Tetrahedron 70 (2014) 4617–4625

Contents lists available at ScienceDirect

Tetrahedron

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

Base-promoted cyclization of 3-alkynylquinoxaline-2-carbonitriles with CH-acids: a new method for the phenazine ring synthesis

Huong T.L. Nguyen, Anna V. Gulevskaya *, Alexander F. Pozharskii, Julia I. Nelina-Nemtseva

Department of Organic Chemistry, Southern Federal University, Zorge 7, Rostov-on-Don 344090, Russian Federation

ARTICLE INFO

Article history:
Received 26 March 2014
Received in revised form 28 April 2014
Accepted 12 May 2014
Available online 16 May 2014

Keywords:
3-Alkynylquinoxaline-2-carbonitriles
Nucleophilic cyclization
Cascade cyclization
Phenazines

ABSTRACT

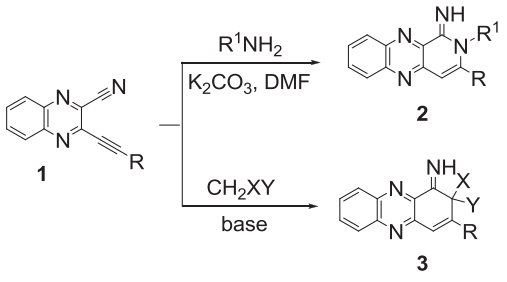
3-Alkynylquinoxaline-2-carbonitriles were directly transformed into 2,3-disubstituted phenazin-1-amines by treating with a CH-acid (diethylmalonate, ethyl cyanoacetate, malononitrile, 2-tosylacetonitrile, 2-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)acetonitrile, nitromethane) and *t*-BuOK in THF or DMSO. A new cascade process includes nucleophilic addition of a CH-acid carbanion to the C≡C bond of 3-alkynylquinoxaline-2-carbonitrile, 6-*exo-dig* cyclization of the intermediate allyl carbanion with the formation of 2,2-disubstituted 1-imino-1,2-dihydrophenazine and its aromatization via elimination of the C(2)-substituent. Several secondary reactions were also disclosed and discussed.

1. Introduction

The phenazine nucleus is an integral component of many biologically active compounds, including more than 100 natural antibiotics, produced by *Pseudomonas*, *Streptomyces*, marine, and other microorganisms. Antibiotic, antitumor, antimalarial, and antiparasitic properties of phenazines are well-documented.[1] The biological activity of phenazines is based on their ability for intercalation, inhibition of topoisomerases and radical oxidation processes, transfer of electrons in the process of methanogenesis and so on.

Until now, no general and effective method for the synthesis of substituted phenazines[1a] has been reported. Commonly, substituents are introduced into the building blocks before phenazine ring formation. The majority of the known methods have some limitations due to the arrangement and the electronic nature of substituents in the starting reagents. The low output of products and rather harsh reaction conditions are other drawbacks in the existing protocols. Currently, catalytic methods for phenazines synthesis, based on the Buchwald–Hartwig and Ullmann reactions, seem to be the most effective. However, the high cost of palladium catalysts and their ligands is a limitation. The development of new strategies to enable the preparation of phenazines therefore remains of major interest.

Recently, we have reported that the reaction of 3-alkynylquinoxaline-2-carbonitriles **1** with primary alkylamines in the presence of a base proceeds via the tandem nucleophilic addition to the C≡C bond—6-*exo-dig* cyclization leading to the formation of pyrido[3,4-*b*]quinoxalin-1(2*H*)-imines **2** (Scheme 1).[2] From this we reasoned that analogous reaction of 3-alkynylquinoxaline-2-carbonitriles **1** with the CH_2-active compounds as pronucleophiles could result in the formation of phenazine derivatives **3**.



Scheme 1.

Herein, we wish to report on the results of this approach allowing to synthesize 2,3-disubstituted phenazin-1-amines in a simple and convenient way.

* Corresponding author. Tel.: +7 863 297 5146; fax: +7 863 297 5151; e-mail addresses: agulevskaya@sfedu.ru, anvasgul@gmail.com (A.V. Gulevskaya).

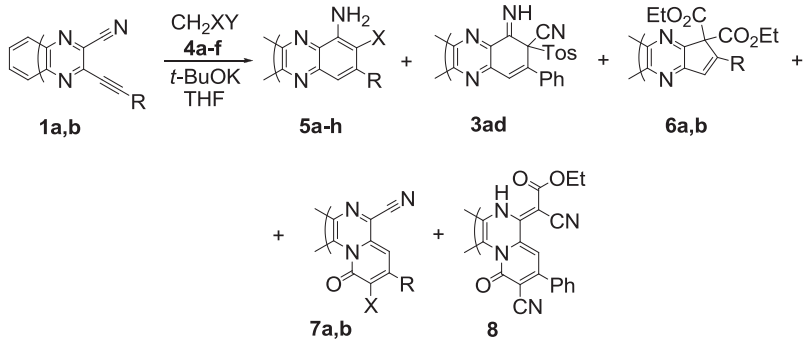
0040-4020/$ – see front matter © 2014 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2014.05.023

2. Results and discussion

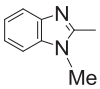
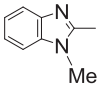
The starting 3-alkynylquinoxaline-2-carbonitriles **1** were prepared from available 3-chloroquinoxaline-2-carbonitrile[3] via the Sonogashira coupling in accordance with a known procedure.[2]

The treatment of 3-(phenylethynyl)quinoxaline-2-carbonitrile **1a** with diethyl malonate (1.2 equiv) and *t*-BuOK (1.2 equiv) in dry THF at room temperature for 24 h gave a mixture of ethyl 1-amino-3-phenylphenazine-2-carboxylate **5a** and diethyl 2-phenyl-1*H*-cyclopenta[*b*]quinoxaline-1,1-dicarboxylate **6a** in 13 and 26% yields, respectively (Table 1, entry 1). The use of diethyl malonate and 2 equiv *t*-BuOK led to an increase in the yields of both products **5a** and **6a** (Table 1, entry 2). From the reaction mixture a small amount of ethyl 6-cyano-10-oxo-8-phenyl-10*H*-pyrido[1,2-*a*]quinoxaline-9-carboxylate **7a** was also isolated. In both cases the starting material **1a** was partly recovered. Increasing the reaction time did not change the reaction output significantly (Table 1, entry 3). In contrast, heating the reaction mixture at 65 °C changed the yields drastically (Table 1, entry 4); diester **6a** was a major product in this case, and only trace amount of phenazine **5a** was formed. The reaction of carbonitrile **1b** with diethyl malonate and *t*-BuOK at room temperature afforded compounds **5b** and **6b** (Table 1, entry 5).

Table 1
Reaction of 3-(arylethynyl)quinoxaline-2-carbonitriles **1** with CH_2-active compounds in the presence of *t*-BuOK in THF



1, 6: R = Ph (**a**); *p*-Tol (**b**)
4: X, Y = CO_2Et, CO_2Et (**a**); CN, CO_2Et (**b**); CN, CN (**c**); CN, Tos (**d**); 1-methyl-1*H*-benzo[*d*]imidazol-2-yl, CN (**e**); NO_2, H (**f**)
5: R, X = Ph, CO_2Et (**a**); *p*-Tol, CO_2Et (**b**); Ph, CN (**c**); *p*-Tol, CN (**d**); Ph, 1-methyl-1*H*-benzo[*d*]imidazol-2-yl (**e**); *p*-Tol, 1-methyl-1*H*-benzo[*d*]imidazol-2-yl (**f**); Ph, NO_2 (**g**); *p*-Tol, NO_2 (**h**)
7: R, X = Ph, CO_2Et (**a**); *p*-Tol, CN (**b**)

Entry	Starting compound	CH_2XY				Reaction conditions	Yields, %	Recovered **1**, %
		X	Y	pK_a (DMSO)[4]	equiv			
1	**1a**	CO_2Et	CO_2Et	16.4	1.2	rt, 24 h	13 (**5a**) 26 (**6a**)	19
2					2	rt, 24 h	23 (**5a**) 29 (**6a**) 1 (**7a**)	7
3					2	rt, 8 days	24 (**5a**) 35 (**6a**) 3 (**7a**)	3
4					2	65 °C, 48 h	Trace (**5a**) 59 (**6a**) 5 (**7a**)	0
5	**1b**	CO_2Et	CO_2Et	16.4	2	rt, 24 h	17 (**5b**) 33 (**6b**)	32
6	**1a**	CN	CO_2Et	13.1	2	rt, 24 h	55 (**5c**) 4 (**8**)	17
7	**1b**	CN	CO_2Et	13.1	2	rt, 24 h	36 (**5d**) 4 (**7b**)	24
8	**1a**	CN	CN	11.1	2	rt, 24 h	64 (**5c**)	Trace
9					2	65 °C, 7 h	60 (**5c**)	Trace
10	**1a**	CN	Tos	12.0	2	rt, 24 h	34 (**5c**)	62
11					2	65 °C, 11 h	40 (**5c**) 19 (**3ad**)	trace
12	**1a**		CN	13.2 (H_2O/acetone)[5]	2	rt, 48 h	24 (**5e**)	25
13					2	65 °C, 16 h	18 (**5e**)	5
14	**1b**		CN	13.2 (H_2O/acetone)[5]	2	rt, 72 h	18 (**5f**)	34
15	**1a**	NO_2	H	17.2	2	rt, 48 h	6 (**5g**)	78
16	**1b**	NO_2	H	17.2	2	rt, 72 h	2 (**5h**)	86

