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## AN EFFICIENT SYNTHETIC ROUTE TOWARDS NOVEL FURO- AND THIENO-TRIAZOLOPYRIDINES

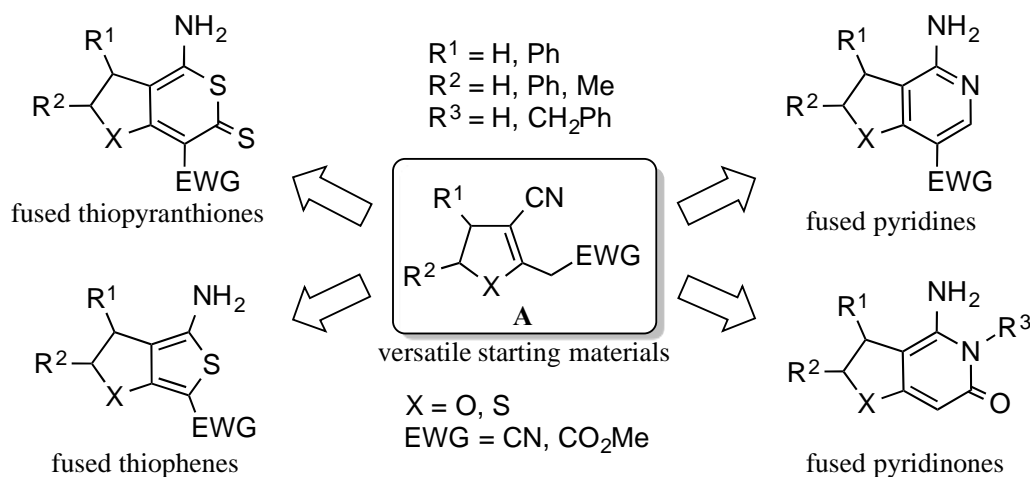
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**Abstract** – An efficient method for the synthesis of novel nitrogen-containing heterotricycles is described. 4,5-Dihydro-3-furan- and -3-thiophene-carbonitriles **1a,b** and **2a,b** having an active methylene group at C-2 position served as the precursor of enamines **3a,b** and **4a,b**, which were followed by an exchange reaction of amines, such as acetohydrazide and benzohydrazide, and subsequent tandem intramolecular cyclization reaction to lead the corresponding furo- and thieno-triazolopyridines **5a,b**, **6a,b**, **7a,b**, and **8a,b**.

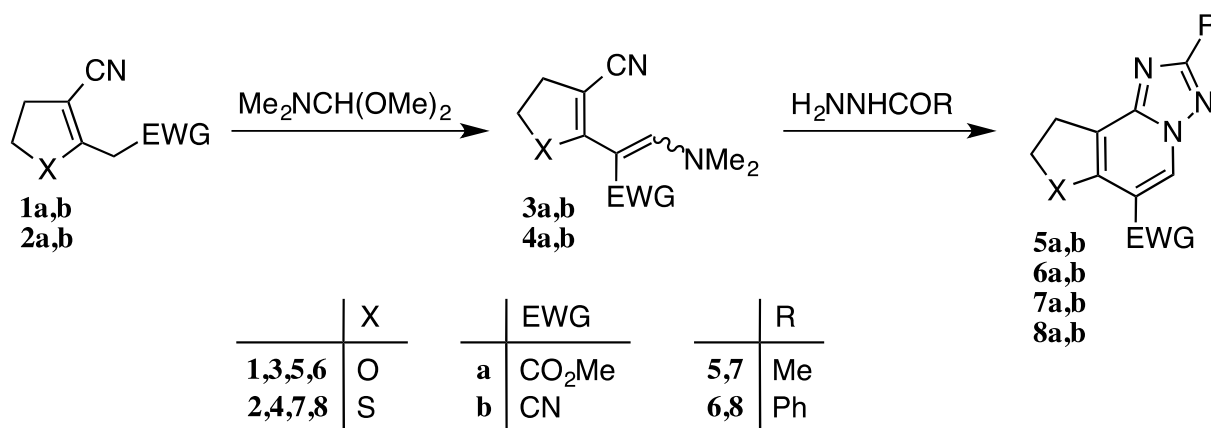
Pyridines and their analogues, especially fused pyridines, are important because of their incidence in nature,<sup>1</sup> their biological properties,<sup>2</sup> and their utilities as intermediates for the design of biologically active compounds.<sup>3</sup> Therefore, a large number of general methods for the preparation of pyridine derivatives have recently been reported.<sup>4</sup> On the other hand, heterocycles containing triazole ring systems also occur in a wide variety of natural and biologically active compounds.<sup>5</sup> Triazole moieties are useful building blocks in chemistry and can be modified to exhibit important roles in pharmacological applications. For these reasons, efficient methods for the synthesis of nitrogen-containing molecules merits further investigations.<sup>6</sup>

