Tetrahedron 69 (2013) 1217–1228

Contents lists available at SciVerse ScienceDirect

Tetrahedron

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

Design, synthesis and transformation of some heteroannulated 3-aminopyridines—purine isosteres with exocyclic nitrogen atom

Viktor O. Iaroshenko [a,b,*], Marcelo Vilches-Herrera [a], Ashot Gevorgyan [a], Satenik Mkrtchyan [a], Knar Arakelyan [a,c], Dmytro Ostrovskyi [a], Muhammad S.A. Abbasi [a], Linda Supe [a], Ani Hakobyan [a,c], Alexander Villinger [a], Dmitriy M. Volochnyuk [d], Andrei Tolmachev [b,d]

[a] Institut für Chemie, Universität Rostock, Albert-Einstein-Str. 3a, 18059 Rostock, Germany
[b] National Taras Shevchenko University, 62 Volodymyrska str., Kyiv-33, 01033, Ukraine
[c] Faculty of Chemistry, Yerevan State University, Alex Manoogian 1, 0025 Yerevan, Armenia
[d] Enamine Ltd, Alexandra Matrosova Str. 23, Kyiv 01103, Ukraine

ARTICLE INFO

Article history:
Received 7 September 2012
Received in revised form 30 October 2012
Accepted 6 November 2012
Available online 21 November 2012

Keywords:
Heterocyclisation
Purine isosteres
Fused pyridines
Electron-excessive aminoheterocycles
Nitro-malonaldehyde

ABSTRACT

The synthesis of 1-deazapurines and isosteres bearing the exocyclic nitrogen atom at position-1 was developed basing on the formal [3+3]-cyclization reaction of nitro-malonaldehyde with the set of electron-excessive aminoheterocycles. Through the functionalization of the purine-like scaffolds synthesized the diversity of compounds furnished in the possition-1 with aryl, alkinyl, and vinyl rests, were obtained.

1. Introduction

Purines and purine-like scaffolds are compounds with extensive application portfolio in the life science and medicine sector.[1,2] The substances from the purine/pseudopurine family have been having a significant impact on drug design and drug-development. Those are the structural part of big number of commercially available drugs and drug candidates, which were developed during the last several decades. For instance three (Valaciclovir, Tenofovir, Abacavir) drugs are belonging to 200 top selling drugs world-wide are compounds with purine framework, four (Sildenafil, Pemetrexed, Temozolomide, Vardenafil) contain heterocyclic scaffolds isosterically close to purine. In the same time modification of the purine scaffold very often results in the gaining new bioactivities and pharmaceutical action.[1]

During the last decade we have concentrated on the development of the new synthetic strategies towards the functionalized and modified purines and isosteres.[3] Recently the laboratories of Hocek,[4] Beal[5] and Iaroshenko[6] have communicated the synthesis of the purine nucleosides furnished with perfluoroalkyl group in the 2- and 6-position. Some of the representatives from this family have showed a strong anti-proliferative action on the endothelium and smooth muscle cells.[7]

We believe that the heterocyclic scaffolds **4** (Figs. 1 and 2) furnished with nitro-group in the position-3 of the fused pyridine ring

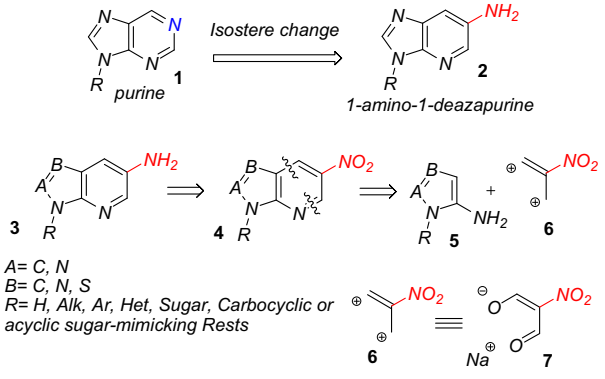


Fig. 1. Retrosynthetic analysis.

* Corresponding author. Tel.: +49 381 4986410; fax: +49 381 49864112; e-mail addresses: viktor.iaroshenko@uni-rostock.de, iva108@googlemail.com (V.O. Iaroshenko).

0040-4020/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2012.11.026

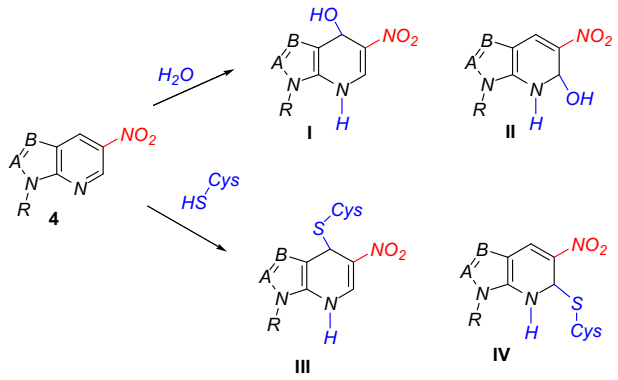


Fig. 2. Heteroannulated 3-nitropyridines as potentional inhibitors of adenosine deaminese (ADA) and inosine monophosphate dehydrohynase (IMPHD).

can find an application as a platform for the design and synthesis of so-called enzyme pitfalls or enzyme killers,[1,8] compounds with the almost irreversible inhibition of the particular enzymes. Additionally, heteroannulated pyridines can be considered as 1-deasopurine isosteres and thus are of great interest as privileged drug-like scaffolds[8] in medicinal chemistry and drug design.[9–12]

The subject of this paper is design and synthesis of the 1-deazapurines and isosteres **3** and **4**, containing the exocyclic nitrogen function in the position-1 of the pseudopurine framework. We have a great interest on the nitro-derivatives **4**, since our[6] recent experience on the mechanism-based design and synthesis of adenosine deaminese (ADA)[1a,5,13] and inosine monophosphate dehydrohynase (IMPHD)[12a,14] inhibitors gave us an understanding of the possible application of **4** as a suitable platform for the development of inhibitors of these enzyme families. The presence of the electron-withdrawing nitro-group can facilitate the addition of the water molecule leading to the formation of hydrated pyridines **I**, **II** (Fig. 2). The latest can be considered from one side, as mimetics of the putative transition state of the ADA,[1a,5,13] and from the other side as compounds mimicking the transition state of IMPHD.[12a,14] Nevertheless, the formation of the Meisenheimer type adducts **III** and **IV** is also possible, this might lead to the irreversible binding on the active site of the current enzyme by the nucleophilic attack of the cysteine rest involved in the transformation of inosine to xanthine, resulting in the enzyme inhibition (Fig. 2). These both aspects have been recently demonstrated, in number of works,[1,12a,14] to be a valuable tool for the mechanism-based design of ADA and IMPHD inhibitors.

We were interested in the elaboration of the principally new synthetic strategy giving possibility to prepare diverse libraries of **3** and **4**. Basing on the retrosynthetic analysis (Fig. 1) and some previously known chemical properties of electron-excessive aminoheterocycles and taking into account recent experience gained in the Iaroshenko's laboratory, we have assumed that the scaffolds **4** can be achieved in two step-synthesis starting from amines **8**–**13**, by the pyridine ring annulation, using commercially available nitromalonaldehyde **7**, which can be handled and stored in a form of a stable sodium salt. The subsequent catalytic reduction of the nitro-group will give rise to correspondent amines **3**.

2. Results and discussion

In the beginning of this research program we have concentrated on the chemical objects for the investigation. As much promising we have identified the electron-excessive heterocyclic amines and anilines, depicted in Fig. 3, and 5-aminoimidazoles **27** (Scheme 3). The latest can be generated in situ by previously communicated method.[4c]

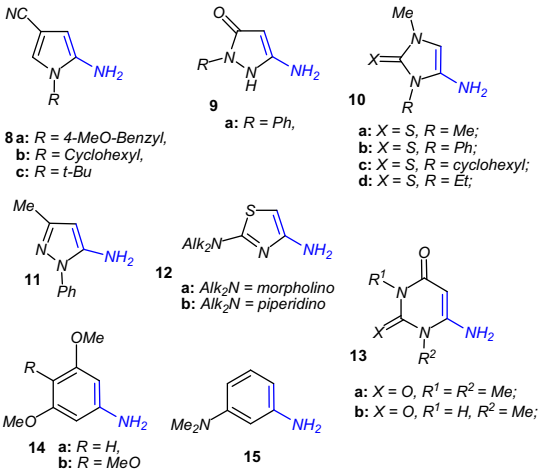
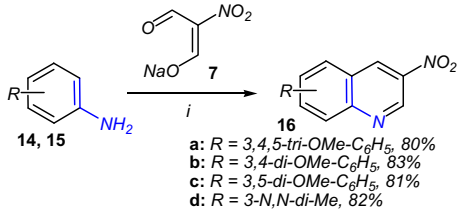


Fig. 3. Structures of the used 1,3-*C*,*N*-dinucleophiles.

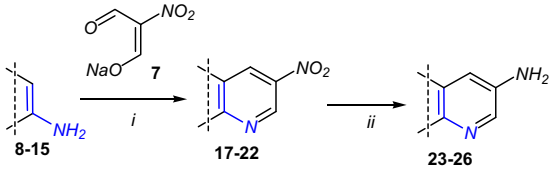
Recently the building block concept towards 3-nitroquinolines was developed by the application of nitro-malonaldehyde **7** onto anilines.[15] Reactions of this type were usually conducted in a hydrochloric acid. We have started the investigation of heteroannulated 3-nitropyridines synthesis by using the previously reported reaction conditions.[15]

To our great disappointment the reaction in the case of unstable heteroamines like **10**, **12**, **27** experienced a failure; in the same time the rest of the heterocycles has demonstrated relatively low yields, never exceeded 45%. With these disappointing results in hand we have turned our attention towards the new, developed during the last decade, water scavenging system, namely DMF/TMSCl-system.[17] As a starting point we have chosen the anilines furnished with electron-excessive groups and studied the reaction with sodium salt of nitro-malonaldehyde **7**, using the DMF/TMSCl as a reaction media. Due to the low stability of the nitro-malonaldehyde we have chosen the correspondent sodium salt **7**. The reaction delivered in good yields hitherto known 3-nitroquinolines **16** (Scheme 1), previously obtained using the same strategy, however instead of DMF/TMSCl mineral acid were applied.[16]

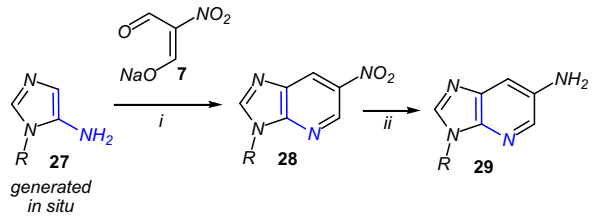
With these new reaction conditions in hand we have turned towards the synthesis of heteroannulated 3-nitropyridines by the method proposed, starting with corresponding electron-excessive aminoheterocycles **8**–**13**. The reaction proceeded smoothly delivering the desired products **17**–**22** in excellent yields (Scheme 2,



Scheme 1. Reagents and conditions: (i): DMF/TMSCl, 100 °C.



Scheme 2. Reagents and conditions: (i): DMF/TMSCl, 100 °C; (ii): MeOH, H_2, Pd/C (10 mol %), 20 °C, 24 h.



Scheme 3. Reagents and conditions: (i): DCM, AcOH, reflux 5–6 h; (ii): MeOH, H_2, Pd/C (10 mol %), 20 °C, 24 h.

Table 1). In the same time the reaction of 5-aminoimidazoles **27** experienced a failure under our standard reaction condition. After some reaction optimization study, the optimal reaction condition for **27** was established, namely, after the generation of the correspondent amine in situ in DCM was completed, the 2 equiv of **7** were added, and then 5 equiv acetic acid were added dropwise at 0 °C. Afterwards the reaction mixture was kept under reflux for 5–6 h. This delivered 1-deazapurines **28** in 32–46 % yields (Scheme 3, Table 2). Increase the yields over this value was not possible.

Table 1
Synthesis of heteroannulated pyridines **17**–**26**

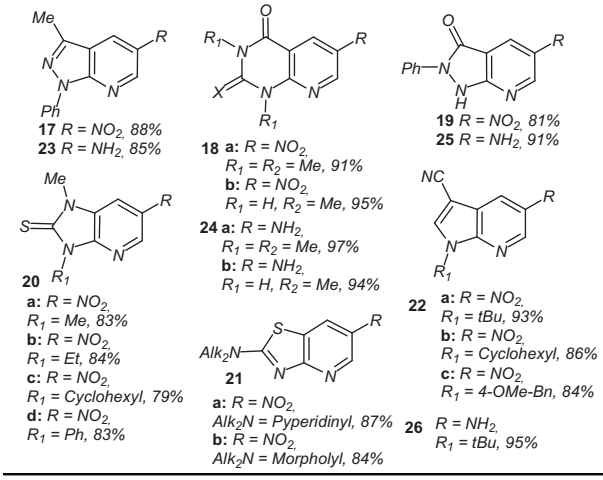
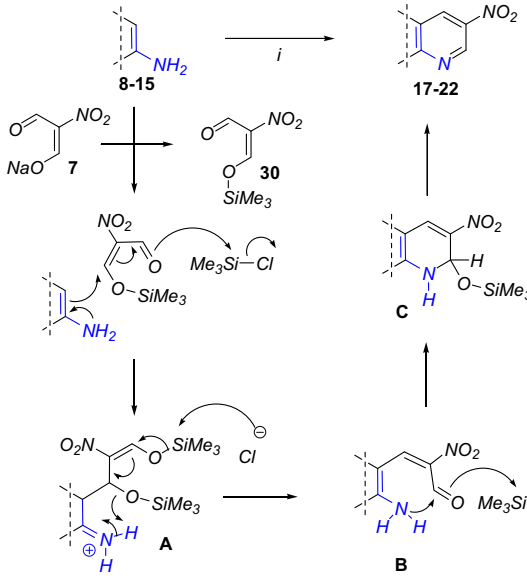


Table 2
Synthesis of imidazo[4,5-*b*]pyridines **28**, **29**

28, **29**	R	(**28**)[a]	(**29**)[a]
a	*n*-Heptyl	40	—[b]
b	*t*-Butyl	35	92
c	Cyclohexyl	36	—[b]
d	Allyl	46	96[c]
e	3,4,5-Trimethoxyphenyl	32	95
f	4-Methoxybenzyl	48	98
g	4-(Methyl)pyridine	45	—[b]
h	3-Phenethyl	42	97
i	3,4-Dimethoxyphenylethyl	45	—[b]

[a] Yields of isolated products.
[b] The hydrogenation was not conducted.
[c] Allyl was reduced to *n*-propyl.

Mechanistically the pyridine ring formation can be explained by the putative mechanism depicted in Scheme 4. The proposed reaction cascade most probably starts from the formation of the moiety **30** as a product of the initial silylation of correspondent nitromalonaldehyde sodium salt. The formation of products **17**–**22** can be explained by conjugate addition of enamine carbon atom of the aminoheterocycle to the C–C-double bond of **30** to give intermediate **A**. The subsequent deprotonation and tautomerisation give rise to intermediate **B**. The intermolecular attack of the amino group onto



Scheme 4. Putative reaction mechanism; reagents and conditions: (i): DMF/TMSCl, 100 °C.

