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**Research Article** 

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# Synthesis and Evaluation of the Biological Activity of New 4-(2- Chloroacetyl) Morpholine Derivatives

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### ABSTRACT

Morpholine derivative were prepared by reacting the morpholine with chloroacetyl chloride in the presence triethylamine as an catalyst and diethylether as a solvent gave the 2-(4-chloroacetyl)morpholine then reaction with substituted 2-amino benzothiazole to give new compounds  $(M_1-M_{10})$  and reaction of 5-substituted-2-amino-1,3,4-oxadiazolein the presence of potassium carbonate anhydrous to give new compounds  $(M_{21}-M_{30})$  respectively. The chemical structure synthesis compound were identified by spectral methods their (FT-IR and H<sup>1</sup>- NMR) and measurement some of its physical properties. The synthesized compounds were screened for antibacterial activity.

Keywords: Morpholine; 2-aminobenzothiazole; 1,3,4-oxadiazolem; Antimicrobial

### INTRODUCTION

Morpholine with the common name of diethylenimide oxide is acolourless, Hygroscopic and versatile organic liquid [1]. Morpholine is a six membered heterocyclic compound [2] and this heterocyclic structure features both amine and either functional groups and an organic chemical compound having the chemical formula O(CH<sub>2</sub>CH<sub>2</sub>)NH [3], Morpholine derivatives plays an important role in the treatment such as antibacterials, anticancers, antimalarials, antitussives, anticonvulsants and analgesics [4]. Morpholine was reacted with Benzothiazole. Benzothiazole is a privileged bicyclic ring system. It contains a benzene ring fused to a thiazole ring. The small and simple benzothiazole nucleus is present in compounds involved in research aimed at evaluating new products that possess interesting biological activities like antimicrobial, antitubercular, antitumor, antimalarial, antimicrobial, anthelmintic, antidiabetic, anticonvulsant, analgesic and anti-inflammatory activity [5]. Morpholine was reacted with 1,3,4-Oxadiazole. 1,3,4-Oxadiazole is a heterocyclic compound containing an oxygen atom and two nitrogen atoms in a five-membered ring. There are three known isomers: 1,2,4-oxadiazole, 1,2,3-oxadiazole and 1,2,5-oxadiazole. However, 1,3,4-oxadiazole and 1,2,4-oxadiazole are better known, and more widely studied by researchers because of their many important chemical and biological properties [6]. It results from convertion of semicarbazones. The semicarbazides, which are the raw material of semicarbazones, have been known to have biological activity against many of the most common species of bacterials [7,8].

#### **EXPERIMENTAL SECTION**

#### **Materials and Methods**

Chemicals used in this work are supplied from Merck, BDH, Sigma Aldirch, Fluka, GCC companies and are used without further purification. Melting points were recorded using digital stuart scientific SMP3 melting points apparatus and are uncorrected. SHIMAZU FT-IR-8400 Fourier transform Infrared spectrophotometer using KBr discs in the (4000 - 6000) cm<sup>-1</sup> spectral range. <sup>1</sup>H-NMR was recorded on mr chabok-sample code: m 10,400 M Hzistrument using DMSO-d6 as solvent and TMS as internal reference.

### Preparation 4-(2- Chloroacetyl) Morpholine [9](M)

To a mixture of Morpholine Diethyl ether (15 ml) and triethylamine (0.025 mol), was added chloroacetylchloride (0.025 mol) drop-wise at 5-10°C. The reaction mixture was then stirred for 6 hrs. And left at room temperature for 24 hours then poured into crushed ice. The solid separated was dried and recrystallized from ethanol and water. Melting points, yield% data are listed in Table 1.

## Preparation of Substituted-2-Aminobenzothiazole [10] (1-10)

Substituted aromatic primary amine (0.03 mol) and ammonium thiocyanate (0.1 mol) were dissolve (150 ml) of glacial acetic acid in a suitable round bottomed flask equipped with a dropping funnel for the addition of bromine, bromine (1.2 ml in 75 ml glacial acetic acid) was added drop wise with stirring and cooling. Stirring was continued for 2 hr. then the resulted solution was poured on ice water with vigorous stirring. The resulting solid was filtered, washed then dried and recrystallized from ethanol/water. Melting points, yield% data are listed in Table 1.