In the course of our investigation of the synthesis of heterobicycles,<sup>7</sup> we have shown the synthesis of fused thiopyranthiones,<sup>8a</sup> thiophenes,<sup>8a</sup> pyridines,<sup>8b</sup> and pyridinones<sup>8b</sup> from 4,5-dihydro-3-furan- and -3-thiophene-carbonitriles **A** having an active methylene group at C-2 position as versatile starting materials (Figure 1). Our general point of interest goes to the synthesis of 4,5-annulated furo- and thieno-pyridines with nitrogen-containing heterocycles, thus providing easy strategies towards the synthesis of novel furo- and thieno-pyridine fused structures. To further extend the utility of **A**, we herein describe an efficient procedure for the synthesis of furo- and thieno-triazolopyridine derivatives **5–8** from key starting materials **1** and **2**.



**Figure 1.** Structures of reported heterobicycles

Initially, we examined condensation reaction of methyl 3-cyano-4,5-dihydro-2-furan- and -2-thiopheneacetates **1a** and **2a** with *N,N*-dimethylformamide dimethyl acetal<sup>2</sup> (DMFDMA). Compounds **1a** and **2a** were easily prepared by Wittig reaction of tetrahydro-2-oxo-3-furan- and -3-thiophene-carbonitriles with methyl (triphenylphosphoranylidene)acetate according to our previous procedure.<sup>8a</sup> Thus, the reaction of compounds **1a,b** and **2a,b** with DMFDMA resulted in the formation of enamines **3a,b** and **4a,b** with 57–76% isolated yields (Scheme 1 and Table 1).



**Scheme 1**

**Table 1.** Synthesis of **3a,b** and **4a,b** according to Scheme 1

Entry	Substrate	X	EWG	Product	Yield (%)
1	<b>1a</b>	O	CO <sub>2</sub> Me	<b>3a</b>	58
2	<b>1b</b>	O	CN	<b>3b</b>	57 <sup>8b</sup>
3	<b>2a</b>	S	CO <sub>2</sub> Me	<b>4a</b>	58
4	<b>2b</b>	S	CN	<b>4b</b>	48 <sup>8b</sup>

Reaction Conditions: DMFDMA (1.2 equiv.), 80 °C, 2 h.

In the next step, we attempted an exchange reaction of amines and subsequent intramolecular cyclization of enamines **3a,b** and **4a,b** with hydrazides (Scheme 1). As a consequence, the reaction of enamines **3a,b** and **4a,b** with acetohydrazide (2 equiv.) and/or benzohydrazide (1 equiv.) in refluxing acetic acid for 0.5 h led to the corresponding furo- and thieno-triazolopyridines **5b**, **6a,b**, **7a,b**, and **8a,b** in moderate to good yields (Table 2). In the case of the reaction of **3a** with acetohydrazide under the same condition, the desired **5a** could not be isolated at all and the reaction was not clean. Fortunately, we found the reaction condition under which compound **5a** could be isolated. Indeed, when a mixture of **3a** and acetohydrazide (2 equiv.) in the presence of acetic acid (1 equiv.) in methanol was refluxed for 3 h, the desired furotriazolopyridine **5a** was obtained in 79% yield.

