Copper-Catalyzed Aerobic Oxidation of Primary Alcohols to Carboxylic Acids

Yibo Yu,[a] Di Zhai,[a] Zhengnan Zhou,[a] Sheng Jiang,[a] Hui Qian, *,[a] and Shengming Ma*,[a,b]

[a] Research Center for Molecular Recognition and Synthesis, Department of Chemistry, Fudan University, 220 Handan Lu, Shanghai 200433, P. R. China.

[b] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Lu, Shanghai 200032, P. R. China.

Supplementary information

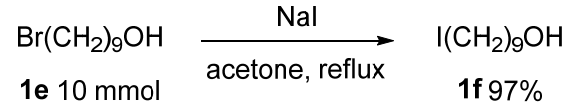
General Information. NMR spectra were taken with an Agilent-400 spectrometer (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR, 376 MHz for ^{19}F NMR). Flue gas analysis experiments were performed with a Testo 350 flue gas analyzer. All reactions were carried out in 25 mL Schlenk tubes unless otherwise mentioned. $Cu(NO_3)_2$•$3H_2O$ and $KHSO_4$ were purchased from Sinopharm Chemical Reagent Co., Ltd; TEMPO (98%) was purchased from Shanghai Darui Fine Chemical Co., Ltd.; DCE was used directly without further treatment. Recovery of substrates was determined by ^{1}H NMR analysis using dibromomethane as the internal standard.

Experimental details and analytical data

1. Preparation of alcohols

Alcohols were prepared following the literature methods[1-4] or used as received without further treatment. (*S*)-**1n,**[5] **5f-5g,**[3] **9a-9c,**[6] and **9d**[2] are known compounds and the analytical data matched those in the literature.

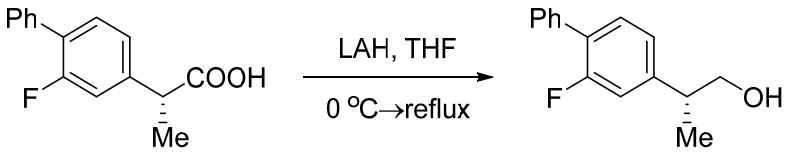
(1) Preparation of 9-iodononan-1-ol[1] (1f, yyb-2-111)



To a flask were added **1e** (2.2961 g, 97% purity, 10 mmol) and NaI (6.0565 g, 99% purity, 40 mmol). Then the flask was degassed and refilled with argon for three times. After the addition of acetone (20 mL), the resulting mixture was heated to 70 ℃ and stirred for 23 h until completion of the reaction as monitored by TLC (petroleum ether/ethyl acetate = 5/1). The resulting mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure. The residual was dissolved with diethyl ether, the organic layer was sequentially washed with water, brine, dried over anhydrous Na_2SO_4, filtered, and evaporated to afford **1f** (2.6341 g, 97%) as yellow oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 3.63 (t, *J* = 6.8 Hz, 2 H, OCH_2), 3.19 (t, *J* = 7.0 Hz, 2 H, CH_2), 1.82 (quintet, *J* = 7.2 Hz, 2 H, CH_2), 1.71 (s, 1 H, OH), 1.56 (quintet, *J* = 6.8 Hz, 2 H, CH_2), 1.45-1.22 (m, 10 H, 5 x CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 62.8, 33.4, 32.6, 30.4, 29.3, 29.2, 28.4, 25.6, 7.2; **IR** (neat, cm^{-1}): 3327, 2924, 2852, 1461,

1428, 1293, 1181, 1054; MS (DART) *m/z*: 271 $(M+H)^+$; HRMS calcd *m/z* for $C_9H_{20}OI$ $[M+H]^+$: 271.0553, found 271.0551.

(2) Preparation of (2*R*)-2-(2-fluoro-4-phenylphenyl)propan-1-ol[2] ((*R*)-9b, yyb-3-144)

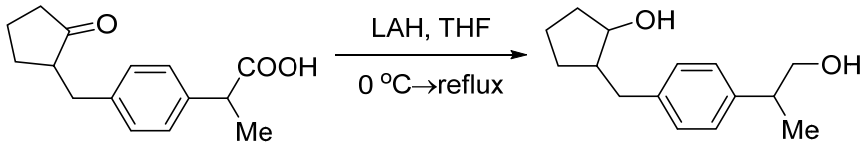


(*R*)-**10b** 4 mmol (*R*)-**9b** 95%, 98% ee

To a three-necked flask was added (*R*)-**10b** (980.1 mg, 4.0 mmol). Then the flask was degassed and refilled with argon for three times. After the addition of anhydrous THF, LAH (6 mL, 1.0 M in THF, 6 mmol) was added dropwise over 25 min at 0 ℃ with an ice-water bath. After stirring for 10 min at the same temperature, the resulting mixture was heated to 80 ℃ and stirred for 3.5 h until completion of the reaction as monitored by TLC (petroleum ether/ethyl acetate = 2/1). The reaction was quenched with ethyl acetate (6 mL) at 0 ℃. The resulting mixture was sequentially washed with 20 mL of 1.0 M HCl (aq.), water, and brine, and dried over anhydrous Na_2SO_4. After filtration and evaporation, the residue was purified by chromatography on silica gel to afford (*R*)-**9b** (873.6 mg, 95%, 98% ee) [eluent: petroleum ether/ethyl acetate = 9/1 (500 mL) to 4/1(400 mL), then 2/3 (200 mL)] as white solid; m.p. 51.0-52.0 ºC (petroleum ether/dichloromethane); HPLC conditions: OD-H column, hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 214 nm, t_R (major) = 13.2 min, t_R (minor) = 11.1 min; $[\alpha]_D^{27}$ = +19.17 (*c* = 1.01, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.54 (d, *J* = 7.6 Hz, 2 H, Ar-H), 7.48-7.29 (m, 4 H, Ar-H), 7.10 (d, *J* = 8.0 Hz, 1 H, Ar-H), 7.05 (d, *J* = 12.0 Hz, 1 H, Ar-H), 3.74 (d, *J* = 6.4 Hz, 2 H, OCH_2), 2.99 (sextet, *J* = 6.8 Hz, 1 H, CH), 1.44 (s, 1 H, OH), 1.31 (d, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 159.8 (d, *J* = 246.5 Hz), 145.5 (d, *J* = 7.1 Hz), 135.7, 130.7 (d, *J* = 3.9 Hz), 128.9 (d, *J* = 3.2 Hz), 128.4, 127.5, 127.2 (d, *J* = 13.5 Hz), 123.5 (d, *J* = 3.1 Hz), 115.0 (d, *J* = 22.9 Hz), 68.4, 42.0, 17.4; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -118.4; **IR** (neat, cm^{-1}): 3243, 2928, 2871, 1624, 1482, 1417, 1376, 1248, 1022; **MS** (70 eV, EI) *m/z* (%): 230 (M^+, 36.53),

199 (100); **Anal. Calcd.** For $C_{15}H_{15}FO$: C 78.24, H 6.57; found C 78.20, H 6.51.

(3) Preparation of 2-((4-(1-hydroxypropan-2-yl)benzyl)cyclopentan-1-ol[2] (9e, yyb-3-166-1)



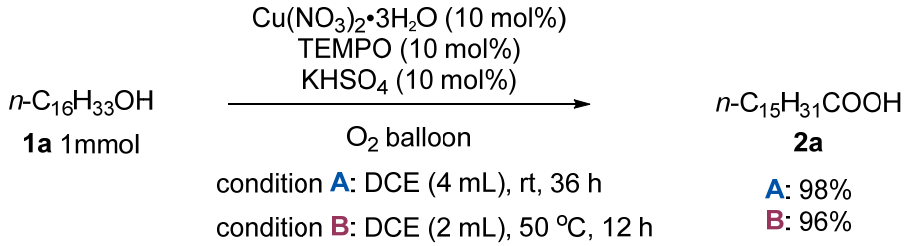
(±)-**10e** 14 mmol **9e** 12%

To a three-necked flask was added (±)-**10e** (3.5248 g, 98% purity, 14 mmol). Then the flask was degassed and refilled with argon for three times. After the addition of anhydrous THF, LAH (35 mL, 1.0 M in THF, 35 mmol) was added dropwise over 20 min at 0 ℃ with an ice-water bath. After stirring for 10 min at the same temperature, the resulting mixture was heated to 80 ℃ and stirred for 20 h until completion of the reaction as monitored by TLC (petroleum ether/ethyl acetate = 1/1). The reaction was quenched with ethyl acetate (20 mL) at 0 ℃. The resulting mixture was sequentially washed with 60 mL of 1.0 M HCl (aq.), water, and brine, and the organic layer was dried over anhydrous Na_2SO_4. After filtration and evaporation, the residue was purified by chromatography on silica gel to afford **9e** (the less polar isomer, 391.9 mg, 12%) and the more polar isomer (2.1873 g, 67%) [eluent: petroleum ether/ethyl acetate = 4/1 (1000 mL) to 1/1(500 mL)] as colorless oil.

9e: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.17 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.12 (d, *J* = 8.0 Hz, 2 H, Ar-H), 4.05 (t, *J* = 3.4 Hz, 1 H, OCH), 3.70-3.57 (m, 2 H, OCH_2), 2.89 (sextet, *J* = 7.0 Hz, 1 H, CH), 2.81 (dd, J_1 = 13.6 Hz, J_2 = 7.6 Hz, 1 H, one proton of CH_2), 2.62 (dd, J_1 = 13.6 Hz, J_2 = 7.6 Hz, 1 H, one proton of CH_2), 2.09 (s, 2 H, 2 x OH), 2.01-1.90 (m, 1 H, CH), 1.88-1.74 (m, 2 H, CH_2), 1.73-1.41 (m, 4 H, 2 x CH_2), 1.24 (d, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 141.0, 140.1, 128.8, 127.3, 74.2, 68.5, 47.4, 41.9, 34.9, 34.6, 28.6, 21.6, 17.5; **IR** (neat, cm^{-1}): 3344, 2957, 2871, 1512, 1451, 1419, 1337, 1029, 1011; **MS** (70 eV, EI) *m/z* (%): 234 (M^+, 5.97), 185 (100); **HRMS** calcd *m/z* for $C_{15}H_{22}O_2$ [M^+]: 234.1614, found: 234.1617.

2. Preparation of acids

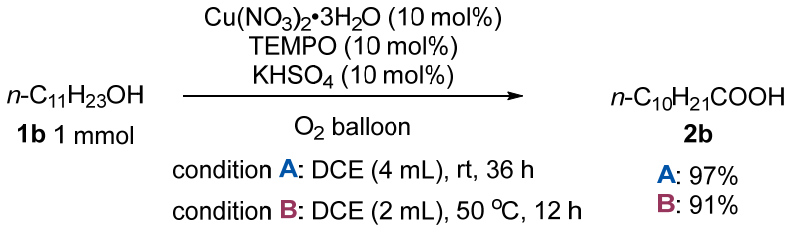
(1) Preparation of hexadecanoic acid (2a, yyb-2-001, yyb-2-002)



Typical Procedure I: A Schlenk tube was degassed to remove the air inside, and refilled with O_2 using an O_2 balloon for three times. Then $Cu(NO_3)_2•3H_2O$ (24.6 mg, 0.1 mmol), TEMPO (16.1 mg, 0.1 mmol), $KHSO_4$ (14.1 mg, 0.1 mmol), **1a** (243.0 mg, 1.0 mmol), and DCE (4 mL) were added sequentially. The resulting mixture was then stirred at room temperature until the completion of the reaction as monitored by TLC (petroleum ether/ethyl acetate = 5/1) (36 h) and filtrated through a short column of silica gel eluted with diethyl ether (3 x 25 mL). After evaporation, the residue was purified by chromatography on silica gel to afford **2a** (252.3 mg, 98%) [eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to 1/1(~100 mL)] as light yellow solid;

Typical Procedure II: A Schlenk tube was degassed to remove the air inside and refilled with O_2 by an O_2 balloon for three times. Then $Cu(NO_3)_2•3H_2O$ (24.5 mg, 0.1 mmol), TEMPO (15.8 mg, 0.1 mmol), $KHSO_4$ (14.1 mg, 0.1 mmol), **1a** (243.0 mg, 1.0 mmol), and DCE (2 mL) were added sequentially. The resulting mixture was then stirred at 50 °C until completion of the reaction as monitored by TLC (petroleum ether/ethyl acetate = 5/1) (12 h) and filtrated through a short column of silica gel eluted with diethyl ether (3 x 25 mL). After evaporation, the residue was purified by chromatography on silica gel to afford **2a**[7] (247.4 mg, 96%) [eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to 1/1 (~100 mL)] as light yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.34 (t, *J* = 7.4 Hz, 2 H, CH_2), 1.63 (quintet, *J* = 7.3 Hz, 2 H, CH_2), 1.39-1.13 (m, 24 H, 12 x CH_2), 0.88 (t, *J* = 6.6 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 180.5, 34.1, 31.9, 29.66, 29.62, 29.61, 29.56, 29.49, 29.40, 29.3, 29.2, 29.0, 24.6, 22.6, 14.0.

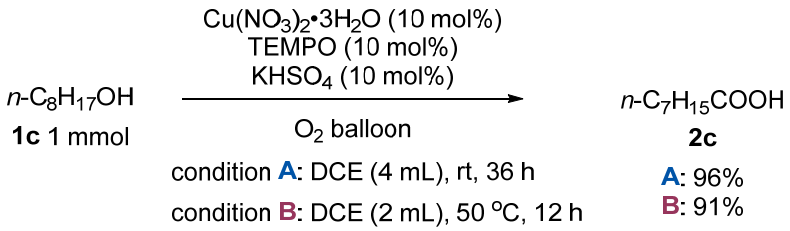
(2) Preparation of undecanoic acid (2b, zzn-1-001, zzn-2-003)



Following Typical Procedure I, the reaction of **1b** (175.0 mg, 99% purity, 1.0 mmol), $Cu(NO_3)_2•3H_2O$ (23.8 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.5 mg, 0.1 mmol) in DCE (4 mL) afforded **2b** (182.6 mg, 97%) [first round eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to 1/1 (~100 mL); second round eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to 1/1 (~100 mL)] as light yellow solid;

Following Typical Procedure II, the reaction of **1b** (173.9 mg, 99% purity, 1.0 mmol), $Cu(NO_3)_2•3H_2O$ (24.0 mg, 0.1 mmol), TEMPO (15.8 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (2 mL) afforded **2b** (168.6 mg, 91%) [eluent: petroleum ether/ethyl acetate = 20/1 (~210 mL) to 1/1 (~100 mL)] as light yellow solid; **2b:**[8] (Low melting point solid, unable to recrystallize to measure the melting point); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.63 (br, 1 H, COOH), 2.34 (t, *J* = 7.6 Hz, 2 H, CH_2), 1.63 (quintet, *J* = 7.2 Hz, 2 H, CH_2), 1.38-1.12 (m, 14 H, 7 x CH_2), 0.88 (t, *J* = 6.8 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 180.6, 34.1, 31.8, 29.5, 29.3, 29.21, 29.16, 29.0, 24.6, 22.6, 14.0; **IR** (neat, cm^{-1}): 3300-2500, 1707, 1465, 1411, 1379, 1242, 1066, 1057; **MS** (70 eV, EI) *m*/*z* (%): 186 (M^+, 17.75), 73 (100).

