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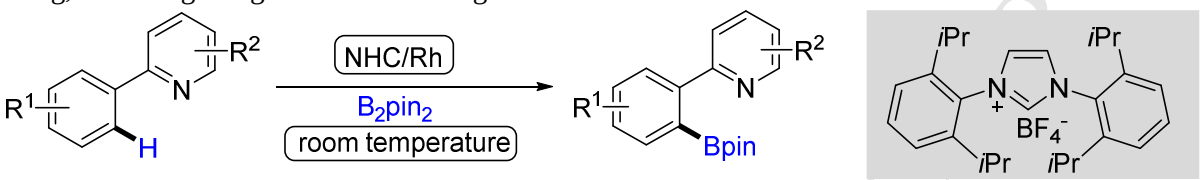

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N-heterocyclic Carbene Enabled Rhodium-Catalyzed *Ortho* C(sp^2)-H Borylation at Room Temperature

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ABSTRACT

We report a rhodium-catalyzed ortho C(sp^2)-H borylation of 2-phenylpyridines using commercially available N-heterocyclic carbenes (NHCs) as ligand and pinacolatodiboron (B_2pin_2) as borylating reagent. The reaction could take place at room temperature, tolerating a wide range of functionalities and affording ortho borylated products in moderate to excellent yields. The current method is also applicable to gram-scale reaction with reduced catalyst loading.

1. Introduction

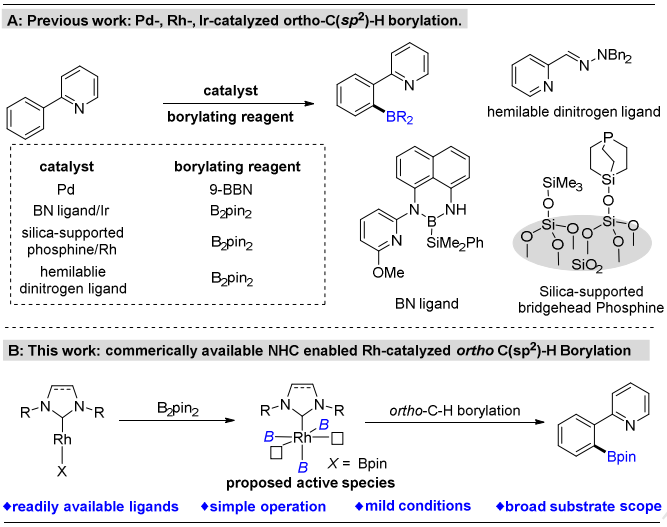
Aryl boronic acids and their derivatives have found wide applications in materials science, medicinal chemistry, organic synthesis, and drug discovery. Traditional methods depend on reaction of aryllithium or Grignard reagent with trialkylborates, which usually requires harsh reaction conditions and has narrow functional group compatibility. Rh- and Ir-catalyzed C-H borylation of aromatic C-H bonds using pinacolborane (HBpin) or B_2pin_2 has become a powerful tool to synthesize numerous of aryl boronates via an atom and step economy, tolerating a variety of functional groups.[1-3] The regioselectivity of this reaction is often governed by steric factor, occurring at the position distal to the substituents,[1] which is complementary to directed ortho metallation (DoM).[4-5] However, the DoM suffered from limitations of substrate scope and harsh reaction conditions due to the use of reactive organolithium reagents. Therefore, the development of Ir-catalyzed ortho selective C-H borylation of arenes is highly demanded in this area.

In the past decade, a number of methods have been developed to achieve ortho C-H borylation of aromatic compounds.[6-11] There are typically two strategies based on d-electron counts of active trisboryl iridium complexes. The first is to utilize 16-electron intermediates. In 2008, Hartwig and coworkers reported a relay directed ortho C-H borylation using silyl as directing groups.[12] Smith and coworkers developed using hydrogen bonding between N-H of substrate and oxygen of one of the boryl groups of triboryl iridium complex.[13-14] The Kanai group developed a Lewis acid tethered bipyridine that could force ortho C-H borylation through Lewis acid-base interaction between catalyst and substrate.[15] The other is chelate directed ortho C-H borylation, which relies on 14-electron triboryl iridium complexes. It is more powerful because the metal center could adopt more diverse directing groups. A proper ligand plays a crucial role in this aspect. Electron poor triarylphosphines,[16] triarylarsines,[17] silica-supported phsosphines,[18-20] hemilabile dinitrogen ligand,[21-23] and bidentate, monoanionic ligands[24-25] are often utilized. A variety of functionalities such as ketone, ester, amide, carbamate, ether, amine, phosphine,[26] and hydrazine, etc. could be used as directing groups. However, there are only few examples related to transition-metal-catalyzed ortho C-H borylation by employing pyridine as a directing group (Scheme 1. A). For example, in 2013, Takai and coworkers reported a palladium-catalyzed ortho-selective C-H borylation of 2-phenylpyridine using 9-BBN as borylating reagent.[27] In 2011, the Sawamura group reported rhodium-catalyzed C-H borylation of 2-phenylpyridine in the presence of silica-supported bridgehead monophosphine.[28] Li and coworkers developed ortho C-H borylation using their anionic boryl nitrogen ligand. Fernández and coworkers reported ortho C-H borylation of this substrate using hemilabile dinitrogen ligands.[21] These methods suffered from some limitations such as relatively unstable borylating reagent, ligands that are not readily available and heating conditions.