**Table 2.** Synthesis of **5–8** according to Scheme 1

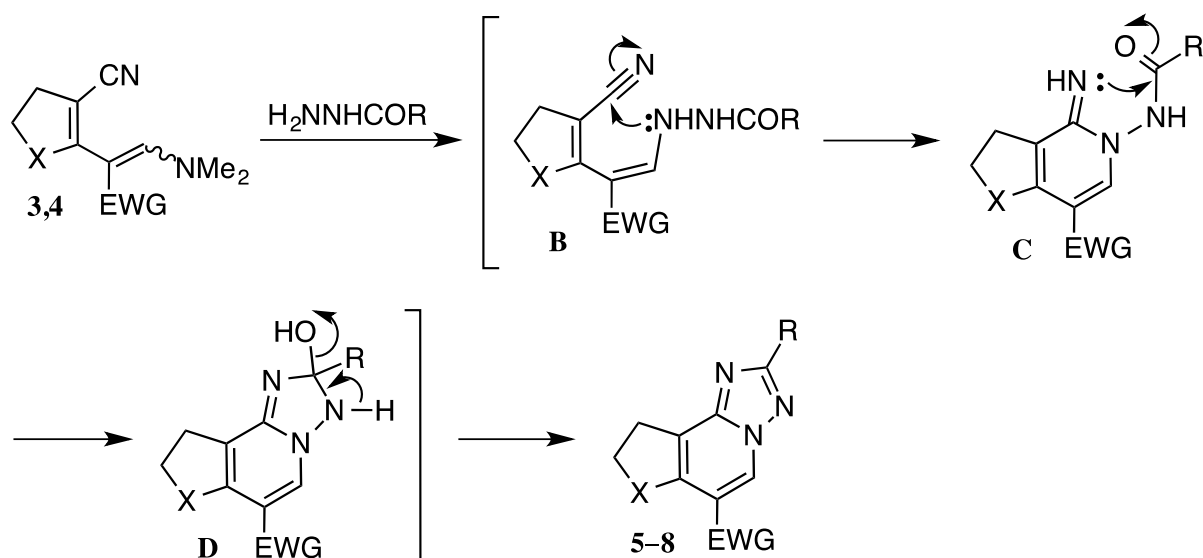
Entry	Substrate	X	R	EWG	Product	Yield (%)
1	<b>3a</b>	O	Me	CO <sub>2</sub> Me	<b>5a</b>	79 <sup>a</sup>
2	<b>3b</b>	O	Me	CN	<b>5b</b>	36 <sup>b</sup>
3	<b>3a</b>	O	Ph	CO <sub>2</sub> Me	<b>6a</b>	84 <sup>c</sup>
4	<b>3b</b>	O	Ph	CN	<b>6b</b>	52 <sup>c</sup>
5	<b>4a</b>	S	Me	CO <sub>2</sub> Me	<b>7a</b>	45 <sup>b</sup>
6	<b>4b</b>	S	Me	CN	<b>7b</b>	67 <sup>b</sup>
7	<b>4a</b>	S	Ph	CO <sub>2</sub> Me	<b>8a</b>	90 <sup>c</sup>
8	<b>4b</b>	S	Ph	CN	<b>8b</b>	62 <sup>c</sup>

Reaction Conditions: <sup>a</sup>acetohydrazide (2 equiv.), AcOH (1 equiv.), MeOH, reflux, 3h. <sup>b</sup>acetohydrazide (2 equiv.), AcOH, reflux, 0.5 h. <sup>c</sup>benzohydrazide (1 equiv.), AcOH, reflux, 0.5 h.

Elemental analyses, MS spectra, <sup>1</sup>H and <sup>13</sup>C NMR spectra of compounds **5–8** are consistent with the assigned structures (see experimental section). For example, the IR spectrum of **5a** reveals a band at 1713 cm<sup>-1</sup> due to an ester carbonyl group. The <sup>1</sup>H NMR spectrum of **5a** in CDCl<sub>3</sub> exhibits a three-proton singlet at δ 2.56 assignable to the methyl protons and a three-proton singlet at δ 3.96 assignable to the methyl protons of the methyl ester. The <sup>13</sup>C NMR spectrum of **5a** in CDCl<sub>3</sub> shows a signal at δ 14.5 because of the methyl carbon, a signal at δ 52.5 because of the methyl carbon of the methyl ester, a signal at δ 151.0 because of the C-9b carbon, a signal at δ 163.1 because of the ester carbonyl carbon, and a signal at δ 166.7 because of the C-2 carbon.

