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Alkylation of Aromatic Amines with Trialkyl Amines Catalyzed by a Defined Iridium Complex with a 2-Hydroxypyridylmethylene Fragment

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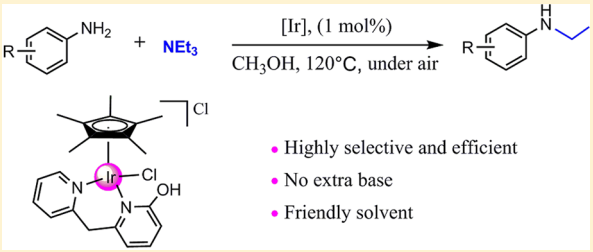
Supporting Information

ABSTRACT: Six Cp*Ir complexes containing NN-bitentate chelate ligands [Cp*IrCl($C_5H_4CH_2C_5H_3OH$)][Cl] (**1**), [Cp*IrCl($C_5H_4CH_2C_5H_3O$)] (**2**), [Cp*IrCl($C_5H_4C_5H_3OH$)] [Cl] (**3**), [Cp*IrCl($C_5H_4CH_2C_5H_4$)][Cl] (**4**), [Cp*IrCl($CH_3OC_5H_3CH_2C_5H_3OCH_3$)][Cl] (**5**), and [Cp*IrCl($CH_3OC_5H_3CH_2C_5H_3OH$)][Cl] (**6**) were synthesized and characterized. Complex **1** could be transformed to **2** when reacted with NaO^{t}Bu or NEt_3 via −OH deprotonation. These six complexes were tested as catalysts for mono-*N*-alkylation of amines with trialkyl amines, and complex **1** exhibited highest activity. The coupling reactions proceed under air condition, with 1 mol % catalyst loading without extra base in methanol at 120 °C and can be further accelerated by adding NR_3·HCl.



INTRODUCTION

Amines have drawn considerable attention, as their motifs are applied in pharmaceuticals, dyes, polymer materials, and agrochemicals.[1] Nevertheless, traditional approaches to amines still suffer from many deficiencies. For instance, the best-known ones for the synthesis of secondary amines are the *N*-alkylation of primary amines utilizing alkyl halides as the alkylating agents, which are mostly toxic and may suffer from overalkylation.[2] Therefore, it is significative to explore more fresh syntheses to afford secondary amines.

The borrowing hydrogen reaction, which is also known as hydrogen autotransfer, has become an efficient protocol to synthesize secondary amines.[3] One of the strategies is to use alcohols,[4] and the other is to use amines,[5,6] as alkylating reagents to react with primary amines. The latter method is less well studied, and only a few examples have been reported in the literature in which homogeneous catalysts were utilized for the reactions of primary amines with trialkyl amines. As shown in Scheme 1, Beller et al. reported an effective transfer process for the reaction of aniline with trialkyl amines by the Shvo catalyst in 24 h in 2008.[6b] In 2009, Williams and co-workers explored an iridium catalyst to achieve the coupling of primary amines with (^{i}Pr)$_2$NH in high yield and excellent selectivity at high temperature, and NEt_3 was also applicable.[6f] Ding and Wang' groups also independently reported the alkylation of aromatic amines with triethylamine in moderate yields in the presence of $AgNTf_2$ or base additive.[6i−k]

In recent years, the Li's group employed a NN-Cp*Ir complex bearing a functional 6,6′-dihydroxy-2,2′-bipyridine ($HOC_5H_3C_5H_3OH$) ligand for the synthesis of different kinds of organic compounds, such as α-alkylated ketones,[7a,b] quinazolinones,[7c] and quinolines,[7d] via borrowing hydrogen strategies (Figure 1, left). On the basis of their works, our group designed a similar iridium complex [Cp*IrCl($HOC_5H_3CH_2C_5H_3OH$)][Cl] with two 2-hydroxypyridyl moieties for methylation of amines and ketones with methanol (Figure 1, middle).[8] In these catalytic cycles, the ligands are converted to bipyridonate forms through a metal−ligand cooperative process. Transition metal complexes bearing mono 2-hydroxypyridyl moiety can also undergo a similar metal−ligand cooperation.[9] Thus, we were curious about the catalytic activity of NN-Cp*Ir complexes containing one 2-hydroxypyridyl fragment. As an update of our continuous interest in borrowing hydrogen reactions,[9g−i] herein we report the synthesis and reactivity of a new Cp*Ir complex [Cp*IrCl($C_5H_4CH_2C_5H_3OH$)][Cl] (**1**) bearing a 2-hydroxy-6-(2-pridinylmethyl)pyridine ligand ($C_5H_4CH_2C_5H_3OH$, $\mathbf{L_1}$) (Figure 1, right). Although the catalytic activity for methylation of amines and ketones with methanol was not discovered, complex **1** shows high catalytic efficiency and selectivity for the mono-*N*-alkylation of aromatic amines with trialkyl amines without extra base. It is worth mentioning that the reaction was carried out under relatively mild conditions (120 °C) in methanol which is regarded as an abundant atom-economical and environmentally friendly solvent.

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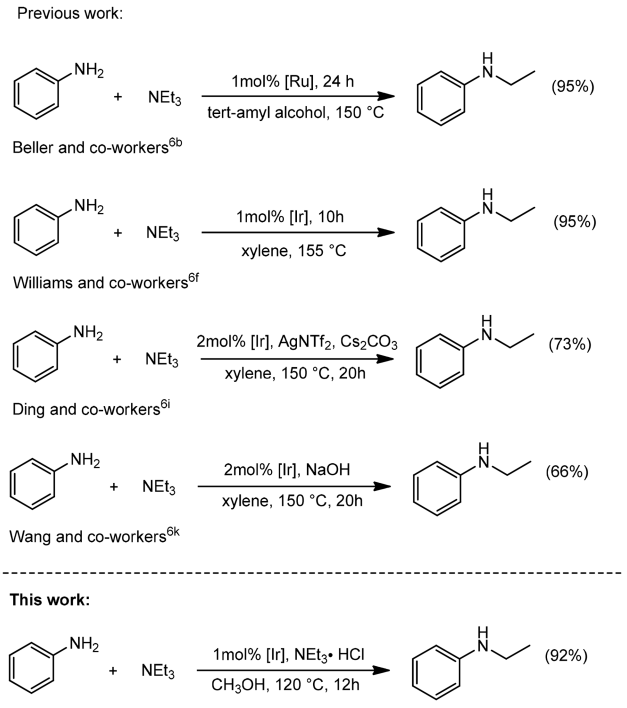
Scheme 1. State-of-the-Art *N*-Alkylation of Aniline with Triethylamine



