



# A reaction for the synthesis of benzimidazoles and 1*H*-imidazo[4,5-*b*]pyridines via a novel rearrangement of quinoxalinones and their aza-analogues when exposed to 1,2-arylenediamines

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NMR data

X-ray diffraction analysis

## ABSTRACT

An efficient and one-step versatile method for the synthesis of benzimidazoles and 1*H*-imidazo[4,5-*b*]pyridines from quinoxalinones and their aza-analogues have been developed on the basis of the novel ring contractions of 3-aryol-quinoxalinones and their aza-analogues with 1,2-arylenediamines.

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## 1. Introduction

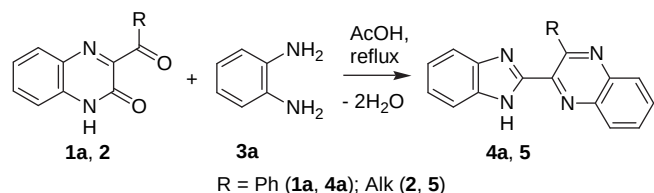
The benzimidazole<sup>1a–g</sup> and imidazopyridine<sup>2a–n</sup> moieties are important pharmacophores, which have proven to be useful for a number of biologically relevant targets. Compounds possessing a benzimidazole moiety have shown significant activity against several viruses, such as HIV,<sup>1d,e</sup> herpes (HSV-1),<sup>1d,f</sup> human cytomegalovirus (HCMV),<sup>1b,d,f</sup> and influenza.<sup>1g</sup> The compounds derived from the imidazopyridine system have recently been evaluated as antagonists of various biological receptors, including angiotensin-II,<sup>2d–f</sup> platelet activating factor,<sup>2c,g,h</sup> and metabotropic glutamate subtype V.<sup>2i</sup> Substituted imidazo[4,5-*b*]pyridines have also been tested for their potential as anticancer,<sup>2b</sup> inotropic,<sup>2j,k</sup> and selective antihistamine (H<sub>1</sub>) agents.<sup>2l</sup> Imidazo[4,5-*b*]pyridine derivatives were also reported as Aurora kinases,<sup>2m</sup> and cyclic PDE inhibitors.<sup>2n</sup> Medicinal chemists consider these heterocycles to be promising compounds. The

preparation of these compounds is usually straightforward, and a number of synthetic methods are already available.<sup>3a–l</sup> However, it is observed that all these methods involve various disadvantages, such as low yields, harsh reaction conditions, such as high reaction temperatures (~200 °C), use of toxic reagents, such as POCl<sub>3</sub>, TMS-Cl, and polyphosphoric acid, use of catalyst/oxidizing agents, such as Pb(OAc)<sub>4</sub>, PCC, and Cu(OAc)<sub>2</sub>, and continuous O<sub>2</sub> bubbling in the course of reaction are also present. Hence, it is imperative to develop a convenient, efficient, and user friendly method for the synthesis of 2-substituted-benzimidazoles and 1*H*-imidazo[4,5-*b*]pyridines.

Recently we have described a highly efficient and versatile method for the synthesis of benzimidazoles **4** and **5** on the basis of the novel ring contraction of 3-benzoyl-**1a** and 3-alkanoylquinoxalin-2(1*H*)-ones **2** with 1,2-phenylenediamine **3a** (Scheme 1) correspondingly.<sup>4a,b</sup>

As is evident from the structure of compounds **4** and **5** the C(2)–C(3)–C(O)Ph and NH<sub>2</sub>C=CNH<sub>2</sub> fragments of quinoxalinone **1a** (or **2**) and 1,2-phenylenediamine **3a** systems are correspondingly involved in the construction of two new heterocyclic systems. These

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**Scheme 1.** A new acid-catalyzed rearrangement, proceeding in the 'quinoxalinone—1,2-phenylenediamine' system.

benzimidazole and quinoxaline systems differ from the initial ones. This one-step ring contraction process represents a conceptually new method for the preparation of substituted benzimidazoles.

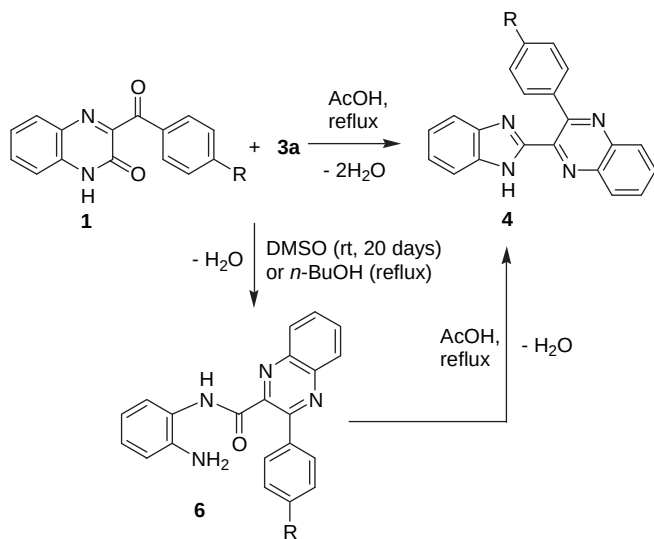
## 2. Results and discussion

We assumed that if instead of 3-benzoyl- and 3-alkanoyl-quinoxalin-2-ones we use aroylquinoxalinones and their aza-analogues—aroylpyrido[2,3-*b*]pyrazines or aroylpyrimido[4,5-*b*]pyrazines (aroylpteridines) in the reaction with 1,2-phenylenediamines this new rearrangement can serve as a simple method for synthesizing not only substituted benzimidazole derivatives but their aza-analogues—1*H*-imidazo[4,5-*b*]pyridines and purines as well. Herein we have reported our results on the feasibility of the above strategy.

Other 3-aryloxyquinoxalin-2(1*H*)-ones **1b–f** behave in a similar way.<sup>5</sup> When exposed to 1,2-phenylenediamine **3a** in boiling acetic acid solution they are converted into rearrangement products **4b–f** with high yields (Table 1). Their structures were unequivocally proved by a variety of 1D/2D NMR correlation methods<sup>6a,b</sup> (see Supplementary data).

**Table 1**

A versatile one-step method for the synthesis of benzimidazoles from quinoxalinones and 1,2-phenylenediamine via a novel rearrangement

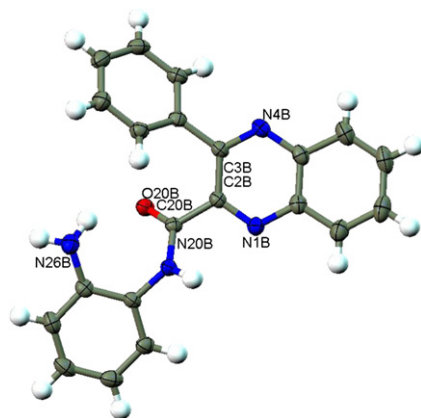


| Entry | R               | Substrates          | Product, Yield (%)                            |
|-------|-----------------|---------------------|-----------------------------------------------|
| 1     | F               | <b>1b</b> <b>3a</b> | <b>4b</b> , 94                                |
| 2     | Cl              | <b>1c</b> <b>3a</b> | <b>4c</b> , 97                                |
| 3     | Br              | <b>1d</b> <b>3a</b> | <b>4d</b> , 95                                |
| 4     | I               | <b>1e</b> <b>3a</b> | <b>4e</b> , 93                                |
| 5     | NO <sub>2</sub> | <b>1f</b> <b>3a</b> | <b>4f</b> , 92                                |
| 6     | H               | <b>1a</b> <b>3a</b> | <b>6a</b> , 80 <sup>a</sup> , 71 <sup>b</sup> |
| 7     | Br              | <b>1d</b> <b>3a</b> | <b>6d</b> , 83 <sup>a</sup>                   |
| 8     | H               | <b>6a</b>           | <b>4a</b> , 87                                |
| 9     | Br              | <b>6b</b>           | <b>4d</b> , 85                                |

<sup>a</sup> Obtained in refluxing *n*-BuOH for 4.5 h.

<sup>b</sup> Obtained in DMSO for 20 days at rt.

It should be noted that carrying out the reaction in DMSO at room temperature for 20 days or in a boiling solution of *n*-BuOH for 4.5 h leads to the formation of *ortho*-aminoanilide quinoxaline 2-carboxylic acid **6**, which when boiled in acetic acid for less than 1 min quantitatively yields 2-benzimidazol-2-ylquinoxalines **4**. This has been illustrated by the reactions of 3-aryloxyquinoxalin-2(1*H*)-ones **1a** and **1d** (Table 1). The structure of **6a** was unambiguously confirmed by the X-ray crystal analysis (see the Supplementary data) (Fig. 1).

