HETEROCYCLES, Vol. 82, No. 1, 2010, pp. 867 - 880. © The Japan Institute of Heterocyclic Chemistry
Received, 7th June, 2010, Accepted, 6th July, 2010, Published online, 7th July, 2010
DOI: 10.3987/COM-10-S(E)47

A CONVENIENT APPROACH TO THE SYNTHESIS OF FURO- AND THIENO-[3,2-*c*]PYRIDINE DERIVATIVES

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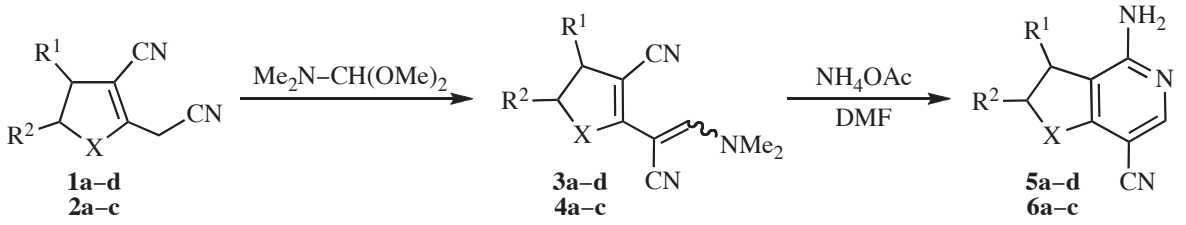
Abstract – The title compounds were prepared from 4,5-dihydro-3-furan- and -3-thiophene-carbonitriles having an active methylene group at C-2 position **1**, **2**, **7**, and **8** as key starting materials. Compounds **1** and **2** condensed with *N,N*-dimethylformamide dimethyl acetal to give the corresponding enamines **3** and **4**. This condensation was followed by exchange reaction of amines and subsequent intramolecular cyclization reaction in the presence of ammonium acetate to lead the corresponding furo- and thieno-[3,2-*c*]pyridines **5** and **6**. On the other hand, the reactions of compounds **7** and **8** with amines such as aqueous ammonium hydroxide and benzylamine afforded the intermediate acetamide derivatives **A**, without isolation of them, which underwent intramolecular cyclization reaction in the presence of sodium methoxide to yield the corresponding furo- and thieno-[3,2-*c*]pyridin-6(2*H*)-ones **9–12**.

In many biologically active compounds, the pyridine core is a privileged substructure. Pyridines are basic structural motifs found in numerous products with interesting medicinal properties such as antimicrobial, myasthenia gravis, multiple sclerosis, spinal cord injuries, botulism, antibacterial, and antifungal.[1-6] Among pyridine derivatives, fused analogues are often of much greater interest biologically than the corresponding monocyclic compounds. Some heterocyclic compounds containing condensed pyridines such as furo- and thieno-[3,2-*c*]pyridines possess a wide spectrum of pharmacological action.[7-12] Hence, the preparation and biological properties of new substituted furo- and thieno-[3,2-*c*]pyridines are of interest.[13-21] The preparation of furo[3,2-*c*]pyridines was first described by Herz and Tocker, who applied Bischler-Napieralski reaction to *N*-acyl derivatives of β-(2-furyl)ethylamine.[22] In addition, thieno[3,2-*c*]pyridines were mentioned for the first time by Steinkopf and Lützkendorf using Skraup reaction starting from 2-aminothiophene.[23]

This paper is dedicated to Prof. Dr. Albert Eschenmoser on the occasion of his 85th birthday.

Although many synthetic methods for such furo- and thieno-[3,2-*c*]pyridines have been reported, there are relatively few methods in the literature describing the preparation of partially hydrogenated furo- and thieno-[3,2-*c*]pyridines.[24-29] Interestingly, hydrogenated heterobicycles are also an important class of natural products and have potential uses in many fields. For example, it is known that the partially hydrogenated furo[2,3-*b*]furan ring is embodied in large number of natural products, particularly in some insect antifeeding compounds such as clerodin and azadirachtin.[30-33] In this context, the preparation and biological properties of new partially hydrogenated heterobicycles such as furo- and thieno-[3,2-*c*]pyridines continues to attract attention and provides an interesting challenge. In the course of our investigation of the synthesis of heterobicycles,[34-37] we have shown the synthesis of fused thiopyranthione and thiophene derivatives from 4,5-dihydro-3-furan- and -3-thiophene-carbonitriles having an active methylene group at C-2 position **1**, **2**, **7**, and **8** as versatile starting materials.[38] To further extend the utility of them, we herein describe a convenient procedure for the synthesis of furo- and thieno-[3,2-*c*]pyridine derivatives **5**, **6**, and **9–12** from key starting materials **1**, **2**, **7**, and **8**.



1a–d **2a–c** **3a–d** **4a–c** **5a–d** **6a–c**

a: R^1 = H, R^2 = H **b**: R^1 = Ph, R^2 = H **c**: R^1 = H, R^2 = Me **d**: R^1 = H, R^2 = Ph

1,3,5: X = O **2,4,6**: X = S

Scheme 1

Initially, we examined condensation reaction of 3-cyano-4,5-dihydro-2-furan- and -2-thiophene-acetonitriles **1a–d** and **2a–c** with *N*,*N*-dimethylformamide dimethyl acetal[39-42] (DMFDMA). Compounds **1a–d** and **2a–c** were easily prepared by Wittig reaction of tetrahydro-2-oxo-3-furan- and -3-thiophene-carbonitriles with (triphenylphosphoranylidene)acetonitrile according to our previous procedure.[38] The reaction of compounds **1a–d** and **2a–c** with DMFDMA resulted in the formation of enamines **3a–d** and **4a–c** with 48–65% isolated yields (Scheme 1 and Table 1). Treatment of **3a–d** and **4a–c** with ammonium acetate[39] followed by exchange reaction of amines effected intramolecular cyclization reaction to lead the corresponding furo- and thieno-[3,2-*c*]pyridines **5a–d** and **6a–c** in moderate yields (Scheme 1 and Table 2). Elemental analyses, MS spectra, ^{1}H and ^{13}C NMR spectra of compounds **3–6** are consistent with the assigned structures (see experimental section). For example, the IR spectra of **3** and **4** display bands in the range of 2205–2170 cm^{-1} due to two conjugated cyano groups. The ^{1}H NMR spectra of **3** and **4** exhibit a signal near δ 7.4 attributable to the olefin proton of the (dimethylamino)methylene. The ^{13}C NMR spectra

of **3** and **4** show a signal near δ 153 due to the olefin carbon of the (dimethylamino)methylene. The IR spectra of **5** and **6** display bands in the range of 3450–3105 cm^{-1} due to a primary amino group. The ^1H NMR spectra of **5** and **6** exhibit a D_2O exchangeable signal near δ 6.7 attributable to the primary amino protons.

