Synthesis and Spectral Characterization of New S-Alkylated 1,2,4-Triazoles as Potential Biological Agents

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In the work we presented the behavior of 5-(4-(4-X-phenylsulfonyl)phenyl)-4-(n-propyl)-2H-1,2,4-triazole-3(4H)-thiones (X= Cl or Br) with some alkylation agents. Thus, new S-alkylated 1,2,4-triazole derivatives were synthesized by reaction of the corresponding 1,2,4-triazole-3-thione derivatives with different á-halogenated compounds (ethyl bromide, ethyl chloroacetate or phenacyl bromide), in basic medium. The structures of synthesized compounds were elucidated by spectral data ([1]H-NMR, [13]C-NMR, mass spectrometry) and elemental analysis.

Keywords: 1,2,4-triazole-3-thione, alkylation, halogenated compound, S-alkylated 1,2,4-triazole

The azoles represent an important class of five-membered heterocyclic compounds recognized for the great number of compounds with biological properties, more of them being used as active substances in composition of many drugs used successfully in clinics for treating of different diseases [1]. Among these, 1,2,4-triazoles represent a class of sustained interest due to the vast range of their biological properties. Moreover, there are known many drugs containing the 1,2,4-triazole ring used as antimycotic, antimigraine, anticancer, antiviral etc [2]. Among 1,2,4-triazoles, compounds containing the 1,2,4-triazole-thione ring deserve special attention since they are reported to possess various biological activities including antimicrobial [3,4], antioxidant [5], carbonic anhydrase inhibitors [6], anticonvulsant [7,8], antitumoral [9]. The biological effect of these compounds depend largely on the nature of the substituents grafted on the 1,2,4-triazole ring [10]. At the same time these compounds are versatile intermediates in organic synthesis as they react with electrophiles at the sulfur and nitrogen atoms. The S-alkylated 1,2,4-triazoles have also increasing importance because various derivatives possess biological activity such as: analgesic [11,12], anti-inflammatory [12-14], antibacterial, antifungal [12,15], antioxidant [16], anticancer [17-19] activity.

In view of these reports and in continuation of our studies on the heterocyclic compounds with potential biological activity [20-24], in this work we extended the research in the 1,2,4-triazoles class, by study of the alkylation reaction of some 1,2,4-triazole-3-thiones with different halogenated compounds. The structures of the alkylation products were established unequivocally by ^{1}H-NMR, ^{13}C-NMR and IR spectrometry.

Experimental part

Melting points were determined on a Böetius apparatus and are uncorrected. The FT-IR spectra were recorded on a Vertex 70 Bruker spectrometer (using KBr pellets). The NMR spectra were recorded on a Varian Gemini 300BB spectrometer at 300 MHz for ^{1}H-NMR and at 75 MHz for ^{13}C-NMR using $CDCl_3$ as solvent; the chemical shifts d, are reported in ppm relative to tetramethylsilane (TMS) as internal standard and coupling constants *J* are in Hz. The content of C, H, and N was assayed using a ECS-40-10-Costeh microdosimeter.

For recording of the mass spectra, a solution (1 µg/mL) of compound in methanol/water (0.1% ammonia) 90/10 was infused into electrospray interface working in positive mode, with 1200 L/MS/MS triple quadrupole, using a Prostar 240 SDM chromatographic pump (Varian) to 20 µL/min flow rate. Nebulising gas was nitrogen at 42 psi, drying gas was air at 19 psi and 200°C, capillary voltage was set up at 4500 V. Protonated molecular ions were fragmented using collision with argon.

