Hydrazinecarbothioamides and 1,3,4-Thia/Oxadiazoles Derivatives with Potential Biological Activity

Synthesis and Spectral Characterization

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This paper presents synthesis of some compounds containing the arylsulfonylphenyl and 4-trifluoromethylphenyl moieties. The hydrazinecarbothioamides were synthesized using 4-(4-X-phenylsulfonyl)benzoic acid hydrazides in reaction with the (4-trifluoromethyl)phenyl isothiocyanate. The 1,3,4-thiadiazoles were obtained from hydrazinecarbothioamides in acidic media and 1,3,4-oxadiazoles by treating of same acyclic compounds with mercury oxide. The synthesized compounds structures were elucidated by spectral data and elemental analysis.

Keywords: 1,3,4-thiadiazole, 1,3,4-oxadiazole, hydrazinecarbothioamide, cyclization

Hydrazinecarbothioamides are building blocks for the construction of a wide variety of molecules especially heterocyclic compounds including thiadiazoles and oxadiazoles [1].

A large number of heterocyclic compounds from 1,3,4-thiadiazole and 1,3,4-oxadiazole class derivatives have been prepared using hydrazinecarbothioamides as raw material by different methods [1-5] and many of these have shown a broad spectrum of biological properties including, anti-inflammatory [3,6,7], antiviral [8,9], antidepressant [10], antitumoral [11-16], analgesic [3,5,16,17], antibacterial, antifungal [18-21], etc.

Also, from the literature it is known that the introduction of a trifluoromethyl group into bioactive molecules, especially in the positions responsible for their physiological profile, has become an important aspect of pharmaceutical research owing to the unique physical and biological properties of fluorine and can have unexpected results on reactivity and biological activity of the fluorinated derivatives [22].

Having regard to our experience in the field of heterocyclic compounds, especially those mentioned above, obtained from hydrazinecarbothioamides having an arylsulfonylphenyl moiety [23-28], we proposed to continue our researches in these classes in order to obtain new derivatives containing additionally in the molecule the (4-trifluoromethyl)phenyl moiety.

Experimental part

Melting points were determined with a Böetius apparatus and are uncorrected. The IR spectra were recorded in KBr disc on a Vertex 70 Bruker spectrometer. The NMR spectra were recorded on a Varian Gemini 300BB spectrometer in DMSO-d_6, at 300 MHz for ^{1}H-NMR and at 75 MHz for ^{13}C-NMR using TMS as internal standard. The ^{1}H-NMR and ^{13}C-NMR spectral data of compounds obtained summarized in table 1 and table 2. The content of C, H, and N was assayed using a ECS-40-10-Costeh microdosimeter. The mass spectra of compounds were recorded 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 and automatic injector Varian Prostar 410. The sample solution (2μg/mL in CH_3OH) was introduced in the ESI interface by direct infusion, after a tenth dilution with methanol/water 0.1 % ammonia 4/1, at a flow rate of 20μL/min. The instrument was operated in positive ions or negative ions mode.

Synthesis of compounds

The reaction of 4-(4-X-phenylsulfonyl)benzoic acid hydrazides **1a-c** [29] with (4-trifluoromethyl)phenyl isothiocyanate occurred with obtaining the corresponding hydrazinecarbothioamides, type of 2-(4-(4-X-phenylsulfonyl)benzoyl)-N-(4-(trifluoromethyl)phenyl)-hydrazinecarbothioamides **2a-c**. By treatment of hydrazinecarbothioamides with sulfuric acid, the dehydrative cyclization took place obtaining the 5-(4-(4-X-phenylsulfonyl)phenyl)-N-(4-(trifluoromethyl)phenyl)-1,3,4-thiadiazol-2-amines **3a-c** and by refluxing of same acyclic compounds with mercury oxide, the desulfurative cyclization took place obtaining the 5-(4-(4-X-phenylsulfonyl)phenyl)-N-(4-(trifluoromethyl)phenyl)-1,3,4-oxadiazol-2-amines **4a-c**.

