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Microwave-assisted, Ir-catalyzed aromatic C–H borylation

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Abstract One-step conversions of 1,3-disubstituted benzenes to aryl boronates and 2,6-disubstituted pyridines to heteroaryl boronates are described. Microwave heating was used for all reactions. $[(COD)Ir(\mu\text{-}OMe)]_2$ and 4,4′-di-*tert*-butyl-2,2′-bipyridine were used as catalysts, in methyl *tert*-butyl ether. Acceleration of the rate of reaction was remarkable compared with that of same reaction under conventional heating conditions.

Keyword Microwave heating · $[(COD)Ir(\mu\text{-}OMe)]_2$ · Dtbpy · Pinacol boronates

Introduction

The aryl boronates, important intermediates in organic synthesis, have been widely used in many useful transformations including Suzukui–Miyaura cross coupling reactions [1], Cu-catalyzed C–O and C–N coupling reactions [2], and Rh-catalyzed conjugate additions to carbonyl compounds [3, 4]. Pinacol boronates, prepared by converting aryl halides to aryl boronates by use of bis(pinacolato)diboron, are their common precursors. The conversion is catalyzed by Pd [5]. Although this method is widely used, it is unsuitable for polyhalogen-substituted compounds. To solve this problem, Hartwig performed C–H borylation of benzene with Re and Rh as catalysts [6, 7]. Later Smith demonstrated aromatic borylation with Hartwig's Rh catalyst [8, 9].

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In recent years, this problem has been overcome by use of Ir-catalyzed C–H borylation, in which the halogen remains on the aromatic heterocyclic compound even when the reactant is an aryl halide. The most widely applied system is $[(COD)Ir(\mu\text{-}OMe)]_2$ with 4,4′-di-*tert*-butyl-2,2′-bipyridine (dtbpy) [10]. Some results suggest that the intermediate $[Ir(Bpin)_3L_2]$ (Bpin = $B(OCMe_2CMe_2O)$) is the active complex for C–H activation. This intermediate is a five-membered ring and steric hindrance could contribute to increasing the selectivity of the reaction [11].

The synthesis of aryl boronates by Ir-catalyzed borylation of arenes has been reported [12–16]. However, improvement for preparation of aryl boronates, for example acceleration of the reactions, has not received much attention. In this work, a series of 1,3-disubstituted benzenes and 2,6-disubstituted pyridines were used as reactants for synthesis of pinacol boronates under microwave heating and conventional heating conditions. The effect on yield of factors such as reaction time, solvent, substituent groups, and electronic and steric effects were investigated systematically. It was found that microwave irradiation substantially accelerated the Ir-catalyzed borylation of aromatic and heterocyclic compounds.

It is generally agreed that the enhanced rate of reaction is a purely thermodynamic effect in most cases [17]. In other words, reaction time will be reduced if a high reaction temperature can be achieved in a short time. Unlike conventional heating, microwave irradiation does not transfer energy to the reaction system through the vessel. It induces very efficient internal heating of the molecules (solvents, reagents, and catalysts) without heating the vessel surface. A solvent which absorbs microwave energy with high efficiency, for example methanol, can be rapidly superheated even above its boiling point when heated under microwave conditions in a sealed vessel. Such a solvent can provide a large amount of energy in a short time to accelerate the reaction.

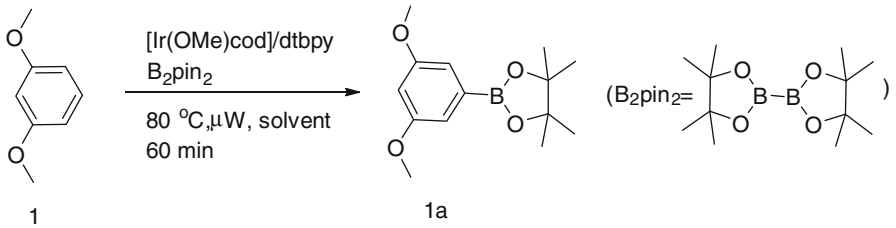
Results and discussion

Tamura et al. [18] have already given a theoretical elucidation of the catalytic cycle of Ir-catalyzed borylation of benzene with diboron. Use of $[(COD)Ir(\mu\text{-}OMe)]_2$ with dtbpy as catalyst was believed to be the most efficient system. In this work, selection of the solvent was further investigated.

