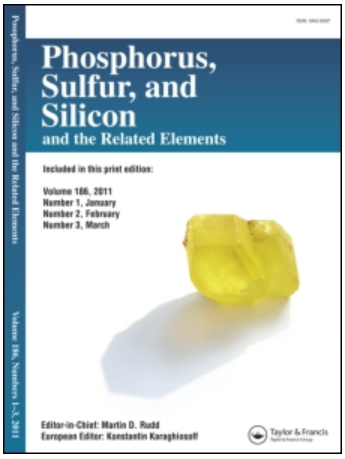

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Synthesis of Some Symmetrical Novel Bis-thiosemicarbazides, 1,2,4-Triazoles, 1,3,4-Thiadiazoles, and Their Derivatives

A. Mobinikhaledi[a]; N. Foroughifar[a]; M. Kalhor[a]; S. Ebrahimi[a]; M. A. Bodaghi Fard[a]
[a] Department of Chemistry, Arak University, Arak, Iran

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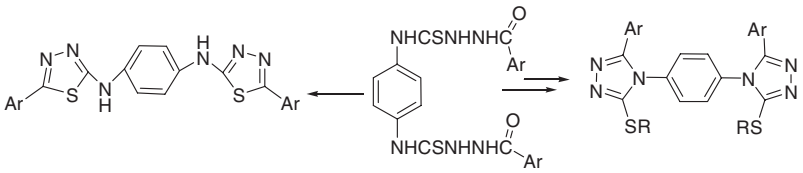
SYNTHESIS OF SOME SYMMETRICAL NOVEL BIS-THIOSEMICARBAZIDES, 1,2,4-TRIAZOLES, 1,3,4-THIADIAZOLES, AND THEIR DERIVATIVES

A. Mobinikhaledi, N. Foroughifar, M. Kalhor, S. Ebrahimi, and M. A. Bodaghi Fard
Department of Chemistry, Arak University, Arak, Iran

GRAPHICAL ABSTRACT



Abstract *Synthesis of some novel bis-1,2,4-triazoles* ***5a–c*** *and 1,3,4-thiadiazoles* ***6a–c*** *bearing a pyridyl unit using 4-(1,4-phenylene)bis-1-(x-picolinoyl)-thiosemicarbazide (x = 2,3,4) in an acidic and alkaline solution, respectively, is reported. The S-alkylation of symmetrical triazole derivatives* ***7a–c*** *and* ***8a–c*** *is also reported. The structures of the synthesized compounds result from the IR and NMR spectroscopic data.*

Keywords Thiadiazole; thiosemicarbazide; triazole

INTRODUCTION

It is well known that thiosemicarbazide derivatives exhibit interesting biological properties such as antitubercular,[1] antidepressant,[2] anti-inflammatory, and analgesic activity.[3] In addition, 1,2,4-triazoles[4–6] or thiadiazoles[7–16] and pyridines[17] have attracted the attention of chemists due to attractive biological activities. On the other hand, incorporating the pyridine ring into active compounds may improve their biological or physiological activities.[18] These heterocyclic systems, especially a combination of these units, 1,2,4-triazoles, thiadiazoles, and pyridine, could result in a large variety of structures and biological activities. Several heterocyclic compounds containing a thiadiazole or triazole moiety have been reported.[4–16] However, the synthesis of novel heterocyclic systems containing a bis(thiadiazole) or bis(triazole) system as well as bis(thiosemicarbazide) derivatives is still a challenge.

As part of our ongoing studies on the synthesis of heterocycles,[19,20] and also due to versatile biological properties of thiadiazole and triazole derivatives, we report the synthesis of some novel symmetrical bis(thiosemicarbazides), 1,3,4-thiadiazoles, and 1,2,4-triazoles.