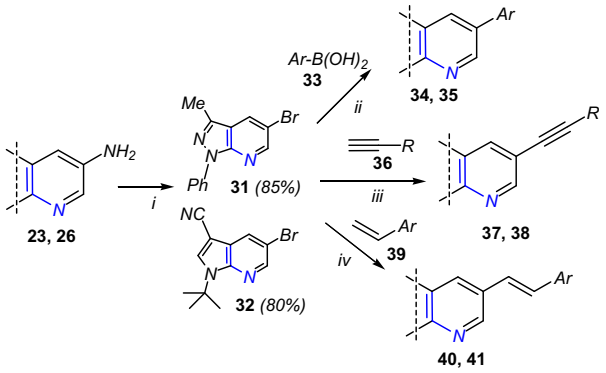
the carbonyl, mediated by TMSCl, affords intermediate **C**, which undergoes aromatization to give fused pyridines **17**–**22** (Scheme 4).

The second step, according to our synthetic plan, to reach the scaffolds **3** was the reduction of the fused 3-nitropyridines **17**–**22**, **28**. The transformation of the nitro-compounds to amines has been conducted in the methanol under normal pressure using the 10% palladium on the charcoal. In many cases the hydrogenation proceeded quantitatively, thus the subsequent purification was not demanded. Under this reaction condition the allyl rest in compound **28d** has been reduced to *n*-propyl (Table 2).

It has become evident that purines and purine-like scaffolds featuring one or two aryl groups in the six-membered ring have a remarkable record in medicinal chemistry and play a continuing role in providing lead compounds for the therapeutic application. Several pronounced examples have to be illustrated here. Hocek et al.,[18] have communicated the synthesis and biological evaluation of the number of purine derivatives, bearing aryl or heteroaryl functionality in the 6-postion of the purine core, using the transition metal catalysed reactions. In the same time 1-deazapurines furnished with aryl or heteroaryl substituents in the position-1 are of current scientific interest as scaffolds with pronounced bioactivities.[19,20] From the other hand, many representatives among these structures have found an application in the material science.[21] During the last two decades there are number of methods were developed for the assembling of the 1-deazopurines and isosteres bearing aryl-,[22] vynil-[23] and alkynil-[24] substituent in the position-1.

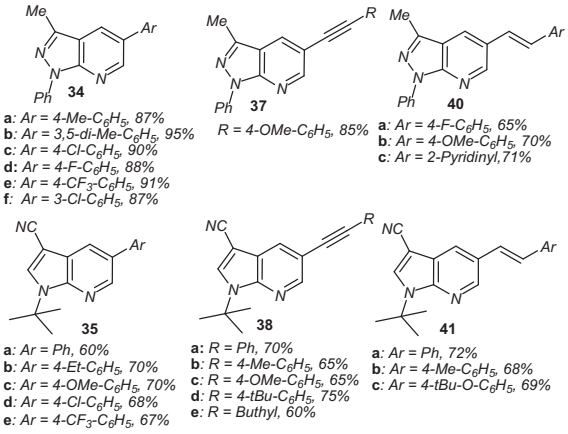
Next, we concentrated on the functionalization of the heteroamines prepared here. As model scaffolds we took heterocycles **23** and **26**, following the deaminative–brominating pathway we have reached bromides **31** and **32** in very good yields. Subsequently, we concentrated on the Pd-mediated C–C coupling protocols, such as Suzuki–Miyaura, Sonogashira and Heck reactions (Scheme 5).

Firstly, the Suzuki–Miyaura reaction was considered as a possible way for the efficient introducing of Ar-substituent in the γ-position of the heteroannulated pyridines **31** and **32**. These two compounds readily reacted with the set of diverse boronic acids in dioxane giving rise to compounds **34** and **35** in yields of 60–95% (Scheme 5, Table 3). In the same time, to save one step we have tried to use directly the intermediary formed diazonium salts, which are known to undergo Pd-catalysed couplings, however, the yields here were always below 30%. Concerning the Sonogashira coupling, the reaction with commercially available acetylenes **36** took place under standard reaction condition, namely copper



Scheme 5. Reagents and conditions: (i): under Ar, 1.5 equiv *tert*-butyl-NO, $CuBr_2$ 1.3 equiv, CH_3CN, rt, 12 h; (ii): under Ar, 1.5 equiv Ar–$B(OH)_2$ and $PdCl_2(PPh_3)_2$ (2 mol %), K_2CO_3, 2 equiv; 1,4-dioxan, 90 °C, 8 h; (iii): under Ar, acetylene 2 equiv, $PdCl_2(PPh_3)_2$ (2 mol %), CuI (5 mol %), NEt_3 1.3 equiv, DMF, 120 °C, 6–8 h; (iv) under Ar, Alkene 3 equiv, $PdCl_2(PPh_3)_2$ 4 (mol %), NEt_3 4 equiv, DMF, 140 °C, 10–14 h.

Table 3
Synthesis of heteroannulated pyridines **34**, **35**, **37**, **38**, **40**, **41**



iodide (5 mol %), triethylamine (1.5 equiv) and $PdCl_2(PPh_3)_2$ (2 mol %), in DMF at 120 °C to deliver the set of derivatives **37**, **38** (Scheme 5, Table 3). Following the purpose the synthesis of the alkene-substituted derivatives of **31** and **32**, the Heck coupling reaction of these bromides with alkenes **39** was performed, resulting the library of purine isosteres **40**, **41** was assembled.

The structures of several scaffolds synthesized, namely compounds **32**, **35d**, **35e**, **38a** and **41b** were corroborated by the means of 1D and 2D NMR methods and X-ray analysis (Figs. 1–5 in SD).[25]

3. Conclusion

Finally, we have proposed the facile synthesis of 1-nitro-, 1-amino-1-deazopurines and isosteres. These scaffolds could be transformed into corresponding 1-bromo derivatives. Subsequent functionalization of the scaffolds obtained by several C–C coupling strategies opened an access to 3-functionalized fused pyridines. The synthesised here libraries can be readily used for the combinatorial synthesis of new complex biologically active molecules using derivatization by synthetic methods and combinatorial equipments.

4. Experimental section

4.1. General

NMR spectra were recorded on a 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 a 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.

*4.1.1. General procedure for **17**–**22**.* **7** (2.0 mmol, 0.38 g) and the corresponding amine (2.0 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 °C during 2–12 h (controlled by TLC). 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.

*4.1.2. General procedure for **23**–**26**, **29**.* In a 50 mL Schlenk flask under a flow of dry argon the corresponding nitro-compound (1.0 mmol) and 0.05 g of Pd/C (10%) were placed. Afterwards, 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 a day 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 examples were purified by preparative chromatography (silica gel, heptane/EtOAc) or recrystallized from appropriate solvent.

*4.1.3. General procedure for **28**.* To a Schlenk flask, set with reflux, CH_2Cl_2 (2.5 mL), correspondent amine (0. 663 mmol), and methyl *N*-(cyanomethyl)-formimidate (0.00663 mol) were added under an argon atmosphere at rt. The reaction mixture was refluxed during 1 h 20 min and after that, the mixture was cooled down to room temperature. Afterwards, the reaction mixture was chilled to 0 °C and compound **7** (0. 73 mmol) was added, subsequently AcOH (5 equiv) was added dropwise and the mixture continued to stir at the same temperature for 45 min and then refluxed for 5–6 h. The solvent was evaporated to dryness and the residue was purified by column chromatography to give desirable product. In a case of anilines (see comments in the main text) one drop of TMS-triflate was added of the first stage, when the correspondent aminoimidazole was generated in situ.

*4.1.4. General procedure for **31**, **32**.* Anhydrous copper halide (1.2 mmol), compound **23** or **26** (1.5 mmol), and anhydrous acetonitrile (40 mL) were placed in a three necked round bottom flask that was equipped with a reflux condenser, addition funnel or solid inlet tube, and a gas outlet tube. The amine (1 mmol) in 5 mL of acetonitrile was slowly added over a period of 5 min to the reaction solution. During this addition, the reaction solution turned completely black from the initial green colour as nitrogen was evolved. After complete gas evolution, the reaction was then poured into 200 mL of 20% aqueous hydrochloric acid and extracted with 200 mL of ether and organic layer was washed once with 200 mL of 20% aqueous hydrochloric acid. The resulting ether solution was dried over anhydrous magnesium sulfate and the ether was removed under reduce pressure.

*4.1.5. General procedure for **34**, **35**.* Under argon atmosphere, appropriate boronic acid (1.2 equiv), compounds **31** or **32** (1 equiv), potassium carbonate (2 equiv) and $PdCl_2(PPh_3)_2$ (2 mol %) were placed into a pressure tube and 4 mL of dry 1,4 dioxane were added. Once the tube was sealed the mixture was heated at 90 °C for

4–6 h. The product was then purified by column chromatography (eluent: *n*-heptane/ethylacetate).

*4.1.6. General procedure for **37**, **38**.* Under argon atmosphere, copper iodide (5 mol %), appropriate acetylene (1.2 equiv), compound **31** or **32** (1 equiv), triethylamine (1.5 equiv) and $PdCl_2(PPh_3)_2$ (2 mol %), were placed into a pressure tube and 4 mL of dry DMF were added. Once the tube was sealed the mixture was heated at 120 °C for 4–6 h. The product was then purified by column chromatography (eluent: *n*-heptane/ethylacetate).

*4.1.7. General procedure for **40**, **41**.* Under argon atmosphere, appropriate styrene (3 equiv), **31** or **32** (1 equiv), triethylamine (4 equiv) and $PdCl_2(PPh_3)_2$ (4 mol %), were placed into a pressure tube and 4 mL of dry dimethylformamide were added. Once the tube was sealed the mixture was heated at 140 °C for 8 h. The product was then purified by column chromatography (eluent: *n*-heptane/ethylacetate).

5. Analytical data

5.1. 3-Methyl-5-nitro-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (17)

The product was isolated as a yellow solid. Yield 88%, mp 130–132 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.71 (s, 3H, Me), 7.32–7.38 (m, 1H, Ph), 7.51–7.56 (m, 2H, Ph), 8.18–8.21 (m, 1H, Ph), 8.90 (d, 1H, ^4J=2.5 Hz, CH_{Ar}), 9.43 (d, 1H, ^4J=2.5 Hz, CH_{Ar}). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=12.5 (Me), 116.0 (C), 121.3, 126.3, 126.9, 129.2 (CH), 138.4, 139.2 (C), 145.0 (CH), 145.2, 151.2 (C). MS (GC, 70 eV): *m*/*z* (%)=254 (M^+, 100), 208 (14), 167 (12), 140 (12), 77 (15). HRMS (ESI): calcd for $C_{13}H_{10}N_4O_2$ (M+H) 255.08765, found 255.08749. IR (ATR, cm^{-1}): $\tilde{\nu}$=3078 (w), 1593 (m), 1522 (m), 1504 (m), 1476 (m), 1437 (m), 1383 (w), 1350 (m), 1328 (s), 1265 (m), 1160 (w), 1123 (m), 1030 (w), 1011 (w), 962 (w), 933 (w), 914 (w), 790 (m), 772 (s), 752 (s), 689 (s), 671 (m), 656 (m), 595 (s).

5.2. 1,3-Dimethyl-6-nitropyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (18a)

The product was isolated as a white solid. Yield 91%, mp 202–204 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.51 (s, 3H, NMe), 3.78 (s, 3H, NMe), 9.20 (d, 1H, ^4J=2.7 Hz, CH_{Ar}), 9.46 (d, 1H, ^4J=2.7 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=28.9, 30.4 (Me), 110.0 (C), 133.5 (CH), 140.0 (C), 149.7 (CH), 150.7, 153.7, 159.7 (C). MS (GC, 70 eV): *m*/*z* (%)=236 (M^+, 100), 208 (11), 124 (53), 78 (11). HRMS (ESI): calcd for $C_9H_8N_4O_4$ (M+H) 237.0618, found 237.0622. IR (ATR, cm^{-1}): $\tilde{\nu}$=3059 (w), 2923 (w), 2853 (w), 1722 (w), 1666 (m), 1591 (s), 1536 (m), 1471 (m), 1412 (m), 1376 (m), 1334 (s), 1280 (s), 1163 (m), 1097 (s), 1005 (m), 981 (m), 949 (m), 910 (w), 829 (m), 796 (s), 751 (s), 733 (s), 711 (m), 675 (m), 580 (m).

5.3. 1-Methyl-6-nitropyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (18b)

The product was isolated as a white solid. Yield 95, mp 202–204 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=3.54 (s, 3H, NMe), 3.78 (s, 3H, NMe), 8.80 (d, 1H, ^4J=2.8 Hz, CH_{Ar}), 9.48 (d, 1H, ^4J=2.8 Hz, CH_{Ar}), 12.13 (s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO): δ=29.0 (Me), 111.0 (C), 131.6 (CH), 139.5 (C), 149.4 (CH), 150.3, 155.0, 160.1 (C). MS (GC, 70 eV): *m*/*z* (%)=222 (M^+, 100), 124 (46). HRMS (ESI): calcd for $C_8H_6N_4O_4$ (M+H) 221.0316, found 221.0317. IR (ATR, cm^{-1}): $\tilde{\nu}$=3183 (w), 3043 (m), 2922 (w), 2848 (w), 1674 (s), 1588 (s), 1525 (m), 1463 (s), 1356 (m), 1327 (s), 1266 (s), 1179 (m), 1147 (m), 1072 (m), 989 (w), 954 (m), 938 (m), 813 (m), 794 (m), 744 (m), 704 (m), 666 (m), 585 (m).

5.4. 1,2-Dihydro-5-nitro-2-phenylpyrazolo[3,4-*b*]pyridin-3-one (19)

The product was isolated as a dark brown solid. Yield 81%, mp 341–345 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.07–7.13 (m, 1H, CH_{Ar}), 7.36–7.41 (m, 2H, CH_{Ar}), 8.20–8.23 (m, 2H, CH_{Ar}), 8.31 (s, 1H, NH), 8.37 (d, 1H, ^4J=2.7 Hz, CH_{Ar}), 8.89 (d, 1H, ^4J=2.8 Hz, CH_{Ar}). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ=105.6 (C), 118.7, 123.4, 128.4, 128.8 (CH), 130.3, 140.6 (C), 148.1 (CH), 155.7, 160.5 (C). MS (GC, 70 eV): *m*/*z* (%)=256 (M^+, 100), 210 (35), 133 (40). HRMS (ESI): calcd for $C_{12}H_8N_4O_3$ (M+H) 257.0669, found 257.0666. IR (ATR, cm^{-1}): $\tilde{\nu}$=3065 (w), 1610 (m), 1532 (w), 1435 (m), 1325 (s), 1174 (m), 1057 (m), 1031 (m), 963 (m), 829 (m), 783 (s), 745 (s), 674 (s), 586 (m).

5.5. 1,3-Dimethyl-6-nitro-1*H*-imidazo[4,5-*b*]pyridine-2(3*H*)-thione (20a)

The product was isolated as an orange solid. Yield 83%, mp 203–205 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.77 (s, 3H, NMe), 3.79 (s, 3H, NMe), 8.08 (d, 1H, ^4J=2.2 Hz, CH_{Ar}), 9.09 (d, 1H, ^4J=2.2 Hz, CH_{Ar}). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=30.3, 31.3 (NMe), 109.7 (CH), 125.7 (C), 140.1 (CH), 140.6, 148.8, 174.7 (C). MS (GC, 70 eV): *m*/*z* (%)=224 (M^+, 100), 178 (35). HRMS (EI): calcd for $C_8H_8N_4S$ (M^+) 224.03625, found 224.035823. IR (ATR, cm^{-1}): $\tilde{\nu}$=3034 (w), 2924 (w), 1615 (w), 1598 (w), 1521 (m), 1487 (m), 1438 (m), 1408 (m), 1330 (s), 1288 (w), 1114 (s), 1070 (m), 1010 (m), 929 (m), 899 (s), 889 (s), 806 (s), 766 (s), 742 (s), 645 (m), 616 (s), 560 (s).

