Synthesis , Identification and Study The Biological Activity of Some Tetrazole Derivatives From Imidazole Derivative

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الخلاصة

تضمن البحث تحضير مشتقات التيترازول بسلسلة من التفاعلات ، تتضمن الخطوة الاولى تفاعل اورثو- فنلين ثنائي امين مع ٥- امينوحامض السالسلك في وسط حامضي للحصول على ٤-امينو-٢-(بنزواميدازول-٢-ايل)فينول (١).المركب(١) يتفاعل مع (٤- ثنائي مثيل امينوبنزالديهايد، ٤- هيدروكسي اسيتوفينون، فانلين، استيل الاسيتون،٤- برومو اسيتوفينون،٣-امينواسيتوفينون،) في وسط حامضي لتكوين قواعد شف (٢,٣,٤,٥,٦,٧) على التوالي.(٧) يتفاعل مع كل من (٤-كلوروبنزالديهايد، ٤- بروموا‌سيتوفينون)في وسط حامضي لتكوين قواعد شف (٨و٩) على التوالي.(١) يتفاعل مع السالسلديهايد في وسط حامضي وبوجود نتريت الصوديوم لنحصل على مشتق الازو(١٨).كل مشتقات قواعد شيف (٢.٣,٤,٥,٦,٧,٨,٩) تتفاعل مع ازايد الصوديوم لنحصل على مشتقات التيترازول (١٠,١١,١٢,١٣,١٤,١٥,١٦,١٧)على التوالي.(١٨) يتفاعل مع ((٣- نيتروانلين،٤- امينواسيتوفينون، ٥- نيترو-٢- امينوثيازول،٢- امينوبنزواميدازول، ٢- امينوبريدين،بنزداين) لنحصل على مشتقات قواعد شيف (١٩,٢٠,٢١,٢٢,٢٣,٢٤) على التوالي ،والتي تتفاعل مع ازايد الصوديوم لنحصل على مشتقات التيترازول(٢٥,٢٦,٢٧,٢٧٨,٢٩,٣٠) على التوالي. كل هذه المركبات تم تشخيصها بواسطة (FT-IR) وبعضها بواسطة طيف الرنين النووي المغناطيسي للبروتون وطيف الرنين النووي المغناطيسي للكاربون 13 وتم متابعة التفاعل بتقنية R_f -TLC وتم قياس درجة الانصهار.

Abstract

This research involved synthesis of tetrazol derivatives by a chain of reaction. The first step includes react between o-phenylenediamin with 5-amino salicylic acid to get 4-amino-2(1H-benzo[d]imidazol-2-yl)phenol(1).(1) react with (4-dimethylamino benzaldehyde ,4-hydroxy acetophenone ,Vanillin, Acetylacetone , 4-Bromoacetophenone and m-aminoacetophenone) to get schiff base derivatives (2,3,4,5,6 and 7) consecutive.(7) react with (4-chlorobenzaldehyde ,4-Bromoacetophenone) to get schiff base derivatives (8,9) consecutive.(1) react with salicylaldehyde and sodium Nitrate in acid medium to get azo derivative (18).All schiff base derivatives (2,3,4,5,6,7,8,9) react with sodium azide to get tetrazol derivatives (10,11,12,13,14,15,16 and17) consecutivly.(18) which react with (3-nitro aniline , 4- amino acetophenone , 2-amino-5-nitrothiazole ,2-aminobenzimidazole ,2-aminopyridine and benzidine) to get schiff base derivatives (19,20,21,22,23 and 24) consecutive,which react with sodium azide to get tetrazole derivatives (25,26,27,28,29 and 30) consecutive.All these compounds characterized by means of FT-IR,and some of the compounds by means of ^{1}H-NMR, and ^{13}C-NMR and follow the reaction by R_f-TLC and measurement of melting point.

Key words:- *Tetrazole, schiff base, azo ,imidazole compounds*

Introduction

A heterocyclic compound or ring structure is a cyclic compound that has atoms of at least two different elements as members of its ring[1]. Heterocyclic Chemistry considered more complex in organic chemistry depending upon nature of different atom in the ring , type of ring , aromaticity or non.Heterocyclic compounds have medicinal biological effectiveness,This Encouraged scientists to synthesis many of these compounds and developed them for using in pharmaceutical field. its Scattered in nature and interference in the synthesis of a lot of biomolecules , vitaminas , dyes and enzymes. In this research; new heterocycle amines compounds were prepared .which have wide uses in medicine and pharmacy[2,3].Imidazole derivatives play important role in medical and industrial fields ,such as Medetomidine which used in surgery and pain relief as well as ornidazole , metronidazole using for antibacterial drugs.Benzimidazole are remarkably ,effective compounds in biochemical researches .This manifested clearly appear in this compounds benzimidazole nucleus: Dabigatran as anticoagulants, Rivoglitazone as antidiabetic , Maribavir as antiviral, Flibanserin drugs in HSDD,Candesartan as antihypertensive and Telmisartan as anti-hypertensive[4-6].Benzimidazole-schiff base derivatives show a possessed biological activities such as anticonvulsant antitumor , antidepressant and cardiac stimulant [7,8].In this research new tetrazole derivatives were prepared by reaction of Schiff base with sodium azide in DMSO as solvent[9]. In recent years, the development of the tetrazole chemistry has been attracted much attention because of their unique structure and applications as antihypertensive, anti allergic, antibiotic and anticonvulsant agents [10,11].Some of tetrazoles containing groups have been used both as anticancer and antimicrobial agents.[12] Tetrazoles played central roles in coordination chemistry and explosives.[13] and can be replacements for carboxylic moiety in drug composition , with the advantage over carboxylic moieties being that they are resistant to many biological metabolic degradation pathways.[14-16]

Experimental Apparatus

(FTIR)Spectra(4000-400 cm^{-1}) used KBr disk were recorded on a SHIMADZU FTIR-8400S fourier.transform. melting point were measured using Stuart, UK. Elemental Analysis 3764,carlo erba Europ,^{1}H-NMR were recorded by fourier transformation bruker spectrometer , operating at (400MHz)with(DMSO-ds) measurements were made at department of chemistry Kashsn university Iran.

Experimental

-Synthesis of imidazole derivative(4-amino-2-(1H-benzo [d] imidazol-2-yl) phenol) (1) [17] Equi molar quantities(0.01) mol of o-phenylenediamine , 5-aminosalicylic acid(0.01) mol in (20ml) of HCl (4N) was refluxed for half hour the mixture is cooled and filtered off.The residue (1) the product was recrystallized from absolute ethanol alcohol .The precipitate was brilliant gray color.

-General method of synthesis Schiff base (2,3,4,6 and 7) [18]Amixture of equimolar quantities (0.01mol)of (1)and(4-(N,N-Dimethylaminobenzaldehyde,4-Hydroxyacetophenone ,Viniline ,4-bromo acetophenone and 3-amino acetophenone) (0.01mol) were refluxed for (2-3)hs in (50)ml of ethanol alcohol .Then it was added (2)drops of glacial acetic acid as catalyst .The reaction mixture was cooled and kept for (24)hours .the crystals products was filtered,dried and recrystallization from ethanol alcoholgive (2,3,4,6 and 7)consecutive.

-Synthesis schiff base derivative4,4'-((1Z,1'E)-pentane-2,4-diylidenebis(azanylylidene))bis(2-(1H-benzo[d] imidazol -2-yl)phenol) (5**)** A mixture of(0.02 mol of (1) and acetyl acetone (0.01) mol was refluxed for (2-3) hs in (50)ml of ethanol alcohol.Then it was added(2)drops of glacial acetic acid to the mixture as catalyst . The reaction mixture was cooled and kept for (24)hours . the crystals found was filtered ,dried and recrystallization from ethanol alcohol to give compound(5).

-Synthesis Schiff base (8,9) Amixture of (0.01) mole of(7)and(4-chlorobenzaldehyde,4-bromo acetophenone (0.01mole) were refluxed for(2-3)hrs. in (50)ml of ethanol alcohol. Then it was added(2)drops of glacial acetic acid to the mixture as catalyst .The reaction mixture was cooled and kept for (24) hours . the crystals found was filtered ,dried and recrystallization from ethanol alcohol to give(8 and 9) consecutives.

-Synthesis of tetrazole derivative (10,11,12,14 and 15) [19]A mixture of Schiff base (2,3,4,6 and 7)(0.001mol) dissolved in 1,4- dioxane (15ml) and sodium azide(0.001mol) was dissolved in 1,4dioxan(15ml) and refluxed for(14-24) hrs.The mixture was cooled and the resulting final (10,11,12,14 and15) consecutive recrystallization from ethanol.

-Synthesis of tetrazole derivative (13,16 and 17)Amixture of Schiff base(5,8 and 9)consecutive (0.001mol) dissolved in 1,4dioxan(15ml) and sodium azide (0.002mol) was dissolved in 1,4-dioxan(15ml) and refluxed for(14-24)hrs .The reaction was cooled and the resulting final (13,16 and 17) consecutive recrystallization from ethanol.

