New heterocyclic Compounds from 1,2,4-triazole-3(4*H*)-thione Class Obtained from Cyclization of New Acylthiosemicarbazides

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*New 1-(4-(4-X-phenylsulfonyl)benzoyl)-4-(4-chlorophenyl)-thiosemicarbazides **2a-c** were obtained by nucleophilic addition of 4-(4-X-phenylsulfonyl)-benzoic acid hydrazides **1a-c** to 4-chloro-phenylisothiocyanate. Cyclization of 1,4-disubstituted thiosemicarbazides **2a-c** in NaOH 8% media afforded 5-(4-(4-X-phenylsulfonyl)phenyl)-4-(4-chlorophenyl)-2H-1,2,4-triazole-3(4H)-thiones **3a-c**. The structures of all the new compounds were established by IR, UV, ^{1}H-NMR, ^{13}C-NMR, MS spectra and elemental analysis.*

Keywords: acylthiosemicarbazide, nucleophilic addition, cyclization, 1,2,4-triazole-3(4H)-thione

1,2,4-Triazoles are a class of heterocyclic compounds which have a significant interes in medicinal chemistry having a wide range of biological activities such as antimicrobial [1,2], anti-inflammatory [3], analgesic [4], antitubercular [5], antitumoral [6], etc. In addition, 1,2,4-triazole and its derivatives have found wide use in the chemical industry and agriculture, because of their insecticidal, herbicidal and fungicidal properties [7].

The most popular method for the construction of 1,2,4-triazol-3-thiones nucleus is the intramolecular cyclization reaction of acylthiosemicarbazides in basic media [1-5].

Thiosemicarbazides, are also compounds known for their biological activity, including antibacterial, antifungal, anti-HIV, analgesic, anti-inflammatory and anti-tumour effects [8-14].

Continuing our research in the domain of biologically active heterocyclic compounds [15, 16], in this paper we describe the syntheses of some new 1,4-disubstituted thiosemicarbazides **2a-c** and their behaviour in basic media aimed to afford 1,2,4-triazoles **3a-c**.

Experimental part

The melting points of compounds were determined with a Boetius apparatus and are uncorrected. The IR spectra were recorded on a Vertex 70 Bruker apparatus in KBr pellets, at 4000-400 cm^{-1}. The NMR spectra were registered on a VARIAN GEMINI 300 BB apparatus working at 300 MHz for ^{1}H and at 75 MHz for ^{13}C, in DMSO-d_6, using TMS as internal standard. The mass spectra were registered with a triple quadrupole mass spectrometer Varian 1200 L/MS/MS, with electrospray interface (ESI), coupled with a high performance liquid chromatograph with Varian ProStar 240 SDM ternar pump. The sample solution (2 µg/mL in cloroform/metanol 2/1, v/v) was introduced in the ESI interface by direct infusion, after a tenth dilution with methanol, at a flow rate of 20µL/. The UV spectra were recorded on a SPECORD 40 Analytik Jena apparatus, at 200-600 nm.

The key intermediates, 4-(4-X-phenylsulfonyl)-benzoic acid hydrazides **1a-c**, were prepared following the reported procedure [17]. The 4-(4-X-phenylsulfonyl)-benzoic acids were obtained by a Friedel-Crafts reaction between benzene or halobenzenes (X=Cl, Br) and *p*-toluenesulfochloride followed by oxidation of diarylsulfones with chromic acid. The 4-(4-X-phenylsulfonyl) - benzoic acids were then converted into the corresponding hydrazides by reaction of these with hydrazine hydrate (scheme 1).

Nucleophilic addition of 4-(4-X-phenylsulfonyl)-benzoic acid hydrazides **1a-c** to 4-chloro-phenylisothiocyanate proceeds easily in boiling ethanol affording the new 1-(4-(4-X-phenylsulfonyl)benzoyl)-4-(4-chlorophenyl)-thiosemicarbazides **2a-c** in high yields (90-97%).

The acylthiosemicarbazides **2a-c**, on refluxing with NaOH 8%, were cyclized into new corresponding 5-(4-(4-X-phenylsulfonyl)phenyl)-4-(4-chlorophenyl)-2*H*-1,2,4-triazole-3(4*H*)-thiones **3a-c**.

