ISSN 1070-4280, Russian Journal of Organic Chemistry, 2009, Vol. 45, No. 2, pp. 248–255. © Pleiades Publishing, Ltd., 2009.
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# 3,3'-Bi(6,8-dialkyl-2,4-dioxa-7-thia-6,8-diazabicyclo[3.3.0]-octane-7,7-dioxides): Structure and Synthesis

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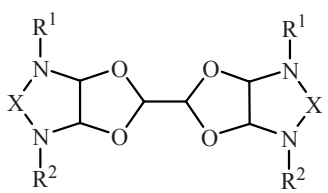
Received May 6, 2008

**Abstract**—Derivatives of a new heterocyclic system, 3,3'-bi(6,8-dialkyl-2,4-dioxa-7-thia-6,8-diazabicyclo[3.3.0]-octane-7,7-dioxides), were synthesized by condensation of 1,3-dialkylsulfamides with glyoxal (as a dihydrate trimer). Their structure was investigated by spectral methods, XRD, and X-ray phase analysis of one among these compounds.

**DOI:** 10.1134/S107042800902016X

Our longstanding interest to the chemistry and stereochemistry of 2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-diones (glycolurils) [1, 2] and their analogs [3, 4] is due to the wide range of practically useful biological activity of these compounds [5, 6]. Glycolurils are commonly obtained from ureas and glyoxal (40% water solution) in water or in the mixture of water and lower alcohols at pH 1 [1, 2, 7, 8]. Recently [9, 10] we studied a reaction of 1,3-dialkylsulfamides with glyoxal under the same conditions. It turned out that only 1,3-dimethyl-sulfamide reacted with glyoxal to give 3,7-dithia-2,4,6,8-tetraazabicyclo[3.3.0]octane-3,3,7,7-tetraoxide [9]. The reaction with the other 1,3-dialkylsulfamides instead of the expected sulfoanalogs of glycolurils yielded the first examples of new heterocyclic system, 3,3'-bi(6,8-dialkyl-2,4-dioxa-7-thia-6,8-diazabicyclo[3.3.0]octane-7,7-dioxides) **I** [10]. Besides, by the reaction of 1,3-dialkylureas with glyoxal we obtained a series of compounds of close structure, 3,3'-bi(6,8-dialkyl-2,4-dioxa-6,8-diazabicyclo[3.3.0]octan-7-ones) **II** whose structure was proved by XRD analysis [11].



X = $SO_2$ (**I**), CO (**II**).

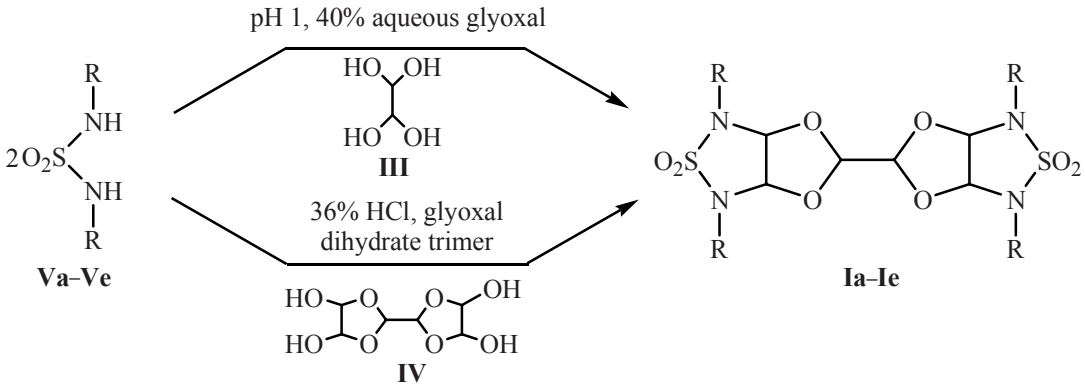
In this study we developed the optimum conditions of the synthesis, and the structure was investigated of derivatives of new heterocyclic system **I**.

The glyoxal is known to exist in solutions in various hydrate forms, among them 1,1,2,2-tetrahydroxyethane (**III**) and 2,2'-bi(4,5-dihydroxy-1,3-dioxolane) (**IV**), with trivial names bisgemdiol and glyoxal dihydrate trimer respectively [12]. Besides the amount of the hydrate forms varies depending on the concentration, and therefore the reactions were carried out applying either commercial 40% water solution of glyoxal and the freshly-prepared solution of dihydate trimer.

Aiming at development of a preparative synthetic procedure for compounds **Ia–Ie** we investigated the effect of various parameters of the process on the yield of the reaction products (pH of the medium or the quantity of concn. HCl, temperature and time of the reaction). By the condensation of 1,3-dialkylsulfamides **Va–Vd** with glyoxal in the form of 40% water solution with the adition of concn. HCl (pH 1) we obtained compounds **Ia–Id** in the yields not exceeding 5–11% (Scheme 1).

