Fused polycyclic nitrogen-containing heterocycles

21.* Condensation of 4-hydroxy-3,5-diphenyl-2-phenyliminothiazolidine with 5-fluoro-4-morpholino- and -4-(4-methylpiperazino)-1,2-phenylenediamines**

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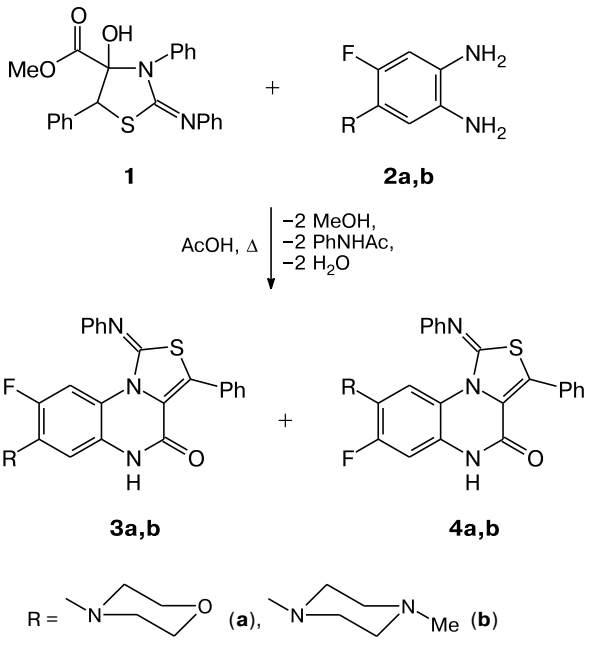
The condensation of 4-hydroxy-3,5-diphenyl-2-phenyliminothiazolidine with 5-fluoro-4-morpholino- and 5-fluoro-4-(4-methylpiperazino)-1,2-phenylenediamines leads to regioisomeric thiazolo[3,4-*a*]quinoxalines differing in substituents in positions 7 and 8 of the benzene ring. From the ratio of isomers formed it follows that the mesomeric effect of a fluorine atom in 1,2-phenylenediamines is comparable with the influence of an aminosubstituent.

Key words: 4-hydroxy-3,5-diphenyl-2-phenyliminothiazolidine, cyclocondensation, thiazolo[3,4-*a*]quinoxalines, IR spectroscopy, NMR spectroscopy, X-ray diffraction analysis.

Quinoxalines as well as fused systems based on them represent fragments of many biologically active compounds and drugs.[2—13] Among cyclizations accompanied by the formation of azolo[3,4-*a*]quinoxalines, the reactions of 4-hydroxy-2-iminothiazolidines with 1,2-phenylenediamines studied by us earlier[14—18] occupy an important place. In order to develop this approach as applied to the synthesis of fluorine-containing thiazolo[3,4-*a*]quinoxalines that are prospective as potential biologically active compounds, in the present work we studied the condensation of 4-hydroxy-3,5-diphenyl-2-phenyliminothiazolidine **1** with 5-fluoro-4-morpholino- and 5-fluoro-4-(4-methylpiperazino)-1,2-phenylenediamines (**2a,b**, respectively).

The use of "nonsymmetrically" substituted 1,2-phenylenediamines **2a,b** in this reaction (see Ref. 1) results in the formation of a mixture of two isomeric thiazoloquinoxalones **3a,b** and **4a,b** in the ratio 2 : 3 with 7-fluoroderivatives **4a,b** prevailing in both cases (Scheme 1). The isomers were separated by column chromatography.

Scheme 1



* For part 20, see Ref. 1.

** Dedicated to Academician A. I. Konovalov on his 75th birthday.

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The structures of thiazoloquinoxalones were established on the basis of ^{1}H and ^{13}C NMR spectral data and X-ray diffraction analysis.

A pecularity of the ^{1}H NMR spectra of compounds **3a**,**b** and **4a**,**b** is the presence of a diagnostic signal of the proton H(9), which appears as a doublet with the spin-spin coupling constant equal to 8.9 or 15.6 Hz. Since J = 15.6 Hz corresponds to the vicinal coupling constant $^{3}J_{H,F}$ (see Ref. 19), the major isomers can be identified as compounds **4a**,**b**, while the minor isomers can be identified as compounds **3a**,**b**. The signals for the protons H(6) resonate in higher fields, apparently, due to the influence of the electron-donating morpholine and piperazine substituents. A more comprehensive substantiation of these assignments is given below.

The structure of isomeric 7,8-substituted thiazolo-[3,4-*a*]quinoxalines **3a**, **4a** and **3b**, **4b** was established based on a series of correlation experiments 2D NMR (COSY, HSQC, HMBC),[20,21] whereby the structure of thiazolo[3,4-*a*]quinoxaline **4a** was examined in detail, whereas the structure of the other compounds was deduced by analogy.

The ^{1}H NMR spectrum of compound **4a** in DMSO-d_6 at 323 K consists of a broadened signal of the NH proton (δ 11.08), two doublet signals (δ 9.42 and 6.93) and a number of lines in the region with δ 7.5—7.1 and 3.8—2.8. The ^{13}C NMR spectrum contains signals in the area with δ 154—150 and δ 134—102 and also two signals at δ 65.87 and 50.59, a portion of the signals is split due to spin-spin coupling with the fluorine atom. With the aid of the 2D COSY method, three spin systems relating to the protons of the two phenyl moieties and a morpholine ring have been distinguished. Two doublet signals (δ 9.42 and 6.93) for which correlations in the COSY spectrum were not detected, correspond to the protons H(6)/H(9) or H(9)/H(6). Taking into account 2D HSQC spectral data, the signals for all the carbon atoms of compound **4a**, which are bound to protons, were determined.

