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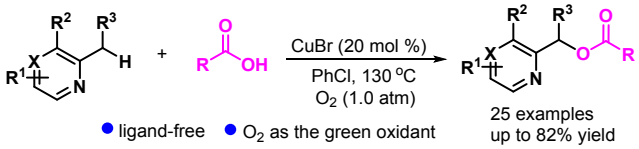
Ligand-free Copper(I)-Catalyzed Benzylic Acyloxylation of 2-Alkylpyridines under Aerobic Conditions

Li Cheng, Yuqian Sun, Wenrong Wang, Changsheng Yao*, Tuan-Jie Li*

School of Chemistry & Materials Science, Jiangsu Key Laboratory of Green Synthetic Chemistry for Functional Materials, Jiangsu Normal University, Xuzhou 221116, P. R. China



Abstract: A ligand-free copper(I)-catalyzed benzylic acyloxylation of 2-alkylpyridines with carboxylic acids was realized by using 1.0 atm of O_2 as a green oxidant. The transformation provided a facile access to a wide range of *N*-heterocyclic esters through C-O bond formation, with broad substrate scope and good functional groups tolerance. Preliminary mechanistic investigations showed that this protocol included a radical process.

Keywords: CuBr-catalysis; benzylic acyloxylation; 2-alkylpyridines; carboxylic acids

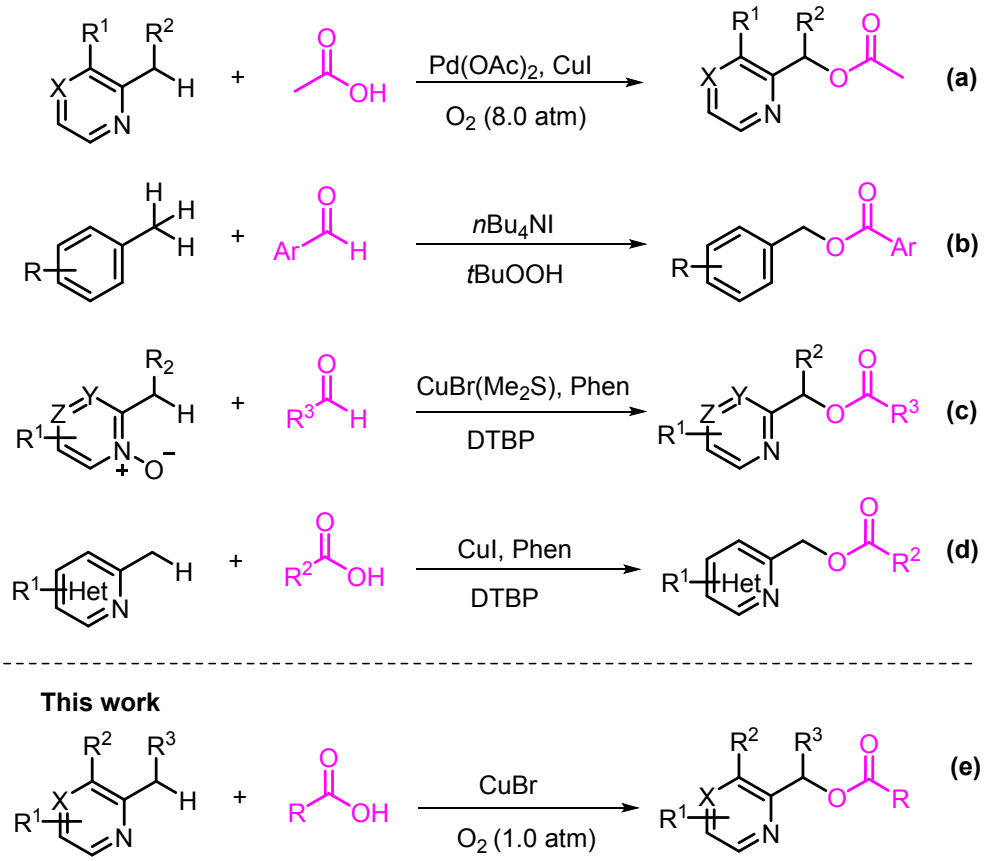
INTRODUCTION

Transition-metal-catalyzed C(sp^3)−H functionalization has emerged as a powerful and appealing tool for the introduction of diverse functional groups into organic molecules through the direct conversion of C(sp^3)−H bonds.[1] In particular, metal-catalyzed acyloxylation of C(sp^3)–H has received increasing attention for the syntheses of functional esters in the past years.[2] Currently, notable progress has been made predominantly with Pd catalyst which allows direct acyloxylation of the C(sp^3)–H bonds into C–O bonds, but these transformations are almost limited to acetoxylation in the presence of ligands and several kinds of oxidants including $PhI(OAc)_2$.[3] In sharp contrast, the use of low-cost copper catalysts for C(sp^3)–H acyloxylation using aromatic acids as coupling partners is quiet less while copper-catalyzed C(sp^3)–H functionalization has been extensively studied.[4] Moreover, molecular oxygen as a safe and environmentally friendly oxidant is typically usually

used in many C–O bond formation reactions.[5] It has become clear that the combination of ligand-free copper catalysis with molecular oxygen to achieve the C(sp^3)–H acyloxylation will provide a green and sustainable entry to construct functional esters.[6]

Over the past years, metal-catalyzed C(sp^3)–H acyloxylation of *N*-heteroaryl compounds has attracted considerable attention as *N*-heteroaryl esters are frequently found in a plethora of natural products and play an important role in the field of medicinal chemistry.[7] In 2010, Jiang and co-workers pioneered a Pd-catalyzed benzylic acetoxylation of 2-alkylheterocycles in AcOH, but this method required 1.0 equivalent of CuI as additive in the presence of 8.0 atm O_2 (Scheme 1a).[8] Besides, Bu_4NI could also catalyze the benzylic acyloxylation of alkylarenes with aromatic aldehydes presented by ^tBuOOH (Scheme 1b).[9] Later, Soulé's group developed a copper-promoted benzylic acyloxylation of 2-alkyheterocycle *N*-oxides for the synthesis of 2-pyridinemethyl ester derivatives *via* tandem oxidative coupling and Boekelheide rearrangement, but this reaction needed 1,10-phenanthroline (Phen) as the ligand and 3.0 equivalents of di-*tert*-butyl peroxide (DTBP) as the oxidant (Scheme 1c).[10] Very recently, Yin et al presented a copper-catalyzed C(sp^3)−H acyloxylation of *N*-heteroaryl methanes *via* oxidative dehydrogenation (Scheme 1 d).[11] In this method, Phen ligand and 3.0 equivalents DTBP were still necessary and 2-metheylpyridine was proven to be ineffective in this transformation. Thus there is an urgent need to develop a cheap metal-catalyzed, ligand-free and additive-free strategy to acyloxylate 2-alkylpyridine in the presence of environmentally compatible and readily available oxidants. Herein, we report a ligand-free copper (I)-catalyzed benzilic acyloxylation of 2-alkylpyridines by using O_2 (1.0 atm) as a green oxidant. The current protocol represents a unique and sustainable procedure to access a wide range of 2-pyridinemethyl ester derivatives. Besides, other fused *N*-heterocycle derivatives such as 6,7-dihydro-5*H*-cyclopenta[*b*]pyridine, 5,6,7,8-tetrahydroquinoline, 3-methylisoquinoline and 2-propylpyrazine are tolerated well in this method (Scheme1 e).

