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A Unified Strategy Towards *N*-Aryl Heterocycles by a One-Pot Copper-Catalyzed Oxidative C–H Amination of Azoles

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Keywords: Synthetic methods / C–H activation / Amination / Nitrogen heterocycles / Copper / Reaction mechanisms

An efficient one-pot synthesis of *N*-aryl-substituted heterocycles by a Cu-catalyzed two-fold C–N bond formation is reported. This strategy involves a Cu^{I}-catalyzed C–N bond-forming reaction between azoles and electron-deficient bromopyridines followed by an intramolecular sp^2 C–H amination. One of the products thus formed has been successfully used as a ligand for the synthesis of a Pd complex.

Introduction

Nitrogen-containing heterocycles continue to attract the attention of synthetic chemists due to their applications in pharmaceuticals,[1] functional materials[2] and agrochemical products.[3] Thus, several methods have been developed to synthesize various heterocycles with different architectures.[4] The last two decades have witnessed a renaissance in the synthesis of heterocycles since the pioneering work of Buchwald on direct sp^2 C–H activation/intramolecular C–N bond formation,[5] leading to various heterocycles such as carbazoles,[6] benzimidazoles,[7] indazoles,[8] indolines,[9] and *N*-methoxylactams.[10]

Although most of these methods involve the use of expensive palladium, rhodium and ruthenium catalysts,[11] they have provided a new dimension in the development of an atom-economic and orthogonal C–N bond formation protocol for the synthesis of nitrogen-containing heterocyclic compounds. Subsequently, several inexpensive methods involving Cu-catalysed sp^2 C–H activation have been developed for the construction of N heterocycles.[12–16] However, the transition-metal-catalysed C–H activation of unsubstituted anilines is susceptible to poisoning of the catalyst[17] due to the basic nature of the amine moiety.[18] Furthermore, a Cu-catalysed route to C–N bond formation with a free amine on a deactivated pyridine nucleus is thus far unexplored. Thus, herein we report a one-pot Cu-catalysed synthesis of *N*-arylimidazobenzimidazoles by a cascade two-fold C–N bond formation from readily available starting materials involving an sp^2 C–H activation.

Owing to their interesting biological properties,[19] considerable efforts have been made to synthesize various imidazobenzimidazole derivatives (Figure 1).[20,21] However, the methods developed thus far suffer from harsh conditions, narrow functional group tolerance, poor atom economy and low yields. During the course of our study, Fu and coworkers[22] reported an elegant synthesis of *N*-arylimidazobenzimidazoles by a copper-catalysed intramolecular C–H amination from pre-arylated 2-(1*H*-imidazol-1-yl)anilines (Scheme 1). This protocol also requires a couple of steps for the construction of imidazobenzimidazoles, including the preparation of the *N*-arylated starting material, which is cumbersome and low yielding (23–60%). However, we anticipated that *N*-pyridyl heterocycles could be accomplished by a cascade two-fold C–N bond formation involving a direct oxidative sp^2 C–H activation.

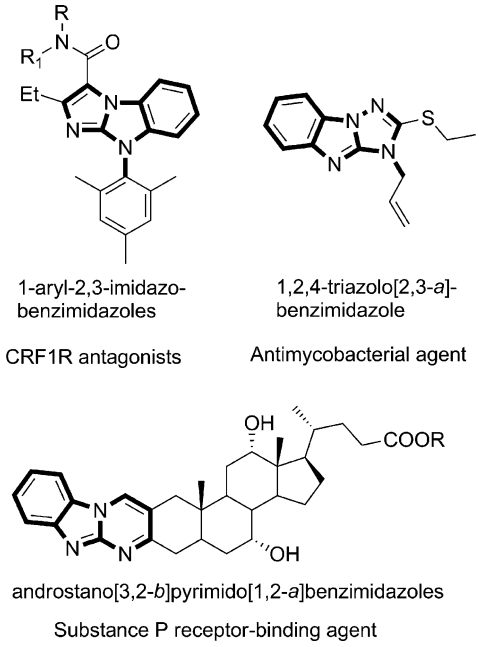

Figure 1. Previously synthesized imidazobenimidazoles.

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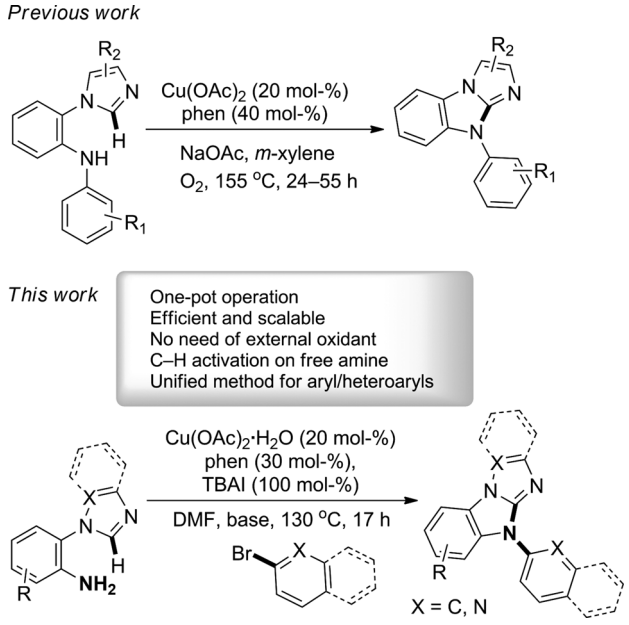
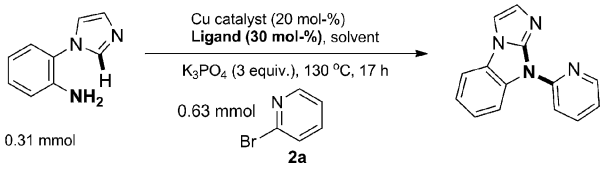


Scheme 1. C–H bond functionalization of heterocycles.

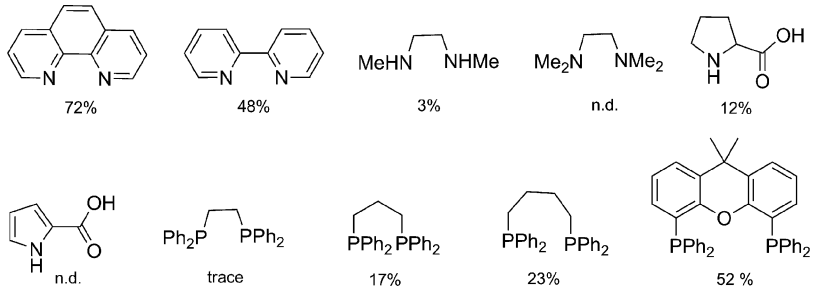
Results and Discussion

To test this hypothesis, we selected 2-(1*H*-imidazol-1-yl)-aniline (**1a**) and 2-bromopyridine (**2a**) as model substrates for the cascade reaction. Our optimization studies commenced with the identification of a suitable catalytic system for the reaction. Our initial attempt with 20 mol-% CuI as catalyst, 30 mol-% phen and K_3PO_4 as base gave the desired product in 23% yield (Table 1; entry 1). Further optimization to improve the yield by using various additives/oxidants along with CuI were unsuccessful. However, encouraged by the formation of the product, we focused our attention on the use of divalent copper salts as catalyst. The use of $CuCl_2$ or $CuBr_2$ as catalyst gave poor yields of 20 and 18%, respectively (entries 2 and 3), whereas $CuSO_4$ was found to be ineffective for this transformation. Nevertheless, an improved yield (50%) was achieved when we used a mixture of 20 mol-% CuI and excess $Cu(OAc)_2·H_2O$ (entry 4). Further to our search for improved reaction conditions, we found that 20 mol-% $CuCl_2$ and excess $Cu(OAc)_2·H_2O$ gave the best yield of 87% (entry 6). Despite the satis-

Table 1. Optimization of the reaction conditions for the cascade reaction.[a]



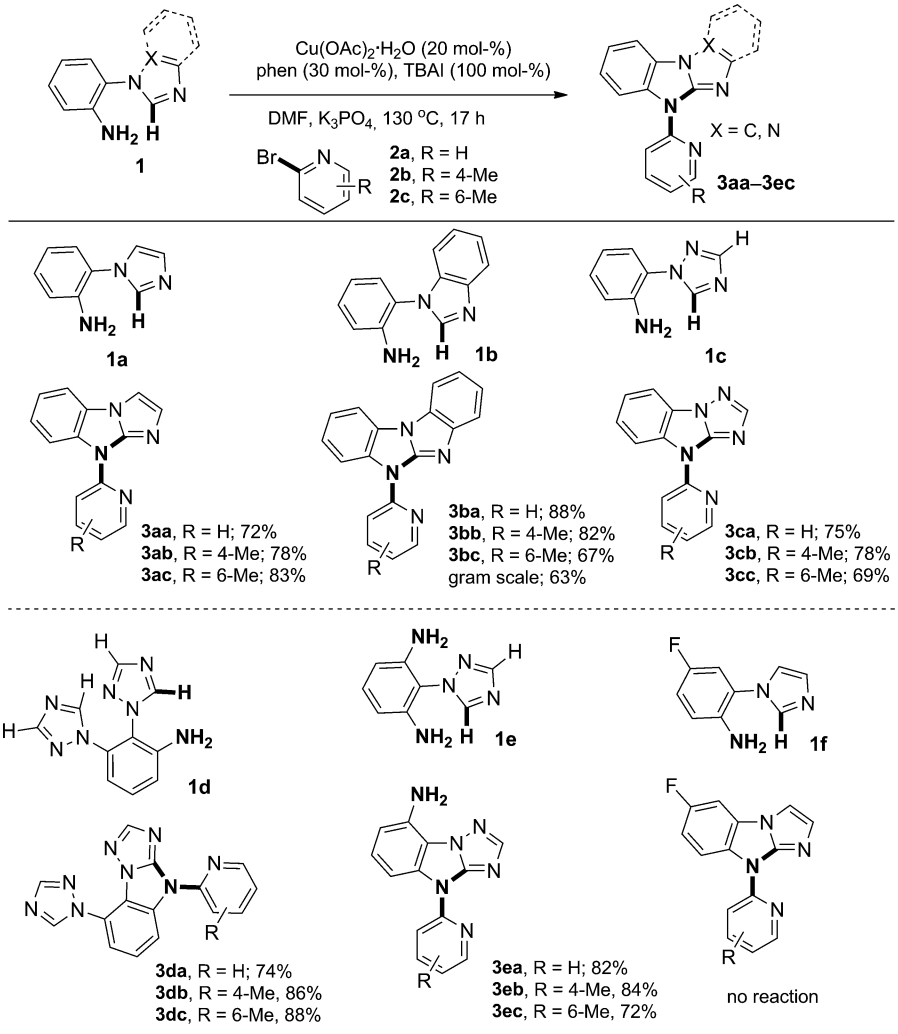
Entry	Catalyst/additive	Ligand[b]	Base	Solvent	Isolated yield[c] [%]
1	20 mol-% CuI	30 mol-% phen	K_3PO_4	DMF	23
2	20 mol-% $CuCl_2$	30 mol-% phen	K_3PO_4	DMF	20
3	20 mol-% $CuBr_2$	30 mol-% phen	K_3PO_4	DMF	18
4	20 mol-% CuI/1 equiv. $Cu(OAc)_2·H_2O$	30 mol-% phen	K_3PO_4	DMF	50
5	20 mol-% CuI/1 equiv. $CuCl_2$	30 mol-% phen	K_3PO_4	DMF	31
6	20 mol-% $CuCl_2$/1 equiv. $Cu(OAc)_2·H_2O$	30 mol-% phen	K_3PO_4	DMF	87
7	1 equiv. $Cu(OAc)_2·H_2O$		K_3PO_4	DMF	39
8	20 mol-% $Cu(OAc)_2·H_2O$	30 mol-% phen		DMF	18 (8)
9	40 mol-% $Cu(OAc)_2·H_2O$	30 mol-% phen		DMF	23 (11)
10	60 mol-% $Cu(OAc)_2·H_2O$	30 mol-% phen		DMF	37 (5)
11	80 mol-% $Cu(OAc)_2·H_2O$	30 mol-% phen		DMF	58 (trace)
12	20 mol-% $Cu(OAc)_2·H_2O$	30 mol-% phen	K_3PO_4	DMF	21 (18)
13	40 mol-% $Cu(OAc)_2·H_2O$	30 mol-% phen	K_3PO_4	DMF	30 (10)
14	60 mol-% $Cu(OAc)_2·H_2O$	30 mol-% phen	K_3PO_4	DMF	67 (7)
15	20 mol-% $Cu(OAc)_2·H_2O$/10 mol-% TBAI	30 mol-% phen	K_3PO_4	DMF	65 (11)
16	20 mol-% $Cu(OAc)_2·H_2O$/50 mol-% TBAI	30 mol-% phen	K_3PO_4	DMF	67 (5)
17	20 mol-% $Cu(OAc)_2·H_2O$/100 mol-% TBAI	30 mol-% phen	K_3PO_4	DMF	72
18	20 mol-% $Cu(OAc)_2·H_2O$/100 mol-% TBAI	30 mol-% phen	K_3PO_4	toluene	n.d.



