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Amine Exchange Reactions of 3-*tert*-Butyl-6-(methylsulfanyl)-1,2,3,4-tetrahydro-1,3,5-triazine Hydroiodide with Amino Acids

Sun Min'yan', S. M. Ramsh, V. S. Fundamenskii, S. Yu. Solov'eva, and V. I. Zakharov

St. Petersburg State Institute of Technology, Moskovskii pr. 26, St. Petersburg, 190013 Russia
e-mail: gsramsh@mail.wplus.net

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Abstract—3-*tert*-Butyl-6-(methylsulfanyl)-1,2,3,4-tetrahydro-1,3,5-triazine hydroiodide enters into the amine exchange reaction with glycine and β-alanine in aqueous solution. The final exchange products are [4-(methylsulfanyl)-5,6-dihydro-1,3,5-triazin-3-ium-1(2*H*)-yl] acetate and 3-[4-(methylsulfanyl)-5, 6-dihydro-1,3,5-triazin-3-ium-1(2*H*)-yl] propanoate, respectively, crystallizing together with *t*-butylamine hydroiodide from aqueous or aqueous alcoholic solutions as ion associates, which also can be detected in solution in DMSO-d_6. [4-(Methylsulfanyl)-5,6-dihydro-1,3,5-triazin-3-ium-1(2*H*)-yl] acetate can be extracted directly from the reaction mixture after carrying out the amine exchange in aqueous isopropanol or 95% ethanol, as well as by "recrystallization" of its associate with *tert*-butylamine hydroiodide from aqueous isopropanol.

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Previously we reported on the synthesis of 3-*tert*-butyl-6-(methylsulfanyl)-1,2,3,4-tetrahydro-1,3,5-triazine hydroiodide [3-*tert*-butyl-6-(methylsulfanyl)-2,3,4,5-tetrahydro-1,3,5-triazin-1-ium iodide, **I**] [1], whose molecule includes a fragment of protonated isothiocarbamide. Trying to carry out an aminolysis of this compound with amino acids, we found that in aqueous solutions the hydoiodide **I** enters in the reaction of amine exchange with glycine and β-alanine. Such reactions, that can be described as transamination, are considered in the chemistry of the Mannich bases as N-alkylation of amine with a Mannich base [2–4]. The amine exchange of tertiary acyclic Mannich bases derived from secondary amines, with primary amines, including amino acids, has been described about half a century ago [5]. The reaction studied by us is a previously unknown type of amine exchange in a series of Mannich bases that consists in the transamination of tertiary cyclic Mannich base derived from a primary amine with another primary amine.

The amine exchange proceeds almost completely in aqueous solution at a molar ratio of reagents 1:1, and the reaction products (**IIa** and **IIb**) can be identified either after complete evaporation of water in the formed solid crystalline mass, or after adding acetone to the reaction solution, that leads to precipitation of an amorphous powder. The ^{1}H NMR spectra of the obtained substances are consistent with their molecular composition and structure. In DMSO-d_6 solution the product of amine exchange of compounds **I** with glycine is not simply a mixture of equimolar quantities of the zwitterion **IIIa** and *tert*-butylamine hydroiodide, but the ion associate **IIa** which is attested by a reliable downfield shift of about 0.1 ppm of the signals of the methyl and cyclic methylene groups as compared with similar signals of individual zwitter-ion **IIIa**. In D_2O the signals of compounds **IIa** and **IIIa** are almost identical, probably due to almost complete dissociation of the associate **IIa** into the ionic components.

The X-ray diffraction analysis of the two crystalline samples of the product of amine exchange with glycine **IIa**, one of which was obtained by complete evaporation of water from the reaction mixture and another by concentrating its water–alcohol solution showed that this product consisted of four molecular and ionic species: The zwitter-ion **IIIa** with equalized bond lengths in isothiuronium and carboxylate fragments, the *tert*-butylammonium cation, the iodide anion, and the water molecule (Tables 1 and 2, Fig. 1), i.e., it can be represented as **IIa**·H_2O = **IIIa**·*t*-$BuNH_3$ + I^-·H_2O.

