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Full Paper

Aminopyrazole Cross-Coupling

4-Arylation of *N*-Acylamino- and Aminopyrazoles by the Suzuki–Miyaura Cross-Coupling Reaction

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Abstract: Halogenated aminopyrazoles have rarely been utilized in metal-catalysed cross-coupling reactions mainly due to the complexation of the aminopyrazoles to the metal center, which deactivates the catalyst. In this paper we reveal that the appropriate combination of palladium source and ligand enables efficient Suzuki–Miyaura cross-coupling reactions with even challenging substrates such as halogenated aminopyrazoles. The combination of $Pd(OAc)_2$ and XPhos allowed efficient coupling of halogenated *N*-acetylaminopyrazoles, whereas XPhos Pd G2 was needed when unprotected aminopyrazoles were used. Generally, the halogenated aminopyrazoles underwent facile cross-coupling reactions with a range of aryl-, heteroaryl-, and styrylboronic acids and esters. The resulting biaryl, bisheteroaryl, or arylalkenyl derivatives were obtained in good-to-high isolated yields.

Introduction

Recently, we reported 4-substituted aminopyrazoles as potent and selective inhibitors of cyclin-dependent kinases, namely CDK2, CDK4, and CDK9.[1–4] These compounds displayed antiproliferative activity, which was proven on several cancer cell lines, including MCF7, K562, and RPMI-8226. To further explore the structure–activity relationship (SAR) and potentially find new compounds with improved CDK inhibition activity, we were interested in the synthesis of amino- and *N*-acylaminopyrazoles with diverse substituents at the 4-position of the pyrazole ring.

Classically, 4-substituted aminopyrazoles can be prepared by traditional methods starting from the corresponding substituted acyclic precursors.[5–10] Although these traditional methods still hold their value, they usually suffer from limited substrate scope and require multiple steps, which make them unattractive for parallel syntheses.[11–15] Therefore, we sought a more efficient and general method for the rapid elaboration of the 4-substituted aminopyrazole scaffold. Among various organic reactions, the Pd-catalyzed Suzuki–Miyaura cross-coupling reaction has enjoyed great attention as it enables straightforward and efficient syntheses of olefins, styrenes, and biaryls, has broad substrate scope, and uses relatively low-toxic and bench-stable organoboron reagents.[16]

Previously, Pd-catalyzed Suzuki–Miyaura cross-coupling reactions involving heteroaromatic substrates represented a substantial challenge,[17–20] presumably due to the complexation of a starting material and/or product to the metal resulting in the inhibition of the catalyst.[21,22] In particular, five-membered nitrogen-rich heterocycles bearing an unprotected amino group were found problematic coupling partners in palladium-catalyzed cross-coupling reactions.[23–26] However, the development of more robust catalysts has overcome this obstacle, allowing the cross-coupling of the previously challenging substrates.[27–31]

Despite the tremendous progress in the development of effective palladium-based catalytic systems, only isolated examples of the Suzuki–Miyaura reaction with halogenated amino- or *N*-acylaminopyrazoles have been published to date.[32,33] The reported procedures often employed less effective catalytic systems based on $[Pd(PPh_3)_4]$, which provided the biaryl product in low yield. Furthermore, no systematic study including reaction optimization and exploration of the substrate scope has been disclosed.[34] Poorly explored cross-coupling methodologies in this field and the potential bioactivity of the target arylated aminopyrazoles encouraged us to further explore the arylation of aminopyrazole derivatives at the 4-position. Herein, we present our results of the Pd-catalyzed C–C cross-coupling reactions of pyrazoles with a range of aryl-, heteroaryl-, and styrylboronic acids or esters. In addition, we have compared the reactivity of 4-chloro-, 4-bromo-, and 4-iodo-aminopyrazoles in the Suzuki–Miyaura reaction.

Results and Discussion

We initiated our study with the model reaction involving pyrazole **1a** and boronic acid **2a**. The reaction was performed in a mixture of dioxane and water, K_2CO_3 was used as base, and $Pd(OAc)_2$ as the palladium source. The reaction mixture was heated in an oil bath at 100 °C for 18 h (Table 1). In the first stage, distinct supporting ligands were evaluated in combination with $Pd(OAc)_2$, including bulky trialkylphosphines, bidentate phosphines, biphenyl-based phosphines, and an NHC-

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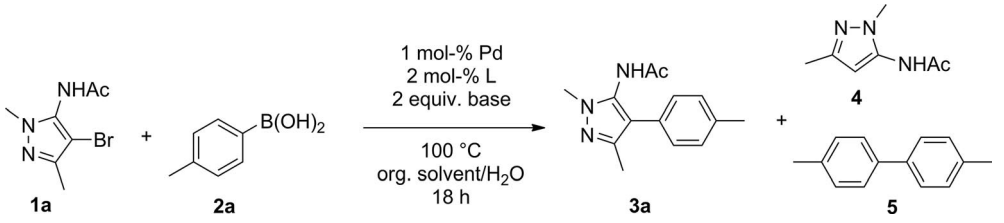
Table 1. Optimization of the reaction parameters[a] (PEPPSI = [1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene](3-chloropyridyl)palladium(II) dichloride).



Entry	[Pd]	Ligand	Base	Solvent	Yield of **3a** [%][b]
1	$Pd(OAc)_2$	PCy_3	K_2CO_3	dioxane	48
2	$Pd(OAc)_2$	PAd_2Bu	K_2CO_3	dioxane	62
3	$Pd(OAc)_2$	dppp	K_2CO_3	dioxane	51
4	$Pd(OAc)_2$	dppf	K_2CO_3	dioxane	33
5	$Pd(OAc)_2$	BINAP	K_2CO_3	dioxane	64
6	$Pd(OAc)_2$	SPhos	K_2CO_3	dioxane	33
7	$Pd(OAc)_2$	XPhos	K_2CO_3	dioxane	74
8	$Pd(OAc)_2$	Aphos	K_2CO_3	dioxane	69
9	PEPPSI	IPr	K_2CO_3	dioxane	45
10	$Pd(OAc)_2$	XPhos	NEt_3	dioxane	32
11	$Pd(OAc)_2$	XPhos	CsF	dioxane	66
12	$Pd(OAc)_2$	XPhos	Cs_2CO_3	dioxane	73
13	$Pd(OAc)_2$	XPhos	K_3PO_4	dioxane	67
14	$Pd(OAc)_2$	XPhos	Na_2CO_3	dioxane	57
15	$Pd(OAc)_2$	XPhos	K_2CO_3	dioxane	43[c]
16	$Pd(OAc)_2$	XPhos	K_2CO_3	dioxane	66[d]
17	$Pd(OAc)_2$	XPhos	K_2CO_3	dioxane	54[e]
18	$Pd(OAc)_2$	XPhos	K_2CO_3	THF	68
19	$Pd(OAc)_2$	XPhos	K_2CO_3	toluene	66
20	$Pd(OAc)_2$	XPhos	K_2CO_3	*i*PrOH	64
21	$Pd(OAc)_2$	XPhos	K_2CO_3	dioxane	59[f]
22	$Pd(OAc)_2$	XPhos	K_2CO_3	dioxane	26[g]
23	$Pd(OAc)_2$	XPhos	K_2CO_3	dioxane	75[h]
24	XPhos Pd G2	XPhos	K_2CO_3	dioxane	75
25	10 % Pd/C	XPhos	K_2CO_3	dioxane	63
26	$[Pd_2dba_3]$	XPhos	K_2CO_3	dioxane	71

[a] Reagents and conditions: **1a** (0.5 mmol), **2a** (1.0 mmol), base (1.0 mmol), organic solvent (2 mL), H_2O (0.5 mL), ligand (0.01 mmol), [Pd] (0.005 mmol), 100 °C, 18 h. [b] Isolated yield. [c] 1 equiv. of K_2CO_3 was used. [d] 3 equiv. of K_2CO_3 was used. [e] 4 equiv. of K_2CO_3 was used. [f] T = 80 °C. [g] T = 40 °C. [h] Reaction time 8 h.

based catalyst (Table 1, entries 1–9). For example, trialkylphosphine PCy_3, which was earlier reported as an efficient supporting ligand for Suzuki reactions involving heteroarenes,[35] gave product **3a** in only 48 % yield, together with 9 % of recovered starting material **1a** and 25 % of debrominated pyrazole **4** (entry 1). Better results were obtained by using PAd_2Bu, BINAP, APhos, and XPhos, with XPhos being the best of all the tested ligands, affording the desired product **3a** in 74 % yield.

Notably, LCMS analyses of the crude reaction mixtures generally showed product **3a**, starting material **1a**, debrominated pyrazole **4**, which results from the reductive hydrodehalogenation of the starting material, boronic acid **2a**, and biphenyl **5**, which results from the oxidative homocoupling of the boronic acid. For cases in which the product was isolated in lower yields (e.g., entries 4, 6, and 10), a substantial amount of the starting material **1a** and/or the hydrodehalogenated pyrazole **4** was detected. The most effective supporting ligand, XPhos, led to the complete consumption of the starting material **1a**, leaving debrominated compound **4** as the sole impurity derived from the parent pyrazole.

Next, other reaction parameters, such as the nature of the base, solvent system, temperature, and reaction time, were optimized. A few other inorganic bases and one organic base were tested (entries 10–14), however, none of them gave better results than K_2CO_3. The amount of base was found to be critical. One equivalent of K_2CO_3 led to the incomplete consumption of the starting material, whereas 3 or 4 equivalents of K_2CO_3 led to an increase in the rate of hydrodehalogenation (entries 15–17). Comparison of different solvent systems (entries 18–20) revealed a mixture of dioxane and water to be optimal for the reaction. We envisioned that a lower reaction temperature could potentially suppress the undesired hydrodehalogenation, however, the impurity **4** was formed even at 40 °C. Moreover, the yield of product **3a** decreased due to the incomplete conversion of the starting pyrazole **1a** (entries 21 and 22). Pleasingly, the reaction time could be reduced to 8 hours without affecting the yield (entry 23). Other palladium sources, such as $[Pd_2dba_3]$, XPhos Pd G2, and 10 % Pd/C, were also effective for the transformation (entries 24–26). Of these Pd sources, the XPhos-derived precatalyst XPhos Pd G2

gave compound **3a** in the highest yield of 75 % (entry 24), which is comparable to the catalytic activity of $Pd(OAc)_2$. Therefore, we chose the less-expensive $Pd(OAc)_2$ for further studies.

