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Sequential Palladium-Catalysed Direct Arylation Followed by Suzuki Coupling of Bromo-2-chloropyridines: Simple Access to a Variety of 2-Arylpyridines

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2-Arylpyridines are an important class of ligands for the synthesis of complexes with physical properties. We observed that the use of 3-, 4- or 5-bromo-2-chloropyridines allows the synthesis of a wide variety of heteroarylated 2-arylpyridines by means of successive direct arylation and Suzuki coupling. For these two reactions, an air-stable catalyst associated to a cheap and nontoxic base was employed as the catalyst. Moreover, a wide range of heteroarenes and functionalised arylboronic acids could be tolerated.

Introduction

Simple access to a wide variety of 2-arylpyridine derivatives is an important area of research in organometallic and material chemistry due to the physical properties of cyclometallated Au, Ir, Pt or Ru complexes that bear 2-phenylpyridine ligands (Figure 1).[1] The tuning of the electronic properties of such ligands requires the introduction of various substituents, including heteroaryls, at different positions. For example, the introduction a terthiophene substituent at C4 on the pyridyl ring of a cationic Ir^{III} bis-cyclometalate $[Ir(C^N)_2(N^N)]PF_6$ led to a drastic modification of the luminescence properties.[1g] The properties of cyclometalated ruthenium complexes that bear thiophene-substituted 2-arylpyridine derivatives have also been recently reported by Berlinguette and co-workers.[1h] In most cases, such functionalisation on 2-arylpyridine are performed by using Suzuki, Stille or Negishi cross-coupling reactions.[1g,2,3] However, these reactions require the preparation of an organometallic derivative of (hetero)aromatics and provide an organometallic salt (MX) as byproduct (Scheme 1).

For example, the diarylation of 2,5-di(trimethyltin)pyridine with 4-iodoanisole has been reported.[4] However, the introduction of two different (hetero)aryl groups by this method is certainly challenging. The diarylation of dihalopyridines or (halopyridin-2-yl)boronic acids derivatives by means of Suzuki couplings has also been described (Scheme 1).[5,6]

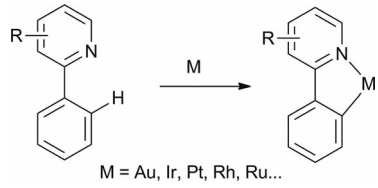

Figure 1. 2-Arylpyridine derivatives are an important class of ligands for the tuning of material properties.

Ohta and co-workers reported in 1990 that arylation by means of the C–H bond functionalisation of several heteroaromatics with aryl halides proceeds in moderate to good yields by using $[Pd(PPh_3)_4]$ as the catalyst.[7] Since these results were reported, palladium-catalysed direct arylation of heteroaryl derivatives with aryl halides has proven to be a very powerful method for the synthesis of a wide variety of arylated heteroarenes.[7–13]

However, palladium-catalysed direct arylation of polyhalopyridines has attracted less attention.[14] Marsais and co-workers have reported the reaction of 2-chloro-5-iodopyridine with a thiazole derivative. The 2-chloro-5-(thiazol-2-yl)pyridine derivative was formed in 58% yield.[14a] Similarly, Greaney and co-workers described the coupling of 2-chloro-4-iodobenzene with 2-phenylindazole.[14b] To the best of our knowledge, only one example of direct arylation of a bromo-2-chloropyridine has been described. Kappe and co-workers have treated 2-methylthiophene with 5-bromo-2-chloropyridine by utilising microwave heating to form 2-chloro-5-(5-methylthiophen-2-yl)pyridine in 64% yield.[15]

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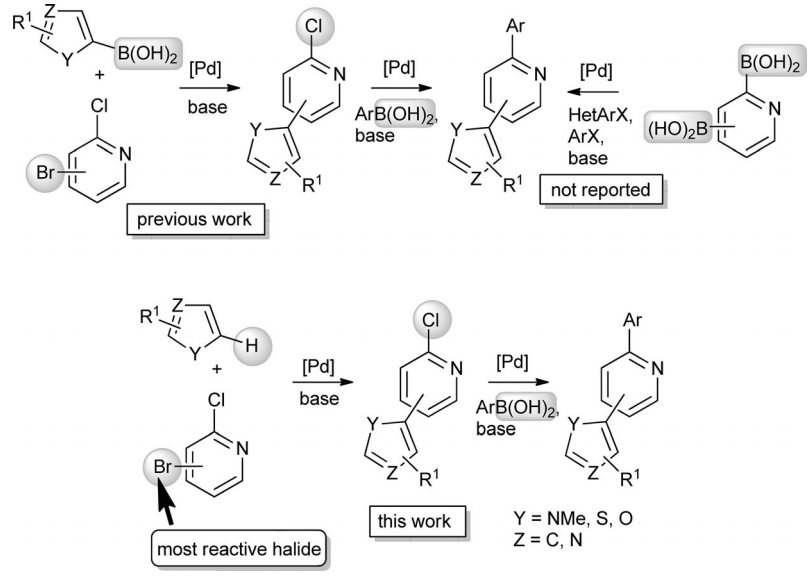


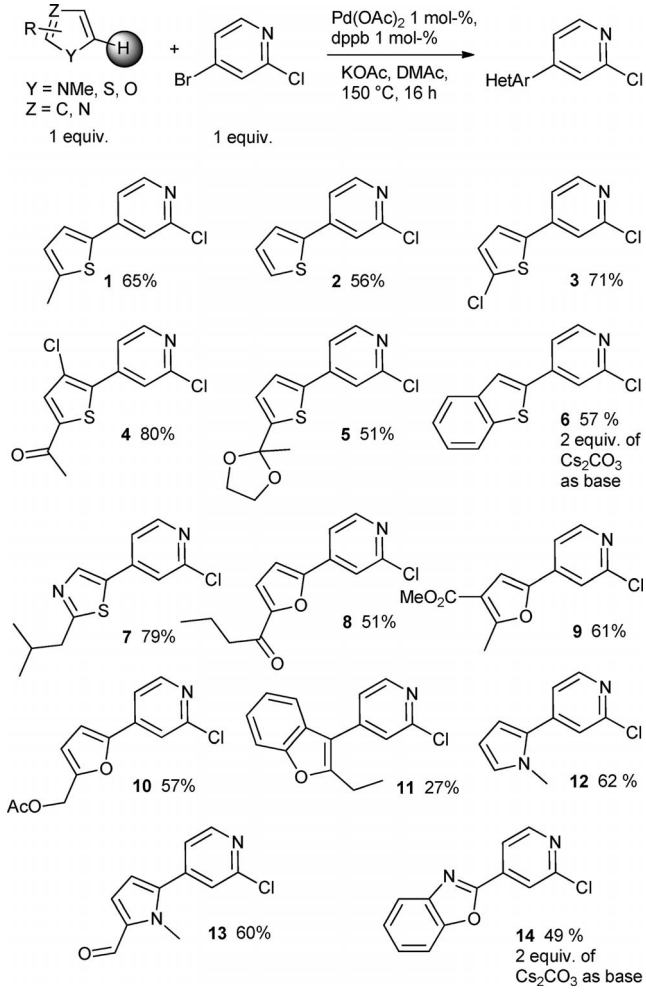
Scheme 1. Synthesis of 2-arylpyridines substituted by heteroarenes.

We now report conditions for the sequential direct monoarylation at C3, C4 or C5 of bromo-2-chloropyridines with a variety of heteroarenes, followed by arylation at C2 of the pyridyl ring by means of Suzuki coupling and by using an air-stable palladium catalyst.