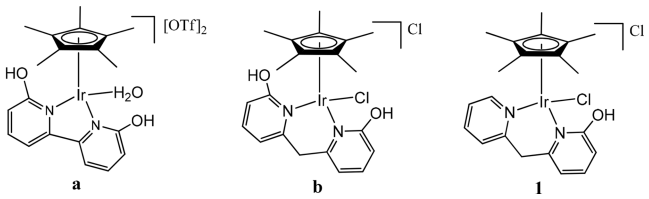
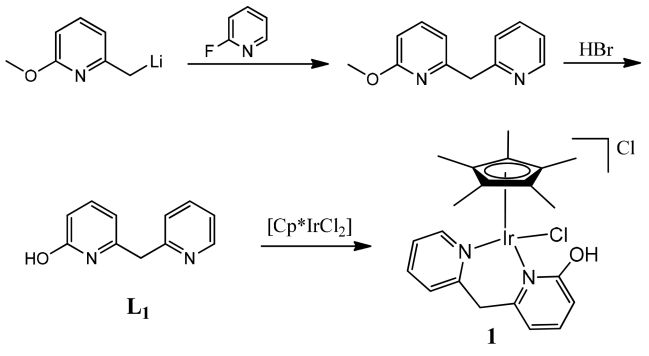


Figure 1. Li's iridium complex **a** (left), our previous iridium complex **b** (middle), and complex **1** in this work (right).

RESULTS AND DISCUSSION

Synthesis and Characterization of the Ligand Precursor and Ir Complexes. As shown in Scheme 2, L_1 was synthesized by the reaction of HBr with 2-methoxy-6-(2-pyridinylmethyl)pyridine at reflux for 3 h in 90% yield. When L_1 was treated with $[Cp^*IrCl_2]_2$ in refluxing CH_3OH for 24 h, complex $[Cp^*IrCl(C_5H_4CH_2C_5H_3OH)][Cl]$ (**1**) was isolated as a yellow solid in 82% yield. The ^1H NMR spectrum of **1** in DMSO-d_6 shows one singlet for the −OH group at 13.03 ppm, seven signals between 8.71 and 7.02 ppm for its aromatic protons, two doublets at 4.68 and 3.70 ppm for the methylene protons, and one singlet for Cp* at 1.56 ppm.

Scheme 2. Synthesis of L_1 and 1



The molecular structure of **1** (Figure 2) was further confirmed by X-ray crystallography. In the solid state, it is a cationic complex with the central Ir atom coordinating with two pyridyl, one Cl atom and one Cp* group. The two pyridine rings of the dipyridyl ligands are not coplanar, and the C(5)−C(6)−C(5A) angle is 111.1(5)°. The C−C bonds in the hydroxypyridyl ring are in the range of 1.385(7)−1.369(6) Å, and the C(1)−O(1) distance (1.428(7) Å) is consistent with a C−O single bond.[10] The distances of Ir(1)−N(1), and Ir(1)−Cl(1) are 2.113(3) and 2.4101(15)Å, respectively.

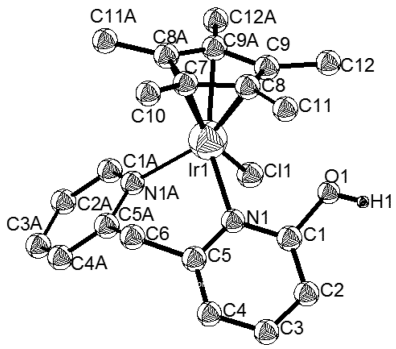
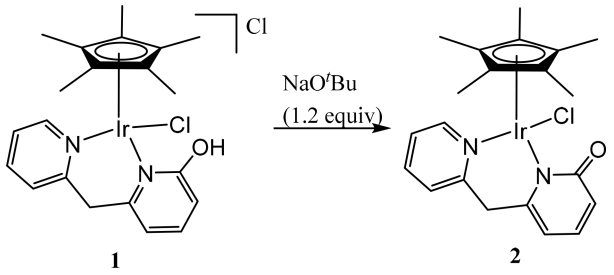


Figure 2. Molecular structure of complex **1**. Hydrogen atoms (except H1), solvent and Cl^- anion have been omitted for clarity. Selected bond distances (Å) and angle (deg): Ir(1)−N(1), 2.113(3); Ir(1)−N(1A), 2.113(3); Ir(1)−Cl(1), 2.4101(15); C(1)−O(1), 1.428(7); C(1)−N(1), 1.354(6); N(1)−C(5), 1.363(5); C(4)−C(5), 1.369(6); C(3)−C(4), 1.385(7); C(2)−C(3), 1.372(7); C(1)−C(2), 1.382(7); N(1)−Ir(1)−N(1A), 85.6(2); N(1)−Ir(1)−Cl(1), 84.44(10); C(5)−C(6)−C(5A), 111.1(5).

Complex **1** was further treated with 1.2 equiv of NaO^tBu in water at room temperature and $[Cp^*IrCl(C_5H_4CH_2C_5H_3O)]$ (**2**) was produced in 79% yield (Scheme 3). The ^1H NMR spectrum of **2** in DMSO-d_6 shows seven signals between 8.72 and 6.48 ppm for its aromatic protons, two doublets for the methylene group at 4.41 and 3.60 ppm, and one singlet at 1.55 ppm for Cp*. **2** could also be generated by treating **1** with 2 equiv of triethylamine in 76% yield. X-ray diffraction analysis shows the iridium center is coordinated with two pyridyl, one Cl atom and one Cp* group (Figure 3), which is similar to **1**. The N(1)−Ir(1)−N(2), N(1)−Ir(1)−Cl(1) and N(2)−Ir(1)−Cl(1) angles are 86.8, 88.1, and 83.6°, respectively. The distances of Ir(1)−N(1), Ir(1)−N(2) and Ir(1)−Cl(1) are 2.125(11), 2.108(13) and 2.421(3) Å, respectively. The

Scheme 3. Synthesis of 2



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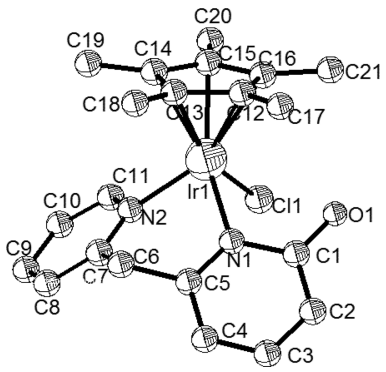
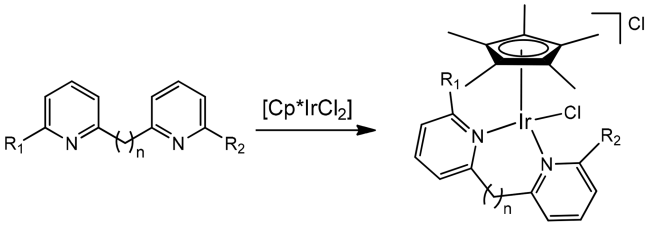