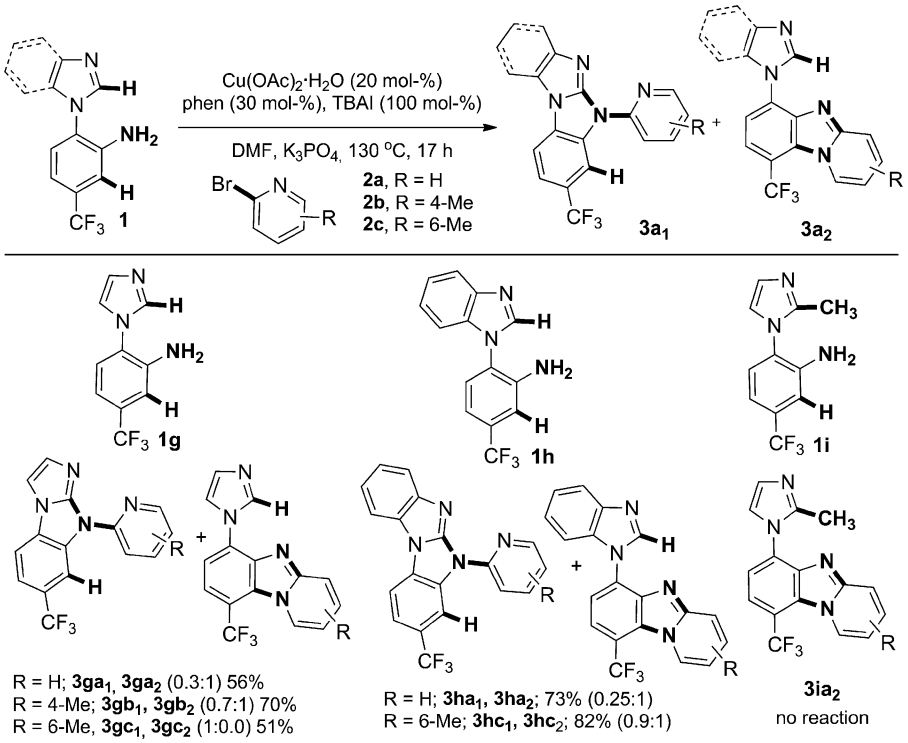
[a] Reaction conditions: **1a** (0.31 mmol), **2a** (0.63 mmol), catalyst (20 mol-%), base (3 equiv.), solvent (3 mL), 130 °C. [b] Ligands tested in screening process are shown below. [c] Yield of byproduct are given in parentheses.

factory yields obtained, it was difficult to identify the nature of the reactive copper species that is responsible for the transformation. Thus, the reaction was carried out without $CuCl_2$ and phenanthroline to examine the role of excess $Cu(OAc)_2{\cdot}H_2O$. Interestingly, this reaction yielded 39% of the required product (entry 7). Then we studied the reaction extensively by using $Cu(OAc)_2{\cdot}H_2O$ as the sole catalyst for this cascade two-fold C–N bond protocol. To determine the required amount of $Cu(OAc)_2{\cdot}H_2O$ for the reaction, we screened various quantities of the catalyst with or without the base. In the absence of base, our initial optimization with 20 mol-% of $Cu(OAc)_2{\cdot}H_2O$ and 30 mol-% phen gave the required product in 18% yield along with 8% of a byproduct with the same molecular mass (entry 8). When 80 mol-% of $Cu(OAc)_2{\cdot}H_2O$ was used, the product was obtained in 58% yield with trace amounts of the byproduct (entry 11). Although the yield of the reaction was improved with 80 mol-% of $Cu(OAc)_2{\cdot}H_2O$ in the absence of base, it was far from satisfactory . Therefore we wanted to explore the influence of base on the catalytic system. The reaction furnished 67% of product when we used 60 mol-% of $Cu(OAc)_2{\cdot}H_2O$ with 30 mol-% phen and 3 equiv. K_3PO_4 (entry 14). To improve the yield further, we used TBAI as an additive with 20 mol-% $Cu(OAc)_2$, 30 mol-% phen and 3 equiv. K_3PO_4 (entries 15–18). Addition of 1 equiv. TBAI improved the yield significantly to 72% and no byproduct was observed (entry 17). Notably, when we performed the reaction under these improved conditions in toluene, no product was obtained. We also examined the use of various ligands in place of phenanthroline under the improved conditions [20 mol-% $Cu(OAc)_2{\cdot}H_2O$, 30 mol-% ligand, 1 equiv. TBAI and 2 equiv. K_3PO_4], however, the yield of the product was not improved. Hence, we chose 20 mol-% $Cu(OAc)_2{\cdot}H_2O$, 30 mol-% phen, 1 equiv. TBAI and 2 equiv. K_3PO_4 (entry 17) as the optimized conditions to scrutinize the substrate scope of the reaction.

To explore the scope and generality of this method, we selected a range of *N*-(*o*-aminoaryl)azoles **1a**–**1i** (Scheme 2 and Scheme 3) and bromopyridines to explore the formation of *N*-pyridyl heterocycles. In all cases, the reaction pro-

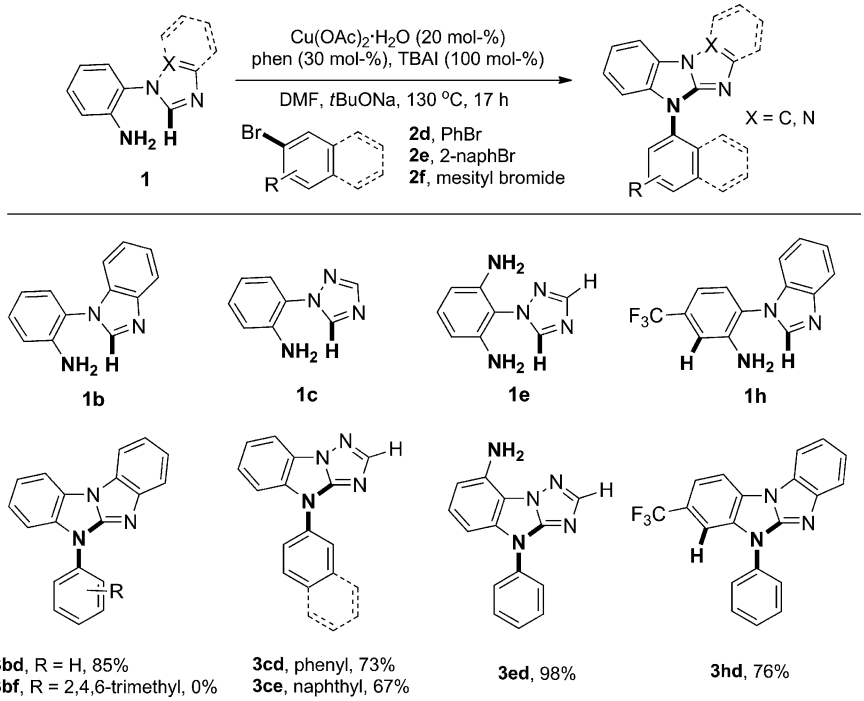


Scheme 2. Substrate scope for the cascade reaction between azoles and 2-bromopyridines.

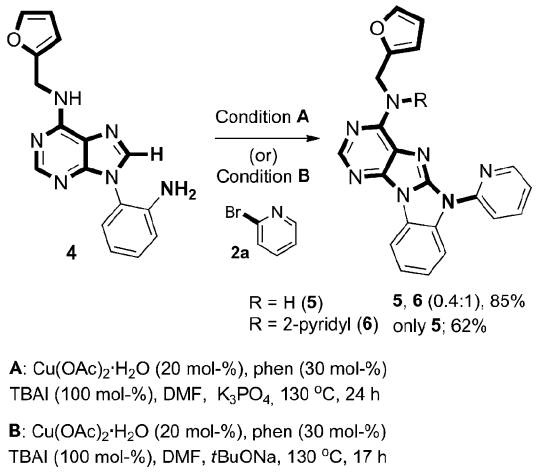


Scheme 3. Substrate scope for the cascade reaction between azoles and 2-bromopyridines and the competitive C–H activations.

ceeded smoothly to provide the expected *N*-pyridyl heterocycles in good-to-excellent yields (Scheme 2). In the case of 2,3-bis(triazol-1-yl)-1-aminobenzene (**1d**), despite the presence of four potentially activated C–H bonds, the reaction with pyridyl bromides proceeded efficiently to afford the desired products (**3da**–**3dc**) in excellent yields. The tolerance of the reaction conditions to the presence of triazole offers an ideal opportunity for further synthetic manipulation towards the preparation of N-heterocyclic carbenes (NHCs) and related products. Remarkably, when we used azole **1e**,