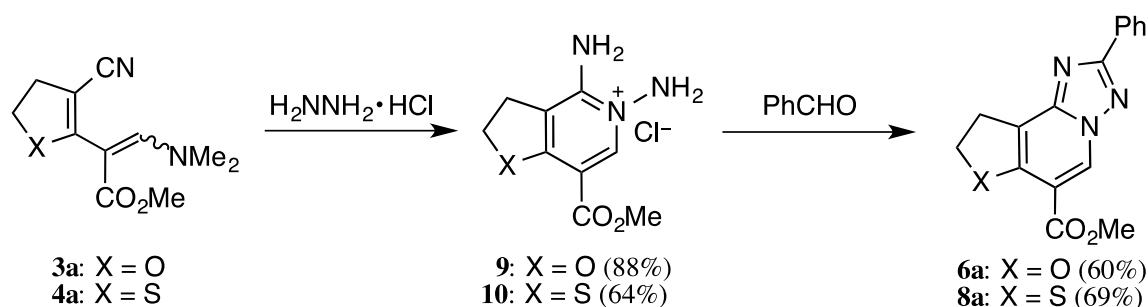
A plausible mechanism for the formation of the furo- and thieno-triazolopyridines **5–8** is shown in Scheme 2. Thermal treatment of enamines **3** and **4** with hydrazides probably causes an exchange reaction of amines to give the non-isolable intermediate **B**, which underwent *in situ* cyclization to result in the formation of the fused pyridines **C**. Subsequently, a ring-closure/dehydration reaction of **C** easily occurs in

the presence of acetic acid and then the corresponding furo- and thieno-triazolopyridines **5–8** would be produced.



Scheme 2

To confirm the structures of furo- and thieno-triazolopyridines, we synthesized compounds **6a** and **8a** by an alternative route (Scheme 3).<sup>10</sup> Thus, the reaction of enamines **3a** and **4a** with hydrazine monohydrochloride in refluxing methanol gave the corresponding 1,2-diaminopyridinium salts **9** (88%) and **10** (64%). Compounds **9** and **10** were readily reacted with benzaldehyde in the presence of sodium methoxide at room temperature to yield **6a** (60%) and **8a** (69%), which were identical with authentic samples prepared according to Scheme 1 on the basis of a comparison of the melting points, IR, and NMR spectra.



Scheme 3

In conclusion, we have demonstrated the synthesis of novel furo- and thieno-triazolopyridines **5–8** starting from 4,5-dihydro-3-furan- and -3-thiophene-carbonitriles **1** and **2** having an active methylene group at C-2 position through a domino reaction. The key exchange reaction of amines and subsequent tandem intramolecular cyclization of enamines **3** and **4** with acetohydrazide and/or benzohydrazide

proceeds smoothly to furnish the corresponding furo- and thieno-triazolopyridines **5–8**. Functionalized nitrogen-containing heterocycles are important synthons in organic synthesis and for the preparation of biologically active compounds with interest in medicinal chemistry.

## EXPERIMENTAL

All melting points are uncorrected. The IR spectra were recorded on a JASCO FT/IR-4100 spectrometer. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were measured with a JEOL JNM-A500 spectrometer at 500.00 and 125.65 MHz, respectively. The  $^1\text{H}$  and  $^{13}\text{C}$  chemical shifts ( $\delta$ ) are reported in parts per million (ppm) relative to TMS as internal standard. Positive(+) or negative(-) FAB MS spectra were obtained on a JEOL JMS-700T spectrometer. Elemental analyses were performed on YANACO MT-6 CHN analyzer. The starting compounds **1a,b** and **2a,b** were prepared in this laboratory according to the procedure reported in literature.<sup>8a</sup>

**The preparation of enamines 3a and 4a from 1a and/or 2a and DMFDMA.** A solution of **1a** and/or **2a** (20 mmol) and DMFDMA (2.86 g, 24 mmol) was stirred at 80 °C for 2 h. After removal of MeOH *in vacuo*, the residue was purified by column chromatography on alumina with Et<sub>2</sub>O as the eluent to afford **3a** and **4a**.

**Methyl 3-cyano-4,5-dihydro- $\alpha$ -[(dimethylamino)methylene]-2-furanacetate (3a):** Colorless columns (2.59 g, 58%), mp 123–124 °C (acetone/petroleum ether); IR (KBr):  $\nu$  2200 (CN), 1686 cm<sup>-1</sup> (CO);  $^1\text{H}$  NMR (CDCl<sub>3</sub>):  $\delta$  3.02 [br s, 6H, N(CH<sub>3</sub>)<sub>2</sub>], 2.96 (t,  $J$  = 9.6 Hz, 2H, 4-H), 3.71 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 4.51 (t,  $J$  = 9.6 Hz, 2H, 5-H), 7.60 (s, 1H, olefin H);  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>):  $\delta$  30.4 (C-4), 39.2, 46.8 [N(CH<sub>3</sub>)<sub>2</sub>], 51.4 (CO<sub>2</sub>CH<sub>3</sub>), 70.4 (C-5), 85.6 [C=CHN(CH<sub>3</sub>)<sub>2</sub>], 85.7 (C-3), 116.9 (CN), 153.9 [C=CHN(CH<sub>3</sub>)<sub>2</sub>], 167.47 (CO), 167.51 (C-2); FAB(+) MS:  $m/z$  223 [M+H]<sup>+</sup>. Anal. Calcd for C<sub>11</sub>H<sub>14</sub>N<sub>2</sub>O<sub>3</sub>: C, 59.45; H, 6.35; N, 12.60. Found: C, 59.26; H, 6.33; N, 12.41.

