Organic & Biomolecular Chemistry

ROYAL SOCIETY OF CHEMISTRY

PAPER

View Article Online
View Journal | View Issue

Cite this: *Org. Biomol. Chem.*, 2021, **19**, 1976

An isoxazole strategy for the synthesis of alkyl 5-amino-4-cyano-1*H*-pyrrole-2-carboxylates – versatile building blocks for assembling pyrrolo-fused heterocycles†

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Received 11th January 2021,
Accepted 2nd February 2021

DOI: 10.1039/d1ob00053e

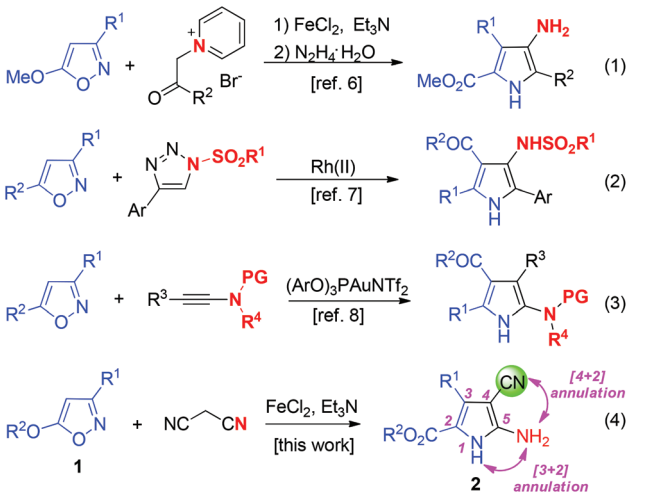
rsc.li/obc

A full atom-economical domino method has been developed for the preparation of alkyl 5-amino-4-cyano-1*H*-pyrrole-2-carboxylates by transannulation of 5-alkoxyisoxazoles with malononitrile under Fe(II) catalysis. Alkyl 5-amino-4-cyano-1*H*-pyrrole-2-carboxylates are excellent building blocks for various annulation reactions, leading to new derivatives of 1*H*-pyrrolo[1,2-*a*]imidazole and pyrrolo[2,3-*d*]pyrimidine. The DFT calculations of mechanistic details of alkyl 5-amino-4-cyano-1*H*-pyrrole-2-carboxylate formation are presented.

Introduction

The pyrrole nucleus is widely present in biologically active natural products, synthetic medicines, and modern materials.[1] Fused polyheterocycles, containing a pyrrole moiety, are of key importance for agrochemical and materials science, in particular, for bioimaging applications and chemosensing systems.[2] Accordingly, many methods have been developed for the synthesis of pyrrole derivatives.[3] One of the successful methodologies for the synthesis of fused pyrrole-containing systems is based on reactions of functionalized pyrroles as building blocks.[4] The end-product of annulation dictates which groups are needed in the pyrrole starting material. Unsubstituted pyrrole nitrogen, amino, carbonyl, and cyano groups, and double and triple bonds are most commonly used in various annulation strategies for the preparation of structurally diverse fused pyrroles.[4]

An effective approach for the assembly of the pyrrole ring is the intermolecular transannulation of isoxazoles.[5–8] It enables the introduction of various functional groups, including ester and amino groups, at different positions of the pyrrole ring. The use of principally different transannulation methods of isoxazoles makes it possible to obtain amino-substituted pyrrolecarboxylates with both 1,2- and 1,3-locations of the ester and amino groups. For example, the transannulation of 5-alkoxyisoxazoles with pyridinium ylides provided good results in the preparation of 4-aminopyrrole-2-carboxylates (Scheme 1, reaction (1)).[6] *N*-Sulfonylated 4-aminopyrrole-3-carboxylates can be prepared by transannulation of 5-alkoxyisoxazoles with 1-sulfonyl-1*H*-1,2,3-triazoles under rhodium catalysis (Scheme 1, reaction (2)).[7] The use of ynamides as transannulation agents under catalysis conditions with Au(I) complexes allows the preparation of N^1-protected 5-aminopyrrole-3-carboxylates (Scheme 1, reaction (3)).[8] The introduction of an additional electrophilic functional group, for example, a



Scheme 1 Synthesis of aminopyrroles *via* transannulation of isoxazoles.

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†Electronic supplementary information (ESI) available: Spectroscopic data for new compounds. CCDC 2053975 (**2b**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d1ob00053e

cyano group, into the target aminopyrrole-3-carboxylate is a great problem for the above-mentioned methods due to both the low availability and low efficiency of cyano-modified transannulation agents.

As part of our ongoing studies on the synthetic applications of Fe(II)-catalysed isomerization of functionalized isoxazole derivatives,[6,7b,9] we found that malononitrile can play the role of a transannulation agent in the reaction with 5-alkoxyisoxazoles **1**, enabling the introduction of a cyano group into the target aminopyrrolecarboxylate **2** (Scheme 1, reaction (4)). Synthesis of the first representatives of the alkyl 5-amino-4-cyano-1*H*-pyrrole-2-carboxylate series by the iodine-catalysed reaction of benzylidene malononitriles with methyl glycinates was reported by Wang *et al.* only in 2020.[10] Alternative methods of obtaining these attractive building blocks for heterocyclizations using less harsh conditions and less expensive catalysts are highly desired.

In this work, we describe a full atom-economical domino method for the preparation of alkyl 5-amino-4-cyano-1*H*-pyrrole-2-carboxylates *via* the $FeCl_2$-catalyzed transannulation of 5-alkoxyisoxazoles with malononitrile. The mechanistic details of the reaction are discussed using DFT calculations. The practical utility of the densely functionalized pyrrole building blocks **2** in the preparation of new 1*H*-pyrrolo[1,2-*a*]imidazole and pyrrolo[2,3-*d*]pyrimidine derivatives is also demonstrated.

Results and discussion

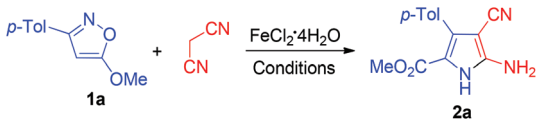
As described in a series of papers,[11] Fe(II) complexes and salts are most often used as effective catalysts for the N–O bond cleavage in 5-alkoxyisoxazoles, while Ni(II) complexes and salts are successfully applied[12] for the reactions of isoxazoles with methylene active compounds, leading to pyrroles. We started the optimization experiments with the reaction of isoxazole **1a** with malononitrile in the presence of a mixed catalyst, $FeCl_2{\cdot}4H_2O$ and $NiCl_2{\cdot}6H_2O$ (Table 1, entry 1), but failed to obtain the target product **2a**. The addition of Et_3N made it possible to obtain pyrrole **2a** using only $FeCl_2{\cdot}4H_2O$ as a catalyst in 48% yield, after chromatography of a complex reaction mixture (Table 1, entry 2).