Results and Discussion

To determine the reactivity of 4-bromo-2-chloropyridine for palladium-catalysed direct arylations, a set of reactions in the presence of 2-methylthiophene as the coupling partner and under various reaction conditions was carried out. Our objective was to obtain the monoheteroarylated compound **1** without cleavage of the C–Cl bond (Scheme 2). To minimise the formation of side products that arise from such C–Cl bond cleavage, we employed an equimolar amount of the heteroarene and 4-bromo-2-chloropyridine. We observed that by using KOAc as the base and 1 mol-% $Pd(OAc)_2$/dppb [dppb = 1,4-bis(diphenylphosphanyl)butane] as the catalytic system in *N*,*N*-dimethylacetamide (DMAc) at 150 °C, the target product **1** was obtained in 65% yield (Scheme 2). Under these conditions, no significant cleavage of the C–Cl bond was observed. It should be noted that at a lower temperature of 120 °C, partial conversion of the 4-bromo-2-chloropyridine was observed.

Then the scope for the mono-heteroarylation of 4-bromo-2-chloropyridine using a variety of heteroarenes was investigated (Scheme 2). Compounds **2** and **5** were obtained in 56 and 51% yields, respectively, from thiophene or 2-methyl-2-(thiophen-2-yl)-1,3-dioxolane. Better yields were obtained from the chloro-substituted thiophenes, 2-chlorothiophene and 2-acetyl-4-chlorothiophene. These heteroarenes gave **3** and **4** in 71 and 80% yields, respectively, without cleavage of the C–Cl bonds of both pyridine and thiophene moieties. A high yield of 79% for **7** was also obtained for the coupling of 4-bromo-2-chloropyridine with 2-isobutylthiazole. Furan derivatives were found to be less reactive. From 1-(furan-2-yl)butan-1-one, methyl 2-methylfuran-3-



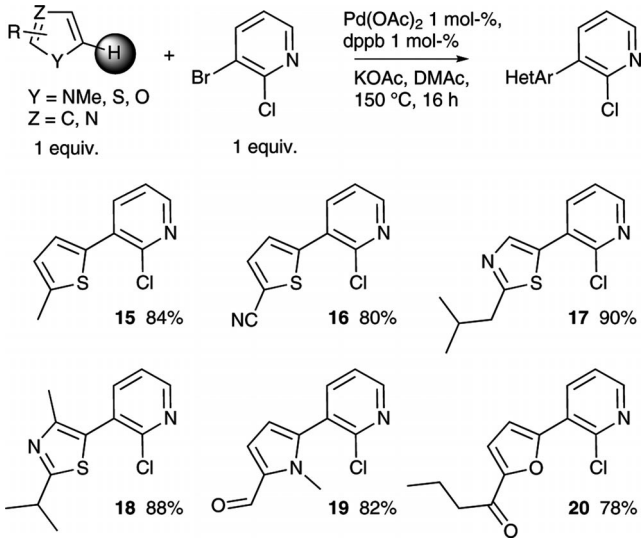
Scheme 2. Direct arylation of 4-bromo-2-chloropyridine.

carboxylate and furfuryl acetate **8**–**10** were obtained in 51–61% yields. A low yield of 27% for **11** was obtained from 2-ethylbenzofuran. On the other hand, 1-methylpyrrole and 1-methylpyrrole-2-carbaldehyde gave **12** and **13** in quite good yields.

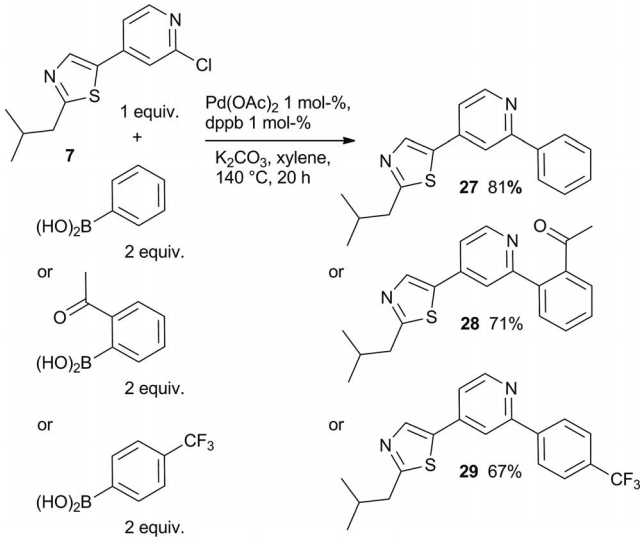
Next we studied the reactivity of 3-bromo-2-chloropyridine by using the same reaction conditions (Scheme 3). Compounds **15** and **16** were produced in 84 and 80% yields, respectively, from 2-methylthiophene and thiophene-2-carbonitrile. Again, thiazole derivatives allowed the formation of **17** and **18** in very high yields. With this pyridine derivative, even 1-methylpyrrole-2-carbaldehyde and 1-(furan-2-yl)butan-1-one led to the target products **19** and **20** in high yields. In all cases, no formation of diheteroarylated products could be detected by GC/MS analysis.

Six heteroarenes have been coupled with 5-bromo-2-chloropyridine (Scheme 4). In all cases, good yields of the desired coupling products **21**–**26** were obtained. Again, from 2-chlorothiophene no significant cleavage of both C–Cl bonds was observed, and **22** was produced in 91% yield. A high yield of **25** was also obtained from methyl 2-methylfuran-3-carboxylate.

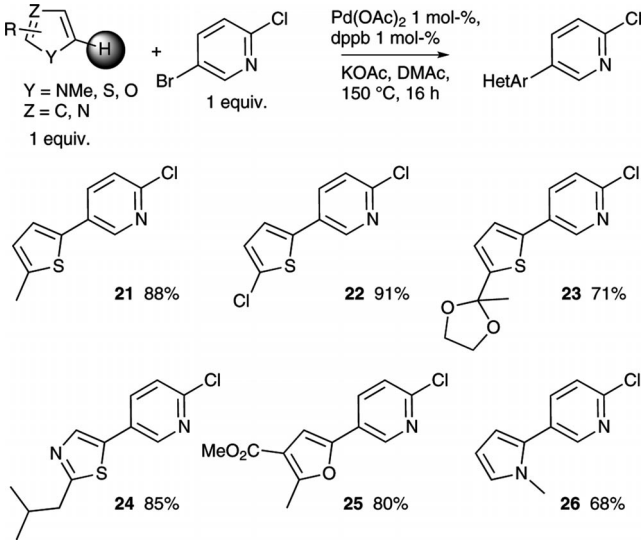
Then the reactivity for Suzuki coupling of some heteroaryl-2-chloropyridines was examined (see Schemes 5, 6, and 7). C–Cl bonds are known to be less reactive than C–Br bonds. However, similar substrates have already been employed successfully in Suzuki couplings.[16] We observed that **7** and benzene boronic acid in the presence of air-stable $Pd(OAc)_2$/dppb (1 mol-%) as the catalytic system using K_2CO_3 as the base in xylene gave **27** in 81% yield, with complete consumption of the starting material. It should be



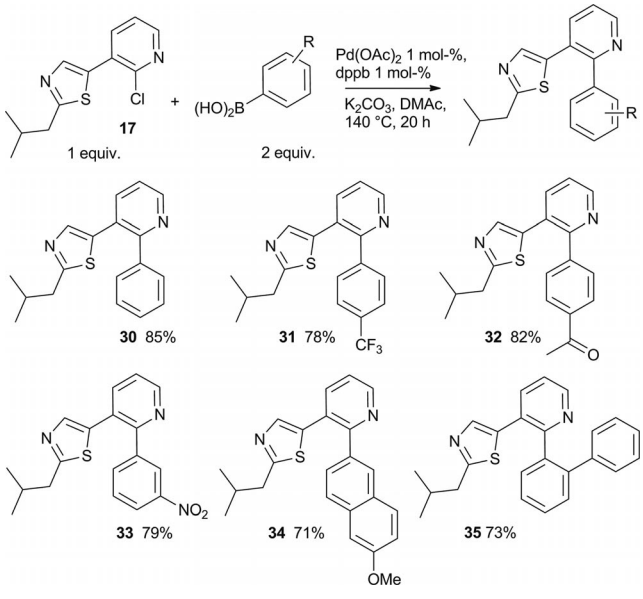
Scheme 3. Direct arylation of 3-bromo-2-chloropyridine.



