Phosphine-free cross-coupling reaction of halopyridines with arylboronic acids in an ionic liquid : water mixture

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Palladium acetate-catalysed Suzuki reaction of halopyridines and arylboronic acids has been investigated in room-temperature ionic liquids in the absence of the phosphine ligand. A significant effect of water on the efficiency of the Suzuki reaction in ionic liquids was observed. The mixture of ionic liquid and water significantly enhanced the rate of the coupling reaction. The separation of the product was easily performed by extraction with diethyl ether and the $Pd(OAc)_2$–[bmim][PF_6] (1-butyl-3-methylimidazolium hexafluorophosphate) can be reused six times with only a small loss of reactivity.

Keywords: heterobiaryl, Suzuki reaction, halopyridine, palladium acetate, ionic liquid

Heterobiaryls are used in the synthesis of biologically active compounds or ligands. The development of new methods for the preparation of heterobiaryls continues to be the subject of investigation.[1,2] The Suzuki reaction, which involves the palladium-catalysed cross-coupling of aryl- or heteroarylboronic acids with aryl or heteroaryl halides (or triflates), has proved to be very versatile.[3-9] The traditional Suzuki reaction usually proceeds with phosphine-based palladium catalysts in organic solvents.[10-13] However, the Suzuki reaction when carried out in conventional organic solvents, suffers from several drawbacks such as high catalyst consumption, high reaction temperature, long reaction times and poor reagent solubility. Furthermore, the expensive palladium complex is often lost at the end of the reaction and many phosphines are toxic and sensitive to air and moisture. Recently, the Suzuki reaction, including the cross-coupling reaction of heteroaryl halides was successfully carried out in aqueous media. The advantages of using an aqueous catalytic system were easier product separation, decreased cost and increased reactivity. For example, the $Pd(PPh_3)_4$-catalysed Suzuki coupling of 2- and 4-chloropyridines with arylboronic acids involving water as the cosolvent was reported by Lohse in 1999.[14] Subsequently Gong *et al*. carried out the synthesis of heteroaryl benzoic acids in aqueous acetonitrile by using $Pd(PPh_3)_4$ as the catalyst.[15] Later, Nishida developed an elegant method of Suzuki reaction of chloro- and bromopyridines with arylboronic acid in aqueous media with Pd/C as the catalyst in the presence of TBAB.[16] However, phosphine ligands in these systems were indispensable for the Suzuki reaction.

Ionic liquids have attracted considerable attention as a novel reaction media in green chemistry.[17-21] We previously reported that the Suzuki reaction involving the cross-coupling reaction of aryl boronic acid with carboxylic and anhydride proceeded with high efficiency in water in the presence of ionic liquid and without the use of a phosphine ligand.[22,23] These catalytic systems are air-stable, insensitive to moisture, and reusable with an impressive reactivity for a wide range of substrates. The presence of ionic liquids played a crucial role in the reaction, and the formation of a separate biphase with other traditional solvents such as diethyl ether significantly simplified the purification of the desired products. In this paper, a highly efficient method for the synthesis of arylpyridines by the Suzuki reaction of halopyridines with arylboronic acids in mixture of ionic liquid and water in high yields under mild reaction conditions is presented. The use of ionic liquids significantly enhanced the reactivity of Suzuki reaction and good recyclable efficiency was obtained.

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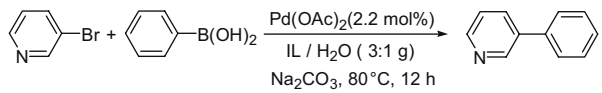
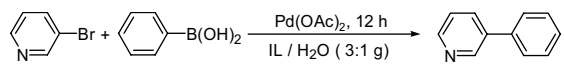
Results and discussion