The structure of **IIa**·H_2O can be regarded as *tert*-butylammonium salt monohydrate of the primary product of amine exchange, **IVa** = **IIIa**×HI. Without

Table 1. The covalent bond lengths, *d*, and bond angles, ω, of the molecular components of the ion associate **IIa**

Bond	*d*, Å	Angle	ω, deg
S–C^4	1.737(8)	C^6SC^4	104.4(4)
S–C^6	1.777(10)	$C^5N^1C^3$	108.4(6)
O^1–C^1	1.229(12)	$C^2N^1C^3$	111.9(6)
O^2–C^1	1.249(11)	$C^2N^1C^5$	112.7(6)
N^1–C^2	1.466(10)	$C^5N^3C^4$	121.0(7)
N^1–C^3	1.439(12)	$O^2C^1C^2$	114.8(8)
N^1–C^5	1.451(9)	$O^1C^1C^2$	120.0(8)
N^3–C^4	1.307(11)	$O^1C^1O^2$	125.1(9)
N^3–C^5	1.485(10)	$C^4N^2C^3$	120.7(7)
C^1–C^2	1.537(10)	SC^4N^2	114.3(6)
N^2–C^4	1.322(11)	$N^3C^4N^2$	120.5(8)
N^2–C^3	1.465(10)	N^3C^4S	125.2(7)
N^4–C^7	1.503(10)	$C^1C^2N^1$	113.1(6)
C^7–C^{10}	1.527(10)	$N^4C^7C^8$	107.1(6)
C^7–C^9	1.514(10)	$C^{10}C^7C^8$	111.5(6)
C^7–C^8	1.517(13)	$C^{10}C^7N^4$	107.5(6)
		$C^9C^7C^8$	111.6(6)
		$C^9C^7N^4$	107.9(6)
		$C^9C^7C^{10}$	111.0(6)
		$N^2C^3N^1$	110.8(7)
		$N^3C^5N^1$	111.3(6)

Table 2. Parameters of hydrogen bonds in the crystal structure of (**IIa**·H_2O)

Bond (D–H···A)	*d*(D···A), Å
O^3···O^2	2.683
N^3···O^2	2.764
N^4···O^1	2.777
N^4···O^3	2.792
O^3···I	3.498
N^2···I	3.471
N^4···I	3.610[a]

[a] Internuclear distance is boundary between hydrogen bond and van der Waals contact.

pointing to a specific localization of the proton of hydrogen iodide, the crystalline product of transamination of compound **I** with glycine can formally be considered as a hydrated hydroiodide of the adduct of **IIIa** with *tert*-butylamine, i.e., as **IIa**·H_2O = **IIIa**·*t*-$BuNH_2$·HI·H_2O. But regardless of the way of describing the associate **IIa**, it can be stated that its precoursors, the hydroiodide **IVa** and *tert*-butylamine, appearing in aqueous solution due to the reaction of amine exchange in equimolar ratio, form instantaneously the *tert*-butylammonium salt, which, in turn, dissociates into separate ions. Probably the associate **IIa** is less soluble in water (has a higher crystal lattice energy) compared with two other molecular components of the dissociative equilibrium, the zwitter-ion **IIIa** and *tert*-butylamine hydroiodide, and at the concentrating the aqueous solution by solvent evaporation it crystallizes first. In other words, the zwitter-ion **IIIa** and *tert*-butylamine hydroiodide

