New Heterocyclic Compounds from 1,2,4-triazole and 1,3,4-thiadiazole Class Having Diphenylsulfone and 2-fluorophenyl Fragments

STEFANIA-FELICIA BARBUCEANU[1]*, GABRIELA LAURA ALMAJAN[1], CONSTANTIN DRAGHICI[2], GABRIEL SARAMET[3], CRISTIAN ENACHE[4], GABRIELA BANCESCU[5]

[1]Organic Chemistry Department, Faculty of Pharmacy, University of Medicine and Pharmacy “Carol Davila”, 6 Traian Vuia Str., 020956, Bucharest, Romania

[2]Centre of Organic Chemistry “Costin D. Neniţescu”, Romanian Academy, 202B Splaiul Independenţei, 060023, Bucharest, Romania

[3]Pharmaceutical Techniques Department, Faculty of Pharmacy, University of Medicine and Pharmacy “Carol Davila”, 6 Traian Vuia Str., 020956, Bucharest, Romania

[4]Central Laboratory for Fito-Sanitary Quarantine, 11 Şoseaua Afumaţi Str., 077190, Bucharest, Romania

[5]Microbiology Department, Faculty of Dentistry, University of Medicine and Pharmacy “Carol Davila”, 19 Calea Plevnei Str., 050051, Bucharest, Romania

In the present study, new 1,2,4-triazole-3-thiones and 1,3,4-thiadiazol-2-amines containing diphenylsulfone and 2-fluorophenyl fragments were synthesized by heterocyclization of corresponding acylthiosemicarbazides. The new 5-(4-(4-X-phenylsulfonyl)phenyl)-4-(2-fluorophenyl)-2H-1,2,4-triazole-3(4H)-thiones ***3a,b*** *were obtained by treatment of corresponding acylthiosemicarbazides* ***2a,b*** *with NaOH 8%. The new 5-(4-(4-X-phenylsulfonyl)phenyl)-N-(2-fluorophenyl)-1,3,4-thiadiazol-2-amines* ***4a,b*** *were synthesized by cyclization of same acylthiosemicarbazides* ***2a,b*** *with $POCl_3$. By treating of these acylthiosemicarbazides with sulfuric acid, the synthesis of 1,3,4-thiadiazoles has not occurred. Synthesis of new N^1-[4-(4-X-phenylsulfonyl)benzoyl]-N^4-(2-fluorophenyl)-thiosemicarbazides* ***2a,b*** *took place by reaction of 4-(4-X-phenylsulfonyl)-benzoic acid hydrazides* ***1a,b*** *with 2-fluorophenyl isothiocyanate. The structure of the new synthesized compounds was established upon their elemental analysis, IR, UV-VIS, ^{1}H-NMR, ^{13}C-NMR and mass spectra.*

Keywords: 1,2,4-triazole-3-thione, 1,3,4-thiadiazol-2-amine, acylthiosemicarbazide, heterocyclization

The recent literature is enriched with progressive findings about the synthesis and pharmacological action of heterocyclic compounds.

The synthesis of new 1,2,4-triazole and 1,3,4-thiadiazole derivatives and investigation of their chemical and biological behavior have gained more importance in recent decades because of their utilization in medicine.

A variety of biological properties like antibacterial [1-6], antifungal [2-4], antitubercular [5-8], analgesic [9-11], anti-inflammatory [9-11] have been reported in mercapto/thione substituted 1,2,4-triazole and 2-aminosubstituted 1,3,4-thiadiazole ring systems.

One of the methods of obtaining heterocyclic compounds from 1,2,4-triazole-3-thiones and 1,3,4-thiadiazoles 2-aminosubstituted class is cyclization of acylthiosemicarbazides. It is known that even these linear intermediates from thiosemicarbazides class show various biological properties, including: antibacterial [12,13,], antifungal [14], antitubercular [15], analgesic [10], anti-inflammatory [10], etc.

The literature data shows that compounds from diphenylsulfones class present biological properties including antimicrobial and anti-inflammatory activity [16,17].

