Tetrahedron xxx (2015) 1–6

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

N-heterocyclic carbene-Pd(II)-1-methylimidazole complex catalyzed C–H bond benzylation of (benzo)oxazoles with benzyl chlorides

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ARTICLE INFO

Article history:
Received 27 May 2015
Received in revised form 7 July 2015
Accepted 10 July 2015
Available online xxx

Keywords:
N-heterocyclic carbene-palladium complex
(Benzo)oxazole
C–H bond functionalization
Benzylation
Synthetic method

ABSTRACT

The first example of phosphine-free, NHC–Pd(II) complex catalyzed direct C–H bond benzylation of (benzo)oxazoles with benzyl chlorides was reported in this paper. Under the suitable conditions, all reactions worked well enough to give the desired C2-benzylated products in good to almost quantitative yields, providing a facile and straight pathway for the C–H bond benzylation of (benzo)oxazoles within short time.

1. Introduction

During the recent years, the transition metal catalyzed direct C–H bond functionalization has become a versatile methodology for the modification of heteroaromatic compounds.[1] Recently, a well-defined *N*-heterocyclic carbene-palladium(II)-1-methylimidazole [NHC–Pd(II)-Im] complex **1** was developed by our group and proven to be a highly efficient catalyst in C–C and C–N coupling reactions.[2,3] In addition, recent studies have shown that this complex was also a good catalyst in the direct C–H bond arylation of heteroaromatic compounds such as (benzo)oxazoles and (benz)imidazoles, and fluorenes with aryl chlorides.[4] These successful experiences thus prompted us to further test the catalytic activity of NHC–Pd(II)-Im complex **1** in organic synthesis. In this case, it was found that 2-substituted (benzo)oxazoles are interesting backbones because of their special biological and physical properties, or being important precursors in organic synthesis.[5] Therefore, based on our results on the NHC–Pd(II)-Im complex **1** catalyzed direct C–H bond arylation of (benzo)oxazoles with aryl chlorides,[4a] we then turned our interest to its application toward direct C–H bond benzylation of (benzo)oxazoles with benzyl chlorides.[6] In addition, to the best of our knowledge, this is the first example of phosphine-free, NHC–Pd(II) complex catalyzed direct C–H bond benzylation of (benzo)oxazoles with benzyl chlorides.[7] Herein, we report these results in detail.

2. Results and discussion

Initially, the reactions between benzoxazole **2a** (0.6 mmol) and benzyl chloride **3a** (0.5 mmol) as the model substrates in the presence of NHC–Pd(II)-Im complex **1** (1.0 mol %) using toluene as the solvent (2.0 mL) at 130 °C for 3 h were carried out to evaluate various bases (Table 1, entries 1–6). Among the bases screened, LiO^tBu gave the best yield (Table 1, entry 3). However, almost no reaction occurred when some other bases such as KO^tBu, NaO^tBu, KOH, Li_2CO_3 and $NaHCO_3$ were used, respectively (Table 1, entries 1, 2 and 4–6). Subsequently, some solvents were also tested using LiO^tBu as the base. For example, when dioxane was used as the solvent, product **4a** was obtained in 68% yield (Table 1, entry 7). Using other solvents such as THF, CH_3CN and DMSO, almost no desired product was detected (Table 1, entries 8–10). Finally, when the catalyst loading was elevated to 2.0 mol %, the yield could be increased to 98% within 3 h (Table 1, entry 11). Further study showed that 130 °C was necessary to give satisfactory result within 3 h. For example, the yield was decreased to 82% when the reaction temperature was lowered to 120 °C, even with increased catalyst loading (2.0 mol %) (Table 1, entry 12). In addition, it was confirmed that in the absence of NHC–Pd(II)-Im complex **1**, no reaction occurred.

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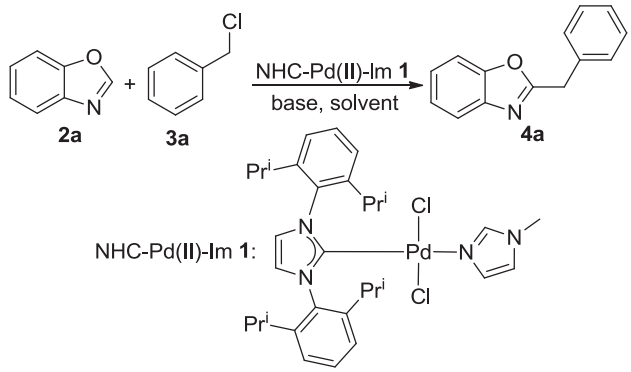
http://dx.doi.org/10.1016/j.tet.2015.07.030
0040-4020/

Table 1
Optimization for the NHC–Pd(II)-Im complex **1** catalyzed reaction of benzoxazole **2a** with benzyl chloride **3a**



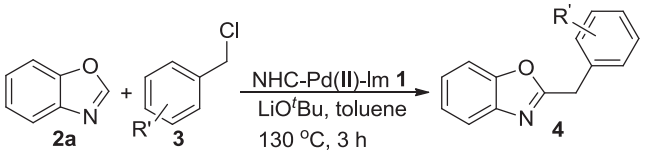
Entry[a]	Solvent	Base	Yield (%)[b]
1	Toluene	KO^{t}Bu	nr
2	Toluene	NaO^{t}Bu	nr
3	Toluene	LiO^{t}Bu	88
4	Toluene	KOH	nr
5	Toluene	Li_2CO_3	<5
6	Toluene	$NaHCO_3$	nr
7	Dioxane	LiO^{t}Bu	68
8	THF	LiO^{t}Bu	<5
9	CH_3CN	LiO^{t}Bu	nr
10	DMSO	LiO^{t}Bu	nr
11[c]	Toluene	LiO^{t}Bu	98
12[d]	Toluene	LiO^{t}Bu	82

[a] Otherwise specified, all reactions were carried out using **2a** (0.6 mmol), **3a** (0.5 mmol), **1** (1.0 mol %), base (2.0 equiv) in solvent (2.0 mL) at 130 °C for 3 h.
[b] Isolated yields.
[c] **1** (2.0 mol %).
[d] **1** (2.0 mol %), 120 °C.