An increase in the reaction time under the same reaction conditions led to complete resinification of the reaction mixture, whereas in ethanol, no reaction was observed (Table 1, entries 3 and 4).

1,4-Dioxane turned out to be the best solvent since the pyrrole product precipitated out in pure form when the reaction mixture was cooled to room temperature and treated with water. After some variation of the conditions (Table 1, entries 5–8), the yield was increased to 63% in the presence of only 1.5 mol% of the cheap catalyst (Table 1, entry 8). The use of THF as a solvent and DMAP or DABCO as a base proved to be ineffective (Table 1, entries 9–11).

The optimized conditions (Table 1, entry 8) were used for the preparation of previously unknown alkyl 5-amino-3-(aryl/alkyl/hetaryl)-4-cyano-1*H*-pyrrole-2-carboxylates **2a–t** (Table 2).

Table 1 Optimization of reaction conditions for the domino synthesis of pyrroles **2**[a]



1a **2a**

Entry	Catalyst (mol%)	$CH_2(CN)_2$ (equiv.)	Base (equiv.)	Solvent, *t* (°C); time (h)	Yield[a] **2a**, %
1	(10/10)[b]	1.5	no base	MeCN, rt; 48	0
2	(30)	3	Et_3N (3)	MeCN, rt; 3	48
3	(30)	3	Et_3N (3)	MeCN, rt; 24	0
4	(50)	3	Et_3N (3)	EtOH, rt; 24	0
5	(10)	3	Et_3N (3)	Dioxane, 100; 1	52
6	(1.5)	3	Et_3N (3)	Dioxane, 80; 1	52
7	(1.5)	1.5	Et_3N (1.5)	Dioxane, 80; 5	0
8	**(1.5)**	**3**	**Et_3N (1)**	**Dioxane, 80; 1**	**63**
9	(1.5)[c]	3	Et_3N (1)	Dioxane, 80; 1	58
10	(1.5)	3	Et_3N (1)	THF, 60; 2	0
11	(1.5)	3	DMAP (0.5)	Dioxane, 80; 2	0
12	(1.5)	3	DABCO (0.5)	Dioxane, 80; 2	0

[a] Isolated yield. [b] $FeCl_2{\cdot}4H_2O/NiCl_2{\cdot}6H_2O$. [c] $FeSO_4{\cdot}7H_2O$.

The reaction tolerates a variety of donor- and acceptor-substituted aryl, alkyl, and 2-thienyl groups at the 3 position (R^1) and alkoxy substituents at the 5 position (R^2O) of isoxazole **1** and affords the desired products in generally good yields (55–95%). The relatively low yields of pyrroles **2f,p** are due to the instability of isoxazoles **1f,p**, leading to resinification of the corresponding reaction mixtures and the need to isolate pyrroles **2f,p** using chromatography. Pyrroles **2a–e,g–o,q–t** simply precipitated out in pure form when the cooled reaction mixtures were diluted with water.

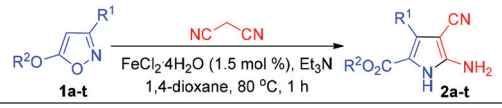
To test the ability to scale-up the synthesis of pyrroles **2**, a gram-scale reaction of isoxazole **1b** (3.10 g, 17.7 mmol) with malononitrile was carried out to give pyrrole **2b** in even higher yield (3.2 g, 75%). Note that 5-morpholino and 5-(phenylsulfanyl)-substituted 3-phenylisoxazoles were inactive in the reaction.

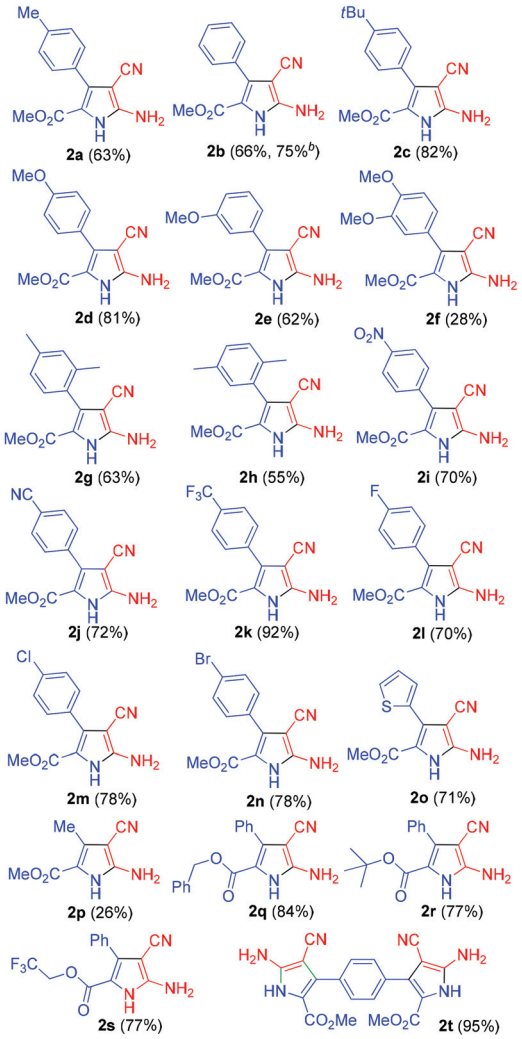
All new compounds were characterized by ^1H NMR, ^{13}C NMR and HRMS methods. Moreover, the structure of **2b** was also confirmed by single-crystal X-ray diffraction analysis. Pyrroles **2a–t** are non-hygroscopic crystalline solids, which are stable under air atmosphere for at least 2 months at rt.

In order to obtain information on the mechanism of pyrrole **3** formation, we performed several control experiments. It was found that isoxazole **1a** was intact in the absence of $FeCl_2{\cdot}4H_2O$ under standard reaction conditions, whereas azirine **3a**, isolated from the $FeCl_2{\cdot}4H_2O$-catalyzed isomerization of isoxazole **1a**, gave pyrrole **2a** in 65% yield upon reaction with malononitrile in the presence of Et_3N (Scheme 2).

