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Palladium-Catalyzed Oxidative Carbonylation of Aromatic C−H Bonds of *N*-Alkylanilines with CO and Alcohols for the Synthesis of *o*-Aminobenzoates

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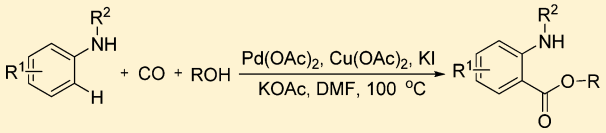
Supporting Information

ABSTRACT: A Pd(II)-catalyzed C−H monocarbonylation of *N*-alkylanilines for the synthesis of *o*-aminobenzoates has been developed. Various aliphatic alcohols and phenol were tolerated in the reaction to afford the corresponding *o*-aminobenzoates in good yields under mild balloon pressure of CO.

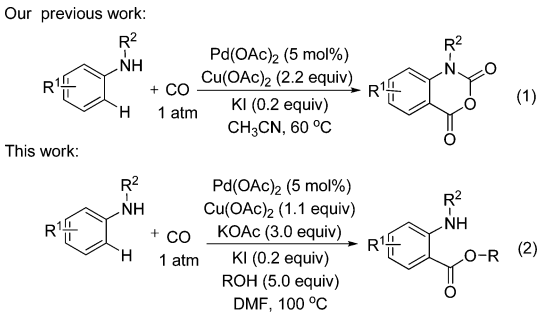


Carbonylation reactions have proven to be a powerful tool in organic synthesis, and they have received considerable attention over the past decades.[1] In particular, the C−H bond carbonylation has become a useful method for the synthesis of carbonyl compounds such as acids,[2] ester,[3] amides,[4] ketone,[5] and anhydrides.[6] In these reactions, the direct carbonylation of C−H bonds with CO and alcohols for the synthesis of aryl esters or vinyl esters have received considerable attention.[7] Recently, Pd-, Ru-, or Rh-catalyzed oxidative carbonylation of urea, *N*,*N*-dimethylbenzylamines, indoles, and 2-phenylpyridine for the synthesis of esters were developed by several research groups including ours.[3a,8] Directing groups play an important role in these reactions. However, only a small number of functional groups can act as the directing groups to assist the *ortho* C−H carbonylation. The search for new and synthetically versatile directing groups is still a challenging task in C−H bond carbonylation.[9]

O-Aminobenzoates and their derivatives are valuable commodity chemicals and highly reactive intermediates.[10] However, the conventional methods for the synthesis of *o*-aminobenzoates generally require multistep procedures under harsh reaction conditions.[11] Thus, the development of a simple and economic method for the synthesis of *o*-aminobenzoates is highly desirable. In 2012, we developed a Pd-catalyzed C−H bond carbonylation of *N*-alkylanilines, affording synthetically useful isatoic anhydrides under mild conditions (Scheme 1, eq 1).[6a] The reaction proceeded through a Pd-catalyzed one-pot double carbonylation of *N*-alkylanilines via an anthranilic acid intermediate.[6a,b] Based on our previous study, we hypothesized that *o*-aminobenzoates may be obtained by the Pd-catalyzed C−H bond carbonylation of *N*-alkylanilines in the presence of an alcohol. In this paper, we report the Pd-catalyzed monocarbonylation of the C−H bond of *N*-alkylanilines for the synthesis of *o*-aminobenzoates (Scheme 1, eq 2).

We began our study by investigating the Pd-catalyzed oxidative carbonylation of *N*-methylaniline **1a** and ethanol **2a** under a balloon pressure of CO. We were pleased to obtain

Scheme 1. Palladium-Catalyzed Oxidative Carbonylation of *N*-Alkylanilines



the product of *o*-aminobenzoate **3aa** in 42% yield along with isatoic anhydride **4aa** in 20% yield when the reaction was performed using $Pd(OAc)_2$ as a catalyst in the presence of $Cu(OAc)_2$ and KI in DMF at 100 °C (Table 1, entry 1).[12] For optimizing the reaction conditions, the effect of bases was investigated, and we found that base plays an important role in this oxidative carbonylation reaction. KOAc was found to be superior to K_2CO_3, K_3PO_4, and Cs_2CO_3 (Table 1, entries 2−5). Various oxidants such as BQ, $CuCl_2$, and $CuBr_2$ were also screened. $Cu(OAc)_2$ was found to be the optimum choice (Table 1, entries 7−9). Further, the effect of different solvents was investigated; however, no improvement was observed (Table 1, entries 10−13). Surprisingly, the yield of *o*-aminobenzoate **3aa** increased to 74% in the presence of 3.0 equiv of KOAc, and only 9% yield of byproduct, isatoic anhydride, was observed (Table 1, entry 14).

