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SYNTHESIS OF FUSED THIOPYRANTHIONE AND THIOPHENE DERIVATIVES FROM 4,5-DIHYDRO-3-THIOPHENE(AND -3-FURAN)-CARBONITRILES HAVING AN ACTIVE METHYLENE GROUP AT C-2 POSITION

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Abstract – A versatile strategy is described for the synthesis of new fused thiopyranthione and thiophene derivatives. The reaction of heterocyclic α,β-unsaturated nitriles **3a–c**, **4a–d**, **5a–c**, and **6a–d**, which were prepared from tetrahydro-2-oxo-3-thiophene- and -3-furan-carbonitriles **1a–c** and/or **2a–d** and alkylidene phosphoranes such as (triphenylphosphoranylidene)acetonitrile and methyl (triphenylphosphoranylidene)acetate through Wittig reaction, with carbon disulfide in the presence of sodium hydride in THF gave the corresponding 6-thioxothieno[3,2-*c*]thiopyran and 6-thioxothiopyrano[4,3-*b*]furan derivatives **7a–c**, **8a–d**, **9a–c**, and **10a–d**. On the other hand, treatment of compounds **3a–c**, **5a–c**, and **6a–d** with sulfur powder in the presence of triethylamine in methanol caused Gewald reaction to provide the corresponding thieno[3,4-*b*]thiophene and -furan derivatives **11a–c**, **12a–c**, and **13a–d**.

INTRODUCTION

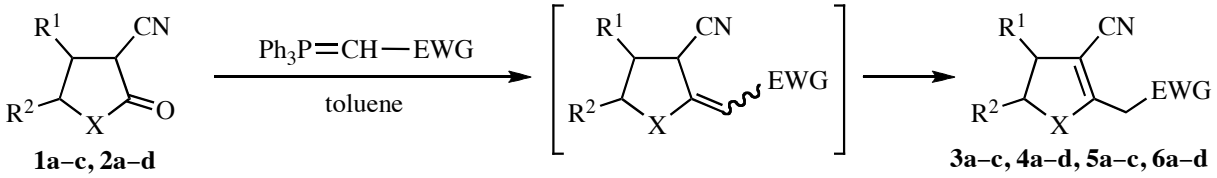
Heterocycles and heterobicycles form, by far, the largest of the classical divisions of organic chemistry.[1–6] Moreover, they are of immense importance not only biologically and industrially but also to the functioning of any developed human society as well. The majority of pharmaceutical products that mimic natural products with biological activity are heterocycles. Therefore, researchers are on a continuous pursuit to design and produce better pharmaceuticals, pesticides, insecticides, rodenticides, and weed killers by natural models. It is easy to understand why both the development of new methods and the

strategic development of known methods for the synthesis of heterocyclic compounds continue to drive the field of synthetic organic chemistry. Organic chemists have been engaged in extensive efforts to produce these heterocyclic compounds by developing new and efficient synthetic transformations. Among them, cyclocondensation reactions are of the most attractive methodologies for synthesizing heterocyclic compounds, and the need for improved cyclocondensation reactions is evident.

In the course of our studies on heterocyclic β-enaminonitriles,[7–11] we became interested in the development of the methods for the synthesis of heterobicycles such as thieno[3,2-*c*]thiopyrans,[12,13] thiopyrano[4,3-*b*]furans,[14] thieno[3,4-*b*]thiophenes,[15–17] and thieno[3,4-*b*]furans. The synthesis of these compounds has been rarely described in the literature. Therefore, there is a need for synthetic methods suitable for their analogues. As part of our current studies on the development of new routes in heterocyclic synthesis, we herein describe an efficient procedure for the synthesis of fused thiopyranthione and thiophene derivatives **7–13** from the reactions of heterocyclic α,β-unsaturated nitriles **3–6** as one of versatile starting materials and carbon disulfide and/or sulfur powder in the presence of sodium hydride or triethylamine.

RESULTS AND DISCUSSION

Initially, we examined Wittig reaction of tetrahydro-2-oxo-3-thiophene- and -3-furan-carbonitriles **1a–c** and **2a–d** with alkylidene phosphoranes (Scheme 1). Compounds **1a–c** and **2a–d** were easily prepared by treatment of 2-amino-4,5-dihydro-3-thiophene- and -3-furan-carbonitriles with hydrochloric acid according to our previous procedure.[18–21] Furthermore, we have also shown Wittig reaction of compounds **1a** and **2a** with (triphenylphosphoranylidene)acetonitrile (entries 1 and 4 in Table 1).[22] Thus, the starting materials, heterocyclic α,β-unsaturated nitriles **3a–c**, **4a–d**, **5a–c**, and **6a–d** were synthesized by Wittig reaction of compounds **1a–c** and **2a–d** with (triphenylphosphoranylidene)acetonitrile and/or methyl (triphenylphosphoranylidene)acetate in refluxing toluene with 55–98% isolated yields (Scheme 1 and Table 1). Elemental analyses, MS spectra, ^{1}H and ^{13}C NMR spectra of compounds **3–6** are consistent with the assigned structures (see experimental section).



1a–c, 2a–d **3a–c, 4a–d, 5a–c, 6a–d**

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

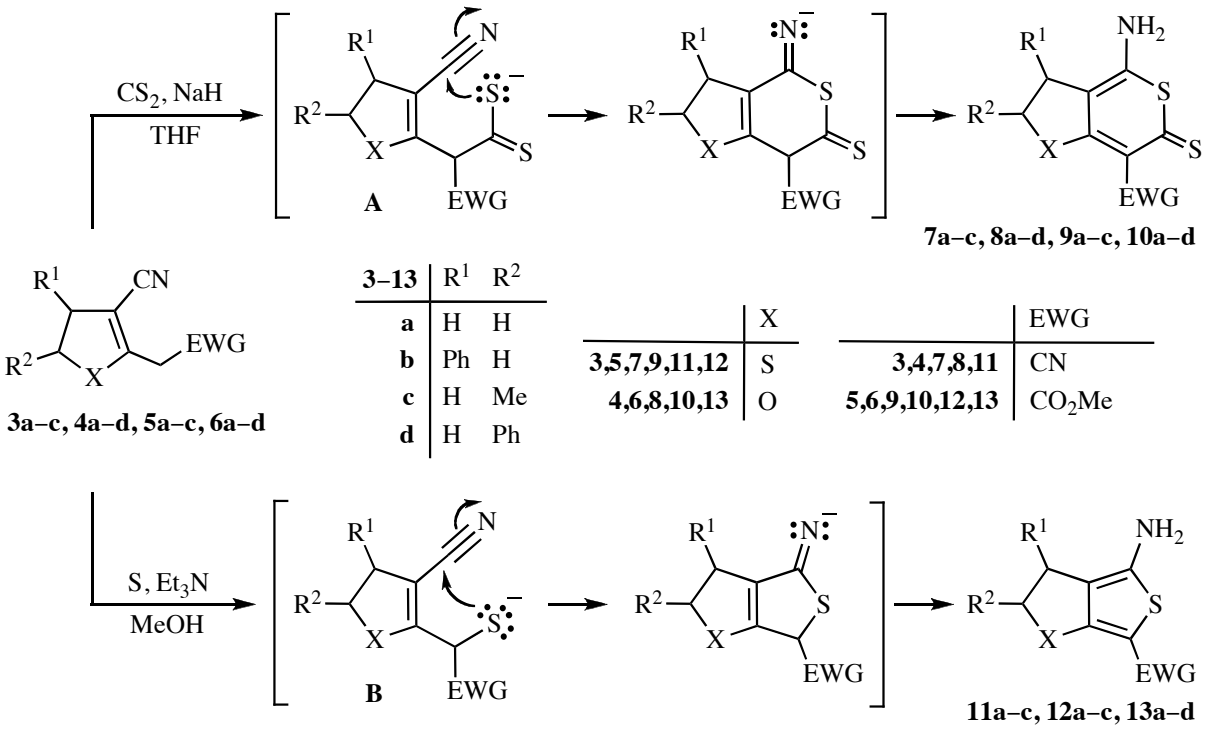
1,3,5: X = S **2,4,6**: X = O **3,4**: EWG = CN **5,6**: EWG = CO_2Me