Synthesis of compounds

The key intermediates, *5-(4-(4-X-phenylsulfonyl) phenyl)-4-(n-propyl)-2H-1,2,4-triazole-3(4H)-thiones* (X= Cl or Br) known in literature [25], were synthesized by cyclization, in basic media, of the corresponding acylthiosemicarbazides. The thiosemicarbazides were obtained by treatment of the corresponding hydrazides with *n*-propylisothiocyanate. For the synthesis of the corresponding hydrazides, we started from chloro/bromo-benzene and tosyl chloride, following several stages: alkylation, oxidation, esterification and hydrazinolysis [25]. By treatment of 1,2,4-triazole-3(4*H*)-thiones **1a,b** with ethyl bromide, in sodium ethoxide media, the 5-(4-(4-X-phenylsulfonyl)phenyl)-3-(ethylthio)-4-propyl-4*H*-1,2,4-triazoles **2a,b** were obtained. Also, *2-(5-(4-(4-X-phenylsulfonyl)phenyl)-4-propyl-4H-1,2,4-triazol-3-ylthio)-1-phenylethanone* **3a,b** and *ethyl 2-(5-(4-(4-X-phenylsulfonyl)phenyl)-4-propyl-4H-1,2,4-triazol-3-ylthio)acetate* **4a,b** were obtained by reaction of the same 1,2,4-triazole-3(4*H*)-thiones **1a,b** with phenacyl bromide and ethyl chloroacetate, respectively. Although both N-2 endocyclic nitrogen atom and sulfur atom from 1,2,4-triazole-3-thiones **1a,b** are accessible to attack by alkylating agents, on the basis of the spectral data it has been demonstrated that alkylation of these compounds took place at the sulfur atom and not nitrogen atom.

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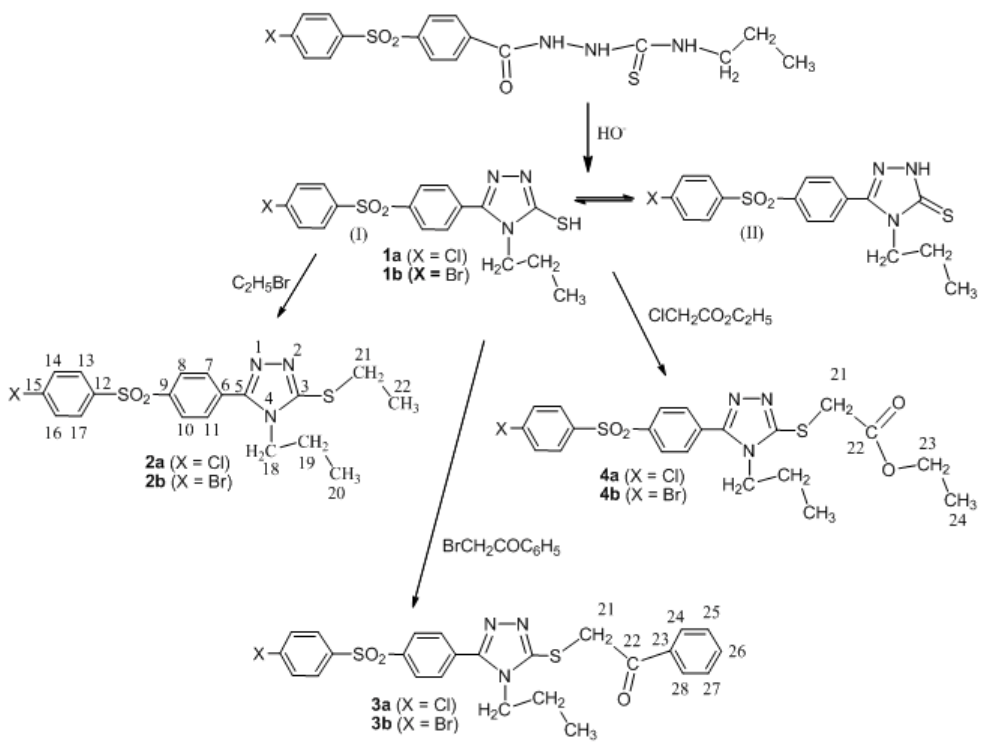

Scheme 1. Synthesis of compounds 2a,b-4a,b

The target 1,2,4-triazole compounds were synthesized according to the synthetic route outlined in scheme 1.

General procedure for the synthesis of S-alkylated 1,2,4-triazoles 2a,b – 4a,b

The 1,2,4-triazole **1** (2mmol) was added to a solution of sodium ethoxide (obtained from 46 mg of sodium and 35 mL absolute ethanol). The mixture was stirred at room temperature until a solution was obtained. Then, the ethyl bromide, phenacyl bromide or ethyl chloroacetate (2mmol) was added to the solution and the mixture was stirred at room temperature for 10 h. The resulting mixture was poured into a small amount of ice-water. The precipitate obtained was filtered off, washed with water, dried and recristalized from ethanol.