**Methyl 3-cyano-4,5-dihydro- $\alpha$ -[(dimethylamino)methylene]-2-thiopheneacetate (4a):** Pale yellow prisms (2.76 g, 58%), mp 95–96 °C (dec.) (Et<sub>2</sub>O); IR (KBr):  $\nu$  2202 (CN), 1685 cm<sup>-1</sup> (CO);  $^1\text{H}$  NMR (CDCl<sub>3</sub>):  $\delta$  3.04 [s, 6H, N(CH<sub>3</sub>)<sub>2</sub>], 3.06 (br s, 2H, 4-H), 3.34 (br s, 2H, 5-H), 3.70 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 7.56 (s, 1H, olefin H);  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>):  $\delta$  32.5 (C-4), 36.1 (C-5), 42.4 [N(CH<sub>3</sub>)<sub>2</sub>], 51.3 (CO<sub>2</sub>CH<sub>3</sub>), 87.7 (C-3), 103.2 [C=CHN(CH<sub>3</sub>)<sub>2</sub>], 116.2 (CN), 152.5 [C=CHN(CH<sub>3</sub>)<sub>2</sub>], 159.1 (C-2), 167.6 (CO); FAB(+) MS:  $m/z$  239 [M+H]<sup>+</sup>. Anal. Calcd for C<sub>11</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>S: C, 55.44; H, 5.92; N, 11.76. Found: C, 55.38; H, 5.99; N, 11.74.

**General procedure for the preparation of furo- and thieno-triazolopyridines 5–8 from enamines 3 and/or 4 and acetohydrazide and/or benzohydrazide.**

**Procedure A.** A mixture of **3a** (1.11 g, 5 mmol), acetohydrazide (0.74 g, 10 mmol), and AcOH (0.30 g, 5 mmol) in MeOH (10 mL) was refluxed for 3 h. After removal of the solvent *in vacuo*, cold water was

added to the residue. The precipitate was collected by filtration, washed with water, dried, and recrystallized from MeOH to give **5a**.

**Procedure B.** A solution of **3b** or **4a,b** (5 mmol) and acetohydrazide (0.74 g, 10 mmol) in AcOH (10 mL) was refluxed for 0.5 h. After work-up as described above, **5b** and **7a,b** were obtained.

**Procedure C.** A solution of **3a,b** or **4a,b** (5 mmol) and benzohydrazide (0.68 g, 5 mmol) in AcOH (10 mL) was refluxed for 0.5 h. After work-up as described above, **6a,b** and **8a,b** were obtained.

**Methyl 8,9-dihydro-2-methylfuro[3,2-*c*][1,2,4]triazolo[1,5-*a*]pyridine-6-carboxylate (5a):** Colorless needles (0.93 g, 79%), mp 198–199 °C (MeOH); IR (KBr):  $\nu$  1713 (CO)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  2.56 (s, 3H,  $\text{CH}_3$ ), 3.46–3.51 (m, 2H, 9-H), 3.96 (s, 3H,  $\text{CO}_2\text{CH}_3$ ), 4.91–4.95 (m, 2H, 8-H), 8.97 (s, 1H, 5-H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  14.5 ( $\text{CH}_3$ ), 27.0 (C-9), 52.5 ( $\text{CO}_2\text{CH}_3$ ), 74.0 (C-8), 105.8 (C-6), 109.4 (C-9a), 131.7 (C-5), 151.0 (C-9b), 160.0 (C-6a), 163.1 (CO), 166.7 (C-2); FAB(+) MS:  $m/z$  234  $[\text{M}+\text{H}]^+$ . Anal. Calcd for  $\text{C}_{11}\text{H}_{11}\text{N}_3\text{O}_3$ : C, 56.65; H, 4.75; N, 18.02. Found: C, 56.49; H, 4.77; N, 18.05.