Scheme 5. Suzuki coupling with **7**.

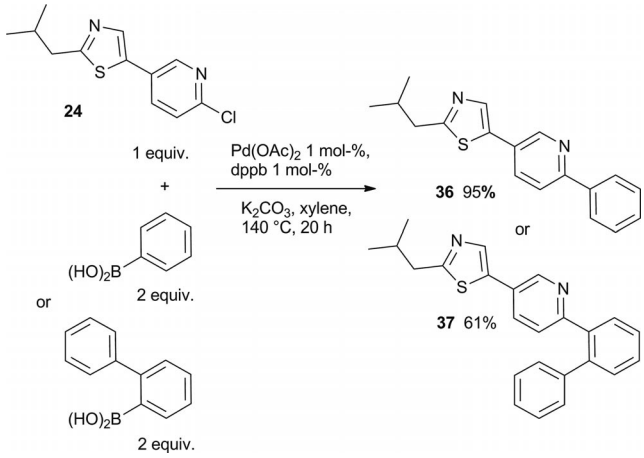


Scheme 4. Direct arylation of 5-bromo-2-chloropyridine.



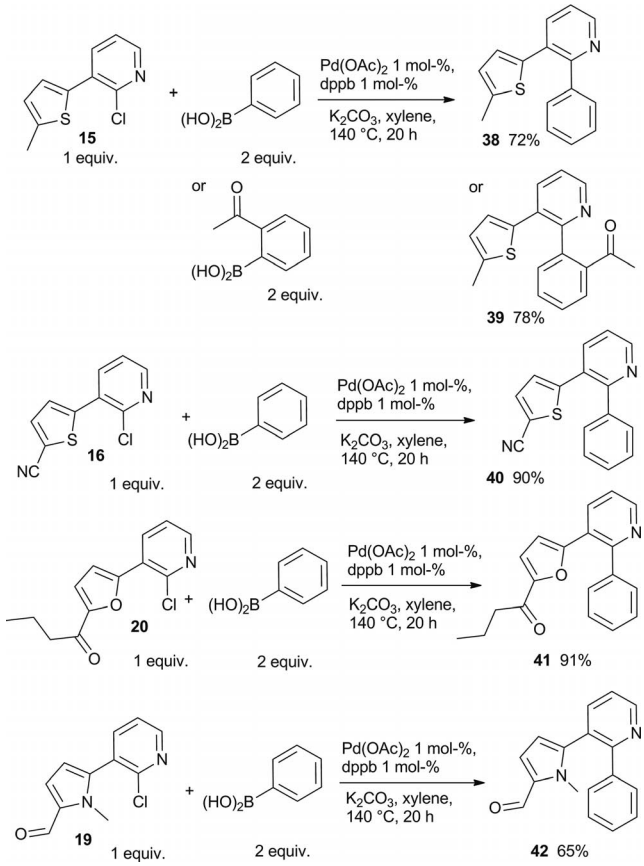
Scheme 6. Suzuki coupling with **17**.

noted that functionalised arylboronic acids are tolerated. The coupling of **7** with 2-acetylbenzeneboronic acid or 4-(trifluoromethyl)benzeneboronic acid gave **28** and **29** in 71 and 67% yields, respectively.



Scheme 7. Suzuki coupling with **24**.

The more congested 2-chloropyridine derivative **17** was found to have a similar reactivity to **7** (Scheme 6). Six benzeneboronic acid derivatives were employed, and in all cases, the desired coupling products **30**–**35** were produced in high yields. The presence of trifluoromethyl, acetyl or nitro substituents on the arylboronic acid was found to have a negligible influence on the yields. Even the use of more congested 2-phenylbenzeneboronic acid was successful in giving **35** in 72% yield.



Scheme 8. Suzuki coupling with **15**, **16**, **19** or **20**.

As expected, the reactivity of **24** was similar to **7** or **17** (Scheme 7). In the presence of benzene boronic acid or 2-phenylbenzeneboronic acid, the desired products **36** and **37** were obtained in 95 and 61% yields, respectively.

Next, benzene boronic acid and 2-acetybenzeneboronic acid were treated with 2-chloro-3-(5-methylthiophen-2-yl)-pyridine **15** (Scheme 8, top). Once again, the desired coupling products **38** and **39** were obtained in high yields of 72 and 78%. Compounds **40** and **41** were isolated in 90 and 91% yields, respectively, from 5-(2-chloropyridin-3-yl)thiophene-2-carbonitrile (**16**) or 1-[5-(2-chloropyridin-3-yl)-furan-2-yl]butan-1-one (**20**) and benzene boronic acid (Scheme 8, middle). Finally, the reaction of **19** with benzene boronic acid gave **42** in 65% yield due to a moderate conversion of this chloropyridine derivative (Scheme 8, bottom).

Conclusion

These results demonstrate that the use of an equimolar amount of commercially available 3-, 4- or 5-bromo-2-chloropyridines and heteroarenes allows the formation of the mono-heteroarylated pyridines with selective activation of the C–Br bond in good yields. A relatively low loading (1 mol-%) of an air-stable catalyst associated to a cheap and nontoxic base can be employed for these couplings. This procedure compares favourably with previously reported procedures for the synthesis of such compounds. With our procedure, satisfactory results were obtained in the presence of a wide variety of heteroarenes. We also observed that the 2-arylpyridines can also be easily obtained from the heteroarylated 2-chloropyridines by means of Suzuki coupling by using 1 mol-% $Pd(OAc)_2$ and dppb as the catalyst system. These sequential reactions allow access to a very wide variety of 2-arylpyridine derivatives with easily tuneable electronic and steric properties, which should be useful to material chemists.

Experimental Section

General: DMAc (99%) was purchased from Acros. Bromo-2-chloropyridines, KOAc (99%), K_2CO_3 (99%), $[\{Pd(C_3H_5)Cl\}_2]$ (56.5%) and dppb (98%) were purchased from Alfa Aesar. These compounds were not purified before use.

General Procedure for Direct Arylations Leading to Products 1–26: As a typical experiment, the reaction of the aryl bromide (1 mmol), heteroarene (1 mmol) and KOAc or Cs_2CO_3 (2 mmol) (see Schemes 1–8) at 150 °C over 16 h in DMAc (3 mL) in the presence of $Pd(OAc)_2$/dppb (1 mol-%) under argon afforded the coupling product after evaporation of the solvent and purification on silica gel.

2-Chloro-4-(5-methylthiophen-2-yl)pyridine (1): From 4-bromo-2-chloropyridine (0.193 g, 1 mmol) and 2-methylthiophene (0.098 g, 1 mmol) compound **1** was obtained in 65% (0.136 g) yield. ^1H

NMR (400 MHz, $CDCl_3$): δ = 8.32 (d, J = 5.1 Hz, 1 H), 7.45 (s, 1 H), 7.35–7.30 (m, 2 H), 6.81 (d, J = 3.8 Hz, 1 H), 2.56 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.2, 149.9, 144.6, 143.4, 137.1, 126.9, 126.3, 119.4, 118.2, 15.6 ppm. $C_{10}H_8ClNS$ (209.70): calcd. C 57.28, H 3.85, N 6.68; found C 57.01, H 3.98, N 6.50.

2-Chloro-4-thiophen-2-ylpyridine (2): From 4-bromo-2-chloropyridine (0.193 g, 1 mmol) and thiophene (0.084 g, 1 mmol) compound **2** was obtained in 56% (0.109 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (d, J = 5.1 Hz, 1 H), 7.48 (m, 2 H), 7.39 (d, J = 5.1 Hz, 1 H), 7.33 (d, J = 5.1 Hz, 1 H), 7.08 (t, J = 3.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.8, 149.5, 143.8, 139.1, 128.0, 127.5, 125.6, 119.5, 118.2 ppm. C_9H_6ClNS (195.67): calcd. C 55.24, H 3.09, N 7.16; found C 55.18, H 3.01, N 7.02.

