



# SYNTHESIS OF SOME NEW HETEROCYCLIC COMPOUND DERIVATIVES FROM 2-CHLORO-3-FORMYL-1,8- NAPHTHYRIDINE

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**Keywords:** Novel heterocycles, 1,8-naphthyridine, 1,3,4-oxadiazole, 1,3,4-thiadiazole, 1,2,4-triazole, Vilsmeier-Haack.

2-Chloro-3-formyl-1,8-naphthyridine (**1**) has been synthesized in a Vilsmeier-Haack type reaction route. Starting from (**1**) a number of novel 1,8-naphthyridines were also synthesized. The structures of synthesized compounds were confirmed by their spectral and physical data. Some of the newly synthesized compounds exhibited antibacterial activity.

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## Introduction

1,8-Naphthyridine derivatives have attracted considerable attention as the 1,8-naphthyridine skeleton is present in many natural compounds show important biological activity.<sup>1,2</sup> For example, 2-amino-N-hydroxy-1,8-naphthyridine-3-carboxamide possesses herbicidal properties and used for selective control of weeds in barley, wheat, maize, sorghum and rice crops.<sup>3</sup> Some 3-phenyl-1,8-naphthyridine derivatives containing piperidyl, piperazinyl or morpholinyl group or an N-diethanolamine side chain show significant activity as inhibitors of human platelets aggregation induced by arachidonate and collagen.<sup>4</sup> Some 1,2,4-triazoles, 1,3,4-thiadiazoles and 1,3,4-oxadiazole derivatives have been attracting widespread attention due to their diverse pharmacological properties as anti-microbial, anti-inflammatory, analgesic and anti-tumor activities.<sup>5-8</sup>

It is well known that the hydrazone group plays an important role in the bioactivity of hydrazone derivatives, e.g. a large number of hydrazones possessed interesting antibacterial and antifungal,<sup>9,10</sup> antiinflammatory,<sup>11,12</sup> and antimalarial<sup>13</sup> properties. With aim of obtaining new hydrazone derivatives with a wide spectrum of pharmaceutical applications, we have investigated the synthesis of new hydrazone derivatives<sup>14,15,16</sup> and their transformation into a series of heterocyclic compounds as 1,3,4-oxadiazole, 1,2,4-triazole and 1,3,4-thiadiazole derivatives of 1,8-naphthyridine.

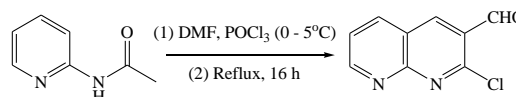
## EXPERIMENTAL

Melting points were recorded on electro-thermal CIA9300 melting point apparatus and are uncorrected, <sup>1</sup>H NMR spectra were recorded on a Bruker NMR spectrometer (300 MHz,

Bruker Co., Germany), using TMS as internal reference and DMSO-d<sub>6</sub> as solvent. IR spectra were recorded on a Bruker Tensor 27 spectrometer by using KBr discs.

### Synthesis of 2-chloro-3-formyl-1,8-naphthyridine (**1**)

To solution of (0.01 mol) of N-(pyridine-2-yl)acetamide (0.15 mol) in dry DMF, POCl<sub>3</sub> (0.06 mol) was added dropwise with stirring at 0-5 °C.<sup>17</sup> The reaction mixture was refluxed for about 16 h with stirring. The reaction mixture was poured into crushed ice and the precipitated solid was filtered, washed with excess of cold water, dried and recrystallized from ethanol (Scheme 1).



**Scheme 1.** Synthesis of 2-chloro-3-formyl-1,8-naphthyridine

### Synthesis of 2-chloro-3-methoxycarbonyl-1,8-naphthyridine (**2**)

To a solution of (**1**) (0.01 mol) in methanol (10 mL) were added N-iodosuccinimide (NIS) (0.025 mol) and potassium carbonate (0.025 mol).<sup>18</sup> The resultant dark mixture was stirred in dark for 4 h. The reaction mixture was then diluted with 5-6 mL of water. Sodium thiosulphate (0.5 g) was added to destroy any remaining NIS or hypoiodite species. The solid product was filtered, dried and recrystallized from ethanol.