Synthesis of 2-(4-(4-X-phenylsulfonyl)benzoyl)-N-(4-(trifluoromethyl)phenyl)hydrazinecarbothioa-mides **2a-c**

Synthesis of compounds was realized similarly with literature data [24, 27, 28].

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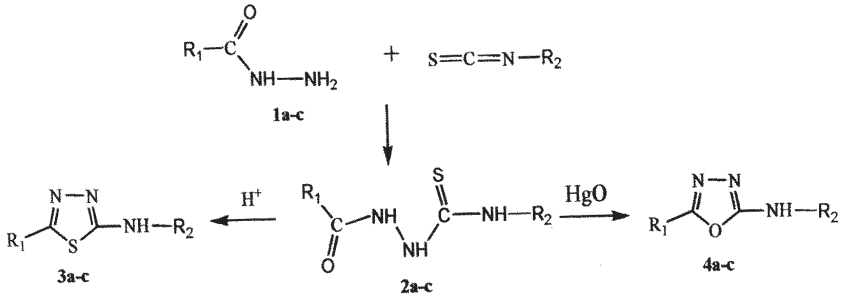
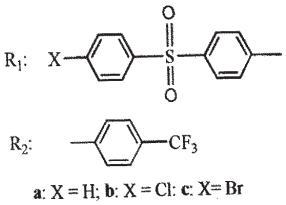


Scheme 1
Synthesis of compounds **2a-c- 4a-c**



a: X = H; **b**: X = Cl: **c**: X= Br

An equimolecular mixture formed by hydrazide **1** and isothiocyanate (4mmol), in ethanol, was refluxed for cca 12h. The product obtained was cooling, filtered off, dried and recrystallized from ethanol.

2-(4-(Phenylsulfonyl)benzoyl)-N-(4-(trifluoromethyl) phenyl)hydrazinecarbothioamide ***2a***

m.p. 186-187 °C; yield: 79 %;

Elemental analysis: anal. calcd for $C_{21}H_{16}F_3N_3O_3S_2$ (479.50): C, 52.60; H, 3.36; N, 8.76. Found: C, 52.55; H, 3.30; N, 8.72%.

ESI-MS, m/z: 480 $[M+H]^+$; 319 $[M\text{-}CF_3C_6H_4NH_2]^+$; 277 $[C_6H_5SO_2C_6H_4CONHNH_2+H]^+$; 245 $[C_6H_5SO_2C_6H_4CO]^+$; 141 $[C_6H_5SO_2]^+$; 125 $[C_6H_5SO]^+$

IR (KBr, ν, cm^{-1}): 3315m, 3250m, 3105w, 3088w, 3046 w, 1681s, 1597 m, 1541s, 1489m, 1325s, 1295s, 1228m, 1157vs, 1127s, 1105s, 1067s, 846s.

2-(4-(4-Chlorophenylsulfonyl)benzoyl)-N-(4-(trifluoromethyl)phenyl)hydrazinecarbothioamide ***2b***

m.p. 194-196 °C; yield: 72 %;

Elemental analysis: anal. calcd for $C_{21}H_{15}ClF_3N_3O_3S_2$ (513.94): C, 49.08; H, 2.94; N, 8.18. Found: C, 49.15; H, 2.87; N, 8.13%.

ESI-MS, *m/z*: 514 $[^{35}Cl\ M+H]^+$, 516 $[^{37}Cl\ M+H]^+$;
353 $[^{35}ClM+H\text{-}CF_3C_6H_4NH_2]^+$; 355 $[^{37}ClM\text{-}CF_3C_6H_4NH]^+$;
311 $[^{35}ClC_6H_4SO_2C_6H_4CONHNH_2+H]^+$;
313 $[^{37}ClC_6H_4SO_2C_6H_4CONHNH_2+H]^+$;
279 $[^{35}ClC_6H_4SO_2C_6H_4CO]^+$; 281 $[^{37}ClC_6H_4SO_2C_6H_4CO]^+$;
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 $[^{37}ClC_6H_4]^+$

IR (KBr, ν, cm^{-1}): 3330s, 3311s, 3172m, 3091m, 3069w, 3039w, 1692s, 1595m, 1547s, 1524s, 1323s, 1293s, 1224m, 1161vs, 1126s, 1106s, 1068s, 832s, 756s.

