Monatshefte für Chemie 135, 201–209 (2004)
DOI 10.1007/s00706-003-0100-7

Monatshefte für Chemie
Chemical Monthly
Printed in Austria

Synthesis of Functionalized (2-Thienylcarbonyl)thiazoles and 4-(2-Thienyl)pyridines by Reaction of (2-Thienylcarbonyl)thioacetanilides and their Enamine Derivatives

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Received July 8, 2003; accepted (revised) July 15, 2003
Published online November 27, 2003

Summary. The condensation of two molecules of 2-(2-thienylcarbonyl)thioacetanilides catalyzed by piperidine yielded thiazole derivatives as confirmed by X-ray crystal structure analysis. The reaction of malononitrile with 3-morpholino-3-(2-thienyl)acrylic acid thioanilides furnished 6-amino-1-aryl-4-(2-thienyl)-1,2-dihydro-2-thioxopyridine-5-carbonitriles. A similar reaction of malononitrile with 3-morpholino-3-(2-thienyl)acrylic acid anilides provided 2-oxopyridine-5-carbonitriles.

Keywords. *Michael* addition; 4-(2-Thienyl)pyridine; (2-Thienylcarbonyl)thioacetanilides; Thiazole; Crystal structure.

Introduction

The chemistry of pyridine and its derivatives has been widely studied because of its importance in the synthesis of compounds exhibiting interesting biological activities [1]. Moreover, various pyridine derivatives are useful precursors for the synthesis of natural products [2, 3], which have found applications as pharmaceuticals [1, 4, 5]. It has been shown that a thiophene ring incorporated into heterocyclic compounds causes modification of their biological properties [6–9], and some thienyl substituted pyridines have been examined as antiradiation drugs [10]. Moreover, various thienylpyridines show fluorescence and they are studied intensively due to their potential in the construction of molecular electronics and chemical sensor devices [11].

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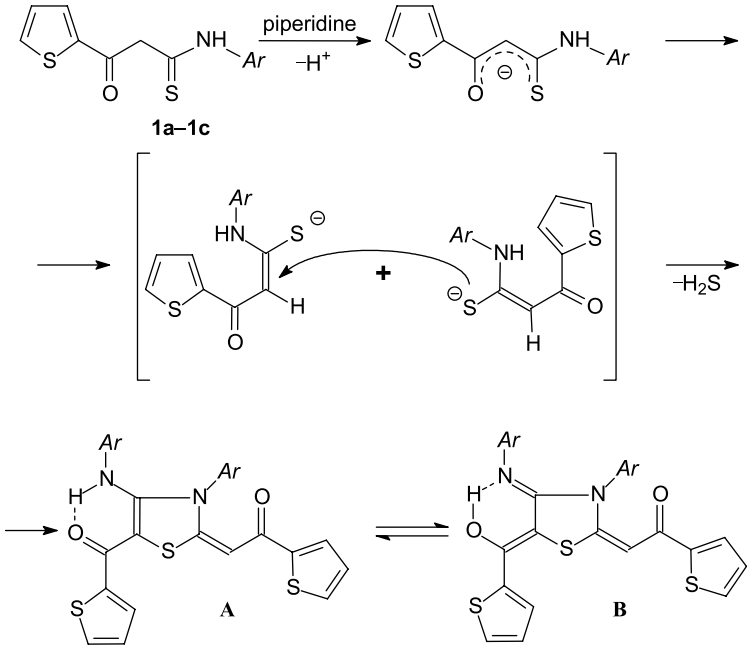
Results and Discussion

We have recently reported an efficient synthesis of polyfunctionalized pyridines *via* tandem *Michael* addition-cyclization of benzoylthioacetanilides [12], cyclic β-ketothioanilides [13, 14], and (2-thienylcarbonyl)thioacetanilides [15] to α,β-unsaturated nitriles. Continuing our studies on the synthesis of potential biological active compounds, we have now directed our interest to the preparation of thienyl substituted pyridines.

To our knowledge, *Ghorab et al*. [10] have tried to obtain 3-(2-thienyl) substituted pyridines by reaction of [1-(2-thienyl)ethylidene]propanedinitrile with phenyl isothiocyanate. They claimed, that instead of the desired target compound the bicyclic pyrido[2,3-*b*]pyrimidine derivative was formed as a result of addition of two molecules of phenyl isothiocyanate to [1-(2-thienyl)ethylidene]propanedinitrile. However, in the reaction with phenyl isocyanate the appropriate pyridine was formed.

