HETEROCYCLES 28. SYNTHESIS AND
CHARACTERIZATION OF SOME BIS AND
POLYHETEROCYCCLIC COMPOUNDS WITH
ANTI-INFLAMMATORY POTENTIAL

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Abstract
The synthesis of some thiazolyl-mercaptotriazolic thioethers and their use in the
obtaining of some potential anti-inflammatory polyheterocyclic compounds with
thiazolo[3,2-b][1,2,4]triazole and pyrazole rings is presented. A structural analysis of the
synthesized compounds was performed by IR, NMR and MS, confirming the structures of
synthesized compounds. A 1H NMR spectrometric analysis confirmed the presence of keto-
enol and ring-chain tautomeric equilibrium for the synthesized thioethers.

Keywords: thiazolyl-thiazolo[3,2-b][1,2,4]triazoles, 3-thiazolyl-5-pyrazolyl-
1,2,4-triazoles, anti-inflammatory activity.

Introduction
Several medicinal chemistry and pharmacologic experimental research revealed the biological potential of thiazole, 1,2,4-triazole and
pyrazole compounds. The 1,2,4-triazolic compounds present a wide variety of biological properties: antimicrobial [1-3], antiviral [4], anti-inflammatory
[5,6], analgesic [7], antitumoral [8,9], insecticide [10] and anticonvulsant [11,12]. Thus, fluotrimazol, ribavirine and furazonal are used in therapy for
their antimicrobial and antiviral properties, while estazolam, alprazolam and
rizatriptan are used for their central nervous system (CNS) activity, all
being 1,2,4-triazole derivatives. The pyrazole ring is present in the structure of some biologically active compounds such as celecoxib and sildenafil or other compounds with antipsychotic [13], antimicrobial [14], anti-inflammatory properties [15].

In previous papers we presented the synthesis of some 1,2,4-triazole and thiazolo-triazole derivatives with antimicrobial and anti-inflammatory potential [16-22]. As a continuation of this research, we intended to synthesize and evaluate the anti-inflammatory potential of some polyheterocyclic compounds which include also 1,2,4-triazole and pyrazole rings, apart from the thiazole ring, well-known for its biologic potential.

Materials and Methods
Melting points were determined in open glass capillary methods with an Electrothermal melting point meter and were uncorrected. Elemental analysis (C, H, N, S) was performed on a VarioEL analyzer. The obtained results were within the admission limits: ±0.4%. Infrared spectra were recorded as KBr pellets with a FTIR spectrophotometer Nicolet 210. Mass spectra were recorded on a MAT 311 mass spectrometer with EI ion source, at an ionization energy of 70 eV with direct inlet probe. ¹H NMR spectra were recorded on a BRUKER DRX 400 instrument operating at 400.13 MHz, with tetramethylsilane (TMS) as internal standard. The chemical shifts were reported in δ units (ppm) relative to the residual peak of the deuterated solvent (CDCl₃ and DMSO-d₆).

