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Synthesis and Functionalization of 3-Ethylquinoxalin-2(1*H*)-one

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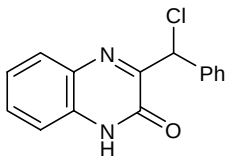
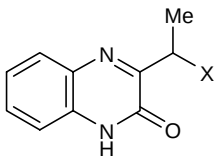
Abstract—A new and effective procedure was developed for the synthesis of 3-ethylquinoxalin-2(1*H*)-one from *o*-phenylenediamine and ethyl 2-oxobutanoate. The latter was prepared by the Grignard reaction of diethyl oxalate with ethylmagnesium bromide or iodide. The ethyl group in 3-ethylquinoxalin-2(1*H*)-one can readily be converted into various functional groups: α-bromoethyl, α-thiocyanato, α-azidoethyl, α-phenylaminoethyl, acetyl, and bromoacetyl. The reaction of 3-(bromoacetyl)quinoxalin-2(1*H*)-one with thiourea and hydrazine-1,2-dicarbothioamide gives the corresponding 3-(2-amino-4-thiazolyl) derivatives.

We previously showed that 3-(α-chlorobenzyl)-quinoxalin-2(1*H*)-one (**I**), which is readily available via reaction of 3-chloro-3-phenyl-2-oxopropionates with *o*-phenylenediamine, is a convenient polyfunctional reagent for the synthesis of various fused quinoxaline derivatives, such as thiazolo[3,4-*a*]-, imidazo-[1,5-*a*]-, pyrrolo[1,2-*a*]-, pyrazolo[3,4-*b*]-, pyrano-[5,6-*b*]-, and indolizino[2,3-*b*]quinoxalines [1–5]. The key factor in the formation of all these compounds is favorable arrangement of the α-chlorobenzyl group with respect to the endocyclic imino and carbamoyl moieties. Replacement of the chlorine atom by appropriate groups gives rise to structural fragments necessary for the subsequent ring closure at the *a* or *b* side of the pyrazine ring in the initial quinoxaline.

Replacement of the phenyl group in molecule **I** by methyl could considerably extend the synthetic potential due to ready transformation of the α-chloroethyl fragment into various functional groups. Therefore, the goal of the present work was to develop procedures for the preparation of 3-ethylquinoxalin-2(1*H*)-one (**IIa**) as a convenient intermediate product for the synthesis of various quinoxaline derivatives which are promising building blocks in the design of macroheterocyclic systems.



I



IIa, **III**

IIa, X = H; **III**, X = Br.

The only reported method for the synthesis of 3-ethylquinoxalin-2(1*H*)-one (**IIa**) includes three steps: (1) reaction of ethyl α-(ethoxalyl)propionate [6] with *o*-phenylenediamine, (2) alkaline hydrolysis of intermediate ethyl α-(2-hydroxyquinoxalin-3yl)propionate, and (3) decarboxylation of the acid thus formed [7]. The procedure based on oxidation of 3-alkyltetrahydroquinoxalin-2-ones formed by condensation of *o*-phenylenediamine with α-halo carboxylic acids also seems to be unreasonable: the yield of the target 3-alkylquinoxalin-2(1*H*)-ones ranges from 8 to 34% [8]. By analogy with the synthesis of 3-(α-chlorobenzyl)quinoxalin-2(1*H*)-one (**I**), one of the simplest procedures for the preparation of 3-(α-bromoethyl)-quinoxalin-2(1*H*)-one (**III**) may be that based on reaction of methyl 3-chloro-2-oxobutanoate with *o*-phenylenediamine [9]. However, unlike 3-chloro-3-phenyl-2-oxopropionates which are readily formed in high yields by the Darzens reaction of dichloroacetates with benzaldehyde [10], 3-chloro-2-oxobutanoates are very difficult to obtain in such a way because of numerous competing processes with participation of acetaldehyde used as electrophilic reagent.

Retrosynthetic analysis [11] shows that molecule **IIa** is built up from synthons **A** and **B** whose synthetic equivalents are, respectively, *o*-phenylenediamine and 2-oxobutanoic acid derivatives **IV** (Scheme 1). Among various methods for the preparation of 2-oxobutanoic acid derivatives **IV**, we selected the Grignard reaction

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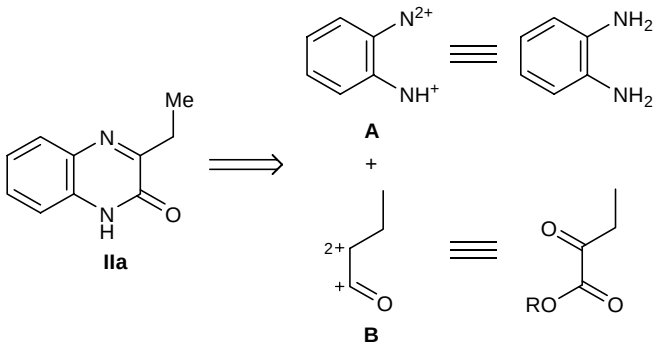
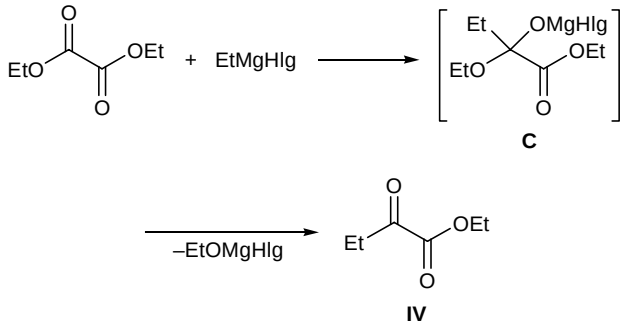
Scheme 1.