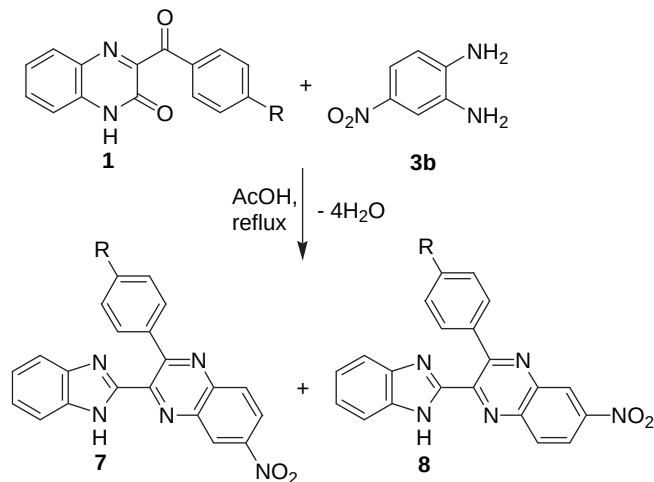


**Fig. 1.** ORTEP drawing one of the two independent **6a** molecules. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

As can be seen from Table 2, the reaction of 3-aryloxyquinoxalin-2(1*H*)-ones with nonsymmetric 1,2-phenylenediamine **3b** proceeds with the formation of almost equal amounts of the mixture of isomeric products, differing in the position of substituents of the benzene ring of quinoxalinone system regardless of the nature of the substituents in 1,2-phenylenediamine. However, in the reactions of 4-nitro-1,2-phenylenediamine **3b** each one of the products, with a high-melting point (>330 °C) precipitated during its formation from a boiling solution of acetic acid and the other one (with the melting point <300 °C) precipitated from the filtrate, after the separation of an isomer with a high-melting point (Table 2).

**Table 2**

An efficient one-step method for the synthesis of benzimidazoles from quinoxalinones and 4-nitro-1,2-phenylenediamine via a novel rearrangement

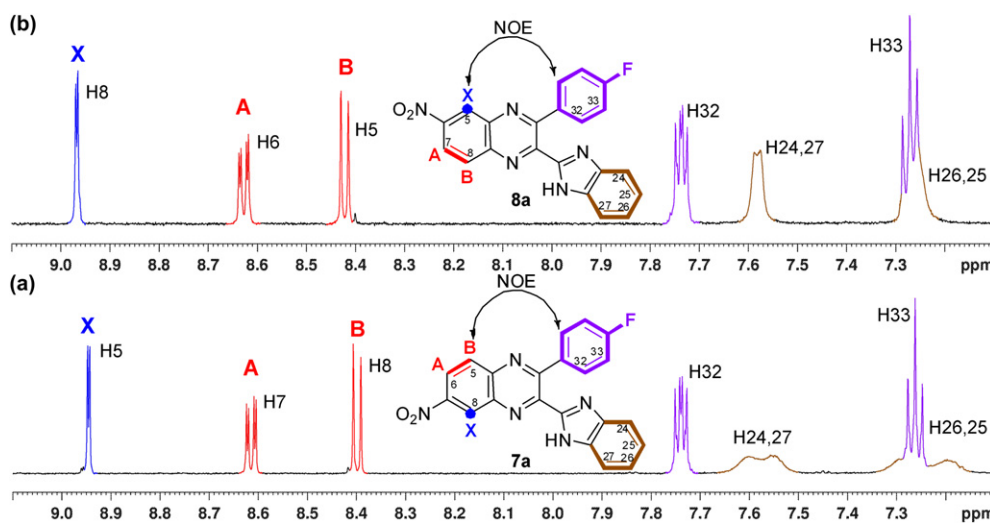


| Entry | R  | Substrate | Products, Yield (%)    |
|-------|----|-----------|------------------------|
| 1     | F  | <b>1b</b> | <b>7a+8a</b> (47) (38) |
| 2     | Cl | <b>1c</b> | <b>7b+8b</b> (42) (36) |
| 3     | Br | <b>1d</b> | <b>7c+8c</b> (45) (43) |
| 4     | I  | <b>1e</b> | <b>7d+8d</b> (44) (45) |

Unfortunately there is no significant difference in the  $^1\text{H}$  NMR spectra of high- and low-melting isomers that could be directly correlated with the isomeric structure. However, a combination of different NMR experiments (see [Supplementary data](#)) makes it possible to unambiguously establish the structures of these compounds. Namely, although the protons of the quinoxaline moiety resonate as ABX systems with practically identical chemical shifts in both isomers ([Fig. 2](#)) the weak but significant NOE's between the aryl *ortho*-protons and the nearest proton of the quinoxaline fragment make it possible to assign exactly the H5 protons. Thus with taking into account that H5 protons characteristically resonate in **7** (as AB part of ABX system with CS ca. 8.4 ppm) and in **8** (as the X part of ABX system with CS ca. 8.9 ppm) isomers the nitro group position (C7 or C6) can be easily deduced.

withdrawing substituents ( $1560\text{--}1540\text{ cm}^{-1}$ ) or to lower frequencies ( $1550\text{--}1490\text{ cm}^{-1}$ ) in the presence of electron-releasing substituents.<sup>9a,b</sup> Taking into account that the benzimidazole substituent at position 2 of the quinoxaline system has a specific  $\pi$ -deficient center, i.e., the  $\mu$ -carbon atom, which bears a substantially higher positive charge<sup>10</sup> than that on the *ipso*-carbon atom of the aryl substituent at position 3. It can be assumed that for low-melting isomers with the  $\text{NO}_2$  group in position 6 the  $\nu_{\text{as}}(\text{NO}_2)$  frequencies must be higher than those for the high-melting isomers with the nitro group in position 7.

In order to confirm our conclusions about the structure of the high- and low-melting isomers **7a–d** and **8a–d**, on the bases of NMR spectroscopic data we have had X-ray diffraction analysis performed for **7a** and **8a**. In fact, X-ray crystallographic analysis of



**Fig. 2.** Fragments of  $^1\text{H}$  NMR spectra (DMSO, 303 K) of **7a** (a) and **8a** (b). Observed NOE's are shown schematically by arrows.

Besides, the carbon CSs of the quinoxaline system are sensitive to the mutual position of aryl and  $\text{NO}_2$  moieties<sup>7</sup> and can be used to provide an additional support to the above conclusions on isomeric structures by comparison with theoretically predicted data<sup>8a,b</sup> (e.g., for **7a/8a** see [Supplementary data](#)). Thus, the high-melting isomers (**7a–d**) are in position 7 with the  $\text{NO}_2$  group while the low-melting isomers (**8a–d**) are in position 6 with the  $\text{NO}_2$  group.

On the whole, the IR spectra of both isomers are similar and have absorption bands characteristic of these structures ([Experimental Section](#)). At the same time, a comparison of the spectra shows that the anti-symmetric vibrations of the  $\text{NO}_2$  group are most sensitive to structural changes ([Table 3](#)).

**Table 3**  
The value of  $\nu_{\text{as}}(\text{NO}_2)$  and  $\nu_{\text{s}}(\text{NO}_2)$  absorption bands of isomers **7** and **8** in IR spectra (KBr)  $\nu/\text{cm}^{-1}$

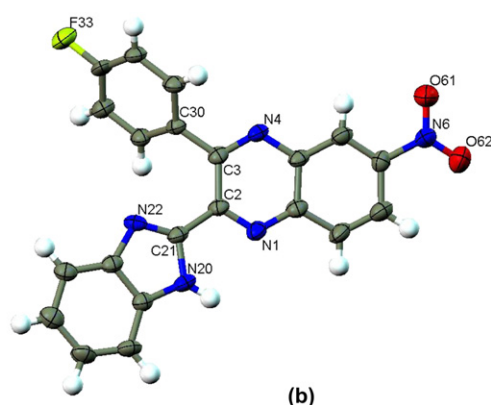
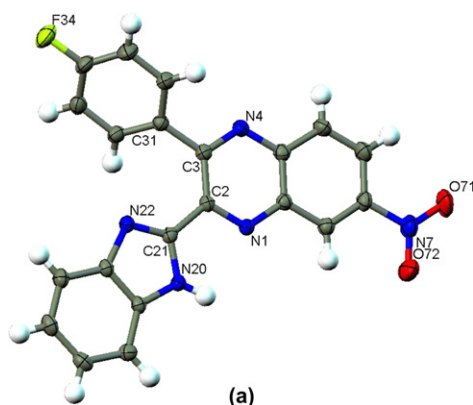
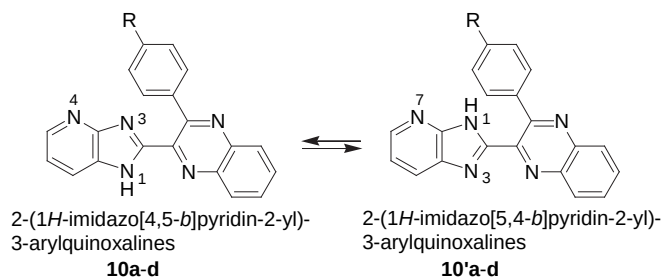
| IR, $\nu/\text{cm}^{-1}$<br>(KBr) | Isomers   |           |           |           |           |           |           |           |
|-----------------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                                   | <b>7a</b> | <b>8a</b> | <b>7b</b> | <b>8b</b> | <b>7c</b> | <b>8c</b> | <b>7d</b> | <b>8d</b> |
| $\nu_{\text{as}}(\text{NO}_2)$    | 1520      | 1532      | 1519      | 1531      | 1519      | 1534      | 1519      | 1532      |
| $\nu_{\text{s}}(\text{NO}_2)$     | 1348      | 1350      | 1348      | 1347      | 1347      | 1348      | 1346      | 1344      |