Scheme 1

Table 1. Wittig reaction of compounds **1a–c** and **2a–d** with alkylidene phosphoranes

Entry	Substrate	X	R^1	R^2	EWG	Product	Yield (%)
1	**1a** ref.[18,19]	S	H	H	CN	**3a** ref.[22]	93
2	**1b** ref.[19]	S	Ph	H	CN	**3b**	96
3	**1c** ref.[19]	S	H	Me	CN	**3c**	98
4	**2a** ref.[18,19]	O	H	H	CN	**4a** ref.[22]	84
5	**2b** ref.[20]	O	Ph	H	CN	**4b**	69
6	**2c** ref.[21]	O	H	Me	CN	**4c**	97
7	**2d** ref.[20]	O	H	Ph	CN	**4d**	74
8	**1a**	S	H	H	CO_2Me	**5a**	65
9	**1b**	S	Ph	H	CO_2Me	**5b**	88
10	**1c**	S	H	Me	CO_2Me	**5c**	94
11	**2a**	O	H	H	CO_2Me	**6a**	55
12	**2b**	O	Ph	H	CO_2Me	**6b**	77
13	**2c**	O	H	Me	CO_2Me	**6c**	83
14	**2d**	O	H	Ph	CO_2Me	**6d**	88

In the next step, we tried to construct fused thiopyranthiones **7–10** from compounds **3–6** and carbon disulfide[23–25] (Scheme 2). To optimize the yield of **7–10**, we carried out several experiments on **3–6**, testing different reaction conditions, *e.g.* solvent, time, and substrate/base molar ratio. Solvent effects were observed with THF giving the highest yield of fused thiopyranthiones, while other solvents such as CH_2Cl_2, hexane, and toluene gave very low yields of fused thiopyranthiones. The results are summarized in Table 2. As a consequence, the reaction of heterocyclic α,β-unsaturated nitriles **3a–c**, **4a–d**, **5a–c**, and **6a–d** with carbon disulfide in the presence of sodium hydride in THF at room temperature for 4 h led to the corresponding 6-thioxothieno[3,2-*c*]thiopyran and 6-thioxothiopyrano[4,3-*b*]furan derivatives **7a–c**, **8a–d**, **9a–c**, and **10a–d** in 24–72% yields. These products **7–10** 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 **7–10** display bands in the range of 3430–3130 cm^{-1} due to a primary amino group. The ^{1}H NMR spectra of **7–10** exhibit a D_2O exchangeable signal near δ 6.0 attributable to the primary amino protons. The ^{13}C NMR spectra of **7–10** show a signal near δ 180.5 due to the thiocarbonyl carbon. The formation of the fused thiopyranthiones **7–10** could be explained by possible mechanism presented in Scheme 2. It is conceivable that the initial event is the formation of the 1:1 adducts **A** from compounds **3–6** and carbon disulfide, which underwent intramolecular cyclization to result in the formation of **7–10**.



Scheme 2

Table 2. Synthesis of fused thiopyranthione derivatives **7–10** according to Scheme 2

Entry	Substrate	X	R^1	R^2	EWG	Product	Yield (%)
1	**3a**	S	H	H	CN	**7a**	66
2	**3b**	S	Ph	H	CN	**7b**	40
3	**3c**	S	H	Me	CN	**7c**	24
4	**4a**	O	H	H	CN	**8a**	47
5	**4b**	O	Ph	H	CN	**8b**	66
6	**4c**	O	H	Me	CN	**8c**	65
7	**4d**	O	H	Ph	CN	**8d**	60
8	**5a**	S	H	H	CO_2Me	**9a**	53
9	**5b**	S	Ph	H	CO_2Me	**9b**	53
10	**5c**	S	H	Me	CO_2Me	**9c**	45
11	**6a**	O	H	H	CO_2Me	**10a**	72
12	**6b**	O	Ph	H	CO_2Me	**10b**	52
13	**6c**	O	H	Me	CO_2Me	**10c**	38
14	**6d**	O	H	Ph	CO_2Me	**10d**	37

Finally, we also attempted Gewald reaction[26,27] of compounds **3**, **5** and **6** with sulfur powder (Scheme 2). Having optimized the Gewald reaction parameters, we then examined several reaction conditions. The best results are shown in Table 3. Indeed, when a mixture of **3a–c**, **5a–c**, or **6a–d** and sulfur powder in the presence of triethylamine in methanol was stirred at room temperature for 24 h, the corresponding thieno[3,4-*b*]thiophene and thieno[3,4-*b*]furan derivatives **11a–c**, **12a–c**, and **13a–d** were obtained in moderate yields. In this case, the reaction of **4a–d** with sulfur powder failed to give the expected

thieno[3,4-*b*]furans and the reaction was not clean. The reason for this change of behavior is not very clear at present. The structures of compounds **11–13** were deduced from their elemental analyses, MS, IR, ^{1}H NMR, and ^{13}C NMR spectra (see experimental section). The IR spectra of **11–13** display bands in the range of 3470–3170 cm^{-1} due to a primary amino group. The ^{1}H NMR spectra of **11–13** exhibit a D_2O exchangeable signal near δ 6.5 attributable to the primary amino protons. A plausible mechanism for the formation of the fused thiophenes **11–13** is shown in Scheme 2. Compounds **3**, **5** and **6** would be thiolated at the methylene carbon by sulfur, followed by ring closure to afford **11–13**.

