

# Efficient Synthesis and Antimicrobial Activity of 2-Pyridyl-4-thiazolidinones from 2-Chloro Nicotinaldehydes

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**ABSTRACT:** Several new 2-pyridyl-4-thiazolidinones are synthesized in an efficient manner evading using any catalyst or base. Simple workup procedure, good yields, and mild reaction conditions are the salient features of this method. All the synthesized compounds are screened for antimicrobial activity against several organisms.

**KEYWORDS:** 2-chloro nicotinaldehyde; Catalyst-free reaction; Thiazolidinone; Antimicrobial activity.

## INTRODUCTION

Pyridine and its analogs have great importance in the field of heterocycles since they entice much attention because of their great practical efficacy, especially, due to their various biological properties [1]. In addition, many pyridines are reported in the literature as herbicides, fungicides, bactericides, insecticides, and pharmaceuticals [2]. Thiazolidinones and correlated motifs have exhibited high biological activity and are present in natural products and pharmaceutical compounds. These are also

considered to be valuable with assorted biological activities in the areas of medicine and agriculture [3-5].

4-Thiazolidinone derivatives have been shown to possess antibacterial [6-9], antifungal [10], anticonvulsant [11,12], anticancer [13,14], antituberculosis [15-17], antitumor [18], antiparasitic [19], anti-inflammatory [20], analgesic [21], antipsychotic [22] and herbicidal [23] properties. These have also been reported to inhibit the bacterial enzyme Mur-B, a precursor in the biosynthesis

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of peptidoglycon [24], a non-nucleoside inhibitor of HIV-RT [25,26]. Furthermore, compounds MKT 077 and HP-236 have been registered as antitumor (Phase-I Clinical Trials) and antipsychotic agents. It has also been found that thiazolidinone derivative CP-060 and its analogues are used for the treatment of diabetes [27]. Furthermore, 1,3-thiazolidin-4-ones are interesting heterocyclic compounds in pharmaceutical chemistry. The most important synthetic route to 1,3-thiazolidin-4-ones involves three components (an aldehyde, an amine, and mercaptoacetic acid), either in a one- or a two-step process [28]. The reactions proceed by initial formation of an imine, which undergoes attack by the sulfur nucleophile, followed by intramolecular cyclization on elimination of water. The most common protocol to remove the water is by azeotropic distillation [29], but use of chemical drying agents (scavengers) such as DCC [30],  $ZnCl_2$  [31], sodium sulphate [32], etc. and use of microwave heating [33,34], solid phase [35] and polymer supported [36] systems has also been demonstrated. Motivated by these findings, and in continuation of our work with nitrogen containing heterocycles [37,38], herein we report the facile synthesis and antimicrobial activity of various 2-pyridyl thiazolidinones. In the present study, two 2-chloro nicotinaldehydes (**1a,b**) are used as active substrates which were developed in our laboratory [39]. The condensation reaction proceeded smoothly under mild conditions, upon treatment of various anilines and mercaptoacetic acid to yield 2-pyridyl thiazolidinone derivatives.

## EXPERIMENTAL SECTION

All reactions involving air-sensitive reagents were performed under a nitrogen atmosphere. Solvents were freshly dried and purified by conventional methods prior to use. The progress of all the reactions was monitored by TLC, using TLC aluminium sheets precoated with silica gel 60 F254 to a thickness of 0.25 mm (Merck). Flash column chromatography was done using silica gel (Merck, 60-120 mesh). Melting points were determined on a MEL-TEMP II melting point apparatus and were uncorrected. IR spectra were recorded on a Perkin-Elmer FT-IR spectrophotometer.  $^1H$  and  $^{13}C$  NMR spectra were recorded on a Varian Gemini 200 MHz, Bruker Avance 300 MHz spectrometer, TMS was used as an internal standard and  $CDCl_3/DMSO-d_6$  are used as solvents. Mass spectra were recorded on VG Micromass 7070 H (EI), QSTAR XL High Resolution Mass Spectrometer (HRMS), Thermofinnigan ESI ion trap Mass Spectrometer and

a GC-MS system on an Agilent 6890 series. 2-chloro nicotinaldehydes were effectively prepared and compared with the literature data [39, 40].

