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Copper Promoted Aerobic Oxidative C(sp^3)-C(sp^3) Bond Cleavage of *N*-(2-(Pyridin-2-yl)-ethyl)anilines

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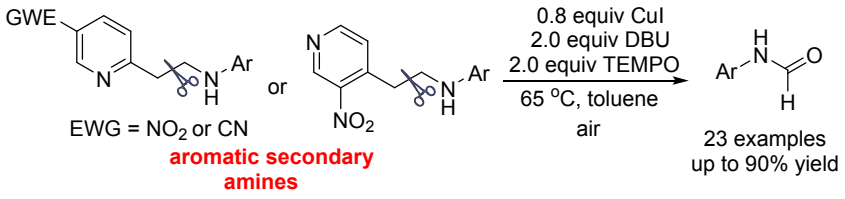
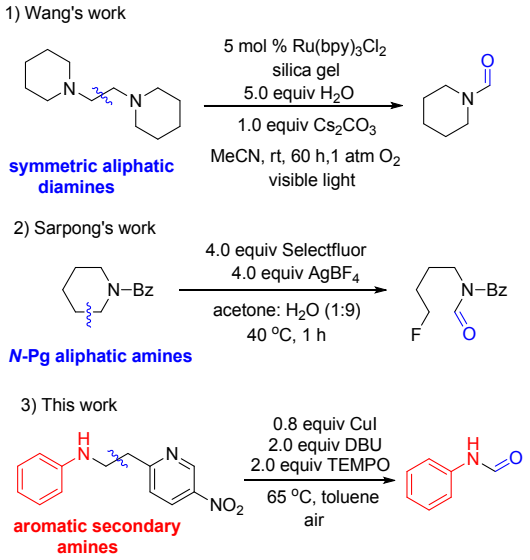
Supporting Information Placeholder



ABSTRACT: A strategy of aerobic oxidative C(sp^3)-C(sp^3) bond cleavage of *N*-ethylaniline derivatives bearing azaarenes for the synthesis of *N*-aryl formamides has been developed. This approach was carried out smoothly with the CuI/TEMPO/air system to give *N*-aryl formamides in yields of 50 to 90%. With this methodology, a mutagenically active compound was constructed in 90% yield. Moreover, the reaction also provided a "one-pot" synthetic tool for accessing a promoter of hematopoietic stem cells by difunctionalization in 61% yield.

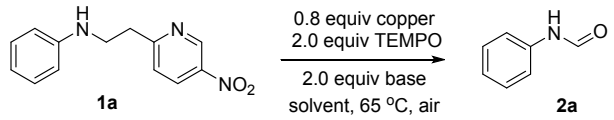
$C(sp^3)$-$C(sp^3)$ bond activation is gaining increasing attention in organic synthesis. Although many examples of strained $C(sp^3)$-$C(sp^3)$ bond activation have been reported,[1] the activation of unstrained $C(sp^3)$-$C(sp^3)$ bond is still a challenging subject due to the high bond-dissociation energy and lack of selectivity.[2] Recently, several strategies to cleave inert $C(sp^3)$-$C(sp^3)$ bonds have been developed: β-elimination,[3] oxidative cleavage,[4] reductive scission,[5] cross alkane metathesis[6] and nucleophilic substitution.[7] Among them, the oxidative cleavage of $C(sp^3)$-$C(sp^3)$ bonds adjacent to tertiary aliphatic amines is of particular interest as the generated electrophilic iminium ions may serve as a reactive intermediate to install a broad range of complex structures. For example, Wang reported that Bu_4NI and TBHP promoted oxidative functionalization of tertiary amines to synthesize methylene-bridged bis-1,3-dicarbonyl compounds.[8] In addition, Opatz demonstrated the σ-bond fragmentation of 1-benzyl-1,2,3,4-tetrahydroisoquinolines.[9] Wang and co-workers realized the $C(sp^3)$-$C(sp^3)$ bond cleavage of 1,2-diamines by a photocatalytic system to obtain iminium ions and C-radicals (Scheme 1, eq 1),[10] and Sarpong developed a new approach for the cleavage of inert $C(sp^3)$-$C(sp^3)$ bond via silver-mediated ring-opening fluorination from *N*-acyl (Bz) unstrained cyclic amines in 2018 (Scheme 1, eq 2).[11] Very recently, a copper-catalyzed selective cleavage of $C(sp^3)$-$C(sp^3)$ single bonds within amines using high pressure air has been developed by Beller's group.[12] However, in contrast to tertiary aliphatic amines and *N*-Bz aliphatic secondary amines, unprotected secondary aromatic amines are able to form stable *N*,*N*,-diphenylhydrazines by a dehydrogenative homocoupling reaction under oxidative conditions[13] (we also found this phenomenon in our study). Additionally, they can easily bind the transition metal catalysts and inhibit catalytic cycles.[14] The scission of unstrained $C(sp^3)$-$C(sp^3)$ bonds in the presence of adjacent secondary aromatic amines is unprecedented.

Scheme 1. The C(sp^3)-C(sp^3) bond cleavage strategies of amines.



Although the C(sp^3)-C(sp) and C(sp^3)-C(sp^2) bond cleavage of unprotected secondary aromatic amine derivatives have been developed by Li and Wang respectively, [15-16] the C(sp^3)-C(sp^3) bond cleavage of secondary aromatic amines has not been realized. Very recently, we introduced a copper-promoted intramolecular C-H oxidative amination reaction for the synthesis of aziridine derivatives.[17] In this C-*N* bond formation reaction, a radical was proposed to form at the benzylic position of azaarenes followed by the annulation with secondary amines. In the continuation of our research concerning potential divergent synthetic methodologies and C-C bond functionalization,[18] we questioned whether the substrates could be oxidized to enamine intermediates and then react with molecular oxygen to form 1,2-dioxetanes. Afterwards, C(sp^3)-C(sp^3) bond and O-O bond cleavage lead to *N*-aryl formamides, which have been widely employed in the preparation of bioactive compounds and fine chemical intermediates (Scheme 1, eq 3).[19] Herein, we reported the cleavage of unstrained C(sp^3)-C(sp^3) bond adjacent to aromatic secondary amines to synthesize *N*-aryl formamides with air as the terminal oxidant under mild condition.