-Synthesis of 5-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-hydroxybenzald- ehyde (18). [20] (1)derivative (0.005mmol,1.12gm) of the aromatic amine was dissolved in 5 ml of concentrated HCl and (8ml) of distilled water.The mixture is cooled to(0C^{o}) and (0.005mmol)of sodium nitrate to added dropwise with continuous stirring .The solution was left for 15 minutes to stable after completing the addition(0.005mmol)of salicylaldehyde dissolved in (1g NaOH in 50ml H_2O) was added,a yellow precipitate was formed,filtered and recrystallization from ethanol.

-Synthesis Schiff base compounds (19,20,21,22 and 23) Amixture of(0.01)mole of(18) and (3-nitroaniline,4-amino acetophenone,2-amino pyridine)(0.01mole) were refluxed for(2-3)hrs in (30)ml of ethanol alcohol. Then it was added(2)drops of glacial acetic acid as catalyst .The reaction mixture was cooled and kept for 24 hours . the crystals and was filtered ,dried and recrystallization from ethanol alcohol to give(19,20,21,22 and 23) consecutive.

-Synthesis Schiffbase 4,4'-((((1E)-([1,1'-biphenyl]-4,4'-diylbis(azanylylidene))bis(methanylylid ene))bis(4-hydroxy-3,1-phenylene))bis(diazene-2,1-diyl))bis(2-(1H-benzo[d]imidazol-2-yl) phenol) (24) A mixture of (0.02)mole of (18) and Benzidine (0.01mol) was refluxed for(2-3)hrs in (30)ml of ethanol alcohol .Then it was added(2)drops of glacial acetic acid to the mixture as catalyst.The reaction mixture was cooled and kept for 24 hours . the crystals and was filtered ,dried and recrystallization from ethanol alcohol to give(24) compound.

-Synthesis of tetrazole derivatives (25,26,27,28 and 29)Amixture of Schiff base (19,20,21,22 and 23) consecutive (0.01mol) dissolved in 1,4-dioxan(15ml) and sodium azide (0.01mol) was dissolved in 1,4-dioxan(15ml) and refluxed for(14-24)hrs .The reaction was cooled and the resulting final (25,26,27,28 29) consecutive recrystallization from ethanol.

-Synthesis of tetrazol derivative4,4'-(((1,1'-([1,1'-biphenyl]-4,4'-diyl) bis(1H-tetrazole-5,1-diyl))bis(4-hydroxy-3,1-phenylene))bis(diazene-2,1-diyl))bis(2-(1H-benzo[d]imidazol-2-yl)
phenol) (30)A mixture of Schiff base (24)(0.01mol) dissolved in 1,4-dioxan(15ml) and sodium azide (0.01mol) was dissolved in 1,4dioxan(15ml) and refluxed for(14-24)hrs.The reaction was cooled and the resulting final (30) recrystallization from ethanol

-preparation of Microbiology culture media: It's wighting about (20 gram) of nutrient agar and dissolved in (500ml) of distillation water,then put in autoclave for (20 minute)at 200C^{o} for sterilization it . Pouring the media after become at 37^{O}C in Petri dishes , made ready for streaking by bacteria.It was getting (*Escherichia coli*) and (*staphylococcus aurous*) isolated

bacteria from hospital . It was cultured and These plates were incubated at 37C° for (24) hrs for both bacteria. [21]

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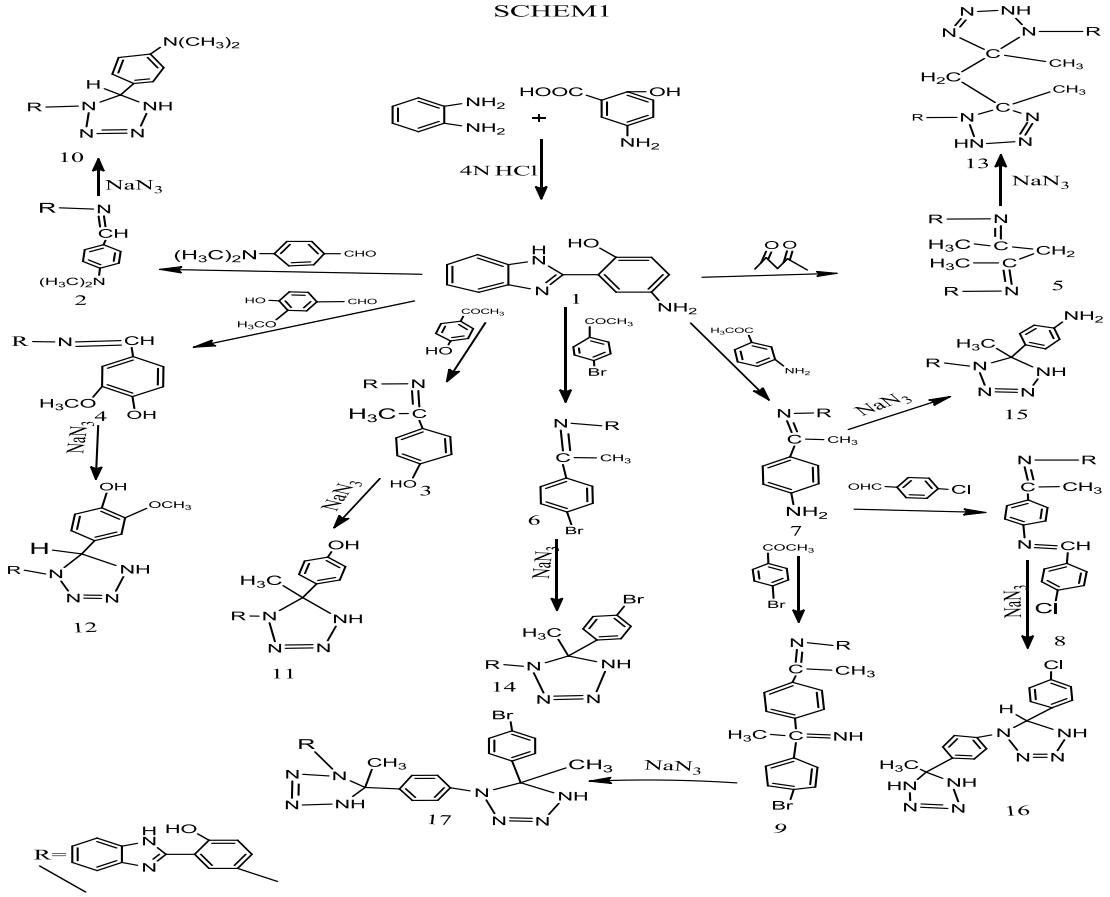
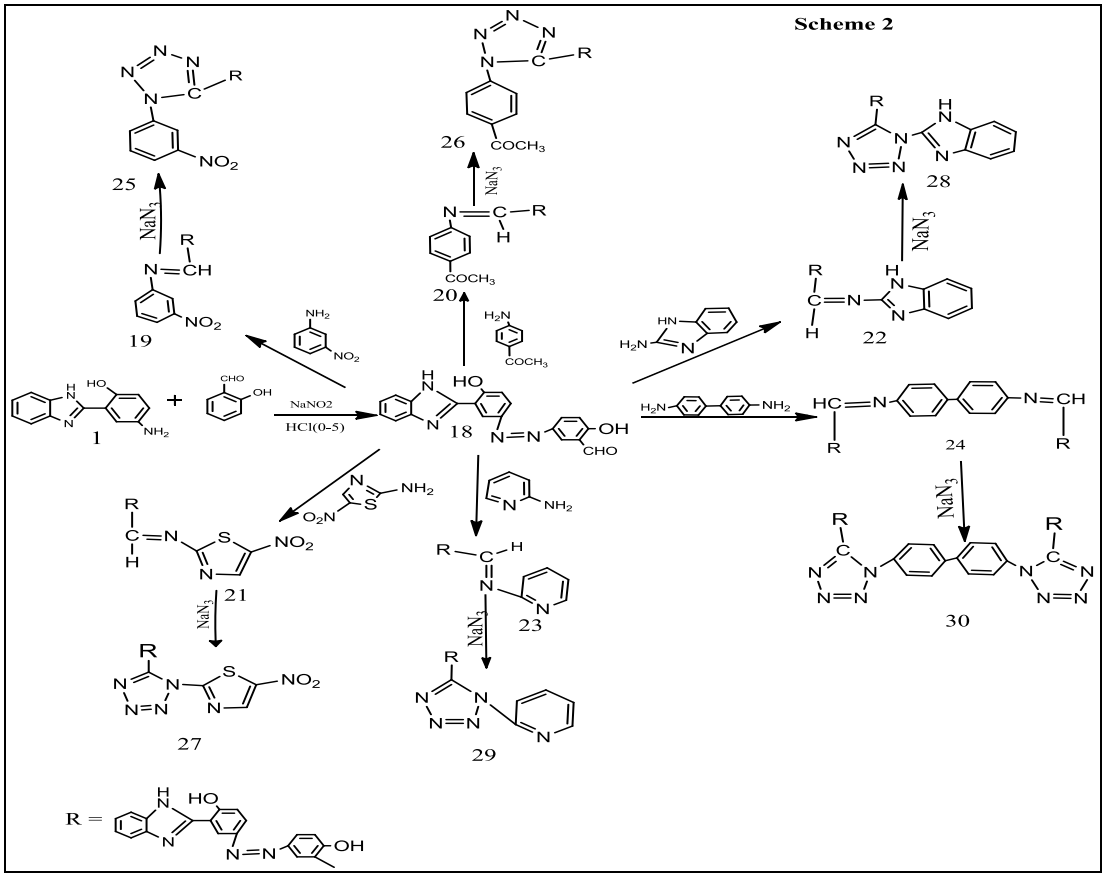
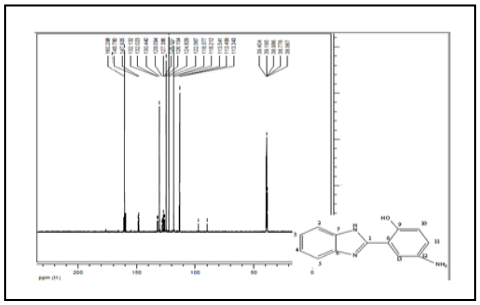