Figure 3. Molecular structure of complex **2**. Hydrogen atoms and solvent have been omitted for clarity. Selected bond distances (Å) and angle (deg): Ir(1)−N(1), 2.125(11); Ir(1)−N(2), 2.108(13); Ir(1)−Cl(1), 2.421(3); C(1)−O(1), 1.25(3); C(1)−N(1), 1.41(3); N(1)−C(5), 1.34(3); C(4)−C(5), 1.39(3); C(3)−C(4), 1.38(3); C(2)−C(3), 1.37(3); C(1)−C(2), 1.40(3); N(1)−Ir(1)−N(2), 86.8(7); N(1)−Ir(1)−Cl(1), 88.1(3); N(2)−Ir(1)−Cl(1), 83.6(4); C(5)−C(6)−C(7), 114.8(16).

C(1)−N(1) bond is 1.41(3) Å, and the C(1)−C(2) distance is 1.40(3) Å, obviously longer than the other bonds in the same ring, suggesting they are more similar to single bonds. The O(1)−C(1) distance (1.25(3) Å) is comparable to those of a pyridonate ruthenium complex supported by deprotonated 6,6′-dihydroxyterpyridine developed by Szymczak's group, suggesting a C═O bond.[10]

Complexes [Cp*IrCl($C_5H_4C_5H_3OH$)][Cl] (**3**), [Cp*IrCl-($C_5H_4CH_2C_5H_4$)][Cl] (**4**), [Cp*IrCl-($CH_3OC_5H_3CH_2C_5H_3OCH_3$)][Cl] (**5**), and [Cp*IrCl-($CH_3OC_5H_3CH_2C_5H_3OH$)][Cl] (**6**) were synthesized following a similar procedure as described for **1** (Scheme 4). When

Scheme 4. Synthesis of 3−6

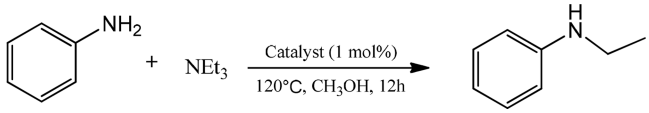


n = 0, R_1 = H, R_2 = OH: **3**
n = 1, R_1 = H, R_2 = H: **4**
n = 1, R_1 = OCH_3, R_2 = OCH_3: **5**
n = 1, R_1 = OCH_3, R_2 = OH: **6**

6-hydroxy-2,2′-bipyridine,[11] 2-(2-pyridylmethyl)pyridine,[12] 2-methoxy-6-((6-methoxypyridin-2-yl)methyl)pyridine,[8] and 2-hydroxy-6-((6-methoxypyridin-2-yl)methyl)pyridine were treated with $[Cp^*IrCl_2]_2$ in refluxing CH_3OH for 24 h, complexes **3**−**6** were isolated as yellow solids in 90, 84, 89, and 91% yields, respectively. The ^{1}H NMR spectrum of **3** exhibits seven signals between 8.93 and 7.31 ppm for its aromatic protons. For complex **4**, besides the aromatic protons, two doublets at 4.90 and 3.78 ppm for its $-CH_2-$ group appear. While for complexes **5** and **6**, the ^{1}H NMR spectra show uncoupled methylene signals at 4.05 and 3.86 ppm, respectively, similar to the complex [Cp*IrCl($HOC_5H_3CH_2C_5H_3OH$)][Cl] reported in another work.[8]

Catalysis. Initially, complexes **1**−**6** were tried as catalysts for methylation of amines and ketones with methanol, while different from complex **b** shown in Figure 1,[8] no activity was discovered, suggesting the bipyridonate structure is important for methanol dehydrogenation. Fortunately, these complexes can catalyze the alkylation of aromatic amines with trialkyl amines. To find the optimal conditions, the reaction of aniline with NEt_3 was selected as the model reaction (Table 1). At

Table 1. Optimization of Reaction Conditions for the Alkylation of Aniline[a]



entry	cat.	NEt_3 (mmol)	NEt_3·HCl (%)	conversion (%)[b]	yield (%)[c]
1	**1**	2	0	74	70
2	**2**	2	0	65	58
3	**3**	2	0	65	62
4	**4**	2	0	17	11
5	**5**	2	0	20	16
6	**6**	2	0	49	41
7	**1**	1	0	55	50
8	**2**	1	0	30	24
9	**1**	2	10	92	87
10	**2**	2	10	93	90
11	**1**	2	20	100	94
12	**2**	2	20	100	96
13[d]	**1**	ethylamine	0	0	0
14[e]	**1**	diethylamine	0	0	0
15[f]	**1**	2	20	100	93
16[g]		2	20	0	0

[a]Aniline (1.0 mmol), methanol (2 mL), air, catalyst (1 mol %), 120 °C, 12 h. [b]Determined by GC analysis on the basis of aniline. [c]Yields determined by GC analysis by using *p*-xylene as the internal standard. [d]Reaction was carried out with 2 mmol ethylamine. [e]Reaction was carried out with 2 mmol diethylamine. [f]Reaction was carried out under N_2. [g]Reaction was carried out without catalyst.

120 °C, in the presence of 1 mol % complexes **1**−**6** and 2 mL of CH_3OH, the reactions proceeded in a 25 mL Schlenk tube under air condition. When 2 equiv of NEt_3 were added, the product *N*-ethylbenzenamine was afforded in 70% yield when **1** was used as catalyst (Table 1, entry 1). Complexes **2**−**6** were not as active as **1** under the same condition, giving yields of 58, 62, 11, 16, and 41%, respectively (Table 1, entries 2−6). If the amount of NEt_3 was decreased to 1 equiv, the yields were lowered, but **1** was still more active than **2** (Table 1, entries 7 and 8). The results were surprising, because as described above, complex **1** can react with NEt_3 to produce complex **2**, so **2** should be the intermediate of **1**. We speculated that the other product of **1** with NEt_3, NEt_3·HCl, might act as a facilitator for this reaction. In order to testify our inference, 10 and 20% NEt_3·HCl were added, respectively, and the yields were increased obviously, no matter if **1** or **2** as the catalyst (Table 1, entries 9−12). The other product, $NHEt_2$, was also detected in around 64% yield by GC analysis under the reaction conditions of entry 11 in Table 1. The results further proved that **2** is the intermediate of **1** and suggest NEt_3·HCl might act as the acceptor of the generated $NHEt_2$. Another two aliphatic amines, ethylamine and diethylamine, were tested, and no conversion was found (Table 1, entries 13 and 14). The N_2 atmosphere had almost no influence on the reaction (Table 1, entry 15). When the reaction was carried out without

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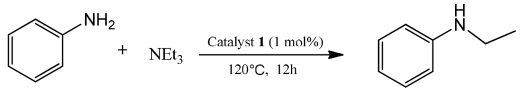
catalyst, no product was detected (Table 1, entry 16). In addition, different solvents had been screened and the results showed that CH_3OH is most suitable for this reaction (Table 2).