of diethyl oxalate with ethylmagnesium bromide or iodide [12]. Taking into account that this reaction usually leads to formation of tertiary alcohols, it was necessary to find out temperature conditions, reactant ratio, and reaction time to force the process to be terminated at the stage of formation of adduct **C** [13] (Scheme 2). The subsequent decomposition of unstable adduct **C** should give highly reactive keto ester **IV** and halomagnesium alkoxide.

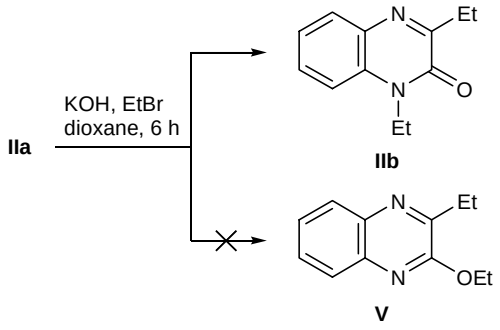
Scheme 2.



The resulting mixture containing diethyl oxalate and keto ester **IV** (without additional purification or separation) was brought into reaction with *o*-phenylenediamine to obtain quinoxaline **IIa**; here, the required amount of *o*-phenylenediamine was calculated from the ^{1}H NMR spectrum of crude product **IV**. Insofar as the reactivity of ethyl 2-oxobutanoate is higher than that of diethyl oxalate, 3-ethylquinoxalin-2(1*H*)-one (**IIa**) was smoothly obtained at room temperature, and it contained no quinoxaline-2,3-dione impurity.

The structure of compound **IIa** was confirmed by elemental analysis and spectral methods, as well as by comparing with published data [6, 7]. 3-Ethylquinoxalin-2(1*H*)-one (**IIa**) can readily be alkylated at the nitrogen atom with ethyl bromide under standard conditions [14] (in boiling dioxane in the presence of potassium hydroxide) to afford 1,3-diethylquinoxalin-2(1*H*)-one (**IIb**) (no *O*-alkyl derivative **V** is formed; Scheme 3). The structure of *N*-ethylquinoxalinone **IIb** is confirmed by the presence in its IR spectrum of absorption bands due to stretching vibrations of C=N and C=O bonds at 1602 and 1655 cm^{-1}, respectively; these bands are displaced to higher frequencies by 5 and 15 cm^{-1}, respectively, relative to the corresponding bands in the spectrum of initial quinoxalinone **IIa**. The ^{1}H NMR spectrum of **IIb** contained signals from protons in the benzo fragment at δ 7.25–7.82 ppm and protons of two nonequivalent methylene groups at δ 2.95 (CCH_2) and 4.29 ppm (NCH_2).

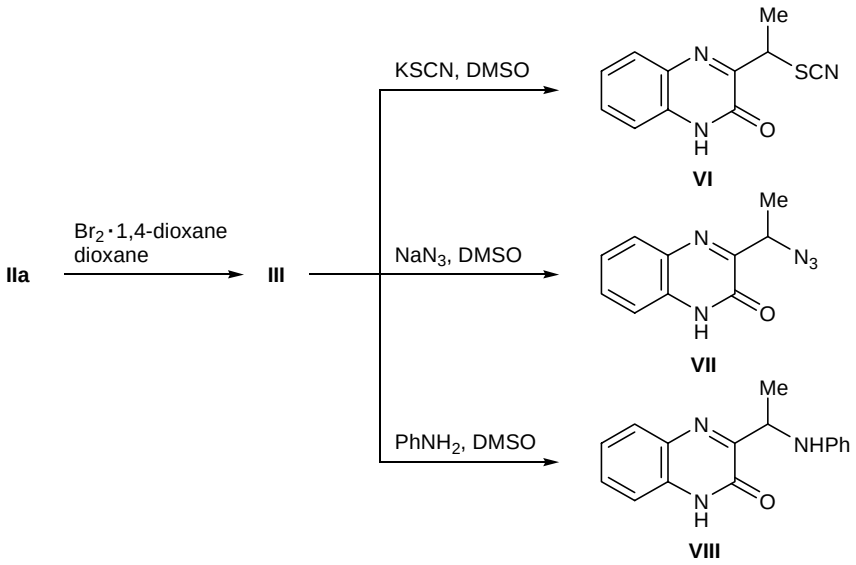
Scheme 3.