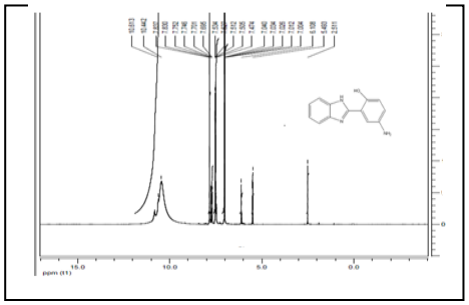


Results and Discussion

Compound(1) 4-amino-2-(1H-benzo[d]imidazol-2-yl)phenol:The infrared spectrum data of compound (1) showed band at (3348) cm^{-1} for(N-H)in(NH_2),(3024)$cm^{-1}$for(Ar-H),(3163)cm^{-1} for(N-H)imidazole,(1666)$cm^{-1}$for(C=N) inside Imidazole ring ,(3450)cm^{-1} for(O-H) (1566) cm^{-1} for(C=C)Aromatic.The ^{1}H NMR (DMSO) spectrum data of compound(1) show δ:6-7.8(m., 6H, Ar- H),10.4 S,1 H OH,5.4(S,2H,NH_2),10.6(S,2H,NH Amidazol ring).The ^{13}C-NMR (DMSO) spectrum data of compound(1) showδ: 113(C_5,C_2) ,130(C_{10}) , 147 (C_{12}), 128 (C_8), 160(C_1),127 (C_{11}),126(C_{13}) 148(C_9) ,123(C_6,C_7),122(C_3,C_4) .



Fig(2)^{13}C-NMRspectrumdatafor(1)compound cm^{-1}



Fig(1)^{1}HNMRspectrum data for(1)compound cm^{-1}

-Schiff Base [2-6].Compound(E)-2-(1H-benzo[d]imidazol-2-yl)-4-((4-(dimethylamino)benzyl idene)amino)phenol (2) The infrared spectrum data of compound (2) showed band at ,(2923)cm^{-1}

for (C-H) in CH_3,(3147) for(N-H)Imidazol, ,(3070) $cm^{-1}$for (Ar-H),(1666) cm^{-1} for(C=N) Imidazol ,(1589)for(C=C)Arom,(3487) cm^{-1} for (O-H) phenol.

-Compound(E)-4-(((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)imino) methyl) -2-methoxy phenol (3) The infrared spectrum data of compound(3) shows band at. (2964)cm^{-1} for (C-H) in CH_3,(3101) cm^{-1} for(N-H)Imidazol, ,(3062) $cm^{-1}$for (Ar-H),(1666) cm^{-1} for(C=N) Imidazol ,(1589) $cm^{-1}$for(C=C)Arom,(3210) $cm^{-1}$for (O-H)phenol.The ^{1}H NMR (DMSO) spectrum data of compound(3) show δ:6-7.8,(m,11H Ar-H), 10.3 (S,2H,2OH,), 2.4(S,3H,CH_3,).The ^{13}C-NMR (DMSO) δ:162.06(C14),160(C19,C9),130.6(C1),62(C2) .

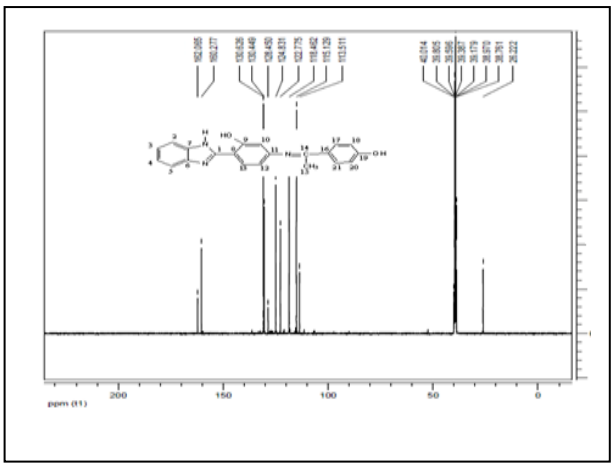


Fig (4) 13C-NMR spectrum for(3) compound cm^{-1}

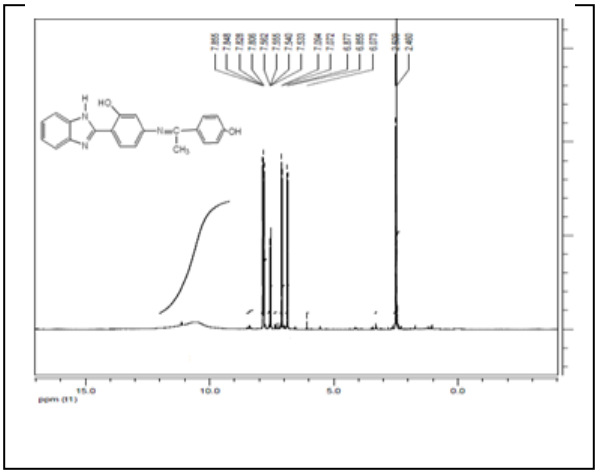


Fig (3) ^{1}H-NMR spectrum for(3)compound cm^{-1}

-Compound 2-(1H-benzo[d]imidazol-2-yl)-5-((1-(4-hydroxyphenyl) ethylidene) amino) phenol(4) The infrared spectrum data of compound (4) showed band at , (2960)cm^{-1} for (C-H) in CH_3,(3120) $cm^{-1}$for(N-H)Imidazol, ,(3024) $cm^{-1}$for (Ar-H),(1650) cm^{-1} for(C=N) Imidazol ,(1589) cm^{-1} for(C=C)Arom,(3271) cm^{-1} for (O-H)phenol(1211) $cm^{-1}$for (C-O-C).

-Compound(E)-2-(1H-benzo[d]imidazol-2-yl)-4-((1-(4-bromophenyl)ethylidene) amino)phenol (5)The infrared spectrum data of compound (5) showed band at , (2862) cm^{-1} for (C-H) in CH_3,(3160) cm^{-1} for (N-H) imidazol, ,(3062) cm^{-1} for (Ar-H),(1666) for(C=N) Imidazol ,(1535) cm^{-1} for(C=C)Arom,(3386) cm^{-1} for (O-H) phenol.

-Compound (E)-4-((1-(4-aminophenyl)ethylidene)amino)-2-(1H-benzo[d] imidazol -2-yl) phenol(6). The infrared spectrum data of compound (6) showed band at , (2950)cm^{-1} for (C-H) in CH_3,(3100) cm^{-1} for(N-H) Imidazol, ,(3062) cm^{-1} for (Ar-H),(1666) cm^{-1} or(C=N)Imidazol ,1535)for(C=C)Arom,(3332)for(O-H)phenol.

-Compound 2-(1H-benzo[d]imidazol-2-yl)-4-((E)-(1-(4-((4-chlorobenzylidene) amino) phenyl) ethylidene)amino)phenol (7).The infrared spectrum data of compound (7) showed band at , (2975)cm^{-1} for (C-H) in CH_3,(3180) cm^{-1} for(N-H)Imidazol, ,(3062) $cm^{-1}$for (Ar-H),(1674) cm^{-1} for (C=N)Imidazol ,(1635) cm^{-1} for (C=C)Arom,(3340)for(O-H)phenol,(3371)for(N-H)NH_2

-Compound 2-(1H-benzo[d]imidazol-2-yl)-4-((E)-(1-(4-((E)-(1-(4-bromophenyl) ethylidene) amino)phenyl)ethylidene)amino)phenol(8). The infrared spectrum data of compound (8) showed band at(3110) cm^{-1} for(N-H) Imidazol, (3025)cm^{-1} for(Ar-H), (1620) cm^{-1} for (C=N) Imidazol,(1689) cm^{-1} for(C=C)Arom,(3320) cm^{-1} for(O-H)phenol,(3366) cm^{-1} for(N-H) NH_2.