Initially, the effect of various ionic liquids on the coupling reaction was studied as shown in Table 1. To determine the standard conditions, the coupling reaction of 3-bromopyridine and phenylboronic acid was chosen as the model reaction using Na_2CO_3 as the base in the presence of 2.2 mol% $Pd(OAc)_2$ at 80 °C for 12 h under N_2(Scheme 1). The separation of the products was easily performed by extraction with diethyl ether. Ionic liquids containing the 1-(2-hydroxyethyl)-3-methylimidazolium cation ([PEG_1mim]) and dialkylimidazolium cation([Rmim]) were studied. It was found that PEG-ILs did not promote the reaction (Table 1, entries 1–3). However, the room temperature ionic liquids (ILs) containing the 1,3-dialkylimidazolium cation improved the cross-coupling reaction. The anion of the ionic liquids markedly influenced the reactivity of the Suzuki reaction. Hydrophobic 1-butyl-3-methylimidazolium hexafluorophosphate [bmim][PF_6] significantly promoted the reactivity (Table 1, entry 6), while 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4]) showed a poor effect on the reactivity (Table 1, entry 5). No reaction was observed in a mixture of water and the hydrophilic 1-butyl-3-methylimidazolium chloride ([bmim][Cl]) under these reaction conditions (Table 1, entry 4). These results suggested that [bmim][PF_6] was superior to [bmim][BF_4]



Scheme 1 The route of synthesis of 3-bromopyridine in IL-H_2O system.

Table 1 Effect of ionic liquid on the coupling reaction of 3-bromopyridine and phenylboronic acid[a]



Entry	Ionic liquid	Yield/%[b]
1	[PEG_1mim] [Cl]	4
2	[PEG_1mim] [BF_4]	6
3	[PEG_1mim] [PF_6]	10
4	[bmim][Cl]	5
5	[bmim][BF_4]	57
6	[bmim][PF_6]	96
7[c]	[bmim][PF_6]	80
8[d]	[bmim][PF_6]	97

[a]Reaction conditions: 3-bromopyridine (1.0 mmol), $PhB(OH)_2$ (1.5 mmol), Na_2CO_3 (2.0 mmol), $Pd(OAc)_2$ (2.2 mol%), IL/H_2O (3 g/1 g), 12 h, 80 °C, under N_2.
[b]Determined by means of GC, based on the 3-bromopyridine.
[c]Reaction was carried out at 60 °C.
[d]Reaction was carried out at 100 °C.

and [bmim][Cl] for the coupling of 3-bromopyridine with phenylboronic acids. Reducing the temperature to 60 °C had a dramatic effect on the reaction with the yield being reduced to 80% in [bmim][PF_6]-H_2O system (Table 1, entry 7). Raising the temperature from 80 to 100 °C had a positive effect on the coupling reaction (Table 1, entry 8), but the formation of the by-product biphenyl from the self-coupling of phenylboronic acid proceeded rapidly. The best conversion was obtained at 80 °C (Table 1, entry 6).

In the Suzuki reaction of arylboronic acids with aryl halides in ionic liquids, water played the crucial role to the reaction of 3-bromopyridine and phenylboronic acid. The coupling reaction rate was found to be dependent on the ratio of the [bmim][PF_6] and water. As expected, the reaction in pure ionic liquid, or pure water gave poor yields together with the formation of large amounts of the byproduct biphenyl from the self-coupling of phenylboronic acid (Table 2, entries 1 and 10). The addition of water to [bmim][PF_6] clearly enhanced the activity of the coupling reaction and an optimum yield was obtained when the mass ratio of [bmim][PF_6] to water was 3 : 1 (96%) (Table 2, entry 3). The generation of the homocoupling by-products was suppressed markedly. Further increase of the amount of water was deleterious to the reaction (Table 2, entries 4–9). Compared with the reaction under N_2, the yield of coupling reaction was slightly decreased in air, and more byproduct of biphenyl was observed (Table 2, entry 11).

The effect of various bases was screened and the results are presented in Table 3. The inorganic bases (NaOAc, KOAc, Na_3PO_4, K_3PO_4, NaOH, KOH, KF, Na_2CO_3, K_2CO_3) and organic base (Et_3N) were examined in the coupling reaction. Et_3N, K_2CO_3, and Na_2CO_3 gave the desired product with high yields(Table 3, entries 8–10) and the best yield was obtained using Na_2CO_3 in 96% GC yield, whereas NaOAc, KOAc and NaOH were found to be poor bases for the coupling reaction(Table 3, entries 1, 2, 5). Moderate yields were afforded by using the bases, Na_3PO_4, K_3PO_4, KOH and KF (Table 3, entries 3, 4, 6, 7). $Pd(OAc)_2$ was shown to be an excellent catalyst in the [bmim][PF_6]–H_2O system (Table 3, entry 10), while $PdCl_2$ and $PdCl_2(CH_3CN)_2$ gave moderate yields (Table 3, entries 11,12). All of the entries described so far employed 2.2 mol% $Pd(OAc)_2$. In entries 13–15 the amount of $Pd(OAc)_2$ was decreased from 1.8 mol% to 0.9 mol% with a negative effect on the conversion.

