Palladium/Tetraphosphine Catalyzed Suzuki Cross-Coupling of Heteroarylboronic Acids with Aryl Halides.

Isabelle Kondolff,[a] Henri Doucet,[b*] Maurice Santelli[a*]

[a]UMR 6180 CNRS and Université d'Aix-Marseille III: "Chirotechnologies: catalyse et biocatalyse", Laboratoire de Synthèse Organique, Faculté des Sciences de Saint Jérôme, Université d'Aix-Marseille III, Avenue Escadrille Normandie-Niemen, 13397 Marseille Cedex 20, France, FAX: (33) 4 91 98 91 12; E-mail: m.santelli@univ-cezanne.fr

[b]Institut Sciences Chimiques de Rennes, UMR 6226 CNRS-Université de Rennes "Catalyse et Organometalliques", Campus de Beaulieu, 35042 Rennes, France. Fax: 02-23-23-69-39; Tel: 02-23-23-62-80; E-mail: henri.doucet@univ-rennes1.fr.

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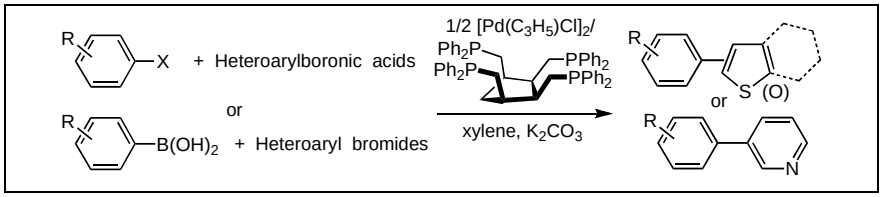

cis,*cis*,*cis*-1,2,3,4-Tetrakis(diphenylphosphinomethyl)cyclopentane/$[PdCl(C_3H_5)]_2$ efficiently catalyses the Suzuki reaction of heteroarylboronic acids with aryl bromides and also the coupling of arylboronic acids with heteroaryl bromides. The coupling of thiophene- or benzothiopheneboronic acids, furan- or benzofuranboronic acids and 3-pyridineboronic acid with a variety of aryl bromides gave the corresponding coupling products in good yields. However, in most cases, better results in terms of ratio substrate/catalyst were obtained for the reverse reaction using heteroaryl bromides with arylboronic acids.

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INTRODUCTION

Due to their important biological properties, the preparation of heterobiaryls is an important industrial goal. The palladium-catalysed Suzuki cross-coupling reaction between heteroaryl halides and arylboronic acids provides a very efficient method for the preparation of heterobiaryl derivatives [1,2]. On the other hand, the reverse reaction using heteroarylboronic acids and aryl halides has attracted much less attention, and most of the results have been described with $Pd(PPh_3)_4$ as catalyst [3–6]. But this ligand can be labile under coupling conditions especially at elevated temperature and gave palladium black which is generally completely inactive for cross-coupling reactions. In recent years, a few other catalysts have been tested on the Suzuki coupling of these heteroarylboronic acid derivatives [7–15]. For example, Fu *et al*. have reported the coupling of 2-thiopheneboronic acid with 4-bromo-*N*,*N*-dimethylaniline using 0.5% $Pd_2(dba)_3$ and 1.2% P(*t*-Bu)$_3$ as catalyst [7]. Two dialkylbiphenylphosphino ligands with 1–3% $Pd_2(dba)_3$ are also efficient catalysts for the coupling of pyridineboronic acids with aryl halides [8,9]. Dppf as ligand gave satisfactory results for the arylation of thiophene, benzofuran and pyridineboronic acids [10-14]. A palladium complex with a di(norbornyl)phosphine and a 2-phenylpyridine ligand catalyses the arylation of 3-furan- and 3-thiopheneboronic acid derivatives using 5 mol % catalyst [15]. Recently, diaminocarbenes were also found to be useful ligands for the coupling of 3-pyridineboronic acid with 2,6-dimethylbromobenzene [16]. $PdCl_2$(ethylenediamine-*N*,*N*,*N*',*N*'-tetraacetic acid) is also an efficient catalyst for the arylation of 3-thiopheneboronic acid [17]. A palladium–metalla-macrocycle supported by an aminofunctionalised ferrocene was used for the coupling of 3-thiophene-boronic acid with 4-bromobenzophenone [18]. A few other coupling reactions using these heteroarylboronic acids have also been described in the presence of palladium nanoparticles, supported catalysts, in ionic liquids as solvent or using microwaves [19-25].

In order to obtain stable and efficient palladium catalysts, we have prepared the tetraphosphine ligand, *cis*,*cis*,*cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)-cyclopentane or Tedicyp [26] (Scheme 1). The presence of four phosphines close to the metal center seems to increase the stability of the catalyst. The palladium is shown by NMR to circulate around the 4 phosphorous atoms under the "pressure to coordinate" of the 4 phosphino groups maintained in a half-space. This "pressure to coordinate" in a half space might be responsible for easy reductive elimination step for several cross-coupling reactions. We have already reported several results obtained in allylic substitution, [27] for Heck, [28] Sonogashira, [29] Suzuki [30] or Negishi [31]. reactions and also for C–H activation/arylation of furans [32] using this ligand. We have also described several results for the Suzuki coupling of heteroaryl halides with arylboronic acids [33]. Recently, we have described preliminary results, for the reverse reaction using heteroarylboronic acids with aryl halides [34]. In order to further establish

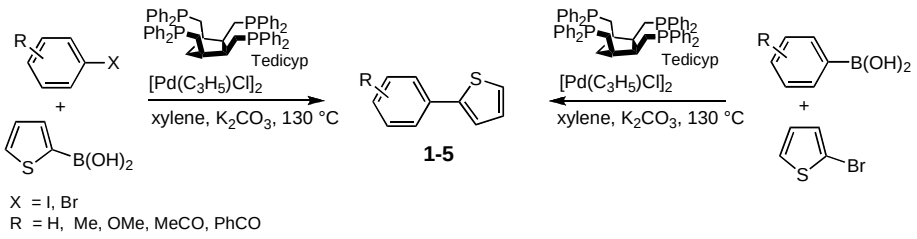
the requirements for successful Suzuki coupling reactions for the synthesis of arylthiophene, arylfuran or arylpyridine derivatives with our catalyst, we herein report on the coupling of heteroarylboronic acids such as thiophene-, benzothiophene-, dibenzothiophene-, furan-, benzofuran-, or pyridineboronic acids with aryl bromides. We have also compared in several cases the relative reaction rates for the coupling of heteroarylboronic acids and aryl bromides with the reverse combination of reactants.

RESULTS AND DISCUSSION

Palladium chemistry involving heterocycles has its unique characteristics stemming from the heterocycles' inherently different structural and electronic properties in comparison to the corresponding carbocyclic aryl compounds. Furthermore, palladium(II) possesses strong thiophilicity. Therefore, when using thiophene derivatives for some palladium-catalysed reactions, a poisoning effect of the sulphur atom can be observed. This poisoning effect has also been observed in the presence of nitrogen atom. For these reasons, the position of the halide on a heteroaromatic ring and the nature of the heteroatom have important effects on the reactions rates.

