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Selective C–N Bond-Forming Reaction of 2,6-Dibromopyridine with Amines

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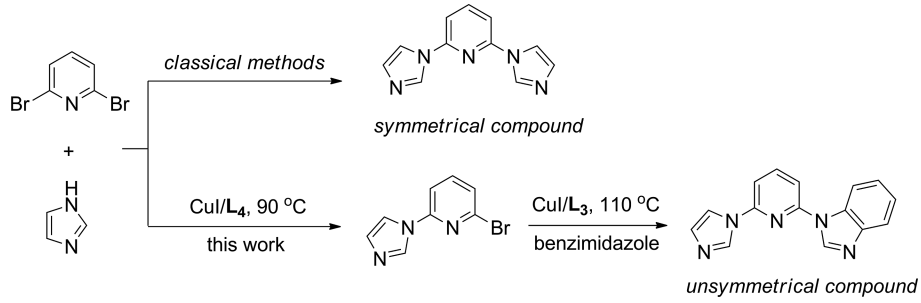
Keywords: Synthetic methods / Nitrogen heterocycles / Cross-coupling / Copper / Amines

A practical and efficient protocol for the syntheses of 6-substituted 2-bromopyridine compounds has been developed by using a selective copper-catalyzed C–N bond-forming reaction between 2,6-dibromopyridine and a range of amines. The major advantage of this protocol is the complete control of selectivity of the pyridine bromine atom for the C–N cross-coupling reaction. There are few reported syntheses of unsymmetrical 2,6-disubstituted pyridine-bridged compounds because of their complicated preparations. Although this is the case, a new series of these unsymmetrical compounds have been successfully prepared in two steps by using this copper-catalyzed coupling approach.

Introduction

2,6-Disubstituted pyridine-bridged compounds have attracted much attention because of their widespread applications in pharmaceutical synthesis,[1] organometallic catalysis,[2] and the field of advanced materials.[3] Generally, symmetrical 2,6-disubstituted pyridine-bridged compounds are prepared by a classical copper-catalyzed C–N bond-forming reaction,[4] but unsymmetrical compounds are difficult to obtain (see Scheme 1). Consequently, it is no surprise that copper-catalyzed coupling reactions with 2,6-dibromopyridine have been developed to give symmetrical 2,6-disubstituted pyridine-bridged compounds.[5] Despite the prevalence of these compounds in pharmaceutical synthesis, organometallic catalysis, and advanced materials synthesis, unsymmetrical 2,6-disubstituted pyridine-bridged compounds are much less studied.

Recent research has shown that unsymmetrical 2,6-disubstituted pyridine-bridged compounds exhibit remarkable performance in pharmaceutical synthesis[6] and organometallic catalysis.[7] Yu and co-workers reported the first example of a selective C–N bond-forming reaction for the preparation of 2-bromo-6-(pyrazol-1-yl)pyridines by employing a palladium-catalyzed coupling reaction of 2,6-dibromopyridine and pyrazoles.[8] This method has been employed to construct a class of unsymmetrical pyridine-bridged pyrazolyl-imidazolyl ligands that exhibit exceptionally high catalytic activity in the Suzuki reaction[9] and the



Scheme 1. The C–N coupling of 2,6-dibromopyridine.

transfer hydrogenation of ketones.[10] Recently, Frech's group also developed a transition-metal-free approach for the preparation of 6-bromopyridine-2-amines.[11] Buckley and co-workers synthesized a series of imidazo[1,2-*a*]pyridines, which are highly potent interleukin-1 receptor associated kinase-4 (IRAK-4) inhibitors with good drug-like properties.[12] However, these unsymmetrical 2,6-disubsti-

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tuted pyridine-bridged compounds are typically prepared by using a stoichiometric method or an expensive palladium catalyst, and, thus, these approaches result in low atom economy and high cost. Because unsymmetrical 2,6-disubstituted pyridine-bridged compounds are important building blocks in pharmaceutical synthesis and organometallic catalysis, there is an urgent need to seek an efficient, atom-economic, and inexpensive synthetic protocol to obtain these compounds.

The copper-catalyzed cross-coupling reaction has more than one hundred year history, and it is still actively employed in the field of organic synthesis as an efficient and versatile method.[13] 2,6-Dibromopyridine contains two bromo groups, and, therefore, some control in the selectivity of the C–N cross-coupling reactions of this compound is unavoidable. In classical synthetic methods, complete control of the selectivity of C–N bond formation with 2,6-dibromopyridine is a challenge (see Scheme 1). To the best of our knowledge, there is no report of a copper-catalyzed selective C–N cross-coupling reaction of 2,6-dibromopyridine and amines to synthesize 6-substituted 2-bromopyridines.

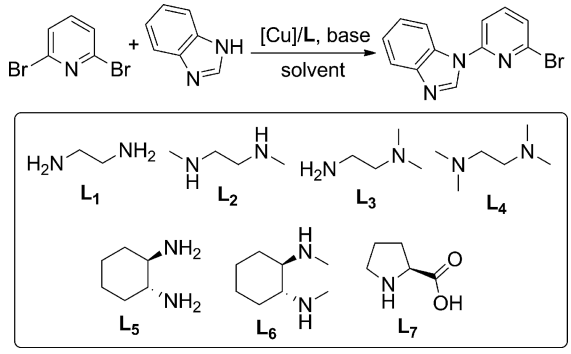
The presence of a ligand is important to the efficiency and selectivity of a reaction. We have a long-standing interest in the development of an efficient catalytic system to resolve the problems of the selective C–N cross-coupling reaction of 2,6-dibromopyridine. Inspired by Buchwald's research,[14] we tried a Cu-catalyzed C–N coupling reaction of 2,6-dibromopyridine with amines. We found that the ligand played an important role in the control of the selectivity with regard to 2,6-dibromopyridine. When 1,2-ethanediamine derivatives (**L**) were used as the ligand, the CuI/**L**/dimethyl sulfoxide (DMSO) catalytic system showed high selectivity in the coupling reaction of 2,6-dibromopyridine to produce 6-substituted 2-bromopyridine compounds as the major product. Therefore, in a copper-catalyzed coupling reaction, the selectivity for the formation of a mono- or disubstituted pyridine product depends on the appropriate choice of a ligand.

Herein, we report an efficient protocol for the selective construction of 6-substituted 2-bromopyridine compounds by using a copper-catalyzed coupling approach. The generation of these compounds provides access to a variety of subsequent transformations. We envisage that the 6-substituted 2-bromopyridine compounds may be useful intermediates in organic synthesis, such as in a Suzuki coupling,[15] a Heck coupling, a Sonogashira coupling,[16] an Ullmann-type reaction,[17] and an *N*-alkylation.

