IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 12, Issue 2 Ver. I (Mar. - Apr.2017), PP 39-47
www.iosrjournals.org

Synthesis, Identification and Evaluation the Biological Activity for Some New Heterocyclic Compounds Derived from Schiff Bases

Khitam T. A. Al-Sultani
(Department of Chemistry, College of Science/ Baghdad University, Iraq)

Abstract: *This research involves synthesis some of new tetrazole, imidazolinone, thiazolidinone, and oxazepine derivatives. The first step includes formation Schiff bases (1-5) from condensation N-[(4-aminophenyl) carbamothioyl] benzamide with different aromatic aldehydein the presence of glacial acetic acid in DMF as a solvent. Four route with different reagents used for the cyclization of the prepared Schiff bases by reagent (sodium azide, 2-amino acetic acid, 2-mercapto acetic acid and phthalic anhydride) to form tetrazole (6-10), imidazolinone (11-15), Thiazolidinone (16-20), oxazepine(21-25) derivatives respectively. The structure of newly synthesized compounds were identified by spectral methods their [FTIR, and some of them by 1HNMR, 13C-NMR] and measurements some of its physical properties and some specific reactions. The chemical structures of synthesized compounds were well characterized by 1HNMR, 13CNMR, FT-IR and TLC. Also, the effects of prepared compounds in some of strains of bacteria were studied.*

Keywords: *Schiff Bases, Tetrazole, Imidazolinone, Thiazolidinone, Oxazepine, Antibacterial*.

I. Introduction

Schiff bases are chemical compounds possess general group (-HC=N-) called azomethine. These compounds can be formed by react the primary amines with aldehydes or ketones in presence either acid, base or heat as a catalyst of the reaction [1]. Great deals of research have reported that Schiff bases which are derived from the heterocyclic compounds are antimicrobial [2], antiproliferative [3], anticonvulsant [4], cytotoxic [5] and anticancer [6]. Like the other organic compounds, schiff bases which consist of four, five and seven membered rings have biological activities based on its spectrum therefore many of industrial and medical applications like pigments and dyes take place in these fields [7-9]. Not only schiff bases are important, but their derivatives considered as one of the compounds which occupies the medical markets. For examples, oxoimidazoline which is also known imidazolinones, this substance has five membered rings with nitrogen atoms in 1 and positions exhibited many of biological activities such as CNS depressant, hypnotic and sedative [10, 11]. Also, thiazolidine derivatives like 4-Thiazolidinones, this substance is formed by attacking the sulphur atom of imine group. This reaction contains cyclisation process to formed product of the schiff bases [12]. By using advanced analysis techniques combine with CHN analysis in order to characterize oxazepine compounds which are used commonly in colorectal cancer which consider as the most cancer type can be diagnosed which occurring because of many reasons like life style or increasing of age of human. The oxazepine can be synthesized by react the schiff bases with malic anhydride [13]. Finally, this paper aims to synthesis and characterize some new tetrazole, imidazolinone, thiazolidinone and oxazepine derivatives.

II. Experimental Part

1.1 Materials and Instruments

Chemicals supplied from Merck, BDH, Sigma Aldrich and Fluka companies and are used without further purification. Melting points were recorded using digital Stuart scientific SMP3 melting point apparatus and are uncorrected. FTIR spectra were recorded on SHIMAZU FTIR-8400 using KBr discs in the (4000-600) cm-1 spectral range. 1HNMR and 13CNMR were recorded on Burker 500MHzistrument using $CDCl_3$-d as solvent and TMS as internal reference. Thin layer chromatography (TLC) was carried out using Fertigfollenpre coated sheets type polygram silica and the plates were developed with iodine vapor.

1.2 Methods

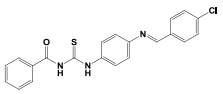
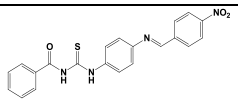
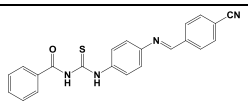
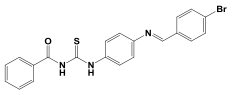
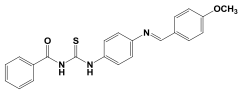
2.2.1 Preparation of N-[(4-aminophenyl) carbamothioyl] benzamide

This compound was prepared according to literature procedure [14].

2.2.2 Preparation of (E)-N-[4-(4-substitutedbenzylideneamino) phenylcarbamothioyl] benzamide (1-5)[15]

Schiff bases have been synthesized by reaction of N-[(4-aminophenyl) carbamothioyl] benzamide (0.01 mol, 0.5 gm.) with different substituted aromatic aldehyde (0.01 mol.) in DMF for (3-6 hour) .in presence of (2-3 drops) of glacial acetic acid. The formed precipitate was filtered and recrystallized by ethanol. Physical properties of dry product and FTIR spectral data are listed in Table (1).