The interaction of 3-(phenylethynyl)quinoxaline-2-carbonitrile **1a** with ethyl cyanoacetate afforded phenazine **5c** as the main product (55%) together with (*Z*)-ethyl 2-cyano-2-(9-cyano-10-oxo-8-phenyl-5*H*-pyrido[1,2-*a*]quinoxalin-6(10*H*)-ylidene)acetate **8** (Table 1, entry 6). The reaction of carbonitrile **1b** with ethyl cyanoacetate under the same conditions led to the formation of phenazine **5d** and pyridoquinoxaline **7b** in 36 and 4% yields, respectively (Table 1, entry 7).

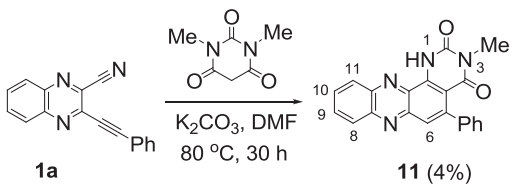
When malonodinitrile was used as the CH-active compound, the reaction selectively gave 1-amino-3-phenylphenazine-2-carbonitrile **5c** in 60–64% yield (Table 1, entries 8 and 9). Following treatment with 2-tosylacetonitrile and *t*-BuOK at room temperature, 3-(phenylethynyl)quinoxaline-2-carbonitrile **1a** was also transformed into compound **5c** (Table 1, entry 10). Heating the reaction mixture at 65 °C led to an increase in yield of **5c** and the appearance of one more product, namely, 1-imino-3-phenyl-2-tosyl-1,2-dihydrophenazine-2-carbonitrile **3ad** (Table 1, entry 11).

The reactions of compounds **1a** and **1b** with 2-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)acetonitrile in the presence of *t*-BuOK afforded phenazine derivatives **5e** and **5f**, respectively, as the only isolable products in 18–24% yield (Table 1, entries 12–14). Heating the reaction mixture resulted in considerable tarring.

The interaction of compounds **1a**,**b** with nitromethane produced only 2–6% of phenazines **5g**,**h** (Table 1, entries 15 and 16). The major part of the starting material in these experiments was recovered. Reaction of 3-(phenylethynyl)quinoxaline-2-carbonitrile **1a** with 1,3-dimethylbarbituric acid and *t*-BuOK in THF did not proceed, probably, because of the low solubility of **1a** salt in this solvent.

We believed that low yields of phenazines **5g**,**h** could be caused by the low CH-acidity of nitromethane (Table 1). Therefore, to achieve better result we tested other base/solvent systems for the cyclization reaction. Refluxing carbonitrile **1a** with a sixfold excess of nitromethane in triethylamine did not improve the yield of compound **5g** (Table 2, entry 1). The use of DBU/acetonitrile system had only a small positive impact on the phenazine **5g** yield (Table 2, entry 2). Besides, one more product, e.g., 3-phenylpyrido[4,3-*b*]quinoxalin-1(2*H*)-one **10**, has been isolated from the reaction mixture. The use of *t*-BuOK base and DMSO solvent afforded phenazine **5g** in 36% yield (Table 2, entry 3); however, the reaction was not selective producing also a comparable amount of 2-(nitromethyl)-3-(phenylethynyl)quinoxaline **9**.

phenylpyrimido[4,5-*a*]phenazine-2,4(1*H*,3*H*)-dione **11** as the only isolated product (Scheme 2).



Scheme 2.

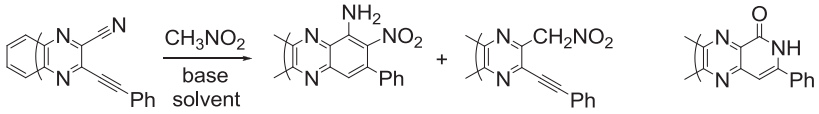
Phenazines **5a**–**h** are red-colored compounds with λ_{max} 478–497 nm and the end absorption ranging between 524 and 537 nm. Their mass spectra included the molecular peak ion, which for **5a**,**c**,**d**,**g**,**h** was the most intensive. The IR spectra of **5** indicated the presence of NH_2 group (ν_{as} 3462–3482 cm^{-1} and ν_s 3339–3378 cm^{-1}). In cases of 1-aminophenazines **5a**,**b** the characteristic $\nu_{C=O}$ band at 1662–1684 cm^{-1} was also registered. The spectra of nitriles **5c**,**d** included a $\nu_{C\equiv N}$ band at ~2200 cm^{-1}. In the ^1H NMR spectra of **5c**–**f** in $CDCl_3$ the protons of the amino group resonated at δ 6.4–6.5 ppm as a broad singlet. The same peak for compounds **5a**,**b**,**g**,**h** was shifted to δ 7.4–7.5 ppm, apparently, due to a weak chelation. In the spectra of **5a**,**d**–**g** the H(4) proton appeared as a one-proton singlet at δ 7.3–7.7 ppm. The structures of **5a** and **5e** were also proved by X-ray single crystal studies (Figs. 1 and 2).

Products **6a** and **8** were identical to authentic samples previously synthesized in our laboratory.[6] The structures **3ad**, **6b**, **7**, **10**, and **11** are supported by a combination of elemental analysis, mass spectrometry, IR, ^1H and ^{13}C NMR spectroscopic measurements.

Plausible mechanisms for the formation of compounds **5**–**8** and **3** are depicted in Scheme 3. First, a CH-acid carbanion adds to one of the triple bonds of **1** forming after a proton transfer an allyl carbanion **12**. Further development of the process depends on the substituents X and Y at the CH-acid termini. A competition of three different pathways is responsible for the outcome.

Path *A* is the main and is realized as 6-*exo*-*dig* carbocyclization of intermediate **12** producing imine **3**. The latter loses one of the C(2) substituents providing arylamide ion **14** and, after protonation,

Table 2
Reaction of 3-(phenylethynyl)quinoxaline-2-carbonitrile **1a** with nitromethane



Entry	CH_3NO_2 (equiv)	Base	Solvent	Reaction conditions	Yields, %	Recovered **1**, %
1	6	Et_3N	—	Reflux, 5 days	4 (**5g**)	66
2	3	DBU	MeCN	Reflux, 7 h	9 (**5g**) 10 (**10**)	Trace
3	2	*t*-BuOK	DMSO	rt, 24 h	36 (**5g**) 29 (**9**)	—

The *t*-BuOK/DMSO system was found to be more effective than *t*-BuOK/THF for the interaction of 3-(phenylethynyl)quinoxaline-2-carbonitrile **1a** with malonodinitrile giving rise to phenazine **5c** in 73% yield. Unfortunately, applying this base and solvent for reaction of **1a** with 1,3-dimethylbarbituric acid even at room temperature led to the formation of complex mixture of products. At the same time, heating **1a** and 1,3-dimethylbarbituric acid with K_2CO_3 in DMF proceeded rather unexpectedly yielding 3-methyl-5-phenazine derivatives **5**. Most likely, elimination of substituent Y from imine **3** is assisted by the nucleophilic attack of *tert*-butoxide ion. Indeed, in all cases the leaving group Y is more electrophilic than the remaining group X (X=CN, Y=CO_2Et, Tos; X=1-methyl-1*H*-benzo[*d*]imidazol-2-yl, Y=CN; X=NO_2, Y=H). A driving force for this process is aromatization. Isolation of compound **3ad** from the reaction of **1a** with 2-tosylacetonitrile is an additional argument in favor of this mechanism.