Table 1. Synthesis of enamines **3** and **4** according to Scheme 1

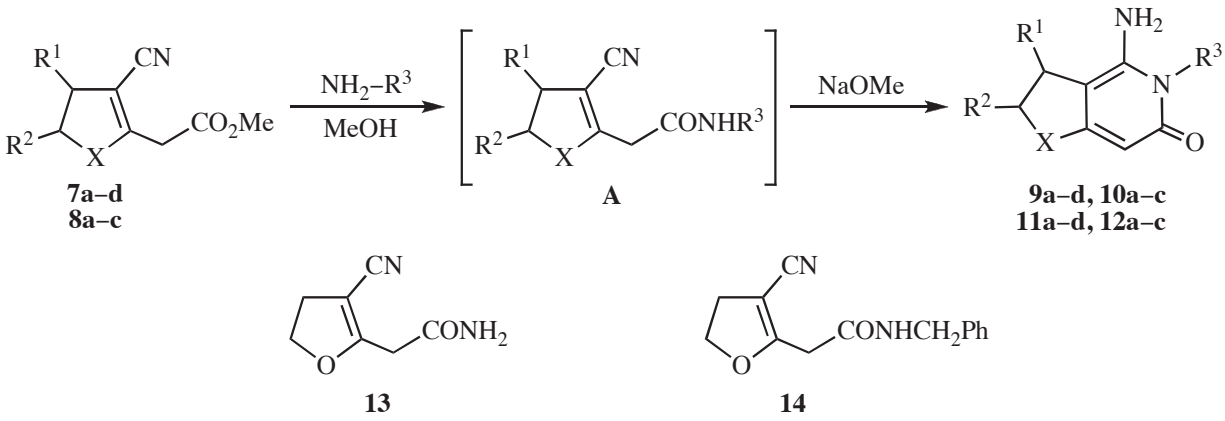
Entry	Substrate	X	R^1	R^2	Product	Yield (%)
1	**1a**	O	H	H	**3a**	57
2	**1b**	O	Ph	H	**3b**	58
3	**1c**	O	H	Me	**3c**	60
4	**1d**	O	H	Ph	**3d**	62
5	**2a**	S	H	H	**4a**	48
6	**2b**	S	Ph	H	**4b**	65
7	**2c**	S	H	Me	**4c**	50

Table 2. Synthesis of furo- and thieno-[3,2-*c*]pyridines **5** and **6** according to Scheme 1

Entry	Substrate	X	R^1	R^2	Product	Yield (%)
1	**3a**	O	H	H	**5a**	67
2	**3b**	O	Ph	H	**5b**	80
3	**3c**	O	H	Me	**5c**	57
4	**3d**	O	H	Ph	**5d**	72
5	**4a**	S	H	H	**6a**	76
6	**4b**	S	Ph	H	**6b**	89
7	**4c**	S	H	Me	**6c**	66

In the next step, we also attempted aminolysis/cyclization reaction of methyl 3-cyano-4,5-dihydro-2-furan- and -2-thiophene-acetates **7a–d** and **8a–c**[38] with amines (Scheme 2). First the aminolysis parameters were optimized and second the base sodium methoxide was investigated because of its ease of handling. As a consequence, the reaction of compound **7a** with aqueous ammonium hydroxide and/or benzylamine in MeOH at room temperature for 24 h led to the corresponding acetamide derivatives **13** (68%) and **14** (73%). Treatment of **13** and **14** with sodium methoxide in MeOH at room temperature for 1 h caused intramolecular cyclization reaction to give the corresponding furo[3,2-*c*]pyridin-6(2*H*)-ones **9a** (59%) and **11a** (90%). On the basis of these results, we have tried to directly construct furo- and thieno-[3,2-*c*]pyridin-6(2*H*)-ones **9–12** starting from **7** and/or **8** and amines in a one-pot process, without isolation of the intermediate acetamide derivatives **A**. The best results are shown in Table 3. Indeed, when a mixture of **7a–d** and/or **8a–c** and aqueous ammonium hydroxide and/or benzylamine in MeOH was stirred at room temperature for 24 h and then the reaction mixture was treated with sodium methoxide at room temperature for 1 h, the desired furo- and thieno-[3,2-*c*]pyridin-6(2*H*)-ones **9a–d**, **10a–c**, **11a–d**, and **12a–c** were obtained in moderate yields.

These products **9–12** gave satisfactory elemental analyses and spectroscopic data (IR, ^{1}H NMR, ^{13}C NMR, and MS) consistent with their assigned structures (see experimental section). For example, the IR spectra of **9–12** display bands in the range of 3480–3180 cm^{-1} due to a primary amino and amido groups. The ^{1}H NMR spectra of **9–12** exhibit two D_2O exchangeable signals near δ 5.9 and 10.0 attributable to the primary amino and amido protons. The ^{13}C NMR spectra of **9–12** show a signal near δ 162 due to the amido carbonyl carbon. In addition, furo[3,2-*c*]pyridin-6(2*H*)-ones **9a** and **11a** were identical with authentic samples prepared by intramolecular cyclization reaction of acetamide derivatives **13** and **14** with sodium methoxide.



a: R^1 = H, R^2 = H **b**: R^1 = Ph, R^2 = H **c**: R^1 = H, R^2 = Me **d**: R^1 = H, R^2 = Ph
9,10: R^3 = H **11,12**: R^3 = CH_2Ph **7,9,11**: X = O **8,10,12**: X = S

Scheme 2

Table 3. One-pot synthesis of furo- and thieno-[3,2-*c*]pyridin-6(2*H*)-ones **9–12** from **7** and **8** according to Scheme 2

Entry	Substrate	X	R^1	R^2	R^3	Product	Yield (%)
1	**7a**	O	H	H	H	**9a**	54
2	**7b**	O	Ph	H	H	**9b**	73
3	**7c**	O	H	Me	H	**9c**	58
4	**7d**	O	H	Ph	H	**9d**	39
5	**8a**	S	H	H	H	**10a**	38
6	**8b**	S	Ph	H	H	**10b**	66
7	**8c**	S	H	Me	H	**10c**	36
8	**7a**	O	H	H	CH_2Ph	**11a**	63
9	**7b**	O	Ph	H	CH_2Ph	**11b**	86
10	**7c**	O	H	Me	CH_2Ph	**11c**	84
11	**7d**	O	H	Ph	CH_2Ph	**11d**	66
12	**8a**	S	H	H	CH_2Ph	**12a**	52
13	**8b**	S	Ph	H	CH_2Ph	**12b**	40
14	**8c**	S	H	Me	CH_2Ph	**12c**	74

In conclusion, we have developed a convenient method for the synthesis of furo- and thieno-[3,2-*c*]pyridine derivatives **5**, **6**, and **9–12** from 4,5-dihydro-3-furan- and -3-thiophene-carbonitriles having an active methylene group at C-2 position **1**, **2**, **7**, and **8**. It is also worth noting that compounds **1**, **2**, **7**, and **8** are versatile building blocks for the synthesis of new heterobicycles. This methodology offers significant advantages with regard to the simplicity of operation. Functionalized fused pyridine derivatives 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 FAB MS spectra were obtained on a JEOL JMS-700T spectrometer. Elemental analyses were performed on YANACO MT-6 CHN analyzer. The starting compounds **1**, **2**, **7**, and **8** were prepared in this laboratory according to our previous procedure.[38]

General procedure for the preparation of enamines 3 and 4 from 1 and/or 2 and DMFDMA.