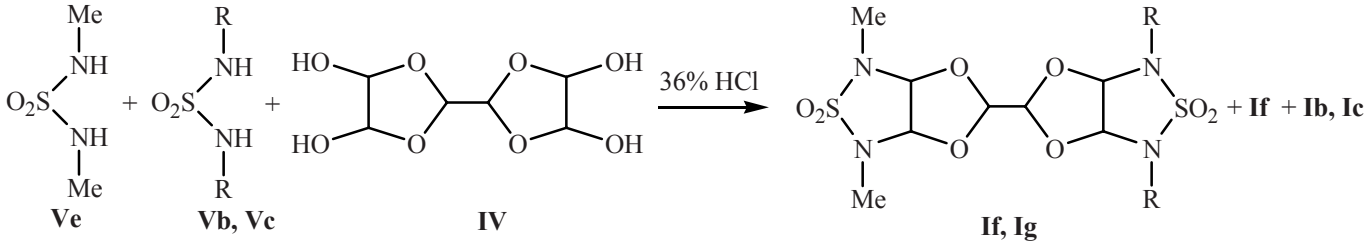
By an example of the reaction of 1,3-dimethyl-(diethyl)sulfamides **Va** and **Ve** with the freshly prepared water solution of the glyoxal in the form **IV** we studied

**Scheme 1.**




R = Et (**a**), Pr (**b**), *i*-Pr (**c**), Bu (**d**), Me (**e**).

**Scheme 2.**




R = Pr (**If, Vb**), *i*-Pr (**Ig,Vc**).

the effect of pH of the environment, of the temperature, and character of substituents on the reaction result. The reaction was carried out in water with addition of HCl (pH 2, 3, 5), and also in 18% and 36% HCl at temperatures 20, 40, and 80°C. At pH 2 compound **Ia** formed in amount of 5–9%, at pH 3 and 5 compounds **Ia** and **Ie** did not form. The raising of the temperature to 80°C did not result in the formation of compound **Ie** or in the larger yield of compound **Ia**. In 18% and 36% hydrochloric acid at 40°C the yield of derivative **Ie** was 56 and 81% respectively. At 20°C in 36% HCl compound **Ie** formed in 80% yield within 6–8 h, whereas at 40°C , in 0.5 h.

Hence the optimum conditions of the synthesis of compounds **I** is 40°C and application of the glyoxal dihydrate trimer (**IV**) in concn. HCl.

In order to extend the range of derivatives of new heterocyclic system **I** by varying the substituents at the nitrogen atoms we brought into the reaction with glyoxal dihydrate trimer (**IV**) a mixture of two different 1,3-dialkylsulfamides **V** in equimolar ratio. The reaction of glyoxal with C 1,3-dimethylsulfamide (**Ve**) and 1,3-dipropyl- and diisopropylsulfamides (**Vb, Vc**) proceeded selectively with prevailing formation of unsymmetrical products **If, Ig** (yields 55–68%, Scheme 2) with tetramethyl and tetrapropyl derivatives **Ib, Ic**, and **Ie** as impurities in amount of 4–10%.

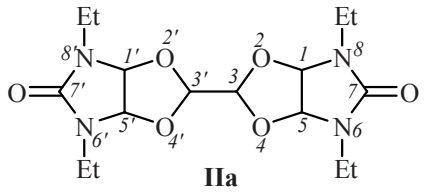
Compound **If** was purified by fractional crystallization from methanol, compound **Ig** was isolated by column chromatography on silica gel. The reaction of glyoxal **IV** with sulfamide **Ve** and 1,3-dibutyl-sulfamide (**Vd**) proceeded nonselectively with the formation of compounds **Id** and **Ie** in approximately equal quantities.

Analogously to the mechanism of glycoluril formation in the reaction of ureas with 4,5-dihydroxyimidazolidin-2-ones [1] it is presumable that the formation of compounds **I** proceeded through the intermediate carbenium ions [**VI**(**VI'**)] or [**VII**(**VII'**)] that require for their generation strong acid medium (Scheme 3).

To prove the structure of the derivatives of the new bisbicyclic system the obtained compounds **I** were investigated by $^{1}H$ and $^{13}C$ NMR spectroscopy, mass spectrometry, X-ray diffraction and X-ray phase analysis.

In particular, a comparative analysis of coupling con-stants was performed for compounds **Ic** and **IIa** (Table 1). The latter substance was synthesized by

procedure [11] and according to XRD had a bidioxolane structure.



