HETEROCYCLES, Vol. 89, No. 4, 2014, pp. 1025 - 1034. © 2014 The Japan Institute of Heterocyclic Chemistry
Received, 6th January, 2014, Accepted, 5th February, 2014, Published online, 7th February, 2014
DOI: 10.3987/COM-14-12931

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,[1] their biological properties,[2] and their utilities as intermediates for the design of biologically active compounds.[3] Therefore, a large number of general methods for the preparation of pyridine derivatives have recently been reported.[4] On the other hand, heterocycles containing triazole ring systems also occur in a wide variety of natural and biologically active compounds.[5] 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.[6]

In the course of our investigation of the synthesis of heterobicycles,[7] we have shown the synthesis of fused thiopyranthiones,[8a] thiophenes,[8a] pyridines,[8b] and pyridinones[8b] 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**.

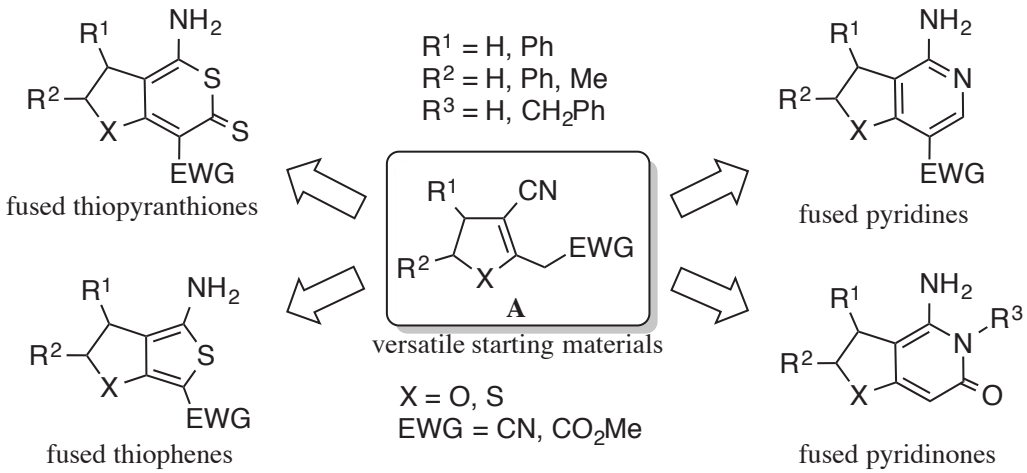
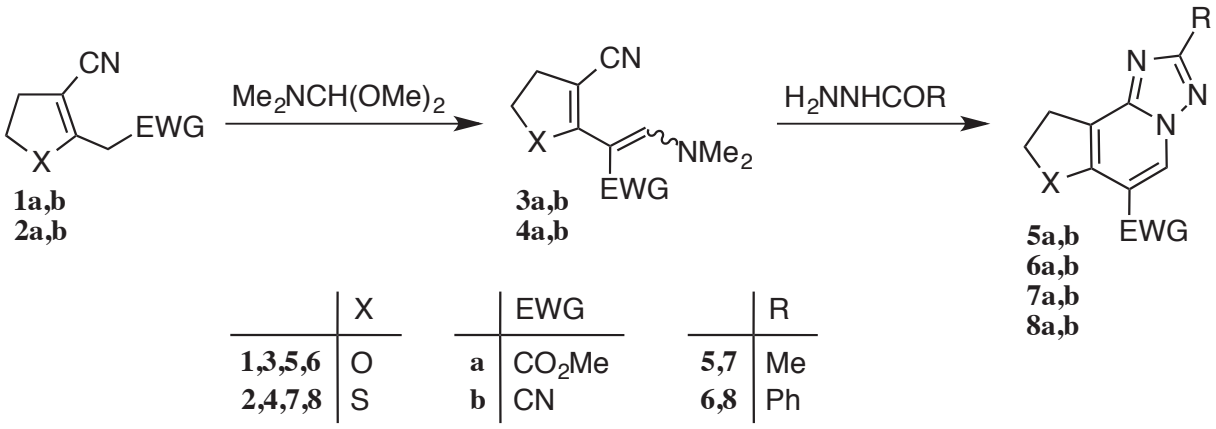


