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Tetraphosphine/palladium catalysed Suzuki cross-coupling reactions of aryl halides with alkylboronic acids

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Abstract—Through the use of $[PdCl(C_3H_5)]_2$/*cis*,*cis*,*cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane as a catalyst, a range of aryl bromides and chlorides undergoes Suzuki cross-coupling with alkylboronic acids in good yields. Several alkyl substituents such as ethyl, *n*-butyl, *n*-octyl, isobutyl or 2,2-dimethylpropyl on the alkylboronic acids have been successfully used. The functional group tolerance on the aryl halide is remarkable; substituents such as fluoro, methyl, methoxy, acetyl, formyl, benzoyl, nitro or nitrile are tolerated. Furthermore, this catalyst can be used at low loading, even for reactions of sterically hindered aryl bromides.

1. Introduction

Arylalkane derivatives are important building blocks in organic synthesis and their preparation is an important industrial goal. The palladium-catalysed so-called Suzuki cross-coupling reaction is a powerful method for the synthesis of these arylalkane compounds.[1] Organoboron reagents exhibit greater functional group compatibility than organozinc or Grignard reagents. However, the procedure suffers generally from high catalyst loading due to the fast decomposition of the catalyst.[2] In recent years, several thermally stable palladium catalysts have been successfully used for Suzuki reactions,[3] but the results which have been described with these catalysts, were generally obtained for the coupling of arylboronic acids. With alkylboronic acids most of the results were described with $Pd(PPh_3)_4$[2b,c] or $PdCl_2$/dppf.[2a,d,e] For example, Molander et al. have reported that $PdCl_2$/dppf is an efficient catalyst for the cross-coupling of 2-phenylethylboronic acid with several arylbromides.[2h] Good results have also been reported recently by Hartwig et al. and by Najera et al.[2f,g] They described that a sterically hindered ferrocenyl dialkylphosphine palladium complex and an oxime-derived palladacycle led to efficient catalysts for the reaction of *n*-butylboronic acid with aryl halides. However, to our knowledge, low-catalyst loading Suzuki cross-coupling reactions with alkylboronic acids have not been described. Thus, an effective method using high substrate/catalyst ratios for the successful coupling of simple primary alkylboronic acids are still subject to significant improvement.

In order to find more efficient palladium catalysts, we have prepared the tetrapodal[4] phosphine ligand, Tedicyp[5] (Fig. 1). We have reported recently several results obtained in allylic substitution,[5] Heck,[6] Sonogashira reactions[7] and Suzuki cross-coupling[8] using Tedicyp as ligand. For example, a TON (turnover number) of 96000000 for the reaction of 4-bromobenzophenone with benzeneboronic acid had been obtained.[8b] We also reported some results for Suzuki cross-coupling reaction using Tedicyp ligand with sterically hindered aryl bromides,[8d] heteroaryl bromides,[8c] aryl chlorides,[8e] vinylhalides,[8g] benzylhalides[8h] and with a variety of arylboronic acids.[8f] Here, in order to further establish the requirements for a successful Suzuki cross-coupling reaction, we wish to report on the reaction of alkylboronic acids with a variety of arylhalides using Tedicyp as the ligand.

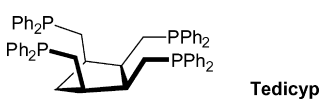

Figure 1.

2. Results and discussion

For this study, based on previous results,[8] xylene was chosen as the solvent and potassium carbonate as the base (Scheme 1). The reactions were performed at 130 °C under argon in the presence of a ratio 1/2 of $[Pd(C_3H_5)Cl]_2$/Tedicyp as catalyst.

First, we have investigated the Suzuki cross-coupling

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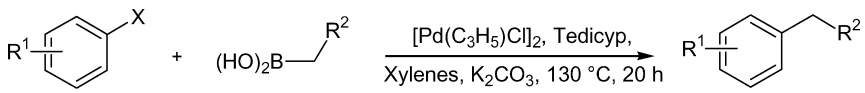

X = Cl, Br
R^1 = Me, *i*-Pr, *t*-Bu, OMe, F, NO_2, CN, COMe, CHO, COPh
R^2 = Me, Et, *n*-Pr, *i*-Pr, *n*-C_7H_{15}, $CH_2CH(CH_3)_2$, cyclohexyl, CH_2Ph, $C(CH_3)_3$

Scheme 1.

