Tetrahedron 71 (2015) 147–157

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

A short and efficient protocol for the synthesis of imidazo[1,5-*a*]quinoxalin-4-ones from 3-aroylquinoxalinones and compounds with the aminomethylene moiety

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ARTICLE INFO

Article history:
Received 14 August 2014
Received in revised form 24 October 2014
Accepted 6 November 2014
Available online 13 November 2014

Keywords:
Synthetic methods
Nitrogen heterocycles
Annulation/cyclization
Imidazo[1,5-*a*]quinoxalin-4-ones

ABSTRACT

The reaction of 3-aroylquinoxalin-2(1*H*)-ones with α-amino acids and their derivatives, amines with various alkyl groups, amino alcohols with alkylene groups of various length, *N*-(3-aminopropyl)morpholine and 1,6-diaminohexane in DMSO at 150 °C proceeds through the oxidative cyclocondensation and makes it possible to synthesize substituted imidazo[1,5-*a*]quinoxalines. Depending on the compound with the aminomethylene fragment used the reaction allows to introduction of any given substituent into position 1.

1. Introduction

Imidazo[1,5-*a*]quinoxalines and related imidazo[1,5-*a*]quinoxalin-4-ones are important heterocycles in the synthesis of a variety of biologically important and medicinally useful agents. In addition to many other pharmacologically active compounds[4–9] e.g., they were used in the synthesis of GABA/benzodiazepine receptor agonists/antagonists,[1] cAMP and cGMP phosphodiesterase inhibitors,[2] and A1- and A2a-adenosine receptor agonists.[3] More recently, among the derivatives of imidazo[1,5-*a*]quinoxalines there appeared the compound BMS-238497 (7,8-dimetoxy-4-(2-chloro-4-methylphenylamino)imidazo[1,5-*a*]quinoxaline), which emerged as a novel and potent inhibitor of the Src-family kinase $p56^{Lck}$.[9–11] BMS-238497 displays an excellent enzymatic activity against Lck (IC_{50}=2 nM) and a good potency in blocking the T cell proliferation (IC_{50}=0.67 μM).[10,11] To support the further characterization and the SAR study of the imidazo[1,5-*a*]quinoxaline derivatives, a ready access to a large amount of them as well as to their precursors is necessary.

Two approaches have been mainly reported in literature for the construction of the imidazo[1,5-*a*]quinoxalin-4-one ring system. In the first approach, an appropriately substituted imidazole derivative is introduced into a substituted *ortho*-halonitrobenzene derivative followed by the intramolecular cyclization of the resulting *ortho*-substituted imidazobenzene.[2,12,13] In spite of the fact that this method is highly efficient, it is not without limitations. It was found that the intramolecular nucleophilic aromatic substitution and ring closure failed with fluoroanilines with electron-donating substituents (e.g., R=OMe). The second approach involves the annulation of an imidazole ring to *N*-protected quinoxalin-2-one mediated by a dipolar cycloaddition of tosylmethyl or benzyl isocyanide as the key step.[1,14,15] While useful for the preparation of certain imidazo[1,5-*a*]quinoxalin-4-ones, this approach suffers a number of drawbacks such as the poor regioselectivity encountered in the formation of quinoxalin-2-ones with nonsymmetrical phenylene-1,2-diamines, the lack of control of the chemoselectivity of N-protection versus O-protection during the protection step,[14] and the difficulties involved in separating the regioisomers. The method requires not easily accessible, air-sensitive, unstable phenylene-1,2-diamines as initial precursors as well (Scheme 1).

Finally, the main drawback of both of these methods is that none of them can be effectively used for the introduction of different substituents in position 1 of the imidazo[1,5-*a*]quinoxalines (synthesis of the imidazo[1,5-*a*]quinoxalines with various substituents in position 1) because of the complexity of the synthesis of the

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http://dx.doi.org/10.1016/j.tet.2014.11.017
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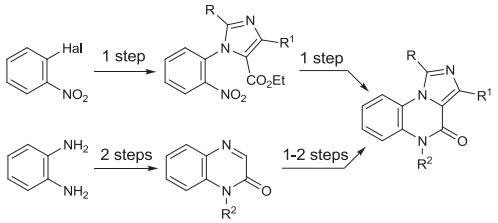


Scheme 1. Two approaches for the construction of imidazo[1,5-*a*]quinoxalin-4-ones.

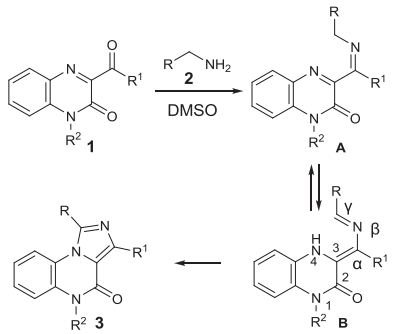
necessary derivatives of *N*-arylimidazoles in the first case and the α-substituted isonitriles in the second.

2. Results and discussion

2.1. Imidazoannulation of 3-aroylquinoxalin-2-ones with amino acids

In the course of our studies of the synthesis and utilization of nitrogen-containing heterocyclic and heteroaromatic compounds,[16] we had reason to explore the chemistry of quinoxalin-2(1*H*)-ones **1**. We have recently reported a novel highly efficient method for the synthesis of the 1-aryl(hetaryl)imidazo[1,5-*a*]quinoxalin-4-one derivatives. The overall strategy involves the benzylamine-mediated heterocyclization of the readily accessible 3-aroylquinoxalin-2(1*H*)-ones and their *N*-alkyl analogues in DMSO, furnishing imidazo[1,5-*a*]quinoxalines in moderate to excellent yields depending on the nature of the substituents on the pyrazine ring of the quinoxalinone system.[17] The analysis of the reaction mechanism shows that the process in DMSO proceeds through the intermediate formation of *N*-(α-quinoxalinylbenzylydene)benzylamine (**A**), which when transformed into an other tautomeric form (**B**) subjected to oxidative cyclocondensation results in imidazo[1,5-*a*]quinoxalines.

As can be seen from Scheme 2 the successful closure of the cycle depends on the presence of tautomer **B** responsible for the imidazo[*a*]annulation due to the intramolecular nucleophilic addition of the *N*4 atom of the quinoxaline system to the *Cγ* atom of the imino-group of the substituent. The presence and predominance of the tautomers **A** or **B** in the reaction mixture depend both on the nature of substituents R and R^1 and the acidic or basic impurities, which can catalyse the processes of the formation of imidazo[1,5-*a*]quinoxalines **3**. In continuation of these studies, we became interested in investigating α-amino acids and their derivatives, amines with various alkyl groups, amino alcohols with alkylene groups varying in length, *N*-(3-aminopropyl)morpholine and 1,6-diaminohexane with aroylquimoxalin-2(1*H*)-ones with a view to develop an efficient simple synthesis of variously substituted imidazo[1,5-*a*]quinoxalines. This class of compounds displayed a broad spectrum of



Scheme 2. Common presentation of the imidazo[1,5-*a*]quinoxalin-4-one formation when 3-aroylquinoxalin-2(1*H*)-ones are exposed to benzylamine.

biological activity. We have successfully achieved this goal, and the results of our studies are presented herein.

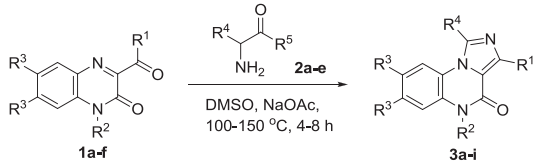
The interaction of 3-benzoylquinoxalin-2(1*H*)-one **1a** with glycine **2a** at 150 °C in DMSO in the presence of sodium acetate leads to the imidazo[1,5-*a*]quinoxalin-4(5*H*)-one **3a** in 90% yield (Table 1, entry 1). The formation of 3-aryl derivatives of imidazo[1,5-*a*]quinoxalin-4(5*H*)-ones **3b**–**e** proceeds in high yields as well (entries 2–5). The use of ***L***-β-phenyl-α-alanine **2b** instead of glycine in the reaction with ketone **1a** under similar conditions also leads to the formation of compound **3a** in good yield (entry 7). Decreasing of the reaction temperature to 120 or 100 °C provides the formation of 1-aryl substituted derivative. However, under these conditions along with the desired compound **3a** allocated the starting compound **1a**. The reaction of ketone **1a** with ***L***-isoleucine **2c** successfully results in a 1-secbutyl derivative **3g**, easily formed even at 100 °C (entry 8). Imidazoannellation also occurred when hydrochlorides of esters or amides of α-amino acids were used as a source of the C–N fragment. Thus, the interactions of compound **1a** with methyl ***L***-leucine hydrochloride **2d** and with ***L***-alaninamide hydrochloride **2e** accordingly results in 1-isobutylimidazo[1,5-*a*]quinoxaline **3h** (entry 9) and 1-methylimidazo[1,5-*a*]quinoxaline **3i** (entry 10) as the major products. Apparently, under the reaction conditions hydrolysis of the ester or amide groups takes place. The structure of compounds **3a**–**i** can be directly proved a by variety of 1D/2D NMR correlation methods.[18,19]