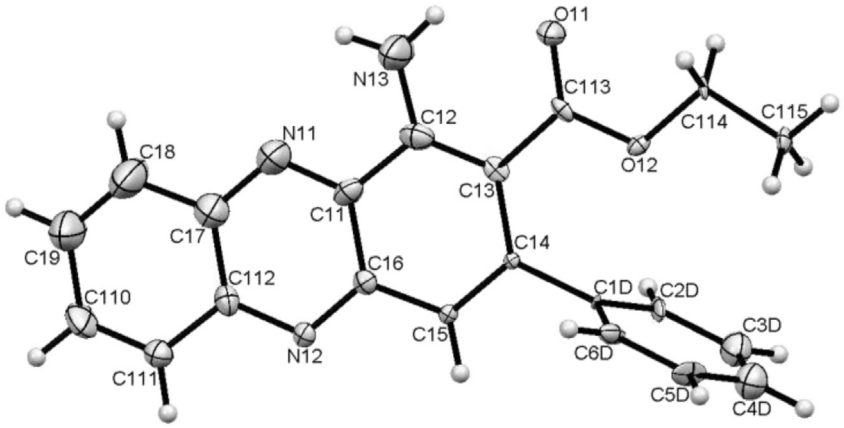


Fig. 1. ORTEP plots for X-ray crystal structure of **5a**.

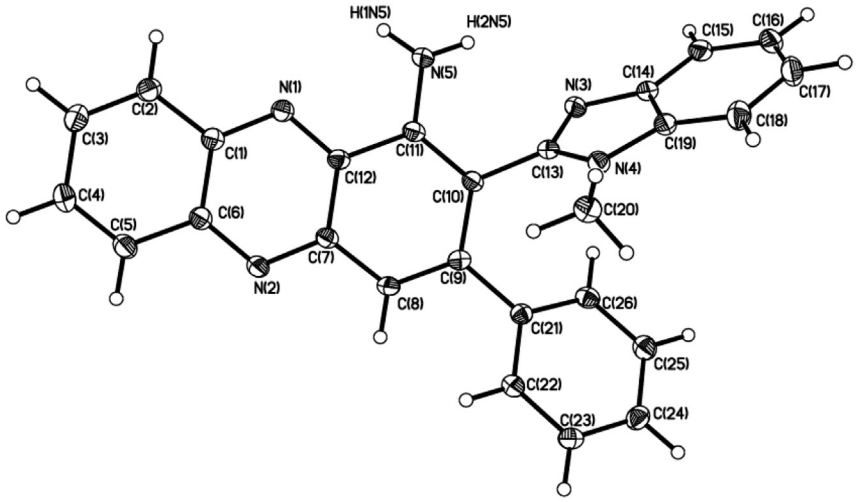


Fig. 2. ORTEP plots for X-ray crystal structure of **5e**.

Path *B* is an intramolecular nucleophilic aromatic substitution of the cyano group in the intermediate **12** leading to cyclopenta[*b*] quinoxaline **6**. This way is realized when diethyl malonate serves as a CH_2-active compound. As it is seen from Table 1, this CH-acid has the greatest pK_a value (excluding nitromethane). Therefore, the corresponding carbanions **12aa** and **12ba** should be the most nucleophilic in the series. Due to this, annelation of the cyclopentane ring to the starting molecule **1** competes with the phenazine ring formation. It seems that the cyclization of carbanion **12** into arylideneamide ion **13** is reversible. Comparing reactions of **1a** with diethyl malonate carried out at room temperature (Table 1, entry 2) and at 65 °C (Table 1, entry 4), one can assume that the formation of phenazine **5a** (Path *A*) is kinetically controlled whereas the cyclization of **1a** into **6a** (Path *B*) is thermodynamically controlled.

Path *C* is based on an intramolecular acylation with participation of the ring nitrogen atom and ethoxycarbonyl group of the intermediate **12**. It is realized only with diethyl malonate and ethyl cyanoacetate as CH-acids and produces pyridoquinoxaline derivatives **7** and **8**, the latter being a product of further substitution of the cyano group with ethyl cyanoacetate residue in the molecule **7c** (R=Ph, X=CN).

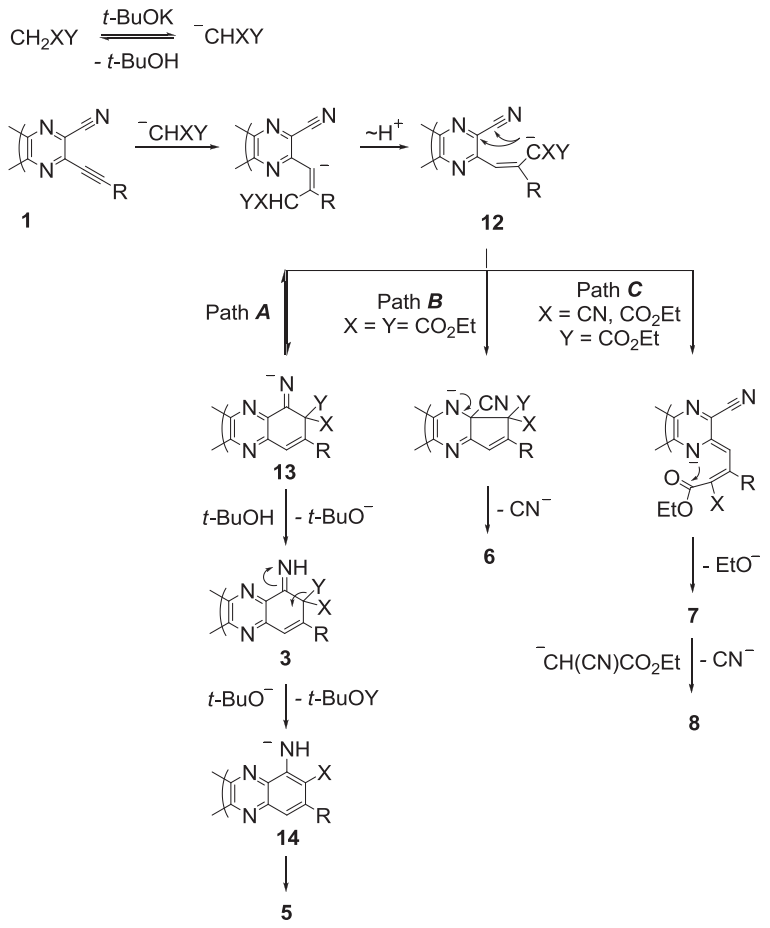
Formation of 2-(nitromethyl)-3-(phenylethynyl)quinoxaline **9** in the reaction of **1a** with nitromethane demonstrates one more possibility, e.g., nucleophilic aromatic substitution of the cyano group in the starting molecule with the CH-acid residue.

Probably, the reaction of **1a** with 1,3-dimethylbarbituric acid in the presence of K_2CO_3 in DMF follows Path *A* producing initially the spirocyclic imine **3ag** (Scheme 4). However, the latter undergoes intramolecular nucleophilic attack of the imine nitrogen atom on the pyrimidine C(2)=O group resulting in the elimination of a methylisocyanate molecule and annelation of the pyrimidine ring to the phenazine system. The ability of 5,5-disubstituted and spirobarbituric acids to undergo the ring contraction is known.[6,7] Nucleophilic reactions of potassium *tert*-butoxide have been also reported.[8]

The formation of compound **10** can be rationalized as a result of partial hydrolysis of the starting carbonitrile **1a** to the corresponding amide followed by a 6-*endo*-*dig* cyclization. We have proved that this transformation proceeded on silica gel during flash column chromatography of the reaction mixture. When a mixture of **1a**, DBU and acetonitrile (without nitromethane) was underwent the same work-up, compound **10** was obtained as the only product in 58% yield.

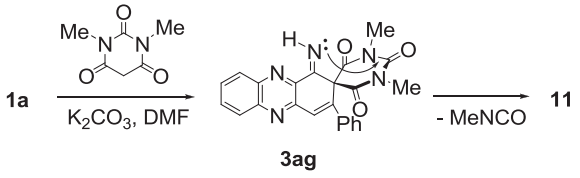
3. Conclusion

We have disclosed a simple and convenient method for the synthesis of 2,3-disubstituted phenazin-1-amines via the cascade interaction of 3-alkynylquinoxaline-2-carbonitriles with CH-acids and potassium *tert*-butoxide in THF or DMSO. One of the advantages of this method is mild reaction conditions. It is also obvious



3,**12**: R, X, Y = Ph, CO_2Et, CO_2Et (**aa**); Ph, CN, CO_2Et (**ab**); Ph, CN, CN (**ac**); Ph, CN, Tos (**ad**); Ph, 1-methyl-1*H*-benzo[*d*]imidazol-2-yl, CN (**ae**); Ph, NO_2, H (**af**); Ph, -C(O)-N(Me)-C(O)-N(Me)-C(O)- (**ag**); *p*-Tol, X, Y = CO_2Et, CO_2Et (**ba**); *p*-Tol, CN, CO_2Et (**bb**); *p*-Tol, CN, CN (**bc**); *p*-Tol, CN, Tos (**bd**); *p*-Tol, 1-methyl-1*H*-benzo[*d*]imidazol-2-yl, CN (**be**); *p*-Tol, NO_2, H (**bf**); *p*-Tol, -C(O)-N(Me)-C(O)-N(Me)-C(O)- (**bg**)

Scheme 3.



