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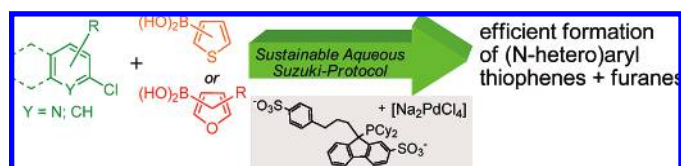
Efficient Suzuki–Miyaura Coupling of (Hetero)aryl Chlorides with Thiophene- and Furanboronic Acids in Aqueous *n*-Butanol

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An efficient Suzuki cross-coupling protocol enables the reaction of *N*-hetero and normal aryl chlorides with thiophene- and furanboronic acids. Coupling is effected in aqueous *n*-butanol as the solvent in near quantitative yield with a catalyst loading of 0.1–1 mol %. For heterocyclic substrates aqueous catalysis is found to be more efficient than Suzuki coupling under anhydrous conditions. The developed Suzuki coupling procedure utilizes biodegradable solvents and is useful for large scale reactions, as it includes the facile product separation from a biphasic solvent mixture without the need for additional organic solvents during workup.

Introduction

Thiophenes are common in natural products and constitute attractive targets in pharmaceutical and fine chemistry because of their potential biological activity,^{1–13} furans are found in

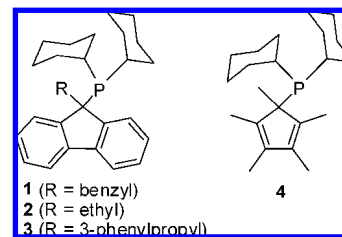
numerous natural products,¹⁴ flavors, and fragrances;^{15,16} molecules bearing a furan moiety often display pharmacological activity.^{13,17–21} (*N*-Hetero)arylthiophenes and -furans such as thiophenylpyridines,^{11,22} furanylpyridines,¹⁷ or furanylquinolines,¹⁸ are ubiquitous in drugs.¹⁹

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2-Arylated furans and thiophenes are accessible via conventional electrophilic substitution reactions²⁰ or CH-activation,²¹ while the 3-position in thiophenes and furans is less easily accessible.^{20,22} The Suzuki coupling^{23,24} can be very useful for the synthesis of arylthiophenes or -furans. Such coupling reactions proceed smoothly only when halogenothiophenes or -furans are reacted with the respective aryl boronic acids. Typically catalyst loadings of 0.05–2.0 mol % tend to be sufficient for the quantitative coupling of chlorothiophenes or chlorofurans with sterically hindered boronic acids,^{25,26} pyridylboronic acid,^{27,28} or phenylboronic acid.²⁹ Quite in contrast, the use of thiophene- or furanboronic acids in Suzuki reactions is fraught with problems, because of the facile decomposition of such metalloids in polar protic reaction media via protodeboronation.^{30–33} This was studied in detail by Roques et al. for furanboronic acids³⁴ and by Brown et al. for thiopheneboronic acids.³⁵ Consequently, the general application of such thiophene and furan metalloids is limited to the use of aryl iodides/bromides or activated aryl chlorides as coupling partners.^{36–39} With thiopheneboronic acid, the more challenging 2-chloropyridine or related compounds are problematic⁴⁰ and require high catalyst loadings (1–10 mol %) for activated *N*-heterocyclic aryl chlorides.^{25,41,42} The Suzuki coupling of furanboronic acid has primarily been explored in combination with iodo- and bromo(hetero)aryl halides,^{18,39,43,44} only few examples are known for the conversion of activated *N*-heteroaryl chlorides.^{45,46} Notable exceptions are efficient catalysts recently reported by Buchwald and Billingsley; the Suzuki protocol developed by Buchwald proved to be efficient for the coupling of various

SCHEME 1. Ligands Tested in Suzuki Cross-Coupling of Thiopheneboronic Acids



furanboronic acids with activated aryl chlorides but failed with *N*-heterocyclic chlorides.²⁷ Only a few examples are known for the coupling of less activated^{47–49} or (hetero)aryl chlorides⁵⁰ with furanboronic acids. Trifluoroborates can be alternatives to the classical boronic acids. However the corresponding thiophene- and furan metalloids also suffer from low stability; thus, efficient Suzuki reactions are facile only with aryl bromides. Only few transformations of aryl chlorides were reported.⁵¹

The limitations in Suzuki couplings with thiophene- and furanboronic acids result from the dichotomy that polar protic solvents are known to facilitate this kind of catalytic reaction, while boronic acids tend to be unstable in these solvents. Hence, in order to improve the efficiency of Suzuki couplings with these heteroarylboronic acids, coupling catalysts need to be developed, which accelerate the respective cross-coupling reactions such that it turns out to be significantly faster than the competitive protodeboronation in polar protic solvents.

On the basis of our recent development of the cataCXium F family of fluorenylphosphines,^{52–54} we report here on Pd-phosphine complex catalysts, which enable the efficient coupling of thiophene- and furanboronic acids in anhydrous and in aqueous media.

Results and Discussion

Suzuki Coupling, with Thiopheneboronic Acids under Anhydrous Conditions. Pd complexes of fluorenyldialkylphosphines constitute highly active catalysts for Suzuki coupling, especially for *N*-heterocyclic compounds.^{28,55} The ligands depicted in Scheme 1 were the most useful ones in various cross-coupling reactions. Consequently, we decided to first evaluate these ligands in the anhydrous Suzuki coupling with thiophene- and furanboronic acids. In a preliminary study we tested three fluorenylphosphines (1–3) and Cp*PCy₂ (4). 2-Chloropyridine

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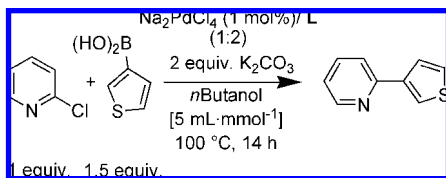
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TABLE 1. Catalytic Activity of Various Pd-Phosphine Complexes in the Suzuki Cross-Coupling of Thiopheneboronic Acids

| entry | ligand L | yield ^a (%) |
|-------|-----------------|------------------------|
| 1 | 1 | 66 |
| 2 | 2 | ≥99 |
| 3 | 3 | 68 |
| 4 | 4 | 86 |

^a Average of two runs, determined by GC using heptadecane as internal standard.

was reacted with 3-thiopheneboronic acid using anhydrous *n*-butanol as the solvent and a 1 mol % catalyst loading.

Of these phosphines the *in situ* formed [Pd/**2**] complex (**2** = 9-(9'-ethylfluorenyl)dicyclohexylphosphine) was the most effective one in the coupling of 2-chloropyridine with 3-thiopheneboronic acid (Table 1).

