# Copper-Catalyzed Formal C−N Bond Cleavage of Aromatic Methylamines: Assembly of Pyridine Derivatives

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S *Supporting Information*

ABSTRACT: An efficient copper-catalyzed C−N bond cleavage of aromatic methylamines was developed to construct pyridine derivatives. With neat conditions and facile operation, the fragment-assembling strategy affords a broad range of 2,4,6-trisubstituted pyridines in up to 95% yield from simple and readily available starting materials. Interestingly, when pyridin-2-yl methylamine was employed as the substrate, α-alkylation reaction of ketones readily occurred to give β-(pyridin-2-yl) ketones instead of the 2,4,6-trisubstituted pyridines.
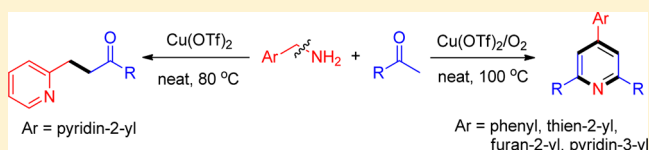
INTRODUCTION

It is known that pyridine forms the structural core of many natural products, pharmaceutical agents, and functionalized materials.[1] In particular, β-(pyridin-2-yl) ketones were identified as lead structures for a series of pyridine derivatives with umami flavor (UF, Figure 1), which were widely applied as wonderful
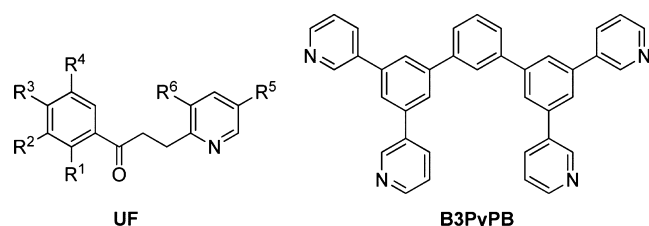

Figure 1. Structure of UF and B3PyPB.

alternatives to monosodium glutamate in the food industry.[1e] Compound B3PyPB (Figure 1), one of the pyridine-based π-conjugated systems, was used in high-performance FIrpic-based organic light-emitting device (OLED).[1d] Consequently, pyridine synthesis remains a topic of considerable interest in modern synthetic chemistry.[2]

Synthetic strategies involving C−N bond cleavage have been widely investigated. Classic examples include deprotection of N-protecting groups[3] and cross-coupling reactions[4] by C−N bond cleavage, both of which are powerful tools having great significance for synthetic and pharmacological chemistry due to the efficiency and versatility for rapid generation of a broad range of functionalized products. Among them, cross-coupling reacions through C−N bond cleavage of N-benzylic sulfonamides[5] provided a convenient access to α-alkylation of ketones,[5a,b] Friedel−Crafts alkylation of indoles,[5c,d] and other C−C bond forming reactions.[5e,f] However, the employment of N-protected benzyl amines in previous work limited the application of this methodology. In this paper, we found pyridin-2-yl methylamine
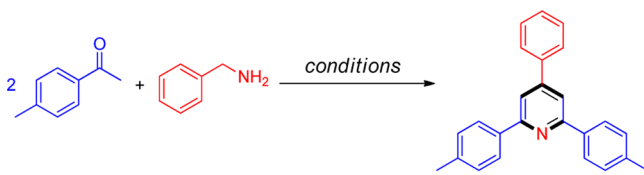
featured high reactivity in the copper-catalyzed α-alkylation reaction of ketones to afford pharmacologically significant β-(pyridin-2-yl) ketones.

Other aromatic methylamines also proceeded C−N bond cleavage in the copper-catalytic system with ketones. Instead of generation of β-aryl ketones, both carbon and nitrogen components of bond-cleavage were trapped by ketones to assemble 2,4,6-trisubstituted pyridine derivatives. This fragment-assembling strategy would be of great interest and potential applications due to the high atom economy, and offer opportunities to achieve desirable synthetic convergence and flexibility to improve overall efficiency. With this strategy, for example, Xi and co-workers reported a novel isomerization for the synthesis of dihydropyrimidine derivatives by C−N bond cleavage of azetidines and intramolecular ring-closing reaction.[6] Herein, for the first time, we report a copper-catalyzed C−N bond cleavage of aromatic methylamines with molecular oxygen as the oxidant for ready generation of 2,4,6-trisubstituted pyridine derivatives. From simple and readily available starting materials, the present protocol features advantages including atom economy, neat conditions (minimized waste), environmentally friendly oxidant, and nonhazardous byproduct (water), and more importantly offers great flexibility in the construction of nitrogen-containing heterocycles under Cu/O$_2$ systems.[7]

RESULTS AND DISCUSSION

Synthesis of 2,4,6-Trisubstituted Pyridines. Initially, 1-(p-tolyl)ethanone (**1b**, 2 mmol) and benzylamine (**2a**, 1.2 mmol), treated with copper catalyst under air and neat conditions, were chosen as the model system (Table 1). To our delight, after heating the mixture at 100 °C for 20 h, this reaction with CuI, CuBr, or CuCl$_2$ afforded a certain yield of 2,4,6-trisubstituted pyridine **3ba** (entries 1−3) bearing symmetrical structure, which

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Table 1. Screening the Reaction Conditions[a]

entry	[Cu] catalyst	oxidant	solvent	temperature (°C)	yield (%)
1	CuI	air	neat	100	32
2	CuBr	air	neat	100	20
3	CuCl$_2$	air	neat	100	29
4	Cu(OAc)$_2$	air	neat	100	trace
5	Cu(OOCCF$_3$)$_2$	air	neat	100	60
6	Cu(OTf)$_2$	air	neat	100	73
7	Cu(OTf)$_2$	air	neat	80	68
8	Cu(OTf)$_2$	air	neat	120	73
9[b]	Cu(OTf)$_2$	air	neat	100	91
10[c]	Cu(OTf)$_2$	O$_2$ (1 atm)	neat	100	75
11[d]	Cu(OTf)$_2$	O$_2$ (1 atm)	neat	100	92
12[e]	Cu(OTf)$_2$	–	neat	100	trace
13[f]	–	O$_2$ (1 atm)	neat	100	trace
14[g]	Cu(OTf)$_2$	O$_2$ (1 atm)	water	100	77
15[g]	Cu(OTf)$_2$	O$_2$ (1 atm)	DMSO	100	80
16[g]	Cu(OTf)$_2$	O$_2$ (1 atm)	toluene	100	89
17[g]	Cu(OTf)$_2$	O$_2$ (1 atm)	DMF	100	47

[a]The reaction was performed in an opened tube (25 mL) with **1b** (2 mmol), **2a** (1.2 mmol) and [Cu] catalyst (0.1 mmol) for 20 h. GC yield based on **1b** was given. [b]Using 1.6 mmol of **2a**. [c]An O$_2$ balloon was attached to the tube. [d]The reaction was performed in a sealed tube (25 mL) filled with O$_2$ (1 atm). [e]Under nitrogen atmosphere. [f]In the absence of Cu(OTf)$_2$. [g]0.5 mL of solvent was used.

indicated a C−N bond cleavage of **2a**/condensation/oxidation reaction sequence in this transformation. Among the copper catalysts screened (entries 3−6), Cu(OTf)$_2$ (5 mol %) was found to be the best catalyst to give the target **3ba** in 73% yield (entry 6), in which benzylamine was converted completely with some ketone **1b** left. Screening different reaction temperature suggested 100 °C was optimal (entries 7−8). Compared with air, the reaction equipped with an O$_2$ (1 atm) balloon gave a slight increase in the yield (entry 10). Gratifyingly, the reaction performed in a sealed tube filled with oxygen atmosphere (1 atm) increased the yield to 92% (entry 11), while with an opened system under air, more than 1.6 equiv (1.6 mmol) of benzylamine were required to facilitate a full conversion of ketone (entry 9). Furthermore, this reaction could not yield the target product under nitrogen atmosphere (entry 12) or without additional copper catalyst (entry 13). The employment of solvent in this system just decreased the yield of **3ba** (entries 14−17), whereas toluene had no obvious influence on the transformation (entry 16). Thus, the optimal reaction condition is ketone (2 mmol, 1 equiv), benzylamine (0.6 equiv), and Cu(OTf)$_2$ (5 mol %) conducted in a sealed tube filled with oxygen atmosphere (1 atm) at 100 °C for 20 h.