5.6. 3-Ethyl-1-methyl-6-nitro-1*H*-imidazo[4,5-*b*]pyridine-2(3*H*)-thione (20b)

The product was isolated as a red solid. Yield 84%, mp 200–202 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.42 (t, 3H, ^3J=7.0 Hz CH_2CH_3), 3.81 (s, 3H, NMe), 4.48 (q, 2H, ^3J=7.0 Hz, CH_2CH_3), 8.12 (d, 1H, ^4J=2.5 Hz, CH_{Ar}), 9.14 (d, 1H, ^4J=2.5 Hz, CH_{Ar}). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=12.9 (Me), 31.2 (CH_2), 39.2 (Me), 109.6 (CH), 125.8 (C), 140.1 (CH), 140.6, 148.4, 173.9 (C). MS (GC, 70 eV): *m*/*z* (%)=238 (M^+, 100), 210 (57), 192 (12), 164 (60), 64 (22). HRMS (EI): calcd for $C_9H_{10}N_4O_2S$ (M^+) 238.05190, found 238.051930. IR (ATR, cm^{-1}): $\tilde{\nu}$=3054 (w), 2981 (w), 2942 (w), 1771 (w), 1619 (w), 1525 (m), 1483 (m), 1458 (m), 1430 (s), 1392 (m), 1361 (m), 1333 (s), 1298 (s), 1262 (s), 1215 (m), 1116 (s), 1087 (s), 1021 (m), 959 (m), 939 (m), 902 (m), 808 (s), 770 (s), 744 (s), 671 (w), 617 (s).

5.7. 3-Cyclohexyl-1-methyl-6-nitro-1*H*-imidazo[4,5-*b*]pyridine-2(3*H*)-thione (20c)

The product was isolated as a yellow solid. Yield 79%, mp 198–200 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=1.24–1.50 (m, 6H, $CH_{2cyclhex}$), 1.63–1.66 (m, 2H, $CH_{2cyclhex}$), 1.77–1.80 (m, 2H, $CH_{2cyclhex}$), 2.89–2.96 (m, 1H, $NCH_{cyclhex}$), 3.45 (s, 3H, Me), 7.62 (d, 1H, ^4J=2.11 Hz, CH_{Ar}), 8.86 (d, 1H, ^3J=8.5 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=24.7, 25.5 (CH_2), 31.4 (Me), 33.4 (CH_2), 64.7 (CH), 106.7 (CH), 125.8 (C), 136.7 (CH), 137.3, 143.1, 155.1 (C). MS (GC, 70 eV): *m*/*z* (%)=292 (M^+, 43), 263 (16), 249 (100), 237 (13), 203 (20). HRMS (EI): calcd for $C_{13}H_{16}O_2N_4S$ (M^+) 292.09885, found 292.099655. IR (ATR, cm^{-1}): $\tilde{\nu}$=3097 (w), 2922 (s), 2852 (s), 1732 (w), 1647 (s), 1583 (m), 1519 (s), 1448 (s), 1430 (s), 1395 (m), 1336 (s), 1285 (s), 1261 (s), 1218 (m), 1147 (s), 1106 (s), 1076 (s), 1013 (m), 970 (s), 916 (s), 892 (m), 871 (m), 822 (s), 795 (m), 743 (s), 600 (s).

5.8. 1-Methyl-6-nitro-3-phenyl-1*H*-imidazo[4,5-*b*]pyridine-2(3*H*)-thione (20d)

The product was isolated as a red solid. Yield 83%, mp 260–262 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=3.86 (s, 3H, NMe),

7.51–7.65 (m, 5H, Ph), 8.78 (d, 1H, ^4J=2.3 Hz, CH_{Ar}), 9.05 (d, 1H, ^4J=2.3 Hz, CH_{Ar}). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=31.6 (Me), 111.9 (CH), 126.2 (C), 128.5, 129.2, 129.3 (CH), 134.0 (C), 137.0 (CH), 141.0, 148.7, 173.8 (C). MS (GC, 70 eV): *m*/*z* (%)=286 (M^+, 100), 239 (45), 224 (12), 77 (12). HRMS (EI): calcd for $C_{13}H_{10}N_2O_2S$ (M^+) 286.05190, found 286.051426. IR (ATR, cm^{-1}): $\tilde{\nu}$=3021 (w), 1597 (w), 1567 (w), 1536 (m), 1486 (w), 1444 (w), 1414 (w), 1393 (w), 1322 (m), 1283 (s), 1248 (m), 1127 (m), 1061 (m), 950 (m), 938 (m), 900 (m), 771 (s), 744 (m), 719 (m), 657 (m), 631 (m), 564 (m).

5.9. 6-Nitro-2-(piperidin-1-yl)thiazolo[4,5-*b*]pyridine (21a)

The product was isolated as a yellow solid. Yield 87%, mp 214–216 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.74 (s, 6H, CH_2), 3.75 (s, 4H, CH_2), 8.60 (s, 1H, ^4J=2.12 Hz, CH_{Ar}), 9.28 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=23.9, 25.4, 50.3 (CH_2), 124.1 (CH), 124.9, 137.8 (C), 143.8 (CH), 168.2, 172.6 (C). MS (EI, 70 eV): *m*/*z* (%)=264 (M^+, 100), 249 (20), 235 (53), 209 (31), 181 (23), 163 (15), 108 (13). HRMS (EI): calcd for $C_{11}H_{12}O_2N_4S$ (M^+) 264.06755, found 264.067764. IR (ATR, cm^{-1}): $\tilde{\nu}$=3048 (w), 2967 (w), 1582 (w), 1563 (m), 1530 (m), 1484 (m), 1438 (m), 1384 (m), 1290 (m), 1260 (m), 1239 (s), 1107 (s), 1067 (m), 1054 (m), 1028 (m), 937 (m), 890 (m), 801 (w), 769 (s), 744 (m), 707 (w), 659 (m).

5.10. 2-Morpholino-6-nitrothiazolo[4,5-*b*]pyridine (21b)

The product was isolated as an orange solid. Yield 84%, mp 248–250 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.80–3.85 (m, 8H, CH_2), 8.66 (d, 1H, CH_{Ar}), 9.24 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): due to bed solubility it was not possible to measure. MS (EI, 70 eV): *m*/*z* (%)=266 (M^+, 67), 222 (11), 209 (100), 181 (35), 163 (21), 108 (14). HRMS (EI): calcd for $C_{10}H_{10}O_3N_4S$ (M^+) 266.04681, found 266.046719. IR (ATR, cm^{-1}): $\tilde{\nu}$=3048 (w), 2967 (w), 1582 (w), 1563 (m), 1531 (m), 1484 (m), 1438 (m), 1384 (m), 1309 (m), 1290 (m), 1260 (m), 1239 (s), 1107 (s), 1066 (m), 1054 (m), 1028 (m), 937 (m), 890 (m), 801 (w), 769 (s), 744 (m), 707 (w), 636 (m), 562 (m).

5.11. 1-*tert*-Butyl-5-nitro-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (22a)

The product was isolated as an orange solid. Yield 93%, mp 218–220 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.79 (s, 9H, $(CH_3)_3$), 8.00 (s, 1H, CH_{Ar}), 8.82 (d, 1H, ^4J=2.6 Hz, CH_{Ar}), 9.24 (d, 1H, ^4J=2.5 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=29.1 $(CH_3)_3$, 59.9, 86.0, 113.7, 120.3 (C), 124.1, 136.6 (CH), 140.0 (C), 140.1 (CH), 148.7 (C). MS (GC, 70 eV): *m*/*z* (%)=244 (M^+, 24), 188 (100), 142 (28). HRMS (ESI): calcd for $C_{12}H_{13}N_4O_2$ (M+H) 245.1033, found 245.1032. IR (ATR, cm^{-1}): $\tilde{\nu}$=3167 (w), 2974 (w), 2222 (s), 1604 (m), 1575 (m), 1515 (s), 1414 (m), 1333 (s), 1292 (s), 1196 (s), 1119 (m), 912 (m), 776 (m), 744 (m), 660 (m), 619 (m).

5.12. 1-Cyclohexyl-5-nitro-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (22b)

The product was isolated as a brown solid. Yield 86%, mp 211–213 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.18–1.33 (m, 1H, CH_2), 1.45–1.81 (m, 5H, CH_2), 1.88–2.15 (m, 4H, CH), 7.94 (s, 1H, CH_{Ar}), 8.86 (d, 1H, ^4J=2.3 Hz, CH_{Ar}), 9.24 (d, 1H, ^4J=2.3 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=25.1, 25.5, 33.3 (CH_2), 55.4 (CH), 87.0, 113.6, 119.0 (C), 124.5, 135.9 (CH), 140.5 (C), 141.1 (CH), 147.9 (C). MS (GC, 70 eV): *m*/*z* (%)=270 (M^+, 46), 189 (61), 188 (100). HRMS (EI): calcd for $C_{14}H_{14}N_4O_2$ (M^+) 270.11113, found 270.11097. IR (ATR, cm^{-1}): $\tilde{\nu}$=3151 (w), 2938 (m), 2226 (s), 1604 (m), 1578 (m), 1521 (m), 1509 (s), 1428 (m), 1327 (s), 1197 (m), 1077 (m), 915 (m), 785 (m), 746 (m), 615 (s).

5.13. 1-(4-Methoxybenzyl)-5-nitro-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (22c)

The product was isolated as a yellow solid. Yield 84%, mp 130–132 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=3.71 (s, 3H, OCH_3), 5.54 (s, 2H, CH_2), 6.89 (d, 2H, ^3J=8.7 Hz, CH_{Ar}), 7.33 (d, 2H, ^3J=8.7 Hz, CH_{Ar}), 8.90 (s, 1H, CH_{Ar}), 8.95 (d, 1H, ^4J=2.5 Hz, CH_{Ar}), 9.30 (d, 1H, ^4J=2.5 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=48.2 (CH_2), 55.0 (OCH_3), 85.5, 113.8 (C), 114.1 (CH), 118.2 (C), 124.5 (CH), 128.0 (C), 129.3 (CH), 140.3 (C), 141.0, 141.4 (CH), 147.6, 159.0 (C). MS (GC, 70 eV): *m*/*z* (%)=121 (M^+, 100), 77 (6). HRMS (EI): calcd for $C_{18}H_{12}N_4O_3$ (M^+) 308.09039, found 308.09124. IR (ATR, cm^{-1}): $\tilde{\nu}$=3104 (w), 2221 (s), 1734 (s), 1603 (m), 1579 (m), 1513 (s), 1342 (s), 1240 (s), 1171 (s), 1027 (m), 948 (w), 795 (m).

5.14. 3-Methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridin-5-amine (23)

The product was isolated as a grey solid. Yield 85%, mp 102–104 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.49 (s, 3H, Me), 5.27 (s, 2H, NH_2), 7.32–7.38 (m, 1H, Ph), 7.19–7.24 (m, 1H, Ph), 7.26 (d, 1H, ^4J=2.5 Hz, CH_{Ar}), 7.46–7.52 (m, 2H, Ph), 8.17 (d, 1H, ^4J=2.5 Hz, CH_{Ar}), 8.25–8.27 (m, 2H, Ph). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ=12.1 (Me), 109.8 (CH), 117.2 (C), 118.7, 124.2, 129.0, 139.6 (CH), 139.7, 140.4, 140.8, 144.8 (C). MS (GC, 70 eV): *m*/*z* (%)=224 (M^+, 100). HRMS (ESI): calcd for $C_{13}H_{12}N_4$ (M+H) 225.11232, found 225.11233. IR (ATR, cm^{-1}): $\tilde{\nu}$=3346 (w), 1632 (w), 1591 (m), 1503 (s), 1441 (w), 1410 (m), 1385 (m), 1268 (m), 1201 (w), 1128 (m), 1066 (m), 966 (m), 906 (m), 862 (m), 754 (s), 717 (m), 691 (s), 671 (s).

5.15. 6-Amino-1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (24a)

The product was isolated as a green solid. Yield 97%, mp 208–210 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.45 (s, 3H, NMe), 3.65 (s, 3H, NMe), 3.80 (br s, 2H, NH_2), 7.23 (d, 1H, ^4J=3.0 Hz, CH_{Ar}), 8.16 (d, 1H, ^4J=3.0 Hz, CH_{Ar}). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=28.5, 29.3 (Me), 110.7 (C), 121.2 (CH), 139.1 (C), 141.9 (CH), 143.9, 151.1, 161.6 (C). MS (GC, 70 eV): *m*/*z* (%)=206 (M^+, 100), 177 (14), 121 (30), 94 (32). HRMS (ESI): calcd for $C_9H_{10}N_4O_2$ (M+H) 207.0877, found 207.0875. IR (ATR, cm^{-1}): $\tilde{\nu}$=3415 (w), 3345 (w), 3239 (w), 2929 (w), 1696 (m), 1640 (s), 1504 (s), 1472 (s), 1421 (s), 1379 (m), 1353 (m), 1323 (m), 1292 (s), 1163 (w), 1070 (m), 1010 (w), 975 (m), 893 (m), 780 (s), 745 (s), 682 (m), 616 (m).

5.16. 6-Amino-1-methylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (24b)

The product was isolated as a green solid. Yield 94%, mp 202–204 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=3.42 (s, 3H, NMe), 5.46 (s, 2H, NH_2), 7.50 (d, 1H, ^4J=2.8 Hz, CH_{Ar}), 8.12 (d, 1H, ^4J=2.8 Hz, CH_{Ar}), 11.45 (s, 1H, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ=27.9 (Me), 111.0 (C), 118.5 (CH), 140.7 (C), 141.5 (CH), 143.0, 150.1, 161.6 (C). MS (GC, 70 eV): *m*/*z* (%)=192 (M^+, 100), 121 (22), 94 (33). HRMS (ESI): calcd for $C_8H_8N_4O_2$ (M+H) 193.072, found 193.0723. IR (ATR, cm^{-1}): $\tilde{\nu}$=3446 (w), 3366 (w), 3181 (w), 3045 (w), 2922 (w), 2850 (w), 1681 (s), 1634 (s), 1582 (m), 1504 (s), 1423 (m), 1383 (m), 1326 (m), 1286 (s), 1231 (m), 955 (m), 688 (m), 807 (m), 780 (m), 745 (m), 727 (m), 669 (m).

5.17. 5-Amino-1,2-dihydro-2-phenylpyrazolo[3,4-*b*]pyridin-3-one (25)

The product was isolated as a green solid. Yield 91%, mp 295–297 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=5.29 (s, 2H, NH_2), 7.19–7.27 (m, 2H, CH_{Ar}), 7.45–7.50 (m, 2H, CH_{Ar}), 8.37 (d, 1H,

^4J=2.7 Hz, CH_{Ar}), 7.90 (d, 1H, ^3J=8.7 Hz, CH_{Ar}), 8.13 (d, 1H, ^4J=2.6 Hz, CH_{Ar}), 10.42 (s, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=111.3 (C), 113.9, 119.0, 124.7, 128.9 (CH), 137.7, 141.6 (C), 142.5 (CH), 151.2, 156.6 (C). MS (GC, 70 eV): m/z (%)=226 (M^+, 100), 197 (49). HRMS (ESI): calcd for $C_{12}H_{10}N_4O$ (M+H) 225.0782, found 225.0776. IR (ATR, cm^{-1}): $\tilde{\nu}$=3207 (w), 3064 (w), 1651 (s), 1593 (m), 1496 (s), 1422 (m), 1359 (m), 1273 (m), 1232 (m), 1198 (m), 1076 (s), 1031 (w), 971 (w), 891 (m), 827 (m), 783 (m), 743 (s), 646 (s), 586 (s).

