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One-Pot Synthesis and Antimicrobial Activity of *O*-Alkyl Hydrazinecarbothioates

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Abstract—*O*-Alkyl hydrazinecarbothioates, which are potential building blocks in the synthesis of heterocycles and antimicrobial agents, were obtained from primary alcohols in 38–89% yields by a one-pot method. The obtained compounds are characterized by thione-thiol tautomerism in a solution. An experimental screening for antibacterial and antifungal activity of hydrazinecarbothioates was performed, the highest activity was found against *B. cereus* and *St. aureus* strains.

Keywords: hydrazinecarbothioates, one-pot synthesis, cascade synthesis, antibacterial activity, antifungal activity

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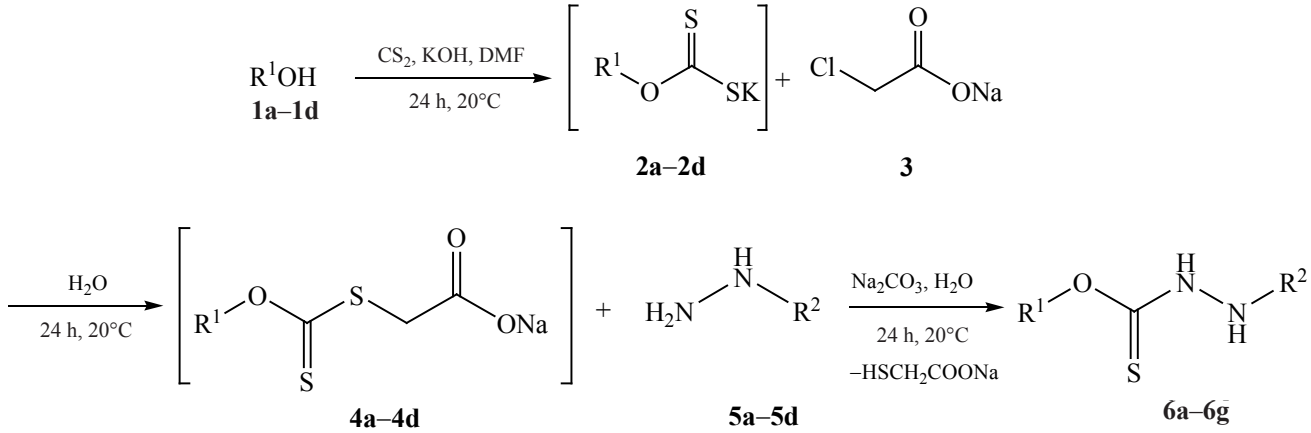
Hydrazinecarbothioates are a class of organic compounds with three nucleophilic sites that are useful in terms of synthetic possibilities and biological research. Due to their high reactivity, these compounds can serve as building blocks in the synthesis of heterocyclic compounds with different biological activities [1–3]. Among the few data on the study of the biological properties of hydrazinecarbothioates, there is information on the manifestation of their antituberculosis and antiparasitic activities [1, 4].

Since the resistance of microorganisms to the drugs used is increasing, the number of new antibacterial and antifungal agents is decreasing, and the volumes of their consumption are increasing [5], the search for new substances with antimicrobial activity is very relevant. Among hydrazine derivatives, hydrazides [6–9] and thiohydrazones [10–12] exhibit high antimicrobial activity; therefore, we can assume a high probability of antimicrobial activity in hydrazine carbothioates, and we have undertaken to improve the method of their synthesis and study the antimicrobial activity.

In general, hydrazinecarbothioates can be obtained by alkylation of sodium/potassium xanthates followed by acylation of hydrazines [3]. Relatively few xanthates are commercially available; the rest must be prepared from alcohols and carbon disulfide [13–15]. To increase the availability of substituted *O*-alkyl hydrazinecarbothioates, we proposed a cascade one-pot scheme for their synthesis directly from alcohols (Scheme 1).

