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Synthesis of heteroannulated 3-nitro- and 3-aminopyridines by cyclocondensation of electron-rich aminoheterocycles with 3-nitrochromone

Viktor O. Iaroshenko [a,b,*], Satenik Mkrtchyan [a,c], Ashot Gevorgyan [a,c], Marcelo Vilches-Herrera [a], Dmitri V. Sevenard [d], Alexander Villinger [a], Tariel V. Ghochikyan [c], Ashot Saghiyan [c], Vyacheslav Ya. Sosnovskikh [e], Peter Langer [a,f,*]

[a] Institut für Chemie, Universität Rostock, Albert-Einstein-Str. 3a, 18059 Rostock, Germany
[b] National Taras Shevchenko University, 62 Volodymyrska st., Kyiv-33 01033, Ukraine
[c] Faculty of Chemistry, Yerevan State University, Alex Manoogian 1, 0025 Yerevan, Armenia
[d] Hansa Fine Chemicals GmbH, BITZ, Fahrenheitstrasse 1, 28359 Bremen, Germany
[e] Department of Chemistry, Ural State University, 51 Lenina Ave., 620083 Ekaterinburg, Russia
[f] Leibniz-Institut für Katalyse e. V. an der Universität Rostock, Albert-Einstein-Str. 29a, 18059 Rostock, Germany

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ABSTRACT

3-Nitrochromone reacts with electron-rich aminoheterocycles (in glacial acetic acid at reflux) and anilines (in a mixture of DMF and TMSCl at 100–140 °C) to give a variety of hetero(carbo)annulated 3-nitropyridines. The reaction, involving a formal [3+3] cyclocondensation, proceeds in high yields and appears not to be influences greatly by the nature of the 1,3-C,N-dinucleophile as seen from the thorough scope study. The synthetic utility of the products was demonstrated by their conversion into the corresponding 3-aminopyridine derivatives. An NMR study and X-ray crystallographic analysis are reported.
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1. Introduction

Nitrogen containing heterocycles are of considerable pharmacological relevance.[1] Heteroannulated pyridines attracted significant attention because of their various pharmacological activities.[2,3] 3-Nitro- and 3-aminopyridines, their heteroannulated analogues,[4] and functionalized quinolines represent attractive lead structures for drug discovery.[5] We have been particularly interested in purine-type scaffolds **I** containing electron-withdrawing substituents (EWG) at the 1-position of the purine core structure. We believe that such structures represent promising patterns for the development of inhibitors of adenosine deaminase (ADA), since some 3-nitropyridines are known to undergo hydration at the 4-position to form stable Meisenheimer type hydrates.[6] 3-Nitropyridines as well as their heteroannulated analogues undergo, depending on the pH of the solution, a reaction with water to give stable hydrates. In the case of 5,6-bicyclic systems, these hydrates **II** are expected to be promising scaffolds for the development of ADA transition state mimetics (Fig. 1).

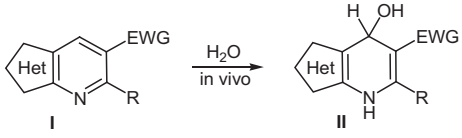

Fig. 1. 5,6-Bicyclic systems as promising scaffolds for the development of ADA transition state mimetics.

On the other hand, 3-substituted chromones (3-acyl-,[7] 3-methoxalyl-,[8] 3-cyanochromones[9]) are used as valuable synthetic intermediates in the preparation of pharmacologically relevant products and new heterocyclic systems. Introduction of an electron-withdrawing group into the 3-position of chromones radically changes the reactivity of the pyrone ring toward nucleophilic reagents and opens up a broad synthetic scope of this important oxygen-containing heterocyclic system. Being essentially *gem*-activated alkenes, 3-substituted chromones exhibit a variety of

* Corresponding authors. Tel.: +49 381 4986410; fax: +49 381 49864112; e-mail addresses: viktor.iaroshenko@uni-rostock.de (V.O. Iaroshenko), peter.langer@uni-rostock.de (P. Langer).

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properties and can undergo additional transformations through opening of the γ-pyrone ring and heterocyclizations at the carbonyl carbon atom because of the presence of a good leaving group (phenolate anion). However, 3-nitrochromones have not received much attention despite their potential interest as building blocks in organic synthesis for the construction of heterocyclic compounds bearing a nitro group.

Based on the retrosynthetic analysis and on our previous work related to the development of new cyclocondensation reactions of electron-rich aminoheterocycles,[10] we envisaged that 3-nitro(thio) chromones are suitable substrates for the synthesis of heteroannulated 3-nitropyridines. We are reporting now on the formation of this type of heterocycles from 3-nitrochromones **1** and various electron-rich heterocyclic amines and anilines **2** (Fig. 2).

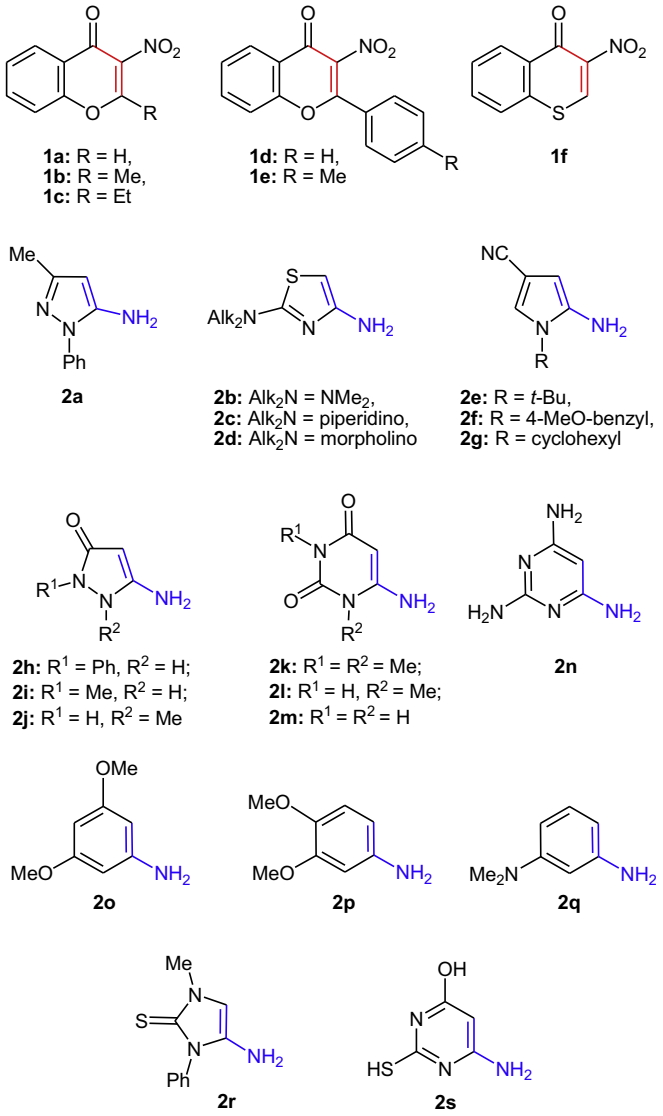
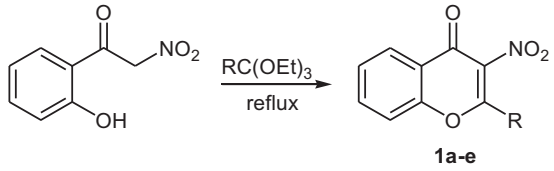


Fig. 2. 3-Nitro(thio)chromones **1** and electron-rich amines **2** used for the synthesis of heteroannulated 3-nitropyridines and 3-nitroquinolines **3**.

2. Results and discussion

Chromones, having electron-withdrawing substituents at the 3-position, undergo reactions with dinucleophiles at the 2-position of the chromone system, followed by pyrone ring opening and intramolecular cyclization via another electrophilic centers.[7] Owing to this, 3-substituted chromones as 1,3-dielectrophiles and electron-rich aminoheterocycles as 1,3-dinucleophiles have attracted attention as excellent building blocks for the preparation of various fused pyridines and pyrimidines.[11,12] These compounds can be considered as purine isosteres and are of a great interest as privileged scaffolds in medicinal chemistry and drug design.[3b,13]

Routes for the synthesis of 2-unsubstituted 3-nitrochromone **1a** are scarce, only two methods are known. The first and the most utilized method follows a three-step procedure via 4-hydroxy-3-nitrocoumarin, starting from commercially available 4-hydroxycoumarin and producing **1a** in moderate yields by formylation of 2′-hydroxy-2-nitroacetophenone with acetic formic anhydride. The latter was prepared by decarbonylation of 4-hydroxy-3-nitrocoumarin with aqueous sodium hydroxide.[14] An alternative synthesis of 6-substituted 3-nitrochromones relies on the nitration of the corresponding 3-hydroxymethyl- or 3-formylchromones, however this reaction worked only when the aromatic ring was deactivated toward electrophilic substitution.[15] Moreover, regioselective method for the radical 3-nitration of flavones that allows the synthesis of 3-nitroflavones has been reported.[16] 2-Methyl-3-nitrochromone **1b** has been previously synthesized by acetylation of 2′-hydroxy-2-nitroacetophenone with acetic anhydride in pyridine in low yield (18%).[14a] Therefore, simpler and high yield approaches toward 3-nitrochromones would be desirable. In this work, the best reaction conditions for the synthesis of 3-nitrochromones **1a**–**e** were found (see Experimental) and of special interest is the formation of these compounds in the reaction of 2′-hydroxy-2-nitroacetophenone with triethyl orthocarboxylates in 82–88% yields (Scheme 1).

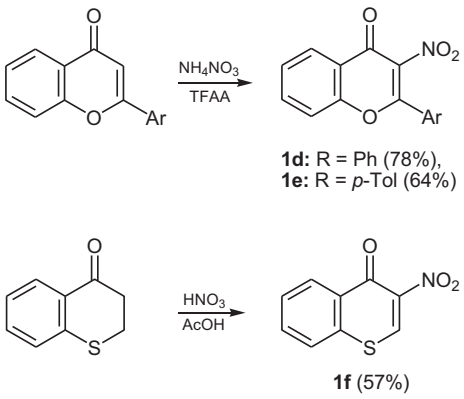


Chromone **1**	R	Reaction time (h)	Yield (%)
a	H	6	82
b	Me	3	84
c	Et	4	83
d	Ph	5	88
e	*p*-Tol	5	85

Scheme 1.

In addition, 3-nitroflavones **1d**,**e** were also prepared by nitration of flavones using ammonium nitrate and trifluoroacetic anhydride,[16] while nitration of thiochroman-4-one with 65% nitric acid in acetic acid produced 3-nitrothiochromone **1f** in 57% yield.[17] The latter reaction is a straightforward and convenient route to **1f**, which makes this little-known compound suitable for further investigations (Scheme 2). All our attempts to prepare 3-nitro-2-(trifluoromethyl)chromone and methyl 3-nitrochromone-2-carboxylate by reactions of 2′-hydroxy-2-nitroacetophenone with trifluoroacetic anhydride and methyl 2-chloro-2-oxoacetate, failed.