(3) Preparation of octanoic acid (2c, yyb-2-026, yyb-2-019)



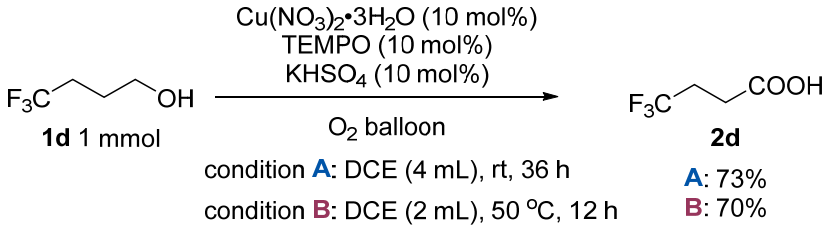
Following Typical Procedure I, the reaction of **1c** (130.0 mg, 1.0 mmol), $Cu(NO_3)_2•3H_2O$ (24.5 mg, 0.1 mmol), TEMPO (16.3 mg, 0.1 mmol), and $KHSO_4$ (13.6 mg, 0.1 mmol) in DCE (4 mL) afforded **2c** (139.0 mg, 96%) [eluent: petroleum ether/ethyl acetate = 20/1 (~210 mL) to 5/1 (~60 mL), then 1/1 (~100 mL)] as light

yellow oil;

Following Typical Procedure II, the reaction of **1c** (130.9 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.2 mg, 0.1 mmol), TEMPO (16.1 mg, 0.1 mmol), and $KHSO_4$ (14.0 mg, 0.1 mmol) in DCE (2 mL) afforded **2c** (131.4 mg, 91%) [eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to 1/1 (~100 mL)] as light yellow oil;

2c:[7] **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 11.45 (br, 1 H, COOH), 2.35 (t, *J* = 7.6 Hz, 2 H, CH_2), 1.64 (quintet, *J* = 7.3 Hz, 2 H, CH_2), 1.42-1.18 (m, 8 H, 4 x CH_2), 0.88 (t, *J* = 6.8 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 180.5, 34.1, 31.5, 28.9, 28.8, 24.6, 22.5, 13.9.

(4) Preparation of 4,4,4-trifluorobutanoic acid (2d, yyb-3-124, yyb-3-117)

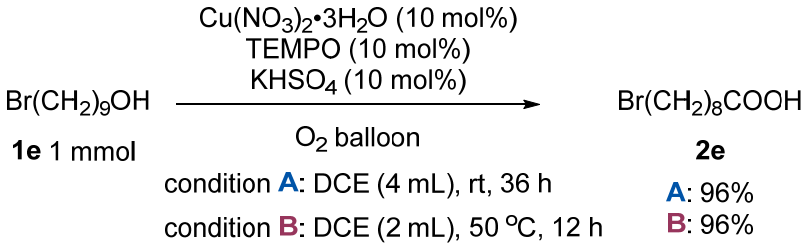


Following Typical Procedure I, the reaction of **1d** (131.2 mg, 98% purity, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.1 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.9 mg, 0.1 mmol) in DCE (4 mL) afforded **2d** (104.2 mg, 73%) [eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to 3/1 (~200 mL)] as yellow solid;

Following Typical Procedure II, the reaction of **1d** (130.0 mg, 98% purity, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.7 mg, 0.1 mmol), TEMPO (15.7 mg, 0.1 mmol), and $KHSO_4$ (13.7 mg, 0.1 mmol) in DCE (2 mL) afforded **2d** (100.8 mg, 70%) [eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to 4/1 (~250 mL)] as yellow solid;

2d:[9] (Low melting point solid, unable to recrystallize to measure melting point); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 10.57 (br, 1 H, COOH), 2.66 (t, *J* = 7.8 Hz, 2 H, CH_2), 2.56-2.37 (m, 2 H, CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 177.3, 126.3 (q, *J* = 274.4 Hz), 29.0 (q, *J* = 30.0 Hz), 26.9 (q, *J* = 3.1 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$): δ = –67.6; **IR** (neat, cm^{-1}): 3250-2250, 1716, 1446, 1427, 1384, 1254, 1228, 1138, 1107; **MS** (70 eV, EI) *m*/*z* (%): 142 (M^+, 0.8), 125 ($(M\text{-}OH)^+$, 21.16), 77 (100).

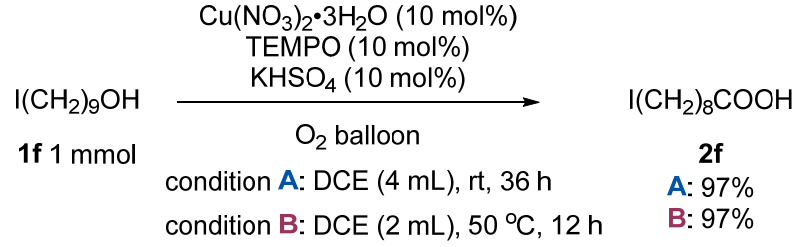
(5) Preparation of 9-bromononanoic acid (2e, zzn-1-009, zzn-1-010)



Following Typical Procedure I, the reaction of **1e** (229.2 mg, 97% purity, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.3 mg, 0.1 mmol), TEMPO (16.2 mg, 0.1 mmol), and $KHSO_4$ (13.6 mg, 0.1 mmol) in DCE (4 mL) afforded **2e** (226.5 mg, 96%) [eluent: petroleum ether/ethyl acetate = 10/1 (~270 mL) to 1/1 (~150 mL)] as white solid;

Following Typical Procedure II, the reaction of **1e** (229.2 mg, 97% purity, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.0 mg, 0.1 mmol), TEMPO (16.2 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (2 mL) afforded **2e** (227.9 mg, 96%) [eluent: petroleum ether/ethyl acetate = 10/1 (~380 mL) to 1/1 (~200 mL)] as light yellow solid; **2e:**[7] **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 3.40 (t, *J* = 6.8 Hz, 2 H, CH_2), 2.35 (t, *J* = 7.4 Hz, 2 H, CH_2), 1.85 (quintet, *J* = 7.1 Hz, 2 H, CH_2), 1.73-1.53 (m, 2 H, CH_2), 1.52-1.38 (m, 2 H, CH_2), 1.38-1.02 (m, 6 H, 3 x CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 180.5, 34.0, 33.8, 32.7, 28.9, 28.8, 28.4, 28.0, 24.5.

(6) Preparation of 9-iodononanoic acid (2f, yyb-2-114, yyb-2-115)



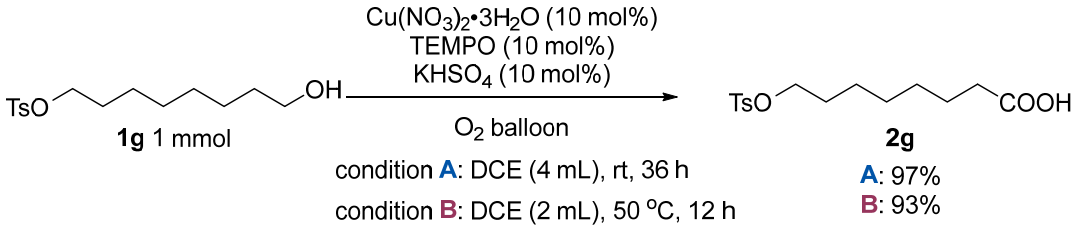
Following Typical Procedure I, the reaction of **1f** (262.6 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.2 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.9 mg, 0.1 mmol) in DCE (4 mL) afforded **2f** (268.1 mg, 97%) [eluent: petroleum ether/ethyl acetate = 10/1 (~160 mL) to 2/1 (~240 mL)] as light yellow solid;

Following Typical Procedure II, the reaction of **1f** (262.5 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.8 mg, 0.1 mmol), TEMPO (16.2 mg, 0.1 mmol), and $KHSO_4$ (14.0 mg, 0.1 mmol) in DCE (2 mL) afforded **2f** (267.3 mg, 97%) [eluent: petroleum

ether/ethyl acetate = 15/1 (~160 mL) to 10/1 (~160 mL), then 2/1 (~300 mL)] as light yellow solid;

2f:[10] m.p. 60.2-60.9 °C (petroleum ether/dichloromethane); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 10.42 (br, 1 H, COOH), 3.18 (t, *J* = 6.8 Hz, 2 H, CH_2), 2.35 (t, *J* = 7.4 Hz, 2 H, CH_2), 1.82 (quintet, *J* = 7.1 Hz, 2 H, CH_2), 1.71-1.53 (m, 2 H, CH_2), 1.46-1.21 (m, 8 H, 4 x CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 180.3, 34.0, 33.4, 30.3, 28.9, 28.8, 28.2, 24.5, 7.1; **IR** (neat, cm^{-1}): 3200-2350, 1689, 1463, 1428, 1301, 1271, 1234, 1195; **MS** (70 eV, EI) *m/z* (%):157 ($(M-I)^+$, 34.7); 55 (100).

(7) Preparation of 8-(toluene-4-sulfonyloxy)octanoic acid (2g, yyb-2-033, yyb-2-034)



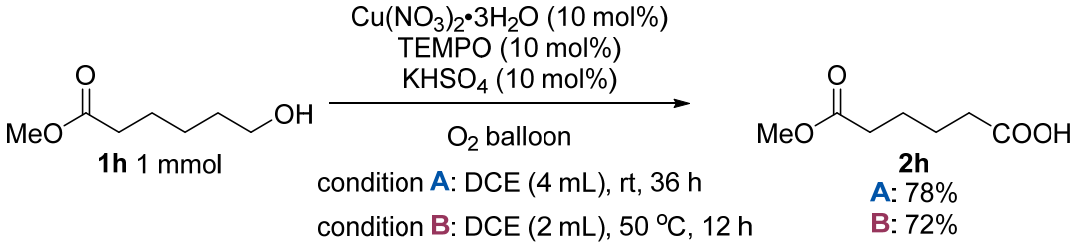
Following Typical Procedure I, the reaction of **1g** (303.7 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.0 mg, 0.1 mmol), TEMPO (16.1 mg, 0.1 mmol), and $KHSO_4$ (14.0 mg, 0.1 mmol) in DCE (4 mL) afforded **2g** (309.3 mg, 97%) [eluent: petroleum ether/ethyl acetate = 5/1 (~180 mL) to 1/1 (~300 mL)] as light yellow solid;

Following Typical Procedure II, the reaction of **1g** (302.2 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.5 mg, 0.1 mmol), TEMPO (16.3 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (2 mL) afforded **2g** (295.4 mg, 93%) [eluent: petroleum ether/ethyl acetate = 5/1 (~240 mL) to 2/1 (~150 mL), then 1/1 (~300 mL)] as light yellow solid;

2g: m.p. 60.3-61.5 °C (petroleum ether/dichloromethane); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.48 (br, 1 H, COOH), 7.78 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.35 (d, *J* = 8.0 Hz, 2 H, Ar-H), 4.02 (t, *J* = 6.4 Hz, 2 H, CH_2), 2.44 (s, 3 H, CH_3), 2.32 (t, *J* = 7.6 Hz, 2 H, CH_2), 1.72-1.49 (m, 4 H, 2 x CH_2), 1.38-1.14 (m, 6 H, 3 x CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 180.0, 144.6, 133.0, 129.7, 127.7, 70.4, 33.8, 28.6, 28.5, 28.3, 24.9, 24.3, 21.4; **IR** (neat, cm^{-1}): 3100-2800, 1694, 1597, 1467, 1352, 1236, 1189, 1096; **MS** (ESI) *m/z*: 315 $(M+H)^+$, 332 $(M+NH_4)^+$, 337 $(M+Na)^+$; **Anal. Calcd.** For $C_{15}H_{22}O_5S$: C 57.31, H 7.05;

found C 57.31, H 6.81.

(8) Preparation of 1,6-hexanedioic acid monomethyl ester (2h, zzn-1-007, zzn-1-006)

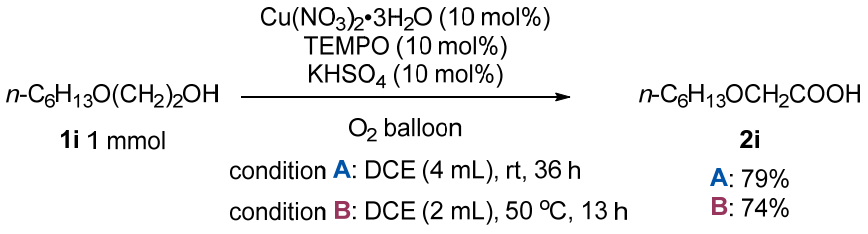


Following Typical Procedure I, the reaction of **1h** (146.8 mg, 1.0 mmol), $Cu(NO_3)_2•3H_2O$ (24.1 mg, 0.1 mmol), TEMPO (15.7 mg, 0.1 mmol), and $KHSO_4$ (13.7 mg, 0.1 mmol) in DCE (4 mL) afforded **2h** (125.8 mg, 78%) [eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to 5/1 (~240 mL), then 1/1 (~100 mL)] as reddish liquid;

Following Typical Procedure II, the reaction of **1h** (146.1 mg, 1.0 mmol), $Cu(NO_3)_2•3H_2O$ (24.2 mg, 0.1 mmol), TEMPO (16.2 mg, 0.1 mmol), and $KHSO_4$ (13.6 mg, 0.1 mmol) in DCE (2 mL) afforded **2h** (116.0 mg, 72%) [eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to 5/1 (~240 mL), then 2/1 (~220 mL) to 1/1 (~100 mL)] as a reddish liquid;

2h:[7] **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 10.89 (br, 1 H, COOH), 3.68 (s, 3 H, CH_3), 2.49-2.20 (m, 4 H, 2 x CH_2), 1.77-1.56 (m, 4 H, 2 x CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 179.4, 173.8, 51.5, 33.5, 24.1, 23.9.

(9) Preparation of 2-(hexyloxy)acetic acid (2i, yyb-2-037, yyb-2-041)

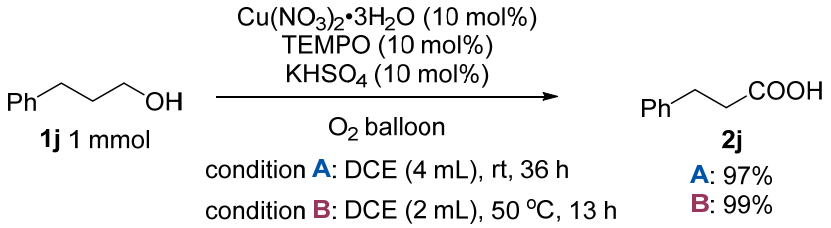


Following Typical Procedure I, the reaction of **1i** (146.3 mg, 1.0 mmol), $Cu(NO_3)_2•3H_2O$ (24.5 mg, 0.1 mmol), TEMPO (15.8 mg, 0.1 mmol), and $KHSO_4$ (14.0 mg, 0.1 mmol) in DCE (4 mL) afforded **2i** (126.5 mg, 79%) [eluent: petroleum ether/ethyl acetate = 5/1 (~240 mL) to 1/1 (~200 mL)] as light yellow oil;

Following Typical Procedure II, the reaction of **1i** (146.9 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.6 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (14.1 mg, 0.1 mmol) in DCE (2 mL) afforded **2i** (119.3 mg, 74%) [eluent: petroleum ether/ethyl acetate = 10/1 (~330 mL) to 5/1 (~120 mL), then 1/1 (~160 mL)] as light yellow oil;

2i:[7] **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.15 (br, 1 H, COOH), 4.13 (s, 2 H, CH_2), 3.56 (t, *J* = 6.6 Hz, 2 H, CH_2), 1.63 (quintet, *J* = 7.0 Hz, 2 H, CH_2), 1.45-1.17 (m, 6 H, 3 x CH_2), 0.89 (t, *J* = 6.8 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 175.7, 72.0, 67.6, 31.4, 29.2, 25.4, 22.4, 13.8.