3-(4-(4-chlorophenylsulfonyl)phenyl)-5-(ethylthio)-4-propyl-4H-1,2,4-triazole **2a**

m.p. 135-137 °C; yield: 76 %;

IR (KBr, n, cm^{-1}): 3094m, 3072m, 3037w, 2973m, 2935m, 2877m, 1600m, 1581m, 1470m, 1321s, 1284m, 1158vs, 769s;

^{1}H-NMR ($CDCl_3$, d ppm, *J* Hz): 0.85 (t, 3H, 7.4, $CH_2CH_2\underline{CH_3}$); 1.46 (t, 3H, 7.4, $SCH_2\underline{CH_3}$), 1.70 (sx, 2H, 7.4, $CH_2\underline{CH_2}CH_3$), 3.35 (q, 2H, 7.4, $S\underline{CH_2}CH_3$), 3.89 (t, 2H, 7.4, $\underline{CH_2}CH_2CH_3$), 7.51 (d, 2H, 8.7, H-14, H-16), 7.78 (d, 2H, 8.5, H-7, H-11), 7.91 (d, 2H, 8.7, H-13, H-17), 8.06 (d, 2H, 8.5, H-8, H-10);

^{13}C-NMR ($CDCl_3$, d ppm): 10.83 ($CH_2CH_2\underline{CH_3}$), 14.87 ($SCH_2\underline{CH_3}$), 23.25 ($CH_2\underline{CH_2}CH_3$), 27.55 ($S\underline{CH_2}CH_3$), 46.34 ($\underline{CH_2}CH_2CH_3$), 128.26 (C-7, C-11), 129.23 (C-8, C-10), 129.41 (C-13, C-17), 129.78 (C-14, C-16), 132.26 (C-6), 133.72 (C-15), 140.36 (C-12), 142.60 (C-9), 152.87 (C-5 triazole ring), 153.57 (C-3 triazole ring);

Elemental analysis: Anal. Calcd for $C_{19}H_{20}ClN_3O_2S_2$ (421.96): C, 54.08; H, 4.78; N, 9.96. Found: C, 54.02; H, 4.83; N, 9.89%;

ESI-MS, *m/z*: 422 $[M+H]^+$ (^{35}Cl), 424 $[M+H]^+$ (^{37}Cl); 380 (100) $[M+H-C_3H_6]^+$; 382 (100) $[M+H-C_3H_6]^+$; 352 $[M+H-C_3H_6-C_2H_4]^+$; 354 $[M+H-C_3H_6-C_2H_4]^+$; 175 $[^{35}ClC_6H_4SO_2]^+$; 177 $[^{37}ClC_6H_4SO_2]^+$.

3-(4-(4-bromophenylsulfonyl)phenyl)-5-(ethylthio)-4-propyl-4H-1,2,4-triazole **2b**

m.p. 128-130 °C; yield: 65 %;

IR (KBr, n, cm^{-1}): 3092m, 3071w, 2972m, 2932m, 2876m, 1600m, 1573s, 1470m, 1322s, 1284m, 1158vs, 581s;

^{1}H-NMR ($CDCl_3$, d ppm, *J* Hz): 0.85 (t, 3H, 7.4, $CH_2CH_2\underline{CH_3}$), 1.47 (t, 3H, 7.1, $SCH_2\underline{CH_3}$), 1.67 (sx, 2H, 7.4, $CH_2\underline{CH_2}CH_3$), 3.34 (q, 2H, 7.1, $S\underline{CH_2}CH_3$), 3.87 (t, 2H, 7.4, $\underline{CH_2}CH_2CH_3$), 7.68 (d, 2H, 8.7, H-14, H-16), 7.78 (d, 2H, 8.7, H-7, H-11), 7.83 (d, 2H, 8.7, H-13, H-17), 8.05 (d, 2H, 8.7, H-8, H-10);

