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Graphical Abstract

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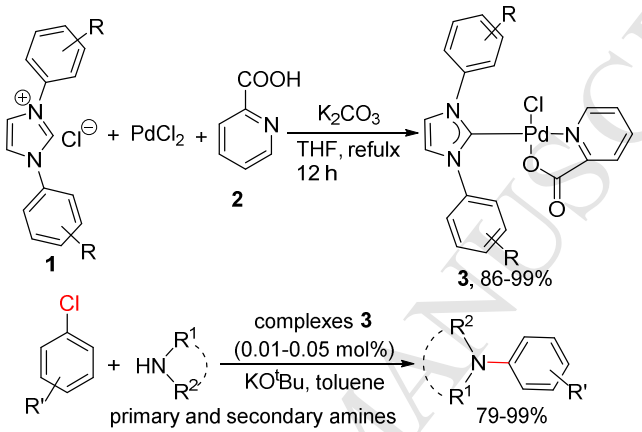

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Synthesis of *N*-heterocyclic carbene-Pd(II) complexes and their catalytic activity in the Buchwald-Hartwig amination of aryl chlorides

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ABSTRACT

Novel *N*-heterocyclic carbene-palladium(II) complexes using 2-picolinic acid as the ancillary ligand have been successfully developed under mild conditions. Their catalytic activity in organic synthesis has been initially tested in the Buchwald-Hartwig amination of secondary and primary amines with aryl chlorides. Various substituents on both substrates can be tolerated, giving the desired coupling products in good to almost quantitative yields. The minimum catalyst loading can be 0.01 mol%, implying their potential application toward industrial processes.

1. Introduction

Nitrogen-containing compounds widely exist in pesticides, materials, pharmaceuticals, natural products and other fields.[1] Transition metals, especially palladium salts, catalyzed C-N coupling seem to be one of the most popular strategies to obtain such compounds.[2] Traditionally, tertiary phosphines are necessary to achieve highly efficient C-N coupling.[2,3] Comparably, from its first isolation of free *N*-heterocyclic carbene (NHC) by Arduengo's group in 1991, NHCs have been interesting ligands in palladium-catalyzed coupling reactions.[4] Consequently, to date, some excellent NHC-Pd(II) complexes have also been developed by different groups to achieve satisfactory C-N coupling, especially for the more challenging substrates such as aryl chlorides.[5] However, most of them still have the following shortcomings which may make them difficult to be ideal candidates in organic synthesis: (1) the NHC skeleton and/or palladium complexes are difficult to be obtained; (2) toxic ancillary ligands are necessary; (3) the catalyst loading is usually too high to be acceptable by industrial chemistry. In order to overcome these obstacles, during the past years, using IPr (commercially IPr·HCl as the precursor) as the NHC skeleton, we have developed some novel NHC-Pd(II) complexes bearing different ancillary ligands in a one-pot procedure in good to high yields. In addition, all of them have been proven to be excellent catalysts toward C-N coupling of primary and secondary amines with aryl chlorides.[6] In these complexes, we found that the ancillary ligands have some effect on the catalytic activity. For instance, using iso-quinoline as the ancillary ligand, the minimum catalyst loading can be 0.005 mol% in some cases.[6b] As a part of our continuous work on the development of efficient NHC-Pd(II) complexes and their application in the C-N coupling reactions, we found novel NHC-Pd(II) complexes using 2-picolinic acid as the ancillary ligand. They were also efficient catalysts in the amination of aryl chlorides under low catalyst loadings. Herein, we report these results in detail.

2. Results and discussion

2.1 Synthesis of NHC-Pd(II) complexes 3.

According to our previously reported methods,[6] the reactions were carried out using commercially available imidazolium salts **1** (X equiv), $PdCl_2$ (0.15 mmol) and picolinic acid **2** (1.0 equiv) as the substrates, K_2CO_3 (3.0 equiv) as the base in refluxing THF (2.0 mL) for 12 h, giving the corresponding NHC-Pd(II) complexes **3** in good to almost quantitative yields (Table 1). The relative amounts of imidazolium salts **1** affected the reactions to some extent. For example, when imidazolium salt **1a** (1.1 equiv) was added, the lowest yield of complex **3a** was obtained in 86% (Table 1, entry 1). Once the amount of **1** increased to 1.3 equiv, the yield of complex **3a** can further increase to 91% (Table 1, entry 2). Finally, when the amount of **1** was elevated to 1.5 equiv, the best yield was achieved (Table 1, entry 3). The amount of K_2CO_3 also affected the reaction evidently. For instance, when it was reduced to 2.0 equivalents, the yield dramatically dropped from 99 to 82% (Table 1, entries 3 *vs* 4). Under the optimal conditions, both imidazolium salts **1b** and **1c** can be also

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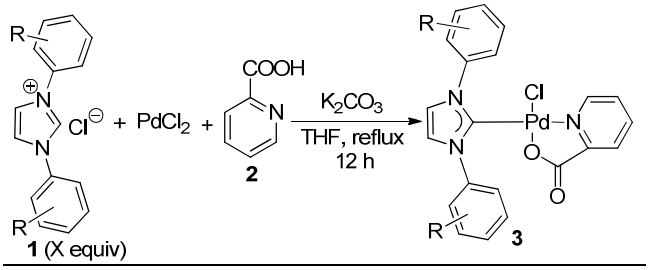
transformed to the corresponding complexes **3b** and **3c** in 94 and 88% yields, respectively (Table 1, entries 5 and 6).

Table 1. Synthesis of complexes **3**.



Entry[a]	**1** (R)	[X]	Yield (%)[b]
1	**1a** (2,6-^{i}Pr$_2$)	1.1	**3a**, 86
2	**1a**	1.3	**3a**, 91
3	**1a**	1.5	**3a**, 99
4[c]	**1a**	1.5	**3a**, 82
5	**1b** (2,6-Me$_2$)	1.5	**3b**, 94
6	**1c** (2,4,6-Me$_3$)	1.5	**3c**, 88

[a] Otherwise specified, the reactions were carried out using **1**, $PdCl_2$ (0.15 mmol), **2** (1.0 equiv) and K_2CO_3 (3.0 equiv) in refluxing THF (2.0 mL) for 12 h. [b] Isolated yields. [c] K_2CO_3 (2.0 equiv).