Table 1: Optimization of Reaction Conditions of C(sp^3)-C(sp^3) bond cleavage.[a]



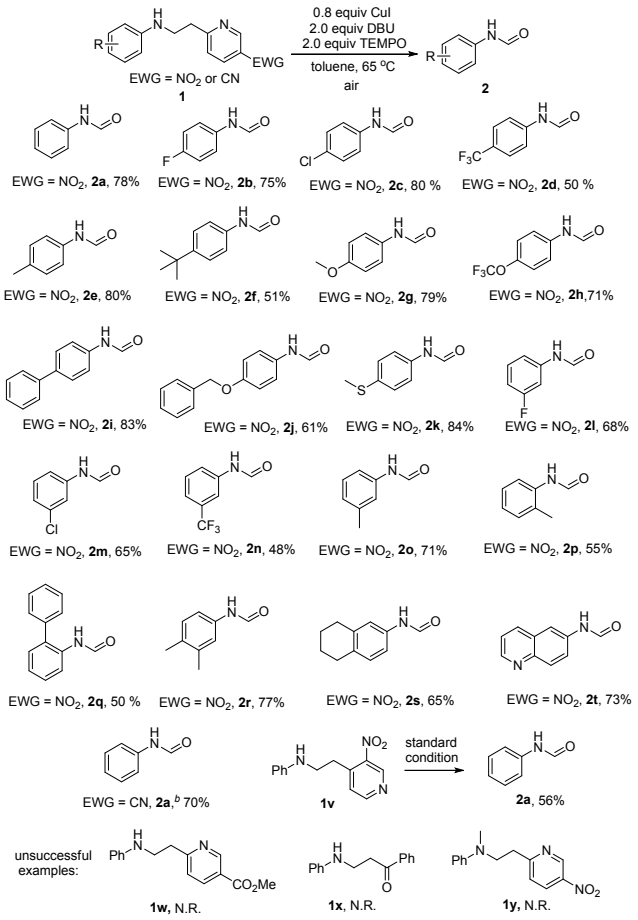
entry	copper	base	solvent	yield (%)[b]
1	CuI	DBU	dioxane	36
2	CuI	DBU	DMSO	N.R.
3	CuI	DBU	DMF	8
4	CuI	DBU	toluene	78
5	CuI	TBD	toluene	N.R.
6	CuI	DMAP	toluene	N.R.
7	CuI	DABCO	toluene	N.R.
8	$Cu(OAc)_2$	DBU	toluene	21
9	CuBr	DBU	toluene	72
10[c]	CuI	DBU	toluene	51
11[d]	CuI	DBU	toluene	62
12[e]	CuI	DBU	toluene	65
13[f]	CuI	DBU	toluene	23

[a] A solution of **1a** (0.2 mmol), copper salt (0.16 mmol) and TEMPO (0.4 mmol) with base (0.4 mmol) in the solvent stated (1.5 mL) was stirred for 2 h at 65 °C. [b] Isolated yield. [c] 0.1 mmol CuI was used. [d] 0.1 mmol TEMPO was used [e] Under O_2 atmosphere. [f] The reaction was carried out at rt.

In an initial attempt on the formation of *N*-aryl formamides, a solution of aniline **1a** (1.0 equiv) in the presence of CuI (0.8 equiv), DBU (2.0 equiv) and TEMPO (2.0 equiv) in dioxane was stirred for 2 h at 65 °C. The desired formamide product **2a** was obtained in 36% yield (Table 1, entry 1). Next, the reaction conditions were optimized to improve the reaction yield. The solvent screening revealed that polar aprotic solvent such as DMSO and DMF afforded the products in very poor yields (entries 2-3). In comparison, the nonpolar solvent toluene afforded a much higher yield (78%, entry 4). In addition to DBU, other organic bases such as 2,3,4,6,7,8-hexahydro-1*H*-pyrimido[1,2-a]pyrimidine (TBD), 1,4-diazabicyclo[2.2.2]octane (DABCO), and *N,N,*-dimethylpyridin-4-amine (DMAP), were

also examined in toluene but only gave trace amount of products (entries 5-7). When screening different copper salts, $Cu(OAc)_2$ was found much less effective (21%, entry 8) and CuBr gave slightly lower yield than CuI (72%, entry 9). Lowering the loading of the copper salt or TEMPO also decreased the reaction yields (entries 10-11). Additionally, when the reaction was carried out under O_2 atmosphere, the desired product was obtained in 65% yield (entry 12). Notably, the yield was significantly lower at room temperature (23%, entry 13).

Scheme 2. Scope of CuI−promoted synthesis of *N*-aryl formamides via C(sp^3)-C(sp^3) cleavage.[a]

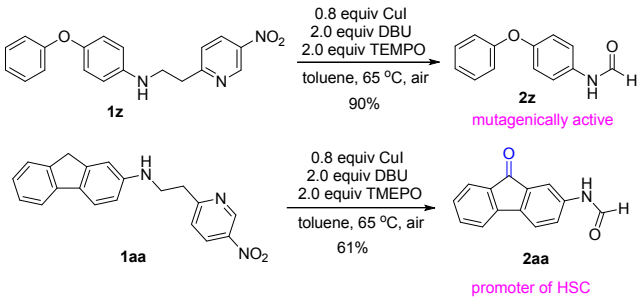


[a] Reaction conditions: a solution of **1** (0.2 mmol), CuI (0.16 mmol), DBU (0.4 mmol) and TEMPO (0.4 mmol) in toluene (1.5 mL) was stirred for 2 h at 65 °C. Isolated yield. [b] 6-(2-(Phenylamino)ethyl)nicotinonitrile **1u** was used as substrate.

With the optimal reaction conditions established, we then examined the substrate scope of CuI-promoted C(sp^3)-C(sp^3) activation process for the formation of *N*-aromatic formamides **2**. As shown in Scheme 2, almost all of the tested combinations produced the desired *N*-aromatic formamides **2** with moderate to good isolated yields. The reaction has a high tolerance to substituents on the para position of the phenyl ring: *para*-F, *para*-Cl, and *para*-Me only had a slight impact on the yield (**2b-2c**, **2e**). Even aniline **1d** bearing a *para*-CF_3 group reacted smoothly to afford *N*-aromatic formamide **2d** in 50% yield. Other anilines bearing various electron-donating para-substituents on the phenyl ring were also suitable substrates for this protocol (**2f-2k**). Similarly, we noted that the *meta*-substituted amines could also smoothly engage in this process to afford the corresponding *N*-aromatic formamides **2l-2o** in moderate to good yields. A steric effect was seen in substrates bearing *ortho*-substituents: *ortho*-Me and *ortho*-Ph afforded the corresponding products in moderate yields (**2p-2q**). Furthermore, the aniline with two substituents of the phenyl ring gave *N*-formylation product **2r** and **2s** in 77% and 65% yields respectively. The reaction was also very effective for the construction of *N*-heterocyclic formamide **2t in** 73% yield. To further expand the scope of the reaction, *N*-ethylaniline derivatives bearing functionalities different from *para*-nitro azaarenes were investigated. By replacing NO_2 in **1a** with the slightly weaker electron-withdrawing group CN (**1u**), the same product **2a** was obtained in 70% yield. When switching from **1a** to *N*-(2-(3-nitropyridin-4-yl)ethyl)aniline (**1v**), the reaction still afforded the corresponding product **2a** in acceptable yield (56%). However, when methyl 6-(2-(phenylamino)ethyl)nicotinate **1w** or 1-phenyl-3-(phenylamino)propan-1-one **1x** were used as the starting substrates, no bond cleavage was observed. When *N*-methyl-*N*-(2-(5-nitropyridin-2-yl)ethyl)aniline **1y** was used as the starting