On the other hand, fluorinated compounds are of growing importance with applications in medicine. It was reported that the introduction of a halogen atom in a molecule augments the antimicrobial activity [18,19].

Starting from the aforesaid biological properties of these molecules, and as a part of our program aimed to continuing interest on the synthesis and development of new heterocyclic compounds with expected biological activity [20-23], we now report the synthesis and characterization of new heterocyclic compounds from 1,2,4-triazole-3-thione and 2-aminosubstituted 1,3,4-thiadiazole class carrying diphenylsulfone (at position 5) and 2-fluorophenyl moieties (at position 4 from 1,2,4-triazole or at amino group from 2-amino-1,3,4-thiadiazole) from cyclization of corresponding acylthiosemicarbazides, with the purpose of investigating in the future their possible antimicrobial, analgesic or anti-inflammatory activities.

Experimental part

All chemical reagents used in synthesis were procured from the Merck, Sigma-Aldrich or Fluka Companies.

Melting points were determined on a Böetius apparatus and were uncorrected. The IR spectra were recorded on a Vertex 70 Bruker spectrophotometer recorded in KBr disc. The UV spectra were determined on a SPECORD 40 Analytik Jena spectrophotometer, using methanolic solutions ($2.5 \cdot 10^{-5}$ M). The ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Varian Gemini 300BB spectrometer (at 300 MHz for ^{1}H-NMR and 75 MHz for ^{13}C-NMR), in DMSO-d_6 as a solvent and tetramethylsilane (TMS) as an internal standard. The chemical shifts δ being reported in ppm and the coupling constants in Hz. The mass spectra ESI-MS were obtained with a triple quadrupole mass spectrometer Varian 1200 L/MS/MS with electrospray interface (ESI), coupled with a high performance liquid chromatograph

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* email: stefaniafelicia_barbuceanu@yahoo.com