Our approach to the synthesis of 3-(2-thienyl)pyridinecarbonitrile consisted in the reaction of (2-thienylcarbonyl)thioacetanilides (**1a**–**1c**) with malononitrile (**2**). The reaction of **1a**–**1c** with **2** carried out in boiling acetonitrile in the presence of piperidine gave orange coloured crystalline products **3a**–**3c** in moderate yields (44–56%) (Scheme 1). To our surprise, **3** were not the expected pyridine derivatives. Their IR spectra revealed only absorption of an amino group ($\bar{\nu} = 3051$–$3324\,\mathrm{cm}^{-1}$), while a nitrile group band was absent. The ^{1}H NMR spectrum of



3a *Ar* = C_6H_5
3b *Ar* = 4-Cl-C_6H_4
3c *Ar* = 4-CH_3-C_6H_4

Scheme 1

3a showed a singlet at $\delta = 6.01$ ppm for a vinyl proton, a multiplet at $\delta = 6.87$–7.97 ppm for aromatic protons, and a singlet at $\delta = 10.35$ ppm for an OH group. The ^{13}C NMR spectrum exhibited two signals at $\delta = 176.1$ and 176.7 ppm for carbonyl carbon atoms. The spectral data for **3b** and **3c** were similar to those of **3a**. The molecular weight of **3** determined by MS (*e.g.* **3a**, $m/z = 486$, 100%) combined with analytical data, suggested, that **3** had been formed by condensation of two molecules of **1**. This assumption was confirmed in separate experiments. Compounds **3a**–**3c** were obtained from **1a**–**1c** in boiling acetonitrile solution in the presence of a catalytic amount piperidine. The reaction was accompanied by vigorous evaporation of hydrogen sulfide. A mechanism of the formation of **3** is outlined in Scheme 1. The tendency of **1** to undergo this reaction probably depends on the strongly acidic character of the CH_2 group. Compounds **1**, similarly to benzoylthioacetanilides, can exist in three tautomeric forms [16, 17].

Among a few possible isomers, which could be obtained from **1**, only the reaction pathway leading to thiazole skeleton turned out to be correct. The structure of thiazole **3c** was finally confirmed by X-ray analysis. The molecular structure of compound **3c** is shown in Fig. 1.

The molecule consists of a thiazole skeleton with two thienylcarbonyl moieties and two 4-tolyl substituents. One of thienylcarbonyl moieties is connected by a methine bond, another directly with C-5 of thiazole. The former, bonded by C5–C6, exhibits ring-flip disorder as is typical for terminal unsubstituted thienyl groups [18]. The major ring component with an occupancy factor of 0.78 is one