Scheme 4.

that the presence of the amino, cyano, and ethoxycarbonyl groups in the synthesized phenazines allows further modification of these molecules.

4. Experimental

4.1. General

Proton (^1H) and carbon (^{13}C) nuclear magnetic resonance (NMR) spectra were recorded on a Bruker DPX-250 spectrometer (250 and 62.9 MHz, respectively). ^1H and ^{13}C NMR chemical shifts are in parts per million (ppm) relative to Me_4Si. Coupling constants are in hertz (Hz). The IR spectra were recorded on an FT FSM-1202 spectrometer (http://infraspek.ru) using Nujol. The UV–vis spectra were recorded on Varian Cary 50 Probe spectrophotometer in $CHCl_3$. Mass spectra were measured on a Finnigan MAT INCOS 50 spectrometer. CHN analysis was accomplished by combustion analysis (Dumas and Pregl method). Melting points were determined in glass capillaries using a Stuart SMP30 device and are uncorrected. Flash column chromatography was performed on silica gel or Al_2O_3 (III–IV activity, Brockman). All commercial reagents were purchased from Acros and Aldrich.

4.2. X-ray structure determination

Atomic coordinates, bond lengths, bond angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC) and allocated the deposition numbers CCDC 993247 (**5a**) and CCDC 993248 (**5e**).

4.3. Reaction of 3-(phenylethynyl)quinoxaline-2-carbonitrile 1a with diethylmalonate

Diethyl malonate (160 mg, 0.15 mL, 1.0 mmol), *t*-BuOK (112 mg, 1.0 mmol), and dry THF (5 mL) were stirred for 30 min at room temperature. To the resulting mixture 3-(phenylethynyl)quinoxaline-2-carbonitrile **1a** (128 mg, 0.5 mmol) was added by portions.

The reaction mixture was stirred for 24 h at room temperature and then evaporated to dryness without heating. The residue was treated with several drops of acetic acid. After evaporation it was mixed with silica gel and purified by flash column chromatography on silica gel (3×40 cm) with CH_2Cl_2 as the eluent. The first fraction was recovered **1a** (9 mg, 7%). The red fraction with R_f 0.7 gave **5a** (39.5 mg, 23%). The yellow fraction with R_f 0.6 gave **7a** (2 mg, 1%). The yellowish fraction with R_f 0.4 gave **6a** (56 mg, 29%).

*4.3.1. Ethyl 1-amino-3-phenylphenazine-2-carboxylate **5a**.* Dark red needles with mp 164–165 °C (heptane); ^{1}H NMR ($CDCl_3$) δ ppm: 0.73 (t, J=7.1 Hz, 3H, CH_2CH_3), 3.95 (q, J=7.1 Hz, 2H, CH_2CH_3), 7.32 (s, 1H, H(4)), 7.34–7.45 (m, 7H, Ph and NH_2), 7.73–7.86 (m, 2H, H(7) and H(8)), 8.15–8.21 (m, 2H, H(6) and H(9)); ^{13}C NMR ($CDCl_3$) δ ppm: 13.6, 60.7, 105.6, 117.3, 127.4, 128.3, 128.4, 129.6, 130.1, 130.2, 131.8, 135.2, 141.4, 143.8, 144.7, 145.4, 146.3, 149.2, 169.5; IR, cm^{-1}: 1662 (C=O), 3339 and 3476 (NH_2); UV–vis, λ_{max} (log ε), nm: 320 (3.92), 365 sh (3.09), 450 (2.90), 481 (2.87), end absorption up to 534 nm; MS m/z: 343 ([M$^+$], 100), 314 (7), 297 (93), 269 (57), 255 (51), 242 (12), 214 (6), 157 (8), 140 (15), 129 (7), 121 (11), 115 (16), 102 (11), 89 (5), 77 (20). Anal. Calcd for $C_{21}H_{17}N_3O_2$: C, 73.45; H, 4.99; N, 12.24. Found: C, 73.51; H, 5.07; N, 12.36.

*4.3.2. Diethyl 2-phenyl-1H-cyclopenta[b]quinoxaline-1,1-dicarboxylate **6a**.* Yellow solid with mp 120–122 °C (heptane, lit.[6] 121–123 °C); ^{1}H NMR ($CDCl_3$) δ ppm: 1.03 (t, J=7.1 Hz, 6H, $2CH_2CH_3$), 4.04–4.26 (m, 4H, $2CH_2CH_3$), 7.41–7.45 (m, 3H, Ph), 7.63 (s, 1H, H(3)), 7.65–7.78 (m, 4H, Ph, H(6) and H(7)), 8.07 (dd, J=8.2, 1.6 Hz, 1H, H(5) or H(8)), 8.17 (dd, J=7.9, 1.9 Hz, 1H, H(8) or H(5)); ^{13}C NMR ($CDCl_3$) δ ppm: 14.1, 63.0, 69.1, 128.1, 129.0, 129.2, 129.3, 130.2, 130.3, 130.5, 130.6, 132.8, 140.7, 143.1, 154.4, 157.2, 157.6, 166.2; IR, cm^{-1}: 1730 and 1770 (C=O); UV–vis, λ_{max} (log ε), nm: 290 (4.25), 360 (4.19), 375 (4.22), 405 (4.08), 425 (4.11); MS m/z: 388 ([M]$^+$, 24), 287 (6), 270 (100), 259 (26), 243 (38), 229 (11), 214 (16), 152 (6), 140 (33), 129 (12), 115 (54), 102 (36), 88 (20), 77 (41). Anal. Calcd for $C_{23}H_{20}N_2O_4$: C, 71.12; H, 5.19; N, 7.21. Found: C, 70.91; H, 5.36; N, 7.28.

*4.3.3. Ethyl 6-cyano-10-oxo-8-phenyl-10H-pyrido[1,2-a]quinoxaline-9-carboxylate **7a**.* Yellow solid with mp 186–187 °C (heptane); ^{1}H NMR ($CDCl_3$) δ ppm: 1.10 (t, J=7.1 Hz, 3H, CH_2CH_3), 4.23 (q, J=7.1 Hz, 2H, CH_2CH_3), 7.32 (s, 1H, H(7)), 7.46–7.55 (m, 5H, Ph), 7.61–7.76 (m, 2H, H(2) and H(3)), 7.95 (dd, J=7.7, 1.9 Hz, 1H, H(4)), 9.91 (dd, J=8.7, 1.4 Hz, 1H, H(1)); ^{13}C NMR ($CDCl_3$) δ ppm: 14.2, 62.5, 109.0, 109.2, 114.0, 127.2, 128.3, 129.0, 129.1, 129.5, 130.5, 131.5, 132.6, 133.4, 135.1, 136.1, 136.7, 148.7, 160.1, 165.7; IR, cm^{-1}: 1652 and 1731 (C=O), 2234 (C≡N); UV–vis, λ_{max} (log ε), nm: 293 (3.66), 314 (3.63), 440 (3.48); MS m/z: 369 ([M$^+$], 15), 296 (10), 269 (88), 140 (21), 113 (11), 102 (19), 76 (16), 29 (100). Anal. Calcd for $C_{22}H_{15}N_3O_3$: C, 71.54; H, 4.09; N, 11.38. Found: C, 71.69; H, 3.92; N, 11.54.

4.4. Reaction of 3-(*p*-tolylethynyl)quinoxaline-2-carbonitrile 1b with diethylmalonate

The reaction was carried out similarly to the described above. The separation of the reaction products was carried out by flash column chromatography on silica gel (3×30 cm) with CH_2Cl_2 as the eluent. The first fraction recovered with R_f 0.7 was **1b** (43 mg, 32%). The red fraction with R_f 0.4 gave **5b** (31 mg, 17%). The yellowish fraction with R_f 0.2 gave **6b** (67 mg, 33%).

