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Synthesis and Antimicrobial screening of some new azo compounds derived from thiazole ring modified

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Abstract : The presented work involved the preparation of new Azocompounds containing aromatic heterocyclic (thiazol ring) derived from substituted aminobenzoic acid. The preparation procedure involves a series of steps the first step includes the reaction of synthesized 2-aminothiazol compounds with nitrous acid at (0)°C to form the corresponding diazonium salts. The second step involved coupling the newly synthesized diazonium salts with different amines and phenols. All the prepared compounds in this work were characterized by melting point and softening points with other physical properties, FTIR, H^1-NMR spectra, Screening of the antimicrobial activity of the prepared azo compounds was tested against two types of bacteria; Gram positive (*Stapylococcus aureus)* andGram negative (*Escherichia coli*).
Keywards : Diazonium salts, Azo compound, Aminothiazole ring

Introduction

Thiazole which forms a part of vitamin B_1[1], the Penicillin[2] and several bioactive agents have been extensively studied and used for various applications. They exhibit wide range of biological activity[3]2-amino thiazole moiety were reported to possess antidepressant[4], fungicidal[5],anti-inflammatory[6],antitubercular[7] antibacterial[8],insecticidal[9]etc. activities.Thiazole exhibit a wide range of biological activities and therefore the derivatives of aminothiazole are expected to be biologically active. Azo-functionalized dyes bearing aromatic heterocyclic components [10]have attracted everincreasing attention in recent years due to their wide range of color, brightness, simplicity and ease ofmanufacturing and good dyeing performance[11-14]. They are used in high tech applications such aslasers and non-linear optical systems [15] thermal transfer printing and fuel cells[16], dye sensitized solarcells[17], photodynamic therapy[18], and metallochromic indicators[19] They are also used in dyeingtextiles, leather, paper, food and cosmetic products [20] Furthermore, azo dye compounds are knownfor their medicinal importance [24-21] and are also known to be involved in a number of biologicalreactions such as inhibition of DNA, RNA and protein synthesis, carcinogenesis and nitrogen fixation [25]In a broader sense, the azo dyes constitute the largest diverse group of all the synthetic colorants.[26,27]

Experimental

- **Material:**

All the chemicals that were used of analytical grade and there were available from CDH, BDH and Fluka companies.

- **Instrument:**

1. Melting points were determined on Galen Kamp capillary melting point apparatus and were uncorrected.

2. FTIR spectra were recorded on Shimadzu FT-IR 8400 Fourier Transform Infrared Spectrophotometer.
3. Softening points were determined on Thermal Microscope Reichert Thermover 160.
4. ^{1}H-NMR were measured in DMSO Solutions on a Bruker-500 MHz spectrophotometer using TMS as an internal standard (chemical shifts in ppm)
5. The antibacterial activity was determined by agar-well diffusion method.

Synthesis methods for the prepared compounds:

- **General procedure for the coupling 2-aminothiazol compounds with amines.**

Literature procedure was used with some modifications[28]. The aminothiazole compounds (0.01 mol) were dissolved in(6 mL, 50%) HCland cooled at (0–5)°C. A solution of sodium nitrite (0.01 mol, 0.69 gm)in water (4 ml) previously cooled at 0°C was added dropwisemaintaining the temperature at 0–5°C; stirring was continuedfor an hour, the prepared diazonium compounds were used for coupling reaction. The amines which are used for the coupling reaction (0.01 mol) were dissolved in glacial aceticacid (30 mL) and cooled below 5°C. Then was added dropwise to the above mentioned diazonium chloride solution with continuous stirring for 3hours at 0–5°C. then reaction mixture waspoured into ice to obtain the dyes, these dyes werefiltered and dried at 70°C and were recrystallized fromGlacial acetic acid, the physical properties of the prepared compounds are listedin table (3).

