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Graphical Abstract

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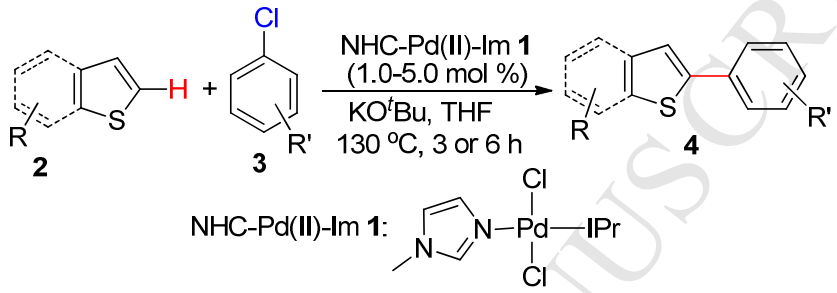

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ABSTRACT

NHC-Pd(II)-Im complex showed efficient catalytic activity toward the direct C-H bond arylation of (benzo)thiophenes with the challenging aryl chlorides. Under the suitable conditions, all reactions proceeded smoothly to give the desired C-H bond arylated products in acceptable to high yields, giving an inexpensive and alternative methodology for the arylation of (benzo)thiophenes.

1. Introduction

During the past decades, the transition metal-catalyzed direct C-H bond arylation of heteroaromatic compounds have attracted much attention and thus got great success.[1] As a result, the transition-metal catalyzed direct C-H bond arylation of (benzo)thiophenes also attracted chemists' attention successfully. However, to the best of our knowledge, there are still some shortcomings remained in the direct C-H bond arylation of (benzo)thiophenes, which thus hampered them to be potentially practical methods in organic synthesis: (1) in most cases, only the more active aryl bromides and iodides were used as the arylating reagents in the presence of phosphine ligands;[2,3] in the very fewer successful examples using the inert aryl chlorides as the arylating reagents; (2) air-sensitive phosphine ligands are necessary;[2j,4] (3) papers using *N*-heterocyclic carbene (NHC)-palladium complexes were also reported recently, however, the reported complexes were all not readily available and/or air-sensitive phosphine ligand was also involved.[5] Therefore, great demand still remains for the direct C-H bond arylation of (benzo)thiophenes with the easily available, cheaper while inert aryl chlorides catalyzed by stable and readily available catalysts.[6] From 2011, we developed a well-defined *N*-heterocyclic carbene-palldium(II)-1-methylimidazole [NHC-Pd(II)-Im] complex **1** from commercially available starting materials IPr·HCl, $PdCl_2$ and 1-methylimidazole in a one-pot procedure, which has been proven to be one of the most versatile NHC-Pd(II) complexes with highly catalytic activity in activating aryl chlorides toward C-C and C-N coupling reactions.[7-9] For example, very recently, we have reported the first example of sole direct C-H bond arylation of benzo[*b*]furans with aryl chlorides in the presence of NHC-Pd(II)-Im complex **1**, giving the C2-arylated benzo[*b*]furans in acceptable to high yields.[9a] These results thus prompted us to further investigate its application to the direct C-H bond arylation of (benzo)thiophenes with aryl chlorides. Herein, we report these results in detail.

2. Results and discussion

The optimization for the reaction conditions was began with the model reaction using benzothiophene **2a** (0.5 mmol) and chlorobenzene **3a** (0.6 mmol) as the substrates, NHC-Pd(II)-Im complex **1** (1.0 mol%) as the catalyst, CuO (10.0 mol%) as the additive in THF (2.0 mL) at 130 °C for 6 h to test various bases (1.0 mmol) (Table 1, entries 1-6). It was found that KO^{t}Bu was the best base, giving the highest yield of 97% (Table 1, entry 1). In the presence of other bases such as NaO^{t}Bu, K_2CO_3, Cs_2CO_3, KOH and K_3PO_4, almost no reaction occurred (Table 1, entries 2-6). Using KO^{t}Bu as the base, a variety of normal solvents was then screened. It was found that good yield can still be achieved when dioxane was used as the solvent (Table 1, entry 8), while in toluene, very low yield was observed (Table 1, entry 7), and in polar solvents such as DMAc and CH_3CN, no desired product can be detected (Table 1, entries 9 and 10). Based on the above results, a series of copper salts was also tested. For example, good yields can be still observed when Cu_2O, CuI and $Cu(OAc)_2$ were selected as the additives, respectively (Table 1, entries 11, 13 and 14). However, in the presence of CuCl, the yield