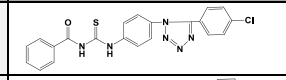
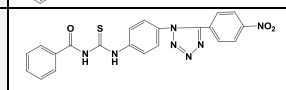
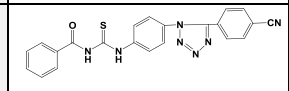
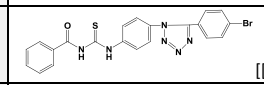
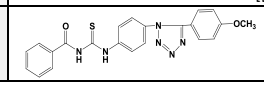
Table 1 - Physical properties and FTIR spectral data $cm^{-1}$for the compounds (1-5).

Com p.No.	Physical Properties				Major FTIR Absorption cm^{-1}					
	Structures	M.P. C°	Yield %	Color	νN-H	νC-H arom.	νC=N	νC=S	νC=O	Other bands
1		197-199	85	Gray	3180	3047	1650	1255	1649	νC-Cl 1091 νp-position 825
2		172-174	90	yellow	3280	3029	1647	1255	1670	NO_2 Asym.1515 sym.1340 νpara-position 837
3		212-214	88	pale yellow	3185	3050	1668	1259	1649	νC≡N 2223
4		110-112	70	brown	3290	3031	1649	1259	1670	νC-Br 970 νp-position 827
5		222-224	83	Off-white	3232	3051	1650	1253	1670	νC-O-C 1107

2.2.3 Preparation of N-[4-(5-(4-substitutedphenyl)-1H-tetrazol-1-yl) phenylcarbamothioyl] benzamide (6-10)[16]

In order to stirring solution of Schiff-bases (1-5) (0.003mol) in (10ml) of tetrahydrofuran, sodium azide (0.003 mol., 0.195g) in 10 ml of tetrahydrofuran was added. The mixture was refluxed for (10-14hours), the end of reaction was checked by TLC which showed the disappearance of the starting materials, then cooled the mixture at room temperature and the precipitate was filtered, washed with cold water, recrystallized with ethanol. Physical properties of dry product and FTIR spectral data are listed in Table (2).

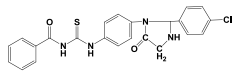
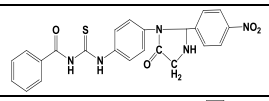
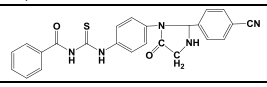
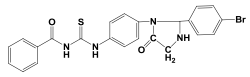
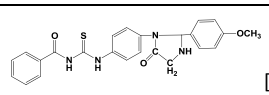
Table 2 - Physical properties and FTIR spectral data $cm^{-1}$for the compounds (6-10).

Comp. No.	Physical Properties				Major FTIR Absorption cm^{-1}					
	Structures	M.P. C°	Yield %	Color	νN-H	νC-H arom.	νC=O	νC=S	νC=N	Other bands
6		207-209	75	Pale-yellow	3180	3047	1649	1255	1600	ν (N=N)1523 ν (C-Cl) 1080 νp-position835
7		210-212	72	yellow	3192	3029	1670	1255	1600	ν (N=N)1515 νNO2 Asym. 1515 Sym. 1342
8		220-221	80	Green	3185	3050	1649	1259	1603	ν (N=N)1514 νC≡N2223
9	 [[	133 decomp.	65	Light brown	3290	3031	1670	1259	1616	ν (N=N) 1521 νC-Br 889 νp-position 835
10		263 decomp.	60	white	3232	3051	1650	1253	1602	ν (N=N) 1515, ν (C-O-C) 1147

2.2.4 Preparation ofN-[4-(2-(4-chlorophenyl)-5-oxoimidazolidin-1-yl)phenylcarbamothioyl]benzamide(11-15) [10]

A solution of appropriate Schiff bases (1-5) (0.0013 mol.) in (15 ml) of tetrahydrofuran as solvent and 2-aminoacetic acid (0.097g.,0.0013mol.) in (5ml.) of tetrahydrofuran was refluxed for (16-20hours), then the reaction mixture was cooled at room temperature and the precipitate was filtered, washed with coldwater and recrystallized by ethanol. Physical properties of dry product and FTIR spectral data are listed in Table (3).

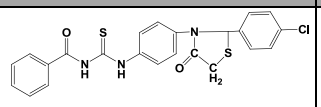
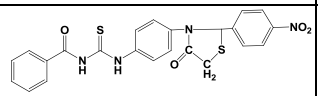
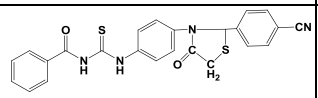
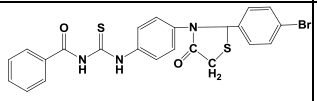
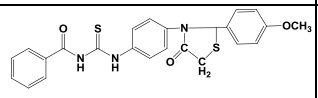
Table 3 - physical properties and FTIR spectral data $cm^{-1}$for the compounds (11-15).