With the optimal conditions established, the reactions between benzoxazole **2a** and a variety of benzyl chlorides **3** were first investigated to show the generality (Table 2). All reactions worked well under suitable conditions. Substituents on the benzyl chlorides affected the reactions to some extent. For example, benzyl chlorides having electron-donating methoxy group such as 4-methoxybenzyl chloride **3c** was not a suitable substrate under the optimal conditions, giving the lowest yield (Table 2, entry 2). To our pleasure, very high yield can also be achieved by simply increasing the catalyst loading to 3.0 mol % under similar conditions (Table 2, entry 3). However, its analogue, 3-methoxybenzyl chloride **3b** was the most suitable substrate in such transformation to give the highest yield (Table 2, entry1). Sterically-hindered substituent slightly affected the reaction. For instance, for the reaction involving 2-methylbenzyl chloride **3d**, product **4d** was observed in 88% yield (Table 2, entry 4), while for its analogue, 3- and 4-methylbenzyl chlorides **3e** and **3f**, higher yields were obtained (Table 2, entries 5 and 6). 4-Fluorobenzyl chloride **3h** was superior substrate than 3-fluorobenzyl chloride **3g**, giving higher yield under identical conditions (Table 2, entries 7 and 8).

Subsequently, the limitation and generality of this reaction was further tested using a variety of benzoxazoles **2** and benzyl chlorides **3** as the substrates under the optimal conditions. The results are summarized in Table 3. All reactions took place well to give the desired C2-benzylated products **4** in good to almost quantitative yields. Substituents on the benzoxazoles **2** have apparent effect on the reactions. For example, for the reactions involving 5-methylbenzoxazole **2b** and 6-methylbenzoxazole **2e**, 3.0 mol % catalyst loading was necessary to achieve satisfactory yields within 3 h, while 1.0 mol % catalyst loading was efficient enough for the reactions involving 5-*tert*-butylbenzoxazole **2c** (Table 3, entries 1–10 and 15–18). On the other hand, it seems that substituents on the benzyl chlorides **3** did not affect the reactions significantly. For instance, electron-donating, -neutral and -withdrawing groups on the phenyl rings of benzyl chlorides are all tolerated to give the corresponding products **4** in good to almost quantitative yields.

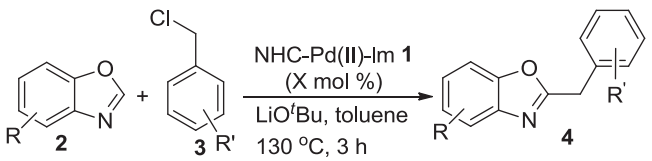
Table 2
NHC–Pd(II)-Im complex **1** catalyzed reactions of benzoxazole **2a** with benzyl chlorides **3**



Entry[a]	**3** (*R*′)	Yield (%)[b]
1	**3b** (3-OMe)	**4b**, 98
2	**3c** (4-OMe)	**4c**, 38
3[c]	**3c** (4-OMe)	**4c**, 97
4	**3d** (2-Me)	**4d**, 88
5	**3e** (3-Me)	**4e**, 95
6	**3f** (4-Me)	**4f**, 92
7	**3g** (3-F)	**4g**, 86
8	**3h** (4-F)	**4h**, 96
9	**3i** (4-^{t}Bu)	**4i**, 86

[a] Otherwise specified, all reactions were carried out using **2a** (0.6 mmol), **3** (0.5 mmol), **1** (2.0 mol %), LiO^{t}Bu (2.0 equiv) in toluene (2.0 mL) at 130 °C for 3 h.
[b] Isolated yields.
[c] **1** (3.0 mol %).

Table 3
NHC–Pd(II)-Im complex **1** catalyzed reactions of benzoxazoles **2** with benzyl chlorides **3**



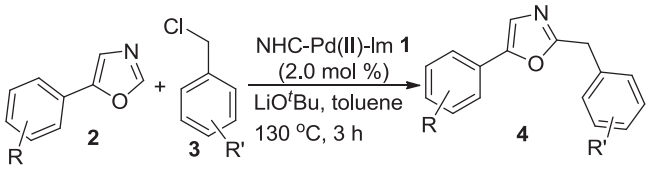
Entry[a]	**2** (*R*)	**3** (*R*′)	[X]	Yield (%)[b]
1	**2b** (5-Me)	**3a** (H)	3.0	**4j**, 90
2	**2b**	**3b** (3-OMe)	3.0	**4k**, 87
3	**2b**	**3d** (3-Me)	3.0	**4l**, 83
4	**2b**	**3f** (4-Me)	3.0	**4m**, 81
5	**2b**	**3g** (3-F)	3.0	**4n**, 83
6	**2b**	**3h** (4-F)	3.0	**4o**, 87
7	**2c** (5-^{t}Bu)	**3a**	1.0	**4p**, 94
8	**2c**	**3c** (4-OMe)	1.0	**4q**, 97
9	**2c**	**3f**	1.0	**4r**, 93
10	**2c**	**3h**	1.0	**4s**, 98
11	**2d** (5-F)	**3a**	2.0	**4t**, 90
12	**2d**	**3c**	2.0	**4u**, 80
13	**2d**	**3f**	2.0	**4v**, 89
14	**2d**	**3h**	2.0	**4w**, 86
15	**2e** (6-Me)	**3a**	3.0	**4x**, 85
16	**2e**	**3c**	3.0	**4y**, 86
17	**2e**	**3f**	3.0	**4z**, 86

[a] All reactions were carried out using **2** (0.6 mmol), **3** (0.5 mmol), **1** (X mol %), LiO^{t}Bu (2.0 equiv) in toluene (2.0 mL) at 130 °C for 3 h.
[b] Isolated yields.