Functionalization of quinoxalinone **IIa** was performed via substitution of the bromine atom in α-bromoethyl derivative **III** by the action of various nucleophiles. Compound **III** is readily obtained by bromination of **IIa** in acetic acid; however, this reaction is accompanied by side bromination at the aromatic ring. In order to avoid this process, we carried out bromination of **IIa** under mild conditions, by treatment of a suspension of **IIa** in dioxane with bromine at 12–15°C; in this case, the brominating agent is a complex of bromine with dioxane. As a result, quinoxalinone **III** thus obtained contained no impurity of dibromo derivative. The bromine atom in **III** is readily replaced by such nucleophiles as KSCN, NaN_3, and $PhNH_2$ in DMSO to give the corresponding 3-(α-X-ethyl)quinoxalines **VI**–**VIII** (Scheme 4).

Compounds **VI**–**VIII** displayed in the IR spectra absorption bands typical of the quinoxalin-2-one system and those corresponding to vibrations of the thiocyanato group (2160 cm^{-1}, **VI**), azido group (2135 cm^{-1}, **VII**), and amino group (3300 cm^{-1}, **VIII**). The ^{1}H NMR spectra of α-substituted 3-ethylquinoxalin-2-one derivatives **VI**–**VIII** contained signals from the CH and CH_3 protons of the substituent in position *3*, which appeared as a quartet and doublet,

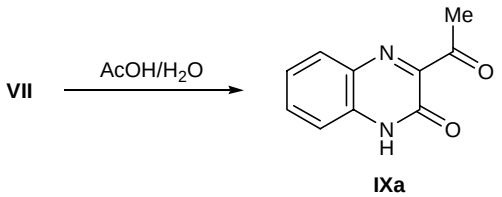
Scheme 4.



respectively, in a stronger field, as compared to the corresponding signals of 3-(1-bromoethyl)quinoxalin-2(1*H*)-one (**III**).

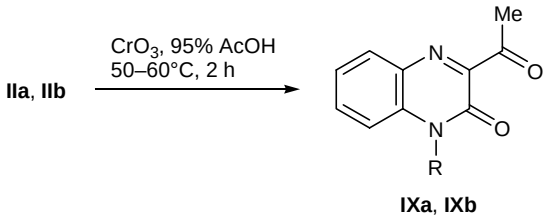
Having such derivatives as 3-(1-bromoethyl), 3-(1-thiocyanatoethyl), and 3-(1-azidoethyl) (compounds **III**, **VI**, and **VII**) at our disposal, it seemed reasonable to obtain a more promising (from the synthetic viewpoint) quinoxaline derivative, namely 3-acetylquinoxalin-2(1*H*)-one (**IXa**) [5]. It can be prepared by analogy with 3-(α-X-benzyl) derivatives, or from bromo and thiocyanato derivatives **III** and **VI** by the Kornblum reaction, or by acid hydrolysis of azido derivative **VII**. However, we failed to obtain the desired results by heating quinoxaline **VI** in DMSO both in the presence and in the absence of base or by heating azide **VII** in dilute hydrochloric acid or in acetic acid. On the other hand, by treatment of azidoethylquinoxaline **VII** with 70% aqueous acetic acid we succeeded in obtaining ketone **IXa** as the major product (Scheme 5).

Scheme 5.



We also made an attempt to directly oxidize the ethyl group in quinoxalines **IIa** and **IIb** to acetyl fragment. Reactions of **IIa** and **IIb** with CrO_3 in 95% acetic acid at 50–60°C (2 h) [15] gave the desired ketones **IXa** and **IXb** (Scheme 6). Their IR spectra contained absorption bands belonging to the ketone and lactam carbonyl groups at 1714 and 1710 cm^{-1}, respectively, and the acetyl fragment in **IXa** and **IXb** gave rise to a singlet at δ ~ 2.7 ppm in the ^1H NMR spectra.

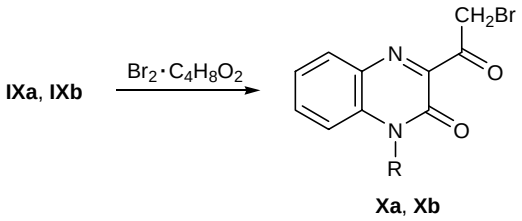
Scheme 6.



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

Further functionalization of 3-acetylquinoxalin-2(1*H*)-ones **IXa** and **IXb** included synthesis of their bromoacetyl analogs; the presence of an α-bromocarbonyl fragment in the latter opens new prospects in the preparation of various heterocyclic systems. The bromination of **IXa** and **IXb** to bromoacetylquinoxalines **Xa** and **Xb** was effected with the use of bromine–1,4-dioxane complex in THF (12–15°C, 30 min; Scheme 7). The structure of products **Xa** and **Xb** is confirmed by a high-frequency shift of the carbonyl absorption bands in the IR spectra (by 10–15 cm^{-1}), as compared to initial ketones **IXa** and **IXb**. The ^1H NMR spectra of **Xa** and **Xb** lacked methyl group singlet at δ 2.7 ppm, but a new singlet appeared at δ 4.7 ppm due to protons of the bromomethyl group.