reactions of *n*-butylboronic acid with several *para*- and *ortho*-substituted arylbromides. The results presented in the Table 1 disclose a strong influence of the substituents on the aryl bromide on the reaction rate. The reaction with *n*-butylboronic acid can be performed with as little as 0.01% catalyst. Electron-withdrawing groups in the aryl bromide support the Suzuki reaction, while electron-donation groups are unfavourable. Turnover numbers of 8000–14,000 can be achieved with this catalyst for activated substrates such as 4-bromoacetophenone, 4-bromobenzaldehyde, 4-bromobenzophenone, 4-bromobenzonitrile and 4-bromonitrobenzene (Table 1, entries 1–10). With the deactivated arylbromides: 4-bromoanisole and 4-*t*-butylbromobenzene lower TONs of 820 and 1000 were obtained (Table 1, entries 11 and 12). Then, we tried to evaluate the importance of the presence of one *ortho* substituent on the arylbromide on the reaction rate. We observed that the coupling of 2-bromoacetophenone, 2-bromobenzaldehyde, 2-bromobenzonitrile or 1-bromonaphthalene with *n*-butylboronic acid in the presence of 0.1 or 0.01% catalyst led to the alkylaryl adducts in TONs of 1000–3800 (Table 1, entries 13–21). Next, we tried to evaluate the difference of reaction rate between mono- and di-*ortho*-substituted arylbromides, and we observed that even very hindered aryl bromides could be coupled efficiently with *n*-butylboronic acid. For example, with 9-bromoanthracene and 1-bromo-2,4,6-triisopropylbenzene high conversions were obtained. The presence of 0.1 and 1% catalyst was necessary for these reactions showing a significant effect of the *ortho*-substituents of the aryl bromide on the reaction rate (Table 1, entries 22 and 23).

In our previous researches on the coupling of phenylboronic acid with these aryl bromides much higher reaction rates had been observed with this catalyst.[8b] In order to obtain more information on the rate-limiting step of this reaction, we performed a competitive reaction using an equimolar mixture of phenylboronic acid (20 mmol) and *n*-butylboronic acid (20 mmol) with 4-bromoacetophenone (10 mmol) in the presence of 0.1% catalyst. After one

Table 1. Palladium-Tedicyp catalysed Suzuki cross-coupling reactions with *n*-butylboronic acid (Scheme 1)

Entry	Aryl halide	Ratio substrate/catalyst	Product number	Yield (%)[a]
1	4-Bromoacetophenone	1000	**1**	(92) 100
2	4-Bromoacetophenone	10,000	**1**	90
3	4-Bromobenzaldehyde	1000	**2**	(85) 100
4	4-Bromobenzaldehyde	10,000	**2**	92
5	4-Bromobenzophenone	10,000	**3**	(94) 100
6	4-Bromobenzophenone	100,000	**3**	14
7	4-Bromobenzonitrile	1000	**4**	(90) 100
8	4-Bromobenzonitrile	10,000	**4**	100
9	4-Nitrobromobenzene	1000	**5**	(82) 100
10	4-Nitrobromobenzene	10,000	**5**	100
11	4-Bromoanisole	1000	**6**	(73) 82
12	4-*t*-Butylbromobenzene	1000	**7**	(84) 100
13	2-Bromoacetophenone	1000	**8**	(78) 85
14	2-Bromoacetophenone	10,000	**8**	38
15	2-Bromobenzaldehyde	1000	**9**	(84) 100
16	2-Bromobenzaldehyde	10,000	**9**	35
17	2-Bromobenzonitrile	1000	**10**	(91) 100
18	2-Bromobenzonitrile	10,000	**10**	28
19	2-Nitrobromobenzene	1000	**11**	(83) 100
20	2-Bromobiphenyl	1000	**12**	(92) 100
21	1-Bromonaphthalene	1000	**13**	(93) 100
22	9-Bromoanthracene	1000	**14**	(91) 100
23	2,4,6-Triisopropylbromobenzene	100	**15**	(88) 100
24	3-Bromoquinoline	1000	**16**	(80) 100
25	3-Bromoquinoline	10,000	**16**	88
26	4-Chlorobenzonitrile	50	**4**	(78) 100
27	4-Chlorobenzonitrile	100	**4**	65
28	4-Chloroacetophenone	50	**1**	(58) 69
29	4-Chloronitrobenzene	50	**5**	(74) 100
30	4-Chloronitrobenzene	100	**5**	97
31	2-Chloroquinoline	100	**17**	(72) 100[b]
32	2-Chloroquinoline	250	**17**	77[b]

Conditions: Pd-tedicyp catalyst, ArX (1 equiv.), *n*-butylboronic acid (2 equiv.), K_2CO_3 (2 equiv.), xylene, 130 °C, 20 h, GC or NMR yields.
[a] Yields in parentheses are isolated.
[b] The formation of 2,2′-biquinoline was also observed.