To further understand the scope and limitations of the cross-coupling reaction in $Pd(OAc)_2$–[bmim][PF_6]–H_2O, a variety of arylboronic acids were examined in the coupling reaction and the results are presented in Table 4. As can be seen that the electron-rich arylboronic acids showed the excellent reactivity and furnished the products in high yields (Table 4, entries 1-3), while the electron-deficient arylboronic acid gave moderate yield (Table 4, entry 4).

The effect of the halopyridine partner on the Suzuki reaction was also investigated (Table 4). 5-Bromo-2-methylpyridine and 5-bromo-3-methylpyridine gave good to high yields (Table 4, entries 5 and 6). However, the sterically demanding bromopyridines delivered poorer yields even after extending the reaction time (Table 4, entries 7 and 8). Encouraged by these results, the activity of 3-chloropyridines was studied. Unfortunately, 3-chloropyridine gave the products in low yields (Table 4, entry 9), while the electron-rich 3-chloropyridines only gave a trace of the desired product (Table 4, entry 10). The influence of the position of the bromo substituent on pyridines on the rate of the coupling with arylboronic acid was studied. 2-Bromopyridine was less active than 3-bromopyridine, and gave lower yield even when the reaction time was extended to 24 h at 80 °C (Table 4, entries 11 and 12). The coupling of 2-bromopyridine with electron-rich arylboronic acid afforded 65% (Table 4, entry 13), while the coupling with electron-deficient arylboronic acid was sluggish (Table 4, entry 15). The sterically demanding bromopyridines gave a poor yield (Table 4, entry 14). It was reported that these α-substituted heteroaryl bromides, a possible interaction between the hetero element and the palladium complex has a decelerating effect on the rate of the reaction.[24]

The reuse of the catalytic system was examined in the coupling reaction of 3-bromopyridine with phenylboronic acid using Na_2CO_3 as the base at 80 °C for 12 h in the presence of 2.2 mol% $Pd(OAc)_2$. Since the ionic liquid was insoluble in diethyl ether, the products were easily isolated by simple extraction with diethyl ether. The remaining ionic liquid and catalyst were recovered and reused without further addition of ionic liquid (Fig. 1). It was found that washing the residue in every cycle with water was important to the efficiency of the recyclability. The reactivity of the catalyst in the cycles was reduced significantly without washing with water after the reaction. A possible reason was that the salt byproducts generated in the coupling reaction retarded the coupling reaction.[25] [Bmim][PF_6] was immiscible with water, and after washing in every cycle with water, high efficiency in the recycling experiment was obtained. The catalytic system could be recycled six times with only a small decrease in activity without the need of activation or addition of the catalyst.

Table 2 Effect of water on the Suzuki reaction of 3-bromopyridine with phenylboronic acid in [bmim][PF_6][a]

Entry	Water added/g	Yield/%[b]
1	0.00	4
2	0.50	89
3	1.00	96
4	1.50	91
5	2.00	88
6	2.50	89
7	3.00	88
8	3.50	82
9	4.50	77
10[c]	6.00	46
11[d]	1.00	91

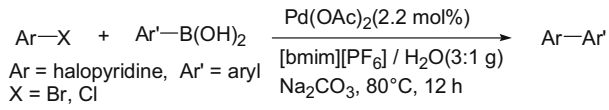
[a]Reaction conditions: 3-bromopyridine (1.0 mmol), $PhB(OH)_2$ (1.5 mmol), Na_2CO_3 (2.0 mmol), $Pd(OAc)_2$ (2.2 mol%), [bmim][PF_6](3 g), 80 °C, 12 h, under N_2.
[b]Determined by means of GC, based on the 3-bromopyridine.
[c]Pure water as solvent.
[d]Reaction was carried out in air.