To the best of our knowledge, very scarce information is available about the reactivity of 3-nitro(thio)chromones **1**. There have been only a handful of papers describing some reactions of **1a** with amines, benzamidine, phenylhydrazine, and enamines, including 5-amino-1-isopropyl-3-methylpyrazole and 5-amino-3-(4-pyridyl)



Scheme 2.

isoxazole,[18] as well as reactions of **1b** with amidines, guanidine, acid hydrazides, *S*-methylisothiourea, and hydroxylamine.[19] We have recently shown[20] that the reaction of **1a** with in situ generated 1-substituted 5-amino-1*H*-imidazoles affords a range of 1-substituted 6-nitro-3*H*-imidazo[4,5-*b*]pyridines, which represent potential adenosine deaminase (ADA) inhibitors.[21] All these reactions proceed by nucleophilic 1,4-addition followed by intramolecular condensation at the carbonyl group to yield various nitro derivatives.

Our efficient procedures for the preparation of 3-nitrochromones **1** allowed us to investigate their chemical properties in more detail. Here we have examined the behavior of **1** in their reactions with a wide set of electron-rich aminoheterocycles and anilines **2** with the purpose of development of a simple and preparative synthetic approach to hetero(carbo)annulated 3-nitropyridines **3**. After some optimization, it was found that treatment of 3-nitrochromone **1a** with amines **2a**–**l**,**s** (1.1 equiv) in glacial acetic acid at reflux for several hours (method A) resulted in the formation of annulated pyridines **3a**–**l**,**s** with an excellent regioselectivity. A wide range of amines **2** can effectively participate in the reaction with high yields (up to 98%). In most cases, the reaction was complete after 1–7 h, and the products could be isolated by simple filtration of the precipitate formed. The progress of the reaction was monitored by TLC, and the results are summarized in Table 1. In a different set of reactions we have used a mixture of DMF and TMSCl as a water scavenger;[22] the reactions were conducted in a pressure tube at 100–140 °C for several hours (method B). The TMSCl-mediated reaction of **1** with pyrimidines **2m**,**n** and 4-amino-1-methyl-3-phenyl-1*H*-imidazole-2(3*H*)-thione **2r**, which is unstable in acetic acid, afforded products **3m**,**n**,**r** (yields 65–95%). It should be noted that formal [3+3] cyclocondensation leading to fused pyridines **3** from 3-nitrochromone **1a** is not limited to the use of the heterocyclic amines. The less reactive electron-rich anilines **2o**–**q** also undergo a similar reaction (DMF/TMSCl) to give 3-nitroquinolines **3o**–**q** as the only isolated products in 62–91% yield (Table 1).

This result clearly shows that the present methodology could be applicable to various types of heterocyclic amines and anilines, providing a rapid route to the synthesis of a great variety of hetero(carbo)annulated pyridines bearing a NO_2 group located at the β-position of the pyridine core. In connection with this, it was of interest to evaluate the reactivity of 2-methyl- and 2-ethyl-3-nitrochromones **1b**,**c**, 3-nitroflavones **1d**,**e**, and 3-nitrothiochromone **1f** toward some heterocyclic amines **2**. Unfortunately, all our attempts to obtain the corresponding fused pyridines by treatment of chromones **1b**–**e** with amines **2** under the same reaction conditions (methods A and B) were unsuccessful and only starting materials were recovered. In some cases, the reaction gave tarry multicomponent mixtures from which no fused pyridines of type **3** could be isolated. Thus, the reaction turned out to be very sensitive to the nature of the substituent at the C-2 atom and afforded pyridines **3** only when the chromone **1a** was used. This is probably a result of the steric and conjugation factors. It was also found that 3-nitrothiochromone **1f** is much less reactive than 3-nitrochromone **1a** and all attempts to obtain the corresponding pyridines under the same and even more drastic conditions (dimethylacetamide, TMSCl, 170 °C), failed. The observed differences in reactivity between **1a** and **1f** appears to be connected with the difficulty met by the nucleophile in cleaving the thiopyrone S–C bond arising from the less electronegative character of the sulfur atom, which strongly reduces the electrophilicity of the 2-position, and the greater aromaticity of the thiochromone system as compared with chromones.[23] Although we were unable to prepare 3-nitro-2-(trifluoromethyl)chromone, the corresponding pyrazolo[3,4-*b*]pyridine **3t** was obtained in low yield (10%) by three-component reaction of 2′-hydroxy-2-nitroacetophenone with trifluoroacetic anhydride and 5-amino-3-methyl-1-phenylpyrazole **2a** (Scheme 3). The low yield logically can be

Table 1
Synthesis of compounds **3** and **4**

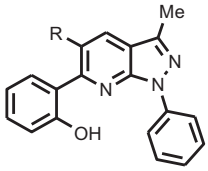
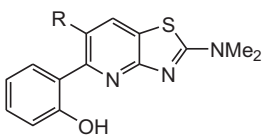
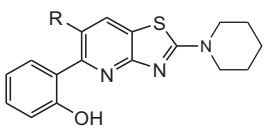
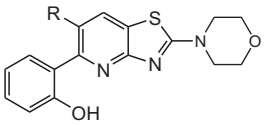
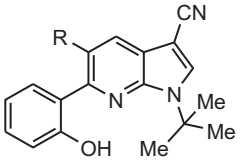
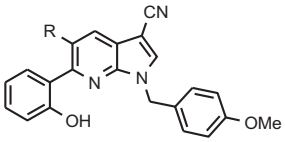
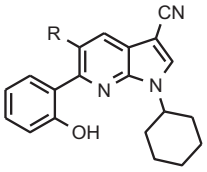
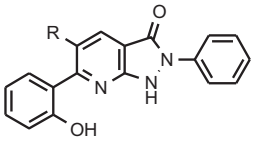
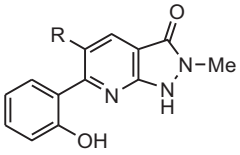
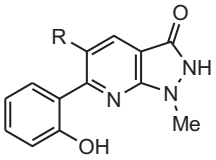
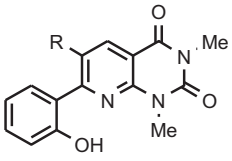
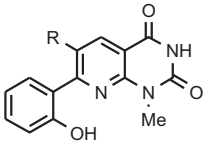
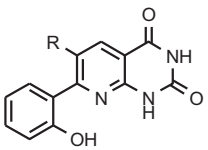
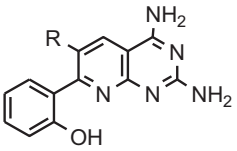
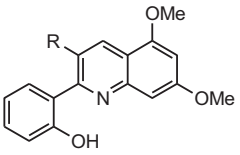
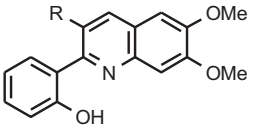
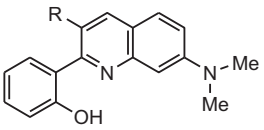
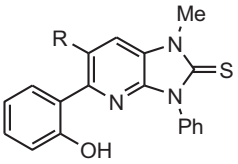
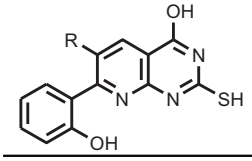
Products	**3** (R=NO_2)	Time[a] (h)	Yield **3**[a,b] (%)	Time[c] (h)	Yield **3**[b,c] (%)	**4** (R=NH_2)	Yield **4**[b] (%)
	**3a**	1	97	1	88	**4a**	87
	**3b**	4	65	4	43	**4b**	48
	**3c**	15	71	15	32	**4c**	70

Table 1 (*continued*)

Products	**3** (R=NO_2)	Time[a] (h)	Yield **3**[a,b] (%)	Time[c] (h)	Yield **3**[b,c] (%)	**4** (R=NH_2)	Yield **4**[b] (%)
	**3d**	1	90	1	44	**4d**	66
	**3e**	7	67	7	28	**4e**	77
	**3f**	1	93	1	31	**4f**	64
	**3g**	1	81	1	27	**4g**	78
	**3h**	5	98	5	77	**4h**	78
	**3i**	2	87	2	63	**4i**	96
	**3j**	4	78	4	54	**4j**	92
	**3k**	4	97	4	44	**4k**	66
	**3l**	6	73	6	32	**4l**	88
	**3m**	2	84	2	40	**4m**	97

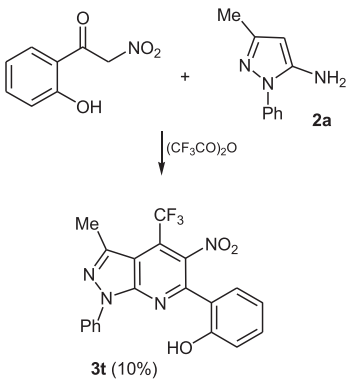
(*continued on next page*)

Table 1 (*continued*)

Products	**3** (R=NO_2)	Time[a] (h)	Yield **3**[a,b] (%)	Time[c] (h)	Yield **3**[b,c] (%)	**4** (R=NH_2)	Yield **4**[b] (%)
	**3n**	2	Mix.	4	65	**4n**	93
	**3o**	2	Mix.	18	62	**4o**	80
	**3p**	2	Mix.	2	83	**4p**	93
	**3q**	2	Mix.	10	91	**4q**	94
	**3r**	2	Mix.	10	95	[d]	—
	**3s**	3	79	3	35	[d]	—

[a] Method A (AcOH, reflux).
[b] Yields of isolated products.
[c] Method B (TMSCl/DMF, 100 °C; 140 °C for **3p**).
[d] Reaction did not occur.

explained by taking into account that the correspondent aminopyrazole **2g** can react with trifluoroacetic anhydride delivering corresponding acylated product, the latest was detected by ^{19}F NMR as a major reaction product.

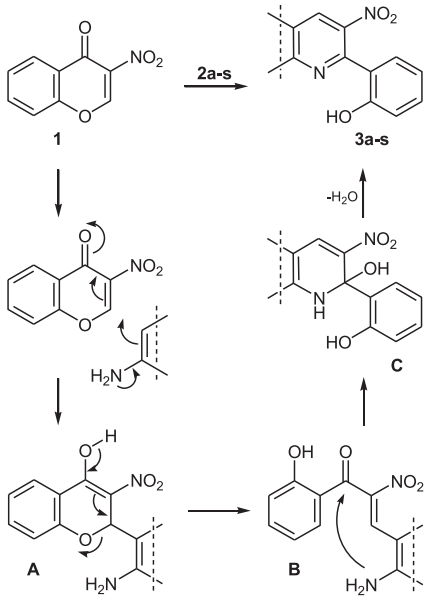


Scheme 3.

The formation of fused pyridines **3** can be explained by conjugate addition of the enamine carbon atom of **2** to the double bond of **1a** to give intermediate **A**. Subsequent pyrone ring opening delivers intermediate type **B**. The intramolecular attack of the amino group to the carbonyl group affords intermediate **C**, which undergoes elimination of water to give products **3** (Scheme 4).

The structures of fused pyridines **3a**,**e**,**f**,**k**,**o**,**r** were confirmed by X-ray crystal structure analyses (Figs. 3 and 4; and Supplementary data).[24] The ORTEP diagram of all investigated crystals shows the planar cores of heterocyclic framework; compounds **3o** and **3r** contain the intramolecular hydrogen bonds O–H·N.

Next, taking into account the availability of the fused 3-nitropyridine **3** and due to the biological importance of 3-aminopyridine derivatives, especially 5-amino-7-azaindoles,[25] we studied their synthesis by hydrogenation of **3** in the presence of Pd/C (10 mol %). The reduction of the nitro group of compounds **3a**–**q** afforded the expected fused 3-aminopyridines and 3-aminoquinolines **4a**–**q** in good to excellent yields (Scheme 5, Table 1). It is noteworthy that, in the case of **3f**, no cleavage of the benzyl group was observed. Taking into account that the amino



Scheme 4. Possible mechanism of the formation of heterocycles **3**. Reagents and conditions see Table 1.