hour, the conversion was complete and we only observed the formation of the coupling product with phenylboronic acid. An other competitive reaction using an equimolar mixture of 4-bromoacetophenone (10 mmol) and 2,4,6-triisopropylbromobenzene (10 mmol) with *n*-butylboronic acid (5 mmol) in the presence of 0.1% catalyst was also perfomed. This reaction led after five hours to a mixture of coupling adducts **1** and **15** in a ratio 97:3. The respective rates of these reactions suggest that, in the presence of this catalyst, the rate-determining step of the reaction is not the oxidative addition of the arylbromide. The rate-determining step of this reaction seems to be the *trans*-metallation of the alkylboronic acid with the palladium centre or the C–C bond formation from the Pd-aryl-alkyl intermediate.

Then, we studied the reaction in the presence of aryl chlorides (Table 1, entries 26–32). We observed that this system is not very active for such compounds: the reactions were performed in the presence of 0.4–2% catalyst. For these substrates, a tetraphosphine electronically similar to $P(t\text{-}Bu)_3$ should lead to better results.

Finally, we have investigated the Suzuki reaction of eight other alkylboronic acids (Table 2). In the presence of *n*-propyl-, 2-methylpropyl-, 3-methylbutyl-, (cyclohexyl)-methyl-, 2-phenylethyl- or *n*-octylboronic acids, very similar results to those observed with *n*-butylboronic acid were obtained (Table 2, entries 1–8 and 15–29). In the presence of ethyl- or 2,2-dimethylpropaneboronic acids lower TONs were obtained (Table 2, entries 12–14 and 30–32).

We also studied the coupling of bromopyridines with *n*-octylboronic acid. As expected,[8c] we observed higher TONs for the coupling of β- and γ-substituted bromopyridines (1000) (Table 2, entries 10 and 11) than with the α-substituted 2-bromopyridine (100) (Table 2, entry 9).

In summary, we have established that the Tedicyp-palladium system is not limited to Suzuki reactions of arylboronic acids; alkylboronic acids are also efficiently coupled. Lower TONs are obtained than for the coupling with arylboronic acids, but the reaction with alkylboronic acids can be performed with as little as 0.01% catalyst with a wide variety of arylbromides. This catalyst seems to be much more efficient than the complexes formed with triphenylphosphine ligand. Due to the high price of palladium, the practical advantage of such low catalyst loadings can become increasingly important for industrial processes. These alkylboronic acids are thermally, air-, and moisture-stable. Moreover, some of them are commercially available. This is a practical advantage of the Suzuki reaction, relative to the other coupling processes. A wide range of functions such as methoxy, fluoro, acetyl, formyl, benzoyl, nitro or nitrile on the arylbromide are tolerated. As expected, the steric hindrance of the arylbromide has an important effect on the reaction rates.

Table 2. Palladium-Tedicyp catalysed Suzuki cross-coupling reactions with various alkylboronic acids (Scheme 1)

