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ARTICLE TYPE

Copper Catalyzed Oxidative *ortho*-C–H Benzoxylation of 2-Phenylpyridines with Benzyl Alcohols and Benzyl Amines as Benzoxylation Sources

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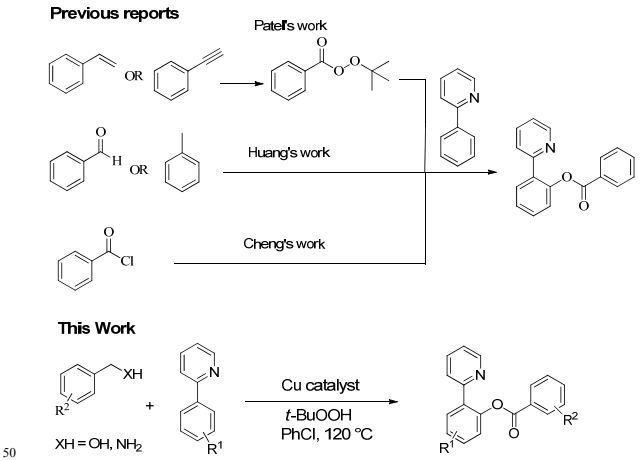
A simple and efficient protocol for the oxidative *ortho* benzoxylation of 2-phenylpyridines with benzyl alcohols and benzyl amines *via* C−H bond activation has been developed. Present protocol uses benzyl alcohol and benzyl amine as inexpensive and easily available starting materials to afford benzoxylation products in moderate to good yields in the presence of Cu/TBHP catalytic system.

The transition metal catalyzed C–H bond functionalization has become a highly efficient and atom-economical protocol in the organic synthesis.[1] The transformation of unreactive *ortho* C–H bond of aromatic compounds to C–C, C–N, C–O and C–X bonds is useful methodology for building complex molecules.[2] The C–O bond formation *via* C–H bond activation is one of the most attractive process. Consequently, various groups have reported the acetoxylation of an sp^2 C–H bond of different aromatic substrates using various oxidizing reagents.[3] Furthermore, Yu, Corey and Sanford have also demonstrated the palladium catalyzed sp^3 C–H bond acetoxylation reactions.[4] However; these protocols were limited upto acetoxylation and hydroxylation reactions.

The benzoxylation *via* transition-metal catalyzed C–H bond activation is also reported by some research groups. In this context, Sanford and co-workers reported the *o*-benzoxylation of 2-phenylpyridine with benzoate iodonium salts using palladium catalyst.[5] Subsequently, some groups have developed a palladium,[6] rhodium[7] and ruthenium[8] catalyzed *o*-benzoxylation protocols using carboxylic acids and aryl acylperoxides as a benzoxylation sources. However, despite of their potential utility, the above reported methods suffer from one or more drawbacks such as the use of air/moisture sensitive phosphine ligands/additives and employing expensive palladium, rhodium and ruthenium catalysts.

To overcome these drawbacks, some groups reported the *o*-benzoxylation of 2-phenylpyridine using copper precursors with different benzoxylation sources such as carboxylic salts,[9] anhydrides,[10] acid chlorides,[11] aldehydes and alkylbenzene.[12] However, longer reaction time and the use of unstable carboxylic salts as well as acyl chlorides were undesirable. Very recently, Rout *et al*., developed the *o*-benzoxylation of 2-phenylpyridine using terminal aryl alkenes and alkynes as arylcarboxy surrogates.[13] Hence, the domino reactions using inexpensive copper catalyst with less reaction time can reduce the environmental impacts as well as productive costs.



Scheme 1: Copper catalyzed benzoxylation of 2-phenylpyridine.

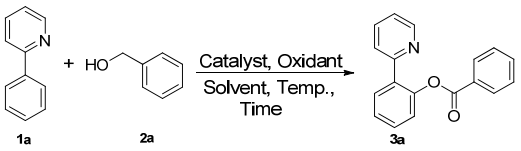
In continuation of our ongoing research on the development of facile and efficient protocols,[14] herein, we have developed a simple, convenient and cost effective methodology for the *o*-benzoxylation of 2-phenylpyridines with benzyl alcohols and benzyl amines using inexpensive and easily available copper catalyst (Scheme 1).

The reaction of 2-phenylpyridine (**1a**) with benzyl alcohol (**2a**) as arylcarboxy source was chosen as a model system for the oxidative benzoxylation reaction. A series of experiments were carried out to optimize reaction parameters such as catalyst, oxidant, solvent, temperature and time on the model reaction and the obtained results were summarized in Table 1.