Comp .No.	Physical Properties				Major FTIR Absorption cm^{-1}				
	Structures	M.P. C°	Yield %	Color	νN-H	νC-H arom.	νC=O	νC=S	Other bands
11		182-184	77	Off-white	3332 3170	3059	1680 1654	1259	ν (C-Cl) 1091 νp-position 831
12		195 decomp.	80	Deep yellow	3328 3286	3033	1700 1670	1253	νNO2 asym 1523 sym 1340
13		144-146	85	white	3338 3244	3055	1670 1630	1257	νC≡N2225
14		156-157	70	white	3290 3230	3055	1670 1620	1255	νC-Br 880 νp-position 833
15	 [[	201 decomp.	75	white	3330 3259	3031	1670 1650	1259	ν (C-O-C) 1149

2.2.5 Preparation of N-[(4-(2-(4-substitutedphenyl)-4-oxothiazolidin-3-yl) phenyl)carbamothioyl] benzamide(16-20) [16]

A mixture of Schiff-bases (1-5) (0.003mol) in tetrahydrofuran (15ml) and mercaptoacetic acid (0.003mol, 0.2ml) in tetrahydrofuran with a pinch of anhydrous zinc chloride was refluxed on water bath (14-16 hours).The separated solid was filtered, dried and crystallized by ethanol. Physical properties of dry product and FTIR spectral data are listed in Table (4).

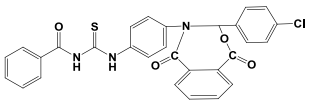
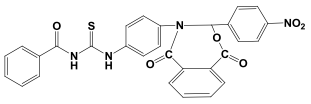
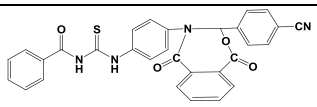
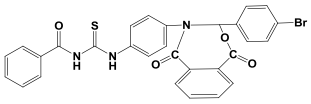
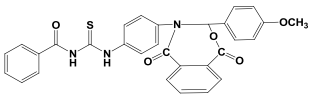
Table 4- physical properties and FTIR spectral data cm-1for the compounds (16-20).

Comp. No.	Physical Properties				Major FTIR Absorption cm^{-1}				
	Structures	M.P. C°	Yield %	Color	νN-H	νC-H arom.	νC=O	νC=S	Other bands
16		193-195	78	white	3145	3051	1679	1257	ν (C-Cl) 1091 νp-position 829
17		209-211	88	Dark-yellow	3190	3035	1670	1255	νNO2 asym 1512 sym 1340
18	 [	218-220	85	Off-white	3185	3012	1670	1255	νC≡N 2223
19		177-179	77	Brown	3220	3031	1672	1257	νC-Br 896 νp-position 835
20		221 decomp.	65	white	3232	3022	1653	1259	ν (C-O-C) 1151

2.2.6 Preparation of N-[(4-(3-(4-chlorophenyl)-1,5-dioxobenzo[e][1,3]oxazepin-4(1H,3H,5H)-yl)phenyl)carbamothioyl]benzamide(21-25)[17]

A mixture of Schiff base (1-5) (0.001mole) and phthalic anhydride (0.001mole) was dissolved in (20mL) in tetrahydrofuran. The mixture was heated for 7hours in water bath at (70°C), excess solvent was distilled, and the precipitate was filtered and recrystallized by ethanol. Physical properties of dry product and FTIR spectral data are listed in Table (5).

Table 5 - Physical properties and FTIR spectral data cm-1for the compounds (21-25).

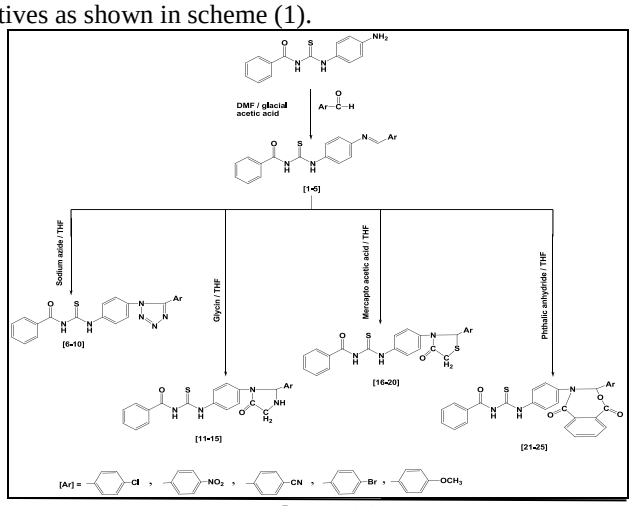
Comp. No.	Physical Properties				Major FTIR Absorption cm^{-1}				
	Structures	M.P. C°	Yield %	Color	νN-H	νC-H arom.	νC=O	νC=S	Other bands
21		132-134	65	white	3190	3034	1672	1257	ν (C=O) phthalic 1770 ν (C-Cl) 1089 νp-position 837
22		215-217	80	Pale yellow	3188	3040	1668	1255	ν (C=O) phthalic 1779 νNO2 asym 1523 sym 1336
23	 [	223-225	66	Gray	3185	3033	1670	1255	ν (C=O) phthalic 1770 νC≡N 2200
24	 [	148-150	60	Brown	3280	3031	1673	1250	ν (C=O) phthalic 1760 νC-Br 880 νp-position 825
25		170-172	75	white	3210	3033	1660	1258	ν (C=O) phthalic 1760 ν (C-O-C) 1142

2.3 Anti-microbial activity test [18]

The test was performed according to the disk diffusion method. Some of prepared compounds were tested against two strain gram +ve (*Staphylococcus aura* and *Bacillus*) and two strain gram –ve bacteria (*pseudomonas* and *Escherichia coli*). Filter paper (Whattman no.1) disk of 5mm diameter were sterilized by autoclaving for 15 min. at 121 °C. The sterile disks were impregnated with different compounds (800µg/disk). Agar plates were surface inoculated uniformly with 100 µL from both culture of tested microorganism. The impregnated disk were placed on the medium suitably spaced a part and the plates incubated at 5 °C for 1 hour. to permit good diffusion and then transferred to an incubator at 37 °C for 24 hours. The inhibition zones caused by various compounds on the microorganisms were examined.