With the optimized conditions in hand, we explored the scope of the cross-coupling reaction by using halogenated *N*-acylpyrazoles **1a**–**d** with aryl-, heteroaryl-, and styrylboronic acids and esters **2a**–**q** (Table 2). Generally, the coupling products were obtained in moderate-to-high isolated yields with both bromides **1a** and **1c**. Both electron-donating and -withdrawing groups at the *para* position of the respective phenylboronic acids (**2c**,**d** for EWG, **2e**,**f** for EDG) were compatible with the

Table 2. Scope and limitation of the Suzuki reaction using *N*-acylaminopyrazoles.

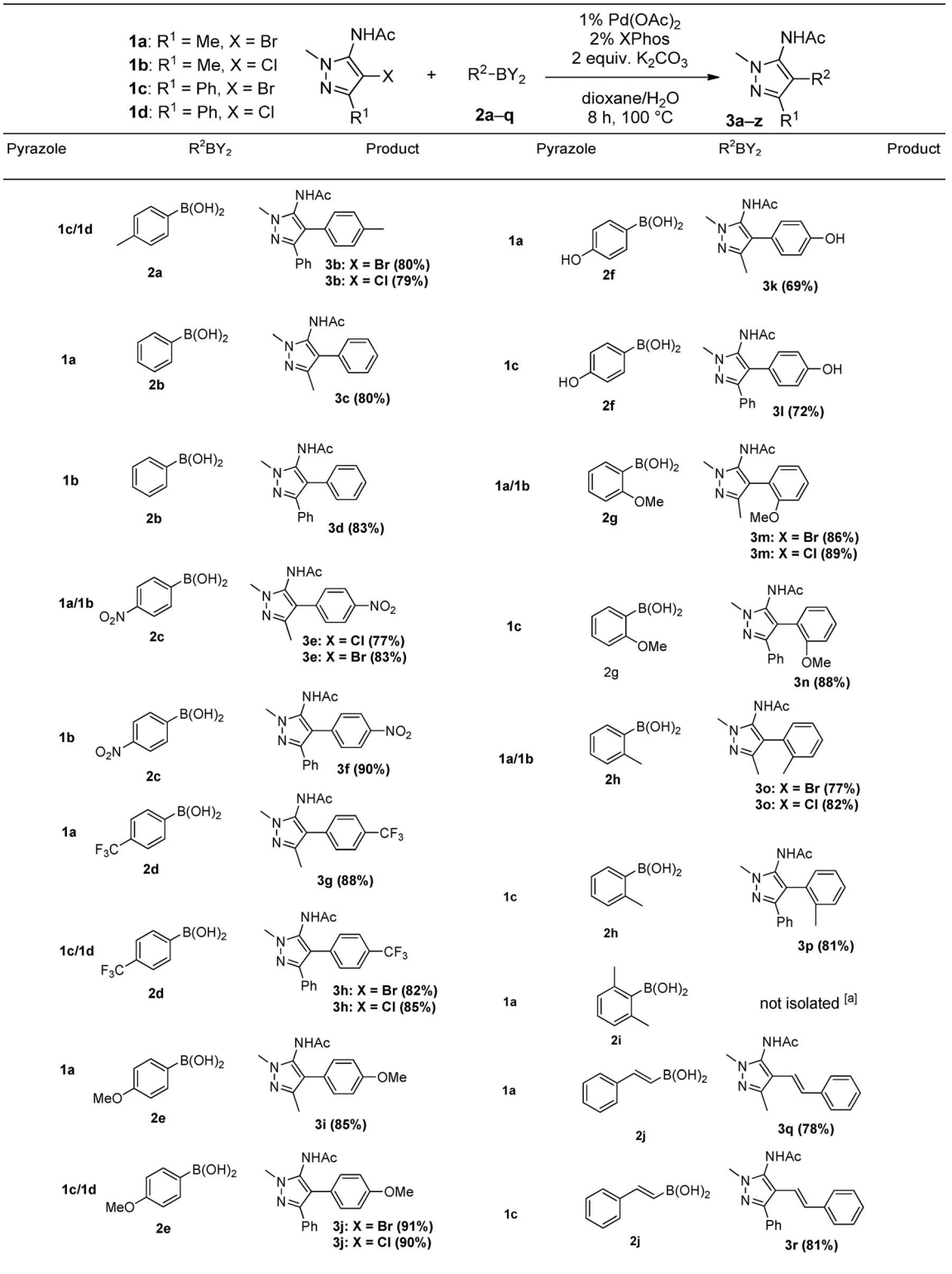
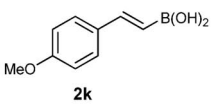
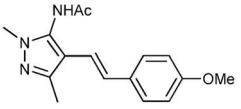
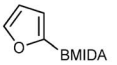
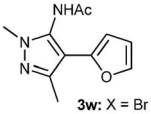
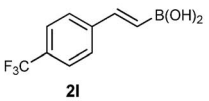
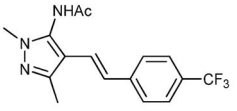
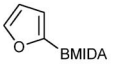
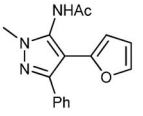
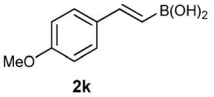
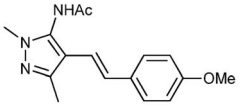
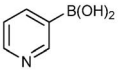
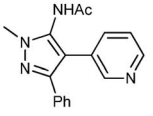
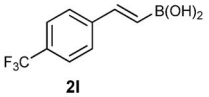
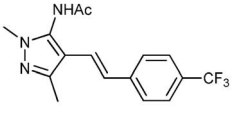
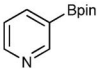
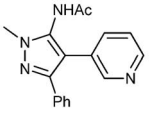
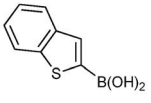
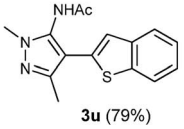
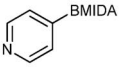
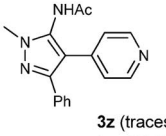
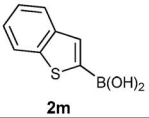
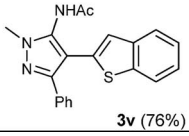


Table 2. *(Continued)*.

Pyrazole	R^2BY_2	Product	Pyrazole	R^2BY_2	Product
1a	 **2k**	 **3s** (83%)	**1a/1b**	 **2n**	 **3w:** X = Br (84%) **3w:** X = Cl (85%)
1a	 **2l**	 **3t** (86%)	**1c/1d**	 **2n**	 **3x:** X = Br (77%) **3x:** X = Cl (80%)
1a	 **2k**	 **3s** (83%)	**1c**	 **2o**	 **3y** (traces) [a]
1a	 **2l**	 **3t** (86%)	**1c**	 **2p**	 **3y** (58%)
1a	 **2m**	 **3u** (79%)	**1c**	 **2q**	 **3z** (traces) **3z** (29%) [b]
1c	 **2m**	 **3v** (76%)			

[a] Only traces of the respective biaryl were detected by LCMS. [b] The reaction was performed in DMF/*i*PrOH (10:1) with 0.5 equiv. of $Cu(OAc)_2$.

reaction. Notably, the *ortho*-substituted phenylboronic acids **2g** and **2h** reacted equally well, producing sterically hindered biaryls **3m**–**p** in yields of 77–88 %. On the other hand, *ortho*-disubstituted boronic acid **2i** failed to give the cross-coupling product when treated with pyrazole **1a** under the optimized conditions. Gratifyingly, (*E*)-styrylboronic acids **2j**–**l** were successfully coupled with pyrazoles **1a** and **1c** allowing the preparation of compounds **3q**–**t** in yields of 78–86 %. The cross-coupling of the styrylboronic acids proceeded with the retention of stereochemistry; compounds **3q**–**t** adopted the *E* configuration, as determined from the values of vicinal coupling constant of the olefinic protons ($^3J \approx 16$ Hz).

Carbon–carbon cross-coupling reactions involving heteroarylboronic acids or their derivatives with heteroaryl halides are versatile transformations in medicinal chemistry. Therefore, we appreciated that the coupling of pyrazoles **1a** and **1c** with 2-benzothienylboronic acid (**2m**) and the MIDA ester of 2-furylboronic acid (**2n**) delivered heterobiaryls **3u**–**x** in good yields of 76–84 %. On the other hand, the use of pyridine as an organoboron nucleophile was found to be more problematic. Only traces of the desired heterobiaryl **3y** were detected by LCMS when 3-pyridylboronic acid (**2o**) was employed in the cross-coupling reaction. At first, we considered that the low solubility of **2o** in dioxane/H_2O could potentially hamper the reaction with **1c**, hence we switched to other solvent systems, including DMF/H_2O and DMF/*i*PrOH. However, this only increased the rate of hydrodehalogenation and no improvement was observed in the conversion to **3y**. The problem was solved by using the pinacol ester of 3-pyridylboronic acid (**2p**), which furnished the desired heterobiaryl **3y** in a moderate yield of 58 %. The MIDA ester of 4-pyridylboronic acid (**2q**) gave only traces of product **3z**. We believe that 4-pyridylboronates could behave similarly to their 2-pyridyl counterparts in that they are susceptible to protodeboronation.[36] Inspired by the previously reported procedures dealing with the "2-pyridyl problem", we switched to a different solvent system (DMF/*i*PrOH) and added 0.5 equiv. of $Cu(OAc)_2$,[37] the co-catalysis with copper allowed us to isolate biaryl **3z** in a poor yield of 29 %.