-Compound4,4'-((1Z,1'E)-pentane-2,4-diylidenebis(azanylylidene))bis(2-(1H-benzo[d]imidazol-2-yl)phenol) (9)The infrared spectrum data of compound (9) showedbandat(3163)for(N-H)Imidazol,(3093)$cm^{-1}$for(Ar-H),(1666) cm^{-1} for (C=N) Imidazol ,(1689) cm^{-1} for(C=C) Arom ,(3417) $cm^{-1}$for(O-H)phenol,(3215) cm^{-1} for(N-H)NH_2.

Tetrazole(10-17) Compound 2-(1H-benzo[d]imidazol-2-yl)-4-(5-(4-(dimethylamino)phenyl) -4,5 -dihydro-1H-tetrazol-1-yl)phenol (10).The infrared spectrum data of compound(10) shows (3001)$cm^{-1}$for(Ar-H), (3433) cm^{-1} for (O-H) , (3209)$cm^{-1}$for(N-H)Imidazole , (2808-2962)cm^{-1} for(C-H)CH_3**.** (N=N)at(1434) cm^{-1}**,** (C=N) at(1542) cm^{-1}**.**The^{1}H NMR (DMSO) spectrum data of -Compound(10) show δ:6.7-7.8**(**m,11Ar-H) (S,1OH,7.1), S,6H,2CH_3,2.3)(S,NH amidazol ring,9.6).The^{13}C-NMR (DMSO) spectrum data of compound(10) show δ :131(C1),106-118(C-Aromatic) ,150(C9) ,160(C18), 125(C15), 121(C12) ,129(C8) .

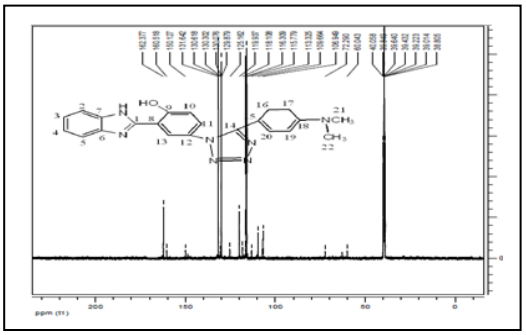


Fig 6^{13}CNMR spectrum for(10) compound cm^{-1}

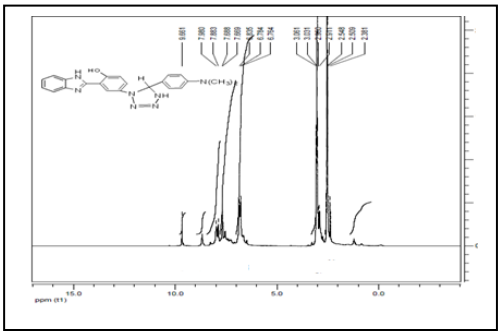


Fig 5 H-NMR spectrum for(10) compound cm^{-1}

-Compound 2-(1H-benzo[d] imidazol-2-yl)-4-(5-(4-hydroxyphenyl)-5-methyl-4,5-dihydro-1H-tetrazol -1-yl)phenol (11).The infrared spectrum data of compound(11) shows (3085)$cm^{-1}$for (Ar-H), (3320)$cm^{-1}$for (O-H),(3116)$cm^{-1}$for(N-H) Imidazole(2923)cm^{-1} for(C-H)CH_3**.** (N=N)at(1434) cm^{-1}**,** (C=N) at(1589) cm^{-1}(3200) cm^{-1} for (N-H) Tetrazol .The^{1}H NMR (DMSO) spectrum data of compound(11) show δ **(**m,11Ar-H**,**6.8-7.8) ,(S,2OH,10.1) ,(S,3H,CH3,2.3) (S,NH amidazol ring,10.4),(S,NH tetrazol ring ;10.6).The^{13}C-NMR (DMSO) spectrum data of compound(10) show δ: 26(C15) , 113-118 (CAromatic) ,125(C9),123(C6,C7), 160(C14) ,131(C1),130(C16).

-Compound 4-(1-(3-(1H-benzo [d]imidazol-2-yl)-4-hydroxyphenyl)-4,5-dihydro-1H-tetrazol-5-yl)-2-methoxyphenol(12). The infrared spectrum data of compound(12) shows (3008)cm^{-1} for(Ar-H), (3348) cm^{-1} for (O-H) ,(3116)$cm^{-1}$for(N-H)Imidazole , (2960-2829)cm^{-1} for(C-H)CH_3**.** (N=N)at(1434) cm^{-1}**,** (C=N) at(1589) cm^{-1}**.**The^{1}H NMR (DMSO) spectrum data of compound(12) show δ,**(**m,10Ar-H**,**6.9-7.7),(s,2OH,8.6),(s,3CH_3,3.8),(s,NH amidazol ring , 9.7).

The^{13}C-NMR (DMSO) spectrum data of compound(10) show δ ,161(C14), 150(C9,C18),114-142(C-Arom),147(C1).

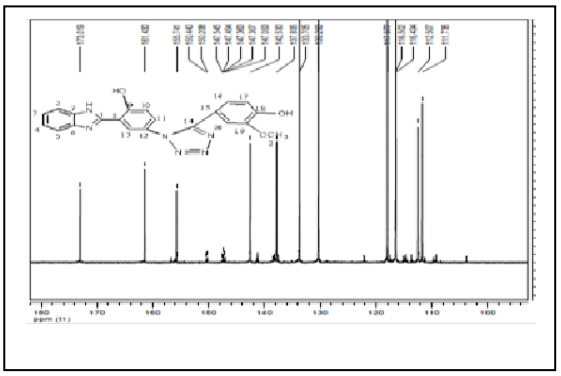


Fig (8)13CNMR spectrum for(12) compound cm^{-1}

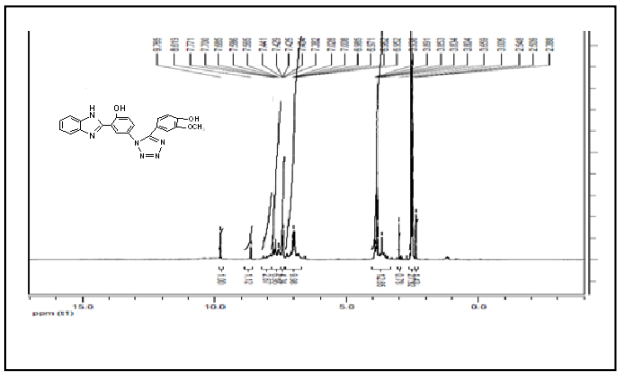


Fig (7)HNMR spectrum for(12) compound cm^{-1}

-CompoundDi[2-(3H-benzo[d]imidazol-2-yl)-4-(5-methyl-2,5-dihydro-1H-tetrazol-1-yl)phenol] Methane(13). The infrared spectrum data of compound(13) shows (3040)$cm^{-1}$for(Ar-H) , (3386) cm^{-1} for (O-H) , (3161)$cm^{-1}$for(N-H)Imidazole , (2939) cm^{-1} for (C-H)CH_3**.** (N=N) at(1450) cm^{-1}**,**

(C=N) at(1581) cm^{-1}.The ^{1}H NMR (DMSO) spectrum data of compound(14) show δ,(m,10Ar-H,6.7-7),(s,2H,OH,9.8),(s,6H,CH3,2.007)(s,NH in amidazol ring,9.8),(s,NH tetrazol ring;10.2)

The ^{13}iC-NMR (DMSO) spectrum data of compound(13) show δ:60(C15,C18), 152 (C6,C7 ,C31 ,C32) ,11-132(C-arom),72(C14,C17) , 163(C1,C26) , 66(C16).

-Compound(14) 2-(1H-benzo[d]imidazol-2-yl)-4-(5-(4-bromophenyl)-5-methyl-4,5-dihydro-1H-tetrazol-1-yl)phenol.The infrared spectrum data of compound(14) shows (3040)$cm^{-1}$for(Ar-H), (3340) cm^{-1} for (O-H) , (3125)$cm^{-1}$for(N-H)Imidazole , (2965)cm^{-1} for(C-H)CH_3. (N=N)at(1404) cm^{-1}, (C=N) at(1589) cm^{-1}.The1HNMR (DMSO δ ppm): 2.5,(m,10Ar-H,7.81-7.4),(s,2OH,8.5) ,(s,1CH3,2)(s,NH in imidazol ring,9.8),(s,NH tetrazol ring;10.1).The13C-NMR(DMSO) δ :26(C15),123(C6,C8),130(C16,125(C9),124(C12),113-118(C_{Arom}), 60(C14),131)(C1).