**8,9-Dihydro-2-methylfuro[3,2-*c*][1,2,4]triazolo[1,5-*a*]pyridine-6-carbonitrile (5b):** Colorless needles (0.36 g, 36%), mp 270–271 °C (MeOH); IR (KBr):  $\nu$  2237 (CN)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{DMSO-}d_6$ ):  $\delta$  2.44 (s, 3H,  $\text{CH}_3$ ), 3.43 (t,  $J = 9.2$  Hz, 2H, 9-H), 4.92 (t,  $J = 9.2$  Hz, 2H, 8-H), 9.46 (s, 1H, 5-H);  $^{13}\text{C}$  NMR ( $\text{DMSO-}d_6$ ):  $\delta$  13.8 ( $\text{CH}_3$ ), 26.9 (C-9), 74.4 (C-8), 86.2 (C-6), 108.8 (C-9a), 112.8 (CN), 134.2 (C-5), 150.2 (C-9b), 159.1 (C-6a), 165.9 (C-2); FAB(+) MS:  $m/z$  201  $[\text{M}+\text{H}]^+$ . Anal. Calcd for  $\text{C}_{10}\text{H}_8\text{N}_4\text{O}$ : C, 59.99; H, 4.03; N, 27.99. Found: C, 59.78; H, 4.09; N, 27.92.

**Methyl 8,9-dihydro-2-phenylfuro[3,2-*c*][1,2,4]triazolo[1,5-*a*]pyridine-6-carboxylate (6a):** Colorless needles (1.24 g, 84%), mp 206–208 °C (MeOH); IR (KBr):  $\nu$  1710 (CO)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{DMSO-}d_6$ ):  $\delta$  3.46 (t,  $J = 9.2$  Hz, 2H, 9-H), 3.87 (s, 3H,  $\text{CO}_2\text{CH}_3$ ), 4.89 (t,  $J = 9.2$  Hz, 2H, 8-H), 7.52–7.55 (m, 3H, aryl H), 8.17–8.19 (m, 2H, aryl H), 9.20 (s, 1H, 5-H);  $^{13}\text{C}$  NMR ( $\text{DMSO-}d_6$ ):  $\delta$  26.6 (C-9), 52.3 ( $\text{CO}_2\text{CH}_3$ ), 73.7 (C-8), 105.9 (C-6), 109.9 (C-9a), 126.9, 128.8, 130.1, 130.4 (C aryl), 131.9 (C-5), 150.9 (C-9b), 159.4 (C-6a), 162.5 (CO), 165.2 (C-2); FAB(+) MS:  $m/z$  296  $[\text{M}+\text{H}]^+$ . Anal. Calcd for  $\text{C}_{16}\text{H}_{13}\text{N}_3\text{O}_3$ : C, 65.08; H, 4.44; N, 14.23. Found: C, 64.93; H, 4.55; N, 14.24.

**8,9-Dihydro-2-phenylfuro[3,2-*c*][1,2,4]triazolo[1,5-*a*]pyridine-6-carbonitrile (6b):** Colorless needles (0.68 g, 52%), mp 239–240 °C (acetone); IR (KBr):  $\nu$  2241 (CN)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{DMSO-}d_6$ ):  $\delta$  3.51 (t,  $J = 9.5$  Hz, 2H, 9-H), 4.95 (t,  $J = 9.5$  Hz, 2H, 8-H), 7.51–7.54 (m, 3H, aryl H), 8.15–8.18 (m, 2H, aryl H), 9.59 (s, 1H, 5-H);  $^{13}\text{C}$  NMR ( $\text{DMSO-}d_6$ ):  $\delta$  27.0 (C-9), 74.5 (C-8), 87.0 (C-6), 109.5 (C-9a), 112.7 (CN), 126.8, 128.6, 129.6, 130.4 (C aryl), 134.7 (C-5), 150.8 (C-9b), 159.5 (C-6a), 165.4 (C-2); FAB(+) MS:  $m/z$  263  $[\text{M}+\text{H}]^+$ . Anal. Calcd for  $\text{C}_{15}\text{H}_{10}\text{N}_4\text{O}$ : C, 68.69; H, 3.84; N, 21.36. Found: C, 68.56; H, 3.96; N, 21.33.