Table 3. Synthesis of fused thiophene derivatives **11–13** according to Scheme 2

Entry	Substrate	X	R^1	R^2	EWG	Product	Yield (%)
1	**3a**	S	H	H	CN	**11a**	51
2	**3b**	S	Ph	H	CN	**11b**	43
3	**3c**	S	H	Me	CN	**11c**	71
4	**5a**	S	H	H	CO_2Me	**12a**	90
5	**5b**	S	Ph	H	CO_2Me	**12b**	64
6	**5c**	S	H	Me	CO_2Me	**12c**	31
7	**6a**	O	H	H	CO_2Me	**13a**	55
8	**6b**	O	Ph	H	CO_2Me	**13b**	29
9	**6c**	O	H	Me	CO_2Me	**13c**	21
10	**6d**	O	H	Ph	CO_2Me	**13d**	66

In conclusion, we have developed a simple and efficient method for the synthesis of 6-thioxothieno[3,2-*c*]thiopyran, 6-thioxothiopyrano[4,3-*b*]furan, thieno[3,4-*b*]thiophene, and thieno[3,4-*b*]furan derivatives **7–13** by the reactions of heterocyclic α,β-unsaturated nitriles **3–6** as one of versatile starting materials with carbon disulfide and/or sulfur powder in the presence of sodium hydride or triethylamine. This methodology offers significant advantages with regard to the simplicity of operation. Functionalized fused thiopyranthione and thiophene 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 sifts (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, heterocyclic α,β-unsaturated nitriles **3–6**, were prepared in this laboratory according to the procedure for

the preparation of **3a** and **4a** reported in literature.[22]

General procedure for the preparation of heterocyclic α,β-unsaturated nitriles 3–6 from 1 and/or 2 and alkylidene phosphoranes.

A mixture of **1a–c** and/or **2a–d** (20 mmol) and (triphenylphosphoranylidene)acetonitrile (7.83 g, 26 mmol) or methyl (triphenylphosphoranylidene)acetate (7.36 g, 22 mmol) in toluene (20 mL) was refluxed for 8 h. After removal of the solvent *in vacuo*, Et_2O (40 mL) was added to the residue. The solid was removed by filtration and washed with Et_2O. The combined filtrates were concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with CH_2Cl_2 as the eluent to afford **3a–c**, **4a–d**, **5a–c**, and **6a–d**.

3-Cyano-4,5-dihydro-4-phenyl-2-thiopheneacetonitrile (3b)

Colorless prisms (4.33 g, 96%), mp 68–69 °C (Et_2O); IR (KBr): 2253, 2207 (CN) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.45 (dd, *J* = 7.6, 11.7 Hz, 1H, 5-H), 3.66–3.76 (m, 2H, CH_2CN), 3.88 (dd, *J* = 9.9, 11.7 Hz, 1H, 5-H), 4.49–4.54 (m, 1H, 4-H), 7.27–7.43 (m, 5H, aryl H); ^{13}C NMR ($CDCl_3$): δ 19.7 (*C*H_2CN), 40.9 (C-5), 54.9 (C-4), 108.8 (C-3), 113.9 (CH_2*C*N), 114.0 (CN), 127.1, 128.5, 129.4, 138.8 (C aryl), 152.2 (C-2); MS: *m/z* 227 $[M+H]^+$. Anal. Calcd for $C_{13}H_{10}N_2S$: C, 69.00; H, 4.45; N, 12.38. Found: C, 69.04; H, 4.56; N, 12.34.

3-Cyano-4,5-dihydro-5-methyl-2-thiopheneacetonitrile (3c)

Red oil (3.21 g, 98%); IR (neat): 2256, 2210 (CN) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.46 (d, *J* = 6.7 Hz, 3H, CH_3), 2.74 (tdd, *J* = 1.4, 6.1, 15.9 Hz, 1H, 4-H), 3.23 (tdd, *J* = 1.7, 8.9, 15.9 Hz, 1H, 4-H), 3.58–3.68 (m, 2H, CH_2CN), 4.01–4.09 (m, 1H, 5-H); ^{13}C NMR ($CDCl_3$): δ 19.5 (*C*H_2CN), 22.0 (CH_3), 44.4 (C-4), 45.8 (C-5), 102.7 (C-3), 114.0 (CH_2*C*N), 114.3 (CN), 151.2 (C-2); MS: *m/z* 165 $[M+H]^+$. Anal. Calcd for $C_8H_8N_2S$: C, 58.51; H, 4.91; N, 17.06. Found: C, 58.37; H, 4.97; N, 16.90.

3-Cyano-4,5-dihydro-4-phenyl-2-furanacetonitrile (4b)

Red oil (2.91 g, 69%); IR (neat): 2265, 2214 (CN) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.55–3.64 (m, 2H, CH_2CN), 4.40–4.44 (m, 1H, 4-H), 4.53–4.57 (m, 1H, 5-H), 4.95–5.00 (m, 1H, 5-H), 7.20–7.43 (m, 5H, aryl H); ^{13}C NMR ($CDCl_3$): δ 17.4 (*C*H_2CN), 49.0 (C-4), 80.4 (C-5), 91.6 (C-3), 112.6 (CH_2*C*N), 113.8 (CN), 127.1, 128.4, 129.4, 138.9 (C aryl), 161.4 (C-2); MS: *m/z* 211 $[M+H]^+$. Anal. Calcd for $C_{13}H_{10}N_2O$: C, 74.27; H, 4.79; N, 13.32. Found: C, 74.30; H, 4.94; N, 13.05.

3-Cyano-4,5-dihydro-5-methyl-2-furanacetonitrile (4c)

Red oil (2.88 g, 97%); IR (neat): 2263, 2214 (CN) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.39 (d, *J* = 6.1 Hz, 3H, CH_3), 2.46–2.52 (m, 1H, 4-H), 2.99–3.05 (m, 1H, 4-H), 3.41–3.42 (m, 2H, CH_2CN), 4.92–4.98 (m, 1H, 5-H); ^{13}C NMR ($CDCl_3$): δ 17.3 (*C*H_2CN), 21.4 (CH_3), 37.3 (C-4), 82.2 (C-5), 85.1 (C-3), 112.7 (CH_2*C*N), 114.6 (CN), 160.4 (C-2); MS: *m/z* 149 $[M+H]^+$. Anal. Calcd for $C_8H_8N_2O$: C, 64.85; H, 5.44; N, 18.91. Found: C, 64.73; H, 5.51; N, 18.64.

3-Cyano-4,5-dihydro-5-phenyl-2-furanacetonitrile (4d)

Red oil (3.12 g, 74%); IR (neat): 2261, 2215 (CN) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.89–2.95 (m, 1H, 4-H), 3.28–3.35 (m, 1H, 4-H), 3.49–3.51 (m, 2H, CH_2CN), 5.74–5.78 (m, 1H, 5-H), 7.17–7.37 (m, 5H, aryl H); ^{13}C NMR ($CDCl_3$): δ 17.3 (*C*H_2CN), 38.2 (C-4), 85.6 (C-3), 86.1 (C-5), 112.6 (CH_2*C*N), 114.1 (CN), 125.6, 129.05, 129.13, 138.8 (C aryl), 160.4 (C-2); MS: *m/z* 211 $[M+H]^+$. Anal. Calcd for $C_{13}H_{10}N_2O$: C, 74.27; H, 4.79; N, 13.32. Found: C, 74.38; H, 4.96; N, 13.12.

Methyl 3-cyano-4,5-dihydro-2-thiopheneacetate (5a)

Pale yellow oil (2.37 g, 65%); IR (neat): 2207 (CN), 1743 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.06 (tt, *J* = 1.4, 8.9 Hz, 2H, 4-H), 3.39 (t, *J* = 8.9 Hz, 2H, 5-H), 3.58 (t, *J* = 1.4 Hz, 2H, C*H*$_2$$CO_2$Me), 3.75 (s, 3H, CO_2Me); ^{13}C NMR ($CDCl_3$): δ 32.9 (C-5), 35.9 (*C*$H_2$$CO_2$Me), 36.4 (C-4), 52.5 ($CO_2$*Me*), 103.3 (C-3), 115.2 (CN), 156.1 (C-2), 168.0 (C=O); MS: *m/z* 184 $[M+H]^+$. Anal. Calcd for $C_8H_9NO_2S$: C, 52.44; H, 4.95; N, 7.64. Found: C, 52.53; H, 5.01; N, 7.74.

