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# Regioselective Synthesis of Novel [*N*-(4-Oxo-3-(2-phenyl-1,8-naphthyridin-3-yl)-thiazolidin-2-ylidene)]acetamide/benzamides and their Biological Activity

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In an attempt to discover the new antibacterial agents to fight the bacterial infections, a series of 1,8-naphthyridine based 2-iminothiazolidin-4-one derivatives was synthesized by a straight-forward regioselective synthesis. 2-Phenyl-1,8-naphthyridin-3-amine (**2**) was reacted with acetyl or aroyl isothiocyantes to give the corresponding *N*-[(2-phenyl-1,8-naphthyridin-3-yl)carbamothioyl)]acetamide or benzamides (**3a-e**). Finally, the target compounds [*N*-(4-oxo-3-(2-phenyl-1,8-naphthyridin-3-yl)thiazolidin-2-ylidene)]acetamide or benzamides (**4a-e**) were obtained by the reaction of thiourea (**3a-e**) with chloroacetyl chloride in presence of pyridine. All the synthesized products were formed in good yields and their structures were characterized by spectral (IR, EI-MS and NMR) and physical data. The biological activity of title compounds was evaluated against the bacterial strains and found to be more potent.

**Keywords: 1,8-Naphthyrdine, Aroyl thiourea, Aroyl isothiocyanate, Iminothiazolidin-4-one, Antibacterial activity.**

## INTRODUCTION

A large number of organo-sulphur compounds have been successfully utilized for the treatment of various diseases and also found in many natural and synthetic products. These are increasingly important with a broad range of applications in biological profiles. Therefore, many researchers have more concentrated to develop the sulphur-containing architectures and investigated their pharmacological properties.

Our current efforts are focused in identifying newer structural elements consisting of both 1,8-naphthyridine and 2-imino-thiazolidin-4-ones. The 1,8-naphthyridine scaffold is a centre of attention in all the nitrogen containing heterocycles due to their biological importance. The significant activities of these compounds have been reported such as antibacterial [1], anti-fungal and antitumor [2], antihypertensive [3], HIV-1 integrase mutant [4], antiplatelet [5], antidepressant [6], DNA stabilizing [7], antiallergic [8] activities, *etc*. Moreover, 2-iminothiazolidinone is a privileged moiety in five-membered heterocyclic system and its derivatives exhibited a large range of interesting bioactivities like antibiofilm [9], S1P1 receptor agonist [10], antithrombotic [11] antibacterial [12], anticancer [13] activities, *etc*.

The synthesis of 1,8-naphthyridine derivatives containing thiazolidin-4-one core is also reported in the literature [14]. In continuation of our studies, a 1,8-naphthyridine based acyl/aroyl thiourea intermediates (**3a-e**) from 2-phenyl-1,8-naphthyridin-3-amine (**2**) in appreciable yields is excuted. In next step, compounds **3a-e** underwent a regioselective reaction with chloroacetyl chloride in presence of a base to afford the highly functionalized [*N*-(4-oxo-3-(2-phenyl-1,8-naphthyridin-3-yl)thiazolidin-2-ylidene)]acetamide or benzamides (**4a-e**). The final compounds were assayed for their biological efficacy against the microorganisms.

## EXPERIMENTAL

All the reagents and solvents were obtained from the commercial sources. Melting points were reported by open end capillaries method and are uncorrected. The IR spectra were measured by employing the KBr pellets technique on a Shimadzu FT-IR instrument. NMR spectra were obtained on Bruker spectro-

meter at 300 MHz for $^1$H NMR, and 100 MHz for $^{13}$C NMR, where the solvent is DMSO-$d_6$ or $CDCl_3$. The chemical shifts are reported in δ ppm scale and TMS as reference. MS determinations were conducted by the ESI method on waters Alliance mass spectroscopic instrument. Elemental analyses were reported by using a Elementar Vario Micro Cube analyser. The reactions and purity were checked by TLC plates (silica gel 60F254, Merck) and the spots visualized under UV irradiation.