Initially, our study focused on the screening of different copper precursors such as $Cu(OAc)_2$, $Cu(OAc)_2{\cdot}H_2O$, $CuBr_2$, CuO, $CuCO_3{\cdot}Cu(OH)_2$, Cu_2O, CuI, CuBr and CuCl for the oxidative benzoxylation reaction using *tert*. butyl hydroperoxide (5.0–6.0 M in decane) (TBHP) as an oxidant at 120 °C (Table 1, entries 1–9). The $CuCO_3{\cdot}Cu(OH)_2$, Cu_2O and CuI provided the desired product **3a** in 54%, 62% and 70% yield respectively (Table 1, entries 5–7). However, the other copper precursors provided the benzoxylation product **3a** in moderate to poor yield. Next, when the reaction was carried out in the closed reaction vessel, the yield of **3a** decreases (Table 1, entry 7). The desired product **3a**

was not observed either in the absence of catalyst or oxidant, indicating that both catalyst as well as oxidant are required for the progress of reaction (Table 1, entries 10 and 11).

Table 1: Optimization of the reaction conditions[a]



Entry	Catalyst (mmol)	Oxidant (mmol)	Solvent (mL)	Yield (%)[b]
1	$Cu(OAc)_2$	TBHP	PhCl	20
2	$Cu(OAc)_2{\cdot}H_2O$	TBHP	PhCl	26
3	CuO	TBHP	PhCl	08
4	$CuBr_2$	TBHP	PhCl	35
5	$CuCO_3{\cdot}Cu(OH)_2$	TBHP	PhCl	54
6	Cu_2O	TBHP	PhCl	62
7	CuI	TBHP	PhCl	70 (20)[c]
8	CuBr	TBHP	PhCl	38
9	CuCl	TBHP	PhCl	27
10	-	TBHP	PhCl	00
11	CuI	-	PhCl	00
12	CuI	TBHP (aq.)	PhCl	34
13	CuI	TBPB	PhCl	30
14	CuI	TBP	PhCl	10
15	CuI	*m*-CPBA	PhCl	00
16	CuI	H2O2	PhCl	00
17	CuI	TBHP	PhCN	20
18	CuI	TBHP	DCE	07
19	CuI	TBHP	DCB	31
20[e]	CuI	TBHP	PhCl	56
21[d]	CuI	TBHP	PhCl	71
22[e]	CuI	TBHP	PhCl	59
23[f]	CuI	TBHP	PhCl	23
24[g]	CuI	TBHP	PhCl	70
25[h]	CuI	TBHP	PhCl	58

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (1 mmol), catalyst (0.1 mmol), oxidant (2 mmol), solvent (2 mL), 120 °C, 11 h, open to air. [b] GC yield. [c] reaction was carried out in closed vessel. [d] **2a** (0.75 mmol). [e] **2a** (1.25 mmol). [f] 130 °C. [g] 110 °C. [h] 15 h. [i] 8 h.

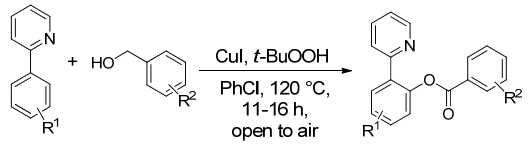
Next, we have tested various oxidants to enhance the yield of **3a** and it was observed that other organic peroxides such as TBHP (aq.), *tert*- butyl perbenzoate (TBPB) and di-tertiary butyl peroxide (TBP) have lower reactivity than TBHP (5.0–6.0 M in decane) (Table 1, entries 7 and 12–14). However, the reaction did not proceed when *m*-CPBA and H_2O_2 were used as oxidants (Table 1, entries 15 and 16). Furthermore, we have investigated the effect of various solvents on the reaction outcome and it was found that chlorobenzene is superior to other solvents (Table 1, entries 7 and 17–19). Further investigations revealed that mole ratio of **1a**:**2a** played an important role to increase the reaction yield. As the mole ratio of **1a**:**2a** was changed from 1:2 to 1:1.5 and 1:2.5, the yield of **3a** was obtained in 70%, 56% and 71% respectively (Table 1, entries 7, 20 and 21). Therefore, 1:2 mole ratio of **1a**:**2a** is the best choice.