(10) Preparation of 3-phenylpropanoic acid (2j, yyb-2-005, yyb-2-006)

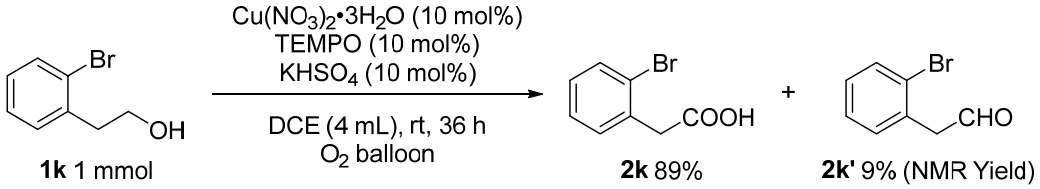


Following Typical Procedure I, the reaction of **1j** (0.14 mL, d = 1.001 g/mL, 98% purity, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.4 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.7 mg, 0.1 mmol) in DCE (4 mL) afforded **2j** (146.9 mg, 97%) [eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to 2/1 (~150 mL)] as light yellow solid;

Following Typical Procedure II, the reaction of **1j** (0.14 mL, d = 1.001 g/mL, 98% purity, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.4 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.5 mg, 0.1 mmol) in DCE (2 mL) afforded **2j** (150.1 mg, 99%) [eluent: petroleum ether/ethyl acetate = 20/1 (~100 mL) to 10/1 (~220 mL),then 5/1 (~120 mL)] as light yellow solid;

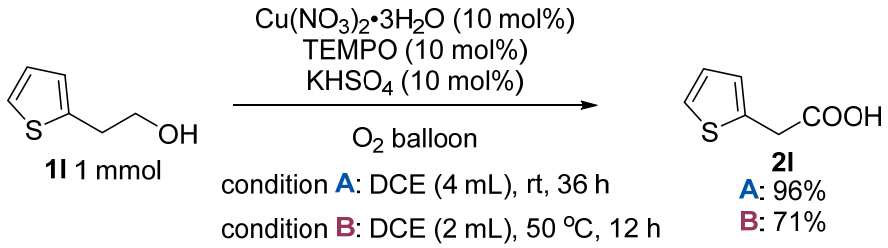
2j:[7] **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.86 (br, 1 H, COOH), 7.33-7.22 (m, 2 H, Ar-H), 7.22-7.07 (m, 3 H, Ar-H), 2.93 (t, *J* = 7.8 Hz, 2 H, CH_2), 2.65 (t, *J* = 8.0 Hz, 2 H, CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 179.6, 140.0, 128.4, 128.1, 126.3, 35.5, 30.4.

(11) Preparation of 2-(*o*-bromophenyl)acetic acid (2k, yyb-2-076)



Following Typical Procedure I, the reaction of **1k** (206.6 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.3 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.9 mg, 0.1 mmol) in DCE (4 mL) afforded **2k**[11] (193.4 mg, 89%) (9% NMR yield of corresponding aldehyde was formed based on ^{1}H NMR analysis of the crude product) [petroleum ether/ethyl acetate = 10/1 (~160 mL) to 2/1 (~300 mL)] as light yellow solid; m.p. 105.2-106.1 ºC (petroleum ether/dichloromethane); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.02 (br, 1 H, COOH), 7.56 (d, *J* = 8.0 Hz, 1 H, Ar-H), 7.32-7.22 (m, 2 H, Ar-H), 7.18-7.08 (m, 1 H, Ar-H), 3.82 (s, 2 H, CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 177.0, 133.5, 132.8, 131.5, 129.1, 127.6, 125.0, 41.3; **IR** (neat, cm^{-1}): 3250-2400, 1698, 1474, 1444, 1345, 1298, 1239, 1197, 1165; **MS** (70 eV, EI) *m/z* (%): 216 (M^+(^{81}Br), 8.01), 214 (M^+(^{79}Br), 6.99), 135 (100).

(12) Preparation of 2-thienylacetic acid (2l, yyb-2-020, yyb-2-021)

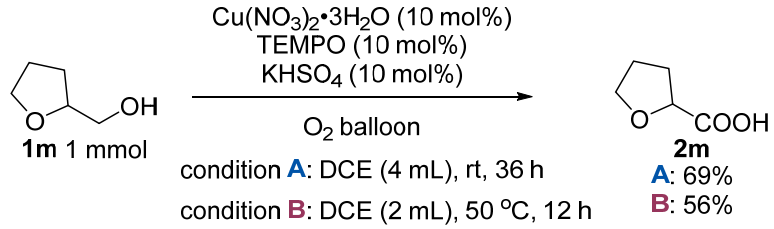


Following Typical Procedure I, the reaction of **1l** (128.8 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.5 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.6 mg, 0.1 mmol) in DCE (4 mL) afforded **2l** (137.7 mg, 96%) [eluent: petroleum ether/ethyl acetate = 5/1 (~240 mL) to 1/1 (~200 mL)] as light yellow solid;

Following Typical Procedure II, the reaction of **1l** (128.3 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.6 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (14.0 mg, 0.1 mmol) in DCE (2 mL) afforded **2l** (107.4 mg, 71%, 94% purity) [eluent: petroleum ether/ethyl acetate = 5/1 (~240 mL) to 1/1 (~120 mL)] as light brown solid; **2l:**[7] **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 11.73 (br, 1 H, COOH), 7.21 (dd, J_1 = 4.4 Hz, J_2

= 2.0 Hz, 1 H, Thiophene-H), 6.99-6.87 (m, 2 H, Thiophene-H), 3.86 (s, 2 H, CH_2); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ = 177.1, 134.0, 127.2, 126.9, 125.3, 35.0.

(13) Preparation of 2-tetrahydrofurancarboxylic acid (2m, yyb-2-027, yyb-2-023)

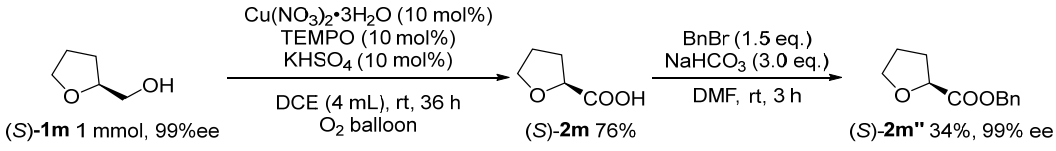


Following Typical Procedure I, the reaction of **1m** (102.7 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.5 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.6 mg, 0.1 mmol) in DCE (4 mL) afforded **2m** (83.0 mg, 69%, 97% purity) [eluent: petroleum ether/ethyl acetate =3/1 (~160 mL) to 1/2 (~150 mL)] as light yellow oil;

Following Typical Procedure II, the reaction of **1m** (102.3 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.3 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.7 mg, 0.1 mmol) in DCE (2 mL) afforded **2m** (65.3 mg, 56%) [eluent: petroleum ether/ethyl acetate =10/1 (~160 mL) to 5/1 (~120 mL), then 2/1 (~180 mL) to 1/1 (~200 mL)] as light yellow oil;

2m:[7] ^{1}**H NMR** (400 MHz, $CDCl_3$): δ = 10.30 (br, 1 H, COOH), 4.51 (dd, J_1 = 8.4 Hz, J_2 = 5.6 Hz, 1 H, CH), 4.04 (q, J = 7.3 Hz, 1 H, one proton of CH_2), 3.95 (q, J = 7.2 Hz, 1 H, one proton of CH_2), 2.41-2.21 (m, 1 H, one proton of CH_2), 2.18-2.04 (m, 1 H, one proton of CH_2), 2.02-1.82 (m, 2 H, CH_2); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ = 177.8, 76.2, 69.5, 30.1, 25.2.

(14) Preparation of (*S*)-tetrahydro-2-furoic acid ((*S*)-2m, yyb-3-125, yyb-4-017)



Following Typical Procedure I, the reaction of (*S*)-**1m** (104.3 mg, 97% purity, 1.0 mmol, 99% ee), $Cu(NO_3)_2$•$3H_2O$ (24.0 mg, 0.1 mmol), TEMPO (15.8 mg, 0.1 mmol), and $KHSO_4$ (13.7 mg, 0.1 mmol) in DCE (4 mL) afforded (*S*)-**2m** (87.6 mg, 76%) [eluent: petroleum ether/ethyl acetate =3/1 (~200 mL) to 1/1 (~200 mL)] as light yellow

oil;

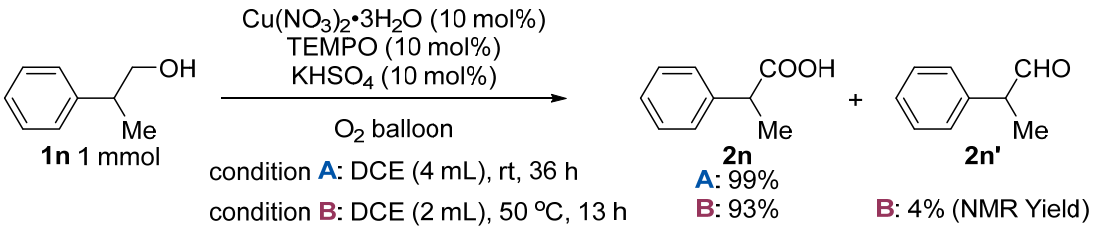
(*S*)-**2m:**[12] $[\alpha]_D^{24}$ = -36.02 (*c* = 1.035, $CHCl_3$) (reported:[12] $[\alpha]_D$ = -36.0 (*c* = 1.21, $CHCl_3$)); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 10.12 (br, 1 H, COOH), 4.51 (dd, J_1 = 8.4 Hz, J_2 = 5.6 Hz, 1 H, CH), 4.11-3.99 (m, 1 H, one proton of CH_2), 3.99-3.86 (m, 1 H, one proton of CH_2), 2.43-2.23 (m, 1 H, one proton of CH_2), 2.19-2.03 (m, 1 H, one proton of CH_2), 2.04-1.86 (m, 2 H, CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 177.8, 76.3, 69.5, 30.1, 25.2; **IR** (neat, cm^{-1}): 3400-2400, 1722, 1449, 1352, 1277, 1198, 1175, 1071; **MS** (70 eV, EI) *m*/*z* (%): 71 ($(M-COOH)^+$, 100).

The ee of (*S*)-**2m** was determined by HPLC analysis after being converted to (*S*)-**2m''**.

To the flask were added $NaHCO_3$ (37.9 mg, 0.45 mmol), (*S*)-**2m** (17.6 mg, 0.15 mmol), BnBr (40.5 mg, 98% purity, 0.23 mmol), and DMF (2.0 mL). After stirring for 3 h at room temperature, the reaction was quenched with H_2O (5 mL). The resulting mixture was extracted with diethyl ether (10 mL x 3), washed with brine, and dried over anhydrous Na_2SO_4. After evaporation, the residue was purified by chromatography on silica gel to afford (*S*)-**2m''** (10.6 mg, 34%, 99% ee) [eluent: petroleum ether/ethyl acetate = 5/1 (~180 mL)] as yellow oil;

(*S*)-**2m'':**[13] **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.51-7.28 (m, 5 H, Ar-H), 5.27-5.03 (m, 2 H, OCH_2), 4.51 (dd, J_1 = 8.4 Hz, J_2 = 5.2 Hz, 1 H, CH), 4.10-3.97 (m, 1 H, one proton of CH_2), 3.96-3.78 (m, 1 H, one proton of CH_2), 2.35-2.15 (m, 1 H, one proton of CH_2), 2.08-1.80 (m, 3 H, one proton of CH_2 and CH_2); HPLC conditions: OJ-H column, hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 214 nm, t_R (major) = 14.8 min, t_R (minor) = 17.4 min.

(15) Preparation of 2-phenylpropionic acid (2n, yyb-3-110, yyb-3-097)



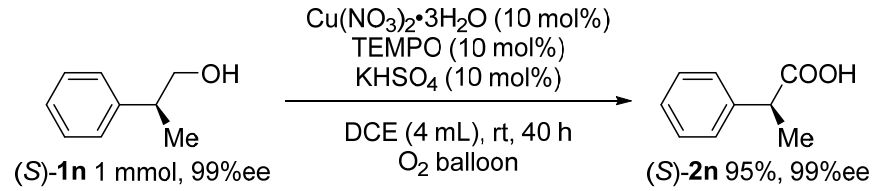
Following Typical Procedure I, the reaction of **1n** (138.1 mg, 98% purity, 1.0

mmol), $Cu(NO_3)_2$•$3H_2O$ (24.7 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.7 mg, 0.1 mmol) in DCE (4 mL) afforded **2n** (147.5 mg, 99%) [eluent: petroleum ether/ethyl acetate = 15/1 (~160 mL) to 4/1 (~250 mL)] as light yellow oil;

Following Typical Procedure II, the reaction of **1n** (139.3 mg, 98% purity, 1.0 mmol), $Cu(NO_3)_2 \cdot 3H_2O$ (23.9 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (2 mL) afforded **2n** (140.3 mg, 93%) (4% NMR yield of corresponding aldehyde was formed based on ^{1}H NMR analysis of the crude product) [eluent: petroleum ether/ethyl acetate = 15/1 (~160 mL) to 10/1 (~270 mL), then 4/1 (~120 mL)] as light yellow oil;

2n:[14] **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.60 (br, 1 H, COOH), 7.37-7.20 (m, 5 H, Ar-H), 3.72 (q, *J* = 7.2 Hz, 1 H, CH), 1.49 (d, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 181.1, 139.6, 128.6, 127.5, 127.3, 45.3, 18.0; **IR** (neat, cm^{-1}): 3250-2300, 1699, 1497, 1453, 1413, 1378, 1264, 1229, 1064; **MS** (70 eV, EI) *m*/*z* (%): 150 (M^+, 25.84), 105 (100).

(16) Preparation of (*S*)-2-phenylpropionic acid ((*S*)-2n, yyb-3-128)

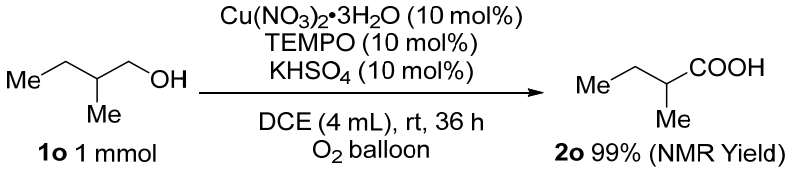


(*S*)-**1n** 1 mmol, 99%ee (*S*)-**2n** 95%, 99%ee

Following Typical Procedure I, the reaction of (*S*)-**1n** (137.0 mg, 1.0 mmol, 99% ee), $Cu(NO_3)_2$•$3H_2O$ (24.3 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (4 mL) afforded (*S*)-**2n** (143.1 mg, 95%, 99% ee) [eluent: petroleum ether/ethyl acetate = 15/1 (~160 mL) to 4/1 (~250 mL)] as light yellow oil;

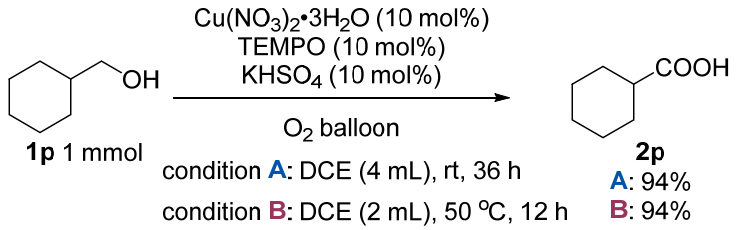
(*S*)-**2n:**[15] HPLC conditions: AD-H column, hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 214 nm, t_R (major) = 9.1 min, t_R (minor) = 8.1 min; $[\alpha]_D^{25}$ = +75.64 (*c* = 0.94, $CHCl_3$) (reported:[16] $[\alpha]_D^{20}$ = +69.2 (*c* = 1.0, $CHCl_3$)); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 10.63 (br, 1 H, COOH), 7.38-7.17 (m, 5 H, Ar-H), 3.71 (q, *J* = 7.2 Hz, 1 H, CH), 1.49 (d, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 181.0, 139.7, 128.6, 127.5, 127.3, 45.3, 18.0; **IR** (neat, cm^{-1}): 3300-2300, 1699, 1497, 1453, 1413, 1378, 1261, 1228, 1064; **MS** (70 eV, EI) *m*/*z* (%): 150 (M^+, 25.05), 105 (100).

(17) Preparation of 2-methylbutanoic acid (2o, yyb-2-051)



Following Typical Procedure I, the reaction of **1o** (89.2 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.2 mg, 0.1 mmol), TEMPO (15.8 mg, 0.1 mmol), and $KHSO_4$ (14.0 mg, 0.1 mmol) in DCE (4 mL) afforded **2o**[17] (99%, NMR Yield was determined by ^1H NMR analysis using dibromomethane as the internal standard.).