**General procedure for the synthesis of 2-phenyl-1,8-naphthyridin-3-amine (2):** A mixture of compound **1** (0.01 mol) and hydrazine monohydrate (0.011 mol) in EtOH (35 mL) was stirred under reflux until the completion of reaction. At the end of this period, the obtained solid was suspended in dilute HCl followed by refluxing again for 0.5 h, solution was cooled and filtered. The filtrate was basified (pH 8-9) with a solution of 4 N NaOH. The formed product was extracted twice by $CHCl_3$ and the organic layers were washed successively with brine and water. The dried extract was evaporated, and the collected crude was recrystallized from the mixture of EtOAc-EtOH (1:2) to furnish pure product **2** as yellow crystals.

**General procedure for the synthesis of *N*-[(2-phenyl-1,8-naphthyridin-3-yl)carbamothioyl]acetamide or *N*-[(2-phenyl-1,8-naphthyridin-3-yl)carbamothioyl]benzamides (3a-e):** Acetyl chloride or substituted benzoyl chloride (0.01 mol) was gradually added during 15 min to a stirred solution of KSCN (0.01 mol) in dry acetone (20 mL) at room temperature. The mixture was refluxed for 20 min, cool and followed by addition of 2-phenyl-1,8-naphthyridin-3-amine (**2**) (0.01 mol) in dry acetone (20 mL) along with stirring. The resulting mixture refluxed for 2-3 h (monitored by TLC) and poured onto an excess of cold water and stirred another 10 min. The formed product was extracted twice by chloroform. The dried organic extract was evaporated and recrystallized by the mixture of dichloromethane and ethanol (2:1) to furnish the desired products **3a-e**.

**Synthesis *N*-(4-oxo-3-(2-phenyl-1,8-naphthyridin-3-yl)thiazolidin-2-ylidene) acetamide or benzamides (4a-e):** To a suspension of compounds **3a-e** (0.01 mol) and pyridine (0.011 mol) in dry acetonitrile (10 mL) with constant stirring at 0 ºC and followed by dropwise addition of a solution of chloroacetyl chloride (0.011 mol) in dry acetonitrile (5 mL) under the nitrogen. Then, the reaction mixture was stirred at room temperature for 30 min and was refluxed for 4-5 h (TLC monitored). The content was concentrated to half of the volume and treated with ice-cold water. The resulting brown solid was filtered, dried and purified by using silica gel column chromatography (hexane-EtOAc, 7:3) (**Scheme-I**).

**Spectral data**

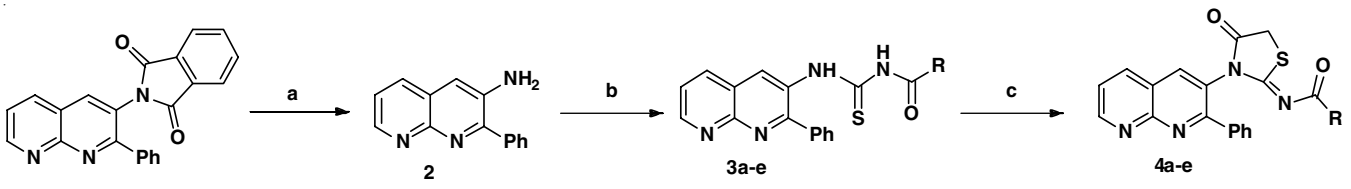
**2-Phenyl-1,8-naphthyridin-3-amine (2):** IR (KBr, $\nu_{max}$, $cm^{-1}$): 3462, 3298 ($NH_2$), 3186, 1616, 1544, 1429; $^1$H NMR (DMSO-$d_6$) δ ppm: 5.51 (s, 2H, -$NH_2$, $D_2O$ exchange), 7.40-7.43 (m, 2H), 7.49-7.58 (m, 3H), 7.79 (d, *J* = 7.0 Hz, 2H), 8.13-8.15 (dd, *J* = 8.1, 1.3 Hz, 1H), 8.70 (d, *J* = 2.3 Hz, 1H,); $^{13}$C NMR (DMSO-$d_6$) δ ppm: 114.71, 122.01, 123.62, 128.51, 128.81, 134.42, 138.18, 140.68, 148.33, 149.72, 152.03; MS (ESI) *m/z*: 222 $[M+H]^+$; Elemental analysis (%) found (calcd.): C 76.00 (76.03); H 5.01 (5.02); N 18.99 (19.03).