### Synthesis of 2-chloro-1,8-naphthyridine-3-hydrazide (**3**)

To a solution of compound (**2**) (0.01 mol) in ethanol, hydrazine hydrate (6.5 mL) was added<sup>19</sup> and the reaction mixture was stirred for 10 h at a temperature below 100 °C. The solvent was evaporated to half under reduced pressure. The precipitate which separated on cooling was collected by filtration and then recrystallized from ethanol.

**Synthesis of 2-chloro-1,8-naphthyridine-3-thiosemicarbazide (4)**

To an EtOH solution of hydrazide (**3**) (0.01 mol), NH<sub>4</sub>SCN (2.28 g, 0.03 mol) and cc. hydrochloric acid (4 mL) was added and stirred for 8 h at a temperature below 100 °C.<sup>19</sup> The solvent was evaporated under reduced pressure and the residue was poured on crushed ice. The solid formed was filtered and recrystallized from EtOH.

**Synthesis of 2-chloro-3-[4-phenyl-1-acetyl thiosemicarbazide]-1,8-naphthyridine (5)**

To ethanolic solution of hydrazide (**3**) (0.01 mole) phenyl isothiocyanate (0.02 mol), and concentrated hydrochloric acid (2 mL) was added and stirred for 10 h at a temperature below 100 °C. The solvent was evaporated under reduced pressure and the residue poured on crushed ice with stirring. The solid formed was filtered and recrystallized from ethanol.

**Synthesis of 2-chloro-3-[5-(1,2,4-triazolo-3-thione)]-1,8-naphthyridine (6)**

To ethanolic solution of compound (**4**) (1.0 mmol), sodium hydroxide (0.056 g, 1.0 mmol) in 5 mL water was added and stirred for 6 h at 90 °C.<sup>19</sup> The solution was filtered and neutralized with dilute hydrochloric acid. The crystalline material was filtered off and recrystallized from ethanol.

**Synthesis of 2-chloro-3-[5-(2-amino-1,3,4-thiadiazolo)]-1,8-naphthyridine (7)**

To a stirred solution of compound (**4**) (1.0 mol) in ethanol (50 mL), concentrated sulfuric acid (6 mL) was added and refluxed for 6 h at 90 °C.<sup>19</sup> The solution was poured onto ice water, ammonia was added until it turns basic. A precipitate was obtained which was filtered and recrystallized from ethanol.

**Synthesis of 2-chloro-3-[5-(2-phenyl amino-1,3,4-thiadiazole)]-1,8-naphthyridine (8)**

To a stirred solution of compound (**5**) (1.0 mol) in ethanol (50 mL), concentrated sulfuric acid (6 mL) was added and refluxed for 6 h at 90 °C. The solution was poured onto ice water, ammonia was added until it turns basic. A precipitate was obtained which was filtered and recrystallized from ethanol.

**Synthesis of 2-chloro-3-[5-(4-phenyl-1,2,4-triazole-3-thione)]-1,8-naphthyridine (9)**

To ethanolic solution of compound (**5**) (0.01 mole), sodium hydroxide (0.056 g, 0.01 mole) in 5 mL water was added and stirred for 8 h at 90 °C. The resulting solution was acidified with 10% hydrochloric acid with cooling. The precipitate then filtered and recrystallized from ethanol.

**Synthesis of 2-chloro-3-[5-(2-phenyl amine-1,3,4-oxadiazole)]-1,8-naphthyridine (10)**

To solution of compound (**5**) (0.01 mol) in methanol (30 mL), mercuric oxide (2.4 g, 0.01 mol) was added then the mixture was refluxed for 8 h and filtered while the solution is hot. The solvent was evaporated to give solid product which was dried and recrystallized from ethanol.

**Synthesis of 2-chloro-N-formyl-1,8-naphthyridine-3-carbohydrazide (11)**

A mixture of acid hydrazide (**3**) (0.01 mol) and formic acid (0.246 g, 0.01 mol) in ethanol (20 mL) was refluxed for 6 h.<sup>13</sup> On cooling a solid appeared, which was filtered, dried and recrystallized from ethanol.

**Synthesis of N-benzylidene-2-chloro-1,8-naphthyridine-3-carbohydrazide (12)**

A mixture of acid hydrazide (**3**) (0.01 mol) and benzaldehyde (0.01 mol) in ethanol (20 mL) was refluxed for 6 h. The solvent was evaporated and the precipitate filtered and recrystallized from ethanol.