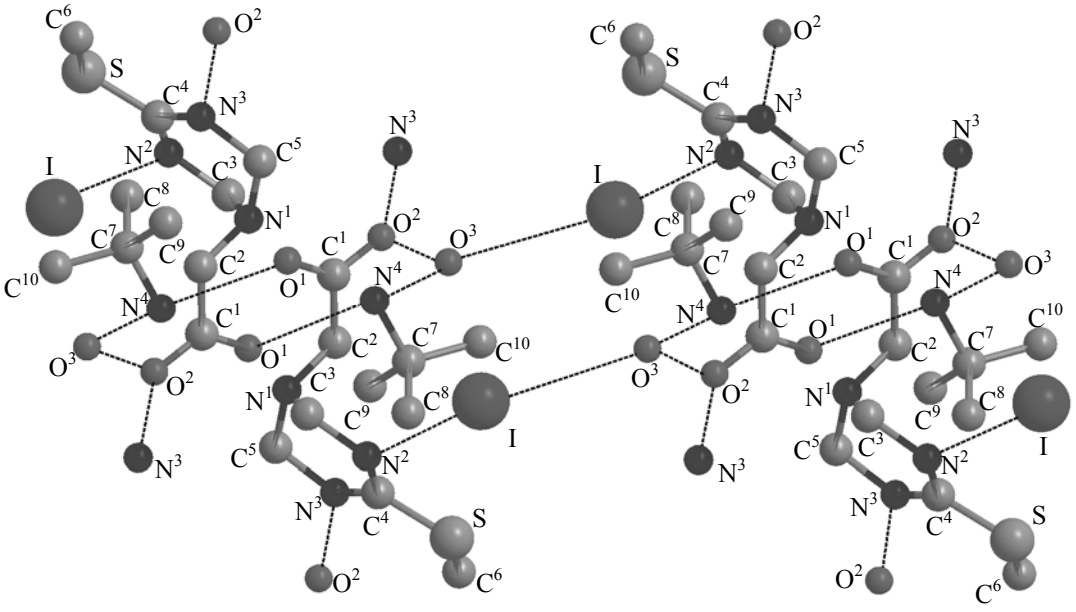
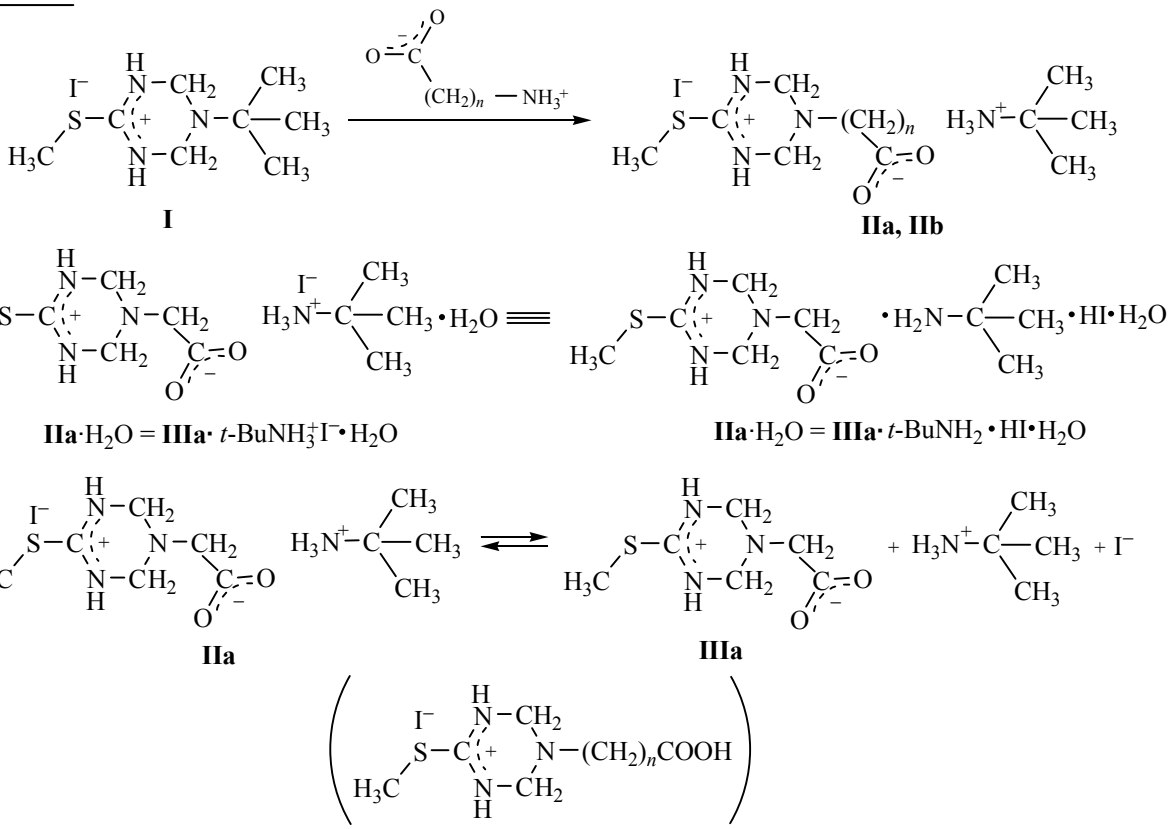


Fig. 1. Molecular structure and hydrogen bonds in the crystal (**IIa**·H_2O) according to the X-ray diffraction analysis.

crystallize from their equimolar aqueous solution jointly in the form of a hydrated ionic associate **IIa**·H_2O, but do not precipitate as a mechanical mixture of crystals of the individual components. Similarly and for the same reason, these components behave at the growing the crystals of associate **IIa**·H_2O from its aqueous alcoholic solution by slow evaporation and change in the solvent composition. Eventually, such co-crystallization of two molecular components is a result of stabilization both on the molecular level due to the formation of ion associates **IIa**, and on the supramolecular level, through the effects of crystal packing.

Since the zwitter-ion **IIIa** is a kind of amino acid, the associate **IIa** = **IIIa**·*t*-$BuNH_3$ + I^- = **IIIa**·*t*-$BuNH_2$·HI) is a salt of this amino acid, and the salt formation occurs both at the acid carboxy group, and at the basic isothiuronium fragment. There are no data in the Cambridge Structural Database [6] concerning a simple crystalline salt of this type, consisting of zwitter-ion of glycine, sodium cation and chlorine anion.



