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Direct transformation of alkylarenes into *N*-(pyridine-2-yl)amides via C(sp^3)-C(sp^3) bond cleavage

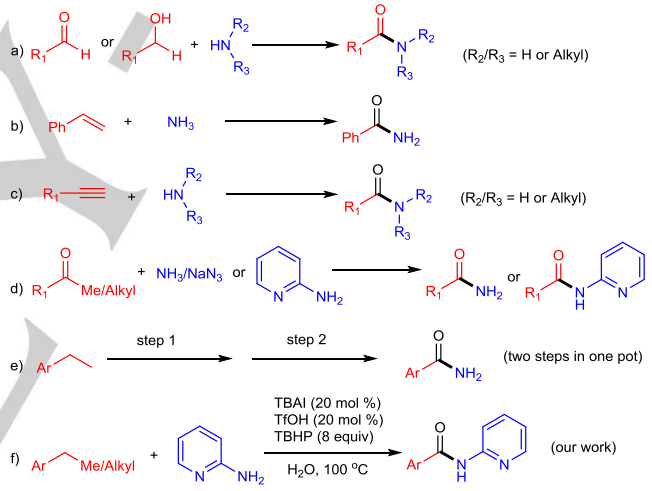
Haipin Zhou,[a] Yanpeng Liu,[b] Haidong Xia,[b] Jinyi Xu,[b] Tingfang Wang*[c] and Shengtao Xu*[a,b]

Abstract: C(sp^3)-H bond functionalization and C(sp^3)-C(sp^3) bond cleavage are very challenging transformations in chemistry. Herein, we report a mild and green methodology for the construction of *N*-(pyridine-2-yl)amides via tandem C(sp^3)-H activation/C-C bond cleavage of alkylarenes. Various *N*-heterocyclic amides were directly synthesized from alkylarenes in water in moderate to good yields.

Introduction

Amide bonds not only play a crucial role in proteins but are also ubiquitous in pharmacologically active compounds and materials (such as nylon, hydrogels, and artificial silks). Indeed, amide bonds are found in 2/3rds of the drug candidates reported in a 2006 survey.[1] The widespread occurrence of amides in organic compounds makes the construction of amide bonds one of the most important topics in organic chemistry. Conventionally, amide bonds are formed by the reaction of carboxylic acid surrogates and amines or carboxylic acids and amine surrogates. These existing methods are remarkably general but have also reached their inherent limits, and concerns about their waste generation and great expense are attracting increasing attention. Therefore, researchers are eager to find new methodologies for the construction of amides from other substrates that were previously considered to be impossible.[2]

In recent years, non-classical approaches to amide bond construction have been developed. Aldehydes[3] and alcohols[4] have been proven to be efficient substrates for the construction of amides in the last twenty years (Scheme 1, a). Amidation by direct C-C bond cleavage is another strategy under development and has attracted considerable attention. C=C and C≡C bonds are relatively active, and the synthesis of amides by C=C[5] or C≡C[6] bond cleavage has been reported (Scheme 1, b or c). C-C single bond is usually considered to be very stable, but its wide existence in organic compounds makes the synthesis of amides via C-C single bond cleavage attractive to organic chemists. Since Ishihara reported the synthesis of carboxamides by LDA-catalyzed Haller-Bauer and Cannizzaro reactions,[7] the construction of primary[8] or *N*-heterocyclic[9] amides via direct C(O)-Me(or Alkyl) bond cleavage (Scheme 1, d) has achieved considerable progress. Recently, we reported the construction of *N*-(pyridine-2-yl)amides from ketones via selective oxidative cleavage of C(O)-C(alkyl) bond.[10] Not long ago, Shimokawa reported the direct transformation of ethylarenes into primary aromatic amides with *N*-bromosuccinimide and I_2/aqueous NH_3[11] (Scheme 1, e), and the corresponding primary aromatic amides were synthesized in good yields via a one pot two steps reaction.



Scheme 1. Non-classical approaches to the construction of amides.

C(sp^3)-H and C(sp^3)-C(sp^3) bonds are two of the most common bonds in organics because of their inertness. Although chemists have devoted considerable effort to selective C(sp^3)-H bond activation/functionalization[12] and C(sp^3)-C(sp^3) bond cleavage,[13] the research is still fundamental and remains full of challenges, thus, new methodologies are still urgently needed. Here, we report the direct transformation of alkylarenes to *N*-(pyridine-2-yl)amides via tandem C(sp^3)-H bond activation/oxidative cyclization/C-C bond cleavage (Scheme 1, f), where the *N*-(pyridine-2-yl)amides are formed via catalysis by TBAI in one step in water.

