JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b01338 • Publication Date (Web): 17 Jul 2019

Just Accepted

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Single-Electron-Transfer-Induced C(sp^3)-N Couplings *via* C-C Bond Cleavage of Cycloketoxime Esters

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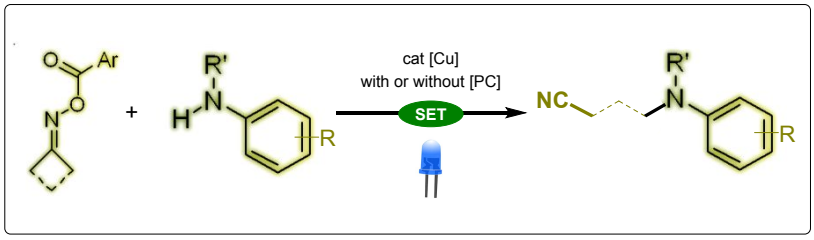


ABSTRACT: A practical single-electron-transfer-induced selective C(sp^3)–N coupling of cycloketoximes with anilines *via* C–C bond cleavage under copper catalytic and synergetic photoredox/copper catalytic reaction systems has been uncovered. These two powerful and simple protocols demonstrated excellent selectivity and good functional groups compatibility without any base or ligand control. Preliminary mechanistic experiments indicated a radical-mediated process was involved in these transformations.

■ INTRODUCTION

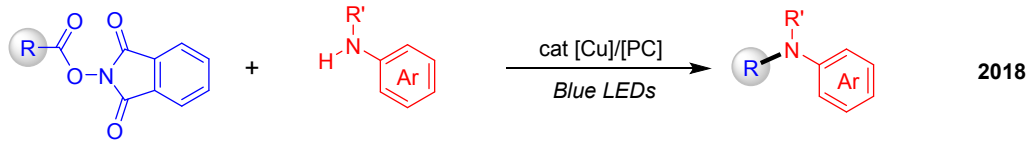
Amines and the derivatives are a privileged class of compounds with wide applications from pharmaceuticals, agrochemicals and material science to diverse mediates for the synthesis of functional molecules.[1] The development of amine chemistry is urgently required, especially to construst varieties of carbon-nitrogen (C–N) bond. Conventional, the alkylation of amines with readily available alkyl halides and alcohols were well developed accompanying with overalkylation and poor functional group compatibility, which seriously hampered its industrial application. [3] Moreover, Buchwald-Hartwig and Ullman-type cross-coupling reactions provided alternative practical pathways for the construction of alkyl or aryl amines in the presence of copper or palladium catalyst, [4] which provided a straightforward protocol to synthesize diaryl amines, while the alkyl arylamines were limited owing to the *β*-elimination of a metal alkyl intermediate. Furthermore, reductive amination of amines with carbonyl compounds is also a classical popular strategy to obtain variable protected amines in the presence of reductants. [5] In spite of these remarkable developments, it is highly desirable and significant to develop an effective mild approach achieving the direct construction of C(sp^3)–N bonds. In recent years, the photo-induced copper-catalyzed Ullman C–N coupling reactions were detailed studied, which mainly proceed *via* photoexcitation of copper-amine complexes with a reductive potential triggering a single-electron-transfer event. [6, 7, 8]

The synergetic photoredox and transition-metal catalyst is a novel catalytic system[9] for the efficient formation of C(sp^3)–N bond. The group of Hu has recently developed a decarboxylative amination of alkyl redox-active esters with arylamines enabled by tandem

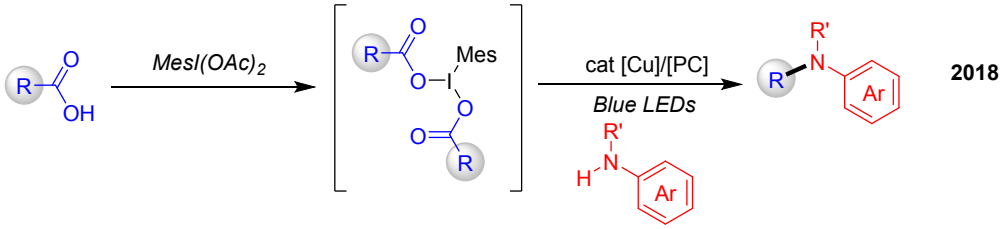
photoredox and copper catalyst (Scheme 1a). [10] Meanwhile, MacMillan and co-workers achieved decarboxylative C(sp^3)–N couplings from active iodonium carboxylates and anilines *via* dual copper and photoredox catalyst (Scheme 1b). [11] The key point of these transformations is that the copper salts can cooperate well with the photoredox catalyst to accomplish the catalyzed cycle

Scheme 1. Single-Electron-Transfer-Induced Selective C(sp^3)-N Couplings.

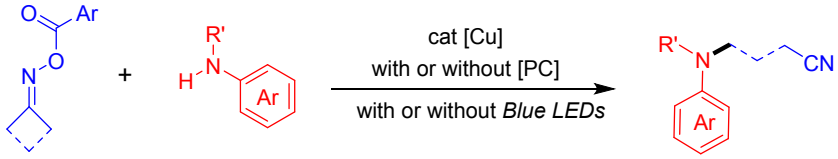
a) Hu's strategy:



b) MacMillan's strategy:



c) This work:



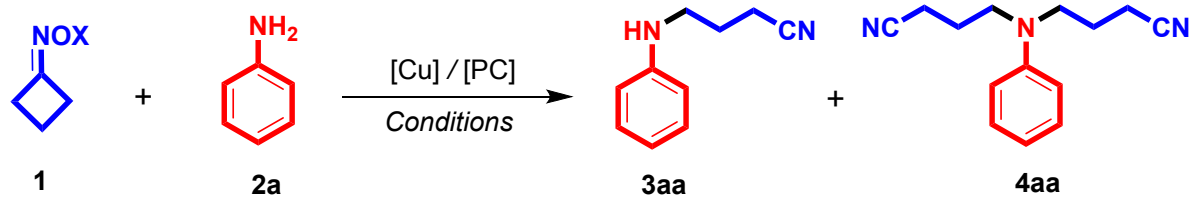
under the irradiation of visible light *via* single electron transfer process. As a sequence, with our ongoing interest in the research of C–C bond cleavage. [12] Herein, we disclosed a C(sp^3)–N cross coupling reaction of anilines with cycloketoximes to generate cyanoalkylated anilines in the presence of copper catalyst with or without synergetic photoredox under mild reaction conditions (Scheme 1c). In this transformation, the non-toxic and stable cycloketoximes were used as presursor of cyano at ambient condition. A wide range of cycloketoximes and anilines are well tolerated to furnish varieties of mono-alkylated products and di-alkylated products in good to excellent yields, respectively.

■ RESULTS AND DISCUSSION

Cycloketoxime derivatives[13-21] were good precursors to achieve cyanoalkylation of diverse radical acceptors *via* the C-C bond cleavage. Initially, we operated the reaction employing cyclobutanone *O*-benzoyl oxime (**1a**) and aniline (**2a**) under our previous reported reaction conditions (Table 1).[12a] As we expected, the desired product 4-(phenylamino)butanenitrile (**3aa**) was obtained in 26% yield (entry 1). After a brief screening of solvents, DMF performed better than other solvents for this conversion (entry 4). When the temperature was reduced to 80 °C, the yield of **3aa** was improved to 49% (entry 5). Further lowering the temperature would suppress the reaction (entry 6). What's more, different copper salts showed different efficiencies for this transformation, a good yield of **3aa** was isolated in the presence of copper bis(dipivaloylmethanate) (5 mol%) (entry 8). Moreover, the isolated yield of product was

improved to 85% with an increasing amount of cyclobutanone *O*-benzoyl oxime (**1a**) to 1.5 equivalent (entry 9). Furthermore, single **3aa** was detected in 90% yield eventhough the amount of **1a** was improved to 3.0 equivalent (entry 10). The copper-catalyzed reaction system was limited to the formation of mono-functionalizated aniline **3aa**. Furthermore, the synergetic photoredox and copper-catalytic condition was investigated under the irradiation of visible light. Surprisingly, when cycloketoxime (**1a'**)

Table 1. Screening of Conditions[a]



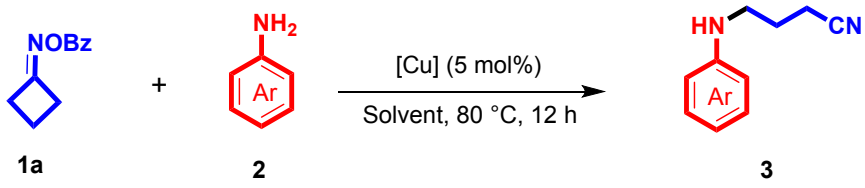
1 **2a** **3aa** **4aa**

Entry	X	[Cu] (mol%)	[PC] (mol%)	Solvent	T (°C)	Yield (%)[b]	
						3aa	**4aa**
1	PhCO (**1a**)	$Cu(OTf)_2$ (5)		1,4-dioxane	100	26	0
2	PhCO (**1a**)	$Cu(OTf)_2$ (5)		$PhCF_3$	100	31	0
3	PhCO (**1a**)	$Cu(OTf)_2$ (5)		CH_3CN	100	38	0
4	PhCO (**1a**)	$Cu(OTf)_2$ (5)		DMF	100	41	0
5	PhCO (**1a**)	$Cu(OTf)_2$ (5)		DMF	80	49	0
6	PhCO (**1a**)	$Cu(OTf)_2$ (5)		DMF	60	45	0
7	PhCO (**1a**)	CuTc (5)		DMF	80	69	0
8	PhCO (**1a**)	$Cu(tmhd)_2$ (5)		DMF	80	81 (75)	0
9[c]	PhCO (**1a**)	$Cu(tmhd)_2$ (5)		DMF	80	93 (85)	0
10[d]	PhCO (**1a**)	$Cu(tmhd)_2$ (5)		DMF	80	90	0
11[c]	4-CF_3PhCO (**1a'**)	$Cu(tmhd)_2$ (5)		DMF	80	88	0
12	4-CF_3PhCO (**1a'**)	$Cu(tmhd)_2$ (5)	*fac*-Ir(ppy)$_3$ (1)	DMF	rt	15	5
13	4-CF_3PhCO (**1a'**)	$Cu(tmhd)_2$ (20)	*fac*-Ir(ppy)$_3$ (1)	DMF	rt	52	10
14	4-CF_3PhCO (**1a'**)	$Cu(OTf)_2$ (20)	*fac*-Ir(ppy)$_3$ (1)	DMF	rt	65	12
15	4-CF_3PhCO (**1a'**)	$Cu(OTf)_2$ (20)	Ir (ppy)$_2$ (dtbbpy)PF_6 (1)	DMF	rt	57	7
16	4-CF_3PhCO (**1a'**)	$Cu(OTf)_2$ (20)	$Ru(bpy)_2PF_6$(1)	DMF	rt	25	5
17[e]	4-CF_3PhCO (**1a'**)	$Cu(OTf)_2$ (20)	*fac*-Ir(ppy)$_3$ (1)	DMF	rt	7	80 (73)
18	PhCO (**1a**)	$Cu(OTf)_2$ (20)	*fac*-Ir(ppy)$_3$ (1)	DMF	rt	0	0
19[e,f]	4-CF_3PhCO (**1a'**)	$Cu(OTf)_2$ (20)	*fac*-Ir(ppy)$_3$ (1)	DMF	rt	trace	0

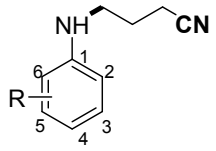
[a] Standard conditions, [Cu]: **1a** (0.2 mmol), **2a** (0.4 mmol), [Cu] 5 mol% in solvent (0.2 M) under Ar for 12 h; [Cu]+[PC]: **1a'** (0.2 mmol), **2a** (0.4 mmol), [Cu] 20 mol%, [PC] 1 mol% in solvent (0.2 M) at room temperature under irradiation of 12 w/m × 5 m blue LEDs for 12 h. [b] GC-MS yield using dodecane as internal standard, isolated yield was in parenthesis. [c] **1** (0.3 mmol), **2a** (0.2 mmol). [d] **1a** (0.6 mmol), **2a** (0.2 mmol). [e] **1a'** (0.6 mmol), **2a** (0.2 mmol). [f] Without blue LEDs irradiation. tmhd = 2,2,6,6-tetramethyl-3,5-heptanedionato.

and free aniline (**2a**) were treated with extra addition of *fac*-Ir(ppy)$_3$ (1 mol%) under the irradiation of 12 w/m × 5 m blue LEDs at room temperature, the *N*, *N*-dialkylanilines **4aa** was detected in GC-MS, albeit with 5% yield (entry 12). According to MacMillan's and Hu's conditions, increasing amount of copper salt to 20 mol% resulted in a sudden improvement yield of **3aa** to 52% with furnishing **4aa** in 10% yield (entry 13). Other photocatalysts were also investigated providing significantly lower yields of amine

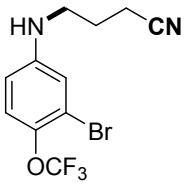
Table 2. Anilines scope of copper-catalyzed selective C(sp^3)-N cross-coupling.[a]



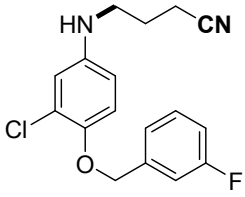
1a **2** **3**



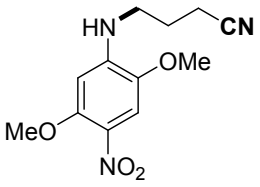
R = 4-Me, **3ba**, 89%
R = 4-^{t}Bu, **3ca**, 93%
R = 4-F, **3da**, 83%
R = 4-CF_3, **3ea**, 58%
R = 2-I, **3fa**, 64%
R = 4-OMe, **3ga**, 78%
R = 4-CH_2CN, **3ha**, 73%



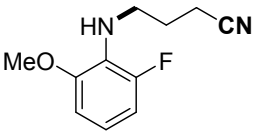
3ia, 73%



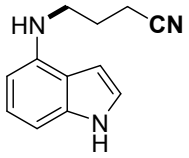
3ja, 78%



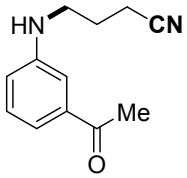
3ka, 70%



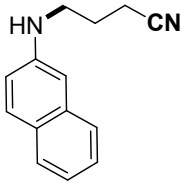
3la, 79%



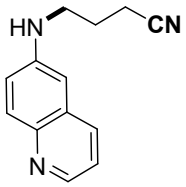
3ma, 85%



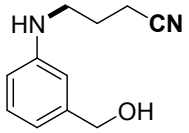
3na, 75%



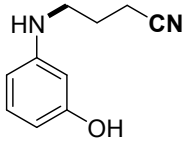
3oa, 80%



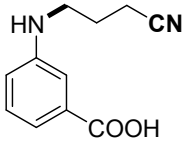
3pa, 64%



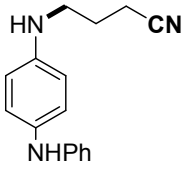
3qa, 72%



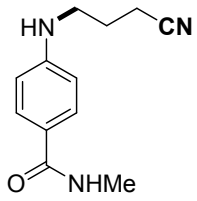
3ra, 55%



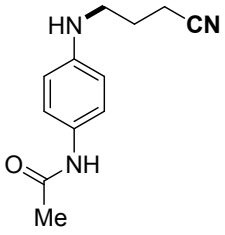
3sa, 48%



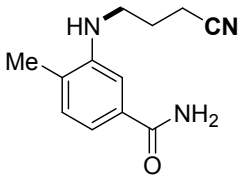
3ta, 73%



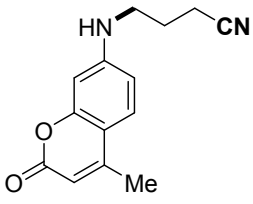
3ua, 71%



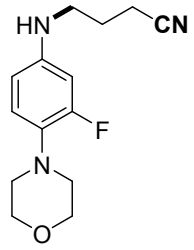
3va, 87%



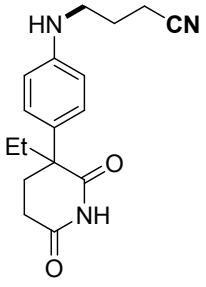
3wa, 58%



3xa, 46%



3ya, 87%



3za, 91%

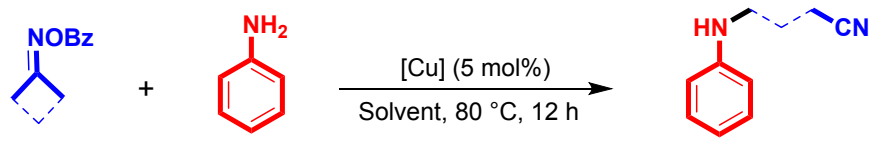
[a] Reaction conditions: **1a** (0.3 mmol), **2** (0.2 mmol), 5 mol% of $Cu(tmhd)_2$ in DMF (0.2 M) under Ar at 80 °C for 12 h, isolated yields.

products (entries 15-16). When $Cu(tmhd)_2$ was changed to $Cu(OTf)_2$ with an improving amount of cycloketoxime (**1a'**) to 3.0 equivalents, the yield of *N*, *N*-disubstituted aniline (**4aa**) was dramatically improved to 80% (entry 17). It was noteworthy that the reaction was inhibited completely in the absence of light (entry 16).