Scheme 1. Direct Benzilic Acyloxylation of 2-Alylpyridines

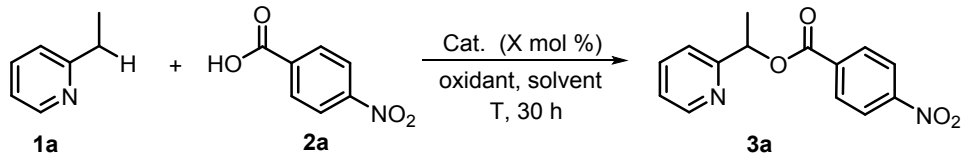


RESULTS AND DISCUSSION

Initial optimization was performed using 2-ethylpyridine (**1a**, 0.1 mmol) and 4-nitrobenzoic acid (**2a**, 0.12 mmol) in PhCl (0.6 mL) (Table 1). The catalytic activity of the different copper salts, such as CuCl, CuBr, CuI, $Cu(OAc)_2$, and $CuBr_2$, was tested under air atmosphere at 120 °C (entries 1-5). Among these salts, CuBr showed the best catalytic performance, resulting in the desired product **3a** in 37 % yield (entry 2). Thus, CuBr was selected as the Cu-catalyst to assess the effect of solvents, including toluene, $PhCF_3$, DCE, CH_3CN and 1,4-dioxane (entries 6-10). All the attempts did not show any improvement on the reaction yield as compared with PhCl. Subsequently, the oxidants including O_2, BQ (benzoquinone), $K_2S_2O_8$, TBHP (*tert*-butyl peroxide) and DTBP (di-*tert*-butyl peroxide) were screened for this transformation (entries 11-15). The experimental results indicated that the presence of O_2 drove the reaction most efficiently, giving 52 % yield of **3a** (entry 11). Then, we explored the other reaction parameters including reaction temperature and the amount of copper catalyst. The yield was raised to 60 % when the reaction was conducted at

130 °C (entry 16). It was found that the CuBr loading had an important impact on the reaction efficiency. An increase of the loading of CuBr was beneficent to the reaction (entries 17-18), and the use of 20 mol% CuBr led to the best yield of **3a** (78 %, entry 18).

Table1. Optimization of Reaction Conditions [a]



1a **2a** **3a**

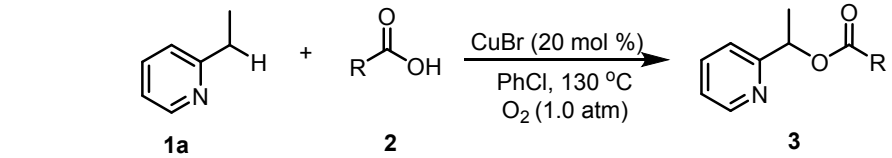
Entry	Cat. (mol %)	Oxidant [b]	Solvent	T (°C)	Yield (%) [f]
1	CuCl (10)	air	PhCl	120	29
2	CuBr (10)	air	PhCl	120	37
3	CuI (10)	air	PhCl	120	10
4	$Cu(OAc)_2$ (10)	air	PhCl	120	15
5	$CuBr_2$ (10)	air	PhCl	120	25
6	CuBr (10)	air	toluene	120	29
7	CuBr (10)	air	$PhCF_3$	120	31
8	CuBr (10)	air	DCE	120	17
9	CuBr (10)	air	CH_3CN	120	22
10	CuBr (10)	air	1,4-dioxane	120	11
11	CuBr (10)	O_2	PhCl	120	52
12	CuBr (10)	BQ [c]	PhCl	120	48
13	CuBr (10)	$K_2S_2O_8$	PhCl	120	36
14	CuBr (10)	TBHP [d]	PhCl	120	41
15	CuBr (10)	DTBP [e]	PhCl	120	43
16	CuBr (10)	O_2	PhCl	130	60
17	CuBr (10)	O_2	PhCl	140	58
18	CuBr (20)	O_2	PhCl	130	78
19	CuBr (30)	O_2	PhCl	130	70

[a] Reactions were performed with **1a** (0.10 mmol, 10.7 mg), **2a** (0.12 mmol, 20.0 mg), cat. (mol %), and oxidant in PhCl (0.6 mL) at T °C, 30 h. [b] O_2 (1.0 atm) and other oxidants (1.2 equivlents), [c] BQ = benzoquinone, [d] TBHP = *tert*-butyl peroxide, [e] DTBP = di-*tert*-butyl peroxide. [f] Isolated yield.

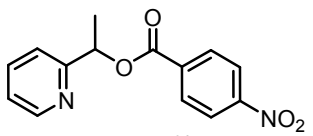
With the optimized reaction conditions in hand, firstly, the scope of aromatic acids as coupling reagents for the acyloxylation of 2-ethylpyridine was investigated. As shown in Table 2, various commercially available aromatic acids and α,β-unsaturated carboxylic acids were exposed to the standard reaction conditions and the desired 1-(pyridin-2-yl)ethyl substituted benzoates were successfully afforded with good yields. Among them, 4-nitrobenzoic acid as the acyloxylation reagent

showed high reactivity due to the acyloxylated product was furnished in 78 % yield. Alternatively, thiophene-2-carboxylic acid as a representative heteroaryl acid was employed to react with substrate **1a** under the standard conditions and the corresponding product **3i** was generated with 63 % yield.

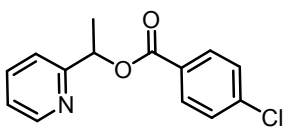
Table 2. Substrate Scope of Aromatic Acids[a,b]



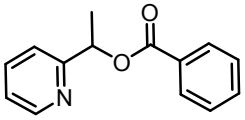
1a **2** **3**



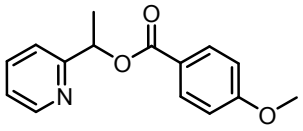
3a, 78 %



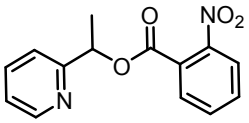
3b, 65 %



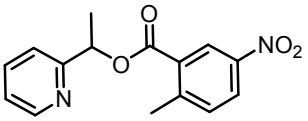
3c, 60 %



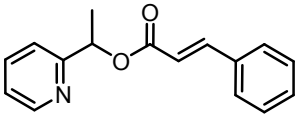
3d, 68 %



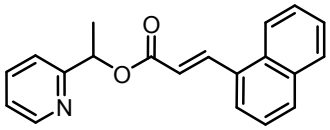
3e, 71 %



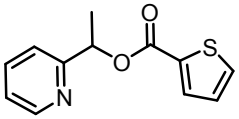
3f, 73 %



3g, 78 %



3h, 60 %



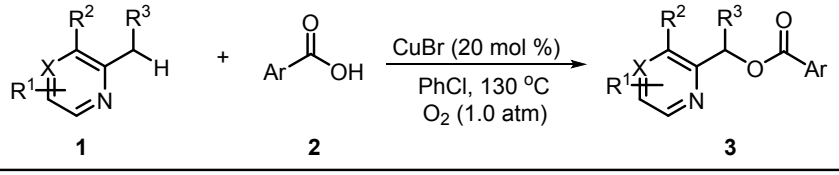
3i 68 %

[a] Reactions were performed with **1** (0.10 mmol), **2** (0.12 mmol), CuBr (20 mol%, 2.86 mg), and O_2 (1.0 atm) in PhCl (0.6 mL) at 130 °C, 30 h. [b]Isolated yields.