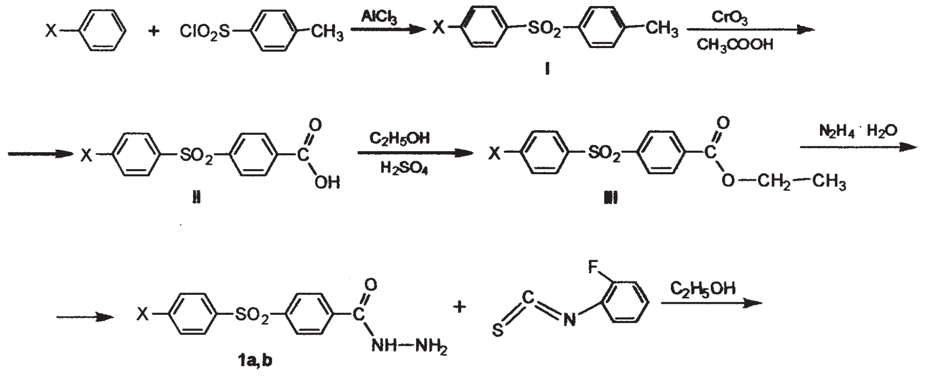


Fig. 1

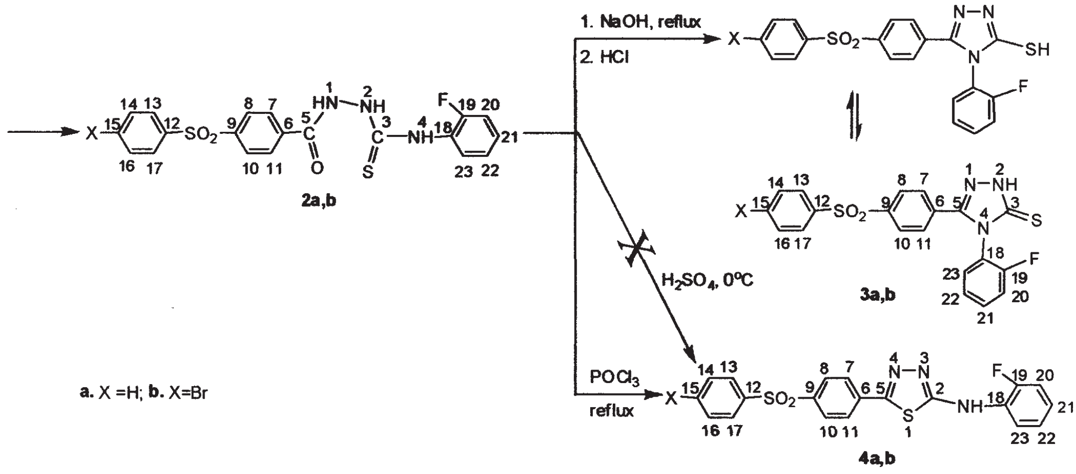
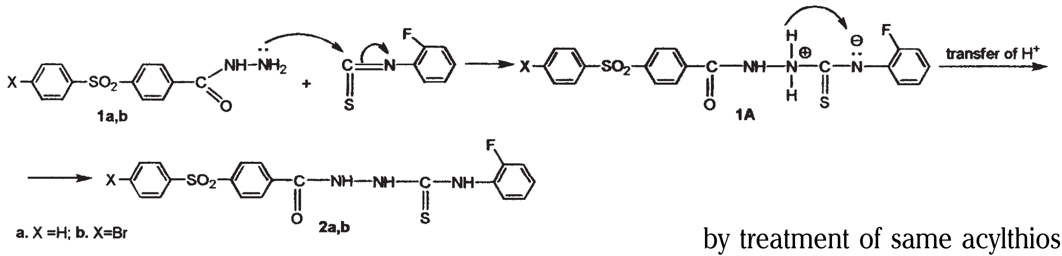


Fig. 2



with Varian ProStar 240 SDM ternar pump and automatic injector Varian Prostar 410. The sample solution (2 µg/mL in $CHCl_3/CH_3OH$ 1/1, v/v) was introduced in the ESI interface by direct infusion, after a tenth dilution with methanol, at a flow rate of 20µL/min.

Synthesis of new compounds

The 4-(4-X-phenylsulfonyl)-benzoic acid hydrazides **1a,b** (X=H, Br) [26] used in the synthesis of new intermediary from acylthiosemicarbazides **2a,b** class, were prepared using several sequences: tosylation, oxidation, esterification and hydrazinolysis [26] according to reaction scheme 1 (fig. 1). The obtained 4-(4-X-phenylsulfonyl)-benzoic acid hydrazides **1a,c** were treated with 2-fluorophenyl isothiocyanate to yield new N^1-[4-(4-X-phenylsulfonyl)benzoyl]-N^4-(2-fluorophenyl)-thiosemicarbazides **2a,b** which were used as key intermediates in synthesis of heterocycles from 1,2,4-triazole and 1,3,4-thiadiazole class. Treatment of these acylthiosemicarbazides **2a,b** with a solution of 8% sodium hydroxide, at reflux, afforded the new 5-(4-(4-X-phenylsulfonyl)phenyl)-4-(2-fluorophenyl)-2*H*-1,2,4-triazole-3(4*H*)-thiones **3a,b** which are in equilibrium with thiol tautomers. In order to obtain the corresponding 2-aminosubstituted 1,3,4-thiadiazoles, under acidic medium, by treatment of same acylthiosemicarbazides **2a,b** with sulfuric acid, reaction did not occur. If instead of sulfuric acid was used phosphorus oxychloride as cyclization agent, new 5-(4-(4-X-phenylsulfonyl)phenyl)-N-(2-fluorophenyl)-1,3,4-thiadiazol-2-amines **4a,b** were obtained.

The title compounds were synthesized according to the route depicted in figure 1.

The mechanism proposed for the obtaining of new acylthiosemicarbazides **2a,b** consists in two steps:

- nucleophile attack of the hydrazine nitrogen atom (NH_2) on the isothiocyanic carbon, positive polarized, with formation of the amphionic intermediary **1A**.;
- stabilization of intermediary **1A** by accepting the proton by anionic nitrogen, and obtaining the acylthiosemicarbazides **2a,b** (fig. 2).

