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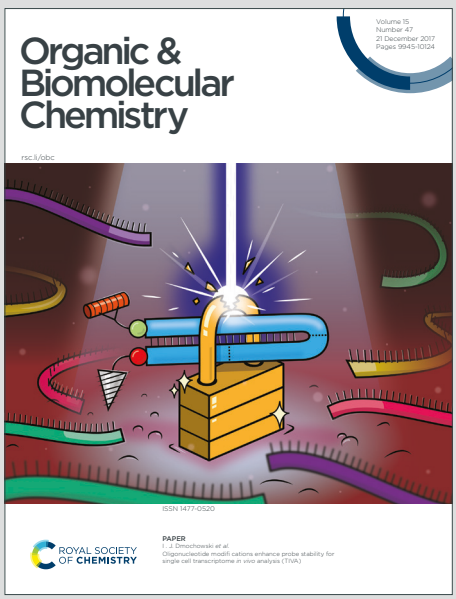

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ARTICLE

Access to 2-Pyridinylamide and Imidazopyridine from 2-Fluoropyridine and Amidine Hydrochloride

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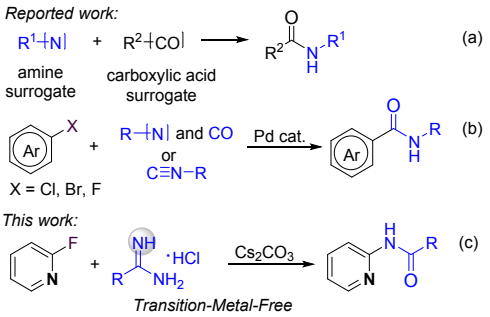
Under catalyst-free conditions, an efficient method to synthesize 2-pyridinylamides has been developed, and the protocol uses inexpensive and readily available 2-fluoropyridine and amidine derivatives as the starting materials. Simultaneously, the Copper-catalysed approach to imidazopyridine derivatives has been established with high chemoselectivity and regiospecificity. The results suggest that the nitrogen-heterocycles containing iodide substituents can also be compatible for the reaction *via* the cascade Ullmann-type coupling, and the nucleophilic substitution reaction provides the target products in a one-pot manner.

Introduction

Amide derivatives are important building blocks found in large number of natural products because of their recognized biological and therapeutic activities. The development of simple and efficient protocols to synthesize amides is an important task in organic synthesis. Amides are the core structure of many drugs such as lidocaine,[1] roflumilast[2] and atorvastatin.[3] Amide bonds are also essential for biological structure because amide bonds are the basis for amino acids to form proteins.[4] The simplest and cheapest method to prepare amides is probably the direct condensation of carboxylic acids and amines. However, it is well known that this amidation process requires severe harsh conditions to prevent the formation of low-activity carboxylate-ammonium salts.[5] Therefore, the more efficient method to synthesize amides is based on the nucleophilic substitution of amines with activated carboxylic acid derivatives such as acid chlorides and carboxylic anhydrides (Scheme 1a). [6] Although this strategy has successfully synthesized amides, the activation of carboxylic acids often requires additional synthetic steps, and the use of some toxic reagents and the byproducts are stoichiometrically generated. In contrast, when carboxylic acid becomes an ester or equivalent, the carboxylic group becomes more electrophilic and will certainly stimulate the amidation reaction. Under certain catalytic conditions, alcohols,[7] aldehydes,[8] ketones,[9] nitriles,[10] and thioacids[11] can be used as equivalents of unactivated esters to participate in the synthesis of amides. The preparation of amides *via* the combination of halogenated aromatics, amines, and CO in the metal-transition catalysis is an effective synthesis strategy (Scheme 1b).[12] Unfortunately, although many synthetic methods have been developed, amines with a strongly electron-withdrawing group or a larger steric hindrance are not suitable to synthesize amide compounds. We also used Pd-catalysed halogenated aromatics and isonitriles in the coupling reaction to prepare amide compounds.[13] Recently, the metal-free catalysed synthesis of pyridyl pyridones[14] and 2-aminopyridines[15] through the hydroxylation and arylation reaction of 2-fluoropyridines was reported by our group. With an increased interest in the potential reactivity of 2-halopyridines, we aimed to develop more 2-halopyridine selective functionalization reactions under metal-free catalysed conditions. Herein, we disclose a controlled nucleophilic substitution and selective amination of amidine hydrochloride with 2-fluoropyridine to synthesize amides and imidazopyridine derivatives.

Scheme 1. Major pathways to synthesize amides



Results and discussion

For optimize the reaction conditions, 2-fluoro-3-iodopyridine **1a**, acetamidine hydrochloride **2a** and H_2O (3.0 equiv.) were selected as the model system. First, dimethyl sulfoxide (DMSO) was selected as the solvent, and ^{t}BuOLi was selected as the base to optimize the reaction conditions. After 18 hours of reaction at 90 °C, we found that this reaction can give the designed product **3a** in 12% yield

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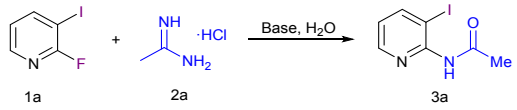
(Table 1, entry 1). Next, we screened the base and found that CsF and KF exhibited no apparent promotion effect (Table 1, entries 2-3). However, moderate yields were obtained when NaOH or ^{t}BuONa were used (Table 1, entries 4-5). In the presence of H_2O, strong base such as NaOH or ^{t}BuONa provides more active -OH groups for nucleophilic substitution and hydrolysis of 2-Pyridinylamide **3a** and give 2-aminopyridine derivatives.[15] Next, we further screened the weak base and found that K_2CO_3 exhibited a better effect (Table 1, entry 6). Surprisingly, when Cs_2CO_3 was used, the yield can be significantly improved to 93% (Table 1, entry 7). The solvent screening shows that DMSO is the optimal solvent (Table 1, entries 8-10); when NMP, DMF and MeCN were used as the solvent, a lower yield was detected. We found that when the temperature was increased or decreased, the yield of this reaction decreased (Table 1, entries 11-12). By decreasing the amount of acetamidine hydrochloride and Cs_2CO_3, the yield was reduced to 87%, 85% and 37%, respectively (Table 1, entries 13-15). Under N_2 and anhydrous condition, the yield of the nucleophilic substitution reaction is significantly affected (Table 1, entry 16) possibly because the progress of the nucleophilic substitution and hydrolysis reaction is hindered. Furthermore, shorten the reaction time, the yield of the amidation reaction is slightly affected (Table 1, entry 17).

