The Alkylation of 1*H*-5-mercapto-3-phenyl -1,2,4-triazole and 4*H*-4-amino-5-mercapto-3-phenyl -1,2,4-triazole

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*The alkylation of in situ prepared sodium salts of 1H-5-mercapto-3-phenyl-1,2,4-triazole (**1a**) and 4H-4-amino-5-mercapto-3-phenyl-1,2,4-triazole (**2a**) with ethyl chloroacetate in absolute ethanol leads with good yields to 1H-5-ethoxycarbonyl-methylsulfanyl-3-phenyl-1,2,4-triazole (**3a**) and 4H-4-amino-3-ethoxycarbonyl-methylsulfanyl-5-phenyl-1,2,4-triazole (**4a**). The alkaline hydrolysis of the esters (**3a**, **4a**) leads to 1H-5-carboxy-methylsulfanyl-3-phenyl-1,2,4-triazole (**6a**) and 4H-4-amino-5-carboxy-methylsulfanyl-3-phenyl-1,2,4-triazole (**5a**), respectively. All the compounds were characterized by mass, IR, ^{1}H-NMR and ^{13}C-NMR spectroscopy, and the confirmation of S-alkylation was proven through 2D NMR spectra.*

Keywords: S-alkylation, mercapto-triazoles, amino-mercapto-triazoles, acetic acid derivatives, NMR data

The constantly interest for 3-substituted 1*H*-5-mercapto-1,2,4-triazoles (**1**) and 4*H*-4-amino-5-mercapto-1,2,4-triazoles (**2**) and their derivatives is due to biological properties (such as antimicrobial, antibacterial, anti-inflammatory and anti-HIV activities) [1-6] and for their cation complexing properties [7-8].

Because it is known that acetic acid derivatives are an important class of non-steroidical anti-inflammatory compounds [9], and on the other hand, the presence of carboxy-methyl moiety grafted on the triazolic nucleus modifies its complexing properties, we set our goal up to synthesis, characterization and afterwards, the study of biological and complexing properties of some 3-substituted 1*H*-5-mercapto-1,2,4-triazoles and 3-substituted-4*H*-4-amino-5-mercapto-1,2,4-triazoles, alkylated at the exocyclic sulfur with -CH_2-$COOC_2H_5$ and -CH_2-COOH moieties (Scheme **1**).

Literature presents different methods for the alkylation of the exocyclic sulphur or endocyclic nitrogen of 3-substituted-1*H*-5-mercapto-1,2,4-triazoles (**1**) and 3-substituted-4*H*-4-amino-5-mercapto-1,2,4-triazoles (**2**).

Thereby, it is affirmed that the S-alkylation of triazoles (**1**)(R=H, Me, Et) occurs in alkaline medium with ethyl bromoacetate[10], and the S-alkylation of triazoles (**2**) (R=aryl) occurs with ethyl chloroacetate in alkaline medium [11], with ethyl bromoacetate in ethanol in the presence of triethylamine [15], with chloroacetic acid in a refluxing mixture of acetic acid and ethanol [12] or with ethyl chloroacetate in ethanol at reflux [13]. On the other hand, it is affirmed that N-alkylation of (**1**) (R=adamantyl) occurs in ethanolic sodium hydroxide with sodium chloroacetate [9] or with ethyl bromoacetate in the presence of sodium ethoxide (R=CH_3, C_6H_5) [14].

It is also affirmed that the alkylation of triazoles (**2**)(R=Ar) with ethyl chloroacetate in ethanol (in the presence of sodium acetate) or with ethyl chloroacetate in basic medium leads to mixtures, while the alkylation with chloroacetic acid in ethanol in presence of sodium acetate leads exclusively to S-alkylated product [12].