5.18. 1-*tert*-Butyl-5-amino-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (26a)

The product was isolated as a brown solid. Yield 95%, mp 129–131 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.71 (s, 9H, $(CH_3)_3$), 3.60 (br s, 2H, NH_2), 7.22 (d, 1H, ^4J=2.6 Hz, CH_{Ar}), 7.65 (s, 1H, CH_{Ar}), 7.89 (d, 1H, ^4J=2.6 Hz, Ar–H). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=28.6 $(CH_3)_3$, 57.6 (C), 79.4 (C), 108.7 (CH), 116.2 (C), 121.7 (C), 133.6 (CH), 134.0 (CH), 140.0 (C), 140.8 (C). MS (GC, 70 eV): m/z (%)=214 (M^+, 20), 158 (100), 130 (10). HRMS (EI): calcd for $C_{12}H_{14}N_4$ (M^+) 214.12130, found 214.12134. IR (ATR, cm^{-1}): $\tilde{\nu}$=3349 (w), 2202 (s), 1613 (w), 1519 (m), 1417 (s), 1305 (m), 1087 (m), 862 (w), 725 (m), 692 (m), 620 (s).

5.19. 3-Heptyl-6-nitro-3*H*-imidazo[4,5-*b*]pyridine (28a)

The product was isolated as a yellow solid. Yield 40%, mp 56–58 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.82–0.86 (m, 3H, $CH_3(CH_2)_4CH_2CH_2$), 1.24–1.33 (m, 8H, $CH_3(CH_2)_4CH_2CH_2$), 1.91–1.96 (m, 2H, $CH_3(CH_2)_4CH_2CH_2$) 4.34 (t, 2H, ^3J=7.3 Hz, $CH_3(CH_2)_4CH_2CH_2$), 8.24 (s, 1H, CH_{Ar}), 8.86 (s, 1H, CH_{Ar}), 9.31 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=11.9 (Me), 22.4, 26.6, 28.6, 29.8, 31.5, 44.4 (CH_2), 123.8 (CH), 134.3 (C), 140.9 (CH), 147.8, 153.6 (C). MS (GC, 70 eV): m/z (%)=262 (M^+, 86), 233 (24), 219 (64), 205 (42), 191 (40), 178 (100), 164 (45), 131 (28), 119 (15). HRMS (ESI): calcd for $C_{13}H_{18}N_4O_2$ (M+H) 263.14112, found 263.14113. IR (ATR, cm^{-1}): $\tilde{\nu}$=3072 (w), 2916 (w), 1589 (s), 1523 (s), 1499 (m), 1456 (m), 1381 (w), 1343 (s), 1325 (s), 1261 (m), 1218 (m), 1076 (m), 929 (m), 847 (w), 793 (s), 748 (s), 722 (m), 665 (m), 633 (s).

5.20. 3-*tert*-Butyl-6-nitro-3*H*-imidazo[4,5-*b*]pyridine (28b)

The product was isolated as a white solid. Yield 35%, mp 112–114 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.86 (s, 9H, NMe_3), 8.35 (s, 1H, CH_{Ar}), 8.85 (d, 1H, ^4J=2.4 Hz, CH_{Ar}), 9.31 (d, 1H, ^4J=2.4 Hz, CH_{Ar}). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=29.0 (Me), 58.3 (C), 123.4 (CH), 135.6 (C), 139.8 (CH), 140.5 (C), 145.6 (CH), 150.6 (C). MS (GC, 70 eV): m/z (%)=220 (M^+, 62), 165 (100), 118 (22), 57 (20). HRMS (EI): calcd for $C_{10}H_{12}N_4O_2$ (M^+) 220.09548, found 220.095401. IR (ATR, cm^{-1}): $\tilde{\nu}$=3093 (w), 2986 (w), 1640 (w), 1585 (m), 1529 (m), 1515 (m), 1481 (m), 1459 (m), 1395 (w), 1368 (w), 1326 (s), 1306 (s), 1264 (m), 1250 (m), 1225 (s), 1193 (s), 1072 (m), 957 (w), 933 (m), 910 (m), 848 (w), 819 (w), 785 (s), 749 (s), 708 (m), 642 (m), 577 (s).

5.21. 3-Cyclohexyl-6-nitro-3*H*-imidazo[4,5-*b*]pyridine (28c)

The product was isolated as a yellow solid. Yield 36%, mp 118–120 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.23–1.58 (m, 3H, $CH_{2cyclhex}$), 1.79–2.01 (m, 5H, $CH_{2cyclhex}$), 2.19–2.24 (m, 2H, $CH_{2cyclhex}$), 4.58–4.69 (m, 1H, $NCH_{cyclhex}$), 8.35 (s, 1H, CH_{Ar}), 8.86 (d, 1H, ^4J=2.3 Hz, CH_{Ar}), 9.30 (d, 1H, ^4J=2.3 Hz, CH_{Ar}). ^{13}C NMR (75.5 MHz, DMSO): δ=24.7, 25.0, 32.0 (CH_2), 54.3 (CH), 123.2 (CH), 133.9 (C), 139.9 (CH), 140.5 (C), 147.9 (CH), 149.6 (C). MS (GC, 70 eV): m/z (%)=246 (M^+, 27), 165 (100), 119 (16), 67 (12). HRMS (ESI): calcd for $C_{12}H_{14}N_4O_2$ (M+1) 247.11895, found 247.11901. IR (ATR, cm^{-1}): $\tilde{\nu}$=2933 (w), 2851 (w), 1643 (w), 1601 (m), 1586 (m), 1515 (m), 1491 (m), 1448 (m), 1401 (w), 1342 (m), 1319 (s), 1275 (m), 1256 (m), 1206 (m), 1178 (m), 1139 (w), 1070 (m), 995 (w), 912 (m), 885 (w), 840 (w), 811 (m), 796 (s), 756 (s), 748 (s), 681 (m), 635 (m).

5.22. 3-Allyl-6-nitro-3*H*-imidazo[4,5-*b*]pyridine (28d)

The product was isolated as a yellow solid. Yield 46%, mp 122–123 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.97 (dt, 2H, ^3J=5.8 Hz, ^4J=1.5 Hz, NCH_2), 5.23–5.40 (m, 2H, $CHCH_2$), 6.00–6.15 (m, 2H, $CHCH_2$), 8.28 (s, 1H, CH_{Ar}), 8.90 (d, 1H, ^4J=2.2 Hz, CH_{Ar}), 9.34 (d, 1H, ^4J=2.2 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=46.2 (CH_2), 119.9 (CH_2), 123.8 (CH), 127.4 (C), 131.0 (CH), 134.0 (C), 141.1 (CH), 147.5, 149.8 (C). MS (GC, 70 eV): m/z (%)=204 (M^+, 100), 176 (12), 157 (31), 131 (23). HRMS (ESI): calcd for $C_9H_8N_4O_2$ (M+H) 205.072, found 205.07185. IR (ATR, cm^{-1}): $\tilde{\nu}$=3035 (w), 1593 (s), 1521 (s), 1496 (m), 1466 (m), 1422 (w), 1401 (m), 1335 (s), 1309 (s), 1256 (m), 1202 (s), 1093 (w), 1069 (m), 991 (m), 917 (s), 839 (w), 796 (m), 769 (s), 748 (s), 691 (m), 634 (s).

5.23. 3-(3,4,5-Trimethoxyphenyl)-6-nitro-3*H*-imidazo[4,5-*b*]pyridine (28e)

The product was isolated as a yellow solid. Yield 32%, mp 173–175 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.91 (s, 3H, OMe), 3.93 (s, 6H, 2× OMe), 4.57 (t, 2H, ^3J=6.8 Hz, CH_2), 6.89 (s, 2H, CH_{Ar}), 8.48 (s, 1H, CH_{Ar}), 8.96 (d, 1H, ^4J=2.4 Hz, CH_{Ar}), 9.37 (d, 1H, ^4J=2.4 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=56.4, 60.9 (OMe), 101.9, 124.2 (CH), 129.5, 134.8, 138.5, 141.2 (C), 141.5, 147.1 (CH), 149.8, 154.1 (C). MS (GC, 70 eV): m/z (%)=330 (M^+, 100), 115 (74), 287 (21), 269 (12), 241 (15). HRMS (EI): calcd for $C_{15}H_{14}N_4O_5$ (M^+) 330.09587, found 330.095802. IR (ATR, cm^{-1}): $\tilde{\nu}$=3085 (w), 2930 (w), 2838 (w), 1813 (w), 1588 (s), 1509 (s), 1460 (m), 1417 (m), 1343 (s), 1318 (s), 1297 (m), 1231 (s), 1218 (s), 1177 (m), 1124 (s), 1074 (m), 1023 (m), 990 (s), 913 (m), 857 (m), 827 (s), 794 (m), 773 (m), 746 (s), 691 (m), 660 (s).

5.24. 3-(4-Methoxybenzyl)-6-nitro-3*H*-imidazo[4,5-*b*]pyridine (28f)

The product was isolated as a yellow solid. Yield 48%, mp 161–163 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.72 (s, 3H, OMe), 5.38 (s, 2H, CH_2), 6.80–6.83 (m, 2H, CH_{Ar}), 7.21–7.24 (m, 2H, CH_{Ar}), 8.13 (s, 1H, CH_{Ar}), 8.80 (d, 1H, ^4J=2.4 Hz, CH_{Ar}), 9.28 (d, 1H, ^4J=2.4 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=47.3 (CH_2), 55.3 (OMe), 114.5, 123.9 (CH), 126.6 (C), 129.6 (CH), 134.2 (C), 141.1, 147.5 (CH), 150.1, 154.9, 159.9 (C). MS (GC, 70 eV): m/z (%)=284 (M^+, 64), 121 (100). HRMS (EI): calcd for $C_{14}H_{12}N_4O_3$ (M+H) 285.09336, found 285.09337. IR (ATR, cm^{-1}): $\tilde{\nu}$=3042 (w), 1767 (w), 1613 (w), 1589 (s), 1528 (m), 1516 (s), 1496 (m), 1469 (s), 1411 (w), 1386 (w), 1352 (s), 1303 (s), 1254 (s), 1234 (s), 1194 (s), 1174 (m), 1117 (m), 1074 (w), 1022 (s), 944 (m), 886 (w), 857 (m), 841 (s), 817 (m), 799 (m), 766 (s), 750 (s), 714 (m), 656 (s).

5.25. 6-Nitro-3-((pyridin-4-yl)methyl)-3*H*-imidazo[4,5-*b*]pyridine (28g)

The product was isolated as a brown solid. Yield 45%, mp 154–156 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=5.67 (s, 2H, CH_2), 7.24–7.26 (m, 2H, CH_{Ar}), 8.51–8.53 (m, 2H, CH_{Ar}), 8.96–8.98 (m, 2H, CH_{Ar}), 9.25 (d, 1H, ^4J=2.3 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=45.8 (CH_2), 122.1, 123.6 (CH), 130.4, 133.8 (C), 140.6 (CH), 140.9, 145.0 (C), 149.9, 150.0 (CH). MS (GC, 70 eV): m/z (%)=255 (M^+, 81), 254 (100), 208 (32), 92 (20). HRMS (EI): calcd for $C_{12}H_9N_5O_2$ (M+H) 256.0829, found 256.08237. IR (ATR, cm^{-1}): $\tilde{\nu}$=3069 (w), 1601 (m), 1590 (m), 1520 (s), 1504 (m), 1466 (m), 1409 (m), 1390 (w), 1346 (s), 1270 (m), 1200 (m), 1158 (w), 1080 (w), 994 (w), 941 (w), 918 (m), 857 (w), 792 (m), 780 (m), 762 (s), 750 (s), 731 (m), 664 (s), 630 (m).

5.26. 6-Nitro-3-phenethyl-3*H*-imidazo[4,5-*b*]pyridine (28h)

The product was isolated as a brown solid. Yield 42%, mp 99–101 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.22 (t, 2H, ^3J=7.1 Hz, CH_2), 4.60 (t, 2H, ^3J=7.1 Hz, CH_2), 7.01–7.04 (m, 2H, CH_{Ar}), 7.22–7.29 (m, 3H, CH_{Ar}), 7.87 (s, 1H, CH_{Ar}), 8.86 (d, 1H, ^4J=2.2 Hz, CH_{Ar}), 9.34 (d, 1H, ^4J=2.2 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=35.9, 46.0 (CH_2), 123.7, 127.3, 128.6, 128.9 (CH), 134.1, 136.8 (C), 141.0 (CH), 147.8 (C). MS (GC, 70 eV): *m*/*z* (%)=268 (M^+, 31), 104 (100), 91 (26). HRMS (EI): calcd for $C_{14}H_{12}N_4O_2$ (M+H) 269.1033, found 269.10343. IR (ATR, cm^{-1}): $\tilde{\nu}$=3051 (w), 2923 (w), 1591 (m), 1519 (s), 1495 (m), 1464 (m), 1406 (m), 1386 (w), 1369 (w), 1346 (s), 1256 (m), 1197 (m), 1152 (w), 1101 (w), 1067 (w), 1006 (w), 956 (m), 914 (m), 871 (w), 839 (w), 796 (m), 783 (m), 758 (m), 745 (s), 702 (s), 634 (m).

5.27. 3-(3,4-Dimethoxyphenethyl)-6-nitro-3*H*-imidazo[4,5-*b*]pyridine (28i)

The product was isolated as a yellow solid. Yield 45%, mp 112–114 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.15 (t, 2H, ^3J=6.8 Hz, CH_2), 3.77 (s, 3H, OMe), 3.83 (s, 3H, OMe), 4.57 (t, 2H, ^3J=6.8 Hz, CH_2), 6.50–6.55 (m, 2H, CH_{Ar}), 6.74 (d, 1H, ^3J=8.0 Hz, CH_{Ar}), 7.86 (s, 1H, CH_{Ar}), 8.86 (d, 1H, ^4J=2.4 Hz, CH_{Ar}), 9.34 (d, 1H, ^4J=2.4 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=35.5, 45.9 (CH_2), 55.8 (OMe), 114.4, 111.6, 120.7, 123.7 (CH), 129.3, 134.1 (C), 140.8 (CH), 140.9 (C), 147.9 (CH), 148.1, 149.1, 149.9 (C). MS (GC, 70 eV): *m*/*z* (%)=328 (M^+, 8), 164 (100), 151 (19). HRMS (EI): calcd for $C_{16}H_{16}N_4O_4$ (M+H) 329.12556, found 329.12557. IR (ATR, cm^{-1}): $\tilde{\nu}$=3034 (w), 1588 (m), 1511 (s), 1456 (m), 1406 (w), 1381 (w), 1337 (s), 1321 (s), 1296 (m), 1257 (s), 1235 (s), 1199 (m), 1154 (s), 1076 (w), 1023 (s), 941 (w), 852 (w), 816 (m), 796 (m), 778 (s), 747 (m), 727 (m), 660 (w), 634 (s).