**Methyl 8,9-dihydro-2-methylthieno[3,2-*c*][1,2,4]triazolo[1,5-*a*]pyridine-6-carboxylate (7a):** Colorless needles (0.57 g, 45%), mp 160–161 °C ( $\text{CH}_2\text{Cl}_2$ /petroleum ether); IR (KBr):  $\nu$  1712 (CO)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR

(CDCl<sub>3</sub>):  $\delta$  2.46 (s, 3H, CH<sub>3</sub>), 3.48 (s, 4H, 8- and 9-H), 3.89 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 9.10 (s, 1H, 5-H); <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  13.9 (CH<sub>3</sub>), 31.98 (C-9), 32.07 (C-8), 52.3 (CO<sub>2</sub>CH<sub>3</sub>), 111.9 (C-6), 123.8 (C-9a), 130.1 (C-5), 144.7 (C-6a), 148.9 (C-9b), 163.7 (CO), 165.4 (C-2); FAB(+) MS:  $m/z$  250 [M+H]<sup>+</sup>. Anal. Calcd for C<sub>11</sub>H<sub>11</sub>N<sub>3</sub>O<sub>2</sub>S: C, 53.00; H, 4.45; N, 16.86. Found: C, 52.84; H, 4.56; N, 16.78.

**8,9-Dihydro-2-methylthieno[3,2-*c*][1,2,4]triazolo[1,5-*a*]pyridine-6-carbonitrile (7b):** Colorless needles (0.72 g, 67%), mp 253–254 °C (CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr):  $\nu$  2232 (CN) cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  2.47 (s, 3H, CH<sub>3</sub>), 3.56–3.60 (m, 2H, 9-H), 3.71–3.75 (m, 2H, 8-H), 9.56 (s, 1H, 5-H); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>):  $\delta$  14.0 (CH<sub>3</sub>), 33.4 (C-9), 33.6 (C-8), 93.8 (C-6), 115.0 (CN), 124.4 (C-9a), 134.0 (C-5), 144.8 (C-6a), 148.9 (C-9b), 165.7 (C-2); FAB(+) MS:  $m/z$  217 [M+H]<sup>+</sup>. Anal. Calcd for C<sub>10</sub>H<sub>8</sub>N<sub>4</sub>S: C, 55.54; H, 3.73; N, 25.91. Found: C, 55.58; H, 3.71; N, 25.89.

**Methyl 8,9-dihydro-2-phenylthieno[3,2-*c*][1,2,4]triazolo[1,5-*a*]pyridine-6-carboxylate (8a):** Colorless needles (1.40 g, 90%), mp 169–170 °C (acetone); IR (KBr):  $\nu$  1719 (CO) cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  3.49–3.57 (m, 4H, 8- and 9-H), 3.89 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 7.51–7.54 (m, 3H, aryl H), 8.16–8.18 (m, 2H, aryl H), 9.20 (s, 1H, 5-H); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>):  $\delta$  32.1 (C-8), 32.2 (C-9), 52.4 (CO<sub>2</sub>CH<sub>3</sub>), 112.5 (C-6), 124.4 (C-9a), 126.8, 128.6, 129.9, 130.3 (C aryl), 130.6 (C-5), 145.3 (C-6a), 149.4 (C-9b), 163.6 (CO), 164.9 (C-2); FAB(+) MS:  $m/z$  312 [M+H]<sup>+</sup>. Anal. Calcd for C<sub>16</sub>H<sub>13</sub>N<sub>3</sub>O<sub>2</sub>S: C, 61.72; H, 4.21; N, 13.50. Found: C, 61.62; H, 4.26; N, 13.42.

**8,9-Dihydro-2-phenylthieno[3,2-*c*][1,2,4]triazolo[1,5-*a*]pyridine-6-carbonitrile (8b):** Colorless needles (0.86 g, 62%), mp 249–250 °C (CH<sub>2</sub>Cl<sub>2</sub>); IR (KBr):  $\nu$  2234 (CN) cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  3.64–3.67 (m, 2H, 9-H), 3.74–3.77 (m, 2H, 8-H), 7.52–7.55 (m, 3H, aryl H), 8.14–8.17 (m, 2H, aryl H), 9.66 (s, 1H, 5-H); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>):  $\delta$  33.5 (C-8), 33.7 (C-9), 94.4 (C-6), 114.9 (CN), 125.0 (C-9a), 127.0, 128.9, 129.5, 130.7 (C aryl), 134.4 (C-5), 145.4 (C-6a), 149.4 (C-9b), 165.0 (C-2); FAB(+) MS:  $m/z$  279 [M+H]<sup>+</sup>. Anal. Calcd for C<sub>15</sub>H<sub>10</sub>N<sub>4</sub>S: C, 64.73; H, 3.62; N, 20.13. Found: C, 64.77; H, 3.61; N, 20.05.

