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# Thiophene -2-carbaldehyde and Benzaldehyde Thiosemicarbazones in Reactions with Propargyl Bromide and 1,3-Dibromopropyne

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**Abstract**—The reaction of thiophene-2-carbaldehyde and benzaldehyde thiosemicarbazones with propargyl bromide in methanol provided S-(2-propyne)thiosemicarbazones hydrobromides of thiophene-2-carbaldehyde and benzaldehyde. Reaction products obtained from thiosemicarbazones and 1,3-dibromopropyne in methanol at heating were 2-thenilydene(benzylidene)azino-4-bromomethylidene-4,5-dihydrothiazol-3-ium bromides.

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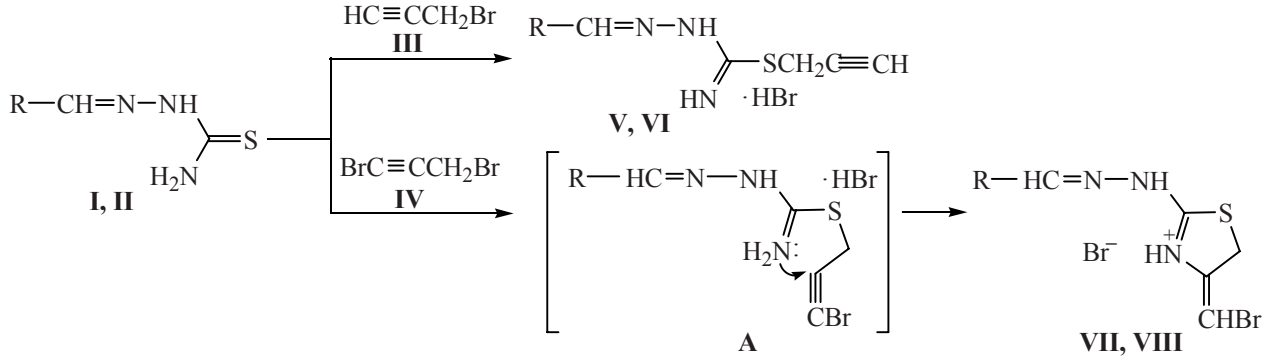
Thiosemicarbazones of aromatic and heterocyclic aldehydes and ketones are efficient ligands for complexing [1–3] and exhibit a high biological activity. Among these compounds substances were found possessing tuberculocidal [4–6], antimicrobial [7, 8], antibacterial [9], antiviral [10], antitumor [11], and malaricidal [12] actions.

Reactions of thiosemicarbazones with acetylene compounds up till now remain poorly understood. We described formerly a synthesis of substituted 1,3-thiazin-4-ones by a reaction of methyl propiolate with thiosemicarbazones in MeOH in the presence of triethylamine [13]. By the reaction of thiosemicarbazones with terminal α-acetylene ketones in MeCN at 20°C substituted 1,3,4-thiadiazolines were obtained in 83–97% yields [14].

It was reported in [15] that the reaction products obtained from thiosemicarbazones and acetylenedicarboxylate or dimethyl acetylenedicarboxylate in methanol at heating were substituted 1,3-thiadiazolidin-4-ones.

In this study we investigated the reaction of thiophene-2-carbaldehyde and benzaldehyde thiosemicarbazones (**I** and **II**) with propargyl bromide (**III**) and 1,3-dibromopropyne (**IV**) in anhydrous methanol at heating. In the reaction with propargyl bromide the only reaction products were S-(2-propyne)thiosemicarbazone hydrobromides of thiophene-2-carbaldehyde (**V**) and benzaldehyde (**VI**). In the IR spectra of the compounds appeared the absorption bands of the acetylene bond at 2120 and 2125 $cm^{-1}$. In the $^1H$ NMR spectra the proton signals of the fragment C≡CH were observed as singlets at 3.46 and 3.51 ppm.

Quite differently proceeded the reaction of thiosemicarbazones of thiophene-2-carbaldehyde (**I**) and

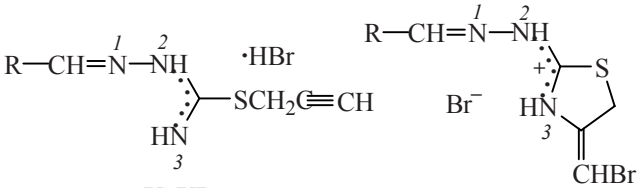



R = 2-thienyl (**I, V, VII**), Ph (**II, VI, VIII**).

benzaldehyde (**II**) with 1,3-dibromopropyne (**IV**) in anhydrous methanol at heating. Presumably intermediately S-(1-bromo-2-propyne)thiosemicarbazone hydrobromides formed of thiophene-2-carbaldehyde and benzaldehyde that under the synthesis conditions underwent the intramolecular cyclization into 2-thenilydeneazino-4-bromomethylidene-4,5-dihydrothiazol-3-ium bromide (**VII**) and 2-benzylideneazino-4-bromomethylidene-4,5-dihydrothiazol-3-ium bromide (**VIII**).