Figure 1. Structures of reported heterobicycles

Initially, we examined condensation reaction of methyl 3-cyano-4,5-dihydro-2-furan- and -2-thiophene-acetates **1a** and **2a** with *N*,*N*-dimethylformamide dimethyl acetal[9] (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.[8a] 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	**1a**	O	CO_2Me	**3a**	58
2	**1b**	O	CN	**3b**	57[8b]
3	**2a**	S	CO_2Me	**4a**	58
4	**2b**	S	CN	**4b**	48[8b]

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

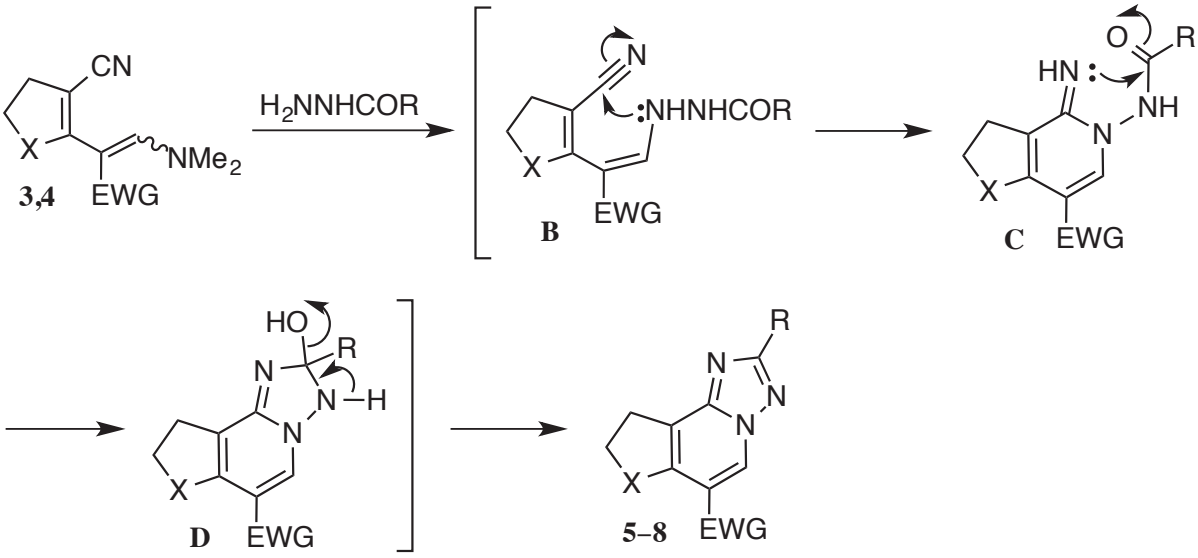
Entry	Substrate	X	R	EWG	Product	Yield (%)
1	**3a**	O	Me	CO_2Me	**5a**	79[a]
2	**3b**	O	Me	CN	**5b**	36[b]
3	**3a**	O	Ph	CO_2Me	**6a**	84[c]
4	**3b**	O	Ph	CN	**6b**	52[c]
5	**4a**	S	Me	CO_2Me	**7a**	45[b]
6	**4b**	S	Me	CN	**7b**	67[b]
7	**4a**	S	Ph	CO_2Me	**8a**	90[c]
8	**4b**	S	Ph	CN	**8b**	62[c]

Reaction Conditions: [a]acetohydrazide (2 equiv.), AcOH (1 equiv.), MeOH, reflux, 3 h. [b]acetohydrazide (2 equiv.), AcOH, reflux, 0.5 h. [c]benzohydrazide (1 equiv.), AcOH, reflux, 0.5 h.

Elemental analyses, MS spectra, ^1H and ^{13}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^{-1} due to an ester carbonyl group. The ^1H NMR spectrum of **5a** in $CDCl_3$ 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 ^{13}C NMR spectrum of **5a** in $CDCl_3$ 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.