With the optimized reaction conditions in hand, firstly we tested the substrate scope of copper-catalyzed C (sp^3)–N cross-couplings and the results were summarized in Table 2. We turned our attention to investigate the applicability of the optimized conditions with various anilines in the presence of $Cu(tmhd)_2$ (5 mmol%). The results showed that anilines with varieties of functional groups were transformed into the corresponding products smoothly. Several mono-substituted anilines bearing 4-Me, 4-^{t}Bu, 4-F, 4-CF_3, 2-I, 4-OMe, and 4-CH_2CN on aryl rings were perfectly tolerated giving the cyanoalkylation products in good to excellent yields (**3ba-3ha**). Moreover, a wide range of multi-substituted anilines containing different kinds of substituents on different substituted positions showed good efficiency to afford the desired products in good yields (**3ia-3la**). It is worthy to note when 1*H*-indol-4-amine (**2m**) containing both a primary amine and an active indole nitrogen was investigated under the optimized conditions, the corresponding product 4-((1*H*-indol-4-yl)amino)butanenitrile (**3ma**) was formed with high selectivity in 85% yield. What's more, 1-(2-aminophenyl)ethan-1-one (**3n**) performed well to provide the alkyl amination product **3na** in 75% yield. Meanwhile, naphthalene and quinolone-substituted amines reacted with cyclobutanone *O*-benzoyl oxime (**1a**) effectively to produce the cyanoalkylation products in 64-80% yields (**3oa-3pa**). Alcohol, phenol, benzoic acid, and their derivatives were also compatible well with this mild copper-catalyzed protocol, only C (sp^3)-N coupling products were observed in moderate to good yields without the detection of any other products (**3qa-3sa**). In addition, other active anilines including secondary amine, *N*-methylbenzamide, and acetamide also reacted with cyclobutanone *O*-benzoyl oxime (**1a**) to give the single products (**3ta-3wa**) in 58-87% yields. Importantly, some natural products and functional amines could also proceed well to furnish the cyanoalkylation products (**3xa-3za**) in 46-91% yields. However, the alkylamines were not good candidates for this copper-catalyzed C(sp3)-N coupling, neither phenylmethanamine nor *N*-methyl-1-phenylmethanamine could provide the desired product under the optimized conditions.

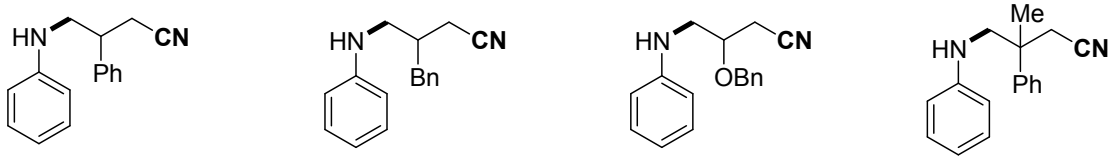
Following these satisfied results with aniline substrates, we further explored the scope of cyclobutanone *O*-benzoyl oximes shown in Table 3. Lowering the amount of oximes to 1.0 equivalent and increasing amount of aniline to 2.0 equivalent, a range of substituted cyclobutanone *O*-benzoyl oximes could generate the diverse 4-(phenylamino)butanenitriles smoothly in the presence of copper catalyst. The mono-substituted cyclobutanone *O*-benzoyl oximes bearing Ph, Bn, and OBn participated in this alkylamination furnishing the products (**3ab-3ad**) in yields of 44-72%. Furthermore, di-substituted oximes showed good performance under the optimized conditions (**3ae-3af**). This reaction was also amenable to the spirocyclic cyclobutanone *O*-benzoyl oxime (**1g**) to afford the cycloketoximes under standard conditions. 2-Phenyl cyclobutan-1-one oxime (**1h**) was also a good candidate for the preparation of amine product (**3ah**). As shown in Table 3, a diverse set of cyclopentanone oxime derivatives (**1i-1o**) and cycloheptyl ketoxime derivative (**1p**) could produce the corresponding products (**3ai-3ap**) in moderate to good yields.

Table 3. Cycloketoximes scope of copper-catalyzed selective C(sp^3)-N cross-coupling.

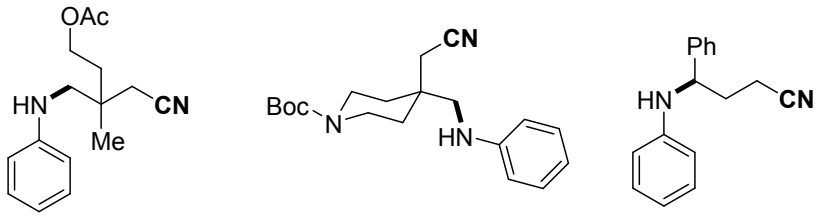


1 **2a** **3**

Variation of strained cycloketoxime motifs [a]

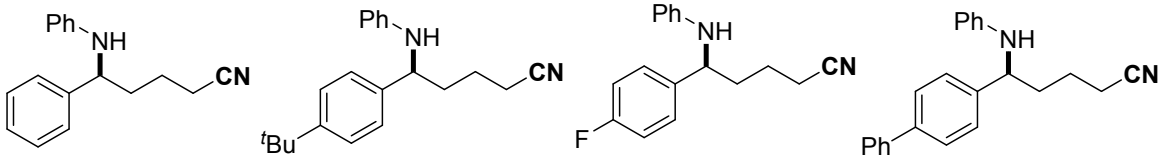


3ab, 65% **3ac**, 72% **3ad**, 44% **3ae**, 61%

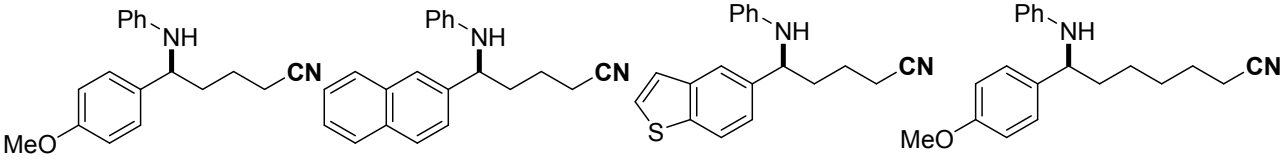


3af, 58% **3ag**, 52% **3ah**, 42%[b]

Variation of less-strained cycloketoxime motifs [b]



3ai, 53% **3aj**, 60% **3ak**, 50% **3al**, 66%

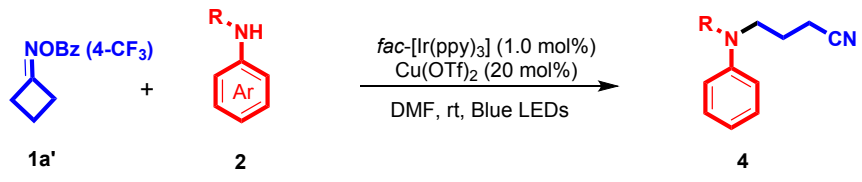


3am, 70% **3an**, 52% **3ao**, 48% **3ap**, 51%

[a] Reaction conditions **A**: **1** (0.2 mmol), **2a** (0.4 mmol), 5 mol% of $Cu(tmhd)_2$ in DMF (0.2 M) under Ar at 80 °C for 12 h, isolated yields. [b]Reaction conditions **B**: **1** (0.2 mmol), **2a** (0.4 mmol), 5 mol% of $Cu(OTf)_2$ in 1,4-dioxane (0.2 M) under Ar at 80 °C for 12 h, isolated yields.

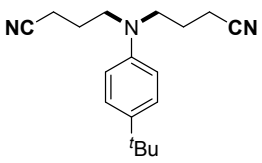
To further prove the potential application of dual copper and photoredox catalyst reaction system, we explored the scope of free anilines and *N*-alkyl anilines (Table 4). A broad range of free anilines were examined, the dialkylfunctionalization products bearing 4-^{t}Bu, 4-OMe, 4-Fluro groups (**4ba-4da**) were generated in good yields. 4-Methyl-3-bromo aniline was also transformed to

Table 4. Substrate scope of photoredox/copper-catalyzed selective C(sp^3)-N cross-coupling.

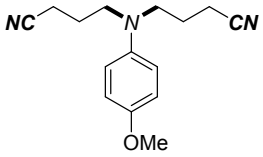


1a' 2 4

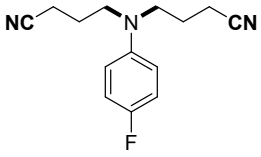
R = H [a]



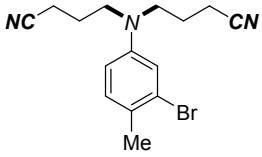
4ba, 78%



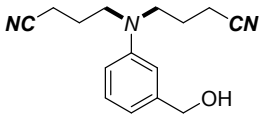
4ca, 85%



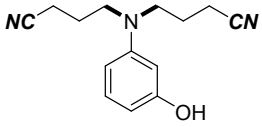
4da, 52%



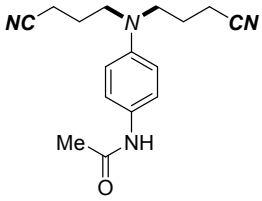
4ea, 52%



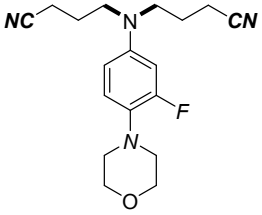
4fa, 68%



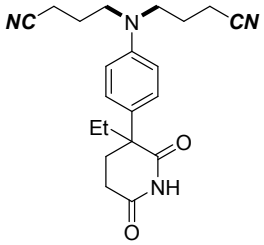
4ga, 62%



4ha, 90%

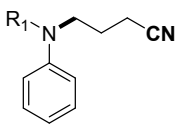


4ia, 65%

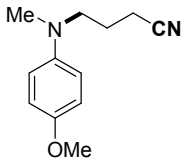


4ja, 66%

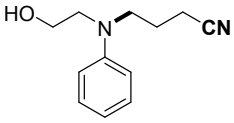
R = Alkyl groups [b]



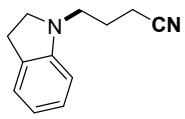
R = Me, R_2 = H, **4ka**, 78%
R = Bn, R_2 = H, **4la**, 68%
R = ^{i}Pr, R_2 = H, **4ma**, 55%
R = Allyl, R_2 = H, **4na**, 72%



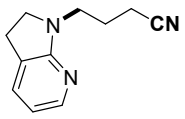
4oa, 74%



4pa, 65%



4qa, 80%



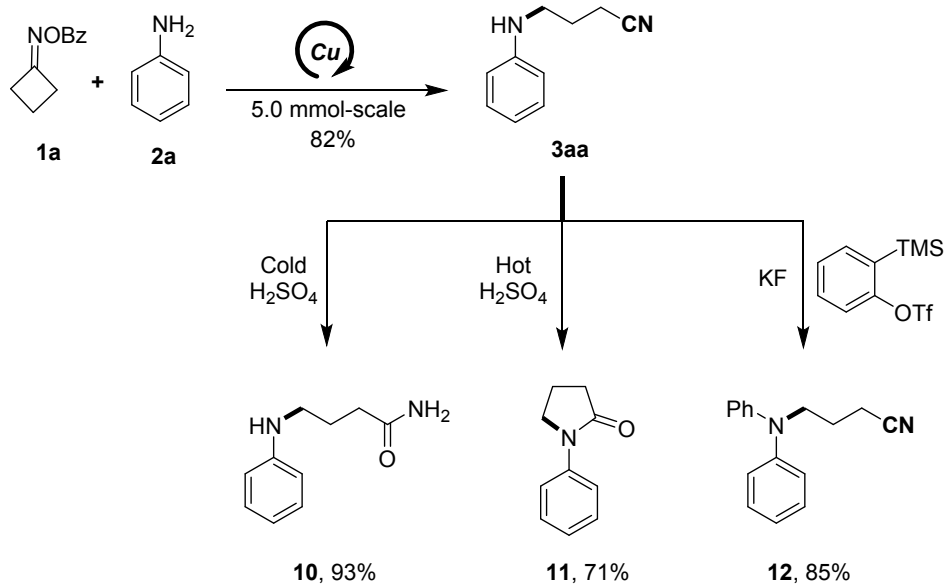
4ra, 59%

[a] Reaction conditions **A**: **1a'** (0.6 mmol), **2** (0.2 mmol), 1 mol% of *fac*-Ir(ppy)$_3$, and 20 mol% of Cu(OTf)$_2$ in DMF (0.2 M) under Ar at room temperature under irradiation of 12 w/m × 5 m blue LEDs for 12 h. [b] Reaction conditions **B**: **1a'** (0.3 mmol), **2** (0.2 mmol), 1 mol% of *fac*-Ir(ppy)$_3$ and 20 mol% of Cu(OTf)$_2$ in DMF (0.2 M) under Ar at room temperature under irradiation of 12 w/m × 5 m blue LEDs for 12 h.

N, *N*-dialkyl aniline (**4ea**) in 52% yield. Meanwhile, the anilines containing aliphatic hydroxyl group, phenolic hydroxyl group, and amide reacted with **1a'** smoothly to afford the desired products (**4fa**-**4ha**) in 62% to 90% yield. The functional natural products were also compatible with the reaction conditions delivering the products (**4ia**-**4ja**) in moderate yields. Notably, *N*-alkyl aniline could not afford the desired product under the single copper-catalytic reaction conditions. However, under the dual copper and photoredox catalyst reaction conditions, the coupling of varieties of *N*-alkyl anilines with cycloketoxime (**1a'**) could be conducted smoothly. *N*-methyl, benzyl, isopropyl, and allyl anilines all performed well to give the corresponding amines (**4ka**-**4na**) in good yields. 4-((4-Methoxyphenyl)(methyl)amino)butanenitrile (**4ao**) was also obtained in 74% yield. Synthetically useful functional group such as free alcohol was well compatible and the aniline product (**4pa**) was prepared in 65% yield under the optimized conditions. Furthermore, indoline was also a suitable amine substrate producing 4-(indolin-1-yl)butanenitrile (**4qa**) in 80% yield. In addition, the alkylated heteroindoline (**4ra**) was generated in 59% yield. However, no desired product was observed when alkylamine such as phenylmethanamine or *N*-methyl-1-phenylmethanamine was investigated under the optimized photoredox/copper-catalytic conditions.