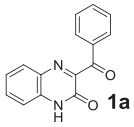
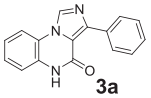
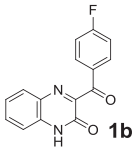
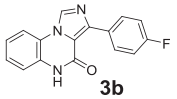
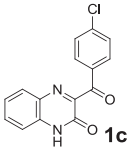
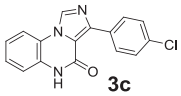
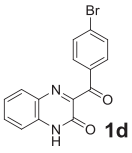
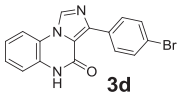
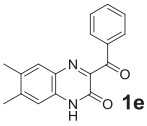
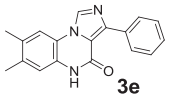
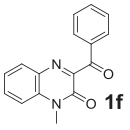
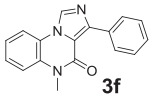
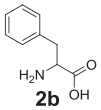
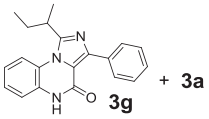
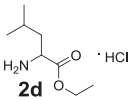
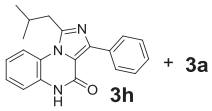
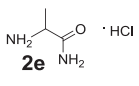
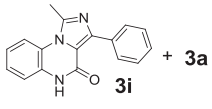
First, nitrogens directly bounded to proton (NH) were unequivocally revealed from the $^1H-^{15}N$ HSQC spectra (see SI). Then the NOE between the NH and H6 protons allows to unequivocally assign the latter, and the following excitation of H6 allows to reveal all the protons of quinoxaline spin system in 1D TOCSY spectra (see e.g., Fig. 1a, b, c for **3g**). In turn, NOE between H9 and the spatially close imidazole unit substituent allowed us to establish its resonances in proton spectra and then to reveal all its spin system by 1D TOCSY experiments (Fig. 1d, e). On the other hand three fragments of the title compounds and the bonding between them were also unequivocally revealed by $^1H-^{13}C$ and $^1H-^{15}N$ HSQC/HMBC connectivities (e.g., on Fig. 1f are shown $^1H-^{15}N$ HMBC connectivities; see SI for all details). Finally good correlations of the calculated[20] versus experimental ^{13}C CSs additionally support this structural hypothesis. Theoretical ^{15}N CSs for **3a**–**i** are also in good agreement with experimental data (see SI).

Based on the results above and the known chemistry of quinoxalines,[16d,e,17] a plausible mechanism for the model reaction has been proposed (Scheme 3). The reaction starts with the condensation of α-amino acid derivative **2a** with 3-aroylquinoxalin-2(1*H*)-one **1a** to form imine **C**, followed by the NaOAc-promoted decarboxylative pathway to generate intermediate **D**. Subsequently, the intermediate **D** can be easily cyclized through an intramolecular nucleophilic addition to give the dihydro derivative of imidazo[1,5-*a*]quinoxaline **F** through an intermediate **E**. Finally, compound **F** in the presence of DMSO loses two hydrogen atoms as water to give the final product **3a**.

The data in Table 1 show, that only in one case, namely, in the case of the reaction of *N*-methylbenzoylqunoxalin-2-one **1f** with α-glycine, due to the lower reactivity of the former, we have doubled the reaction time and the quantity of α-glycine as compared to the other cases. In this case the second portion of α-glycine was added to the reaction mixture four hours after the beginning of the process and the reaction was continued for another four hours. The low reactivity of *N*-methylbenzoylqunoxalin-2-one **1f** as regards the imidazo[*a*]annulation is apparently due to the its low aromaticity as compared with the quinoxalin-2(1*H*)-ones **1a**–**e**. As can be seen from Fig. 2 compounds **1a**–**e** in the reaction conditions can easily be transferred to the 2-hydroxy form (hydroxy tautomer) **1′′a**–**e**, in which the *N*3 nitrogen atom becomes more nucleophilic and consequently more reactive. The lack of this opportunity in the

Table 1
The synthesis of imidazo[1,5-*a*]quinoxalin-4-ones **3a**–**i**



Entry	Ketone	Amino acid and its derivatives (equiv)	Temp., °C (time, h)	Product	Yield of **3a**–**i**,[a] %
1[b]	 **1a**	 **2a** (1.3)	150 (4)	 **3a**	90
2[b]	 **1b**	**2a** (1.3)	150 (4)	 **3b**	74
3[b]	 **1c**	**2a** (1.3)	150 (4)	 **3c**	81
4[b]	 **1d**	**2a** (1.3)	150 (4)	 **3d**	82
5[b]	 **1e**	**2a** (1.3)	150 (4)	 **3e**	78
6[c]	 **1f**	**2a** (2.6)[c]	150 (8)	 **3f**	63
7[b]	**1a**	 **2b** (1.3)	150 (4)	**3a**	65
8[b]	**1a**	 **2c** (1.3)	100 (6)	 **3g** + **3a**	66+3[e]
9[d]	**1a**	 **2d** (1.3)	150 (4)	 **3h** + **3a**	60+4[e]
10[d]	**1a**	 **2e** (1.3)	150 (4)	 **3i** + **3a**	58+3[e]

[a] Yields refer to isolated analytically pure materials.
[b] In the presence of 1.3 equiv of NaOAc.
[c] Second portion of 1.3 equiv of NaOAc has been added to the reaction mixture obtained after heating the reagents in DMSO for 4 h in the presence of 1.3 equiv of NaOAc.
[d] In the presence of 2.6 equiv of NaOAc.
[e] Yields refer to those based on ^{1}H NMR.

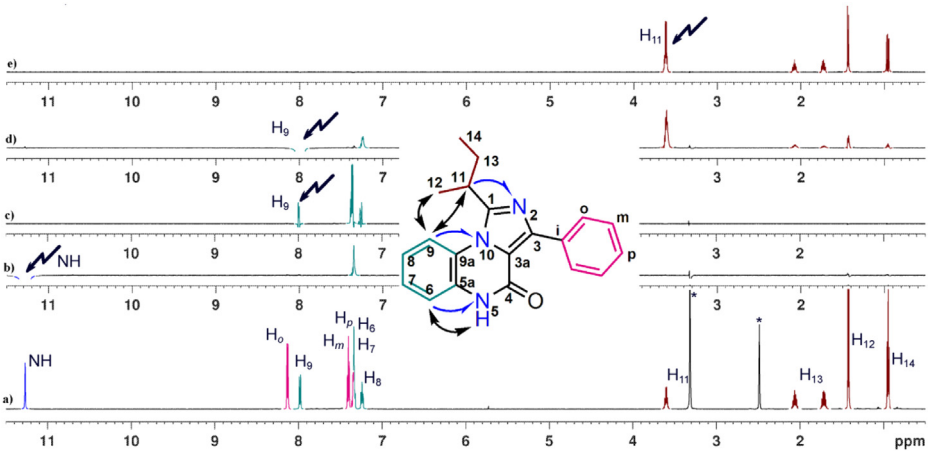
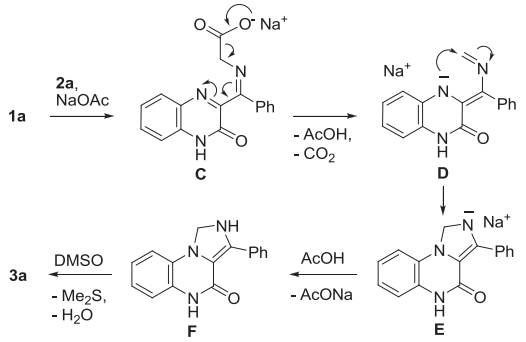


Fig. 1. ^{1}H NMR spectra of **3g** in DMSO-d_6 at 303 K: (a) ^{1}H spectrum; (b, d) 1D NOESY spectra; (c, e) 1D TOCSY spectrum (excited protons are marked by arrows); (f) The structure, principal NOE's (black arrows) and ^{1}H–^{15}N HMBC connectivity's (blue arrows) for **3g**.



Scheme 3. Proposed mechanism for the decarboxylative cyclization.

N-methylbenzoylqunoxalin-2-one **1f** decreases the nucleophilicity of the *N*3 nitrogen atom, thus making it less reactive.

As can be seen from Table 2 the introduction of a methyl substituent in position 1 of 3-benzoylquinoxalin-2(1*H*)-one **1a** slows down the reaction with glycine and the formation of product **3f** with an only 16% yield (entry 2), that of 5.5 times less than at the interaction of **1**a and **2**a in similar conditions (entry 1). The increase in the yield of imidazo[1,5-*a*]quinoxaline **3f** achieved, either in the presence of a two-fold excess of glycine and a twice increase in the reaction time (entry 3), or when replacing sodium acetate by a stronger base, i.e. a sodium hydrocarbonate (entry 4).