*4.4.1. Ethyl 1-amino-3-p-tolylphenazine-2-carboxylate **5b**.* Dark red needles with mp 151–152 °C (heptane); ^{1}H NMR ($CDCl_3$) δ ppm: 0.77 (t, J=7.1 Hz, 3H, CH_2CH_3), 2.40 (s, 3H, CH_3), 3.97 (q, J=7.1 Hz, 2H, CH_2CH_3), 7.21 (d, J=7.8 Hz, 2H, *p*-Tol), 7.31–7.40 (m, 5H, H(4), *p*-Tol and NH_2), 7.73–7.86 (m, 2H, H(7) and H(8)), 8.15–8.21 (m, 2H, H(6) and H(9)); ^{13}C NMR ($CDCl_3$) δ ppm: 13.6, 21.6, 60.8, 105.9, 117.1, 128.2, 129.0, 129.6, 130.0, 130.2, 131.7, 135.2, 137.2, 140.8, 141.3, 144.8, 145.4, 146.3, 149.0, 169.6; IR, cm^{-1}: 1684 (C=O), 3361 and 3472 (NH_2); UV–vis, λ_{max} (log ε), nm: 319 (4.50), 364 sh (3.57), 450 (3.36), 486 (3.33), end absorption up to 535 nm; MS m/z: 357 ([M$^+$], 33), 311 (28), 282 (17), 269 (18), 127 (7), 102 (11), 77 (14), 51 (8), 39 (8), 29 (100). Anal. Calcd for $C_{22}H_{19}N_3O_2$: C, 73.93; H, 5.36; N, 11.76. Found: C, 73.81; H, 5.45; N, 11.91.

*4.4.2. Diethyl 2-p-tolyl-1H-cyclopenta[b]quinoxaline-1,1-dicarboxylate **6b**.* Off-white needles with mp 130–131 °C (heptane); ^{1}H NMR ($CDCl_3$) δ ppm: 1.04 (t, J=7.2 Hz, 6H, $2CH_2CH_3$), 2.38 (s, 3H, CH_3), 4.04–4.26 (m, 4H, $2CH_2CH_3$), 7.23 (d, J=8.2 Hz, 2H, *p*-Tol), 7.57 (s, 1H, H(3)), 7.65 (d, J=8.2 Hz, 2H, *p*-Tol), 7.68–7.79 (m, 2H, H(6) and H(7)), 8.05 (dd, J=8.1, 1.4 Hz, 1H, H(5) or H(8)), 8.16 (dd, J=7.7, 1.8 Hz, 1H, H(8) or H(5)); ^{13}C NMR ($CDCl_3$) δ ppm: 14.2, 21.8, 63.0, 69.0, 128.1, 129.1, 129.2, 129.3, 129.8, 130.0, 130.2, 130.5, 140.6, 140.9, 143.1, 154.5, 157.3, 157.9, 166.3; IR, cm^{-1}: 1730 and 1764 (C=O); UV–vis, λ_{max} (log ε), nm: 306 (4.50), 365 (4.76), 381 (4.75); MS m/z: 402 ([M]$^+$, 18), 284 (41), 273 (12), 255 (20), 127 (9), 115 (6), 102 (7), 77 (7), 29 (100). Anal. Calcd for $C_{24}H_{22}N_2O_4$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.49; H, 5.35; N, 7.04.

4.5. Reaction of 3-(phenylethynyl)quinoxaline-2-carbonitrile 1a with ethyl cyanoacetate

Ethyl cyanoacetate (160 mg, 0.15 mL, 1.0 mmol), *t*-BuOK (112 mg, 1.0 mmol), and dry THF (5 mL) were stirred for 30 min at room temperature. To the resulting mixture 3-(phenylethynyl)quinoxaline-2-carbonitrile **1a** (128 mg, 0.5 mmol) was added by portions. The reaction mixture was stirred for 24 h at room temperature and filtered. The orange precipitate over the filter was rinsed with diethyl ether. Then filtrate and precipitate were treated separately.

The orange precipitate was purified by flash column chromatography on silica gel (3×30 cm) with CH_2Cl_2 as the eluent. The red fraction with R_f 0.7 gave **5c** (65 mg, 44%). The next orange fraction with R_f 0.6 gave **8** (6 mg, 3%).

The filtrate was evaporated to dryness without heating. The residue was treated with several drops of acetic acid. After evaporation it was mixed with silica gel and purified by flash column chromatography on silica gel (3×30 cm) with CH_2Cl_2 as the eluent. The first fraction was recovered **1a** (22 mg, 17%). The red fraction with R_f 0.7 gave **5c** (16 mg, 11%). The orange fraction with R_f 0.6 gave **8** (2 mg, 1%).

*4.5.1. 1-Amino-3-phenylphenazine-2-carbonitrile **5c**.* Red-orange needles with mp 264–265 °C (MeCN); ^{1}H NMR ($CDCl_3$) δ ppm: 6.40 (br s, 2H, NH_2), 7.48–7.57 (m, 4H, Ph and H(4)), 7.69–7.73 (m, 2H, Ph), 7.81–7.95 (m, 2H, H(7) and H(8)), 8.22–8.28 (m, 2H, H(6) and H(9)); ^{13}C NMR (pyridine-d_5) δ ppm: 87.7, 116.3, 118.7, 129.2, 129.3, 129.5, 129.9, 130.2, 130.7, 132.3, 134.3, 139.8, 141.6, 145.0, 145.4, 145.7, 153.6; IR, cm^{-1}: 2201 (C≡N), 3378 and 3482 (NH_2); UV–vis, λ_{max} (log ε), nm: 314 (3.93), 364 sh (2.96), 385 sh (2.84), 445 (2.80), 479 (2.68), end absorption up to 534 nm; MS m/z: 296 ([M$^+$], 100), 268 (9), 168 (9), 148 (9), 140 (8), 134 (6), 121 (7), 102 (9), 77 (12). Anal. Calcd for $C_{19}H_{12}N_4$: C, 77.01; H, 4.08; N, 18.91. Found: C, 77.13; H, 4.28; N, 18.77.

*4.5.2. (Z)-Ethyl 2-cyano-2-(9-cyano-10-oxo-8-phenyl-5H-pyrido[1,2-a]quinoxalin-6(10H)-ylidene)acetate **8**.* Orange needles with mp 218–220 °C (CH_2Cl_2/EtOH, 100:1 v/v; lit.[6] 218–220 °C); ^{1}H NMR ($CDCl_3$) δ ppm: 1.40 (t, J=7.2 Hz, 3H, CH_2CH_3), 4.38 (q, J=7.2 Hz, 2H, CH_2CH_3), 7.20–7.25 (m, 1H, H_{arom}), 7.28–7.35 (m, 1H, H_{arom}), 7.39–7.45 (m, 1H, H_{arom}), 7.56–7.58 (m, 3H, H_{arom}), 7.83–7.87 (m, 2H, H_{arom}), 8.33 (s, 1H, H(7)), 9.31 (d, J=8.5 Hz, 1H, H(1)), 13.54 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ ppm: 14.6, 62.8, 71.9, 106.5, 111.6, 115.3, 117.9, 118.5, 121.6, 125.0, 126.1, 126.7, 129.1, 129.3, 129.9, 132.3, 133.8, 134.3, 150.8, 156.5, 160.7, 169.9; IR, cm^{-1}: 1648 and 1662 (C=

O), 2206 (C≡N), 3000–3500 (N–H); UV–vis, λ_{max} (log ε), nm: 242 (4.23), 260 (4.25), 327 (4.14), 422 (4.10), 485 sh (3.75); MS *m*/*z*: 408 ([M]$^+$, 46), 362 (100), 334 (39), 305 (31), 280 (17), 269 (7), 253 (5), 235 (14), 209 (6), 169 (7), 153 (11), 140 (33), 127 (8), 113 (16), 102 (33), 88 (9), 77 (49). Anal. Calcd for $C_{24}H_{16}N_4O_3$: C, 70.58; H, 3.95; N, 13.72. Found: C, 70.72; H, 4.13; N, 13.89.

4.6. Reaction of 3-(*p*-tolylethynyl)quinoxaline-2-carbonitrile 1b with ethyl cyanoacetate

The reaction was carried out similarly to the described in Section 4.5. The separation of the reaction products was carried out by flash column chromatography on silica gel (2.5×60 cm) with $CHCl_3$ as the eluent. The first fraction with R_f 0.5 was recovered **1b** (32 mg, 24%). The red fraction with R_f 0.2 gave **5d** (56 mg, 36%). The yellowish fraction with R_f 0.1 gave **7b** (7 mg, 4%).