Table 2. Solvent Screening[a]



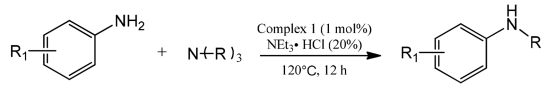
entry	solvent	conversion (%)[b]	yield (%)[c]
1	CH_3OH	100	94
2	CH_3CH_2OH	89	85
3	H_2O	27	20
4	toluene	5	2
5	THF	16	12

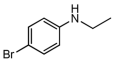
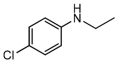
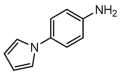
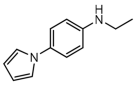
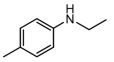
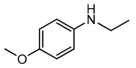
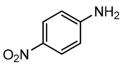
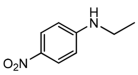
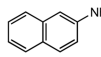
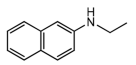
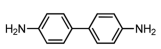
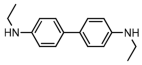
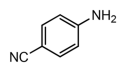
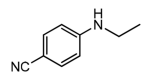
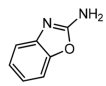
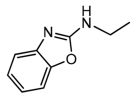
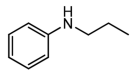
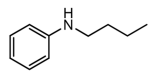
[a]Aniline (1.0 mmol), methanol (2 mL), NEt_3 (2.0 mmol), NEt_3·HCl (20%, 0.2 mmol), catalyst **1** (1 mol %), 120 °C, 12 h, air. [b]Determined by GC analysis on the basis of aniline. [c]Yields determined by GC analysis by using *p*-xylene as the internal standard.

With the optimized reaction conditions, various aromatic amines were tested for the alkylation reaction and these results are listed in Table 3. In general, the reaction is applicable to most aromatic amines. Reactions of *ortho*-, *meta*-, and *para*-brominated anilines gave the corresponding products in 83−95% yields (Table 3, entries 2−4). Other para-substituted anilines, such as 4-chloroaniline, 4-(1*H*-pyrrol-1-yl)aniline, *p*-toluidine, and 4-methoxyaniline, also reacted with NEt_3 to afford mono-*N*-alkylated aniline derivatives in high yields (83−94%) (Table 3, entries 4−8). A strong electron-withdrawing group in the para position (4-nitroaniline) decreased the isolated yield to 69% (Table 3, entry 9). The *ortho*-methyl and -methoxy substituted anilines gave relatively lower yields, probably due to steric hindrance effect (Table 3, entries 10 and 11). 2-Naphthylamine was also tested, and the corresponding product was isolated in moderate yield (Table 3, entries 12). When two amino groups were present, both could be monoalkylated (Table 3, entry 13). For the substrates containing a coordination group, such as 2-aminopyridine, 4-cyanoaniline, and benzooxazol-2-ylamine, the yields were much lower (30−55%) (Table 3, entries 14−16). In addition, when the reaction was carried out with 2 mmol of *N*,*N*-dipropyl-1-propanamine, it afforded the product *N*-propylaniline in 83% yield. Similarly, if 20% HCl was added, the reaction was accelerated (Table 3, entry 17). When the alkylating reagent was replaced by an unsymmetrical trialkylamine, *N*-butyldimethylamine, the ratio of *N*-methylbenzenamine and *N*-butylbenzenamine was about 5:95 according to GC analysis, and the isolated yield of *N*-butylbenzenamine was about 85% (Table 3, entry 18).

The reaction mechanism of our work may proceed through a borrowing hydrogen mechanism (Scheme 5).[5,6] In the presence of NEt_3, complex **1** is first transformed to **2**. The Cl atom then leaves as an anion, and intermediate **A** with an open site forms. After the coordination with NEt_3, *β*-hydride elimination occurs, with the conversion of **B** to **C**, accompanied by the formation of iminium ion **D**. It is possible that one of the pyridyl rings dissociates from the Ir center during this step, because *β*-hydride elimination needs an open site. Aromatic amine then attacks the iminium ion, followed by the release of $NHEt_2$. At last, the hydride connecting with Ir transfers to newly formed iminium ion **F**, and the final

Table 3. Ir-Catalyzed Selective Mono-Alkylation of Anilines[a]



Entry	substrate	Product	Isolated yield[b](%)
1			92
2			95
3			83
4			89
5			88
6			90
7			94
8			83
9			69
10			80
11			66
12			73
13			91
14			35
15			30
16			55
17			83[c] 96[d]
18			85[e]

[a]Aniline (1.0 mmol), methanol (2 mL), NEt_3 (2.0 mmol), NEt_3·HCl (20%, 0.2 mmol), catalyst **1** (1 mol %), 120 °C, 12 h, air. [b]Yields of isolated product. [c]Reaction was carried out with 2 mmol *N*,*N*-dipropyl-1-propanamine, without NEt_3·HCl. [d]Reaction was carried out with 2 mmol *N*,*N*-dipropyl-1-propanamine and 20% HCl, without NEt_3·HCl. [e]Reaction was carried out with 2 mmol *N*-butyldimethylamine without NEt_3·HCl.

secondary amine is formed, with the regeneration of **A**. As described in Table 1, $NHEt_2$ and NH_2Et are not suitable for this methodology, probably due to iminium ion **D** being less

