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Palladium-catalyzed direct heteroarylation of chloropyridines and chloroquinolines

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ABSTRACT

The direct coupling of aryl chlorides with heteroarenes would be a considerable advantage for sustainable development due to their lower cost, lower mass, the wider diversity of available compounds and also because of the formation of only HCl associated to a base as by-product and the reduction of the number of steps to prepare these compounds. We observed that through the use of $PdCl(dppb)(C_3H_5)$ as a catalyst, a range of heteroaryl derivatives undergoes coupling via C–H bond activation/functionalization reaction with chloropyridines or chloroquinolines in low to high yields. This air-stable catalyst can be used with a wide variety of substrates. The position of the chloro substituent on pyridines has a minor influence on the yields. On the other hand, the nature on the heteroaryl derivative has a large influence. The highest yields were obtained using benzoxazole, thiophene or thiazole derivatives. The coupling of chloropyridines with furans also gave the expected products, but in low to moderate yields.

1. Introduction

The palladium-catalyzed cross-coupling reactions between pyridyl halides and heteroarenes represent a powerful access to heteroarylated pyridines, which are important pharmaceutical compounds [1]. Negishi [2], Stille [3], Kumada [4] or Suzuki [5] cross-coupling reactions have been largely employed for the preparation of such compounds. However, these methods are not very convenient due to the limited access and various stabilities of several heteroaromatic organometallic derivatives. Moreover, these reactions are not environmentally attractive as they provides an organometallic or salt (MX) as by-product. Over the last years, very interesting results for the coupling of pyridyl halides with heteroaromatic derivatives by C–H bond activation have been reported and provide an economically and environmentally attractive procedure for the preparation of such compounds [6]. However, so far most of the results were obtained with reactive, but expensive bromopyridines or iodopyridines [7–10]. The use of chloropyridines for such coupling reactions would be a considerable advantage for sustainable development due to their lower cost, lower mass and the wider diversity of available compounds. This reaction provides only HCl associated to a base as by-product and therefore is very interesting both in terms of atom-economy and inert wastes. However, for this coupling, aryl chlorides are relatively uncommon partners [11]. This is due to the fact that the oxidative addition of pyridyl chlorides to palladium is slower than with bromides or iodides. One of the first examples of such reaction was reported by Zhuravlev [11a]. He observed that the coupling product of 2-chloropyridine with an oxazolopyridine derivative could be obtained in 33% yield using $Pd(OAc)_2$ (5 mol%) / PPh_3 (20 mol%), Cs_2CO_3 and acetone as reaction conditions. Better yields were obtained using palladium associated to electron-rich monophosphines. For example, Daugulis and co-worker have been able to couple 2-chloro-6-methoxypyridine with benzothiophene in 72% yield using $Pd(OAc)_2$ (5 mol%)/butyldi-1-adamantylphosphine (10 mol%) as catalyst. This catalyst also gave good results for the coupling of 2-chloropyridine with benzoxazole [11b]. A relatively similar procedure has been described recently for the 2-arylation of a 4-thiazolecarboxylate. Using 5–10 mol% $Pd(OAc)_2$ and 10–20 mol% P(biphenyl-2-yl)Cy_2 as catalyst, the coupling of 2-chloro and 3-chloropyridines gave the expected products in high yields [11d].

If monophosphine ligands such as PPh_3 or the air-sensitive P(biphenyl-2-yl)Cy_2 and butyldi-1-adamantylphosphine have been successfully used for the direct coupling of heteroaromatics with pyridyl chlorides, the efficiency of bidentate phosphine ligands for such couplings has not been demonstrated. Moreover, it should be noted that, so far, relatively few pyridyl chloride derivatives and heteroaromatics have been employed for this reaction [11]. For example, to our knowledge, the 2-arylation of furans and the 5-arylation of thiazoles using pyridyl chlorides or the reactivity of 4-chloropyridines have not been reported. Therefore, the discovery of an effective and selective method, using a low loading of an air-stable catalyst, for the direct coupling of both electron-excessive and electron-deficient 2-, 3- or 4-pyridyl chlorides with a wide variety of heteroaromatics still needs to be developed.

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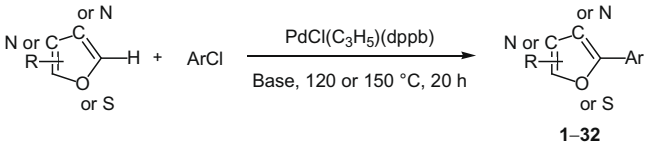
So far, most of the coupling reactions of heteroaryl derivatives with aryl chlorides *via* a C–H bond activation require relatively high catalyst loadings (1–10 mol%) and have been performed at elevated temperature (120–150 °C) [6]. At these temperatures, when $Pd(OAc)_2$ is employed as catalyst precursor, soluble palladium(0) colloids or nanoparticles are generally formed, and then, especially under high palladium concentrations (typically when 1–10 mol% catalyst is employed), so-called "palladium black" forms rapidly. This "palladium black" is inactive for the coupling of most aryl chlorides with arenes. Therefore, for the direct coupling of chloropyridines with aryl chlorides, the stabilization of monomeric palladium species or small clusters is necessary. Such stabilization can be performed using either ammonium salts or ligands. Consequently, we have prepared the air-stable $PdCl(C_3H_5)$(dppb) complex (dppb = 1,4-bis(diphenylphosphino)butane) [12]. The idea was that intermediate Pd(0) species have to be protected by internal ligation against decomposition pathways through under-ligation and subsequent colloid and "Pd black" formation [13–16]. The presence of the bidentate ligand dppb on palladium might also reduce the poisoning of the catalyst due to the presence of heteroaromatics. We have already reported some results for the direct coupling of heteroaromatics with aryl and vinyl bromides [14,15] and also with aryl chlorides [9e,11c] using this catalyst. Herein, we report that this catalyst provides a powerful system for the cross-coupling of chloropyridine or chloroquinoline derivatives with a wide variety of heteroaromatics.

2. Results and discussion

We describe here successively the reactions of 2-chloro, 3-chloro and 4-chloropyridine derivatives with a range of heteroaromatics (Scheme 1, Tables 1–4). We initially examined the influence of several reaction parameters on the yield for the coupling of 2-chloropyridine with benzoxazole or 2-*n*propylthiazole (Table 1). The best results for the reaction with benzoxazole were obtained using Cs_2CO_3 associated to DMF and $PdCl(C_3H_5)$(dppb) as catalyst at 150 °C (Table 1, entry 4). With this substrate, KOAc as base or ligand-free catalysts gave very low yields of target product (Table 1, entries 1, 2, 6 or 7). In absence of catalyst no formation of product was detected by GC (Table 1, entry 9). On the other hand, with 2-*n*propylthiazole, the highest yield was obtained using KOAc as base and DMAc as solvent (Table 1, entry 13). The reactions conducted at 100 °C instead of 150 °C gave lower yields (Table 1, entries 5 and 14).



Scheme 1.

Therefore, for this study, DMF and Cs_2CO_3 were chosen as reaction conditions for the 2-arylation of benzoxazole and benzothiazole. For the 5-arylation of thiazoles, thiophenes or furans, DMAc and KOAc were employed as the solvent and the base. The reactions were performed under argon in the presence of 2.5 mol% of $PdCl(C_3H_5)$(dppb) as catalyst. Most of the substrates and products are thermally stable so, in order to obtain higher yields, we have performed the reactions at an elevated temperature: 150 °C. However, in some cases, a lower reaction temperature of 120 °C had to be employed due to partial decomposition of the starting material or coupling product.

