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1,3-Dipolar cycloaddition of azomethine imines to ethynyl hetarenes: A synthetic route to 2,3-dihydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-one based heterobiaryls

Julia I. Nelina-Nemtseva [a], Anna V. Gulevskaya [a, *], Vitaliy V. Suslonov [b], Alexander D. Misharev [b]

[a] Department of Organic Chemistry, Southern Federal University, Zorge 7, Rostov-on-Don, 344090, Russian Federation
[b] Center for X-ray Diffraction Studies and Chemical Analysis and Materials Research Centre, Saint Petersburg State University, Universitetskii Pr., 26, Peterhof, 198504, Russian Federation

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Heterobiaryls

ABSTRACT

π-Deficient ethynyl hetarenes were used as dipolarophiles in a 1,3-dipolar cycloaddition reaction with azomethine imines (2-arylidene-5-oxopyrazolidin-2-ium-1-ides). Both CuI-catalyzed and catalyst-free thermally induced reactions proceeded with high regioselectivity providing 6-hetaryl-5-aryl-2,3-dihydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-ones in moderate to excellent yields. The ethynyl hetarenes (pyridines, pyrazines, quinoxalines, pteridines and pyrimido[4,5-*c*]pyridazines) with *ortho*-methyl, *ortho*-cyano and *ortho*-alkynyl substituents were applicable to this reaction. 1,3-Dipolar cycloaddition reactions of alkynyl hetarenes with azomethine imines or other 1,3-dipole reagents can be considered as an alternative synthetic approach to heterobiaryls.

1. Introduction

Tetrahydropyrazolo[1,2-*a*]pyrazolones have been studied since the late 1980s as analogues of penicillin and cephalosporin antibiotics[1a-f] and have been developed as herbicides and pesticides,[1g,h] antitumor agents,[1i] calcitonin agonist[1j] and as potent drugs for treatment of cognitive dysfunctions such as Alzhheimer's disease. Among a variety of reported synthetic approaches to these compounds,[2] 1,3-dipolar cycloaddition[3] of azomethine imines with alkynes is one of the most useful and straightforward tool. Dorn an Otto were the first to report on the synthesis of dimethyl 3,3-dimethyl-7-oxo-3,5,6,7-tetrahydropyrazolo[1,2-*a*]pyrazole-1,2-dicarboxylate by refluxing 5-oxo-2-(propan-2-ylidene)pyrazolidin-2-ium-1-ide with dimethyl acetylenedicarboxylate (DMAD) in CH_2Cl_2 (Scheme 1, ***a***).[4] The method was very useful,[5] however, the reaction with other azomethine imines required rather harsh conditions (refluxing in toluene, xylenes, anisole *etc.*)[5b-g] and at using asymmetric acetylenes led to mixtures of regioisomers in variable yields.[5b,c,f] In most cases, strongly activated esters of acetylenedicarboxylic, propiolic and tetrolic acids were used as dipolarophiles. Thermal cycloaddition of 2-benzylidene-3-methyl-5-oxopyrazolidin-2-ium-1-ide with less electron-deficient acetylenic sulfones gave poor yields of the cycloaddition products (Scheme 1, ***b***).[5h] In 2003 Fu's group demonstrated that 1,3-dipolar cycloaddition of azomethine imines with 1-alkynes can be catalyzed by CuI (Scheme 1, ***c***).[6a,b] Moreover, the reaction afforded a single regioisomer and, at using a chiral ligand, generated the product in very good enantiomeric excess. Since then, various copper catalysts, including heterogeneous, ligand-free Cu(I) zeolites,[6c] $[Cu(\mu\text{-}OH)(TMEDA)_2Cl_2]$,[6d] $(Bu^n{}_4N^+)_4[\gamma\text{-}H_2SiW_{10}O_{36}Cu_2(\mu\text{-}1,1\text{-}N_3)_2]$,[6e] ligand-free, heterogeneous supported $Cu(OH)_x/Al_2O_3$,[6f] CuHMDS/(*S*)-DIP-BINAP,[6g,h] and some others.[6i-l] Notably, CuHMDS/(*S*)-DIP-BINAP[6g,h] system afforded the cycloadducts in an unique 5,7-disubstituted manner (Scheme 1, ***d***). The catalytic reaction presumably involves the transient formation of a copper acetylide to enhance the reactivity of the dipolarophile. That is why all the catalytic methods are limited to the use of terminal alkynes. 1,3-Dipolar cycloaddition of azomethine imines with internal alkynes,

* Corresponding author.
E-mail address: agulevskaya@sfedu.ru (A.V. Gulevskaya).

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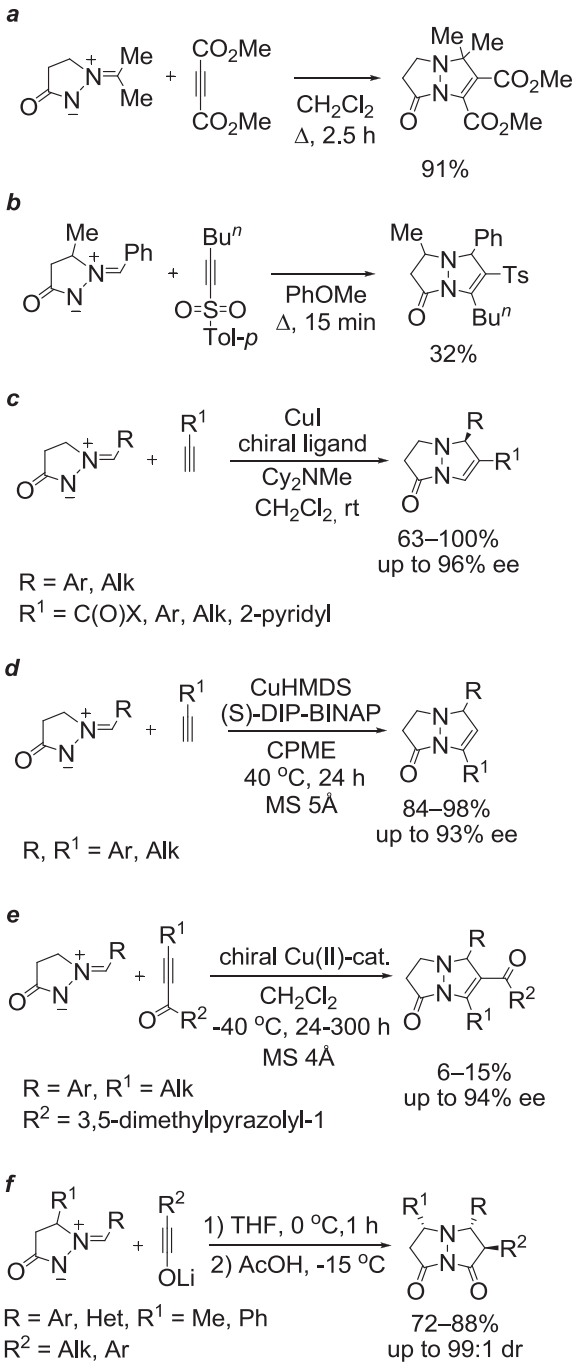

Scheme 1.

