Supporting Information for

Process Development of CuI/ABNO/NMI-Catalyzed Aerobic Alcohol Oxidation

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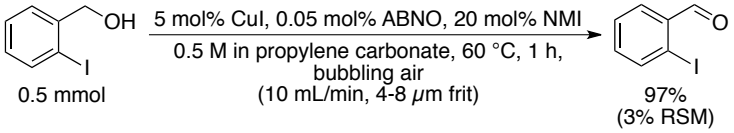
I. General Method for Screening Reaction Conditions.

A solution of Cu salt and NMI was added to a solution of alcohol (0.5 mmol) and biphenyl (internal standard; 0.25 mmol) in a 13 x 100 mm test tube. A solution of ABNO was then added, and the test tube was fitted with an Ace glass gas dispersion tube (7x135 mm, 4-8 μm frit) and sealed with a septum (cf. apparatus described in Representative Procedure for 10 mmol Scale Batch Reactions in the Experimental Section of the manuscript). The reaction was stirred at room temperature or at 60 °C in an oil bath and monitored by GC for 2 h. At this point, an aliquot (50 μL) of the reaction mixture was removed via syringe and diluted with 1 mL EtOAc and filtered through a pipet silica plug. The plug was rinsed with an additional 3 mL EtOAc, and an aliquot of filtrate was taken up for GC analysis.

Scheme S1. Oxidation of 2-Iodobenzyl Alcohol in Propylene Carbonate According to the General Procedure. Yield and RSM determined by ^{1}H NMR spectroscopy using biphenyl as int. standard.

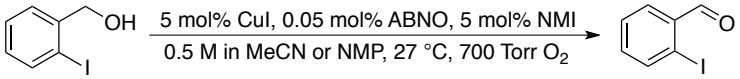


II. Method for Gas Uptake Analyses

Comparison of Solvents in the (NMI)Cu^I/ABNO-Catalyzed Aerobic Oxidation of 2-Iodobenzyl Alcohol (reaction shown in Figure 1).

For each reaction, 25 mL round-bottom flasks with stirbars were attached to an apparatus with a calibrated volume and a pressure transducer designed to measure the gas pressure within each of 5 sealed reaction vessels. The apparatus was evacuated and filled with O_2 to 500 Torr seven times. The pressure was established at 700 Torr and the flasks were heated to 27 °C. Solution A (below) was added *via* syringe through a septum, and then the pressure and temperature were allowed to equilibrate. When the pressure and temperature stabilized, Solution B was added *via* syringe through a septum. Data were acquired using custom software written within LabVIEW (National Instruments).

Table S1. Solution compositions for gas uptake experiment in Figure 1.



Reaction	Solution A	Solution B
1	2-iodobenzyl alcohol (234 mg, 1 mmol) in 1.5 mL MeCN	CuI (9.52 mg, 0.05 mmol), NMI (4 μL, 0.05 mmol), ABNO (0.07 mg, 0.0005 mmol) in 500 μL MeCN
2	2-iodobenzyl alcohol (234 mg, 1 mmol) in 1.5 mL NMP	CuI (9.52 mg, 0.05 mmol), NMI (4 μL, 0.05 mmol), ABNO (0.07 mg, 0.0005 mmol) in 500 μL NMP

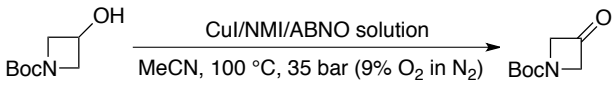
III. Stability of Catalyst Solutions for Flow Experiments

A solution of CuI and NMI or CuI, NMI, and ABNO stored for 1 day or 3 weeks (Table S2) was added to a solution of alcohol (0.25 mmol) and biphenyl (internal standard; 0.125 mmol) in a 10 x 75 mm heavy-walled test tube. A solution of ABNO was added to tubes containing only CuI, NMI, alcohol, and biphenyl. The reactions were loaded into a HEL CAT24 high pressure Hastelloy vessel, pressurized to 35 bar of 9% O_2 in N_2, heated to 100 °C, and shaken for 1 h. At this point, the apparatus was de-pressurized and the reactions were diluted with EtOAc (1 mL) and filtered through a pipet silica plug. Each plug was rinsed with additional EtOAc (3 mL), and filtrate was concentrated in vacuo before being taken up in $CDCl_3$ for ^1H NMR analysis. Yields are described in Table S3.