Table 1. Optimization of the Reaction Conditions[a]

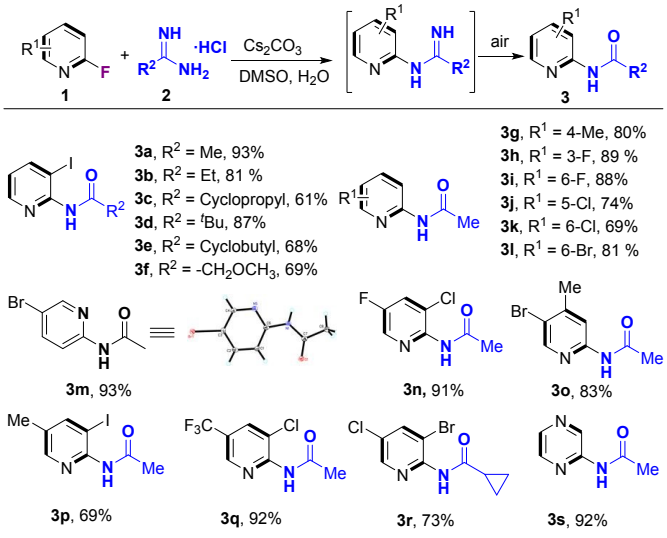


Entry	Solve	Base (mmol)	T/°C	yield/%[b]
1	DMSO	^{t}BuOLi (3)	90	12
2	DMSO	CsF (3)	90	<5
3	DMSO	KF (3)	90	<5
4	DMSO	NaOH (3)	90	37
5	DMSO	^{t}BuONa (3)	90	47
6	DMSO	K_2CO_3 (3)	90	85
7	**DMSO**	**Cs_2CO_3** (3)	**90**	**93**
8	NMP	Cs_2CO_3 (3)	90	81
9	DMF	Cs_2CO_3 (3)	90	63
10	MeCN	Cs_2CO_3 (3)	90	79
11	DMSO	Cs_2CO_3 (3)	80	87
12	DMSO	Cs_2CO_3 (3)	100	90
13[c]	DMSO	Cs_2CO_3 (3)	90	87
14	DMSO	Cs_2CO_3 (2)	90	85
15	DMSO	Cs_2CO_3 (1)	90	37
16[d]	DMSO	Cs_2CO_3 (3)	90	<5
17[e]	DMSO	Cs_2CO_3 (3)	100	82

[a]Reaction conditions: 2-fluoro-3-iodopyridine **1a** (1.0 mmol), acetamidine hydrochloride (1.3 mmol), base (3.0 mmol), H_2O (3.0 mmol) in solvent (3 mL) for 18 h; [b]Isolated Yield; [c]acetamidine hydrochloride (1.0 mmol) was used; [d]N_2 and anhydrous condition. [e]12 h.

With the optimal conditions in hand (Table 1, entry 6), the substrates for this amidation with high chemoselectivity were developed. The results suggest that when the iodine groups were embedded into the pyridine ring, the amidation can be smoothly completed with a high yield of the target product (Scheme 2, **3a**-**3f**). It is remarkable that iodopyridine was reserved in this transformation, since further functionalization of the product can be made to C-I bond. It was also mechanistically interesting, since it is well-known that the C(sp^2)-I bond is notably susceptible in a transition metal catalyzed cross coupling reaction. This reaction is also tolerant to other substituent groups such as cyclopropyl, cyclobutyl, -F, -Cl, -Br, -CF_3, -OMe and -Me groups. Among these amide products, the structure of N-(5-bromopyridin-2-yl)acetamide **3m** was confirmed by crystal X-ray diffraction analysis (**CCDC** 2023439). More importantly, when the fluorine, chlorine, bromine and iodine substituents are embedded into pyridine, the reaction takes priority at the 2-position fluorine to give designed product in good yields, while the halogen atoms at other positions are fully compatible (Scheme 2, **3n-3r**). When 2-fluoropyrazine was used as the raw material for the amination reaction, the reaction could also smoothly proceed and gave N-(pyrazin-2-yl)acetamide **3s** in 92% yield.

Scheme 2. Synthesis of amide derivatives[a]

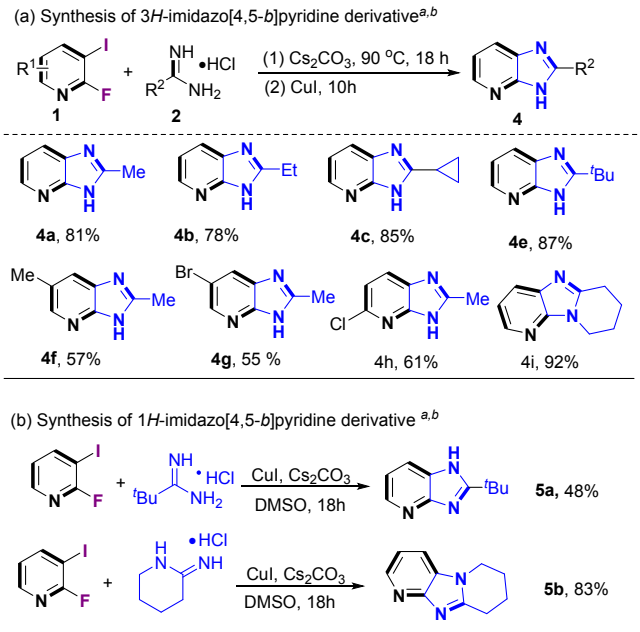


[a]Reaction conditions: 2-fluoropyridine (1.0 mmol), acetamidine hydrochloride (1.3 mmol), Cs_2CO_3 (3.0 mmol), H_2O (3.0 mmol) in DMSO (3 ml) at 90 °C for 18 h under open air; [b] Isolated yields.