Unlike the frequencies of  $\nu_{\text{s}}(\text{NO}_2)$ , which are virtually identical in the spectra of both compounds, the frequencies  $\nu_{\text{as}}(\text{NO}_2)$  for high-melting isomers are  $\sim 15\text{ cm}^{-1}$  higher than those for low-melting isomers. Asymmetric vibrations of  $\text{NO}_2$ , which are known to be sensitive to the electronic properties of the *para* substituent, are shifted to higher frequencies in the presence of electron-

**7a** and **8a** demonstrated that the  $\text{NO}_2$  group in the high-melting isomer is in position 7 ([Fig. 3 a](#)), and in the low-melting one it is in position 6 ([Fig. 3 b](#)).

The use of pyrido[2,3-*b*]pyrazin-3(4*H*)-ones **9** instead of quinoxalinones **1** in the rearrangement considered here makes it possible to synthesize aza-analogues of benzimidazoles—1*H*-imidazo[4,5-*b*]pyridines **10**, which are not easily accessible by classical Filips–Ladenburg<sup>3a,11a,b</sup> and Weidenhagen<sup>12a–c</sup> reactions. The formation of 2-(1*H*-imidazo[4,5-*b*]pyridin-2-yl)-3-arylquinoxalines **10a–d** from pyrido[2,3-*b*]pyrazin-2(1*H*)-ones **9a–d** and 1,2-phenylenediamine **3a** proceeds in AcOH under reflux for 35–47 h. It should be noted, that carrying out the reaction with refluxed AcOH for 3 h leads to the formation of 2-amino-3-azaanylide quinoxaline 3-phenyl-2-carboxylic acids **11**. This has been illustrated by the reaction of 2-(1*H*-imidazo[4,5-*b*]pyridin-2-yl)-3-phenylquinoxaline **9a** and 1,2-phenylenediamine **3a** ([Table 4](#)). Single crystal of **10a** suitable for X-ray diffraction study was obtained by recrystallization from AcOH ([Fig. 4](#)).

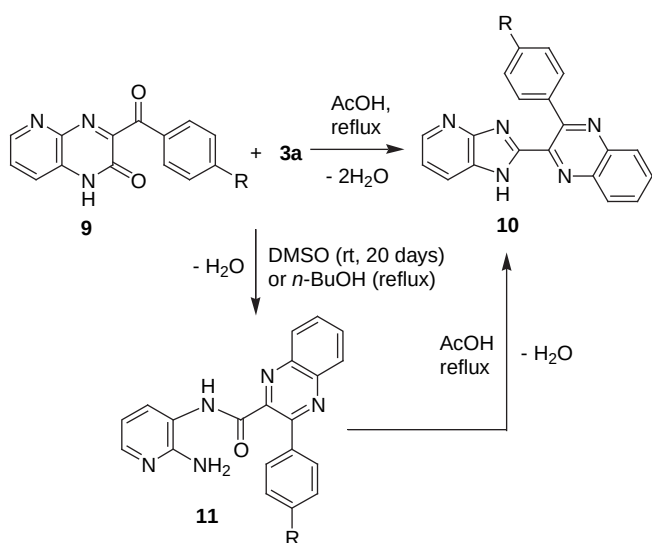
As evident from the  $^1\text{H}$  NMR data (see [Experimental Section](#) and [Supplementary data](#)), compounds **10a–d**, in contrast to the compounds **4a–f**, **7a–d**, and **8a–d** with the benzimidazole system in the investigated solutions of DMSO- $d_6$  exist as a tautomeric mixture of **10a–d**  $\rightleftharpoons$  **10'a–d**, resulting in the dissymmetric 1*H*-imidazo[4,5-*b*]pyridine system. Benzimidazoles as imidazoles with a ring *N*-hydrogen are subjected to tautomerism, which becomes evident in unsymmetrically substituted compounds.<sup>13</sup> In the cases of imidazo[4,5-*b*]pyridines **10a–d** the dissymmetry was caused by a nitrogen atom of the pyridine ring.



**Fig. 3.** ORTEP drawing of **7a** (a) and **8a** (b) molecules. Displacement ellipsoids are drawn at the 30% probability level. H atoms are represented by circles of arbitrary radii. The solvent molecule in (a) was omitted for clarity.

**Table 4**

A new 1H-imidazo[4,5-b]pyridine synthesis from pyrido[2,3-b]pyrazin-2(1H)-ones and 1,2-phenylenediamine via a novel rearrangement

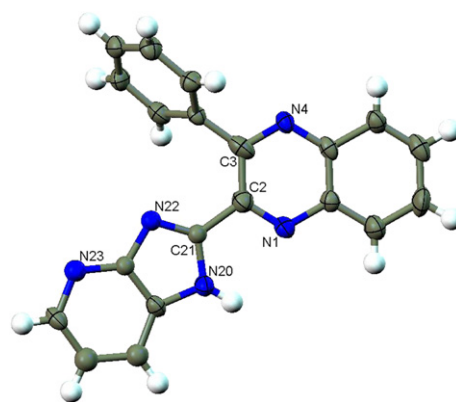


| Entry | R  | Substrates          | Product, Yield (%)                             |
|-------|----|---------------------|------------------------------------------------|
| 1     | H  | <b>9a</b> <b>3a</b> | <b>10a</b> , 69                                |
| 2     | F  | <b>9b</b> <b>3a</b> | <b>10b</b> , 44                                |
| 3     | Cl | <b>9c</b> <b>3a</b> | <b>10c</b> , 41                                |
| 4     | Br | <b>9d</b> <b>3a</b> | <b>10d</b> , 43                                |
| 5     | H  | <b>9a</b> <b>3a</b> | <b>11a</b> , 64 <sup>a</sup> , 72 <sup>b</sup> |
| 6     | H  | <b>11a</b>          | <b>10a</b> , 84                                |

<sup>a</sup> Obtained in refluxing pyridine.

<sup>b</sup> Obtained in refluxing AcOH.

On the basis of the known chemistry of quinoxalinones,<sup>14a–d</sup> 1,2-phenylenediamines<sup>15</sup> and above data (the formation of compounds **6a,b** and **11a**) it is reasonable to assume that the formation of 2-benzimidazol-2-ylquinoxaline **4** involves addition of the amino group of **3** at the C(3) atom of quinoxalin-2(1H)-one **1** as the first step. The next step involves the nucleophilic attack of the second amino group of **3** at the benzoyl carbonyl group to form the spiro-quinoxaline derivative **6'**. Rearrangement of the spiroquinoxalinone **6'** is then assumed to occur according to **Scheme 2**, which proceeds by cascade reactions involving: (a) acid catalysis ring-opening with cleavage of the C(3)–N(4) bond in spiro-compound **6'** with the intermediate formation of quinoxaline derivative **6**, (b) intramolecular nucleophilic attack by the amino group on the carbonyl group with the intermediate formation of hydroxy-de-



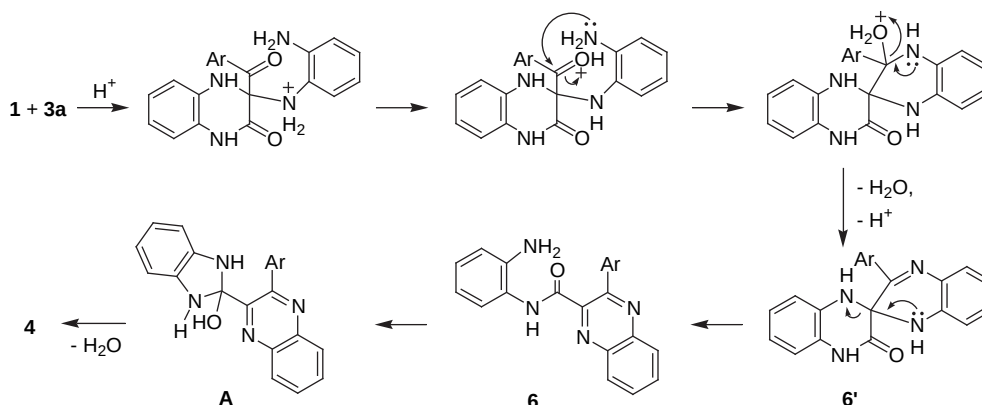
**Fig. 4.** ORTEP plot of compound **10a**. Displacement ellipsoids are drawn at the 30% probability level. The solvent water molecules were omitted for clarity.

riative **A**, and (c) elimination of water leading to the formation of the final product **4** (**Scheme 2**).