**IIa**

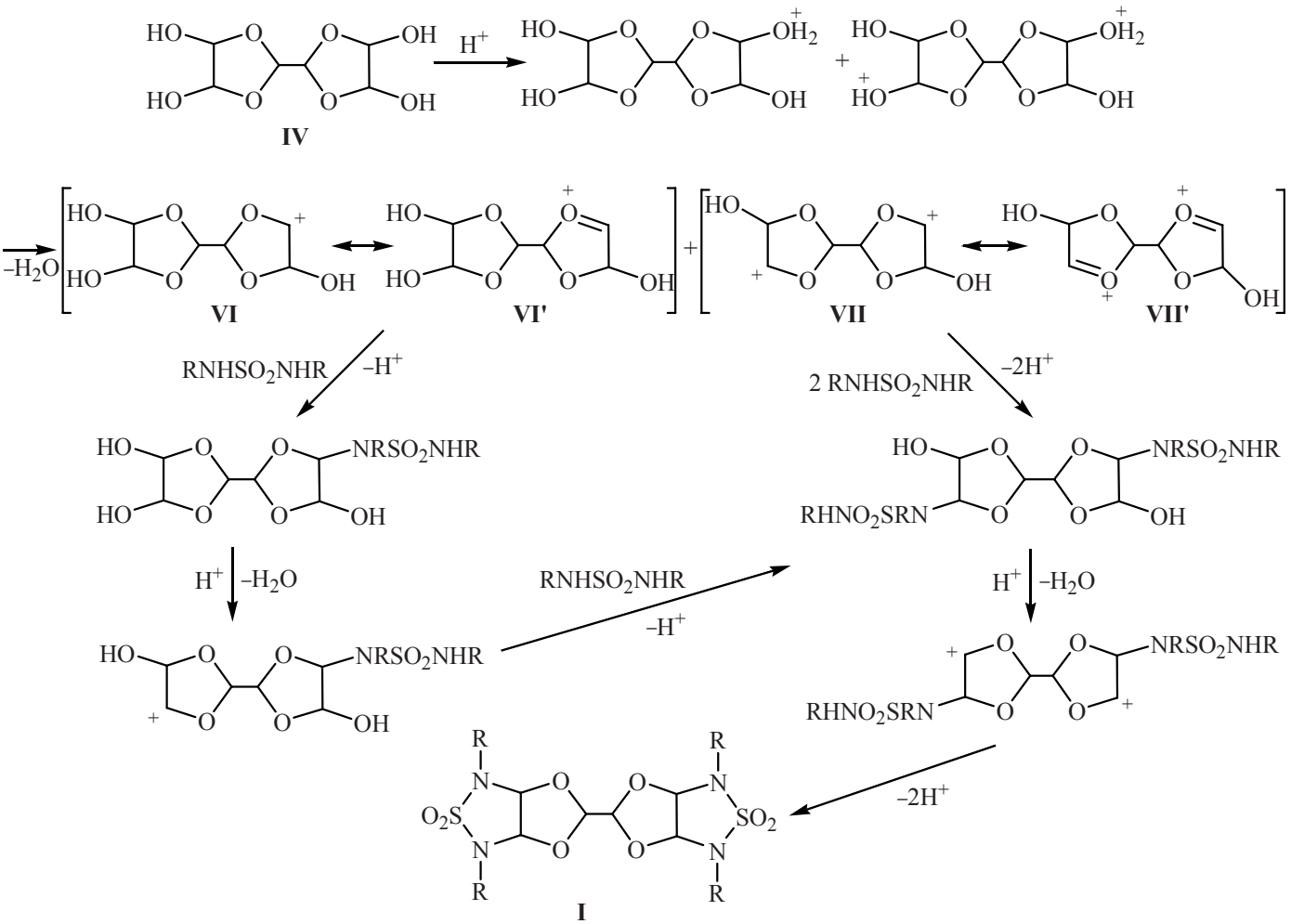
The value of the direct coupling constant $^1J$(CH) in compounds **Ic** and **IIa** varying with the changing length of the C–H bond is notably larger for the protons at the bicyclic atoms $C^{1,1',5,5'}$ than for the protons at the bridging atoms $C^{3,3'}$. The value of the vicinal coupling constant $^3J$(HH) varying at the change of the dihedral angle between the coupling protons also is larger for the protons at the bicyclic carbon atoms than for the protons at the bridging carbon atoms. Therewith the value of the vicinal coupling constant for the protons at the bridging carbon atoms is an average value depending on the conformational equilibrium at the free rotation around the bridging C–C bond. The value of the direct coupling constant $^1J$(CH) is considerably larger for $H^1$ than for $H^3$. The value of vicinal coupling constant $^3J$(HH) for $H^{1,5}$ is also larger than that for $H^{3,3'}$.