Results and Discussion

The cross-coupling reaction of 2,6-dibromopyridine and benzimidazole was selected as a model to optimize the reaction conditions, in which a diverse range of temperatures, solvents, copper sources, ligands, and bases were evaluated. Initially, the effect of temperature on the cross-coupling reaction was investigated, and the results show that the product yield increased as the temperature increased from 70 to 90 °C (see Table 1, Entries 1 and 2). However, with a temperature of 110 °C, the monosubstituted product rapidly converted into the disubstituted one (see Table 1, Entry 3). At the higher temperature, the monosubstituted product was prone to undergo a further C–N coupling to give 72% yield of the disubstituted product (see Table 1, Entry 3). The effect of using different solvents was also examined, and DMSO was determined to be the optimal solvent (see Table 1, Entries 4 vs. 5, 6, and 7).

Table 1. Optimization of copper-catalyzed *N*-arylation.[a]



Entry	Solvent	Copper	L	Base	% Yield[b]
1[c]	DMSO	CuI	L_3	K_2CO_3	69 (8)
2[d]	DMSO	CuI	L_3	K_2CO_3	81 (13)
3[e]	DMSO	CuI	L_3	K_2CO_3	20 (72)
4	DMSO	CuI	L_3	K_2CO_3	68 (9)
5	DMF[f]	CuI	L_3	K_2CO_3	34 (trace)
6	DMA[f]	CuI	L_3	K_2CO_3	37 (trace)
7	NMP[f]	CuI	L_3	K_2CO_3	55 (6)
8	DMSO	CuCl	L_3	K_2CO_3	61 (17)
9	DMSO	Cu_2O	L_3	K_2CO_3	65 (13)
10	DMSO	$CuSO_4$	L_3	K_2CO_3	49 (8)
11	DMSO	$Cu(OAc)_2$	L_3	K_2CO_3	37 (11)
12	DMSO	$Cu(NO_3)_2$	L_3	K_2CO_3	53 (13)
13	DMSO	CuO	L_3	K_2CO_3	45 (15)
14	DMSO	Cu	L_3	K_2CO_3	47 (28)
15	DMSO	CuI	none	K_2CO_3	32 (12)
16	DMSO	CuI	L_1	K_2CO_3	15 (trace)
17	DMSO	CuI	L_2	K_2CO_3	27 (trace)
18	DMSO	CuI	L_4	K_2CO_3	73 (12)
19	DMSO	CuI	L_5	K_2CO_3	50 (26)
20	DMSO	CuI	L_6	K_2CO_3	37 (47)
21	DMSO	CuI	L_7	K_2CO_3	47 (8)
22	DMSO	CuI	L_3	K_3PO_4	44 (7)
23	DMSO	CuI	L_3	Na_2CO_3	42 (trace)
24	DMSO	CuI	L_3	$NaHCO_3$	38 (trace)
25	DMSO	CuI	L_3	KOH	9 (53)
26	DMSO	CuI	L_3	NaOH	trace (41)
27	DMSO	CuI	L_3	Cs_2CO_3	6 (47)
28	DMSO	CuI	L_3	KO*t*Bu	trace (17)
29	DMSO	CuI	L_3	Et_3N	7 (trace)

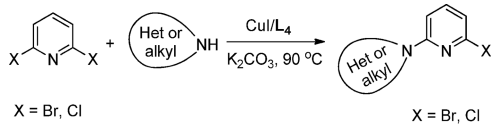
[a] Reagents and conditions: 2,6-dibromopyridine (0.5 mmol), benzimidazole (1.0 mmol), Cu (20 mol-%), ligand (40 mol-%), and base (1.5 mmol) in DMSO (2 mL), 90 °C, 12 h. [b] Isolated yield. Data in parentheses correspond to yield of 2,6-bis(benzimidazol-1-yl)pyridine. [c] 70 °C, 24 h. [d] 90 °C, 24 h. [e] 110 °C, 24 h. [f] DMF = *N*,*N*-dimethylformamide, DMA = *N*,*N*-dimethylacetamide, NMP = *N*-methyl-2-pyrrolidone.

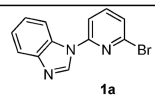
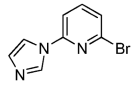
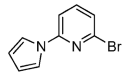
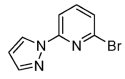
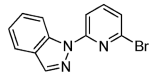
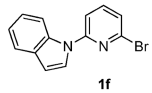
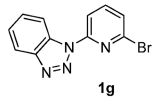
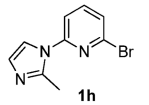
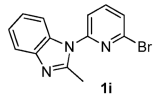
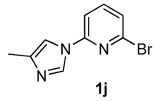
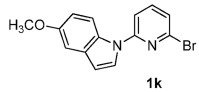
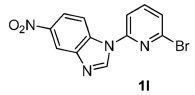
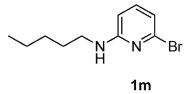
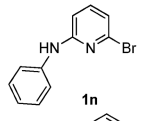
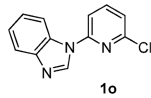
A range of different copper sources (Cu^{I}, Cu^{II}, and Cu^{0}) were subsequently evaluated. The results show that the copper(I) compounds were more catalytically active than the other copper sources, and CuI provided the best results (see Table 1, Entry 4). A control experiment revealed that a lower product yield was obtained in the presence of CuI but in the absence of a ligand (see Table 1, Entry 15). By using CuI as the copper source, we investigated the potential catalytic efficiency of different ligands, such as 1,2-ethanediamine (**L_1**), *N*,*N*′-dimethyl-1,2-ethanediamine (**L_2**), and *N*,*N*-dimethylethylenediamine (**L_3**). Among the three ligands, **L_3** efficiently assisted in the catalysis of the cross-coupling reaction (see Table 1, Entry 4), and the reactivity decreased when **L_3** was replaced with either **L_1** or **L_2** (see Table 1, Entries 4 vs. 16 and 17). Encouraged by these results, we employed *N*,*N*,*N*′,*N*′-tetramethylethane-1,2-diamine (**L_4**) as a ligand in the reaction. Interestingly, **L_4** was superior to the other ligands, and the reaction proceeded slightly faster than it did with **L_3** (see Table 1, Entries 18 vs. 4). Inspired by the structure–activity relationship of **L_1** and **L_2**, the activities of *trans*-1,2-diaminocyclohexane (**L_5**) and *N*,*N*′-dimethyl-*trans*-cyclohexane-1,2-diamine (**L_6**) were also investigated. As expected, **L_6** exhibited a higher activity than **L_5** (see Table 1, Entries 20 vs. 19), however there was an obvious increase in the disubstituted product formation. The L-proline (**L_7**) ligand provided moderate conversion (see Table 1, Entry 21).

Generally, the nature of the base is an important factor to determine the efficiency of a copper-catalyzed C–N bond-forming reaction. Among the examined inorganic bases, the weaker ones afforded better results than the stronger ones (see Table 1, Entries 4, 22, 23, and 24 vs. 25, 26, 27, and 28). It is noteworthy that cesium carbonate and potassium *tert*-butoxide, which are stronger bases, gave poor conversion (see Table 1, Entries 27 and 28). The stronger bases promoted the formation of the disubstituted product. Among the potassium bases, potassium carbonate was superior to the others, with potassium phosphate, hydroxide, and *tert*-butoxide giving a lower conversion (see Table 1, Entries 4 vs. 22, 25, and 28). The organic base triethylamine was also examined in the cross-coupling reaction and followed the same trend as the stronger bases (see Table 1, Entry 29).