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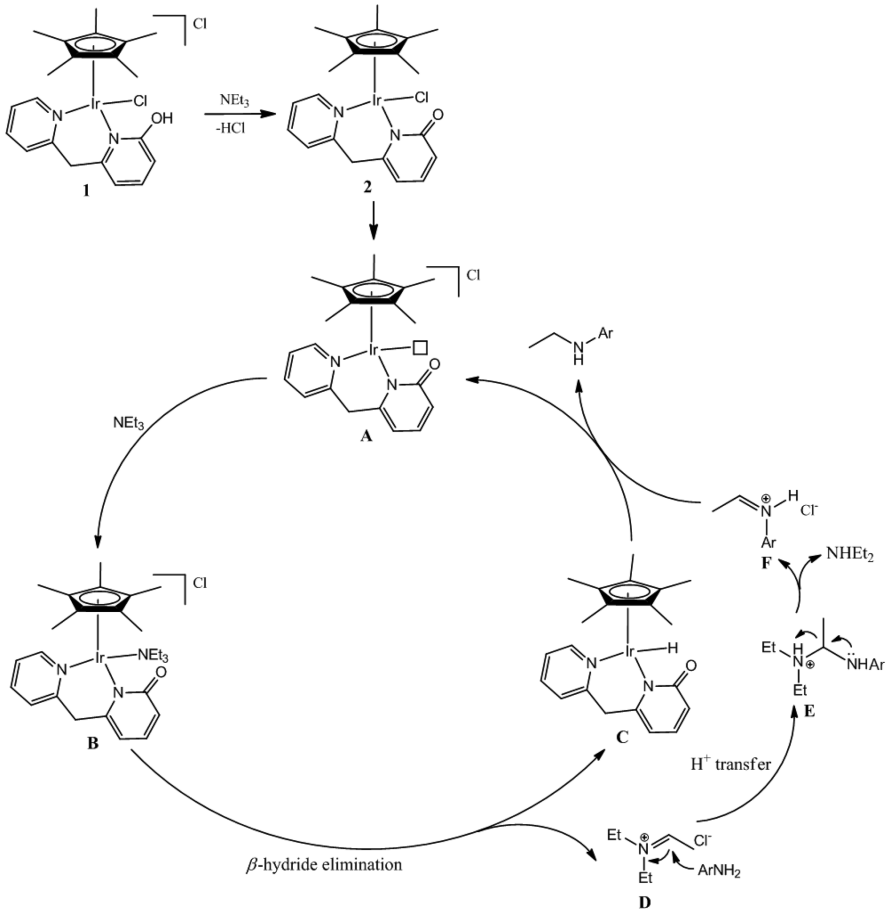
Scheme 5. Proposed Mechanism of Alkylation with Iridium Catalyst



stable, which also explains the selectivity when *N*-butyldimethylamine was selected as the alkylating reagent (Table 3, entry 18).

CONCLUSIONS

In summary, six well-defined Cp*Ir complexes (**1**–**6**) containing NN-bitentate chelate ligands were synthesized and characterized. Complex **1** contains a 2-hydroxypyridyl fragment, which was translated into pyridonate complex **2** in the presence of a base. Complex **1** is an efficient catalyst for monoalkylation of amines with trialkyl amines, and **2** is its intermediate. The catalytic reaction proceeds under relatively mild conditions (120 °C) in methanol under air. No extra base is needed, and the reaction can be promoted by NR_3·HCl. Furthermore, it is highly selective, and no imine derivatives and disubstituted aniline were detected. Our current work provides an alternative method for the monoalkylation of primary amines, and other experimental studies are ongoing to explore more active transition-metal catalysts.

EXPERIMENTAL SECTION

All the manipulations were carried out under an atmosphere of dry nitrogen using vacuum-line and oven-dried standard Schlenk techniques if not otherwise mentioned. All solvents were distilled from appropriate drying agents under N_2 before use. All reagents were obtained from commercial suppliers and used without further purification. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrometer. The ^{1}H NMR chemical shifts were referenced to the residual solvent as determined relative to Me_4Si (δ = 0 ppm). The ^{13}C{1H} chemical shifts were reported in parts per million (ppm) relative to the carbon resonance of $CDCl_3$ (77.0 ppm) or DMSO-d_6 (39.5 ppm). Elemental analyses were performed on a PerkinElmer 240C analyzer. The high-resolution mass spectrum (HR-MS) was recorded on a Varian 7.0 T FTICR-MS by the ESI technique. Single-crystal X-ray diffraction was carried out as follows: Suitable crystals were placed in a cooled N_2 stream at 173(2) K on a Bruker D8 Quest X-ray diffractometer. Data collections were performed using four-circle kappa diffractometers equipped with CCD detectors. Data were reduced and then corrected for absorption.[13] Solution, refinement, and geometrical calculations for all crystal structures were performed by SHELXTL.[14] All the GC measurements were performed on Agilent GC7890A equipment using Agilent 19091B-102 (25 m, 220 μm) column.

Synthesis of 2-Methoxy-6-((pyridinyl)methyl)pyridine. A solution of *n*-BuLi (16.7 mL, 2.4 M, 40.0 mmol) was added to 2-methoxy-6-methylpyridine (4.9 g, 40.0 mmol) in 50 mL of THF at −78 °C. When temperature naturally warmed to −20 °C, 2-fluoropyridine (1.9 g, 20.0 mmol) was added. The reaction mixture was stirred at −20 °C for 3 h and refluxed overnight. After addition of 25 mL of water, the water phase was extracted with CH_2Cl_2. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, v/v = 10:1) to give 2-methoxy-6-((pyridinyl)methyl)pyridine (3.5 g, 87%) as a yellow liquid. HR-MS (ESI) Calcd for $C_{12}H_{12}N_2O$ + H: 201.1028. Found: 201.1025. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 8.56 (d, J = 4.8 Hz, 1H), 7.63 (t, J = 8.0 Hz, 1H), 7.50 (d, J = 8.4 Hz, 1H), 7.33 (t, J = 5.2 Hz, 1H), 7.17–1.14 (m, 1H), 6.81 (d, J = 7.2 Hz, 1H), 6.59 (d, J = 8.0 Hz, 1H), 4.26 (s, 2H), 3.91 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 163.7, 159.7, 157.0, 149.2, 138.9, 123.7, 121.3, 115.9, 108.1, 53.2, 46.9.

Synthesis of L_1. A solution of 2-methoxy-6-((pyridinyl)methyl)-pyridine (2.65 g, 13.3 mmol) in 10 mL of HBr (40% in water) was heated at reflux for 3 h. After cooling to room temperature, the yellow

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solution was neutralized by slow addition of a saturated aqueous solution of NaOH. The water phase was extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated to afford $\mathbf{L_1}$ as a white solid (2.30 g, 93%). Mp: 155−159 °C. HR-MS (ESI) Calcd for $C_{11}H_{10}N_2O$ + H: 187.0871. Found: 187.0872. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 8.62 (d, J = 4.0 Hz, 1H), 7.70 (t, J = 8.0 Hz, 1H), 7.38−7.34 (m, 2H), 7.27−7.24 (m, 1H), 6.45 (d, J = 8.8 Hz, 1H), 6.14 (d, J = 6.8 Hz, 1H), 4.04 (s, 2H) (the −OH proton did not appear). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 165.3, 156.6, 149.5, 146.6, 141.7, 137.1, 123.7, 122.2, 117.7, 106.0, 41.2.