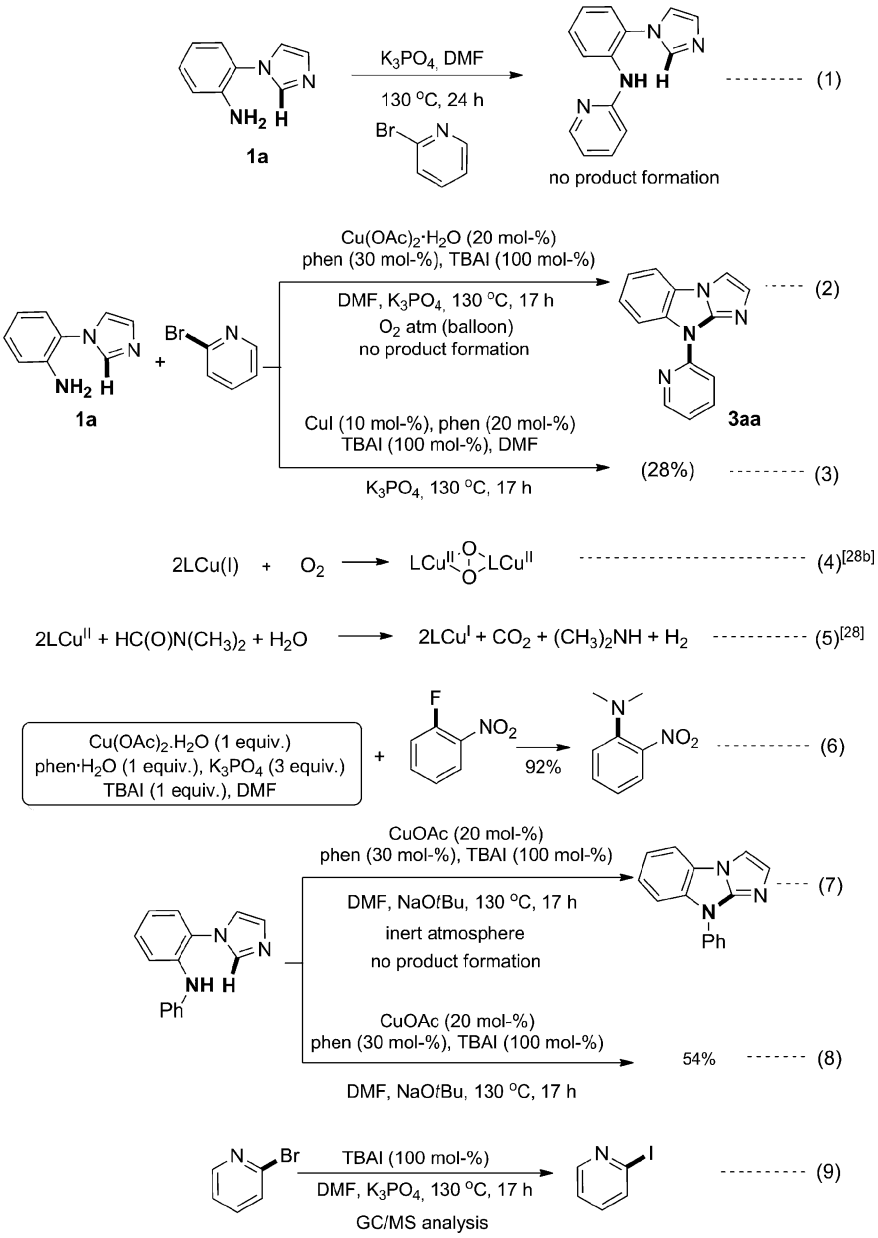
Scheme 4. Reaction of azoles and aryl bromides.



Scheme 5. Synthesis of benzimidazokinetin.

we could selectively functionalize one of the amine moieties to provide products **3ea**–**3ec** in good yields. This desymmetrization could be useful in further structural modifications. Unfortunately, azole **1f** was found to be unreactive under the optimized conditions.

In the case of CF_3-substituted *N*-(*o*-aminoaryl)azoles **1g** and **1h**, an inseparable regioisomeric mixture of the expected *N*-pyridyl heterocycles and benzimidazo[1,2-*a*]pyridines were obtained in good yields (Scheme 3). Such benzimidazo[1,2-*a*]pyridine motifs are of synthetic[23] and biological interest.[24] The formation of regioisomers may be due to the CF_3 substituent enhancing the acidity of the *ortho*-H and hence the *o*-C–H activation resulting in the regioisomeric mixture of products. The formation of the benzimidazo[1,2-*a*]pyridines was confirmed unambiguously by various NMR studies of the representative compounds



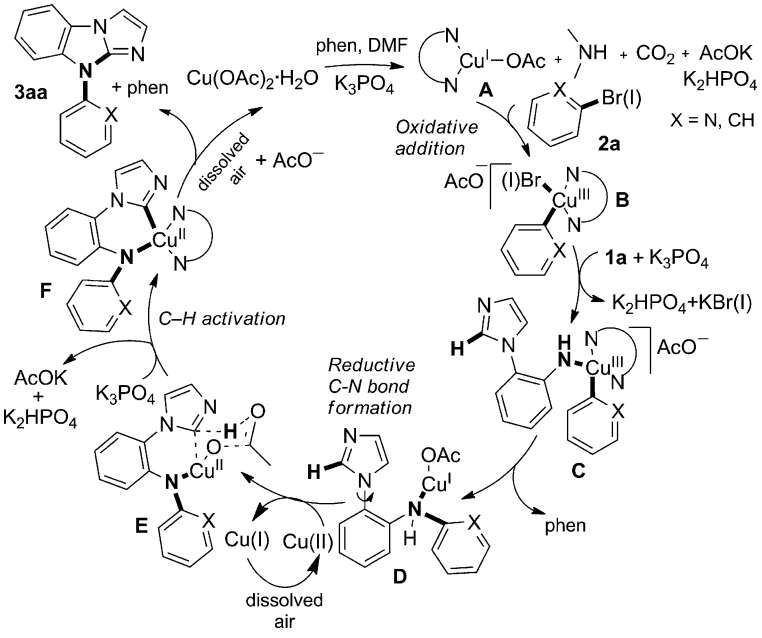
Scheme 6. Reactions carried out during a study of the mechanism.

3ga$_2$ and **3ha$_2$**. Interestingly, when **1g** was treated with 2-bromo-6-methylpyridine (**2c**), only the *N*-pyridyl heterocycle **3gc$_1$** was obtained in 51% yield. With the intention of obtaining only the product **3a$_2$** from the competing reaction, we performed this reaction with 2-methylimidazole **1i**. However, to our surprise, this substrate was very reluctant to couple with various 2-bromopyridines under our optimized conditions.

Having successfully accomplished the one-pot synthesis of *N*-aryl heterocycles with 2-bromopyridines, we then looked at extending the scope of this reaction to simple aryl bromides **2d**–**f** (Scheme 4). Our initial attempts with azole **1b** and bromobenzene (**2d**) under our optimized conditions provided only 7% of the *N*-phenyl heterocycle **3bd**. Nevertheless, encouraged by the formation of the product, we looked at changing the base to improve the yield of this reaction. After a thorough screening, this reaction successfully furnished the desired *N*-phenyl heterocycle **3bd** in 85% yield when *t*BuONa was used instead of K_3PO_4. Then we explored the scope of the reaction with various azoles and a few aryl bromides. All of them gave good yields and, interestingly, the reaction of azole **1e** with **2d** provided the best yield (98%). In addition, the reaction of azole **1h** with bromobenzene (**2d**) afforded heterocycle **3hd** as the sole product (76%) without affecting other competitive C–H bonds. As expected, the sterically demanding mesityl bromide (**2f**) was found to be unreactive under the optimized conditions with azole **1b**.

This strategy has also been extended to the biologically important anti-aging drug analogue[25] benzimidazokinetin (Scheme 5). In our initial attempts to synthesize this hybrid natural product, *N*-pyridylbenzimidazokinetin **5**, the azole **4** under the optimized conditions A gave a mixture of products **5** and **6** in a ratio of 0.4:1 in 85% yield, whereas conditions B exclusively provided the product *N*-pyridylbenzimidazokinetin **5** in 62% yield. Thus, the cascade two-fold C–N bond methodology becomes more general for the C–H activation of similar kinds of azoles and the synthesis of the corresponding heterocyclic compounds.

To gain more insight into the reaction mechanism, several control experiments were carried out (Scheme 6). Initially a blank reaction was carried out without the Cu catalyst to rule out the possibility of a S_NAr displacement reaction [Equation (1)]. The reaction was then studied under oxygen; it was found that product formation was completely inhibited [Equation (2)]. It is thus likely that the Cu^I catalyst generated in situ under the reaction conditions might be completely re-oxidized to Cu^{II} by oxygen [Equation (4)],[26b] and that the unavailability of the active Cu^I catalyst led to isolation of unchanged starting materials. This explains the importance of the Cu^I species, which is required for the polarization of the 2-bromopyridines. In further support of a mechanism involving Cu^I, when this reaction was carried out in the presence of CuI as catalyst, 28% of the required product was isolated [Equation (3)]. Moreover, it is well established that Cu^{II} can be reduced to Cu^I by the mild reducing action of DMF.[26] During this process, the reaction should produce an equivalent amount of dimethylamine [DMA; Equation (5)], which was also observed under our reaction conditions.[27] The DMA generated was successfully trapped with 1-fluoro-2-nitrobenzene to give *N*,*N*-dimethyl-2-nitroaniline in 92% yield [Equation (6)]. When the reaction was carried out with the *N*-phenyl intermediate using CuOAc as a catalyst and degassed solvent under an inert atmosphere [Equation (7)], product formation was not observed. However, when the solvent was not degassed, the product was obtained in 54% yield [Equation (8)]. These observations lead to the conclusions that Cu^{II} is the active species involved in the C–H activation reaction; also, this active species could be generated in situ by the oxidation of



Scheme 7. Proposed mechanism.

Cu^{I} with small quantities of dissolved oxygen present in the solvent system.[23b,28] Although the role of tetrabutylammonium iodide (TBAI) as an additive is not yet clear, GC–MS analysis showed that a substantial amount of iodine exchange[29] had taken place under the blank reaction conditions – see Equation (9) – which might facilitate the initial oxidative addition.

Based on the above investigations, a plausible mechanism for the synthesis of *N*-aryl or *N*-pyridyl heterocycles using $Cu(OAc)_2 \cdot H_2O$ is outlined here (Scheme 7). According to literature precedent,[26,27] the reductive generation of the active catalyst phenCu^{I} **A** was achieved from $Cu(OAc)_2 \cdot H_2O$ by the mild reducing action of DMF.[23] Then phen-Cu^{I} **A** undergoes oxidative addition[30] of 2-bromo- or 2-iodopyridine to yield the Cu^{III} species **B**. Subsequently, reductive C–N coupling takes place to give the Cu^{I} species **D**. This Cu^{I} species is oxidized in situ to provide Cu^{II} intermediate **E**,[23b,28] which in turn undergoes acetate-ligand-assisted, concerted C–H activation to afford **F**. Finally, reductive elimination gives product **3aa** and concomitant Cu^{0} oxidation regenerates the Cu^{II} catalyst.

In addition to the biological relevance of these heterocycles, we explored the coordination of the products with metals. Thus, a representative electron-rich product, *N*-pyridyl heterocycle **3bc** was chosen as a ligand for the preparation of a Pd complex[31] (Figure 2).

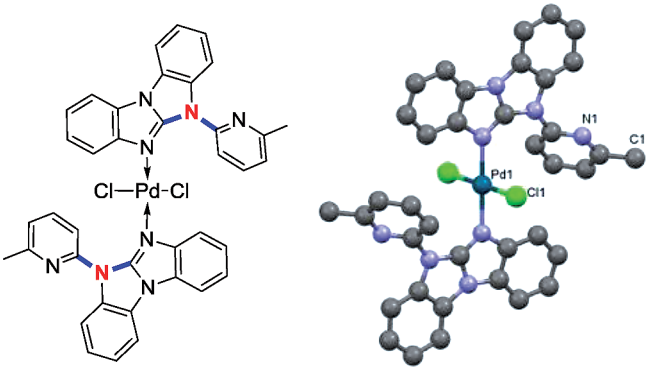


Figure 2. Coordination of product **3bc** to palladium.

Conclusions

We have developed an efficient, one-pot, copper-catalysed sp^2 C–H cascade amination to synthesize various *N*-aryl and -pyridyl heterocycles from various azoles and aryl bromides or 2-bromopyridines. To the best of our knowledge, this is the first report of the use of an inexpensive Cu^{II} salt as catalyst for a cascade two-fold C–N bond-forming reaction involving an oxidative sp^2 C–H activation. Furthermore, we believe that many of the synthesized electron-rich triazole derivatives could serve as ligands for metal catalysis and also be elaborated (**3da**–**3dc**) as N-heterocyclic carbenes by using known *N*-alkylation protocols. Thus, the method described herein serves as a straightforward protocol for the synthesis of *N*-pyridyl heterocycles and also allows access to biologically active heterocyclic hybrid natural products.