(18) Preparation of cyclohexanecaboxylic acid (2p, yyb-2-052, yyb-2-053)

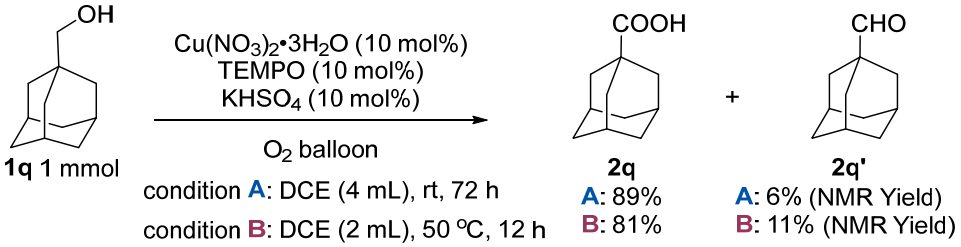


Following Typical Procedure I, the reaction of **1p** (113.8 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (23.9 mg, 0.1 mmol), TEMPO (16.1 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (4 mL) afforded **2p** (120.4 mg, 94%) [eluent: petroleum ether/ethyl acetate = 20/1 (~310 mL) to 1/1 (~200 mL)] as light yellow oil;

Following Typical Procedure II, the reaction of **1p** (114.9 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.7 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (2 mL) afforded **2p** (121.4 mg, 94%) [eluent: petroleum ether/ethyl acetate = 20/1 (~310 mL) to 2/1 (~180 mL)] as light yellow oil;

2p:[7] **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.43 (br, 1 H, COOH), 2.33 (tt, J_1 = 11.2 Hz, J_2 = 3.7 Hz, 1 H, CH), 1.99-1.85 (m, 2 H, CH_2), 1.82-1.68 (m, 2 H, CH_2), 1.68-1.55 (m, 1 H, one proton of CH_2), 1.54-1.37 (m, 2 H, CH_2), 1.36-1.15 (m, 3 H, CH_2 and one proton of CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 182.8, 42.9, 28.7, 25.6, 25.3.

(19) Preparation of 1-adamantanecarboxylic acid (2q, yyb-2-035, yyb-2-044)

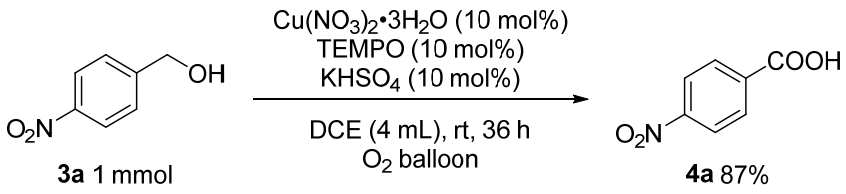


Following Typical Procedure I, the reaction of **1q** (167.4 mg, 1.0 mmol), $Cu(NO_3)_2•3H_2O$ (24.3 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (4 mL) afforded **2q** (161.1 mg, 89%) (6% NMR yield of corresponding aldehyde was formed based on ^{1}H NMR analysis of the crude product) [eluent: petroleum ether (100 mL), petroleum ether/ethyl acetate = 20/1 (~210 mL) to 10/1 (~110 mL), then 5/1 (~120 mL)] as white solid;

Following Typical Procedure II, the reaction of **1q** (167.5 mg, 1.0 mmol), $Cu(NO_3)_2•3H_2O$ (24.3 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.9 mg, 0.1 mmol) in DCE (2 mL) afforded **2q** (147.9 mg, 81%) (11% NMR yield of corresponding aldehyde was formed based on ^{1}H NMR analysis of the crude product) [eluent: petroleum ether/ethyl acetate = 20/1 (~210 mL) to 10/1 (~220 mL), then 5/1 (~120 mL), ethyl acetate (150 mL)] as white solid;

2q:[18] m.p. 172.0-175.4 °C (we were not able to obtain the crystal from the solvent tested, the m.p. of **2q** was determined by using the solid right after evaporation of the eluent); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.85 (br, 1 H, COOH), 2.09-1.97 (m, 3 H, 3 x CH), 1.96-1.82 (m, 6 H, 3 x CH_2), 1.78-1.59 (m, 6 H, 3 x CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 184.6, 40.5, 38.5, 36.4, 27.8; **IR** (neat, cm^{-1}): 3250-2400, 1687, 1450, 1409, 1324, 1281, 1252, 1183, 1084; **MS** (70 eV, EI) *m/z* (%): 180 (M^+, 10.28), 135 (100).

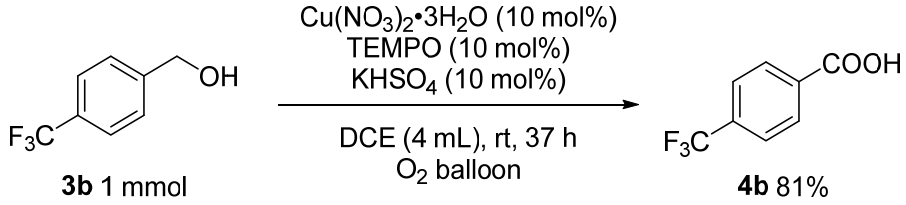
(20) Preparation of 4-nitrobenzoic acid (4a, yyb-2-038)



Following Typical Procedure I, the reaction of **3a** (154.3 mg, 99% purity, 1.0 mmol), $Cu(NO_3)_2•3H_2O$ (24.2 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and

$KHSO_4$ (13.6 mg, 0.1 mmol) in DCE (4 mL) afforded **4a**[19] (145.4 mg, 87%) [eluent: petroleum ether/ethyl acetate = 5/1 (~120 mL), ethyl acetate (200 mL)] as light yellow solid; **^{1}H NMR** (400 MHz, CD_3OD) δ = 8.32 (d, *J* = 8.4 Hz, 2 H, Ar-H), 8.23 (d, *J* = 8.8 Hz, 2 H, Ar-H); **^{13}C NMR** (100 MHz, CD_3OD): δ = 167.6, 152.0, 137.6, 131.9, 124.5.

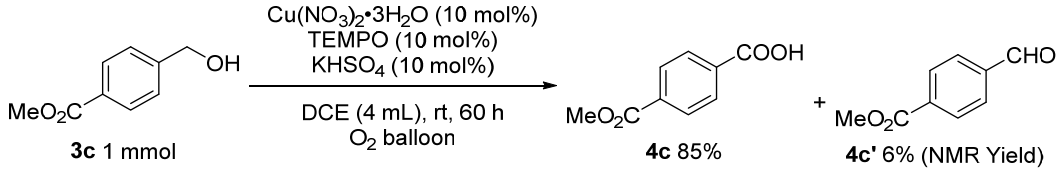
(21) Preparation of 4-(trifluoromethyl)benzoic acid (4b, yyb-2-112)



3b 1 mmol **4b** 81%

Following Typical Procedure I, the reaction of **3b** (176.1 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.3 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (4 mL) afforded **4b**[19] (153.5 mg, 81%) [eluent: petroleum ether/ethyl acetate = 5/1 (~120 mL) to 1/1 (~300 mL)] as light yellow solid; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 13.49 (br, 1 H, COOH), 8.18 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.88 (d, *J* = 8.4 Hz, 2 H, Ar-H); **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 166.3, 134.7, 132.6 (q, *J* = 31.9 Hz), 130.1, 125.6 (q, *J* = 3.7 Hz), 123.8 (q, *J* = 271.0 Hz); **^{19}F NMR** (376 MHz, DMSO-d_6): δ = – 61.5.

(22) Preparation of 4-(methoxycarbonyl)benzoic acid (4c, yyb-2-128-2)

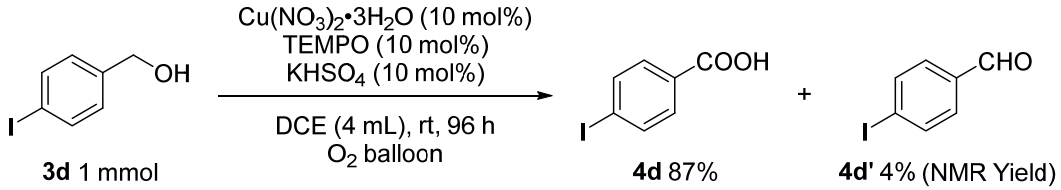


3c 1 mmol **4c** 85% **4c'** 6% (NMR Yield)

A Schlenk tube was degassed to remove the air inside and refilled with O_2 using an O_2 balloon for three times. Then $Cu(NO_3)_2$•$3H_2O$ (25.4 mg, 0.1 mmol), TEMPO (16.2 mg, 0.1 mmol), $KHSO_4$ (13.7 mg, 0.1 mmol), **3c** (170.0 mg, 98% purity, 1.0 mmol), and DCE (4 mL) were added sequentially. The resulting mixture was stirred at room temperature for 60 h as monitored by TLC (petroleum ether/ethyl acetate = 2/1), filtrated through a short column of silica gel eluted with diethyl ether (3 x 25 mL), and

concentrated under reduced pressure (92% NMR yield of **4c** and 6% NMR yield of corresponding aldehyde **4c'** were determined based on ^{1}H NMR analysis of the crude product using dibromomethane as the internal standard in DMSO-d_6). The sample was diluted with ethyl acetate (10 mL), and H_2O (10 mL) was added. The resulting mixture was extracted with ethyl acetate (10 mL×3) and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the crude product was purified by column chromatography on silica gel to afford **4c**[19] (154.3 mg, 85%) [eluent: petroleum ether/ethyl acetate = 10/1 (~160 mL) to 5/1 (~120 mL), then 1/1 (~400 mL)] as white solid; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 13.36 (br, 1 H, COOH), 8.18-7.86 (m, 4 H, Ar-H), 3.90 (s, 3 H, OCH_3); **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 166.6, 165.6, 134.8, 133.2, 129.6, 129.4, 52.4.

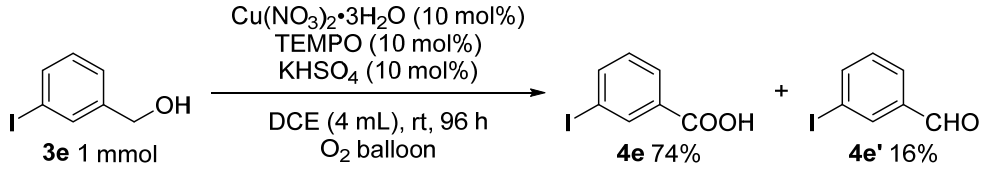
(23) Preparation of 4-iodobenzoic acid (4d, yyb-2-109)



A Schlenk tube was degassed to remove the air inside and refilled with O_2 using an O_2 balloon for three times. Then $Cu(NO_3)_2$•$3H_2O$ (26.5 mg, 0.1 mmol), TEMPO (16.4 mg, 0.1 mmol), $KHSO_4$ (14.0 mg, 0.1 mmol), **3d** (242.0 mg, 97% purity, 1.0 mmol), and DCE (4 mL) were added sequentially. The resulting mixture was then stirred at room temperature for 96 h as monitored by TLC (petroleum ether/ethyl acetate = 2/1), filtrated through a short column of silica gel eluted with diethyl ether (3 x 25 mL), and concentrated under reduced pressure (88% NMR yield of **4d** and 4% NMR yield of corresponding aldehyde were determined based on ^{1}H NMR analysis of the crude product using dibromomethane as the internal standard in DMSO-d_6). The sample was diluted with ethyl acetate (10 mL) and H_2O (10 mL) was added. The resulting mixture was extracted with ethyl acetate (10 mL×3) and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the crude product was purified by column chromatography on silica gel to afford **4d**[19] (216.9 mg, 87%) [eluent: petroleum ether/ethyl acetate = 10/1 (~160 mL) to 5/1 (~120 mL), then 2/1

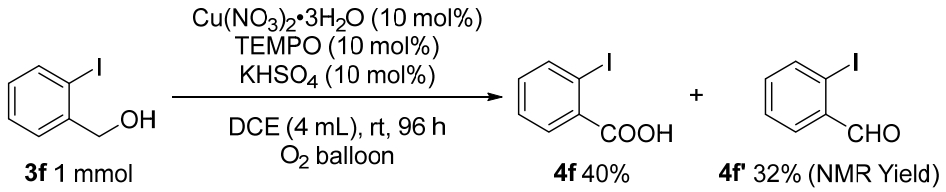
(~450 mL)] as light yellow solid; **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 13.13 (br, 1 H, COOH), 7.90 (d, J = 8.0 Hz, 2 H, Ar-H), 7.21 (d, J = 8.0 Hz, 2 H, Ar-H); **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 166.9, 137.6, 131.1, 130.3, 101.1.

(24) Preparation of 3-iodobenzoic acid (4e, yyb-3-095-2)



Following Typical Procedure I, the reaction of **3e** (236.0 mg, 98% purity, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.4 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.9 mg, 0.1 mmol) in DCE (4 mL) afforded **4e**[20] (181.9 mg, 74%) (16% NMR yield of corresponding aldehyde was formed based on ^{1}H NMR analysis of the crude product) [petroleum ether/ethyl acetate = 15/1 (~160 mL) to 5/1 (~120 mL), then 1/1 (~200 mL)] as white solid**:** m.p. 185.8-186.4 ºC (petroleum ether/ethyl acetate) (reported:[21] m.p. 184-185 ºC (*i*-PrOH)); **^{1}H NMR** (400 MHz, CD_3OD) δ = 8.34 (s, 1 H, Ar-H), 8.00 (d, J = 8.0 Hz, 1 H, Ar-H), 7.92 (d, J = 8.0 Hz, 1 H, Ar-H), 7.24 (t, J = 7.8 Hz, 1 H, Ar-H); **^{13}C NMR** (100 MHz, CD_3OD): δ = 168.0, 142.8, 139.6, 133.9, 131.3, 129.9, 94.4; **IR** (neat, cm^{-1}): 3100-2250, 1677, 1587, 1561, 1428, 1411, 1295, 1260, 1170, 1058; **MS** (70 eV, EI) *m/z* (%): 248 (M^+, 100).

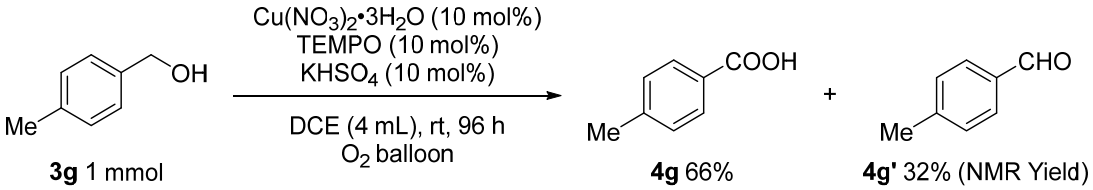
(25) Preparation of 2-iodobenzoic acid (4f, yyb-3-094-2)



Following Typical Procedure I, the reaction of **3f** (238.5 mg, 98% purity, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.4 mg, 0.1 mmol), TEMPO (16.1 mg, 0.1 mmol), and $KHSO_4$ (13.5 mg, 0.1 mmol) in DCE (4 mL) afforded **4f**[22] (99.9 mg, 40%) (32% NMR yield of corresponding aldehyde was formed based on ^{1}H NMR analysis of the crude product) [petroleum ether/ethyl acetate = 20/1 (~100 mL) to 4/1 (~250 mL), then 2/1

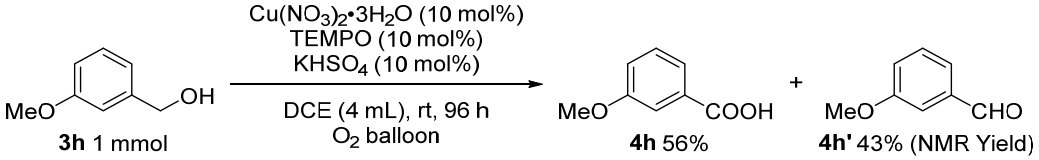
(~150 mL)] as white solid; m.p. 161.0-162.2 ºC (petroleum ether/ethyl acetate); **^{1}H NMR** (400 MHz, CD_3OD) δ = 8.00 (d, J = 7.6 Hz, 1 H, Ar-H), 7.79 (dd, J_1 = 7.8 Hz, J_2 = 1.4 Hz, 1 H, Ar-H), 7.44 (td, J_1 = 7.6 Hz, J_2 = 0.5 Hz, 1 H, Ar-H), 7.18 (td, J_1 = 7.6 Hz, J_2 =1.6 Hz, 1 H, Ar-H); **^{13}C NMR** (100 MHz, CD_3OD): δ = 170.0, 142.3, 137.7, 133.5, 131.6, 129.0, 94.2; **IR** (neat, cm^{-1}): 3200-2300, 1670, 1579, 1560, 1464, 1401, 1293, 1250, 1145, 1012; **MS** (70 eV, EI) *m*/*z* (%): 248 (M^+, 100).

