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Synthesis of 3,6-diaryl-1*H*-pyrazolo[3,4-*b*]pyridines *via* one-pot sequential Suzuki–Miyaura coupling†

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A practical synthesis of diarylpyrazolo[3,4-*b*]pyridine derivatives by a combination of chemoselective Suzuki–Miyaura cross-coupling reactions was developed. The sequential arylation strategy can be performed in a one-pot manner without much loss of efficiency when compared to the corresponding stepwise synthesis. These conditions are applicable to the coupling of a wide variety of aryl and heteroaryl-boronic acids with pyrazolo[3,4-*b*]pyridines with high selectivity of the C3 over the C6 position, thus enabling the rapid construction of a diverse array of medicinally important diarylpyrazolo [3,4-*b*]pyridines.

1. Introduction

The transition-metal-catalysed cross-coupling reaction has been well-established as a powerful synthetic tool in C–C bond formation. In particular, the Suzuki–Miyaura cross-coupling reaction has shown widespread applications in natural product synthesis, the synthesis of medicinally important pharmacophores and organic materials.[1] To explore further synthetic applications of transition-metal-catalyzed cross-coupling reactions, organocatalytic reactions and arylation of heteroaromatics have attracted attention in recent years.[2] In the last decade a selective arylation strategy in a sequential manner has emerged as a valuable tool for cross-coupling techniques.[3a–d] In pursuit of this, selective and/or sequential arylation were studied on a few pharmaceutically important heterocycles *e.g.* indazoles,[3e,f] azaindoles,[3g,h] and imidazopyrazines.[3i] This strategy, which explores the different reactivities of electrophilic and nucleophilic cross-coupling partners, allows for multiple C-aryl bond formations in a "controlled" manner to rapidly construct functional molecules with complex structures applicable to pharmaceutical and material science.[4,5]

Pyrazolo[3,4-*b*]pyridine, a privileged heterocyclic core, has been actively pursued in medicinal research due to its wide spectrum of biological activities; *viz*: glycogen synthase kinase-3 (GSK-3) inhibitors[6] and A^1 adenosine receptors[7] (Fig. 1). Recently, arylated pyrazolo[3,4-*b*]pyridine has been outlined as a fibroblast growth factor inhibitor (FGF-R and FGFR3) specific for the treatment of bladder cancer,[8] as a Raf inhibitor to inhibit B-Raf^{V600E},[9] as metabotropic glutamate receptor 5 (mGluR5) positive allosteric modulators (PAM's)[10] and as a neuroprotector in MPP^+-induced neurodegeneration (Fig. 1).[11]

A number of methods have been developed to functionalize this fused heterocyclic system.[12] Recently, Guillaumet reported the direct heteroarylation of 2*H*-pyrazolo[3,4-*b*]pyridines using "on water" conditions[13a] whereas, Popowycz has reported Pd-catalyzed late-stage C-3 functionalization of pyrazolo[3,4-*b*]pyridines.[13b] Despite many advances in the synthesis of C-arylated pyrazolopyridines, a selective and high-yielding method from accessible starting materials remains a goal within the synthetic community. Herein, we report an efficient synthesis of 3,6-diarylpyrazolo[3,4-*b*]pyridine *via* site selective sequential Suzuki–Miyaura coupling (SMC).[14] The salient features of this protocol are its high chemoselectivity, easy removal of the protecting group and tolerance towards functional groups. The designed 3,6-diarylpyrazolo[3,4-*b*]pyridines can be synthesized sequentially in a one-pot reaction.

2. Results and discussion

The synthesis of the 6-chloro-3-iodo-1-(4-methoxybenzyl)-1*H*-pyrazolo[3,4-*b*]pyridine (**1**) core was accomplished through cyclisation of 2-chloro-3-cyanopyridine and hydrazine followed by *in situ* diazotization and iodination at the C3 position of the ring.[12a] C6-chlorination was undertaken on its N-oxide product and, lastly, removal of the N-protection.[15] We commenced the optimization of arylation by coupling 6-chloro-3-iodo-1-(4-methoxybenzyl)-1*H*-pyrazolo[3,4-*b*]pyridine (**1**) with phenylboronic acid (**2**) using $Pd(OAc)_2$ as a catalyst (5 mol%) and dppf as a ligand (5 mol%) in the presence of Cs_2CO_3 at 60 °C in THF, giving 68% yield (Table 1, entry 1). Whereas other solvents, *e.g.* acetonitrile and 1,4-dioxane, failed to provide higher yields (Table 1, entries 2 and 3). However, in combination with 1,4-

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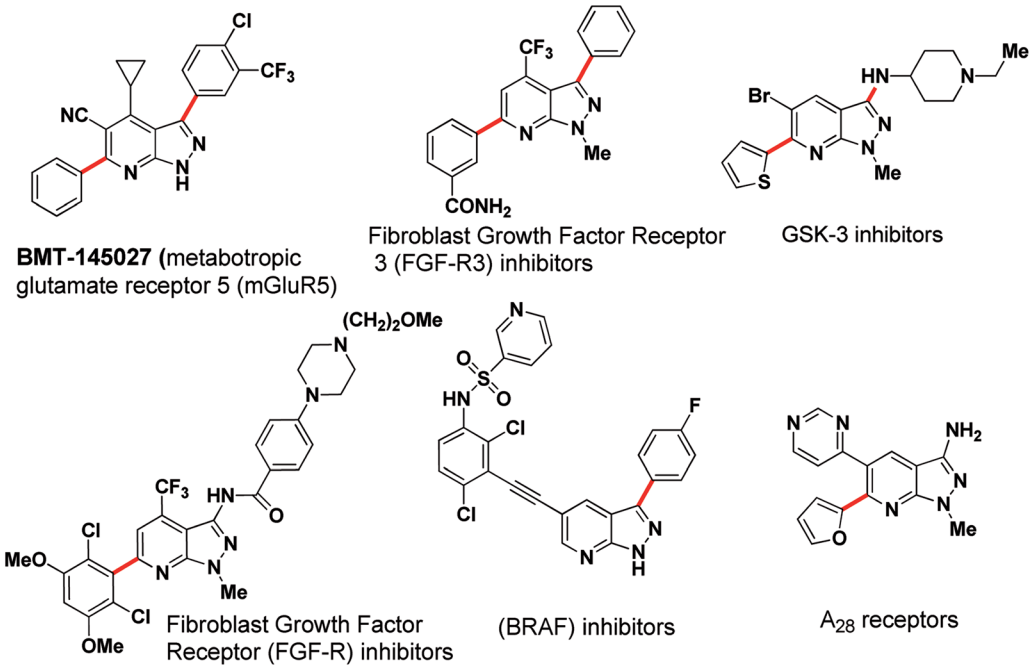
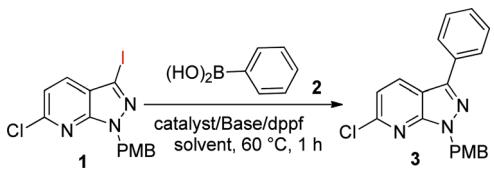


Fig. 1 Medicinal interest in arylated 1*H*-pyrazolo[3,4-*b*]pyridines.

Table 1 Optimization of reaction conditions for the C3-arylpyrazolo [3,4-*b*]pyridines[a]

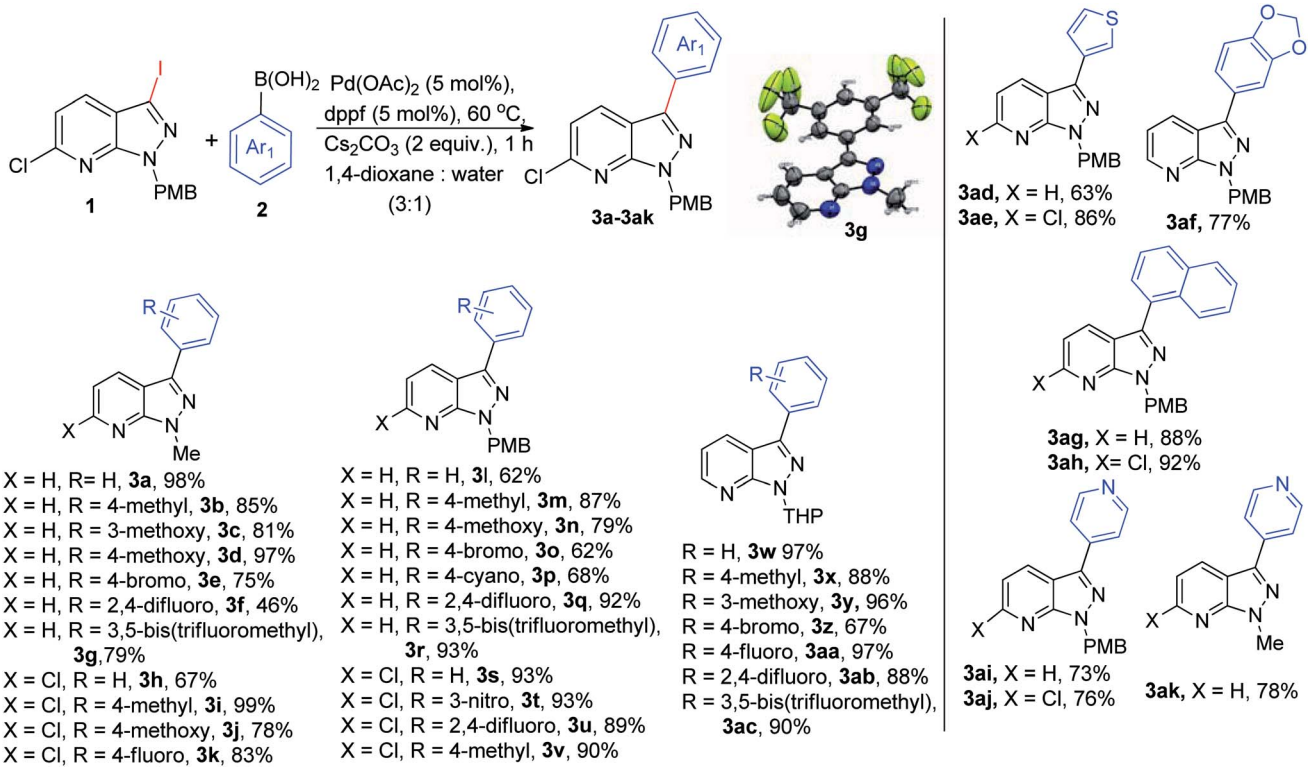


Entry	Catalyst	Ligand	Base	Solvent	Yield[b]
1	$Pd(OAc)_2$	dppf	Cs_2CO_3	THF	68
2	$Pd(OAc)_2$	dppf	Cs_2CO_3	CH_3CN	45
3	$Pd(OAc)_2$	dppf	Cs_2CO_3	Dioxane	62
4	**$Pd(OAc)_2$**	**dppf**	**Cs_2CO_3**	**Dioxane : water (3 : 1)**	**93**
5	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	Dioxane : water (3 : 1)	69
6	$PdCl_2(PPh_3)_4$	dppf	Cs_2CO_3	Dioxane : water (3 : 1)	73
7	$Pd(PPh_3)_4$	dppf	Cs_2CO_3	Dioxane : water (3 : 1)	80
8	$PdCl_2$	dppf	Cs_2CO_3	Dioxane : water (3 : 1)	78
9	$Pd(OAc)_2$	dppf	K_2CO_3	Dioxane : water (3 : 1)	75
10	$Pd(OAc)_2$	dppf	Na_2CO_3	Dioxane : water (3 : 1)	63
11	$Pd(OAc)_2$	dppf	Cs_2CO_3	Dioxane : water (1 : 1)	82
12[c]	$Pd(OAc)_2$	dppf	Cs_2CO_3	Dioxane : water (3 : 1)	77
13[d]	$Pd(OAc)_2$	dppf	Cs_2CO_3	Dioxane : water (3 : 1)	86
14	$Pd(OAc)_2$	dppf	—	Dioxane : water (3 : 1)	n.r.
15[e]	$Pd(OAc)_2$	dppf	Cs_2CO_3	Dioxane : water (3 : 1)	n.r.