Experimental Section

General Methods: Unless otherwise noted, all starting materials and reagents were obtained from commercial suppliers and used after further purification as detailed below. *N*,*N*-Dimethylformamide and MeOH were freshly distilled from calcium hydride. All solvents for routine isolation of products and chromatography were reagent grade and glass distilled. Reaction flasks were dried in an oven at 130 °C for 12 h. Air- and moisture-sensitive reactions were performed under argon/UHP nitrogen. Column chromatography was performed by using silica gel (100–200 mesh, Acme) with indicated solvents. Thin-layer chromatography (TLC) was conducted with Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized with UV, potassium permanganate, ceric ammonium molybdate, and iodine staining. Optical rotation was recorded with an Autopol IV automatic polarimeter. Melting points of the compounds were determined by using a Büchi B-545 melting point apparatus. IR spectra were recorded with a Thermo Nicolet Avater 320 FTIR and a Nicolet Impact 400 machine. Mass spectra were obtained with a Waters Micromass-Q-Tof microTM (YA105) spectrometer. GCMS analysis was done with an Agilent 7890A GC system connected with 5975C inert XL EI/CI MSD (with triple axis detector). ^{1}H NMR spectra were recorded with a Bruker 400 MHz and a Bruker 500 MHz spectrometer and are reported in ppm by using the solvent as an internal standard [$CDCl_3$ at δ = 7.26 ppm, $(CD_3)_2SO$ at δ = 2.50 ppm]. Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, m = multiplet, br. = broad, ap =apparent; coupling constant(s) in Hz; integration. Proton-decoupled ^{13}C NMR spectra were recorded with a Bruker 400 MHz and a Bruker 500 MHz spectrometer and are reported in ppm using the solvent as an internal standard [$CDCl_3$ at δ = 77.2 ppm, $(CD_3)_2SO$ at δ = 39.5 ppm].

General Procedure for the Synthesis of *N*-Pyridyl Heterocycles: The azole **1** (1 equiv.) and 2-bromopyridine **2** (2 equiv.) were added to an oven-dried screw-cap reaction tube charged with a magnetic stirring bar, $Cu(OAc)_2 \cdot H_2O$ (20 mol-%), 1,10-phenanthroline monohydrate (30 mol-%), K_3PO_4 (3 equiv.) and TBAI (1 equiv.) in dry DMF (3 mL) at room temp. Then the reaction tube was closed with the screw cap, and the mixture was stirred at 130 °C for 17 h. The reaction mixture was cooled to room temperature, water (5 mL) was added and the mixture extracted with ethyl acetate (3 × 5 mL). Then the combined organic layers were further washed with water (7 × 5 mL), dried with anhyd. Na_2SO_4 and concentrated to give the crude product. Purification by silica gel column chromatography afforded the *N*-pyridyl heterocycles.

3aa: Following the general procedure, the reaction was carried out between 2-(1*H*-imidazol-1-yl)aniline (**1a**; 50 mg, 0.314 mmol, 1 equiv.) and 2-bromopyridine (**2a**; 60 µL, 0.63 mmol, 2.0 equiv.). Column chromatography (10% ethyl acetate in hexanes) on silica gel yielded 53 mg (72%) of the title compound **3aa** as a white solid. R_f = 0.45 (20% ethyl acetate in hexanes); m.p. 141–143 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.80 (dd, *J* = 8.3, 0.7 Hz, 1 H), 8.71 (d, *J* = 8.4 Hz, 1 H), 8.55 (ddd, *J* = 4.8, 2.8, 0.7 Hz, 1 H), 7.89 (ddd, *J* = 8.4, 7.3, 2.8 Hz, 1 H), 7.56 (dd, *J* = 7.7, 0.6 Hz, 1 H), 7.44 (d, *J* = 1.6 Hz, 1 H), 7.38 (td, *J* = 7.7, 0.7 Hz, 1 H), 7.30 (td, *J* = 8.3, 0.6 Hz, 1 H), 7.26 (d, *J* = 1.6 Hz, 1 H), 7.16 (ddd, *J* = 7.7, 4.8, 0.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.5, 147.8, 138.6, 134.1, 131.4, 125.3, 124.3, 122.4, 119.7, 117.3, 114.2,

110.6, 106.7 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 1591, 1574, 1561, 1338, 1262, 771 cm^{-1}. HRMS (ESI): calcd. for $C_{14}H_{11}N_4$ $[M + H]^+$ 235.0984; found 235.0983.

3ab: Following the general procedure, the reaction was carried out between 2-(1*H*-imidazol-1-yl)aniline (**1a**; 50 mg, 0.314 mmol, 1 equiv.) and 2-bromo-4-methylpyridine (**2b**; 70 μL, 0.628 mmol, 2.0 equiv.). Column chromatography on silica gel (7% ethyl acetate in hexanes) yielded 61 mg (78%) of the title compound **3ab** as a white solid. R_f = 0.50 (20% ethyl acetate in hexanes); m.p. 104–107 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.85 (dd, J = 8.4, 0.5 Hz, 1 H), 8.50 (s, 1 H), 8.40 (d, J = 5.0 Hz, 1 H), 7.54 (dd, J = 7.8, 0.8 Hz, 1 H), 7.43 (d, J = 1.3 Hz, 1 H), 7.37 (td, J = 7.8, 1.3 Hz, 1 H), 7.28 (td, J = 8.4, 1.2 Hz, 1 H), 7.29 (d, J = 1.4 Hz, 1 H), 6.99 (d, J = 5.0 Hz, 1 H), 2.50 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.5, 150.1, 147.6, 134.2, 131.3, 125.2, 124.2, 122.3, 121.2, 117.2, 114.6, 110.6, 106.7, 21.6 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 1608, 1568, 1453, 1218, 769 cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{13}N_4$ $[M + H]^+$ 249.1140; found 249.1140.

3ac: Following the general procedure, the reaction was carried out between 2-(1*H*-imidazol-1-yl)aniline (**1a**; 50 mg, 0.314 mmol, 1 equiv.) and 2-bromo-6-methylpyridine (**2c**; 71 μL, 0.628 mmol, 2.0 equiv.). Column chromatography on silica gel (7% ethyl acetate in hexanes) yielded 65 mg (83%) of the title compound **3ac** as a white solid. R_f = 0.50 (20% ethyl acetate in hexanes); m.p. 118–121 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.87 (d, J = 8.3 Hz, 1 H), 8.46 (d, J = 8.2 Hz, 1 H), 7.78 (t, J = 7.8 Hz, 1 H), 7.56 (d, J = 7.7 Hz, 1 H), 7.43 (d, J = 1.5 Hz, 1 H), 7.39 (td, J = 8.5, 1.1 Hz, 1 H), 7.31 (td, J = 7.7, 1.1 Hz, 1 H), 7.28 (d, J = 1.5 Hz, 1 H), 7.02 (d, J = 7.4 Hz, 1 H), 2.51 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.4, 150.5, 139.0, 134.1, 130.7, 125.2, 124.4, 122.4, 119.4, 117.3, 111.1, 110.7, 106.7, 24.5 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 2922, 1609, 1494, 1156, 743 cm^{-1}. (ESI): calcd. for $C_{15}H_{13}N_4$ $[M + H]^+$ 249.1140; found 249.1137.

3ba: Following the general procedure, the reaction was carried out between 2-(1*H*-benzimidazol-1-yl)aniline (**1b**; 50 mg, 0.239 mmol, 1 equiv.) and 2-bromopyridine (**2a**; 45 μL, 0.478 mmol, 2.0 equiv.). Column chromatography on silica gel (10% ethyl acetate in hexanes) yielded 60 mg (88%) of the title compound **3ba** as a white solid. R_f = 0.50 (20% ethyl acetate in hexanes); m.p. 155–157 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.87–8.83 (m, 2 H), 8.60 (dd, J = 4.2, 1.1 Hz, 1 H), 7.97 (ddd, J = 9.2, 7.4, 1.9 Hz, 1 H), 7.87–7.80 (m, 3 H), 7.44–7.39 (m, 3 H), 7.38–7.39 (m, 1 H), 7.26–7.22 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.3, 151.1, 148.0, 146.8, 138.8, 133.9, 127.7, 125.9, 123.9, 123.3, 123.1, 121.0, 120.4, 119.2, 116.9, 115.1, 110.4, 110.2 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 1632, 1606, 1566, 1548, 1455, 1400, 1235, 1217, 750, 736 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{13}N_4$ $[M + H]^+$ 285.1140; found 285.1149.

3bb: Following the general procedure, the reaction was carried out between 2-(1*H*-benzimidazol-1-yl)aniline (**1b**; 50 mg, 0.239 mmol, 1 equiv.) and 2-bromo-4-methylpyridine (**2b**; 50 μL, 0.478 mmol, 2.0 equiv.). Column chromatography on silica gel (8% ethyl acetate in hexanes) yielded 58 mg (82%) of the title compound **3bb** as a white solid. R_f = 0.50 (20% ethyl acetate in hexanes); m.p. 131–133 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.82–8.80 (m, 1 H), 8.63 (t, J = 0.5 Hz, 1 H), 8.45 (d, J = 5.0 Hz, 1 H), 7.86–7.83 (m, 2 H), 7.82–7.78 (m, 1 H), 7.42–7.37 (m, 3 H), 7.33 (td, J = 7.8, 1.2 Hz, 1 H), 7.06 (dd, J = 4.5, 0.6 Hz, 1 H), 2.55 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.3, 151.1, 150.3, 147.6, 146.8, 134.0, 127.6, 125.8, 123.7, 123.2, 122.9, 121.7, 120.9, 119.1, 116.8, 115.5, 110.3, 110.1, 21.7 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 1633, 1551, 1498, 1443, 1237, 1216, 1160, 768 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{15}N_4$ $[M + H]^+$ 299.1297; found 299.1287.

3bc: Following the general procedure, the reaction was carried out between 2-(1*H*-benzimidazol-1-yl)aniline (**1b**; 50 mg, 0.239 mmol, 1 equiv.) and 2-bromo-6-methylpyridine (**2c**; 57 μL, 0.478 mmol, 2.0 equiv.). Column chromatography on silica gel (7% ethyl acetate in hexanes) yielded 48 mg (67%) of the title compound **3bc** as a white solid. R_f = 0.53 (20% ethyl acetate in hexanes); m.p. 137–140 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.88 (dd, J = 5.1, 3.6 Hz, 1 H), 8.60 (d, J = 8.3 Hz, 1 H), 7.86–7.82 (m, 3 H), 7.78–7.76 (m, 1 H), 7.41–7.36 (m, 3 H), 7.32 (td, J = 7.9, 1.0 Hz, 1 H), 7.07 (d, J = 7.5 Hz, 1 H), 2.66 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.3, 151.5, 150.5, 146.9, 139.1, 134.0, 127.7, 125.9, 123.8, 123.3, 123.0, 121.0, 119.8, 119.2 117.1, 111.9, 110.4, 110.2, 24.4 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 1641, 1606, 1557, 1442, 1324, 1231, 1163, 750 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{15}N_4$ $[M + H]^+$ 299.1297; found 299.1296.

3bc – Gram-Scale Reaction: Azole **1b** (1 g, 4.78 mmol, 1 equiv.) and 2-bromo-6-methylpyridine (**2c**; 1.07 mL, 9.56 mmol, 2 equiv.) were added to a mixture of $Cu(OAc)_2{\cdot}H_2O$ (189 mg, 0.956 mmol, 20 mol-%), 1,10-phenanthroline monohydrate (284 mg, 1.43 mmol, 30 mol-%), K_3PO_4 (3.02 g, 14.35 mmol, 3 equiv.) and TBAI (1.73 g, 1 equiv.) in dry DMF (8 mL) at room temp. Then the reaction tube was closed with a screw cap and stirred at 130 °C for 17 h. The reaction mixture was then cooled to room temperature, water (7 mL) was added and the mixture extracted with ethyl acetate (3 × 15 mL). Then the combined organic layers were further washed with water (7 × 20 mL), dried with anhyd. Na_2SO_4 and concentrated to give the crude product. Purification by column chromatography (7% ethyl acetate in hexanes) afforded the *N*-pyridyl heterocycle (0.89 g, 63%).