## Synthesis of N-(2-Aminoacetyl Substituted Benzothiazole-2yl)Morpholine (M<sub>1</sub>-M<sub>10</sub>) [11]

A mixture of 2-(4-Chloroacetyl)morpholine (0.008 mol) in absolute ethanol (25 ml) and potassium carbonate anhydrous (0.008 mol) was refluxed and added drop wise to a solution of (0.008 mol) of substituted-2-aminobenzothiazole dissolved in (30 ml) of absolute ethanol, the reaction mixture was refluxed for (8-10) hrs. After cooling the separated precipitate was filtered and recrystalized from a suitable solvent. Physical properties for compounds are listed in Table 2.

## Preparation of Semicarbazone Derivatives [11] (11-20)

An equimolar of semicarbazide hydrochloride and different aromatic aldehyde were dissolved in the mixture were refluxed for (1 hr), then cooled and precipitated by water, filtered to obtain semicarbazone. Melting points, yield% data are listed in Table 3.

## Preparation of 2-Amino-5-Substituted-1,3,4 Oxadiazole [11] (21-30)

Semicarbazone (0.01 mol) and sodium acetate (1.4 gm, 0.01 mol) were dissolve 40-50 ml of glacial acetic acid in a suitable round bottomed flask equipped with a dropping funnel for the addition of bromine, bromine (0.6 ml in 5 ml glacial acetic acid) was added drop wise with stirring and cooling. Stirring was continued for 1 hr then the resulted solution was poured on ice water with vigorous stirring. The resulting solid was filtered, washed then dried and recrystallized from ethanol/water. Melting points, yield% data are listed in Table 4.

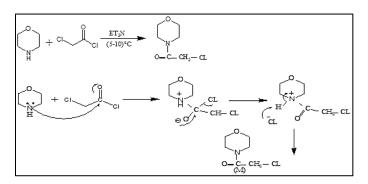
## Synthesis of N-(2-Aminoacetyl-5-Substituted-1,3,4-Oxadiazoles-2-yl) Morpholine [11] (M<sub>21</sub>-M<sub>30</sub>)

A mixture of compound (1) (1 gm, 0.004 mol) in absolute ethanol (10 ml) and potassium carbonate anhydrous (0.56 gm, 0.004 mol) was refluxed and added dropwise to a solution of (0.004 mol) of 2-amino-5-substituted-1,3,4oxadiazole dissolved in (10 ml) abs. ethanol, the mixture was refluxed for 6-8 hrs. The resulted mixture was cooled to room temperature before pouring into crushed ice. The obtained precipitate was filtered; washed thorough by with water and dried then was purified by recrystallization from a suitable solvent. Melting points, yield% data are listed in Table 5.

### **RESULTS AND DISCUSSION**

### Preparation 4-(2- Chloroacetyl) Morpholine

Morpholine was converted to 4-(2-chloroacetyl) morpholine by the reaction with chloroacetyl chloride at 5-10°C in the presence of triethylamine and diethylether as a solvent, as shown in the following equation. The mechanism for this reaction involves nucleophilic attack of amino group in morpholine on reaction with carbonyl group in chloroacetylchloride give the final product (M), as shown in the following (Scheme 1) [12].

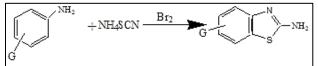


Scheme 1: Morpholine on reaction with carbonyl group in chloroacetylchloride

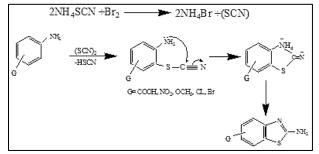
The FT-IR spectra show the absence at v(3421) cm<sup>-1</sup> for imide(NH) in the starting material and appearance of the (C=O) group band at (1654) cm<sup>-1</sup> and(C-CL) at v(1037) cm<sup>-1</sup> which is agood indication of successful condensation listed in Table 6.

#### Preparation of Substituted -2- Aminobenzothiazole (1-10)

Aniline derivatives were reacted with Ammonium thiocyanate with the addition of bromine in the presence of glacial acetic acid as a solvent as shown in the following equation:



The mechanism of reaction involves a nuclephilic addition as shown below (Scheme 2) [13].