***N*-[(2-Phenyl-1,8-naphthyridin-3-yl)carbamothioyl]-acetamide (3a):** IR (KBr, $\nu_{max}$, $cm^{-1}$): 3225 (NH), 3009, 1692 (carbonyl), 1531 1243; $^1$H NMR (DMSO-$d_6$) δ ppm: 2.11 (s, 3H), 7.48-7.51 (m, 3H), 7.66-7.69 (dd, 1H, *J* = 8.1, 4.2 Hz), 7.74-7.76 (m, 2H), 8.53-8.56 (dd, 1H, *J* = 8.2, 2.0 Hz), 8.70 (s, 1H), 9.13 (s, 1H), 11.53 (s, 1H, NH), 12.34 (s, 1H, NH); $^{13}$C NMR (DMSO-$d_6$) δ ppm: 23.51, 121.02, 122.75, 123.81, 128.63, 128.89, 133.98, 136.84, 137.00, 153.84, 158.37, 167.49 (C=O), 177.84 (C=S); MS (ESI) *m/z*: 323 $[M+H]^+$. Elemental analysis (%) found (calcd.): C 63.33 (63.38); H 4.38 (4.39); N 17.38 (17.41); O 4.96 (4.99); S 9.95 (9.97).

***N*-[(2-phenyl-1,8-naphthyridin-3-yl)carbamothioyl]-benzamide (3b):** IR (KBr, $\nu_{max}$, $cm^{-1}$): 3136(NH), 3061, 3003, 1658 (carbonyl), 1537, 1269; $^1$H NMR ($CDCl_3$) δ ppm: 7.50-7.55 (m, 6H), 7.63-7.67 (t, *J* = 7.44 Hz, 1H), 7.81-7.85 (m, 4H), 8.27-8.30 (dd, *J* = 8.14, 1.78 Hz, 1H), 9.14-9.16 (dd, *J* = 5.23, 2.88 Hz, 2H), 9.24 (s, 1H, NH), 12.68 (s, 1H, NH); $^{13}$C NMR ($CDCl_3$) δ ppm: 121.53, 122.50, 127.60, 128.01, 128.40, 128.51, 128.59, 129.19, 129.46, 129.68, 130.03, 130.68, 131.22, 133.51, 133.90, 136.71, 137.00, 153.98, 155.21, 158.48, 166.60 (C=O), 179.40 (C=S). MS (ESI) *m/z*: 385 $[M+H]^+$. Elemental analysis (%) found (calcd.): C 68.73 (68.77); H 4.19 (4.22); N 14.57 (14.58); O 4.16 (4.19); S 8.34 (8.37).

2-Chloro-*N*-((2-phenyl-1,8-naphthyridin-3-yl)carbamothioyl)benzamide (3c): IR (KBr, $\nu_{max}$, $cm^{-1}$): 3284 (NH), 3085, 1660 (carbonyl), 1544, 1262; $^1$H NMR (DMSO-$d_6$): δ ppm: 7.49-7.58 (m, 5H), 7.65-7.82 (m, 5H), 8.34-8.37 (dd, *J* = 8.07, 1.65 Hz, 1H), 9.10-9.12 (dd, *J* = 4.83, 1.92 Hz, 2H), 9.23 (s, 1H, NH), 12.60 (s, 1H, NH); $^{13}$C NMR (DMSO-$d_6$) δ ppm: 121.58, 125.32, 127.15, 128.37, 128.40, 128.83, 128.91, 129.28, 129.74, 130.51, 130.68, 132.14, 134.66, 136.37, 139.04, 143.23, 151.81, 155.35, 157.18, 166.74 (C=O), 178.28 (C=S); MS (ESI) *m/z*: 419 $[M+H]^+$. Elemental analysis (%) found (calcd.): C 63.08 (63.11); H 3.61 (3.62); Cl 8.46 (8.50); N 13.37 (13.38); O 3.82 (3.84); S 7.65 (7.69).