Reaction mechanisms of heterocyclic compounds from 1,2,4-triazole and 1,3,4-thiadiazole class are similar to those presented in a previous work [27].

Synthesis of N^1-[4-(4-X-phenylsulfonyl)benzoyl]-N^4-(2-fluorophenyl)-thiosemicarbazides 2a,b

A mixture of 4-(4-X-phenylsulfonyl)-benzoic acid hydrazide **1a,b** (2 mmol) and 2-fluorophenyl isothiocyanate (2 mmol) in absolute ethanol (10 mL) was refluxed for 19 h. The reaction mixture was cooled, filtered off and washed with a less cold alcohol. The solid thus obtained was recrystallized from ethanol yielding **2a,b**.

N^1-[4-(phenylsulfonyl)benzoyl]-N^4-(2-fluorophenyl)-thiosemicarbazide 2a

m.p.=173-175°C; yield = 91.4%

IR (KBr; cm^{-1}): 3316s, 3250m, 3169m, 3092m, 3068m, 1694s, 1598m, 1547s, 1524s, 1485m, 1310s, 1294s, 1264m, 1241m, 1158vs

^{1}H-NMR (DMSO-d_6, δ, ppm, *J*, Hz): 8.10 (d; 8.8; 2H; H-7;H-11); 8.15 (d; 8.8; 2H; H-8;H-10); 8.00 (dd, 7.4;1.4; 2H; H-13;H-17); 7.64 (t, 7.4; 2H; H-14;H-16); 7.71 (tt; 7.4;1.4; 1H; H-15); 7.10-7.38 (m; 4H; H-20;H-21;H-22;H-23); 9.63 (ws; 1H; NH-1); 9.96 (ws; 1H; NH-2); 10.86 (ws; 1H; NH-4)

^{13}C-NMR (DMSO-d_6, δ, ppm): 182.21 (C-3); 164.28 (C-5); 137.03 (C-6); 127.35 (C-7;C-11); 128.30 (C-8;C-10); 143.74 (C-9); 140.61 (C-12); 127.49 (C-13;C-17); 129.63 (C-14;C-16); 133.97 (C-15); 127.11 (d; *J* = 11.9 Hz; C-18); 158.35 (d; *J* = 254.2 Hz; C-19); 115.69 (d; *J* = 19.8 Hz; C-20); 129.26 (d; *J* = 7.2 Hz; C-21); 123.94 (d; *J* = 3.0 Hz; C-22); 127.35 (d; *J* = 8.3 Hz; C-23)

UV (CH_3OH, λ_{max} (nm), logε): 246.7 (4.39); 356.8 (3.37)

Elemental analysis: found: C:55.88; H:3.70; N:9.85%; calcd. for $C_{20}H_{16}FN_3O_3S_2$ (429.49g/mol): C:55.93;H:3.76; N:9.79%

ESI-MS, *m/z* : 430 [M+H]$^+$; 319 [M-FPhNH]$^+$; 277 [$PhSO_2PhCONHNH_2$]$^+$; 245 [$PhSO_2PhCO$]$^+$; 219 [$PhSO_2Ph$]$^+$

N^1-[4-(4-bromophenylsulfonyl)benzoyl]-N^4-(2-fluorophenyl)-thiosemicarbazide 2b

m.p.=201-203°C; yield = 91.8%

IR (KBr; cm^{-1}): 3400s, 3317s, 3145w, 3082m, 3050w, 3014w, 1682s, 1595w, 1572m, 1542s, 1523s, 1483m, 1310s, 1297s, 1264m, 1246m, 1157vs, 575m

^{1}H-NMR (DMSO-d_6, δ, ppm, *J*, Hz): 8.12 (d; 9.0; 2H; H-7;H-11); 8.16 (d; 9.0; 2H; H-8;H-10); 7.94 (d, 8.8; 2H; H-13;H-17); 7.86 (d, 8.8; 2H; H-14,H-16); 7.10-7.35 (m; 4H; H-20;H-21;H-22;H-23); 9.64 (s; 1H; NH-1); 9.97 (s; 1H; NH-2); 10.88 (ws; 1H; NH-4)

