Polyfused nitrogen-containing heterocycles 18.* 2′-Amino-5-methyl-1,2,3,4,4′,5′-hexahydrospiro[quinoxaline-2,4′-thiazol]-3-ones. Synthesis, structure, and recyclization

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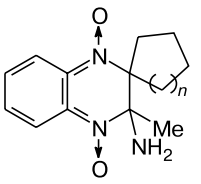
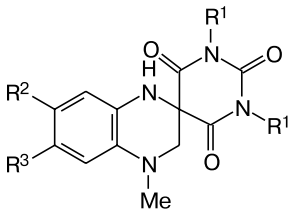
Bis-3-(α-bromoethyl)quinoxalin-2-ones with 3-oxapentane or 3,6-dioxaoctane spacer binding two heterocyclic fragments react with thiourea to give the corresponding bis-spirothiazoloquinoxalines, which upon treatment with acetic anhydride can be converted to podands with terminal thiazoloannulated quinoxaline fragments. X-Ray data for 2′-amino-4-ethyl-5-methyl-1,2,3,4,4′,5′-hexahydrospiro[quinoxaline-2,4′-thiazol]-3-one indicate for this compound a potentiality to form clathrate structures with various solvate molecules.

Key words: 3-(α-bromoethyl)quinoxalin-2-ones, spirothiazoloquinoxalines, thiazolo[3,4-*a*]quinoxalines, recyclization, podands, IR spectroscopy, NMR spectroscopy, X-ray analysis.

Heterocyclic compounds with endo- and exocyclic functional groups are convenient starting materials in the synthesis of their fused derivatives. For example, 3-(α-haloethyl)quinoxalin-2-ones, containing alkyl halogenide fragment, imine and carbamoyl groups, allow one to synthesize various pyrrolo[*a*]-, pyrrolo[*b*]-, azolo[*a*]-, and azolo[*b*]-annulated fused quinoxaline derivatives depending on the bifunctional reagent used.[2—8] Such an approach is also used for the synthesis of other heterocyclic systems, first of all, quinoxalines showing a wide range of biological activity.[9—13] It is well known that compounds containing spirocarbocyclic and spiroheterocyclic frag-



1a—c



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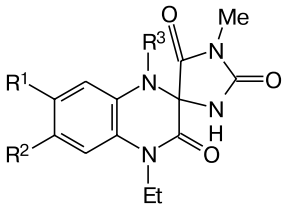

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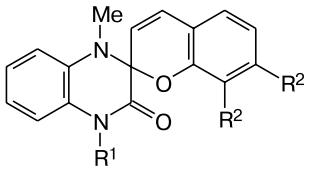

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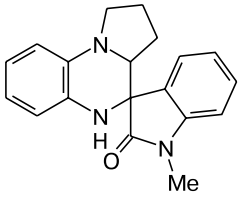

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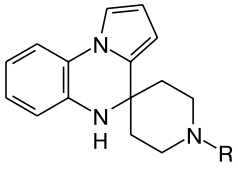

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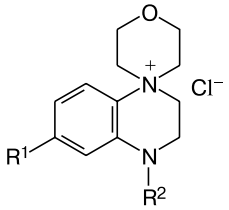

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n = 1 (**1a**), 2 (**1b**), 3 (**1c**)

* For Part 17, see Ref. 1.

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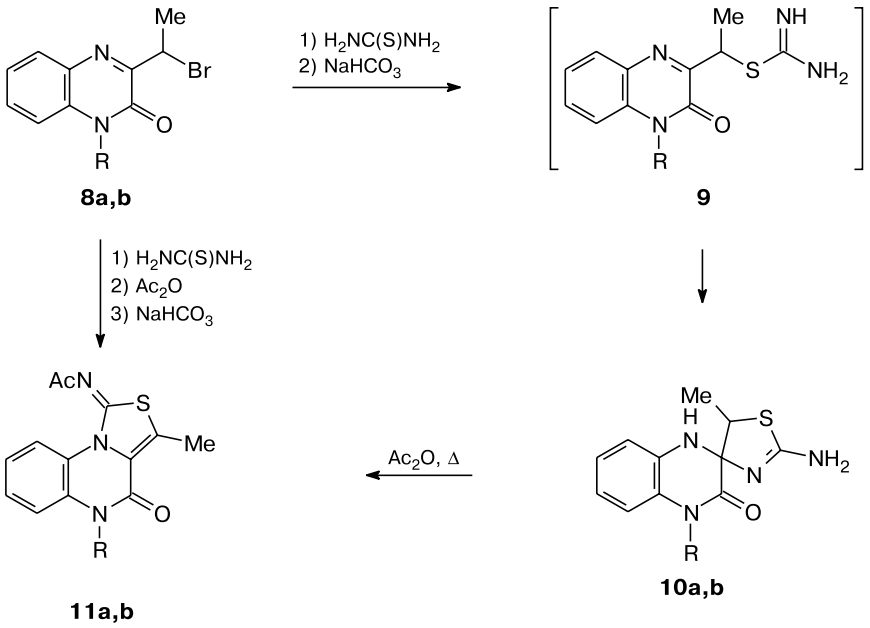
Scheme 1



R = H (**a**), Et (**b**)

ments, which are the structural components of many biologically active natural compounds,[14–16] can be synthesized by means of rather uncommon reactions.