Finally, the reactions between various 5-aryloxazoles **2** and benzyl chlorides **3** were also investigated under the optimal conditions. The results are shown in Table 4. All reactions also took place smoothly to give the desired C2-benzylated products **4** in good to excellent yields. It seems that electron-rich, -neutral and -poor groups on the phenyl rings of both substrates **2** and **3** had no effect on the reactions. For example, Electron-donating groups such as methoxy (**3c**) and methyl (**3f**) groups, electron-withdrawing group such as fluorine atom (**3h**) on the phenyl rings of benzyl

Please cite this article in press as: Ji, Y.-Y.; et al., Tetrahedron (2015), http://dx.doi.org/10.1016/j.tet.2015.07.030

Table 4
NHC–Pd(II)-Im complex **1** catalyzed reactions of aryloxazoles **2** with benzyl chlorides **3**



Entry[a]	2 (*R*)	3 (*R'*)	Yield (%)[b]
1	**2e** (H)	**3a** (H)	**4aa**, 83
2	**2e**	**3c** (4-OMe)	**4ab**, 83
3	**2e**	**3f** (4-Me)	**4ac**, 84
4	**2e**	**3h** (4-F)	**4ad**, 94
5	**2f** (4-F)	**3a**	**4ae**, 87
6	**2f**	**3c**	**4af**, 85
7	**2f**	**3f**	**4ag**, 87
8	**2g** (4-Me)	**3a**	**4ah**, 83
9	**2g**	**3c**	**4ai**, 82
10	**2g**	**3f**	**4aj**, 83
11	**2h** (2-Me)	**3a**	**4ak**, 87
12	**2h**	**3c**	**4al**, 84
13	**2h**	**3f**	**4am**, 93

[a] All reactions were carried out using **2** (0.5 mmol), **3** (0.6 mmol), **1** (2.0 mol%), LiO^{t}Bu (2.0 equiv) in toluene (2.0 mL) at 130 °C for 3 h.
[b] Isolated yields.

chlorides are all tolerated. In addition, sterically-hindered substituent on the phenyl ring of 2-aryloxazoles **2** did not affect the reaction significantly. For instance, *ortho*-substituted 5-(2-methylphenyl)oxazole **2h** was also a suitable substrate in such transformation to give products **4ak**–**4am** in good to high yields under the optimal conditions (Table 4, entries 11–13).

3. Conclusion

In conclusion, the first example of phosphine ligand-free, NHC–Pd(II) complex catalyzed direct C–H bond benzylation of (benzo)oxazoles with benzyl chlorides was reported in this paper. In the presence of a well-defined NHC–Pd(II)-Im complex, all reactions proceeded well to give the desired C2-benzylated (benzo) oxazoles in good to almost quantitative yields. Various substituents such as electron-donating, -neutral, -withdrawing and sterically hindered ones are tolerated in such transformation, giving a facile and straight pathway for the functionalization of (benzo)oxazoles.

4. Experimental section

4.1. General remarks

Melting points are uncorrected. NMR spectra were recorded at 300/500 (for ^{1}H NMR) or 125 MHz (for ^{13}C NMR), respectively. ^{1}H NMR 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, LiO^{t}Bu (1.0 mmol), benzoxazole **2a** (0.6 mmol), NHC–Pd(II)-Im complex **1** (2.0 mol%), dry toluene (2.0 mL) and benzyl chloride **3a** (0.5 mmol) were successively added into a sealed tube. The mixture was stirred vigorously at 130 °C for 3 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**[7c] yellow liquid.* ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.70–7.66 (m, 1H), 7.45–7.41 (m, 1H), 7.36 (d, *J*=7.0 Hz, 2H), 7.32 (t, *J*=7.5 Hz, 2H), 7.28–7.23 (m, 3H), 4.25 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 151.1, 141.3, 134.8, 129.0, 128.8, 127.3, 124.7, 124.2, 119.8, 110.4, 35.3.

*4.2.2. Compound **4b**[8] yellow liquid.* ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.69–7.67 (m, 1H), 7.45–7.41 (m, 1H), 7.29–7.22 (m, 3H), 6.95 (d, *J*=7.5 Hz, 1H), 6.92 (s, 1H), 6.80 (dd, *J*=8.5, 2.5 Hz, 1H), 4.22 (s, 2H), 3.76 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 159.8, 151.0, 141.3, 136.1, 129.7, 124.6, 124.1, 121.2, 119.7, 114.7, 112.7, 110.3, 55.1, 35.1.

*4.2.3. Compound **4c**[7d] yellow liquid.* ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.69–7.65 (m, 1H), 7.45–7.41 (m, 1H), 7.29–7.24 (m, 4H), 6.87 (d, *J*=8.5 Hz, 2H), 4.19 (s, 2H), 3.76 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 158.8, 150.8, 140.7, 130.0, 126.5, 124.7, 124.2, 119.6, 114.2, 110.4, 55.2, 34.2.

*4.2.4. Compound **4d**[7d] yellow liquid.* ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.67–7.66 (m, 1H), 7.42–7.40 (m, 1H), 7.29–7.23 (m, 3H), 7.17–7.14 (m, 3H), 4.23 (s, 2H), 2.38 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 150.9, 141.3, 136.7, 133.2, 130.5, 129.9, 127.5, 126.3, 124.5, 124.0, 119.7, 110.3, 32.9, 19.5.

*4.2.5. Compound **4e** yellow liquid.* ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.70–7.66 (m, 1H), 7.45–7.41 (m, 1H), 7.28–7.23 (m, 2H), 7.21 (t, *J*=7.5 Hz, 1H), 7.17–7.15 (m, 2H), 7.06 (d, *J*=7.5 Hz, 1H), 4.21 (s, 2H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 151.0, 141.3, 138.4, 134.6, 129.6, 128.6, 127.9, 125.9, 124.5, 124.0, 119.7, 110.3, 35.1, 21.2. MS (ESI): 246 $[M+Na]^+$; HRMS (ESI) calcd for $C_{15}H_{13}NNaO$ $[M+Na]^+$: 246.0889; found: 246.0888. IR (neat) ν 3021, 2937, 1610, 1565, 1236, 1141, 997, 837, 795, 746, 692 cm^{-1}.

*4.2.6. Compound **4f**[7d] pale yellow liquid.* ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.69–7.65 (m, 1H), 7.43–7.40 (m, 1H), 7.28–7.23 (m, 4H), 7.13 (d, *J*=8.0 Hz, 2H), 4.21 (s, 2H), 2.30 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4, 151.1, 141.4, 137.0, 131.7, 129.5, 128.9, 124.6, 124.1, 119.8, 110.4, 34.9, 21.1.