2-(4-(4-Bromophenylsulfonyl)benzoyl)-N-(4-(trifluoromethyl)phenyl)hydrazinecarbothioamide ***2c***

m.p. 204-206 °C; yield: 87 %;

Elemental analysis: anal. calcd for $C_{21}H_{15}BrF_3N_3O_3S_2$ (558.39): C, 45.17; H, 2.71; N, 7.53. Found: C, 45.21; H, 2.64; N, 7.49%.

ESI-MS, *m/z*: 558 $[^{79}Br\ M+H]^+$; 560 $[^{81}Br\ M+H]^+$; 397 $[^{79}Br\ M+H\text{-}CF_3C_6H_4NH_2]^+$; 399 $[^{81}Br\ M+H\text{-}CF_3C_6H_4NH_2]^+$; 355$[^{79}BrC_6H_4SO_2C_6H_4CONHNH_2+H]^+$;357 $[^{81}BrC_6H_4SO_2C_6H_4CONHNH_2+H]^+$

IR (KBr, ν, cm^{-1}): 3332s, 3306s, 3169m, 3091m, 3069w, 3054w, 1692s, 1596m, 1547s, 1524s, 1481m, 1322s, 1292s, 1262m, 1225m, 1161vs, 1126s, 1104s, 1069s, 844m, 570s.

Synthesis of 5-(4-(4-X-phenylsulfonyl)phenyl)-N-(4-(trifluoromethyl)phenyl)-1,3,4-thiadiazol-2-amines **3a-c**

Synthesis of compounds was realized similarly with literature data [23,27].

A mixture formed by the hydrazinecarbothioamide **2** (2mmol) and phosphorous oxychloride (10 mL) was refluxed for 5h. The residue obtained by distillation under reduced pressure was put into water and ice. To the precipitate was added a diluted aqueous solution of $NaHCO_3$ until slightly basic *p*H. The product was filtered off, washed with water, dried and purified from chloroform/ petroleum ether (~ 1:2, v/v).

5-(4-(Phenylsulfonyl)phenyl)-N-(4-(trifluoromethyl)phenyl)-1,3,4-thiadiazol-2-amine ***3a***

m.p. 240-243 °C; yield: 73 %;

Elemental analysis: anal. calcd for $C_{21}H_{14}F_3N_3O_2S_2$ (461.48): C, 54.66; H, 3.06; N, 9.11. Found: C, 54.72; H, 3.00; N, 9.03%.

ESI-MS, *m/z*: 462 $[M+H]^+$; 160 $[F_3CC_6H_4NH]^+$; 125 $[C_6H_5SO]^+$; 77 $[C_6H_5]^+$;

ESI-MS, *m/z*: 460 $[M-H]^-$; 185 $[F_3CC_6H_4NCN]^-$

IR (KBr, ν, cm^{-1}): 3338m, 3061w, 3006w, 1615m, 1573w, 1550m, 1493m, 1326s, 1290m, 1157s, 1108s, 1068m, 841m.

5-(4-(4-Chlorophenylsulfonyl)phenyl)-N-(4-(trifluoromethyl)phenyl)-1,3,4-thiadiazol-2-amine ***3b***

m.p. 246 °C (dec.); yield: 77 %;

Elemental analysis: anal. calcd for $C_{21}H_{13}ClF_3N_3O_2S_2$ (495.93): C, 50.86; H, 2.64; N, 8.47. Found: C, 50.70; H, 2.76; N, 8.38%.

ESI-MS, *m/z*: 496 $[^{35}Cl\ M+H]^+$; 498 $[^{37}Cl\ M+H]^+$; 321 $[M+H\text{-}ClC_6H_4SO_2]^+$; 219 $[F_3CC_6H_4NHCNS+H]^+$; 160 $[F_3CC_6H_4NH]^+$

ESI-MS, *m/z*: 494 $[^{35}Cl\ M-H]^-$; 496 $[^{37}Cl\ M-H]^-$; 263 $[^{35}ClC_6H_4SO_2C_6H_4C]^-$; 265 $[^{37}ClC_6H_4SO_2C_6H_4C]^-$; 185 $[F_3CC_6H_4NCN]^-$; 175 $[^{35}ClC_6H_4SO_2]^-$; 177 $[^{37}ClC_6H_4SO_2]^-$

IR (KBr, ν, cm^{-1}): 3344m, 3094w, 3061w, 1615m, 1551m, 1491m, 1326vs, 1280m, 1158s, 1108m, 1117m, 1068m, 839m, 764m.