N-heterocyclic carbenes (NHCs) have been widely used as organocatalysts and ancillary ligands in transition-metal catalysis.[29-31] In most cases of NHC-metal complexes the ratio of ligand to metal is 1:1. This property reminded us of silica-supported bridgehead monophosphine ligand in Rh-catalyzed ortho C(sp^2)-H borylation.[28] In fact, NHC-Rh complexes as well

as other transition-metal's NHC complexes have been widely used in C-H functionalization.[32-36] However, sporadic examples have been realized by NHC-Rh complexes.[11, 37] And We hypothesized that the reaction of NHC-Rh complex with HBpin or B_2pin_2 would give rise to NHC-Rh(III)(Bpin)$_3$ containing two vacant or weekly coordinating sites. This species would probably enable ortho C(sp^2)-H borylation when reacting with 2-phenylpyridine. Giving the fact that the NHCs have stronger σ donating abilities, their Rh complexes would probably show higher reactivity. Herein, we disclose NHC enabled Rh-catalyzed C(sp^2)-H borylation at room temperature (Scheme 1. B).[37] The reaction could be compatible with a number of functionalities, affording a vast array of ortho borylated products.

Scheme 1. Recent advance of Transtion-Metal-Catalyzed Directed *ortho* C(sp^2)-H Borylation of 2-Phenylpyridine.

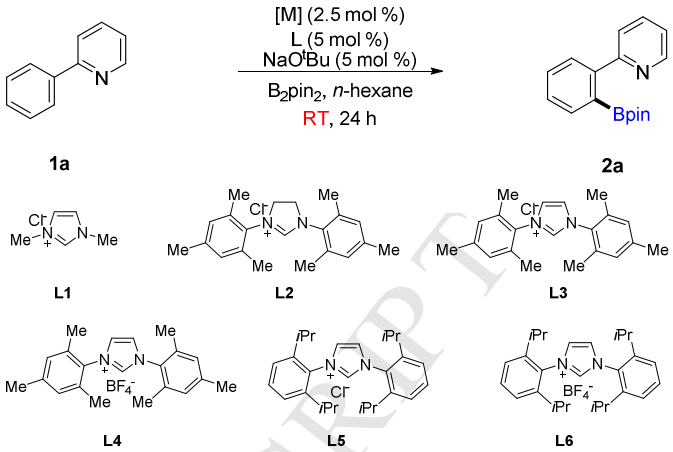


2. Results and Discussion

2-Phenylpyridine **1a** were chose as our pilot substrate to initiate study. Reaction of **1a** with B_2pin_2 in the presence of 2.5 mol% $[RhCl(COD)]_2$, 5 mol % **L1**, 5 mol% ^{t}BuOK in *n*hexane at room temperature for 24 h afforded corresponding ortho borylated product **2a** in 94% isolated yield (Table 1, entry 1). The reaction could not occur without **L1** (Table 1, entry 2) or with 4,4'-di-tert-butyl-2,2'-bipydine (dtbpy) as ligand (Table 1, entry 3). When using $[IrCl(COD)]_2$ instead of $[RhCl(COD)]_2$, at least three components were observed (Table 1, entry 4). Without a ligand, $[IrCl(COD)]_2$ gave trace amount of desired product (Table 1, entry 5). The type of NHC ligand also played an important role in controlling reactivity. For example, the use of **L2**-**L6** instead of L1 resulted in inferior yields (Table 1, entries 6-9). The borylating reagent HBpin gave rise to decreased yield under otherwise identical reaction conditions (Table 1, entry 10). Further study showed that n-hexane was the optimal in terms of reactivity (Table 1, entry 11).

With optimized reaction conditions identified, then the substrate scope of the current borylation process was determined. As shown in Table 2, a variety of functionalities could tolerate under reaction conditions. Substrates bearing substituents at the *para*-positions gave rise to moderate to excellent yields (64-90% yield) in most cases (**2c-k**). Notably, the regioselectivities was governed by pyridine even in the presence of other directing groups such as ester and ketone (**2g** and **2j**). Reactions of substrates containing *meta*-substituents of phenyl ring afforded borylated products in moderate to good yields (**2l-2o**, 65-85% yield). Interestingly, substrate (**1p**) containing 3,5-ditrifluoromethyl groups could also proceed reaction smoothly, delivering corresponding product **2p** in moderate yield (48%). It is

Table 1. Optimization of Reaction Conditions.[a]



Entry	variations from standard conditions	yield (%)[c]
1	none	94
2	no ligand	n.r.
3	dtbpy instead of NHC	n.r.
4	$[IrCl(COD)]_2$	36
5	**L1** instead of **L6**	78
6	**L2** instead of **L6**	84
7	**L3** instead of **L6**	92
8	**L4** instead of **L6**	89
9	**L5** instead of **L6**	83
10[b]	HBpin instead of B_2pin_2	82
11	THF instead of n-hexane	89

[a]**Standard conditions:** Unless otherwise noted, all the reactions were carried out with L6 (0.01 mmol), $[RhCl(COD)]_2$ (0.005 mmol), ^{t}BuOK (0.01 mmol), 1a (0.2 mmol), and B_2pin_2 (0.2 mmol) in *n*-hexane (1.0 mL) at 25 °C for 24 h. [b]HBpin (0.3 mmol).