After optimization of the reaction conditions, the substrate scope of the carbonylation was investigated, and the results are listed in Table 2. This oxidative carbonylation was found to be a good methodology for the synthesis of *o*-amino-

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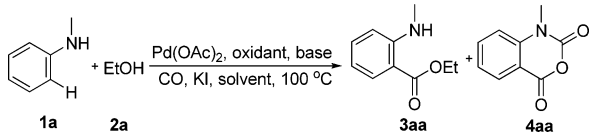
Table 1. Optimization of Reaction Conditions for the Carbonylation of *N*-Methylaniline[a]



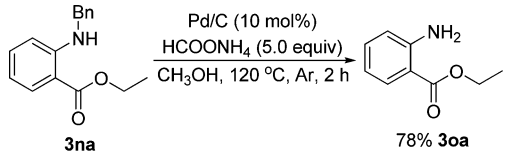
entry	oxidant	base	solvent	yield **3aa** (%)	yield **4aa** (%)
1	$Cu(OAc)_2$		DMF	42	20
2	$Cu(OAc)_2$	K_2CO_3	DMF	47	7
3	$Cu(OAc)_2$	KOAc	DMF	68	11
4	$Cu(OAc)_2$	K_3PO_4	DMF	53	15
5	$Cu(OAc)_2$	Cs_2CO_3	DMF	56	11
6	$Cu(OAc)_2$	KOAc	DMF	67	12[b]
7	BQ	KOAc	DMF	11	0
8	$CuCl_2$	KOAc	DMF	56	0
9	$CuBr_2$	KOAc	DMF	56	0
10	$Cu(OAc)_2$	KOAc	toluene	20	5
11	$Cu(OAc)_2$	KOAc	THF	0	0
12	$Cu(OAc)_2$	KOAc	DMA	67	14
13	$Cu(OAc)_2$	KOAc	DMSO	50	10
14	$Cu(OAc)_2$	KOAc	DMF	74	9[c]

[a]Reaction conditions: *N*-methylaniline **1a** (0.2 mmol), $Pd(OAc)_2$ (5 mol %), oxidant (1.1 equiv), KI (20 mol %), base (1.5 equiv), ethanol (5.0 equiv), CO (1 atm), solvent (2.0 mL), at 100 °C. [b]KI (1.0 equiv). [c]3.0 equiv of base.

benzoates. Notably, the reaction was successfully performed on a 1.0 mmol scale to afford *o*-aminobenzoate **3aa** in 65% yield (Table 2, entry 1). *N*-Methylanilines with electron-donating or -withdrawing groups such as methyl, methoxyl, chloro, and bromo groups on phenyl rings were tolerated under the reaction conditions, and the corresponding *o*-aminobenzoates **3ba**–**ia** were obtained in moderate to good yields (Table 2, entries 2–9). In general, the electron-rich substrates were more reactive because of their slightly stronger nucleophilicity. For example, methyl-substituted *o*-aminobenzoates **3ba** and **3da** were obtained in 72% yield (Table 2, entries 2 and 4). However, the strong electron-donating methoxy group on the phenyl ring decreased the yield of the reactions because of the formation of an isatoic anhydride byproduct (Table 2, entries 5–6). *m*-Chloro- and -bromo-substituted *N*-methylanilines **1h** and **1i** were transformed into the corresponding *o*-aminobenzoates **3ha** and **3ia** in 44% and 37% yield, respectively, indicating that the carbonylation was sensitive to electronic features of the *N*-methylanilines.[13] Similarly, the carboxylic ester **3ja** from the carbonylation of 2-naphthylamine **1j** was obtained in 50% yield (Table 2, entry 10). In addition, different alkyl substituents on the anilines were also investigated. *N*-Ethyl- and propyl-substituted anilines and tetrahydroquinoline **1k**–**m** were used, and the anticipated *o*-aminobenzoates were obtained in 48–67% yields (Table 2, entries 11–13). *N*-Benzylaniline **1n** also afforded *o*-aminobenzoate **3na** in 43% yield (Table 2, entry 14), and the benzyl group can be easily removed under reductive condition with Pd/C as catalyst to afforded *o*-aminobenzoate **3oa** in 78% yield (Scheme 2).[14]

Under the optimized conditions, the effect of directing group was next investigated. When aniline **1o** was used as the substrate, the product, ethyl phenylcarbamate (52%), was formed along with *N*,*N*′-diphenylurea (18%).[3e] A secondary amine such as diphenylamine **1p** was also examined under the