III. Results And Discussion

The synthetic sequences for preparation of new series of Tetrazole,Thiazolidinone, Imidazolinone and Oxazepine all these derivatives as shown in scheme (1).



Scheme (1)

Schiff bases (1-5) were prepared by reaction of compound N-[(4-aminophenyl) carbamothioyl] benzamide with different aromatic aldehydes in presence of glacial acetic acid ,the structure for these compounds were confirmed by physical properties listed in Table(1). FTIR spectrum showed disappearance of absorption band for NH_2 group and appearance of the absorption band at (1668-1647)cm^{-1} to (C=N) [19] and show other different absorption bands for the substituted groups that are listed in Table (1).^{1}HNMR spectrum for compound (2) show signals at υ 7.30-8.42 ppm; υ8.65 ppm (s, 1H, -N=CH-); υ 9.16 ppm (s, 1H, -CS-NH-Ph); (m, 13H, Ar-H) and υ10.30 ppm (s, 1H, -CO-NH-CS-) [20 figure (1). ^{13}CNMR spectrum for this compound show signals listed in Table (7) and figure (2). Schiff bases were cyclized by using four different steps with different reagents.

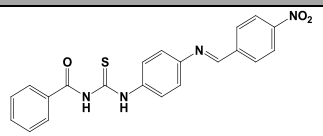
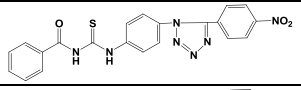
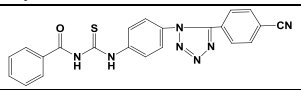
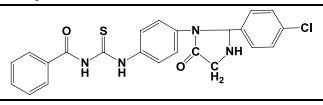
First step include treatment schiff bases with sodium azide to give tetrazole derivatives (6-10), the synthetic steps are shown in scheme (1). The mechanism of the reaction systematically investigated as [3+2] cyclo additions which christened as a 1, 3 -dipolar cyclo additions. Involved the addition of unsaturated systems to 1, 3-dipoles, a molecule possessing resonance contributors in which positive and negative charges are located in 1, 3-position relative to each other. The addition results five membered rings. Physical properties of compounds (6-10) are listed in Table (2). FTIR spectra of compounds (6-10) showed bands at (1523-1514) cm^{-1} are due to the cyclic (N=N) stretching of tetrazole ring. Also , the FTIR for these compounds show the other absorptions bands at (3290-3180) cm^{-1}, (1670-1649) cm^{-1}, (1616-1600) cm^{-1}, and (1259-1253) cm^{-1}, due to υ(NH), υ(C=O), υ(C=N) and υ(C=S) respectively, the other substituted groups are listed in Table (2).^{1}HNMR spectral data of compounds (7 and 8) shows disappearance of the proton of azomethene group, the results listed in Table (6), figure (3) for compound (7) and ^{13}CNMR spectral data of compounds (7 and 8) show results listed in Table (7), figure (4) for compound (7).

The second step of cyclization of Schiff bases was achieved by using 2-aminoaceticacid in tetrahydrofuran to give imdazolidone derivatives (11-15).FTIR spectra of compounds (11-15)showeddisappearance of absorption band at (1668-1647)cm^{-1} for υ(C=N) and appearance of absorption bands at(3338-3170) cm^{-1} and (1670-1620)cm^{-1} and υ(C=O) band of imidazolidone ring respectively. All details of FTIR spectral data of compounds (11-15) are listed in Table(3).^{1}HNMR spectral data of compound (11) show the disappearance of signal proton of azomethene group (-N=CH-) and appearance of new signals for the imidazolidone ring that are listed in Table (6) and ^{13}CNMR spectral data are listed in Table (7).

The third cyclization step of Schiff bases with 2-mercapto acetic acid in THF to give thiazolidinone derivatives (15-20). FTIR spectra of compounds (15-20) showed disappearance of absorption bands at (1668-1647) cm^{-1} for υ(C=N) and appearance of absorption band at (1679-1653) cm^{-1} due to υ (C=O) of thiazolidinonerings. All details of FTIR spectral data of compounds (15-20) are listed in Table(4).^{1}HNMR spectral data of compound (16, 18)show disappearance signals proton of azomethane group (-N=CH-) and appearance new signals for the thiazolidinone rings listed in Table (6) and ^{13}CNMRspectral data listed in Table (7).