We first studied the reactivity of 2-thiopheneboronic acid with a range of aryl bromides (Scheme 1, Table 1). For this study, based on previous results [33], xylene was used as the solvent and K_2CO_3 as the base. The reactions were performed at 130°C under argon in the presence of a 1:2 ratio of $[Pd(C_3H_5)Cl]_2$/Tedicyp as catalyst (Scheme 1). The coupling of 2-thiopheneboronic acid with iodobenzene, bromobenzene, 4-bromoacetophenone, 4-bromoanisole or 2-bromotoluene gave the expected 2-arylthiophenes **1**–**5** in good yields in the presence of 1–5% catalyst (Table 1, entries 1, 2, 4, 5, 7–9, 11 and 12). Similar reaction rates were observed with electron-poor and electron-rich aryl bromides indicating that with this heteroarylboronic acid, the oxidative addition of the aryl bromide to palladium is not rate-limiting. The reverse reaction using 2-bromothiophene and arylboronic acids led to much faster reactions and very high substrate/catalyst ratios of 1000–1,000,000 have been successfully employed (Table 1, entries 3, 6, 10 and 13). These results seem to indicate that the catalyst might be partially poisoned by 2-thiopheneboronic acid. Using the functionalised 2-acetyl-5-thiopheneboronic acid we also obtained the arylation product **6** in good yield (Scheme 2). It should be noted that such 2-arylthiophenes can also be prepared directly by palladium catalysed C–H activation/fonctionalisation using simple thiophenes and aryl halides [36]. Therefore, the coupling reaction using 2-thiopheneboronic acid is probably not economically attractive compared to the Suzuki arylation reaction of 2-bromothiophene which proceeds at high substrate/catalyst ratios or to the C–H activation/functionalisation of thiophene which does not require the use of an arylboronic acid.

Scheme 1



X = I, Br
R = H, Me, OMe, MeCO, PhCO

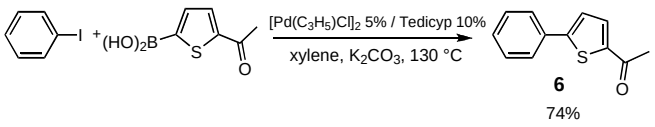
Table 1

Suzuki reaction with 2-thiopheneboronic acid catalysed by the Tedicyp-palladium complex (Scheme 1).

Entry	Aryl halide	Arylboronic acid	Ratio substrate/catalyst	Product	Yield (%)[a]
1	Iodobenzene	2-Thiopheneboronic acid	100	**1**	82 (96)
2	Bromobenzene	2-Thiopheneboronic acid	50	**1**	(47)
3	2-Bromothiophene	Benzeneboronic acid	100000	**1**	88
4	4-Bromoacetophenone	2-Thiopheneboronic acid	100	**2**	80 (86)
5	4-Bromoacetophenone	2-Thiopheneboronic acid	250	**2**	(64)
6	2-Bromothiophene	4-Acetylphenylboronic acid	1000	**2**	90
7	4-Bromobenzophenone	2-Thiopheneboronic acid	50	**3**	39 (44)
8	4-Bromoanisole	2-Thiopheneboronic acid	20	**4**	(100)
9	4-Bromoanisole	2-Thiopheneboronic acid	50	**4**	81
10	2-Bromothiophene	4-Methoxyphenylboronic acid	1000000	**4**	85
11	2-Bromotoluene	2-Thiopheneboronic acid	20	**5**	87 (100)
12	2-Bromotoluene	2-Thiopheneboronic acid	50	**5**	(40)
13	2-Bromothiophene	2-Methylphenylboronic acid	100000	**5**	89

Conditions: catalyst $[Pd(C_3H_5)Cl]_2$ / Tedicyp 1:2, see ref. 26, ArX (1 equiv.), arylboronic acid (2 equiv.), K_2CO_3 (2 equiv.), xylene, 20 h, 130 °C, under argon, isolated yields, ratio substrate/catalyst based on the aryl halide. [a] Yields in parenthesis correspond to GC and NMR yields.

Scheme 2



2-Benzothiopheneboronic acid was found to be less reactive than 2-thiopheneboronic acid (Scheme 3, Table 2). Using iodobenzene or 4-bromoacetophenone, low yields of 2-arylbenzothiophenes **7** and **8** have been obtained. With this heteroarylboronic acid, the best result was obtained using the sterically congested and electron-rich 2-bromotoluene (Table 2, entry 4). Again, for the cross-coupling reactions with 2-benzothiopheneboronic acid, the oxidative addition of the aryl bromide to palladium is certainly not the rate-limiting step of the catalytic cycle.

Scheme 3

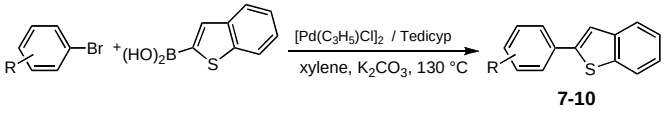


Table 2

Suzuki reaction with 2-benzothiopheneboronic acid catalysed by the Tedicyp-palladium complex (Scheme 3).

Entry	Aryl halide	Ratio substrate/ catalyst	Product	Yield (%)[a]
1	Iodobenzene	20	7	26 (34)
2	4-Bromoacetophenone	20	8	6 (10)
3	4-Bromobenzonitrile	100	9	41 (53)
4	2-Bromotoluene	50	10	92 (100)

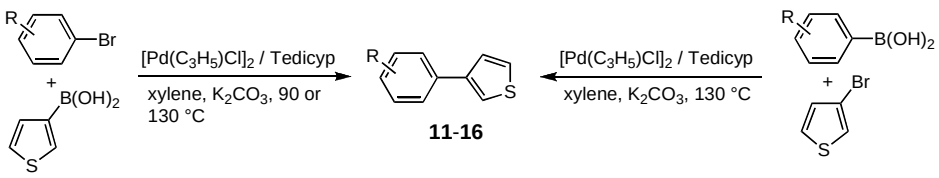
Conditions: catalyst $[Pd(C_3H_5)Cl]_2$ / Tedicyp 1:2, see ref. 26, ArX (1 equiv.), 2-benzothiopheneboronic acid (2 equiv.), K_2CO_3 (2 equiv.), xylene, 20 h, 130 °C, under argon, isolated yields, ratio substrate/catalyst based on the aryl halide. [a] Yields in parenthesis correspond to GC and NMR yields.

Then we examined the coupling of 3-thiopheneboronic acid with several aryl bromides to give 3-arylated thiophenes (Scheme 4, Table 3). These compounds can not be obtained by palladium catalysed C–H activation of thiophene. Therefore, the classical cross-coupling reactions remain the most powerful method for their preparation. We observed that higher reactions rates were observed for the coupling reactions in the presence of 3-thiopheneboronic acid than with 2-thiopheneboronic acid. Using 4-bromoacetophenone, 4-bromobenzaldehyde, 4-bromobenzophenone or 4-bromoanisole the reactions were performed using as little as 0.4–0.1% catalyst. Employing these reaction conditions, the products **11**–**14** were obtained in high yields (Table 3, entries 1–4, 6–13). The sterically congested aryl bromides 2-bromotoluene and bromomesitylene were also found to be suitable reactants for coupling with 3-thiopheneboronic acid (Table 3, entries 15, 17 and 18). However, the coupling with bromomesitylene required the presence of 5 mol % catalyst. Again, in order to determine the most powerful method for the synthesis of these compounds via Suzuki coupling, we determined the reactions rates for the coupling reactions using 3-bromothiophene with 4-acetylphenylboronic acid (Table 3, entry 5). For this reaction a TON of 215 was obtained, which is quite similar to the TON of 550 obtained for the coupling of 3-thiopheneboronic acid with 4-bromoacetophenone. On the other hand, the coupling of 3-bromothiophene with 4-methoxy- or 2-methylphenylboronic acids led to a very high TONs of 750000 and 930000, respectively, and the reverse reactions to TONs of 420 and 900 (Table 3, entries 11 and 14–16). In fact, the functions on the arylboronic acid have an important influence on the reactions rates of the coupling reactions.

