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Aerobic Oxidative Conversion of Aromatic Aldehydes to Nitriles Using a Nitroxyl/NO_x Catalyst System

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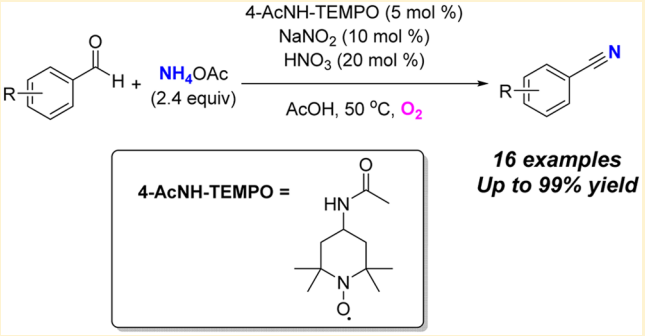
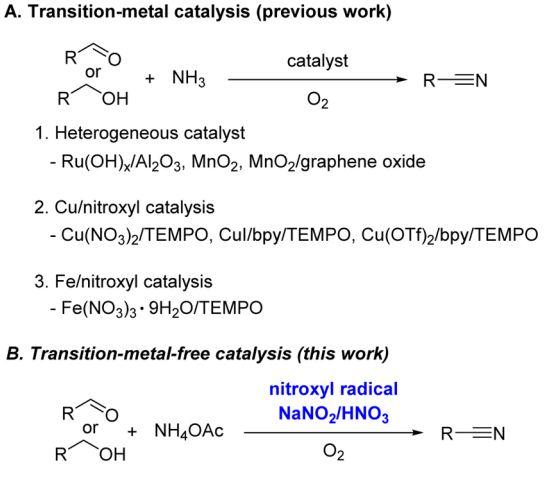
Supporting Information

ABSTRACT: The first transition-metal-free aerobic oxidative conversion of aldehyde catalyzed by a nitroxyl radical/NO_x system is presented for the synthesis of nitrile. In the presence of a catalytic amount of 4-AcNH-TEMPO (4-acetamido-2,2,6,6-tetramethylpiperidine-*N*-oxyl), $NaNO_2$, and HNO_3, benzaldehydes bearing a variety of functional groups underwent condensation with NH_4OAc and following aerobic oxidation to produce nitriles selectively under an O_2 balloon. Aerobic oxidative conversion of a primary alcohol instead of aldehyde is also achieved by a one-pot sequential strategy.



Nitrile is an important functional group in organic synthesis, serving not only as a versatile intermediate for transformations to other functional groups, such as amides, amines, ketones, carboxylic acids, and tetrazoles[1] but also as a crucial moiety for the production of agrochemicals, dyes, and pharmaceuticals.[2] In general, nitriles are prepared by nucleophilic substitution of leaving groups with toxic cyanide sources, such as KCN, NaCN, or ZnCN. To avoid the use of toxic metal cyanide, a variety of protocols using less toxic cyanation sources have been developed in recent decades;[3] however, most reported protocols depend on transition metal-catalyzed cross couplings of aryl halides, which generate halide byproducts and are laborious to prepare.[4] In terms of green chemistry, aerobic oxidative conversion of aldehydes with an ammonia source would be an attractive approach to generate nitriles because only water is produced during both condensation of aldehyde with ammonia and aerobic oxidation of the in situ generated imine intermediate. However, there are only a few examples of aerobic oxidative conversions of aldehyde with an ammonia source to nitrile, whereas a lot of anaerobic methods using stoichiometric oxidants, such as $(Bu_4N)_2S_2O_8$, trichloroisocyanuric acid (TCCA), I_2, NBS, $NaICl_2$, *tert*-butyl hydroperoxide (TBHP), hypervalent iodine, $NaIO_4$, H_5OI_6, and chloramine-T/KI have been developed.[5] In 2009, the Mizuno group reported that a heterogeneous ruthenium catalyst facilitates the aerobic oxidative conversion of aldehydes or primary alcohols to nitriles (Scheme 1, A-1).[6,7] Homogeneous catalytic systems for this transformation were developed by Tao, Huang, Muldoon, and Stahl with Cu/TEMPO catalyst systems (Scheme 1, A-2).[8] Recently, Batra achieved $Fe(NO_3)_3{\cdot}9H_2O$-catalyzed aerobic oxidative nitrile synthesis from alcohol or aldehyde (Scheme 1, A-3).[9] However, transition-metal-free aerobic oxidative approaches have not been investigated. Herein, we describe the first example of nitrile synthesis via aerobic oxidative conversion of aldehydes or primary alcohols using a nitroxyl/NO_x system (Scheme 1, B).