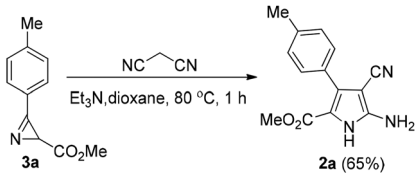
From these experiments, we can conclude that the domino process leading to pyrroles **2** involves Fe(II)-catalyzed isomerization of isoxazole **1** to azirine **3** by a mechanism which is well established,[11a,b,13] followed by a base-catalysed reaction of azirine **3** with malononitrile. A plausible mechanism for the

Table 2 Synthesis of pyrroles **2a–t** [a]



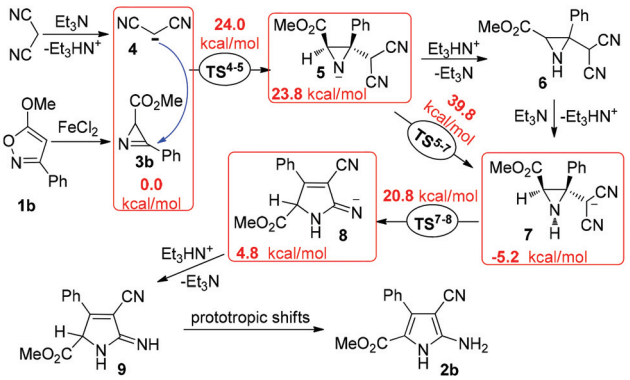


[a] Isolated yields. [b] Gram-scale.



Scheme 2 Synthesis of pyrrole **2a** from azirine **3a**.

formation of pyrroles **2**, confirmed by DFT calculations at the DFT B3LYP-D3/6-311+G(d,p) level of theory with the SMD model for 1,4-dioxane (for details of the calculations, see the ESI†), is shown in Scheme 3. Since the reaction of azirine **3** with malononitrile occurs only in the presence of an Et_3N base, it must proceed through equilibrium formation of anion



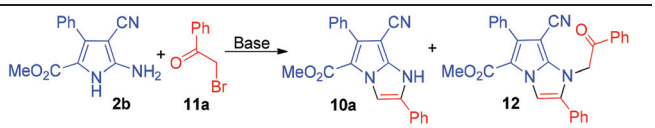
Scheme 3 Plausible reaction mechanism for the formation of pyrroles **2** (free Gibbs energy in kcal mol^{-1} (in red), 298 K, DFT B3LYP-D3/6-311+G(d,p) level with the SMD model for 1,4-dioxane).

4 from the most acidic compound in the reaction system, malononitrile. According to the calculation, the addition of anion **4** to azirine **3b**, leading to aziridinide **5**, proceeds at the reaction temperature through a surmountable energy barrier of 24.0 kcal mol^{-1} ($\mathbf{TS}^{4-5}$). In contrast, the energy of the transition state for an intramolecular H-shift in anion **5** with the formation of anion **7** ($\mathbf{TS}^{5-7}$) is too high, and therefore, the conversion of anion **5** to anion **7** most likely occurs by a stepwise protonation/deprotonation pathway *via* intermediate **6**. The energy barrier for recyclization of anion **7** to anion **8**, proceeding according to the calculation *via* the concerted aziridine ring-opening/cyclization sequence, is low enough ($\mathbf{TS}^{7-8}$, 20.8 kcal mol^{-1}) and should be easily overcome under the experimental conditions. Furthermore, anion **8** is stabilized by protonation, and subsequent prototropic shifts lead to the formation of the aromatic structure of pyrrole **2b**.

Having in our hands a set of highly functionalized pyrroles **2**, we further demonstrated their usefulness for the preparation of fused pyrrole-containing heterocycles *via* an annulation reaction. First, we have tried to prepare the pyrrolo[1,2-*a*]imidazole system using the unsubstituted pyrrole nitrogen and the amino group of pyrroles **2** for the annulation. Although some fully unsaturated 1*H*-pyrrolo[1,2-*a*]imidazoles have been found to exhibit antiproliferative[14a] and antiviral[14b] activities, not many such compounds and methods for their preparation are known.[14,15] We assumed that hitherto unknown 2-aryl-substituted 1*H*-pyrrolo[1,2-*a*]imidazoles **10** can be prepared *via* [3 + 2] annulation of pyrroles **2** with phenacyl bromides **11** as 1,2-biselectrophiles, and we began to search for the reaction conditions (Table 3).

It was found that pyrrole **2b** does not react with phenacyl bromide **11a** in the absence of a base. The reaction of **2b** with **11a** in the presence of potassium carbonate in DMF at room temperature for 3 d afforded *N*-alkylated pyrrolo[1,2-*a*]imidazole **12** in 42% yield, but no desired product **10a** was detected (Table 3, entry 2). Compound **10a** was obtained in 11% yield when heated at higher temperature for 6 h but was accompanied by a byproduct **12** (4%). The product **10a** yield

Table 3 Optimization of reaction conditions for the domino synthesis of pyrroles **2** [a]



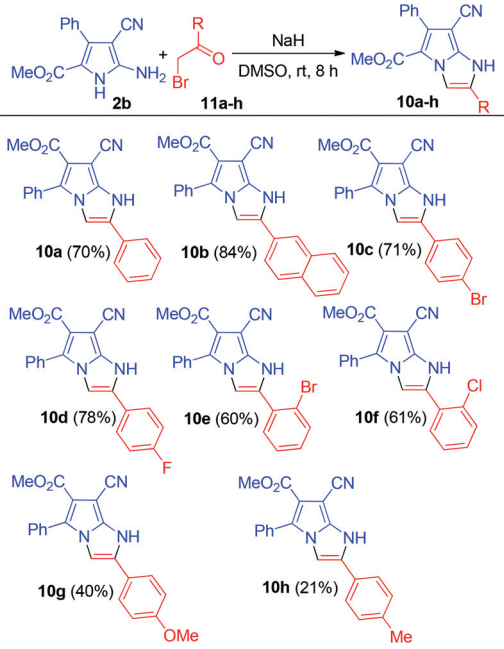
Entry	**11a** (equiv.)	Base (equiv.)	Solvent, *t* (°C); time (h)	Yield[a] **10a**, %	Yield[a] **12a**, %
1	1	No base	Me_2CO rt; 24	0	0
2	2.5	K_2CO_3, 3	DMF, rt; 72	0	42
3	2.5	K_2CO_3, 3	DMF, 100; 6	11	4
4	2.5	NaH, 3	DMF, rt; 24	37	0
5	1.5	NaH, 3	DMF, rt; 1.5	54	0
6	2.5	*t*BuOK, 5	DMF, rt; 72	0	0
7	2.5	Cs_2CO_3, 3	DMF, rt; 8	0	10
8	2.5	NaH, 3	DME, rt; 24	0	0
9	1.5	NaH, 4	HMPA, rt; 1.5	30	0
10	**1.3**	**NaH, 2**	**DMSO, rt; 8**	**70**	**0**

[a] Isolated yield.

was increased to 70% by selecting NaH as the base and DMSO as the solvent (Table 3, entries 3–9). The optimized conditions (Table 3, entry 9) were used for the preparation of pyrrolo[1,2-*a*]imidazoles **10a–h** (Table 4).