Methyl 3-cyano-4,5-dihydro-4-phenyl-2-thiopheneacetate (5b)

Colorless prisms (4.55 g, 88%), mp 79–80 °C (Et_2O); IR (KBr): 2207 (CN), 1737 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.35 (dd, *J* = 7.0, 11.6 Hz, 1H, 5-H), 3.62–3.71 (m, 2H, C*H*$_2$$CO_2$Me), 3.78 (s, 3H, CO_2Me), 3.82 (dd, *J* = 10.1, 11.6 Hz, 1H, 5-H), 4.45–4.50 (m, 1H, 4-H), 7.29–7.40 (m, 5H, aryl H); ^{13}C NMR ($CDCl_3$): δ 36.1 (*C*$H_2$$CO_2$Me), 41.0 (C-5), 52.6 ($CO_2$*Me*), 54.6 (C-4), 108.0 (C-3), 115.1 (CN), 127.2, 128.2, 129.2, 139.6 (C aryl), 156.5 (C-2), 168.0 (C=O); MS: *m/z* 260 $[M+H]^+$. Anal. Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40. Found: C, 64.92; H, 5.11; N, 5.38.

Methyl 3-cyano-4,5-dihydro-5-methyl-2-thiopheneacetate (5c)

Yellow oil (3.72 g, 94%); IR (neat): 2206 (CN), 1744 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.42 (d, *J* = 6.7 Hz, 3H, CH_3), 2.70 (tdd, *J* = 1.2, 5.8, 15.6 Hz, 1H, 4-H), 3.18 (tdd, *J* = 1.4, 8.5, 15.6 Hz, 1H, 4-H), 3.56–3.58 (m, 2H, C*H*$_2$$CO_2$Me), 3.75 (s, 3H, CO_2Me), 3.89–3.99 (m, 1H, 5-H); ^{13}C NMR ($CDCl_3$): δ 22.0 (CH_3), 36.1 (*C*$H_2$$CO_2$Me), 44.2 (C-4), 45.4 (C-5), 52.5 (CO_2*Me*), 101.8 (C-3), 115.4 (CN), 155.3 (C-2), 168.1 (C=O); MS: *m/z* 198 $[M+H]^+$. Anal. Calcd for $C_9H_{11}NO_2S$: C, 54.80; H, 5.62; N, 7.10. Found: C, 54.86; H, 5.52; N, 7.01.

Methyl 3-cyano-4,5-dihydro-2-furanacetate (6a)

Colorless oil (1.85 g, 55%); IR (neat): 2211 (CN), 1746 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.92–2.98 (m, 2H, 4-H), 3.42–3.43 (m, 2H, C*H*$_2$$CO_2$Me), 3.75 (s, 3H, CO_2Me), 4.55–4.60 (m, 2H, 5-H); ^{13}C NMR ($CDCl_3$): δ 30.3 (C-4), 33.5 (*C*$H_2$$CO_2$Me), 52.6 ($CO_2$*Me*), 72.2 (C-5), 85.3 (C-3), 115.7 (CN), 166.3 (C-2), 167.1 (C=O); MS: *m/z* 168 $[M+H]^+$. Anal. Calcd for $C_8H_9NO_3$: C, 57.48; H, 5.43; N, 8.38. Found: C, 57.50; H, 5.31; N, 8.40.

Methyl 3-cyano-4,5-dihydro-4-phenyl-2-furanacetate (6b)

Colorless prisms (3.74 g, 77%), mp 46–47 °C (Et_2O); IR (KBr): 2212 (CN), 1739 (C=O) cm^{-1}; ^1H NMR

($CDCl_3$): δ 3.48–3.58 (m, 2H, C*H*$_2$$CO_2$Me), 3.78 (s, 3H, CO_2Me), 4.37 (dd, *J* = 6.4, 10.5 Hz, 1H, 4-H), 4.46 (dd, *J* = 6.4, 9.4 Hz, 1H, 5-H), 4.90 (dd, *J* = 9.4, 10.5 Hz, 1H, 5-H), 7.24–7.27 (m, 2H, aryl H), 7.28–7.32 (m, 1H, aryl H), 7.35–7.39 (m, 2H, aryl H); ^{13}C NMR ($CDCl_3$): δ 33.7 (*C*$H_2$$CO_2$Me), 48.9 (C-4), 52.7 ($CO_2$*Me*), 80.1 (C-5), 91.0 (C-3), 115.1 (CN), 127.2, 128.0, 129.2, 140.0 (C aryl), 166.5 (C-2), 167.1 (C=O); MS: *m/z* 244 $[M+H]^+$. Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.21; H, 5.47; N, 5.77.

Methyl 3-cyano-4,5-dihydro-5-methyl-2-furanacetate (6c)

Pale yellow oil (3.02 g, 83%); IR (neat): 2210 (CN), 1747 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.41 (d, *J* = 6.1 Hz, 3H, CH_3), 2.49–2.55 (m, 1H, 4-H), 3.02–3.09 (m, 1H, 4-H), 3.40 (dd, *J* = 1.2, 2.1 Hz, 2H, C*H*$_2$$CO_2$Me), 3.75 (s, 3H, CO_2Me), 4.91–4.97 (m, 1H, 5-H); ^{13}C NMR ($CDCl_3$): δ 21.4 (CH_3), 33.7 (*C*$H_2$$CO_2$Me), 37.2 (C-4), 52.5 ($CO_2$*Me*), 81.3 (C-5), 84.3 (C-3), 115.9 (CN), 165.4 (C-2), 167.2 (C=O); MS: *m/z* 182 $[M+H]^+$. Anal. Calcd for $C_9H_{11}NO_3$•0.1H_2O: C, 59.07; H, 6.17; N, 7.65. Found: C, 59.20; H, 6.04; N, 7.64.

Methyl 3-cyano-4,5-dihydro-5-phenyl-2-furanacetate (6d)

Pale yellow oil (4.28 g, 88%); IR (neat): 2211 (CN), 1747 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.91–2.96 (m, 1H, 4-H), 3.33–3.40 (m, 1H, 4-H), 3.46–3.55 (m, 2H, C*H*$_2$$CO_2$Me), 3.76 (s, 3H, CO_2Me), 5.73–5.78 (m, 1H, 5-H), 7.32–7.42 (m, 5H, aryl H); ^{13}C NMR ($CDCl_3$): δ 33.7 (*C*$H_2$$CO_2$Me), 38.4 (C-4), 52.6 ($CO_2$*Me*), 84.7 (C-3), 85.5 (C-5), 115.5 (CN), 125.7, 128.8, 128.9, 139.9 (C aryl), 165.5 (C-2), 167.1 (C=O); MS: *m/z* 244 $[M+H]^+$. Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.09; H, 5.45; N, 5.77.

