Synthesis of 2-Amino-3,5-dicarbonitrile-6-thiopyridines Using Silica-bonded N-Propyldiethylenetriamine as a Heterogeneous Solid Base Catalyst

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(Received 30 June 2016, Accepted 17 October 2016)

Silica-bonded N-propyldiethylenetriamine (7) is employed as a recyclable heterogeneous solid base catalyst for the synthesis of 2-amino-3,5-dicarbonitrile-6-thiopyridines through pseudo four-component condensation reaction between aromatic aldehydes, malononitrile, and 2-amino-thiophenol in refluxing ethanol. Silica-bonded N-propyldiethylenetriamine showed much the same efficiency when used in consecutive reaction runs.

Keywords: 2-Amino-3,5-dicarbonitrile-6-thiopyridines, Heterogeneous catalysts, Solid bases, Synthesis, Multi-component reactions

INTRODUCTION

Multi-component reactions (MCRs) play an important role in combinatorial chemistry because of their ability to synthesize small drug-like molecules with several degrees of structural diversity. MCRs have performed quantitative revolutions in molecular architecting, access to multifunctional molecules, and combinatorial chemistry in recent years [1-3].

The pyridine ring systems represent a major class of heterocycles and their analogues exhibit diverse biological and physiological activities [4]. In particular, 2-amino-3,5-dicarbonitrile-6-thio-pyridines serve as 'privileged scaffold' due to their potential therapeutic applications [5-18]. These structures represent such a class of medicinally significant compounds, libraries of which demonstrate activity against a wide range of biological targets (Fig. 1). For example, compounds 1 and 2 displays efficacy as selective human adenosine receptor modulators [5,6], relevant for treatment of a range of conditions, and compound 3 as anti-prion agents [7].

Compound 4 showed varying degrees of efficacy as an anti-proliferative agent [18]. Compounds 5 and 6 were reported to inhibit PrPSc accumulation in scrapie-infected mouse neuroblastoma cells (ScN2a) and modulate androgen receptor function [17]. In addition, 2-amino-3,5-dicarbonitrile-6-thio-pyridines skeleton is often used as anti-prion [7,12,13], anti-hepatitis B virus [14], anti-bacterial [15] and anti-cancer [8] agents. Recently, some of these compounds have been recognized as potential targets for the development of new drugs for the treatment of Parkinson’s disease, hypoxia, asthma, kidney disease, epilepsy, cancer [16] and Creutzfeldt-Jacob disease [7,12,17].

Many synthetic methods have been developed for the construction of 2-amino-6-thiopyridine-3,5-dicarbonitrile derivatives. Among these reported methods, three-component condensation reaction between aldehydes, malononitrile, and thiophenols catalyzed by Lewis/Bronsted bases is the most common approach. The reported Lewis/Bronsted base catalysts include DBU [19], Et3N [20,21], piperidine [22,23], KF/alumina [24,25], K2CO3/KMnO4 [26], etc. Besides bases, Lewis acids, Bronsted acids, nanoparticles, and ionic liquids, such as ZnCl2 [27], boric acid [28], silica nanoparticles [29], nano MgO [30], ZrOCl2 [31], [bmim]OH [32], [bmim]Br [33], Zn(II) and Cd(II) metal-organic frameworks (MOFs) [34], 2-hydroxyethylammonium acetate [35], K2CO3 in PEG-400 [36], and phosphotungstic acid [37], are also occasionally
Several types of propyl amine functionalized silica, hydrotalcites, and basic zeolites (microporous and mesoporous) have been synthesized and applied as an alternative to traditional amines in base catalyzing chemical transformations [38-48].

Recently, we prepared some silica immobilized amines such as; silica-bonded N-propyldiethylenetriamine (7) [43], silica-bonded N-propyltriethylenetetramine (8) [44], silica-bonded N-propylpiperazine (9) [49,50], silica-bonded N-propylpiperazine sodium N-propionate (10) [49,50], silica-bonded N-propylmorpholine (11) [51] and 3-silicapropyl amine (12) [52], and investigated their applications as heterogeneous solid bases in organic reactions [49-54] or using as ligand for stabilizing Pd nano particles [51,55-57] (Fig. 2).