3ca: Following the general procedure, the reaction was carried out between 2-(1*H*-1,2,4-triazol-1-yl)aniline (**1c**; 50 mg, 0.312 mmol, 1 equiv.) and 2-bromopyridine (**2a**; 60 μL, 0.624 mmol, 2.0 equiv.). Column chromatography on silica gel (14% ethyl acetate in hexanes) yielded 55 mg (75%) of the title compound **3ca** as a white solid. R_f = 0.40 (20% ethyl acetate in hexanes); m.p. 163–166 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.93 (dd, J = 8.9, 1.1 Hz, 1 H), 8.60 (dd, J = 4.7, 0.9 Hz, 1 H) 8.52 (d, J = 8.4 Hz, 1 H), 8.13 (s, 1 H), 7.93 (ddd, J = 9.2, 6.5, 1.8 Hz, 1 H), 7.88 (dd, J = 7.5, 1.3 Hz, 1 H), 7.49–7.41 (m, 2 H), 7.25–7.23 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.6, 152.3, 150.7, 148.3, 138.9, 133.5, 125.1, 124.9, 123.6, 120.7, 117.7, 114.3, 110.9 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 1575, 1562, 1504, 1480, 1467, 1326, 1176, 1160, 775, 745 cm^{-1}. HRMS (ESI): calcd. for $C_{13}H_{10}N_5$ $[M + H]^+$ 236.0936; found 236.0943.

3cb: Following the general procedure, the reaction was carried out between 2-(1*H*-1,2,4-triazol-1-yl)aniline (**1c**; 50 mg, 0.312 mmol, 1 equiv.) and 2-bromo-4-methylpyridine (**2b**; 60 μL, 0.624 mmol, 2.0 equiv.). Column chromatography on silica gel (12% ethyl acetate in hexanes) yielded 61 mg (78%) of the title compound **3cb** as a white solid. R_f = 0.45 (20% ethyl acetate in hexanes); m.p. 165–168 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.90 (dd, J = 8.9, 1.2 Hz, 1 H), 8.42 (d, J = 5.0 Hz, 1 H), 8.29 (s, 1 H), 8.13 (s, 1 H), 7.87 (dd, J = 7.4, 0.8 Hz, 1 H), 7.47–7.39 (m, 2 H), 7.06 (d, J = 5.0 Hz, 1 H), 2.50 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.5, 152.3, 150.8, 150.6, 147.9, 133.6, 125.1, 124.8, 123.4, 122.0, 117.7, 114.7, 110.8, 21.6 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 1612, 1561, 1505, 1471, 1373, 1164, 744 cm^{-1}. HRMS (ESI): calcd. for $C_{14}H_{12}N_5$ $[M + H]^+$ 250.1093; found 250.1094.

3cc: Following the general procedure, the reaction was carried out between 2-(1*H*-1,2,4-triazol-1-yl)aniline (**1c**; 50 mg, 0.312 mmol, 1 equiv.) and 2-bromo-6-methylpyridine (**2c**; 57 μL, 0.624 mmol, 2.0 equiv.). Column chromatography on silica gel (12% ethyl acet-

ate in hexanes) yielded 54 mg (69%) of the title compound **3cc** as a white solid. R_f = 0.45 (20% ethyl acetate in hexanes); m.p. 152–155 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.89 (dd, J = 7.5, 1.2 Hz, 1 H), 8.43 (d, J = 5.1 Hz, 1 H), 8.30 (s, 1 H), 8.13 (s, 1 H), 7.88–7.86 (m, 1 H), 7.48–7.39 (m, 2 H), 7.07 (dd, J = 5.0, 0.4 Hz, 1 H), 2.51 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.5, 152.3, 150.8, 150.6, 147.9, 133.6, 125.1, 124.8, 123.4, 122.0, 117.7, 114.7, 110.8, 21.6 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 1612, 1561, 1504, 1471, 1373, 1164, 754, 744 cm^{-1}. HRMS (ESI): calcd. for $C_{14}H_{12}N_5$ [M + H]$^+$ 250.1093; found 250.1100.

3da: Following the general procedure, the reaction was carried out between 2,3-di(1*H*-1,2,4-triazol-1-yl)aniline (**1d**; 50 mg, 0.220 mmol, 1.0 equiv.) and 2-bromopyridine (**2a**; 41 μL, 0.440 mmol, 2.0 equiv.). Column chromatography on silica gel (17% ethyl acetate in hexanes) yielded 49 mg (74%) of the title compound **3da** as a white solid. R_f = 0.25 (20% ethyl acetate in hexanes); m.p. 242–245 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.44 (s, 1 H), 9.05 (dd, J = 8.4, 0.9 Hz, 1 H), 8.64–8.62 (m, 1 H), 8.55 (d, J = 8.3 Hz, 1 H), 8.24 (s, 1 H), 8.12 (s, 1 H), 8.00–7.96 (m, 1 H), 7.85 (dd, J = 8.2, 0.9 Hz, 1 H), 7.60 (t, J = 8.3 Hz, 1 H), 7.33–7.30 (m, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 154.9, 152.8, 152.8, 148.4, 145.5, 139.2, 135.1, 125.7, 121.4, 118.7, 117.4, 114.8 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 2925, 1564, 1485, 1278, 773 cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{10}N_8Na$ [M + Na]$^+$ 325.0921; found 325.0921.

3db: Following the general procedure, the reaction was carried out between 2,3-di-(1*H*-1,2,4-triazol-1-yl)aniline (**1d**; 50 mg, 0.220 mmol, 1.0 equiv.) and 2-bromo-4-methylpyridine (**2b**; 49 μL, 0.440 mmol, 2.0 equiv.). Column chromatography on silica gel (15% ethyl acetate in hexanes) yielded 60 mg (86%) of the title compound **3db** as a white solid. R_f = 0.35 (20% ethyl acetate in hexanes); m.p. 243–247 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.44 (s, 1 H), 8.99 (d, J = 8.5, 0.9 Hz, 1 H), 8.45 (d, J = 5.0 Hz, 1 H), 8.32 (s, 1 H), 8.24 (s, 1 H), 8.12 (s, 1 H), 7.82 (dd, J = 8.2, 0.9 Hz, 1 H), 7.57 (t, J = 8.2 Hz, 1 H), 7.21 (dd, J = 5.0, 0.4 Hz, 1 H), 2.53 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.8, 152.2, 150.9, 150.3, 147.9, 145.5, 135.1, 125.6, 122.8, 122.7, 118.5, 117.3, 117.2, 115.2, 21.6 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 1668, 1611, 1568, 1482, 1278, 756, 734 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{13}N_8$ [M + H]$^+$ 317.1263; found 317.1252.

3dc: Following the general procedure, the reaction was carried out between 2,3-di(1*H*-1,2,4-triazol-1-yl)aniline (**1d**; 50 mg, 0.220 mmol, 1.0 equiv.) and 2-bromo-6-methylpyridine (**2c**; 49 μL, 0.440 mmol, 2.0 equiv.). Column chromatography on silica gel (15% ethyl acetate in hexanes) yielded 61 mg (88%) of the title compound **3dc** as a white solid. R_f = 0.35 (20% ethyl acetate in hexanes); m.p. 258–261 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.44 (s, 1 H), 9.07 (dd, J = 8.4, 0.8 Hz, 1 H), 8.33 (d, J = 8.4 Hz, 1 H), 8.24 (s, 1 H), 8.11 (s, 1 H), 7.86 (t, J = 7.6 Hz, 1 H), 7.84 (d, J = 7.6 Hz, 1 H), 7.59 (t, J = 8.4 Hz, 1 H), 7.16 (d, J = 7.6 Hz, 1 H), 2.69 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.9, 154.9, 152.9, 152.7, 149.6, 145.5, 139.4, 135.1, 125.6, 122.8, 120.8, 118.6, 117.5, 111.6, 24.4 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 1635, 1483, 1213, 788, 771 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{13}N_8$ [M + H]$^+$ 317.1263; found 317.1266.

3ea: Following the general procedure, the reaction was carried out between 2-(1*H*-1,2,4-triazol-1-yl)benzene-1,3-diamine (**1e**; 50 mg, 0.285 mmol, 1 equiv.) and 2-bromopyridine (**2a**; 54 μL, 0.570 mmol, 2.0 equiv.). Column chromatography on silica gel (20% ethyl acetate in hexanes) yielded 58.4 mg (82%) of the title compound **3ea** as a white solid. R_f = 0.25 (30% ethyl acetate in hexanes); m.p. 175–178 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.56 (ddd, J = 4.8, 1.9, 0.9 Hz, 1 H), 8.46 (dt, J = 8.3, 0.9 Hz, 1 H), 8.18 (dd, J = 8.4, 0.7 Hz, 1 H), 8.08 (s, 1 H), 7.90 (ddd, J = 8.3, 7.4, 1.9 Hz, 1 H), 7.26–7.19 (m, 2 H), 6.70 (dd, J = 8.4, 0.7 Hz, 1 H), 4.60 (br. s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8, 151.4, 150.7, 148.2, 138.7, 134.3, 133.1, 125.9, 120.5, 114.1, 113.3, 109.5, 106.8 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 3340, 2926, 1652, 1593, 1481, 1378, 1019, 767 cm^{-1}. HRMS (ESI): calcd. for $C_{13}H_{11}N_6$ [M + H]$^+$ 251.1045; found 251.1040.

3eb: Following the general procedure, the reaction was carried out between 2-(1*H*-1,2,4-triazol-1-yl)benzene-1,3-diamine (**1e**; 50 mg, 0.285 mmol, 1 equiv.) and 2-bromo-4-methylpyridine (**2b**; 63 μL, 0.570 mmol, 2.0 equiv.). Column chromatography on silica gel (18% ethyl acetate in hexanes) yielded 63.2 mg (84%) of the title compound **3eb** as a white solid. R_f = 0.30 (30% ethyl acetate in hexanes); m.p. 148–151 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.41 (d, J = 5.0 Hz, 1 H), 8.25 (d, J = 0.5 Hz, 1 H), 8.17 (dd, J = 8.3, 0.6 Hz, 1 H), 8.09 (s, 1 H), 7.21 (t, J = 8.1 Hz, 1 H), 7.04 (dd, J = 5.0, 0.5 Hz, 1 H), 6.70 (dd, J = 8.0, 0.6, Hz, 1 H) 4.60 (br. s, 2 H), 2.50 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.6, 153.9, 150.1, 143.9, 139.0, 134.5, 133.1, 125.9, 119.9, 113.3, 111.0, 109.5, 107.1, 24.4 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 3351, 2925, 1597, 1555, 1480, 1455, 1377, 1218, 1033, 768 cm^{-1}. HRMS (ESI): calcd. for $C_{14}H_{13}N_6$ [M + H]$^+$ 265.1202; found 265.1193.

3ec: Following the general procedure, the reaction was carried out between 2-(1*H*-1,2,4-triazol-1-yl)benzene-1,3-diamine (**1e**; 50 mg, 0.285 mmol, 1 equiv.) and 2-bromo-6-methylpyridine (**2c**; 63 μL, 0.570 mmol, 2.0 equiv.). Column chromatography on silica gel (18% ethyl acetate in hexanes) yielded 53.5 mg (72%) of the title compound **3ec** as a white solid. R_f = 0.30 (30% ethyl acetate in hexanes); m.p. 147–150 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (d, J = 8.2 Hz, 1 H), 8.24 (dd, J = 8.3, 0.7 Hz, 1 H), 7.78 (t, J = 8.3 Hz, 1 H), 8.07 (s, 1 H), 7.22 (t, J = 8.2 Hz, 1 H), 7.06 (d, J = 8.2 Hz, 1 H), 6.70 (dd, J = 8.3, 0.7 Hz, 1 H), 4.60 (br. s, 2 H), 2.64 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8, 151.3, 150.8, 150.3, 147.8, 134.4, 133.0, 125.8, 121.8, 114.5, 113.2, 109.6, 106.8, 21.5 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 3435, 3342, 2924, 1651, 1556, 1477, 1417, 1161, 761 cm^{-1}. HRMS (ESI): calcd. for $C_{14}H_{13}N_6$ [M + H]$^+$ 265.1202; found 265.1207.