General procedure for the preparation of fused thiopyranthiones 7–10 from 3–6 and carbon disulfide in the presence of sodium hydride.

To an ice-cooled and stirred solution of **3a–c**, **4a–d**, **5a–c**, and **6a–d** (5 mmol) in THF (5 mL) was added 60% NaH (0.20 g, 5 mmol). The stirring was continued at rt until evolution of gas ceased. To the obtained mixture was added carbon disulfide (0.42 g, 5.5 mmol) with stirring and then the mixture was stirred at rt for 4 h. The reaction mixture was neutralized with acetic acid (0.30 g, 5 mmol) with stirring and ice-cooling. After removal of the solvent *in vacuo*, cold water was added to the residue. Further processing of the resulting mixture is described in the following paragraphs.

(A) The precipitate was isolated by filtration, washed with water, dried, and recrystallized from an appropriate solvent to give **7a–c**, **8a–d**, **9a**, and **10a**.

(B) The resulting mixture was extracted with CH_2Cl_2. The extract was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography on alumina with CH_2Cl_2-acetone (4:1) as the eluent to afford **9b–c** and **10b–d**.

4-Amino-2,3-dihydro-6-thioxo-6*H*-thieno[3,2-*c*]thiopyran-7-carbonitrile (7a)

Pale yellow prisms (0.75 g, 66%), mp >300 °C (DMSO/H_2O); IR (KBr): 3427, 3311, 3207, 3140 (NH), 2200 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.17 (t, *J* = 8.4 Hz, 2H, 3-H), 3.53 (t, *J* = 8.4 Hz, 2H, 2-H), 8.77 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 31.9 (C-2), 33.4 (C-3), 101.0 (C-7), 113.3 (C-3a), 116.7 (CN), 161.6 (C-4), 167.8 (C-7a), 187.2 (C=S); MS: *m/z* 227 $[M+H]^+$. Anal. Calcd for $C_8H_6N_2S_3$: C, 42.45; H, 2.67; N, 12.38. Found: C, 42.36; H, 2.82; N, 12.14.

4-Amino-2,3-dihydro-3-phenyl-6-thioxo-6*H*-thieno[3,2-*c*]thiopyran-7-carbonitrile (7b)

Orange prisms (0.60 g, 40%), mp 237–238 °C (acetone/petroleum ether); IR (KBr): 3384, 3292, 3184 (NH), 2210 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.26 (dd, *J* = 0.9, 11.6 Hz, 1H, 2-H), 4.09 (dd, *J* = 8.4, 11.6 Hz, 1H, 2-H), 4.89–4.92 (m, 1H, 3-H), 7.21–7.24 (m, 2H, aryl H), 7.26–7.31 (m, 1H, aryl H), 7.33–7.37 (m, 2H, aryl H), 8.65 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 41.7 (C-2), 49.1 (C-3), 101.2 (C-7), 115.1 (C-3a), 116.6 (CN), 126.8, 127.3, 128.6, 139.5 (C aryl), 162.4 (C-4), 168.6 (C-7a), 187.8 (C=S); MS: *m/z* 303 $[M+H]^+$. Anal. Calcd for $C_{14}H_{10}N_2S_3$: C, 55.60; H, 3.33; N, 9.26. Found: C, 55.51; H, 3.52; N, 9.02.

4-Amino-2,3-dihydro-2-methyl-6-thioxo-6*H*-thieno[3,2-*c*]thiopyran-7-carbonitrile (7c)

Yellow prisms (0.29 g, 24%), mp 280 °C (dec.) (acetone); IR (KBr): 3378, 3303, 3161 (NH), 2212 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.42 (d, *J* = 6.7 Hz, 3H, CH_3), 2.86 (dd, *J* = 5.6, 15.4 Hz, 1H, 3-H), 3.28–3.34 (m, 1H, 3-H), 4.13–4.21 (m, 1H, 2-H), 8.78 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 22.2 (CH_3), 41.1 (C-3), 44.5 (C-2), 101.0 (C-7), 112.2 (C-3a), 116.6 (CN), 162.0 (C-4), 166.7 (C-7a), 187.1 (C=S); MS: *m/z* 241 $[M+H]^+$. Anal. Calcd for $C_9H_8N_2S_3 \cdot 0.1\ H_2O$: C, 44.64; H, 3.41; N, 11.57. Found: C, 44.48; H, 3.44; N, 11.41.

4-Amino-2,3-dihydro-6-thioxo-6*H*-thiopyrano[4,3-*b*]furan-7-carbonitrile (8a)

Pale yellow prisms (0.50 g, 47%), mp 276 °C (dec.) (DMSO/H_2O); IR (KBr): 3386, 3277, 3177 (NH), 2213 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.98 (t, *J* = 8.9 Hz, 2H, 3-H), 4.83 (t, *J* = 8.9 Hz, 2H, 2-H), 8.67 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 26.8 (C-3), 74.8 (C-2), 94.1 (C-7), 102.4 (C-3a), 114.5 (CN), 163.1 (C-4), 173.6 (C-7a), 190.3 (C=S); MS: *m/z* 211 $[M+H]^+$. Anal. Calcd for $C_8H_6N_2OS_2 \cdot 0.2H_2O$: C, 44.93; H, 3.02; N, 13.10. Found: C, 44.97; H, 2.97; N, 13.06.

4-Amino-2,3-dihydro-3-phenyl-6-thioxo-6*H*-thiopyrano[4,3-*b*]furan-7-carbonitrile (8b)

Pale yellow needles (0.95 g, 66%), mp 230–231 °C (acetone/petroleum ether); IR (KBr): 3418, 3294, 3183 (NH), 2222 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 4.63 (dd, *J* = 3.1, 9.0 Hz, 1H, 3-H), 4.66 (dd, *J* = 3.1, 9.0 Hz, 1H, 2-H), 5.12 (t, *J* = 9.0 Hz, 1H, 2-H), 7.20–7.24 (m, 2H, aryl H), 7.26–7.30 (m, 1H, aryl H), 7.33–7.37 (m, 2H, aryl H), 8.49 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 44.0 (C-3), 82.5 (C-2), 94.1 (C-7), 105.3 (C-3a), 114.4 (CN), 126.9, 127.3, 128.7, 140.2 (C aryl), 163.9 (C-4), 173.6 (C-7a), 191.0 (C=S); MS: *m/z* 287 $[M+H]^+$. Anal. Calcd for $C_{14}H_{10}N_2OS_2$: C, 58.72; H, 3.52; N, 9.78. Found: C, 58.59; H, 3.62; N, 9.71.

4-Amino-2,3-dihydro-2-methyl-6-thioxo-6*H*-thiopyrano[4,3-*b*]furan-7-carbonitrile (8c)

Pale yellow needles (0.73 g, 65%), mp 286 °C (dec.) (acetone/petroleum ether); IR (KBr): 3306, 3172 (NH), 2222 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.47 (d, J = 6.4 Hz, 3H, CH_3), 2.56 (dd, J = 7.2, 14.9 Hz, 1H, 3-H), 3.51 (dd, J = 9.2, 14.9 Hz, 1H, 3-H), 5.23–5.30 (m, 1H, 2-H), 8.64 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 21.2 (CH_3), 33.7 (C-3), 84.3 (C-2), 94.0 (C-7), 102.1 (C-3a), 114.6 (CN), 163.2 (C-4), 172.7 (C-7a), 190.3 (C=S); MS: m/z 225 $[M+H]^+$. Anal. Calcd for $C_9H_8N_2OS_2$: C, 48.19; H, 3.59; N, 12.49. Found: C, 48.24; H, 3.63; N, 12.23.