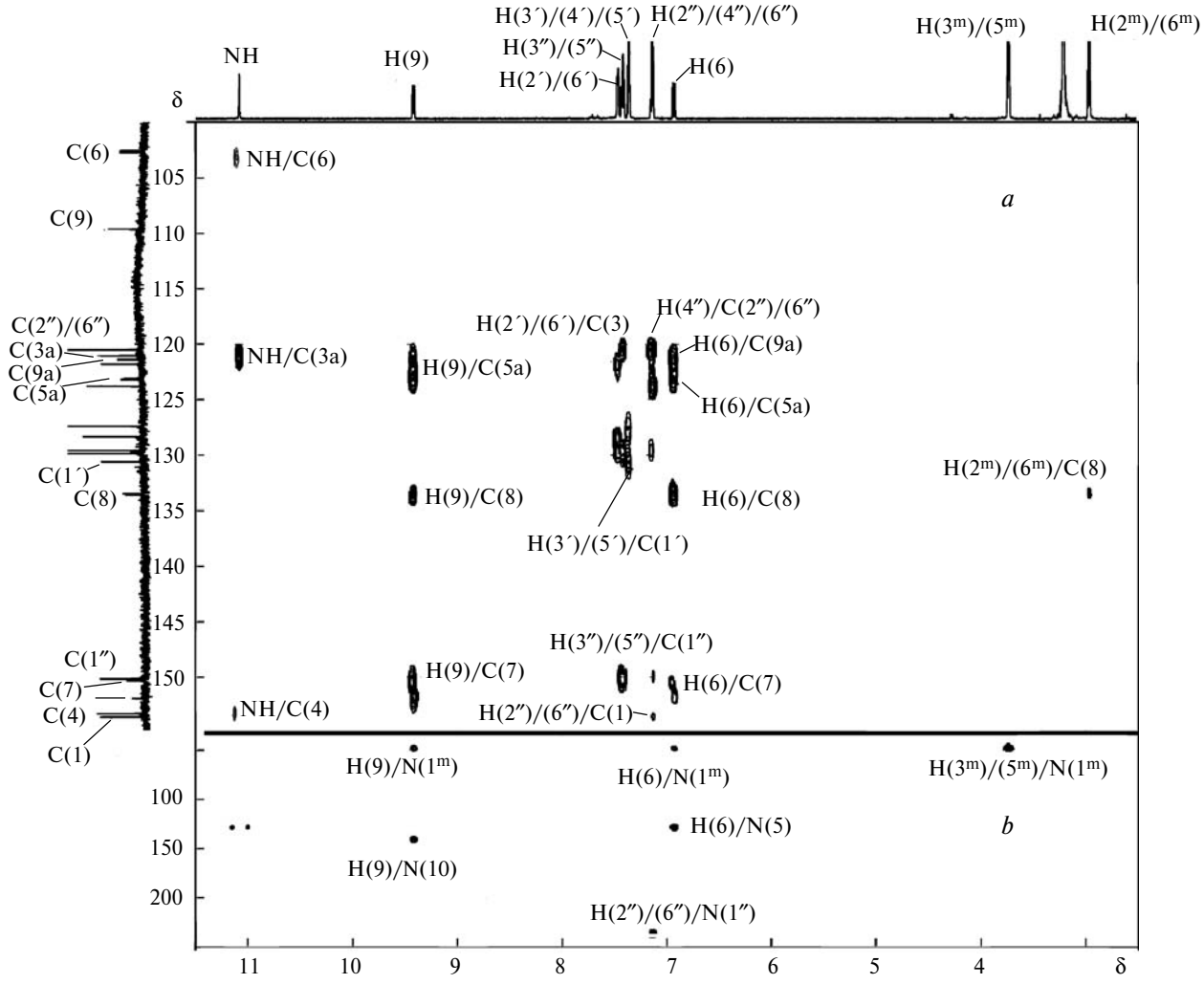
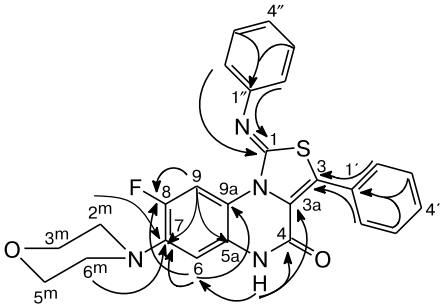


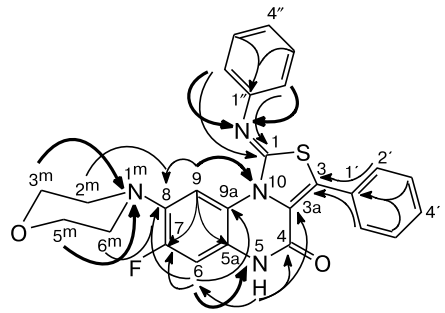
Fig. 1. Fragments of the 2D HMBC $^{1}H—^{13}C$ (*a*) and 2D HMBC $^{1}H—^{15}N$ (*b*) spectra of compound **4a**.

Ultimately, the structure of the molecule was established on the basis of 2D HMBC $^1H—^{13}C$, 2D HSQC $^1H—^{15}N$, and HMBC $^1H—^{15}N$ methods (Figs 1 and 2). The principal HMBC-correlations demonstrating the connectivities between fragments in molecule **4a** are as follows (see Fig. 2): between H(2´)/H(6´) and C(3), between H(2")/H(6") and N(1"), between H(2")/H(6") and C(1) (the attachment of the Ph´ and Ph´´ groups to the thiazole ring, respectively). In the 2D HMBC $^1H—^{15}N$ spectrum these are between $C(3^m)H_2/C(5^m)H_2$ and $N(1^m)$ (the structure of the morpholine ring).