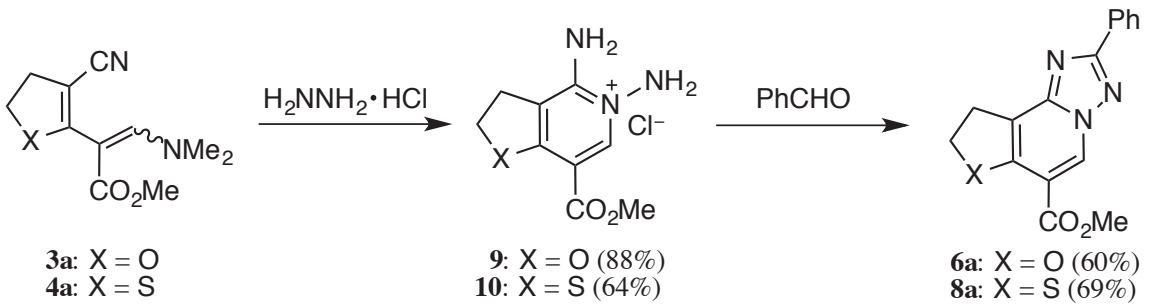
A plausible mechanism for the formation of the furo- and thieno-triazolopyridines **5–8** is shown in Scheme 2. Thermal treatment of enamines **3** and **4** with hydrazides probably causes an exchange reaction of amines to give the non-isolable intermediate **B**, which underwent *in situ* cyclization 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).[10] 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.



3a: X = O
4a: X = S

9: X = O (88%)
10: X = S (64%)

6a: X = O (60%)
8a: X = S (69%)

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 heterotricycles 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}H and ^{13}C NMR spectra were measured with a JEOL JNM-A500 spectrometer at 500.00 and 125.65 MHz, respectively. The ^{1}H and ^{13}C chemical shifts (δ) 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.[8a]

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_2O as the eluent to afford **3a** and **4a**.

Methyl 3-cyano-4,5-dihydro-α-[(dimethylamino)methylene]-2-furanacetate (3a): Colorless columns (2.59 g, 58%), mp 123–124 °C (acetone/petroleum ether); IR (KBr): ν 2200 (CN), 1686 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$): δ 3.02 [br s, 6H, $N(CH_3)_2$] , 2.96 (t, J = 9.6 Hz, 2H, 4-H), 3.71 (s, 3H, CO_2CH_3), 4.51 (t, J = 9.6 Hz, 2H, 5-H), 7.60 (s, 1H, olefin H); ^{13}C NMR ($CDCl_3$): δ 30.4 (C-4), 39.2, 46.8 [$N(CH_3)_2$], 51.4 (CO_2CH_3), 70.4 (C-5), 85.6 [C=CHN$(CH_3)_2$], 85.7 (C-3), 116.9 (CN), 153.9 [C=CHN$(CH_3)_2$], 167.47 (CO), 167.51 (C-2); FAB(+) MS: m/z 223 $[M+H]^+$. Anal. Calcd for $C_{11}H_{14}N_2O_3$: 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-α-[(dimethylamino)methylene]-2-thiopheneacetate (4a): Pale yellow prisms (2.76 g, 58%), mp 95–96 °C (dec.) (Et_2O); IR (KBr): ν 2202 (CN), 1685 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$): δ 3.04 [s, 6H, $N(CH_3)_2$], 3.06 (br s, 2H, 4-H), 3.34 (br s, 2H, 5-H), 3.70 (s, 3H, CO_2CH_3), 7.56 (s, 1H, olefin H); ^{13}C NMR ($CDCl_3$): δ 32.5 (C-4), 36.1 (C-5), 42.4 [$N(CH_3)_2$], 51.3 (CO_2CH_3), 87.7 (C-3), 103.2 [C=CHN$(CH_3)_2$], 116.2 (CN), 152.5 [C=CHN$(CH_3)_2$], 159.1 (C-2), 167.6 (CO); FAB(+) MS: m/z 239 $[M+H]^+$. Anal. Calcd for $C_{11}H_{14}N_2O_2S$: 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): ν 1713 (CO) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.56 (s, 3H, CH_3), 3.46–3.51 (m, 2H, 9-H), 3.96 (s, 3H, CO_2CH_3), 4.91–4.95 (m, 2H, 8-H), 8.97 (s, 1H, 5-H); ^{13}C NMR ($CDCl_3$): δ 14.5 (CH_3), 27.0 (C-9), 52.5 (CO_2CH_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 $[M+H]^+$. Anal. Calcd for $C_{11}H_{11}N_3O_3$: 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): ν 2237 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.44 (s, 3H, 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}C NMR (DMSO-d_6): δ 13.8 (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 $[M+H]^+$. Anal. Calcd for $C_{10}H_8N_4O$: 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): ν 1710 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.46 (t, *J* = 9.2 Hz, 2H, 9-H), 3.87 (s, 3H, CO_2CH_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}C NMR (DMSO-d_6): δ 26.6 (C-9), 52.3 (CO_2CH_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 $[M+H]^+$. Anal. Calcd for $C_{16}H_{13}N_3O_3$: 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): ν 2241 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 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}C NMR (DMSO-d_6): δ 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 $[M+H]^+$. Anal. Calcd for $C_{15}H_{10}N_4O$: 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 (CH_2Cl_2/petroleum ether); IR (KBr): ν 1712 (CO) cm^{-1}; ^1H NMR