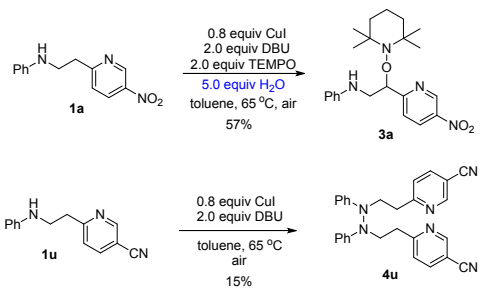
substrate under the standard reaction condition, no *N*-methyl-*N*-phenylformamide was detected at all. This revealed that the proton of *N*-H is also essential in this reaction.

Scheme 3. The application of C(sp^3)-C(sp^3) bond cleavage process.



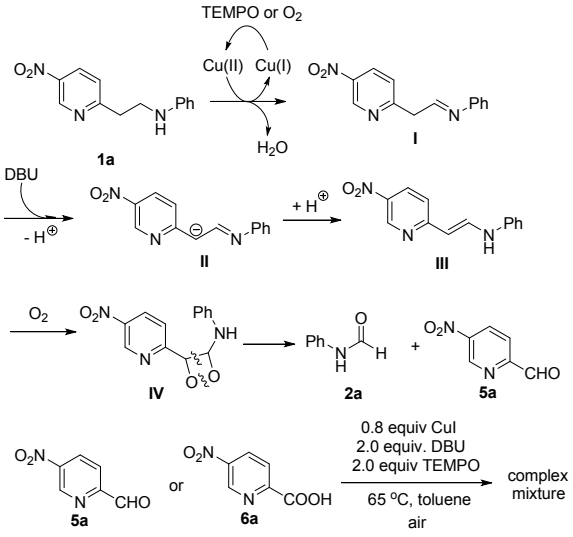
Formamide substructures are frequently encountered in many bioactive compounds. To test the applicability of our methodology, the mutagenically active molecule **2z** was synthesized by this C(sp^3)-C(sp^3) activation strategy.[19b] The process proceeded readily with higher yield than any other reported method (90%). Furthermore, by unifying oxidative benzylic C-H cabonylation and C(sp^3)-C(sp^3) activation in one-pot, we successfully realized the difunctionalization of **1aa** to obtain fluorenone formamide **2aa** which has been used in maintaining and expanding of hematopoietic stem cells (HSC) in 61% yield (Scheme 3).[19f] To test the practicality of this methodology, a gram-scale reaction using substrate **1a** was carried out to give product **2a** in 70% yield.

Scheme 4. Control experiments.



In order to understand the reaction mechanism, two control experiments were performed (Scheme 4). When 5.0 equiv of H_2O was added into the reaction system under air atmosphere, the reaction gave TEMPO addition product **3a** in 57% yield, and no desired *N*-phenylformamide **2a** was obtained. The addition of H_2O was thought to inhibit the formation of iminium intermediate. Additionally, without the addition of TEMPO, *N,N,*-diphenylhydrazine **4u** was formed by using **1u** as the substrate in 15% yield, indicating a vital role of TEMPO as an additive in the transformation.

Scheme 5. The proposed mechanism for C(sp^3)-C(sp^3) bond cleavage.



Although the details of this C(sp^3)-C(sp^3) bond cleavage remains uncertain, a plausible mechanism is illustrated in Scheme 5. The iminium intermediate **I** is generated in the existence of copper salt and oxidant (TEMPO or O_2).[16] With the strong electron withdrawing group NO_2, intermediate **I** is easily deprotonated to intermediate **II** by DBU. Enamine intermediate **III** is formed and reacts with oxygen to form 1,2-dioxetane intermediate **IV**. Finally, the fragmentation of **IV** sequentially underwent the C-C bond and O-O bond cleavage to furnish the desired product **2a**.[20] In addition, we

tried to identify the pyridine component by using commercially available 5-nitropicolinaldehyde (**5a**) and 5-nitropicolinic acid (**6a**) as reference standards. Unfortunately, neither **5a** nor **6a** was stable under the standard conditions. However, a mass peak corresponding to **5a** was detected in the study of the reaction mixture (Supporting Information).

In summary, we have developed an efficient copper-promoted oxidative cleavage of $C(sp^3)$-$C(sp^3)$ bond adjacent to secondary aromatic amines providing *N*-aromatic formamides. A wide scope of substituents on the aniline portion was tolerated to give the products in moderate to good yields. Both TEMPO and oxygen played very important roles in this reaction. The methodology has been successfully applied for the synthesis of a mutagenically active molecule in 90% yield and a HSC active molecule in 61% yield, respectively. Further exploration of this organic transformation and the application of this methodology in the synthesis of more biologically relevant molecules are underway in our laboratories.

EXPERIMENT SECTION

General Information

Unless otherwise noted, all reagents were obtained commercially and used without further purification. Unless otherwise specified, all other reagents were purchased from Acros, Aldrich, Fisher, Adamas-beta Co. Ltd. or TCI and used without further purification. ^{1}H NMR spectra was recorded at 400 MHz, ^{13}C NMR spectra was recorded at 100 MHz. ^{1}H NMR spectra was recorded with tetramethylsilane (δ = 0.00 ppm) as internal reference; ^{13}C NMR spectra was recorded with $CDCl_3$ (δ = 77.00 ppm) as internal reference. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). Chromatography was carried out

with silica gel (200-300 mesh) using mixtures of petroleum ether (Bp 60-80 ºC) and ethyl acetate as eluents. Mass Spectra were obtained from the mass spectrometry facility of East China University of Science and Technology.