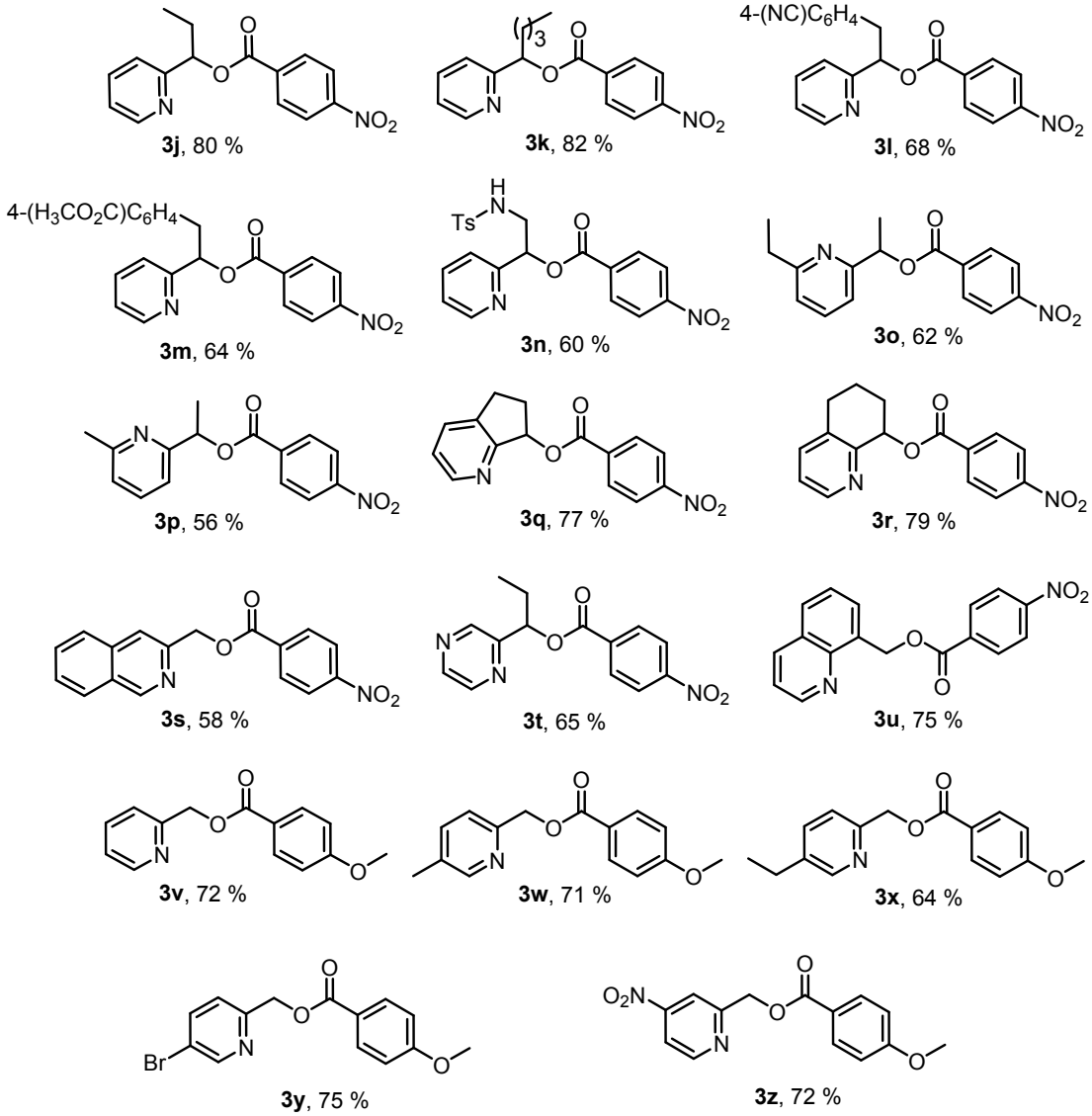
Next, we explored the acyloxylation reaction of a variety of 2-ethylpyridine derivatives in combination with 4-nitrobenzoic acid as coupling partner under the standard conditions. The results are summarized in Table 3. Various substituents, such as methyl (**1b**), propyl (**1c**), aryl (**1d** and **1e**) and sulfonamido (**1f**) functionalities linked to the ethyl group of 2-ethylpyridines, were proven to be suitable as the corresponding products **3j-3n** were smoothly obtained with 60 %-82 % yields under the standard conditions. Moreover, both ethyl (**1g**) and methyl (**1h**) groups located at 6-postion of pyridine unit also worked well in the transformations, delivering the desired acyloxylation products **3o** and **3p** in 62 % and 56 % yields, respectively. Notably, fused pyridines such as 6,7-dihydro-5*H*-cyclopenta[*b*]pyridine and

5,6,7,8-tetrahydroquinoline were successfully engaged in this copper catalysis, accessing the corresponding acyloxylation products **3q** and **3r** efficiently, respectively. Furthermore, 3-methylisoquinoline could take part in this protocol and afforded product **3s** in 58 % yield. 2-Propylpyrazine was an effective component, leading to

Table 3. **Substrate Scope of 2-Alkylpyridines**[a,b]



1 **2** **3**



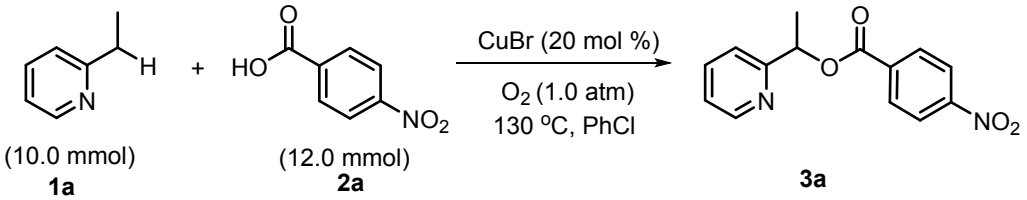
[a] Reactions were performed with **1** (0.10 mmol), **2** (0.12 mmol), CuBr (20 mol%, 2.86 mg), and O_2 (1.0 atm) in PhCl (0.6 mL) at 130 °C for 30 h. [b]Isolated yields

the formation of product **3t** in 65 % yield. The reaction of 8-methylisoquinoline with

4-nitrobenzolic acid proceeded smoothly to give the corresponding product **3u** in 75 % yield under the standard conditions. To expand the scope of this transformation, 4-methoxylbenzoic acid was selected as a representative electron-donating aryl acid to probe the feasibility of the copper(I)-catalyzed benzylic acyloxylation of 2-alkylpyridines. Delightfully, the reaction worked well to provide the acyloxylated products **3v-3z** 64 %-75 % yields when 2-methylpyridines bearing electronically neutral (H), rich (methyl and ethyl) and poor (bromo and nitro) groups were reacted with 4-methoxylbenzoic acid. These results indicated that the electronic property of the substitutes attached by pyridine ring had little effect on the transformations.