- **General procedure for the coupling 2-aminothiazol compounds with phenols.**

The same procedure above was carried out in the synthesis except for one difference: the phenols were dissolved in 20% NaOH instead of GAA. The physical properties if the prepared compounds are listed in table (3)

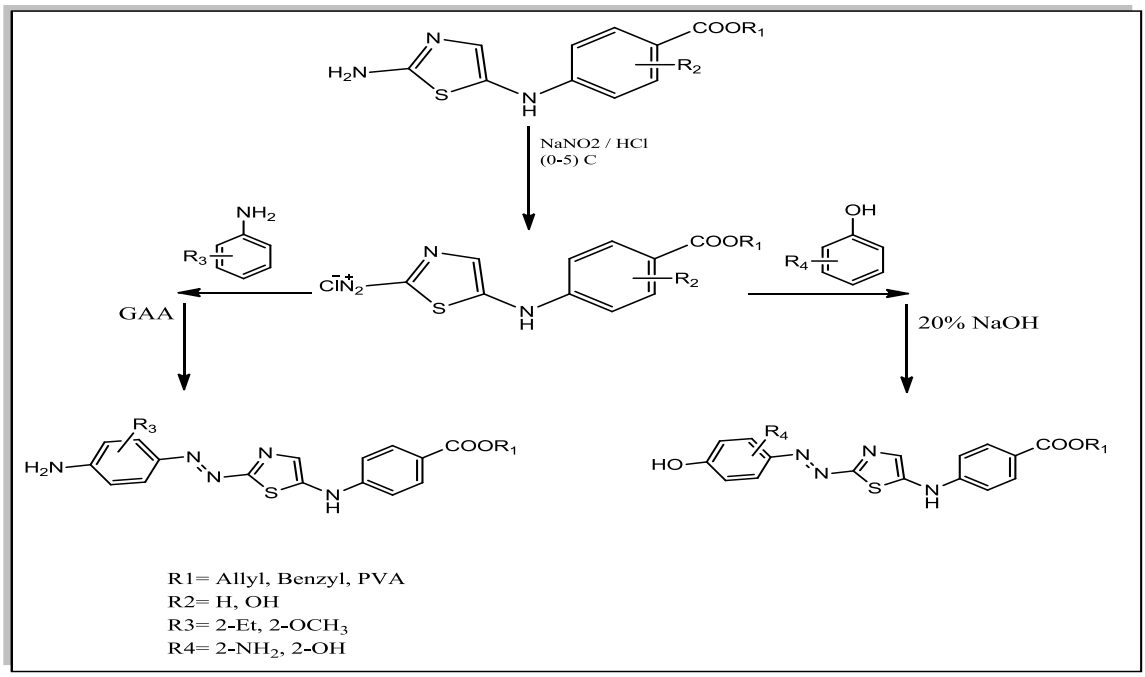
Note: In case of reacting the polymers containing the aminothiazole ring; the same procedures above were carried out except the products were purified by dissolving them in DMSO then reprecipitating from H_2O.

- **The Biological activity[28,29]**

The synthesized compounds were exposed to antimicrobial activity. Antimicrobial activities were observed for some of the compounds using strain of gram positive such as (Staphylococcus aureus), gram negative (E. coli). The antimicrobial activities of the synthesized compounds were studied by disc diffusion method. Bacterial inoculums were spread on Nutrient agar. After the inoculums dried, 6 mm diameter wells were made in the agar plate with a sterile cork borer. The synthesized compounds were dissolved in DMSO at concentration of 10^{-2}M,Cefotaxime 10^{-2} M was used as standard for the antibacterial activity. The Petri plates were incubated at 37ºC for 24 hours. The Zone of inhibition was measured in mm and the results are listed in Table (5)

Result and discussion:

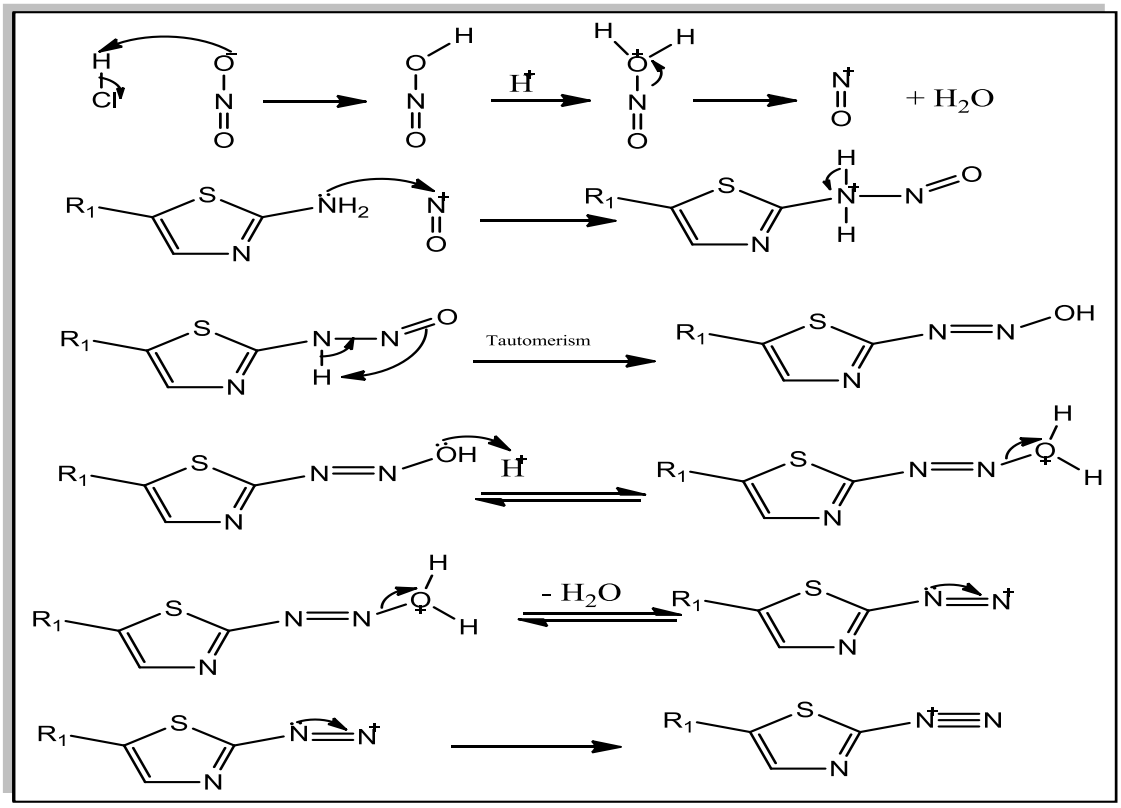
All the Azo Compounds were prepared by the diazotization and coupling. The following scheme shows the reaction steps



Scheme -1-

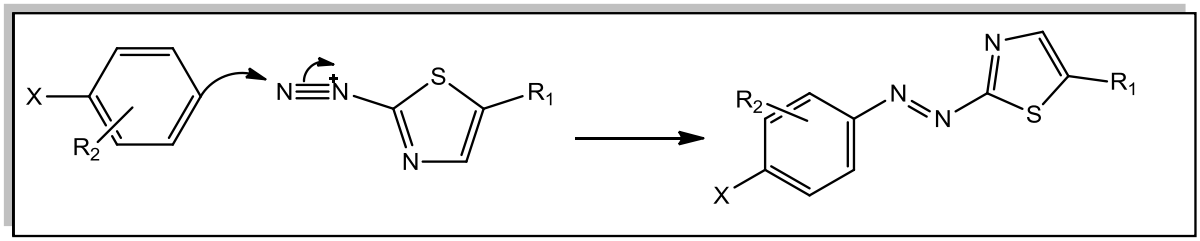
The starting material for the synthetic substituted thiazole-2-azo compounds is substituted 2-aminothiazole ring which reacted with Nitrous acid at (0-5)°C then coupled with different aromatic amines and phenols. The coupling mechanism for step1 to form the diazonium salts is shown in the scheme -2- and the is shown is the scheme -3[30,31]

Step1. Formation of diazonium salt[32]



Scheme -2-

Step2. Coupling reaction[31]