As to the spiro derivatives of quinoxaline, methods for the synthesis of only few their representatives are known, for example, spirocyclopentane- (**1a**),[17] spirocyclohexane- (**1b**),[17,18] spirocycloheptane- (**1c**),[17] spiropyrimidine- (**2**),[19] spiroimidazole- (**3**),[20,21] and spirobenzopyranquinoxalines (**4**),[22] as well as spiroindole- (**5**)[19,23] and spiropyridinepyrrolo[1,2-*a*]quinoxalines (**6**),[24] in which the carbon atom in position 2 or 3 of the quinoxaline system serves as the spiro-atom, and only in case of spiromorpholine derivative (**7**),[25] it is the nitrogen atom. The syntheses of these compounds are mainly based on the intramolecular cyclization of *o*-phenylenediamine derivatives,[18,19,21,26] on the recyclization of the more complicated heterocyclic systems containing quinoxaline fragment,[20,21,23] on the reaction of benzofuroxan with various ketones,[17] and only in one case, on the reaction of quinoxaline derivative with salicylaldehyde and its benzo derivative.[24]

Earlier, we found that 3-(α-bromoethyl)quinoxalin-2-ones (**8a,b**) reacted with thiourea through the formation of the intermediate compounds **9a,b** to give spiroquinoxalinethiazoles (**10a,b**), which upon a short-time heating in acetic anhydride were converted to thiazolo[3,4-*a*]quinoxalines **11a,b**[27] (Scheme 1).

Thiazolo[3,4-*a*]quinoxalines can be also obtained in good yields without isolation of the intermediate spiroquinoxalinethiazoles **10a,b**.

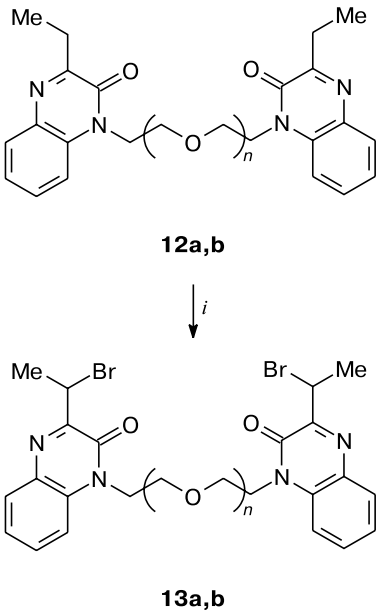
Results and Discussion

The present work deals with the application of the new approach to the synthesis of thiazolo-4,2′-spiro[quinoxaline-2,4′-thiazoles] and thiazolo[3,4-*a*]quinoxalines for the preparation of their bis-analogs with 3-oxapentane and 3,6-dioxaoctane spacers, since, as a rule, they are not inferior to the corresponding monosystems in biological activity,[28] whereas methods for their preparation are few.[29,30] In this work, the structure of spiro compounds is also studied in more details.

Bromination of bis-3-ethylquinoxalin-2-ones **12a,b** under conditions similar to the bromination of 3-ethylquinoxalinones with the complex of bromine with dioxane in a dioxane solution, proceeds smoothly to form the corresponding α-bromoethyl derivatives of bis-quinoxalinones **13a,b** (Scheme 2). It can be seen from the disappearance of triplet and quartet signals of the ethyl group at δ 1.30 and 2.90, respectively, in the ^{1}H NMR spectra of compounds **12a,b** and from the appearance of doublet and quartet signals of the —CH(Br)—CH_3 group at δ 2.10 and 5.60, respectively, in the spectra of bis-alkyl bromides **13a,b**.

In the reaction of bis-quinoxalinones **13** with thiourea, the presence of two α-bromoethyl fragments in their structure suggests the formation not only of bis-spiroquinoxalines **14** similarly to the mono(α-bromoethyl)quinoxalinone **8**, but also of compounds **15** and **16** or their tautomeric forms (Scheme 3). However, in the ^{1}H NMR spectra of the products of the reaction of com-

Scheme 2



12a,b

13a,b

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

i. Br_2, dioxane, 8—12 °C, 4 h.

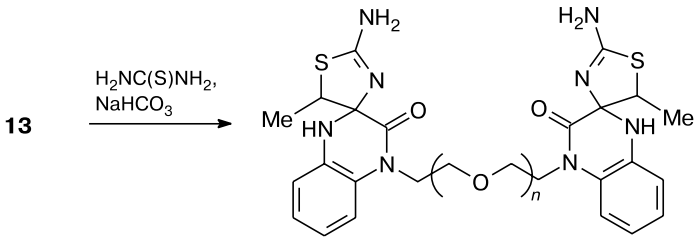
pounds **8a,b** with thiourea, positions and multiplicity of signals of the aromatic protons and protons of the —$CHCH_3$ group virtually are similar to those in the ^{1}H NMR spectra of the spiroquinoxalines **10a,b**, which indicates the formation of bis(spiroquinoxalinethiazolyl)-alkanes **14a,b** as a result of these reactions. In the ^{13}C NMR spectra of compound **14b**, the presence of a signal of the spiro carbon atom at δ 88 (along with signals of 14 carbon atoms) confirms the formation of compounds **14a,b**.