Scheme 2. Debenzylation of the *o*-Aminobenzoate

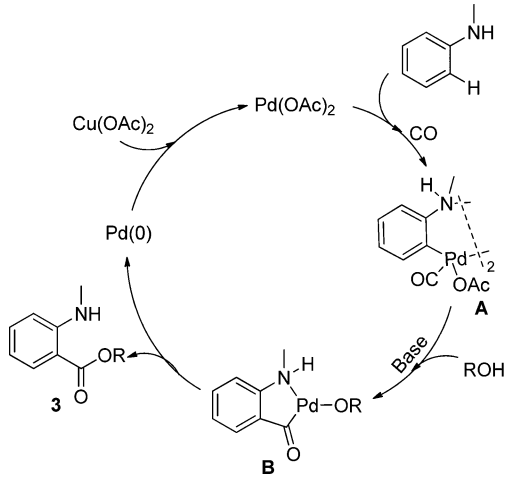


standard conditions. However, no reaction was observed (Table 2, entry 16). Tertiary anilines such as *N*,*N*-dimethylaniline **1q** only afforded a trace of ethyl 2-(dimethylamino)benzoate (Table 2, entry 17).[6a]

Furthermore, we investigated different alcohols for this carbonylation, and the results are listed in Table 3. To our delight, we found that both primary and secondary alcohols afforded the corresponding *o*-aminobenzoates in good yields. When methanol was used as a substrate, 70% yield of **3ab** was obtained. Simple alkyl alcohols such as propanol and butanol were also suitable for this transformation (**3ac**–**ad**). However, the sterically hindered 2-propanol exhibited lower efficiency. Fortunately, when benzyl alcohol was used as the nucleophile, the desired products **3af** was obtained in 77% yield. In particular, the reaction proceeded smoothly to afford **3ag** in 68% yield when phenol was used as the substrate. However, the reaction failed to synthesize *o*-aminobenzamides when amines, such as piperidine and morpholine, were used instead of alcohols.

On the basis of the previous studies,[6a] a plausible mechanism for this carbonylation is proposed in Scheme 3.

Scheme 3. Tentative Mechanism for the Reaction



The C–H bond activation of *N*-methylaniline by $Pd(OAc)_2$ results in dimeric palladium intermediate **A** in the presence of CO,[6a] followed the insertion of CO into **A**, and subsequent coordination to alcohols forms intermediate **B** assisted by KOAc. Finally, the reductive elimination of **B** affords carbonylation product **3** and Pd(0), which is oxidized to Pd(II) by $Cu(OAc)_2$ to regenerate the catalyst and complete the catalytic cycle.

In summary, we developed an efficient Pd-catalyzed oxidative C–H bond carbonylation of *N*-alkylanilines with CO and alcohols for the synthesis of *o*-aminobenzoates. This novel Pd-catalyzed carbonylation reaction is an alternative protocol for the synthesis of valuable *o*-aminobenzoates in moderate to good yield under balloon pressure of CO.

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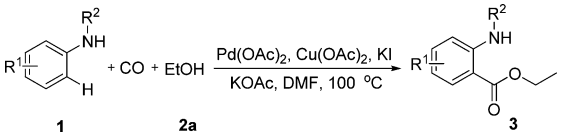
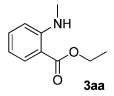
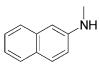
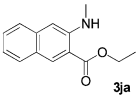
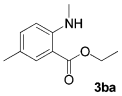
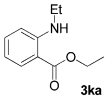
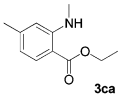
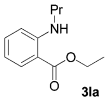
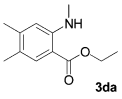
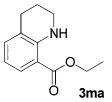
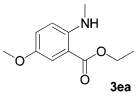
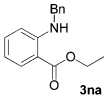
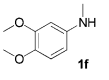
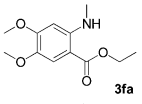
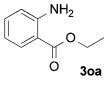
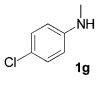
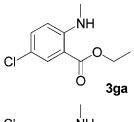
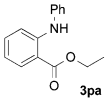
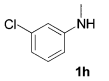
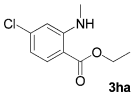
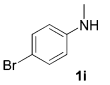
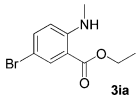
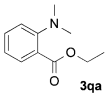
Table 2. Substrate Scope for Carbonylation of *N*-Alkylaniline Derivatives[a]