Scheme 1. Aerobic Oxidative Conversion of Aldehyde to Nitrile



Stable nitroxyl radicals, such as 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO) and related derivatives, have been utilized in Cu-catalyzed alcohol oxidation as a cocatalyst. Since Sammelhack et al. reported Cu/TEMPO-catalyzed alcohol oxidation in 1984 for the first time,[10] various Cu/nitroxyl radical catalyst systems have been developed for the enhancement of catalytic reactivity and wide substrate scope.[11,12] In 2004, the first transition-metal-free TEMPO-catalyzed aerobic oxidation of

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alcohol was developed by the Hu group.[13] They achieved aerobic catalytic turnover of TEMPO using Br_2/$NaNO_2$. After their pioneering work, a variety of TEMPO-catalyzed aerobic alcohol oxidations employing cocatalysts such as *tert*-butyl nitrite, NH_2OH, and NH_4NO_3 have been published.[14] Recently, the use of less sterically hindered bicyclic nitroxyl radicals, such as 2-azaadamantane-*N*-oxyl (AZADO), 9-azabicyclo[3.3.1]nonane-*N*-oxyl (ABNO), and their derivatives, facilitated secondary and sterically hindered primary alcohol oxidation, which are challenging in TEMPO-catalyzed aerobic oxidation.[15] Despite significant progress of the nitroxyl/NO_x catalyst system in preparing aldehyde or ketone from alcohol,[16] the application of nitroxyl/NO_x in nitrile synthesis has not been investigated.

Recently, Bailey et al. achieved oxidative nitrile synthesis from primary amines as well as aldehydes using a stoichiometric amount of 4-acetamido-2,2,6,6-tetramethylpiperidine-1-oxoammonium tetrafluoroborate (Scheme 2).[17] From Bailey's results, we envisioned that the nitroxyl/NO_x system is able to facilitate aerobic imine oxidation as well as aerobic alcohol/amine oxidation. To prove our hypothesis, we investigate the aerobic oxidative conversion of 4-methyl benzaldehyde (**1a**) to 4-methyl

Scheme 2. Oxoammonium Salt-Mediated Amine to Nitrile Oxidation

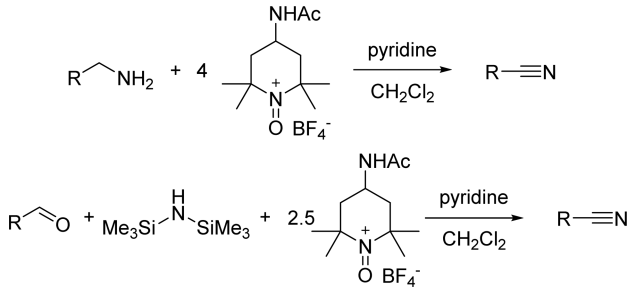
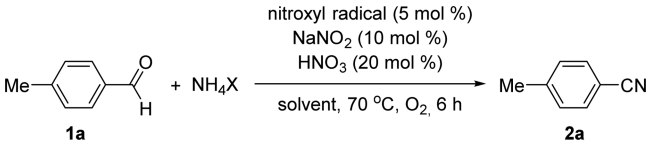
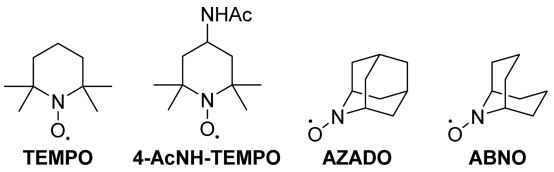