4.6.1. 1-Amino-3-p-tolylphenazine-2-carbonitrile ***5d***. Red-orange needles with mp 267–268 °C (*i*-PrOH); ^{1}H NMR ($CDCl_3$) δ ppm: 2.43 (s, 3H, CH_3), 6.35 (br s, 2H, NH_2), 7.28 (d, *J*=8.0 Hz, 2H, *p*-Tol), 7.35 (s, 1H, H(4)), 7.61 (d, *J*=8.0 Hz, 2H, *p*-Tol), 7.79–7.91 (m, 2H, H(7) and H(8)), 8.18–8.24 (m, 2H, H(6) and H(9)); ^{13}C NMR (pyridine-d_5) δ ppm: 21.3, 87.9, 116.0, 118.8, 129.4, 129.8, 129.9, 130.2, 130.7, 132.3, 134.3, 136.9, 139.1, 141.5, 145.1, 145.5, 145.7, 153.6; IR, cm^{-1}: 2202 (C≡N), 3372 and 3478 (NH_2); UV–vis, λ_{max} (log ε), nm: 316 (4.29), 369 sh (3.35), 387 sh (3.25), 444 (3.18), 478 (3.06), end absorption up to 534 nm; MS *m*/*z*: 310 ([M$^+$], 100). Anal. Calcd for $C_{20}H_{14}N_4$: C, 77.40; H, 4.55; N, 18.05. Found: C, 77.22; H, 4.38; N, 17.93.

4.6.2. 10-Oxo-8-p-tolyl-10H-pyrido[1,2-a]quinoxaline-6,9-dicarbonitrile ***7b***. Yellow solid with mp 298–299 °C (*i*-PrOH); ^{1}H NMR ($CDCl_3$) δ ppm: 2.46 (s, 3H, CH_3), 7.37 (d, *J*=0.8 Hz, 1H, H(7)), 7.40 (d, *J*=8.2 Hz, 2H, *p*-Tol), 7.67 (d, *J*=8.2 Hz, 2HH, *p*-Tol), 7.72–7.75 (m, 1H, H(3)), 7.78–7.86 (m, 1H, H(2)), 8.01 (dd, *J*=7.8, 1.7 Hz, 1H, H(4)), 9.88 (dm, *J*=8.8 Hz, 1H, H(1)); ^{13}C NMR ($CDCl_3$) δ ppm: 22.0, 107.8, 113.7, 115.6, 121.8, 128.1, 128.8, 128.9, 129.7, 130.5, 130.6, 131.6, 131.8, 134.2, 134.5, 134.6, 137.0, 142.9, 157.1; IR (KBr), cm^{-1}: 1673 (C=O), 2223 (C≡N); UV–vis, λ_{max} (log ε), nm: 280 (3.89), 309 (3.82), 342 (3.72), 431 sh (3.56), 456 (3.65), 481 sh (3.52); MS *m*/*z*: 336 ([M]$^+$, 100), 308 (72), 292 (6), 168 (6), 154 (11), 140 (10), 127 (12), 102 (10), 76 (9). Anal. Calcd for $C_{21}H_{12}N_4O$: C, 74.99; H, 3.60; N, 16.66. Found: C, 75.13; H, 3.45; N, 16.83.

4.7. Reaction of 3-(phenylethynyl)quinoxaline-2-carbonitrile 1a with malonodinitrile

Malonodinitrile (66 mg, 1.0 mmol), *t*-BuOK (112 mg, 1.0 mmol), and dry THF (5 mL) were stirred for 30 min at room temperature. To the resulting mixture 3-(phenylethynyl)quinoxaline-2-carbonitrile **1a** (128 mg, 0.5 mmol) was added by portions. The reaction mixture was stirred for 24 h at room temperature and then evaporated to dryness without heating. The residue was treated with some drops of acetic acid. After evaporation it was mixed with Al_2O_3 and purified by flash column chromatography on Al_2O_3 (2×40 cm) with CH_2Cl_2 as the eluent. The first fraction recovered was **1a** (trace). The red fraction with R_f 0.4 gave **5c** (95 mg, 64%).

Reaction of **1a** (128 mg, 0.5 mmol) with malonodinitrile (66 mg, 1.0 mmol), *t*-BuOK (112 mg, 1.0 mmol), and dry DMSO (5 mL) was carried out similarly.

4.8. Reaction of 3-(phenylethynyl)quinoxaline-2-carbonitrile 1a with 2-tosylacetonitrile

2-Tosylacetonitrile (195 mg, 1.0 mmol), *t*-BuOK (112 mg, 1.0 mmol), and dry THF (5 mL) were stirred for 30 min at room temperature. To the resulting mixture 3-(phenylethynyl) quinoxaline-2-carbonitrile **1a** (128 mg, 0.5 mmol) was added by portions. The reaction mixture was stirred for 11 h at 65 °C and then evaporated to dryness without heating. The residue was treated with some drops of acetic acid. After evaporation it was mixed with silica gel and purified by flash column chromatography on silica gel (3×40 cm) with CH_2Cl_2 as the eluent. The first fraction recovered was **1a** (trace). The red fraction with R_f 0.7 gave **5c** (59 mg, 40%). The yellow fraction with R_f 0.1 gave **3ad** (43 mg, 19%).

4.8.1. 1-Imino-3-phenyl-2-tosyl-1,2-dihydrophenazine-2-carbonitrile ***3ad***. Yellow solid with mp 319–320 °C (*i*-PrOH); ^{1}H NMR ($CDCl_3$) δ ppm: 2.30 (s, 3H, Me), 6.70 (br s, 1H, NH), 7.21 (d, *J*=8.2 Hz, 2H, Tos), 7.45–7.60 (m, 5H, Ph), 7.82–7.96 (m, 2H, H(7) and H(8)), 8.08 (d, *J*=8.2 Hz, 2H, Tos), 8.12–8.23 (m, 2H, H(6) and H(9)); ^{13}C NMR (DMSO-d_6) δ ppm: 21.8, 90.1, 116.7, 121.1, 128.5, 128.7, 128.9, 129.2, 129.5, 129.6, 130.2, 132.7, 133.1, 134.3, 139.0, 140.6, 141.5, 141.8, 143.6, 143.7, 150.9, 155.1; IR (KBr), cm^{-1}: 1150 (SO_2, s), 1319 (SO_2, as), 2214 (C≡N), 3311 (NH); UV–vis, λ_{max} (log ε), nm: 304 (4.02), 353 (3.41), 366 (3.32), 437 (3.28), 486 sh (2.87); MS *m*/*z*: 295 (33, [M–Tos]$^+$), 294 (27, [M–TosH]$^+$), 293 (34, [M–TosH$_2$]$^+$), 139 (16), 91 (78), 89 (15), 77 (36), 65 (100). Anal. Calcd for $C_{26}H_{18}N_4O_2S$: C, 69.32; H, 4.03; N, 12.44; S, 7.12. Found: C, 69.47; H, 3.88; N, 12.51.

4.9. Reaction of 3-(phenylethynyl)quinoxaline-2-carbonitrile 1a with 2-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)acetonitrile

2-(1-Methyl-1*H*-benzo[*d*]imidazol-2-yl)acetonitrile (171 mg, 1.0 mmol), *t*-BuOK (112 mg, 1.0 mmol), and dry THF (5 mL) were stirred for 30 min at room temperature. To the resulting mixture 3-(phenylethynyl)quinoxaline-2-carbonitrile **1a** (128 mg, 0.5 mmol) was added by portions. The reaction mixture was stirred for 48 h at room temperature and then evaporated to dryness without heating. The residue was treated with some drops of acetic acid. After evaporation it was mixed with silica gel and purified by flash column chromatography on silica gel (2.5×40 cm) with $CHCl_3$ as the eluent. The first fraction recovered was **1a** (32 mg, 25%). The orange fraction was collected and purified additionally by flash column chromatography on Al_2O_3 (2.5×20 cm) with $CHCl_3$ as the eluent. The orange red fraction with R_f 0.65 gave **5e** (48 mg, 24%).

4.9.1. 2-(1-Methyl-1H-benzo[d]imidazol-2-yl)-3-phenylphenazin-1-amine ***5e***. Red solid with mp 199–200 °C (heptane); ^{1}H NMR ($CDCl_3$) δ ppm: 3.02 (s, 3H, CH_3), 6.47 (br s, 2H, NH_2), 7.14–7.42 (m, 8H, H_{arom}), 7.70 (s, 1H, H(4)), 7.76–7.91 (m, 3H, H_{arom}), 8.21–8.26 (m, 2H, H(6) and H(9)); ^{13}C NMR ($CDCl_3$) δ ppm: 31.0, 106.2, 110.0, 116.9, 119.9, 122.8, 123.1, 128.3, 128.9, 129.1, 129.7, 130.2, 130.3, 131.5, 135.0, 135.6, 140.7, 141.8, 143.4, 144.5, 145.1, 145.4, 146.8, 151.6; IR (KBr), cm^{-1}: 3374 and 3477 (NH_2); UV–vis, λ_{max} (log ε), nm: 321 (4.14), 380 sh (3.42), 439 (3.12), 486 (3.06), end absorption up to 524 nm; MS *m*/*z*: 401 ([M$^+$], 9), 384 (7), 282 (20), 201 (15), 192 (14), 140 (14), 119 (14), 102 (39), 92 (17), 77 (100). Anal. Calcd for $C_{26}H_{19}N_5$: C, 77.79; H, 4.77; N, 17.44. Found: C, 77.64; H, 4.95; N, 17.36.