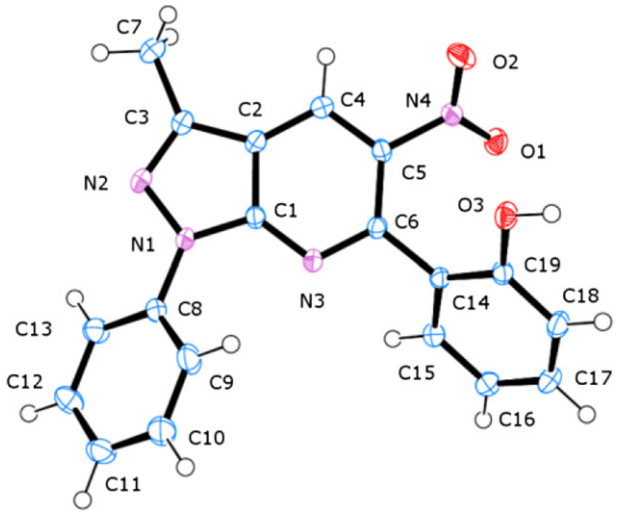


Fig. 3. Molecular structure of compound **3a**.

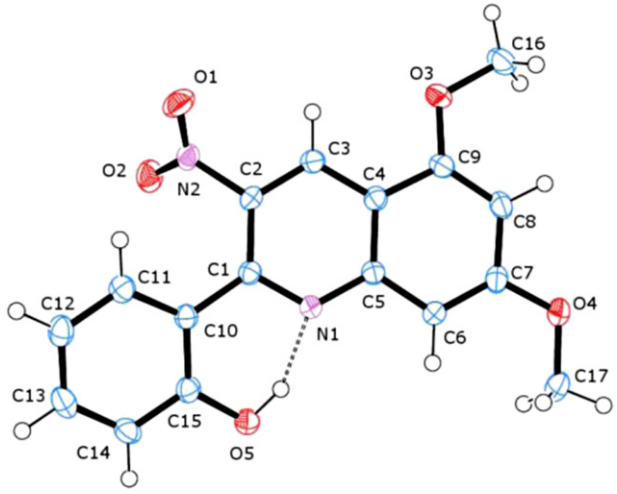
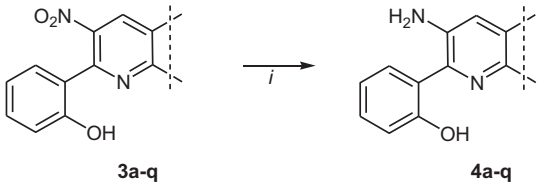


Fig. 4. Molecular structure of compound **3o**.

group can easily be removed by desamination, this is also a method for preparation of novel 3-unsubstituted pyridines and quinolines derivatives bearing 2-hydroxyphenyl moiety at the α-position of the pyridine core. In the same time the reduction reaction of products **3r** and **3s** experienced a failure, here we have most probably encountered with the poisoning effect that sulfur-containing compounds tending to demonstrate. Given the actual interest in these compounds as pharmaceutical intermediates,[3b,13] this simple entry to pyridine derivatives is useful and complements the published synthetic methods.



Scheme 5. Reagents and conditions: (i) MeOH, H_2, Pd/C (10 mol %), 20 °C, 2 days.

3. Conclusion

In conclusion, we have developed a simple and convenient method for the synthesis of functionalized heteroannulated 3-nitropyridines and 3-nitroquinolines by [3+3] cyclocondensation of 3-nitrochromone with electron-rich aminoheterocycles and anilines. The reduction of the nitro group afforded the corresponding heteroannulated 3-aminopyridines and 3-aminoquinolines. The products are drug-like scaffolds, which are not readily available by other methods. The biological evaluation of the synthesized compounds is currently studied in our laboratories.

4. Experimental

4.1. General

NMR spectra were recorded on a Brucker Avance 250 II and Brucker AV 300 instruments. IR spectra were recorded on a Perkin–Elmer FT IR 1600 spectrometer (ATR). Mass spectra were obtained on a Hewlett–Packard HPGC/MS 5890/5972 instrument (EI, 70 eV) by GC inlet or on an MX-1321 instrument (EI, 70 eV) by direct inlet. Column chromatography was performed on silica gel (63–200 mesh, Merck), silica gel Merck 60F_{254} plates were used for TLC. All solvents were purified and dried by standard methods. 3-Nitrothiochromone **1f** was prepared according to described procedure.[17]

4.1.1. 4-Hydroxy-3-nitrocoumarin. To a suspension of 4-hydroxycoumarin (40.0 g, 0.25 mol) and sodium nitrite (0.8 g, 0.012 mol) in acetic acid (120 mL) was added 65% nitric acid (35 mL) in small portions with stirring at room temperature. The reaction mixture was heated with stirring at 60 °C for 15 min and the resulting solid was filtered and washed with water to give green crystals in 87% yield (44.6 g), mp 174–175 °C (lit.[14a] mp 177 °C).

4.1.2. 2′-Hydroxy-2-nitroacetophenone. 4-Hydroxy-3-nitrocoumarin (12.6 g, 0.06 mol) was dissolved in 450 mL of 5% aqueous solution of sodium hydroxide and the resulting reddish solution was heated at 60 °C for 3 h. After cooling, the reaction mixture was acidified with stirring by dropwise addition of acetic acid to the pH 5. The solid that formed was rapidly filtered and washed with water to afford a colorless solid in 81% yield (8.8 g), mp 106 °C (lit.[14a] mp 106–107 °C).

*4.1.3. 3-Nitrochromone (**1a**).* To a solution of 2′-hydroxy-2-nitroacetophenone (13.3 g, 0.074 mol) in trimethyl orthoformate (66.4 mL) was added concentrated sulfuric acid (0.36 g). The

reaction mixture was then refluxed for 6 h and distilled to a dry residue. The solid that formed was washed with water and recrystallized from methanol to give a brown solid in 84% yield (11.7 g), mp 149–150 °C (lit.[14b,c] mp 149–151 °C, 151–152 °C). Chromones **1b**–**e** were obtained by the analogous procedure.

*4.1.4. 2-Ethyl-3-nitrochromone (**1c**).* Colorless solid, mp 178–179 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.40 (t, 3H, ^3J=7.5 Hz, Me), 2.82 (q, 2H, ^3J=7.5 Hz, CH_2), 7.42–7.52 (m, 2H, H-6, H-8), 7.71–7.76 (m, 1H, H-7), 8.19 (dd, 2H, ^3J=8.0 Hz, ^4J=1.5 Hz, H-5); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 11.0, 25.1, 118.1, 122.5, 123.3, 126.3, 134.9, 138.3, 155.2, 167.2, 168.2; MS (GC, 70 eV) *m*/*z* (%) 219 (M^+, 100); HRMS (EI): calcd for $C_{11}H_9NO_4$ (M^+) 219.0522, found 219.0523; IR (ATR, cm^{-1}) ν 2993 (w), 1732 (w), 1654 (s), 1615 (m), 1568 (w), 1519 (s), 1456 (s), 1372 (s), 1326 (m), 1209 (w), 1140 (m), 1042 (m), 969 (w), 902 (m), 787 (s), 768 (s), 596 (m).

4.2. General procedures for the synthesis of compounds 3

Method A (*in acetic acid*). 3-Nitrochromone **1a** (2 mmol, 0.38 g) and the corresponding amine **2** (2.2 mmol) were dissolved in acetic acid (20 mL) and heated under reflux in an inert atmosphere during 1–15 h (controlled by TLC, Table 1). Then this solution was evaporated under reduced pressure, treated with water, filtrated, and dried on the air and recrystallized from an appropriate solvent, or was subjected to a column chromatography over silica gel.

Method B (*in DMF/TMSCl*). 3-Nitrochromone **1a** (2 mmol, 0.38 g) and the corresponding amine **2** (2.2 mmol) were placed in pressure tube under the flow of dry argon and dissolved in dry DMF (10 mL) containing 1 mL of TMSCl. The mixture was heated at 100–140 °C during 2–12 h (controlled by TLC, Table 1). Then this solution was evaporated under reduced pressure, treated with water, filtrated, and dried on the air and recrystallized from an appropriate solvent, or was subjected to a column chromatography over silica gel.

*4.2.1. 2-(3-Methyl-5-nitro-1-phenyl-1H-pyrazolo[3,4-b]pyridin-6-yl) phenol (**3a**).* Method A, the compound was precipitated from the reaction mixture, filtered off and washed with water. Yellow solid, mp 204–206 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.69 (s, 3H, Me), 6.87 (d, 1H, ^3J=7.6 Hz), 7.01 (t, 1H, ^3J=7.2 Hz), 7.30–7.37 (m, 2H), 7.55 (t, 2H, ^3J=7.6 Hz), 7.65 (m, 1H), 8.22 (d, 2H, ^3J=7.6 Hz), 9.09 (s, 1H, Py), 10.05 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 12.3, 114.5, 115.1, 119.6, 120.5, 125.2, 126.3, 128.3, 129.3, 130.5, 130.9, 138.4, 142.3, 145.2, 149.3, 150.9, 154.7; MS (GC, 70 eV) *m*/*z* (%) 346 (M^+, 100), 316 (10), 300 (63), 283 (30), 221 (10), 77 (18); HRMS (ESI): calcd for $C_{19}H_{14}N_4O_3$ (M+1) 347.1136, found 347.1141; IR (ATR, cm^{-1}) ν 3393 (m), 3085 (w), 2917 (w), 1606 (w), 1592 (m), 1575 (m), 1523 (m), 1495 (s), 1452 (m), 1421 (m), 1383 (w), 1364 (w), 1322 (w), 1308 (s), 1286 (m), 1212 (m), 1193 (m), 1154 (w), 1118 (m), 1103 (m), 1176 (w), 1039 (w), 1013 (w), 982 (w), 916 (m), 897 (w), 861 (w), 845 (m), 807 (w), 780 (m), 752 (s), 691 (s), 682 (m), 672 (m), 653 (w), 639 (m), 632 (m), 564 (m), 540 (m).

*4.2.2. 2-[2-(Dimethylamino)-6-nitrothiazolo[4,5-b]pyridin-5-yl]phenol (**3b**).* Method A, the compound was purified by a column chromatography (heptane/EtOAc/1:5, R_f=0.58 (MeOH/EtOAc/2:1)). Brown solid, mp 266–268 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.25 (s, 6H, Me_2N), 6.82 (d, 1H, ^3J=8.0 Hz), 6.94 (t, 1H, ^3J=7.4 Hz), 7.25 (t, 1H, ^3J=7.4 Hz), 7.48 (d, 1H, ^3J=7.0 Hz), 8.86 (s, 1H, Py), 9.81 (s, 1H, OH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 39.7, 114.9, 119.2, 123.2, 125.7, 126.3, 130.1, 130.2, 139.8, 149.0, 154.4, 166.0, 173.1; MS (GC, 70 eV) *m*/*z* (%) 316 (M^+, 39), 270 (100), 254 (17), 227 (17), 207 (49); HRMS (ESI): calcd for $C_{14}H_{12}N_4O_3S$ (M+1) 317.0703, found 317.0707; IR (ATR, cm^{-1}) ν 3090 (w), 2921 (w), 2852 (w), 1601 (w), 1549 (s), 1497 (w), 1450 (w), 1408 (m), 1345 (w), 1325 (m), 1307 (s), 1279 (s), 1228 (s), 1181 (m), 1153 (m), 1115 (m), 1098 (s), 1079 (m), 1035 (m), 972 (w), 936 (w), 901 (s), 861 (m), 827 (m), 781 (m), 765 (s), 745 (s), 729 (s), 695 (m), 667 (s), 619 (m), 581 (m), 537 (s).