This method for the selective C–N bond formation to give a monosubstituted pyridine is important because of 6-substituted 2-bromopyridine compounds are difficult to synthesize through other methods. Therefore, the scope of the catalytic system was explored by using a range of amines under the optimized reaction conditions (see Table 2). The copper-catalyzed cross-coupling products were obtained in moderate to good yields through the *N*-arylation of 2,6-dibromopyridine with various amines. The coupling of 2,6-dibromopyridine with benzimidazole, imidazole, pyrrole, and pyrazole afforded the corresponding product in 81, 72, 76, and 60% yield, respectively (see Table 2, Entries 1, 2, 3 and 4). Nitrogen heterocycles such as indazole, indole and benzotriazole gave products in relatively lower yields than the those obtained from the other

Table 2. Synthesis of 6-substituted 2-bromopyridine compounds.[a]



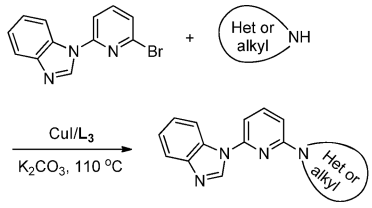
Entry	Products	Yield[b] (%)
1	 **1a**	81 (16)
2	 **1b**	72 (23)
3	 **1c**	76 (19)
4	 **1d**	60 (13)
5	 **1e**	41 (21)
6	 **1f**	42 (15)
7	 **1g**	48 (25)
8	 **1h**	58 (8)
9	 **1i**	48 (trace)
10	 **1j**	63 (13)
11	 **1k**	46 (32)
12	 **1l**	70 (15)
13	 **1m**	61 (28)
14	 **1n**	trace
15	 **1o**	53 (9)

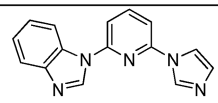
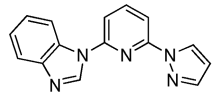
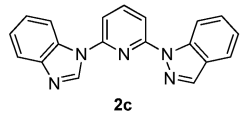
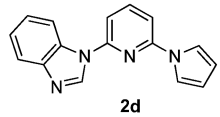
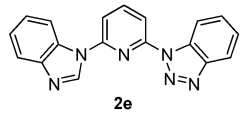
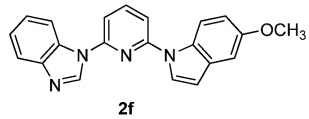
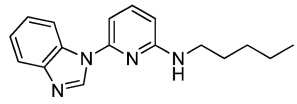
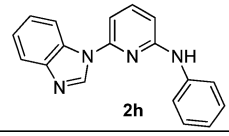
[a] Reagents and conditions: 2,6-dibromopyridine (0.5 mmol), amines (1.0 mmol), CuI (20 mol-%), **L_4** (40 mol-%), and K_2CO_3 (1.5 mmol) in DMSO (2 mL), 90 °C, 24 h. [b] Isolated yield. Data in parentheses correspond to the yield of 2,6-disubstituted pyridine.

N-heterocyclic compounds (see Table 2, Entries 5, 6, and 7 vs. 1, 2, 3, and 4). The reason for these poorer results was that the monosubstituted products were prone to further C–N coupling to give the corresponding disubstituted product. The optimized reaction conditions were also applied in the *N*-arylation of sterically hindered 2-methyl-1*H*-imidazole and 2-methyl-1*H*-benzimidazole. The effect of this steric hindrance on the coupling reaction was obvious, and the desired cross-coupling products were only afforded in moderate yields (see Table 2, Entries 8 and 9). In general, the *N*-arylation was not affected by the nature of the substituent on either the imidazole or indole substrate, and, thus, these reactions provided the corresponding product with either an electron-donating or -withdrawing substituent such as a methyl, methoxy, or nitro group (see Table 2, Entries 10, 11, and 12). To extend the scope of the *N*-arylation, the copper-catalyzed C–N bond-forming reactions between 2,6-dibromopyridine and an alkyl or arylamine were examined. For example, *n*-pentylamine underwent a moderate conversion to give the desired product in 61% yield (see Table 2, Entry 13), whereas the coupling of aniline failed to furnish the desired product (see Table 2, Entry 14). Because 2,6-dichloropyridine is less expensive and more readily available than 2,6-dibromopyridine, we examined its coupling reaction with benzimidazole under the optimized conditions, and a moderate yield of the product was obtained (see Table 2, Entry 15).

Symmetrical 2,6-disubstituted pyridine-bridged compounds have been extensively investigated and explored,[18] but little attention has been paid to the synthesis and application of unsymmetrical 2,6-disubstituted pyridine-bridged compounds because of their complicated synthetic preparation. We became interested in the synthesis of the unsymmetrical compounds that contain different nitrogen heterocycles, as they exhibit some hemilability to transition metals to produce an efficient transition-metal catalyst. Inspired by the effect of temperature on the coupling reaction (see Table 1) and that the higher temperature could favorably generate the disubstituted product, we examined the copper-catalyzed C–N coupling reaction between the 6-substituted 2-bromopyridine compounds and a range of amines by using $\mathbf{L_3}$ and K_2CO_3 at a higher reaction temperature (see Table 3). The results show that these C–N coupling reactions with imidazole, pyrazole, indazole, pyrrole, and benzotriazole took place smoothly to give good to excellent yields of the unsymmetrical compounds (see Table 3, Entries 1–5). However, 5-methoxyindole was slightly less reactive, and the coupling reaction proceeded with moderate conversion (see Table 3, Entry 6). Encouraged by the success of the heteroarylamines, alkyl and arylamines were also evaluated. *n*-Pentylamine was employed under the same reaction conditions to give the desired product in 40% yield (see Table 3, Entry 7). Aniline was then submitted to the reaction, and no product formation was observed, despite the extended reaction times (see Table 3, Entry 8). These findings are important as unsymmetrical 2,6-disubstituted pyridine-bridged compounds are difficult to synthesize by others methods.

Table 3. Synthesis of unsymmetrical 2,6-disubstituted pyridine-bridged compounds.[a]



Entry	Products	Yield[b] (%)
1	 **2a**	83
2	 **2b**	95
3	 **2c**	76
4	 **2d**	79
5	 **2e**	82
6	 **2f**	50
7	 **2g**	40
8[c]	 **2h**	no reaction

[a] Reagents and conditions: 1-(6-bromopyridin-2-yl)-1*H*-benzo[d]-imidazole (0.5 mmol), amines (0.5 mmol), CuI (20 mol-%), $\mathbf{L_3}$ (40 mol-%), and K_2CO_3 (1.0 mmol) in DMSO (2 mL), 110 °C, 48 h. [b] Isolated yield. [c] 72 h.