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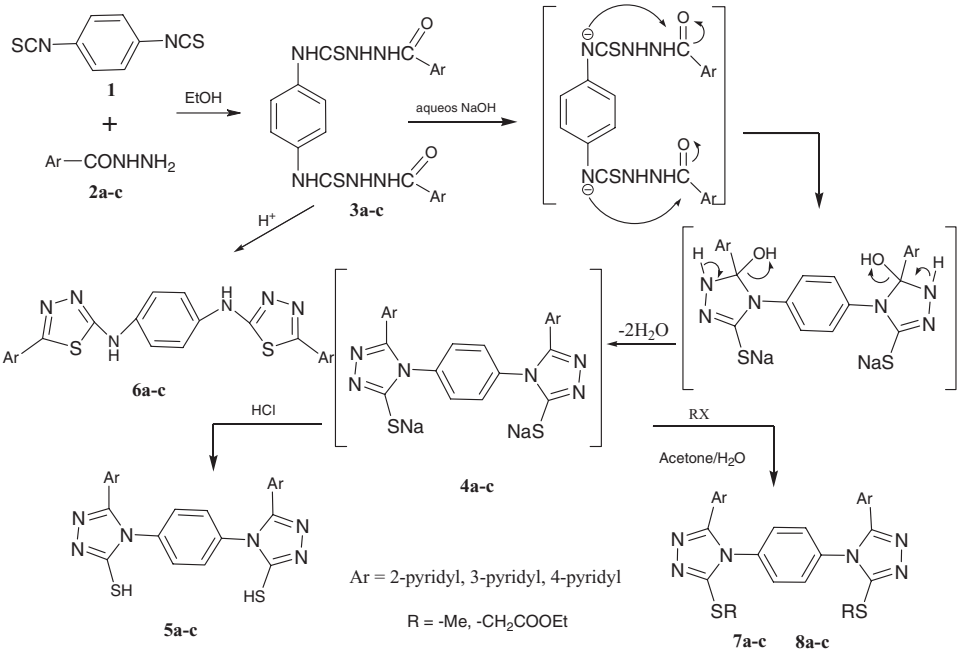
Address correspondence to A. Mobinikhaledi, Department of Chemistry, Arak University, Arak 38156-879, Iran. E-mail: akbar_mobini@yahoo.com

RESULTS AND DISCUSSION

The synthesis of the title compounds is illustrated in Scheme 1. The required pyridine carboxylic acid hydrazides **2a–c** were prepared via reaction of the appropriate pyridine carboxylic acid with hydrazine according to the literature.[21] The preparation of thiosemicarbazides **3a–c** was achieved by the reaction of the corresponding substituted hydrazides with 1,4-phenylenediisothiocyanate **1**. Thiosemicarbazide derivatives **3a–c** underwent an intramolecular cyclization under basic or acidic conditions to produce bis(1,2,4-triazoles) **5a–c** and bis(1,3,4-thiadiazoles) **6a–c** in high yields (Table 1). The reaction yields for **5c** and **6c** are higher than other respective isomers, which may be attributed to the stereoelectronic effects of the nitrogen atom of the pyridine ring and also to the more symmetrical structure of these products. The corresponding bis(1,2,4-triazolate) salts **4a–c** were further converted to the related symmetrically *S*-alkylated bis(1,2,4-triazole) derivatives **7a–c** and **8a–c**, when treated separately with methyl iodide or ethyl 2-chloro acetate.

The IR spectra of thiosemicarbazides **3a–c** showed characteristic absorption at 1149–1157, 1676–1683, and 3128–3493 cm^{-1} for the −C=S, C=O, and −NH stretching vibrations, respectively. ^1H NMR spectra of **3a–c** showed singlets at 9.73–10.81 ppm due to the resonance of −NH−CS−NH and −CO−NH protons, which disappeared upon D_2O addition. The ^{13}C NMR spectrum of compound **3a** showed nine signals, including a signal at 164 ppm for the >C=S and a signal at 180 ppm for the carbonyl carbon atoms.

The bis-triazole-3-thiols **5a–c** were obtained by refluxing the corresponding bis(thiosemicarbazides) in 4N NaOH solution, followed by acidification. The ^1H NMR spectra of compounds **5a–c** showed singlets at 14.28–14.40 ppm attributed to the resonance of the SH protons, which disappeared upon D_2O addition. In the ^{13}C NMR spectra of compounds **5a–c**, the appearance of signals at the region between 169.0–169.4 ppm



Scheme 1 Synthesis of bis(thiosemicarbazides), 1,2,4-triazoles, and 1,3,4-thiadiazoles.

Table 1 Reaction time, melting point, and yield of compounds **3** through **8a–c**

Compound	Time (h)	Mp (°C)	Yield (%)[a]
3a	0.08	225–227	82
3b	0.3	198–199	80
3c	0.03	229	84
5a	1.0	385–387	87
5b	0.6	395–397	88
5c	1.5	390–393	90
6a	8.0	357–358	90
6b	8.0	341	83
6c	8.0	369–370	94
7a	0.05	295	75
7b	0.4	276–277	52
7c	0.5	297–300	52
8a	4.5	208–209	40
8b	3.0	203–204	55
8c	4.0	202	47

[a]Isolated yield.

attributed to the carbon resonance of the C═N group in triazole rings is in support of the expected thiol structures.

