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Copper-catalyzed aerobic oxidative synthesis of aryl nitriles from benzylic alcohols and aqueous ammonia†

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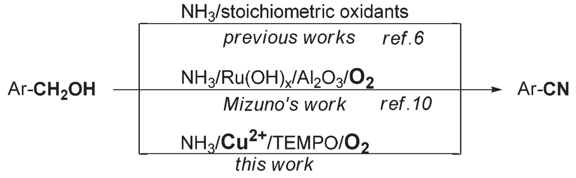
Copper-catalyzed direct conversion of benzylic alcohols to aryl nitriles was realized using NH_3(aq.) as the nitrogen source, O_2 as the oxidant and TEMPO as the co-catalyst. Furthermore, copper-catalyzed one-pot synthesis of primary aryl amides from alcohols was also achieved.

Introduction

Aryl nitriles are versatile building blocks in the synthesis of natural products, pharmaceuticals, agricultural chemicals and dyes.[1] Development of newer methods for the synthesis of aryl nitriles is of significant interest. General synthetic methods include Sandmeyer's reaction,[2] transition metal-catalyzed cross-coupling of aryl halides or direct C–H functionalization of arenes.[3] However, inorganic cyanide salts, generally toxic, were used and the reactions produce large amounts of inorganic salts as waste. Environmentally benign approaches are considerably attractive, and many excellent examples have been reported. For instance, metal-catalyzed dehydration of aryl oximes or amides,[4] changing the CN source to DMF *via* the C–H functionalization of arenes,[5] and especially, oxidative dehydrogenation of benzylic alcohols,[6] azides[7] or methyl arenes[8] have been extensively investigated.

As alcohols are inexpensive and easily available, it would be advantageous to synthesize nitriles directly from alcohols. Oxidative reaction of alcohols and ammonia to produce nitriles has been studied using reagents such as I_2/DIH,[6a] I_2/TBHP,[6b] $NiSO_4/K_2S_2O_8$/NaOH,[6c] $MnO_2/MgSO_4$,[6d] and $(Bu_4N)_2S_2O_8$/Cu$(HCO_2)_2$/Ni$(HCO_2)_2$/KOH[6e] (Scheme 1). However, one drawback has been that stoichiometric amounts of reactive oxidants were needed, not to mention their high cost and the generation of environmentally hazardous/toxic byproducts. Obviously, molecular oxygen as an oxidant has remarkable advantages, including its abundance, low cost, and benign byproducts (usually only H_2O). The development of catalytic aerobic oxidation methodologies would be highly desirable.[9]



Scheme 1 Ammoxidation of alcohols to nitriles.

Recently, Mizuno *et al.* reported a highly efficient $Ru(OH)_x/Al_2O_3$-catalyzed aerobic synthesis of aryl nitriles from alcohols and the hydration of nitriles to yield primary amides (Scheme 1).[10] The reaction represents a major advance in the nitrile synthesis, but is carried out at 120–130 °C in an autoclave in many cases.

Aerobic oxidation of alcohols to aldehydes catalyzed by copper has been well studied,[11] and the catalyst Cu^{2+}/TEMPO/Bipy/KOBu^t was usually used to synthesize aldehydes with oxygen as an oxidant. Meanwhile, in Mizuno's work,[10b] Schiff-bases were regarded as intermediates which would oxidatively dehydrogenate to produce nitriles. If ammonia, as a nitrogen source, is introduced into the reaction of copper-catalyzed aerobic oxidative synthesis of aldehydes, it would probably condense with aldehydes to produce Schiff-bases which would subsequently be converted into nitriles catalyzed by copper. This hypothesis prompted us to examine copper-catalyzed synthesis of aryl nitriles directly from benzylic alcohols. To the best of our knowledge, employing copper as a catalyst in aerobic oxidative synthesis of nitriles has not been disclosed. Herein, we demonstrate a copper-catalyzed aerobic catalytic system for the synthesis of aryl nitriles from benzylic alcohols (Scheme 1). This catalyst system expands the toolbox for synthesis of nitriles through transition metal-catalyzed aerobic oxidation of alcohols. Moreover, it is a highly desirable method not only because copper is cheap, readily available and environmentally benign, but also because of the mild reaction conditions to give a high conversion.

