Monatsh Chem 139, 1055–1060 (2008)
DOI 10.1007/s00706-008-0881-9
Printed in The Netherlands

Monatshefte für Chemie
Chemical Monthly

Synthesis and characterization of mono- and bicyclic heterocyclic derivatives containing 1,2,4-triazole, 1,3,4-thia-, and -oxadiazole rings

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Received 6 December 2007; Accepted 20 December 2007; Published online 1 February 2008

Abstract A series of new N- and S-substituted 1,3,4-oxadiazole derivatives were synthesized. 5-Pyridin-3-yl-3-[2-(5-thioxo-4,5-dihydro-l,3,4-thiadiazol-2-yl)ethyl]-1,3,4-oxadiazole-2(3*H*)-thione and 5-[(5-(pyridin-3-yl)-1,3,4-oxadiazol-2-ylthio)methyl]-*N*-phenyl-1,3,4-thiadiazol-2-amine were formed by cyclization of 3-(5-pyridin-3-yl-2-thioxo-1,3,4-oxadiazol-3(2*H*)-ylpropanimidohydrazide and 2-[(5-pyridin-3-yl-1,3,4-oxadiazol-2-yl)thio]thiosemicarbazide with CS_2 and H_2SO_4. On the other hand, a number of new bicyclic 1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazole derivatives were synthesized. 6-Pyridin-3-ylbis[1,2,4]-triazolo[3,4-*b*:4′,3′-*d*][1,3,4]thiadiazole-3(2*H*)-thione was synthesized by reaction of 6-(hydrazino)-3-pyridine-3-yl[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazole with CS_2/KOH/*Et*OH. The structures of the newly synthesized compounds were elucidated by the spectral and analytical data IR, Mass, and ^{1}H NMR spectra.

Introduction

During recent years there has been intense investigation of different classes of 1,3,4-oxadiazoles and the related thiadiazole derivatives, many of which have demonstrated a broad spectrum of biological activity in both agrochemical and pharmaceutical fields showing antibacterial [1], antimicrobial [2], insecticidal [3], herbicidal/fungicidal [4], antiinflammatory [5], hypoglycaemic [6], hypotension [7], and antitumor activity [8]. In the field of medicinal chemistry, oxadiazoles are utilized as ester or amide surrogates. A number of biologically relevant entities containing the 1,3,4-oxadiazole motif are used as HIV integrase inhibitor and angiogenesis inhibitor [9, 10]. In addition, compounds incorporating both 1,2,4-triazole and 1,3,4-thiadiazole rings have been attracting widespread attention due to their diverse pharmacological prosperities such as antimicrobial, antiinflammatory, analgesic, and antitumoral activities [11–20]. Acylhydrazides and their derivatives have been, in general, used as the starting materials for the synthesis of 1,3,4-oxadiazoles, 1,3,4-thiadiazoles, and 1,2,4-triazoles [21, 22]. Furthermore, heterocyclic hydrazines are generally utilized as intermediates for the synthesis of several condensed systems containing triazoles and other ring systems [23, 24]. Consequently, in view of the above facts and as a part of an ongoing investigation into biologically more active and less toxic substances, our current interest is focused on the synthesis of a series of new 1,3,4-oxadiazoles and condensed 1,2,4-triazolothiadiazole derivatives.