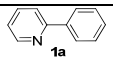
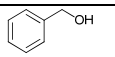
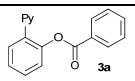
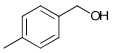
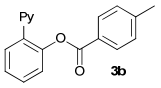
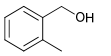
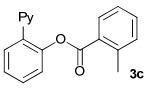
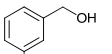
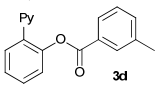
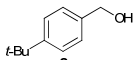
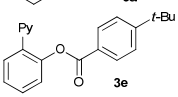
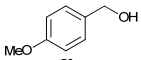
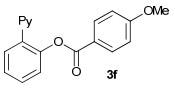
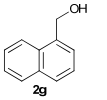
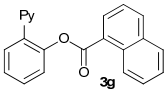
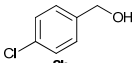
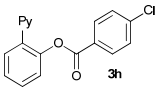
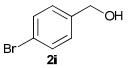
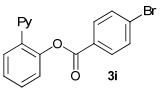
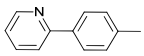
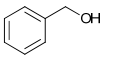
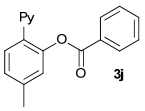
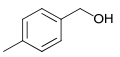
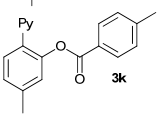
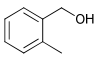
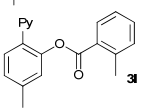
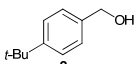
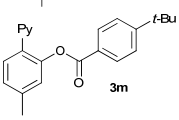
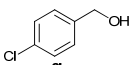
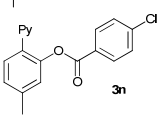
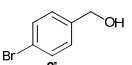
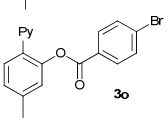
The effect of variation in the reaction temperature was also studied for the effective progress of benzoxylation reaction and 120 °C was found to be the optimum temperature (Table 1, entry 7). With increase or decrease in the reaction temperature, the yield of **3a** was found to decrease (Table 1, entries 22 and 23). Furthermore, with increase in the reaction time does not affect the reaction yield (Table 1, entry 24), whereas decrease in the reaction time from 11 h to 8 h resulted in low yield of **3a** (Table 1, entry 25). It shows that 11 h was an optimum reaction time to afford the high yield of **3a** (Table 1, entry 7). The lower loading of CuI or TBHP led to decrease in the reaction yield. Hence, optimized reaction parameters were: 2-phenylpyridine (0.5 mmol), benzyl alcohol (1 mmol), CuI (0.1 mmol), TBHP (2 mmol) in 2 mL chlorobenzene at 120 °C for 11 h.

With these optimized reaction conditions in hand, we have investigated the scope of the developed protocol for the synthesis of diverse *ortho* benzoxylated products from various *ortho*, *meta* and *para*-substituted benzyl alcohols with 2-phenylpyridine (Table 2). The reaction of **1a** with **2a** under the optimized reaction conditions provided 63% yield of the desired product **3a** (Table 2, entry 1). The *p*–Me, *o*–Me and *m*–Me benzyl alcohols were smoothly reacts with **1a** and furnished benzoxylated products **3b**–**3d** with 75%, 69% and 73% yields respectively (Table 2, entries 2–4). It shows that the position of the methyl substituent on the phenyl ring of benzyl alcohol marginally affects the reaction yield. Next, *p*-*tert*-butyl benzyl alcohol (**2e**) efficiently undergoes oxidative benzoxylation reaction with **1a** to deliver **3e** in 78% yield (Table 2, entry 5). The oxidative benzoxylation reaction of *p*-methoxy benzyl alcohol (**2f**) with **1a** also provided the desired product **3f** in good yield (Table 2, entry 6). Notably, the 1-naphthalenemethanol was also served as surrogate of the benzoxy group providing naphthylcarboxylation product **3g** in good yield (Table 2, entry 7). Furthermore, the halogen substituents like –Cl, –Br on the phenyl ring of benzyl alcohols were compatible under the present reaction conditions and deliver the corresponding benzoxylation products **3h** and **3i** in good yields (Table 2, entries 8 and 9). On the other hand, highly electron-deficient *p*-nitro benzyl alcohol and aliphatic alcohols such as 1-ethanol as well as 2-phenyl-1-ethanol were failed to provide the corresponding products. Moreover, the benzoxylation of 2-(*p*-tolyl) pyridine (**1b**) was also explored with a variety of benzyl alcohols under the optimized reaction conditions and the obtained results were summarised in table 2. It was observed that **1b** shows the same pattern of reactivity as observed for **1a** (Table 2, entries 10–15).