3-[5-(2-Phenyl-thiazol-4-yl)-1,2,4-triazol-3-yl-thio]-pentan-2,4-dione (2a)[18]
0.002 Moles of 1a were suspended in 10 mL anhydrous acetone; 0.40 g sodium acetate and 0.002 moles of 3-chloro-acetylacetone were added. The mixture was stirred for two hours at room temperature, then poured into ice-water, filtered and re-crystallized from ethanol-water. M.p. 161-63°C; C₁₆H₁₄N₄O₂S₂ (358.42); IR(νcm⁻¹): 3411, 3101, 2974, 2826, 2712(νNH, νOH, νCH), 1733, 1714(νCO); EIMS(m/z): 358(M⁺, 24%), 341, 316, 301, 274, 260, 149, 104, 83, 70, 43(100%); ¹H NMR 300 MHz (CDCl₃), δ( ppm):
x: 2.44(s, 6H, CH₃CO); 4.01(s, 1H, CH-acetylacetone); 7.44(m, 3H, C₆H₅-m+p); 7.90(m, 2H, C₆H₅-Br); 8.04(s, 1H, thiazole);
y: 2.35(s, 3H, COCH₂); 2.77(s, 3H, CH₃); 7.44(m, 3H, C₆H₅-m+p); 7.90(m, 2H, C₆H₅-Br); 7.97(s, 1H, thiazole); 8.03(s, OH enol);
z: 2.36(s, 3H, CH₃); 2.42(s, 3H, COCH₂); 4.16(s, 1H, CH-acetylacetone); 7.44(m, 3H, C₆H₅-m+p); 7.90(m, 2H, C₆H₅-Br); 8.01(s, 1H, thiazole).
3-[5-(4-Methyl-2-phenyl-thiazol-5-yl)-1,2,4-triazol-3-yl-thio]-pentan-2,4-dione (2b)[20]
The same method as for 2a. M.p. 142-4° C; C_{17}H_{16}Na_{2}O_{2}S_{2} (372.45); IR (cm⁻¹): 3434, 3089, 2965, 2908, 2751 (νNH, νOH, νCH), 1735 (νCO); EIMS (m/z): 372(M⁺, 58%), 330 (100%), 287, 201, 185, 104, 97, 83, 70, 43; ¹H-RMN 300 MHz (CDCl₃), δ (ppm): 2.47 (s, 6H, COCH₃); 2.81 (s, 3H, CH₃); 7.45 (m, 3H, C₆H₅-m+p); 7.96 (m, 2H, C₆H₅-o).

3-[N-Acetyl-5-(2-Phenyl-thiazol-4-yl)-1,2,4-triazol-3-yl-thio]-pentan-2,4-dione (3a)
0.001 Moles of 2a were treated with 2 mL acetic anhydride, 2 drops of pyridine were added and then the mixture was heated on a water bath until solvation and then left for 24 h at room temperature. The obtained substance was filtered and re-crystallized from ethanol. M.p. 183-5° C; C_{18}H_{16}N₄O₃S₂ (400.46); EIMS (m/z): 400 (M⁺, 20%), 358, 341, 315 (100%), 301, 287, 273, 242, 187, 104, 83; ¹H-RMN 300 MHz (CDCl₃), δ (ppm): 2.38 (s, 6H, COCH₃); 2.87 (s, 3H, N-COCH₃); 7.48 (m, 3H, C₆H₅-m+p); 8.04 (s, 1H, thiazole); 8.06 (m, 2H, C₆H₅-o).

3-[N-Acetyl-5-(4-Methyl-2-phenyl-thiazol-5-yl)-1,2,4-triazol-3-yl-thio]-pentan-2,4-dione (3b)
The same method as for 3a. M.p. 157-9° C; C_{19}H_{18}N₄O₃S₂ (414.48); EIMS (m/z): 414 (M⁺, 47%), 372, 354, 329 (100%), 301, 287, 201, 104, 71, 43; ¹H-RMN 300 MHz (CDCl₃), δ (ppm): 2.39 (s, 6H, COCH₃); 2.78 (s, 3H, N-COCH₃); 2.80 (s, 3H, CH₃); 7.46 (m, 3H, C₆H₅-m+p); 7.99 (m, 2H, C₆H₅-o).