At the first stage, primary alcohols **1a**–**1d** were reacted with carbon disulfide and potassium hydroxide in a dimethylformamide medium; an aqueous solution of sodium chloroacetate **3** was added to the resulting potassium alkyl xanthates **2a**–**2d** without isolating them from the reaction mixture, and intermediate 2-[(alkoxycarbonothioyl)sulfanyl] acetates **4a**–**4d** were obtained. Their subsequent reaction with substituted hydrazines **5a**–**5d** in the presence of sodium carbonate leads to hydrazinecarbothioates **6a**–**6g**. The reactions proceed at room temperature without the use of expensive catalysts. The developed procedure is suitable for using primary monohydric (R^1OH) and dihydric (HOR^2OH) alcohols with different chain lengths (R^1 = ethyl, butyl, decyl; R^2 = hexanediyl), on the one hand, and for various substituted phenyl- and benzylhydrazines, on the other hand. Yields of target hydrazinecarbothioates reach 89%. Structure of the obtained compounds was confirmed by ^1H, ^{13}C NMR and HRMS-ESI mass spectrometry data.

Scheme 1.



1, **2**, **4:** R^1 = Et (**a**), Bu (**b**), $C_{10}H_{21}$ (**c**), $HO(CH_2)_6$ (**d**); **5**, R^2 = Ph (**a**), 2-$CH_3C_6H_4$ (**b**), $C_6H_4CH_2$ (**c**), 4-FPh (**d**); **6**, R^1 = Bu (**a**, **c**), Et (**b**, **d**), $C_{10}H_{21}$ (**e**, **f**), PhNHNHC(=S)O$(CH_2)_6$ (**g**); R^2 = Ph (**a**, **e**, **g**), 2-$CH_3C_6H_4$ (**b**, **c**), Bn (**d**), 4-FPh (**f**).

Compounds **6a**–**6g** can exist in two tautomeric forms (Scheme 2), which is confirmed by NMR spectroscopy data. The NMR spectra of compound **6a** showed a double set of signals in a 1 : 1 ratio. The ^{1}H NMR spectrum shows broadened singlets at 7.86 and 8.02 ppm, which belong to the protons of two N^2H groups in two tautomers, as well as signals at 10.53 and 10.83 ppm, corresponding to the protons of the SH group of tautomer **6a′** and the N^1H group of tautomer **6a**. A similar signal splitting is observed in the ^{13}C NMR spectrum. The ratio of tautomers is not the same for all compounds (1 : 1), in a solution of compound **6d** it is 3 : 1 with a predominance of the N^1H tautomer, while in solutions of compounds **6e**–**6g**, the predominance of the N^1H tautomer is insignificant (3 : 2).

We performed primary screening of compounds **6a**–**6g** against test cultures *C. albicans*, *C. tropicalis*, *E. coli*, *St. aureus* and *B. cereus* (Table 1). When studying the antifungal activity of the obtained compounds, it was found that hydrazinecarbothioates **6a**–**6g** inhibit the growth of *Candida* yeasts, especially *C. albicans*. Compound **6a** turned out to be the most effective, for which the minimum cidal concentration (MCC) is on the same level as the reference drug, fluconazole (16.0 μg/mL). Compounds **6b** and **6c** also had a pronounced antifungal effect against *C. albicans*: the minimum inhibitory concentration (MIC) was 62.5 μg/mL. The remaining compounds are much less active (MIC 125.0 μg/mL). With respect to *C. tropicalis*, hydrazinecarbothioates showed a significantly lower antifungal effect.

The antimicrobial effect of compounds **6a**–**6g** was observed against gram-positive bacteria. They had a bacteriostatic effect on the culture of *B. cereus* at concentrations from 4.0 to 31.0 μg/mL, and the bactericidal effect was manifested when the concentration was doubled. Compounds **6a**–**6e** are the most active (MIC 4.0 μg/mL, MCC 8.0 μg/mL), their activity is higher than that of the reference drug vancomycin. With regard to *St. aureus*, compounds **6e** and **6g** showed the greatest antibacterial effect. The obtained compounds did not show pronounced antibacterial activity against the gram-negative bacterium *E. coli* (MCC in the range of 125.0–250.0 μg/mL).

A comparison of the structure of the synthesized hydrazinecarbothioates with their antimicrobial activity shows that with an increase in the alkyl chain R^1 length (with an increase in lipophilicity), the activity of the compounds with respect to *St. aureus* increases: cytotoxic concentration c_{cyt} 62.5 (R^1 = ethyl), 31.0 (R^1 = butyl),

Scheme 2.