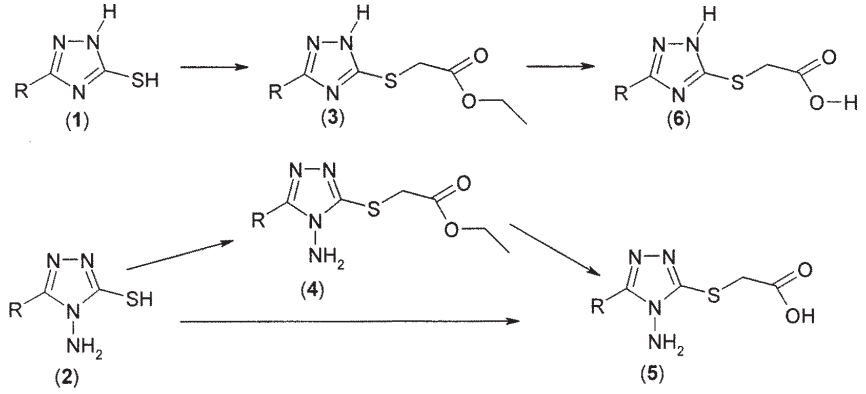
Such differences have led us to try to establish the conditions for the S-alkylation reaction of compounds (**1**) and (**2**) (where R=C_6H_5), and then to apply them to the alkylation of other mercapto-triazoles and amino-mercapto-triazoles(**1**, **2**).

Experimental part

Materials and methods

The reagents were commercial products (Merck, Fluka, Aldrich) and used without further purification. 1*H*-5-mercapto-3-phenyl-1,2,4-triazole (**1**)(R=C_6H_5) and 4*H*-4-amino-5-mercapto-3-phenyl-1,2,4-triazole (**2**) were prepared according to the literature [13,16].

Melting points were determined on a Böetius PHMK (Veb Analytik Dresden) instrument, and thin-layer



Scheme 1. S-alkylation reactions for 3-substituted 1*H*-5-mercapto-1,2,4-triazoles (**1**) and 4*H*-4-amino-5-mercapto-1,2,4-triazoles (**2**)

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chromatography was carried out on silica gel-coated plates 60 F_{254} Merck using benzene:methanol 7:3, benzene:methanol 3:7 or benzene:ethyl acetate 1:1 (v/v) as eluant.

Mass spectra GC-MS were performed on an Agilent G1701DA apparatus using methanol as carrying solvent.

IR spectra were recorded in KBr pellet on a Jasco FT/IR-410 spectrophotometer. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker Avance AC200 or on Bruker Avance III 400 spectrometers in DMSO-d_6, using TMS as reference, chemical shifts being reported in ppm and the coupling constants in Hz.

*Synthesis of 1H-5-ethoxycarbonyl-methylsulfanyl-3-phenyl-1,2,4-triazole (**3**)*

Route A

To a suspension of 1*H*-3-phenyl-5-mercapto-1,2,4-triazole(0.5g, 2.82 mmol) (**1a**) in absolute ethanol (10 mL), ethyl chloroacetate (0.346g, 0.30 mL, 2.82 mmol) is added. The mixture is heated under reflux for 7 hours, then cooled at room temperature and filtered under vacuum.

White crystals (0.71g, η=96%), m.p.= 137-139 °C (EtOH);

IR(cm^{-1}): 3436, 2936, 2845 (-CH_2-) , 2651 (large, -NH_2^+), 1730 (i, C=O), 1614, 1502, 1311, 1181, 1024, 867, 694.

GC-MS (70eV):m/e= 263 (M^+, 73%); 217 (M^+-C_2H_5OH, 36 %); 190 (M^+- $COOC_2H_5$, 100 %)

^{1}H-NMR δ_H (DMSO-d_6, 400 MHz): 9.89 (br.,s., 2H, NH_2^+); 8.00-7.98 (m, 2H, 2'-H, 6'-H); 7.53-7.48 (m, 3H, 3'-H, 4'-H, 5'-H); 4.12(q, 2H, J=7.1Hz, -O-C$\underline{H}_2$-CH_3); 4.07(s, 2H,-S-C$\underline{H}_2$-); 1.18(t, 3H, J=7.1Hz, -O-CH_2-C$\underline{H}_3$)

^{13}C-NMR δ_C (DMSO-d_6, 100 MHz): 168.6 (C=O); 156.7 (3-C); 156.6 (5-C); 130.0 (4'-C); 128.9 (3'-C, 5'-C); 127.5 (1'-C); 125.9 (2'-C, 6'-C); 60.1 (-O-$\underline{C}H_2$-CH_3); 33.5 (-S-CH_2); 13.9 (-O-CH_2-$\underline{C}H_3$).