*4.2.3. 2-[6-Nitro-2-(piperidin-1-yl)thiazolo[4,5-b]pyridin-5-yl]phenol (**3c**).* Method A, the compound was purified by a column chromatography (heptane/EtOAc/1.5:1, R_f=0.65 (EtOAc)). Yellow solid, mp 109–110 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.74 (s, 6H, $3CH_2$), 3.72 (s, 4H, $2CH_2$), 6.86 (m, 1H), 7.02 (dd, 1H, ^3J=8.2 Hz, ^4J=1.0 Hz), 7.22–7.31 (m, 2H), 8.34 (s, 1H, Py), 9.95 (br s, 1H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 23.9, 25.4, 50.1, 118.1, 119.8, 119.9, 123.0, 126.5, 129.4, 131.6, 138.8, 149.8, 156.1, 164.8, 172.6; MS (EI, 70 eV) *m*/*z* (%) 356 (M^+, 54), 310 (100); HRMS (EI): calcd for $C_{17}H_{16}N_4O_3S$ (M^+) 356.09376, found 356.09383; IR (ATR, cm^{-1}) ν 3066 (w), 2937 (w), 2855 (w), 1595 (w), 1537 (s), 1447 (m), 1416 (w), 1306 (s), 1213 (m), 1157(w), 1118 (m), 1037 (w), 1009 (m), 969 (w), 952 (w), 904 (w), 886 (m), 832 (w), 782 (m), 750 (s), 709 (m), 680 (w), 629 (w), 595 (m), 568 (w).

*4.2.4. 2-(2-Morpholino-6-nitrothiazolo[4,5-b]pyridin-5-yl)phenol (**3d**).* Method A, the compound was precipitated from the reaction mixture, filtered off and washed with *i*-PrOH/EtOAc/2:1. Yellow solid, mp 229–231 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.72–3.76 (m, 8H, $4CH_2$), 6.82 (dd, 1H, ^3J=8.1 Hz, ^4J=0.8 Hz), 6.94 (td, 1H, ^3J=7.5 Hz, ^4J=1.0 Hz), 7.26 (m, 1H), 7.49 (dd, 1H, ^3J=7.6 Hz, ^4J=1.7 Hz), 8.89 (s, 1H, Py), 9.84 (s, 1H, OH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 48.1, 65.4, 114.9, 119.2, 122.7, 125.5, 126.6, 130.2, 130.3, 140.2, 149.0, 154.4, 165.6, 173.2; MS (EI, 70 eV) *m*/*z* (%) 358 (M^+, 34), 312 (100), 69 (13); HRMS (ESI): calcd for $C_{16}H_{14}N_4O_4S$ (M+1) 359.0809, found 359.0805; IR (ATR, cm^{-1}) ν 3517 (w), 3408 (w), 1599(w), 1540 (s), 1492 (m), 1470 (w), 1448 (w), 1433 (w), 1409 (m), 1394 (w), 1345 (m), 1329 (s), 1311 (s), 1283 (s), 1238 (m), 1212 (w), 1182 (w), 1126 (w), 1112 (s), 1083 (w), 1068 (w), 1028 (m), 931 (w), 896 (s), 864 (w), 840 (w), 821 (w), 781 (w), 759 (s), 711 (w), 674 (w), 631 (m), 609 (m), 543 (w).

*4.2.5. 1-tert-Butyl-6-(2-hydroxyphenyl)-5-nitro-1H-pyrrolo[2,3-b] pyridine-3-carbonitrile (**3e**).* Method A, the compound was precipitated from the reaction mixture, filtered off and washed with MeOH. Colorless solid, mp 244–245 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.78 (s, 9H, *t*-Bu), 6.86 (dd, 1H, ^3J=8.0 Hz, ^4J=0.8 Hz), 7.00 (td, 1H, ^3J=7.5 Hz, ^4J=0.9 Hz), 7.29 (m, 1H), 7.56 (dd, 1H, ^3J=7.6 Hz, ^4J=1.6 Hz), 8.72 (s, 1H), 8.78 (s, 1H), 10.01 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 28.6, 59.4, 83.5, 114.5, 115.1, 118.3, 119.6, 124.6, 125.2, 130.3, 130.5, 139.6, 142.7, 145.1, 146.3, 154.7; MS (GC, 70 eV) *m*/*z* (%) 336 (M^+, 96), 306 (15), 280 (100), 263 (10), 250 (47), 234 (84), 206 (34), 195 (16), 180 (13), 152 (10), 57 (68), 41 (33); HRMS (ESI): calcd for $C_{18}H_{16}N_4O_3$ (M+1) 337.1295, found 337.1292; IR (ATR, cm^{-1}) ν 3293 (w), 2980 (w), 2240 (m), 1671 (w), 1605 (w), 1595 (w), 1567 (m), 1522 (s), 1450 (m), 1412 (m), 1400 (w), 1372 (m), 1352 (s), 1341 (s), 1295 (m), 1255 (m), 1197 (s), 1123 (m), 1101 (m), 1092 (m), 1043 (s), 1007 (w), 945 (w), 920 (m), 852 (w), 838 (m), 819 (w), 784 (s), 761 (s), 700 (m), 667 (s), 625 (s), 615 (s), 600 (m), 557 (m), 532 (m).

*4.2.6. 1-(4-Methoxybenzyl)-6-(2-hydroxyphenyl)-5-nitro-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile (**3f**).* Method A, the compound was precipitated from the reaction mixture, filtered off and washed with water. Colorless solid, mp 166–167 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.71 (s, 3H, MeO), 5.50 (s, 2H, CH_2), 6.85–6.92 (m, 3H), 7.01 (td, 1H, ^3J=7.5 Hz, ^4J=0.9 Hz), 7.27–7.37 (m, 3H), 7.56 (dd, 1H, ^3J=7.6 Hz, ^4J=1.6 Hz), 8.77 (s, 1H), 8.83 (s, 1H), 10.00 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 48.1, 55.1, 84.7, 114.1, 114.2, 115.1, 116.9, 119.5, 125.0, 125.1, 128.2, 129.5, 130.5, 130.6, 140.9, 143.2, 145.9, 146.7, 154.6, 159.0; MS (EI, 70 eV) *m*/*z* (%) 400 (M^+, 27), 121 (100), 91 (13), 77 (20); HRMS (ESI): calcd for $C_{22}H_{16}N_4O_4$ (M+1) 401.1244, found 401.1242; IR (ATR, cm^{-1}) ν 3116 (w), 3020 (w), 2841 (w), 1609

(m), 1581 (w), 1573 (w), 1515 (s), 1475 (w), 1462 (w), 1437 (s), 1389 (m), 1361 (w), 1341 (s), 1324 (m), 1305 (w), 1282 (m), 1252 (s), 1216 (m), 1174 (s), 1160 (m), 1121 (w), 1094 (w), 1029 (m), 953 (w), 910 (w), 884 (w), 868 (w), 845 (m), 817 (m), 790 (m), 766 (s), 727 (m), 700 (w), 686 (w), 666 (w), 644 (m), 627 (w), 609 (m), 569 (w), 554 (m), 528 (w).

*4.2.7. 1-Cyclohexyl-6-(2-hydroxyphenyl)-5-nitro-1H-pyrrolo[2,3-b] pyridine-3-carbonitrile (**3g**).* Method A, the compound was precipitated from the reaction mixture, filtered off and washed with water. Yellow solid, mp 226–227 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.23–2.06 (m, 10H, 5CH$_2$), 4.78 (m, 1H, CHN), 6.87 (d, 1H, ^3J=8.0 Hz), 7.01 (t, 1H, ^3J=7.5 Hz), 7.31 (td, 1H, ^3J=8.0 Hz, ^4J=1.6 Hz), 7.56 (dd, 1H, ^3J=7.6 Hz, ^4J=1.5 Hz), 8.78 (s, 1H), 8.92 (s, 1H), 9.97 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 24.7, 25.0, 32.2, 54.5, 84.5, 114.4, 115.0, 116.9, 119.3, 124.9, 125.1, 130.4, 138.9, 143.1, 145.6, 146.3, 154.6; MS (GC, 70 eV) *m*/*z* (%) 362 (M$^+$, 96), 280 (100), 234 (58), 206 (17), 55 (19); HRMS (ESI): calcd for $C_{20}H_{18}N_4O_3$ (M+1) 363.1452, found 363.1446; IR (ATR, cm^{-1}): ν 3117 (w), 2942 (w), 2856 (w), 2227 (m), 1607 (m), 1580 (w), 1563 (w), 1531 (s), 1496 (w), 1478 (m), 1450 (w), 1431 (s), 1395 (m), 1311 (w), 1289 (w), 1263 (m), 1230 (w), 1202 (m), 1161 (w), 1142 (w), 1114 (w), 1094 (w), 1034 (w), 995 (w), 948 (w), 921 (w), 891 (w), 875 (w), 822 (w), 788 (m), 766 (s), 756 (m), 703 (w), 641 (m), 623 (m), 543 (w).

*4.2.8. 6-(2-Hydroxyphenyl)-5-nitro-2-phenyl-1,2-dihydropyrazolo [3,4-b]pyridin-3-one (**3h**).* Method A, the compound was precipitated from the reaction mixture, filtered off and washed with water. Green solid, mp 248–250 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.88 (d, 1H, ^3J=8.0 Hz), 6.99 (t, 1H, ^3J=7.4 Hz), 7.28–7.37 (m, 2H), 7.51–7.56 (m, 3H, Ph), 7.92 (d, 2H, ^3J=8.0 Hz, Ph), 8.75 (s, 1H, Py), 10.14 (s, 1H, OH), 12.0–13.5 (br s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6) δ 107.9, 115.3, 119.4, 119.9, 124.0, 125.8, 129.2, 130.2, 131.2, 131.4, 136.8, 140.3, 153.8, 154.7, 157.3; MS (EI, 70 eV) *m*/*z* (%) 348 (M$^+$, 47), 318 (48), 303 (100), 289 (9), 274 (19), 183 (22), 156 (12), 77 (42); HRMS (ESI): calcd for $C_{18}H_{12}N_4O_4$ (M+1) 349.0931, found 349.0926; IR (ATR, cm^{-1}) ν 3055 (w), 1652 (w), 1635 (w), 1605 (m), 1583 (m), 1527 (m), 1497 (w), 1483 (w), 1453 (w), 1407 (m), 1339 (s), 1310 (m), 1275 (m), 1240 (m), 1195 (m), 1179 (m), 1157 (m), 1113 (w), 1098 (w), 1072 (w), 1042 (w), 982 (w), 950 (w), 918 (w), 885 (w), 843 (w), 815 (w), 791 (s), 763 (m), 746 (s), 702 (s), 679 (s), 650 (s), 639 (s), 611 (s), 596 (m), 558 (m).