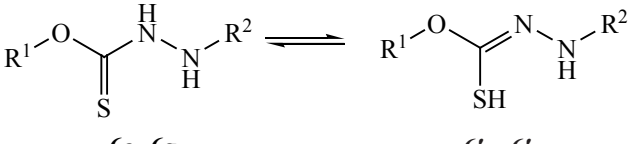


Table 1. Antimicrobial activity of hydrazinecarbothioates **6a–6g**

Compound	*B. cereus*		*St. aureus*		*E. coli*		*C. albicans*		*C. tropicalis*	
	MCC, μg/mL	MIC, μg/mL	MCC, μg/mL	MIC, μg/mL	MCC, μg/mL	MIC, μg/mL	MCC, μg/mL	MIC, μg/mL	MCC, μg/mL	MIC, μg/mL
6a	8.0	4.0	31.0	8.0	125.0	62.5	16.0	8.0	62.5	31.0
6b	8.0	4.0	62.5	16.0	125.0	62.5	62.5	31.0	125.0	62.5
6c	8.0	4.0	31.0	8.0	250.0	125.0	62.5	31.0	125.0	125.0
6d	8.0	4.0	62.5	31.0	250.0	125.0	125.0	31.0	125.0	62.5
6e	8.0	4.0	8.0	4.0	250.0	125.0	125.0	31.0	125.0	125.0
6f	62.5	31.0	31.0	16.0	250.0	125.0	125.0	31.0	125.0	62.5
6g	16.0	8.0	8.0	4.0	250.0	125.0	125.0	31.0	125.0	125.0
Fluconazole	–	–	–	–	–	–	16.0	4.0	62.5	31.0
Vancomycin	16.0	8.0	16.0	8.0	–	–	–	–	–	–

8.0 μg/mL (R^1 = decyl or hexyl). The introduction of an electron-withdrawing fluorine atom into the aryl fragment R^2 (compound **6e**) leads to a noticeable decrease in activity against *St. aureus* and *B. cereus*.

In conclusion, we developed a cascade one-pot method for the preparation of *O*-alkyl hydrazinecarbothioates from primary monohydric and dihydric alcohols with yields up to 89%. The thione-thiol tautomerism of hydrazinecarbothioates was detected for the first time using NMR spectroscopy method. An experimental screening of the antibacterial and antifungal activity of hydrazinecarbothioates was performed; it was found that the highest antimicrobial activity (comparable to commercial antimicrobial agents) is observed in *O*-butyl-2-phenylhydrazinecarbodithioate.

EXPERIMENTAL

All reagents were purchased from Sigma Aldrich, Scharlau, and Fisher Chemical. Melting points were determined by the capillary method and were not corrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III HD spectrometer (400.13 and 100.62 MHz, respectively). High resolution mass spectra (HRMS) were recorded on a Bruker micrOTOF spectrometer (Positive Ion Electrospray Ionization).

General procedure for the synthesis of compounds 6a–6g. To 0.1 mol of primary alcohol **1a**–**1d** and 50 mL of dimethylformamide was added 6.2 g (0.11 mol) of powdered KOH. The resulting mixture was stirred for 30 min at room temperature, then 7.2 mL (9.1 g, 0.12 mol) of carbon disulfide was rapidly added dropwise. The mixture warmed up slightly and turned orange in color. After stirring for 1 day at room temperature, a solution of 11.6 g (0.1 mol) of sodium chloroacetate **3** in 150 mL of water was added. The resulting mixture was stirred for 1 day, then were added 0.1 mol of arylhydrazine hydrochloride **5a**–**5d**, 8.5 g (0.1 mol) of sodium bicarbonate and the mixture was stirred for 24 h. The precipitate was filtered off, washed with water, dried in air, and recrystallized from hexane. The obtained compounds were crystalline substances stable in air.