**Fig. 1.** Structure of some bio-active compounds containing 2-amino-pyridine-3,5-dicarbonitriles.

**Fig. 2.** The structure of silica-bonded amines.
EXPERIMENTAL

General

Chemicals were purchased from Merck and Aldrich chemical companies. For recorded $^1$H NMR spectra we used Bruker Ultrashield (400 MHz) in pure deuterated CDCl$_3$, or DMSO-d$_6$ solvent with tetramethylsilane (TMS) as internal standard. Melting points were determined in open capillaries tubes in a Barnstead Electrothermal 9100 BZ circulating oil melting point apparatus. The reaction monitoring was accomplished by TLC on silica gel Poly Gram SILG/UV254 plates. All the products are known compounds and were characterized by comparison of their IR, $^1$H NMR and $^{13}$C NMR spectroscopic data and their melting points with reported values [24-37]. Solid bases 7-12 [43,44,49-52] were prepared according to our previously reported procedure.

General Procedure for the Synthesis of 2-Amino-3,5-dicarbonitrile-6-thio-pyridines

A mixture of aromatic aldehyde (1 mmol), malononitrile (2 mmol), 2-amino-thiophenol (1 mmol), catalyst 7 (0.1 g, 5 × 10$^{-3}$ mmol of OH$^-$) [43], in refluxing ethanol (5 ml) for the time specified in Table 2 (the progress of the reaction was monitored by TLC). After completion, warm ethanol (10 ml) was added and filtered. The remaining was washed with warm ethanol (2 × 5 ml) to separate catalyst. After cooling the organic phase the crude was precipitated and filtered to obtain products. For further purification the crude was recrystallized from ethanol (95%). The recovered catalyst was dried and reused for the subsequent runs.

2-Amino-6-(2-amino-phenylsulfanyl)-4-(4-chlorophenyl)-pyridine-3,5-dicarbonitrile (13a). M.p.: 230-232 ℃ (Lit. [28] 234-236 ℃); IR (KBr): 3419, 3325, 3214, 2214, 1634, 1538, 1427, 1094, 1029, 874, 804 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ (ppm) 4.27 (s, 2H), 5.64 (s, 2H), 6.82-6.87 (m, 2H), 7.32-7.36 (m, 1H), 7.39-7.42 (m, 1H), 7.50-7.52 (m, 2H), 7.56-7.58 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ (ppm) 87.1, 96.1, 109.9, 115.1, 115.8, 118.9, 129.5, 129.8, 129.9, 131.5, 132.3, 137.5, 137.9, 149.5, 159.4.

2-Amino-6-(2-amino-phenylsulfanyl)-4-(3-chlorophenyl)-pyridine-3,5-dicarbonitrile (13b). M.p.: 162-164 ℃; IR (KBr): 3455, 3389, 3218, 2215, 1635, 1538, 1472, 1257, 1472, 1257, 1030, 874, 783 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ (ppm) 4.07 (s, 2H), 5.71 (s, 2H), 6.82-6.87 (m, 2H), 7.31-7.36 (m, 1H), 7.40-7.43 (m, 2H), 7.51-7.58 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ (ppm) 87.4, 96.1, 114.6, 114.8, 115.8, 118.9, 126.7, 128.5, 130.5, 131.1, 132.4, 134.8, 135.1, 137.9, 149.5, 156.9, 159.3, 168.6.

2-Amino-6-(2-amino-phenylsulfanyl)-4-(4-bromophenyl)-pyridine-3,5-dicarbonitrile (13c). M.p.: 236-238 ℃; IR (KBr): 3409, 3347, 3220, 2213, 1632, 1536, 1409, 1260, 1024, 876, 803 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ (ppm) 4.27 (s, 2H), 5.66 (s, 2H), 6.82-6.87 (m, 2H), 7.32-7.36 (m, 1H), 7.40-7.45 (m, 3H), 7.73 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ (ppm) 86.7, 93.8, 107.9, 115.6, 115.9, 116.0, 116.9, 124.6, 131.1, 132.2, 132.3, 133.8, 137.7, 151.6, 160.0, 167.3.