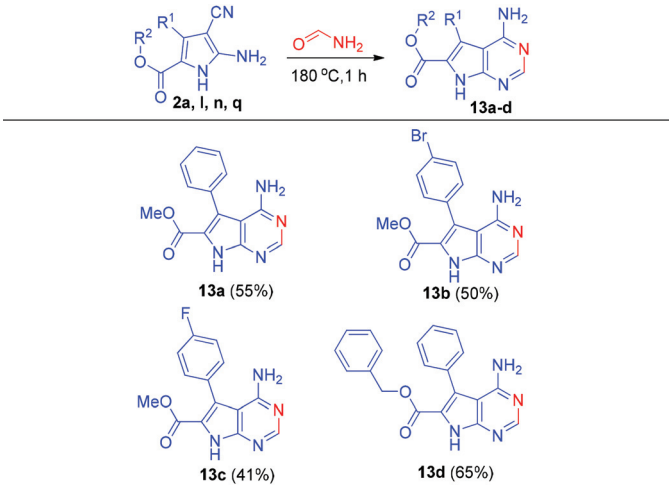
The reaction tolerates phenyl-, halogenophenyl- and naphthyl-substituted 2-bromoethanones **11**, affording pyrrolo [1,2-*a*]imidazoles **10a–f** in 60–84% yields, while the yields of Me- and MeO-substituted products **10g,h** are somewhat lower due to the fact that chromatography was used to isolate them. Note that 4-/3-nitro-, 4-hydroxy-, and 2,4,6-trimethyl-substituted phenacyl bromides were inactive in the reaction. Pyrrolo [1,2-*a*]imidazoles **10a–h** are non-hygroscopic crystalline solids, which are stable under air atmosphere for at least 2 months at rt.

Table 4 Synthesis of pyrrolo[1,2-*a*]imidazoles **10a–h** [a]



[a] Isolated yields.

Table 5 Synthesis of pyrrolo[2,3-*d*]pyrimidines **13a–d** [a]



[a] Isolated yields.

Our next goal was to use the pyrrole building block **2** to obtain the pyrrolo[2,3-*d*]pyrimidine heterocyclic system, C-analogues of purine bases that exhibit substantial bioactivity.[16] For example, we mention here only the FDA-approved drugs with a pyrrolo[2,3-*d*]pyrimidine core, such as baricitinib, ribociclib, ruxolitinib, and tofacitinib.[17] Accordingly, a plethora of methods for the synthesis of functionalized derivatives of this (5,6)-nitrogen heterocyclic system have been developed.[16,18] Unexpectedly, we found that substituted alkyl 5-aryl-7*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxylates have not been synthesized until now. We supposed that such derivatives could be prepared by [4 + 2] annulation of the amino and cyano groups of building blocks **2**, and therefore performed the reaction of pyrroles **2** with formamide. Heating pyrroles **2a, l, n,q** in formamide at 180 °C for 1 h afforded alkyl 4-amino-5-aryl-7*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxylates **13a–d** in 41–65% yields (Table 5). Chromatography was not required for the isolation of compounds **13** since they precipitated from solution upon cooling. 4-Amino-5-aryl-7*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxylates **13a–d** are non-hygroscopic crystalline solids, which are stable under air atmosphere for at least 2 months at rt.

Conclusions

Alkyl 5-amino-4-cyano-1*H*-pyrrole-2-carboxylates, highly functionalized building blocks for annulation reactions, were synthesized by the intermolecular transannulation of 5-alkoxyisoxazoles with malononitrile under Fe(II) catalysis. A plausible mechanism was proposed for the formation of pyrroles using a

full atom-economical domino method, and this was supported by DFT calculations at the DFT B3LYP-D3/6-311+G(d,p) level of theory. Alkyl 5-amino-4-cyano-1*H*-pyrrole-2-carboxylates were transformed into 1*H*-pyrrolo[1,2-*a*]imidazole derivatives by annulation with phenacyl bromides. Their reaction with formamide allowed the preparation of hitherto unknown alkyl 5-aryl-7*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxylates.

Experimental

Melting points were determined on a melting point apparatus SMP30. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on a Bruker AVANCE 400 spectrometer in $CDCl_3$. Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane. Electrospray ionization (ESI), positive mode, and mass spectroscopy were performed on a Bruker MaXis mass spectrometer, HRMS-ESI-QTOF. Thin-layer chromatography (TLC) was performed on aluminum sheets precoated with SiO_2 ALUGRAM SIL G/UV254. Column chromatography was performed on Macherey-Nagel silica gel 60M (0.04–0.063 mm). Isoxazoles **1a,b,d,g,j,m,n**,[19a] **1c**,[9d] **1e,o**,[19b] **1f**,[19d] **1h,q**,[11c] **1i,p,r**,[7b] **1l**[19c] and azirine **3a**[19c] were synthesized by the reported procedures.

General procedure for the preparation of isoxazoles 1

To a stirred suspension of NaH (60% in oil, prewashed with hexane) in dry THF (20 mL), the corresponding alcohol was added at rt, and the reaction mixture was stirred for 0.5 h. Then, 5-chloro-3-arylisoxazole (5.6 mmol) was added as a solid, and the mixture was refluxed for 1 h. After cooling to rt, the mixture was quenched with water (20 mL). The reaction mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo* to give the pure product.

3-Phenyl-5-(2,2,2-trifluoroethoxy)isoxazole (1s). Colorless solid (1.32 g, yield 97%). Mp: 100–101 °C (Et_2O–hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82–7.74 (m, 2H), 7.52–7.43 (m, 3H), 5.72 (s, 1H), 4.66 (q, J = 7.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 164.7, 130.4, 129.0, 128.9, 126.5, 122.2 (q, J = 278.1 Hz), 78.0, 67.6 (q, J = 37.6 Hz). HRMS-ESI $[M + Na]^+$ calcd for $C_{11}H_8F_3NNaO_2^+$, 266.0399; found, 266.0388.

1,4-bis (5-Methoxyisoxazol-3-yl)benzene (1t). Colorless solid (1.34 g, yield 88%). Mp: 209–210 °C (Et_2O–hexane). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.05–7.90 (m, 4H), 6.29 (s, 2H), 4.08 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.8, 162.9, 130.6, 126.7, 75.9, 59.7. HRMS-ESI $[M + H]^+$ calcd for $C_{14}H_{13}N_2O_4^+$, 273.0870; found, 273.0878.