^{13}C-NMR ($CDCl_3$, d ppm): 11.00 ($CH_2CH_2\underline{CH_3}$), 15.05 ($SCH_2\underline{CH_3}$), 23.44 ($CH_2\underline{CH_2}CH_3$), 27.67 ($S\underline{CH_2}CH_3$), 46.44 ($\underline{CH_2}CH_2CH_3$), 128.41 (C-7, C-11), 129.07 (C-14, C-16), 129.42 (C-8, C-10), 129.52 (C-13, C-17), 132.69 (C-6), 132.91 (C-14, C-16), 140.11 (C-12), 142.54 (C-9), 152.98 (C-5 triazole ring), 153.79 (C-3 triazole ring);

Elemental analysis: Anal. Calcd for $C_{19}H_{20}BrN_3O_2S_2$ (466.42): C, 48.93; H, 4.32; N, 9.01. Found: C, 48.87; H, 4.27; N, 8.94%;

ESI-MS, *m/z*: 466 $[M+H]^+$ (^{79}Br), 468 $[M+H]^+$ (^{81}Br); 424 $[M+H-C_3H_6]^+$; 426 $[M+H-C_3H_6]^+$; 396 $[M+H-C_3H_6-C_2H_4]^+$; 398 $[M+H-C_3H_6-C_2H_4]^+$; 322 $[^{79}BrC_6H_4SO_2C_6H_4CN+H]^+$; 324 $[^{81}BrC_6H_4SO_2C_6H_4CN+H]^+$; 219 $[^{79}BrC_6H_4SO_2]^+$; 221 $[^{81}BrC_6H_4SO_2]^+$; 177 $[C_6H_5TriazoleSH]^+$; 155 $[^{79}BrC_6H_4]^+$; 157 $[^{81}BrC_6H_4]^+$.

2-(5-(4-(4-chlorophenylsulfonyl)phenyl)-4-propyl-4H-1,2,4-triazol-3-ylthio)-1-phenylethanone ***3a***

m.p. 145-147°C; yield: 64 %;

IR (KBr, n, cm^{-1}): 3090m, 3066m, 2986m, 2970m, 2937s, 2924m, 2881m, 1705s, 1598m, 1581m, 1475m, 1315s, 1284s, 1205m, 1159vs, 769s;

^{1}H-NMR ($CDCl_3$, d ppm, *J* Hz): 0.86 (t, 3H, 7.5, $CH_2CH_2\underline{CH_3}$), 1.73 (sx, 2H, 7.5, $CH_2\underline{CH_2}CH_3$), 3.96 (t, 2H, 7.5, $\underline{CH_2}CH_2CH_3$), 5.00 (s, 2H, SCH_2), 7.50 (t, 2H, 7.5, H-25, H-27), 7.62 (tt, 1H, 7.5, 1.8, H-26), 7.68 (d, 2H, 8.7, H-14, H-16), 7.77 (d, 2H, 8.3, H-7, H-11), 7.83 (d, 2H, 8.7, H-13, H-17), 8.02 (dd, 2H, 1.8, 7.5, H-24, H-28), 8.06 (d, 2H, 8.3, H-8, H-10);

^{13}C-NMR ($CDCl_3$, d ppm): 11.02 ($CH_2CH_2\underline{CH_3}$), 23.54 ($CH_2\underline{CH_2}CH_3$), 41.98 (SCH_2), 46.66 ($\underline{CH_2}CH_2CH_3$), 128.41 (C-7, C-11), 128.64 (C-24, C-28), 128.99 (C-25, C-27), 129.39 (C-8, C-10), 129.53 (C-13, C-17), 129.92 (C-14, C-16), 132.44 (C-6), 134.18

(C-26), 135.23 (C-23), 139.54 (C-15), 140.50 (C-12), 142.73 (C-9), 152.14 (C-5 triazole ring), 154.10 (C-3 triazole ring), 193.08 (C=O);

Elemental analysis: Anal. calcd for $C_{25}H_{22}ClN_3O_3S_2$ (512.04): C, 58.64; H, 4.33; N, 8.21. Found: C, 58.57; H, 4.26; N, 8.17%;

ESI-MS, *m/z*: 512 $[M+H]^+$ (^{35}Cl), 514 $[M+H]^+$ (^{37}Cl); 470 $[M+H-C_3H_6]^+$; 472 $[M+H-C_3H_6]^+$; 364 $[M+H-C_3H_6-C_6H_5CHO]^+$; 366 $[M+H-C_3H_6-C_6H_5CHO]^+$; 278 $[^{35}ClC_6H_4SO_2C_6H_4CN+H]^+$;280 $[^{37}ClC_6H_4SO_2C_6H_4CN+H]^+$; 175 $[^{35}ClC_6H_4SO_2]^+$; 177 $[^{37}ClC_6H_4SO_2]^+$; 159 $[^{35}ClC_6H_4SO]^+$; 161 $[^{37}ClC_6H_4SO]^+$; 111 $[^{35}ClC_6H_4]^+$; 113 $[^{37}ClC_6H_4]^+$.