A mixture of **1a–d** and/or **2a–c** (10 mmol) and DMFDMA (1.43 g, 12 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 CH_2Cl_2 as the eluent to give **3a–d** and **4a–c**.

3-Cyano-4,5-dihydro-α-[(dimethylamino)methylene]-2-furanacetonitrile (3a)

Colorless prisms (1.07 g, 98%), mp 110–111 °C (acetone/petroleum ether); IR (KBr): 2203, 2185 (CN) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.95 (t, *J* = 9.2 Hz, 2H, 4-H), 3.10–3.45 [m, 6H, $N(CH_3)_2$], 4.45 (t, *J* = 9.2 Hz, 2H, 5-H), 7.42 (s, 1H, olefin H); ^{13}C NMR ($CDCl_3$): δ 31.4 (C-4), 38.5, 47.7 [$N(CH_3)_2$], 68.4 [*C*=CHN$(CH_3)_2$], 70.8 (C-5), 72.4 (C-3), 116.5, 117.8 (CN), 152.9 [C=*C*HN$(CH_3)_2$], 165.3 (C-2); MS: *m/z* 190 $[M+H]^+$. Anal. Calcd for $C_{10}H_{11}N_3O$: C, 63.48; H, 5.86; N, 22.21. Found: C, 63.49; H, 5.83; N, 22.37.

3-Cyano-4,5-dihydro-α-[(dimethylamino)methylene]-4-phenyl-2-furanacetonitrile (3b)

Colorless prisms (1.53 g, 58%), mp 181–182°C (acetone/petroleum ether); IR (KBr): 2201, 2186 (CN) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.10–3.45 [m, 6H, $N(CH_3)_2$], 4.35 (dd, *J* = 6.4, 11.4 Hz, 2H, 4- and 5-H), 4.77 (t, *J* = 11.4 Hz, 1H, 5-H), 7.22–7.37 (m, 5H, aryl H), 7.53 (s, 1H, olefin H); ^{13}C NMR ($CDCl_3$): δ 38.6, 47.7 [$N(CH_3)_2$], 49.7 (C-4), 68.3 [*C*=CHN$(CH_3)_2$], 78.2 (C-3), 78.4 (C-5), 116.4, 117.4 (CN), 127.1, 127.7, 129.0, 140.8 (C aryl), 153.2 [C=*C*HN$(CH_3)_2$], 165.6 (C-2); MS: *m/z* 266 $[M+H]^+$. Anal. Calcd for $C_{16}H_{15}N_3O$: C, 72.43; H, 5.70; N, 15.84. Found: C, 72.43; H, 5.76; N, 15.81.

3-Cyano-4,5-dihydro-5-methyl-α-[(dimethylamino)methylene]-2-furanacetonitrile (3c)

Colorless prisms (1.64 g, 62%), mp 163–164 °C (acetone/petroleum ether); IR (KBr): 2204, 2181 (CN)

cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.39 (d, *J* = 6.4 Hz, 3H, 5-CH_3), 2.55 (dd, *J* = 7.6, 13.4 Hz, 1H, 4-H), 3.05 (dd, *J* = 9.5, 13.4 Hz, 1H, 4-H), 3.10–3.45 [m, 6H, $N(CH_3)_2$], 4.77–4.83 (m, 1H, 5-H), 7.40 (s, 1H, olefin H); ^{13}C NMR ($CDCl_3$): δ 21.2 (5-CH_3), 38.3 (C-4), 38.6, 47.6 [$N(CH_3)_2$], 68.6 [*C*=$CHN(CH_3)_2$], 71.8 (C-3), 79.7 (C-5), 116.6, 118.0 (CN), 152.9 [C=*C*$HN(CH_3)_2$], 164.4 (C-2); MS: *m/z* 204 $[M+H]^+$. Anal. Calcd for $C_{11}H_{13}N_3O$: C, 65.01; H, 6.45; N, 20.67. Found: C, 65.00; H, 6.42; N, 20.71.

3-Cyano-4,5-dihydro-α-[(dimethylamino)methylene]-5-phenyl-2-furanacetonitrile (3d)

Colorless prisms (1.64 g, 62%), mp 163–164°C (acetone/petroleum ether); IR (KBr): 2205, 2190 (CN) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.96 (dd, *J* = 8.5, 14.0 Hz, 1H, 4-H), 3.10–3.45 [m, 7H, 4-H and $N(CH_3)_2$], 5.61 (dd, *J* = 8.5, 10.1 Hz, 1H, 5-H), 7.26–7.41 (m, 5H, aryl H), 7.43 (s, 1H, olefin H); ^{13}C NMR ($CDCl_3$): δ 38.6 [$N(CH_3)_2$], 39.4 (C-4), 47.6 [$N(CH_3)_2$], 68.4 [*C*=$CHN(CH_3)_2$], 72.1 (C-3), 83.9 (C-5), 116.4, 117.4 (CN), 125.7, 128.6, 128.8, 140.0 (C aryl), 153.0 [C=*C*$HN(CH_3)_2$], 164.3 (C-2); MS: *m/z* 266 $[M+H]^+$. Anal. Calcd for $C_{16}H_{15}N_3O$: C, 72.43; H, 5.70; N, 15.84. Found: C, 72.38; H, 5.76; N, 15.75.