Reaction of compound **1** (1,3-dimethoxybenzene), as typical reactant, in different solvents was catalyzed by $[(COD)Ir(\mu\text{-}OMe)]_2$ and dtbpy (Scheme 1; Table 1). All reactions were carried out with 1,3-dimethoxybenzene (1 mmol), B_2pin_2 (1.1 mmol), $[Ir(OMe)cod]_2$ (1.5 mmol %), dtbpy (3.0 mmol %), and solvent (2.4 mL) in a microwave heating reactor at 80 °C for 1 h [19].

The results indicated that methyl *tert*-butyl ether (MTBE) is the most effective solvent, which is consistent with a previous report [20] (Table 1). This may be because of the better solubility of the reactant in MBTE than in other solvents.

A series of 1,3-disubstituted benzenes were chosen as reactants to prepare pinacol boronates under conventional heating and microwave irradiation conditions (Scheme 2; Table 2).

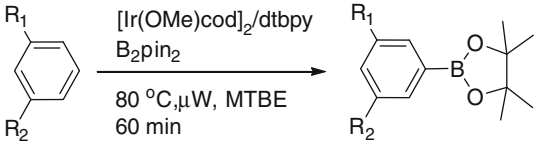


Scheme 1 Reaction of 1,3-dimethoxybenzene with B_2pin_2 catalyzed by $[Ir(OMe)cod]_2$ and dtbpy under microwave conditions

Table 1 Synthesis of **1a** in different solvents

Entry	Solvent	Catalyst	Ligand	Time (min)	Temperature (°C)	Yield (%)
1	THF	$[(COD)Ir(\mu\text{-}OMe)]_2$	dtbpy	60	80	75
1	DMF	$[(COD)Ir(\mu\text{-}OMe)]_2$	dtbpy	60	80	64
1	Dioxane	$[(COD)Ir(\mu\text{-}OMe)]_2$	dtbpy	60	80	78
1	MTBE	$[(COD)Ir(\mu\text{-}OMe)]_2$	dtbpy	60	80	90
1	Hexane	$[(COD)Ir(\mu\text{-}OMe)]_2$	dtbpy	60	80	80

All reactions were conducted with 1,3-dimethoxybenzene (1 mmol), B_2pin_2 (1.1 mmol), $[Ir(OMe)cod]_2$ (1.5 mmol %), dtbpy (3.0 mmol %), and solvent (2.4 mL) in a microwave heating reactor



Scheme 2 Reaction of 1,3-disubstituted benzenes with B_2pin_2 catalyzed by $[Ir(OMe)cod]_2$ and dtbpy at 80 °C

Under conventional heating conditions, complete conversion for entry 1 in Table 2 required 80 °C for 8 h and strict N_2 atmosphere [21]. Also, the concentrations of catalyst and substrate had to be higher than for microwave heating [22], otherwise the yield might be substantially reduced. In contrast, it took only 60 min to complete the conversion for entry 1 under microwave irradiation, even though the amounts of catalyst and ligand were half those under conventional heating conditions. In addition, a higher yield was achieved under microwave irradiation than with conventional heating. Similar results were observed for entry 2. The reaction time was significantly reduced under microwave irradiation.

Asymmetric 1,3-disubstituted benzenes (entries 3–13 in Table 2) were used as reactants with microwave heating at 80 °C for 30 or 60 min. All reaction conditions were similar except for the different starting material. GC–MS was used to monitor the amount of reactant remaining. An important aspect of this kind of reaction is the selectivity of conversion of asymmetric 1,3-disubstituted benzenes into aryl boronates. The starting materials in entries 3–7 are bromo-substituted and meta-