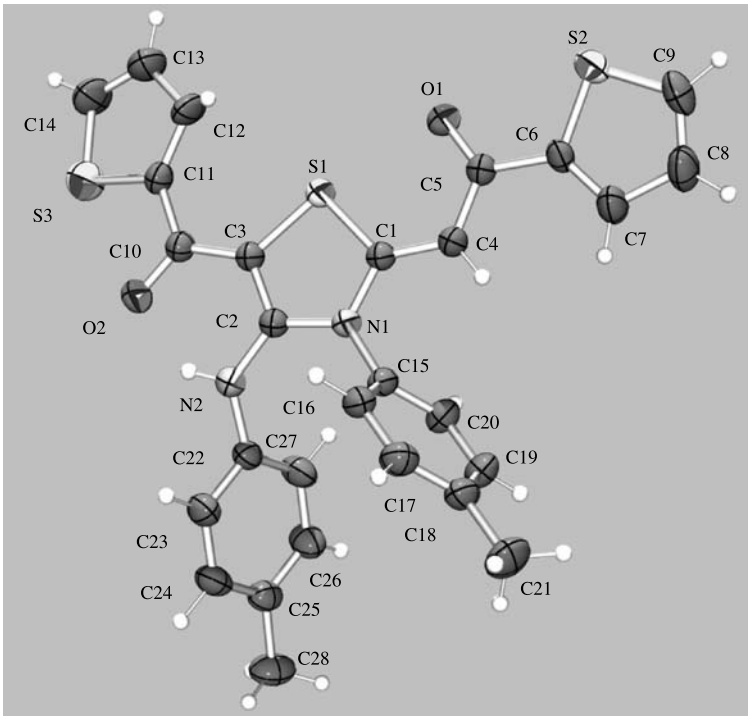


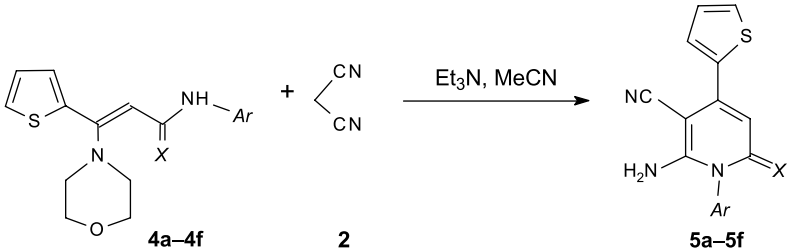
Fig. 1. A perspective view of the molecule of **3c** with crystallographic atom numbering; for clarity, only the predominant ring position of the disordered thienyl group (S2–C6–C7–C8–C9) is shown

with the sulfur atom in the *cis* position with respect to the carbonyl group oxygen atom O1 (see Fig. 1), whereas the minor component (occupancy is 0.22) has the sulfur atom in *trans* position. The *cis* position corresponds to conjugative interaction of the ring heteroatom and a carbonyl group [19].

One of the 4-tolyl moieties is bonded with C-4 atom of thiazole by the amine nitrogen and the other is bonded directly to the nitrogen atom of thiazole. Crystal structure analysis revealed that the hydrogen atom is connected to the amine nitrogen with a slightly longer bond. The bond length O2–C10 is 1.237 Å, which indicates a carbonyl group. The distance O2–N2 equals 2.674 Å and both atoms are bridged by an angular (134°) hydrogen bond. Inspection of bond lengths O2–C10, C10–C3, C3–C2, and C2–N2 indicates that the form present in the solid state corresponds to the A tautomer of **3c**.

Since **1** was found to be non-reactive towards **2** we used another way leading to the construction of the pyridine skeleton. It consisted in using appropriate enamines. The enamine procedure has been successfully applied earlier to these β-ketoacid derivatives, which reacted reluctantly with malononitrile [20–22]. To our knowledge, the morpholine enamines of (2-thienylcarbonyl)thioacetanilides **4a**–**4c** have not been described so far. They were obtained from morpholine enamine of 2-acetylthiophene and the appropriate aryl isothiocyanates in chloroform solution. In a similar way we obtained **4d**–**4f**. Among the methods for the preparation of the enamine of 2-acetylthiophene, only the reaction involving the morpholine-$TiCl_4$ complex proved to be effective [23–25]. The analytical and spectral features of **4a**–**4f** were consistent with their structures.

The reactions of **4a**–**4c** with **2** carried out in acetonitrile solution in the presence of a catalytic amount of triethylamine resulted in good yields of 4-(2-thienyl)pyridines **5a**–**5c** (Scheme 2). The IR spectrum of **5a** revealed a band at $\bar{\nu} = 2220\,\mathrm{cm}^{-1}$ for the nitrile group and four bands in the range of 3450–3205 cm^{-1} for the NH_2 group. In the ^{1}H NMR spectrum of **5a** a singlet at $\delta = 6.97$ ppm corresponding to proton CH-5 of the pyridine ring was observed. The protons of the amino group appeared as a singlet at $\delta = 7.14$ ppm and aromatic protons of phenyl and thienyl groups resonated as multiplets in the range of



4a–4f **2** **5a–5f**

4, 5	X	Ar	4, 5	X	Ar
a	S	C_6H_5	d	O	C_6H_5
b	S	4-Cl-C_6H_4	e	O	4-Cl-C_6H_4
c	S	4-CH_3-C_6H_4	f	O	4-CH_3-C_6H_4

Scheme 2

$\delta = 7.50–7.85$ ppm. The ^{13}C NMR spectrum exhibited signals for a thiocarbonyl group at $\delta = 181.6$ ppm.

The above reaction is assumed to proceed *via* a tandem *Michael* addition-elimination mechanism. The resulting intermediate underwent *in situ* cyclisation to the pyridine skeleton. The analogous reaction of **4d–4f** with **2** afforded **5d–5f** (Scheme 2). Their analytical and spectral data were consistent with the proposed structures. Although compound **5d** has been earlier described by *Ghorab et al.* [10], the ^1H NMR data of our sample and those reported by these authors were slightly different. The differences concerned the resonance of protons of the amino group in the ^1H NMR spectrum and the melting point.