Scheme -3-

Structures of the starting material (Substituted 2-aminothiazol ring) (24-27) were confirmed by the physical properties listed in table (1). FTIR spectra showed absorptions at the regions (3456-3420) cm^{-1} of υNH_2 group, (3190-3234) cm^{-1} of υNH group, (3010-3085) cm^{-1} of υC-H aromatic, (2900-2989) cm^{-1} of υC-H Aliphatic, (1755-1785) cm^{-1} of υC=O ester, (1630-1650) cm^{-1} of υC=N, (1514-1610) cm^{-1} of υC=C aromatic, (1323-1375) cm^{-1} of υC-N and (1155-1265) cm^{-1} due to υC-O. Some of the starting compounds have an additional absorption peak at (3540-3550) cm^{-1} of υO-H phenol. The rest of the IR data are listed in table (2).^{1}H-NMR spectrum of compound 25 showed signal at δ10.1ppm for (s,1H,OH), δ9.3ppm for (s,2H,NH_2), δ8.6ppm for (s,1H,NH), (7.0-7.8)ppm for (m,8H,Ar-H), and δ 4.5ppm for(s,2H,Ph-CH_2-CO)

Compounds (42-45) were prepared by the coupling reaction of anisidine with the substituted amino thiazole ring in the presence of Nitrous acid at (0-5)°C, all the produced compounds were confirmed by the physical properties listed in table (3). FTIR spectra showed the formation of new absorption region at (1500-1521) cm^{-1} of υN=N group and some compounds (43-45) have an additional absorption region at (3517-3578) cm^{-1} of υO-H phenol and (1624-1632) cm^{-1} due to υC=C group. The rest of the IR data are listed in table (4).^{1}H-NMR spectrum of compound 38 showed signal at δ8.1ppm for (s,2H,NH_2), δ7.6ppm for (s,1H,NH), δ7.3 ppm for (m,4H,Ar-H), δ6.8ppm for (s,2H,CH_2=CH),δ 3.9ppm of (m,1H,CH_2-CH=CH_2) and δ3.5 of(t,2H, CH_2-CH=),and δ1.8ppm(s,3H,OCH_3)

Compounds (50,51) were prepared by the coupling reaction of 2-hydroxy aniline with the substituted amino thiazole ring in the presence of Nitrous acid at (0-5)°C, all the produced compounds were confirmed by the physical properties listed in table (3).FTIR spectra showed the formation of new absorption region at (1507-1517) cm^{-1} due to υN=N group, (3501-3596) cm^{-1} of υO-H phenol and some compounds have an absorption peak at (1621-1669) cm^{-1} of υC=C. The rest of the IR data are listed in table (4).^{1}H-NMR spectrum of compound 50 showed signal at δ10.5ppm for (s,1H,OH), δ9.4ppm for (s,2H,NH_2), δ8.2ppm for (s,1H,NH), δ(7.2-7.7)ppm for (m,6H,Ar-H),δ 3.9ppm of (s,2H,CH_2-ph), and δ3.5 of(s,1H, thiazole ring)

Compounds (56-65) were prepared by the coupling reaction of phenol with the substituted amino thiazole ring in the presence of Nitrous acid at (0-5)°C, all the produced compounds formation of new absorption region at (1499-1517) cm^{-1} due to υN=N group and (3511-3591) cm^{-1} of υO-H phenol. The rest of the IR data are listed in table(4).^{1}H-NMR spectrum of compound 65 showed signal at δ12.1ppm for (s,1H,OH phenolic), δ10.2ppm for (s,1H,HO-Ar), δ8.5ppm for (s,1H,NH), δ(7.4-8.2) ppm for (m,7H,Ar-H),δ(4.3)ppm of (s,1H,thiazol ring),δ 4.0 ppm (t,1H, CH-CH_2),δ 2.7ppm(d,2H, CH-CH_2)