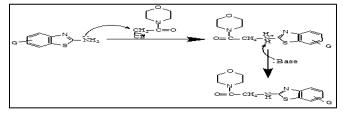
Scheme 2: Mechanism of reaction involves a nuclephilic addition

The FT-IR spectra show compounds (1-10) give absorption band at (3406- 3479) cm<sup>-1</sup> for (NH<sub>2</sub>) group, (1400-1496) cm<sup>-1</sup> (C=N), (605-725) cm<sup>-1</sup> (C-S) and (1600-1712) cm<sup>-1</sup> (C=C) listed in Table 6.

#### Synthesis of N-(2-Aminoacetyl Substituted Benzothiazole-2-yl)Morpholine

The reaction compound (M) with 2-amino benzothiazole derivatives in the presence of potassium carbonate anhydrous and diethylether as a solvent, as shown in the following equation:

The mechanism of reaction as shown in the following (Scheme 3) [14].

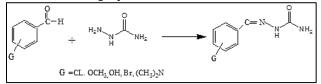


Scheme 3: Mechanism of reaction 2-amino benzothiazole derivatives in the presence of potassium carbonate anhydrous and diethylether

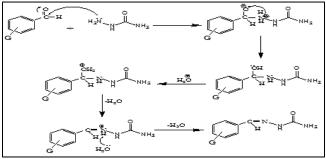
The FTIR spectra show compounds  $(M_1-M_{10})$  have absorption bands at (3028-3421) cm<sup>-1</sup> for (N-H), (3024-3140) cm<sup>-1</sup> (C-H) aromatic, (1616-1701) cm<sup>-1</sup> (C=O) and (1404-1566) cm<sup>-1</sup> (C=N) listed at Table 7). In the 1H-NMR spectrum of compound (M10) showed the signal at  $\delta(1.4-2.4)(s,2H,CH2-N)$ ,  $\delta(3.0-3.3)(s,2H,CH2-O)$ ,  $\delta(7.1)(s,1H,NH)$ ,  $\delta(7.2)(s,2H,CH2C=O)$ , $\delta(7.3)(s,3H,aromatic)$ .

#### Preparation of Semicarbazone Derivatives (11-20)

Semicarbazone are obtained by the condensation of semicarbazide with aldehyde aromatic were dissolved in ethanol absolute and refluxed as shown in the following equation:



The mechanism for this reaction involves nucleophilic attack of amino group in semicarbazide on reaction with carbonyl group in aldehyde and then a proton is transferred from the nitrogen to the oxygen anion. The hydroxy group is protonated to yield an oxonium ion, which easily liberates a water molecule. An unshared pair of electrons on the nitrogen migrates toward the positive oxygen, causing the loss of a water molecule. A proton from the positively charged nitrogen is transferred to water, leading to the imine's formation (Scheme 4) [15].

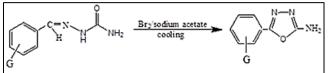


Scheme 4: Reaction involves nucleophilic attack of amino group in semicarbazide

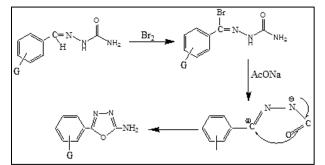
The FTIR spectra show compounds (11-20) showing absorbance band at (3421-3488) cm<sup>-1</sup> (NH2), (1681-1732) cm<sup>-1</sup> for (C=O), (3244-3475) cm<sup>-1</sup> (N-H), (1551-1670) cm<sup>-1</sup> (C=N) and (1508-1612) cm<sup>-1</sup> (C=C) listed in Table 8.