General procedure for the preparation of substrates: To a solution of 5-nitro-2-vinylpyridine (0.4 mmol, 120 mg) and aromatic amines **7** (0.8 mmol, 2 equiv) in toluene (2 mL) was added $Yb(OTf)_3$ (0.02 mmol, 12.4 mg). The resulting solution was stirred for 2 h at 65 ºC by oil bath. After the reaction was completed, the reaction mixture was directly purified by column chromatography (petroleum ether: ethyl acetate = 20:1~4:1) to give the corresponding product. Other Michael addition product was prepared according to the literature.[17]

4-(tert-Butyl)-*N*-(2-(5-nitropyridin-2-yl)ethyl)aniline(1f), yellowish solid, 87 mg (81%). Mp 84-86 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.31 (d, J = 2.4 Hz, 1H), 8.31 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.29 (d, J = 8.4 Hz, 1H), 7.14 (d, J = 8.8 Hz, 1H), 6.52 (d, J = 8.8 Hz, 1H), 3.53 (t, J = 6.0 Hz, 2H), 3.15 (t, J = 6.0 Hz, 2H), 1.20 (s, 9H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 165.8, 144.2, 143.8, 141.8, 139.6, 130.3, 125.1, 122.5, 111.7, 42.2, 36.8, 32.8, 30.5 ppm. HRMS (EI-TOF) m/z calcd for $C_{17}H_{21}N_3O_2$: 299.1634, found 299.1630.

4-Methoxy-*N*-(2-(5-nitropyridin-2-yl)ethyl)aniline(1g), yellowish solid, 94 mg (86%). Mp 69-71 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.39 (d, J = 2.4 Hz, 1H), 8.38 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 6.79 (m, 2H), 6.61 (m, 2H), 3.75 (s, 3H), 3.57 (t, J = 6.0 Hz, 2H), 3.21 (t, J = 6.0 Hz, 2H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.8, 152.4, 144.9, 142.8, 141.7, 131.4, 123.6, 115.0, 114.5, 55.8, 44.0, 37.7 ppm. HRMS (EI-TOF) m/z calcd for $C_{14}H_{15}N_3O_3$: 273.1113, found 273.1111.

***N*-(2-(5-Nitropyridin-2-yl)ethyl)-4-(trifluoromethoxy)aniline(1h)**, orange solid, 99 mg (76%). Mp 101-103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.39 (d, J = 2.8 Hz, 1H), 8.40 (dd, J_1 = 8.4 Hz, J_2 = 2.8 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H), 6.59 (m, 2H), 4.19 (brs, 1 H), 3.60 (t, J = 6.0 Hz, 2H), 3.22 (t, J = 6.0 Hz, 2H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.4, 146.5, 144.9, 142.9, 140.6, 131.5, 123.6, 122.5, 118.2 ($J_{C\text{-}F}$ = 253.7 Hz), 113.2, 43.0, 37.4 ppm. HRMS (EI-TOF) m/z calcd for $C_{14}H_{12}N_3O_3F_3$: 327.0831, found 327.0832.

***N*-(2-(5-Nitropyridin-2-yl)ethyl)-[1,1'-biphenyl]-4-amine(1i)**, yellow solid, 73 mg (57%). Mp 119-121 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.41 (d, J = 2.8 Hz, 1H), 8.40 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.53 (dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 2H), 7.44 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 2H), 7.41-7.36 (m, 3H), 7.27 (m, 1H), 6.70 (m, 2H), 4.15 (brs, 1H), 3.67 (t, J = 7.2 Hz, 2H), 3.15 (t, J = 6.4 Hz, 2H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.6, 147.0, 145.0, 142.9, 141.1, 131.5, 130.8, 128.7, 128.1, 126.3, 126.2, 123.6, 113.2, 42.6, 37.6 ppm. HRMS (EI-TOF) m/z calcd for $C_{19}H_{17}N_3O_2$: 319.1321, found 319.1322.

4-(Benzyloxy)-*N*-(2-(5-nitropyridin-2-yl)ethyl)aniline(1j), yellowish solid, 126 mg (80%). Mp 80-82 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.39 (d, J = 2.4 Hz, 1H), 8.30 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.42- 7.31 (m, 6H), 6.85 (d, J = 8.8 Hz, 1H), 6.59 (d, J = 8.8 Hz, 1H), 4.99 (s, 2H), 3.57 (t, J = 6.0 Hz, 2H), 3.13 (t, J = 6.0 Hz, 2H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.8, 151.6, 144.9, 142.8, 142.0, 137.5, 131.4, 128.5, 127.8, 127.5, 123.6, 116.2, 114.3, 70.8, 43.9, 37.7 ppm. HRMS (EI-TOF) m/z calcd for $C_{20}H_{19}N_3O_3$: 349.1426, found 349.1424.

4-(Methylthio)-*N*-(2-(5-nitropyridin-2-yl)ethyl)aniline(1k), yellowish solid, 61 mg (53%). Mp 76-78 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.30 (d, J = 2.4 Hz, 1H), 8.29 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.26 (d, J = 8.4 Hz, 1H), 7.13 (m, 2H), 6.48 (m, 2H), 4.07 (brs, 1H), 3.50 (t, J = 6.0 Hz, 2H),

3.13 (t, J = 6.0 Hz, 2H), 2.32 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.5, 145.4, 143.8, 141.8, 130.4, 130.3, 123.7, 122.6, 112.5, 41.8, 36.4, 18.0 ppm. HRMS (EI-TOF) m/z calcd for $C_{14}H_{15}N_3O_2S$: 289.0885, found 289.0883.

2-Methyl-*N*-(2-(5-nitropyridin-2-yl)ethyl)aniline(1p), yellowish solid, 67 mg (65%). Mp 60-62 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 9.30 (d, J = 2.4 Hz, 1H), 8.29 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.26 (d, J = 8.4 Hz, 1H), 7.05 (m, 1H), 6.96 (d, J = 8.0 Hz, 1H), 6.59 (m, 2H), 4.00 (brs, 1H), 3.55 (t, J = 6.4 Hz, 2H), 3.18 (t, J = 6.4 Hz, 2H), 2.00 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.8, 144.6, 143.7, 141.8, 130.4, 129.2, 126.1, 122.6, 122.5, 121.2, 116.2, 108.6, 41.8, 36.4, 16.4 ppm. HRMS (EI-TOF) m/z calcd for $C_{14}H_{15}N_3O_2$: 257.1164, found 257.1165.

***N*-(2-(5-Nitropyridin-2-yl)ethyl)-[1,1'-biphenyl]-2-amine(1q)**, yellowish solid, 73 mg (57%). Mp 126-128 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 9.20 (d, J = 2.8 Hz, 1H), 8.32 (dd, J_1 = 8.4 Hz, J_2 = 2.8 Hz, 1H), 7.42-7.34 (m, 3H), 7.28-7.23 (m, 4H), 7.07 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1H), 6.80-6.76 (m, 2H), 3.61 (t, J = 6.4 Hz, 2H), 3.18 (t, J = 6.4 Hz, 2H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.5, 144.7, 144.5, 142.7, 139.2, 131.3, 130.3, 129.4, 128.8, 128.7, 127.3, 123.5, 117.4, 110.6, 43.0, 37.3 ppm. HRMS (EI-TOF) m/z calcd for $C_{19}H_{17}N_3O_2$: 319.1321, found 319.1320.