Route B

To a suspension of 1*H*-5-mercapto-3-phenyl-1,2,4-triazole(**1a)** (2.2g, 12.42 mmol) in distilled water (20 mL) a NaOH 1M solution (12.5 mL) is added. The mixture is treated while hot with active charcoal, filtered off and the pale yellow solution is distilled to dryness at 40°C under vacuum. The solid product is suspended in absolute ethanol (20 mL), heated under reflux, then ethyl chloroacetate is added (1.53g, 1.33mL, 12.5 mmol). After 15 min of reflux, it is cooled at room temperature and distilled water is added (10 mL), then the suspension is kept for 24h at +5°C. Ethanol is removed by distillation and the white aqueous suspension is filtered under vacuum.

White crystals (3.07g, η=94%), m.p. = 137-139°C,

IR(cm^{-1}): 3430, 2978, 2854 (-CH_2-), 1724 (i, C=O), 1631, 1502, 1304, 1177, 1020, 867, 690.

^{1}H-NMR δ_H (DMSO-d_6 , 400 MHz): 14.45 (br.,s., 1H, NH); 7.98-7.96 (m, 2H, 2'-H, 6'-H); 7.54-7.48 (m, 3H, 3'-H, 4'-H, 5'-H); 4.13(q, 2H, -O-C$\underline{H}_2$-CH_3); 4.08(s, 2H,-S-C$\underline{H}_2$-); 1.19 (t, 3H, -O-CH_2-C$\underline{H}_3$)

^{13}C-NMR δ_C (DMSO-d_6, 100 MHz): 168.7 (C=O); 165.8 (3-C); 165.7 (5-C); 129.9 (4'-C); 128.9 (3'-C, 5'-C); 127.4 (1'-C); 125.9 (2'-C, 6'-C); 61.0 (-O-$\underline{C}H_2$-CH_3); 33.5 (-S-CH_2); 13.9 (-O-CH_2-$\underline{C}H_3$).

*Synthesis of 4H-4-amino-5-ethoxycarbonyl-methylsulfanyl-3-phenyl-1,2,4-triazole (**4a**)*

Route A

To a suspension of 4*H*-4-amino-5-mercapto-3-phenyl-1,2,4-triazole(**2a**) (3.84g, 20 mmol) in distilled water (30 mL), solid NaOH is added (0.8g, min. 98%). The brown solution is filtered hot with active charcoal, then distilled to dryness under vacuum at room temperature. The solid product is suspended in absolute ethanol (60 mL), ethyl chloroacetate is added (2.66g, 2.4 mL, 21 mmol), heated under reflux for 2 h, then cooled at room temperature and distilled to dryness under vacuum. The white product is suspended in distilled water and filtered.

White powder (4.82g, η=87%), m.p. = 174-175°C

IR(cm^{-1}): 3258 (-NH_2), 3136, 2985, 2940(CH_2), 1738 (C=O), 1645, 1454, 1309, 1179, 1031, 693, 530

GC-MS(70eV):m/e= 278 (M^+, 27 %); 233 (M^+-C_2H_5, 17 %); 205 (M^+-$COOC_2H_5$, 100 %)

^{1}H-NMR δ_H (DMSO-d_6, 200 MHz): 8.01-7.97 (m, 2H, 2'-H, 6'-H); 7.50-7.48 (m, 3H, 3'-H, 4'-H, 5'-H); 6.20 (s, 2H, -NH_2); 4.15(q, 2H, J=7.0 Hz, -O-C$\underline{H}_2$-CH_3); 4.08 (s, 2H,-S-C$\underline{H}_2$-); 1.21 (t, 3H, J=7.0 Hz, -O-CH_2-C$\underline{H}_3$)

^{13}C-NMR δ_C (DMSO-d_6, 50 MHz): 168.4 (C=O); 154.1 (3-C); 152.8 (5-C); 129.5 (4'-C); 128.4 (3'-C, 5'-C); 127.7 (1'-C); 126.8 (2'-C, 6'-C); 61.2 (-O-$\underline{C}H_2$-CH_3); 33.1 (-S-CH_2); 13.9 (-O-CH_2-$\underline{C}H_3$).