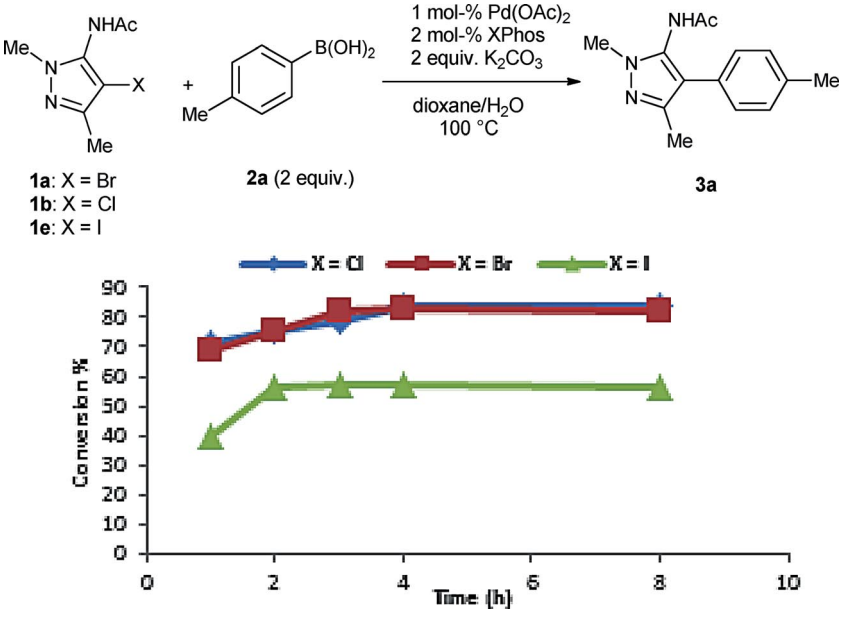
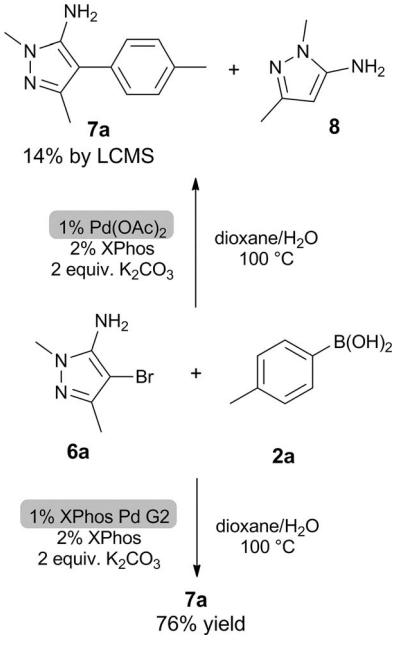


Figure 1. Reactivity of Cl-, Br-, and I-substituted pyrazoles **1a**,**b**,**e** in the Suzuki–Miyaura cross-coupling reaction.

Similarly to the bromides **1a** and **1c**, the chlorides **1b** and **1d** proved to be eligible electrophiles for the reaction, providing the respective heterobiaryls **3b**, **3e**, **3h**, **3j**, **3m**, **3o**, **3w**, and **3x** in yields of 77–90 %. Generally, the yields achieved with chlorides **1b** and **1d** were comparable or even better than those obtained with bromides **1a** and **1c**. This prompted us to further investigate the reactivity of chloride **1b**, bromide **1a**, and iodide **1e** with *p*-tolylboronic acid (**2a**). The formation of biaryl **3a** was studied by HPLC over the course of 8 hours, and the results are depicted in Figure 1. Under the optimized conditions, the cross-coupling reactions with both chloride **1b** and bromide **1a** proceeded with approximately 70 % conversion after 1 h. Conversions of 82 % for the bromide and 84 % for the chloride were achieved after 4 h. At that point, the starting materials **1a** and **1b** were completely consumed and the product **3a** was accompanied by approximately 13 % of the hydrodehalogenated pyrazole **4**. On the other hand, iodide **1e** exhibited a greater propensity for hydrodehalogenation, which led to a higher amount of impurity **4** (39 %).

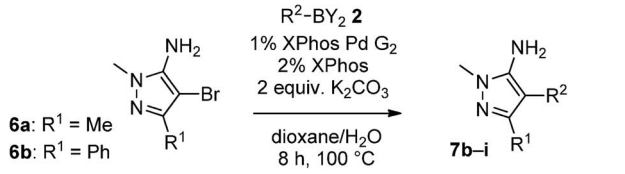
To extend the scope of the procedure to pyrazoles bearing an unprotected amino group, we turned our attention to the cross-coupling of pyrazole **6a** and *p*-tolylboronic acid (**2a**) (Scheme 1). Disappointingly, only a small amount of the desired product **7a** was observed together with unreacted starting material **6a** and hydrodebrominated pyrazole **8**. We assumed that strong complexation of the metal to the substrate terminated the reaction. This inhibition can be eliminated by the proper choice of palladium source. For example, 2-aminobiphenyl-based palladacycles (e.g., XPhos Pd G2) combined with bulky electron-rich phosphines have been reported to be superior to traditional Pd sources such as $[Pd_2dba_3]$ or $Pd(OAc)_2$.[38] Fortunately, this was the case, switching to the precatalyst XPhos Pd G2 allowed us to isolate the NH_2-unprotected biaryl **7a** in 76 % yield. This modified procedure was then applied to the synthesis of biaryls **7b**–**k** (Table 3) from unprotected aminopyrazoles

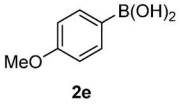
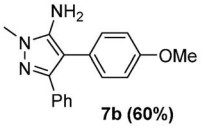
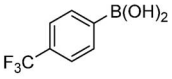
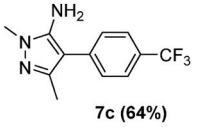
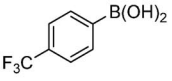
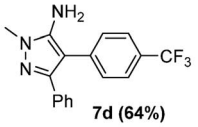
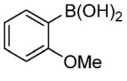
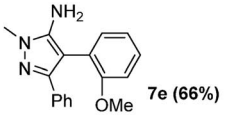
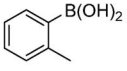
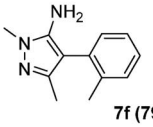
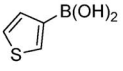
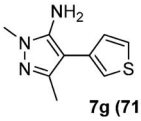
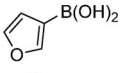
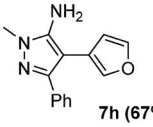
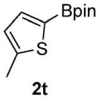
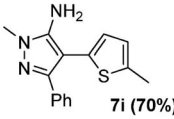
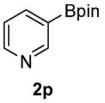
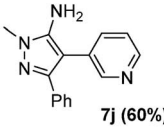
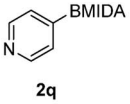
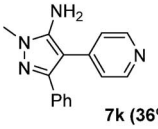


Scheme 1. Suzuki–Miyaura cross-coupling reaction of unprotected aminopyrazole **6a**.

6a and **6b**. Various boronic acids or esters bearing an electron-donating (**2e**) and -withdrawing functionality (**2d**), *ortho*-substituted boronic acids (**2g**,**h**), and heterocyclic moieties (**2p**–**t**) were all compatible with the reaction, affording the desired products **7b**–**j** in yields of 60–79 %. The coupling of pyrazole **6b** and 4-pyridylboronic acid MIDA ester (**2q**) was co-catalyzed with $Cu(OAc)_2$, as in the previous series of reactions (see Table 2). This modification was necessary to obtain good conversion, although the biaryl **7k** was still only obtained in a low yield of 36 %. When styrylboronic acid (**2j**) was treated with pyrazole **6a**, the starting material **6a** was completely consumed

Table 3. Scope of the Suzuki–Miyaura cross-coupling reaction using unprotected aminopyrazoles.

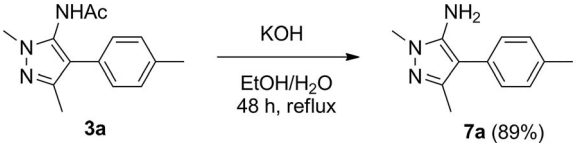


Pyrazole	R^2BY_2	Product
6b	 **2e**	 **7b (60%)**
6a	 **2d**	 **7c (64%)**
6b	 **2d**	 **7d (64%)**
6b	 **2g**	 **7e (66%)**
6a	 **2h**	 **7f (79%)**
6a	 **2r**	 **7g (71%)**
6b	 **2s**	 **7h (67%)**
6b	 **2t**	 **7i (70%)**
6b	 **2p**	 **7j (60%)**
6b	 **2q**	 **7k (36%)** [a]

[a] 0.5 equiv. of $Cu(OAc)_2$ were added.

to give a complex mixture of unidentified compounds. This was presumably due to side-reactions between the unprotected amino group and the styryl moiety.

Alternatively, unprotected aminopyrazoles **7** could be obtained from their *N*-acetyl analogues **3** by a simple hydrolysis of the amide group. As an example, pyrazole **7a** was easily prepared in high yield from the corresponding amide **3a** using KOH in a mixture of ethanol and water (Scheme 2). This alternative approach avoids the use of the more expensive XPhos Pd G2.



Scheme 2. Hydrolysis of the *N*-acetamide group in **3a**.

Conclusions

An efficient method for the Suzuki–Miyaura reactions of 4-halogenated pyrazoles bearing an *N*-acylamino and unprotected amino functionality has been developed. The reported procedure enables the efficient cross-coupling reaction of 4-chloro-, 4-bromo-, and 4-iodopyrazoles with a range of aryl-, heteroaryl-, and styrylboronic acids and/or esters. The chloro- and bromopyrazoles were found to be superior electrophilic coupling partners, as the iodo derivative suffers from considerable hydrodeiodination. The cross-coupling products bearing the *N*-acylamino group on the pyrazole ring were generally obtained in high yields with $Pd(OAc)_2$ and XPhos as the catalytic system. On the other hand, the use of the precatalyst XPhos Pd G2 instead of $Pd(OAc)_2$ was found to be essential for the efficient cross-coupling reaction of bromopyrazoles containing a free amino group. This procedure with its broad substrate scope has allowed the rapid synthesis of a library of functionalized aminopyrazoles and *N*-acylaminopyrazoles, which have the potential to evince significant protein kinase inhibitory activity.