Entry	Aryl bromide	Alkylboronic acid	Ratio substrate/catalyst	Product number	Yield (%)[a]
1	4-Bromoacetophenone	*n*-Octylboronic acid	10,000	**18**	(93) 100
2	4-Bromobenzaldehyde	*n*-Octylboronic acid	10,000	**19**	(74) 78
3	4-Fluorobromobenzene	*n*-Octylboronic acid	250	**20**	(95) 100
4	4-Fluorobromobenzene	*n*-Octylboronic acid	1000	**20**	41
5	2-Bromoanisole	*n*-Octylboronic acid	250	**21**	(82) 100
6	2-Bromoanisole	*n*-Octylboronic acid	1000	**21**	48
7	2,4,6-Trimethylbromobenzene	*n*-Octylboronic acid	250	**22**	(82) 100
8	2,4,6-Trimethylbromobenzene	*n*-Octylboronic acid	1000	**22**	55
9	2-Bromopyridine	*n*-Octylboronic acid	100	**23**	(52) 100[b]
10	3-Bromopyridine	*n*-Octylboronic acid	1000	**24**	(87) 100
11	4-Bromopyridine	*n*-Octylboronic acid	1000	**25**	(80) 100
12	4-Bromoacetophenone	*n*-Ethylboronic acid	250	**26**	(89) 100
13	4-Bromoacetophenone	*n*-Ethylboronic acid	1000	**26**	63
14	2-Bromobenzaldehyde	*n*-Ethylboronic acid	1000	**27**	(58) 64
15	4-Bromoacetophenone	*n*-Propylboronic acid	10,000	**28**	(74) 81
16	4-Bromoacetophenone	3-Methylbutylboronic acid	10,000	**29**	(92) 100
17	4-Bromobenzonitrile	3-Methylbutylboronic acid	1000	**30**	(94) 100
18	4-Bromobenzonitrile	3-Methylbutylboronic acid	10,000	**30**	100
19	4-Bromoacetophenone	2-Methylpropylboronic acid	1000	**31**	(91) 99
20	4-Bromoacetophenone	2-Methylpropylboronic acid	10,000	**31**	42
21	2-Bromoacetophenone	2-Methylpropylboronic acid	1000	**32**	(92) 100
22	2-Bromoacetophenone	2-Methylpropylboronic acid	10,000	**32**	41
23	4-*t*Butylbromobenzene	2-Methylpropylboronic acid	1000	**33**	(75) 78
24	4-Bromoacetophenone	(Cyclohexyl)methylboronic acid	1000	**34**	(95) 100
25	4-Bromoacetophenone	(Cyclohexyl)methylboronic acid	10,000	**34**	74
26	4-Bromobenzonitrile	(Cyclohexyl)methylboronic acid	1000	**35**	(92) 100
27	4-Bromobenzonitrile	(Cyclohexyl)methylboronic acid	10,000	**35**	67
28	4-Bromoacetophenone	2-Phenylethylboronic acid	1000	**36**	(94) 100
29	4-Bromoacetophenone	2-Phenylethylboronic acid	10,000	**36**	93
30	4-Bromoacetophenone	2,2-Dimethylpropylboronic acid	250	**37**	(79) 100
31	4-Bromoacetophenone	2,2-Dimethylpropylboronic acid	1000	**37**	95
32	4-Bromobenzaldehyde	2,2-Dimethylpropylboronic acid	250	**38**	(77) 90

Conditions: Pd-tedicyp catalyst, ArBr (1 equiv.), alkylboronic acid (2 equiv.), K_2CO_3 (2 equiv.), xylene, 130 °C, 20 h, GC or NMR yields.
[a] Yields in parentheses are isolated.
[b] The formation of 2,2′-bipyridine was also observed.

3. Experimental

3.1. General remarks

All reactions were run under argon in Schlenk tubes using vacuum lines. Xylene analytical grade was not distilled before use. Some of the aryl halides were distilled before use. Potassium carbonate (99+) was used without drying. Alkenylboronic acids were prepared according to reported procedures by addition of 2 equiv. of $B(OMe)_3$ to alkenylmagnesium bromide solutions in THF at −90 °C, then the solution was allowed to room temperature, poured on ice, extracted with ether, dried ($MgSO_4$) and evaporated. The reactions were followed by GC and NMR for high boiling point substrates and by GC for low boiling point substrates. GC/MS was recorded with a Varian Saturn 2100T spectrometer. ^1H spectrum were recorded with a Bruker 300 MHz spectrometer in $CDCl_3$ solutions. Chemical shift are reported in ppm relative to $CDCl_3$ (7.25). Flash chromatography were performed on silica gel (230–400 mesh) GC and NMR yields in the tables are conversions of the aryl halides into the products calculated with GC and ^1H NMR spectrum of the crude mixtures.

3.2. General procedure

The reaction of the arylhalide (10 mmol), alkylboronic acid (20 mmol) and K_2CO_3 (2.76 g, 20 mmol) at 130 °C during 20 h in anhydrous xylene (20 mL) in the presence of *cis*,*cis*,*cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane/$[PdCl(C_3H_5)]_2$ complex under argon affords the corresponding adduct after extraction with ether, evaporation and filtration on silica gel (pentane/ether).

3.3. Preparation of the Pd-Tedicyp catalyst

An over-dried 40-mL Schlenk tube equipped with a magnetic stirring bar under argon atmosphere, was charged with $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (30 mg, 81 μmol) and Tedicyp (140 mg, 162 μmol). 10 mL of anhydrous THF were added, then the solution was stirred at room temperature for 10 min and the THF was evaporated. The appropriate catalyst concentration was obtained by successive dilutions. ^{31}P NMR (162 MHz, $CDCl_3$) δ 25 (w=80 Hz), 19.4 (w=110 Hz).

3.3.1. 4-*n*-Butylacetophenone 1. From 4-bromoacetophenone (1.99 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **1** was obtained in 92% (1.62 g) yield.

3.3.2. 4-*n*-Butylbenzaldehyde 2. From 4-bromobenzaldehyde (1.85 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **2** was obtained in 85% (1.38 g) yield.