Consequently we studied complex [Pd/**2**] in more detail for Suzuki cross-coupling of 2- and 3-thiopheneboronic acids. Because of its higher stability, 3-thiopheneboronic acid allows lower catalyst loadings for quantitative Suzuki cross-coupling. Applying 0.1 mol % [Pd/**2**]-complex as catalyst, 2-chloropyridine was successfully cross-coupled with 3-thiopheneboronic acid in pure *n*-butanol at 100 °C using K₂CO₃ as base with an 89% conversion. Quantitative conversion was accomplished at 0.5 mol % catalyst loading (Table 2, entry 1). In the same manner 2-chloro-4-picoline and 2-chloro-isonicotinamide were reacted with 3-thiopheneboronic acid affording near quantitative

TABLE 2. Suzuki Reaction with 3- and 2-Thiopheneboronic Acid Utilizing Anhydrous *n*-Butanol Reaction Media^a

| Entry | Aryl Chloride | Boronic Acid | Product | Pd [mol %] | Conversion ^b [%] | Yield ^c [%] |
|-------|---------------|--------------|---------|------------|-----------------------------|------------------------|
| 1 | | | | 0.1 0.5 | 89 ≥99 | 93 |
| 2 | | | | 0.5 | ≥99 | 89 |
| 3 | | | | 0.5 | ≥99 | 91 |
| 4 | | | | 0.5 | ≥99 | 79 |
| 5 | | | | 1 | 98 | 93 |
| 6 | | | | 1 | ≥99 | 91 ^d |
| 7 | | | | 1 | 73 | 51 ^d |
| 8 | | | | 1 | 17 | [d], [e] |
| 9 | | | | 1 | <5 | 0 ^d |
| 10 | | | | 0.5 | ≥99 | 89 ^d |

^a Reaction conditions: 1.0 equiv of aryl halide, 1.5 equiv of boronic acid, 3.2 equiv of K₂CO₃, 100 °C, 14 h, cat.: the respective volume of catalyst stock solution (in *n*-butanol) (*c*_{Pd} = 0.01 mol/L, Na₂PdCl₄/ligand **2** L/Pd = 2:1). Reaction times and temperature were not optimized. ^b Average of two runs, determined by GC using heptadecane as internal standard. ^c Average of two runs, products were isolated via column chromatography (silica (20 × 3 cm), cyclohexane:EtOAc:NEt₃ (10:1:1) as eluent). ^d Degassed *tert*-amyl alcohol (5 mL mmol⁻¹) in addition to 0.25 g of molecular sieves 4 Å was used instead *n*-butanol of as reaction solvent and for *in situ* preparation of the precatalyst. ^e Product not isolated.

TABLE 3. Suzuki Reaction with 3-Thiopheneboronic Acid Using *n*-Butanol/Water as Solvent^a

| Entry | Aryl Chloride | Boronic Acid | Product | Pd [mol %] | Conversion ^[b] [%] | Yield ^[c] [%] |
|-------|---------------|--------------|---------|------------|-------------------------------|--------------------------|
| 1 | | | | 0.1 | >99 | 90 |
| 2 | | | | 0.25 | ≥99 | 95 |
| 3 | | | | 0.25 | ≥99 | 91 |
| 4 | | | | 0.25 | ≥99 | 93 |
| 5 | | | | 0.25 | ≥99 | 93 |
| 6 | | | | 0.25 | ≥99 | 95 |
| 7 | | | | 0.1 | ≥99 | 95 |
| 8 | | | | 1.0 0.5 | ≥99 83 | 92 |

^a Reaction conditions: 1.0 equiv of aryl halide, 1.5 equiv of boronic acid, 3.2 equiv of K₂CO₃, degassed *n*-butanol (5 mL mmol⁻¹), degassed water (2 mL mmol⁻¹), 100 °C, 12 h, cat.: the respective volume of catalyst stock solution (in *n*-butanol) (*c*_{Pd} = 0.005 mol/L, Na₂PdCl₄/ligand **5** L/Pd = 2:1). Reaction times and temperature were not optimized. ^b Average of two runs, determined by GC using heptadecane as internal standard. ^c Average of two runs, products were isolated via column chromatography (silica (20 × 3 cm), cyclohexane:EtOAc:NEt₃ (10:1:1) as eluent).

yield (89%, 91%) at 0.5 mol % catalyst loading (Table 2, entries 2 + 3). 4-Chlorotoluene is coupled with the same metalloid quantitatively using 1 mol % catalyst (Table 2, entry 5). Interestingly, when *n*-butanol was used as a solvent, the highly active 2-chloropyrimidine preferably underwent an S_NAr-mechanism instead of the slower Suzuki cross-coupling reaction to form the undesired product 2-butoxypyrimidine in 79% yield (Table 2, entry 4).⁵⁶ Consequently, we switched to *tert*-amyl alcohol under anhydrous conditions (in combination with molecular sieves) as solvent with the more labile 2-thiopheneboronic acid. Then the activated 2-chloropyrimidine reacted smoothly and selectively with 2-thiopheneboronic acid in *tert*-amyl alcohol as solvent, affording 89% isolated yield with 0.5 mol % catalyst loading (Table 2, entry 10). Under these conditions, formation of the respective ether was not detected. When 1 mol % catalyst loading was applied, 2-chloropyridine was quantitatively cross-coupled with 2-thiopheneboronic acid using *tert*-amyl alcohol as solvent (Table 2, entry 6). However more deactivated *N*-heterocyclic aryl chlorides like 2-chlorolopidine or 2-chloro-6-methoxypyridine were not quantitatively Suzuki cross-coupled using 1 mol % [Pd/2]-complex as catalyst (Table 2, entries 7 + 8, 73% and 17% conversion, respectively).

(56) 2-Butoxypyrimidine is also formed in the absence of catalyst under otherwise identical reaction conditions.

Unfortunately, the catalyst failed with the most challenging substrate combination of 4-amino-2-chloropyridine and 2-thiopheneboronic acid (Table 2, entry 9).

In conclusion, the fluorenylphosphine-based catalysts show activity comparable to the best systems reported so far for Suzuki coupling of aryl chlorides with thiopheneboronic acids.²⁷

Suzuki Coupling Using an Aqueous Reaction Protocol. Very recently we reported that water as a (co)solvent drastically enhances the Suzuki coupling of *N*-heterocyclic substrates.^{28,55,57,58} In this context, the use of Pd complexes with highly water soluble disulfonated fluorenyldialkylphosphine **5** (Scheme 2)⁵⁹ led to unprecedented activities in the Suzuki coupling of heteroaryl chlorides. According to our hypothesis, the nitrogen moieties of the applied substrates preferentially engage in hydrogen bonding⁶⁰ with water rather than coordinating to the Pd-center of the active catalyst. In this manner poisoning of the catalyst by the heterocyclic substrates³⁹ is minimized.