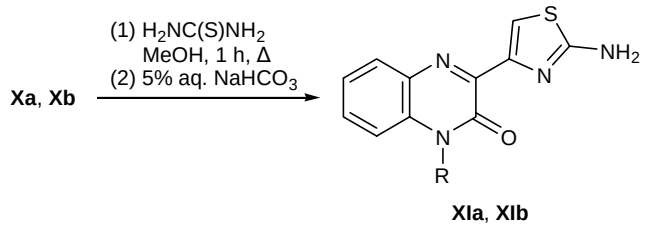
Scheme 7.



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

One of the most typical reactions of α-halo ketones is the reaction with thioamides or thiourea, which underlies the main procedure for the synthesis of thiazoles (Hantzsch reaction [16]). Moreover, this reaction may be used to identify α-halo ketones. We performed reactions of α-bromo ketones **Xa** and **Xb** with thiourea under standard conditions, i.e., by heating the reactants in boiling methanol, followed by treatment of the reaction mixture with a solution of sodium hydrogen carbonate [16] (Scheme 8).

Scheme 8.



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

Closure of thiazole ring follows from the presence of a singlet at δ 8.27±1 ppm from the 5-H proton and of a broadened singlet at δ 6.5 ppm from the amino group in the ^{1}H NMR spectra of the products. The structure of compound **XIb** was proved by the X-ray diffraction data. Compound **XIb** crystallizes to form monoclinic crystals containing one molecule in the asymmetric part of a unit cell. The quinoxaline fragment is planar within 0.050(3) Å, and it forms a dihedral angle of 15.9(1)° with the thiazole ring plane (Fig. 1). The ethyl group on C^1 strongly declines from the quinoxaline plane. The crystalline structure is characterized by an extended system of intra- and intermolecular contacts, the main kinds of which are N–H···N, C–H···N, and C–H···O. Thus, a couple of identical intermolecular contacts between protons of the amino group and thiazole nitrogen atoms in two molecules related through a symmetry center give rise to dimers shown in Fig. 2. The parameters of these contacts are as follows: $d(H^{322}\cdots N^{33'})$ = 2.35 Å, $\angle(N^{32}–H^{322}\cdots N^{33'})$ = 135°. The dimers are linked together through contacts between protons of the thiazole rings and carbonyl oxygen atoms: $d(H^{35}\cdots O^{2''})$ = 2.38 Å, $\angle(C^{35}–H^{35}\cdots O^{2''})$ = 129.3°; symmetry transformation –1/2 – *x*, 1/2 – *y*, 1/2 – *z*. As a result, infinite chains of H-bonded molecules are formed along the crystallographic 0*x* axis (Fig. 2). Intermolecular contacts involving the H^{321} atom (amino group) and 5-H atom of the fused benzene ring link the above chains to a three-dimensional supramolecular structure in crystal (Fig. 3). These interactions are characterized by the following parameters: $d(H^{321}\cdots N^{4''})(–1/2 + x, –y, z)$ = 3.12(1) Å, $\angle(N^{32}–H^{321}\cdots N^{4''})$ = 148°; $d(H^{5}\cdots N^{32'''})$ $(1/2 + x, –y, z)$ = 3.40(1) Å, $\angle(C^{5}–H^{5}\cdots N^{32'''})$ = 144°.

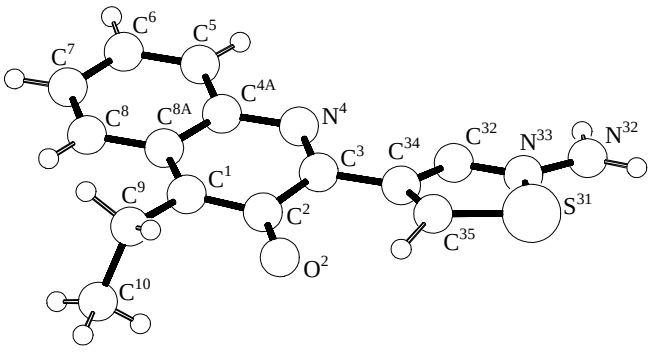


Fig. 1. Structure of the molecule of 3-(2-aminothiazol-4-yl)-quinoxalin-2(1*H*)-one (**XIb**) according to the X-ray diffraction data.

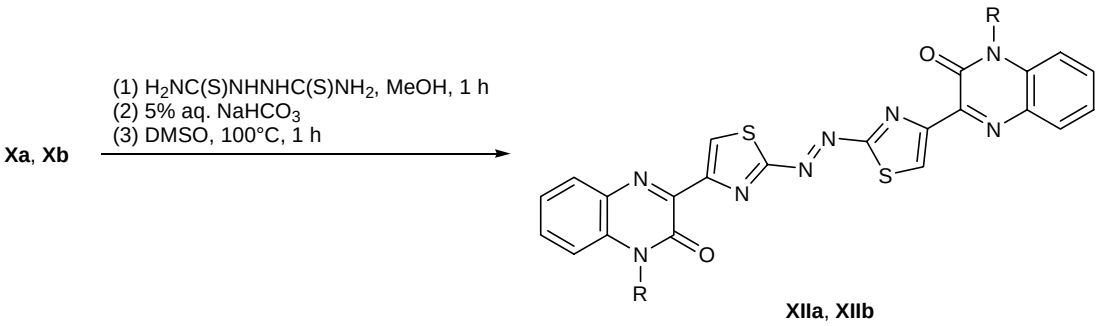
Likewise, α-bromo ketones **Xa** and **Xb** reacted with hydrazine-1,2-dicarbothioamide to afford the corresponding bis-thiazolyl-substituted hydrazines which were not isolated due to their ready oxidation with atmospheric oxygen; furthermore, these products are poorly soluble in common organic solvents, except for dimethyl sulfoxide which also acts as oxidant. Therefore, we failed to obtain their satisfactory ^{1}H NMR spectra, and the isolated products were azo compounds **XII**, which were readily formed by heating in DMSO for 1 h at ~100°C (Scheme 9).