6 - Acetyl - 5 - methyl - 2 - (2-phenyl-thiazol-4-yl) - thiazolo [3,2-b] [1,2,4]-triazole (4a)
a. 0.002 Moles of 3a were dissolved in sulphuric acid and maintained 3 h at room temperature, then poured into ice, the deposed substance filtered and re-crystallized from ethanol.
b. 0.002 Moles of 1a were suspended in 5 mL ethanol, then 0.002 moles of 3-chloro-acetylacetone was added, the mixture was heated on a water bath for 4 h. After the solution was cooled, the deposed substance was filtered and re-crystallized from ethanol. M.p. 196-8° C; IR (cm⁻¹): 3092, 3029, 2970, 2852, 2713 (νCH), 1650 (νCO ketone); EIMS (m/z): 340 (M⁺, 100%), 325, 237, 222, 83, 71; ¹H-RMN 300 MHz (DMSO-d₆), δ (ppm): 2.66 (s, 3H, COCH₃); 2.95 (s, 3H, CH₃); 7.56 (m, 3H, C₆H₅-m+p); 8.04 (m, 2H, C₆H₅-o); 8.41 (s, 1H, thiazole).
6-Acetyl-5-methyl-2-(4-methyl-2-phenyl-thiazol-5-yl)-thiazolo[3,2-b][1,2,4]-triazole (4b)
The same method as for 4a. M.p. 229-30°C; C_{12}H_{14}N_{4}OS_{2} (354.43); IR (cm^{-1}): 3090, 2980, 2921 (vCH), 1659 (vCO ketone); EIMS (m/z): 354 (M^{+}, 100%), 251, 182, 104, 71, 43; 1H-RMN 300 MHz (CDCl_{3}), δ (ppm): 2.62 (s, 3H, CH_{3}), 7.93 (s, 3H, CH); 2.97 (s, 3H, CH_{3}) 7.47 (m, 3H, C_{6}H_{5}-m+p); 8.00 (m, 2H, C_{6}H_{5}-o).

3-(4-Methyl-2-phenyl-thiazol-5-yl)-5-(3,5-dimethyl-pyrazol-4-yl-thio)-1,2,4-triazole (5b)
0.001 Moles of 3b were dissolved in 5 mL ethanol, treated with 0.05 mL hydrazine hydrate and then heated on a water bath for 2 h. The solution was cooled and the deposed substance was filtered and re-crystallized from DMFA-water. M.p. 250-52°C; C_{17}H_{16}N_{6}S_{2} (364.47); IR (cm^{-1}): 3200, 3074, 2963, 2872, 2734 (vNH, vCH), 1573 (vC=N); EIMS (m/z): 368 (M^{+}, 100%), 335, 274, 265, 171, 141, 104, 97, 95, 45, 42; 1H-RMN 300 MHz (CDCl_{3}), δ (ppm): 2.22 (s, large, 6H, 2CH_{3}); 2.70 (s, 3H, CH_{3}); 7.50 (m, 3H, C_{6}H_{5}-m+p); 7.95 (m, 2H, C_{6}H_{5}-o).

N-Acetyl-3-(4-Methyl-2-phenyl-thiazol-5-yl)-5-(1-acetyl-3,5-dimethyl-pyrazol-4-yl-thio)-1,2,4-triazole (6b)
0.001 Moles of 5b were treated with 2 mL acetic anhydride, 2 drops of pyridine were added; the mixture was heated on a water bath until solution and then left for 24 h at room temperature. The deposed substance was filtered and washed with ethanol. Mp. 193-4°C; C_{21}H_{20}N_{6}O_{2}S_{2} (452.54); IR (cm^{-1}): 2969, 2923 (vCH), 1733 (vCO amidic), 1557 (vC=N); EIMS (m/z): 452 (M^{+}, 90%), 410 (100%), 368, 335, 274, 200, 171, 141, 104, 97, 70, 43; 1H-RMN 300 MHz (DMSO-d_{6}), δ (ppm): 2.32 (s, 3H, CH_{3}); 2.67 (s, 3H, CH_{3}); 2.72 (s, 3H, CH_{3}) 2.76 (s, 3H, COCH_{3}) 2.79 (s, 3H, COCH_{3}) 7.45 (m, 3H, C_{6}H_{5}-m+p); 7.96 (m, 2H, C_{6}H_{5}-o).

3-(4-Methyl-2-phenyl-thiazol-5-yl)-5-(3,5-dimethyl-1-phenyl-pyrazol-4-yl-thio)-1,2,4-triazole (7b)
0.001 Moles of 3b were dissolved in 5 mL ethanol, then treated with 0.11g phenyl-hydrazine and heated on a water bath for 2 h. The solution was cooled and the deposed substance was filtered and re-crystallized from ethanol. M.p. 217°C; C_{23}H_{20}N_{6}S_{2} (444.56); IR (cm^{-1}): 3069, 2969, 2923, 2873, 2733 (vNH, vCH), 1596 (vC=N); EIMS (m/z): 444 (M^{+}, 92%), 411, 272, 244, 222, 171 (100%), 118, 171, 104, 77.