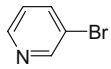
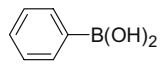
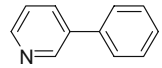
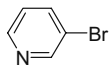
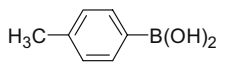
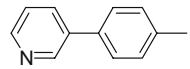
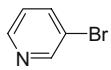
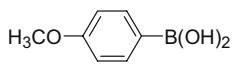
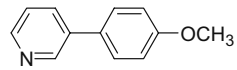
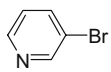
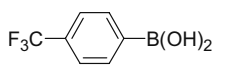
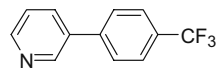
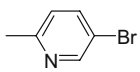
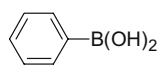
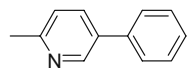
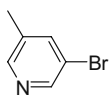
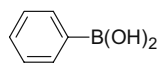
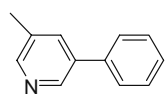
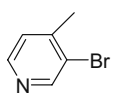
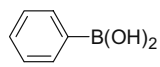
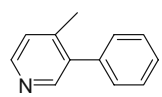
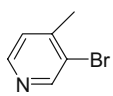
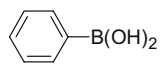
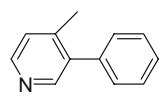
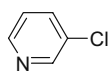
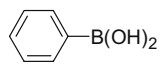
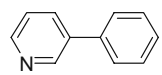
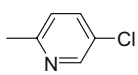
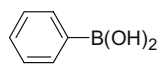
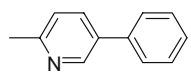
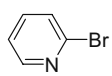
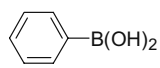
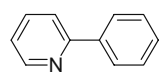
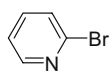
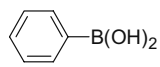
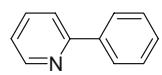
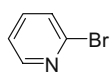
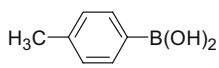
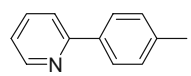
Table 3 Effect of bases and catalysts on the Suzuki reaction of 3-bromopyridine with phenylboronic acid in [bmim][PF_6][a]

Entry	Base	Pd/mol%	Yield/%[b]
1	NaOAc	$Pd(OAc)_2$	58
2	KOAc	$Pd(OAc)_2$	52
3	Na_3PO_4	$Pd(OAc)_2$	67
4	K_3PO_4	$Pd(OAc)_2$	72
5	NaOH	$Pd(OAc)_2$	49
6	KOH	$Pd(OAc)_2$	76
7	KF	$Pd(OAc)_2$	70
8	Et_3N	$Pd(OAc)_2$	86
9	K_2CO_3	$Pd(OAc)_2$	89
10	Na_2CO_3	$Pd(OAc)_2$	96
11	Na_2CO_3	$PdCl_2$	79
12	Na_2CO_3	$PdCl_2(CH_3CN)_2$	88
13[c]	Na_2CO_3	$Pd(OAc)_2$	91
14[d]	Na_2CO_3	$Pd(OAc)_2$	86
15[e]	Na_2CO_3	$Pd(OAc)_2$	70

[a]Reaction conditions: 3-bromopyridine (1.0 mmol), $PhB(OH)_2$ (1.5 mmol), base (2.0 mmol), cat. (2.2 mol%), [bmim][PF_6]/H_2O(3 g/1 g), 80 °C, 12 h, under N_2.
[b]Determined by means of GC, based on the 3-bromopyridine.
[c]1.8 mol% $Pd(OAc)_2$ was used.
[d]1.32 mol% $Pd(OAc)_2$ was used.
[e]0.9 mol% $Pd(OAc)_2$ was used.