Table1. Physical properties of the starting thiazole compounds

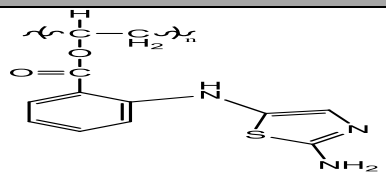
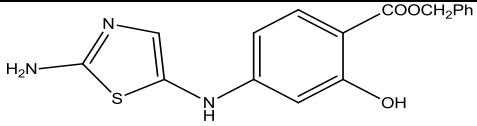
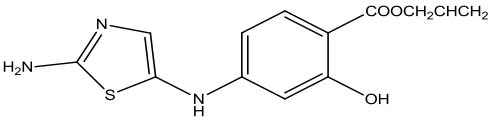
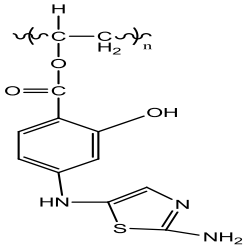
Comp. NO.	Structure	Color	M.P °C	S.P °C	Yield %
24	 *poly ethylene* 2-(2,5-aminothiazol)benzoate	Brown	-	107	63
25	 benzyl 4-((2,5-diaminothiazol)-2-hydroxybenzoate	Dark red	97	-	80
26	 allyl 4-(2,5-diaminothiazol)-2-hydroxybenzoate	Brown	120	-	87
27	 *poly ethylene* 4-(2,5-diaminothiazol)-2-hydroxybenzoate	Dark Brown	-	111	72

Table2 . FTIR spectral data of the starting compounds

Comp. No.	υNH_2 1° amine	υNH 2° amine	υC-H aromatic	υC-H Aliphatic	υC=O ester	υC=N	υC=C aromatic	υC-N	υC-O	others
24	3450	3192	3046	2916	1770	1639	1608	1369	1180	-
25	3450	3210	3085	2954	1776	1650	1612	1373	1155	υO-H Phenol 3550
26	3420	3200	3069	2989	1755	1642	1620	1370	1223	υO-H Phenol 3540
27	3422	3199	3062	2916	1760	1648	1604	1372	1265	υO-H Phenol 3542

Table3. Physical properties of the preparedazo compounds

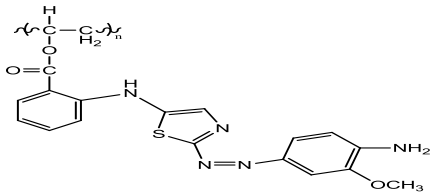
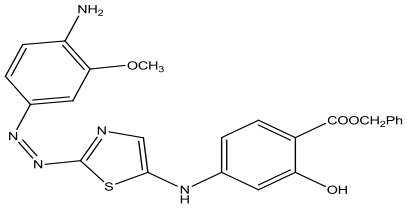
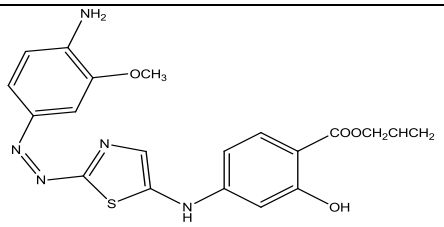
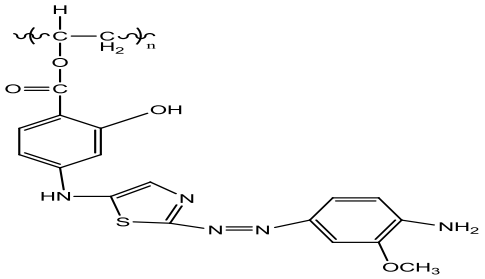
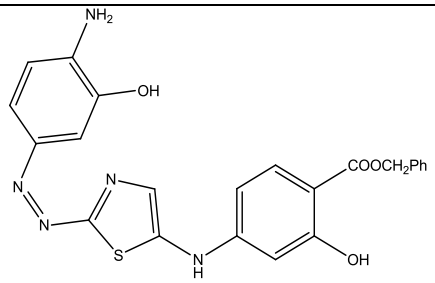
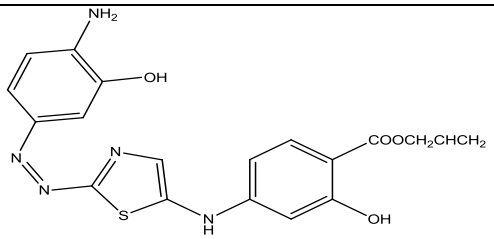
Comp. NO.	Structure	Color	M.P °C	S.P °C	Yield %
42	 poly ethyl 2-[2-(4-amino-3-methoxyphenyldiazenyl)5-aminothiazole]benzoate	red	-	114	72
43	 benzyl 4-[2-(4-amino-3-methoxyphenyldiazenyl)5-aminothiazole]-2-hydroxybenzoate	Deep red	183	-	79
44	 allyl 4-[2-(4-amino-3-methoxyphenyldiazenyl)5-aminothiazole]-2-hydroxybenzoate	Deep red	169	-	68
45	 poly ethyl 4-[2-((4-amino-3-methoxyphenyldiazenyl)5-aminothiazole]-2-hydroxybenzoate	red	-	95	78
50	 benzyl 4-[2-(4-amino-3-hydroxyphenyldiazenyl)5-aminothiazole]-2-hydroxybenzoate	orange	183	-	82
51	 allyl 4-[2-(4-amino-3-hydroxyphenyldiazenyl)5-aminothiazple]-2-hydroxybenzoate	orange	167	-	75