In conclusion we have demonstrated that only the reaction of the enamine of 2-(2-thienylcarbonyl)thioacetanilides with malononitrile leads to thienyl substituted pyridines. This procedure provides an easy entry into a variety of functionalized heterocyclic systems containing a pyridine nucleus. Efforts to use these and related reactions in synthesis of other heterocycles are ongoing in our laboratory.

Experimental

Melting points were determined on a *Boetius* hot stage apparatus. IR spectra: Bruker IFS 48 in KBr pellets. NMR spectra: Bruker AMX 500 (^1H: 500.14 MHz ^{13}C: 125.76 MHz) in *DMSO*-d_6 with *TMS* as internal standard. Mass spectra: Finningan Mat 95 (EI, 70 eV). X-Ray analysis was carried out on a KappaCCD (Nonius) diffractometer. Microanalyses were performed with Euro EA 3000 Elemental Analyzer; their results agreed satisfactorily with the calculated values. Compounds **1a–1c** were prepared from acetylthiophene and appropriate aryl isothiocyanates [26].

*General Procedure for the Preparation of 3-Aryl-4-arylamino-5-(2-thienylcarbonyl)-2,3-dihydro-2-(2-thienylacylidene)thiazole **3a–3c***

A solution of 5 mmol of (2-thienylcarbonyl)thioacetanilide **1a–1c** in 50 cm^3 of ethanol with a catalytic amount of piperidine was refluxed for 4 h. The intensive red reaction mixture was concentrated. After cooling the orange precipitate was filtered off. Compounds **3a–3c** were purified by crystallization from CH_3CN.

3-Phenyl-4-phenylamino-2,3-dihydro-5-(2-thienylcarbonyl)-2-(2-thienylacylidene)thiazole (**3a**, $C_{26}H_{18}N_2O_2S_3$)

Orange needles; mp 294–296°C; yield 44%; IR (KBr): $\bar{\nu} = 3465–3092$ (br., OH), 1611 (C=O), 1591 (C=C) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 6.01$ (s, =CH), 6.87–6.88 (m, 3CH arom), 7.02–6.99 (m, 2CH arom), 7.06 (dd, $J = 5.0$, 3.8 Hz, CH thienyl), 7.42–7.29 (m, 7CH arom), 7.72 (dd, $J = 5.0$, 1.2 Hz, CH thienyl), 7.95 (dd, $J = 5.0$, 1.0 Hz, CH thienyl), 7.98 (dd, $J = 3.8$, 1.0 Hz, CH thienyl), 10.35 (s, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 89.9$, 96.7 (C=C), 122.6, 123.9, 127.8, 128.1, 128.3, 128.4, 129.4, 129.5, 130.8, 131.0, 131.2, 135.2, 138.6, 144.0, 145.4, 150.6, 159.6 (C arom, C=C), 176.1 (C=O), 176.7 (C=O) ppm; MS: m/z (%) = 486 (100, $[M]^{+\bullet}$), 228 (45), 156 (13), 111 (65).

3-(4-Chlorophenyl)-4-(4-chlorophenylamino)-2,3-dihydro-5-(2-thienylcarbonyl)-2-(2-thienylacylidene)thiazole (**3b**, $C_{26}H_{16}Cl_2N_2O_2S_3$)

Orange crystals; mp 282–284°C; yield 44%; IR (KBr): $\bar{\nu} = 3450–3105$ (br., OH), 1598 (C=O), 1569 (C=C) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 6.01$ (s, =CH), 6.89 (d, $J = 8.8$ Hz, 2CH arom), 7.07 (m, 4CH

arom), 7.27 (dd, $J = 3.8$, 5.0 Hz, CH thienyl), 7.43 (dd, $J = 3.8$, 1.2 Hz, CH thienyl), 7.51 (m, 5CH arom), 7.71 (dd, $J = 3.8$, 5.0 Hz, CH thienyl), 7.93 (dd, $J = 3.8$, 1.2 Hz, CH thienyl), 7.97 (dd, $J = 5.0$, 1.2 Hz, CH thienyl), 9.82 (s, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 89.7$, 96.7 (C=C), 122.9, 123.9, 128.2, 128.3, 129.9, 130.6, 131.3, 131.5, 133.5, 134.2, 134.5, 144.0, 145.6, 148.9, 150.6, 159.5 (C arom, C=C), 176.1, 176.8 (C=O) ppm; MS: m/z (%) = 554 (45, $[M]^{+\bullet}$), 555 (16, $[M+1]^{+\bullet}$), 556 (37, $[M+2]^{+\bullet}$), 262 (25), 156 (19), 111 (100).