Table 1. Optimization of Nitroxyl/NO_x-Catalyzed Oxidative Nitrile Synthesis from Aldehyde[a]



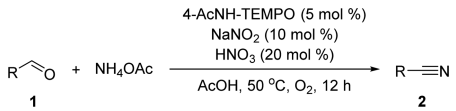
1a **2a**

entry	nitroxyl radical	NH_4X	solvent	yield (%)[b]
1	TEMPO	NH_3 (aq)	CH_3CN	5
2	TEMPO	NH_4Cl	CH_3CN	trace
3	TEMPO	NH_4OAc	CH_3CN	11
4	TEMPO	NH_4OAc	DMF	trace
5	TEMPO	NH_4OAc	DMSO	trace
6	TEMPO	NH_4OAc	AcOH	54
7	4-AcNH-TEMPO	NH_4OAc	AcOH	63
8	AZADO	NH_4OAc	AcOH	17
9	ABNO	NH_4OAc	AcOH	11
10[c]	4-AcNH-TEMPO	NH_4OAc	AcOH	91
11[c,d]	4-AcNH-TEMPO	NH_4OAc	AcOH	85
12[c,e]	4-AcNH-TEMPO	NH_4OAc	AcOH	63

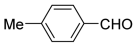
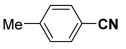
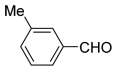
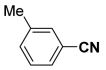
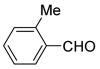
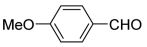
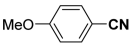
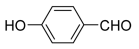
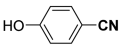
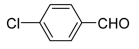
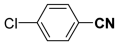
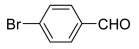
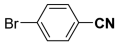
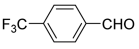
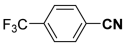
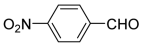
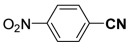
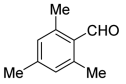
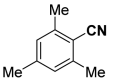
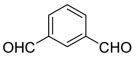
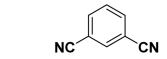
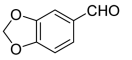
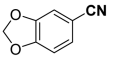


[a]Reaction conditions: **1a** (0.5 mmol), NH_4X (2.4 equiv), nitroxyl radical (5 mol %), $NaNO_2$ (10 mol %), and HNO_3 (20 mol %) in solvent (1.0 mL) under an O_2 balloon at 70 °C for 6 h. [b]Yield determined by ^1H NMR (internal standard: 1,1,2,2-tetrachloroethane). [c]Carried out at 50 °C for 12 h. [d]Without $NaNO_2$. [e]Under air.

Table 2. Nitroxyl/NO_x-Catalyzed Aerobic Oxidative Conversion of Aldehydes to Nitriles[a]



1 **2**

entry	aldehyde	nitrile	yield (%)
1			90
2			92
3			96
4			90, 99[b]
5			43
6			94
7			97
8			87
9			91
10			56
11			68[c,d]
12			88, 94[b]
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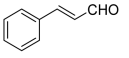
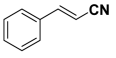
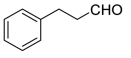
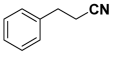
16			40, 99[b]
17			-

[a]Reaction conditions: **1** (0.5 mmol), NH_4OAc (2.4 equiv), 4-AcNH-TEMPO (5 mol %), $NaNO_2$ (10 mol %), and HNO_3 (20 mol %) in AcOH (1.0 mL) under an O_2 balloon at 50 °C for 12 h. [b]Used 10 mol % of 4-AcNH-TEMPO. [c]Used 4.8 equiv of NH_4OAc. [d]^1H NMR yield because of volatile product.