In some cases, coupling reactions at elevated temperatures are not suitable due to the decomposition of the substrates or products. So, we performed a few reactions with 3-thiopheneboronic acid at a lower temperature (90°C). The reactions were slower, but satisfactory TONs of 300 and 225 were obtained with 4-bromoacetophenone and 4-bromoanisole (Table 1, entries 3, 4, 12 and 13).

The Suzuki reaction with 3-thiopheneboronic acid is not limited to the reaction with aryl bromides. A benzyl bromide has also been successfully used as coupling partner (Scheme 5). Moreover, this reaction proceeds in good yield using as little as 0.1 mol % catalyst.

Scheme 4



R = Me, OMe, MeCO, CHO, PhCO

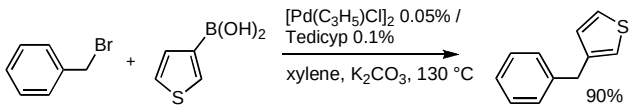
Table 3

Suzuki reaction with 3-thiopheneboronic acid catalysed by the Tedicyp-palladium complex (Scheme 4).

Entry	Aryl bromide	Arylboronic acid	Ratio substrate/catalyst	Product	Yield (%)[a]
1	4-Bromoacetophenone	3-Thiopheneboronic acid	250	**11**	77 (82)
2	4-Bromoacetophenone	3-Thiopheneboronic acid	1000	**11**	(55)
3	4-Bromoacetophenone	3-Thiopheneboronic acid	250	**11**	(84)[b]
4	4-Bromoacetophenone	3-Thiopheneboronic acid	1000	**11**	(30)[b]
5	3-Bromothiophene	4-Acetylphenylboronic acid	250	**11**	86
6	4-Bromobenzaldehyde	3-Thiopheneboronic acid	250	**12**	81 (90)
7	4-Bromobenzaldehyde	3-Thiopheneboronic acid	1000	**12**	(45)
8	4-Bromobenzophenone	3-Thiopheneboronic acid	50	**13**	91 (97)
9	4-Bromobenzophenone	3-Thiopheneboronic acid	1000	**13**	(60)
10	4-Bromoanisole	3-Thiopheneboronic acid	250	**14**	84 (97)
11	4-Bromoanisole	3-Thiopheneboronic acid	1000	**14**	(42)
12	4-Bromoanisole	3-Thiopheneboronic acid	250	**14**	(90)[b]
13	4-Bromoanisole	3-Thiopheneboronic acid	1000	**14**	0[b]
14	3-Bromothiophene	4-Methoxyphenylboronic acid	1000000	**14**	75
15	2-Bromotoluene	3-Thiopheneboronic acid	1000	**15**	84 (90)
16	3-Bromothiophene	2-Methylphenylboronic acid	1000000	**15**	93
17	2,4,6-Trimethylbromobenzene	3-Thiopheneboronic acid	20	**16**	74 (78)
18	2,4,6-Trimethylbromobenzene	3-Thiopheneboronic acid	100	**16**	(56)

Conditions: catalyst $[Pd(C_3H_5)Cl]_2$ / Tedicyp 1:2, see ref. 26, ArBr (1 equiv.), arylboronic acid (2 equiv.), K_2CO_3 (2 equiv.), xylene, 20 h, 130 °C, under argon, isolated yields, ratio substrate/catalyst based on the aryl halide. [a] Yields in parenthesis correspond to GC and NMR yields. [b] Reaction temperature: 90 °C.

Scheme 5



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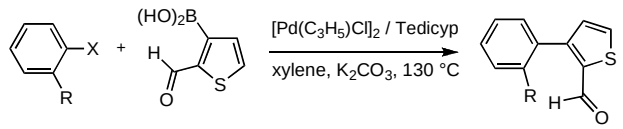
Then, we examined the reactivity of 2-formyl-3-thiopheneboronic acid (Scheme 6). Even if this functionalised arylboronic acid is less reactive than 3-thiopheneboronic acid, the products **18** and **19** were obtained in good yields using 1–2 mol % catalyst.

Scheme 6

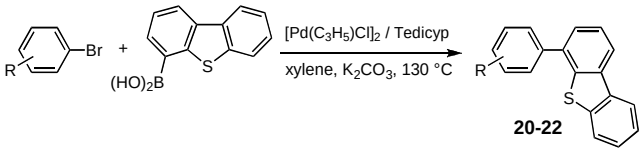


18, **19**

R = H and X = I: catalyst 1 mol % yield of **18**: 90%
R = OMe and X = Br: catalyst 2 mol % yield of **19**: 75%

The Suzuki reaction with 2-dibenzothiopheneboronic acid gave the expected 2-aryldibenzothiophene derivatives **20**–**22** in high yields (Scheme 7, Table 4). This reaction led to a higher TON of 6700 using the electron-deficient 4-bromoacetophenone than with bromobenzene. With this substrate, the oxidative addition of the aryl bromide to palladium might be rate-limiting.

Scheme 7



20-22

Table 4

Suzuki reaction with 2-dibenzothiopheneboronic acid catalysed by the Tedicyp-palladium complex (Scheme 7).

Entry	Aryl bromide	Ratio substrate/ catalyst	Product	Yield (%)[a]
1	Bromobenzene	100	20	93 (100)
2	4-Bromoacetophenone	1000	21	89 (100)
3	4-Bromoacetophenone	10000	21	(67)
4	2-Bromobenzaldehyde	100	22	92 (100)

Conditions: catalyst $[Pd(C_3H_5)Cl]_2$ / Tedicyp 1:2, see ref. 26, ArBr (1 equiv.), 2-dibenzothiopheneboronic acid (2 equiv.), K_2CO_3 (2 equiv.), xylene, 20 h, 130 °C, under argon, isolated yields, ratio substrate/catalyst based on the aryl halide. [a] Yields in parenthesis correspond to GC and NMR yields.

The reactions rates using 3-furanboronic acid and aryl halides were quite similar to those obtained with 3-thiopheneboronic acid (Scheme 8, Table 5). With this heteroarylboronic acid, iodobenzene, 4-bromoaceto-phenone, 4-bromobenzonitrile or 2-bromotoluene gave the arylfuran derivatives **23**–**26** in good yields in the presence of 0.4–0.1% catalyst (Table 5, entries 1, 2, 4, 5, 7–11). The reverse reaction using 3-bromofuran and arylboronic acids also gave the expected 3-arylfuranes in the presence of 0.4–0.1% catalyst (Table 5, entries 3, 6 and 13).

Scheme 8

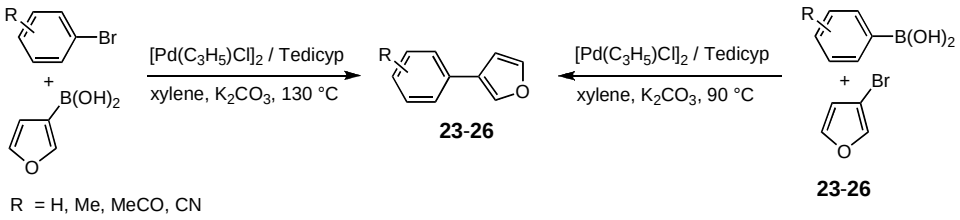


Table 5

Suzuki reaction with 3-furanboronic acid catalysed by the Tedicyp-palladium complex (Scheme 8).