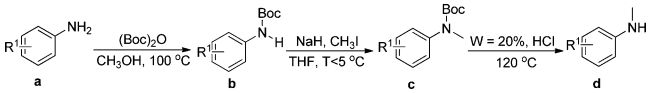
Entry	substrate	product	t (h)	yield (%)	Entry	substrate	product	t (h)	yield (%)
1	 1a	 3aa	12	74 (65)[b]	10	 1j	 3ja	24	50[d]
2	 1b	 3ba	12	72	11	 1k	 3ka	22	67[d]
3	 1c	 3ca	21	60	12	 1l	 3la	48	48
4	 1d	 3da	13	72	13	 1m	 3ma	8	49[d]
5	 1e	 3ea	9	56	14	 1n	 3na	46	43[c]
6	 1f	 3fa	13	54	15	 1o	 3oa	24	0[e]
7	 1g	 3ga	5	65[c]	16	 1p	 3pa	24	0
8	 1h	 3ha	6	44[c]					
9	 1i	 3ia	13	37[c]	17	 1q	 3qa	24	5

[a]Reaction conditions: *N*-alkylaniline **1** (0.2 mmol), $Pd(OAc)_2$ (5 mol %), $Cu(OAc)_2$ (1.1 equiv), KI (20 mol %), KOAc (3 equiv), and ethanol (5.0 equiv) under CO (1 atm) in 2.0 mL of DMF at 100 °C. [b]**1a** (1 mmol), DMF (8 mL), 24 h. [c]In the absence of KOAc and at 120 °C. [d]1.5 equiv of KOAc. [e]The product ethyl phenylcarbamate was formed in 52% yield, along with *N*,*N*′-dipehnylurea in 18% yield.

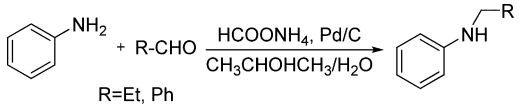
EXPERIMENTAL SECTION

General Information. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad. Coupling constants *J* were reported in hertz. All products were characterized by HRMS (ESI-TOF-Q); copies of their ^1H NMR and ^{13}C NMR spectra are provided in the Supporting Information. Unless otherwise stated, all reagents and solvents were purchased from commercial suppliers and used without further purification.

Typical Procedure for Synthesis of *N*-Alkylanilines.



Method 1: Substituted aniline **a** (10.0 mmol) was protected with $(Boc)_2O$ (12 mmol, 2.1824 g) in CH_3OH (30 mL) at 100 °C for 6 h to afford products **b** in quantitative yields. Then, anhydrous THF (8 mL) was added to the pure **b**, followed by addition of NaH (12 mmol, 288 mg) at <5 °C in an ice bath with vigorous stirring for 1 min. Subsequently, CH_3I (12 mmol, 0.75 mL) was injected in the reaction mixture, and the resulting reaction mixture was stirred for 4−24 h and monitored by TLC until reaction completion. Crude product **c** was further by silica gel chromatography with hexane/ethyl acetate (20:1). Finally, **c** was deprotected by mass fraction 20% HCl (5 mL) at 120 °C. After the completion, the reaction mixture was cooled to room temperature, and the reaction mixture was washed with 3 M NaOH (15 mL) and extracted with ethyl acetate. The crude product was purified by silica gel chromatography to afford corresponding products **d** in 90% yield.[15]



Method 2, synthesis *N*-benzylaniline: A mixture of 2-propanol (10 mL) with Pd/C (10 mol %, 424 mg) and ammonium formate (20 mmol, 1.2612 g) was stirred in a flask, followed by additionof 1 mL of H_2O to the flask, and the mixture was vigorously stirred for 1 min to activate Pd/C. Then, aniline (2.0 mmol, 186.1 mg) and benzaldehyde (2.0 mmol, 212.1 mg) were immediately added to the reaction mixture, and the reaction mixture was stirred at room temperature. The progress of the reaction was monitored by TLC. After reaction completion, the Pd/C catalyst was filtered off on

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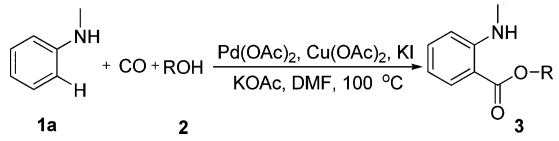
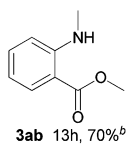
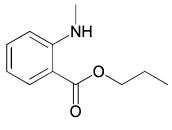
Table 3. Substrate Scope for Carbonylation of *N*-Methylaniline and Alcohols[a]



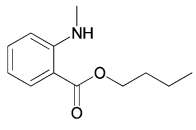
1a 2 3



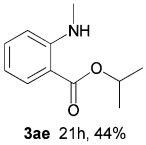
3ab 13h, 70%[b]