i.e. propiolylpyrazoles, using chiral Cu(II) complex of 3-(2-naphthyl)-L-alanine amide as a Lewis acid catalyst has been reported by Ishihara group (Scheme 1, ***e***).[7] Although good regio- and enantioselectivity have been reached, the yields of the cycloaddition products did not exceed 15%. Two-step synthesis of pyrazolopyrazolones, including [3+2] cycloaddition of azomethine imines with 1-alkynyl Fisher carbene complexes and subsequent oxidative demetalation, has been elaborated.[8] Recently, thermal 1,3-dipolar cycloaddition of azomethine imines with internal aroyl alkynes under microwave irradiation has also been realized.[9] Lithium ynolates has also been used as dipolarophiles (Scheme 1, ***e***).[10]

Surprisingly, only one example[6a] of using alkynyl hetarene, *i.e.* 2-ethynylpyridine, as a dipolarophile in the above reactions was reported (for a review on 1,3-cycloaddition of azomethine imines, see ref.3o). In general, there are many examples of the use of alkynyl hetarenes as dipolarophiles in the azide-alkyne Huisgen cycloaddition.[11] The reactions of alkynyl hetarenes with dipoles of other types (nitrones,[12a] azomethine ylides,[12b] nitrile oxides,[12c,d] diazoalkanes,[12e-g]) are rare.

Herein, we wish to describe 1,3-dipolar cycloaddition reactions of ethynyl derivatives of some π-deficient hetarenes with azomethine imines, *i.e.* 2-arylidene-5-oxopyrazolidin-2-ium-1-ides, allowing the synthesis of tetrahydropyrazolo[1,2-*a*]pyrazole based heterobiaryls. Heteroaryl-heteroaryl or heteroaryl-aryl motifs are frequently present in the naturally occurring compounds, pharmaceuticals, ligands and functional materials.[13] It was additional motivation for this study.

2. Results and discussion

Ethynyl derivatives of quinoxaline **1**, pyrazine **2**, pyridine **3**, 1,3-dimethylpteridine-2,4(1*H*,3*H*)-dione **4** and 6,8-dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-dione **5** have been chosen to be dipolarophiles (Fig. 1). All these heterocycles constitute the core structures of many biologically active compounds.[14] Moreover, compounds **1**–**5** are ready available via the Sonogashira coupling of the corresponding halides with trimethylsilylacetylene and subsequent desilylation (see Experimental Section). 2-Arylidene-5-oxopyrazolidin-2-ium-1-ides **6a-c** were synthesized in accordance with the reported procedure.[15]

For our initial experiment, azomethine imine **6a** was exposed to 2-ethynylquinoxaline **1a** under conditions described in Ref. [6a,b] (CuI, Cy_2NMe, CH_2Cl_2, rt) without chiral ligand. The reaction afforded 5-phenyl-6-(quinoxalin-2-yl)-2,3-dihydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-one **7a** in 13% yield for 48 h (Table 1, Entry 1). The use of acetonitrile as solvent led to decrease in yield (Entry 2). The CuI/Et_3N/DMSO catalytic system was also less effective (Entry 3). In

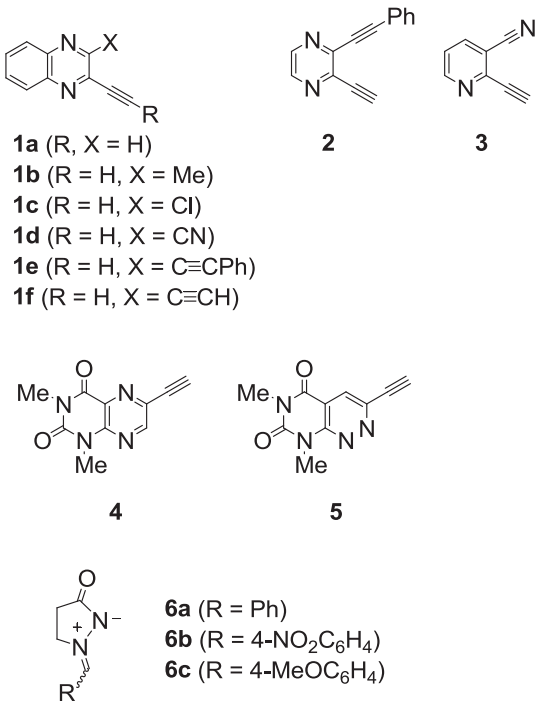

Fig. 1. Dipolarophiles and dipoles used in this study.

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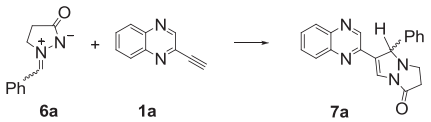
Table 1
Screening of reaction conditions.[a]



Entry	R	Base	Catalyst	Solvent	Reaction conditions	Yield **7a**, %	Recov. **1a**, %
1	H	Cy_2NMe	CuI	CH_2Cl_2	rt, 48 h	13	65
2	H	Cy_2NMe	CuI	MeCN	rt, 48 h	3	24
3	H	Et_3N (1 equiv.)	CuI	DMSO	rt, 48 h	9	41
4	H	Cy_2NMe	CuI	CH_2Cl_2	reflux, 48 h	38	60
5	**H**	**Cy_2NMe**	**CuI**	**$CHCl_3$**	**reflux, 22 h**	**96**	–
6	H	Cy_2NMe	–	$CHCl_3$	reflux, 144 h	trace	87

[a] The reaction was carried out in 0.3 mmol scale. In all cases, with the exception of Entry 3, 0.5 equiv. of a base and 5 mol.% of a catalyst were used.

both cases, complicated reaction mixtures were obtained, which made the chromatographic separation of the products difficult. Refluxing of the reaction mixture in CH_2Cl_2 improved the yield of **7a** (Entry 4). The best result in terms of yield (98%) was obtained at using chloroform as solvent under reflux (Entry 5). Blank experiment without catalyst gave **7a** in trace amounts even after prolonged heating (Entry 6). This indicates the presence of CuI catalyst is essential for this transformation.