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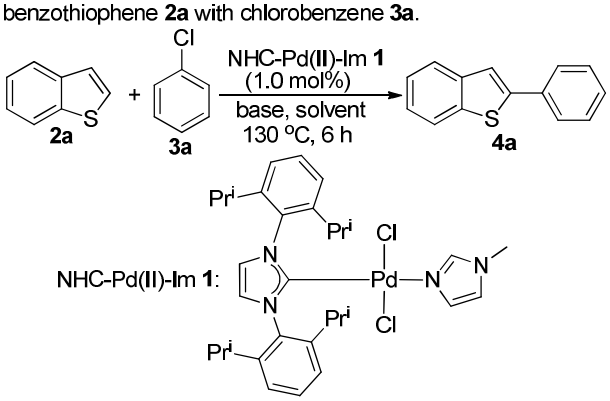
decreased dramatically to 52% (Table 1, entry 12). It is worth noting here that the addition of the copper additive is essential for such transformation, because in the absence of any copper additive, almost no reaction took place (Table 1, entry 15).

Table 1. Optimization for the complex **1** catalyzed reaction of benzothiophene **2a** with chlorobenzene **3a**.

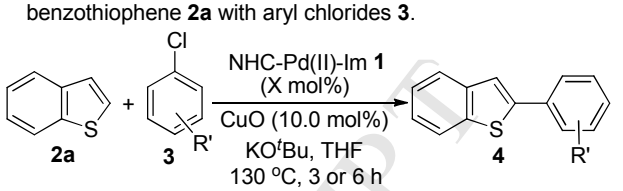


Entry[a]	Base	Solvent	Additive	Yield (%)[b]
1	KO^{t}Bu	THF	CuO	97
2	NaO^{t}Bu	THF	CuO	NR
3	K_2CO_3	THF	CuO	NR
4	Cs_2CO_3	THF	CuO	NR
5	KOH	THF	CuO	<5
6	K_3PO_4	THF	CuO	NR
7	KO^{t}Bu	toulene	CuO	29
8	KO^{t}Bu	dioxane	CuO	87
9	KO^{t}Bu	DMAc	CuO	NR
10	KO^{t}Bu	CH_3CN	CuO	NR
11	KO^{t}Bu	THF	Cu_2O	89
12	KO^{t}Bu	THF	CuCl	52
13	KO^{t}Bu	THF	CuI	90
14	KO^{t}Bu	THF	$Cu(OAc)_2$	90
15	KO^{t}Bu	THF	——	<5

[a] All reactions were carried out using **2a** (0.5 mmol), **3a** (0.6 mmol), **1** (1.0 mol%), additive (0 or 10.0 mol%), base (2.0 equiv) in solvent (2.0 mL) at 130 °C for 6 h. [b] Isolated yields.

Once the optimal conditions in hand, we first investigated the reactions of benzothiophene **2a** with various aryl chlorides to test the generality and limitation. The results are shown in Table 2. As can be seen from Table 2, under suitable conditions, most reactions took place smoothly to give the desired C2-arylated products in good to high yields. It seems that substituents on the aryl chlorides affected the reactions to some extent. For example, under identical conditions, the reactions involving 4-methylphenyl chloride **3b**, 3-methylphenyl chloride **3c** and 2-methylphenyl chloride **3d**, gave very low yields (Table 2, entries 1, 3 and 5). Satisfyingly, increasing the catalyst loading to 2.0 or 3.0 mol%, high to almost quantitative yields can be achieved within 3 h (Table 2, entries 2, 4 and 7). When 4-vinylphenyl chloride **3g** was chosen as the substrate, good yield can be observed under the optimal conditions (Table 2, entry 11), which can also increase to 92% within shorter time when the catalyst loading was increased to 2.0 mol% (Table 2, entry 12). The lowest yield was found when 4-fluorophenyl chloride **3h** was used (Table 2, entries 13-15). By decreasing the amount of KO^{t}Bu to 1.2 equiv, the best yield was achieved in 56% (Table 2, entry 15).