5.28. 3-*tert*-Butyl-3*H*-imidazo[4,5-*b*]pyridin-6-amine (29b)

The product was isolated as a green solid. Yield 92%, mp 155–157 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=1.71 (s, 9H, NMe_3), 4.94 (s, 2H, NH_2), 7.15 (d, 1H, ^4J=2.5 Hz, CH_{Ar}), 7.82 (d, 1H, ^4J=2.5 Hz, CH_{Ar}), 8.13 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=28.6 (Me), 55.8 (C), 110.2, 132.4 (CH), 136.9, 140.1, 140.8 (C), 141.7 (CH). MS (GC, 70 eV): *m*/*z* (%)=190 (M^+, 35), 134 (100). HRMS (ESI): calcd for $C_{10}H_{14}N_4$ (M^+) 190.1213, found 190.121307. IR (ATR, cm^{-1}): $\tilde{\nu}$=3326 (w), 3218 (w), 2938 (w), 1650 (w), 1605 (w), 1495 (s), 1474 (s), 1400 (s), 1369 (m), 1331 (m), 1291 (m), 1232 (s), 1157 (s), 1026 (w), 860 (s), 839 (m), 762 (m), 652 (s).

5.29. 3-Propyl-3*H*-imidazo[4,5-*b*]pyridin-6-amine (29d)

The product was isolated as a green solid. Yield 96%, mp 80–81 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=0.82 (t, 3H, ^3J=7.5 Hz, C$H_3$$CH_2$), 1.78–1.85 (m, 2H, CH_3CH_2), 4.10 (t, 2H, ^4J=6.7 Hz, NCH_2), 4.96 (s, 2H, NH_2), 7.18 (d, 1H, ^4J=2.3 Hz, CH_{Ar}), 7.83 (d, 1H, ^4J=2.3 Hz, CH_{Ar}), 8.17 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=11.0 (Me), 22.6, 44.4 (CH_2), 110.4, 133.0 (CH), 135.6, 139.9, 141.2 (C), 144.2 (CH). MS (GC, 70 eV): *m*/*z* (%)=176 (M^+, 77), 147 (57), 134 (100). HRMS (ESI): calcd for $C_9H_{12}N_4$ (M+H) 177.11256, found 177.11257. IR (ATR, cm^{-1}): $\tilde{\nu}$=3364 (w), 3207 (w), 3103 (w), 2960 (w), 1640 (w), 1604 (w), 1505 (s), 1488 (m), 1447 (m), 1409 (s), 1364 (m), 1301 (m), 1262 (w), 1226 (s), 1162 (s), 1120 (m), 975 (w), 866 (s), 831 (w), 795 (w), 765 (m), 652 (s).

5.30. 3-(3,4,5-Trimethoxyphenyl)-3*H*-imidazo[4,5-*b*]pyridin-6-amine (29e)

The product was isolated as a yellow solid. Yield 95%, mp 168–171 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=3.71 (s, 3H, OMe), 3.85 (s, 6H, 2× OMe), 5.16 (s, 2H, NH_2), 7.26–7.27 (m, 3H, CH_{Ar}), 7.89 (d, 1H, ^4J=2.4 Hz, CH_{Ar}), 8.65 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=56.2, 60.2 (OMe), 110.4, 110.6 (CH), 131.5 (C), 133.4 (CH), 136.1, 136.4, 139.1, 142.0 (C), 143.3 (CH), 153.2 (C). MS (GC, 70 eV): *m*/*z* (%)=300 (M^+, 100), 285 (76), 227 (10). HRMS (EI): calcd for $C_{15}H_{16}N_4O_3$ (M+1) 300.12169, found 300.121338. IR (ATR, cm^{-1}): $\tilde{\nu}$=3376 (w), 2961 (w), 1599 (s), 1512 (s), 1466 (m), 1427 (m), 1382 (m), 1291 (w), 1237 (s), 1167 (m), 1124 (s), 1002 (s), 876 (m), 835 (m), 811 (m), 764 (s), 727 (s), 643 (s), 626 (s).

5.31. 3-(4-Methoxybenzyl)-3*H*-imidazo[4,5-*b*]pyridin-6-amine (29f)

The product was isolated as a yellow solid. Yield 98%, mp 76–78 °C. ^{1}H NMR (250 MHz, DMSO-d_6): δ=3.70 (s, 3H, OMe), 4.97 (s, 2H, NH_2), 5.28 (s, 2H, CH_2), 6.85–6.89 (m, 2H, CH_{Ar}), 7.16 (d, 1H, ^4J=2.4 Hz, CH_{Ar}), 7.26–7.29 (m, 2H, CH_{Ar}), 7.82 (d, 1H, ^4J=2.4 Hz, CH_{Ar}), 8.26 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO): δ=45.5 (CH_2), 55.0 (OMe), 110.3, 113.9, 129.0 (CH), 129.5 (C), 133.2 (CH), 135.6, 139.6, 141.4 (C), 144.1 (CH), 158.7 (C). MS (GC, 70 eV): *m*/*z* (%)=254 (M^+, 69), 121 (100). HRMS (EI): calcd for $C_{14}H_{14}N_4O$ (M^+) 254.11621, found 254.116180. IR (ATR, cm^{-1}): $\tilde{\nu}$=3 (s), 1363 (m), 1292 (m), 1269 (w), 1244 (s), 1225 (s), 1176 (m), 1151 (s), 1118, 1035 (s), 971 (s), 916 (w), 867 (m), 836 (m), 808 (s), 772 (m), 653 (s).

5.32. 3-Phenethyl-3*H*-imidazo[4,5-*b*]pyridin-6-amine (29h)

The product was isolated as a white solid. Yield 97%, mp 113–115 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.14 (t, 2H, ^3J=7.1 Hz, CH_2), 4.40 (t, 2H, ^3J=7.1 Hz, CH_2), 4.96 (s, 2H, NH_2), 7.12–7.28 (m, 6H, CH_{Ar}), 7.84 (d, 1H, ^4J=2.4 Hz, CH_{Ar}), 7.96 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=35.1, 44.1 (CH_2), 110.4, 126.4, 128.3, 128.6, 133.0 (CH), 135.6, 138.2, 139.7, 141.3 (C), 144.1 (CH). MS (GC, 70 eV): *m*/*z* (%)=238 (M^+, 46), 147 (33), 134 (100). HRMS (EI): calcd for $C_{14}H_{14}N_4$ (M+1) 239.12336, found 239.12340. IR (ATR, cm^{-1}): $\tilde{\nu}$=3371 (m), 3204 (m), 2925 (w), 1641 (w), 1604 (w), 1581 (w), 1504 (s), 1455 (m), 1410 (s), 1379 (m), 1362 (s), 1302 (m), 1248 (m), 1230 (s), 1171 (s), 1153 (s), 1103 (m), 1030 (m), 862 (s), 840 (m), 767 (s), 721 (s), 693 (s).

5.33. 5-Bromo-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (31)

The product was isolated as a white solid. Yield 85%, mp 110–112 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.56 (s, 3H, Me), 7.28–7.34 (m, 1H, CH_{Ar}), 7.50–7.56 (m, 2H, CH_{Ar}), 8.15–8.19 (m, 2H, CH_{Ar}), 8.66 (dd, 2H, ^3J=9.1 Hz, ^4J=2.2 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=12.0 (Me), 112.2, 118.3 (C), 119.9, 125.6, 129.1, 132.6 (CH), 138.7, 142.4, 148.4 (C), 149.5 (CH). MS (GC, 70 eV): *m*/*z* (%)=287 (M^+, 100), 272 (13), 207 (18), 167 (12), 140 (130), 77 (40). HRMS (ESI): calcd for $C_{13}H_{10}N_3Br$ (M^+) 287.00526, found 287.004794. IR (ATR): ν=1592 (m), 1564 (w), 1504 (s), 1438 (m), 1414 (s), 1380 (m), 1321 (m), 1266 (s), 1209 (w), 117 (w), 1114 (m), 1070 (m), 1010 (w), 949 (m), 904 (w), 883 (m), 820 (m), 766 (s), 744 (s), 688 (s), 668 (s), 651 (m).

5.34. 1-*tert*-Butyl-5-bromo-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (32)

The product was isolated as a white solid. Yield 80%, mp 183 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.73 (s, 9H, $(CH_3)_3$), 7.78 (s, 1H, CH_{Ar}), 8.08 (d, 1H, ^4J=2.3 Hz, CH_{Ar}), 8.36 (d, 1H, ^4J=2.3 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=29.0 $(CH_3)_3$, 58.9, 82.9, 114.1, 114.8 (C), 122.8 (C), 129.9, 134.1, 144.9 (CH), 145.4 (C). MS (GC, 70 eV): *m*/*z* (%)=279 (M^+, 16), 223 (100), 142 (28); HRMS (ESI): calcd for $C_{12}H_{13}BrN_3$ (M+H) 278.02866, found 278.02874; IR (ATR, cm^{-1}): ν=2972 (w),

2217 (s), 1519 (s), 1407 (m), 1372 (m), 1271 (s), 1190 (s), 1073 (w), 881 (m), 832 (m), 617 (s).

5.35. 3-Methyl-1-phenyl-5-*p*-tolyl-1*H*-pyrazolo[3,4-*b*]pyridine (34a)

The product was isolated as a yellow solid. Yield 87%, mp 130–132 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.36 (s, 3H, Me), 2.63 (s, 3H, Me), 7.27–7.32 (m, 3H, CH_{Ar}), 7.54 (t, 2H, ^3J=8.2 Hz, CH_{Ar}), 7.68 (d, 1H, ^3J=7.8 Hz, CH_{Ar}), 8.30 (d, 2H, ^3J=8.2 Hz, CH_{Ar}), 8.53 (s, 1H, CH_{Ar}), 8.90 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=12.1, 20.6 (Me), 116.9 (C), 125.2, 126.8, 127.6, 129.1, 129.6, 129.7 (CH), 134.4, 137.0, 139.2, 143.2 (C), 148.1 (CH), 149.5 (C). MS (GC, 70 eV): *m*/*z* (%)=299 (M^+, 100). HRMS (EI): calcd for $C_{20}H_{17}N_3$ (M^+) 299.14170, found 299.141349. IR (ATR, cm^{-1}): ν=3023 (w), 1612 (w), 1594 (s), 1504 (s), 1416 (s), 1381 (m), 1344 (m), 1279 (m), 1256 (m), 1212 (w), 1118 (m), 1078 (m), 1011 (w), 957 (w), 903 (m), 852 (w), 816 (s), 760 (s), 695 (s), 665 (s), 589 (m), 569 (m).

5.36. 3-Methyl-5-(3,5-dimethylphenyl)-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (34b)

The product was isolated as an orange solid. Yield 95%, mp 96–98 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.36 (s, 6H, 2× Me), 2.65 (s, 3H, Me), 7.05 (s, 1H, CH_{Ar}), 7.30 (t, 1H, ^3J=7.2 Hz, CH_{Ar}), 7.41 (s, 2H, CH_{Ar}), 7.52–7.58 (m, 2H, CH_{Ar}), 8.30 (d, 2H, ^3J=7.9 Hz, CH_{Ar}), 8.57 (d, 1H, ^4J=2.0 Hz, CH_{Ar}), 8.91 (d, 1H, ^4J=2.0 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=12.2, 21.0 (Me), 116.9 (C), 119.7, 124.8, 125.2, 128.0, 129.0, 129.1 (CH), 130.0, 137.2, 138.1, 139.2, 143.3 (C), 148.3 (CH), 149.6 (C). MS (GC, 70 eV): *m*/*z* (%)=313 (M^+, 100). HRMS (EI): calcd for $C_{21}H_{19}N_3$ (M^+) 313.15735, found 313.156954. IR (ATR, cm^{-1}): ν=2914 (w), 1589 (m), 1504 (m), 1430 (m), 1411 (m), 1365 (w), 1272 (m), 1219 (m), 1181 (w), 1118 (m), 1030 (w), 960 (w), 898 (m), 880 (w), 836 (s), 757 (s), 683 (s), 669 (s), 603 (m), 589 (m).

5.37. 5-(4-Chlorophenyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (34c)

The product was isolated as a yellow solid. Yield 90%, mp 157–159 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.64 (s, 3H, Me), 7.30 (t, 1H, ^3J=7.6 Hz, CH_{Ar}), 7.52–7.59 (m, 4H, CH_{Ar}), 7.84 (d, 1H, ^3J=8.4 Hz, CH_{Ar}), 8.29 (d, 1H, ^3J=8.4 Hz, CH_{Ar}), 8.63 (d, 1H, ^4J=1.8 Hz, CH_{Ar}), 8.95 (d, 1H, ^4J=1.8 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=12.2 (Me), 116.8 (C), 119.7, 125.3, 128.2, 128.5, 128.7, 129.0, 129.1 (CH), 132.6, 136.2, 139.1, 143.4 (C), 148.2 (CH), 149.7 (C). MS (GC, 70 eV): *m*/*z* (%)=232 (M^+, 100), 304 (10). HRMS (EI): calcd for $C_{19}H_{14}N_3Cl$ (M^+) 319.08708, found 319.086462. IR (ATR, cm^{-1}): ν=3037 (w), 1611 (w), 1593 (m), 1558 (w), 1500 (s), 1440 (m), 1414 (s), 1343 (m), 1277 (m), 1255 (m), 1210 (w), 1118 (m), 1093 (m), 1076 (m), 1010 (m), 956 (w), 902 (m), 849 (m), 827 (s), 762 (s), 695 (s), 647 (m), 586 (m).

5.38. 5-(4-Fluorophenyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (34d)

The product was isolated as a yellow solid. Yield 88%, mp 168–169 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.63 (s, 3H, Me), 7.27–7.38 (m, 3H, CH_{Ar}), 7.50–7.56 (m, 2H, CH_{Ar}), 7.81–7.86 (m, 2H, CH_{Ar}), 8.27–8.30 (m, 2H, CH_{Ar}), 8.57 (d, 1H, ^4J=2.2 Hz, CH_{Ar}). ^{19}F NMR (282 MHz, DMSO-d_6): δ=−115.1. ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=12.1 (Me), 115.7, 116.0 (CH), 116.8 (C), 119.7, 125.2, 128.1, 128.8, 129.0, 129.1, 129.2 (CH), 133.8 (d, *J*=3.0 Hz, C), 139.1, 143.3 (C), 148.2 (CH), 149.5, 162.0 (d, *J*=245 Hz, C). MS (GC, 70 eV): *m*/*z* (%)=303 (M^+, 100). HRMS (EI): calcd for $C_{19}H_{14}N_3F$ (M^+) 303.11663, found 303.116054. IR (ATR, cm^{-1}): ν=1610 (w), 1594 (s), 1563 (w), 1504 (s), 1490 (s), 1416 (s), 1346 (w), 1259 (m), 1224 (s), 1163 (m), 1117 (m), 1076 (m), 1012 (w), 957 (w), 901 (m), 855 (m), 834 (s), 804 (m), 762 (s), 969 (s), 665 (s), 588 (m).