#### Preparation of 2-Amino-5-Substituted-1,3,4 Oxadiazole(21-30)

The compounds (21-30) were synthesized from the convertion of semicarbazone to 1,3,4 oxadiazole by the reaction with sodium acetate at  $5-10^{\circ}$ C in the presence of Bromine and glacial acetic acid as a solvent, as shown in the following equation:



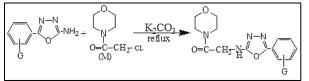
The mechanism of reaction involves the oxidative intramolecular cyclization reactions of semicarbazones with bromine in acetic acid solution (Scheme 5) [15]. The FTIR spectra show compounds (21-30) have absorption band at (3417-3479) cm<sup>-1</sup> for (NH<sub>2</sub>) group, (1654-1732) cm<sup>-1</sup> (C=N), (1211-1280) cm<sup>-1</sup> (C-O-C) and (1570-1658) cm<sup>-1</sup> (C=C) listed in Table 9.



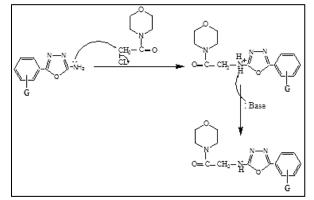
Scheme 5: Oxidative intramolecular cyclization reactions of semicarbazones with bromine in acetic acid solution

#### Synthesis of N-(2-aminoacetyl-5-substituted-1,3,4-oxadiazoles-2- yl) morpholine (M21-M30)

The reaction compound (M) with 5- substituted-2-amino-1,3,4-oxadiazole in the presence of potassium carbonate anhydrous and Diethylether as a solvent, as shown in the following equation:



The mechanism of reaction involves the amine N functions as the nucleophile and attacks the electrophilic C of the alkyl halide displacing the chloride and creating the new C-N bond. The base deprotonates the positive N (ammonium) center creating the alkylation product, here a secondary amine (Scheme 6) [14].



Scheme 6: Amine N functions as the nucleophile and attacks the electrophilic C of the alkyl halide

The FTIR spectra show compounds ( $M_{21}$ - $M_{30}$ ) have absorption band at (3340-3479) cm<sup>-1</sup> for (N-H), (1662-1732) cm<sup>-1</sup> (C=O), (1566-1666) cm<sup>-1</sup> (C=N) and (1113-1180) cm<sup>-1</sup> (C-O-C) listed at Table 10. In the 1H-NMR spectrum of compound ( $M_{25}$  and  $M_{28}$ ) showed the signal at  $\delta$ (1.1-1.9)(s,2H,CH2-N),  $\delta$ (3.3)(s,2H,CH2-O),  $\delta$ (6.5-6.9)(s,1H,NH),  $\delta$  (7.6-8.1) (s,2H,CH2C=O),  $\delta$  (7.3-7.4) (s,3H,aromatic) these spectrum and other are shown in Table 11.

#### **Biological Study**

The cup plate method using nutrient agar medium was employed in studying the antibacterial activity of some of the prepared compounds  $(M_2, M_7, M_{26})$  against two types of bacteria, *Staphylococcus aureus* (Gram positive) and *Escherichia coli* (Gram negative) respectively and DMSO was used as sample solution. Using a sterilized corn borer cups were scooped out of agar medium contained in a petri dish which was previously inoculated with the microorganisms. The test compound solution (0.1 mL) was added in the cups and the petri dishes were subsequently incubated at (37°C) for 48 hrs. Zones of inhibition produced by each compound were measured in mm and the results are listed in Table 12. As shown in Figures 1-6.

Compd. No.	Structure product	Yield %	Color	M.P °C
М	$O = C - CH_2 - CL$	95	White	79-80
1	Br S NH <sub>2</sub>	60	White	200-202
2		90	Black	71-73
3		99	Yellow	276-278
4	OCH3 NH2	95	Off-white	>300
5	NG <sub>2</sub> NG <sub>2</sub> NH <sub>2</sub>	60	Green	174-176
6		98	Green	64-66
7		95	Orange	82-84
8		85	Off-white	216-218
9		90	Off-white	162-164
10		98	Black	Oily

## Table 2: Physical properties of compound (M1-M10)

Compd. No.	Structure product	Yield %	Color	M.P. ℃
$M_1$		80	Off white	114-116
<b>M</b> <sub>2</sub>		80	Brown	46-48
$M_3$		90	Dark brown	80-82
$M_4$	O-C-CH <sub>2</sub> -N-C-CH <sub>3</sub> -N-C-CH <sub>3</sub>	75	Gray	>300
M <sub>5</sub>		70	Yellow	>300
$M_6$	$O = CH_2 - N - V$	90	Pale yellow	>300
$\mathbf{M}_7$		98	Orange	>300
$\mathbf{M}_8$		70	Gray	>300
M9		75	Brown	110-112
$M_{10}$	O=C-CH <sub>2</sub> -N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N	95	Brown	>300