The IR spectra of **6a–c** showed absorption bands at 3256–3265 cm^{-1} characteristic for the NH group. Also in the ^1H NMR spectra of all bis(1,3,4-thiadiazoles), the singlet at 10.59–10.74 ppm was attributed to the resonance of the NH proton. *S*-Alkylated 1,2,4-triazoles, **7a–c** and **8a–c**, were obtained by refluxing the appropriate triazole salts **4a–c** with methyl iodide and ethyl 2-chloroacetate in aqueous acetone, respectively. In the ^1H NMR spectra of **7a–c** and **8a–c**, the absence of the -SH resonance and the appearance of a singlet in the aliphatic region, related to the resonance of the -SR group, supports the formation of the alkylated products.

EXPERIMENTAL

All chemicals used were purchased from Merck or Fluka. Melting points were determined using an electrothermal digital apparatus and are uncorrected. Elemental analyses were performed with an Elemental Analyzer (Elemental, Vario EL III) at Arak University. IR spectra were obtained with a galaxy series FT-IR 5000 spectrometer using KBr discs. NMR spectra were recorded on a Bruker (300 MHz) spectrometer. Chemical shifts (ppm) are referenced to tetramethylsilane (TMS) as an internal standard. Reactions were monitored by thin layer chromatography.

Preparation of Bis(thiosemicarbazides) 3a–c: General Procedure

A solution of 1,4-phenylenediisothiocyanate (0.2 g, 1 mmol) in ethanol (30 mL) was added to a solution of pyridyl acid hydrazide **2a–c** (0.28 g, 2.0 mmol) in absolute ethanol (15 mL) with stirring. The reaction mixture was refluxed for 2–30 min. The solution was cooled to ambient temperature, and the precipitate was filtered to give the crude product, which was then recrystallized from DMF:EtOH (15:1) to give pure **3a–c**.

4,4-(1,4-Phenylene)bis-1-(2-picolinoyl)-thiosemicarbazide (3a). IR (KBr): $\nu = 1149$ (C=S), 1271, 1373 (C=C), 1518, 1572 (C=N), 1683 (C=O), 3094 (C−H_{arom}), 3159, 3229, 3354 (N−H) cm^{-1}; ^1H NMR (DMSO-d_6): $\delta = 7.39$ (s, 4H, C−$H_{phenylene}$), 7.64 (m, 2H, C−$H_{pyridyl}$), 8.02 (d, $J = 9.5$ Hz, 4H, C−H_{pyridy}), 8.67 (d, $J = 9.5$ Hz, 2H, C−H_{pyridy}), 9.71 (s, 4H, NH−CS−NH), 10.70 (s, 2H, NH); ^{13}C NMR (DMSO-d_6): $\delta =$ 122.9, 125.3, 127.3, 136.4, 138.1, 148.9, 149.8, 164.1, 180.9; Ms: m/z 465 (5), 436 (7), 192 (30), 99 (35), 85 (100), 71 (90), 57 (83), 43(92); Anal. Calcd. for $C_{20}H_{18}N_8O_2S_2$: C, 51.49; H, 3.89; N, 24.02; S, 13.75. Found: C, 51.76; H, 4.08; N, 23.96; S, 13.97%.

4,4-(1,4-Phenylene)bis-1-(3-picolinoyl)-thiosemicarbazide (3b). IR (KBr): $\nu = 115\ 7$ (C=S), 1255, 1371 (C=C), 1514, 1570 (C=N), 1678 (C=O), 3050 (C−H_{arom}), 3171, 3232, 3493 (N−H) cm^{-1}; ^1H NMR (DMSO-d_6): $\delta = 7.4$ (s, 4H, C−$H_{phenylene}$), 7.54 (t, $J = 5.1$ Hz, 2H, C−$H_{pyridyl}$), 8.28 (d, $J = 7.1$ Hz, 2H, C−H_{pyridy}), 8.75 (d, $J = 6.8$ Hz, 2H, C−H_{pyridy}), 9.12 (s, 2H, C−H_{pyridy}), 9.89 (s, 4H, NH−CS−NH), 10.81 (s, 2H, NH); Anal. Calcd. for $C_{20}H_{18}N_8O_2S_2$: C, 51.49; H, 3.89; N, 24.02; S, 13.75. Found: C, 51.26; H, 3.67; N, 24.32; S, 13.47%.