General procedure for the preparation of pyrroles 2

A mixture of isoxazole **1** (0.6 mmol), malononitrile (119 mg, 1.8 mmol), Et_3N (61 mg, 0.6 mmol) and $FeCl_2{\cdot}4H_2O$ (1.8 mg, 0.009 mmol) in dioxane (4 mL) was refluxed for 1 h. After the reaction was completed, the resulting mixture was diluted with H_2O (20 mL) and cooled at 0 °C for 1 h. The precipitate was filtered off, washed with Et_2O and dried to give the pure product.

Methyl 5-amino-4-cyano-3-(*p*-tolyl)-1*H*-pyrrole-2-carboxylate (2a). Grey solid (96 mg, yield 63%). Mp: 209–210 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.87 (s, 1H), 7.34–7.27 (m, 2H), 7.22–7.17 (m, 2H), 6.10 (s, 2H), 3.59 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.8, 149.4, 137.0, 133.2, 129.4, 129.3, 128.2, 116.4, 109.4, 75.5, 50.7, 20.8. HRMS-ESI $[M + Na]^+$ calcd for $C_{14}H_{13}N_3NaO_2^+$, 278.0900; found, 278.0896.

Methyl 5-amino-4-cyano-3-phenyl-1*H*-pyrrole-2-carboxylate (2b). Brown solid (96 mg, yield 66%). Mp: 209–210 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.93 (s, 1H), 7.51–7.28 (m, 5H), 6.13 (s, 2H), 3.60 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.7, 149.4, 133.1, 132.3, 129.5, 127.7, 127.6, 116.3, 109.6, 75.5, 50.8. HRMS-ESI $[M + Na]^+$ calcd for $C_{13}H_{11}N_3NaO_2^+$, 264.0743; found, 264.0742.

Methyl 5-amino-3-(4-(*tert*-butyl)phenyl)-4-cyano-1*H*-pyrrole-2-carboxylate (2c). Grey solid (146 mg, yield 82%). Mp: 253–255 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.88 (s, 1H), 7.50–7.30 (m, 4H), 6.11 (s, 2H), 3.61 (s, 3H), 1.31 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.6, 150.1, 149.4, 133.1, 129.2, 124.4, 116.5, 109.3, 75.4, 50.7, 34.3, 31.1 (3C). HRMS-ESI $[M + Na]^+$ calcd for $C_{17}H_{19}N_3NaO_2^+$, 320.1369; found, 320.1365.

Methyl 5-amino-4-cyano-3-(4-methoxyphenyl)-1*H*-pyrrole-2-carboxylate (2d). Beige solid (132 mg, yield 81%). Mp: 242–243 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.84 (s, 1H), 7.55–7.23 (m, 2H), 7.09–6.84 (m, 2H), 6.10 (s, 2H), 3.79 (s, 3H), 3.60 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.8, 158.9, 149.3, 133.1, 130.8, 124.4, 116.5, 113.1, 109.2, 75.5, 55.1, 50.7. HRMS-ESI $[M + Na]^+$ calcd for $C_{14}H_{13}N_3NaO_3^+$, 294.0849; found, 294.0838.

Methyl 5-amino-4-cyano-3-(3-methoxyphenyl)-1*H*-pyrrole-2-carboxylate (2e). Brown solid (101 mg, yield 62%). Mp: 208–209 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.93 (s, 1H), 7.40–7.24 (m, 1H), 7.12–6.84 (m, 3H), 6.12 (s, 2H), 3.77 (s, 3H), 3.61 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.7, 158.5, 149.4, 133.5, 132.8, 128.6, 121.9, 116.3, 115.2, 113.4, 109.6, 75.5, 55.0, 50.8. HRMS-ESI $[M + Na]^+$ calcd for $C_{14}H_{13}N_3NaO_3^+$, 294.0849; found, 294.0847.

Methyl 5-amino-4-cyano-3-(3,4-dimethoxyphenyl)-1*H*-pyrrole-2-carboxylate (2f). Beige solid (51 mg, yield 28%). Mp: 219–220 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.84 (s, 1H), 7.42–6.74 (m, 3H), 6.10 (s, 2H), 3.78 (s, 6H), 3.63 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.9, 149.4, 148.5, 147.7, 133.1, 124.6, 121.9, 116.6, 113.9, 111.0, 109.3, 75.5, 55.4, 50.7. HRMS-ESI $[M + Na]^+$ calcd for $C_{15}H_{15}N_3NaO_4^+$, 324.0955; found, 324.0955.

Methyl 5-amino-4-cyano-3-(2,4-dimethylphenyl)-1*H*-pyrrole-2-carboxylate (2g). Brown solid (102 mg, yield 63%). Mp: 219–220 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.90 (s, 1H), 7.08–7.04 (m, 1H), 7.01–6.97 (m, 2H), 6.10 (s, 2H), 3.53 (s, 3H), 2.30 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.6, 149.1, 136.7, 135.9, 132.8, 130.2, 129.8, 125.7, 116.2, 110.4, 76.4, 50.7, 20.7, 19.4. HRMS-ESI $[M + H]^+$ calcd for $C_{15}H_{16}N_3O_2^+$, 270.1237; found, 270.1236.

Methyl 5-amino-4-cyano-3-(2,5-dimethylphenyl)-1*H*-pyrrole-2-carboxylate (2h). Brown solid (89 mg, yield 55%). Mp: 228–229 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.91 (s,

1H), 7.17–7.09 (m, 1H), 7.09–7.01 (m, 2H), 6.96–6.86 (m, 1H), 6.11 (s, 2H), 3.53 (s, 3H), 2.27 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.5, 149.1, 133.8, 133.0, 132.9, 132.5, 130.3, 129.3, 128.3, 116.2, 110.4, 76.3, 50.7, 20.5, 19.0. HRMS-ESI $[M + H]^+$ calcd for $C_{15}H_{16}N_3O_2^+$, 270.1237; found, 270.1237.

Methyl 5-amino-4-cyano-3-(4-nitrophenyl)-1*H*-pyrrole-2-carboxylate (2i). Brown solid (120 mg, yield 70%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.20 (s, 1H), 8.38–8.09 (m, 2H), 7.83–7.53 (m, 2H), 6.25 (s, 2H), 3.62 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.4, 149.7, 146.7, 139.3, 130.9, 130.3, 122.8, 115.9, 110.5, 75.1, 51.0. HRMS-ESI $[M + Na]^+$ calcd for $C_{13}H_{10}N_4NaO_4^+$, 309.0594; found, 309.0591.

Methyl 5-amino-4-cyano-3-(4-cyanophenyl)-1*H*-pyrrole-2-carboxylate (2j). Grey solid (115 mg, yield 72%). Mp 264–265 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.15 (s, 1H), 8.00–7.76 (m, 2H), 7.75–7.50 (m, 2H), 6.22 (s, 2H), 3.61 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.5, 149.6, 137.3, 131.6, 130.8, 130.6, 118.8, 115.9, 110.3, 75.1. HRMS-ESI $[M + Na]^+$ calcd for $C_{14}H_{10}N_4NaO_2^+$, 289.0696; found, 289.0693.