Table S2. Composition of prepared (NMI)Cu^I/ABNO solutions in MeCN at 22 °C.

solution number	solution composition	storage conditions
1	50 mM CuI, 50 mM NMI	air
2	50 mM CuI, 50 mM NMI	N_2
3	50 mM CuI, 50 mM NMI, 3 mM ABNO	air
4	50 mM CuI, 50 mM NMI, 3 mM ABNO	N_2
5	50 mM CuI, 100 mM NMI, 3 mM ABNO	air
6	50 mM CuI, 100 mM NMI, 3 mM ABNO	N_2
7	50 mM CuI, 150 mM NMI, 3 mM ABNO	air
8	50 mM CuI, 150 mM NMI, 3 mM ABNO	N_2

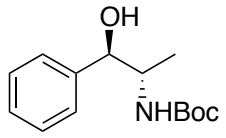
Table S3. Evaluation of catalyst solution activity after storage at 22 °C.



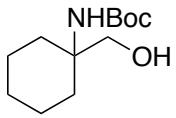
solution number	% yield (1 day)	% yield (3 weeks)
1	95	91
2	96	100
3	96	60
4	97	100
5	97	93
6	97	78
7	99	84
8	98	98

IV. Synthesis and Characterization of Substrates.

Representative Procedure for the Synthesis of Boc-Protected Aminoalcohols.

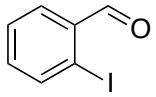


_N_-Boc-LD-norephedrine.
Boc_2O (3.32 g, 15.2 mmol, 1.15 equiv) was added to a stirred solution of norephedrine (2 g, 13.2 mmol, 1 equiv) in CH_2Cl_2 (55 mL) under N_2 at 0 °C. NEt_3 (2.3 mL, 13.2 mmol, 1 equiv) was then added dropwise *via* syringe. The resulting colorless solution was slowly warmed to r.t. and stirred for 48 h. At this point, the rxn was neutralized with aq. citric acid and the organic layer was washed with sat. aq. $NaHCO_3$, H_2O, and brine. The organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude material was purified by silica column chromatography (20-40% EtOAc/hexanes gradient elution) to yield the product as a white solid (3.05 g, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.22 (m, 5H), 4.84 (dd, J = 3.6, 3.6 Hz, 1H), 4.66 (d, J = 8 Hz, 1H), 4.00 (s, 1H), 3.30 (s, 1H), 1.46 (s, 9H), 0.98 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.39, 140.85, 128.14, 127.44, 126.35, 79.80, 76.80, 52.03, 28.42, 14.82. Spectral properties are consistent with literature values.[1]



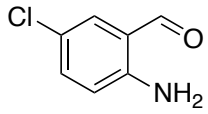
1-[1-(tert-butoxycarbonylamino)cyclohexyl]methanol.
The crude material was purified by silica column chromatography (30-100% EtOAc/hexanes gradient elution). A white crystalline solid (1.59 g, 75%) was isolated. ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.02 (s, 1H), 4.54 (t, J = 5.7 Hz, 1H), 3.37 (d, J = 5.8 Hz, 2H), 1.92 (d, J = 13.0 Hz, 2H), 1.54 – 1.13 (m, 8H), 1.39 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 155.34, 78.00, 66.79, 56.28, 31.34, 29.23, 26.33, 22.01. Spectral properties are consistent with literature values.[2]

V. Characterization of Aldehyde and Ketone Products.



1

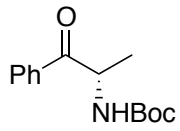
2-iodobenzaldehyde.
The product was isolated as a yellow oil (2.17 g, 94 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.07 (s, 1H), 7.96 (d, J = 7.9 Hz, 1H), 7.89 (d, J = 7.7 Hz, 1H), 7.47 (t, J = 7.4 Hz, 1H), 7.29 (dd, J = 7.7, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.79, 140.67, 135.50, 135.14, 130.28, 128.74, 100.73. Spectral properties are consistent with literature values.[3]



2

2-amino-5-chlorobenzaldehyde.