3-Cyano-4,5-dihydro-α-[(dimethylamino)methylene]-2-thiopheneacetonitrile (4a)

Pale yellow needles (0.99 g, 48%), mp 104–105°C (acetone/petroleum ether); IR (KBr): 2174 (CN) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.05–3.09 (m, 2H, 4-H), 3.13–3.40 [m, 8H, 5-H and $N(CH_3)_2$], 7.35 (s, 1H, olefin H); ^{13}C NMR ($CDCl_3$): δ 31.7 (C-4), 38.0 (C-5), 39.2, 47.2 [$N(CH_3)_2$], 71.5 [*C*=$CHN(CH_3)_2$], 90.1 (C-3), 117.2, 117.5 (CN), 153.4 [C=*C*$HN(CH_3)_2$], 157.3 (C-2); MS: *m/z* 206 $[M+H]^+$. Anal. Calcd for $C_{10}H_{11}N_3S$: C, 58.51; H, 5.40; N, 20.47. Found: C, 58.55; H, 5.31; N, 20.71.

3-Cyano-4,5-dihydro-α-[(dimethylamino)methylene]-4-phenyl-2-thiopheneacetonitrile (4b)

Colorless prisms (1.83 g, 65%), mp 150–151°C (acetone); IR (KBr): 2198, 2185 (CN) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.10–3.50 [m, 7H, 5-H and $N(CH_3)_2$], 3.67 (dd, *J* = 9.1, 11.4 Hz, 1H, 5-H), 4.47 (dd, *J* = 7.0, 9.1 Hz, 1H, 4-H), 7.28–7.38 (m, 5H, aryl H), 7.48 (s, 1H, olefin H); ^{13}C NMR ($CDCl_3$): δ 38.9 [$N(CH_3)_2$], 39.5 (C-5), 47.4 [$N(CH_3)_2$], 55.8 (C-4), 71.5 [*C*=$CHN(CH_3)_2$], 94.6 (C-3), 117.3, 117.7 (CN), 127.3, 127.9, 129.0, 140.2 (C aryl), 153.4 [C=*C*$HN(CH_3)_2$], 158.0 (C-2); MS: *m/z* 282 $[M+H]^+$. Anal. Calcd for $C_{16}H_{15}N_3S$: C, 68.30; H, 5.37; N, 14.93. Found: C, 68.26; H, 5.49; N, 14.74.

3-Cyano-4,5-dihydro-5-methyl-α-[(dimethylamino)methylene]-2-thiopheneacetonitrile (4c)

Colorless prisms (1.10 g, 50%), mp 79–81°C (acetone/petroleum ether); IR (KBr): 2200, 2182 (CN) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.40 (d, *J* = 6.7 Hz, 3H, 5-CH_3), 2.73 (dd, *J* = 5.8, 15.0 Hz, 1H, 4-H), 3.10–3.40 [m, 7H, 4-H and $N(CH_3)_2$], 3.77–3.82 (m, 1H, 5-H), 7.34 (s, 1H, olefin H); ^{13}C NMR ($CDCl_3$): δ 21.4 (5-CH_3), 39.7 [$N(CH_3)_2$], 43.6 (C-5), 45.7 (C-4), 47.5 [$N(CH_3)_2$], 71.6 [*C*=$CHN(CH_3)_2$], 88.8 (C-3), 117.4, 117.5 (CN), 153.4 [C=*C*$HN(CH_3)_2$], 156.5 (C-2); MS: *m/z* 220 $[M+H]^+$. Anal. Calcd for $C_{11}H_{13}N_3S$: C, 60.24; H, 5.97; N, 19.16. Found: C, 60.30; H, 5.98; N, 19.17.

General procedure for the preparation of furo- and thieno-[3,2-*c*]pyridines 5 and 6 from 3 and/or 4 and ammonium acetate.

A mixture of **3a–d** and/or **4a–c** (5 mmol) and ammonium acetate (0.77 g, 10 mmol) in DMF (5 mL) was stirred at 100 °C for 5 h. After removal of the solvent *in vacuo*, cold water was added to the residue. The precipitate was isolated by filtration, washed with water, dried, and recrystallized from an appropriate solvent to yield **5a–d** and **6a–c**.

4-Amino-2,3-dihydrofuro[3,2-*c*]pyridine-7-carbonitrile (5a)

Pale red prisms (0.54 g, 67%), mp >300 °C (DMF/H_2O); IR (KBr): 3381, 3332, 3125 (NH), 2228 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.97 (t, J = 8.9 Hz, 2H, 3-H), 4.72 (t, J = 8.9 Hz, 2H, 2-H), 6.77 (br s, 2H, NH_2), 8.08 (s, 1H, 6-H); ^{13}C NMR (DMSO-d_6): δ 25.8 (C-3), 73.3 (C-2), 81.5 (C-7), 102.3 (C-3a), 115.9 (CN), 152.3 (C-6), 158.7 (C-4), 166.9 (C-7a); MS: m/z 162 $[M+H]^+$. Anal. Calcd for $C_8H_7N_3O$: C, 59.62; H, 4.38; N, 26.07. Found: C, 59.50; H, 4.47; N, 26.00.

4-Amino-2,3-dihydro-3-phenylfuro[3,2-*c*]pyridine-7-carbonitrile (5b)

Pale yellow prisms (0.95 g, 80%), mp 202–203 °C (acetone/petroleum ether); IR (KBr): 3433, 3302, 3119 (NH), 2225 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 4.55 (dd, J = 3.7, 9.2 Hz, 1H, 2-H), 4.62 (dd, J = 3.7, 9.2 Hz, 1H, 3-H), 5.03 (t, J = 9.2 Hz, 1H, 2-H), 6.48 (br s, 2H, NH_2), 7.15–7.18 (m, 2H, aryl H), 7.30–7.34 (m, 2H, aryl H), 7.23–7.27 (m, 1H, aryl H), 8.19 (s, 1H, 6-H); ^{13}C NMR (DMSO-d_6): δ 43.5 (C-3), 81.4 (C-2), 81.8 (C-7), 105.6 (C-3a), 115.7 (CN), 127.0, 127.1, 128.6, 141.0 (C aryl), 153.2 (C-6), 158.5 (C-4), 166.9 (C-7a); MS: m/z 238 $[M+H]^+$. Anal. Calcd for $C_{14}H_{11}N_3O$: C, 70.87; H, 4.67; N, 17.71. Found: C, 70.92; H, 4.77; N, 17.62.

4-Amino-2,3-dihydro-2-methylfuro[3,2-*c*]pyridine-7-carbonitrile (5c)

Pale red prisms (0.50 g, 57%), mp 221–222 °C (acetone/petroleum ether); IR (KBr): 3408, 3327, 3145 (NH), 2218 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.43 (d, J = 6.4 Hz, 3H, CH_3), 2.55 (dd, J = 7.2, 15.3 Hz, 1H, 3-H), 3.13 (dd, J = 9.2, 15.3 Hz, 1H, 3-H), 5.10–5.18 (m, 1H, 2-H), 6.73 (br s, 2H, NH_2), 8.08 (s, 1H, 6-H); ^{13}C NMR (DMSO-d_6): δ 21.4 (CH_3), 33.0 (C-3), 81.4 (C-7), 82.6 (C-2), 102.0 (C-3a), 116.0 (CN), 152.4 (C-6), 158.7 (C-4), 166.1 (C-7a); MS: m/z 176 $[M+H]^+$. Anal. Calcd for $C_9H_9N_3O$: C, 61.70; H, 5.18; N, 23.99. Found: C, 61.78; H, 5.25; N, 24.01.