^{13}C-NMR (DMSO-d_6, δ, ppm): 182.18 (C-3); 164.58 (C-5); 137.23 (C-6); 127.44 (C-7;C-11); 128.26 (C-8;C-10); 143.21 (C-9); 139.83 (C-12); 129.50 (C-13;C-17); 132.95 (C-14;C-16); 128.26 (C-15); 127.00 (d; *J* = 12.0 Hz; C-18); 158.29 (d; *J* = 246.8 Hz; C-19); 115.70 (d; *J* = 20.0 Hz; C-20); 129.33 (d; *J* = 3.0 Hz; C-21); 123.95 (d; *J* = 3.0 Hz; C-22); 128.00 (d; *J* = 8.2 Hz; C-23)

UV (CH_3OH, λ_{max} (nm), logε): 253.7 (4.49); 363 (3.45)

Elemental analysis: found: C:47.30; H:2.91; N:8.23 %; calcd. for $C_{20}H_{15}BrFN_3O_3S_2$ (508.38 g/mol): C:47.27; H:2.97; N:8.27 %

ESI-MS, *m/z*: 508 [M+H]$^+$ (^{79}Br), 510 [M+H]$^+$ (^{81}Br); 397/399 [M-FPhNH]$^+$; 355/357 [$BrPhSO_2PhCONHNH_2$]$^+$

Synthesis of 5-(4-(4-X-phenylsulfonyl)phenyl)-4-(2-fluorophenyl)-2H-1,2,4-triazole-3(4H)-thiones 3a,b

To corresponding acylthiosemicarbazide **2a,b** (1 mmol) a solution of NaOH 8% (15 mL) was added. The reaction mixture was refluxed for 5 h and then, the obtained solution was filtered and the filtrate was cooled and acidified with a diluted solution of HCl till pH ~ 5. The obtained solid was filtered off and washed with water till neutral *p*H, dried and recrystallized from $CHCl_3$/petroleum ether (1:2, v/v).

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

m.p.=220-222°C; yield = 60.5%

IR (KBr; cm^{-1}): 3297s, 3088m, 3063m, 3037m, 1628m, 1585w, 1508s, 1466s, 1310s, 1291m, 1267m, 1237m, 1156vs

^{1}H-NMR (DMSO-d_6, δ, ppm, *J*, Hz): 7.57 (d; 8.8; 2H; H-7;H-11); 7.97 (wd, 8.8; 2H; H-8;H-10); 7.98 (wd, 7.4; 2H; H-13;H-17); 7.61 (wt; 7.4; 2H; H-14;H-16); 7.69 (wt; 7.4; 1H; H-15); 7.30-7.45 (m; 2H; H-20;H-21); 7.55-7.65 (m; 2H; H-23;H-23); 14.60 (s; 1H; NH)

^{13}C-NMR (DMSO-d_6, δ, ppm): 169.48 (C-3); 149.07 (C-5); 130.11 (C-6); 128.74 (C-7;C-11); 127.63 (C-8;C-10); 142.77 (C-9); 140.28 (C-12); 129.95 (C-13;C-17); 127.95 (C-14;C-16); 134.19 (C-15); 130.03 (d; *J* = 12.0 Hz; C-18); 156.84 (d; *J* = 250.5 Hz; C-19); 116.87 (d; *J* = 18.9 Hz; C-20); 121.68 (d; *J* = 12.8 Hz; C-21); 125.57 (d; *J* = 3.4 Hz; C-22); 132.84 (d; *J* = 8.3 Hz; C-23)

UV (CH_3OH, λ_{max} (nm), logε): 252.9 (4.41); 311.9 (3.97)

Elemental analysis: found: C:58.41; H:3.35; N:10.14 %; calcd. for $C_{20}H_{14}FN_3O_2S_2$ (411.47 g/mol): C:58.38; H:3.43; N:10.21 %

ESI-MS, *m/z*: 412 [M+H]$^+$; 271 [M+H-$PhSO_2$]$^+$;