3-(2-Phenyl-thiazol-5-yl)-5-[p-bromophenyl-3,5-dimethyl-pyrazol-4-yl-thio]-1,2,4-triazole (8a)
0.001 Moles of 3a were dissolved in 5 mL ethanol and then treated with 0.25g p-bromo-phenylhydrazine dissolved in 5 mL ethanol and heated on a
water bath for 6 h. The solution was cooled and the deposed substance was filtered and re-crystallized from ethanol. M.p. 253-4ºC; C_{22}H_{17}N_{3}S_{2}Br (509.44); IR (cm^{-1}): 3207, 2916 (vCH), 159 (vC=N); C_{22}H_{17}N_{3}S_{2}Br (509.44); EIMS (m/z): 510, 508 (M^+, 100%), 430, 338, 299, 254, 171, 91, 83, 39; 1H- RMN 300 MHz (CDCl_3), δ (ppm): 2.35 (s, 3H, CH_3); 2.88 (s, 3H, CH_3); 7.04 (d, 2H, C_6H_4Br, 3J_HH=8.20 Hz); 7.42 (d, 2H, C_6H_4Br, 3J_HH=8.20 Hz); 7.48 (m, 3H, C_6H_5-m+p); 8.07 (s, 1H, thiazole); 8.12 (m, 2H, C_6H_5-o).

N-Acetyl-3-(4-methyl-2-phenyl-thiazol-5-yl)-5-(3,5-dimethyl-1-phenylpyrazol-4-yl-thio)-1,2,4-triazole (9b)
The same method as for 6b. M.p. 160-2ºC; C_{25}H_{22}N_{6}OS_{2} (486.60); IR (cm^{-1}): 3067, 2919 (vCH), 1728 (vC=O amide), 1598 (vC=N); EIMS (m/z): 486 (M^+, 73%), 444, 411, 214, 200, 171 (100%), 130, 118, 104, 77, 43; 1H- RMN 300 MHz (CDCl_3), δ (ppm): 2.38 (s, 3H, CH_3); 2.39 (s, 3H, CH_3); 2.75 (s, 3H, CH_3); 2.80 (s, 3H, COCH_3); 7.43-7.55 (m, 2H, C_6H_5-o, 6H, C_6H_5-m+p); 7.97 (m, 2H, C_6H_5 o phenyl-thiazole).

N-Acetyl-3-(2-phenyl-thiazol-5-yl)-5-[p-bromophenyl-3,5-dimethylpyrazol-4-yl-thio]-1,2,4-triazole (10a)
The same method as for 6b. M.p. 202-4ºC; C_{24}H_{19}N_{3}OS_{2}Br (551.45); IR (cm^{-1}): 3120, 3067, 2926 (vCH), 1727 (vC=O amide), 1573 (vC=N); EIMS (m/z): 552, 550 (M^+, 8.5%), 510, 430, 249, 196, 187, 170, 155, 129, 104, 76, 43 (100%); 1H- RMN 300 MHz (CDCl_3), δ (ppm): 2.37 (s, 3H, CH_3); 2.41 (s, 3H, CH_3); 2.89 (s, 3H, N-COCH_3); 7.43 (d, 2H, C_6H_4Br o, 3J_HH=8.7 Hz); 7.47 (m, 3H, C_6H_5-m+p); 7.65 (d, 2H, C_6H_4Br-m, 3J_HH=8.7 Hz); 7.95 (s, 1H, thiazole); 8.05 (m, 2H, C_6H_5-o).