Similarly to spiroquinoxalinethiazole **10**, bis-thiazolospiroquinoxaline **14a** upon treatment with acetic anhydride readily undergoes recyclization to form bis-thiazolo[3,4-*a*]quinoxaline **17** (Scheme 4).

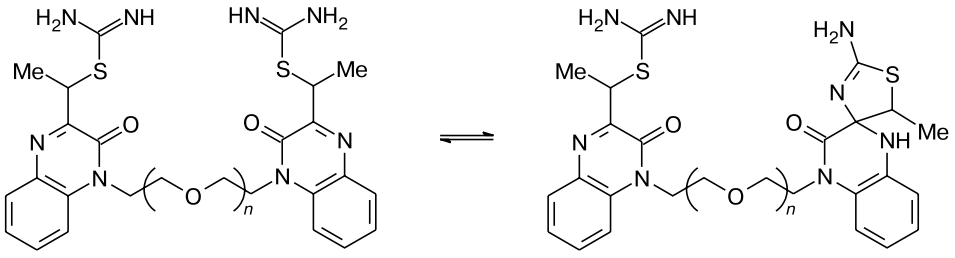
Thiazolo[*a*]annulation, apparently, proceeds through the open-chain acylated isothioureide tautomeric form **9a** (or **15a**), formed as a result of the spiro compound opening with acetic anhydride. This form undergoes further acylation at the most nucleophilic isothioureide nitrogen atoms to give diacyl derivatives of 3-(α-isothioureido)ethylquinoxalin-2-one containing highly electrophilic isothioureide carbon atom. A nucleophilic attack of the nitrogen atom of the pyrazine ring at the isothioureide carbon atom leads to the thiazole ring closure at the *a* side of the quinoxaline. This thiazolo[*a*]annulation can proceed with elimination of NH_3, $AcNH_2$, or Ac_2NH (Scheme 5).

The upfield shift by ~1 ppm of signals of the benzo fragment of the quinoxaline system in the ^{1}H NMR spectra and the presence of a signal characteristic of the spiro atom at δ 89 in the ^{13}C NMR spectra[31,32] testify to spiro-