Imidazopyridine is the core structure of nitrogen-containing heterocyclic compounds.[16] Because of its unique biological activity, such as antibacterial,[17] anticancer,[18] and anti-virus characteristics,[19] it has been widely applied in biology, pesticide and medicinal chemistry. The two-fold amination of amidine with 2,3-

dihalopyridines is an alternative strategy to synthesize imidazopyridines. However, the reported Cu-catalysed double amination of 2,3-dihalopyridine required the difficult-to-access *ortho*-halopyridine iodides.[20] In fact, the most of two-fold amination methods gave low regioselectivity and yields, which greatly diminished the practical application and academic value of this amination process. Here, we adopt two methods to achieve the regioselective synthesis of imidazo[4,5-*b*]pyridine products starting from amidine hydrochloride, which constituted a general and highly regiospecific method to synthesize the structurally diverse 2-substituted 3*H*-imidazo[*4,5-b*]pyridine and 2-substituted 1*H*-imidazo[*4,5-b*]pyridine (Scheme 3). First, the tandem base-promoted nucleophilic substitution and Cu-catalysed intermolecular amination gave the 2-substituted 3*H*-imidazo[*4,5-b*]pyridine products (Scheme 4a). In this case, when the Cs_2CO_3-promoted nucleophilic substitution reaction is complete, the CuI catalyst was added and completed the subsequent amination reaction. The reaction conditions enabled the two-fold amination to proceed with electron-donating and electron-withdrawing groups to produce the design product in moderate to good yield. As shown in Scheme 3, *ortho*-fluoropyridines with different substituents such as -Me, -^{t}Bu, -Br and -Cl groups were well tolerated (Scheme 3, **4a-4h**). With 2-iminopiperidine hydrochloride as the substrates, the amination reaction gave the highest yield (**4i**, 92%). Correspondingly, when CuI was directly added to the reaction system as a catalyst in a one-pot manner, the double amination of 2-fluoro-3-iodopyridine gave 2-substituted 1*H*-imidazo[*4,5-b*]pyridine products **5a** and **5b** in moderate yields.

Scheme 3. Synthesis of imidazo[4,5-*b*]pyridine derivative

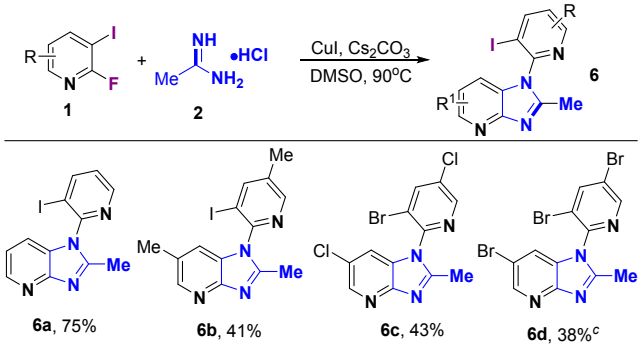


[a]Reaction conditions a: 2-fluoropyridine **1** (1.0 mmol), amidine hydrochloride **2** (1.3 mmol), Cs_2CO_3 (3.0 mmol) in DMSO (3 mL) at 90 °C for 18 h; then, CuI (10 mol%) was added and reacted at 90 °C for 10 h; [b] Isolated yield.

[b]Reaction conditions b: 2-fluoropyridine **1** (1.0 mmol), amidine hydrochloride (1.3 mmol), CuI (10 mol%), and Cs_2CO_3 (3.0 mmol) in DMSO (3 mL) at 90 °C for 18 h; [b] Isolated yield.

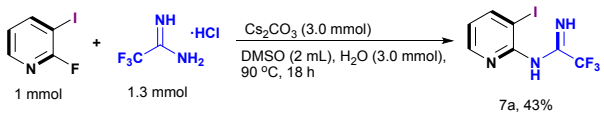
This methodology was also applicable to the preparation of 1,2-disubstituted imidazo[4,5-*b*]pyridines in a three-component reaction. As shown in Scheme 4, *ortho*-fluoropyridines with different substituents such as –Me, -Cl, -Br and -I groups were well tolerated. The -Br or I group embedded into the *ortho*-fluoropyridines did not significantly affect the reaction yields and produced the desired products in 38-75% yields. Importantly, this method provides a concise entry to iodide substituents polycyclic pyrimidines by using 2-fluoro-3-iodopyridines as a suitable substrate, which was not easily accessed in the copper catalyst amination system.

Scheme 4. Cu-catalysed Domino Synthesis of Imidazo[4,5-*b*]pyridines *via* Ullmann-Type Coupling Reaction



[a]Reaction conditions: halopyridine (2.2 mmol), acetamidine hydrochloride (1.0 mmol), Cs_2CO_3 (3.0 mmol), CuI (10 mol%) in DMSO (3 mL) at 110 °C for 24 h; [b]Isolated yield; [c]3,5-dibromo-2-fluoropyridine was used as the substrate.

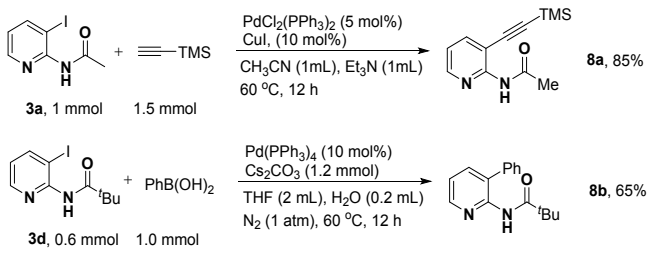
To further verify the reaction mechanism and expand the practicability of this reaction, we chose a few acetamidine derivatives with electron withdrawing group for the amination with 2-fluoropyridine to synthesize amidine derivatives [Eq. (1)]. The reaction successfully obtained 2,2,2-trifluoro-N-(3-iodopyridin-2-yl)acetimidamide (7a, 43%), which can be used to prepare 2-pyridinylamides through hydrolysis. Due to the influence of the strong electron-withdrawing group (CF_3), 2,2,2-trifluoro-N-(3-iodopyridin-2-yl)acetimidamide **7a** is not prone to hydrolysis reaction to give the amide products under current reaction conditions.



Eq. (1)

The obtained N-(3-iodopyridin-2-yl)acetamides are highly attractive as intermediates to prepare more functionalized alkynylpyridines. N-(3-iodopyridin-2-yl)acetamide **3a** was further functionalized into useful moieties such as N-(3-((trimethylsilyl)ethynyl)pyridin-2-yl)acetamide **8a** in 85% yield by the palladium-catalysed Sonogashira coupling reaction (Scheme 5). Next, The Pd-catalyzed

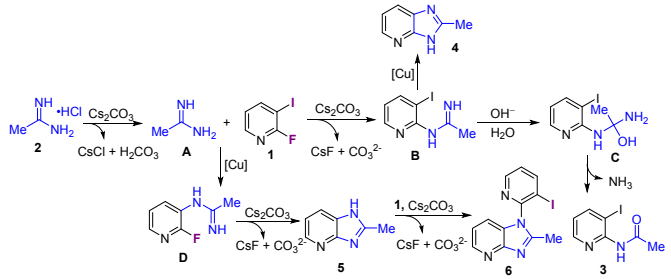
coupling of N-(3-iodopyridin-2-yl)pivalamide **3d** with phenylboronic acid gave N-(3-phenylpyridin-2-yl)pivalamide **8b** in 65% yield (Scheme 5).



