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Dedicated to the 115th anniversary of B.A. Arbuzov's birth

Synthesis and Antimicrobial Activity of Amines Containing Carbamoylmethylsulfonyl Fragments

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Abstract—A series of amines containing long hydrocarbon substituents and carbamoylmethylsulfonyl fragments have been synthesized. Antimicrobial activity of the prepared amines and their hydrochlorides against several test microorganisms has been investigated.

Keywords: antimicrobial activity, antimycobacterial activity, amines, carbamoylmethylsulfonyl group

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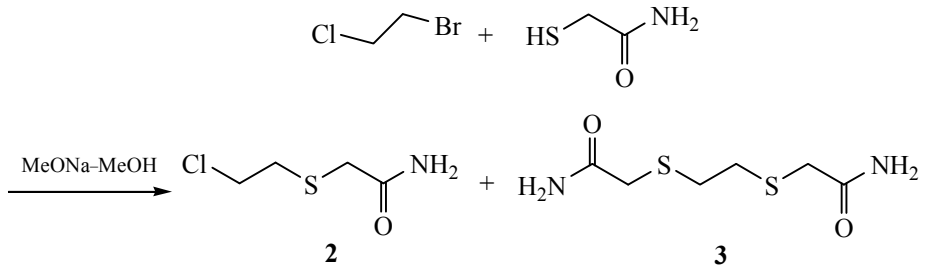
Many of tertiary ammonium compounds are known to exhibit bacteriostatic and bactericide properties and have been widely used as antiseptics in medicine [1–3]. The mechanism of their action is based on the interaction with phospholipids of cytoplasmatic membrane of a bacterial cell which causes its disorganization, flowing out of intracellular low-molecular compounds, decomposition of the proteins and nucleic acids, and lysis of cell wall [4, 5]. Low doses of tertiary ammonium compounds cause less deep changes and disorder the membrane functions: change the osmotic pressure, permeability, and rate of transfer of molecules and ion through the membrane, inhibit the metabolic processes and biological oxidation, and retard cell fission [5]. However, majority of the drugs of this group is inactive against intracellularly localized viruses, endospore form of bacteria, and tuberculosis mycobacteria [5–7]. On the other hand, it is known that different alkyl derivatives containing terminal carbamoylmethylsulfonyl group exhibit antimycobacterial properties but at the same time do not exhibit antimicrobial action against other microorganisms [8–10]. The investigation of *n*-octylsulfonylacetamide has shown that such compounds can affect the ATP-synthetase and components of respiretory chain of mycobacteria [11, 12]. The functionalization of such structures with alkylamine or alkylammonium groups may result in new properties, in particular, the combination of antimycobacterial and antimicrobial activity against different microorganisms.

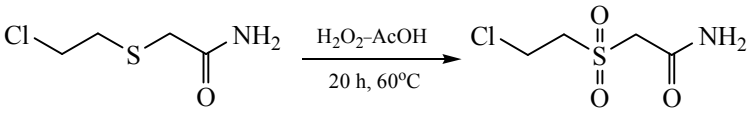
In this study, we synthesized a series of amines containing long hydrocarbon substituents and carbamoylmethylsulfonyl fragments in the *N*-alkyl chain. It was supposed that such compounds might exhibit a wide range of antimicrobial activity including that against tuberculosis mycobacteria. The key starting 2-[(2-chloroethyl)sulfonyl]acetamide **1** was prepared via the reaction of amide of thioglycolic acid with 1-bromo-2-chloroethane with further oxidation of the formed 2-[(2-chloroethyl)sulfanyl]acetamide **2** with hydrogen peroxide (Schemes 1 and 2). Significant amount of bis-1,2-(carbamoylmethylsulfanyl)ethane **3** was formed during the alkylation of thioglyconate [9]. To avoid its formation, the reaction should be carried out with large excess of 1-bromo-2-chloroethane. The optimal temperature for oxidation of 2-chloroethylsulfide **2** with hydrogen peroxide in acetic acid was found to be of 50–60°C; otherwise the yield of sulfone **1** was critically decreased.

The target tertiary (**4a**–**5c**) and secondary (**6a**, **6b**) amines containing carbamoylmethylsulfonyl fragments in the *N*-alkyl chain were prepared via the reaction of 2-[(2-chloroethyl)sulfonyl]acetamide **1** with different primary and secondary amines in the presence of carbonates (Schemes 3 and 4). The corresponding

Scheme 1.