Scheme 3



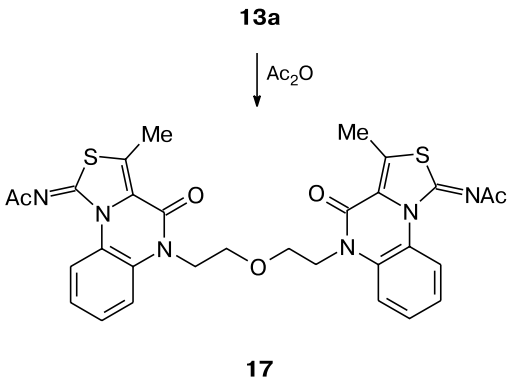
14a,b



15a,b **16a,b**

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

Scheme 4

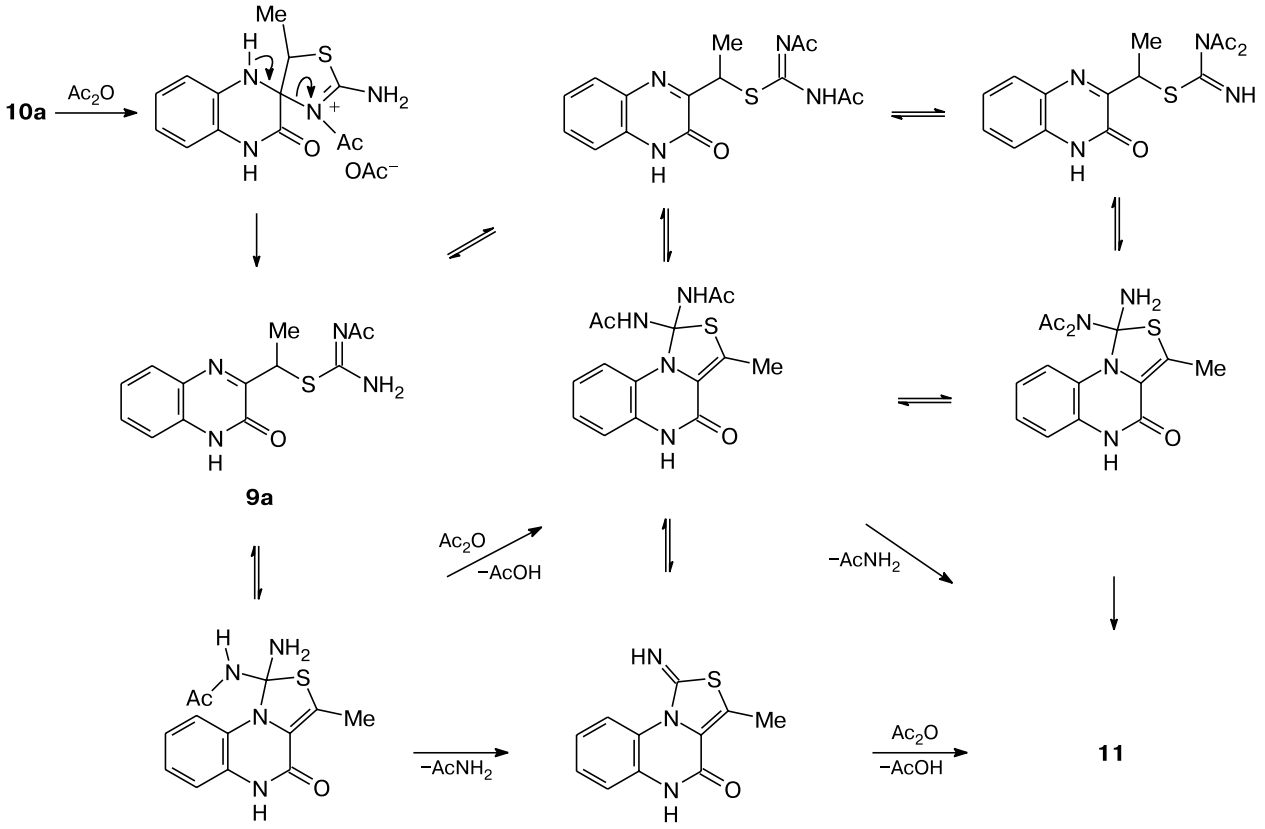


quinoxalinethiazoles formation, whereas the formation of 1-iminothiazolo[3,4-*a*]quinoxaline system is indicated by the presence of a signal of H(9) proton in the ^{1}H NMR spectrum, which is diagnostic of the azolo[*a*]annulation of quinoxalines and is observed in the relatively downfield part (δ 9.9)[18,33] as compared with the other aromatic protons.

Analysis of the ^{1}H NMR spectra of compounds synthesized shows that positions of signals and their multiplicity for each type of compounds (3-α-bromoethylquinoxalin-2-one and its bis-analog, spiroquinoxalinethiazole and its bis-analog, thiazolo[3,4-*a*]quinoxaline and its bis-analog) remain virtually unchanged. For example, methyl and methyne protons of the ethylidene CH_3CH= group in the ^{1}H NMR spectra of compounds **8** and **13a,b**, **10a,b** and **14a,b** resonate at δ 2.1 and 5.7, 1.4 and 4.9, respectively. Protons of the methyl groups of the thiazole ring and of the iminoacyl group in thiazolo[3,4-*a*]quinoxalines **11a,b** and their bis-analogs **17** resonate at δ 2.3 and 2.7, respectively. It should be noted that the breaking of aromaticity of the pyrazine ring in spiroquinoxalinethiazoles **10a,b** and **14a,b** results in the upfield shift of signals of the protons of the benzene ring by ~1.0 ppm as compared with signals of the protons of aromatic derivatives of quinoxaline **8**, **11a,b**, **13a,b**, and **17**. Signals of H(9) protons of thiazolo[3,4-*a*]quinoxaline systems **11a,b** and **17**, being diagnostic for these systems,[6,8,29,33,34] are observed in the region δ 9.0—10.1, whereas signals of H(5) protons of quinoxalines **8**, **11a,b**, **13a,b**, and **17** and spiroquinoxalinethiazoles **10a,b** and **14a,b**, at δ 7.87 and 6.7—7.1, respectively.

Furthermore, the presence of two and four asymmetric centers in compounds **10a,b** and **14a,b**, respectively, suggests the formation of other diastereomers in addition to the isolated ones. However, a comparison of the

Scheme 5



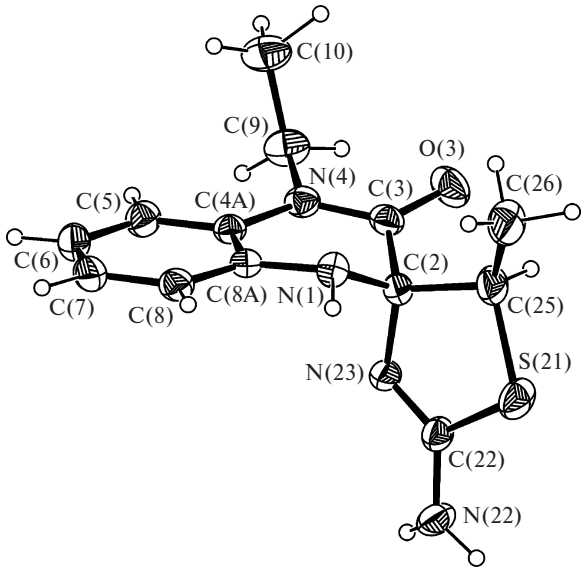


Fig. 1. ORTEP Diagram of molecule **10b** in a crystal. Ellipsoids of thermal vibrations of nonhydrogen atoms are shown with probability of 30%, hydrogen atoms are shown by spheres of arbitrary radii. Molecules of DMSO are not shown.