The positions of substituents in the benzene ring of the quinoxaline system were determined in the following way. In the HMBC $^1H—^{13}C$ spectrum (see Fig. 1, *a*), a correlation between the NH proton and the C atom of a CH group (δ 102.64) is observed; given that $^3J_{C,H} > {}^{2,4}J_{C,H}$ (hence, the corresponding cross-peak is more intensive[22]), this peak was assigned to the atom C(6). This allowed the differentiation of the atoms C(6) and C(9) and the assignment of the corresponding protons H(6) and H(9). ^{15}N NMR data for compound **4a** additionally support the assignment of the proton H(6): in the 2D HMBC $^1H—^{15}N$ spectrum (see Fig. 1, *b*) a cross-peak between the atom N(5) (the signal of which was determined from the 2D HSQC $^1H—^{15}N$ spectrum) and the proton H(6) is present, whereas for the proton H(9) there is no such a peak ($^3J_{N,H} > {}^4J_{N,H}$).



3a



4a

Fig. 2. Basic HMBC-correlations from protons to carbon atoms (thin arrows) and nitrogen atoms (thick arrows) for compounds **3a** and **4a**.

In the 2D HMBC $^1H—^{13}C$ spectrum (see Fig. 1, *a*), cross-peaks of different intensities between the protons H(6), H(9) and the carbon atom C(7) (δ 151.08) with $J_{F,C} = 244.5$ Hz (see Ref. 22) are observed. Among them the peak from the proton H(9) is the most intensive, which makes it possible to assign this carbon atom as C(7) since $^3J_{C,H} > {}^{2,4}J_{C,H}$. Therefore, it has been established that the fluorine atom in compound **4a** is attached to the atom C(7). In addition, in the HMBC $^1H—^{13}C$ spectrum (see Fig. 1, *a*) a cross-peak between the protons $C(2^m)H_2/C(6^m)H_2$ and the atom C(8) is present, which suggests the presence of a covalent bond between the morpholine ring and the benzene ring of the quinoxaline system, the morpholine residue being bound to the atom C(8). Also, in the HMBC $^1H—^{13}C$ spectrum (see Fig. 1, *a*) there are correlations between the NH protons and the

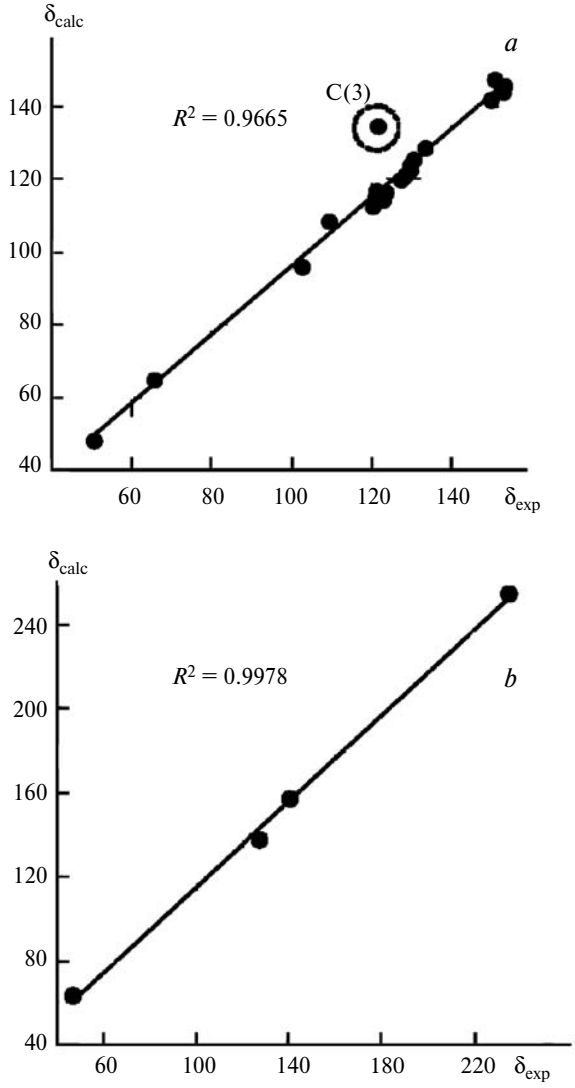


Fig. 3. The correlation of calculated (δ_{calc}) and experimental (δ_{exp}) chemical shifts ^{13}C (*a*) and ^{15}N (*b*) for compound **4a**.

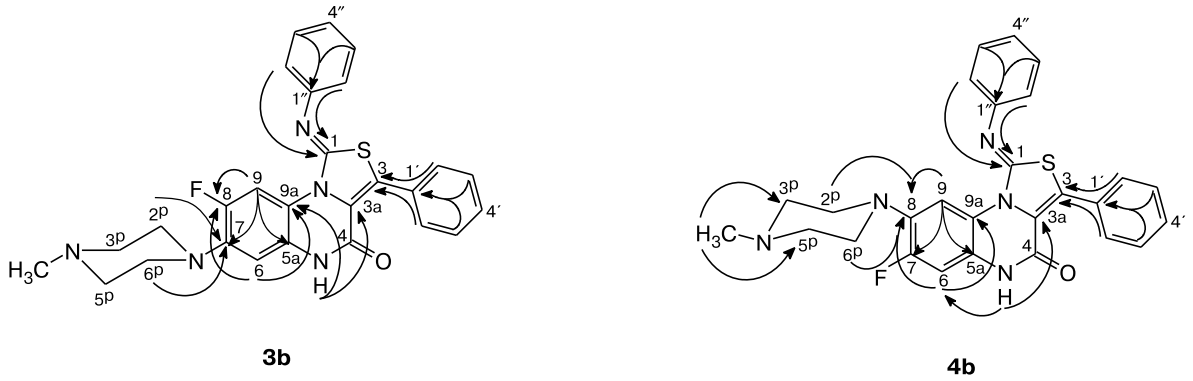


Fig. 4. Basic HMBC-correlations from protons to carbon atoms for compounds **3b** and **4b**.

atoms C(3a) and C(4), between H(6) and C(9a), H(9) and C(5a), and in the 2D HMBC $^{1}H—^{15}N$ spectrum (see Fig. 1, *b*) they are between the proton H(9) and the atom N(10), which eventually enables the determination of the complete structure of quinoxaline **4a**.