Scheme 2.

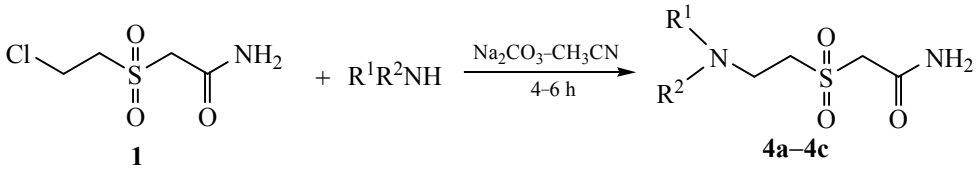


hydrochlorides **7a**, **7b** were prepared via the reaction of dodecyl(methyl)amine **4a** and hexadecylamine **6b** with HCl.

Dinonylamine **4b** and didecylamine **4c** were tar-like substances, other amines **4**–**6** were isolated as crystalline substances which did not exhibit a distinct melting point. Amines **4**–**6** were soluble in methanol and acetone, poorly soluble in ethyl acetate and acetonitrile, and insoluble in water.

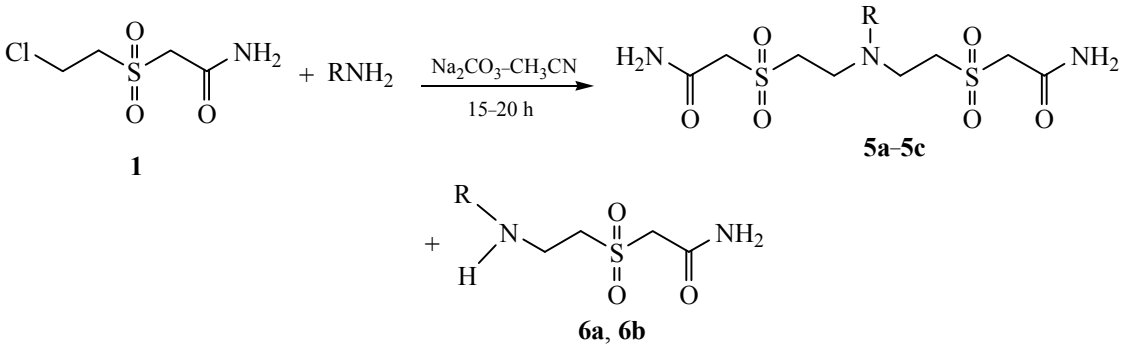
The screening of antimicrobial activity against a series of test microorganisms was performed for the prepared amines **4**–**6** and their hydrochlorides **7a**, **7b**. The results are given in Table 1. According to the obtained data, dodecyl(methyl)amine **4a** and its hydrochloride **7a** exhibited the highest bacteriostatic activity against *Staphylococcus aureus* and *Bacillus cereus* as compared with other studied compounds. The MIC value was 31.3 and 15.6 μg/mL, respectively, 2–4 times higher than that of reference drug

Scheme 3.



$R^1 = CH_3$, $R^2 = C_{12}H_{25}$ (**4a**); $R^1 = R^2 = C_9H_{19}$ (**4b**), $R^1 = R^2 = C_{10}H_{21}$ (**4c**).

Scheme 4.



R = C_8H_{17} (**5a**, **6a**), C_9H_{19} (**5b**), $C_{16}H_{33}$ (**5c**, **6b**).

Table 1. Bacteriostatic, fungistatic (MIC), bactericide (MBC), and fungicide (MFC) activity of 2-(carbamoylmethylsulfonyl)-ethylamines **4**–**6**[a] and their hydrochlorides **7**

Compound	*Staphylococcus aureus*		*Bacillus cereus*		*Candida albicans*	
	MIC, μg/mL	MBC/MFC, μg/mL	MIC, μg/mL	MBC/MFC, μg/mL	MIC, μg/mL	MBC/MFC, μg/mL
4a	15.6±1.2	15.6±1.2	31.3±2.7	–	62.5±5.7	62.5±5.7
4b	62.5±5.7	125.0±11.0	–	–	31.3±2.6	31.3±2.6
6b	125.0±11.0	–	–	–	–	–
7a	15.6±1.2	15.6±1.3	15.6±1.3	31.3±2.6	31.3±2.5	31.3±2.5
7b	–	125.0±12.0	–	–	–	–
Chloramphenicol	62.5±5.8		62.5±5.6		–	–