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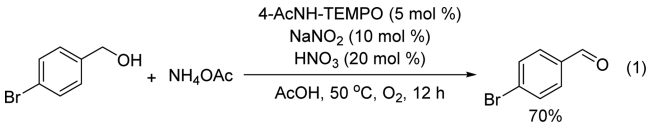
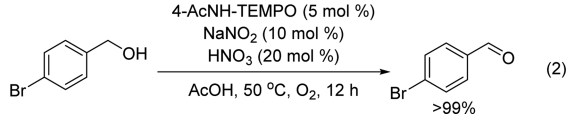
benzonitrile (**2a**) in the presence of nitroxyl radical, $NaNO_2$, and HNO_3 (Table 1). Gratifyingly, the TEMPO/$NaNO_2$/HNO_3 system catalyzed oxidative conversion of aldehyde to nitrile, and NH_4OAc showed the best result among the ammonia sources tested (entries 1−3). The effect of solvent was crucial. When acetic acid (AcOH) was employed as a solvent, **2a** was obtained in 54% yield, whereas other polar solvents, such as DMF and DMSO, produced a negligible amount of nitrile (entries 4−6).[18] The use of 4-acetamido-2,2,6,6-tetramethylpiperidine-*N*-oxyl (4-AcNH-TEMPO) instead of TEMPO showed better yield than TEMPO; however, bicyclic nitroxyl radicals, such as AZADO[19] and ABNO,[20] gave poor results (entries 7−9). During the optimization, we observed that 4-methyl benzoic acid was produced as a major side product, which is generated by direct oxidation of aldehyde.[21] To reduce benzoic acid formation, we decreased the reaction temperature and increased the reaction time, and this delicate tuning produced nitriles selectively in 91% yield (entry 10). Control experiments revealed that 4-AcNH-TEMPO, HNO_3, and O_2 are necessary for successful transformation.[22] It is noteworthy that the present method occurred without $NaNO_2$ or under ambient conditions (entries 11 and 12). However, we decided to use $NaNO_2$ cocatalyst and O_2 balloon in further studies for the high yield of nitriles.[23]

With the optimized conditions in hand (Table 1, entry 10), we next examined the scope and limitations of the present method (Table 2). A variety of tolualdehydes (*o*-, *m*-, and *p*-) and 4-methoxybenzaldehyde underwent oxidative conversions to afford the corresponding nitriles in good to excellent yields (entries 1−4). The conversion of 4-hydroxybenzaldehyde, which was a problematic substrate in Cu/TEMPO-catalyzed aerobic oxidation[12a] produced 4-hydroxybenzonitrile in moderate yield (entry 5). Halide substituents that can be used in subsequent coupling reactions were tolerated in the reaction (entries 6 and 7). Benzaldehydes bearing electron-withdrawing substituents also underwent oxidative conversion to produce nitriles in high yields (entries 8 and 9). Sterically hindered substrates like mesitaldehyde (2,4,6-trimethylbenzaldehyde) showed moderate yield in the optimized conditions (entry 10). The oxidation of isophthalaldehyde, which has two aldehyde groups, generated 1,3-dicyanobenzene in the presence of 4.8 equiv of NH_4OAc (entry 11). Polycyclic and heteroaromatic substrates, such as piperonal, 1-naphthaldehyde, furfural, and 2-thiophenecarboxaldehyde, showed effective transformation to the corresponding nitriles (entries 12−15). The reaction of allylic aldehydes, such as cinnamaldehyde, was sluggish under the optimized conditions, but high yield of cinnamonitrile was obtained by increasing the 4-AcNH-TEMPO catalyst loading to 10 mol % (entry 16). Oxidative conversion of the aliphatic aldehyde was problematic (entry 17).