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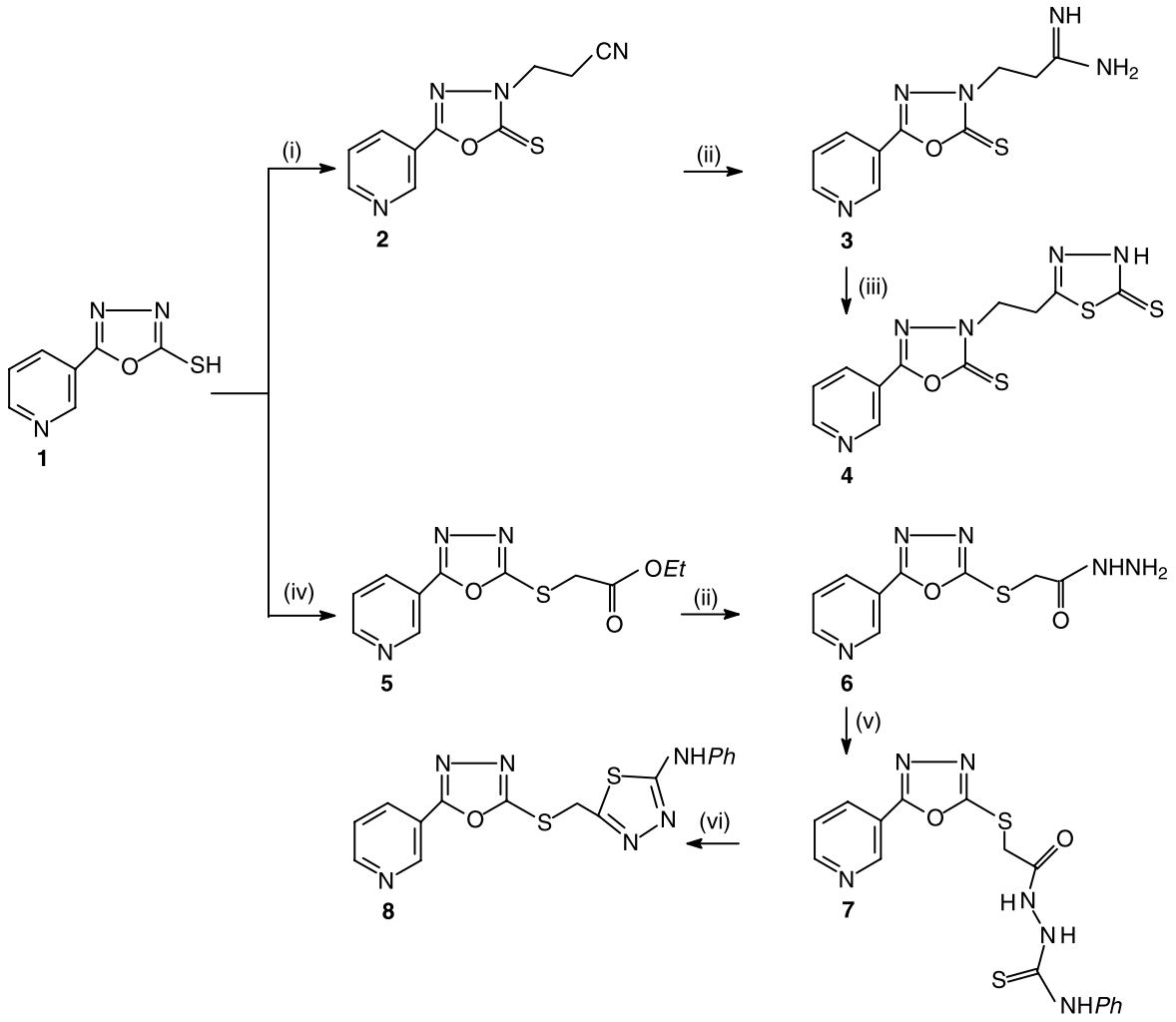
Results and discussion

The starting material 5-pyridin-3-yl-1,3,4-oxadiazole-2-thiol (**1**) [23] was synthesized by refluxing nicotinic acid hydrazide and CS_2/KOH/*Et*OH.

Reaction of the thiol **2** with acrylonitrile in ethanol afforded 3-(5-pyridin-3-yl-2-thioxo-1,3,4-oxadiazole-3(2*H*)-yl)propanenitrile (**2**) in 75% yield.