***O*-Butyl 2-phenylhydrazinecarbothioate (6a).** Yield 89%, colorless needles, mp 71–73°C, R_f 0.50 (hexane–ethyl acetate, 3 : 1). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.73 t (3H, Me, ^3J 8.0 Hz, **6′a**), 0.93 t (3H, Me, ^3J 8.0 Hz, **6a**), 1.04–1.13 m (2H, CH_2, **6′a**), 1.36–1.50 m (4H, CH_2, **6a**, **6′a**), 1.64–1.71 m (2H, CH_2, **6a**), 4.36 t (2H, CH_2, ^3J 8.0 Hz, **6a**), 4.42 t (2H, CH_2, ^3J 8.0 Hz, **6′a**), 6.65–6.76 m (6H, Ph, **6a**, **6′a**), 7.14–7.19 m (4H, Ph, **6a**, **6′a**), 7.86 s (1H, N^{2}H, **6′a**), 8.02 s (1H, N^{2}H, **6a**), 10.53 br. s (1H, SH, **6′a**), 10.83 br. s (1H, N^{1}H, **6a**). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.81 t (3H, Me, J 7.3 Hz, **6′a**), 1.00 t (3H, Me, ^3J 7.3 Hz, **6a**), 1.11–1.16 m (2H, CH_2, **6′a**), 1.43–1.49 m (2H, CH_2, **6a**), 1.54–1.58 m (2H, CH_2, **6′a**), 1.74–1.78 m (2H, CH_2, **6a**), 4.46–4.53 m (4H, CH_2, **6a**, **6′a**), 5.93 s (1H, N^{2}H, **6′a**), 6.47 s (1H, N^{2}H, **6a**), 6.78–6.99 m (6H, Ph, **6a**, **6′a**), 7.23–7.30 m (4H, Ph, **6a**, **6′a**), 8.11 br. s (1H, SH, **6′a**), 8.31 br. s (1H, N^{1}H, **6a**). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 14.52,14.68, 18.61, 19.00, 30.64, 30.82, 70.14, 70.45, 112.40, 112.91, 119.40, 129.24 (2C), 129.28 (2C), 148.50, 149.04, 191.32, 192.43. ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.81, 13.56, 18.68, 19.08, 30.37, 30.62, 71.47, 72.22, 113.16, 114.14,

121.39, 121.78, 129.27 (4C), 147.08, 147.17, 192.24, 192.33. Mass spectrum (HRMS-ESI), *m/z*: 225.1073 $[M + H]^+$ (calculated for $C_{11}H_{16}N_2OS$: 225.1062).

***O*-Ethyl 2-(2-methylphenyl)hydrazinecarbothioate (6b).** Yield 81%, colorless needles, mp 62–64°C, R_f 0.44 (hexane–ethyl acetate, 3 : 1). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.11 t (3H, Me, ^3J 8.0 Hz, **6′b**), 1.30 t (3H, Me, ^3J 8.0 Hz, **6b**), 2.13 s (3H, MePh, **6′b**), 2.19 s (3H, MePh, **6b**), 4.39–4.49 m (4H, CH_2, ^3J 8.0 Hz, **6b**, **6′b**), 6.55–6.73 m (4H, Ph, **6b**, **6′b**), 7.00–7.04 m (4H, Ph, **6b**, **6′b**), 7.22 s (1H, N^{2}H, **6′b**), 7.53 s (1H, N^{2}H, **6b**), 10.54 br. s (1H, SH, **6′b**), 11.00 br. s (1H, N^{1}H, **6b**). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 14.48, 14.74, 17.65, 66.40, 66.68, 111.45, 111.79, 119.41, 119.71, 122.03, 122.58, 126.92 (2C), 130.48, 130.55, 146.00, 146.44, 191.01, 191.43. Mass spectrum (HRMS-ESI), *m/z*: 211.3088 $[M + H]^+$ (calculated for $C_{10}H_{14}N_2OS$: 211.3087).