3-(4-Methylphenyl)-4-(4-methylphenylamino)-2,3-dihydro-5-(2-thienylcarbonyl)-2-(2-thienylacylidene)thiazole (**3c**, $C_{28}H_{22}N_2O_2S_3$)

Orange crystals; mp 323–325°C; yield 56%; IR (KBr): $\bar{\nu} = 3463$–3105 (br., OH), 1598 (C=O), 1574 (C=C) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 2.14$ (s, CH_3), 2.27 (s, CH_3), 5.99 (s, =CH) 6.75 (d, $J = 8.3$ Hz, 2CH arom), 6.82 (d, $J = 8.3$ Hz, 2CH arom), 7.06 (dd, $J = 4.9$, 3.7 Hz, CH thienyl), 7.15 (d, $J = 8.2$ Hz, 2CH arom), 7.24 (d, $J = 8.2$ Hz, 2CH arom), 7.29–7.32 (m, 2CH thienyl), 7.73 (dd, $J = 4.9$, 1.0 Hz, CH thienyl), 7.93 (dd, $J = 3.7$, 1.0 Hz, CH thienyl), 7.98 (dd, $J = 5.0$, 1.0 Hz, CH thienyl), 10.54 (s, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 19.8$ (CH_3), 20.2 (CH_3), 89.9, 95.1 (C=C), 123.3, 127.9, 128.1, 128.2, 128.4, 128.7, 129.4, 129.9, 130.5, 131.4, 133.5, 135.6, 139.2, 144.2, 145.4, 151.5, 159.7 (C arom, C=C), 175.7, 176.7 (C=O) ppm; MS: m/z (%) = 514 (82, $[M]^{+\bullet}$), 242 (55), 161 (14), 156 (68), 111 (100).

Compound **3c** with formula $C_{28}H_{22}N_2O_2S_3$ crystallizes in the triclinic system, space group $P\bar{1}$, with unit cell parameters $a = 10.0566(1)$, $b = 10.1785(2)$, $c = 13.0362(2)$ Å, $\alpha = 92.451(1)$, $\beta = 110.857(1)$, $\gamma = 93.324(1)°$, $V = 1241.98(3)$ Å^3, $Z = 2$. A total of 7960 independent reflections (R(int) = 0.0293) were collected on a sample (size $0.3 \times 0.25 \times 0.15$ mm^3) using MoKα radiation. The structure was solved by direct methods and refined by the full-matrix least-squares method on F^2 using SHELX97 program system. One thienyl group was found to exhibit ring-flip disorder. The disorder model used in refinement consisted of two superimposed flipped thienyl rings, with exchanged positions of S2 and C7 atoms. The following restraints for the disordered atoms were applied: geometry of both flipped rings was restrained to be similar as that of the other, non-disordered thienyl group; and atomic displacement components of bonded atoms along the line joining them were restrained to be equal. Final R indices for $I > 2\sigma(I)$ were equal $R1 = 0.0482$ and for all data $R1 = 0.078$, w$R2 = 0.1458$. The final difference *Fourier* map of electron density revealed largest peak and hole 0.315 and -0.605 e · Å^{-3}, respectively, the latter value being connected with the presence of disorder. The structural data were deposited at the Cambridge Crystallographic Data Centre. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk) under reference number CCDC 216533.

*General Procedure for the Synthesis of Enamines of (2-Thienylcarbonyl)thioacetanilides **4a–4f***

4-[1-(2-Thienyl)ethenyl]-morpholine was synthesized according to the general procedure of Refs. [24, 25]. Compounds **4a–4f** were prepared from morpholine enamine and appropriate aryl isothiocyanates, or aryl isocyanates according to the procedure described previously in Ref. [27]. Crystallization from *Me*OH afforded yellow prisms.

3-(4-Morpholinyl)-N-phenyl-3-(2-thienyl)thioacrylamide (**4a**, $C_{17}H_{18}N_2OS_2$)

Yellow crystals; mp 155–157°C; yield 64%; IR (KBr): $\bar{\nu} = 3444$, 3230–3180 (NH), 1548 (C=C) cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 3.07$ (t, $J = 4.7$ Hz, 2NCH_2), 3.73 (t, $J = 4.7$ Hz, 2OCH_2), 5.89 (s, =CH), 7.05–7.53 (m, 8CH arom), 8.15 (s, NH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 48.9$ (NCH_2), 66.5 (OCH_2), 122.8, 125.8, 128.1, 128.5, 129.5, 130.4, 135.7, 139.1 (C arom, C=C), 194.1 (C=S) ppm; MS: m/z (%) = 330 (14, $[M]^{+\bullet}$), 296 (100), 265 (14), 239 (28), 153 (13), 135 (18).