All complexes **3** have been fully confirmed by ^{1}H and ^{13}C NMR, MS and elemental analysis. To our delight, the yellow crystals of complex **3a**, which are suitable for single crystal diffraction analysis, were obtained in a mixture of ethyl acetate and dichloromethane by slow evaporation of the solvents. As shown in Figure 1, the Pd centre of complex **3a** is coordinated by four different ligands such as one carbene carbon atom, one N atom and one O atom from picolinic acid, and one Cl atom, giving a very slightly distorted square-planar geometry. In such structure, the NHC and the N atom are *trans* to each other [the bond angles of C(7)-Pd(1)-N(2) = 172.4(3), O(2)-Pd(1)-Cl(1) = 176.8(2)].

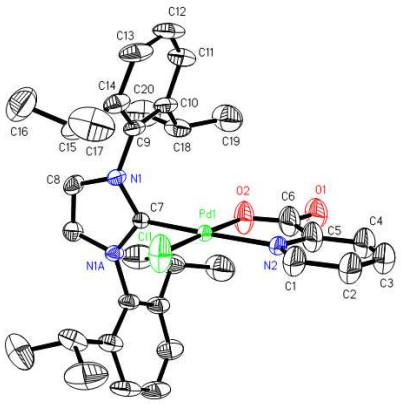
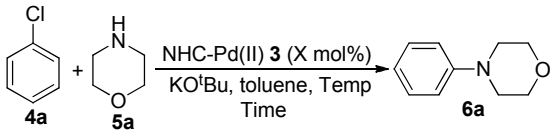


Fig. 1 The molecular structure of complex **3a** showing 30% probability ellipsoids; all hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (°): Selected bond distances (Å) and angles (°): Pd(1)-C(7) = 1.974(6), Pd(1)-O(2) = 2.045(6), Pd(1)-N(2) = 2.071(6), Pd(1)-Cl(1) = 2.212(2); C(7)-Pd(1)-O(2) = 92.1(2), C(7)-Pd(1)-N(2) = 172.4(3), O(2)-Pd(1)-N(2) = 80.3(2), C(7)-Pd(1)-Cl(1) = 91.10(19), O(2)-Pd(1)-Cl(1) = 176.8(2), N(2)-Pd(1)-Cl(1) = 96.5(2).

2.2 Buchwald-Hartwig amination of aryl chlorides

Once the structures of complexes **3** were fully characterized, we chose Buchwald-Hartwig amination of aryl chlorides to evaluate their catalytic activity. Initial examinations were carried out using chlorobenzene **4a** (0.7 mmol) and morpholine **5a** (1.2 equiv) as the substrates, complex **3a** (0.1 mol%) as the catalyst, toluene (1.0 mL) as the solvent in 90 °C for 1 h to screen various bases (1.3 equiv). Among them, KO^{t}Bu gave the best yield (Table 2, entry 1). Product **6a** can also be obtained in moderate yield (74%) when NaO^{t}Bu was added. However, in the presence of other bases such as Cs_2CO_3, LiO^{t}Bu, LiOH, Li_2CO_3, NaOH, Na_2CO_3, $NaHCO_3$, KOH, K_2CO_3, $KHCO_3$ and K_3PO_4, no reaction occurred. Using KO^{t}Bu as the base, a variety of solvents was also tested. For instance, when THF and dioxane were chosen as the solvents, high yields of product **6a** can also be achieved (94 and 91%, respectively). When other polar solvents such as DMSO, DMF and DMAc were used, very low yields were observed (22, 12 and 24%, respectively). Further studies were then performed based on the result shown in Table 2, entry 1. For instance, if the catalyst loading was reduced to 0.05 mol%, the yield drastically lowered to 59% (Table 2, entry 2). To our pleasure, the yields increased gradually when the time was prolonged (Table 2, entries 3 and 4), and the best same yield can be observed when the reaction was carried out for 6 h (Table 2, entry 4). If the catalyst loading was further reduced to 0.03 mol%, the reaction should take place at 110 or 130 °C for 12 h to give good yields (Table 2, entries 7 and 8). Under the same conditions shown in Table 1, entry 4, complexes **3b** and **3c** were also tested, giving very low yields in both cases (Table 2, entries 9 and 10).

Table 2. Optimization for the complex **3**-catalysed reaction of chlorobenzene **4a** with morpholine **5a**.



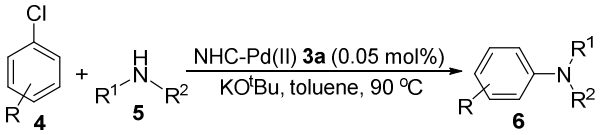
Entry[a]	**3** [X]	Temp (°C)	Time (h)	Yield (%)[b]
1	**3a** (0.10)	90	1	99
2	**3a** (0.05)	90	1	59
3	**3a** (0.05)	90	3	87
4	**3a** (0.05)	90	6	98
5	**3a** (0.03)	90	6	66
6	**3a** (0.03)	90	12	76
7	**3a** (0.03)	110	12	87
8	**3a** (0.03)	130	12	89
9	**3b** (0.05)	90	6	7
10	**3c** (0.05)	90	6	7

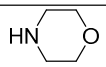
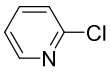
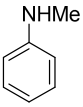
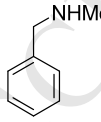
[a] Reaction conditions: **4a** (0.7 mmol), **5a** (0.84 mmol), KO^{t}Bu (0.91 mmol), **3** (X mol%), toluene (1.0 mL). [b] Isolated yields.