The 6-substituted 2-bromopyridine compounds are of great use and versatility in organic synthesis, as they can be converted into useful pharmaceuticals, organocatalysts, and advanced material intermediates through transition-metal-catalyzed Suzuki couplings, Ullmann-type reactions, and Sonogashira couplings as well as through simple *N*-alkylation reactions. As illustrated in Figure 1, all these reactions proceeded smoothly to give four new unsymmetrical 2,6-disubstituted pyridine-bridged compounds in good yields.

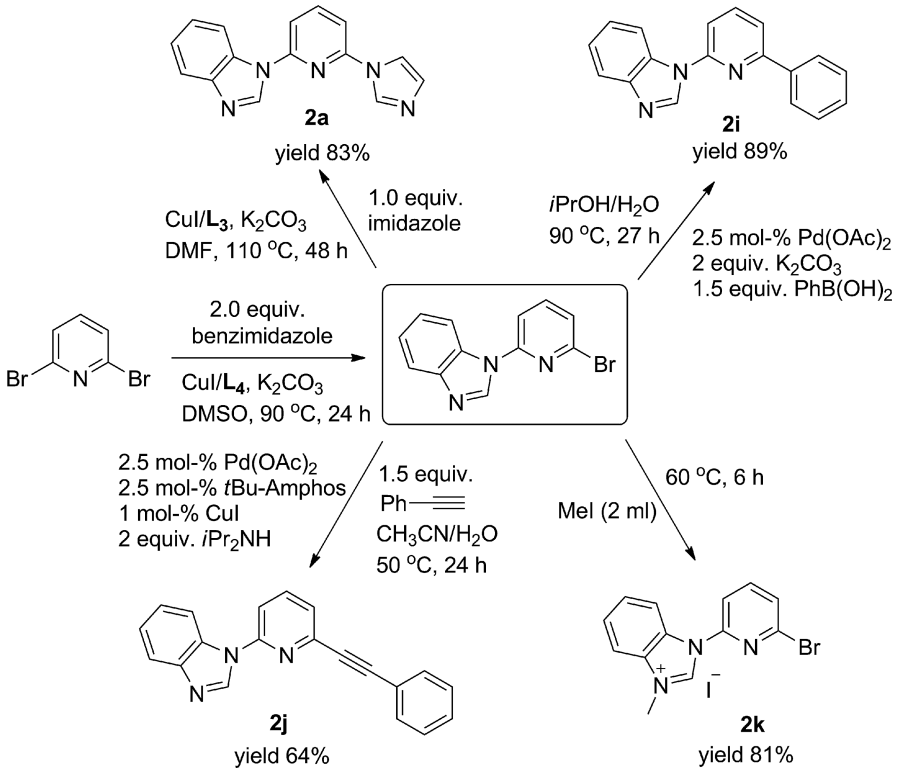


Figure 1. Functionalization of 6-substituted 2-bromopyridine compounds [*t*Bu-Amphos = 2-(di-*tert*-butylphosphino)ethyltrimethylammonium chloride].

Conclusions

In summary, the valuable and cost-effective copper-catalyzed selective C–N coupling of 2,6-dibromopyridine and amines was developed for the preparation of 6-substituted 2-bromopyridine compounds, which are common core structures for a number of pharmaceuticals, organocatalysts, and advanced material intermediates. Furthermore, a series of the unsymmetrical 2,6-disubstituted pyridine-bridged compounds were obtained in good yields. We predict that the new methods developed herein will have wide synthetic utility in medicinal chemistry, organometallic catalysis, and materials science.

Experimental Section

General Methods: All reactions were carried out in Schlenk tubes under nitrogen. DMSO was distilled from molecular sieves (4 Å). All solvents and reagents were purchased from Alfa Aesar, Acros, and Adamas-beta. The NMR spectroscopic were recorded with a Varian Inova-400 spectrometer by using TMS as internal standard (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR). Mass spectrometry data were collected with a Bruker ultrafleXtreme mass spectrometer. All products were isolated by short chromatography on a silica gel (300–400 mesh) column.

Typical Procedure for the Synthesis of 6-Substituted 2-Bromopyridine Compounds: A mixture of 2,6-dibromopyridine (0.5 mmol), the amine (1.0 mmol), the Cu compound (0.1 mmol), the ligand (0.2 mmol), and K_2CO_3 (1.5 mmol) in DMSO (2 mL) was combined under nitrogen. The reaction mixture was stirred at room temperature for 30 min and then heated to 90 °C for 24 h. The reaction mixture was then added to brine (15 mL), and the resulting solution was extracted with dichloromethane (3× 15 mL). The combined extracts were concentrated under vacuum, and the crude product was isolated by short chromatography on a silica gel (300–400 mesh) column.

1-(6-Bromopyridin-2-yl)-1*H*-benzo[*d*]imidazole (1a): Purification by flash chromatography (petroleum ether/EtOAc, 2:1) afforded **1a** (111 mg, 81%) as a white solid; m.p. 145–148 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.60 (s, 1 H), 8.10 (d, J = 8.0 Hz, 1 H), 7.87 (d, J = 8.0 Hz, 1 H), 7.76 (t, J = 8.0 Hz, 1 H), 7.56 (d, J = 8.0 Hz, 1 H), 7.49 (dd, J = 8.0 Hz, J = 4.0 Hz, 1 H), 7.45–7.37 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.60, 144.66, 141.15, 140.92, 140.84, 131.79, 125.75, 124.63, 123.72, 120.79, 112.88, 112.14 ppm. HRMS (MALDI): calcd. for $C_{12}H_8BrN_3$ $[M + H]^+$ 273.9974; found 273.9977.

2-Bromo-6-(1*H*-imidazol-1-yl)pyridine (1b): Purification by flash chromatography (petroleum ether/EtOAc, 2:1) afforded **1b** (80 mg, 72%) as a white solid; m.p. 92–94 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32 (s, 1 H), 7.67 (t, J = 8.0 Hz, 1 H), 7.61 (s, 1 H), 7.41 (dd, J = 8.0 Hz, 1 H), 7.31 (dd, J = 8.0 Hz, 1 H), 7.19 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.81, 141.01, 140.91, 134.99, 131.01, 126.04, 116.12, 110.60 ppm. HRMS (EI): calcd. for $C_8H_6BrN_3$ $[M]^+$ 222.9740; found 222.9737.

2-Bromo-6-(1*H*-pyrrol-1-yl)pyridine (1c): Purification by flash chromatography (petroleum ether) afforded **1c** (85 mg, 76%) as a white solid; m.p. 72–74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 (t, J = 8.0 Hz, 1 H), 7.47–7.46 (m, 2 H), 7.25 (dd, J = 12.0 Hz, J = 8.0 Hz, 2 H), 6.35 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.58, 140.39, 127.03, 123.87, 118.21, 111.90, 109.40 ppm. HRMS (EI): calcd. for $C_9H_7BrN_2$ $[M]^+$ 221.9787; found 221.9789.