*4.2.9. 6-(2-Hydroxyphenyl)-2-methyl-5-nitro-1,2-dihydropyrazolo [3,4-b]pyridin-3-one (**3i**).* Method A, the compound was precipitated from the reaction mixture, filtered off and washed with water. Red solid, mp 295–297 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.48 (s, 3H, Me), 6.85 (d, 1H, ^3J=8.1 Hz), 6.95 (td, 1H, ^3J=7.4 Hz, ^4J=0.7 Hz), 7.30 (m, 1H), 7.48 (dd, 1H, ^3J=7.6 Hz, ^4J=1.6 Hz), 8.65 (s, 1H, Py), 10.01 (s, 1H, OH), 12.5–13.0 (br s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 30.6, 105.7, 115.1, 119.3, 125.1, 130.1, 130.9, 140.8, 153.0, 154.4, 154.5, 157.1; MS (EI, 70 eV) *m*/*z* (%) 286 (M$^+$, 32), 256 (79), 241 (37), 183 (23), 169 (23), 156 (16), 131 (26), 119 (25), 105 (18), 77 (29), 69 (100); HRMS (ESI): calcd for $C_{13}H_{10}N_4O_4$ (M+1) 287.07748, found 287.07720; IR (ATR, cm^{-1}) ν 2929 (w), 2746 (w), 1645 (m), 1621 (m), 1582 (m), 1532 (m), 1504 (m), 1447 (m), 1318 (m), 1292 (m), 1240 (m), 1177 (w), 1116 (w), 1092 (w), 1033 (w), 999 (w), 961 (w), 939 (w), 861 (m), 793 (s), 755 (s), 701 (s), 634 (s).

*4.2.10. 6-(2-Hydroxyphenyl)-1-methyl-5-nitro-1,2-dihydropyrazolo [3,4-b]pyridin-3-one (**3j**).* Method A, the compound was precipitated from the reaction mixture, filtered off and washed with water. Yellow solid, mp 272–274 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.86 (s, 3H, Me), 6.83 (d, 1H, ^3J=8.1 Hz), 6.97 (td, 1H, ^3J=7.5 Hz, ^4J=0.8 Hz), 7.29 (m, 1H), 7.53 (dd, 1H, ^3J=7.6 Hz, ^4J=1.5 Hz), 8.77 (s, 1H, Py), 9.91 (s, 1H, OH), 11.63 (s, 1H, NH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 33.2, 102.0, 115.0, 119.3, 125.7, 127.9, 130.2, 130.5, 140.5, 148.9, 151.2, 154.0, 154.5; MS (EI, 70 eV) *m*/*z* (%) 286 (M$^+$, 52), 241 (100); HRMS (ESI): calcd for $C_{13}H_{10}N_4O_4$ (M+1) 287.06789, found 287.03788; IR (ATR, cm^{-1}) ν 256(w), 1488 (w), 1453 (w), 1404 (w), 1369 (w), 1349 (m), 1288 (w), 1230 (m), 1160 (m), 1116 (w), 1063 (w), 1015 (w), 933 (w), 920 (w), 844 (w), 820 (w), 769 (m), 751 (s), 684 (m), 672 (m), 656 (m), 617 (m), 599 (m).

*4.2.11. 7-(2-Hydroxyphenyl)-1,3-dimethyl-6-nitropyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (**3k**).* Method A, the compound was precipitated from the reaction mixture, filtered off and washed with water. Yellow solid, mp 280–282 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.33 (s, 3H, Me), 3.61 (s, 3H, Me), 6.87 (d, 1H, ^3J=7.9 Hz), 7.01 (t, 1H, ^3J=7.3 Hz), 7.36 (td, 1H, ^3J=8.0 Hz, ^4J=1.6 Hz), 7.64 (dd, 1H, ^3J=7.6 Hz, ^4J=1.5 Hz), 8.73 (s, 1H, Py), 10.29 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 28.3, 29.7, 108.5, 115.2, 119.6, 123.8, 130.6, 131.9, 133.2, 141.8, 150.9, 151.3, 154.4, 155.0, 159.7; MS (GC, 70 eV) *m*/*z* (%) 328 (M$^+$, 1), 281 (100), 253 (28), 196 (12), 169 (41); HRMS (ESI): calcd for $C_{15}H_{12}N_4O_5$ (M+1) 329.0880, found 329.0883; IR (ATR, cm^{-1}) ν 3256 (w), 3076 (w), 2952 (w), 1706 (m), 1650 (s), 1594 (s), 1582 (s), 1537 (m), 1504 (w), 1488 (w), 1446 (m), 1419 (m), 1401 (w), 1372 (m), 1353 (s), 1289 (m), 1268 (m), 1197 (m), 1163 (w), 1116 (w), 1096 (m), 1067 (w), 1038 (w), 1010 (w), 969 (w), 949 (w), 928 (w), 844 (w), 827 (w), 795 (m), 779 (m), 765 (s), 756 (s), 700 (s), 679 (m), 650 (m), 593 (m), 546 (m).

*4.2.12. 7-(2-Hydroxyphenyl)-1-methyl-6-nitropyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (**3l**).* Method A, the compound was precipitated from the reaction mixture, filtered off and washed with water. Yellow solid, mp 230–232 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.53 (s, 3H, Me), 6.86 (d, 1H, ^3J=8.0 Hz), 7.00 (td, 1H, ^3J=7.4 Hz, ^4J=0.7 Hz), 7.35 (m, 1H), 7.63 (dd, 1H, ^3J=7.6 Hz, ^4J=1.6 Hz), 8.67 (s, 1H, Py), 10.28 (s, 1H, OH), 12.01 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 28.8, 109.3, 115.3, 119.6, 123.9, 130.6, 131.9, 132.9, 141.6, 150.6, 152.7, 154.4, 155.0, 160.1; MS (GC, 70 eV) *m*/*z* (%) 314 (M$^+$, 100), 281 (11), 267 (55), 225 (57), 207 (27), 195 (15), 168 (63), 140 (17), 115 (13), 92 (13); HRMS (ESI): calcd for $C_{14}H_{10}N_4O_5$ (M+1) 315.0724, found 315.0725; IR (ATR, cm^{-1}) ν 3288 (w), 3153 (w), 3014 (w), 2820 (w), 1707 (w), 1674 (m), 1602 (m), 1536 (m), 1498 (w), 1446 (m), 1426 (w), 1402 (m), 1372 (m), 1343 (s), 1284 (m), 1196 (m), 1155 (m), 1077 (m), 1038 (w), 976 (m), 935 (w), 863 (m), 842 (m), 815 (m), 781 (m), 765 (s), 749 (s), 737 (s), 677 (m), 659 (m), 588 (m), 551 (s).

*4.2.13. 7-(2-Hydroxyphenyl)-6-nitropyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (**3m**).* Method B, the compound was precipitated from the reaction mixture, filtered off and washed with MeOH/H_2O/1:1. Yellow solid, mp 317–319 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.86 (d, 1H, ^3J=8.1 Hz), 6.98 (t, 1H, ^3J=7.5 Hz), 7.34 (m, 1H), 7.50 (dd, 1H, ^3J=7.5 Hz, ^4J=1.0 Hz), 8.64 (s, 1H, Py), 10.19 (s, 1H, OH), 11.75 (s, 1H, NH), 12.24 (s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 108.4, 115.2, 119.3, 123.8, 130.4, 131.6, 132.8, 141.9, 150.3, 153.5, 154.8, 155.5, 161.2; MS (GC, 70 eV) *m*/*z* (%) 300 (M$^+$, 96), 270 (100), 255 (40), 231 (13), 211 (35), 182 (11), 168 (21), 156 (17), 128 (10); HRMS (ESI): calcd for $C_{13}H_8N_4O_5$ (M+1) 301.05675, found 301.05635; IR (ATR, cm^{-1}) ν 3306 (w), 3012 (w), 2824 (w), 1722 (w), 1668 (m), 1599 (m), 1574 (m), 1537 (m), 1494 (w), 1348 (s), 1300 (m), 1274 (m), 1203 (m), 1145 (w), 1114 (w), 1096 (w), 1017 (w), 978 (w), 884 (w), 841 (w), 808 (w), 794 (w), 751 (s), 656 (m), 590 (m), 559 (m).

*4.2.14. 2-(2,4-Diamino-6-nitropyrido[2,3-d]pyrimidin-7-yl)phenol (**3n**).* Method B, the compound was precipitated from the reaction mixture, filtered off and washed with *i*-PrOH/heptane/10:1. Yellow solid, mp 285–287 °C; ^{1}H NMR (250 MHz, DMSO-d_6) δ 6.91–7.03 (m, 2H), 7.33–7.39 (m, 1H), 7.53–7.57 (m, 1H), 8.08 (s, 1H, NH), 8.84

(s, 1H, NH), 9.31 (s, 1H, NH), 9.49 (s, 1H, Py), 9.62 (s, 1H, NH), 10.41 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 103.6, 115.3, 119.4, 123.4, 130.3, 131.8, 132.0, 142.6, 151.0, 155.0, 156.0, 156.7, 162.7; MS (GC, 70 eV) m/z (%) 298 (M^+, 100), 282 (15), 266 (33), 220 (28); HRMS (ESI): calcd for $C_{13}H_{10}N_6O_3$ (M+1) 299.08871, found 299.08841; IR (ATR, cm^{-1}) ν 3324 (w), 3119 (w), 1681 (w), 1645 (m), 1606 (m), 1515 (m), 1464 (w), 1450 (w), 1425 (m), 1402 (m), 1358 (m), 1300 (m), 1200 (m), 1158 (m), 989 (w), 977 (w), 921 (w), 870 (w), 795 (m), 755 (m), 650 (m).

*4.2.15. 2-(5,7-Dimethoxy-3-nitroquinolin-2-yl)phenol (**3o**).* Method B, the compound was purified by a column chromatography (heptane/EtOAc/4:1, R_f=0.60 (EtOAc)). Yellow solid, mp 208–209 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.97 (s, 3H, MeO), 4.00 (s, 3H, MeO), 6.55 (m, 1H), 6.86–6.94 (m, 2H), 7.08 (dd, 1H, ^3J=8.3 Hz, ^4J=1.0 Hz), 7.27 (dd, 1H, ^3J=8.0 Hz, ^4J=1.4 Hz), 7.34 (m, 1H), 8.88 (s, 1H, Py), 11.70 (s, 1H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 56.0, 56.1, 98.8, 99.9, 113.5, 118.3, 118.5, 119.6, 129.1, 129.7, 132.3, 140.8, 148.5, 151.5, 156.8, 157.5, 165.0; MS (GC, 70 eV) m/z (%) 326 (M^+, 73), 318 (48), 280 (100), 265 (27), 222 (20), 194 (12); HRMS (ESI): calcd for $C_{17}H_{14}N_2O_5$ (M+1) 327.0975, found 327.0976; IR (ATR, cm^{-1}) ν 3108 (w), 2971 (w), 1609 (m), 1582 (m), 1500 (m), 1452 (s), 1382 (m), 1237 (s), 1204 (m), 1160 (s), 1135 (s), 1039 (m), 970 (w), 939 (m), 831 (s), 797 (s), 774 (m), 751 (s), 742 (s), 722 (m), 703 (m), 667 (m), 641 (s).