Table 2
Comparison of the conditions and yields in the reactions of 3-benzoylquinoxalin-2(1*H* and 1-methyl)-ones **1a**,**f** with glycine **2a**

Entry	Reagents/ratio	Base	Time, h	Yield, %
1	**1a**:**2a**/1:1.3	NaOAc	4	90 (**3a**)
2	**1f**:**2a**/1:1.3	NaOAc	4	16 (**3f**)
3	**1f**:**2a**/1:2.6	NaOAc	8	63 (**3f**)
4	**1f**:**2a**/1:1.3	$NaHCO_3$	4	60 (**3f**)

2.2. Imidazoannulation of 3-benzoylquinoxalin-2-ones with alkylamines

The interaction of the 3-benzoylquinoxalin-2(1*H*)-one **1a** with alkylamines leads to the 1-alkyl-substituted imidazo[1,5-*a*]quinoxalines **3j**–**m** (Table 3, entries 2–5). In the case of isobutylamine the formation of imidazo[1,5-*a*]quinoxaline **3a** along with the formation of compound **3k**, takes place (Table 3, entry 3). The reaction of methylamine hydrochloride with a ketone **1a** as well as with glycine leads to imidazo[1,5-*a*]quinoxaline **3a** (Table 3, entry 1). In this case the complete transformation of the 3-benzoylquinoxalin-2(1*H*)-one **1a** has been achieved with a large excess of methylamine hydrochloride.

The interaction of butylamine **2g** and ketone **1a** has been studied under acid catalysis. When the reaction has been carried out in the presence of excess AcOH and *p*-TsOH, and 0.1 equiv of

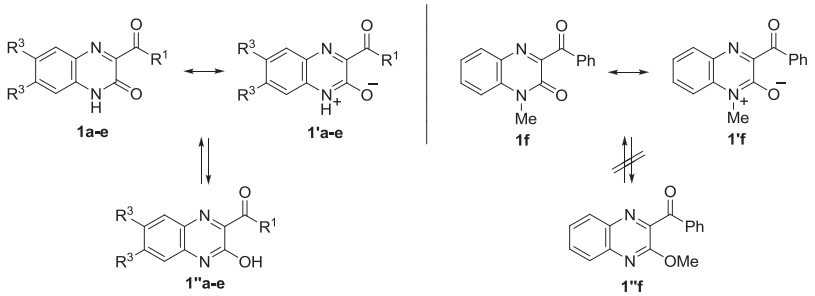
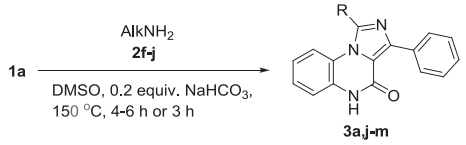


Fig. 2. The resonance structures of 3-benzoylquinoxalin-2(1*H*)-ones **1**.

Table 3
The synthesis of 1-alkylimidazo[1,5-*a*]quinoxalin-4(5*H*)-ones **3j**–**m**



Entry	Amine (equiv)	Product	Yield, %	
			In the absence of $NaHCO_3$	In the presence of $NaHCO_3$
1	—NH_2·HCl **2f** (4.0)	**3a**	20[a]	78[c]
2	**2g** NH_2 (1.7)	**3j**	52[a]	70
3	**2h** NH_2 (1.7)	+ **3a** **3k**	(20+10)[b]	24+22
4	**2i** NH_2 (1.1)	**3l**	43[b]	51
5	**2j** NH_2 (1.1)	**3m**	46[b]	56

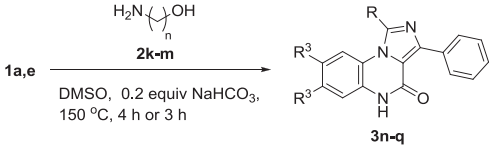
The reaction was carried out [a] for 4 h, [b] for 6 h, [c] in the presence of 3.0 equiv $MeNH_2$·HCl and 3.5 equiv $NaHCO_3$.

p-TsOH the formation of compound **3j** occurs in 24, 15 and 20% yields, respectively and in these cases in a considerable amount of unreacted 3-benzoylquinoxalin-2(1*H*)-one **1a** is allocated. Whereas in the presence of 0.2 equiv of $NaHCO_3$ as a basic catalyst the above reaction has been completed in less than 3 h with formation of the desired imidazo[1,5-*a*]quinoxaline **3j**. The yields of products **3j**–**m** have increased by 8–58%. The temperature influence has been studied on the example of the interaction of isobutylamine with 3-benzoylquinoxalin-2(1*H*)-one **1a**. Thus, the four hours reaction of compound **1a** with an excess of isobutylamine **2h** without addition of an acid or a base catalyst at 100 °C does not lead to the compound **3k** at all. The interaction of reagents even in the presence of $NaHCO_3$ at 135 °C does not take place completely.

2.3. Imidazoannulation of 3-aroylquinoxalin-2-ones with amino alcohols

The reactions of 2-aminoethanol **2k**, 3-aminopropanol **2l**, 4-aminobutanol **2m** with 3-benzoylquinoxalin-2(1*H*)-one **1a** and its 6,7-dimethyl derivative **1e** lead to the 1-hydroxyalkylimidazo[1,5-*a*]quinoxalin-4(5*H*)-ones **3n**–**q** (Table 4). In the absence of an acid or base catalyst the yields of the products of imidazoannulation **3o**–**q** are 30–39% and in these cases a significant amount (~30%) of unreacted starting compounds **1a**,**e** is allocated from the reaction mixture. In the presence of 0.1 equiv of *p*-TsOH (for 4 h), or 0.2 equiv of ***L***-proline (for 3 h) the reaction of butanolamine with 3-benzoylquinoxalin-2(1*H*)-one **1a** resulted in 13 and 11% of the imidazo[1,5-*a*]quinoxalin-4(5*H*)-one **3q**, respectively. Carrying out the reactions of 3-benzoylquinoxalin-2(1*H*)-one **1a** with amino alcohols in the presence of $NaHCO_3$ significantly increase the yield of compounds **3** (Table 4). The formation of compound **3a** as a minor product both in the presence of $NaHCO_3$ and without it occurs along with the formation of 1-hydroxymethylimidazo[1,5-*a*]quinoxalin-4(5*H*)-one **3n** in the case of ethanolamine (Table 4, entry

Table 4
The synthesis of 1-hydroxyalkylimidazo[1,5-*a*]quinoxalin-4(5*H*)-ones **3n**–**q**

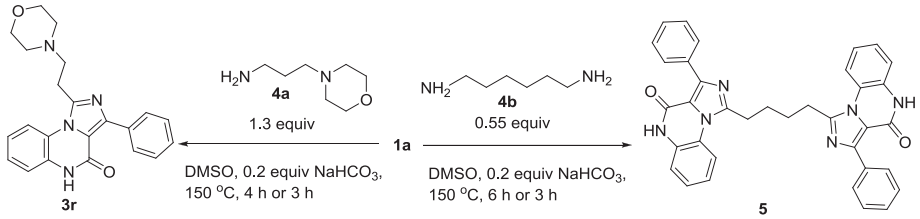


Entry	Amino alcohol (equiv)	Ketone	Product	Yield, %	
				In the absence of $NaHCO_3$	In the presence of $NaHCO_3$
1	**2k** (1.3)	**1a**	+ **3a** **3n**	15+15	36+25
2	**2l** (1.3)	**1a**	**3o**	37	65
3	**2l** (1.3)	**1e**	**3p**	39	—
4	**2m** (1.3)	**1a**	**3q**	35	51

1). Reducing the reaction temperature to 135 °C does not lead to noticeable decrease the formation of compound **3a** and slows down of imidazoannulation (from the reaction mixture in large amount was allocated starting compound **1a**).

2.4. Imidazoannulation of 3-aroylquinoxalin-2-ones with diamines

The interaction of 3-benzoylquinoxalin-2(1*H*)-one **1a** with the 3-aminopropylmorpholine **4a** leads to the formation of 1-morpholineethylimidazo[1,5-*a*]quinoxaline **3r**. When 1,6-diaminohexane **4b** in is used as a supplier of the C1–N2 fragment the reaction results in the formation of 1,6-bis(imidazo[1,5-*a*]quinoxalin-4-on-1-yl)butane **5**. $NaHCO_3$ as in the previous cases increases the yields of compounds **3r** and **5** (Scheme 4).



Scheme 4. The synthesis of imidazo[1,5-*a*]quinoxalin-4(5H)-ones **3r** and **5**.