*4.2.7. Compound **4g** yellow liquid.* ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.70–7.68 (m, 1H), 7.47–7.45 (m, 1H), 7.31–7.27 (m, 3H), 7.14 (d, *J*=7.5 Hz, 1H), 7.09 (d, *J*=9.5 Hz, 1H), 6.96 (t, *J*=8.5 Hz, 1H), 4.25 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4, 162.9 (d, J_{C-F}=245.125 Hz), 151.0, 141.2, 137.0 (d, J_{C-F}=7.5 Hz), 130.2 (d, J_{C-F}=8.375 Hz), 124.7 (d, J_{C-F}=20.625 Hz), 124.6, 124.2, 119.9, 116.0 (d, J_{C-F}=21.75 Hz), 114.3 (d, J_{C-F}=20.875 Hz), 110.4, 34.8 (d, J_{C-F}=1.5 Hz). MS (ESI): 250 $[M+Na]^+$; HRMS (ESI) calcd for $C_{14}H_{10}FNNaO$ $[M+Na]^+$: 250.0639; found: 250.0635. IR (neat) ν 2976, 2914, 2363, 2329, 1610, 1590, 1570, 1486, 1452, 1236, 1138, 834, 793 cm^{-1}.

*4.2.8. Compound **4h**[9] yellow liquid.* ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.69–7.66 (m, 1H), 7.46–7.44 (m, 1H), 7.34 (dd, *J*=8.5, 5.0 Hz, 2H), 7.30–7.28 (m, 2H), 7.04–7.00 (m, 2H), 4.23 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1, 162.1 (d, J_{C-F}=244.5 Hz), 150.8, 140.5, 130.6 (d, J_{C-F}=8.0 Hz), 130.1, 125.0 (d, J_{C-F}=5.25 Hz), 124.5 (d, J_{C-F}=5.375 Hz), 119.6 (d, J_{C-F}=3.125 Hz), 115.7 (d, J_{C-F}=21.375 Hz), 110.6, 34.3.

*4.2.9. Compound **4i** brown liquid.* ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.69–7.66 (m, 1H), 7.44–7.42 (m, 1H), 7.36 (d, *J*=8.5 Hz, 2H), 7.31 (d, *J*=8.5 Hz, 2H), 7.27–7.25 (m, 2H), 4.23 (s, 2H), 1.29 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4, 151.0, 150.1, 141.4, 131.7, 128.6, 125.7, 124.6, 124.1, 119.8, 110.4, 34.7, 34.4, 31.3. MS (ESI): 288 $[M+Na]^+$; HRMS (ESI) calcd for $C_{18}H_{19}NNaO$ $[M+Na]^+$: 288.1359; found:

288.1359. IR (neat) ν 2961, 2909, 2861, 1613, 1564, 1514, 1454, 1365, 1269, 1242, 1139, 1103, 1020, 1000, 828, 806, 743 cm^{-1}.

4.2.10. Compound ***4j*** [7c] *yellow solid.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.47 (t, J=1.0 Hz, 1H), 7.36–7.29 (m, 5H), 7.26–7.22 (m, 1H), 7.06 (dd, J=8.5, 1.0 Hz, 1H), 4.23 (s, 2H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 149.3, 141.6, 134.9, 134.0, 129.0, 128.8, 127.3, 125.7, 119.7, 109.8, 35.3, 21.4.

4.2.11. Compound ***4k*** *yellow liquid.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.46 (s, 1H), 7.30 (d, J=8.0 Hz, 1H), 7.23 (t, J=8.0 Hz, 1H), 7.06 (d, J=8.0 Hz, 1H), 6.94 (d, J=8.0 Hz, 1H), 6.90 (s, 1H), 6.79 (dd, J=8.0, 2.5 Hz, 1H), 4.20 (s, 2H), 3.76 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 159.8, 149.2, 141.5, 136.2, 133.8, 129.6, 125.6, 121.2, 119.6, 114.6, 112.6, 109.7, 55.0, 35.2, 21.3. MS (ESI): 276 $[M+Na]^+$; HRMS (ESI) calcd for $C_{16}H_{15}NNaO_2$ $[M+Na]^+$: 276.0095; found: 276.0098. IR (neat) ν 2965, 2926, 2357, 2341, 1604, 1585, 1570, 1492, 1452, 1433, 1256, 1191, 1146, 1051, 968, 840, 796 cm^{-1}.

4.2.12. Compound ***4l*** *yellow liquid.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.46 (s, 1H), 7.30 (d, J=8.5 Hz, 1H), 7.22–7.19 (m, 1H), 7.15 (d, J=7.5 Hz, 2H), 7.06 (d, J=8.0 Hz, 2H), 4.19 (s, 2H), 2.43 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 149.3, 141.6, 138.4, 134.8, 133.8, 129.6, 128.6, 127.9, 125.9, 125.6, 119.7, 109.7, 35.2, 21.33, 21.26. MS (ESI): 260 $[M+Na]^+$; HRMS (ESI) calcd for $C_{16}H_{15}NNaO$ $[M+Na]^+$: 260.1046; found: 260.1045. IR (neat) ν 2954, 2920, 2357, 2318, 1573, 1478, 1261, 1191, 1146, 965, 843, 799 cm^{-1}.

4.2.13. Compound ***4m*** *yellow liquid.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.45 (s, 1H), 7.29 (d, J=8.5 Hz, 1H), 7.24 (d, J=8.0 Hz, 2H), 7.13 (d, J=8.0 Hz, 2H), 7.08–7.05 (m, 1H), 4.19 (s, 2H), 2.42 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.5, 149.3, 141.6, 136.9, 133.9, 131.8, 129.5, 128.9, 125.7, 119.7, 109.8, 34.9, 21.4, 21.0. MS (ESI): 238 $[M+H]^+$; HRMS (ESI) calcd for $C_{16}H_{16}NO$ $[M+H]^+$: 238.1226, found 238.1236. IR (neat) ν 3014, 1567, 1427, 1331, 1262, 1060, 1033, 959, 906, 861, 798, 731 cm^{-1}.