To evaluate the practicality of this protocol, a gram-scale benzilic acyloxylation reaction of 2-ethylpyridine (**1a**, 10 mmol) with 4-nitrobenzoic acid (**2a**, 12 mmol) was conducted under the standard conditions. Gratifyingly, the reaction proceeded smoothly, affording product **3a** in 64 % yield (Scheme 2).

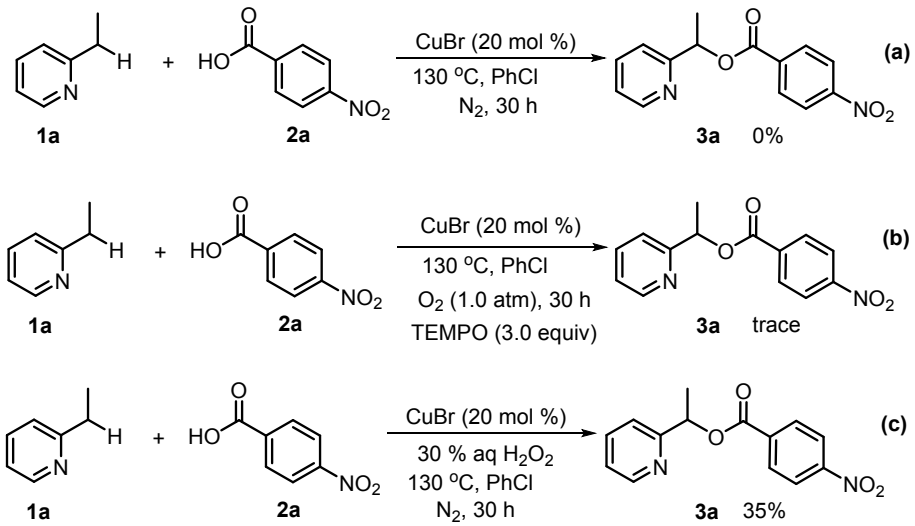
Scheme 2. Gram Scale Experiment for the Synthesis of 3a



(10.0 mmol) **1a** (12.0 mmol) **2a** **3a**

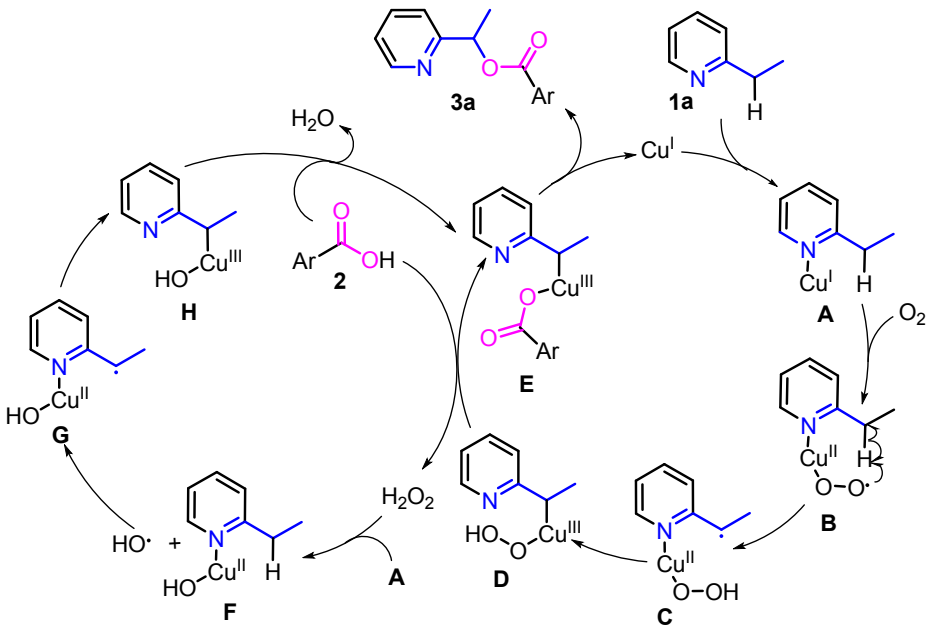
To gain mechanistic insight into this reaction, several control experiments were conducted. When the model reaction was carried out under a nitrogen atmosphere, the desired product **3a** was not obtained, indicating that molecular oxygen was necessary in this protocol (Scheme 3 a). Then, the reaction was subjected with 3.0 equivalents of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) under the standard conditions and only a trace amount of **3a** was detected (Scheme 3 b). These results showed that these processes included the possibility of a radical mechanism. For H_2O_2 generated in situ from O_2 *via* copper catalysis could act as the oxidant for the acyloxylation, the model reaction was performed with 2.0 equivalents of H_2O_2 (30 % aqueous H_2O_2 was used) under a nitrogen atmosphere and the C(sp^3)-H acyloxylation of 2-ethylpyridine took place efficiently, affording **3a** in 35 % yield (Scheme 3 c).

Scheme 3. Control Experiments



Based on the abovementioned analysis and literature survey,[6b,12] a reasonable mechanism for this copper(I)-catalyzed benzylic acyloxylation reaction was proposed to occur *via* a Cu(I)/Cu(II)/Cu(III) catalytic cycle (Scheme 4). This transformation pathway was initiated by the coordination of Cu(I) salt with substrate **1a** to afford intermediate **A**, which underwent oxidation to yield radical species **B** (Cu(I) to Cu(II)) (detected by HRMS, $[M + H]^+ = 203.0$, see the Surporting Information (SI)) in the presence of O_2. Then, intermediate **B** was converted into intermediate **D** (detected by HRMS, $[M + H]^+ = 203.0$) *via* intramolecular hydrogen atom transfer (HAT) and subsequent oxidative addition (Cu(II) to Cu(III)). The following ligand exchange gave intermediate **E** (detected by HRMS, $[M + H]^+ = 336.0$). Subsequently, the reductive elimination of the intermediate **E** afforded the final product **3a** and completed the catalytic cycle to regenerate the Cu catalyst. The resulting H_2O_2 served as the oxidant to participate in this transformation. Moreover, the intermediates **F** ($[M + H]^+ = 188.0$) and **G** or **H** ($[M + H]^+ = 187.0$) were observed by HRMS.

Scheme 4. Possible Reaction Pathway



CONCLUSIONS

In summary, starting from easily available aromatic acids, a new ligand-free copper(I)-catalyzed C(sp^3)−H acyloxylation of 2-alkylpyridines has been established by means of O_2 as an environmentally friendly oxidant. This transformation features broad substrate scope and good functional group tolerance. Further mechanistic studies are currently underway in our laboratory.

EXPERIMENTAL SECTION

General Information. Unless otherwise mentioned, all reactions sealed by 10 mL LH-20 Schlenk and were monitored by analytical thin-layer chromatography (TLC), which was visualized by ultraviolet light (254 nm or 365 nm). All reagents were commercially available and were used without further purification. Purification of the products was accomplished by flash chromatography using silica gel (200-300 mesh). Melting points were determined in open capillaries and were uncorrected. ^{1}H NMR spectra were measured on a 400 MHz spectrometer in $CDCl_3$ (100 MHz, $^{13}C\{^1H\}$ NMR) or DMSO-d_6 with a chemical shift (δ) given in ppm relative to TMS as an internal standard. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartets, m = multiplet), coupling constants (Hz), integration. High-resolution mass spectra (HRMS) were obtained on a HRMS/MS

instrument with the technique of atmospheric pressure chemical ionization (APCI) and TOF analyzer.