[a] Reaction conditions: 6-chloro-3-iodo-1-(4-methoxybenzyl)-1*H*-pyrazolo [3,4-*b*]pyridine (1.0 equiv.), arylboronic acid (1.0 equiv.), catalyst (5 mol%), dppf (5 mol%), base (2.0 equiv.), 1,4-dioxane : water (3 : 1) (5 mL), 60 °C, 1 h, air. [b] Isolated yields. [c] 1.0 equiv. base used. [d] Reaction performed for 4 h. [e] At room temperature; n.r. = no reaction.

dioxane : water (3 : 1), the desired product was isolated in 93% yield. On substituting dppf with a PPh_3 ligand we observed an inferior result (Table 1, entry 5). Different Pd-catalysts were screened but no fruitful results were obtained (Table 1, entries 6–8). Moderate yields (63–75%) were recorded with other bases; *viz*: K_2CO_3 and Na_2CO_3 (Table 1, entries 9 and 10). Increasing the water content in the reaction solvent did not lead to a satisfactory result (Table 1, entry 11), suggesting that dioxane : water in a ratio of 3 : 1 is the best solvent combination. The reaction yield decreased to 77% (Table 1, entry 12) using one equivalent base and in the absence of a base the reaction did not work (Table 1, entry 14). The reaction did not proceed at rt (Table 1, entry 15). Thus, we identified $Pd(OAc)_2$ (5 mol%)/dppf (5 mol%)/Cs_2CO_3 (2 equiv.)/1,4-dioxane : water (3 : 1)/60 °C as the standard conditions for the coupling reaction (Table 1, entry 4). This reaction is selective for C3-arylation and in no case was any C6-arylation product detected.

With the optimized protocol in hand, we evaluated the scope of the substrate for coupling reactions (Scheme 1). Interestingly, our standard conditions proved to be efficient for both electron-rich (–Me, –OMe), and electron-deficient (–Br, –F, $–CF_3$, $–NO_2$) boronic acids, leading to the desired product within a range of 62–98% yield with different N-protected pyrazolo[3,4-*b*]pyridine molecules (Me, PMB, THP) in 1 h. First, we examined coupling of the 3-iodo derivative of *N*-Me-pyrazolo[3,4-*b*]pyridine with electronically diverse boronic acids and observed a yield in the range of 75–98% (**3a–3g**), except for 2,4-difluorophenylboronic acid (**3f**, 46% yield). Implementation of standard reaction conditions on 6-chloro-3-iodopyrazolopyridines led to the desired product (**3h–3k**) in excellent yields and to our delight the reaction was chemoselective. A reaction between *N*-PMB-pyrazolo[3,4-*b*]pyridines and electron-rich boronic acids gave good yields of **3m-3n**, while **3o-3p** were obtained in slightly lower yields with electron-deficient partners. The difluoro and bis-(trifluoromethyl)-containing boronic acids proved to be



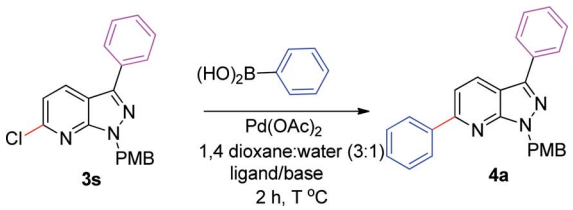
Scheme 1 Synthesis of C3-arylpyrazolo[3,4-*b*]pyridines and their derivatives.[a,b] [a]Reaction conditions: 6-chloro-3-iodo-1-(4-methoxybenzyl)-1*H*-pyrazolo[3,4-*b*]pyridine (1.0 equiv.), arylboronic acid (1.0 equiv.), catalyst (5 mol%), dppf (5 mol%), base (2.0 equiv.), 1,4 dioxane : water (3 : 1) (5 mL), 60 °C, 1 h, air; [b]isolated yields.

effective in giving 92% and 93% yields for **3q** & **3r** respectively. High yields (89–93%, **3s–3v**) were obtained in the case of 3-iodo-6-chloro-*N*-PMB-pyrazolo[3,4-*b*]pyridine and a similar pattern was observed with the single halogenated *N*-THP-pyrazolo[3,4-*b*] pyridines (**3w–3ac**). The thiophene, **3ad–3ae**, 63–86% and 6-membered heteroyclic (pyridyl, **3ai-3aj**, 73–76%) boronic acids gave desired products in significantly good yields. We were also successful in introducing naphthyl (**3ag-3ah**) and benzo[*d*][1,3] dioxole groups (**3af**) onto the pyrazolo[3,4-*b*]pyridine core moiety in excellent yields. The crystal structure of **3g** was confirmed by X-ray crystallography.

We extended the above findings to C6-arylation on 6-chloro-1-(4-methoxybenzyl)-3-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine (**3s**) with phenylboronic acid to yield 1-(4-methoxybenzyl)-3,6-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine, **4a** (Table 2). Only 54% of the diarylated product was formed on applying the earlier optimized conditions (Table 2, entry 1). Changing the ligand to PPh_3 decreased the yield of coupled product to 48% (Table 2, entry 2). Incomplete conversion was observed on using a milder base, such as K_2CO_3 and Na_2CO_3 (Table 2, entries 3 and 4). The reaction yield was enhanced to 95% on increasing the temperature to 100 °C. No new spot was formed at rt (Table 2, entry 7). Experimentation showed that the combination of $Pd(OAc)_2$ (5 mol%) and dppf (5 mol%) with 2.0 equiv. of Cs_2CO_3 in 1,4-dioxane and water (3 : 1) at 100 °C for 2 h afforded the C6-arylated product in the best yield (Table 2, entry 6).

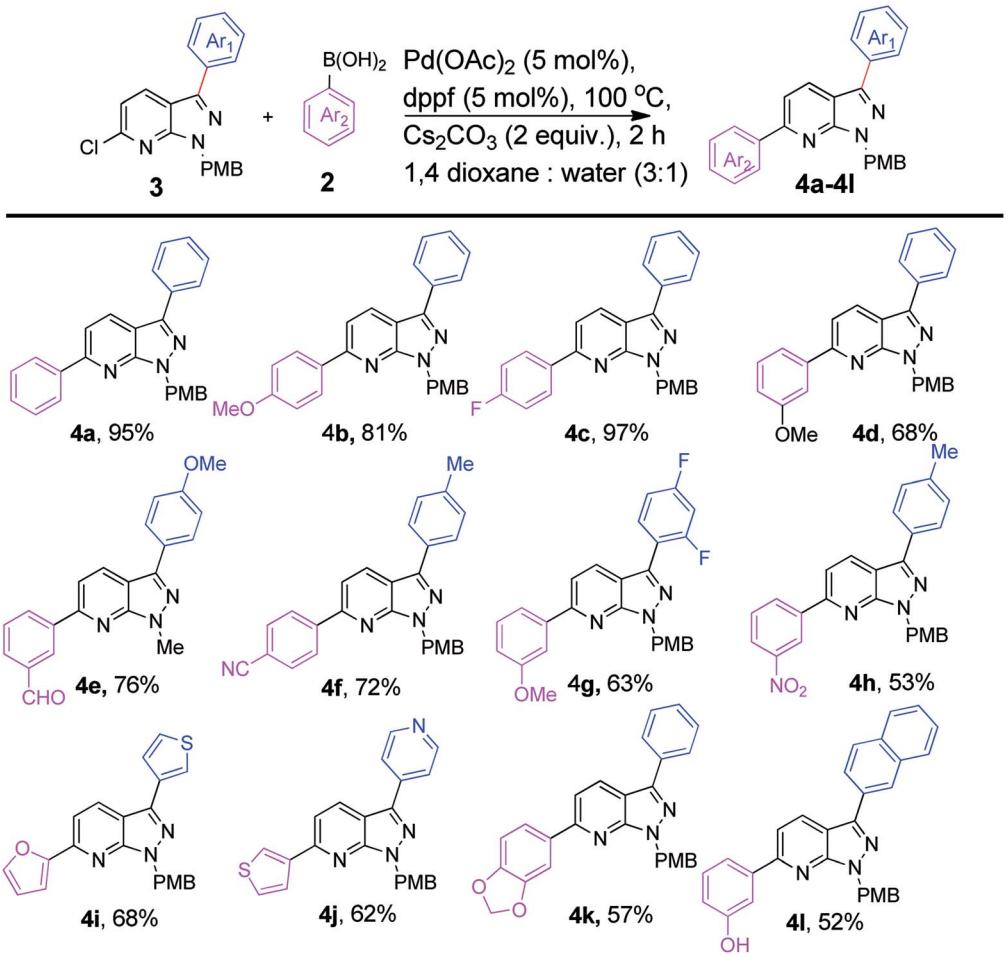
For substrate scope, coupling with 4-fluorophenylboronic acid facilitates excellent reaction yield (97%), when compared to coupling with electron-donating 4-methoxyphenylboronic acid resulted in 81% yield (**4b** & **4c**, Scheme 2). The formyl group functionalized compound, **4e** can be utilized for beneficial organic transformations. The reaction of electron-withdrawing

Table 2 Optimization studies for C6-arylation of 3-arylpyrazolo[3,4-*b*]pyridines[a]



Entry	Ligand [5mol%]	Base	*T* (°C)	Yield[b] (%)
1	dppf	Cs_2CO_3	60	54
2	PPh_3	Cs_2CO_3	60	48
3[c]	dppf	K_2CO_3	60	62
4[d]	dppf	Na_2CO_3	60	55
5	dppf	Cs_2CO_3	80	78
6	**dppf**	**Cs_2CO_3**	**100**	**95**
7	dppf	Cs_2CO_3	rt	n.r.