To further demonstrate the potential application of this transformation, we operated the copper-catalyzed C(sp^3)-N coupling reaction on a 5.0 mmol scale, 82% yield of the desired product **3aa** was isolated (Scheme 2). Meanwhile, the corresponding amide products **10** and **11** were prepared in excellent to good yields when **3aa** were treated with cold H_2SO_4 and hot H_2SO_4, respectively. Moreover, **3aa** reacted with 2-(trimethylsilyl)phenyl trifluoromethanesulfonate smoothly to furnish the aryl product **12** in 85% yield in the presence of KF.

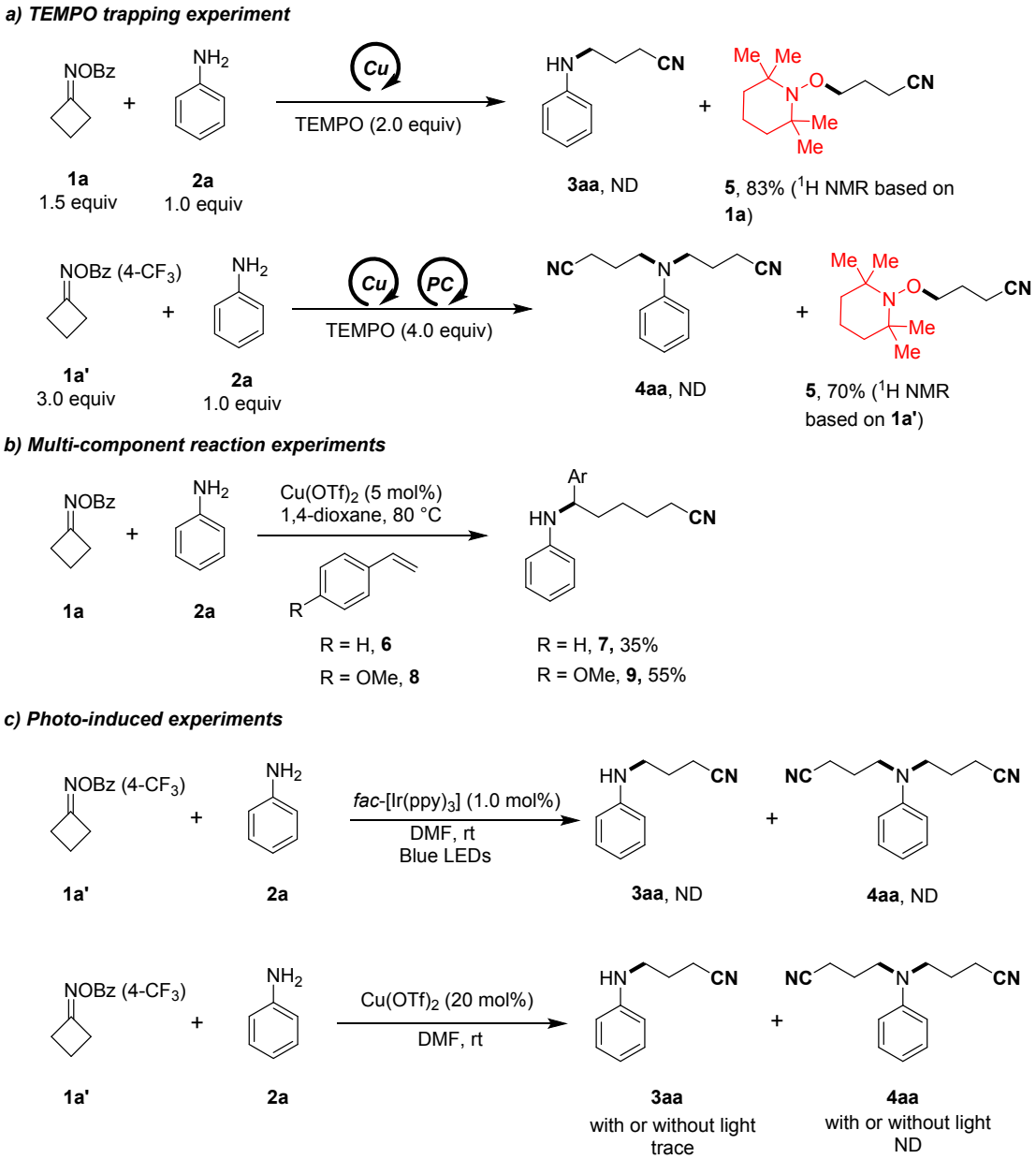
Scheme 2. Further Transformations



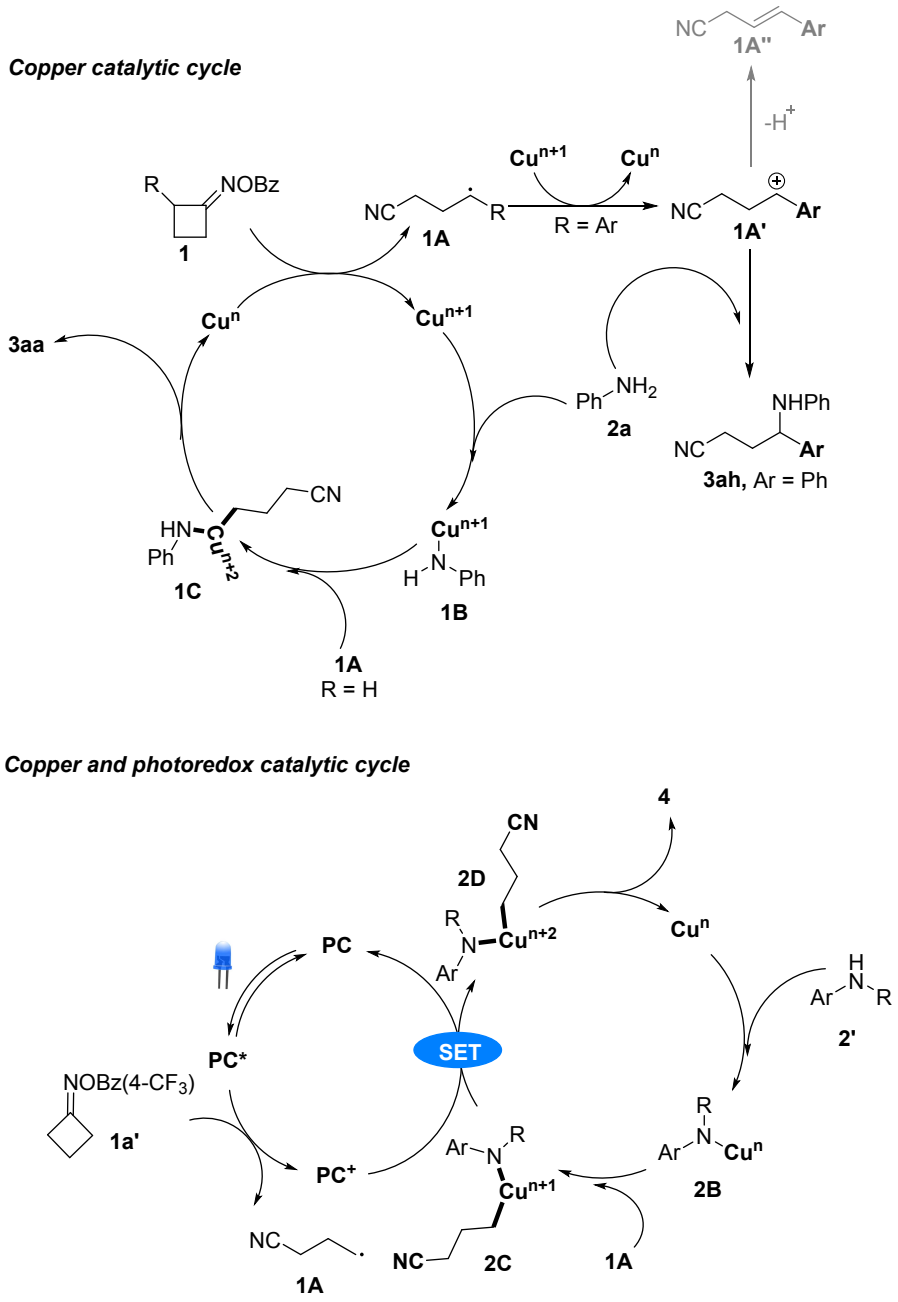
In order to understand the possible mechanism of copper-catalyzed and synergetic catalyzed selective C(sp^3)–N coupling, TEMPO trapping experiments were operated with an extra addition of TEMPO. The distal carbon-TEMPO adduct **5** were formed in 83% and

70% yield respectively, with no observation of alkylated products **3aa** and **4aa** (Scheme 3a), indicating that a radical-mediated pathway was involved in this reaction. To our delight, multi-component radical cascade reactions could also be realized affording products (**7**, **9**) in modest yields when styrenes (**6**, **8**) were added to the copper-catalytic reaction system (Scheme 3b). To evaluate the possibility of association between photoredox catalyst and copper salt, a series of photo-induced experiments were operated. When *fac*-Ir(ppy)$_3$ (1 mol%) was employed in the absence of copper salts, we didn't detect any alkylation product. Meanwhile, copper salt performed hypodynamic transformation in the absence of photoredox catalyst (Scheme 3c). These results indicated that the combination of photoredox catalyst and copper catalyst under the irradiation of blue LEDs was crucial to achieve the C(sp^3)–N couplings.

Scheme 3. Mechanistic Experiments



Scheme 4. Plausible Mechanism



Based on the experimental results and previous reports, plausible mechanisms including copper catalytic cycle and dual photoredox-copper catalytic cycle were shown in Scheme 4. For copper-catalyzed selective C(sp^3)–N couplings, initially a distal radical **1A** was formed in the presence of copper *via* a SET reduction and *β*-scission of iminyl radical process with a release of Cu^{n+1}species. Radical **1A** (R = H) was trapped by a copper amido complex **1B**, which generated from an incorporation of aniline (**2**) with Cu^{n+1}, to give a high-valent copper alkyl amido complex **1C**. Then the desired mono-alkylated product was formed along with the regeneration of a low-valent copper catalyst. When *α*-aryl cycloketoximes was employed, a highly reductive potential intermediate **1A** (R = Ar) would be oxidized to generate a benzyl cation species **1A'**. Then the corresponding product **3ah** would be formed through

nucleophilic attack of anilines along with the generation of the β-H elimination byproduct. For copper and photoredox catalytic cycle, the photoredox catalyst *fac*-[Ir(ppy)$_3$] was excited under the light irradiation producing a long-lived triplet excited state (PC*), which has a reductive potential to promote cyclo ketoximes (**1a'**) producing a distal radical **1A** *via* an known process. Concurrently, the aniline **2'** coordinated with a low-valent copper catalyst formed a copper amido complex **2B**. Subsequently, the active radical **1A** was captured by complex **2B** to produce complex **2C**. Then a high-valent copper alkyl amido complex **2D** was obtained *via* a single-electron oxidation between **PC**$^+$ and complex **2C** with a regeneration of **PC**.[22] Finally, complex **2D** was expected to yield the amine product **4** through a reductive elimination to complete the cycle.

■ CONCLUSIONS

In conclusion, we have reported a single-electron-transfer-induced selective C(sp^3)–N coupling of cycloketoximes with anilines *via* C–C bond cleavage. Both copper catalytic and synergetic photoredox/copper catalytic protocols were developed for the efficient preparation of varieties of mono-alkylamination products and di-alkylamination products, respectively. These amines containing cynao groups are of great importance in organic synthesis of functional molecules. These two mild and operationally simple approaches complementing each other were suitable for the modification of different anilines and exhibited good functional group tolerance. This work provided practical strategy for the C(sp^3)–N couplings.

■ EXPERIMENTAL SECTION

All new compounds were fully characterized. NMR-spectra were recorded on Bruker ARX-400 MHz or ARX-500 MHz Associated. Mass spectra were conducted at Micromass Q-Tof instrument (ESI) and Agilent Technologies 5973N (EI). All reactions were carried out in flame-dried reaction vessels with Teflon screw caps under argon. Cu(tmhd)$_2$ and Cu(OTf)$_2$ were purchased from TCI, *fac*-[Ir(ppy)$_3$] was purchased from Acros. All of the cyclobutanone *O*-acyl oximes **1** were synthesized from the corresponding cycloketones and carboxylic acids according to the literatures.[12a-c] All of the NMR spectra of the know compounds were in full accordance with the data in the literature. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification.

Characterization of New Starting Materials. ***2-Phenylcyclobutan-1-one O-benzoyl oxime (1h).*** A brown soild, mp 76-78 ^{o}C (5.0 mmol scale, 420.2 mg, 41%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 – 8.03 (m, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.8 Hz, 2H), 7.42 (d, J = 7.4 Hz, 2H), 7.36 (t, J = 7.7 Hz, 2H), 7.27 – 7.25 (m, 1H), 4.70 – 4.66 (m, 1H), 3.28 – 3.08 (m, 2H), 2.70 – 2.55 (m, 1H), 2.35 – 2.15 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.8, 163.9, 138.7, 133.2, 129.6, 129.0, 128.6, 128.4, 127.1, 127.0, 49.6, 29.5, 23.3; ATR-FTIR (cm $^{-1}$):1739, 1650, 1544, 1463, 1259, 1119, 710; HRMS m/z (ESI) calcd for $C_{17}H_{15}NNaO_2$ $(M + Na)^+$ 288.0995, found 288.0998.

2-Phenylcyclopentan-1-one O-benzoyl oxime (1i). A white soild, mp 82-84 ^{o}C (5.0 mmol scale, 749.6 mg, 53%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.1 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 7.34 – 7.33 (m, 4H), 7.26 – 7.22 (m, 1H), 4.05 (t, J = 7.2 Hz, 1H), 2.98 – 2.78 (m, 2H), 2.36 – 2.29 (m, 1H), 2.09 – 1.79 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.5, 163.7,

140.3, 133.1, 129.5, 129.1, 128.5, 128.4, 127.8, 126.7, 49.0, 34.6, 29.8, 22.4; ATR-FTIR (cm^{-1}): 1739, 1599, 1450, 1266, 710; HRMS m/z (ESI) calcd for $C_{18}H_{18}NO_2$ $(M + H)^+$ 280.1332, found 280.1336.

2-(4-(tert-Butyl)phenyl)cyclopentan-1-one O-benzoyl oxime (1j). A white soild, mp 102-104 °C (5.0 mmol scale, 838.5 mg, 50%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 – 8.05 (m, 1H), 7.58 – 7.41 (m, 2H), 7.37 – 7.32 (m, 3H), 7.27 – 7.19 (m, 2H), 7.14 – 7.12 (m, 1H), 4.07 – 4.03 (m, 1H), 2.97 – 2.75 (m, 2H), 2.44 – 2.26 (m, 1H), 2.09 – 1.74 (m, 3H), 1.30 – 1.29 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 175.9, 163.9, 163.8, 149.5, 149.4, 138.6, 137.2, 133.1, 132.8, 129.54, 129.49, 129.3, 128.8, 128.4, 128.0, 127.5, 126.8, 125.6, 125.5, 48.6, 48.3, 36.7, 34.5, 34.4, 33.1, 31.4 31.3, 29.9, 23.8, 22.5; ATR-FTIR (cm^{-1}): 1739, 1650, 1550, 1454, 1260, 712; HRMS m/z (ESI) calcd for $C_{22}H_{25}NNaO_2$ $(M + Na)^+$ 358.1778, found 358.1780.