5.39. 5-(4-(Trifluoromethyl)phenyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (34e)

The product was isolated as a yellow solid. Yield 91%, mp 144–145 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.65 (s, 3H, Me), 7.29–7.33 (m, 1H, CH_{Ar}), 7.55 (t, 2H, ^3J=8.0 Hz, CH_{Ar}). 7.86 (d, 2H, ^3J=8.0 Hz, CH_{Ar}), 8.04 (d, 2H, ^3J=8.0 Hz, CH_{Ar}), 8.29 (d, 2H, ^3J=7.8 Hz, CH_{Ar}), 8.71 (d, 1H, ^4J=2.1 Hz, CH_{Ar}), 9.00 (d, 1H, ^4J=2.1 Hz, CH_{Ar}). ^{19}F NMR (282 MHz, DMSO-d_6): δ=−60.9. ^{13}C NMR (62.9 MHz, DMSO-d_6): due to bed solubility it was not possible to measure. MS (GC, 70 eV): *m*/*z* (%)=353 (M^+, 100), 338 (14). HRMS (EI): calcd for $C_{20}H_{14}N_3F_3$ (M^+) 353.11343, found 353.113271. IR (ATR, cm^{-1}): ν=1612 (m), 1598 (m), 1505 (m), 1408 (w), 1441 (w), 1418 (m), 1384 (w), 1324 (s), 1283 (m), 1258 (m), 1163 (s), 1104 (s), 1067 (s), 1012 (m), 955 (m), 904 (m), 849 (m), 837 (s), 773 (m), 752 (s), 702 (m), 689 (s), 668 (m), 635 (w), 594 (s), 552 (w).

5.40. 5-(3-Chlorophenyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-*b*]pyridine (34f)

The product was isolated as an orange solid. Yield 87%, mp 140–142 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.64 (s, 3H, Me), 7.30 (t, 1H, ^3J=7.2 Hz, CH_{Ar}), 7.46–7.57 (m, 4H, CH_{Ar}), 7.79 (d, 1H, ^3J=7.5 Hz, CH_{Ar}), 7.91 (s, 1H, CH_{Ar}), 8.29 (d, 1H, ^3J=7.5 Hz, CH_{Ar}), 8.68 (d, 1H, ^4J=2.0 Hz, CH_{Ar}), 8.97 (d, 1H, ^4J=2.0 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=12.7 (Me), 116.9 (C), 119.8, 125.4, 125.7, 126.8, 127.4 (CH), 128.3 (C), 128.6, 129.1, 130.8 (CH), 133.9, 139.1, 139.5, 143.5 (C), 148.3 (CH), 149.8 (C). MS (GC, 70 eV): *m*/*z* (%)=319 (M^+, 100). HRMS (EI): calcd for $C_{19}H_{14}N_3Cl$ (M^+) 319.08708, found 319.087283. IR (ATR, cm^{-1}): ν=3031 (w), 1594 (m), 1569 (m), 1497 (m), 1460 (m), 1436 (m), 1412 (m), 1383 (m), 1273 (m), 1251 (m), 1176 (w), 1097 (m), 1075 (m), 1045 (m), 957 (w), 896 (m), 878 (m), 787 (s), 775 (m), 742 (s), 697 (s), 683 (s), 607 (m), 589 (s).

5.41. 1-*tert*-Butyl-5-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (35a)

The product was isolated as a white solid. Yield 60%, mp 182 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=1.84 (s, 9H, $(CH_3)_3$), 7.42–7.58 (m, 3H, CH_{Ar}), 7.85 (d, 2H, ^3J=7.4 Hz, CH_{Ar}), 8.36 (s, 1H, CH_{Ar}), 8.60 (s, 1H, CH_{Ar}), 8.80 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=28.7 $(CH_3)_3$, 58.6, 82.0, 115.6, 120.9 (C), 125.4, 127.3, 127.7, 129.1 (CH), 130.4 (C), 136.7 (CH), 137.7 (C), 143.0 (CH), 146.1 (C). MS (GC, 70 eV): *m*/*z* (%)=275 (M^+, 17), 219 (100). HRMS (EI): calcd for $C_{18}H_{17}N_3$ (M^+) 275.14170, found 275.14181. IR (ATR, cm^{-1}): ν=3138 (w), 2212 (m), 1603 (w), 1523 (m), 1407 (m), 1396 (m), 1208 (s), 891 (m), 760 (s), 702 (s).

5.42. 1-*tert*-Butyl-5-(4-ethylphenyl)-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (35b)

The product was isolated as a white solid. Yield 70%, mp 160 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=1.24 (t, 3H, ^3J=7.6 Hz, CH_3), 1.81 (s, 9H, $(CH_3)_3$), 2.68 (q, 2H, ^3J=7.4 Hz, CH_2), 7.35 (d, 2H, ^3J=8.1 Hz, CH_{Ar}), 7.72 (d, 2H, ^3J=8.1 Hz, CH_{Ar}), 8.29 (d, 1H, ^4J=2.3 Hz, CH_{Ar}), 8.57 (s, 1H, CH_{Ar}), 8.74 (d, 1H, ^4J=2.1 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=15.5 (CH_3), 27.8 (CH_2), 28.5 $(CH_3)_3$, 58.4, 81.8, 115.5, 120.8 (C), 124.9, 127.1, 128.4 (CH), 130.3, 134.9 (C), 136.4, 142.7 (CH), 143.2, 145.9 (C). MS (GC, 70 eV): *m*/*z* (%)=303 (M^+, 29), 247 (100), 232 (62). HRMS (EI): calcd for $C_{20}H_{21}N_3$ (M) 303.1730, found 303.1732. IR (ATR, cm^{-1}): ν=3150 (w), 2216 (m), 1526 (w), 1366 (w), 1208 (m), 903 (w), 833 (s), 777 (m).

5.43. 1-*tert*-Butyl-5-(4-methoxyphenyl)-1*H*-pyrrolo[2,3-*b*] pyridine-3-carbonitrile (35c)

The product was isolated as a white solid. Yield 70%, mp 130 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.77 (s, 9H, $(CH_3)_3$), 3.79 (s, 3H, OCH_3), 6.95 (d, 2H, ^3J=9 Hz, CH_{Ar}), 7.49 (d, 2H, ^3J=9 Hz, CH_{Ar}), 7.79 (s, 1H, CH_{Ar}), 8.07 (d, 2H, ^4J=2 Hz, CH_{Ar}), 8.55 (d, 2H, ^4J=2 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=29.1 $(CH_3)_3$, 55.4 (OCH_3), 58.5, 83.1 (C), 114.6 (CH), 115.6, 121.5 (C), 125.4, 128.5 (CH), 130.8, 131.1 (C), 133.4, 143.2 (CH), 146.2, 159.4 (C). MS (GC, 70 eV): *m*/*z* (%)=305 (M^+, 36), 249 (100), 234 (29). HRMS (EI): calcd for $C_{19}H_{19}N_3O$ (M^+) 305.15226, found 305.15261. IR (ATR, cm^{-1}): ν=3145 (w), 2213 (m), 1606 (m), 1519 (m), 1399 (m), 1295 (m), 1246 (m), 830 (s).

5.44. 1-*tert*-Butyl-5-(4-chlorophenyl)-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (35d)

The product was isolated as a white solid. Yield 68%, mp 189–190 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.78 (s, 9H, $(CH_3)_3$), 7.36–7.41 (m, 2H, CH_{Ar}), 7.45–7.50 (m, 2H, CH_{Ar}), 7.82 (s, 1H, CH_{Ar}), 8.08 (d, 1H, ^4J=2 Hz, CH_{Ar}), 8.54 (d, 1H, ^4J=2 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=29.1 $(CH_3)_3$, 58.7, 83.4, 115.4, 121.5 (C), 125.8, 128.6, 129.3 (CH), 130.2 (C), 133.8 (CH), 133.9, 136.9 (C), 143.1 (CH), 146.6 (C). MS (GC, 70 eV): *m*/*z* (%)=309 (M^+, 17), 253 (100). HRMS (EI): calcd for $C_{18}H_{16}N_3Cl$ (M^+) 309.10273, found 309.10261. IR (ATR, cm^{-1}): ν=3145 (w), 2217 (m), 1608 (w), 1524 (m), 1469 (m), 1414 (m), 1368 (m), 1207 (s), 1089 (m), 830 (s).

5.45. 1-*tert*-Butyl-5-(4-(trifluoromethyl)phenyl)-1*H*-pyrrolo [2,3-*b*]pyridine-3-carbonitrile (35e)

The product was isolated as a white solid. Yield 67%, mp 177–179 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.79 (s, 9H, $(CH_3)_3$), 7.68 (s, 4H, CH_{Ar}), 7.85 (s, 1H, CH_{Ar}), 8.15 (s, 1H, ^4J=2 Hz, CH_{Ar}), 8.60 (d, 1H, ^4J=2 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=29.1 $(CH_3)_3$, 58.8, 83.5, 115.3, 121.5 (C), 126.1 (q, CF_3, ^1J=3.36, ^2J=7.78 Hz), 126.2 (C), 127.7 (CH), 129.5, 129.9 (C), 134.0 (CH), 142.0 (C), 143.3 (CH), 144.0, 146.9 (C). ^{19}F NMR (300 MHz, $CDCl_3$): δ=−62.48 Hz. MS (GC, 70 eV): *m*/*z* (%)=343 (M^+, 11), 287 (100). HRMS (EI): calcd for $C_{19}H_{16}N_3F_3$ (M^+) 343.1290, found 343.1289. IR (ATR, cm^{-1}): ν=3143 (w), 2218 (m), 1608 (m), 1523 (m), 1399 (m), 1322 (s), 1208 (m), 1164 (m), 1111 (s), 1070 (m), 835 (m).

5.46. 5-(2-(4-Methoxyphenyl)ethynyl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (37)

The product was isolated as a yellow solid. Yield 85%, mp 92–94 °C. ^{1}H NMR (250 MHz, DMSO-d_6): δ=2.62 (s, 3H, Me), 3.81 (s, 3H, OMe), 7.01 (d, 2H, ^3J=8.9 Hz, CH_{Ar}), 7.29–7.35 (m, 1H, CH_{Ar}), 7.53–7.59 (m, 4H, CH_{Ar}), 8.523 (d, 2H, ^3J=8.3 Hz, CH_{Ar}), 8.56–8.57 (m, 1H, CH_{Ar}), 8.76–8.77 (m, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=12.0 (Me), 55.2 (OMe), 85.3, 90.9, 113.0, 113.9 (C), 114.4 (CH), 116.3 (C), 120.0, 125.6, 129.1, 132.9 (CH), 138.8, 143.3, 148.5 (C), 151.3 (CH), 159.6 (C). MS (GC, 70 eV): *m*/*z* (%)=339 (M^+, 100), 324 (31). HRMS (EI): calcd for $C_{22}H_{17}N_3O$ (M^+) 339.13661, found 339.136346. IR (ATR): ν=2916 (w), 1595 (s), 1556 (m), 1504 (s), 1455 (m), 1438 (s), 1413 (s), 1382 (s), 1351 (m), 1299 (s), 1265 (m), 1242 (s), 1206 (m), 1173 (s), 1117 (s), 1066 (m), 1031 (s), 970 (m), 911 (m), 896 (m), 824 (s), 772 (s), 746 (s), 671 (s), 649 (m), 593 (s), 563 (m), 531 (s).

5.47. 1-*tert*-Butyl-5-(2-phenylethynyl)-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (38a)

The product was isolated as a brown solid. Yield 70%, mp 136–138 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.76 (s, 9H, $(CH_3)_3$), 7.27–7.33 (m, 3H, CH_{Ar}), 7.47–7.52 (m, 2H, CH_{Ar}), 7.80 (s, 1H, CH_{Ar}), 8.11 (d, 1H, ^4J=1.9 Hz, CH_{Ar}), 8.49 (d, 1H, ^4J=2.1 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=29.1 $(CH_3)_3$, 58.8, 83.4, 86.7, 91.3, 114.3, 115.0, 120.8, 122.9 (C), 128.4, 128.5, 130.4, 131.6, 133.9 (CH), 145.9 (C), 146.9 (CH). MS (GC, 70 eV): *m*/*z* (%)=299 (M^+, 23), 243 (100). HRMS (EI): calcd for $C_{20}H_{17}N_3$ (M^+) 299.1417, found 299.14203. IR (ATR, cm^{-1}): ν=3144 (w), 2217 (m), 1610 (w), 1491 (m), 1407 (m), 1208 (s), 896 (m), 753 (s), 688 (s), 634 (m), 584 (m). The structure was independently confirmed by X-ray analysis.

5.48. 1-*tert*-Butyl-5-(2-*p*-tolylethynyl)-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (38b)

The product was isolated as an orange solid. Yield 65%, mp 185–187 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.74 (s, 9H, $(CH_3)_3$), 2.30 (s, 3H, CH_3), 7.10 (d, 2H, ^3J=7.9 Hz, CH_{Ar}), 7.38 (d, 2H, ^3J=8.1 Hz, CH_{Ar}), 7.78 (s, 1H, CH_{Ar}), 8.09 (d, 1H, ^4J=2.1 Hz, CH_{Ar}), 8.47 (d, 1H, ^4J=1.9 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=21.6, 29.1 (CH_3), 58.8, 83.4, 86.0, 91.5, 114.5, 115.1, 119.8, 120.8 (C), 129.2, 130.3, 131.5, 133.9 (CH), 138.7, 145.8 (C), 146.9 (CH). MS (GC, 70 eV): *m*/*z* (%)=313 (M^+, 31), 257 (100). HRMS (EI): calcd for $C_{21}H_{19}N_3$ (M^+) 313.15735, found 313.15732. IR (ATR, cm^{-1}): ν=3149 (w), 2219 (m), 1609 (w), 1509 (w), 1407 (s), 1361 (m), 1206 (s), 894 (m), 812 (s), 774 (m), 634 (m).

5.49. 1-*tert*-Butyl-5-(2-(4-methoxyphenyl)ethynyl)-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (38c)

The product was isolated as a white solid. Yield 65%, mp 211–213 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.75 (s, 9H, $(CH_3)_3$), 3.76 (s, 3H, OCH_3), 6.82 (d, 2H, ^3J=9 Hz, CH_{Ar}), 7.42 (d, 2H, ^3J=9 Hz, CH_{Ar}), 7.78 (s, 1H, CH_{Ar}), 8.08 (d, 1H, ^4J=2 Hz, CH_{Ar}), 8.46 (d, 1H, ^4J=2 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=29.1 $(CH_3)_3$, 55.3 (OCH_3), 58.8, 83.3, 85.4, 91.3, 114.1, 114.7 (C), 114.9 (CH), 115.1, 120.8 (C), 130.1 (CH), 133.1, 133.8 (CH), 145.7 (C), 146.8 (CH), 159.8 (C). MS (GC, 70 eV): *m*/*z* (%) 329 (M^+, 49), 273 (100), 258 (35). HRMS (EI): calcd for $C_{21}H_{19}N_3O$ (M^+) 329.15226, found 329.15221. IR (ATR, cm^{-1}): ν=3119 (w), 2212 (m), 1738 (w), 1511 (s), 1406 (w), 1242 (m), 1211 (m), 1033 (m), 821 (s), 636 (m).

5.50. 1-*tert*-Butyl-5-(2-(4-*tert*-butylphenyl)ethynyl)-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (38d)

The product was isolated as an orange solid. Yield 75%, mp 143–145 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.26 (s, 9H, $(CH_3)_3$), 1.75 (s, 9H, $(CH_3)_3$), 7.29–7.35 (m, 2H, CH_{Ar}), 7.39–7.46 (m, 2H, CH_{Ar}), 7.79 (s, 1H, CH_{Ar}), 8.09 (d, 1H, ^4J=1.9 Hz, CH_{Ar}), 8.48 (d, 1H, ^4J=1.9 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=29.1, 31.2 (CH_3), 34.8, 58.8, 83.4, 86.0, 91.5, 114.6, 115.1, 119.9, 120.8 (C), 125.5, 130.3, 131.4, 133.8 (CH), 145.8 (C), 146.9 (CH), 151.9 (C). MS (GC, 70 eV): *m*/*z* (%)=355 (M^+, 47), 299 (32), 284 (100). HRMS (EI): calcd for $C_{24}H_{25}N_3$ (M^+) 355.2043, found 355.2042. IR (ATR, cm^{-1}): ν=3143 (w), 2218 (m), 1604 (w), 1520 (w), 1405 (s), 1347 (m), 1266 (m), 1205 (s), 894 (m), 831 (s), 775 (m), 635 (m).