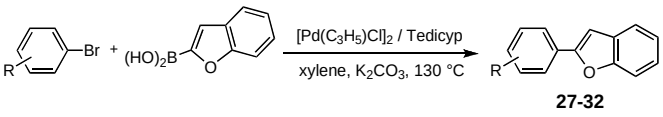
Entry	Aryl halide	Arylboronic acid	Ratio substrate/catalyst	Product	Yield (%)[a]
1	Iodobenzene	3-Furanboronic acid	250	23	83 (100)
2	Iodobenzene	3-Furanboronic acid	1000	23	(68)
3	3-Bromofuran	Benzeneboronic acid	1000	23	91 (100) [b]
4	4-Bromoacetophenone	3-Furanboronic acid	250	24	81 (98)
5	4-Bromoacetophenone	3-Furanboronic acid	1000	24	(84)
6	3-Bromofuran	4-Acetylphenylboronic acid	250	24	87 (94) [b]
7	4-Bromobenzonitrile	3-Furanboronic acid	100	25	(98)
8	4-Bromobenzonitrile	3-Furanboronic acid	250	25	68
9	2-Bromotoluene	3-Furanboronic acid	100	26	(100)
10	2-Bromotoluene	3-Furanboronic acid	250	26	81 (90)
11	2-Bromotoluene	3-Furanboronic acid	1000	26	(28)
12	2-Bromotoluene	3-Furanboronic acid	100	26	0 [b]
13	3-Bromofuran	2-Methylphenylboronic acid	250	26	70 [b]

Conditions: catalyst $[Pd(C_3H_5)Cl]_2$ / Tedicyp 1:2, see ref. 26, ArX (1 equiv.), 3-furanboronic acid (2 equiv.), K_2CO_3 (2 equiv.), xylene, 20 h, 130 °C, under argon, isolated yields, ratio substrate/catalyst based on the aryl halide. [a] Yields in parenthesis correspond to GC and NMR yields. [b] Reaction temperature: 90 °C.

However, these reactions were performed at a lower temperature (90 °C) due to the low boiling point of 3-bromofuran. In order to compare the respective rates of the reactions, a coupling was also performed with 3-furanboronic acids and 2-bromotoluene at 90 °C but, the aryl bromide was recovered unreacted (Table 5, entry 12). We had previously reported that the coupling of 5-bromo-2-furaldehyde with arylboronic acids proceeds in very high TONs [33].

The direct arylation of benzofuran *via* C–H function-alisation has been reported by Ohta in 1990, but the yields were low (12–50%) [36]. To our knowledge, high yield arylations of benzofuran *via* C–H activation have not been reported so far. Therefore, the arylation of 2-benzofuran-boronic acid remains a simple process for the formation of 2-arylbenzothiophenes. We found that 2-benzofuran-boronic acid is less reactive than 3-furanboronic acid (Scheme 9, Table 6). However, with electron-deficient aryl bromides such as 4-bromo-benzophenone, 4-bromo-benzaldehyde or 4-bromo-benzonitrile high yields of products **27**–**30** were obtained using 1–5 mol % catalyst (Table 6, entries 1–6). With the electron-excessive or the sterically congested aryl bromides, 4-bromoanisole or 2-bromotoluene, similar results were obtained (Table 6, entries 7–10). These results indicate that for the reaction with 2-benzofuranboronic acid and aryl bromides, the oxidative addition is not the rate limiting-step of the catalytic cycle.

Scheme 9



Finally, we studied the synthesis of 3-arylpyridines by coupling of 3-pyridineboronic acid with several aryl bromides and also by reaction of 3-bromopyridine with arylboronic acids (Scheme 10, Table 7). Relatively slow reactions were observed with 3-pyridineboronic acid, and 2–10% catalyst had to be used in order to obtain high yields of adducts (Table 7, entries 1, 3, 4, 6, 8, 10, 11, 13, 14, 16 and 18). The results unfold a minor substituent effect of the aryl bromide on the reaction rate, indicating that again, with 3-pyridineboronic acid as coupling partner, the rate-limiting step of the reaction is not the oxidative addition of the aryl bromide. The reverse coupling reactions using 3-bromopyridine and arylboronic acids gave much more satisfactory results in terms of ratio substrate/catalyst. The reactions were performed using 0.1–0.001% catalyst (Table 7, entries 2, 5, 7, 9, 12, 15, 17 and 18). For example, a TON of 8 was obtained for the

Table 6

Suzuki reaction with 2-benzofuraneboronic acid catalysed by the Tedicyp-palladium complex (Scheme 9).

Entry	Aryl halide	Ratio substrate/catalyst	Product	Yield (%)[a]
1	4-Bromoacetophenone	20	**27**	66 (81)
2	4-Bromobenzaldehyde	100	**28**	95 (100)
3	4-Bromobenzaldehyde	250	**28**	(27)
4	4-Bromobenzophenone	20	**29**	85 (92)
5	4-Bromobenzonitrile	20	**30**	88 (100)
6	4-Bromobenzonitrile	100	**30**	(52)
7	4-Bromoanisole	20	**31**	62 (80)
8	4-Bromoanisole	100	**31**	(60)
9	2-Bromotoluene	20	**32**	75 (88)
10	2-Bromotoluene	100	**32**	(34)

Conditions: catalyst $[Pd(C_3H_5)Cl]_2$ / Tedicyp 1:2, see ref. 26, ArX (1 equiv.), 2-Benzofuraneboronic acid (2 equiv.), K_2CO_3 (2 equiv.), xylene, 20 h, 130 °C, under argon, isolated yields, ratio substrate/catalyst based on the aryl halide. [a] Yields in parenthesis correspond to GC and NMR yields.

coupling of 3-pyridineboronic acid with 1-bromo-naphthalene; and a TON of 56000 for the reaction of 3-bromopyridine with 1-naphthaleneboronic acid (Table 7, entries 16 and 18).

In summary, in the presence of the Tedicyp/palladium complex, the Suzuki cross-coupling of heteroarylboronic acids such as 3-thiopheneboronic acid or 3-furanboronic acid with aryl bromides can be performed with as little as 0.1% catalyst. On the other hand, with 2-thiophene-, 2-benzothiophene-, 2-benzofuran- and 3-pyridineboronic acids, the reactions are quite slow and were generally performed with 1–10% catalyst. Pyridines are π-electron deficient heterocycles. Thiophenes or furans are π-electron excessive. These results seem to demonstrate that the electron-density on the heteroarylboronic acid is not a determining factor for the success of such couplings. On the other hand, palladium(II) possesses strong thiophilicity. This is reflected in the poisoning effects of

Scheme 10

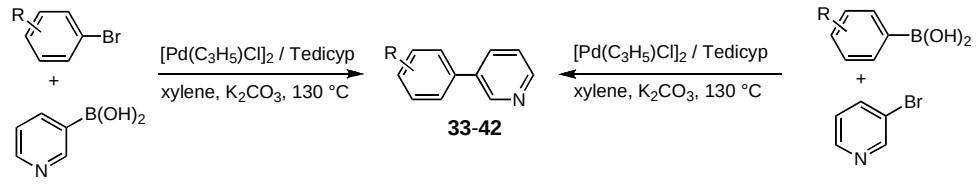


Table 7

Suzuki reaction with pyridine derivatives catalysed by the Tedicyp-palladium complex (Scheme 10).