3,4-Dimethyl-*N*-(2-(5-nitropyridin-2-yl)ethyl)aniline(1r), orange solid, 77 mg (71%). Mp 61-63 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 9.32 (s, 1H), 8.30 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.28 (d, J = 8.4 Hz, 1H), 6.87 (d, J = 8.0 Hz, 1H), 6.38 (m, 1H), 6.33 (dd, J_1 = 8.0 Hz, J_2 = 2.8 Hz, 1H), 3.52 (t, J = 6.0 Hz, 2H), 3.13 (t, J = 6.0 Hz, 2H), 2.12 (s, 3H), 2.08 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.9, 145.7, 144.8, 137.5, 131.4, 130.3, 125.9, 123.6, 115.0, 110.5, 42.3, 37.8, 20.1, 18.7 ppm. HRMS (EI-TOF) m/z calcd for $C_{15}H_{17}N_3O_2$: 271.1321, found 271.1317.

***N*-(2-(5-Nitropyridin-2-yl)ethyl)-5,6,7,8-tetrahydronaphthalen-1-amine(1s)**, yellow solid, 86 mg (72%). Mp 64-66 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.38 (d, J = 2.8 Hz, 1H), 8.38 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 7.03 (t, J = 8.0 Hz, 1H), 6.51 (m, 2H), 4.04 (brs, 1H), 3.61 (t, J = 6.4 Hz, 2H), 3.25 (t, J = 6.4 Hz, 2H), 2.72 (t, J = 6.4 Hz, 2H), 2.32 (t, J = 6.4 Hz, 2H), 1.84 (m, 2H), 1.72 (m, 2H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.9, 145.3, 144.8, 142.9, 137.9, 131.5, 126.1, 123.6, 121.4, 118.6, 106.8, 42.9, 37.5, 30.1, 23.8, 23.1, 22.7 ppm. HRMS (EI-TOF) m/z calcd for $C_{17}H_{19}N_3O_2$: 297.1477, found 297.1476.

***N*-(2-(5-Nitropyridin-2-yl)ethyl)quinolin-6-amine(1t)**, yellow solid, 66 mg (56%). Mp 129-131 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.41 (d, J = 2.4 Hz, 1H), 8.62 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 8.39 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 9.2 Hz, 1H), 7.38 (d, J = 8.4 Hz, 1H), 7.29 (m, 1H), 7.08 (dd, J_1 = 9.2 Hz, J_2 = 2.8 Hz, 1H), 6.75 (d, J = 2.4 Hz, 1H), 3.73 (t, J = 6.4 Hz, 2H), 3.30 (t, J = 6.4 Hz, 2H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 174.3, 166.4, 146.1, 145.6, 144.9, 143.0, 142.9, 134.0, 131.6, 130.1, 123.7, 121.5, 103.2, 103.1, 42.7, 37.1 ppm. HRMS (EI-TOF) m/z calcd for $C_{16}H_{14}N_4O_2$: 294.1117, found 294.1118.

6-(2-(Phenylamino)ethyl)nicotinonitrile(1u), orange solid, 63 mg (70%). Mp 72-74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.83 (d, J = 1.6 Hz, 1H), 7.85 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 1H), 7.17 (m, 1H), 6.71 (t, J = 1.6 Hz, 2H), 6.63 (m, 1H), 6.60 (m, 2H), 4.05 (br, 1H), 3.58 (t, J = 6.8 Hz, 2H), 3.16 (t, J = 6.8 Hz, 2H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 164.5, 152.2, 147.7, 139.5, 129.4, 123.5, 117.7, 116.8, 113.0, 107.7, 42.8, 37.8 ppm. HRMS (ESI-TOF) calcd for $[M+H]^+$ $C_{14}H_{14}N_3$: 224.1188, found 224.1189.

***N*-(2-(5-Nitropyridin-2-yl)ethyl)-4-phenoxyaniline(1z)**, orange solid, 84 mg (63%). Mp 111-113 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.40 (d, J = 2.4 Hz, 1H), 8.40 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.38 (dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 7.29 (m, 2H), 7.00 (t, J = 8.8 Hz, 1H), 6.91 (m, 4H), 6.63 (m, 2H), 4.00 (brs, 1H), 3.60 (t, J = 6.0 Hz, 2H), 3.24 (t, J = 6.0 Hz, 2H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.6, 159.0, 148.0, 144.9, 144.2, 142.9, 131.5, 129.5, 123.6, 122.0, 121.3, 117.1, 114.0, 43.5, 37.6 ppm. HRMS (EI-TOF) m/z calcd for $C_{19}H_{17}N_3O_3$: 335.1270, found 335.1269.

***N*-(2-(5-Nitropyridin-2-yl)ethyl)-9H-fluoren-2-amine(1aa)**, orange solid, 27 mg (20%). Mp 154-156 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.34 (d, J = 2.8 Hz, 1H), 8.31 (dd, J_1 = 8.4 Hz, J_2 = 2.8 Hz, 1H), 7.53 (m, 2H), 7.38 (d, J = 7.6 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H), 7.10 (m, 1H), 6.76 (m, 1H), 6.57 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 3.74 (s, 2H), 3.61 (t, J = 6.4 Hz, 2H), 3.18 (t, J = 6.4 Hz, 2H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 165.6, 146.1, 144.2, 143.9, 141.2, 141.1, 131.3, 130.4, 125.6, 123.9, 123.7, 122.6, 119.7, 117.5, 111.1, 110.1, 108.4, 42.2, 36.6, 35.9 ppm. HRMS (EI-TOF) m/z calcd for $C_{20}H_{17}N_3O_2$: 331.1321, found 331.1317.

Typical procedure for synthesis of C(sp^3)-C(sp^3) bond cleavage product (2a as an example): A 10 mL round bottom flask was equipped with magnetic stir bar and cooling coil was charged with *N*-(2-(5-nitropyridin-2-yl)ethyl)aniline (**1a**, 0.2 mmol, 49 mg), toluene (1.5 mL). Then, DBU (0.4 mmol, 60 μL), TEMPO (0.4 mmol, 62 mg) and CuI (0.16 mmol, 38 mg) were added to the solution. The reaction mixture was exposed to the open air and was stirred for 2 h at 65 °C by oil bath. After the reaction was completed, the reaction mixture was directly purified by column chromatography [100 g silica gel was treated with 2 mL aqua ammonia (25% m/m)] with petroleum ether/CH_2Cl_2 = 1:1 to give C(sp^3)-C(sp^3) bond cleavage product **2a** in 78% yield.