6-Bromoacetyl-5-methyl-2-(2-phenyl-thiazol-4-yl)-thiazolo[3,2-b][1,2,4]triazole (11a)
0.34 g (0.001 moles) of 4a were dissolved in 10 mL tetrachloromethane; 0.05 mL bromine were added and then refluxed for 4 h on a water bath. The solvent was evaporated and the obtained residue was re-crystallized from ethanol. M.p. 203-5ºC; C_{16}H_{11}N_{3}OS_{2}Br (419.31); IR (cm^{-1}): 3062, 2917, 2848 (vCH), 1654 (vC=O ketone); EIMS (m/z): 420, 418 (M^+, 42%), 339 (100%), 325, 297, 236, 162, 151, 126, 103, 83, 70, 43; 1H- RMN 300 MHz (CDCl_3), δ (ppm): 2.64 (s, 3H, CH_3); 3.04 (s, 3H, CH_3); 7.49 (m, 3H, C_6H_5-m+p); 8.01 (m, 2H, C_6H_5-o); 8.12 (s, 1H, thiazole).

Methyl 5-methyl-2-(2-phenyl-thiazol-4-yl)-thiazolo[3,2-b][1,2,4]-triazol-6-yl cetoxime (12a)
0.34 g (0.001 moles) of 4a were dissolved in 10 mL ethanol. A solution obtained from 0.14 g (0.002 moles) hydroxylamine hydrochloride and 0.164 g (0.002 moles) sodium acetate was added. The mixture was refluxed for 3 h, then the solution was cooled and the deposed oxime was filtered and
re-crystallized from ethanol. M.p. 287-88°C; C_{16}H_{13}N_{2}OS_{2} (355.42); IR(\text{cm}^{-1}): 3162(\nu\text{OH}), 3082, 2916(\nu\text{CH}), 1557(\nu\text{C=N}); EIMS(m/z): 355(M^{+}, 100%), 339, 313, 252, 187, 104, 83, 77, 57, 39;
\textsuperscript{1}H-RMN 300 MHz (DMSO-d_{6}), \delta(ppm): 2.32(s, 3H, CH_{3}); 2.76(s, 3H, CH_{3}); 7.56(m, 3H, C_{6}H_{5}-m+p); 8.04(m, 2H, C_{6}H_{5}-o); 8.31(s, 1H, thiazole).

5-Methyl-2-((2-phenyl-thiazol-4-yl)-thiazolo[3,2-b][1,2,4]triazol-6-carboxylic acid (13a)

0.34g (0.001 moles) of 4a were dissolved in 15 mL dioxane and then added to a cooled solution obtained from 10 g sodium hydroxide, 40 mL water and 2.5 mL bromine. The mixture was stirred for 12 h. The solution was acidulated with hydrochloric acid and then NaHSO_{3} was added to remove the excess of bromide. The deposed carboxylic acid was filtered and re-crystallized from DMFA-water (DMFA – dimethyl formamide). M.p. 279-80°C; C_{16}H_{13}N_{2}O_{2}S_{2} (342.38); IR(\text{cm}^{-1}): 3107, 3062, 2960, 2930, 2853(\nu\text{OH carboxyl}, \nu\text{CH}), 1701(\nu\text{CO carboxyl}); EIMS(m/z): 342(M^{+}, 85%), 298(100%), 274, 239, 195, 187, 162, 149, 112, 104, 83, 71, 44;

5-Methyl-2-((4-methyl-2-phenyl-thiazol-5-yl)-thiazolo[3,2-b][1,2,4]triazol-6-carboxylic acid (13b)

The same method as for 14a. M.p. >283°C; C_{16}H_{12}N_{2}O_{2}S_{2} (356.41); IR(\text{cm}^{-1}): 3057, 3013, 2855, 2557(\nu\text{OH carboxyl}, \nu\text{CH}), 1671(\nu\text{CO carboxyl}); EIMS(m/z): 356(M^{+}, 18%), 312(100%), 253, 209, 176, 164, 156, 140, 114, 104, 96, 77, 70, 44;

5-Methyl-2-((2-phenyl-thiazol-4-yl)-thiazolo[3,2-b][1,2,4]-triazol-6-yl)-ethandial (14a)