Thus we have developed a simple and convenient procedure for the synthesis of 3-ethylquinoxalin-2(1*H*)-one and shown that the ethyl group therein is readily transformed into various functional groups which can be successfully used in further syntheses.

EXPERIMENTAL

The IR spectra were recorded in mineral oil on a Bruker Vector-22 Fourier spectrometer. The ^{1}H NMR spectra were measured on a Bruker MCL-250 instrument (250.13 MHz) using signals from residual

Scheme 9.



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

protons in the solvent as reference. The melting points were determined on a Boetius melting point apparatus.

X-Ray analysis of a single crystal of compound **XIb** was performed on an Enraf–Nonius CAD-4 automatic four-circle diffractometer ($\lambda Cu K_\alpha$ irradiation, graphite monochromator, $\omega/2\theta$ scanning, $\theta \geq 74.2°$). Monoclinic crystals, $C_{13}H_{11}N_4OS$, with the following unit cell parameters (at 20°C): a = 8.977(7), b = 18.698(1), c = 14.923(1) Å; β = 93.26(2)°; V = 2500(1) Å^3; Z = 8, d_{calc} = 1.44 g/cm^3; space group $I2/a$. Total of 5424 reflections were measured, 2602 of which were with $I \geq 4\sigma(I)$. No drop in the intensity of three control reflections was observed during data acquisition. The structure was solved by the direct method using SIR program [17] and was refined first in isotropic and then in anisotropic approximation. The positions of hydrogen atoms were determined from the difference electron density series; their contributions to structural amplitudes were taken into account with fixed temperature and positional parameters. The final divergence factors were R = 0.084 and R_w = 0.111 (from 2602 reflections with $F^2 \geq 4\sigma$). All calculations were performed on an AlphaStation 200 computer using MolEN software package [18]. The coordinates of atoms are available from the authors. The molecular structure and crystal packing were plotted, and intra- and intermolecular interactions were calculated, using PLATON software [19].

3-Ethylquinoxalin-2(1*H*)-one (IIa). Isopropyl alcohol, 300 ml, and *o*-phenylenediamine, 17 g (157.41 mmol), were added to 41 g of a mixture of compound **IV** and diethyl oxalate. The mixture was stirred for 6 h (a solid began to separate in 5 min) and was left to stand overnight. The precipitate was filtered off and washed with isopropyl alcohol. The filtrate was poured into water and was left overnight, and the precipitate was filtered off. Yield 93%, mp 192–194°C (from acetone). IR spectrum, ν, cm^{-1}: 1605 (C=N), 1660 (C=O), 2380–3220 (NH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.33 t (3H, CH_3, J = 7.40 Hz), 2.91 q (2H, CH_2, J = 7.40 Hz), 7.30–7.58 m (3H, 6-H, 7-H, 8-H), 7.80 d (1H, 5-H, J = 7.85 Hz), 11.21 br.s (1H, NH). Found, %: C 68.75; H 5.97; N 16.35. $C_{10}H_{10}N_2O$. Calculated, %: C 68.95; H 5.79; N 16.08.

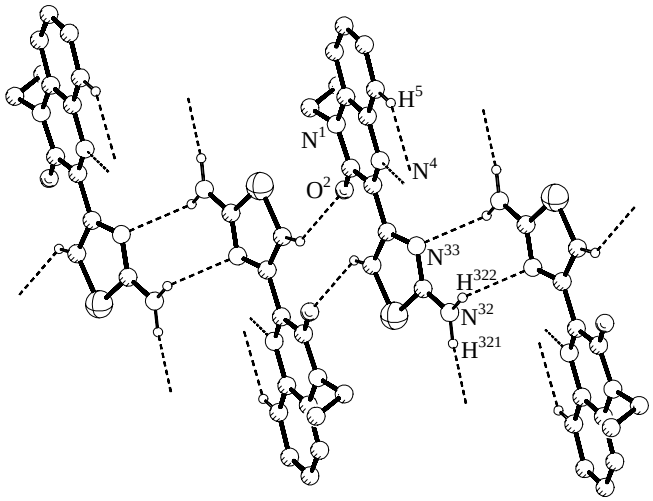


Fig. 2. Formation of H-bonded chains of molecules **XIb** in crystal (hydrogen bonds are shown as dashed lines).