3.3.3. 4-*n*-Butylbenzophenone 3. From 4-bromobenzophenone (2.61 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **3** was obtained in 94% (2.24 g) yield. ^1H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, 2H, J=8.2 Hz), 7.73 (d, 2H, J=8.2 Hz), 7.56 (t, 1H, J=7.6 Hz), 7.46 (t, 2H, J=7.6 Hz), 7.27 (d, 2H, J=8.2 Hz), 2.69 (t, 2H, J=7.8 Hz), 1.61 (m, 2H), 1.36 (m, 2H), 0.94 (t, 3H, J=7.2 Hz).

3.3.4. 4-*n*-Butylbenzonitrile 4. From 4-bromobenzonitrile (1.82 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **4** was obtained in 90% (1.43 g) yield.

3.3.5. 4-*n*-Butylnitrobenzene 5. From 4-bromonitrobenzene (2.02 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **5** was obtained in 82% (1.47 g) yield. ^1H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, 2H, J=8.7 Hz), 7.35 (d, 2H, J=8.7 Hz), 2.70 (t, 2H, J=7.8 Hz), 1.60 (m, 2H), 1.36 (m, 2H), 0.92 (t, 3H, J=7.2 Hz).

3.3.6. 4-*n*-Butylanisole 6. From 4-bromoanisole (1.87 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **6** was obtained in 73% (1.20 g) yield. ^1H NMR (300 MHz, $CDCl_3$) δ 7.10 (d, 2H, J=8.5 Hz), 6.83 (d, 2H, J=8.5 Hz), 3.80 (s, 3H), 2.58 (t, 2H, J=7.8 Hz), 1.58 (m, 2H), 1.33 (m, 2H), 0.92 (t, 3H, J=7.2 Hz).

3.3.7. 1-*n*-Butyl-4-*t*-butylbenzene 7. From 4-*t*-butylbromobenzene (2.13 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **7** was obtained in 84% (1.60 g) yield. ^1H NMR (300 MHz, $CDCl_3$) δ 7.30 (d, 2H, J=8.1 Hz), 7.13 (d, 2H, J=8.1 Hz), 2.58 (t, 2H, J=7.8 Hz), 1.59 (m, 2H), 1.35 (m, 2H), 1.32 (s, 9H), 0.92 (t, 3H, J=7.2 Hz).

3.3.8. 2-*n*-Butylacetophenone 8. From 2-bromoacetophenone (1.99 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **8** was obtained in 52% (0.92 g) yield. ^1H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, 1H, J=7.7 Hz), 7.40–7.15 (m, 3H), 2.83 (t, 2H, J=7.8 Hz), 2.63 (s, 3H), 1.54 (m, 2H), 1.40 (m, 2H), 0.91 (t, 3H, J=7.2 Hz).

3.3.9. 2-*n*-Butylbenzaldehyde 9. From 2-bromobenzaldehyde (1.85 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **9** was obtained in 84% (1.37 g) yield. ^1H NMR (300 MHz, $CDCl_3$) δ 10.29 (s, 1H), 7.82 (d, 1H, J=7.8 Hz), 7.49 (t, 1H, J=7.6 Hz), 7.34 (t, 1H, J=7.6 Hz), 7.26 (d, 1H, J=7.8 Hz), 3.02 (t, 2H, J=7.8 Hz), 1.59 (m, 2H), 1.40 (m, 2H), 0.93 (t, 3H, J=7.2 Hz).

3.3.10. 2-*n*-Butylbenzonitrile 10. From 2-bromobenzonitrile (1.82 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **10** was obtained in 91% (1.45 g) yield. ^1H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, 1H, J=7.5 Hz), 7.49 (t, 1H, J=7.5 Hz), 7.30 (d, 1H, J=7.5 Hz), 7.26 (t, 1H, J=7.7 Hz), 2.83 (t, 2H, J=7.8 Hz), 1.65 (m, 2H), 1.40 (m, 2H), 0.93 (t, 3H, J=7.2 Hz).

3.3.11. 2-*n*-Butylnitrobenzene 11. From 2-bromonitrobenzene (2.02 g, 10 mmol), and *n*-butylboronic acid (2.04 g, 20 mmol), product **11** was obtained in 83% (1.48 g) yield. ^1H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, 1H, J=8.3 Hz), 7.49 (t, 1H, J=7.7 Hz), 7.31 (m, 2H), 2.87 (t, 2H, J=7.8 Hz), 1.61 (m, 2H), 1.36 (m, 2H), 0.92 (t, 3H, J=7.2 Hz).