[a] Compounds **4c** and **5a**–**c** did not exhibit activity.

chloramphenicol. At the same time, the studied compounds limited the growth of yeast fungus *C. albicans* at concentrations 62.5 and 31.3 μg/mL, in contrast to chloramphenicol, and did not affect negatively on *E. coli*. The hydrochloride **7a** was found to be more active than the amine **4a**, probably because of the higher solubility in water. Dinonylamine **4b** exhibited bacteriostatic activity comparable with chloramphenicol against bacteria *St. aureus* (MIC 62.5 μg/mL) and fungistatic activity against fungi *C. albicans* (MIC 31.3 μg/mL). The investigated compounds were inactive against bacteria *Escherichia coli*, *Pseudomonas aeruginosa*, *Aspergillus niger*, and *Trichophyton mentagrophytes*.

The investigation of bactericide and fungicide action of the prepared compounds showed that compound **7a** at concentrations 15.6–31.3 μg/mL inhibited growth and caused death of microorganisms (Table 1). For example, hydrochloride **7a** exhibited bactericide action against *St. aureus* and *B. cereus* strains (MBC 15.6 and 31.3 μg/mL, respectively) and fungicide action against *C. albicans* (MFC 31.3 μg/mL).

Moreover, tuberculostatic activity of hydrochloride **7a** against lab strain *M. tuberculosis* H37Rv was investigated. Compound **7a** inhibited the growth of mycobacteria at concentration 12.5 μg/mL.

The degree of hemolysis of erythrocytes of human blood was measured for the most active compounds (Table 2). Compounds **4a**, **4b**, and **7a** at concentrations 15.6–62.5 μg/mL exhibited low hemolytic activity (0.4–5.2%). Hemolytic activity of the reference drug gramicidin S under the same conditions was 98–100%.

In summary, novel derivatives of amines containing long alkyl substitutes and carbamoylmethylsulfonyl fragments were synthesized. Some of them, in particular, [2-(carbamoylmethylsulfonyl)ethyl]dodecylamine **4a** and its hydrochloride **7a**, exhibited antimicrobial action against *Staphylococcus aureus* and *Bacillus cereus* as well as yeast fungus *Candida albicans* at concentrations 15.6–62.5 μg/mL and against lab strain of tuberculosis mycobacteria at concentration 12.5 μg/mL. Those compounds were not cytotoxic for human blood erythrocytes at concentrations suppressing the growth of bacteria and fungi. Taking into account the mentioned facts, the search of novel antiseptic drugs in the discussed class of the compounds is promising.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra (DMSO-d_6) were registered using AVANCE-600 and Bruker MSL-400

Table 2. Hemolytic activity of compounds **4a**, **4b**, and **7a**

Compound	Concentration, μg/mL	Hemolysis, %
4a	15.6	0.9
	31.3	0.4
	62.5	0.9
4b	31.3	0.4
	62.5	5.2
7a	15.6	0.5
	31.3	1.1
Gramicidin S	15.6	98
	31.3	99
	62.5	100

spectrometers (internal reference—Me_4Si). Thin-layer chromatography was performed on Silufol-254 plates (developer – iodine). Melting points were measured using a Boëtius heating bench. Mass spectra (MALDI-TOF) were registered using an Ultraflex III (Bruker) device (matrix—*p*-nitroaniline). The C, H, and N contents in the prepared compounds were determined using a CHN-3 device. The assessment of hemolytic activity of the synthesized compounds was performed using an AP-101 digital photoelectrocalorimeter (Apel).