Table 2. NHC-Pd(II)-Im complex **1** catalyzed reactions of benzothiophene **2a** with aryl chlorides **3**.



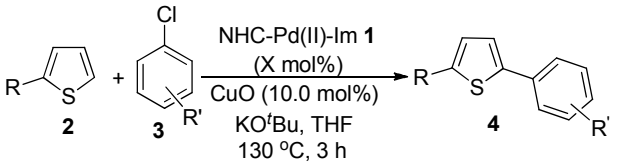
Entry[a]	**3** (R')	[X]	Time (h)	Yield (%)[b]
1	**3b** (4-Me)	1	6	**4b**, 33
2	**3b**	2	3	**4b**, 98
3	**3c** (3-Me)	1	6	**4c**, 32
4	**3c**	2	3	**4c**, 99
5	**3d** (2-Me)	1	6	**4d**, 33
6	**3d**	2	6	**4d**, 52
7	**3d**	3	3	**4d**, 90
8	**3e** (4-OMe)	2	3	**4e**, 62
9	**3e**	3	3	**4e**, 86
10	**3f** (3-OMe)	3	3	**4f**, 82
11	**3g** (4-vinyl)	1	6	**4g**, 81
12	**3g**	2	3	**4g**, 92
13	**3h** (4-F)	1	6	**4h**, 20
14	**3h**	3	3	**4h**, 35
15[c]	**3h**	3	3	**4h**, 56

[a] Otherwise specified, all reactions were carried out using **2a** (0.5 mmol), **3** (0.6 mmol), **1** (X mol%), CuO (10.0 mol%), KO^{t}Bu (2.0 equiv) in THF (2.0 mL) at 130 °C for 3 or 6 h. [b] Isolated yields. [c] KO^{t}Bu: 1.2 equiv.

Encouraged by the above successful results for the reactions between benzothiophene **2a** and aryl chlorides **3**, we subsequently turned our attention to the reactions of thiophenes such as 2-phenylthiophene **2b** and 2-methylthiophene **2c** to further test the limitation and generality of this methodology. The results are summarized in Table 3. For the reactions of 2-phenylthiophene **2b** with a variety of aryl chlorides **3**, all reactions worked well to give the desired C-H bond arylated products **4i-p** in moderate to almost quantitative yields (Table 3, entries 1-8). Electron-rich, -neutral and -sterically hindered substitutents on the aryl chlorides **3** did not affect the reactions significantly. For instance, for the reaction of 2-phenylthiophene **2b** with 2-methylphenyl chloride **3d**, good yield can be still obtained (Table 3, entry 4). Moderate yield was observed for the reaction of 4-fluorophenyl chloride **4p** (Table 3, entry 8). Under the optimal conditions, even if the catalyst loading was increased to 5.0 mol%, the yield was still very low for the reaction of 2-methylthiophene **2c** with 3-methylphenyl chloride **3c** (Table 3, entry 9). Therefore, to develop efficient method for such transformation, more effort was performed. To our pleasure, after some errors and trials, it was found that by adjusting the substrate

ratio (**2c**:**3c** = 2:1), increasing the catalyst loading (5.0 mol%) and prolonging the reaction time (12 h), the yield can drastically elevate to 79% (Table 3, entry 11). Based on this result, a series of aryl chlorides **3** was then subjected to such conditions. All reactions performed well to give the corresponding C-H bond arylated products **4** in moderate yields (Table 3, entries 10-14). For all aryl chlorides tested, the substituents on the phenyl rings did not affect the reactions evidently.

Table 3. NHC-Pd(II)-Im complex **1** catalyzed reactions of 2-substituted thiophenes **2** with aryl chlorides **3**.