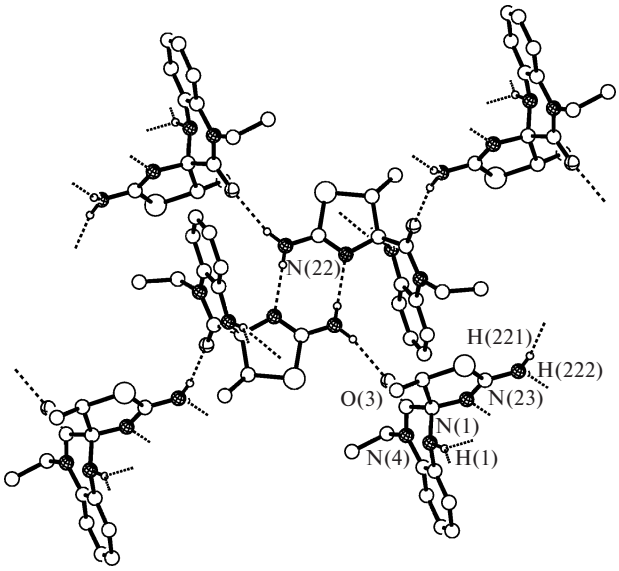


Fig. 2. Hydrogen bonds in crystal **10b**; only hydrogen atoms participating in hydrogen bonds are shown (dotted lines). Molecules of DMSO are not shown.

^{1}H NMR spectra of the crude products and the samples, obtained after recrystallization, showed the presence of only one diastereomer in every case, which point out the high stereoselectivity in the spiro system formation.

The structure of spiroquinoxalinethiazole **10b** was also established by X-ray analysis. Molecule **10b** is located in a general position of a rhombic cell (Fig. 1) and crystallizes with participation of DMSO molecule. The solvate molecule in the crystal is disordered over two positions with relative occupancies being 0.7 : 0.3. Though molecule of **10b** is chiral, it forms racemic crystals. The relative configurations of C(2) and C(25) carbon atoms are *S* and *R*, respectively. The thiazole ring of the molecule is in the envelope conformation with the angle between the plane fragments C(2)—C(25)—S(21) and C(2)—N(23)—C(22)—S(21) being 152°, whereas quinoxaline system is in the twisted envelope conformation with the deflection of C(2) and C(3) atoms from the plane (within 0.036(2) Å) fragment formed by the fused benzene ring and N(1) and N(4) nitrogen atoms being −0.674(3) and −0.116(3) Å, respectively. Carbon atom C(9) of the ethyl substituent is also deflected from this plane by 0.342(3) Å.

The presence of the spiro fragment in molecule **10b** prevents formation of the π—π interaction in the crystal, characteristic of the crystal packing of the thiazoloquinoxaline systems.[2] However, strong intermolecular hydrogen bonds of various types (N—H...O, N—H...N, C—H...O) are formed in the crystal of **10b**. Analysis of the crystal packing shows that a bilayers, bordered from both sides with the solvate molecules of DMSO, are formed in the crystal owing to classical hydrogen bonds. The N—H...N interaction in pairs with participation of one hydrogen atom of the amino group leads to the formation of dimeric molecules with center of symmetry (Fig. 2) with parameters of N(22)—H(222)...N(23″) interaction as follows: H(222)...N(23″) is 2.15 Å, N(22)...N(23″) is 3.039(3) Å, the angle N(22)—H(222)...N(23″) is 166°, operation of symmetry is $-x, -y, -z$.

The second hydrogen atom of the amino group interacts with the oxygen atom of the carbonyl group of the neighboring molecules to form N(22)—H(221)...O(3′) bond (H(221)...O(3′) is 2.08 Å, N(22)...O(3′) is 2.952(3) Å, the angle N(22)—H(221)...O(3′) is 168° ($1/2 - x$, $-1/2 + y$, z)). Since each molecule of the dimer participates in two such interactions (as the donor and as the acceptor), the H-dimers of the molecules are bound in two directions in endless double layer parallel to the crystallographic plane 0*ab* (Fig. 3). The solvate molecules of DMSO, disordered over two positions, are located on the external sides of this bilayer. The disordering of the molecules does not prevent participation of their oxygen atom in N(1)—H(1)...O(1) hydrogen bond with the hydrogen atom of the NH group (H(1)...O(1) is 1.95 Å, N(1)...O(1) is 2.965(3) Å, the angle N(1)—H(1)...O(1) is 155°). Such bilayers are anti-parallel so that cylindrical cavities are observed in the crystal, filled with DMSO molecules in our case (see Fig. 3).

Taking into account the presence of the strong intermolecular hydrogen bonds between the compound molecules in the crystal and special conformations of the molecules, together leading to the formation of the supramolecular structure described, one can suggest that this compound rather belongs to the clathrate type of structures, in which guest molecules are located in the already formed

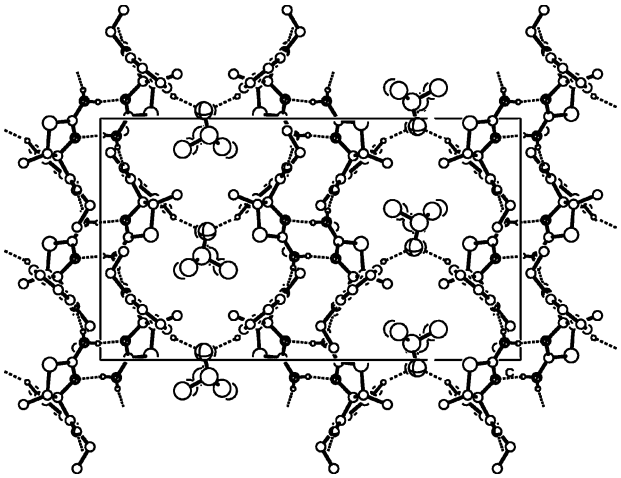


Fig. 3. Formation of the bilayer supramolecular structure in a crystal of compound **10b**. View along 0*a* axis, only hydrogen atoms participating in hydrogen bonds are shown (dotted lines). Nonhydrogen atoms of DMSO molecule (in position with occupancy of 0.7) are given in large spheres.

cavities of the crystal lattice of host compounds than to inclusion compounds or inclusion complexes. These data indirectly indicate the potential possibility of cocrystallization of this compound with solvate molecules of other types without significant changes of the crystal pack.