Experimental Section

General: Boronic acids and esters, precatalysts, ligands, 1,3-dimethyl-1*H*-pyrazol-5-amine, and 1-methyl-3-phenyl-1*H*-pyrazol-5-amine were bought from commercial suppliers. Solvents were purified by standard techniques and deoxygenated with a stream of nitrogen immediately before use. All reactants and catalysts were weighed in air and then transferred to a sealed tube. All cross-coupling reactions were performed in a sealed tube, which was thoroughly flushed with a stream of nitrogen before closing with a screw cap. The reaction tube was then inserted into a preheated oil bath. Progress of the reaction was monitored by LCMS and TLC (Kiesegel 60, visualization by UV). Crude products were purified by column chromatography on silica gel. Mixtures of dichloromethane and methanol were used as eluents. Purified products were characterized by NMR spectroscopy and HRMS. The NMR spectra were recorded with a Jeol 400 MHz spectrometer in deuteriated chloroform or DMSO. Chemical shifts are reported in ppm and referenced to the residual solvent peak. HRMS data were recorded with an

Orbitrap Elite HRMS operating in the positive full scan mode in the range of m/z = 200–900.

Preparation of Halogenated Pyrazoles 1a–e and 6a,b

***N*-(4-Bromo-1,3-dimethyl-1*H*-pyrazol-5-yl)acetamide (1a):** A mixture of 1,3-dimethyl-1*H*-pyrazol-5-amine (5.55 g, 50.0 mmol) and acetic anhydride (5.25 mL, 55.0 mmol) in DCM (40 mL) was stirred at ambient temperature for 18 h. Then the mixture was cooled to 0 °C and bromine (2.71 mL, 52.5 mmol) was added dropwise. After stirring the mixture for 3 h at ambient temperature, the reaction was quenched with 2 N K_2CO_3 (30 mL) and 1 N $Na_2S_2O_3$ (10 mL). The organic layer was separated and the aqueous layer extracted with ethyl acetate (2 × 20 mL). The combined organic layers were dried with Na_2SO_4 and concentrated under vacuum. The residue was purified by crystallization from a mixture of DCM and toluene. Pyrazole **1a** was obtained as white needles (10.5 g, 91 %), m.p. 122–123 °C (DCM/toluene). ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 2.06 (s, 3 H), 2.09 (s, 3 H), 3.54 (s, 3 H), 9.86 (s, 1 H) ppm; minor conformer: δ = 1.73, 2.12, 3.64, 9.28 ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 12.3, 22.4, 36.1, 89.4, 134.8, 144.1, 169.2 ppm. HRMS (ESI-TOF): calcd. for $C_7H_{11}BrN_3O$ [M + H]$^+$ 232.0080; found 232.0091, 234.0064.

***N*-(4-Chloro-1,3-dimethyl-1*H*-pyrazol-5-yl)acetamide (1b):** A mixture of 1,3-dimethyl-1*H*-pyrazol-5-amine (1.110 g, 10.0 mmol) and acetic anhydride (1.13 mL, 12.0 mmol) in DCM (20 mL) was stirred at ambient temperature for 20 h. Then the mixture was immersed in an ice–water bath and *N*-chlorosuccinimide (1.469 g, 11.0 mmol) was added. The resulting mixture was warmed to room temperature and stirred for an additional 4 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography (silica gel, 0–3 % MeOH in DCM). Crystallization from a mixture of DCM and toluene afforded pyrazole **1b** as white needles (1.458 g, 78 %), m.p. 140–142 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.07 (s, 3 H), 2.09 (s, 3 H), 3.53 (s, 3 H), 9.89 (s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 11.4, 22.4, 36.1, 102.6, 133.0, 142.5, 169.3 ppm. HRMS (ESI-TOF): calcd. for $C_7H_{11}ClN_3O$ [M + H]$^+$ 188.0585; found 188.0586.

***N*-(4-Bromo-1-methyl-3-phenyl-1*H*-pyrazol-5-yl)acetamide (1c):** A mixture of 1-methyl-3-phenyl-1*H*-pyrazol-5-amine (5.25 g, 30.33 mmol) and acetic anhydride (3.72 mL, 39.42 mmol) in DCM (100 mL) was stirred at ambient temperature for 22 h. Then the mixture was cooled in an ice bath and bromine (1.72 mL, 33.36 mmol) was added dropwise. The mixture was stirred for 3 h at 5 °C. The reaction was then quenched with 2 N K_2CO_3 (30 mL) and 1 N $Na_2S_2O_3$ (10 mL). The organic layer was separated and the aqueous layer extracted with dichloromethane (3 × 50 mL). The combined organic layers were dried with Na_2SO_4 and concentrated under vacuum. The crude product was crystallized from a mixture of DCM and toluene to yield pyrazole **1c** as a white crystalline solid (8.53 g, 96 %), m.p. 183–184 °C (DCM/toluene). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.12 (s, 3 H), 3.70 (s, 3 H), 7.39 (t, J = 7.5 Hz, 1 H), 7.46 (t, J = 7.5 Hz, 2 H), 7.82 (d, J = 7.5 Hz, 2 H), 10.01 (s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 22.4, 36.6, 88.1, 126.7, 128.1, 128.5, 132.1, 136.3, 145.4, 169.4 ppm. HRMS (ESI-TOF): calcd. for $C_{12}H_{13}BrN_3O$ [M + H]$^+$ 294.0237; found 294.0211, 296.0183.

***N*-(4-Chloro-1-methyl-3-phenyl-1*H*-pyrazol-5-yl)acetamide (1d):** A mixture of 1-methyl-3-phenyl-1*H*-pyrazol-5-amine (1.73 g, 10.0 mmol) and acetic anhydride (1.13 mL, 12.0 mmol) in dichloromethane (0 mL) was stirred at a room temperature for 18 h, then the mixture was cooled in an ice–water bath and *N*-chlorosuccinimide (1.47 g, 11.0 mmol) was added in one portion. The reaction mixture was stirred at room temperature for another 18 h and evaporated under reduced pressure (evaporated twice with toluene to remove residual acetic acid). The crude product was crystallized twice, first from a mixture of dichloromethane/hexanes, then from MeOH/H_2O to remove residual succinimide. The title product **1d** was obtained as a white fine powder (2.09 g, 84 %), m.p. 156–158 °C (MeOH/H_2O). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.12 (s, 3 H), 3.68 (s, 3 H), 7.38 (td, J = 7.3, 1.3 Hz, 1 H), 7.46 (dd, J = 7.5, 7.3 Hz, 2 H), 7.81 (dd, J = 7.5, 1.3 Hz, 2 H), 10.06 (s, 1 H) ppm. ^{13}C NMR (101 MHz, [D$_6$]DMSO): δ = 22.5, 36.6, 101.8, 126.4, 128.1, 128.6, 131.7, 134.7, 143.8, 169.5 ppm.

***N*-(4-Iodo-1,3-dimethyl-1*H*-pyrazol-5-yl)acetamide (1e):** A mixture of 1,3-dimethyl-1*H*-pyrazol-5-amine (0.555 g, 5.0 mmol) and acetic anhydride (0.565 mL, 6.0 mmol) in MeCN (30 mL) was stirred at ambient temperature for 18 h. Then iodine (3.036 g, 12.0 mmol) was slowly added in several portions and the resulting mixture was stirred at ambient temperature for an additional 3 d. Then 2 N K_2CO_3 (15 mL) and 1 N $Na_2S_2O_3$ (15 mL) were added and the mixture was thoroughly shaken until all unreacted iodine was reduced. The organic layer was separated and the aqueous layer extracted with ethyl acetate (2 × 30 mL). The combined organic layers were dried with Na_2SO_4 and the solvents removed under reduced pressure. The crude product was triturated with water (20 mL), filtered, and washed with water (ca. 20 mL) to yield the iodopyrazole **1e** as a white powder (0.865 g, 62 %), m.p. 144–146 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.06 (s, 3 H), 2.08 (s, 3 H), 3.56 (s, 3 H), 9.79 (s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 14.0, 22.5, 36.1, 59.9, 138.4, 147.5, 169.2 ppm. HRMS (ESI-TOF): calcd. for $C_7H_{11}IN_3O$ [M + H]$^+$ 279.9941; found 279.9941.

4-Bromo-1,3-dimethyl-1*H*-pyrazol-5-amine (6a): A mixture of 1,3-dimethyl-1*H*-pyrazol-5-amine (0.22 g, 2.0 mmol), and *N*-bromosuccinimide (0.37 g, 2.1 mmol) in DCM (10 mL) was stirred at ambient temperature for 19 h. Then the mixture was washed with aqueous sodium carbonate and the aqueous layer extracted with dichloromethane (2 × 10 mL). The combined organic layers were dried with Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, *i*PrOH/hexanes, gradient from 2:100 to 4:100). The bromopyrazole **6a** was obtained as a yellow oil (0.29 g, 77 %). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.95 (s, 3 H), 3.48 (s, 3 H), 5.26 (br. s, 2 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 12.3, 34.9, 74.0, 143.1, 144.5 ppm.

4-Bromo-1-methyl-3-phenyl-1*H*-pyrazol-5-amine (6b): A mixture of 1-methyl-3-phenyl-1*H*-pyrazol-5-amine (1.73 g, 10.0 mmol) and *N*-bromosuccinimide (1.78 g, 10.0 mmol) was stirred in DCM (20 mL) at ambient temperature for 18–24 h. Then the mixture was washed with aqueous sodium carbonate. The organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluting with 0–2 % MeOH in dichloromethane). The title compound **6b** was obtained as a pink solid (1.91 g, 76 %), m.p. 89–92 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.64 (s, 3 H), 5.47 (s, 2 H), 7.32 (t, J = 7.3 Hz, 1 H), 7.40 (t, J = 7.3 Hz, 2 H), 7.77 (d, J = 7.3 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 35.5, 72.1, 126.5, 127.6, 128.2, 132.9, 144.5, 145.8 ppm. HRMS (ESI-TOF): calcd. for $C_{10}H_{11}BrN_3$ [M + H]$^+$ 252.0135; found 252.0135, 254.0108.