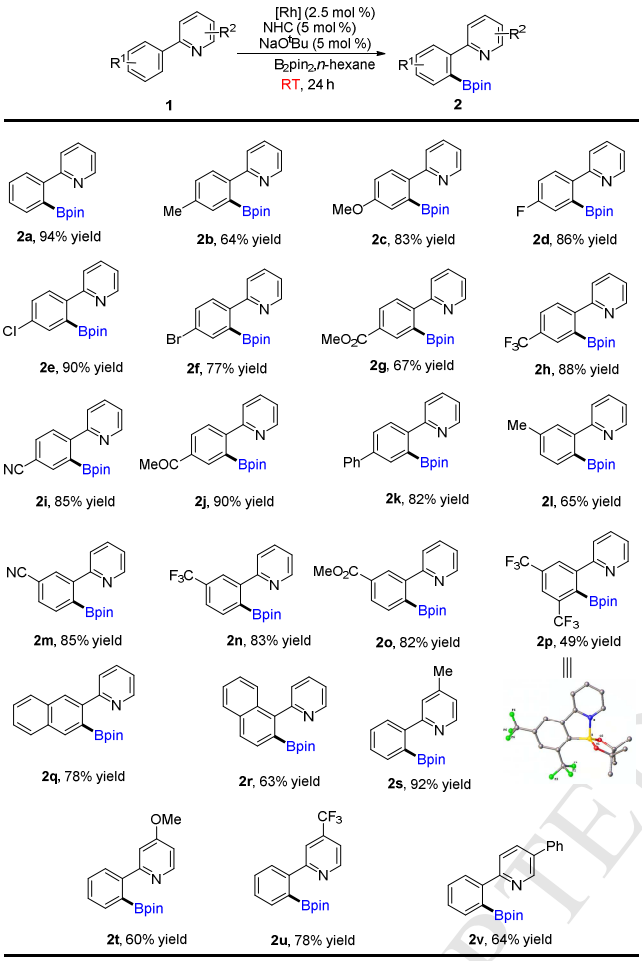
contrast to other steric sensitive systems. The single crystal structure of **2p** also unambiguously confirmed its bond connections. 2-naphthyl and 1-naphthylpyridine (**1q** and **1r**) could also undergo reaction smoothly to produce products **2q** and **2r** in 78% and 63% yields respectively. Notably, compound **2r** was previously prepared by Ir-catalyzed C-H borylation using hemilable dinitrogen ligand[21] and was not realized by recent reported Cp*Rh-NHC complex catalytic system.[37] We next examined the substituent effect of pyridiyl ring on reaction. *para*-Me, MeO, and CF_3 and *meta*-Ph were compatible with the reaction conditions, affording corresponding products (**2s-v**) in moderate to excellent yields (60-92% yield).

To demonstrate the synthetic utility of current method, a gram-scale borylation of **1a** as shown in Scheme 2. Reaction of **1a** (1.08 grams) in the presence of reduced catalyst loading (1.0 mol %) at room temperature for 36 h afforded corresponding **2a** in 84% isolated yield (1.65 grams). The C-B bond of **2a** could be converted to C-O bond by $NaBO_3$ in THF/H_2O at room temperature for 12 h to furnish hydroxylated product **3** in 82% yield. In addition, Suzuki-Miyaura coupling of **2a** with *parp*-bormotoluene in the presence of $Pd(OAc)_2$/Sphos (5 mol %) and

NaOH in THF/H_2O at 80 ˚C for 12 h gave arylated product **4** in 61% yield.[38]

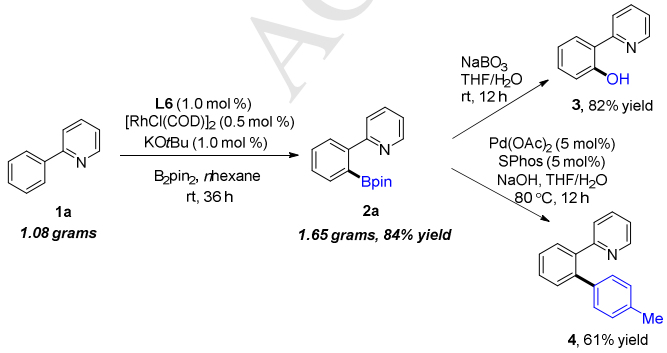
A plausible reaction mechanism was outlined in Scheme 3. Giving the fact that HBpin showed lower reactivity (Table 1), we hypothesized the active species might be a trisboryl NHC-Rh(III) complex **A** which contains two vacant or weekly coordinated sites.

Table 2 Substrate Scope of NHC-Rh-Catalyzed C-H Borylation of 2-Phenylpyridines **1**.[a]



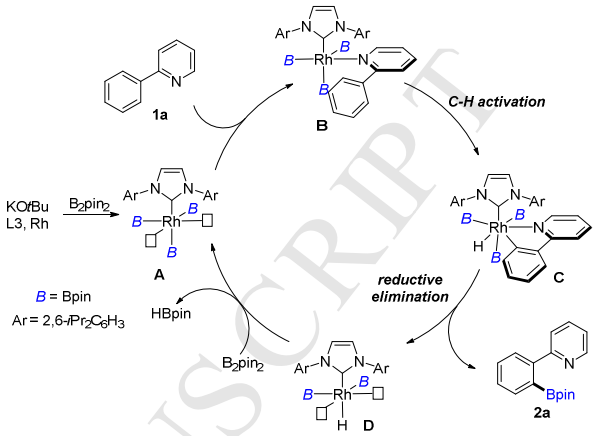
[a]Unless otherwise noted, all the reactions were carried out with **L1** (0.01 mmol), [RhCl(COD)]$_2$ (0.005 mmol), tBuOK (0.01 mmol), **1** (0.2 mmol), and B_2pin_2 (0.3 mmol) in *n*-hexane (2.0 mL) at 25 ˚C for 24 h. The yields refer to isolated products.