The last cyclization step of Schiff bases with phthalic anhydride to result seven membered rings by cyclo addition reaction is classified as a [5+2] implying 5-atome component plus 2-atom component leading to 7-membered cyclic ring. Physical properties of oxazepin derivatives (21-25) are listed in Table (5). FTIR spectra of compounds (21-25) showed bands at (1779-1760) cm^{-1} due to the cyclic (C=O) stretching of ketone imide ring, the other substituted groups are listed in Table (5).^{1}HNMR spectral data of compounds (21 and 22) shows disappearance of proton of azomethane group and appearance signal for proton oxazepin ring, the results listed in Table (6) and ^{13}CNMRspectral data of compounds (21 and 22) show results listed in Table (7).

Table 6: 1H-NMR spectral data (δ ppm) for the selected compounds

Comp. No.	Structures	^{1}HNMR Spectral data(δ ppm)
2		7.30-8.42 (m, 13H, Ar-H); 8.65 (s, 1H,-N=CH-); 9.16 (s, 1H, -CS-NH-Ph); 10.30 (s, 1H, -CO-NH-CS-)
7		7.355-8.375 (m, 13H, Ar-H); 9.15 (s, 1H, -CS-NH-Ph); 10.20 (s, 1H, -CO-NH-CS-)
8		7.30-8.20 (m, 13H, Ar-H); 9.20 (s, 1H, -CS-NH-Ph); 10.28 (s, 1H, -CO-NH-CS-)
11		3.20 (s, 1H, -CH_2-NH-CH-); 5.33 (s, 2H, -CH_2-NH-CH-); 7.47-7.91 (m, 13H, Ar-H); 9.28 (s, 1H, -CS-NH-Ph); 10.15 (s, 2H, -CH_2-NH-CH- overlap with -CO-NH-CS-)

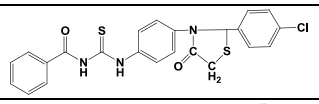
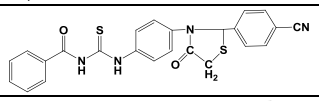
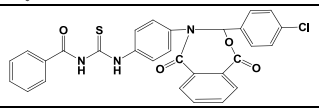
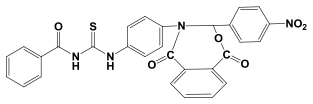
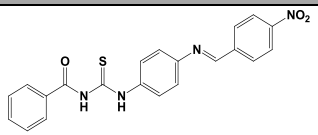
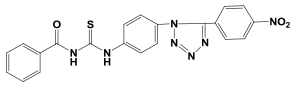
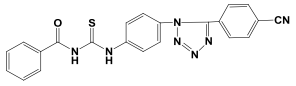
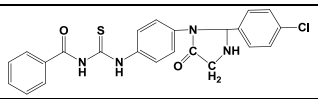
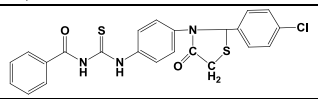
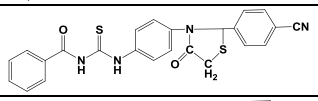
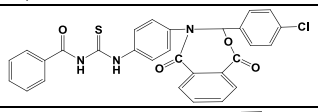
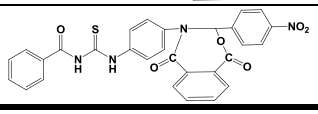
16		3.85 (s, 1H, -CH_2-S-C<u>H</u>-); 5.44 (s, 2H, -C<u>H_2</u>-S-CH-); 7.47-8.08 (m, 13H, Ar-<u>H</u>); 9.30 (s, 1H, -CS-N<u>H</u>-Ph); 10.28 (s, 1H, -CO-N<u>H</u>-CS-)
18		3.82 (s, 1H, -CH_2-S-C<u>H</u>-); 5.42 (s, 2H, -C<u>H_2</u>-S-CH-); 7.53-7.95 (m, 13H, Ar-<u>H</u>); 9.21 (s, 1H, -CS-N<u>H</u>-Ph); 10.30 (s, 1H, -CO-N<u>H</u>-CS-)
21		7.10 (s, 1H, -CO-O-C<u>H</u>-); 7.45-7.95 (m, 17H, Ar-<u>H</u>); 9.25 (s, 1H, -CS-N<u>H</u>-Ph); 10.50 (s, 1H, -CO-N<u>H</u>-CS-)
22		7.12 (s, 1H, -CO-O-C<u>H</u>-); 7.54-8.44 (m, 17H, Ar-<u>H</u>); 9.13 (s, 1H, -CS-N<u>H</u>-Ph); 10.19 (s, 1H, -CO-N<u>H</u>-CS-)

Table 7: 13CNMR spectral data (δ ppm) for the selected compounds.