Scheme 5. Transformations of iodopyridine

The plausible reaction mechanism for this amination reaction is as follows (Scheme 6): [21] first, acetamidine hydrochloride **2** reacts with Cs_2CO_3 to produce acetamidine **A**, which reacts with 2-fluoropyridine **1** *via* nucleophilic substitution under the assistance of Cs_2CO_3 to yield N-(3-iodopyridin-2-yl)acetimidamide **B**. Then, with the aid of water, Cs_2CO_3 provides hydroxy groups for the nucleophilic attack of N-(3-iodopyridin-2-yl)acetimidamide **B** to yield **C**. Intermediate **C** may be converted into amide **3** and release NH_3. In addition, the copper-catalysed Ullmann-type coupling of 2-fluoro-3-iodopyridine with acetamidine **A** provides N-(2-fluoropyridin-3-yl)acetimidamide **D**. Intermediate **D** experiences a nucleophilic substitution with the assistance of Cs_2CO_3 to yield 1*H*-imidazo[4,5-*b*]pyridine product **5**. Next, 1*H*-imidazo[4,5-*b*]pyridine product **5** reacts with excess 2-fluoro-3-iodopyridine in the nucleophilic substitution process to give product **6** instead of participating in an Ullmann-type coupling reaction. Similarly, with the copper catalyst, the imine group of amidine intermediate **B** coupling with C-I bond gives 3*H*-imidazo[4,5-*b*]pyridine product **4**.

Scheme 6. Possible mechanism to synthesize amides and imidazo [4,5-b] pyridine



Conclusions

In conclusion, we reported a transition-metal-free method to synthesize 2-pyridinylamide derivatives from 2-fluoropyridine and amidine derivatives. The Cu-catalysed approach to produce imidazo[4,5-*b*]pyridine derivatives has been established with high chemoselectivity in good yield. The reaction uses inexpensive and relatively safe amidine hydrochloride as the ammonium source to produce amides and imidazo[4,5-*b*]pyridines with high chemoselectivity and regiospecificity. This method provides a convenient option to synthesize amide and imidazo[4,5-*b*]pyridines, which are important intermediates for medicinal syntheses.

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Experimental section

Materials and methods

Unless otherwise noted, all commercial materials and solvents were used without further purification and all the reactions were carried out in a Schlenk tube equipped with magnetic stir bar. ^{1}H NMR spectra were recorded in $CDCl_3$ at 400 MHz (500 MHz or 600 MHz) and ^{13}C NMR NMR spectra were recorded in $CDCl_3$ at 100 MHz (125 MHz or 150 MHz) respectively, ^{1}H and ^{13}C NMR NMR were referenced to $CDCl_3$ at δ 7.26 (DMSO-d_6 at δ 2.50) and 77.0 (DMSO-d_6 at δ 39.52) respectively. GC–MS was obtained using electron ionization (Agilent Technologies 7890A/5975C). HRMS spectra were acquired using an Agilent 6210 ESI/TOF mass spectrometer and MAT 95XP (Double-focusing Magnetic Sector Analyzer), Thermo (EI, 70eV). TLC was performed using commercially prepared 100-400 mesh silica gel plates (GF_{254}), and visualization was effected at 254 nm. All the other chemicals were purchased from Aldrich Chemicals. Commercial reagents were used without further purification.

General methods for the synthesis of N-(3-iodopyridin-2-yl)acetamide 3a: A 25 mL Schlenk tube was charged with 2-fluoro-3-iodopyridine **1a** (1.0 mmol, 223 mg), acetamidine hydrochloride **2a** (1.3 mmol, 123 mg), Cs_2CO_3 (3.0 mmol, 978 mg), DMSO (3 mL), H_2O (3.0 mmol, 48 mg) and a magnetic stirring bar. The Schlenk tube was then immersed in an oil bath at 90 °C stirring for 18h. After the reaction finished, the mixture was diluted with ethyl acetate and passed through Celite. After evaporation of the solvent the residue was adsorbed on silica gel and the crude product was purified by column chromatography using petroleum/ethyl acetate = 1:1 as eluent.

General methods for the synthesis of 3*H*-imidazo[4,5-*b*]pyridine 4a: A 25 mL Schlenk tube was charged with 2-fluoro-3-iodopyridine **1a** (1.0 mmol, 223 mg), acetamidine hydrochloride **2a** (1.3 mmol, 123 mg), Cs_2CO_3 (3.0 mmol, 978 mg), DMSO (3 mL) and a magnetic stirring bar. The Schlenk tube was then immersed in an oil bath at 90 °C stirring for 18 h, the CuI (10 mol%, 19 mg) was add and reaction at 90 °C stirring for 10 h again. After the reaction finished, the mixture was diluted with ethyl acetate and passed through Celite. After evaporation of the solvent the residue was adsorbed on silica gel and the crude product was purified by column chromatography using petroleum/ethyl acetate = 1:1 as eluent.

General methods for the synthesis of 1*H*-imidazo[4,5-*b*]pyridine 5a: A 25 mL Schlenk tube was charged with 2-fluoro-3-iodopyridine **1a** (1.0 mmol, 223 mg), pivalimidamide hydrochloride **2a** (1.3 mmol, 177 mg), CuI (10 mol%, 19 mg), Cs_2CO_3 (3.0 mmol, 978 mg), DMSO (3 mL) and a magnetic stirring bar. The Schlenk tube was then immersed in an oil bath at 90 °C stirring for 18h. After the reaction finished, the mixture was diluted with ethyl acetate and passed through Celite. After evaporation of the solvent the residue was

adsorbed on silica gel and the crude product was purified by column chromatography using petroleum/ethyl acetate = 1:1 as eluent.

General methods for the synthesis of imidazo[4,5-*b*]pyridine 6a: A 25 mL Schlenk tube was charged with 2-fluoro-3-iodopyridine **1a** (2.2 mmol, 491 mg), acetamidine hydrochloride **2a** (1.0 mmol, 94 mg), CuI (10 mol%, 19 mg), Cs_2CO_3 (3.0 mmol, 978 mg), DMSO (3 mL) and a magnetic stirring bar. The Schlenk tube was then immersed in an oil bath at 110 °C stirring for 24h. After the reaction finished, the mixture was diluted with ethyl acetate and passed through Celite. After evaporation of the solvent the residue was adsorbed on silica gel and the crude product was purified by column chromatography using petroleum/ethyl acetate = 1:1 as eluent.