Under the conditions shown in Table 2, entry 4, kinds of aryl chlorides **4** and secondary amines **5** were first applied to test the scope and limitation of this reaction. The results are illustrated in

Table 3. All reactions took place smoothly to give the desired C-N coupling products in good to high yields. Substituents on the aryl chlorides **4** did not affect the reactions evidently. Electron-neutral, -poor, -rich and sterically-hindered substituents on aryl chlorides were all tolerated. For example, all reactions of 4-methylphenyl chloride **4d**, 3-methoxyphenyl chloride **4e** and 3-fluorophenyl chloride **4f** with morpholine **5a** gave products **6d-f** in high yields (Table 3, entries 3-5). The heteroaryl chloride such as 2-chloropyridine **4h** was also tolerated to give product **6h** in 92% yield within 12 h. Other secondary amines such as pyrrolidine **5b**, piperidine **5c**, *N*-methylaniline **5d** and *N*-methylbenzylamine **5e** are all suitable substrates in the reactions with various aryl chlorides **4** to give the desired products **6i-u** in good to high yields (Table 3, entries 8-20).

Table 3. Complex **3a**-catalyzed C-N coupling of aryl chlorides **4** with secondary amines **5**.

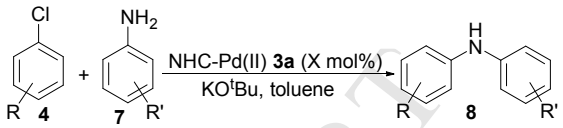


Entry[a]	**4** (R)	**5**	Time (h)	Yield (%)[b]
1	**4b** (2-Me)	**5a** 	6	**6b**, 89
2	**4c** (3-Me)	**5a**	6	**6c**, 93
3	**4d** (4-Me)	**5a**	6	**6d**, 94
4	**4e** (3-OMe)	**5a**	6	**6e**, 96
5	**4f** (3-F)	**5a**	6	**6f**, 91
6	**4g** (4-F)	**5a**	12	**6g**, 84
7	**4h** 	**5a**	12	**6h**, 92
8	**4e**	**5b** 	6	**6i**, 91
9	**4a** (H)	**5c** 	12	**6j**, 85
10	**4c**	**5c**	6	**6k**, 82
11	**4e**	**5c**	12	**6l**, 96
12	**4h**	**5c**	12	**6m**, 80
13	**4a**	**5d** 	12	**6n**, 91
14	**4c**	**5d**	12	**6o**, 94
15	**4e**	**5d**	6	**6p**, 93
16	**4a**	**5e** 	6	**6q**, 94
17	**4c**	**5e**	6	**6r**, 93
18	**4e**	**5e**	6	**6s**, 92
19	**4f**	**5e**	12	**6t**, 93
20	**4g**	**5e**	12	**6u**, 85

[a] All reactions were carried out using **4** (0.70 mmol), **5** (0.84 mmol), KO^{t}Bu (0.91 mmol), **3a** (0.05 mol%) in toluene (1.0 mL) at 90 °C. [b] Isolated yields.

Based on the above successful results on the NHC-Pd(II) complex **3a**-catalyzed C-N coupling of aryl chlorides **4** with secondary amines **5**, anilines **7** were then tested with a variety of aryl chlorides **4** under the similar conditions. To our delight, all reactions also performed well enough to give the corresponding coupled products **8** in good to almost quantitative yields (Table 4). Substituents such as electron-rich, -neutral, -poor and sterically-hindered ones are all compatible in these transformations. Special attention was paid on the reactions involving sterically-hindered substituents on one or both of the substrates. It seems that these substituents did not affect the reactions dramatically except for the reaction involving 2-methoxyphenyl chloride **4i**, which gave the lowest yield, maybe partially due to the coordination of the oxygen atom to the palladium centre (Table 4, entry 15). Among the reactions examined, the lowest catalyst loading can be 0.01 mol%, implying their potential application toward industrial processes (Table 4, entries 2-6 and 16).

Table 4. Complex **3a**-catalyzed C-N coupling of aryl chlorides **4** with anilines **7**.

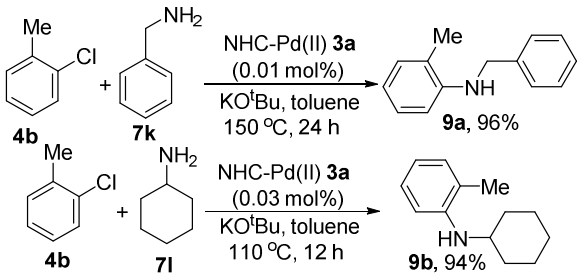


Entry[a]	**4** (R)	**7** (R')	[X]	Temp (°C)	Time (h)	Yield (%)[b]
1	**4b** (2-Me)	**7a** (H)	0.03	130	24	**8a**, 95
2	**4b**	**7b** (2-Me)	0.01	110	3	**8b**, 96
3	**4b**	**7c** (4-Me)	0.01	110	12	**8c**, 97
4	**4b**	**7d** (2,4-Me$_2$)	0.01	110	3	**8d**, 98
5	**4b**	**7e** (2,6-Me$_2$)	0.01	110	3	**8e**, 91
6	**4b**	**7f** (2,4,6-Me$_3$)	0.01	110	12	**8f**, 96
7	**4b**	**7g** (2,6-^{i}Pr$_2$)	0.02	110	12	**8g**, 91
8	**4b**	**7h** (2-OMe)	0.02	130	24	**8h**, 91
9	**4b**	**7i** (4-OMe)	0.02	130	24	**8i**, 90
10	**4b**	**7j** (4-F)	0.02	130	24	**8j**, 93
11	**4a** (H)	**7d**	0.03	130	24	**8k**, 95
12	**4c** (3-Me)	**7d**	0.03	130	24	**8l**, 99
13	**4d** (4-Me)	**7d**	0.05	130	24	**8m**, 89
14	**4e** (3-OMe)	**7d**	0.03	130	24	**8n**, 95
15	**4i** (2-OMe)	**7d**	0.03	130	24	**8o**, 79
16	**4j** (2,6-Me$_2$)	**7d**	0.01	110	12	**8p**, 97
17	**4k** (2,4,6-Me$_3$)	**7d**	0.02	110	6	**8q**, 94
18	**4l** (2,6-^{i}Pr$_2$)	**7d**	0.05	130	24	**8r**, 88

[a] All reactions were carried out using **4** (0.70 mmol), **7** (0.84 mmol), KO^{t}Bu (0.91 mmol), **3** (X mol%) in toluene (0.5 mL). [b] Isolated yields.