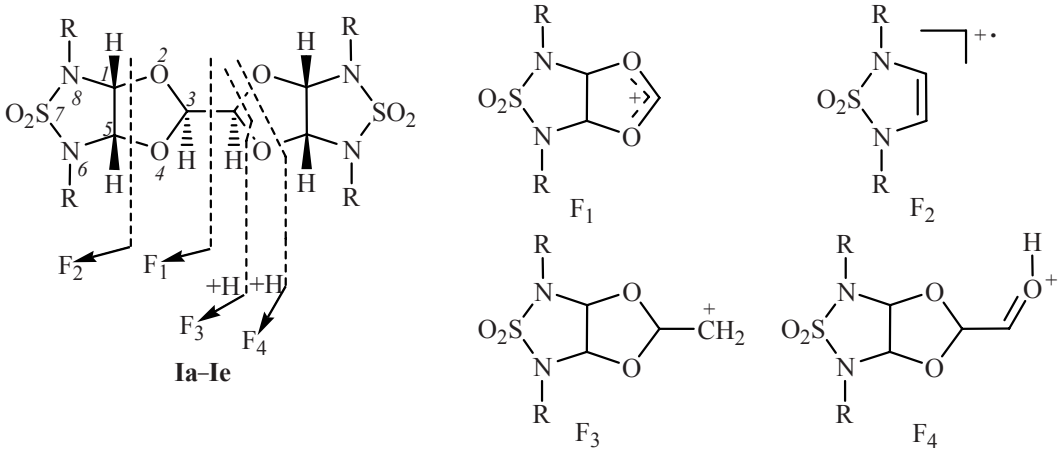
**Table 1.** Direct and vicinal coupling constants of protons at bridging (*3*,*3*') and bicyclic (*1*, *5*) carbon atoms in the spectra HMQC (hmqcndld) of compounds **Ic** and **IIa**

| Compd. no. | $^1J$[CH(*1*)] | $^3J$[HH(*1*–*5*)] | $^1J$[CH(*3*)] | $^3J$[HH(*3*–*3*')] |
|---|---|---|---|---|
| **Ic** | 185.3 | 5.3 | 173.6 | 3.7 |
| **IIa** | 181.6 | 5.2 | 171.9 | 4.1 |

The comparative analysis of the experimentally measured coupling constants in the solutions of compounds **Ic** and **IIa** suggests that their structures are similar. The difference in the values of the coupling constants of

**Scheme 3.**

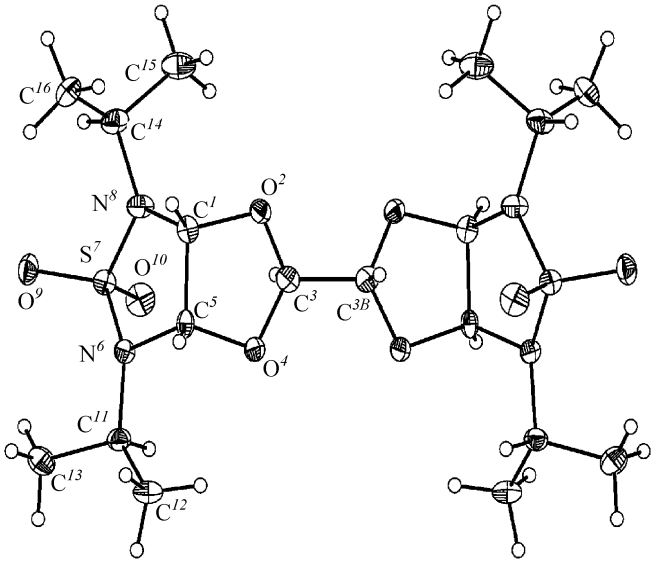





compounds **Ic** and **IIa** may be due to the distortion of the rings in going from C=O to $SO_2$, and also by the shift in the conformational equilibrium at the free rotation around the bridging C–C bond.

The specific feature of the mass spectra of compounds **I** consists in the low intensity or even absence of the molecular ion peaks, and the primary fragment ions $F_1$ and $F_2$ apparently form from $M^+$ by the rupture of the $C^3$–$C^{3'}$ bond or the dioxolane ring [13] in structures **I**.

The peaks of ions $F_1$ with *m/z* 1/2 *M* possess the maximum intensity. The formation of ions $F_3$ and $F_4$ is accompanied by hydrogen migration probably from atoms $C^1$ or $C^5$ to $C^3$ or $O^2$ respectively. The secondary fragment ions form from the primary ones by elimination of R as radicals or the corresponding olefins, and also of molecules CO, HCOOH, and $SO_2$.



General view of one of independent molecules (A) of compound **Ic** represented by ellipsoids of thermal oscillations (*p* 50%).

Analysis of the mass spectra of compound **IIa** published in [11] shows the total analogy of the fragmentation.

The structure of the bibicycle **Ic** was unambiguously established from the XRD analysis and X-ray phase analysis that demonstrated the identity of the obtained X-rayogram of the powder to that calculated from the data of XRD analysis of a single crystal (see the figure).

As showed the XRD analysis compound **Ic** crystallized with two independent molecules in the unit cell (A and B), and each of the molecules is located in the symmetry center coinciding with the center of bonds $C^{3}$–$C^{3B}$ and $C^{3A}$–$C^{3AA}$. In both molecules the bicyclic fragment is built by a *cis*-junction of a thiadiazolidine and dioxolane rings, and atoms $H^{3,3A}$ are axial and are mutually *trans*-oriented. In all cases the thiadiazolidine ring is present in the envelop conformation, but the atoms deviating from the plane of the others are different ($N^6$ in molecule A by 0.38 Å and $S^{7A}$ in molecule B by 0.54 Å). Analogously the conformations of the dioxolane ring are also different: in molecule A a *twist*-conformation is observed with deviations of atoms $C^3$ and $O^2$ by 0.27 and –0.25 Å, whereas in molecule B an envelop conformation is present with the deviation of $C^{3A}$ by 0.39 Å. The relative configurations of the asymmetric centers in the bicyclic fragment are $C^1$, *R**; $C^5$, *S**, and of the pseudoasymmetric atom $C^3$, *s**.