Results and Discussion

Originally, ethylbenzene (**1a**) and 2-aminopyridine (**2a**) were treated in a reaction system containing a catalytic amount of I_2 and excess TBHP in toluene at 80 °C, and to our delight, *N*-(pyridin-2-yl)benzamide (**3**) was obtained in 22% yield (Table 1, entry 1). Subsequent screening of solvents showed that H_2O

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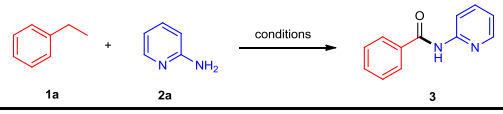
was a substantially better solvent, giving a yield of 34% (Table 1, entry 6). Then, the yield increased slightly to 38% when TBAI was used as the catalyst (Table 1, entry 10). After that, we screened peroxides, and the results showed that DTBP, $K_2S_2O_8$ and O_2 (balloon) were not effective oxidants (Table 1, entries 11-13). These results indicated that TBHP was crucial for this reaction. Since we had not yet achieved a synthetically useful yield, acid additives were introduced into the reaction system to improve the yield. To our delight, an enhancement was observed when 0.2 equivalents of a protic acid were used (Table 1, entries 14-16), but the addition of more acid did not further increase the yield (Table 1, entry 18). Finally, with the increase of temperature from 80 to 100 °C, *N*-(pyridine-2-yl)benzamide (**3**) was isolated in a moderate yield of 61% (Table 1, entry 20).

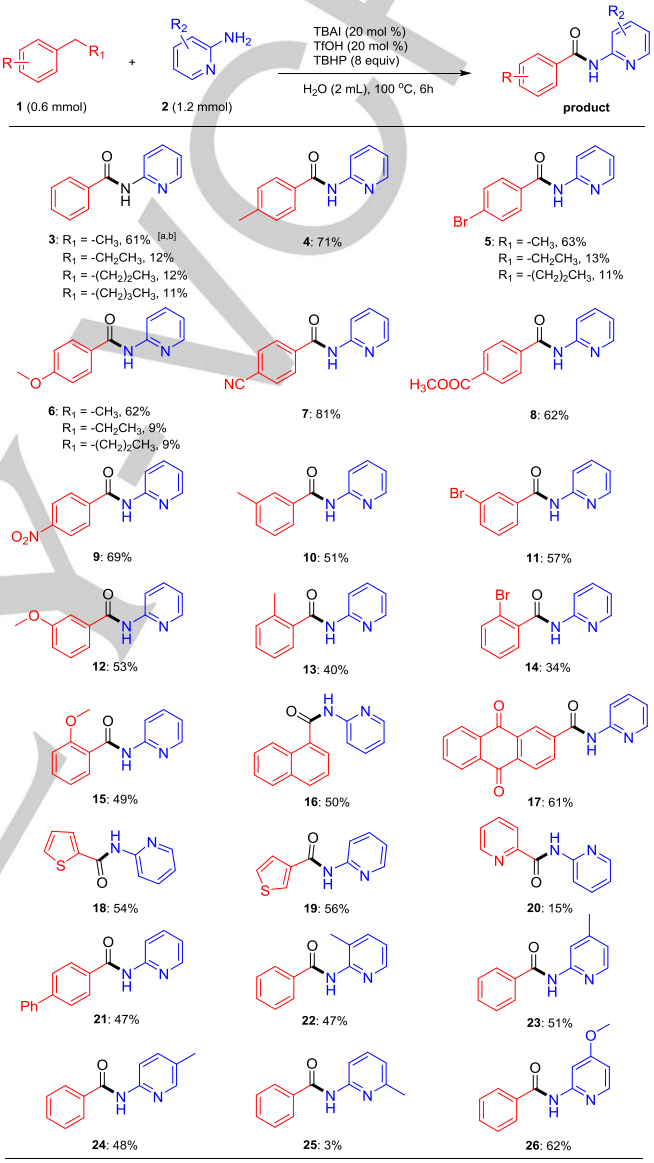
Table 1. Optimization of the reaction conditions.[a]



Entry	Solvent	Catalyst (20 mol%)	Oxidant (8 equiv)	Additives (20 mol%)	Temp (°C)	Yield[b] (%)
1	Toluene	I_2	TBHP	-	80	22
2	DMSO	I_2	TBHP	-	80	17
3	DMF	I_2	TBHP	-	80	5
4	DCE	I_2	TBHP	-	80	17
5	CH_3CN	I_2	TBHP	-	80	25
6	H_2O	I_2	TBHP	-	80	34
7	H_2O	KI	TBHP	-	80	32
8	H_2O	CuI	TBHP	-	80	3
9	H_2O	NIS	TBHP	-	80	34
10	H_2O	TBAI	TBHP	-	80	38
11	H_2O	TBAI	DTBP	-	80	trace
12	H_2O	TBAI	$K_2S_2O_8$	-	80	-
13[c]	H_2O	TBAI	O_2	-	80	-
14	H_2O	TBAI	TBHP	CH_3COOH	80	43
15	H_2O	TBAI	TBHP	CF_3COOH	80	42
16	H_2O	TBAI	TBHP	TfOH	80	56
17	H_2O	TBAI	TBHP	$FeCl_3$	80	13
18[d]	H_2O	TBAI	TBHP	TfOH	80	56
19	H_2O	TBAI	TBHP	TfOH	60	49
20	**H_2O**	**TBAI**	**TBHP**	**TfOH**	**100**	**61**