4-Amino-2,3-dihydro-2-phenyl-6-thioxo-6*H*-thiopyrano[4,3-*b*]furan-7-carbonitrile (8d)

Pale yellow prisms (0.86 g, 60%), mp 264 °C (dec.) (acetone/petroleum ether); IR (KBr): 3340, 3263, 3142 (NH), 2216 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.94 (dd, J = 7.5, 15.2 Hz, 1H, 3-H), 3.50 (dd, J = 9.7, 15.2 Hz, 1H, 3-H), 6.17 (dd, J = 7.5, 9.7 Hz, 1H, 2-H), 7.39–7.48 (m, 5H, aryl H), 8.76 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 34.8 (C-3), 87.4 (C-2), 93.8 (C-7), 101.6 (C-3a), 114.5 (CN), 126.2, 128.8, 128.9, 139.2 (C aryl), 163.3 (C-4), 172.4 (C-7a), 190.6 (C=S); MS: m/z 287 $[M+H]^+$. Anal. Calcd for $C_{14}H_{10}N_2OS_2$: C, 58.72; H, 3.52; N, 9.78. Found: C, 58.62; H, 3.71; N, 9.59.

Methyl 4-amino-2,3-dihydro-6-thioxo-6*H*-thieno[3,2-*c*]thiopyran-7-carboxylate (9a)

Pale yellow prisms (0.69 g, 53%), mp 214 °C (dec.) (acetone); IR (KBr): 3392, 3302, 3188 (NH), 1697 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.08 (t, J = 8.1 Hz, 2H, 3-H), 3.38 (t, J = 8.1 Hz, 2H, 2-H), 3.70 (s, 3H, CO_2Me), 8.21 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 31.7 (C-2), 32.6 (C-3), 51.8 ($CO_2\mathit{Me}$), 112.3 (C-3a), 123.6 (C-7), 160.7 (C-4), 162.5 (C-7a), 166.9 (C=O), 181.9 (C=S); MS: m/z 260 $[M+H]^+$. Anal. Calcd for $C_9H_9NO_2S_3$: C, 41.68; H, 3.50; N, 5.40. Found: C, 41.70; H, 3.57; N, 5.21.

Methyl 4-amino-2,3-dihydro-3-phenyl-6-thioxo-6*H*-thieno[3,2-*c*]thiopyran-7-carboxylate (9b)

Yellow prisms (0.89 g, 53%), mp 194 °C (dec.) (acetone/petroleum ether); IR (KBr): 3400, 3308, 3205 (NH), 1717 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.15 (dd, J = 1.2, 11.5 Hz, 1H, 2-H), 3.72 (s, 3H, CO_2Me), 3.93 (dd, J = 8.2, 11.5 Hz, 1H, 2-H), 4.82–4.84 (m, 1H, 3-H), 7.20–7.23 (m, 2H, aryl H), 7.25–7.29 (m, 1H, aryl H), 7.33–7.37 (m, 2H, aryl H), 8.09 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 41.2 (C-2), 48.2 (C-3), 51.9 ($CO_2\mathit{Me}$), 114.2 (C-3a), 123.6 (C-7), 126.8, 127.2, 128.4, 139.9 (C aryl), 161.6 (C-4), 163.1 (C-7a), 166.9 (C=O), 182.8 (C=S); MS: m/z 336 $[M+H]^+$. Anal. Calcd for $C_{15}H_{13}NO_2S_3$: C, 53.70; H, 3.91; N, 4.18. Found: C, 53.84; H, 3.96; N, 4.14.

Methyl 4-amino-2,3-dihydro-2-methyl-6-thioxo-6*H*-thieno[3,2-*c*]thiopyran-7-carboxylate (9c)

Yellow prisms (0.61 g, 45%), mp 169 °C (dec.) (acetone/petroleum ether); IR (KBr): 3342, 3287, 3145 (NH), 1714 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.36 (d, J = 6.7 Hz, 3H, CH_3), 2.78 (dd, J = 6.0, 15.4 Hz, 1H, 3-H), 3.23 (dd, J = 8.1, 15.4 Hz, 1H, 3-H), 3.69 (s, 3H, CO_2Me), 3.99–4.06 (m, 1H, 2-H), 8.20 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 21.9 (CH_3), 40.4 (C-3), 43.9 (C-2), 51.9 ($CO_2\mathit{Me}$), 111.4 (C-3a), 123.6 (C-7), 161.2 (C-4), 161.6 (C-7a), 166.9 (C=O), 181.8 (C=S); MS: m/z 274 $[M+H]^+$. Anal. Calcd for

$C_{10}H_{11}NO_2S_3$: C, 43.93; H, 4.06; N, 5.12. Found: C, 43.99; H, 4.10; N, 5.08.

Methyl 4-amino-2,3-dihydro-6-thioxo-6*H*-thiopyrano[4,3-*b*]furan-7-carboxylate (10a)

Colorless plates (0.88 g, 72%), mp 190 °C (dec.) (methanol); IR (KBr): 3379, 3303, 3184 (NH), 1698 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.93 (t, *J* = 8.7 Hz, 2H, 3-H), 3.68 (s, 3H, CO_2Me), 4.71 (t, *J* = 8.7 Hz, 2H, 2-H), 8.17 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 26.4 (C-3), 51.9 (CO_2*Me*), 73.8 (C-2), 101.7 (C-3a), 116.0 (C-7), 162.5 (C-4), 165.1 (C=O), 169.5 (C-7a), 184.2 (C=S); MS: *m*/*z* 244 $[M+H]^+$. Anal. Calcd for $C_9H_9NO_3S_2$: C, 44.43; H, 3.73; N, 5.76. Found: C, 44.42; H, 3.76; N, 5.67.

Methyl 4-amino-2,3-dihydro-3-phenyl-6-thioxo-6*H*-thiopyrano[4,3-*b*]furan-7-carboxylate (10b)

Pale yellow prisms (0.82 g, 52%), mp 208 °C (dec.) (acetone/petroleum ether); IR (KBr): 3366, 3280, 3140 (NH), 1719 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.71 (s, 3H, CO_2Me), 4.50 (dd, *J* = 2.9, 9.1 Hz, 1H, 2-H), 4.61 (dd, *J* = 2.9, 9.1 Hz, 1H, 3-H), 4.99 (t, *J* = 9.1 Hz, 1H, 2-H), 7.17–7.20 (m, 2H, aryl H), 7.25–7.29 (m, 1H, aryl H), 7.33–7.37 (m, 2H, aryl H), 7.99 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 43.6 (C-3), 52.0 (CO_2*Me*), 81.6 (C-2), 104.7 (C-3a), 116.0 (C-7), 126.8, 127.1, 128.7, 140.6 (C aryl), 163.3 (C-4), 165.0 (C=O), 169.4 (C-7a), 185.1 (C=S); MS: *m*/*z* 320 $[M+H]^+$. Anal. Calcd for $C_{15}H_{13}NO_3S_2$: C, 56.41; H, 4.10; N, 4.39. Found: C, 56.38; H, 4.10; N, 4.35.