**Synthesis of 2-chloro-3-(1,3,4-oxadiazol-2-yl)-1,8-naphthyridine (13-14)**

To separate homogenous solutions of carbohydrazide (**11**) and (**12**) (0.01 mol) in glacial acetic acid, PbO<sub>2</sub> (2.34 g, 0.01 mole) was added the mixture then stirred at 25 °C for 4 h. The reaction mixture was diluted with ice-water and left to stand for 24 h. The precipitate was filtered, washed well with cold water and recrystallized from ethanol.

**Synthesis of 2-chloro-3-[5-(1,3,4-oxadiazolo-2-thione)]-1,8-naphthyridine (15)**

To ethanolic solution of hydrazide (**3**) (1.0 mmol), potassium hydroxide (0.056 g, 1.0 mmol) and carbon disulfide (2 mmol) was added. The mixture was heated under reflux until the evolution of hydrogen sulfide ceased.<sup>19</sup> The solvent was then removed, water was added and the solution was filtered off. The filtrate was acidified with diluted hydrochloric acid. The precipitate formed was collected, washed with water and recrystallized from ethanol.

Some physical properties and spectral data of compounds (**1**) – (**15**) are presented in Table 1 and 2.

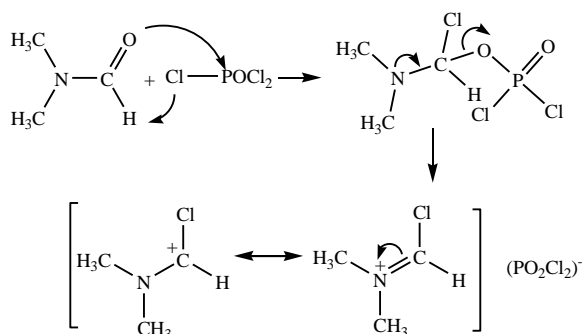
**RESULTS AND DISCUSSION**

Although many reaction routes have been developed for functionalized 1,8-naphthyridines,<sup>20,21,22</sup> the Vilsmeier approach is found to be the most efficient for achieving useful transformation and heteroannulations.

Thus in this communication we have reported the synthesis of 2-chloro-3-formyl-1,8-naphthyridine from the reaction of N-(pyridin-2-yl)acetamide with Vilsmeier reagent and transformation of 2-chloro- and 3-formyl groups into different functionalities.

The Vilsmeier cyclization of N-(pyridin-2-yl)acetamide was carried out by adding POCl<sub>3</sub> to the substrate in DMF at (0-5 °C) following by heating the mixture until 90°C to afford 2-chloro-3-formyl-1,8-naphthyridine. The mechanism of reaction is given in Scheme 2.

Structures of synthesized compounds were elucidated by mean of physical data (Table 1).



**Scheme 2.** The mechanism of Vilsmeier-Haack reaction.

The IR spectrum of compound (1) showed a sharp absorption at 1705 cm<sup>-1</sup> belongs to the aldehyde group and an absorption band at 2820 cm<sup>-1</sup> belongs to the aldehyde proton and an absorption band at 765 cm<sup>-1</sup> for C-Cl group. Its <sup>1</sup>H NMR spectrum shows a singlet at δ = 9.83 and 7.26 for aldehyde and C-H protons, respectively, two doublets at 8.49 and 7.48 for C-7 and C-5 protons and a triplet at δ 7.31 for C-6 proton.

The formyl group was first oxidized to an ester group. Among the various available methods,<sup>23</sup> the conversion of formyl group was made with using of N-iodosuccinimide(NIS)-K<sub>2</sub>CO<sub>3</sub> mixture in methanol at room temperature to afford the corresponding 2-chloro-3-methoxycarbonyl-1,8-naphthyridine (2) in good yield (Scheme 3). The IR spectra of the compound (2) showed a strong absorption band at 1732 cm<sup>-1</sup> belongs to the carbonyl group of the ester formed. The <sup>1</sup>H NMR spectrum of the compound showed a singlet at δ 4.3 and 7.92 for methoxy and C-4 hydrogens, respectively, two doublets at δ 7.42 and 8.38 for C-5 and C-7 protons and a triplet at δ 7.27 for C-6 proton.

The methyl ester (2) formed was treated with hydrazine hydrate in ethanol to give the corresponding acid hydrazide (3). The hydrazide group shows an absorption band at 3410 cm<sup>-1</sup> for N-H and at another at 1680 cm<sup>-1</sup> for C=O group .