***N*-Phenylformamide(2a)**, yellow oil, 19 mg (78%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.2 (brs, 0.78H), 8.78 (d, J = 11.2 Hz, 0.22H), 8.27 (d, J = 2.0 Hz, 0.60H), 7.59 (d, J = 7.6 Hz, 1.22H), 7.32 (t, J = 7.6 Hz, 1.66H), 7.19 (d, J = 7.6 Hz, 0.44H), 7.07 (q, J = 5.6 Hz, 0.84H) ppm. ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 163.0, 160.1, 138.7, 138.6, 129.8, 129.3, 124.1, 124.0, 119.6, 118.0 ppm. The spectroscopic data matched that previously reported[20b].

***N*-(4-Fluorophenyl)formamide(2b)**, brown solid, 21 mg (75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (d, J = 11.2 Hz, 0.40H), 8.29 (s, 0.58H), 7.74 (brs, 0.39H), 7.45 (m, 1.15H), 7.23 (m, 0.87H), 7.01-6.93 (m, 2.57H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.3, 159.4 (d, $J_{C\text{-}F}$ = 243.2 Hz), 158.7, 158.5 (d, $J_{C\text{-}F}$ = 242.7 Hz), 132.0, 131.8, 121.0, 120.0, 115.5 (d, $J_{C\text{-}F}$ = 22.8 Hz), 114.6 (d, $J_{C\text{-}F}$ = 22.8 Hz) ppm. The spectroscopic data matched that previously reported[21a].

***N*-(4-Chlorophenyl)formamide(2c)**, yellow solid, 25 mg (80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (d, J = 11.2 Hz, 0.41H), 8.30 (s, 0.60H), 8.12 (brs, 0.37H), 7.43 (m, 1.23H), 7.34-7.27 (m, 0.42H), 7.25-7.21 (m, 0.92H), 7.21-7.19 (m, 0.75H), 6.97 (m, 0.80H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.3, 157.9, 134.3, 134.2, 129.8, 129.7, 128.9, 128.1, 120.2, 119.1 ppm. The spectroscopic data matched that previously reported[21a].

***N*-(4-(Trifluoromethyl)phenyl)formamide(2d)**, brown solid, 19 mg (50%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73 (m, 0.28H), 8.37 (brs, 0.61H), 7.62-7.51 (m, 2.59H), 7.19-7.12 (m, 0.55H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.7, 159.7, 140.0, 139.9, 138.8, 126.3 (q, $J_{C\text{-}F}$ = 33.8 Hz), 126.4, 124.1 (q, $J_{C\text{-}F}$ = 270.0 Hz), 119.8, 117.9 ppm. The spectroscopic data matched that previously reported[21a].

***N*-p-Tolylformamide(2e)**, yellow solid, 22 mg (80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (d, J = 11.6 Hz, 0.49H), 8.38 (s, 0.92H), 7.42 (d, J = 8.0 Hz, 0.39H), 7.15 (t, J = 8.8 Hz, 0.98H), 7.11 (m,

1.98H), 6.98 (d, J = 8.0 Hz, 1.09H), 2.33 (m, 3.00H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 163.0, 159.1, 135.1, 134.5, 134.3, 134.1, 130.2, 129.5, 120.1, 119.1, 20.9, 20.8 ppm. The spectroscopic data matched that previously reported[21a].

***N*-(4-(tert-Butyl)phenyl)formamide(2f)**, yellow solid, 18 mg (51%). ^1H NMR (400 MHz, $CDCl_3$): δ 8.58 (d, J = 11.2 Hz, 0.45H), 8.29 (s, 0.39H), 7.72 (br, 0.40H), 7.39 (d, J = 8.8 Hz, 0.82H), 7.29 (t, J = 8.8 Hz, 1.86H), 6.95 (d, J = 8.4 Hz, 0.94H), 1.24 (m, 9.00H) ppm.$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 161.8, 158.0, 147.5, 146.8, 133.2, 133.0, 125.6, 124.9, 118.8, 117.8, 33.4, 33.3, 30.3, 28.7 ppm. The spectroscopic data matched that previously reported[21a].

***N*-(4-Methoxyphenyl)formamide(2g)**, yellow solid, 24 mg (79%). ^1H NMR (400 MHz, $CDCl_3$): δ 8.43 (m, 0.46H), 8.26 (d, J = 1.6 Hz, 0.52H), 7.39 (brs, 0.47H), 7.38 (dd, J_1 = 10.8 Hz, J_2 = 2.4 Hz, 1.08H), 6.96 (dd, J_1 = 6.4 Hz, J_2 = 2.4 Hz, 1.01H), 8.84 (brs, 0.47H), 6.81-6.79 (m, 2.02H), 3.73 (m, 3H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 161.8, 157.7, 156.7, 155.7, 128.8, 128.4, 120.8, 120.7, 113.9, 113.3, 54.6, 54.4 ppm. The spectroscopic data matched that previously reported[21a].

***N*-(4-(Trifluoromethoxy)phenyl)formamide(2h)**, yellow oil, 29 mg (71%). ^1H NMR (400 MHz, $CDCl_3$): δ 8.61 (d, J = 6.0 Hz, 0.37H), 8.33 (s, 0.62H), 8.03 (brs, 0.32H), 7.52 (d, J = 8.0 Hz, 1.28H), 7.31 (s, 0.64H), 7.15 (m, 2.00H), 7.05 (m, 0.75H) ppm.$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 162.2, 158.9, 154.5, 152.9, 147.0 (q, $J_{C\text{-}F}$ = 113.1 Hz), 145.7, 135.4, 135.3, 122.7, 121.9, 121.1, 119.1 (q, $J_{C\text{-}F}$ = 253.3 Hz) ppm. The spectroscopic data matched that previously reported[21b].

***N*-([1,1'-Biphenyl]-4-yl)formamide (2i)**, yellow solid, 33 mg (83%). ^1H NMR (400 MHz, $CDCl_3$): δ 8.65 (d, J = 11.6 Hz, 0.47H), 8.35 (d, J = 2.0 Hz, 0.53H), 7.56-7.49 (m, 5.50H), 7.39-7.35 (m, 2.06H), 7.30-7.26 (m, 1.11H), 7.08 (m, 1.45H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 161.2,

157.8, 139.3, 139.0, 137.4, 136.8, 135.1, 134.8, 127.9, 127.7, 127.4, 126.7, 126.4, 126.2, 125.9, 125.8, 119.2, 118.1 ppm. The spectroscopic data matched that previously reported[21b].