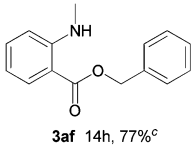
3ac 15h, 73%



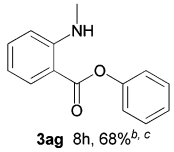
3ad 20h, 72%



3ae 21h, 44%



3af 14h, 77%[c]



3ag 8h, 68%[b, c]

[a]Reaction conditions: *N*-Methylaniline **1a** (0.2 mmol), $Pd(OAc)_2$ (5 mol %), $Cu(OAc)_2$ (1.1 equiv), KI (20 mol %), KOAc (3 equiv), and alcohol (5.0 equiv) under CO (1 atm) in 2.0 mL of DMF at 100 °C. [b]KOAc (1.5 equiv). [c]Alcohol (2.0 equiv).

Celite, and the solvent was removed by rotary evaporation. The residue was purified by silica gel column chromatography with hexane/ethyl acetate (50:1) as the eluent.[16]

Typical Procedure for Carbonylation of *N*-Alkylanilines for Synthesis of *o*-Aminobenzoates. A mixture of *N*-alkylaniline **1** (0.2 mmol), ROH (1.0 mmol), $Pd(OAc)_2$ (5 mol %, 2.2 mg), $Cu(OAc)_2$ (0.22 mmol, 40 mg), KI (0.04 mmol, 6.6 mg), KOAc (0.6 mmol, 58.8 mg), and DMF (2 mL) was charged in a 10 mL round-bottom flask. Then, the flask was evacuated and backfilled with CO (three times, balloon) and stirred at 100 °C. When the reaction was completed (detected by TLC), the mixture was cooled to room temperature and vented to discharge the excess CO. The reaction was quenched with H_2O (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and then evaporated in vacuo. The residue was purified by column chromatography on silica gel to afford the corresponding *o*-aminobenzoates **3** with hexane/ethyl acetate (40/1) as the eluent.

Ethyl 2-(methylamino)benzoate (**3aa**): yield 74% (26.5 mg), colorless liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.92 (d, J = 8.0 Hz, 1 H), 7.66 (br s, 1 H), 7.37 (t, J = 7.2 Hz, 1 H), 6.66 (d, J = 8.4 Hz, 1 H), 6.58 (t, J = 7.2 Hz, 1 H), 4.33−4.28 (m, 2 H), 2.90 (d, J = 3.2 Hz, 3 H), 1.37 (t, J = 7.2 H, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.7, 152.0, 134.5, 131.5, 114.2, 110.6, 110.1, 60.1, 29.5, 14.3; HRMS calcd (ESI) m/z for $C_{10}H_{13}NNaO_2$ $[M + Na]^+$ 202.0838, found 202.0844.

Ethyl 5-methyl-2-(methylamino)benzoate (**3ba**): yield 72% (27.8 mg), colorless liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.74 (s, 1 H), 7.48 (br s, 1 H), 7.22 (d, J = 8.4 Hz, 1 H), 6.61 (d, J = 8.4 Hz, 1 H), 4.35−4.31 (m, 2 H), 2.90 (s, 3 H), 2.26 (s, 3 H), 1.41−1.38 (m, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.6, 150.1, 135.5, 131.2, 123.1, 110.7, 109.8, 60.1, 29.6, 20.1, 14.3. HRMS calcd (ESI) m/z for $C_{11}H_{15}NNaO_2$ $[M + Na]^+$ 216.0995, found 216.1000.

Ethyl 4-methyl-2-(methylamino)benzoate (**3ca**): yield 60% (23.2 mg), white solid; mp 49−50 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.80 (d, J = 8.0 Hz, 1 H), 7.63 (br s, 1 H), 6.45 (s, 1 H), 6.40 (d, J = 8.0 Hz, 1 H), 4.31−4.26 (m, 2 H), 2.88 (d, J = 4.4 Hz, 3 H), 2.32 (s, 3 H), 1.35 (t, J = 7.2 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.6, 152.0, 145.2, 131.4, 115.6, 110.8, 107.6, 59.9, 29.4, 22.1, 14.3; HRMS calcd (ESI) m/z for $C_{11}H_{15}NNaO_2$ $[M + Na]^+$ 216.0995, found 216.0999.

Ethyl 4,5-dimethyl-2-(methylamino)benzoate (**3da**): yield 72% (29.8 mg), white solid; mp 48−49 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.65 (s, 1 H), 7.41 (br s, 1 H), 6.46 (s, 1 H), 4.31−4.26 (m, 2 H), 2.87 (s, 3 H), 2.23 (d, J = 6.4 Hz, 3 H), 2.14 (d, J = 6.4 Hz, 3 H), 1.36 (t, J = 6.8 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.6, 150.5, 144.1, 131.6, 122.4, 111.8, 107.8, 59.9, 29.6, 20.6, 18.5, 14.4; HRMS calcd (ESI) m/z for $C_{12}H_{17}NNaO_2$ $[M + Na]^+$ 230.1151, found 230.1158.