Notwithstanding the different conformations the main bond distances and bond angles in the two independent molecules have close values (Tables 2 and 3). One of the interesting features of compound **Ic** are essential difference in the bond lengths of C–N and S–N bonds for two nitrogen atoms of the thiadiazolidine ring. As seen, in molecules A and B the bonds $S^7$–$N^8$ and $S^{7A}$–$N^{8A}$ are significantly shortened to 1.616(2)–1.623(2) Å compared with $S^7$–$N^6$ and $S^{7A}$–$N^{6A}$ [1.656(2)–1.658(2) Å], and the bonds $C^1$–$N^8$ and $C^{1A}$–$N^{8A}$ are on the contrary elongated

compared with $C^5$–$N^6$ and $C^{5A}$–$N^{6A}$. The observed variations in the bond lengths involving nitrogen are also accompanied by different degree of the pyramidal structure of their valence surroundings. For instance, the sum of the bond angles for atoms $N^6$ and $N^{6A}$ is 342 and 347 deg indicating the essentially pyramidal structure, whereas the analogous values for atoms $N^8$ and $N^{8A}$ amount to 359 and 356.7 deg and thus the valence surrounding of these nitrogen atoms is flattened. The significant difference in the reciprocal position of the isopropyl substituents with respect to the S–N bond of the ring also should be stressed. For atoms $N^8$ and $N^{8A}$ the bond $C^{14}$–$H^{14A}$ is periplanar to the S–N bond whereas for atoms $N^6$ and $N^{6A}$ the corresponding $C^{11}$–$H^{11A}$ bond is normal to the average plane of the thiadiazolidine ring. Taking into consideration that among the C–H bonds the "eclipsed" bonds are commonly those with the largest π-component [14] it is presumable that the S–N bonds of atom $N^8$ are characterized by the larger contribution of the *p*-orbitals of the nitrogen atom. The like nonequivalence of bond distances in the thiadiazolidine ring we have observed before and attributed it to the presence of stereoelectronic interactions [9, 15] that in compound **Ic** might consist in a charge transfer from the lone electron pair of the nitrogen atom to the antibonding orbitals of S–O, S–N, or C–O bond. However in this structure the analysis of the pseudotorsion angles shows that the lone electron pairs of nitrogens, both $N^6$ and $N^8$, are directed antiperiplanar to S–O and C–O bonds of the dioxolane ring and consequently their stereoelectronic interactions should be identical, and the observed differences cannot be attributed to the charge transfer. In its turn the analysis of the crystal packing shows that all the intermolecular contacts correspond to weak interactions that cannot result in essential variation of the bond lengths. Therefore it is possible to conclude that beside the stereoelectrinic interactions the variation of the bond lengths in this heterocycle can be affected by the other factors, namely, the electronegativity of the substituents (here $SO_2$) at the nitrogen atom that might stabilize the flat configuration of the nitrogen and consequently the change in its hybridization. We formerly observed similar effects, for instance, in azophosphorinane rings [16].

The antimicrobial and fungicidal activity of compounds **Ic** and **Ie** respectively was tested.*

**Table 2.** Main bond distances (*d*) in molecules of compound **Ic**

| A | | B | |
|---|---|---|---|
| Bond | *d*, Å | Bond | *d*, Å |
| $C^1$–$O^2$ | 1.409(3) | $C^{1A}$–$O^{2A}$ | 1.425(3) |
| $C^1$–$N^8$ | 1.436(3) | $C^{1A}$–$N^{8A}$ | 1.434(3) |
| $C^1$–$C^5$ | 1.540(3) | $C^{1A}$–$C^{5A}$ | 1.540(3) |
| $O^2$–$C^3$ | 1.411(3) | $O^{2A}$–$C^{3A}$ | 1.411(3) |
| $C^3$–$O^4$ | 1.420(3) | $C^{3A}$–$O^{4A}$ | 1.415(3) |
| $C^3$–$C^{3B}$ | 1.489(5) | $C^{3A}$–$C^{3AA}$ | 1.495(5) |
| $O^4$–$C^5$ | 1.437(3) | $O^{4A}$–$C^{5A}$ | 1.427(3) |
| $C^5$–$N^6$ | 1.451(3) | $C^{5A}$–$N^{6A}$ | 1.463(3) |
| $N^6$–$S^7$ | 1.658(2) | $N^{6A}$–$S^{7A}$ | 1.656(2) |
| $S^7$–$O^9$ | 1.436(2) | $S^{7A}$–$O^{9A}$ | 1.432(2) |
| $S^7$–$O^{10}$ | 1.437(2) | $S^{7A}$–$O^{10A}$ | 1.441(2) |
| $S^7$–$N^8$ | 1.616(2) | $S^{7A}$–$N^{8A}$ | 1.623(2) |