3.3.12. 2-*n*-Butylbiphenyl 12. From 2-bromobiphenyl (2.33 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **12** was obtained in 92% (1.93 g) yield. ^1H NMR (300 MHz, $CDCl_3$) δ 7.60–7.10 (m, 9H), 2.76 (t, 2H, J=7.8 Hz), 1.66 (m, 2H), 1.39 (m, 2H), 0.97 (t, 3H, J=7.2 Hz).

3.3.13. 1-*n*-Butylnaphthalene 13. From 1-bromonaphthalene (2.07 g, 10 mmol) and *n*-butylboronic acid (2.04 g,

20 mmol), product **13** was obtained in 93% (1.71 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, 1H, J=8.1 Hz), 7.86 (d, 1H, J=7.9 Hz), 7.71 (d, 1H, J=7.9 Hz), 7.55–7.30 (m, 4H), 3.09 (t, 2H, J=7.8 Hz), 1.76 (m, 2H), 1.49 (m, 2H), 0.99 (t, 3H, J=7.2 Hz).

3.3.14. 9-*n*-Butylanthracene 14. From 9-bromoanthracene (2.57 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **14** was obtained in 91% (2.13 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.27 (d, 2H, J=8.1 Hz), 8.00 (d, 2H, J=7.7 Hz), 7.47 (m, 4H), 3.60 (t, 2H, J=7.8 Hz), 1.81 (m, 2H), 1.61 (m, 2H), 1.03 (t, 3H, J=7.2 Hz).

3.3.15. 1-*n*-Butyl-2,4,6-triisopropylbenzene 15. From 2,4,6-triisopropylbromobenzene (2.83 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **15** was obtained in 88% (2.29 g) yield. Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.97 (s, 2H), 3.16 (sept., 2H, J= 6.8 Hz), 2.85 (sept., 1H, J=6.9 Hz), 2.61 (t, 2H, J=7.8 Hz), 1.45 (m, 4H), 1.25 (d, 6H, J=6.9 Hz), 1.24 (d, 12H, J= 6.9 Hz), 0.97 (t, 3H, J=7.3 Hz); MS (EI, 70 eV): Calcd 260.2. Found 260 (34%) (M^+). $C_{19}H_{32}$ (260.46): Calcd C 87.62, H 13.38. Found C 87.29, H 13.28.

3.3.16. 3-*n*-Butylquinoline 16. From 3-bromoquinoline (2.08 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **16** was obtained in 80% (1.48 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.76 (d, 1H, J=2.3 Hz), 8.10 (d, 1H, J=8.5 Hz), 7.90 (s, 1H), 7.75 (d, 1H, J=8.5 Hz), 7.60 (t, 1H, J=8.5 Hz), 7.50 (t, 1H, J=8.5 Hz), 2.78 (t, 2H, J=7.8 Hz), 1.69 (m, 2H), 1.38 (m, 2H), 0.94 (t, 3H, J=7.2 Hz).

3.3.17. 2-*n*-Butylquinoline 17. From 2-chloroquinoline (1.63 g, 10 mmol) and *n*-butylboronic acid (2.04 g, 20 mmol), product **17** was obtained in 72% (1.33 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (m, 2H), 7.76 (d, 1H, J=7.0 Hz), 7.67 (t, 1H, J=7.9 Hz), 7.47 (t, 1H, J=7.9 Hz), 7.28 (d, 1H, J=7.0 Hz), 2.97 (t, 2H, J=7.8 Hz), 1.76 (m, 2H), 1.40 (m, 2H), 0.96 (t, 3H, J=7.2 Hz).

3.3.18. 4-*n*-Octylacetophenone 18. From 4-bromoacetophenone (1.99 g, 10 mmol) and *n*-octylboronic acid (3.16 g, 20 mmol), product **18** was obtained in 93% (2.16 g) yield.

3.3.19. 4-*n*-Octylbenzaldehyde 19. From 4-bromobenzaldehyde (1.85 g, 10 mmol) and *n*-octylboronic acid (3.16 g, 20 mmol), product **19** was obtained in 74% (1.61 g) yield.

3.3.20. 4-*n*-Octylfluorobenzene 20. From 4-bromofluorobenzene (1.75 g, 10 mmol) and *n*-octylboronic acid (3.16 g, 20 mmol), product **20** was obtained in 95% (1.97 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14 (dd, 2H, J=8.5, 5.5 Hz), 6.97 (dd, 2H, J=8.5, 8.5 Hz), 2.59 (t, 2H, J=7.5 Hz), 1.60 (m, 2H), 1.29 (m, 10H), 0.90 (t, 3H, J=7.2 Hz).