2-(5-(4-(4-bromophenylsulfonyl)phenyl)-4-propyl-4H-1,2,4-triazol-3-ylthio)-1-phenylethanone ***3b***

m.p. 142-144 °C; yield: 78 %;

IR (KBr, n, cm^{-1}): 3088m, 3066m, 2969m, 2936s, 2923s, 2879m, 1705s, 1598m, 1572m, 14757m, 1315s, 1283s, 1205m, 1159vs, 588m;

^{1}H-NMR ($CDCl_3$, d ppm, *J* Hz): 0.88 (t, 3H, 7.4, $CH_2CH_2\underline{CH_3}$), 1.75 (sx, 2H, 7.4, $CH_2\underline{CH_2}CH_3$), 3.97 (t, 2H, 7.4, $\underline{CH_2}CH_2CH_3$), 5.02 (s, 2H, SCH_2), 7.51 (t, 2H, 7.8, H-25, H-27), 7.63 (t, 1H, 7.8, H-26), 7.69 (d, 2H, 8.7, H-14, H-16), 7.77 (d, 2H, 8.6, H-7, H-11), 7.84 (d, 2H, 8.7, H-13, H-17), 8.04 (bd, 2H, 7.8, H-24, H-28), 8.05 (d, 2H, 8.6, H-8, H-10);

^{13}C-NMR ($CDCl_3$, d ppm): 11.03 ($CH_2CH_2\underline{CH_3}$), 23.56 ($CH_2\underline{CH_2}CH_3$), 42.00 (SCH_2), 46.67 ($\underline{CH_2}CH_2CH_3$), 128.30 (C-24, C-28), 128.43 (C-7, C-11), 128.65 (C-8, C-10), 129.11 (C-15), 129.44 (C-25, C-27), 129.55 (C-13, C-17), 132.46 (C-6), 132.93 (C-14, C-16), 134.19 (C-26), 135.23 (C-23), 140.08 (C-12), 142.70 (C-9), 152.17 (C-5 triazole ring), 154.10 (C-3 triazole ring), 193.09 (C=O);

Elemental analysis: Anal. Calcd for $C_{25}H_{22}BrN_3O_3S_2$ (556.49): C, 53.96; H, 3.98; N, 7.55. Found: C, 54.07; H, 3.89; N, 7.49%;

ESI-MS, *m/z*: 556 $[M+H]^+$ (^{79}Br); 558 $[M+H]^+$ (^{81}Br); 514 $[M+H-C_3H_6]^+$; 516 $[M+H-C_3H_6]^+$; 436 $[M+H-C_3H_6-C_6H_6]^+$; 438 $[M+H-C_3H_6-C_6H_6]^+$; 408 $[M+H-C_3H_6-C_6H_6CO]^+$; 410 $[M+H-C_3H_6-C_6H_6CO]^+$; 219 $[^{79}BrC_6H_4SO_2]^+$; 221 $[^{81}BrC_6H_4SO_2]^+$; 155 $[^{79}BrC_6H_4]^+$; 157 $[^{81}BrC_6H_4]^+$.

ethyl 2-(5-(4-(4-chlorophenylsulfonyl)phenyl)-4-propyl-4H-1,2,4-triazol-3-ylthio)acetate ***4a***

m.p. 109-110 °C; yield: 76 %;

IR (KBr, n, cm^{-1}): 3090m, 3070m, 2980m, 2968m, 2937m, 1740s, 1600m, 1579m, 1475m, 1458m, 1318s, 1285m, 1164vs, 768s;