With the optimized reaction conditions in hand, we employed various methyl ketones with benzylamine to explore the generality of the pyridine assembly under the Cu/O$_2$ system (Table 2). Phenyl methyl ketones with electron-donating or electron-withdrawing substituents on the aromatic ring reacted well to give the corresponding products (Table 2, entries 1−10). Slight steric effect was observed when the substituents were presented on the *para*, *meta*, and *ortho* positions of the benzene ring,

such as **1e**, **1f**, and **1g** (Table 2, entries 5−7). Morpholino substituent (**1j**) and naphthalene (**1k**), with toluene as the solvent for convenience of operation, were tolerated to afford moderate yields of pyridine products. Both thiophen-2-yl and furan-2-yl methyl ketones **1l,m** showed high reactivities (Table 2, entries 12, 13); however, the desired 2,4,6-trisubstituted pyridine products were obtained with considerably different yields (94% of **3la** and 42% of **3ma**, respectively). Then alkyl methyl ketones were subjected to this reaction to react with **2a**. Generally, 2,6-dialkyl-substituted pyridines were obtained in moderate yields (Table 2, entries 14−19), including alkenyl substituent tolerated well (entry 19). It should be noted that acetone was also productive under the standard conditions and gave the corresponding product in 50% yield (entry 18). Unfortunately, nonmethyl ketones, such as cyclohexanone, propiophenone, and 3-pentanone, led to the desired pyridines in very low GC yields.

Next, substituted benzyl amines were employed to give the expected pyridines in excellent yields (80−92%, Table 3, entries 1−5). Heteroaryl methylamines featured considerably different reactivities. While furan-2-yl, thien-2-yl, and pyridin-3-yl methyl-amines could efficiently yield pyridines (Table 3, entries 6−8), 2-pyridyl and 4-pyridyl methylamines failed to transfer to the corresponding products. Furanyl methylamine and thienyl ketone gave 2,4,6-triheteroaryl pyridine **3lg** in good yield (Table 3, entry 9).

Surprisingly, *N*-methyl or *N*-benzyl benzylamines **2j−l** were also successfully subjected to this reaction system and provided pyridine **3aa** in moderate to excellent yields with cleavage of two or three C−N bonds (Table 4, entries 1−3), although *N*-isopropyl benzylamine (**2m**) failed to react under the optimized reaction conditions (Table 4, entry 4). Likewise, benzylamine with α-carboxylic acid or ester substituent could transfer to pyridine **3aa** with C−N bond cleavage and decarboxylation (Table 4, entries 5−6).

Two-fold C−N bond cleavage of xylylenediamine (**2p**) enabled 2-fold pyridine assembly and readily provided bis-(pyridin-4-yl)benzene **3ap** in good yield [eq 1]. Such multifold cyclizations may serve as an attractive route to extended π-conjugated systems for potential applications in OLED.[1c,d]
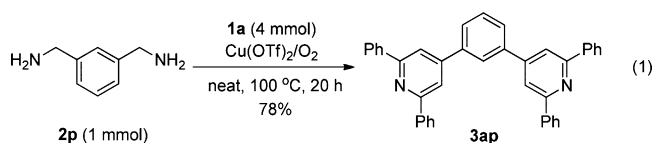
In this copper/oxygen catalytic system, cross reactions with two different methyl ketones provided asymmetrically substituted pyridines as major products. As shown in Scheme 1, 1-(4-methoxyphenyl)ethanone (**1e**, 1 mmol) and benzylamine (**2a**, 1.2 mmol), when treated with methyl ketone (1 mmol), such as **1a**, **1c**, **1l**, and **1o**, smoothly afforded pyridines **4a**, **4b**, **4c**, and **4d**, respectively, in moderate yields.

To shed light on the reaction mechanism, several controlled experiments were conducted. Aerobic oxidation of benzylamine to imine **5** efficiently occurred under this Cu/O$_2$ system [eq 2]. When treated with 4-methylbenzaldehyde (1 equiv), ketone **1a** and benzylamine **2a** (1 equiv) afforded 4-(*p*-tolyl)-pyridine **3ak** as the main product [eq 3], which indicated that the aldehyde was probably the key intermediate in this chemical process. With the experimental results obtained, a circular reaction pathway is proposed as shown in Scheme 2. First, Cu(II)-mediated single-electron oxidation[7d] of benzylamine and aminolysis
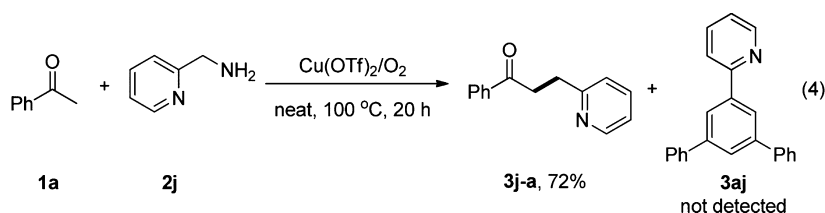
Table 2. Synthesis of 2,4,6-Trisubstituted Pyridines via C−N Bond Cleavage[a]

Entry	Ketone	Pyridine	Yield (%)	Entry	Ketone	Pyridine	Yield (%)
				13[c]	1m	3ma	42
1	1a, R' = H	3aa, R' = H	91				
2	1b, R' = 4-Me	3ba, R' = 4-Me	90	14	1n	3na	61
3	1c, R' = 4-F	3ca, R' = 4-F	91				
4	1d, R' = 4-Cl	3da, R' = 4-Cl	75				
5	1e, R' = 4-OMe	3ea, R' = 4-OMe	87	15	1o	3oa	75
6	1f, R' = 3-OMe	3fa, R' = 3-OMe,	85				
7	1g, R' = 2-OMe	3ga, R' = 2-OMe	70				
8	1h, R' = 4-OCF$_3$	3ha, R' = 4-OCF$_3$	90	16	1p	3pa	70
9	1i, R' = 4-SMe	3ia, R' = 4-SMe	85				
10[b]	1j, R'= 4-morpholino	3ja, R' = 4-morpholino	54				
11[b]	1k	3ka	48	17	1q	3qa	55
12[c]	1l	3la	94	18	1r	3ra	50
				19	1s	3sa	42

[a]Reagents and conditions: 1 (2 mmol), 2 (1.2 mmol), and Cu(OTf)$_2$ (0.1 mmol) at 100 °C for 20 h. Isolated yields were given. [b]Using toluene (0.5 mL) as the solvent. [c]At 80 °C for 8 h.

provided imine 5.[8] Then hydrolysis of imine would give benzaldehyde and benzylamine, which is a reversible process (Scheme 2, path A). Subsequently, promoted by Lewis acidic Cu(II), the condensation[9] of ketone, benzylamine, and benzaldehyde afforded intermediate 1,4-dihydropyridine intermediate II. Finally, II was readily oxidized to the final product 3aa and generated benzaldehyde via oxidative hydrolysis under Cu/O$_2$ catalytic system. The benzaldehyde would participate in the next pyridine formation (Scheme 2, path B). Additionally, either imine 5 replacing benzaldehyde or ammonia replacing benzylamine could serve as corresponding component in the condensation process.