Having identified the optimal reaction conditions for the dipolar cycloaddition, we then examined other azomethine imines and alkynes in this reaction. As shown in Table 2, azomethine imine **6b**, derived from 4-nitrobenzaldehyde, reacted with **1a** giving rise cycloadduct **7b** in quantitative yield (Entry 1). Evidently, in this case electron-withdrawing 4-nitrophenyl substituent is located at the positive end of the dipole making it more reactive. On the contrary, azomethine imine **6c** bearing electron-releasing 4-methoxyphenyl substituent at the positive end of the dipole afforded compound **7c** in significantly reduced yield (Entry 2). The reaction was sensitive to the presence and nature of the *ortho*-substituent on the hetaryl moiety of the starting alkyne. Alkyne **1b** bearing 2-methylquinoxalinyl substituent provided cycloadduct **7d** in 37% yield only (Entry 3). The reaction of dipole **6a** with 2-chloro-3-ethynylquinoxaline **1c** was accompanied by tarring; we were unable to isolate either the starting material or the product (Entry 4). 3-Ethynylquinoxaline-2-carbonitrile **1d** and 2-ethynyl-3-(phenylethynyl)quinoxaline **1e** were both suitable substrates affording corresponding products in 79% and 78% yields, respectively (Entries 5, 6). It should be noted that the cyano group of **1d** remained intact, although the reaction of 1,3-dipolar cycloaddition between potassium cyanide and dipole similar to **6** was described earlier.[5d] Exposure of 2,3-diethynylquinoxaline **1f** to the reaction with 2 equivalents of azomethine imine **6a** delivered pyrazolo[1,2-*a*]pyrazol-1(5*H*)-one **7h** in 51% yield (Entry 7), which is significantly lower than in the two previous cases. No product of double cycloaddition was observed. It is easy to see that in all cases the presence of an *ortho* substituent in the quinoxaline nucleus of the hetaryl acetylene **1** led to a decrease in the yield of the cycloaddition product **7** (Entries 3, 5–7), which is particularly noticeable in the case of the methyl derivative **1b** (Entry 3). Apparently, the reason for this is the steric factor. The π-deficiency of the heterocyclic ring attached to the C≡C bond also affects the reaction outcome. The reaction of dipole **6a** with 6-ethynyllumazine **4**, which is less π-deficient than compound **1a**, gave the corresponding cycloadduct **7i** in moderate yield (Entry 8). However, isomeric to **4** 3-ethynylpyridazinopyrimidine **5** was a more successful dipolarophile providing cycloaddition product **7j** in 72% yield (Entry 9). When 2-ethynyl-3-(phenylethynyl)pyrazine **2** and 2-ethynylnicotinonitrile **3** were used as dipolarophiles, the desired cycloadducts **7k** and **7l** were obtained in 73 and 79% yields, respectively (Entry 10, 11).

We also tested catalyst-free thermally induced 1,3-dipolar cycloaddition of azomethine imines to ethynyl hetarenes. Heating 2-ethynylqinoxaline **1a** with azomethine imine **6a** in *p*-xylene (130 °C, 7 h) gave cycloadduct **7a** in 35% yield. Similar reaction of 3-ethynylquinoxaline-2-carbonitrile **1d** with **6a** provided product **7f** in 35% yield. It should be noted that in contrast to the previously described thermal reactions of azomethine imines with alkyl propiolates or other asymmetric acetylenes[5b,c,f] both above reactions proceeded regioselectively. It is known that 1,3-dipolar cycloaddition to acetylenes can be concerted or stepwise.[16] It is known that 1,3-dipolar cycloaddition to acetylenes can be concerted or stepwise.[16] On the one hand, π-deficient hetaryl moiety activates the C≡C bond of **1** towards nucleophilic attack and can stabilize zwitterionic intermediate **8** via delocalization of the negative charge favoring a stepwise mechanism and regioselective formation of compounds **7a** and **7f** (Scheme 2). However, recently mechanism of [3+2]-cycloaddition of azomethine imines to methyl propiolate was evaluated by computational and experimental methods (which is especially important) supporting a polar concerted cycloaddition mechanism with high asynchronicity.[16c]

The structures of synthesized compounds **7** were supported by a combination of elemental analysis, mass-spectrometry, IR, UV–vis, ^1H and ^{13}C NMR spectroscopic measurements. All of the compounds are yellow-colored with λ_{max} 359–407 nm. Their IR spectra indicated the presence of C=O group (ν 1685–1719 cm^{-1}). In cases of alkynyl derivatives **7g,h,k** the characteristic $\nu_{C\equiv C}$ band at 2105–2207 cm^{-1} was also registered. The spectra of nitriles **7f,l** included a $\nu_{C\equiv N}$ band at 2220–2232 cm^{-1}. In the ^1H NMR spectra the H(5) proton of **7** appeared as a doublet at 5.6–5.8 ppm with a coupling constant $J = 1.3–1.4$ Hz or as a broad singlet. This corresponds to the regioisomers depicted in Table 2. The structure of **7f** was proved by X-ray single crystal study (Fig. 2).

3. Conclusions

We have described regioselective CuI-catalyzed and catalyst-free thermally induced 1,3-dipolar cycloaddition reactions of π-deficient ethynyl hetarenes and 2-arylidene-5-oxopyrazolidin-2-ium-1-ides, which are expected to be a general route for the facile synthesis of a wide range of 2,3-dihydropyrazolo[1,2-*a*]pyrazole based heterobiaryls. The 1,3-dipolar cycloaddition process operates efficiently with ethynyl derivatives of pyridine, pyrazine, quinoxaline, pteridine and pyrimido[4,5-*c*]pyridazine. The ethynyl hetarenes with *ortho*-methyl, *ortho*-cyano and *ortho*-alkynyl

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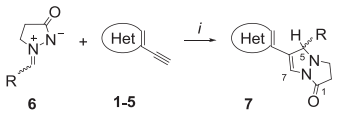
Table 2
Synthesis of 6-hetaryl-3-R-2,3-dihydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-ones **7**.



i - Cy_2NMe, CuI, $CHCl_3$, reflux, 22 h

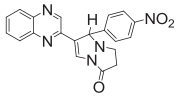
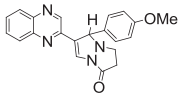
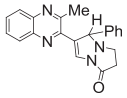
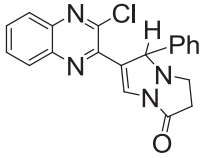
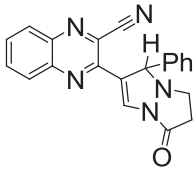
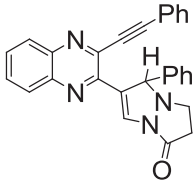
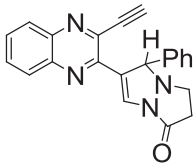
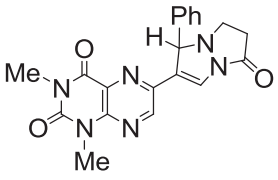
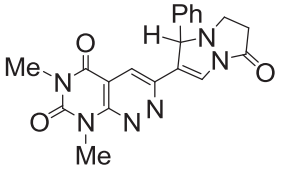
Entry	Ylide, R	Alkyne	Product **7**		Yield **7**%	Recov. alkyne %
1	**6b**, R = 4-$NO_2C_6H_4$	**1a**		**7b**	98	–
2	**6c**, R = 4-$MeOC_6H_4$	**1a**		**7c**	56	35
3	**6a**	**1b**		**7d**	37	60
4	**6a**	**1c**		**7e**	–	tarring
5	**6a**	**1d**		**7f**	79	trace
6	**6a**	**1e**		**7g**	78	trace
7	**6a**	**1f**		**7h**	51	28
8	**6a**	**4**		**7i**	56	trace
9	**6a**	**5**		**7j**	72	18

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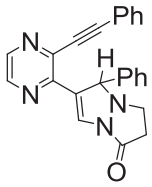
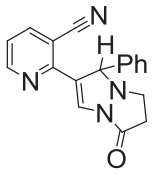
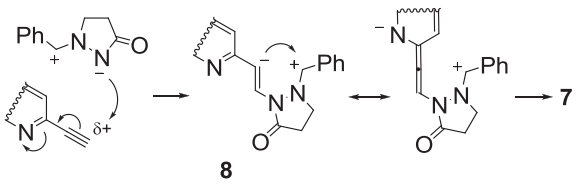
Table 2 (*continued*)

Entry	Ylide, R	Alkyne	Product **7**		Yield **7**%	Recov. alkyne %
10	**6a**	**2**		**7k**	73	21
11	**6a**	**3**		**7l**	79	20



Scheme 2.