Route B

To a suspension of 4*H*-4-amino-5-mercapto-3-phenyl-1,2,4-triazole (**2a)** (0.5g, 2.6 mmol) in absolute ethanol (5 mL), chloroacetic acid is added (0.25g, 2.6 mmol). The mixture is heated under reflux for 14 h, then it is cooled at room temperature and filtered under vacuum. The crude product (0.25g, m.p.=152-154°C) was recrystallised from ethanol.

White powder (0.1g, η=14%), m.p.=174-176°C

IR(cm^{-1}): 3256 (-NH_3^+), 3137, 2984, 2938(CH_2), 1737 (C=O), 1645, 1455, 1310, 1180, 1033, 692, 530

GC-MS(70eV):m/e= 278 (M^+, 25 %); 233 (M^+-C_2H_5, 16 %); 205 (M^+- $COOC_2H_5$, 100 %)

^{1}H-NMR δ_H (DMSO-d_6, 200 MHz): 8.02-7.98 (m, 2H, 2'-H, 6'-H); 7.52-7.49 (m, 3H, 3'-H, 4'-H, 5'-H); 6.38 (br.,s, 3H, -NH_3^+); 4.16(q, 2H, J=7.1 Hz, -O-C$\underline{H}_2$-CH_3); 4.05 (s, 2H,-S-C$\underline{H}_2$-); 1.20 (t, 3H, J=7.1 Hz, -O-CH_2-C$\underline{H}_3$)

^{13}C-NMR δ_C (DMSO-d_6, 50 MHz): 168.3 (C=O); 153.9 (3-C); 153.1 (5-C); 129.8 (4'-C); 128.4 (3'-C, 5'-C); 127.8 (1'-C); 126.1 (2'-C, 6'-C); 61.2 (-O-$\underline{C}H_2$-CH_3); 33.1 (-S-CH_2); 13.9 (-O-CH_2-$\underline{C}H_3$).

Route C [13]

To a suspension of 4*H*-4-amino-3-phenyl-5-mercapto-1,2,4-triazole(**2a**) (1.0g, 5.2 mmol) in absolute ethanol (25 mL), ethyl chloroacetate (1.5g, 12.2 mmol)is added. The mixture is heated under reflux for 6 h, then distilled to dryness. The crude product (1.7g) is suspended in a mixture of NaOH 1M solution (10mL) and distilled water (25 mL) for 30 min at room temperature, then filtered, and the resulting product (0.43g) was recrystallised from absolute ethanol (8.6 mL).

White powder (0.36g, η=25%), m.p. = 172-174°C (m.p.= 172-173°C [13])

IR(cm^{-1}): 3255, 3136, 2983, 2940 (CH_2), 1735 (C=O), 1643, 694, 566

*Alkaline hydrolysis of 4H-4-amino-5-ethoxycarbonyl-methylsulfanyl-3-phenyl-1,2,4-triazole (**4a**)*

A suspension of 4*H*-4-amino-5-ethoxycarbonyl-methylsulfanyl-3-phenyl-1,2,4-triazole (**4a**) (2.5g, 9 mmol) in a NaOH 1M solution (20 mL) is heated under reflux for 1 hour. The solution is then acidified with diluted HCl to *p*H~3 and distilled to dryness. The white product is recrystallised from absolute ethanol.

