Copper-catalyzed aerobic conversion of C=O bond of ketones to C≡N bond using ammonium salt as nitrogen source

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Supporting Information

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1. General information

Unless otherwise noted, all reagents and solvents were obtained from commercial suppliers and used without further purification. All products were characterized by GC-MS, $^1$H NMR and $^{13}$C NMR. Mass spectra were measured on a mass instrument (El). $^1$H NMR and $^{13}$C NMR spectra were recorded at 400 MHz and 101 MHz in CDCl$_3$ or DMSO-$d_6$ using TMS as internal standard. Multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quintet), and m (multiplet), and coupling constants ($J$) are reported in hertz. The yield of benzonitrile and conversion of acetophenone were detected by gas phase chromatography, using a RTX-5 capillary column and a frame ionization detector (FID).

2. Typical procedure for the synthesis of nitriles from ketones

A Schlenk tube was charged with ketones 1 or 3 (1.0 mmol), Cu(OAc)$_2$ (54 mg, 0.3 mmol), TBAI (111 mg, 0.3 mmol), (NH$_4$)$_2$CO$_3$ (157 mg, 1.0 mmol), and DMSO (3.0 mL), and the reaction mixture was stirred at 120°C under oxygen atmosphere for 5 h. After cooling to room temperature, the solution was then diluted with ethyl acetate ($3 \times 10$ mL). The organic layers were combined, dried over Na$_2$SO$_4$, filtered and concentrated under vacuum and purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 10/1) to obtain the desired product 2.

3. Optimization of reaction conditions

Table S1. Screening of Reaction Conditions.*

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<th>Solvent</th>
<th>Conv.(%)$^b$</th>
<th>Yield(%)$^b$</th>
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The detection of benzaldimine and cleavage fragment by GC-MS could be determined by GC-MS.

In order to verify if imines can be formed from aldehydes in the presence of ammonium salts, benzoaldehyde was chosen to react with (NH₄)₂CO₃ under N₂ atmosphere. Not only trace (<5%) of benzonitrile was obtained, but also trace amount (<1%) of the corresponding benzaldimine (5) could be determined by GC-MS.

4. The detection of benzaldimine and cleavage fragment by GC-MS
In order to identify the fragment of the ketones, substrate acetophenone (1a), propiophenone (3a) and valerophenone (3e) were tested under the standard conditions. As expected, apart from the generation of benzonitrile (2a), trace amount of formamide (7a), acetamide (7b) and n-butyramide (7e) could be detected by GC-MS, respectively.

In order to explain why only trace amount of amide was detected for 1a, 3a and 3e, n-butyramide was used as the substrate under the standard conditions to test the stability of the
aliphatic amides under the copper/O₂ catalyst system. The amount of the n-butyramide was quantified by GC using bromobenzene as the internal standard before and after the reaction (the spectrum of GC were shown as below). Before reaction, the n-butyramide was quantified as 87 mg (the ratio of the peak area of n-butyramide to bromobenzene was 236136/284648). After reaction, the n-butyramide was quantified as 32 mg (the ratio of the peak area of n-butyramide to bromobenzene was 128214/425740). Which revealed that the amount of n-butyramide was declined dramatically after reaction. These results implied the aliphatic amides may be unstable under the copper/O₂ catalyst system, so only trace amount of formamide, acetamide and n-butyramide could be detected by GC-MS, but 40% yield of benzamide could be isolated from 1,2-diphenylethanone (3i).

5. Characterization data of products

(1) Benzonitrile (2a).

Following general procedure, 2a was obtained from 1a, 3a, 3c, 3i, 4a, 6, 7 and 8 in 80% (82 mg), 46% (47 mg), 49% (50 mg), 62% (64 mg), 87% (90 mg), 92% (95 mg), 61% (63 mg) and 86% (89 mg) yield as colorless oil, respectively (the yield was detected by GC using bromobenzene as internal standard). ¹H NMR (CDCl₃, 400 MHz): δ = 7.67–7.58 (m, 3H), 7.50–7.45 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz,): δ = 132.8, 132.1, 129.2, 118.9, 112.4; LRMS (El 70 ev): m/z (%): 103 (M⁺, 100); Known compound.¹

(2) 4-Methoxybenzonitrile (2b).