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Results and discussion

Our study began with an examination of the conversion of benzyl alcohols to benzonitriles with Sheldon's catalyst ($CuCl_2$/TEMPO/Bipy/$KOBu^t$),[11] and aqueous ammonia was added as a nitrogen source (Table 1). Delightfully, the desired product was obtained in excellent yield (94%) at 80 °C (entry 1). We speculated that aqueous ammonia could act both as a ligand and a base, replacing the 2,2′-bipyridine and $KOBu^t$ in the reaction. Thus, phenyl nitrile was obtained in good yield (77–78%; entries 2, 3), indicating that $KOBu^t$ was not necessary for the transformation. Using $CuCl_2$ as a catalyst under ligand-free and base-free conditions, different solvents were examined (entries 4–7). It was found that good yields of the desired products were obtained in DMSO (entry 4) and DMF (entry 7), lower yields were obtained in dioxane and H_2O. Copper and TEMPO are critical for the conversion, and no products were detected in the absence of $CuCl_2$ or TEMPO (entries 8, 9). Next, we screened the copper sources with different valences. Gratifyingly, $CuBr_2$, $Cu(NO_3)_2$, and $Cu(OAc)_2$ all gave excellent yields (entries 10–12) and the yield was up to 98% with $Cu(NO_3)_2$. However, no products were obtained with $CuSO_4$ or CuO (entries 13, 14). Additionally, cuprous salts also exhibited high activity and good yields were obtained (entries 15, 16).

The above results show that $Cu(NO_3)_2$/TEMPO/NH_3(aq.)/O_2 is an efficient combination for the synthesis of aryl nitriles directly from benzyl alcohols. Using the optimized conditions, we next explored the scope and generality of the process (Table 2). It was found that benzylic alcohols carrying electron-donating and electron-withdrawing groups could be smoothly converted into the desired products with excellent isolated yields (91–95%, entries 1–5). Benzylic alcohols carrying an *ortho*-substituent were also found to readily participate in the reaction (87–97%, entries 6–9). Furthermore, the method could be applied to the transformation of allylic alcohols to unsaturated nitriles. Cinnamyl nitrile could be quantitatively obtained from cinnamyl alcohol without isomerization, hydrogenation, and hydration of the double bonds (entry 10). Heteroatom-containing alcohols also reacted smoothly to afford the corresponding nitriles in high yields (83–89%, entries 11, 12). However, aliphatic primary alcohols could not be converted under the standard conditions (entries 13, 14).

During the reaction, aldehydes were supposed to form initially[11] and subsequently converted into nitriles. Thus, we evaluated the $Cu(NO_3)_2/NH_3(aq.)/O_2$ system in the direct transformation of aryl aldehydes into nitriles (Table 3). With the standard conditions, electron-rich aryl aldehydes could be smoothly converted into the desired products with high isolated yields (84–89%, entries 1–3, 6). The transformation of aryl aldehydes containing weak electron-withdrawing groups could also be realized (entry 4). However, aryl aldehydes carrying strong electron-withdrawing groups gave poor results. For example, the isolated yield is only 5% for 4-nitrobenzaldehyde (entry 5). It is noteworthy that the yield from $Cu(NO_3)_2$-catalyzed oxidation of 4-nitrobenzylalcohol (Table 2, entry 5, 92%) is much higher than 4-nitrobenzaldehyde (5%). Similarly, cinnamyl and 3-pyridyl aldehyde were found to be poor substrates (entries 7, 8). Electron-rich heteroaryl aldehydes gave satisfactory results. For instance, 60% isolated yield was obtained for thiophene-3-aldehyde (entry 9). Also, aliphatic aldehydes could not be obtained from aliphatic primary alcohols with the standard conditions (entry 10).