I **IIa, IIb**

IIa·H_2O = **IIIa**· *t*-$BuNH_3^+I^-$•H_2O **IIa**·H_2O = **IIIa**·*t*-$BuNH_2$•HI•H_2O

IIa **IIIa**

IVa, IVb = IIIa, IIIb·IH

n = 1 (**a**), 2 (**b**).

The zwitter-ion **IIIa** in the crystal structure of **IIa** is significantly nonplanar. The five atoms of the heterocycle and alkylthio group lie approximately in one plane, while the N^1 atom is located out of the plane, and the N^1–C^2 bond is almost perpendicular to the flat fragment (envelope) (Fig. 1). The iodide ion is bound by three hydrogen bonds with the cyclic nitrogen atom N^2 (3.471 Å), nitrogen atom N^4 of *tert*-butylammonium cation (3.610 Å) (in Fig. 1, this hydrogen bond is not shown) and the atom O^3 of hydration water (3.498 Å) (Fig. 1, Table. 2).

Due to the systems of hydrogen bonds, there are the intermolecular contacts of two types, representing "macrocycles" of different size (Fig. 1). The smaller "macrocycle" is built by a pair of systems of hydrogen bonds linking the oxygen atom O^1 with the nitrogen atom of *tert*-butylammonium cation N^4, hydrate

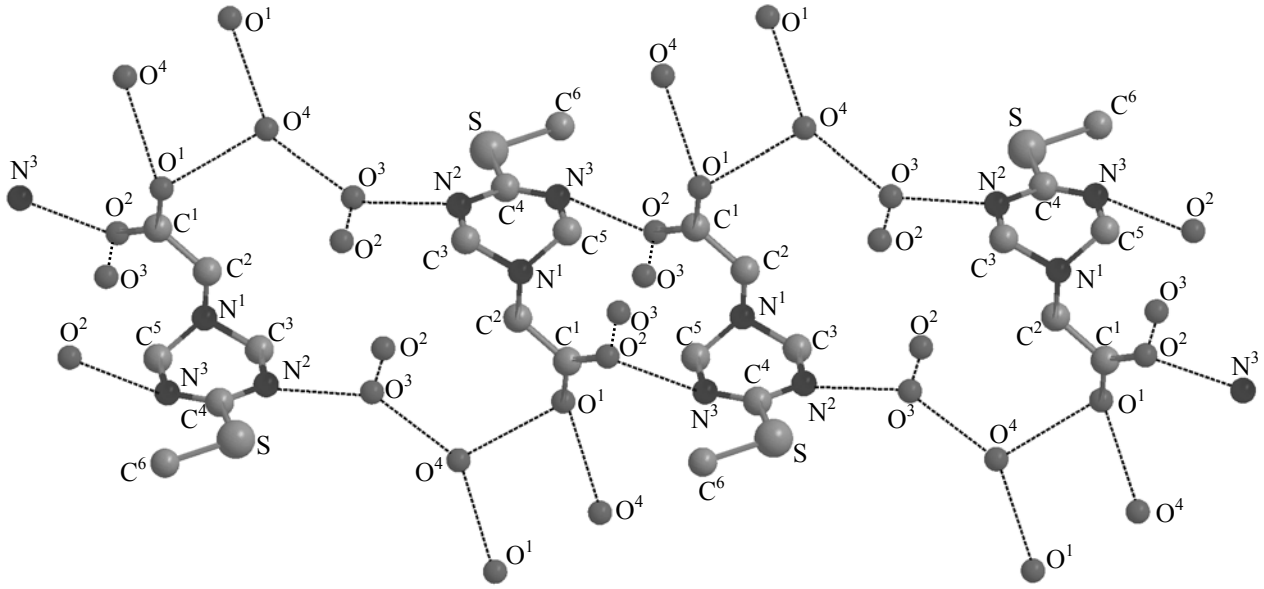


Fig. 2. Molecular structure and hydrogen bonds in the crystal (**IIIa**·H_2O) according to the X-ray diffraction analysis.

oxygen atom O^3, and the oxygen atom O^2 of another zwitter-ion formed from the basic zwitter-ion by inversion of the cell. The larger "macrocycle" is constructed similarly with a pair of systems of hydrogen bonds between the oxygen O^2 and nitrogen N^2 with involvement of the oxygen O^3 of hydrate water and iodide anion.