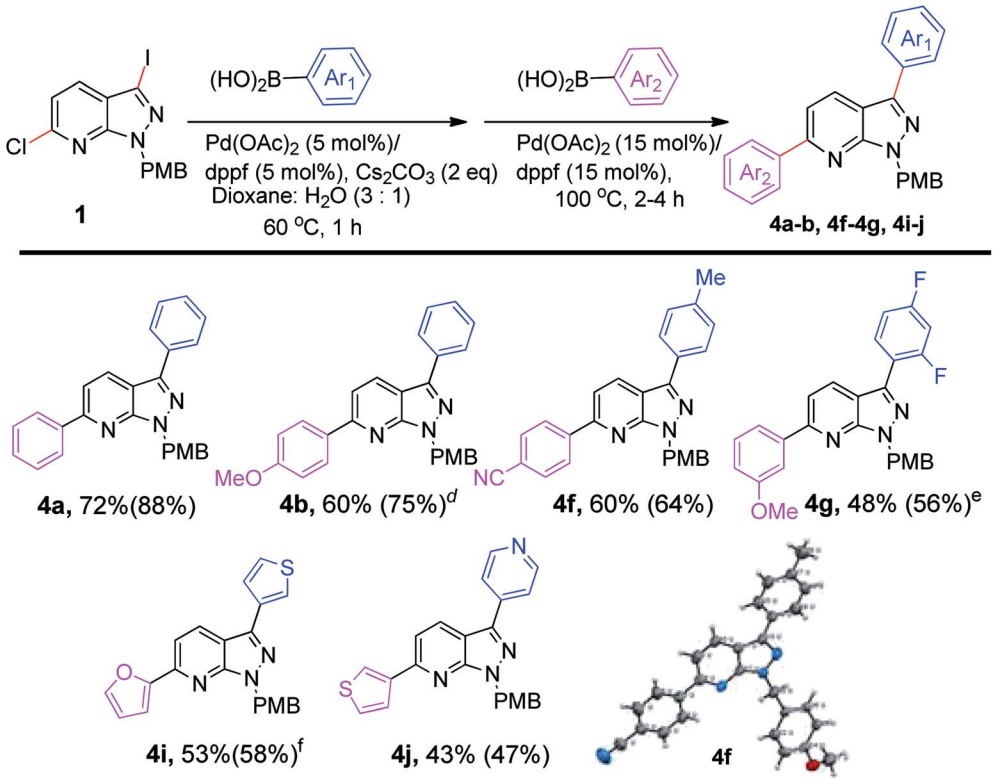
[a] Reaction conditions: 6-chloro-1-(4-methoxybenzyl)-3-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine **3** (1.0 equiv.), arylboronic acid **2** (1.0 equiv.), $Pd(OAc)_2$ (5 mol%), ligand (5 mol%), base (2.0 equiv.), 1,4-dioxane : water (3 : 1) (5 mL), 2 h. [b] Isolated yields. [c] 15% of starting material recovered; n.r. = no reaction. [d] 25% of starting material recovered; n.r. = no reaction.



Scheme 2 Pd-catalyzed C6-arylation of 3-arylpyrazolo[3,4-*b*]pyridines.[a,b] [a]Reaction conditions: 6-chloro-1-(4-methoxybenzyl)-3-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine **3** (1.0 equiv.), arylboronic acid **2** (1.0 equiv.), $Pd(OAc)_2$ (5 mol%), dppf (5 mol%), Cs_2CO_3 (2.0 equiv.), 1,4-dioxane : water (3 : 1) (5 mL), 100 °C, 2 h; [b]isolated yields.

(–CN, $–NO_2$) boronic acid also proceeded smoothly with the present starting moiety, giving 72% and 53% of desired products (**4f** & **4h**). The difluorophenyl group containing pyrazolopyridine coupled with 3-methoxyphenylboronic acid produced **4g** in 63% yield. The present strategy is efficient enough to couple with heteroaromatic boronic acids producing diarylated product (**4i-j**) in 62–68% yield. In addition, we successfully arylated the pyrazolo[3,4-*b*]pyridine with benzo[*d*][1,3]dioxol-5-ylboronic acid, giving 57% of **4k**. The 3-hydroxyphenylboronic acid was quite stable under these conditions, as the coupled product (**4l**) was isolated in 52% yield.

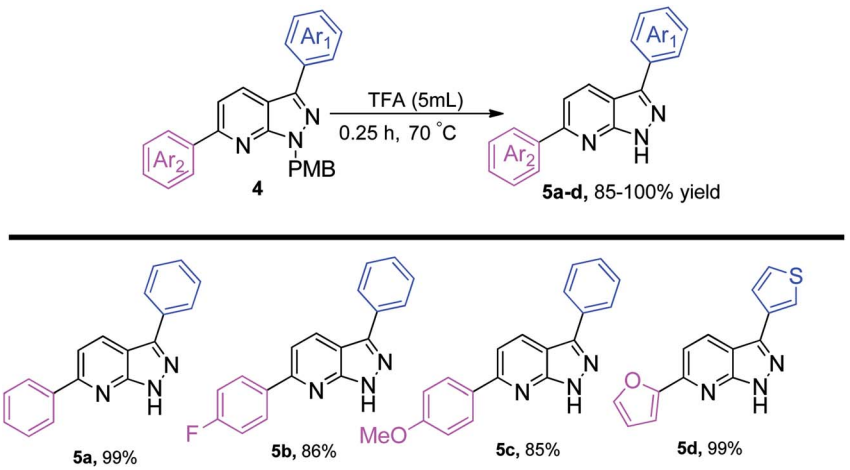
After successful stepwise sequential diarylation, we turned our focus to the one-pot arylation reaction to synthesize 3,6-diarylated pyrazolopyridines (Scheme 3). The combinations of boronic acids that showed the best overall yield in our previous stepwise synthesis of diarylated pyrazolo[3,4-*b*]pyridines (Scheme 2) were selected for one-pot sequential arylation of 6-chloro-3-iodo-1-(4-methoxybenzyl)-1*H*-pyrazolo[3,4-*b*]pyridine (**1**). The Suzuki cross-coupling was first performed with $Pd(OAc)_2$/dppf as the catalyst in the presence of Cs_2CO_3 as base and $Ar_1B(OH)_2$ at 60 °C. Upon completion of the coupling, a second arylation was accomplished with $Ar_2B(OH)_2$ and the same Pd $(OAc)_2$/dppf (15 mol%) catalyst, at 100 °C without purification of the intermediate. The one-pot coupling reaction afforded diaryl-1*H*-pyrazolo[3,4-*b*]pyridines (**4a-b**; **4f-g**; **4i-j**) in moderate to good yields (43–72%). In a one-pot reaction diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine (**4a**) was isolated in 72% yield. Insertion of 4-methoxyphenylboronic acid as a second arylating agent was successful, as **4b** was isolated in 60% yield in **4h**. The combination of 4-methylphenylboronic acid as the first arylating agent and 4-cyanophenylboronic acid as the second proved to be successful, with an isolated yield of 60% (**4f**). The structure of **4f** was determined by X-ray crystallography. Further, when 3-methoxyphenylboronic acid reacted with 6-chloro-3-(2,4-difluorophenyl)-1-(4-methoxybenzyl)-1*H*-pyrazolo[3,4-*b*]pyridine, the product (**4g**) was isolated in 48% yield in 6 h. The combinations of 5/5 or 5/6 member heterocyclic boronic acids were screened and afforded moderate yields of 53% (**4i**) and 43% (**4j**) respectively. The study suggested that the overall yield of biarylated product in the one pot method is comparable to the stepwise sequential method. We have observed that C3 arylation was preferred over C6 arylation, in our reaction conditions. But, we cannot neglect the role of I *vs.* Cl as one of the governing factors. Thus the one-pot method can



Scheme 3 Sequential one-pot synthesis of 3,6-diarylpyrazolo[3,4-*b*]pyridines.[a,b,c] [a]Reaction conditions: 6-chloro-3-iodo-1-(4-methoxybenzyl)-1*H*-pyrazolo[3,4-*b*]pyridine **1** (1.0 equiv.), arylboronic acid **2** (1.0 equiv.), $Pd(OAc)_2$ (5 mol%), dppf (5 mol%), Cs_2CO_3 (2.0 equiv.), 1,4-dioxane : water (3 : 1) (5 mL), 60 °C for 1 h; after consumption of pyrazolopyridine **1**, addition of $Pd(OAc)_2$ (15 mol%), dppf (15 mol%), arylboronic acid **2** (1.2 equiv.), 100 °C, 2–4 h; [b]isolated yields; [c]formal average yields of the two steps shown in parentheses; [d]10% of starting material recovered; [e]6 h for second arylation and 15% of starting material recovered; [f]6–8 h for second arylation.

be used as a time and cost-effective method for the diarylation of pyrazolopyridines (Scheme 3).

The *p*-methoxybenzyl protecting group (PMB) was easily cleaved by the action of trifluoroacetic acid (TFA) at 70 °C within 0.25 h.[16a] We performed a THP de-protection reaction of **3w** with methanolic HCl, giving 97% yield of the required product.[16b] A rapid screening showed that diarylated pyrazolo[3,4-*b*]pyridines can be de-protected to produce **5a–5d**, in excellent yields (Scheme 4). The electron-withdrawing and electron-donating groups do not greatly influence the yield of final compounds. It is important to mention here that the di-heteroarylated product, *e.g.* a combination of thiophene and furan, remained intact under de-protection conditions to give **5d** in 99% yield.



Scheme 4 De-protection of the PMB group.[a,b] [a]Reaction conditions: 3,6-diaryl-1*H*-pyrazolo[3,4-*b*]pyridine **4** (1 equiv.), TFA (5 mL), 70 °C, 0.25 h; [b]isolated yields.

3. Conclusion

In conclusion, we have developed catalytic systems for the stepwise sequential arylation of pyrazolo[3,4-*b*]pyridines at the C3 and C6 positions *via* Suzuki–Miyaura reactions. The chemoselective sequential arylation strategy was also performed in one pot without a loss of efficiency when compared to the corresponding stepwise synthesis. This route offers significant flexibility to access heteroaromatic frameworks with challenging substitution patterns. We hope that this new methodology will open access to synthesizing new chemotypes and to discovering functionalized pyrazolo[3,4-*b*]pyridines with therapeutic potential.

4. Experimental

General information

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All Suzuki–Miyaura reactions were performed in a round bottom flask and monitored through thin layer chromatography (TLC silica gel F_{254}, glass plates) and analysed using 254 nm UV light and iodine, ninhydrin stains. Melting points were recorded on a Büchi Melting Point B-545 instrument and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded with a 400 MHz (^{1}H = 400 and ^{13}C = 100 MHz) or 500 MHz (^{1}H = 500 and ^{13}C = 125 MHz) spectrometer. Chemical shift values of ^{1}H NMR were recorded in parts per million (ppm, δ) relative to tetramethylsilane (TMS, 0.00 ppm). Multiplicities are indicated as s(singlet), d(doublet), t(triplet), q(quartet), m(multiplet), coupling constants (J) were reported in Hertz (Hz) and integration value. Chemical shift values of ^{13}C NMR were recorded in parts per million (ppm, δ) and calibrated to the residual peak as an internal standard ($CDCl_3$: δ = 77.0 ppm and DMSO: δ = 39.0 ppm). High-resolution mass spectra (HRMS) were obtained using the ESI-TOF method.

General procedure for the synthesis of monoarylpyrazolo [3,4-*b*]pyridines and their derivatives. To a round bottom flask, were added 3-iodo-1-methyl-1*H*-pyrazolo[3,4-*b*]pyridine **1** (0.5 mmol) dissolved in 5 mL of dioxane : water (3 : 1), catalyst and ligand 5 mol% each. Arylboronic acid **2** (0.5 mmol, 1.0 equiv.) and base (2 equiv.), were added to the above after 5 min of stirring and started heating at 60 °C. When the TLC indicated the total consumption of starting material, the reaction mixture was allowed to cool at ambient temperature. The reaction mixture was extracted with ethyl acetate and organic layer was washed with brine. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc) to give the desired products (**3a–3ak**).