(26) Preparation of 4-methylbenzoic acid (4g, yyb-2-078-2)



Following Typical Procedure I, the reaction of **3g** (125.1 mg, 98% purity, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.6 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.6 mg, 0.1 mmol) in DCE (4 mL) afforded **4g**[19] (89.8 mg, 66%) (32% NMR yield of corresponding aldehyde was formed based on ^{1}H NMR analysis of the crude product) [eluent: petroleum ether/ethyl acetate = 10/1 (~160 mL) to 1/1 (~200 mL)] as light yellow solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.42 (br, 1 H, COOH), 8.01 (d, J = 8.0 Hz, 2 H, Ar-H), 7.27 (d, J = 8.0 Hz, 2 H, Ar-H), 2.43 (s, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 172.5, 144.6, 130.2, 129.2, 126.6, 21.7.

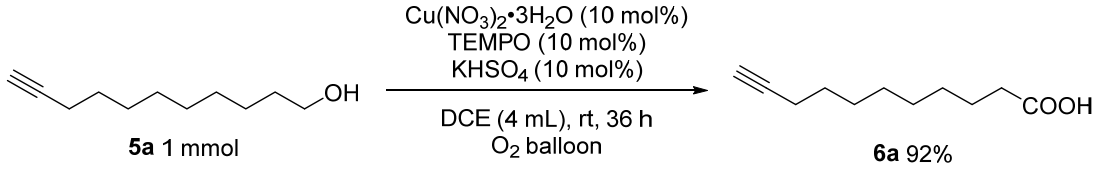
(27) Preparation of 3-methoxybenzoic acid (4h, yyb-3-107)



Following Typical Procedure I, the reaction of **3h** (140.7 mg, 98% purity, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.4 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.6 mg, 0.1 mmol) in DCE (4 mL) afforded **4h**[19] (85.1 mg, 56%) (43% NMR yield of corresponding aldehyde was formed based on ^{1}H NMR analysis of the crude product) [eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to 2/1 (~300 mL)] as white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 12.32 (br, 1 H, COOH), 7.73 (d, J = 7.6

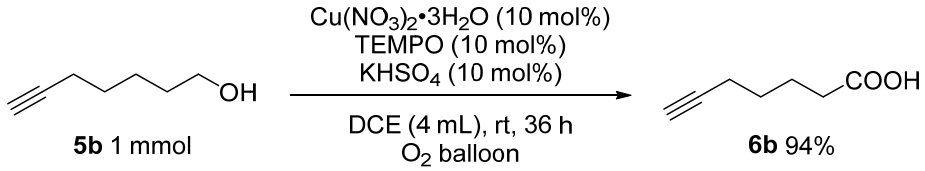
Hz, 1 H, Ar-H), 7.63 (s, 1 H, Ar-H), 7.38 (t, J = 8.0 Hz, 1 H, Ar-H), 7.16 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1 H, Ar-H), 3.86 (s, 3 H, OCH_3); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ = 172.4, 159.6, 130.5, 129.5, 122.7, 120.5, 114.4, 55.4.

(28) Preparation of 10-undecynoic acid (6a, yyb-2-036)



Following Typical Procedure I, the reaction of **5a** (168.7 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.3 mg, 0.1 mmol), TEMPO (16.2 mg, 0.1 mmol), and $KHSO_4$ (14.0 mg, 0.1 mmol) in DCE (4 mL) afforded **6a**[7] (167.4 mg, 92%) [eluent: petroleum ether/ethyl acetate = 10/1 (~160 mL) to 1/1 (~200 mL)] as white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.68 (br, 1 H, COOH), 2.35 (t, J = 7.6 Hz, 2 H, CH_2), 2.18 (td, J_1 = 7.0 Hz, J_2 = 2.7 Hz, 2 H, CH_2), 1.94 (t, J = 2.6 Hz, 1 H, CH), 1.63 (quintet, J = 7.3 Hz, 2 H, CH_2), 1.52 (quintet, J = 7.2 Hz, 2 H, CH_2), 1.47-1.11 (m, 8 H, 4 x CH_2); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ = 180.5, 84.6, 68.1, 34.0, 29.0, 28.9, 28.8, 28.5, 28.3, 24.5, 18.3.

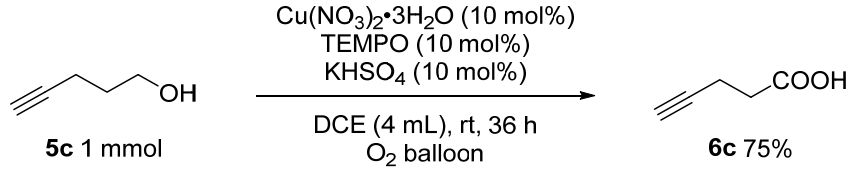
(29) Preparation of 6-heptynoic acid (6b, yyb-3-098)



Following Typical Procedure I, the reaction of **5b** (114.4 mg, 97% purity, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.1 mg, 0.1 mmol), TEMPO (16.2 mg, 0.1 mmol), and $KHSO_4$ (13.9 mg, 0.1 mmol) in DCE (4 mL) afforded **6b**[23] (117.0 mg, 94%) [eluent: petroleum ether/ethyl acetate = 5/1 (~240 mL) to 2/1 (~150 mL)] as light yellow oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.67 (br, 1 H, COOH), 2.40 (t, J = 7.4 Hz, 2 H, CH_2), 2.51 (td, J_1 = 6.9 Hz, J_2 = 2.5 Hz, 2 H, CH_2), 1.97 (t, J = 2.6 Hz, 1 H, CH), 2.40 (quintet, J = 7.6 Hz, 2 H, CH_2), 2.40 (quintetq, J = 7.4 Hz, 2 H, CH_2); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ = 180.1, 83.7, 68.7, 33.4, 27.6, 23.6, 18.0; **IR** (neat, cm^{-1}): 3296, 3200-2250,

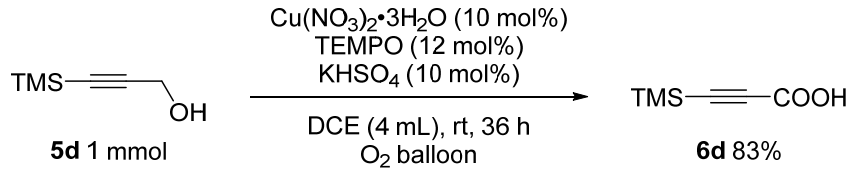
2117, 1702, 1456, 1412, 1332, 1289, 1233, 1147; **MS** (ESI) *m/z*: 127 $(M+H)^+$.

(30) Preparation of 4-pentynoic acid (6c, yyb-2-004)



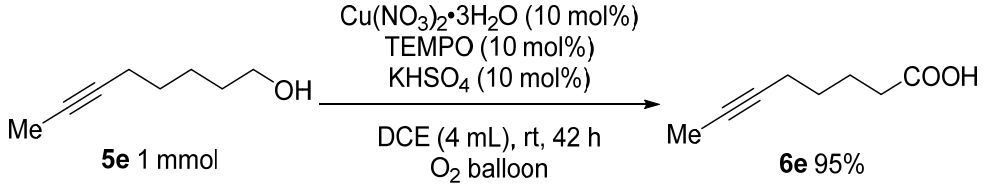
Following Typical Procedure I, the reaction of **5c** (84.2 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.1 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (4 mL) afforded **6c**[7] (74.0 mg, 75%) [eluent: petroleum ether/ethyl acetate = 5/1 (~240 mL) to 1/1 (~120 mL)] as white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.60 (br, 1 H, COOH), 2.62 (t, *J* = 7.2 Hz, 2 H, CH_2), 2.57-2.38 (m, 2 H, CH_2), 2.01 (s, 1 H, CH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 178.3, 82.0, 69.2, 33.1, 14.0.

(31) Preparation of 3-(trimethylsilyl)propiolic acid (6d, yyb-3-106)



Following Typical Procedure I, the reaction of **5d** (127.8 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.2 mg, 0.1 mmol), TEMPO (19.0 mg, 0.12 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (4 mL) afforded **6d**[7] (117.5 mg, 83%) [eluent: petroleum ether/ diethyl ether = 4/1 (~250 mL) to 1/1 (~200 mL)] as yellow oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 10.90 (br, 1 H, COOH), 0.26 (s, 9 H, 3 x CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 157.6, 97.2, 93.9, -1.1.

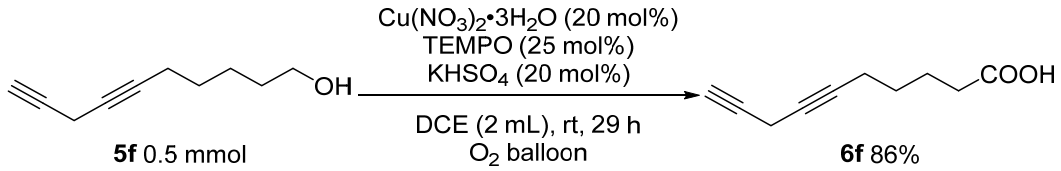
(32) Preparation of oct-6-ynoic acid (6e, yyb-3-109)



Following Typical Procedure I, the reaction of **5e** (127.8 mg, 1.0 mmol),

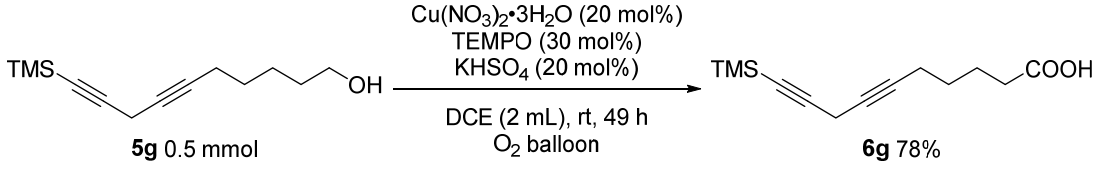
$Cu(NO_3)_2•3H_2O$ (24.3 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.6 mg, 0.1 mmol) in DCE (4 mL) afforded **6e**[24] (134.9 mg, 95%) [eluent: petroleum ether/ethyl acetate = 5/1 (~240 mL) to 2/1 (~150 mL)] as light yellow solid; m.p. 42.4-43.2 °C (petroleum ether); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.40 (br, 1 H, COOH), 2.38 (t, *J* = 7.4 Hz, 2 H, CH_2), 2.26-2.07 (m, 2 H, CH_2), 1.86-1.65 (m, 5 H, CH_3 and CH_2), 1.53 (quintet, *J* = 7.2 Hz, 2 H, CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 180.2, 78.4, 75.9, 33.6, 28.2, 23.8, 18.3, 3.4; **IR** (neat, cm^{-1}): 3250-2400, 1689, 1457, 1438, 1413, 1316, 1295, 1245, 1147; **MS** (ESI) *m/z*: 141 $(M+H)^+$.

(33) Preparation of deca-6,9-diynoic acid (6f, yyb-4-045)



Following Typical Procedure I, the reaction of **5f** (75.4 mg, 0.5 mmol), $Cu(NO_3)_2•3H_2O$ (24.2 mg, 0.1 mmol), TEMPO (20.1 mg, 0.125 mmol), and $KHSO_4$ (13.7 mg, 0.1 mmol) in DCE (2 mL) afforded **6f**[25] (70.8 mg, 86%) [eluent: petroleum ether/ethyl acetate = 5/1 (~300 mL) to 2/1 (~210 mL)] as yellow oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 10.45 (br, 1 H, COOH), 3.15 (q, *J* = 2.4 Hz, 2 H, CH_2), 2.38 (t, *J* = 7.4 Hz, 2 H, CH_2), 2.20 (tt, J_1 = 6.9 Hz, J_2 = 2.4 Hz, 2 H, CH_2), 2.07 (t, *J* = 2.6 Hz, 1 H, CH), 1.82-1.67 (m, 2 H, CH_2), 1.64-1.47 (m, 2 H, CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 179.9, 80.4, 78.7, 73.6, 68.4, 33.5, 27.8, 23.7, 18.3, 9.5; **IR** (neat, cm^{-1}): 3293, 3300-2800, 1703, 1458, 1413, 1311, 1289, 1233, 1148; **MS** (ESI) *m/z*: 163 $(M-H)^-$.

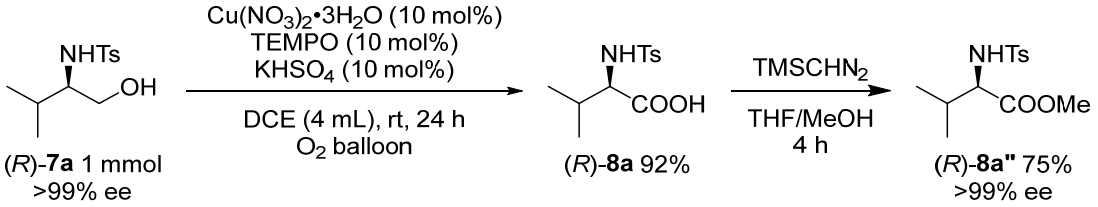
(34) Preparation of 10-(trimethylsilyl)deca-6,9-diynoic acid (6g, yyb-4-060)



Following Typical Procedure I, the reaction of **5g** (111.1 mg, 0.5 mmol), $Cu(NO_3)_2•3H_2O$ (24.3 mg, 0.1 mmol), TEMPO (24.1 mg, 0.15 mmol), and $KHSO_4$

(13.8 mg, 0.1 mmol) in DCE (2 mL) afforded **6g** (92.6 mg, 78%) [eluent: petroleum ether/ethyl acetate = 5/1 (~240 mL) to 3/1 (~200 mL)] as yellow oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 3.18 (t, *J* = 2.4 Hz, 2 H, CH_2), 2.38 (t, *J* = 7.6 Hz, 2 H, CH_2), 2.20 (tt, J_1 = 6.9 Hz, J_2 = 2.4 Hz, 2 H, CH_2), 1.79-1.68 (m, 2 H, CH_2), 1.62-1.51 (m, 2 H, CH_2), 0.16 (s, 9 H, 3 x CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 180.0, 100.6, 84.7, 80.2, 73.9, 33.5, 27.8, 23.7, 18.4, 10.8, -0.1; **IR** (neat, cm^{-1}): 3150-2750, 2182, 1707, 1412, 1308, 1291, 1249, 1149; **MS** (ESI) *m/z*: 235 $(M-H)^-$; **HRMS** calcd *m/z* for $C_{13}H_{21}O_2Si$ $[M+H]^+$: 237.1305, found 237.1302.