5-(4-(4-bromophenylsulfonyl)phenyl)-4-(2-fluorophenyl)-2H-1,2,4-triazole-3(4H)-thione 3b

m.p.=252-254°C; yield = 62.5%

IR (KBr; cm^{-1}): 3289m, 3092m, 3050m, 1598m, 1573m, 1508s, 1470s, 1332s, 1289m, 1261m, 1240m, 1159vs, 578s

^{1}H-NMR (DMSO-d_6, δ, ppm, *J*, Hz): 7.80 (d; 8.4; 2H; H-7;H-11); 7.97 (d, 8.4; 2H; H-8;H-10); 7.86 (d, 8.4; 2H; H-13;H-17); 7.81 (d; 8.4; 2H; H-14;H-16); 7.58 (m; 2H; H-20;H-23); 7.30-7.45 (m; 2H; H-21;H-22); 14.48 (s; 1H; NH)

^{13}C-NMR (DMSO-d_6, δ, ppm): 169.49 (C-3); 149.05 (C-5); 130.26 (C-6); 128.82 (C-7;C-11); 128.05 (C-8;C-10); 143.31 (C-9); 139.49 (C-12); 129.66 (C-13;C-17); 133.06 (C-14;C-16); 128.50 (C-15); 130.26 (d; *J* = 12.2 Hz; C-18); 157.11 (d; *J* = 250.5 Hz; C-19); 116.89 (d; *J* = 18.6 Hz; C-20); 121.78 (d; *J* = 12.7 Hz; C-21); 125.66 (d; *J* = 3.5 Hz; C-22); 132.71 (d; *J* = 8.3 Hz; C-23)

UV (CH_3OH, λ_{max} (nm), logε): 256.4 (4.42); 322.5 (3.85)

Elemental analysis: found: C:48.90; H:2.59; N:8.51 %; calcd. for $C_{20}H_{13}BrFN_3O_2S_2$ (490.37 g/mol): C:48.99; H:2.67; N:8.57 %

ESI-MS, *m/z*: 490 [M+H]$^+$ (^{79}Br); 492 [M+H]$^+$ (^{81}Br); 271 [M+H-$BrPhSO_2$]$^+$

Synthesis of 5-(4-(4-X-phenylsulfonyl)phenyl)-N-(2-fluorophenyl)-1,3,4-thiadiazol-2-amines 4a,b

A mixture of the appropriate acylthiosemicarbazide **2a,b** (1 mmol) and phosphorous oxychloride (5 mL) was heated under reflux for 4 h. The resulting mixture was evaporated under reduced pressure and the residue was then added in ice when a precipitate was obtained. To resulting precipitate was added a diluted solution of sodium hydrogen carbonate till *p*H ~8, and the obtained product was filtered off, washed with water till neutral *p*H, dried and recrystallized from $CHCl_3$/petroleum ether (1:2, v/v) to give **4a,b**.

5-(4-phenylsulfonyl)phenyl)-N-(2-fluorophenyl)-1,3,4-thiadiazol-2-amine 4a

m.p.= 247-249°C; yield = 67.3%

IR (KBr; cm^{-1}): 3355s, 3087m, 3058m, 1623m, 1596w, 1547s, 1494s, 1477s, 1321s, 1293s, 1255m, 1156vs

^{1}H-NMR (DMSO-d_6, δ, ppm, *J*, Hz): 8.09 (s; 2H; H-7, H-11); 8.09 (s; 2H; H-8;H-10); 7.99 (dd, 8.5; 1.4; 2H; H-13;H-17); 7.55 (t; 8.5; 2H; H-14;H-16); 7.70 (tt, 8.5;1.4; H-15); 8.37 (wt, 8.5; H-20); 7.05-7.40 (m; 3H; H-21;H-22;H-23); 10.51 (ws, 1H; NH)