General Procedure for the Synthesis of Biaryls or Arylalkenyls 3a–z by the Suzuki–Miyaura Reaction: See Table 2. The corresponding pyrazole **1** (1.0 mmol), boronic acid **2** (2.0 mmol), potassium carbonate (0.272 g, 2.0 mmol), and XPhos (0.009 g, 0.020 mmol) were weighed into a pressure tube. Dioxane (3 mL) and water (1 mL) were successively added to the reaction flask. The mixture was then degassed for 5 min by using a needle connected to a nitrogen supply. Then $Pd(OAc)_2$ (0.002 g, 0.010 mmol) was

added while maintaining a flow of nitrogen. The tube was quickly closed with a screw cap and inserted into an oil bath preheated to 100 °C. The mixture was stirred at approximately 700 rpm for 8 h. After that, the mixture was filtered through Celite, washed with EtOAc, and partitioned between EtOAc and water. The organic layer was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (DCM/MeOH, 100:0–100:3) to give the desired biaryl. The title product was sufficiently pure according to NMR and HPLC–MS analyses; however, it was further crystallized from a mixture of DCM and hexanes or other solvent systems before measurement of the melting point.

***N*-[1,3-Dimethyl-4-(*p*-tolyl)-1*H*-pyrazol-5-yl]acetamide (3a):** White solid (0.180 g, 74 %), m.p. 108–110 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 2.01 (s, 3 H), 2.17 (s, 3 H), 2.30 (s, 3 H), 3.53 (s, 3 H), 7.16–7.22 (m, 4 H), 9.70 (s, 1 H) ppm; minor conformer: δ = 1.48 (s, 3 H), 2.19 (s, 3 H), 2.31 (s, 3 H), 3.64 (s, 3 H), 9.26 (s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 13.1, 20.1, 22.4, 35.0, 114.4, 128.0, 129.0, 129.6, 133.0, 135.3, 143.2, 170.1 ppm. HRMS (ESI-TOF): calcd. for $C_{14}H_{18}N_3O$ [M + H]$^+$ 244.1444; found 244.1434.

***N*-[1-Methyl-3-phenyl-4-(*p*-tolyl)-1*H*-pyrazol-5-yl]acetamide (3b):** White solid (0.244 g, 80 %), m.p. 174–176 °C (toluene). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.02 (s, 3 H), 2.30 (s, 3 H), 3.67 (s, 3 H), 7.03 (d, *J* = 7.9 Hz, 2 H), 7.14 (d, *J* = 7.9 Hz, 2 H), 7.23–7.31 (m, 3 H), 7.33–7.36 (m, 2 H), 9.76 (s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 20.7, 22.4, 35.5, 114.4, 127.3, 127.3, 128.2, 129.0, 129.0, 129.3, 133.6, 134.5, 135.8, 146.1, 170.3 ppm. HRMS (ESI-TOF): calcd. for $C_{19}H_{20}N_3O$ [M + H]$^+$ 306.1601; found 306.1601.

***N*-(1,3-Dimethyl-4-phenyl-1*H*-pyrazol-5-yl)acetamide (3c):** Colorless oil that solidified upon standing (0.183 g, 80 %), m.p. 120–123 °C. ^{1}H NMR (400 MHz, CDCl$_3$): major conformer: δ = 2.12 (s, 3 H), 2.24 (s, 3 H), 3.66 (s, 3 H), 7.22 (d, *J* = 7.5 Hz, 2 H), 7.28 (t, *J* = 7.5 Hz, 1 H), 7.38 (t, *J* = 7.5 Hz, 2 H), 7.58 (s, 1 H) ppm; minor conformer: δ = 1.67 (s, 3 H), 2.30 (s, 3 H), 3.71 (s, 3 H), 7.17 (s, 1 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): major conformer: δ = 12.8, 22.8, 35.5, 115.6, 126.8, 128.6, 128.7, 132.0, 132.5, 144.8, 170.5 ppm; minor conformer: δ = 13.2, 20.3, 34.9, 116.7, 127.0, 128.4, 128.8, 131.6, 132.9, 145.7, 173.0 ppm. HRMS (ESI-TOF): calcd. for $C_{13}H_{16}N_3O$ [M + H]$^+$ 230.1288; found 230.1280.

***N*-(1-Methyl-3,4-diphenyl-1*H*-pyrazol-5-yl)acetamide (3d):** White solid (0.241 g, 83 %), m.p. 198–201 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 2.03 (s, 3 H), 3.68 (s, 3 H), 7.13–7.16 (m, 2 H), 7.25–7.30 (m, 4 H), 7.32–7.36 (m, 4 H), 9.81 (s, 1 H) ppm; minor conformer: δ = 1.55 (s), 3.79 (s), 9.33 (s, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 22.4, 35.6, 114.5, 126.7, 127.3, 127.4, 128.2, 128.4, 129.2, 132.3, 133.5, 134.6, 146.2, 170.3 ppm. HRMS (ESI-TOF): calcd. for $C_{18}H_{18}N_3O$ [M + H]$^+$ 292.1445; found 292.1445.

***N*-[1,3-Dimethyl-4-(4-nitrophenyl)-1*H*-pyrazol-5-yl]acetamide (3e):** Yellow solid (0.211 g, 77 %), m.p. 162–164 °C (DCM/hexanes). ^{1}H NMR (400 MHz, CDCl$_3$): major conformer: δ = 2.22 (s, 3 H), 2.30 (s, 3 H), 3.73 (s, 3 H), 7.39 (d, *J* = 8.8 Hz, 2 H), 7.60 (br. s, 1 H), 8.17 (d, *J* = 8.8 Hz, 2 H) ppm; minor conformer: δ = 1.71 (s, 3 H), 2.36 (s, 3 H), 3.79 (s, 3 H), 7.31 (br. s, 1 H), 7.47 (d, *J* = 8.8 Hz, 2 H), 8.25 (d, *J* = 8.8 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): major conformer: δ = 13.0, 23.0, 35.7, 114.1, 123.9, 129.0, 132.2, 139.3, 144.9, 146.1, 170.3 ppm; minor conformer: δ = 13.6, 20.4, 35.2, 124.2, 128.7, 131.4, 138.8, 145.9 ppm. HRMS (ESI-TOF): calcd. for $C_{13}H_{15}N_4O_3$ [M + H]$^+$ 275.1139; found 275.1137.

***N*-[1-Methyl-4-(4-nitrophenyl)-3-phenyl-1*H*-pyrazol-5-yl]acetamide (3f):** Yellow solid (0.302 g, 90 %), m.p. 142–144 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 2.06 (s, 3 H), 3.72 (s, 3 H), 7.31–7.35 (m, 5 H), 7.39 (d, *J* = 8.8 Hz, 2 H), 8.20 (d, *J* = 8.8 Hz, 2 H), 9.97 (s, 1 H) ppm; minor conformer: δ = 1.56 (s), 3.82 (s), 7.45 (d, *J* = 8.8 Hz), 8.25 (d, *J* = 8.8 Hz), 9.49 (NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 22.9, 36.1, 113.1, 124.2, 128.2, 128.3, 129.0, 130.3, 133.3, 135.7, 140.1, 146.3, 147.3, 170.7 ppm. HRMS (ESI-TOF): calcd. for $C_{18}H_{17}N_4O_3$ [M + H]$^+$ 337.1295; found 337.1297.

***N*-{1,3-Dimethyl-4-[4-(trifluoromethyl)phenyl]-1*H*-pyrazol-5-yl}acetamide (3g):** White solid (0.261 g, 88 %), m.p. 177–178 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 2.04 (s, 3 H), 2.22 (s, 3 H), 3.57 (s, 3 H), 7.51 (d, *J* = 7.9 Hz, 2 H), 7.75 (d, *J* = 7.9 Hz, 2 H), 9.84 (s, 1 H) ppm; minor conformer: δ = 1.51 (s, 3 H), 2.25 (s, 3 H), 3.67 (s, 3 H), 7.57 (d, *J* = 7.9 Hz, 2 H), 7.79 (d, *J* = 7.9 Hz, 2 H), 9.40 (s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): major conformer: δ = 13.2, 22.5, 35.1, 113.1, 124.4 (q, *J* = 272 Hz), 125.4 (q, *J* = 4 Hz), 126.5 (q, *J* = 32 Hz), 128.5, 133.8, 137.1, 143.7, 170.1 ppm. HRMS (ESI-TOF): calcd. for $C_{14}H_{15}F_3N_3O$ [M + H]$^+$ 298.1162; found 298.1145.

***N*-{1-Methyl-3-phenyl-4-[4-(trifluoromethyl)phenyl]-1*H*-pyrazol-5-yl}acetamide (3h):** White solid (0.294 g, 82 %), m.p. 176–178 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 2.04 (s, 3 H), 3.69 (s, 3 H), 7.26–7.32 (m, 5 H), 7.34 (d, *J* = 8.3 Hz, 2 H), 7.69 (d, *J* = 8.3 Hz, 2 H), 9.88 (s, 1 H) ppm; minor conformer: δ = 1.54 (s), 3.80 (s), 7.40 (d, *J* = 8.3 Hz), 7.74 (d, *J* = 8.3 Hz), 9.42 (s, NH) ppm. ^{13}C NMR (101 MHz, [D$_6$]DMSO): δ = 22.4, 35.6, 113.1, 124.4 (q, *J* = 272 Hz, CF_3), 125.3 (q, *J* = 4 Hz), 127.1 (q, *J* = 32 Hz), 127.6, 127.7, 128.4, 129.6, 133.0, 135.0, 136.7, 146.6, 170.3 ppm. HRMS (ESI-TOF): calcd. for $C_{19}H_{17}F_3N_3O$ [M + H]$^+$ 360.1318; found 360.1319.