4-Amino-2,3-dihydro-2-phenylfuro[3,2-*c*]pyridine-7-carbonitrile (5d)

Pale yellow needles (0.85 g, 72%), mp 239–240 °C (acetone/petroleum ether); IR (KBr): 3431, 3317, 3105 (NH), 2212 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.90–2.96 (m, 1H, 3-H), 3.46–3.52 (m, 1H, 3-H), 6.05 (dd, J = 7.5, 9.9 Hz, 1H, 2-H), 6.83 (br s, 2H, NH_2), 7.36–7.45 (m, 5H, aryl H), 8.16 (s, 1H, 6-H); ^{13}C NMR (DMSO-d_6): δ 34.1 (C-3), 81.3 (C-7), 86.0 (C-2), 101.6 (C-3a), 115.8 (CN), 125.8, 128.4, 128.7, 140.4 (C aryl), 152.7 (C-6), 158.6 (C-4), 166.1 (C-7a); MS: m/z 238 $[M+H]^+$. Anal. Calcd for $C_{14}H_{11}N_3O$: C, 70.87; H, 4.67; N, 17.71. Found: C, 70.77; H, 4.80; N, 17.56.

4-Amino-2,3-dihydrothieno[3,2-*c*]pyridine-7-carbonitrile (6a)

Pale red prisms (0.67 g, 76%), mp 283–284 °C (DMF/H_2O); IR (KBr): 3404, 3310, 3134 (NH), 2216

(CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.12 (t, J = 8.3 Hz, 2H, 3-H), 3.50 (t, J = 8.3 Hz, 2H, 2-H), 6.80 (br s, 2H, NH_2), 8.13 (s, 1H, 6-H); ^{13}C NMR (DMSO-d_6): δ 31.7 (C-3), 32.1 (C-2), 90.6 (C-7), 115.8 (C-3a), 117.6 (CN), 151.8 (C-6), 154.9 (C-7a), 156.6 (C-4); MS: m/z 178 $[M+H]^+$. Anal. Calcd for $C_8H_7N_3S$: C, 54.22; H, 3.98; N, 23.71. Found: C, 54.20; H, 4.08; N, 23.68.

4-Amino-2,3-dihydro-3-phenylthieno[3,2-*c*]pyridine-7-carbonitrile (6b)

Colorless prisms (1.12 g, 89%), mp 253–255 °C (acetone/petroleum ether); IR (KBr): 3449, 3288, 3138 (NH), 2214 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.26–3.30 (m, 1H, 2-H), 4.04 (dd, J = 8.9, 11.6 Hz, 1H, 2-H), 4.82 (dd, J = 1.8, 8.9 Hz, 1H, 3-H), 6.57 (br s, 2H, NH_2), 7.15–7.18 (m, 2H, aryl H), 7.23–7.33 (m, 3H, aryl H), 8.24 (s, 1H, 6-H); ^{13}C NMR (DMSO-d_6): δ 41.2 (C-2), 48.3 (C-3), 90.8 (C-7), 117.6 (CN), 118.0 (C-3a), 127.0, 127.1, 128.4, 140.3 (C aryl), 152.7 (C-6), 155.9 (C-7a), 156.7 (C-4); MS: m/z 254 $[M+H]^+$. Anal. Calcd for $C_{14}H_{11}N_3S$: C, 66.38; H, 4.38; N, 16.59. Found: C, 66.49; H, 4.50; N, 16.59.

4-Amino-2,3-dihydro-2-methylthieno[3,2-*c*]pyridine-7-carbonitrile (6c)

Colorless prisms (0.63 g, 66%), mp 228–229 °C (acetone); IR (KBr): 3415, 3326, 3122 (NH), 2209 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.40 (d, J = 7.0 Hz, 3H, CH_3), 2.82 (dd, J = 5.6, 16.0 Hz, 1H, 3-H), 3.23–3.29 (m, 1H, 3-H), 4.15–4.20 (m, 1H, 2-H), 6.79 (br s, 2H, NH_2), 8.14 (s, 1H, 6-H); ^{13}C NMR (DMSO-d_6): δ 22.4 (CH_3), 40.0 (C-3), 44.7 (C-2), 90.6 (C-7), 114.8 (C-3a), 117.6 (CN), 151.8 (C-6), 154.1 (C-7a), 156.8 (C-4); MS: m/z 192 $[M+H]^+$. Anal. Calcd for $C_9H_9N_3S$: C, 56.52; H, 4.74; N, 21.97. Found: C, 56.58; H, 4.79; N, 21.89.

General procedure for the preparation of furo- and thieno-[3,2-*c*]pyridin-6(2*H*)-ones 9–12 from 7 and/or 8 and amines in the presence of sodium methoxide.

A mixture of **7a–d** and **8a–c** (5 mmol) and 28% aqueous ammonium hydroxide (5 mL, 0.128 mol) and/or benzylamine (5 mL, 45.8 mmol) in MeOH (5 mL) was stirred at rt for 24 h. To the obtained reaction mixture was added a solution of sodium (0.12 g, 5 mmol) in anhydrous MeOH (3 mL) with stirring and then the resulting mixture was stirred at rt for 1 h. After removal of the solvent *in vacuo*, cold water was added to the residue. The precipitate was isolated by filtration, washed with water, dried, and recrystallized from an appropriate solvent to afford **9a–d**, **10a–c**, **11a–d**, and **12a–c**.

4-Amino-3,5-dihydrofuro[3,2-*c*]pyridin-6(2*H*)-one (9a)

Colorless prisms (0.41 g, 54%), mp >300 °C ($CHCl_3$/MeOH); IR (KBr): 3403, 3319, 3195 (NH), 1678 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.75 (t, J = 8.2 Hz, 2H, 3-H), 4.48 (t, J = 8.2 Hz, 2H, 2-H), 4.83 (s, 1H, 7-H), 5.81 (br s, 2H, NH_2), 9.78 (br s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 24.4 (C-3), 72.5 (C-2), 81.4 (C-7), 86.0 (C-3a), 146.0 (C-4), 163.7 (CO), 172.4 (C-7a); MS: m/z 153 $[M+H]^+$. Anal. Calcd for $C_7H_8N_2O_2$: C, 55.26; H, 5.30; N, 18.41. Found: C, 55.09; H, 5.35; N, 18.26.