The IR spectrum showed a characteristic absorption band at $\bar{\nu} = 2248\,\mathrm{cm}^{-1}$ corresponding to the CN group. The ^{1}H NMR spectrum showed the two CH_2 groups as triplets in addition to the protons of the pyridyl ring. Treatment of **2** with hydrazine hydrate in ethanol at reflux temperature afforded 3-(5-pyridin-3-yl-2-thioxo-1,3,4-oxadiazole-3(2*H*)-yl)propanimidohydrazide (**3**) in 90% yield. Its ^{1}H NMR spectrum showed the two CH_2 groups as triplets, the NH_2 as singlet in addition to the protons of the pyridyl ring. When **3** was refluxed with CS_2 in butanol, 5-pyridin-3-yl-3-[2-(5-thioxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)ethyl]-1,3,4-oxadiazole-2(3*H*)-thione (**4**) was obtained. Its IR spectrum showed characteristic absorption bands at $\bar{\nu} = 3419$ and $1652\,\mathrm{cm}^{-1}$ corresponding to the NH and C=N groups and its ^{1}H NMR agrees with the assigned structure. Reaction of **1** with ethyl chloroacetate and NaOH/*Et*OH gave ethyl[(5-pyridin-3-yl-l,3,4-oxadiazol-2-yl)thio]-acetate (**5**) in 70% yield. Its IR spectrum showed a characteristic adsorption band in the carbonyl frequency region at $\bar{\nu} = 1739\,\mathrm{cm}^{-1}$ corresponding to the ester group. The ^{1}H NMR spectrum showed the signals as triplet at $\delta = 1.18$ ppm for the CH_3 group, quartet at $\delta = 4.14$ ppm for the CH_2 group, and SCH_2 as singlet at $\delta = 4.30$ ppm in addition to the protons of the pyridyl ring. Treatment of **5** with hy-

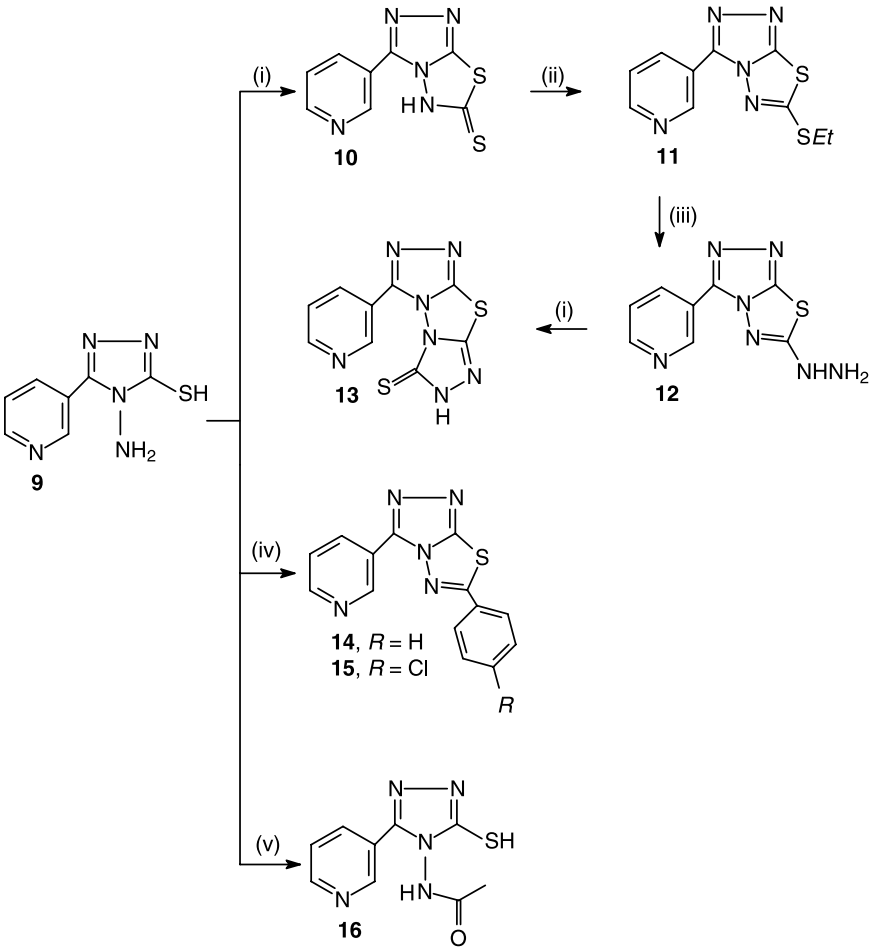


(i) CH_2=CH-CN/*TEA*/*Et*OH/reflux; (ii) $N_2H_4.H_2O$/*Et*OH/reflux; (iii) CS_2/*Bu*OH/reflux; (iv) NaOH/*Et*OH/$ClCH_2CO_2Et$/reflux; (v) *Ph*NCS/*Et*OH/reflux; (vi) H_2SO_4/rt