Proceeding further toward the substrate exploration of this protocol, a broad range of readily available benzyl amines were also screened for the oxidative benzoxylation of 2-phenylpyridine, as summarized in Table 3. The optimized reaction parameters using benzyl amine as arylcarboxy surrogate were: 2-phenylpyridine (0.5 mmol), benzyl amine (1 mmol), $Cu(OAc)_2$ (0.1 mmol), TBHP (2.5 mmol) at 120 °C for 17 h (See ESI for optimization table and plausible reaction mechanism of **1a** with **2j**). The reaction of 2-phenylpyridine with *ortho*, *meta* and *para* substituents like –Me, –*t*-Bu, –OMe and –Cl on the

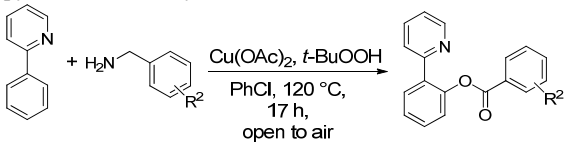
Table 2: Substrate scope for oxidative benzoxylation of 2-arylpyridine with benzyl alcohols.[a]

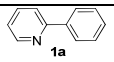
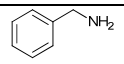
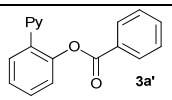
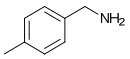
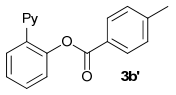
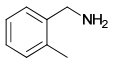


Entry	2-arylpyridines	Benzyl alcohols	Product	Yield (%)[b]
1				63
2	**1a**			75
3	**1a**			69
4	**1a**			73
5	**1a**			78
6	**1a**			63
7	**1a**			57
8	**1a**			60[c]
9	**1a**			60[c]
10				71
11	**1b**			77
12	**1b**			74
13	**1b**			80
14	**1b**			62[c]
15	**1b**			61[c]

[a] Reaction conditions: 2-phenylpyridine (0.5 mmol), benzyl alcohols (1 mmol), CuI (0.1 mmol), TBHP (2 mmol), PhCl (2 mL), 120 °C, 11 h, open to air. [b] Isolated yield. [c] 16 h.

Table 3: Substrate scope for oxidative benzoxylation of 2-arylpyridine with benzyl amines.[a]

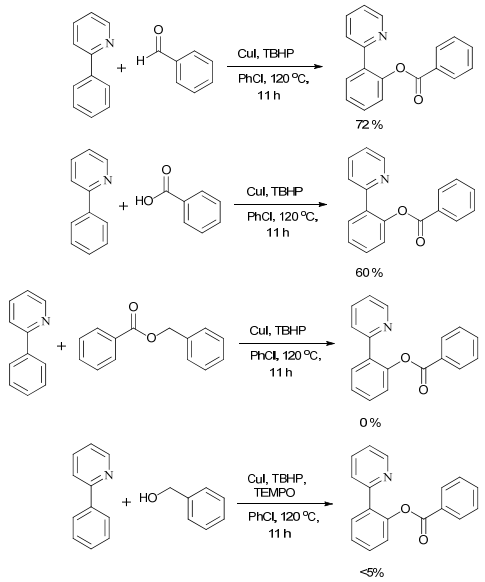


Entry	2-phenylpyridine	Benzyl amines	Product	Yield (%)[b]
1				41
2	**1a**			49
3	**1a**			46
4	**1a**			47
5	**1a**			51
6	**1a**			36
7	**1a**			36
8	**1a**			41

[a] Reaction conditions: **1a** (0.5 mmol), benzyl amines (1 mmol), $Cu(OAc)_2$ (0.1 mmol), TBHP (2 mmol), PhCl (2 mL), 120 °C, 17 h, open to air. [b] Isolated yield.

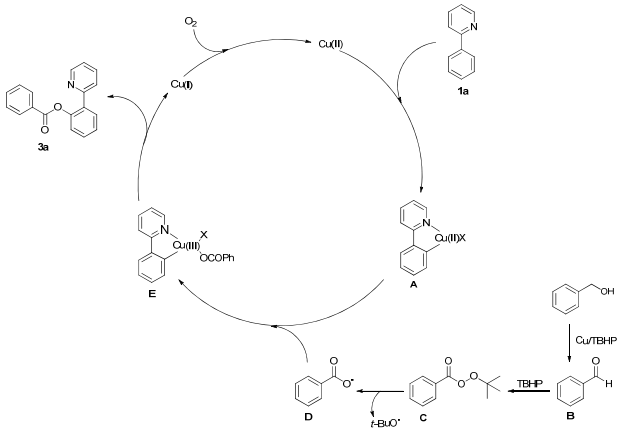
phenyl ring of benzyl amines delivered the corresponding benzoxylation products in moderate yields (Table 3, entries 1–7). Furthermore, the *N*-methyl benzylamine (**2q**) was also served as surrogate of the benzoxy group to provide the product **3a** in moderate yield (Table 3, entry 8). However, the *N*,*N*-dimethyl benzylamine was failed to provide the desired product **3a** under the optimized reaction conditions.