Methyl 5-amino-4-cyano-3-(4-(trifluoromethyl)phenyl)-1*H*-pyrrole-2-carboxylate (2k). Grey solid (171 mg, yield 92%). Mp: 260–262 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.11 (s, 1H), 8.06–7.41 (m, 4H), 6.21 (s, 2H), 3.62 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.5, 149.6, 136.6, 131.2, 130.4, 128.0 (q, J = 31.8 Hz), 124.5 (q, J = 3.8 Hz), 124.3 (q, J = 271.9 Hz), 116.0, 110.2, 75.3, 50.9. HRMS-ESI $[M + Na]^+$ calcd for $C_{14}H_{10}F_3N_3NaO_2^+$, 332.0617; found, 332.0614.

Methyl 5-amino-4-cyano-3-(4-fluorophenyl)-1*H*-pyrrole-2-carboxylate (2l). Grey solid (109 mg, yield 70%). Mp: 240–241 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.96 (s, 1H), 7.55–7.40 (m, 2H), 7.30–7.15 (m, 2H), 6.15 (s, 2H), 3.60 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.7 (d, J = 244.9 Hz), 159.6, 149.4, 132.0, 131.6 (d, J = 8.3 Hz), 128.6 (d, J = 3.5 Hz), 116.3, 114.5 (d, J = 21.6 Hz), 109.7, 75.5, 50.8. HRMS-ESI $[M + Na]^+$ calcd for $C_{13}H_{10}FN_3NaO_2^+$, 282.0649; found, 282.0649.

Methyl 5-amino-3-(4-chlorophenyl)-4-cyano-1*H*-pyrrole-2-carboxylate (2m). Brown solid (109 mg, yield 66%). Mp: 256–257 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.01 (s, 1H), 7.62–7.29 (m, 4H), 6.17 (s, 2H), 3.62 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.6, 149.4, 132.4, 131.6, 131.4, 131.1, 127.7, 116.2, 109.8, 75.3, 50.8. HRMS-ESI $[M + Na]^+$ calcd for $C_{13}H_{10}{}^{35}ClN_3NaO_2^+$, 298.0354; found, 298.0358.

Methyl 5-amino-3-(4-bromophenyl)-4-cyano-1*H*-pyrrole-2-carboxylate (2n). Brown solid (150 mg, yield 78%). Mp: 268–269 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.01 (s, 1H), 7.77–7.50 (m, 2H), 7.50–7.23 (m, 2H), 6.17 (s, 2H), 3.61 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.6, 149.4, 131.63, 131.59, 131.5, 130.6, 121.1, 116.1, 109.7, 75.2, 50.8. HRMS-ESI $[M + Na]^+$ calcd for $C_{13}H_{10}{}^{81}BrN_3NaO_2^+$, 343.9829; found, 343.9828.

Methyl 5-amino-4-cyano-3-(thiophen-2-yl)-1*H*-pyrrole-2-carboxylate (2o). Grey solid (105 mg, yield 71%). Mp: 237–238 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.99 (s, 1H), 7.68–7.54 (m, 1H), 7.46–7.35 (m, 1H), 7.19–7.05 (m, 1H), 6.16 (s, 2H), 3.68 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.5, 149.7, 132.5, 128.3, 126.8, 126.7, 125.0, 116.4, 109.7, 75.2, 50.9. HRMS-ESI $[M + Na]^+$ calcd for $C_{11}H_9N_3NaO_2S^+$, 270.0308; found, 270.0307.

Methyl 5-amino-4-cyano-3-methyl-1*H*-pyrrole-2-carboxylate (2p). Colorless solid (28 mg, yield 26%). Mp: 209–210 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.57 (s, 1H), 6.02 (s, 2H), 3.70 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.2, 148.8, 130.3, 116.2, 110.3, 76.1, 50.7, 11.2. HRMS-ESI $[M + Na]^+$ calcd for $C_8H_9N_3NaO_2^+$, 202.0587; found, 202.0597.

Benzyl 5-amino-4-cyano-3-phenyl-1*H*-pyrrole-2-carboxylate (2q). Beige solid (160 mg, yield 84%). Mp: 116–117 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.89 (s, 1H), 7.43–7.39 (m, 2H), 7.37–7.27 (m, 6H), 7.23–7.17 (m, 2H), 6.18 (s, 2H), 5.12 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.1, 149.5, 136.1, 133.6, 132.3, 129.6, 128.2, 127.8, 127.64, 127.61, 116.3, 109.6, 75.8, 64.9. HRMS-ESI $[M + Na]^+$ calcd for $C_{19}H_{15}N_3NaO_2^+$, 340.1056; found, 340.1057.

***tert*-Butyl 5-amino-4-cyano-3-phenyl-1*H*-pyrrole-2-carboxylate (2r).** Brown solid (131 mg, yield 77%). Mp: 115–117 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.65 (s, 1H), 7.56–7.19 (m, 5H), 6.08 (s, 2H), 1.30 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.1, 149.1, 132.7, 132.0, 129.7, 127.5, 127.4, 116.5, 111.4, 79.8, 75.2, 27.8. HRMS-ESI $[M + Na]^+$ calcd for $C_{16}H_{17}N_3NaO_2^+$, 306.1213; found, 306.1211.

2,2,2-Trifluoroethyl 5-amino-4-cyano-3-phenyl-1*H*-pyrrole-2-carboxylate (2s). Grey solid (143 mg, yield 77%). Mp: 232–233 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.03 (s, 1H), 7.54–7.26 (m, 5H), 6.31 (s, 2H), 4.71 (q, J = 9.1 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.4, 150.0, 135.4, 131.8, 129.5, 127.9, 127.6, 123.5 (q, J = 278.8 Hz), 108.0, 76.5, 59.0 (q, J = 35.1 Hz). HRMS-ESI $[M + Na]^+$ calcd for $C_{14}H_{10}F_3N_3NaO_2^+$, 332.0617; found, 332.0621.

Dimethyl 3,3′-(1,4-phenylene)bis (5-amino-4-cyano-1*H*-pyrrole-2-carboxylate) (2t). Brown solid (230 mg, yield 95%). Mp: >400 °C (Et_2O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.96 (s, 2H), 7.78–7.21 (m, 4H), 6.15 (s, 4H), 3.63 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.7, 149.5, 132.6, 131.5, 128.8, 116.4, 109.7, 75.3, 50.8. HRMS-ESI $[M + Na]^+$ calcd for $C_{20}H_{16}N_6NaO_4^+$, 427.1125; found, 427.1114.