***N*-(4-(Benzyloxy)phenyl)formamide(2j)**, yellow solid, 28 mg (61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, J = 11.6 Hz, 0.44H), 8.21 (brs, 0.49H), 8.01 (d, J = 11.2 Hz, 0.40H), 7.37-7.24 (m, 6.74H), 6.95-6.83 (m, 3.01H), 4.96 (m, 2.00H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.2, 158.9, 145.7, 135.4, 135.3, 122.7, 121.9, 121.1, 119.1 (q, J_{C-F} = 253.3 Hz) ppm. The spectroscopic data matched that previously reported[21c].

***N*-(4-(Methylthio)phenyl)formamide(2k)**, yellow oil, 28 mg (84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (d, J = 8.0 Hz, 0.44H), 8.27 (s, 0.87H), 7.40 (d, J = 8.4 Hz, 1.25H), 7.19-7.15 (m, 2.22H), 6.96 (d, J = 8.4 Hz, 0.91H), 2.40 (m, 3.00H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.7, 159.4, 135.3, 134.5, 134.4, 134.2, 128.4, 127.9, 120.8, 119.7, 16.6, 16.5 ppm. The spectroscopic data matched that previously reported[21b].

***N*-(3-Fluorophenyl)formamide(2l)**, yellow oil, 19 mg(68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.63 (d, J = 11.2 Hz, 0.41H), 8.32 (brs, 0.58H), 7.58 (brs, 0.43H), 7.43 (m, 0.68H), 7.28-7.20 (m, 1.16H), 7.11 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 0.70H), 6.85-6.72 (m, 1.63H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.3 (d, J_{C-F} = 245.6 Hz), 162.9 (d, J_{C-F} = 243.7 Hz), 162.8, 159.6, 138.5 (d, J_{C-F} = 10.1 Hz), 138.4 (d, J_{C-F} = 10.1 Hz), 131.2, 130.3, 115.3, 114.0, 112.1 (d, J_{C-F} = 21.0 Hz), 111.6 (d, J_{C-F} = 21.0 Hz), 107.7 (d, J_{C-F} = 26.1 Hz), 105.9 (d, J_{C-F} = 26.1 Hz) ppm. The compound was reported previously[20b].

***N*-(3-Chlorophenyl)formamide(2m)**, yellow solid, 20 mg (65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (m, 0.43H), 8.39 (brs, 0.59H), 7.80 (m, 0.40H), 7.67 (t, J = 2.0 Hz, 0.67H), 7.38 (d, J = 8.4 Hz, 0.76H), 7.31-7.28 (m, 0.37H), 7.25 (m, 0.49H), 7.18-7.12 (m, 1.04H), 6.97 (d, J = 8.4 Hz, 0.42H)

ppm. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 161.9, 158.8, 137.1, 137.0, 134.3, 133.5, 129.8, 129.1, 124.3, 123.8, 119.2, 117.7, 117.1, 115.6 ppm. The spectroscopic data matched that previously reported[21d].

***N*-(3-(Trifluoromethyl)phenyl)formamide(2n)**, brown solid, 18 mg (48%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (d, J = 11.2 Hz, 0.37H), 8.49 (brs, 0.34H), 8.35 (s, 0.62H), 7.77 (s, 0.63H), 7.68 (m, 1.16H), 7.45-7.21 (m, 2.71H) ppm. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 162.3, 159.2, 137.4, 132.3 (q, J_{C-F} = 32.7 Hz), 131.7, 131.3, 130.5, 129.7, 123.7 (q, J_{C-F} = 270.8 Hz), 123.5 (q, J_{C-F} = 270.7 Hz), 122.9, 121.9 (q, J_{C-F} = 3.8 Hz), 121.7, 121.4 (q, J_{C-F} = 3.8 Hz), 116.7 (q, J_{C-F} = 3.8 Hz), 115.4 (q, J_{C-F} = 3.8 Hz) ppm. The spectroscopic data matched that previously reported[21e].

***N*-m-Tolylformamide(2o)**, yellow oil, 19 mg (71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (d, J = 11.6 Hz, 0.54H), 8.78 (d, J = 1.2 Hz, 0.48H), 7.70 (brs, 0.49H), 7.41 (m, 0.50H), 7.30 (m, 0.50H), 7.23 (m, 0.93H), 7.01 (brs, 0.34H), 6.96 (d, J = 7.6 Hz, 1.04H), 6.88 (m, 1.08H) ppm. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 162.4, 158.8, 139.9, 139.2, 136.7, 136.5, 129.6, 129.0, 126.1, 125.7, 120.6, 119.6, 117.0, 115.9, 21.5, 21.4 ppm. The spectroscopic data matched that previously reported[21b].

***N*-o-Tolylformamide(2p)**, brown solid, 15 mg (55%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (m, 0.62H), 8.37 (brs, 0.39H), 7.85 (d, J = 8.0 Hz, 0.39H), 7.16-7.01 (m, 3.80H), 2.23 (s, 3H) ppm. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 163.9, 159.6, 135.2, 134.7, 131.3, 130.6, 130.1, 129.1, 127.1, 126.7, 126.1, 125.6, 123.3, 120.9, 17.7, 17.6 ppm. The spectroscopic data matched that previously reported[21b].

***N*-([1,1'-Biphenyl]-2-yl)formamide(2q)**, yellow solid, 20 mg (50%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (d, J = 11.2 Hz, 0.44H), 8.32 (d, J = 7.6 Hz, 0.52H), 8.23 (d, J = 2.0 Hz, 0.49H), 7.46-7.21 (m, 7.46H), 7.17-7.13 (m, 1.31H) ppm. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 161.9, 158.9,

137.8, 137.3, 133.8, 133.7, 132.9, 131.9, 131.2, 130.2, 129.3, 129.2, 129.1, 128.8, 128.7, 128.2, 128.1, 125.3, 124.6, 121.4, 121.3, 118.1 ppm. The spectroscopic data matched that previously reported[21f].

***N*-(3,4-Dimethylphenyl)formamide(2r)**, yellow solid, 23 mg (77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (m, 0.49H), 8.33 (m, 0.45H), 8.23 (m, 0.45H), 7.43 (brs, 0.36H), 7.24 (m, 0.46H), 7.05 (m, 0.64H), 6.85 (m, 1.05H), 6.82 (t, J = 9.2 Hz, 1.14H), 2.23 (m, 6H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.9, 159.1, 138.2, 137.4, 134.6, 134.4, 133.8, 133.2, 130.7, 130.0, 121.4, 120.5, 117.5, 116.4, 19.9, 19.2, 19.1 ppm. The spectroscopic data matched that previously reported[21f].