Table 4 Suzuki cross-coupling reaction of halopyridine with arylboronic acid in the mixture of [bmim][PF_6] and water[a]



Entry	Ar–X	Ar′-B(OH)$_2$	Product	Yield/%[b]
1				93
2				94
3				96
4				84
5				86
6				88
7				75
8[c]				83
9[c]				36
10				trace
11				57
12[c]				68
13				65
14				51
15				48

[a]Reaction conditions: halopyridine (1.0 mmol), arylboronic acid (1.5 mmol), Na_2CO_3 (2.0 mmol), $Pd(OAc)_2$ (2.2 mol%), [bmim][PF_6]/H_2O(3 g/1 g), 80 °C, 12 h, under N_2.
[b]Isolated yield.
[c]Reaction time prolonged to 24 h.

In conclusion, the [bmim][PF_6]–H_2O solvent system was shown to be a useful and alternative reaction medium for cross-coupling of bromopyridines with arylboronic acids using $Pd(OAc)_2$ as the catalyst, avoiding the use of phosphine. Water was found to have a remarkable accelerating effect on the Suzuki reaction in ionic liquids. The $Pd(OAc)_2$-[bmim][PF_6] can be reused six times only with a small loss of reactivity. This procedure represents an environmentally friendly method for the preparation of heterobiaryl compounds.

Experimental

Starting materials and solvents were purchased from common commercial sources and were used without additional purification. Column chromatography was carried out on silica gel (300–400 mesh). ^{1}H NMR spectra were recorded at 400 MHz, using TMS as internal standard. Mass spectroscopy data of the product of the Suzuki reaction was collected on MS-EI. Elemental analyses were performed by Dezhou University. Melting points were measured on X-4 melting-point device.

Representative procedure for the Suzuki reaction of halopyridine with arylboronic acid

A mixture of halopyridine (1.0 mmol), arylboronic acid (1.5 mmol), $Pd(OAc)_2$ (5 mg, 2.2 mol%), Na_2CO_3 (0.21 g, 2.0 mmol), and [bmim][PF_6]/H_2O (3 g/1 g) was stirred at 80 °C for 12 h under N_2. After the reaction, the solution was cooled to room temperature, and the resultant suspension was extracted with diethyl ether (5 ml) four

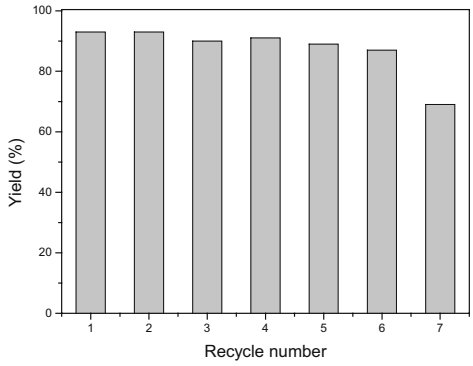


Fig. 1 Recycling of $Pd(OAc)_2$-[bmim][PF_6]-H_2O catalytic system. Reaction conditions: 3-bromopyridine (1.0 mmol), $PhB(OH)_2$ (1.5 mmol), Na_2CO_3 (2.0 mmol), $Pd(OAc)_2$ (2.2 mol%), [bmim][PF_6]/H_2O (3/1 g), 80 °C, 12 h, under N_2.

times. The combined diethyl ether phase was concentrated, and further purification of the product was achieved by flash chromatography on a silica gel column(300–400 mesh). In the recycling experiment, the residue after the extraction was washed with water (3 × 6 ml) and then was subjected to a second run of the coupling reaction by charging with the same substrates (3-bromopyridine, phenylboronic acid, water, and Na_2CO_3) without further addition of [bmim][PF_6] or $Pd(OAc)_2$.

*3-Phenylpyridine***(T1):** Yellow oil.[26] NMR (400 MHz, $CDCl_3$, TMS) δ 8.83 (d, 1 H, *J* = 7.5 Hz), 8.56–8.55 (m, 1 H), 7.83–7.80 (m, 1 H), 7.55–7.53 (m, 2 H), 7.45–7.42 (m, 2 H), 7.38–7.29 (m, 2 H). MS (EI): *m/z* (%): 155 (100) [M^+], 154 (22), 153 (15), 76 (9). Anal. Calcd for $C_{11}H_9N$: C, 85.1; H, 5.85; N, 9.0. Found: C, 85.1; H, 5.9; N, 9.1%.