4.10. Reaction of 3-(*p*-tolylethynyl)quinoxaline-2-carbonitrile 1b with 2-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)acetonitrile

The reaction was carried out similarly to the above reaction with 2-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)acetonitrile (171 mg, 1.0 mmol), *t*-BuOK (112 mg, 1.0 mmol), dry THF (5 mL), and 3-(*p*-tolylethynyl)quinoxaline-2-carbonitrile **1b** (135 mg, 0.5 mmol) for 72 h at room temperature.

4.10.1. 2-(1-Methyl-1H-benzo[d]imidazol-2-yl)-3-p-tolylphenazin-1-amine ***5f***. Red solid with mp 282–283 °C (heptane); ^{1}H NMR

($CDCl_3$) δ ppm: 2.27 (s, 3H, CH_3), 3.05 (s, 3H, CH_3), 6.46 (br s, 2H, NH_2), 7.01 (d, J=8.0 Hz, 2H, *p*-Tol), 7.16–7.38 (m, 5H, H_{arom}), 7.67 (s, 1H, H(4)), 7.75–7.91 (m, 3H, H_{arom}), 8.20–8.25 (m, 2H, H(6) and H(9)); ^{13}C NMR ($CDCl_3$) δ ppm: 21.6, 31.0, 106.3, 110.1, 116.7, 119.9, 122.7, 123.0, 124.6, 128.9, 129.7, 130.1, 130.3, 131.5, 135.0, 135.6, 137.8, 138.2, 141.7, 143.4, 144.6, 145.1, 145.4, 146.7, 151.8; IR (KBr), cm^{-1}: 3364 and 3478 (NH_2); UV–vis, λ_{max} (log ε), nm: 328 (3.78), 391 (3.21), 438 (3.07), 490 (2.85), end absorption up to 524 nm; MS *m*/*z*: 415 ([M^+], 4), 208 (11), 200 (12), 119 (15), 115 (12), 102 (42), 91 (23), 77 (100). Anal. Calcd for $C_{27}H_{21}N_5$: C, 78.05; H, 5.09; N, 16.86. Found: C, 78.16; H, 5.29; N, 16.70.

4.11. Reaction of 3-(phenylethynyl)quinoxaline-2-carbonitrile 1a with nitromethane

Method A: Nitromethane (61 mg, 0.054 mL, 1.0 mmol), *t*-BuOK (112 mg, 1.0 mmol), and dry THF (5 mL) were stirred for 30 min at room temperature. To the resulted mixture 3-(phenylethynyl)quinoxaline-2-carbonitrile **1a** (128 mg, 0.5 mmol) was added by portions. The reaction mixture was stirred for 48 h at room temperature and then evaporated to dryness without heating. The residue was treated with some drops of acetic acid. After evaporation it was mixed with silica gel and purified by flash column chromatography on silica gel (2.5×40 cm) with $CHCl_3$ as the eluent. The first fraction recovered was **1a** (99 mg, 78%). The orange fraction with R_f 0.2 gave **5g** (9 mg, 6%).

Method B: The reaction of **1a** (128 mg, 0.5 mmol) with nitromethane (61 mg, 0.054 mL, 1.0 mmol), *t*-BuOK (112 mg, 1.0 mmol), and dry DMSO (3 mL) was carried out similarly for 24 h at room temperature. The reaction mixture was diluted with saturated solution of NH_4Cl (50 mL) and extracted with $CHCl_3$ (6×30 mL). The extract was evaporated to dryness under reduced pressure. The residue was mixed with silica gel and purified by flash column chromatography on silica gel (2.5×60 cm) with CH_2Cl_2 as the eluent. The yellow fraction with R_f 0.7 gave **9** (42 mg, 29%). The next orange fraction gave **5g** (57 mg, 36%).

Method C: A mixture of **1a** (128 mg, 0.5 mmol), nitromethane (92 mg, 0.081 mL, 1.5 mmol), DBU (228 mg, 1.5 mmol), and dry acetonitrile (5 mL) was stirred under reflux for 7 h. The reaction mixture was then evaporated to dryness without heating. The residue was treated with some drops of acetic acid. After evaporation it was mixed with silica gel and purified by flash column chromatography on silica gel (2.5×40 cm) with CH_2Cl_2 as the eluent. The first fraction recovered was **1a** (2 mg). The orange fraction with R_f 0.5 gave **5g** (15 mg, 9%). The yellowish fraction with R_f 0.1 gave **10** (14 mg, 10%).

4.11.1. 2-Nitro-3-phenylphenazin-1-amine ***5g***. Red-orange solid with mp 216–217 °C (heptane/ethanol, 10:1 v/v); ^1H NMR ($CDCl_3$) δ ppm: 7.34 (s, 1H, H(4)), 7.38–7.48 (m, 5H, Ph), 7.71 (br s, 2H, NH_2), 7.82–7.95 (m, 2H, H(7) and H(8)), 8.20–8.26 (m, 2H, H(6) and H(9)); ^{13}C NMR ($CDCl_3$) δ ppm: 118.9, 127.6, 128.4, 129.0, 129.1, 129.9, 130.1, 131.2, 132.8, 135.4, 139.9, 141.0, 141.5, 144.1, 144.6, 145.8; IR (KBr), cm^{-1}: 3350 and 3462 (NH_2); UV–vis, λ_{max} (log ε), nm: 275 (4.06), 352 (3.91), 398 sh (3.44), 447 sh (3.01), 485 sh (2.84), end absorption up to 533 nm; MS *m*/*z*: 316 ([M^+], 100), 299 (18), 259 (27), 286 (11), 270 (23), 258 (7), 243 (10), 193 (6), 140 (7), 115 (11), 102 (11), 77 (14). Anal. Calcd for $C_{18}H_{12}N_4O_2$: C, 68.35; H, 3.82; N, 17.71. Found: C, 68.49; H, 4.00; N, 17.57.

4.11.2. 2-(Nitromethyl)-3-(phenylethynyl)quinoxaline ***9***. Beige solid with mp 173–174 °C (hexane); ^1H NMR ($CDCl_3$) δ ppm: 6.14 (s, 2H, CH_2), 7.44–7.55 (m, 3H, Ph), 7.71 (dd, J=7.6, 1.9 Hz, 2H, Ph), 7.86–7.97 (m, 2H, H(6) and H(7)), 8.16–8.23 (m, 2H, H(5) and H(8)); ^{13}C NMR ($CDCl_3$) δ ppm: 78.9, 84.7, 97.5, 120.7, 128.7, 129.1, 129.5, 130.3, 131.3, 131.9, 132.4, 139.3, 140.3, 142.2, 145.6; IR (KBr), cm^{-1}: 1354 and 1556 (NO_2), 2212 (C≡C), 2931 (C–H); UV–vis, λ_{max} (log ε), nm: 292 (4.16), 352 (4.06), 362 (4.03), 436 (3.04), 490 (2.69); MS *m*/*z*: 289 ([M^+], 6), 259 (28), 243 ([$M-NO_2$]$^+$, 73), 127 (9), 121 (15), 115 (100), 89 (24), 76 (15). Anal. Calcd for $C_{17}H_{11}N_3O_2$: C, 70.58; H, 3.83; N, 14.53. Found: C, 70.40; H, 3.72; N, 14.45.

4.11.3. 3-Phenylpyrido[4,3-b]quinoxalin-1(2H)-one ***10***. Yellow needles decomp. >310 °C (EtOH); ^1H NMR (DMSO-d_6) δ ppm: 7.09 (s, 1H, H(4)), 7.33–7.53 (m, 3H, Ph), 7.79 (d, J=7.4 Hz, 2H, Ph), 7.95–8.07 (m, 2H, H(7) and H(8)), 8.25–8.37 (m, 2H, H(6) and H(9)); ^{13}C NMR (DMSO-d_6) δ ppm: 107.6, 128.6, 129.3, 129.4, 129.8, 130.2, 131.0, 131.2, 132.8, 134.0, 142.8, 143.3, 143.6, 149.9, 165.0; IR (KBr), cm^{-1}: 1725 (C=O), 3238 (N–H); UV–vis (MeCN), λ_{max} (log ε), nm: 321 (4.13), 346 sh (3.91), 402 (3.41), 442 sh (3.30), 483 (2.93); MS *m*/*z*: 273 ([M^+], 84), 272 (100), 244 (11), 116 (13), 102 (16), 89 (25), 76 (7). Anal. Calcd for $C_{17}H_{11}N_3O$: C, 74.71; H, 4.06; N, 15.38. Found: C, 74.87; H, 3.97; N, 15.54.