Table 2 Microwave-assisted Ir-catalyzed borylation of disubstituted benzenes

Entry	R1	R2	Product	Microwave heating		Standard heating	
				Time (min)	Yield[a] (%)	Time (min)	Yield[a] (%)
1	OMe	OMe	**1a**	60	90	480	87
2	Cl	Cl	**1b**	60	94	720	93
3	Me	Br	**1c**	30	84	480	82
4	$CH(CH_3)_2$	Br	**1d**	30	91	480	88
5	OMe	Br	**1e**	60	77	1,080	79
6	OEt	Br	**1f**	60	75	960	73
7	$OCH_2C(OEt)_2$	Br	**1g**	60	84	1,080	85
8	OMe	Cl	**1h**	60	80	1,080	83
9	Me	CN	**1i**	60	85	1,080	80
10	CF_3	F	**1j**	60	73	900	69
11	OMe	CN	**1k**	60	81	1,080	84
12	COOMe	I	**1l**	60	82	480	84
13	Me	CHO	**1m**	60	85	360	80

[a] Purified isolated yield of reaction achieving 100 % conversion

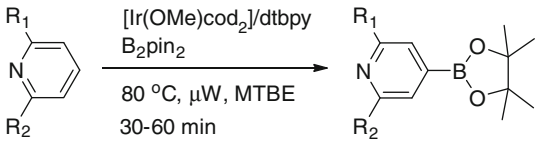
group compounds. The large size of the substituent group leads to steric hindrance. The results showed that the steric hindrance and the electron-donating groups contributed to the improved yield. Product **1c** was synthesized by the microwave method for the first time, i.e. it is a new compound. The starting materials for entries 5–7 are derivatives of 3-bromophenol, whose hydroxyl groups were all protected. If the phenols had been unprotected, the active proton may have deactivated the catalyst. The reaction in entry 5 required 16 h to complete according to a literature report [23]; with microwave heating only 1 h was needed. Products **1f** and **1g** were also synthesized for the first time by this method. These results suggest that the scope of application might be dramatically increased by use of appropriate protective groups.

The reaction time for entries 8, 9 and 11 was also substantially shortened, from 18 to 1 h, by use of microwaves.

The reactant in entry 10 is well known; it was difficult to convert completely. This might be because of the fluorine atom—because of its electron-donating effect and weak steric hindrance. By analysis of the GC–MS data, it was found that the purity of compound **1j** was approximately 86.1 %. For entry 12 the yield was 80 % when the reagents were heated at 80 °C for 8 h in MTBE; microwave heating afforded 82 % within 1 h.

This was the first synthesis of compound **1m** (entry 13), a boronate which contains an aldehyde group. This result suggested that the active proton of the aldehyde did not affect the Ir catalyst.

According to the ^{1}H NMR spectra of the products in Table 2, all of the pinacol boronates were located at C-5. This result suggested the method has high selectivity



Scheme 3 Reaction of 2,6-disubstituted pyridines with B_2pin_2 catalyzed by $[Ir(OMe)cod]_2$ and dtbpy at 80 °C

Table 3 Microwave-assisted Ir-catalyzed borylation of disubstituted pyridines

Entry	R1	R2	Product	Microwave heating		Standard heating	
				Time (min)	Yield[a] (%)	Time (min)	Yield[a] (%)
14	Br	Br	**2n**	5	95	30	94
15	Me	Me	**2o**	5	98	30	95
16	$C(CH_3)_3$	$C(CH_3)_3$	**2p**	30	88	480	80
17	$C(CH_3)_3$	COOMe	**2q**	30	90	480	88
18	Me	Cl	**2r**	30	85	900	80
19	CF_3	Cl	**2s**	30	90	480	83
20	OMe	Cl	**2t**	30	79	900	75

[a] Purified isolated yield of reaction achieving 100 % conversion

for both symmetric and asymmetric 1,3-disubstituted arenes. The main reason for this result might be that the less hindered location was substituted selectively.