*3-(4-Methylphenyl)pyridine***(T4-2):** Yellow oil.[27] NMR (400 MHz, $CDCl_3$, TMS) δ8.85 (d, 1 H, *J* = 7.5 Hz), 8.57 (q, 1 H, *J* = 6.5 Hz), 7.88–7.85 (m, 1 H), 7.49 (t, 2 H, *J* = 7.0 Hz), 7.36–7.33 (m, 1 H), 7.29 (t, 2 H, *J* = 4.5 Hz), 2.42 (s, 3 H). MS (EI): *m/z* (%): 169 (100) [M^+], 154 (30), 153 (20), 76 (10). Anal. Calcd for $C_{12}H_{11}N$: C, 85.2; H, 6.55; N, 8.3. Found: C, 85.1; H, 6.6; N, 8.3%.

*3-(4-Methoxyphenyl)pyridine***(T4-3):** Colourless oil.[26] NMR (400 MHz, $CDCl_3$, TMS) δ 8.80 (s, 1 H), 8.53 (d, 1 H, *J* = 4.4 Hz), 7.81 (d, 1 H, *J* = 7.6 Hz), 7.51 (d, 2 H, *J* = 8.8 Hz), 7.32 (q, 1 H, *J* = 6.6 Hz), 7.00 (d, 2 H, *J* = 5.2 Hz), 3.85 (s, 3 H). MS (EI): *m/z* (%):186 (16) [M^+ + 1], 185 (100) [M^+], 170 (50), 142 (37), 115 (16), 89 (7), 63 (5). Anal. Calcd for $C_{12}H_{11}NO$: C, 77.8; H, 6.0; N, 7.6. Found: C, 77.8; H, 6.0; N, 7.6%.

*3-(4-(Trifluoromethyl)phenyl)pyridine***(T4-4):** White solid, m.p. 33–36 °C.[26] NMR (400 MHz, $CDCl_3$, TMS) δ 8.78 (d, 1 H, *J* = 4.6 Hz), 8.57 (q, 1 H, *J* = 1.2 Hz), 7.82–7.79 (m, 1 H), 7.66 (d, 2 H, *J* = 8.4 Hz), 7.60 (d, 2 H, *J* = 8.0 Hz), 7.33–7.30 (m, 1 H). MS (EI): *m/z* (%):224 (17) [M^+ + 1], 223 (100) [M^+], 204 (10), 191 (26), 154 (19), 127 (8). Anal. Calcd for $C_{12}H_8F_3N$: C, 64.6; H, 3.6; F, 25.5; N, 6.3. Found: C, 64.55; H, 3.6; F, 25.5; N, 6.3%.

*2-Methyl-5-phenylpyridine***(T4-5)**: Yellow oil.[28] NMR (400 MHz, $CDCl_3$, TMS) δ8.97 (d, 1 H, *J* = 5.0 Hz), 8.52 (q, 1 H, *J* = 7.6 Hz), 7.86–7.82 (m, 1 H), 7.48 (t, 2 H, *J* = 5.5 Hz), 7.34–7.30 (m, 1 H), 7.29 (t, 2 H, *J* = 3.6 Hz), 2.55 (s, 3 H). MS (EI): *m/z* (%): 169 (100) [M^+], 154 (54), 153 (17), 76 (15). Anal. Calcd for $C_{12}H_{11}N$: C, 85.2; H, 6.55; N, 8.3. Found: C, 85.1; H, 6.6; N, 8.3%.

*3-Methyl-5-phenylpyridine***(T4-6)**: Yellow oil.[29] NMR (400 MHz, $CDCl_3$, TMS) δ8.86 (d, 1 H, *J* = 7.6 Hz), 8.52 (q, 1 H, *J* = 7.0 Hz), 7.85–7.81 (m, 1 H), 7.50 (t, 2 H, *J* = 5.5 Hz), 7.35–7.31 (m, 1 H), 7.30 (t, 2 H, *J* = 6.5 Hz), 2.44 (s, 3 H). MS (EI): *m/z* (%): 169 (100) [M^+], 154 (20), 153 (36), 76 (20). Anal. Calcd for $C_{12}H_{11}N$: C, 85.2; H, 6.55; N, 8.3. Found: C, 85.1; H, 6.6; N, 8.3%.