4-Amino-3,5-dihydro-3-phenylfuro[3,2-*c*]pyridin-6(2*H*)-one (9b)

Colorless prisms (0.83 g, 73%), mp >300 °C ($CHCl_3$/MeOH); IR (KBr): 3482, 3375 (NH), 1652 (CO)

cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 4.29 (dd, J = 3.4, 8.9 Hz, 1H, 2-H), 4.39 (dd, J = 3.4, 8.9 Hz, 1H, 3-H), 4.80 (t, J = 8.9 Hz, 1H, 2-H), 4.95 (s, 1H, 7-H), 5.56 (br s, 2H, NH_2), 7.15–7.17 (m, 2H, aryl H), 7.19–7.23 (m, 1H, aryl H), 7.28–7.32 (m, 2H, aryl H), 9.90 (br s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 42.5 (C-3), 80.8 (C-2), 81.6 (C-7), 90.3 (C-3a), 126.6, 126.9, 128.5, 142.8 (C aryl), 146.6 (C-4), 163.9 (CO), 172.4 (C-7a); MS: *m*/*z* 229 [M+H]$^+$. Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.49; H, 5.38; N, 12.20.

4-Amino-3,5-dihydro-2-methylfuro[3,2-*c*]pyridin-6(2*H*)-one (9c)

Colorless plates (0.33 g, 39%), mp >300 °C ($CHCl_3$/MeOH); IR (KBr): 3386, 3184 (NH), 1691 (CO) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 1.32 (d, J = 6.9 H, 3H, CH_3), 2.33 (dd, J = 6.8, 14.0 Hz, 1H, 3-H), 2.92 (dd, J = 8.5, 14.0 Hz, 1H, 3-H), 4.81 (s, 1H, 7-H), 4.83–4.90 (m, 1H, 2-H), 5.78 (br s, 2H, NH_2), 9.80 (br s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 21.6 (CH_3), 31.9 (C-3), 81.2 (C-2), 81.3 (C-7), 86.1 (C-3a), 146.0 (C-4), 163.7 (CO), 171.7 (C-7a); MS: *m*/*z* 167 [M+H]$^+$. Anal. Calcd for $C_8H_{10}N_2O_2$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.86; H, 6.10; N, 16.77.

4-Amino-3,5-dihydro-2-phenylfuro[3,2-*c*]pyridin-6(2*H*)-one (9d)

Colorless prisms (0.66 g, 58%), mp >300 °C ($CHCl_3$/MeOH); IR (KBr): 3391, 3187 (NH), 1688 (CO) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.68 (dd, J = 6.7, 14.3 Hz, 1H, 3-H), 3.28 (dd, J = 9.2, 14.3 Hz, 1H, 3-H), 4.95 (s, 1H, 7-H), 5.80 (dd, J = 6.7, 9.2 Hz, 1H, 2-H), 5.87 (br s, 2H, NH_2), 7.30–7.34 (m, 3H, aryl H), 7.37–7.41 (m, 2H, aryl H), 9.90 (br s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 33.2 (C-3), 81.4 (C-7), 85.0 (C-2), 85.4 (C-3a), 125.5, 128.0, 128.5, 141.6 (C aryl), 146.1 (C-4), 163.9 (CO), 171.8 (C-7a); MS: *m*/*z* 229 [M+H]$^+$. Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.38; H, 5.37; N, 12.23.

4-Amino-3,5-dihydrothieno[3,2-*c*]pyridin-6(2*H*)-one (10a)

Colorless needles (0.32 g, 38%), mp >300 °C ($CHCl_3$/MeOH); IR (KBr): 3377, 3328, 3184 (NH), 1672 (CO) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.86 (t, J = 7.6 Hz, 2H, 3-H), 3.28 (t, J = 7.6 Hz, 2H, 2-H), 5.36 (s, 1H, 7-H), 5.76 (br s, 2H, NH_2), 10.05 (br s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 29.6 (C-3), 32.3 (C-2), 94.4 (C-7), 96.9 (C-3a), 145.2 (C-4), 159.8 (C-7a), 161.3 (CO); MS: *m*/*z* 169 [M+H]$^+$. Anal. Calcd for $C_7H_8N_2OS$: C, 49.98; H, 4.79; N, 16.65. Found: C, 49.75; H, 4.79; N, 16.41.

4-Amino-3,5-dihydro-3-phenylthieno[3,2-*c*]pyridin-6(2*H*)-one (10b)

Green prisms (0.81 g, 66%), mp >300 °C ($CHCl_3$/MeOH); IR (KBr): 3436, 3357, 3297 (NH), 1613 (CO) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 3.04 (dd, J = 1.7, 11.3 Hz, 1H, 2-H), 3.84 (dd, J = 8.2, 11.3 Hz, 1H, 2-H), 4.57 (dd, J = 1.7, 8.2 Hz, 1H, 3-H), 5.45 (s, 1H, 7-H), 5.53 (br s, 2H, NH_2), 7.18–7.23 (m, 3H, aryl H), 7.27–7.31 (m, 2H, aryl H), 10.13 (br s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 41.8 (C-2), 46.2 (C-3), 94.5 (C-7), 99.7 (C-3a), 126.6, 127.0, 128.2, 142.6 (C aryl), 145.9 (C-4), 160.3 (C-7a), 161.5 (CO); MS: *m*/*z* 245 [M+H]$^+$. Anal. Calcd for $C_{13}H_{12}N_2OS \bullet 0.1H_2O$: C, 63.44; H, 5.00; N, 11.38. Found: C, 63.39; H,

4.97; N, 11.33.

4-Amino-3,5-dihydro-2-methylthieno[3,2-*c*]pyridin-6(2*H*)-one (10c)

Brown prisms (0.33 g, 36%), mp >300 °C (EtOH); IR (KBr): 3385, 3192 (NH), 1671 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.34 (d, *J* = 6.7 Hz, 3H, CH_3), 2.52 (dd, *J* = 6.3, 14.3 Hz, 1H, 3-H), 3.01 (dd, *J* = 7.6, 13.4 Hz, 1H, 3-H), 3.90–3.97 (m, 1H, 2-H), 5.32 (s, 1H, 7-H), 5.73 (br s, 2H, NH_2), 10.06 (br s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 22.2 (CH_3), 37.9 (C-3), 44.7 (C-2), 94.5 (C-7), 96.3 (C-3a), 145.4 (C-4), 159.3 (C-7a), 161.3 (CO); MS: *m/z* 183 $[M+H]^+$. Anal. Calcd for $C_8H_{10}N_2OS$: C, 52.72; H, 5.53; N, 15.37. Found: C, 52.58; H, 5.58; N, 15.15.