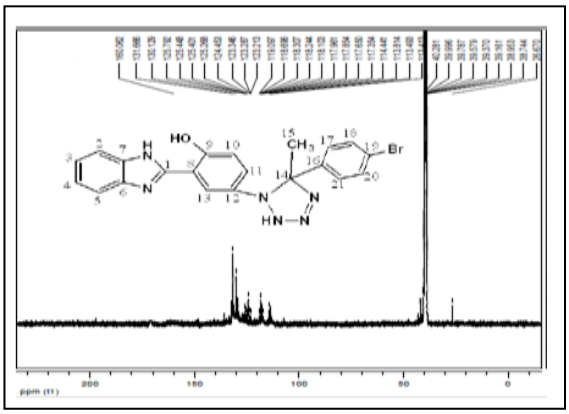


Fig10HNMR spectrum for(14) compound cm^{-1}

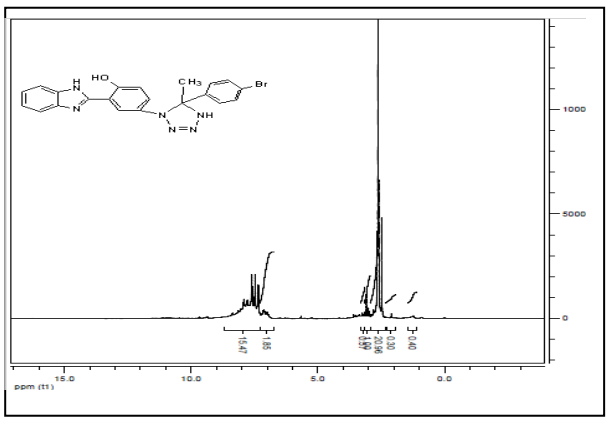


Fig 9 HNMR spectrum for(14) compound cm^{-1}

Compound(15) 4-(5-(4-aminophenyl)-5-methyl-4,5-dihydro-1H-tetrazol-1-yl)-2-(1H-benzo[d] imidazol-2-yl)phenol The infrared spectrum data of compound(15) shows (3008)$cm^{-1}$for(Ar-H), (3332) cm^{-1} for (O-H) , (3139)$cm^{-1}$for(N-H)Imidazole , (2955)cm^{-1} for(C-H)CH_3. (N=N)at(1415) cm^{-1}, (C=N) at(1527) cm^{-1}.The ^{1}HNMR (DMSO δ ppm):(m,11H,Ar-H,6.6-8),(s,1OH,8.9) ,(s,3H,CH3,1.5)(s,NH amidazol ring,9.7),(s,NH tetrazol ring;10.2),5.2(s,2H,NH_2) .The ^{13}C-NMR (DMSO δ ppm) :131(C6,C7),($C_{Aromatic}$;115-130),(C1;158) ,(C19;154) , (C12;137),59(C15).

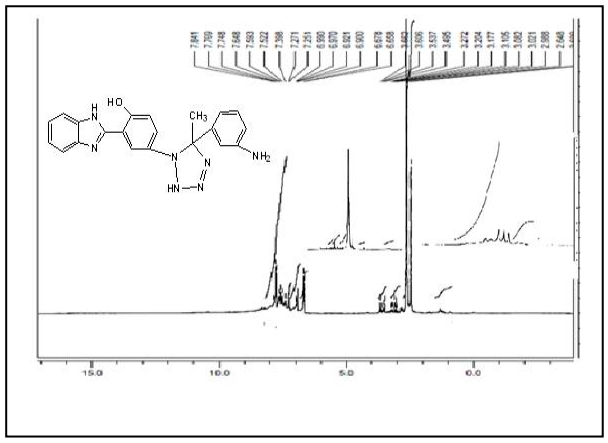


Fig (12^{13}CNMR spectrum for(15) compound cm^{-1}

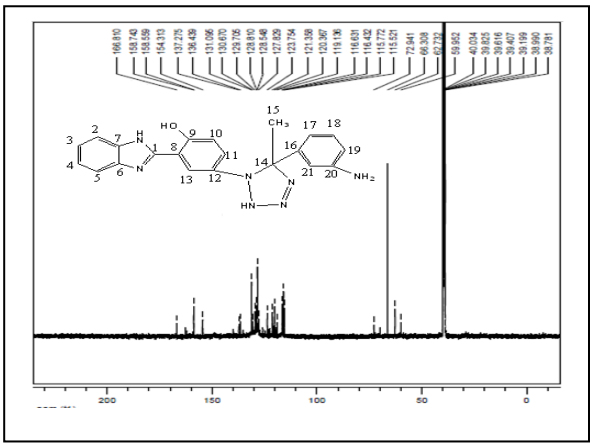


Fig 11 HNMR spectrum for(15) compound cm^{-1}

-Compound(16) 2-(1H-benzo[d]imidazol-2-yl)-4-(5-(4-(5-(4-chlorophenyl)-4,5-dihydro -1H-tetrazol-1-yl)phenyl)-5-methyl-4,5-dihydro-1H-tetrazol-1-yl)phenol .The infrared spectrum data of compound(16) shows (3062)cm^{-1}for(Ar-H), (3371) cm^{-1} for (O-H) , (3139)cm^{-1}for(N-H) Imidazole ,(2955)cm^{-1}for(C-H)CH_3**.** (N=N)at(1450) cm^{-1}**,**(C=N) at(1589) cm^{-1}. (N=N)at(1450) cm^{-1}**,**(C=N)tetrazol ring at(1589)cm^{-1},(825)cm-1for(C-Cl),(H-N)tetrazol ringat(3371) cm^{-1} .The^{1}HNMR (DMSO δ ppm): 2.5,**(**m,15Ar-H,6.6-7.7),(s,1OH,7.8),(s,3CH_3;3.4) (s,NH amidazol ring,9.3),(s,1H,NH tetrazol ring;10.4).The13C-NMR (DMSO)δ: 62(C15),130(C6,C7),112-119(CArom) ,153(C14) ,148(C1) ,138(C8) ,135(C16) ,129(C1)

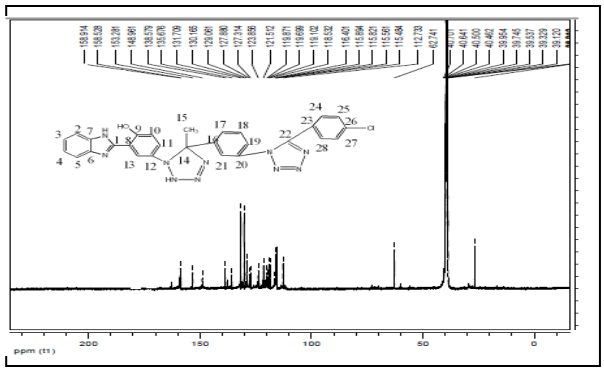


Fig 14^{13}CNMRspectrum for(16) compound cm^{-1}

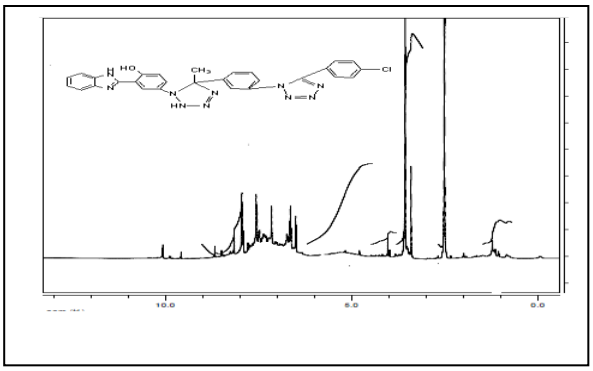


Fig 131 HNMR spectrum for(16) compound cm^{-1}

-Compound(17) 2-(1H-benzo[d]imidazol-2-yl)-4-(5-(4-(5-(4-bromophenyl) -5-methyl-4,5-di ydro-1H-tetrazol-1-yl)phenyl)-5-methyl-4,5-dihydro-1H-tetrazol-1-yl) phenol.The infrared spectrum data of compound(17) shows (3062) $cm^{-1}$for(Ar-H), (3348) cm^{-1} for (O-H) , (3224)cm^{-1} for(N-H)Imidazole , (2023)cm^{-1} for(C-H)CH_3**.** (N=N)at(1415) cm^{-1}**,** (C=N) at(1527) cm^{-1} ,(666)$cm^{-1}$for(C-Br), (H-N) tetrazole ring at(3348) cm^{-1} .The^{1}HNMR(DMSO)δ:**(**m,15Ar-H**,**6.2-7.7**),**(s,1OH,9.72),(s,6H,CH3;3.4,1.2)**,(**s,1H,NH amidazol ring, 9.77) ,(s,1H,NH tetrazol ring;9.8) .The^{13}C-NMR(DMSO δ):130(C8),112-124(C- Aromatic) ,153(C14), 66(C23),62.7(15) , 126 (C6 ,C7) .