Table 3. Synthesis of 2,4,6-Trisubstituted Pyridines via C−N Bond Cleavage[a]

$$2 \; \underset{Ar^1}{\overset{O}{\parallel}} + Ar^2 \diagdown NH_2 \xrightarrow[\text{neat, 100 °C, 20 h}]{Cu(OTf)_2/O_2} \underset{Ar^1 \diagup N \diagdown Ar^1}{Ar^2}$$

Entry	1	2 (Ar²)	3	Yield (%)
1	1a	2b (4-FC₆H₄)	3ab, R = 4-F	92
2	1a	2c (3-ClC₆H₄)	3ac, R = 3-Cl	89
3	1a	2d (2-ClC₆H₄)	3ad, R = 2-Cl	80
4	1a	2e (4-OMeC₆H₄)	3ae, R = 4-OMe	90
5	1a	2f (2-OMeC₆H₄)	3af, R = 2-OMe	88
6	1a	2g (furan-2-yl)	3ag	88
7	1a	2h (thiophen-2-yl)	3ah	95
8	1a	2i (pyridin-3-yl)	3ai	65
9	1l	2g	3lg	88

[a]Reagents and conditions: 1 (2 mmol), 2 (1.2 mmol), and Cu(OTf)₂ (0.1 mmol) at 100 °C for 20 h.

Synthesis of β-(Pyridin-2-yl)-ketones. As described above, under the copper-catalyzed system, 2-pyridyl methylamine 2j with ketone 1a could not generate 2,4,6-trisubstituted pyridine. Instead, the chain product 3j−a was obtained in 72% yield via

Table 4. Pyridine Synthesis via Cleavage of C−C and C−N Bonds[a]

$$\underset{Ph}{\overset{O}{\parallel}} + \underset{R^2}{\overset{R}{\underset{|}{Ph \diagdown N \diagdown R^1}}} \xrightarrow[\text{neat, 100 °C, 20 h}]{Cu(OTf)_2/O_2} \underset{Ph \diagup N \diagdown Ph}{Ph}$$

entry	2 (R/R¹/R²)	yield (%)
1	2j (H/H/Me)	78
2	2k (H/Me/Me)	54
3	2l (H/H/Bn)	90
4	2m (H/H/i-Pr)	trace
5	2n (COOH/H/H)	80
6	2o (COOMe/H/H)	55

[a]Reagents and conditions: 1a (2 mmol), 2 (1.2 mmol), and Cu(OTf)₂ (0.1 mmol) at 100 °C for 20 h.

Scheme 1. Synthesis of Asymmetrical Pyridines

4a, R = Ph, 56%
4b, R = 4-FC₆H₄, 48%
4c, R = thiophen-2-yl, 60%
4d, R = cyclopropyl, 42%

deamination cross-coupling reaction [eq 4]. To the best of our knowledge, this is the first exmple of α-alkylation reaction of

$$Ph \diagdown NH_2 \xrightarrow[\text{neat, 100 °C, 20 h}]{Cu(OTf)_2/O_2} Ph \diagdown N \diagdown Ph + NH_3 \quad (2)$$

5, 96%

$$1a + 2a + \overset{\text{p-tol}}{\underset{Ph \diagup N \diagdown Ph}{\text{CHO}}} \xrightarrow{\text{as above}} \overset{p\text{-tol}}{\underset{Ph \diagup N \diagdown Ph}{}} + \overset{Ph}{\underset{Ph \diagup N \diagdown Ph}{}} \quad (3)$$

3ak, 72%   3aa, 8%

Scheme 2. Plausible Reaction Mechanism for the Synthesis of 2,4,6-Trisubstituted Pyridines

path A:

$$Ph \diagdown NH_2 \xrightarrow[-H_2O]{O_2, Cu(II) \to Cu(I)} Ph \diagdown NH \xrightarrow[-NH_3]{2a} Ph \diagdown N \diagdown Bn$$

2a   I   5

$$\xrightarrow[H_2O]{} PhCHO + 2a$$

path B:

$$\underset{Ph}{\overset{O}{\parallel}} + Ph \diagdown NH_2 + PhCHO \xrightarrow{\text{condensation}} \left[\underset{Ph \diagup \underset{Bn}{N} \diagdown Ph}{Ph} \right]$$

1a   2a   II

$$\xrightarrow[-PhCHO]{O_2, Cu(II) \to Cu(I)} \underset{Ph \diagup N \diagdown Ph}{Ph}$$

3aa

ketones using primary monoaryl methylamine as the reaction partner. After simple optimization of the reaction conditions, this reaction could afford **3j−a** in 95% yield at 80 °C for 12 h (Scheme 3). Other ketones such as substituted phenyl ketones,

**Scheme 3. Scope of the Deamination Cross-Coupling Reaction**
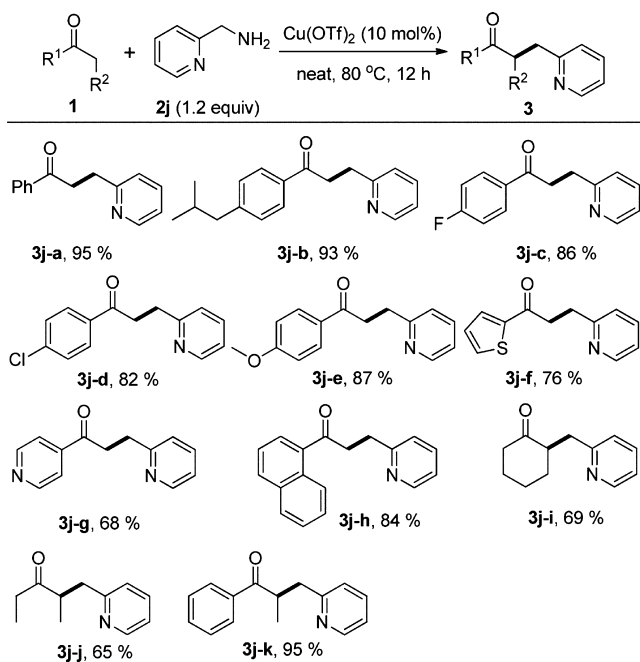
naphthyl ketone, thienyl ketone, and pyridyl ketone could be also converted to the corresponding chain products in good yields with C(sp³)−C(sp³) bond formation. It is surprising that nonmethyl ketones, such as cyclohexanone, propiophenone, and 3-pentanone, also featured high activities in this reaction system, giving the corresponding β-(pyridin-2-yl)-ketones in good to excellent yields.