2-Amino-6-(2-amino-phenylsulfanyl)-4-p-tolyldipyridine-3,5-dicarbonitrile (13d). M.p.: 210-212 ℃ (Lit. [28] 208-210 ℃); IR (KBr): 3421, 3322, 3212, 2215, 1630 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$): δ (ppm) 2.25 (s, 3H, CH$_3$), 4.32 (brs, 2H, NH$_2$), 6.26 (brs, 2H, NH$_2$), 6.55 (t, 1H, $^J$= 5.0 Hz, Ar), 6.65 (d, 1H, $^J$= 8.1 Hz, Ar), 7.06 (dt, 1H, $^J$= 7.7 Hz, $^J$= 1.3 Hz, Ar), 7.14-7.18 (m, 3H, Ar), 7.23 (d, 2H, $^J$= 8.1 Hz, Ar); $^{13}$C NMR (125 MHz, CDCl$_3$ & two drops of DMSO-d$_6$): δ (ppm) 21.8, 87.5, 95.4, 110.2, 115.8, 115.8, 116.1, 118.5, 128.7, 129.9, 130.9, 132.3, 133.7, 137.9, 141.3, 150.4, 158.8, 160.2, 168.0.

2-Amino-6-(2-amino-phenylsulfanyl)-4-(4-methoxyphenyl)-pyridine-3,5-dicarbonitrile (13e). M.p.: 229-231 ℃ (Lit. [28] 230-232 ℃); IR (KBr): 3426, 3324, 3210, 2214, 1620 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-d$_6$): δ (ppm) 3.90 (s, 3H), 4.45 (s, 2H), 5.29 (s, 2H), 7.40 (d, 2H, $^J$= 7.6 Hz), 7.54 (d, 2H, $^J$= 7.6 Hz), 7.65-7.67 (m, 1H), 8.03-8.05 (m, 3H); $^{13}$C NMR (100 MHz, DMSO-d$_6$): δ (ppm) 43.9, 87.0, 94.1, 107.9, 115.6, 115.8, 116.1, 116.3, 116.5, 116.9, 130.9, 131.5, 132.2, 137.7, 151.7, 157.9, 160.1.

2-Amino-6-(2-amino-phenylsulfanyl)-4-(4-ethoxyphenyl)-pyridine-3,5-dicarbonitrile (13f). M.p.: 201-204 ℃; IR (KBr): 3425, 3323, 3211, 2215, 1620 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-d$_6$): δ (ppm) 1.15 (t, 3H, $^J$= 7.2 Hz), 3.58-3.64 (m, 2H), 4.65 (s, 2H), 5.59 (s, 2H), 6.82-6.87 (m, 2H), 7.33 (m, 2H), 7.53-7.55 (m, 3H), 7.74 (m, 1H); $^{13}$C NMR (100 MHz, DMSO-d$_6$): δ (ppm) 23.1, 65.7, 86.7, 93.8, 108.0, 115.5, 115.8, 116.0, 116.3, 124.5, 131.1, 132.2, 132.3, 133.8, 137.6, 151.6, 157.8, 160.1.

2-Amino-6-(2-aminophenylsulfanyl)-4-(3-nitrophenyl)pyridine-3,5-dicarbonitrile (13g). M.p.: 191-192 °C; IR (KBr): 3424, 3321, 3212, 2214, 1621 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ (ppm) 4.27 (s, 2H), 5.51 (s, 2H), 7.15 (m, 1H), 7.20-7.24 (t, 2H, J = 8.8 Hz), 7.33 (m, 1H), 7.35 (s, 1H), 7.68 (s, 1H), 8.01-8.13 (m, 2H). ¹³C NMR (100 MHz, DMSO-d₆): δ (ppm) 86.7, 93.8, 107.0, 115.6, 115.9, 116.8, 116.9, 124.1, 131.6, 132.2, 132.3, 133.6, 137.7, 151.8, 157.8, 160.3, 167.1.