As a result, the crystal structure of **IIa**·H_2O can be considered as a chain consisting of H-bonded dimeric units connected by hydrogen bonds, the chains in turn are linked together in a crystal frame by the intermolecular hydrogen bonds $N^3\cdots O^2$ (Fig. 1).

It should be noted that the majority of hydrogen bonds (4 of 7) are between the atoms bearing single or half charge, and only three bonds involve oxygen of hydrate water O^3.

At an attempt to recrystallize hydrated associate **IIa**·H_2O from aqueous isopropanol, in the resulting crystalline precipitate along with the original associate was detected the zwitter-ion **IIIa** (^{1}H NMR data, in DMSO-d_6). As a result of several such "recrystallizations" the zwitter-ion was isolated in the form of individual dihydrate **IIIa**·$2H_2O$, whose structure was confirmed by X-ray diffraction analysis (without localization of the hydrogens of water molecules). The explanation lies in the fact that at the dissolving the ion associate **IIa** in aqueous isopropanol it dissociates into individual ions, and the crystalline substance formed after cooling the concentrated solution in the aqueous isopropanol (possibly with partial evaporation and some change in the solvent composition) depends on the relative solubility of all molecular components: the associate **IIa**, the zwitter-ion **IIIa**, and *tert*-butylamine hydroiodide. Perhaps, in contrast to water, in the aqueous isopropanol the least soluble is the zwitter-ion **IIIa**. This explanation is consistent with the fact that the zwitter-ion **IIIa** can be extracted directly from the reaction mixture after amine exchange of compound **I** with glycine when the reaction is carried out in aqueous isopropanol or 95% ethanol, but in the latter case with a small yield. It is possible that the crystallization of the dihydrate **IIIa**·$2H_2O$ is favored by hydrolysis of *tert*-butylamine hydroiodide occurring in a hot water–isopropanol solution, i.e., accompanied by partial evaporation of *tert*-butylamine from the solution.

Structure of the zwitter-ion in the crystal structure **IIIa**·$2H_2O$ differs from that in **IIa**·H_2O (Fig. 2, Table 3). Each oxygen atom of the carboxy group participates in two intermolecular hydrogen bonds (Table 4). The O^1 atom forms a system of hydrogen bonds with two atoms O^4 of symmetrically bound water molecules (the distances are 2.777 and 2.719 Å, respectively). Another O^2 atom forms a hydrogen bond with the oxygen atom of water O^3 and the cyclic nitrogen atom N^3 (the distances are 2.781 and 2.882 Å, respectively). The oxygen atom of hydration water O^3, in addition to participating in the aforementioned hydrogen bond $O^3\cdots O^2$, forms a hydrogen bond with the cyclic

Table 3. Bond lengths, *d*, and bond angles, ω, of zwitter-ion **IIIa**

Bond	*d*, Å	Angle	ω, deg
S–C^4	1.751(9)	C^6SC^4	101.5(4)
S–C^6	1.801(9)	$C^4N^2C^3$	120.5(7)
N^2–C^4	1.337(10)	$C^5N^1C^3$	109.2(7)
N^2–C^3	1.498(10)	$C^2N^1C^3$	110.9(6)
O^1–C^1	1.265(10)	$C^2N^1C^5$	114.1(6)
O^2–C^1	1.240(10)	$C^5N^3C^4$	119.9(7)
N^1–C^5	1.438(10)	N^2C^4S	114.4(6)
N^1–C^2	1.469(10)	N^3C^4S	123.8(6)
N^1–C^3	1.462(10)	$N^3C^4N^2$	121.7(8)
N^3–C^4	1.296(10)	$O^1C^1C^2$	113.3(8)
N^3–C^5	1.496(10)	$O^2C^1C^2$	121.5(7)
C^1–C^2	1.520(10)	$O^2C^1O^1$	125.2(8)
		$N^3C^5N^1$	111.1(6)
		$N^1C^2C^1$	115.6(7)
		$N^1C^3N^2$	109.3(7)

nitrogen atom N^2 (the distance is 2.751 Å), and the oxygen atom of the second hydration water O^4, in addition to participating in two hydrogen bonds $O^4\cdots O^1$, forms a hydrogen bond with the atom O^3 (the distance is 2.731 Å).

Like the previous case, the system of hydrogen bonds leads to the intermolecular contacts of two types, representing "macrocycles" of various sizes. First, smaller in size, is formed by a pair of hydrogen bonds of oxygen O^2 and nitrogen N^3, a second, larger, is formed by a pair of systems of hydrogen bonds between the oxygen O^1 and nitrogen N^2, with the participation of oxygen bridges O^3 and O^4 of two hydration water molecules (Fig. 2).