**Table 3.** Main bond angles (ω) in molecules of compound **Ic**

| A | | B | |
|---|---|---|---|
| Angle | ω, deg | Angle | ω, deg |
| $C^5N^6C^{11}$ | 120.0(2) | $C^{5A}N^{6A}C^{11A}$ | 115.85(19) |
| $C^5N^6S^7$ | 110.31(17) | $C^{5A}N^{6A}S^{7A}$ | 109.19(16) |
| $C^{11}N^6S^7$ | 116.73(16) | $C^{11A}N^{6A}S^{7A}$ | 117.00(17) |
| $O^9S^7O^{10}$ | 114.84(11) | $O^{9A}S^{7A}O^{10A}$ | 114.74(11) |
| $O^9S^7N^8$ | 109.42(12) | $O^{9A}S^{7A}N^{8A}$ | 109.08(11) |
| $O^{10}S^7N^8$ | 113.04(12) | $O^{10A}S^{7A}N^{8A}$ | 113.94(11) |
| $O^9S^7N^6$ | 111.88(11) | $O^{9A}S^{7A}N^{6A}$ | 112.60(11) |
| $O^{10}S^7N^6$ | 111.36(11) | $O^{10A}S^{7A}N^{6A}$ | 111.26(10) |
| $N^8S^7N^6$ | 94.57(11) | $N^{8A}S^{7A}N^{6A}$ | 93.33(10) |
| $C^1N^8C^{14}$ | 123.0(2) | $C^{1A}N^{8A}C^{14A}$ | 123.3(2) |
| $C^1N^8S^7$ | 115.04(17) | $C^{1A}N^{8A}S^{7A}$ | 113.31(16) |
| $C^{14}N^8S^7$ | 121.02(17) | $C^{14A}N^{8A}S^{7A}$ | 120.05(17) |

The study of the antimicrobial activity of compound compound **Ic** revealed that it exhibited a weak antimicrobial action showing a bacteriostatic effect with respect to *Staphylococcus aureus* at a concentration >1000 μg/ml.

Compound **Ie** exhibited a fungicidal activity with respect patogenes causing root rots and seed mold of agricultural crops: *Botrytis cinerea*, *Fusarium oxysporum*, *Helminthosporium sativum,* and *Fusarium graminearum*; however, this activity is twice and more lower than that of thiram.

* The fungicidal activity was investigated in FGUP "VNIIKhSZP" under supervision of V.A. Abelentsev, the antimicrobial activity was studied in FGNU "Institute of Natural Sciences" at the Perm State University and under supervision of G.A. Aleksandrova.

By and large a simple one-stage method was developed for the synthesis of derivatives of a new heterocyclic system of [1,3]dioxolano[4,5-*c*][1,2,5]thiadiazolidine, 3,3'-bi(6,8-dialkyl-2,4-dioxa-7-thia-6,8-diazabicyclo[3.3.0]-octane-7,7-dioxides) from accessible components: 1,3-dialkylsulfamides and glyoxal dihydrate trimer. The structure of the new heterocyclic system was proved by the sum of physicochemical analytical methods and by X-ray diffraction study.

## EXPERIMENTAL

NMR spectra were registered on spectrometers Bruker AM-250 ($^1$H, 250.13 MHz) and Bruker AM-300 ($^{13}$C, 75.5 MHz) in DMSO-$d_6$, chemical shifts were reported relative to an internal reference TMS. The coupling constants were estimated from the data of 1D HMQC spectra (HMQCNDLD) [17]. IR spectra were recorded on a spectrophotometer SPECORD M82 from pellets with KBr. Mass spectra were obtained on MS-30 Kratos instrument at the energy of ionizing electrons 70 eV. Melting points were measured on Sanyo Gallenkamp instrument. 1,3-Dialkylsulfamides were obtained by procedures [18–20]. TLC was performed on Silufol UV-254 plates, eluent ethyl acetate–petroleum ether, 1:1.

**3,3'-Bi{(1*R**,3*s**,5*S**)-6,8-dialkyl-2,4-dioxa-7-thia-6,8-diazabicyclo[3.3.0]octane-7,7-dioxides}. General procedure.** To 10 mmol of 1,3-dialkylsulfamide and 1.05 g (5 mmol) of glyoxal dihydrate trimer was added 10 ml of concn. HCl, and the mixture was stirred at 35–40°C for 2 h for **Ia**, 1 h for **Ib** and **Ic**, 30 min for **Ie**. The separated colorless precipitate of compound **Ia–Ic** and **Id** was filtered off, washed with water (4–5 × 5 ml), and recrystallized from methanol (**Ia–Ic**) or from a large amount of dioxane (**Ie**).