2-(4-Fluorophenyl)cyclopentan-1-one O-benzoyl oxime (1k). A white soild, mp 85-87 °C (5.0 mmol scale, 628.2 mg, 42%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 – 8.05 (m, 2H), 7.60 – 7.56 (m, 1H), 7.46 (t, J = 7.7 Hz, 2H), 7.31 – 7.28 (m, 2H), 7.04 – 7.00 (m, 2H), 4.02 (t, J = 7.6 Hz, 1H), 2.99 – 2.74 (m, 2H), 2.36 – 2.29 (m, 1H), 2.04 – 1.81 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.3, 163.8, 161.71 (d, J = 245.0 Hz), 135.9 (d, J = 2.8 Hz), 133.2, 129.5, 129.4 (d, J = 8.0 Hz), 129.1, 128.5, 115.4 (d, J = 21.4 Hz), 48.5, 34.8, 29.8, 22.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.3; ATR-FTIR (cm^{-1}): 2245, 1738, 1644, 1495, 1454, 1266, 708; HRMS m/z (ESI) calcd for $C_{18}H_{16}FNNaO_2$ $(M + Na)^+$ 320.1057, found 320.1060.

2-([1,1'-Biphenyl]-4-yl)cyclopentan-1-one O-benzoyl oxime (1l). A white soild, mp 134-136 °C (5.0 mmol scale, 837.8 mg, 47%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.1 Hz, 1H), 7.61 – 7.40 (m, 10H), 7.36 – 7.33 (m, 1H), 7.28 (d, J = 8.2 Hz, 1H), 7.21 – 7.17 (m, 1H), 4.18 – 4.09 (m, 1H), 3.00 – 2.79 (m, 2H), 2.50 – 2.32 (m, 1H), 2.14 – 1.80 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.6, 175.5, 163.9, 163.8, 140.9, 140.8, 140.7, 139.7, 139.5, 139.4, 133.2, 132.9, 129.6, 129.5, 128.8, 128.7, 128.5, 128.3, 128.1, 127.6, 127.5, 127.3, 127.2, 127.1, 127.0, 126.9, 48.9, 48.4, 36.7, 34.7, 33.1, 29.9, 23.8, 22.5; ATR-FTIR (cm^{-1}): 1742, 1732, 1654, 1501, 1454, 1266, 708; HRMS m/z (ESI) calcd for $C_{24}H_{22}NO_2$ $(M + H)^+$ 356.1645, found 356.1650.

2-(4-Methoxyphenyl)cyclopentan-1-one O-benzoyl oxime (1m). A white soild, mp 125-127 °C (5.0 mmol scale, 821.5 mg, 53%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 7.4 Hz, 1.51H), 7.58 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.26 – 7.24 (m, 2H), 7.12 (d, J = 8.5 Hz, 0.5H), 6.88 – 6.84 (m, 2H), 4.10 – 3.99 (m, 1H), 3.79 (s, 3H), 2.94 – 2.76 (m, 2H), 2.37 – 2.27 (m, 1H), 2.04 – 1.80 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.7, 175.9, 163.8, 158.4, 158.2, 133.8, 133.1, 132.9, 132.2, 129.52, 129.45, 129.2, 128.8, 128.4, 128.11, 128.09, 114.1, 114.0, 55.3, 55.2, 48.4, 47.7, 36.7, 34.6, 32.9, 29.8, 23.6, 22.4; ATR-FTIR (cm^{-1}): 1740, 1640, 1451, 1263, 708; HRMS m/z (ESI) calcd for $C_{19}H_{20}NO_3$ $(M + H)^+$ 310.1438, found 310.1441.

2-(Naphthalen-2-yl)cyclopentan-1-one O-benzoyl oxime (1n). A white soild, mp 130-132 °C (5.0 mmol scale, 958.6 mg, 58%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 – 8.07 (m, 1H), 7.84 – 7.78 (m, 3H), 7.75 – 7.68 (m, 1H), 7.61 – 7.42 (m, 4H), 7.34 – 7.28 (m, 1H), 7.24 – 7.22 (m, 1H), 6.96 – 6.93 (m, 1H), 4.30 – 4.22 (m, 1H), 3.03 – 2.83 (m, 2H), 2.51 – 2.34 (m, 1H), 2.21 – 1.81 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.4, 175.4, 163.84, 163.77, 139.1, 137.7, 133.5, 133.4, 133.1, 132.8, 132.4, 132.1, 129.6, 129.3, 129.2, 128.7, 128.51, 128.45, 128.3, 127.9, 127.8, 127.6, 127.52, 127.47, 126.4, 126.3, 126.1, 126.0, 125.7, 125.6, 125.4, 36.6, 34.5,

33.1, 29.9, 23.8, 22.5; ATR-FTIR (cm^{-1}): 1739, 1651, 1545, 1464, 1260, 1120, 711; HRMS m/z (ESI) calcd for $C_{22}H_{19}NNaO_2$ $(M + Na)^+$ 352.1308, found 352.1305.

2-(Benzo[b]thiophen-5-yl)cyclopentan-1-one O-benzoyl oxime (1o). A yellow soild, mp 135-137 °C (5.0 mmol scale, 754.2 mg, 45%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 – 8.06 (m, 1H), 7.84 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.77 – 7.67 (m, 1H), 7.61 – 7.56 (m, 0.5H), 7.48 – 7.42 (m, 2H), 7.38 – 7.24 (m, 3H), 7.20 (dd, *J* = 8.3, 1.7 Hz, 0.5H), 7.07 – 7.03 (m, 1H), 4.25 – 4.17 (m, 1H), 3.02 – 2.82 (m, 2H), 2.50 – 2.33 (m, 1H), 2.16 – 1.80 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.6, 175.6, 163.9, 163.8, 140.0, 139.9, 138.2, 137.9, 136.5, 133.1, 132.8, 129.6, 129.4, 129.2, 128.6, 128.5, 128.0, 127.1, 126.7, 124.4, 123.8, 123.7, 123.6, 122.9, 122.7, 122.6, 122.0, 49.1, 48.7, 37.0, 34.9, 33.1, 29.9, 23.8, 22.5; ATR-FTIR (cm^{-1}): 1738, 1625, 1593, 1454, 1259, 707; HRMS m/z (ESI) calcd for $C_{20}H_{17}NNaO_2S$ $(M + Na)^+$ 358.0872, found 358.0877.

2-(4-Methoxyphenyl)cycloheptan-1-one O-benzoyl oxime (1p). A white soild, mp 84-86 °C (3.0 mmol scale, 633.9 mg, 63%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 – 8.05 (m, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.30 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.09 – 4.05 (m, 1H), 3.78 (s, 3H), 3.14 – 3.10 (m, 1H), 2.39 – 2.32 (m, 1H), 2.11 – 2.05 (m, 1H), 1.98 – 1.88 (m, 4H), 1.63 – 1.57 (m, 1H), 1.46 – 1.39 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 164.0, 158.5, 133.1, 132.7, 129.5, 129.4, 128.5, 128.3, 113.9, 55.2, 47.6, 31.0, 30.8, 27.4, 26.2, 25.4; ATR-FTIR (cm^{-1}): 2222, 1692, 1480, 1371, 1276, 1174, 758; HRMS m/z (ESI) calcd for $C_{21}H_{23}NNaO_3$ $(M + Na)^+$ 360.1570, found 360.1573.

General Procedure A of Copper-Catalyzed Selective C (sp^3)-N Cross-Couplings.

Flame-dried 25 mL Schlenk tube filled with argon, cyclobutanone oxime **1a** (56.7 mg, 0.3 mmol), aniline **2a** (18.6 mg, 0.2 mmol), $Cu(tmhd)_2$ (4.3 mg, 5 mol%), and absolute dry DMF (1.0 mL) were added under Ar. The formed mixture was stirred at 80 °C with the heating mantle under Ar for 12 h as monitored by TLC. The solution was then cooled to room temperature, the mixture was extracted with EA and saturated $NaHCO_3$ solution, dried ($MgSO_4$) and concentrated to give a crude product. The crude product was purified by flash column chromatography on silica gel (PE : EA = 8 : 1) to afford **3aa**.

4-(Phenylamino)butanenitrile (3aa). A yellow oil (27.1 mg, 85%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.20 (t, *J* = 7.9 Hz, 2H), 6.75 (t, *J* = 7.3 Hz, 1H), 6.63 (d, *J* = 7.7 Hz, 2H), 3.72 (br s, 1H), 3.32 (t, *J* = 6.6 Hz, 2H), 2.47 (t, *J* = 7.1 Hz, 2H), 2.07 – 1.89 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.5, 129.3, 119.3, 117.9, 112.8, 42.2, 25.2, 14.7; ATR-FTIR (cm^{-1}): 2245, 1596, 1452, 1385, 1267, 1115, 1071, 741; HRMS m/z (ESI) calcd for $C_{10}H_{13}N_2$ $(M + H)^+$ 161.1073, found 161.1076.

4-(p-Tolylamino)butanenitrile (3ba). A yellow oil (30.9 mg, 89%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.01 (d, *J* = 8.0 Hz, 2H), 6.57 – 6.54 (m, 2H), 3.57 (br s, 1H), 3.29 (t, *J* = 6.6 Hz, 2H), 2.47 (t, *J* = 7.1 Hz, 2H), 2.25 (s, 3H), 1.99 – 1.92 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2, 129.8, 127.1, 119.4, 113.0, 42.6, 25.2, 20.3, 14.7; ATR-FTIR (cm^{-1}): 2247, 1550, 1446, 1381, 1267, 1060, 749; HRMS m/z (ESI) calcd for $C_{11}H_{15}N_2$ $(M + H)^+$ 175.1230, found 175.1229.

4-((4-(tert-Butyl)phenyl)amino)butanenitrile (3ca). A yellow oil (40.3 mg, 93%): ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.4 Hz, 2H), 6.61 (d, *J* = 8.4 Hz, 2H), 3.31 (t, *J* = 6.5 Hz, 2H), 2.48 (t, *J* = 7.1 Hz, 2H), 1.97 – 1.90 (m, 2H), 1.31 (s, 9H); ^{13}C NMR (126

MHz, $CDCl_3$) δ 145.1, 140.6, 126.1, 119.4, 112.5, 42.4, 33.8, 31.4, 25.3, 14.7; ATR-FTIR (cm^{-1}): 2246, 1603, 1462, 1378, 1123, 751; HRMS m/z (ESI) calcd for $C_{14}H_{21}N_2$ $(M + H)^+$ 217.1699, found 217.1702.

4-((4-Fluorophenyl)amino)butanenitrile (3da). A yellow oil (29.6 mg, 83%): ^1H NMR (400 MHz, $CDCl_3$) δ 6.90 – 6.86 (m, 2H), 6.58 – 6.52 (m, 2H), 3.26 (t, *J* = 6.6 Hz, 2H), 2.47 (t, *J* = 7.1 Hz, 2H), 1.98 – 1.91 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.9 (d, *J* = 235.5 Hz), 143.8, 119.3, 115.7 (d, *J* = 22.4 Hz), 113.7 (d, *J* = 7.4 Hz), 42.9, 25.1, 14.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -127.5; ATR-FTIR (cm^{-1}): 2245, 1719, 1452, 1385, 1267, 1115, 1071, 741; HRMS m/z (ESI) calcd for $C_{10}H_{12}FN_2$ $(M + H)^+$ 179.0979, found 179.0978.

4-((4-(Trifluoromethyl)phenyl)amino)butanenitrile (3ea). A yellow oil (26.3 mg, 58%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.4 Hz, 2H), 6.62 (d, *J* = 8.4 Hz, 2H), 4.13 (br s, 1H), 3.37 – 3.32 (m, 2H), 2.47 (t, *J* = 7.0 Hz, 2H), 2.04 – 1.94 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0, 126.7 (q, *J* = 3.7 Hz), 124.8 (q, *J* = 270.3 Hz), 119.3 (q, *J* = 32.7 Hz), 119.1, 111.9, 41.8, 24.9, 14.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ -61.1; ATR-FTIR (cm^{-1}): 2246, 1550, 1459, 1383, 1223, 1050, 736; HRMS m/z (ESI) calcd for $C_{11}H_{12}F_3N_2$ $(M + H)^+$ 229.0947, found 229.0950.

4-((2-Iodophenyl)amino)butanenitrile (3fa). A yellow oil (36.3 mg, 64%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.24 – 7.20 (m, 1H), 6.59 (dd, *J* = 8.1, 1.0 Hz, 1H), 6.48 (td, *J* = 7.7, 1.4 Hz, 1H), 4.18 (br s, 1H), 3.39 – 3.34 (m, 2H), 2.49 (t, *J* = 7.1 Hz, 2H), 2.04 – 1.97 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.4, 139.2, 129.5, 119.2, 119.1, 110.5, 85.7, 42.4, 24.9, 14.8; ATR-FTIR (cm^{-1}): 2248, 1505, 1452, 1378, 1236, 1125, 756; HRMS m/z (ESI) calcd for $C_{10}H_{12}IN_2$ $(M + H)^+$ 287.0040, found 287.0043.

4-((4-Methoxyphenyl)amino)butanenitrile (3ga). A yellow oil (29.7 mg, 78%). ^1H NMR (400 MHz, $CDCl_3$) δ 6.85 – 6.74 (m, 2H), 6.65 – 6.54 (m, 2H), 3.75 (s, 3H), 3.25 (t, *J* = 6.6 Hz, 2H), 2.47 (t, *J* = 7.1 Hz, 2H), 1.97 – 1.90 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.4, 141.7, 119.4, 114.9, 114.2, 55.7, 43.2, 25.3, 14.8; ATR-FTIR (cm^{-1}): 2247, 1596, 1505, 1378, 1264, 1120, 1069, 750; HRMS m/z (ESI) calcd for $C_{11}H_{15}N_2O$ $(M + H)^+$ 191.1179, found 191.1182.

4-((4-(Cyanomethyl)phenyl)amino)butanenitrile (3ha). A yellow oil (28.9 mg, 73%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.6 Hz, 2H), 6.69 – 6.53 (m, 2H), 3.88 (br s, 1H), 3.62 (s, 2H), 3.30 (t, *J* = 6.6 Hz, 2H), 2.47 (t, *J* = 7.0 Hz, 2H), 1.99 – 1.92 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.2, 129.0, 119.3, 118.53, 118.47, 113.1, 42.1, 25.0, 22.7, 14.7; ATR-FTIR (cm^{-1}): 2247, 1590, 1509, 1378, 1220, 1116, 746; HRMS m/z (ESI) calcd for $C_{12}H_{14}N_3$ $(M + H)^+$ 200.1182, found 200.1185.

4-((3-Bromo-4-(trifluoromethoxy)phenyl)amino)butanenitrile (3ia). A yellow oil (47.3 mg, 73%): ^1H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.8 Hz, 1H), 6.81 (d, *J* = 2.7 Hz, 1H), 6.51 (dd, *J* = 8.9, 2.7 Hz, 1H), 3.88 (br s, 1H), 3.31 – 3.26 (m, 2H), 2.48 (t, *J* = 7.0 Hz, 2H), 2.00 – 1.94 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.0, 137.8, 123.6, 120.6 (q, *J* = 257.8 Hz), 119.0, 117.3, 116.5, 112.3, 42.3, 24.8, 14.8; ^{19}F NMR (471 MHz, $CDCl_3$) δ -58.2; ATR-FTIR (cm^{-1}): 2248, 1603, 1545, 1372, 1246, 752; HRMS m/z (ESI) calcd for $C_{11}H_{11}BrF_3N_2O$ $(M + H)^+$ 323.0001, found 323.0006.