*5-(4-(4-Bromophenylsulfonyl)phenyl)-N-(4-(trifluoromethyl)phenyl)-1,3,4-thiadiazol-2-*amine ***3c***

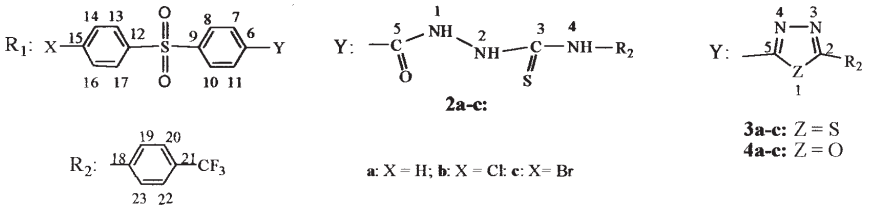
m.p. 259 °C (dec.); yield: 79 %;

Elemental analysis: anal. calcd for $C_{21}H_{13}BrF_3N_3O_2S_2$ (540.38): C, 46.68; H, 2.42; N, 7.78. Found: C, 46.51; H, 2.31; N, 7.70%.

ESI-MS, *m/z*: 540 $[^{79}Br\ M+H]^+$; 542 $[^{81}Br\ M+H]^+$; 321 $[M+H\text{-}BrC_6H_4SO_2]^+$; 219 $[F_3CC_6H_4NHCNS+H]^+$; 160 $[F_3CC_6H_4NH]^+$

ESI-MS, *m/z*: 538 $[^{79}Br\ M-H]^-$; 540 $[^{81}Br\ M-H]^-$; 335 $[^{79}BrC_6H_4SO_2C_6H_4NCN]^-$; 337 $[^{81}BrC_6H_4SO_2C_6H_4NCN]^-$; 185 $[F_3CC_6H_4NCN]^-$; 219 $[^{79}BrC_6H_4SO_2]^-$; 221 $[^{81}BrC_6H_4SO_2]^-$;

IR (KBr, ν, cm^{-1}): 3327m, 3090w, 3061w, 1614m, 1573m, 1553m, 1492m, 1325vs, 1291m, 1158s, 1118m, 1105m, 1069s, 840m, 571m.



2a-c:

a: X = H; **b**: X = Cl; **c**: X= Br

3a-c: Z = S
4a-c: Z = O

Table 1
THE ^{1}H-NMR SPECTRAL DATA OF COMPOUNDS **2a-c - 4a-c** (DMSO-d_6, δ ppm, *J* Hz)

No	H-7, H-11	H-8, H-10	H-13, H-17	H-14, H-16	H-15	H-19, H-23	H-20, H-22	NH
2a (65 °C)	8.14d (8.8)	8.09d (8.8)	7.99dd (7.5; 1.7)	7.64bt (7.5)	7.77tt (7.5; 1.7)	7.67bd (8.2)	7.79d (8.2)	9.98bs 10.05bs 10.85bs
2b (65 °C)	8.15d (8.8)	8.10d (8.8)	7.99d (8.8)	7.69d (8.8)	-	7.67d (8.8)	7.79d (8.8)	9.96bs 10.08bs 10.90bs
2c (70 °C)	8.15d (8.7)	8.10d (8.8)	7.94d (8.8)	7.86d (8.8)	-	7.67d (8.8)	7.80bd (8.8)	9.90bs 10.50bs
3a	8.09s	8.09s	7.99bd (7.4)	7.64bt (7.4)	7.69bt (7.4)	7.76d (8.8)	7.96d (8.8)	11.10s
3b	8.10s	8.010s	8.01d (8.8)	8.01d (8.8)	-	7.76d (8.8)	7.96d (8.8)	11.10s
3c	8.09s	8.09s	7.92bd (8.8)	7.84d (8.8)	-	7.75d (8.6)	7.96d (8.6)	11.08s
4a	8.10d (8.8)	8.16d (8.8)	8.10dd (7.8; 1.7)	7.70tt (7.8; 1.7)	7.65tt (7.8; 1.7)	7.81d (8.8)	7.71d (8.8)	11.31s
4b	8.11d (8.8)	8.16d (8.8)	8.02d (8.5)	7.73d (8.5)	-	7.81d (8.8)	7.73d (8.8)	11.30bs
4c	8.10d (8.8)	8.16d (8.8)	7.94d (8.6)	7.87d (8.6)	-	7.81d (8.8)	7.72d (8.8)	11.32s