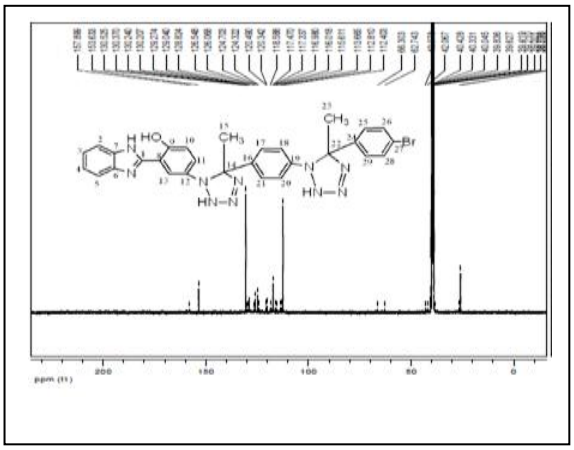


Fig16 1HNMR spectrum for(17) compound cm^{-1}

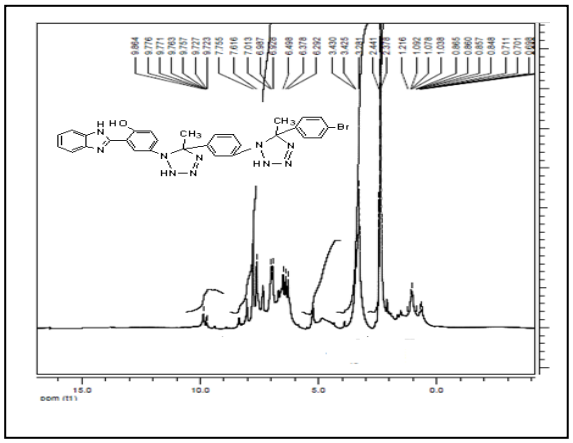


Fig 15 HNMRspectrum for(17) compound cm^{-1}

-Compound 5-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-hydroxybenz ald ehyde (18).The infrared spectrum data of compound(18) shows (3031) $cm^{-1}$for(Ar-H), (3420) cm^{-1} for (O-H) , (3232)$cm^{-1}$for(N-H)Imidazole , (1481) cm^{-1} for(N=N),(1712) $cm^{-1}$for (C=O) Aldehydegroup ,(1558) cm^{-1} for(C=C)Aromatic(C-H) Ald. at(2669)cm^{-1}. The^{1}H NMR (DMSO δ ppm): 2.5,**(**m,10Ar-H**,**6.6-8) ,(s,2OH,10.1) ,(s,1CHO,16.3)(s,NH amidazol ring,10.7) .

-Schiff Bases (19-24): Compound4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl) -2-((E)-((3-nitrophenyl)imino)methyl)phenol: (19)The infrared spectrum data of (19) compound shows(H-N) Imidazole at(3224) cm^{-1} (1612)cm^{-1} or C=N) Imidazole, (3070)$cm^{-1}$for(C-H)Arom, (C=C)at(1527) cm^{-1}(3371) $cm^{-1}$for (O-H) ,(N=N)at(1450) cm^{-1}, (O-N-O)NO_2 at(1527-1350) cm^{-1}

-Compound(20)1-(4-((E)-(5-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl)-2-hydroxybenzylidene)amino)phenyl)ethanone.The infrared spectrum data of (20) compound shows(H-N) Imidazole at(3116) cm^{-1} (1666)$cm^{-1}$for(C=N) Imidazole, (3008)$cm^{-1}$for(C-H)Arom,(C=C)at(1581) cm^{-1} (3456-3240)) cm^{-1} for (O-H) ,(N=N)at(1442) cm^{-1},(2854-2983)$cm^{-1}$for(C-H)CH_3, (C=O) Ketone at(1715)cm^{-1}.

-Compound (21)4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl)-2-((E)-((1H-benzo [d]imidazol-2-yl)imino)methyl)phenol(21).The infrared spectrum dataof (21)compound shows(H-N) Imidazole at(3116) cm^{-1} (1666)cm^{-1} or C=N) Imidazole, (3010$cm^{-1}$for(C-H)Arom ,(C=C)at(1542cm^{-1} (3425) cm^{-1} for (O-H) ,(N=N)at(1442) cm^{-1}, (O-N-O)NO_2 at(1522-1351), (1249)$Cm^{-1}$for(C=S)Thiozole ring.

-Compound(22) 4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-((E)-((5-nitro thiazol-2-yl)imino)methyl)phenol(22)The infrared spectrum data of compound(22) showd (H-N) Imidazole at(3116) cm^{-1} (1165)cm^{-1} (C=N) Imidazole, (3012)$cm^{-1}$for(C-H)Arom,(C=C)at(1581) cm^{-1} (3420) $cm^{-1}$for(O-H) (N=N)at(1481)cm^{-1}.

-Compound 4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-((E)-(pyridin-2-ylimino)methyl)phenol(23)The infrared spectrum data of compound(23) showd (H-N) Imidazole at(3115) cm^{-1} (1666)$cm^{-1}$for(C=N) Imidazole, (3070)$cm^{-1}$for(C-H)Arom,(C=C)at(1589) cm^{-1} (3300) $cm^{-1}$for(O-H),(N=N)at(1450)cm^{-1} (1589)$cm^{-1}$for(C=N)Pyridine ring.^{1}HNMR (DMSO δ ppm): 2.5,(m,14Ar-H,6.5-8)(s,2OH,10.1),(s,1CH=N,8.4)(s,NH amidazol ring,10.8) .The13C-NMR (DMSO) δ :147(C20),111-125(CAromatic),142 (C21),129(C1), 28(C12),126(C8)

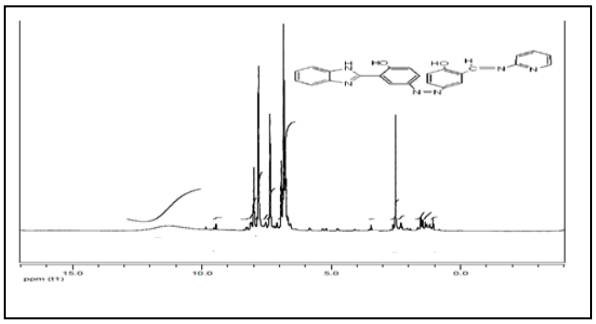


Fig18^{13}CNMR pectrum for(23) compound cm-^{1}

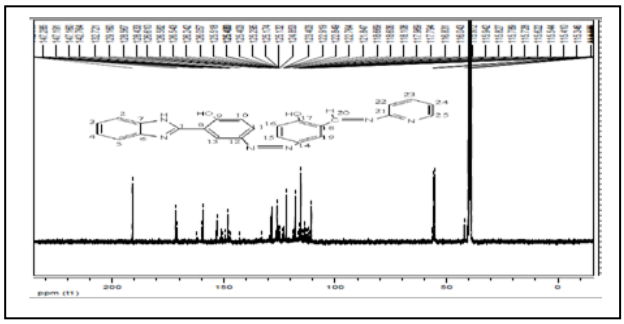


Fig17 ^{1} HNMR spectrum for(23) compound cm-^{1}

-Compound4,4'-((((1E)-([1,1'-biphenyl]-4,4'-diylbis(azanylylidene))bis(methanylylidene)) bis (4-hydroxy-3,1-phenylene))bis(diazene-2,1-diyl))bis(2-(1H-benzo[d]imidazol-2-yl)phenol)(24)

The infrared spectrum data of compound(24) shows(C=N) at (1542-1527) cm^{-1} (3055-3008)cm^{-1} or(Ar-H), (3440-3402)$cm^{-1}$for(O-H), (3230)$cm^{-1}$for(N-H) Imidazole, (N=N)at(1458) cm^{-1} (C=C) Aromatic at(1560)cm^{-1}.

-Tetrazol(25-30) Compound(25)4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-(1-(3-nitrophenyl)-1H-tetrazol-5-yl)phenol.The infrared spectrum data of compound(25) shows(3209)$cm^{-1}$for(N-H)Imidazole , (C=N) at(1598) cm^{-1}, in tetrazole ring (3070)$cm^{-1}$for(Ar-H) (3386)cm-1for(O-H),(N=N)Tetrazol at(1465) cm^{-1}.The ^{1}HNMR (DMSO) δ : (m,14Ar-H,6.7-7.4) ,(s,2OH,7.8),(s,NH amidazol ring,11.1)^{13}C-NMR (DMSO) δ: 157 (C20), 111-121 (CAromatic),124 (C25) ;131 (C1), ;125 (C21) .

-Compound1-(4-(5-(5-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl)-2-hydrox phenyl)-1H-tetrazol-1-yl)phenyl)ethanone (26)The infrared spectrum data of compound(26) shows(3200)$cm^{-1}$for(N-H)Imidazole , (C=N) (1598) cm^{-1}, in tetrazole ring (3055)cm-1for(Ar-H) (3363)$cm^{-1}$for(O-H),(N=N)Tetrazol at(1450)cm^{-1} (2993)for(C-H)CH_3(C=O)keton at(1735)cm^{-1}.

The1H NMR (DMSO δ): ,(m,14Ar-H,6.1-7.9) ,(s,2OH,8.07),(s,NH amidazol ring,10.5) 3.5 (S,3H,CH3).The 13C-NMR (DMSO δ): 162 (C20), 112-129 (C-arom), 130C21) ;138C1), 32 (C14,C12) 124(C25),60(C28),172(C22).