The structure of **5** was unequivocally established by NMR. First, structure of half of it up to the linker's middle can be 'directly' derived by a variety of NMR correlations (see SI). After measuring the self diffusion coefficient (SDC) the weight of **5** is estimated and then concluded that it consists of two such halves because its SDC ($2.17\cdot10^{-10}$ m^2/s) is lower by ca. 30% than that of **3i** ($3.19\cdot10^{-10}$ m^2/s)) used as mass-reference.[21] The results of these NMR experiments were then confirmed by the MS (MALDI TOF).

3. Conclusion

In summary, we have developed a facile decarboxylative cyclization to construct imidazo[1,5-*a*]quinoxalin-4(5*H*)-ones by virtue of the amino acid derivatives and 3-aroylquinoxalinones. The process proceeds with azomethines generated in situ, which when subjected to oxidative cyclocondensation in the presence of DMSO results in imidazo[1,5-*a*]quinoxalin-4(5*H*)-ones. As compared to previous reports, the substrate scope of the compounds responsible for the incorporation of the C1–N2 fragment and the substituents in position 1 of imidazo[1,5-*a*]quinoxalin-4(5*H*)-ones was largely extended. In particular, no metal was required in the reaction, in order to avoid the metal residue in the products. Besides, the compounds constructed by this methodology bear great research significance for their potentially photophysical and biological activities.

4. Experimental section

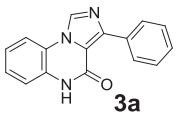
4.1. General methods

The melting points were determined on a Boetius hot-stage apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Bruker Vector-22 FT-IR spectrometer. All NMR experiments were performed with a Bruker AVANCE-600 and 400 MHz (600 and 400 MHz for ^1H NMR, 376 MHz for ^{19}F NMR, 150 and 100 MHz for ^{13}C NMR, 60 MHz for ^{15}N NMR, respectively) spectrometers 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^{-1}. NMR experiments were carried out at 303 K. ^{15}N CSs determined from inverse 2D HSQC and HMBC experiments.[18] DPFGNOE,[19] DPFGROE and TOCSY spectra were obtained using a Hermite-shaped pulse for selective excitation. Chemical shifts (δ in ppm) are referenced to the solvent DMSO-d_6 (δ=2.49 ppm for ^1H and 39.5 ppm for ^{13}C NMR) and to external CD_3NO_2 (380.2 ppm) for ^{15}N NMR spectra (conversion factor to NH_3: −380.2 ppm).[22] The quantum chemical calculations were performed using a Gaussian 98w software package.[23] Full geometry optimizations have been carried out within the framework of DFT (B3LYP) method using 6-31G(d) basis sets. Chemical shifts (CSs) were calculated by the GIAO method at the same level of theory. All data were referred to as TMS (^1H and ^{13}C) and NH_3 (^{15}N) chemical shifts, which were calculated under the same conditions. The MALDI mass spectra were obtained on a Bruker UltraFlex III MALDI TOF/TOF instrument with 2,5-dihydroxybenzoic acid (2,5-DHB) as a matrix. The elemental analyses were carried out at the microanalysis laboratory of the Arbuzov Institute of Organic and Physical Chemistry, Russian Academy of Sciences. The 3-aroylquinoxalin-2-ones were synthesized according to the reported methods.[24–27]

4.2. General procedure for the synthesis of 3a–h

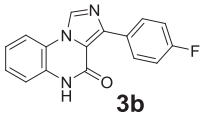
A mixture of 3-aroylquinoxalin-2-one **1** (1.0 mmol), amino acid (1.3 mmol) and NaOAc (1.3 or 2.6 mmol) in DMSO (2 mL) was stirred at 100–150 °C for 4–8 h (Table 1). After cooling to room temperature, the reaction mixture was poured into water (15 mL). After collection by suction filtration the crude product was washed with water (5 mL), dried in air and purified by recrystallization from the appropriate solvent (when synthesizing **3a**–**e**) or by column chromatography on silica gel (CH_2Cl_2/hexane=9:1) (when synthesizing **3f**–**h**).

4.2.1. 3-Phenylimidazo[1,5-a]quinoxalin-4(5H)-one (*3a*).[1,28]



Yield: 234 mg (90%), 174 (67%), 169 mg (65%), 52 mg (20%), 203 mg (78%), 26 mg (10%), 57 mg (22%), 39 mg (15%), 65 mg (25%) in the reactions of compound **1a** with glycine **2a** in the presence of NaOAc, glycine **2a** without adding NaOAc, ***L*** -β-phenyl-α-alanine **2b**, methylamine hydrochloride **2f**, methylamine hydrochloride **2f** in the presence of $NaHCO_3$, isobutylamine **2h**, isobutylamine **2h** in the presence of $NaHCO_3$, aminoethanol **2k**, aminoethanol **2k** in the presence of $NaHCO_3$, respectively (Tables 1–4). White powder, mp >360 °C (DMSO:CH_3CN=1:1) (lit.[28] >360 °C). $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 154.9 (C-4), 143.7 (C-3), 133.0 (C-*i*), 132.4 (C-1), 128.9 (C-*o*), 128.8 (C-5a), 127.8 (C-*p*), 127.6 (C-*m*), 127.0 (C-7), 122.6 (C-8), 120.2 (C-9a), 116.8 (C-3a), 116.2 (C-6), 115.5 (C-9).

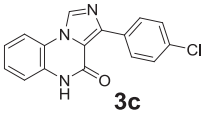
*4.2.2. 3-(4-Fluorophenyl)imidazo[1,5-a]quinoxalin-4(5H)-one (**3b**).*[1]



3b

Yield: 207 mg (74%). White powder, mp >360 °C (DMSO). IR (Nujol mull) ν 3200–2500, 1663, 1617, 1559, 1541, 1507, 1495, 1441, 1340, 1309, 1297, 1262, 1231, 1155, 1109, 1002, 961, 841, 815, 749, 736, 677, 656, 627 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ 7.21–7.39 (5H, m, Ar, H-6, H-7, H-8), 8.18 (1H, d, J=8.4 Hz, H-9), 8.35–8.40 (2H, m, Ar), 9.11 (1H, s, H-1), 11.34 (1H, s, NH); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 161.9 (d, $^1J_{CF}$=245.2 Hz, C-*p*), 155.0 (C-4), 142.7 (C-3), 132.5 (C-1), 130.9 (d, $^3J_{CF}$=8.1 Hz, C-*o*), 129.5 (d, $^4J_{CF}$=3.0 Hz, C-*i*), 128.6 (C-5a), 127.1 (C-7), 122.7 (C-8), 120.2 (C-9a), 116.7 (C-3a), 116.2 (C-6), 115.5 (C-9), 114.5 (d, $^2J_{CF}$=21.3 Hz, C-*m*); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 269.5 (N-2), 184.0 (N-10), 135.2 (N-5); $^{19}F\{^1H\}$ NMR (DMSO-d_6, 376 MHz) δ −113.9. MS (MALDI TOF) 280 $[MH]^+$.

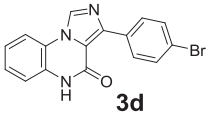
*4.2.3. 3-(4-Chlorophenyl)imidazo[1,5-a]quinoxalin-4(5H)-one (**3c**).*



3c

Yield: 243 mg (81%). White powder, mp >360 °C (DMSO). Anal. Calcd for $C_{16}H_{10}N_3OCl$: C, 64.66; H, 3.35; N, 14.37; Cl, 11.79. Found: C, 64.98; H, 3.41; N, 14.21; Cl, 11.99%. IR (Nujol mull) ν 3200–2500, 1663, 1618, 1570, 1533, 1512, 1487, 1438, 1429, 1406, 1357, 1324, 1310, 1291, 1260, 1234, 1182, 1165, 1132, 1108, 1095, 1047, 1014, 1000, 979, 960, 933, 903, 840, 749, 715, 674, 656, 628, 555, 506 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ 7.25 (1H, dd, J=8.1, 7.2 Hz, H-8), 7.32 (1H, dd, J=8.1, 7.2 Hz, H-6), 7.37 (1H, dd, J=8.3, 7.1, 1.3 Hz, H-7), 7.48 (2H, d, J=8.6 Hz, Ar), 8.19 (1H, d, J=8.2 Hz, H-9), 8.37 (2H, d, J=8.6 Hz, Ar), 9.13 (1H, s, H-1), 11.38 (1H, s, NH); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 154.9 (C-4), 142.3 (C-3), 132.6 (C-1), 132.5 (C-*p*), 131.9 (C-*i*), 130.5 (C-*o*) 128.7 (C-5a), 127.7 (C-*m*), 127.1 (C-7), 122.7 (C-8), 120.2 (C-9a), 117.1 (C-3a), 116.2 (C-6), 115.5 (C-9); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 269.6 (N-2), 184.1 (N-10), 135.4 (N-5). MS (MALDI TOF) 296 $[MH]^+$, 298 $[MH]^+$.