4*H*-4-*amino-5-carboxy-methylsulfanyl-3-phenyl-1,2,4-triazole*(**5a**)

White powder (1.65g, η=73%), m.p.= 182-184°C. (m.p.=183-184°C [13])

IR(cm^{-1}): 3620 (OH), 3545, 3338, 3262, 3196, 2934 (CH_2), 1714 (C=O), 1617, 1402, 1250 (OH), 695, 566

^{1}H-NMR δ_H (DMSO-d_6, 200 MHz): 8.02-7.98 (m, 2H, 2'-H, 6'-H); 7.50-7.49 (m, 3H, 3'-H, 4'-H, 5'-H); 6.49 (br.,s, 3H, -NH_3^+); 3.96 (s, 2H,-S-C<u>H</u>$_2$-).

^{13}C-NMR δ_C (DMSO-d_6, 50 MHz): 169.9 (C=O); 153.9 (3-C); 153.2 (5-C); 129.5 (4'-C); 128.3 (3'-C, 5'-C); 127.7 (1'-C); 126.8 (2'-C, 6'-C); 34.8 (-S-CH_2).

*Alkaline hydrolysis of 1H-5-ethoxycarbonyl-methylsulfanyl-3-phenyl-1,2,4-triazole (**3a**)*

A suspension of 1H-5-ethoxycarbonyl-methylsulfanyl-3-phenyl-1,2,4-triazole (**3a**) (8.1g, 30.8 mmol) in a NaOH 5% solution (50 mL) is heated under reflux for 1 hour, then treated with active charcoal and filtered hot. The filtrate is then acidified with diluted HCl to pH~3, and the white suspension is filtered under vacuum.

1*H-5-carboxy-methylsulfanyl-3-phenyl-1,2*,4-*triazole* (**6a**)

White powder (7.0g, η=97%), m.p.=172-174°C

IR(cm^{-1}):3488 (OH), 3261,3188, 2937, 2877 (-CH_2-), 2546, 1728 (i, C=O), 1611, 1489, 1468, 1330, 1185, 903, 723, 683.

^{1}H-NMR δ_H (DMSO-d_6, 200 MHz): 13.7 (br., s, 1H, COO<u>H</u>); 8.03-8.01 (m, 2H, 2'-H, 6'-H); 7.54-7.48 (m, 3H, 3'-H, 4'-H, 5'-H); 4.04 (s, 2H,-S-C<u>H</u>$_2$-).

^{13}C-NMR δ_C (DMSO-d_6, 50 MHz): 169.9 (C=O); 156.9 (3-C); 156.8 (5-C); 129.9 (4'-C); 128.9 (3'-C, 5'-C); 127.9 (1'-C); 125.9 (2'-C, 6'-C); 34.0 (-S-CH_2).

*Diazotation of 4H-4-amino-5-carboxy-methylsulfanyl-3-phenyl-1,2,4-triazole (**5a**) and the displacement of the diazo group*

To a suspension of 4*H*-4-amino-5-carboxy-methylsulfanyl-3-phenyl-1,2,4-triazole (**5a**) (0.5g, 2.0 mmol) in a water-ethanol mixture (1:3, v/v, 10 mL) and HCl 1M (5 mL), a $NaNO_2$ 0.5M solution (5 mL) is added dropwise, under intense stirring. After 30 min of stirring, distilled water is added (10 mL), the mixture is concentrated under vacuum at room temperature and then filtered.

1H-5-carboxy-methylsulfanyl-3-phenyl-1,2,4-triazole (**6a**)

White powder (0.31g, η=66%), m.p.= 172-173°C.

IR(cm^{-1}):3471(OH), 3261, 3189, 2937, 2875 (-CH_2-), 2549, 1728 (i, C=O), 1611, 1489, 1469, 1331, 1186, 903, 723, 685.