***O*-Butyl 2-(2-methylphenyl)hydrazinecarbothioate (6c).** Yield 71%, colorless needles, mp 76–78°C. R_f 0.51 (hexane–ethyl acetate, 3 : 1). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.72 t (3H, Me, ^3J 8.0 Hz, **6′c**), 0.93 t (3H, Me, ^3J 8.0 Hz, **6c**), 1.03–1.12 m (2H, CH_2, **6′c**), 1.36–1.49 m (4H, CH_2, **6c**, **6′c**), 1.65–1.72 m (2H, CH_2, **6c**), 2.13 t (3H, MePh, ^3J 8.0 Hz, **6′c**), 2.19 t (3H, MePh, ^3J 8.0 Hz, **6c**), 4.33 t (2H, CH_2, ^3J 8.0 Hz, **6′c**), 4.43 t (2H, CH_2, ^3J 8.0 Hz, **6c**), 6.56–6.73 m (2H, Ph, **6′c**), 6.66–6.73 m (2H, Ph, **6c**), 7.00–7.06 m (4H, Ph, **6c**, **6′c**), 7.21 s (1H, N^{2}H, **6′c**), 7.51 s (1H, N^{2}H, **6c**), 10.56 br. s (1H, SH, **6′c**), 10.99 br. s, (1H, N^{1}H, **6c**). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 13.86, 14.09, 17.65, 18.63, 19.02, 30.56, 30.79, 70.24, 70.38, 111.40, 111.77, 119.77, 121.94, 122.45, 126.50 (2C), 130.51 (2C), 146.00, 146.61, 191.14, 191.92. Mass spectrum (HRMS-ESI), *m/z*: 239.1212 $[M + H]^+$ (calculated for $C_{12}H_{18}N_2OS$: 239.1218).

***O*-Ethyl 2-benzylhydrazinecarbothioate (6d)** was obtained according to the general procedure and further purified using acid-base reprecipitation. Compound **6d** was stirred in 3% NaOH solution, insoluble impurities were filtered off, the filtrate was neutralized with acetic acid. The precipitate was filtered off, washed with water, dried, and recrystallized from heptane. Yield 38%, colorless needles, mp 80–82°C, R_f 0.33 (hexane–ethyl acetate, 3 : 1). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.24 t (12H, Me, ^3J 8.0 Hz, **6d**, **6′d**), 3.89 s (2H, C$\underline{H}_2$Ph, **6′d**), 3.95 s (6H, C$\underline{H}_2$Ph, **6d**), 4.36–4.46 m (8H, Ph, **6d**, **6′d**), 7.24–7.39 m (20H, Ph, **6d**, **6′d**), 5.31 s (3H, N^{2}H, **6′d**), 5.51 s (1H, N^{2}H, **6d**), 10.07 br. s (1H, SH, **6′d**), 10.76 br. s (3H, N^{1}H, **6d**). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 14.56, 14.73, 54.23, 54.82, 66.08, 66.29, 127.51, 127.68, 128.52, 128.78, 128.97, 129.08, 137.94, 138.56, 188.52, 188.97. Mass spectrum (HRMS-ESI), *m/z*: 211.0910 $[M + H]^+$ (calculated for $C_{10}H_{14}N_2OS$: 211.0905).

***O*-Decyl 2-phenylhydrazinecarbothioate (6e).** Yield 84%, colorless needles, mp 73–75°C, R_f 0.68 (hexane–ethyl acetate, 3 : 1). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.87 t (5H, ^3J 8.0 Hz, **6′e**, **6e**), 1.02–1.38 m (24H, CH_2, **6′e**, **6e**), 1.43–1.50 m (2H, CH_2, **6′e**), 1.64–1.71 m (1.4H, CH_2, **6e**), 4.33 t (12H, CH_2, ^3J 8.0 Hz, **6′e**), 4.40 t (1.4H, CH_2, ^3J 8.0 Hz, **6e**), 6.63–6.75 m (5H, Ph, **6′e**), 7.15 t (3.4H, Ph, ^3J 8.0 Hz, **6e**), 7.87 s (0.7H, N^{2}H, **6f**), 8.02 s (1H, N^{2}H, **6′f**), 10.53 br. s (1H, SH, **6′f**), 10.82 br. s (0.7H, N^{1}H, **6f**). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 14.43, 22.59, 28.57, 28.70, 29.03, 29.19, 29.33, 29.44, 29.48, 31.75, 31.78, 70.36, 70.72, 112.33, 112.88, 119.29, 129.20, 148.52, 149.03, 191.31, 192.42. Mass spectrum (HRMS-ESI), *m/z*: 309.2023 $[M + H]^+$ (calculated for $C_{17}H_{28}N_2OS$: 309.2001).