2-[(2-Chloroethyl)sulfonyl]acetamide (1). 15.5 mL of 35% solution of H_2O_2 was added dropwise to a solution of 9.27 g (0.06 mol) of 2-[(2-chloroethyl)-sulfanyl]acetamide **2** in 100 mL of glacial acetic acid so that temperature of the reaction mixture did not exceed 60°C. The mixture was heated at 55–60°C for 20 h, then cooled down, and filtered. The filtrate was evaporated off under reduced pressure (not to dryness). 100 mL of Et_2O–MeOH mixture (10 : 1) was added to the residue, the precipitate was triturated, filtered, and dried. Yield 8.17 g (73%), white crystalline substance, mp 126–127°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.81 t (2H, CH_2SO_2, $^3J_{HH}$ = 7.1), 3.97 t (2H, CH_2Cl, $^3J_{HH}$ = 7.1), 4.12 s (2H, CH_2CO), 7.50 s and 7.77 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 36.61 ($ClCH_2$), 55.15 (CH_2SO_2), 59.07 (SO_2CH_2CO), 164.11 (C=O). Found, %: C 25.83; H 4.31; Cl 19.06; N 7.52; S 17.28. $C_4H_8ClNO_3S$. Calculated, %: C 25.88; H 4.34; Cl 19.10; N 7.55; S 17.27.

2-[(Chloroethyl)sulfanyl]acetaminde (2). A solution of 9 g (0.1 mmol) of amide of sulfanylacetic acid in 100 mL of MeOH was added dropwise to sodium methylate prepared from 2.3 g (0.1 mol) of sodium in 100 mL of MeOH. The obtained solution of thiolate was slowly added to 12.3 mL (21.45 g, 0.15 mol) of 1-bromo-2-cloroethane at 15–20°C. The reaction mixture was kept overnight and filtered. The filtrate was evaporated off under reduced pressure. 100 mL of EtOAc was added. The mixture was filtered and evaporated off after a day. Yield 9.3 g (62%), thick oil crystallizing during storage, mp 60–61°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.94 t (2H, CH_2S, $^3J_{HH}$ = 7.6), 3.13 s (2H, CH_2CO), 3.78 t (2H, CH_2Cl, $^3J_{HH}$ = 7.6), 7.03 s and 7.46 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 36.61 (CH_2Cl), 55.15 (CH_2SO_2), 59.07 (SO_2CH_2CO), 164.11 (C=O). Found, %: C 31.22; H 5.18; Cl 23.06; N 9.08; S 20.83. C_4H_8ClNOS. Calculated, %: C 31.27; H 5.25; Cl 23.08; N 9.12; S 20.87.

2-({[2-Dodecyl(methyl)amino]ethyl}sulfonyl)acetamide (4a). 0.51 g (0.004 mol) of sodium carbonate and 0.79 g (0.004 mmol) of dodecyl(metyl)amine were added to 0.74 g (0.004 mol) of 2-[2-(chloroethyl)-sulfonyl]acetamide in 40 mL of anhydrous acetonitrile. The mixture was refluxed for 4 h, then cooled down and kept for 1 day. White crystals were filtered off, triturated in water, filtered, and dried. Yield 1.05 g (75.5%), mp 75–80°C. IR spectrum (KBr), ν, cm^{-1}: 3391 s, 3196 s (N–H), 2976 m, 2920 s, 2850 s (C–H), 1670 s (amide I), 1629 m (amide II), 1467 m, 1421 m, 1378 m, 1313 s (S=O), 1172 s, 1123 s (S=O), 863 m, 831 cm, 697 m, 655 m, 572 m, 536 m, 500 m. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.86 t (3H, CH_3, $^3J_{HH}$ = 7.1), 1.25 br. s (18H, CH_2), 1.39 m (2H, CH_2), 2.17 s (3H, CH_3N), 2.30 t (2H, CH_2N, $^3J_{HH}$ = 7.0), 2.75 t (2H, CH_2N, $^3J_{HH}$ = 6.8), 3.41 t (2H, CH_2SO_2, $^3J_{HH}$ = 6.8), 4.07 s (2H, CH_2CO), 7.40 s and 7.70 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 14.40 (CH_3), 22.58, 27.15, 27.33, 29.20, 29.53, 31.79 (CH_2, $C_{12}H_{25}$), 41.83 (NCH_3), 50.30 (NCH_2, $C_{12}H_{25}$), 50.53 (NCH_2), 57.17 (CH_2SO_2), 59.28 (SO_2CH_2CO), 164.38 (C=O). Mass spectrum (MALDI-TOF), *m/z*: 349.3 $[M + H]^+$, 371.3 $[M + Na]^+$ (calculated for $C_{17}H_{36}N_2O_3S$: 348.5).