We were interested to learn whether enhanced Suzuki

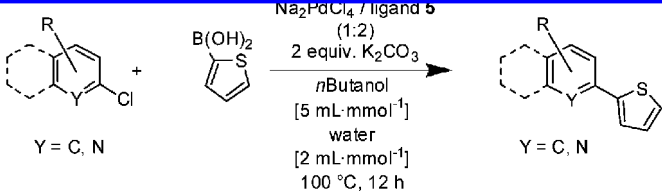





















(57) Fleckenstein, C. A.; Roy, S.; Leuthäusser, S.; Plenio, H. *Chem. Commun.* **2007**, 2870–2872.

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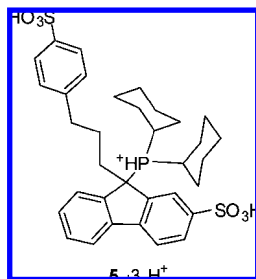
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TABLE 4. Suzuki Reaction with 2-Thiopheneboronic Acid Using *n*-Butanol/Water as Solvent^a

|  | | | | | | |
|--|--|--|--|------------|-------------------------------|--------------------------|
| Entry | Aryl Chloride | Boronic Acid | Product | Pd [mol %] | Conversion ^[b] [%] | Yield ^[c] [%] |
| 1 |  |  |  | 1 | ≥99 | 90 |
| 2 |  |  |  | 1 | ≥99 | 94 |
| 3 |  |  |  | 1 | ≥99 | 95 |
| 4 |  |  |  | 1 | 31 | 31 ^[b,d] |
| 5 |  |  |  | 1 | 6 | 6 ^[b,d] |
| 6 |  |  |  | 0.5 | ≥99 | 94 |
| 7 |  |  |  | 0.5 | 98 | 89 |

^a Reaction conditions: 1.0 equiv of aryl halide, 1.5 equiv of boronic acid, 3.2 equiv of K₂CO₃, degassed *n*-butanol (5 mL mmol⁻¹), degassed water (2 mL·mmol⁻¹), 100 °C, 12 h, cat.: the respective volume of catalyst stock solution (in *n*-butanol) (*c*_{Pd} = 0.005 mol/L, Na₂PdCl₄/ligand **5** L/Pd = 2:1). Reaction times and temperature were not optimized. ^b Average of two runs, determined by GC using heptadecane as internal standard. ^c Average of two runs, products were isolated via column-chromatography (silica (20 × 3 cm), cyclohexane:EtOAc:NEt₃ (10:1:1) as eluent). ^d Product not isolated.

SCHEME 2. High Water Soluble Disulfonated Dicyclohexylfluorenylphosphine Ligand **5**·3H⁺



reactivity in water/*n*-butanol mixtures can be realized with labile thiophene- and furanboronic acids. This approach boldly ignores the fact that the decomposition of the thiophene- and furanboronic acids in water is drastically accelerated. On the other hand, the chosen aqueous/organic reaction medium is convenient as it is cheap, safe, and biodegradable. We were pleased to see, that in a preliminary test with Pd/**5** as catalyst (formed *in situ* from Na₂PdCl₄ and the phosphonium salt of **5**), 2-chloropyridine was smoothly coupled with 3-thiopheneboronic acid in water/*n*-butanol (2:5) as solvent and K₂CO₃ as base at 100 °C utilizing only 0.1 mol % catalyst (Table 3, entry 1). This indicates that the aqueous reaction protocol is superior to the anhydrous one, which requires a fivefold higher catalyst loading to achieve full conversion (see Table 2, entry 1; 0.5 mol %). In order to

substantiate the robustness of the aqueous cross-coupling protocol, we coupled a variety of *N*-heterocyclic and normal aryl chlorides with 2-thiophene- and 3-thiopheneboronic acids.

Suzuki Coupling of 3-Thiopheneboronic Acid. Utilizing a catalyst loading of 0.25 mol % a number of activated and deactivated chloropyridines and chloroquinolines were quantitatively Suzuki coupled with 3-thiopheneboronic acid in water/*n*-butanol as solvent (Table 3, entries 2–6). This reaction protocol enables efficient coupling of 4-chlorotoluene with 3-thiopheneboronic acid affording 83% conversion at a catalyst loading of 0.5 mol % and quantitative coupling applying 1 mol % catalyst, respectively (Table 3, entry 8). The reaction of 2-chloropyrimidine with 3-thiopheneboronic acid using 0.1 mol % catalyst selectively and quantitatively affords the desired Suzuki biaryl in water/*n*-butanol as solvent. The formation of 2-*n*-butoxypyrimidine, which was isolated as main product when working under anhydrous conditions, was not observed. Obviously, the use of water effectively inhibits the undesired ether formation.

Suzuki Coupling of 2-Thiopheneboronic Acid. Suzuki coupling of 2-thiopheneboronic acids required higher catalyst loadings because of the increased propensity of this metalloids toward protodeboronation, which is about 120 times faster than that of 3-thiopheneboronic acid.³⁵ When 1 mol % of Pd/**5** was applied, the substrates 2-chloropyridine, 2-chloroquinoline, and 2-chlorolepidine were smoothly coupled with this heteroboronic

TABLE 5. Suzuki Reaction with Furanboronic Acids Using *n*-Butanol/Water as Solvent^a

| $ \begin{array}{c} \text{R} \\ \\ \text{C}_6\text{H}_3\text{Y}(\text{Cl}) + (\text{HO})_2\text{B}(\text{C}_4\text{H}_3\text{O})\text{R}' \xrightarrow[\text{nButanol / water (5:2)}]{\text{Na}_2\text{PdCl}_4 (1 \text{ mol}\%)/\text{ligand } \mathbf{5} (1:2), 2 \text{ equiv. K}_2\text{CO}_3} \text{R-C}_6\text{H}_3\text{Y-C}_4\text{H}_3\text{O-R}' \\ \text{Y = C, N} \qquad \qquad \qquad \text{Y = C, N} \\ [7 \text{ mL}\cdot\text{mmol}^{-1}] \\ 100^\circ\text{C}, 12 \text{ h} \end{array} $ | | | | | | |
|--|---------------|--------------|---------|------------|-----------------------------|------------------------|
| Entry | Aryl Chloride | Boronic Acid | Product | Pd [mol %] | Conversion ^b [%] | Yield ^c [%] |
| 1 | | | | 1 | ≥99 | 93 |
| 2 | | | | 1 | ≥99 | 97 |
| 3 | | | | 1 | ≥99 | 96 |
| 4 | | | | 1 | ≥99 | 92 |
| 5 | | | | 1 | ≥99 | 93 |
| 6 | | | | 1 | 94 | 90 |
| 7 | | | | 1 | ≥99 | 95 |
| 8 | | | | 1 | ≥99 | 97 |