(35) Preparation of *N*-tosyl-*D*-valine ((*R*)-8a, yyb-2-194, yyb-2-196)



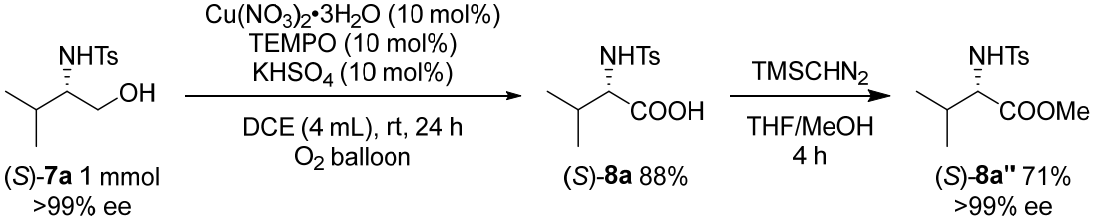
Following Typical Procedure I, the reaction of (*R*)-**7a** (257.9 mg, 1.0 mmol, >99% ee), $Cu(NO_3)_2$•$3H_2O$ (24.2 mg, 0.1 mmol), TEMPO (16.2 mg, 0.1 mmol), and $KHSO_4$ (13.9 mg, 0.1 mmol) in DCE (4 mL) afforded (*R*)-**8a**[26] (250.9 mg, 92%) [petroleum ether/ethyl acetate = 3/1 (~200 mL) to 1/1 (~250 mL)] as white solid; m.p. 146.7-147.5 ^{o}C (petroleum ether/acetone); $[\alpha]_D^{26}$ = -4.49 (*c* = 0.99, $CHCl_3$); **^{1}H NMR** (400 MHz, CD_3OD) δ = 7.72 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.32 (d, *J* = 8.0 Hz, 2 H, Ar-H), 3.62 (d, *J* = 5.6 Hz, 1 H, CH), 2.40 (s, 3 H, CH_3), 2.01 (sextet, *J* = 6.6 Hz, 1 H, CH), 0.94 (d, *J* = 6.4 Hz, 3 H, CH_3), 0.88 (d, *J* = 6.8 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, CD_3OD): δ = 174.3, 144.5, 139.1, 130.5, 128.2, 62.7, 32.4, 21.4, 19.6, 18.1; **IR** (neat, cm^{-1}): 3291, 3200-2400, 1705, 1597, 1464, 1331, 1288, 1159, 1088; **MS** (70 eV, EI) *m/z* (%): 226 ($(M-COOH)^+$, 80.18), 91 (100).

The ee of (*R*)-**8a** was determined by HPLC analysis after being converted to (*R*)-**8a''**.

Typical Procedure III: The flask containing (*R*)-**8a** (54.5 mg, 0.2 mmol) were sequentially added THF/MeOH (4.0 mL, 3:1/v:v) and $TMSCHN_2$ (0.12 mL, 2.0 M in hexane, 0.24 mmol) under argon atmosphere. The resulting mixture was stirred at room temperature for 4 h. After diluting with CH_2Cl_2 (20 mL) and sequential washing with

$NaHCO_3$ (sat.) and brine, the organic layer was dried over Na_2SO_4. After filtration and evaporation, the residue was purified by chromatography on silica gel to afford (*R*)-**8a''**[27] (42.9 mg, 75%, >99% ee) [eluent: petroleum ether/ethyl acetate = 4/1 (~250 mL)] as white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.71 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.28 (d, *J* = 8.0 Hz, 2 H, Ar-H), 5.10 (d, *J* = 10.0 Hz, 1 H, NH), 3.73 (q, *J* = 5.1 Hz, 1 H, CH), 3.44 (s, 3 H, OCH_3), 2.41 (s, 3 H, CH_3), 2.02 (sextet, *J* = 6.5 Hz, 1 H, CH), 0.95 (d, *J* = 6.8 Hz, 3 H, CH_3), 0.87 (d, *J* = 6.8 Hz, 3 H, CH_3); HPLC conditions: OJ-H column, hexane/*i*-PrOH = 95/5, 0.5 mL/min, λ = 214 nm, t_R (major) = 43.8 min.

(36) Preparation of *N*-tosyl-*L*-valine ((*S*)-8a, yyb-2-195, yyb-2-197)



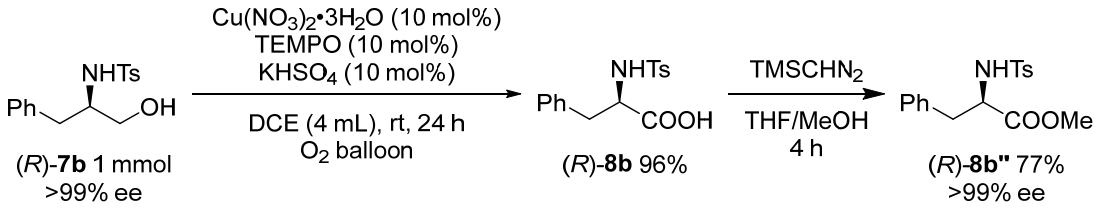
Following Typical Procedure I, the reaction of (*S*)-**7a** (258.4 mg, 1.0 mmol, >99% ee), $Cu(NO_3)_2$•$3H_2O$ (23.9 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (4 mL) afforded (*S*)-**8a**[28] (239.3 mg, 88%) [petroleum ether/ethyl acetate = 3/1 (~200 mL) to 1/1 (~200 mL)] as white solid; m.p. 146.8-147.5 °C (petroleum ether/acetone) (reported:[29] m.p. 146.4-147.7 °C (water)); $[\alpha]_D^{27}$ = +4.14 (*c* = 1.00, $CHCl_3$) (reported:[30] $[\alpha]_D^{25}$ = +17.1 (*c* = 2.23, $CHCl_3$)); **^{1}H NMR** (400 MHz, CD_3OD) δ = 7.72 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.32 (d, *J* = 8.0 Hz, 2 H, Ar-H), 3.62 (d, *J* = 5.6 Hz, 1 H, CH), 2.39 (s, 3 H, CH_3), 2.01 (sextet, *J* = 6.6 Hz, 1 H, CH), 0.94 (d, *J* = 6.8 Hz, 3 H, CH_3), 0.88 (d, *J* = 6.8 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, CD_3OD): δ = 174.3, 144.5, 139.1, 130.5, 128.2, 62.7, 32.4, 21.4, 19.6, 18.1; **IR** (neat, cm^{-1}): 3291, 3150-2350, 1703, 1597, 1464, 1331, 1288, 1159, 1088; **MS** (70 eV, EI) *m*/*z* (%): 226 ($(M\text{-}COOH)^+$, 87.14), 91 (100).

The ee of (*S*)-**8a** was determined by HPLC analysis after being converted to (*S*)-**8a''**.

Following Typical Procedure III, the reaction of (*S*)-**8a** (54.2 mg, 0.2 mmol) and $TMSCHN_2$ (0.12 mL, 2.0 M in hexane, 0.24 mmol) in THF/MeOH (4.0 mL, 3:1/v:v)

afforded (*S*)-**8a''** [31] (40.3 mg, 71%, >99% ee) [eluent: petroleum ether/ethyl acetate = 4/1 (~250 mL)] as white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.71 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.28 (d, *J* = 8.4 Hz, 2 H, Ar-H), 5.13 (d, *J* = 10.0 Hz, 1 H, NH), 3.73 (q, *J* = 5.1 Hz, 1 H, CH), 3.44 (s, 3 H, OCH_3), 2.41 (s, 3 H, CH_3), 2.02 (sextet, *J* = 6.5 Hz, 1 H, CH), 0.95 (d, *J* = 6.8 Hz, 3 H, CH_3), 0.87 (d, *J* = 6.8 Hz, 3 H, CH_3); HPLC conditions: OJ-H column, hexane/*i*-PrOH = 95/5, 0.5 mL/min, λ = 214 nm, t_R (major) = 46.5 min.

(37) Preparation of *N*-tosyl-*D*-phenylalanine ((*R*)-8b, yyb-2-182, yyb-2-189)



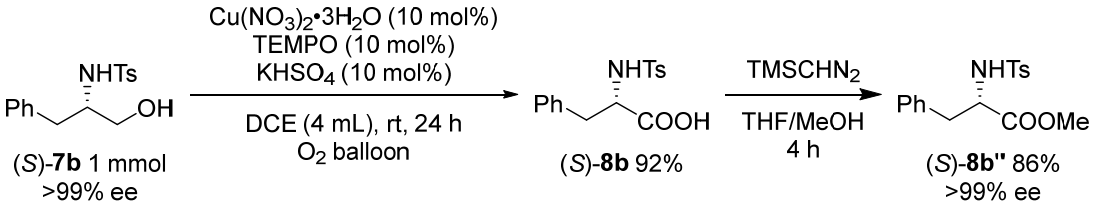
Following Typical Procedure I, the reaction of (*R*)-**7b** (311.6 mg, 1.0 mmol, >99% ee), $Cu(NO_3)_2$•$3H_2O$ (24.7 mg, 0.1 mmol), TEMPO (16.2 mg, 0.1 mmol), and $KHSO_4$ (13.7 mg, 0.1 mmol) in DCE (4 mL) afforded (*R*)-**8b**[28] (313.7 mg, 96%) [petroleum ether/ethyl acetate = 3/1 (~200 mL) to 1/1 (~300 mL)] as white solid; m.p. 150.8-151.4 °C (petroleum ether/ethyl acetate) (reported:[28] m.p. 160 °C (diethyl ether/ethanol)); $[\alpha]_D^{27}$ = +9.28 (*c* = 1.00, $CHCl_3$) (reported:[32] $[\alpha]_D^{27}$ = +12.3, (*c* = 1.00, acetone)); **^{1}H NMR** (400 MHz, CD_3OD) δ = 7.54 (d, *J* = 7.6 Hz, 2 H, Ar-H), 7.28-7.00 (m, 7 H, Ar-H), 4.00 (t, *J* = 6.8 Hz, 1 H, CH), 3.02 (dd, J_1 = 13.6 Hz, J_2 = 5.6 Hz, 1 H, one proton of CH_2), 2.83 (dd, J_1 = 13.4 Hz, J_2 = 8.2 Hz, 1 H, one proton of CH_2), 2.38 (s, 3 H, CH_3); **^{13}C NMR** (100 MHz, CD_3OD): δ = 174.3, 144.4, 139.0, 137.7, 130.5, 130.4, 129.3, 128.0, 127.7, 58.7, 39.8, 21.4; **IR** (neat, cm^{-1}): 3318, 3200-2800, 1709, 1597, 1388, 1328, 1273, 1159, 1088; **MS** (70 eV, EI) *m*/*z* (%): 274 ((M-COOH)$^+$, 228 ((M-Bn)$^+$, 11.45), 5.60), 91 (100).

The ee of (*R*)-**8b** was determined by HPLC analysis after being converted to (*R*)-**8b''**.

Following Typical Procedure III, the reaction of (*R*)-**8b** (64.5 mg, 0.2 mmol) and $TMSCHN_2$ (0.12 mL, 2.0 M in hexane, 0.24 mmol) in THF/MeOH (4.0 mL, 3:1/v:v) afforded (*R*)-**8b''** [33] (52.1 mg, 77%, >99% ee) [eluent: petroleum ether/ethyl acetate =

4/1 (~250 mL)] as white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.63 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.33-7.14 (m, 5 H, Ar-H), 7.12-6.97 (m, 2 H, Ar-H), 5.17 (s, 1 H, NH), 4.20 (t, *J* = 6.0 Hz, 1 H, CH), 3.48 (s, 3 H, OCH_3), 3.09-2.91 (m, 2 H, CH_2), 2.39 (s, 3 H, CH_3); HPLC conditions: OJ-H column, hexane/*i*-PrOH = 80/20, 1.0 mL/min, λ = 214 nm, t_R (major) = 18.4 min.

(38) Preparation of *N*-tosyl-*L*-phenylalanine ((*S*)-8b, yyb-2-185, yyb-2-190)



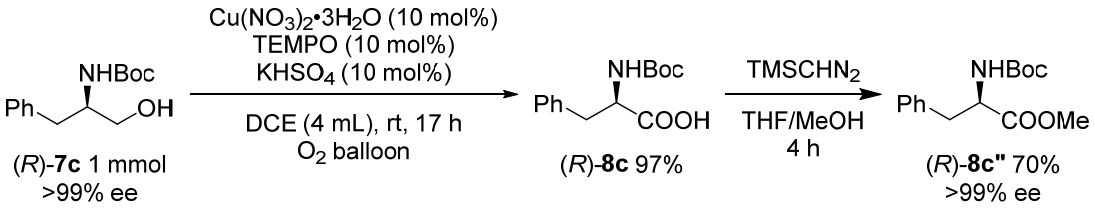
Following Typical Procedure I, the reaction of (*S*)-**7b** (305.4 mg, 1.0 mmol, >99% ee), $Cu(NO_3)_2$•$3H_2O$ (23.9 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.7 mg, 0.1 mmol) in DCE (4 mL) afforded (*S*)-**8b**[28] (294.7 mg, 92%) [petroleum ether/ethyl acetate = 3/1 (~200 mL) to 1/1 (~200 mL)] as white solid; m.p. 150.8-151.5 °C (petroleum ether/ethyl acetate) (reported:[29] m.p. 150.4-152.9 °C (water)); $[\alpha]_D^{27}$ = -10.75 (*c* = 1.02, $CHCl_3$) (reported:[32] $[\alpha]_D^{27}$ = -11.8, (*c* = 1.00, acetone)); **^{1}H NMR** (400 MHz, CD_3OD) δ = 7.54 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.30-7.00 (m, 7 H, Ar-H), 4.02 (t, *J* = 6.8 Hz, 1 H, CH), 3.02 (dd, J_1 = 14.0 Hz, J_2 = 5.6 Hz, 1 H, one proton of CH_2), 2.84 (dd, J_1 = 13.8 Hz, J_2 = 8.2 Hz, 1 H, one proton of CH_2), 2.37 (s, 3 H, CH_3); **^{13}C NMR** (100 MHz, CD_3OD): δ = 174.3, 144.4, 139.1, 137.8, 130.5, 130.4, 129.4, 128.0, 127.7, 58.7, 39.9, 21.4; **IR** (neat, cm^{-1}): 3319, 3200-2800, 1709, 1694, 1597, 1388, 1328, 1274, 1159, 1088; **MS** (70 eV, EI) *m*/*z* (%): 274 ($(M\text{-}COOH)^+$, 5.97), 228 ($(M\text{-}Bn)^+$, 11.95), 91 (100).

The ee of (*S*)-**8b** was determined by HPLC analysis after being converted to (*S*)-**8b''**.

Following Typical Procedure III, the reaction of (*S*)-**8b** (63.8 mg, 0.2 mmol) and $TMSCHN_2$ (0.12 mL, 2.0 M in hexane, 0.24 mmol) in THF/MeOH (4.0 mL, 3:1/v:v) afforded (*S*)-**8b''** [34] (57.5 mg, 86%, >99% ee) [eluent: petroleum ether/ethyl acetate = 4/1 (~250 mL)] as white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.63 (d, *J* = 8.4 Hz, 2

H, Ar-H), 7.30-7.14 (m, 5 H, Ar-H), 7.13-6.97 (m, 2 H, Ar-H), 5.17 (d, J = 9.2 Hz, 1 H, NH), 4.20 (dt, J_1 = 11.1 Hz, J_2 = 4.6 Hz, 1 H, CH), 3.48 (s, 3 H, OCH_3), 3.10-2.94 (m, 2 H, CH_2), 2.39 (s, 3 H, CH_3); HPLC conditions: OJ-H column, hexane/*i*-PrOH = 80/20, 1.0 mL/min, λ = 214 nm, t_R (major) = 37.1 min.