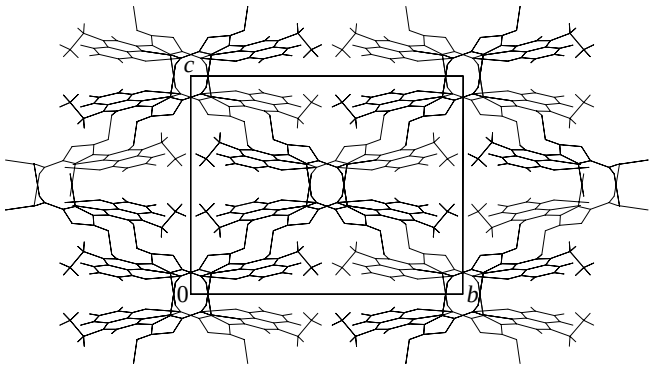


Fig. 3. Packing of molecules **XIb** in crystal (projection along the 0*a* crystallographic axis).

1,3-Diethylquinoxalin-2(1*H*)-one (IIb). A mixture of 2.32 g (13.3 mmol) of 3-ethylquinoxalin-2(1*H*)-one (**IIa**) and 1.12 g (20.0 mmol) of potassium hydroxide in 70 ml of dioxane was heated to the boiling point. A solution of 1.67 g (15.3 mmol) of ethyl bromide was added, and the mixture was heated for 5 h under reflux. The solvent was removed under reduced pressure (water-jet pump), the residue was treated with water, the mixture was left to stand for 0.5 h, and the precipitate was filtered off and washed with a solution of potassium hydroxide and water. Yield 66%, mp <70°C (from hexane). IR spectrum, ν, cm^{-1}: 1602 (C=N), 1655 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.33 t (3H, C**H**$_3$CH$_2$C, *J* = 7.25 Hz), 1.37 t (3H, C**H**$_3$CH$_2$N, *J* = 7.85 Hz), 2.95 q (2H, CH$_3$C**H**$_2$C, *J* = 7.25 Hz), 4.29 q (2H, CH$_3$C**H**$_2$N, *J* = 7.25 Hz), 7.26 d (1H, 8-H, *J* = 8.13 Hz), 7.28 d.d (1H, 7-H, *J* = 8.13, 6.38 Hz), 7.46 d.d.d (1H, 6-H, *J* = 7.28, 7.26, 1.28 Hz), 7.82 d.d (1H, 5-H, *J* = 8.55, 1.73 Hz). Found, %: C 71.32; H 6.71; N 13.57. $C_{12}H_{14}N_2O$. Calculated, %: C 71.26; H 6.98; N 13.85.

3-(1-Bromoethyl)quinoxalin-2(1*H*)-one (III). A mixture of 0.16 ml (3.88 mmol) of bromine and 5 ml of dioxane was added under stirring at 12–15°C to a suspension of 0.62 g (3.56 mmol) of quinoxaline **IIa** in 30 ml of dioxane. The mixture was stirred for 4 h, and the precipitate was filtered off and washed with isopropyl alcohol, a solution of sodium carbonate, and water. Yield 99%, mp 206–210°C (from acetone). IR spectrum, ν, cm^{-1}: 1605 (C=N), 1665 (C=O), 2380–3180 (NH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.14 d (3H, CH_3, *J* = 6.58 Hz), 5.76 q (1H, CHBr, *J* = 6.58 Hz), 7.30–7.62 m (3H, 6-H, 7-H, 8-H), 7.90 d (1H, 5-H, *J* = 7.90 Hz), 11.83 br.s (1H, NH). Found, %: C 47.62; H 3.50; Br 31.73; N 11.32. $C_{10}H_9BrN_2O$. Calculated, %: C 47.46; H 3.58; Br 31.60; N 11.07.

Ethyl 2-oxobutanoate (IV). A solution of 39.4 g (361.54 mmol) of ethyl bromide in 100 ml of THF was added dropwise under stirring to a mixture of 8.8 g (361.96 mmol) of magnesium turnings and 200 ml of THF. The mixture became turbid and warmed up to the boiling point. When the addition was complete, the mixture was heated for 0.5 h under reflux and cooled to –60°C, and a solution of 52.78 g (361.51 mmol) of diethyl oxalate in 100 ml of THF was added, maintaining the temperature below –20°C. The mixture was stirred for 2 h at –20°C, and dilute hydrochloric acid was added dropwise to a weakly acidic reaction. The organic phase was separated, washed with water (2×150 ml), and dried over sodium sulfate, and the aqueous phase was extracted with chloroform (3×250 ml). The extracts were washed with water (2×150 ml), dried over sodium sulfate, filtered, and evaporated to obtain 41 g of a mixture of compound **IV** and diethyl oxalate at a ratio of 1:1 (according to the ^{1}H NMR data).

3-(1-Thiocyanatoethyl)quinoxalin-2(1*H*)-one (VI). Potassium thiocyanate, 0.24 g (2.53 mmol), was added to a solution of 0.4 g (1.58 mmol) of compound **III** in 10 ml of DMSO. The mixture was stirred for 6 h, left to stand overnight, and poured into water, and the precipitate was filtered off and washed with water. Yield 78%, mp 186–188°C (from isopropyl alcohol). IR spectrum, ν, cm^{-1}: 1603 (C=N), 2160 (SCN), 1670 (C=O), 2500–3220 (NH). ^{1}H NMR spectrum (CD_3OD), δ, ppm: 1.91 d (3H, CH_3, *J* = 6.80 Hz), 4.98 d (1H, CHSCN, *J* = 6.80 Hz), 7.30–7.42 m (2H, 6-H or 7-H, 8-H), 7.57 d.d.d (1H, 7-H or 6-H, *J* = 7.43, 7.43, 1.2 Hz), 7.85 d.d (1H, 5-H, *J* = 8.03 Hz). Found, %: C 57.23; H 3.65; N 18.15; S 14.02. $C_{11}H_9N_3OS$. Calculated, %: C 57.13; H 3.92; N 18.17; S 13.86.