^a Reaction conditions: 1.0 equiv of aryl halide, 1.5 equiv of boronic acid, 3.2 equiv of K₂CO₃, degassed *n*-butanol (5 mL mmol⁻¹), degassed water (2 mL mmol⁻¹), 100 °C, 12 h, cat.: the respective volume of catalyst stock solution (in *n*-butanol) (*c*_{Pd} = 0.005 mol/L, Na₂PdCl₄/ligand **5** L/Pd = 2:1). Reaction times and temperature were not optimized. ^b Average of two runs, determined by GC using heptadecane as internal standard. ^c Average of two runs, products were isolated via column chromatography (silica (20 × 3 cm), cyclohexane:EtOAc:NEt₃ (10:1:1) as eluent). ^d Product not isolated.

acid (Table 4, entries 1–3). Again the aqueous coupling protocol demonstrates its superiority over the anhydrous protocol where full conversion of 2-chlorolepidine with 2-thiophenylboronic acid was not feasible using Pd/2 at the same catalyst-loading (Table 2, entry 7, 73% conversion); such limitations in the conversion of *N*-heteroaryl chlorides were also reported in the Buchwald protocol.²⁷ Nonetheless, deactivated *N*-heterocyclic aryl chlorides did not undergo full conversion under aqueous conditions but still performed significantly better than under anhydrous conditions (Table 4, entries 4, 5). Pharmaceutically interesting chloroazines like 2-chloropyrimidine and 2-chloro-3,5-dimethoxytriazine (another biological active moiety)^{61,62} are smoothly coupled with 2-thiophenylboronic acid using the aqueous reaction conditions, affording 94% and 89% isolated yield, respectively, with 0.5 mol % catalyst loading (Table 4, entries 6 + 7). Formation of undesired *N*-arylbutoxide byproducts was not observed.

Suzuki Coupling of Furanboronic Acids. Next we studied the applicability of our aqueous reaction protocol to the coupling

of the more labile furanboronic acids. We were pleased to observe the smooth coupling of 3-furanboronic acid with a large variety of activated and deactivated 2-chloropyridines and 2-chloroquinolines and 2-chloropyrimidine including the notorious 4-amino-2-chloropyridine (typically 92–97% yield, 1 mol % Pd/5) (Table 5, entries 1–5). Suzuki coupling with 3-furanboronic acid is not limited to *N*-heteroaryl chlorides: *p*-chloroacetophenone or 6-chloro-5-methylbenzothiazole are arylated using the same conditions as for the heteroaryl chlorides (Table 5, entries 7 and 8). Thus, the reactivity of this catalytic system is significantly higher than that of other protocols which are limited to activated (*N*-hetero)aryl chlorides.²⁷ Our aqueous reaction protocol enables Suzuki coupling of electron-deficient and thus more labile 2-furanboronic acids. Unfortunately, the rapid decomposition of 2-furanboronic acids still prevents coupling of nonactivated aryl chlorides.

Other than providing high Suzuki reactivity, the developed reaction protocol is very convenient in many respects: (a) the water/*n*-butanol mixture is cheap and nontoxic, and the organic component is biodegradable; (b) anhydrous conditions are not required; (c) a convenient base (K₂CO₃) is used. When working on larger scale, product separation is simple since additional organic solvents such as ethers or alkanes are not required.

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(62) Menicagli, R.; Samaritani, S.; Signore, G.; Vaglini, F.; Via, L. D. *J. Med. Chem.* **2004**, *47*, 4649–4652.

Instead, addition of more water to the reaction mixture ensures an effective separation of the product-containing *n*-butanol layer from the water layer containing salts as well as excess of boronic acid. In cases of quantitative conversion of the aryl chloride, simple phase separation, drying of the alcoholic solution, and solvent removal afforded the desired product in excellent isolated yield and high purity (>95% judged by GC and NMR) without additional chromatographic purification.

Summary and Conclusion

In summary, we have developed a highly efficient Suzuki cross-coupling protocol enabling conversion of *N*-hetero- and normal aryl chlorides with thiophene- and furanboronic acids in aqueous *n*-butanol as the solvent. The facile coupling reactions are based on the Pd complex of the highly water soluble disulfonated fluorenylphosphine **5**, obtained *in situ* from Na₂PdCl₄ and the respective phosphonium salt of **5**. For heterocyclic substrates, aqueous catalysis was found to be significantly more efficient than Suzuki coupling under anhydrous conditions. Using the aqueous catalysis protocol, a variety of different *N*-heterocyclic and nonheterocyclic aryl chlorides was Suzuki coupled with 2- and 3-thiopheneboronic acids as well as furanboronic acids in near quantitative yield at catalyst loadings of 0.1–1 mol %. The undesired ether formation observed for some substrate combinations in anhydrous *n*-butanol as the solvent is suppressed in the presence of water. Furthermore, on a large scale the developed system enables efficient and sustainable Suzuki coupling including the facile product separation without the need for additional organic solvents during workup.

Experimental Section

All chemicals were purchased as reagent grade from commercial suppliers and used without further purification, unless otherwise noted. Used solvents (water, *n*-butanol) were all technical grade) were deaerated via freeze and thaw technique (2×). For cross-coupling reactions under anhydrous conditions, *n*-butanol (technical grade, dried over molecular sieves, 4 Å) was used. Potassium carbonate, used in cross-coupling reactions, was technical grade. The phosphine ligands were prepared according to published procedures: **1**,⁵⁴ **2**,⁵² **3**,⁵⁴ **4**,⁵³ **5**;²⁸ these ligands are also commercially available under the trade name cataCXium F from Evonik-Degussa GmbH. All “phosphines” mentioned in this publication were used in the form of their air stable phosphonium salts and deprotonated *in situ* during the catalyst preparation. All experiments were carried out under an argon atmosphere, unless otherwise noted. Proton (¹H NMR), carbon (¹³C NMR), phosphorus (³¹P NMR), and nitrogen (¹⁵N NMR) nuclear magnetic resonance spectra were recorded on Bruker DRX 500 at 500 MHz, 125.75, 202.46, and 50.69 MHz, respectively, at 293 K. The chemical shifts are given in parts per million (ppm) on the delta scale (δ) and are referenced to tetramethylsilane (δ = 0 ppm), ¹H NMR, 65% aq H₃PO₄ (δ = 0 ppm), ³¹P NMR and nitromethane (δ = 0 ppm), ¹⁵N NMR. Abbreviations for NMR data: s = singlet; d = doublet; t = triplet; q = quartet; qi = quintet; dd = doublet of doublets; dt = doublet of triplets; dq = doublet of quartets; tt = triplet of triplets; m = multiplet. Mass spectra were recorded on a Finnigan MAT 95 magnetic sector spectrometer. Thin layer chromatography (TLC) was performed using Fluka silica gel 60 F 254 (0.2 mm) on aluminum plates. Silica gel columns for chromatography were prepared with E. Merck silica gel 60 (0.063–0.20 mesh ASTM). GC experiments were run on a Clarus 500 GC with autosampler and FID detector. Column: Varian CP-Sil 8 CB (*l* = 15 m, diam = 0.25 mm, *d_F* = 1.0 μm), N₂ (flow: 17 cm/s; split 1:50); injector

temperature: 270 °C, detector temperature: 350 °C. Temperature program: isotherm 150 °C for 5 min, heating to 300 °C with 25 °C/min, isotherm for 15 min.