Table3. Physical properties of the preparedazo compounds

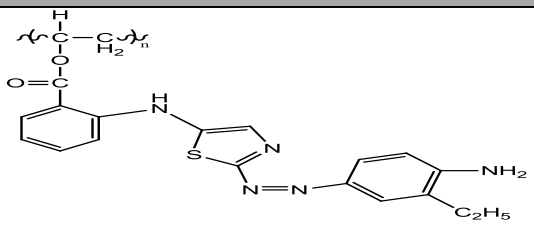
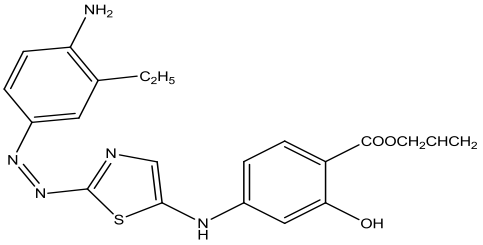
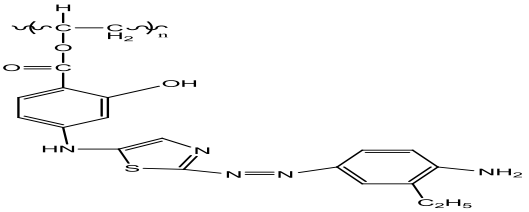
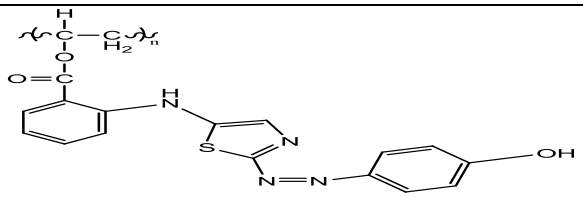
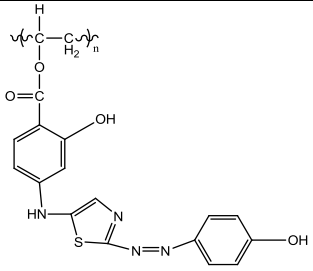
Comp. NO.	Structure	Color	M.P °C	S.P °C	Yield %
56	 polyethyl 2-[2-((4-amino-3-ethylphenyl)diazenyl)5-aminothiazole]benzoate	orange	-	107	86
57	 allyl 4-[2-(4-amino-3-ethylphenyldiazenyl)5-aminothiazole]-2-hydroxybenzoate	red	181	-	84
58	 poly ethyl 4-[2-(4-amino-3-ethylphenyl)diazenyl)5-aminothiazole)-2-hydroxybenzoate	red	-	117	80
63	 poly ethylene 2-[2-(4-hydroxyphenyl)diazenyl)5-aminothiazole]benzoate	red	-	132	75
65	 poly ethylene(2-hydroxy-4-[2-(4-hydroxyphenyl)diazenyl)5-aminothiazole])benzoate	red	-	137	82