General procedure for the preparation of pyrrolo[1,2-*a*] imidazoles 10

To a stirred suspension of NaH (in 60% mineral oil, 40 mg, 1 mmol, prewashed with hexane) in anhydrous DMSO (3 mL) was added pyrrole **3b** (120 mg, 0.5 mmol) at ambient temperature, and the reaction mixture was stirred for 1 h. Then, the appropriate 2-bromo-1-phenylethanone (0.65 mmol) was added, and the reaction mixture was stirred for other 8 h. Then, the reaction mixture was diluted with H_2O (15 mL) and the resulting precipitate was collected and recrystallized from a Et_2O–acetone (20 : 1) mixture. For **4g** and **4h**, the reaction mixture was extracted with EtOAc (5 × 15 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc–hexane from 1 : 10 to 1 : 1).

Methyl 7-cyano-2,6-diphenyl-1*H*-pyrrolo[1,2-*a*]imidazole-5-carboxylate (10a). Beige solid (119 mg, yield 70%). Mp: 278–280 °C (Et_2O–acetone). ^1H NMR (400 MHz, DMSO-d_6) δ 13.13 (s, 1H), 8.28 (d, J^4 = 1.6 Hz, 1H), 7.92–7.85 (m, 2H), 7.53–7.40 (m, 8H), 3.70 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.9, 139.9, 138.7, 133.0, 132.3, 130.0, 129.0, 128.5, 128.4, 128.1, 127.7, 124.9, 116.02, 107.0, 105.1, 68.2, 50.9. HRMS-ESI $[M - H]^-$ calcd for $C_{21}H_{14}N_3O_2^-$, 340.1092; found, 340.1073.

Methyl 7-cyano-2-(naphthalen-2-yl)-6-phenyl-1*H*-pyrrolo[1,2-*a*]imidazole-5-carboxylate (10b). Beige solid (164 mg, yield 84%). Mp: 309–310 °C (Et_2O–acetone). ^1H NMR (400 MHz, DMSO-d_6) δ 13.25 (s, 1H), 8.42–8.35 (m, 2H), 8.02–7.98 (m, 2H), 7.96–7.90 (m, 2H), 7.60–7.52 (m, 4H), 7.49–7.41 (m, 3H), 3.71 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.9, 140.1, 138.7, 133.0, 132.9, 132.6, 132.3, 130.0, 128.6, 128.1, 127.9, 127.7, 126.9, 126.5, 126.0, 123.3, 123.0, 116.0, 107.6, 105.2, 68.2, 50.9. HRMS-ESI $[M + H]^+$ calcd for $C_{25}H_{18}N_3O_2^+$, 392.1394; found, 392.1394.

Methyl 2-(4-bromophenyl)-7-cyano-6-phenyl-1*H*-pyrrolo[1,2-*a*]imidazole-5-carboxylate (10c). Brown solid (147 mg, yield 70%). Mp: 324–325 °C (Et_2O–acetone). ^1H NMR (400 MHz, DMSO-d_6) δ 13.16 (s, 1H), 8.32 (s, 1H), 7.88–7.79 (m, 2H), 7.73–7.65 (m, 2H), 7.54–7.48 (m, 2H), 7.48–7.40 (m, 3H), 3.69 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.8, 140.0, 138.8, 132.3, 132.0, 131.9, 129.9, 128.1, 127.8, 127.7, 126.9, 121.4, 115.9, 107.6, 105.1, 68.1, 50.9. HRMS-ESI $- H]^-$ calcd for $C_{21}H_{13}{}^{81}BrN_3O_2^-$, 420.0176; found, 420.0168.

Methyl 7-cyano-2-(4-fluorophenyl)-6-phenyl-1*H*-pyrrolo[1,2-*a*]imidazole-5-carboxylate (10d). Grey solid (140 mg, yield 78%). Mp: 280–282 °C (Et_2O–acetone). ^1H NMR (400 MHz, DMSO-d_6) δ: 13.16 (s, 1H), 8.32 (s, 1H), 7.88–7.79 (m, 2H), 7.73–7.65 (m, 2H), 7.54–7.48 (m, 2H), 7.48–7.40 (m, 3H), 3.69 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.0 (d, J = 246.2 Hz), 159.9, 139.3 (d, J = 129.0 Hz), 132.3, 132.2, 130.0, 128.1, 127.7, 127.2 (d, J = 8.4 Hz), 125.2 (d, J = 3.0 Hz), 116.1, 116.0, 115.9, 107.0, 105.1, 68.1, 50.9. HRMS-ESI $[M + H]^+$ calcd for $C_{21}H_{15}FN_3O_2^+$, 360.1143; found, 360.1160.

Methyl 2-(2-bromophenyl)-7-cyano-6-phenyl-1*H*-pyrrolo[1,2-*a*]imidazole-5-carboxylate (10e). Brown solid (147 mg, yield 70%). Mp: 238–239 °C (Et_2O–acetone). ^1H NMR (400 MHz, DMSO-d_6) δ 13.13 (s, 1H), 8.13 (s, 1H), 7.87–7.80 (m, 1H), 7.74–7.69 (m, 1H), 7.58–7.51 (m, 3H), 7.49–7.40 (m, 4H), 3.67 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.0, 139.3, 138.8, 133.6, 132.3, 131.6, 130.9, 130.8, 129.9, 129.3, 128.1, 128.0, 127.7, 121.8, 115.9, 109.7, 104.9, 68.0, 50.9. HRMS-ESI $[M + Na]^+$ calcd for $C_{21}H_{14}{}^{79}BrN_3NaO_2^+$, 442.0162; found, 442.0167.

Methyl 2-(2-chlorophenyl)-7-cyano-6-phenyl-1*H*-pyrrolo[1,2-*a*]imidazole-5-carboxylate (10f). Colorless solid (115 mg, yield 61%). Mp: 253–254 °C (Et_2O–acetone). ^1H NMR (400 MHz, DMSO-d_6) δ 13.15 (s, 1H), 8.17 (s, 1H), 7.81–7.76 (m, 1H), 7.68–7.63 (m, 1H), 7.54–7.42 (m, 7H) 3.67 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.0, 139.4, 138.9, 132.3, 131.1, 130.5, 130.5, 130.3, 129.9, 129.4, 128.2, 127.7, 127.6, 127.1, 115.9, 110.0, 104.9, 68.1, 50.9. HRMS-ESI $[M + Na]^+$ calcd for $C_{21}H_{14}{}^{35}ClN_3NaO_2^+$, 398.0667; found, 398.0657.