***N*-[4-(4-Methoxyphenyl)-1,3-dimethyl-1*H*-pyrazol-5-yl]acetamide (3i):** White solid (0.220 g, 85 %), m.p. 185–186 °C (DCM/toluene). ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 2.02 (s, 3 H), 2.16 (s, 3 H), 3.53 (s, 3 H), 3.76 (s, 3 H), 6.96 (d, *J* = 8.8 Hz, 2 H), 7.20 (d, *J* = 8.8 Hz, 2 H), 9.69 (s, 1 H) ppm; minor conformer: δ = 1.50 (s, 3 H), 2.18 (s, 3 H), 3.64 (s, 3 H), 3.77 (s, 3 H), 6.99 (d, *J* = 8.8 Hz, 2 H), 7.25 (d, *J* = 8.8 Hz, 2 H), 9.24 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): major conformer: δ = 13.1, 22.4, 35.0, 55.1, 114.0, 114.2, 124.8, 129.3, 132.9, 143.1, 157.7, 170.1 ppm; minor conformer: δ = 13.1, 20.5, 34.6, 114.8, 124.4, 129.3, 133.9, 143.6, 157.9, 171.4 ppm. HRMS (ESI-TOF): calcd. for $C_{14}H_{18}N_3O_2$ [M + H]$^+$ 260.1394; found 260.1379.

***N*-[4-(4-Methoxyphenyl)-1-methyl-3-phenyl-1*H*-pyrazol-5-yl]acetamide (3j):** White solid (0.292 g, 91 %), m.p. 160–162 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 2.02 (s, 3 H), 3.67 (s, 3 H), 3.75 (s, 3 H), 6.91 (d, *J* = 8.8 Hz, 2 H), 7.06 (d, *J* = 8.8 Hz, 2 H), 7.24–7.31 (m, 3 H), 7.33–7.36 (m, 2 H), 9.75 (s, 3 H) ppm; minor conformer: δ = 1.55 (s), 3.77 (s), 3.78 (s), 6.95 (d, *J* = 8.8 Hz), 7.11 (d, *J* = 8.8 Hz), 9.27 (s, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): major conformer: δ = 22.4, 35.5, 55.0, 113.9, 114.3, 124.4, 127.2, 127.3, 128.2, 130.3, 133.6, 134.4, 146.0, 158.1, 170.3 ppm; minor conformer: δ = 20.7, 35.2 ppm. HRMS (ESI-TOF): calcd. for $C_{19}H_{20}N_3O_2$ [M + H]$^+$ 322.1550; found 322.1550.

***N*-[4-(4-Hydroxyphenyl)-1,3-dimethyl-1*H*-pyrazol-5-yl]acetamide (3k):** White solid (0.169 g, 69 %), m.p. 110–112 °C (acetone/DCM). ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 2.01 (s, 3 H), 2.14 (s, 3 H), 3.62 (s, 3 H), 6.78 (d, *J* = 8.3 Hz, 2 H), 7.07 (d, *J* = 8.3 Hz, 2 H), 9.37 (s, 1 H), 9.65 (s, 1 H) ppm; minor conformer: δ = 1.50 (s, 3 H), 2.16 (s, 3 H), 3.62 (s, 3 H), 6.80 (d, *J* = 8.3 Hz, 2 H), 7.12 (d, *J* = 8.3 Hz, 2 H), 9.19 (s, 1 H), 9.43 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): major conformer: δ = 13.1, 22.4, 35.0, 114.5,

115.3, 123.1, 129.3, 132.7, 143.0, 155.9, 170.2 ppm; minor conformer: δ = 13.2, 20.6, 34.6, 115.5, 129.4, 143.5, 156.0, 171.5 ppm. HRMS (ESI-TOF): calcd. for $C_{13}H_{16}N_3O_2$ $[M + H]^+$ 246.1237; found 246.1224.

***N*-[4-(4-Hydroxyphenyl)-1-methyl-3-phenyl-1*H*-pyrazol-5-yl]-acetamide (3l):** White solid (0.221 g, 72 %), m.p. 251–252 °C (acetone/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 2.02 (s, 3 H), 3.66 (s, 3 H), 6.73 (d, J = 8.8 Hz, 2 H), 6.94 (d, J = 8.8 Hz, 2 H), 7.22–7.30 (m, 3 H), 7.34–7.37 (m, 2 H), 9.41 (s, 1 H), 9.71 (s, 1 H) ppm; minor conformer: δ = 1.56 (s), 3.77 (s), 6.76 (d, J = 8.8 Hz), 6.99 (d, J = 8.8 Hz), 9.23 (s), 9.49 (s) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): major conformer: δ = 22.4, 35.5, 114.6, 115.3, 122.7, 127.1, 127.2, 128.2, 130.4, 133.7, 134.3, 145.9, 156.3, 170.3 ppm; minor conformer: δ = 20.7, 35.2, 115.6 ppm. HRMS (ESI-TOF): calcd. for $C_{18}H_{18}N_3O_2$ $[M + H]^+$ 308.1394; found 308.1393.

***N*-[4-(2-Methoxyphenyl)-1,3-dimethyl-1*H*-pyrazol-5-yl]acetamide (3m):** White solid (0.222 g, 86 %), m.p. 66–70 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 1.97 (s, 3 H), 2.00 (s, 3 H), 3.54 (s, 3 H), 3.72 (s, 3 H), 6.95 (td, J = 7.3, 1.0 Hz, 1 H), 7.04 (d, J = 7.8 Hz, 1 H), 7.07 (dd, J = 7.3, 1.6 Hz, 1 H), 7.29 (td, J = 7.3, 1.6 Hz, 1 H), 9.49 (s, 1 H) ppm; minor conformer: δ = 1.54 (s), 3.64 (s), 9.06 (s) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): major conformer: δ = 13.1, 22.4, 35.2, 55.1, 111.2, 120.2, 121.1, 128.3, 130.9, 133.8, 144.5, 156.7, 169.7 ppm; minor conformer: δ = 12.9, 20.3, 34.7, 55.2, 112.3, 119.5, 120.7, 128.8, 131.2, 134.8, 145.0, 156.8, 171.5 ppm. HRMS (ESI-TOF): calcd. for $C_{14}H_{18}N_3O_2$ $[M + H]^+$ 260.1394; found 260.1394.

***N*-[4-(2-Methoxyphenyl)-1-methyl-3-phenyl-1*H*-pyrazol-5-yl]-acetamide (3n):** White foam (0.282 g, 88 %), m.p. 70–74 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 1.98 (s, 3 H), 3.41 (s, 3 H), 3.67 (s, 3 H), 6.92–6.97 (m, 1 H), 6.99 (d, J = 8.3 Hz, 1 H), 7.06 (dd, J = 7.3, 1.6 Hz, 1 H), 7.18–7.25 (m, 3 H), 7.29–7.33 (m, 3 H), 9.58 (s, 1 H) ppm; minor conformer: δ = 1.61 (s), 3.50 (s), 3.78 (s), 9.12 (s) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 22.4, 35.7, 54.8, 110.8, 111.5, 120.4, 121.3, 126.0, 127.0, 128.0, 128.9, 131.2, 134.4, 135.1, 146.6, 151.0, 170.0 ppm. HRMS (ESI-TOF): calcd. for $C_{19}H_{20}N_3O_2$ $[M + H]^+$ 322.1550; found 322.1550.

***N*-[1,3-Dimethyl-4-(*o*-tolyl)-1*H*-pyrazol-5-yl]acetamide (3o):** White foam (0.187 g, 77 %). ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 1.93 (s, 3 H), 1.94 (s, 3 H), 2.07 (s, 3 H), 3.55 (s, 3 H), 7.03 (dd, J = 7.3, 1.6 Hz, 1 H), 7.17 (td, J = 7.3, 1.6 Hz, 1 H), 7.22 (td, J = 7.3, 1.6 Hz, 1 H), 7.26 (d, J = 7.3 Hz, 1 H), 9.61 (s, 1 H) ppm; minor conformer: δ = 1.51 (s), 1.97 (s), 2.11 (s), 3.66 (s), 9.23 (s) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 12.5, 19.6, 22.4, 35.3, 114.1, 125.5, 127.2, 129.9, 130.8, 131.8, 133.7, 137.0, 143.7, 169.6 ppm. HRMS (ESI-TOF): calcd. for $C_{14}H_{18}N_3O$ $[M + H]^+$ 244.1444; found 244.1445.

***N*-[1-Methyl-3-phenyl-4-(*o*-tolyl)-1*H*-pyrazol-5-yl]acetamide (3p):** White foam (0.247 g, 81 %), m.p. 80–84 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 1.90 (s, 3 H), 1.95 (s, 3 H), 3.70 (s, 3 H), 7.09–7.12 (m, 1 H), 7.19–7.31 (m, 8 H), 9.66 (s, 1 H) ppm; minor conformer: δ = 1.60 (s), 3.81 (s), 9.29 (s) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 19.7, 22.3, 35.7, 113.9, 125.8, 125.9, 127.2, 127.7, 128.3, 130.0, 130.7, 132.3, 134.0, 134.9, 137.1, 145.8, 169.9 ppm. HRMS (ESI-TOF): calcd. for $C_{19}H_{20}N_3O$ $[M + H]^+$ 306.1601; found 306.1602.

***(E)*-*N*-(1,3-Dimethyl-4-styryl-1*H*-pyrazol-5-yl)acetamide (3q):** White solid (0.199 g, 78 %), m.p. 143–145 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 2.14 (s, 3 H), 2.30 (s, 3 H), 3.53 (s, 3 H), 6.74 (d, J = 16.7 Hz, 1 H), 6.89 (d, J = 16.7 Hz, 1 H), 7.21 (t, J = 7.5 Hz, 1 H), 7.34 (t, J = 7.5 Hz, 2 H), 7.49 (d, J = 7.5 Hz, 2 H), 9.92 (s, 1 H) ppm; minor conformer: δ = 1.71 (s, 3 H), 2.32 (s, 3 H), 3.62 (s, 3 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): major conformer: δ = 13.9, 22.7, 35.2, 110.4, 119.0, 125.5, 125.7, 126.8, 128.6, 134.3, 137.9, 144.0, 169.5 ppm. HRMS (ESI-TOF): calcd. for $C_{15}H_{18}N_3O$ $[M + H]^+$ 256.1444; found 256.1430.