### General procedure for the synthesis of 2-pyridyl thiazolidinones (2a-j):

In a 25 mL round bottom flask, aniline (1 mmol), mercapto acetic acid (1.2 mmol), and 2-chloro nicotinaldehyde (**1a/1b**) (1 mmol) were added successively under stirring and refluxed in 1,2-dichloroethane (3 mL) for 10-12 h. After completion of the reaction as indicated by TLC, the reaction mixture was washed with a saturated solution of sodium hydrogen carbonate ( $2 \times 5$  mL). The reaction mixture was extracted with dichloromethane, dried ( $Na_2SO_4$ ), concentrated under reduced pressure and the residue was purified by column chromatography on silica gel using ethyl acetate:hexane (3:7) as eluent to afford pure compounds.

### 2-(2-Chloro-5-phenyl-3-pyridyl)-3-phenyl-1,3-thiazolidin-4-one (2a)

Yield: 80%, Yellowish solid, mp 96-98 °C. IR (KBr):  $\nu_{max}$  = 3012, 2925, 2855, 1692, 1376, 1225, 1077, 757, 695  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  = 3.87 (m, 2H,  $CH_2$ ), 6.58 (s, 1H, CH), 7.16-7.5 (m, 10H, Ar), 7.78 (d,  $J$  = 2.26 Hz 1H, Ar), 8.48 (d,  $J$  = 2.26 Hz 1H, Ar).  $^{13}C$  NMR (75 MHz,  $DMSO-d_6$ ):  $\delta$  = 32.9, 61.2, 120.0, 124.2, 127.0, 127.2, 128.8, 129.2, 129.4, 133.6, 134.3, 135.6, 136.5, 147.5, 170.9; ESI-MS:  $m/z$  367  $[M+H]^+$ . HRMS (ESI):  $m/z$  calcd for  $C_{20}H_{15}N_2ONaSCl$ :  $[M+Na]^+$  389.0491, found: 389.0498; Anal. Calcd. for  $C_{20}H_{15}ClN_2OS$ : C 65.48; H 4.12; N 7.64. Found: C 65.38; H 4.32; N 7.72.

### 2-(2-Chloro-5-phenyl-3-pyridyl)-3-(4-fluorophenyl)-1,3-thiazolidin-4-one (2b)

Yield: 82%, Yellowish solid; mp 118-120 °C. IR (KBr):  $\nu_{max}$  = 3059, 2926, 1693, 1508, 1433, 1228, 1077, 831, 761, 697  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  = 3.80 (m, 2H,  $CH_2$ ), 6.51 (s, 1H, CH), 7.04 (t,  $J$  = 8.31 Hz 2H, Ar), 7.28-7.32 (m, 2H, Ar), 7.36-7.47 (m, 5H, Ar), 7.73 (d,  $J$  = 2.26 Hz 1H, Ar), 8.48 (d,  $J$  = 2.26 Hz 1H, Ar).  $^{13}C$  NMR (75 MHz,  $DMSO-d_6$ ):  $\delta$  = 32.0, 60.2, 115.1, 115.4, 125.8, 125.9, 126.0, 127.8, 128.3, 132.0, 132.1, 132.3, 134.2, 134.4, 135.4, 146.6, 146.9, 158.1, 161.4, 169.9. ESI-MS:  $m/z$  385  $[M+H]^+$ . HRMS (ESI):  $m/z$  calcd for  $C_{20}H_{15}N_2OFSCl$ :  $[M+H]^+$  385.0577, found: 385.0573; Anal. Calcd. for  $C_{20}H_{14}ClFN_2OS$ : C 62.42; H 3.67; N 7.28. Found: C 62.51; H 3.62; N 7.23.