**The preparation of diaminopyridinium salts 9 and 10 from 3a and/or 4a and hydrazine monohydrochloride.** A mixture of **3a** or **4a** (5 mmol) and hydrazine monohydrochloride (0.45 g, 6.5 mmol, in the case of the reaction of **3a**) or (0.69 g, 10 mmol, in the case of the reaction of **4a**) in MeOH (10 mL) was refluxed for 2 h (in the case of **3a**) or for 4 h (in the case of **4a**). After removal of the solvent *in vacuo*, Et<sub>2</sub>O was added to the residue. The precipitate was collected by filtration, washed with Et<sub>2</sub>O, dried, and recrystallization from MeOH to give **9** and **10**.

**4,5-Diamino-2,3-dihydro-7-(methoxycarbonyl)furo[3,2-*c*]pyridinium chloride (9):** Colorless prisms (1.08 g, 88%), mp 281–283 °C (dec.) (MeOH); IR (KBr):  $\nu$  3271, 3186 (NH<sub>2</sub>), 1732 (CO) cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  3.13 (t,  $J$  = 9.3 Hz, 2H, 3-H), 3.82 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 4.92 (t,  $J$  = 9.3 Hz, 2H, 2-H), 6.80 (br s, 2H, NH<sub>2</sub>), 8.46 (br s, 2H, NH<sub>2</sub>), 8.53 (s, 1H, 6-H); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>):  $\delta$  28.4 (C-3), 55.8 (CO<sub>2</sub>CH<sub>3</sub>),

79.2 (C-2), 106.9 (C-7), 111.3 (C-3a), 150.4 (C-6), 156.3 (C-4), 166.4 (CO), 170.0 (C-7a); FAB(-) MS:  $m/z$  244 [M-H]<sup>-</sup>. Anal. Calcd for C<sub>9</sub>H<sub>12</sub>ClN<sub>3</sub>O<sub>3</sub>: C, 44.00; H, 4.92; N, 17.10. Found: C, 43.97; H, 4.90; N, 16.98.

**4,5-Diamino-2,3-dihydro-7-(methoxycarbonyl)thieno[3,2-c]pyridinium chloride (10):** Pale yellow prisms (0.72 g, 64%), mp 283–285 °C (dec.) (MeOH); IR (KBr):  $\nu$  3287, 3243 (NH<sub>2</sub>), 1715 (CO) cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  3.26 (t,  $J$  = 8.9 Hz, 2H, 3-H), 3.51 (t,  $J$  = 8.9 Hz, 2H, 2-H), 3.86 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 6.89 (br s, 2H, NH<sub>2</sub>), 8.54 (br s, 2H, NH<sub>2</sub>), 8.57 (s, 1H, 6-H); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>):  $\delta$  31.8 (C-3), 32.1 (C-2), 52.7 (CO<sub>2</sub>CH<sub>3</sub>), 109.2 (C-7), 121.3 (C-3a), 143.6 (C-6), 149.6 (C-4), 158.0 (C-7a), 162.7 (CO); FAB(+) MS:  $m/z$  226 [M-HCl+H]<sup>+</sup>. Anal. Calcd for C<sub>9</sub>H<sub>12</sub>ClN<sub>3</sub>O<sub>2</sub>S: C, 41.30; H, 4.62; N, 16.05. Found: C, 41.18. H, 4.58; N, 16.10.

**The preparation of furo- and thieno-triazolopyridines 6a and 8a from 9 and/or 10 and benzaldehyde.** A mixture of **9** or **10** (5 mmol), benzaldehyde (1.06 g, 10 mmol), and sodium methoxide (0.41 g, 7.5 mmol) in MeOH (50 mL) was stirred at rt for 1 h. After removal of the solvent *in vacuo*, cold water was added to the residue. The precipitate was collected by filtration, washed with water, dried, and recrystallized from an appropriate solvent to afford **6a** (0.89 g, 60%) and **8a** (1.08 g, 69%). The melting points, IR, and NMR spectra of these compounds coincided with authentic samples prepared from **3a** and/or **4a** and benzohydrazide.

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