The composition and structure of synthesized compounds **V–VIII** were proved by elemental analysis and IR and $^{1}H$,$^{13}C$, $^{15}N$ NMR spectra. The IR spectra of compounds **VII** and **VIII** lack the absorption bands of the acetylene bond. In the $^{1}H$ NMR spectra the signals of the protons from the fragment =CHBr give rise to singlets at 6.53 and 6.69 ppm, the signals from the NH group of the ring and HN appear as broad singlets at 10.08 and 11.00 ppm. In the $^{13}C$ NMR spectra of compounds **VII** and **VIII** the carbon atoms of the group =CHBr are observed at 87.68 and 90.06 ppm.

In 2D $^{1}H$–$^{15}N$ HMBC spectra of compounds **V–VIII** only two nitrogen signals are observed: of imine nitrogen atom (CH=N) in the region – 70–82 ppm and amine nitrogen atom (–NH–) in the region –204–207 ppm. The imine atom $N^{1}$ gives a cross-peak with the proton CH=N, whereas the amine nitrogen atom gives cross-peaks with the protons of fragments $CH_2$, =CHBr, and CH=N. Therefore it is presumable that the atoms $N^{2}$ and $N^{3}$ are structurally equivalent, and the structure of the compounds may be depicted as follows:




## EXPERIMENTAL

IR spectra were recorded on a spectrophotometer Specord 75IR from KBr pellets. $^{1}H$, $^{13}C$, and $^{15}N$ NMR spectra were registered from solutions of compounds in DMSO-$d_6$ at 20°C on a spectrometer Bruker DPX-400 (at operating frequencies 400.13, 100.62, and 40.54 MHz respectively). As internal reference for $^{1}H$ and $^{13}C$ NMR spectra was used HMDS, for $^{15}N$ NMR spectra, $MeNO_2$.

**S-(2-Propyne)thiosemicarbazone hydrobromide of thiophene-2-carbaldehyde (V).** To a solution of 0.93 g (5 mmol) of thiophene-2-carbaldehyde thiosemicarbazone (**I**) in 20 ml of anhydrous methanol was added at stirring a solution of 0.6 g (5 mmol) of propargyl bromide (**III**) in 15 ml of anhydrous methanol. The reaction mixture was brought to boiling, it was stirred for 2 h, the solvent was partially evaporated, the solution was cooled to 0°C, the precipitated crystals were filtered off, washed on the filter with cold methanol, and dried in a vacuum. Yield 1.03 g (67%), colorless crystals, mp 189–191°C. IR spectrum, ν, $cm^{-1}$: 590 (C–S), 1420 ($CH_2$, bend.), 1580, 1635 (C=N, C=C), 2120 (C≡C), 2940 ($CH_2$), 3220 ($NH_2$). $^{1}H$ NMR spectrum, δ, ppm: 3.46 s (1H, a"CH), 4.27 s (2H, $CH_2$), 7.18–7.70 m (3H, $C_4H_3S$), 8.61 s (1H, CH=N), 9.65 s (2H, $NH_2$). $^{13}C$ NMR spectrum, δ, ppm: 20.32 ($CH_2$), 76.10 (≡CH), 77.93 ($CH_2C$≡), 128.39, 132.23, 134.47, 136.59 ($C_{arom}$), 148.11 (CH=N), 161.71 (N=CS). $^{15}N$ NMR spectrum, δ, ppm: –76.2 (CH=N), –206.2 (NH). Found, %: C 35.15; H 3.19; Br 26.39; N 13.55; S 20.74. $C_9H_{10}BrN_3S_2$. Calculated, %: C 35.53; H 3.29; Br 26.32; N 13.82; S 21.05.