3ga$_1$ and 3ga$_2$: Following the general procedure, the reaction was carried out between 2-(1*H*-imidazol-1-yl)-5-(trifluoromethyl)aniline (**1g**; 100 mg, 0.440 mmol, 1 equiv.) and 2-bromopyridine (**2a**; 84 μL, 0.88 mmol, 2.0 equiv.). Column chromatography on silica gel (10% ethyl acetate in hexanes) yielded 75 mg (56%) of an inseparable mixture of regioisomeric products **3ga$_1$*** and **3ga$_2$** (0.3:1) as a white solid. R_f = 0.50 (20% ethyl acetate in hexanes); m.p. 134–137 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.25* (s, 0.3 H), 8.75* (s, 0.3 H), 8.71 (d, 8.3 Hz, 1 H), 8.60* (dd, J = 4.5, 0.8 Hz, 0.3 H), 8.46 (dd, J = 4.8, 1.0 Hz, 1 H), 8.11 (d, J = 2.76 Hz, 1 H), 8.08 (s, 1 H), 7.94 (td, J = 6.6, 1.8 Hz, 1 H), 7.92* (td, J = 8.1, 1.8 Hz, 0.3 H) 7.70 (d, J = 8.3 Hz, 1 H), 7.66–7.58* (m, 0.9 H), 7.48–7.47 (m, 1 H), 7.47–7.46* (m, 0.3 H), 7.43 (d, J = 2.7 Hz, 1 H), 7.31* (d, J = 1.5 Hz, 0.3 H), 7.21 (dd, J = 7.2, 4.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.0, 148.6, 148.5, 148.1, 146.7, 139.2, 138.8, 132.3, 128.8, 126.4, 125.4, 120.9, 120.3, 119.6, 116.8, 116.7, 116.7, 116.6, 116.6, 115.1, 114.1, 113.2, 110.6, 110.3, 107.0, 106.9 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –60.5 (1.0), –60.8 (0.3) ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 2928, 2851, 2101, 1640, 1446, 1321, 1102, 772, 667 cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{10}N_4F_3$ [M + H]$^+$ 303.0858; found 303.0851.

Note: The identity of **3ga$_2$** was confirmed by a partial purification of the above isomeric mixtures. The experimental data for pure compound **3ga$_2$** is given below.

M.p. 141–143 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.68 (d, J = 8.2 Hz, 1 H), 8.46–8.44 (m, 1 H), 8.08 (d, J = 2.7 Hz, 1 H), 8.06 (s, 1 H), 7.93–7.89 (m, 1 H), 7.65 (dd, J = 8.4, 0.5 Hz, 1 H), 7.46–7.44 (m, 1 H), 7.41 (d, J = 2.8 Hz, 1 H), 7.19 (ddd, J = 7.3, 4.8, 0.9 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.9, 148.6, 148.5, 146.7, 139.2, 128.8, 126.1, 125.4, 123.9, 120.9, 116.8, 116.6, 113.2, 110.3, 106.9 ppm. HRMS (ESI): calcd. for $C_{15}H_{10}F_3N_4$ [M + H]$^+$ 303.0852; found 303.0855.

3gb$_1$ and 3gb$_2$: Following the general procedure, the reaction was carried out between 2-(1*H*–imidazol-1-yl)-5-(trifluoromethyl)aniline (**1g**; 100 mg, 0.440 mmol, 1 equiv.) and 2-bromo-4-methylpyridine (**2b**; 95 μL, 0.880 mmol, 2.0 equiv.). Column chromatography on silica gel (6% ethyl acetate in hexanes) yielded 98 mg (70%) of an inseparable mixture of the regioisomeric products **3gb$_1$*** and **3gb$_2$** (0.7:1) as a white solid. R_f = 0.50 (20% ethyl acetate in hexanes); m.p. 126–129 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.22 (s, 1 H), 8.52 (s, 1 H), 8.52* (s, 0.7 H), 8.43 (d, J = 5.0 Hz, 1 H), 8.30* (d, J = 5.0 Hz, 0.7 H), 8.09* (s, 0.7 H), 8.08 (s, 1 H), 7.68* (d, J = 8.3 Hz, 0.7 H), 7.62 (d, J = 8.3 Hz, 1 H), 7.57* (dd, J = 1.1 Hz, 0.7 H), 7.46 (d, J = 1.4 Hz, 1 H), 7.48–7.45* (m, 0.7 H), 7.41* (d, J = 2.7 Hz, 0.7 H), 7.32 (d, J = 1.1 Hz, 1 H), 7.03 (d, J = 4.32 Hz, 1 H), 7.05–7.01* (m, 0.7 H), 2.53* (s, 2.1 H), 2.50 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.1, 151.0, 150.4, 148.7, 148.0, 147.7, 133.9, 132.3, 127.1, 126.6, 126.3, 122.2, 121.6, 119.5, 119.5, 117.0, 116.6, 115.2, 115.1, 114.5, 113.6, 110.6, 110.2, 106.9, 106.7, 21.6 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –60.5 (0.7), –60.8 (1.0) ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 2927, 2852, 2104, 1644, 1609, 1571, 1448, 1325, 1158, 1118, 755, 668 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{12}N_4F_3$ [M + H]$^+$ 317.1014; found 317.1027.

3gc$_1$: Following the general procedure, the reaction was carried out between 2-(1*H*-imidazol-1-yl)-5-(trifluoromethyl)aniline (**1g**; 100 mg, 0.440 mmol, 1 equiv.) and 2-bromo-6-methylpyridine (**2c**; 95 μL, 0.880 mmol, 2.0 equiv.). Column chromatography on silica gel (7% ethyl acetate in hexanes) yielded 71 mg (51%) of the title compound **3gc$_1$** as a white solid. R_f = 0.50 (20% ethyl acetate in hexanes); m.p. 136–139 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.30 (s, 1 H), 8.50 (d, J = 8.2 Hz, 1 H), 7.79 (t, J = 7.8 Hz, 1 H), 7.63 (d, J = 8.2 Hz, 1 H), 7.57 (dd, J = 8.2, 0.9 Hz, 1 H), 7.46 (d, J = 0.9 Hz, 1 H), 7.30 (s, 1 H), 7.05 (d, J = 7.8 Hz, 1 H), 2.65 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.4, 150.3, 139.1, 133.8, 132.2, 127.1, 123.2, 119.7, 119.4, 119.4, 115.2, 115.1, 110.9, 110.6, 106.9, 24.3 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –61.1 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 2927, 2852, 2102, 1730, 1597, 1577, 1456, 1123, 770, 669 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{12}N_4F_3$ [M + H]$^+$ 317.1014; found 317.1005.

3ha$_1$ and 3ha$_2$: Following the general procedure, the reaction was carried out between 2-(1*H*-benzo[*d*]imidazol-1-yl)-5-(trifluoromethyl)aniline (**1h**; 50 mg, 0.180 mmol, 1 equiv.) and 2-bromopyridine (**2a**; 40 μL, 0.451 mmol, 2.5 equiv.). Column chromatography on silica gel (9% ethyl acetate in hexanes) yielded 46 mg (73%) of an inseparable mixture of the regioisomeric products **3ha$_1$*** and **3ha$_2$** (0.2:1) as a white solid. R_f = 0.53 (20% ethyl acetate in hexanes); m.p. 107–110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9 ppm. 17* (s, 0.2 H), 8.82* (d, J = 8.3 Hz, 0.2 H), 8.81 (dd, J = 9.0, 2.5 Hz, 1 H), 8.75 (d, J = 8.3 Hz, 1 H), 8.62–7.89* (m, 0.2 H), 8.57 (d, J = 4.0 Hz, 1 H), 8.05 (s, 1 H), 7.96–7.93* (m, 0.2 H), 7.95 (td, J = 8.7, 1.7 Hz, 1 H), 7.84 (d, J = 8.3 Hz, 1 H), 7.79–7.76* (m, 0.4 H), 7.73 (dd, J = 5.3, 2.1 Hz, 1 H), 7.65* (d, J = 8.2 Hz, 0.2 H), 7.55 (d, J = 8.2 Hz, 1 H), 7.42–7.38* (m, 0.2 H), 7.41–7.36 (m, 2 H), 7.32* (t, J = 8.3 Hz, 0.2 H), 7.24 (dd, J = 7.5, 2.6 Hz, 1 H), 7.25–7.22* (m, 0.4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.3, 150.8, 148.1, 146.5, 138.9, 138.8, 133.9, 129.4, 125.3, 124.5, 124.0, 123.4, 121.5, 120.7, 119.5, 118.0, 117.9, 117.2, 116.7, 116.6, 115.1, 114.9, 110.5, 110.4, 109.9 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –60.5 (1.0), –60.8 (0.23) ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 3019, 2927, 1732, 1609, 1571, 1448, 1325, 1284, 1158, 756, 667 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{12}N_4F_3$ [M + H]$^+$ 353.1014; found 353.1025.

Note: The identity of **3ha$_2$** was confirmed through a partial purification of the above isomeric mixtures. The experimental data for the pure compound **3ha$_2$** is noted below.

R_f = 0.53 (20% ethyl acetate in hexanes); m.p. 121–124 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.87–8.82 (m, 1 H), 8.78 (d, J = 8.4 Hz, 1 H), 8.59 (d, J = 3.7 Hz, 1 H), 8.08 (s, 1 H), 7.97 (ddd, J = 8.4, 7.4, 1.9 Hz, 1 H), 7.88 (d, J = 8.3 Hz, 1 H), 7.78 (td, J = 4.0, 1.6 Hz, 1 H), 7.58 (dd, J = 8.3, 0.8 Hz, 1 H), 7.46–7.39 (m, 2 H), 7.26 (td, J = 4.0, 0.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.8, 148.1, 146.6, 138.9, 134.0, 125.4, 124.6, 123.6, 123.4, 120.8, 118.1, 118.0, 117.2, 116.7, 116.6, 115.2, 110.5, 110.5 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –60.5 ppm.

3hc$_1$ and 3hc$_2$: Following the general procedure, the reaction was carried out between 2-(1*H*-benzo[*d*]imidazol-1-yl)-5-(trifluoromethyl)aniline (**1h**; 50 mg, 0.180 mmol, 1 equiv.) and 2-bromo-6-methylpyridine (**2c**; 50 μL, 0.451 mmol, 2.5 equiv.). Column chromatography on silica gel (9% ethyl acetate in hexanes) yielded 55 mg (82%) of an inseparable mixture of the regioisomeric products **3hc$_1$* and 3hc$_2$** (0.9:1) as a white solid. R_f = 0.53 (20% ethyl acetate in hexanes); m.p. 132–135 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.26* (s, 0.9 H), 8.89–8.87* (dd, J = 4.7, 0.9 Hz, 0.9 H), 8.56 (d, J = 8.2 Hz, 1 H), 8.09 (s, 1 H), 7.90–7.79* (m, 3.6 H), 7.90–7.79 (m, 4 H), 7.68 (d, J = 8.1 Hz, 1 H), 7.58 (d, J = 7.8 Hz, 1 H), 7.45–7.40* (m, 1.8 H), 7.45–7.40 (m, 1 H), 7.35* (t, J = 7.6 Hz, 0.9 H), 7.11* (dd, J = 7.4, 1.8 Hz, 0.9 H), 7.11 (dd, J = 7.4, 1.8 Hz, 1 H), 2.68* (s, 2.7 H), 2.68 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.5, 157.5, 152.5, 151.7, 150.1, 150.0, 147.0, 146.6, 139.3, 139.2, 134.1, 133.8, 129.5, 127.9, 127.4, 125.8, 125.5, 125.4, 124.5, 124.0, 123.3, 121.5, 120.3, 120.3, 120.2, 119.6, 117.9, 117.9, 117.3, 116.6, 116.6, 114.8, 114.8, 112.0, 111.7, 110.5, 110.5, 110.4, 110.0, 24.4, 24.3 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –60.5 (1.0), –61.0 (0.93) ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 3020, 1729, 1640, 1556, 1457, 1324, 1215, 758, 669 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{14}N_3F_3$ [M + H]$^+$ 367.1171; found 367.1186.