Compd. No.	Structure product	Yield %	Color	M.P.℃
11	$\bigcup_{H}^{OH} \bigcup_{H}^{O} \bigcup_{NH}^{O} \bigcup_{-C-NH_2}^{OH}$	86	Off white	176-178
12	$\bigcup_{H} \bigcup_{H} \bigcup_{H$	75	Off white	190-192
13	$CH_{3}O \qquad O \\ H = N - NH - C - NH_{2}$ $CH_{3}O \qquad H$	70	Yellow	210-212
14	CH <sub>3</sub> O O H CH <sub>3</sub> O OCH <sub>3</sub>	98	Orange	205-207
15	$C = N - NH - C - NH_2$	90	Yellow	175-177
16	$CL \qquad \qquad$	98	white	202-204
17	$CL \qquad 0 \\ H = N - NH - C - NH_2$	88	white	254-256
18	$CL \qquad 0 \\ I \\ H = N - NH - C - NH_2$	86	Off white	176-178
19		95	white	210-212
20	$\begin{array}{c} 0\\ H_{3C} - N \\ H_{3C} - N \\ C \\ H_{3C} \\ C \\ H_{3} \end{array}$	77	Yellow	162-164

Table 3: Physical properties of compound (11-20)

#### Table 4: Physical properties of compound (21-30)

Compd. No.	Structure product	Yield %	Color	M.P.°C
21		70	Brown	160-162
22		75	Orange	160-162
23	CH <sub>3</sub> O-NH <sub>2</sub>	80	White	202-204
24	CH <sub>3</sub> O CH <sub>3</sub> O OCH <sub>3</sub> NH <sub>2</sub>	85	Green	170-172
25	HO-NH2	75	Orange	198-200
26		75	Pale yellow	167-168
27		70	Off white	246-248
28		65	White	204-206
29		60	White	>300
30	$H_3C-N$	90	green	oily

Compd. No.	Structure product	Yield %	Color	M.P.°C
M <sub>21</sub>		80	Brown	148-150
M <sub>22</sub>	$ \begin{array}{c} \begin{array}{c} & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & $	75	Dark grey	>300
M <sub>23</sub>	$\bigcap_{\substack{N \\ O=C-CH_2-N}}^{O} \bigcap_{\substack{N-N \\ H}}^{CH_3O} OCH_3$	70	Pale yellow	218-220
M <sub>24</sub>	$O = C - CH_2 - M - M - CH_3O - OCH_3$	80	Brown	156-158
M <sub>25</sub>	O O O O O O O O O O	80	Black	188-190
M <sub>26</sub>	O O O O O O O O O O	90	Lead	196-198
M <sub>27</sub>	$ \begin{array}{c} & & \\ & & $	70	Pale yellow	248-250
$M_{28}$	$O = C - CH_2 - N - CL$	85	White	230-232
M <sub>29</sub>	$ \begin{array}{c} & & \\ & & $	60	Gray	> 300
$M_{30}$	$ \begin{array}{c} O \\ \\ \\ \\ \\ \\ \\ O = C - CH_2 - N - V \\ H \end{array} \begin{array}{c} CH_3 \\ \\ \\ \\ \\ O = C - CH_3 \end{array} $	70	Gray	202-204

Table 5: Physical properties of compound (M21-M30)