**2-(2-Chloro-5-phenyl-3-pyridyl)-3-(4-chlorophenyl)-1,3-thiazolidin-4-one (2c)**

Yield: 77%, Yellowish solid; mp 128-130 °C. IR (KBr):  $\nu_{\max}$  = 3061, 2923, 1698, 1542, 1492, 1377, 1283, 1090, 763  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 3.81 (m, 2H,  $\text{CH}_2$ ), 6.53 (s, 1H, CH), 7.11 (t,  $J$  = 9.1 Hz 2H, Ar), 7.39-7.48 (m, 5H, Ar), 7.65 (d,  $J$  = 8.31 Hz 2H, Ar), 7.71 (d,  $J$  = 2.26 Hz 1H, Ar), 8.51 (d,  $J$  = 2.26 Hz 1H, Ar).  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  = 32.9, 61.1, 121.2, 125.3, 127.0, 128.9, 129.3, 129.5, 132.7, 133.2, 134.4, 135.4, 136.7, 147.7, 171.0. ESI-MS:  $m/z$  401  $[\text{M}+\text{H}]^+$ . HRMS (ESI):  $m/z$  calcd for  $\text{C}_{20}\text{H}_{15}\text{N}_2\text{OSCl}_2$ :  $[\text{M}+\text{H}]^+$  401.0282, found: 401.0267; Anal. Calcd. for  $\text{C}_{20}\text{H}_{14}\text{Cl}_2\text{N}_2\text{OS}$ : C 59.86; H 3.52; N 6.98. Found: C 59.94; H 3.71; N 6.88.

**2-(2-Chloro-5-phenyl-3-pyridyl)-3-(4-bromophenyl)-1,3-thiazolidin-4-one (2d)**

Yield: 75%, Yellowish solid; mp 130-132 °C. IR (KBr):  $\nu_{\max}$  = 3060, 2924, 1700, 1489, 1370, 1233, 1074, 759, 697  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 3.82 (m, 2H,  $\text{CH}_2$ ), 6.54 (s, 1H, CH), 7.23 (d,  $J$  = 9.1 Hz 2H, Ar), 7.41-7.52 (m, 7H, Ar) 7.73 (d,  $J$  = 2.26 Hz 1H, Ar), 8.51 (d,  $J$  = 2.26 Hz 1H, Ar).  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  = 32.9, 60.9, 120.5, 124.6, 125.5, 127.0, 128.9, 129.3, 132.5, 133.2, 134.2, 135.4, 136.0, 136.6, 147.7, 170.8. ESI-MS:  $m/z$  445  $[\text{M}+\text{H}]^+$ . HRMS (ESI):  $m/z$  calcd for  $\text{C}_{20}\text{H}_{15}\text{N}_2\text{OSCl}_2$ :  $[\text{M}+\text{H}]^+$  445.0297, found: 445.0282; Anal. Calcd. for  $\text{C}_{20}\text{H}_{14}\text{BrClN}_2\text{OS}$ : C 53.89; H 3.17; N 6.28. Found: C 53.95; H 3.22; N 6.31.

**2-(2-Chloro-5-phenyl-3-pyridyl)-3-(4-iodophenyl)-1,3-thiazolidin-4-one (2e)**

Yield: 78%, Brownish red solid; mp 142-144 °C; IR (KBr):  $\nu_{\max}$  = 3057, 2923, 1735, 1486, 1358, 1294, 1073, 760, 695  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 3.77 (m, 2H,  $\text{CH}_2$ ), 6.51 (s, 1H, CH), 7.1 (d,  $J$  = 8.7 Hz 2H, Ar), 7.36-7.46 (m, 5H, Ar), 7.63-7.67 (m, 3H, Ar), 8.49 (d,  $J$  = 2.45 Hz 1H, Ar).  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  = 32.9, 60.9, 124.2, 125.6, 127.0, 128.9, 129.3, 133.2, 134.1, 135.4, 136.6, 136.7, 138.4, 147.7, 170.8. ESI-MS:  $m/z$  493  $[\text{M}+\text{H}]^+$ . HRMS (ESI):  $m/z$  calcd for  $\text{C}_{20}\text{H}_{15}\text{N}_2\text{OISCl}$ :  $[\text{M}+\text{H}]^+$  492.9638, found: 492.9658; Anal. Calcd. for  $\text{C}_{20}\text{H}_{14}\text{ClIN}_2\text{OS}$ : C 48.75; H 2.86; N 5.68. Found: C 48.84; H 2.91; N 5.72.