N-(4-Chlorophenyl)-3-(4-morpholinyl)-3-(2-thienyl)thioacrylamide (**4b**, $C_{17}H_{17}ClN_2OS_2$)

Yellow crystals; mp 140–142°C; yield 41%; IR (KBr): $\bar{\nu} = 3450$, 3199–3177 (NH), 1542 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 3.07$ (t, $J = 4.8$ Hz, $2NCH_2$), 3.85 (t, $J = 4.8$ Hz, $2OCH_2$), 5.87 (s, =CH), 7.10–7.53 (m, 7CH arom), 8.10 (s, NH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 48.9$ (NCH_2), 66.5 (OCH_2), 123.7, 123.9, 128.2, 128.6, 129.7, 130.5, 130.9, 135.6, 137.6 (C arom, C=C), 194.4 (C=S) ppm; MS: m/z (%) = 364 (22, $M]^{+\bullet}$), 331 (100), 238 (16), 205 (37), 169 (45), 195 (22), 153 (27).

N-(4-Methylphenyl)-3-(4-morpholinyl)-3-(2-thienyl)thioacrylamide (**4c**, $C_{18}H_{20}N_2OS_2$)

Yellow crystals; mp 150–152°C; yield 52%; (KBr): $\bar{\nu} = 3444$, 3268–3186 (NH), 1528 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 2.33$ (s, CH_3), 3.71 (t, $J = 4.5$ Hz, $2NCH_2$), 3.80 (t, $J = 4.5$ Hz, $2OCH_2$), 5.90 (s, =CH), 6.98–7.52 (m, 7CH arom), 8.05 (s, NH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 20.9$ (CH_3), 49.0 (NCH_2), 66.6 (OCH_2), 123.0, 125.8, 128.2, 129.2, 129.4, 130.4, 135.9, 136.6 (C arom), 194.1 (C=S) ppm; MS: m/z (%) = 344 (22, $[M]^{+\bullet}$), 311 (100), 238 (15), 205 (26), 149 (30), 195 (20), 153 (18).

3-(4-Morpholinyl)-N-phenyl-3-(2-thienyl)acrylamide (**4d**, $C_{17}H_{18}N_2O_2S$)

Yellow crystals; mp 157–158°C; yield 77%; IR (KBr): $\bar{\nu} = 3437$, 3287–3178 (NH), 1664 (C=O), 1594 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 3.04$ (t, $J = 4.7$ Hz, $2NCH_2$), 3.74 (t, $J = 4.7$ Hz, $2OCH_2$), 5.17 (s, =CH), 6.74 (s, NH), 6.99–7.55 (m, 8CH arom) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 48.9$ (NCH_2), 66.5 (OCH_2), 101.3 (C=C), 119.4, 123.3, 127.8, 128.7, 128.9, 129.9, 136.1, 138.4, 150.6 (C arom, C=C), 165.7 (C=O) ppm; MS: m/z (%) = 314 (4, $[M]^{+\bullet}$), 222 (100), 194 (20), 137 (18).

N-(4-Chlorophenyl)-3-(4-morpholinyl)-3-(2-thienyl)acrylamide (**4e**, $C_{17}H_{17}ClN_2OS$)

Yellow crystals; mp 181–183°C; yield 54%; IR (KBr): $\bar{\nu} = 3460$, 3282–3180 (NH), 1654 (C=O), 1589 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 3.02$ (t, $J = 4.5$ Hz, $2NCH_2$), 3.72 (t, $J = 4.5$ Hz, $2OCH_2$), 5.14 (s, =CH), 6.84 (s, NH), 7.10–7.54 (m, 7CH arom) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 48.8$ (NCH_2), 66.5 (OCH_2), 100.6 (C=C), 120.5, 127.8, 128.7, 129.0, 129.9, 136.0, 137.1, 151.0 (C arom, C=C), 165.6 (C=O) ppm; MS: m/z (%) = 348 (3, $[M]^{+\bullet}$), 222 (100), 194 (10), 137 (14).