First, we tested several reaction conditions for the coupling of 2-chloropyridines with seven heteroaromatics (Table 2). 2-Chloro-6-methylpyridine, 2-chloropyridine or 2-chloroquinoline reacted with benzoxazole gave the target products 1–3 in 65–79% yields (Table 2, entries 1–3). To determine the electronic influence of the pyridine substituents on this coupling reaction, we studied the reactivity of substituted 2-chloropyridines. The presence of electron donating or withdrawing substituents appears to have a minor effect on the reaction yields. 5-Trifluoromethyl-2-chloropyridine and 6-methoxy-2-chloropyridine gave the expected coupling products 4 and 5 in similar yields of 77% and 78%, respectively (Table 2, entries 4 and 5). Then, we studied the 2-arylation of benzothiazole using 2-chloropyridines. We obtained lower yields of desired products than in the presence of benzoxazole. However, the target compounds 6-8 were formed in all cases using either 2-chloro-6-methylpyridine, 2-chloroquinoline or 5-trifluoromethyl-2-chloropyridine (Table 2, entries 6–8). In the literature, the 2-arylation of a 4-thiazolecarboxylate using pyridyl chlorides has been reported [11d]. In order to extend the scope of this reaction; we examined the 5-arylation of 2-substituted thiazoles. 2-*n*Propylthiazole was coupled with 2-chloropyridine, 2-chloroquinoline or 6-methoxy-2-chloropyridine. As expected, the 5-arylated thiazoles 9–11 were selectively obtained in 38–64% yields (Table 2, entries 9–11). In the same manner, two 2,4-substituted thiazoles: 2-ethyl-4-methylthiazole and 2-phenyl-4-methylthiazole were reacted affording 12–14 in very similar yields (Table 2, entries 12–14). Finally, the reactivity of 2-substituted thiophenes with 2-chloro-6-methoxypyridine has been studied, and again,

Table 1
Palladium-catalyzed direct arylation of 2-chloropyridine, influence of the reaction conditions.

Entry	Heteroarene	Base	Solvent	Catalyst	Temperature (°C)	Yield (%)[a]
1	Benzoxazole	KOAc	DMF	$PdCl(C_3H_5)$(dppb)	150	27
2	Benzoxazole	KOAc	DMAc	$PdCl(C_3H_5)$(dppb)	150	5
3	Benzoxazole	Cs_2CO_3	DMAc	$PdCl(C_3H_5)$(dppb)	150	67
4	Benzoxazole	Cs_2CO_3	DMF	$PdCl(C_3H_5)$(dppb)	150	72 (69)
5	Benzoxazole	Cs_2CO_3	DMF	$PdCl(C_3H_5)$(dppb)	100	25
6	Benzoxazole	Cs_2CO_3	DMF	$Pd(OAc)_2$	150	3
7	Benzoxazole	Cs_2CO_3	DMF	$[PdCl(C_3H_5)]_2$	150	2
8	Benzoxazole	Cs_2CO_3	DMF	$[PdCl(C_3H_5)]_2$/2 PPh_3	150	58
9	Benzoxazole	Cs_2CO_3	DMF	–	150	0
10	2-*n*propylthiazole	KOAc	DMF	$PdCl(C_3H_5)$(dppb)	150	26
11	2-*n*propylthiazole	Cs_2CO_3	DMAc	$PdCl(C_3H_5)$(dppb)	150	2
12	2-*n*propylthiazole	Cs_2CO_3	DMF	$PdCl(C_3H_5)$(dppb)	150	12
13	2-*n*propylthiazole	KOAc	DMAc	$PdCl(C_3H_5)$(dppb)	150	45 (38)
14	2-*n*propylthiazole	KOAc	DMAc	$PdCl(C_3H_5)$(dppb)	100	2

[a] Conditions: catalyst: [Pd] (0.025 mmol), 2-chloropyridine (1 mmol), heteroarene (1.2 mmol), base (1.2 mmol), solvent (5 mL), 20 h, GC and NMR yields, yields in parenthesis are isolated.

Table 2
Palladium-catalyzed arylation of 2-chloropyridines or quinolines (Scheme 1).

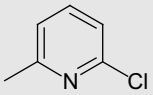
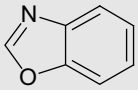
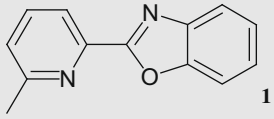
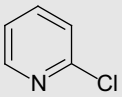
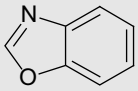
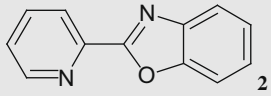
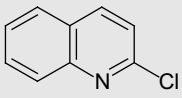
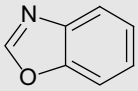
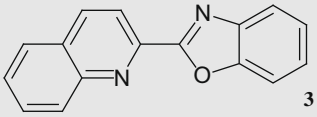
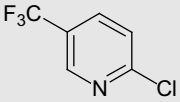
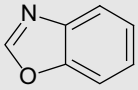
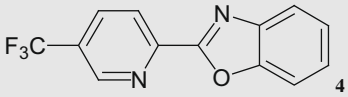
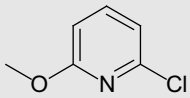
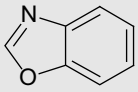
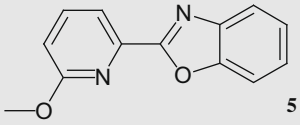
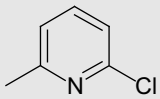
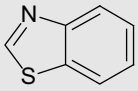
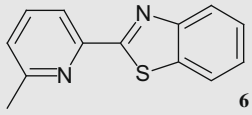
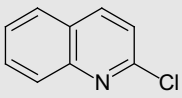
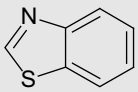
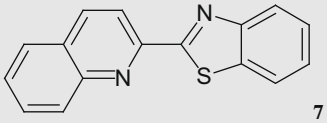
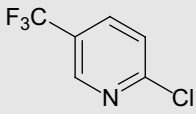
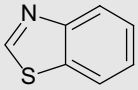
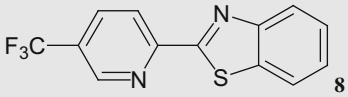
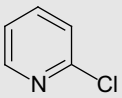
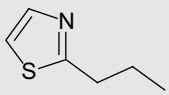
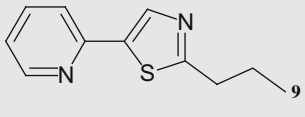
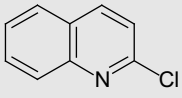
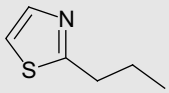
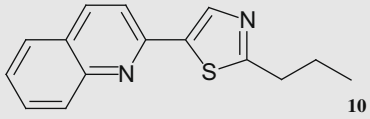
Entry	2-Chloropyridine or quinoline	Heteroarene	Product	Yield (%)[a]
1			 **1**	65
2			 **2**	69
3			 **3**	79
4			 **4**	77
5			 **5**	78
6			 **6**	58
7			 **7**	54
8			 **8**	52
9			 **9**	38[b]
10			 **10**	50[b,c]