^{13}C-NMR (DMSO-d_6, δ, ppm): 165.28 (C-2); 156.97 (C-5); 134.79 (C-6); 128.36 (C-7;C-11); 127.82 (C-8;C-10); 141.86 (C-9); 140.72 (C-12); 127.43 (C-13;C-17); 129.88 (C-14;C-16); 133.96 (C-15); 128.04 (d; *J* = 10.5 Hz; C-18);

152.11 (d, J = 243.0 Hz; C-19); 115.39 (d, J = 18.8 Hz; C-20); 123.64 (d, J = 7.5 Hz; C-21); 124.80 (d, J = 2.9 Hz; C-22); 120.94 (d, J = 8.0 Hz; C-23);

UV (CH_3OH) (λ_{max}/nm, (log ε)): 257.9 (4.11); 341.7 (4.25)

Elemental analysis: found: C:58.29; H:3.38; N:10.17 %; calcd. for $C_{20}H_{14}FN_3O_2S_2$ (411.47 g/mol): C:58.38; H:3.43; N:10.21 %

ESI-MS, *m/z*: 412 $[M+H]^+$; 301 $[M+H\text{-}FPhNH]^+$; 271 $[M+H\text{-}PhSO_2]^+$; 110 $[FPhNH]^+$

5-(4-(4-bromophenylsulfonyl)phenyl)-N-(2-fluorophenyl)-1,3,4-thiadiazol-2-amine 4b

m.p.= 220-222°C; yield = 75.2%

IR (KBr; cm^{-1}): 3359m, 3087m, 3059w, 1622m, 1596w, 1572s, 1547s, 1496s, 1478s, 1322s, 1291m, 1255m, 1158vs, 572m

^{1}H-NMR (DMSO-d_6, δ, ppm, J, Hz): 8.08 (s; 2H; H-7;H-11); 8.08 (s; 2H; H-8;H-10); 7.93 (d, 8.5; 2H; H-13;H-17); 7.85 (d; 8.5; 2H; H-14;H-16); 8.36 (wt, 8.5; H-20); 7.05-7.35 (m; 3H; H-21;H-22; H-23); 10.50 (ws, 1H; NH)

^{13}C-NMR (DMSO-d_6, δ, ppm): 165.38 (C-2); 156.89 (C-5); 135.05 (C-6); 128.50 (C-7;C-11); 127.93 (C-8;C-10); 141.38 (C-9); 140.00 (C-12); 128.50 (C-13;C-17); 133.04 (C-14;C-16); 128.26 (C-15); 128.10 (d; J = 10.2 Hz; C-18); 152.17 (d, J = 244.5 Hz; C-19); 115.45 (d, J = 18.6 Hz; C-20); 123.75 (d, J = 7.2 Hz; C-21); 124.87 (d, J = 3.0 Hz; C-22); 121.00 (d, J = 8.2 Hz; C-23);

UV (CH_3OH) (λ_{max}/nm, (log ε)): 257.3 (4.26); 341.9 (4.22);

Elemental analysis: found: C:49.05; H:2.58; N:8.63 %; calcd. for $C_{20}H_{13}BrFN_3O_2S_2$ (490.37 g/mol): C:48.99; H:2.67; N:8.57 %

ESI-MS, *m/z* (%): 490 $[M+H]^+$ (^{79}Br); 492 $[M+H]^+$ (^{81}Br); 271 $[M+H\text{-}BrPhSO_2]^+$

Results and discussions

The spectral data are in good agreement with the proposed structures.

In the IR spectra of compounds from acylthiosemicarbazides class **2a,b** obtained by reaction between hydrazides **1a,b** and 2-fluorophenyl isothiocyanate is characteristic stretching vibration of C = S group at ~ 1245 cm^{-1}. Also, important are absorption bands of C=O and NH groups that appear in the region 1694 cm^{-1} (νC=O for **2a**) and 1682 cm^{-1} (νC=O for **2b**) and 3145-3400 cm^{-1} (νNH) respectively. The ^{1}H-NMR spectra of these compounds showed three NH proton singlet signals in region 9.63-10.88 ppm and the ^{13}C-NMR spectra present two characteristic signals of carbon atoms from C=O and C=S groups at ~ 164 ppm and ~ 182 ppm respectively.