Syntheses of 1d and 1e according to the method reported in the literature.[13] A flame-dried 10 mL LH-20 Schlenk equipped with a magnetic stir bar was charged with 2-ethylpyridine (64.0 mg, 0.6 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), AgOAc (210.0 mg, 1.26 mmol) and atrial iodine (5 mmol) were mixed with acetic acid (1.5 mL) and heated at 130 ^oC for 47 h. Purification by flash chromatography (silicagel, mixtures of petroleum ether/ethyl acetate, 10:1, v/v) gave **1d** and **1e**.

4-(2-(Pyridin-2-yl)ethyl)benzonitrile (1d): Colorless oil (49.9 mg, 40 % yield); ^1H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.72 (d, J = 5.6 Hz, 1H), 8.29 (t, J = 7.8 Hz, 1H), 7.80 (t, J = 6.6 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 8.0 Hz, 2H), 7.43 (d, J = 8.0 Hz, 2H), 3.56 (t, J = 8.0 Hz, 2H), 3.31 (t, J =8.0 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.9, 145.4, 144.1, 141.1, 132.5, 129.4, 126.9, 124.7, 118.7, 110.7, 35.5, 34.5; HRMS (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{13}N_2$ 209.1079; Found 209.1085.

***Methyl 4-(2-(pyridin-2-yl)ethyl)benzoate (1e)*:** Colorless oil (65.1 mg, 45 % yield); ^1H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.71 (d, J =5.6 Hz, 1H), 8.22 (t, J =7.6 Hz, 1H), 7.89 - 7.86 (m, 2H), 7.75 (t, J =6.4 Hz, 1H), 7.49 (d, J =7.6 Hz, 1H), 7.28 (d, J =8.0 Hz, 2H), 3.86 (s, 3H), 3.54 (t, J =7.4 Hz, 2H), 3.27 (t, J =7.4 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.7, 156.2, 145.1, 143.8, 141.1, 129.9, 128.6, 127.0, 124.5, 52.0, 35.2, 34.6; HRMS (APCI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{16}NO_2$ 242.1181; Found 242.1176.

Synthesis of 1f according to the method reported in the literature.[14]

A flame-dried 50 mL round-bottomed flask equipped with a magnetic stir bar was charged with 4-toluenesulfonyl chloride (2.3 g, 12 mmol) capped with a rubber septum and flushed with N_2, anhydrous CH_2Cl_2 (30 mL) was added and then it was cooled to 0 ^oC. 2-(pyridin-2-yl) ethanamine (1.2 g, 10 mmol) was added dropwise, and the resulting mixture was stirred at 0 ^oC for 3 min. After this time, triethylamine (TEA, 2.0 g, 20 mmol) was added in one portion. The reaction mixture was stirred for 3 h and slowly allowed to warm to room temperature over that time. The resulting

mixture was quenched by addition of water and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic fractions were washed with brine (30 mL), dried over Na_2SO_4 and filtrated. After the solvent was removed under reduced pressure, the residue was recrystallized from CH_2Cl_2/petroleum ether to afford sulfonyl protected **1f**.

4-Methyl-N-(2-(pyridin-2-yl)ethyl)benzenesulfonamide (1f): White solid (2.0 g, 70 % yield); m.p. 114 - 115 °C (reported 120 - 122 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, J = 4.7 Hz, 1H), 7.73 (d, J = 7.9 Hz, 2H), 7.58 (t, J = 7.7 Hz, 1H), 7.26 (d, J = 7.7 Hz, 2H), 7.15 - 7.12 (m, 1H), 7.07 (d, J = 7.8 Hz, 1H), 6.14 (t, J = 5.6 Hz, 1H), 3.35 (q, J = 6.0 Hz, 2H), 2.93 (t, J = 6.1 Hz, 2H), 2.40 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.8, 148.8, 143.0, 137.1, 136.8, 129.5, 127.0, 123.5, 121.7, 42.3, 36.3, 21.4; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{16}N_2O_2SNa$ 299.0830l; Found 299.0846.

General Procedure for the Preparation of Products 3. A 10-mL LH-20 Schlenk tube equipped with a magnetic stir bar was charged with CuBr (2.9 mg, 0.02 mmol), 2-alkylpyridines **1** (0.1 mmol), aromatic acids **2** (0.12 mmol), PhCl (0.6 mL). This tube was evacuated, and refilled with oxygen (1.0 atm). The mixture was stirred at 130 ^{o}C for 30 h, at which time complete consumption of starting material was observed by TLC. The reaction mixture was diluted with ethyl acetate (30 mL). The mixture was washed with saturated Na_2CO_3 solution three times. The organic layer was separated and dried with $MgSO_4$ filtered. After removal of the solvent under reduced pressure, the resulting was purified by column chromatography (silicagel, mixtures of petroleum ether/ethyl acetate, 8:1, v/v) to afford the desired product **3**.

Scale-up Experiment. In a dried 50 mL round-bottomed flask equipped with a magnetic stirrer, add CuBr (286.9 mg, 2.0 mmol), 2-ethylpyridine (1.1 g, 10 mmol), 4-nitrobenzoic acid (2.0 g, 12.0 mmol), PhCl (15 mL). This flask was evacuated, and refilled with oxygen. The mixture was stirred at 130 ^{o}C until complete consumption of starting material observed by TLC (about 36 h). The reaction mixture was diluted with ethyl acetate and washed with saturated Na_2CO_3 solution three times. The organic layer was separated and dried with $MgSO_4$ filtered. After the removal of the solvent under reduced pressure, the residue was purified by column chromatography

(silicagel, mixtures of petroleum ether/ethyl acetate, 8:1, v/v) to afford the desired product **3a** (1.73 g, 64%).

1-(Pyridin-2-yl)ethyl 4-nitrobenzoate (3a). Colorless oil (21.2 mg, 78 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.40 - 8.30 (m, 5H), 7.85 - 7.84 (m, 2H), 6.50 (d, J = 6.0 Hz, 1H), 1.98 (d, J = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.7, 155.9, 150.9, 144.5, 143.6, 134.1, 131.4, 125.6, 123.7, 123.5, 70.9, 21.2; IR (KBr) (ν, cm^{-1}) 2922, 2360, 2341, 2341, 1728, 1528, 1343, 1102, 1014; HRMS (APCI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{14}H_{12}N_2O_4Na$ 295.0695; Found 295.0701.

1-(Pyridin-2-yl)ethyl 4-chlorobenzoate (3b). Colorless oil (17.0 mg, 65 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.82 (d, J = 5.2 Hz, 1H), 8.27 (t, J = 7.8 Hz, 1H), 8.09 (d, J =11.2 Hz, 2H), 7.81 - 7.74 (m, 2H), 7.45 (d, J = 8.8 Hz, 2H), 6.46 (q, J = 6.8 Hz, 1H), 1.94 (d, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.6, 156.7, 144.4, 143.0, 140.4, 131.5, 129.0, 127.2, 125.2, 123.2, 70.1, 21.2; IR (KBr) (ν, cm^{-1}) 1723, 1593, 1270, 1103, 1092, 1070, 1014; HRMS (APCI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{14}H_{12}ClNO_2Na$ 284.0454; Found 284.0457.