Ethyl 5-methoxy-2-(methylamino)benzoate (**3ea**): yield 56% (23.4 mg), colorless liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.44 (s, 1 H), 7.29 (br s, 1 H), 7.04 (d, J = 8.8 Hz, 1 H), 6.61 (d, J = 8.8 Hz, 1 H), 4.32−4.28 (m, 2 H), 3.75 (s, 3 H), 2.86 (s, 3 H), 1.36 (t, J = 6.8 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.2, 149.0, 147.3, 122.9, 114.5, 111.9, 109.8, 60.2, 55.9, 29.9, 14.3. HRMS calcd (ESI) m/z for $C_{11}H_{15}NNaO_3$ $[M + Na]^+$ 232.0944, found 232.0947.

Ethyl 4,5-dimethoxy-2-(methylamino)benzoate (**3fa**): yield 54% (25.8 mg), white solid; mp 103−104 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.62 (br s, 1 H), 7.39 (s, 1 H), 6.11 (s, 1 H), 4.31−4.26 (m, 2 H), 3.91 (s, 3 H), 3.82 (s, 3 H), 2.89 (s, 3 H), 1.38−1.35 (m, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 167.8, 155.1, 149.1, 138.6, 113.6, 100.6, 93.3, 59.6, 56.3, 55.3, 29.5, 14.2. HRMS calcd (ESI) m/z for $C_{12}H_{17}NNaO_4$ $[M + Na]^+$ 262.1050, found 262.1057.

Ethyl 5-chloro-2-(methylamino)benzoate (**3ga**): yield 65% (27.7 mg), white solid; mp 62−63 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.86 (s, 1 H), 7.64 (br s, 1 H), 7.29 (d, J = 7.2 Hz, 1 H), 6.58 (d, J = 9.2 Hz, 1 H), 4.33−4.27 (m, 2 H), 2.88 (d, J = 4.8 Hz, 3 H), 1.37 (t, J = 7.2 Hz, 3 H), ; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 167.6, 150.5, 134.3, 130.6, 118.8, 112.1, 110.8, 60.5, 29.6, 14.3; HRMS calcd (ESI) m/z for $C_{10}H_{12}ClNNaO_2$ $[M + Na]^+$ 236.0449, found 236.0451.

Ethyl 4-chloro-2-(methylamino)benzoate (**3ha**): yield 44% (18.7 mg), yellow liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.82 (d, J = 8.4 Hz, 1 H), 7.76 (br s, 1 H), 6.62 (s, 1 H), 6.54 (d, J = 8.4 Hz, 1 H), 4.32−4.27 (m, 2 H), 2.88 (d, J = 5.2 Hz, 3 H), 1.37 (t, J = 7.2 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.1, 152.6, 140.7, 132.8, 114.5, 110.4, 108.6, 60.4, 29.5, 14.3; HRMS calcd (ESI) m/z for $C_{10}H_{12}ClNNaO_2$ $[M + Na]^+$ 236.0449, found 236.0452.

Ethyl 5-bromo-2-(methylamino)benzoate (**3ia**): yield 37% (19.0 mg), colorless liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.99 (s, 1 H), 7.67 (br s, 1 H), 7.41 (d, J = 9.2 Hz, 1 H), 6.54 (d, J = 9.2 Hz, 1 H), 4.33−4.28 (m, 2 H), 2.88 (d, J = 4.8 Hz, 3 H), 1.38 (t, J = 6.8 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 167.6, 150.8, 137.0, 133.6, 112.5, 111.4, 105.5, 60.6, 29.6, 14.3; HRMS calcd (ESI) m/z for $C_{10}H_{12}BrNNaO_2$ $[M + Na]^+$ 279.9944, found 279.9942.

Ethyl 3-(methylamino)-2-naphthoate (**3ja**): yield 50% (22.9 mg), brown liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.49 (s, 1 H), 7.69 (d, J = 8.0 Hz, 1 H), 7.58 (d, J = 8.0 Hz, 1 H), 7.39 (t, J = 7.2 Hz, 2 H), 7.14 (t, J = 7.2 Hz, 1 H), 6.79 (s, 1 H), 4.40−4.35 (m, 2 H), 2.95 (s, 3 H), 1.43 (t, J = 6.8 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.3, 147.8, 137.8, 133.6, 129.2, 128.7, 125.4, 124.7, 121.8, 114.4, 103.8, 60.7, 29.9, 14.3; HRMS calcd (ESI) m/z for $C_{14}H_{15}NNaO_2$ $[M + Na]^+$ 252.0995, found 252.1000.