^{1}H-NMR ($CDCl_3$, d ppm, *J* Hz): 0.87 (t, 3H, 7.4, $CH_2CH_2\underline{CH_3}$), 1.28 (t, 3H, 7.1, $-OCH_2\underline{CH_3}$), 1.72 (sx, 2H, 7.4, $CH_2\underline{CH_2}CH_3$), 3.95 (t, 2H, 7.4, $\underline{CH_2}CH_2CH_3$), 4.15 (s, 2H, SCH_2), 4.22 (q, 2H, 7.1, $-OCH_2$), 7.51 (d, 2H, 8.5, H-14, H-16), 7.76 (d, 2H, 8.4, H-7, H-11), 7.90 (d, 2H, 8.5, H-13, H-17), 8.05 (d, 2H, 8.4, H-8, H-10);

^{13}C-NMR ($CDCl_3$, d ppm): 10.99 ($CH_2CH_2\underline{CH_3}$), 14.19 ($-OCH_2\underline{CH_3}$), 23.60 ($CH_2\underline{CH_2}CH_3$), 35.37 ($-SCH_2$), 46.65 ($\underline{CH_2}CH_2CH_3$), 62.28 ($-OCH_2$), 128.38 (C-7, C-11), 128.41 (C-8, C-10), 129.52 (C-13, C-17), 129.93 (C-14, C-16), 132.46 (C-6), 139.55 (C-15), 140.51 (C-12), 142.78 C-9), 151.55 (C-5 triazole ring), 154.12 (C-3 triazole ring), 168.30 (C=O);

Elemental analysis: Anal. Calcd for $C_{21}H_{22}ClN_3O_4S_2$ (480.00): C, 52.55; H, 4.62; N, 8.75. Found: C, 52.43; H, 4.72; N, 8.66%;

ESI-MS, *m/z*: 480 $[M+H]^+$ (^{35}Cl), 482 $[M+H]^+$ (^{37}Cl); 392 $[M+H-C_3H_6-C_2H_4-H_2O]^+$; 394 $[M+H-C_3H_6-C_2H_4-H_2O]^+$; 364 $[M+H-C_3H_6-C_2H_4-H_2O-CO]^+$; 366 $[M+H-C_3H_6-C_2H_4-H_2O-CO]^+$; 335 $[M+H-C_3H_6-C_2H_4-H_2O-CO-CH_2NH]^+$; 337 $[M+H-C_3H_6-C_2H_4-H_2O-CO-CH_2NH]^+$; 278 $[^{35}ClC_6H_4SO_2C_6H_4CN+H]^+$; 280 $[^{37}ClC_6H_4SO_2C_6H_4CN+H]^+$; 175 $[^{35}ClC_6H_4SO_2]^+$; 177 $[^{37}ClC_6H_4SO_2]^+$;159 $[^{35}ClC_6H_4SO]^+$; 161 $[^{37}ClC_6H_4SO]^+$; 111 $[^{35}ClC_6H_4]^+$; 113 $[^{37}ClC_6H_4]^+$.

ethyl 2-(5-(4-(4-bromophenylsulfonyl)phenyl)-4-propyl-4H-1,2,4-triazol-3-ylthio)acetate ***4b***

m.p. 117-119 °C; yield: 91 %;

IR (KBr, n, cm^{-1}): 3089m, 3068m, 2968m, 2936m, 2880m, 1740s, 1600m, 1572m, 1479m, 1457m, 1317s, 1285s, 1164vs, 585m;

^{1}H-NMR ($CDCl_3$, d ppm, *J* Hz): 0.87 (t, 3H, 7.4, $CH_2CH_2\underline{CH_3}$), 1.28 (t, 3H, 7.1, $-OCH_2\underline{CH_3}$), 1.71 (sx, 2H, 7.4, $CH_2\underline{CH_2}CH_3$), 3.95 (t, 2H, 7.4, $\underline{CH_2}CH_2CH_3$), 4.15 (s, 2H, SCH_2), 4.21 (q, 2H, 7.1, $-OCH_2$), 7.68 (d, 2H, 8.7, H-14, H-16), 7.77 (d, 2H, 8.6, H-7, H-11), 7.83 (d, 2H, 8.7, H-13, H-17), 8.05 (d, 2H, 8.6, H-8, H-10);