4.2.14. Compound ***4n*** *yellow solid; mp: 43–44* °*C.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.47 (s, 1H), 7.32 (d, J=8.0 Hz, 1H), 7.30–7.24 (m, 1H), 7.13 (d, J=8.0 Hz, 1H), 7.10–7.07 (m, 2H), 6.95 (td, J=8.0, 2.0 Hz, 1H), 4.22 (s, 2H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4, 162.9 (d, J_{C-F}=245.0 Hz), 149.2, 141.4, 137.2 (d, J_{C-F}=7.5 Hz), 134.1, 130.2 (d, J_{C-F}=8.25 Hz), 125.9, 124.6 (d, J_{C-F}=2.875 Hz), 119.8, 116.0 (d, J_{C-F}=21.75 Hz), 114.2 (d, J_{C-F}=20.875 Hz), 109.8, 34.9 (d, J_{C-F}=1.5 Hz), 21.3. MS (ESI): 264 $[M+Na]^+$; HRMS (ESI) calcd for $C_{15}H_{12}FNNaO$ $[M+Na]^+$: 264.0795; found: 264.0799. IR (neat) ν 2921, 2849, 1590, 1567, 1484, 1444, 1259, 1239, 1186, 1139, 896, 841, 796 cm^{-1}.

4.2.15. Compound ***4o*** *yellow solid; mp: 67–68* °*C.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.46 (s, 1H), 7.33–7.30 (m, 3H), 7.08 (d, J=8.5 Hz, 1H), 7.02–6.98 (m, 2H), 4.19 (s, 2H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 162.0 (d, J_{C-F}=244.125 Hz), 149.2, 141.4, 134.0, 130.5 (d, J_{C-F}=8.0 Hz), 125.7, 119.7, 115.6 (d, J_{C-F}=21.375 Hz), 109.7, 34.4, 21.3. MS (ESI): 264 $[M+Na]^+$; HRMS (ESI) calcd for $C_{15}H_{12}FNNaO$ $[M+Na]^+$: 264.0795; found: 264.0800. IR (neat) ν 2971, 2926, 2369, 1613, 1565, 1506, 1256, 1219, 1185, 1141, 963, 903, 834, 826, 798 cm^{-1}.

4.2.16. Compound ***4p*** *yellow liquid.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.71 (s, 1H), 7.36–7.30 (m, 6H), 7.26–7.22 (m, 2H), 4.23 (s, 2H), 1.35 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 149.0, 147.6, 141.3, 134.9, 128.9, 128.7, 127.2, 122.2, 116.3, 109.5, 35.2, 34.8, 31.7. MS (ESI): 288 $[M+Na]^+$; HRMS (ESI) calcd for $C_{18}H_{19}NNaO$ $[M+Na]^+$: 288.1359; found: 288.1363. IR (neat) ν 2954, 2908, 2868, 1564, 1477, 1361, 1265, 1119, 962, 881, 859, 809 cm^{-1}.

4.2.17. Compound ***4q*** *yellow liquid.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.71 (s, 1H), 7.35 (d, J=8.5 Hz, 1H), 7.32 (d, J=8.5 Hz, 1H), 7.28 (d, J=8.5 Hz, 2H), 6.85 (d, J=8.5 Hz, 2H), 4.17 (s, 2H), 3.75 (s, 3H), 1.35 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 158.7, 149.0, 147.6, 141.2, 129.9, 126.9, 122.1, 116.2, 114.1, 109.4, 55.1, 34.7, 34.3, 31.7. MS (ESI): 318 $[M+Na]^+$; HRMS (ESI) calcd for $C_{19}H_{21}NNaO_2$ $[M+Na]^+$: 318.1465; found: 318.1465. IR (neat) ν 2959, 2909, 2357, 2324, 1613, 1573, 1511, 1483, 1242, 1174, 1034, 961, 834, 809 cm^{-1}.

4.2.18. Compound ***4r*** *yellow liquid.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.70 (s, 1H), 7.35 (d, J=9.0 Hz, 1H), 7.32 (d, J=9.0 Hz, 1H), 7.24 (d, J=7.5 Hz, 2H), 7.12 (d, J=7.5 Hz, 2H), 4.20 (s, 2H), 2.31 (s, 3H), 1.35 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.5, 149.0, 147.6, 141.3, 136.8, 131.8, 129.4, 128.8, 122.2, 116.3, 109.5, 34.8, 31.7, 21.0. MS (ESI): 302 $[M+Na]^+$; HRMS (ESI) calcd for $C_{19}H_{21}NNaO$ $[M+Na]^+$: 302.1515; found: 318.1523. IR (neat) ν 2965, 2352, 2329, 1573, 1520, 1483, 1427, 1363, 1264, 1124, 1079, 1062, 958, 878, 807 cm^{-1}.

4.2.19. Compound ***4s*** *yellow liquid.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.71 (s, 1H), 7.38–7.31 (m, 4H), 7.00 (t, J=8.5 Hz, 2H), 4.20 (s, 2H), 1.35 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 162.0 (d, J_{C-F}=244.125 Hz), 149.0, 147.8, 141.2, 130.6 (d, J_{C-F}=3.25 Hz), 130.5 (d, J_{C-F}=8 Hz), 122.4, 116.3, 115.6 (d, J_{C-F}=21.375 Hz), 109.5, 34.8, 34.4, 31.7. MS (ESI): 306 $[M+Na]^+$; HRMS (ESI) calcd for $C_{18}H_{18}FNNaO$ $[M+Na]^+$: 306.1265; found: 306.1270. IR (neat) ν 2954, 2901, 2868, 1577, 1507, 1477, 1424, 1361, 1275, 1222, 1152, 1123, 960, 932, 879, 861, 834, 809, 780, 740 cm^{-1}.