General procedure for preparation of 1-(4-(4-X-phenylsulfonyl)benzoyl)-4-(4-chlorophenyl)-thiosemicarbazide **2a-c**

A mixture of hydrazide **1a-c** (5 mmol), 4-chlorophenylisothiocyanate (5mmol) and ethanol (13 mL), was refluxed for 10 h. The solid product was filtered, washed with cold ethanol and recrystalized from methanol.

4-(4-chlorophenyl)-1-(4-phenylsulfonyl)benzoyl)-thiosemicarbazide **2a**

m.p.: 206-207°C; yield 91.6%

Elemental analysis (%) - Found C:53.91; H:3.57; S:14.31; N:9.50; Calcd. for $C_{20}H_{16}ClN_3O_3S_2$ (445.95g/mol): C:53.87; H:3.62; S:14.38; N:9.42

IR (KBr; cm^{-1}): 3314s, 3172s, 3096m, 3070m, 3043m, 1686s, 1543s, 1493s, 1313s, 1297s, 1261s, 1159s, 763s

^{1}H-NMR (DMSO-d_6, δ, ppm, *J*, Hz): 8.12 (s, 2H; H-7; H-11); 8.12 (s, 2H; H-8, H-10); 8.01 (dd, 7.0;1.4; 2H; H-13, H-17); 7.62 (dd, 7.7;1.4 2H; H-14, H-16); 7.70 (tt, 7.7;1.4; 1H, H-15); 7.45 (ws, 1H; H-19); 7.38 (d, 8.5; 1H; H-20); 7.38 (d, 8.5; 1H; H-22); 7.45 (ws; 1H; H-23); 9.82 (ws, 1H, NH); 9.91 (ws, 1H; NH); 10.81 (s, 1H, NH)

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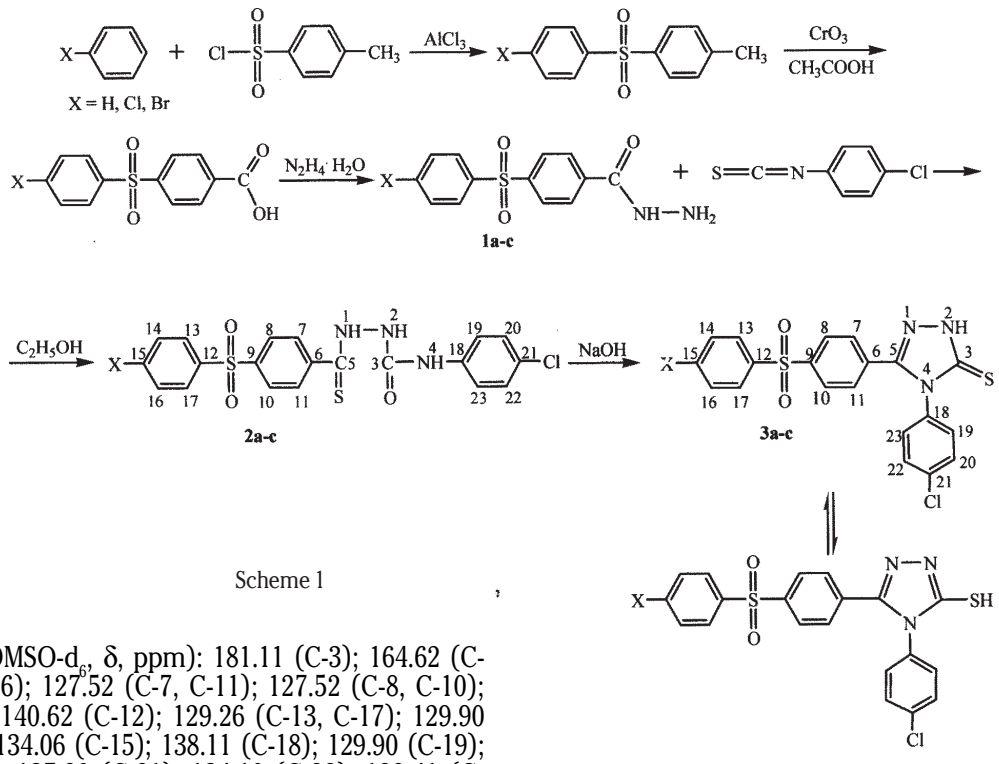