This proposed mechanism of the rearrangement is indirectly confirmed by the formation of spiro-compounds with a structure similar to that of **6'** in the reactions of quinoxalinones with other binucleophilic compounds<sup>14c,d</sup> and in the reactions of aza-quinoxalinones with 1,2-phenylenediamine. The formation of quinoxaline derivative **6** in the reaction of quinoxalin-2(1H)-ones with 1,2-phenylenediamine in DMSO at room temperature, and in boiling *n*-BuOH, also occurs.

### 3. Conclusion

To summarize, we have found an efficient and versatile one-step method for the preparation of a series of benzimidazoles as well as



Scheme 2. A probable mechanism of the rearrangement.

1*H*-imidazo[4,5-*b*]pyridines. This was accomplished by the novel rearrangement of 3-arylquinoxalin-2(1*H*)-ones and their aza-analogues of benzimidazoles on exposure to 1,2-phenylenediamines. The reaction is readily applicable to large scale synthesis. Application of this methodology to the synthesis of other heterocyclic ring systems is currently under investigation and the results will be published in due time.

## 4. Experimental section

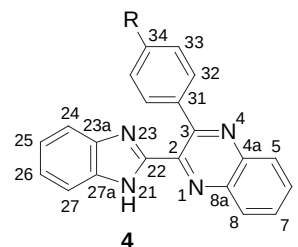
### 4.1. General methods

NMR investigations were carried out in the NMR Department of the Federal Collective Spectral Analysis Center for the physical and chemical investigations of the structure, properties, and composition of matter and materials. All NMR experiments were performed with a Bruker AVANCE-600 spectrometer (14.1 T) equipped with a 5 mm diameter gradient inverse broad band probehead and a pulsed gradient unit capable of producing magnetic field pulse gradients in the *z*-direction of 53.5 G cm<sup>-1</sup>. Frequencies are 400 MHz in <sup>1</sup>H, 100 MHz in <sup>13</sup>C, and 60 MHz in <sup>15</sup>N experiments. Chemical shifts are reported in the  $\delta$  (ppm) scale relative to the <sup>1</sup>H and <sup>13</sup>C signals of tetramethylsilane (TMS) (0.00 ppm). <sup>15</sup>N, <sup>19</sup>F chemical shifts were referenced to the <sup>15</sup>N signal of CH<sub>3</sub>CN (235.50 ppm) and <sup>19</sup>F signal of C<sub>6</sub>F<sub>6</sub> (−164.9 ppm), respectively. The ab initio quantum chemical calculations were performed using Gaussian 98.<sup>16</sup> Chemical shifts were determined by the GIAO method within the DFT framework using a hybrid exchange-correlation functional, B3LYP, at the 6-31G(d) level if not commented otherwise. All data were referred to TMS (0.00 ppm) for <sup>1</sup>H and <sup>13</sup>C chemical shifts calculated in the same conditions. Melting points were determined on a Boetius hot-stage apparatus. IR spectra were recorded on a Bruker Vector-22 FT-IR spectrometer in KBr pellets. Mass spectra of electron ionization (EI) were measured on a Thermo Fisher Sci. DFS mass spectrometer. The insertion of the sample was performed with direct injection combined with a water cooling system. The peaks of fragment ions with the intensity of less than 10% are omitted. The elemental analyses were given for the pure compounds after removing the solvate molecule and were carried out at the Microanalysis Laboratory of the Arbuzov Institute of Organic and Physical Chemistry, Russian Academy of Sciences.

### 4.2. Typical procedure 1: synthesis of 2-(benzimidazol-2-yl)-3-arylquinoxalines 4

A solution of 3-arylquinoxaline-2(1*H*)one **1** (0.93 mmol) and 1,2-phenylenediamine **3a** (0.93 mmol) in acetic acid (9 mL) was heated at reflux for 1 h. After cooling to room temperature, the

crystals of **4** that precipitated were collected by suction filtration and compound **4** was obtained in ~90% yield. The filtrate was evaporated and the residue was treated with water. The crystals formed were filtered off, washed with water, and dried. An additional 3–5% compound **4** was thus obtained.



**4.2.1. 2-(Benzimidazol-2-yl)-3-(4-fluorophenyl)quinoxaline (4b).** Pale orange crystals, mp 251–253 °C; [found C, 74.22; H, 3.89; N, 16.40. C<sub>21</sub>H<sub>13</sub>FN<sub>4</sub> requires C, 74.11; H, 3.85; N, 16.46%];  $\nu_{\max}$  (KBr) 3243, 3066, 1697, 1513, 1429, 1361, 1338, 1284, 1272, 1223, 845, 744 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (400 MHz, DMSO-*d*<sub>6</sub>) 7.20–7.26 (2H, m, H25, H26), 7.21 (2H, dd, <sup>3</sup>*J*<sub>HH</sub> 9.1, <sup>3</sup>*J*<sub>HF</sub> 9.1 Hz, 2×H33), 7.53–7.59 (2H, m, H24, H27), 7.66 (2H, dd, <sup>3</sup>*J*<sub>HH</sub> 9.1, <sup>4</sup>*J*<sub>HF</sub> 5.6 Hz, 2×H32), 7.93–7.99 (2H, m, H6, H7), 8.19–8.25 (2H, m, H5, H8), 13.20 (1H, br s, H21);  $\delta_{\text{C}}$  (100 MHz, DMSO-*d*<sub>6</sub>) 114.6 (d, <sup>2</sup>*J*<sub>FC</sub> 21.8 Hz, C33), 117.0 (br, C24, C27), 122.7 (br, C25, C26), 128.6 (C8), 128.9 (C5), 130.9 (C6), 131.5 (C7), 131.7 (d, <sup>3</sup>*J*<sub>FC</sub> 8.6 Hz, C32), 135.1 (d, <sup>4</sup>*J*<sub>FC</sub> 3.4 Hz, C31), 139.0 (br, C23a, C27a), 139.7 (C8a), 140.8 (C4a), 143.3 (C2), 149.2 (C22), 152.3 (C3), 162.6 (d, <sup>1</sup>*J*<sub>FC</sub> 246 Hz, C34);  $\delta_{\text{F}}$  (376 MHz, DMSO-*d*<sub>6</sub>) 112.8 (F34).

**4.2.2. 2-(Benzimidazol-2-yl)-3-(4-chlorophenyl)quinoxaline (4c).** Off-white crystals, mp 233–235 °C; [found C, 70.61; H, 3.71; N, 15.66. C<sub>21</sub>H<sub>13</sub>ClN<sub>4</sub> requires C, 70.69; H, 3.67; N, 15.70%];  $\nu_{\max}$  (KBr) 3203, 3061, 1690, 1429, 1364, 1336, 1293, 1094, 1011, 838, 742 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (400 MHz, DMSO-*d*<sub>6</sub>) 7.16–7.30 (2H, m, H25, H26), 7.40 (2H, d, *J* 8.6 Hz, 2×H33), 7.42–7.56 (2H, m, H24, H27), 7.57 (2H, d, *J* = 8.6 Hz, 2×H32), 7.90–7.94 (2H, m, H6, H7), 8.13–8.16 (1H, m, H5), 8.17–8.20 (1H, m, H8), 13.20 (1H, br s, H21);  $\delta_{\text{C}}$  (100 MHz, DMSO-*d*<sub>6</sub>) 115.0 (br, C24, C27), 122.9 (C25, C26), 127.7 (C33), 128.7 (C8), 128.8 (C5), 131.1 (C6, C32), 131.7 (C7), 133.8 (C34), 137.3 (C31), 138.8 (br, C23a, C27a), 139.7 (C8a), 140.7 (C4a), 143.1 (C2), 149.1 (C22), 152.0 (C3).

**4.2.3. 2-(Benzimidazol-2-yl)-3-(4-bromophenyl)quinoxaline (4d).** Yellow crystals, mp 234–236 °C; [found C, 62.72; H, 3.23; N, 13.90. C<sub>21</sub>H<sub>13</sub>BrN<sub>4</sub> requires C, 62.86; H, 3.27; N, 13.96%];  $\nu_{\max}$  (KBr) 3297, 3241, 3063, 3027, 2881, 1712, 1479, 1428, 1341, 1263, 768, 746 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (400 MHz, DMSO-*d*<sub>6</sub>) 7.16–7.19 (1H, m, H25), 7.26–7.28 (1H, m, H26), 7.52–7.64 (6H, m, 2×H32, 2×H33, H24,



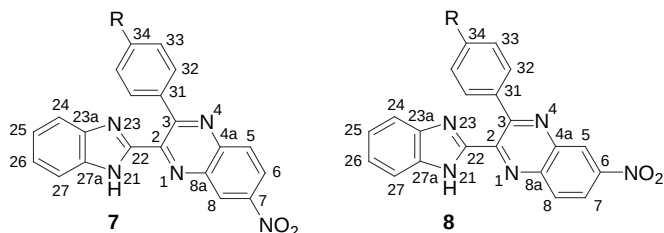
H27), 7.93–7.96 (2H, m, H6, H7), 8.17–8.23 (2H, m, H5, H8), 13.20 (1H, br s, H21);  $\delta_C$  (100 MHz, DMSO- $d_6$ ) 111.9 (br, C27), 119.7 (br, C24), 121.9 (br, C25), 122.5 (C34), 123.6 (br, C26), 128.6 (C8), 128.9 (C5), 130.6 (C32), 131.1 (C6), 131.47 (C33), 131.52 (C7), 134.4 (br, C27a), 137.9 (C31), 139.7 (C8a), 140.7 (C4a), 143.2 (C2), 143.4 (br, C23a), 149.1 (C22), 152.1 (C3).