To further validate this method, a series of 2,6-disubstituted pyridines were selected as reactants (Scheme 3). As is apparent from Table 3, reaction time was dramatically reduced by microwave heating compared with conventional heating. In Table 3, the starting materials in entries 14 and 15 were completely converted in 5 min, in agreement with a literature report [24]. Because of the high polarity, the products were difficult to separate from B_2pin_2 and a small amount of dimer remained in the products. The starting materials in entries 16 and 17 were highly sterically hindered, which led to excellent selectivity. The reaction took only 30 min to give compounds **2p** (88 % yield) and **2q** (90 % yield). The starting materials in entries 18–20 contained a chlorine atom and were also converted to compounds **2r**, **2s**, and **2t** with excellent yields.

Further comparison of the results in Tables 2 and 3 revealed that the reaction time was shorter when substituted pyridines were used as reactants [25]. Because pyridine derivatives coordinate extremely strongly with Lewis acids, the Ir metal or the boron atom binds reversibly to the basic nitrogen.

Conclusions

In summary, an efficient, highly selective, and environmental friendly method has been developed for iridium-catalyzed borylation of 1,3-disubstituted benzenes and 2,6-disubstituted pyridines. This borylation reaction proceeded much more quickly

when microwave irradiation, rather than conventional heating, was used. In addition, because of the affinity of the basic nitrogen in pyridine for the Ir catalyst, the reaction time for pyridine borylation was significant shorter than for benzene borylation.

Compounds **1d**, **1g**, **1l**, **1m**, **2p**, and **2q** have not been reported previously, i.e. they are all new compounds. The other known compounds except **2o** have been synthesized previously by conventional methods. In this work, microwave irradiation significantly accelerated the reaction rate and resulted in a higher yield than conventional heating.

In particular, compound **1m** is the first pinacol boronate containing an aldehyde group to be synthesized successfully by use of iridium as catalyst and microwave heating. In general, if a substrate contains an active proton, the catalyst is deactivated. For this reason, the active proton must be protected during borylation. To our surprise, **1m** was synthesized without such protection. To extend the range of substrates other heterocyclic compounds, for example indoles, furans, pyrroles and thiophenes, are being investigated.

Experimental

All starting materials were purchased from commercial sources. Reactions were carried out in identical thick-walled glass reaction tubes with crimp-top septum seals. ^{1}H NMR and ^{13}C spectra were recorded on a Bruker 400 MHz spectrometer in $CDCl_3$ or DMSO-d_6 using TMS as internal standard. The reactions were monitored at regular intervals by GC–MS to measure conversion and for product identification.

A mixture of the substrate (1 mmol), $[(COD)Ir(\mu\text{-}OMe)]_2$ (1.5 mmol.%), dtbpy (3.0 mmol.%), and B_2pin_2 (1.1 mmol) was dissolved in MTBE (2.4 mL) and the solution was heated at 80 °C for 60 min by microwave irradiation until GC–MS analysis indicated the starting material was consumed completely. The mixture was washed with water and extracted with ethyl acetate (EA; 15 mL × 3). The combined extracts were dried with anhydrous $MgSO_4$ and the solvent was removed in vacuo. The product was purified by chromatography over silica gel.

A mixture of the substrate (1 mmol), $[(COD)Ir(\mu\text{-}OMe)]_2$ (3.0 mmol.%), dtbpy (6.0 mmol.%) and B_2pin_2 (1.1 mmol) was dissolved in MTBE (5.0 mL) and the solution was then heated at 80 °C overnight under N_2. Analysis by GC–MS indicated the starting material was consumed completely. The mixture was washed with water and extracted with EA (15 mL × 3). Combined extracts were dried with anhydrous $MgSO_4$ and the solvent was removed in vacuo. The product was purified by chromatography over silica gel.

Spectroscopic data for representative products

2-(3,5-Dimethoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**1a**)

^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.34 (12H, s, CH_3), 3.81 (6H, s, OCH_3), 6.56 (1H, t, J = 2.4 Hz, ArH), 6.95 (2H, t, J = 2.4 Hz, ArH); ^{13}C NMR (400 MHz,

$CDCl_3$) (δ, ppm): 24.87, 55.44, 83.90, 104.54, 111.58, 160.38; GC–MS (EI): $m/z = 264.1$ $[M]^+$.