[a] Reaction conditions: **1a** (0.6 mmol), **2a** (1.2 mmol), catalyst (0.12 mmol), additive (0.12 mmol), oxidant (4.8 mmol), solvent (2 mL), 6 h.
[b] Isolated yields.
[c] O_2 (1 atm; balloon)
[d] 1.2 equivalent of TfOH was used.

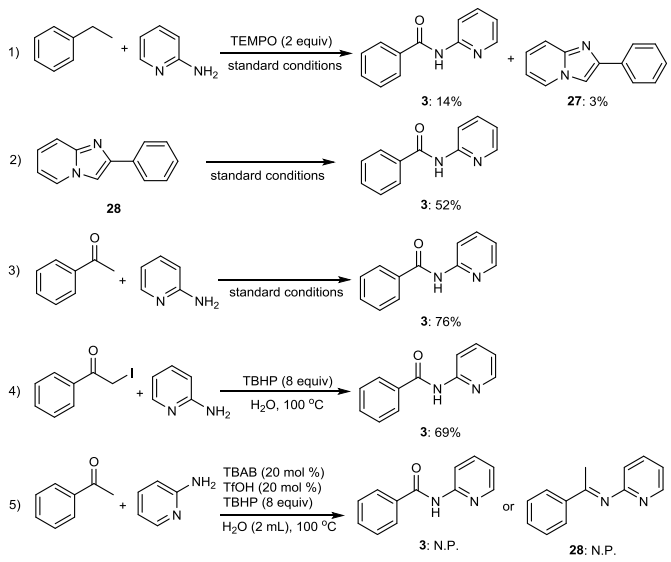
With the optimized reaction conditions in hand, the scope of suitable alkylarenes was explored (Scheme 2). First, alkylbenzenes with substituents in the para position were examined to determine whether electron-donating substituents **(4, 6)** or electron-withdrawing substituents (**5, 7-9**) could be applied to this reaction. Then, different long chains-substituted alkylbenzenes were treated under the standard conditions. Unexpectedly, the corresponding amide products were also obtained by selective C(sp^3)-C(sp^3) bond cleavage (**3, 5, 6**). In addition, meta- or ortho-substituted derivatives were also explored, and the results showed that the yield decreased slightly for the meta-substituted derivatives (**10-12**), whereas the yields of the ortho-substituent derivatives decreased dramatically to 34%-49% (**13-15**). Additionally, polycyclic alkylarenes (**16, 17**) and five-membered heterocycles (**18, 19**) could be transformed into the corresponding amides in moderate yields. The six-membered heterocycle 2-ethylpyridine gave the amide product in low yield (**20**), and 4-ethylbiphenyl also exhibited acceptable yield (**21**). Finally, substituted 2-aminopyridines were examined, and all substrates were suitable for the reaction except 6-substituted 2-aminopyridine, which had a low yield of 3% (**22-26**).



Scheme 2. Amidation of alkylbenzenes by C(sp^3)-C(sp^3) bond cleavage.
[a] (Unless otherwise stated, R_1 = -CH_3)
[b] Isolated yields.

To elucidate the mechanism of this reaction, several control experiments were conducted. TEMPO, a well-known radical trapping reagent, was added into the standard reaction system, which caused a decline of the yield of *N*-(pyridin-2-yl)benzamide (**3**) to 14%, and a new product **27**, whose structure was confirmed later, was detected in a yield of 3% (Scheme 3, entry 1). Using **27** as the starting material, product **3** was obtained smoothly under the standard conditions (Scheme 3, entry 2), indicating that the reaction might proceed through a radical

process and that **27** might be a key intermediate. Next, amide **3** was synthesized in a yield of 76% from acetophenone under the standard conditions (Scheme 3, entry 3), and *α*-iodoacetophenone could also be successfully transformed into **3** under oxidation by TBHP (Scheme 3, entry 4). Finally, no **3** or imine **28** could detected when replacing TBAI with TBAB (Scheme 3, entry 5).