Scheme 2 Transtion-Metal-Catalyzed Directed *ortho* C(sp^2)-H Borylation of 2-Phenylpyridine.



One site of A would coordinate with 2-phenylpyridine to generate NHC-Rh(III) complex **B** and the other would enable C-H activation through oxidative addition to form NHC-Rh(V) complex **C**. **C** would undergo reductive elimination to liberate product **2a** with concurrent formation of hydrido bisboryl NHC-Rh(III) complex **D** which would react with B_2pin_2 to regenerate active species **A**.

Scheme 3. Plausible Mechanism for the NHC-Rh catalyzed ortho C-H borylation of 2-phenylpydidine **1a**.



3. Conclusions

In conclusion, we have developed a Rh-catalyzed ortho C(sp^2)-H borylation of 2-phenylpyridines at room temperature using commercially available NHCs. The reaction can tolerate a vast array of functionalities, providing borylated products in moderate to excellent yields. This protocol is also applicable for sterically congested substrate. We also demonstrated that current method is also amendable for gram-scale reaction with reduced catalyst loading. Mechanistic studies and further application of this method are currently underway in our laboratory.

4. Experimental Section

4.1. General Information

All oxygen- and moisture-sensitive manipulations were carried out under an inert atmosphere using standard Schlenk techniques or glovebox. THF, toluene, CH_3CN, *n*-hexane and methanol were purified by passing through a neutral alumina column under argon. All other chemicals and solvents were purchased and used as received. ^{1}H NMR and ^{13}C NMR spectra were recorded on Zhongke-Niujin 400, Bruker 400, Bruker 600 NMR spectrometer at ambient temperature. ^{13}C shifts were obtained with ^{1}H decoupling. High-resolution mass spectroscopy data were obtained on Agilent 6530, Agilent 6224 TOF LC/MS spectrometer.

4.2. Synthesis of Products

In a nitrogen-filled glovebox, to an oven-dried 25-mL Schlenk tube was charged with [Rh(COD)Cl]$_2$ (2.5 mg, 2.5 mol%), L6 (4.8 mg, 5.0 mol%) and KO^{t}Bu (1.1 mg, 5.0 mol%) and *n*-hexane (1.0 mL). The reaction mixture was allowed to stir for 2 hours at room temperature, followed by adding **1a** (0.2 mmol) and B_2pin_2 (50.8 mg, 0.2 mmol, 1.0 equiv). The reaction was then stirred for the determined time at 25 ˚C. The solvent was concentrated under vacuum, and the product was isolated by short-column chromatography (petroleum ether/ethyl acetate/triethylamine 4:1:1% to ethyl acetate/triethylamine 1:1%) on neutral Al_2O_3 (300–400 mesh). The reactions were repeated two runs.

4.3. Characterizing Data for All Products.

2-[2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine (**2a**). Yellow solid, 51.9 mg, 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.66 (d, J = 5.6 Hz, 1H), 7.95 (t, J = 7.6 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 7.2 Hz, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.41 (t, J = 7.2 Hz, 1H), 7.38–7.33 (m, 1H), 7.29 (t, J = 7.6 Hz, 1H), 1.43 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 156.5, 143.1, 141.8, 137.1, 131.4, 127.8, 122.6, 121.2, 117.4, 80.2, 26.9.

2-[4-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine(**2b**). White solid, 37.6 mg, 64% yield .The product was isolated by short-column chromatography (petroleum ether/ethyl acetate/triethylamine 4:1:1% to 0:1:1%) on silica gel (300-400 mesh). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.62 (d, J = 4.8 Hz, 1H), 7.91 (t, J = 7.6 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.58-7.46 (m, 2H), 7.30 (m, 1H), 7.09 (d, J = 7.6 Hz, 1H), 2.39 (s, 3H), 1.43 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 156.7, 143.0, 141.6, 141.6, 134.6, 132.2, 128.6, 122.1, 121.1, 117.1, 80.1, 27.0.

2-[4-methoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine(**2c**). White solid, 51.2 mg, 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.58 (d, J = 5.2 Hz, 1H), 7.89 (t, J = 7.6 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 8.4 Hz, 1H), 7.29-7.20 (m, 2H), 6.80 (d, J = 8.4 Hz, 1H), 3.87 (s, 3H), 1.42 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 162.6, 156.5, 142.8, 141.8, 129.9, 122.7, 121.3, 116.6, 116.2, 113.6, 80.0, 55.2, 27.0.