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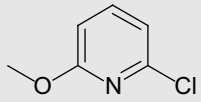
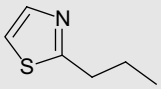
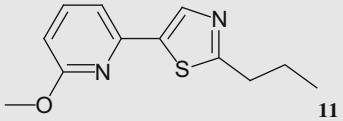
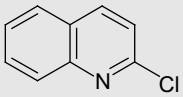
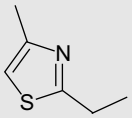
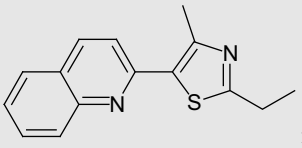
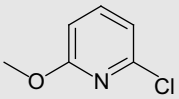
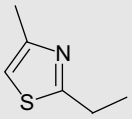
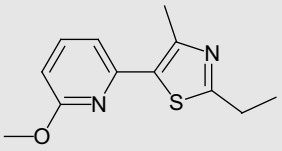
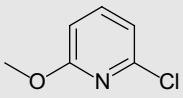
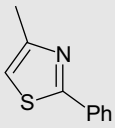
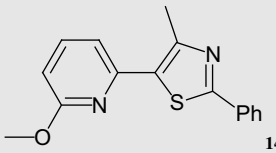
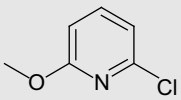
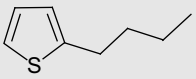
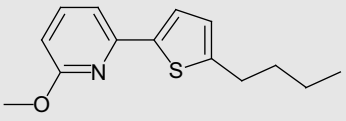
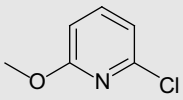
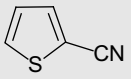
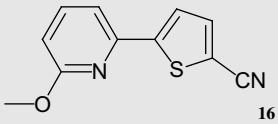
Table 2 (*continued*)

Entry	2-Chloropyridine or quinoline	Heteroarene	Product	Yield (%)[a]
11			 **11**	64[b,c]
12			 **12**	52[b,c]
13			 **13**	60[b,c]
14			 **14**	62[b,c]
15			 **15**	53[b,c]
16			 **16**	63[b,c]

[a] Conditions: catalyst: $PdCl(C_3H_5)(dppb)$ (0.025 mmol), aryl chloride (1 mmol), heteroarene (1.2 mmol), Cs_2CO_3 (1.2 mmol), DMF (5 mL), 20 h, 150 °C, isolated yields.
[b] KOAc and DMAc were employed as base and solvent.
[c] Reaction temperature 120 °C.

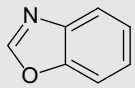
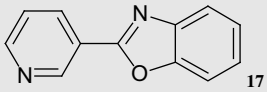
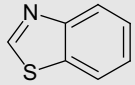
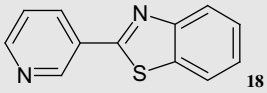
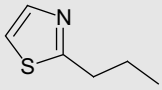
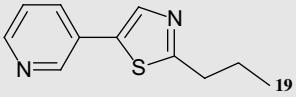
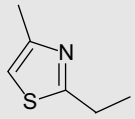
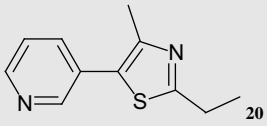
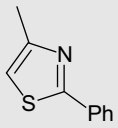
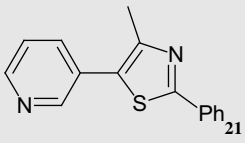
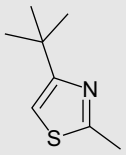
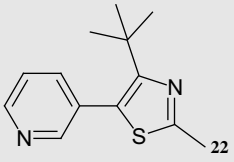
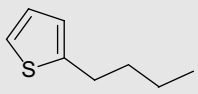
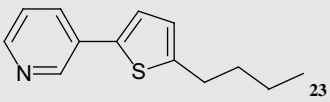
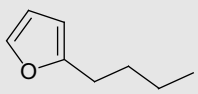
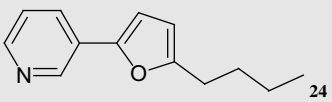
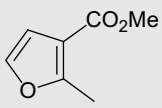
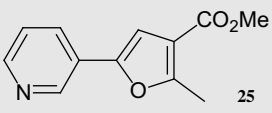
the desired compounds 15 and 16 were formed in satisfactory yields of 53% and 63% (Table 2, entries 15 and 16). It should be noted that quantitative conversion of the pyridyl chlorides was observed in most cases.

Then, we studied the influence of position of the chloro substituent on pyridines for this reaction. Due to the electronegativity of the nitrogen atom, the α and γ positions of halopyridines should be the most susceptible to the oxidative addition to Pd(0). In fact, the reactivity of 3-chloropyridine is quite similar to 2-chloropyridine (Table 3). Coupling reaction with benzoxazole or benzothiazole gave 17 and 18 in 80% and 79% yields, respectively. Moreover, no formation of side-products was observed. Four thiazole derivatives were also employed, and again, satisfactory results were obtained except with sterically congested 2-methyl-4*t*butylthiazole (Table 3, entries 3–6). With this substrate a low yield of 33% was obtained. 2-*n*Butylthiophene led to 23 in 61% yield (Table 3, entry 7). Furan derivatives were found to be less reactive. The coupling reaction was selective in favour of the 5-arylation of furans, but the formation of relatively large amount of 3,3′-bipyridine as side-product was also observed. Using 2-*n*butylfuran and methyl 2-methyl-3-furoate, 24 and 25 were formed in only 41% and 30% yields, respectively (Table 3, entries 8 and 9).

With 4-chloropyridine we observed behaviour similar to that of 2- or 3-chloropyridine. Satisfactory yields were also obtained using several heteroaromatics (Table 4). Again, using benzoxazole, benzothiazole or 2-*n*propylthiazole, the selective formation of the expected products 26–28 was observed in high yields (Table 4, entries 1-3). Using 2-ethyl-4-methylthiazole, a low yield of 29 (34%) was produced due to a partial conversion of 4-chloropyridine (Table 4, entry 4). Ethyl thiazole-2-carboxylate, also led to a moderate yield of 37% in 30. With this substrate unidentified side-products were formed in the course of the reaction (Table 4, entry 5). Here also, using similar reaction conditions, a higher yield was obtained using 2-*n*butylthiophene than in the presence of 2-*n*butylfuran (Table 4, entries 6 and 7).

This procedure is not limited to chloropyridines. 2-Chloropyrimidine has been successfully coupled with benzoxazole (Scheme 2). The desired product 33 was obtained in very high yield. Finally,

Table 3
Palladium-catalyzed arylation of 3-chloropyridine (Scheme 1).