*1-Methyl-3-phenyl-1H-pyrazolo[3,4-b]pyridine (**3a**).* Light yellow solid; 98% yield (102 mg); mp 86–87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (dd, J = 4.5, 1.5 Hz, 1H), 8.38 (dd, J = 7.6, 1.5 Hz, 1H), 8.01–7.90 (m, 2H), 7.56 (t, J = 7.6 Hz, 2H), 7.48–7.45 (m, 1H), 7.22 (dd, J = 8.4, 4.6, 1H), 4.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 148.6, 142.4, 133.1, 130.4, 128.9, 128.2, 126.9, 116.8, 113.4, 33.9. HRMS (ESI): m/z calcd. for $C_{13}H_{11}N_3$[M + H]$^+$: 210.1031; found: 210.1015.

*1-Methyl-3-(p-tolyl)-1H-pyrazolo[3,4-b]pyridine (**3b**).* Light brown solid; 85% yield (94.4 mg) mp 52–53 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (dd, J = 4.6, 1.4 Hz, 1H), 8.25–8.22 (m, 1H), 7.78 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.2 Hz, 2H), 7.07 (dd, J = 8.2, 4.6, 1H), 4.14 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.2, 148.4, 142.4, 138.0, 130.3, 130.2, 129.5, 126.7, 116.6, 113.8, 33.8, 21.2. HRMS (ESI): m/z calcd. for $C_{14}H_{13}N_3$[M + H]$^+$: 224.1187; found: 224.1182.

*3-(3-Methoxyphenyl)-1-methyl-1H-pyrazolo[3,4-b]pyridine (**3c**).* Dusky white solid; 81% yield (96.5 mg); mp 85–86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63–8.61 (m, 1H), 8.40–8.38 (m, 1H), 7.59–7.55 (m, 2H), 7.49–7.45 (m, 1H), 7.24–7.20 (m, 1H), 7.03–7.00 (m, 1H), 4.27 (s, 3H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 151.3, 148.6, 142.3, 134.4, 130.4, 129.9, 119.4, 116.8, 114.1, 113.4, 112.0, 55.3, 33.9. HRMS (ESI): m/z calcd. for $C_{14}H_{13}N_3O$[M + H]$^+$: 240.1136; found: 240.1138.

*3-(4-Methoxyphenyl)-1-methyl-1H-pyrazolo[3,4-b]pyridine (**3d**).* Dusky white solid, 97% yield (115.5 mg), mp 76–77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (dd, J = 4.6, 0.9 Hz, 1H), 8.29 (dd, J = 8.2, 0.9 Hz, 1H), 7.88–7.86 (m, 2H), 7.16–7.13 (m, 1H), 7.04 (d, J = 8.2, 2H), 4.19 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 151.3, 148.5, 142.3, 130.4, 128.1, 125.8, 116.5, 114.3, 113.3, 55.3, 33.8. HRMS (ESI): m/z calcd. for $C_{14}H_{13}N_3O$[M + H]$^+$: 240.1136; found: 240.1141.

*3-(4-Bromophenyl)-1-methyl-1H-pyrazolo[3,4-b]pyridine (**3e**).* White solid; 75% yield (107.1 mg); mp 104–105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (dd, J = 4.6, 0.92 Hz, 1H), 8.32 (dd, J = 8.6, 1.36 Hz, 1H), 7.87–7.85 (m, 2H), 7.67–7.65 (m, 2H), 7.24–7.20 (m, 1H), 4.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 148.7, 141.2, 132.1, 132.0, 130.0, 128.3, 122.2, 117.0, 113.2, 33.9. HRMS (ESI): m/z calcd. for $C_{13}H_{10}BrN_3$[M + H]$^+$: 288.0136; found: 288.0129.

*3-(2,4-Difluorophenyl)-1-methyl-1H-pyrazolo[3,4-b]pyridine (**3f**).* White solid; 46% yield (56.1 mg); mp 92–93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (dd, J = 4.6, 1.5 Hz, 1H), 8.25–8.22 (m, 1H), 7.95–7.87 (m, 1H), 7.24–7.20 (m, 1H), 7.10–7.01 (m, 2H), 4.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0 (dd, J = 247.9, 10.9 Hz, 1C), 159.9 (dd, J = 249.8, 11.4 Hz, 1C), 151.0, 148.9, 137.4, 131.3 (dd, J = 9.5, 5.7 Hz, 1C), 131.1, 131.0, 116.9, 114.1, 112.0 (dd, J = 20.9, 2.86 Hz, 1C), 104.4 (t, J = 25.7 Hz, 1C), 34.0. HRMS (ESI): m/z calcd. for $C_{13}H_9F_2N_3$[M + H]$^+$: 246.0842; found: 246.0858.

*3-(3,5-Bis(trifluoromethyl)phenyl)-1-methyl-1H-pyrazolo[3,4-b] pyridine (**3g**).* Off white solid; 79% yield (135.7 mg); mp 118–119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (dd, J = 4.5, 1.5 Hz, 1H), 8.41 (s, 2H), 8.32 (d, J = 8.4 Hz, 1H), 7.89 (s, 1H), 7.26 (dd, J = 8.4, 4.6, 1H), 4.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 149.2, 139.2, 135.4, 132.2 (q, J = 34.3 Hz, 1C), 129.5, 126.4, 124.6, 121.9, 121.49–121.42 (m, 1C), 117.8, 113.0, 34.2. HRMS (ESI): m/z calcd. for $C_{15}H_9F_6N_3$[M + H]$^+$: 346.0778; found: 346.0771.

*6-Chloro-1-methyl-3-phenyl-1H-pyrazolo[3,4-b]pyridine (**3h**).* Creamy white solid; 67% yield (81.1 mg); mp 75–76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21–8.19 (m, 1H), 7.87 (d, J = 7.8 Hz, 2H), 7.50–7.46 (m, 2H), 7.41–7.39 (m, 1H), 7.14–7.12 (m, 1H), 4.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.6, 150.4, 142.9, 132.5,

132.5, 128.9, 128.5, 126.8, 117.3, 112.0, 34.1; HRMS (ESI): *m*/*z* calcd. for $C_{13}H_{10}ClN_3[M + H]^+$: 244.0641; found: 244.0621.

6-Chloro-1-methyl-3-(p-tolyl)-1H-pyrazolo[3,4-b]pyridine ***(3i).*** White solid; 99% yield (126.8 mg); mp 141–142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22–8.20 (m, 1H), 7.78 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 7.8 Hz, 2H), 7.14 (dd, J = 8.7, 1.3 Hz, 1H), 4.15 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.6, 150.3, 143.0, 138.5, 132.5, 129.7, 129.6, 126.7, 117.2, 112.0, 34.0, 21.3; HRMS (ESI): *m*/*z* calcd. for $C_{14}H_{12}ClN_3[M + H]^+$: 258.0797; found: 258.0796.

6-Chloro-3-(4-methoxyphenyl)-1-methyl-1H-pyrazolo[3,4-b]pyridine ***(3j).*** White solid; 78% yield (106.1 mg); mp 137–138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 8.2 Hz, 1H), 7.83 (d, J = 8.2 Hz, 2H), 7.15–7.13 (m, 1H), 7.03 (d, J = 8.2 Hz, 2H), 4.14 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 150.6, 150.3, 142.8, 132.5, 128.1, 125.2, 117.1, 114.4, 111.9, 55.3, 34.0; HRMS (ESI): *m*/*z* calcd. for $C_{14}H_{12}ClN_3O[M + H]^+$: 274.0746; found: 274.0745.

6-Chloro-3-(4-fluorophenyl)-1-methyl-1H-pyrazolo[3,4-b]pyridine ***(3k).*** White solid; 83% yield (107.9 mg); mp 149–150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19–8.17 (m, 1H), 7.89–7.85 (m, 2H), 7.26–7.15 (m, 3H), 4.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9 (d, J = 246.9 Hz, 1C), 150.6, 142.0, 132.2, 128.8, 128.5 (d, J = 7.6 Hz, 1C), 117.5, 116.1, 115.9, 111.8, 34.1; HRMS (ESI): *m*/*z* calcd. for $C_{13}H_9ClFN_3[M + H]^+$: 262.0541; found: 262.0545.

1-(4-Methoxybenzyl)-3-phenyl-1H-pyrazolo[3,4-b]pyridine ***(3l).*** Dusky brown solid; 62% yield (97.4 mg); mp 115–116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (dd, J = 4.6, 1.5 Hz, 1H), 8.39–8.37 (m, 1H), 8.01 (d, J = 7.6 Hz, 2H), 7.55 (t, J = 7.6 Hz, 2H), 7.48–7.44 (m, 3H), 7.24–7.20 (m, 1H), 6.88 (dd, J = 6.8, 2.2 Hz, 2H), 5.78 (s, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 59.0, 151.1, 148.7, 142.8, 133.2, 130.3, 129.3, 129.2, 128.8, 128.2, 127.0, 117.0, 113.8, 113.6, 55.1, 50.2. HRMS (ESI): *m*/*z* calcd. for $C_{20}H_1N_3O[M + H]^+$: 316.1449; found: 316.1468.

1-(4-Methoxybenzyl)-3-(p-tolyl)-1H-pyrazolo[3,4-b]pyridine ***(3m).*** Light brown solid; 87% yield (142.7 mg); mp 76–77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, J = 4.5, 1H), 8.23 (d, J = 7.6 Hz, 1H), 7.84 (d, J = 7.6 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 7.29–7.26 (m, 2H), 7.09–7.06 (m, 1H), 6.85–6.80 (m, 2H), 5.70 (s, 2H), 3.69 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 150.9, 148.4, 142.7, 137.9, 130.2, 129.4, 129.2, 128.3, 126.8, 116.7, 113.7, 113.6, 113.4, 54.9, 50.0, 21.1. HRMS (ESI): *m*/*z* calcd. for $C_{21}H_{19}N_3O[M + H]^+$: 330.1606; found: 330.1607.

1-(4-Methoxybenzyl)-3-(4-methoxyphenyl)-1H-pyrazolo[3,4-b]pyridine ***(3n).*** White solid; 79% yield (135.9 mg); mp 125–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 4.6, 1H), 8.36 (dd, J = 8.4, 1.5 Hz, 1H), 7.96 (d, J = 9.1 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 7.24–7.20 (m, 1H), 7.10 (d, J = 9.1 Hz, 2H), 6.90 (d, J = 9.1 Hz, 2H), 5.78 (s, 2H), 3.99 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 159.0, 151.0, 148.6, 142.7, 130.3, 129.3, 129.2, 128.3, 125.9, 116.7, 114.2, 113.8, 113.5, 55.3, 55.1, 50.1. HRMS (ESI): *m*/*z* calcd. for $C_{21}H_{19}N_3O[M + H]^+$: 346.1555; found: 346.1555.