N-Methyl-1-(pyridin-2-yl)methanamine (**2k**) also smoothly reacted with ketone **1a** under this reaction system, affording the desired product **3j−a** in 77% yield [eq 5]. However, N-tosyl-1-(pyridin-2-yl)methanamine (**2l**) failed to give the final pyridine [eq 6], probably because the protonation of the tosyl-protected amine did not easily occur. Finally, it was found that pyridin-2-ylmethanol (**2m**) was unable to yield the corresponding product, which suggested that **2m** was not the intermediate product in this transformation.

Interestingly, this cross-coupling reaction occurred only in the case of 2-pyridyl methylamine, which suggested the coordination interaction between copper catalyst and 2-pyridyl methylamine would play a key role in the transformation. A plausible reaction mechanism is proposed as shown in Scheme 4. Interaction of Cu(OTf)₂ and ketone **1a** afforded alkenyloxy copper species **A**, and simultaneously generated HOTf, which would react with 2-pyridyl methylamine (**2j**) to give ammonium **B**. Subsequently,

intermediate **C**, formed via coordination interaction between **A** and **B**, underwent intramolecular nucleophilic attack and
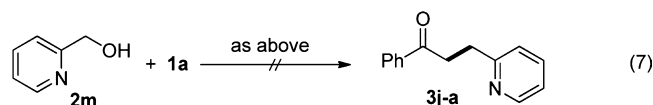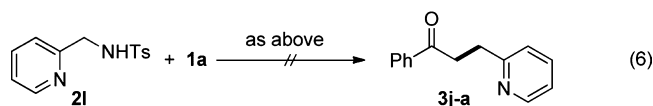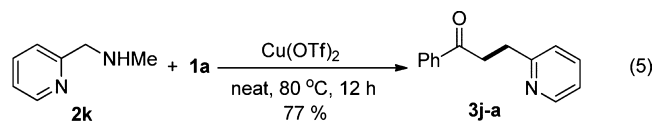
Scheme 4. Plausible Reaction Mechanism for the Cross-Coupling Reaction
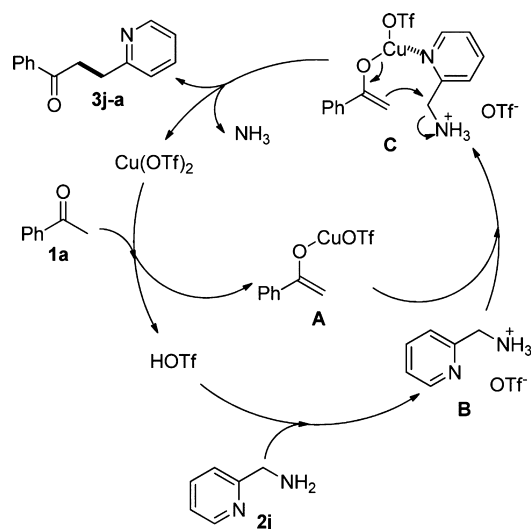
carbon−nitrogen bond cleavage in an S_N2 manner to provide the final product **3j−a**.

■ CONCLUSIONS

In summary, a practical copper-catalyzed C−N bond cleavage of aromatic methylamines was developed to construct functionalized pyridine derivatives. A series of 2,4,6-trisubstituted pyridines was efficiently obtained in moderate to excellent yields. This process should be initiated by copper-catalyzed aerobic oxidative cleavage of C−N bond of aromatic methylamines. A wide range of ketones and aromatic methylamines were tolerated well in this Cu/O₂ catalytic system. This fragment-assembling strategy is highly compatible with the goal of sustainable and green chemistry. In particular, pyridin-2-yl methylamine could transfer to different β-(pyridin-2-yl) ketones in good yields via α-alkylation of ketones. The finding that different aromatic methylamines show different reaction selectivity under copper catalysis system might open up a new way to design functionalized molecules in organic synthesis.

■ EXPERIMENTAL SECTION

General Methods. ^{1}H and ^{13}C NMR spectra were recorded using a 400 MHz NMR spectrometer. The chemical shifts were referenced to signals at 7.26 and 77.0 ppm, respectively, and CDCl$_3$ was used as the solvent with TMS as the internal standard. High-resolution mass spectra were obtained with a LCMS-IT-TOF mass spectrometer. TLC was performed by using commercially prepared 100−400 mesh silica gel plates (GF$_{254}$), and visualization was effected at 254 nm. Unless otherwise noted, all commercial materials and solvents were used without further purification.

General Procedure for the Synthesis of 2,4,6-Trisubstituted Pyridines. To a 25 mL pressure tube was added a mixture of ketone **1** (2 mmol), benzylamine **2** (1.2 mmol), and Cu(OTf)$_2$ (36 mg, 0.1 mmol), successively. Subsequently, the tube was evacuated with a vacuum pump, filled with oxygen (1 atm), and sealed with Teflon stopper. The mixture was stirred at 100 °C for 20 h. Upon completion, the crude product was cooled to room temperature and then directly separated by flash column chromatography on silica gel to give the pure product **3**. Pyridines **3ja** and **3ka** were prepared using toluene (0.5 mL) as the solvent for convenience of stirring. Pyridines **3la** and **3ma** were obtained at 80 °C for 8 h. Asymmetrical pyridines **4a−d** were synthesized according to this procedure using two different ketones (1 mmol for each).

2,4,6-Triphenylpyridine (3aa).[10] In 91% yield (279 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.22 (d, J = 7.1 Hz, 4H), 7.91 (s, 2H), 7.77 (d, J = 7.0 Hz, 2H), 7.57−7.43 (m, 9H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 157.5, 150.3, 139.5, 139.0, 129.1, 129.1, 129.0, 128.7, 127.2, 127.2, 117.2; HRMS (ESI) calc. C$_{23}$H$_{17}$N [M + H]$^+$ 308.1434, found 308.1442.

4-Phenyl-2,6-di-p-tolylpyridine (3ba).[9b] In 90% yield (301 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.08 (d, J = 7.9 Hz, 4H), 7.79 (s, 2H), 7.68 (d, J = 7.8 Hz, 2H), 7.49−7.38 (m, 3H), 7.28 (d, J = 7.9 Hz, 4H), 2.39 (s, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 157.3, 149.9, 139.2, 138.9, 136.8, 129.3, 129.0, 128.8, 127.1, 126.9, 116.4, 21.3; HRMS (ESI) calc. C$_{25}$H$_{21}$N [M + H]$^+$ 336.1747, found 336.1750.

2,6-Bis(4-fluorophenyl)-4-phenylpyridine (3ca).[9b] In 91% yield (312 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.18 (dd, J = 8.2, 5.6 Hz, 4H), 7.82 (s, 2H), 7.73 (d, J = 7.6 Hz, 2H), 7.58−7.46 (m, 3H), 7.20 (t, J = 8.5 Hz, 4H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 163.6, 156.4, 150.4, 138.8, 135.5, 129.1, 129.1, 128.9, 127.1, 116.7, 115.5; HRMS (ESI) calc. C$_{23}$H$_{15}$F$_2$N [M + H]$^+$ 344.1245, found 344.1246.

2,6-Bis(4-chlorophenyl)-4-phenylpyridine (3da).[9b] In 75% yield (281 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.13 (d, J = 7.9 Hz, 4H), 7.85 (s, 2H), 7.72 (d, J = 7.7 Hz, 2H), 7.57−7.46 (m, 7H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 156.3, 150.6, 138.6, 137.7, 135.3, 129.2, 129.1, 128.9, 128.3, 127.1, 117.1; HRMS (ESI) calc. C$_{23}$H$_{15}$Cl$_2$N [M + H]$^+$ 376.0654, found 376.0699.