Entry	Heteroarene	Temperature (°C)	Product	Yield (%)[a]
1		120	 **17**	80[b]
2		120	 **18**	79[b]
3		120	 **19**	78
4		120	 **20**	74
5		120	 **21**	58
6		120	 **22**	33
7		120	 **23**	61
8		120	 **24**	41
9		120	 **25**	30

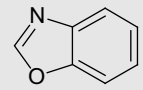
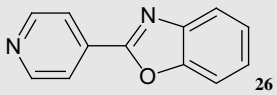
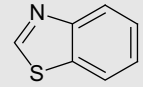
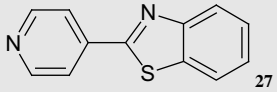
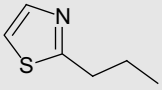
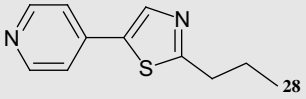
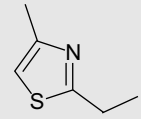
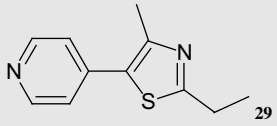
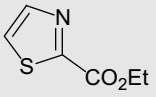
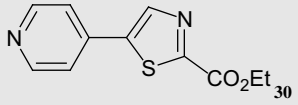
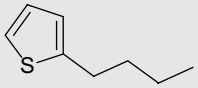
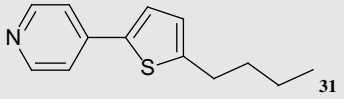
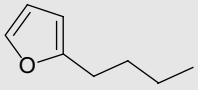
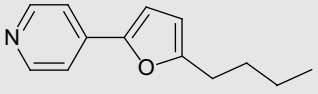
[a] Conditions: catalyst: $PdCl(C_3H_5)(dppb)$ (0.025 mmol), 3-chloropyridine (1 mmol), heteroarene (1.2 mmol), KOAc (1.2 mmol), DMAc (5 mL), 20 h, isolated yields.
[b] Cs_2CO_3 and DMF were employed as base and solvent.

2-chlorobenzothiazole was reacted with benzoxazole or benzothiazole to give 34 and 35 in 54% and 63% yields, respectively (Schemes 3 and 4).

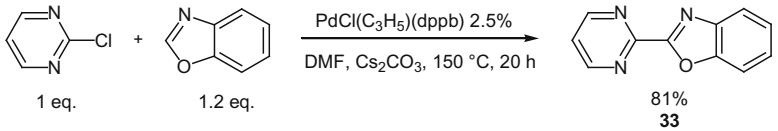
3. Conclusion

In summary, the complex $PdCl(dppb)(C_3H_5)$ provides an efficient catalyst for the direct coupling of chloropyridines or chloroquinolines with a wide variety of heteroarenes. 2-, 3- or 4-chloropyridine derivatives have been employed successfully. The position of the halide on the heteroaromatic appears to have a minor influence on the reactions yields. Several heteroaromatics were also employed successfully. In general, better results were obtained for the coupling with benzoxazole, benzothiazole, thiazoles or thiophenes than with furans. This procedure is very simple, economically attractive and uses commercially available ligand and

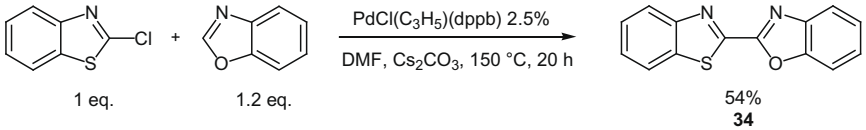
Table 4
Palladium-catalyzed arylation of 4-chloropyridine (Scheme 1).

Entry	Heteroarene	Temperature (°C)	Product	Yield (%)[a]
1		120	 **26**	71[b]
2		120	 **27**	65[b]
3		120	 **28**	76
4		120	 **29**	34
5		120	 **30**	37
6		120	 **31**	50
7		120		34

[a] Conditions: catalyst: $PdCl(C_3H_5)(dppb)$ (0.025 mmol), 4-chloropyridine hydrochloride (1 mmol), heteroarene (1.2 mmol), KOAc (2.2 mmol), DMAc (5 mL), 20 h, isolated yields.
[b] Cs_2CO_3 and DMF were employed as base and solvent.

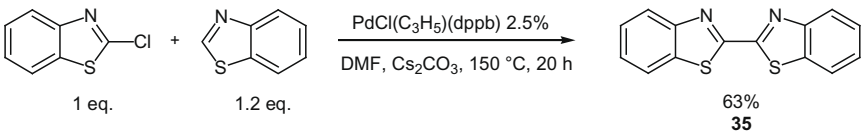


Scheme 2.



Scheme 3.

catalyst precursors. The air-stability of this catalyst makes this procedure more convenient than those using bulky electron-rich phosphanes that are often employed to activate aryl chlorides in palladium-catalyzed reactions [11b,11d]. To the best of our knowledge, this work represents one of the most wide-ranging study reported so far for the preparation of heteroarylpyridines via a C–H bond activation/functionalization. The only by-product is HCl associated to AcOK or Cs_2CO_3 instead of metallic salts with classical



Scheme 4.

cross-coupling procedures. Moreover, no preparation of an organometallic derivative is required, reducing the number of steps to prepare these compounds.

4. Experimental

4.1. General remarks

All reactions were run under argon in Schlenk tubes using vacuum lines. DMF or DMAc analytical grade were not distilled before use. Cesium carbonate or potassium acetate (99+) were used. Commercial aryl chlorides and heteroarene derivatives were used without purification. ^1H and ^{13}C spectrum were recorded with a Bruker 200 MHz spectrometer in $CDCl_3$ solutions. Chemical shift are reported in ppm relative to $CDCl_3$ (7.25 for ^1H NMR and 77.0 for ^{13}C NMR). Flash chromatography was performed on silica gel (230–400 mesh). Cyclic voltammetric experiments were carried out using an EDAQ potentiostat unit, with the EChem software package. A platinum wire working electrode, a platinum wire auxiliary electrode, and a saturated calomel reference electrode (SCE) were used in a standard three-electrode configuration. Electrochemical measurements were performed in dimethylformamide, containing 0.1 M tetrabutylammonium tetrafluoroborate, at a 100 mV s^{-1} scan rate, under a dinitrogen atmosphere.

4.2. Preparation of the PdCl(dppb)(C_3H_5) catalyst [12]

An oven-dried 40 mL Schlenk tube equipped with a magnetic stirring bar under argon atmosphere, was charged with $[Pd(C_3H_5)Cl]_2$ (182 mg, 0.5 mmol) and dppb (426 mg, 1 mmol). 10 mL of anhydrous dichloromethane were added, then the solution was stirred at room temperature for twenty minutes. The solvent was removed in vacuum. The yellow powder was used without purification. ^{31}P NMR (81 MHz, $CDCl_3$) δ = 19.3 (s).

4.3. General procedure for coupling reactions

In a typical experiment, the aryl chloride (1 mmol), heteroarene derivative (1.2 mmol), Cs_2CO_3 (0.390 g, 1.2 mmol) or KOAc (0.118 g, 1.2 mmol) and $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) were dissolved in DMF or DMAc (5 mL) under an argon atmosphere. The reaction mixture was stirred at 120 or 150 °C (see tables) for 20 h. The solution was diluted with an H_2O/KOH solution 1 M (20 mL), then the product was extracted three times with CH_2Cl_2. The combined organic layer was dried over $MgSO_4$ and the solvent was removed in vacuo. The crude product was purified by silica gel column chromatography.

4.4. 2-(6-Methylpyridin-2-yl)-benzoxazole (**1**)

The reaction of 2-chloro-6-methylpyridine (0.128 g, 1 mmol), benzoxazole (0.143 g, 1.2 mmol) and Cs_2CO_3 (0.390 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 150 °C affords the corresponding product 1 in 65% (0.137 g) isolated yield.

^1H NMR (200 MHz, $CDCl_3$) δ 7.98 (d, J = 8.2 Hz, 1H), 7.62 (m, 1H), 7.45 (t, J = 7.8 Hz, 1H), 7.42 (m, 1H), 7.15 (m, 2H), 6.99 (d, J = 8.2 Hz, 1H), 2.47 (s, 3H).