***O*-Decyl 2-(4-fluorophenyl)hydrazinecarbothioate (6f).** Yield 80%, colorless crystals, mp 57–59°C, R_f 0.62 (hexane–ethyl acetate, 3 : 1). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.86 t (5H, ^3J 8.0 Hz, **6′f**, **6f**), 0.99–1.36 m (24H, CH_2, **6′f**, **6f**), 1.43–1.50 m (2H, CH_2, **6′f**), 1.65–1.69 m (1.4H, CH_2, **6f**), 4.32 t (2H, CH_2, ^3J 8.0 Hz, **6′f**), 4.39 t (1.4H, CH_2, ^3J 8.0 Hz, **6f**), 6.62–6.72 m (5H, Ph, **6′f**), 6.96–7.00 m (3.4H, Ph, **6f**), 7.82 s (0.7H, N^{2}H, **6f**), 8.00 s (1H, N^{2}H, **6′f**), 10.55 br. s (1H, SH, **6′f**), 10.84 br. s (0.7H, N^{1}H, **6f**). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 14.39, 22.58, 25.48, 25.76, 28.57, 28.70, 29.07, 29.19, 29.38, 29.43, 29.48, 31.73, 31.78, 70.40, 70.76, 113.61 d ($^3J_{CF}$ 6.0 Hz), 114.22, 115.50 d ($^2J_{CF}$ 22.0 Hz), 115.57 d ($^2J_{CF}$ 22.0 Hz), 115.72, 115.79, 145.05, 145.63, 155.32 d ($^1J_{CF}$ 233.0 Hz), 155.41 d ($^1J_{CF}$ 233.0 Hz), 157.65, 157.74, 191.28, 192.40. Mass spectrum (HRMS-ESI), *m/z*: 327.1802 $[M + H]^+$ (calculated for $C_{17}H_{27}FN_2OS$: 327.1906).

***O*,*O*'-Hexane-1,6-diylbis(2-phenylhydrazinecarbothioate) (6g)** was recrystallized from isopropyl alcohol. Yield 83%, colorless crystals, mp 120–122°C, R_f 0.62 (hexane–ethyl acetate, 3 : 1). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.84 m (1.7H, CH_2, **6′g, 6g**), 1.04–1.08 m (1.4H, CH_2, **6′g, 6g**), 1.18–1.22 m (1.4H, CH_2, **6′g, 6g**), 1.29–1.33 m (1.7H, CH_2, **6′g, 6g**), 1.43–1.54 m (1.7H, CH_2, ^3J 8.0 Hz, **6′g**), 1.70–1.73 m (1H, CH_2, **6g**),

4.23–4.43 m (3.4H, CH_2, **6′g**), 4.23–4.44 m (2.8H, CH_2, **6′g, 6g**), 4.43 t (1H, CH_2, ^3J 8.0 Hz, **6g**), 6.62–6.76 m (7.7H, Ph, **6′g**), 7.12–7.19 m (5H, Ph, **6g**), 7.88 s (1H, N^2H, **6g**), 8.01 s (0.7H, N^2H, **6′g**), 8.04 s (0.7H, N^2H, **6′g**), 10.53 br. s (0.7H, SH, **6′g**), 10.56 br. s (0.7H, SH, **6′g**), 10.83 br. s (1H, N^1H, **6g**). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 25.13, 24.93, 25.29, 25.51, 28.56, 28.70, 70.30, 70.66, 112.36, 112.90, 119.44, 129.21, 129.28, 148.51, 149.01, 191.29, 192.41. Mass spectrum (HRMS-ESI), *m/z*: 419.1568$[M + H]^+$ (calculated for $C_{20}H_{26}N_4O_2S_2$: 419.1575).

Antimicrobial activity of hydrazinecarbothioates was determined *in vitro* by the method of two-fold serial dilutions in liquid nutrient media, followed by inoculation on solid nutrient media in order to identify the nature of the antimicrobial effect (cid) [16] in relation to the following test microorganisms: *Staphylococcus aureus* ATCC 6538, *B. cereus* ATCC 10702, *Escherichia coli* ATCC 25922, *Candida albicans* ATCC 10231, *Candida tropicalis* ATCC 66029. To determine the minimum inhibitory concentration of the compound, meat-peptone broth was used for bacteria, and Sabouraud broth was used for yeast. The minimum cidal concentrations were determined by inoculation on the appropriate dense nutrient media. Working solutions of hydrazinecarbothioates were prepared at a concentration of 1000 μg/mL in a 50% DMSO aqueous solution. Microbial load was 10^4 cells per 1 mL. The tests were carried out in triplicate.