**4.2.4. 2-(Benzimidazol-2-yl)-3-(4-iodophenyl)quinoxaline (4e).** Light-yellow crystals, mp 264–265 °C; [found C, 56.16; H, 2.95; N, 12.55.  $C_{21}H_{13}IN_4$  requires C, 56.27; H, 2.92; N, 12.50%];  $\nu_{max}$  (KBr) 3393, 3049, 1711, 1479, 1417, 1387, 1334, 1323, 1196, 1141, 997, 765, 747  $cm^{-1}$ ;  $\delta_H$  (400 MHz, DMSO- $d_6$ ) 7.20–7.26 (2H, m, H25, H26), 7.42 (2H, d,  $J$  8.0 Hz, 2×H32), 7.55–7.59 (2H, m, H24, H27), 7.77 (2H, d,  $J$  8.0 Hz, 2×H33), 7.94–7.99 (2H, m, H6, H7), 8.18–8.25 (2H, m, H5, H8), 13.21 (1H, br s, H21);  $\delta_C$  (100 MHz, DMSO- $d_6$ ) 95.9 (C34), 122.8 (br, C25, C26), 128.6 (C8), 128.9 (C5), 131.1 (C6), 131.5 (C7, C32), 136.5 (C33), 138.2 (C31), 139.7 (C8a), 140.8 (C4a), 143.2 (C2), 145.8 (br, C23a, C27a), 149.1 (C22), 152.3 (C3), the signals of C24, C27 are extremely broadened.

**4.2.5. 2-(Benzimidazol-2-yl)-3-(4-nitrophenyl)quinoxaline (4f).** Bright-yellow crystals, mp 304–306 °C; [found C, 68.52; H, 3.52; N, 18.99.  $C_{21}H_{13}N_5O_2$  requires C, 68.66; H, 3.57; N, 19.06%];  $\nu_{max}$  (KBr) 3384, 3056, 1510, 1480, 1348, 1324, 1201, 855, 765, 740, 704  $cm^{-1}$ ;  $\delta_H$  (400 MHz, DMSO- $d_6$ ) 7.13–7.29 (2H, m, H25, H26), 7.47–7.61 (2H, m, H24, H27), 7.90 (2H, d,  $J$  8.9 Hz, 2×H32), 7.94–8.02 (2H, m, H6, H7), 8.20–8.28 (2H, m, H5, H8), 8.27 (2H, d,  $J$  8.9 Hz, 2×H33), 13.24 (1H, br, H21);  $\delta_C$  (100 MHz, DMSO- $d_6$ ) 111.9 (br, C27), 119.8 (br, C24), 121.9 (br, C25), 122.6 (C33), 123.7 (br, C26), 128.5 (C8), 129.0 (C5), 130.8 (C32), 131.5 (C6, C7), 134.3 (br, C27a), 140.0 (C8a), 140.5 (C4a), 142.8 (C2), 143.3 (br, C23a), 145.6 (C31), 147.4 (C34), 148.7 (C22), 151.4 (C3).

### 4.3. Typical procedure 2: synthesis of 2-(benzimidazol-2-yl)quinoxalines 7 and 8

A solution of 3-arylquinoxaline-2(1H)one **1** (0.65 mmol) and 4-nitro-1,2-phenylenediamine **3b** (0.65 mmol) in acetic acid (7 mL) was refluxed for 1.5 h. After ca. 30 min the precipitation of crystals occurred, which was completed during the following 1 h. The crystals were collected by hot suction filtration. Thus, 40% of the analytically pure sample of a high-melting isomer **7** was obtained. After evaporation of the solvent from the filtrate under reduced pressure the resulting solid was refluxed at 80 °C for 10 min in *i*-PrOH and was hot filtered. After cooling the filtrate to room temperature the precipitated crystals of isomer **8** were collected by suction filtration and ca. a 40% compound **8** was obtained. 5–10% of the solid residue, which was not dissolved in refluxed *i*-PrOH proved to be isomer **7**.



**4.3.1. 2-(Benzimidazol-2-yl)-3-(4-fluorophenyl)-7-nitroquinoxaline (7a).** Bright-orange powder, mp 336–337 °C (AcOH); [found C, 65.39; H, 3.18; N, 18.15.  $C_{21}H_{12}FN_5O_2$  requires C, 65.45; H, 3.14; N, 18.17%];  $\nu_{max}$  (KBr) 3360, 1602, 1520 ( $\nu_{as}$  ( $NO_2$ )), 1348 ( $\nu_s$  ( $NO_2$ )), 1331, 1309, 1224, 1205, 1160, 1069, 833, 743  $cm^{-1}$ ;  $\delta_H$  (400 MHz, DMSO- $d_6$ ) 7.18–7.32 (2H, m, H25, H26), 7.26 (2H, dd,  $^3J_{HH}$  8.8,  $^3J_{HF}$  8.8 Hz, 2×H33), 7.52–7.64 (2H, m, H24, H27), 7.74 (2H, dd,  $^3J_{HH}$  8.8,

$^4J_{HF}$  5.5 Hz, 2×H32), 8.40 (1H, d,  $J$  9.3 Hz, H5), 8.61 (1H, dd,  $J$  9.3, 2.5 Hz, H6), 8.95 (1H, d,  $J$  2.5 Hz, H8), 13.30 (1H, br s, H21);  $\delta_C$  (100 MHz, DMSO- $d_6$ ) 114.8 (d,  $J$  21.9 Hz, C33), 112.1 (br, C27), 120.0 (br, C24), 122.2 (br, C25), 124.1 (br, C26), 124.4 (C6), 124.5 (C8), 130.9 (C5), 132.0 (d,  $J$  8.9 Hz, C32), 134.4 (br, C27a), 134.4 (d,  $J$  3.1 Hz, C31), 138.5 (C8a), 143.1 (C4a), 143.4 (br, C23a), 145.3 (C2), 147.9 (C7), 148.4 (C22), 155.1 (C3), 163.0 (d,  $J$  247.2 Hz, C34);  $\delta_F$  (376 MHz, DMSO- $d_6$ ) 111.6 (F34);  $m/z$  385 (26  $M^{+}$ ), 384 (60), 354 (100), 353 (14), 339 (14), 338 (44), 337 (16), 326 (13), 177 (13), 169 (13%).

**4.3.2. 2-(Benzimidazol-2-yl)-3-(4-fluorophenyl)-6-nitroquinoxaline (8a).** Bright-yellow powder, mp 246–249 °C (*i*-PrOH); [found C, 65.34; H, 3.09; N, 18.12.  $C_{21}H_{12}FN_5O_2$  requires C, 65.45; H, 3.14; N, 18.17%];  $\nu_{max}$  (KBr) 3073, 2968, 2929, 1602, 1532 ( $\nu_{as}$  ( $NO_2$ )), 1514, 1431, 1350 ( $\nu_s$  ( $NO_2$ )), 1334, 1309, 1230, 849, 751  $cm^{-1}$ ;  $\delta_H$  (400 MHz, DMSO- $d_6$ ) 7.18 (1H, dd,  $J$  8.0, 8.0 Hz, H26), 7.26 (2H, dd,  $^3J_{HH}$  8.6,  $^3J_{HF}$  8.6 Hz, 2×H33), 7.30 (1H, dd,  $J$  8.0, 8.0 Hz, H25), 7.53 (1H, d,  $J$  8.0 Hz, H24), 7.61 (1H, d,  $J$  8.0 Hz, H27), 7.73 (2H, dd,  $^3J_{HH}$  8.5,  $^4J_{HF}$  5.6 Hz, 2×H32), 8.40 (1H, d,  $J$  9.1 Hz, H8), 8.61 (1H, dd,  $J$  9.1, 2.4 Hz, H7), 8.95 (1H, d,  $J$  2.4 Hz, H5), 13.32 (1H, br s, H21);  $\delta_C$  (100 MHz, DMSO- $d_6$ ) 112.1 (C27), 114.6 (d,  $J$  21.8 Hz, C33), 120.0 (C24), 122.2 (C25), 1124.1 (C7), 124.2 (C26), 124.9 (C5), 130.5 (C8), 131.9 (d,  $J$  9.0 Hz, C32), 134.5 (C31, C27a), 139.5 (C4a), 142.2 (C8a), 143.5 (C23a), 145.7 (C2), 148.1 (C6), 148.4 (C22), 154.4 (C3), 162.9 (d,  $J$  246.6 Hz, C34);  $\delta_F$  (376 MHz, DMSO- $d_6$ ) 112.0 (F34);  $m/z$  385 (6  $M^{+}$ ), 384 (15), 355 (9), 354 (100), 338 (11), 337 (16), 177 (11%).