**Compound Ia.** Yield 1.19–1.24 g (54–56%), mp 219–221°C (decomp.), $R_f$ 0.39. IR spectrum, ν, cm$^{-1}$: 2990, 2945 (Et), 1307, 1148 ($SO_2$), 1175, 1090, 1025 (OCO). $^1$H NMR spectrum, δ, ppm: 1.23 t (12H, 4Me, *J* 6.7 Hz), 3.22–3.30 m (8H, 4$NCH_2$), 5.03 s (2H, CHCH), 5.79 s (4H, 2CHCH). $^{13}$C NMR spectrum, δ, ppm: 13.9 (Me), 39.1 ($NCH_2$), 87.2 (CH), 102.3 (CH). Mass spectrum, *m/z* ($I_{rel}$, %): 441 (0.8), 251 (3), 221 (96), 193 (63), 176 (92). Found, %: C 38.03; H 5.90; N 12.68; S 14.45. $C_{14}H_{26}N_4O_8S_2$. Calculated, %: C 38.00; H 5.92; N 12.66; S 14.49. *M* 442.50.

**Compound Ib.** Yield 1.79–1.84 γ (72–74%), mp 173–175°C (decomp.), $R_f$ 0.72. IR spectrum, ν, cm$^{-1}$: 2969, 2930, 2890 (Pr), 1310, 1155 ($SO_2$), 1167, 1095, 1044 (OCO). $^1$H NMR spectrum, δ, ppm: 0.93 t (12H, 4Me, *J* 7.3 Hz), 1.58–1.73 m (8H, 4$CH_2$), 3.09–3.23 m (8H, 4$NCH_2$), 5.06 s (2H, CHCH), 5.83 s (4H, 2CHCH). Mass spectrum, *m/z* ($I_{rel}$, %): 279 (1), 249 (87), 221 (47), 204 (70), 179 (72), 111 (100). Found, %: C 43.39; H 6.89; N 11.28; S 12.82. $C_{18}H_{34}N_4O_8S_2$. Calculated, %: C 43.36; H 6.87; N 11.24; S 12.86. *M* 408.61.

**Compound Ic.** Yield 1.34–1.42 γ (54–57%), mp 229–231°C (decomp.), $R_f$ 0.59. IR spectrum, ν, cm$^{-1}$: 2984, 2936 (*i*-Pr), 1304, 1160 ($SO_2$), 1196, 1096, 1064 (OCO). $^1$H NMR spectrum, δ, ppm: 1.29 d (24H, 8Me, *J* 6.6 Hz), 3.73–3.83 m (4H, 4NCH), 5.07 s (2H, CHCH), 5.90 s (4H, 2CHCH). Mass spectrum, *m/z* ($I_{rel}$, %): 498 (0.8), 279 (3), 263 (6.5), 249 (61), 204 (62.5). Found, %: C 43.35; H 6.91; N 11.21; S 12.81. $C_{18}H_{34}N_4O_8S_2$. Calculated, %: C 43.36; H 6.87; N 11.24; S 12.86. *M* 498.61.

**Compound Ie.** Yield 1.56–1.64 g (81–85%), mp 253–254°C (decomp.). IR spectrum, ν, cm$^{-1}$: 2976, 2928 (Me), 1308, 1144 ($SO_2$), 1181, 1120, 1096, 1048 (OCO). $^1$H NMR spectrum, δ, ppm: 2.84 s (12H, 4$NCH_3$), 5.02 s (2H, CHCH), 5.72 s (4H, 2CHCH). Mass spectrum, *m/z* ($I_{rel}$, %): 193 (26), 165 (9.5), 148 (36), 124 (5), 83 (42). Found, %: C 31.12; H 4.71; N 14.46; S 16.57. $C_{10}H_{18}N_4O_8S_2$. Calculated, %: C 31.08; H 4.70; N 14.50; S 16.59. *M* 386.39.

**3,3'-Bi{(1*R**,3*s**,5*S**)-6,8-dibutyl-2,4-dioxa-7-thia-6,8-diazabicyclo[3.3.0]octane-7,7-dioxide} (Id).** To a solution of 1.04 g (5 mmol) of 1,3-dibutylsulfamide **Vd** in a minimal volume of methanol was added 0.53 g (2.5 mmol) of glyoxal dihydrate trimer and 10 ml of concn. HCl. The reaction mixture was stirred for 2 h at 35–40°C. The separated colorless precipitate of compound **Id** was filtered off, washed with water (4–5×5 ml), and recrystallized from methanol. Yield 0.99–1.02 g (71–73%), mp 180–182°C (decomp.), $R_f$ 0.68. IR spectrum, ν, cm$^{-1}$: 2960, 2944, 2872 (Bu), 1312, 1168 ($SO_2$), 1192, 1184, 1092, 1040 (OCO). $^1$H NMR spectrum, δ, ppm: 0.93 t (12H, 4Me), 1.30–1.44 m (8H, 4$CH_2$), 1.56–1.68 m (8H, 4$CH_2$), 3.11–3.25 m (8H, 4$NCH_2$), 5.00 s (2H, CHCH), 5.75 s (4H, 2CHCH). Mass spectrum, *m/z* ($I_{rel}$, %): 307 (2.5), 277 (100), 232 (81), 205 (52), 137 (42). Found, %: C 47.59; H 7.65; N 10.11; S 11.51. $C_{22}H_{42}N_4O_8S_2$. Calculated, %: C 47.63; H 7.63; N 10.10; S 11.56. *M* 554.72.