***N*-(5,6,7,8-Tetrahydronaphthalen-1-yl)formamide(2s)**, brown solid, 23 mg (65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (d, J = 11.2 Hz, 0.66H), 8.43 (s, 0.28H), 7.89 (m, 0.63H), 7.30 (d, J = 7.6 Hz, 0.29H), 7.12 (m, 1.25H), 6.96 (m, 1.62H), 2.79 (m, 2H), 2.61 (m, 2H), 1.85 (d, J = 5.6 Hz, 2H), 1.77 (d, J = 5.6 Hz, 2H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.4, 159.1, 139.2, 138.3, 134.8, 134.3, 128.8, 127.7, 127.1, 126.6, 126.1, 125.9, 120.5, 117.9, 29.8, 29.7, 24.6, 24.5, 22.8, 22.7, 22.5, 22.4 ppm. HRMS (EI-TOF) m/z calcd for $C_{11}H_{13}NO$:175.0997, found 175.0999. The compound was reported previously [21g].

***N*-(Quinolin-6-yl)formamide(2t)**, black solid, 25 mg (73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.48 (d, J = 11.2 Hz, 0.21H), 9.33 (s, 0.46H), 8.85-8.73 (m, 0.97H), 8.43 (s, 0.50H), 8.36 (d, J = 2.4 Hz, 0.51H), 8.00 (d, J = 8.4 Hz, 0.97H), 7.93 (d, J = 5.2 Hz, 0.52H), 7.56 (dd, J_1 = 9.2 Hz, J_2 = 2.4 Hz, 0.51H), 7.44 (m, 0.48H), 7.34 (m, 0.24H), 7.29 (q, J = 4.4 Hz, 0.51H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.9, 159.8, 149.7, 149.4, 145.8, 145.4, 136.2, 135.6, 135.4, 135.3, 131.2, 129.9,

128.9, 123.3, 122.3, 122.2, 121.8, 116.8, 114.4 ppm. The spectroscopic data matched that previously reported[21h].

***N*-(4-Phenoxyphenyl)formamide(2z)**, yellow solid, 38 mg (90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, *J* = 11.6 Hz, 0.44H), 8.29 (d, *J* = 1.6 Hz, 0.56H), 7.62 (brs, 0.41H), 7.43(m, 1.18H), 7.26 (m, 2.05H), 7.23 (brs, 0.51H), 7.07-6.91 (m, 5.96H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.6, 158.8, 157.3, 157.1, 155.1, 154.0, 132.2, 131.8, 129.9, 129.8, 123.6, 123.3, 121.8, 121.3, 120.1, 119.6, 118.8, 118.6 ppm. The spectroscopic data matched that previously reported[19b].

***N*-(9-oxo-9H-Fluoren-2-yl)formamide (2aa)**, brown solid, 27 mg (61%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.42 (s, 0.79H), 10.28 (d, *J* = 11.6 Hz, 0.21H), 8.85 (d, *J* = 11.2 Hz, 0.22H), 8.26 (m, 0.85H), 7.91 (d, *J* = 8.8 Hz, 0.21H), 7.86 (d, *J* = 1.6 Hz, 0.84H), 7.68-7.63 (m, 3.00H), 7.54-7.50 (m, 2.33H), 7.38-7.32 (m, 0.54H), 7.28-7.24 (m, 1.10H), 7.00 (m, 0.18H), 6.48 (m, 0.23H) ppm. ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 192.8, 192.7, 162.5, 160.0, 144.0, 139.7, 139.4, 139.3, 138.7, 138.6, 135.5, 135.4, 134.6, 134.0, 133.4, 133.2, 128.7, 128.6, 124.7, 124.0, 122.8, 122.2, 121.8, 120.7, 114.7, 112.8 ppm. HRMS (EI-TOF) m/z calcd for $C_{14}H_9NO_2$: 223.0633, found 223.0636. The compound was reported previously [19f].

Gram-scale reaction for the synthesis of 2a: A 50 mL round bottom flask was equipped with magnetic stir bar and cooling coil was charged with *N*-(2-(5-nitropyridin-2-yl)ethyl)aniline (**1a**, 3.5 mmol, 0.85 g), toluene (12 mL). Then, DBU (7 mmol, 1.05 mL), TEMPO (7 mmol, 1.05 g) and CuI (2.8 mmol, 0.53 g) were added to the solution. The reaction mixture was exposed to the open air and was stirred for 2 h at 65 ^{o}C by oil bath. After the reaction was completed, the reaction mixture was directly purified by column chromatography [100 g silica gel was treated with 2 mL aqua ammonia

(25% m/m)] with petroleum ether/CH_2Cl_2 = 1:1 to give C(sp^3)-C(sp^3) bond cleavage product **2a** in 70% yield (0.27 g).

Synthesis of *N*,*N*-diphenylhydrazine 4u : To a solution of 6-(2-(phenylamino)ethyl)nicotinonitrile (**1u**, 0.2 mmol, 44.6 mg) in toluene (1.5 mL) was added DBU (0.4 mmol, 60 μL) and CuI (0.16 mmol, 38 mg). The resulting solution was stirred for 2 h at 65 °C under air atmosphere by oil bath. After the reaction was completed, the reaction mixture was directly purified by column chromatography with petroleum ether/CH_2Cl_2 = 2:1 to give **4u** in 15% yield (6.8 mg).

6,6'-((1,2-Diphenylhydrazine-1,2-diyl)bis(ethane-2,1-diyl))dinicotinonitrile (4u), orange solid, Mp 167-169 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.70 (d, J = 2.0 Hz, 1H), 7.73 (dd, J_1 = 8.0 Hz, J_2 = 2.4 Hz, 1H), 7.15-7.09 (m, 3H), 6.77-6.69 (m, 3H), 3.84 (m, 2H), 3.16 (t, J = 7.6 Hz, 2H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.7, 152.2, 148.0, 139.6, 129.4, 123.6, 119.1, 116.8, 113.0, 107.7, 49.4, 36.7 ppm. HRMS (ESI-TOF) calcd for $[M+Na]^+$ $C_{28}H_{24}N_6Na$: 467.1960, found 467.1961.

5-Nitropicolinaldehyde (5a), ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.09 (d, J = 0.8 Hz, 1H), 9.56 (s, 1H), 8.81 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.17 (d, J = 8.4 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 192.4, 155.7, 146.5, 145.8, 133.8, 122.9 ppm. The spectroscopic data matched that previously reported[22].

5-Nitropicolinic acid (6a), ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.47 (bs, 1H), 8.76 (bs, 1H), 8.29 (bs, 1H) ppm. ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 165.23, 153.4, 146.1, 145.1, 133.5, 125.8 ppm. The spectroscopic data matched that previously reported[23].

ASSOCIATED CONTENT

Supporting Information

Experiment details and spectroscopic 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 interests.

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