4-((3-Chloro-4-((3-fluorobenzyl)oxy)phenyl)amino)butanenitrile (3ja). A yellow oil (49.8 mg, 78%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.30 (m, 1H), 7.22 – 7.18 (m, 2H), 7.03 – 6.96 (m, 1H), 6.81 (d, *J* = 8.8 Hz, 1H), 6.67 (d, *J* = 2.8 Hz, 1H), 6.43 (dd, *J* = 8.8, 2.8 Hz, 1H), 5.02 (s, 2H), 3.22 (t, *J* = 6.6 Hz, 2H), 2.45 (t, *J* = 7.1 Hz, 2H), 1.95 – 1.89 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8 (d, *J* = 245.9 Hz), 146.2, 143.1, 139.6 (d, *J* = 7.3 Hz), 130.0 (d, *J* = 8.2 Hz), 124.7, 122.6 (d, *J* = 2.4 Hz), 119.3, 117.1, 114.7, 114.6 (d, *J* = 21.1 Hz), 114.1 (d, *J* = 22.1 Hz), 111.9, 71.4, 42.7, 25.0, 14.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.9; ATR-FTIR (cm $^{-1}$): 2246, 1603, 1460, 1372, 1264, 1056, 753; HRMS m/z (ESI) calcd for $C_{17}H_{17}ClFN_2O$ $(M + H)^+$ 319.1008, found 319.1012.

4-((2,5-Dimethoxy-4-nitrophenyl)amino)butanenitrile (3ka) . A yellow oil (36.9 mg, 70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 6.13 (s, 1H), 5.13 (t, *J* = 5.5 Hz, 1H), 3.94 (s, 3H), 3.85 (s, 3H), 3.44 (q, *J* = 6.6 Hz, 2H), 2.51 (t, *J* = 6.9 Hz, 2H), 2.08 – 2.02 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.8, 144.5, 139.1, 126.4, 118.9, 107.2, 92.7, 56.8, 56.0, 41.2, 24.9, 14.8; ATR-FTIR (cm $^{-1}$): 2248, 1598, 1505, 1382, 1265, 1125, 1068, 753; HRMS m/z (ESI) calcd for $C_{12}H_{16}N_3O_4$ $(M + H)^+$ 266.1135, found 266.1137.

4-((2-Fluoro-6-methoxyphenyl)amino)butanenitrile (3la). A yellow oil (32.8 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.64 (dd, *J* = 8.3, 5.0 Hz, 1H), 6.35 – 6.29 (m, 2H), 4.39 (br s, 1H), 3.81 (s, 3H), 3.28 (t, *J* = 5.7 Hz, 2H), 2.47 (t, *J* = 7.1 Hz, 2H), 2.02 – 1.95 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2 (d, *J* = 235.9 Hz), 142.8, 138.6 (d, *J* = 10.9 Hz), 119.2, 109.7 (d, *J* = 10.1 Hz), 101.3 (d, *J* = 23.0 Hz), 97.4 (d, *J* = 28.2 Hz), 55.8, 41.8, 25.0, 14.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.9; ATR-FTIR (cm $^{-1}$): 2248, 1601, 1505, 1380, 1265, 1065, 752; HRMS m/z (ESI) calcd for $C_{11}H_{14}FN_2O$ $(M + H)^+$ 209.1085, found 209.1087.

4-((1H-indol-4-yl)amino)butanenitrile (3ma). A brown oil (33.8 mg, 85%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (br s, 1H), 7.12 – 7.07 (m, 2H), 6.86 (d, *J* = 8.2 Hz, 1H), 6.45 (t, *J* = 2.2 Hz, 1H), 6.30 (d, *J* = 7.6 Hz, 1H), 4.01 (br s, 1H), 3.47 (t, *J* = 6.6 Hz, 2H), 2.50 (t, *J* = 7.1 Hz, 2H), 2.09 – 2.02 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.6, 136.4, 123.4, 122.2, 119.6, 116.8, 101.8, 99.3, 98.4, 42.3, 25.3, 14.8; ATR-FTIR (cm $^{-1}$): 2248, 1603, 1506, 1452, 1372, 1265, 1123, 1068, 755; HRMS m/z (ESI) calcd for $C_{12}H_{14}N_3$ $(M + H)^+$ 200.1182, found 200.1185.

4-((3-Acetylphenyl)amino)butanenitrile (3na). A brown oil (30.4 mg, 75 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 2H), 7.23 – 7.19 (m, 1H), 6.85 – 6.82 (m, 1H), 4.04 (br s, 1H), 3.37 (t, *J* = 6.6 Hz, 2H), 2.59 (s, 3H), 2.50 (t, *J* = 7.1 Hz, 2H), 2.03 – 1.96 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.6, 147.7, 138.1, 129.4, 119.3, 118.2, 117.6, 111.2, 42.1, 26.7, 25.0, 14.7; ATR-FTIR (cm $^{-1}$): 2247, 1736, 1605, 1460, 1379, 1256, 1120, 752; HRMS m/z (ESI) calcd for $C_{12}H_{15}N_2O$ $(M + H)^+$ 203.1179, found 203.1182.

4-(Naphthalen-2-ylamino)butanenitrile (3oa). A yellow oil (33.5 mg, 80 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.60 (m, 3H), 7.39 – 7.34 (m, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 6.83 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.78 (d, *J* = 1.7 Hz, 1H), 3.85 (br s, 1H), 3.34 (t, *J* = 6.6 Hz, 2H), 2.42 (t, *J* = 7.1 Hz, 2H), 1.99 – 1.92 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.1, 135.0, 129.0, 127.6, 126.4, 125.9, 122.2, 119.4, 117.8, 104.3, 42.2, 24.9, 14.7; ATR-FTIR (cm $^{-1}$): 2248, 1601, 1505, 1462, 1380, 1127, 1065, 751; HRMS m/z (ESI) calcd for $C_{14}H_{15}N_2$ $(M + H)^+$ 211.1230, found 211.1235.

4-(Quinolin-6-ylamino)butanenitrile (3pa) . A yellow oil (26.8 mg, 64%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (dd, *J* = 4.2, 1.4 Hz, 1H), 7.90 (dd, *J* = 18.1, 8.5 Hz, 2H), 7.26 – 7.25 (m, 1H), 7.07 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.70 (d, *J* = 2.5 Hz, 1H), 4.19 (br s, 1H),

3.40 (t, *J* = 6.6 Hz, 2H), 2.49 (t, *J* = 7.0 Hz, 2H), 2.06 – 1.99 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.3, 145.5, 143.1, 133.9, 130.2, 130.0, 121.5, 121.3, 119.2, 103.0, 42.2, 24.8, 14.8; ATR-FTIR (cm $^{-1}$): 2246, 1595, 1464, 1380, 1265, 1132, 1066, 749; HRMS m/z (ESI) calcd for $C_{13}H_{14}N_3$ $(M + H)^+$ 212.1182, found 212.1179.

4-((3-(Hydroxymethyl)phenyl)amino)butanenitrile (3qa) . A colorless oil (27.5 mg, 72%): H NMR (400 MHz, $CDCl_3$) δ 7.15 (t, *J* = 7.8 Hz, 1H), 6.69 (d, *J* = 7.5 Hz, 1H), 6.62 (s, 1H), 6.53 (dd, *J* = 8.0, 1.8 Hz, 1H), 4.58 (s, 2H), 3.28 (t, *J* = 6.5 Hz, 2H), 2.43 (t, *J* = 7.0 Hz, 2H), 1.96 – 1.89 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.8, 142.2, 129.4, 119.5, 116.2, 111.8, 111.2, 65.1, 42.1, 25.0, 14.6; ATR-FTIR (cm $^{-1}$): 2247, 1605, 1466, 1378, 1250, 1065, 762; HRMS m/z (ESI) calcd for $C_{11}H_{15}N_2O$ $(M + H)^+$ 191.1179, found 191.1182.

4-((3-Hydroxyphenyl)amino)butanenitrile (3ra) . A colorless oil (19.4, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (t, *J* = 8.0 Hz, 1H), 6.26 – 6.14 (m, 2H), 6.10 (s, 1H), 4.55 (br s, 1H), 3.20 (t, *J* = 6.7 Hz, 2H), 2.40 (t, *J* = 7.1 Hz, 2H), 1.91 – 1.85 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 149.1, 130.3, 119.6, 105.7, 105.0, 99.8, 42.2, 25.0, 14.6; ATR-FTIR (cm $^{-1}$): 2246, 1709, 1506, 1446, 1378, 1264, 1069, 735; HRMS m/z (ESI) calcd for $C_{10}H_{13}N_2O$ $(M + H)^+$ 177.1022, found 177.1025.

3-((3-Cyanopropyl)amino)benzoic acid (3sa). A white solid, mp 157-159 °C (19.7 mg, 48%). ^{1}H NMR (400 MHz, DMSO) δ 7.20 – 7.11 (m, 3H), 6.80 – 6.77 (m, 1H), 5.97 (br s, 1H), 3.16 – 3.06 (m, 2H), 2.59 (t, *J* = 7.2 Hz, 2H), 1.86 – 1.79 (m, 2H); ^{13}C NMR (101 MHz, DMSO) δ 167.9, 148.7, 131.5, 129.1, 120.6, 116.8, 116.1, 112.6, 41.4, 24.4, 14.1; ATR-FTIR (cm $^{-1}$): 2246, 1728, 1631, 1565, 1511, 1263, 1096, 850; HRMS m/z (ESI) calcd for $C_{11}H_{13}N_2O_2$ $(M + H)^+$ 205.0972, found 205.0970.

4-((4-(Phenylamino)phenyl)amino)butanenitrile (3ta). A yellow oil (36.4 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.17 (m, 2H), 7.04 – 7.01 (m, 2H), 6.87 – 6.84 (m, 2H), 6.80 (t, *J* = 7.3 Hz, 1H), 6.63 – 6.59 (m, 2H), 5.43 (br s, 1H), 3.30 (t, *J* = 6.6 Hz, 2H), 2.49 (t, *J* = 7.1 Hz, 2H), 2.00 – 1.93 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.9, 143.5, 133.3, 129.2, 123.5, 119.4, 118.9, 114.9, 113.8, 42.8, 25.3, 14.8; ATR-FTIR (cm $^{-1}$): 2246, 1590, 1452, 1377, 1265, 1123, 1068, 746; HRMS m/z (ESI) calcd for $C_{16}H_{18}N_3$ $(M + H)^+$ 252.1495, found 252.1493.

4-((3-Cyanopropyl)amino)-N-methylbenzamide (3ua). A yellow oil (30.9 mg, 71%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.5 Hz, 2H), 6.55 (d, *J* = 8.5 Hz, 2H), 6.32 (br s, 1H), 4.32 (br s, 1H), 3.31 (t, *J* = 6.6 Hz, 2H), 2.94 (d, *J* = 4.6 Hz, 3H), 2.45 (t, *J* = 7.0 Hz, 2H), 1.97 – 1.91 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 150.2, 128.6, 123.1, 119.3, 111.7, 41.7, 26.6, 24.9, 14.7; ATR-FTIR (cm $^{-1}$): 2247, 1715, 1509, 1450, 1383, 1264, 1150, 1069, 735; HRMS m/z (ESI) calcd for $C_{12}H_{16}N_3O$ $(M + H)^+$ 218.1288, found 218.1289.

N-(4-((3-Cyanopropyl)amino)phenyl)acetamide (3va). A yellow oil (37.6 mg, 87%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (br s, 1H), 7.28 (d, *J* = 8.8 Hz, 2H), 6.55 (d, *J* = 8.8 Hz, 2H), 3.26 (t, *J* = 6.6 Hz, 2H), 2.46 (t, *J* = 7.0 Hz, 2H), 2.12 (s, 3H), 1.97 – 1.90 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.5, 144.6, 128.6, 122.4, 119.4, 112.9, 42.5, 25.1, 24.1, 14.7; ATR-FTIR (cm $^{-1}$): 2248, 1732, 1605, 1553, 1381, 1259, 1115, 742; HRMS m/z (ESI) calcd for $C_{12}H_{16}N_3O$ $(M + H)^+$ 218.1288, found 218.1290.

3-((3-Cyanopropyl)amino)-4-methylbenzamide (3wa). A white oil (25.1 mg, 58%): ^{1}H NMR (400 MHz, DMSO) δ 7.79 (br s, 1H), 7.14 (br s, 1H), 7.07 – 6.99 (m, 3H), 5.04 (br s, 1H), 3.20 (t, *J* = 6.6 Hz, 2H), 2.60 (t, *J* = 7.2 Hz, 2H), 2.11 (s, 3H), 1.93 – 1.86 (m, 2H); ^{13}C NMR (101 MHz, DMSO) δ 168.6, 146.0, 132.9, 129.4, 125.6, 120.8, 115.3, 107.9, 41.7, 24.3, 17.7, 14.2; ATR-FTIR (cm $^{-1}$): 2246, 1729, 1603, 1455, 1379, 1129, 1032, 733; HRMS m/z (ESI) calcd for $C_{12}H_{16}N_3O$ $(M + H)^+$ 218.1288, found 218.1289.

4-((4-Methyl-2-oxo-2H-chromen-7-yl)amino)butanenitrile (3xa). A yellow oil (22.4 mg, 46%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 1H), 6.58 – 6.51 (m, 2H), 5.98 (d, *J* = 1.1 Hz, 1H), 4.67 (br s, 1H), 3.37 (q, *J* = 6.5 Hz, 2H), 2.50 (t, *J* = 7.0 Hz, 2H), 2.33 (d, *J* = 1.1 Hz, 3H), 2.06 – 1.97 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 155.8, 153.1, 151.0, 125.7, 119.1, 110.9, 110.0, 109.6, 98.4, 41.8, 24.7, 18.5, 14.8; ATR-FTIR (cm $^{-1}$): 2248, 1725, 1556, 1463, 1382, 1263, 1036, 752; HRMS m/z (ESI) calcd for $C_{14}H_{15}N_2O_2$ $(M + H)^+$ 243.1128, found 243.1132.

4-((3-Fluoro-4-morpholinophenyl)amino)butanenitrile (3ya). A yellow oil (45.7 mg, 87%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (t, *J* = 9.2 Hz, 1H), 6.41 – 6.28 (m, 2H), 3.84 – 3.82 (m, 4H), 3.64 (br s, 1H), 3.23 (t, *J* = 6.6 Hz, 2H), 2.94 – 2.93 (m, 4H), 2.45 (t, *J* = 7.1 Hz, 2H), 1.96 – 1.89 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.9 (d, *J* = 245.1 Hz), 144.2 (d, *J* = 10.2 Hz), 131.0 (d, *J* = 9.8 Hz), 120.3 (d, *J* = 4.5 Hz), 119.2, 108.2 (d, *J* = 2.8 Hz), 101.5 (d, *J* = 24.5 Hz), 67.0, 51.7, 51.6, 42.5, 25.0, 14.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -122.4; ATR-FTIR (cm $^{-1}$): 2246, 1559, 1456, 1380, 1264, 1120, 1065, 749; HRMS m/z (ESI) calcd for $C_{14}H_{19}FN_3O$ $(M + H)^+$ 264.1507, found 264.1505.

4-((4-(4-Ethyl-2,6-dioxopiperidin-4-yl)phenyl)amino)butanenitrile (3za). A yellow oil (54.7 mg, 91%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (br s, 1H), 7.05 (d, *J* = 8.7 Hz, 2H), 6.57 (d, *J* = 8.7 Hz, 2H), 3.28 (t, *J* = 6.6 Hz, 2H), 2.61 – 2.50 (m, 1H), 2.47 (t, *J* = 7.1 Hz, 2H), 2.44 – 2.38 (m, 1H), 2.32 – 2.27 (m, 1H), 2.14 (td, *J* = 13.7, 4.6 Hz, 1H), 2.02 – 1.83 (m, 4H), 0.83 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.7, 172.9, 146.7, 127.2, 127.1, 119.3, 112.9, 50.0, 42.0, 32.8, 29.2, 26.7, 25.0, 14.7, 8.9; ATR-FTIR (cm $^{-1}$): 2248, 1729, 1515, 1460, 1379, 1123, 1065, 752; HRMS m/z (ESI) calcd for $C_{17}H_{22}N_3O_2$ $(M + H)^+$ 300.1707, found 300.1709.