2-Chloro-4-(5-chlorothiophen-2-yl)pyridine (3): From 4-bromo-2-chloropyridine (0.193 g, 1 mmol) and 2-chlorothiophene (0.119 g, 1 mmol) compound **3** was obtained in 71% (0.163 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (d, J = 5.1 Hz, 1 H), 7.34 (s, 1 H), 7.25–7.20 (m, 2 H), 6.89 (d, J = 3.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.5, 150.2, 143.5, 137.9, 133.0, 127.8, 125.6, 119.6, 118.2 ppm. $C_9H_5Cl_2NS$ (230.11): calcd. C 46.98, H 2.19, N 6.09; found C 46.80, H 2.04, N 5.89.

1-[4-Chloro-5-(2-chloropyridin-4-yl)thiophen-2-yl]ethanone (4): From 4-bromo-2-chloropyridine (0.193 g, 1 mmol) and 2-acetyl-4-chlorothiophene (0.161 g, 1 mmol) compound **4** was obtained in 80% (0.218 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.40 (d, J = 5.1 Hz, 1 H), 7.61 (s, 1 H), 7.52 (s, 1 H), 7.47 (d, J = 5.1 Hz, 1 H), 2.51 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.5, 152.3, 150.2, 143.1, 141.7, 139.2, 133.7, 124.4, 122.9, 121.2, 26.5 ppm. $C_{11}H_7Cl_2NOS$ (272.15): calcd. C 48.55, H 2.59, N 5.15; found C 48.37, H 2.50, N 5.39.

2-Chloro-4-[5-(2-methyl-1,3-dioxolan-2-yl)thiophen-2-yl]pyridine (5): From 4-bromo-2-chloropyridine (0.193 g, 1 mmol) and 2-methyl-2-thiophen-2-yl-1,3-dioxolane (0.170 g, 1 mmol) compound **5** was obtained in 51% (0.143 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34 (d, J = 5.1 Hz, 1 H), 7.48 (s, 1 H), 7.40–7.33 (m, 2 H), 7.08 (d, J = 3.8 Hz, 1 H), 4.08 (m, 4 H), 1.80 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.3, 150.7, 150.1, 144.4, 138.9, 126.1, 125.5, 119.8, 118.5, 106.9, 65.1, 27.4 ppm. $C_{13}H_{12}ClNO_2S$ (281.76): calcd. C 55.42, H 4.29, N 4.97; found C 55.40, H 4.37, N 5.30.

4-Benzo[*b*]thiophen-2-yl-2-chloropyridine (6): From 4-bromo-2-chloropyridine (0.193 g, 1 mmol) and benzothiophene (0.134 g, 1 mmol) compound **6** was obtained in 57% (0.140 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42 (d, J = 5.1 Hz, 1 H), 7.90–7.80 (m, 2 H), 7.76 (s, 1 H), 7.62 (s, 1 H), 7.50 (d, J = 5.2 Hz, 1 H), 7.45–7.38 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.2, 149.9, 144.2, 139.8, 139.7, 139.0, 125.7, 124.9, 124.2, 122.8, 122.3, 120.5, 119.0 ppm. $C_{13}H_8ClNS$ (245.73): calcd. C 63.54, H 3.28, N 5.70; found C 63.67, H 3.17, N 5.49.

2-Chloro-4-(2-isobutylthiazol-5-yl)pyridine (7): From 4-bromo-2-chloropyridine (0.193 g, 1 mmol) and 2-isobutylthiazole (0.141 g, 1 mmol) compound **7** was obtained in 79% (0.199 g) yield. ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 8.29 (d, J = 5.1 Hz, 1 H), 7.98 (s, 1 H), 7.37 (s, 1 H), 7.26 (d, J = 5.1 Hz, 1 H), 2.85 (d, J = 7.5 Hz, 2 H), 2.04 (m, 1 H), 0.96 (d, J = 7.5 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.4, 152.2, 150.0, 141.7, 140.5, 134.0, 120.5, 119.1, 42.4, 29.6, 22.0 ppm. $C_{12}H_{13}ClN_2S$ (252.76): calcd. C 57.02, H 5.18, N 11.08; found C 57.14, H 5.11, N 10.87.

1-[5-(2-Chloropyridin-4-yl)furan-2-yl]butan-1-one (8): From 4-bromo-2-chloropyridine (0.193 g, 1 mmol) and 1-(furan-2-yl)butan-1-one (0.138 g, 1 mmol) compound **8** was obtained in 51% (0.127 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.43 (d, J = 5.1 Hz, 1 H), 7.66 (s, 1 H), 7.55 (d, J = 5.1 Hz, 1 H), 7.26 (d, J = 3.5 Hz, 1 H), 7.00 (d, J = 3.5 Hz, 1 H), 2.87 (t, J = 7.6 Hz, 2 H), 1.78 (sext., J = 7.6 Hz, 2 H), 1.03 (t, J = 7.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.3, 153.2, 152.6, 152.5, 150.3, 139.3, 118.9, 118.1, 117.3, 111.3, 40.4, 17.6, 13.7 ppm. $C_{13}H_{12}ClNO_2$ (249.69): calcd. C 62.53, H 4.84, N 5.61; found C 62.59, H 4.90, N 5.42.

Methyl 5-(2-Chloropyridin-4-yl)-2-methylfuran-3-carboxylate (9): From 4-bromo-2-chloropyridine (0.193 g, 1 mmol) and methyl 2-methylfuran-3-carboxylate (0.140 g, 1 mmol) compound **9** was obtained in 61% (0.153 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29 (d, J = 5.1 Hz, 1 H), 7.45 (s, 1 H), 7.31 (d, J = 5.1 Hz, 1 H), 7.08 (s, 1 H), 3.79 (s, 3 H), 2.60 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.6, 161.0, 152.3, 150.1, 147.8, 139.5, 117.8, 116.3, 115.9, 110.6, 51.6, 14.0 ppm. $C_{12}H_{10}ClNO_3$ (251.67): calcd. C 57.27, H 4.01, N 5.57; found C 57.34, H 3.87, N 5.80.

5-(2-Chloropyridin-4-yl)furan-2-ylmethyl Acetate (10): From 4-bromo-2-chloropyridine (0.193 g, 1 mmol) and furfuryl acetate (0.140 g, 1 mmol) compound **10** was obtained in 57% (0.143 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.35 (d, J = 5.1 Hz, 1 H), 7.56 (s, 1 H), 7.42 (d, J = 5.1 Hz, 1 H), 6.87 (s, 1 H), 6.54 (s, 1 H), 5.10 (s, 2 H), 2.11 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.1, 152.0, 151.2, 150.1, 149.7, 139.5, 117.7, 116.3, 112.7, 110.3, 57.5, 20.5 ppm. $C_{12}H_{10}ClNO_3$ (251.67): calcd. C 57.27, H 4.01, N 5.57; found C 57.14, H 4.04, N 5.48.

2-Chloro-4-(2-ethylbenzofuran-3-yl)pyridine (11): From 4-bromo-2-chloropyridine (0.193 g, 1 mmol) and 2-ethylbenzofuran (0.146 g, 1 mmol) compound **11** was obtained in 27% (0.069 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.41 (d, J = 5.1 Hz, 1 H), 7.50 (d, J = 8.2 Hz, 1 H), 7.43 (d, J = 8.2 Hz, 1 H), 7.38 (s, 1 H), 7.30–7.17 (m, 3 H), 2.86 (q, J = 7.6 Hz, 2 H), 1.33 (t, J = 7.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.2, 154.1, 152.2, 150.0, 144.3, 127.2, 124.4, 123.7, 123.3, 122.2, 118.9, 113.1, 111.3, 20.5, 12.7 ppm. $C_{15}H_{12}ClNO$ (257.71): calcd. C 69.91, H 4.69, N 5.43; found C 69.98, H 4.57, N 5.09.