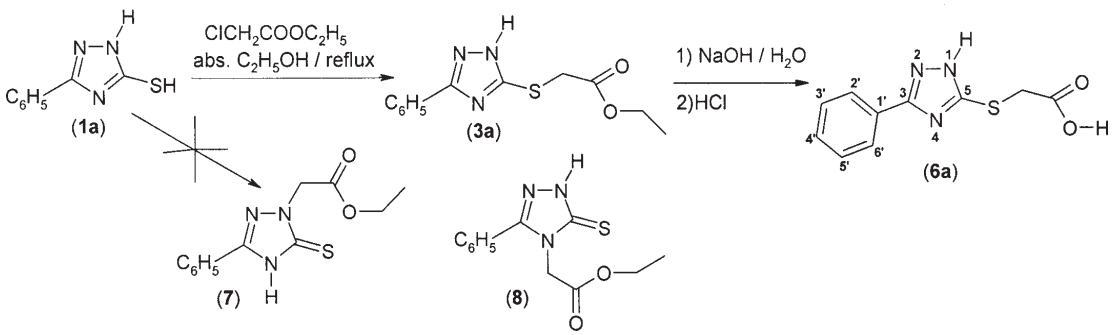
Results and discussion

The alkylation of 1*H*-5-mercapto-3-phenyl-1,2,4-triazole (**1a**) with ethyl chloroacetate to 1*H*-5-ethoxycarbonyl-methylsulfanyl-3-phenyl-1,2,4-triazole (**3a**) was performed according to literature data for the alkylation of 4*H*-4-amino-5-mercapto-3-phenyl-1,2,4-triazole (**2a**) and (**3a**) was obtained with 96% yield. The fact that the alkylation of (**1a**) with ethyl chloroacetate does not require the use of a base is determined by the increased basicity of the triazolic nucleus, which makes it able to bind the hydrochloric acid formed in reaction, and suggest that the thiol form of 1*H*-5-mercapto-3-phenyl-1,2,4-triazole (**1a**) is favored by the alcoholic medium.

Formation of an alkylated product is proven by the characteristic vibrations of the esteric carbonyl group (ν_{CO}=1730i, 1728i) from IR spectra and by mass spectrometry, regarding molecular ion peak and its fragmentation, characteristic for esters: M^+-C_2H_5, M^+-$COOC_2H_5$.

Formation of the S-alkylated product (**3a**) and not of those N-alkylated (**7**) or (**8**), was confirmed by ^{13}C-NMR spectra, where the chemical shift characteristic for C=S group (δ=180 ppm), possible only in N-alkylated compounds (**7**) or (**8**) no longer appears.

At the same time, analyzing 2D NMR ^{1}H-^{13}C HMBC spectra of (**3a**), long-distance couplings ^{3}J of triazolic carbon atoms 3-C with phenylic protons 2'-H and 6'-H, $^3J_{2',6'\text{-H},\ 3\text{-C}}$, respectively 5-C with methylenic protons –S-CH_2-, $^3J_{\text{-S-C}\underline{\text{H}}\text{2-},\ 5\text{-C}}$ are observed. It also notes that a long-distance coupling ^{2}J of the carbon atom from carbonyl group C=O with methylenic protons –S-CH_2- $^2J_{\text{C=O, -S-CH2-}}$ occurs, and a ^{3}J coupling with methylenic protons O-C<u>H</u>$_2$-, $^3J_{\text{C=O, O-C}\underline{\text{H}}\text{2-}}$.(fig. 1) By the analysis of 2D NMR ^{1}H–^{13}C HMBC spectra of the hydrolysis product (**6a**), long distance couplings ^{3}J of triazolic carbon 3-C with 2'-H and 6'-H, $^3J_{2',6'\text{-H},\ 3\text{-C}}$, respectively 5-C with methylenic protons –S-CH_2-, $^3J_{\text{-S-C}\underline{\text{H}}\text{2-},\ 5\text{-C}}$ are observed. Another long-distance coupling ^{2}J of the carbon atom from carboxylic C=O group with methylenic protons –S-CH_2- $^2J_{\text{C=O, -S-CH2-}}$ is observed. These long-distance couplings confirm the structure of the synthesized compound and allow a correct assign of chemical shifts from ^{1}H-NMR and ^{13}C-NMR spectra.