**S-(2-Propyne)thiosemicarbazone hydrobromide of benzaldehyde (VI)** was obtained similarly to compound **V** from 0.6 g (5 mmol) of benzaldehyde thiosemicarbazone (**II**) and 0.6 g (5 mmol) of propargyl bromide (**III**) in anhydrous methanol at 65°C. Yield 1.22 g (82%), colorless crystals, mp 206–208°C. IR spectrum, ν, $cm^{-1}$: 585 (CS), 1420 ($CH_2$, bend.), 1585, 1640 (C=N, C=C), 2125 (C≡C), 2945 ($CH_2$), 3245 ($NH_2$). $^{1}H$ NMR spectrum, δ, ppm: 3.51 s (1H, ≡CH), 4.39 s (2H, $CH_2$), 7.47–7.96 m (5H, $C_6H_5$), 8.50 s (1H, CH=N), 9.98 br.s (2H, $NH_2$). $^{13}C$ NMR spectrum, δ, ppm: 20.44 ($CH_2$), 76.09 (≡CH), 77.70 ($CH_2C$≡), 128.54, 128.80, 131.78, 132.37 ($C_{arom}$), 152.99 (CH=N), 162.58 (N=CS). $^{15}N$ NMR spectrum, δ, ppm: –70.2 (CH=N), –207.3 (NH). Found, %: C 44.12; H 3.89; Br 26.76; N 14.24; S 11.07. $C_{11}H_{12}BrN_3S$. Calculated, %: C 44.30, H 4.03; Br 26.85; N 14.09; S 10.74.

The reaction carried out in dioxane at microwave activation (4 min, power 360 W) gave the product in 55% yield, mp 208°C. The microwave activation significantly reduced the reaction time, but the yield was smaller due to the tarring of the reaction mixture.

**2-Thenylideneazino-4-bromomethylidene-4,5-dihydrothiazol-3-ium bromide (VII).** To a solution of 0.93 g (5 mmol)of thiophene-2-carbaldehyde thiosemicarbazone (**I**) in 15 ml of anhydrous methanol added at stirring 0.99 g (5 mmol) of 1,3-dibromopropyne (**IV**) in 15 ml of anhydrous methanol. The reaction mixture was

brought to boiling, it was stirred for 2.5 h, methanol was partly evaporated, the solution was cooled to 0°C, the precipitated crystals were filtered off, washed on the filter with cold methanol, and dried in a vacuum. Yield 1.74 g (91%), colorless crystals, mp 162–164°C. IR spectrum, ν, $cm^{-1}$: 585 (CS), 1430 ($CH_2$, bend.), 1590, 1630 (C=N, C=C), 2930 ($CH_2$), 3440 (NH, $HN^+$). $^1H$ NMR spectrum, δ, ppm: 4.38 s (2H, $CH_2$), 6.53 s (1H, =CHBr), 7.29–8.04 m (3H, $C_4H_3S$), 8.86 s (1H, CH=N), 10.00 br.s (1H, NH), 10.80 br.s (1H, NH in the ring). $^{13}C$ NMR spectrum, δ, ppm: 34.62 ($CH_2$), 87.68 (=CHBr), 128.58, 134.37, 135.25, 136.72 ($C_{arom}$), 136.46 (C=CHBr), 162.04 (CH=N), 169.11 (N=CS). $^{15}N$ NMR spectrum, δ, ppm: –82.8 (CH=N), –204.0 (NH). Found, %: C 28.54; H 2.12; Br 42.05; N 10.71; S 16.54. $C_9H_9Br_2N_3S_2$. Calculated, %: C 28.20; H 2.35; Br 41.78; N 10.97; S 16.71.

**2-Benzylideneazino-4-bromomethylidene-4,5-dihydrothiazol-3-ium bromide (VIII)** was obtained similarly to compound **VII** from 3 g (5 mmol) of benzaldehyde thiosemicarbazone (**II**) and 0.99 g (5 mmol) of 1,3-dibromopropyne in anhydrous methanol at heating. Yield 1.45 g (77%), colorless crystals, mp 189–190°C. IR spectrum, ν, $cm^{-1}$: 580 (CS), 1435 ($CH_2$, bend.), 1585, 1640 (C=N, C=C), 2935 ($CH_2$), 3150 (NH). $^1H$ NMR spectrum, δ, ppm: 4.02 s (2H, $CH_2$), 6.69 s (1H, =CHBr), 7.52–8.03 m (5H, $C_6H_5$), 8.53 s (1H, CH=N), 10.20 br.s (1H, HN), 11.00 br.s (1H, NH in the ring). $^{13}C$ NMR spectrum, δ, ppm: 35.20 ($CH_2$), 90.06 (=CHBr), 129.09, 129.38, 131.69, 132.82 ($C_{arom}$), 135.94 (C=CHBr), 164.39 (CH=N), 169.99 (N=CS). $^{15}N$ NMR spectrum, δ, ppm: –78.3 (CH=N), –204.6 (NH). Found, %: C 35.40; H 2.98; Br 42.34; N 10.98; S 8.30. $C_{11}H_{11}Br_2N_3S$. Calculated, %: C 35.01; H 2.92; Br 42.44; N 11.14; S 8.49.

The reaction carried out in dioxane at microwave activation in 4 min gave the product in 48% yield.

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