3.3.21. 2-*n*-Octylanisole 21. From 2-bromoanisole (1.87 g, 10 mmol) and *n*-octylboronic acid (3.16 g, 20 mmol), product **21** was obtained in 82% (1.81 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (m, 2H), 6.90 (t, 1H, J=7.5 Hz), 6.84 (d, 1H, J=8.3 Hz), 3.82 (s, 3H), 2.61 (t, 2H, J=7.5 Hz), 1.58 (m, 2H), 1.30 (m, 10H), 0.89 (t, 3H, J=7.2 Hz).

3.3.22. 1-*n*-Octyl-2,4,6-trimethylbenzene 22. From 2,4,6-trimethylbromobenzene (1.99 g, 10 mmol) and *n*-octylboronic acid (3.16 g, 20 mmol), product **22** was obtained in 82% (1.90 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.82 (s, 2H), 2.56 (t, 2H, J=7.5 Hz), 2.28 (s, 6H), 2.24 (s, 3H), 1.55 (m, 2H), 1.27 (m, 10H), 0.89 (t, 3H, J= 7.2 Hz).

3.3.23. 2-*n*-Octylpyridine 23. From 2-bromopyridine (1.58 g, 10 mmol) and *n*-octylboronic acid (3.16 g, 20 mmol), product **23** was obtained in 52% (0.99 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (d, 1H, J=5.0 Hz), 7.60 (t, 1H, J=7.8 Hz), 7.10 (m, 2H), 2.80 (t, 2H, J=7.5 Hz), 1.70 (m, 2H), 1.27 (m, 10H), 0.88 (t, 3H, J=7.2 Hz).

3.3.24. 3-*n*-Octylpyridine 24. From 3-bromopyridine (1.58 g, 10 mmol) and *n*-octylboronic acid (3.16 g, 20 mmol), product **24** was obtained in 87% (1.66 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (m, 2H), 7.46 (d, 1H, J=7.8 Hz), 7.16 (dd, 1H, J=7.5, 4.7 Hz), 2.58 (t, 2H, J=7.5 Hz), 1.57 (m, 2H), 1.28 (m, 10H), 0.86 (t, 3H, J=7.2 Hz).

3.3.25. 4-*n*-Octylpyridine 25. From 4-bromopyridine (1.58 g, 10 mmol) and *n*-octylboronic acid (3.16 g, 20 mmol), product **25** was obtained in 80% (1.53 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (d, 2H, J=6.0 Hz), 7.22 (d, 2H, J=6.0 Hz), 2.69 (t, 2H, J=7.5 Hz), 1.66 (m, 2H), 1.33 (m, 10H), 0.94 (t, 3H, J=7.2 Hz).

3.3.26. 4-Ethylacetophenone 26. From 4-bromoacetophenone (1.99 g, 10 mmol) and ethylboronic acid (1.48 g, 20 mmol), product **26** was obtained in 89% (1.32 g) yield.

3.3.27. 2-Ethylbenzaldehyde 27. From 2-bromobenzaldehyde (1.85 g, 10 mmol) and ethylboronic acid (1.48 g, 20 mmol), product **27** was obtained in 58% (0.78 g) yield.

3.3.28. 4-*n*-Propylacetophenone 28. From 4-bromoacetophenone (1.99 g, 10 mmol) and *n*-propylboronic acid (1.76 g, 20 mmol), product **28** was obtained in 74% (1.20 g) yield.

3.3.29. 4-(3-Methylbutyl)acetophenone 29. From 4-bromoacetophenone (1.99 g, 10 mmol) and 3-methylbutylboronic acid (2.32 g, 20 mmol), product **29** was obtained in 92% (1.75 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, 2H, J=8.3 Hz), 7.26 (d, 2H, J=8.3 Hz), 2.66 (t, 2H, J=7.7 Hz), 2.57 (s, 3H), 2.52 (m, 3H), 0.93 (d, 6H, J=6.4 Hz).

3.3.30. 4-(3-Methylbutyl)benzonitrile 30. From 4-bromobenzonitrile (1.82 g, 10 mmol) and 3-methylbutylboronic acid (2.32 g, 20 mmol), product **30** was obtained in 94% (1.63 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, 2H, J=8.3 Hz), 7.26 (d, 2H, J=8.3 Hz), 2.65 (t, 2H, J=7.7 Hz), 2.52 (m, 3H), 0.93 (d, 6H, J=6.4 Hz).

3.3.31. 4-(2-Methylpropyl)acetophenone 31. From 4-bromoacetophenone (1.99 g, 10 mmol) and 2-methylpropylboronic acid (2.04 g, 20 mmol), product **31** was obtained in 91% (1.60 g) yield.