Scheme 2. S-alkylation of 1*H*-5-mercapto-3-phenyl-1,2,4-triazole

A further proof for the S-alkylation is the formation of 1*H*-5-carboxy-methylsulfanyl-3-phenyl-1,2,4-triazole (**6a**) at the diazotation of 4*H*-4-amino-5-carboxy-methylsulfanyl-3-phenyl-1,2,4-triazole (**5a**) in the presence of nitrous acid (generated *in situ* from sodium nitrite and hydrochloric acid) at room temperature (Scheme 4). Thus, the compound obtained *via* diazotation is identical to that obtained at alkaline hydrolysis of 1*H*-5-ethoxycarbonyl-methylsulfanyl-3-phenyl-1,2,4-triazole (**3a**) (scheme 2), as evidenced by the physicals properties and by the similarity of the two IR spectra (fig. **2**).

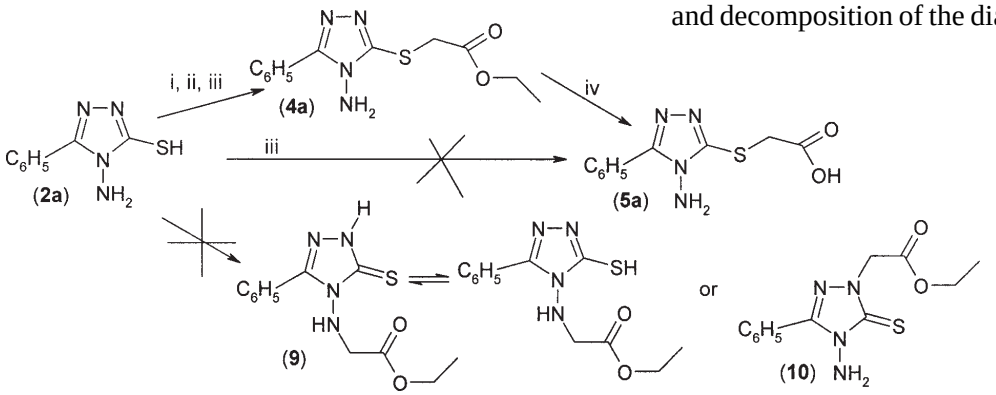
The alkylation of 4*H*-4-amino-5-mercapto-3-phenyl-1,2,4-triazole (**2a**) with ethyl chloroacetate and the alkaline hydrolysis of 4*H*-4-amino-5-ethoxycarbonyl-methylsulfanyl-3-phenyl-1,2,4-triazole (**4a**) to 4*H*-4-amino-5-carboxy-methylsulfanyl-3-phenyl-1,2,4-triazole (**5a**) was carried out accordingly to literature [13].

The attempt of direct alkylation of 4*H*-4-amino-5-mercapto-3-phenyl-1,2,4-triazole (**2a**) to 4*H*-4-amino-5-carboxy-methylsulfanyl-3-phenyl-1,2,4-triazole (**5a**) using chloroacetic acid in absolute ethanol at reflux led in ~23% yield to the (**4a**) ester, as confirmed by same physical and spectroscopic properties of the compound with the ones of the products obtained *via* routes i and ii. (scheme **3**).

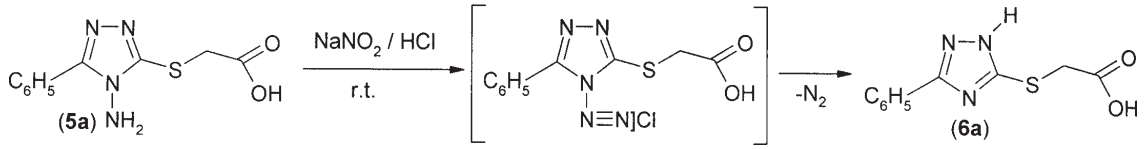
Low yields of alkylation reactions with ethyl chloroacetate and chloroacetic acid respectively, have led us to try another method of synthesis, namely, the alkylation of the sodium salt of 4*H*-4-amino-5-mercapto-3-phenyl-1,2,4-triazole (**2a**), prepared *in situ*, with ethyl chloroacetate in absolute ethanol at reflux. By this method, the yield increased to 87%, and the obtained ester (**4a**) has identical properties with the one previously prepared.