2-Chloro-4-(1-methylpyrrol-2-yl)pyridine (12): From 4-bromo-2-chloropyridine (0.193 g, 1 mmol) and 1-methylpyrrole (0.081 g, 1 mmol) compound **12** was obtained in 62% (0.119 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26 (d, J = 5.1 Hz, 1 H), 7.26 (s, 1 H), 7.18 (d, J = 5.1 Hz, 1 H), 6.72 (s, 1 H), 6.38 (s, 1 H), 6.15 (s, 1 H), 3.68 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.1, 148.8, 142.7, 129.5, 126.4, 121.0, 119.8, 111.2, 108.1, 35.0 ppm. $C_{10}H_9ClN_2$ (192.64): calcd. C 62.35, H 4.71, N 14.54; found C 62.51, H 4.52, N 14.71.

5-(2-Chloropyridin-4-yl)-1-methylpyrrole-2-carbaldehyde (13): From 4-bromo-2-chloropyridine (0.193 g, 1 mmol) and 1-methylpyrrole-2-carbaldehyde (0.109 g, 1 mmol) compound **13** was obtained in 60% (0.132 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.63 (s, 1 H), 8.46 (d, J = 5.1 Hz, 1 H), 7.38 (s, 1 H), 7.27 (d, J = 5.1 Hz, 1 H), 6.99 (d, J = 3.9 Hz, 1 H), 6.43 (d, J = 3.9 Hz, 1 H), 3.97 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.2, 152.1, 149.9, 141.6, 139.1, 134.3, 124.0, 123.6, 121.8, 112.1, 34.5 ppm. $C_{11}H_9ClN_2O$ (220.65): calcd. C 59.88, H 4.11, N 12.70; found C 59.98, H 4.24, N 12.58.

2-(2-Chloropyridin-4-yl)benzooxazole (14): From 4-bromo-2-chloropyridine (0.193 g, 1 mmol) and benzooxazole (0.119 g, 1 mmol) compound **14** was obtained in 49% (0.113 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.59 (d, J = 5.1 Hz, 1 H), 8.14 (s, 1 H), 8.02 (d, J = 5.1 Hz, 1 H), 7.84 (d, J = 7.0 Hz, 1 H), 7.64 (d, J = 7.0 Hz, 1 H), 7.50–7.40 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.9, 152.3, 150.5, 150.3, 141.2, 136.8, 126.4, 125.0,

121.4, 120.5, 119.3, 110.7 ppm. $C_{12}H_7ClN_2O$ (230.65): calcd. C 62.49, H 3.06, N 12.15; found C 62.29, H 3.01, N 12.41.

2-Chloro-3-(5-methylthiophen-2-yl)pyridine (15): From 3-bromo-2-chloropyridine (0.193 g, 1 mmol) and 2-methylthiophene (0.098 g, 1 mmol) compound **15** was obtained in 84% (0.176 g) yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.32 (dd, J = 4.7, 1.8 Hz, 1 H), 7.83 (dd, J = 7.7, 1.9 Hz, 1 H), 7.30–7.25 (m, 2 H), 6.83–6.79 (m, 1 H), 2.56 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.1, 147.1, 141.6, 138.4, 134.9, 129.8, 127.9, 125.2, 121.9, 14.7 ppm. $C_{10}H_8ClNS$ (209.70): calcd. C 57.28, H 3.85, N 6.68; found C 57.38, H 3.95, N 6.58.

5-(2-Chloropyridin-3-yl)thiophene-2-carbonitrile (16): From 3-bromo-2-chloropyridine (0.193 g, 1 mmol) and thiophene-2-carbonitrile (0.109 g, 1 mmol) compound **16** was obtained in 80% (0.176 g) yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.38 (dd, J = 4.7, 1.8 Hz, 1 H), 7.79 (d, J = 7.7 Hz, 1 H), 7.57 (d, J = 3.5 Hz, 1 H), 7.34 (d, J = 3.5 Hz, 1 H), 7.29 (dd, J = 7.7, 4.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.7, 149.1, 145.0, 139.5, 137.3, 128.4, 128.0, 122.7, 113.7, 111.1 ppm. $C_{10}H_5ClN_2S$ (220.68): calcd. C 54.43, H 2.28, N 12.69; found C 54.37, H 2.19, N 12.47.

2-Chloro-3-(2-isobutylthiazol-5-yl)pyridine (17): From 3-bromo-2-chloropyridine (0.193 g, 1 mmol) and 2-isobutylthiazole (0.141 g, 1 mmol) compound **17** was obtained in 90% (0.227 g) yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.30 (d, J = 4.7 Hz, 1 H), 7.84 (s, 1 H), 7.77 (d, J = 7.7 Hz, 1 H), 7.22 (dd, J = 7.7, 4.8 Hz, 1 H), 2.86 (d, J = 7.5 Hz, 2 H), 2.10 (m, 1 H), 0.96 (d, J = 7.5 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.4, 148.4, 147.9, 141.6, 138.5, 131.3, 126.9, 121.8, 41.6, 29.0, 21.6 ppm. $C_{12}H_{13}ClN_2S$ (252.76): calcd. C 57.02, H 5.18, N 11.08; found C 57.01, H 5.27, N 10.89.

2-Chloro-3-(2-isopropyl-4-methylthiazol-5-yl)pyridine (18): From 3-bromo-2-chloropyridine (0.193 g, 1 mmol) and 2-isopropyl-4-methylthiazole (0.141 g, 1 mmol) compound **18** was obtained in 88% (0.222 g) yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.35 (d, J = 4.7 Hz, 1 H), 7.62 (d, J = 7.7 Hz, 1 H), 7.23 (dd, J = 7.7, 4.7 Hz, 1 H), 3.24 (sept., J = 7.5 Hz, 1 H), 2.20 (s, 3 H), 1.35 (d, J = 7.5 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.1, 151.0, 149.8, 148.9, 140.8, 127.8, 124.0, 121.5, 33.0, 22.7, 15.5 ppm. $C_{12}H_{13}ClN_2S$ (252.76): calcd. C 57.02, H 5.18, N 11.08; found C 57.08, H 5.04, N 11.20.

5-(2-Chloropyridin-3-yl)-1-methylpyrrole-2-carbaldehyde (19): From 3-bromo-2-chloropyridine (0.193 g, 1 mmol) and 1-methylpyrrole-2-carbaldehyde (0.109 g, 1 mmol) compound **19** was obtained in 82% (0.180 g) yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.57 (s, 1 H), 8.44 (d, J = 4.7 Hz, 1 H), 7.63 (d, J = 7.7 Hz, 1 H), 7.30 (dd, J = 7.7, 4.8 Hz, 1 H), 6.95 (d, J = 3.9 Hz, 1 H), 6.23 (d, J = 3.9 Hz, 1 H), 3.71 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.0, 151.5, 150.2, 141.0, 138.3, 132.8, 127.3, 123.7, 122.3, 111.7, 33.9 ppm. $C_{11}H_9ClN_2O$ (220.65): calcd. C 59.88, H 4.11, N 12.70; found C 59.78, H 4.04, N 12.88.

1-[5-(2-Chloropyridin-3-yl)furan-2-yl]butan-1-one (20): From 3-bromo-2-chloropyridine (0.193 g, 1 mmol) and 1-(furan-2-yl)butan-1-one (0.138 g, 1 mmol) compound **20** was obtained in 78% (0.194 g) yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.37 (d, J = 4.7 Hz, 1 H), 8.30 (d, J = 7.7 Hz, 1 H), 7.37 (dd, J = 7.7, 4.8 Hz, 1 H), 7.35 (d, J = 3.5 Hz, 1 H), 7.27 (d, J = 3.5 Hz, 1 H), 2.85 (t, J = 7.6 Hz, 2 H), 1.78 (sext., J = 7.6 Hz, 2 H), 1.01 (t, J = 7.6 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.3, 152.2, 151.2, 148.8, 147.4, 137.0, 125.2, 122.7, 118.5, 113.9, 40.5, 17.8, 13.9 ppm. $C_{13}H_{12}ClNO_2$ (249.69): calcd. C 62.53, H 4.84, N 5.61; found C 62.40, H 4.81, N 5.79.