Thus, the crystal structure of **IIIa**·$2H_2O$ can be considered as a chain consisting of H-bonded dimeric units connected by hydrogen bonds, and these chains, in turn, are linked in a crystalline frame by intermolecular hydrogen bonds $O^4\cdots O^1$ and $O^3\cdots O^2$. Note that among the six existing hydrogen bonds, only one, $N^3\cdots O^2$, is formed between two charged atoms with 0.5 units of elementary charge, while in other participate the oxygen atoms of hydrate water O^3 and O^4 (Fig. 2).

As a result of comparing the two crystal structures, **IIa** and **IIIa**, it should be noted that although both include the same substituted six-membered heterocycle, the presence in the first structure of *tert*-butylamine hydroiodide (*tert*-butylammonium iodide) leads to substantially different molecular packing.

Table 4. Parameters of hydrogen bonds in the crystal structure of **IIIa**·$2H_2O$)

Bond (D–H···A)	*d*(D···A), Å
$N^2\cdots O^3$	2.751
$O^3\cdots O^4$	2.731
$O^4\cdots O^1$	2.777
$O^4\cdots O^1$	2.719
$O^3\cdots O^2$	2.781
$N^3\cdots O^2$	2.882

Unfortunately, we failed to grow a single crystal of compound **IIb**, however, judging from the absence of characteristic bands of hydration water in its IR spectrum and from the data of elemental analysis, we suggest that it is obtained in an anhydrous (non-hydrated) form.

The amine exchange of compound **I** with glycine or β-alanine can be traced at carrying out the reaction in an ampule of NMR spectrometer by the appearance of new signals in the spectra, when an equimolar mixture of compound **I** and respective amino acid is dissolved in D_2O. The amine exchange occurs also in DMSO-d_6: by adding a solvent in the ampoule with an equimolar mixture of compound **I** with glycine or β-alanine the amino acid is gradually "dissolved," while in the spectrum along with the signals of the parent compound **I** appear the signals of the amine exchange product **II** whose intensity gradually increases, reaching in 2–3 weeks about 80% of the total intensity, while at the bottom of the ampoule there are incompletely dissolved amino acids. The exchange process is clearly manifested by the appearance in the spectrum of signals of the amino acid fragment of the formed complex **II**, because the amino acids themselves are virtually insoluble in dry DMSO-d_6 and respective spectra contain only the signals of the solvent.

It is known that isothiocarbamide derivatives display an inhibitory effect on NO-synthase [7–9]. In this regard, combining the amino acid and the isothiuronium fragment can lead to an appearance of unique biological activity in compounds **II** and **III**.

EXPERIMENTAL

The ^1H NMR spectra were recorded on Bruker AM-400 (400 MHz) and Bruker AM-200 (200 MHz) instruments in DMSO-d_6 and D_2O. The IR spectra were recorded on a spectrophotometer Shimadzu FTIR-8400S from KBr tablets. Elemental analysis was performed on the analyzer LECO CHNS(O) 942. The

TLC was performed on Silufol UV-254 plates, eluent ethanol–chloroform 1:10. Acetone was purified and dried by the method [10].

The X-ray diffraction analysis was carried out on an automatic single-crystal diffractometer IPDS 2T STOE, Mo $K_{\square}$-radiation. The structures were solved and refined using the program of SIR complex to R = 0.406.

For the X-ray diffraction analysis of the associate **IIa**·H_2O was used a single crystal selected from the crystalline mass obtained along the procedure described below, as well as a single crystal specially grown from a solution of this mass in 80% alcohol (the listed results of the analysis relate to the last sample). The **IIa**·H_2O structure crystallizes in the monoclinic crystal system, space group $P2_1/c$, with the unit cell parameters: a = 7.5201 (8), b = 20.6153 (23), c = 11.9262 (18), β = 106.43 (1), V = 1773.21, Z = 4. A set of 3082 reflections ($F > 4\sigma$) collected in the range of angles 2θ from 0 to 60° was obtained from a colorless single crystal of 0.30×0.37×0.49 mm size.

For the X-ray diffraction analysis of the zwitter-ion **III**·2H_2O was used a single crystal selected from the sample obtained by method *a* (see below). Structure **III**·2H_2O crystallizes in the triclinic space group $P4$, the unit cell parameters are as follows: a = 8.034 (7), b = 8.290(7), c = 8.306(7), α = 83.23(6), β = 88.44(7), γ = 75.88(6), V = 532.77, Z = 2. A set of 1248 reflections ($F > 4\sigma$) collected in the range of angles 2θ from 0° to 60° was obtained from a colorless single crystal of 0.33×0.31×0.42 mm size.