***(E)*-*N*-(1-Methyl-3-phenyl-4-styryl-1*H*-pyrazol-5-yl)acetamide (3r):** White solid (0.257 g, 81 %), m.p. 78–80 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.16 (s, 3 H), 3.67 (s, 3 H), 6.78 (d, J = 16.7 Hz, 1 H), 6.96 (d, J = 16.7 Hz, 1 H), 7.22 (t, J = 7.5 Hz, 1 H), 7.33 (t, J = 7.5 Hz, 2 H), 7.37–7.42 (m, 3 H), 7.47 (t, J = 7.5 Hz, 2 H), 7.59 (m, 2 H), 10.04 (s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 22.6, 35.7, 110.5, 118.5, 125.8, 127.2, 127.7, 127.8, 128.0, 128.6, 128.7, 133.6, 134.3, 137.5, 147.4, 169.8 ppm. HRMS (ESI-TOF): calcd. for $C_{20}H_{20}N_3O$ $[M + H]^+$ 318.1601; found 318.1600.

***(E)*-*N*-[4-(4-Methoxystyryl)-1,3-dimethyl-1*H*-pyrazol-5-yl]acetamide (3s):** White solid (0.237 g, 83 %), m.p. 157–159 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.12 (s, 3 H), 2.27 (s, 3 H), 3.51 (s, 3 H), 3.76 (s, 3 H), 6.67 (d, J = 16.7 Hz, 1 H), 6.72 (d, J = 16.7 Hz, 1 H), 6.91 (d, J = 8.8 Hz, 2 H), 7.42 (d, J = 8.8 Hz, 2 H), 9.86 (s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 13.9, 22.6, 35.2, 55.1, 110.7, 114.1, 116.8, 125.3, 126.9, 130.6, 133.9, 143.7, 158.4, 169.5 ppm. HRMS (ESI-TOF): calcd. for $C_{16}H_{20}N_3O_2$ $[M + H]^+$ 286.1550; found 286.1520.

***(E)*-*N*-{4-[4-(Trifluoromethyl)styryl]-1,3-dimethyl-1*H*-pyrazol-5-yl}acetamide (3t):** White solid (0.278 g, 86 %), m.p. 188–190 °C (DCM). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.14 (s, 3 H), 2.31 (s, 3 H), 3.53 (s, 3 H), 6.80 (d, J = 16.6 Hz, 1 H), 7.05 (d, J = 16.6 Hz, 1 H), 7.67 (d, J = 8.6 Hz, 2 H), 7.71 (d, J = 8.6 Hz, 2 H), 9.94 (s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 13.8, 22.7, 35.3, 110.1, 122.0, 123.6, 124.4 (q, J = 271 Hz), 125.4 (q, J = 4 Hz), 126.1, 126.6 (q, J = 32 Hz), 134.9, 142.1, 144.4, 169.5 ppm. HRMS (ESI-TOF): calcd. for $C_{16}H_{17}F_3N_3O$ $[M + H]^+$ 324.1318; found 324.1290.

***N*-[4-(Benzo[*b*]thiophen-2-yl)-1,3-dimethyl-1*H*-pyrazol-5-yl]-acetamide (3u):** White solid (0.225 g, 79 %), m.p. 149–152 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 2.14 (s, 3 H), 2.38 (s, 3 H), 3.58 (s, 3 H), 7.30 (dd, J = 7.5, 6.9 Hz, 1 H), 7.36 (dd, J = 7.5, 6.9 Hz, 1 H), 7.39 (s, 1 H), 7.82 (d, J = 7.5 Hz, 1 H), 7.93 (d, J = 7.5 Hz, 1 H), 9.98 (s, 1 H) ppm; minor conformer: δ = 1.65 (s), 3.68 (s), 9.42 (s) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): major conformer: δ = 14.0, 22.7, 35.1, 108.5, 119.7, 122.0, 123.0, 123.8, 124.4, 133.9, 134.5, 138.1, 139.8, 143.7, 170.0 ppm; minor conformer: δ = 12.3, 22.4, 36.1 ppm. HRMS (ESI-TOF): calcd. for $C_{15}H_{16}N_3OS$ $[M + H]^+$ 286.1009; found 286.1009.

***N*-[4-(Benzo[*b*]thiophen-2-yl)-1-methyl-3-phenyl-1*H*-pyrazol-5-yl]acetamide (3v):** White solid (0.263 g, 76 %), m.p. 196–198 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.10 (s, 3 H), 3.71 (s, 3 H), 7.19 (s, 1 H), 7.27–7.39 (m, 5 H), 7.45–7.53 (m, 2 H), 7.77 (dd, J = 6.7, 1.5 Hz, 1 H), 7.90 (dd, J = 7.6, 1.0 Hz, 1 H), 9.99 (s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 22.6, 35.8, 107.7, 122.2, 122.5, 123.4, 124.1, 124.4, 127.9, 128.0, 128.4, 132.9, 133.8, 135.6, 139.3, 139.7, 147.0, 170.2 ppm. HRMS (ESI-TOF): calcd. for $C_{20}H_{18}N_3OS$ $[M + H]^+$ 348.1165; found 348.1166.

***N*-[4-(Furan-2-yl)-1,3-dimethyl-1*H*-pyrazol-5-yl]acetamide (3w):** Prepared from pyrazole **1a** and the MIDA ester of furan-2-ylboronic acid (**2n**). White solid (0.184 g, 84 %), m.p. 139–141 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.09 (s, 3 H), 2.28 (s, 3 H), 3.54 (s, 3 H), 6.35 (dd, J = 3.2, 0.7 Hz, 1 H), 6.52 (dd, J = 3.2, 1.8 Hz, 1 H), 7.65 (dd, J = 1.8, 0.7 Hz, 1 H), 9.87 (s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 13.8, 22.6, 35.1, 104.8, 105.8, 111.1, 132.9, 141.2, 142.8, 147.3, 169.7 ppm. HRMS (ESI-TOF): calcd. for $C_{11}H_{14}N_3O_2$ $[M + H]^+$ 220.1081; found 220.1081.

***N*-[4-(Furan-2-yl)-1-methyl-3-phenyl-1*H*-pyrazol-5-yl]acetamide (3x):** Prepared from pyrazole **1c** and the MIDA ester of furan-2-ylboronic acid (**2n**). Pale-yellow solid (0.216 g, 77 %), m.p. 131–134 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.08 (s, 3 H), 3.68 (s, 3 H), 6.34 (dd, *J* = 3.4, 0.7 Hz, 1 H), 6.53 (dd, *J* = 3.4, 1.8 Hz, 1 H), 7.30–7.45 (m, 5 H), 7.63 (dd, *J* = 1.8, 0.7 Hz, 1 H), 9.93 (s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 22.5, 35.8, 105.1, 107.8, 111.3, 127.2, 127.7, 128.2, 133.3, 135.3, 142.2, 145.7, 146.5, 169.9 ppm. HRMS (ESI-TOF): calcd. for $C_{16}H_{16}N_3O_2$ [M + H]$^+$ 282.1237; found 282.1237.

***N*-[1-Methyl-3-phenyl-4-(pyridin-3-yl)-1*H*-pyrazol-5-yl]acetamide (3y):** Prepared from pyrazole **1c** and 3-pyridylboronic acid pinacol ester (**2p**). White solid (0.169 g, 58 %), m.p. 188–189 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): major conformer: δ = 2.04 (s, 3 H), 3.71 (s, 3 H), 7.29–7.33 (m, 5 H), 7.37 (ddd, *J* = 7.9, 4.8, 0.9 Hz, 1 H), 7.53 (dt, *J* = 7.9, 2.2 Hz, 1 H), 8.34 (d, *J* = 2.2 Hz, 1 H), 8.47 (dd, *J* = 4.8, 1.3 Hz, 1 H), 9.92 (s, 1 H) ppm; minor conformer: δ = 1.59 (s), 3.82 (s) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 22.4, 35.7, 111.2, 123.6, 127.4, 127.6, 128.3, 128.4, 133.1, 135.1, 136.4, 146.6, 147.7, 149.5, 170.2 ppm. HRMS (ESI-TOF): calcd. for $C_{17}H_{17}N_4O$ [M + H]$^+$ 293.1397; found 293.1397.

***N*-[1-Methyl-3-phenyl-4-(pyridin-4-yl)-1*H*-pyrazol-5-yl]acetamide (3z):** Prepared from pyrazole **1a** and 4-pyridylboronic acid MIDA ester (**2q**). The reaction was performed in a mixture of DMF and 2-propanol (5 mL, 10:1) in the presence of Cu(OAc)$_2$ (0.031 g, 0.5 mmol). Biaryl **3z** was obtained after purification by column chromatography as a white solid (0.064 g, 29 %), m.p. 184–186 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.07 (s, 3 H), 3.71 (s, 3 H), 7.14 (dd, *J* = 4.6, 1.6 Hz, 2 H), 7.30–7.35 (m, 5 H), 8.51 (dd, *J* = 4.6, 1.6 Hz, 2 H), 10.02 (s, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 22.5, 35.7, 111.9, 123.6, 127.7, 127.9, 128.5, 132.9, 135.3, 140.3, 146.9, 149.6, 170.3 ppm. HRMS (ESI-TOF): calcd. for $C_{17}H_{17}N_4O$ [M + H]$^+$ 293.1397; found 293.1397.

General Procedure for the Synthesis of Biaryls 7a–i by the Suzuki–Miyaura Reaction: See Table 3. The corresponding pyrazole (1.0 mmol), boronic acid (2.0 mmol), potassium carbonate (0.272 g, 2.0 mmol), and XPhos (0.009 g, 0.020 mmol) were weighed into a pressure tube and dioxane (3 mL) and water (1 mL) were added successively. The mixture was degassed for 5 min by using a needle connected to a nitrogen supply. XPhos Pd G2 (0.008 g, 0.010 mmol) was added while maintaining a flow of nitrogen. The tube was quickly closed with a screw cap and inserted into an oil bath preheated to 100 °C. The mixture was stirred at approximately 700 rpm for 8 h. After that, the mixture was filtered through Celite, washed with EtOAc, and partitioned between EtOAc and water. The organic layer was separated, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (DCM/MeOH, 100:0–100:5) to give the desired biaryl. The title product was sufficiently pure according to NMR and HPLC–MS; however, it was further crystallized from a mixture of DCM and hexanes or other solvent systems before measurement of the melting point.