4-Amino-3,5-dihydro-5-(phenylmethyl)furo[3,2-*c*]pyridin-6(2*H*)-one (11a)

Colorless prisms (0.76 g, 63%), mp 217–218 °C (acetone); IR (KBr): 3458, 3310 (NH), 1672 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.82 (t, *J* = 8.2 Hz, 2H, 3-H), 4.50 (t, *J* = 8.2 Hz, 2H, 2-H), 5.05 (s, 1H, 7-H), 5.17 (br s, 2H, CH_2Ph), 6.19 (br s, 2H, NH_2), 7.15–7.17 (m, 2H, aryl H), 7.19–7.22 (m, 1H, aryl H), 7.26–7.30 (m, 2H, aryl H); ^{13}C NMR (DMSO-d_6): δ 25.4 (C-3), 42.7 (*C*H_2Ph), 72.1 (C-2), 80.9 (C-7), 86.7 (C-3a), 126.48, 126.53, 128.1, 137.5 (C aryl), 146.8 (C-4), 162.9 (CO), 170.1 (C-7a); MS: *m/z* 243 $[M+H]^+$. Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.46; H, 5.90; N, 11.57.

4-Amino-3,5-dihydro-3-phenyl-5-(phenylmethyl)furo[3,2-*c*]pyridin-6(2*H*)-one (11b)

Colorless prisms (1.37 g, 86%), mp 190–191 °C (acetone); IR (KBr): 3464, 3307, 3194 (NH), 1665 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 4.29 (dd, *J* = 3.1, 8.5 Hz, 1H, 2-H), 4.46 (dd, *J* = 3.1, 8.5 Hz, 1H, 3-H), 4.81 (t, *J* = 8.5 Hz, 1H, 2-H), 5.02 (br d, *J* = 16.5 Hz, 1H CH_2Ph), 5.17 (s, 1H, 7-H), 5.31 (br d, *J* = 16.5 Hz, 1H, CH_2Ph), 5.94 (br s, 2H, NH_2), 7.11–7.22 (m, 6H, aryl H), 7.26–7.31 (m, 4H, aryl H); ^{13}C NMR (DMSO-d_6): δ 42.7 (*C*H_2Ph), 43.1 (C-3), 80.5 (C-2), 80.9 (C-7), 90.7 (C-3a), 126.3, 126.5, 126.6, 126.9, 128.1, 128.4, 137.3, 142.8 (C aryl), 147.4 (C-4), 163.0 (CO), 170.2 (C-7a); MS: *m/z* 319 $[M+H]^+$. Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.42; H, 5.75; N, 8.79.

4-Amino-3,5-dihydro-2-methyl-5-(phenylmethyl)furo[3,2-*c*]pyridin-6(2*H*)-one (11c)

Colorless needles (1.07 g, 84%), mp 241–242 °C (acetone); IR (KBr): 3474, 3311, 3277, 3204 (NH), 1672 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.35 (d, *J* = 6.4 Hz, 3H, CH_3), 2.39 (dd, *J* = 6.7, 13.9 Hz, 1H, 3-H), 2.99 (dd, *J* = 8.5, 13.9 Hz, 1H, 3-H), 4.86–4.91 (m, 1H, 2-H), 5.02 (s, 1H, 7-H), 5.15 (AB q, *J* = 16.2 Hz, 2H, CH_2Ph), 6.13 (br s, 2H, NH_2), 7.15–7.22 (m, 3H, aryl H), 7.26–7.30 (m, 2H, aryl H); ^{13}C NMR (DMSO-d_6): δ 21.6 (CH_3), 32.8 (C-3), 42.7 (*C*H_2Ph), 80.8 (C-2), 80.9 (C-7), 86.3 (C-3a), 126.5, 128.0, 137.5 (C aryl), 146.7 (C-4), 163.0 (CO), 169.4 (C-7a); MS: *m/z* 257 $[M+H]^+$. Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.19; H, 6.25; N, 10.95.

4-Amino-3,5-dihydro-2-phenyl-5-(phenylmethyl)furo[3,2-*c*]pyridin-6(2*H*)-one (11d)

Colorless prisms (1.05 g, 66%), mp 196–197 °C (acetone); IR (KBr): 3445, 3407, 3312, 3276 (NH), 1682 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.74 (dd, *J* = 6.9, 14.3 Hz, 1H, 3-H), 3.34 (dd, *J* = 9.3, 14.3 Hz, 1H,

3-H), 5.14 (br d, *J* = 15.3 Hz, 1H, C*H*$_2$Ph), 5.15 (s, 1H, 7-H), 5.23 (br d, *J* = 15.3 Hz, 1H, C*H*$_2$Ph), 5.81 (dd, *J* = 6.9, 9.3 Hz, 1H, 2-H), 6.24 (br s, 2H, NH_2), 7.18–7.23 (m, 3H, aryl H), 7.27–7.42 (m, 7H, aryl H); ^{13}C NMR (DMSO-d_6): δ 34.1 (C-3), 42.8 (*C*H$_2$Ph), 80.8 (C-7), 84.6 (C-2), 85.9 (C-3a), 125.5, 126.5, 126.6, 127.9, 128.1, 128.5, 137.4, 141.5 (C aryl), 146.8 (C-4), 163.0 (CO), 169.5 (C-7a); MS: *m*/*z* 319 $[M+H]^+$. Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.48; H, 5.82; N, 8.77.

4-Amino-3,5-dihydro-5-(phenylmethyl)thieno[3,2-*c*]pyridin-6(2*H*)-one (12a)

Pale brown plates (0.67 g, 52%), mp 205–206 °C (acetone); IR (KBr): 3446, 3305, 3282 (NH), 1622 (CO) cm^{-1}; ^{1}H NMR (DMF): δ 2.93 (t, *J* = 7.6 Hz, 2H, 3-H), 3.29 (t, *J* = 7.6 Hz, 2H, 2-H), 5.20 (br s, 2H, C*H*$_2$Ph), 5.54 (s, 1H, 7-H), 6.15 (br s, 2H, NH_2), 7.16–7.18 (m, 2H, aryl H), 7.19–7.23 (m, 1H, aryl H), 7.27–7.31 (m, 2H, aryl H); ^{13}C NMR (DMSO-d_6): δ 30.9 (C-3), 31.8 (C-2), 43.0 (*C*H$_2$Ph), 93.7 (C-7), 97.1 (C-3a), 126.5, 126.6, 128.1, 137.0 (C aryl), 145.5 (C-4), 157.7 (C-7a), 160.5 (CO); MS: *m*/*z* 259 $[M+H]^+$. Anal. Calcd for $C_{14}H_{14}N_2OS$: C, 65.09; H, 5.46; N, 10.84. Found: C, 65.12; H, 5.49; N, 10.76.