Accordingly, based on the data from a series of 2D-heterocorrelation experiments ($^{1}H—^{13}C$ и $^{1}H—^{15}N$) the structure of compound **4a** has unambiguously been established.

With the aim of the evaluation of the potential of theoretical methods for the determination of NMR-parameters, in this work the calculation of the chemical shifts of ^{1}H, ^{13}C, and ^{15}N (GIAO B3LYP/6-31G(d)//HF/6-31G) has been carried out for compound **4a** (correlation plots for ^{13}C and ^{15}N are depicted in Fig. 3). Making allowance for the underestimation of the chemical shifts of ^{13}C which is characterstic for this computational method (see Refs 23—26), and a marked[27,28] deviation of the chemical shift of ^{13}C vicinal to atoms of the third period (P, S, Cl), on the whole, good agreement of theoretical and experimental data is observed ($R^2 = 0.967$ (for all ^{13}C), $R^2 = 0.994$ (without C(3)). For the resonance signals of the nitrogen atom a virtually ideal agreement with the theory is observed ($R^2 = 0.998$). The calculated chemical shifts of ^{1}H also correlate well with experimental ones: $R^2 = 0.975$.

Analogously, the structure of thiazolo[3,4-*a*]quinoxalines **3a,b** and **4b** was determined (Figs 2 and 4). In addition, the structures of compounds **3b** and **4a** were confirmed by the results of X-ray diffraction analyses (Figs 5 and 6).

Both compounds crystallize with incorporation of DMSO molecules in the ratio of 1 : 1, and in the crystal of compound **4a** the solvate molecule is disordered over two positions with a 0.87 : 0.13 occupancy ratio.

The planarity of the tricyclic fragment of thiazolo[3,4-*a*]quinoxalines in crystals is disturbed. Thus in the tricyclic portion of molecule **3b** the planes of the thiazole ring and the fused benzene fragment constitute a dihedral angle equal to 6.7(1)°, in which the planes of the benzene and thiazole ring deviate in the same direction from the plane of the nitrogen-containing heterocycle with angles

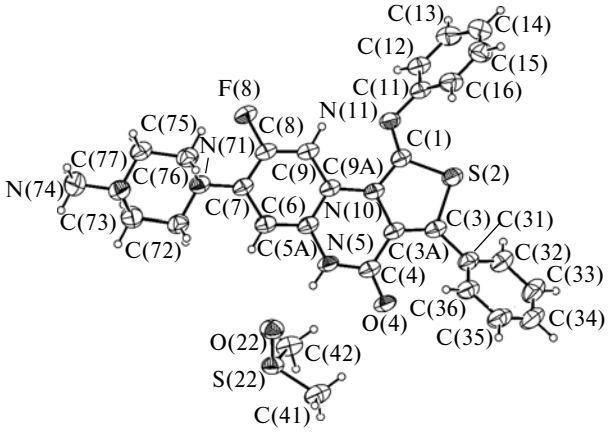


Fig. 5. The geometry of a molecule of compound **3b** in the crystal. Non-hydrogen atoms are represented with probability ellipsoids of thermal vibrations ($p = 50\%$), hydrogen atoms are depicted as spheres of an arbitrary radius.

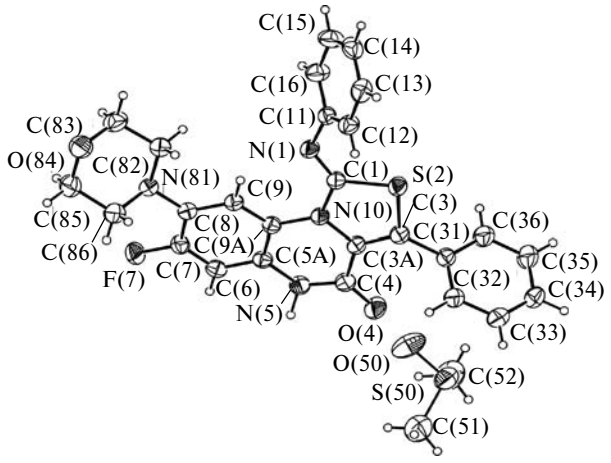


Fig. 6. The geometry of a molecule **4a** in the crystal. A disordered DMSO molecule is shown in the position with higher occupancy.

of 4.3(1) and 4.7(1)°, respectively. Even more appreciable deviations are observed in the molecule of compound **4a**, whose tricyclic fragment proves to be "twisted" (the torsion angle C(1)—N(10)—C(9A)—C(9) amounts to 9.2(4)°), while the planes of the thiazole ring and the fused benzene fragment form a dihedral angle of 10.2(1)°. Such distortions of the tricyclic system seem to be associated with the presence of bulky substituents in the *ortho*-positions of the fused benzene fragment of the molecules since they are absent in thiazolo[3,4-*a*] quinoxalines with small substituents in the benzene moiety.