4.2.20. Compound ***4t*** *yellow solid; mp: 48–49* °*C.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.40–7.34 (m, 6H), 7.31–7.27 (m, 1H), 7.02 (td, J=7.5, 1.0 Hz, 1H), 4.26 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 159.9 (d, J_{C-F}=238.625 Hz), 147.4, 142.2 (d, J_{C-F}=13.125 Hz), 134.5, 128.9 (d, J_{C-F}=15.0 Hz), 127.4, 112.3 (d, J_{C-F}=26.125 Hz), 110.7 (d, J_{C-F}=10.0 Hz), 106.3 (d, J_{C-F}=25.375 Hz), 35.3. MS (ESI): 228 $[M+H]^+$; HRMS (ESI) calcd for $C_{14}H_{10}FNO$ $[M+H]^+$: 228.0819, found.228.0820. IR (neat) ν 3080, 1732, 1576, 1470, 1235, 1006, 856, 807, 751, 714 cm^{-1}.

4.2.21. Compound ***4u*** *yellow solid; mp: 53–54* °*C.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.35 (d, J=8.5 Hz, 2H), 7.28 (d, J=8.0 Hz, 2H), 7.00 (t, J=8.5 Hz, 1H), 6.88 (d, J=8.0 Hz, 2H), 4.18 (s, 2H), 3.77 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 159.8 (d, J_{C-F}=238.5 Hz), 158.9, 147.3, 142.1 (d, J_{C-F}=13.0 Hz), 130.0, 126.4, 114.2, 112.1 (d, J_{C-F}=26.125 Hz), 110.6 (d, J_{C-F}=10 Hz), 106.2 (d, J_{C-F}=25.5 Hz), 55.2, 34.4. MS (ESI): 280 $[M+Na]^+$; HRMS (ESI) calcd for $C_{15}H_{12}FNNaO_2$ $[M+Na]^+$: 280.0744; found: 280.0749. IR (neat) ν 2999, 2959, 2919, 2352, 2341, 1615, 1568, 1511, 1483, 1438, 1245, 1174, 1124, 1031, 968, 944, 907, 854, 817, 809 cm^{-1}.

4.2.22. Compound ***4v*** *yellow solid; mp: 51–52* °*C.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.36–7.33 (m, 2H), 7.25 (d, J=8.0 Hz, 2H), 7.15 (d, J=8.0 Hz, 2H), 6.99 (td, J=9.0, 2.0 Hz, 1H), 4.20 (s, 2H), 2.32 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 169.8 (d, J_{C-F}=238.75 Hz), 147.3, 142.2 (d, J_{C-F}=13 Hz), 137.0, 131.4, 129.5, 128.8, 112.1 (d, J_{C-F}=26.125 Hz), 110.6 (d, J_{C-F}=10 Hz), 106.2 (d, J_{C-F}=25.5 Hz), 34.9, 21.0. MS (ESI): 264 $[M+Na]^+$; HRMS (ESI) calcd for $C_{15}H_{12}FNNaO$ $[M+Na]^+$: 264.0795; found: 264.0798. IR (neat) ν 3080, 3027, 2928, 2862, 1623, 1607, 1567, 1511, 1474, 1434, 1272, 1245, 1126, 969, 942, 906, 856, 806, 775, 765 cm^{-1}.

4.2.23. Compound ***4w*** *yellow solid; mp: 52–53* °*C.* ^1H NMR (300 MHz, $CDCl_3$, TMS) δ 7.41–7.32 (m, 4H), 7.07–7.00 (m, 3H), 4.23 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 162.1 (d,

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J_{C-F}=244.625 Hz), 159.9 (d, J_{C-F}=239.375 Hz), 147.2, 141.5, 130.6 (d, J=8.125 Hz), 129.9, 115.8 (d, J_{C-F}=21.375 Hz), 112.59 (d, J=26.125 Hz), 112.57 (d, J_{C-F}=26.125 Hz), 110.82 (d, J_{C-F}=10 Hz), 110.81 (d, J=9.875 Hz), 106.2 (d, J_{C-F}=25.625 Hz), 34.4. MS (ESI): 246 $[M+H]^+$; HRMS (ESI) calcd for $C_{17}H_9FNO$ $[M+H]^+$: 246.0714; found: 246.0710. IR (neat) ν 2981, 2941, 2352, 1567, 1504, 1474, 1222, 1133, 973, 907, 872, 834, 803 cm^{-1}.

4.2.24. Compound ***4x***[7g] *yellow liquid.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.54 (d, J=8.5 Hz, 1H), 7.37–7.32 (m, 4H), 7.28–7.25 (m, 2H), 7.10 (d, J=8.5 Hz, 1H), 4.24 (s, 2H), 2.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.6, 151.4, 139.2, 135.02, 134.97, 129.0, 128.8, 127.2, 125.3, 119.1, 110.6, 35.3, 21.6.

4.2.25. Compound ***4y*** *yellow liquid.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.53 (d, J=8.0 Hz, 1H), 7.28 (d, J=8.5 Hz, 2H), 7.24 (s, 1H), 7.09 (d, J=8.0 Hz, 1H), 6.86 (d, J=8.5 Hz, 2H), 4.17 (s, 2H), 3.77 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 158.8, 151.3, 139.1, 134.9, 130.0, 126.9, 125.2, 119.0, 114.2, 110.5, 55.2, 34.3, 21.6. MS (ESI): 254 $[M+H]^+$; HRMS (ESI) calcd for $C_{16}H_{16}NO_2$ $[M+H]^+$: 254.1176; found: 254.1169. IR (neat) ν 3002, 2961, 2920, 2833, 2359, 2337, 1613, 1567, 1510, 1487, 1458, 1426, 1342, 1301, 1244, 1173, 1148, 1109, 1034, 941, 895, 809, 778, 756, 733, 697 cm^{-1}.

4.2.26. Compound ***4z*** *yellow liquid.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.53 (d, J=8.5 Hz, 1H), 7.24 (d, J=8.0 Hz, 2H), 7.23 (s, 1H), 7.13 (d, J=8.0 Hz, 2H), 7.08 (dd, J=8.5, 1.0 Hz, 1H), 4.19 (s, 2H), 2.43 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.8, 151.3, 139.2, 136.8, 134.9, 131.8, 129.4, 128.8, 125.2, 119.0, 110.6, 34.8, 21.6, 21.0. MS (ESI): 238 $[M+H]^+$; HRMS (ESI) calcd for $C_{16}H_{16}NO$ $[M+H]^+$: 238.1226; found: 238.1222. IR (neat) ν 3027, 2915, 2862, 2359, 2332, 1610, 1567, 1511, 1484, 1454, 1428, 1335, 1245, 1146, 1109, 942, 894, 852, 806, 768, 728 cm^{-1}.