Following general procedure, 2b was obtained from 1b, 3b, 3f in 90% (119 mg), 48% (64 mg) and 59% (78 mg) yield as colorless solid, respectively. ¹H NMR (CDCl₃, 400 MHz): δ = 7.59 (d, J = 8.8 Hz, 2H), 6.95 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ = 162.9, 134.0, 119.3, 114.8, 104.0, 55.6; LRMS (El 70 ev): m/z (%): 133 (M⁺, 100); Known compound.¹

(3) 4-Ethoxybenzonitrile (2c).
Following general procedure, 2c was obtained from 1c in 88% (129 mg) yield as colorless solid. \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta = 7.57\) (d, \(J = 8.9\) Hz, 2H), 6.93 (d, \(J = 8.9\) Hz, 2H), 4.08 (q, \(J = 7.0\) Hz, 2H), 1.44 (t, \(J = 7.0\) Hz, 3H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz,): \(\delta = 162.3, 134.0, 119.3, 115.2, 103.6, 64.0, 14.6\); LRMS (EI 70 ev): \(m/\zeta\) (%): 147 (M\(^+\), 100); Known compound.\(^2\)

(4) **4-**-**tert-butylbenzonitrile (2d).**

Following general procedure, 2d was obtained from 1d in 80% (127 mg) yield as colorless oil. \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta = 7.59\) (d, \(J = 8.0\) Hz, 2H), 7.48 (d, \(J = 8.0\) Hz, 2H), 1.33 (s, 9H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz,): \(\delta = 156.7, 132.0, 126.2, 119.2, 109.3, 35.3, 31.0\); LRMS (EI 70 ev): \(m/\zeta\) (%): 159 (M\(^+\), 100); Known compound.\(^1\)

(5) **4-Methylbenzonitrile (2e).**

Following general procedure, 2e was obtained from 1e and 3c in 86% (101 mg) and 45% (53 mg) yield as colorless oil, respectively. \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta = 7.54\) (d, \(J = 8.0\) Hz, 2H), 7.48 (d, \(J = 8.0\) Hz, 2H), 2.42 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz,): \(\delta = 142.7, 131.0, 128.8, 118.2, 108.3, 20.8\); LRMS (EI 70 ev): \(m/\zeta\) (%): 117 (M\(^+\), 100); Known compound.\(^1\)

(6) **2-Methylbenzonitrile (2f).**

Following general procedure, 2f was obtained from 1f in 68% (79 mg) yield as colorless oil. \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta = 7.59\) (d, \(J = 7.7\) Hz, 1H), 7.48 (t, \(J = 7.6\) Hz, 1H), 7.34 – 7.24 (m, 2H), 2.55 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz,): \(\delta = 141.9, 132.7, 132.5, 130.2, 126.2, 118.2, 112.8, 20.5\); LRMS (EI 70 ev): \(m/\zeta\) (%): 117 (M\(^+\), 100); Known compound.\(^3\)

(7) **3-Methylbenzonitrile (2g).**

Following general procedure, 2g was obtained from 1g in 75% (84 mg) yield as colorless oil. \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta = 7.46\) (s, 2H), 7.41 (d, \(J = 7.7\) Hz, 1H), 7.38 – 7.32 (m, 1H), 2.39 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz,): \(\delta = 139.2, 133.7, 132.5, 129.3, 129.0, 119.1, 112.2, 21.2\); LRMS (EI 70 ev): \(m/\zeta\) (%): 117 (M\(^+\), 100); Known compound.\(^4\)

(8) **3,4-Dimethoxybenzonitrile (2h).**

Following general procedure, 2h was obtained from 1h in 89% (145 mg) yield as white solid. \(^1\)H NMR
(CDCl$_3$, 400 MHz): $\delta$ = 7.29 (dd, $J$ = 8.4, 1.9 Hz, 1H), 7.08 (d, $J$ = 1.8 Hz, 1H), 6.91 (d, $J$ = 8.4 Hz, 1H), 3.94 (s, 3H), 3.91 (s, 3H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ = 152.9, 149.2, 126.5, 119.2, 113.9, 111.2, 103.8, 56.1; LRMS (EI 70 ev): m/z (%): 163 (M$^+$, 100); Known compound.$^2$

(9) 2,4,6-Trimethylbenzonitrile (2i).