Gram-scale synthesis of N-(3-iodopyridin-2-yl)acetamide 3a: A 50 mL Schlenk tube was charged with 2-fluoro-3-iodopyridine **1a** (4.48 mmol, 1 g), acetamidine hydrochloride **2a** (6.0 mmol, 1.5 equiv., 0.64 g), Cs_2CO_3 (13.5 mmol, 3.0 equiv., 4.4 g), DMSO (15 mL), H_2O (13.5 mmol, 0.24 g) and a magnetic stirring bar. The Schlenk tube was then immersed in an oil bath at 90 °C stirring for 36 h under open air. After the reaction finished, the mixture was diluted with ethyl acetate and passed through Celite. After evaporation of the solvent the residue was adsorbed on silica gel and the crude product was purified by column chromatography using petroleum/ethyl acetate = 3:1 as eluent, affording the N-(3-iodopyridin-2-yl)acetamide **3a** (0.97 g, 83 %) as a yellow liquid.

N-(3-iodopyridin-2-yl)acetamide (3a): Yellow liquid, (243.7 mg, 93% yield); R_f = 0.34 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.12 (s, 1H), 8.42 (dd, *J* = 5.0, 2.0 Hz, 1H), 8.29 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.05 (dd, *J* = 7.5, 4.5 Hz, 1H), 2.01 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 168.5, 152.5, 148.3, 148.1, 123.3, 94.0, 23.0; ESI-HRMS m/z [M+H]$^+$calcd for $C_7H_8IN_2O$ 262.9676, found 262.9670.

N-(3-iodopyridin-2-yl)propionamide (3b): Yellow solid, (223.6 mg, 81% yield); mp. 94-96 °C; R_f = 0.24 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, Acetone-d_6) δ 9.01 (s, 1H), 8.40 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.28 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.00 (dd, *J* = 7.8, 4.8 Hz, 1H), 2.49 (q, *J* = 7.8, 15.6 Hz, 2H), 1.17 (t, *J* = 7.8 , 7.2 Hz, 3H); ^{13}C NMR (150 MHz, Acetone-d_6) δ 172.9, 153.4, 149.2, 148.9, 123.3, 91.7, 29.9, 9.6; ESI-HRMS m/z [M+H]$^+$calcd for $C_8H_{10}IN_2O$ 276.9832, found 276.9825.

N-(3-iodopyridin-2-yl)cyclopropanecarboxamide (3c): Yellow liquid, (175.7 mg, 61% yield); R_f = 0.35 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.62 (s, 1H), 8.15 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.06 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.52 (dd, *J* = 7.8, 4.8 Hz, 1H), 1.38-1.33 (m, 1H), 1.26 – 1.23 (m, 2H), 0.88 – 0.84 (dt, *J* = 7.2, 3.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.4, 160.7, 147.1, 145.8, 117.8, 94.7, 17.0, 8.9 (2C); ESI-HRMS m/z [M+H]$^+$calcd for $C_9H_{10}IN_2O$ 288.9832, found 288.9824.

N-(3-iodopyridin-2-yl)pivalamide (3d)[22]: Yellow liquid, (264.5 mg, 87% yield); R_f = 0.26 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.79 (s, 1H), 8.24 (s, 1H), 7.88 (s, 1H), 7.13 (m 1H), 1.39 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 170.0, 161.3, 147.5, 146.1, 118.3, 95.3, 38.9, 28.7; ESI-HRMS m/z [M+H]$^+$calcd for $C_{10}H_{14}IN_2O$ 305.0145, found 305.0137.

N-(3-iodopyridin-2-yl)cyclobutanecarboxamide (3e): Yellow liquid, (205.4 mg, 68% yield); R_f = 0.35 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.3 (s, 1H), 8.20 (t, *J* = 5.4 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 6.60 – 6.58 (m, 1H), 3.23 – 3.16 (m, 1H), 2.52 – 2.45 (m, 2H), 2.24 (t, *J* = 10.2 Hz, 2H), 2.03 – 1.90 (m, 2H); ^{13}C NMR (150 MHz, DMSO) δ 165.8, 160.9, 147.3, 146.0, 118.4, 94.6, 41.4, 26.2 (2C), 25.2, 17.9; ESI-HRMS m/z [M+H]$^+$calcd for $C_{10}H_{12}IN_2O$ 302.9989, found 302.9981.

N-(3-iodopyridin-2-yl)-2-methoxyacetamide (3f): Yellow liquid, (201 mg, 69% yield); R_f = 0.22 (petroleum ether/ethyl acetate = 2:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.47 (s, 1H), 8.11 (d, J = 7.2 Hz, 1H), 6.86 – 6.84 (m, 1H), 4.11 (s, 2H), 3.56 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 167.8, 150.3, 148.5, 148.1, 121.8, 86.1, 72.6, 59.8; ESI-HRMS m/z [M+H]$^+$calcd for $C_8H_{10}IN_2O_2$ 292.9781, found 292.9775.

N-(4-methylpyridin-2-yl)acetamide (3g)[23]: Yellow liquid, (120.1 mg, 80% yield); R_f = 0.56 (petroleum ether/ethyl acetate = 2:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.38 (s, 1H), 8.14 (dd, J = 5.0, 0.5 Hz, 1H), 7.91 (s, 1H), 6.91 (dq, J = 2.0, 1.5, 1.0 Hz, 1H), 2.29 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.2, 152.2, 148.7, 147.5, 120.2, 113.7, 23.9, 21.0; ESI-HRMS m/z [M+H]$^+$calcd for $C_8H_{11}N_2O$ 151.0866, found 151.0861.

N-(3-fluoropyridin-2-yl)acetimidamide (3h): Yellow liquid, (137.1 mg, 89% yield); R_f = 0.24 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.25 (s, 1H), 8.23 (d, *J* = 4.8 Hz, 1H), 7.73(dd, *J* = 9.6, 7.8 Hz, 1H), 7.33 – 7.29 (m, 1H), 2.07 (d, *J* = 1.8 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.5, 152.2 (d, *J* = 259.1 Hz), 143.9 (d, *J* = 5.1 Hz), 140.2 (d, *J* = 12.8 Hz), 124.7 (d, *J* = 18.3 Hz), 122.78 (d, *J* = 3.6 Hz), 22.9; ESI-HRMS m/z [M+H]$^+$calcd for $C_7H_8FN_2O$ 155.0615, found 155.0608.