Very recently, Lu *et al.* reported copper-catalyzed hydration of nitriles with the aid of acetaldoxime in which coordination of copper salts to nitriles results in an enhanced electrophilicity of the nitrile carbon to hydroxy in acetaldoxime.[12] Then

Table 1 Copper-catalyzed transformation of benzyl alcohol (**1a**) to benzonitrile (**2a**)[a]

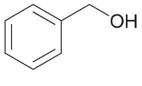
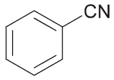
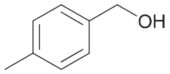
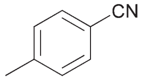
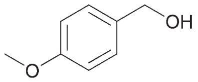
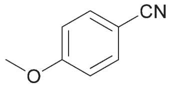
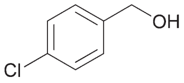
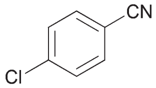
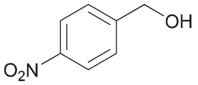
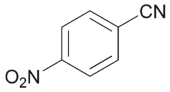
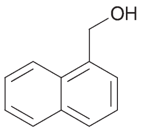
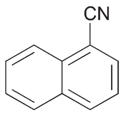
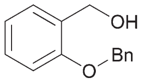
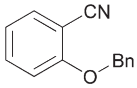
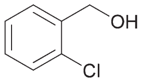
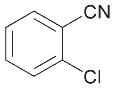
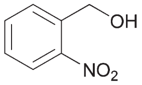
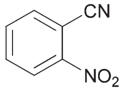
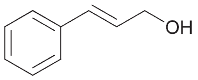
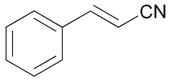
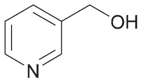
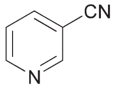
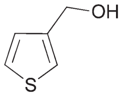
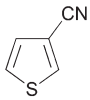
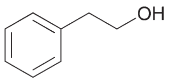
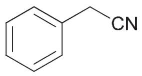
$$\underset{\textbf{1a}}{\text{Ph-CH}_2\text{OH}} \xrightarrow{\text{Cu / NH}_3\text{(aq.)}} \underset{\textbf{2a}}{\text{Ph-CN}}$$

Entry	Cat. (5 mol%)	Co-cat. (5 mol%)	Ligand (5 mol%)	Base (5 mol%)	NH_3	Solvent	Yield[b] (%)
1	$CuCl_2$	TEMPO	2,2′-Bipyridine	$KOBu^t$	NH_3(aq.)	CH_3CN	94
2	$CuCl_2$	TEMPO	—	$KOBu^t$	NH_3(aq.)	CH_3CN	77
3	$CuCl_2$	TEMPO	—	—	NH_3(aq.)	CH_3CN	78
4	$CuCl_2$	TEMPO	—	—	NH_3(aq.)	DMSO	80
5	$CuCl_2$	TEMPO	—	—	NH_3(aq.)	DMF	79
6	$CuCl_2$	TEMPO	—	—	NH_3(aq.)	Dioxane	5
7	$CuCl_2$	TEMPO	—	—	NH_3(aq.)	H_2O	35
8	$CuCl_2$	—	—	—	NH_3(aq.)	DMSO	0
9	—	TEMPO	—	—	NH_3(aq.)	DMSO	0
10	$CuBr_2$	TEMPO	—	—	NH_3(aq.)	DMSO	96
11	$Cu(NO_3)_2$	TEMPO	—	—	NH_3(aq.)	DMSO	98(62[c])
12	$Cu(OAc)_2$	TEMPO	—	—	NH_3(aq.)	DMSO	92
13	$CuSO_4$	TEMPO	—	—	NH_3(aq.)	DMSO	0
14	CuO	TEMPO	—	—	NH_3(aq.)	DMSO	<1
15	CuCl	TEMPO	—	—	NH_3(aq.)	DMSO	86
16	CuBr	TEMPO	—	—	NH_3(aq.)	DMSO	94

[a] Reaction conditions: benzyl alcohol (1 mmol), catalyst (5 mol%), TEMPO (5 mol%), 25% NH_3(aq.) (3 mmol), solvent (1 mL), O_2 (1 atm.), 5 h, 80 °C. [b] GC yield. [c] At 50 °C, 10 h.