(39) Preparation of *N*-Boc-*D*-phenylalanine ((*R*)-8c, yyb-3-023, yyb-3-028)



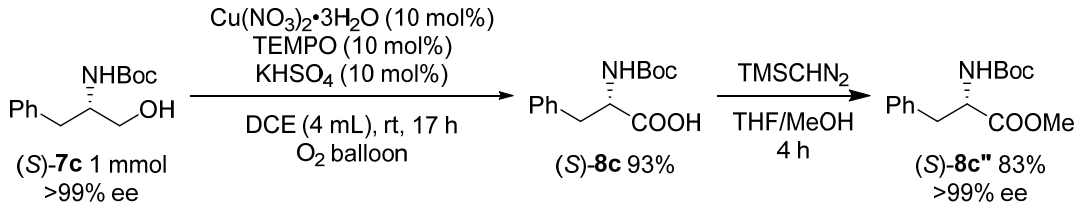
Following Typical Procedure I, the reaction of (*R*)-**7c** (251.4 mg, 1.0 mmol, >99% ee), $Cu(NO_3)_2$•$3H_2O$ (24.2 mg, 0.1 mmol), TEMPO (16.1 mg, 0.1 mmol), and $KHSO_4$ (13.7 mg, 0.1 mmol) in DCE (4 mL) afforded (*R*)-**8c**[35] (257.4 mg, 97%) [petroleum ether/ethyl acetate = 3/1 (~200 mL) to 1/1 (~300 mL)] as yellow oil; $[\alpha]_D^{25}$ = -21.75 (*c* = 1.21, $CHCl_3$) (reported:[36] $[\alpha]_D^{25}$ = -24.8 (*c* = 1.00, EtOH)); **^{1}H NMR** (400 MHz, CD_3Cl, rotamers present) δ = 11.44 (br, 1 H, COOH), 7.38-7.07 (m, 5 H, Ar-H), [6.65 (d, J = 7.2 Hz, 0.40 H), 5.10 (d, J = 8.0 Hz, 0.54 H), 1 H, NH], [4.70-4.56 (m, 0.55 H), 4.57-4.30 (m, 0.41 H), 1 H, CH], 3.28-3.11 (m, 1 H, one proton of CH_2), [3.07 (dd, J_1 = 13.6 Hz, J_2 = 6.0 Hz, 0.58 H), 2.95-2.80 (m, 0.41 H), 1 H, one proton of CH_2], [1.41 (s, 5 H), 1.29 (s, 4 H), 9 H, 3 x CH_3]; **^{13}C NMR** (100 MHz, CD_3Cl, rotamers present): δ = 176.1, 175.8, 156.6, 155.3, 136.4, 135.8, 129.34, 129.29, 128.4, 126.9, 126.8, 81.5, 80.1, 56.0, 54.1, 38.9, 37.7, 28.1, 27.8; **IR** (neat, cm^{-1}): 2980, 3200-2800, 1713, 1663, 1497, 1395, 1368, 1159, 1052; **MS** (70 eV, EI) *m/z* (%): 265 (M^+, 0.36), 164 ($(M\text{-Boc})^+$, 9.64), 57 (100).

The ee of (*R*)-**8c** was determined by HPLC analysis after being converted to (*R*)-**8c''**.

Following Typical Procedure III, the reaction of (*R*)-**8c** (57.2 mg, 0.2 mmol) and $TMSCHN_2$ (0.12 mL, 2.0 M in hexane, 0.24 mmol) in THF/MeOH (4.0 mL, 3:1/v:v) afforded (*R*)-**8c''**[37] (42.3 mg, 70%, >99% ee) [eluent: petroleum ether/ethyl acetate = 4/1 (~120 mL)] as light yellow oil; **^{1}H NMR** (400 MHz, CD_3Cl, rotamers present) δ =

7.37-7.19 (m, 3 H, Ar-H), 7.18-7.07 (m, 2 H, Ar-H), [5.13-4.86 (m, 0.85 H), 4.84-4.68 (m, 0.14 H), 1 H, NH], [4.65-4.47 (m, 0.85 H), 4.46-4.32 (m, 0.14 H), 1 H, CH], 3.81-3.60 (m, 3 H, OCH_3), 3.19-2.88 (m, 2 H, CH_2), 1.41 (s, 9 H, 3 x CH_3); HPLC conditions: OJ-H column, hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 214 nm, t_R (major) = 5.6 min.

(40) Preparation of *N*-Boc-*L*-phenylalanine ((*S*)-8c, yyb-3-024, yyb-3-029)



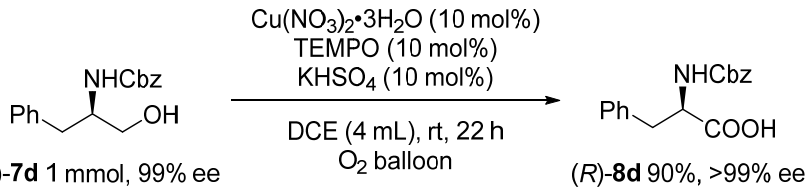
Following Typical Procedure I, the reaction of (*S*)-**7c** (252.4 mg, 1.0 mmol, >99% ee), $Cu(NO_3)_2$•$3H_2O$ (24.3 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (4 mL) afforded (*S*)-**8c**[32] (246.4 mg, 93%) [petroleum ether/ethyl acetate = 3/1 (~200 mL) to 1/1 (~300 mL)] as yellow oil; $[\alpha]_D^{26}$ = +21.98 (*c* = 1.06, $CHCl_3$) (reported:[36] $[\alpha]_D^{25}$ = +24.9 (*c* = 1.20, EtOH)); **^{1}H NMR** (400 MHz, CD_3Cl, rotamers present) δ = 11.39 (br, 1 H, COOH), 7.42-7.03 (m, 5 H, Ar-H), [6.63 (d, *J* = 7.2 Hz, 0.38 H), 5.06 (d, *J* = 8.0 Hz, 0.53 H), 1 H, NH], [4.70-4.57 (m, 0.55 H), 4.48-4.32 (m, 0.39 H), 1 H, CH], 3.28-3.12 (m, 1 H, one proton of CH_2), [3.07 (dd, J_1 = 13.8 Hz, J_2 = 6.2 Hz, 0.58 H), 2.95-2.80 (m, 0.38 H), 1 H, one proton of CH_2], [1.41 (s, 5 H), 1.29 (s, 4 H), 9 H, 3 x CH_3]; **^{13}C NMR** (100 MHz, CD_3Cl, rotamers present): δ = 176.3, 176.0, 156.6, 155.3, 136.4, 135.8, 129.4, 129.3, 128.5, 126.9, 126.9, 81.6, 80.2, 56.1, 54.2, 39.0, 37.7, 28.2, 27.9; **IR** (neat, cm^{-1}): 2979, 3200-2800, 1713, 1662, 1497, 1395, 1368, 1159, 1052; **MS** (70 eV, EI) *m*/*z* (%): 265 (M^+, 0.57), 164 ($(M\text{-Boc})^+$, 10.47), 57 (100).

The ee of (*S*)-**8c** was determined by HPLC analysis after being converted to (*S*)-**8c''**.

Following Typical Procedure III, the reaction of (*S*)-**8c** (42.3 mg, 0.16 mmol) and $TMSCHN_2$ (0.10 mL, 2.0 M in hexane, 0.20 mmol) in THF/MeOH (4.0 mL, 3:1/v:v) afforded (*S*)-**8c''**[38] (36.9 mg, 83%, >99% ee) [eluent: petroleum ether/ethyl acetate = 4/1 (~120 mL)] as light yellow oil; **^{1}H NMR** (400 MHz, CD_3Cl, rotamers present) δ =

7.40-7.19 (m, 3 H, Ar-H), 7.18-7.04 (m, 2 H, Ar-H), [5.13-4.87 (m, 0.84 H), 4.82-4.68 (m, 0.14 H), 1 H, NH], [4.68-4.20 (m, 0.83 H), 4.45-4.29 (m, 0.13 H), 1 H, CH], 3.71 (s, 3 H, OCH_3), 3.26-2.75 (m, 2 H, CH_2), 1.41 (s, 9 H, 3 x CH_3); HPLC conditions: OJ-H column, hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 214 nm, t_R (major) = 6.1 min.

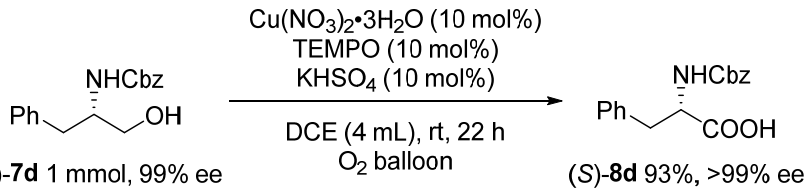
(41) Preparation of *N*-Cbz-*D*-phenylalanine ((*R*)-8d, yyb-3-071)



(*R*)-**7d** 1 mmol, 99% ee (*R*)-**8d** 90%, >99% ee

Following Typical Procedure I, the reaction of (*R*)-**7d** (285.2 mg, 1.0 mmol, 99% ee), $Cu(NO_3)_2$•$3H_2O$ (24.4 mg, 0.1 mmol), TEMPO (16.1 mg, 0.1 mmol), and $KHSO_4$ (13.9 mg, 0.1 mmol) in DCE (4 mL) afforded (*R*)-**8d**[39] (269.7 mg, 90%, >99% ee) [petroleum ether/ethyl acetate = 3/1 (~200 mL) to 1/1 (~300 mL)] as light yellow oil; HPLC conditions: AD-H column, hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 214 nm, t_R (major) = 18.1 min; $[\alpha]_D^{31}$ = -31.24 (*c* = 0.895, $CHCl_3$); **^{1}H NMR** (400 MHz, CD_3Cl, rotamers present) δ = 10.59 (br, 1 H, COOH), 7.60-7.18 (m, 8 H, Ar-H), 7.13 (d, *J* = 6.8 Hz, 2 H, Ar-H), [6.33 (d, *J* = 6.8 Hz, 0.21 H), 5.27 (d, *J* = 8.0 Hz, 0.77 H), 1 H, NH], 5.15-4.91 (m, 2 H, CH_2), [4.77-4.61 (m, 0.75 H), 4.57-4.45 (m, 0.22 H), 1 H, CH], 3.28-2.87 (m, 2 H, CH_2); **^{13}C NMR** (100 MHz, CD_3Cl, rotamers present): δ = 176.3, 176.0, 156.6, 155.9, 136.0, 135.7, 135.4, 129.3, 128.6, 128.5, 128.2, 128.1, 127.9, 127.2, 67.6, 67.1, 55.6, 54.6, 38.5, 37.7; **IR** (neat, cm^{-1}): 2960, 3200-2800, 1713, 1515, 1497, 1375, 1345, 1213, 1049; **MS** (ESI) *m/z*: 298 $(M-H)^-$.

(42) Preparation of *N*-Cbz-*L*-phenylalanine ((*S*)-8d, yyb-3-070)

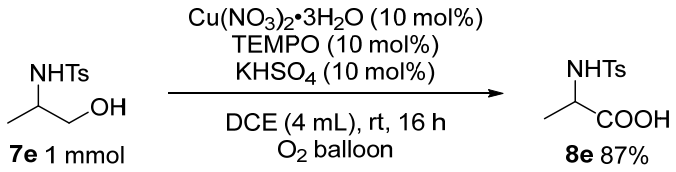


(*S*)-**7d** 1 mmol, 99% ee (*S*)-**8d** 93%, >99% ee

Following Typical Procedure I, the reaction of (*S*)-**7d** (285.7 mg, 1.0 mmol, 99% ee), $Cu(NO_3)_2$•$3H_2O$ (24.1 mg, 0.1 mmol), TEMPO (16.2 mg, 0.1 mmol), and $KHSO_4$

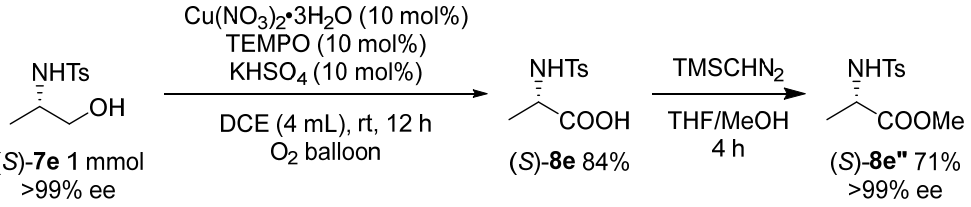
(13.9 mg, 0.1 mmol) in DCE (4 mL) afforded (*S*)-**8d**[40] (277.7 mg, 93%, >99% ee) [petroleum ether/ethyl acetate = 3/1 (~200 mL) to 1/1 (~300 mL)] as light yellow oil; HPLC conditions: AD-H column, hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 214 nm, t_R (major) = 22.7 min; $[\alpha]_D^{31}$ = +33.76 (*c* = 0.85, $CHCl_3$); **^{1}H NMR** (400 MHz, CD_3Cl, rotamers present) δ = 11.14 (br, 1 H, COOH), 7.40-7.15 (m, 8 H, Ar-H), 7.12 (d, *J* = 7.2 Hz, 2 H, Ar-H), [6.45 (d, *J* = 7.2 Hz, 0.23 H), 5.34 (d, *J* = 8.0 Hz, 0.75 H), 1 H, NH], 5.16-4.90 (m, 2 H, CH_2), [4.75-4.60 (m, 0.74 H), 4.58-4.40 (m, 0.25 H), 1 H, CH], 3.27-2.84 (m, 2 H, CH_2); **^{13}C NMR** (100 MHz, CD_3Cl, rotamers present): δ = 176.1, 175.9, 156.7, 155.9, 136.0, 135.7, 135.5, 129.3, 128.5, 128.4, 128.1, 128.0, 127.9, 127.1, 67.6, 67.1, 55.6, 54.6, 38.4, 37.6; **IR** (neat, cm^{-1}): 2945, 3200-2800, 1712, 1515, 1497, 1375, 1345, 1157, 1048; **MS** (ESI) *m/z*: 298 $(M-H)^-$.

(43) Preparation of *N*-tosyl-*DL*-alanine (8e, yyb-2-074)



Following Typical Procedure I, the reaction of **7e** (229.3 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.2 mg, 0.1 mmol), TEMPO (16.1 mg, 0.1 mmol), and $KHSO_4$ (13.7 mg, 0.1 mmol) in DCE (4 mL) afforded **8e**[34] (211.0 mg, 87%) [petroleum ether/ethyl acetate = 5/1 (~180 mL) to 1/1 (~200 mL)] as white solid; m.p. 138.3-139.4 °C (petroleum ether/acetone) (reported:[41] m.p. 138-139 °C (water)); **^{1}H NMR** (400 MHz, CD_3OD) δ = 7.73 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.34 (d, *J* = 8.0 Hz, 2 H, Ar-H), 3.88 (q, *J* = 7.1 Hz, 1 H, CH), 2.40 (s, 3 H, CH_3), 1.29 (d, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, CD_3OD): δ = 175.4, 144.7, 139.2, 130.6, 128.1, 52.6, 21.4, 19.5; **IR** (neat, cm^{-1}): 3273, 2434, 1709, 1495, 1339, 1289, 1243, 1168, 1090; **MS** (70 eV, EI) *m/z* (%): 198 ($(M-COOH)^+$, 10.28), 91 (100).