General Procedure B of Copper-Catalyzed Selective C (*sp*^{3})-N Cross-Couplings.

Flame-dried 25 mL Schlenk tube filled with argon, cyclobutanone oxime **1b** (53.0 mg, 0.2 mmol), aniline **2a** (37.2 mg, 0.4 mmol), $Cu(tmhd)_2$ (4.3 mg, 5 mol%), and absolute dry DMF (1.0 mL) were added under Ar. The formed mixture was stirred at 80 ºC with heating mantle under Ar for 12 h as monitored by TLC. The solution was then cooled to room temperature, the mixture was extracted with EA and saturated $NaHCO_3$ solution, dried ($MgSO_4$) and concentrated to give a crude product. The crude product was purified by flash column chromatography on silica gel (PE : EA = 8 : 1) to afford **3ab**.

3-Phenyl-4-(phenylamino)butanenitrile (3ab). A yellow oil (30.6 mg, 65%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (t, *J* = 7.4 Hz, 2H), 7.39 (t, *J* = 7.1 Hz, 1H), 7.31 (d, *J* = 7.5 Hz, 2H), 7.24 (t, *J* = 7.8 Hz, 2H), 6.80 (t, *J* = 7.3 Hz, 1H), 6.66 (d, *J* = 8.1 Hz, 2H), 3.73 (br s, 1H), 3.63 (dd, *J* = 13.1, 6.9 Hz, 1H), 3.49 (dd, *J* = 13.1, 7.3 Hz, 1H), 3.40 – 3.33 (m, 1H), 2.84 – 2.73 (m, 2H); ^{13}C NMR (126

MHz, $CDCl_3$) δ 147.2, 139.3, 129.4, 129.1, 128.0, 127.3, 118.3, 118.1, 113.0, 47.9, 41.3, 22.1; ATR-FTIR (cm^{-1}): 2247, 1550, 1452, 1380, 1126, 1066, 755; HRMS m/z (ESI) calcd for $C_{16}H_{17}N_2$ $(M + H)^+$ 237.1386, found 237.1388.

3-Benzyl-4-(phenylamino)butanenitrile (3ac). A colorless oil (36.1 mg, 72%): ^1H NMR (500 MHz, $CDCl_3$) δ 7.38 (t, *J* = 7.4 Hz, 2H), 7.32 – 7.29 (m, 1H), 7.26 – 7.20 (m, 4H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.61 (d, *J* = 7.7 Hz, 2H), 3.83 (br s, 1H), 3.34 (dd, *J* = 13.8, 5.3 Hz, 1H), 3.24 (dd, *J* = 13.7, 7.9 Hz, 1H), 2.92 (dd, *J* = 13.8, 5.9 Hz, 1H), 2.76 (dd, *J* = 13.8, 8.1 Hz, 1H), 2.50 (td, *J* = 6.8, 3.3 Hz, 1H), 2.40 – 2.34 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.4, 138.1, 129.3, 128.9, 128.7, 126.8 118.3 117.8, 112.8 46.6, 37.7, 37.2, 19.4; ATR-FTIR (cm^{-1}): 2247, 1602, 1556, 1377, 1123, 1069, 748; HRMS m/z (ESI) calcd for $C_{17}H_{19}N_2$ $(M + H)^+$ 251.1543, found 251.1540.

3-(Benzyloxy)-4-(phenylamino)butanenitrile (3ad). A yellow oil (23.4 mg, 44%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.32 (m, 5H), 7.20 – 7.16 (m, 2H), 6.75 (t, *J* = 7.3 Hz, 1H), 6.60 – 6.58 (m, 2H), 4.71 (d, *J* = 11.6 Hz, 1H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.00 – 3.94 (m, 1H), 3.91 (br s, 1H), 3.43 – 3.28 (m, 2H), 2.68 (d, *J* = 5.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.4, 137.0, 129.4, 128.7, 128.3, 128.0, 118.2, 117.3, 113.1, 73.0, 72.3, 46.3, 21.2; ATR-FTIR (cm^{-1}): 2247, 1556, 1453, 1380, 1262, 1133, 1020, 753; HRMS m/z (ESI) calcd for $C_{17}H_{19}N_2O$ $(M + H)^+$ 267.1492, found 267.1496.

3-Methyl-3-phenyl-4-(phenylamino)butanenitrile (3ae). A yellow oil 30.5 mg, 61%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.31 (m, 5H), 7.20 – 7.13 (m, 2H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.58 (d, *J* = 7.7 Hz, 2H), 3.53 – 3.48 (m, 1H), 3.44 – 3.39 (m, 1H), 3.30 (br s, 1H), 2.85 (s, 2H), 1.63 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.8, 142.0, 129.3, 129.1, 127.5, 125.8, 118.1, 118.0, 113.2, 53.5, 41.5, 28.4, 24.3; ATR-FTIR (cm^{-1}): 2248, 1603, 1556, 1455, 1382, 1265, 1075, 736; HRMS m/z (ESI) calcd for $C_{17}H_{19}N_2$ $(M + H)^+$ 251.1543, found 251.1543.

4-Cyano-3-methyl-3-((phenylamino)methyl)butyl acetate (3af). A yellow oil (30.3 mg, 58%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.17 (m, 2H), 6.76 – 6.72 (m, 1H), 6.69 – 6.66 (m, 2H), 4.24 – 4.12 (m, 2H), 3.84 (br s, 1H), 3.14 (s, 2H), 2.44 (s, 2H), 2.06 (s, 3H), 1.84 (t, *J* = 6.7 Hz, 2H), 1.17 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 148.1, 129.3, 118.1, 117.9, 113.1, 60.3, 51.5, 36.9, 35.3, 27.0, 22.7, 20.9; ATR-FTIR (cm^{-1}): 2248, 1726, 1559, 1446, 1377, 1269, 1125, 1067, 739; HRMS m/z (ESI) calcd for $C_{15}H_{21}N_2O_2$ $(M + H)^+$ 261.1598, found 261.1596.

tert-Butyl 4-(cyanomethyl)-4-((phenylamino)methyl)piperidine-1-carboxylate (3ag). A yellow oil (34.1 mg, 52%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.17 (m, 2H), 6.77 – 6.72 (m, 1H), 6.70 – 6.68 (m, 2H), 3.70 – 3.60 (m, 2H), 3.30 – 3.21 (m, 4H), 2.53 (s, 2H), 1.66 – 1.60 (m, 4H), 1.46 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.6, 148.0, 129.4, 118.3, 117.6, 113.2, 80.0, 50.6, 36.4, 32.3, 28.4, 23.7; ATR-FTIR (cm^{-1}): 2247, 1726, 1562, 1463, 1378, 1259, 1036, 759; HRMS m/z (ESI) calcd for $C_{19}H_{28}N_3O_2$ $(M + H)^+$ 330.2176, found 330.2173.

General Procedure C of Copper-Catalyzed Selective C (sp^3)-N Cross-Couplings.

Flame-dried 25 mL Schlenk tube filled with argon, 2-phenylcyclobutan-1-one *O*-benzoyl oxime **1h** (53.0 mg, 0.2 mmol), aniline **2a** (37.2 mg, 0.4 mmol), $Cu(OTf)_2$ (3.6 mg, 5 mol%), and absolute dry 1,4-dioxane (1.0 mL) were added under Ar. The formed

mixture was stirred at 80 ºC under Ar for 12 h as monitored by TLC. The solution was then cooled to room temperature, the mixture was extracted with EA and saturated $NaHCO_3$ solution, dried ($MgSO_4$) and concentrated to give a crude product. The crude product was purified by flash column chromatography on silica gel (PE : EA = 7 : 1) to afford **3ah**.

4-Phenyl-4-(phenylamino)butanenitrile (3ah). A yellow oil (19.7 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 4H), 7.30 – 7.27 (m, 1H), 7.15 – 7.09 (m, 2H), 6.72 – 6.66 (m, 1H), 6.59 – 6.57 (m, 2H), 4.51 (t, *J* = 7.0 Hz, 1H), 4.05 (br s, 1H), 2.52 – 2.32 (m, 2H), 2.25 – 2.08 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.5, 141.6, 129.3, 129.0, 127.8, 126.3, 119.3, 118.2, 113.7, 56.9, 33.6, 14.5; ATR-FTIR (cm $^{-1}$): 2245, 1601, 1524, 1451, 1383, 1207, 1062, 750; HRMS m/z (ESI) calcd for $C_{16}H_{17}N_2$ $(M + H)^+$ 237.1386, found 237.1385.

5-Phenyl-5-(phenylamino)pentanenitrile (3ai). A yellow oil (26.5 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.33 (m, 4H), 7.27 – 7.24 (m, 1H), 7.12 – 7.08 (m, 2H), 6.66 (t, *J* = 7.3 Hz, 1H), 6.54 (d, *J* = 7.8 Hz, 2H), 4.36 (t, *J* = 6.8 Hz, 1H), 4.05 (br s, 1H), 2.35 (td, *J* = 7.0, 1.6 Hz, 2H), 2.03 – 1.93 (m, 2H), 1.85 – 1.77 (m, 1H), 1.72 – 1.66 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.9, 142.9, 129.2, 128.8, 127.3, 126.2, 119.3, 117.6, 113.3, 57.4, 37.3, 22.4, 17.1; ATR-FTIR (cm $^{-1}$): 2246, 1556, 1454, 1380, 1209, 1065, 745; HRMS m/z (ESI) calcd for $C_{17}H_{19}N_2$ $(M + H)^+$ 251.1543, found 251.1540.

5-(4-(tert-Butyl)phenyl)-5-(phenylamino)pentanenitrile (3aj). A yellow oil (36.7 mg, 60%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.34 (m, 2H), 7.25 (d, *J* = 8.3 Hz, 2H), 7.13 – 7.10 (m, 2H), 6.67 (t, *J* = 7.3 Hz, 1H), 6.60 – 6.47 (m, 2H), 4.35 (t, *J* = 6.8 Hz, 1H), 2.34 (td, *J* = 7.1, 2.2 Hz, 2H), 2.00 – 1.92 (m, 2H), 1.83 – 1.78 (m, 1H), 1.71 – 1.65 (m, 1H), 1.31 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.1, 147.0, 139.7, 129.1, 125.9, 125.6, 119.4, 117.4, 113.2, 56.9, 37.2, 34.4, 31.3, 22.4, 17.0; ATR-FTIR (cm $^{-1}$): 2247, 1560, 1446, 1383, 1216, 1032, 746; HRMS m/z (ESI) calcd for $C_{21}H_{27}N_2$ $(M + H)^+$ 307.2169, found 307.2170.

5-(4-Fluorophenyl)-5-(phenylamino)pentanenitrile (3ak). A yellow oil (26.9 mg, 50%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.12 – 7.08 (m, 2H), 7.02 (t, *J* = 8.6 Hz, 2H), 6.68 (t, *J* = 7.3 Hz, 1H), 6.51 (d, *J* = 7.7 Hz, 2H), 4.35 (t, *J* = 6.8 Hz, 1H), 2.36 (td, *J* = 7.0, 1.8 Hz, 2H), 1.98 – 1.88 (m, 2H), 1.82 – 1.77 (m, 1H), 1.72 – 1.64 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9 (d, *J* = 245.4 Hz), 146.7, 138.6 (d, *J* = 3.1 Hz), 129.2, 127.7 (d, *J* = 8.1 Hz), 119.2, 117.8, 115.6 (d, *J* = 21.4 Hz), 113.4, 56.8, 37.4, 22.3, 17.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.3; ATR-FTIR (cm $^{-1}$): 2246, 1602, 1507, 1427, 1318, 1223, 1157, 752; HRMS m/z (ESI) calcd for $C_{17}H_{18}FN_2$ $(M + H)^+$ 269.1449, found 269.1447.

5-([1,1'-Biphenyl]-4-yl)-5-(phenylamino)pentanenitrile (3al). A yellow oil (42.9 mg, 66%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.53 (m, 4H), 7.45 – 7.30 (m, 5H), 7.10 (t, *J* = 7.9 Hz, 2H), 6.66 (t, *J* = 7.3 Hz, 1H), 6.55 (d, *J* = 7.9 Hz, 2H), 4.39 (t, *J* = 6.8 Hz, 1H), 4.09 (br s, 1H), 2.36 – 2.30 (m, 2H), 2.01 – 1.93 (m, 2H), 1.85 – 1.76 (m, 1H), 1.75 – 1.66 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.9, 142.0, 140.6, 140.2, 129.2, 128.7, 127.5, 127.2, 127.0, 126.7, 119.3, 117.6, 113.3, 57.1, 37.3, 22.3, 17.0; ATR-FTIR (cm $^{-1}$): 2246, 1559, 1450, 1377, 1223, 1113, 1068, 751; HRMS m/z (ESI) calcd for $C_{23}H_{23}N_2$ $(M + H)^+$ 327.1856, found 327.1860.

5-(4-Methoxyphenyl)-5-(phenylamino)pentanenitrile (3am). A yellow oil (39.4 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.19 (m, 2H), 7.12 – 7.04 (m, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.64 (t, *J* = 7.3 Hz, 1H), 6.55 – 6.48 (m, 2H), 4.29 (t, *J* = 6.8 Hz, 1H),

4.02 (br s, 1H), 3.76 (s, 3H), 2.29 (td, *J* = 7.0, 1.5 Hz, 2H), 1.99 – 1.82 (m, 2H), 1.79 – 1.69 (m, 1H), 1.69 – 1.57 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 146.9, 134.8, 129.1, 127.3, 119.3, 117.4, 114.1, 113.3, 56.7, 55.2, 37.3, 22.3, 17.0; ATR-FTIR (cm $^{-1}$): 2246, 1604, 1508, 1313, 1245, 1177, 831; HRMS m/z (ESI) calcd for $C_{18}H_{21}N_2O$ $(M + H)^+$ 281.1648, found 281.1654.

5-(Naphthalen-2-yl)-5-(phenylamino)pentanenitrile (3an). A yellow oil (31.4 mg, 52%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.77 (m, 4H), 7.51– 7.45 (m, 3H), 7.12– 7.08 (m, 2H), 6.67 (t, *J* = 7.3 Hz, 1H), 6.59 (d, *J* = 7.7 Hz, 2H), 4.53 (t, *J* = 6.8 Hz, 1H), 4.17 (br s, 1H), 2.34 (td, *J* = 7.0, 2.4 Hz, 2H), 2.08 – 1.98 (m, 2H), 1.87 – 1.79 (m, 1H), 1.74 – 1.67 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.9, 140.4, 133.3, 132.8, 129.1, 128.7, 127.7, 127.6, 126.2, 125.8, 125.1, 124.2, 119.3, 117.6, 113.4, 57.6, 37.2, 22.3, 17.0; ATR-FTIR (cm $^{-1}$): 2246, 1601, 1552, 1455, 1315, 1125, 1069, 752; HRMS m/z (ESI) calcd for $C_{21}H_{21}N_2$ $(M + H)^+$ 301.1699, found 301.1696.

5-(Benzo[b]thiophen-5-yl)-5-(phenylamino)pentanenitrile (3ao). A yellow oil (29.5 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.3 Hz, 1H), 7.80 – 7.79 (m, 1H), 7.45 (d, *J* = 5.4 Hz, 1H), 7.34 – 7.26 (m, 2H), 7.11 – 7.07 (m, 2H), 6.66 (t, *J* = 7.3 Hz, 1H), 6.56 (d, *J* = 7.7 Hz, 2H), 4.48 (t, *J* = 6.8 Hz, 1H), 4.14 (br s, 1H), 2.35 (td, *J* = 7.0, 2.1 Hz, 2H), 2.08 – 1.95 (m, 2H), 1.86 – 1.76 (m, 1H), 1.76 – 1.63 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.9, 139.9, 139.3, 138.7, 129.2, 127.0, 123.8, 122.9, 122.7, 121.2, 119.3, 117.7, 113.4, 57.5, 37.6, 22.4, 17.1; ATR-FTIR (cm $^{-1}$): 2245, 1600, 1545, 1320, 1151, 1071, 750; HRMS m/z (ESI) calcd for $C_{19}H_{19}N_2S$ $(M + H)^+$ 307.1263, found 307.1258.