Entry	Aryl bromide	Arylboronic acid	Ratio substrate/catalyst	Product	Yield (%)a
1	Bromobenzene	3-Pyridineboronic acid	33	33	75
2	3-Bromopyridine	Benzeneboronic acid	1000000	33	98[b,c]
3	4-Bromobenzophenone	3-Pyridineboronic acid	20	34	82 (100)
4	3-Bromobenzaldehyde	3-Pyridineboronic acid	20	35	84 (100)
5	3-Bromopyridine	3-Formylphenylboronic acid	100	35	87 (100)
6	4-Fluorobromobenzene	3-Pyridineboronic acid	10	36	84
7	3-Bromopyridine	4-Fluorophenylboronic acid	100000	36	96[b,d]
8	4-Bromoanisole	3-Pyridineboronic acid	20	37	80
9	3-Bromopyridine	4-Methoxyphenylboronic acid	100000	37	82[b]
10	2-Bromoacetophenone	3-Pyridineboronic acid	20	38	80 (100)
11	2-Bromoacetophenone	3-Pyridineboronic acid	50	38	(49)
12	3-Bromopyridine	2-Acetylphenylboronic acid	1000	38	77
13	2-Bromoanisole	3-Pyridineboronic acid	10	39	61 (70)
14	2-Bromotoluene	3-Pyridineboronic acid	20	40	85 (100)
15	3-Bromopyridine	2-Methylphenylboronic acid	10000	40	87b
16	1-Bromonaphthalene	3-Pyridineboronic acid	10	41	84
17	3-Bromopyridine	1-Naphthaleneboronic acid	10000	41	77
18	3-Bromopyridine	1-Naphthaleneboronic acid	100000	41	(56)
19	2,6-Dimethylbromobenzene	3-Pyridineboronic acid	20	42	85 (98)

Conditions: catalyst $[Pd(C_3H_5)Cl]_2$ / Tedicyp 1:2, see ref. 26, ArBr (1 equiv.), arylboronic acid (2 equiv.), K_2CO_3 (2 equiv.), xylene, 20 h, 130 °C, under argon, isolated yields, ratio substrate/catalyst based on the aryl halide. [a] Yields in parenthesis correspond to GC and NMR yields. [b] Ref. 33b. [c] $PhB(OH)_2$ 1.5 equiv., 115 h. [d] $PhB(OH)_2$ 1.5 equiv., 90 h.

the sulphur atom on some palladium-catalysed reactions. This poisoning effect has also been observed in the presence of nitrogen atoms. For this reason, the halide position on the heteroaroaryl boronic acid has an important effect on the reactions rates. This could partially explain the differences of reactivity between these heteroarylboronic acids. With most of these heteroarylboronic acid derivatives similar reaction rates were generally observed in the presence of 4-bromoacetophenone or 4-bromoanisole indicating that the rate-limiting step of these reactions does not seem to be the oxidative addition of the aryl halides to palladium. In order to obtain higher TONs for the synthesis of these products, we also studied the reverse reactions using arylboronic acids and heteroaryl bromides. We observed that, in most cases, much higher reaction rates were obtained for the coupling of bromothiophenes or 3-bromopyridine with arylboronic acids. For this reason, for the synthesis of arylthiophene or arylpyridine derivatives, the boronic acid function should preferably be located on the aryl and the halide on the heteroaryl rather than the reverse.

EXPERIMENTAL

General. All reactions were run under argon using vacuum lines in Schlenk tubes in oven-dried glassware. Xylene was not distilled before use. Commercial arylboronic acids and aryl halides were used without purification. ^{1}H (300 MHz) and ^{13}C (75 MHz) spectra were recorded in $CDCl_3$ solutions. Chemical shift (δ) are reported in ppm relative to $CDCl_3$. Flash chromatographies were performed on silica gel (230–400 mesh).

Preparation of the Pd-Tedicyp Catalyst [26]**.** An oven-dried 40-mL Schlenk tube equipped with a magnetic stirring bar, under argon atmosphere, was charged with $[Pd(C_3H_5)Cl]_2$ (4.2 mg, 11.6 μmol) and Tedicyp (20 mg, 23.2 μmol). 2.5 mL of anhydrous DMF were added then the solution was stirred at room temperature for 10 min. The appropriate amount of catalyst (see tables) was transferred to the mixture of aryl halide, arylboronic acid and base in xylene.

Catalytic procedure for Suzuki reactions. As a typical experiment, the reaction of the arylboronic acid (2 mmol), aryl bromide (1 mmol) and K_2CO_3 (276 mg, 2 mmol) at 130 °C over 20 h in xylene (3 mL) in the presence of *cis*,*cis*,*cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane/$[PdCl(C_3H_5)]_2$ complex under argon afforded the corresponding products after addition of water, extraction with dichloromethane, separation, drying ($MgSO_4$), evaporation and chromatography on silica gel.

2-Phenylthiophene (1). (Table 1, entry 1) Iodobenzene (204 mg, 1 mmol), 2-thiopheneboronic acid (256 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (10 μmol) gave **1** in 82% (131 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.08 (dd, J = 5.1, 3.6 Hz, 1H), 7.19 (d, J = 5.1 Hz, 1H), 7.25–7.34 (m, 2H), 7.38 (t, J = 7.5 Hz, 2H), 7.62 (dd, J = 7.5, 1.5 Hz, 2H).

4-(Thiophen-2-yl)acetophenone (2). (Table 1, entry 4) 4-Bromoacetophenone (199 mg, 1 mmol), 2-thiopheneboronic acid (256 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (10 μmol) gave **2** in 80% (162 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.59 (s, 3H), 7.11 (dd, J = 5.1, 3.6 Hz, 1H), 7.36 (d, J = 5.1 Hz, 1H), 7.42 (d, J = 3.6 Hz, 1H), 7.68 (d, J = 8.3 Hz, 2H), 7.95 (d, J = 8.3 Hz, 2H).

4-(Thiophen-2-yl)benzophenone (3). (Table 1, entry 7) 4-Bromobenzophenone (261 mg, 1 mmol), 2-thiopheneboronic acid (256 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (20 μmol) gave **3** in 39% (103 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.12 (dd, J = 5.0, 3.7 Hz, 1H), 7.37 (d, J = 5.0 Hz, 1H), 7.44 (d, J = 3.7 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H), 7.58 (t, J = 7.7 Hz, 1H), 7.71 (d, J = 8.5 Hz, 2H), 7.80 (d, J = 7.7 Hz, 2H), 7.83 (d, J = 8.5 Hz, 2H). ^{13}C nmr (300 MHz, $CDCl_3$): δ = 124.5, 125.4, 126.4, 128.3, 128.4, 129.9, 130.9, 132.3, 136.1, 137.7, 138.3, 143.0, 195.9. MS (EI, 70 eV): m/z (%) = 264 (100) [M^+]. Anal. Calcd. for $C_{17}H_{12}OS$, C, 77.24; H, 4.58; found C, 77.42; H, 4.42. White solid mp = 127 °C.

2-(4-Methoxyphenyl)thiophene (4). (Table 1, entry 9) 4-Bromoanisole (187 mg, 1 mmol), 2-thiopheneboronic acid (256 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (20 μmol) gave **4** in 81% (154 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 3.83 (s, 3H), 6.91 (d, J = 8.9 Hz, 2H), 7.04 (dd, J = 5.1, 3.7 Hz, 1H), 7.19 (d, J = 3.7 Hz, 1H), 7.21 (d, J = 5.1 Hz, 1H), 7.54 (d, J = 8.9 Hz, 2H).