Scheme 1

^{13}C-NMR (DMSO-d$_6$, δ, ppm): 181.11 (C-3); 164.62 (C-5); 137.07 (C-6); 127.52 (C-7, C-11); 127.52 (C-8, C-10); 143.82 (C-9); 140.62 (C-12); 129.26 (C-13, C-17); 129.90 (C-14, C-16); 134.06 (C-15); 138.11 (C-18); 129.90 (C-19); 127.98 (C-20); 137.20 (C-21); 134.10 (C-22); 128.41 (C-23)

ESI-MS, *m/z* (%): [M+H]$^+$ 446 (^{35}Cl), [M+H]$^+$ 448 (^{37}Cl)

UV (methanol, λ_{max} (nm), lgε): 203 (4.56); 245 (4.45)

4-(4-chlorophenyl)-1-(4-(4-chlorophenylsulfonyl) benzoyl)-thiosemicarbazide **2b**

m.p.: 196-197°C; yield 97.2%

Elemental analysis (%) - Found C:50.07; H:3.09; S:13.30; N:8.83; Calcd. for $C_{20}H_{15}Cl_2N_3O_3S_2$ (480.39g/mol): C:50.00; H:3.15; S:13.35, N:8.75;

IR (KBr; cm^{-1}): 3290s, 3150w, 3090m, 3049w, 1684s, 1541s, 1526s, 1492s, 1319s, 1299m, 1260m, 1158vs, 767s

^{1}H-NMR (DMSO-d$_6$, δ, ppm, *J*, Hz): 8.13 (d, 8.8; 2H; H-7; H-11); 8.09 (d, 8.8; 2H; H-8, H-10); 8.00 (d, 8.5; 2H; H-13, H-17); 7.71 (d, 8.5, 2H; H-14, H-16); 7.50 (ws, 1H; H-19); 7.35 (d, 8.8; 1H; H-20); 7.35 (d, 8.8; 1H; H-22); 7.50 (ws; 1H; H-23); 9.80 (ws, 1H, NH); 10.00 (ws, 1H; NH); 10.85 (s, 1H, NH)

^{13}C-NMR (DMSO-d$_6$, δ, ppm): 181.43 (C-3); 164.57 (C-5); 137.21 (C-6); 127.56 (C-7, C-11); 127.99 (C-8, C-10); 143.32 (C-9); 139.42 (C-12); 129.32 (C-13, C-17); 130.05 (C-14, C-16); 138.10 (C-15); 139.20 (C-18); 129.54 (C-19); 130.05 (C-20); 137.01 (C-21); 130.05 (C-22); 129.54 (C-23)

ESI-MS, *m/z* (%): [M+H]$^+$ 480 (^{35}Cl, ^{35}Cl), [M+H]$^+$ 442 (^{35}Cl, ^{37}Cl), [M+H]$^+$ 484 (^{37}Cl, ^{37}Cl)

UV (methanol, λ_{max} (nm), lgε): 203 (4.57); 249 (4.45)

1-(4-(4-bromophenylsulfonyl)benzoyl)-4-(4-chlorophenyl)-thiosemicarbazide **2c**

m.p.: 204-205°C (C_2H_5OH); yield 90%

Elemental analysis (%) - Found C:45.71; H:2.81; S:12.17, N:8.09; Calcd. For $C_{20}H_{15}BrClN_3O_3S_2$ (524.84g/mol): C:45.77; H:2.88; S:12.22; N:8.01

IR (KBr; cm^{-1}): 3437m, 3284s, 3145m, 3089m, 3045w, 1683s, 1541s, 1492s, 1316s, 1293s, 1260m, 1157vs, 751s, 575m

^{1}H-NMR (DMSO-d$_6$, δ, ppm, *J*, Hz): 8.13 (s, 2H; H-7; H-11); 8.13 (s, 2H; H-8, H-10); 7.95 (d, 8.8; 2H; H-13, H-17); 7.86 (d, 8.8, 2H; H-14, H-16); 7.48 (ws, 1H; H-19); 7.39 (d, 8.8; 1H; H-20); 7.39 (d, 8.8; 1H; H-22); 7.48 (ws; 1H; H-23); 9.80 (ws, 1H, NH); 9.95 (ws, 1H; NH); 10.81 (s, 1H, NH)