Table 2
THE ^{13}C-NMR SPECTRAL DATA OF COMPOUNDS **2a-c - 4a-c** (DMSO-d_6, δ ppm, *J* Hz)

No	C-2	C-3	C-5	C-6	C-7, C-11	C-8, C-10	C-9	C-12	C-13, C-17	C-14, C-16	C-15	C-18	C-19, C-23	C-20, C-22	C-21	CF_3
2a	-	180.92	164.61	136.96	129.22	127.51	142.93	140.59	127.51	129.85	134.02	143.82	125.78	125.18	126.08q (29.8)	124.28q (270.1)
2b	-	180.87	164.19	137.13	129.99	128.36	142.91	139.38	127.58	129.99	139.16	143.32	125.68	125.17	126.07q (29.9)	124.35q (271.5)
2c	-	180.94	164.57	137.17	127.59	128.39	142.58	139.81	129.52	132.97	128.30	143.31	125.78	125.13	125.78q (30.2)	124.60q (272.0)
3a	164.43	-	156.94	124.13	128.39	127.91	141.99	140.72	127.47	129.90	133.99	143.87	116.91	126.44q (3.5)	122.90q (32.1)	124.18q (270.5)
3b	164.50	-	156.89	124.08	128.54	128.08	141.54	139.56	129.51	130.11	139.18	143.97	116.99	126.45q (3.4)	122.91q (32.4)	124.30q (270.8)
3c	164.53	-	156.86	124.27	128.57	128.11	141.53	140.00	129.57	133.09	128.34	143.96	117.02	126.44q (3.4)	125.90q (31.3)	124.45q (271.2)
4a	159.96	-	157.03	128.08	126.75	128.45	142.72	141.87	127.49	129.88	134.04	140.48	117.14	126.44q (3.4)	122.87q (32.1)	124.58q (271.3)
4b	159.97	-	156.99	128.25	126.80	128.53	142.22	141.85	129.48	130.04	139.20	139.27	117.14	126.45q (3.6)	122.87q (32.1)	124.26q (270.9)
4c	159.98	-	157.00	128.26	126.81	128.53	142.19	141.85	129.50	133.00	128.31	139.70	117.14	126.45q (3.6)	122.88q (32.1)	124.40q (271.6)

Synthesis of 5-(4-(4-X-phenylsulfonyl)phenyl)-N-(4-(trifluoromethyl)phenyl)-1,3,4-oxadiazol-2-amines ***4a-c***

Synthesis of compounds was realized similarly with literature data [23,24].

To a solution of hydrazinecarbothioamide **2** (2mmol) in ethanol the mercury oxide (4 mmol) was added and the mixture was refluxed for 10h. The mixture obtained was filtered off for removing the mercury sulfide obtained. The precipitate obtained by concentration of the filtrate was filtered off, dried and recrystallized from ethanol.

5-(4-(Phenylsulfonyl)phenyl)-N-(4-(trifluoromethyl)phenyl)-1,3,4-oxadiazol-2-amine ***4a***

m.p. 289-290 °C; yield: 38 %;

Elemental analysis: anal. calcd for $C_{21}H_{14}F_3N_3O_3S$ (445.41): C, 56.63; H, 3.17; N, 9.43. Found: C, 56.59; H, 3.09; N, 9.50%.