Scheme 1

drazine hydrate in ethanol at reflux temperature gave 2-[(5-pyridin-3-yl-1,3,4-oxadiazol-2-yl)thio]acetohydrazide (**6**). The IR spectrum of this compound showed a characteristic carbonyl frequency at $\bar{\nu} = 1684\,cm^{-1}$ in addition to the C=N group at $\bar{\nu} = 1652\,cm^{-1}$. Its ^1H NMR spectrum agrees with the assigned structure. Reaction of the hydrazide **6** with phenyl isothiocyanate afforded the corresponding thiosemicarbazide derivative **7** in a good yield (84%) [25]. The IR spectrum of **7** showed a characteristic absorption band at $1596\,cm^{-1}$ corresponding to the C=N group in addition to the amino frequencies at $\bar{\nu} = 3117–3216\,cm^{-1}$ and at $\bar{\nu} = 3444\,cm^{-1}$. The ^1H NMR spectrum showed the SCH_2 and NH as singlets in addition to the protons of the pyridyl ring. The thiosemicarbazide **7** was treated with H_2SO_4 at room temperature to form *N*-phenyl-5-[(5-pyridin-3-yl-1,3,4-oxadiazol-2-yl)thio]methyl-1,3,4-thiadiazol-2-amine (**8**). Its IR spectrum showed the two peak frequencies at $\bar{\nu} = 3418$ and $1663\,cm^{-1}$ corresponding to NH and C=N and its ^1H NMR spectrum agrees with the assigned structure (Scheme 1).

Because one of the most important methods for the synthesis of bicyclic triazole systems is the cyclization of 1-amino-2-thio- or 2-hydrazino-derivatives to give the bicyclic ring systems, 4-amino-5-pyridin-3-yl-4H-1,2,4-triazole-3-thiol (**9**) [24], formally synthesized from potassium 2-(pyridin-3-ylcarbonyl)hydrazinecarbodithioate, was used as a starting material for the synthesis of a series of condensed heterocyclic compounds. Thus, reaction of the 1-amino-1,2,4-triazole derivative **9** with benzoic acid or chlorobenzoic acid afforded 6-phenyl-3-pyridin-3-yl[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazole (**14**)



(i) CS_2/KOH/*Et*OH/reflux; (ii) *Et*I/KOH; (iii) $N_2H_4.H_2O$/*Et*OH/reflux; (iv) *R*-C_6H_4-CO_2H/$POCl_3$/reflux; (v) Ac_2O/Py/reflux

Scheme 2

or 6-(4-chlorophenyl)-3-pyridin-3-yl[1,2,4]triazolo-[3,4-*b*][1,3,4]thiadiazole (**15**). When **9** was treated with CS_2 and ethanolic KOH it gave 3-pyridin-3-yl[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazole-6-thiol (**10**). The ^{1}H NMR spectrum showed the NH group as a singlet at $\delta = 14.0$ ppm in addition to the protons of the pyridyl ring in the range $\delta = 56$–8.76 ppm. Treatment of **10** with ethyl iodide in aqueous solution of KOH gave **11**, which was allowed to react with $N_2H_4 \cdot H_2O$/*Et*OH to give **12**. The ^{1}H NMR spectrum of **11** showed the CH_3 group as a triplet at $\delta = 1.45$ ppm and the CH_2 group as a quartet at $\delta = 3.40$ ppm in addition to the protons of the pyridyl ring at $\delta = 7.62$–9.99 ppm. 6-Hydrazino-3-pyridine-3-yl[l,2,4]triazolo[3,4-*b*][1,3,4]thiadiazole (**12**) was treated with CS_2/KOH/*Et*OH to give 6-pyridin-3-ylbis[1,2,4]triazolo[3,4-*b*:4′,3′-*d*][1,3,4]thiadiazole-3(2*H*)-thione (**13**). Its IR spectrum showed an absorption band at $\bar{\nu} = 1614\ cm^{-1}$ corresponding to the C=N group. The ^{1}H NMR showed the NH group at $\delta = 12.86$ ppm and the protons of the pyridyl ring at $\delta = 7.05$–8.56 ppm. Acetylation of **9** with acetic anhydride gave *N*-(3-mercapto-5-pyridin-3-yl-(4*H*)-1,2,4-triazol-4-yl)acetamide (**16**). Its IR spectrum showed a characteristic absorption band in the carbonyl frequency region for the NH–CO group (Scheme 2).