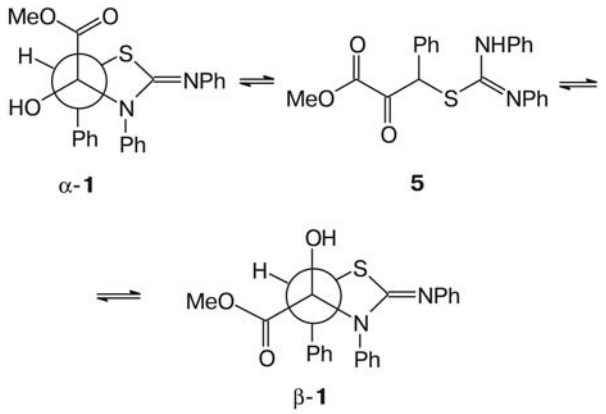
In molecule **4a** (see Fig. 6), the morpholine substituent is somewhat turned relative to the benzene fragment of the molecule (the average plane of the substituent constitute a dihedral angle of 36.3(1)° with the plane of the fused benzene ring). The planes of the phenyl sunstituents C(11)—C(16) and C(31)—C(36) constitute dihedral angles with the plane of the thiazole ring, which amount to 57.2(1) and 64.4(1)°, respectively. Virtually the same arrangement of substituents is also observed in molecule **3b** (see Fig. 5).

As has been observed earlier,[1] in the crystals of thiazolo[3,4-*a*]quinoxalines **3b** and **4a** the solvate molecule of DMSO prevents the formation of an H-dimer of molecules owing to the creation of classical hydrogen bonds and itself forms a hydrogen bond between the sulfinyl group of the DMSO molecule and the hydrogen atom of the amide group. The parameters of the hydrogen bond in the crystal of compound **3b** are as follows: the bond H(5)...O(22), 1.93 Å; N(5)...O(22), 2.783(4) Å; the angle N(5)—H(5)...O(22), 169°; in the crystals of compound **4a**: the bond H(5)...O(50), 1.73 Å; N(5)...O(50), 2.775(3) Å, the angle N(5)—H(5)...O(50), 165°.

Interactions of the π—π-type in crystals of the studied compounds were analyzed by using formal criteria of the existence of π—π-interactions[29] and also literature data.[30]

In the crystals of compound **3b**, the stacking effect is observed: on account of interactions of electron systems the triacyclic fragments of thiazolo[3,4-*a*]quinoxaline make up sloping piles along the axis 0*a* with two distances alternating in the piles 3.58 and 3.92 Å between root-mean-square planes of molecules arranged according to the "head-to-tail" type (Fig. 7, *a*). As a result of packing of such piles according to the hexagonal type and the presence of bulky substituents, the solvate DMSO molecules are pairwise isolated in the crystal by surrounding molecules of thiazolo[3,4-*a*]quinoxaline. The inconvenience of mutual packing of bulky substituents also accounts for a low value of the calculated packing coefficient of molecules, 66.3%.