ESI-MS, m/z: 446 $[M+H]^+$; 285 $[M-CF_3PhNH_2]^+$; 217 $[C_6H_5SO_2C_6H_4]^+$

IR (KBr, ν, cm^{-1}): 3287m, 3067m, 3032m, 1616s, 1594m, 1578s, 1552m, 1335vs, 1310m, 1292m, 1159vs, 1121 s, 1072m, 839s.

5-(4-(4-Chlorophenylsulfonyl)phenyl)-N-(4-(trifluoromethyl)phenyl)-1,3,4-oxadiazol-2-amine ***4b***

m.p. 275-278 °C; yield: 33 %;

Elemental analysis: anal. calcd for $C_{21}H_{13}ClF_3N_3O_3S$ (479.86): C, 52.56; H, 2.73; N, 8.76. Found: C, 52.50; H, 2.64; N, 8.71%.

ESI-MS, *m/z*: 480 $[^{35}Cl\ M+H]^+$, 482 $[^{37}Cl\ M+H]^+$; 319 $[M+H-CF_3C_6H_4NH_2]^+$; 321 $[M+H-CF_3C_6H_4NH_2]^+$;

ESI-MS, *m/z*: 478 $[^{35}Cl\ M-H]^-$, 480 $[^{37}Cl\ M-H]^-$; 291 $[^{35}ClC_6H_4SO_2C_6H_4CNN]^-$; 293 $[^{37}ClC_6H_4SO_2C_6H_4CNN]^-$; 263 $[^{35}ClC_6H_4SO_2C_6H_4C]^-$; 265 $[^{37}ClC_6H_4SO_2C_6H_4C]^-$; 185 $[CF_3C_6H_4NCN]^-$

IR (KBr, ν, cm^{-1}): 3301m, 3086m, 3071m, 3032w, 1615s, 1594s, 1578s, 1552m, 1329s, 1292m, 1158s, 1119s, 1071s, 840s, 767s.

5-(4-(4-Bromophenylsulfonyl)phenyl)-N-(4-(trifluoromethyl)phenyl)-1,3,4-oxadiazol-2-amine ***4c***

m.p. 292-294 °C; yield: 39 %;

Elemental analysis: anal. calcd for $C_{21}H_{13}BrF_3N_3O_3S$ (524.31): C, 48.11; H, 2.50; N, 8.01. Found: C, 48.19; H, 2.45; N, 7.94%.

ESI-MS, *m/z*: 524 [^{79}Br M+H]$^+$, 526 [^{81}Br M+H]$^+$; 203 [^{79}Br C_6H_4SO]$^+$; 205 [^{81}Br C_6H_4SO]$^+$

ESI-MS, *m/z*: 522 [^{79}Br M-H]$^-$, 524 [^{81}Br M-H]$^-$; 335 [$^{79}BrC_6H_4SO_2C_6H_4NCN]^-$; 337 [^{81}Br $C_6H_4SO_2C_6H_4NCN]^-$; 307 [$^{79}BrC_6H_4SO_2C_6H_4C]^-$; 309 [$^{81}BrC_6H_4SO_2C_6H_4C]^-$; 219 [$^{79}BrC_6H_4SO_2]^-$; 221 [$^{81}BrC_6H_4SO_2]^-$; 185 $[CF_3C_6H_4NCN]^-$

IR (KBr, ν, cm^{-1}): 3297m, 3083m, 3031w, 1617s, 1594s, 1578s, 1552m, 1334s, 1292m, 1159s, 1135m, 1118m, 1071s, 840s, 570m.

Results and discussions

Acyclic compounds **2a-c** shown the characteristic stretching absorption bands due to NH (three bands), C=O and C=S functions present in the following intervals in their IR spectra: at 3105-3332 cm^{-1}, 1681-1692 cm^{-1} and 1224-1228 cm^{-1} respectively. The ^{1}H-NMR spectra shown characteristic singlet signals to NH groups with chemical shift ä in region 9.90-10.90 ppm. On the other hand, the ^{13}C-NMR spectra shown the characteristic signals of C=O and C=S at 164.19-164.61 ppm and 180.87-180.94 ppm, respectively. The CF_3 carbon signal appeared as quartet at δ = ≈ 124 ppm with coupling constants *J* = 270.1-272.0 Hz.