**2-(2-Chloro-5-ethyl-3-pyridyl)-3-phenyl-1,3-thiazolidin-4-one (2f)**

Yield: 88%, Yellowish solid; mp 84-86 °C. IR (KBr):

$\nu_{\max}$  = 3051, 2967, 2927, 1693, 1372, 1287, 1068, 753, 692  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.17 (t,  $J$  = 7.75 Hz, 3H,  $-\text{CH}_2-\text{CH}_3$ ), 2.55 (q,  $J$  = 7.74 Hz, 15.3 Hz 2H,  $-\text{CH}_2-\text{CH}_3$ ), 3.78 (m, 2H,  $\text{CH}_2$ ), 6.48 (s, 1H, CH), 7.11-7.36 (m, 5H, Ar), 7.39 (d,  $J$  = 2.27 Hz 1H, Ar), 8.11 (d,  $J$  = 2.46 Hz 1H, Ar).  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  = 15.0, 25.3, 33.0, 61.2, 124.2, 127.0, 129.3, 133.3, 135.7, 137.0, 139.3, 146.3, 148.7, 170.9. ESI-MS:  $m/z$  319  $[\text{M}+\text{H}]^+$ . HRMS (ESI):  $m/z$  calcd for  $\text{C}_{16}\text{H}_{15}\text{N}_2\text{ONaCl}$ :  $[\text{M}+\text{Na}]^+$  341.0479, found: 341.0491; Anal. Calcd. for  $\text{C}_{16}\text{H}_{15}\text{ClN}_2\text{OS}$ : C 60.28; H 4.74; N 8.79. Found: C 60.24; H 4.71; N 8.89.

**2-(2-Chloro-5-ethyl-3-pyridyl)-3-(4-fluorophenyl)-1,3-thiazolidin-4-one (2g)**

Yield: 81%, Yellowish solid; mp 124-126 °C. IR (KBr):  $\nu_{\max}$  = 3059, 1693, 1508, 1378, 1227, 1077, 831, 761  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.15 (t,  $J$  = 7.55 Hz 3H,  $-\text{CH}_2-\text{CH}_3$ ), 2.56 (q,  $J$  = 7.55 Hz, 15.11 Hz 2H,  $-\text{CH}_2-\text{CH}_3$ ), 3.77 (m, 2H,  $\text{CH}_2$ ), 6.43 (s, 1H, CH), 6.97 (d,  $J$  = 9.1 Hz 2H, Ar), 7.21-7.27 (m, 2H, Ar), 7.38 (d,  $J$  = 2.27 Hz 1H, Ar), 8.11 (d,  $J$  = 2.27 Hz 1H, Ar);  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  = 14.9, 25.2, 32.9, 61.2, 116.1, 116.4, 126.2, 126.3, 132.8, 135.8, 139.3, 146.5, 149.0, 159.3, 162.5, 171.1. ESI-MS:  $m/z$  337  $[\text{M}+\text{H}]^+$ . HRMS (ESI):  $m/z$  calcd for  $\text{C}_{16}\text{H}_{14}\text{N}_2\text{OFNaCl}$ :  $[\text{M}+\text{Na}]^+$  359.0397, found: 359.0386; Anal. Calcd. for  $\text{C}_{16}\text{H}_{14}\text{ClFN}_2\text{OS}$ : C 57.06; H 4.19; N 8.32. Found: C 57.16; H 4.21; N 8.21.