Comp. No.	Compound structure	^{13}CNMR spectral data (δ ppm)
2		120.33-135.92 (C- aromatic rings); 157.45 (C=N); 166.99 (C=O); 178.20 (C=S)
7		120.34-149.39 (C- aromatic rings); 157.55 (C=N tetrazole); 167.05 (C=O); 178.31 (C=S)
8		118.44 (C≡N); 120.35-149.28 (C- aromatic rings); 160.95 (C=N tetrazole); 167.06 (C=O); 178.33 (C=S)
11		58.30 (-<u>C</u>H_2-NH-CH-); 77.24 (-CH_2-NH-<u>C</u>H-); 120.36-134.82 (C- aromatic rings); 168.00 (C=O amide); 171.2 (C=O imidazolin ring); 178.40 (C=S)
16		52.30 (-<u>C</u>H_2-S-CH-); 77.24 (-CH_2-S-<u>C</u>H-); 120.36-133.87 (C- aromatic rings); 167.20 (C=O amide); 171.00 (C=O thiazolidine ring); 179.00 (C=S)
18		60.21 (-<u>C</u>H_2-S-CH-); 77.35 (-CH_2-S-<u>C</u>H-); 117.90 (C≡N); 121.20-135.80 (C- aromatic rings); 167.22-168.20 (C=O amide with C=O thiazolidine ring); 179.00 (C=S)
21		120.36 (-CO-O-<u>C</u>H-); 124.37-142.20 (C- aromatic rings); 167.20 (C=O amide); 173.42 (C=O oxazepin ring); 178.50 (C=S)
22		120.40 (-CO-O-<u>C</u>H-); 124.36-142.40 (C- aromatic rings); 167.70 (C=O amide); 174.00 (C=O oxazepin ring); 178.60 (C=S)

Anti-microbial activity:

The results of antibacterial activity are listed in Table (8). The results referred that all synthetic compounds possess moderate activity against certain types of bacteria, while it did not possess any activity against others. Compounds (3 and 24) possess strong activity against *Escherichia coli*, while compounds (13 and 22) possess strong activity against *Staphylococcus aureus.* Compounds (3, 9, 13, and 24) showed weak activity against *Bacillus*. However, compounds (5, 8, 11, 17, and 22) showed no inhibition for the same bacteria. As far as compounds (8 and 24) possess modest activity against *Pseudomonas*, while no inhibition activity was found for compounds (3, 11, 13, and 19).

Table 8: Anti-microbial activity of some of the prepared compounds

Comp. No.	*Staphylococcus aureus*+ve	*Bacillus* +ve	*Pseudomonas* –ve	*Escherichia coli*– ve
3	8	3	-	11
5	6	-	4	9
8	-	-	10	6
9	10	5	4	8
11	9	-	-	10
13	13	3	-	9
17	4	-	9	3
19	6	7	-	-
22	12	-	3	9
24	9	4	7	12

Solvent: DMSO; [C]: 800µg/ml, Zone of inhibition: (-) no inhibition zone; (3-6) weak; (7-10) moderate; (11-15) strong.

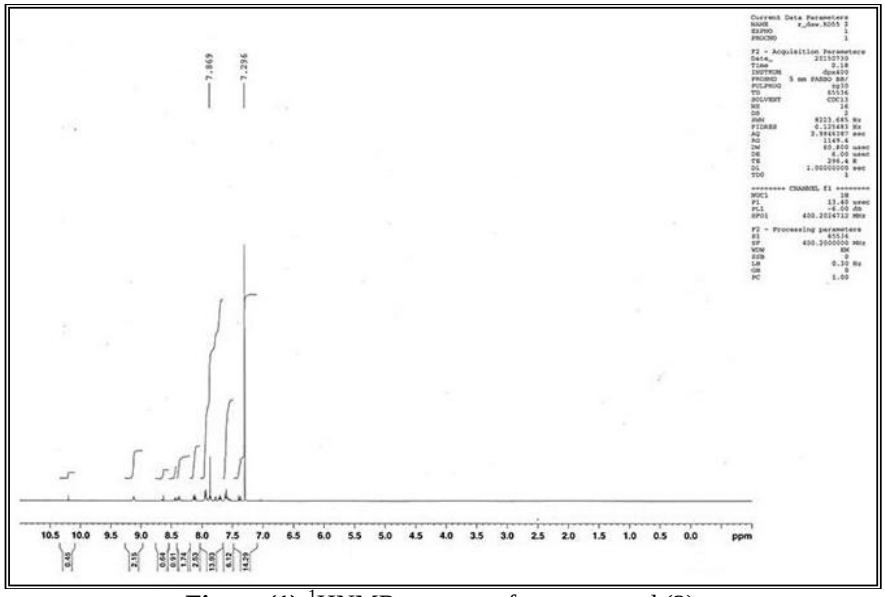


Figure (1):[1]HNMR spectrum for compound (2).