Following general procedure, 2i was obtained from 1i in 71% (103 mg) yield as white solid. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ = 6.93 (d, $J$ = 0.4 Hz, 2H), 2.48 (s, 6H), 2.32 (s, 3H); $^{13}$C NMR (CDCl$_3$, 100 MHz,): $\delta$ = 142.8, 142.0, 128.2, 117.8, 110.6, 21.6, 20.6; LRMS (EI 70 ev): m/z (%): 145 (M$^+$, 100); Known compound.$^1$

(10) 4-Fluorobenzonitrile (2j).

Following general procedure, 2j was obtained from 1j and 3g in 65% (79 mg) and 49% (59 mg) yield as colorless solid, respectively. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ = 7.69 (dd, $J$ = 8.7, 5.2 Hz, 2H), 7.19 (t, $J$ = 8.5 Hz, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz,): $\delta$ = 165.0 (d, $J$ = 256.5 Hz), 134.6 (d, $J$ = 9.3 Hz), 118.0, 116.8 (d, $J$ = 22.7 Hz), 108.5 (d, $J$ = 3.7 Hz); LRMS (EI 70 ev): m/z (%): 121 (M$^+$, 100); Known compound.$^5$

(11) 4-Chlorobenzonitrile (2k).

Following general procedure, 2k was obtained from 1k and 3c in 85% (117 mg) and 49% (67 mg) yield as colorless solid, respectively. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ = 7.61 (d, $J$ = 8.5 Hz, 2H), 7.47 (d, $J$ = 8.5 Hz, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz,): $\delta$ = 139.5, 133.3, 129.6, 117.8, 110.7; LRMS (EI 70 ev): m/z (%): 137 (M$^+$, 100); Known compound.$^1$

(12) 4-Bromobenzonitrile (2l).

Following general procedure, 2l was obtained from 1l in 77% (141 mg) yield as yellow solid. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ = 7.64 (d, $J$ = 8.5 Hz, 2H), 7.53 (d, $J$ = 8.5 Hz, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz,): $\delta$ = 133.4, 132.7, 128.0, 118.1, 111.3; LRMS (EI 70 ev): m/z (%):183 (M$^+$, 100), 181 (95); Known compound.$^1$

(13) 2-Bromobenzonitrile (2m).

Following general procedure, 2m was obtained from 1m in 70% (127 mg) yield as colorless solid. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ = 7.69 (ddd, $J$ = 10.9, 7.9, 1.8 Hz, 2H), 7.51 – 7.39 (m, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz,): $\delta$ = 134.3, 133.9, 133.2, 127.6, 125.4, 117.2, 115.9; LRMS (EI 70 ev): m/z (%):183 (M$^+$, 100), 181 (95); Known compound.$^1$

(14) 3-Bromobenzonitrile (2n).
Following general procedure, 2n was obtained from 1n in 72% (130 mg) yield as colorless solid. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta = 7.81$ (s, 1H), 7.75 (d, $J = 8.1$ Hz, 1H), 7.61 (d, $J = 7.7$ Hz, 1H), 7.37 (t, $J = 8.0$ Hz, 1H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta =$ 136.1, 134.7, 130.7, 130.6, 122.9, 117.3, 114.2. LRMS (EI 70 ev): $m/z$ (%) 183 (M$^+$, 100), 181 (95); Known compound.$^1$

(15) 4-iodobenzonitrile (2o).