3-(4-Bromophenyl)-1-(4-methoxyphenyl)-1H-pyrazolo[3,4-b]pyridine ***(3o).*** Off white solid; 62% yield (121.4 mg); mp 75–76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (dd, J = 4.1, 0.9 Hz, 1H), 8.23 (dd, J = 8.2, 1.4 Hz, 1H), 7.81–7.79 (m, 2H), 7.60–7.58 (m, 2H), 7.37–7.32 (m, 2H), 7.15 (d, J = 8.2, 4.6 Hz, 1H), 6.82–6.80 (m, 2H), 5.68 (s, 2H), 3.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 151.1, 148.8, 141.6, 132.1, 131.9, 130.0, 129.3, 129.0, 128.4, 122.2, 117.2, 113.8, 113.4, 55.1, 50.3. HRMS (ESI): *m*/*z* calcd. for $C_{20}H_{16}BrN_3O[M + H]^+$: 394.0554; found: 394.0546.

4-(1-(4-Methoxybenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl)benzonitrile ***(3p).*** Light yellow solid; 68% yield (115.3 mg); mp 175–176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (dd, J = 4.5, 1.8 Hz, 1H), 8.33 (dd, J = 8.2, 1.3 Hz, 1H), 8.09 (dd, J = 6.88, 1.8 Hz, 2H), 7.76 (dd, J = 6.8, 1.8 Hz, 2H), 7.40–7.38 (m, 2H), 7.23 (dd, J = 8.2, 4.6 Hz, 1H), 6.83 (dd, J = 6.88, 2.2 Hz, 2H), 5.72 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 151.2, 149.1, 140.6, 137.7, 132.6, 129.9, 129.5, 128.8, 127.2, 118.8, 117.8, 114.0, 113.5, 111.4, 55.2, 50.5. HRMS (ESI): *m*/*z* calcd. for $C_{21}H_{16}N_4O[M + H]^+$: 341.1402; found: 341.1391.

3-(2,4-Difluorophenyl)-1-(4-methoxybenzyl)-1H-pyrazolo[3,4-b] pyridine ***(3q).*** Pale yellow solid; 92% yield (161.0 mg); mp 60–61 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (dd, J = 4.6, 1.5 Hz, 1H), 8.25–8.22 (m, 1H), 7.93 (q, J = 8.4 Hz, 1H), 7.48–7.45 (m, 2H), 7.21 (dd, J = 8.4, 4.6 Hz, 1H), 7.09–7.02 (m, 2H), 6.92–6.89 (m, 2H), 5.80 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$). ^{13}C NMR showed one less carbon, it might be due to one carbon peak got merged at 129.3 ppm. δ 162.9 (dd, J = 248.8, 11.4 Hz, 1C), 159.3 (dd, J = 250.7, 12.4 Hz, 1C), 159.0, 150.7, 148.9, 137.7, 131.5 (dd, J = 9.5, 5.7 Hz, 1C), 130.9 (d, J = 10.4, 1C), 129.3 (b, 1C), 129.0, 117.0, 114.2, 113.8, 111.9 (d, J = 20.9 Hz, 1C), 104.6–104.0 (m, 1C), 55.2–54.9 (m, 1C), 50.2. HRMS (ESI): *m*/*z* calcd. for $C_{20}H_{15}F_2N_3O[M + H]^+$: 352.1261; found: 352.1264.

3-(3,5-Bis(trifluoromethyl)phenyl)-1-(4-methoxybenzyl)-1H-pyrazolo[3,4-b]pyridine ***(3r).*** White solid; 93% yield (209.1 mg); mp 127–128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (dd, J = 4.5, 1.5 Hz, 1H), 8.40 (s, 2H), 8.31–8.29 (m, 1H), 7.87 (s, 1H), 7.40 (d, J = 8.4 Hz, 2H), 7.28–7.26 (m, 1H), 6.84 (dd, J = 6.84, 2.2 Hz, 2H), 5.73 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 151.2, 149.3, 139.6, 135.5, 132.2 (q, J = 32.3 Hz, 1C), 129.5, 128.7, 126.6, 124.6, 121.9, 121.4 (b, 1C), 117.9, 114.0, 113.2, 55.2, 50.6. HRMS (ESI): *m*/*z* calcd. for $C_{22}H_{15}F_6N_3O[M + H]^+$: 452.1197; found: 452.1191.

6-Chloro-1-(4-methoxybenzyl)-3-phenyl-1H-pyrazolo[3,4-b]pyridine ***(3s).*** White solid; 93% yield (162 mg); mp 85–86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22–8.19 (m, 1H), 7.90–7.88 (m, 2H), 7.49–7.45 (m, 2H), 7.41–7.38 (m, 3H), 7.16–7.13 (m, 1H), 6.83 (dd, J = 3.6, 1.4 Hz, 2H), 5.63 (s, 2H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 150.5, 150.3, 143.2, 132.7, 132.4, 129.5, 128.8, 128.7, 128.5, 127.0, 117.6, 113.8, 112.2, 55.1, 50.3; HRMS (ESI): *m*/*z* calcd. for $C_{20}H_{16}ClN_3O[M + H]^+$: 350.1059; found: 350.1041.

6-Chloro-1-(4-methoxybenzyl)-3-(3-nitophenyl)-1H-pyrazolo[3,4-b]pyridine ***(3t).*** Light yellow solid; 93% yield (182.7 mg); mp 155–156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76–8.75 (m, 1H), 8.27–8.22 (m, 3H), 7.65 (t, J = 7.7 Hz, 1H), 7.42–7.40 (m, 2H), 7.26–7.23 (m, 1H), 6.85 (dd, J = 6.8, 1.8 Hz, 2H), 5.65 (s, 2H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 151.0, 150.3, 148.6, 140.6, 134.5, 132.5, 131.8, 129.9, 129.7, 128.2, 122.9, 121.5, 118.4, 114.0, 111.8, 55.2, 50.6; HRMS (ESI): *m*/*z* calcd. for $C_{20}H_{15}ClN_4O[M + H]^+$: 395.0910; found: it decompose during mass analysis.

*6-Chloro-3-(2,4-difluorophenyl)-1-(4-methoxybenzyl)-1H-pyrazolo [3,4-b]pyridine (**3u**).* White solid; 89% yield (170.9 mg); mp 87–88 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (dd, J = 8.4, 3.2 Hz, 1H), 7.87 (q, J = 8.3 Hz, 1H), 7.42 (d, J = 8.5 Hz, 2H), 7.19 (d, J = 8.4 Hz, 1H), 7.04–6.97 (m, 2H), 6.87 (d, J = 8.5 Hz, 2H), 5.68 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.1 (dd, J = 249.2, 32.7 Hz, 1C), 159.9 (dd, J = 249.7, 11.7 Hz, 1C), 159.3, 150.8, 150.1, 138.2, 133.3 (d, J = 10.8 Hz, 1C), 131.5 (dd, J = 9.7, 5.6 Hz, 1C), 129.6, 128.6, 117.8, 116.7 (dd, J = 14.8, 2.5 Hz, 1C), 114.0, 112.9, 112.1 (d, J = 20.8 Hz, 1C), 104.4 (t, J = 25.8 Hz, 1C), 55.2, 50.5; HRMS (ESI): m/z calcd. for $C_{20}H_{14}ClF_2N_3O[M + H]^+$: 386.0871; found: 386.0859.

*6-Chloro-1-(4-methoxybenzyl)-3-(p-tolyl)-1H-pyrazolo[3,4-b]pyridine (**3v**).* White solid; 90% yield (162.9 mg); mp 110–111 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, J = 8.2 Hz, 1H), 7.81 (d, J = 7.2 Hz, 2H), 7.42 (d, J = 7.6 Hz, 2H), 7.33–7.28 (m, 2H), 7.17 (d, J = 8.3 Hz, 1H), 6.86 (d, J = 7.5 Hz, 2H), 5.66 (s, 2H), 3.78 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 150.5, 150.4, 143.4, 138.5, 132.5, 129.9, 129.6, 129.6, 128.9, 126.9, 117.5, 113.9, 112.2, 55.2, 50.3, 21.3; HRMS (ESI): m/z calcd. for $C_{21}H_{18}ClN_3O[M + H]^+$: 364.1216; found: 364.1201.

*3-Phenyl-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-b]pyridine (**3w**).* Light brown solid; 97% yield (135 mg); mp 74–75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, J = 4.6 Hz, 1H), 8.13 (d, J = 7.6 Hz, 1H), 7.86 (d, J = 7.6 Hz, 2H), 7.35 (t, J = 7.6 Hz, 2H), 7.27–7.24 (m, 1H), 7.01–6.98 (m, 1H), 6.09 (dd, J = 10.7, 2.3 Hz, 1H), 4.04–4.01 (m, 1H), 3.74–3.69 (m, 1H), 2.73–2.64 (m, 1H), 2.03 (b, 1H), 1.91–1.88 (m, 1H), 1.70–1.60 (m, 2H), 1.48–1.46 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.0, 148.3, 143.3, 132.6, 130.0, 128.4, 128.0, 126.8, 117.3, 113.7, 82.0, 67.8, 29.0, 24.6, 22.7. HRMS (ESI): m/z calcd. for $C_{17}H_{17}N_3O[M + H]^+$: 280.1449; found: 280.1442.

*1-(Tetrahydro-2H-pyran-2-yl)-3-(p-tolyl)-1H-pyrazolo[3,4-b]pyridine (**3x**).* Brown solid; 88% yield (128.5 mg); mp 76–77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (dd, J = 4.6, 1.3 Hz, 1H), 8.32 (dd, J = 8.2, 1.8 Hz, 1H), 7.88 (d, J = 7.7 Hz, 2H), 7.31–7.29 (m, 2H), 7.21–7.18 (m, 1H), 6.19 (dd, J = 10.5, 2.3 Hz, 1H), 4.18–4.15 (m, 1H), 3.89–3.86 (m, 1H), 2.83–2.74 (m, 1H), 2.43–2.42 (m, 3H), 2.18–2.17 (m, 1H), 2.04–2.01 (m, 1H), 1.84–1.83 (m, 2H), 1.65 (b, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 148.6 (d, J = 2.8 Hz, 1C), 143.9, 138.3, 130.5 (d, J = 2.8 Hz, 1C), 130.1, 129.4 (d, J = 4.7 Hz, 1C), 127.2, 117.5 (d, J = 6.67 Hz, 1C), 114.2, 82.3 (d, J = 9.5 Hz, 1C), 68.3, 29.5, 25.0, 23.1, 21.3 (d, J = 3.8 Hz, 1C). HRMS (ESI): m/z calcd. for $C_{18}H_{19}N_3O[M + H]^+$: 294.1606; found: 294.1605.