General Procedures for the Suzuki Cross-Coupling Reactions. Preparation of Catalyst Stock Solution for Suzuki Coupling in Anhydrous Alcohols. [Na₂PdCl₄] (11.8 mg, 0.04 mmol), the respective phosphine (**1–4**) (0.08 mmol), and K₂CO₃ (69 mg, 0.5 mmol) were placed in a 10 mL Schlenk tube, evacuated, and backfilled with Ar thrice. Degassed dry *n*-butanol (4 mL) was added and the mixture stirred at 55 °C for 3 h to obtain a yellow suspension. *c*_{Pd} of this catalyst stock solution is 0.01 mmol·mL^{−1}. When the cross-coupling reaction was performed in *tert*-amyl alcohol as solvent, this alcohol was used for the stock solution.

Cross-Coupling Reaction in Anhydrous Alcohols (*n*-butanol or *tert*-amyl alcohol) as Solvent. Boronic acid (1.2 mmol) and K₂CO₃ (440 mg, 3.2 mmol) were placed in a 25 mL Schlenk tube, evacuated, and backfilled with Ar thrice. For cross-coupling reactions with 2-thiopheneboronic acids more molecular sieve (0.25, g 4 Å) was added prior to the degassing sequence. Then degassed *n*-butanol (or *tert*-amyl alcohol, respectively) (5 mL), the aryl halide (1 mmol), and the respective volume of catalyst stock solution were added. The reaction mixture was stirred for 12 h at 100 °C and then cooled to room temperature. Water (5 mL) was added, and the product was extracted with methyl *tert*-butyl ether (2 × 5 mL). The organic layer was concentrated *in vacuo* and the residue purified via column chromatography (silica (20 × 3 cm), cyclohexane:EtOAc:NEt₃ (10:1:1)), to afford the pure cross-coupling product in 51–93% yield, respectively.

Preparation of Catalyst Stock Solution for Suzuki Coupling in Aqueous *n*-Butanol. [Na₂PdCl₄] (5.9 mg, 0.02 mmol), phosphine **5** (30 mg, 0.04 mmol), and K₂CO₃ (33 mg, 0.24 mmol) were placed in a 25 mL Schlenk tube, evacuated, and backfilled with Ar thrice. Degassed water (4 mL) was added and the mixture stirred at 55 °C for 3 h to obtain a clear, nearly colorless solution. *c*_{Pd} of this catalyst stock solution is 0.005 mmol·mL^{−1}.

Cross-Coupling Reaction in Water/*n*-Butanol (screening experiments). Boronic acid (1.2 mmol) and K₂CO₃ (440 mg, 3.2 mmol) were placed in a 25 mL Schlenk tube, evacuated, and backfilled with Ar thrice. Then degassed *n*-butanol (5 mL) was added as well as the aryl halide (1 mmol) and the respective volume of catalyst stock solution. The amount of water in the reaction mixture was adjusted to 2 mL total volume. The reaction mixture was stirred for 12 h at 100 °C and then cooled to room temperature. Water (5 mL) was added, and the product was extracted with methyl *tert*-butyl ether (2 × 5 mL). The organic layer was concentrated *in vacuo* and the residue purified via column chromatography (silica (20 × 3 cm), cyclohexane:EtOAc:NEt₃ (10:1:1)) to afford the pure respective cross-coupling product in 89–97% yield.

Preparative Scale Cross-Coupling Reaction in Water/*n*-Butanol. 3-Thiopheneboronic acid (1.66 g, 13 mmol), 2-chloroquinoline (1.66 g, 10 mmol), and K₂CO₃ (4.14 g, 30 mmol) were placed in a 50 mL Schlenk flask, evacuated, and backfilled with Ar thrice. Then degassed *n*-butanol (25 mL) was added as well as the catalyst stock solution (0.5 mol % catalyst loading). After the reaction mixture was stirred for 12 h at 100 °C, quantitative conversion was observed via GC chromatography. The reaction mixture was then cooled to room temperature, water (10 mL) was added, and the organic layer separated, dried over MgSO₄, and filtered. Removal of the volatiles *in vacuo* afforded the crude product 2-thiophen-3-ylquinoline (1.92 g, 91%) as an off white solid (purity checked by GC and ¹H NMR: >95%).

2-Thiophen-3-ylpyridine (Table 2, entry 1/Table 3, entry 1). ¹H NMR (500 MHz, CDCl₃) δ 8.61 (dq, ³*J* = 4.7 Hz, *J* = 1.0 Hz, 1 H, CH, ar), 7.89 (dd, ³*J* = 3.2 Hz, *J* = 1.3 Hz, 1 H, CH, ar), 7.69–7.64 (m, 2 H, CH, ar), 7.59 (dt, ³*J* = 8.0 Hz, *J* = 1.0 Hz, 1 H, CH, ar), 7.38 (dd, ³*J* = 5.0 Hz, *J* = 3.0 Hz, 1 H, CH, ar), 7.14 (ddd, ³*J* = 7.6 Hz, *J* = 4.6 Hz, *J* = 1.2 Hz, 1 H, CH, ar); ¹³C{¹H}

NMR (125.77 MHz, CDCl₃) δ 154.0, 150.0, 142.6, 137.1, 126.7, 126.6, 123.9, 122.2, 120.7; HRMS calcd for C₉H₇NS: 161.03, found 161.02985.

2-Thiophen-3-ylquinoline (Table 3, entry 2). ¹H NMR (500 MHz, CDCl₃) δ 8.13 (d, ³J = 8.5 Hz, 1 H, CH, ar), 8.11 (d, ³J = 8.8 Hz, 1 H, CH, ar), 8.03 (dd, ³J = 3.0 Hz, ³J = 1.3 Hz, 1 H, CH, ar), 7.87 (dd, ³J = 5.1 Hz, ³J = 1.3 Hz, 1 H, CH, ar), 7.77 (dd, ³J = 8.0 Hz, ³J = 1.0 Hz, 1 H, CH, ar), 7.75 (d, ³J = 8.6 Hz, 1 H, CH, ar), 7.69 (ddd, ³J = 8.5 Hz, ³J = 7.0 Hz, ³J = 1.5 Hz, 1 H, CH, ar), 7.49 (ddd, ³J = 8.2 Hz, ³J = 7.0 Hz, ³J = 1.3 Hz, 1 H, CH, ar), 7.43 (dd, ³J = 5.0 Hz, ³J = 3.0 Hz, 1 H, CH, ar); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 153.7, 148.7, 143.1, 137.1, 130.1, 129.9, 127.9, 127.5, 127.3, 126.8, 126.5, 125.0, 119.4; HRMS calcd for C₁₃H₉NS: 211.0456, found 211.04371.