Formation of an alkylated product is also proven by characteristic vibrations of esteric carbonyl (ν_{CO}=1737cm^{-1}) groups. In this case, N-alkylation was excluded due to the fact that the chemical shift characteristic for C=S group (δ=180 ppm), no longer appears in ^{13}C-NMR spectra. The existence of thiol tautomeric form for (**9**) is also excluded, being known the property of 5-mercapto-1,2,4-triazoles to exist in thione tautomeric form [17].

As above mentioned, another proof for the S-alkylation is the deamination of the compound **5a** *via* diazotation and decomposition of the diazonium salt, leading to **6a.**



Scheme 3. S-alkylation of 4*H*-4-amino-5-mercapto-3-phenyl-1,2,4-triazole (**2a**)



Scheme 4. The removal of N-amino group by diazotation

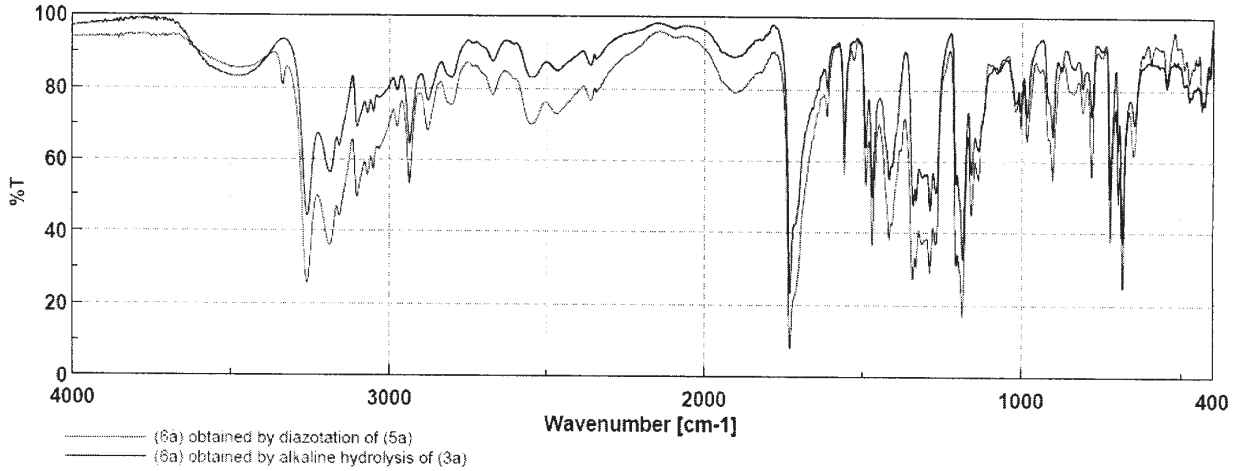


Fig. 1. Superposing of IR spectra for (**6a**) obtained by different routes

An interesting property of **4a, 5a** triazoles is the increased basicity of the exocyclic -NH_2 group, that can bind the proton even in aqueous medium.

Thus, the ^{1}H-NMR spectrum for **4a**, synthesized *via* route B, indicates the protonation of the exocyclic -NH_2 group by reaction-generated HCl (broad signal at δ=6.38, corresponding to three protons), while for **4a** synthesized from sodium salt of the triazole **2a** (route A), this signal is not observed (even if the melting point of the two compounds is identical).

Analyzing ^{1}H-NMR spectrum of **5a**, the protonation of exocyclic-NH_2 group is observed due to the amphionic structure, proven by the absence of carboxylic proton chemical shift (at δ=12.3 ppm) and by the presence of a broad signal at δ=6.49 ppm, corresponding to the three protons from -NH_3^+ group.

Conclusions

The alkylation of sodium salts of 1*H*-5-mercapto-3-phenyl-1,2,4-triazole (**1a**) and 4*H*-4-amino-5-mercapto-3-phenyl-1,2,4-triazole(**2a**), prepared *in situ*, with ethyl chloroacetate in absolute ethanol, is a simple and general method for the synthesis of S-alkylated compounds in good yields. This alkylation method can be extended to other α-halogenated esters, and other mercapto-triazoles.

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