To probe the reaction mechanism of this transformation, a series of experiments were performed (Scheme 2). When the reaction mixture of **1a** with **2a** was examined using GC–MS analysis, it shows the presence of benzaldehyde, benzoic acid and benzyl benzoate in the reaction medium. To ascertain the reaction pathway the reaction of **1a** with benzaldehyde, benzoic acid and benzyl benzoate were performed separately and the benzoxylation product **3a** was obtained in 72%, 60% and 0% yields respectively (Scheme 2). Furthermore, the reaction of **1a** with **2a** in the presence of the radical scavenger TEMPO provided very low yield of **3a** (<5%) (Scheme 2). This result indicates that the benzoxylation reaction may proceed through a radical pathway.



Scheme 2: Control experiments.

On the basis of the above mechanistic investigation and previous reports,[13,15] a tentative mechanism for the copper-catalyzed *ortho*-C–H benzoxylation of **1a** is depicted in Scheme 3. The oxidative benzoxylation of 2-phenylpyridine (**1a**) is probably initiated by oxidation of Cu(I) to active Cu(II) species. Then, the active Cu(II) species forms a chelation with the 2-phenylpyridine *via* C-H bond activation to give the intermediate **A**. Meanwhile, benzyl alcohol gets converted to benzaldehyde **B** *via* C–H bond activation in the presence of Cu/ TBHP catalytic system. Next, benzaldehyde reacts with *tert*-butylperoxy radical generated from TBHP which gives *tert*-butyl perester **C**.[13] Homolytic cleavage of *tert*-butyl perester **C** provides the benzoxy radical **D** along with *tert*-butoxyl radical.[13] Then, benzoxy radical **D** reacts with a intermediate **A** to provide the Cu(III) intermediate **E**, which undergo reductive elimination to give the desired product **3a** and regenerate the Cu(I) catalyst for the next catalytic cycle.



Scheme 3: Plausible reaction mechanism of **1a** with **2a** .

In summary, a simple and efficient protocol has been developed for the benzoxylation of 2-phenylpyridine *via* C–H bond activation using commercially available copper catalyst and TBHP as an oxidant. Present catalytic system uses inexpensive, facile and readily available benzyl alcohols and benzyl amines as benzoxylation sources. The developed protocol gives benzoxylation products of 2-phenylpyridine in moderate to good yields under the present reaction conditions.

Experimental Section:

General:

All the chemicals were purchased from Sigma Aldrich, S.D. Fine chemical and commercial suppliers and were used without further purification. The progress of the reaction was monitored by gas chromatography Perkin Elmer Clarus 400 GC equipped with flame ionization detector (FID) with a capillary column (30 m × 0.25 mm × 0.25 μm) and thin layer chromatography using Merck silica gel 60 F254 plates. The products were visualized with a 254 nm UV lamp. GC-MS-QP 2010 instrument (Rtx-17, 30 m × 25 mm ID, film thickness (df) = 0.25 μm) (column flow 2 $mLmin^{-1}$, 80 °C to 240 °C at 10 °C/min rise) was used for the mass analysis of the products. Products were purified by column chromatography on 100–200 mesh silica gel. The ^1H NMR spectra were recorded on 300 MHz and 400 MHz spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as internal standard. The ^{13}C NMR spectra were recorded on 75 MHz and 100 MHz spectrometer in $CDCl_3$. Chemical shifts were reported in parts per million (δ) relative to tetramethylsilane as internal standard. *J* (coupling constant) values were reported in hertz. Splitting patterns of proton were described as s (singlet), d (doublet), dd (doublet of doublets), t (triplet) and m (multiplet). The products were confirmed by GC–MS, ^1H and ^{13}C NMR spectroscopic analysis.

General experimental procedure for oxidative benzoxylation of 2–phenylpyridine with benzyl alcohol:

2-phenylpyridine (**1a**, 0.5 mmol), benzyl alcohol (**2a**, 1 mmol) and CuI (0.1 mmol) in 2 mL chlorobenzene was charged in an oven dried 10 mL two-necked round bottom flask. At room temperature TBHP (5–6 M in decane, 2 mmol) was added dropwise to the reaction flask with stirring. The flask was then equipped with a condenser and the reaction mixture was stirred at 120 °C for 11 h in open air and progress of reaction was monitored by TLC and GC. After completion, the reaction mixture was allowed to cool to room temperature, diluted with ethyl acetate (10 mL) and filtered through a celite bed. The celite bed was washed with ethyl acetate (3 × 5 mL). Consequently, the ethyl acetate layer was washed with 5% aqueous solution of sodium bicarbonate (2 × 5 mL) followed by water (2 × 5 mL). The combined ethyl acetate extracts were dried over Na_2SO_4 and the solvent was evaporated by rotary evaporation to obtain the crude product which was then purified by column chromatography (silica gel, 100–200 mesh size), with petroleum ether/ethyl acetate as eluent to afford a pure product. The products were confirmed by GC-MS, ^1H and ^{13}C NMR spectroscopic analysis.