2,6-Bis(4-methoxyphenyl)-4-phenylpyridine (3ea).[9b] In 87% yield (319 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.19 (d, J = 8.7 Hz, 4H), 7.79 (s, 2H), 7.75 (d, J = 7.2 Hz, 2H), 7.56−7.45 (m, 3H), 7.06 (d, J = 8.7 Hz, 4H), 3.89 (s, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 160.5, 156.9, 149.9, 139.3, 132.3, 129.0, 128.8, 128.3, 127.1, 115.6, 114.0, 55.3; HRMS (ESI) calc. C$_{25}$H$_{21}$NO$_2$ [M + H]$^+$ 368.1645, found 368.1650.

2,6-Bis(3-methoxyphenyl)-4-phenylpyridine (3fa).[9b] In 85% yield (312 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.91 (s, 2H), 7.87 (s, 2H), 7.81−7.75 (m, 4H), 7.57−7.44 (m, 5H), 7.04 (dd, J = 8.1, 2.3 Hz, 2H), 3.95 (s, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 160.0, 157.0, 150.0, 140.9, 138.8, 129.6, 129.0, 128.9, 127.1, 119.4, 117.2, 114.6, 112.6, 55.3; HRMS (ESI) calc. C$_{25}$H$_{21}$NO$_2$ [M + H]$^+$ 368.1645, found 368.1654.

2,6-Bis(2-methoxyphenyl)-4-phenylpyridine (3ga). In 70% yield (257 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.05 (s, 2H), 8.02 (d, J = 7.6 Hz, 2H), 7.78 (d, J = 7.3 Hz, 2H), 7.58−7.37 (m, 5H), 7.15 (t, J = 7.4 Hz, 2H), 7.06 (d, J = 8.2 Hz, 2H), 3.92 (s, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 157.0, 155.9, 147.6, 139.4, 131.5, 129.7, 129.6, 128.9, 128.5, 127.3, 121.3, 121.0, 111.4, 55.7; HRMS (ESI) calc. C$_{25}$H$_{21}$NO$_2$ [M + H]$^+$ 368.1645, found 368.1648.

4-Phenyl-2,6-bis(4-(trifluoromethoxy)phenyl)pyridine (3ha). In 90% yield (427 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.21 (d, J = 8.7 Hz, 4H), 7.86 (s, 2H), 7.73 (d, J = 6.9 Hz, 2H), 7.59−7.48 (m, 3H), 7.37 (d, J = 8.3 Hz, 4H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 156.2, 150.6, 150.0, 138.6, 137.9, 129.3, 129.2, 128.6, 127.1, 121.0, 120.5, 117.2; HRMS (ESI) calc. C$_{25}$H$_{15}$F$_6$NO$_2$ [M + H]$^+$ 476.1080, found 476.1103.

2,6-Bis(4-(methylthio)phenyl)-4-phenylpyridine (3ia). In 85% yield (339 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.14 (d, J = 8.4 Hz, 4H), 7.83 (s, 2H), 7.73 (d, J = 7.1 Hz, 2H), 7.58−7.47 (m, 3H), 7.38 (d, J = 8.4 Hz, 4H), 2.55 (s, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 156.8, 150.2, 139.9, 139.0, 136.2, 129.1, 128.9, 127.4, 127.1, 126.4, 116.5, 15.6; HRMS (ESI) calc. C$_{25}$H$_{21}$NS$_2$ [M + H]$^+$ 400.1188, found 400.1192.

4,4′-((4-Phenylpyridine-2,6-diyl)bis(4,1-phenylene))-dimorpholine (3ja). In 54% yield (258 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.17 (d, J = 8.8 Hz, 4H), 7.75 (d, J = 10.0 Hz, 4H), 7.55−7.45 (m, 3H), 7.02 (d, J = 8.8 Hz, 4H), 3.88 (t, J = 4.8 Hz, 8H), 3.25 (t, J = 4.8 Hz, 8H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 156.9, 151.7, 149.7, 139.4, 131.0, 128.9, 128.7, 127.9, 127.1, 115.1, 115.1, 66.7, 48.7; HRMS (ESI) calc. C$_{31}$H$_{31}$N$_3$O$_2$ [M + H]$^+$ 478.2489, found 478.2497.

2,6-Di(naphthalen-2-yl)-4-phenylpyridine (3ka).[9b] In 48% yield (195 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.71 (s, 2H), 8.45 (dd, J = 8.6, 1.2 Hz, 2H), 8.06−8.01 (m, 6H), 7.96−7.90 (m, 2H), 7.83 (d, J = 7.3 Hz, 2H), 7.62−7.50 (m, 7H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 157.4, 150.2, 139.0, 136.9, 133.7, 133.5, 129.1, 129.0, 128.7, 128.4, 127.7, 127.2, 126.5, 126.4, 126.2, 124.9, 117.4; HRMS (ESI) calc. C$_{31}$H$_{21}$N [M + H]$^+$ 408.1747, found 408.1750.

4-Phenyl-2,6-di(thiophen-2-yl)pyridine (3la).[11] In 94% yield (300 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.70−7.56 (m, 6H), 7.50−7.33 (m, 5H), 7.08 (t, J = 4.1 Hz, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 152.5, 145.0, 144.8, 138.4, 129.0, 129.0, 127.9, 127.7, 126.9, 124.7, 114.9; HRMS (ESI) calc. C$_{19}$H$_{13}$NS$_2$ [M + H]$^+$ 320.0562, found 320.0570.

2,6-Di(furan-2-yl)-4-phenylpyridine (3ma).[12] In 42% yield (121 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.81 (s, 2H), 7.76 (d, J = 7.0 Hz, 2H), 7.60−7.44 (m, 5H), 7.23 (d, J = 3.2 Hz, 2H), 6.57 (dd, J = 3.3, 1.7 Hz, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 153.7, 149.9, 149.6, 143.3, 138.3, 129.2, 129.0, 127.0, 114.8, 112.1, 109.3; HRMS (ESI) calc. C$_{19}$H$_{13}$NO$_2$ [M + H]$^+$ 288.1019, found 288.1031.

2,6-Diphenethyl-4-phenylpyridine (3na). In 61% yield (221 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.51−7.38 (m, 5H), 7.30−7.18 (m, 10H), 7.10 (s, 2H), 3.21−3.08 (m, 8H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 160.8, 149.6, 148.6, 141.4, 138.4, 129.0, 128.6, 128.3, 127.1, 126.0, 118.9, 39.8, 36.1; HRMS (ESI) calc. C$_{27}$H$_{25}$N [M + H]$^+$ 364.2060, found 364.2068.

2,6-Dicyclopropyl-4-phenylpyridine (3oa). In 75% yield (176 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.63 (d, J = 7.8 Hz, 2H), 7.50−7.38 (m, 3H), 7.10 (d, J = 0.4 Hz, 2H), 2.12−1.94 (m, 2H), 1.12−1.03 (m, 4H), 0.97−0.90 (m, 4H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 162.3, 148.1, 139.2, 128.8, 128.4, 127.0, 116.2, 17.1, 9.4; HRMS (ESI) calc. C$_{17}$H$_{17}$N [M + H]$^+$ 236.1434, found 236.1435.