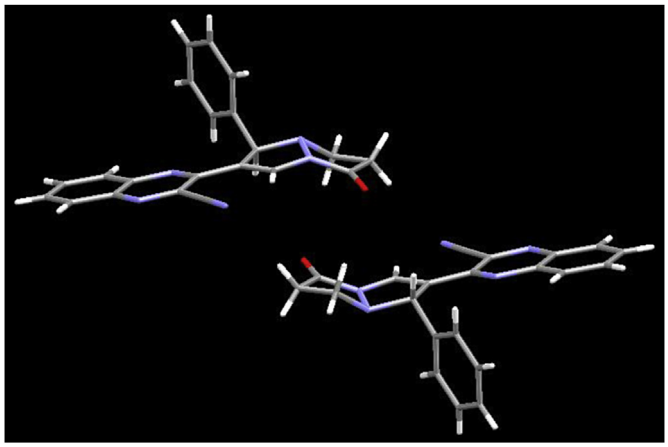


Fig. 2. X-Ray crystal structure of **7f** (a pair of (*R*)- and (*S*)-enantiomers of **7f** connected by inversion centre are present in the crystal unit cell).

substituents are well-tolerated. Considering the importance of 2,3-dihydropyrazolo[1,2-*a*]pyrazoles as core structures in pharmacologically active substances, this method may became attractive for both synthetic and medicinal chemistry.

4. Experimental

4.1. General

Proton (^{1}H) and carbon (^{13}C) nuclear magnetic resonance (NMR) spectra were recorded on a Bruker DPX−250 spectrometer (250 and 62.9 MHz, respectively). ^{1}H and ^{13}C NMR chemical shifts are in parts per million relative to Me_4Si. Coupling constants are in Hertz. The IR spectra were recorded on a FT FSM-1202 spectrometer (http://infraspek.ru) using KBr or Nujol. The UV−vis spectra were recorded on a Varian Cary 50 Probe spectrophotometer in $CHCl_3$. Mass spectra were measured on a Finnigan MAT INCOS 50 spectrometer. The HR-ESI mass-spectra were obtained on a BRUKER maXis spectrometer equipped with an electrospray ionization (ESI) source. The instrument was operated in positive mode using an *m/z* range of 50−1200. The capillary voltage of the ion source was set at 4000 V. The nebulizer gas pressure was 1.0 bar, and the drying gas flow was 4.0 L/min. 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. 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 1590043 (**7f**).

4.3. Synthesis of the starting compounds

2,3-Dichloropyrazine, 2-chloro- and 2,3-dichloroquinoxalines were purchased from Aldrich. 2-Chloro-3-methylquinoxaline,[17] 2-chloro-3-(phenylethynyl)quinoxaline,[18] 3-chloroquinoxaline-2-carbonitrile,[19] 6-chloro-1,3-dimethylpteridine-2,4(1*H*,3*H*)-dione,[20] 3-chloro-6,8-dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-dione,[21] 2-chloro-3-(phenylethynyl)pyrazine,[12] 2-chloronicotinonitrile,[22] 2-ethynylquinoxaline **1a**,[23] 2-chloro-3-ethynylquinoxaline **1c**[24] were synthesized in accordance with literature procedures.

4.4. General procedure for the synthesis of alkynyl azines

A mixture of azine chloride (0.50 mmol), $Pd(PPh_3)_2Cl_2$ (42 mg, 0.06 mmol), CuI (6 mg, 0.03 mmol) and Et_3N (6 mL) was stirred under argon for 20 min at room temperature. Then a solution of ethynyltrimethylsilane (63 mg, 0.09 mL, 0.64 mmol) was added dropwise. The flask was closed tightly. The resulting mixture was stirred for 24 h at 50−55 °C. The reaction mixture was evaporated to dryness without heating. The residue was mixed with silica gel and purified by flash column chromatography on silica gel (3 × 30 cm) with $CHCl_3$ as the eluent.

We were unable to obtain by chromatography pure samples of (trimethylsilyl)ethynyl derivatives because of their partial desilylation. Thus, pure (trimethylsilyl)ethynyl derivatives or partially desilylated products were subjected to desilylation according to the

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following procedure. To a solution of (trimethylsilyl)ethynyl azine (0.5 mmol) in methanol (5 mL), KF•2H$_2$O (56 mg, 0.6 mmol) was added. The reaction mixture was stirred for 24 h at room temperature and then evaporated to dryness. The residue was purified by flash column chromatography on silica gel with CH_2Cl_2 as the eluent. R_f, yield and characteristics for each compound are given below. All alkynes decompose when stored.

4.4.1. 2-Methyl-3-((trimethylsilyl)ethynyl)quinoxaline

R_f 0.3, 38%. Brown solid with mp 45–48 °C; ^{1}H NMR ($CDCl_3$) δ ppm: 0.35 (s, 9H), 2.89 (s, 3H), 7.68–7.75 (m, 2H), 7.99 (dd, J = 7.7, 1.8 Hz, 1H), 8.05 (dd, J = 7.7, 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: −0.4, 23.2, 101.6, 102.5, 128.4, 128.9, 129.5, 130.5, 139.3, 140.6, 140.7, 155.3; IR, cm^{-1}: 2161 (C≡C); MS (ESI) *m/z*: found 241.1163 [M+H]$^+$, calcd for $C_{14}H_{16}N_2Si$ 241.1156 [M+H]$^+$.

*4.4.2. 2-Ethynyl-3-methylquinoxaline (**1b**)*

R_f 0.4, 89%. Brown solid with mp 97–99 °C; ^{1}H NMR ($CDCl_3$) δ ppm: 2.90 (s, 3H), 3.58 (s, 1H), 7.70–7.77 (m, 2H), 8.00 (dd, J = 7.9, 1.5 Hz, 1H), 8.05 (dd, J = 7.9, 1.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 23.1, 80.9, 83.2, 128.5, 128.9, 129.6, 130.8, 138.6, 140.7, 140.9, 155.2; IR, cm^{-1}: 2098 (C≡C); MS (ESI) *m/z*: found 169.0767 [M+H]$^+$, calcd for $C_{11}H_8N_2$ 169.0760 [M+H]$^+$.

*4.4.3. 3-Ethynylquinoxaline-2-carbonitrile (**1d**)*

R_f 0.6, 74%. Off-white solid with mp 163–165 °C (decomp.); ^{1}H NMR ($CDCl_3$) δ ppm: 3.73 (s, 1H), 7.87–7.99 (m, 2H), 8.10–8.19 (m, 2H); ^{13}C NMR ($CDCl_3$) δ ppm: 78.2, 85.9, 114.8, 129.4, 129.8, 131.8, 132.6, 134.0, 138.9, 140.4, 142.0; IR, cm^{-1}: 2107 (C≡C), 2234 (C≡N); MS *m/z*: 179 ([M$^+$], 100), 127 (60), 76 (35), 50 (22). Anal. calcd for $C_{11}H_5N_3$: C, 73.74; H, 2.81; N, 23.45. Found: C, 73.47; H, 2.94; N, 23.66.