5.51. 1-*tert*-Butyl-5-(2-(4-butylphenyl)ethynyl)-1*H*-pyrrolo [2,3-*b*]pyridine-3-carbonitrile (38e)

The product was isolated as a white solid. Yield 60%, mp 102–104 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.89 (t, 3H, ^3J=7.2 Hz, CH_3), 1.39–1.57 (m, 4H, CH_2), 1.73 (s, 9H, $(CH_3)_3$), 2.37 (t, 2H, ^3J=6.9 Hz, CH_2), 7.76 (s, 1H, CH_{Ar}), 7.96 (d, 1H, ^4J=1.9 Hz, CH_{Ar}), 8.35 (d, 1H, ^4J=2.1 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=29.0, 13.6 (CH_3), 19.1, 22.0, 30.7 (CH_2), 58.6, 83.1, 92.4, 115.1, 115.2, 120.7 (C), 130.3, 133.6 (CH), 138.2, 145.5 (C), 146.9 (CH). MS (GC, 70 eV): *m*/*z* (%)=279 (M^+, 49), 223 (100), 208 (89), 194 (58); HRMS (EI): calcd for $C_{18}H_{21}N_3$ (M^+) 279.17300, found 279.17307; IR (ATR, cm^{-1}):

ν=2975 (w), 2225 (s), 1545 (s), 1398 (m), 1372 (m), 1268 (s), 1183 (s), 880 (m), 825 (m), 612 (s).

5.52. 5-(4-Fluorostyryl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (40a)

The product was isolated as a yellow solid. Yield 65%, mp 115–117 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.60 (s, 3H, Me), 7.19–7.30 (m, 3H, CH_{Ar}), 7.37–7.39 (m, 2H, CH_{Ar}), 7.50–7.55 (m, 2H, CH_{Ar}), 7.62–7.67 (m, 4H, CH_{Ar}), 8.26 (d, 2H, ^3J=7.6 Hz, CH_{Ar}), 8.50 (d, 1H, ^4J=1.9 Hz, CH_{Ar}), 8.81 (d, 1H, ^4J=1.9 Hz, CH_{Ar}). ^{19}F NMR (62.9 MHz, DMSO-d_6): δ=−114.1. ^{13}C NMR (62.9 MHz, DMSO-d_6): due to bed solubility it was not possible to measure. MS (GC, 70 eV): m/z (%)=329 (M^+, 100). HRMS (EI): calcd for $C_{21}H_{16}N_3F$ (M^+) 329.13228, found 329.131861. IR (ATR, cm^{-1}): ν=3035 (w), 1593 (s), 1505 (s), 1440 (m), 1413 (s), 1384 (m), 1280 (m), 1228 (s), 1158 (m), 1118 (m), 1069 (w), 1030 (w), 1012 (w), 950 (m), 900 (m), 853 (m), 771 (m), 750 (s), 687 (m), 668 (m), 588 (m).

5.53. 5-(4-Methoxystyryl)-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (40b)

The product was isolated as a yellow solid. Yield 70%, mp 131–133 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.61 (s, 3H, Me), 3.78 (s, 3H, OMe), 7.25–7.32 (m, 2H, CH_{Ar}), 6.97 (d, 2H, ^3J=8.5 Hz, CH_{Ar}), 7.22–7.40 (m, 3H, CH_{Ar}), 7.51–7.57 (m, 4H, CH_{Ar}), 8.27 (dd, 2H, ^3J=8.6 Hz, ^4J=1.1 Hz, CH_{Ar}), 8.49 (d, 1H, ^4J=2.0 Hz, CH_{Ar}), 8.81 (d, 1H, ^4J=2.0 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=12.2 (Me), 55.1 (OMe), 114.2 (CH), 117.0 (C), 119.6, 122.7, 125.2, 125.9 (CH), 127.4 (C), 127.7, 128.6, 129.1 (CH), 129.5, 139.2, 143.1 (C), 148.8 (CH), 149.4, 159.0 (C). MS (GC, 70 eV): m/z (%)=341 (M^+, 100). HRMS (EI): calcd for $C_{22}H_{19}N_3O$ (M^+) 341.15226, found 341.152368. IR (ATR, cm^{-1}): ν=1593 (m), 1559 (w), 1504 (s), 1436 (m), 1414 (m), 1385 (m), 1281 (m), 1250 (m), 1213 (m), 1176 (m), 1119 (m), 1068 (w), 1019 (m), 964 (m), 951 (s), 902 (m), 581 (s), 810 (m), 773 (s), 747 (s), 688 (s), 671 (m), 588 (s).

5.54. 3-Methyl-1-phenyl-5-((*E*)-2-(pyridin-2-yl)vinyl)-1*H*-pyrazolo[3,4-*b*]pyridine (40c)

The product was isolated as a yellow oil. Yield 71%. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.63 (s, 3H, Me), 7.25–7.32 (m, 2H, CH_{Ar}), 7.47–7.56 (m, 4H, CH_{Ar}), 7.78–7.89 (m, 2H, CH_{Ar}), 8.27 (d, 2H, ^3J=7.6 Hz, CH_{Ar}), 8.59–8.65 (m, 2H, CH_{Ar}), 8.92 (d, 1H, ^4J=1.7 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ=12.2 (Me), 117.0 (C), 119.7, 122.3, 1224, 125.3 (CH), 126.4 (C), 127.3, 128.4, 128.8, 129.1, 136.9 (CH), 139.1, 143.4, 149.5, 149.7, 154.7 (C). MS (GC, 70 eV): m/z (%)=312 (M^+, 29), 311 (100). HRMS (ESI): calcd for $C_{20}H_{17}N_4$ (M+H) 313.14477, found 313.14502. IR (ATR, cm^{-1}): ν=2919 (w), 1595 (w), 1582 (s), 1561 (m), 1504 (s), 1467 (s), 1430 (s), 1413 (s), 1384 (m), 1259 (m), 1218 (m), 1148 (m), 1115 (m), 1069 (m), 1011 (w), 964 (s), 604 (m), 849 (w), 752 (s), 739 (s), 689 (s), 670 (s), 588 (s), 568 (m).

5.55. 1-*tert*-Butyl-5-styryl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (41a)

The product was isolated as a yellow solid. Yield 72%, mp 146–148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.72 (s, 9H, $(CH_3)_3$), 7.08 (s, 2H, CH_{Ar}), 7.15–7.22 (m, 1H, CH_{Ar}), 7.24–7.32 (m, 2H, CH_{Ar}), 7.42–7.47 (m, 2H, CH_{Ar}), 7.73 (s, 1H, CH_{Ar}), 8.03 (d, 1H, ^4J=2 Hz, CH_{Ar}), 8.43 (d, 1H, ^4J=2 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=28.1 $(CH_3)_3$, 57.6, 82.2, 114.6, 120.6 (C), 123.1, 124.2, 125.5 (CH), 126.6 (C), 126.9, 127.8, 128.5, 132.6 (CH), 135.9 (C), 142.8 (CH), 145.6 (C). MS (GC, 70 eV): m/z (%)=301 (M^+, 38), 244 (100). HRMS (EI): calcd for $C_{20}H_{19}N_3$ (M^+) 301.15735, found 301.1577. IR (ATR, cm^{-1}): ν=3155 (w), 2979 (m), 2214 (m), 1520 (m), 1397 (m), 1371 (m), 1363 (m), 1204 (s), 1083 (w), 949 (s), 746 (s), 687 (s), 631 (s).

5.56. 5-(4-Methyl)-1-*tert*-butyl-1*H*-pyrrolo[2,3-b]pyridine-3-carbonitrile (41b)

The product was isolated as a yellow solid. Yield 68%, mp 179–181 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.75 (s, 9H, $(CH_3)_3$), 2.30 (s, 3H, CH_3), 7.08 (s, 2H, CH_{Ar}), 7.12 (d, 2H, ^3J=8 Hz, CH_{Ar}), 7.37 (d, 2H, ^3J=8 Hz, CH_{Ar}), 7.76 (s, 1H, CH_{Ar}), 8.07 (d, 1H, ^4J=2 Hz, CH_{Ar}), 8.46 (d, 1H, ^4J=2 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=21.3, 29.1 $(CH_3)_3$, 58.6, 83.1, 115.6, 121.6 (C), 124.0, 124.3, 126.5 (CH), 127.9 (C), 129.5, 129.6, 133.5 (CH), 134.2, 137.9 (C), 143.8 (CH), 146.5 (C). MS (GC, 70 eV): m/z (%)=315 (M^+, 64), 258 (100), 244 (45). HRMS (EI): calcd for $C_{21}H_{21}N_3$ (M^+) 315.17300, found 315.1728. IR (ATR, cm^{-1}): ν=3142 (w), 2976 (m), 2214 (m), 1522 (m), 1414 (m), 1366 (m), 1206 (s), 1089 (w), 972 (m), 854 (m), 806 (m), 744 (m), 633 (s).

5.57. 5-(4-*tert*-Butoxystyryl)-1-*tert*-butyl-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (41c)

The product was isolated as a yellow solid. Yield 69%, mp 143–145 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.31 (s, 9H, $(CH_3)_3$), 1.76 (s, 9H, $O(CH_3)_3$), 6.94 (d, 2H, ^3J=8 Hz, CH_{Ar}), 7.06 (d, 2H, ^3J=8 Hz, CH_{Ar}), 7.39 (d, 2H, ^3J=8 Hz, CH_{Ar}), 7.77 (s, 1H, CH_{Ar}), 8.07 (s, 1H, CH_{Ar}), 8.46 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=27.9 $(OCH_3)_3$, 28.1 $(CH_3)_3$, 57.5, 77.9, 82.1, 114.6, 120.6 (C), 122.9, 123.0, 123.3, 126.1 (CH), 126.9 (C), 128.1 (CH), 131.1 (C), 132.5, 142.7 (CH), 145.5, 154.4 (C). MS (GC, 70 eV): m/z (%)=373 (M^+, 6), 317 (60), 261 (100). HRMS (EI): calcd for $C_{24}H_{27}N_3O$ (M^+) 373.21486, found 373.21453. IR (ATR, cm^{-1}): ν=3134 (w), 2963 (m), 2210 (m), 1504 (m), 1406 (m), 1364 (m), 1257 (s), 893 (m), 859 (m), 796 (s), 633 (m).

Acknowledgements

Financial support by the BMBF 'REMEDIS'-project 'Höhere Lebensqualität durch neuartige Mikroimplantate' (Grant No. 03IS2081A) is gratefully acknowledged. Financial support by the DAAD (scholarships for S.M, M.V.-H., L.S., M.S.A.A. and A.G.) is acknowledged.

Supplementary data

Experimental procedures, characterization data and ^{1}H and ^{13}C NMR spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org. Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.tet.2012.11.026.

References and notes

1. (a) Silverman, R. B. *The Organic Chemistry of Drug Design, and Drug Action*, 2nd ed.; Elsevier Academic: 2004; 617, ISBN 0-12-643732-7; (b) Palmer, M.; Honek, J. F.; Dieckmann, T. *Biochemical Pharmacology*, 1st ed.; John Wiley & Sons: 2012; 428, ISBN-13: 978-0-470-17445-6.
2. Begue, J.-P.; Bonnet-Delpont, D. *Bioorganic and Medicinal Chemistry of Fluorine*, 1st ed.; John Wiley & Sons: 2008; p 366, ISBN-10: 0470278307.
3. (a) Iaroshenko, V. O.; Wang, Y.; Sevenard, D. V.; Volochnyuk, D. M. *Synthesis* **2009**, 1851–1857; (b) Iaroshenko, V. O.; Wang, Y.; Zhang, B.; Volochnyuk, D. M.; Sosnovskikh, V. Y. *Synthesis* **2009**, 2393–2402; (c) Mkrtchyan, S.; Iaroshenko, V. O.; Dudkin, S.; Gevorgyan, A.; Vilches-Herrera, M.; Ghazaryan, G.; Volochnyuk, D.; Ostrovskyi, D.; Ahmed, Z.; Villinger, A.; Sosnovskikh, V. Y.; Langer, P. *Org. Biomol. Chem.* **2010**, *8*, 5280–5284; (d) Iaroshenko, V. O.; Mkrtchyan, S.; Volochnyuk, D. M.; Langer, P.; Sosnovskikh, V. Y.; Ostrovskyi, D.; Dudkin, S.; Kotljarov, A. V.; Miliutina, M.; Savych, I.; Tolmachev, A. A. *Synthesis* **2010**, 2749–2759; (e) Ostrovskyi, D.; Iaroshenko, V. O.; Ali, I.; Mkrtchyan, S.; Villinger, A.; Tolmachev, A.; Langer, P. *Synthesis* **2011**, 133–141; (f) Iaroshenko, V. O.; Mkrtchyan, S.; Ghazaryan, G.; Hakobyan, A.; Maalik, A.; Supe, L.; Villinger, A.; Tolmachev, A.; Ostrovskyi, D.; Sosnovskikh, V. Y.; Langer, P. *Synthesis* **2011**,