Table 2 Copper-catalyzed synthesis of aryl nitriles (**2**) from benzylic alcohols (**1**)[a]

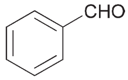
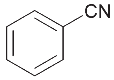
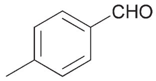
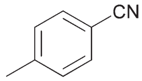
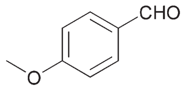
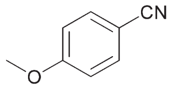
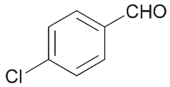
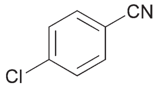
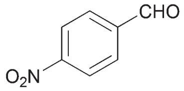
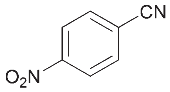
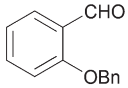
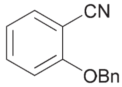
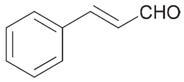
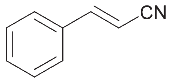
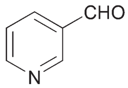
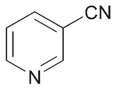
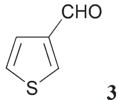
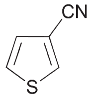
$$\underset{\mathbf{1}}{\text{Ar-CH}_2\text{OH}} \xrightarrow[\text{NH}_3\text{(aq.): 3eq., O}_2\text{(1atm), 80}^{\text{o}}\text{C}]{\text{Cu(NO}_3)_2\text{: 5mol\%, TEMPO: 5mol\%}} \underset{\mathbf{2}}{\text{Ar-CN}}$$

Entry	1	2	Yield[b] (%)
1	 **1a**	 **2a**	92
2	 **1b**	 **2b**	93
3	 **1c**	 **2c**	95
4	 **1d**	 **2d**	91
5	 **1e**	 **2e**	92
6	 **1f**	 **2f**	97
7	 **1g**	 **2g**	87
8	 **1h**	 **2h**	95[c]
9	 **1i**	 **2i**	93[c]
10	 **1j**	 **2j**	98
11	 **1k**	 **2k**	89
12	 **1l**	 **2l**	83
13	 **1m**	 **2m**	0[d]
14	$CH_3(CH_2)_{10}$–CH_2OH **1n**	$CH_3(CH_2)_{10}$–CN **2n**	0[d]

[a] Reaction conditions: alcohol (3 mmol), $Cu(NO_3)_2$ (5 mol%), TEMPO (5 mol%), 25% NH_3(aq.) (9 mmol), DMSO (3 mL), O_2 (1 atm.), 5 h, 80 °C. [b] Isolated yield. [c] Reaction time is 7 h. [d] Reaction time is 20 h.

Table 3 Copper-catalyzed synthesis of aryl nitriles (**2**) from aryl aldehydes (**3**)[a]

$$\underset{\mathbf{3}}{\text{Ar-CHO}} \xrightarrow[\text{NH}_3\text{(aq.): 3eq., O}_2\text{(1atm), 80}^{\text{o}}\text{C}]{\text{Cu(NO}_3)_2\text{: 5mol\%}} \underset{\mathbf{2}}{\text{Ar-CN}}$$

Entry	3	2	Yield[b] (%)
1	 **3a**	 **2a**	85
2	 **3b**	 **2b**	84
3	 **3c**	 **2c**	86
4	 **3d**	 **2d**	84
5	 **3e**	 **2e**	5
6	 **3f**	 **2g**	89
7	 **3g**	 **2j**	16
8	 **3h**	 **2k**	11
9	 **3i**	 **2l**	60
10	$CH_3(CH_2)_{10}$–CHO **3j**	$CH_3(CH_2)_{10}$–CN **2n**	0[c]

[a] Reaction conditions: aldehyde (3 mmol), $Cu(NO_3)_2$ (5 mol%), 25% NH_3(aq.) (9 mmol), DMSO (3 mL), O_2 (1 atm.), 5 h, 80 °C. [b] Isolated yield. [c] Reaction time is 20 h.