^{13}C-NMR (DMSO-d$_6$, δ, ppm): 181.40 (C-3); 164.55 (C-5); 137.97 (C-6); 127.55 (C-7, C-11); 127.98 (C-8, C-10); 142.27 (C-9); 139.83 (C-12); 129.31 (C-13, C-17); 133.00 (C-14, C-16); 128.32 (C-15); 138.97 (C-18); 129.54 (C-19); 129.31 (C-20); 137.21 (C-21); 129.31 (C-22); 129.54 (C-23)

ESI-MS, *m/z* (%): [M+H]$^+$ 524 (^{35}Cl, ^{79}Br), [M+H]$^+$ 526 (^{37}Cl, ^{79}Br), [M+H]$^+$ 528 (^{37}Cl, ^{81}Br)

UV (methanol, λ_{max} (nm), lgε): 203 (4.61); 253 (4.49)

General procedure for preparation of 5-(4-(4-X-phenylsulfonyl)phenyl)-4-(4-chlorophenyl)-2H-1,2,4-triazole-3(4H)-thione **3a-c**

The thiosemicarbazides **2a-c** (1 mmol) was dissolved in 8 ml NaOH 8%. The reaction mixture was refluxed for 4 h and then hot filtered and cooled at room temperature. The filtrate was neutralized with a diluted solution of HCl. The product obtained was filtered, washed with cold water and recrystallized from $CHCl_3$/petroleum ether (1:1, v/v) [15].

5-(4-(phenylsulfonyl)phenyl)-4-(4-chlorophenyl)-2H-1,2,4-triazole-3(4H)-thione **3a**

m.p.: 285°C ; yield 70.2%

Elemental analysis (%) - Found C:56.20; H:3.22; S:14.94, N:9.90; Calcd. for $C_{20}H_{14}ClN_3O_2S_2$ (427.93): C:56.13; H:3.30; S:14.99; N:9.82

IR (KBr; cm^{-1}): 3421m, 3092s, 3023m, 1599w, 1533m, 1494vs, 1475m, 1324vs, 1290s, 1239m, 1160vs, 719s

^{1}H-NMR (DMSO-d$_6$, δ, ppm, *J*, Hz): 7.92-8.00 (m, 6H; H-7, H-8, H-10, H-11, H-13, H-17); 7.62 (tt, 7.4; 2H, H-14, H-16,); 7.70 (wt, 7.4; 1H; H-15); 7.43 (d, 8.5; 1H; H-19); 7.50 (d, 8.5; 1H; H-20); 7.38 (d, 8.5; 1H; H-22); 7.43 (d, 8.5; 1H; H-23)

^{13}C-NMR (DMSO-d$_6$, δ, ppm): 168.85 (C-3); 148.94 (C-5); 130.96 (C-6); 129.46 (C-7, C-11); 127.70 (C-8, C-10); 142.48 (C-9); 140.33 (C-12); 127.59 (C-13, C-17); 129.58 (C-14, C-16); 134.11 (C-15); 134.31 (C-18); 129.90 (C-19);

130.63 (C-20); 130.34 (C-21); 129.90 (C-22); 130.63 (C-23)

ESI-MS, *m/z* (%): $[M+H]^+$ 428 (^{35}Cl), $[M+H]^+$ 430 (^{37}Cl)

UV (mehanol, λ_{max} (nm), lgε): 203 (4.55); 249 (4.33); 317 (3.81)

5-(4-(4-chlorophenylsulfonyl)phenyl)-4-(4-chlorophenyl)-2H-1,2,4-triazole-3(4H)-thione **3b**

m.p.: 286-288°C; yield 77%

Elemental analysis (%) - Found: C:52.03; H:2.78; S:13.82, N:9.01; Calcd. for $C_{20}H_{13}Cl_2N_3O_2S_2$ (462.37): C:51.95; H:2.83; S:13.87; N:9.09

IR (KBr; cm^{-1}): 3421w, 3089m, 3063m, 3031w, 1582w, 1539w, 1497s, 1476m, 1323vs, 1283m, 1240m, 1159vs, 770m

^{1}H-NMR (DMSO-d_6, δ, ppm, *J*, Hz): 7.68 (d, 8.5; 2H; H-7, H-11); 7.98 (d, 8.5; 2H; H-8, H-10); 7.93 (d, 8.8; 2H; H-13, H-17); 7.54 (d, 8.8; 2H; H-14, H-16); 7.43 (d, 8.8; 1H; H-19); 7.57 (d, 8.8; 1H; H-20); 7.57 (d, 8.8; 1H; H-22); 7.43 (d, 8.8; 1H; H-23)