2-{[2-(Dinonylamino)ethyl]sulfonyl}acetamide (4b) was prepared similarly from 0.68 g (3.8 mmol) 2-[(2-chloroethyl)sulfonyl]acetamide, 0.39 g (3.8 mmol) of sodium carbonate, and 1.12 g (3.8 mmol) dinonyl-amine hydrochloride; reaction duration 5 h. Yield 1.22 g (80%), light yellow tranparent thick oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.90 t (6H, CH_3, $^3J_{HH}$ = 6.8), 1.28 br. s (24H, CH_2), 1.48 br. s (4H, CH_2), 2.51 t (4H, CH_2N, $^3J_{HH}$ = 7.6), 3.07 t (2H, CH_2N, $^3J_{HH}$ = 6.5), 3.38 t (2H, CH_2SO_2, $^3J_{HH}$ = 6.4), 4.14 s (2H, CH_2CO), 7.46 s and 7.77 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 14.38 (CH_3), 22.59, 26.66, 27.20, 29.26, 29.40, 29.50, 31.80 (CH_2, C_9H_{19}), 46.67 (NCH_2, C_9H_{19}), 49.70 (NCH_2), 53.33 (CH_2SO_2), 59.10 (SO_2CH_2CO), 164.32 (C=O). Mass spectrum (MALDI-TOF), *m/z*: 419.4 $[M + H]^+$, 441.3 $[M + Na]^+$, 457.2 $[M + K]^+$ (calculated for $C_{22}H_{46}N_2O_3S$: 418.7).

2-{[2-(Didecylamino)ethyl]sulfonyl}acetamide (4c) was prepared similarly from 0.86 g (4.6 mmol) 2-[(2-chloroethyl)sulfonyl]acetamide, 0.49 g (4.6 mmol) of sodium carbonate, and 1.54 g (4.6 mmol) didecylamine hydrochloride; reaction duration 6 h. Yield 1.20 g (58%), light yellow transparent thick oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.86 t (6H, CH_3, $^3J_{HH}$ = 6.7), 1.25 br. s (28H, CH_2), 1.37 br. s (4H, CH_2), 2.36 t (4H, CH_2N, $^3J_{HH}$ = 7.1), 2.85 t (2H, CH_2N, $^3J_{HH}$ = 7.1), 3.38 t (2H, CH_2SO_2, $^3J_{HH}$ = 6.7), 4.06 s (2H, CH_2CO), 7.40 s and 7.69 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm:

14.36 (CH_3), 22.57, 26.80, 27.21, 29.18, 29.38, 29.45, 29.52, 31.78 (CH_2, $C_{10}H_{21}$), 46.73 (NCH_2, $C_{10}H_{21}$), 49.79 (NCH_2), 53.34 (CH_2SO_2), 59.12 (SO_2CH_2CO), 164.34 (C=O). Mass spectrum (MALDI-TOF), *m/z*: 446.4 $[M]^+$, 469.4 $[M + Na]^+$, 485.4 $[M + K]^+$ (calculated for $C_{24}H_{50}N_2O_3S$: 446.7).

Bis-[2-(carbamoylmethylsulfonyl)ethyl]octylamine (5a). 0.53 g (3.8 mmol) of sodium carbonate and 0.25 g (1.9 mmol) of octylamine were added to 0.79 g (4.2 mmol) of 2-[(2-chloroethyl)sulfonyl]acetamide in 40 mL of anhydrous acetonitrile. The obtained mixture was refluxed for 15 h, then cooled down and kept for 1 day. The precipitate was filtered off, the filtrate was evaporated off. The residue was washed with ethyl acetate, dried, and ground in water. Yield 0.48 g (57%), white crystals, mp 85–90°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.86 t (3H, CH_3, $^3J_{HH}$ = 6.8), 1.26 br. s (10H, CH_2), 1.41 br. s (2H, CH_2), 2.45 t (2H, CH_2N, $^3J_{HH}$ = 7.1), 2.92 t (4H, CH_2N, $^3J_{HH}$ = 6.8), 3.45 t (4H, CH_2SO_2, $^3J_{HH}$ = 6.8), 4.06 s (4H, CH_2CO), 7.44 s and 7.73 s (4H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 14.44 (CH_3), 22.51, 26.65, 27.15, 29.00, 29.03, 31.63 (CH_2, C_8H_{17}), 46.48 (NCH_2, C_8H_{17}), 50.23 (NCH_2), 52.92 (CH_2SO_2), 58.94 (SO_2CH_2CO), 164.27 (C=O). Mass spectrum (MALDI-TOF), *m/z*: 428.2 $[M + H]^+$, 450.1 $[M + Na]^+$ (calculated for $C_{16}H_{33}N_3O_6S_2$: 427.6).

