₁₂ N ₂ O ₆ (328.28)	red	191	0.83	98
14	C ₁₇ H ₁₅ N ₃ O ₆ 357.32	yellow	225	0.9	80
15	C ₁₇ H ₁₅ N ₃ O ₅ S 373.38	yellow	200	0.93	90
16	C ₁₉ H ₁₃ N ₃ O ₆ (379.33)	orange	182	0.4	96
17	C ₁₉ H ₁₄ N ₄ O ₅ (378.34)	brown	228	0.53	97

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