2,6-Diisobutyl-4-phenylpyridine (3pa). In 70% yield (187 mg), colorless oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.73−7.58 (m, 2H), 7.50−7.34 (m, 3H), 7.15 (s, 2H), 2.72 (d, J = 7.3 Hz, 4H), 2.22−2.10 (m, 2H), 0.97 (d, J = 6.7 Hz, 12H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 161.3, 148.2, 138.9, 128.8, 128.5, 126.9, 118.6, 47.6, 29.2, 22.3; HRMS (ESI) calc. C$_{19}$H$_{25}$N [M + H]$^+$ 268.2060, found 268.2065.

2,6-Dipentyl-4-phenylpyridine (3qa). In 55% yield (162 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.62 (d, J = 7.1 Hz, 2H), 7.48−7.37 (m, 3H), 7.17 (s, 2H), 2.87−2.77 (m, 4H), 1.81−1.70 (m, 4H), 1.43−1.30 (m, 8H), 0.90 (t, J = 7.0 Hz, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 162.3, 148.9, 139.0, 128.9, 128.6, 127.0, 117.8, 38.6, 31.7, 29.9, 22.5, 14.0; HRMS (ESI) calc. C$_{21}$H$_{29}$N [M + H]$^+$ 296.2373, found 296.2379.

2,6-Dimethyl-4-phenylpyridine (3ra).[13] In 50% yield (92 mg), colorless oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.54 (d, J = 6.9 Hz, 2H), 7.43−7.33 (m, 3H), 7.12 (s, 2H), 2.53 (s, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 158.0, 149.1, 138.6, 128.9, 128.7, 127.0, 118.4, 24.5; HRMS (ESI) calc. C$_{13}$H$_{13}$N [M + H]$^+$ 184.1121, found 184.1124.

2,6-Bis(4-methylpent-3-en-1-yl)-4-phenylpyridine (3sa). In 42% yield (134 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$)

δ 7.61 (d, J = 7.2 Hz, 2H), 7.48−7.37 (m, 3H), 7.16 (s, 2H), 5.21 (t, J = 7.1 Hz, 2H), 2.85 (t, J = 7.7 Hz, 4H), 2.45 (dd, J = 15.0, 7.4 Hz, 4H), 1.68 (s, 6H), 1.55 (s, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 161.7, 148.7, 139.0, 132.1, 128.9, 128.6, 127.0, 123.6, 118.1, 38.5, 28.6, 25.7, 17.6; HRMS (ESI) calc. C$_{23}$H$_{29}$N [M + H]$^+$ 320.2373, found 320.2387.

4-(4-Fluorophenyl)-2,6-diphenylpyridine (3ab).[9b] In 92% yield (299 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.14 (d, J = 7.3 Hz, 4H), 7.72 (s, 2H), 7.59 (dd, J = 8.6, 5.3 Hz, 2H), 7.48−7.36 (m, 6H), 7.12 (t, J = 8.6 Hz, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 163.3, 157.4, 148.9, 139.3, 134.9, 129.0, 128.8, 128.6, 127.0, 116.9, 116.0; HRMS (ESI) calc. C$_{23}$H$_{16}$FN [M + H]$^+$ 326.1340, found 326.1348.

4-(3-Chlorophenyl)-2,6-diphenylpyridine (3ac). In 89% yield (303 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.13 (d, J = 7.3 Hz, 4H), 7.71 (s, 2H), 7.63 (s, 1H), 7.50−7.31 (m, 9H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 157.4, 148.5, 140.7, 139.2, 134.9, 130.2, 129.1, 128.8, 128.6, 127.2, 127.0, 125.2, 116.7; HRMS (ESI) calc. C$_{23}$H$_{16}$ClN [M + H]$^+$ 342.1044, found 342.1047.

4-(2-Chlorophenyl)-2,6-diphenylpyridine (3ad).[9b] In 80% yield (273 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.18 (d, J = 7.3 Hz, 4H), 7.73 (s, 2H), 7.52−7.26 (m, 10H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 156.8, 148.5, 139.3, 138.4, 132.2, 130.8, 130.2, 129.6, 129.0, 128.6, 127.1, 127.0, 119.3; HRMS (ESI) calc. C$_{23}$H$_{16}$ClN [M + H]$^+$ 342.1044, found 342.1052.

4-(4-Methoxyphenyl)-2,6-diphenylpyridine (3ae).[9b] In 90% yield (303 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.25 (d, J = 7.2 Hz, 4H), 7.88 (s, 2H), 7.72 (d, J = 8.8 Hz, 2H), 7.58−7.46 (m, 6H), 7.07 (d, J = 8.8 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 160.4, 157.3, 149.5, 139.6, 131.1, 128.9, 128.6, 128.2, 127.1, 116.5, 114.4, 55.3; HRMS (ESI) calc. C$_{24}$H$_{19}$NO [M + H]$^+$ 338.1539, found 338.1540.

4-(2-Methoxyphenyl)-2,6-diphenylpyridine (3af).[9b] In 88% yield (297 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.17 (d, J = 7.3 Hz, 4H), 7.84 (s, 2H), 7.49−7.34 (m, 8H), 7.04 (t, J = 7.5 Hz, 1H), 6.97 (d, J = 8.2 Hz, 1H), 3.78 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 156.6, 156.5, 147.8, 139.8, 130.4, 130.0, 128.7, 128.5, 128.4, 127.0, 121.0, 119.6, 111.4, 55.5; HRMS (ESI) calc. C$_{24}$H$_{19}$NO [M + H]$^+$ 338.1539, found 338.1548.

4-(Furan-2-yl)-2,6-diphenylpyridine (3ag).[10] In 88% yield (261 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.22 (d, J = 7.1 Hz, 4H), 7.95 (s, 2H), 7.61−7.45 (m, 7H), 6.99 (d, J = 3.4 Hz, 1H), 6.58 (dd, J = 3.3, 1.7 Hz, 1H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 157.5, 151.9, 143.6, 139.4, 139.0, 129.0, 128.6, 127.0, 112.9, 112.1, 108.4; HRMS (ESI) calc. C$_{21}$H$_{15}$NO [M + H]$^+$ 298.1226, found 298.1229.

2,6-Diphenyl-4-(thiophen-2-yl)pyridine (3ah).[10] In 95% yield (297 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.19 (d, J = 7.3 Hz, 4H), 7.88 (s, 2H), 7.63 (d, J = 3.0 Hz, 1H), 7.58−7.42 (m, 7H), 7.19 (dd, J = 4.9, 3.8 Hz, 1H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 157.6, 143.1, 141.8, 139.1, 129.2, 128.7, 128.4, 127.1, 127.0, 125.4, 115.4; HRMS (ESI) calc. C$_{21}$H$_{15}$NS [M + H]$^+$ 314.0998, found 314.1003.

2′,6′-Diphenyl-3,4′-bipyridine (3ai). In 65% yield (200 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.00 (d, J = 1.3 Hz, 1H), 8.72 (d, J = 3.7 Hz, 1H), 8.20 (d, J = 7.2 Hz, 4H), 7.98 (d, J = 8.0 Hz, 1H), 7.83 (s, 2H), 7.55−7.40 (m, 7H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 157.6, 149.9, 148.1, 146.8, 139.0, 134.5, 134.4, 129.2, 128.6, 127.0, 123.7, 116.7; HRMS (ESI) calc. C$_{22}$H$_{16}$N$_2$ [M + H]$^+$ 309.1386, found 309.1389.