2-(3,5-Didichlorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**1b**)

^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.34 (12H, s, CH_3), 7.43 (1H, t, $J = 2.0$ Hz, ArH), 7.65 (2H, t, $J = 2.0$ Hz, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 23.81, 83.48, 130.04, 131.68, 133.68; GC–MS (EI): $m/z = 257.0$ $[M - 15]^+$.

2-(3-Bromo-5-methylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**1c**)

^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 1.29 (12H, s, CH_3), 3.32 (3H, s, CH_3), 7.47 (1H, s, ArH), 7.54 (2H, t, $J = 2.4$ Hz, ArH); ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 20.28, 24.53, 83.94, 121.47, 133.49, 133.78, 140.10; GC–MS (EI): $m/z = 281.0$ $[M - 15]^+$.

2-(3-Bromo-5-isopropylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**1d**)

^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 1.19 (6H, d, $J = 7.2$ Hz, CH_3), 1.29 (12H, s, CH_3), 2.92 (1H, m, CH), 7.49 (1H, s, ArH), 7.57 (1H, d, $J = 5.2$ Hz, ArH), 7.58 (1H, d, $J = 6.0$ Hz, ArH); ^{13}C NMR (400 MHz, DMSO-d_6) (δ, ppm): 24.11, 25.11, 33.62, 84.55, 122.31, 131.54, 132.65, 134.63, 151.50; GC–MS (EI): $m/z = 309.1$ $[M - 15]^+$.

2-(3-Bromo-5-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**1e**)

^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.34 (12H, s, CH_3), 3.81 (3H, s, OCH_3), 6.99 (1H, s, ArH), 7.15 (1H, s, ArH), 7.23 (1H, s, ArH), 7.52 (1H, d, $J = 1.2$ Hz, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm):19.61, 50.31, 78.96, 112.72, 115.37, 117.45, 124.52, 154.68; GC–MS (EI): $m/z = 312.1$ $[M]^+$.

2-(3-Bromo-5-ethoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**1f**)

^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.33 (12H, s, CH_3), 1.39 (3H, t, $J = 6.8$ Hz, CH_3), 4.04 (2H, t, $J = 6.8$ Hz, OCH_2), 7.14 (1H, t, $J = 2.0$ Hz, ArH), 7.23 (1H, d, $J = 2.0$ Hz, ArH), 7.50 (1H, d, $J = 0.8$ Hz, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 9.52, 19.61, 58.57, 78.92, 113.44, 115.84, 117.42, 124.35, 154.05; GC–MS (EI): $m/z = 326.1$ $[M]^+$.

2-(3-Bromo-5-(2,2-diethoxyethoxy)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**1g**)

^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.25 (6H, t, $J = 7.2$ Hz, CH_3),1.33 (12H, s, CH_3), 3.63 (2H, q, $J = 7.2$ Hz, OCH_2), 3.76 (2H, q, $J = 7.2$ Hz, OCH_2), 4.01 (2H, d, $J = 5.2$ Hz, OCH_2), 4.81 (2H, d, $J = 5.2$ Hz, OCH_2), 7.18 (1H, t, $J = 2.0$ Hz, ArH), 7.26 (1H, d, $J = 2.0$ Hz, ArH), 7.52 (1H, d, $J = 1.6$ Hz, ArH); ^{13}C NMR

(400 MHz, $CDCl_3$) (δ, ppm): 15.34, 24.85, 62.66, 68.85, 84.20, 100.42, 118.67, 121.33, 122.64, 130.08, 158.90; GC–MS (EI): $m/z = 399.1$ $[M - 15]^+$.

2-(3-Chloro-5-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**1h**)

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.34 (12H, s, CH_3), 3.82 (3H, s, OCH_3), 6.99 (1H, s, ArH), 7.19 (1H, d, $J = 2.4$ Hz, ArH), 7.37 (1H, d, $J = 1.6$ Hz, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 24.88, 55.58, 84.22, 117.48, 117.77, 126.90, 134.63, 159.94; GC–MS (EI): $m/z = 268.1$ $[M]^+$.