4-Methyl-2-thiophen-3-ylpyridine (Table 2, entry 2/Table 3, entry 3). ¹H NMR (500 MHz, CDCl₃) δ 8.46 (d, ³J = 5.0 Hz, 1 H, CH, ar), 7.87 (dd, ³J = 2.9 Hz, ³J = 1.3 Hz, 1 H, CH, ar), 7.64 (dd, ³J = 5.0 Hz, ³J = 1.2 Hz, 1 H, CH, ar), 7.43–7.41 (m, 1 H, CH, ar), 7.37 (dd, ³J = 5.0 Hz, ³J = 2.8 Hz, 1 H, CH, ar), 6.97 (dq, ³J = 5.0 Hz, ³J = 0.8 Hz, 1 H, CH, ar), 2.36 (s, 3 H, CH₃); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 153.4, 149.4, 147.7, 142.3, 126.2, 126.2, 123.3, 122.9, 121.2, 21.1; HRMS calcd for C₁₀H₉NS: 175.0456, found 175.04453.

4-Methyl-2-thiophen-3-ylquinoline (Table 3, entry 4). ¹H NMR (500 MHz, CDCl₃) δ 8.10 (dq, ³J = 8.5 Hz, ³J = 0.6 Hz, 1 H, CH, ar), 7.99 (dd, ³J = 1.2 Hz, ³J = 3.0 Hz, 1 H, CH, ar), 7.90 (dd, ³J = 8.5 Hz, ³J = 1.2 Hz, 1 H, CH, ar), 7.84 (dd, ³J = 5.1 Hz, ³J = 1.3 Hz, 1 H, CH, ar), 7.66 (ddd, ³J = 8.5 Hz, ³J = 7.0 Hz, ³J = 1.5 Hz, 1 H, CH, ar), 7.55 (d, ³J = 1.0 Hz, 1 H, CH, ar), 7.47 (ddd, ³J = 8.5 Hz, ³J = 7.0 Hz, ³J = 1.2 Hz, 1 H, CH, ar), 7.39 (dd, ³J = 5.0 Hz, ³J = 3.0 Hz, 1 H, CH, ar), 2.67 (d, ³J = 1.0 Hz, 3 H, CH₃); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 153.4, 148.5, 145.1, 143.2, 130.5, 129.7, 127.6, 127.3, 126.6, 126.2, 124.8, 124.0, 120.1, 19.3; HRMS calcd for C₁₄H₁₁NS: 225.0613, found 225.05940.

2-Thiophen-3-ylisonicotinamide (Table 2, entry 3/Table 3, entry 5). ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.71 (dd, ³J = 5.0 Hz, ³J = 0.6 Hz, 1 H, CH, ar), 8.28 (s (br), 1 H, NH₂), 8.25–8.23 (m, 2 H, CH, ar), 7.80 (dd, ³J = 5.0 Hz, ³J = 1.3 Hz, 1 H, CH, ar), 7.76 (s (br), 1 H, NH₂), 7.67 (dd, ³J = 5.0 Hz, ³J = 3.2 Hz, 1 H, CH, ar), 7.65 (dd, ³J = 5.0 Hz, ³J = 1.6 Hz, 1 H, CH, ar); ¹³C{¹H} NMR (125.77 MHz, DMSO-*d*₆) δ 166.7, 153.8, 150.5, 142.7, 141.9, 127.6, 126.6, 125.0, 120.1, 118.1; ¹⁵N NMR (50.69 MHz, DMSO-*d*₆) δ –275.1 (NH₂), –66.5 (pyridyl); HRMS calcd for C₁₀H₈N₂O₂: 204.0358, found 204.03597.

2-Methoxy-6-thiophen-3-ylpyridine (Table 3, entry 6). ¹H NMR (500 MHz, CDCl₃) δ 7.90 (dd, ³J = 3.0 Hz, ³J = 1.2 Hz, 1 H, CH, ar), 7.63 (dd, ³J = 5.0 Hz, ³J = 1.2 Hz, 1 H, CH, ar), 7.55 (dd, ³J = 8.2 Hz, ³J = 7.4 Hz, 1 H, CH, ar), 7.35 (dd, ³J = 5.0 Hz, ³J = 3.0 Hz, 1 H, CH, ar), 7.17 (dd, ³J = 7.5 Hz, ³J = 0.5 Hz, 1 H, CH, ar), 6.62 (dd, ³J = 8.0 Hz, ³J = 0.5 Hz, 1 H, CH, ar), 4.00 (s, 3 H, OCH₃); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 164.1, 151.4, 142.6, 139.5, 126.6, 126.4, 123.7, 113.0, 109.3, 53.6; HRMS calcd for C₁₀H₉NOS: 191.0405, found 191.04062.

2-Thiophen-3-ylpyrimidine (Table 3, entry 7). ¹H NMR (500 MHz, CDCl₃) δ 8.73 (d, ³J = 5.0 Hz, 2 H, CH, ar), 8.30 (dd, ³J = 3.1 Hz, ³J = 1.2 Hz, 1 H, CH, ar), 7.90 (dd, ³J = 5.0 Hz, ³J = 1.2 Hz, 1 H, CH, ar), 7.38 (dd, ³J = 5.0 Hz, ³J = 3.1 Hz, 1 H, CH, ar), 7.10 (t, ³J = 4.9 Hz, 1 H, CH, ar); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 160.9, 156.2, 140.6, 127.0, 126.3, 125.1, 117.6; ¹⁵N NMR (50.69 MHz, CDCl₃) δ –95.4; HRMS calcd for C₈H₆N₂S: 162.0253, found 162.02548.

2-Butoxypyrimidine (Table 2, entry 4). ¹H NMR (500 MHz, CDCl₃) δ 8.43 (d, ³J = 4.8 Hz, 2 H, CH, ar), 6.83 (t, ³J = 4.8 Hz, 1 H, CH, ar), 4.28 (t, ³J = 6.8 Hz, 2 H, OCH₂), 1.76–1.70 (m, 2 H, CH₂), 1.44 (qui, ³J = 7.4 Hz, 2 H, CH₂), 0.90 (t, ³J = 7.5 Hz, 2 H, CH₃); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 164.35, 158.2, 113.7, 66.4, 29.9, 18.1, 12.8; HRMS calcd for C₈H₁₂N₂O: 152.0949, found 152.06218.

3-*p*-Tolylthiophene (Table 2, entry 5/Table 3 entry 8). ¹H NMR (500 MHz, CDCl₃) δ 7.41 (d, ³J = 8.0 Hz, 2 H, CH, ar), 7.32 (t, ³J = 2.0 Hz, 1 H, CH, ar), 7.29 (s, 1 H, CH, ar), 7.29 (t, ³J = 1.0 Hz, 1 H, CH, ar), 7.29 (d, ³J = 8.0 Hz, 2 H, CH, ar), 2.29 (s, 3 H, CH₃); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 141.3, 135.8, 132.1, 128.5 (2x), 125.3, 125.0, 118.6, 20.1; HRMS calcd for C₁₁H₁₀S: 174.0504, found 174.04988.