The product was isolated as a brown crystalline solid (1.52 g, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.81 (s, 1H), 7.45 (d, J = 2.6 Hz, 1H), 7.26 (dd, J = 8.8, 4 Hz, 1H), 6.62 (d, J = 8.8 Hz, 1H), 6.13 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.85, 148.35, 135.28, 134.32, 120.79, 119.31, 117.68. Spectral properties are consistent with literature values.[4]

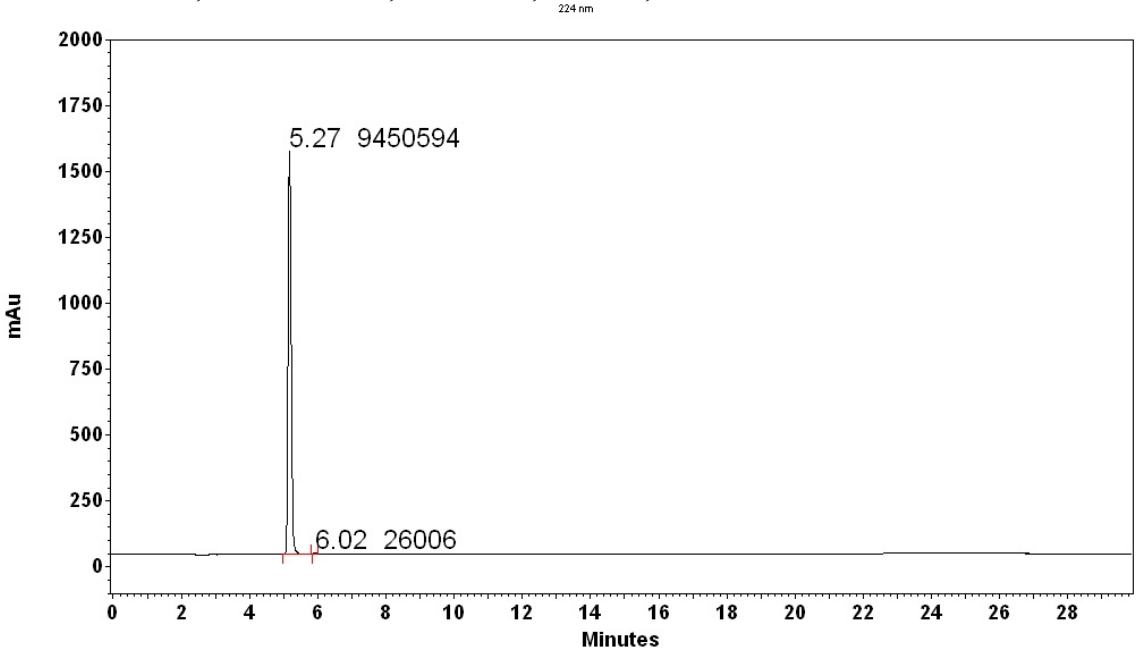


3

(*S*)-*N*-Boc-cathinone.

The product was isolated as a light yellow solid (2.41 g, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 7.1 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 5.57 (d, J = 6.9 Hz, 1H), 5.30 (m, 1H), 1.46 (s, 9H), 1.40 (d, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.48, 155.19, 134.22, 133.73, 128.84, 128.68, 79.72, 51.11, 28.40, 19.94. Spectral properties are consistent with literature values.[1]