Following general procedure, 2o was obtained from 1o in 82% (188 mg) yield as white solid. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta =$ 7.77 (d, $J = 8.4$ Hz, 2H), 7.29 (d, $J = 8.4$ Hz, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz,): $\delta =$ 138.5, 133.2, 118.3, 111.8, 100.4; LRMS (EI 70 ev): $m/z$ (%) 229 (M$^+$, 100); Known compound.$^1$

(16) 4-Nitrobenzonitrile (2p).

Following general procedure, 2p was obtained from 1p in 75% (111 mg) as colorless solid. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta =$ 8.37 (d, $J = 8.3$ Hz, 2H), 7.91 (d, $J = 8.3$ Hz, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz,): $\delta =$ 150.1, 133.5, 124.3, 118.4, 116.8; LRMS (EI 70 ev): $m/z$ (%) 148 (M$^+$, 100); Known compound.$^1$

(17) 1,4-Benzenedicarbonitrile (2q).

Following general procedure, 2q was obtained from 1q in 49% (63 mg) yield as white solid; $^1$H NMR (DMSO-d$_6$, 400 MHz): $\delta =$ 8.10 (s, 4H); $^{13}$C NMR (DMSO-d$_6$, 100 MHz,): $\delta =$ 133.7, 118.0, 116.2; LRMS (EI 70 ev): $m/z$ (%) 128 (M$^+$, 100); Known compound.$^1$

(18) 2-Naphthonitrile (2r).

Following general procedure, 2r was obtained from 1r in 63% (96 mg) yield as yellow solid. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta =$ 8.23 (s, 1H), 7.90 (t, $J = 8.4$ Hz, 3H), 7.69 – 7.56 (m, 3H); $^{13}$C NMR (CDCl$_3$, 100 MHz,): $\delta =$ 134.6, 134.2, 132.2, 129.2, 129.0, 128.4, 128.1, 127.7, 126.3, 119.3, 109.4; LRMS (EI 70 ev): $m/z$ (%) 153 (M$^+$, 100); Known compound.$^1$

(19) Thiophene-2-carbonitrile (2s).

Following general procedure, 2s was obtained from 1s in 59% (64 mg) yield as colorless oil. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta =$ 7.67 – 7.60 (m, 2H), 7.15 (dd, $J = 5.0$, 3.9 Hz, 1H); $^{13}$C NMR (CDCl$_3$, 100 MHz,): $\delta =$ 137.5, 132.7, 127.7, 114.3, 109.9; LRMS (EI 70 ev): $m/z$ (%) 10 (M$^+$, 100); Known compound.$^1$

(20) 3-Phenyl-acrylonitrile (2t).

Following general procedure, 2t was obtained from 3h in 35% (46 mg) yield as colorless oil. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta =$ 7.48 – 7.33 (m, 6H), 5.87 (d, $J = 16.7$ Hz, 1H); $^{13}$C NMR (CDCl$_3$, 100 MHz,): $\delta =$
Following general procedure, 3d was obtained from 3i and 4b in 40% (48 mg) and 48% (58 mg) yield as white solid, respectively. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta = 7.82$ (d, $J = 8.6$ Hz, 2H), 7.53 (t, $J = 7.4$ Hz, 1H), 7.45 (t, $J = 7.5$ Hz, 2H), 6.21 (s, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta = 169.7$, 133.2, 132.0, 128.7, 127.4; LRMS (EI 70 ev): m/z (%): 121 (M$^+$, 100); Known compound.\textsuperscript{8}

(22) 3,5-diphenyl-1,2,4-oxadiazole (10).

Following general procedure, 10 was obtained from 9 in 42% (47 mg) yield as white solid. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.23$ (d, $J = 7.3$ Hz, 2H), 8.18 (dd, $J = 6.6$, 2.7 Hz, 2H), 7.60 (d, $J = 7.2$ Hz, 1H), 7.58 – 7.50 (m, 5H); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta = 175.7$, 169.0, 132.8, 131.2, 129.1, 128.9, 128.2, 127.6, 127.0, 124.3; LRMS (EI 70 ev): m/z (%): 222 (M$^+$, 100); Known compound.\textsuperscript{9}
Reference


6. NMR Spectra of Products