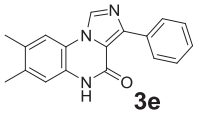
*4.2.4. 3-(4-Bromophenyl)imidazo[1,5-a]quinoxalin-4(5H)-one (**3d**).*



3d

Yield: 279 mg (82%). White powder, mp >340 °C (dec) (DMSO:CH_3CN=1:1). Anal. Calcd for $C_{16}H_{10}N_3OBr$: C, 55.62; H, 3.00; N, 11.74; Br, 23.39. Found: C, 56.49; H, 2.96; N, 12.35; Br, 23.49%. IR (Nujol mull) ν 3200–2500, 1670, 1615, 1567, 1541, 1511, 1488, 1400, 1321, 1296, 1263, 1180, 1155, 1137, 1106, 1074, 1043, 1015, 1004, 960, 930, 834, 746, 718, 707, 660, 629 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ 7.24 (1H, ddd, J=8.2, 7.1, 1.3 Hz, H-8), 7.32 (1H, dd, J=8.3, 1.3 Hz, H-6), 7.37 (1H, ddd, J=8.3, 7.1, 1.3 Hz, H-7), 7.60–7.64 (2H, m, Ar), 8.18 (1H, d, J=8.2 Hz, H-9), 8.28–8.32 (2H, m, Ar), 9.12 (1H, s, H-1), 11.37 (1H, s, NH); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 155.0 (C-4), 142.4 (C-3), 132.7 (C-1), 132.3 (C-*i*), 130.0 (C-*o*), 130.7 (C-*m*), 128.8 (C-5a), 127.2 (C-7), 122.8 (C-8), 121.3 (C-*p*), 120.2 (C-9a), 117.2 (C-3a), 116.3 (C-6), 115.6 (C-9); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 269.8 (N-2), 184.8 (N-10), 135.5 (N-5). MS (MALDI TOF) 340 $[MH]^+$, 342 $[MH]^+$.

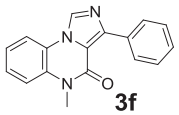
*4.2.5. 7,8-Dimethyl-3-phenylimidazo[1,5-a]quinoxalin-4(5H)-one (**3e**).*



3e

Yield: 226 mg (78%). White powder, mp >360 °C (DMSO). Anal. Calcd for $C_{18}H_{15}N_3O$: C, 74.72; H, 5.23; N, 14.52. Found: C, 74.84; H, 5.16; N, 14.35%. IR (KBr) ν 3176, 3105, 3079, 3024, 2969, 2918, 2859, 1658, 1612, 1580, 1520, 1491, 1444, 1407, 1363, 1332, 1321, 1296, 1262, 1237, 1164, 1128, 1071, 1023, 925, 869, 749, 713, 687, 672, 584, 499 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ 2.25 (3H, s, CH_3), 2.30 (3H, s, CH_3), 7.08 (1H, s, H-6), 7.33 (1H, dd, J=7.4, 7.4 Hz, *p*-Ph), 7.41 (2H, dd, J=7.6, 7.4 Hz, *m*-Ph), 7.99 (1H, s, H-9), 8.29 (2H, d, J=7.6 Hz, *o*-Ph), 9.01 (1H, s, H-1), 11.17 (1H, s, NH); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 154.9 (C-4), 143.5 (C-3), 135.5 (C-7), 133.2 (C-*i*), 131.9 (C-1), 131.1 (C-8), 128.9 (C-*o*), 127.7 (C-*p*), 127.6 (C-*m*), 126.5 (C-5a), 118.0 (C-9a), 116.8 (C-3a), 116.5 (C-6), 115.9 (C-9), 19.1 (C-7), 18.9 (C-8); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 269.7 (N-2), 184.0 (N-10), 134.2 (N-5). MS (MALDI TOF) 290 $[MH]^+$.

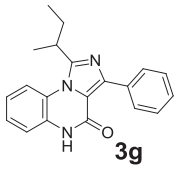
*4.2.6. 5-Methyl-3-phenylimidazo[1,5-a]quinoxalin-4(5H)-one (**3f**).*



3f

Yield: 176 mg (63%). White powder, mp 208–210 °C (DMSO:CH_3CN=1:1). Anal. Calcd for $C_{17}H_{13}N_3O$: C, 74.17; H, 4.76; N, 15.26. Found: C, 74.28; H, 4.86; N, 15.12%. IR (KBr) ν 3091, 3061, 3034, 2978, 2943, 2894, 1650, 1614, 1598, 1536, 1517, 1476, 1446, 1399, 1363, 1348, 1337, 1312, 1294, 1241, 1177, 1165, 1125, 1100, 1072, 1050, 976, 956, 925, 869, 839, 779, 749, 691, 678, 665, 634, 467 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ 3.56 (3H, s, CH_3), 7.30–7.37 (2H, m, *p*-Ph, H-8), 7.40–7.44 (2H, m, *m*-Ph), 7.47 (1H, ddd, J=8.3, 7.2, 1.3 Hz, H-7), 7.51 (1H, dd, J=8.3, 1.3 Hz, H-6), 8.20–8.23 (2H, m, *o*-Ph), 8.24 (1H, dd, J=8.0, 1.3 Hz, H-9), 9.12 (1H, s, H-1). $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 154.4 (C-4), 143.9 (C-3), 133.1 (C-*i*), 132.1 (C-1), 129.9 (C-5a), 129.1 (C-*o*), 127.8 (C-*p*), 127.5 (C-*m*), 127.3 (C-7), 123.0 (C-8), 120.9 (C-9a), 116.1 (C-6), 116.1 (C-3a), 115.6 (C-9), 28.4 (N5–CH_3); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 270.6 (N-2), 182.1 (N-10), 128.4 (N-5). MS (MALDI TOF) 276 $[MH]^+$, 298 $[M+Na]^+$, 314 $[M+K]^+$.

*4.2.7. 1-(sec-Butyl)-3-phenylimidazo[1,5-a]quinoxalin-4(5H)-one (**3g**).*

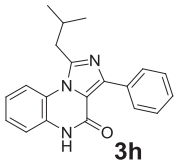


3g

Yield: 211 mg (66%). White powder, mp 236–238 °C (DMSO:CH_3CN=1:2). Anal. Calcd for $C_{20}H_{19}N_3O$: C, 75.69; H, 6.03; N, 13.24. Found: C, 75.75; H, 6.00; N, 13.19%. IR (KBr) ν 3200–2500, 1659, 1611, 1552, 1490, 1439, 1403, 1377, 1331, 1183, 925, 835, 779, 742, 692, 667 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ 0.99 (3H, t, J=7.0 Hz, CH_3CH_2), 1.46 (3H, d, J=6.5 Hz, CH_3CH), 1.67–1.75 (1H, m, $CH_AH_BCH_3$), 2.02–2.10 (1H, m, $CH_AH_BCH_3$), 3.57–3.64 (1H, m, $CH_3CHCH_2CH_3$), 7.22–7.26 (1H, m, H-8), 7.31–7.43 (5H, m, *m,p*-Ph, H-6, H-7), 7.98 (1H, d, J=8.4 Hz, H-9), 8.13 (2H, d, J=7.8 Hz, o-Ph), 11.27 (1H, s, NH); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 155.1 (C-4), 151.1 (C-1), 142.3 (C-3), 133.4 (C-*i*), 129.7 (C-5a), 129.6 (C-*o*), 127.8 (C-*p*), 127.4 (C-*m*), 126.6 (C-7), 122.6 (C-8), 121.8 (C-9a), 117.8 (C-3a),

117.3 (C-9), 116.5 (C-6), 35.1 (C-11), 27.9 (C-13), 18.8 (C-12), 11.5 (C-14); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 269.3 (N-2), 176.0 (N-10), 135.2 (N-5). MS (MALDI TOF) 318 $[MH]^+$, 340 $[M+Na]^+$, 356 $[M+K]^+$.