2-{[(2-Octylamino)ethyl]sulfonyl]}acetamide (6a). The precipitate obtained after filtration of the reaction mixture was washed with acetonitrile and dried. Yield 0.30 g (36%), white crystals, mp 70–75°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.86 t (3H, CH_3, $^3J_{HH}$ = 8.1), 1.25 br. s (10H, CH_2), 1.39 br. s (2H, CH_2), 2.60 t (2H, CH_2N, $^3J_{HH}$ = 7.1), 2.90 t (2H, CH_2N, $^3J_{HH}$ = 7.2), 3.71 t (2H, CH_2SO_2, $^3J_{HH}$ = 6.8), 4.18 s (2H, CH_2CO), 7.42 s and 7.72 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 14.39 (CH_3), 22.51, 26.65, 29.18, 28.97, 31.63 (CH_2, $C_{16}H_{33}$), 46.48 (NCH_2, $C_{16}H_{33}$), 50.71 (NCH_2), 52.93 (CH_2SO_2), 58.94 (SO_2CH_2CO), 164.09 (C=O). Mass spectrum (MALDI-TOF), *m/z*: 279.2 $[M + H]^+$, 301.11 $[M + Na]^+$ (calculated for $C_{12}H_{26}N_2O_3S$: 278.4).

Bis-[2-(carbamoylmethylsulfonyl)ethyl]nonylamine (5b) was prepared similalry from 0.90 g (4.8 mmol) 2-[(2-chloroethyl)sulfonyl]acetamide, 0.46 g (4.4 mmol) sodium carbonate, and 0.32 g (2.2 mmol) of nonylamine; reaction duration 20 h. Yield 0.65 g (66%), white crystals, mp 92–95°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.86 t (3H, CH_3, $^3J_{HH}$ = 6.6), 1.25 br. s (12H, CH_2), 1.40 br. s (2H, CH_2), 2.43 t (2H, CH_2N, $^3J_{HH}$ = 7.1), 2.90 t (4H, CH_2N, $^3J_{HH}$ = 6.6), 3.43 t (4H, CH_2SO_2, $^3J_{HH}$ = 6.8), 4.04 s (4H, CH_2CO), 7.43 s and 7.71 s (4H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 14.43 (CH_3), 22.57, 26.85, 27.28, 29.15, 29.47, 29.51, 31.77 (CH_2, C_9H_{19}), 46.53 (NCH_2, $C_{10}H_{21}$), 50.13 (NCH_2), 52.99 (CH_2SO_2), 59.08 (SO_2CH_2CO), 164.30 (C=O). Mass spectrum (MALDI-TOF), *m/z*: 442.2 $[M + H]^+$, 464.2 $[M + Na]^+$ (calculated for $C_{17}H_{35}N_3O_6S_2$: 441.6).

Bis-[2-(carbamoylmethylsulfonyl)ethyl]hexadecylamine (5c) was prepared similalry from 1.5 g (8.1 mmol) 2-[(2-chloroethyl)sulfonyl]acetamide, 0.78 g (7.2 mmol) sodium carbonate, and 0.88 g (3.6 mmol) of hexadecylamine; reaction duration 15 h. Yield 0.40 g (20%), white crystals, mp 103–108°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.86 t (3H, CH_3, $^3J_{HH}$ = 6.9), 1.24 br. s (26H, CH_2), 1.40 br. s (2H, CH_2), 2.43 br. s (2H, CH_2N), 2.90 t (4H, CH_2N, $^3J_{HH}$ = 7.0), 3.43 t (4H, CH_2SO_2, $^3J_{HH}$ = 7.0), 4.05 s (4H, CH_2CO), 7.43 s and 7.72 s (4H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 14.38 (CH_3), 22.53, 27.24, 29.15, 29.50, 31.74 (CH_2, $C_{16}H_{33}$), 46.47 (NCH_2, $C_{16}H_{33}$), 50.03 (NCH_2), 52.97 (CH_2SO_2), 59.00 (SO_2CH_2CO), 164.26 (C=O). Mass spectrum (MALDI-TOF), *m/z*: 540.4 $[M + H]^+$, 562.3 $[M + Na]^+$ (calculated for $C_{24}H_{49}N_3O_6S_2$: 539.8).