Experimental

Melting points were determined on a Boetius heating stage. IR spectra were recorded on a Bruker Vector-22 Fourier spectrometer in Nujol. ^{1}H NMR spectra were recorded on a Bruker MSL-400 spectrometer (400.13 MHz), ^{13}C NMR spectra were recorded on a Bruker Avance-600 Fourier spectrometer (150.86 MHz) at 35 °C. Chemical shifts are given in δ scale. Signals of residual protons of the corresponding solvents were used as the internal standard.

Analysis of a monocrystal of **10b** was carried out at the X-ray Crystallography Department of the Center for Community Use on the basis of Laboratory of the Diffractional Research Methods, A. E. Arbuzov Institute of Organic and Physical Chemistry of the Kazan Research Center, Russian Academy of Sciences. The experiment was performed on a Nonius B.V. CAD-4 automatic X-ray diffractometer.

Crystals of **10b** are rhombic, $C_{13}H_{16}N_4OS \cdot C_2H_6OS$. At 20 °C, a = 10.249(2), b = 13.9868(6), c = 24.391(2) Å, V = 3496(1) Å^3, d_{calc} = 1.35 g cm^{-3}, Z = 8, space group *Pbca*. The unit cell parameters and the intensities of 4015 reflections, 2893 of which are with $I \geq 3\sigma$, were measured at 20 °C (graphite monochromator, λ(Cu-Kα), ω/2θ-scanning technique, $\theta \leq 74.20°$). The intensities of three control reflections showed no decrease in the course of the experiment, the absorption correction was made by the azimuthal scan method (μ(Cu) = 28.33 cm^{-1}). The structure was solved by direct method with the use of the SIR program[35] and refined first isotropically and then anisotropically. The hydrogen atoms were revealed from differential electron density maps. Their contribution to the structure amplitudes were taken into consideration with the fixed positional and isotropic temperature parameters. The final R factors were R = 0.060 and R_w = 0.090 based on 2893 independent reflections with $F^2 \geq 3\sigma$. All the calculations were carried out with the use of the MOLEN programs,[36] analysis of the intermolecular interactions and figures of the molecules were performed with the use of the PLATON program.[37] The X-ray diffraction data for compound **10b** were deposited with the Cambridge Structural Database (CCDC 635520).

3-(α-Bromoethyl)quinoxalin-2(1*H*)-one (8a),[38] 3-(α-bromoethyl)-1-ethylquinoxalin-2(1*H*)-one (8b),[27] and **1,*n*-bis(3-ethyl-2-oxoquinoxalin-1-yl)alkanes 12[39,40]** were obtained according to the procedures published earlier.

1,*n*-Bis[3-(α-bromoethyl)-2-oxoquinoxalin-1-yl]alkanes 13. A solution of bromine (0.22 mL, 4.32 mmol) in dioxane (10 mL) was added to a stirred mixture of compound **12** (2.21 mmol) and dioxane (30 mL) at 8—12 °C. The reaction mixture was stirred at this temperature for 4 h. The crystals formed were filtered off, washed with aqueous soda and water to obtain analytically pure compounds **13**.

1,5-Bis[3-(α-bromoethyl)-2-oxoquinoxalin-1-yl]-3-oxapentane (13a). The yield was 70%, m.p. 186—188 °C. Found (%): C, 50.20; H, 4.25; N, 9.72. $C_{24}H_{24}Br_2N_4O_3$. Calculated (%): C, 50.00; H, 4.17; N, 9.72. IR, ν/cm^{-1}: 463, 760, 1066, 1132, 1172, 1312, 1343, 1603, 1656. ^{1}H NMR ($CDCl_3$), δ: 2.09 (d, 6 H, Me, J = 6.8 Hz); 3.85 (t, 4 H, OCH_2, J = 5.6 Hz); 4.43 (t, 4 H, NCH_2, J = 5.6 Hz); 5.57—5.74 (m, 2 H, BrCH); 7.34 (dd, 2 H, H(6) or H(7), quinoxaline, J = 7.6 Hz, J = 7.6 Hz); 7.37 (d, 2 H, H(8), quinoxaline, J = 8.6 Hz); 7.48 (dd, 2 H, H(6) or H(7), quinoxaline, J = 8.1 Hz, J = 7.6 Hz); 7.87 (d, 2 H, H(5), quinoxaline, J = 7.8 Hz).