Synthesis of 2-(*tert*-Butoxy)-6-((6-methoxypyridin-2-yl)-methyl)pyridine. A solution of *n*-BuLi (11.7 mL, 2.4 M, 28.1 mmol) was added to 2-methoxy-6-methylpyridine (3.6 g, 28.1 mmol) in 50 mL of THF at −78 °C. When temperature naturally warmed to −20 °C, 2-bromo-6-*tert*-butoxypyridine (3.2 g, 13.9 mmol) was added. The reaction mixture was stirred at −20 °C for 3 h and refluxed overnight. After addition of 25 mL of water, the water phase was extracted with CH_2Cl_2. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, v/v = 5:1) to give 2-(*tert*-butoxy)-6-((6-methoxypyridin-2-yl)methyl)-pyridine (3.0 g, 80%) as a yellow liquid. HR-MS (ESI) Calcd for $C_{16}H_{20}N_2O_2$ + H: 273.1603. Found: 273.1601. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.48−7.40 (M, 2H), 6,78−6.76 (M, 2H), 6.55 (d, J = 8.4 Hz, 1H), 6.47 (d, J = 8.4 Hz, 1H), 4.08 (s, 2H), 3.90 (s, 3H), 1.51 (s, 9H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 163.6, 163.3, 157.7, 156.8, 138.7, 116.1, 115.4, 110.4, 107.7, 79.3, 53.2, 46.6, 28.6.

Synthesis of 2-Hydroxy-6-((6-methoxypyridin-2-yl)methyl)-pyridine. A solution of 2-(*tert*-butoxy)-6-((6-methoxypyridin-2-yl)methyl)pyridine (0.6 g, 2.2 mmol) in 5 mL of CH_2Cl_2 and 8 mL of CF_3COOH was stirred for 30 min at room temperature. The solution was neutralized by slow addition of a saturated aqueous solution of NaOH. The water phase was extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated to afford 2-hydroxy-6-((6-methoxypyridin-2-yl)methyl)-pyridine as a yellow solid (0.44 g, 91%). Mp: 146 °C. HR-MS (ESI) Calcd for $C_{12}H_{12}N_2O_2$ + H: 217.0977. Found: 217.0979. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 12.43 (s, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.36−7.32 (m, 1H), 6.87 (d, J = 7.2 Hz, 1H), 6.63 (d, J = 8.0 Hz, 1H), 6.43 (d, J = 9.2 Hz, 1H), 6.10 (d, J = 6.8 Hz, 1H), 3.94 (s, 2H), 3.93 (s, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 164.9, 163.8, 153.8, 146.5, 141.5, 139.4, 117.7, 115.9, 109.3, 105.6, 53.5, 40.7.

Synthesis of 1. A solution of $\mathbf{L_1}$ (0.09 g, 0.48 mmol) and $[Cp^*IrCl_2]_2$ (0.2 g, 0.25 mmol) was refluxed in dried CH_3OH (20 mL) with stirring for 24 h. The mixture was allowed to cool to room temperature and the yellow precipitate was collected, washed with acetone, and dried under vacuum to provide **1** as a yellow solid (0.23 g, 82%). Single crystals suitable for X-ray crystallographic determination were grown with CH_3OH/ether at 0 °C. Mp: 195 °C (dec.). Anal. Calcd for $C_{21}H_{25}Cl_2IrN_2O$: C, 43.15; H, 4.31; N, 4.79. Found: C, 43.43; H, 4.32; N, 4.81. ^{1}H NMR (400 MHz, DMSO-d_6, ppm): 13.03 (s, 1H), 8.71 (d, J = 5.6 Hz, 1H), 8.04 (t, J = 7.6 Hz, 1H), 7.83 (d, J = 7.6 Hz, 1H), 7.78 (t, J = 8.0 Hz, 1H), 7.52 (t, J = 6.4 Hz, 1H), 7.26 (d, J = 7.2 Hz, 1H), 7.02 (d, J = 8.4 Hz, 1H), 4.68 (d, J = 14.8 Hz, 1H), 3.70 (d, J = 14.8 Hz, 1H), 1.56 (s, 15H). ^{13}C NMR (100 Hz, DMSO-d_6, ppm):165.6, 157.4, 155.7, 153.4, 142.6, 141.0, 125.6, 125.3, 116.7, 111.4, 88.1, 49.1, 9.2.

Synthesis of 2. *Method A.* NaO^{t}Bu (0.039 g, 0.41 mmol) was added into a solution of **1** (0.2 g, 0.34 mmol) in H_2O (10 mL) under stirring for 1 h. Then, the precipitate was filtered off, and the filtrate was concentrated. The crude product was recrystallized with CH_3OH/ether to give **2** as a yellow powder (0.15 g, 79%). Mp: 180 °C (dec.). Anal. Calcd for $C_{21}H_{24}ClIrN_2O$: C, 46.02; H, 4.41; N, 5.11. Found: C, 46.31; H, 4.54; N, 5.06. ^{1}H NMR (400 MHz, DMSO-d_6, ppm): 8.72 (d, J = 5.6 Hz, 1H), 7.99 (t, J = 7.6 Hz, 1H), 7.76 (d, J = 7.6 Hz, 1H), 7.47 (t, J = 6.8 Hz, 1H), 7.37 (br s, 1H), 6.69 (br s, 1H), 6.48 (br s, 1H), 4.41 (d, J = 14.4 Hz, 1H), 3.60 (d, J = 14.4 Hz, 1H), 1.55 (s, 15H). ^{13}C NMR (100 Hz, DMSO-d_6, ppm): 168.4, 159.3, 155.8, 150.7, 140.1, 136.6, 124.7, 124.2, 115.5, 104.1, 86.7, 47.9, 9.4.

Method B. NEt_3 (0.017 g, 0.16 mmol) was added into a solution of **1** (0.05 g, 0.08 mmol) in CH_3OH (5 mL) under stirring for 1 h. Then, the precipitate was filtered off and the filtrate was concentrated. The crude product was washed with ether to give **2** as a yellow powder (0.036 g, 76%).