3-Methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (**1i**)

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.35 (12H, s, CH_3), 2.39 (3H, s, CH_3), 7.53 (1H, s, ArH), 7.82 (1H, s, ArH), 7.89 (1H, s, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 20.98, 24.88, 84.44, 111.98, 119.02, 134.79, 135.60, 138.39, 139.62; GC–MS (EI): $m/z = 228.1$ $[M - 15]^+$.

2-(3-Fluoro-5-(trifluoromethyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**1j**)

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.36 (12H, s, CH_3), 7.29 (1H, d, $J = 9.2$ Hz ArH), 7.40 (1H, d, $J = 6.8$ Hz, ArH), 7.85 (1H, d, $J = 6.0$ Hz, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 19.58, 79.38, 115.05, 119.34, 129.97, 132.42, 160.22, 162.73; ^{19}F NMR (400 MHz, $CDCl_3$) (δ, ppm): -100.64, -63.14; GC–MS (EI): $m/z = 275.1$ $[M - 15]^+$.

3-Methoxy-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (**1k**)

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.35 (12H, s, CH_3), 3.85 (3H, s, OCH_3), 7.21 (1H, q, $J = 1.2$ Hz, ArH), 7.52 (1H, d, $J = 2.8$ Hz, ArH), 7.67 (1H, s, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm):19.61, 50.37, 79.28, 107.67,113.43, 114.72, 118.91, 125.38, 153.86; GC–MS (EI): $m/z = 244.1$ $[M - 15]^+$.

Methyl 3-iodo-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (**1l**)

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.35 (12H, s, CH_3), 3.92 (3H, s, OCH_3), 8.30 (1H, d, $J = 0.4$ Hz, ArH), 8.40 (1H, s, ArH), 8.45 (1H, t, $J = 1.6$ Hz, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 24.87, 52.32, 84.47, 93.95, 131.47, 134.77, 140.93, 147.6242, 165.70; GC–MS (EI): $m/z = 388.1$ $[M]^+$.

3-Methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (**1m**)

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.27 (12H, s, CH_3), 2.44 (3H, s, CH_3), 8.30 (1H, d, $J = 0.4$ Hz, ArH), 7.44 (1H, d, $J = 1.2$ Hz, ArH), 7.55 (1H, d, $J = 10.4$ Hz, ArH), 7.69 (1H, s, ArH), 9.99 (1H, s, CHO); ^{13}C NMR (400 MHz,

$CDCl_3$) (δ, ppm): 21.24, 35.04, 83.53, 127.26, 128.90, 130.04, 135.31, 136.46, 138.93, 192.67; GC–MS (EI): $m/z = 239.2$ $[M - 15]^+$.

2,6-Dibromo-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (**2n**)

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.26 (12H, s, CH_3), 7.45 (2H, m, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 25.05, 83.51, 127.07, 140.09, 140.91; GC–MS (EI): $m/z = 363.1$ $[M]^+$.

2,6-Di-*tert*-butyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (**2o**)

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.35 (18H, s, CH_3), 1.36 (12H, s, CH_3), 7.44 (2H, s, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 24.87, 30.23, 37.63, 84.09, 120.30, 166.88; GC–MS (EI): $m/z = 303.3.1$ $[M - 15]^+$.

Methyl 6-(*tert*-butyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)picolinate (**2p**)

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.37 (12H, s, CH_3), 1.41 (9H, s, CH_3), 3.97 (3H, s, OCH_3), 7.85 (1H, d, $J = 0.4$ Hz, ArH), 8.24 (1H, d, $J = 0.8$ Hz, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 24.74, 30.21, 52.65, 84.63, 127.70, 136.86, 146.41, 166.45, 169.10; GC–MS (EI): $m/z = 304.1$ $[M - 15]^+$.

2-Chloro-6-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (**2q**)

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.35 (12H, s, CH_3), 2.53 (3H, s, CH_3), 7.41 (1H, s, ArH) 7.48 (1H, s, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 23.96, 24.85, 84.78, 126.18, 126.73, 150.54, 158.90; GC–MS (EI): $m/z = 238.1$ $[M - 15]^+$.