2-Bromo-6-(1*H*-pyrazol-1-yl)pyridine (1d):[19] Purification by flash chromatography (petroleum ether/EtOAc, 20:1) afforded **1d** (66 mg, 60%) as a white solid; m.p. 55–58 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.53 (s, 1 H), 7.93 (d, J = 8.0 Hz, 1 H), 7.73 (s, 1 H), 7.65 (t, J = 8.0 Hz, 1 H), 7.35 (d, J = 8.0 Hz, 1 H), 6.46 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.39, 142.66, 140.68, 139.86, 127.52, 125.19, 110.83, 108.19 ppm. HRMS (EI): calcd. for $C_8H_6BrN_3$ $[M]^+$ 222.9740; found 222.9737.

1-(6-Bromopyridin-2-yl)-1*H*-indazole (1e): Purification by flash chromatography (petroleum ether/EtOAc, 20:1) afforded **1e** (56 mg, 41%) as a white solid; m.p. 102–105 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 (d, J = 8.0 Hz, 1 H), 8.18 (d, J = 4.0 Hz, 1 H), 7.98 (dd, J = 8.0 Hz, J = 4.0 Hz, 1 H), 7.75 (d, J = 8.0 Hz, 1 H), 7.63 (t, J = 8.0 Hz, 1 H), 7.55 (t, J = 8.0 Hz, 1 H), 7.31–7.27 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.69, 140.25, 139.29, 138.75, 137.64, 128.42, 126.10, 123.40, 122.98, 120.79, 115.33, 111.52 ppm. HRMS (EI): calcd. for $C_{12}H_8BrN_3$ $[M]^+$ 272.9896; found 272.9890.

1-(6-Bromopyridin-2-yl)-1*H*-indole (1f): Purification by flash chromatography (petroleum ether/EtOAc, 20:1) afforded **1f** (58 mg, 42%) as a white viscous solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 (d, J = 8.0 Hz, 1 H), 7.67 (d, J = 4.0 Hz, 1 H), 7.64 (t, J = 8.0 Hz, 2 H), 7.41 (d, J = 8.0 Hz, 1 H), 7.33 (t, J = 8.0 Hz, 2 H), 7.22 (t, J = 8.0 Hz, 1 H), 6.71 (d, J = 4.0 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.18, 140.47, 140.32, 134.97, 130.60, 125.44, 123.63, 123.55, 121.82, 121.15, 113.50, 112.04, 106.58 ppm. HRMS (EI): calcd. for $C_{13}H_9BrN_2$ $[M]^+$ 271.9944; found 271.9939.

1-(6-Bromopyridin-2-yl)-1*H*-benzo[*d*][1,2,3]triazole (1g):[20] Purification by flash chromatography (petroleum ether/EtOAc, 20:1) afforded **1g** (66 mg, 48%) as a white solid; m.p. 114–116 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.59 (d, J = 8.0 Hz, 1 H), 8.27 (d, J = 8.0 Hz, 1 H), 8.12 (d, J = 8.0 Hz, 1 H), 7.78 (t, J = 8.0 Hz, 1 H), 7.64 (t, J = 8.0 Hz, 1 H), 7.51–7.46 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.08, 146.74, 140.83, 140.02, 131.24, 129.28, 126.14, 125.25, 119.91, 114.70, 112.58 ppm. HRMS (EI): calcd. for $C_{11}H_7BrN_4$ $[M]^+$ 273.9849; found 273.9841.

2-Bromo-6-(2-methyl-1*H*-imidazol-1-yl)pyridine (1h): Purification by flash chromatography (EtOAc): afforded **1h** (69 mg, 58%) as a white solid; m.p. 98–101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (t, J = 8.0 Hz, 1 H), 7.48 (dd, J = 8.0 Hz, J = 0.8 Hz, 1 H), 7.30–7.28 (m, 2 H), 7.01 (d, J = 1.6 Hz, 1 H), 2.63 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.30, 145.12, 140.69, 140.62, 128.23, 126.36, 118.68, 115.07, 15.67 ppm. HRMS (MALDI): calcd. for $C_9H_8BrN_3$ $[M + H]^+$ 237.9974; found 237.9973.

1-(6-Bromopyridin-2-yl)-2-methyl-1*H*-benzo[*d*]imidazole (1i): Purification by flash chromatography (petroleum ether/EtOAc, 1:1) afforded **1i** (69 mg, 48%) as a white solid; m.p. 102–104 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (t, J = 8.0 Hz, 1 H), 7.73 (d, J = 8.0 Hz, 1 H), 7.58 (d, J = 8.0 Hz, 1 H), 7.44 (d, J = 8.0 Hz, 1 H), 7.40 (d, J = 8.0 Hz, 1 H), 7.31–7.23 (m, 2 H), 2.71 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.35, 149.46, 142.67, 141.33, 140.69, 134.48, 127.18, 123.23, 123.12, 119.39, 118.05, 110.15, 15.54 ppm. HRMS (MALDI): calcd. for $C_{13}H_{10}BrN_3$ $[M + H]^+$ 288.0131; found 288.0140.

2-Bromo-6-(4-methyl-1*H*-imidazol-1-yl)pyridine (1j): Purification by flash chromatography (petroleum ether/EtOAc, 1:1) afforded **1j** (74 mg, 63%) as a white solid; m.p. 72–74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (d, J = 1.6 Hz, 1 H), 7.64 (t, J = 8.0 Hz, 1 H), 7.37 (dd, J = 8.0 Hz, J = 0.8 Hz, 1 H), 7.31 (t, J = 1.2 Hz, 1 H), 7.24 (dd, J = 8.0 Hz, J = 0.4 Hz, 1 H), 2.28 (d, J = 4.0 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.85, 140.92, 140.80, 140.27, 134.24, 125.54, 112.34, 110.19, 13.74 ppm. HRMS (MALDI): calcd. for $C_9H_8BrN_3$ $[M + H]^+$ 237.9974; found 237.9980.

1-(6-Bromopyridin-2-yl)-5-methoxy-1*H*-indole (1k): Purification by flash chromatography (petroleum ether/EtOAc, 20:1) afforded **1k** (70 mg, 46%) as a pale brown solid; m.p. 59–60 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (d, J = 8.0 Hz, 1 H), 7.64 (d, J = 4.0 Hz, 1 H), 7.61 (t, J = 8.0 Hz, 1 H), 7.36 (d, J = 8.0 Hz, 1 H), 7.28 (d, J = 8.0 Hz, 1 H), 7.09 (d, J = 4.0 Hz, 1 H), 6.96 (dd, J = 8.0 Hz, J = 4.0 Hz, 1 H), 6.64 (d, J = 4.0 Hz, 1 H), 3.87 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.31, 152.18, 140.38, 140.25, 131.34, 130.02, 125.69, 123.14, 114.67, 112.98, 111.35, 106.45, 103.13, 55.72 ppm. HRMS (MALDI): calcd. for $C_{14}H_{11}BrN_2O$ $[M]^+$ 302.0049; found 302.0054.