Chiralcel OJ-*H*, 5-25% iPrOH, 1 mL/min, 254 nm, >99 % ee

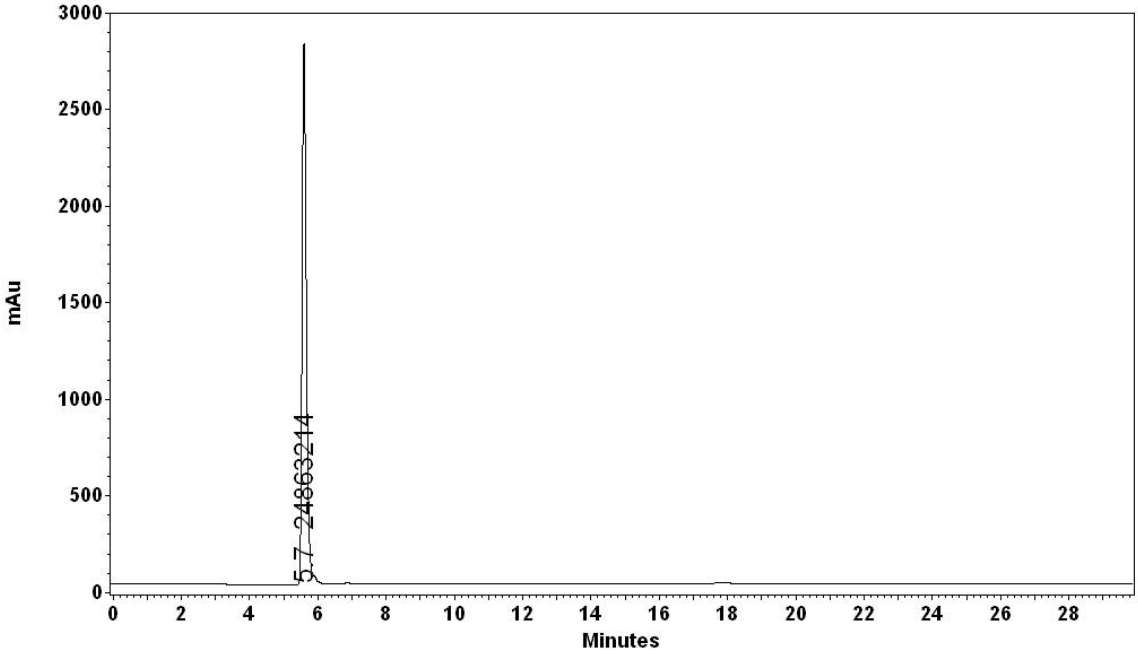


Method for independent preparation of (*S*)-*N*-Boc-cathinone.[5]

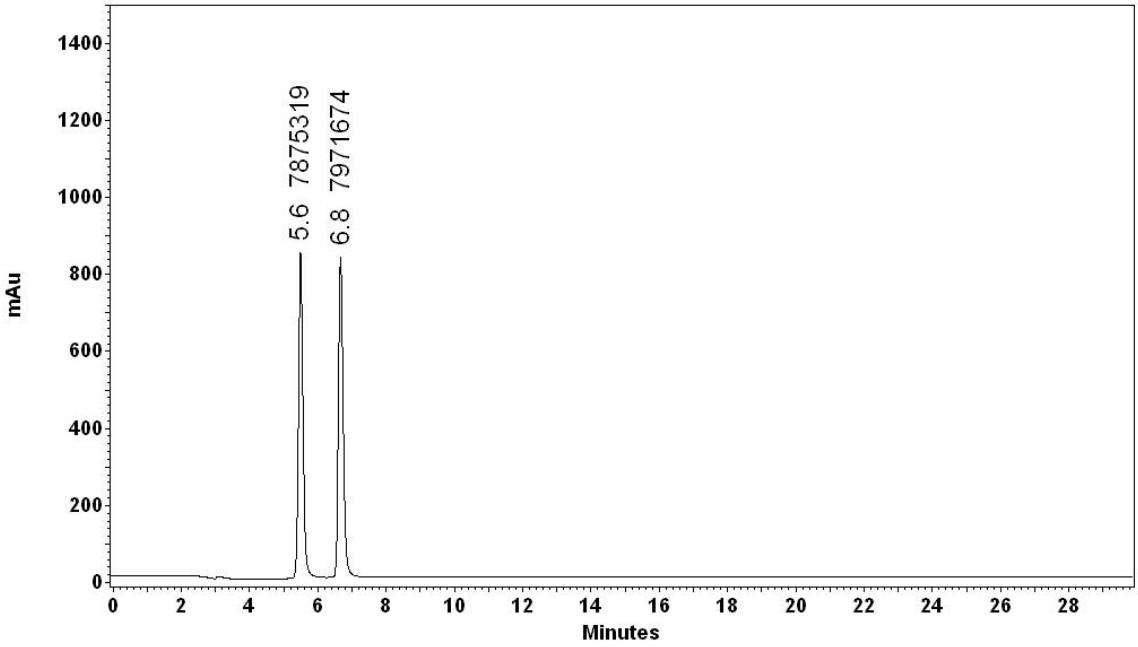
Dess Martin periodinane (445 mg, 1.05 mmol, 2.1 equiv) was added in one portion to a stirred solution of Boc-LD-norephedrine (126 mg, 0.5 mmol, 1 equiv) in H_2O-saturated CH_2Cl_2 (2 mL) at room temperature. The reaction was stirred for 20 min, then diluted with Et_2O (10 mL), sat. aq. $NaHCO_3$ (8 mL), and H_2O (2 mL). The reaction was stirred