Table 4. FTIR spectral data of the prepared compounds

Comp. No.	υO-H phenol	υNH_2 1° amine	υN-H 2°amine	υC-H aromatic	υC-H Aliphatic	υC=O ester	υC=C aromatic	υN=N Azo	υC-N	υC-O	others
42	-	3498	3276	3045	2953	1750	1618	1512	1303	1240	-
43	3527	3397	3200	3041	2910	1778	1600	1502	1325	1267	-
44	3517	3410	3218	3015	2920	1798	1601	1500	1329	1217	υC=C Olef. 1624
45	3578	3460	3217	3012	2902	1783	1608	1504	1323	1265	-
50	3596	3419	3252	3066	2979	1769	1606	1508	1348	1230	-
51	3541	3399	3244	3026	2925	1789	1600	1508	1345	1239	υC=C Olef. 1621
56	-	3424	3227	3016	2969	1710	1601	1500	1305	1244	-
57	3578	3419	3281	3009	2952	1763	1596	1503	1307	1229	υC=C Olef. 1629
58	3592	3385	3217	3047	2920	1747	1593	1498	1328	1240	-
63	3564	-	3247	3088	2931	1720	1639	1517	1338	1251	-
65	3561	-	3249	3083	2958	1768	1629	1520	1340	1265	-

Table5 .antimicrobial activity of some of the prepared compounds.

Comp. No.	Inhibition Zone in mm against *Stapylococcusaureus* (Gram positive)	Inhibition Zone in mm against*Escherichia coli*(Gram negative)
Reference Cefotaxime	48	40
43	17	13
44	20	15
50	18	5
51	14	9
57	20	11