1-(6-Bromopyridin-2-yl)-5-nitro-1*H*-benzo[*d*]imidazole (1l): Purification by flash chromatography (petroleum ether/EtOAc, 2:1) afforded **1l** (113 mg, 70%) as a pale yellow solid; m.p. 201–202 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (d, J = 2.0 Hz, 1 H), 8.68 (s, 1 H), 8.36 (dd, J = 2.0 Hz, J = 8.0 Hz, 1 H), 8.28 (d, J = 8.0 Hz, 1 H), 7.84 (t, J = 8.0 Hz, 1 H), 7.58 (t, J = 8.0 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.79, 144.58, 144.17, 143.72, 141.50, 141.24, 135.93, 126.94, 120.23, 117.19, 113.62, 112.46 ppm. HRMS (MALDI): calcd. for $C_{12}H_7BrN_4O_2$ $[M + H]^+$ 318.9825; found 318.9830.

6-Bromo-*N*-pentylpyridin-2-amine (1m): Purification by flash chromatography (petroleum ether/EtOAc, 20:1) afforded **1m** (75 mg, 61%) as a pale brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24 (t, J = 8.0 Hz, 1 H), 6.69 (d, J = 8.0 Hz, 1 H), 6.26 (d, J = 8.0 Hz, 1 H), 4.72 (br., 1 H), 3.19 (t, J = 8.0 Hz, 2 H), 1.63–1.56 (m, 2 H), 1.38–1.32 (m, 4 H), 0.92–0.89 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.02, 140.24, 139.50, 115.43, 103.89, 42.26, 29.09, 28.95, 22.39, 14.00 ppm. HRMS (MALDI): calcd. for $C_{10}H_{15}BrN_2$ $[M + H]^+$ 243.0491; found 243.0490.

1-(6-Chloropyridin-2-yl)-1*H*-benzo[*d*]imidazole (1o): Purification by flash chromatography (petroleum ether/EtOAc, 2:1) afforded **1o** (61 mg, 53%) as a white solid; m.p. 122–124 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.57 (s, 1 H), 8.10–8.08 (m, 1 H), 7.86 (t, J = 8.0 Hz, 2 H), 7.51 (dd, J = 8.0 Hz, J = 0.8 Hz, 1 H), 7.44–7.35 (m, 2 H), 7.32 (dd, J = 8.0 Hz, J = 0.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.89, 149.53, 144.67, 141.20, 140.96, 131.80, 124.59, 123.69, 121.90, 120.79, 112.89, 111.83 ppm.

Typical Procedure for the Synthesis of Unsymmetrical 2,6-Disubstituted Pyridine-Bridged Compounds: A mixture of 1-(6-bromopyridin-2-yl)-1*H*-benzo[*d*]imidazole (0.5 mmol), the amine (0.5 mmol), CuI (0.1 mmol), **L$_3$** (0.2 mmol), and K_2CO_3 (1.0 mmol) in DMSO (2 mL) was combined under nitrogen. The reaction mixture was stirred at room temperature for 30 min and then heated to 110 °C for 48 h. The mixture was then added to brine (15 mL), and the resulting solution was extracted with dichloromethane (3 × 15 mL). The combined extracts were concentrated under vacuum, and the product was isolated by short chromatography on a silica gel (300–400 mesh) column.

1-[6-(1*H*-Imidazol-1-yl)pyridin-2-yl]-1*H*-benzo[*d*]imidazole (2a): Purification by flash chromatography (EtOAc) afforded **2a** (108 mg, 83%) as a white solid; m.p. 144–146 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.59 (s, 1 H), 8.44 (s, 1 H), 8.10 (d, J = 8.0 Hz, 1 H), 8.04 (t, J = 8.0 Hz, 1 H), 7.89 (d, J = 8.0 Hz, 1 H), 7.71 (s, 1 H), 7.50 (d, J = 8.0 Hz, 1 H), 7.45–7.38 (m, 2 H), 7.34 (d, J = 8.0 Hz, 1 H), 7.27 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.30, 148.58, 144.72, 142.04, 140.99, 135.07, 131.86, 131.21, 124.68, 123.77, 120.92, 116.19, 112.81, 111.37, 109.36 ppm. HRMS (EI): calcd. for $C_{15}H_{11}N_5$ $[M]^+$ 261.1009; found 261.1014.

1-[6-(1*H*-Pyrazol-1-yl)pyridin-2-yl]-1*H*-benzo[*d*]imidazole (2b): Purification by flash chromatography (petroleum ether/EtOAc, 2:1) afforded **2b** (124 mg, 95%) as a white solid; m.p. 116–119 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.60 (s, 2 H), 8.08 (d, J = 8.0 Hz, 1 H), 8.02 (t, J = 8.0 Hz, 1 H), 7.98 (d, J = 8.0 Hz, 1 H), 7.90 (d, J = 8.0 Hz, 1 H), 7.80 (d, J = 4.0 Hz, 1 H), 7.45–7.37 (m, 3 H), 6.54 (d, J = 4.0 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.06, 148.36, 144.70, 142.75, 141.69, 141.24, 132.02, 127.28, 124.44, 123.54, 120.88, 112.57, 111.01, 109.97, 108.47 ppm. HRMS (EI): calcd. for $C_{15}H_{11}N_5$ $[M]^+$ 261.1009; found 261.1005.

1-[6-(1*H*-Benzo[*d*]imidazol-1-yl)pyridin-2-yl]-1*H*-indazole (2c): Purification by flash chromatography (petroleum ether/EtOAc, 2:1) afforded **2c** (118 mg, 76%) as a white solid; m.p. 129–132 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.70 (d, J = 8.0 Hz, 1 H), 8.64 (s, 1 H), 8.21 (s, 1 H), 8.04–7.91 (m, 4 H), 7.76 (d, J = 8.0 Hz, 1 H), 7.47 (t, J = 8.0 Hz, 1 H), 7.39–7.25 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.67, 147.75, 144.72, 141.55, 141.00, 138.65, 137.71, 132.09, 128.43, 126.20, 124.25, 123.39, 122.99, 120.97, 120.83, 115.09, 112.31, 111.21, 109.92 ppm. HRMS (EI): calcd. for $C_{19}H_{13}N_5$ $[M]^+$ 311.1165; found 311.1167.

1-[6-(1*H*-Pyrrol-1-yl)pyridin-2-yl]-1*H*-benzo[*d*]imidazole (2d): Purification by flash chromatography (petroleum ether/EtOAc, 2:1) afforded **2d** (103 mg, 79%) as a white solid; m.p. 119–120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.58 (s, 1 H), 8.11 (d, J = 8.0 Hz, 1 H), 7.90 (q, J = 8.0 Hz, 2 H), 7.57 (s, 2 H), 7.43–7.35 (m, 2 H), 7.32 (d, J = 8.0 Hz, 1 H), 7.26 (d, J = 8.0 Hz, 1 H), 6.41 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.87, 148.85, 144.72, 141.36, 141.20, 132.03, 124.38, 123.45, 120.76, 118.22, 112.87, 112.07, 109.44, 108.45 ppm. HRMS (EI): calcd. for $C_{16}H_{12}N_4$ $[M]^+$ 260.1056; found 260.1053.