The main proof of heterocyclisation of hydrazinecarbothioamides **2a-c** is disappearance from IR spectra of compounds **3** and **4** of absorption bands due to stretching vibrations of the C=O and C=S groups. Also, comparatively with acyclic compounds **2**, the IR spectra of compounds **3** and **4** showed a single band at 3327-3344 cm^{-1} for **3a-c** and at 3287-3301 cm^{-1} for **4a-c** characteristic to NH group. The stretching vibration bands of SO_2 group appeared in the IR spectra of all compounds at 1322-1335 cm^{-1} (ν_{as} SO_2) and 1157-1161 cm^{-1} (ν_{sym} SO_2), respectively. Unlike the hydrazinecarbothioamides, the ^{1}H-NMR spectra presented a single singlet signal at 11.08-11.10 ppm for **3a-c** and at 11.30-11.32 ppm for **4a-c** for proton of NH group, more deshielded than those of compounds **2**. In the ^{13}C-NMR spectra of these compounds, the signal from ≈ 164 ppm and ≈ 181 ppm characteristic to C=O and C=S from hydrazinecarbothioamides disappeared. Instead, new signals appeared at 164.43-164.53 ppm and 156.86-156.94 ppm in case of compounds **3a-c** and at 159.96-159.98 ppm and 156.99-157.03 ppm in case of compounds **4a-c** which belong to C-2 and C-5 quaternary heterocyclic carbon from 1,3,4-thiadiazole and 1,3,4-oxadiazole nucleus. Moreover, the carbon signal from CF_3 group from thiadiazoles and oxadiazoles appeared as quartet at δ ≈ 124 ppm, with *J* ≈ 270.5-271.6 Hz ppm.

The protons and carbon atoms signals from (4-trifluoromethyl)phenyl and arylsulfonylphenyl fragments were found at the corresponding chemical shifts (tables 1 and 2).

The structures of these compounds are also confirmed by their mass spectra, the molecular ions and the main fragments are presented in the experimental part. These compounds couldn't be analyzed by traditionally procedure by injecting them in gas chromatograph coupled with a mass spectrometer because haven't enough volatility and are thermally unstable. For this reason another ionization source must be used for these substances. Probably the most used atmospheric pressure ionization source is electrospray (ESI). Main advantage is that substances dissolved in an appropriate liquid phase will be ionized by spraying it under high voltage. Every fine charged liquid drop by evaporation will ionize dissolved substances. Ions will enter in mass spectrometer passing from atmospheric pressure to high vacuum. Generally ESI conserve molecular ion in protonated [M+H]$^+$ form if ESI operated in positive mode or as [M-H]$^-$ if ESI operated in negative mode and molecules have mobile protons, like acids, for example. For structural determination we need fragments that could be obtained using collision of molecular ions by an inert gas like nitrogen, helium or argon. Generally ESI MS do not offer a large number of fragments, usually up to ten fragments by collision.

These compounds studied have both acidic and basic centers. Therefore, they could be ionized both in positive and negative mode. Mass spectrometer is able to detect isotope contribution in molecular ions. The compounds obtained have similar fragmentation. In case of hydrazinecarbothioamide **2a** the main fragments are summarized in Scheme 3:

Using fragmentations both in positive and in negative mode for molecules that posses both acidic and basic center we can obtain supplementary structural information for a better assignment of synthons in molecule.

Conclusions

The aim of the present study was the synthesis and characterization of some compounds containing 4-trifluoromethylphenyl and arysulfonylphenyl moieties. The structure of hydrazinecarbothioamides which were synthesized by treatment of some arylsulfonylbenzoic acid hydrazides with an aromatic isothiocyanate having a trifluoromethyl radical in para- position on the phenyl moiety and the structure of 1,3,4-thiadiazoles/1,3,4-oxadiazoles obtained by dehydrative/desulfurative cyclization of these acyclic compounds was confirmed by spectroscopic techniques.

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