**2-(2-Chloro-5-ethyl-3-pyridyl)-3-(4-chlorophenyl)-1,3-thiazolidin-4-one (2h)**

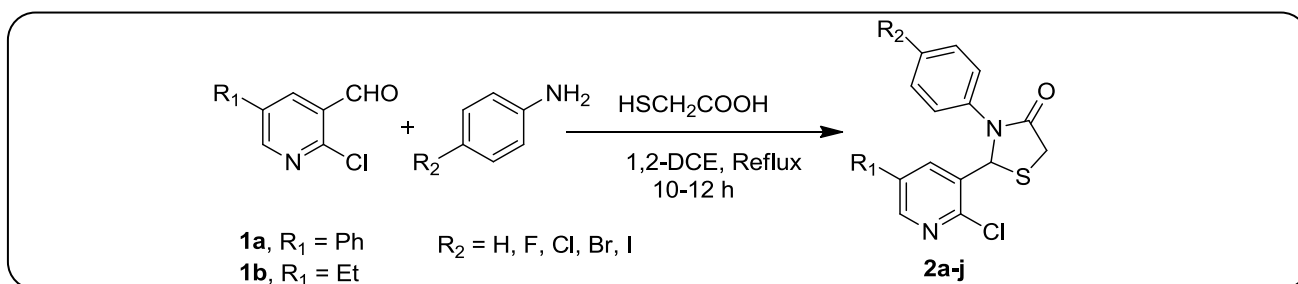
Yield: 75%, Yellowish solid; mp 98-100 °C. IR (KBr):  $\nu_{\max}$  = 3040, 2969, 2929, 1695, 1492, 1369, 1285, 1092, 830  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.16 (t,  $J$  = 7.55 Hz 3H,  $-\text{CH}_2-\text{CH}_3$ ), 2.56 (q,  $J$  = 7.55 Hz, 15.11 Hz 2H,  $-\text{CH}_2-\text{CH}_3$ ), 3.76 (m, 2H,  $\text{CH}_2$ ), 6.44 (s, 1H, CH), 7.22-7.30 (dd,  $J$  = 9.0 Hz, 14.0 Hz 4H, Ar), 7.34 (d,  $J$  = 2.27 Hz 1H, Ar), 8.13 (d,  $J$  = 2.27 Hz 1H, Ar).  $^{13}\text{C}$  NMR (75 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  = 14.9, 25.2, 32.9, 61.0, 125.2, 129.3, 132.4, 132.7, 135.5, 135.4, 139.3, 146.5, 149.1, 170.8. ESI-MS:  $m/z$  353  $[\text{M}+\text{H}]^+$ . HRMS (ESI):  $m/z$  calcd for  $\text{C}_{16}\text{H}_{15}\text{N}_2\text{OSCl}_2$ :  $[\text{M}+\text{H}]^+$  353.0282, found: 353.0278; Anal. Calcd. for  $\text{C}_{16}\text{H}_{14}\text{Cl}_2\text{N}_2\text{OS}$ : C 54.40; H 3.99; N 7.93. Found: C 54.48; H 3.97; N 7.97.

**2-(2-Chloro-5-ethyl-3-pyridyl)-3-(4-bromophenyl)-1,3-thiazolidin-4-one (2i)**

Yield: 79%, Yellowish solid; mp 114-116 °C. IR (KBr):

Table 1: Effect of reaction parameters on the synthesis of 2-Pyridyl-4-thiazolidinones.

S. No	Solvent (reflux)	Base	Dehydrating agent	Yield (%)
1	DCM	Et <sub>3</sub> N	MgSO <sub>4</sub>	69
2	Benzene	DIPEA	MgSO <sub>4</sub>	75
3	Toluene	Pyridine	4 °A M.S	81
4	Xylene	K <sub>2</sub> CO <sub>3</sub>	Na <sub>2</sub> SO <sub>4</sub>	79
5	1,2-DCE	-	-	80



Scheme 1: Synthesis of 2-Pyridyl-4-thiazolidinones 2a-j.

$\nu_{\max}$  = 3094, 2971, 2929, 1696, 1490, 1360, 1282, 1067, 823 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.15 (t,  $J$  = 7.55 Hz 3H, -CH<sub>2</sub>-CH<sub>3</sub>), 2.56 (q,  $J$  = 7.36 Hz, 14.92 Hz 2H, -CH<sub>2</sub>-CH<sub>3</sub>), 3.74 (m, 2H, CH<sub>2</sub>), 6.43 (s, 1H, CH), 7.16 (m, 2H, Ar), 7.33 (d,  $J$  = 2.1 Hz 1H, Ar), 7.39 (m, 2H, Ar), 8.12 (s, 1H, Ar). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  = 14.9, 25.2, 32.9, 60.9, 120.3, 125.4, 132.3, 132.7, 135.4, 136.0, 139.3, 146.4, 149.0, 170.8. ESI-MS:  $m/z$  397 [M+H]<sup>+</sup>. HRMS (ESI):  $m/z$  calcd for C<sub>16</sub>H<sub>15</sub>N<sub>2</sub>OSCIBr: [M+H]<sup>+</sup> 396.9776, found: 396.9763; Anal. Calcd. for C<sub>16</sub>H<sub>14</sub>BrClN<sub>2</sub>O: C 48.32; H 3.55; N 7.04. Found: C 48.30; H 3.66; N 7.07.