*4.2.16. 2-(6,7-Dimethoxy-3-nitroquinolin-2-yl)phenol (**3p**).* Method B, the compound was purified by a column chromatography (heptane/EtOAc/4:1, R_f=0.45 (EtOAc)). Red solid, mp 202–204 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.94 (s, 3H, MeO), 4.01 (s, 3H, MeO), 6.79 (s, 1H), 6.85 (d, 1H, ^3J=7.9 Hz), 6.98 (t, 1H, ^3J=7.5 Hz), 7.09 (s, 1H), 7.27–7.33 (m, 1H), 7.59 (dd, 1H, ^3J=7.5 Hz, ^4J=1.3 Hz), 8.82 (s, 1H, Py), 9.95 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d6) δ 56.0, 56.5, 99.7, 100.1, 112.8, 114.9, 119.3, 125.3, 127.1, 130.3, 130.6, 141.9, 150.4, 150.8, 154.6, 156.5, 164.3; MS (GC, 70 eV) m/z (%) 326 (M^+, 73), 280 (100), 265 (27), 236 (13), 222 (21), 194 (11); HRMS (ESI): calcd for $C_{17}H_{14}N_2O_5$ (M+1) 327.09755, found 327.09798; IR (ATR, cm^{-1}) ν 2970 (w), 1609 (w), 1591 (m), 1525 (m), 1499 (w), 1453 (m), 1382 (m), 1346 (s), 1237 (m), 1204 (m), 1160 (s), 1134 (s), 1039 (m), 939 (m), 831 (s), 797 (m), 751 (s), 742 (s), 703 (m), 667 (m), 641 (s).

*4.2.17. 2-(7-(Dimethylamino)-3-nitroquinolin-2-yl)phenol (**3q**).* Method B, the compound was precipitated from the reaction mixture, filtered off and washed with H_2O/MeOH/1:2. Dark red solid, mp 236–238 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.18 (s, 6H, Me_2N), 6.98–7.03 (m, 2H), 7.19 (s, 1H), 7.38 (m, 1H), 7.52 (m, 1H), 7.59 (dd, 1H, ^3J=7.5 Hz, ^4J=1.2 Hz), 8.11 (d, 1H, ^3J=9.5 Hz), 9.13 (s, 1H, Py), 10.0–10.8 (br s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 48.6, 100.3, 115.3, 118.2, 118.8, 119.2, 121.8, 130.3, 131.0, 131.7, 135.5, 138.9, 146.1, 149.2, 154.4, 155.0; MS (GC, 70 eV) m/z (%) 309 (M^+, 45), 263 (100), 247 (35), 219 (15); HRMS (EI): calcd for $C_{17}H_{15}N_3O_3$ (M^+) 309.11079, found 309.11112; IR (ATR, cm^{-1}) ν 3202 (w), 2914 (w), 2562 (w), 1644 (w), 1603 (w), 1573 (m), 1515 (m), 1443 (w), 1421 (w), 1331 (m), 1268 (m), 1216 (w), 1158 (m), 1101 (w), 1066 (w), 1017 (m), 956 (w), 900 (m), 858 (w), 823 (m), 771 (m), 755 (s), 713 (m), 623 (m), 611 (m).

*4.2.18. 5-(2-Hydroxyphenyl)-1-methyl-6-nitro-3-phenyl-1H-imidazo[4,5-b]pyridine-2(3H)-thione (**3r**).* Method B, the compound was purified by a column chromatography (heptane/EtOAc/1:1, R_f=0.58 (EtOAc)). Orange solid, mp 164–166 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.86 (s, 3H, Me), 6.79–6.92 (m, 2H), 7.19–7.30 (m, 2H), 7.51–7.59 (m, 5H, Ph), 7.93 (s, 1H, Py), 8.58 (s, 1H, OH); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 31.6, 112.8, 117.9, 119.7, 120.5, 124.7, 127.7, 129.3, 129.7, 129.9, 131.9, 133.3, 142.1, 145.5, 145.8, 155.1, 174.5; MS (EI, 70 eV) m/z (%) 378 (M^+, 100), 348 (60), 332 (90), 316 (12), 77 (14), 57 (10); HRMS (ESI): calcd for $C_{19}H_{14}N_4O_3S$ (M+1) 379.0859, found 379.0860; IR (ATR, cm^{-1}) ν 3082 (w), 2249 (w), 1615 (w), 1602 (w), 1576 (w), 1534 (m), 1500 (m), 1466 (s), 1424 (s), 1376 (m), 1347 (m), 1323 (s), 1286 (s), 1245 (m), 1226 (m), 1198 (s), 1158 (m), 1114 (m), 1079 (m), 1043 (w), 1027 (w), 1003 (w), 988 (w), 956 (w), 936 (w), 904 (s), 894 (m), 830 (w), 806 (s), 782 (w), 766 (s), 753 (s), 726 (s), 711 (s), 686 (s), 647 (s), 603 (m), 556 (s).

*4.2.19. 7-(2-Hydroxyphenyl)-2-mercapto-6-nitropyrido[2,3-d]pyrimidin-4-ol (**3s**).* Method A, the compound was precipitated from the reaction mixture, filtered off and washed with water. Yellow solid, mp 307–309 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.86 (d, 1H, ^3J=8.2 Hz), 6.99 (td, 1H, ^3J=7.5 Hz, ^4J=0.8 Hz), 7.35 (m, 1H), 7.52 (dd, 1H, ^3J=7.6 Hz, ^4J=1.7 Hz), 8.64 (s, 1H, Py), 10.25 (s, 1H, OH), 12.86 (s, 1H, SH), 13.53 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 110.5, 115.2, 119.4, 123.5, 130.5, 131.5, 132.7, 142.5, 152.3, 154.8, 155.7, 158.7, 176.7; MS (GC, 70 eV) m/z (%) 316 (M^+, 100), 286 (11), 270 (48), 253 (19); HRMS (ESI): calcd for $C_{13}H_8N_4O_4S$ (M+1) 317.0339, found 317.0336; IR (ATR, cm^{-1}) ν 3188 (w), 3014 (w), 2887 (w), 1683 (m), 1621 (w), 1605 (m), 1584 (m), 1520 (m), 1505 (m), 1485 (w), 1464 (m), 1455 (m), 1417 (w), 1352 (s), 1308 (m), 1262 (m), 1236 (m), 1194 (w), 1159 (m), 1131 (s), 969 (w), 948 (m), 857 (m), 805 (s), 792 (s), 744 (s), 692 (s), 659 (s), 629 (s), 592 (m), 558 (s), 535 (s).

*4.2.20. 2-(3-Methyl-5-nitro-1-phenyl-4-trifluoromethyl-1H-pyrazolo[3,4-b]pyridin-6-yl)phenol (**3t**).* To a solution of 2′-hydroxy-2-nitroacetophenone (0.30 g, 1.66 mmol) in dry dioxane (4.5 mL) was added dry pyridine (0.28 g, 3.5 mmol) and trifluoroacetic anhydride (0.73 g, 3.5 mmol). The reaction mixture was kept at 90 °C for 2 h and 5-amino-3-methyl-1-phenylpyrazole **2a** (0.32 g, 1.82 mmol) was added. Again, the resulting mixture was kept at 90 °C for 2 h, distilled to a dry residue, dried under reduced pressure, subjected to flash-chromatography (4.5 g of silica gel, $CHCl_3$), and recrystallized from methanol to give yellow crystals. Yield 67 mg (10%), mp 224–226 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.73 (q, 3H, ^6J=1.6 Hz, Me), 6.88–6.96 (m, 2H), 7.32–7.41 (m, 2H), 7.53–7.58 (m, 2H), 8.07–8.10 (m, 2H), 8.44 (dd, 1H, ^3J=8.0 Hz, ^4J=1.8 Hz), 12.23 (s, 1H, OH); ^{19}F NMR (300 MHz, DMSO-d_6) δ −65.9 (s, CF_3); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 14.4 (q, ^5J=3.8 Hz, Me), 108.5, 117.9, 118.2, 119.5, 120.7 (q, ^1J=277 Hz, CF_3), 121.5, 127.3, 127.6, 129.3, 129.7, 134.1, 137.7, 142.9, 148.4 (q, ^2J=39.8 Hz, C–CF_3), 153.9, 160.4, 161.3; MS (GC, 70 eV) m/z (%) 414 (M^+, 1), 370 (100); HRMS (ESI): calcd for $C_{20}H_{13}N_4O_3F_3$ (M+1) 415.1552, found 415.1554; IR (ATR, cm^{-1}) ν 2928 (w), 1580 (m), 1512 (w), 1479 (w), 1446 (m), 1375 (m), 1344 (m), 1304 (w), 1248 (m), 1212 (s), 1140 (s), 1084 (w), 1060 (m), 1033 (m), 993 (m), 908 (w), 877 (w), 859 (w), 811 (m), 752 (s), 739 (s), 685 (m), 660 (m), 649 (m), 637 (m).

4.3. General procedure for the synthesis of compounds 4

In a 50 mL Schlenk flask under a flow of dry argon were placed the corresponding pyridine **3** (1.0 mmol) and 0.05 g of Pd/C (10%). Afterward, 25 mL of degassed methanol was added. The system was washed three times with hydrogen. The hydrogenation was conducted with the help of a glass burette under atmospheric pressure. After 3 equiv of hydrogen was consumed, the mixture was stirred for 2 days at 20 °C (controlled by TLC). The reaction mixture was filtered through a Celite pad (2–3 cm). The Celite was washed three times with methanol. The solvent of the filtrate was removed under reduced pressure. In many cases, the compounds isolated did not demand further purification, however, some of substances were purified by a column chromatography (silica gel, heptane/EtOAc) or recrystallized from an appropriate solvent.

*4.3.1. 2-(5-Amino-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridin-6-yl)phenol (**4a**).* The compound was precipitated from the reaction mixture, filtered off and washed with heptane/*i*-PrOH/1:1. Brown

solid, mp 160–162 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.55 (s, 3H, Me), 4.0–6.0 (br s, 2H, NH_2), 6.94–7.03 (m, 2H), 7.19 (tt, 1H, ^3J=7.4 Hz, ^4J=1.0 Hz), 7.31 (m, 1H), 7.41 (dd, 1H, ^3J=7.6 Hz, ^4J=1.6 Hz), 7.44–7.49 (m, 2H), 7.52 (s, 1H, Py), 8.28–8.31 (m, 2H), 9.5–10.5 (br s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 12.3, 112.8, 116.5, 118.7, 119.9, 124.2, 126.5, 129.0, 129.8, 131.5, 138.0, 139.8, 140.8, 145.1, 147.2, 155.0, 162.3; MS (GC, 70 eV) *m*/*z* (%) 315 (M^+, 100), 300 (10).

*4.3.2. 2-[6-Amino-2-(dimethylamino)thiazolo[4,5-b]pyridin-5-yl] phenol (**4b**).* The compound was purified by a column chromatography (heptane/EtOAc/1:1, R_f=0.45 (EtOAc)). Yellow solid, mp 158–160 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.14 (s, 6H, Me_2N), 4.85 (s, 2H, NH_2), 6.88–6.95 (m, 2H), 7.20–7.26 (m, 1H), 7.54 (dd, 1H, ^3J=7.8 Hz, ^4J=1.6 Hz), 7.61 (s, 1H, Py), 10.75 (br s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 39.4, 116.6, 117.5, 119.0, 124.5, 125.2, 129.0, 130.5, 136.1, 140.4, 155.0, 156.3, 167.0; MS (EI, 70 eV) *m*/*z* (%) 286 (M^+, 90), 270 (25); HRMS (EI): calcd for $C_{14}H_{14}N_4OS$ (M^+) 286.08046, found 286.08045; IR (ATR, cm^{-1}) ν 3324 (w), 2923 (w), 1583 (s), 1537 (s), 1487 (w), 1435 (m), 1403 (s), 1351 (m), 1274 (m), 1233 (m), 1204 (m), 1121 (m), 1073 (m), 1039 (w), 975 (w), 920 (w), 859 (m), 826 (m), 755 (s), 729 (s), 615 (m), 572 (m), 553 (m).