General experimental procedure for oxidative benzoxylation of 2–phenylpyridine with benzyl amine:

A mixture of 2-phenylpyridine (**1a**, 0.5 mmol), benzyl amine (**2j**, 1 mmol) and $Cu(OAc)_2$ (0.1 mmol) in 2 mL chlorobenzene was placed in an oven dried 10 mL two-necked round bottom flask.

At room temperature TBHP (5–6 M in decane, 2.5 mmol) was added dropwise to the reaction flask with stirring. The flask was then equipped with a condenser and the reaction mixture was stirred at 120 °C for 17 h in open air. The progress of the reaction was monitored by TLC and GC. After completion, the reaction mixture was allowed to cool to room temperature, diluted with ethyl acetate (10 mL) and filtered through a celite bed. The celite bed was washed with ethyl acetate (3 × 5 mL). Consequently, the ethyl acetate layer was washed with 5% solution of sodium bicarbonate solution (2 × 5 mL) followed by water (2 × 5 mL). The ethyl acetate extracts were dried over Na_2SO_4 and the solvent was evaporated by rotary evaporation to obtain the crude product which was then purified by column chromatography (silica gel, 100–200 mesh size), with petroleum ether/ethyl acetate as eluent to afford a pure product. All compounds were confirmed by GC–MS, ^{1}H NMR and ^{13}C NMR spectroscopic analysis.

Characterisation data of products:

2-(pyridin-2-yl)phenyl benzoate (**3a**). Yellow oil; 86 mg (63%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62–8.60 (m, 1H), 8.10–8.07 (m, 2H), 7.79–7.77 (m, 1H), 7.64–7.56 (m, 3H), 7.50–7.39 (m, 4H), 7.32–7.29 (m, 1H), 7.18–7.16 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.16, 155.54, 149.58, 148.30, 136.19, 133.45, 133.30, 130.93, 130.17, 129.74, 129.48, 128.59, 126.41, 123.74, 123.32, 122.16; GCMS (EI, 70 eV): *m/z* (%): 275 (14, M^+), 105 (100), 77 (33).

2-(pyridin-2-yl)phenyl 4-methylbenzoate (**3b**). Yellow oil; 108 mg (75%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61–8.60 (m, 1H), 7.97 (d, J = 8.0 Hz, 2H), 7.78 (dd, J = 7.6, 1.8 Hz, 1H), 7.63–7.54 (m, 2H), 7.49–7.45 (m, 1H), 7.41–7.37 (m, 1H), 7.30 (dd, J = 8.0, 1.2 Hz, 1H), 7.25 (d, J = 8.0 Hz, 2H), 7.16–7.13 (m, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.20, 155.57, 149.62, 148.35, 144.29, 136.12, 133.35, 130.91, 130.24, 129.69, 129.22, 126.71, 126.32, 123.76, 123.37, 122.10, 21.73; GCMS (EI, 70 eV): *m/z* (%): 289 (9, M^+), 119 (100), 91 (29), 40 (13).

2-(pyridin-2-yl)phenyl 2-methylbenzoate (**3c**). Yellow oil; 99 mg (69%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (d, J = 5.0 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 8.4 Hz, 1H), 7.66–7.63 (m, 1H), 7.56–7.54 (m, 1H), 7.50–7.47 (m, 1H), 7.43–7.38 (m, 2H), 7.30–7.24 (m, 4H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.71, 155.83, 149.54, 148.33, 141.21, 136.22, 133.51, 132.49, 131.76, 131.07, 130.88, 129.73, 128.56, 126.33, 125.77, 123.73, 123.42, 122.15, 21.60; GCMS (EI, 70 eV): *m/z* (%): 289 (3, M^+), 119 (100), 91 (36), 40 (5).

2-(pyridin-2-yl)phenyl 3-methylbenzoate (**3d**). Yellow oil; 105 mg (73%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64–8.62 (m, 1H), 7.90–7.86 (m, 2H), 7.77 (d, J = 8.0 Hz, 1H), 7.61–7.53 (m, 2H), 7.45 (d, J = 8.0 Hz, 1H), 7.40–7.30 (m, 4H), 7.17–7.12 (m, 1H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.27, 155.42, 149.42, 148.31, 138.30, 136.36, 134.27, 133.14, 130.93, 130.69, 129.78, 129.28, 128.37, 127.29, 126.36, 123.86, 123.27, 122.23; GCMS (EI, 70 eV): *m/z* (%): 289 (13.6, M^+), 119 (100), 91 (37.4), 65 (10.5).