1,8-Bis[3-(α-bromoethyl)-2-oxoquinoxalin-1-yl]-3,6-dioxaoctane (13b). The yield was 78%, m.p. 183—185 °C. Found (%): C, 50.44; H, 4.76; N, 9.07. $C_{26}H_{28}Br_2N_4O_4$. Calculated (%): C, 50.34; H, 4.55; N, 9.03. IR, ν/cm^{-1}: 463, 500, 538, 602, 614, 671, 761, 871, 891, 968, 1006, 1064, 1082, 1120, 1137, 1170, 1256, 1307, 1561, 1603, 1652. ^{1}H NMR ($CDCl_3$), δ: 2.09 (d, 6 H, Me, J = 6.9 Hz); 3.54 (s, 4 H, OCH_2CH_2O); 3.76 (t, 4 H, $NCH_2C\underline{H}_2O$, J = 5.8 Hz); 4.41 (t, 4 H, $NC\underline{H}_2CH_2O$, J = 5.8 Hz); 5.70 (q, 2 H, BrCH, J = 6.9 Hz); 7.32 (dd, 2 H, H(6) or H(7), quinoxaline, J = 7.9 Hz, J = 7.2 Hz); 7.44 (d, 2 H, H(8), quinoxaline, J = 8.4 Hz); 7.52 (dd, 2 H, H(6) or H(7), quinoxaline, J = 8.6 Hz, J = 7.2 Hz); 7.85 (d, 2 H, H(5), quinoxaline, J = 7.9 Hz).

4-R-2′-Amino-5′-methyl-1,2,3,4,4′,5′-hexahydrospiro[quinoxaline-2,4′-thiazol]-3-ones 10 and α,ω-bis[2′-amino-5′-methyl-3-oxo-1,2,3,4,4′,5′-hexahydrospiro[quinoxaline-2,4′-thiazol-4-yl]oxaalkanes 14 (general procedure). Thiourea (1.5 or 3 mmol, respectively) was added to a solution of compound **8** or **13** (1.25 mmol) in dioxane (10 mL). The reaction mixture was stirred for 5 h at ~20 °C and left for ~14 h, then the tar-like matter formed was separated from the solvent, dissolved in water, and treated with 5% aq. $NaHCO_3$. The crystals formed were filtered off and washed with water. Compounds **10a,b** were described in our letter to the Editor.[27]

2′-Amino-5′-methyl-1,2,3,4,4′,5′-hexahydrospiro-[quinoxaline-2,4′-thiazol]-3-one (10a). The yield was 85%, m.p. 183—185 °C. Found (%): C, 53.44; H, 4.76; N, 22.80; S, 12.78. $C_{11}H_{12}N_4OS$. Calculated (%): C, 53.21; H, 4.87; N, 22.56; S, 12.91. IR, ν/cm^{-1}: 435, 709, 740, 822, 858, 972, 1148, 1184, 1274, 1315, 1505, 1578, 1606, 1633, 1691, 2500—3445. ^{1}H NMR

(DMSO-d_6), δ: 1.37 (d, 3 H, Me, J = 6.9 Hz); 4.89 (q, 1 H, SCH, J = 7.0 Hz); 6.35 (s, 1 H, NH), 6.49 (br.s, 2 H, NH_2); 6.59—6.66 (m, 1 H, H(6) or H(7)); 6.71—6.79 (m, 2 H, H(7) or H(6), H(5) or H(8)); 6.89 (d, 1 H, H(5) or H(8), J = 6.9 Hz); 10.33 (s, 1 H, NHC(O)). ^{13}C {^1H} NMR (DMSO-d_6), δ: 14.88, 49.82, 89.03, 114.64, 114.85, 118.24, 122.63, 126.09, 133.89, 159.95, 165.51.

2´-Amino-4-ethyl-5´-methyl-1,2,3,4,4´,5´-hexahydrospiro[quinoxaline-2,4´-thiazol]-3-one (10b). The yield was 79%, m.p. 170—173 °C. Found (%): C, 56.38; H, 5.75; N, 20.40; S, 11.53. $C_{13}H_{16}N_4OS$. Calculated (%): C, 56.50; H, 5.84; N, 20.27; S, 11.60. IR, ν/cm^{-1}: 723, 993, 1140, 1173, 1256, 1308, 1350, 1403, 1508, 1582, 1657, 2600—3100, 3305, 3363. ^1H NMR (DMSO-d_6), δ: 1.39 (t, 3 H, C$\underline{H}_3$CH$_2$, J = 7.0 Hz); 1.37 (d, 3 H, C$\underline{H}_3$CH, J = 6.6 Hz); 3.80—4.10 (m, 2 H, C$\underline{H}_2$CH$_3$); 4.93 (q, 1 H, CH$_3$C$\underline{H}$, J = 6.6 Hz); 6.46 (s, 1 H, NH); 6.77 (dd, 1 H, H(6) or H(7), J = 8.0 Hz, J = 6.6 Hz); 6.81 (dd, 1 H, H(7) or H(6), J = 8.0 Hz, J = 7.32 Hz); 6.97 (d, 1 H, H(5) or H(8), J = 7.6 Hz); 7.01 (d, 2 H, H(5) or H(8), J = 7.3 Hz). ^{13}C {^1H} NMR (DMSO-d_6), δ: 12.77, 14.74, 37.15, 49.86, 88.67, 113.98, 115.51, 118.61, 122.84, 127.11, 135.12, 160.06, 164.34.