1-[6-(1*H*-Benzo[*d*]imidazol-1-yl)pyridin-2-yl]-1*H*-benzo[*d*][1,2,3]triazole (2e): Purification by flash chromatography (petroleum ether/EtOAc, 2:1) afforded **2e** (128 mg, 82%) as a white solid; m.p. 156–158 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.67 (s, 1 H), 8.55 (d, J = 8.0 Hz, 1 H), 8.33 (d, J = 8.0 Hz, 1 H), 8.18 (t, J = 8.0 Hz, 2 H), 8.03–8.01 (m, 1 H), 7.95–7.93 (m, 1 H), 7.62–7.58 (m, 2 H), 7.49 (t, J = 8.0 Hz, 1 H), 7.43–7.41 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.08, 148.46, 146.86, 144.79, 141.93, 141.32, 131.98, 131.25, 129.41, 125.31, 124.58, 123.73, 121.05, 120.18, 114.34, 112.44, 112.25, 112.14 ppm. HRMS (EI): calcd. for $C_{18}H_{12}N_6$ $[M]^+$ 312.1118; found 312.1115.

1-[6-(5-Methoxy-1*H*-indol-1-yl)pyridin-2-yl]-1*H*-benzo[*d*]imidazole (2f): Purification by flash chromatography (petroleum ether/EtOAc, 2:1) afforded **2f** (85 mg, 50%) as a brown solid; m.p. 167–168 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.70 (s, 1 H), 8.25 (d, J = 8.0 Hz, 1 H), 8.14–8.11 (m, 1 H), 8.01 (t, J = 8.0 Hz, 1 H), 7.93–7.91 (m, 1 H), 7.77 (d, J = 4.0 Hz, 1 H), 7.45 (d, J = 8.0 Hz, 1 H), 7.42–7.39 (m, 3 H), 7.14 (d, J = 2.8 Hz, 1 H), 6.94 (dd, J = 9.2 Hz, J = 2.4 Hz, 1 H), 6.71 (dd, J = 3.6 Hz, J = 0.8 Hz, 1 H), 3.89 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.41, 152.17, 148.79, 144.51, 141.36, 141.26, 132.07, 131.49, 130.08, 126.00, 124.53, 123.62, 120.74, 114.79, 113.08, 113.01, 110.82, 109.12, 106.62, 103.31, 55.77 ppm. HRMS (MALDI): calcd. for $C_{21}H_{16}N_4O$ $[M + H]^+$ 341.1397; found 341.1397.

6-(1*H*-Benzo[*d*]imidazol-1-yl)-*N*-pentylpyridin-2-amine (2g): Purification by flash chromatography (petroleum ether/EtOAc, 1:1) afforded **2g** (56 mg, 40%) as a white solid; m.p. 91–93 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.55 (s, 1 H), 8.04 (d, J = 8.0 Hz, 1 H), 7.85 (d, J = 8.0 Hz, 1 H), 7.58 (t, J = 8.0 Hz, 1 H), 7.37–7.31 (m, 2 H), 6.78 (d, J = 8.0 Hz, 1 H), 6.34 (d, J = 8.0 Hz, 1 H), 4.70 (br., 1 H), 3.39–3.34 (m, 2 H), 1,71–1.64 (m, 2 H), 1.43–1.36 (m, 4 H), 0.93 (t, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.60, 148.61, 144.54, 141.59, 139.64, 132.26, 123.73, 122.87, 120.41, 112.90, 104.55, 101.87, 42.15, 29.25, 29.23, 22.45, 14.02 ppm. HRMS (MALDI): calcd. for $C_{17}H_{20}N_4$ $[M + H]^+$ 281.1761; found 281.1755.

1-(6-Phenylpyridin-2-yl)-1*H*-benzo[*d*]imidazole (2i): Purification by flash chromatography (petroleum ether/EtOAc, 2:1) afforded **2i** (121 mg, 89%) as a white solid; m.p. 138–140 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.67 (s, 1 H), 8.16 (d, J = 8.0 Hz, 1 H), 8.10 (d, J = 8.0 Hz, 2 H), 7.92 (t, J = 8.0 Hz, 2 H), 7.72 (d, J = 8.0 Hz, 1 H), 7.54–7.45 (m, 4 H), 7.41–7.37 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.26, 149.59, 144.46, 141.34, 139.75, 137.99, 132.20, 129.76, 128.95, 126.95, 124.31, 123.37, 120.63, 118.09, 112.97, 112.33 ppm. HRMS (EI): calcd. for $C_{18}H_{13}N_3$ $[M]^+$ 271.1104; found 271.1100.

1-[6-(Phenylethynyl)pyridin-2-yl]-1*H*-benzo[*d*]imidazole (2j): Purification by flash chromatography (petroleum ether/EtOAc, 2:1) afforded **2j** (94 mg, 64%) as a yellow solid; m.p. 91–94 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.63 (s, 1 H), 8.09 (d, J = 8.0 Hz, 1 H), 7.89 (t, J = 8.0 Hz, 2 H), 7.66–7.63 (m, 2 H), 7.53 (t, J = 8.0 Hz, 2 H), 7.43–7.35 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.83, 144.69, 143.21, 141.36, 139.13, 132.16, 132.03, 129.36, 128.48, 125.23, 124.35, 123.42, 121.81, 120.71, 113.47, 112.66, 90.51, 87.88 ppm. HRMS (MALDI): calcd. for $C_{20}H_{13}N_3$ $[M + H]^+$ 296.1182; found 296.1189.

1-(6-Bromopyridin-2-yl)-3-methyl-1*H*-benzo[*d*]imidazol-3-ium Iodide (2k): Purification by flash chromatography (petroleum ether/EtOAc, 2:1) afforded **2k** (168 mg, 81%) as a white solid; m.p. 230–232 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.53 (s, 1 H), 8.43–8.40 (m, 1 H), 8.25 (t, J = 8.0 Hz, 1 H), 8.18–8.15 (m, 1 H), 8.10 (d, J = 8.0 Hz, 1 H), 7.99 (d, J = 8.0 Hz, 1 H), 7.84–7.81 (m, 2 H), 4.21 (s, 3 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 147.16, 143.51, 143.24, 140.03, 132.43, 129.29, 129.25, 128.14, 127.43, 116.16, 115.60, 114.31, 34.07 ppm. HRMS (ESI): calcd. for $C_{13}H_{11}BrIN_3$ $[M - I]^+$ 288.0131; found 288.0132.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H NMR and ^{13}C NMR spectra of all compounds.