Images of crystal structures are obtained using the program "Mercury 2.2" [11].

3-*tert*-Butyl-6-(methylsulfanyl)-1,2,3,4-tetrahydro-1,3,5-triazine hydroiodide (3-*tert*-butyl-6-(methylsulfanyl)-2,3,4,5-tetrahydro-1,3,5-triazin-1-ium iodide, I) was obtained by the improved method [1]. 10.68 g (61.6 mmol) of 5-*tert*-butyl-1,3,5-triazinan-2-thione in 110 ml of anhydrous acetone was stirred for 20 min at room temperature, then to the formed suspension was added 5.0 ml (11.40 g, 80.3 mmol) of methyl iodide. After a few hours the precipitate formed was filtered off, washed with acetone and dried in a vacuum over P_2O_5. Yield 9.50 g (48.9%), mp 138°C (138–140°C [1]).The ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.17 [9H, s, $C(CH_3)_3$], 2.55 s (3H, SCH_3), 4.47 s (4H, C^2H_2, C^4H_2), 9.80 (2H, NH). IR spectrum (thin layer), ν, cm^{-1}: 1544 (C–N, def. NH^+), 1603 (C=N), 2873, 2918, 2964, 3050 (CH_2, CH_3), 3111, 3154 , 3205, 3422 (NH). Found, %: C 30.50; H 5.70; N 13.21. $C_8H_{17}N_3S\times HI$ ($C_8H_{18}IN_3S$). Calculated, %: C 30.48; H 5.76; N 13.33.

[4-(Methylsulfanyl)-5,6-dihydro-1,3,5-triazin-3-ium-1(2*H*)-yl] acetate, a compound with 2-methylpropane-2-amine iodide (1:1) ([4-(methylsulfanyl)-3,6-dihydro-1,3,5-triazine-1(2*H*)-yl]acetic acid, compound with *tert*-butylamine (1:1), hydrobromide, IIa), hydrate. At room temperature 0.540 g (7.193 mmol) of glycine was dissolved in 14 ml of water. To the resulting solution was added with stirring 2.267 g (7.193 mmol) of compound **I** and 14 ml of water. After 10 min compound **I** dissolved completely. The reaction solution was poured into a Petri dish and left to evaporate in air at room temperature. After 3 days at the bottom of the Petri dish remained a transparent film, and after 6 days appeared a conglomerate of large white crystals, which were dried in a vacuum desiccator over $CaCl_2$. Yield 2.633 g (89.6%), mp 127–129° C. The ^{1}H NMR spectrum (400 MHz, D_2O), δ, ppm: 1.33 s [9H, C $(CH_3)_3$], 2.54 s (3H, SCH_3), 3.33 s (2H, CH_2 COO), 4.41 s (4H, C^2H_2, C^6H_2). The ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 1.26 s [9H, $C(CH_3)_3$], 2.35 s (3H, SCH_3), 3.23 s (2H, CH_2COO), 4.23 s (4H, C^2H_2, C^6H_2). The IR spectrum (thin layer), ν, cm^{-1} : 1543 (C–N, def. NH^+), 1603 (CO_2^-), 2802, 2885, 2973 (CH_2, CH_3), 3070, 3132 (NH), 3466 (OH). Found, %: C 29.15, H 6.62; N 13.01; S 7.87. $C_6H_{11}N_3O_2S\cdot C_4H_{12}IN\cdot H_2O$ ($C_6H_{11}N_3O_2S\cdot C_4H_{11}N\cdot HI\cdot H_2O$, $C_{10}H_{23}IN_4O_2S\cdot H_2O$). Calculated, %: C 29.42, H 6.17; N 13.72; S 7.85.

3-[4-(Methylsulfanyl)-5,6-dihydro-1,3,5-triazin-3-ium-1(2*H*)-yl] propanoate, a compound with 2-methylpropane-2-aminium iodide (1: 1) (3-[4-(methylsulfanyl)-3,6-dihydro-1,3,5-triazine-1(2*H*)-yl]propanic acid, compound with *tert*-butylamine (1:1) hydroiodide, IIb). To a solution of 0.640 g (7.184 mmol) of β-alanine in 14 ml of water was added with stirring 2.264 g (7.182 mmol) of compound **I** and 14 ml of water, and the stirring was continued for 10 min to complete dissolution of compound **I**. After keeping for 24 h the reaction mixture was poured into a Petri dish and solvent was allowed to evaporate in air at room temperature. After 4 days at the bottom of the Petri dish formed a transparent film. In next 7 days it turned into a hard white residue, which was scraped from the bottom of the Petri dish and dried in a vacuum desiccator over $CaCl_2$. Yield 2.511 g (86.5%), mp 127–130°C. The ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (J, Hz): 1.24 s [9H, $C(CH_3)_3$], 2.24