2-{[(2-Hexadecylamino)ethyl]sulfonyl]}acetamide (6b). Yield 0.88 g (45%), white crystals, mp 97–101°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.86 t (3H, CH_3, $^3J_{HH}$ = 6.8), 1.25 br. s (26H, CH_2), 1.53 br. s (2H, CH_2), 2.60 t (2H, CH_2N, $^3J_{HH}$ = 7.1), 3.03 t (2H, CH_2N, $^3J_{HH}$ = 7.1), 3.47 t (2H, CH_2SO_2, $^3J_{HH}$ = 7.1), 4.11 s (2H, CH_2CO), 7.44 s and 7.76 s (2H, NH_2). ^{13}C NMR spectrum, δ_C, ppm: 14.42 (CH_3), 22.57, 27.18, 29.18, 29.51, 31.77 (CH_2, $C_{16}H_{33}$), 42.47 (NCH_2, $C_{16}H_{33}$), 49.00 (NCH_2), 52.68 (CH_2SO_2), 59.29 (SO_2CH_2CO), 164.27 (C=O). Mass spectrum (MALDI-TOF), *m/z*: 391.4 $[M + H]^+$, 413.3 $[M + Na]^+$ (calculated for $C_{20}H_{42}N_2O_3S$: 390.6).

Hydrochlorides 7a, 7b *(general procedure)*. 0.1 M solution of HCl (1.1 mol of HCl per 1 mol of amine) was added to a solution of compound **4a** or **6b** in 20 mL of methanol. The obtained mixture was kept at room temperature for 5–15 days. The solution was filtered and evaporated off. The residue was ground in acetone–diethyl ether mixture (1 : 2).

[2-(Carbamoylmethylsulfonyl)ethyl](dodecyl)(methyl)amine hydrochloride (7a). Yield 85%, white crystals. There was no clear melting point, the substance became transparent at temperature above 110°C and melted at further heating. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.86 t (3H, CH_3, $^3J_{HH}$ = 6.9), 1.26 s and 1.28 br. s (18H, CH_2), 1.67 br. s (2H, CH_2),

2.76 s (3H, CH_3N), 3.03 br. s and 3.12 br. s (2H, CH_2N), 3.49 br. s and 3.56 br. s (2H, CH_2N), 3.90 t (2H, CH_2SO_2, $^3J_{HH}$ = 7.6), 4.22 s (2H, CH_2CO), 7.54 s and 7.93 s (2H, NH_2). Found, %: C 53.34; H 9.12; Cl 9.18; N 7.11; S 8.04. $C_{17}H_{36}N_2O_3S{\cdot}HCl$. Calculated, %: C 53.03; H 9.67; Cl 9.21; N 7.28; S 8.33.

[2-(Carbamoylmethylsulfonyl)ethyl]hexadecylamine hydrochloride (7b). Yield 69%, white crystals. There was no clear melting point, the substance became transparent at temperature above 130°C and melted at further heating. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.86 t (3H, CH_3, $^3J_{HH}$ = 6.7), 1.25 br. s (26H, CH_2), 1.60 br. s (2H, CH_2), 2.94 br. s (2H, CH_2N), 3.34 br. s (2H, CH_2N), 3.78 t (2H, CH_2SO_2, $^3J_{HH}$ = 7.7), 4.23 s (2H, CH_2CO), 7.56 s and 7.91 s (2H, NH_2), 9.13 br. s (2H, NH_2). Found, %: C 56.85; H 9.43; Cl 8.12; N 6.41; S 7.48. $C_{20}H_{42}N_2O_3S{\cdot}HCl$. Calculated, %: C 56.24; H 10.15; Cl 8.30; N 6.56; S 7.51.