Finally, primary alkyl amines such as benzyl amine **7k** and cyclohexyl amine **7l** were also investigated with 2-methylphenyl chloride **4b** under the similar conditions (Scheme 1). Both reactions performed well enough in 0.01 or 0.03 mol% catalyst loading, giving products **9a** and **9b** in 96 and 94% yields, respectively.

Scheme 1. NHC-Pd(II) complex **3a** catalyzed reactions of 2-methylphenyl chloride **4b** with alkyl amines.



3. Conclusion

In conclusion, a series of novel NHC-Pd(II) complexes using 2-picolinic acid as the ancillary ligand has been developed in a one-pot procedure under mild conditions. All complexes have

been fully characterized by standard methods such as ^{1}H and ^{13}C NMR, MS and elemental analysis. Their catalytic activity was initially tested in the Buchwald-Hartwig amination of various secondary and primary amines with aryl chlorides, giving good to almost quantitative yields. The minimum catalyst loading can be 0.01 mol%, and this work will thus enrich the NHC chemistry in organic synthesis.

4. Experimental section

4.1 General remarks

NMR spectra were recorded at 500 MHz (for ^{1}H NMR) or 125 MHz (for ^{13}C NMR), respectively. ^{1}H and ^{13}C NMR spectra recorded in $CDCl_3$ solutions were referenced to TMS (0.00 ppm) and the residual solvent peak (77.0 ppm), respectively. *J*-values are given in Hz. All solvents were dried by standard methods. The mass analyzer type for the high resolution mass spectra (HRMS) is quadrupole. All amines were distilled prior to using. Other commercially obtained reagents were used without further purification. Flash column chromatography was performed on silica gel (300-400 mesh).

4.2 Experimental procedure

4.2.1 General procedure for the synthesis of NHC-Pd(II) complexes 3. Under a N_2 atmosphere, a mixture of imidazolium salts **1** (0.225 mmol), $PdCl_2$ (0.15 mmol), K_2CO_3 (0.45 mmol) and picolinic acid **2** (0.15 mmol) was stirred in anhydrous THF (2.0 mL) under reflux for 12 h. Then the solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (SiO_2) to give complexes **3** as yellow solids.

*4.2.1.1 Compound **3a***: yellow solid. m.p. 248 ^{o}C (decomposed). ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 8.55 (d, *J* = 5.5 Hz, 1H), 7.83-7.77 (m, 2H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.34 (d, *J* = 7.5 Hz, 4H), 7.31-7.28 (m, 1H), 7.17 (s, 2H), 2.95 (hept, *J* = 7.0 Hz, 4H), 1.42 (d, *J* = 7.0 Hz, 12H), 1.14 (d, *J* = 7.0 Hz, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 157.4, 151.3, 146.8, 146.5, 139.1, 134.5, 130.4, 126.6, 126.2, 125.1, 124.0, 28.6, 26.2, 22.9. IR (neat) ν 2964, 1668, 1600, 1458, 1408, 1337, 1291, 1047, 944, 800, 771, 755, 713 cm^{-1}. HRMS (ESI) calcd for $C_{33}H_{41}ClN_3O_2Pd$ $[M+H]^+$: 654.1920; found: 654.1917. Anal. calcd for $C_{33}H_{40}ClN_3O_2Pd$: C, 60.47%; H, 6.18%; N, 6.44%; found: C, 60.62%; H, 6.11%; N, 6.31%.

*4.2.1.2 Compound **3b***: yellow solid. m.p. 182 ^{o}C (decomposed). ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 8.53 (d, *J* = 4.5 Hz, 1H), 7.86-7.79 (m, 2H), 7.33-7.30 (m, 3H), 7.25-7.22 (m, 4H), 7.18-7.17 (m, 2H), 2.34 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 155.2, 151.0, 146.5, 139.3, 137.2, 136.7, 129.6, 128.6, 126.7, 126.2, 124.0, 18.3. IR (neat) ν 3160, 3087, 2915, 1668, 1478, 1330, 1288, 1229, 1158, 1046, 942, 848, 778, 758, 709 cm^{-1}. HRMS (ESI) calcd for $C_{25}H_{24}ClN_3O_2PdNa$ $[M+Na]^+$: 564.0487; found: 564.0496. Anal. calcd for $C_{25}H_{24}ClN_3O_2Pd$: C, 55.57%; H, 4.48%; N, 7.78%; found: C, 55.51%; H, 4.55%; N, 7.69%.

*4.2.1.3 Compound **3c***: yellow solid. m.p. 260 ^{o}C (decomposed). ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 8.53 (d, *J* = 5.5 Hz, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.80 (t, *J* = 7.5 Hz, 1H), 7.30 (t, *J* = 6.5 Hz, 1H), 7.13 (s, 2H), 7.02 (s, 4H), 2.33 (s, 6H), 2.28 (s, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 155.0, 150.9, 146.4, 139.3, 139.2, 134.7, 129.2, 126.7, 126.1, 124.1, 21.1, 18.2. IR (neat) ν 2961, 2921, 1729, 1666, 1650, 1597, 1484, 1341, 1328, 1285, 1232, 1159, 1089, 1043, 927, 859, 773, 766, 741, 705 cm^{-1}. HRMS (ESI) calcd for $C_{27}H_{28}ClN_3O_2PdNa$ $[M+Na]^+$: 592.0800; found: 592.0803. Anal. calcd for $C_{27}H_{28}ClN_3O_2Pd{\cdot}1/2CH_3CO_2Et$: C, 56.87%; H, 5.27%; N, 6.86%; found: C, 56.81%; H, 5.33%; N, 6.85%.