1-(Pyridin-2-yl)ethyl benzoate (3c). Colorless oil (13.6 mg, 60 % yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 4.4 Hz, 1H), 8.12 (d, J = 8.0 Hz, 2H), 7.69 (t, J = 7.6 Hz, 1H), 7.57 (t, J = 7.4 Hz, 1H), 7.47 - 7.43 (m, 3H), 7.23 - 7.19 (m, 1H), 6.17 (q, J = 6.8 Hz, 1H), 1.74 (d, J = 6.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.8, 160.5, 149.3, 136.8, 133.0, 130.2, 129.7, 128.4, 122.7, 120.2, 73.6, 20.8; IR (KBr) (ν, cm^{-1}) 1717, 1590, 1573, 1474, 1451, 1435, 1338, 1315, 1270, 1109, 1177, 1070, 1048, 1026, 1001; HRMS (APCI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{14}H_{13}NO_2Na$ 250.0844; Found 250.0866.

1-(Pyridin-2-yl)ethyl 4-methoxybenzoate (3d). Colorless oil (17.5 mg, 68 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.59 (d, J = 3.6 Hz, 1H), 8.06 (d, J = 8.8 Hz, 2H), 7.68 (t, J = 7.6 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 7.21 - 7.18 (m, 1H), 6.92 (d, J = 8.8 Hz, 2H), 6.14 (q, J = 6.8 Hz, 1H), 3.85 (s, 3H), 1.71 (d, J = 6.8 Hz,

3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 165.5, 163.4, 160.6, 149.1, 136.9, 131.7, 122.6, 122.5, 120.2, 113.6, 73.2, 55.4, 20.8; IR (KBr) (ν, cm^{-1}) 1711, 1606, 1511, 1269, 1256, 1168, 1101; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{15}NO_3Na$ 280.0950; Found 280.0940.

1-(Pyridin-2-yl)ethyl 2-nitrobenzoate (3e). Colorless oil (19.3 mg, 71 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.78 (d, J = 4.0 Hz, 1H), 8.38 (t, J = 7.4 Hz, 1H), 7.96 - 7.83 (m, 4H), 7.75 - 7.65 (m, 2H), 6.57 (q, J = 6.4 Hz, 1H), 1.88 (d, J = 6.8 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 164.1, 155.7, 147.9, 144.8, 142.5, 133.3, 132.3, 130.6, 126.3, 125.5, 123.9, 123.6, 71.2, 20.6; IR (KBr) (ν, cm^{-1}) 2924, 1732, 1591, 1574, 1537, 1457, 1445, 1436, 1350, 1286, 1255, 1131, 1072, 1047, 788, 736; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{12}N_2O_4Na$ 295.0695; Found 295.0708.

1-(Pyridin-2-yl)ethyl 2-methyl-5-nitrobenzoate (3f). Colorless oil (20.9 mg, 73 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.85 - 8.82 (m, 2H), 8.41 (s, 1H), 8.25 - 8.22 (m, 1H), 7.92 - 7.88 (m, 2H), 7.44 (d, J = 8.4 Hz, 1H), 6.58 (q, J =6.8 Hz, 1H), 2.76 (s, 3H), 1.94 (d, J =6.4 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 163.9, 156.2, 148.8, 145.9, 145.3, 142.3, 133.1, 129.0, 126.9, 125.8, 125.7, 123.2, 70.1, 22.1, 21.1; IR (KBr) (ν, cm^{-1}) 3419, 1732, 1614, 1522, 1350, 1317, 1272, 1249, 1125, 1070, 781, 737; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{14}N_2O_4Na$ 309.0851; Found 309.0846.

1-(Pyridin-2-yl)ethyl cinnamate (3g). Colorless oil (19.7 mg, 78 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.61 (d, J = 2.8 Hz, 1H), 7.75 - 7.67 (m, 2H), 7.54 - 7.51 (m, 2H), 7.40 - 7.37 (m, 4H), 7.21 (dd, J = 6.6 Hz, J = 4.3 Hz, 1H), 6.54 (d, J = 16.0 Hz, 1H), 6.06 (q, J =6.4 Hz, 1H), 1.68 (d, J =6.8 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 166.1, 160.3, 149.2, 145.2, 136.9, 134.3, 130.3, 128.8, 128.1, 122.7, 120.5, 118.0, 73.0, 20.8; IR (KBr) (ν, cm^{-1}) 1711, 1636, 1590, 1449, 1331, 1306, 1270, 1256, 1202, 1170, 1071, 979, 767; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{15}NO_2Na$ 276.1001; Found 276.1012.

1-(Pyridin-2-yl)ethyl 3-(naphthalen-1-yl)acrylate (3h). Colorless oil (18.2 mg, 60 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.94 - 7.67 (m, 7H), 7.52 - 7.47 (m, 3H), 7.28 - 7.26 (m, 1H), 6.67 (d, J = 15.6 Hz, 1H), 6.13 (s, 1H), 1.73 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.2, 145.4, 137.7, 134.3, 134.2, 133.2, 131.8, 130.1, 128.7, 128.6, 127.8, 127.3, 126.7, 123.5, 123.1, 120.9, 118.1, 72.8, 21.0; IR (KBr) (ν, cm^{-1}) 2359, 2341, 1715, 1450, 1307, 1270, 1202, 1171, 1071, 768, 713; HRMS (APCI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{20}H_{17}NO_2Na$ 326.1157; Found 326.1151.

1-(Pyridin-2-yl)ethyl thiophene-2-carboxylate (3i). Colorless oil (15.8 mg, 68 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.31 (s, 1H), 7.97 (d, J = 3.3 Hz, 1H), 7.85 - 7.78 (m, 2H), 7.62 (d, J = 4.8 Hz, 1H), 7.14 - 7.12 (m, 1H), 6.48 (q, J = 6.3 Hz, 1H), 1.91 (d, J = 6.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.7, 156.8, 144.7, 142.7, 134.9, 133.6, 132.0, 128.2, 125.3, 123.0, 69.8, 21.4; IR (KBr) (ν, cm^{-1}) 3069, 3026, 2986, 2562, 2076, 2003, 1708, 1630, 1618, 1523, 1415, 1368, 1358, 1279, 1265, 1229, 1095, 1075.; HRMS (APCI-TOF) m/z: [M + H]$^+$ Calcd for $C_{12}H_{12}NO_2S$ 234.0588; found 234.0589.

1-(Pyridin-2-yl)propyl 4-nitrobenzoate (3j). Colorless oil (22.9 mg, 80 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.85 (s, 1H), 8.40 - 8.26 (m, 5H), 7.77 (s, 2H), 6.27 (s, 1H), 2.38 - 2.32 (m, 2H), 1.08 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.9, 155.4, 150.9, 144.2, 143.6, 134.2, 131.4, 125.4, 123.8, 123.7, 75.8, 28.4, 9.8; IR (KBr) (ν, cm^{-1}) 3450, 1728, 1640, 1528, 1345, 1299, 1240, 1116, 1102, 1083, 1014, 872, 784; HRMS (APCI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{15}H_{14}N_2O_4Na$ 309.0851; Found 309.0840.