**Table 1.** Physical and IR Spectral data of compounds (1) – (15).

Comp No.	M.p. °C	Yield %	Formula	C=O	C=N	NH	C=S	C-H (aromatic)	C-O-C	C-Cl
1	165-167	60	C <sub>9</sub> H <sub>5</sub> N <sub>2</sub> OCl	1705	1580	----	----	3085	----	765
2	96-98	65	C <sub>10</sub> H <sub>7</sub> N <sub>2</sub> O <sub>2</sub> Cl	1732	1618	----	----	3040	----	770
3	172-175	60	C <sub>9</sub> H <sub>7</sub> N <sub>4</sub> OCl	1680	1620	341	----	3035	----	775
4	235-238	65	C <sub>10</sub> H <sub>8</sub> N <sub>5</sub> OSC 1	1690	1585	325	1210	3083	----	768
5	252-254	60	C <sub>11</sub> H <sub>12</sub> N <sub>5</sub> OS Cl	1695	1575	338	1220	3066	----	775
6	256-259	55	C <sub>10</sub> H <sub>5</sub> N <sub>5</sub> S Cl	----	1587	----	1235	3045	----	780
7	246-249	55	C <sub>10</sub> H <sub>5</sub> N <sub>6</sub> S Cl	----	1595	342	----	3035	----	768
8	269-271	55	C <sub>16</sub> H <sub>10</sub> N <sub>5</sub> S Cl	----	1605	322	----	3056	----	780
9	252-254	60	C <sub>16</sub> H <sub>10</sub> N <sub>5</sub> S Cl	---	1529	328	1210	3085	----	775
10	273-275	55	C <sub>16</sub> H <sub>10</sub> N <sub>5</sub> Cl O	---	1605	338	----	3080	1210	778
11	221-223	60	C <sub>10</sub> H <sub>7</sub> N <sub>4</sub> Cl O <sub>2</sub>	1715, 1685	1585	338	----	3035	----	785
12	230-232	55	C <sub>16</sub> H <sub>11</sub> N <sub>4</sub> Cl O	1675	1605	332	----	3035	----	775
13	274-276	50	C <sub>10</sub> H <sub>4</sub> N <sub>4</sub> O Cl	----	1595	---	----	3055	1085	720
14	268-271	50	C <sub>16</sub> H <sub>9</sub> N <sub>4</sub> O Cl	---	1605	----	----	3035	1125	780
15	212-215	45	C <sub>10</sub> H <sub>5</sub> N <sub>4</sub> O S 1	----	1575	332	1225	3085	----	775