4-(Furan-2-yl)-2,6-di(thiophen-2-yl)pyridine (3lg). In 88% yield (272 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.76−7.69 (m, 4H), 7.59 (d, J = 1.2 Hz, 1H), 7.42 (dd, J = 5.0, 1.0 Hz, 2H), 7.14 (dd, J = 5.0, 3.7 Hz, 2H), 6.96 (d, J = 3.2 Hz, 1H), 6.57 (dd, J = 3.4, 1.8 Hz, 1H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 152.6, 151.4, 144.7, 143.8, 139.0, 127.9, 127.9, 125.0, 112.1, 111.0, 108.9; HRMS (ESI) calc. C$_{17}$H$_{11}$NOS$_2$ [M + H]$^+$ 310.0355, found 310.0365.

1,3-Bis(2,6-diphenylpyridin-4-yl)benzene (3ap). In 78% yield (418 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.26 (d, J = 7.4 Hz, 8H), 8.08 (s, 1H), 7.97 (s, 4H), 7.86 (d, J = 7.6 Hz, 2H), 7.71 (t, J = 7.7 Hz, 1H), 7.56 (t, J = 7.4 Hz, 8H), 7.48 (t, J = 7.2 Hz, 4H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 157.7, 149.8, 140.2, 139.4, 129.9, 129.1, 128.7, 127.8, 127.1, 126.0, 117.2; HRMS (ESI) calc. C$_{40}$H$_{28}$N$_2$ [M + H]$^+$ 537.2325, found 537.2342.

2-(4-Methoxyphenyl)-4,6-diphenylpyridine (4a).[9b] In 56% yield (189 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.18−8.11 (m, 4H), 7.76 (d, J = 4.6 Hz, 2H), 7.67 (d, J = 7.0 Hz, 2H), 7.49−7.37 (m, 6H), 6.99 (d, J = 8.8 Hz, 2H), 3.79 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 160.4, 157.1, 156.9, 149.9, 139.6, 139.0, 132.1, 129.0, 128.9, 128.8, 128.6, 128.3, 127.1, 127.0, 116.3, 116.1, 113.9, 55.2; HRMS (ESI) calc. C$_{24}$H$_{19}$NO [M + H]$^+$ 338.1539, found 338.1544.

2-(4-Fluorophenyl)-6-(4-methoxyphenyl)-4-phenylpyridine (4b).[9b] In 48% yield (170 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.22−8.08 (m, 4H), 7.79−7.66 (m, 4H), 7.52−7.41 (m, 3H), 7.16 (t, J = 8.7 Hz, 2H), 7.01 (d, J = 8.8 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 163.5, 160.6, 157.1, 156.2, 150.1, 139.0, 135.7, 132.0, 129.0, 128.9, 128.8, 128.3, 127.1, 116.2, 116.0, 115.5, 114.0, 55.3; HRMS (ESI) calc. C$_{24}$H$_{18}$FNO [M + H]$^+$ 356.1445, found 356.1460.

2-(4-Methoxyphenyl)-4-phenyl-6-(thiophen-2-yl)pyridine (4c). In 60% yield (206 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.11 (d, J = 8.7 Hz, 2H), 7.70−7.66 (m, 5H), 7.49−7.37 (m, 4H), 7.13−7.09 (m, 1H), 7.00 (d, J = 8.7 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 160.6, 156.8, 152.5, 145.0, 145.6, 138.8, 131.6, 129.0, 128.9, 128.3, 127.9, 127.5, 127.0, 124.4, 115.9, 114.5, 114.0, 55.3; HRMS (ESI) calc. C$_{22}$H$_{17}$NOS [M + H]$^+$ 344.1104, found 344.1107.

2-Cyclopropyl-6-(4-methoxyphenyl)-4-phenylpyridine (4d). In 42% yield (126 mg), white solid: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.05 (d, J = 8.8 Hz, 2H), 7.72−7.61 (m, 3H), 7.53−7.41 (m, 3H), 7.25 (s, 1H), 7.01 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H), 2.21−2.10 (m, 1H), 1.26−1.18 (m, 2H), 1.08−0.98 (m, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 162.7, 160.3, 156.6, 149.0, 139.3, 132.4, 128.9, 128.6, 128.2, 127.1, 117.3, 114.7, 113.9, 55.3, 17.4, 9.8; HRMS (ESI) calc. C$_{21}$H$_{19}$NO [M + H]$^+$ 302.1539, found 302.1547.

General Procedure for the Synthesis of β-(Pyridin-2-yl) Ketones. To a 10 mL tube was added a mixture of ketone 1 (1 mmol), pyridin-2-ylmethanamine 2 (1.2 mmol), and Cu(OTf)$_2$ (36 mg, 0.1 mmol), successively. The mixture was stirred at 80 °C for 12 h. Upon completion, the crude product was cooled to room temperature and then directly separated by flash column chromatography on silica gel to give the pure product.

1-Phenyl-3-(pyridin-2-yl)propan-1-one (3j−a). In 95% yield (200 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.50 (d, J = 4.5 Hz, 1H), 7.98 (d, J = 7.6 Hz, 2H), 7.58−7.50 (m, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.25 (d, J = 8.2 Hz, 1H), 7.12−7.06 (m, 1H), 3.50 (t, J = 7.3 Hz, 2H), 3.23 (t, J = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 199.2, 160.6, 149.1, 136.8, 136.4, 132.9, 128.5, 128.0, 123.3, 121.2, 37.7, 31.9; HRMS (ESI) calc. C$_{14}$H$_{13}$NO [M + H]$^+$ 212.1070, found 212.1077.

1-(4-Isobutylphenyl)-3-(pyridin-2-yl)propan-1-one (3j−b). In 93% yield (248 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.45 (d, J = 4.5 Hz, 1H), 7.86 (d, J = 8.2 Hz, 2H), 7.51 (td, J = 7.7, 1.7 Hz, 1H), 7.19 (d, J = 7.8 Hz, 1H), 7.15 (d, J = 8.1 Hz, 2H), 7.02 (dd, J = 7.0, 5.3 Hz, 1H), 3.43 (t, J = 7.3 Hz, 2H), 3.18 (t, J = 7.3 Hz, 2H), 2.45 (d, J = 7.2 Hz, 2H), 1.90−1.75 (m, 1H), 0.84 (d, J = 6.6 Hz, 6H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 198.6, 160.6, 149.0, 147.2, 136.1, 134.5, 129.0, 127.9, 123.1, 121.0, 45.1, 37.5, 31.9, 29.9, 22.1; HRMS (ESI) calc. C$_{18}$H$_{21}$NO [M + H]$^+$ 268.1696, found 268.1691.

1-(4-Fluorophenyl)-3-(pyridin-2-yl)propan-1-one (3j−c). In 86% yield (197 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.45 (d, J = 4.2 Hz, 1H), 8.01−7.91 (m, 2H), 7.52 (td, J = 7.7, 1.8 Hz, 1H), 7.19 (d, J = 7.8 Hz, 1H), 7.10−6.98 (m, 3H), 3.43 (t, J = 7.2 Hz, 2H), 3.18 (t, J = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 197.5, 165.5, 160.4, 149.1, 136.2, 133.2, 130.5, 123.2, 121.1, 115.4, 37.4, 31.8; HRMS (ESI) calc. C$_{14}$H$_{12}$FNO [M + H]$^+$ 230.0976, found 230.0980.