4,4-(1,4-Phenylene)bis-1-(4-picolinoyl)-thiosemicarbazide (3c). IR (KBr): $\nu = 1149$ (C=S), 1228, 1263 (C=C), 1518, 1602 (C=N), 1676 (C=O), 3047 (C−H_{arom}), 3128, 3244 (N−H) cm^{-1}; ^1H NMR (DMSO-d_6): $\delta = 7.28$ (s, 4H, C−$H_{phenylene}$), 7.75 (d, $J = 4.8$ Hz, 4H, C−$H_{phenylene}$), 8.67 (d, $J = 4.7$ Hz, 4H, C−$H_{pyridyl}$), 9.73 (s, 2H, CS−NH), 9.76 (s, 2H, NH−CS), 10.78 (s, 2H, CONH); Anal. Calcd. for $C_{20}H_{18}N_8O_2S_2$: C, 51.49; H, 3.89; N, 24.02; S, 13.75. Found: C, 51.43; H, 4.17; N, 24.23; S, 13.96%.

Preparation of 5,5-Substituted Bis-3-mercapto-1,2,4-triazoles 5a–c: General Procedure

Bis(thiosemicarbazide) **3a–c** (0.5g, 1 mmol) was added slowly to a solution of 4N sodium hydroxide (10–15 mL). The reaction mixture was refluxed for the proper time (Table 1) to give the corresponding salt, which was then filtered and washed with 1N sodium hydroxide solution and water to give the intermediate compounds **4a–c**. The filtrate was refluxed for 1 h and after cooling to ambient temperature was acidified with 2N hydrochloric acid. The precipitate was filtered and washed thoroughly with water (5 mL), dried, and recrystallized from DMSO:H_2O (6:0.5) to give the pure products.

4,4-(1,4-Phenylene)bis-5-(2-pyridyl)-1,2,4-triazole-3-thiol (5a). IR (KBr): $\nu = 1280$ (C=S), 1336 (C=C), 1604 (C=N), 3050 (C−H_{arom}), 3117, 3188 (N−H) cm^{-1}; ^1H NMR (DMSO-d_6): $\delta = 7.36$ (s, 4H, C−$H_{phenylene}$), 7.41 (q, $J = 10.1$ Hz, 2H, C−$H_{pyridyl}$), 7.79 (d, $J = 7.9$ Hz, 2H, C−$H_{pyridyl}$), 7.89 (t, $J = 7.7$ Hz, 2H, C−$H_{pyridyl}$), 8.33 (d, $J = 4.6$ Hz, 2H, C−$H_{pyridyl}$), 14.28 (s, 2H, S−H); ^{13}C NMR (DMSO-d_6): $\delta = 124.4$, 125.5, 129.2, 135.6, 137.8, 145.4, 149.5, 150.0, 169.4; Anal. Calcd. for $C_{20}H_{14}N_8S_2$: C, 55.80; H, 3.28; N, 26.03; S, 14.90. Found: C, 55.70; H, 3.37; N, 26.33; S, 15.07%.

4,4-(1,4-Phenylene)bis-5-(3-pyridyl)-1,2,4-triazole-3-thiol (5b). IR (KBr): $\nu = 1400$, 1438 (C=C), 1550, 1610 (C=N), 2688 (SH), 3061 (C−H_{arom}) cm^{-1}; ^1H NMR (DMSO-d_6): $\delta = 7.42$ (t, $J = 6.7$ Hz, 2H, C−$H_{pyridyl}$), 7.50–7.57 (m, 6H, C−$H_{pyridyl}$ and C−$H_{phenylene}$), 8.56 (s, 2H, C−$H_{pyridyl}$), 8.65 (t, $J = 6.7$ Hz, 2H, C−$H_{pyridyl}$), 14.33 (s, 2H, N−H), The SH protons disappeared upon D_2O addition; ^{13}C NMR (DMSO-d_6): $\delta = 122.5$, 123.8, 130.4, 135.3, 136.1, 148.9, 149.2, 151.5, 169.0; Anal. Calcd. for $C_{20}H_{14}N_8S_2$: C, 55.80; H, 3.28; N, 26.03; S, 14.90. Found: C, 56.14; H, 3.34; N, 25.61; S, 14.59%.