***N*-(4-Oxo-3-(2-phenyl-1,8-naphthyridin-3-yl)thiazolidin-2-ylidene)acetamide (4a):** IR (KBr, $\nu_{max}$, $cm^{-1}$): 3059 (ring




**Reagents and conditions:** (a) $N_2H_4.H_2O$/ethanol, reflux (b) KSCN/RCOCl, acetone, reflux (c) Chloroacetyl chloride, Py, ACN, Reflux; **3a-e** and **4a-e**: R = methyl, phenyl,2-chlorophenyl, 4-nitrophenyl, 4-methoxyphenyl

**Scheme-I:** Regioselective synthesis of compounds **4a-e**

$CH_2$), 1732 (carbonyl), 1644 (carbonyl), 1520 (C=N), 1165 (C-S); $^1$H NMR (DMSO-$d_6$) δ ppm: 2.14 (s, 3H), 3.75-3.94 (dd, *J* = 56.88, 18.45 Hz, 2H, $CH_2$), 7.45-7.50 (m, 3H), 7.66-7.76 (m, 3H), 8.49-8.52 (dd, *J* = 8.17, 2.03 Hz, 2H), 9.13-9.15 (d, *J* = 8.17 Hz, 1H ); $^{13}$CNMR (DMSO-$d_6$) δ ppm: 23.51, 33.25, 121.22, 122.81, 123.59, 128.74, 128.68, 133.05, 135.77, 137.12, 148.61, 153.47, 156.29, 167.60 (C=O), 170.85 (C=O); MS (ESI) *m/z*: 363 $[M+H]^+$. Elemental analysis (%) found (calcd.): C 62.97 (63.00); H 3.89 (3.94); N 15.46 (15.49); O 8.83 (8.86); S 8.85 (8.89).

***N*-[4-Oxo-3-(2-phenyl-1,8-naphthyridin-3-yl)thiazolidin-2-ylidene]benzamide (4b):** IR (KBr, $\nu_{max}$, $cm^{-1}$): 3059 (ring $CH_2$), 1732 (carbonyl), 1644 (carbonyl), 1514 (C=N), 1168 (C-S); $^1$H NMR (DMSO-$d_6$) δ ppm: 3.75-3.94 (dd, *J* = 56.88, 18.45 Hz, 2H, $CH_2$), 7.31-7.38 (m, 5H), 7.47-7.54 (m, 3H), 7.80-7.92 (m, 3H), 8.29-8.34 (dd, *J* = 12.96, 6.41 Hz, 2H), 9.15-9.17 (d, *J* = 8.17 Hz, 1H); $^{13}$CNMR (DMSO-$d_6$) δ ppm: 33.23, 121.15, 122.39, 125.62, 127.57, 128.41, 128.73, 128.81, 128.99, 129.34, 129.46, 129.68, 131.18, 133.67, 135.21, 137.43, 148.38, 151.53, 154.72, 156.14, 167.61 (C=O), 170.88 (C=O). MS (ESI) *m/z*: 425 $[M+H]^+$. Elemental analysis (%) found (calcd.): C 67.91 (67.96); H 3.80 (3.83); N 13.20 (13.21); O 7.54 (7.58); S 7.55 (7.59).

**2-Chloro-*N*-(4-oxo-3-(2-phenyl-1,8-naphthyridin-3-yl)thiazolidin-2-ylidene)benzamide (4c):** IR (KBr, $\nu_{max}$, $cm^{-1}$): 3064 (ring $CH_2$), 1735 (carbonyl), 1649 (carbonyl), 1518 (C=N), 1162 (C-S); $^1$H NMR (DMSO-$d_6$) δ ppm: 3.79-3.98 (dd, *J* = 56.88, 18.45 Hz, 2H, $CH_2$), 7.35-7.61 (m, 7H), 7.70-7.91 (m, 3H), 8.24-8.29 (dd, *J* = 12.87, 6.31 Hz, 2H), 9.11-9.13 (d, *J* = 8.15 Hz, 1H); $^{13}$CNMR (DMSO-$d_6$) δ ppm: 33.16, 121.35, 122.25, 124.89, 127.45, 128.12, 128.64, 128.90, 129.07, 129.37, 129.81, 129.93, 131.59, 133.35, 135.47, 137.61, 148.49, 150.82, 153.48, 155.10, 158.23, 167.60 (C=O), 170.85 (C=O). MS (ESI) *m/z*: 459 $[M+H]^+$. Elemental analysis (%) found (calcd.): C 62.81 (62.85); H 3.29 (3.31); Cl 7.73 (7.76); N 12.21 (12.25); O 6.97 (7.00); S 6.99 (7.02).