4.12. Reaction of 3-(*p*-tolylethynyl)quinoxaline-2-carbonitrile 1b with nitromethane

The reaction was carried out similarly to the above reaction with 3-(*p*-tolylethynyl)quinoxaline-2-carbonitrile **1b** (135 mg, 0.5 mmol) for 72 h at room temperature.

4.12.1. 2-Nitro-3-p-tolylphenazin-1-amine ***5h***. Red-orange solid with mp 233–234 °C (heptane/ethanol, 10:1 v/v); ^1H NMR ($CDCl_3$) δ ppm: 2.41 (s, 3H, CH_3), 7.27 (d, J=8.0 Hz, 2H, *p*-Tol), 7.32–7.37 (m, 3H, *p*-Tol and H(4)), 7.64 (br s, 2H, NH_2), 7.81–7.95 (m, 2H, H(7) and H(8)), 8.17–8.24 (m, 2H, H(6) and H(9)); ^{13}C NMR ($CDCl_3$) δ ppm: 21.7, 118.6, 127.5, 127.6, 129.8, 129.9, 130.1, 131.1, 132.7, 135.3, 136.9, 138.3, 141.0, 141.4, 143.9, 144.6, 145.8; IR (KBr), cm^{-1}: 3351 and 3462 (NH_2); UV–vis, λ_{max} (log ε), nm: 276 (4.09), 356 (3.95), 406 sh (3.51), 454 sh (3.16), 497 sh (3.02), end absorption up to 537 nm; MS *m*/*z*: 330 ([M^+], 100), 313 (27), 300 (14), 285 (22), 269 (20), 256 (10), 246 (8), 232 (13), 193 (9), 140 (10), 128 (14), 115 (15), 102 (16), 77 (17). Anal. Calcd for $C_{19}H_{14}N_4O_2$: C, 69.08; H, 4.27; N, 16.96. Found: C, 68.89; H, 4.15; N, 16.78.

4.13. Reaction of 3-(phenylethynyl)quinoxaline-2-carbonitrile 1a with 1,3-barbituric acid

1,3-Barbituric acid (94 mg, 0.6 mmol), K_2CO_3 (83 mg, 0.6 mmol), and dry DMF (5 mL) were stirred for 30 min at 80 °C. To the resulting mixture 3-(phenylethynyl)quinoxaline-2-carbonitrile **1a** (128 mg, 0.5 mmol) was added by portions. The reaction mixture was stirred for 30 h at 80 °C and then treated with saturated aqueous solution of NH_4Cl (50 mL). The resulted mixture was extracted with $CHCl_3$ (5×20 mL). The extract was dried over Na_2SO_4 and evaporated to dryness. The residue was mixed with silica gel and purified by flash column chromatography on silica gel (2.5×30 cm) with $CHCl_3$ as the eluent. The yellowish fraction with R_f 0.1 gave **11** (7 mg, 4%).

4.13.1. 3-Methyl-5-phenylpyrimido[4,5-a]phenazine-2,4(1H,3H)-dione ***11***. Yellow solid with mp 252–253 °C (*i*-PrOH); ^1H NMR ($CDCl_3$) δ ppm: 3.43 (s, 3H, CH_3), 7.40–7.49 (m, 5H, Ph), 7.77 (s, 1H, H(6)), 7.89–8.00 (m, 2H, H(9) and H(10)), 8.26–8.31 (m, 2H, H(8) and H(11)), 10.02 (br s, 1H, NH); ^{13}C NMR (pyridine-d_5) δ ppm: 27.8, 110.1, 125.2, 127.8, 128.1, 129.5, 129.9, 130.3, 131.7, 132.8, 133.5, 141.0, 142.2, 142.4, 144.4, 144.5, 145.8, 158.7, 161.7; IR (KBr), cm^{-1}: 1668 and 1674 (C=O); UV–vis, λ_{max} (log ε), nm: 301 (3.98), 356 (3.31), 366 (3.29), 428 (3.13); MS *m*/*z*: 354 ([$M]^+$, 32), 297 (10), 269 (43), 255 (41), 177 (32), 165 (11), 140 (62), 127 (11), 114 (51), 102 (94), 88

(29), 77 (100). Anal. Calcd for $C_{21}H_{14}N_4O_2$: C, 71.18; H, 3.98; N, 15.81. Found: C, 71.03; H, 4.15; N, 15.98.

4.14. Synthesis of 3-phenylpyrido[4,3-*b*]quinoxalin-1(2*H*)-one 10

A mixture of **1a** (128 mg, 0.5 mmol), DBU (228 mg, 1.5 mmol), and dry acetonitrile (5 mL) was stirred for 24 h at room temperature. The reaction mixture was then evaporated to dryness without heating. The residue was treated with some drops of acetic acid. After evaporation it was mixed with silica gel and purified by flash column chromatography on silica gel (2.5×15 cm) with CH_2Cl_2 as the eluent. The yellowish fraction with R_f 0.1 gave **10** (79 mg, 58%).

Acknowledgements

We gratefully acknowledge the Russian Foundation for Basic Research (grant no. 14-03-00032-a) for financial support of this research. We also thank Drs. Anna Tkachuk and Oleg Burov for technical assistance.

Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2014.05.023. These data include MOL files and InChiKeys of the most important compounds described in this article.

References and notes

1. (a) Laursen, J. B.; Nielsen, J. *Chem. Rev.* **2004**, *104*, 1663–1685; (b) Mavrodi, D. V.; Blankenfeldt, W.; Thomashow, L. S. *Annu. Rev. Phytopathol.* **2006**, *44*, 417–445; (c) Pierson, L. S.; Pierson, E. A. *Appl. Microbiol. Biotechnol.* **2010**, *86*, 1659–1670; (d) Mavrodi, D. V.; Pareiko, J. A.; Mavrodi, O. V.; Kwak, Y.-S.; Weller, D. M.; Blankenfeldt, W.; Thomashow, L. S. *Environ. Microbiol.* **2013**, *15*, 675–686; (e) Van Rensburg, C. E. J.; Jooné, G. K.; Sirgel, F. A.; Matlola, N. M.; O'Sullivan, J. F. *Chemotheraphy* **2000**, *46*, 43–48; (f) Cimmino, A.; Evidente, A.; Mathieu, V.; Andolfi, A.; Lefranc, F.; Kornienko, A.; Kiss, R. *Nat. Prod. Rep.* **2012**, *29*, 487–501; (g) Gloster, D. F.; Cincotta, L.; Foley, J. W. *J. Heterocycl. Chem.* **1999**, *36*, 25–32; (h) Conda-Sheridan, M.; Marler, L.; Park, E.-J.; Kondratyuk, T. P.; Jermihov, K.; Mesecar, A. D.; Pezzuto, J. M.; Asolkar, R. N.; Fenical, W.; Cushman, M. *J. Med. Chem.* **2010**, *53*, 8688–8699; (i) Borrero, N. V.; Bai, F.; Perez, C.; Duong, B. Q.; Rocca, J. R.; Jin, S.; Huigens, R. W. *Org. Biomol. Chem.* **2014**, *12*, 881–886.
2. Tyaglivy, A. S.; Gulevskaya, A. V.; Pozharskii, A. F.; Askalepova, O. I. *Tetrahedron* **2013**, *69*, 9804–9812.
3. (a) Moustafa, O. S.; Badr, M. Z. A.; Kamel, E. M. *Pharmazie* **2000**, *55*, 896–899; (b) Carlier, L.; Baron, M.; Chamayou, A.; Couarraze, G. *Tetrahedron Lett.* **2011**, 4686–4689.
4. Bordwell pK_a table (acidity in DMSO) (http://www.chem.wisc.edu/areas/reich/pkatable/).
5. Anisimova, V. A.; Askalepova, O. I.; Bagdasarov, K. N.; Chernov'yants, M. S. *Chem. Heterocycl. Compd.* **1988**, *24*, 281–284.
6. Gulevskaya, A. V.; Nguyen, H. T. L.; Tyaglivy, A. S.; Pozharskii, A. F. *Tetrahedron* **2012**, *68*, 488–498.
7. (a) Meusel, M.; Ambrożak, A.; Hecker, T. K.; Gütschow, M. *J. Org. Chem.* **2002**, *68*, 4684–4692; (b) Ambrożak, A.; Gütschow, M. *J. Heterocycl. Chem.* **2006**, *43*, 807–811; (c) Krasnov, K. A.; Kartsev, V. G.; Khrustalev, V. N. *Heterocycles* **2007**, *71*, 13–18.
8. Astruc, D.; Djankovitch, L.; Aranzaes, J. R. *ARKIVOC* **2006**, *iv*, 173–188.