Entry[a]	**2** (R)	**3** (R')	[X]	Yield (%)[b]
1	**2b** (Ph)	**3a** (H)	2	**4i**, 99
2	**2b**	**3b** (4-Me)	2	**4j**, 93
3	**2b**	**3c** (3-Me)	2	**4k**, 94
4	**2b**	**3d** (2-Me)	3	**4l**, 87
5	**2b**	**3e** (4-OMe)	3	**4m**, 89
6	**2b**	**3f** (3-OMe)	3	**4n**, 81
7	**2b**	**3g** (4-vinyl)	2	**4o**, 98
8[c]	**2b**	**3h** (4-F)	3	**4p**, 62
9	**2c** (Me)	**3c**	5	**4q**, 32
10[d]	**2c**	**3b**	5	**4r**, 69
11[d]	**2c**	**3c**	5	**4q**, 79
12[d]	**2c**	**3d**	5	**4s**, 70
13[d]	**2c**	**3e**	5	**4t**, 68

[a] Otherwise specified, all reactions were carried out using **2** (0.5 mmol), **3** (0.6 mmol), **1** (X mol%), CuO (10.0 mol%), KO^{t}Bu (2.0 equiv) in THF (2.0 mL) at 130 °C for 3 h.
[b] Isolated yields. [c] KO^{t}Bu: 1.2 equiv.
[d] The reactions were carried out using **2c** (1.0 mmol), **3** (0.5 mmol), KO^{t}Bu (1.2 equiv), **1** (5.0 mol%), Cu_2O (10.0 mol%) in THF (2.0 mL) at 130 °C for 12 h.

3. Conclusion

In conclusion, we report herein the first example of phosphine ligand-free, NHC-Pd(II) complex catalyzed direct C-H bond arylation of (benzo)thiophenes with the inert, while easily available aryl chlorides as the arylating reagents. Using a well-defined NHC-Pd(II)-Im complex as the catalyst, all reactions performed well to give the desired C-H bond arylated (benzo)thiophenes in moderate to high yields, affording an inexpensive and alternative methodology for the arylation of (benzo)thiophenes.

4. Experimental section

4.1 General remarks.

Melting points are uncorrected. NMR spectra were recorded at 500 (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 in Hertz. Flash column chromatography was performed on silica gel (300-400 mesh).

4.2 Experimental procedure

Under N_2 atmosphere, NHC-Pd(II)-Im complex **1** (1.0 mol%), CuO (10.0 mol%), benzothiophene **2a** (0.5 mmol), KO^{t}Bu (1.0 mmol), dry THF (2.0 mL) and chlorobenzene **3a** (0.6 mmol) were successively added into a sealed tube. The mixture was stirred vigorously at 130 °C for 6 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel to afford pure product **4a**.

4.2.1 Compound ***4a***[2a]: white solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.83 (d, *J* = 7.5 Hz, 1H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.72 (d, *J* = 7.5 Hz, 2H), 7.54 (s, 1H), 7.42 (t, *J* = 7.5, 2H), 7.36-7.29 (m, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 144.3, 140.7, 139.5, 134.3, 128.9, 128.3, 126.5, 124.5, 124.3, 123.6, 122.3, 119.5.

4.2.2 Compound ***4b***[2a]: white solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.46 (s, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.27 (t, *J* = 8.0 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 2.36 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 144.4, 140.8, 139.3, 138.2, 131.5, 129.6, 126.3, 124.4, 124.1, 123.4, 122.2, 118.8, 21.2.

4.2.3 Compound ***4c***[2e]: white solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.82 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 7.5 Hz, 1H), 7.53-7.52 (m, 3H), 7.36-7.29 (m, 3H), 7.16 (d, *J* = 8.0 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 144.4, 140.7, 139.4, 138.6, 134.2, 129.0, 128.8, 127.2, 124.4, 124.2, 123.6, 123.5, 122.2, 119.3, 21.4.

4.2.4 Compound ***4d***[2a]: white solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.84 (d, *J* = 7.5 Hz, 1H), 7.78 (d, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.0 Hz, 1H), 7.38-7.22 (m, 6H), 2.47 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 143.5, 140.2, 140.1, 136.4, 134.2, 130.8, 130.6, 128.3, 125.9, 124.3, 124.1, 123.5, 123.0, 122.0, 21.0.