2-(pyridin-2-yl)phenyl 4-(*tert*-butyl)benzoate (**3e**). Yellow oil; 129 mg (78%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 4.9 Hz, 1H), 8.01 (d, J = 8.4 Hz, 2H), 7.79 (d, J = 7.6 Hz, 1H), 7.65–7.61 (m, 1H), 7.57 (d, J = 7.6 Hz, 1H), 7.49–7.45 (m, 3H), 7.39 (t, J = 7.6 Hz, 1H), 7.28 (t, J = 8.0 Hz, 1H), 7.18–7.15 (m, 1H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.15, 157.26, 155.56, 149.65, 148.33, 136.15, 133.36, 130.96, 130.08, 129.69, 126.64, 126.31, 125.51, 123.81, 123.34, 122.12, 35.18, 31.10; GCMS (EI, 70 eV): *m/z* (%): 331 (7, M^+), 162 (12), 161 (100).

2-(pyridin-2-yl)phenyl 4-methoxybenzoate6c (**3f**). Yellow oil; 96 mg (63%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 4.8 Hz, 1H), 8.04 (d, J = 8.8 Hz, 2H), 7.77 (dd, J = 7.6, 1.7 Hz, 1H), 7.62–7.59 (m, 1H), 7.56–7.54 (m, 1H), 7.48–7.45 (m, 1H), 7.40–7.36 (m, 1H), 7.30–7.28 (m, 1H), 7.17–7.14 (m, 1H), 6.92 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.86, 163.82, 155.58, 149.58, 148.38, 136.14, 133.34, 132.31, 130.90, 129.69, 126.25, 123.80, 123.40, 122.11, 121.74, 113.78, 55.48; GCMS (EI, 70 eV): *m/z* (%): 305 (5, M^+), 135 (100), 77 (12), 40 (6).

2-(pyridin-2-yl)phenyl 1-naphthoate (**3g**). Yellow oil; 92 mg (57%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (d, J = 8.8 Hz, 1H), 8.59 (d, J = 5.0 Hz, 1H), 8.31 (d, J = 8.8 Hz, 1H), 8.06 (d, J = 7.8 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.62–7.49 (m, 6H), 7.45–7.42 (m, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.17–7.13 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.70, 155.84, 149.54, 148.38, 136.31, 134.01, 133.80, 133.59, 131.58, 131.03, 130.91, 129.81, 128.53, 128.01, 126.45, 126.33, 125.96, 125.81, 124.46, 123.65, 123.50, 122.18; GCMS (EI, 70 eV): *m/z* (%): 325 (5, M^+), 155 (100), 127 (48).

2-(pyridin-2-yl)phenyl 4-chlorobenzoate (**3h**). Yellow oil; 92 mg (60%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57–8.56 (m, 1H), 8.01 (d, J = 8.8 Hz, 2H), 7.76 (dd, J = 8.0, 1.6 Hz, 1H), 7.66–7.62 (m, 1H), 7.55–7.45 (m, 2H), 7.44–7.40 (m, 3H), 7.30 (d, J = 8.0 Hz, 1H), 7.18–7.15 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.35, 155.55, 149.53, 148.12, 139.98, 136.29, 133.19, 131.54, 131.08, 130.90, 129.80, 128.85, 126.55, 123.63, 123.26, 122.23; GCMS (EI, 70 eV): *m/z* (%): 309 (10.2, M^+), 141 (33.8), 139 (100), 111 (26.9), 75 (9.4), 44 (9.7).

2-(pyridin-2-yl)phenyl 4-bromobenzoate (**3i**). Yellow oil; 105 mg (60%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 8.5 Hz, 2H), 7.73 (dd, J = 7.6, 1.6 Hz, 1H), 7.60–7.38 (m, 6H), 7.29 (d, J = 7.9 Hz, 1H), 7.18–7.13 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.49, 155.46, 149.46, 148.08, 136.41, 133.08, 131.87, 131.53, 130.90, 129.84, 128.71, 128.49, 126.57, 123.69, 123.24, 122.29; GCMS (EI, 70 eV): *m/z* (%): 355 (18.7, $(M+2)^+$), 353 (18.9, M^+), 185 (95), 183 (100), 157 (22.5), 155 (24.2), 76 (16.6), 75 (12.3).