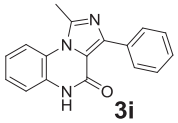
*4.2.8. 1-(iso-Butyl)-3-phenylimidazo[1,5-a]quinoxalin-4(5H)-one (**3h**).*



3h

Yield: 192 mg (60%). White powder, mp 258–260 °C (DMSO:CH_3CN=1:2). Anal. Calcd for $C_{20}H_{19}N_3O$: C, 75.69; H, 6.03; N, 13.24. Found: C, 75.77; H, 6.12; N, 13.10%. IR (KBr) ν 3200–2500, 1672, 1609, 1542, 1497, 1440, 1404, 1379, 1331, 1276, 856, 744, 694, 668 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.05 (6H, d, J=6.6 Hz, CH_3), 2.31–2.42 (1H, m, $CH(CH_3)_2$), 3.19 (2H, d, J=6.9 Hz, CH_2), 7.24 (1H, ddd, J=8.4, 6.7, 2.2 Hz, H-8), 7.30–7.44 (5H, m, *m*,*p*-Ph, H-6, H-7), 7.98 (1H, d, J=8.4 Hz, H-9), 8.13–8.19 (2H, m, *o*-Ph), 11.22 (1H, s, NH). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) δ 154.9 (C-4), 146.1 (C-1), 142.2 (C-3), 133.2 (C-*i*), 129.5 (C-5a), 129.4 (C-*o*), 127.7 (C-*p*), 127.4 (C-*m*), 126.5 (C-7), 122.4 (C-8), 121.7 (C-9a), 117.9 (C-3a), 117.0 (C-9), 116.3 (C-6), 39.3 (C-10), 25.9 (C-11), 22.3 (C-12); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 273.0 (N-2), 177.1 (N-10), 135.2 (N-5). MS (MALDI TOF) 318 $[MH]^+$, 340 $[M+Na]^+$, 356 $[M+K]^+$.

*4.2.9. 1-Methyl-3-phenylimidazo[1,5-a]quinoxalin-4(5H)-one (**3i**).*



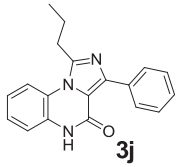
3i

Yield: 162 mg (58%). White powder, mp 258–260 °C (AcOH/H_2O=1:1). Anal. Calcd for $C_{17}H_{13}N_3O$: C, 74.17; H, 4.76; N, 15.26. Found: C, 74.02; H, 4.37; N, 15.05%. IR (KBr) ν 3185, 3114, 3049, 3031, 2981, 2907, 2867, 2764, 1666, 1612, 1578, 1556, 1515, 1496, 1486, 1441, 1401, 1369, 1333, 1302, 1276, 1247, 1182, 1162, 1131, 1074, 1014, 780, 743, 716, 694, 667, 551 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 2.97 (3H, s, CH_3), 7.22–7.26 (1H, m, H-8), 7.33–7.38 (3H, m, *p*-Ph, H-6, H-7), 7.42 (1H, dd, J=8.1, 7.4 Hz, *m*-Ph), 8.08 (1H, d, J=8.1 Hz, H-9), 8.18 (2H, d, J=8.3 Hz, o-Ph), 11.23 (1H, s, NH). ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) δ 154.9 (C-4), 143.3 (C-1), 142.1 (C-3), 133.1 (C-*i*), 129.5 (C-5a), 129.3 (C-*o*), 127.7 (C-*p*), 127.4 (C-*m*), 126.5 (C-7), 122.4 (C-8), 121.9 (C-9a), 117.9 (C-3a), 116.8 (C-9), 116.2 (C-6), 18.3 (C-11); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 272.9 (N2), 177.4 (N-10), 135.1 (N-5). MS (MALDI TOF) 276 $[MH]^+$, 298 $[M+Na]^+$, 314 $[M+K]^+$.

4.3. General procedure for the synthesis of 3a,j–r and 5

a. A mixture of 3-benzoylquinoxalin-2-one **1a** or 3-benzoyl-6,7-dimethylquinoxalin-2-one **1e** (1.0 mmol) and $NH_2Me\cdot HCl$ (4 mmol) or alkylamine (1.7 mmol when alkyl=Bu, *i*-Bu and 1.1 mmol when alkyl=$C_{16}H_{33}$, $C_{18}H_{37}$) or amino alcohol (1.3 mmol) or 1,6-diaminohexane (0.55 mmol), in DMSO (2 mL) was stirred at 150 °C for 4–6 h (Tables 3 and 4, Scheme 4). When synthesizing **3a**,**j**,**k**,**n**–**q** after cooling to room temperature, the reaction mixture was poured into water (15 mL). After collection by suction filtration the crude product was washed with water (5 mL), dried in air and purified by column chromatography on silica gel (CH_2Cl_2/hexane=9:1→ CH_2Cl_2 for **3j**,**k**; $CH_2Cl_2\rightarrow CH_2Cl_2$:EtOH=30:1 for **3n**–**r**) or recrystallized (**3a**). When synthesizing **3l**,**m** and **3** the reaction mixture was left overnight at room temperature, wherein the crystals of the product were precipitated out. The crystals were collected by suction filtration, washed with CH_3CN (5 mL) and dried. Hexane (5 mL) was added to the residue and left for 2 h. The precipitate was filtered and dried. ***b***. General procedure was (*b*) implemented in a similar manner as the procedure (*a*) except that $NaHCO_3$ (16 mg, 0.2 mmol when synthesizing **3j**–**r**, **5** and 294 mg, 3.5 mmol when synthesizing **3a**) was used, and the reaction time was reduced to 3 h, and $NH_2Me\cdot HCl$ (when synthesizing **3a**) was reduced to 3 mmol.

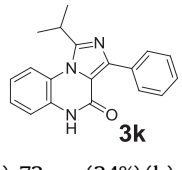
*4.3.1. 1-Propyl-3-phenylimidazo[1,5-a]quinoxalin-4(5H)-one (**3j**).*



3j

Yield: 158 mg (52%) (*a*), 210 mg (70%) (*b*). White powder, mp 255–257 °C (DMSO). Anal. Calcd for $C_{19}H_{17}N_3O$: C, 75.23; H, 5.65; N, 13.85. Found: C, 75.18; H, 5.60; N, 13.92%. IR (KBr) ν 3200–2500, 1674, 1610, 1544, 1515, 1497, 1467, 1441, 1406, 1376, 1332, 1277, 741, 693 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.07 (3H, t, J=7.3 Hz, CH_3), 1.86–2.01 (2H, m, CH_2CH_3), 3.26 (3H, t, J=7.4 Hz, $CH_2CH_2CH_3$), 7.23 (1H, dd, J=8.0, 6.8 Hz, H-8), 7.30–7.37 (3H, m, *p*-Ph, H-6, H-7), 7.40 (2H, dd, J=7.6, 7.5 Hz, *m*-Ph), 7.99 (1H, d, J=8.2 Hz, H-9), 8.15 (2H, dd, J=7.9, 1.3 Hz, o-Ph), 11.26 (1H, s, NH); ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) δ 155.0 (C-4), 146.8 (C-1), 142.2 (C-3), 133.3 (C-*i*), 129.6 (C-5a), 129.5 (C-*o*), 127.8 (C-*p*), 127.5 (C-*m*), 126.6 (C-7), 122.6 (C-8), 121.8 (C-9a), 117.9 (C-3a), 117.1 (C-9), 116.3 (C-6), 32.6 (C-11), 19.8 (C-12), 13.7 (C-13); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 271.4 (N-2), 176.7 (N-10), 135.3 (N-5). MS (MALDI TOF): 304 $[MH]^+$, 326 $[M+Na]^+$, 342 $[M+K]^+$.

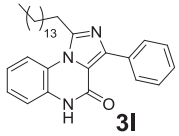
*4.3.2. 1-(iso-Propyl)-3-phenylimidazo[1,5-a]quinoxalin-4(5H)-one (**3k**).*



3k

Yield: 60 mg (20%) (*a*), 72 mg (24%) (b). White powder, mp >190 (dec) (DMSO:CH_3CN=1:1). Anal. Calcd for $C_{19}H_{17}N_3O$: C, 75.23; H, 5.65; N, 13.85. Found: C, 75.15; H, 5.68; N, 13.74%. IR (KBr) ν 3200–2500, 1659, 1610, 1494, 1439, 1406, 1376, 1329, 1084, 925, 867, 772, 746, 694 cm^{-1}. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.45 (6H, d, J=6.7 Hz, $(CH_3)_2$), 3.80–3.87 (1H, m, $CH(CH_3)_2$), 7.22–7.26 (1H, m, H-8), 7.31–7.37 (2H, m, *m*-Ph), 7.38–7.43 (3H, *p*-Ph, H-6, H-7), 8.02 (1H, d, J=8.3 Hz, H-9), 8.14 (2H, dd, J=8.3, 1.3 Hz, o-Ph), 11.22 (1H, s, NH); ^{13}C{^{1}H} NMR (DMSO-d_6, 100 MHz) δ 155.1 (C-4), 151.9 (C-1), 142.1 (C-3), 133.3 (C-*i*), 129.6 (C-5a), 129.6 (C-*o*), 127.8 (C-*p*), 127.5 (C-*m*), 126.6 (C-7), 122.6 (C-8), 121.7 (C-9a), 117.9 (C-3a), 117.4 (C-9), 116.5 (C-6), 28.6 (C-10), 21.3 (C-11); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 268.6 (N-2), 175.3 (N-10), 135.2 (N-5). MS (MALDI TOF): 304 $[MH]^+$.