**4.3.3. 2-(Benzimidazol-2-yl)-3-(4-chlorophenyl)-7-nitroquinoxaline (7b).** Orange powder, mp 338–339 °C (AcOH); [found C, 62.85; H, 2.99; N, 17.35.  $C_{21}H_{12}ClN_5O_2$  requires C, 62.77; H, 3.01; N, 17.43%];  $\nu_{max}$  (KBr) 3369, 3095, 1615, 1519 ( $\nu_{as}$  ( $NO_2$ )), 1348 ( $\nu_s$  ( $NO_2$ )), 1330, 740  $cm^{-1}$ ;  $\delta_H$  (400 MHz, DMSO- $d_6$ ) 7.18–7.32 (2H, m, H25, H26), 7.48 (2H, d,  $J$  8.7 Hz, 2×H33), 7.52–7.64 (2H, m, H24, H27), 7.70 (2H, d,  $J$  8.7 Hz, 2×H32), 8.39 (1H, d,  $J$  9.3 Hz, H5), 8.60 (1H, dd,  $J$  9.3, 2.4 Hz, H6), 8.93 (1H, d,  $J$  2.4 Hz, H8), 13.34 (1H, br s, H21);  $\delta_C$  (100 MHz, DMSO- $d_6$ ) 115.9 (br, C24, C27), 122.7 (C25, C26), 124.1 (C6), 124.3 (C8), 127.5 (C33), 130.7 (C5), 131.3 (C32), 134.3 (C34), 136.8 (C31), 138.5 (C8a), 139.3 (br, C23a, C27a), 142.9 (C4a), 145.5 (br, C2), 147.9 (C7), 148.6 (br, C22), 154.8 (C3);  $m/z$  403 (6), 402 (20), 401 (17  $M^{+}$ ), 400 (57), 372 (32), 371 (28), 370 (100), 369 (11), 356 (12), 355 (12), 354 (34), 168 (11%).

**4.3.4. 2-(Benzimidazol-2-yl)-3-(4-chlorophenyl)-6-nitroquinoxaline (8b).** Orange red crystals, mp 291–292 °C (*i*-PrOH); [found C, 62.89; H, 3.04; N, 17.36.  $C_{21}H_{12}ClN_5O_2$  requires C, 62.77; H, 3.01; N, 17.43%];  $\nu_{max}$  (KBr) 3394, 2926, 1615, 1531 ( $\nu_{as}$  ( $NO_2$ )), 1347 ( $\nu_s$  ( $NO_2$ )), 1332, 738  $cm^{-1}$ ;  $\delta_H$  (400 MHz, DMSO- $d_6$ ) 7.16–7.34 (2H, m, H25, H26), 7.49 (2H, d,  $J$  8.7 Hz, 2×H33), 7.52–7.64 (2H, m, H24, H27), 7.69 (2H, d,  $J$  8.7 Hz, 2×H32), 8.40 (1H, d,  $J$  9.3 Hz, H8), 8.61 (1H, dd,  $J$  9.3, 2.4 Hz, H7), 8.95 (1H, d,  $J$  2.4 Hz, H5), 13.37 (1H, s, H21);  $\delta_C$  (100 MHz, DMSO- $d_6$ ) 115.9 (br, C24, C27), 123.2 (C25, C26), 124.2 (C7), 124.9 (C5), 127.7 (C33), 130.5 (C8), 131.4 (C32), 134.2 (C34), 137.0 (C31), 138.6 (br, C23a, C27a), 139.5 (C4a), 142.3 (C8a), 145.7 (C2), 148.2 (C6), 148.4 (C22), 154.3 (C3);  $m/z$  403 (4), 402 (11), 401 (11  $M^{+}$ ), 400 (27), 373 (11), 372 (40), 371 (34), 370 (100), 354 (15), 335 (12), 154 (14%).

**4.3.5. 2-(Benzimidazol-2-yl)-3-(4-bromophenyl)-7-nitroquinoxaline (7c).** Orange yellow powder, mp 343–345 °C (AcOH); [found C, 56.41; H, 2.68; N, 15.64.  $C_{21}H_{12}BrN_5O_2$  requires C, 56.52; H, 2.71; N, 15.69%];  $\nu_{max}$  (KBr) 3360, 3096, 3066, 2919, 1519 ( $\nu_{as}$  ( $NO_2$ )), 1347 ( $\nu_s$  ( $NO_2$ )), 1329, 1071, 746  $cm^{-1}$ ;  $\delta_H$  (400 MHz, DMSO- $d_6$ ) 7.16–7.34 (2H, m, H25, H26), 7.54–7.66 (2H, m, H24, H27), 7.60–7.66 (4H, m, 2×H32, 2×H33), 8.39 (1H, d,  $J$  9.3 Hz, H5), 8.60 (1H, dd,  $J$  9.1, 2.4 Hz, H6), 8.94 (1H, d,  $J$  2.4 Hz, H8), 13.32 (1H, br s, H21);  $\delta_C$  (100 MHz, DMSO- $d_6$ ) 111.9 (br, C27), 119.8 (br, C24), 122.0 (br, C25), 123.1 (C34), 123.9 (br, C26), 124.2 (C6), 124.3 (C8), 130.5 (C32), 130.8 (C5), 131.5 (C33), 134.3 (br, C27a), 137.2 (C31), 138.5 (C8a), 142.9 (C4a), 143.3 (br,

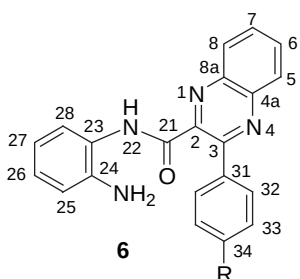
C23a), 145.1 (C2), 147.9 (C7), 148.1 (C22), 154.9 (C3);  $m/z$  447 (13), 446 (37), 445 (14  $M^{+}$ ), 444 (36), 417 (30), 416 (100), 415 (36), 414 (99), 400 (20), 398 (19), 336 (28), 335 (38), 334 (22), 168 (33), 154 (14%).

**4.3.6. 2-(Benzimidazol-2-yl)-3-(4-bromophenyl)-6-nitroquinoxaline (8c).** Yellow crystals, mp 287–289 °C (AcOH); [found C, 56.71; H, 2.68; N, 15.63.  $C_{21}H_{12}BrN_5O_2$  requires C, 56.52; H, 2.71; N, 15.69%];  $\nu_{\max}$  (KBr) 3236, 3103, 2924, 1708, 1534 ( $\nu_{as}$  (NO<sub>2</sub>)), 1430, 1361, 1348 ( $\nu_s$  (NO<sub>2</sub>)), 1334, 1292, 1072, 756, 741  $cm^{-1}$ ;  $\delta_H$  (400 MHz, DMSO- $d_6$ ) 7.16–7.34 (2H, m, H25, H26), 7.54–7.64 (2H, m, H24, H27), 7.60–7.66 (4H, m, 2×H32, 2×H33), 8.38 (1H, d,  $J$  9.3 Hz, H8), 8.59 (1H, dd,  $J$  9.2, 2.4 Hz, H7), 8.91 (1H, d,  $J$  2.4 Hz, H5), 13.30 (1H, br s, H21);  $\delta_C$  (100 MHz, DMSO- $d_6$ ) 112.1 (br, C27), 119.3 (br, C24), 122.9 (br, C25, C26), 123.1 (C34), 124.2 (C7), 124.9 (C5), 130.5 (C8), 130.7 (C32), 131.7 (C33), ~134.0 (br, C27a), 137.4 (C31), 139.5 (C4a), 142.3 (C8a), ~143.0 (br, C23a), 145.6 (C2), 148.2 (C22), 148.3 (C6), 154.3 (C3);  $m/z$  447 (9), 446 (22), 445 (9  $M^{+}$ ), 444 (21), 417 (27), 416 (100), 415 (31), 414 (99), 400 (13), 398 (12), 336 (24), 335 (32), 334 (21), 168 (23), 154 (25%).