4-Amino-3,5-dihydro-3-phenyl-5-(phenylmethyl)thieno[3,2-*c*]pyridin-6(2*H*)-one (12b)

Gray prisms (1.24 g, 74%), mp 224–226 °C ($CHCl_3$/MeOH); IR (KBr): 3464, 3320 (NH), 1630 (CO) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 3.03 (dd, *J* = 1.2, 11.3 Hz, 1H, 2-H), 3.86 (dd, *J* = 7.9, 11.3 Hz, 1H, 2-H), 4.67 (dd, *J* = 1.2, 7.9 Hz, 1H, 3-H), 5.06 (br d, *J* = 16.2 Hz, 1H, C*H*$_2$Ph), 5.33 (br d, *J* = 16.2 Hz, 1H, C*H*$_2$Ph), 5.64 (s, 1H, 7-H), 5.96 (br s, 2H, NH_2), 7.11–7.13 (m, 2H, aryl H), 7.16–7.22 (m, 4H, aryl H), 7.26–7.30 (m, 4H, aryl H); ^{13}C NMR (DMSO-d_6): δ 41.5 (C-2), 43.0 (*C*H$_2$Ph), 47.1 (C-3), 93.7 (C-7), 99.9 (C-3a), 126.3, 126.6, 127.0, 128.10, 128.12, 136.8, 142.3 (C aryl), 146.3 (C-4), 158.3 (C-7a), 160.6 (CO); MS: *m*/*z* 335 $[M+H]^+$. Anal. Calcd for $C_{20}H_{18}N_2OS$: C, 71.83; H, 5.42; N, 8.38. Found: C, 71.64; H, 5.55; N, 8.31.

4-Amino-3,5-dihydro-2-methyl-5-(phenylmethyl)thieno[3,2-*c*]pyridin-6(2*H*)-one (12c)

Colorless prisms (0.54 g, 40%), mp 196–197 °C (acetone); IR (KBr): 3466, 3312, 3202 (NH), 1672 (CO) cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 1.36 (d, *J* = 6.7 Hz, 3H, CH_3), 2.60 (dd, *J* = 6.4, 14.6 Hz, 1H, 3-H), 3.10 (dd, *J* = 7.8, 14.6 Hz, 1H, 3-H), 3.94–3.99 (m, 1H, 2-H), 5.19 (AB q, *J* = 16.0 Hz, 2H, C*H*$_2$Ph), 5.50 (s, 1H, 7-H), 6.11 (br s, 2H, NH_2), 7.16–7.23 (m, 3H, aryl H), 7.27–7.31 (m, 2H, aryl H); ^{13}C NMR (DMSO-d_6): δ 22.2 (CH_3), 39.2 (C-3), 42.9 (C-2), 44.3 (*C*H$_2$Ph), 93.7 (C-7), 96.5 (C-3a), 126.56, 126.63, 128.1, 137.0 (C aryl), 145.6 (C-4), 157.2 (C-7a), 160.5 (CO); MS: *m*/*z* 273 $[M+H]^+$. Anal. Calcd for $C_{15}H_{16}N_2OS$: C, 66.15; H, 5.92; N, 10.29. Found: C, 66.05; H, 5.96; N, 10.13.

The preparation of acetamide derivatives 13 and 14 from 7a and amines.

A mixture of **7a** (0.84 g, 5 mmol) and 28% aqueous ammonium hydroxide (5 mL, 0.128 mol) and/or benzylamine (5 mL, 45.8 mmol) in MeOH (5 mL) was stirred at rt for 24 h. After removal of the solvent *in vacuo*, Et_2O (in the case of the preparation of **13**) or cold water (in the case of the preparation of **14**) was added to the residue. The precipitate was isolated by filtration, washed with Et_2O (in the case of the

preparation of **13**) or water (in the case of the preparation of **14**), dried, and recrystallized from MeOH/Et_2O (in the case of the preparation of **13**) or acetone/petroleum ether (in the case of the preparation of **14**) to give **13** and **14**.

3-Cyano-4,5-dihydro-2-furanacetamide (13)

Colorless needles (0.52 g, 68%), mp 115–116 °C; IR (KBr): 3425, 3398, 3179 (NH), 2206 (CN), 1677 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.84–2.89 (m, 2H, 4-H), 3.20 (t, J = 1.3 Hz, 2H, CH_2CO), 4.51 (t, J = 9.2 Hz, 2H, 5-H), 7.08, 7.48 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 29.4 (C-4), 34.7 (CH_2CO), 71.9 (C-5), 83.6 (C-3), 116.5 (CN), 167.1 (CO), 168.6 (C-2); MS: m/z 153 $[M+H]^+$. Anal. Calcd for $C_7H_8N_2O_2$: C, 55.26; H, 5.30; N, 18.41. Found: C, 55.16; H, 5.36; N, 18.23.

3-Cyano-4,5-dihydro-*N*-(phenylmethyl)-2-furanacetamide (14)

Colorless needles (0.89 g, 73%), mp 217–218 °C; IR (KBr): 3261, 3083 (NH), 2208 (CN), 1649 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.88 (t, J = 9.6 Hz, 2H, 4-H), 3.31 (s, 2H, CH_2CO), 4.28 (d, J = 5.8 Hz, 2H, $NHCH_2$), 4.52 (t, J = 9.6 Hz, 2H, 5-H), 7.22–7.27 (m, 3H, aryl H), 7.30–7.34 (m, 2H, aryl H), 8.57 (br s, 1H, NH); ^{13}C NMR (DMSO-d_6): δ 29.4 (C-4), 34.9 (CH_2CO), 42.4 ($NHCH_2$), 71.9 (C-5), 83.7 (C-3), 116.4 (CN), 126.8, 127.1, 128.2, 138.8 (C aryl), 165.2 (CO), 168.4 (C-2); MS: m/z 243 $[M+H]^+$. Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.54; H, 5.90; N, 11.59.

The preparation of furo- and thieno-[3,2-*c*]pyridin-6(2*H*)-ones 9a and 11a from 13 and 14 in the presence of sodium methoxide.

A mixture of **13** and/or **14** (3 mmol) in a solution of sodium (69 mg, 3 mmol) in anhydrous MeOH (3 mL) was stirred at rt for 1 h. After the same work-up as described above for the preparation of **9–12**, **9a** (0.27 g, 59%) and **11a** (0.65 g, 92%) were obtained. The melting points and IR spectra of **9a** and **11a** coincided with those of authentic samples prepared from **7a** and amines.

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