Experimental

Melting Points were taken on a digital melting point apparatus. Infrared spectra were measured on KBr using a Bruker-Vector 22. Mass spectra were measured on a Hewlett-Packard 5988 A (1000 Hz) instrument. ^{1}H NMR spectra were obtained using a Varian Gemini (300 MHz) spectrometer (*DMSO*-d_6) with *TMS* as internal standard. All reactions were monitored by TLC. The microanalyses were performed at the microanalytical unit, Cairo University, Egypt and were found to agree favourably with the calculated values. 5-Pyridin-3-yl-1,3,4-oxadiazole-2-thiol (**1**) was obtained as reported [23], by refluxing nicotinic acid hydrazide with CS_2/KOH/*Et*OH. 4-Amino-5-pyridin-3-yl-(4*H*)-1,2,4-triazole-3-thiol (**9**) was obtained by refluxing potassium salt of nicotinic acid hydrazide with $N_2H_4 \cdot H_2O$ [24].

3-(5-Pyridin-3-yl-2-thioxo-1,3,4-oxadiazol-3(2H)-yl)propanenitrile (**2**, $C_{10}H_8N_4OS$)
A mixture of 10.1 g **1** [23] (56.5 mmol), 2.9 g acrylonitrile (56.5 mmol), and 1.8 g Et_3N (20 mmol) was dissolved in 30 cm^3 absolute *Et*OH. The reaction mixture was heated under reflux for 3 h and then cooled to room temperature. The obtained precipitate was filtered off, dried, and recrystallized from *Et*OH to give 7.5 g **2** as white crystals in 75% yield. *Rf* = 0.65 (chloroform). Mp 233–235°C; IR (KBr): $\bar{\nu} = 2248$ (C≡N), 1614 (C=N) cm^{-1}; ^{1}H NMR (*DMSO*-d_6, 300 MHz): $\delta = 3.11$ (t, $J = 6.4$ Hz, CH_2CH_2CN), 4.40 (t, $J = 6.4$ Hz, CH_2CH_2CN), 7.62–7.71 (m, pyridyl-H), 8.27 (d, $J = 7.9$ Hz, pyridyl-H), 8.81 (d, $J = 6.6$ Hz, pyridyl-H), 9.05 (s, pyridyl-H) ppm; MS: m/z (%) = 255 ($M^+ + Na$, 25).

3-(5-Pyridin-3-yl-2-thioxo-1,3,4-oxadiazol-3(2H))-ylpropanimidohydrazide (**3**, $C_{10}H_{12}N_6O_S$)
A mixture of 10.7 g **2** (46.3 mmol), 8.5 cm^3 *Et*OH, and 6.9 g $N_2H_4 \cdot H_2O$ (138 mmol) was refluxed for 1 h and the solvent was removed under reduced pressure. The remaining precipitate was collected, dried, and recrystallized from *Et*OH to afford 9.6 g **3** in 90% yield as yellow solids. $R_f = 0.25$ (ethyl acetate/chloroform, 1/1). Mp 195–197°C; IR (KBr): $\bar{\nu} =$ 3439 (NH), 3278–3163 (NH_2) cm^{-1}; ^{1}H NMR (*DMSO*-d_6, 300 MHz): $\delta = 3.80$ (br, s, NH_2), 4.56 (t, $J = 7.1$ Hz, CH_2), 5.88 (t, $J = 7.1$ Hz, CH_2), 7.58–7.61 (m, pyridyl-H), 8.34 (d, $J = 7.4$ Hz, pyridyl-H), 8.72 (d, $J = 5.9$ Hz, pyridyl-H), 9.03 (s, pyridyl-H), 9.12 (br, s, NH) ppm.