**Table 2.**  $^1\text{H}$  NMR data of compounds (1) – (15).

Comp. No.	$^1\text{H}$ NMR $\delta$ ppm, Solvent: DMSO- $d_6$
1	7.31(1H, t, C-6-H), 7.48(1H, d, C-5-H), 7.86(1H, s, C-4-H), 8.49(1H, d, C-7-H), 9.83(1H, s, CHO)
2	4.3(3H, s, OCH <sub>3</sub> ), 7.27-7.31(1H, t, C-6-H), 7.41-7.47(1H, d, C-5-H), 7.42(1H, s, C-4-H), 8.38-8.40(1H, d, C-7-H)
3	4.70(2H, s, NH <sub>2</sub> ), 7.33-7.35(1H, t, C-6-H), 7.45-7.47(1H, d, C-5-H), 8.01(1H, s, C-4-H), 8.42-8.44(1H, d, C-7-H), 9.95(1H, s, NH)
4	4.56-4.59(2H, s, NH <sub>2</sub> ), 7.56-7.59(1H, t, C-6-H), 7.83-7.86(1H, d, C-5-H), 8.01(1H, s, C-4-H), 8.56-8.59(1H, d, C-7-H), 8.96(1H, s, NH), 10.01(1H, s, NH)
5	7.25-7.32(5H, m, Ar-H), 7.58-7.60(1H, t, C-6-H), 7.84-7.85(1H, d, C-5-H), 7.94(1H, s, C-4-H), 8.59-8.61(1H, d, C-7-H), 8.84(1H, s, NH), 9.16(1H, s, NH), 10.56(1H, s, NH)
6	7.357.37(1H, t, C-6-H), 7.52-7.54(1H, d, C-5-H), 7.88(1H, s, C-4), 8.55-8.57(1H, d, C-7-H), 10.0 (1H, s, NH)
7	4.56(2H, s, NH <sub>2</sub> ), 7.33-7.35(1H, t, C-6-H), 7.48-7.51 (1H, d, C-5-H), 7.85(1H, s, C-4-H), 8.32-8.35(1H, d, C-7-H)
8	4.68(1H, s, NH), 7.11-7.32(5H, m, Ar-H), 7.36-7.37(1H, t, C-6-H), 7.51-7.53 (1H, d, C-5-H), 7.88(1H, s, C-4-H), 8.36-8.38(1H, d, C-7-H)
9	7.18-7.35(5H, m, Ar-H), 7.41-7.43(1H, t, C-6-H), 7.72-7.74(1H, d, C-5-H), 7.95(1H, s, C-4-H), 8.36-8.38(1H, d, C-7-H), 10.65 (1H, s, NH)
10	4.85(1H, s, NH), 7.21-7.31(5H, m, Ar-H), 7.30-7.33(1H, t, C-6-H), 7.44-7.46 (1H, d, C-5-H), 7.81(1H, s, C-4-H), 8.29-8.31(1H, d, C-7-H)
11	4.85(1H, s, NH), 7.12-7.21(5H, m, Ar-H), 7.30-7.33(1H, t, C-6-H), 7.44-7.46 (1H, d, C-5-H), 7.81(1H, s, C-4-H), 8.29-8.31(1H, d, C-7-H)
12	6.23-6.25(1H, m, =CH), 7.12-7.24(3H, m, Ar-H), 7.35-7.38(1H, t, C-6-H), 7.46-7.48(1H, d, C-5-H), 7.85(1H, s, C-4-H), 8.33-8.35(1H, d, C-7-H), 9.05(1H, s, NH)
13	7.31-7.33(1H, t, C-6-H), 7.39-7.41 (1H, d, C-5-H), 7.81(1H, s, C-4-H), 7.95(1H, s, heterocyclic proton), 8.28-8.30(1H, d, C-7-H)
14	7.11-7.23(5H, m, Ar-H), 7.31-7.33(1H, t, C-6-H), 7.49-7.51(1H, d, C-5-H), 7.86(1H, s, C-4-H), 8.42-8.44(1H, d, C-7-H)
15	7.29-7.31(1H, t, C-6-H), 7.46-7.48 (1H, d, C-5-H), 7.83(1H, s, C-4-H), 8.40-8.42(1H, d, C-7-H), 9.68 (1H, s, N-H)

The  $^1\text{H}$ NMR spectrum of compound (3) showed absorption a singlet at  $\delta$  9.70 for NH<sub>2</sub> proton and at  $\delta$  7.33, 7.45, 8.01 and 8.42 for C-6, C-5, C-4, C-7 proton respectively and at  $\delta$  9.95 for NH proton. The synthesis of compound 4 and 5 was performed by the reaction of compound (3) with ammonium thiocyanate for compound (4) or phenyl isocyanate for compound (5) (Scheme-3), and the products 4 and 5 were characterized by their physical and spectral data.

IR spectra of the compounds 4 and 5 showed NH stretching bands between 3380 and 3252  $\text{cm}^{-1}$  and absorption bands for C=O (1690 and 1695  $\text{cm}^{-1}$ ) and for C=S groups (1210 and 1220  $\text{cm}^{-1}$ ). In the  $^1\text{H}$ NMR spectra of the compounds 4 and 5 the NH proton absorptions are appeared as singlets at  $\delta$  8.85 and 10.56 ppm, respectively.