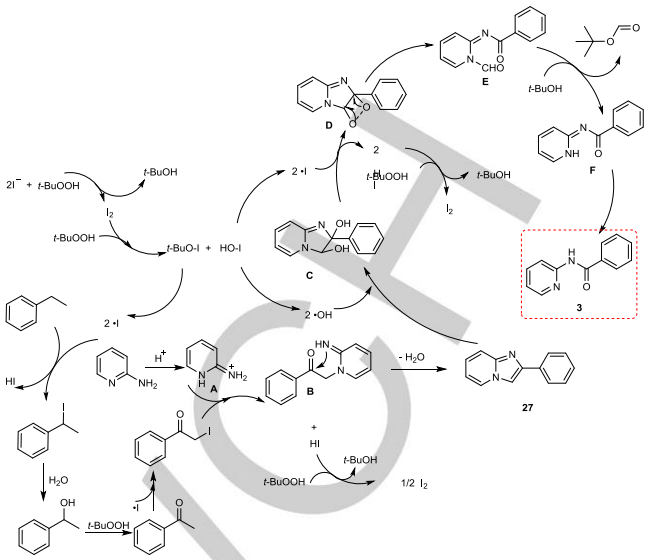


Scheme 3. Control experiments.

Based on the above investigation, a plausible mechanism was proposed (Scheme 4). First, (1-iodoethyl)benzene is formed from ethylbenzene and subsequently transformed into 1-phenylethanol. 1-Phenylethanol is then oxidized to acetophenone by TBHP, and subsequent reaction of acetophenone with iodine forms *α*-iodoacetophenone, which reacts with **A** to produce the imine **B**.[14] **B** is subsequently transferred to the key intermediate, **27**.[15] The addition of two hydroxyl radicals to the double bond of **27** affords diol **C**. Then, a four-membered peroxide ring **D** is formed by the abstraction of hydrogens from the diol by two iodine radicals. The strained four-membered ring is unstable, and the C-C bond is cleaved to form aldehyde **E**.[16] Finally, *tert*-butyl formate is released from **E**, leading to the formation of amide **F**,[17] which undergoes isomerization to afford the desired amide **3**.

Conclusion

In summary, we have developed a mild and green methodology for the construction of *N*-(pyridine-2-yl)amides from alkylarenes and 2-aminopyridine in one step. Various alkylarenes were directly transformed into the corresponding *N*-(pyridine-2-yl)amides via tandem C(sp^3)-H bond activation/oxidative cyclization/C-C bond cleavage. Mechanistic investigations showed that cyclization was a key step of C-C bond cleavage. Direct amidation via C(sp^3)-C(sp^3) bond cleavage has been rarely reported, and this is the first work to report the synthesis of *N*-heterocyclic amides via C(sp^3)-C(sp^3) bond cleavage of alkylarenes.



Scheme 4. Proposed mechanism.

Experimental Section

General Information. All chemicals were of chemical pure grade quality and used without further purification, all organic solvents were analytical pure grade quality, water was ordinary domestic water and used without further purification, *tert*-butyl hydroperoxide (TBHP) was 70% aqueous solution purchased from Sinopharm Chemical Reagent Co.,Ltd. Reactions were monitored by TLC (Merck silica gel 60 F_{254}), column chromatography was performed on silica gel 200~300 mesh. All ^{1}H NMR (300 MHz), ^{13}C{^{1}H} NMR (75 MHz) spectra were recorded on a Bruker Avance 300 spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard and reported in parts per million (ppm, *δ*). High-resolution mass spectrums (HRMS) were measured on Finnigan MAT 95 spectrometer (Finnigan, Germany).

General Procedure for the Synthesis of *N*-heterocyclic Amides from Alkylbenzene. To a solution of alkylbenzene (0.6 mmol), 2-aminopyridine (1.2 mmol) and tetrabutylazanium iodide (TBAI) (0.12 mmol) in water in sealed tube, was added triflic acid (TfOH) (0.12 mmol) and tert-butyl hydroperoxide (TBHP) (4.8 mmol). The solution was heated at 100 °C for 5-6 h and monitored by thin layer chromatography. The reaction mixture was cooled to room temperature and added saturated sodium thiosulfate, then the inorganic layer was extracted and separated with dichloromethane for 3 times. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate as the eluent, typically 100:5-100:10).

***N*-(Pyridin-2-yl)benzamide (3)**. White solid; 73 mg, 61% yield; m.p. 84-87 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 8.93 (s, 1H), 8.40 (d, *J* = 8.4 Hz, 1H), 8.20 (d, *J* = 3.2 Hz, 1H), 7.93 (d, *J* = 6.9 Hz, 2H), 7.78-7.72 (m, 1H), 7.59-7.54 (m, 1H), 7.51-7.49 (m, 2H), 7.06-7.02 (m, 1H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 166.4, 151.9, 147.5, 138.3, 134.5, 131.9, 128.5, 127.4, 119.6, 114.5; HRMS (ESI-TOF) *m/z*: calcd for $C_{12}H_{11}N_2O$ $[M+H]^+$ 199.0866, found 199.0864.