2-[4-fluoro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine(**2d**). White solid, 51.4mg, 86% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.64 (d, J = 4.8 Hz, 1H), 7.95 (t, J = 7.6 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.62 (dd, J = 8.4 Hz , 4.8 Hz , 1H), 7.36 (m, 2H), 6.96 (t, J = 8.0 Hz, 1H), 1.42 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 165.6 (q, J_{CF} = 250.9 Hz) , 155.5, 143.0, 142.1, 132.8, 123.0 (q, J_{CF} = 8.6 Hz) , 122.3, 118.0 (q , J_{CF} = 19.9 Hz) , 117.1, 114.9 (q, J_{CF} = 23.6 Hz) , 80.2, 26.9.

2-[4-chloro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine(**2e**). White solid, 56.7 mg, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.64 (d, J = 5.6 Hz, 1H), 7.96 (m, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 1.2 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.40-7.34 (m, 1H), 7.29-7.22 (m, 1H), 1.42 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.3, 143.1, 142.1, 137.9, 135.3, 131.5, 127.9, 122.9, 122.3, 117.4, 80.3, 27.0 ; HRMS (ESI) calcd for $C_{17}H_{20}BClNO_2$ ($[M+H]^+$): 316.1270, found: 316.1276.

2-[4-bromo-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine(**2f**). Yellow solid, 55.2 mg, 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.65 (d, J = 5.2 Hz, 1H), 7.96 (t, J = 7.6 Hz, 1H), 7.81 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.40 (dd, J = 8.4 Hz , 6.8 Hz , 2H), 1.42 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.4, 143.1, 142.1, 135.7, 134.5, 130.8, 127.1, 123.0, 122.6, 117.4, 80.3, 27.0.

2-[4-Methoxycarbonyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine(**2g**). Yellow solid, 45.4 mg, 67% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.72 (d, J = 5.2 Hz, 1H), 8.36 (s, 1H), 8.01 (t, J = 6.8 Hz, 2H), 7.87 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.44 (t, J = 6.0 Hz, 1H), 3.93 (s, 3H), 1.45 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 167.3, 155.0, 143.5, 142.0, 141.1, 132.5, 132.2, 129.5, 123.6, 121.0, 118.2, 80.4, 52.0, 27.0; HRMS (ESI) calcd for $C_{19}H_{23}BNO_4$ ($[M+H]^+$): 340.1715, found: 340.1718.

2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethyl)phenyl]pyridine(**2h**). Yellow solid, 61.3 g, 88% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.74 (d, J = 5.2 Hz, 1H), 8.05 (t, J = 7.6 Hz, 1H), 7.94 (s, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 7.6 Hz, 1H), 7.48 (t, J = 7.2 Hz, 1H), 1.45 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.8, 143.6, 142.1, 140.2, 132.7 (d, J_{CF} = 31.4 Hz), 128.1 (q, J_{CF} = 3 Hz) , 125.1 (q, J_{CF} = 3.6 Hz) , 124.4 (q, J_{CF} = 271.3 Hz) , 123.8, 121.2, 118.1, 80.6, 26.9; HRMS (ESI) calcd for $C_{18}H_{20}BF_3NO_2$ ($[M+H]^+$): 350.1534, found: 350.1539.

2-[4-cyano-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine(**2i**). White solid, 52.1 mg, 85% yield; the reaction was carried in acetronile instead of hexane. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.75 (d, J = 5.6 Hz, 1H), 8.08 (t, J = 8.0 Hz 1H), 7.99 (s, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.60 (m, 1H), 7.55 -7.49 (m, 1H), 1.43 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.1, 143.6, 142.4, 140.6, 135.2, 131.7, 124.3, 121.4, 119.4, 118.4, 114.5, 80.6, 26.9; HRMS (ESI) calcd for $C_{18}H_{20}BN_2O_2$ ($[M+H]^+$): 307.1612, found: 307.1615.

2-[4-acetyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine(**2j**). Yellow solid, 58.2 mg, 90% yield; the reaction was carried in acetronile instead of *n*-hexane. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.73 (d, J = 5.6 Hz, 1H), 8.26 (s, 1H), 8.06 - 8.00 (m, 1H), 7.95-7.86 (m, 2H), 7.74 (d, J = 8.0 Hz, 1H), 7.50 – 7.43 (m, 1H), 2.65 (s, 3H), 1.45 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.0, 143.6, 142.1, 131.4, 128.2, 127.3, 127.0, 126.0, 123.7, 121.2, 118.3, 80.5, 26.9; HRMS (ESI) calcd for $C_{19}H_{23}BNO_3$ ($[M+Na]^+$): 324.1766, found: 324.1762.

2-[4-Phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine(**2k**). Yellow solid, 58.3 mg, 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.66 (d, J = 4.8 Hz, 1H), 7.96 - 7.88 (m, 2H), 7.79 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.68 - 7.62 (m, 2H), 7.50 (d, J = 8.0 Hz , 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.34 (dd, J = 7.2 Hz , 5.6 Hz , 2H), 1.45 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 156.2, 144.0, 143.1, 141.8, 141.7, 136.3, 130.3, 128.6, 127.3, 127.0, 122.5, 121.5, 117.4, 80.2, 27.0, 24.7; HRMS (ESI) calcd for $C_{23}H_{25}BNO_2$ ($[M+H]^+$): 358.1973, found: 358.1976.