*3-(3-Methoxyphenyl)-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo [3,4-b]pyridine (**3y**).* Yellow liquid; 96% yield (147.9 mg); liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (dd, J = 4.6, 1.4 Hz, 1H), 8.35 (dd, J = 8.2, 1.3 Hz, 1H), 7.59–7.57 (m, 2H), 7.43 (t, J = 8.0 Hz, 1H), 7.21 (d, J = 8.2, 4.6 Hz, 1H), 7.00–6.97 (m, 1H), 6.23 (dd, J = 10.5, 2.2 Hz, 1H), 4.21–4.11 (m, 1H), 3.91 (s, 3H), 3.89–3.85 (m, 1H), 2.88–2.78 (m, 1H), 2.21–2.18 (m, 1H), 2.06–2.03 (m, 1H), 1.86–1.82 (m, 2H), 1.67–1.65 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 151.3, 148.6, 143.6, 134.1, 130.4, 129.6, 119.7, 117.6, 114.2, 114.1, 112.4, 82.3, 68.2, 55.2, 29.53, 24.9, 23.0; HRMS (ESI): m/z calcd. for $C_{18}H_{19}N_3O_2[M + H]^+$: 310.1555; found: 310.1538.

*3-(4-Bromophenyl)-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-b]pyridine (**3z**).* Creamy white solid; 67% yield (119.1 mg); mp 112–113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (dd, J = 4.6, 1.8 Hz, 1H), 8.28 (dd, J = 8.2, 1.8 Hz, 1H), 7.88–7.85 (m, 2H), 7.63–7.60 (m, 2H), 7.22 (q, J = 4.6 Hz, 1H), 6.20 (dd, J = 10.5, 2.3 Hz, 1H), 4.18–4.14 (m, 1H), 3.89–3.83 (m, 1H), 2.81–2.72 (m, 1H), 2.19–2.16 (m, 1H), 2.03–2.00 (m, 1H), 1.86–1.79 (m, 2H), 1.65–1.63 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$). ^{13}C NMR showed one less carbon, it might be due to one carbon peak got merged at 131.9 ppm. δ 151.3, 148.8, 142.7, 131.9, 130.2, 128.7, 122.5, 117.8, 113.9, 82.3, 68.3, 29.9, 24.9, 23.0; HRMS (ESI): m/z calcd. for $C_{18}H_{16}BrN_3O[M + H]^+$: 358.0554; found: 358.0547.

*3-(4-Fluorophenyl)-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-b]pyridine (**3aa**).* White solid; 97% yield (143.6 mg); mp 92–93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (dd, J = 4.6, 1.4 Hz, 1H), 8.28 (dd, J = 8.2, 1.4 Hz, 1H), 7.97–7.93 (m, 2H), 7.23–7.16 (m, 3H), 6.20 (dd, J = 10.5, 2.7 Hz, 1H), 4.18–4.11 (m, 1H), 3.89–3.83 (m, 1H), 2.82–2.72 (m, 1H), 2.19–2.16 (m, 1H), 2.04–2.01 (m, 1H), 1.89–1.79 (m, 2H), 1.68–1.63 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9 (d, J = 246.9 Hz, 1C), 151.4, 148.8 (d, J = 3.8 Hz, 1C), 143.0, 130.2 (d, J = 3.82 Hz, 1C), 129.1 (d, J = 2.86 Hz, 1C), 129.0 (d, J = 8.58 Hz, 1C), 117.7 (d, J = 5.72 Hz, 1C), 115.6 (dd, J = 20.2, 5.7 Hz, 1C), 114.0, 82.3 (d, J = 9.5 Hz, 1C), 68.4, 29.5, 25.0, 23.1; HRMS (ESI): m/z calcd. for $C_{17}H_{16}FN_3O[M + H]^+$: 298.1355; found: 298.1324.

*3-(2,4-Difluorophenyl)-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo [3,4-b]pyridine (**3ab**).* Light brown liquid; 88% yield (138.1 mg); liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59–8.58 (m, 1H), 8.19–8.17 (m, 1H), 7.96–7.90 (m, 1H), 7.21–7.18 (m, 1H), 7.04–6.95 (m, 2H), 6.22 (dd, J = 10.5, 2.2 Hz, 1H), 4.18–4.11 (m, 1H), 3.89–3.84 (m, 1H), 2.79–2.71 (m, 1H), 2.18 (b, 1H), 2.05–2.01 (m, 1H), 1.85–1.80 (m, 2H), 1.65–1.63 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1 (dd, J = 249.8, 11.4 Hz, 1C), 160.0 (dd, J = 250.7, 12.3 Hz, 1C), 150.9, 148.9, 138.9, 131.7 (q, J = 4.7 Hz, 1C), 131.1 (d, J = 10.4 Hz, 1C), 117.6, 116.8 (dd, J = 14.3, 3.8 Hz, 1C), 114.8, 111.9 (dd, J = 20.9, 2.8 Hz, 1C), 104.2 (t, J = 25.7 Hz, 1C), 82.3, 68.3, 29.4, 24.9, 23.0; HRMS (ESI): m/z calcd. for $C_{17}H_{15}F_2N_3O[M + H]^+$: 316.1261; found: 316.1259.

*3-(3,5-Bis(trifluoromethyl)phenyl)-1-(tetrahydro-2H-pyran-2-yl)-1H-pyrazolo[3,4-b]pyridine (**3ac**).* Creamy white solid; 90% yield (186.2 mg); mp 160–161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, J = 4.5 Hz, 1H), 8.46 (s, 2H), 8.33 (dd, J = 7.3, 0.92 Hz, 1H), 7.91 (s, 1H), 7.33–7.31 (m, 1H), 6.25 (dd, J = 10.5, 2.3 Hz, 1H), 4.20–4.17 (m, 1H), 3.91–3.85 (m, 1H), 2.84–2.75 (m, 1H), 2.22–2.18 (m, 1H), 2.05–2.02 (m, 1H), 1.87–1.82 (m, 2H), 1.68–1.66 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 149.4, 140.7, 135.2, 132.2 (q, J = 32.4 Hz, 1C), 129.7, 126.9, 124.6, 121.9–121.7 (m, 1C), 118.5, 113.6, 82.5, 68.6, 29.5, 24.9, 23.0; HRMS (ESI): m/z calcd. for $C_{19}H_{15}F_6N_3O[M + H]^+$: 416.1197; found: 416.1183.

*1-(4-Methoxybenzyl)-3-(thiophen-3-yl)-1H-pyrazolo[3,4-b]pyridine (**3ad**).* Brown solid; 63% yield (100.8 mg); mp 108–109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (dd, J = 4.6, 1.3 Hz, 1H), 8.26 (dd, J = 7.8, 1.4 Hz, 1H), 7.76 (dd, J = 3.2, 1.4 Hz, 1H), 7.68 (dd, J = 5.0, 1.4 Hz, 1H), 7.43 (dd, J = 5.0, 3.2 Hz, 1H), 7.36–7.34 (m, 2H), 7.15 (dd, J = 7.8, 4.6 Hz, 1H), 6.81 (dd, J = 6.8, 2.2 Hz, 2H), 5,68 (s, 2H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$). ^{13}C NMR

showed one less carbon, it might be due to one carbon peak got merged at 129.2 ppm. δ 159.0, 150.8, 148.8, 139.2, 134.3, 130.0, 129.2, 126.4, 126.1, 121.8, 116.9, 113.8, 113.5, 55.1, 50.1; HRMS (ESI): *m*/*z* calcd. for $C_{18}H_{15}N_3OS[M + H]^+$: 322.1013; found: 322.1001.

*6-Chloro-1-(4-methoxybenzyl)-3-(thiophen-3-yl)-1H-pyrazolo[3,4-b]pyridine (**3ae**).* Orange solid; 86% yield (152.2 mg); mp 130–131 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, J = 8.3 Hz, 1H), 7.74–7.74 (m, 1H), 7.65 (d, J = 5.0 Hz, 1H), 7.45–7.44 (m, 1H), 7.38 (d, J = 8.5 Hz, 2H), 7.17 (d, J = 8.3 Hz, 1H), 6.84 (d, J = 8.6 Hz, 2H), 5.62 (s, 2H), 3.76 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$). ^{13}C NMR showed one less carbon, it might be due to one carbon peak got merged at 126.3 ppm. δ 159.2, 150.6, 150.1, 139.6, 133.9, 132.1, 129.5, 128.8, 126.3 (b, 1C), 122.2, 117.6, 113.9, 112.1, 55.2, 50.2; HRMS (ESI): *m*/*z* calcd. for $C_{18}H_{14}ClN_3OS[M + H]^+$: 356.0624; found: it decomposes during mass analysis.

*3-(Benzo[d][1,3]dioxo-5-yl)-1-(4-methoxybenzyl)-1H-pyrazolo[3,4-b]pyridine (**3af**).* White solid; 77% yield (137.8 mg); mp 97–98 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.20 (s, 1H), 7.37–7.31 (m, 4H), 7.09 (s, 1H), 6.87–6.76 (m, 3H), 5.95 (s, 2H), 5.62 (s, 2H), 3.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 151.2, 148.7, 148.2, 147.8, 142.6, 130.2, 129.4, 127.5, 120.9, 116.9, 113.9, 113.5, 108.6, 107.6, 101.2, 55.2, 50.2; HRMS (ESI): *m*/*z* calcd. for $C_{21}H_{17}N_3O_3[M + H]^+$: 360.1347; found: 360.1225.

*1-(4-Methoxybenzyl)-3(naphthalen-2-yl)-1H-pyrazolo[3,4-b]pyridine (**3ag**).* Creamy white solid, 88% yield (160.1 mg); mp 96–97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (dd, J = 4.5, 1.8 Hz, 1H), 8.46 (dd, J = 8.2, 1.4 Hz, 1H), 8.42 (s, 1H), 8.17 (dd, J = 8.72, 1.8 Hz, 1H), 7.99–7.96 (m, 2H), 7.92–7.89 (m, 1H), 7.56–7.53 (m, 2H), 7.48–7.46 (m, 2H), 7.22–7.20 (m, 1H), 6.89–6.87 (m, 2H), 5.80 (s, 2H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 151.1, 148.7, 142.7, 133.4, 133.0, 130.6, 130.4, 129.3, 129.2, 128.5, 128.1, 127.7, 126.3, 126.1, 125.8, 124.9, 117.0, 113.8, 113.8, 55.1, 50.2; HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{19}N_3O[M + H]^+$: 366.1606; found: 366.1592.

*6-Chloro-1-(4-methoxybenzyl)-3-(naphthalen-2-yl)-1H-pyrazolo [3,4-b]pyridine (**3ah**).* White solid; 92% yield (183.1 mg); mp 143–144 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38–8.36 (m, 2H), 8.11–8.07 (m, 1H), 8.02–7.89 (m, 3H), 7.57–7.54 (m, 2H), 7.49–7.45 (m, 2H), 7.23 (d, J = 8.3 Hz, 1H), 6.83 (d, J = 8.5 Hz, 2H), 5.71 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 150.6, 143.2, 133.4, 133.2, 132.6, 130.2, 129.8, 129.6, 128.8, 128.7, 128.2, 127.8, 126.5, 126.4, 126.0, 124.8, 117.7, 114.0, 112.4, 55.2, 50.4; HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{18}ClN_3O[M + H]^+$: 400.1216; found: 400.1202.