2-Amino-6-(2-aminophenylsulfanyl)-4-(4-nitrophenyl)pyridine-3,5-dicarbonitrile (13h). M.p.: 207-209 °C, (Lit. [28] 206-208 °C); IR (KBr): 3426, 3320, 3214, 2215, 1622 cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ (ppm) 4.59 (s, 2H), 5.57 (s, 2H), 6.82-6.88 (m, 2H), 7.33-7.34 (m, 1H), 7.45-7.49 (m, 3H), 7.75-7.77 (m, 2H). ¹³C NMR (100 MHz, DMSO-d₆): δ (ppm) 88.86, 97.2, 111.1, 117.1, 125.8, 128.1, 129.7, 130.3, 130.4, 133.0, 133.8, 140.0, 140.3, 155.5, 158.0, 160.2.

2-Amino-6-(2-aminophenylsulfanyl)-4-(4-cyano-phenyl)pyridine-3,5-dicarbonitrile (13i). M.p.: 245-246 °C; IR (KBr): 3428, 3321, 3210, 2214, 1619 cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ (ppm) 3.93 (s, 2H), 5.30 (s, 2H), 7.08 (d, 2H, J = 8.0 Hz), 7.55 (m, 2H), 7.65-7.67 (m, 2H), 8.01 (d, 2H, J = 8.0 Hz). ¹³C NMR (100 MHz, DMSO-d₆): δ (ppm) 86.7, 93.9, 107.9, 115.5, 115.8, 116.0, 116.9, 124.5, 131.0, 132.2, 133.8, 137.6, 146.2, 151.6, 157.8, 160.0.

2-Amino-4-phenyl-6-p-tolylsulfanyl)pyridine-3,5-dicarbonitrile (13j). M.p.: 216-218 °C, (Lit. [25] 218-220 °C); IR (KBr): 3450, 3322, 3208, 2214, 1618, 1547, 1524, 1490, 1264, 808, 704 cm⁻¹. ¹H NMR (300 MHz, DMSO-d₆): δ (ppm) 2.43 (s, 3H), 5.37 (s, 2H), 7.24 (d, 2H, J = 8.2 Hz), 7.43 (d, 2H, J = 8.2 Hz), 7.51-7.58 (m, 5H). ¹³C NMR (75 MHz, DMSO-d₆): δ (ppm) 20.8, 86.9, 93.1, 114.9, 115.2, 123.4, 128.3, 128.6, 130.0, 130.2, 133.9, 134.8, 139.5, 158.5, 159.6, 166.5.

RESULTS AND DISCUSSION

In continuation our research on the design and application silica functionalized solid acids and bases as heterogeneous catalysts in organic transformations [43,44,49-57], we describe the application of silica-bonded amines (7-12) in the synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridine derivatives via pseudo four-component condensation reaction of aromatic aldehydes, malononitrile, thiophenols in refluxing ethanol (Scheme 1).

To this end, the reaction between 4-chloro-benzaldehyde (1 mmol), malononitrile (2 mmol), and 2-aminothiophenol (1 mmol) was selected as a model reaction to establish the feasibility of the strategy and optimize the reaction conditions. As shown in Table 1, the catalytic effect of solid bases 7-12 was studied as heterogeneous base catalysts. All of these silica immobilized amines were accomplished this pseudo four-component condensation reaction in refluxing ethanol.

The model reaction was converted into corresponding product in a higher yield using solid amine 7 as catalyst (Table 1, entry 4). The lower amounts of 7 (0.05 and 0.07 g) was converted the model reaction in longer reaction time and lower yield (Table 1, entries 2 and 3) and using higher amounts of the catalyst (0.15 g) did not improve the result to an appreciable extent (Table 1, entry 5). The model reaction was treated in solvents such as methanol, dichloromethane, chloroform, water, and acetonitrile in the presence of 7 (0.1 g) at reflux conditions (Table 1, entries 6-10). The condensation reaction under solvent-free conditions at 100 °C gave corresponding product in 85% yield after 50 min (Table 1, entry 11). So, the optimum conditions was aromatic aldehyde (1 mmol), malononitrile (2 mmol), thiophenol (1 mmol), and 7 (0.1 g) in refluxing ethanol.