4,4-(1,4-Phenylene)bis-5-(4-pyridyl)-1,2,4-triazole-3-thiol (5c). This compound was obtained as light yellow precipitate. IR (KBr): $\nu = 1197$ (C=S), 1334, 1428

(C=C), 1516, 1606 (C=N), 3092 (C−H_{arom}), 3194 (N−H) cm^{-1}; ^1H NMR (DMSO-d_6): $\delta = 7.23$ (d, $J = 4.6$ Hz, 4H, C−$H_{pyridyl}$), 7.58 (s, 4H, C−$H_{phenylene}$), 8.58 (d, $J = 4.7$ Hz, 4H, C−$H_{pyridyl}$), 14.43 (bs, 2H, S−H); ^{13}C NMR (DMSO-d_6): $\delta = 122.6, 130.4, 133.6, 135.4, 148.9, 150.4, 169.4$; Anal. Calcd. for $C_{20}H_{14}N_8S_2$: C, 55.80; H, 3.28; N, 26.03; S, 14.90. Found: C, 55.61; H, 3.18; N, 26.13; S, 14.70%.

Preparation of 2, 2-Substituted Bis-(pyridyl)-1,3,4-thiadiazoles 6a–c: General Procedure

The thiosemicarbazides **3a–c** (0.39 g, 0.6 mmol) were added slowly to concentrated sulfuric acid (10–15 mL), which was stirred and kept at 0 °C. The reaction mixture was stirred at room temperature for 8 h. It was then poured into ice-water (50 g) and neutralized with concentrated aqueous ammonia. The precipitate was filtered, washed with water (15 mL), dried, and recrystallized from DMF:H_2O (10:1) to give pure **6a–c**.

2,2-(1,4-Phenylendiamine)bis-5-(2-pyridyl)-1,3,4-thiadiazole (6a). This compound was obtained as a dark yellow precipitate. IR (KBr): $\nu = 1415, 1485$ (C=C), 1525, 1593 (C=N), 3065 (C−H_{arom}), 3257 (N−H) cm^{-1};^1H NMR (DMSO-d_6): $\delta = 7.49$ (t, $J = 6.8$ Hz, 2H, C−$H_{pyridyl}$), 7.68 (s, 4H, C−$H_{phenylene}$), 7.97 (d, $J = 7.7$ Hz, 2H, C−$H_{pyridyl}$), 8.13 (d, $J = 7.9$ Hz, 2H, C−$H_{pyridyl}$), 8.63 (d, $J = 4.4$ Hz, 2H, C−$H_{pyridyl}$), 10.60 (s, 2H, N−H); Anal. Calcd. for $C_{20}H_{14}N_8S_2$: C, 55.80; H, 3.28; N, 26.03; S, 14.90. Found: C, 56.05; H, 3.54; N, 25.76; S, 14.63%.

2,2-(1,4-Phenylendiamine)bis-5-(3-pyridyl)-1,3,4-thiadiazole (6b). This compound was obtained as a dark yellow precipitate. IR (KBr): $\nu = 1236, 1415$ (C=C), 1510, 1608 (C=N), 3025 (C−H_{arom}), 3169, 3256 (N−H) cm^{-1}.^1H NMR (DMSO-d_6): $\delta =$ 7.51 (t, $J = 7.4$ Hz, 2H, C−$H_{pyridyl}$), 7.66 (s, 4H, C−$H_{phenylene}$), 8.19 (d, $J = 7.6$ Hz, 2H, C−$H_{pyridyl}$), 8.63 (d, $J = 4.2$ Hz, 2H, C−$H_{pyridyl}$), 9.02 (s, 2H, C−$H_{pyridyl}$), 10.59 (s, 2H, N−H). ^{13}C NMR (DMSO-d_6): $\delta = 119.1, 124.6, 127.1, 134.3, 135.8, 147.7, 151.1, 154.6, 165.2$; Anal. Calcd. for $C_{20}H_{14}N_8S_2$: C, 55.80; H, 3.28; N, 26.03; S, 14.90. Found: C, 55.52; H, 3.56; N, 25.77; S, 14.58%.