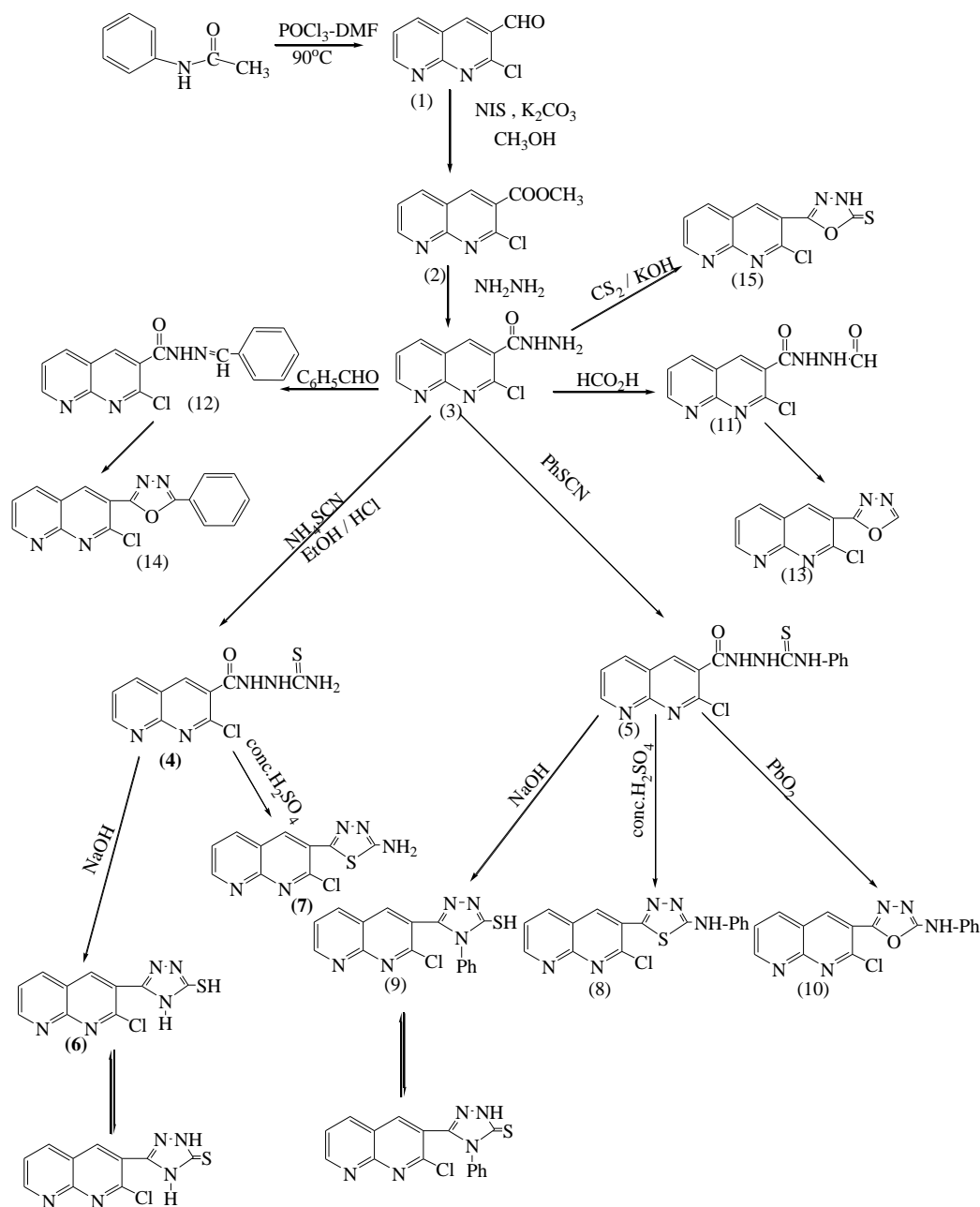
The intramolecular cyclization of compounds 4 and 5 (Scheme 3) was performed by alkaline treatment of these intermediates under reflux conditions. It is well known that in case of these type of compounds thion-mercapto tautomerism can be occurred (6 and 7) and the SH signal due to thiol form is a more defined singlet than the NH signal diarized from triplets observed.<sup>24,25</sup>

The  $^1\text{H}$ NMR spectra of the compounds 6 and 9 show the expected chemical shifts (Table 2). In the IR spectrum of 6 and 9 the stretching bands representing NH at 3314 and 3268  $\text{cm}^{-1}$  are appeared and the signals due to C=O group are absent. The cyclization of compounds 4 and 5 in acidic medium yielded the compounds 7 and 8. In the IR spectrum of compounds 7 and 8 the stretching bands due to NH at 3365 and 3215  $\text{cm}^{-1}$  are appeared and the signal due to C=O group are completely absent.