3-(1-Azidoethyl)quinoxalin-2(1*H*)-one (VII). Sodium azide, 0.16 g (2.5 mmol), was added to a solution of 0.40 g (1.58 mmol) of compound **III** in 12 ml of DMSO. The mixture was stirred for 6 h, left to stand overnight, and poured into water, and the precipitate was filtered off and washed with water. Yield 84%, mp 199–200°C (from isopropyl alcohol). IR spectrum, ν, cm^{-1}: 1605 (C=N), 1673 (C–O), 2091, 2134 (N_3), 2390–3240 (NH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.72 d (3H, CH_3, *J* = 6.78 Hz), 4.92 q (1H, CHN_3, *J* = 67.8 Hz), 7.29–7.62 m (3H, 6-H, 7-H, 8-H), 7.92 d (1H, 5-H, *J* = 7.75 Hz), 12.62 br.s (1H, NH). Found, %: C 55.61; H 4.46; N 32.41. $C_{10}H_9N_5O$. Calculated, %: C 55.81; H 4.22; N 32.54.

3-(1-Phenylaminoethyl)quinoxalin-2(1*H*)-one (VIII). Aniline, 0.15 g (1.6 mmol), was added to a solution of 0.20 g (0.8 mmol) of compound **III** in 12 ml of DMSO. The mixture was stirred for 6 h, left to stand overnight, and poured into water, and the precipitate was filtered off and washed with water. Yield 71%, mp 163–166°C (from isopropyl alcohol). IR spectrum, ν, cm^{-1}: 1605 (C=N), 1673 (C–O), 2390–3450 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.49 d (3H, CH_3, *J* = 6.43 Hz), 4.93–5.15 m (1H, CHN), 5.82 d (1H, N**H**Ph, *J* = 8.58 Hz), 6.52 d.d (1H, *p*-H, *J* = 7.30, 6.88 Hz), 6.65 d.d (2H, *o*-H, *J* = 7.75 Hz), 6.95–7.55 m (5H, 6-H, 7-H, 8-H, *m*-H), 7.75 d (1H, 5-H, *J* = 7.75 Hz), 12.36 br.s (1H, NH). Found, %: C 72.20; H 6.04; N 15.76. $C_{16}H_{15}N_3O$. Calculated, %: C 72.44; H 5.70; N 15.84.

3-Acetylquinoxalin-2(1*H*)-one (IXa). A solution of 5.17 g (52 mmol) of chromium(VI) oxide in 3 ml of water and 5 ml of acetic acid was added under stirring to a solution of 6.00 g (34 mmol) of compound **IIa** in 50 ml of acetic acid. The mixture was stirred for 2 h at 55–60°C, poured into water, and extracted with chloroform (3×25 ml). The extract was dried over sodium sulfate and passed through a column (300×15 mm) charged with 10 g of silica gel, and the column was washed with 200 ml of chloroform. The solvent was removed under reduced pressure (water-jet pump) to isolate analytically pure compound **IXa**. Yield 40%, mp 173–175°C. IR spectrum, ν, cm^{-1}: 1610 (C=N), 1659 (C=O), 1712 (C=O), 2500–3220 (NH). ^{1}H NMR spectrum (CD_3OD), δ, ppm: 2.66 s (3H, CH_3), 7.33 d (1H, 8-H, *J* = 8.33 Hz), 7.39 d.d.d (1H, 6-H or 7-H, *J* = 7.74, 7.73, 1.13 Hz), 7.64 d.d.d (1H, 7-H or 6-H, *J* = 7.77, 7.76, 1.13 Hz), 7.87 d.d (1H, 5-H, *J* = 8.14, 1.15 Hz). Found, %: C 63.98; H 4.58; N 14.61. $C_{10}H_8N_2O_2$. Calculated, %: C 63.83; H 4.22; N 14.89.

3-Acetyl-1-ethylquinoxalin-2(1*H*)-one (IXb) was synthesized as described above for **IXa** from compound **IIb**. Yield 45%, mp 84–85°C. IR spectrum, ν, sm^{-1}: 1604 (C=N), 1670 (C=O), 1714 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.40 t (3H, C**H**$_3$CH$_2$, *J* = 6.83 = Hz), 2.68 s (3H, CH_3CO), 4.32 q (2H, CH_3C**H**$_2$, *J* = 6.83 Hz), 7.34 d (1H, 8-H, *J* = 7.70 Hz), 7.35 d.d (1H, 7-H, *J* = 7.70, 7.67 Hz), 7.63 d.d.d (1H, 6-H, *J* = 8.38, 7.46, 1.30 Hz), 7.92 d.d (1H, 5-H, *J* = 8.53, 1.70 Hz). Found, %: C 66.45; H 5.45; N 12.73. $C_{12}H_{12}N_2O_2$. Calculated, %: C 66.66; H 5.59; N 12.95.