4-Methyl-*N*-(pyridin-2-yl)benzamide (4). Yellow solid; 90 mg, 71% yield; m.p. 107-108 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 8.79 (s, 1H), 8.32 (d, *J* = 8.4 Hz, 1H), 8.16-8.14 (m, 1H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.70-7.64 (m, 1H), 7.21 (d, *J* = 7.9 Hz, 2H), 6.99-6.94 (m, 1H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 165.9, 151.8, 148.0, 143.0, 138.6, 131.5, 129.6, 127.4, 119.90, 114.3, 21.6; HRMS (ESI-TOF) *m/z*: calcd for $C_{13}H_{13}N_2O$ [M+H]$^+$ 213.1022, found 213.1024.

4-Bromo-*N*-(pyridin-2-yl)benzamide (5). White solid; 105 mg, 63% yield; m.p. 132-134 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 8.71 (s, 1H), 8.36 (d, *J* = 8.4 Hz, 1H), 8.27-8.25 (m, 1H), 7.81-7.74 (m, 3H), 7.66-7.62 (m, 2H), 7.10-7.06 (m, 1H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 164.9, 151.5, 148.1, 138.7, 133.3, 132.3, 128.9, 127.3, 120.3, 114.4; HRMS (ESI-TOF) *m/z*: calcd for $C_{12}H_{10}BrN_2O$ [M+H]$^+$ 276.9971, found 276.9974.

4-Methoxy-*N*-(pyridin-2-yl)benzamide (6). Yellow solid; 85 mg, 62% yield; m.p. 88-90 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 8.94 (s, 1H), 8.37 (d, *J* = 8.5 Hz, 1H), 8.19 (d, *J* = 4.0 Hz, 1H), 7.89 (d, *J* = 8.7 Hz, 2H), 7.75-7.69 (m, 1H), 7.03-6.99 (m, 1H), 6.97-6.92 (m, 2H), 3.85 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 165.5, 162.9, 152.0, 147.9, 138.5, 129.3, 126.6, 119.8, 114.3, 114.1, 55.6; HRMS (ESI-TOF) *m/z*: calcd for $C_{13}H_{13}N_2O_2$ [M+H]$^+$ 229.0972, found 229.0969.

4-Cyano-*N*-(pyridin-2-yl)benzamide (7). White solid; 108 mg, 81% yield; m.p. 198-200 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 9.20 (s, 1H), 8.37 (d, *J* = 8.4 Hz, 1H), 8.18-8.16 (m, 1H), 8.03 (d, *J* = 8.1 Hz, 2H), 7.81-7.77 (m, 3H), 7.26-7.07 (m, 1H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 164.2, 151.3, 148.0, 138.9, 138.3, 132.7, 128.1, 120.6, 118.0, 115.9, 114.7; HRMS (ESI-TOF) *m/z*: calcd for $C_{13}H_{10}N_3O$ [M+H]$^+$ 224.0818, found 224.0815.

Methyl 4-(pyridin-2-ylcarbamoyl)benzoate (8). White solid; 95 mg, 62% yield; m.p. 200-202 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 8.68 (s, 1H), 8.38 (d, *J* = 8.4 Hz, 1H), 8.31-8.28 (m, 1H), 8.17 (d, *J* = 8.1 Hz, 2H), 7.99 (d, *J* = 8.1 Hz, 2H), 7.78 (t, *J* = 8.0 Hz, 1H), 7.10 (m, 1H), 3.96 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 166.3, 165.0, 151.4, 148.1, 138.7, 138.2, 133.5, 130.2, 127.4, 120.4, 114.4, 52.6; HRMS (ESI-TOF) *m/z*: calcd for $C_{14}H_{13}N_2O_3$ [M+H]$^+$ 257.0921, found 257.0924.

4-Nitro-*N*-(pyridin-2-yl)benzamide (9). White solid; 101 mg, 69% yield; m.p. 235-236 °C; ^{1}H NMR (300 MHz, DMSO-d_6): *δ* 11.20 (s, 1H), 8.42-8.32 (m, 3H), 8.23-8.18 (m, 3H), 7.90-7.85 (m, 1H), 7.22-7.19 (m, 1H); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): *δ* 164.6, 151.9, 149.3, 148.1, 139.9, 138.3, 129.6, 123.4, 120.3, 114.9; HRMS (ESI-TOF) *m/z*: calcd for $C_{12}H_{10}N_3O_3$ [M+H]$^+$ 244.0717, found 244.0718.