**4.3.7. 2-(Benzimidazol-2-yl)-3-(4-iodophenyl)-7-nitroquinoxaline (7d).** Orange crystals, mp 338–340 °C (AcOH); [found C, 51.33; H, 2.42; N, 14.14.  $C_{21}H_{12}IN_5O_2$  requires C, 51.14; H, 2.45; N, 14.20%];  $\nu_{\max}$  (KBr) 3361, 3098, 3053, 1585, 1519 ( $\nu_{as}$  (NO<sub>2</sub>)), 1346 ( $\nu_s$  (NO<sub>2</sub>)), 1332, 743  $cm^{-1}$ ;  $\delta_H$  (400 MHz, DMSO- $d_6$ ) 7.20–7.32 (2H, m, H25, H26), 7.48 (2H, d,  $J$  8.5 Hz, 2×H32), 7.56–7.64 (2H, m, H24, H27), 7.81 (2H, d,  $J$  8.5 Hz, 2×H33), 8.39 (1H, d,  $J$  9.3 Hz, H5), 8.61 (1H, dd,  $J$  9.3, 2.5 Hz, H6), 8.94 (1H, d,  $J$  2.5 Hz, H8), 13.30 (1H, br s, H21);  $\delta_C$  (100 MHz, DMSO- $d_6$ ) 109.5 (C34), 112.4 (br, C27), 120.2 (br, C24), 122.2 (br, C25), 124.2 (br, C26), 124.5 (C6, C8), 130.9 (C5), 131.6 (C32), 134.1 (br, C27a), 136.5 (C33), 137.6 (C31), 138.5 (C8a), 142.8 (br, C23a), 143.1 (C4a), 145.2 (C2), 148.0 (C7), 148.3 (C22), 155.2 (C3);  $m/z$  493 (20  $M^{+}$ ), 492 (51), 463 (32), 462 (100), 446 (20), 337 (12), 336 (50), 335 (50), 334 (25), 320 (10), 319 (20), 168 (23), 155 (11%).

**4.3.8. 2-(Benzimidazol-2-yl)-3-(4-iodophenyl)-6-nitroquinoxaline (8d).** Yellow crystals, mp 283–285 °C (AcOH); [found C, 50.97; H, 2.41; N, 14.25.  $C_{21}H_{12}IN_5O_2$  requires C, 51.14; H, 2.45; N, 14.20%];  $\nu_{\max}$  (KBr) 3238, 3099, 3066, 2922, 1706, 1532 ( $\nu_{as}$  (NO<sub>2</sub>)), 1430, 1344 ( $\nu_s$  (NO<sub>2</sub>)), 1333, 1292, 999, 756, 740  $cm^{-1}$ ;  $\delta_H$  (400 MHz, DMSO- $d_6$ ) 7.18–7.22 (1H, m, H25), 7.28–7.32 (1H, br, H26), 7.46 (2H, d,  $J$  8.5 Hz, 2×H32), 7.56–7.64 (2H, m, H24, H27), 7.79 (2H, d,  $J$  8.5 Hz, 2×H33), 8.38 (1H, d,  $J$  9.2 Hz, H8), 8.59 (1H, dd,  $J$  9.2, 2.3 Hz, H7), 8.92 (1H, d,  $J$  2.3 Hz, H5), 13.30 (1H, br s, H21);  $\delta_C$  (100 MHz, DMSO- $d_6$ ) 96.6 (C34), 112.1 (C27), 120.1 (C24), 122.2 (C25), 124.2 (C7, C26), 124.9 (C5), 130.5 (C8), 131.6 (C32), 134.5 (C27a), 136.5 (C33), 137.6 (C31), 139.5 (C4a), 142.2 (C8a), 143.5 (C23a), 145.6 (C2), 148.2 (C6), 148.3 (C22), 154.5 (C3);  $m/z$  493 (36  $M^{+}$ ), 492 (100), 463 (18), 462 (63), 447 (11), 446 (35), 336 (12), 335 (21), 334 (13), 320 (12), 319 (28), 168 (12), 160 (14%).

#### 4.4. Typical procedure 3: synthesis of the 2-aminoanilide quinoxaline 3-aryl-2-carboxylic acid 6



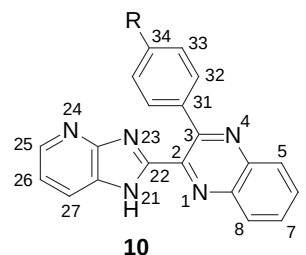
A solution of 3-arylquinoxaline-2(1H)-one **1** (0.81 mmol) and 1,2-phenylenediamine **3a** (0.81 mmol) in *n*-BuOH (10 mL) was

heated at reflux for 4.5 h. After cooling to room temperature the precipitated crystals were collected by suction filtration, washed with *i*-PrOH (2×5 mL), and dried in air, providing an analytically pure sample of compound **6**.

**4.4.1. 2-Aminoanilide quinoxaline 3-phenyl-2-carboxylic acid (6a).** Light-yellow crystals, mp 203–204 °C; [found C, 74.49; H, 4.67; N, 16.34.  $C_{21}H_{16}N_4O$  requires C, 74.10; H, 4.74; N, 16.46%];  $\nu_{\max}$  (KBr) 3362, 3238, 1660, 1638, 1537, 1503, 1449, 1326, 1309, 1103, 762, 700  $cm^{-1}$ ;  $\delta_H$  (400 MHz, DMSO- $d_6$ ) 4.84 (2H, br s, H24), 6.61 (1H, dd,  $J$  7.1, 7.6 Hz, H27), 6.77 (1H, d,  $J$  7.6 Hz, H25), 6.97 (1H, dd,  $J$  7.1, 7.2 Hz, H26), 7.30 (1H, d,  $J$  7.6 Hz, H28), 7.50–7.62 (3H, m, 2×H33, H34), 7.88–7.90 (2H, m, 2×H32), 7.94–8.02 (2H, m, H6, H7), 8.18–8.28 (2H, m, H5, H8), 10.05 (1H, br s, H22);  $\delta_C$  (100 MHz, DMSO- $d_6$ ) 115.9 (C25), 116.3 (C27), 122.3 (C23), 124.8 (C28), 126.4 (C26), 128.4 (C33), 128.6 (C32), 128.8 (C8), 128.9 (C5), 129.5 (C34), 130.8 (C7), 131.5 (C6), 137.4 (C31), 139.0 (C8a), 141.3 (C4a), 141.7 (C24), 149.2 (C2), 151.4 (C3), 165.0 (C21).

#### 4.5. Typical procedure 4: synthesis of 2-(1H-imidazo[4,5-b]pyridin-2-yl)-3-arylquinoxalines 10

A solution of 2-arylpyrido[2,3-*b*]pyrazin-3(4H)-one **9** (1.59 mmol) and 1,2-phenylenediamine **3a** (1.59 mmol) in acetic acid (15 mL) was heated at reflux for 35–47 h. After cooling to room temperature, the precipitated crystals of compound **10** were collected by suction filtration, washed with *i*-PrOH, dried in air and an analytically pure sample of compound **10** was obtained in yields indicated in Table 4.



**4.5.1. 2-(1H-Imidazo[4,5-*b*]pyridin-2-yl)-3-phenylquinoxaline (10a).** Gray brown crystals, mp 267–270 °C; [found C, 74.37; H, 4.01; N, 21.71.  $C_{20}H_{13}N_5$  requires C, 74.29; H, 4.05; N, 21.66%];  $\nu_{\max}$  (KBr) 3054, 2978, 2793, 1590, 1480, 1428, 1408, 1277, 1253, 1216, 1090, 950, 772, 760, 695, 528  $cm^{-1}$ ;  $\delta_H$  (400 MHz, DMSO- $d_6$ ) 7.25–7.32 (2H, m, 2×H25), 7.37–7.47 (6H, m, 4×H33, 2×H34), 7.57–7.63 (4H, m, 4×H32), 7.96–8.03 (6H, m, 2×H6, 2×H7, 2×H27), 8.22–8.27 (4H, m, 2×H5, 2×H8), 8.39 (2H, dd,  $J$  4.8, 1.6 Hz, 2×H26), 13.40 (1H, br s, H21), 13.70 (1H, br s, H21).

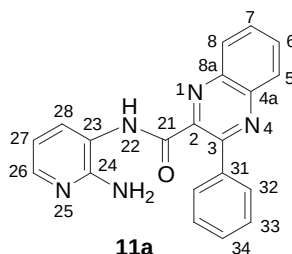
**4.5.2. 2-(1H-Imidazo[4,5-*b*]pyridin-2-yl)-3-(4-fluorophenyl)quinoxaline (10b).** Light-gray crystals, mp 313–314 °C (DMF); [found C, 70.45; H, 3.52; N, 20.46.  $C_{20}H_{12}FN_5$  requires C, 70.37; H, 3.54; N, 20.52%];  $\nu_{\max}$  (KBr) 3112, 3061, 3018, 2956, 1593, 1513, 1479, 1433, 1408, 1275, 1255, 1220, 1164, 952, 841, 776, 761, 524  $cm^{-1}$ ;  $\delta_H$  (400 MHz, DMSO- $d_6$ ) 7.20–7.32 (6H, m, 4×H33, 2×H25), 7.60–7.70 (4H, m, 4×H32), 7.96–8.03 (6H, m, 2×H6, 2×H7, 2×H27), 8.22–8.27 (4H, m, 2×H5, 2×H8), 8.39 (2H, dd,  $J$  4.6, 1.6 Hz, 2×H26), 13.40 (1H, br s, H21), 13.80 (1H, br s, H21);  $\delta_F$  (376 MHz, DMSO- $d_6$ ) 112.5 (F34), 112.8 (F34').