To explore the generality and efficiency of the current protocol, malononitrile and 2-aminothiophenol were reacted with different aromatic aldehyde derivatives and the corresponding products were obtained in high yields. Results indicate that both electron-donating and electron-withdrawing substituents on the benzaldehyde ring were well tolerated under optimized conditions. As it is clear in Table 2, the reactions of benzaldehyde having substituents such as 4-Me-, 4-OMe- and 4-OTf- with malononitrile and 2-aminothiophenol were proceeded efficiently to generate the 2-amino-3,5-dicarbonitrile-6-thiopyridine derivatives in high yields. Also, benzaldehyde substituted halogens (such as 4-Cl-, 3-Cl- and 4-Br-) and electron-withdrawing groups (such as 3-NO₂-, 4-NO₂-, 4-CN-) converted into the corresponding products after 30 to 45 min in high yields (Table 2, entries 1-3 and 7-9). In addition, the reaction of malononitrile, benzaldehyde and 4-methyl-thiophenol gave the corresponding product in high yields (Table 2, entry 10).


Scheme 1. Synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines

\begin{align*}
\text{ArCHO} \quad + \quad 2 \text{ NC} \equiv \text{CN} \quad + \quad \text{Solid amine (7-12)} \quad \rightarrow \quad \text{NC}_2\text{HC} \equiv \text{CN} \quad \text{Ar} \quad \text{NH}_2 \\
\text{G} = \text{CH}_3, \text{NH}_2
\end{align*}

Table 1. Investigation the Effect of Catalysts and Solvents on the Reaction of 4-Chloro-benzaldehyde, Malononitrile and 2-Amino-thiophenol in Different Conditions$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>loading (g)</th>
<th>Solvent</th>
<th>Time (min)</th>
<th>Yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>-</td>
<td>Ethanol</td>
<td>24 h</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>0.05</td>
<td>Ethanol</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>0.07</td>
<td>Ethanol</td>
<td>45</td>
<td>70</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>0.1</td>
<td>Ethanol</td>
<td>30</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
<td>0.15</td>
<td>Ethanol</td>
<td>30</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>7</td>
<td>0.1</td>
<td>Methanol</td>
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<td>90</td>
</tr>
<tr>
<td>7</td>
<td>7</td>
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<td>Dichloromethane</td>
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<td>Chloroform</td>
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</tr>
<tr>
<td>9</td>
<td>7</td>
<td>0.1</td>
<td>Water</td>
<td>80</td>
<td>-</td>
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<td>10</td>
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<td>Acetonitrile</td>
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<td>65</td>
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<tr>
<td>11</td>
<td>7</td>
<td>0.1</td>
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<td>50</td>
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<td>Ethanol</td>
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<td>14</td>
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<td>0.1</td>
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<td>50</td>
<td>87</td>
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<td>15</td>
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<td>Ethanol</td>
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<td>75</td>
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<td>16</td>
<td>12</td>
<td>0.1</td>
<td>Ethanol</td>
<td>50</td>
<td>75</td>
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</table>

$^a$Reaction conditions; aromatic aldehyde (1 mmol), malononitrile (2 mmol), and 2-amino-thiophenol in 5 ml of solvent under reflux conditions. $^b$Isolated yield.
The first step of the process involves the nitrile of the α-efluxing C-3 and 2-thioethanol (G). Nitrification produces dihydropyridine intermediate III. Finally, intermediate III after cyclization of the second molecule of malononitrile to produce to form intermediate II which followed by Michael addition thiolate addition t Knoevenagel product I. The reaction proceeds through and its solid acid moiety (NH$_2$) activates the malononitrile and thiol, 6- or NH) activates the nitrile of the malononitrile, and thiocarbamoyl chloride (Scheme 2). T

diaminocinnamonicitrile (I). The solid base moiety of the catalyst (NH$_2$ or NH) activates the malononitrile and thiol, and its solid acid moiety (NH$_3$) activates the nitrile of the Knoevenagel product I. The reaction proceeds through thiolate addition to nitrile of the α-cyanocinnamonicitrile (I) to form intermediate II which followed by Michael addition of the second molecule of malononitrile to produce intermediate III. Finally, intermediate III after cyclization and tautomerization produces dihydropyridine. Air oxidation of dihydropyridine adduct under the reaction conditions gives corresponding 2-amino-3,5-dicarbonitrile-6-thio-pyridine derivatives (Scheme 2).