N-(6-fluoropyridin-2-yl)acetamide (3i): Yellow solid, (135.5 mg, 88% yield); mp. 119-121 °C; R_f = 0.24 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.81 (s, 1H), 7.14 (dd, *J* = 7.8, 2.4 Hz, 1H), 7.09 (dd, *J* = 16.2, 7.8 Hz, 1H), 5.98 (dd, *J* = 7.2, 1.8 Hz, 1H) , 1.24 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 169.5, 161.3 (d, *J* = 236.5 Hz), 150.5 (d, *J* = 14.9 Hz), 143.9 (d, *J* = 8.0 Hz), 110.2 (d, *J* = 4.1 Hz), 103.3 (d, *J* = 35.6 Hz), 23.9; ESI-HRMS m/z [M+H]$^+$calcd for $C_7H_8FN_2O$ 155.0615, found 155.0611.

N-(5-chloropyridin-2-yl)acetamide (3j)[24]: White solid, (125.8 mg, 74% yield); mp. 172-174 °C; R_f = 0.22 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.66 (s, 1H), 8.33 (t, *J* = 2.9 Hz, 1H), 8.10 (d, *J* = 8.9 Hz, 1H), 7.85 (ddd, *J* = 9.0, 4.0, 2.3 Hz, 1H), 2.09 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.44, 150.8, 146.3, 137.8, 124.8, 114.4, 23.9; ESI-HRMS m/z [M+H]$^+$calcd for $C_7H_8ClN_2O$ 171.0320, found 171.0314.

N-(6-chloropyridin-2-yl)acetamide (3k)[25]: White solid, (117.3 mg, 69% yield); mp. 150-152 °C; R_f = 0.22 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.77 (s, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.81 – 7.62 (m, 1H), 7.16 – 7.11 (m, 1H), 2.08 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.6, 152.2, 148.0, 141.7, 118.9, 111.9, 23.9; ESI-HRMS m/z [M+H]$^+$calcd for $C_7H_8ClN_2O$ 171.0320, found 171.0314.

N-(6-bromopyridin-2-yl)acetamide (3l)[26]: White solid, (194.7 mg, 91% yield); mp. 155-157 °C; R_f = 0.24 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.78 (s, 1H), 8.07 (d,

J = 8.4 Hz, 1H), 7.69 (t, *J* = 7.8 Hz, 1H), 7.28 (d, *J* = 7.8 Hz, 1H), 2.08 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d$_6$) *δ* 169.5, 152.3, 141.3, 138.7, 122.7, 112.1, 23.9; ESI-HRMS m/z [M+H]$^+$calcd for $C_7H_8BrN_2O$ 214.9815, found 214.9808.

N-(5-bromopyridin-2-yl)acetamide (3m)[27]: White solid, (162.6 mg, 76% yield); mp. 169-171 °C; R_f = 0.24 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, DMSO-d$_6$) *δ* 10.64 (s, 1H), 8.41 (dd, *J* = 2.4, 0.6 Hz, 1H), 8.06 (d, *J* = 9.6 Hz, 1H), 7.97 (dd, *J* = 9.0, 3.0 Hz, 1H), 2.09 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d$_6$) *δ* 169.4, 151.1, 148.4, 140.5, 115.0, 113.2, 23.9; ESI-HRMS m/z [M+H]$^+$calcd for $C_7H_8BrN_2O$ 214.9815, found 214.9809.

N-(3-chloro-5-fluoropyridin-2-yl)acetamide (3n): White solid, (172.0 mg, 91% yield); mp. 86-88 °C; R_f = 0.32 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (400 MHz, DMSO-d$_6$) *δ* 10.17 (s, 1H), 8.44 (t, *J* = 2.4 Hz, 1H), 8.13 (dd, *J* = 8.0, 2.8 Hz, 1H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d$_6$) *δ* 168.6, 156.7 (d, *J* = 257.95 Hz), 144.9 (d, *J* = 2.93 Hz), 134.7 (d, *J* = 23.9 Hz), 127.2 (d, *J* = 5.5 Hz), 126.2 (d, *J* = 22.5 Hz), 22.7; ESI-HRMS m/z [M+H]$^+$calcd for $C_7H_7FClN_2O$ 189.0225, found 189.0218.

N-(5-bromo-4-methylpyridin-2-yl)acetamide (3o)[23]: Brown solid, (189.2 mg, 83% yield); mp. 150-152 °C; R_f = 0.36 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (400 MHz, DMSO-d$_6$) *δ* 10.49 (s, 1H), 8.32 (s, 1H), 8.06 (s, 1H), 2.31 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d$_6$) *δ* 169.2, 151.4, 148.6, 147.9, 116.0, 115.1, 23.9, 22.2; ESI-HRMS m/z [M+H]$^+$calcd for $C_8H_{10}BrN_2O$ 228.9971, found 228.9965.

N-(3-iodo-5-methylpyridin-2-yl)acetamide (3p): Yellow liquid, (190.4 mg, 69% yield); R_f = 0.30 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, DMSO-d$_6$) *δ* 9.99 (s, 1H), 8.24 (dd, *J* = 1.2, 2.4 Hz, 1H), 8.13 (dd, *J* = 0.6, 1.8 Hz, 1H), 2.23 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d$_6$) *δ* 168.7, 150.1, 148.2, 133.1, 93.9, 40.4, 23.0, 16.7; ESI-HRMS m/z [M+H]$^+$calcd for $C_8H_{10}IN_2O$ 276.9832, found 276.9824.

N-(3-chloro-5-(trifluoromethyl)pyridin-2-yl)acetamide (3q): Yellow liquid, (219.0 mg, 92% yield); R_f = 0.46 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (400 MHz, DMSO-d$_6$) *δ* 10.45 (s, 1H), 8.75 (s, 1H), 8.42 (s, 1H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d$_6$) *δ* 168.7, 151.9, 143.6 (d, *J* = 4.4 Hz), 136.1 (d, *J* = 2.4 Hz), 125.4, 123.8 (d, *J* = 74.44 Hz), 123.3 (d, *J* = 33.43 Hz), 121.5, 23.2; ESI-HRMS m/z [M+H]$^+$calcd for $C_8H_7F_3ClN_2O$ 239.0194, found 239.0191.

N-(3-bromo-5-chloropyridin-2-yl)cyclopropanecarboxamide (3r)[26]: Yellow liquid, (200.0 mg, 73% yield); R_f = 0.26 (petroleum ether/ethyl acetate = 3:1); ^{1}H NMR (600 MHz, CDCl$_3$) *δ* 8.10 (d, *J* = 2.4 Hz, 1H), 7.82 (d, *J* = 2.4 Hz, 1H), 1.44 – 1.39 (m, 1H), 1.22 – 1.19 (m, 2H), 0.90 – 0.86 (m, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) *δ* 165.7, 157.9, 143.3, 140.3, 123.3 , 117.7, 17.2, 9.0.