5-Pyridin-3-yl-3-[2-(5-thioxo-4,5-dihydro-1,3,4-thiadiazol-2-yl)ethyl]-1,3,4-oxadiazole-2(3H)-thione (**4**, $C_{11}H_9N_5OS_3$)
Carbon disulfide (5 cm^3, 16 mmol) was added to a solution of 2.1 g **3** (8 mmol) in 30 cm^3 *Bu*OH. The mixture was refluxed for 5 h and the solvent was removed under reduced pressure. The formed precipitate was recrystallized from *Bu*OH to give 0.7 g **4** in 35% yield as pink crystals. $R_f = 0.65$ (chloroform/methanol, 2/1). Mp 235–237°C; IR (KBr): $\bar{\nu} = 1652$ (C=N), 3419 (NH) cm^{-1}; ^{1}H NMR (*DMSO*-d_6, 300 MHz): $\delta = 4.45$ (t, $J = 6.7$ Hz, CH_2), 5.88 (t, $J = 6.8$ Hz, CH_2), 7.22–7.32 (m, pyridyl-H), 8.17 (d, $J = 7.2$ Hz, pyridyl-H), 8.33 (d, $J =$ 7.1 Hz, pyridyl-H), 9.02 (s, pyridyl-H), 12.10 (br, s, NH) ppm; MS: m/z (%) = 323 (M^+, 44).

Ethyl [(5-pyridin-3-yl-1,3,4-oxadiazol-2-yl)thio]acetate (**5**, $C_{11}H_{11}N_3O_3S$)
A solution of compound 1.79 g **1** (10 mmol), 0.4 g NaOH (10 mmol), and 30 cm^3 *Et*OH was heated under reflux for 45 min followed by addition of 1.22 g ethyl chloroacetate (10 mmol). The resulting mixture was heated for 6 h, filtered, cooled and poured on crushed ice. The precipitate was filtered off and recrystallized from *Et*OH to afford 1.2 g **5** in 70% yield as pink crystals. $R_f = 0.65$ (chloroform/methanol, 2/1). Mp 175–177°C; IR (KBr): $\bar{\nu} = 1739$ (C=O), 1605 (C=N) cm^{-1}; ^{1}H NMR (*DMSO*-d_6, 300 MHz): $\delta = 1.18$ (t, $J = 7.1$ Hz, CH_2CH_3), 4.15 (q, $J = 7.1$ Hz, CH_2CH_3), 4.30 (s, SCH_2), 7.62–7.72 (m, pyridyl-H), 8.32 (d, $J = 7.8$ Hz, pyridyl-H), 8.77 (d, $J = 6.4$ Hz, pyridyl-H), 9.24 (s, pyridyl-H) ppm; MS: m/z (%) = 304 ($M^+ + K$, 45).

2-[(5-Pyridin-3-yl-1,3,4-oxadiazol-2-yl)thio]acetohydrazide (**6**,$C_9H_9N_5O_2S$)
A mixture of 2.65 g **2** (10 mmol), 4 cm^3 *Et*OH, and 1.5 g $N_2H_4 \cdot H_2O$ (30 mmol) was refluxed for 4 h and the solvent was removed under reduced pressure. The remaining precipitate was collected, dried, and recrystallized from *Et*OH to afford 1.6 g **6** in 63% yield as yellow crystals. $R_f = 0.65$ (chloroform/methanol, 2/1). Mp 140–142°C; IR (KBr): $\bar{\nu} = 3321$ (NH),

3207–3143 (NH_2), 1616 (C=N), 1684 (C=O) cm^{-1}; ^1H NMR (*DMSO*-d_6, 300 MHz): $\delta = 3.91$ (s, NH_2), 4.64 (s, SCH_2), 7.33–7.91 (m, pyridyl-H), 8.01 (s, pyridyl-H), 8.76 (br, s, NH) ppm.

2-[(5-Pyridin-3-yl-1,3,4-oxadiazol-2-yl)thio]thiosemicarbazide (**7**,$C_{16}H_{14}N_6O_2S_2$)
Phenyl isothiocyanate (2.7 g, 20 mmol) was added to a solution of 7.7 g **6** (20 mmol) in 100 cm^3 *Et*OH. The reaction mixture was heated under reflux for 12 h. The solid product which separated on cooling was filtered off, washed with *Et*OH, dried, and recrystallized from *Et*OH to give 6.5 g **7** in 86% yield as brown crystals. $R_f = 0.53$ (chloroform). Mp 233–235°C; IR (KBr): $\bar{\nu} = 3446$ (NH), 3216–3117 (NH_2), 1596 (C=O) cm^{-1}; ^1H NMR (*DMSO*-d_6, 300 MHz): $\delta = 3.44$ (s, CH_2), 4.49 (br, s, NH), 7.12–7.38 (m, *Ar*–H), 7.42–7.51 (m, pyridyl-H), 7.95 (s, pyridyl-H), 9.88 (s, NH), 11.01 (br, s, NH) ppm; MS: m/z (%) = 287 (M^+, 45).