Scheme 2



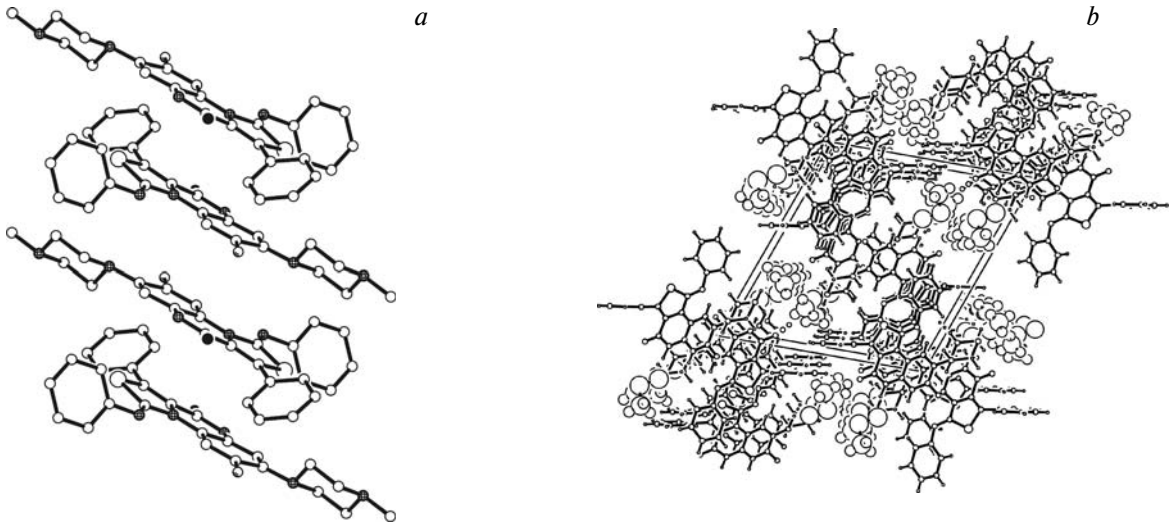
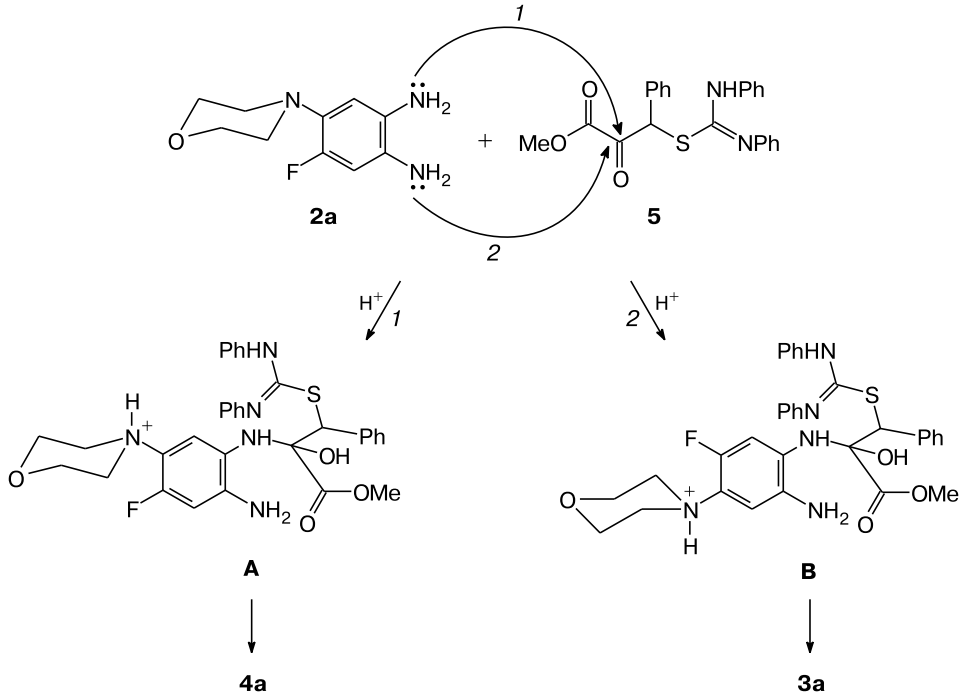
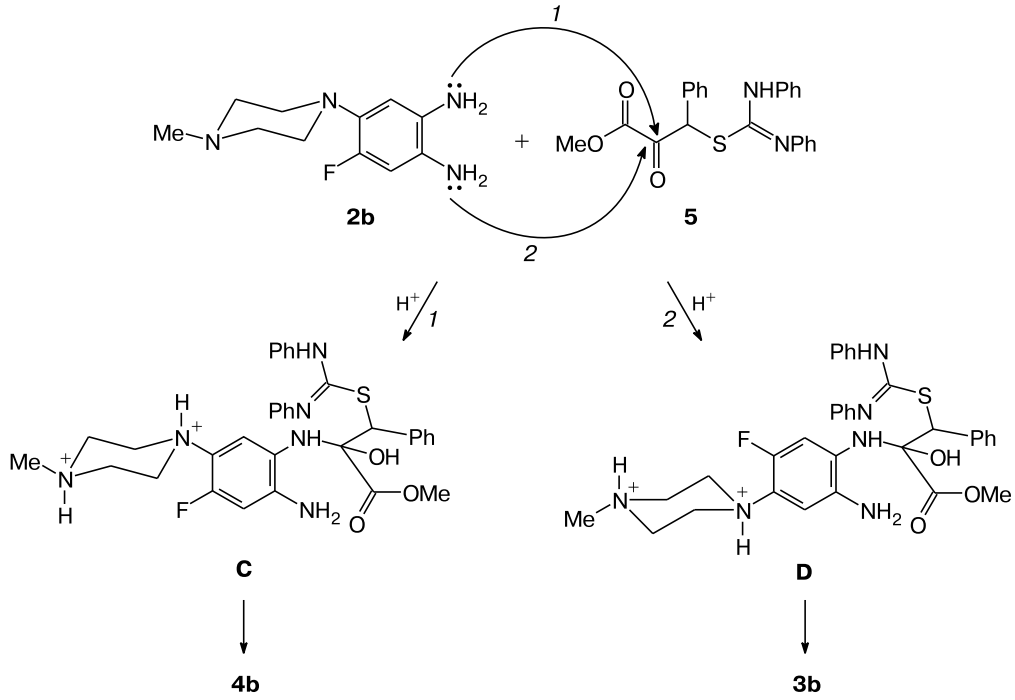


Fig. 7. *a*. A fragment of the packing of molecules in the crystal of compound **4a** (a projection along the axis 0*b*); DMSO molecules are not shown. *b*. The formation of zigzag chains by DMSO molecules in the crystal **4a** (a projection along the axis 0*b*); the DMSO molecules are depicted as large spheres.

Scheme 3



Scheme 4



The molecules of thiazoloquinoxaline **4a** form dimers in crystals owing to π—π-interactions between the aromatic systems of the triacyclic fragments of the molecules (the distance between the arbitrary centers of the triacyclic systems of the molecules is 4.63 Å, the dihedral angle between their root-mean-square planes is 0°, the shortest

distance between these planes is 3.46 Å). The molecules of the dimer, in turn, are connected with each other by a combination of interactions of different types (C—H...π, C—H...O, C—H...F) in a three-dimensional network of hydrogen-bonded molecules. In this network in a crystal, pseudochannels parallel to the axis 0*b* are formed in which the solvate DMSO molecules disordered over two sites are located (see Fig. 7, *b*). Despite the fact that according to the calculations there are no cavities potentially accessible to additional solvent molecules in the crystal, the packing coefficient of molecules in the crystal turns out to be extremely low, 65.2%.

The reasons for the observed ratio of isomeric products in the investigated coupling of diamines **2a,b** in favor of the preferential formation of 7-fluroderivatives **4a,b** are the same as those established earlier[1] for the reaction of 4-methyl- and 4-nitro-1,2-phenylenediamines (taking into consideration that the reaction was carried out in acetic acid). The protonation of the nitrogen atoms of the morpholine and piperazine substituents in 4-substituted 1,2-phenylenediamines **2a,b** decreases the electron-donating properties of the amino group. The mesomeric effect of a fluorine atom is comparable to the effect of an ammonium group.

Of three possible variants of the first step of the reaction,[15–17] *viz.*, amidation or imination involving cyclic tautomers α-**1**, β-**1** or imination of open-chain tautomer **5** (Scheme 2), we give preference to the latter option, which most probably demonstrates the formation of the 3a-hydroxythiazoloquinoxalines isolated earlier[1,18] and characterized as intermediate compounds (Schemes 3 and 4).