2-Thiophen-2-ylpyridine (Table 2, entry 6/Table 4, entry 1). ¹H NMR (500 MHz, CDCl₃) δ 8.56 (dt, ³J = 4.5 Hz, ³J = 1.2 Hz, 1 H, CH, ar), 7.68–7.62 (m, 2 H, CH, ar), 7.56 (dd, ³J = 3.8 Hz, ³J = 1.2 Hz, 1 H, CH, ar), 7.38 (dd, ³J = 5.0 Hz, ³J = 1.0 Hz, 1 H, CH, ar), 7.14–7.09 (m, 2 H, CH, ar); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 151.6, 148.5, 143.8, 135.6, 127.0, 127.5, 123.5, 120.9, 117.8; HRMS calcd for C₉H₇NS: 161.03, found 161.02942.

2-Thiophen-2-ylquinoline (Table 4, entry 2). ¹H NMR (500 MHz, CDCl₃) δ 8.11 (d, ³J = 8.6 Hz, 1 H, CH, ar), 8.08 (d, ³J = 8.5 Hz, 1 H, CH, ar), 7.78 (d, ³J = 8.5 Hz, 1 H, CH, ar), 7.75 (dd, ³J = 8.2 Hz, ³J = 1.3 Hz, 1 H, CH, ar), 7.72 (dd, ³J = 3.8 Hz, ³J = 1.2 Hz, 1 H, CH, ar), 7.68 (ddd, ³J = 8.5 Hz, ³J = 7.0 Hz, ³J = 1.5 Hz, 1 H, CH, ar), 7.47 (ddd, ³J = 8.0 Hz, ³J = 6.7 Hz, ³J = 1.0 Hz, 1 H, CH, ar), 7.46 (dd, ³J = 5.0 Hz, ³J = 1.0 Hz, 1 H, CH, ar), 7.15 (dd, ³J = 5.0 Hz, ³J = 3.8 Hz, 1 H, CH, ar); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 151.3, 147.1, 144.4, 135.6, 128.8, 128.3, 127.5, 127.0, 126.4, 126.2, 125.1, 124.8, 116.6; HRMS calcd for C₁₃H₉NS: 211.0456, found 211.04476.

4-Methyl-2-thiophen-2-ylquinoline (Table 2, entry 7/Table 4, entry 3). ¹H NMR (500 MHz, CDCl₃) δ 8.05 (d, ³J = 8.2 Hz, 1 H, CH, ar), 7.81 (dd, ³J = 8.2 Hz, ³J = 1.3 Hz, 1 H, CH, ar), 7.63 (dd, ³J = 3.5 Hz, ³J = 1.0 Hz, 1 H, CH, ar), 7.61 (ddd, ³J = 8.6 Hz, ³J = 7.0 Hz, ³J = 1.6 Hz, 1 H, CH, ar), 7.51 (s, 1 H, CH, ar), 7.40 (ddd, ³J = 8.3 Hz, ³J = 7.0 Hz, ³J = 1.3 Hz, 1 H, CH, ar), 7.39 (dd, ³J = 5.0 Hz, ³J = 1.3 Hz, 1 H, CH, ar), 2.59 (s, 3 H, CH₃); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 152.4, 148.4, 146.0, 145.1, 130.2, 129.8, 128.7, 128.4, 127.7, 126.2, 126.1, 124.0, 118.6, 19.2; HRMS calcd for C₁₄H₁₁NS: 225.0613, found 225.05936.

2-Thiophen-2-ylpyrimidine (Table 2, entry 10/Table 4, entry 6). ¹H NMR (500 MHz, CDCl₃) δ 8.62 (d, ³J = 5.0 Hz, 2 H, CH, ar), 7.94 (dd, ³J = 3.8 Hz, ³J = 1.3 Hz, 1 H, CH, ar), 7.41 (dd, ³J = 5.0 Hz, ³J = 1.3 Hz, 1 H, CH, ar), 7.08 (dd, ³J = 5.0 Hz, ³J = 3.7 Hz, 1 H, CH, ar), 7.02 (t, ³J = 5.0 Hz, 1 H, CH, ar); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 160.6, 156.2, 142.2, 128.9, 128.0, 127.3, 117.5; HRMS calcd for C₈H₆N₂S: 162.0253, found 162.02788.

2,4-Dimethoxy-6-thiophen-2-yl-[1,3,5]triazine (Table 4, entry 7). ¹H NMR (500 MHz, CDCl₃) δ 8.15 (dd, ³J = 3.8 Hz, ³J = 1.3 Hz, 1 H, CH, ar), 7.59 (dd, ³J = 5.0 Hz, ³J = 1.3 Hz, 1 H, CH, ar), 7.16 (dd, ³J = 5.0 Hz, ³J = 3.8 Hz, 1 H, CH, ar), 4.09 (s, 6 H, OCH₃); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 171.6, 169.7, 139.7, 131.5, 130.9, 127.3, 54.2; HRMS calcd for C₉H₉N₃O₂S: 223.0416, found 223.03932.

2-Furan-3-ylpyridine (Table 5, entry 1). ¹H NMR (500 MHz, CDCl₃) δ 8.58 (dq, ³J = 4.8 Hz, ³J = 0.9 Hz, 1 H, CH, ar), 8.02 (dd, ³J = 1.5 Hz, ³J = 0.9 Hz, 1 H, CH, ar), 7.65 (dt, ³J = 7.8 Hz, ³J = 1.8 Hz, 1 H, CH, ar), 7.49 (t, ³J = 1.8 Hz, 1 H, CH, ar), 7.44 (dt, ³J = 7.9 Hz, ³J = 1.0 Hz, 1 H, CH, ar), 7.12 (ddd, ³J = 7.6 Hz, ³J = 4.8 Hz, ³J = 1.1 Hz, 1 H, CH, ar), 6.89 (dd, ³J = 1.8 Hz, ³J = 0.8 Hz, 1 H, CH, ar); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 152.2, 150.1, 144.2, 141.6, 136.9, 127.5, 122.1, 120.5, 109.0; ¹⁵N NMR (50.69 MHz, CDCl₃) δ –76.7; HRMS calcd for C₉H₇NO: 145.0528, found 145.05257. The ¹H NMR spectrum was identical to that in the literature.⁶³

2-Furan-3-ylquinoline-3-carbaldehyde (Table 5, entry 2). ¹H NMR (500 MHz, CDCl₃) δ 10.41 (s, 1 H, CHO), 8.74 (s, 1 H, CH, ar), 8.13 (dq, ³J = 8.5 Hz, ³J = 0.8 Hz, 1 H, CH, ar), 7.95 (d, ³J = 8.3 Hz, 1 H, CH, ar), 7.90–7.89 (m, 1 H, CH, ar), 7.83 (ddd, ³J = 8.5 Hz, ³J = 6.9 Hz, ³J = 1.4 Hz, 1 H, CH, ar), 7.61 (t, ³J = 1.7 Hz, 1 H, CH, ar), 7.59 (ddd, ³J = 8.1 Hz, ³J = 7.1 Hz, ³J = 1.2 Hz, 1 H, CH, ar), 6.95 (q, ³J = 0.9 Hz, 1 H, CH, ar); ¹³C{¹H} NMR

(63) Ribereau, P.; Queguiner, G. *Can. J. Chem.* **1983**, *61*, 334–342.