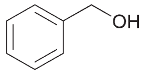
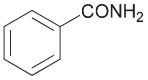
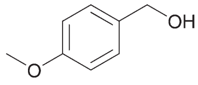
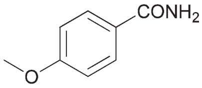
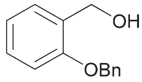
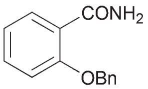
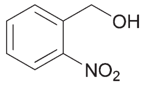
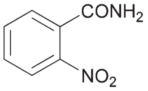
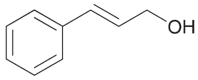
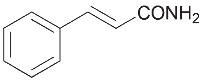
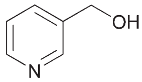
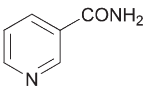
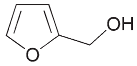
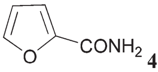
we explored the one-pot method for the synthesis of primary aryl amides directly from benzylic alcohols. After the transformation from benzylic alcohol to nitrile, acetaldoxime and H_2O were introduced into the reaction. As shown in Table 4, the practical utility of this one-pot procedure has been demonstrated by synthesizing a number of primary aryl amides with good to excellent yields (65–97%).

Conclusions

To sum up, in the present study we report a new and efficient method for the synthesis of aryl nitriles directly from the corresponding benzylic alcohols. It was found that benzylic alcohols could be easily converted into aryl nitriles by using aqueous ammonia (25%) as a nitrogen source, $Cu(NO_3)_2$–TEMPO as the catalyst and O_2 as the oxidant. Furthermore, one-pot synthesis of primary aryl amides could also be achieved. The present procedure is simple, efficient and environmentally benign,

Table 4 Copper-catalyzed one-pot synthesis of aryl amides (**4**) from benzylic alcohols (**1**)[a]

$$\underset{\mathbf{1}}{\text{Ar-CH}_2\text{OH}} \xrightarrow[\text{(2) MeCH=NOH}]{\text{(1) Cu(NO}_3)_2\text{/TEMPO/NH}_3\text{(aq.)/O}_2} \underset{\mathbf{4}}{\text{Ar-CONH}_2}$$

Entry	1	4	Yield[b] (%)
1	 **1a**	 **4a**	94
2	 **1c**	 **4b**	97
3	 **1g**	 **4c**	70
4	 **1i**	 **4d**	85
5	 **1j**	 **4e**	92
6	 **1k**	 **4f**	89
7	 **1o**	 **4g**	65

[a] Reaction conditions: (1) alcohol (3 mmol), $Cu(NO_3)_2$ (5 mol%), TEMPO (5 mol%), 25% NH_3(aq.) (9 mmol), DMSO (3 mL), O_2 (1 atm.), 5 h, 80 °C. (2) Acetaldoxime (6 mmol), H_2O (15 mL), 100 °C, 24 h. [b] Isolated yield.

allowing for a practical route to aryl nitriles and amides. The convenience of aqueous ammonia and the low cost of the catalytic copper system give this method potential to production on an industrial scale.

Experimental

General experimental: all chemicals were obtained from a commercial source and used without further purification. Flash column chromatography was performed on silica 230–400 mesh. ^{1}H-NMR, ^{13}C-NMR spectra were recorded on a Bruker Advance 400 spectrometer at ambient temperature in $CDCl_3$. Chemical shifts are reported in ppm relative to TMS. Melting points were measured on a SGW X-4 microscope, and are uncorrected.

Optimization of reaction conditions: copper-catalyzed transformation of benzyl alcohol (1a) to benzonitrile (2a)

To a 100 mL round-bottomed flask equipped with a magnetic stirrer, 0.05 mmol of the catalyst, 0.05 mmol of TEMPO, 1.0 mmol of benzyl alcohol (**1a**) and 1 mL of solvent were added. The vessel was flushed with O_2 and 3.0 mmol of NH_3 (aq., 25–28%) was added. The vessel was sealed and the reaction mixture was stirred in an oil bath at 80 °C for 5 hours. After cooling to room temperature, the mixture was diluted with 20 mL CH_2Cl_2. 1.0 mmol of bromobenzene was added as an internal standard. The product was yielded by GC.