**3-{(1'*R**,3*s**,5'*S**)-6',8'-Dimethyl-2',4'-dioxa-7'-thia-6',8'-diazabicyclo[3.3.0]octane-7',7'-dioxid-3'-**

**yl}-{(1*R**,3*s**,5*S**)-6,8-dipropyl(isopropyl)-2,4-dioxa-7-thia-6,8-diazabicyclo[3.3.0]-octane-7,7-dioxides} If and Ig.** *General procedure.* A mixture of 1,3-dimethylsulfamide **Ve**, glyoxal dihydrate trimer, 1,3-dipropyl- or 1,3-diisopropylsulfamide **Vb** and **Vc**, each taken by 5 mmol, and 10 ml of concn. HCl (~36%), was stirred for 1 h at 35–40°C. The separated precipitate was filtered off and washed with water (4–5×5 ml), then 10 ml of methanol was added. The precipitate of compound **Ie** insoluble in methanol was filtered off (yield 7–10%), compounds **Ib** and **If** were separated by fractional crystallization from the filtrate, separation of compounds **Ic** and **Ig** was performed by column chromatography on $SiO_2$ (100 × 160), eluent ethyl acetate–petroleum ether, 1:1. $R_f$ 0.59 (**Ic**), 0.48 (**Ig**).

**Compound If.** Yield 1.44–1.50 g (65–68%), mp 211–213°C. IR spectrum, ν, cm$^{-1}$: 2976, 2936, 2880 (Me, Pr), 1304, 1156 ($SO_2$), 1192, 1112, 1088, 1048 (OCO). $^1$H NMR spectrum, δ, ppm: 0.90 t (6H, 2Me, *J* 7.2 Hz), 1.55–1.67 m (4H, 2$CH_2$), 2.81 s (6H, 2Me), 3.05–3.22 m (4H, 2$NCH_2$), 5.02 s (2H, CHCH), 5.75 s (2H, CHCH), 5.80 s (2H, CHCH). Mass spectrum, *m/z* ($I_{rel}$, %): 249 (63), 204 (63), 193 (43), 179 (18), 148 (55), 111 (100), 83 (70). Found, %: C 38.05; H 5.96; N 12.64; S 14.44. $C_{14}H_{26}N_4O_8S_2$. Calculated, %: C 47.63; H 7.63; N 10.10; S 11.56.*M* 442.50.

**Compound Ig.** Yield 1.17–1.22 g (53–55%), mp 239–241°C. IR spectrum, ν, cm$^{-1}$: 2982, 2936 (Me, *i*-Pr), 1306, 1149 ($SO_2$), 1194, 1095, 1050 (OCO). $^1$H NMR spectrum, δ, ppm: 1.28 d (12H, 4Me, *J* 6.6 Hz), 2.82 s (6H, 2Me), 3.72–3.82 m (2H, 2NCH), 5.03 s (2H, CHCH), 5.77 s (2H, CHCH), 5.87 C (2H, CHCH).

Crystals for XRD study were obtained by crystallizing compound **Ic** from methanol. $C_{18}H_{34}N_4O_8S_2$, *M* 498.61. Crystals at 100 K monoclinic: *a* 21.243(3), *b* 10.356(2), *c* 21.912(4) Å, β 97.516(5)°, *V* 4779.4(15) Å$^3$, $d_{calc}$ 1.386 g cm$^{-3}$, space group *C*2/*c*, *Z* 8. Intensities of 16347 reflections were measured on an automatic diffractometer Smart APEX II CCD at 100 K (MO$K_\alpha$-radiation, graphite monochromator, ω-scanning, $2\theta_{max}$ 56°), 5749 of observed reflections were used in the subsequent calculations. The structure was solved by the direct method and refined in the full-matrix least-mean-square method in the anisotropic-isotropic approximation by $F^2$. The positions of hydrogen atoms were localized from the difference synthesis of the electron density and were refined in the *rider* model. The final divergence factors are as follows: w$R_2$ 0.0779, *GOF* 1.004, $R_1$ 0.0496 [calculated for 3236 reflexions with $I > 2\sigma(I)$ by software SHELXTL PLUS].

Powder X-rayogram was obtained on a diffractometer Bruker D8 Advance (*T* 298 K, λCu$K_\alpha$-radiation, Gobel mirrors, θ/2θ scanning with a step 0.02).

The study was carried out under a financial support of the Russian Academy of Sciences (program OKh-10).

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