The possibility of recycling the catalyst 7 was examined using by the reaction of 4-chlorobenzaldehyde, malononitrile, and 2-aminothiophenol under the optimized conditions. Upon completion, the reaction mixture was filtered while hot. The remaining was washed with warm ethanol (2 × 5 ml). The separated catalyst was dried and reused as such for subsequent experiments under similar reaction conditions. The results showed that the catalyst could be effectively used for at least nine consecutive cycles without much appreciable loss in its catalytic activity (Fig. 3).

Table 2. Synthesis of 2-Amino-3,5-dicarbonitrile-6-thio-pyridines Using 7 as Catalyst in Refluxing Ethanol

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>G</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)</th>
<th>M.p. (°C)</th>
<th>Lit. M.p. (°C)</th>
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<td>1</td>
<td>4-Cl-C$_6$H$_5$-</td>
<td>2-NH$_2$</td>
<td>13a</td>
<td>30</td>
<td>90</td>
<td>230-232</td>
<td>234-236 [28]</td>
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<tr>
<td>2</td>
<td>3-Cl-C$_6$H$_5$-</td>
<td>2-NH$_2$</td>
<td>13b</td>
<td>35</td>
<td>85</td>
<td>162-164</td>
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<tr>
<td>3</td>
<td>4-Br-C$_6$H$_5$-</td>
<td>2-NH$_2$</td>
<td>13c</td>
<td>40</td>
<td>80</td>
<td>236-238</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>4-Me-C$_6$H$_5$-</td>
<td>2-NH$_2$</td>
<td>13d</td>
<td>30</td>
<td>90</td>
<td>210-212</td>
<td>208-210 [28]</td>
</tr>
<tr>
<td>5</td>
<td>4-MeO-C$_6$H$_5$-</td>
<td>2-NH$_2$</td>
<td>13e</td>
<td>35</td>
<td>80</td>
<td>229-231</td>
<td>230-232 [28]</td>
</tr>
<tr>
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<td>4-EtO-C$_6$H$_5$-</td>
<td>2-NH$_2$</td>
<td>13f</td>
<td>30</td>
<td>85</td>
<td>201-204</td>
<td>-</td>
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<tr>
<td>7</td>
<td>3-O$_2$N-C$_6$H$_5$-</td>
<td>2-NH$_2$</td>
<td>13g</td>
<td>40</td>
<td>80</td>
<td>191-192</td>
<td>-</td>
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<tr>
<td>8</td>
<td>4-O$_2$N-C$_6$H$_5$-</td>
<td>2-NH$_2$</td>
<td>13h</td>
<td>35</td>
<td>80</td>
<td>207-208</td>
<td>206-208 [28]</td>
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<tr>
<td>9</td>
<td>4-NC-C$_6$H$_5$-</td>
<td>2-NH$_2$</td>
<td>13i</td>
<td>45</td>
<td>75</td>
<td>245-246</td>
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</tr>
<tr>
<td>10</td>
<td>C$_6$H$_5$-</td>
<td>4-Me</td>
<td>13j</td>
<td>40</td>
<td>88</td>
<td>216-218</td>
<td>218-220 [25]</td>
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</table>

*Isolated yield.
CONCLUSIONS

In conclusion, this work shows that silica-bonded amines as solid bases which can be prepared by simple operation from commercially available and relative cheap starting materials; efficiently catalyzed the synthesis of 2-amino-3,5-dicarbonitrile-6-thio-pyridines. It could also be recovered and reused for several times without noticeable loss of reactivity.

ACKNOWLEDGEMENTS

We are thankful to the Persian Gulf University Research Council for the partial support of this work.

REFERENCES