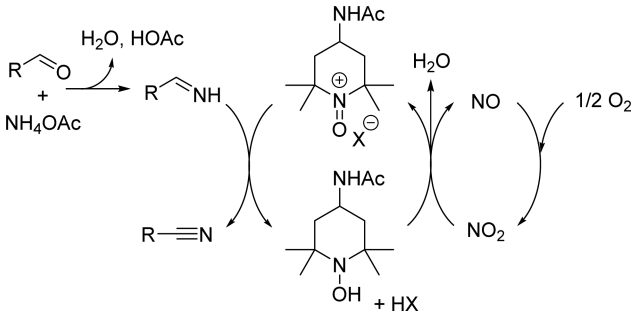


Next, we envisioned oxidative conversion of primary alcohol to nitrile using our method. The oxidative conversion of 4-bromobenzyl alcohol under the optimized conditions gave only 4-bromobenzaldehyde in 70% yield (eq 1). However, the same reaction without NH_4OAc produced 4-bromobenzaldehyde in a quantitative yield (eq 2). These results indicate that aerobic alcohol oxidation into aldehyde was interrupted by NH_4OAc, which is required for the synthesis of nitriles. To accomplish alcohol to nitrile transformation using the present method, we tried to carry out a one-pot sequential reaction. After initial alcohol oxidation in the presence of 4-AcNH-TEMPO, $NaNO_2$, and HNO_3 for 1 h, the solution of NH_4OAc in AcOH was added. After 12 h, the one-pot operation of the two oxidations was successful to generate 4-bromobenzonitrile in good overall yield as expected (Scheme 3).

Scheme 3. One-Pot Aerobic Oxidative Conversion of Alcohol to Nitrile

The proposed mechanism of the present aerobic oxidative conversion of aldehydes to nitriles is described in Scheme 4.[15]

Scheme 4. Proposed Mechanism for Aerobic Oxidative Nitrile Synthesis from Aldehyde Using the Nitroxyl/NO_x System



The combination of two redox cycles (oxoammonium/hydroxylamine and NO/NO_2) facilitates the use of molecular oxygen as a terminal oxidant in the present reaction.

In summary, we have developed a nitroxyl/NO_x system catalyzed oxidative conversion of aldehydes to nitriles under aerobic conditions. Various benzaldehydes underwent condensation with NH_4OAc and following aerobic oxidation to produce benzonitriles selectively. In addition, oxidative conversion of primary alcohol to nitrile was achieved by a one-pot strategy. The proposed mechanism was depicted on the basis of our insight and previously reported references.

EXPERIMENTAL SECTION

General Considerations. All commercially available compounds and solvents were purchased and used as received unless otherwise noted. Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 F254 plates. Visualization on TLC was achieved by the use of UV light (254 nm) and treatment with phosphomolybdic acid stain followed by heating. Flash chromatography was performed using Silica gel (particle size 40−63 um, 230−400 mesh). ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded on a 400 MHz NMR (400 MHz for ^1H, 101 MHz for ^{13}C) spectrometer. Chemical shift values are given in parts per million relative to internal TMS (0.00 ppm for ^1H) or $CDCl_3$ (77.06 ppm for ^{13}C). The following abbreviations were used to describe peak splitting patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet,

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dd = double of doublet, dt = double of triplet, and td = triple of doublet. Coupling constants (J) were reported in hertz unit (Hz).

Procedure for Optimization of Nitroxyl/NO_x-Catalyzed Aerobic Oxidative Conversion of Aldehydes to Nitriles (Table 1). A 15 mm flame-dried test tube, which was equipped with a magnetic stir bar and charged with nitroxyl radical (5 mol %, 0.025 mmol), NH_4X (2.4 equiv, 1.2 mmol), and $NaNO_2$ (10 mol %, 0.05 mmol, 3.5 mg), was evacuated and backfilled with oxygen (this process was repeated 3 times). After 0.5 mL of solvent was added, 4-methylbenzaldehyde (0.5 mmol, 59.0 μL), HNO_3 (20 mol %, 0.1 mmol, 6.4 μL), and solvent (0.5 mL) were added in sequence. The solution was stirred at 70 °C under an O_2 balloon. After the indicated time, the reaction was cooled to room temperature and diluted by adding EtOAc and water. Two layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The ^{1}H NMR yield of the desired product was determined by integration using an internal standard (1,1,2,2-tetrachloroethane).