4.2.5 Compound ***4e***[2a]: yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.80 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 9.0 Hz, 2H), 7.42 (s, 1H), 7.33 (td, *J* = 8.0, 1.0 Hz, 1H), 7.28 (td, *J* = 8.0, 1.0 Hz, 1H), 6.95 (d, *J* = 9.0 Hz, 2H), 3.85 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.8, 144.2, 140.9, 139.2, 127.7, 127.1, 124.4, 123.9, 123.2, 122.2, 118.2, 114.4, 55.4.

4.2.6 Compound ***4f***[2n]: yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.82 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 7.5 Hz, 1H), 7.53 (s, 1H), 7.36-7.20 (m, 4H), 7.24 (s, 1H), 6.89 (dt, *J* = 7.5, 2.0 Hz, 1H), 3.87 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.9, 144.0, 140.5, 139.4, 135.6, 129.9, 124.5, 124.3, 123.6, 122.2, 119.6, 119.0, 113.7, 112.1, 55.3.

4.2.7 Compound ***4g***[10]: white solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.82 (d, *J* = 7.5 Hz, 1H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.55 (s, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 6.74 (dd, *J* = 18.0, 11.0 Hz, 1H), 5.80 (d, *J* = 18.0 Hz, 1H), 5.30 (d, *J* = 11.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 143.9, 140.7, 139.5, 137.5, 136.2, 133.7, 126.7, 126.6, 124.5, 124.4, 123.5, 122.2, 119.4, 114.4.

4.2.8 Compound ***4h***[2e]: white solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.82 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.67 (dd, *J* = 8.5, 5.0 Hz, 2H), 7.46 (s, 1H), 7.37-7.25 (m, 2H), 7.12 (t,

J = 8.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 162.8 (d, J_{C-F} = 246.875 Hz), 143.1, 140.7, 139.5, 130.6 (d, J_{C-F} = 3.375 Hz), 128.2 (d, J_{C-F} = 8.125 Hz), 124.6, 124.4, 123.5, 122.2, 119.4, 115.9 (d, J_{C-F} = 21.75 Hz).

4.2.9 Compound ***4i***[2j]: white solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.64 (d, *J* = 7.5 Hz, 4H), 7.40 (t, *J* = 7.5 Hz, 4H), 7.30-7.27 (m, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 143.6, 134.3, 128.9, 127.5, 125.6, 124.0.

4.2.10 Compound ***4j***[2b]: white solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.63 (d, *J* = 7.5 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.39 (t, *J* = 8.0 Hz, 2H), 7.29-7.24 (m, 3H), 7.20 (d, *J* = 8.0 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 143.8, 143.0, 137.4, 134.4, 131.5, 129.6, 128.9, 127.4, 125.6, 125.5, 123.9, 123.5, 21.2.

4.2.11 Compound ***4k***[11]: white solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.30-7.27 (m, 4H), 7.11 (d, *J* = 8.0 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 143.8, 143.4, 138.5, 134.3, 134.2, 128.9, 128.8, 128.3, 127.4, 126.3, 125.6, 123.9, 123.8, 122.7, 21.4.

4.2.12 Compound ***4l***[11]: white solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.63 (d, *J* = 8.0 Hz, 2H), 7.46-7.44 (m, 1H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.30-7.22 (m, 5H), 7.04 (d, *J* = 3.5 Hz, 1H), 2.49 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 143.9, 142.5, 135.9, 134.3, 134.0, 130.8, 130.2, 128.9, 127.8, 127.4, 126.0, 125.6, 123.1, 21.2.

4.2.13 Compound ***4m***[2f]: yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.62 (d, *J* = 7.5 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.28-7.25 (m, 2H), 7.17 (s, 1H), 6.92 (d, *J* = 8.0 Hz, 2H), 3.84 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.2, 143.6, 142.6, 134.4, 128.9, 127.3, 127.2, 126.9, 125.5, 123.9, 122.9, 114.3, 55.4.