4.2.2 General procedure for the complex 3a-catalyzed Buchwald-Hartwig amination of aryl chlorides. Under a N_2 atmosphere, KO^{t}Bu (102.1 mg, 1.3 equiv) and a solution of complex **3a** (10-50 μL, 0.01-0.05 mol%, prepared from 4.6 mg of complex **3a** in 1.0 mL dichloromethane) were added into a Schlenk reaction tube. The tube was sealed and the solvent was removed under reduced pressure. Then toluene (0.5 mL), amines (0.84 mmol) and aryl chlorides (0.70 mmol) were successively added. The mixture was stirred vigorously at the specified temperature for 3-24 h. Then the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (SiO_2) to give the corresponding products.

*4.2.2.1 Compound **6a***[6a]: white solid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.26 (t, *J* = 7.5 Hz, 2H), 6.90-6.85 (m, 3H), 3.83 (t, *J* = 4.5 Hz, 4H), 3.12 (t, *J* = 4.5 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.2, 129.1, 119.9, 115.6, 66.8, 49.3.

4.2.2.2 Compound **6b**[6a]: colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.16 (t, *J* = 7.5 Hz, 2H), 7.01-6.97 (m, 2H), 3.83 (t, *J* = 4.5 Hz, 4H), 2.89 (t, *J* = 4.5 Hz, 4H), 2.30 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.2, 132.5, 131.1, 126.6, 123.3, 118.9, 67.4, 52.2, 17.8.

4.2.2.3 Compound **6c**[6a]: colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.15 (t, *J* = 8.0 Hz, 1H), 6.72-6.69 (m, 3H), 3.82 (t, *J* = 4.5 Hz, 4H), 3.11 (t, *J* = 4.5 Hz, 4H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.3, 138.7, 128.9, 120.8, 116.4, 112.8, 66.8, 49.4, 21.6.

4.2.2.4 Compound **6d**[6a]: white solid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.07 (d, *J* = 8.0 Hz, 2H), 6.81 (d, *J* = 8.0 Hz, 2H), 3.82 (t, *J* = 4.5 Hz, 4H), 3.07 (t, *J* = 4.5 Hz, 4H), 2.26 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.1, 129.6, 129.3, 115.9, 66.8, 49.8, 20.3.

4.2.2.5 Compound **6e**[6a]: colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.16 (d, *J* = 8.0 Hz, 1H), 6.51 (d, *J* = 8.5 Hz, 1H), 6.44-6.42 (m, 2H), 3.82 (t, *J* = 4.5 Hz, 4H), 3.77 (s, 3H), 3.12 (t, *J* = 4.5 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.6, 152.6, 129.7, 108.3, 104.6, 102.1, 66.7, 55.0, 49.2.

4.2.2.6 Compound **6f**[6a]: colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.18 (dd, *J* = 15.0, 8.0 Hz, 1H), 6.654 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.58-6.52 (m, 2H), 3.82 (t, *J* = 4.5 Hz, 4H), 3.12 (t, *J* = 4.5 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.8 (d, $J_{C\text{-}F}$ = 241.875 Hz), 152.9 (d, $J_{C\text{-}F}$ = 9.625 Hz), 130.1 (d, $J_{C\text{-}F}$ = 9.875 Hz), 110. 7 (d, $J_{C\text{-}F}$ = 2.375 Hz), 106.0 (d, $J_{C\text{-}F}$ = 21.25 Hz), 102.3 (d, $J_{C\text{-}F}$ = 25.0 Hz), 66.6, 48.7.

4.2.2.7 Compound **6g**[6a]: colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 6.97 (t, *J* = 9.5 Hz, 2H), 6.86 (dd, *J* = 9.5, 5.5 Hz, 2H), 3.85 (t, *J* = 4.5 Hz, 4H), 3.07 (t, *J* = 4.5 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3 (d, $J_{C\text{-}F}$ = 237.625 Hz), 147.9 (d, $J_{C\text{-}F}$ = 2.0 Hz), 117.4 (d, $J_{C\text{-}F}$ = 7.5 Hz), 115.5 (d, $J_{C\text{-}F}$ = 22.0 Hz), 66.9, 50.3.

4.2.2.8 Compound **6h**[6a]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 8.20 (d, *J* = 3.0 Hz, 1H), 7.49 (td, *J* = 8.5, 1.5

Hz, 1H), 6.67-6.62 (m, 2H), 3.81 (t, *J* = 4.5 Hz, 4H), 3.49 (t, *J* = 4.5 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.5, 147.9, 137.3, 113.6, 106.8, 66.6, 45.5.

4.2.2.9 Compound **6i**[6a]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.11 (t, *J* = 8.0 Hz, 1H), 6.23 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.19 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.10 (t, *J* = 2.0 Hz, 1H), 3.78 (s, 3H), 3.25 (quintet, *J* = 4.5 Hz, 4H), 1.97 (quintet, *J* = 4.5 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7, 149.3, 129.7, 104.9, 100.5, 97.9, 55.0, 47.6, 25.4.

4.2.2.10 Compound **6j**[6b]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.23 (t, *J* = 8.0 Hz, 2H), 6.93 (d, *J* = 8.0 Hz, 2H), 6.80 (t, *J* = 8.0 Hz, 1H), 3.14 (t, *J* = 5.5 Hz, 4H), 1.69 (quintet, *J* = 5.5 Hz, 4H), 1.56 (quintet, *J* = 5.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.2, 128.9, 119.1, 116.5, 50.6, 25.8, 24.3.