Methyl 4-amino-2,3-dihydro-2-methyl-6-thioxo-6*H*-thiopyrano[4,3-*b*]furan-7-carboxylate (10c)

Pale yellow prisms (0.49 g, 38%), mp 182 °C (dec.) (acetone/petroleum ether); IR (KBr): 3330, 3303, 3167 (NH), 1699 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.39 (d, *J* = 6.1 Hz, 3H, CH_3), 2.51 (dd, *J* = 7.0, 15.0 Hz, 1H, 3-H), 3.10 (dd, *J* = 8.9, 15.0 Hz, 1H, 3-H), 3.68 (s, 3H, CO_2Me), 5.08–5.16 (m, 1H, 2-H), 8.13 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 21.3 (CH_3), 33.4 (C-3), 51.9 (CO_2*Me*), 83.0 (C-2), 101.4 (C-3a), 116.0 (C-7), 162.5 (C-4), 165.1 (C=O), 168.6 (C-7a), 184.1 (C=S); MS: *m*/*z* 258 $[M+H]^+$. Anal. Calcd for $C_{10}H_{11}NO_3S_2$: C, 46.67; H, 4.31; N, 5.44. Found: C, 46.71; H, 4.32; N, 5.39.

Methyl 4-amino-2,3-dihydro-2-phenyl-6-thioxo-6*H*-thiopyrano[4,3-*b*]furan-7-carboxylate (10d)

Pale yellow needles (0.59 g, 37%), mp 199 °C (dec.) (acetone/petroleum ether); IR (KBr): 3315, 3138 (NH), 1706 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.87 (dd, *J* = 6.8, 15.3 Hz, 1H, 3-H), 3.46 (dd, *J* = 9.5, 15.3 Hz, 1H, 3-H), 3.68 (s, 3H, CO_2Me), 6.06 (dd, *J* = 6.8, 9.5 Hz, 1H, 2-H), 7.34–7.45 (m, 5H, aryl H), 8.24 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 34.7 (C-3), 52.0 (CO_2*Me*), 86.0 (C-2), 100.7 (C-3a), 115.8 (C-7), 125.6, 128.5, 128.7, 140.0 (C aryl), 162.7 (C-4), 165.1 (C=O), 168.5 (C-7a), 184.6 (C=S); MS: *m*/*z* 320 $[M+H]^+$. Anal. Calcd for $C_{15}H_{13}NO_3S_2$: C, 56.41; H, 4.10; N, 4.39. Found: C, 56.32; H, 4.08; N, 4.33.

General procedure for the preparation of fused thiophenes 11–13 from 3, 5 and/or 6 and sulfur powder in the presence of triethylamine.

A mixture of **3a–c**, **5a–c**, and/or **6a–d** (5 mmol), sulfur powder (0.16 g, 5 mmol), and triethylamine (1.45 g, 14.3 mmol) in MeOH (5 mL) was stirred at rt for 24 h. After removal of the solvent *in vacuo*, the residue was purified by column chromatography on silica gel with CH_2Cl_2 as the eluent to yield **11a–c**,

12a–c, and **13a–d**.

4-Amino-2,3-dihydrothieno[3,4-*b*]thiophene-6-carbonitrile (11a)

Pale yellow columns (1.32 g, 51%), mp 125–126 °C (Et_2O); IR (KBr): 3338, 3295, 3198 (NH), 2194 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.81 (t, J = 7.5 Hz, 2H, 3-H), 3.79 (t, J = 7.5 Hz, 2H, 2-H), 6.68 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 27.3 (C-3), 40.6 (C-2), 73.1 (C-6), 115.9 (CN), 120.4 (C-3a), 150.5 (C-4), 155.1 (C-6a); MS: m/z 183 $[M+H]^+$. Anal. Calcd for $C_7H_6N_2S_2$: C, 46.13; H, 3.32; N, 15.37. Found: C, 46.06; H, 3.38; N, 15.31.

4-Amino-2,3-dihydro-3-phenylthieno[3,4-*b*]thiophene-6-carbonitrile (11b)

Colorless prisms (0.55 g, 43%), mp 137–138 °C (Et_2O/petroleum ether); IR (KBr): 3399, 3325, 3220 (NH), 2189 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.54 (dd, J = 2.4, 11.3 Hz, 1H, 2-H), 4.37 (dd, J = 7.9, 11.3 Hz, 1H, 2-H), 4.47 (dd, J = 2.4, 7.9 Hz, 1H, 3-H), 6.53 (br s, 2H, NH_2), 7.20–7.26 (m, 3H, aryl H), 7.30–7.34 (m, 2H, aryl H); ^{13}C NMR (DMSO-d_6): δ 44.1 (C-3), 49.4 (C-2), 73.3 (C-6), 115.8 (CN), 122.1 (C-3a), 126.8, 127.0, 128.3, 141.2 (C aryl), 151.8 (C-4), 155.1 (C-6a); MS: m/z 259 $[M+H]^+$. Anal. Calcd for $C_{13}H_{10}N_2S_2$: C, 60.43; H, 3.90; N, 10.84. Found: C, 60.55; H, 4.02; N, 10.80.

4-Amino-2,3-dihydro-2-methylthieno[3,4-*b*]thiophene-6-carbonitrile (11c)

Colorless prisms (0.70 g, 71%), mp 69–71 °C (Et_2O/petroleum ether); IR (KBr): 3307, 3187 (NH), 2198 (CN) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.44 (d, J = 6.7 Hz, 3H, CH_3), 2.48 (dd, J = 6.4, 15.0 Hz, 1H, 3-H), 2.99 (dd, J = 7.5, 15.0 Hz, 1H, 3-H), 4.44–4.51 (m, 1H, 2-H), 6.67 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 22.4 (CH_3), 35.7 (C-3), 54.1 (C-2), 73.3 (C-6), 115.9 (CN), 119.2 (C-3a), 150.9 (C-4), 154.2 (C-6a); MS: m/z 197 $[M+H]^+$. Anal. Calcd for $C_8H_8N_2S_2$: C, 48.95; H, 4.11; N, 14.27. Found: C, 49.03; H, 4.11; N, 14.20.

Methyl 4-amino-2,3-dihydrothieno[3,4-*b*]thiophene-6-carboxylate (12a)

Colorless columns (0.97 g, 90%), mp 130–131 °C (acetone/petroleum ether); IR (KBr): 3423, 3321, 3204 (NH), 1651 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.76 (t, J = 7.8 Hz, 2H, 3-H), 3.63 (s, 3H, CO_2Me), 3.64 (t, J = 7.8 Hz, 2H, 2-H), 6.46 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 26.5 (C-3), 39.1 (C-2), 50.8 (CO_2*Me*), 96.5 (C-6), 120.9 (C-3a), 150.5 (C-4), 152.5 (C-6a), 161.9 (C=O); MS: m/z 216 $[M+H]^+$. Anal. Calcd for $C_8H_9NO_2S_2$: C, 44.63; H, 4.21; N, 6.51. Found: C, 44.52; H, 4.20; N, 6.48.