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[1] a) S. Dey, S. Sarkar, H. Paul, E. Zangrando, P. Chattopadhyay, *Polyhedron* **2010**, *29*, 1583–1587; b) G. Evano, N. Blanchard, M. Toumi, *Chem. Rev.* **2008**, *108*, 3054–3131; c) G. M. Buckley, L. Gowers, A. P. Higueruelo, K. Jenkins, S. R. Mack, T. Morgan, D. M. Parry, W. R. Pitt, O. Rausch, M. D. Richard, V. Sabin, J. L. Fraser, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 3211–3214; d) G. M. Buckley, R. Fosbeary, J. L. Fraser, L. Gowers, A. P. Higueruelo, L. A. James, K. Jenkins, S. R. Mack, T. Morgan, D. M. Parry, W. R. Pitt, O. Rausch, M. D. Richard, V. Sabin, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 3656–3660.

[2] a) A. Herbst, C. Bronner, P. Dechambenoit, O. S. Wenger, *Organometallics* **2013**, *32*, 1807–1814; b) F. Godoy, C. Segarra, M. Poyatos, E. Peris, *Organometallics* **2011**, *30*, 684–688; c) G. Papini, M. Pellei, G. G. Lobbia, A. Burini, C. Santini, *Dalton Trans.* **2009**, 6985–6990; d) F. E. Hahn, M. C. Jahnke, V. Gomez-Benitez, D. Morales-Morales, T. Pape, *Organometallics* **2005**, *24*, 6458–6463.

[3] a) M. Burnworth, S. J. Rowan, C. Weder, *Macromolecules* **2012**, *45*, 126–132; b) H. Y. Gong, B. M. Rambo, E. Karnas, V. M.

Lynch, J. L. Sessler, *Nature Chem.* **2010**, *2*, 406–409; c) T. Tu, X. L. Bao, W. Assenmacher, H. Peterlik, J. Daniels, K. H. Dötz, *Chem. Eur. J.* **2009**, *15*, 1853–1861.

[4] a) T. Tu, X. Feng, Z. Wang, X. Liu, *Dalton Trans.* **2010**, *39*, 10598–10600; b) K. Inamoto, J. Kuroda, K. Hiroya, Y. Noda, M. Watanabe, T. Sakamoto, *Organometallics* **2006**, *25*, 3095–3098; c) B. Inés, R. SanMartin, M. J. Moure, E. Domínguez, *Adv. Synth. Catal.* **2009**, *351*, 2124–2132.

[5] a) X. T. Zhou, H. B. Ji, S. G. Liu, *Tetrahedron Lett.* **2013**, *54*, 3882–3885; b) L. Y. Li, L. Zhu, D. G. Chen, X. L. Hu, R. H. Wang, *Eur. J. Org. Chem.* **2011**, 2692–2696; c) T. Tu, W. Assenmacher, H. Peterlik, G. Schnakenburg, K. H. Dötz, *Angew. Chem. Int. Ed.* **2008**, *47*, 7127–7131; *Angew. Chem.* **2008**, *120*, 7236; d) T. Tu, J. Malineni, K. H. Dötz, *Adv. Synth. Catal.* **2008**, *350*, 1791–1795.

[6] S. Roy, A. J. Zych, R. J. Herr, C. Cheng, G. W. Shipps Jr., *Tetrahedron* **2010**, *66*, 1973–1979.

[7] a) S. Heider, H. Petzold, G. Chastanet, S. Schlamp, T. Rüffer, B. Weber, J. F. Létard, *Dalton Trans.* **2013**, *42*, 8575–8584; b) R. Pritchard, C. A. Kilner, M. A. Halcrow, *Tetrahedron Lett.* **2009**, *50*, 2484–2486.

[8] X. J. Sun, Z. K. Yu, S. Z. Wu, W.-J. Xiao, *Organometallics* **2005**, *24*, 2959–2963.

[9] F. L. Zeng, Z. K. Yu, *J. Org. Chem.* **2006**, *71*, 5274–5281.

[10] a) F. L. Zeng, Z. K. Yu, *Organometallics* **2008**, *27*, 2898–2901; b) F. Zeng, Z. Yu, *Organometallics* **2008**, *27*, 6025–6028.

[11] J. L. Bolliger, M. Oberholzer, C. M. Frech, *Adv. Synth. Catal.* **2011**, *353*, 945–954.

[12] G. M. Buckley, T. A. Ceska, J. L. Fraser, L. Gowers, C. R. Groom, A. P. Higueruelo, K. Jenkins, S. R. Mack, T. Morgan, D. M. Parry, W. R. Pitt, O. Rausch, M. D. Richard, V. Sabin, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 3291–3295.

[13] a) D. W. Ma, Q. Cai, *Acc. Chem. Res.* **2008**, *41*, 1450–1460; b) H. H. Rao, H. Fu, *Synlett* **2011**, 745–769; c) F. Monnier, M. Taillefer, *Angew. Chem. Int. Ed.* **2009**, *48*, 6954–6971; *Angew. Chem.* **2009**, *121*, 7088.

[14] a) D. S. Surry, S. L. Buchwald, *Chem. Sci.* **2010**, *1*, 13–31; b) J. C. Antilla, J. M. Baskin, T. E. Barder, S. L. Buchwald, *J. Org. Chem.* **2004**, *69*, 5578–5587; c) J. C. Antilla, A. Klapars, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 11684–11688; d) A. Klapars, J. C. Antilla, X. Huang, S. L. Buchwald, *J. Am. Chem. Soc.* **2001**, *123*, 7727–7729.

[15] C. Liu, W. B. Yang, *Chem. Commun.* **2009**, 6267–6269.

[16] R. B. DeVasher, L. R. Moore, K. H. Shaughnessy, *J. Org. Chem.* **2004**, *69*, 7919–7927.

[17] Z. X. Xi, F. H. Liu, Y. B. Zhou, W. Z. Chen, *Tetrahedron* **2008**, *64*, 4254–4259.

[18] a) C. J. Serpell, R. Chall, A. L. Thompson, P. D. Beer, *Dalton Trans.* **2011**, *40*, 12052–12055; b) F. Jean-Baptiste dit Dominique, H. Gornitzka, A. Sournia-Saquet, C. Hemmert, *Dalton Trans.* **2009**, 340–352; c) T. Tu, W. Assenmacher, H. Peterlik, R. Weisbarth, M. Nieger, K. H. Dötz, *Angew. Chem. Int. Ed.* **2007**, *46*, 6368–6371; *Angew. Chem.* **2007**, *119*, 6486; d) A. Caballero, E. Díez-Barra, F. A. Jalón, S. Merino, J. Tejeda, *J. Organomet. Chem.* **2001**, *617–618*, 395–398.

[19] S. Heider, H. Petzold, G. Chastanet, S. Schlamp, T. Rüffer, B. Weber, J. F. Létard, *Dalton Trans.* **2013**, *42*, 8575–8584.

[20] W. Du, P. Wu, Q. Wang, Z. K. Yu, *Organometallics* **2013**, *32*, 3083–3090.

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