*1-(4-Methoxybenzyl)-3-(pyridin-4-yl)-1H-pyrazolo[3,4-b]pyridine (**3ai**).* Brown solid; 73% yield (114.9 mg); mp 88–89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (dd, J = 4.5, 1.3 Hz, 2H), 8.46 (dd, J = 4.6, 1.3 Hz, 1H), 8.34 (dd, J = 8.2, 1.3 Hz, 1H), 7.85 (dd, J = 4.1, 1.3 Hz, 2H), 7.38 (d, J = 8.2 Hz, 2H), 7.22 (m, 1H), 6.83–6.81 (m, 2H), 5,71 (s, 2H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 151.1, 150.3, 149.0, 140.6, 139.8, 129.8, 129.5, 128.7, 121.0, 117.7, 113.9, 113.6, 55.1, 50.5; HRMS (ESI): *m*/*z* calcd. for $C_{19}H_{16}N_4O[M + H]^+$: 317.1402; found: 317.1405.

*6-Chloro-1-(4-methoxybenzyl)-3-(pyridin-4-yl)-1H-pyrazolo[3,4-b]pyridine (**3aj**).* Light brown solid; 76% yield (132.6 mg); mp 149–150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, J = 5.5 Hz, 2H), 8.26–8.24 (m, 1H), 7.81 (d, J = 5.0 Hz, 2H), 7.40 (d, J = 8.6 Hz, 2H), 7.24–7.22 (m, 1H), 6.84 (d, J = 8.2 Hz, 2H), 5.65 (s, 2H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$). ^{13}C NMR showed one less carbon, it might be due to one carbon peak got merged. δ 159.3, 150.9, 150.3, 140.2, 140.0, 131.9, 129.7, 128.2, 120.9, 118.5, 113.9, 112.1, 55.2, 50.6; HRMS (ESI): *m*/*z* calcd. for $C_{19}H_{15}ClN_4O[M + H]^+$: 351.1012; found: 351.1003.

*1-Methyl-3-(pyridin-4-yl)-1H-pyrazolo[3,4-b]pyridine (**3ak**).* Brown solid; 78% yield (81.6 mg); mp 70–71 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 4.1 Hz, 2H), 8.59 (dd, J = 4.1, 1.3 Hz, 1H), 8.34 (dd, J = 8.2, 1.3 Hz, 1H), 7.86–7.85 (m, 2H), 7.23–7.20 (m, 1H), 4.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 150.2, 148.9, 140.6, 139.3, 129.8, 120.8, 117.6, 113.4, 34.1; HRMS (ESI): *m*/*z* calcd. for $C_{12}H_{10}N_4[M + H]^+$: 211.0983; found: 211.0981.

General procedure for the synthesis of monoarylpyrazolo [3,4-*b*]pyridines and their derivatives (4a–4l). To a round bottom flask, were added 6-chloro-1-(4-methoxybenzyl)-3-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine **3** (0.5 mmol) dissolved in 5 mL of dioxane : water (3 : 1), catalyst and ligand 5 mol% each. Arylboronic acid **2** (0.5 mmol, 1.0 equiv.) and base (2 equiv.) were added to the above after 5 min of stirring and started heating at 100 °C. When the TLC indicated the total consumption of starting material, the reaction mixture was allowed to cool at ambient temperature. The reaction mixture was extracted with ethyl acetate and organic layer was washed with brine and distilled water. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc) to give the desired products (**4a–4l**).

*1-(4-Methoxybenzyl)-3,6-diphenyl-1H-pyrazolo[3,4-b]pyridine (**4a**).* White solid; 95% yield (185.3 mg); mp 118–119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 8.2 Hz, 1H), 8.18–8.16 (m, 2H), 7.96 (dd, J = 8.7, 1.3 Hz, 2H), 7.64 (d, J = 8.7 Hz, 1H), 7.52–7.45 (m, 7H), 7.40–7.36 (m, 1H), 6.83 (dd, J = 6.6, 0.9 Hz, 2H), 5.76 (s, 2H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 156.2, 151.5, 142.7, 139.2, 133.4, 130.7, 129.6, 126.5, 129.3, 128.8, 128.7, 128.1, 127.4, 127.0, 114.6, 113.8, 112.3, 55.2, 50.2; HRMS (ESI): *m*/*z* calcd. for $C_{26}H_{21}N_3O[M + H]^+$: 392.1762; found: 392.1746.

*1-(4-Methoxybenzyl)-6-(4-methoxyphenyl)-3-phenyl-1H-pyrazolo [3,4-b]pyridine (**4b**).* White solid; 81% yield (170.1 mg); mp 123–124 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 8.5 Hz, 1H), 8.16 (d, J = 8.8 Hz, 2H), 7.97 (d, J = 7.15 Hz, 2H), 7.60 (d, J = 8.4 Hz, 1H), 7.52–7.47 (m, 4H), 7.40 (t, J = 7.4, 1H), 7.05 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 5.76 (s, 2H), 3.90 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.8, 159.1, 156.0, 151.6, 142.8, 133.5, 131.8, 130.7, 129.6, 128.8 (d, J = 2.7 Hz, 1C), 128.1, 127.0, 116.0, 114.8, 114.2, 114.1, 113.9, 111.9, 55.4, 55.2, 50.2; HRMS (ESI): *m*/*z* calcd. for $C_{27}H_{23}N_3O_2[M + H]^+$: 422.1868; found: 422.1857.

*6-(4-Fluorophenyl)-1-(4-methoxyphenyl)-3-phenyl-1H-pyrazolo [3,4-b]pyridine (**4c**).* White solid; 97% yield (197.9 mg); mp 136–137 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.37–8.34 (m, 1H), 8.20–8.16 (m, 2H), 7.97 (d, J = 7.2 Hz, 2H), 7.61 (d, J = 8.4 Hz, 1H), 7.51 (t, J = 7.5 Hz, 2H), 7.46 (d, J = 8.6 Hz, 2H), 7.41 (t, J = 7.4 Hz, 1H), 7.22 (t, J = 8.6, 2H), 6.85 (d, J = 8.6 Hz, 2H), 5.76 (s, 2H),

3.76 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.8 (d, J = 247.8 Hz, 1C), 159.1, 155.2, 151.5, 142.8, 135.3 (d, J = 2.9 Hz, 1C), 133.3, 130.9, 129.6, 129.5, 129.3 (d, J = 8.3 Hz, 1C), 128.8, 128.2, 127.0, 115.7 (d, J = 21.4 Hz, 1C), 114.3, 113.9, 112.3, 55.2, 50.2; HRMS (ESI): m/z calcd. for $C_{26}H_{20}FN_3O[M + H]^+$: 410.1668; found: 410.1681.

*1-(4-Methoxybenzyl)-6-(3-methoxyphenyl)-3-phenyl-1H-pyrazolo [3,4-b]pyridine (**4d**).* White solid; 68% yield (142.8 mg); mp 95.9–96.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$): 8.33 (d, J = 8.2 Hz, 1H), 7.97–7.95 (m, 2H), 7.77–7.76 (m, 1H), 7.72–7.70 (m, 1H), 7.63 (d, J = 8.2, 1H), 7.48–7.38 (m, 6H), 7.02–6.99 (m, 1H), 6.82 (d, J = 8.7 Hz, 2H), 5.75 (s, 2H), 3.92 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 160.0, 159.0, 157.0, 156.0, 151.4, 142.7, 140.6, 133.3, 130.7, 130.0, 129.7, 129.6, 129.4, 128.8, 128.1, 127.0, 119.9, 114.9, 114.8, 113.8, 113.0, 112.4, 55.1, 50.2; HRMS (ESI): m/z calcd. for $C_{27}H_{23}N_3O_2[M + H]^+$: 422.1868; found: 422.1841.

*3-(3-(4-Methoxyphenyl)-1-methyl-1H-pyrazolo[3,4-b]pyridin-6-yl)benzaldehyde (**4e**).* Creamy white solid; 76% yield (129.9 mg); mp 179–180 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.17 (s, 1H), 8.67 (s, 1H), 8.46 (d, J = 7.4 Hz, 1H), 8.38–0.36 (m, 1H), 7.98 (d, J = 7.3 Hz, 1H), 7.92 (d, J = 8.0 Hz, 2H), 7.71–7.67 (m, 2H), 7.07 (d, J = 7.9 Hz, 2H), 4.26 (s, 3H), 3.90 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.2, 159.8, 154.6, 151.7, 142.4, 140.2, 136.9, 133.2, 131.1, 130.3, 129.5, 128.6, 128.1, 125.8, 114.4, 114.0, 112.4, 55.3, 33.8; HRMS (ESI): m/z calcd. for $C_{21}H_{17}N_3O_2[M + H]^+$: 344.1398; found: 344.1371.

*4-(1-(4-Methoxybenzyl)-3-(p-tolyl)-1H-pyrazolo[3,4-b]pyridin-6-yl)benzonitrile (**4f**).* Light yellow solid; 72% yield (154.5 mg); mp 186–187 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, J = 8.4 Hz, 1H), 8.28 (d, J = 8.2 Hz, 2H), 7.86 (d, J = 8.0 Hz, 2H), 7.81 (d, J = 8.2 Hz, 2H), 7.64 (t, J = 8.4 Hz, 1H), 7.44 (d, J = 8.6 Hz, 2H), 7.32 (d, J = 7.9 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 5.76 (s, 2H), 3.76 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 153.7, 151.1, 143.4, 143.0, 138.3, 132.5, 131.3, 130.2, 129.6, 129.6, 129.3, 127.9, 126.9, 118.8, 114.5, 113.9, 113.1, 112.6, 55.2, 50.3, 21.3; HRMS (ESI): m/z calcd. for $C_{28}H_{22}N_4O[M + H]^+$: 431.1871; found: 431.1888.

*3-(2,4-Difluorophenyl)-1-(4-methoxybenzyl)-6-(3-methoxyphenyl)-1H-pyrazolo[3,4-b]pyridine (**4g**).* White solid; 63% yield (143.6 mg); mp 100–101 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (dd, J = 8.4, 3.4 Hz, 1H), 7.89 (q, J = 6.8 Hz, 1H), 7.78 (s, 1H), 7.74 (d, J = 7.2 Hz, 1H), 7.65 (d, J = 8.5 Hz, 1H), 7.49–7.43 (m, 3H), 7.04–6.97 (m, 3H), 6.85 (d, J = 8.5, 2H), 5.78 (s, 2H), 3.94 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.05 (dd, J = 248.9, 11.7 Hz, 1C), 160.0, 159.9 (dd, J = 249.8, 11.9 Hz, 1C), 159.2, 156.3, 151.1, 140.7, 137.7, 131.5 (t, J = 2.4 Hz, 1C), 131.5 (t, J = 3.4 Hz, 1C), 129.8, 129.7, 129.3, 120.0, 117.3 (dd, J = 14.7, 3.7 Hz, 1C), 115.0, 114.9, 113.9, 113.2, 113.1, 112.0 (dd, J = 21.1, 3.3 Hz, 1C), 104.4 (t, J = 25.6 Hz, 1C), 55.4, 55.2, 50.4; HRMS (ESI): m/z calcd. for $C_{27}H_{21}F_2N_3O_2[M + H]^+$: 458.1679; found: 458.1664.