Methyl 4-amino-2,3-dihydro-3-phenylthieno[3,4-*b*]thiophene-6-carboxylate (12b)

Colorless prisms (0.93 g, 64%), mp 151–152 °C (acetone/petroleum ether); IR (KBr): 3443, 3327, 3208 (NH), 1656 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.41 (dd, J = 2.6, 11.4 Hz, 1H, 2-H), 3.65 (s, 3H, CO_2Me), 4.23 (dd, J = 8.2, 11.4 Hz, 1H, 2-H), 4.42 (dd, J = 2.6, 8.2 Hz, 1H, 3-H), 6.28 (br s, 2H, NH_2), 7.20–7.24 (m, 3H, aryl H), 7.28–7.32 (m, 2H, aryl H); ^{13}C NMR (DMSO-d_6): δ 43.5 (C-3), 48.2 (C-2), 50.9 (CO_2*Me*), 96.5 (C-6), 123.0 (C-3a), 126.6, 127.0, 128.3, 142.0 (C aryl), 151.8 (C-4), 152.4 (C-6a), 161.9 (C=O); MS: m/z 292 $[M+H]^+$. Anal. Calcd for $C_{14}H_{13}NO_2S_2$: C, 57.71; H, 4.50; N, 4.81. Found: C,

57.94; H, 4.55; N, 4.77.

Methyl 4-amino-2,3-dihydro-2-methylthieno[3,4-*b*]thiophene-6-carboxylate (12c)

Colorless needles (0.35 g, 31%), mp 117–119 °C (acetone/petroleum ether); IR (KBr): 3448, 3313, 3204 (NH), 1671 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.40 (d, J = 6.7 Hz, 3H, CH_3), 2.41 (dd, J = 6.4, 15.0 Hz, 1H, 3-H), 2.95 (dd, J = 7.6, 15.0 Hz, 1H, 3-H), 3.62 (s, 3H, CO_2Me), 4.26–4.34 (m, 1H, 2-H), 6.44 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 22.7 (CH_3), 35.1 (C-3), 50.8 (CO_2Me), 51.9 (C-2), 96.6 (C-6), 119.8 (C-3a), 150.9 (C-4), 151.6 (C-6a), 161.8 (C=O); MS: m/z 230 $[M+H]^+$. Anal. Calcd for $C_9H_{11}NO_2S_2$: C, 47.14; H, 4.83; N, 6.11. Found: C, 47.40; H, 4.90; N, 6.06.

Methyl 4-amino-2,3-dihydrothieno[3,4-*b*]furan-6-carboxylate (13a)

Colorless prisms (0.55 g, 55%), mp 173–174 °C (acetone/petroleum ether); IR (KBr): 3425, 3380 3323, 3206 (NH), 1660 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.75 (t, J = 8.2 Hz, 2H, 3-H), 3.57 (s, 3H, CO_2Me), 4.89 (t, J = 8.2 Hz, 2H, 2-H), 6.54 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 24.6 (C-3), 50.3 (CO_2Me), 80.2 (C-2), 82.4 (C-6), 108.9 (C-3a), 149.8 (C-4), 161.1 (C=O), 165.9 (C-6a); MS: m/z 200 $[M+H]^+$. Anal. Calcd for $C_8H_9NO_3S$: C, 48.23; H, 4.55; N, 7.03. Found: C, 48.27; H, 4.53; N, 7.01.

Methyl 4-amino-2,3-dihydro-3-phenylthieno[3,4-*b*]furan-6-carboxylate (13b)

Colorless needles (0.40 g, 29%), mp 152–154 °C (acetone/petroleum ether); IR (KBr): 3470, 3288, 3177 (NH), 1653 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.60 (s, 3H, CO_2Me), 4.37 (dd, J = 3.7, 8.6 Hz, 1H, 3-H), 4.65 (dd, J = 3.7, 8.6 Hz, 1H, 2-H), 5.24 (t, J = 8.6 Hz, 1H, 2-H), 6.45 (br s, 2H, NH_2), 7.17–7.20 (m, 2H, aryl H), 7.21–7.25 (m, 1H, aryl H), 7.30–7.35 (m, 2H, aryl H); ^{13}C NMR (DMSO-d_6): δ 42.7 (C-3), 50.4 (CO_2Me), 82.5 (C-6), 87.9 (C-2), 111.6 (C-3a), 126.6, 126.9, 128.5, 141.8 (C aryl), 150.9 (C-4), 161.1 (C=O), 165.5 (C-6a); MS: m/z 276 $[M+H]^+$. Anal. Calcd for $C_{14}H_{13}NO_3S$: C, 61.07; H, 4.76; N, 5.09. Found: C, 61.18; H, 4.71; N, 5.09.

Methyl 4-amino-2,3-dihydro-2-methylthieno[3,4-*b*]furan-6-carboxylate (13c)

Colorless needles (0.27 g, 21%), mp 156–157 °C (acetone/petroleum ether); IR (KBr): 3432, 3330, 3216 (NH), 1658 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 1.41 (d, J = 6.4 Hz, 3H, CH_3), 2.34 (dd, J = 7.2, 14.5 Hz, 1H, 3-H), 2.90 (dd, J = 8.4, 14.5 Hz, 1H, 3-H), 3.57 (s, 3H, CO_2Me), 5.24–5.32 (m, 1H, 2-H), 6.51 (br s, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 21.9 (CH_3), 32.2 (C-3), 50.3 (CO_2Me), 82.4 (C-6), 89.6 (C-2), 108.5 (C-3a), 149.9 (C-4), 161.1 (C=O), 165.1 (C-6a); MS: m/z 214 $[M+H]^+$. Anal. Calcd for $C_9H_{11}NO_3S$: C, 50.69; H, 5.20; N, 6.57. Found: C, 50.69; H, 5.13; N, 6.52.

Methyl 4-amino-2,3-dihydro-2-phenylthieno[3,4-*b*]furan-6-carboxylate (13d)

Colorless prisms (0.91 g, 66%), mp 181–182 °C (acetone/petroleum ether); IR (KBr): 3453, 3330, 3206 (NH), 1663 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.69 (dd, J = 7.0, 14.6 Hz, 1H, 3-H), 3.25 (dd, J = 8.9, 14.6 Hz, 1H, 3-H), 3.58 (s, 3H, CO_2Me), 6.18 (dd, J = 7.0, 8.9 Hz, 1H, 2-H), 6.61 (br s, 2H, NH_2), 7.33–7.43 (m, 5H, aryl H); ^{13}C NMR (DMSO-d_6): δ 33.3 (C-3), 50.4 (CO_2Me), 82.6 (C-6), 93.0 (C-2),

107.9 (C-3a), 125.8, 128.2, 128.5, 141.1 (C aryl), 150.1 (C-4), 161.1 (C=O), 164.8 (C-6a); MS: *m/z* 276 $[M+H]^+$. Anal. Calcd for $C_{14}H_{13}NO_3S$: C, 61.07; H, 4.76; N, 5.09. Found: C, 61.29; H, 4.77; N, 5.01.

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