Benzimidazokinetins 5 and 6: Following the general procedure, the reaction was carried out between kinetin-derived azole **4** (100 mg, 0.326 mmol, 1 equiv.) and 2-bromopyridine (**2a**; 100 μL, 0.816 mmol, 2.5 equiv.). Column chromatography on silica gel yielded 126 mg (85%) of **5** and **6** (0.4:1) as a viscous liquid. R_f = 0.30 (50% ethyl acetate in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.90–8.87 (m, 1 H), 8.63 (s, 1 H), 8.55–8.51 (m, 2 H), 8.38 (d, J = 8.4 Hz, 1 H), 8.12–8.10 (m, 1 H), 7.76–7.35 (m, 2 H), 7.44–7.35 (m, 3 H), 7.31–7.30 (m, 1 H), 7.18–7.14 (m, 2 H), 6.26–6.23 (m, 2 H), 5.84 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.8, 152.4, 152.3, 150.9, 150.0, 148.4, 147.9, 147.7, 141.7, 138.6, 138.2, 137.0, 134.3, 125.1, 124.5, 124.4, 123.5, 120.8, 120.2, 117.3, 114.4, 112.4, 110.3, 108.0, 45.5 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 3414, 3066, 1644, 1442, 1025, 773 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{19}N_8O$ [M + H]$^+$ 459.1676; found 459.1675.

General Procedure for the Synthesis of *N*-Aryl Heterocycles: The starting amine **1** (100 mg, 1 equiv.) and aryl bromide (2 equiv.) were added to an oven-dried screw-cap reaction tube charged with a magnetic stirring bar, $Cu(OAc)_2{\cdot}H_2O$ (20 mol-%), 1,10-phenanthroline monohydrate (30 mol-%), *t*BuONa (3 equiv.) and TBAI (1 equiv.) in dry DMF at room temp. Then the reaction mixture was closed with a screw cap and the mixture was stirred at 130 °C for 17 h. It was then cooled to room temperature, water (5 mL) was

added and the mixture extracted with ethyl acetate (3× 5 mL). Then the combined organic layers were washed with water (7× 5 mL), dried with anhyd. Na_2SO_4 and concentrated to give the crude product. Purification by column chromatography afforded the *N*-aryl heterocycles.

3bd: Following the general procedure, the reaction was carried out between 2-(1*H*-benz[*d*]imidazol-1-yl)aniline (**1b**; 100 mg, 0.478 mmol, 1 equiv.) and bromobenzene **2d** (100 μL, 0.956 mmol, 2.0 equiv.). Column chromatography on silica gel (15% ethyl acetate in hexanes) yielded 115 mg (85%) of the title compound **3bd** as a white solid. R_f = 0.20 (20% ethyl acetate in hexanes); m.p. 128–131 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.82 (m, 4 H), 7.78 (d, J = 7.9 Hz, 1 H), 7.62 (t, J = 7.6 Hz, 2 H), 7.56–7.54 (m, 1 H), 7.44 (t, J = 7.5 Hz, 1 H), 7.39–7.28 (m, 4 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.2, 135.3, 135.3, 130.2, 128.2, 127.7, 125.7, 124.8, 123.5, 123.3, 122.3, 120.4, 119.1, 111.0, 110.9, 110.3 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 2924, 1630, 1324, 1122, 746 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{14}N_3$ $[M + H]^+$ 284.1182; found 284.1176.

3cd: Following the general procedure, the reaction was carried out between 2-(1*H*-triazol-1-yl)aniline (**1c**; 100 mg, 0.624 mmol, 1 equiv.) and bromobenzene (**2d**; 130 μL, 1.24 mmol, 2.0 equiv.). Column chromatography on silica gel (19% ethyl acetate in hexanes) yielded 107 mg (73%) of the title compound **3cd** as a white solid. R_f = 0.35 (30% ethyl acetate in hexanes); m.p. 104–106 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05 (s, 1 H), 7.90–7.88 (m, 1 H), 7.76 (d, J = 1.1 Hz, 1 H), 7.75–7.74 (m, 1 H), 7.65–7.63 (m, 1 H), 7.60–7.57 (m, 2 H), 7.44–7.41 (m, 1 H), 7.39–7.35 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.8, 153.3, 135.1, 134.4, 130.1, 127.8, 124.6, 124.5, 123.8, 122.7, 111.9, 111.5 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 2923, 1563, 1160, 747 cm^{-1}. HRMS (ESI): calcd. for $C_{14}H_{11}N_4$ $[M + H]^+$ 235.0978; found 235.0982.

3ce: Following the general procedure, the reaction was carried out between 2-(1*H*-triazol-1-yl)aniline (**1c**; 100 mg, 0.624 mmol, 1 equiv.) and 2-bromonaphthalene (**2e**; 259 mg, 1.24 mmol, 2.0 equiv.). Column chromatography on silica gel (23% ethyl acetate in hexanes) yielded 119 mg (67%) of the title compound **3ce** as a white solid. R_f = 0.40 (20% ethyl acetate in hexanes); m.p. 177–180 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.20 (d, J = 1.8 Hz, 1 H), 8.09 (s, 1 H), 8.07 (d, J = 8.7 Hz, 1 H), 7.96–7.92 (m, 3 H), 7.89 (dd, J = 8.7, 2.1 Hz, 1 H), 7.75–7.71 (m, 1 H), 7.60–7.55 (m, 2 H), 7.43–7.40 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 154.8, 153.3, 135.1, 134.4, 130.1, 127.8, 124.6, 124.5, 123.8, 122.7, 111.9, 111.5 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 2931, 1566, 1476, 1160, 747 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{12}N_4Na$ $[M + Na]^+$ 307.0954; found 307.0952.

3ed: Following the general procedure, the reaction was carried out between 2-(1*H*-1,2,4-triazol-1-yl)benzene-1,3-diamine (**1e**; 200 mg, 1.142 mmol, 1 equiv.) and bromobenzene (**2d**; 359 μL, 2.28 mmol, 2.0 equiv.). Column chromatography on silica gel (27% ethyl acetate in hexanes) yielded 279 mg (98%) of the title compound **3ed** as a white solid. R_f = 0.30 (40% ethyl acetate in hexanes); m.p. 154–157 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.02 (s, 1 H), 7.76 (d, J = 7.8 Hz, 2 H), 7.58 (t, J = 7.6 Hz, 2 H), 7.41 (t, J = 7.4 Hz, 1 H), 7.16 (t, J = 8.1 Hz, 1 H), 7.01 (d, J = 8.2 Hz, 1 H), 6.66 (d, J = 7.9 Hz, 1 H) ppm; Note: When the ^{1}H NMR spectrum of compound **3ed** in $CDCl_3$ was recorded, we did not observe the presence of an NH_2 peak. Therefore the ^{1}H NMR spectrum was re-analysed in [D_6]DMSO (see the spectrum in the Supporting Information). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.2, 136.4, 135.3, 133.7, 130.0, 127.5, 125.5, 123.7, 108.5, 101.3 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 3431, 2923, 1629, 1458, 1156, 746 cm^{-1}. HRMS (ESI): calcd. for $C_{13}H_{10}N_5Na$ $[M + Na]^+$ 272.0907; found 272.0907.

3hd: Following the general procedure, the reaction was carried out between 2-(1*H*-benzo[*d*]imidazol-1-yl)-5-(trifluoromethyl)aniline (**1h**; 100 mg, 0.360 mmol, 1 equiv.) and 2-bromobenzene (**2d**; 75 μL, 0.72 mmol, 2.0 equiv.). Column chromatography on silica gel yielded 96 mg (76%) of the title compound **3hd** as a white solid. R_f = 0.35 (20% ethyl acetate in hexanes); m.p. 169–172 °C ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.02 (s, 1 H), 7.89 (d, J = 8.3 Hz, 1 H), 7.85–7.81 (m, 3 H), 7.65–7.62 (t, J = 8.3 Hz, 2 H), 7.58–7.55 (m, 2 H), 7.47 (t, J = 7.5 Hz, 1 H), 7.42–7.37 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.7, 146.9, 135.4, 134.9, 130.3, 128.1, 126.1, 125.5, 124.8, 124.2, 123.9, 122.6, 117.4, 116.4, 111.3, 111.2, 110.3 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 2923, 1640, 1321, 1095, 797 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{13}N_3F_3$ $[M + H]^+$ 352.1056; found 352.1058.

Benzimidazokinetin 5: Following the general procedure, the reaction was carried out between kinetin-derived azole **4** (100 mg, 0.326 mmol, 1 equiv.) and 2-bromopyridine (**2a**; 100 μL, 0.956 mmol, 2.5 equiv.) in the presence of *t*BuONa (241 mg, 1.14 mmol, 3 equiv.). Column chromatography on silica gel yielded 92 mg (62%) of the title compound **5** as a white solid. R_f = 0.30 (50% ethyl acetate in hexanes); m.p. 236–239 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 (dd, J = 6.9, 1.6 Hz, 1 H), 8.67 (d, J = 8.3 Hz, 1 H), 8.54 (dd, J = 4.8, 1.1 Hz, 1 H), 8.46 (s, 1 H), 8.04–8.07 (m, 1 H), 7.90–7.85 (m, 1 H), 7.40–7.33 (m, 3 H), 7.24–7.16 (m, 1 H), 6.29 (s, 2 H), 5.86 (br. t, J = 5.3 Hz, 1 H), 4.86 (br. d, J = 5.4 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.9, 148.3, 148.2, 142.4, 138.7, 134.4, 125.1, 124.8, 123.6, 120.6, 117.0, 114.9, 112.6, 110.6, 107.7, 38.1 ppm. FTIR (neat, KBr): $\tilde{\nu}$ = 2960, 1616, 1441, 771 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{15}N_7NaO$ $[M + Na]^+$ 404.1230; found 404.1238.

Supporting Information (see footnote on the first page of this article): Starting material preparations, mechanistic studies, NMR spectra, XRD data.

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[1] a) M. C. Bagley, J. W. Dale, E. A. Merritt, X. Xiong, *Chem. Rev.* **2005**, *105*, 685–714; b) J. Kim, M. Movassaghi, *Chem. Soc. Rev.* **2009**, *38*, 3035–3050.
[2] a) E. Hao, B. Fabre, F. R. Fronczek, M. G. H. Vicente, *Chem. Mater.* **2007**, *19*, 6195–6205; b) Y. G. Lee, Y. Koyama, M. Yonekawa, T. Takata, *Macromolecules* **2009**, *42*, 7709–7717.
[3] a) Q. Du, W. Zhu, Z. Zhao, X. Qian, Y. Xu, *J. Agric. Food Chem.* **2012**, *60*, 346–353; b) N. Jacobsen, L.-E. K. Pedersen, *Pestic. Sci.* **1983**, *14*, 90–97.
[4] a) I. Nakamura, Y. Yamamoto, *Chem. Rev.* **2004**, *104*, 2127–2198; b) K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem. Int. Ed.* **2005**, *44*, 4442–4489; *Angew. Chem.* **2005**, *117*, 4516; c) D. Zhao, J. You, C. Hu, *Chem. Eur. J.* **2011**, *17*, 5466–5492.
[5] W. C. P. Tsang, N. Zheng, S. L. Buchwald, *J. Am. Chem. Soc.* **2005**, *127*, 14560–14561.
[6] a) W. C. P. Tsang, R. H. Munday, G. Brasche, N. Zheng, S. L. Buchwald, *J. Org. Chem.* **2008**, *73*, 7603–1610; b) J. A. Jordan-Hore, C. C. C. Johansson, M. Gulias, E. M. Beck, M. J. Gaunt, *J. Am. Chem. Soc.* **2008**, *130*, 16184–16186.