Experimental

The NMR spectra were recorded on a Bruker-AVANCE-600 spectrometer (600 (^{1}H), 150.926 (^{13}C) and 60.796 MHz (^{15}N)) at 30 °C in DMSO-d_6 (for compounds **3a** and **4a**) and $CDCl_3$ (for compounds **3b** and **4b**). The residual signal of $CDCl_3$ (δ_H 7.26, δ_C 77.00) or DMSO (δ_H 2.50, δ_C 39.43) was used as the internal standard. Chemical shifts in the ^{15}N NMR spectra were measured relative to the signal of an external standard CD_3CN (δ_N 0). The IR spectra were measured on a Vector-22 FTIR spectrometer (Bruker) in KBr pellets. Melting points were determined on a Boetius heating stage. 4-Hydroxy-4-methoxycarbonyl-3,5-diphenyl-2-phenyliminothiazolidine (**1**) was obtained by the reaction of methyl 3-chloro-2-oxo-3-phenylpropionate with *N*,*N*′-diphenylthiocarbamide using a procedure developed by us earlier.[31]

The study of compounds by ^{1}H NMR spectroscopy was performed at the NMR Department of the Federal Collective Spectral Analytical Center of Physicochemical Research of Structure, Propeties, and Composition of Compounds and Materials and the Federal Center of Collective Use for Physicochemical Research of Compounds and Materials with support from the Ministry of Education and Science of the Russian Federation (State Contract Nos 02.451.11.7036 and 02.451.11.7019).

8-Fluoro-7-morpholino-3-phenyl-1-phenyliminothiazolo[3,4-*a*]quinoxalin-4(5*H*)-one (3a) and 7-fluoro-8-morpholino-3-phenyl-1-phenyliminothiazolo[3,4-*a*]quinoxalin-4(5*H*)-one (4a) (a mixture of isomers **3a** + **4a**, 40 : 60). To a solution of 0.5 g (2.07 mmol) 1-amino-5-fluoro-4-morpholino-2-nitrobenzene in 30 mL of anhydrous ethanol 96% hydrazine (0.6 mL, 18.9 mmol) was added. The reaction mixture was heated on a water bath until complete dissolution of the precipitate, after which it was cooled to 30 °C, a catalyst (Raney-Ni)[32] (0.1 g) in 20 mL of anhydrous ethanol was added, and the mixture was refluxed for 6 h. The reaction mixture was cooled to room temperature, the catalyst was filtered off, and the solvent was evaporated *in vacuo*. To a solution of thus prepared diamine **2a** in AcOH (30 mL) was added 4-hydroxythiazolidine **1** (0.83 g, 2.14 mmol). The mixture was refluxed for 5 h, cooled, and acidified with 5% HCl. The mustard-colored precipitate that formed was filtered off and recrystallized from CH_3CN to give a mixture of **3a** and **4a** (0.85 g, 87%), m.p. 239—241 °C. The separation of the isomers was carried out by column chromatography on Kieselgel (chloroform—hexane, 6 : 4). R_f values are given for a fixed layer of SiO_2 (Silufol) in a chloroform—hexane—methanol (6 : 4 : 1) system. The yield of compound **3a** is 0.03 g (4%), yellow-colored crystals, R_f 0.45, m.p. 331—335 °C. Found (%): C, 65.74; H, 4.22; N, 11.61; S, 6.65. $C_{26}H_{21}FN_4O_2S$. Calculated (%): C, 65.95; H, 4.30; N, 11.56; S, 6.72. IR (Nujol), ν/cm^{-1}: 2930—2855 (NH), 1674 (C=O), 1615 (C=N), 1587, 1514. ^{1}H NMR, δ: 3.00—3.02 (m, H, $N(CH_2)_2$); 3.74—3.76 (m, 4 H, $O(CH_2)_2$); 6.82 (d, 1 H, H(6), J = 8.7 Hz); 7.07—7.14 (m, 3 H, 2 *o*-H + *p*-H of phenylimine); 7.33—7.36 (m, 3 H, 2 *o*-H + *p*-H_{Ph}); 7.40 (d.d, 2 H, 2 *m*-H of phenylimine, J = 7.7 Hz, J = 7.7 Hz); 7.42—7.46 (m, 2 H, 2 *m*-H_{Ph}); 9.26 (d, 1 H, H(9), $J_{H,F}$ = 15.9 Hz); 11.03 (s, 1 H, NH). The yield of compound **4a** is 0.43 g (50%), yellow-colored crystals, R_f 0.62, m.p. 281—282 °C. Found (%): C, 65.74; H, 4.22; N, 11.61; S, 6.65. $C_{26}H_{21}FN_4O_2S$. Calculated (%): C, 66.09; H, 4.48; N, 11.86; S, 6.78. IR (Nujol), ν/cm^{-1}: 2953—2854 (NH), 1667 (C=O), 1616 (C=N), 1589, 1514. ^{1}H NMR, δ: 2.94—2.96 (m, 4 H, $N(CH_2)_2$); 3.72—3.74 (m, 4 H, $O(CH_2)_2$); 6.92 (d, 1 H, H(6), $J_{H,F}$ = 12.6 Hz); 7.12—7.15 (m, 3 H, 2 *o*-H + *p*-H of phenylimine); 7.35—7.37 (m, 3 H, 2 *o*-H_{Ph} + *p*-H_{Ph}); 7.42 (d.d, 2 H, 2 *m*-H of phenylimine, J = 7.7 Hz, J = 8.1 Hz); 7.45—7.47 (m, 2 H, 2 *m*-H_{Ph}); 9.42 (d, 1 H, H(9), J = 9.0 Hz); 11.15 (s, 1 H, NH).