4.2.27. Compound ***4aa***[10] *yellow solid.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.58–7.56 (m, 2H), 7.38–7.31 (m, 6H), 7.29–7.22 (m, 3H), 4.16 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 151.4, 135.4, 128.73, 128.65, 128.1, 128.0, 127.0, 124.0, 122.0, 34.7.

4.2.28. Compound ***4ab*** *yellow solid; mp: 76–77* °C. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.57 (d, J=8.0 Hz, 2H), 7.36 (t, J=7.5 Hz, 2H), 7.28–7.22 (m, 4H), 6.87 (d, J=8.0 Hz, 2H), 4.10 (s, 2H), 3.76 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.9, 158.6, 151.3, 129.8, 128.7, 128.1, 128.0, 127.4, 123.9, 121.9, 114.1, 55.1, 33.8. MS (ESI): 288 $[M+Na]^+$; HRMS (ESI) calcd for $C_{17}H_{15}NNaO_2$ $[M+Na]^+$: 288.0995; found: 288.1004. IR (neat) ν 2981, 2895, 2352, 2332, 1607, 1550, 1504, 1239, 1179, 1116, 1056, 1020, 937, 906, 823, 783, 758 cm^{-1}.

4.2.29. Compound ***4ac*** *yellow solid; mp: 74–75* °C. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.57 (d, J=7.5 Hz, 2H), 7.36 (t, J=7.5 Hz, 2H), 7.28–7.22 (m, 4H), 7.13 (d, J=7.5 Hz, 2H), 4.11 (s, 2H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.8, 151.3, 136.6, 132.4, 129.3, 128.7, 128.6, 128.1, 128.0, 124.0, 121.9, 34.3, 21.0. MS (ESI): 272 $[M+Na]^+$; HRMS (ESI) calcd for $C_{17}H_{15}NNaO$ $[M+Na]^+$: 272.1046; found: 272.1053. IR (neat) ν 2915, 2842, 2365, 2313, 1646, 1554, 1511, 1444, 1113, 1060, 973, 944, 897, 828, 771 cm^{-1}.

4.2.30. Compound ***4ad*** *yellow solid; mp: 73–74* °C. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.56 (d, J=7.5 Hz, 2H), 7.36 (t, J=7.5 Hz, 2H), 7.30–7.27 (m, 3H), 7.23 (s, 1H), 7.00 (t, J=8.5 Hz, 2H), 4.11 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.2, 161.8 (d, J_{C-F}=243.875 Hz), 151.4, 131.0 (d, J_{C-F}=3.25 Hz), 130.2 (d, J_{C-F}=8 Hz), 128.7, 128.2, 127.8, 123.9, 121.9, 115.4 (d, J_{C-F}=21.25 Hz), 33.8. MS (ESI): 276 $[M+Na]^+$; HRMS (ESI) calcd for $C_{16}H_{12}FNNaO$ $[M+Na]^+$: 276.0795; found: 276.0802. IR (neat) ν 2968, 2935, 2372, 2313, 1603, 1554, 1501, 1222, 1109, 1050, 944, 828, 785 cm^{-1}.

4.2.31. Compound ***4ae*** *yellow liquid.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.53 (dd, J=8.5, 5.5 Hz, 2H), 7.34–7.31 (m, 4H), 7.27–7.24 (m, 1H), 7.17 (s, 1H), 7.06 (t, J=8.5 Hz, 2H), 4.15 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 162.4 (d, J_{C-F}=247.0 Hz), 150.6, 135.4, 128.7 (d, J_{C-F}=6.125 Hz), 127.0, 125.8 (d, J_{C-F}=8.125 Hz), 124.3 (d, J_{C-F}=3.375 Hz), 121.6 (d, J_{C-F}=1.0 Hz), 115.8 (d, J_{C-F}=21.875 Hz), 34.7. MS (ESI): 276 $[M+Na]^+$; HRMS (ESI) calcd for $C_{16}H_{12}FNNaO$ $[M+Na]^+$: 276.0795; found: 276.0805. IR (neat) ν 3067, 3034, 2921, 1597, 1580, 1554, 1497, 1451, 1229, 1162, 1113, 1056, 973, 940, 834, 821, 728, 692 cm^{-1}.

4.2.32. Compound ***4af*** *yellow solid; mp: 57–58* °C. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.54 (dd, J=8.5, 5.5 Hz, 2H), 7.26 (d, J=8.5 Hz, 2H), 7.16 (s, 1H), 7.06 (t, J=8.5 Hz, 2H), 6.87 (d, J=8.5 Hz, 2H), 4.09 (s, 2H), 3.77 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.9, 162.4 (d, J_{C-F}=246.875 Hz), 158.7, 150.5, 129.8, 127.4, 125.8 (d, J_{C-F}=8 Hz), 124.4, 121.6, 115.8 (d, J_{C-F}=21.875 Hz), 114.1, 55.2, 33.8. MS (ESI): 306 $[M+Na]^+$; HRMS (ESI) calcd for $C_{17}H_{14}NNaO_2$ $[M+Na]^+$: 306.0901; found: 306.0898. IR (neat) ν 3007, 2961, 2842, 1550, 1501, 1467, 1295, 1242, 1179, 1119, 839, 823, 816 cm^{-1}.

4.2.33. Compound ***4ag*** *yellow solid; mp: 58–59* °C. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.52 (dd, J=8.0, 5.5 Hz, 2H), 7.22 (d, J=7.5 Hz, 2H), 7.16 (s, 1H), 7.13 (d, J=7.5 Hz, 2H), 7.05 (t, J=8.0 Hz, 2H), 4.10 (s, 2H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.7, 162.4 (d, J_{C-F}=246.875 Hz), 150.5, 136.6, 132.3, 129.3, 128.6, 125.8 (d, J_{C-F}=8.125 Hz), 124.4 (d, J_{C-F}=3.375 Hz), 121.6 (d, J_{C-F}=1 Hz), 115.8 (d, J_{C-F}=21.875 Hz), 34.2, 20.9. MS (ESI): 290 $[M+Na]^+$; HRMS (ESI) calcd for $C_{17}H_{14}FNNaO$ $[M+Na]^+$: 290.0952; found: 290.0949. IR (neat) ν 2915, 1557, 1507, 1232, 1159, 1106, 1046, 940, 829, 775 cm^{-1}.