4.5. 2-Pyridin-2-ylbenzoxazole (**2**)

The reaction of 2-chloropyridine (0.114 g, 1 mmol), benzoxazole (0.143 g, 1.2 mmol) and Cs_2CO_3 (0.390 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 150 °C affords the corresponding product 2 in 69% (0.135 g) isolated yield.

^1H NMR (200 MHz, $CDCl_3$) δ 8.70 (d, J = 4.6 Hz, 1H), 8.24 (d, J = 8.2 Hz, 1H), 7.70–7.55 (m, 2H), 7.55 (m, 1H), 7.60–7.20 (m, 3H).

4.6. 2-Benzoxazol-2-ylquinoline (**3**)

The reaction of 2-chloroquinoline (0.164 g, 1 mmol), benzoxazole (0.143 g, 1.2 mmol) and Cs_2CO_3 (0.390 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 150 °C affords the corresponding product 3 in 79% (0.194 g) isolated yield.

^1H NMR (200 MHz, $CDCl_3$) δ 8.46 (d, J = 8.2 Hz, 1 H), 8.37 (d, J = 8.2 Hz, 1H), 8.33 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.2 Hz, 1H), 7.88 (m, 1H), 7.77 (t, J = 7.8 Hz, 1H), 7.76 (m, 1H), 7.66 (t, J = 7.8 Hz, 1H), 7.43 (m, 2H).

4.7. 2-(5-Trifluoromethylpyridin-2-yl)-benzoxazole (**4**)

The reaction of 2-chloro-5-(trifluoromethyl)pyridine (0.182 g, 1 mmol), benzoxazole (0.143 g, 1.2 mmol) and Cs_2CO_3 (0.390 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 150 °C affords the corresponding product 4 in 77% (0.203 g) isolated yield.

^1H NMR (200 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.43 (d, J = 8.0 Hz, 1H), 8.09 (d, J = 8.0 Hz, 1H), 7.81 (m, 1H), 7.64 (m, 1H), 7.50–7.30 (m, 2H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 159.9, 150.9, 148.8, 147.0 (q, J = 4.0 Hz), 141.4, 134.3 (q, J = 3.5 Hz), 127.7 (q, J = 33.4 Hz), 126.6, 125.2, 122.9 (q, J = 272.4 Hz), 122.8, 120.8, 111.2.

Anal. Calc. for $C_{13}H_7F_3N_2O$: C, 59.10; H, 2.67. Found: C, 59.14; H, 2.84%.

4.8. 2-(6-Methoxypyridin-2-yl)-benzoxazole (**5**)

The reaction of 2-chloro-6-methoxypyridine (0.144 g, 1 mmol), benzoxazole (0.143 g, 1.2 mmol) and Cs_2CO_3 (0.390 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 150 °C affords the corresponding product 5 in 78% (0.177 g) isolated yield.

^1H NMR (200 MHz, $CDCl_3$) δ 7.89 (d, J = 8.2 Hz, 1H), 7.83 (m, 1H), 7.68 (t, J = 7.8 Hz, 1H), 7.63 (m, 1H), 7.36 (m, 2H), 6.86 (d, J = 8.2 Hz, 1H), 4.10 (s, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 164.7, 162.1, 151.3, 143.8, 142.3, 139.5, 126.1, 125.2, 121.0, 117.3, 114.2, 111.4, 54.2.

Anal. Calc. for $C_{13}H_{10}N_2O$: C, 69.02; H, 4.46. Found: C, 69.20; H, 4.57%.

4.9. 2-(6-Methylpyridin-2-yl)-benzothiazole (**6**)

The reaction of 2-chloro-6-methylpyridine (0.128 g, 1 mmol), benzothiazole (0.162 g, 1.2 mmol) and Cs_2CO_3 (0.390 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 150 °C affords the corresponding product 6 in 58% (0.131 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.18 (d, J = 8.2 Hz, 1H), 8.10 (d, J = 8.2 Hz, 1H), 7.96 (d, J = 8.2 Hz, 1H), 7.73 (t, J = 7.8 Hz, 1H), 7.52 (t, J = 7.8 Hz, 1H), 7.41 (t, J = 7.8 Hz, 1H), 7.24 (d, J = 7.8 Hz, 1H), 2.66 (s, 3H).

4.10. 2-Benzothiazol-2-ylquinoline (**7**)

The reaction of 2-chloroquinoline (0.164 g, 1 mmol), benzothiazole (0.162 g, 1.2 mmol) and Cs_2CO_3 (0.390 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 150 °C affords the corresponding product 7 in 54% (0.142 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.87 (d, J = 8.2 Hz, 1H), 8.51 (d, J = 8.2 Hz, 1H), 8.40–8.10 (m, 3H), 7.99 (d, J = 8.2 Hz, 1H), 7.88 (t, J = 7.8 Hz, 1H), 7.78 (t, J = 7.8 Hz, 1H), 7.62-7.40 (m, 2H).

4.11. 2-(5-Trifluoromethylpyridin-2-yl)-benzothiazole (**8**)

The reaction of 2-chloro-5-(trifluoromethyl)pyridine (0.182 g, 1 mmol), benzothiazole (0.162 g, 1.2 mmol) and Cs_2CO_3 (0.390 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 150 °C affords the corresponding product 8 in 52% (0.146 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.52 (d, J = 8.3 Hz, 1H), 8.14 (d, J = 8.2 Hz, 1H), 8.09 (d, J = 8.2 Hz, 1H), 8.00 (d, J = 8.2 Hz, 1H), 7.57 (t, J = 7.8 Hz, 1H), 7.48 (t, J = 7.8 Hz, 1H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 167.9, 154.8, 154.6, 147.0 (q, J = 4.0 Hz), 136.8, 134.7 (q, J = 3.5 Hz), 127.7 (q, J = 33.4 Hz), 127.4, 127.0, 124.4, 122.9 (q, J = 272.4 Hz), 122.6, 120.8.

Anal. Calc. for $C_{13}H_7F_3N_2S$: C, 55.71; H, 2.52. Found: C, 55.94; H, 2.60%.

4.12. 2-(2-Propylthiazol-5-yl)-pyridine (**9**)

The reaction of 2-chloropyridine (0.113 g, 1 mmol), 2-*n*propylthiazole (0.153 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 150 °C affords the corresponding product 9 in 38% (0.078 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.58 (d, J = 4.7 Hz, 1H), 8.10 (s, 1H), 7.73 (t, J = 7.8 Hz, 1H), 7.66 (d, J = 7.8 Hz, 1H), 7.19 (dd, J = 7.8 and 4.7 Hz, 1H), 3.02 (t, J = 7.5 Hz, 2H), 1.87 (sext., J = 7.5 Hz, 2H), 1.06 (t, J = 7.5 Hz, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 173.3, 150.9, 149.8, 139.3, 139.2, 136.7, 122.3, 119.5, 35.7, 23.3, 13.7.

Anal. Calc. for $C_{11}H_{12}N_2S$: C, 64.67; H, 5.92. Found: C, 64.57; H, 5.91%.