7-(4-Methoxyphenyl)-7-(phenylamino)heptanenitrile (3ap). A yellow oil (31.3 mg, 51%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.6 Hz, 2H), 7.08 (t, *J* = 7.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.73 – 6.58 (m, 1H), 6.51 (d, *J* = 8.5 Hz, 2H), 4.26 (t, *J* = 6.8 Hz, 1H), 4.01 (br s, 1H), 3.78 (s, 3H), 2.30 (t, *J* = 7.0 Hz, 2H), 1.84 – 1.72 (m, 2H), 1.67 – 1.58 (m, 2H), 1.50 – 1.42 (m, 3H), 1.36 – 1.30 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 147.3, 135.8, 129.1, 127.3, 119.6, 117.2, 114.0, 113.3, 57.4, 55.2, 38.4, 28.5, 25.5, 25.2, 17.0; ATR-FTIR (cm $^{-1}$): 2246, 1603, 1455, 1380, 1221, 1119, 1063, 752; HRMS m/z (ESI) calcd for $C_{20}H_{25}N_2O$ $(M + H)^+$ 309.1961, found 309.1958.

General Procedure A of Dual Photoredox and Copper-Catalyzed Selective C (*sp*^{3})-N Cross-Couplings.

Flame-dried 25 mL Schlenk tube filled with argon, cyclobutanone *O*-(4-(trifluoromethyl)benzoyl) oxime **1a'** (154.2 mg, 0.6 mmol), aniline **2a** (18.6 mg, 0.2 mmol), *fac*-Ir(ppy)$_3$ (1.3 mg, 1 mol%), $Cu(OTf)_2$ (14.4 mg, 20 mol%), and absolute DMF (1.0 mL) were added under Ar. The formed mixture was stirred into a crystallizing basin equipped with a 5 m length blue LED strips (12 w/m) under constant irradiation at room temperature for 12 h as monitored by TLC. The mixture was extracted with EA and saturated $NaHCO_3$ solution, dried ($MgSO_4$) and concentrated to give a crude product. The crude product was purified by flash column chromatography on silica gel (PE : EA = 4 : 1) to afford **4aa.**

4,4'-(Phenylazanediyl)dibutanenitrile (4aa) . A yellow oil (33.1 mg, 73%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 2H), 6.82 – 6.74 (m, 3H), 3.48 – 3.41 (m, 4H), 2.39 (t, *J* = 7.0 Hz, 4H), 1.97 – 1.90 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.0, 129.6,

119.2, 118.2, 114.1, 50.2, 23.0, 14.7; ATR-FTIR (cm $^{-1}$): 2245, 1598, 1503, 1325, 1112, 780; HRMS m/z (ESI) calcd for $C_{14}H_{18}N_3$ $(M + H)^+$ 228.1495, found 228.1496.

4,4'-((4-(tert-Butyl)phenyl)azanediyl)dibutanenitrile (4ba). A yellow oil (44.3 mg, 78%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.9 Hz, 2H), 6.73 – 6.71 (m, 2H), 3.40 (t, *J* = 7.1 Hz, 4H), 2.39 (t, *J* = 7.0 Hz, 4H), 1.98 – 1.89 (m, 4H), 1.29 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 141.3, 126.3, 119.3, 114.2, 50.5, 33.8, 31.4, 23.1, 14.7; ATR-FTIR (cm $^{-1}$): 2246, 1601, 1550, 1335, 1118, 1069, 753; HRMS m/z (ESI) calcd for $C_{18}H_{26}N_3$ $(M + H)^+$ 284.2121, found 284.2126.

4,4'-((4-Methoxyphenyl)azanediyl)dibutanenitrile (4ca) **.** A yellow oil (43.7 mg, 85%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (s, 4H), 3.77 (s, 3H), 3.25 (t, *J* = 6.8 Hz, 4H), 2.39 (t, *J* = 7.0 Hz, 4H), 1.86 – 1.79 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.2, 141.7, 119.6, 119.4, 114.9, 55.6, 52.1, 23.2, 14.7; ATR-FTIR (cm $^{-1}$): 2246, 1602, 1505, 1336, 1121, 1067, 751; HRMS m/z (ESI) calcd for $C_{15}H_{20}N_3O$ $(M + H)^+$ 258.1601, found 258.1603.

4,4'-((4-Fluorophenyl)azanediyl)dibutanenitrile (4da). A yellow oil. (25.4 mg, 52%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 – 6.94 (m, 2H), 6.80 – 6.73 (m, 2H), 3.35 (t, *J* = 7.0 Hz, 4H), 2.39 (t, *J* = 6.9 Hz, 4H), 1.91 – 1.84 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.8 (d, *J* = 239.0 Hz), 143.9, 119.2, 117.4 (d, *J* = 7.5 Hz), 116.1 (d, *J* = 22.2 Hz), 51.3, 23.0, 14.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.9; ATR-FTIR (cm $^{-1}$): 2245, 1605, 1509, 1332, 1220, 1109, 1026, 752; HRMS m/z (ESI) calcd for $C_{14}H_{17}FN_3$ $(M + H)^+$ 246.1401, found 246.1400.

4,4'-((3-Bromo-4-methylphenyl)azanediyl)dibutanenitrile (4ea). A yellow oil (33.1 mg, 52%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.4 Hz, 1H), 6.92 (d, *J* = 2.6 Hz, 1H), 6.64 (dd, *J* = 8.4, 2.6 Hz, 1H), 3.40 (t, *J* = 7.0 Hz, 4H), 2.38 (t, *J* = 7.0 Hz, 4H), 2.29 (s, 3H), 1.96 – 1.88 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.2, 131.4, 127.5, 125.9, 119.1, 118.0, 113.7, 50.4, 23.0, 21.6, 14.7; ATR-FTIR (cm $^{-1}$): 2246, 1545, 1446, 1378, 1230, 1121, 1065, 752; HRMS m/z (ESI) calcd for $C_{15}H_{19}BrN_3$ $(M + H)^+$ 320.0757, found 320.0760.

4,4'-((3-(Hydroxymethyl)phenyl)azanediyl)dibutanenitrile (4fa). A yellow oil (34.8 mg, 68%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.21 (m, 1H), 6.80 (s, 1H), 6.77 (d, *J* = 7.5 Hz, 1H), 6.67 (dd, *J* = 8.2, 2.4 Hz, 1H), 4.65 (s, 2H), 3.47 (t, *J* = 7.1 Hz, 4H), 2.39 (t, *J* = 7.0 Hz, 4H), 1.98 – 1.91 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.3, 142.5, 129.8, 119.2, 116.7, 113.0, 112.3, 65.5, 50.1, 23.1, 14.7; ATR-FTIR (cm $^{-1}$): 2246, 1550, 1446, 1336, 1228, 1109, 1066, 739; HRMS m/z (ESI) calcd for $C_{15}H_{20}N_3O$ $(M + H)^+$ 258.1601, found 258.1605.

4,4'-((3-Hydroxyphenyl)azanediyl)dibutanenitrile (4ga). A yellow oil (30.3 mg, 62%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (t, *J* = 8.1 Hz, 1H), 6.33 – 6.21 (m, 3H), 5.69 (br s, 1H), 3.53 – 3.30 (m, 4H), 2.38 (t, *J* = 7.0 Hz, 4H), 1.96 – 1.89 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1, 148.5, 130.5, 119.3, 106.0, 105.0, 100.6, 50.0, 23.0, 14.6; ATR-FTIR (cm $^{-1}$): 2247, 1617, 1579, 1503, 1375, 1165, 759; HRMS m/z (ESI) calcd for $C_{14}H_{18}N_3O$ $(M + H)^+$ 244.1444, found 244.1443.

N-(4-(Bis(3-cyanopropyl)amino)phenyl)acetamide (4ha). A yellow oil (50.9 mg, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (br s, 1H), 7.35 (d, *J* = 8.9 Hz, 2H), 6.71 (d, *J* = 9.0 Hz, 2H), 3.37 (t, *J* = 7.0 Hz, 4H), 2.36 (t, *J* = 6.9 Hz, 4H), 2.11 (s, 3H), 1.88 (p, *J* = 7.1

Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 144.1, 129.4, 122.2, 119.3, 115.2, 50.5, 24.2, 22.9, 14.6; ATR-FTIR (cm $^{-1}$): 2246, 1732, 1661, 1519, 1420, 1372, 1265, 1062, 818; **HRMS m/z (ESI)** calcd for $C_{16}H_{21}N_4O$ $(M + H)^+$ 285.1710, found 285.1715.

4,4'-((3-Fluoro-4-morpholinophenyl)azanediyl)dibutanenitrile (4ia). A yellow oil (42.7 mg, 65%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.88 (t, *J* = 9.4 Hz, 1H), 6.57 – 6.45 (m, 2H), 3.91 – 3.80 (m, 4H), 3.36 (t, *J* = 7.0 Hz, 4H), 3.00 – 2.98 (m, 4H), 2.38 (t, *J* = 7.0 Hz, 4H), 1.93 – 1.87 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.8 (d, *J* = 245.7 Hz), 143.7 (d, *J* = 9.5 Hz), 131.9 (d, *J* = 9.4 Hz), 120.2 (d, *J* = 4.6 Hz), 119.1, 110.6 (d, *J* = 2.7 Hz), 103.7 (d, *J* = 24.4 Hz), 67.1, 51.52 (d, *J* = 2.4 Hz), 50.7, 23.1, 14.7; ^{19}F NMR (471 MHz, $CDCl_3$) δ -121.1; ATR-FTIR (cm $^{-1}$): 2245, 1629, 1518, 1452, 1301, 1238, 737; HRMS m/z (ESI) calcd for $C_{18}H_{24}FN_4O$ $(M + H)^+$ 331.1929, found 331.1930.

4, 4'-((4-(3-Ethyl-2,6-dioxopiperidin-3-yl)phenyl)azanediyl)dibutanenitrile (4ja). A yellow oil (50.4 mg, 66%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (br s, 1H), 7.14 (d, *J* = 8.9 Hz, 2H), 6.70 (d, *J* = 8.8 Hz, 2H), 3.45 (t, *J* = 7.2 Hz, 4H), 2.62 – 2.55 (m, 1H), 2.50 – 2.43 (m, 1H), 2.39 (t, *J* = 6.9 Hz, 4H), 2.35 – 2.29 (m, 1H), 2.17 (td, *J* = 13.7, 4.6 Hz, 1H), 2.03 – 1.84 (m, 6H), 0.85 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.4, 172.5, 146.0, 127.5, 119.1, 113.6, 50.1, 40.0, 32.8, 29.3, 26.7, 22.9, 14.7, 9.0; ATR-FTIR (cm $^{-1}$): 2246, 1699, 1520, 1461, 1355, 1192, 819; HRMS m/z (ESI) calcd for $C_{21}H_{26}N_4NaO_2$ $(M + Na)^+$ 389.1948, found 389.1951.

General Procedure B of Dual Photoredox and Copper-Catalyzed Selective C (*sp*^{3})-N Cross-Couplings.

Flame-dried 25 mL Schlenk tube filled with argon, cyclobutanone *O*-(4-(trifluoromethyl)benzoyl) oxime **1a'** (77.1 mg, 0.3 mmol), aniline **2k'** (21.4 mg, 0.2 mmol), *fac*-Ir(ppy)$_3$ (1.3 mg, 1 mol%), $Cu(OTf)_2$ (14.4 mg, 20 mol%), and absolute DMF (1.0 mL) were added under Ar. The formed mixture was stirred into a crystallizing basin equipped with a 5 m length blue LED strips (12 w/m) under constant irradiation at room temperature for 12 h as monitored by TLC. The mixture was extracted with EA and saturated $NaHCO_3$ solution, dried ($MgSO_4$) and concentrated to give a crude product. The crude product was purified by flash column chromatography on silica gel (PE : EA = 8 : 1) to afford **4ka.**

4-(Methyl(phenyl)amino)butanenitrile (4ka) . A yellow oil (27.2 mg, 78%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.24 (m, 2H), 6.82 – 6.66 (m, 3H), 3.47 (t, *J* = 6.9 Hz, 2H), 2.96 (s, 3H), 2.40 (t, *J* = 7.1 Hz, 2H), 2.00 – 1.93 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.9, 129.3, 119.4, 117.0, 112.5, 51.2, 38.7, 23.1, 14.7; ATR-FTIR (cm $^{-1}$): 2245, 1605, 1450, 1339, 1220, 1067, 752; HRMS m/z (ESI) calcd for $C_{11}H_{15}N_2$ $(M + H)^+$ 175.1230, found 175.1228.

4-(Benzyl(phenyl)amino)butanenitrile (4la). A yellow oil (33.8 mg, 68%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 2H), 7.25 – 7.15 (m, 5H), 6.73 – 6.65 (m, 3H), 4.52 (s, 2H), 3.55 – 3.41 (m, 2H), 2.32 (t, *J* = 7.1 Hz, 2H), 1.98 – 1.91 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.0, 138.3, 129.4, 128.6, 127.0, 126.6, 119.2, 117.2, 112.9, 55.1, 49.6, 23.2, 14.7; ATR-FTIR (cm $^{-1}$): 2246, 1595, 1505, 1378, 1229, 1108, 1066, 750; HRMS m/z (ESI) calcd for $C_{17}H_{19}N_2$ $(M + H)^+$ 251.1543, found 251.1543.

4-(Isopropyl(phenyl)amino)butanenitrile (4ma) . A yellow oil (22.1 mg, 55%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.22 (m, 2H), 6.87 – 6.75 (m, 3H), 4.02 – 3.95 (m, 1H), 3.29 – 3.21 (m, 2H), 2.39 (t, *J* = 7.0 Hz, 2H), 1.92 – 1.85 (m, 2H), 1.19 (d, *J* = 6.7

Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.4, 129.2, 119.6, 118.2, 116.0, 51.1, 41.8, 24.1, 20.0, 14.6; ATR-FTIR (cm $^{-1}$): 2246, 1602, 1552, 1377, 1121, 1069, 748; HRMS m/z (ESI) calcd for $C_{13}H_{19}N_2$ $(M + H)^+$ 203.1543, found 203.1545.

4-(Allyl(phenyl)amino)butanenitrile (4na). A yellow oil. (28.7 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.17 (m, 2H), 6.83 – 6.68 (m, 3H), 5.92 – 5.83 (m, 1H), 5.22 – 5.18 (m, 2H), 3.96 (dt, *J* = 5.0, 1.6 Hz, 2H), 3.63 – 3.41 (m, 2H), 2.43 (t, *J* = 7.1 Hz, 2H), 2.03 – 1.96 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.8, 133.7, 129.3, 119.3, 117.0, 116.6, 112.7, 53.9, 49.1, 23.4, 14.7; ATR-FTIR (cm $^{-1}$): 2245, 1559, 1462, 1338, 1208, 1105, 1059, 739; HRMS m/z (ESI) calcd for $C_{13}H_{17}N_2$ $(M + H)^+$ 201.1386, found 201.1384.