2-[5-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine(**2l**). White solid, 38.2 mg, 65% yield. The product was isolated by flash-column chromatography (petroleum ether/ethyl acetate/triethylamine 4:1:1% to 0:1:1%) on silica gel (300-400 mesh). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.63 (d, J = 5.2 Hz, 1H), 7.90 (m, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.59 (d, J = 7.2 Hz, 1H), 7.45 (s, 1H), 7.30 (t, J = 6.0 Hz, 1H), 7.22 (d, J = 6.8 Hz, 1H), 2.36 (s, 3H), 1.41 (s, 12H); ^{13}C NMR (100 MHz, CDCl3) δ (ppm) 156.6, 143.2, 141.6, 137.4, 137.3, 132.3, 131.2, 122.4, 121.8, 117.2, 80.1, 26.9, 21.3.

2-[5-cyano-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine(**2m**). Yellow solid, 52.0 mg, 85% yield; the reaction was carried in acetronile instead of hexane. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.73 (d, J = 5.6 Hz, 1H), 8.07 (t, J = 7.6 Hz, 1H), 7.93 (s, 1H), 7.89–7.82 (m, 2H), 7.68 (d, J = 7.6 Hz, 1H), 7.54–7.48 (m, 1H), 1.43 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.0, 143.5, 142.5, 137.8, 134.3, 132.2, 124.4, 124.1, 119.0, 118.0, 111.6, 80.6, 26.9; HRMS (ESI) calcd for $C_{18}H_{20}BN_2O_2$ ($[M+H]^+$): 307.1612, found: 307.1614.

2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trifluoromethyl)phenyl]pyridine(**2n**). Yellow solid, 57.8 mg, 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.70 (d, J = 5.6 Hz, 1H), 8.01 (dd, J = 7.6, 7.6 Hz, 1H), 7.85 (dd, J = 8.0 Hz , J = 7.2 Hz, 3H) , 7.65 (d, J = 7.6 Hz, 1H), 7.44 (t, J = 6.4 Hz, 1H), 1.43 (d, J = 2.0 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.8, 143.3, 142.3, 137.5, 131.8, 130.3 (q, J_{CF} =31.8 Hz) , 127.8

(q, J_{CF} =3.1 Hz) , 124.2 (q, J_{CF} =270.0 Hz) , 123.6, 117.80, 80.44, 26.90; HRMS (ESI) calcd for $C_{18}H_{20}BF_3NO_2$ ($[M+H]^+$): 350.1534, found: 350.1538.

2-[5-acetyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine(**2o**). Yellow solid, 55.6 mg, 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.69 (d, J = 5.2 Hz, 1H), 8.34 (s, 1H), 8.08 (d, J = 7.6 Hz, 1H), 8.03 (t, J = 7.6 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 7.6 Hz, 1H), 7.43 (t, J = 6.4 Hz, 1H), 3.94 (s, 3H), 1.43 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 167.0, 155.3, 143.2, 142.3, 137.4, 132.2, 131.4, 129.8, 123.34, 122.2, 117.8, 80.4, 77.3, 76.7, 52.1, 26.9.

2-*[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,5-bis(trifluoromethyl)phenyl]pyridine*(**2p**). Yellow solid, 40.7 mg, 49% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.79 (d, J = 5.6 Hz, 1H), 8.12-8.01 (m, 2H), 7.98-7.90 (m, 2H), 7.56-7.47 (m, 1H), 1.46 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 152.8, 143.5, 141.5, 141.0, 135.1 (q, J_{CF} = 33.0 Hz) , 131.3 (q, J_{CF} = 33.0 Hz), 124.5, 124.3, 123.8 (q, J_{CF} = 272.8 Hz) , 123.4 (q, J_{CF} = 270.9 Hz) , 121.4, 118.3, 82.4, 28.4; HRMS (ESI) calcd for $C_{19}H_{19}BF_6NO_2$ ($[M+H]^+$): 418.1408, found: 418.1414.

2-[3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)naphthalen-2-yl]pyridine(**2q**). White solid, 51.6 mg, 78% yield, ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.72 (d, J = 5.6 Hz, 1H), 8.14 (d, J = 8.4 Hz, 2H), 8.01-7.95 (m, 2H), 7.84 (t, 2H), 7.51-7.35 (m, 3H), 1.48 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 156.2, 143.1, 141.6, 136.0, 135.5, 133.2, 131.0, 128.5, 128.5, 126.8, 125.7, 123.1, 121.0, 118.1, 80.2, 27.1; HRMS (ESI) calcd for $C_{21}H_{23}BNO_2$ ($[M+H]^+$): 332.1816, found: 332.1821.

2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)naphthalen-1-yl]pyridine(**2r**). White solid, 41.7 mg, 63% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.75 (d, J = 5.2 Hz, 1H), 8.32 (d, J = 8.4 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H), 7.99 (t, J = 7.2 Hz, 1H), 7.93-7.85 (m, 3H), 7.54 (t, J = 7.2 Hz, 1H), 7.46 (t, J = 7.2 Hz, 1H), 7.36 (t, J = 6.0 Hz, 1H), 1.43 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 157.5, 144.2, 141.4, 134.5, 133.5, 131.5, 129.6, 129.5, 128.3, 127.0, 125.1, 122.7, 121.8, 121.6, 80.6, 27.0.