^{13}C-NMR ($CDCl_3$, d ppm): 11.01 ($CH_2CH_2\underline{CH_3}$), 14.20 ($-OCH_2\underline{CH_3}$), 23.61 ($CH_2\underline{CH_2}CH_3$), 35.37 ($-SCH_2$), 46.65 ($\underline{CH_2}CH_2CH_3$), 62.29 ($-OCH_2$), 128.42 (C-7, C-11), 129.10 (C-15), 129.43 (C-8, C-10), 129.53 (C-13, C-17), 132.47 (C-6), 132.92 (C-14, C-16), 140.07 (C-12), 142.71 (C-9), 151.56 (C-5 triazole ring), 154.12 (C-3 triazole ring), 168.32 (C=O);

Elemental analysis: Anal. Calcd for $C_{21}H_{22}BrN_3O_4S_2$ (524.45): C, 48.09; H, 4.23; N, 8.01. Found: C, 48.22; H, 4.34; N, 7.93%;

ESI-MS, *m/z*: 524 $[M+H]^+$ (^{79}Br), 526 $[M+H]^+$ (^{81}Br); 482 $[M+H-C_3H_6]^+$; 484 $[M+H-C_3H_6]^+$; 454 $[M+H-C_3H_6-C_2H_4]^+$; 456 $[M+H-C_3H_6-C_3H_6]^+$; 436 $[M+H-C_3H_6-C_2H_4-H_2O]^+$; 438 $[M+H-C_3H_6-C_2H_4-H_2O]^+$; 408 $[^{79}BrC_6H_4SO_2C_6H_4$ TriazoleSCH$_2]^+$; 410 $[^{81}BrC_6H_4SO_2C_6H_4$TriazoleSCH$_2]^+$; 395 $[^{79}BrC_6H_4SO_2C_6H_4$Triazole S$+H]^+$; 397 $[^{81}BrC_6H_4SO_2C_6H_4$TriazoleS$+H]^+$; 322 $[^{79}BrC_6H_4SO_2C_6H_4CN+H]^+$; 324 $[^{81}BrC_6H_4SO_2C_6H_4CN+H]^+$; 219 $[^{79}C_6H_4SO_2]^+$; 221 $[^{81}BrC_6H_4SO_2]^+$; 203 $[^{79}BrC_6H_4SO]^+$; 205 $[^{81}BrC_6H_4SO]^+$; 177 $[C_6H_5$TriazoleSH$]^+$; 155 $[^{79}BrC_6H_4]^+$; 157 $[^{81}BrC_6H_4]^+$.

Results and discussions

The structures of the compounds synthesized were elucidated by ^{1}H-NMR, ^{13}C-NMR, IR and mass spectrometry.

In compounds synthesized, new signals due to $-CH_2CH_3$, $-CH_2COC_6H_5$ or $-CH_2COOCH_2CH_3$ moieties were detected in the ^{1}H-NMR and ^{13}C-NMR spectra.

Thus, in the ^{1}H-NMR spectra of compounds **2a,b** obtained by treatment of 1,2,4-triazole with ethyl bromide, two new signals appeared: a quartet signal at chemical shift d ~ 3.35 ppm corresponding to two protons from CH_2 group and a triplet signal at d ~ 1.47 ppm for three protons from CH_3 group. The ^{13}C-NMR spectra of these compounds displayed the signals of the carbons from CH_2 and CH_3 group at ~ 27 and ~ 15 ppm, respectively.

Compounds **3a,b** obtained from reaction of **1a,b** with phenacyl bromide showed in the ^{1}H-NMR spectra three new signals corresponding to phenyl fragment and in the ^{13}C-NMR spectra other four signals for the same fragment (see the ^{13}C-NMR spectra). The most important signal from ^{13}C-NMR spectra is that characteristic to the carbon from C=O group which resonated at ~ 193 ppm. In the IR spectra of these compounds **3a,b,** the presence of absorption band from 1705 cm^{-1} characteristic to C=O group from phenacyl fragment is a proof that the reaction of 1,2,4-triazoles **1a,b** with phenacyl bromide took place.