2-Chloro-5-(5-methylthiophen-2-yl)pyridine (21): From 5-bromo-2-chloropyridine (0.193 g, 1 mmol) and 2-methylthiophene (0.098 g, 1 mmol) compound **21** was obtained in 88% (0.184 g) yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.55 (s, 1 H), 7.74 (d, J = 8.2 Hz, 1 H), 7.29 (d, J = 8.2 Hz, 1 H), 7.12 (d, J = 5.2 Hz, 1 H), 6.75 (d, J = 5.2 Hz, 1 H), 2.51 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.7, 146.4, 141.7, 136.7, 135.5, 130.0, 126.9, 124.9, 124.5, 15.7 ppm. $C_{10}H_8ClNS$ (209.70): calcd. C 57.28, H 3.85, N 6.68; found C 57.39, H 3.70, N 6.89.

2-Chloro-5-(5-chlorothiophen-2-yl)pyridine (22): From 5-bromo-2-chloropyridine (0.193 g, 1 mmol) and 2-chlorothiophene (0.119 g, 1 mmol) compound **22** was obtained in 91% (0.209 g) yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.47 (s, 1 H), 7.66 (d, J = 8.2 Hz, 1 H), 7.27 (d, J = 8.2 Hz, 1 H), 7.05 (d, J = 5.2 Hz, 1 H), 6.87 (d, J = 5.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.4, 146.2, 137.4, 135.3, 131.1, 128.7, 127.5, 124.4, 124.0 ppm. $C_9H_5Cl_2NS$ (230.11): calcd. C 46.98, H 2.19, N 6.09; found C 46.99, H 2.34, N 6.40.

2-Chloro-5-[5-(2-methyl-1,3-dioxolan-2-yl)thiophen-2-yl]pyridine (23): From 5-bromo-2-chloropyridine (0.193 g, 1 mmol) and 2-methyl-2-thiophen-2-yl-1,3-dioxolane (0.170 g, 1 mmol) compound **23** was obtained in 71% (0.200 g) yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.53 (s, 1 H), 7.71 (d, J = 8.2 Hz, 1 H), 7.25 (d, J = 8.2 Hz, 1 H), 7.12 (d, J = 5.2 Hz, 1 H), 6.97 (d, J = 5.2 Hz, 1 H), 3.95 (m, 4 H), 1.73 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.0, 147.8, 145.4, 137.3, 134.5, 128.4, 124.3, 123.4, 123.3, 106.0, 64.0, 26.4 ppm. $C_{13}H_{12}ClNO_2S$ (281.76): calcd. C 55.42, H 4.29, N 4.97; found C 55.58, H 4.40, N 5.15.

2-Chloro-5-(2-isobutylthiazol-5-yl)pyridine (24): From 5-bromo-2-chloropyridine (0.193 g, 1 mmol) and 2-isobutylthiazole (0.141 g, 1 mmol) compound **24** was obtained in 85% (0.214 g) yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.54 (s, 1 H), 7.85 (s, 1 H), 7.77 (d, J = 8.2 Hz, 1 H), 7.35 (d, J = 8.2 Hz, 1 H), 2.89 (d, J = 7.6 Hz, 2 H), 2.14 (m, 1 H), 1.01 (d, J = 7.6 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.3, 150.6, 147.1, 139.1, 136.2, 133.2, 126.9, 124.5, 42.6, 29.8, 22.3 ppm. $C_{12}H_{13}ClN_2S$ (252.76): calcd. C 57.02, H 5.18, N 11.08; found C 56.87, H 5.14, N 11.39.

Methyl 5-(6-Chloropyridin-3-yl)-2-methylfuran-3-carboxylate (25): From 5-bromo-2-chloropyridine (0.193 g, 1 mmol) and methyl 2-methylfuran-3-carboxylate (0.140 g, 1 mmol) compound **25** was obtained in 80% (0.201 g) yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.65 (s, 1 H), 7.84 (d, J = 8.2 Hz, 1 H), 7.35 (d, J = 8.2 Hz, 1 H), 6.97 (s, 1 H), 3.85 (s, 3 H), 2.65 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.9, 159.9, 150.0, 147.8, 144.9, 133.4, 125.1, 124.2, 115.5, 107.5, 51.5, 14.0 ppm. $C_{12}H_{10}ClNO_3$ (251.67): calcd. C 57.27, H 4.01, N 5.57; found C 57.08, H 3.89, N 5.57.

2-Chloro-5-(1-methylpyrrol-2-yl)pyridine (26): From 5-bromo-2-chloropyridine (0.193 g, 1 mmol) and 1-methylpyrrole (0.081 g, 1 mmol) compound **26** was obtained in 68% (0.131 g) yield. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.36 (d, J = 2.3 Hz, 1 H), 7.59 (dd, J = 8.2 and 2.3 Hz, 1 H), 7.27 (d, J = 8.2 Hz, 1 H), 6.70 (m, 1 H), 6.22 (m, 1 H), 6.15 (m, 1 H), 1.44 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.4, 148.7, 138.1, 129.4, 128.2, 125.1, 123.9, 110.2, 108.4, 35.1 ppm. $C_{10}H_9ClN_2$ (192.64): calcd. C 62.35, H 4.71, N 14.54; found C 62.18, H 4.58, N 14.44.

General Procedure for Suzuki Coupling Reactions Leading to Products 27–42: In a typical experiment, the reaction of the heteroarylated pyridyl chloride (1 mmol), aryl boronic acid (2 mmol) and K_2CO_3 (2 mmol) at 140 °C over 20 h in xylene (3 mL) in the presence of $Pd(OAc)_2$/dppb (1 mol-%) under argon afforded the coupling product after evaporation of the solvent and purification on silica gel.

4-(2-Isobutylthiazol-5-yl)-2-phenylpyridine (27): From **7** (0.253 g, 1 mmol) and benzeneboronic acid (0.244 g, 2 mmol) compound **27**

was obtained in 81% (0.238 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.59 (d, J = 4.7 Hz, 1 H), 7.99 (s, 1 H), 7.94 (d, J = 7.2 Hz, 2 H), 7.73 (s, 1 H), 7.43 (t, J = 7.2 Hz, 2 H), 7.36 (t, J = 7.5 Hz, 1 H), 7.27 (d, J = 4.7 Hz, 1 H), 2.84 (d, J = 7.6 Hz, 2 H), 2.09 (m, 1 H), 0.96 (d, J = 7.6 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.8, 158.4, 150.3, 139.9, 139.8, 139.0, 136.0, 129.3, 128.8, 127.6, 119.0, 117.6, 42.7, 29.9, 22.3 ppm. $C_{18}H_{18}N_2S$ (294.41): calcd. C 73.43, H 6.16, N 9.51; found C 73.27, H 6.08, N 9.28.

1-{2-[4-(2-Isobutylthiazol-5-yl)pyridin-2-yl]phenyl}ethanone (28): From **7** (0.253 g, 1 mmol) and 2-acetylbenzeneboronic acid (0.328 g, 2 mmol) compound **28** was obtained in 71% (0.239 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54 (d, J = 4.7 Hz, 1 H), 8.00 (s, 1 H), 7.62 (s, 1 H), 7.58 (d, J = 7.3 Hz, 1 H), 7.52–7.44 (m, 2 H), 7.42 (t, J = 6.8 Hz, 1 H), 7.31 (d, J = 4.1 Hz, 1 H), 2.85 (d, J = 7.5 Hz, 2 H), 2.23 (s, 3 H), 2.09 (m, 1 H), 0.97 (d, J = 7.5 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.8, 158.5, 149.6, 141.4, 139.9, 139.7, 138.2, 135.4, 130.2, 129.0, 128.7, 127.5, 119.2, 119.0, 42.5, 30.2, 29.6, 22.0 ppm. $C_{20}H_{20}N_2OS$ (336.45): calcd. C 71.40, H 5.99, N 8.33; found C 71.19, H 6.10, N 8.04.