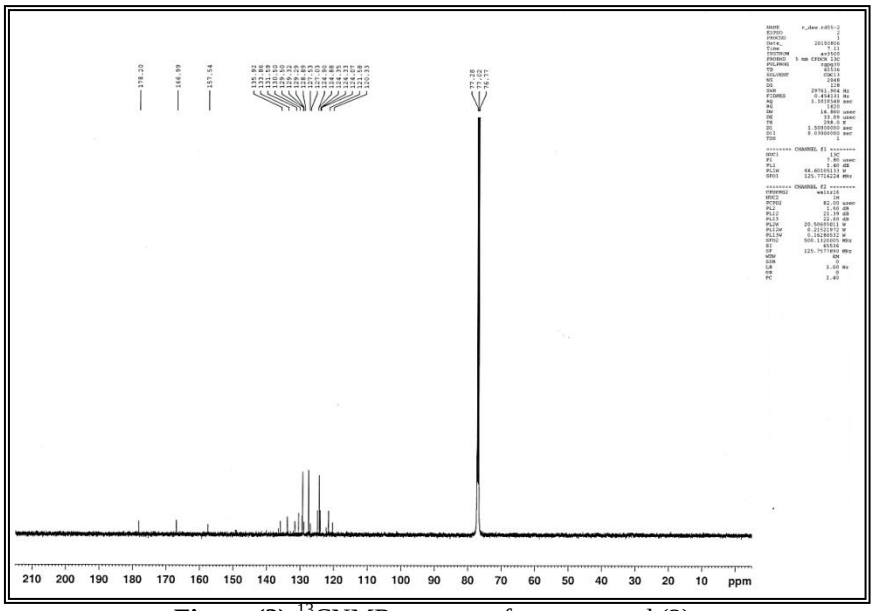


Figure (2):[13]CNMR spectrum for compound (2).

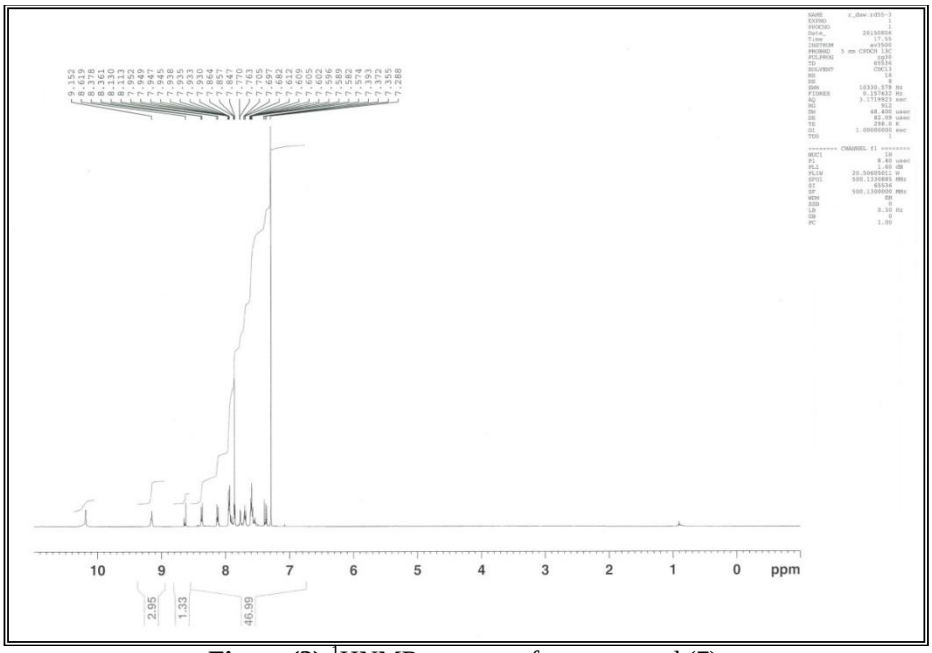


Figure (3):^{1}HNMR spectrum for compound (7).

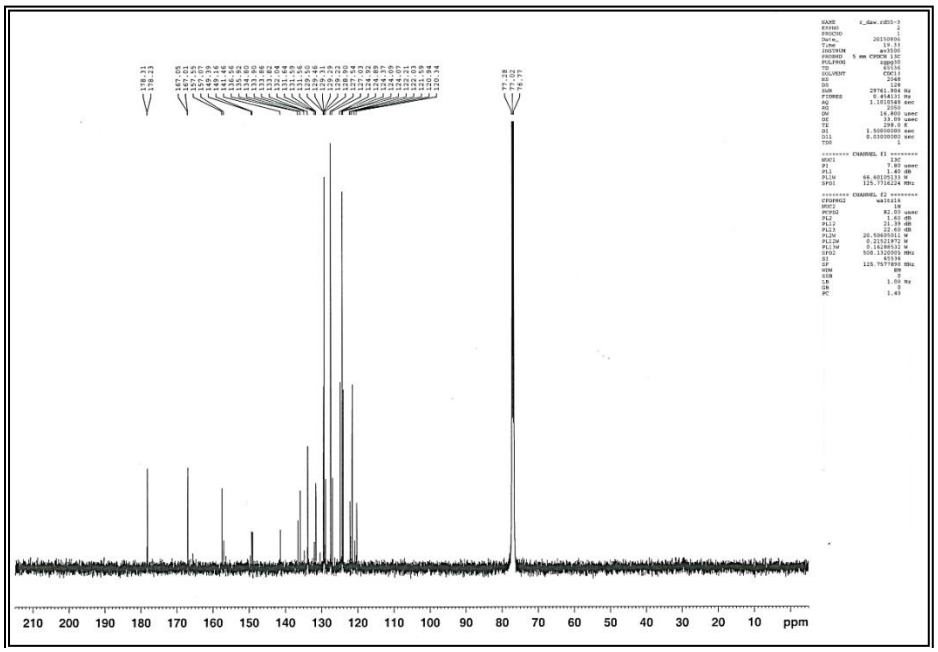


Figure (4):13CNMR spectrum for compound (7).