3-Bromoacetylquinoxalin-2(1*H*)-one (Xa). A mixture of 0.30 ml (5.8 mmol) of bromine and 2 ml of dioxane was added under stirring at 12–15°C to a solution of 1.00 g (5.3 mmol) of compound **IXa** in 30 ml of THF. The mixture was stirred for 1 h, poured into water, and extracted with chloroform (3×15 ml). The extract was dried over sodium sulfate, filtered, and evaporated under reduced pressure (water-jet pump). The product was used in further syntheses without additional purification.

3-Bromoacetyl-1-ethylquinoxalin-2(1*H*)-one (Xb) was synthesized in a similar way from compound **IXb**.

3-(2-Aminothiazol-4-yl)quinoxalin-2(1*H*)-one (XIa). Thiourea, 0.06 g (0.79 mmol), was added to a solution of 0.20 g (0.75 mmol) of compound **Xa** in 10 ml of methanol, and the mixture was heated for 1.5 h under reflux. The precipitate was filtered off and washed with an aqueous solution of sodium hydrogen carbonate and water. Yield 86%, mp > 360°C (from DMSO–CH_3CN, 1:1). IR spectrum, ν, cm^{-1}: 1606, 1619 (C=C, C=N); 1664 (C=O); 2500–3650 (NH, NH_2). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.38 d (1H, 8-H, *J* = 7.75 Hz), 7.39 d.d (1H, 6-H or 7-H, *J* = 7.75, 6.88 Hz), 7.59 d.d (1H, 7-H or 6-H, *J* = 7.30, 6.88 Hz), 7.90 d (1H, 5-H, *J* = 7.73 Hz), 8.26 s (1H, 5'-H), 12.50 s (1H, NH). Found, %: C 61.23; H 3.49; N 25.99; S 13.03. $C_{11}H_8N_4OS$. Calculated, %: C 61.09; H 3.73; N 25.91; S 13.12.

3-(2-Aminothiazol-4-yl)-3-ethylquinoxalin-2(1*H*)-one (XIb) was synthesized in a similar way from compound **Xb**. Yield 84%, mp 159–161°C (from DMSO–CH_3CN, 1:1). IR spectrum, ν, cm^{-1}: 1600, 1603 (C=C, C=N); 1665 (C=O); 2750–3470 (NH_2). ^{1}H NMR spectrum (CD_3OD), δ, ppm: 1.38 t (3H, CH_3, *J* = 6.93 Hz), 4.43 q (3H, CH_2, *J* = 6.93 Hz), 7.41 d.d.d (1H, 6-H or 7-H, *J* = 7.16, 7.16, 1.4 Hz), 7.55–7.65 m (2H, 7-H or 6-H, 8-H), 7.96 d (1H, 5-H, *J* = 7.40 Hz), 8.28 s (1H, 5'-H). Found, %: C 63.69; H 4.95; N 22.87; S 11.93. $C_{13}H_{12}N_4OS$. Calculated, %: C 63.91; H 4.95; N 22.93; S 11.77.

4,4'-Bis(2-oxo-1,2-dihydroquinoxalin-3-yl)-2,2'-azothiazole (XIIa). Hydrazine-1,2-dicarbothioamide, 0.06 g (0.37 mmol), was added to a solution of 0.20 g (0.75 mmol) of compound **Xa** in 10 ml of methanol, and the mixture was heated for 1.5 h under reflux. The precipitate was filtered off, washed with aqueous sodium hydrogen carbonate and water, dried, and dispersed in DMSO. The suspension was heated for 1 h at 100°C and cooled, and the precipitate was filtered off and washed with isopropyl alcohol. Yield 60%, mp >360°C (from DMSO). IR spectrum, ν, cm^{-1}: 1607 (C=N), 1664 (C=O). Found, %: C 54.38; H 2.67; N 23.32; S 13.07. $C_{22}H_{12}N_8O_2S_2$. Calculated, %: C 54.55; H 2.50; N 23.12; S 13.23.

4,4'-Bis(1-ethyl-2-oxo-1,2-dihydroquinoxalin-3-yl)-2,2'-azothiazole (XIIb) was synthesized in a similar way from compound **Xb**. Yield 63%, mp >360°C (from DMSO). IR spectrum, ν, cm^{-1}: 1601 (C=N), 1646 (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.37 t (3H, CH_3, *J* = 7.18 Hz), 4.45 q (3H, CH_2, *J* = 8.08 Hz), 7.46–7.55 m (1H, 6-H or 7-H), 7.71–7.78 m (2H, 7-H or 6-H, 8-H), 8.04 d (1H, 5-H, *J* = 7.63 Hz), 9.30 s (5'-H). Found, %: C 57.49; H 3.89; N 20.54; S 12.05. $C_{26}H_{20}N_8O_2S_2$. Calculated, %: C 57.76; H 3.73; N 20.72; S 11.86.

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