4-(2-Isobutylthiazol-5-yl)-2-(4-trifluoromethylphenyl)pyridine (29): From **7** (0.253 g, 1 mmol) and 4-(trifluoromethyl)benzeneboronic acid (0.380 g, 2 mmol) compound **29** was obtained in 67% (0.243 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.63 (d, J = 5.1 Hz, 1 H), 8.05 (d, J = 8.1 Hz, 2 H), 8.01 (s, 1 H), 7.75 (s, 1 H), 7.67 (d, J = 8.1 Hz, 2 H), 7.33 (d, J = 5.1 Hz, 1 H), 2.84 (d, J = 7.5 Hz, 2 H), 2.09 (m, 1 H), 0.92 (d, J = 7.5 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.8, 156.8, 150.5, 142.2, 140.2, 140.1, 135.6, 131.2 (q, J = 32.2 Hz), 127.3, 125.7 (q, J = 3.7 Hz), 124.0 (q, J = 272.2 Hz), 119.8, 117.8, 42.7, 29.8, 22.2 ppm. $C_{19}H_{17}F_3N_2S$ (362.41): calcd. C 62.97, H 4.73, N 7.73; found C 63.08, H 4.69, N 7.60.

3-(2-Isobutylthiazol-5-yl)-2-phenylpyridine (30): From **17** (0.253 g, 1 mmol) and benzeneboronic acid (0.244 g, 2 mmol) compound **30** was obtained in 85% (0.250 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.64 (d, J = 4.7 Hz, 1 H), 7.78 (d, J = 7.7 Hz, 1 H), 7.44–7.20 (m, 7 H), 2.86 (d, J = 7.5 Hz, 2 H), 2.10 (m, 1 H), 0.96 (d, J = 7.5 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.6, 157.1, 148.3, 140.3, 138.8, 137.6, 134.6, 128.7, 127.7, 127.4, 125.4, 121.4, 41.4, 29.0, 21.4 ppm. $C_{18}H_{18}N_2S$ (294.41): calcd. C 73.43, H 6.16, N 9.51; found C 73.50, H 6.24, N 9.38.

3-(2-Isobutylthiazol-5-yl)-2-(4-trifluoromethylphenyl)pyridine (31): From **17** (0.253 g, 1 mmol) and 4-(trifluoromethyl)benzeneboronic acid (0.380 g, 2 mmol) compound **31** was obtained in 78% (0.282 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.72 (d, J = 4.7 Hz, 1 H), 7.85 (d, J = 7.7 Hz, 1 H), 7.60 (d, J = 8.2 Hz, 2 H), 7.55 (d, J = 8.2 Hz, 2 H), 7.45 (s, 1 H), 7.37 (dd, J = 7.7, 4.8 Hz, 1 H), 2.80 (d, J = 7.5 Hz, 2 H), 2.04 (m, 1 H), 0.96 (d, J = 7.5 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.8, 156.3, 149.2, 143.1, 141.3, 138.7, 134.6, 130.2 (q, J = 32.4 Hz), 129.8, 126.3, 125.1 (q, J = 3.8 Hz), 123.9 (q, J = 273.9 Hz), 122.8, 42.2, 29.7, 22.0 ppm. $C_{19}H_{17}F_3N_2S$ (362.41): calcd. C 62.97, H 4.73, N 7.73; found C 63.07, H 4.80, N 7.58.

1-{4-[3-(2-Isobutylthiazol-5-yl)pyridin-2-yl]phenyl}ethanone (32): From **17** (0.253 g, 1 mmol) and 4-acetylbenzeneboronic acid (0.328 g, 2 mmol) compound **32** was obtained in 82% (0.276 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.62 (d, J = 4.7 Hz, 1 H), 7.84 (d, J = 8.2 Hz, 2 H), 7.76 (d, J = 7.7 Hz, 1 H), 7.46 (d, J = 8.2 Hz, 2 H), 7.38 (s, 1 H), 7.27 (dd, J = 7.7, 4.8 Hz, 1 H), 2.72 (d, J = 7.5 Hz, 2 H), 2.53 (s, 3 H), 1.96 (m, 1 H), 0.86 (d, J = 7.5 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.7, 170.7, 155.7, 148.2, 143.2, 140.3, 137.6, 135.7, 133.7, 128.8, 127.2, 125.4, 121.7, 41.3, 28.7, 25.7, 21.1 ppm. $C_{20}H_{20}N_2OS$ (336.45): calcd. C 71.40, H 5.99, N 8.33; found C 71.47, H 6.14, N 8.20.

3-(2-Isobutylthiazol-5-yl)-2-(3-nitrophenyl)pyridine (33): From **17** (0.253 g, 1 mmol) and 3-nitrobenzeneboronic acid (0.334 g, 2 mmol) compound **33** was obtained in 79% (0.268 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.65 (s, 1 H), 8.20 (s, 1 H), 8.13 (d, J = 7.5 Hz, 1 H), 7.78 (d, J = 7.8 Hz, 1 H), 7.70 (d, J = 7.5 Hz, 1 H), 7.42 (t, J = 7.5 Hz, 1 H), 7.40–7.35 (m, 2 H), 2.72 (d, J = 7.5 Hz, 2 H), 1.94 (m, 1 H), 0.85 (d, J = 7.5 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.1, 155.2, 149.5, 148.1, 141.5, 141.2, 139.0, 135.6, 134.2, 129.2, 126.4, 124.7, 123.3, 123.1, 42.3, 29.8, 22.1 ppm. $C_{18}H_{17}N_3O_2S$ (339.41): calcd. C 63.70, H 5.05, N 12.38; found C 63.79, H 5.14, N 12.52.

3-(2-Isobutylthiazol-5-yl)-2-(6-methoxynaphthalen-2-yl)pyridine (34): From **17** (0.253 g, 1 mmol) and 6-methyoxynaphthalene-2-boronic acid (0.404 g, 2 mmol) compound **34** was obtained in 71% (0.265 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.64 (d, J = 4.7 Hz, 1 H), 7.83 (s, 1 H), 7.76 (d, J = 7.7 Hz, 1 H), 7.62–7.58 (m, 2 H), 7.44 (s, 1 H), 7.39 (d, J = 8.0 Hz, 1 H), 7.27 (dd, J = 7.7, 4.8 Hz, 1 H), 7.08–7.04 (m, 2 H), 3.85 (s, 3 H), 2.66 (d, J = 7.5 Hz, 2 H), 1.89 (m, 1 H), 0.81 (d, J = 7.5 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.6, 158.2, 157.8, 149.2, 141.1, 138.5, 135.5, 134.7, 134.4, 130.0, 129.1, 128.6, 127.5, 126.6, 126.3, 122.0, 119.0, 105.6, 55.3, 42.2, 29.8, 22.1 ppm. $C_{23}H_{22}N_2OS$ (374.50): calcd. C 73.76, H 5.92, N 7.48; found C 73.50, H 6.04, N 7.64.

2-Biphenyl-2-yl-3-(2-isobutylthiazol-5-yl)pyridine (35): From **17** (0.253 g, 1 mmol) and 2-phenylbenzeneboronic acid (0.396 g, 2 mmol) compound **35** was obtained in 73% (0.270 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.57 (d, J = 4.7 Hz, 1 H), 7.52–7.10 (m, 6 H), 7.01 (t, J = 8.0 Hz, 1 H), 6.94 (t, J = 8.0 Hz, 2 H), 6.70 (s, 1 H), 6.64 (d, J = 8.0 Hz, 2 H), 2.63 (d, J = 7.5 Hz, 2 H), 1.91 (m, 1 H), 0.88 (d, J = 7.5 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 158.2, 148.8, 141.3, 141.0, 140.7, 138.8, 137.3, 134.8, 131.0, 130.1, 129.5, 129.3, 128.2, 128.1, 127.8, 126.8, 122.7, 42.5, 30.1, 22.6 ppm. $C_{24}H_{22}N_2S$ (370.51): calcd. C 77.80, H 5.98, N 7.56; found C 77.91, H 5.94, N 7.50.