3-Methyl-*N*-(pyridin-2-yl)benzamide (10). White solid; 65 mg, 51% yield; m.p. 77-81 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 9.02 (s, 1H), 8.41 (d, *J* = 8.3 Hz, 1H), 8.20-8.18 (m, 1H), 7.78-7.74 (m, 3H), 7.37 (s, 2H), 7.06-7.02 (m, 1H), 2.40 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 166.2, 151.8, 147.9, 138.8, 138.6, 134.4, 133.1, 128.8, 128.1, 124.4, 119.9, 114.3, 21.5; HRMS (ESI-TOF) *m/z*: calcd for $C_{13}H_{13}N_2O$ [M+H]$^+$ 213.1022, found 213.1021.

3-Bromo-*N*-(pyridin-2-yl)benzamide (11). White solid; 95 mg, 57% yield; m.p. 110-112 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 9.16 (s, 1H), 8.29 (d, *J* = 8.4 Hz, 1H), 8.08-8.06 (m, 1H), 8.01-7.99 (m, 1H), 7.77-7.73 (m, 1H), 7.71-7.64 (m, 1H), 7.61-7.57 (m, 1H), 7.28-7.23 (m, 1H), 6.99-6.95 (m, 1H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 164.6, 151.6, 148.0, 138.7, 136.5, 135.2, 130.8, 130.4, 125.9, 123.1, 120.3, 114.6; HRMS (ESI-TOF) *m/z*: calcd for $C_{12}H_{10}BrN_2O$ [M+H]$^+$ 276.9971, found 276.9966.

3-Methoxy-*N*-(pyridin-2-yl)benzamide (12). White semisolid; 73 mg, 53% yield; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 9.53 (s, 1H), 8.42-8.39 (m, 1H), 8.07-8.04 (m, 1H), 7.74-7.69 (m, 1H), 7.48-7.44 (m, 2H), 7.35-7.29 (m, 1H), 7.08-7.04 (m, 1H), 7.01-6.96 (m, 1H), 3.80 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 166.1, 159.9, 151.9, 147.8, 138.5, 135.9, 129.7, 119.8, 119.3, 118.5, 114.5, 112.5, 55.4; HRMS (ESI-TOF) *m/z*: calcd for $C_{13}H_{12}N_2O_2$ [M+H]$^+$ 251.0792, found 251.0794.

2-Methyl-*N*-(pyridin-2-yl)benzamide (13). White solid; 51 mg, 40% yield; m.p. 112-113 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 9.54 (s, 1H), 8.39 (d, *J* = 8.2 Hz, 1H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.64-7.62 (m, 1H), 7.50 (d, *J* = 7.4 Hz, 1H), 7.39-7.34 (m, 1H), 7.26-7.20 (m, 2H), 6.93-6.89 (m, 1H), 2.50 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 168.8, 151.9, 147.7, 138.6, 136.5, 136.3, 131.4, 130.6, 127.1, 126.1, 119.9, 114.4, 19.9; HRMS (ESI-TOF) *m/z*: calcd for $C_{13}H_{13}N_2O$ [M+H]$^+$ 213.1022, found 213.1025.

2-Bromo-*N*-(pyridin-2-yl)benzamide (14). White solid; 56 mg, 34% yield; m.p. 160-162 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 9.32 (s, 1H), 8.39 (d, *J* = 8.4 Hz, 1H), 7.94-7.91(m, 1H), 7.75 (td, *J* = 8.8, 8.4, 1.9 Hz, 1H), 7.64-7.60 (m, 2H), 7.40 (td, *J* = 7.5, 1.4 Hz, 1H), 7.33 (td, *J* = 7.7, 1.9 Hz, 1H), 7.02-6.97 (m, 1H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 166.2, 151.4, 147.8, 138.7, 137.8, 133.7, 131.9, 129.6, 127.8, 120.3, 119.6, 114.6; HRMS (ESI-TOF) *m/z*: calcd for $C_{12}H_{10}BrN_2O$ [M+H]$^+$ 276.9971, found 276.9972.

2-Methoxy-*N*-(pyridin-2-yl)benzamide (15). White solid; 67 mg, 49% yield; m.p. 56-60 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 10.37 (s, 1H), 8.43 (d, *J* = 8.4 Hz, 1H), 8.29-8.23 (m, 2H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.9 Hz, 1H), 7.08 (t, *J* = 7.6 Hz, 1H), 7.02-6.95 (m, 2H), 3.99 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 163.7, 157.7, 152.1, 148.1, 138.4, 133.8, 132.6, 121.6, 121.5, 119.8, 114.9, 111.7, 56.4; HRMS (ESI-TOF) *m/z*: calcd for $C_{13}H_{13}N_2O_2$ [M+H]$^+$ 229.0972, found 229.0970.