1,3-Dimethyl-4-(*p*-tolyl)-1*H*-pyrazol-5-amine (7a): White solid (0.152 g, 76 %), m.p. 100–102 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.04 (s, 3 H), 2.30 (s, 3 H), 3.51 (s, 3 H), 4.98 (s, 2 H), 7.12–7.18 (m, 4 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 13.2, 20.7, 34.0, 101.8, 127.8, 129.1, 131.4, 133.6, 142.8, 143.6 ppm. HRMS (ESI-TOF): calcd. for $C_{12}H_{16}N_3$ [M + H]$^+$ 202.1056; found 202.1056.

4-(4-Methoxyphenyl)-1-methyl-3-phenyl-1*H*-pyrazol-5-amine (7b): White solid (0.167 g, 60 %), m.p. 139–142 °C (MeOH/H$_2$O). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.64 (s, 3 H), 3.75 (s, 3 H), 4.96 (s, 2 H), 6.90 (d, *J* = 8.8 Hz, 2 H), 7.04 (d, *J* = 8.8 Hz, 2 H), 7.18–7.24 (m, 3 H), 7.2–7.31 (m, 2 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 34.6, 55.0, 101.2, 114.0, 126.1, 126.7, 127.1, 127.9, 130.6, 134.5, 144.7, 145.7, 157.3 ppm. HRMS (ESI-TOF): calcd. for $C_{17}H_{18}N_3O$ [M + H]$^+$ 280.1444; found 280.1444.

1,3-Dimethyl-4-[4-(trifluoromethyl)phenyl]-1*H*-pyrazol-5-amine (7c): White solid (0.163 g, 64 %), m.p. 109–111 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.10 (s, 3 H), 3.52 (s, 3 H), 5.33 (s, 2 H), 7.49 (d, *J* = 8.4 Hz, 2 H), 7.67 (d, *J* = 8.4 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 12.9, 33.5, 100.4, 124.5 (q, *J* = 271 Hz), 124.6 (q, *J* = 32 Hz), 125.2 (m), 127.7 (q, *J* = 7 Hz), 138.9, 143.2, 144.5 ppm. HRMS (ESI-TOF): calcd. for $C_{12}H_{13}F_3N_3$ [M + H]$^+$ 256.1056; found 256.1056.

1-Methyl-3-phenyl-4-[4-(trifluoromethyl)phenyl]-1*H*-pyrazol-5-amine (7d): White solid (0.202 g, 64 %), m.p. 168–170 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.66 (s, 3 H), 5.38 (s, 2 H), 7.21–7.28 (m, 5 H), 7.31 (dd, *J* = 8.7, 0.6 Hz, 2 H), 7.63 (dd, *J* = 8.6, 0.5 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 34.6, 99.9, 124.6 (q, *J* = 271 Hz, CF$_3$), 125.2 (q, *J* = 4 Hz), 125.4 (q, *J* = 32 Hz), 127.2, 127.6, 128.2, 129.4, 134.0, 138.5, 145.4, 146.4 ppm. HRMS (ESI-TOF): calcd. for $C_{17}H_{15}F_3N_3$ [M + H]$^+$ 318.1213; found 318.1212.

4-(2-Methoxyphenyl)-1-methyl-3-phenyl-1*H*-pyrazol-5-amine (7e): White solid (0.184 g, 66 %), m.p. 182–184 °C (MeOH/H$_2$O). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.61 (s, 3 H), 3.64 (s, 3 H), 4.78 (s, 2 H), 6.87 (dd, *J* = 7.40, 1.2 Hz, 1 H), 6.96 (dd, *J* = 7.40, 1.69 Hz, 1 H), 7.03 (dd, *J* = 8.3, 0.9 Hz, 1 H), 7.11–7.21 (m, 3 H), 7.22–7.29 (m, 3 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 34.6, 55.0, 98.1, 111.5, 120.4, 122.5, 126.4, 126.5, 127.8, 127.9, 132.0, 134.9, 145.1, 146.1, 156.9 ppm. HRMS (ESI-TOF): calcd. for $C_{17}H_{18}N_3O$ [M + H]$^+$ 280.1444; found 280.1444.

1,3-Dimethyl-4-(*o*-tolyl)-1*H*-pyrazol-5-amine (7f): Pale-yellow solid (0.158 g, 79 %), m.p. 103–105 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.84 (s, 3 H), 2.0 (s, 3 H), 3.51 (s, 3 H), 4.73 (s, 2 H), 6.99–7.05 (m, 1 H), 7.09–7.16 (m, 2 H), 7.18–7.23 (m, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 12.5, 19.7, 34.0, 101.7, 125.5, 126.4, 129.9, 131.2, 133.2, 137.3, 143.2, 143.6 ppm. HRMS (ESI-TOF): calcd. for $C_{12}H_{16}N_3$ [M + H]$^+$ 202.1339; found 202.1339.

1,3-Dimethyl-4-(thiophen-3-yl)-1*H*-pyrazol-5-amine (7g): White solid (0.137 g, 71 %), m.p. 93–95 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.09 (s, 3 H), 3.50 (s, 3 H), 5.07 (s, 2 H), 7.21 (dd, *J* = 4.7, 1.0 Hz, 1 H), 7.23 (dd, *J* = 3.1, 1.0 Hz, 1 H), 7.54 (d, *J* = 4.7, 3.1 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 13.6, 34.0, 97.8, 117.9, 125.4, 127.2, 134.3, 142.9, 143.7 ppm. HRMS (ESI-TOF): calcd. for $C_9H_{12}N_3S$ [M + H]$^+$ 194.0746; found 194.0746.

4-(Furan-3-yl)-1-methyl-3-phenyl-1*H*-pyrazol-5-amine (7h): Prepared from pyrazole **6b** and furan-3-ylboronic acid (**2s**). Pale-yellow solid (0.160 g, 67 %), m.p. 142–144 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.63 (s, 3 H), 5.10 (s, 2 H), 6.17 (t, *J* = 1.6 Hz, 1 H), 7.22–7.27 (m, 1 H), 7.30 (t, *J* = 7.3 Hz, 2 H), 7.42–7.46 (m, 2 H), 7.61–7.64 (m, 2 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 34.6, 92.0, 111.6, 117.3, 127.0, 127.2, 128.0, 134.5, 139.1, 142.9, 145.0, 146.3 ppm. HRMS (ESI-TOF): calcd. for $C_{14}H_{14}N_3O$ [M + H]$^+$ 240.1131; found 240.1132.

1-Methyl-4-(5-methylthiophen-2-yl)-3-phenyl-1*H*-pyrazol-5-amine (7i): Prepared from pyrazole **6b** and 4,4,5,5-tetramethyl-2-(5-methylthiophen-2-yl)-1,3,2-dioxaborolane (**2t**). White solid (0.188 g, 70 %), m.p. 121–123 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.36 (d, *J* = 1.0 Hz, 3 H), 3.58 (s, 3 H), 5.12 (s, 2 H), 6.61 (d, *J* = 3.4 Hz), 6.70 (dd, *J* = 3.4, 1.0 Hz, 1 H), 7.15–7.25 (m, 3 H), 7.34–7.39 (m, 2 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 15.0, 34.7, 94.3, 125.7, 126.3, 127.0, 127.1, 128.0, 132.9, 134.0, 138.3,

145.8, 146.3 ppm. HRMS (ESI-TOF): calcd. for $C_{15}H_{16}N_3S$ $[M + H]^+$ 270.9941; found 270.9941.

1-Methyl-3-phenyl-4-(pyridin-3-yl)-1*H*-pyrazol-5-amine (7j): Prepared from pyrazole **6b** and 3-pyridylboronic acid pinacol ester (**2p**). White solid (0.150 g, 60 %), m.p. 140–142 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.66 (s, 3 H), 5.33 (s, 2 H), 7.21–7.28 (m, 5 H), 7.32 (ddd, J = 7.8, 4.7, 0.7 Hz, 1 H), 7.50 (dd, J = 7.8, 1.6 Hz, 1 H), 8.32 (d, J = 1.6 Hz, 1 H), 8.39 (dd, J = 4.7, 1.4 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 34.6, 97.9, 123.5, 127.1, 127.4, 128.1, 130.0, 134.1, 136.4, 145.4, 146.4, 149.9 ppm. HRMS (ESI-TOF): calcd. for $C_{15}H_{15}N_4$ $[M + H]^+$ 251.1291; found 251.1291.

1-Methyl-3-phenyl-4-(pyridin-4-yl)-1*H*-pyrazol-5-amine (7k): Prepared from pyrazole **6b** and 4-pyridylboronic acid MIDA ester (**2q**). The reaction was carried out in the presence of $Cu(OAc)_2$ (50 mol-%). Product **7k** was isolated as a pale-yellow solid (0.090 g, 36 %), m.p. 193–195 °C (DCM/hexanes). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.62 (s, 3 H), 5.48 (s, 2 H), 7.03 (d, J = 4.5 Hz, 2 H), 7.22–7.27 (m, 5 H), 8.36 (d, J = 4.5 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 34.6, 98.6, 123.3, 127.3, 127.7, 128.2, 134.0, 141.7, 145.6, 146.7, 149.5 ppm. HRMS (ESI-TOF): calcd. for $C_{15}H_{15}N_4$ $[M + H]^+$ 251.1291; found 251.1291.

Hydrolysis of *N*-Acetamide 3a: A mixture of pyrazole **3a** (0.243 g, 1.0 mmol) and KOH (0.168 g, 3.0 mmol) in EtOH/H_2O (2:1, 6 mL) was heated at reflux with a condenser for 48 h. Then the reaction mixture was diluted with EtOAc and brine and the organic layer was separated. The aqueous layer was extracted twice with EtOAc and the combined organic layers were dried with Na_2SO_4. The crude product was purified by column chromatography to yield the biaryl **7a** as a white solid (0.178 g, 89 %). Analytical data are identical to those of the same compound prepared by the Suzuki coupling reaction using XPhos Pd G2.

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