References

[1] ZahraaS. M., Ivan H. R. and Ali H. R., synthesis and characterization of new aminoacid-schiff bases and studies their effects on the activity of acp, pap and npa enzymes (*in vitro*), *e-journal of chemistry, 9(2),* 2012, 962-969.

[2] Kahveci B.,Bekircan O. and Karaoglu S., Synthesis and antimicrobial activity of some 3-alkyl-4-(arylmethyleneamino)-4,5-dihydro-1H-1,2,4-triazol-5-ones,*Indian J. Chem., 44B,* 2005, 2614-2617.

[3] Vicini P.,GeronikakiA.,Incerti M.,Busonera B.,Poni G.,Kabras C.A.,Colla P.L., Synthesis and biological evaluation of benzo[d]isothiazole, benzothiazole and thiazole Schiff bases, *Bio. org. Med. Chem,.11,* 2003, 4785-4789.

[4] KuçukguzelI.,KuçukguzelS.G.,Rollas S.,Otuk-Sanıs G.,Ozdemir O.,BayrakI.,AltugT. and STables J.P., 3-(Arylalkylthio)-4-alkyl/aryl-5-(4-aminophenyl)-4H-1,2,4-triazole derivatives and their anticonvulsant activity, *Farmaco.59,* 2004, 893-901.

[5] Tarafder M.T.,Kasbollah A.,Saravan N., Crouse K.A., Ali A.M., Tin O.K., S-methyldithiocarbazate and its schiff bases: Evaluation of bondings and biological properties, *J.Biochem. Mol. Biol. Biophs., 6,* 2002, 85-91.

[6] Aletti S.P., Hemminge S. Y., Badiadka N. and Balladka K. S., Synthesis and spectroscopic characterization of some novel Schiff bases of benzylidene derivatives, *Der PharmaChemica,6(1),* 2014, 1-6.

[7] Hamid L. S., Amjid I., Saeed A. and George W. W., Synthesis and Spectroscopic Studies of New Schiff Bases, *Molecules,11,* 2006, 206-211.

[8] Ismaeel Y. M., Duhaa S. and Shaimaa A. S., Synthesis and characterization of some new compounds derivatives from paraaminobenzoic acid, *International Journal for Sciences and Technology,* 8(3), 2013, 6-11.

[9] Ezzat H. Z., Synthesis, Characterization and Study Biological activity of some new Sulphadiazine derivatives, *International Journal of Chemical and Natural Sciences,2(4),* 2014, 109-115.
[10] Suaad M.H. and Lawand H.K, Synthesis and antimicrobial evaluation activity of some new substituted spiro-thiazolidine, Imidazolinone and azetidine derivatives of 5- BromoIsatine, *Journal of Zankoisulaimani ,17(1),* 2015,49-59.
[11] Rakesh N. M. and Desai K. R., Studies on Synthesis of Some Novel Heterocyclic Azlactone Derivatives and Imidazolinone Derivatives andtheir Antimicrobial Activity, *E-Journal of Chemistry,2(1),* 2005, 42 -51.
[12] Hilal. M. A., Ibtisam K.J. and Malak N. S., Synthesis and characterization of newheterocyclic compounds with studying its biological activity, *Kerbala Journal of Pharmaceutical Sciences,4,* 2012, 119-135.
[13] Dhanya S., Ranjitha C., Rama M .,Ksr P., Oxazepine Derivative as an Antitumor Agent and Snail1 Inhibitor against Human Colorectal Adenocarcinoma, *International Journal of Innovative Research in Science, Engineering and Technology, 3(8),* 2014, 15357- 15363.
[14] Uday H. R. , Suaad M. H. and Khulood A. S., Corrosion Inhibition Effects of Some New Synthesized N-Aroyl-N\-Aryl thiourea Derivatives for Carbon Steel in Sulfuric Acid Media, *Journal of Al-Nahrain University,16 (4),* 2013, 80-93.
[15] Zainab H., Emad Y., Ahmed A. and Ali A., Synthesis and characterization of Schiff's bases of Sulfamethoxazole, *Organic and Medicinal Chemistry Letters,4(1),* 2014,1-4.
[16] Mohammed R. A., Suaad M. H. and Ayad K. K., Synthesis, Evaluation Antimicrobial Activity of Some New *N*-substituted Naphthalimides Containing Different Heterocyclic Rings, *Iraqi Journal of Science, 54(4),* 2013, 761-774.
[17] Ruaa M., Synthesis and Characterization of Some Heterocyclic Compounds (Oxazepine, Tetrazole) Derived from Schiff Bases, *Journal of Al-Nahrain University,15 (4),* 2012, 60-67.
[18] Anesini C. and Perez C., Screening of plants used in argentic folk medicine for antibacterial activity, *J. Ethnrophrmacol,39(2),* 1993, 35-47.
[19] Ralph L., Christin K. Hermann T. Morrill D. and Curtin R., *Systematic Identification of Organic Compounds* (8th edition, John and Sons 2004).
[20] Silverstein, R.M. and Bassler, G.C., *Spectrometric identification of organic compounds* (4th edition, John and Son 1981).