N-(pyrazin-2-yl)acetamide (3s)[28]: White solid, (126.1 mg, 92% yield); R_f = 0.26 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (400 MHz, DMSO) *δ* 10.71 (s, 1H), 9.30 (s, 1H), 8.33 (d, J = 14.4 Hz, 2H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, DMSO) *δ* 169.5, 148.8, 142.5 , 139.4, 136.2, 23.6; ESI-HRMS m/z [M+H]$^+$calcd for $C_6H_8N_3O$ 138.0662, found 138.0666.

2-methyl-3H-imidazo[4,5-*b*]pyridine (4a)[29]: Yellow solid, (107.7mg, 81% yield); R_f = 0.23 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, DMSO-d$_6$) *δ* 12.70 (s, 1H), 8.22 (dd, *J* = 5.5 Hz, 1H), 7.85 (s, 1H), 7.14 (dd, *J* = 7.5, 4.5 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d$_6$) *δ* 153.6, 151.9, 142.6 131.8, 122.6, 117.2, 15.0; ESI-HRMS m/z [M+H]$^+$calcd for $C_7H_8N_3$ 134.0713, found 134.0707.

2-ethyl-3H-imidazo[4,5-*b*]pyridine (4b)[30]: Yellow liquid, (114.7 mg, 78% yield); R_f = 0.22 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, CDCl$_3$) *δ* 8.32 (d, *J* = 4.8 Hz, 1H), 8.02 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.23 (dd, *J* = 7.9, 4.9 Hz, 1H), 3.49 (s, 1H), 3.08 (q, *J* = 7.6 Hz, 2H), 1.54 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) *δ* 158.9, 150.0, 142.0, 134.8, 125.7, 117.8, 23.1, 12.0; ESI-HRMS m/z [M+H]$^+$calcd for $C_8H_{10}N_3$ 148.0869, found 148.0868.

2-cyclopropyl-3H-imidazo[4,5-*b*]pyridine (4c): White solid, (135.2 mg, 85% yield); mp. 173-175 °C; R_f = 0.21 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, DMSO-d$_6$) *δ* 12.77 (s, 1H), 8.19 (d, *J* = 5.0 Hz, 1H), 7.79 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.09 (dd, *J* = 8.0, 5.0 Hz, 1H), 2.29 – 2.13 (m, 1H), 2.16 – 2.10 (m, 2H), 1.09 – 1.06 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) *δ* 159.9, 149.6, 141.21, 135.6, 125.6, 117.7, 10.6, 9.6; ESI-HRMS m/z [M+H]$^+$calcd for $C_9H_{10}N_3$ 160.0869, found 160.0867.

2-tert-butyl-3H-imidazo[4,5-*b*]pyridine (4d): White solid, (152.3 mg, 87% yield); mp. 155-157 °C; R_f = 0.20 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (600 MHz, CDCl$_3$) *δ* 13.86 (s, 1H), 8.36 (t, *J* = 4.8 Hz, 1H), 8.09 (d, *J* = 6.6 Hz, 1H), 7.25 (dd, *J* = 3.6, 8.4 Hz, 1H), 1.61 (s, 9H); ^{13}C NMR (150 MHz, CDCl$_3$) *δ* 165.06, 149.47, 142.04, 136.05, 127.45, 117.86, 34.09, 29.50; ESI-HRMS m/z [M+H]$^+$calcd for $C_{10}H_{14}N_3$ 176.1182, found 176.1180.

2,6-dimethyl-3H-imidazo[4,5-*b*]pyridine (4e): Brown solid, (83.8 mg, 57% yield); mp. 213-215 °C; R_f = 0.22 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, DMSO-d$_6$) *δ* 12.50 (s, 1H), 8.07 (s, 1H), 7.64 (s, 1H), 2.49 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d$_6$) *δ* 153.5, 148.1, 142.7, 135.5, 127.5, 126.3, 18.8, 15.7; ESI-HRMS m/z [M+H]$^+$calcd for $C_8H_{10}N_3$ 148.0869, found 148.0867.

6-bromo-2-methyl-3H-imidazo[4,5-b]pyridine(4f)[29]: Brown solid, (116.1 mg, 55% yield); R_f = 0.21 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, DMSO) δ 12.90 (s, 1H), 8.30 (d, *J* = 2.0 Hz, 1H), 8.11 (d, *J* = 2.0 Hz, 1H), 2.51 (d, *J* = 5.3 Hz, 3H); ^{13}C NMR (125 MHz, DMSO) *δ* 155.9, 143.3, 112.6, 15.56.(Three carbon signals of ^{13}C NMR are missing).

6,7,8,9-tetrahydroimidazo[1,2-*a*:5,4-*b*']dipyridine (4g)[31]: Yellow liquid, (159.2 mg, 92% yield); R_f = 0.24 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (600 MHz, DMSO-d$_6$) *δ* 7.35 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.02 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.32 (dd, *J* = 7.8, 4.8 Hz, 1H), 3.24 (t, *J* =6.0 Hz, 2H), 2.09 (t, *J* =6.0 Hz, 2H), 1.17 – 1.12 (m, 2H), 1.07 – 1.02 (m, 2H); ^{13}C NMR (150 MHz, DMSO-d$_6$) *δ* 153.4, 147.6, 142.1, 134.5, 125.4, 117.9, 41.2, 25.2, 21.7, 20.0; ESI-HRMS m/z [M+H]$^+$calcd for $C_{10}H_{12}N_3$ 174.1026, found 174.1016.

2-tert-butyl-1H-imidazo[4,5-*b*]pyridine (5a): White solid, (84 mg, 48% yield); mp. 247-249 °C; R_f = 0.34 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (600 MHz, DMSO-d$_6$) *δ* 12.78 (s, 1H), 8.24 (s, 1H), 7.88 (s, 1H), 7.13 (dd, *J* = 7.8, 3.2 Hz, 1H), 1.39 (s, 9H); ^{13}C NMR (150 MHz, DMSO-d$_6$) *δ* 163.8, 149.4, 142.7, 134.4, 125.7, 117.2, 33.5, 28.9 (3C); ESI-HRMS m/z [M+H]$^+$calcd for $C_{10}H_{12}N_3$ 176.1182, found 176.1174.