-Compound4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-(1-(5-nitrothiazol-2-yl)-1H-tetrazol-5-yl)phenol(27).The infrared spectrum data of compound(27) shows(3209)cm-1for(N-H)Imidazole , (C=N)at(1598) cm^{-1}, in tetrazole ring (3070)cm-1for(Ar-H) (3394-3386)cm-1for(O-H),(N=N)Tetrazol at(1458) cm^{-1} ,(1218)$cm^{-1}$for(S-C)Thiozol,(1388,1520)cm^{-1} for(O-N-O)NO_2.The ^{1}H NMR (DMSO δ ppm): 2.5,(m,11Ar-H,6.6-7.1) ,(s,2OH,8.2),(s,NH amidazol ring,9.1The^{13}C NMR(DMSO) : 131C20), 115.6-114.8CArom), 116C22), 118C1) ,115.7(C12,C14)

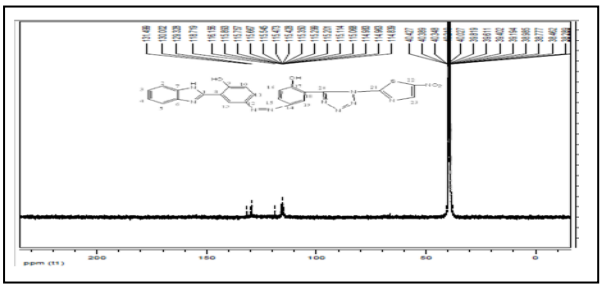


Fig20 ^{13}CNMR spectrum for(27) compound cm^{-1}

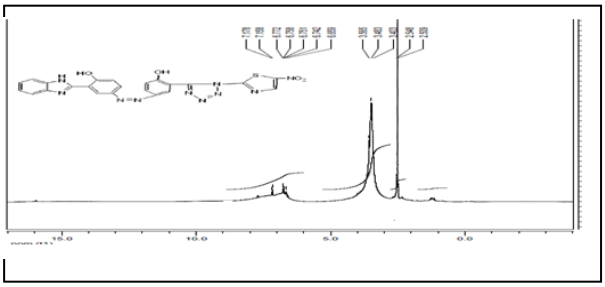


Fig19 ^{1} HNMR spectrum for(27) compound cm^{-1}

-Compound2-(1-(1H-benzo[d]imidazol-2-yl)-1H-tetrazol-5-yl)-4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)phenol(28).The infrared spectrum data of compound(28) shows(3170)cm^{-1}for(N-H)Imidazole , (C=N)at(1598) cm^{-1}, in tetrazole ring (3001)cm^{-1}for(Ar-H) (3390)cm-1for(O-H), (N=N)Tetrazol at(1458) cm^{-1} .The ^{1}HNMR (DMSO δ ppm): 2.5,(m,14Ar-H,6.7-7.8) ,(s,2OH,9.03),(s,NH amidazol ring,10.6) .The^{13}C-NMR (DMSO δ ppm): ;167 (C20), 116-125 (CAromatic)159(C1,C21),157(C12,C14) .

-Compound4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-(1-(pyridin-2-yl)-1H-tetrazol-5-yl)phenol(29). The infrared spectrum data of compound(29) shows(3109-3200)cm^{1}for(N-H)Imidazole , (C=N)at(1598) cm^{-1}, in tetrazole ring (3078)cm^{-1}for(Ar-H) (3340) cm^{-1} for(O-H),(N=N)Tetrazol at(1458) cm^{-1} (C=N)at(1635) cm^{-1}, in Pyridine ring.The^{1}H NMR (DMSO δ):(m,14Ar-H,7.3-8.4) ,(s,2OH,8.7),(s,NH amidazol ring,9.1)The^{13}C-NMR (DMSO δ ppm): 161 (C20), 130-111 (CAromatic) ;139 (C21) ;141 (C1)(C21;139),156(C9,C8) **(23)**.

-Compound4,4'-(((1,1'-([1,1'-biphenyl]-4,4'-diyl)bis(1H-tetrazole-5,1-diyl))bis(4-hydroxy-3,1-phenylene))bis(diazene-2,1-diyl))bis(2-(1H-benzo[d]imidazol-2-yl) phenol) (30)The infrared spectrum data of compound(30) shows(3109)cm^{-1}for(N-H)Imidazole , (C=N)at(1598) cm^{-1}, in tetrazole ring (3070)cm-1for(Ar-H) (3394-3386)cm-1for(O-H), N=N)Tetrazol at(1458) cm^{-1}

Biological activity

In this work, the antibacterial test was performed according to the wells method. Compounds (1-30) were assayed for their antimicrobial activity in vitro against Gram-negative bacteria (*Escherichia coli*) and Gram-positive bacteria *(staphylococcus aurous)*. Prepared agar and Petri dishes were sterilized by autoclaving for 20min at200C°. These plates

were incubated at 37C° for 24h for both bacteria. DMSO was used as a solvent to prepare solutions of the various compounds were examined(0.02gram of comp./5ml DMSO). The inhibition zones caused by the various compounds were examined,where compounds which appeared good activity(1,8,18and 28) agnist*(staphylococcus aurous*) on other hand ;compounds (1 and17) which appeared good activity agnist (*Escherichia coli*). The results of the preliminary screening tests are listed in table(7). [25]

Table(7) Biological activity for compounds(1-30)

Compound .NO	*E. coli*	*Staph. Aureus*	Compound .NO	*E. coli*	*Staph. Aureus*
1	**-**	+++	**16**	**R**	++
2	**-**	++	**17**	++	-
3	**-**	-	**18**	+	+++
4	**-**	-	**19**	-	++
5	-	++	**20**	-	++
6	+	-	**21**	-	+
7	+	-	**22**	-	+++
8	-	+++	**23**	-	++
9	+	++	**24**	+	-
10	-	++	**25**	**R**	-
11	**R**	+++	**26**	**R**	+++
12	**R**	+++	**27**	**R**	-
13	**R**	-	**28**	**R**	-
14	**R**	-	**29**	**R**	-
15	**R**	++	**30**	+	-

- = No inhibition = inactive. + = (5-10) mm = slightly active.

++ = (11-20) mm = moderately active +++=(more than 20) mm = Goodactive. Resistance(+-)=R.

Fig 20 Biological activity for compounds(1-30)

Table (8) Physical properties of compounds(1-30)

No	Name of comp	M. F	M. W	m.p (°C)	R_f	Colour	%
1	4-amino-2-(1H-benzo[d]imidazol-2-yl)phenol	$C_{13}H_{11}N_3O$	225.25	210-208	0.5	Brillient Gray	85
2	E)-2-(1H-benzo[d]imidazol-2-yl)-4-((4-)(dimethylamino)benzylidene)amino)phenol	$C_{22}H_{20}N_4O$	356.16	245-243	0.3	Reddish Pink	80
3	2-(1H-benzo[d]imidazol-2-yl)-5-((1-(4-hydroxyphenyl)ethylidene)amino)phenol	$C_{12}H_{17}N_3O_2$	343.13	18178	0.4	Yellowish Green	84
4	(E)-4-(((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)imino)methyl)-2-methoxyphenol	C21H17N3O3	359.13	250-248	0.4	Brown	76
5	4,4'-((1Z,1'Z)-pentane-2,4-diylidenebis(azanylylidene))bis(2-(1H-benzo[d]imidazol-2-yl)phenol)	$C_{31}H_{26}N_6O_2$	514.55	200-198	0.5	Dark Green	55
6	(E)-2-(1H-benzo[d]imidazol-2-yl)-4-((1-(4-bromophenyl)ethylidene)amino)phenol	$C_{21}H_{16}BrN_3O$	405.05	240-238	0.2	Dark Green	75
7	(E)-4-((1-(4-aminophenyl)ethylidene)amino)-2-(1H-benzo[d]imidazol-2-yl)phenol	$C_{21}H_{18}N_40$	342.39	180-178	0.3	Dark Brown	83
8	2-(1H-benzo[d]imidazol-2-yl)-4-((E)-(1-(4-((4-chlorobenzylidene)amino)phenyl)ethylidene)amino)phenol	$C_{28}H_{21}ClN_4O$	464.95	240-238	0.3	Gray	73
9	2-(1H-benzo[d]imidazol-2-yl)-4-((E)-(1-(4-((1-(4-bromophenyl)ethylidene)amino)phenyl)ethylidene)amino)phenol	$C_{28}H_{23}BrN_4O$	522.11	150-148	0.5	Reddish Brown	76
10	2-(1H-benzo[d]imidazol-2-yl)-4-(5-(4-(dimethylamino)phenyl)-4,5-dihydro-1H-tetrazol-1-yl)phenol	$C_{22}H_{21}N_7O$	399	215-213	0.4	Brown	80
11	2-(1H-benzo[d]imidazol-2-yl)-4-(5-(4-hydroxyphenyl)-5-methyl-4,5-dihydro-1H-tetrazol-1-yl)phenol	C21H18N6O2	386.41	180-178	0.4	Violet	74
12	4-(1-(3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)-4,5-dihydro-1H-tetrazol-5-yl)-2-methoxyphenol	$C_{21}H_{18}N_6O$	402.4	116-114	0.3	Black	77
13	Di[2-(3H-benzo[d]imidazol-2-yl)-4-(5,5-dimethyl-2,5-dihydro-1H-tetrazol-1-yl)phenol]Methane	$C_{31}H_{28}N_{12}O_2$	600.03	184-182	0.4	Violet	76
14	2-(1H-benzo[d]imidazol-2-yl)-4-(5-(4-bromophenyl)-5-methyl-4,5-dihydro-1H-tetrazol-1-yl)phenol	$C_{21}H_{17}BrN_6O$	449.3	92-90	0.4	Brown	82
15	4-(5-(4-aminophenyl)-5-methyl-4,5-dihydro-1H-tetrazol-1-yl)-2-(1H-benzo[d]imidazol-2-yl)phenol	$C_{21}H_{19}N_7O$	385.4	160-158	0.4	Brown	81
16	2-(1H-benzo[d]imidazol-2-yl)-4-(5-(4-(5-(4-chlorophenyl)-4,5-dihydro-1H-tetrazol-1-yl)phenyl)-5-methyl-4,5-dihydro-1H-tetrazol-1-yl)phenol	$C_{28}H_{23}ClN_{10}O$	551	100-98	0.4	Brown	89
17	2-(1H-benzo[d]imidazol-2-yl)-4-(5-(4-(5-(4-bromophenyl)-5-methyl-4,5-dihydro-1H-tetrazol-1-yl)phenyl)-5-methyl-4,5-dihydro-1H-tetrazol-1-yl)phenol	$C_{29}H_{25}BrN_{10}O$	608	140-138	0.3	Black	74
18	5-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-hydroxybenzaldehyde	$C_{20}H_{14}N_4O_3$	358.35	178-176	0.4	Dark yellow	83
19	H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-١)-٣))-٤((E)-((3-nitrophenyl)imino)methyl)phenol	$C_{26}H_{18}N_6O_4$	478.64	300-298	0.3	Dark Green	82
20	E)-(5-((3-(1H-benzo[d]imidazol-2-yl)-4-))-٤)-١ hydroxyphenyl)diazenyl)-2-hydroxybenzylidene)amino)phenyl)ethanone	$C_{28}H_{21}N_5O_3$	475.50	149-147	0.4	Dark Red	88