The  $^1\text{H}$ NMR spectra of compounds 5 and 10 contain the expected chemical shifts (Table 2). The thiosemicarbazide (5) was treated with mercuric oxide in methanol to give substituted 1,3,4-oxadiazole (10) derivative. The IR spectra of the compound 10 shows absorption bands at 3380  $\text{cm}^{-1}$ , 1605  $\text{cm}^{-1}$  and at 1210  $\text{cm}^{-1}$  for NH, C=N and C-O-C linkages, respectively. In order to perform the synthesis of monosubstituted oxadiazole, the acid hydrazide (3) was treated with formic acid to give 2-chloro-N-formyl-1,8-naphthyridine-3-carbohydrazide (11) which was transformed into substituted 1,3,4-oxadiazole (13) in a reaction with PbO<sub>2</sub> (Table 2). The compound 11 showed absorption bands at 1715  $\text{cm}^{-1}$  and 1653  $\text{cm}^{-1}$  for C=O and a band at 1585  $\text{cm}^{-1}$  for C=N group, furthermore two bands at 3380 and 3315  $\text{cm}^{-1}$  for NH and a band at 2815  $\text{cm}^{-1}$  for aldehyde group.

The  $^1\text{H}$  NMR spectrum of compound 11 showed singlet at  $\delta$  4.85 for NH and a group of signals at  $\delta$  7.21-7.29 belong to phenyl ring and a triplet signal  $\delta$  7.33 for C-6, two doublet signals at  $\delta$  7.46 and 8.31 for C-5 and C-7, respectively and a signal at  $\delta$  7.81 for C-4. Compound 11 was cyclized by PbO<sub>2</sub> to give 2-substituted-1,3,4-oxadiazole (13). The IR spectrum of the compound 13 showed absorption bands at 1595  $\text{cm}^{-1}$  for C=N and at 1085  $\text{cm}^{-1}$  for C-O-C groups.

The  $^1\text{H}$ NMR spectrum of the compound 13 contained the expected chemical shifts (Table 2). The acid hydrazide (3) was treated with benzaldehyde to give hydrazone (12). The IR spectrum of the compound 12 showed IR absorption bands at 1675  $\text{cm}^{-1}$  for C=O group and at 3325  $\text{cm}^{-1}$  for NH group.



**Scheme 3.** A flow chart of synthesis of compounds (1) – (15).

The  $^1\text{H}$  NMR spectrum of the compound **12** showed the NH signals at  $\delta 9.05$  as a singlet. The hydrazone **12** was then cyclized to 2,5-disubstituted-1,3,4-oxadiazole (**14**) by  $\text{PbO}_2$ .

The compound **14** showed IR absorption at  $1185\text{ cm}^{-1}$  for C-O-C and at  $1605\text{ cm}^{-1}$  for C=N groups. The  $^1\text{H}$  NMR of the compound **14** showed the expected chemical shifts (Table 2).

The base catalyzed cyclization of hydrazone (**3**) with carbon disulfide give 1,3,4-oxadiazole derivative (**15**) in good yield under reflux condition (Table 2). The IR and  $^1\text{H}$  NMR of these compound are listed in Table 1 and 2.

#### Biological activity.

The anti-microbial activity of compounds (**6**) – (**10**) and (**13**) – (**15**) were evaluated against *Escherichia Coli*, *Proteus Vulgaris*, *Staphylococcus Epidermidis* and *Staphylococcus Aureus*. The results (Table 3) showed that these compounds have a good anti-microbial activity against *S. Aureus* and *S. Epidermidis*. Ciprofloxacin (Cipro) and chloramphenicol (Camph) were used as control. The concentration of the new compounds was 10 mg/disk while that of Cipro and Camph dose were selected to be 5 mg/disk and 39 mg/disk respectively.

**Table 3.** Antibacterial activity data of compound (6-10,13-15).

No.	Zone of inhibition in mm			
	<i>S. Aureus</i>	<i>S. Epidermidis</i>	<i>E. Coli</i>	<i>P. Vulgaris</i>
6	26	24	12	10
7	23	22	11	10
8	19	17	13	9
9	21	12	13	12
10	23	21	16	11
13	18	19	14	15
14	15	14	15	14
15	18	22	13	10
Cipro	-	-	15	14
Camph	17	16	14	-

## CONCLUSION

In conclusion, we have developed a simple and efficient method for the synthesis of some new 1,8-naphthyridine derivatives and characterized them by spectral studies. The newly synthesized compounds (**6**, **7**, **8**, **9**, **10**, **13**, **14** and **15**) were evaluated for their antibacterial activities. The results obtained indicated that these compounds had a good activity against *Staphylococcus aureus* and *Staphylococcus epidermidis*.

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