Synthesis of 3. A solution of 6-hydroxy-2,2′-bipyridine (0.1 g, 0.58 mmol) and $[Cp^*IrCl_2]_2$ (0.24 g, 0.29 mmol) was refluxed in dried CH_3OH (15 mL) with stirring for 24 h. The mixture was allowed to cool to room temperature, and the yellow precipitate was collected, washed with acetone, and dried under vacuum to provide **3** as a yellow powder (0.15 g, 90%). Mp: 178 °C (dec.). Anal. Calcd for $C_{20}H_{23}Cl_2IrN_2O$: C, 42.10; H, 4.06; N, 4.91. Found: C, 42.26; H, 4.07; N, 4.88. ^{1}H NMR (400 MHz, DMSO-d_6, ppm): 13.78 (s, 1H), 8.93 (d, J = 4.8 Hz, 1H), 8.64 (d, J = 8.4 Hz, 1H), 8.26 (t, J = 8.0 Hz, 1H), 8.14 (d, J = 7.6 Hz, 1H), 8.05 (t, J = 8.0 Hz, 1H), 7.80 (t, J = 6.4 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 1.60 (s, 15H). No satisfactory ^{13}C NMR data could be obtained due to low solubility.

Synthesis of 4. A solution of 2-(2-pyridylmethyl)pyridine (0.25 g, 1.47 mmol) and $[Cp^*IrCl_2]_2$ (0.6 g, 0.74 mmol) was refluxed in dried CH_3OH (20 mL) with stirring for 24 h. The mixture was allowed to cool to room temperature, and the yellow precipitate was collected, washed with acetone, and dried under vacuum to provide **4** as a yellow powder (0.23 g, 84%). Mp: 175−177 °C (dec.). Anal. Calcd for $C_{21}H_{25}Cl_2IrN_2$: C, 44.36; H, 4.43; N, 4.93. Found: C, 44.23; H, 4.47; N, 4.84. ^{1}H NMR (400 MHz, DMSO-d_6, ppm): 8.76 (d, J = 5.8 Hz, 2H), 8.09 (t, J = 7.6 Hz, 2H), 7.91 (d, J = 7.6 Hz, 2H), 7.57 (t, J = 5.8 Hz, 2H), 4.90 (d, J = 15.6 Hz, 1H), 3.78 (d, J = 15.6 Hz, 1H), 1.55 (s, 15H). ^{13}C NMR (100 Hz, DMSO-d_6, ppm): 156.3, 155.6, 141.3, 126.3, 126.1, 88.6, 46.0, 8.8.

Synthesis of 5. A solution of 2-methoxy-6-((6-methoxypyridin-2-yl)methyl)pyridine (0.10 g, 0.43 mmol) and $[Cp^*IrCl_2]_2$ (0.18 g, 0.22 mmol) was refluxed in dried CH_3OH (15 mL) with stirring for 24 h. The mixture was allowed to cool to room temperature, and the precipitate was collected, washed with acetone, and dried under vacuum to provide **5** as a yellow powder (0.12 g, 89%). Mp: 171 °C (dec.). Anal. Calcd for $C_{23}H_{29}Cl_2IrN_2O_2$: C, 43.95; H, 4.65; N, 4.46. Found: C, 43.93; H, 4.65; N, 4.69. ^{1}H NMR (400 MHz, DMSO-d_6, ppm): 7.62 (t, J = 7.6 Hz, 2H), 6.86 (d, J = 7.2 Hz, 2H), 6.64 (d, J = 8.0 Hz, 2H), 4.05 (s, 2H), 3.81 (s, 6H), 1.63 (s, 15H). ^{13}C NMR (100 Hz, DMSO-d_6, ppm): 163.5, 157.4, 139.9, 116.6, 108.4, 92.6, 55.4, 53.3, 8.7.

Synthesis of 6. A solution of 2-hydroxy-6-((6-methoxypyridin-2-yl)methyl)pyridine (0.10 g, 0.46 mmol) and $[Cp^*IrCl_2]_2$ (0.19 g, 0.23 mmol) was refluxed in dried CH_3OH (15 mL) with stirring for 24 h. The mixture was allowed to cool to room temperature and the precipitate was collected, washed with acetone and dried under vacuum to provide **6** as a yellow powder (0.13 g, 91%). Mp: 170 °C (dec.). Anal. Calcd for $C_{22}H_{27}Cl_2IrN_2O_2$: C, 42.99; H, 4.43; N, 4.56. Found: C, 42.78; H, 4.55; N, 4.55. ^{1}H NMR (400 MHz, DMSO-d_6, ppm): 11.6 (s, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.34 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 7.2 Hz, 1H), 6.69 (d, J = 8.4 Hz, 1H), 6.17 (d, J = 8.4 Hz, 1H), 5.98 (d, J = 5.6 Hz, 1H), 3.86 (s, 2H), 3.81 (s, 3H), 1.63 (s, 15H). ^{13}C NMR (100 Hz, DMSO-d_6, ppm): 163.6, 163.5, 155.4, 147.5, 141.5, 140.3, 117.5, 116.3, 109.0, 105.0, 92.6, 55.4, 53.4, 8.7.

General Procedure for the Alkylation of Anilines. Under air condition, in a 25 mL Schlenk tube, a mixture of amines (1.0 mmol), methanol (2 mL), complex **1** (5.8 mg, 1 mol %), trialkyl amines (2.0 mmol), and NEt_3·HCl (20%, 0.2 mmol) were stirred at 120 °C for 12 h. Then, it was allowed to cool to room temperature, and 0.1 mL of the reaction mixture was sampled and immediately diluted with 5 mL of CH_3OH precooled to 0 °C for GC analysis for calculating conversation and product selectivity of the reaction. After the reaction was completed, the reaction mixture was condensed under reduced pressure and subjected to purification by flash silica gel column chromatography to afford the target product, which was identified by NMR analyses. All analytical data of the known compounds are consistent with those reported in the literature.

N-Ethylaniline.[6h] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.17 (t, J = 7.2 Hz, 2H), 6.69 (t, J = 7.6 Hz, 1H), 6.61 (d, J = 7.6 Hz, 2H), 3.16

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(q, J = 7.2 Hz, 2H), 1.25 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 148.5, 129.3, 117.2, 112.8, 38.5, 14.9.

2-Bromo-N-ethylaniline.[6i] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.40 (d, J = 7.6 Hz, 1H), 7.17 (t, J = 7.2 Hz, 1H), 6.61 (d, J = 8.0 Hz, 1H), 6.55 (t, J = 7.6 Hz, 1H), 3.19 (q, J = 7.2 Hz, 2H), 1.30 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 145.2, 132.4, 128.5, 117.5, 111.3, 109.6, 38.4, 14.7.