2-(2-Methylphenyl)thiophene (5). (Table 1, entry 11) 2-Bromotoluene (171 mg, 1 mmol), 2-thiopheneboronic acid (256 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 μmol) gave **5** in 87% (151 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.42 (s, 3H), 7.04–7.11 (m, 2H), 7.15–7.25 (m, 3H), 7.33 (dd, J = 5.0, 1.3 Hz, 1H), 7.40 (dd, J = 5.7, 2.7 Hz, 1H).

2-Acetyl-5-phenylthiophene (6). (Scheme 2) Iodobenzene (204 mg, 1 mmol), 2-acetyl-5-thiopheneboronic acid (340 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (100 μmol) gave **6** in 74% (150 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.56 (s, 3H), 7.32 (d, J = 4.2 Hz, 1H), 7.38 (d, J = 4.2 Hz, 1H), 7.40 (t, J = 7.1 Hz, 2H), 7.63–7.65 (m, 1H), 7.66 (d, J = 7.1 Hz, 2H).

2-Phenylbenzothiophene (7). (Table 2, entry 1) Iodobenzene (204 mg, 1 mmol), 2-benzothiopheneboronic acid (356 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 μmol) gave **7** in 26% (55 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.27–7.38 (m, 3H), 7.41 (t, J = 7.6 Hz, 2H), 7.54 (s, 1H), 7.71 (d, J = 7.6 Hz, 2H), 7.77 (d, J = 6.8 Hz, 1H), 7.85 (d, J = 7.1 Hz, 1H).

2-(4-Acetylphenyl)benzothiophene (8). (Table 2, entry 2) 4-Bromoacetophenone (199 mg, 1 mmol), 2-benzothiopheneboronic acid (356 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 μmol) gave **8** in 6% (15 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.62 (s, 3H), 7.35 (ddd, J = 6.0, 4.2, 3.2 Hz, 2H), 7.66 (s, 1H), 7.78 (d, J = 8.5 Hz, 2H), 7.80–7.86 (m, 2H), 8.00 (d, J = 8.5 Hz, 2H).

2-(4-Benzonitrile)benzothiophene (9). (Table 2, entry 3) 4-Bromobenzonitrile (182 mg, 1 mmol), 2-benzothiopheneboronic acid (356 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (10 μmol) gave **9** in 41% (96 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.37 (t, J = 4.5 Hz, 2H), 7.64 (s, 1H), 7.68 (d, J = 8.6 Hz, 2H), 7.79 (d, J = 8.6 Hz, 2H), 7.80–7.86 (m, 2H).

2-(2-Methylphenyl)benzothiophene (10). (Table 2, entry 4) 2-Bromotoluene (171 mg, 1 mmol), 2-benzothiopheneboronic acid (356 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (20 μmol) gave **10** in 92% (206 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.48 (s, 3H), 7.27–7.50 (m, 7H), 7.79 (d, J = 7.2 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H).

3-(4-Acetylphenyl)thiophene (11). (Table 3, entry 1) 4-Bromoacetophenone (199 mg, 1 mmol), 3-benzothiopheneboronic acid (356 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (4 μmol) gave **10** in 77% (0.156 g) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.61 (s, 3H), 7.39–7.44 (m, 2H), 7.56 (t, J = 2.1 Hz, 1H), 7.67 (d, J = 8.5 Hz, 2H), 7.98 (d, J = 8.5 Hz, 2H).

4-Thiophen-3-yl-benzaldehyde (12). (Table 3, entry 6) 4-Bromobenzaldehyde (185 mg, 1 mmol), 3-benzothiopheneboronic acid (356 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (4 μmol) gave **12** in 81% (152 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.40–7.47 (m, 2H), 7.61 (t, J = 2.2 Hz, 1H), 7.75 (d, J = 8.1 Hz, 2H), 7.91 (d, J = 8.1 Hz, 2H), 10.02 (s, 1H).

Phenyl-(4-thiophen-3-yl-phenyl)-methanone (13). (Table 3, entry 8) 4-Bromobenzophenone (261 mg, 1 mmol), 3-benzothiopheneboronic acid (356 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (20 μmol) gave **13** in 91% (240 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.40–7.46 (m, 2H), 7.48 (t, J = 8.0 Hz, 2H), 7.55–7.60 (m, 2H), 7.69 (d, J = 8.7 Hz, 2H), 7.80 (d, J = 8.0 Hz, 2H), 7.85 (d, J = 8.7 Hz, 2H). ^{13}C nmr (300 MHz, $CDCl_3$): δ = 121.9, 126.1, 126.2, 126.7, 128.3, 129.9, 130.9, 132.3, 135.9, 137.8, 139.7, 141.1, 196.1. MS (EI, 70 eV): m/z (%) = 264 (100) [M^+]. Anal. Calcd. For $C_{17}H_{12}OS$: C, 77.24; H, 4.58, found C, 76.96; H, 4.82. White solid mp = 155 °C.

3-(4-Methoxyphenyl)thiophene (14). (Table 3, entry 10) 4-Bromoanisole (187 mg, 1 mmol), 3-benzothiopheneboronic acid (356 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (4 μmol) gave **14** in 84% (160 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 3.82 (s, 3H), 6.92 (d, J = 8.9 Hz, 2H), 7.30–7.36 (m, 3H), 7.51 (d, J = 8.9 Hz, 2H).

3-(2-Methylphenyl)thiophene (15). acid (356 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (1 μmol) gave **15** in 84% (146 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.37 (s, 3H), 7.16 (dd, J = 4.9, 1.4 Hz, 1H), 7.21–7.28 (m, 4H), 7.30 (m, 1H), 7.36 (dd, J = 4.9, 3.0 Hz, 1H).

3-(2,4,6-Trimethylphenyl)thiophene (16): (Table 3, entry 17) 2,4,6-Trimethylbromobenzene (199 mg, 1 mmol), 3-benzothiopheneboronic acid (356 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 μmol) gave **16** in 74% (150 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.04 (s, 6H), 2.30 (s, 3H), 6.86–6.93 (m, 3H), 7.00–7.04 (m, 1H), 7.36–7.40 (m, 1H).

3-Benzylthiophene (17). (Scheme 5) Benzyl bromide (171 mg, 1 mmol), 3-thiopheneboronic acid (256 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (1 μmol) gave **17** in 90% (157 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 4.02 (s, 2H), 7.24–7.40 (m, 6H), 7.95 (m, 2H).

2-Formyl-3-phenylthiophene (18). (Scheme 6) Iodobenzene (204 mg, 1 mmol), 2-formyl-3-thiopheneboronic acid (312 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (10 μmol) gave **18** in 90% (169 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.22 (d, J = 4.9 Hz, 1H), 7.43–7.50 (m, 5H), 7.73 (dd, J = 4.9, 1.3 Hz, 1H), 9.88 (d, J = 1.3 Hz, 1H).

2-Formyl-3-(2-methoxyphenyl)thiophene (19): (Scheme 6) 2-Bromoanisole (187 mg, 1 mmol), 2-formyl-3-thiopheneboronic acid (312 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (20 μmol) gave **19** in 75% (164 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 3.79 (s, 3H), 6.95–7.10 (m, 2H), 7.18 (d, J = 5.0 Hz, 1H), 7.25–7.30 (m, 1H), 7.40 (td, J = 7.5, 4.4 Hz, 1H), 7.68 (dd, J = 5.0, 1.1 Hz, 1H), 9.71 (d, J = 1.1 Hz, 1H).