4.4.4. 2-(Phenylethynyl)-3-((trimethylsilyl)ethynyl)quinoxaline

R_f 0.6, 87%. Brown solid with mp 123–125 °C; ^{1}H NMR ($CDCl_3$) δ ppm: 0.34 (s, 9H), 7.38–7.42 (m, 3H), 7.70 (dd, J = 7.5, 1.6 Hz, 2H), 7.73–7.76 (m, 2H), 8.04–8.06 (m, 2H); ^{13}C NMR ($CDCl_3$) δ ppm: −0.3, 86.7, 95.7, 101.1, 102.5, 121.7, 128.5, 128.9, 129.0, 129.8, 130.9, 131.1, 132.4, 140.3, 140.4140.6, 140.8; IR, cm^{-1}: 2104, 2221 (C≡C); MS *m/z*: 254 ([M+H−SiMe$_3$]$^+$, 100), 253 ([M−SiMe$_3$]$^+$, 26), 204 (10), 176 (10), 127 (81), 100 (190), 77 (12), 74 (20). Anal. calcd for $C_{21}H_{18}N_2Si$: C, 77.26; H, 5.56; N, 8.58; Si, 8.60. Found: C, 77.01; H, 5.80; N, 8.87.

*4.4.5. 2-Ethynyl-3-(phenylethynyl)quinoxaline (**1e**)*

R_f 0.7, 87%. Brown solid with mp 119–121 °C; ^{1}H NMR ($CDCl_3$) δ ppm: 3.65 (s, 1H), 7.41–7.47 (m, 3H), 7.72 (dd, J = 7.8, 1.5 Hz, 2H), 7.76–7.82 (m, 2H), 8.07–8.10 (m, 2H); ^{13}C NMR ($CDCl_3$) δ ppm: 80.5, 83.2, 86.4, 96.1, 121.6, 128.6, 128.9, 129.1, 129.9, 131.0, 131.4, 132.4, 139.8, 140.3, 140.8(0), 140.8(3); IR, cm^{-1}: 2103, 2218 (C≡C); MS *m/z*: 254 ([M$^+$], 100), 253 (24), 203 (55), 127 (62), 100 (14), 76 (61). Anal. calcd for $C_{18}H_{10}N_2$: C, 85.02; H, 3.96; N, 11.02. Found: C, 85.13; H, 4.09; N, 11.11.

*4.4.6. 2,3-Diethynylquinoxaline (**1f**)*

R_f 0.6, 78%. Tan solid, decomp. > 170 °C (mp 175–176 °C (decomp.)[25]); ^{1}H NMR ($CDCl_3$) δ ppm: 3.61 (s, 1H), 7.81 (dd, J = 6.4, 3.4 Hz, 1H), 8.08 (dd, J = 6.4, 3.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 80.0, 83.5, 129.0, 131.5, 139.7, 140.6; IR, cm^{-1}: 2129 (C≡C); HRMS (ESI): found 179.0609 [M+H]$^+$, calcd for $C_{12}H_6N_2$ 179.0604 [M+H]$^+$.

*4.4.7. 2-Ethynyl-3-(phenylethynyl)pyrazine (**2**)*

R_f 0.6, 85%. Off-white solid, with mp 73–75 °C; ^{1}H NMR ($CDCl_3$) δ ppm: 3.57 (s, 1H), 7.32–7.43 (m, 3H), 7.59–7.63 (m, 2H), 8.43 (d, J = 2.4 Hz, 2H), 8.49 (d, J = 2.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ ppm: 79.9, 84.0, 85.5, 96.5, 121.5, 128.5, 129.8, 132.3, 140.8, 142.3, 142.4, 143.1; IR, cm^{-1}: 2199, 2220 (C≡C); MS (ESI) *m/z*: found 205.0768 [M+H]$^+$, calcd for $C_{14}H_8N_2$ 205.0760 [M+H]$^+$.

*4.4.8. 2-Ethynylnicotinonitrile (**3**)*

R_f 0.5, 89%. Off-white solid, with mp 115–117 °C (125 °C[26]); ^{1}H NMR ($CDCl_3$) δ ppm: 3.56 (s, 1H), 7.39 (dd, J = 8.0, 4.9 Hz, 1H), 7.96 (dd, J = 8.0, 1.7 Hz, 1H), 8.75 (dd, J = 4.9, 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 79.4, 83.8, 113.4, 115.6, 123.0, 140.0, 144.7, 152.9; IR, cm^{-1}: 2114 (C≡C), 2239 (C≡N); MS (ESI) *m/z*: found 129.0451 [M+H]$^+$, calcd for $C_8H_4N_2$ 129.0447 [M+H]$^+$.

4.4.9. 1,3-Dimethyl-6-((trimethylsilyl)ethynyl)pteridine-2,4(1H,3H)-dione

R_f 0.2, 74%. Off-white solid with mp 115–117 °C (decomp.) (112–115 °C[27]); ^{1}H NMR ($CDCl_3$) δ ppm: 0.26 (s, 9H), 3.51 (s, 3H), 3.68 (s, 3H), 8.65 (s, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: −0.5, 29.1, 29.5, 99.7, 100.5, 127.1, 135.1, 146.4, 150.3, 150.6, 159.2; IR, cm^{-1}: 1653, 1724 (C=O), 2167 (C≡C); MS *m/z*: 288 ([M$^+$], 43), 273 (100), 108 (11), 81 (13), 67 (11), 56 (13), 43 (22), 15 (33). Anal. calcd for $C_{13}H_{16}N_4O_2Si$: C, 54.14; H, 5.59; N, 19.43; Si, 9.74. Found: C, 54.34; H, 5.63; N, 19.17.

*4.4.10. 6-Ethynyl-1,3-dimethylpteridine-2,4(1H,3H)-dione (**4**)*

R_f 0.1, 83%. Off-white solid, decomp. >230 °C (decomp.) (236–238 °C (decomp.)[28]); ^{1}H NMR ($CDCl_3$) δ ppm: 3.34 (s, 1H), 3.51 (s, 3H), 3.69 (s, 3H), 8.69 (s, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 29.2, 29.6, 79.1, 81.7, 127.3, 134.3, 146.8, 150.3, 150.6, 159.0; IR, cm^{-1}: 1653, 1724 (C=O), 2108 (C≡C); MS *m/z*: 216 ([M$^+$], 100), 159 (14), 131 (34), 104 (39), 77 (25), 56 (15), 28 (17), 18 (19), 15 (17). Anal. calcd for $C_{10}H_8N_4O_2$: C, 55.55; H, 3.73; N, 25.91. Found: C, 55.41; H, 3.99; N, 25.84.