IR spectra of compounds **3a,b** and **4a,b** obtained from acylthiosemicarbazides **2a,b** do not show the absorption band characteristic of C=O group, confirming that the cyclization reaction of these new intermediates **2a,b** took place.

Thus, the IR spectra of 1,2,4-triazole **3a,b** showed NH absorption band at ~ 3300 cm^{-1} and C=S band at ~ 1240 cm^{-1}. In the region of 2550-2600 cm^{-1} [28,29] is not present characteristic absorption band of stretching vibration of SH group. The ^{1}H-NMR spectra of the compounds **3a,b** showed singlet signal at δ 14.60 ppm (for **3a**) and 14.48 ppm (for **3b**) indicating the presence of NH proton [28,30]. In the ^{13}C-NMR spectra of these compounds **3a,b** are not present carbon atoms signals of the C=O and C=S groups from acylthiosemicarbazides, but there are two new signals characteristic of quaternary carbon atoms C-3 and C-5 of triazole nucleus at ~ 169.50 ppm and ~ 149.10 ppm respectively. Presence in the ^{13}C-NMR of C-3 carbon atom signal which resonates at ~ 169.5 ppm indicate the existence of C=S [30-32] and not C-SH group for which the value of δ would have to be at a higher field, around 150 ppm [24,33]. Thus, the results of NMR and IR spectra show that these compounds from 1,2,4-triazole class **3a,b** are found predominantly in the thione tautomeric form.

The ^{1}H-NMR spectra of 1,3,4-thiadiazoles **4a,b** show the N-H signal as singlet at ~ 10.50 ppm and IR spectra of same compounds present characteristic absorption band of stretching vibrations of NH group at ~ 3360 cm^{-1}. Also, in IR spectra of 1,3,4-thiadiazoles and 1,2,4-triazoles absorption band in region 1598-1628 cm^{-1} showed the presence of C=N group. Like in the case of heterocycles from 1,2,4-triazole class, in the ^{13}C-NMR spectra of compounds **4a,b**, the carbon atoms signals of carbonyl and thiocarbonyl from thiosemicarbazides are not found, but there are two new signals characteristic of the quaternary atoms from the 1,3,4-thiadiazole nucleus : C-2 carbon at ~165.3 ppm and C-5 at ~156.9 ppm.

Further evidence for the formation of these new compounds **2-4a-c** were obtained by recording its mass spectra. The molecular ion and main fragments for these new compounds are reported in experimental protocols.

Conclusions

In this paper we reported the synthesis and characterization of some new heterocyclic compounds from 1,2,4-triazole and 1,3,4-thiadiazole class which containing diphenylsulfone and 2-fluorophenyl moieties. These new heterocyclic compounds were synthesized by heterocyclization of some acylthiosemicarbazides. The new acylthiosemicarbazides **2a,b**, key intermediates required to obtain heterocyclic compounds from 1,2,4-triazole and 1,3,4-thiadiazole class, were synthesized by nucleophilic addition of 4-(4-X-phenylsulfonyl)-benzoic acid hydrazides **1a,b** to 2-fluorophenyl isothiocyanate. 1,2,4-Triazole-3-thiones **3a,b** were synthesized by intramolecular cyclization of acylthiosemicarbazides **2a,b**, in basic medium, using natrium hydroxide as the cyclization agent. 1,3,4-Thiadiazole 2-aminosubstituted **4a,b** have been obtained by intramolecular cyclization of same acylthiosemicarbazides in presence of phosphorus oxychloride. Treatment of these acylthiosemicarbazides **2a,b** with sulfuric acid in order to obtain 1,3,4-tiadiazoles **4a,b** has not led to any result. The structure of these new compounds was determined by spectral data and elemental analysis. These new compounds that we synthesized will be tested for their biological activity.

Acknowledgements

This paper is partially supported by the Sectoral Operational Programme Human Resources Development, financed from the European Social Fund and by the Romanian Government under the contract number POSDRU/89/1.5/S/64109

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Manuscript received: 31.01.2011