The ^{1}H-NMR spectra of compounds **4a,b** obtained by treatment of 1,2,4-triazole-3-thiones **1a,b** with ethyl chloroacetate displayed the signals derived from ester group belonging to $-OCH_2CH_3$ group: the quartet signal of protons from CH_2 group at ~ 4.2 ppm with coupling constant *J* = 7.1 Hz and the triplet signal of protons from CH_3 group at 1.28 ppm (*J* = 7.1 Hz). In the ^{13}C NMR

spectra of these compounds, the signals belonging to the same groups were recorded at ~ 62.29 ppm (CH_2) and ~14.20 ppm (CH_3), respectively. Also, the new signal of carbon from COO ester group appeared at ~168.30 ppm. The presence of the stretching absorption band of C=O ester group in the IR spectra of the compounds **4a,b** which appeared at 1740 cm^{-1} is another proof that the reaction of 1,2,4-triazole-3-thione **1a,b** with ethyl chloroacetate occurred.

The ^1H NMR spectra of all new compounds **3** and **4** displayed the singlet signals due to S-C$\underline{H}_2$CO group at ~ 5.00 ppm (for **3**) and 4.15 ppm (for **4**), integrating for two protons. The same S-$\underline{C}H_2$ carbon signal was observed in the ^{13}C-NMR spectra at ~ 42 ppm (for **3**) and ~35 ppm (for **4**), respectively .

Under basic conditions, 1,2,4-triazoles **1a,b** exist, in solution, in two tautomeric forms (I and II) [26].

Due to the thiole-thione tautomeric equilibrium, alkylation of 1,2,4-triazole compounds may occur at one of the two centers (or both) with high electron density: the nitrogen atom or sulfur atom. Elucidation of the structure of these new derivatives obtained was possible by spectral analysis. On the basis of IR and NMR data, it was demonstrated that only S-alkylated compounds were obtained.

Thus, the absence of the NH and C=S stretching vibration bands in the IR spectra of new compounds **2a,b** – **4a,b** is a proof of S-alkylation. The íNH bands of 1,2,4-triazole-3-thiones **1a,b** appeared at 3435 cm^{-1} for **1a** and 3431 for **1b** and the nC=S band appeared at 1256 cm^{-1} (**1a**) and 1238 cm^{-1} (**1b**), respectively [25].

On the other hand, the attachment of these new moiety (CH_2CH_3, $CH_2COC_6H_5$ and $COOCH_2CH_3$) to sulfur atom and not nitrogen was clearly evidenced from the ^{13}C-NMR spectra of compounds **2a,b** – **4a,b** which showed the C-3 signal of triazole in range 153.57-154.12 ppm, more shielded that the C-3 carbon from 1,2,4-triazole-3-thione **1a,b** (~167.6 ppm) [25], indicating the absence of C=S signal. The signal of the C-5 triazole appeared in the new compounds **2-4** at d ~ 151.55-152.98 ppm.

As it was expected, the signals of propyl groups appeared at the corresponding chemical shifts: ~3.9 ppm as triplet signal integrated for two protons ($\underline{CH}_2CH_2CH_3$), ~ 1.7 ppm as sextet signal integrated for two protons ($CH_2\underline{CH}_2CH_3$), and ~ 0.9 ppm as triplet signal integrated for three protons ($CH_2CH_2\underline{CH}_3$), with coupling constant J = 7.4 -7.5 ppm. The carbon signals from the same groups propyl appeared at ~ 46 ppm ($\underline{CH}_2CH_2CH_3$), ~23 ppm ($CH_2\underline{CH}_2CH_3$) and ~11 ppm ($(CH_2)_2\underline{CH}_3$) [25].

Also, the protons and carbons signals from phenylsulfonylphenyl fragment appeared at the values of chemical shifts in the expected region [25].

The molecular mass spectra were the additional support for the proposed structures of the compounds, the molecular ions corresponding to the halogens isotopes ($^{35}Cl/^{37}Cl$ and $^{79}Br/^{81}Br$) being in agreement with their molecular formula.

Conclusions

In this paper we present synthesis and characterization of new S-alkylated 1,2,4-triazoles by reaction of some 1,2,4-triazole-3-thiones containing arylsulfonylphenyl and *n*-propyl moieties with ethyl bromide, phenacyl bromide or ethyl chloroacetate. The structures of these compounds were confirmed by spectral techniques (NMR, IR, MS) and elemental analysis.

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