*4.3.3. 2-[6-Amino-2-(piperidin-1-yl)thiazolo[4,5-b]pyridin-5-yl]phenol (**4c**).* The compound was purified by a column chromatography (heptane/EtOAc/1.5:1, R_f=0.18 (EtOAc)). Yellow solid, mp 126–128 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.63 (s, 6H, $3CH_2$), 3.55 (s, 4H, $2CH_2$), 4.86 (br s, 2H, NH_2), 6.88–6.95 (m, 2H), 7.22 (t, 1H, ^3J=7.05 Hz), 7.52 (d, 1H, ^3J=8.05 Hz), 7.59 (s, 1H, Py), 10.3–11.0 (br s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 23.6, 24.8, 48.8, 116.6, 117.4, 119.0, 124.2, 125.3, 129.1, 130.6, 136.4, 140.4, 155.0, 156.0, 166.8; MS (EI, 70 eV) *m*/*z* (%) 326 (M^+, 100), 310 (41), 257 (13); HRMS (ESI): calcd for $C_{17}H_{18}N_4OS$ (M+1) 327.12013, found 327.12830; IR (ATR, cm^{-1}) ν 2935 (w), 2852 (w), 1558 (m), 1531 (s), 1418 (s), 1307 (s), 1246 (s), 1195 (m), 1155 (m), 1120 (m), 1074 (m), 1010 (m), 885 (m), 851 (m), 749 (s), 679 (m), 629 (m), 586 (s).

*4.3.4. 2-(6-Amino-2-morpholinothiazolo[4,5-b]pyridin-5-yl)phenol (**4d**).* The compound was precipitated from the reaction mixture, filtered off and washed with heptane/*i*-PrOH/1:1. Brown solid, mp 148–150 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.72–3.75 (m, 8H, $4CH_2$), 4.87–4.91 (br s, 2H, NH_2), 6.82 (d, 1H, ^3J=8.6 Hz), 6.94 (t, 1H, ^3J=7.2 Hz), 7.25 (m, 1H), 7.50 (dd, 1H, ^3J=7.7 Hz, ^4J=1.6 Hz), 8.89 (s, 1H, Py), 9.83 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 47.8, 65.5, 116.5, 117.2, 119.1, 124.0, 125.3, 129.1, 130.7, 136.9, 140.8, 154.9, 155.5, 167.4; MS (EI, 70 eV) *m*/*z* (%) 328 (M^+, 100), 312 (14), 91 (17); HRMS (ESI): calcd for $C_{16}H_{16}N_4O_2S$ (M+1) 329.10667, found 329.10649; IR (ATR, cm^{-1}) ν 3333 (w), 2961 (w), 2850 (w), 1564 (m), 1525 (s), 1486 (w), 1422 (s), 1375 (m), 1339 (m), 1275 (m), 1234 (s), 1211 (m), 1182 (m), 1111 (s), 1073 (m), 1025 (m), 974 (w), 937 (w), 896 (m), 860 (m), 755 (s), 679 (m), 646 (s), 597 (m).

*4.3.5. 5-Amino-1-tert-butyl-6-(2-hydroxyphenyl)-1H-pyrrolo[2,3-b] pyridine-3-carbonitrile (**4e**).* Colorless solid, mp 191–193 °C (from heptane/*i*-PrOH/1:3); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.73 (s, 9H, *t*-Bu), 4.91 (br s, 2H, NH_2), 6.93–7.00 (m, 2H), 7.25–7.30 (m, 1H), 7.38 (dd, 1H, ^3J=7.6 Hz, ^4J=1.5 Hz), 7.43 (s, 1H, Py), 8.29 (s, 1H, =CHN), 10.09 (br s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 28.7, 57.8, 79.4, 112.0, 116.3, 116.4, 119.5, 120.9, 126.8, 129.3, 131.6, 134.7, 138.1, 140.6, 141.1, 154.6; MS (GC, 70 eV) *m*/*z* (%) 306 (M^+, 50), 249 (100), 233 (13); HRMS (ESI): calcd for $C_{18}H_{18}N_4O$ (M+1) 307.1553, found 307.1554; IR (ATR, cm^{-1}) ν 3376 (w), 3305 (w), 3128 (w), 1607 (w), 1575 (w), 1519 (m), 1484 (w), 1462 (w), 1407 (m), 1368 (m), 1350 (m), 1304 (w), 1270 (m), 1231 (m), 1211 (s), 1154 (m), 1097 (m), 1046 (w), 1012 (w), 941 (w), 881 (m), 858 (m), 753 (s), 695 (m), 675 (m), 624 (s).

*4.3.6. 5-Amino-1-(4-methoxybenzyl)-6-(2-hydroxyphenyl)-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile (**4f**).* Yellow solid, mp 78–80 °C (from heptane/*i*-PrOH/1:3); ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.70 (s, 3H, MeO), 4.90 (br s, 2H, NH_2), 5.35 (s, 2H, CH_2), 6.87–6.90 (m, 2H), 6.94–7.01 (m, 2H), 7.26–7.32 (m, 3H), 7.38 (dd, 1H, ^3J=7.6 Hz, ^4J=1.0 Hz), 7.46 (s, 1H, Py), 8.36 (s, 1H, =CHN), 9.5–10.5 (br s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 47.0, 55.0, 80.5, 112.1, 114.0, 115.9, 116.4, 119.4, 119.5, 126.2, 129.1, 129.2, 129.5, 131.5, 136.3, 138.9, 140.0, 142.2, 154.7, 158.8; MS (EI, 70 eV) *m*/*z* (%) 370 (M^+, 46), 121 (100); HRMS (ESI): calcd for $C_{22}H_{18}N_4O_2$ (M+1) 371.1431, found 371.1430; IR (ATR, cm^{-1}) ν 3348 (w), 3114 (w), 2929 (w), 2215 (m), 1609 (w), 1581 (w), 1512 (m), 1484 (w), 1428 (m), 1372 (m), 1303 (m), 1276 (m), 1244 (s), 1172 (s), 1124 (m), 1026 (m), 819 (m), 757 (s), 675 (m), 652 (m), 626 (m), 608 (s).

*4.3.7. 5-Amino-1-cyclohexyl-6-(2-hydroxyphenyl)-1H-pyrrolo[2,3-b] pyridine-3-carbonitrile (**4g**).* Yellow solid, mp 206–208 °C (from heptane/*i*-PrOH/1:3); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.2–2.0 (m, 10H, $5CH_2$), 4.58 (m, 1H, CHN), 4.82 (br s, 2H, NH_2), 6.92–6.98 (m, 2H), 7.25–7.35 (m, 2H), 7.42 (s, 1H, Py), 8.41 (s, 1H, =CHN), 9.89 (br s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 24.9, 25.1, 32.5, 53.5, 80.2, 111.8, 115.8, 116.2, 119.4, 119.6, 126.3, 129.4, 131.6, 134.0, 138.9, 139.7, 141.8, 154.7; MS (GC, 70 eV) *m*/*z* (%) 332 (M^+, 47), 250 (100); HRMS (ESI): calcd for $C_{20}H_{20}N_4O$ (M+1) 333.1710, found 333.1711; IR (ATR, cm^{-1}) ν 3329 (w), 3131 (w), 2931 (w), 2853 (w), 1607 (w), 1575 (w), 1523 (m), 1435 (s), 1395 (m), 1374 (m), 1300 (m), 1260 (m), 1232 (m), 1175 (m), 1147 (m), 1121 (w), 1052 (w), 989 (m), 935 (m), 887 (m), 859 (m), 808 (m), 747 (s), 697 (m), 666 (m), 627 (m), 613 (s).

*4.3.8. 5-Amino-6-(2-hydroxyphenyl)-2-phenyl-1,2-dihydropyrazolo [3,4-b]pyridin-3-one (**4h**).* Green solid, mp 195–196 °C (from *i*-PrOH/EtOAc/1:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.5–5.5 (br s, 2H, NH_2), 6.93–7.02 (m, 2H), 7.23–7.54 (m, 6H), 7.95 (m, 2H), 10.0–11.0 (br s, 1H, OH), 15.01 (br s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6) δ 110.3, 116.4, 117.0, 119.0, 119.3, 124.7, 125.6, 128.9, 130.0, 131.1, 137.9, 138.6, 150.0, 151.5, 154.7, 159.4; MS (EI, 70 eV) *m*/*z* (%) 318 (M^+, 100), 302 (28); HRMS (ESI): calcd for $C_{18}H_{14}N_4O_2$ (M+1) 319.1132, found 319.1130; IR (ATR, cm^{-1}) ν 3301 (w), 1645 (m), 1593 (m), 1487 (m), 1455 (w), 1422 (s), 1343 (w), 1304 (m), 1292 (m), 1274 (m), 1211 (m), 1150 (m), 1116 (w), 1082 (w), 1038 (w), 949 (w), 911 (w), 845 (w), 815 (w), 788 (w), 753 (s), 705 (m), 684 (s), 664 (s), 603 (s).

*4.3.9. 5-Amino-6-(2-hydroxyphenyl)-2-methyl-1,2-dihydropyrazolo [3,4-b]pyridin-3-one (**4i**).* The compound was precipitated from the reaction mixture, filtered off and washed with heptane/*i*-PrOH/1:1. Red solid, mp 281–283 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.34 (s, 3H, Me), 4.5–5.3 (br s, 2H, NH_2), 6.91–7.00 (m, 2H), 7.26–7.35 (m, 2H), 7.46 (s, 1H, Py), 9.7–10.7 (br s, 1H, OH), 12.6 (br s, 1H, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 30.4, 109.9, 116.4, 117.0, 119.3, 125.6, 129.8, 131.1, 138.0, 148.8, 151.1, 154.6, 159.8; MS (EI, 70 eV) *m*/*z* (%) 256 (M^+, 100), 73 (21), 44 (29); HRMS (ESI): calcd for $C_{13}H_{12}N_4O_2$ (M+1) 257.10330, found 257.10293; IR (ATR, cm^{-1}) ν 3363 (w), 3017 (w), 1637 (m), 1569 (m), 1478 (m), 1449 (m), 1426 (m), 1325 (w), 1295 (w), 1259 (m), 1234 (m), 1184 (m), 1161 (m), 1098 (w), 1055 (w), 1035 (w), 1018 (w), 959 (w), 904 (w), 851 (w), 834 (w), 759 (s), 685 (s), 654 (m).

*4.3.10. 5-Amino-6-(2-hydroxyphenyl)-1-methyl-1,2-dihydropyrazolo [3,4-b]pyridin-3-one (**4j**).* The compound was precipitated from the reaction mixture, filtered off and washed with heptane/*i*-PrOH/1:1. Red solid, mp 255–257 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.66 (s, 3H, Me), 4.0–6.0 (br s, 2H, NH_2), 6.92–6.98 (m, 2H), 7.26–7.32 (m, 1H), 7.40 (dd, 1H, ^3J=7.6 Hz, ^4J=1.6 Hz), 7.44 (s, 1H, Py), 9.0–12.0 (br

s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 33.3, 104.4, 114.1, 116.6, 126.5, 129.7, 131.4, 135.6, 147.2, 148.2, 152.0, 154.8; MS (EI, 70 eV) *m*/*z* (%) 256 (M^+, 32), 240 (27), 201 (26), 183 (23), 152 (11), 77 (21); HRMS (ESI): calcd for $C_{13}H_{12}N_4O_2$ (M+1) 257.10330, found 257.10349; IR (ATR, cm^{-1}) ν 2931 (w), 2672 (w), 1605 (m), 1582 (m), 1550 (m), 1504 (w), 1475 (w), 1455 (w), 1425 (w), 1379 (w), 1299 (w), 1247 (m), 1229 (m), 1153 (m), 1112 (w), 1068 (w), 1014 (w), 885 (w), 809 (m), 759 (s), 699 (m), 682 (m), 647 (s), 614 (m).