Compd. No.	Compounds structure	v(N- H) amine	υ(C=O)	v(C=N)	v(C- S)	v(C=C)	Others
М	$\sim$ $\sim$ $\sim$ $\sim$ $\sim$ $\sim$ $\sim$ $\sim$ $\sim$ $\sim$ $\sim$ $\sim$ $\sim$ $\sim$	-	1654	-	-	-	υ(C- H)aliphatic 2974, υ(C- CL) 1037
1	Br S NH <sub>2</sub>	3414	-	1454	671	1616	υ(C-Br) aromatic 1064
2		3421	-	1462	709	1616	υ(C-CL) aromatic 1072
3	NO <sub>2</sub> NO <sub>2</sub> NH <sub>2</sub>	3448	-	1496	713	1631	υ(NO2) 1519
4	OCH <sub>3</sub> NH <sub>2</sub>	3406	-	1400	605	1712	υ(OCH3) 1091
5		3479	-	1473	694	1608	υ(NO2) 1500
6		3452	-	1400	624	1612	υ(C=O) 1639
7		3471	-	1450	725	1631	υ(C-NO2) 1500,υ(C- CL) 1122

Table 6: The FT-IR spectra data  $\mbox{cm}^{\cdot 1}\mbox{of}$  the prepared compounds (M-10)

8		3469	-	1450	690	1600	υ(C=O) 1678, υ(OH) 3549
9	O CH3	3471	-	1485	624	1666	υ(C=O) 1782
10		3448	-	1400	628	1624	v(OH) 3410

Table 7. The TT-IK spectra data chi of the prepared compounds (MT-MTO)									
Compd. No.	Compd. Structure	v(N-H)	υ(C-H) aromatic	υ(C=O)	v(C=N)	Others			
$M_1$	O <sup>N</sup> O <sup>N</sup> C <sup>-</sup> CH <sub>2</sub> -N-V <sub>3</sub> H	3414	3074	1616	1454	υ(C-Br) Aromatic 1068			
M <sub>2</sub>	CL $C = C = CH_2 - N$ CL CL CL CL CL CL	3360	3074	1616	1462	υ(C-CL) Aromatic 1072			
M <sub>3</sub>	NO <sub>2</sub> O=C-CH <sub>2</sub> -N-V H	3340	3039	1635	1566	υ(NO2) 1415			
$\mathbf{M}_4$		3421	3024	1620	1404	υ(OCH <sub>3</sub> ) 1404			
M5		3167	3039	1670	1442	υ(NO2) 1400			
$M_6$	$O$ $O$ $C$ $CH_2$ $O$ $CH_3$ $O$ $C$ $CH_3$ $O$	3028	3028	1701	1408	v(C=O) 1616			
M <sub>7</sub>		3367	3086	1697	1408	υ(NO2) 1408, υ(C-CL) Aromatic 1002			
$M_8$	$O^{\bullet}$ COOH $O^{\bullet}$ CH <sub>2</sub> -N-V-V-V-V-V-V-V-V-V-V-V-V-V-V-V-V-V-V-	3062	3062	1735	1516	υ(C=O) 1701, υ(OH) 3390			
M9	$\bigcap_{\substack{n=0-CH_2-N-K}}^{O} \bigcap_{\substack{n=0-CH_2-N-K}}^{N} \bigcap_{\substack{n=0-CH_2}}^{O} \bigcap_{\substack{n=0-CH_2}}^$	3224	3140	1700	1450	υ(C=O) 1666			
$\mathbf{M}_{10}$	O* C- CH <sub>2</sub> -N- H S OH	3118	3024	1620	1404	υ(OH) 3200			

## Table 7: The FT-IR spectra data cm<sup>-1</sup> of the prepared compounds (M1-M10)

Table 8: FTIR spectra data cm<sup>-1</sup> of the prepared compounds (11-20)

Compd. No.	Compounds structure	υ(N-H) amine	v(C=O)	υ(N-H)	v(C=N)	υ(C=C)	others
11	$C = N - NH - C - NH_2$	3421	1681	3309	1551	1527	υ(OH) 3259
12	$C = N - NH - C - NH_2$	3460	1689	3286	1647	1600	-
13	$CH_{3O} \xrightarrow{C = N - NH - C - NH_2} C$	3267	1685	3475	1612	1612	υ(OCH <sub>3</sub> ) 1346,1311
14	CH <sub>3</sub> O O CH <sub>3</sub> O C=N-NH-C-NH <sub>2</sub> CH <sub>3</sub> O OCH <sub>3</sub>	3476	1685	3286	1585	1508	v(OCH <sub>3</sub> ) 1384,1361,1303