4-Phenyldibenzothiophene (20). (Table 4, entry 1) Bromobenzene (157 mg, 1 mmol), 2-dibenzothiopheneboronic acid (456 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (10 μmol) gave **20** in 93% (242 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.45–7.61 (m, 7H), 7.77 (d, J = 7.0 Hz, 2H), 7.85 (m, 1H), 8.13-8.22 (m, 2H).

4-(4-Acetylphenyl)dibenzothiophene (21). (Table 4, entry 2) 4-Bromoacetophenone (199 mg, 1 mmol), 2-dibenzothiopheneboronic acid (456 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (1 μmol) gave **21** in 89% (269 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.67 (s, 3H), 7.45–7.52 (m, 3H), 7.58 (t, J = 7.6 Hz, 1H), 7.83–7.86 (m, 1H), 7.84 (d, J = 8.2 Hz, 2H), 8.11 (d, J = 8.2 Hz, 2H), 8.16–8.21 (m, 2H). ^{13}C nmr (300 MHz, $CDCl_3$): δ = 26.7, 121.2, 121. 8, 122.6, 124.5, 125.2, 126.9, 127.0, 128.5, 128.9, 135.6, 135.8, 136.5, 138.4, 139.4, 145.3, 197.7. Anal. Calcd. For $C_{20}H_{14}OS$: C, 79.44; H, 4.67, found C, 79.57; H, 4.84. MS (EI, 70 eV): m/z (%) = 302 (81) [M^+]. White solid mp = 129 °C.

2-Dibenzothiophen-4-ylbenzaldehyde (22). (Table 4, entry 4) 2-Bromobenzaldehyde (185 mg, 1 mmol), 2-dibenzothiopheneboronic acid (456 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (10 μmol) gave **22** in 92% (265 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.39 (dd, J = 7.4, 1.2 Hz, 1H), 7.47 (ddd, J = 6.5, 4.3, 2.2 Hz, 2H), 7.55–7.63 (m, 3H), 7.68–7.81 (m, 2H), 8.13 (dd, J = 8.5, 1.9 Hz, 1H), 8.17–8.25 (m, 2H), 9.81 (s, 1H).

3-Phenylfuran (23). (Table 5, entry 1) Iodobenzene (204 mg, 1 mmol), 3-furanboronic acid (224 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (4 μmol) gave **23** in 83% (120 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 6.70 (dd, J = 1.3, 0.9 Hz, 1H), 7.25–7.30 (m, 1H), 7.37 (t, J = 7.6 Hz, 2H), 7.46 (t, J = 1.3 Hz, 1H), 7.49 (d, J = 7.6 Hz, 2H), 7.72 (bs, 1H).

1-(4-Furan-3-ylphenyl)-ethanone (24). (Table 5, entry 4) 4-Bromoacetophenone (199 mg, 1 mmol), 3-furanboronic acid (224 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (4 μmol) gave **24** in 81% (151 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.60 (s, 3H), 6.74 (dd, J = 1.8, 0.9 Hz, 1H), 7.50 (t, J = 1.8 Hz, 1H), 7.56 (d, J = 8.3 Hz, 2H), 7.82 (bs, 1H), 7.96 (d, J = 8.3 Hz, 2H). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 26.5, 108.6, 125.7, 129.0, 135.6, 137.2, 139.6, 144.1, 197.4. MS (EI, 70 eV): m/z (%) = 186 (53) [M^+]. Anal. Calcd. For $C_{12}H_{10}O_2$: C, 77.40; H, 5.41, found C, 77.23; H, 5.36. White solid mp = 96 °C.

4-Furan-3-ylbenzonitrile (25). (Table 5, entry 8) 4-Bromobenzonitrile (182 mg, 1 mmol), 3-furanboronic acid (224 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (4 μmol) gave **25** in 68% (115 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 6.70 (dd, J = 1.9, 0.9 Hz, 1H), 7.51 (t, J = 1.9 Hz, 1H), 7.56 (d, J = 9.6 Hz, 2H), 7.64 (d, J = 9.6 Hz, 2H), 7.81 (t, J = 0.9 Hz, 1H).

3-*o*-Tolylfuran (26). (Table 5, entry 10) 2-Bromotoluene (171 mg, 1 mmol), 3-furanboronic acid (224 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (4 μmol) gave **26** in 81% (128 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.38 (s, 3H), 6.58 (dd, J = 1.7, 0.9 Hz, 1H), 7.17–7.35 (m, 4H), 7.47 (t, J = 1.7 Hz, 1H), 7.52 (d, J = 0.9 Hz, 1H).

1-(4-Benzofuran-2-yl-phenyl)-ethanone (27). (Table 6, entry 1) 4-Bromoacetophenone (199 mg, 1 mmol), 2-benzofuranboronic acid (324 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 μmol) gave **27** in 66% (156 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.62 (s, 3H), 7.15 (s, 1H), 7.27 (td, J = 7.8, 1.2 Hz, 1H), 7.33 (td, J = 7.8, 1.2 Hz, 1H), 7.53 (d, J = 7.8 Hz, 1H), 7.59 (d, J = 7.8 Hz, 1H), 7.93 (d, J = 8.4 Hz, 2H), 8.03 (d, J = 8.4 Hz, 2H).

4-Benzofuran-2-yl-benzaldehyde (28). (Table 6, entry 2) 4-Bromobenzaldehyde (185 mg, 1 mmol), 2-benzofuranboronic acid (324 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (10 μmol) gave **28** in 95% (211 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.19 (s, 1H), 7.28 (td, J = 7.8, 1.5 Hz, 1H), 7.32 (td, J = 7.8, 1.5 Hz, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.92 (d, J = 8.4 Hz, 2H), 8.01 (d, J = 8.4 Hz, 2H), 10.02 (s, 1H).

(4-Benzofuran-2-yl-phenyl)-phenylmethanone (29). (Table 6, entry 4) 4-Bromobenzophenone (261 mg, 1 mmol), 2-benzofuranboronic acid (324 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 μmol) gave **29** in 85% (253 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.18 (d, J = 0.8 Hz, 1H), 7.26 (td, J = 8.0, 1.3 Hz, 1H), 7.33 (td, J = 8.0, 1.3 Hz, 1H), 7.46–7.64 (m, 5H), 7.82 (dd, J = 7.0, 1.3 Hz, 2H), 7.90 (d, J = 8.6 Hz, 2H), 7.97 (d, J = 8.6 Hz, 2H). ^{13}C nmr (300 MHz, $CDCl_3$): δ = 103.5, 111.4, 121.3, 123.2, 124.5, 125.1, 128.3, 128.9, 129.9, 130.7, 132.5, 134.1, 137.0, 137.6, 154.6, 155.2, 195.9. MS (EI, 70 eV): m/z (%) = 298 (100) [M^+]. Anal. Calcd. For $C_{21}H_{14}O_2$: C, 84.54; H, 4.73, found C, 84.38; H, 4.84. White solid mp = 192 °C.