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CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

SUPPLEMENTARY INFORMATION

The online version contains supplementary material available at https://doi.org/10.1134/S1070363222080035.

REFERENCES

1. Patent US 5095024-A, 1990.
2. Sandström, J., *Acta Chem. Scand.*, 1960, vol. 14, no. 9, p. 1939.
3. Forsgren, B. and Sandstrom, J., *Acta Chem. Scand*., 1960, vol. 14, no. 4, p. 789.
4. Jensen, K.A., *Acta Chem. Scand*., 1961, vol. 15, no. 5, p. 1067.
5. Marston, H.D., Dixon, D.M., Knisely, J.M., Palmore, T.N., and Fauci, A.S., *J. Am. Med. Ass*., 2016, vol. 316, no. 11, p. 1193. https://doi.org/10.1001/jama.2016.11764
6. Pitucha, M., Karczmarzyk, Z., Swatko-Ossor, M., Wysocki, W., Wos, M., Chudzik, K., Ginalska, G., and Fruzinski, A., *Molecules*, 2019, vol. 24, no. 2, p. 251. https://doi.org/10.3390/molecules24020251
7. Turan-Zitouni, G., Altıntop, M. D., Özdemir, A., Demirci, F., Mohsen, U.A., and Kaplancıklı, Z.A., *J. Enzyme Inhib. Med. Chem*., 2013, vol. 28, no. 6, p. 1211. https://doi.org/10.3109/14756366.2012.723208
8. Brown, A.K., Aljohani, A.K.B., Alsalem, F.M.A., Broadhead, J.L., Gill, J.H., Lu, Y., and Sellars, J.D., *Molecules*, 2020, vol. 25, p. 2387. https://doi.org/10.3390/molecules25102387
9. Eldehna, W., Fares, M., Abdel-Aziz, M., and Abdel-Aziz, H., *Molecules*, 2015, vol. 20, p. 8800. https://doi.org/10.3390/molecules20058800
10. Kumar, A., Chaudhary, P., Singh, R., and Kaushik, N.K., *Main Group Chem*., 2016, vol. 15, p. 163. https://doi.org/10.3233/MGC-150196
11. Mishra, A.K., Manav, N., and Kaushik, N.K., *Spectrochim. Acta. (A)*, 2005, vol. 61, no. 13–14, p. 3097. https://doi.org/10.1016/j.saa.2004.11.035
12. Mishra, A.K., Mishra, S.B., Manav, N., and Kaushik, N.K., *J. Thermal Biol*., 2006, vol. 31, no. 8, p. 611. https://doi.org/10.1016/j.jtherbio.2006.07.003

13. Almanqur, L., Vitorica-yrezabal, I., Whitehead, G., Lewis, D.J., and O'Brien, P., *RSC Adv.*, 2018, vol. 8, no. 51, p. 29096. https://doi.org/10.1039/C8RA04917C
14. Liebing, P., Schmeide, M., Kühling, M., and Witzorke, J., *Eur. J. Inorg. Chem*., 2020, vol. 2020 N 25, p. 2428. https://doi.org/10.1002/ejic.202000258
15. Alanazi, A.M., Alam, F., Salhi, A., Missous, M., Thomas, A.G., O'Brien, P., and Lewis, D.J., *RSC Adv*., 2019, vol. 9 N 42, p. 24146. https://doi.org/10.1039/C9RA02926E
16. *Rukovodstvo po provedeniyu doklinicheskikh issledovaniy lekarstvennykh sredstv* (Guidelines for Conducting Preclinical Studies of Drugs), Mironov, A.N., Bunyatyan, N.D., Vasilyev, A.N., Verstakova, O.L., Zhuravleva, M.V., Lepakhin, V.K., Korobov, N.V., Merkulov, V.A., Orekhov, S.N., Sakaeva, I.V., Uteshev, D.B., and Yavorsky, A.N., Eds., Moscow: Grif and K, 2012, Pt. 1.