*4.3.3. 1-Pentadecyl-3-phenylimidazo[1,5-a]quinoxalin-4(5H)-one (**3l**).*

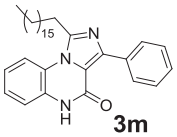


3l

Yield: 203 mg (43%) (*a*), 240 mg (51%) (*b*). White powder, mp 136–138 °C (DMSO). Anal. Calcd for $C_{31}H_{41}N_3O$: C, 78.94; H, 8.76; N, 8.91. Found: C, 78.85; H, 8.68; N, 8.89%. IR (KBr) ν 3200–2500, 1660, 1614, 1578, 1543, 1515, 1498, 1469, 1443, 1408,

1376, 1330, 1303, 1267, 840, 779, 744, 691, 666, 589 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ 0.83 (3H, t, J=6.9 Hz, CH_3), 1.15–1.29 (20H, m, $(CH_2)_4(CH_2)_{10}CH_3$), 1.30–1.35 (2H, m, $(CH_2)_3CH_2(CH_2)_{10}CH_3$), 1.42–1.50 (2H, m, $(CH_2)_2CH_2(CH_2)_{11}CH_3$), 1.84–1.96 (2H, m, $CH_2CH_2(CH_2)_{12}CH_3$), 3.33 (2H, t, J=7.9 Hz, $CH_2(CH_2)_{13}CH_3$), 7.20–7.26 (1H, m, H-8), 7.30–7.36 (3H, m, *p*-Ph, H-6, H-7), 7.37–7.42 (2H, m, *m*-Ph), 7.98 (1H, d, J=8.2 Hz, H-9), 8.15 (2H, d, J=7.8 Hz, o-Ph), 11.21 (1H, s, NH). $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 155.0 (C-4), 146.9 (C-1), 142.2 (C-3), 133.3 (C-*i*), 129.6 (C-5a), 129.5 (C-*o*), 127.8 (C-*p*), 127.5 (C-*m*), 126.6 (C-7), 122.5 (C-8), 121.8 (C-9a), 118.0 (C-3a), 117.1 (C-9), 116.4 (C-6), 31.2 (C-13′), 30.7 (C-1′), 28.9–28.6 ((C-5′)-(C-12′)), 28.57 (C-4′), 28.4 (C-3′), 26.2 (C-2′), 21.9 (C-14′), 13.8 (C-15′). MS (MALDI TOF): 472 $[MH]^+$, 494 $[M+Na]^+$.

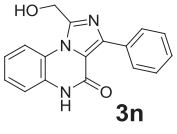
*4.3.4. 1-Heptadecyl-3-phenylimidazo[1,5-a]quinoxalin-4(5H)-one (**3m**).*



3m

Yield: 230 mg (46%) (*a*), 280 mg (56%) (*b*). White powder, mp 134–136 °C (DMSO). Anal. Calcd for $C_{33}H_{45}N_3O$: C, 79.31; H, 9.08; N, 8.41. Found: C, 79.44; H, 9.14; N, 8.30%. IR (KBr) ν 3200–2500, 1662, 1616, 1492, 1471, 1441, 1407, 1375, 1332, 1276, 743, 692, 589 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 0.88 (3H, t, J=6.9 Hz, CH_3), 1.19–1.37 (24H, m, $(CH_2)_4(CH_2)_{12}CH_3$), 1.37–1.46 (2H, m, $(CH_2)_3CH_2(CH_2)_{12}CH_3$), 1.51–1.60 (2H, m, $(CH_2)_2CH_2(CH_2)_{13}CH_3$), 1.96–2.06 (2H, m, $CH_2CH_2(CH_2)_{14}CH_3$), 3.34 (3H, t, J=7.4 Hz, $CH_2(CH_2)_{15}CH_3$), 7.22 (1H, ddd, J=8.2, 7.3, 1.8 Hz, H-8), 7.27 (1H, ddd, J=8.2, 1.8 Hz, H-6), 7.31 (1H, dd, J=8.2, 7.3, Hz, H-7), 7.37–7.42 (1H, *p*-Ph), 7.43–7.49 (2H, m, *m*-Ph), 7.87 (1H, d, J=8.2 Hz, H-9), 8.18–8.22 (2H, m, o-Ph), 10.93 (1H, s, NH); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 156.8 (C-4), 147.6 (C-1), 144.1 (br, C-3), 132.5 (br, C-*i*), 130.1 (C-*o*), 129.3 (C-5a), 128.5 (C-*p*), 127.7 (C-*m*), 126.9 (C-7), 123.1 (C-8), 122.6 (C-9a), 117.7 (C-3a), 117.2 (C-6), 116.7 (C-9), 31.9 (C-15′), 31.4 (br, C-1′), 29.68–29.45 ((C-5′)-(C-14′)), 29.34 (C-4′), 29.32 (C-3′), 27.1 (C-2′), 22.7 (C-16′), 14.1 (C-17′). MS (MALDI TOF): 500 $[MH]^+$.

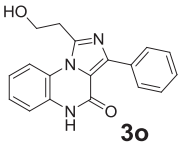
*4.3.5. 1-Hydroxymethyl-3-phenylimidazo[1,5-a]quinoxalin-4(5H)-one (**3n**).*



3n

Yield: 44 mg (15%) (*a*), 104 mg (36%) (*b*). Light-yellow powder, mp >290 (dec) (DMSO). Anal. Calcd for $C_{17}H_{13}N_3O_2$: C, 70.09; H, 4.50; N, 14.42. Found: C, 70.20; H, 4.55; N, 14.30%. IR (KBr) ν 3200–2500, 1622, 1613, 1560, 1510, 1489, 1440, 1414, 1389, 1340, 1303, 1278, 1243, 1166, 1045, 781, 747, 692, 669 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ 5.00 (2H, s, CH_2), 7.26 (1H, ddd, J=8.3, 6.8, 1.7 Hz, H-8), 7.31–7.38 (3H, m, *p*-Ph, H-6, H-7), 7.42 (2H, dd, J=7.8, 7.1 Hz, *m*-Ph), 8.12–8.18 (2H, m, o-Ph), 8.29 (1H, d, J=8.3 Hz, H-9), 11.38 (1H, s, NH); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 154.9 (C-4), 145.3 (C-1), 142.0 (C-3), 133.0 (C-*i*), 129.4 (C-*o*), 129.3 (C-5a), 127.9 (C-*p*), 127.6 (C-*m*), 126.9 (C-7), 122.7 (C-8), 121.3 (C-9a), 118.5 (C-3a), 118.3 (C-9), 116.1 (C-6), 57.5 (C-11); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 275.3 (N-2), 178.4 (N-10), 135.7 (N-5). MS (MALDI TOF): 292 $[MH]^+$, 314 $[M+Na]^+$, 330 $[M+K]^+$.

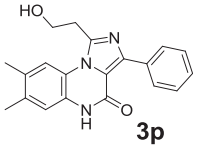
*4.3.6. 1-(2-Hydroxyethyl)-3-phenylimidazo[1,5-a]quinoxalin-4(5H)-one (**3o**).*



3o

Yield: 113 mg (37%) (*a*), 202 mg (65%) (*b*). White powder, mp >220 °C (dec) (DMSO). Anal. Calcd for $C_{18}H_{15}N_3O_2$: C, 70.81; H, 4.95; N, 13.76. Found: C, 70.89; H, 5.00; N, 13.63%. IR (KBr) ν 3220–2500, 1672, 1613, 1578, 1560, 1488, 1415, 1337, 1304, 1278, 1261, 1230, 1181, 1163, 1064, 1051, 935, 853, 779, 748, 697, 667, 594 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ 3.47 (3H, t, J=6.9 Hz, CH_2CH_2OH), 4.00 (3H, td, J=6.9, 5.4 Hz, CH_2OH), 4.85 (1H, t, J=5.4 Hz, OH), 7.23 (1H, ddd, J=8.4, 6.7, 1.7 Hz, H-8), 7.31–7.37 (m, 3H, *p*-Ph, H-6, H-7), 7.38–7.42 (2H, m, *m*-Ph), 8.07 (1H, d, J=8.4 Hz, H-9), 8.15 (2H, d, J=7.5 Hz, o-Ph), 11.22 (1H, s, NH). $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 154.9 (C-4), 144.9 (C-1), 142.4 (C-3), 133.2 (C-*i*), 129.6 (C-5a), 129.5 (C-*o*), 127.8 (C-*p*), 127.5 (C-*m*), 126.7 (C-7), 122.5 (C-8), 121.8 (C-9a), 117.9 (C-3a), 117.2 (C-9), 116.4 (C-6), 58.7 (C-12), 34.3 (C-11); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 270.9 (N-2), 177.8 (N-10), 135.2 (N-5). MS (MALDI TOF): 306 $[MH]^+$, 328 $[M+Na]^+$, 344 $[M+K]^+$.