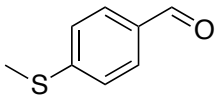
until both layers were clear, then diluted with sat. aq. $NaHCO_3$ and extracted with Et_2O (3 x 30 mL). The organic layers were combined, washed with H_2O (2x), brine, and dried over $MgSO_4$. The filtrate was concentrated in vacuo, yielding a white solid (121 mg, 97%) that was consistent with the desired product by ^1H NMR spectroscopy.

Chiralcel OJ-*H*, 5-25% iPrOH, 1 mL/min, 254 nm: analysis of (*S*)-*N*-Boc-cathinone.



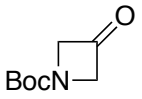
Chiralcel OJ-*H*, 5-25% iPrOH, 1 mL/min, 254 nm: analysis of racemic *N*-Boc-cathinone.





4

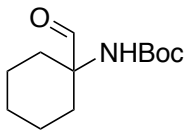
The product was isolated as a pale yellow oil (1.41 g, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.92 (s, 1H), 7.76 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 2.53 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.35, 148.05, 133.08, 130.12, 125.32, 14.83. Spectral properties are consistent with literature values.[3]



5

1-Boc-3-azetidinone.

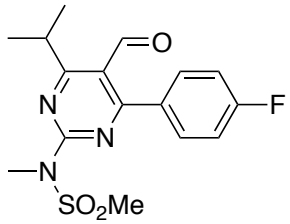
The product was isolated as a white crystalline solid (1.57 g, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.69 (s, 4H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.87, 156.24, 81.19, 71.23, 28.47. Spectral properties are consistent with commercially available product.



6

1-[1-(tert-butoxycarbonylamino)cyclohexyl]carboxaldehyde.

The product was isolated as a white solid (2.00 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (s, 1H), 4.86 (s, 1H), 1.76 – 1.65 (m, 8H), 1.44 (s, 9H), 1.37 – 1.22 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.93, 154.80, 80.29, 61.47, 29.68, 28.27, 25.05, 20.96. Spectral properties are consistent with literature values.[3]



Product in Scheme 2: *N*-[4-(4-Fluorophenyl)-5-formyl-6-isopropylpyrimidin-2-yl]-*N*-methylmethanesulfonamide.

The product was isolated as a white solid (3.44 g, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.67 – 7.59 (m, 2H), 7.29 – 7.18 (m, 2H), 4.01 (hept, J = 6.7 Hz, 1H), 3.64 (s, 3H), 3.55 (s, 3H), 1.32 (d, J = 6.7 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.72, 179.27, 170.02, 164.69 ($J_{C–F}$ = 253.5 Hz), 159.02, 132.86 ($J_{C–F}$ = 9.0 Hz), 132.35 ($J_{C–F}$ = 3.0 Hz), 119.74, 116.2 ($J_{C–F}$ = 22.2 Hz), 42.76, 33.32, 32.23, 21.93. Spectral properties are consistent with literature values.[6]

VI. References.

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