8-Fluoro-7-(4-metylpiperazino)-3-phenyl-1-phenyliminothiazolo[3,4-*a*]quinoxalin-4(5*H*)-one (3b) and 7-fluoro-8-(4-metylpiperazino)-3-phenyl-1-phenyliminothiazolo[3,4-*a*]quinoxalin-4(5*H*)-one (4b) (a mixture of isomers **3b** + **4b** in a ratio of 26 : 74). The reduction of 0.5 g (1.97 mmol) of 5-fluoro-1-amino-4-(4-methylpiperazino)-2-nitrobenzene in 40 mL of anhydrous ethanol with hydrazine (0.6 mL, 18.9 mmol) and Raney-Ni (0.1 g) in 20 mL of anhydrous ethanol was carried out as described above (3 h). The reaction mixture was cooled to room temperature, the catalyst was filtered off, and the solvent was evaporated *in vacuo*. A solution of thus prepared diamine **2b** and 4-hydroxythiazolidine **1** (0.79 g, 2.04 mmol) in AcOH (30 mL) was refluxed for 3 h. The solvent was evaporated, the residue was triturated with ether. The dark green-colored precipitate that formed was filtered off to give a mixture of **3b** + **4b** (0.63 g, 69%) with m.p. 251—256 °C. The separation of the isomers was carried out by column chromatography on Kieselgel (chloroform—hexane, 4 : 1). R_f values are given for a fixed layer of SiO_2 (Silufol) in the system chloroform—hexane—methanol

(1 : 1 : 6). The yield of compound **3b** is 0.11 g (17%), yellow-colored crystals, R_f 0.18, m.p. 309—310 °C. Found (%): C, 66.77; H, 5.10; N, 14.36; S, 6.45. $C_{27}H_{24}FN_5OS$. Calculated (%): C, 66.79; H, 4.98; N, 14.42; S, 6.60. IR, ν/cm^{-1}: 3200—2700 (NH), 1675 (C=O), 1617 (C=N), 1590. ^{1}H NMR, δ: 1.25 (s, 3 H, Me); 2.41—3.05 (m, 8 H, 4 CH_2); 6.33 (d, 1 H, H(6), J = 7.6 Hz); 7.07—7.47 (m, 10 H, 2 Ph); 9.38 (d, 1 H, H(9), $J_{H,F}$ = 15.4 Hz); 9.55 (s, 1 H, NH). The yield of compound **4b** is 0.30 g (48%), yellow-colored crystals, R_f 0.34, m.p. 275—280 °C. Found (%): C, 66.82; H, 4.92; N, 14.44; S, 6.50. $C_{27}H_{24}FN_5OS$. Calculated (%): C, 66.79; H, 4.98; N, 14.42; S, 6.60. IR, ν/cm^{-1}: 3200—2700 (NH), 1681 (C=O), 1614 (C=N), 1582. ^{1}H NMR, δ: 1.26 (s, 3 H, Me); 2.58—3.30 (m, 8 H, 4 CH_2); 6.53 (d, 1 H, H(6), $J_{H,F}$ = 12.0 Hz); 7.09—7.44 (m, 10 H, 2 Ph); 9.47 (d, 1 H, H(9), J = 8.8 Hz); 10.33 (s, 1 H, NH).

The X-ray diffraction analysis of single crystals of compounds **3b**, **4a** was conducted at the Department of X-ray Diffraction Research of the Center of Collective Use based on the laboratory of X-ray diffraction research methods of the A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Research Center of the Russian Academy of Sciences. The X-ray diffraction characteristics of compounds, experiment parameters and structure refinements are given in Table 1. The experiments were perfomed on an automatic four-circle CAD-4 diffractometer (NONIUS B.V.) at 20 °C (graphite monochromator, Cu-Kα radiation), preliminary data processing was carried out by using the MolEN software[33] on an AlphaStation 200 computer. No drop of intensities of three test reflections over the time of experiments was observed. The absorption was taken into account empirically. All the structures were solved by the direct method based on the SIR software[34] and were refined first in the isotropic and then anisotropic approximation with the use of the SHELXL-97 (Ref. 35) and WinGX (Ref. 36) software. The hydrogen atoms of amino groups were determined from difference series of electron density (the positions of the other hydrogen atoms were calculated on the basis of stereochemical criteria) and refined by the corresponding riding models. The analysis of intermolecular interactions and images was performed using the PLATON software.[29]

The atomic coordinates of structures **3b** and **4a** and their temperature parameters were deposited with the Cambridge Crystallographic Data Centre (http://www.ccdc.cam.ac.uk; the deposition numbers are CCDC 671 885 and 671 886, respectively).

Table 1. The parameters of the crystals of compounds **3b**, **4a** and conditions of the X-ray experiment

Parameter	**3b**	**4a**
Color, habitus	Yellow (prismatic form)	
Molecular formula	$C_{27}H_{24}FN_5OS \cdot C_2H_6OS$	$C_{26}H_{21}FN_4O_2S \cdot C_2H_6OS$
Molecular weight	563.70	550.66
Crystal system	Triclinic	Monoclinic
Space group	$P\bar{1}$	$P2_1/n$
a/Å	8.586(2)	16.619(2)
b/Å	12.083(7)	9.8750(6)
c/Å	13.819(5)	17.711(2)
α/deg	99.19(4)	90
β/deg	91.24(4)	109.809(9)
γ/deg	96.94(3)	90
V/Å^3	1403.6(10)	2734.6(5)
Z	2	4
d_{calc}/g cm^{-3}	1.334	1.338
μ/cm^{-1}	20.71	21.32
Absorption correction	Refdelf	Psi-scan
Radiation (λ/Å)	Cu-Kα (1.54184)	
F(000)	592	1152
Number of measured reflections	8745	5757
R_{int}	0.0000	0.0368
Number of observed reflections with c $I > 2\sigma(I)$	3428	4001
Residual disagreement factors	R = 0.0682, Rw = 0.2008	R = 0.0527, Rw = 0.1464
Goodness-of-fit	1.053	1.044
Number of refined parameters	355	347

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