4.13. 2-(2-Propylthiazol-5-yl)-quinoline (**10**)

The reaction of 2-chloroquinoline (0.164 g, 1 mmol), 2-*n*propylthiazole (0.153 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 10 in 50% (0.127 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.14 (d, J = 7.8 Hz, 1H), 8.07 (d, J = 7.8 Hz, 1H), 7.80–7.60 (m, 3H), 7.50 (t, J = 7.8 Hz, 1H), 3.04 (t, J = 7.5 Hz, 2H), 1.90 (sext., J = 7.5 Hz, 2H), 1.07 (t, J = 7.8 Hz, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 174.7, 151.1, 148.6, 140.7, 140.4, 137.1, 130.4, 129.6, 128.0, 127.6, 127.0, 118.2, 36.2, 23.8, 14.1.

Anal. Calc. for $C_{15}H_{14}N_2S$: C, 70.83; H, 5.55. Found: C, 70.90; H 5.41%.

4.14. 2-Methoxy-6-(2-propylthiazol-5-yl)-pyridine (**11**)

The reaction of 2-chloro-6-methoxypyridine (0.144 g, 1 mmol), 2-*n*propylthiazole (0.153 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 11 in 64% (0.150 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.52 (t, J = 7.8 Hz, 1H), 7.15 (d, J = 8.2 Hz, 1H), 6.59 (d, J = 8.2 Hz, 1H), 3.95 (s, 3H), 2.97 (t, J = 7.5 Hz, 2H), 1.83 (sext., J = 7.5 Hz, 2H), 1.02 (t, J = 7.5 Hz, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 173.0, 164.0, 148.6, 139.7, 139.5, 139.4, 112.4, 109.8, 53.7, 36.0, 23.8, 14.1.

Anal. Calc. for $C_{12}H_{14}N_2OS$: C, 61.51; H, 6.02. Found: C, 61.45; H, 6.10%.

4.15. 2-(2-Ethyl-4-methylthiazol-5-yl)-quinoline (**12**)

The reaction of 2-chloroquinoline (0.164 g, 1 mmol), 2-ethyl-4-methylthiazole (0.153 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 12 in 52% (0.132 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.18 (d, J = 7.8 Hz, 1H), 8.09 (d, J = 7.8 Hz, 1H), 7.80-7.60 (m, 3H), 7.53 (t, J = 7.8 Hz, 1H), 3.04 (q, J = 7.4 Hz, 2H), 2.78 (s, 3H), 1.45 (t, J = 7.8 Hz, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 173.0, 152.4, 150.4, 148.5, 137.0, 132.5, 130.4, 129.7, 127.9, 126.9, 126.8, 120.6, 27.5, 18.0, 14.7.

Anal. Calc. for $C_{15}H_{14}N_2S$: C, 70.83; H, 5.55. Found: C, 70.68; H, 5.54%.

4.16. 2-(2-Ethyl-4-methylthiazol-5-yl)-6-methoxypyridine (**13**)

The reaction of 2-chloro-6-methoxypyridine (0.144 g, 1 mmol), 2-ethyl-4-methylthiazole (0.153 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 13 in 60% (0.141 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 7.55 (t, J = 7.8 Hz, 1H), 7.05 (d, J = 8.2 Hz, 1H), 6.60 (d, J = 8.2 Hz, 1H), 3.95 (s, 3H), 3.00 (q, J = 7.5 Hz, 2H), 2.69 (s, 3H), 1.39 (t, J = 7.5 Hz, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 171.8, 163.7, 149.6, 149.5, 139.4, 132.1, 114.6, 109.1, 53.8, 27.4, 18.2, 14.7.

Anal. Calc. for $C_{12}H_{14}N_2OS$: C, 61.51; H, 6.02. Found: C, 61.40; H, 6.01%.

4.17. 2-Methoxy-6-(4-methyl-2-phenylthiazol-5-yl)-pyridine (**14**)

The reaction of 2-chloro-6-methoxypyridine (0.144 g, 1 mmol), 2-phenyl-4-methylthiazole (0.210 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 14 in 62% (0.175 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.00–7.95 (m, 2H), 7.57 (t, J = 7.8 Hz, 1H), 7.45–7.35 (m, 3H), 7.12 (d, J = 8.2 Hz, 1H), 6.64 (d, J = 8.2 Hz, 1H), 4.00 (s, 3H), 2.79 (s, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 166.2, 163.8, 151.1, 149.4, 139.4, 134.1, 133.6, 130.4, 129.3, 126.8, 114.7, 109.5, 53.9, 18.6.

Anal. Calc. for $C_{16}H_{14}N_2OS$: C, 68.06; H, 5.00. Found: C, 68.10; H, 4.87%.

4.18. 2-(5-Butylthiophen-2-yl)-6-methoxypyridine (**15**)

The reaction of 2-chloro-6-methoxypyridine (0.144 g, 1 mmol), 2-*n*butylthiophene (0.168 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 15 in 53% (0.131 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 7.55 (t, J = 7.9 Hz, 1H), 7.42 (d, J = 3.6 Hz, 1H), 7.18 (d, J = 7.4 Hz, 1H), 6.78 (d, J = 3.6 Hz, 1H), 6.58 (d, J = 7.4 Hz, 1H), 4.01 (s, 3H), 2.85 (t, J = 7.5 Hz, 2H), 1.65 (quint., J = 7.4 Hz, 2H), 1.41 (sext., J = 7.4 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 163.9, 150.8, 148.5, 142.6, 139.4, 125.5, 124.6, 111.2, 108.7, 53.7, 34.2, 30.5, 22.6, 14.3.

Anal. Calc. for $C_{14}H_{17}NOS$: C, 67.98; H, 6.93. Found: C, 67.87; H, 7.04%.

4.19. 5-(6-Methoxypyridin-2-yl)-thiophene-2-carbonitrile (**16**)

The reaction of 2-chloro-6-methoxypyridine (0.144 g, 1 mmol), thiophene-2-carbonitrile (0.131 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 16 in 63% (0.136 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 7.63 (t, J = 7.4 Hz, 1H), 7.58 (d, J = 4.0 Hz, 1H), 7.48 (d, J = 4.0 Hz, 1H), 7.27 (d, J = 7.4 Hz, 1H), 6.74 (d, J = 7.4 Hz, 1H), 4.00 (s, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 164.1, 152.8, 148.3, 139.8, 138.6, 123.8, 115.1, 112.3, 111.8, 110.4, 54.0.

Anal. Calc. for $C_{11}H_8N_2OS$: C, 61.09; H, 3.73. Found: C, 61.01; H, 3.68%.

4.20. 2-Pyridin-3-ylbenzooxazole (**17**)

The reaction of 3-chloropyridine (0.113 g, 1 mmol), benzoxazole (0.143 g, 1.2 mmol) and Cs_2CO_3 (0.390 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 120 °C affords the corresponding product 17 in 80% (0.157 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 9.48 (s, 1H), 8.77 (d, J = 4.2 Hz, 1H), 8.52 (d, J = 8.2 Hz, 1H), 7.81 (m, 1H), 7.62 (m, 1H), 7.54–7.30 (m, 3H).

4.21. 2-Pyridin-3-ylbenzothiazole (**18**)

The reaction of 3-chloropyridine (0.113 g, 1 mmol), benzothiazole (0.156 g, 1.2 mmol) and Cs_2CO_3 (0.390 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 150 °C affords the corresponding product 18 in 79% (0.168 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 9.30 (s, 1H), 8.71 (d, J = 4.2 Hz, 1H), 8.36 (d, J = 8.1 Hz, 1H), 8.10 (d, J = 8.2 Hz, 1H), 7.92 (d, J = 8.2 Hz, 1H), 7.60–7.30 (m, 3H).