2-Chloro-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-6-(trifluoromethyl)pyridine (**2r**)

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.36 (12H, s, CH_3), 7.87 (1H, s, ArH) 7.93 (1H, s, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 24.84, 85.40, 119.48, 122.21, 123.68, 132.82, 148.04, 151.81; GC–MS (EI): $m/z = 292.1$ $[M - 15]^+$.

2-Chloro-6-methoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) pyridine (**2s**)

^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 1.35 (12H, s, CH_3), 3.93 (3H, s, OCH_3), 7.01 (1H, s, ArH) 7.22 (1H, s, ArH); ^{13}C NMR (400 MHz, $CDCl_3$) (δ, ppm): 24.84, 54.06, 84.73, 114.58, 120.82, 148.19, 163.74; GC–MS (EI): $m/z = 269.1$ $[M]^+$.

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References

1. N. Miyaura, A. Suzuki, Chem. Rev. **95**, 2457 (1995)
2. D.M.T. Chan, K.L. Monaco, R. Li, D. Bonne, C.G. Clarke, P.Y.S. Lam, Tetrahedron Lett. **44**, 3863 (2003)
3. M.P. Sibi, H. Tatamidani, K. Patil, Org. Lett. **7**, 2571 (2005)
4. G. Chen, N. Tokunaga, T. Hayashi, Org. Lett. **7**, 2881 (2005)
5. T. Ishiyama, M. Murata, N. Miyaura, J. Org. Chem. **60**, 7508–7510 (1995)
6. H. Chen, J.F. Hartwig, Angew. Chem. Int. Ed. **38**, 3391 (1999)
7. H. Chen, S. Schlecht, T.C. Semple, J.F. Hartwig, Science **287**, 1995 (2000)
8. M.K. Tse, J.-Y. Cho, M.R. Smith III, Org. Lett. **3**, 2831 (2001)
9. J.-Y. Cho, C.N. Iverson, M.R. Smith III, J. Am. Chem. Soc. **122**, 12868 (2000)
10. T. Ishiyama, N. Miyaura, J. Org. Chem. **680**, 3 (2003)
11. H. Tamura, H. Yamazaki, H. Sato, S. Sakaki, J. Am. Chem. Soc. **125**, 16114 (2003)
12. F. Shi, M.R. Smith III, R.E. Maleczka Jr, Org. Lett. **8**, 1411–1414 (2006)
13. J.M. Murphy, C.C. Tzschucke, J.F. Hartwig, Org. Lett. **9**, 757–760 (2007)
14. D. Holmes, G.A. Chotana, R.E. Maleczka Jr, M.R. Smith III, Org. Lett. **8**, 1407–1410 (2006)
15. J.M. Murphy, X. Liao, J.F. Hartwig, J. Am. Chem. Soc. **129**, 15434 (2007)
16. R.E. Maleczka Jr, F. Shi, D. Holmes, M.R. Smith III, J. Am. Chem. Soc. **125**, 2003 (2002)
17. C.O. Kappe, Angew. Chem. Int. Ed. **43**, 6250–6284 (2004)
18. H. Tamura, H. Yamazaki, H. Sato, S. Sakaki, J. Am. Chem. Soc. **125**, 16115 (2003)
19. T.A. Boebel, J.F. Hartwig, Tetrahedron **64**, 6824–6830 (2008)
20. P. Harrisson, J. Morris, P.G. Steel, T.B. Marder, Synlett **1**, 147 (2009)
21. T. Ishiyama, J. Takagi, J.F. Hartwig, N. Miyaura, Angew. Chem. **41**, 3056 (2002)
22. P. Harrisson, J. Morris, T.B. Marder, P.G. Steel, Org. Lett. **11**, 3586–3589 (2009)
23. T. Ishiyama, J. Takagi, K. Ishida, N. Miyaura, N.R. Anastasi, J.F. Hartwig, J. Am. Chem. Soc. **124**, 390 (2002)
24. T. Ishiyama, N. Miyaura, Pure Appl. Chem. **78**, 1369–1375 (2006)
25. T. Ishiyama, N. Miyaura, J. Org. Chem. **680**, 7 (2003)