^{13}C-NMR (DMSO-d_6, δ, ppm): 168.90 (C-3); 148.92 (C-5); 130.06 (C-6); 129.52 (C-7, C-11); 127.79 (C-8, C-10); 142.03 (C-9); 139.26 (C-12); 129.59 (C-13, C-17); 130.06 (C-14, C-16); 139.27 (C-15); 134.34 (C-18); 130.63 (C-19); 130.63 (C-20); 133.09 (C-21); 130.63 (C-22); 130.63 (C-23)

ESI-MS, *m/z* (%): $[M+H]^+$ 462 (^{35}Cl, ^{35}Cl), $[M+H]^+$ 464 (^{35}Cl, ^{37}Cl), $[M+H]^+$ 466 (^{37}Cl, ^{37}Cl)

UV (methanol, λ_{max} (nm), lgε): 203.5 (4.56); 254 (4.38); 319 (3.81)

5-(4-(4-bromophenylsulfonyl)phenyl)-4-(4-chlorophenyl)-2H-1,2,4-triazole-3(4H)-thione **3c**

m.p.=288-290°C; yield 73%

Elemental analysis (%) - Found C:47.48; H:2.55; S:12.58; N:8.36; Calcd. for $C_{20}H_{13}BrClN_3O_2S_2$ (506.82): C:47.40; H:2.59; S:12.65: N:8.29

IR (KBr; cm^{-1}): 3420w, 3090m, 3062m, 3031w, 1599w, 1573m, 1497s, 1473m, 1323vs, 1282s, 1240m, 1159vs, 766s, 575m

^{1}H-NMR (DMSO-d_6, δ, ppm, *J*, Hz): 7.82 (d, 8.8; 2H; H-7, H-11); 7.83 (d, 8.8; 2H; H-8, H-10); 8.01 (d, 8.5; 2H; H-13, H-17); 7.58 (d, 8.5; 2H; H-14, H-16); 7.44 (d, 8.5; 1H; H-19); 7.59 (d, 8.5; 1H; H-20); 7.59 (d, 8.5; 1H; H-22); 7.44 (d, 8.5; 1H; H-23)

^{13}C-NMR (DMSO-d_6, δ, ppm): 169.00 (C-3); 148.91 (C-5); 130.40 (C-6); 133.03 (C-7, C-11); 129.51 (C-8, C-10); 141.97 (C-9); 139.56 (C-12); 127.78 (C-13, C-17); 129.60 (C-14, C-16); 139.00 (C-15); 134.33 (C-18); 130.62 (C-19); 129.60 (C-20); 128.40 (C-21); 129.60 (C-22); 130.62 (C-23)

ESI-MS, *m/z* (%): $[M+H]^+$ 506 (^{35}Cl, ^{79}Br), $[M+H]^+$ 508 (^{37}Cl, ^{79}Br), $[M+H]^+$ 510 (^{37}Cl, ^{81}Br)

UV (methanol, λ_{max} (nm), lgε): 204 (4.58); 255.5 (4.42); 320 (3.83);

Cyclization of acylthiosemicarbazides **2a-c** to 1,2,4-triazoles **3a-c** could be explained by the mechanism from scheme 2 .

The intermediate tautomer anion **B** was formed by cyclization of the initially anion **A** obtained in alkaline media from thiosemicarbazide **2a-c**. The tautomer anion **B'** is converted by water elimination into the sodium salt **C** of 1,2,4-triazole **3a-c** .