#### 2-(2-Chloro-5-ethyl-3-pyridyl)-3-(4-iodophenyl)-1,3-thiazolidin-4-one (2j)

Yield: 83%, Greyish solid; mp 138-140 °C. IR (KBr):  $\nu_{\max}$  = 3041, 2971, 2930, 1695, 1487, 1358, 1281, 1065, 822 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.16 (t,  $J$  = 7.55 Hz 3H, -CH<sub>2</sub>-CH<sub>3</sub>), 2.56 (q,  $J$  = 7.55 Hz, 14.92 Hz 2H, -CH<sub>2</sub>-CH<sub>3</sub>), 3.76 (m, 2H, CH<sub>2</sub>), 6.44 (s, 1H, CH), 7.10 (d,  $J$  = 8.9 Hz 2H, Ar), 7.32 (d,  $J$  = 2.6 Hz 1H, Ar), 7.61 (d,  $J$  = 8.9 Hz 2H, Ar), 8.14 (s, 1H, Ar). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  = 14.9, 25.2, 32.9, 60.8, 125.6, 129.2, 132.7, 135.2, 136.8, 138.3, 139.3, 146.5, 149.1, 170.8. ESI-MS:  $m/z$  445 [M+H]<sup>+</sup>. HRMS (ESI):  $m/z$  calcd for C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>NaISCl: [M+Na]<sup>+</sup> 466.9293, found: 466.9300; Anal. Calcd. for C<sub>16</sub>H<sub>14</sub>ClIN<sub>2</sub>O<sub>2</sub>S: C 43.21; H 3.17; N 6.30. Found: C 43.31; H 3.20; N 6.28.

## RESULTS AND DISCUSSION

In this context, it is our interest to develop a new methodology for the synthesis of thiazolidin-4-ones (**2a-j**) avoiding the drawbacks encountered by previous methods. Hence, the number of experiments was performed to optimize the reaction parameters, such as effect of solvent, use of different catalysts, variation of reaction temperature and time to obtain the desired compounds in good yields. In a typical reaction, 2-chloro-5-phenyl nicotinaldehyde (**1a**), aniline and mercaptoacetic acid were refluxed in different solvents in presence of different catalysts, dehydrating agents and bases and the yields obtained are reported in Table 1. The results of this study led to the development of a process with increased yield of the desired product (80%), and avoiding use of base and catalyst (Scheme 1). We also performed solvent optimization and 1,2-dichloroethane is chosen as best solvent in terms of yield and time.

To demonstrate the general utility of the method, we applied these conditions to a variety of anilines with two 2-chloro nicotinaldehydes which are developed in our laboratory. In all the cases, the reactions occurred smoothly, obtaining corresponding 2-pyridyl thiazolidinones in very good yields. The results and yields of products **2a-i** are shown in Table 2.

All the synthesized new compounds (**2a-j**) are screened for their antimicrobial activity by the broth dilution method recommended by NCCL standards [41].

Table 2: Synthesis of 2-Pyridyl4-thiazolidinone derivatives 2a-j.