4.2.2.11 Compound **6k**[6a]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.12 (t, *J* = 7.5 Hz, 1H), 6.75-6.73 (m, 2H), 6.64 (d, *J* = 7.5 Hz, 1H), 3.12 (t, *J* = 5.5 Hz, 4H), 2.30 (s, 3H), 1.69 (quintet, *J* = 5.5 Hz, 4H), 1.55 (quintet, *J* = 5.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.3, 138.5, 128.8, 120.1, 117.4, 113.6, 50.7, 25.9, 24.3, 21.7.

4.2.2.12 Compound **6l**[6a]: colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.13 (t, *J* = 8.0 Hz, 1H), 6.54 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.47 (t, *J* = 2.0 Hz, 1H), 6.36 (dd, *J* = 8.0, 2.0 Hz, 1H), 3.76 (s, 3H), 3.13 (t, *J* = 5.0 Hz, 4H), 1.68 (quintet, *J* = 5.5 Hz, 4H), 1.55 (quintet, *J* = 5.5 Hz, 2H). ^{13}C NMR (125MHz, $CDCl_3$) δ 160.5, 153.5, 129.5, 109.2, 103.9, 102.7, 55.0, 50.4, 25.7, 24.3.

4.2.2.13 Compound **6m**[6b]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 8.16 (d, *J* = 3.5 Hz, 1H), 7.41 (t, *J* = 8.5 Hz, 1H), 6.61 (d, *J* = 8.5 Hz, 1H), 6.53 (t, *J* = 5.5 Hz, 1H), 3.50 (s, 4H), 1.62 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.6, 147.8, 137.1, 112.2, 106.9, 46.1, 25.4, 24.6.

4.2.2.14 Compound **6n**[6b]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.25 (t, *J* = 8.0 Hz, 4H), 7.01 (d, *J* = 8.0 Hz, 4H), 6.94 (t, *J* = 7.0 Hz, 2H), 3.29 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.0, 129.1, 121.2, 120.4, 40.1.

4.2.2.15 Compound **6o**[6b]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.25 (t, *J* = 7.5 Hz, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.92 (t, *J* = 7.5 Hz, 1H), 6.85-6.82 (m, 2H), 6.78 (d, *J* = 7.5 Hz, 1H), 3.28 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.1, 149.0, 138.9, 129.1, 129.0, 122.3, 121.4, 120.9, 120.1, 117.9, 40.2, 21.5.

4.2.2.16 Compound **6p**[6b]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.27 (t, *J* = 8.0 Hz, 2H), 7.14 (t, *J* = 8.0 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.97 (t, *J* = 8.0 Hz, 1H), 6.57 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.53 (t, *J* = 2.0 Hz, 1H), 6.47 (dd, *J* = 8.0, 2.0 Hz, 1H), 3.73 (s, 3H), 3.28 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5, 150.4, 148.9, 129.7, 129.2, 121.9, 121.6, 112.2, 105.9, 105.6, 55.1, 40.2.

4.2.2.17 Compound **6q**[6b]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.27 (t, *J* = 7.5 Hz, 2H), 7.20-7.17 (m, 5H), 6.73-6.67 (m, 3H), 4.48 (s, 2H), 2.96 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.7, 139.0, 129.1, 128.5, 126.8, 126.7, 116.5, 112.4, 56.6, 38.4.

4.2.2.18 Compound **6r**[6a]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.28 (t, *J* = 7.0 Hz, 2H), 7.21 (d, *J* = 7.0 Hz, 3H), 7.08 (t, *J* = 8.0 Hz, 1H), 6.57-6.52 (m, 3H), 4.48 (s, 2H), 2.95 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.9, 139.1, 138.7, 129.0, 128.5, 126.8, 117.6, 113.1, 109.7, 56.6, 38.3, 21.9.

4.2.2.19 Compound **6s**[6a]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.27 (t, *J* = 7.5 Hz, 2H), 7.20-7.19 (m, 3H), 7.09 (t, *J* = 8.0 Hz, 1H), 6.35 (d, *J* = 8.0 Hz, 1H), 6.29-6.26 (m, 2H), 4.48 (s, 2H), 3.71 (s, 3H), 2.96 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7, 151.1, 138.9, 129.7, 128.4, 126.8, 126.6, 105.5, 101.3, 98.9, 56.5, 54.9, 38.4.

4.2.2.20 Compound **6t**: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.25 (t, *J* = 7.0 Hz, 2H), 7.18 (d, *J* = 7.0 Hz, 1H), 7.14 (d, *J* = 7.5 Hz, 2H), 7.05 (dd, *J* = 15.0, 7.5 Hz, 1H), 6.43 (d, *J* = 8.5 Hz, 1H), 6.39-6.33 (m, 2H). 4.42 (s, 2H), 2.91 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.1 (d, $J_{C\text{-}F}$ = 240.375 Hz), 151.4 (d, $J_{C\text{-}F}$ = 10.625 Hz), 138.3, 130.1 (d, $J_{C\text{-}F}$ = 10.25 Hz), 128.6, 127.0, 126.6, 107.8, 102.8 (d, $J_{C\text{-}F}$ = 21.5 Hz), 99.2 (d, $J_{C\text{-}F}$ = 25.875 Hz), 56.3, 38.5. IR (neat) ν 2895, 2399, 1620, 1573, 1501, 1451, 1372, 1351, 1232, 1159, 1010, 955, 822, 754, 732, 693, 680 cm^{-1}. HRMS (ESI) calcd for $C_{14}H_{15}FN$ $[M+H]^+$: 216.1183; found: 216.1184.

4.2.2.21 Compound **6u**: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.28 (t, *J* = 7.0 Hz, 2H), 7.22-7.18 (m, 3H), 6.88 (t, *J* = 8.5 Hz, 2H), 6.65-6.64 (m, 2H), 4.42 (s, 2H), 2.91 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.5 (d, $J_{C\text{-}F}$ = 233.75 Hz), 146.5, 138.8, 128.5, 126.9 (d, $J_{C\text{-}F}$ = 11.625 Hz), 115.4 (d, $J_{C\text{-}F}$ = 21.875 Hz), 113.7 (d, $J_{C\text{-}F}$ = 7.25 Hz), 57.5, 39.0. IR (neat) ν 2882, 2815, 1603, 1514, 1448, 1368, 1351, 1225, 1113, 945, 811, 751, 733, 708, 693 cm^{-1}. HRMS (ESI) calcd for $C_{14}H_{15}FN$ $[M+H]^+$: 216.1183; found: 216.1189.