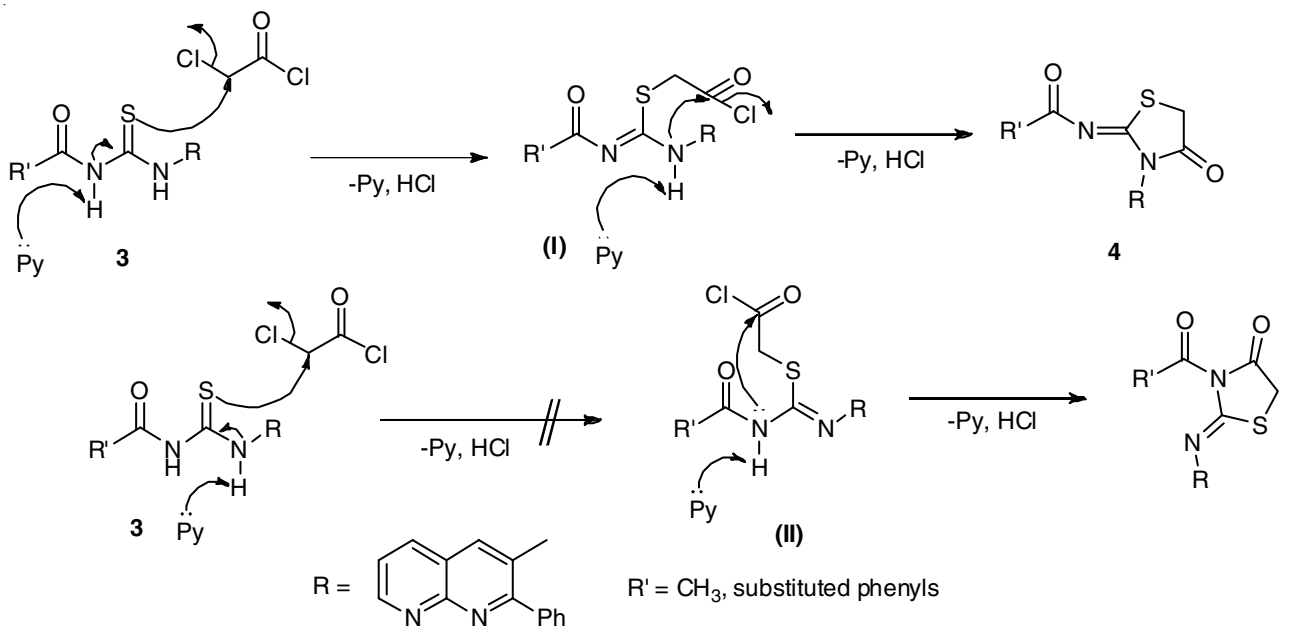
## RESULTS AND DISCUSSION

A reaction of 2-(2-phenyl-1,8-naphthyridin-3-yl)isoindoline-1,3-dione (**1**) with hydrazine monohydrate in alcohol to give 2-phenyl-1,8-naphthyridin-3-amine (**2**). The intermediates of *N*-[4-oxo-3-(2-phenyl-1,8-naphthyridin-3-yl)thiazolidin-2-ylidene]acetamide or benzamides (**3a-e**) were obtained by the reaction of compound **2** with acid chlorides and potassium thiocyanate in anhydrous acetone. It is found that compounds **3a-e** can react with chloroacetyl chloride or ethyl chloroacetate in presence of base under reflux to give the regioselective product *N*-[4-oxo-3-(2-phenyl-1,8-naphthyridin-3-yl)thiazolidin-2-ylidene]acetamide or benzamides (**4a-e**) in high yield. In the final step, the optimized reaction conditions were described under the varying solvent, base, model reagents and compound **3b** was chosen as the model compound (Table-1). In our preliminary observations based on the formation of compound **4b**, triethylamine and potassium carbonate bases (entry 5, 6, 7) gave poor results. The solvents DMF, ethanol and dioxane (entry 1, 3, 4) were also provided low yields. Thus, the model reaction was carried out at refluxing acetonitrile in presence of pyridine (entry 2), leading to the cyclized product (**4b**) in