General Procedure for Aerobic Oxidative Conversion of Aldehydes to Nitriles Catalyzed by 4-AcNH-TEMPO/$NaNO_2$/HNO_3 (Table 2). A 15 mm flame-dried test tube, which was equipped with a magnetic stir bar and charged with aldehyde (0.5 mmol, in case of solid), 4-AcNH-TEMPO (5 mol %, 0.025 mmol, 5.4 mg), NH_4OAc (2.4 equiv, 1.2 mmol, 92.5 mg), and $NaNO_2$ (10 mol %, 0.05 mmol, 3.5 mg), was evacuated and backfilled with oxygen (this process was repeated 3 times). After 0.5 mL of AcOH was added, aldehyde (0.5 mmol, in case of liquid), HNO_3 (20 mol %, 0.1 mmol, 6.4 μL), and AcOH (0.5 mL) were added in sequence. The solution was stirred at 50 °C under an O_2 balloon. After 12 h, the reaction was cooled to room temperature and diluted by adding EtOAc and a saturated aqueous Na_2CO_3 solution. Two layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were concentrated to a volume of approximately 20 mL by an evaporator. To eliminate the remaining aldehyde, we added aqueous 1 M sodium metabisulfite solution (20 mL) to the organic layer and stirred for 2 h.[8c] The reaction mixture was then transferred to a separating funnel, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by column chromatography to give nitrile products.

4-Methylbenzonitrile[8b] *(Table 2, entry 1).* EA/hexane = 1:5, 90% (52.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 7.9 Hz, 2H), 2.45 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 143.7, 132.0, 129.8, 119.1, 109.3, 21.8.

3-Methylbenzonitrile[24] *(Table 2, entry 2).* EA/hexane = 1:5, 92% (53.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 2H), 7.41 (d, J = 7.4 Hz, 1H), 7.35 (t, J = 7.8 Hz, 1H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 139.2, 133.6, 132.5, 129.2, 129.0, 119.0, 112.2, 21.1.

2-Methylbenzonitrile[23] *(Table 2, entry 3).* EA/hexane = 1:5, 96% (56.1 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.7 Hz, 1H), 7.48 (t, J = 7.5 Hz, 1H), 7.31 (d, J = 7.8 Hz, 1H), 7.27 (t, J = 7.4 Hz, 1H), 2.55 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 141.9, 132.6, 132.5, 130.2, 126.2, 118.1, 112.8, 20.5.

4-Methoxybenzonitrile[8c] *(Table 2, entry 4).* EA/hexane = 1:5, 90% (59.8 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 9.0 Hz, 2H), 6.95 (d, J = 8.9 Hz, 2H), 3.86 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.8, 133.9, 119.2, 114.7, 103.9, 55.5.

4-Hydroxybenzonitrile[25] *(Table 2, entry 5).* EA/hexane = 1:5, 43% (25.4 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.6 Hz, 2H), 6.94 (d, J = 8.6 Hz, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.3, 134.3, 119.3, 116.5, 103.0.

4-Chlorobenzonitrile[8c] *(Table 2, entry 6).* EA/hexane = 1:5, 94% (64.5 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.6 Hz, 2H), 7.47 (d, J = 8.6 Hz, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 139.5, 133.4, 129.7, 117.9, 110.8.

4-Bromobenzonitrile[8c] *(Table 2, entry 7).* EA/hexane = 1:5, 97% (88.2 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.5 Hz, 2H), 7.53 (d, J = 8.6 Hz, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 133.4, 132.6, 128.0, 118.0, 111.2.

4-(Trifluoromethyl)benzonitrile[26] *(Table 2, entry 8).* EA/hexane = 1:5, 87% (74.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.4 Hz, 2H), 7.77 (d, J = 8.3 Hz, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 134.5 (q, J_2 = 33.4 Hz), 132.7, 126.2 (q, J_3 = 3.7 Hz), 123.0 (q, J_1 = 273.0 Hz), 117.4, 116.0.