The bacteriostatic and fungistatic activities of the prepared compounds against strains of bacteria *Pseudomonas aeruginosa* ATCC 9027, *Escherichia coli* CDC F-50, *Staphylococcus aureus* ATCC 209-P, *Bacillus cereus* ATCC 8035 and fungi *Trichophyton mentagrophytes var. gypseum* 1773, *Aspergillus niger* BKMF-1119, and *Candida albicans* NCTC 885-653 were determined using twofold serial dilutions method in liquid nutrient media [13]. The bactericide and fungicide activities were determined as described in [14].

The hemolytic action of the compounds was estimated using a method based on the comparation of absorbance of blood in the presence of the tested compound with that of the blood after complete hemolysis [15]. The investigation of tuberculostatic activity was performed by vertical diffusion method using lab strain H37Rv on solid medium “Novaya”. The growth of tuberculosis mycobacteria was estimated using a standard procedure [16].

CONFLICT OF INTERESTS

No conflict of interest was declared by the authors.

REFERENCES

1. Karaev, A.L., *Dezinfekts. Antisept*., 2011, vol. 2, no. 7, p. 38.
2. Kruchenok, T.B., *Probl. Dezinfekt. Steriliz*., 1985, p. 6.
3. Tischer, M., Pradel, G., Ohlsen, K., and Holzgrabe, U., *ChemMedChem*., 2012, vol. 7, p. 22. doi 10.1002/cmdc.201100404
4. Gel’man, N.S., Lukoyanova, M.A., and Ostrovskii, D.N., *Membrany bakterii i dykhatel’naya tsep’* (Bacteria Membranes and Respiratory Chain), Moscow: Nauka, 1972, p. 83.
5. McDonnell, G. and Russell, A.D., *Clin. Microbiol. Rev*., 1999, vol. 12, p. 147. doi 10.1128/CMR.12.1.147
6. Best, M., Sattar, S.A., Springthorpe, V.S., and Kennedy, M.E., *J. Clin. Microbiol*., 1990, vol. 28, no. 10, p. 2234.
7. Russell, A.D., *Clin. Microbiol. Rev*., 1990, vol. 3, p. 99. doi 10.1128/CMR.3.2.99
8. Parrish, N.M., Houston, T., Jones, P.B., Townsed, C., and Dick, J.D., *Antimicrob. Agents Chemother*., 2001, vol. 45, p. 1143. doi 10.1128/AAC.45.4.1143-1150.2001
9. RF Patent 2591256, 2016.
10. Shulaeva, M.M., Fattakhov, S.G., Saifina, L.F., Reznik, V.S., Valijev, R.S., and Mingaleev, D.N., *Russ. Chem. Bull*., 2015, vol. 64, no. 9, p. 2215. doi 10.1007/s11172-015-1141-x
11. Parrish, N.M., Ko, C.G., Hughes, M.A., Townsend, C.A., and Dick, J.D., *J. Antimicrob. Chemother*., 2004, vol. 54, p. 722. doi 10.1093/jac/dkh408
12. Parrish, N.M., Ko, C.G., Dick, J.D., *Tuberculosis*, 2009, vol. 89, p. 325. doi 10.1016/j.tube.2009.05.002
13. Semenov, V.E., Voloshina, A.D., Kulik, N.V., Strobykina, A.S., Giniyatullin, R.Kh., Saifina, L.F., Nikolaev, A.E., Krylova, E.S., Zobov, V.V., and Reznik, V.S., *Russ. Chem. Bull*., 2015, vol. 64, no. 12, p. 2885. doi 10.1007/s11172-015-1243-5
14. Voloshina, A.D., Semenov, V.E., Strobykina, A.S., Kulik, N.V., Krylova, E.S., Zobov, V.V., and Reznik, V.S., *Russ. J. Bioorg. Chem*., 2017, vol. 43, no. 2, p. 170. doi 10.1134/S1068162017020170
15. Tatarinov, D.A., Kuznetsov, D.M., Voloshina, A.D., Lyubina, A.P., Strobykina, A.S., Mukhitova, F.K., Polyancev, F.M., and Mironov, V.F., *Tetrahedron*, 2016, vol. 72, p. 8493. doi 10.1016/j.tet.2016.11.023
16. Belenok, M.G., Andreeva, O.V., Garifullin, B.F., Strobykina, A.S., Kravchenko, M.A., Voloshina, A.D., and Kataev, V.E., *Russ. J. Org. Chem*., 2017, vol. 87, no. 12, p. 2816. doi 10.1134/S1070363217120106