1-(Pyridin-2-yl)pentyl 4-nitrobenzoate (3k). Colorless oil (25.8 mg, 82 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.30 (s, 4H), 7.85 (s, 1H), 7.49 - 7.38 (m, 2H), 6.11 (t, J = 5.8 Hz, 1H), 2.19 - 2.15 (m, 2H), 1.41 - 1.38 (m, 4H), 0.89 (t, J = 6.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.1, 164.0, 158.0, 150.7, 148.0, 138.8, 135.2, 131.00, 130.97, 123.7, 123.6, 123.5, 121.8, 77.2, 34.6, 27.5, 22.3, 13.9; IR (KBr) (ν, cm^{-1}) 3113, 1726, 1528, 1401, 1346, 1270, 1101, 718;

HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{18}N_2O_4Na$ 337.1164; Found 337.1142.

2-(4-Cyanophenyl)-1-(pyridin-2-yl)ethyl 4-nitrobenzoate (3l). Colorless oil (25.4 mg, 68 % yield); ^1H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.29 (d, J = 8.8 Hz, 2H), 8.20 (d, J = 8.8 Hz, 2H), 7.81 - 7.77 (m, 1H), 7.53 (d, J = 8.0 Hz, 2H), 7.39 - 7.32 (m, 4H), 6.36 (t, J = 6.2 Hz, 1H), 3.63 - 3.52 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.6, 156.4, 150.8, 148.4, 141.8, 134.6, 132.4, 132.2, 130.9, 130.3, 124.0, 123.7, 122.1, 118.6, 111.0, 76.9, 40.8; IR (KBr) (ν, cm^{-1}) 2926, 2225, 1729, 1606, 1590, 1533, 1505, 1469, 1438, 1348, 1273, 1258, 1113, 1099, 1048, 1014, 1006, 991, 874, 855, 837, 817, 779; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{15}N_3O_4Na$ 396.0960; Found 396.0959.

2-(4-(Methoxycarbonyl)phenyl)-1-(pyridin-2-yl)ethyl 4-nitrobenzoate (3m). Colorless oil (26.0 mg, 64 % yield); ^1H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 8.31 - 8.13 (m, 5H), 7.93 (d, J = 4.8 Hz, 2H), 7.94 - 7.92 (m, 1H), 7.55 (s, 1H), 7.38 - 7.37 (m, 2H), 6.59 (s, 1H), 3.88 (s, 3H), 3.77 - 3.69 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.7, 163.6, 154.6, 151.0, 140.2, 140.1, 133.9, 131.3, 130.0, 129.7. 129.4, 125.6, 124.0, 123.8, 75.0, 52.2, 41.0; IR (KBr) (ν, cm^{-1}) 2360, 2341, 1723, 1717, 1528, 1344, 1285, 1270, 1103, 1015; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{18}N_2O_6Na$ 429.1063; Found 429.1046.

2-(4-Methylphenylsulfonamido)-1-(pyridin-2-yl)ethyl 4-nitrobenzoate (3n). Colorless oil (26.5 mg, 60 % yield); ^1H NMR (hydrochloride salt; 400 MHz, DMSO-d_6) δ 8.63 (d, J = 5.2 Hz, 1H), 8.38 (d, J =11.2 Hz, 2H), 8.30 (d, J =10.8 Hz, 2H), 8.18 (t, J = 6.2 Hz, 1H), 8.01 - 7.97 (m, 1H), 7.65 (d, J = 8.4 Hz, 2H), 8.60 (d, J = 7.6 Hz, 1H), 7.53 - 7.50 (m, 1H), 7.33 (d, J = 8.0 Hz, 2H), 6.04 (t, J = 5.6 Hz, 1H), 3.48 (t, J = 5.8 Hz, 2H), 2.35 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 164.0, 155.6, 151.0, 148.7, 143.2, 138.3, 135.1, 131.6, 130.2, 126.8, 124.5, 124.3, 122.4, 76.0, 46.3, 21.4; IR (KBr) (ν, cm^{-1}) 2361, 1733, 1521, 1338, 1154, 1106, 792, 666; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{19}N_3O_6SNa$ 464.0892; Found 464.0899.

1-(6-Ethylpyridin-2-yl)ethyl 4-nitrobenzoate (3o). Colorless oil (18.6 mg, 62 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.31 - 8.27 (m, 4H), 8.14 (t, J = 7.2 Hz, 1H), 7.59 (d, J = 7.6 Hz, 1H), 7.53 (d, J = 7.6 Hz, 1H), 6.69 (d, J = 6.4 Hz, 1H), 3.35 (d, J = 6.4 Hz, 2H), 1.95 (d, J = 6.4 Hz, 3H), 1.44 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.5, 161.1, 156.7, 150.8, 134.4, 131.1, 124.1, 123.7, 119.7, 70.9, 27.3, 21.4, 13.5; IR (KBr) (ν, cm^{-1}) 1727, 1525, 1348, 1293, 1124, 1103, 1082; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{16}N_2O_4Na$ 323.1008; Found 323.0986.

1-(6-Methylpyridin-2-yl)ethyl 4-nitrobenzoate (3p). Colorless oil (16.0 mg, 56 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, DMSO-d_6) δ 8.38 (d, J = 9.2 Hz, 2H), 8.30 (d, J = 8.8 Hz, 2H), 8.21 (t, J = 7.8 Hz, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.64 (d, J = 7.6 Hz, 1H), 6.30 (q, J = 6.8 Hz, 1H), 2.71 (s, 3H), 1.75 (d, J = 6.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 164.0, 155.9, 151.0, 135.1, 131.5, 126.1, 124.4, 120.3, 71.7, 21.0; IR (KBr) (ν, cm^{-1}) 1705, 1651, 826, 777, 629; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{14}N_2O_4Na$ 309.0851; Found 309.0835.

6,7-Dihydro-5H-cyclopenta[b]pyridin-7-yl 4-nitrobenzoate (3q). Colorless oil (21.9 mg, 77 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.74 (d, J = 4.0 Hz, 1H), 8.32 (d, J = 8.4 Hz, 2H), 8.25 (d, J = 8.4 Hz, 2H), 8.19 (d, J = 7.6 Hz, 1H), 7.77 (t, J =5.6 Hz, 1H), 6.69 (t, J = 6.4 Hz, 1H), 3.37 - 3.02 (m, 3H), 2.39 - 2.32 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.3, 157.9, 150.6, 146.2, 139.5, 136.3, 135.2, 131.2, 124.7, 123.4, 77.5, 31.0, 28.1; IR (KBr) (ν, cm^{-1}) 3734, 3648, 2359, 2342, 1733, 1716, 1697, 1683, 1653, 1646, 1558, 1540, 1521, 1507, 1457; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{12}N_2O_4Na$ 307.0695; Found 307.0699.