Ethyl 2-(ethylamino)benzoate (**3ka**): yield 67% (25.9 mg), colorless liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.92 (d, J = 8.0 Hz, 1 H), 7.62 (br s, 1 H), 7.34 (t, J = 7.6 Hz, 1 H), 6.66 (d, J = 7.6 Hz, 1 H), 6.57 (t, J = 7.6 Hz, 1 H), 4.33−4.28 (m, 2 H), 3.24−3.21 (m, 2 H), 1.37 (t, J = 6.8 Hz, 3 H), 1.31 (t, J = 6.8 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.7, 151.1, 134.4, 131.6, 114.1, 111.1, 109.8, 60.1, 37.3, 14.5, 14.3; HRMS calcd (ESI) m/z for $C_{11}H_{15}NNaO_2$ $[M + Na]^+$ 216.0995, found 216.1000.

Ethyl 2-(propylamino)benzoate (**3la**): yield 48% (19.9 mg), colorless liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.91 (d, J = 7.6 Hz, 1 H), 7.71 (br s, 1 H), 7.34 (t, J = 7.2 Hz, 1 H), 6.67 (d, J = 8.4 Hz, 1 H), 6.56 (t, J = 7.6 Hz, 1 H), 4.33−4.28 (m, 2 H), 3.18−3.13 (m, 2 H), 1.74−1.68 (m, 2 H), 1.38 (t, J = 6.8 Hz, 3 H), 1.03 (t, J = 7.2 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.7, 151.3, 134.4, 131.6, 114.0, 111.1, 109.8, 60.1, 44.6, 22.3, 14.3, 11.7; HRMS calcd (ESI) m/z for $C_{12}H_{17}NNaO_2$ $[M + Na]^+$ 230.1151, found 230.1148.

Ethyl 1,2,3,4-tetrahydroquinoline-8-carboxylate (**3ma**): yield 49% (20.1 mg), colorless liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.79 (br s, 1 H), 7.72 (d, J = 8.0 Hz, 1 H), 7.03 (d, J = 6.8 Hz, 1 H), 6.44 (t, J = 7.6 Hz, 1 H), 4.31−4.26 (m, 2 H), 3.41 (s, 2 H), 2.78−2.75 (m, 2 H), 1.90 (t, J = 5.6 Hz, 2 H), 1.36 (t, J = 6.8 Hz, 3

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H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.8, 148.3, 133.6, 129.3, 122.0, 113.4, 108.6, 60.0, 41.1, 27.8, 20.8, 14.3; HRMS calcd (ESI) m/z for $C_{12}H_{15}NNaO_2$ $[M + Na]^+$ 228.0995, found 228.0998.

*Ethyl 2-(benzylamino)benzoate (**3na**):* yield 43% (21.9 mg), yellow liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.18 (br s, 1 H), 7.94 (d, J = 7.6 Hz, 1 H), 7.35−7.24 (m, 6 H), 6.63−6.57 (m, 2 H), 4.44 (d, J = 4.8 Hz, 2 H), 4.34−4.29 (m, 2 H), 1.38 (t, J = 6.0 Hz, 3 H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.7, 150.9, 138.8, 134.5, 131.6, 128.6, 127.1, 127.0, 114.8, 111.6, 110.4, 60.3, 46.9, 14.3; HRMS calcd (ESI) m/z for $C_{16}H_{17}NNaO_2$ $[M + Na]^+$ 278.1151, found 278.1157.

*Ethyl 2-aminobenzoate (**3oa**):* yield 78% (8.1 mg), yellow liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.88 (dd, J = 8.0 Hz J = 1.2 Hz, 1 H), 7.26 (dd, J = 15.6 Hz, J = 1.6 Hz, 1 H), 6.66−6.62 (m, 2 H), 5.73 (br s, 2 H), 4.35−4.30 (m, 2 H), 1.38 (t, J = 7.2 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.1, 150.4, 133.9, 131.1, 116.6, 116.1, 110.9, 60.2, 14.3; HRMS Calcd (ESI) m/z for $C_9H_{11}NNaO_2$ $[M + Na]^+$ 188.0682, found 188.0685.