***N*-(Pyridin-2-yl)-1-naphthamide (16)**. White solid; 75 mg, 50% yield; m.p. 143-146 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 9.33 (s, 1H), 8.48 (d, *J* = 8.4 Hz, 1H), 8.42-8.38 (m, 1H), 7.98 (d, *J* = 8.3 Hz, 1H), 7.92-7.89 (m, 1H), 7.84-7.82 (m, 1H), 7.79-7.72 (m, 2H), 7.61-7.52 (m, 2H), 7.51-7.46 (m, 1H), 6.97-6.92 (m, 1H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 168.2, 151.9, 147.8, 138.6, 134.0, 133.9, 131.4, 130.2, 128.6, 127.54, 126.7, 125.6, 125.3, 124.8, 119.9, 114.4; HRMS (ESI-TOF) *m/z*: calcd for $C_{16}H_{13}N_2O$ [M+H]$^+$ 249.1022, found 249.1018.

9,10-Dioxo-*N*-(pyridin-2-yl)-9,10-dihydroanthracene-2-carboxamide (17). Yellow solid; 120 mg, 61% yield; m.p. 211-213 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 8.91 (s, 1H), 8.79 (s, 1H), 8.46-8.32 (m, 6H), 7.87-7.77 (m, 3H), 7.15-7.11 (m, 1H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 182.5, 182.4, 164.0, 151.2, 148.2, 139.3, 138.8, 135.7, 134.7, 133.8, 133.5, 133.2, 128.3, 127.7, 127.6, 125.6, 120.7, 114.5; HRMS (ESI-TOF) *m/z*: calcd for $C_{20}H_{13}N_2O_3$ [M+H]$^+$ 329.0921, found 329.0924.

***N*-(Pyridin-2-yl)thiophene-2-carboxamide (18)**. White soild; 66 mg, 54% yield; m.p. 117-120 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 8.97 (s, 1H), 8.32 (dt, *J* = 8.4, 1.1 Hz, 1H), 8.24-8.22 (m, 1H), 7.75-7.70 (m, 1H), 7.69-7.67 (m, 1H), 7.57-7.55 (m, 1H), 7.11-7.08 (m, 1H), 7.06-7.02 (m, 1H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 160.2, 151.5, 147.9, 139.1, 138.6, 131.7, 129.1, 128.0, 120.0, 114.5; HRMS (ESI-TOF) *m/z*: calcd for $C_{10}H_9N_2OS$ [M+H]$^+$ 205.0430, found 205.0432.

***N*-(Pyridin-2-yl)thiophene-3-carboxamide (19)**. White solid; 69 mg, 56% yield; m.p. 103-105 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 9.01 (s, 1H), 8.37-8.33 (m, 1H), 8.20-8.17 (m, 1H), 8.06-8.03 (m, 1H), 7.75-7.69 (m, 1H), 7.56-7.53 (m, 1H), 7.38-7.35 (m, 1H), 7.04-7.00 (m, 1H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 161.2, 151.6, 147.9, 138.7, 137.4, 129.6, 127.1, 126.4, 120.0, 114.4; HRMS (ESI-TOF) *m/z*: calcd for $C_{10}H_9N_2OS$ $[M+H]^+$ 205.0430, found 205.0431.

***N*-(Pyridin-2-yl)picolinamide (20)**. White solid; 13 mg, 11% yield; m.p. 117-119 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 10.53 (s, 1H), 8.61-8.60 (m, 1H), 8.40 (d, *J* = 8.4 Hz, 1H), 8.36-8.33 (m, 1H), 8.26 (d, *J* = 7.8 Hz, 1H), 7.88 (td, *J* = 7.7, 1.7 Hz, 1H), 7.76-7.70 (m, 1H), 7.48-7.44 (m, 1H), 7.07-7.03 (m, 1H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 162.7, 151.2, 149.4, 148.3, 138.3, 137.6, 126.8, 122.5, 119.9, 114.0; HRMS (ESI-TOF) *m/z*: calcd for $C_{11}H_{10}N_3O$ $[M+H]^+$ 200.0818, found 200.0816.

***N*-(Pyridin-2-yl)-[1,1'-biphenyl]-4-carboxamide (21)**. White solid; 78 mg, 47% yield; m.p. 154-156 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 9.19 (s, 1H), 8.44 (d, *J* = 8.4 Hz, 1H), 8.20-8.18 (m, 1H), 8.03-7.99 (m, 2H), 7.78-7.73 (m, 1H), 7.71-7.68 (m, 2H), 7.64-7.61 (m, 2H), 7.50-7.45 (m, 2H), 7.43-7.37 (m, 1H), 7.06-7.02 (m, 1H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 165.8, 151.8, 148.0, 145.1, 139.8, 138.6, 133.0, 129.1, 128.3, 128.0, 127.5, 127.3, 120.0, 114.5; HRMS (ESI-TOF) *m/z*: calcd for $NaC_{18}H_{14}N_2O$ $[M+Na]^+$ 297.0998, found 297.1001.