15	$C = N - NH - C - NH_2$	3475	1685	3286	1585	1508	υ(OH) 3286
16	$C = N - NH - C - NH_2$	3464	1708	3278	1670	1593	υ(C-CL)Aromatic 1091
17	$CL \qquad O \qquad $	3552	1728	3468	1658	1593	υ(C-CL)Aromatic 1094
18	$CL \qquad O \\ C = N - NH - C - NH_2$	3458	1732	3244	1658	1600	υ(C-CL)Aromatic 1095
19	$ \begin{array}{c} Br & O \\ \parallel \\ C = N - NH - C - NH_2 \end{array} $	3488	1728	3305	1654	1600	υ(C-Br)Aromatic 1091
20	$ \begin{array}{c} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 $	3429	1681	3321	1612	1581	υ(N(CH <sub>3</sub> ) <sub>2</sub> ) 1438

 Table 9: The FT-IR spectra data cm<sup>-1</sup> of the prepared compounds (21-30)

Compd. No.	Compd. structure	υ(N-H) amine	υ(C=N)	v(C-O-C)	v(C=C)	Others
21		3421	1665	1211	1581	υ(OH) 3309
22		3417	1685	1211	1581	-
23	CH <sub>3</sub> O- CH <sub>3</sub> O- NH <sub>2</sub> NH <sub>2</sub>	3479	1689	1276	1612	υ(OCH <sub>3</sub> ) 1346,1311
24	CH <sub>3</sub> O- OCH <sub>3</sub> OCH <sub>3</sub> NH <sub>2</sub>	3475	1716	1219	1612	υ(OCH <sub>3</sub> ) 1381,1342
25	HO-NH2	3471	1681	1292	1597	υ(OH) 3255
26		3433	1670	1215	1643	υ(C-CL) 1180
27		3468	1728	1219	1658	υ(C-CL) 1099
28		3468	1732	1280	1658	υ(C-CL) 1099
29		3448	1654	1242	1570	υ(C-Br) 1028
30	H <sub>3</sub> C-N-N-N CH <sub>3</sub> C-N-N-N-NH <sub>2</sub>	2417	1678	1219	1577	υ(N(CH <sub>3</sub> ) <sub>2</sub> ) 1400

Compd.No.	Comp.srtucture	v(N-H)	v(C=O)	υ(C=N)	v(C-O-C)	Others
M <sub>21</sub>		3387	1681	1620	1141	υ(OH) 3332
M <sub>22</sub>	$\bigcap_{\substack{i=1\\i \in C^{-} CH_{2}-N_{H}^{-}H}}^{N-N}$	3340	1662	1604	1114	-
M <sub>23</sub>	$O$ $CH_{10}$ $CH_{10}$ $O$ $OCH_{3}$ $O$ $OCH_{3}$ $OC$	3479	1689	1612	1113	υ(OCH <sub>3</sub> ) 11346,1311
M <sub>24</sub>	O O O O $CH_{10}$ O O $CH_{10}$ O O O O $CH_{10}$ O O O O O O O O O O	3460	1685	1643	1157	υ(OCH <sub>3</sub> ) 1392,1361,1330

M <sub>25</sub>	$O = C - CH_2 - N - N - N - OH$	3475	1674	1608	1165	υ(OH) 3371
M <sub>26</sub>	$ \begin{array}{c}                                     $	3464	1708	1666	1141	υ(C-CL)aromatic 1037
M <sub>27</sub>	O $CL$ $O$ $O$ $O$ $CL$ $O$ $O$ $O$ $CL$ $O$	3150	1728	1658	1181	v(C-CL)aromatic 1049
M <sub>28</sub>	$\bigcup_{\substack{N = C - CH_2 - N}{H}}^{O} \bigcup_{\substack{N = N \\ O}}^{OL} \bigcup_{\substack{N \\ O}$	3468	1732	1658	1157	υ(C-CL) aromatic 1095
M <sub>29</sub>	$O = C - CH_2 - N - N$	3444	1662	1566	1176	υ(C-Br) aromatic 1014
M <sub>30</sub>	$ \begin{array}{c} \begin{array}{c} \begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \end{array} \end{array} \\ \begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \end{array} \\ \begin{array}{c} \\ \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \\ \\ \end{array} $	3398	1662	1608	1180	υ (N(CH3)2) 1458