0.34 g (0.001 moles) of 4a were dissolved in 5 mL warm acetic acid. 0.30g selenium dioxide dissolved in 2 mL of water were added and then the solution was refluxed for 1 h. The warm solution was filtered, diluted with water and then the dicarbonyl compound was separated and re-crystallized from ethanol. M.p. 205°C; C_{16}H_{10}N_{4}O_{2}S_{2} (354.39); IR(\text{cm}^{-1}): 2916, 2848(\nu\text{CH}), 1716, 1664(\nu\text{CO aldehyde and ketone}); EIMS(m/z): 354(M^{+}, 36%), 326(100%), 298, 237, 222, 186, 149, 111, 103, 83, 70, 43;

5-Methyl-2-((4-methyl-2-phenyl-thiazol-5-yl)-thiazolo[3,2-b][1,2,4]-triazol-6-yl)-ethandial (14b)

The same method as for 15a. M.p. 221-3°C; C_{17}H_{12}N_{4}O_{2}S_{2} (368.42); EIMS(m/z): 368(M^{+}, 3%), 339, 251(100%), 182, 141, 104, 96, 83, 71;

2-[5-Methyl-2-((2-phenyl-thiazol-4-yl)-thiazolo[3,2-b][1,2,4]-triazol-6-yl)-quinoxaline (15a)

0.35g (0.001 moles) of 15a were dissolved in 5 mL ethanol, then 0.11g (0.001 moles) o-phenylenediamine dissolved in 2 mL ethanol were added. The mixture was refluxed for 2 h and then the deposed substance was
filtered after cooling and re-crystallized from ethanol. M.p. 234-6°C; C_{22}H_{14}N_{6}S_{2} (426.50); IR(cm⁻¹): 3066, 2916, 2848(νCH), 1664(νC=N); EIMS(m/z): 426(M⁺, 100%), 323, 251, 213, 199, 168, 129, 102, 83, 77; ¹H- RMN 300 MHz (DMSO-d₆), δ(ppm): 3.11(s, 3H, CH₃); 7.57(m, 2H, quinoxaline); 7.93(m, 2H, quinoxaline); 8.06(m, 3H, C₆H₅-m+p); 8.17(m, 2H, C₆H₅-o); 8.42(s, 1H, thiazole); 9.48(s, 1H, quinoxaline-3).

Results and Discussion

For the synthesis of the compounds, we applied the condensation reaction of the thiazolyl-mercaptotriazoles obtained previously [18, 20] with 3-chloro-acetylacetone (Figure 1). According to the reaction conditions, different results were obtained. Thus, if the reaction was performed in acetone, at room temperature and in the presence of a base (sodium acetate, sodium carbonate), the 2a and 2b thioethers were obtained, which were transformed in the corresponding derivates 3a and 3b by reacting with acetic anhydride. If no base was present, apart from the 2a,b thioethers, the cyclisation products with a triazolo[3,2-b][1,2,4]triazolic structure 4a,b were obtained. The cyclisation products were directly obtained, with very good results, if the condensation reaction was performed in ethanol at reflux. These compounds may also be obtained by the action of the concentrated sulphuric acid on the 2a,b and 3a,b thioethers, or by heating at boiling temperature the 2a,b thioethers in ethanolic solution, in the presence of hydrochloric acid.

![Figure 1: Synthesis and cyclisation of thiazolyl-mercaptotriazolic thioethers](image-url)
Due to the acetyl-acetone fragment from 2a,b, which renders them sensitive to binucleophils action, these compounds were transformed into the corresponding pyrazoles, 5b, 7b and 8a by reacting with hydrazine, phenylhydrazine and p-bromo-phenylhydrazine (Figure 2). The obtained pyrazoles were transformed into the acetyl derivatives 6b, 9b and 10a by reacting with acetic anhydride. By the acetylation of 5b, the 6b diacetylderivative was obtained due to the unsubstituted position 1 from the pyrazole ring.