5-[5-(pyridin-3-yl)-1,3,4-oxadiazol-2-ylthio]methyl-N-phenyl-1,3,4-thiadiazol-2-amine (**8**, $C1_6H_{12}N_6OS_2$)
A suspension of 0.38 g **7** (1 mmol) in 15 cm^3 cold cone. H_2SO_4 was stirred until dissolution and then left at room temperature for 6 h. The reaction mixture was poured onto crushed ice and the precipitated product was filtered off, washed with water, and recrystallized from *Et*OH to afford 0.2 g **8** in 63% yield as a white powder. $R_f = 0.36$ (ethyl acetate/chloroform, 1/1). Mp 193–195°C; IR (KBr): $\bar{\nu} = 3418$ (NH), 1663 (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6, 300 MHz): $\delta = 3.87$ (s, SCH_2), 4.49 (br, s, NH), 7.12–7.21 (m, *Ar*–H), 7.38 (m, *Ar*–H) 7.42–7.51 (m, pyridyl-H), 7.62 (s, pyridyl-H) ppm; MS: m/z (%) = 408 ($M^+ + K + 1$, 22).

3-Pyridin-3-yl[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole-6-thiol (**10**,$C_8H_5N_5S_2$)
Carbon disulfide (3.3 cm^3, 10 mmol) was added to a mixture of 1.9 g **9** (10 mmol) in ethanolic KOH solution (0.56 g, 10 mmol of KOH in 30 cm^3 *Et*OH). The reaction mixture was heated under reflux for 6 h, most of the solvent was then distilled off under reduced pressure, and the residue was dissolved after being cooled in 10% KOH solution and filtered, the cold filtrate was acidified with conc. HCl and the separated solid was filtered off, washed with water and recrystallized from aqueous *Et*OH to give 1.0 g **10** in 53% yield as a white powder. $R_f = 0.56$ (chloroform/methanol, 2/1). Mp 276–278°C; IR (KBr): $\bar{\nu} = 1602$ (C=N), 3110 (SH) cm^{-1}; ^1H NMR (*DMSO*-d_6, 300 MHz): $\delta = 7.56$–7.61 (m, pyridyl-H), 8.36 (d, $J = 5.8$ Hz, pyridyl-H), 8.71 (d, $J = 6.2$ Hz, pyridyl-H), 9.13 (s, pyridyl-H), 14.0 (s, NH) ppm; MS: m/z (%) = 235 (M^+, 7).

6-(Ethylthio)-3-pyridin-3-yl[1,2,4]triazolo[3,4-b][1,3,4]-thiadiazole (**11**, $C_{10}H_9N_5S_2$)
The thiol derivative **10** (0.71 g, 3 mmol) was dissolved in an aqueous solution of KOH (0.16 g, 3 mmol in 20 cm^3 H_2O). Ethyl iodide (0.47 g, 3 mmol) was added with continuous shaking for a few minutes until the product separated. The excess of ethyl iodide was removed by heating on a water bath and the crude ethyl thioether was separated by filtration and recrystallized from aqueous *Et*OH to give 0.5 g **11** in 80% yield as white crystals. $R_f = 0.56$ (chloroform/methanol, 2/1). Mp 168–170°C; IR (KBr): $\bar{\nu} = 1614$ (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6, 300 MHz): $\delta = 1.45$ (t, $J = 7.2$ Hz, CH_2CH_3), 3.40 (q, $J = 7.2$ Hz, CH_2CH_3), 7.62–7.72 (m, pyridyl-H), 8.48 (d, $J = 5.8$ Hz, pyridyl-H), 8.72 (d, $J = 6.2$ Hz, pyridyl-H), 9.33 (s, pyridyl-H) ppm; MS: m/z (%) = 263 (M^+, 35).