*1-(4-Methoxybenzyl)-6-(3-nitrophenyl)-3-(p-tolyl)-1H-pyrazolo [3,4-b]pyridine (**4h**).* Yellow solid; 53% yield (118.9 mg); mp 160–161 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.49 (d, J = 7.4 Hz, 1H), 8.38 (dd, J = 8.3, 2.4 Hz, 1H), 8.30 (d, J = 7.9 Hz, 1H), 7.86 (d, J = 7.8 Hz, 2H), 7.70–7.66 (m, 2H), 7.48 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 7.7 Hz, 2H), 6.87 (d, J = 8.3 Hz, 2H), 5.77 (s, 2H), 3.76 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 153.2, 151.3, 148.8, 143.0, 140.9, 138.3, 133.1, 131.4, 130.2, 129.7, 129.6, 129.2, 126.9, 123.8, 122.4, 114.1, 113.9, 113.2, 55.2, 50.5, 21.3; HRMS (ESI): m/z calcd. for $C_{27}H_{22}N_4O_3[M + H]^+$: 451.1769; found: 451.1775.

*6-(Furan-2-yl)-1-(4-methoxybenzyl)-3-(thiophen-3-yl)-1H-pyrazolo [3,4-b]pyridine (**4i**).* White solid; 68% yield (131.3 mg); mp 163–164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 8.4 Hz, 1H),7.77 (d, J = 1.5 Hz, 1H), 7.69 (d, J = 4.9 Hz, 1H), 7.63–7.60 (m, 2H), 7.44–7.41 (m, 3H), 7.24 (d, J = 3.1 Hz, 1H), 6.83 (d, J = 8.4 Hz, 2H), 6.60 (s, 1H), 5.70 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$). [We found less 1C.] δ 159.1, 153.9, 151.0, 148.2, 143.8, 139.3, 134.5, 130.3, 129.6, 129.5, 126.4, 126.1, 121.8, 113.9, 113.0, 112.3, 109.8, 55.2, 50.1. HRMS (ESI): m/z calcd. for $C_{27}H_{17}N_3O_2S[M + H]^+$: 388.1119; found: 388.1103.

*1-(4-Methoxybenzyl)-3-(pyridine-4-yl)-6-(thiophen-3-yl)-1H-pyrazolo[3,4-b]pyridine (**4j**).* White solid; 62% yield (123.1 mg); mp 150–151 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 (d, J = 5.6 Hz, 2H), 8.31 (d, J = 8.3 Hz, 1H), 8.06 (d, J = 1.7 Hz, 1H), 7.88–7.86 (m, 3H), 7.59 (d, J = 8.2 Hz, 1H), 7.47–7.45 (m, 3H), 6.85 (d, J = 8.6 Hz, 2H), 5.74 (s, 2H), 3.76 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 152.6, 151.4, 150.3, 142.0, 140.8, 139.8, 130.2, 129.7, 129.0, 126.7, 126.5, 124.9, 120.9, 115.4, 114.0, 112.1, 55.2, 50.5. HRMS (ESI): m/z calcd. for $C_{23}H_{18}N_4OS[M + H]^+$: 399.1279; found: 399.1269.

*6-(Benzo[d][1,3]dioxol-5-yl)-1-(4-methoxybenzyl)-3-phenyl-1H-pyrazolo[3,4-b]pyridine (**4k**).* White solid; 57% yield (123.6 mg); mp 143–144 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (d, J = 2.6 Hz, 1H), 8.43 (d, J = 2.5 Hz, 1H), 7.99–7.96 (m, 2H), 7.63–7.61 (m, 2H), 7.52–7.47 (m, 4H), 7.43–7.38 (m, 4H), 6.85–6.82 (m, 2H), 5.73 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$).^{13}C NMR showed one less carbon, it might be due to one carbon peak got merged. δ 159.3, 150.5, 150.4, 148.2, 148.0, 143.0, 132.4, 129.6, 129.5, 128.8, 127.0, 126.9, 121.7, 120.9, 117.5, 113.9, 112.0, 108.7, 107.5, 101.3, 55.2, 50.3; HRMS (ESI): m/z calcd. for $C_{27}H_{21}N_3O_3[M + H]^+$: 436.1660; found: 436.1648.

*3-(1-(4-Methoxybenzyl)-3-(naphthalen-2-yl)-1H-pyrazolo[3,4-b] pyridin-6-yl)phenol (**4l**).* White solid; 52% yield (118.5 mg); mp 179.6–180.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.45–8.41 (m, 2H), 8.15 (d, J = 8.5 Hz, 1H), 7.98–7.95 (m, 2H), 7.89 (d, J = 7.1 Hz, 1H), 7.735–7.731 (b, 2H), 7.63 (d, J = 8.4 Hz, 1H), 7.55–7.51 (m, 2H), 7.47 (d, J = 8.5 Hz, 2H), 7.40 (t, J = 8.1 Hz, 1H), 6.96 (dd, J = 7.9, 1.7 Hz, 1H), 6.83 (d, J = 8.5 Hz, 2H), 5.91 (s, 1H), 5.79 (s, 2H), 3.74 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 159.1, 156.2, 156.0, 151.5, 142.8, 140.6, 133.5, 133.1, 131.0, 130.7, 130.0, 129.6, 129.4, 128.6, 128.2, 127.8, 126.4, 126.2, 125.9, 125.0, 119.9, 116.6, 114.9, 114.4, 113.9, 112.7, 55.2, 50.2. HRMS (ESI): m/z calcd. for $C_3H_{23}N_3O_2[M + H]$: 458.1868; found: 458.1846.

General procedure for sequential one-pot Suzuki–Miyaura cross-coupling reactions. To a round bottom flask were added 6-chloro-3-iodo-1-(4-methoxybenzyl)-1*H*-pyrazolo[3,4-*b*]pyridine **1** (0.5 mmol) dissolved in 5 mL of dioxane : water (3 : 1), catalyst and ligand 5 mol% each. Arylboronic acid **2** (0.5 mmol, 1.0 equiv.) and base (2 equiv.) were added to the above after 5 min of stirring and started heating at 60 °C. When the TLC indicated the total consumption of starting material, the condenser fitted to the RB, next 15 mol% of catalyst and 15 mol% of ligand were added to the same pot. Arylboronic acid **2** (0.5 mmol, 1 equiv.)

was added after 5 min of stirring and stirring continued at 100 °C. After the reaction was completed as monitored by TLC the reaction mixture was allowed to cool at ambient temperature. The reaction mixture was extracted with ethyl acetate and the organic layer was washed with brine and distilled water. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc) to give the desired products. The characterisation of **4a-4b**, **4f-4g**, **4i-4j** is given above.

General procedure for the de-protection of diarylpyrazolo [3,4-*b*]pyridines and their derivatives. To a round bottom flask equipped with a condensor was added appropriate the pyrazolo [3,4-*b*]pyridine (0.1 mmol) and it was kept in ice water for the addition of TFA. TFA (2–5 mL) was carefully added to the above and heating started at 70 °C. On completion, as indicated by TLC, the reaction mixture was quenched with the satd. $NaHCO_3$ solution and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc) to give the desired products (**5a–5d**).

*3,6-Diphenyl-1H-pyrazolo[3,4-b]pyridine (**5a**).* White solid; 99% yield (25.9 mg); mp 207.7–208.2 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.8 (s, 1H), 8.61 (d, J = 8.4 Hz, 1H), 8.18 (d, J = 7.4 Hz, 2H), 8.05 (d, J = 7.5 Hz, 2H), 7.84 (d, J = 8.5 Hz, 1H), 7.54–7.51 (m, 4H), 7.49–7.41 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 155.9, 153.7, 143.0, 139.0, 133.6, 131.7, 129.9, 129.4, 129.3, 128.6, 127.6, 126.9, 115.1, 111.5; HRMS (ESI): *m*/*z* calcd. for $C_{18}H_{13}N_3[M + H]^+$: 272.1187; found: 272.1167.

*6-(4-Fluorophenyl)-3-phenyl-1H-pyrazolo[3,4-b]pyridine (**5b**).* White solid; 86% yield (24.7 mg); mp 250–251 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.8 (s, 1H), 8.61 (d, J = 8.0 Hz, 1H), 8.24–8.17 (m, 2H), 8.04 (d, J = 7.3 Hz, 2H), 7.83 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 7.2 Hz, 2H), 7.42 (t, J = 7.1 Hz, 1H), 7.35 (t, J = 8.4 Hz, 2H); ^{1}H NMR-deutrated (500 MHz, DMSO-d_6) δ 8.45 (d, J = 8.4 Hz, 1H), 8.09–8.06 (m, 2H), 7.89 (d, J = 7.6 Hz, 2H), 7.67 (d, J = 8.4 Hz, 1H), 7.43 (t, J = 7.4 Hz, 2H), 7.32 (t, J = 7.2 Hz, 1H), 7.22 (t, J = 8.6 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 163.5 (d, J = 245.7 Hz, 1C), 162.6, 154.8, 153.5, 143.1, 135.5, 133.6, 131.8, 129.8 (d, J = 33.7 Hz, 1C), 129.4, 128.6, 126.9, 116.2 (d, J = 21.4 Hz, 1C), 114.9, 111.4; HRMS (ESI): *m*/*z* calcd. for $C_{18}H_{12}FN_3[M + H]^+$: 290.1093; found: 290.1075.

*6-(4-Methoxyphenyl)-3-phenyl-1H-pyrazolo[3,4-b]pyridine (**5c**).* White solid; 85% yield (25.5 mg); mp 252–253 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.6 (s, 1H), 8.46 (d, J = 8.5 Hz, 1H), 8.07 (d, J = 8.6 Hz, 2H), 7.96 (d, J = 7.7 Hz, 2H), 7.71 (d, J = 8.5 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.34 (t, J = 7.4 Hz, 1H), 6.99 (d, J = 8.7 Hz, 2H), 3.74 (s, 3H); ^{1}H NMR-deutrated (500 MHz, DMSO-d_6) δ 8.42 (d, J = 8.2 Hz, 1H), 8.01 (d, J = 8.4 Hz, 2H), 7.89 (d, J = 7.9 Hz, 2H), 7.66 (d, J = 8.4 Hz, 1H), 7.43 (t, J = 7.5 Hz, 2H), 7.33 (t, J = 7.0 Hz, 1H), 6.97 (d, J = 8.4 Hz, 2H), 3.70 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.0, 155.6, 153.7, 143.0, 133.7, 131.5, 131.4, 129.4, 129.0, 128.5, 126.8, 114.7, 114.5, 111.0, 55.7; HRMS (ESI): *m*/*z* calcd. for $C_{19}H_{15}N_3O[M + H]^+$: 302.1293; found: 302.1273.

*6-(Furan-2-yl)-3-(thiophen-3-yl)-1H-pyrazolo[3,4-b]pyridine (**5d**).* White solid; 99% yield (25.9 mg); mp 252–253 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.7 (s, 1H), 8.66 (d, J = 8.3 Hz, 1H), 8.23 (s, 1H), 7.93 (s, 1H), 7.74 (d, J = 8.9 Hz, 2H), 7.67 (d, J = 8.4 Hz, 1H), 7.29 (s, 1H), 6.73 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 153.4, 152.9, 147.9, 145.3, 140.0, 134.6, 131.6, 127.4, 126.5, 122.8, 113.2, 113.0, 111.2, 110.6; HRMS (ESI): *m*/*z* calcd. for $C_{14}H_9N_3OS$ $[M + H]^+$: 268.0544; found: 268.0524.

Conflicts of interest

There are no conflicts of interest.

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