3-Bromo-N-ethylaniline.[15] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.00 (t, J = 8.0 Hz, 1H), 6.79 (d, J = 7.6 Hz, 1H), 6.72 (t, J = 2.0 Hz, 1H), 6.49 (d, J = 7.6 Hz, 1H), 3.12 (q, J = 6.8 Hz, 2H), 1.24 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 149.7, 130.5, 123.3, 119.8, 115.1, 111.5, 38.3, 14.7.

4-Bromo-N-methylaniline.[16] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.23 (d, J = 8.8 Hz, 2H), 6.46 (d, J = 8.8 Hz, 2H), 3.11 (q, J = 6.8 Hz, 2H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 147.5, 131.9, 114.3, 108.6, 38.5, 14.8.

4-Chloro-N-ethylaniline.[6i] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.10 (d, J = 8.8 Hz, 2H), 6.50 (d, J = 8.8 Hz, 2H), 3.11 (q, J = 7.2 Hz, 2H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 147.1, 129.0, 121.6, 113.8, 38.6, 14.8.

4-(Cyclopenta-2,4-dien-1-yl)-N-ethylaniline. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.20 (d, J = 8.8 Hz, 2H), 6.96 (t, J = 2.0 Hz, 2H), 6.64 (d, J = 8.8 Hz, 2H), 6.29 (t, J = 2.0 Hz, 2H), 3.18 (q, J = 7.2 Hz, 2H), 1.28 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 146.7, 131.9, 122.5, 119.8, 113.2, 109.3, 38.8, 14.9. HR-MS (ESI) Calcd for $C_{12}H_{14}N_2$ + H: 187.1235. Found: 187.1232.

N-Ethyl-4-methylaniline.[6h] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 6.98 (d, J = 8.0 Hz, 2H), 6.54 (d, J = 8.4 Hz, 2H), 3.13 (q, J = 7.2 Hz, 2H), 2.23 (s, 3H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 146.4, 129.8, 126.5, 113.1, 38.9, 20.5, 15.0.

N-Ethyl-4-methoxyaniline.[6h] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 6.78 (d, J = 9.2 Hz, 2H), 6.58 (d, J = 8.8 Hz, 2H), 3.74 (s, 3H), 3.11 (q, J = 7.2 Hz, 2H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 152.1, 142.9, 114.9, 114.1, 55.8, 39.4, 15.0.

N-Ethyl-2-methylaniline.[16] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.12 (d, J = 7.6 Hz, 1H), 7.04 (d, J = 7.2 Hz, 1H), 6.67−6.60 (m, 2H), 3.19 (q, J = 7.2 Hz, 2H), 2.13 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 146.4, 130.0, 127.2, 121.7, 116.8, 109.7, 38.4, 17.5, 15.0.

N-Ethyl-2-methoxyaniline.[17] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 6.87 (T, J = 7.6 Hz, 1H), 6.76 (d, J = 8.0 Hz, 1H), 6.68−6.60 (m, 2H), 3.84 (s, 3H), 3.17 (q, J = 7.2 Hz, 2H), 1.29 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 146.8, 138.4, 121.3, 116.3, 109.8, 109.3, 55.4, 38.2, 14.9.

N-Ethylnaphthalen-2-amine.[18] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.66 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 8.8 Hz, 2H), 7.35 (t, J = 7.6 Hz, 1H), 7.18 (t, J = 7.6 Hz, 1H), 6.85 (d, J = 8.8 Hz, 1H), 6.79 (d, J = 2.4 Hz, 1H), 3.24 (q, J = 7.2 Hz, 2H), 1.30 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 146.3, 129.0, 127.9, 127.7, 126.5, 126.2, 122.1, 118.3, 104.4, 38.6, 14.9.

N,N′-Diethylbenzidine.[19] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.37 (d, J = 7.6 Hz, 4H), 6.65 (d, J = 8.8 Hz, 4H), 3.18 (q, J = 7.2 Hz, 4H), 1.26 (t, J = 7.2 Hz, 6H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 147.0, 130.7, 127.2, 113.2, 38.7, 15.0.

N-Ethylpridin-2-amine.[6h] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 8.08 (d, J = 5.2 Hz, 1H), 7.42 (t, J = 6.4 Hz, 1H), 6.57−6.54 (m, 1H), 6.37 (d, J = 8.4 Hz, 1H), 3.30 (q, J = 7.2 Hz, 2H), 1.26 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 158.9, 148.1, 137.4, 112.6, 106.4, 36.8, 14.8.

N-Ethyl-4-cyanoaniline.[20] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.41 (d, J = 8.8 Hz, 2H), 6.54 (d, J = 8.8 Hz, 2H), 3.19 (q, J = 7.2 Hz, 2H), 1.28 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 151.6, 133.6, 120.8, 112.1, 97.9, 37.8, 14.4.

N-Ethyl-4-nitroaniline.[21] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 8.08 (d, J = 9.2 Hz, 2H), 6.52 (d, J = 9.2 Hz, 2H), 3.27 (q, J = 7.2 Hz, 2H), 1.31 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 153.5, 137.6, 126.5, 110.9, 38.0, 14.4.

2-(N-Ethylamino)benzoxazole.[22] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.35 (d, J = 7.6 Hz, 1H), 7.24 (d, J = 7.6 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 7.01 (t, J = 7.6 Hz, 1H), 3.53 (q, J = 7.2 Hz, 2H), 1.32 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 162.2, 148.5, 143.0, 123.9, 120.7, 116.1, 108.7, 38.0, 15.2.

N-Propylaniline.[5c] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.16 (t, J = 8.8 Hz, 2H), 6.68 (t, J = 7.6 Hz, 1H), 6.60 (d, J = 3.6 Hz, 2H), 3.07 (t, J = 6.8 Hz, 2H), 1.68−1.59 (m, 2H), 0.99 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 148.5, 129.2, 117.1, 112.7, 45.8, 22.8, 11.7.

N-Butylaniline.[5c] ^{1}H NMR (400 MHz, $CDCl_3$, ppm): 7.17 (t, J = 8.4 Hz, 2H), 6.69 (t, J = 7.6 Hz, 1H), 6.60 (d, J = 7.6 Hz, 2H), 3.11 (t, J = 6.8 Hz, 2H), 1.64−1.57 (m, 2H), 1.47−1.38 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 Hz, $CDCl_3$, ppm): 148.6, 129.2, 117.1, 112.7, 43.7, 31.7, 20.3, 14.0.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.9b00172.

Crystallographic details for complexes **1** and **2**, and NMR spectra of the new compounds (PDF)

Accession Codes

CCDC 1880041 and 1880042 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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