21	H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-ˈ)-3))-4 ((E)-((5-nitrothiazol-2-yl)imino)methyl)phenol	$C_{23}H_{15}N_7O_4S$	485.4	138-136	0.3	Dark Orang	85
22	H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-ˈ)-3))-4 ((E)-((1H-benzo[d]imidazol-2-yl)imino)methyl)phenol	$C_{27}H_{19}N_7O_2$	473.49	118-116	0.3	Light Brown	79
23	H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-ˈ)-3))-4 ((E)-(pyridin-2-ylimino)methyl)phenol	$C_{25}H_{18}N_6O_2$	434.4	148-146	0.3	Red	88
24	4,4'-((1Z,1'Z)-(((1E)-([1,1'-biphenyl]-4,4'-diyl)bis(azanylylidene))bis(methanylylidene))bis(4-hydroxy-3,1-phenylene))bis(diazene-2,1-diyl))bis(2-(1H-benzo[d]imidazol-2-yl)phenol)	$C_{52}H_{36}N_{10}O_4$	864.9	100-99	0.5	Brown	77
25	4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-(1-(3-nitrophenyl)-1H-tetrazol-5-yl)phenol	$C_{26}H_{17}N_9O_4$	519.4	240-238	0.4	Reddish Brown	76
26	1-(4-(5-(5-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-hydroxyphenyl)-1H-tetrazol-1-yl)phenyl)ethanone	$C_{28}H_{20}N_8O_3$	516.5	157-155	0.5	Dark Red	78
27	4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl) diazenyl)-2-(1-(5-nitrothiazol-2-yl)-1H-tetrazol-5-yl)phenol	$C_{23}H_{14}N_{10}O_4S$	526.09	300-298	0.4	Black	80
28	2-(1-(1H-benzo[d]imidazol-2-yl)-1H-tetrazol-5-yl)-4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)phenol	$C_{27}H_{18}N_{10}O_2$	514	175-173	0.2	Brown Light	75
29	4-((3-(1H-benzo[d]imidazol-2-yl)-4-hydroxyphenyl)diazenyl)-2-(1-(pyridin-2-yl)-1H-tetrazol-5-yl)phenol	$C_{25}H_{17}N_9O_2$	475.4	137-135	0.3	Dark Brown	73
30	4,4'-(((1,1'-([1,1'-biphenyl]-4,4'-diyl)bis(1H-tetrazole-5,1-diyl))bis(4-hydroxy-3,1-phenylene))bis(diazene-2,1-diyl))bis(2-(1H-benzo[d]imidazol-2-yl)phenol)	$C_{52}H_{34}N_{16}O_4$	946.9	236-234	0.3	Brown	71

References

[1] Arunkumar; S Suvarna .[2015]**.*Res. J. Chem. Sci***. 5(10) , p67-72 .

[2] Balasaheb V. Shitole, Nana V. Shitole, Suraj B. Ade, and Gopal K. Kakde.[2015].***Electron. J. Chem***. 7 (3) ,*p 240-244*.

[3] Haleh Sanaeishoar, Haman Tavakkoli, Mahsa Asareh and Fouad Mohave .[2016]. ***Iranian Journal of Catalysis***. 6(2).

[4] Delia Hernández Romero, Víctor E. Torres Heredia, Oscar García-Barradas, Ma. Elizabeth Márquez López1 & Esmeralda Sánchez Pavón.[2014]. ***Journal of Chemistry and Biochemistry,* 2(2)**,p 45-85 .

[5] S. D. Pardeshi, S. N. Thore . *[2015]***.IJCPS** Vol. 4,p,300-307.

[6] Jerzy W. Suwinski[2015] . ***ARKIVOC*** , p 97-135

[7] Roman Sívek, Filip Bureš, Oldřich Pytela and Jiří Kulhánek .[2008]. ***Molecules* .**13 p,2326-2337.

[8] Mahesh R , Ramya K , Ashok Kumar HG and Satyanarayana S .[2015]. ***Afr. J. Biotechnol*** , 14(15) ,p 1297-1303 .

[9] Ikhlass Abbas, Sobhi Gomha, Mahmoud ELAasser and Mohammed Bauomi [2015]. ***Turk J Chem*** , p39- 334 .

[10] C. M. Mahalakshmi, M. Karthick, M. Shanmugam and V. Chidambaranathan .[2015].***Der Pharma Chemica***, 7 (1***)***,*p14-19*.

[11] Xiangxiong Chen, Seung Woo Lee, Akbar Idhayadhulla, Radhakrishnan Surendra Kumar and Aseer Manilal .[2015] ***Pharm Res***, 14(8)p 1435.

[12] Fábio L. Pissetti, Pedro L. de Araújo, Fábio A. B. Silvaa and Gaël Y. Poirier .[2015]. ***J. Braz. Chem. Soc***. 26(2),p 266-272.

[13] Iftikhar Ahsan and K.K. Sharma .[2015]. ***The Pharma Innovation Journal***. **4(3),**p 68-73.

[14] A.M.Grozav, A.O.Palamar, V.O.Chornous, I.M.Yaremiy and M.V.Vovk .[2014].***ВІСНИК ФАРМАЦІЇ*** .4(80) ,p8-12.

[15] Fatmah A. S. Alasmary , Anna M. Snelling, Mohammed E. Zain 3, Ahmed M. Alafeefy,Amani S. Awaad and Nazira Karodia .[2015].***Molecules*** ,20.

[16] Hassan Y Aboul-Enein , and Ahemd A El Rashedy .[2015] ***Medicinal chemistry ,*** 5(7), p 318-325 .

[17] P. P.Radhika ,S-Janaraj and A.Siva Knmax.[2011].***J.Resarch in Biotechnology***,2(3)p50-57.

[18] Muzammil K, Trivedi P and Khetani DB .[2015].***Res. J. Chem. Sci.*** 5(5**)**,p 52-55.

[19] Zeid H. Abood and Nooralhuda M.Abdul Hussain. .[2015]. ***Journal of Kerbala University*** . 13 (3) ,p188-204 .

[20] Rajiv A. Shah K. S. Nimavat2 and Dipti K. Dodiya . [2016]**.** ***J PharmSciBioscientific Res***. 6(3)**,**p*304-307*.

[21] Hamak KF1 and Eissa H.[2013]. ***Organic Chem Curr Res .*** 2(3) ,p 3-7.

[22] S.AGolal,A.S.Abdel samie and M.L.Rodrguez.[2010] ***European Journal chemistry***. (112).p67-72.

[23]W.B.Blantosn. [2002]. Chemistry Department, Berkeley, University of California ,**D.Thesis**

[24] J.B.Lamber t.[2004]: Nuclear Magnetic Reonance Spectroscopy. 2nd Edition. Pearson Prentic hall,New Jersy

[25] Haitham.K.Dakhil .[2011].Chemistry Department,College of Education, University of Al-Qadisiyah. **M.Sc.Thesis**

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