2,2-(1,4-Phenylendiamine)bis-5-(4-pyridyl)-1,3,4-thiadiazole (6c). This compound was obtained as a dark yellow precipitate. IR (KBr): $\nu = 1415$ (C=C), 1491, 1601 (C=N), 3053 (C−H_{arom}), 3265 (N−H) cm^{-1};^1H NMR (DMSO-d_6): $\delta = 7.69$ (s, 4H, C−$H_{phenylene}$), 7.81 (d, $J = 4.6$ Hz, 4H, C−$H_{pyridyl}$), 8.70 (d, $J = 3.2$ Hz, 4H, C−$H_{pyridyl}$), 10.74 (s, 2H, N−H); Anal. Calcd. for $C_{20}H_{14}N_8S_2$: C, 55.80; H, 3.28; N, 26.03; S, 14.90. Found: C, 54.52; H, 3.39; N, 25.68; S, 14.59%.

Preparation of (3-Methylthio)-1,2,4-triazoles 7a–c: General Procedure

A solution of the triazole salt **4a–c** (0.1 g, 0.2 mmol) and methyl iodide (0.025 mL, 0.4 mmol) in a mixture of acetone and water (20–30 mL, 3:2), was refluxed for the proper time (Table 1). The solution was cooled to ambient temperature and filtered to give compound **7a–c**.

4,4-(1,4-Phenylene)bis-[(3-methylthio)-5-(2-pyridyl)-1,2,4-triazole] (7a). IR (KBr): $\nu = 704$ (C−S−C), 1402, 1444 (C=C), 1518, 1585 (C=N), 2935 (CH_3), 3072 (C−H_{arom}) cm^{-1}.;^1H NMR (DMSO-d_6): $\delta = 2.65$ (s, 6H, CH_3), 7.42 (q, $J = 7.3$ Hz, 2H, C−$H_{pyridyl}$), 7.49 (s, 4H, C−$H_{phenylene}$), 7.94 (d, $J = 7.6$ Hz, 2H, C−$H_{pyridyl}$), 8.02 (d, $J = 7.4$ Hz, 2H, C−$H_{pyridyl}$), 8.30 (d, $J = 4.6$ Hz, 2H, C−$H_{pyridyl}$); Anal. Calcd. for $C_{22}H_{18}N_8S_2$: C, 57.62; H, 3.96; N, 24.44; S, 13.99. Found: C, 57.35; H, 4.21; N, 24.58; S, 13.78%.

4, 4-(1,4-Phenylene)bis-[(3-methylthio)-5-(3-pyridyl)-1,2,4-triazole] (7b). IR (KBr): $\nu = 705$ (C—S—C), 1403, 1442 (C=C), 1516, 1572 (C=N), 2930 (C—H_{aliph}), 3065 (C—H_{arom}) cm^{-1}; ^1H NMR (DMSO-d_6): $\delta = 2.65$ (s, 6H, CH_3),7.42 (t, $J = 7.5$ Hz, 2H, C—$H_{pyridyl}$), 7.60 (d, $J = 7.9$ Hz, 2H, C—$H_{pyridyl}$), 7.71 (s, 4H, C—$H_{phenylene}$), 8.60 (s, 2H, C—$H_{pyridyl}$), 8.63 (t, $J = 7.1$ Hz, 2H, C—$H_{pyridyl}$); ^{13}C NMR (DMSO-d_6): $\delta = 15.0$, 123.2, 123.9, 130.1, 135.3, 135.7, 148.9, 151.1, 152.7, 153.5; Anal. Calcd. for $C_{22}H_{18}N_8S_2$: C, 57.62; H, 3.96; N, 24.44; S, 13.99. Found: C, 57.91; H, 4.11; N, 24.14; S, 14.19%.

4,4-(1,4-Phenylene)bis-[(3-methylthio)-5-(4-pyridyl)-1, 2, 4-triazole] (7c). This compound was obtained as a dark brown precipitate. IR (KBr): $\nu = 700$ (C—S—C), 1377, 1440 (C=C), 1514, 1602 (C=N), 2930 (CH_3), 3055 (C—H_{arom}) cm^{-1};^1H NMR (DMSO-d_6): $\delta = 2.67$ (s, 6H, CH_3), 7.30 (d, $J = 2.9$ Hz, 2H, C—$H_{pyridyl}$), 7.74 (s, 4H, C—$H_{phenylene}$), 8.61 (d, $J = 2.9$ Hz, 4H, C—$H_{pyridyl}$); Anal. Calcd. for $C_{22}H_{18}N_8S_2$: C, 57.62; H, 3.96; N, 24.44; S, 13.99. Found: C, 57.69; H, 3.85; N, 24.53; S, 14.09%.