5-methyl-2-(pyridin-2-yl)phenyl benzoate (**3j**). Yellow oil; 102 mg (71%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57–8.54 (m, 1H), 8.10–8.06 (m, 2H), 7.68 (d, J = 8.0 Hz, 1H), 7.60–7.50 (m, 3H), 7.46–7.38 (m, 2H), 7.21–7.17 (m, 1H), 7.12–7.02 (m, 2H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.32, 155.54, 149.52, 148.15, 140.24, 136.22, 133.48, 130.70, 130.36, 130.17, 129.55, 128.52, 127.33, 123.81, 123.62, 121.98, 21.22; GCMS (EI, 70 eV): *m/z* (%): 289 (11.3, M^+), 105 (100), 77 (34.4).

5-methyl-2-(pyridin-2-yl)phenyl 4-methylbenzoate (**3k**). Yellow oil; 116 mg (77%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58–8.57 (m, 1H), 7.97 (d, J = 8.2 Hz, 2H), 7.69 (d, J = 7.8 Hz, 1H), 7.60–7.52 (m, 2H), 7.24 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.6 Hz, 1H), 7.13–7.09 (m, 2H), 2.42 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.32, 155.58, 149.54, 148.16, 144.23, 140.13, 136.06, 130.64, 130.41, 130.22, 129.21, 127.20, 126.79, 123.80, 123.59, 121.86, 21.72, 21.19; GCMS (EI, 70 eV): *m/z*

(%): 303 (11, M^+), 120 (9), 119 (100), 91 (28).

5-methyl-2-(pyridin-2-yl)phenyl 2-methylbenzoate (3l). Yellow oil; 112 mg (74%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59–8.57 (m, 1H), 8.02–7.99 (m, 1H), 7.70–7.39 (m, 4H), 7.26–7.10 (m, 5H), 2.53 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.80, 155.78, 149.41, 148.08, 141.12, 140.18, 136.18, 132.42, 131.72, 131.03, 130.57, 130.48, 128.60, 127.18, 125.73, 123.82, 123.57, 121.90, 21.59, 21.17; GCMS (EI, 70 eV): *m/z* (%): 303 (2.5, M^+), 119 (100), 91 (37.2), 65 (10.4).

5-methyl-2-(pyridin-2-yl)phenyl 4-(*tert*-butyl)benzoate (3m). Yellow oil; 138 mg (80%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62–8.59 (m, 1H), 8.06–7.98 (m, 1H), 7.87–7.84 (m, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.62–7.54 (m, 2H), 7.48–7.38 (m, 3H), 7.26–7.23 (m, 1H), 7.11–7.06 (m, 1H), 2.43 (s, 3H), 1.35 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.28, 157.23, 155.53, 149.51, 148.17, 140.19, 136.23, 130.72, 130.10, 130.00, 127.23, 126.72, 125.52, 125.41, 123.80, 121.96, 35.18, 31.12, 21.23; GCMS (EI, 70 eV): *m/z* (%): 345 (8.6, M^+), 162 (12.2), 161 (100), 118 (9.4).

5-methyl-2-(pyridin-2-yl)phenyl 4-chlorobenzoate (3n). Yellow oil; 100 mg (62%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 4.8 Hz, 1H), 8.00 (d, J = 8.8 Hz, 2H), 7.65 (d, J = 8.0 Hz, 1H), 7.63–7.58 (m, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.42 (d, J = 8.6 Hz, 2H), 7.21 (d, J = 8.6 Hz, 1H), 7.14–7.10 (m, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.48, 155.60, 149.49, 147.94, 140.29, 139.91, 136.21, 131.53, 130.61, 130.25, 128.85, 128.04, 127.42, 123.71, 123.45, 121.96, 21.20; GCMS (EI, 70 eV): *m/z* (%): 323 (16, M^+), 141 (34), 140 (8), 139 (100), 111 (24).

5-methyl-2-(pyridin-2-yl)phenyl 4-bromobenzoate (3o). Yellow oil; 112 mg (61%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51–8.50 (m, 1H), 7.94–7.90 (m, 2H), 7.61–7.55 (m, 3H), 7.49 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.17–7.09 (m, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.60, 155.50, 149.37, 147.90, 140.35, 136.36, 131.86, 131.63, 131.41, 130.61, 128.47, 128.42, 127.43, 123.68, 123.54, 122.05, 21.20; GCMS (EI, 70 eV): *m/z* (%): 369 (20.1, $(M+2)^+$), 367 (20.4, M^+), 185 (96.9), 184 (12.1), 183 (100), 157 (21.5), 155 (23.4), 76 (14.2), 75 (9.8).

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