1-(4-Chlorophenyl)-3-(pyridin-2-yl)propan-1-one (3j−d). In 82% yield (201 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.44 (d, J = 4.3 Hz, 1H), 7.86 (d, J = 8.6 Hz, 2H), 7.52 (td, J = 7.7, 1.8 Hz, 1H), 7.34 (d, J = 8.6 Hz, 2H), 7.18 (d, J = 7.8 Hz, 1H), 7.03 (dd, J = 6.9, 5.3 Hz, 1H), 3.42 (t, J = 7.2 Hz, 2H), 3.17 (t, J = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 197.8, 160.2, 149.0, 139.1, 136.2, 135.0, 129.3, 128.6, 123.2, 121.1, 37.4, 31.7; HRMS (ESI) calc. C$_{14}$H$_{12}$ClNO [M + H]$^+$ 246.0680, found 246.0688.

1-(4-Methoxyphenyl)-3-(pyridin-2-yl)propan-1-one (3j−e). In 87% yield (210 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.45 (d, J = 4.2 Hz, 1H), 7.91 (d, J = 8.9 Hz, 2H), 7.52 (td, J = 7.7, 1.8 Hz, 1H),

7.19 (d, J = 7.8 Hz, 1H), 7.03 (dd, J = 6.9, 5.3 Hz, 1H), 6.85 (d, J = 8.9 Hz, 2H), 3.77 (s, 3H), 3.39 (t, J = 7.3 Hz, 2H), 3.17 (t, J = 7.3 Hz, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 197.6, 163.2, 160.7, 148.9, 136.2, 130.1, 129.8, 123.2, 121.0, 113.5, 55.2, 37.3, 32.0; HRMS (ESI) calc. C$_{15}$H$_{15}$NO$_2$ [M + H]$^+$ 242.1176, found 242.1179.

3-(Pyridin-2-yl)-1-(thiophen-2-yl)propan-1-one (3j–f). In 76% yield (165 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.47 (d, J = 4.2 Hz, 1H), 7.70 (dd, J = 3.8, 0.9 Hz, 1H), 7.57−7.50 (m, 2H), 7.20 (d, J = 7.8 Hz, 1H), 7.08−7.03 (m, 2H), 3.40 (t, J = 7.3 Hz, 2H), 3.19 (t, J = 7.3 Hz, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 192.1, 160.2, 149.0, 144.0, 136.3, 133.3, 131.8, 127.9, 123.2, 121.2, 38.2, 32.0; HRMS (ESI) calc. C$_{12}$H$_{11}$NOS [M + H]$^+$ 218.0634, found 218.0635.

3-(Pyridin-2-yl)-1-(pyridin-4-yl)propan-1-one (3j–g). In 68% yield (144 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.76 (dd, J = 4.5, 1.5 Hz, 2H), 8.46 (d, J = 4.2 Hz, 1H), 7.73 (dd, J = 4.5, 1.6 Hz, 2H), 7.58 (td, J = 7.7, 1.8 Hz, 1H), 7.23 (d, J = 7.8 Hz, 1H), 7.09 (dd, J = 6.9, 5.3 Hz, 1H), 3.49 (t, J = 7.1 Hz, 2H), 3.23 (t, J = 7.0 Hz, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 198.8, 159.7, 150.8, 149.0, 142.7, 136.5, 123.4, 121.4, 121.0, 37.7, 31.4; HRMS (ESI) calc. C$_{13}$H$_{12}$N$_2$O [M + H]$^+$ 213.1022, found 213.1025.

1-(Naphthalen-1-yl)-3-(pyridin-2-yl)propan-1-one (3j–h). In 84% yield (219 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.56 (d, J = 8.5 Hz, 1H), 8.49 (d, J = 4.3 Hz, 1H), 7.95−7.90 (dd, J = 11.0, 7.8 Hz, 2H), 7.84 (d, J = 7.7 Hz, 1H), 7.59−7.42 (m, 4H), 7.24 (d, J = 7.5 Hz, 1H), 7.08 (dd, J = 6.9, 5.3 Hz, 1H), 3.56 (t, J = 7.2 Hz, 2H), 3.31 (t, J = 7.1 Hz, 2H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 203.5, 160.4, 149.1, 136.3, 136.0, 133.8, 132.4, 130.0, 128.3, 127.7, 127.4, 126.3, 125.8, 124.3, 123.2, 121.1, 40.9, 32.4; HRMS (ESI) calc. C$_{18}$H$_{15}$NO [M + H]$^+$ 262.1226, found 262.1237.

2-(Pyridin-2-ylmethyl)cyclohexanone (3j–i). In 69% yield (130 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.50 (d, J = 4.8 Hz, 1H), 7.56 (td, J = 7.7, 1.8 Hz, 1H), 7.19 (d, J = 7.8 Hz, 1H), 7.08 (dd, J = 6.8, 5.2 Hz, 1H), 3.34 (dd, J = 14.2, 6.1 Hz, 1H), 3.07−2.93 (m, 1H), 2.58 (dd, J = 14.2, 7.4 Hz, 1H), 2.47−2.30 (m, 2H), 2.13−2.01 (m, 2H), 1.88−1.78 (m, 1H), 1.73−1.60 (m, 2H), 1.48−1.35 (m, 1H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 212.2, 160.3, 149.0, 136.0, 123.9, 120.9, 50.6, 42.1, 37.7, 34.0, 28.0, 25.1; HRMS (ESI) calc. C$_{12}$H$_{15}$NO [M + H]$^+$ 190.1226, found 190.1242.

2-Methyl-1-(pyridin-2-yl)pentan-3-one (3j–j). In 65% yield (115 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.50 (d, J = 4.7 Hz, 1H), 7.56 (td, J = 7.6, 1.7 Hz, 1H), 7.14−7.06 (m, 2H), 3.23−3.14 (m, 2H), 2.82−2.68 (m, 1H), 2.58−2.33 (m, 2H), 1.11 (d, J = 6.8, Hz, 3H), 1.00 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 214.5, 159.6, 149.1, 136.1, 123.6, 121.1, 45.5, 40.9, 34.7, 16.6, 7.6; HRMS (ESI) calc. C$_{11}$H$_{15}$NO [M + H]$^+$ 178.1226, found 178.1235.

2-Methyl-1-phenyl-3-(pyridin-2-yl)propan-1-one (3j–k). In 95% yield (214 mg), yellowish oil: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.43 (d, J = 5.5 Hz, 1H), 7.92 (d, J = 8.6 Hz, 2H), 7.48−7.31 (m, 4H), 7.08 (d, J = 7.8 Hz, 1H), 6.98 (dd, J = 7.0, 5.4 Hz, 1H), 4.15−4.06 (m, 1H), 3.29 (dd, J = 14.0, 7.1 Hz, 1H), 2.81 (dd, J = 14.0, 7.0 Hz, 1H), 1.16 (d, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 203.5, 159.5, 149.1, 136.2, 135.9, 132.6, 128.3, 128.2, 123.7, 121.0, 41.2, 40.6, 17.4; HRMS (ESI) calc. C$_{15}$H$_{15}$NO [M + H]$^+$ 226.1226, found 226.1229.

ASSOCIATED CONTENT

Ⓢ Supporting Information

Full experimental details and copies of NMR spectral data. 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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