Preparation of Compounds 8a–c: General Procedure

Triazole salt **4a–c** (0.1 g, 0.2 mmol) was dissolved in a mixture of acetone and water (3:2, 20–30 mL). Ethyl 2-chloro acetate (0.43 mL, 0.4 mmol) was then added with stirring. The reaction mixture was refluxed for the proper time (Table 1) and cooled to room temperature to give a precipitate, which was filtered and washed with water (2 mL).

Diethyl 4,4-(1,4-phenylene)bis-[5-(2-pyridyl)-1,2,4-triazole-3-ylthio]diacetate (8a). IR (KBr): $\nu = 700$ (C—S—C), 1178 (C—O), 1300, 1448 (C=C), 1516, 1591 (C=N), 1722 (C=O), 2974 (C—H_{aliph}), 3057 (C—H_{arom}) cm^{-1};^1H NMR (DMSO-d_6): $\delta =$ 1.20 (t, $J = 7.0$ Hz, 6H, CH_3), 4.10–4.17 (m, 8H, OCH_2 and SCH_2), 7.40 (t, $J = 6.2$ Hz, 2H, C—$H_{pyridyl}$), 7.51 (s, 4H, C—$H_{phenylene}$), 7.94 (d, $J = 7.4$, 2H, C—$H_{pyridyl}$), 8.02 (d, $J = 7.9$ Hz, 2H, C—$H_{pyridyl}$), 8.31 (d, $J = 7.4$ Hz, 2H, C—$H_{pyridyl}$); Anal. Calcd. for $C_{28}H_{26}N_8O_4S_2$: C, 55.80; H, 4.35; N, 18.59; S, 10.64. Found: C, 56.08; H, 4.17; N, 18.73; S, 10.61%.

Diethyl 4,4-(1,4-phenylene)bis-[5-(3-pyridyl)-1,2,4-triazole-3-ylthio]diacetate (8b). IR (KBr): $\nu = 705$ (C—S—C), 1178 (C—O), 1311, 1389 (C=C), 1438, 1516 (C=N), 1726 (C=O), 2978 (C—H_{aliph}), 3074 (C—H_{arom}) cm^{-1}; ^1H NMR (DMSO-d_6): $\delta =$ 1.20 (t, $J = 7.0$ Hz, 6H, CH_3), 4.10–4.17 (m, 8H, OCH_2 and SCH_2), 7.45 (d, $J = 6.9$ Hz, 2H, C—$H_{pyridyl}$), 7.60 (d, $J = 8.1$, 2H, C—$H_{pyridyl}$), 7.73 (s, 4H, C—$H_{phenylen}$), 8.61 (m, 4H, C—$H_{pyridyl}$); Anal. Calcd. for $C_{28}H_{26}N_8O_4S_2$: C, 55.80; H, 4.35; N, 18.59; S, 10.64. Found: C, 55.74; H, 4.64; N, 18.37; S, 10.73%.

Diethyl 4,4-(1,4-phenylene)bis-[5-(4-pyridyl)-1,2,4-triazole-3-ylthio]diacetate (8c). This compound was obtained as a light yellow precipitate. IR (KBr): $\nu =$ 702 (C—S—C), 1176 (C—O), 1309, 1437 (C=C), 1516, 1601 (C=N), 1734 (C=O), 2984 (C—H_{aliph}), 3051 (C—H_{arom}) cm^{-1}; ^1H NMR (DMSO-d_6): $\delta = 1.20$ (t, $J = 7.1$ Hz, 6H, CH_3), 4.10–4.16 (m, 8H, OCH_2 and SCH_2), 7.31 (d, $J = 5.9$ Hz, 4H, C—$H_{pyridyl}$), 7.75 (s, 4H, C—$H_{phenylen}$), 8.61 (d, $J = 5.9$ Hz, 4H, C—$H_{pyridyl}$); ^{13}C NMR (DMSO-d_6): $\delta =$ 14.4, 34.5, 61.9, 122.3, 130.1, 134.0, 135.3, 150.5, 152.6, 152.9, 168.4; Anal. Calcd. for $C_{28}H_{26}N_8O_4S_2$: C, 55.80; H, 4.35; N, 18.59; S, 10.64. Found: C, 55.54; H, 4.47; N, 18.27; S, 10.87%.