*Methyl 2-(methylamino)benzoate (**3ab**):* yield 70% (23.1 mg), colorless liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.89 (d, J = 8.0 Hz, 1 H), 7.63 (br s, 1 H), 7.38 (t, J = 7.2 Hz, 1 H), 6.66 (d, J = 8.8 Hz, 1 H), 6.58 (t, J = 7.6 Hz, 1 H), 3.85 (s, 3 H), 2.90 (s, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 169.0, 151.9, 134.6, 131.5, 114.3, 110.7, 109.8, 51.4, 29.5; HRMS Calcd (ESI) m/z for $C_9H_{11}NNaO_2$ $[M + Na]^+$ 188.0682, found 188.0688.

*Propyl 2-(methylamino)benzoate (**3ac**):* yield 73% (28.2 mg), colorless liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.92 (d, J = 7.6 Hz, 1 H), 7.66 (br s, 1 H), 7.37 (t, J = 7.6 Hz, 1 H), 6.66 (d, J = 8.4 Hz, 1 H), 6.58 (t, J = 7.2 Hz, 1 H), 4.21 (t, J = 6.4 Hz, 2 H), 2.90 (d, J = 4.8 Hz, 3 H), 1.80−1.74 (m, 2 H), 1.02 (t, J = 7.2 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.7, 152.0, 134.5, 131.5, 114.2, 110.6, 110.1, 65.7, 29.5, 22.1, 10.6; HRMS Calcd (ESI) m/z for $C_{11}H_{15}NNaO_2$ $[M + Na]^+$ 216.0995, found 216.1000.

*Butyl 2-(methylamino)benzoate (**3ad**):* yield 72% (29.8 mg), colorless liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.91 (d, J = 7.6 Hz, 1 H), 7.66 (br s, 1 H), 7.37 (t, J = 7.6 Hz, 1 H), 6.66 (d, J = 8.0 Hz, 1 H), 6.59 (t, J = 7.6 Hz, 1 H), 4.25 (t, J = 6.4 Hz, 2 H), 2.90 (d, J = 4.4 Hz, 3 H), 1.73 (t, J = 6.8 Hz, 2 H), 1.48−1.45 (m, 2 H), 0.97 (t, J = 7.2 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.7, 151.9, 134.4, 131.4, 114.2, 110.6, 110.0, 64.0, 30.7, 29.4, 19.3, 13.7; HRMS calcd (ESI) m/z for $C_{12}H_{17}NNaO_2$ $[M + Na]^+$ 230.1151, found 230.1158.

*Isopropyl 2-(methylamino)benzoate (**3ae**):* yield 44% (17.0 mg), colorless liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.91 (d, J = 7.6 Hz, 1 H), 7.68 (br s, 1 H), 7.37 (t, J = 7.6 Hz, 1 H), 6.65 (d, J = 8.0 Hz, 1 H), 6.58 (t, J = 7.2 Hz, 1 H), 5.22−5.16 (m, 1 H), 2.90 (d, J = 4.0 Hz, 3 H), 1.34 (d, J = 6.0 Hz, 6 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.2, 152.0, 134.4, 131.5, 114.2, 110.6, 110.5, 67.4, 29.5, 22.0; HRMS calcd (ESI) m/z for $C_{11}H_{16}NO_2$ $[M + H]^+$ 194.1176, found 194.1179.

*Benzyl 2-(methylamino)benzoate (**3af**):* yield 77% (37.1 mg), yellow liquid; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.96 (d, J = 7.6 Hz, 1 H), 7.66 (br s, 1 H), 7.41−7.29 (m, 6 H), 6.63 (d, J = 8.4 Hz, 1 H), 6.56 (t, J = 7.6 Hz, 1 H), 5.28 (s, 2 H), 2.85 (d, J = 4.8 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 168.3, 152.0, 136.3, 134.7, 131.5, 128.4, 128.2, 127.9, 127.8, 114.2, 110.6, 109.6, 65.8, 29.4; HRMS calcd (ESI) m/z for $C_{15}H_{15}NNaO_2$ $[M + Na]^+$ 264.0995, found 264.0992.

*Phenyl 2-(methylamino)benzoate (**3ag**):* yield 68% (30.9 mg), yellow liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.14 (d, J = 8.0 Hz, 1 H), 7.63 (br s, 1 H), 7.47−7.40 (m, 3 H), 7.27−7.23 (m, 1 H), 7.16 (d, J = 7.6 Hz, 2 H), 6.72−6.64 (m, 2 H), 2.90 (d, J = 4.8 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ 167.3, 152.6, 150.8. 135.4, 131.9, 129.4, 125.7, 122.0, 114.4, 110.8, 108.6, 29.5; HRMS calcd (ESI) m/z for $C_{14}H_{13}NNaO_2$ $[M + Na]^+$ 250.0838, found 250.0841.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^1H and ^{13}C NMR spectra for products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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