NMR (125.77 MHz, CDCl₃) δ 190.2, 151.3, 148.9, 142.7, 142.5, 137.5, 131.6, 128.4, 128.3, 126.8, 126.4, 125.1, 123.3, 110.7; ¹⁵N NMR (50.69 MHz, CDCl₃) δ -71.2; HRMS calcd for C₁₄H₉NO₂: 223.0633, found 223.06263.

2-Furan-3-yl-6-methoxypyridine (Table 5, entry 3). ¹H NMR (500 MHz, CDCl₃) δ 8.00 (dd, J = 1.6 Hz, J = 0.9 Hz, 1 H, CH, ar), 7.53 (dd, 3J = 8.2 Hz, 3J = 7.4 Hz, 1 H, CH, ar), 7.46 (t, J = 1.7 Hz, 1 H, CH, ar), 7.01 (dd, 3J = 7.4 Hz, J = 0.6 Hz, 1 H, CH, ar), 6.85 (dd, J = 1.9 Hz, J = 0.9 Hz, 1 H, CH, ar), 7.59 (dd, 3J = 8.2 Hz, J = 0.6 Hz, 1 H, CH, ar), 3.96 (s, 3 H, OCH₃); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 162.7, 148.2, 142.6, 140.2, 137.9, 126.0, 111.4, 107.7, 107.6, 52.1; ¹⁵N NMR (50.69 MHz, CDCl₃) δ -120.8; HRMS calcd for C₁₀H₉NO₂: 175.0633, found 175.06154.

2-Furan-3-ylpyridin-4-ylamine (Table 5, entry 4). ¹H NMR (500 MHz, CDCl₃) δ 8.17 (dd, 3J = 5.7 Hz, 1 H, CH, ar), 7.94 (s, 1 H, CH, ar), 7.45–7.43 (m, 1 H, CH, ar), 6.81–6.78 (m, 1 H, CH, ar), 6.67 (d, J = 2.0 Hz, 1 H, CH, ar), 6.38 (dd, 3J = 5.6 Hz, J = 2.1 Hz, 1 H, CH, ar), 4.44 (s (br), 1 H, NH₂); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 152.6, 151.2, 149.0, 142.6, 140.0, 126.2, 107.6, 107.1, 104.8; ¹⁵N NMR (50.69 MHz, CDCl₃) δ -317.6 (NH₂); HRMS calcd for C₉H₈N₂O: 116.00637, found 160.06261.

2-Furan-3-ylpyrimidine (Table 5, entry 5). ¹H NMR (500 MHz, CDCl₃) δ 8.69 (d, 3J = 4.8 Hz, 2 H, CH, ar), 8.27–8.26 (m, 1 H, CH, ar), 7.50 (t, J = 1.7 Hz, 1 H, CH, ar), 7.08 (t, 3J = 4.9 Hz, 1 H, CH, ar), 7.07–7.06 (m, 1 H, CH, ar); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 160.4, 156.1, 143.8, 142.9, 126.0, 117.5, 108.4; ¹⁵N NMR (50.69 MHz, CDCl₃) δ -95.4; HRMS calcd for C₈H₆N₂O: 146.048, found 146.04496.

5-Pyridin-2-ylfuran-2-carbaldehyde (Table 5, entry 6). ¹H NMR (500 MHz, CDCl₃) δ 9.72 (s, 1 H, CHO), 8.66 (dq, 3J = 4.7 Hz, J = 0.9 Hz, 1 H, CH, ar), 7.92 (dt, 3J = 7.9 Hz, J = 0.9 Hz, 1 H, CH, ar), 7.79 (dt, 3J = 7.8 Hz, J = 1.8 Hz, 1 H, CH, ar), 7.36 (d, J = 3.8 Hz, 1 H, CH, ar), 7.29 (ddd, 3J = 7.6 Hz, J = 4.7 Hz, J = 1.2 Hz, 1 H, CH, ar), 7.26 (d, J = 3.8 Hz, 1 H, CH, ar); ¹³C-

{¹H} NMR (125.77 MHz, CDCl₃) δ 176.7, 157.3, 151.6, 149.0, 146.8, 135.9, 122.8, 121.9, 119.1, 109.7; ¹⁵N NMR (50.69 MHz, CDCl₃) δ -76.3; HRMS calcd for C₁₀H₇NO₂: 173.0477, found 173.04588.

1-(4-Furan-3-ylphenyl)ethanone (Table 5, entry 7). ¹H NMR (500 MHz, CDCl₃) δ 7.96 (d, 3J = 8.2 Hz, 2 H, CH, ar), 7.82–7.81 (m, 1 H, CH, ar), 7.56 (d, 3J = 8.2 Hz, 2 H, CH, ar), 7.51–7.50 (m, 1 H, CH, ar), 6.74–6.73 (m, 1 H, CH, ar), 2.60 (s, 3 H, CH₃); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 196.4, 143.1, 138.6, 136.2, 134.6, 128.0, 124.7, 124.6, 107.6, 25.5; HRMS calcd for C₁₂H₁₀O₂: 186.068, found 186.06642. The NMR spectra were identical to those in the literature.²²

5-Furan-3-yl-2-methylbenzothiazole (Table 5, entry 8). ¹H NMR (500 MHz, CDCl₃) δ 8.06 (d, J = 1.6 Hz, 1 H, CH, ar), 7.80 (dd, 3J = 8.2 Hz, J = 0.6 Hz, 1 H, CH, ar), 7.80 (dd, J = 1.6 Hz, J = 0.9 Hz, 1 H, CH, ar), 7.51 (t, J = 1.7 Hz, 1 H, CH, ar), 7.49 (dd, 3J = 8.3 Hz, J = 1.7 Hz, 1 H, CH, ar), 6.77 (dd, J = 1.8 Hz, J = 0.9 Hz, 1 H, CH, ar), 2.84 (s, 3 H, CH₃); ¹³C{¹H} NMR (125.77 MHz, CDCl₃) δ 166.7, 153.1, 142.8, 137.7, 133.1, 129.7, 125.2, 121.9, 120.6, 118.4, 108.0, 19.2; ¹⁵N NMR (50.69 MHz, CDCl₃) δ -73.9; HRMS calcd for C₁₂H₉NOS: 215.0405, found 215.03914.

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Supporting Information Available: Contains the full set of ¹H, ¹³C and ¹⁵N NMR spectra of all compounds synthesized. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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