Note: *In order to supply enough O_2, a 100 mL reaction vessel was used.*

Copper-catalyzed synthesis of aryl nitriles (2) from benzylic alcohols (1): general procedure

To a 250 mL round-bottomed flask equipped with a magnetic stirrer, 0.15 mmol of $Cu(NO_3)_2$, 0.15 mmol of TEMPO, 3.0 mmol of benzylic alcohol (**1**) and 3 mL of DMSO were added. The vessel was flushed with O_2 and 9.0 mmol of NH_3 (aq., 25–28%) was added. The vessel was sealed and the reaction mixture was stirred in an oil bath at 80 °C for 5 hours. After cooling to room temperature, the mixture was partitioned between ethyl acetate and brine. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate twice. The combined organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc-PE) to afford the product (**2**). The products obtained herein are all known compounds, and ^{1}H NMR and ^{13}C NMR are presented below.

Note: *In order to supply enough O_2, a 250 mL reaction vessel was used.*

Copper-catalyzed synthesis of aryl nitriles (2) from aryl aldehydes (3): general procedure

To a 250 mL round-bottomed flask equipped with a magnetic stirrer, 0.15 mmol of $Cu(NO_3)_2$, 3.0 mmol of aryl aldehyde (**3**) and 3 mL of DMSO were added. The vessel was flushed with O_2 and 9.0 mmol of NH_3 (aq., 25–28%) was added. The vessel was sealed and the reaction mixture was stirred in an oil bath at 80 °C for 5 hours. After cooling to room temperature, the mixture was partitioned between ethyl acetate and brine. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate twice. The combined organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc–PE) to afford the product (**2**). The products obtained herein are all known compounds, and ^{1}H NMR and ^{13}C NMR are presented below.

Note: *In order to supply enough O_2, a 250 mL reaction vessel was used.*

Benzonitrile (2a).[13] Liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67–7.54 (m, 3H), 7.45 (t, J = 7.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.5, 131.7, 128.8, 118.5, 112.0.

4-Methylbenzonitrile (2b).[14] M.P.: 21–22 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, J = 8.1 Hz, 2H), 7.23 (t, J = 7.1 Hz, 2H), 2.38 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.5, 131.8, 129.7, 118.9, 109.1, 21.6.

4-Methoxybenzonitrile (2c).[14] M.P.: 63–64 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60–7.53 (m, 2H), 6.99–6.91 (m, 2H), 3.85

(s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.8, 133.8, 119.1, 114.7, 103.8, 55.4.

4-Chlorobenzonitrile (2d).[14] M.P.: 90–91 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (dd, J = 8.7, 2.1 Hz, 2H), 7.43–7.36 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 132.3, 128.6, 116.9, 109.8.

4-Nitrobenzonitrile (2e).[14] M.P.: 116–117 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40–8.32 (m, 2H), 7.95–7.87 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.5, 124.3, 118.4, 116.8.

1-Naphthonitrile (2f).[15] M.P.: 28–29 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J = 8.2 Hz, 1H), 8.01 (d, J = 8.3 Hz, 1H), 7.90–7.82 (m, 2H), 7.63 (ddd, J = 8.3, 7.0, 1.2 Hz, 1H), 7.60–7.54 (m, 1H), 7.45 (dd, J = 8.3, 7.2 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.2, 132.8, 132.5, 132.2, 128.6, 128.5, 127.5, 125.0, 124.8, 117.7, 110.1.

2-(Benzyloxy)benzonitrile (2g).[15] M.P.: 69–70 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59–7.24 (m, 7H), 7.05–6.88 (m, 2H), 5.14 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.2, 135.6, 134.3, 133.7, 128.6, 128.1, 126.9, 121.0, 116.4, 112.9, 102.3, 70.5.

2-Chlorobenzonitrile (2h).[16] M.P.: 42–43 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (dd, J = 7.7, 1.6 Hz, 1H), 7.61–7.48 (m, 2H), 7.39 (td, J = 7.4, 1.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.7, 134.0, 133.9, 130.5, 127.2, 115.9, 113.3.

2-Nitrobenzonitrile (2i).[13] M.P.: 55–56 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41–8.33 (m, 1H), 7.97 (dt, J = 7.6, 3.8 Hz, 1H), 7.95–7.87 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.5, 135.6, 134.5, 133.9, 125.5, 115.0, 107.8.

Cinnamonitrile (2j).[14] Liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50–7.19 (m, 6H), 5.84 (d, J = 16.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.3, 133.4, 131.0, 128.9, 127.2, 118.0, 96.2.