4.2.14 Compound ***4n***[12]: yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.62 (d, *J* = 7.0 Hz, 2H), 7.38 (t, *J* = 7.0 Hz, 2H), 7.31-7.23 (m, 5H), 7.16 (s, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 3.84 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.9, 143.7, 143.4, 135.6, 134.2, 129.9, 128.9, 127.5, 125.6, 124.2, 123.9, 118.2, 113.0, 111.2, 55.3.

4.2.15 Compound ***4o***: yellow solid. mp: 189-190 °C. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.63 (d, *J* = 7.5 Hz, 2H), 7.60 (d, *J* = 7.5 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.30-7.27 (m, 3H), 6.73 (dd, *J* = 17.5, 11.0 Hz, 1H), 5.78 (d, *J* = 17.5 Hz, 1H), 5.27 (d, *J* = 11.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 143.6, 143.3, 136.8, 136.2, 134.3, 133.7, 128.9, 127.5, 126.7, 125.63, 125.61, 124.04, 123.97, 113.9. IR (neat) ν 3055, 2920, 2858, 1624, 1601, 1489, 1455, 1407, 1278, 1202, 1180, 1118, 990, 938, 903, 840, 805 cm^{-1}. MS (ESI): 263 $[M+H]^+$; HRMS (ESI) calcd for $C_{18}H_{15}S$ $[M+H]^+$: 263.0899; found: 263.0896.

4.2.16 Compound ***4p***: white solid. mp: 158-159 °C. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.62 (d, *J* = 7.5 Hz, 2H), 7.58 (t, *J* = 6.5 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.30-7.24 (m, 2H), 7.20 (s, 1H), 7.07 (t, *J* = 8.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 162.3 (d, J_{C-F} = 245.875 Hz), 143.6, 142.4, 134.2, 130.6 (d, J_{C-F} = 3.375 Hz), 128.9, 127.6, 127.3 (d, J_{C-F} = 8.0 Hz), 125.6, 124.0, 116.9 (d, J_{C-F} = 21.75 Hz). IR (neat) ν 2346, 1590, 1540, 1511, 1494, 1455, 1238, 1159, 1101, 937, 906, 864, 835, 801, 755 cm^{-1}. MS (ESI): 255 $[M+H]^+$; HRMS (ESI) calcd for $C_{16}H_{12}FS$ $[M+H]^+$: 255.0638; found: 255.0647.

4.2.17 Compound ***4q***[5]: colorless liquid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.34 (d, *J* = 9.0 Hz, 2H), 7.21 (t, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 4.0 Hz, 1H), 7.03 (d, *J* = 7.5 Hz, 1H), 6.69-6.68 (m, 1H), 2.48 (s, 3H), 2.35 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 142.1, 139.2, 138.3, 134.6, 128.7, 127.8, 126.2, 126.1, 122.7, 122.6, 21.4, 15.4.

4.2.18 Compound ***4r***[2a]: white solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.43 (d, *J* = 8.5 Hz, 2H), 7.13 (d, *J* = 8.5 Hz, 2H), 7.04 (d, *J* = 3.5 Hz, 1H), 6.69-6.68 (m, 1H), 2.48 (s, 3H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 142.1, 138.8, 136.7, 131.9, 129.4, 126.0, 125.4, 122.3, 21.1, 15.4.

4.2.19 Compound ***4s***[2a]: colorless liquid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.38-7.36 (m, 1H), 7.24-7.16 (m, 3H), 6.84 (d, *J* = 3.0 Hz, 1H), 6.73-6.72 (m, 1H), 2.50 (s, 3H), 2.42 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 140.8, 139.6, 135.9, 134.5, 130.7, 130.2, 127.4, 126.2, 125.8, 125.3, 21.2, 15.2.

4.2.20 Compound ***4t***[2a]: yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.47-7.44 (m, 2H), 6.97 (d, *J* = 3.5 Hz, 1H), 6.89-6.86 (m, 2H), 6.68-6.67 (m, 1H), 3.80 (s, 3H), 2.48 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 158.8, 141.9, 138.4, 127.6, 126.7, 126.0, 121.8, 114.2, 55.3, 15.3.

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