469–480; (g) Ostrovskyi, D.; Iaroshenko, V. O.; Petrosyan, A.; Dudkin, S.; Ali, I.; Villinger, A.; Tolmachev, A.; Langer, P. *Synlett* **2010**, 2299–2303.
4. (a) Hocek, M.; Holy, A. *Collect. Czech. Chem. Commun.* **1999**, *64*, 229–241; (b) Hockova, D.; Hocek, M.; Dvorakova, H.; Votruba, I. *Tetrahedron* **1999**, *55*, 11109–11118; (c) Silhar, P.; Pohl, R.; Votruba, I.; Hocek, M. *Synthesis* **2006**, 1848–1852.
5. Veliz, E. A.; Stephens, O. M.; Beal, P. A. *Org. Lett.* **2001**, *3*, 2969–2972.
6. (a) Iaroshenko, V. O.; Sevenard, D. V.; Kotljarov, A. V.; Volochnyuk, D. M.; Tolmachev, A. O.; Sosnovskikh, V. Y. *Synthesis* **2009**, 731–740; (b) Iaroshenko, V. O. *Synthesis* **2009**, 3967–3974; (c) Iaroshenko, V. O.; Ostrovskyi, D.; Petrosyan, A.; Mkrtchyan, S.; Villinger, A.; Langer, P. *J. Organomet. Chem.* **2011**, 2899–2903.
7. Hussner, J.; Begunk, R.; Iaroshenko, V.; Mkrtchyan S.; Hein, M.; Supe, L.; Sternberg, K.; Langer, P.; Bien, S.; Schmitz, K.-P.; Kroemer, H. K.; Meyer zu Schwabedissen, H. 2011, Vol. 383, p 19, Deutsche Gesellschaft für Experimentelle und Klinische Pharmakologie und Toxikologie e.V., Abstracts of the 77th Annual Meeting, March 30–April 1, 2011, Frankfurt a. M., Germany Vol. 383, Title: 'Pyrazolinone-Derivatives selectively influence the proliferation of HCASMC—a new approach of preventing in-stent restenosis'.
8. (a) Evans, B. E.; Rittle, K. E.; Bock, M. G.; DiPardo, R. M.; Freidinger, R. M.; Whitter, W. L.; Lundell, G. F.; Veber, D. F.; Anderson, P. S.; Chang, R. S. L.; Lotti, V. J.; Cerino, D. J.; Chen, T. B.; Kling, P. J.; Kunkel, K. A.; Springer, J. P.; Hirshfield, J. *J. Med. Chem.* **1988**, *31*, 2235–2246; (b) Duarte, C. D.; Barreiro, E. J.; Fraga, C. A. *Mini-Rev. Med. Chem.* **2007**, *7*, 1108–1119; (c) DeSimone, R. W.; Currie, K. S.; Mitchell, S. A.; Darrow, J. W.; Pippin, D. A. *Comb. Chem. High Throughput Screening* **2004**, *7*, 473–494; (d) Costantino, L.; Barlocco, D. *Curr. Med. Chem.* **2006**, *13*, 65–85.
9. (a) Dubey, P. K.; Kumar, R. V.; Naidu, A.; Kulkarni, S. M. A. *Asian J. Chem.* **2002**, *14*, 1129–1138; (b) Lee, S. C.; Choi, J. S.; Oh, J. H.; Park, B.; Kim, Y. E.; Lee, J. H.; Shin, D.; Kim, C. M.; Hyun, Y.-L.; Lee, C. S.; Cho, J.-M.; Ro, S., WO 2007083978, 2007; *Chem. Abstr.* **2007**, *147*, 817587. (c) Kelly, M. G.; Kincaid, J.; Duncton, M.; Sahasrabudhe, K.; Janagani, S.; Upasani, R. B.; Wu, G.; Fang, Y.; Wei, Z.-L., U.S. 2,006,194,801, 2006; *Chem. Abstr.* **2006**, *145*, 889269. (d) Randolph, J. T.; Chen, H.; Degoey, D. A.; Flentge, C. A.; Flosi, W. J.; Grampovnik, D. J.; Huang, P. P.; Hutchinson, D. K.; Kempf, D. J.; Klein, L. L.; Yeung, M. C., U.S. 2,005,159,469, 2005; *Chem. Abstr.* **2005**, *143*, 641882. (e) Kivlighn, S. D.; Zingaro, G. J.; Gabel, R. A.; Broten, T. P.; Schorn, T. W.; Schaffer, L. W.; Naylor, E. M.; Chakravarty, P. K.; Patchett, A. A. *Am. J. Hypertens.* **1995**, *8*, 58–66.
10. (a) Stasch, J. P.; Becker, E. M.; Alonso-Alija, C.; Apeler, H.; Dembowsky, K.; Feurer, A.; Gerzer, R.; Minuth, T.; Perzborn, E.; Pleiss, U.; Schroder, H.; Schroeder, W.; Stahl, E.; Steinke, W.; Straub, A.; Schramm, M. *Nature* **2001**, *410*, 212–215; (b) Witherington, J.; Bordas, V.; Gaiba, A.; Garton, N. S.; Naylor, A.; Rawlings, A. D.; Slingsby, B. P.; Smith, D. G.; Takle, A. K.; Ward, R. W. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3055–3057; (c) Mantovanini, M.; Melillo, G.; Daffonchio, L. , WO 9504742, 1995; *Chem. Abstr.* **1995**, *122*, 314537. (d) Tsushima, M.; Kano, I., EP 0605836, 1994; *Chem. Abstr.* **1995**, *122*, 31198. (e) Sunagava, M.; Yamaga, H.; Sumita, I., WO 9958536, 1999; *Chem. Abstr.* **1999**, *131*, 336878. (f) Kiyoaki, K.; Tamako, T.; Hiroko, O.; Naoki, Y.; Fumiya, H.; Yasukakatsu, Y.; Fukio, K.; Motohiro, N.; Tomoya, M.; Seiji, S.; Tacashi, T.; Shigeharu, I., U.S. 5,200,407, 1991; *Chem. Abstr.* **1991**, *114*, 228904. (g) Walczynski, K.; Zuiderveld, O. P.; Timmerman, H. *Eur. J. Med. Chem.* **2005**, *40*, 15–24.
11. (a) Connolly, C. J. C.; Hamby, J. M.; Schroeder, M. C.; Barvian, M.; Lu, G. H.; Panek, R. L. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 2415–2420; (b) Thompson, A. M.; Delaney, A. M.; Hamby, J. M.; Schroeder, M. C.; Spoon, T. A.; Crean, S. M.; Showalter, H. D. H.; Denny, W. A. *J. Med. Chem.* **2005**, *48*, 4628–4653; (c) Grand, E. K.; Chase, A. J.; Heath, C.; Rahemtulla, A.; Cross, N. C. P. *Leukemia* **2004**, *18*, 962–966; (d) Trudel, S.; Ely, S.; Farooqi, Y.; Affer, M.; Robbiani, D. F.; Chesi, M.; Bergsagel, P. L. *Blood* **2004**, *103*, 3521–3528.
12. (a) Cristalli, G.; Costanzi, S.; Lambertucci, C.; Lupidi, G.; Vittori, S.; Volpini, R.; Camaioni, E. *Med. Res. Rev.* **2001**, *21*, 105–128; (b) Maydanovych, O.; Beal, P. A. *Chem. Rev.* **2006**, *106*, 3397–3411; (c) Santaniello, E.; Ciuffreda, P.; Alessandrini, L. *Synthesis* **2005**, 509–526.
13. (a) Mader, M. M.; Bartlett, P. A. *Chem. Rev.* **1997**, *97*, 1281–1301; (b) Wolfenden, R.; Snider, M. J. *Acc. Chem. Res.* **2001**, *34*, 938–945; (c) Carlow, D. C.; Carter, C. W., Jr.; Mejlhede, N.; Neuhard, J.; Wolfenden, R. *Biochemistry* **1999**, *38*, 12258–12265; (d) Erion, M. D.; Reddy, M. R. *J. Am. Chem. Soc.* **1998**, *120*, 3295–3304.
14. (a) Nair, V. IMPDH inhibitors: discovery of antiviral agents against emerging diseases In *Antiviral Drug Discovery for Emerging Diseases and Bioterrorism Threats*; Torrence, P. F., Ed.; John Wiley & Sons: Hoboken, 2005; Chapter 8, pp 179–202; (b) Shu, Q.; Nair, V. *Med. Res. Rev.* **2008**, 219–232; (c) Erion, M. D.; Reddy, M. R. *J. Am. Chem. Soc.* **1998**, *120*, 3295–3307; (d) Hedstrom, L. *Chem. Rev.* **2009**, *109*, 2903–2928.
15. (a) Novartis A.G., WO 2007/84786 A1, 2007; *Chem. Abstr.* **2007**, *147*, 189196. (b) Takeuchi, I.; Hamada, Y.; Hirota, M. *Chem. Pharm. Bull.* **1993**, *41*, 747–751.
16. (a) Rusinov, V. L.; Petrov, A. Y.; Chupakhin, O. N. *Chemistry of Heterocyclic Compounds,* New York, NY, United States, 1992, pp 1335–1339; Khimiya Geterotsiklicheskikh Soedinenii, **1992**, pp 1560–1564; (b) Qi, J.; Virga, K. G.; Lee, R. E.; Das, S.; Zhao, Y.; Yun, M. K.; White, S. W. *Bioorg. Med. Chem. Lett.* **2011**, 1298–1305; (c) Wenglowsky, S.; Ren, L.; Ahrendt, K. A.; Laird, E. R.; Buckmelter, A. J.; Dinkel, V.; Gloor, S. L.; Gross, S.; Hansen, J. D.; Newhouse, B.; Raddatz, N. J.; Rana, S.; Randolph, N.; Risom, T.; Selby, L. T.; Shrag, M.; Sturgis, H. L.; Voegtli, W. C.; Willis, B. S.; Woessner, R. D.; Wu, W.-I.; Grina, J.; Aliagas, I.; Alicke, B.; Choo, E. F.; Feng, B.; Gould, S. E.; Gunzner-Toste, J.; Hatzivassiliou, G.; Liu, B.; Malesky, K.; Mathieu, S.; Ran, Y.; Rudolph, J.; Savage, S.; Song, K.; Wen, Z.; Young, W. B. *ACS Med. Chem. Lett.* **2011**, 342–347; (d) Pfleiderer, M.; Pfleiderer, W. *Heterocycles* **1992**, *33*, 905–929.
17. Volochnyuk, D. M.; Ryabukhin, S. V.; Plaskon, A. S.; Grygorenko, O. O. *Synthesis* **2009**, 3719–3743.
18. (a) Čerňa, I.; Pohl, R.; Klepetářová, B.; Hocek, M. *J. Org. Chem.* **2008**, *73*, 9048–9054; (b) Kuchař, M.; Hocek, M.; Pohl, R.; Votruba, I.; Shih, I.; Mabery, E.; Mackman, R. *Bioorg. Med. Chem.* **2008**, *16*, 1400–1424; (c) Čerňa, I.; Pohl, R.; Klepetářová, B.; Hocek, M. *Org. Lett.* **2006**, *8*, 5389–5392; (d) Turek, P.; Novák, P.; Pohl, R.; Hocek, M.; Kotora, M. *J. Org. Chem.* **2006**, *71*, 8978–8981; (e) Hocek, M.; Šilhár, P.; Pohl, R. *Collect. Czech. Chem. Commun.* **2006**, *71*, 1484–1496; (f) Hocek, M.; Šilhár, P.; Shih, I.; Mabery, E.; Mackman, R. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5290–5293; (g) Hocek, M.; Nauš, P.; Pohl, R.; Votruba, I.; Furman, P. A.; Tharnish, P. M.; Otto, M. J. *J. Med. Chem.* **2005**, *48*, 5869–5873; (h) Turek, P.; Kotora, M.; Hocek, M.; Votruba, I. *Collect. Czech. Chem. Commun.* **2005**, *70*, 339–349; (i) Spáčilová, P.; Nauš, P.; Pohl, R.; Votruba, I.; Snášel, J.; Zábranská, H.; Pichová, I.; Ameral, R.; Birkuš, G.; Cihlář, T.; Hocek, M. *ChemMedChem* **2010**, *5*, 1386–1396.
19. (a) Fuchss, T.; Martin, T.; Boer, R.; Strub, A.; Eltze, M.; Lehner, M.; Wolf-Ruediger, U. WO 2005/30771 A1, 2005; *Chem. Abstr.* **2005**, *142*, 373838. (b) Kim, N. J.; Bae, M.-A.; Yoo, S.-E.; Kang, N.; Heo, J. N.; Yi, K. Y.; Suh, J. N.; Yi, K. Y.; Suh, J. H.; Chang, S. Y.; Hang, E. S.; Hong, J.-H. U.S. 2010/305324 A1, 2010; *Chem. Abstr.* **2010**, *54*, 10896. (c) Lundquist, IV J. T.; Bowen, S. M.; Mehlmann, J. F.; Pelletier, J. C.; Vera, M. D. U.S. 2009/69319 A1, 2009; *Chem. Abstr.* **2009**, *150*, 306649. (d) Iwata, H.; Kohara, Y.; Cao, S. X.; Guntupalli, P.; Gwaltney, S. L.; Hosfield, D. J.; Liu, Y.; Stafford, J. A.; Throop, B. U.S. 2010/69431 A1, 2010; *Chem. Abstr.* **2010**, *146*, 316915. (e) Collins, I.; Reader, J. C.; Cheung, K. M.; Matthews, T. P.; Proisy, N.; Klair, S. S. WO 2008/75007 A1, 2008; *Chem. Abstr.* **2008**, *149*, 104737. (f) Hammond, M.; Washburn, D. G.; Hoang, T. H.; Manns, S.; Frazee, J. S.; Patterson, J. R.; Thompson, S. K.; Trizna, W.; Wu, C.; Laping, N. J.; Schnackenberg, C. G.; Azzarano, L. M.; Nagilla, R.; Nord, M.; Trejo, R.; Nakamura, H.; Head, M. S.; Zhao, B.; Smallwood, A. M.; Hightower, K. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 4441–4445.
20. (a) Bilodeau, M. T.; Cunningham, A. M.; Koester, T. J.; Ciecko, P. A.; Coll, K. E.; Huckle, W. R.; Hungate, R. W.; Kendall, R. L.; MacFall, R. C.; Mao, X.; Rutledge, R. Z.; Thomas, K. A. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 2485–2488; (b) Bavetsias, V.; Sun, C.; Bouloc, N.; Reynisson, J.; Workman, P.; Linardopoulos, S.; McDonald, E. *Bioorg. Med. Chem. Lett.* **2007**, 6567–6571; (d) Graedler, U.; Fuchss, T.; Ulrich, W.-R.; Boer, R.; Strub, A.; Hesslinger, C.; Anezo, C.; Zaliani, A.; Diederichs, K. *Bioorg. Med. Chem. Lett.* **2011**, 4228–4232.
21. Kim, C. S.; Kim, Y. G.; Cho, Y. J.; Kwon, H. J.; Kim, B. O.; Kim, S. M. WO 2011/055911 A1, 2011; *Chem. Abstr.* **2011**, *154*, 576322.
22. (a) Linstroem, S.; Eriksson, M.; Grivas, S. *Acta Chem. Scand.* **1993**, *47*, 805–812; (b) Ren, H.; Knochel, P. *Chem. Commun.* **2006**, 726–728; (c) Wu, Z.; Robinson, R. G.; Fu, S.; Barnett, S. F.; Defeo-Jones, D.; Jones, R. E.; Kral, A. M.; Huber, H. E.; Kohl, N. E.; Hartman, G. D.; Bilodeau, M. T. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 2211–2214; (d) Lavecchia, G.; Berteina-Raboin, S.; Guillaumet, G. *Tetrahedron Lett.* **2004**, *45*, 6633–6636.
23. (a) Gray, N.; Chang, J. W.; Zhang, J.; Thoreen, C. C.; Kang, S.; Woo, A.; Sabatini, D. M.; Liu, Q. WO 2010/44885 A2, 2010; *Chem. Abstr.* **2010**, *152*, 501357. (b) Khan, A.; Medland, D. P.; Bhatia, G. S. EP1749829 A1, 2007; *Chem. Abstr.* **2007**, *146*, 206286.
24. (a) Varnes, J. G.; Marcus, A. P.; Mauger, R. C.; Throner, S. R.; Hoesch, V.; King, M. M.; Wang, X.; Sygowski, L. A.; Spear, N.; Gadient, R.; Brown, D. G.; Campbell, J. B. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 1402–1406; (b) Deng, X.; Lim, S. M.; Zhang, J.; Gray, N. S. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 4196–4200; (c) Hou, Z.; Suzuki, Y.; Oishi, S.; Fujii, N.; Ohno, H. *Tetrahedron* **2012**, *68*, 1695–1703; (d) Huang, W.-S.; Metcalf, C. A.; Sundaramoorthi, R.; Wang, Y.; Zou, D.; Thomas, R. M.; Zhu, X.; Cai, L.; Wen, D.; Liu, S.; R.,, J.; Qi, J.; Chen, I.; Banda, G.; Lentini, S. P.; Das, S.; Xu, Q.; Keats, J.; Wang, F.; Wardwell, S.; Ning, Y.; Snodgrass, J. T.; Broudy, M. I.; Russian, K.; Zhou, T.; Commodore, L.; Narasimhan, N. I.; Mohemmad, Q. K.; Iuliucci, J.; Rivera, V. M.; Dalgarno, D. C.; Sawyer, T. K.; Clackson, T.; Shakespeare, W. C. *J. Med. Chem.* **2010**, *53*, 4701–4719.
25. Crystallographic data (excluding structure factors) for the structure **32**, **35d**, **35e**, **38a** and **41b**, reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. 880546, 880547, 887970–887972 and 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.