TABLE-1
OPTIMIZED REACTION CONDITIONS FOR THE SYNTHESIS OF **4a-e**

| Entry | Solvent | Reagent* | Base | Reflux time (h) | Yield (%)[a] |
|---|---|---|---|---|---|
| 1 | EtOH | A/B | Py | 8-9 | traces[b] |
| 2 | ACN | A/B | Py | 4 | 71 |
| 3 | DMF | A | Py | 4 | 49 |
| 4 | Dioxane | A | Py | 8 | 35 |
| 5 | ACN | A | TEA | 3 | 44 |
| 6 | DMF | A | TEA | 3 | 31 |
| 7 | DMF | A | $K_2CO_3$ | 6 | traces[b] |

A = Chloroacetyl chloride B = Ethyl chloroacetate; [a]Isolated yields, [b]Reaction was not completed; Reaction conditions: Compound **3b** (1 eq.), A or B (1.1 eq), base (1.1 eq) and solvent (15 mL).




**Scheme-II:** Probable mechanism for the formation of compound **4** series

good yields. Consequently, the best reaction conditions were optimized in acetonitrile and the using pyridine as base at refluxing temperature. The titled products (**4a-e**) were produced by initially, *S*-alkylation followed by cyclization with $N^1$ or $N^2$ and the plausible mechanism is described in **Scheme-II**. The physico-chemical data of the synthesized compounds (**2**, **3a-e** and **4a-e**) are depicted in Table-2. All the synthetic products were identified in this study by physical, spectral, analytical data, which are in good agreement with the assigned structures.

TABLE-2
PHYSICO-CHEMICAL DATA OF COMPOUNDS **2-4**

| Entry | Compd. | R | m.f. | m.p. (°C) | Yield (%)[a] |
|---|---|---|---|---|---|
| 1 | **2** | – | $C_{14}H_{11}N_3$ | 238-240 | 62 |
| 2 | **3a** | Methyl | $C_{17}H_{14}N_4OS$ | 216-218 | 83 |
| 3 | **3b** | Phenyl | $C_{22}H_{16}N_4OS$ | 203-205 | 84 |
| 4 | **3c** | 2-Chlorophenyl | $C_{22}H_{15}ClN_4OS$ | 252-254 | 80 |
| 5 | **3d** | 4-Nitrophenyl | $C_{22}H_{15}N_5O_3S$ | 197-199 | 77 |
| 6 | **3e** | 4-Methoxyphenyl | $C_{23}H_{18}N_4O_2S$ | 224-226 | 79 |
| 7 | **4a** | Methyl | $C_{19}H_{14}N_4O_2S$ | 190-192 | 65 |
| 8 | **4b** | Phenyl | $C_{24}H_{16}N_4O_2S$ | 185-187 | 73 |
| 9 | **4c** | 2-Chlorophenyl | $C_{24}H_{15}ClN_4O_2S$ | 230-232 | 71 |
| 10 | **4d** | 4-Nitrophenyl | $C_{24}H_{15}N_5O_4S$ | 241-243 | 68 |
| 11 | **4e** | 4-Methoxyphenyl | $C_{25}H_{18}N_4O_3S$ | 208-210 | 62 |

[a]Isolated yields after purification.

IR spectra frequencies obtained at 3298-3205 $cm^{-1}$ indicated the appearance of amine function (-$NH_2$) in compound **2**. The characteristic bands for amine (NH), carbonyl (C=O) and thiocarbonyl (C=S) in aroyl/acoylthioureas (**3a-e**) were found at the region of 3225-3300, 1692-1658 and 1265-1242 $cm^{-1}$, respectively. The lack of NH frequencies and the appearance of additional C=O and C=N bands for 2-iminothizolidn-4-one (**4a-e**) were observed at 1735-1732 and 1520-1514 $cm^{-1}$, respectively.