Table 11: 1H-NMR spectral data	(onpm) for selected compounds
Table 11, 111-1 will specifial data	( ppm) for sciected compounds

Compd. No.	1H-NMR spectral data ( <sup>6</sup> ppm)			
M <sub>10</sub>	δ(1.4-2.4)(s,2H,CH2-N), δ(3.0-3.3)(s,2H,CH2-O), δ(7.1)(s,1H,NH), δ(7.2)(s,2H,CH2C=O), δ(7.3)(s,3H,aromatic)			
M <sub>25</sub>	δ(1.7-1.8)(s,2H,CH2-N), δ(3.3-3.4)(s,2H,CH2-O), δ(6.9)(s,1H,NH), δ (7.6)(s,2H,CH2C=O), δ(7.3-7.4)(s,3H,aromatic), δ(10.0-10.6)(s,1H,OH)			
M <sub>28</sub>	δ(1.1)(s,2H,CH2-N), δ(3.3)(s,2H,CH2-O), δ(6.5)(s,1H,NH), δ(8.1)(s,2H,CH2C=O), δ(7.3-7.4)(s,3H,aromatic)			

Table 12: Antibacterial activity data of morpholine derivatives

		Gram Positive			Gram negative		
Compd. No.	Compd. Structure.	Staphylococcus aureus			Escherichia coli		
		Conc. Of extract g/ml			Conc. Of extract g/ml		
		25	50	100	25	50	100
<b>M</b> <sub>2</sub>	O $CL$ $O$ $CL$ $O$ $CL$ $O$ $O$ $CL$ $O$ $O$ $CL$ $O$ $O$ $O$ $CL$ $O$ $O$ $O$ $CL$ $O$	17	29	19	15	13	18
$\mathbf{M}_7$	$O = C - CH_2 - H \leq CL$	17	31	32	16	17	20
M <sub>26</sub>	$ \begin{array}{c} O \\ \\ O \\ O \\ O \\ - \\ C \\ - \\ C \\ - \\ C \\ - \\ C \\ H \\ - \\ C \\ $	15	19	19	15	22	17

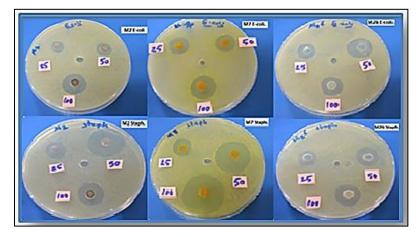
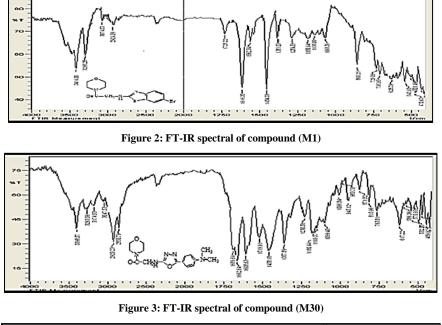


Figure 1: The effect on Staphylococcus aureus and E. coli



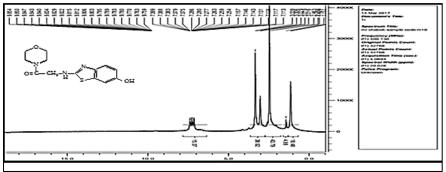


Figure 4: 1H-NMR spectral of compound (M10)

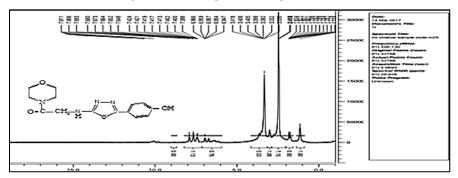


Figure 5: 1H-NMR spectral of compound (M25)

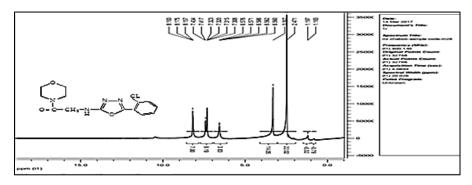


Figure 6: 1H-NMR Spectral of compound (M28)

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