4.22. 3-(2-Propylthiazol-5-yl)-pyridine (**19**)

The reaction of 3-chloropyridine (0.113 g, 1 mmol), 2-*n*propylthiazole (0.153 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 19 in 78% (0.159 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.55 (d, J = 4.2 Hz, 1H), 7.87 (s, 1H), 7.84 (d, J = 7.2 Hz, 1H), 7.33 (dd, J = 7.2 and 4.2 Hz, 1H), 3.01 (t, J = 7.5 Hz, 2H), 1.86 (sext., J = 7.5 Hz, 2H), 1.05 (t, J = 7.5 Hz, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 172.3, 149.4, 147.9, 139.1, 134.9, 134.0, 128.3, 124.1, 36.0, 23.7, 14.1.

Anal. Calc. for $C_{11}H_{12}N_2S$: C, 64.67; H, 5.92. Found: C, 64.57; H, 5.99%.

4.23. 3-(2-Ethyl-4-methylthiazol-5-yl)-pyridine (**20**)

The reaction of 3-chloropyridine (0.113 g, 1 mmol), 2-ethyl-4-methylthiazole (0.153 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 20 in 74% (0.151 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.69 (s, 1H), 8.56 (d, J = 4.8 Hz, 1H), 7.70 (d, J = 7.2 Hz, 1H), 7.37 (dd, J = 7.2 and 4.8 Hz, 1H), 3.01 (q, J = 7.5 Hz, 2H), 2.47 (s, 3H), 1.41 (t, J = 7.5 Hz, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 171.7, 150.1, 148.9, 148.7, 136.6, 129.2, 127.3, 123.8, 27.4, 16.4, 14.7.

Anal. Calc. for $C_{11}H_{12}N_2S$: C, 64.67; H, 5.92. Found: C, 64.80; H, 5.81%.

4.24. 3-(4-Methyl-2-phenylthiazol-5-yl)-pyridine (**21**)

The reaction of 3-chloropyridine (0.113 g, 1 mmol), 2-phenyl-4-methylthiazole (0.210 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 21 in 58% (0.146 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.58 (d, J = 4.1 Hz, 1H), 7.96–7.85 (m, 2H), 7.75 (d, J = 7.2 Hz, 1H), 7.50–7.20 (m, 4H), 2.55 (s, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 166.5, 150.5, 150.1, 149.2, 136.6, 133.8, 130.6, 129.4, 128.9, 128.6, 126.8, 123.9, 16.7.

Anal. Calc. for $C_{15}H_{12}N_2S$: C, 71.40; H, 4.79. Found: C, 71.42; H, 4.89%.

4.25. 3-(4-tert-Butyl-2-methylthiazol-5-yl)-pyridine (**22**)

The reaction of 3-chloropyridine (0.113 g, 1 mmol), 2-methyl-4-*t*butylthiazole (0.187 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 22 in 33% (0.077 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.63 (s, 2H), 7.69 (d, J = 7.2 Hz, 1H), 7.32 (dd, J = 7.2 and 4.8 Hz, 1H), 2.68 (s, 3H), 1.23 (s, 9H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 163.4, 160.7, 151.6, 149.5, 138.6, 132.2, 129.9, 122.5, 32.1, 30.1, 19.4.

Anal. Calc. for $C_{13}H_{16}N_2S$: C, 67.20; H, 6.94. Found: C, 67.35; H, 6.80%.

4.26. 3-(5-Butylthiophen-2-yl)-pyridine (**23**)

The reaction of 3-chloropyridine (0.113 g, 1 mmol), 2-*n*butylthiophene (0.168 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 23 in 61% (0.133 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.85 (s, 1H), 8.49 (d, J = 4.8 Hz, 1H), 7.82 (d, J = 7.8 Hz, 1H), 7.28 (dd, J = 7.8 and 4.8 Hz, 1H), 7.20 (d, J = 3.8 Hz, 2H), 6.80 (d, J = 3.8 Hz, 2H), 2.86 (t, J = 7.5 Hz, 2H), 1.75 (quint., J = 7.5 Hz, 2H), 1.41 (sext., J = 7.5 Hz, 2H), 0.97 (t, J = 7.5 Hz, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 147.9, 147.1, 146.6, 137.6, 132.4, 130.7, 125.3, 123.9, 123.6, 33.7, 29.9, 22.1, 13.8.

Anal. Calc. for $C_{13}H_{15}NS$: C, 71.84; H, 6.96. Found: C,71.97; H, 6.99%.

4.27. 3-(5-Butylfuran-2-yl)-pyridine (**24**)

The reaction of 3-chloropyridine (0.113 g, 1 mmol), 2-*n*butylfuran (0.149 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 24 in 41% (0.083 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.52–8.40 (m, 1H), 7.89 (d, J = 5.9 Hz, 1H), 7.28 (m, 1H), 6.65 (d, J = 3.0 Hz, 1H), 6.10 (d, J = 3.0 Hz, 1H), 2.71 (t, J = 7.6 Hz, 2H), 1.70 (quint., J = 7.5 Hz, 2H), 1.45 (sext., J = 7.5 Hz, 2H), 0.97 (t, J = 7.5 Hz, 3H).

4.28. Methyl 2-methyl-5-pyridyl-3-furoate (**25**)

The reaction of 3-chloropyridine (0.113 g, 1 mmol), methyl 2-methyl-3-furoate (0.168 g, 1.2 mmol) and KOAc (0.118 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 25 in 30% (0.065 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 9.00–8.80 (m, 1H), 8.60–8.40 (m, 1H), 7.92 (d, J = 7.8 Hz, 1H), 7.40–7.25 (m, 1H), 7.00 (s, 1H), 3.87 (s, 3H), 2.68 (s, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 164.6, 160.1, 149.3, 148.9, 145.6, 131.1, 126.5, 124.0, 115.8, 107.4, 52.0, 14.3.

Anal. Calc. for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10. Found: C, 66.18; H, 5.21%.

4.29. 2-Pyridin-4-ylbenzoxazole (**26**)

The reaction of 4-chloropyridine hydrochloride (0.150 g, 1 mmol), benzoxazole (0.143 g, 1.2 mmol) and Cs_2CO_3 (0.715 g, 2.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 120 °C affords the corresponding product 26 in 71% (0.139 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.83 (d, J = 7.0 Hz, 2H), 8.10 (d, J = 7.0 Hz, 2H), 7.81 (m, 1H), 7.64 (m, 1H), 7.50–7.30 (m, 3H).

4.30. 2-Pyridin-4-ylbenzothiazole (**27**)

The reaction of 4-chloropyridine hydrochloride (0.150 g, 1 mmol), benzothiazole (0.162 g, 1.2 mmol) and Cs_2CO_3 (0.715 g, 2.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 150 °C affords the corresponding product 27 in 65% (0.138 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.79 (d, J = 6.5 Hz, 2H), 8.14 (d, J = 8.2 Hz, 1H), 7.98-7.90 (m, 3H), 7.55 (t, J = 7.8 Hz, 1H), 7.47 (t, J = 7.8 Hz, 1H).