4.4.11. 6,8-Dimethyl-3-((trimethylsilyl)ethynyl)pyrimido[4,5-c]pyridazine-5,7(6H,8H)-dione

R_f 0.2, 70%. Off-white solid with mp 123–124 °C (120–121 °C[29]); ^{1}H NMR ($CDCl_3$) δ ppm: 0.27 (s, 9H), 3.45 (s, 3H), 3.85 (s, 3H), 8.11 (s, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: −0.47, 28.9, 30.0, 99.5, 101.0, 112.4, 128.0, 144.4, 149.5, 150.2, 159.8; IR, cm^{-1}: 1674, 1730 (C=O), 2184 (C≡C); MS *m/z*: 288 ([M$^+$], 49), 273 (100). Anal. calcd for $C_{13}H_{16}N_4O_2Si$: C, 54.14; H, 5.59; N, 19.43; Si, 9.74. Found: C, 54.28; H, 5.47; N, 19.55.

*4.4.12. 3-Ethynyl-6,8-dimethylpyrimido[4,5-c]pyridazine-5,7(6H,8H)-dione (**5**)*

R_f 0.2, 85%. Off-white solid, with mp 201–203 °C; ^{1}H NMR ($CDCl_3$) δ ppm: 3.45 (s, 1H), 3.48 (s, 3H), 3.89 (s, 3H), 8.18 (s, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 28.9, 30.1, 79.0, 82.2, 112.5, 128.2, 143.7, 149.7, 150.2, 159.7; IR, cm^{-1}: 1661, 1711 (C=O), 2108 (C≡C); MS *m/z*: 216 ([M$^+$], 100), 159 (14), 131 (19), 104 (31), 88 (29), 81 (27), 62 (12), 56 (14), 53 (16), 15 (22). Anal. calcd for $C_{10}H_8N_4O_2$: C, 55.55; H, 3.73; N, 25.91. Found: C, 55.32; H, 4.01; N, 25.78.

4.5. General procedure for the synthesis of 6-hetaryl-5-phenyl-2,3-dihydropyrazolo[1,2-a]pyrazol-1(5H)-ones 7

Method A. To a stirred for 5 min mixture of 2-arylidene-5-oxopyrazolidin-2-ium-1-ide **6** (0.3 mmol), CuI (3 mg, 0.015 mmol) and $CHCl_3$ (2 mL), a solution of the corresponding ethynyl hetarene **1**–**5** (0.3 mmol) and Cy_2NMe (29 mg, 0.032 mL, 0.15 mmol) in $CHCl_3$ (2 mL) was added dropwise. The reaction mixture was heated under reflux for 22 h and evaporated to dryness. The residue was mixed with silica gel and purified by flash column chromatography on silica gel (3 × 40 cm) with CH_2Cl_2 – Et_2O (1:1, v/v) as the eluent. The first colorless fraction gave unreacted starting alkyne. The next

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yellow fraction gave 6-hetaryl-5-phenyl-2,3-dihydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-one **7**. Starting compounds and yields are indicated in Table 2. R_f and other characteristics of the products **7** are indicated below.

Method B. A solution of 2-benzylidene-5-oxopyrazolidin-2-ium-1-ide **6a** (35 mg, 0.2 mmol), ethynyl hetarene **1a** or **1d** (0.3 mmol) in *p*-xylene (1 mL) was stirred at 130 °C for 7 h. The reaction mixture was evaporated to dryness. Isolation of the product **7** was carried out similarly to the above method A.

4.5.1. 5-Phenyl-6-(quinoxalin-2-yl)-2,3-dihydropyrazolo[1,2-a] pyrazol-1(5H)-one (**7a**)

R_f 0.4. Yellow solid, with mp 208–211 °C (*i*-PrOH); ^{1}H NMR ($CDCl_3$) δ ppm: 2.76–3.00 (m, 2H), 3.15 (pseudoquartet, $J = 8.6$ Hz, 1H), 3.39 (ddd, $J = 8.1$, 8.1, 4.8 Hz, 1H), 5.64 (d, 1H), 7.26–7.35 (m, 3H), 7.44–7.48 (m, 2H), 7.56–7.67 (m, 2H), 7.78–7.83 (m, 2H), 7.89–7.95 (m, 1H), 8.68 (s, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 36.0, 51.1, 73.6, 121.8, 125.5, 128.5, 128.6(8), 128.7(1), 129.0, 129.1, 129.2, 130.2, 137.8, 140.7, 142.2, 142.7, 147.0, 163.7; IR, cm^{-1}: 1693 (C = O); UV–vis, λ_{max} (lg ε), nm: 269 sh (4.37), 340 sh (3.95), 396 (4.11), end absorption up to 484 nm; MS *m/z*: 328 ([M$^+$], 39), 300 (38), 299 (100), 285 (31), 271 (24), 258 (21), 251 (60), 243 (20), 231 (14), 197 (58), 155 (16), 140 (12), 129 (45), 115 (28), 102 (50), 89 (12), 76 (40), 55 (79), 51 (21), 42 (30), 28 (22). Anal. calcd for $C_{20}H_{16}N_4O$: C, 73.15; H, 4.91; N, 17.06. Found: C, 73.22; H, 4.79; N, 17.23.

4.5.2. 5-(4-Nitrophenyl)-6-(quinoxalin-2-yl)-2,3-dihydropyrazolo [1,2-a]pyrazol-1(5H)-one (**7b**)

R_f 0.2. Yellow solid, with mp 164–166 °C (*i*-PrOH); ^{1}H NMR ($CDCl_3$) δ ppm: 2.80 (ddd, $J = 16.0$, 7.0, 2.2 Hz, 1H), 2.96–3.10 (m, 1H), 3.15–3.26 (m, 1H), 3.59 (td, $J = 8.2$, 2.0 Hz, 1H), 5.73 (d, $J = 1.5$ Hz, 1H), 7.58–7.68 (m, 2H), 7.71–7.78 (m, 4H), 7.93–7.97 (m, 1H), 8.14–8.18 (m, 2H), 8.85 (s, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 35.7, 52.5, 73.9, 122.1, 123.5, 124.4, 128.7, 129.2, 129.5, 129.7, 130.5, 140.6, 141.7, 142.7, 146.5, 146.8, 147.7, 164.4; IR, cm^{-1}: 1705 (C = O); UV–vis, λ_{max} (lg ε), nm: 277 sh (4.38), 335 sh (3.94), 392 (4.33), end absorption up to 483 nm; MS *m/z*: 373 ([M$^+$], 31), 344 (100), 330 (34), 318 (11), 316 (14), 298 (11), 257 (11), 251 (42), 242 (16), 197 (41), 129 (13), 102 (15), 55 (27), 28 (15). Anal. calcd for $C_{20}H_{15}N_5O_3$: C, 64.34; H, 4.05; N, 18.76. Found: C, 64.19; H, 4.20; N, 18.93.