4.2.2.22 Compound **8a**[6a]: colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.21 (t, *J* = 7.5 Hz, 3H), 7.16 (d, *J* = 7.5 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.91-6.85 (m, 4H), 5.30 (s, 1H), 2.20 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.0, 141.2, 130.9, 129.2, 128.4, 126.7, 122.0, 120.3, 119.0, 117.3, 17.8.

4.2.2.23 Compound **8b**[6a]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.16 (d, *J* = 7.5 Hz, 2H), 7.08 (t, *J* = 7.5 Hz, 2H), 6.96 (d, *J* = 7.5 Hz, 2H), 6.87 (t, *J* = 7.5 Hz, 2H), 5.10 (s, 1H), 2.23 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.0, 130.8, 127.5, 126.7, 121.3, 118.3, 17.7.

4.2.2.24 Compound **8c**[6a]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.13 (d, *J* = 8.0 Hz, 2H), 7.07 (t, *J* = 7.5 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.87-6.83 (m, 3H), 5.22 (s, 1H), 2.27 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.0, 141.1, 130.8, 130.3, 129.7, 127.1, 126.7, 121.1, 118.5, 117.5, 20.5, 17.7.

4.2.2.25 Compound **8d**[6a]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.13 (d, *J* = 7.5 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 7.00 (s, 1H), 6.92 (s, 2H), 6.81 (d, *J* = 7.5 Hz, 2H), 5.01 (s, 1H), 2.27 (s, 3H), 2.23 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.9, 138.9, 131.7, 131.5, 130.6, 129.2, 127.2, 126.7, 125.9, 120.5, 120.2, 116.4, 20.6, 17.7, 17.6.

4.2.2.26 Compound **8e**[6a]: white solid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.12-7.05 (m, 4H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.69 (t, *J* = 7.5 Hz, 1H), 6.14 (d, *J* = 8.0 Hz, 1H), 4.91 (s, 1H), 2.32 (s, 3H), 2.17 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.1, 138.8, 135.5, 130.2, 128.5, 126.9, 125.5, 122.4, 118.1, 111.8, 18.2, 17.6.

4.2.2.27 Compound **8f**[6a]: white solid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.09 (d, *J* = 7.5 Hz, 1H), 6.95-6.93 (m, 3H), 6.66 (t, *J* = 7.5 Hz, 1H), 6.12 (d, *J* = 7.5 Hz, 1H), 4.82 (s, 1H), 2.29 (s,

6H), 2.13 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.5, 136.0, 135.6, 135.1, 130.2, 129.2, 126.9, 122.0, 117.7, 111.4, 20.8, 18.0, 17.5.

4.2.2.28 Compound **8g**[6a]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.28 (t, *J* = 7.5 Hz, 1H), 7.22 (d, *J* = 7.5 Hz, 2H), 7.11 (d, *J* = 7.5 Hz, 1H), 6.93 (t, *J* = 7.5 Hz, 1H), 6.65 (t, *J* = 7.5 Hz, 1H), 6.11 (d, *J* = 7.5 Hz, 1H), 4.89 (s, 1H), 3.11 (hept, *J* = 6.5 Hz, 2H), 2.33 (s, 3H), 1.17 (d, *J* = 6.5 Hz, 6H), 1.11 (d, *J* = 6.5 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.2, 146.0, 135.7, 130.1, 127.0, 126.9, 123.8, 121.2, 117.5, 111.5, 28.2, 24.7, 23.0, 17.6.

4.2.2.29 Compound **8h**[6a]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.30 (d, *J* = 8.0 Hz, 1H), 7.19 (d, *J* = 7.5 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 6.93 (t, *J* = 7.5 Hz, 1H), 6.87-6.80 (m, 3H), 5.86 (s, 1H), 3.87 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 140.8, 133.9, 130.8, 129.3, 126.6, 122.1, 120.8, 119.6, 119.3, 114.4, 110.4, 55.6, 17.8.

4.2.2.30 Compound **8i**[6a]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.13 (d, *J* = 7.5 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 3H), 6.84 (d, *J* = 8.0 Hz, 2H), 6.80 (t, *J* = 7.5 Hz, 1H), 5.19 (s, 1H), 3.77 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.1, 143.3, 136.4, 130.7, 126.7, 125.4, 122.0, 120.0, 115.4, 114.7, 55.5, 17.7.

4.2.2.31 Compound **8j**[6a]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.15 (d, *J* = 7.5 Hz, 1H), 7.10-7.05 (m, 2H), 6.94-6.86 (m, 5H), 5.22 (s, 1H), 2.21 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.8 (d, $J_{C\text{-}F}$ = 237.875 Hz), 142.0, 139.8, 130.9, 127.3, 126.8, 121.5, 120.0 (d, $J_{C\text{-}F}$ = 7.625 Hz), 117.4, 115.8 (d, $J_{C\text{-}F}$ = 22.375 Hz), 17.7.

4.2.2.32 Compound **8k**[7]: yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.21-7.16 (m, 2H), 7.11 (d, *J* = 8.0 Hz, 1H), 7.01 (s, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.84-6.80 (m, 3H), 5.24 (s, 1H), 2.28 (s, 3H), 2.19 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.0, 138.2, 132.3, 131.6, 129.9, 129.2, 127.2, 120.9, 119.6, 116.2, 20.7, 17.8.