4-((4-Methoxyphenyl)(methyl)amino)butanenitrile (4oa). A yellow oil (30.4 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 – 6.82 (m, 2H), 6.78 – 6.72 (m, 2H), 3.76 (s, 3H), 3.34 (t, *J* = 6.8 Hz, 2H), 2.86 (s, 3H), 2.40 (t, *J* = 7.1 Hz, 2H), 1.95 – 1.88 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.4, 144.1, 119.5, 115.5, 114.8, 55.7, 52.5, 39.6, 23.1, 14.7; ATR-FTIR (cm $^{-1}$): 2246, 1606, 1556, 1339, 1216, 1108, 1065, 752; HRMS m/z (ESI) calcd for $C_{12}H_{17}N_2O$ $(M + H)^+$ 205.1335, found 205.1336.

4-((2-Hydroxyethyl)(phenyl)amino)butanenitrile (4pa). A yellow oil (26.5 mg, 65%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.07 (m, 2H), 7.00 – 6.47 (m, 3H), 3.79 (t, *J* = 5.7 Hz, 2H), 3.51 – 3.47 (m, 4H), 2.39 (t, *J* = 7.0 Hz, 2H), 1.99 – 1.89 (m, 2H), 1.89 (br s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.6, 129.4, 119.4, 117.8, 113.6, 59.9, 54.0, 50.3, 22.9, 14.7; ATR-FTIR (cm $^{-1}$): 2245, 1595, 1545, 1463, 1378, 1125, 1066, 750; HRMS m/z (ESI) calcd for $C_{12}H_{17}N_2O$ $(M + H)^+$ 205.1335, found 205.1336.

4-(Indolin-1-yl)butanenitrile (4qa). A yellow oil (29.7 mg, 80%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (t, *J* = 7.8 Hz, 2H), 6.70 (t, *J* = 7.3 Hz, 1H), 6.52 (d, *J* = 7.7 Hz, 1H), 3.34 (t, *J* = 8.3 Hz, 2H), 3.21 (t, *J* = 6.6 Hz, 2H), 3.00 (t, *J* = 8.3 Hz, 2H), 2.50 (t, *J* = 7.1 Hz, 2H), 2.01 – 1.95 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.2, 129.8, 127.3, 124.5, 119.5, 118.0, 106.9, 53.5, 48.1, 28.5, 23.9, 14.6; ATR-FTIR (cm $^{-1}$): 2245, 1615, 1546, 1339, 1228, 1068, 746; HRMS m/z (ESI) calcd for $C_{12}H_{15}N_2$ $(M + H)^+$ 187.1230, found 187.1224.

4-(2, 3-Dihydro-1H-pyrrolo[2,3-b]pyridin-1-yl)butanenitrile (4ra). A yellow oil (22.1 mg, 59%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (t, *J* = 7.8 Hz, 1H), 6.70 (t, *J* = 7.3 Hz, 1H), 6.52 (d, *J* = 7.7 Hz, 1H), 3.34 (t, *J* = 8.3 Hz, 4H), 3.21 (t, *J* = 6.6 Hz, 2H), 3.00 (t, *J* = 8.3 Hz, 2H), 2.50 (t, *J* = 7.1 Hz, 2H), 2.05 – 1.98 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 145.7, 131.0, 122.9, 119.7, 112.7, 50.2, 44.8, 26.0, 24.0, 14.8; ATR-FTIR (cm $^{-1}$): 2245, 1608, 1556, 1382, 1208, 1121, 1069, 755; HRMS m/z (ESI) calcd for $C_{11}H_{14}N_3$ $(M + H)^+$ 188.1182, found 188.1185.

TEMPO Trapping Experiments

(a) Flame-dried 25 mL Schlenk tube filled with argon, cyclobutanone oxime 1a (56.7 mg, 0.3 mmol), aniline 2a (18.6 mg, 0.2 mmol), $Cu(tmhd)_2$ (4.3 mg, 5 mol%), TEMPO (62.5 mg, 0.4 mmol), and absolute dry DMF (1.0 mL) were added under Ar. The formed mixture was stirred at 80 ºC under Ar for 12 h as monitored by TLC. The solution was then cooled to room temperature, the reaction mixture was analyzed by GC-MS and ^{1}H NMR. The yield of 5 was determined by ^{1}H NMR using CH_2Br_2 as internal standard based on 1a.

(b) Flame-dried 25 mL Schlenk tube filled with argon, cyclobutanone *O*-(4-(trifluoromethyl)benzoyl) oxime **1a'** (77.1 mg, 0.3 mmol), aniline **2a** (18.6 mg, 0.2 mmol), *fac*-Ir(ppy)$_3$ (1.3 mg, 1 mol%), Cu(OTf)$_2$ (14.4 mg, 20 mol%), TEMPO (125.0 mg, 0.8 mmol), and absolute DMF (1.0 mL) were added under Ar. The formed mixture was stirred into a crystallizing basin equipped with a 5 m length blue LED strips (12 w/m) under constant irradiation at room temperature for 12 h as monitored by TLC. the reaction mixture was analyzed by GC-MS and ^{1}H NMR. The yield of **5** was determined by ^{1}H NMR using CH_2Br_2 as internal standard based on **1a'**.

Multi-component Reaction Experiments

(a) Flame-dried 25 mL Schlenk tube filled with argon, cyclobutanone oxime **1a** (56.7 mg, 0.3 mmol), aniline **2a** (18.6 mg, 0.2 mmol), styrene **6** (41.6 mg, 0.4 mmol), Cu(OTf)$_2$ (3.6 mg, 5 mol%), and absolute 1,4-dioxane (1.0 mL) were added under Ar. The formed mixture was stirred at 80 ºC under Ar for 12 h as monitored by TLC. The solution was then cooled to room temperature, the mixture was extracted with EA and saturated $NaHCO_3$ solution, dried ($MgSO_4$) and concentrated to give a crude product. The crude product was purified by flash column chromatography on silica gel (from PE : EA = 7 : 1) to afford 18.4 mg (35%) of **7** as a yellow oil: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.33 – 7.32 (m, 4H), 7.25 – 7.21 (m, 1H), 7.11 – 7.07 (m, 2H), 6.65 (t, *J* = 7.3 Hz, 01H), 6.54 – 6.50 (m, 12H), 4.32 (t, *J* = 6.8 Hz, 1H), 4.06 (br s, 1H), 2.37 – 2.29 (m, 2H), 1.90 – 1.79 (m, 2H), 1.69 – 1.57 (m, 3H), 1.53 – 1.42 (m, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 147.1, 143.5, 129.1, 128.7, 127.1, 126.3, 119.5, 117.4, 113.3, 57.8, 37.9, 25.5, 25.2, 17.1; **ATR-FTIR (cm $^{-1}$)**: 2246, 1601, 1560, 1452, 1382, 1123, 1059, 753; **HRMS m/z (ESI)** calcd for $C_{18}H_{21}N_2$ $(M + H)^+$ 265.1699, found 265.1700.

(b) Flame-dried 25 mL Schlenk tube filled with argon, cyclobutanone oxime **1a** (56.7 mg, 0.3 mmol), aniline **2a** (18.6 mg, 0.2 mmol), 4-methoxystyrene **6** (53.6 mg, 0.4 mmol), Cu(OTf)$_2$ (3.6 mg, 5 mol%), and absolute 1,4-dioxane (1.0 mL) were added under Ar. The formed mixture was stirred at 80 ºC under Ar for 12 h as monitored by TLC. The solution was then cooled to room temperature, the mixture was extracted with EA and saturated $NaHCO_3$ solution, dried ($MgSO_4$) and concentrated to give a crude product. The crude product was purified by flash column chromatography on silica gel (from PE : EA = 5 : 1) to afford 32.4 mg (55%) of **9** as a yellow oil: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.25 (d, *J* = 8.6 Hz, 2H), 7.11 – 7.08 (m, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.65 (t, *J* = 7.3 Hz, 1H), 6.55 – 6.51 (m, 2H), 4.28 (t, *J* = 6.8 Hz, 1H), 4.03 (br s, 1H), 3.79 (s, 3H), 2.31 (td, *J* = 7.0, 1.3 Hz, 2H), 1.89 – 1.82 (m, 1H), 1.80 – 1.73 (m, 1H), 1.70 – 1.64 (m, 2H), 1.60 – 1.54 (m, 1H), 1.50 – 1.40 (m, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 158.6, 147.1, 135.4, 129.1, 127.3, 119.5, 117.3, 114.0, 113.3, 57.2, 55.2, 37.8, 25.5, 25.2, 17.0; **ATR-FTIR (cm $^{-1}$)**: 2246, 1602, 1559, 1380, 1209, 1128, 1066, 753; **HRMS m/z (ESI)** calcd for $C_{19}H_{23}N_2O$ $(M + H)^+$ 295.1805, found 295.1802.

Photo-induced Experiments

(a) Flame-dried 25 mL Schlenk tube filled with argon, cyclobutanone *O*-(4-(trifluoromethyl)benzoyl) oxime **1a'** (77.1 mg, 0.3 mmol), aniline **2a** (18.6 mg, 0.2 mmol), *fac*-Ir(ppy)$_3$ (1.3 mg, 1 mol%), and absolute DMF (1.0 mL) were added under Ar. The formed

mixture was stirred into a crystallizing basin equipped with a 5 m length blue LED strips (12 w/m) under constant irradiation at room temperature for 12 h as monitored by TLC. the reaction mixture was analyzed by GC-MS.

(b) Flame-dried 25 mL Schlenk tube filled with argon, cyclobutanone *O*-(4-(trifluoromethyl)benzoyl) oxime **1a'** (77.1 mg, 0.3 mmol), aniline **2a** (18.6 mg, 0.2 mmol), Cu $(OTf)_2$ (14.4 mg, 20 mol%), and absolute DMF (1.0 mL) were added under Ar. The formed mixture was stirred into a crystallizing basin equipped with a 5 m length blue LED strips (12 w/m) under constant irradiation at room temperature for 12 h as monitored by TLC. the reaction mixture was analyzed by GC-MS.

(c) Flame-dried 25 mL Schlenk tube filled with argon, cyclobutanone *O*-(4-(trifluoromethyl)benzoyl) oxime **1a'** (77.1 mg, 0.3 mmol), aniline **2a** (18.6 mg, 0.2 mmol), Cu $(OTf)_2$ (14.4 mg, 20 mol%), and absolute DMF (1.0 mL) were added under Ar. The stirred mixture was wrapped up in tinfoil to avoid light at room temperature for 12 h as monitored by TLC. the reaction mixture was analyzed by GC-MS.

Functional Group Transformations

Reaction on 5.0 mmol scale: Flame-dried 100 mL Schlenk tube filled with argon, cyclobutanone oxime **1a** (1.4 g, 7.5 mmol), aniline **2a** (465.6 mg, 5.0 mmol), $Cu(tmhd)_2$ (107.5 mg, 5 mol%), and absolute dry DMF (25.0 mL) were added under Ar. The formed mixture was stirred at 80 ºC in an oil bath under Ar for 12 h as monitored by TLC. The solution was then cooled to room temperature, the mixture was extracted with EA and saturated $NaHCO_3$ solution, dried ($MgSO_4$) and concentrated to give a crude product. The crude product was purified by flash column chromatography on silica gel (PE : EA = 8 : 1) to afford 652.8 mg (82%) of **3aa** as a yellow oil.

4-(Phenylamino)butanamide (10) To a solution of **3aa** (32.0 mg, 0.2 mmol) in toluene (1.0 mL) was added a cooled solution of conc. sulfuric acid in H_2O (100.0 µL H_2SO_4/16.0 µL) (The ratio of toluene to acid/H_2O is very important and should be followed strictly). Stir the biphasic mixture at room temperature for 0.5 h and warm to 35°C and stir for 22 h. The reaction was cooled to room temperature and quenched with 68.7 mg of Na_2CO_3 in water (add slowly some foaming). Separate the organic and extract 2 × EtOAc. Combine all the organics and wash the organics with brine, dry over $MgSO_4$, filter and concentrate to afford 33.1 mg (93%) of **10** as a white solid, mp 63-65 ºC: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.20 – 7.14 (m, 2H), 6.69 (t, *J* = 7.3 Hz, 1H), 6.60 (d, *J* = 7.7 Hz, 2H), 5.69 (br s, 1H), 5.57 (br s, 1H), 3.18 (t, *J* = 6.7 Hz, 2H), 2.34 (t, *J* = 7.2 Hz, 2H), 2.00 – 1.93 (m, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.1, 148.2, 129.2, 117.3, 112.7, 43.3, 33.2, 24.9; **ATR-FTIR (cm $^{-1}$)**: 3389, 1650, 1600, 1505, 1376, 1206, 1067, 740; **HRMS m/z (ESI)** calcd for $C_{10}H_{14}N_2NaO$ $(M + Na)^+$ 201.0998, found 201.0999.

1-Phenylpyrrolidin-2-one (11) A mixture of **3aa** (32.0 mg, 0.2 mmol) in absolute ethanol (0.5 mL), concentrated sulfuric acid 66.7 (µL) was stirred under reflux for 12 h. The excess alcohol removed by distillation and the residue was diluted with water, basified with Na_2CO_3 solution (1.0 mL, 30%) and extracted with ether. The ethereal layer was separated, washed with water and dried over $MgSO_4$. The solvent was evaporated under vacuum to give a crude product. The crude product was purified by flash column chromatography on silica gel (PE : EA = 3 : 1) to afford 22.9 mg (71%) of **11** as a white solid, mp 65-67 ºC: **^{1}H NMR (400 MHz,**

$CDCl_3$) δ 7.72 – 7.50 (m, 2H), 7.42 – 7.28 (m, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 3.84 (t, *J* = 7.0 Hz, 2H), 2.59 (t, *J* = 8.1 Hz, 2H), 2.17 – 2.10 (m, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 174.1, 139.3, 128.7, 124.4, 119.8, 48.7, 32.7, 17.9; **ATR-FTIR (cm $^{-1}$)**: 1675, 1555, 1462, 1383, 1236, 1128, 1067, 756; **HRMS m/z (ESI)** calcd for $C_{10}H_{11}NNaO$ $(M + Na)^+$ 184.0733, found 184.0738.

4-(Diphenylamino)butanenitrile (12) To a 25 mL flame-dried schlenk tube was added KF (34.8 mg, 0.6 mmol) and 18-crown-6 (158.4 mg, 0.6 mmol) jin a glove box. The mixture was dissolved in THF (1.0 mL) under argon atmosphere. **3aa** (32.0 mg, 0.2 mmol) was added under argon atmosphere. To the stirred solution, 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (89.4 mg, 0.3 mmol) was added. Then the reaction mixture was allowed to react at 30 ºC for 12 h. After 12 h, the reaction was stopped, the solvent was evaporated and the crude product was purified by flash column chromatography on silica gel (PE : EA = 10 : 1) to afford 40.2 mg (85%) of **12** as a colorless oil: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.31 – 7.23 (m, 4H), 7.01 – 6.94 (m, 6H), 3.85 (t, *J* = 7.1 Hz, 2H), 2.41 (t, *J* = 7.1 Hz, 2H), 2.04 – 1.97 (m, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 147.6, 129.4, 121.9, 121.1, 119.3, 50.5, 23.5, 14.7; **ATR-FTIR (cm $^{-1}$)**: 2246, 1605, 1556, 1465, 1380, 1267, 1109, 1067, 752; **HRMS m/z (ESI)** calcd for $C_{16}H_{16}N_2Na$ $(M + Na)^+$ 259.1206, found 259.1210.

■ASSOCIATED CONTENT

Supporting Information

Full spectroscopic data for all new compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.xxxxxxx

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Notes

The authors declare no competing financial interest.

■ACKNOWLEDGMENTS

We thank the "1000-Youth Talents Plan", the "Jiangsu Specially-Appointed Professor Plan", the National Natural Science Foundation of China (grant 21672097), and National Natural Science Foundation of Jiangsu Province (BK 20170632) for financial support. This work was also supported by a Project Funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions and the program A for Outstanding PhD candidate of Nanjing University.

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