6,7,8,9-tetrahydroimidazo[1,2-*a*:4,5-*b*']dipyridine (5b): Yellow solid, (143.6 mg, 83% yield); mp. 95-97 °C; R_f = 0.32 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (600 MHz, CDCl$_3$) *δ* 8.15 (dd, *J* = 4.8, 1.8 Hz, 1H), 7.78 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.04 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.08 (t, *J* = 6.0 Hz, 2H), 2.96 (t, *J* = 6.6 Hz, 2H), 2.00 – 1.97 (m, 2H), 1.92 – 1.87 (m, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) *δ* 153.1,

147.5, 142.5, 134.8, 125.9, 118.0, 41.3, 25.5, 21.2, 20.34; ESI-HRMS m/z $[M+H]^+$calcd for $C_{10}H_{12}N_3$ 174.1026, found 174.1023.

1-(3-iodopyridin-2-yl)-2-methyl-1H-imidazo[4,5-*b*]pyridine (6a): Yellow liquid, 252 mg, 75% yield); R_f = 0.26 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.73 (dd, J = 4.4, 1.6 Hz, 1H), 8.65 (dd, J = 8.0, 1.6 Hz, 1H), 8.43 (d, J = 3.6 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.23 (dd, J = 8.0, 4.8 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 155.0, 153.4, 149.8, 149.6, 149.5, 144.3, 127.1, 126.8, 118.5, 118.2, 95.2, 14.2; ESI-HRMS m/z $[M+H]^+$calcd for $C_{12}H_{10}IN_4$ 336.9945, found 336.9934.

1-(3-iodo-5-methylpyridin-2-yl)-2,6-dimethyl-1H-imidazo[4,5-*b*]pyridine (6b): White solid, (149 mg, 41% yield); mp. 152-154 °C; R_f = 0.24 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.55 (dd, J = 1.8, 0.6 Hz, 1H), 8.49 (dd, J = 1.8, 0.6 Hz, 1H), 8.26 (d, J = 2.4, 0.6 Hz, 1H), 7.27 (dd, J = 1.8, 0.6 Hz, 1H), 2.41 (s, 3H), 2.36 (d, J = 2.4 Hz, 6H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 153.3, 152.8, 150.0, 149.3, 147.2, 144.9, 136.9, 127.5, 127.2, 118.2, 94.6, 18.0, 17.0, 14.1; ESI-HRMS m/z $[M+H]^+$calcd for $C_{14}H_{14}IN_4$ 365.0258, found 365.0254.

1-(3-bromo-5-chloropyridin-2-yl)-6-chloro-2-dimethyl-1H-imidazo[4,5-*b*]pyridine (6c): White solid, (153 mg, 43% yield); mp. 177-179 °C; R_f = 0.20 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.82 (t, J = 2.5 Hz, 2H), 8.45 (d, J = 2.5 Hz, 1H), 8.01 (d, J = 2.5 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 155.3, 153.5, 147.9, 144.4, 143.0, 142.8, 133.1, 127.6, 125.3, 119.6, 118.9, 14.1; ESI-HRMS m/z $[M+H]^+$calcd for $C_{12}H_8BrCl_2N_4$ 356.9304, found 356.9304.

6-bromo-1-(3,5-dibromopyridin-2-yl)-2-methyl-1H-imidazo[4,5-*b*]pyridine (6d): Yellow liquid, (168.7 mg, 38% yield); R_f = 0.24 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.90 (d, J = 2.0 Hz, 1H), 8.80 (d, J = 2.0 Hz, 1H), 8.51 (d, J = 2.0 Hz, 1H), 8.12 (d, J = 2.0 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 155.1, 153.7, 150.1, 145.4, 145.0, 144.7, 128.2, 122.1, 121.6, 119.9, 113.6, 14.1; ESI-HRMS m/z $[M+H]^+$calcd for $C_{12}H_8Br_3N_4$ 444.8294, found 444.8301.

2,2,2-trifluoro-N-(3-iodopyridin-2-yl)acetimidamide (7a): Yellow liquid, (135.5 mg, 43% yield); R_f = 0.85 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.30 (dd, J = 4.8, 1.6 Hz, 1H), 8.21 (dd, J = 7.8, 1.7 Hz, 1H), 6.77 (dd, J = 7.8, 4.8 Hz, 1H), 6.02 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.6, 148.4 (q, J = 35.5 Hz, 1C), 148.2, 146.0, 120.8, 118.0 (q, J = 276.8 Hz, 1C), 95.3. ESI-HRMS m/z $[M+H]^+$calcd for $C_7H_6F_3IN_3$ 315.9553, found 315.9552.

N-(3-((trimethylsilyl)ethynyl)pyridin-2-yl)acetamide (8a)[32]: Yellow liquid, (197.2 mg, 85% yield); R_f = 0.48 (petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (dd, J =5.0, 2.0 Hz, 1H), 8.15(s, 1H), 7.71 (dd, J = 7.5, 1.5 Hz, 1H), 6.97 (dd, J = 7.5, 4.5 Hz, 1H), 0.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.1, 147.8, 140.7, 118.5, 104.6, 98.5, 25.1, -0.09 (3C); ESI-HRMS m/z $[M+H]^+$ calcd for $C_{12}H_{17}SiON_2$ 233.1105, found 233.1097.

N-(3-phenylpyridin-2-yl)pivalamide (8b): Yellow liquid, (99.1 mg, 65% yield); R_f = 0.50 (petroleum ether/ethyl acetate = 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.74 (S, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.45 (t, J = 8.0 Hz, 2H), 7.40-7.37 (m, 3H), 7.24-7.20 (m, 1H), 1.11 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) 175.7, 148.3, 147.4, 139.0, 137.5, 130.8, 128.8 (2C), 128.4 (2C), 128.0, 120.9, 39.6, 27.2 (3C). ESI-HRMS m/z $[M+H]^+$calcd for $C_{16}H_{19}N_2O$ 255.1492, found 255.1490.

Conflicts of interest

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There are no conflicts to declare.

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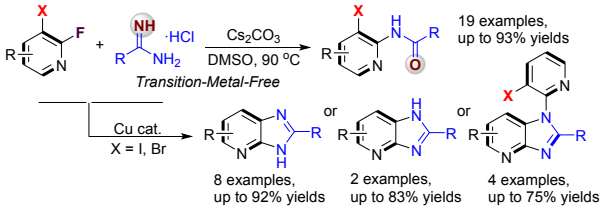

An efficient method to synthesize 2-pyridinylamides and Imidazopyridine has been developed, and the protocol uses inexpensive and readily available 2-fluoropyridine and amidine derivatives as the starting materials.