5-(2-Isobutylthiazol-5-yl)-2-phenylpyridine (36): From **24** (0.253 g, 1 mmol) and benzeneboronic acid (0.244 g, 2 mmol) compound **36** was obtained in 95% (0.279 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.86 (d, J = 1.8 Hz, 1 H), 8.01 (d, J = 7.2 Hz, 2 H), 7.91 (s, 1 H), 7.85 (dd, J = 8.3, 2.3 Hz, 1 H), 7.74 (d, J = 8.2 Hz, 1 H), 7.48 (t, J = 7.3 Hz, 2 H), 7.43 (d, J = 7.1 Hz, 1 H), 2.91 (d, J = 7.2 Hz, 2 H), 2.16 (m, 1 H), 1.03 (d, J = 6.6 Hz, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.6, 156.5, 147.2, 138.5, 138.4, 134.6, 134.2, 129.2, 128.8, 126.7, 126.2, 120.3, 42.5, 29.8, 22.2 ppm. $C_{18}H_{18}N_2S$ (294.41): calcd. C 73.43, H 6.16, N 9.51; found C 73.51, H 6.01, N 9.25.

2-Biphenyl-2-yl-5-(2-isobutylthiazol-5-yl)pyridine (37): From **24** (0.253 g, 1 mmol) and 2-phenylbenzeneboronic acid (0.396 g, 2 mmol) compound **37** was obtained in 61% (0.226 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.86 (d, J = 1.9 Hz, 1 H), 7.90 (s, 1 H), 7.79 (dd, J = 5.8, 3.1 Hz, 1 H), 7.60–7.45 (m, 5 H), 7.36–7.28 (m, 3 H), 7.28–7.21 (m, 1 H), 6.95 (d, J = 8.2 Hz, 1 H), 2.95 (d, J = 7.2 Hz, 2 H), 2.19 (m, 1 H), 1.08 (d, J = 6.6 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.6, 158.5, 146.9, 141.2, 140.6, 138.6, 138.5, 134.6, 132.7, 130.6, 130.4, 129.6, 128.7, 128.2, 127.7, 126.8, 125.4, 125.3, 42.5, 29.8, 22.2 ppm. $C_{24}H_{22}N_2S$ (370.51): calcd. C 77.80, H 5.98, N 7.56; found C 77.78, H 5.81, N 7.39.

3-(5-Methylthiophen-2-yl)-2-phenylpyridine (38): From **15** (0.210 g, 1 mmol) and benzeneboronic acid (0.244 g, 2 mmol) compound **38** was obtained in 72% (0.181 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$):

δ = 8.54 (d, J = 4.7 Hz, 1 H), 7.71 (d, J = 7.7 Hz, 1 H), 7.40–7.36 (m, 2 H), 7.28–7.15 (m, 4 H), 6.48 (s, 2 H), 2.36 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.2, 148.1, 141.0, 140.4, 138.7, 128.1, 129.5, 129.4, 128.1, 128.0, 127.4, 125.6, 122.0, 15.3 ppm. $C_{16}H_{13}NS$ (251.35): calcd. C 76.46, H 5.21, N 5.57; found C 76.72, H 5.34, N 5.69.

1-{2-[3-(5-Methylthiophen-2-yl)pyridin-2-yl]phenyl}ethanone (39): From **15** (0.210 g, 1 mmol) and 2-acetylbenzeneboronic acid (0.328 g, 2 mmol) compound **39** was obtained in 78% (0.229 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.48 (s, 1 H), 7.73 (d, J = 7.7 Hz, 1 H), 7.62 (d, J = 7.7 Hz, 1 H), 7.43–7.18 (m, 4 H), 6.45 (s, 1 H), 6.41 (s, 1 H), 2.32 (s, 3 H), 2.12 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.2, 155.7, 146.3, 140.0, 138.9, 138.0, 136.6, 135.7, 130.0, 129.7, 128.4, 127.1, 126.8, 126.1, 124.2, 121.1, 27.3, 13.9 ppm. $C_{18}H_{15}NOS$ (293.38): calcd. C 73.69, H 5.15, N 4.77; found C 73.80, H 5.21, N 5.02.

5-(2-Phenylpyridin-3-yl)thiophene-2-carbonitrile (40): From **16** (0.221 g, 1 mmol) and benzeneboronic acid (0.244 g, 2 mmol) compound **40** was obtained in 90% (0.236 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.71 (d, J = 3.8 Hz, 1 H), 7.81 (d, J = 7.6 Hz, 1 H), 7.48–7.28 (m, 7 H), 6.79 (d, J = 3.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.7, 149.7, 148.7, 139.0, 138.3, 137.4, 129.3, 128.7, 128.3, 127.5, 126.9, 122.2, 113.8, 110.0 ppm. $C_{16}H_{10}N_2S$ (262.33): calcd. C 73.26, H 3.84, N 10.68; found C 73.19, H 3.71, N 10.40.

1-[5-(2-Phenylpyridin-3-yl)furan-2-yl]butan-1-one (41): From **20** (0.250 g, 1 mmol) and benzeneboronic acid (0.244 g, 2 mmol) compound **41** was obtained in 91% (0.265 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.64 (dd, J = 4.7, 1.5 Hz, 1 H), 8.14 (dd, J = 7.9, 1.5 Hz, 1 H), 7.57–7.30 (m, 6 H), 7.02 (d, J = 3.7 Hz, 1 H), 5.96 (d, J = 3.7 Hz, 1 H), 2.57 (t, J = 7.4 Hz, 2 H), 1.76–1.56 (m, 2 H), 0.91 (t, J = 7.4 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.3, 157.1, 154.3, 151.9, 149.1, 140.3, 135.7, 128.6, 128.4, 128.3, 124.2, 122.1, 117.8, 111.8, 40.0, 17.5, 13.7 ppm. $C_{19}H_{17}NO_2$ (291.34): calcd. C 78.33, H 5.88, N 4.81; found C 78.50, H 6.07, N 5.08.

1-Methyl-5-(2-phenylpyridin-3-yl)pyrrole-2-carbaldehyde (42): From **19** (0.221 g, 1 mmol) and benzeneboronic acid (0.244 g, 2 mmol) compound **42** was obtained in 65% (0.170 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.48 (s, 1 H), 8.75 (d, J = 4.7 Hz, 1 H), 7.70 (d, J = 7.7 Hz, 1 H), 7.45–7.20 (m, 6 H), 6.97 (d, J = 3.9 Hz, 1 H), 6.27 (d, J = 3.9 Hz, 1 H), 3.23 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 179.4, 157.6, 151.3, 141.2, 139.6, 139.3, 132.0, 128.5, 128.4, 128.2, 125.1, 124.1, 121.7, 33.3 ppm. $C_{17}H_{14}N_2O$ (262.31): calcd. C 77.84, H 5.38, N 10.68; found C 77.99, H 5.47, N 10.34.

Supporting Information (see footnote on the first page of this article): UV/Vis absorption spectra for compounds **1**–**42**.

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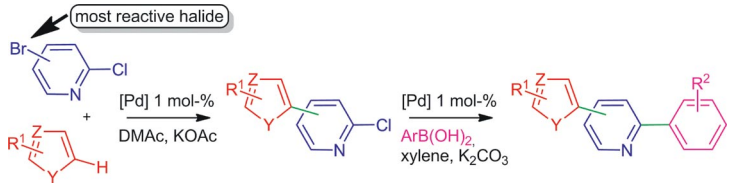
Palladium-Catalysed Arylation



The palladium-catalysed direct heteroarylation of bromo-2-chloropyridines followed by Suzuki coupling allows the synthesis of a variety of heteroarylated 2-arylpyridines in only two steps.

Keywords: Synthetic methods / Homogeneous catalysis / Cross-coupling / C–H bond activation / Arylation / Palladium / Nitrogen heterocycles