Nicotinonitrile (2k).[17] M.P.: 48–49 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.96–8.89 (m, 1H), 8.85 (dd, J = 5.0, 1.6 Hz, 1H), 8.01 (dt, J = 8.0, 1.9 Hz, 1H), 7.48 (ddd, J = 7.9, 5.0, 0.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.9, 152.3, 139.2, 123.6, 116.4, 110.0.

Thiophene-3-carbonitrile (2l).[14] Liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.42 (s, 1H), 7.29 (d, J = 4.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.5, 126.2, 125.3, 112.5, 108.6.

Copper-catalyzed synthesis of primary aryl amides (4) from benzylic alcohols (1): general procedure

To a 250 mL round-bottomed flask equipped with a magnetic stirrer, 0.15 mmol of $Cu(NO_3)_2$, 0.15 mmol of TEMPO, 3.0 mmol of benzylic alcohol (**1**) and 3 mL of DMSO were added. The vessel was flushed with O_2 and 9.0 mmol of NH_3 (aq., 25–28%) was added. The vessel was sealed and the reaction mixture was stirred in an oil bath at 80 °C for 5 hours. The reaction mixture was cooled to room temperature and the seal was removed. The vessel was flushed with N_2 and 6 mmol of acetaldoxime was added to the solution followed by addition of 15 mL of H_2O. The vessel was sealed and the reaction mixture was stirred in an oil bath at 110 °C for 24 hours. After cooling to room temperature, the mixture was quenched with ethyl acetate. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate twice. The combined organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, EtOAc–PE) to afford the product (**4**). The products obtained herein are all known compounds, and ^{1}H NMR and ^{13}C NMR are presented below.

Note: *In order to supply enough O_2, a 250 mL reaction vessel was used.*

Benzamide (4a).[18] M.P.: 128–129 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87–7.78 (m, 2H), 7.56–7.47 (m, 1H), 7.42 (ddt, J = 8.3, 6.7, 1.4 Hz, 2H), 6.45 (s, br, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0, 133.7, 131.9, 128.6, 127.5.

4-Methoxybenzamide (4b).[18] M.P.: 164–165 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 9.0 Hz, 2H), 6.92 (d, J = 8.9 Hz, 2H), 5.90 (s, br, 2H), 3.85 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 162.8, 130.9, 129.4, 114.0, 55.6.

2-(Benzyloxy)benzamide (4c).[19] M.P.: 115–116 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (dd, J = 7.8, 1.8 Hz, 1H), 7.73 (s, br, 1H), 7.50–7.33 (m, 6H), 7.07 (ddd, J = 8.3, 6.9, 3.0 Hz, 2H), 6.38 (s, br, 1H), 5.17 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 157.2, 135.6, 133.3, 132.6, 129.0, 128.7, 127.9, 121.5, 121.3, 112.8, 71.3.

2-Nitrobenzamide (4d).[18] M.P.: 169–170 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10–8.00 (m, 1H), 7.73–7.55 (m, 3H), 5.84 (s, br, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.6, 131.0, 130.9, 129.0, 128.8, 124.7.

Cinnamamide (4e).[18] M.P.: 134–135 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, J = 15.7 Hz, 1H), 7.54–7.49 (m, 2H), 7.37 (dd, J = 10.1, 5.7 Hz, 3H), 6.48 (d, J = 15.7 Hz, 1H), 5.90 (s, br, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.1, 142.4, 131.0, 130.0, 128.9, 128.0, 119.8.

Nicotinamide (4f).[10b] M.P.: 129–130 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.76 (s, 1H), 8.17 (d, J = 5.8 Hz, 1H), 7.81–7.32 (m, 1H), 6.21 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.8, 148.4, 135.6, 131.0, 128.9, 123.7.

Furan-2-carboxamide (4g).[18] M.P.: 84–85 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48–7.43 (m, 1H), 7.14 (d, J = 3.5 Hz, 1H), 6.50 (dd, J = 3.4, 1.7 Hz, 1H), 6.37 (s, br, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5, 147.7, 144.4, 115.0, 112.2.

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