4.31. 4-(2-Propylthiazol-5-yl)-pyridine (**28**)

The reaction of 4-chloropyridine hydrochloride (0.150 g, 1 mmol), 2-*n*propylthiazole (0.153 g, 1.2 mmol) and KOAc (0.216 g, 2.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 28 in 76% (0.155 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.61 (d, J = 6.4 Hz, 2H), 8.00 (s, 1H), 7.40 (d, J = 6.4 Hz, 2H), 3.01 (t, J = 7.5 Hz, 2H), 1.88 (sext., J = 7.5 Hz, 2H), 1.04 (t, J = 7.5 Hz, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 173.4, 150.9, 140.3, 139.5, 135.9, 121.0, 36.1, 23.7, 14.0.

Anal. Calc. for $C_{11}H_{12}N_2S$: C, 64.67; H, 5.92. Found: C, 64.80; H, 5.81%.

4.32. 4-(2-Ethyl-4-methylthiazol-5-yl)-pyridine (**29**)

The reaction of 4-chloropyridine hydrochloride (0.150 g, 1 mmol), 2-ethyl-4-methylthiazole (0.153 g, 1.2 mmol) and KOAc (0.216 g, 2.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 29 in 34% (0.069 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.64 (d, J = 6.4 Hz, 2H), 7.33 (d, J = 6.4 Hz, 2H), 3.01 (q, J = 7.6 Hz, 2H), 2.53 (s, 3H), 1.41 (t, J = 7.6 Hz, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 172.3, 150.5, 149.7, 140.8, 128.5, 123.5, 27.4, 17.0, 14.6.

Anal. Calc. for $C_{11}H_{12}N_2S$: C, 64.67; H, 5.92. Found: C, 64.50; H, 5.99%.

4.33. 5-Pyridin-4-ylthiazole-2-carboxylic acid ethyl ester (**30**)

The reaction of 4-chloropyridine hydrochloride (0.150 g, 1 mmol), ethyl thiazole-2-carboxylate (0.189 g, 1.2 mmol) and KOAc (0.216 g, 2.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 30 in 37% (0.087 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.70 (d, J = 6.3 Hz, 2H), 8.29 (s, 1H), 7.52 (d, J = 6.3 Hz, 2H), 3.22 (q, J = 7.6 Hz, 2H), 1.28 (t, J = 7.6 Hz, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 194.9, 167.6, 151.2, 143.6, 142.3, 138.3, 121.5, 32.1, 8.3.

Anal. Calc. for $C_{11}H_{10}N_2O_2S$: C, 56.39; H, 4.30. Found C, 56.21; H, 4.41%.

4.34. 4-(5-Butylthiophen-2-yl)-pyridine (**31**)

The reaction of 4-chloropyridine hydrochloride (0.150 g, 1 mmol), 2-*n*butylthiophene (0.168 g, 1.2 mmol) and KOAc (0.216 g, 2.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 31 in 50% (0.109 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.70–8.40 (m, 2H), 7.43 (d, J = 6.4 Hz, 2H), 7.34 (d, J = 3.8 Hz, 1H), 6.82 (d, J = 3.8 Hz, 1H), 2.86 (t, J = 7.5 Hz, 2H), 1.75 (quint., J = 7.5 Hz, 2H), 1.41 (sext., J = 7.5 Hz, 2H), 0.97 (t, J = 7.5 Hz, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 150.6, 149.0, 142.1, 138.7, 126.0, 125.6, 119.9, 34.0, 30.4, 22.6, 14.2.

Anal. Calc. for $C_{13}H_{15}NS$: C, 71.84; H, 6.96. Found: C, 71.70; H, 6.79%.

4.35. 4-(5-Butylfuran-2-yl)-pyridine (**32**)

The reaction of 4-chloropyridine hydrochloride (0.150 g, 1 mmol), 2-*n*butylfuran (0.149 g, 1.2 mmol) and KOAc (0.216 g, 2.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMAc at 120 °C affords the corresponding product 32 in 34% (0.069 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.65–8.40 (m, 2H), 7.48 (d, J = 6.3 Hz, 2H), 6.80 (d, J = 3.8 Hz, 1H), 6.14 (d, J = 3.8 Hz, 1H), 2.72 (t, J = 7.5 Hz, 2H), 1.75 (quint., J = 7.5 Hz, 2H), 1.41 (sext., J = 7.5 Hz, 2H), 0.97 (t, J = 7.5 Hz, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 159.1, 150.3, 138.2, 122.5, 117.7, 110.2, 108.0, 30.5, 28.3, 22.7, 14.2.

Anal. Calc. for $C_{13}H_{15}NO$: C, 77.58; H, 7.51. Found: C, 77.41; H, 7.47%.

4.36. 2-Pyrimidin-2-ylbenzoxazole (**33**)

The reaction of 2-chloropyrimidine (0.115 g, 1 mmol), benzoxazole (0.143 g, 1.2 mmol) and Cs_2CO_3 (0.390 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 150 °C affords the corresponding product 33 in 81% (0.160 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.91 (d, J = 7.3 Hz, 2H), 7.82 (d, J = 7.8 Hz, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.50–7.30 (m, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 158.5, 157.0, 154.2, 150.2, 140.6, 126.0, 124.3, 120.9, 120.5, 110.4.

Anal. Calc. for $C_{11}H_7N_3O$: C, 67.00; H, 3.58. Found: C, 67.11; H, 3.67%.

4.37. 2-Benzothiazol-2-ylbenzoxazole (**34**)

The reaction of 2-chlorobenzothiazole (0.170 g, 1 mmol), benzoxazole (0.143 g, 1.2 mmol) and Cs_2CO_3 (0.390 g, 1.2 mmol) with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 150 °C affords the corresponding product 34 in 54% (0.136 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.26 (d, J = 8.2 Hz, 1H), 8.01 (d, J = 8.2 Hz, 1H), 7.88 (d, J = 8.2 Hz, 1H), 7.72 (d, J = 8.2 Hz, 1H), 7.60 (t, J = 7.8 Hz, 1H), 7.53 (t, J = 7.8 Hz, 1H), 7.50–7.40 (m, 2H).

4.38. [2,2′]Bibenzothiazolyl (**35**)

The reaction of 2-chlorobenzothiazole (0.170 g, 1 mmol), benzothiazole (0.162 g, 1.2 mmol) and Cs_2CO_3 (0.390 g, 1.2 mmol)

with $PdCl(C_3H_5)$(dppb) (0.015 g, 0.025 mmol) in DMF at 150 °C affords the corresponding product 35 in 63% (0.169 g) isolated yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ 7.80 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.44 (t, J = 7.8 Hz, 1H), 7.28 (t, J = 7.8 Hz, 1H).

4.39. Cyclic voltammetry

Compounds **3** and **4** exhibited in cyclic voltammetry a reversible wave at $-1.55V_{SCE}$ and $-1.47V_{SCE}$, corresponding to the formation of a radical anion, as previously reported for similar benzothiazole and benzoxazole derivatives [17]. The substitution of the pyridine group by a quinoline in **3** and the introduction of an electron-attracting substituent on the pyridine ring in **4** rendered the nucleus more easily reducible, as seen by the cathodic shift of the reduction potentials ($-1.87V_{SCE}$ for 2). The electronic effect in **4** also affected the second reduction wave, observed at a less cathodic potential than other analogues ($-2.47V_{SCE}$ for **1** and $-2.05V_{SCE}$ for **4**).

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