N-(4-Methylphenyl)-3-(4-morpholinyl)-3-(2-thienyl)acrylamide (**4f**, $C_{18}H_{20}N_2O_2S$)

Yellow crystals; mp 180–181°C; yield 54%; IR (KBr): $\bar{\nu} = 3437$, 3299–3186 (NH), 1650 (C=O), 1589 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 2.25$ (s, CH_3), 3.01 (t, $J = 4.5$ Hz, $2NCH_2$), 3.72 (t, $J = 4.5$ Hz, $2OCH_2$), 5.16 (s, =CH), 6.79 (s, NH), 6.99–7.52 (m, 7CH arom) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 20.7$ (CH_3), 48.9 (NCH_2), 66.5 (OCH_2), 101.3 (C=C), 119.5, 127.7, 128.7, 129.2, 129.3, 132.8, 135.9, 136.3, 150.5 (C arom, C=C), 165.6 (C=O) ppm; MS: m/z (%) = 328 (4, $[M]^{+\bullet}$), 222 (100), 194 (2), 137 (15).

*General Procedure for Preparation of Pyridines **5a–5f***

A mixture of thioanilide **1a–1c** (5 mmol), malonodinitrile **2** (7.5 mmol), and a catalytic amount of triethylamine was heated under reflux in 50 cm^3 of acetonitrile for 2 h. After cooling the orange precipitate was filtered off. Compounds **5a–5c** were purified by crystallization from *Et*OH or CH_3CN.

6-Amino-4-(2-thienyl)-1,2-dihydro-2-thioxo-1-phenylpyridine-5-carbonitrile (**5a**, $C_{16}H_{11}N_3S_2$)

Yellow crystals; mp 325°C; yield 68%; IR (KBr): $\bar{\nu} = 3450$–3205 (NH), 2220 (CN) cm^{-1}; ^1H NMR (*DMSO*-d_6): $\delta = 6.99$ (s, CH), 7.08 (s, NH_2), 7.27–7.67 (m, 6CH arom), 7.80 (dd, $J = 4.0$, 1.0 Hz, CH

thienyl), 7.87 (dd, $J = 5.0$, 0.5 Hz, CH thienyl) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 75.7$ (C-5), 116.9 (CN), 119.2 (C-3), 128.1, 128.5, 129.4, 129.8, 130.3, 131.0, 136.6, 138.1, 139.5 (C arom), 156.7 (C-6), 181.6 (C=S) ppm; MS: m/z (%) = 309 (100, $[M]^{+\bullet}$), 276 (12), 265 (15), 146 (12).

6-Amino-4-(2-thienyl)-1,2-dihydro-2-thioxo-1-(4-chlorophenylpyridine)-5-carbonitrile (**5b**, $C_{16}H_{10}ClN_3S_2$)

Yellow crystals; mp 241°C; yield 57%; IR (KBr): $\bar{\nu} = 3449$–3211 (NH), 2203 (CN) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 6.96$ (s, CH), 7.06 (s, NH_2), 7.25–7.66 (m, 6CH arom), 7.78 (dd, $J = 3.4$, 1.0 Hz, CH thienyl), 7.87 (dd, $J = 5.1$, 1.0 Hz, CH thienyl) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 75.9$ (C-5), 117.1 (CN), 119.0 (C-3), 128.7, 129.6, 130.1, 130.5, 130.6, 134.2, 136.7, 137.3, 140.0 (C arom), 156.9 (C-6), 181.5 (C=S) ppm; MS: m/z (%) = 343 (100, $[M]^{+\bullet}$), 310 (60), 299 (18), 146 (9).

6-Amino-4-(2-thienyl)-1,2-dihydro-2-thioxo-1-(4-methylphenylpyridine)-5-carbonitrile (**5c**, $C_{17}H_{13}N_3S_2$)

Yellow crystals; mp 220°C; yield 52%; IR (KBr): $\bar{\nu} = 3463$–3205 (NH), 2201 (CN) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 2.39$ (s, CH_3), 6.98 (s, CH), 7.05 (s, NH_2), 7.15 (d, $J = 8.1$ Hz, 2CH arom), 7.27 (dd, $J = 5.1$, 3.7 Hz, CH thienyl), 7.38 (d, $J = 8.1$ Hz, 2CH arom), 7.79 (dd, $J = 3.7$, 1.1 Hz, CH thienyl), 7.87 (dd, $J = 5.1$, 1.0 Hz, CH thienyl) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 20.8$ (CH_3), 75.7 (C-5), 116.9 (CN), 119.2 (C-3), 127.8, 128.5, 129.4, 129.8, 130.9, 135.6, 136.6, 138.9, 139.4 (C arom), 156.8 (C-6), 181.8 (C=S) ppm; MS: m/z (%) = 323 (100, $[M]^{+\bullet}$), 290 (36), 279 (14), 146 (11).