4.5.3. 5-(4-Methoxyphenyl)-6-(quinoxalin-2-yl)-2,3-dihydropyrazolo[1,2-a]pyrazol-1(5H)-one (**7c**)

R_f 0.4. Yellow solid, with mp 172–174 °C (*i*-PrOH); ^{1}H NMR ($CDCl_3$) δ ppm: 2.76–2.96 (m, 2H), 3.11 (pseudoquartet, $J = 8.4$ Hz, 1H), 3.29–3.37 (m, 1H), 3.74 (s, 3H), 5.60 (s, 1H), 6.84 (d, $J = 8.4$ Hz, 2H), 7.36 (d, $J = 8.4$ Hz, 2H), 7.57–7.66 (m, 2H), 7.77 (s, 1H), 7.81–7.84 (m, 1H), 7.91–7.94 (m, 1H), 8.65 (s, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 36.1, 50.6, 55.3, 72.7, 114.2, 121.7, 125.8, 129.0 (2C), 129.2, 129.4, 129.8, 130.2, 140.7, 142.2, 142.7, 147.0, 159.8, 163.5; IR, cm^{-1}: 1714 (C = O); UV–vis, λ_{max} (lg ε), nm: 288 (4.05), 335 sh (3.82), 397 (4.23), end absorption up to 499 nm; MS *m/z*: 358 ([M$^+$], 49), 329 (100), 315 (30), 303 (22), 288 (20), 274 (10), 259 (17), 251 (35), 231 (18), 229 (14), 197 (38), 129 (26), 102 (26), 76 (14), 55 (48), 42 (11), 28 (26), 15 (16). Anal. calcd for $C_{21}H_{18}N_4O_2$: C, 70.38; H, 5.06; N, 15.63. Found: C, 70.52; H, 4.89; N, 15.35.

4.5.4. 6-(3-Methylquinoxalin-2-yl)-5-phenyl-2,3-dihydropyrazolo [1,2-a]pyrazol-1(5H)-one (**7d**)

R_f 0.4. Yellow solid, with mp 155–157 °C (*n*-heptane); ^{1}H NMR ($CDCl_3$) δ ppm: 2.75–2.86 (m, 4H), 2.92–3.02 (m, 1H), 3.09–3.19 (m, 1H), 3.44 (ddd, $J = 8.1$, 8.1, 4.0 Hz, 1H), 5.82 (d, $J = 1.5$ Hz, 1H), 7.13–7.28 (m, 3H), 7.43–7.50 (m, 3H), 7.52–7.62 (m, 2H), 7.72–7.78 (m, 1H), 7.83–7.90 (m, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 25.0, 36.0, 51.6, 75.6, 122.0, 126.4, 128.0, 128.1, 128.3, 128.5, 128.6, 129.1, 129.5, 138.9, 139.5, 140.5, 147.0, 151.7, 163.8; IR, cm^{-1}: 1703 (C = O); UV–vis, λ_{max} (lg ε), nm: 283 (4.34), 335 sh (4.10), 391 (4.49), end absorption up to 480 nm; MS *m/z*: 342 ([M$^+$], 19), 313 (100), 299 (32), 287 (11), 271 (21), 257 (11), 211 (27), 143 (14), 102 (162), 77 (16), 55 (37), 14 (13). Anal. calcd for $C_{21}H_{18}N_4O$: C, 73.67; H, 5.30; N, 16.36. Found: C, 73.54; H, 5.42; N, 16.17.

4.5.5. 3-(5-Oxo-1-phenyl-1,5,6,7-tetrahydropyrazolo[1,2-a] pyrazol-2-yl)quinoxaline-2-carbonitrile (**7f**)

R_f 0.7. Orange solid, with mp 212–214 °C (*i*-PrOH); ^{1}H NMR ($CDCl_3$) δ ppm: 2.84–3.09 (m, 2H), 3.17–3.27 (m, 1H), 3.50 (ddd, $J = 8.0$, 7.8, 4.3 Hz, 1H), 5.85 (d, $J = 1.4$ Hz, 1H), 7.25–7.39 (m, 3H), 7.52–7.58 (m, 2H), 7.72–7.88 (m, 3H), 8.03 (dd, $J = 7.5$, 1.2 Hz, 1H), 8.25 (d, $J = 0.9$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 35.9, 51.3, 74.7, 116.6, 122.4, 124.4, 126.6, 128.3, 128.5, 128.7, 128.8, 129.5, 130.8, 133.4, 138.1, 139.3, 142.0, 147.3, 164.2; IR, cm^{-1}: 1701 (C = O), 2232 (C≡N); UV–vis, λ_{max} (lg ε), nm: 259 (4.53), 309 sh (3.96), 382 (4.12), end absorption up to 525 nm; MS *m/z*: 353 ([M$^+$], 62), 324 (29), 310 (25), 298 (21), 283 (22), 276 (100), 269 (13), 256 (12), 222 (18), 140 (11), 115 (10), 102 (17), 77 (13), 55 (40), 42 (11), 28 (11). Anal. calcd for $C_{21}H_{15}N_5O$: C, 71.38; H, 4.28; N, 19.82. Found: C, 71.43; H, 4.03; N, 20.04.

4.5.6. 5-Phenyl-6-(3-(phenylethynyl)quinoxalin-2-yl)-2,3-dihydropyrazolo[1,2-a]pyrazol-1(5H)-one (**7g**)

R_f 0.8. Yellow solid, with mp 245–246 °C (*i*-PrOH); ^{1}H NMR ($CDCl_3$) δ ppm: 2.77–3.01 (m, 2H), 3.17 (pseudoquartet, $J = 8.6$ Hz, 1H), 3.41 (ddd, $J = 8.1$, 8.1, 4.9 Hz, 1H), 5.83 (d, $J = 1.3$ Hz, 1H), 7.17–7.32 (m, 3H), 7.43–7.51 (m, 5H), 7.55–7.63 (m, 2H), 7.69–7.77 (m, 3H), 7.90–7.98 (m, 1H), 8.42 (d, $J = 0.9$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 36.0, 51.2, 74.8, 88.1, 96.0, 121.2, 123.7, 124.7, 128.1, 128.4, 128.6 (2C), 128.7, 128.8, 129.8, 130.1, 130.6, 132.3, 136.7, 138.6, 139.7, 140.3, 147.3, 164.1; IR, cm^{-1}: 1702 (C = O), 2204 (C≡C); UV–vis, λ_{max} (lg ε), nm: 269 (4.52), 296 (4.49), 407 (4.20), end absorption up to 515 nm; MS *m/z*: 428 ([M$^+$], 42), 373 (11), 351 (20), 343 (35), 297 (27), 140 (11), 127 (26), 115 (14), 102 (32), 77 (51), 55 (100), 51 (18), 42 (16), 28 (40), 16 (27), 14 (58). Anal. calcd for $C_{28}H_{20}N_4O$: C, 78.49; H, 4.70; N, 13.08. Found: C, 78.37; H, 4.82; N, 13.21.

4.5.7. 6-(3-Ethynylquinoxalin-2-yl)-5-phenyl-2,3-dihydropyrazolo [1,2-a]pyrazol-1(5H)-one (**7h**)

R_f 0.7 (Et_2O – hexane, 3:1, v/v). Yellow solid, with mp 123–125 °C (*i*-PrOH); ^{1}H NMR ($CDCl_3$) δ ppm: 2.86 (ddd, $J = 16.3$, 7.6, 4.4 Hz, 1H), 2.93–3.04 (m, 1H), 3.17 (pseudoquartet, $J = 8.6$ Hz, 1H), 3.43 (ddd, $J = 8.1$, 8.1, 4.5 Hz, 1H), 3.73 (s, 1H), 5.81 (s, 1H), 7.22–7.25 (m, 1H), 7.29–7.33 (m, 2H), 7.51 (d, $J = 7.2$ Hz, 2H), 7.61–7.66 (m, 2H), 7.74–7.76 (m, 1H), 7.93–7.96 (m, 1H), 8.38 (s, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 36.0, 51.1, 74.6, 82.0, 84.2, 123.7, 124.5, 128.0, 128.3, 128.5, 128.6(8), 128.7(1), 129.9, 131.0, 135.4, 138.6, 139.4, 140.6, 147.3, 164.0; IR, cm^{-1}: 1706 (C = O), 2105 (C≡C); UV–vis, λ_{max} (lg ε), nm: 254 (4.51), 262 (4.50), 364 (3.97), 404 (4.01), end absorption up to 480 nm; MS (ESI) *m/z*: found 353.1397 [M+H]$^+$, calcd for $C_{22}H_{17}N_4O$ 353.1397 [M+H]$^+$.