4.2.34. Compound ***4ah*** *yellow solid; mp: 63–64* °C. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.47 (d, J=8.0 Hz, 2H), 7.35–7.30 (m, 4H), 7.26–7.22 (m, 1H), 7.18 (s, 1H), 7.17 (d, J=9.0 Hz, 2H), 4.15 (s, 2H), 2.34 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.1, 151.6, 138.1, 135.5, 129.4, 128.7, 128.6, 126.9, 125.3, 123.9, 121.3, 34.7, 21.2. MS (ESI) 250 $[M+H]^+$; HRMS (EI): calcd for $C_{17}H_{16}NO$ $[M+H]^+$: 250.1226, found: 250.1244. IR (neat) ν 3318, 3252, 3034, 2941, 1693, 1643, 1603, 1520, 1494, 1451, 1355, 1322, 1298, 1242, 1159, 1123, 1030, 1013, 911, 859, 809, 783, 718, 690 cm^{-1}.

4.2.35. Compound ***4ai*** *yellow solid; mp: 78–79* °C. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.46 (d, J=8.0 Hz, 2H), 7.25 (t, J=7.5 Hz, 2H), 7.171 (d, J=7.5 Hz, 2H), 7.166 (s, 1H), 6.86 (d, J=8.0 Hz, 2H), 4.08 (s, 2H), 3.76 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 158.6, 151.5, 138.1, 129.8, 129.4, 127.5, 125.3, 123.9, 121.2, 114.1, 55.1, 33.8, 21.2. MS (ESI): 302 $[M+Na]^+$; HRMS (ESI) calcd for $C_{18}H_{17}NNaO_2$ $[M+Na]^+$: 302.1151; found: 302.1154. IR (neat) ν 2954, 2908, 2365, 2313, 1610, 1554, 1507, 1428, 1239, 1179, 1027, 977, 812, 785 cm^{-1}.

4.2.36. Compound ***4aj*** *yellow solid; mp: 75–76* °C. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.46 (d, J=8.0 Hz, 2H), 7.22 (d, J=8.0 Hz, 2H), 7.17 (s, 1H), 7.16 (d, J=7.5 Hz, 2H), 7.13 (d, J=7.5 Hz, 2H), 4.10 (s, 2H), 2.33 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.4, 151.5, 150.0, 138.0, 136.5, 132.4, 129.4, 129.3, 128.6, 123.9, 121.3, 34.3, 21.2, 20.9. MS (ESI): 286 $[M+Na]^+$; HRMS (ESI) calcd for $C_{18}H_{17}NNaO$ $[M+Na]^+$: 286.1202; found: 286.1208. IR (neat) ν 2982, 2920, 2363, 2335, 1554, 1517, 1506, 1112, 1051, 970, 941, 906, 813 cm^{-1}.

4.2.37. Compound ***4ak*** *yellow liquid.* ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.61 (d, J=6.5 Hz, 1H), 7.36–7.31 (m, 4H), 7.26 (d, J=6.5 Hz,

1H), 7.24–7.20 (m, 3H), 7.14 (s, 1H), 4.17 (s, 2H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.1, 150.8, 135.5, 134.7, 131.0, 128.8, 128.7, 128.1, 127.3, 127.0, 126.7, 126.0, 124.8, 34.7, 21.7. MS (ESI): 272 $[M+Na]^+$; HRMS (ESI) calcd for $C_{17}H_{15}NNaO$ $[M+Na]^+$: 272.1046; found: 272.1043. IR (neat) ν 3066, 3021, 2931, 2858, 1551, 1500, 1430, 1455, 1287, 1222, 1112, 1048, 969, 941, 907, 847, 809, 724, 694, 678 cm^{-1}.

*4.2.38. Compound **4al** yellow liquid.* ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.61 (d, J=7.5 Hz, 1H), 7.27 (d, J=8.0 Hz, 2H), 7.23–7.21 (m, 3H), 7.12 (s, 1H), 6.86 (d, J=8.0 Hz, 2H), 4.11 (s, 2H), 3.76 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 158.6, 150.7, 134.6, 131.0, 129.8, 128.9, 128.1, 127.5, 127.3, 126.6, 126.0, 124.7, 114.1, 55.1, 33.8, 21.7. MS (ESI): 302 $[M+Na]^+$; HRMS (ESI) calcd for $C_{18}H_{17}NNaO_2$ $[M+Na]^+$: 302.1151; found: 302.1155. IR (neat) ν 2976, 2931, 2897, 2363, 2329, 1702, 1613, 1509, 1247, 1171, 1124, 1031, 941, 904, 826 cm^{-1}.

*4.2.39. Compound **4am** yellow liquid.* ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.61 (d, J=6.5 Hz, 1H), 7.24–7.21 (m, 5H), 7.13 (d, J=8.0 Hz, 2H), 7.12 (s, 1H), 4.12 (s, 2H), 2.41 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.4, 150.7, 136.6, 134.6, 132.4, 131.0, 129.3, 128.6, 128.1, 127.3, 126.6, 126.0, 124.8, 34.3, 21.7, 21.0. MS (ESI): 286 $[M+Na]^+$; HRMS (ESI) calcd for $C_{18}H_{17}NNaO$ $[M+Na]^+$: 286.1202; found: 286.1203. IR (neat) ν 2982, 2909, 2357, 2329, 1697, 1556, 1514, 1486, 1458, 1126, 1034, 940, 904, 824 cm^{-1}.

Acknowledgements

YZ thanks the University Students' Innovative Undertaking Training Program for financial support. We thank Mr. Shun-Chao Yin for his kind help in preparing the revised version.

Supplementary data

Copies of the ^{1}H NMR and ^{13}C NMR spectra of all key intermediates and final products. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2015.07.030. These data include MOL files and InChiKeys of the most important compounds described in this article.

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