4-methyl-2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine(**2s**). Yellow solid, 54.3 g, 92% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.50 (d, J = 5.6 Hz, 1H), 7.71 (d, J = 7.2 Hz, 1H), 7.64 - 7.58 (m, 2H), 7.39 (t, J = 7.2 Hz, 1H), 7.28 (d, J = 7.6 Hz, 1H), 7.16 (d, J = 5.6 Hz, 1H), 2.51 (s, 3H), 1.42 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 154.4, 142.4, 137.0, 131.3, 127.6, 123.6, 120.9, 117.8, 80.0, 27.0, 21.7; HRMS (ESI) calcd for $C_{18}H_{22}BN_2NaO_2$ ($[M+Na]^+$): 318.1636, found: 318.1638.

4-methoxy-2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pheny]pyridine(**2t**). White solid, 36.7 mg, 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.47 (d, J = 6.4 Hz, 1H), 7.72 (d, J = 7.2 Hz, 1H), 7.60 (d, J = 7.6 Hz, 1H), 7.40 (t, J = 7.2 Hz, 1H), 7.27 (d, J = 2.4 Hz , 1H), 7.19 (d, J = 2.4 Hz, 1H), 6.81 (dd, J = 2.4 Hz , 2.4 Hz , 1H), 3.99 (s, 3H), 1.41 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.1, 158.6, 144.1, 136.9, 131.5, 131.2, 127.5, 120.7, 109.1, 101.9, 79.8, 56.2, 27.0. HRMS (ESI) calcd for $C_{18}H_{23}BNO_3$ ($[M+H]^+$): 312.1766, found: 312.1764.

2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]-4-(trifluoromethyl)pyridine(**2u**). Yellow solid, 54.4 mg, 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.80 (d, J = 5.2 Hz, 1H), 7.95 (s, 1H), 7.71 (dd, J = 7.6 Hz , 7.2 Hz, 2H), 7.53-7.36 (m, 3H), 1.39 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 158.9, 147.0, 141.0 (q, J_{CF} = 33.3 Hz), 139.3, 132.9, 130.6, 129.0, 125.3 (q, J_{CF} = 271.9 Hz) , 124.4, 118.0, 115.4, 82.2, 25.8; HRMS (ESI) calcd for $C_{18}H_{19}BF_3NNaO_2$ ($[M+Na]^+$): 372.1353, found: 372.1532.

5-phenyl-2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine(**2v**)Yellow solid, 45.5 mg, 64% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.86 (s, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 6.8 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.59 (d, J = 7.2 Hz, 2H), 7.53 (t, J = 7.2 Hz, 2H), 7.47 (d, J = 7.2 Hz, 1H), 7.42 (t, J = 7.2 Hz, 1H), 7.31 (t, J = 7.2 Hz, 1H), 1.44 (d, J = 11.2 Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.0, 141.6, 140.0, 137.0, 136.3, 136.0, 131.4, 131.3, 129.4, 128.8, 127.9, 126.7, 121.3, 117.4, 80.3, 26.9; HRMS (ESI) calcd for $C_{23}H_{25}BNO_2$ ($[M+H]^+$): 358.1973, found: 358.1976.

2-（4-hydroxylphenyl）pyridine(**3**)Yellow solid, 28.1 mg, 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 14.34 (s, 1H), 8.50 (d, J = 3.6 Hz, 1H), 7.91 (d, J = 8.4 Hz, 1H), 7.87-7.76 (m, 3H), 7.35-7.27 (m, 1H), 7.23 (m, 1H), 7.03 (d, J = 8.4 Hz, 1H), 6.90 (t, J = 6.8 Hz,1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 160.0, 157.9, 145.8, 137.7, 131.5, 126.1, 121.4, 119.0, 118.7, 118.6.

2-（4-methylphenyl）pyridine(**4**). White solid, 30.0 mg, 61% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.64 (d, J = 4.4 Hz, 1H), 7.68 (dd, J = 2.4 Hz , 3.6 Hz , 1H), 7.48-7.41 (m, 3H), 7.38 (dd, J = 1.6 Hz , 1.6 Hz , 1H), 7.14-7.07 (m, 1H), 7.04 (s, 4H), 6.90 (d, J = 8.0 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 159.4, 149.4, 140.6, 139.4, 138.4, 136.3, 135.2, 130.5, 129.6, 128.8, 128.5, 127.4, 125.4, 121.2, 21.1.

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References and notes

1. Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890-931.
2. Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 390-391.
3. Cho, J. Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E.; Smith, M. R. *Science.* **2002**, *295*, 305-308.
4. Schneider, C.; Broda, E.; Snieckus, V. *Org. Lett.* **2011**, *13*, 3588-3591.
5. Hurst, T. E.; Macklin, T. K.; Becker, M.; Hartmann, E.; Kuegel, W.; Parisienne-La Salle, J. C.; Batsanov, A. S.; Marder, T. B.; Snieckus, V.*Chem. Eur. J.* **2010**, *16*, 8155-8161.
6. Ros, A.; Fernandez, R.; Lassaletta, J. M. *Chem. Soc. Rev.* **2014**, *43*, 3229-3243.
7. Xiao, B.; Li, Y.M.; Liu, Z.J.; Yang, H.Y.; Fu, Y. *Chem. Commun.* **2012**, *48*, 4854-4856.
8. Jiang, Q.; Duan-Mu, D.; Zhong, W.; Chen, H.; Yan, H. *Chem. Eur. J.* **2013**, *19*, 1903-1907.
9. Fernandez-Salas, J. A.; Manzini, S.; Piola, L.; Slawin, A. M. Z.; Nolan, S. P. *Chem. Commun.* **2014**, *50*, 6782-6784.
10. Kallaene, S. I.; Braun, T. *Angew. Chem. Int. Ed.* **2014**, *53*, 9311-9315.
11. Keske, E. C.; Moore, B. D.; Zenkina, O. V.; Wang, R.; Schatte, G.; Crudden, C. M. *Chem. Commun.* **2014**, *50*, 9883-9886.