4.2.2.33 Compound **8l**: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.11-7.06 (m, 2H), 7.00 (s, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.64 (d, *J* = 8.0 Hz, 3H), 5.19 (s, 1H), 2.28 (s, 3H), 2.26 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.9, 139.0, 138.3, 132.1, 131.6, 129.8, 129.0, 127.2, 120.9, 120.5, 116.9, 113.4, 21.4, 20.7, 17.7. IR (neat) ν 3371, 3021, 2915, 2855, 2365, 2346, 1603, 1590, 1504, 1491, 1312, 1159, 1113, 1033, 993, 944, 871, 814, 804, 768, 688 cm^{-1}. HRMS (ESI) calcd for $C_{15}H_{18}N$ $[M+H]^+$: 212.1434; found: 212.1437.

4.2.2.34 Compound **8m**: pale yellow liquid. 1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.06 (d, *J* = 8.0 Hz, 1H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.99 (s, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 2H), 5.16 (s, 1H), 2.270 (s, 3H), 2.265 (s, 3H), 2.19 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.2, 139.1, 131.5, 131.4, 129.7, 129.4, 128.7, 127.2, 119.5, 117.3, 20.6, 20.5, 17.7. IR (neat) ν 3385, 3021, 2921, 2855, 1607, 1507, 1298, 1119, 872, 806, 708 cm^{-1}. HRMS (ESI) calcd for $C_{15}H_{18}N$ $[M+H]^+$: 212.1434; found: 212.1434.

4.2.2.35 Compound **8n**: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.12-7.06 (m, 2H), 7.00 (s, 1H), 6.93 (d, *J* = 8.0 Hz, 1H), 6.41-6.37 (m, 3H), 5.26 (s, 1H), 3.71 (s, 3H), 2.27 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.8, 146.6, 137.9, 132.6, 131.6, 130.3, 129.9, 127.2, 121.7, 108.8, 104.8, 101.8, 55.1, 20.7, 17.8. IR (neat) ν 3371, 3007, 2915, 2829, 1905, 1597, 1491, 1461, 1434, 1305, 1262, 1152, 1033, 816, 756, 688 cm^{-1}. HRMS (ESI) calcd for $C_{15}H_{18}NO$ $[M+H]^+$: 228.1383; found: 228.1385.

4.2.2.36 Compound **8o**: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.16 (d, *J* = 8.0 Hz, 1H), 7.01 (s, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.79 (t, *J* = 7.5 Hz, 1H), 6.74 (t, *J* = 7.5 Hz, 1H), 5.77 (s, 1H), 3.84 (s, 3H), 2.27 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6, 137.9, 134.9, 132.3, 131.5, 130.5, 127.1, 121.4, 120.9, 118.5, 113.4, 110.2, 55.5, 20.6, 17.7. IR (neat) ν 3418, 2921, 2829, 1600, 1517, 1454, 1338, 1292, 1235, 1172, 1116, 1027, 806, 776, 736 cm^{-1}. HRMS (ESI) calcd for $C_{15}H_{18}NO$ $[M+H]^+$: 228.1383; found: 228.1389.

4.2.2.37 Compound **8p**[6b]: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.10 (d, *J* = 7.0 Hz, 2H), 7.04 (t, *J* = 7.0 Hz, 1H), 6.95 (s, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 6.07 (d, *J* = 8.0 Hz, 1H), 4.81 (s, 1H), 2.29 (s, 3H), 2.22 (s, 3H), 2.16 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.7, 139.2, 135.1, 131.1, 128.5, 127.4, 127.2, 125.1, 122.8, 112.2, 20.4, 18.2, 17.5.

4.2.2.38 Compound **8q**[6b]: white solid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.19 (s, 1H), 6.90 (s, 2H), 6.73 (d, *J* = 8.0 Hz, 1H), 6.04 (d, *J* = 8.0 Hz, 1H), 4.70 (s, 1H), 2.27 (s, 3H), 2.26 (s, 3H), 2.20 (s, 3H), 2.11 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.1, 136.4, 135.2, 134.7, 131.0, 129.1, 127.2, 126.9, 122.3, 111.7, 20.8, 20.3, 18.0, 17.5.

4.2.2.39 Compound **8r**: pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.25 (t, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.94 (s, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 6.03 (d, *J* = 8.0 Hz, 1H), 4.79 (s, 1H), 3.10 (hept, *J* = 6.5 Hz, 2H), 2.30 (s, 3H), 2.21 (s, 3H), 1.14 (d, *J* = 6.5 Hz, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.0, 143.7, 136.2, 131.0, 127.3, 126.8, 126.6, 123.7, 121.4, 111.7, 28.2, 24.7, 23.0, 20.3, 17.5. IR (neat) ν 3418, 2961, 2921, 2855, 2359, 1620, 1583, 1510, 1457, 1437, 1328, 1295, 1269, 1053, 871, 811, 788, 741 cm^{-1}. HRMS (ESI) calcd for $C_{20}H_{28}N$ $[M+H]^+$: 282.2216; found: 282.2233.

4.2.2.40 Compound **9a**[6b]: white solid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.38-7.32 (m, 4H), 7.26 (t, *J* = 7.0 Hz, 1H), 7.10-7.05 (m, 2H), 6.66 (t, *J* = 7.0 Hz, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 4.35 (s, 2H), 3.83 (s, 1H), 2.25 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.0, 139.5, 130.0, 128.6, 127.5, 127.2, 127.1, 121.9, 117.2, 110.0, 48.3, 17.5.

4.2.2.41 Compound **9b**[6a]: colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.08 (t, *J* = 8.0 Hz, 1H), 7.02 (d, *J* = 7.0 Hz, 1H), 6.62-6.58 (m, 2H), 3.32-3.26 (m, 1H), 2.09-2.05 (m, 5H), 1.77-1.73 (m, 2H), 1.66-1.62 (m, 1H), 1.42-1.33 (m, 2H), 1.28-1.14 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.2, 130.2, 127.0, 121.5, 116.2, 110.2, 51.4, 33.6, 26.0, 25.0, 17.4.

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