4-Benzofuran-2-ylbenzonitrile (30). (Table 6, entry 5) 4-Bromobenzonitrile (182 mg, 1 mmol), 2-benzofuranboronic acid (324 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 μmol) gave **30** in 88% (193 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.16 (s, 1H), 7.26 (td, J = 7.8, 1.3 Hz, 1H), 7.34 (td, J = 7.8, 1.3 Hz, 1H), 7.53 (d, J = 7.9 Hz, 1H), 7.61 (d, J = 7.9 Hz, 1H), 7.71 (d, J = 8.6 Hz, 2H), 7.94 (d, J = 8.6 Hz, 2H).

2-(4-Methoxyphenyl)-benzofuran (31). (Table 6, entry 7) 4-Bromoanisole (187 mg, 1 mmol), 2-benzofuranboronic acid (324 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 μmol) gave **31** in 62% (139 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 3.85 (s, 3H), 6.88 (s, 1H), 6.97 (d, J = 9.0 Hz, 2H), 7.17–7.25 (m, 2H), 7.49 (dd, J = 7.4, 1.1 Hz, 1H), 7.55 (dd, J = 7.4, 1.1 Hz, 1H), 7.79 (d, J = 9.0 Hz, 2H).

2-*o*-Tolylbenzofuran (32). (Table 6, entry 9) 2-Bromotoluene (171 mg, 1 mmol), 2-benzofuranboronic acid (324 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 μmol) gave **32** in 75% (156 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.58 (s, 3H), 6.89 (s, 1H), 7.24–7.35 (m, 5H), 7.52 (dd, J = 7.2, 1.0 Hz, 1H), 7.61 (dd, J = 7.2, 1.0 Hz, 1H), 7.85 (m, 1H).

3-Phenylpyridine (33). (Table 7, entry 1) Bromobenzene (157 mg, 1 mmol), 3-pyridineboronic acid (246 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (33 μmol) gave **33** in 75% (116 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.33–7.42 (m, 2H), 7.48 (t, J = 7.1 Hz, 2H), 7.58 (d, J = 7.1 Hz, 2H), 7.87 (dt, J = 8.0, 1.9 Hz, 1H), 8.58 (dd, J = 4.7, 1.9 Hz, 1H), 8.84 (d, J = 2.2 Hz, 1H).

Phenyl-(4-pyridin-3-yl-phenyl)-methanone (34). (Table 7, entry 3) 4-Bromobenzophenone (261 mg, 1 mmol), 3-pyridineboronic acid (246 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 μmol) gave **34** in 82% (210 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.45 (dd, J = 7.9, 4.9 Hz, 1H), 7.54 (t, J = 7.1 Hz, 2H), 7.63 (t, J = 7.1 Hz, 1H), 7.75 (d, J = 8.4 Hz, 2H), 7.88 (d, J = 8.4 Hz, 2H), 7.93–8.03 (m, 3H), 8.70 (dd, 1H, J = 4.8, 1.8 Hz, 1H), 8.95 (d, J = 1.8 Hz, 1H).

3-Pyridin-3-yl-benzaldehyde (35). (Table 7, entry 4) 3-Bromobenzaldehyde (185 mg, 1 mmol), 3-pyridineboronic acid (246 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 μmol) gave **35** in 84% (174 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.42 (dd, J = 7.6, 4.9 Hz, 1H), 7.66 (t, J = 7.8 Hz, 1H), 7.85 (dt, J = 7.6, 1.0 Hz, 1H), 7.93 (dd, J = 7.8, 1.3 Hz, 2H), 8.08 (s, 1H), 8.64 (bs, 1H), 8.89 (bs, 1H), 10.09 (s, 1H).

3-(4-Fluorophenyl)-pyridine (36). (Table 7, entry 6) 4-Fluorobromobenzene (175 mg, 1 mmol), 3-pyridineboronic acid (246 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (100 μmol) gave **36** in 84% (145 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.14 (dd, J = 8.8, 8.6 Hz, 2H), 7.35 (dd, J = 7.7, 4.9 Hz, 1H), 7.54 (dd, J = 8.8, 5.3 Hz, 2H), 7.83 (dt, J = 7.7, 1.4 Hz, 1H), 8.59 (bs, 1H), 8.81 (bs, 1H).

3-(4-Methoxyphenyl)-pyridine (37). (Table 7, entry 8) 4-Bromoanisole (187 mg, 1 mmol), 3-pyridineboronic acid (246 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 μmol) gave **37** in 80% (148 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 3.85 (s, 3H), 7.00 (d, J = 8.9 Hz, 2H), 7.35 (dd, J = 7.5, 4.7 Hz, 1H), 7.50 (d, J = 8.9 Hz, 2H), 7.82 (dt, J = 7.5, 1.5 Hz, 1H), 8.54 (dd, J = 4.7, 1.5 Hz, 1H), 8.80 (d, J = 1.5 Hz, 1H).

1-(2-Pyridin-3-ylphenyl)-ethanone (38). (Table 7, entry 10) 2-Bromoacetophenone (199 mg, 1 mmol), 3-pyridineboronic acid (246 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 μmol) gave **38** in 80% (147 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.19 (s, 3H), 7.32–7.38 (m, 2H), 7.47 (td, J = 7.6, 1.3 Hz, 1H), 7.55 (td, J = 7.6, 1.5 Hz, 1H), 7.62–7.68 (m, 2H), 8.58 (bs, 1H), 8.62 (d, J = 3.4 Hz, 1H).

3-(2-Methoxyphenyl)pyridine (39). (Table 7, entry 13) 2-Bromoanisole (187 mg, 1 mmol), 3-pyridineboronic acid (246 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (100 μmol) gave **39** in 61% (113 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 3.81 (s, 3H), 6.67–7.10 (m, 2H), 7.30–7.40 (m, 3H), 7.85 (dt, J = 8.0, 2.1 Hz, 1H), 8.54 (d, J = 3.7 Hz, 1H), 8.76 (bs, 1H).

3-(2-Methylphenyl)pyridine (40). (Table 7, entry 14) 2-Bromotoluene (171 mg, 1 mmol), 3-pyridineboronic acid (246 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 μmol) gave **40** in 85% (144 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.27 (s, 3H), 7.18–7.31 (m, 4H), 7.34 (dd, J = 7.8, 4.8 Hz, 1H), 7.65 (dt, J = 7.8, 1.9 Hz, 1H), 8.56 (dd, J = 4.8, 1.9 Hz, 1H), 8.59 (s, 1H).

3-(1-Naphthyl)pyridine (41). (Table 7, entry 16) 1-Bromonaphthalene (207 mg, 1 mmol), 3-pyridineboronic acid (246 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-

palladium complexe (100 µmol) gave **41** in 84% (172 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 7.38–7.60 (m, 5H), 7.76–7.84 (m, 2H), 7.86–7.96 (m, 2H), 8.68 (bs, 1H), 8.75 (bs, 1H).

3-(2,6-Dimethylphenyl)pyridine (42). (Table 7, entry 19) 2,6-Dimethylbromobenzene (185 mg, 1 mmol), 3-pyridineboronic acid (246 mg, 2 mmol), K_2CO_3 (276 mg, 2 mmol), xylene (3 mL), Tedicyp-palladium complexe (50 µmol) gave **42** in 85% (156 mg) isolated yield. ^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.02 (s, 6H), 7.12 (d, J = 7.3 Hz, 2H), 7.16–7.21 (m, 1H), 7.37 (dd, J = 7.6, 4.7 Hz, 1H), 7.50 (dt, J = 7.6, 1.9 Hz, 1H), 8.43 (bs, 1H), 8.60 (d, J = 4.7 Hz, 1H).

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