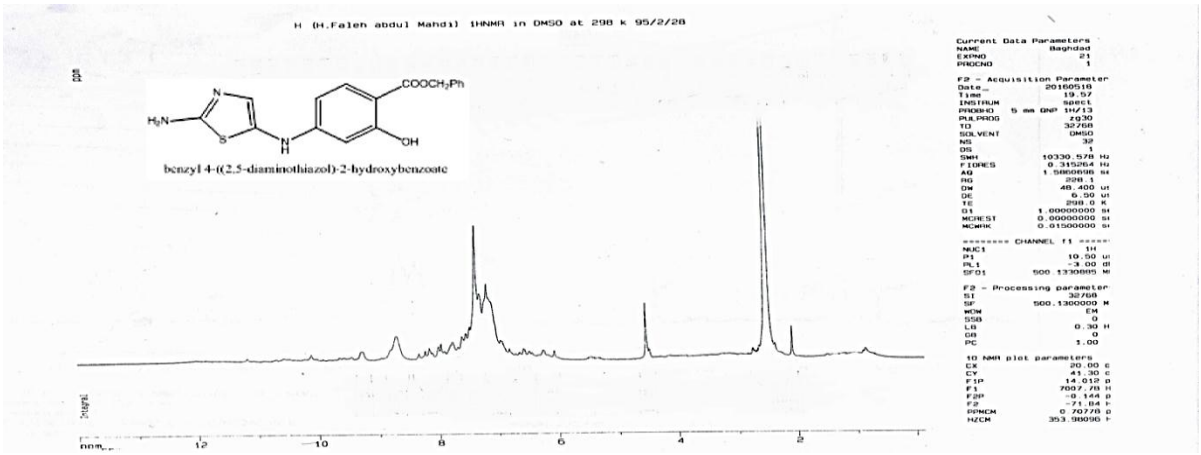


Figure1.[1]HNMR spectra of compound 25

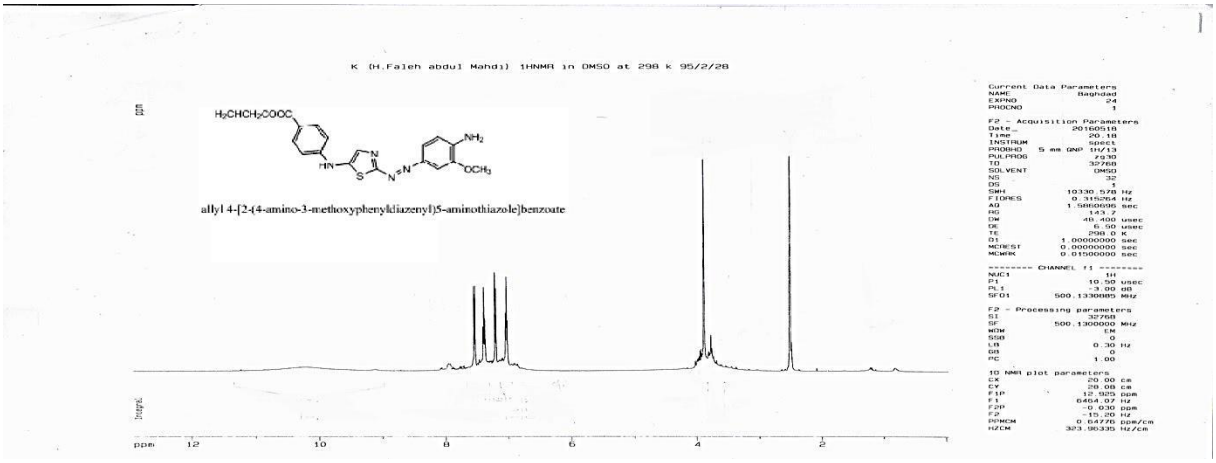


Figure2.[1]HNMR spectra of compound 38

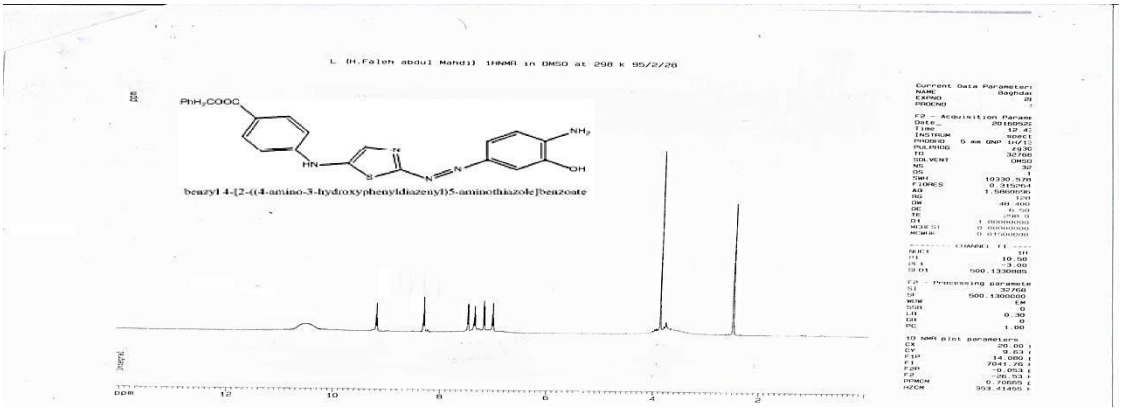


Figure3.[1]HNMR spectra of compound 50

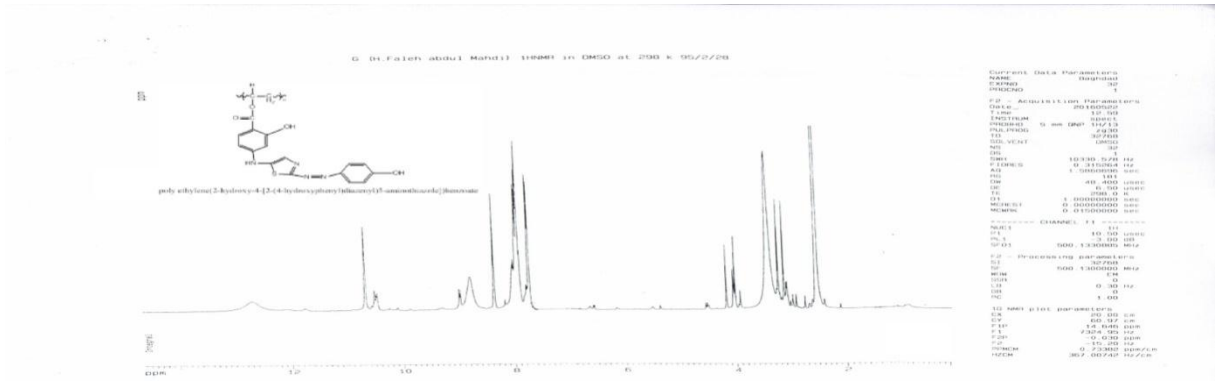


Figure4.[1]HNMR spectra of compound 65

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