Compounds **5d**–**5f** were obtained in a similar way as **5a**–**5c** from anilides **1d**–**1f** (5 mmol) and malonodinitrile **2** (7.5 mmol). Crystallization from *Et*OH afforded colourless prisms.

6-Amino-4-(2-thienyl)-1,2-dihydro-2-oxo-1-phenylpyridine-5-carbonitrile (**5d**, $C_{16}H_{11}N_3OS$)

Colourless crystals; mp 260°C (Ref. [10] 250–252°C); yield 53%; IR (KBr): $\bar{\nu} = 3431$–3174 (NH), 2195 (CN), 1647 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 5.87$ (s, CH), 6.82 (s, NH_2), 7.23 (dd, $J = 5.0$, 3.7 Hz, CH thienyl), 7.31–7.59 (m, 4CH arom), 7.66 (dd, $J = 3.6$, 1.0 Hz, CH thienyl), 7.78 (dd, $J = 5.0$, 1.0 Hz, CH thienyl) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 68.5$ (C-5), 103.6 (C-3), 117.6 (CN), 128.0, 128.3, 128.5, 128.7, 129.3, 130.0, 134.4, 137.6, 145.0 (C arom), 157.0 (C-6), 160.1 (C=O) ppm; MS: m/z (%) = 293 (100, $[M]^{+\bullet}$), 265 (89), 233 (8), 161 (12).

6-Amino-4-(2-thienyl)-1,2-dihydro-2-oxo-1-(4-chlorophenyl)pyridine-5-carbonitrile (**5e**, $C_{16}H_{10}ClN_3OS$)

Colourless crystals; mp 305°C; yield 76%; IR (KBr): $\bar{\nu} = 3460$–3177 (NH), 2194 (CN), 1655 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 5.86$ (s, CH), 7.06 (s, NH_2), 7.23 (dd, $J = 5.0$, 3.6 Hz, CH thienyl), 7.37 (d, $J = 8.7$ Hz, 2CH arom), 7.61 (d, $J = 8.7$ Hz, 2CH arom), 7.66 (dd, $J = 3.8$, 1.2 Hz, CH thienyl), 7.78 (dd, $J = 5.0$, 1.0 Hz, CH thienyl) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 65.5$ (C-5), 103.3 (C-3), 117.6 (CN), 128.0, 128.3, 128.7, 130.0, 130.6, 133.5, 134.0, 137.6, 145.2 (C arom), 157.1 (C-6), 160.1 (C=O) ppm; MS: m/z (%) = 327 (100, $[M]^{+\bullet}$), 299 (78), 215 (23).

6-Amino-4-(2-thienyl)-1,2-dihydro-2-oxo-1-(4-methylphenyl)pyridine-5-carbonitrile (**5f**, $C_{17}H_{13}N_3OS$)

Colourless crystals; mp 259°C; yield 53%; IR (KBr): $\bar{\nu} = 3431$–3174 (NH), 2195 (CN), 1647 (C=O) cm^{-1}; ^{1}H NMR (*DMSO*-d_6): $\delta = 2.38$ (s, CH_3), 5.87 (s, CH), 6.89 (s, NH_2), 7.10 (d, $J = 8.0$ Hz, 2CH arom), 7.23 (dd, $J = 5.0$, 3.7 Hz, CH thienyl), 7.37 (d, $J = 8.0$ Hz, 2CH arom), 7.66 (dd, $J = 3.7$, 1.0 Hz,

CH thienyl), 7.78 (dd, $J = 5.0$, 1.0 Hz, CH thienyl) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 20.6$ (CH_3), 68.4 (C-5), 103.6 (C-3), 117.6 (CN), 128.0, 128.2, 128.3, 128.6, 130.5, 131.7, 137.6, 138.8, 144.9 (C arom), 157.1 (C-6), 160.2 (C=O) ppm; MS: m/z (%) = 307 (93, $[M]^{+\bullet}$), 279 (100), 247 (15), 237 (10), 198 (7), 149 (12).

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