Results and discusion

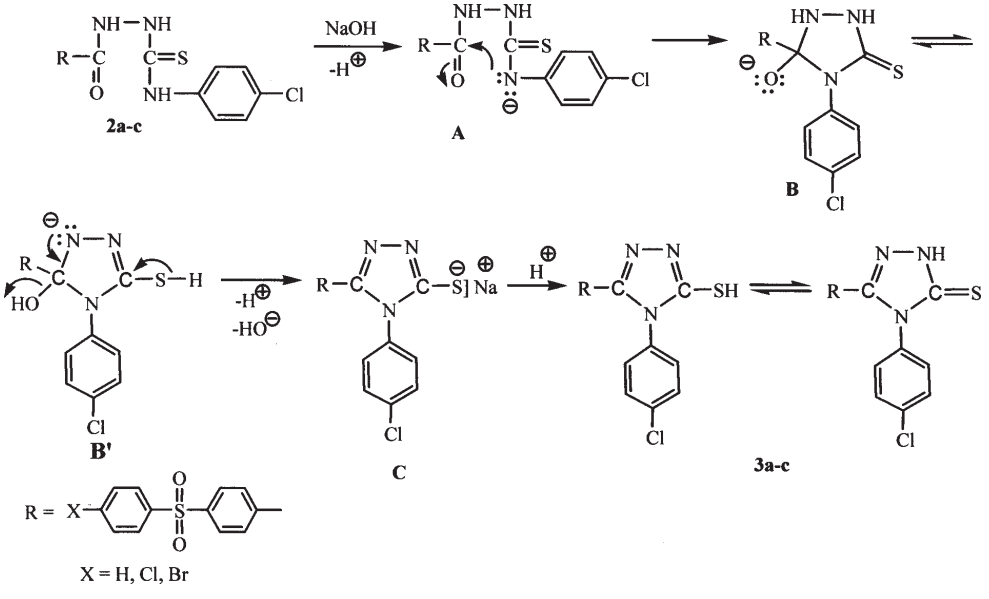
The spectral data of these new compounds are in good agreement with the proposed structures.

Thus, in the IR spectra of acylthiosemicarbazides **2a-c**, the absorption bands of NH (3145-3437 cm^{-1}) and C=O (1683-1686 cm^{-1}) group are observed. The C=S absorption band appears at ~1261 cm^{-1}.

In the IR spectra of new compounds **3a-c** no absorption bands were detected about 1683-1686 cm^{-1} indicating the absence of C=O group of acylthiosemicarbazides which is an evidence of the conversion of these compounds **2a-c** to 1,2,4-triazoles. Although two types of tautomers (thione or thiole) could be expected from the cyclization of thiosemicarbazides **2a-c** under alkaline conditions, only the thione type compounds (**3a-c**) were observed. The formation of thione tautomer is demonstrated in IR spectra by the presence of absorption bands at ~ 1240 cm^{-1} belonging to the C=S group and at ~ 3420 cm^{-1} corresponding to the NH group. The absence of any absorption band about 2550-2600 cm^{-1}, range cited for SH group [18, 19], confirmed that these compounds were in the thionic form in the solid state. The absorption bands due to the C=N and C=C groups appeared at 1582-1599 cm^{-1} and 1473-1573 cm^{-1}, respectively.

The absorption bands associated with other functional groups appeared in the expected regions.

The UV spectra of acylthiosemicarbazides **2a-c** exhibited two absorption maxima in the region of 203 nm and



Scheme 2

245-253 nm. In the UV spectra of compounds **3a-c**, a new absorption maxima was observed at 317-320 nm.

In the ^{1}H-NMRspectra of acylthiosemicarbazides **2a-c** NH signals were observed as singlets at 9.80-9.82 ppm, 9.91-10.00 ppm and 10.81-10.85 ppm.

The ^{13}C-NMR spectra of the new acylthiosemicarbazides **2a-c** show characteristic signals atributed to the carbonyl group at ~ 165 ppm and to the thiocarbonyl group at ~ 181 ppm (the most deshielded carbon).

Cyclization of these acylthiosemicarbazides to 1,2,4-triazoles was proved in the ^{13}C-NMR spectra by presence of two new signals characteristic to C-5 heterocyclic carbon (~ 149.00 ppm) and to C-3 heterocyclic carbon (~ 169.00 ppm). Presence of this signal at ~ 169.00 ppm, characteristic to C=S, indicated that these compounds from 1,2,4-triazole class exist predominantly in the thione form in solution [20,21]. Also, in ^{13}C-NMR spectra of these new heterocyclic compounds, signals corresponding to C=O and C=S from acylthiosemi-carbazides disappears.

The signals from 4-chlorophenylene or diarylsulfone moiety appeared in the expected regions [15, 22].

The structure of these new compounds was further confirmed by the mass spectral analysis. Mass spectra of all the new compounds showed a molecular ion $[M+H]^+$ peak, in agreement with their molecular mass.

Conclusions

New acylthiosemicarbazides **2a-c** bearing arylsulfonyl-benzoyl groups were obtained from nucleophilic addition of corresponding acid hydrazides to 4-chlorophenylisothiocianates. Intramolecular cyclization of these compounds in alkaline media afforded the corresponding 1,2,4-triazole-3-thione **3a-c**. All the new compounds were characterized by elemental analysis and spectroscopic methods.