12. Boebel, T. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 7534-7535.

13. Roosen, P. C.; Kallepalli, V. A.; Chattopadhyay, B.; Singleton, D. A.; Maleczka, R. E.; Smith, M. R. *J. Am. Chem. Soc.* **2012**, *134*, 11350-11353.

14. Preshlock, S. M.; Plattner, D. L.; Maligres, P. E.; Krska, S. W.; Maleczka, R. E.; Smith, M. R. *Angew. Chem. Int. Ed.* **2013**, *52*, 12915-12919.

15. Liang, L. H.; Yoichiro, K.; Motomu, K. *Angew. Chem. Int. Ed.* **2017**, *56*, 1495-1499.

16. Takaya, J.; Ito, S.; Nomoto, H.; Saito, N.; Kirai, N.; Iwasawa, N. *Chem. Commun.* **2015**, *51*, 17662-17665.

17. Sasaki, I.; Taguchi, J.; Hiraki, S.; Ito, H.; Ishiyama, T. *Chem. Eur. J.* **2015**, *21*, 9236-9241.

18. Kawamorita, S.; Ohmiya, H.; Hara, K.; Fukuoka, A.; Sawamura, M. *J. Am. Chem. Soc.* **2009**, *131*, 5058-5059.

19. Kawamorita, S.; Ohmiya, H.; Sawamura, M. *Eur. J. Org. Chem.* **2010**, *75*, 3855-3858.

20. Yamazaki, K.; Kawamorita, S.; Ohmiya, H.; Sawamura, M. *Organic Lett.* **2010**, *12*, 3978-3981.

21. Ros, A.; Estepa, B.; López-Rodríguez, R.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. *Angew. Chem. Int. Ed.* **2011**, *50*, 11724-11728.

22. Ros, A.; López-Rodríguez, R.; Estepa, B.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. *J. Am. Chem. Soc.* **2012**, *134*, 4573-4576.

23. Roering, A. J.; Hale, L. V. A.; Squier, P. A.; Ringgold, M. A.; Wiederspan, E. R.; Clark, T. B. *Organic Lett.* **2012**, *14*, 3558-3561.

24. Wang, G.; Liu, L.; Wang, H.; Ding, Y.-S.; Zhou, J.; Mao, S.; Li, P. *J. Am. Chem. Soc.* **2017**, *139*, 91-94.

25. Ghaffari, B.; Preshlock, S. M.; Plattner, D. L.; Staples, R. J.; Maligres, P. E.; Krska, S. W.; Maleczka, R. E.; Smith, M. R. *J. Am. Chem. Soc.* **2014**, *136*, 14345-14348.

26. Crawford, K. M.; Ramseyer, T. R.; Daley, C. J. A.; Clark, T. B. *Angew. Chem. Int. Ed.* **2014**, *53*, 7589-7593.

27. Kuninobu, Y.; Iwanaga, T.; Omura, T.; Takai, K. *Angew. Chem. Int. Ed.* **2013**, *52*, 4431-4434.

28. Kawamorita, S.; Miyazaki, T.; Ohmiya, H.; Iwai, T.; Sawamura, M.*J. Am. Chem. Soc.* **2011**, *133*, 19310-19313.

29. Zhao, D.; Candish, L.; Paul, D.; Glorius, F. *ACS Catalysis* **2016**, *6*, 5978-5988.

30. Janssen-Muller, D.; Schlepphorst, C.; Glorius, F.*Chemical Society Rev.* **2017**, *46*, 4845-4854.

31. Enders, D.; Niemeier, O.; Henseler, A. *Chemical Rev.* **2007**, *107*, 5606-5655.

32. Kim, J. H.; Gressies, S.; Boultadakis-Arapinis, M.; Daniliuc, C.; Glorius, F. *ACS Catal.* **2016**, *6*, 7652-7656.

33. Kwak, J.; Kim, M.; Chang, S. *J. Am. Chem. Soc.***2011**, *133*, 3780-3783.

34. Ye, S.; Yang, W.; Coon, T.; Fanning, D.; Neubert, T.; Stamos, D.; Yu, J.Q. *Chemistry A European Journal*. **2016**, *22*, 4748-4752.

35. Hsiao, C.-C.; Lin, Y.K.; Liu, C.J.; Wu, T.C.; Wu, Y.T. *Advanced Synthesis & Catalysis* **2010**, *352*, 3267-3274.

36. Fernández-Salas, J. A.; Marelli, E.; Nolan, S. P. *Chemical Science.* **2015**, *6*, 4973-4977.

37. Thongpaen, J.; E. Schmid, T.; Toupet, L.; Dorcet, V.; Mauduit, M.; Baslé, O. *Chem. Commun*. **2018**, *54*, 8202-8205.

38. Meng, F.; McGrath, K. P.; Hoveyda, A. H. *Nature.* **2014**, *513*, 367-374.