4.5.8. 1,3-Dimethyl-6-(5-oxo-1-phenyl-1,5,6,7-tetrahydropyrazolo [1,2-a]pyrazol-2-yl)pteridine-2,4(1H,3H)-dione (**7i**)

R_f 0.2. Yellow solid, with mp 239–242 °C (*i*-PrOH); ^{1}H NMR ($CDCl_3$) δ ppm: 2.74–2.99 (m, 2H), 3.13 (pseudoquartet, $J = 8.8$ Hz, 1H), 3.39 (ddd, $J = 8.1$, 8.1, 4.2 Hz, 1H), 3.48 (s, 3H), 3.59 (s, 3H), 5.55 (br s, 1H), 7.28–7.37 (m, 3H), 7.45–7.48 (m, 2H), 7.71 (br s, 1H), 8.25 (s, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 29.0, 29.4, 35.6, 51.2, 73.5, 121.4, 123.3, 126.9, 128.7, 128.8, 128.9, 137.2, 143.5, 144.1, 145.9, 150.4, 159.5, 163.6; IR, cm^{-1}: 1668, 1677, 1714 (C = O); UV–vis, λ_{max} (lg ε), nm: 351 (4.25), 407 (4.08), end absorption up to 541 nm; MS *m/z*: 390 ([M$^+$], 57), 361 (63), 347 (33), 334 (24), 320 (17), 313 (81), 306

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(22), 259 (82), 206 (10), 193 (11), 179 (13), 140 (20), 91 (12), 77 (24), 55 (100), 42 (16), 28 (21). Anal. calcd for $C_{20}H_{18}N_6O_3$: C, 61.53; H, 4.65; N, 21.53. Found: C, 61.34; H, 4.56; N, 21.80.

4.5.9. 6,8-Dimethyl-3-(5-oxo-1-phenyl-1,5,6,7-tetrahydropyrazolo[1,2-a]pyrazol-2-yl)pyrimido[4,5-c]pyridazine-5,7(6H,8H)-dione (**7j**)

R_f 0.3. Yellow solid, with mp 226–228 °C (*i*-PrOH); ^{1}H NMR ($CDCl_3$) δ ppm: 2.75–2.96 (m, 2H), 3.13 (pseudoquartet, $J = 8.4$ Hz, 1H), 3.27–3.35 (m, 1H), 3.42 (s, 3H), 3.79 (s, 3H), 5.61 (br s, 1H), 7.28–7.41 (m, 5H), 7.71 (br s, 1H), 7.81 (s, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 28.8, 29.9, 36.0, 50.6, 73.3, 113.0, 121.2, 121.4, 123.4, 128.6, 128.9, 129.0, 136.8, 149.3, 150.2, 151.8, 160.2, 163.5; IR, cm^{-1}: 1670, 1698, 1719 (C = O); UV–vis, λ_{max} (lg ε), nm: 359 (4.29), end absorption up to 514 nm; MS *m/z*: 390 ([M$^+$], 96), 361 (76), 320 (18), 313 (57), 306 (16), 292 (11), 259 (50), 206 (13), 192 (17), 177 (11), 166 (10), 164 (11), 152 (14), 139 (12), 115 (11), 91 (16), 77 (19), 55 (100), 15 (17). Anal. calcd for $C_{20}H_{18}N_6O_3$: C, 61.53; H, 4.65; N, 21.53. Found: C, 61.41; H, 4.39; N, 21.47.

4.5.10. 5-Phenyl-6-(3-(phenylethynyl)pyrazin-2-yl)-2,3-dihydropyrazolo[1,2-a]pyrazol-1(5H)-one (**7k**)

R_f 0.8. Yellow solid, with mp 161–163 °C (*i*-PrOH); ^{1}H NMR ($CDCl_3$) δ ppm: 2.80–3.01 (m, 2H), 3.12–3.22 (m, 1H), 3.32–3.40 (m, 1H), 5.75 (d, $J = 1.3$ Hz, 1H), 7.27–7.44 (m, 5H), 7.47–7.51 (m, 3H), 7.71–7.75 (m, 2H), 8.25 (d, $J = 2.4$ Hz, 1H), 8.28 (d, $J = 2.4$ Hz, 1H), 8.33 (d, $J = 1.3$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 36.0, 50.8, 74.2, 87.3, 97.1, 121.4, 123.1, 124.0, 128.2, 128.5 (2C), 128.8, 129.9, 132.1, 136.1, 138.1, 140.7, 141.9, 148.7, 163.8; IR, cm^{-1}: 1685 (C = O), 2207 (C≡C); UV–vis, λ_{max} (lg ε), nm: 283 (4.33), 366 (4.18); MS (ESI) *m/z*: found 379.1569 [M+H]$^+$, calcd for $C_{24}H_{18}N_4O$ 379.1559 [M+H]$^+$.

4.5.11. 2-(5-Oxo-1-phenyl-1,5,6,7-tetrahydropyrazolo[1,2-a]pyrazol-2-yl)nicotinonitrile (**7l**)

R_f 0.4. Yellow solid, with mp 185–187 °C (*i*-PrOH); ^{1}H NMR ($CDCl_3$) δ ppm: 2.78–3.08 (m, 2H), 3.17 (pseudoquartet, $J = 8.6$ Hz, 1H), 3.42 (ddd, $J = 8.0$, 8.0, 4.4 Hz, 1H), 5.77 (s, 1H), 7.11 (dd, $J = 7.9$, 4.8 Hz, 1H), 7.27–7.38 (m, 3H), 7.34–7.46 (m, 2H), 7.87 (d, $J = 7.9$ Hz, 1H), 7.99 (s, 1H), 8.55 (d, $J = 4.8$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ ppm: 35.9, 51.3, 74.5, 105.6, 117.4, 120.4, 123.7, 124.4, 128.3, 128.5, 128.7, 138.2, 141.2, 152.2, 153.9, 163.9; IR, cm^{-1}: 1708 (C = O), 2220 (C≡N); UV–vis, λ_{max} (lg ε), nm: 368 (4.04), end absorption up to 474 nm; MS (ESI) *m/z*: found 303.1251 [M+H]$^+$, calcd for $C_{18}H_{14}N_4O$ 303.1240 [M+H]$^+$.

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Appendix ASupplementary data

Supplementary data associated with this article can be found in the online version, at https://doi.org/10.1016/j.tet.2018.01.046. These data include MOL files and InChiKeys of the most important compounds described in this article.

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