*4.3.11. 6-Amino-7-(2-hydroxyphenyl)-1,3-dimethylpyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (**4k**).* The compound was precipitated from the reaction mixture, filtered off and washed with heptane/*i*-PrOH/1:1. Green solid, mp 299–301 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.30 (s, 3H, Me), 3.50 (s, 3H, Me), 4.5–5.7 (br s, 2H, NH_2), 6.91–7.02 (m, 2H), 7.28–7.41 (m, 2H), 7.80 (s, 1H, Py), 9.4–11.0 (br s, 1H, OH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 28.0, 28.9, 109.4, 116.3, 119.3, 121.5, 125.2, 130.2, 131.4, 139.1, 141.8, 148.3, 150.6, 154.7, 161.0; MS (GC, 70 eV) *m*/*z* (%) 298 (M^+, 100), 281 (18), 207 (19); HRMS (ESI): calcd for $C_{15}H_{14}N_4O_5$ (M+1) 299.1139, found 299.1138; IR (ATR, cm^{-1}) ν 3427 (w), 3349 (w), 3271 (w), 3078 (w), 2945 (w), 1694 (m), 1634 (s), 1604 (s), 1470 (m), 1447 (s), 1427 (m), 1356 (s), 1300 (s), 1257 (m), 1228 (m), 1105 (m), 1066 (m), 1018 (m), 981 (m), 911 (m), 834 (w), 804 (w), 781 (m), 738 (s), 692 (m), 675 (m), 638 (m).

*4.3.12. 6-Amino-7-(2-hydroxyphenyl)-1-methylpyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (**4l**).* The compound was precipitated from the reaction mixture, filtered off and washed with heptane/*i*-PrOH/1:1. Brown solid, mp 290–292 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.44 (s, 3H, Me), 5.10 (br s, 2H, NH_2), 6.92–7.01 (m, 2H), 7.30 (m, 1H), 7.40 (dd, 1H, ^3J=7.6 Hz, ^4J=1.5 Hz), 7.76 (s, 1H, Py), 10.0–12.0 (br s, 2H, OH, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 28.0, 110.2, 116.4, 119.3, 121.4, 125.2, 130.2, 131.2, 138.9, 143.1, 148.1, 150.4, 154.7, 161.5; MS (GC, 70 eV) *m*/*z* (%) 284 (M^+, 100), 240 (14), 78 (15); HRMS (ESI): calcd for $C_{14}H_{12}N_4O_5$ (M+1) 285.09822, found 285.09838; IR (ATR, cm^{-1}) ν 3341 (w), 3152 (w), 3041 (w), 2844 (w), 1681 (s), 1610 (m), 1586 (m), 1468 (m), 1451 (m), 1411 (s), 1379 (m), 1286 (m), 1229 (m), 1206 (w), 1149 (w), 1103 (w), 1077 (w), 998 (w), 943 (m), 914 (w), 813 (m), 788 (m), 765 (w), 734 (s), 723 (s), 687 (m), 665 (w), 636 (m), 583 (s), 566 (m).

*4.3.13. 6-Amino-7-(2-hydroxyphenyl)pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (**4m**).* The compound was precipitated from the reaction mixture, filtered off and washed with heptane/*i*-PrOH/1:1. Brown solid, mp 309–311 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.00 (br s, 2H, NH_2), 6.91 (t, 1H, ^3J=7.4 Hz), 6.99 (d, 1H, ^3J=7.8 Hz), 7.28 (m, 1H), 7.35 (dd, 1H, ^3J=7.8 Hz, ^4J=1.5 Hz), 7.68 (s, 1H, Py), 10.0–12.0 (br s, 3H, OH, NH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 109.0, 116.4, 119.0, 120.7, 124.6, 130.2, 130.9, 139.0, 143.4, 149.1, 150.2, 154.9, 162.6; MS (GC, 70 eV) *m*/*z* (%) 270 (M^+, 96), 224 (16), 160 (17), 128 (100), 97 (31); HRMS (ESI): calcd for $C_{13}H_{10}N_4O_3$ (M+1) 271.08257, found 271.08298; IR (ATR, cm^{-1}) ν 3246 (w), 3043 (w), 1682 (m), 1608 (m), 1487 (w), 1416 (m), 1385 (m), 1299 (w), 1275 (w), 1239 (w), 1215 (w), 1101 (w), 1043 (w), 888 (w), 851 (m), 813 (w), 749 (m), 677 (w), 624 (m), 574 (s).

*4.3.14. 2-(2,4,7-Triaminopyrido[3,2-d]pyrimidin-6-yl)phenol (**4n**).* The compound was precipitated from the reaction mixture, filtered off and washed with heptane/*i*-PrOH/1:1. Green solid, mp 169–171 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.04 (br s, 2H, NH_2), 6.94 (m, 1H), 7.07 (d, 1H, ^3J=8.0 Hz), 7.30 (m, 2H), 7.94 (s, 1H, Py), 8.84 (s, 1H, NH), 9.10 (s, 1H, NH), 10.33 (br s, 1H, OH), 12.50 (br s, 2H, NH_2); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 104.5, 116.3, 119.3, 124.2, 130.5, 130.9, 140.5, 141.2, 151.4, 154.7, 155.1, 162.3, 162.9; MS (GC, 70 eV) *m*/*z* (%) 267 (M^+, 100), 252 (22), 207 (15), 84 (17); HRMS (ESI): calcd for $C_{13}H_{12}N_6O$ (M+1) 269.11454, found 269.11528; IR (ATR, cm^{-1}) ν 3306 (w), 3108 (w), 1633 (m), 1595 (m), 1514 (w), 1479 (w), 1434 (m), 1409 (m), 1384 (m), 1352 (m), 1293 (m), 1241 (m), 1154 (w), 1100 (w), 1007 (w), 831 (w), 753 (m), 701 (m).

*4.3.15. 2-(3-Amino-5,7-dimethoxyquinolin-2-yl)phenol (**4o**).* The compound was precipitated from the reaction mixture, filtered off and washed with *i*-PrOH/EtOAc/1:1. Brown solid, mp 166–168 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.84 (s, 3H, MeO), 3.94 (s, 3H, MeO), 5.04 (br s, 2H, NH_2), 6.56 (m, 1H), 6.84 (m, 1H), 6.91–7.02 (m, 2H), 7.30 (m, 1H), 7.57 (d, 1H, ^3J=7.5 Hz), 7.70 (s, 1H, Py), 10.5–11.5 (br s, 1H, OH); ^{13}C NMR (75.5 MHz, DMSO-d_6) δ 55.2, 55.8, 98.0, 98.9, 112.2, 116.3, 116.4, 119.0, 124.8, 129.8, 130.5, 138.5, 142.1, 149.1, 154.0, 155.5, 157.5; MS (EI, 70 eV) *m*/*z* (%) 296 (M^+, 92), 280 (35); HRMS (ESI): calcd for $C_{17}H_{16}N_2O_3$ (M+1) 297.12337, found 297.12324; IR (ATR, cm^{-1}) ν 3386 (w), 2934 (w), 2833 (w), 1626 (w), 1582 (m), 1446 (m), 1422 (w), 1396 (m), 1347 (w), 1331 (w), 1273 (m), 1204 (s), 1156 (s), 1104 (m), 975 (w), 950 (w), 935 (w), 911 (m), 827 (m), 753 (s), 700 (s), 642 (m), 626 (s), 576 (s).

*4.3.16. 2-(3-Amino-6,7-dimethoxyquinolin-2-yl)phenol (**4p**).* The compound was precipitated from the reaction mixture, filtered off and washed with heptane/*i*-PrOH/1:1. Brown solid, mp 177–179 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.84 (s, 3H, MeO), 3.94 (s, 3H, MeO), 5.16 (br s, 2H, NH_2), 6.56 (s, 1H), 6.85 (s, 1H), 6.89–7.01 (m, 2H), 7.29 (m, 1H), 7.56 (d, 1H, ^3J=7.6 Hz), 7.69 (s, 1H, Py), 10.93 (s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 55.2, 55.8, 97.9, 98.9, 112.2, 116.4, 116.5, 118.8, 125.0, 129.8, 130.6, 138.6, 142.2, 149.3, 154.0, 155.8, 157.5; MS (GC, 70 eV) *m*/*z* (%) 295 (M^+, 100), 280 (27); HRMS (ESI): calcd for $C_{17}H_{16}N_2O_3$ (M^+) 296.11554, found 296.11544; IR (ATR, cm^{-1}) ν 3314 (w), 2936 (w), 2834 (w), 1626 (w), 1582 (m), 1504 (w), 1445 (m), 1396 (w), 1348 (w), 1330 (w), 1272 (m), 1204 (s), 1155 (m), 1126 (m), 1104 (m), 1046 (m), 935 (w), 911 (m), 826 (m), 751 (s), 700 (m), 642 (m), 626 (m), 575 (m).

*4.3.17. 2-(3-Amino-7-(dimethylamino)quinolin-2-yl)phenol (**4q**).* The compound was precipitated from the reaction mixture, filtered off and washed with heptane/*i*-PrOH/1:1. Brown solid, mp 240–242 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.98 (s, 6H, Me_2N), 4.91 (br s, 2H, NH_2), 6.91–6.99 (m, 3H), 7.18–7.31 (m, 2H), 7.41 (s, 1H), 7.55 (d, 1H, ^3J=8.5 Hz), 7.68 (dd, 1H, ^3J=7.5 Hz, ^4J=1.4 Hz), 11.0–11.8 (br s, 1H, OH); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 40.4, 106.3, 116.6, 117.3, 117.8, 118.9, 121.2, 124.6, 125.8, 130.0, 130.2, 137.5, 142.3, 148.7, 148.8, 155.9; MS (GC, 70 eV) *m*/*z* (%) 279 (M^+, 100), 262 (37); HRMS (ESI): calcd for $C_{17}H_{17}N_3O$ (M+1) 280.14444, found 280.14436; IR (ATR, cm^{-1}) ν 3392 (w), 3324 (w), 2919 (w), 1623 (m), 1602 (w), 1573 (w), 1553 (w), 1505 (m), 1428 (m), 1280 (m), 1244 (m), 1223 (m), 1184 (m), 1148 (m), 1008 (m), 971 (w), 936 (w), 918 (w), 884 (w), 823 (m), 793 (m), 757 (s), 725 (m), 693 (s).

4.4. X-ray crystallographic data

X-ray crystallographic data (excluding structure factors) for the structure **3a**, **3e**, **3f**, **3k**, **3o**, and **3r**, reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. 829051–829056, can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk, or via www.ccdc.cam.ac.uk/data_request/cif.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.06.101.

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24. Crystallographic data (excluding structure factors) for the structures **3a**, **e**, **f**, **k**, **o**, **r** reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. 829051–829056 can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk, or via www.ccdc.cam.ac.uk/data_request/cif.
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