4-Nitrobenzonitrile[8c] *(Table 2, entry 9).* EA/hexane = 1:5, 91% (67.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.8 Hz, 2H), 7.91 (d, J = 8.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 150.0, 133.5, 124.3, 118.3, 116.8.

2,4,6-Trimethylbenzonitrile[27] *(Table 2, entry 10).* EA/hexane = 1:5, 56% (40.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (s, 2H), 2.48 (s, 6H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.8, 141.9, 128.2, 117.6, 110.3, 21.6, 20.6.

Isophthalonitrile[26] *(Table 2, entry 11).* Crude ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.93 (d, J = 8.0 Hz, 2H), 7.68 (t, J = 7.9 Hz, 1H).

Piperonitrile[8b] *(Table 2, entry 12).* EA/hexane = 1:5, 88% (64.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, J = 8.1 Hz, 1H), 7.03 (s, 1H), 6.87 (d, J = 8.1 Hz, 1H), 6.07 (s, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 151.5, 148.0, 128.2, 118.9, 111.4, 109.1, 104.9, 102.2.

1-Naphthonitrile[8b] *(Table 2, entry 13).* EA/hexane = 1:5, 92% (70.5 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.3 Hz, 1H), 8.06 (d, J = 8.3 Hz, 1H), 7.90 (t, J = 7.4 Hz, 2H), 7.67 (t, J = 7.6 Hz, 1H), 7.60 (t, J = 7.5 Hz, 1H), 7.50 (t, J = 7.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 133.3, 132.9, 132.6, 132.3, 128.6, 128.6, 127.5, 125.1, 124.9, 117.8, 110.2.

2-Furonitrile[8c] *(Table 2, entry 14).* Crude ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.1 (d, J = 3.3 Hz, 1H), 6.56 (d, J = 1.6 Hz, 1H).

Thiophene-2-carbonitrile[8c] *(Table 2, entry 15).* EA/hexane = 1:5, 73% (39.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65−7.61 (m, 2H), 7.15−7.13 (m, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 137.4, 132.5, 127.6, 114.2, 109.9.

Cinnamonitrile[8c] *(Table 2, entry 16).* EA/hexane = 1:5, 40% (25.9 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.37 (m, 6H), 5.87 (d, J = 16.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 150.6, 133.5, 131.2, 129.1, 127.4, 118.2, 96.3.

One-Pot Procedure for the Oxidative Conversion of Alcohol to Nitrile (Scheme 3). A 15 mm flame-dried test tube, which was equipped with a magnetic stir bar and charged with 4-bromobenzylalcohol (0.5 mmol, 92.5 mg), 4-AcNH-TEMPO (5 mol %, 0.025 mmol, 5.4 mg), and $NaNO_2$ (10 mol %, 0.05 mmol, 3.5 mg) was evacuated and backfilled with oxygen (this process was repeated 3 times). After 0.5 mL of AcOH was added, HNO_3 (20 mol %, 0.1 mmol, 6.4 μL) and AcOH (0.5 mL) were added in sequence. The solution was stirred at 50 °C under an O_2 balloon. After no alcohol spot was observed on TLC (~1 h), NH_4OAc (2.4 equiv, 1.2 mmol, 92.5 mg) in AcOH (1 mL) solution was added. After an additional 12 h, the reaction was cooled to room temperature and diluted by adding EtOAc and a saturated aqueous Na_2CO_3 solution. Two layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were concentrated to a volume of approximately 20 mL by evaporator. To eliminate any remaining aldehyde, we added aqueous 1 M sodium metabisulfite solution (20 mL) to the organic layer and stirred for 2 h. The reaction mixture was then transferred to a separating funnel, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by column chromatography to give 4-bromobenzonitrile in 88% (80 mg) yield.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02333.

Control experiments and ^{1}H and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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