REFERENCES

1. Brown, R. K.; Snider, R. F.; Stevenson, M. D. *J. Org. Chem.* **1956**, *21*, 261.
2. Allais, A.; Meier, J. French Patent 1, 363,855; *Chem. Abstr.* **1964**, *61*, 14641.
3. Alvarex, E. F.; Pajares, M. B.; Lopez, O. N. Spanish Patent; *Chem. Abstr.* **1967**, *67*, 32590.

4. Eweiss, N. F.; Bahajaj, A. A.; Elsherbini, E. A. *J. Heterocycl. Chem.* **1986**, *2*, 1451.
5. Moreno-Manas, M.; Arredondo, Y.; Pleixats, R.; Teixido, M.; Haga, M. M.; Palacin, C.; Castello, J. M.; Oritizz, J. A. *J. Heterocycl. Chem.* **1992**, *29*, 1557.
6. Misra, U.; Hitkari, A.; Saxena, A.; Gurtu, S.; Shanker, K. *Eur. J. Med. Chem.* **1996**, *31*, 629.
7. Turner, S.; Myers, M.; Gadie, B.; Nelson, A. J.; Pape, R.; Saville, J. F.; Doxey, J. C.; Berridge, T. L. *J. Med. Chem.* **1988**, *31*, 902.
8. Gawande, N. G.; Shingare, M. S. *Indian J. Chem.* **1987**, *26B*, 387.
9. Mamolo, G.; Vio, L.; Banfi, E. *Il Farmaco* **1996**, *51*, 71.
10. Mullican, M. D.; Wilson, M. W.; Connor, D. T.; Kostlan, C. R.; Schrier, D. J.; Dyer, R. D. *J. Med. Chem.* **1993**, *36*, 1090.
11. Song, Y.; Connor, D. T.; Sercel, A. D.; Sorenson, R. J.; Doubleday, R.; Unangst, P. C.; Roth, B. D.; Beylin, V. G.; Gilbertsen, R. B.; Chan, K.; Schrier, D. J.; Guglietta, A.; Bornemeier, D. A.; Dyer, R. D. *J. Med. Chem.* **1999**, *42*, 1161.
12. Labanauskas, L.; Kalcas, V.; Udrenaite, E.; Gaidelis, P.; Brukstus, A.; Dauksas, A. *Pharmazie* **2001**, *56*, 617.
13. Shucla, H. K.; Desai, N. C.; Astik, R. R.; Thaker, K. A. *J. Indian Chem. Soc.* **1984**, *61*, 168.
14. Turner, S.; Myers, M.; Gadie, B.; Nelson, A. J.; Pape, R.; Saville, J. F.; Doxey, J. C.; Berridge, T. L. *J. Med. Chem.* **1988**, *31*, 902.
15. Turner, S.; Myers, M.; Gadie, B.; Hale, S. A.; Horsley, A.; Nelson, A. J.; Pape, R.; Saville, J. F.; Doxey, J. C.; Berridge, T. L. *J. Med. Chem.* **1988**, *31*, 907.
16. Chou, J. Y.; Lai, S. Y.; Pan, S. L.; Jow, G. M.; Chern, J. W.; Guh, J. H. *Biochem. Pharmacol.* **2003**, *66*, 115.
17. Allen, R. D.; Johnston, G. A. R. *Med. Res. Rev.* **1983**, *3*, 91.
18. Mavel, S.; Renou, J. L.; Galtier, C.; Allouchi, H.; Snoeck, R.; Andrei, G.; Clercq, E. D.; Gueiffier, J. *Bioorg. Med. Chem.* **2002**, *10*, 941.
19. Mobinikhaledi, A.; Foroughifar, N.; Alipour Safari, J.; Mosleh, T. *Phosphorus, Sulfur Silicon Relat. Elem.* **2007**, *182*, 2329.
20. Mobinikhaledi, A.; Foroughifar, N.; Goodarzi, F. *Phosphorus, Sulfur Silicon Relat. Elem.* **2004**, *179*, 507.
21. Iqubal, R.; Malik, F. *J. Chem. Soc. Pak.* **1984**, *6*, 43.