1,5-Bis{2´-amino-5´-methyl-3-oxo-1,2,3,4,4´,5´-hexahydrospiro[quinoxaline-2,4´-thiazol]-4-yl}-3-oxapentane (14a). The yield was 79%, m.p. >180 °C (decomp.). Found (%): C, 55.44; H, 5.15; N, 19.80; S, 11.23. $C_{26}H_{28}N_8O_3S_2$. Calculated (%): C, 55.30; H, 5.00; N, 19.84; S, 11.36. IR, ν/cm^{-1}: 467, 678, 722, 752, 991, 1060, 1126, 1126, 1160, 1220, 1308, 1378, 1459, 1504, 1600, 1654, 2400—2435. ^1H NMR (DMSO-d_6), δ: 2.50 (d, 6 H, Me, J = 7.2 Hz); 3.55—3.65 (m, 4 H, OCH_2); 3.9—4.15 (m, 4 H, NCH_2); 4.80—4.95 (m, 2 H, CHS); 6.65 (br.s, 2 H, 2 NH, quinoxaline); 6.77 (dd, 2 H, 2 H(6) or 2 H(7), quinoxaline, J = 7.4 Hz, J = 7.0 Hz); 6.80—6.87 (m, 2 H, 2 H(6) or 2 H(7), quinoxaline); 6.97 (d, 2 H, 2 H(5) or 2 H(8), quinoxaline, J = 7.9 Hz); 7.08 (m, 2 H, 2 H(5) or 2 H(8), quinoxaline).

1,8-Bis{[2´-amino-5´-methyl-3-oxo-1,2,3,4,4´,5´-hexahydrospiro[quinoxaline-2,4´-thiazol]-4-yl}-3,6-dioxaoctane (14b). The yield was 73%, m.p. 146—148 °C. Found (%): C, 55.07; H, 5.17; N, 18.50; S, 10.45. $C_{28}H_{32}N_8O_4S_2$. Calculated (%): C, 55.25; H, 5.30; N, 18.41; S, 10.53. IR, ν/cm^{-1}: 750, 992, 1111, 1219, 1309, 1507, 1601, 1655, 2750—3450. ^1H NMR (DMSO-d_6), δ: 1.37 (d, 6 H, Me, J = 6.8 Hz); 3.54—4.15 (m, 12 H, $CH_2(CH_2OCH_2)_2CH_2$); 4.91 (q, 2 H, SCH, J = 7.1 Hz); 6.58 (s, 2 H, NH, quinoxaline); 6.75 (dd, 2 H, H(6) or H(7), quinoxaline, J = 7.7 Hz, J = 7.4 Hz); 6.87 (dd, 2 H, H(7) or H(6), quinoxaline, J = 7.7 Hz, J = 7.4 Hz); 6.97 (d, 2 H, H(5) or H(8), quinoxaline, J = 7.7 Hz); 7.09 (d, 2 H, H(5) or H(8), quinoxaline, J = 7.7 Hz). ^{13}C {^1H} NMR (DMSO-d_6), δ: 14.77, 42.21, 49.84, 66.72, 70.24, 88.28, 114.72, 115.48, 118.66, 123.15, 127.55, 134.92, 160.81, 164.74.

1,5-Bis(1-acetylimino-3-methyl-4-oxothiazolo[3,4-*a*]-quinoxalin-5-yl)-3-oxapentane (17). ***A.*** Thiourea (0.15 g, 2 mmol) was added to a mixture of compound **13** (0.48 g, 0.83 mmol) in THF (20 mL), the mixture was stirred for 6 h at ~20 °C and left for ~14 h. Then acetic anhydride (10 mL) was poured in, the reaction mixture was refluxed for 10 min and cooled. The crystals formed were filtered off, washed with THF, 5% aq. $NaHCO_3$, and water.

B. A mixture of compound **14a** (0.24 g, 0.42 mmol) and acetic anhydride (1 mL) was refluxed for 10 min. The reaction mixture was cooled, the crystals formed were filtered off, washed with Pr^{i}OH. The yield was 23%, m.p. 262—264 °C (DMSO). Found (%): C, 58.47; H, 4.47; N, 13.52; S, 10.48. $C_{30}H_{28}N_6O_5S_2$. Calculated (%): C, 58.43; H, 4.58; N, 13.63; S, 10.40. IR, ν/cm^{-1}: 460, 555, 573, 645, 665, 709, 721, 729, 758, 852, 874, 891, 943, 978, 1011, 1037, 1061, 1075, 1127, 1171, 1250, 1284, 1346, 1505, 1585, 1616, 1653. ^1H NMR (DMSO-d_6), δ: 2.35 (s, 6 H, MeC(O)); 2.67 (s, 6 H, C(3)Me); 3.80 (t, 4 H, OCH_2, J = 5.6 Hz); 4.24 (t, 4 H, NCH_2, J = 5.6 Hz); 7.13—7.18 (m, 2 H, H(6) or H(7), or H(8)); 7.20—7.26 (m, 2 H, H(6) or H(7), or H(8)); 7.38—7.43 (m, 2 H, H(6) or H(7), or H(8)); 9.96 (d, 2 H, H(9), J = 9.7 Hz).

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