($CDCl_3$): δ 2.46 (s, 3H, CH_3), 3.48 (s, 4H, 8- and 9-H), 3.89 (s, 3H, CO_2CH_3), 9.10 (s, 1H, 5-H); ^{13}C NMR ($CDCl_3$): δ 13.9 (CH_3), 31.98 (C-9), 32.07 (C-8), 52.3 (CO_2CH_3), 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 $[M+H]^+$. Anal. Calcd for $C_{11}H_{11}N_3O_2S$: 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_2Cl_2); IR (KBr): ν 2232 (CN) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.47 (s, 3H, CH_3), 3.56–3.60 (m, 2H, 9-H), 3.71–3.75 (m, 2H, 8-H), 9.56 (s, 1H, 5-H); ^{13}C NMR (DMSO-d_6): δ 14.0 (CH_3), 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 $[M+H]^+$. Anal. Calcd for $C_{10}H_8N_4S$: 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): ν 1719 (CO) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 3.49–3.57 (m, 4H, 8- and 9-H), 3.89 (s, 3H, CO_2CH_3), 7.51–7.54 (m, 3H, aryl H), 8.16–8.18 (m, 2H, aryl H), 9.20 (s, 1H, 5-H); ^{13}C NMR (DMSO-d_6): δ 32.1 (C-8), 32.2 (C-9), 52.4 (CO_2CH_3), 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 $[M+H]^+$. Anal. Calcd for $C_{16}H_{13}N_3O_2S$: 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_2Cl_2); IR (KBr): ν 2234 (CN) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 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); ^{13}C NMR (DMSO-d_6): δ 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 $[M+H]^+$. Anal. Calcd for $C_{15}H_{10}N_4S$: 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_2O was added to the residue. The precipitate was collected by filtration, washed with Et_2O, 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): ν 3271, 3186 (NH_2), 1732 (CO) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 3.13 (t, J = 9.3 Hz, 2H, 3-H), 3.82 (s, 3H, CO_2CH_3), 4.92 (t, J = 9.3 Hz, 2H, 2-H), 6.80 (br s, 2H, NH_2), 8.46 (br s, 2H, NH_2), 8.53 (s, 1H, 6-H); ^{13}C NMR (DMSO-d_6): δ 28.4 (C-3), 55.8 (CO_2CH_3),

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 $[M-H]^-$. Anal. Calcd for $C_9H_{12}ClN_3O_3$: 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): ν 3287, 3243 (NH_2), 1715 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 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_2CH_3), 6.89 (br s, 2H, NH_2), 8.54 (br s, 2H, NH_2), 8.57 (s, 1H, 6-H); ^{13}C NMR (DMSO-d_6): δ 31.8 (C-3), 32.1 (C-2), 52.7 (CO_2CH_3), 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 $[M-HCl+H]^+$. Anal. Calcd for $C_9H_{12}ClN_3O_2S$: 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.

ACKNOWLEDGEMENTS

The authors thank Hiroshi Hanazono and Yukiko Iwase for obtaining MS and NMR spectra and Junko Honda for her valuable help with elemental analyses.

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