***N*-(3-Methylpyridin-2-yl)benzamide (22)**. Yellow semisolid; 60 mg, 47% yield; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 9.24 (s, 1H), 8.19 (d, *J* = 4.8 Hz, 1H), 7.93 (d, *J* = 7.2 Hz, 2H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.3 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.11 (dd, *J* = 7.6, 4.8 Hz, 1H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 166.3, 150.1, 145.5, 140.2, 134.2, 132.1, 129.5, 128.7, 127.8, 121.9, 18.5; HRMS (ESI-TOF) *m/z*: calcd for $C_{13}H_{13}N_2O$ $[M+H]^+$ 213.1022, found 213.1023.

***N*-(4-Methylpyridin-2-yl)benzamide (23)**. Yellow solid; 65 mg, 51% yield; m.p. 107-110 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 8.94 (s, 1H), 8.25 (s, 1H), 8.04 (d, *J* = 5.1 Hz, 1H), 7.93-7.90 (m, 2H), 7.59-7.53 (m, 1H), 7.50-7.45 (m, 2H), 6.87 (d, *J* = 5.0 Hz, 1H), 2.40 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 166.0, 151.7, 150.2, 147.5, 134.5, 132.3, 128.9, 127.4, 121.2, 114.9, 21.6; HRMS (ESI-TOF) *m/z*: calcd for $C_{13}H_{13}N_2O$ $[M+H]^+$ 213.1022, found 213.1020.

***N*-(5-Methylpyridin-2-yl)benzamide (24)**. Yellow solid; 61 mg, 48% yield; m.p. 89-93 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 8.86 (s, 1H), 8.29 (d, *J* = 8.5 Hz, 1H), 8.01 (s, 1H), 7.94-7.90 (m, 2H), 7.58-7.53 (m, 2H), 7.50-7.45 (m, 2H), 2.29 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 165.8, 149.6, 147.9, 139.1, 134.6, 132.2, 129.4, 128.9, 127.3, 113.8, 17.9; HRMS (ESI-TOF) *m/z*: calcd for $C_{13}H_{13}N_2O$ $[M+H]^+$ 213.1022, found 213.1021.

***N*-(6-Methylpyridin-2-yl)benzamide (25)**. Yellow solid; 4 mg, 3% yield; m.p. 107-110 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 8.56 (s, 1H), 8.19 (d, *J* = 8.2 Hz, 1H), 7.96-7.89 (m, 2H), 7.65 (t, *J* = 7.9 Hz, 1H), 7.59-7.53 (m, 1H), 7.51-7.46 (m, 2H), 6.93 (d, *J* = 7.5 Hz, 1H), 2.47 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 165.8, 157.1, 150.9, 138.9, 134.5, 132.3, 128.9, 127.3, 119.6, 111.1, 24.1; HRMS (ESI-TOF) *m/z*: calcd for $C_{13}H_{13}N_2O$ $[M+H]^+$ 213.1022, found 213.1020.

***N*-(4-Methoxypyridin-2-yl)benzamide (26)**. White solid; 85 mg, 62% yield; m.p. 59-61 °C; ^{1}H NMR (300 MHz, Chloroform-*d*): *δ* 9.73 (s, 1H), 8.06-8.05 (m, 1H), 7.91-7.88 (m, 2H), 7.74-7.72 (m, 1H), 7.55-7.49 (m, 1H), 7.45-7.39 (m, 2H), 6.52-6.48 (m, 1H), 3.86 (s, 3H); ^{13}C{^{1}H} NMR (75 MHz, Chloroform-*d*): *δ* 167.6, 166.5, 153.7, 148.4, 134.6, 132.1, 128.7, 127.5, 107.8, 99.0, 55.4; HRMS (ESI-TOF) *m/z*: calcd for $C_{13}H_{13}N_2O_2$ $[M+H]^+$ 229.0972, found 229.0972.

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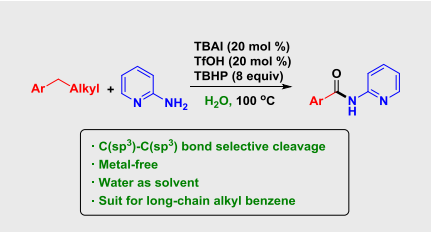
Entry for the Table of Contents

Amides Synthesis



A mild and green methodology for the construction of *N*-(pyridine-2-yl)amides from alkylarenes and 2-aminopyridine in one step was developed. Various alkylarenes were directly transformed into the corresponding *N*-(pyridine-2-yl)amides via tandem C(sp^3)-H bond activation/oxidative cyclization/C-C bond cleavage.