Subsequently, the chemical behaviour of the acetyl group from position 6 of the thiazolo[3,2-b][1,2,4]triazole system was studied. Thus, the ketone 4a was subjected to a bromination reaction, obtaining the compound 11a and transformed in the corresponding oxime 12a by reacting with hydroxylamine (Figure 3). The compounds 2a,b were subjected to a haloforme reaction, obtaining the carboxylic acids 13a,b, which were also obtained by base hydrolysis of the corresponding ethyle esters. Considering the methylene-active character of the methyl from the acetyl group, we intended to obtain the ketoaldehyde 14a by the reaction of the ketone 4a with selenium dioxide. Although an excess of oxidant was used (4 mol
SeO$_2$:1 mol ketone), the dicarbonylic compound was obtained with a low yield. This was characterized by the transformation into the corresponding 2,4-dinitro-phenylhydrazone, a corresponding quinoxaline, 15a, being also obtained for the 14a compound.

![Chemical behavior of thiazolo[3,2-b][1,2,4]triazoles 4a,b](image)

The IR, MS and NMR spectra confirmed the structures of the obtained compounds. A molecular peak was present in the mass spectra of all the synthesised compounds. Apart from the thioethers 2 and 3 and 14 dicarbonilic compounds, the molecular peak is relatively abundant or it is the base peak of the spectrum. The fragmentation peaks from the spectra are due to the fragmentations in the heterocyclic systems or in the functional groups from the molecule.

In the IR spectra of the thioethers 2a,b several peaks can be associated with the vibrations of the NH, enolic OH/alcoholic OH and CO functional groups, which is an argument in favour of the existence of keto-enol and ring-chain tautomeric equilibrium (Figure 4). The IR spectra are simplified by cyclisation, because the peaks attributed to the OH and NH groups are missing and the peaks of $\nu$C=O vibrations were shifted toward lower wavelength values (1650, 1659 cm$^{-1}$). The $\nu$C=O peaks were also missing from the IR spectra of pyrazoles (apart from the acetylated...
compounds 6, 9, 10) which confirmed the fact that the reaction of thioethers 2 with the hydrazine derivatives has occurred. The vibrations bands of the functional groups from the thiazolo[3,2-b][1,2,4]triazoles 11, 12, 13 and 14: carbonyl (aldehyde, ketone, carboxyl) and hydroxyl (oxime and carboxyl), were also present.

The $^1$H NMR spectra of the compounds 2 confirmed the existence of some tautomers derived from acetylacetone rest, like in the case of some 1,2,4-triazole acetoacetate derivatives [23]. The $^1$H NMR spectrum of the compound 2a presented signals which were attributed to the protons from the tautomeric forms in equilibrium (Figure 4).

Thus, for the keto tautomer (x), the signal at 2.44 ppm was attributed to the six equivalent protons from the acetyl rest, at the proton from position 3 of the acetyl-acetone rest being attributed the signal at 4.01 ppm. For the enolic tautomer (y) the signals from 2.35 ppm (CO-CH$_3$), 2.77 ppm (CH$_3$) and 8.03 ppm (OH enolic) were attributed, while the signals at 2.36 ppm (CH$_3$) and 2.42 ppm (CO-CH$_3$) were assigned to the cyclic tautomer (z). The existence of keto-enolic tautomerism was confirmed, also, by the positive reaction with Fe(III) and Cu(II) (enol tautomer) and, also, with 2,4-dinitrophenylhydrazine (ketone tautomer).

**Conclusions**

A series of polyheterocyclic compounds with isolated and condensed rings, with biologic potential, were synthetised: thiazolyl-mercapto-1,2,4-triazolic thioethers (2,3), thiazolyl-thiazolo[3,2-b][1,2,4]triazoles (4,11-15) and thiazolyl-1,2,4-triazolyl-thio-pyrazoles (5-10).
The synthesized compounds were characterised by IR, $^1$H NMR and MS analysis. For the thioethers $2a,b$ the presence of keto-enolic and ring-chain tautomeric equilibriums, suggested by the chemical behaviour of these compounds, was confirmed by IR and $^1$H NMR spectra.

The chemical behaviour of the functional groups from the position 6 of the thiazolo[3,2-b][1,2,4]triazole system was studied.

Acknowledgements

This work was supported by CNCSIS-UEFISCSU, project number PN II-IDEI code 1269/2008.

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*Manuscript received: November 20th 2010*