s (3H, SCH_3), 2.35 t (2H, J = 6.9 Hz, NCH_2CH_2COO), 2.75 t (2H, J = 6.9 Hz, NCH_2CH_2COO), 4.08 s (4H, C^2H_2, C^6H_2). ^{1}H NMR (400 MHz, D_2O), δ, ppm (J, Hz): 1.36 s [9H, $C(CH_3)_3$], 2.43 t (2H, J = 7.0 Hz, NCH_2CH_2COO), 2.57 s (3H, SCH_3), 2.96 t (2H, J = 7.0 Hz, NCH_2CH_2COO), 4.43 s (4H, C^2H_2, C^6H_2). IR spectrum (thin layer), ν, cm^{-1}: 1567, 1584 (C–N, def. NH^+), 1608 (CO_2^-), 2925, 2966 (CH_2, CH_3), 3170 sh. (NH), 3439 (NH). Found, %: C 32.08; H 6.42; N 13.14; S 7.80. $C_7H_{13}N_3O_2S{\cdot}C_4H_{12}IN$ ($C_7H_{13}N_3O_2S{\cdot}C_4H_{11}N{\cdot}HI$, $C_{11}H_{25}IN_4O_2S$). Calculated, %: C 32.68, H 6.23; N 13.86; S 7.93.

[4-(Methylsulfanyl)-5,6-dihydro-1,3,5-triazin-3-ium-1(2*H*)-yl] acetate ([4-(methylsulfanyl)-3,6-dihydro-1,3,5-triazin-1(2*H*)-yl]acetic acid, IIIa), dihydrate. *a***.** 2.000 g (4.898 mmol) of compound **IIa** was "recrystallized" successively from 25 and 15 ml of isopropanol–water 9:1 mixture. The precipitate after the second "recrystallisation" was left for 24 h and then filtered off and dried in a vacuum over $CaCl_2$. Yield 1.010 g (65%), mp 125°C. The ^{1}H NMR spectrum (400 MHz, D_2O), δ, ppm: 2.56 s (3H, SCH_3), 3.37 s (2H, CH_2COO), 4.43 s (4H, C^2H_2, C^6H_2). ^{1}H NMR (400 MHz, DMSO-d_6), δ, ppm: 2.21 s (3H, SCH_3), 3.27 s (2H, CH_2COO), 4.11 s (4H, C^2H_2, C^6H_2). IR spectrum (thin layer), ν, cm^{-1}: 1573, 1580 (C–N, def. NH^+), 1604 (CO_2^-), 1657 (def. NH^+), 2895, 2927 (CH_2, CH_3), 3192 (NH), 3375 (OH). Found, %: C 31.88; H 6.99; N 17.58; S 14.32. $C_6H_{11}N_3O_2S{\cdot}2H_2O$. Calculated, %: C 31.99; H 6.71; N 18.65; S 14.23. This sample was used for X-ray diffraction study.

b. A portion 0.680 g (1.665 mmol) of compound **IIa** was boiled in 10 ml of an isopropanol–water 18:1 mixture to complete dissolution (about 15 min), the solution was cooled to room temperature and left standing. A day latter the needle precipitate formed on the walls of the flask was filtered off, washed three times with isopropyl alcohol, and dried in a vacuum. Yield 0.125 g (33.3%), mp 136–138°C.

c. To a solution of 0.630 g (1.999 mmol) of compound **I** in 9 ml of isopropanol was added a solution of 0.150 g (1.998 mmol) of glycine in 1 ml of water. The reaction mixture was boiled for 1 h under reflux, and then left standing in a closed vessel. A week later the large crystals formed on the bottom of the vessel were filtered off, washed with ethanol, and dried in a vacuum. Yield 0.152 g (33.8%), mp 130°C.

d. To a solution of 0.315 g (0.999 mmol) of compound **I** in 10 ml of 95% ethanol was added 0.075 g (0.999 mmol) of glycine, and the reaction mixture was refluxed with vigorous stirring for 1 h (all dissolved in 20 min), then left overnight. The oil formed on the next day was crystallized from ethanol and dried in a vacuum. Yield is low (the sample obtained was used for the NMR spectroscopy).

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