Methyl 7-cyano-2-(4-methoxyphenyl)-6-phenyl-1*H*-pyrrolo[1,2-*a*]imidazole-5-carboxylate (10g). Colorless solid (74 mg, yield 40%). Mp: 257–258 °C (Et_2O). ^1H NMR (400 MHz, DMSO-d_6) δ 12.97 (s, 1H), 8.12 (s, 1H), 7.81–7.76 (m, 2H), 7.53–7.49 (m, 2H), 7.46–7.40 (m, 3H), 7.08–7.02 (m, 2H), 3.81 (s, 3H), 3.69 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.9, 159.4, 139.7, 138.3, 133.1, 132.4, 130.0, 128.0, 127.6, 126.4, 121.0, 116.1, 114.4, 105.8, 105.0, 68.1, 55.2, 50.8. HRMS-ESI $[M + Na]^+$ calcd for $C_{22}H_{17}N_3NaO_3^+$, 394.1162; found, 394.1163.

Methyl 7-cyano-6-phenyl-2-(*p*-tolyl)-1*H*-pyrrolo[1,2-*a*]imidazole-5-carboxylate (10h). Colorless solid (37 mg, yield 21%). Mp: 271–272 °C (Et_2O). ^1H NMR (400 MHz, DMSO-d_6) δ 13.06 (s, 1H), 8.22 (s, 1H), 7.80–7.73 (m, 2H), 7.54–7.41 (m, 5H), 7.34–7.28 (m, 2H), 3.70 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.9, 139.8, 138.5, 138.0, 133.1, 132.4, 130.0, 129.5, 128.1, 127.7, 125.7, 124.9, 116.0, 106.5, 105.0, 68.1, 50.8, 20.79. HRMS-ESI $[M + Na]^+$ calcd for $C_{22}H_{17}N_3NaO_2^+$, 378.1213; found, 378.1215.

Procedure for the preparation of pyrroloimidazole 12

A suspension of pyrrole **2b** (120 mg, 0.5 mmol), 2-bromo-1-phenylethanone (249 mg, 1.25 mmol) and K_2CO_3 (207 mg, 1.5 mmol) in DMF (3 mL) was stirred for 72 h at ambient temperature. The reaction mixture was concentrated *in vacuo*, and the residue was purified by column chromatography on silica gel (EtOAc–hexane from 1 : 20 to 1 : 3) to give methyl 7-cyano-1-(2-oxo-2-phenylethyl)-2,6-diphenyl-1*H*-pyrrolo[1,2-*a*]imidazole-5-carboxylate **12**. Colorless solid (96 mg, yield 42%). Mp: 180–181 °C (Et_2O). ^1H NMR (400 MHz, $CDCl_3$) δ 7.98–7.93 (m, 2H), 7.91 (s, 1H), 7.67–7.62 (m, 1H), 7.61–7.56 (m, 2H), 7.53–7.41 (m, 10H), 5.56 (s, 2H), 3.79 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 191.7, 161.1, 140.9, 139.5, 135.3, 134.5, 133.7, 132.3, 130.2, 129.8, 129.4, 129.2, 129.1, 128.3, 128.2, 127.8, 127.3, 115.8, 109.4, 106.5, 69.3, 51.1, 50.4. HRMS-ESI $[M + Na]^+$ calcd for $C_{29}H_{21}N_3NaO_3^+$, 482.1475; found, 482.1473.

General procedure for the preparation of pyrrolopyrimidine 13

A solution of pyrrole **2** (1 mmol) in formamide (5 mL) was heated at 180 °C for 1 h. After the reaction was completed, the resulting mixture was cooled to rt. The precipitate formed was filtered off, washed with formamide (3 mL) and then recrystallized from the DMSO–H_2O mixture (1 : 2).

Methyl 4-amino-5-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxylate (13a). Grey solid (148 mg, yield 55%). Mp: 285–286 °C (dec.). ^1H NMR (400 MHz, DMSO-d_6) δ 12.48 (s, 1H), 8.20 (s, 1H), 7.53–7.39 (m, 5H), 3.64 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.9, 158.5, 154.7, 150.2, 133.6, 129.9, 128.2, 127.9, 122.3, 119.9, 102.1, 51.4. HRMS-ESI $[M + H]^+$ calcd for $C_{14}H_{13}N_4O_2^+$, 269.1033; found, 269.1031.

Methyl 4-amino-5-(4-bromophenyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxylate (13b). Grey solid (174 mg, yield 50%). Mp: 340–343 °C (dec.). ^1H NMR (400 MHz, DMSO-d_6) δ 11.01 (s, 1H), 7.77–7.50 (m, 2H), 7.50–7.23 (m, 2H), 6.17 (s, 2H), 3.61 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.8, 158.5, 154.7, 150.3, 132.7, 132.1, 131.1, 121.3, 121.0, 120.1, 101.8, 51.5.

HRMS-ESI $[M + H]^+$ calcd for $C_{14}H_{12}{}^{79}BrN_4NaO_2{}^+$, 347.0138; found, 347.0136.

Methyl 4-amino-5-(4-fluorophenyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxylate (13c). Grey solid (117 mg, yield 41%). Mp: 320–322 °C (dec.). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.48 (s, 1H), 8.19 (s, 1H), 7.50–7.43 (m, 2H), 7.33–7.25 (m, 2H), 3.65 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.8 (d, J = 244.3 Hz), 160.8, 158.5, 154.7, 150.2, 132.03 (d, J = 8.3 Hz), 129.7 (d, J = 3.1 Hz), 121.3, 120.1, 115.1 (d, J = 21.7 Hz), 102.0, 51.5. HRMS-ESI $[M + H]^+$ calcd for $C_{14}H_{12}FN_4O_2{}^+$, 287.0939; found, 287.0939.

Benzyl 4-amino-5-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidine-6-carboxylate (13d). Grey solid (224 mg, yield 65%). Mp: 320–322 °C (dec.). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.59 (s, 1H), 8.21 (s, 1H), 7.53–7.38 (m, 5H), 7.32–7.19 (m, 3H), 7.16–7.00 (m, 2H), 5.16 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.5, 158.6, 154.8, 150.3, 135.6, 133.8, 129.9, 128.3, 128.1, 127.9, 127.7, 127.3, 122.5, 120.0, 102.3, 65.6. HRMS-ESI $[M + H]^+$ calcd for $C_{20}H_{17}N_4O_2{}^+$, 345.1346; found, 345.1334.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We gratefully acknowledge the financial support from the Russian Science Foundation (Grant no. 19-13-00039). This research used resources of the Magnetic Resonance Research Centre, Chemical Analysis, Materials Research Centre, Centre for X-ray Diffraction Studies, and the Computer Centre of the Science Park of Saint Petersburg State University.

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