[7] a) Q. Xiao, W.-H. Wang, G. Liu, F.-K. Meng, J.-H. Chen, Z. Yang, Z.-J. Shi, *Chem. Eur. J.* **2009**, *15*, 7292–7296; b) R. K. Kumar, T. Punniyamurthy, *RSC Adv.* **2012**, *2*, 4616–4619.

[8] a) K. Inamoto, T. Saito, M. Katsuno, T. Sakamoto, K. Hiroya, *Org. Lett.* **2007**, *9*, 2931–2939; b) D. Eom, Y. Jeong, Y. R. Kim, E. Lee, W. Choi, P. H. Lee, *Org. Lett.* **2013**, *15*, 5210–5213.

[9] a) T.-S. Mei, X. Wang, J.-Q. Yu, *J. Am. Chem. Soc.* **2009**, *131*, 10806–10807; b) J. J. Neumann, S. Rakshit, T. Dröge, F. Glorius, *Angew. Chem. Int. Ed.* **2009**, *48*, 6892–6895; *Angew. Chem.* **2009**, *121*, 7024.

[10] M. Wasa, J.-Q. Yu, *J. Am. Chem. Soc.* **2008**, *130*, 14058–14059.

[11] a) L. Ackermann, R. Vicente, A. R. Kapdi, *Angew. Chem. Int. Ed.* **2009**, *48*, 9792–9826; *Angew. Chem.* **2009**, *121*, 9976; b) J. Wencel-Delord, T. Drçge, F. Liu, F. Glorius, *Chem. Soc. Rev.* **2011**, *40*, 4740–4761; c) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215–1292; d) C. Liu, H. Zhang, W. Shi, A. Lei, *Chem. Rev.* **2011**, *111*, 1780–1824; e) H. Wang, C. Grohmann, C. Nimphius, F. Glorius, *J. Am. Chem. Soc.* **2012**, *134*, 19592–19595.

[12] a) X. Chen, X.-S. Hao, C. E. Goodhue, J.-Q. Yu, *J. Am. Chem. Soc.* **2006**, *128*, 6790–6791; b) D. Monguchi, T. Fujiwara, H. Furukawa, A. Mori, *Org. Lett.* **2009**, *11*, 1607–1610; c) Q. Wang, S. L. Schreiber, *Org. Lett.* **2009**, *11*, 5178–5180; d) A. E. King, L. M. Huffman, A. Casitas, M. Costas, X. Ribas, S. S. Stahl, *J. Am. Chem. Soc.* **2010**, *132*, 12068–12073; e) A. Armstrong, J. C. Collins, *Angew. Chem. Int. Ed.* **2010**, *49*, 2282–2285; *Angew. Chem.* **2010**, *122*, 2332; f) T. Kawano, K. Hirano, T. Satoh, M. Miura, *J. Am. Chem. Soc.* **2010**, *132*, 6900–6901; g) Y. Xie, R. Zhang, K. Jin, X. Wang, C. Duan, *J. Org. Chem.* **2011**, *76*, 5444–5449; h) A. John, K. M. Nicholas, *J. Org. Chem.* **2011**, *76*, 4158–4162; i) N. Matsuda, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2011**, *13*, 2860–2863; j) M. Miyasaka, K. Hirano, T. Satoh, R. Kowalczyk, C. Bolm, M. Miura, *Org. Lett.* **2011**, *13*, 359–361; k) S. Guo, B. Qian, Y. Xie, C. Xia, H. Huang, *Org. Lett.* **2011**, *13*, 522–525; l) H.-Q. Do, O. Daugulis, *J. Am. Chem. Soc.* **2011**, *133*, 13577–13586.

[13] a) G. Brasche, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2008**, *47*, 1932–1934; *Angew. Chem.* **2008**, *120*, 1958; b) S. Ueda, H. Nagasawa, *Angew. Chem. Int. Ed.* **2008**, *47*, 6411–6413; *Angew. Chem.* **2008**, *120*, 6511; c) J. Lu, Y. Jin, H. Liu, Y. Jiang, H. Fu, *Org. Lett.* **2011**, *13*, 3694–3697; d) S. H. Cho, J. Yoon, S. Chang, *J. Am. Chem. Soc.* **2011**, *133*, 5996–6005; e) Y. Oda, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2012**, *14*, 664–667; f) M. M. Guru, T. Punniyamurthy, *J. Org. Chem.* **2012**, *77*, 5063–5073; g) S. H. Cho, J. Yoon, S. Chang, *J. Am. Chem. Soc.* **2013**, *133*, 5996–6005.

[14] a) F. Collet, R. H. Dodd, P. Dauban, *Chem. Commun.* **2009**, 5061–5074; b) A. Armstrong, J. C. Collins, *Angew. Chem. Int. Ed.* **2010**, *49*, 2282–2285; *Angew. Chem.* **2010**, *122*, 2332; c) S. Guo, B. Qian, Y. Xie, C. Xia, H. Huang, *Org. Lett.* **2010**, *12*, 522–525; d) K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2011**, *13*, 2395–2397; e) T. Ikawa, T. Nishiyama, T. Shigeta, S. Mohri, S. Morita, S.-i. Takayanagi, Y. Terauchi, Y. Morikawa, A. Takagi, Y. Ishikawa, S. Fujii, Y. Kita, S. Akai, *Angew. Chem. Int. Ed.* **2011**, *50*, 5674–5677; f) H. Xu, H. Fu, *Chem. Eur. J.* **2012**, *18*, 1180–1186; g) M.-L. Louillat, F. W. Patureau, *Org. Lett.* **2013**, *15*, 164–167.

[15] For reviews, see: a) S. S. Stahl, *Angew. Chem. Int. Ed.* **2004**, *43*, 3400–3420; *Angew. Chem.* **2004**, *116*, 3480; b) T. Punniyamurthy, S. Velusamy, J. Iqbal, *Chem. Rev.* **2005**, *105*, 2329–2364.

[16] a) D. Lubriks, I. Sokolovs, E. Suna, *J. Am. Chem. Soc.* **2012**, *134*, 15436–15442; b) Z.-L. Wang, L. Zhao, M.-X. Wang, *Chem. Commun.* **2012**, *48*, 9418–9420; c) Q. Liu, H. Yang, Y. Jiang, Y. Zhao, H. Fu, *RSC Adv.* **2013**, *3*, 15636–15644; d) M. Wang, Y. Jin, H. Yang, H. Fu, L. Hu, *RSC Adv.* **2013**, *3*, 8211–8214; e) P. Hu, Q. Wang, Y. Yan, S. Zhang, B. Zhang, Z. Wang, *Org. Biomol. Chem.* **2013**, *11*, 4304–4307; f) G. Li, C. Jia, K. Sun, *Org. Lett.* **2013**, *15*, 5198–5201; g) T. W. Liwosz, S. R. Chemler, *Chem. Eur. J.* **2013**, *19*, 12771–12777; h) T. Liu, H. Yang, Y. Jiang, H. Fu, *Adv. Synth. Catal.* **2013**, *355*, 1169–1176; i) X. Li, L. He, H. Chen, W. Wu, H. Jiang, *J. Org. Chem.* **2013**, *78*, 3636–3646; j) Á. M. Martínez, N. Rodriguez, R. G. Arrayas, J. C. Carretero, *Chem. Commun.* **2014**, *50*, 2801–2803.

[17] C. Tang, N. Jiao, *J. Am. Chem. Soc.* **2012**, *134*, 18924–18927.

[18] a) Q. Shen, S. Shekhar, J. P. Stambuli, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2005**, *44*, 1371–1375; *Angew. Chem.* **2005**, *117*, 1395; b) Q. Shen, J. F. Hartwig, *J. Am. Chem. Soc.* **2007**, *129*, 7734–7735; c) P. Subramanian, K. P. Kaliappan, *Eur. J. Org. Chem.* **2013**, 595–604; d) M. Su, N. Hoshiya, S. L. Buchwald, *Org. Lett.* **2014**, *16*, 832–835.

[19] a) X. Han, S. S. Pin, K. Burris, L. K. Fung, S. Huang, M. T. Taber, J. Zhang, G. M. Dubowchik, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 4029–4032; b) M. S. Christodoulou, F. Colombo, D. Passarella, G. Ieronimo, V. Zuco, M. D. Cesare, F. Zunino, *Bioorg. Med. Chem.* **2011**, *19*, 1649–1657.

[20] V. A. Anisimova, A. A. Spasov, V. A. Kosolapov, I. E. Tolpygin, V. I. Porotikov, A. F. Kucheryavenko, V. A. Sysoeva, E. V. Tibir'kova, L. V. El'tsova, *Pharm. Chem. J.* **2009**, *43*, 491–494.

[21] K. M. Dawood, N. M. Elwan, B. F. Abdel-Wahab, *ARKIVOC* **2011**, 111–195.

[22] X. Wang, Y. Jin, Y. Zhao, L. Zhu, H. Fu, *Org. Lett.* **2012**, *14*, 452–455.

[23] a) S. Ueda, H. Nagasawa, *J. Am. Chem. Soc.* **2009**, *131*, 15080–15081; b) H. Wang, Y. Wang, C. Peng, J. Zhang, Q. Zhu, *J. Am. Chem. Soc.* **2010**, *132*, 13217–13219; c) K.-S. Masters, T. R. M. Rauws, A. K. Yadav, W. A. Herrebout, B. Van der Veken, B. U. W. Maes, *Chem. Eur. J.* **2011**, *17*, 6315–6320.

[24] a) L. Almirante, L. Polo, A. Mugnaini, E. Provinciali, P. Rugarli, A. Biancotti, A. Gamba, W. Murmann, *J. Med. Chem.* **1965**, *8*, 305–312; b) H. T. Swainston, G. M. Keating, *CNS Drugs* **2005**, *19*, 65–89.

[25] a) S. I. S. Rattan, *J. Anti-Aging Med.* **2002**, *5*, 113–116.

[26] a) J. J. Teo, Y. Chang, H. C. Zeng, *Langmuir* **2006**, *22*, 7369–7377; b) A. Y. S. Malkhasian, M. E. Finch, B. Nikolovski, A. Menon, B. E. Kucera, F. A. Chavez, *Inorg. Chem.* **2007**, *46*, 2950–2952; c) Y.-F. Wang, K. K. Toh, J.-Y. Lee, S. Chiba, *Angew. Chem. Int. Ed.* **2011**, *50*, 5927–5931.

[27] Unable to trace the product when the reaction was carried out in toluene.

[28] a) G. Brasche, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2008**, *47*, 1932–1934; *Angew. Chem.* **2008**, *120*, 1958; b) P. Sang, Y. Xie, J. Zou, Y. Zhang, *Org. Lett.* **2012**, *14*, 3894–3897; c) G.-R. Qu, L. Liang, H. Y. Niu, W.-H. Rao, H.-M. Guo, J. S. Fossey, *Org. Lett.* **2012**, *14*, 4494–4497.

[29] a) S. Iyer, C. Ramesh, *Tetrahedron Lett.* **2000**, *41*, 8981–8984; b) F. Karimi, B. Långström, *J. Chem. Soc. Perkin Trans. 1* **2002**, 2111–2115.

[30] a) L. M. Huffman, S. S. Stahl, *Dalton Trans.* **2011**, *40*, 8959–8963; b) S. Zhang, Y. Ding, *Organometallics* **2011**, *30*, 633–641.

[31] M. Trivedi, G. Singh, R. Nagarajan, N. P. Rath, *Inorg. Chim. Acta* **2013**, *394*, 107–116.

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