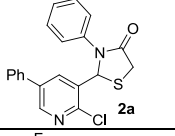
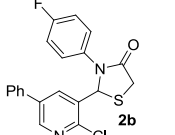
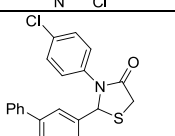
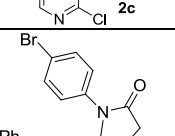
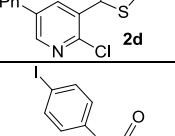
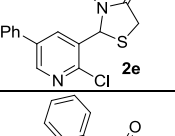
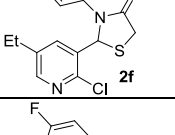
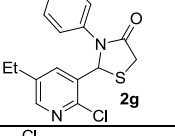
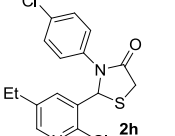
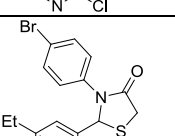
Entry	Aldehyde	Amine	Time (h)	Product	Isolated yield
1	<b>1a</b>	R <sub>2</sub> =H	10		80
2	<b>1a</b>	R <sub>2</sub> =F	12		82
3	<b>1a</b>	R <sub>2</sub> =Cl	11		77
4	<b>1a</b>	R <sub>2</sub> =Br	12		75
5	<b>1a</b>	R <sub>2</sub> =I	12		78
6	<b>1b</b>	R <sub>2</sub> =H	10		88
7	<b>1b</b>	R <sub>2</sub> =F	12		81
8	<b>1b</b>	R <sub>2</sub> =Cl	11		75
9	<b>1b</b>	R <sub>2</sub> =Br	12		79
10	<b>1b</b>	R <sub>2</sub> =I	12		83

Table 3: Antibacterial activity of thiazolidinone compounds.

Entry	MIC ( $\mu\text{g/mL}$ )					
	<i>B.subtilis</i>	<i>S.aurues</i>	<i>S.epidermidis</i>	<i>E.coli</i>	<i>P.aeruginosa</i>	<i>K.pneumoniae</i>
2a	150	150	75	150	18.75	150
2b	150	150	150	150	18.75	150
2c	150	150	150	150	37.5	150
2d	150	150	150	150	9.375	150
2e	150	150	150	150	9.375	150
2f	150	150	150	150	18.75	150
2g	150	150	150	150	37.5	75
2h	150	150	75	150	9.375	75
2i	75	75	75	75	9.375	150
2j	150	150	75	150	18.75	150
Penicillin	1.56	1.56	3.12	12.5	12.5	6.25
Strepto- mycin	6.25	6.25	3.12	6.25	1.56	3.12

Table 4: Antifungal activity of thiazolidinone compounds.

Entry	Zone of Inhibition in MM					
	<i>C. albicans</i>		<i>C. rugosa</i>		<i>S. cerevisiae</i>	
	100 $\mu\text{g}$	150 $\mu\text{g}$	100 $\mu\text{g}$	150 $\mu\text{g}$	100 $\mu\text{g}$	150 $\mu\text{g}$
2a	-	-	-	-	10	15
2d	7	10	7	10	7	12
2i	7	10	7	10	-	-
Amphoter- icin B (50)	23.5		21		22	

The antibacterial activity is tested on six different organisms (Gram-positive and Gram-negative), *Bacillus subtilis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* with respect to the references Penicillin and Streptomycin. Interestingly, out of six organisms, almost all the pyridyl thiazolidinones displayed good antibacterial activity against the most promising resistant strain, *P. aeruginosa*. Compounds **2i** and **2j** showed moderate activity against several strains. Minimum Inhibitory Concentration (MIC) in  $\mu\text{g/mL}$  values for all the compounds are listed in Table 3.

All the compounds are also screened for their antifungal activity against two representative microorganisms *Yeast* and *Filamentous fungi* viz.

*Candida albicans*, *Candida rugosa*, *Saccharomyces cerevisiae* with respect to standard Amphotericin B (50) by paper disc diffusion method. Zone of inhibition (mm) were determined for the compounds and the screening results indicate that only compounds **2a**, **2d** and **2i** of all the compounds exhibited significant antifungal activities as shown in Table 4. Compounds **2a** and **2d** exhibited antifungal activity especially on *S. cerevisiae* strain, whereas compound **2i** have an antifungal effect against *C. albicans* and *C. rugosa* strains.

## CONCLUSIONS

In summary, we have synthesized various new 4-thiazolidinone derivatives in an efficient manner under catalyst-free/base-free conditions. Simple workup procedure, good yields, and mild conditions are the key

features of this method. All the synthesized compounds were screened for antimicrobial activity against several organisms and most of the compounds exhibited very good antibacterial activity against *P. aeruginosa* strain compared to Penicillin. Further, this methodology was used to produce a library of compounds and will be reported in due course with profound properties.

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