5,6,7,8-Tetrahydroquinolin-8-yl 4-nitrobenzoate (3r). Colorless oil (23.5 mg, 79 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.24 (s, 4H), 8.14 (d, J = 7.2 Hz, 1H), 7.83 - 7.73 (m, 1H), 6.55 (s, 1H), 3.12 - 2.96 (m, 2H), 2.43 - 2.27 (m, 2H), 2.06 - 2.03 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.7, 150.5, 148.4, 144.8, 141.6, 138.2, 135.1, 131.3, 125.6, 123.4, 68.2, 27.9, 27.8, 18.1; IR (KBr) (ν, cm^{-1}) 3860, 3813, 3799, 3794, 3777, 3742, 3730, 3708, 3686, 1732, 1529,

1347, 1297, 1234, 1159, 1083, 1014, 956, 872, 851; HRMS (APCI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{16}H_{14}N_2O_4Na$ 321.0851; Found 321.0850.

Isoquinolin-3-ylmethyl 4-nitrobenzoate (3s). Light brown oil (17.9 mg, 58 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 9.31 (s, 1H), 8.32 - 8.28 (m, 4H), 8.03 (d, J = 8.0 Hz, 1H), 7. 89 - 7.86 (m, 2H), 7.76 (t, J = 7.6 Hz, 1H), 7. 67 (t, J =7.4 Hz, 1H), 5.69 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.5, 152.6, 150.6, 147.7, 136.2, 135.3, 131.2, 131.0, 128.1, 128.0, 127.8, 126.7, 123.6, 119.6, 68.0; IR (KBr) (ν, cm^{-1}) 2955, 2924, 2868, 2851, 1726, 1519, 1460, 1283; HRMS (APCI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{17}H_{12}N_2O_4Na$ 331.0695; Found 331.0693.

1-(Pyrazin-2-yl)propyl 4-nitrobenzoate (3t). Colorless oil (18.7 mg, 65 % yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.59 - 8.54 (m, 2H), 8.32 - 8.25 (m, 4H), 6.06 - 6.02 (m, 1H), 2.23 - 2.15 (m, 2H), 1.03 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.0, 154.2, 150.7, 144.24, 144.19, 143.2, 135.1, 130.9, 123.6, 29.7, 27.6, 9.6; IR (KBr) (ν, cm^{-1}) 2359, 2342, 1717, 1540, 1526, 1507, 1270, 1102; HRMS (APCI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{14}H_{13}N_3O_4Na$ 310.0804; Found 310.0782.

Quinolin-8-ylmethyl 4-nitrobenzoate (3u). White solid (23.1 mg, 75 % yield); m.p. 153 - 154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, J = 4.0 Hz, 1H), 8.26 (s, 4H), 8.20 (d, J = 8.4 Hz, 1H), 7.86 - 7.84 (m, 2H), 5.57 (t, J = 7.6 Hz, 1H), 7.47 (dd, J = 8.3, 4.2 Hz, 1H), 6.14 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.7, 150.5, 150.0, 146.2, 136.3, 135.8, 133.5, 130.8, 128.9, 128.5, 128.2, 126.2, 123.5, 121.5, 64.2; IR (KBr) (ν, cm^{-1}) 2360, 2342, 1719, 1526, 1346, 1128, 1103, 845, 825; HRMS (APCI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{17}H_{12}N_2O_4Na$ 331.0695; Found 331.0677.

Pyridin-2-ylmethyl 4-methoxybenzoate (3v). Colorless oil (17.5 mg, 72 % yield); ^{1}H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.78 (d, J = 4.0 Hz, 1H), 8.25 (t, J = 7.4 Hz, 1H), 8.08 (d, J = 8.8 Hz, 2H), 7.83 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 5.8 Hz, 1H), 6.94 (d, J = 8.8 Hz, 2H), 5.82 (s, 2H), 3.86 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.4, 164.0, 152.9, 143.7, 143.1, 132.2, 125.2, 124.8, 120.8, 113.9, 62.1, 55.5; IR (KBr) (ν, cm^{-1}) 2359, 1716, 1605, 1507, 1269, 1264, 1253, 1169, 1102;

HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{13}NO_3Na$ 266.0793; Found 266.0785.

(5-Methylpyridin-2-yl)methyl 4-methoxybenzoate (3w). Colorless oil (18.3 mg, 71 % yield); ^1H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.08 (d, J = 8.8 Hz, 2H), 8.01 (d, J = 7.6 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 6.94 (d, J = 8.8 Hz, 2H), 5.76 (s, 2H), 3.87 (s, 3H), 2.52 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.5, 164.0, 149.7, 144.1, 142.9, 136.1, 132.2, 124.6, 121.0, 113.9, 62.1, 55.5, 18.4; IR (KBr) (ν, cm^{-1}) 3730, 2953, 2918, 2849, 2360, 2341, 1731, 1704, 1513, 1462, 1293, 1236, 1168, 1101, 1083, 1013; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{15}NO_3Na$ 280.0950; Found 280.0930.

(5-Ethylpyridin-2-yl)methyl 4-methoxybenzoate (3x). Colorless oil (17.4 mg, 64 % yield); ^1H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.06 (d, J = 8.8 Hz, 2H), 7.82 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 6.92 (d, J = 9.2 Hz, 2H), 5.61 (s, 2H), 3.85 (s, 3H), 2.74 (q, J = 7.6 Hz, 2H), 1.28 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.7, 163.7, 151.3, 145.1, 140.5, 140.1, 132.0, 123.4, 121.5, 113.7, 64.1, 55.4, 25.8, 14.8; IR (KBr) (ν, cm^{-1}) 3445, 1715, 1575, 1510, 1456, 1317, 1278, 1258, 1168, 1101, 1027, 846, 769; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{17}NO_3Na$ 294.1106; Found 294.1120.

(5-Bromopyridin-2-yl)methyl 4-methoxybenzoate (3y). Colorless oil (24.1 mg, 75 % yield); ^1H NMR (hydrochloride salt; 400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.05 (d, J = 8.4 Hz, 2H), 7.85 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 6.93 (d, J = 8.8 Hz, 2H), 5.41 (s, 2H), 3.87 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.8, 163.6, 154.7, 150.3, 139.6, 131.9, 123.1, 121.9, 119.8, 113.7, 66.2, 55.5; IR (KBr) (ν, cm^{-1}) 1728, 1710, 1607, 1576, 1510, 1472, 1452, 1365, 1333, 1317, 1251, 1114, 1103, 1090, 1023, 1006, 841, 830, 769; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{12}BrNO_3Na$ 343.9898; Found 343.9918.

(4-Nitropyridin-2-yl)methyl 4-methoxybenzoate (3z). White solid (20.7 mg, 72 % yield); m.p. 87 - 88 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, J = 5.2 Hz, 1H), 8.14

(d, J =1.6 Hz, 1H), 8.08 (d, J = 9.2 Hz, 2H), 7.98 - 7.96 (m, 1H), 6.97 (d, J = 7.2 Hz, 2H), 5.58 (s, 2H), 3.88 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.7, 163.8, 160.1, 154.5, 151.7, 131.9, 121.9, 115.3, 113.9, 66.0, 55.5; IR (KBr) (v, cm^{-1}) 1728, 1607, 1576, 1534, 1509, 1464, 1422, 1357, 1286, 1263, 1170, 1101, 1032, 846, 764, 738, 686; HRMS (APCI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{12}N_2O_5Na$ 311.0644; Found 311.0639.

ASSOCIATED CONTENT

Supporting Information.

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

AUTHOR INFORMATION

Corresponding Authors

E-mail: csyao@jsnu.edu.cn; ltj2008@jsnu.edu.cn

Notes

The authors declare no competing financial interest.

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