3.3.32. 2-(2-Methylpropyl)acetophenone 32. From

2-bromoacetophenone (1.99 g, 10 mmol) and 2-methylpropylboronic acid (2.04 g, 20 mmol), product **32** was obtained in 46% (0.81 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, 1H, J=7.7 Hz), 7.42–7.15 (m, 3H), 2.74 (d, 2H, J=6.2 Hz), 2.56 (s, 3H), 1.80 (m, 1H), 0.91 (d, 6H, J=6.4 Hz).

3.3.33. 4-(2-Methylpropyl)-*t*-butylbenzene 33. From 4-*t*-butylbromobenzene (2.13 g, 10 mmol) and 2-methylpropylboronic acid (2.04 g, 20 mmol), product **33** was obtained in 75% (1.43 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (d, 2H, J=8.3 Hz), 7.06 (d, 2H, J=8.3 Hz), 2.43 (d, 2H, J=7.1 Hz), 1.89 (m, 1H), 1.30 (s, 9H), 0.92 (d, 6H, J=6.4 Hz).

3.3.34. 4-(Cyclohexyl)methylacetophenone 34. From 4-bromoacetophenone (1.99 g, 10 mmol) and (cyclohexyl)-methylboronic acid (2.84 g, 20 mmol), product **34** was obtained in 95% (2.05 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, 2H, J=8.2 Hz), 7.21 (d, 2H, J=8.2 Hz), 2.57 (s, 3H), 2.52 (d, 2H, J=7.0 Hz), 1.75–0.75 (m, 11H).

3.3.35. 4-(Cyclohexyl)methylbenzonitrile 35. From 4-bromobenzonitrile (1.82 g, 10 mmol) and (cyclohexyl)methylboronic acid (2.84 g, 20 mmol), product **35** was obtained in 92% (1.83 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, 2H, J=8.1 Hz), 7.22 (d, 2H, J=8.1 Hz), 2.53 (d, 2H, J=7.0 Hz), 1.75–0.75 (m, 11H).

3.3.36. 1-Phenyl-2-(4-acetylphenyl)ethane 36. From 4-bromoacetophenone (1.99 g, 10 mmol) and 2-phenylethylboronic acid (3.00 g, 20 mmol), product **36** was obtained in 94% (2.11 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, 2H, J=8.1 Hz), 7.35–7.15 (m, 7H), 2.99 (m, 4H), 2.61 (s, 3H).

3.3.37. 4-(2,2-Dimethylpropyl)acetophenone 37. From 4-bromoacetophenone (1.99 g, 10 mmol) and 2,2-dimethylpropylboronic acid (2.32 g, 20 mmol), product **37** was obtained in 79% (1.50 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, 2H, J=8.1 Hz), 7.20 (d, 2H, J=8.1 Hz), 2.57 (s, 3H), 2.54 (s, 2H), 0.90 (s, 9H).

3.3.38. 4-(2,2-Dimethylpropyl)benzaldehyde 38. From 4-bromobenzaldehyde (1.85 g, 10 mmol) and 2,2-dimethylpropylboronic acid (2.32 g, 20 mmol), product **38** was obtained in 77% (1.36 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.01 (s, 1H), 7.82 (d, 2H, J=8.3 Hz), 7.32 (d, 2H, J=8.3 Hz), 2.61 (s, 2H), 0.97 (s, 9H).

Registry no.: **1**, 37920-25-5; **2**, 1200-14-2; **3**, 55363-57-0; **4**, 20651-73-4; **5**, 20651-75-6; **6**, 8272-84-9; **7**, 14011-00-8; **8**, 58632-85-2; **9**, 59059-42-6; **10**, 57775-05-0; **11**, 7137-55-5; **12**, 54532-97-7; **13**, 1634-09-9; **14**, 1498-69-7; **16**, 59321-68-5; **17**, 5058-19-5; **18**, 10541-56-7; **19**, 49763-66-8; **20**, 28593-20-6; **21**, 20056-59-1; **22**, 207114-16-7; **23**, 33841-61-1; **24**, 58069-37-7; **25**, 40089-91-6; **26**, 937-30-4; **27**, 22927-13-5; **28**, 2932-65-2; **29**, 65189-85-7; **30**, 7089736; **31**, 38861-78-8; **32**, 100585-54-4; **33**, 68018-45-1; **34**, 68266-59-1; **35**, 98446-82-3; **36**, 785-78-4; **37**, 52380-60-6; **38**, 52986-52-4.

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