In $^1$H NMR spectra, compound **2** displayed a peak of 5.51 ppm as singlet and confirmed for the amine function (-$NH_2$) with $D_2O$ exchange. The characteristic singlets for NH (1) and NH (2) functions were appeared at around 9.24-11.53 and 12.60-12.68 ppm in compounds **3a-e** and $^{13}$C NMR of compounds **3a-e** was showed most deshielded thiocarbonyl (C=S) at about 177.84-179.40 ppm and carbonyl carbon (C=O) resonated at around 166.60-167.49 ppm, respectively. It was evidently indicated that the formation of acyl or aroyl thiourea core in compounds **3a-e**.

The methylene protons (ring -$CH_2$-) of compounds 4a-e was observed as a doublet of doublet at the region of 3.75-3.98 ppm in $^1$H NMR due to deshielded by the adjacent sulphur atom and carbonyl function. In $^{13}$C NMR, the methylene and carbonyl carbon signals of compounds **4a-e** were displayed at 33.16-33.25 ppm and 167.60-170.88 ppm region, respectively. The aromatic protons in all the compounds were found at the region 7.31-9.17 ppm in $^1$H NMR, which was assigned to the peaks of phenyl and 1,8-naphthyridine system. In $^{13}$C NMR, the other carbon signals appeared in their expected region.

In mass spectra, all the compounds furnish the corresponding $[M+1]^+$ peaks, which were matched with the calculated molecular weight. In addition, 2-imino-thiazolidin-4-one derivatives **4a-e** were investigated for their antibacterial activity and showed remarkable results.

The mechanism involves the sulphur attack to α-carbon of chloroacetyl chloride to generate an acyclic intermediate I or II (**Scheme-II**) followed by cyclization of carbonyl with nitrogen (1 or 2) to afford the products **4a-e**. In this case, regioselectivity was played a key role in product formation, but only one regioisomer has been formed under the present reaction conditions. The formation of -CO-$CH_2$-S- linkage in acyclic intermediate-I is supported by the spectral data. The $^1$H NMR spectra results found that the signal disappearance of NH-1 at 12.40 ppm, whereas the 9.0 ppm signal of NH-2 was intact and a new peak was also displayed at 4.05 ppm for methylene group in intermediate-I. Consequently, predominant product was obtained from an intermediate I over II, also supported by the available literature [15,16]. Finally, all the compounds **4a-e** were obtained as a single regioisomer from compounds **3a-e**.

**Biological evaluation:** Antibacterial activity of the final analogues **4a-e** was screened against the several bacteria such as *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Psuedomonas auroginosa* by cup plate agar diffusion method [17]. The test results were compared with reference drug ampicilin and using DMSO as control. The compounds were evaluated at a concentration of 50 μg/mL stock solution in DMSO. The minimum inhibition zone was measured in mm and the bioassay results are summarized in Table-3. The preliminary results of antibacterial activity indicated that compound **4c** was most potent and **4a** was exhibited least activity as comparable to ampicillin, and the remaining compounds showed moderate activity against the bacterial strains.

TABLE-3
ANTIBACTERIAL ACTIVITY OF THE SYNTHETIC COMPOUNDS **4a-e**

| Entry | Microorganism inhibition zone (mm) | | | |
|---|---|---|---|---|
| | Gram-positive bacteria | | Gram-negative bacteria | |
| | *S. aureus* | *B. subtilis* | *E. coli* | *P. aeruginosa* |
| **4a** | 10 | 05 | 14 | 02 |
| **4b** | 25 | 10 | 27 | 08 |
| **4c** | 27 | 14 | 32 | 11 |
| **4d** | 22 | 09 | 21 | 05 |
| **4e** | 10 | 05 | 25 | 08 |
| Ampicillin (std.) | 30 | 12 | 30 | 10 |

## Conclusion

In this work, 2-phenyl-1,8-naphthyridin-3-amine was efficiently prepared and converted into various acyl or aroyl thiourea derivatives (**3a-e**) bearing 1,8-naphthyridine skeleton. A series of [*N*-(4-oxo-3-(2-phenyl-1,8-naphthyridin-3-yl)thiazolidin-2-ylidene]acetamide or benzamides (**4a-e**) were prepared by the cyclization of **3a-e** with chloroacetyl chloride in the presence of pyridine in good yields. The new synthetic products were successfully characterized and their biological results exhibited that most of the 1,8-naphthyridine derivatives have shown significant antibacterial activity against the microorganisms.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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