**4.5.3. 2-(1H-Imidazo[4,5-*b*]pyridin-2-yl)-3-(4-chlorophenyl)quinoxaline (10c).** Gray brown crystals, mp 337–338 °C; [found C, 67.41; H, 3.43; N, 19.48.  $C_{20}H_{12}ClN_5$  requires C, 67.14; H, 3.38; N, 19.57%];  $\nu_{\max}$  (KBr) 3060, 2957, 2788, 1592, 1477, 1431, 1406, 1274,

1091, 951, 837, 775, 759, 528  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (400 MHz, DMSO- $d_6$ ) 7.25–7.33 (2H, m, 2 $\times$ H25), 7.47 (2H, d,  $J$  8.5 Hz, 2 $\times$ H33), 7.49 (2H, d,  $J$  8.5 Hz, 2 $\times$ H33), 7.62 (2H, d,  $J$  8.2 Hz, 2 $\times$ H32), 7.66 (2H, d,  $J$  8.2 Hz, 2 $\times$ H32), 7.96–8.04 (6H, m, 2 $\times$ H6, 2 $\times$ H7, 2 $\times$ H27), 8.20–8.28 (4H, m, 2 $\times$ H5, 2 $\times$ H8), 8.40 (2H, br d,  $J$  4.4 Hz, 2 $\times$ H26).

**4.5.4. 2-(1*H*-Imidazo[4,5-*b*]pyridin-2-yl)-3-(4-bromophenyl)quinoxaline (10d).** Gray green crystals, mp 334–336 °C; [found C, 59.98; H, 2.96; N, 17.49.  $\text{C}_{20}\text{H}_{12}\text{BrN}_5$  requires C, 59.72; H, 3.01; N, 17.41%];  $\nu_{\text{max}}$  (KBr) 3058, 2971, 2791, 1591, 1478, 1431, 1408, 1278, 1254, 1217, 1091, 950, 835, 801, 761, 528  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (400 MHz, DMSO- $d_6$ ) 7.26–7.33 (2H, m, 2 $\times$ H25), 7.55 (2H, d,  $J$  8.6 Hz, 2 $\times$ H33), 7.58–7.62 (4H, m, 2 $\times$ H32, 2 $\times$ H33), 7.63 (2H, d,  $J$  8.6 Hz, 2 $\times$ H32), 7.99–8.03 (6H, m, 2 $\times$ H6, 2 $\times$ H7, 2 $\times$ H27), 8.22–8.27 (4H, m, 2 $\times$ H5, 2 $\times$ H8), 8.40 (2H, br d,  $J$  4.7 Hz, 2 $\times$ H26), 13.46 (1H, br, H21), 13.82 (1H, br, H21).

#### 4.6. Synthesis of the 2-amino-3-azaanylide quinoxaline 3-phenyl-2-carboxylic acid (11a)



A solution of 2-benzoylpyrido[2,3-*b*]pyrazin-3(4*H*)one **9a** (0.42 mmol) and 1,2-phenylenediamine **3a** (0.42 mmol) in acetic acid (3 mL) was heated at reflux for 3 h. After evaporation of the solvent, the residue was triturated with water, the precipitated crystals were collected by suction filtration, then washed with water, dried in air, and an analytically pure sample of compound **11a** was obtained as a brown powder in 0.21 g (72%) yields, mp 216–218 °C; [found C, 70.62; H, 4.38; N, 20.38.  $\text{C}_{20}\text{H}_{15}\text{N}_5\text{O}$  requires C, 70.37; H, 4.43; N, 20.52%];  $\nu_{\text{max}}$  (KBr) 3471, 3261, 3102, 3027, 2928, 1655, 1637, 1596, 1528, 1476, 777, 765, 701, 533  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (400 MHz, DMSO- $d_6$ ) 5.78 (2H, br s, H24), 6.63 (1H, dd,  $J$  7.8, 4.8 Hz, H27), 7.51–7.55 (3H, m, 2 $\times$ H33, H34), 7.73 (1H, dd,  $J$  7.8, 1.8 Hz, H28), 7.84–7.88 (3H, m, 2 $\times$ H32, H26), 7.95–8.02 (2H, m, H6, H7), 8.22–8.27 (2H, m, H5, H8), 10.10 (1H, br s, H22);  $\delta_{\text{C}}$  (100 MHz, DMSO- $d_6$ ) 112.3 (C27), 117.7 (C23), 128.4 (C32), 128.6 (C31), 128.8 (C8), 129.0 (C5), 129.5 (C34), 130.9 (C7), 131.3 (C28), 131.7 (C6), 137.3 (C31), 139.0 (C8a), 141.4 (C4a), 144.5 (C26), 148.7 (C2), 151.4 (C3), 152.7 (C24), 165.4 (C21);  $\delta_{\text{N}}$  (60 MHz, DMSO- $d_6$ ) 125.9 (N22), 268.7 (N25), 323.5 (N1), 328.6 (N4).

#### 4.7. Crystal structure determination of 6a, 7a, 8a, and 10a

Single crystal X-ray diffraction study was carried out at the department of X-ray Diffraction Studies of the Center of Collaborative Research on the basis of the Laboratory of X-ray Diffraction Methods of the A.E. Arbuzov Institute of Organic and Physical Chemistry, the Kazan Research Center of the Russian Academy of Sciences. The X-ray diffraction data for the crystals of compounds **6a**, **7a**, **8a**, **10a** were collected at 296 K on a Bruker AXS Smart Apex II CCD diffractometer in the  $\omega$  and  $\phi$ -scan modes using graphite monochromated Mo  $K_{\alpha}$  ( $\lambda$  0.71073 Å) radiation. Data were corrected for the absorption effect using SADABS program.<sup>17</sup> Data collections: images were indexed, integrates, and scaled using the APEX2<sup>18</sup> data reduction package. All figures were made using PLATON.<sup>19</sup> The

structures were solved by direct method and refined by the full matrix least-squares using SHELXTL<sup>20</sup> and WinGX<sup>21</sup> programs. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms of NH and NH<sub>2</sub> groups of the two independent **6a** molecules were found from differential electron density map and were refined isotropically. Hydrogen atom of NH group of **7a** molecule and OH group of solvate molecule were found from differential electron density map and were refined isotropically. Hydrogen atom of NH group of **8a** molecule was found from differential electron density map and refined by using the riding model. Hydrogen atom of NH group of the molecule **10a** was found from differential electron density map and refined by using the riding model, the hydrogen atoms of two solvate water molecules were found from the calculated scheme of hydrogen bonds and were refined with fixed positional and temperature parameters. One of two independent water molecules is disordered over two position with relative occupancies 0.74:0.26. All other hydrogen atoms of compounds **6a**, **7a**, **8a**, **10a** were placed in idealized positions and refined by using the riding model. X-ray crystal structure data for compounds **6a** (CCDC 774493), **7a** (CCDC 774491), **8a** (CCDC 774494), and **10a** (CCDC 774492) were deposited with the Cambridge Crystallographic Data Center (CCDC). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44 (0)1223 336033 or e-mail: [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)).

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#### Supplementary data

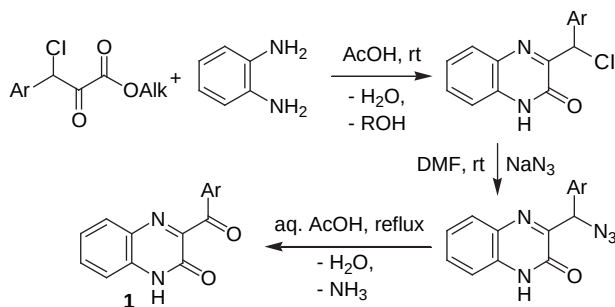
Characterization data, 1D and 2D NMR spectra for all new compounds, calculated CSs for compounds **7a**, **8a**, and X-ray crystallographic file (CIF) for compounds **6a**, **7a**, **8a** and **10a**. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.10.026. These data include MOL files and InChIKeys of the most important compounds described in this article.

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- 1b** (Ar = *p*-FC<sub>6</sub>H<sub>4</sub>, mp 257–259 °C); **1c** (Ar = *p*-ClC<sub>6</sub>H<sub>4</sub>, mp 242–244 °C);  
**1d** (Ar = *p*-BrC<sub>6</sub>H<sub>4</sub>, mp 263–265 °C); **1e** (Ar = *p*-IC<sub>6</sub>H<sub>4</sub>, mp 274–276 °C);  
**1f** (Ar = *p*-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>, mp 270–272 °C)

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