References

1. SERWAR, M., AKHTAR, T., HAMEED, S., KHAN, K. M., Arkivoc, **vii**, 2009, p. 210
2. GÜLERMAN, N.N., DOGAN, H.N., ROLLAS, S., JOHANSSON, C., ÇELIK, C., Il Farmaco, **56**, 2001, p. 953
3. SAHIN, G., PALASKA, E., KELICEN, P., DEMIRDAMAR, R., ALTMOK, G., Arzneim. Forsch., **51**, 2001, p. 478
4. MEKUSKIENE, G., GAIDELIS, P., VAINILAVICIUS, P., *Pharmazie*, **53**, 1998, p. 94
5. CHAUDHARI, B.R., SHINDE, D.B., SHINGARE, M.S., J. Heterocycl. Chem., **4**, nr. 3, 1995, p.187
6. DOGAN, H.N., DURAN, A., ROLLAS, S., Indian J. Chem. Sect. B., **44**, 2005, p. 2301
7. JANKULOVSKA, M., SPIREVSKA, I., COLANCESKA-RAGENOVIK, K., Bull. Chem.Technol. Macedonia, **25**, 2006, p. 29
8. YAMAGUCHI, M. U., BARBOSA DA SILVA, A. P., UEDA-NAKAMURA, T., PRADO DIAS FILHO, B., CONCEIÇÃO DA SILVA, C., NAKAMURA, C. V., Molecules, **14**, 2009, p. 1796
9. AGARWAL, R.K., SINGH, L., SHARMA, D.K., Bioinorg. Chem. Appl., **2006**, 2006, p. 1
10. DEMIRBAS, N., KARAOGLU, S.A., DEMIRBAS, A., SANCAK, K., Eur. J. Med. Chem., **39**, 2004, p. 793
11. DOGAN, N.H., ROLLAS, S., ERDENIZ, H., Il Farmaco, **30**, 1998, p. 462
12. PANDEYA, S.N., SRIRAM, D., NATH, G., DECLERCQ, E., Eur. J. Pharm. Sci., **9**, 1999, p. 25
13. LI, X.Y., WANG, S.H., LI, Z.M., SU, N., ZHAO, W.Z., Carbohydr. Res., **341**, 2006, p. 2867
14. SALGIN-GÖKSEN, U., GÖKHAN-KELEKÇI, N., GÖKTAŞ, O., KÖYSAL, Y., KILIÇ, E., IŞIK, S., AKTAY, G., OZALP, M., Bioorg. Med. Chem. **15**, 2007, p. 5738
15. BĂRBUCEANU, Ş.F., ALMĂJAN, G.L., ŞARAMET, I., DRĂGHICI, C., Rev. Chim. (Bucureşti), **57**, nr.4, 2006, p. 355
16. SUPURAN, C.T., SARAMET, I., BANCIU, M.D., Rev. Roum. Chim., **1995**, 40 (11-12), p. 1227
17. MAVRODIN, A., ZOTTA, V., STOENESCU, M., OŢELEANU, D., Pharm. Zentralhalle, **9**, 1956, p. 353
18. SHAKER, R.M., MAHMOUD A.F., ABDEL-LATIF F.F., Phosphorus, Sulfur Silicon Relat. Elem. **180**, 2005, p. 397
19. TURAN-ZITOUNI, G., KAPLANCIKH, Z.A., YILDIZ, M.T., CHEVALLET, P., KAYA, D., Eur. J. Med. Chem., **40**, 2005, p. 607
20. AL-DEEB, O.A., AL-OMAR, M.A., EL-BROLLOSY, N.R., HABIB, E.E., IBRAHIM, T.M., EL-EMAM, A.A., Arzneim.-Forsch. Drug Res., **56**, 2006, p.40
21. COLANCESKA-RAGENOVIK, K., DIMOVA, V., KAKURINOV, V., MOLNAR, D.G., BUZAROVSKA, A., Molecules, **6**, 2001, p. 815
22. BĂRBUCEANU Ş.-F., ALMĂJAN G. L., ŞARAMET I., DRĂGHICI B., Rev. Chim. (Bucureşti), **58**, nr. 10, 2007, p. 945

Manuscript received: 9.06.2009