6-(Hydrazino)-3-pyridine-3-yl[1,2,4]triazolo[3,4-b][1,3,4]-thiadiazole (**12**, $C_8H_7N_7S$)
A solution of 1.3 g **11** (5 mmol) in 10 cm^3 *Et*OH and 0.75 g $N_2H_4 \cdot H_2O$ (15 mmol) was heated under reflux for 3 h. The solvent was removed under reduced pressure and the precipitated solid was filtered off, washed with *Et*OH, and recrystallized from *Et*OH to afford 1.0 g **12** in 79% yield as grey crystals. $R_f = 0.65$ (chloroform/methanol, 2/1). Mp 244–246°C; IR (KBr): $\bar{\nu} = 3444$ (NH), 3329–3207 (NH_2) cm^{-1}.

6-Pyridin-3-ylbis[1,2,4]triazolo[3,4-b:4′,3′-d][1,3,4]-thiadiazole-3(2H)-thione (**13**, $C_9H_5N_7S_2$)
A mixture of an alcoholic KOH solution (0.28 g, 5 mmol in 7 cm^3 *Et*OH) and 3 cm^3 H_2O was added to a solution of 1.16 g **12** (5 mmol) in 25 cm^3 *Et*OH with stirring. CS_2 (0.38 g, 5 mmol) was added dropwise with continuous stirring and the reaction mixture was refluxed until the H_2S ceased (20 h). The reaction mixture was concentrated, cooled to room temperature and poured into 100 cm^3 of an ice-water mixture, then acidified with conc. HCl. The precipitate was filtered off and recrystallized from dioxane to give 0.98 g **13** in 85% yield as brown solids. $R_f = 0.45$ (chloroform/methanol, 2/1). Mp 254–256°C; IR (KBr): $\bar{\nu} = 1614$ (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6, 300 MHz): $\delta = 4.62$ (s, SH), 7.05–8.05 (m, pyridyl-H), 8.56 (s, pyridyl-H), 12.68 (s, NH) ppm; MS: m/z (%) = 275 (M^+, 20).

6-Phenyl-3-pyridin-3-yl[1,2,4]triazolo[3,4-b][1,3,4]-thiadiazole (**14**, $C_{14}H_9N_5S$) *and 6-(4-chlorophenyl)-3-pyridin-3-yl[1 ,2,4]triazolo[3,4-b][1,3,4]thiadi-azole* (**15**, $C_{14}H_8ClN_5S$)
A mixture of 0.96 g **9** (5 mmol), benzoic acid or 4-chlorobenzoic acid (5 mmol), and 25 cm^3 $POCl_3$ was refluxed for 5–6 h. The excess of $POCl_3$ was removed under reduced pressure and the residue was poured onto crushed ice to give a solid product which was washed with 20 cm^3 aqueous solution of $NaHCO_3$ (20%) and 20 cm^3 H_2O. The collected solid was filtered off, dried, and recrystallized from *Et*OH to give **14** and **15** in 50–64% yields as white crystals.

*Compound **14***: 1.0 g (64%). $R_f = 0.45$ (chloroform/methanol, 2/1). Mp 203–205°C; IR (KBr): $\bar{\nu} = 1578$ (C=N) cm^{-1}; ^1H NMR (*DMSO*-d_6, 300 MHz): $\delta = 7.46$ (m, *Ar*–H), 7.63 (m, *Ar*–H), 7.82 (m, pyridyl-H), 7.93 (s, pyridyl-H) ppm; MS m/z (%) = 279 (M^+, 34).

*Compound **15***: 0.88 g (50%). $R_f = 0.43$ (chloroform/methanol, 2/1). Mp 215–217°C; IR (KBr): $\bar{\nu} = 1614$ (C=N) cm^{-1}; MS: m/z (%) = 313 (M^+, 22).

N-(3-Mercapto-5-pyridin-3-yl-4H-1,2,4-triazol-4-yl)-acetamide (**16**, $C_9H_9N_5OS$)
A mixture of 0.96 g **9** (5 mmol) and 5 cm^3 *Ac*OH in 25 cm^3 dry pyridine was refluxed for 8 h. The reaction mixture poured

into 100 cm^3 H_2O. The solid product which formed was filtered off, dried, and recrystallized from *Ac*OH to afford 0.33 g **16** in 35% yield as brownish crystals. $R_f = 0.53$ (chloroform). Mp 182–184°C; IR (KBr): $\bar{\nu} = 3421$ (NH), 1702 (C=O), 1558 (C=N) cm^{-1}; MS: m/z (%) = 236 ($M^+ + 1$, 17).

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