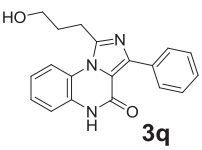
*4.3.7. 1-(2-Hydroxyethyl)-7,8-dimethyl-3-phenylimidazo[1,5-a]quinoxalin-4(5H)-one (**3p**).*



3p

Yield: 130 mg (39%) (*a*). White powder, mp >280 °C (dec) (DMSO). Anal. Calcd for $C_{20}H_{19}N_3O_2$: C, 72.05; H, 5.74; N, 12.60. Found: C, 72.17; H, 5.77; N, 12.51%. IR (KBr) ν 3450–3250, 3220–2500, 1662, 1619, 1515, 1495, 1417, 1400, 1343, 1268, 1163, 1057, 873, 861, 829, 781, 760, 697 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ 2.27 (3H, s, CH_3), 2.34 (3H, s, CH_3), 3.50 (2H, t, J=6.9 Hz, CH_2CH_2OH), 4.03 (2H, td, J=6.9, 5.5 Hz, CH_2CH_2OH), 4.91 (1H, t, J=5.5 Hz, CH_2CH_2OH), 7.11 (1H, s, H-6), 7.35 (1H, ddd, J=7.3, 7.3, 1.2 Hz, *p*-Ph), 7.43 (2H, ddd, J=8.3, 7.3, 1.2 Hz, *m*-Ph), 7.83 (1H, s, H-9), 8.11 (2H, ddd, J=8.3, 7.3, 1.2 Hz, *o*-Ph), 11.05 (1H, s, NH); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 154.9 (C-4), 144.4 (C-1), 142.2 (C-3), 135.2 (C-7), 133.3 (C-*i*), 130.7 (C-8), 129.5 (C-*o*), 127.7 (C-*p*), 127.5 (C-*m*), 127.4 (C-5a), 119.7 (C-9a), 118.0 (C-3a), 117.5 (C-9), 116.8 (C-6), 58.7 (C-12), 34.2 (C-11), 19.3 (C-8), 19.0 (C-7); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 269.8 (N-2), 177.6 (N-10), 134.1 (N-5). MS (MALDI TOF): 334 $[MH]^+$, 356 $[M+Na]^+$, 372 $[M+K]^+$.

*4.3.8. 1-(3-Hydroxypropyl)-7,8-dimethyl-3-phenylimidazo[1,5-a]quinoxalin-4(5H)-one (**3q**).*

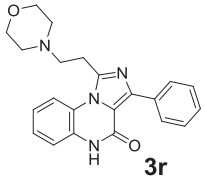


3q

Yield: 112 mg (35%) (*a*), 163 mg (51%) (*b*). White powder, mp 249–250 °C (dec) (DMSO). Anal. Calcd for $C_{19}H_{17}N_3O_2$: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.39; H, 5.41; N, 13.03%. IR (Nujol mull) 3245, 3220–2500, 1671, 1615, 1485, 1426, 1408, 1366, 1337, 1324, 1301, 1274, 1241, 1161, 1042, 1019, 895, 763, 695 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ 2.06–2.12 (2H, m, $CH_2CH_2CH_2OH$), 3.35 (3H, t, J=7.7 Hz, $CH_2(CH_2)_2OH$), 3.64 (3H, td, J=6.0, 5.2 Hz, CH_2OH), 4.61 (1H, t, J=5.2 Hz, OH), 7.24 (1H, ddd, J=8.4, 6.5, 1.8, H-8), 7.32–7.30

(3H, m, *p*-Ph, H-6, H-7), 7.42 (2H, dd, *J*=8.0, 7.6 Hz, *m*-Ph), 8.07 (1H, d, *J*=8.3 Hz, H-9), 8.17 (2H, d, *J*=8.0 Hz, o-Ph), 11.23 (1H, s, NH). $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 155.0 (C-4), 146.9 (C-1), 142.2 (C-3), 133.3 (C-*i*), 129.6 (C-5a), 129.5 (C-*o*), 127.8 (C-*p*), 127.5 (C-*m*), 126.6 (C-7), 122.5 (C-8), 121.9 (C-9a), 118.0 (C-3a), 117.2 (C-9), 116.3 (C-6), 59.9 (C-13), 29.8 (C-12), 27.5 (C-11); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 270.8 (N-2), 176.8 (N-10), 135.2 (N-5). MS (MALDI TOF): 320 $[MH]^+$, 342 $[M+Na]^+$, 359 $[M+K]^+$.

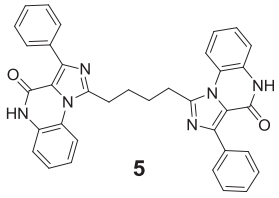
*4.3.9. 1-(2-N-Morpholinylethyl)-3-phenylimidazo[1,5-a]quinoxalin-4(5H)-one (**3r**).*



3r

Yield: 81 mg (22%) (*a*), 189 mg (51%) (*b*). Light-yellow powder, mp >190 °C (dec) (DMSO:CH_3CN=1:2). Anal. Calcd for $C_{22}H_{22}N_4O_2$: C, 70.57; H, 5.92; N, 14.96. Found: C, 70.68; H, 5.91; N, 14.83%. IR (KBr) ν 3185, 3129, 3054, 2969, 2926, 2901, 2849, 1665, 1614, 1559, 1510, 1488, 1448, 1425, 1399, 1389, 1334, 1258, 1237, 1197, 1116, 1073, 1006, 870, 752, 699, 683, 666, 577 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ 2.50–2.55 (4H, m, morphol.), 2.95 (2H, t, *J*=7.4 Hz, CH_2CH_2N), 3.48 (3H, t, *J*=7.4 Hz, CH_2CH_2N), 3.61 (4H, t, *J*=4.6 Hz, morphol.), 7.25 (1H, ddd, *J*=8.3, 6.7, 2.0 Hz, H-8 quinoxal.), 7.32–7.39 (3H, m, *p*-Ph, H-6, H-7 quinoxal.), 7.40–7.44 (2H, m, *m*-Ph), 8.06 (1H, d, *J*=8.3 Hz, H-9 quinoxal.), 8.14–8.18 (2H, m, o-Ph), 11.24 (1H, s, NH); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 154.9 (C-4), 145.3 (C-1), 142.2 (C-3), 133.2 (C-*i*), 129.5 (C-5a), 129.5 (C-*o*), 127.8 (C-*p*), 127.5 (C-*m*), 126.7 (C-7), 122.6 (C-8), 121.8 (C-9a), 118.1 (C-3a), 117.2 (C-9), 116.3 (C-6), 66.2 (C-15), 55.3 (C-12), 53.2 (C-14), 28.7 (C-11); ^{15}N NMR (DMSO-d_6, 60 MHz) δ 270.9 (N-2), 177.3 (N-10), 135.2 (N-5). MS (MALDI TOF): 375 $[MH]^+$, 397 $[M+Na]^+$, 413 $[M+K]^+$.

*4.3.10. 1,4-Bis(3-phenylimidazo[1,5-a]quinoxalin-4(5H)-on-1-yl)butane (**5**).*



5

Yield: 173 mg (30%) (*a*), 290 mg (50%) (*b*). White powder, mp >360 °C (DMSO). Anal. Calcd for $C_{36}H_{28}N_6O_2$: C, 74.98; H, 4.89; N, 14.57. Found: C, 75.07; H, 4.79; N, 14.46%. IR (KBr) ν 3186, 3120, 3033, 2979, 2946, 2906, 2864, 1674, 1613, 1557, 1489, 1438, 1410, 1378, 1331, 1304, 1279, 1262, 1057, 1028, 996, 868, 782, 740, 695, 684, 666, 594, 535 cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz) δ 2.17–2.22 (4H, m, $CH_2(CH_2)_2CH_2$), 3.40–3.46 (4H, br s, $CH_2(CH_2)_2CH_2$), 7.14–7.19 (2H, m, H-8 quinoxal.), 7.30–7.35 (3H, m, *p*-Ph, H-6 quinoxal., H-7 quinoxal.), 7.38 (2H, dd, *J*=8.1, 7.3 Hz, *m*-Ph), 8.04 (2H, d, *J*=8.2 Hz, H-9 quinoxal.), 8.13 (2H, d, *J*=8.1 Hz, o-Ph), 11.21 (1H, s, NH); $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100 MHz) δ 154.9 (C-4), 146.8 (C-1), 142.1 (C-3), 133.2 (C-*i*), 129.5 (C-5a), 129.4 (C-*o*), 127.6 (C-*p*), 127.4 (C-*m*), 126.5 (C-7), 122.4 (C-8), 121.8 (C-9a), 118.0 (C-3a), 117.1 (C-9), 116.2 (C-6), 30.5 (C-11), 25.8 (C-12). MS (MALDI TOF): 577 $[MH]^+$, 599 $[M+Na]^+$.

Acknowledgements

This work was supported by the Russian Scientific Foundation (grant №14-23-00073).

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.11.017.

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