*4-Methyl-3-phenylpyridine***(T4-7)**: Colourless oil.[28] NMR (400 MHz, $CDCl_3$, TMS) δ8.88 (d, 1 H, *J* = 7.8 Hz), 8.54 (q, 1 H, *J* = 5.6 Hz), 7.88–7.85 (m, 1 H), 7.48 (t, 2 H, *J* = 6.7 Hz), 7.36–7.32 (m, 1 H), 7.31 (t, 2 H, *J* = 7.2 Hz), 2.44 (s, 3 H). MS (EI): *m/z* (%): 169 (100) [M^+], 154 (45), 153 (20), 76 (16). Anal. Calcd for $C_{12}H_{11}N$: C, 85.2; H, 6.55; N, 8.3. Found: C, 85.15; H, 6.6; N, 8.3%.

*2-Phenylpyridine***(T 4-11):** Colourless oil.[30] NMR (400 MHz, $CDCl_3$, TMS) δ8.68 (d, 1 H, *J* = 4.4 Hz), 7.98 (t, 2 H, *J* = 7.7 Hz), 7.71–7.69 (m, 2 H), 7.48–7.40 (m, 3 H), 7.20–7.19 (m, 1 H). MS (EI): *m/z* (%): 155 (100) [M^+], 154 (21), 153 (7), 115 (7), 76 (11). Anal. Calcd for $C_{11}H_9N$: C, 85.1; H, 5.85; N, 9.0. Found: C, 85.1; H, 5.9; N, 9.05%.

*2-p-Tolylpyridine***(T4-13):** Colourless oil.[30] NMR (400 MHz, $CDCl_3$, TMS) δ8.74 (d, 1 H, *J* = 5.8 Hz), 8.58 (q, 1 H, *J* = 8.0 Hz), 7.89–7.85 (m, 1 H), 7.50 (t, 2 H, *J* = 6.6 Hz), 7.37–7.34 (m, 1 H), 7.27 (t, 2 H, *J* = 7.4 Hz), 2.47 (s, 3 H). MS (EI): *m/z* (%): 169 (100) [M^+], 154 (22), 153 (15), 76 (9). Anal. Calcd for $C_{12}H_{11}N$: C, 85.2; H, 6.55; N, 8.3. Found: C, 85.2; H, 6.55; N, 8.3%.

*2-o-Tolylpyridine***(T4-14):** Colourless oil.[30] NMR (400 MHz, $CDCl_3$, TMS) δ8.76 (d, 1 H, *J* = 4.6 Hz), 8.75 (q, 1 H, *J* = 5.9 Hz), 7.90–7.84 (m, 1 H), 7.48 (t, 2 H, *J* = 6.7 Hz), 7.35–7.31 (m, 1 H), 7.28 (t, 2 H, *J* = 4.8 Hz), 2.56 (s, 3 H). MS (EI): *m/z* (%): 169 (100) [M^+], 154 (25), 153 (18), 76 (14). Anal. Calcd for $C_{12}H_{11}N$: C, 85.2; H, 6.55; N, 8.3. Found: C, 85.15; H, 6.5; N, 8.3%.

*2-(4-(Trifluoromethyl)phenyl)pyridine***(T4-15):** White solid, m.p. 39–41 °C.[31] NMR (400 MHz, $CDCl_3$, TMS) δ 8.80 (d, 1 H, *J* = 4.6 Hz), 8.58 (q, 1 H, *J* = 1.2 Hz), 7.80–7.77 (m, 1 H), 7.67 (d, 2 H, *J* = 8.4 Hz), 7.63 (d, 2 H, *J* = 8.0 Hz), 7.35–7.31 (m, 1 H). MS (EI): *m/z* (%):224 (17) [M^+ + 1], 223 (100) [M^+], 204 (15), 191 (30), 154 (22), 127 (10). Anal. Calcd for $C_{12}H_8F_3N$: C, 64.6; H, 3.6; F, 25.5; N, 6.3. Found: C, 64.6; H, 3.6; F, 25.5; N, 6.3%.

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