(44) Preparation of *N*-tosyl-*L*-alanine ((*S*)-8e, yyb-2-080, yyb-2-131)

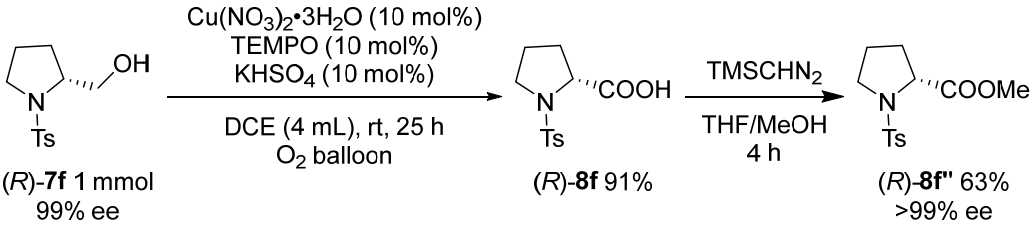


Following Typical Procedure I, the reaction of (*S*)-**7e** (229.9 mg, 1.0 mmol, >99% ee), $Cu(NO_3)_2$•$3H_2O$ (24.2 mg, 0.1 mmol), TEMPO (16.1 mg, 0.1 mmol), and $KHSO_4$ (13.9 mg, 0.1 mmol) in DCE (4 mL) afforded (*S*)-**8e**[42] (205.7 mg, 84%) [petroleum ether/acetone = 5/1 (~180 mL) to 1/1 (~300 mL)] as white solid; $[\alpha]_D^{30}$ = -13.3 (*c* = 0.29, MeOH) (reported:[42] $[\alpha]_D^{20}$ = -11, (*c* = 1.6, MeOH)); m.p. 132.3-133.2 °C (petroleum ether/acetone) (reported:[43] m.p. 129-131 °C (ethyl acetate)); **^{1}H NMR** (400 MHz, CD_3OD) δ = 7.73 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.34 (d, *J* = 8.0 Hz, 2 H, Ar-H), 3.87 (q, *J* = 7.1 Hz, 1 H, CH), 2.40 (s, 3 H, CH_3), 1.28 (d, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, CD_3OD): δ = 175.4, 144.7, 139.2, 130.6, 128.1, 52.7, 21.4, 19.5; **IR** (neat, cm^{-1}): 3269, 3300-2800, 1710, 1653, 1379, 1290, 1230, 1149, 1090; **MS** (70 eV, EI) *m*/*z* (%): 198 ($(M\text{-}COOH)^+$, 10.28), 91 (100).

The ee of (*S*)-**8e** was determined by HPLC analysis after being converted to (*S*)-**8e''**.

Following Typical Procedure III, the reaction of (*S*)-**8e** (49.0 mg, 0.2 mmol) and $TMSCHN_2$ (0.12 mL, 2.0 M in hexane, 0.24 mmol) in THF/MeOH (4.0 mL, 3:1/v:v) afforded (*S*)-**8e'':**[44] (37.0 mg, 71%, >99% ee) [eluent: petroleum ether/ethyl acetate = 4/1 (~250 mL)] as light yellow oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.73 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.30 (d, *J* = 8.0 Hz, 2 H, Ar-H), 5.37 (d, *J* = 8.4 Hz, 1 H, NH), 3.99 (quintet, *J* = 7.4 Hz, 1 H, CH), 3.54 (s, 3 H, OCH_3), 2.42 (s, 3 H, CH_3), 1.38 (d, *J* = 7.2 Hz, 3 H, CH_3); HPLC conditions: OJ-H column, hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 214 nm, t_R (major) = 24.1 min.

(45) Preparation of *N*-tosyl-*D*-proline ((*R*)-8f, yyb-2-160, yyb-2-165)

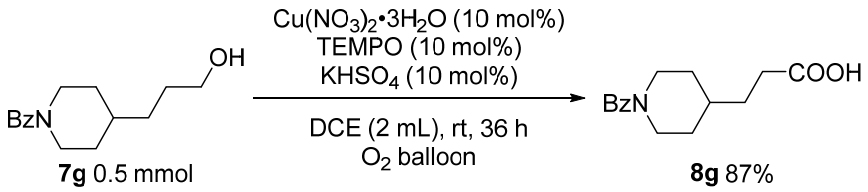


Following Typical Procedure I, the reaction of (*R*)-**7f** (254.9 mg, 1.0 mmol, 99% ee), $Cu(NO_3)_2$•$3H_2O$ (24.5 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (4 mL) afforded (*R*)-**8f**[45] (245.7 mg, 91%) [eluent: ethyl acetate (150 mL)] as light yellow oil; $[\alpha]_D^{24}$ = +90.60 (*c* = 1.13, $CHCl_3$) (reported:[45] $[\alpha]_D$ = +92.3 (*c* = 1.0, $CHCl_3$)); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 9.97 (br, 1 H, COOH), 7.76 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.34 (d, *J* = 8.0 Hz, 2 H, Ar-H), 4.46-4.21 (m, 1 H, CH), 3.60-3.41 (m, 1 H, one proton of CH_2), 3.35-3.19 (m, 1 H, one proton of CH_2), 2.43 (s, 3 H, CH_3), 2.18-1.89 (m, 3 H, one proton of CH_2 and CH_2), 1.81-1.62 (m, 1 H, one proton of CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 176.9, 143.9, 134.3, 129.7, 127.3, 60.2, 48.5, 30.6, 24.4, 21.3; **IR** (neat, cm^{-1}): 3563, 3200-2750, 1743, 1706, 1334, 1282, 1233, 1154, 1091; **MS** (70 eV, EI) *m*/*z* (%): 224 ($(M\text{-}COOH)^+$, 97.75), 91 (100).

The ee of (*R*)-**8f** was determined by HPLC analysis after being converted to (*R*)-**8f''**.

Following Typical Procedure III, the reaction of (*R*)-**8f** (54.4 mg, 0.2 mmol) and $TMSCHN_2$ (0.12 mL, 2.0 M in hexane, 0.24 mmol) in THF/MeOH (4.0 mL, 3:1/v:v) afforded (*R*)-**8f''**[46] (36.3 mg, 63%, >99% ee) [eluent: petroleum ether/ethyl acetate = 3/1 (~200 mL)] as light yellow oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.75 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.32 (d, *J* = 8.0 Hz, 2 H, Ar-H), 4.34-4.25 (m, 1 H, CH), 3.72 (s, 3 H, OCH_3), 3.54-3.45 (m, 1 H, one proton of CH_2), 3.37-3.25 (m, 1 H, one proton of CH_2), 2.43 (s, 3 H, CH_3), 2.08-1.89 (m, 3 H, one proton of CH_2 and CH_2), 1.82-1.68 (m, 1 H, one proton of CH_2); HPLC conditions: OJ-H column, hexane/*i*-PrOH = 90/10, 1.0 mL/min, λ = 214 nm, t_R (major) = 36.8 min.

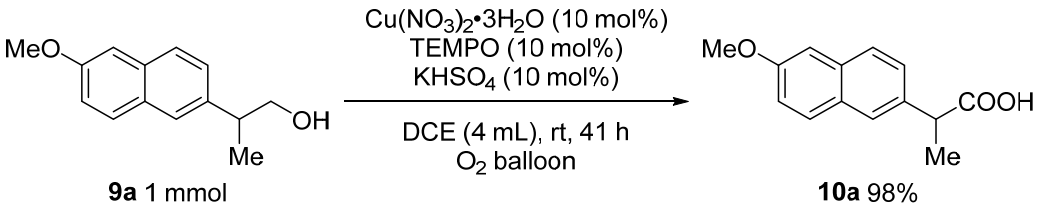
(46) Preparation of 3-(1-benzoylpiperidin-4-yl)propanoic acid (8g, yyb-7-129)



7g 0.5 mmol **8g** 87%

Following Typical Procedure I, the reaction of **7g** (124.6 mg, 0.5 mmol), $Cu(NO_3)_2•3H_2O$ (12.0 mg, 0.05 mmol), TEMPO (8.0 mg, 0.05 mmol), and $KHSO_4$ (7.1 mg, 0.05 mmol) in DCE (2 mL) afforded **8g:**[47] (114.2 mg, 87%) [petroleum ether/ethyl acetate = 1/1 (~200 mL), then ethyl acetate (~200 mL)] as white solid; m.p. 148.9-149.4 °C (petroleum ether/dichloromethane) (reported:[48] m.p. 149-150 °C (toluene)); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 10.44 (br, 1 H, COOH), 7.39 (s, 5 H, Ar-H), 4.85-4.53 (m, 1 H, one proton of CH_2), 3.92-3.57 (m, 1 H, one proton of CH_2), 3.09-2.86 (m, 1 H, one proton of CH_2), 2.85-2.60 (m, 1 H, one proton of CH_2), 2.36 (t, *J* = 6.8 Hz, 2 H, CH_2), 1.92-1.74 (m, 1 H, CH), 1.70-1.49 (m, 4 H, 2 x CH_2), 1.35-1.03 (m, 2 H, CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 178.4, 170.5, 135.9, 129.5, 128.4, 126.8, 47.9, 42.4, 35.4, 32.5, 31.5, 31.2, 30.9; **IR** (neat, cm^{-1}): 1720, 1594, 1566, 1449, 1272, 1215, 1192, 1077; **MS** (70 eV, EI) *m/z* (%): 261 (M^+, 23.37), 105 (100).

(47) Preparation of 2-(6-methoxynaphthalen-2-yl)propanoic acid (10a, yyb-3-139)

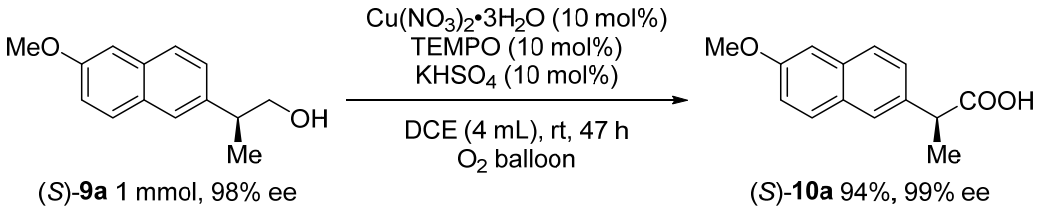


9a 1 mmol **10a** 98%

Following Typical Procedure I, the reaction of **9a** (217.1 mg, 1.0 mmol), $Cu(NO_3)_2•3H_2O$ (24.3 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.9 mg, 0.1 mmol) in DCE (4 mL) afforded **10a**[49] (225.6 mg, 98%) [eluent: petroleum ether/ethyl acetate = 8/1 (~180 mL) to 1/1 (~200 mL)] as light yellow solid; m.p. 154.4-156.2 °C (petroleum ether/dichloromethane); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.81-7.65 (m, 3 H, Ar-H), 7.41 (d, *J* = 8.4 Hz, 1 H, Ar-H), 7.18-6.98 (m, 2 H, Ar-H), 4.00-3.76 (m, 4 H, CH and OCH_3), 1.58 (d, *J* = 6.8 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 180.7, 157.7, 134.9, 133.8, 129.3, 128.9, 127.2, 126.2, 126.1, 119.0, 105.6,

55.3, 45.2, 18.1; **IR** (neat, cm^{-1}): 3200-2700, 1706, 1603, 1458, 1391, 1264, 1230, 1029; **MS** (70 eV, EI) *m*/*z* (%): 230 (M^+, 48.9), 185 (100).

(48) Preparation of (2*S*)-2-(6-methoxynaphthalen-2-yl)propanoic acid (Naproxen) ((*S*)-10a, yyb-3-121)

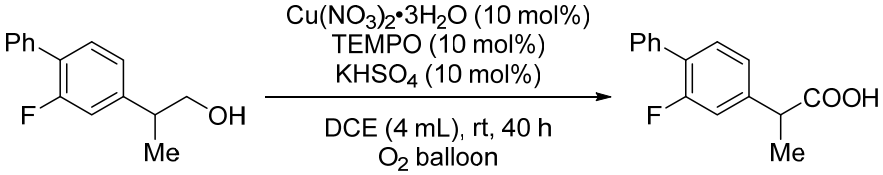


(*S*)-**9a** 1 mmol, 98% ee

(*S*)-**10a** 94%, 99% ee

Following Typical Procedure I, the reaction of (*S*)-**9a** (215.2 mg, 1.0 mmol, 98% ee), $Cu(NO_3)_2•3H_2O$ (24.2 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (4 mL) afforded (*S*)-**10a**[15] (215.5 mg, 94%, 99% ee) [eluent: petroleum ether/ethyl acetate = 5/1 (~180 mL) to 1/1 (~200 mL)] as white solid; m.p. 152.0-153.1 °C (petroleum ether/dichloromethane) (reported:[50] m.p. 152-154 °C (hexane/dichloromethane)); HPLC conditions: AD-H column, hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 214 nm, t_R (major) = 22.2 min, t_R (minor) = 20.4 min; $[\alpha]_D^{25}$ = +66.52 (*c* = 1.08, $CHCl_3$) (reported:[51] $[\alpha]_D^{26}$ = +64.9 (*c* = 1.8, $CHCl_3$)); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.80-7.60 (m, 3 H, Ar-H), 7.40 (d, *J* = 8.4 Hz, 1 H, Ar-H), 7.18-7.03 (m, 2 H, Ar-H), 4.02-3.78 (m, 4 H, CH and OCH_3), 1.58 (d, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 180.8, 157.7, 134.8, 133.8, 129.3, 128.9, 127.2, 126.2, 126.1, 119.0, 105.6, 55.3, 45.2, 18.1; **IR** (neat, cm^{-1}): 3300-2700, 1725, 1681, 1453, 1393, 1263, 1174, 1156; **MS** (70 eV, EI) *m*/*z* (%): 230 (M^+, 47.23), 185 (100).

(49) Preparation of 2-(2-fluoro-[1,1'-biphenyl]-4-yl)propanoic acid (Flurbiprofen) (10b, yyb-3-132)



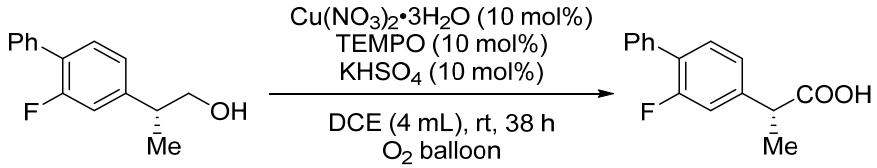
9b 1 mmol

10b 98%

Following Typical Procedure I, the reaction of **9b** (230.4 mg, 1.0 mmol), $Cu(NO_3)_2•3H_2O$ (25.0 mg, 0.1 mmol), TEMPO (16.1 mg, 0.1 mmol), and $KHSO_4$ (13.9

mg, 0.1 mmol) in DCE (4 mL) afforded **10b**[52] (240.2 mg, 98%) [eluent: petroleum ether/ethyl acetate = 15/1 (~160 mL) to 4/1 (~250 mL), then 2/1 (~150 mL)] as white solid; m.p. 112.6-113.7 ºC (petroleum ether/dichloromethane); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.60-7.48 (m, 2 H, Ar-H), 7.47-7.27 (m, 4 H, Ar-H), 7.21-7.04 (m, 2 H, Ar-H), 3.78 (q, *J* = 7.1 Hz, 1 H, CH), 1.55 (d, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 180.2, 159.7 (d, *J* = 247.3 Hz), 140.9 (d, *J* = 7.2 Hz), 135.4, 130.9 (d, *J* = 4.0 Hz), 128.9 (d, *J* = 2.3 Hz), 128.4, 128.1 (d, *J* = 13.5 Hz), 127.7, 123.7 (d, *J* = 4.0 Hz), 115.4 (d, *J* = 23.7 Hz), 44.8, 18.0; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -117.9; **IR** (neat, cm^{-1}): 3100-2400, 1695, 1460, 1415, 1296, 1216, 1074; **MS** (70 eV, EI) *m*/*z* (%): 244 (M^+, 55.23), 199 (100).

(50) Preparation of (2*R*)-(-)-2-(2-fluoro-[1,1'-biphenyl]-4-yl)propanoic acid ((*R*)-Flurbiprofen) ((*R*)-10b, yyb-3-145)

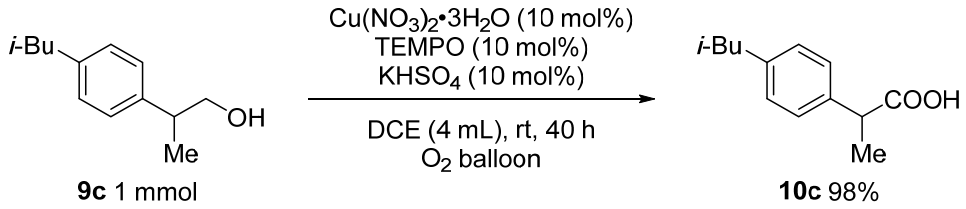


(*R*)-**9b** 1 mmol, 98% ee (*R*)-**10b** 98%, 99% ee

Following Typical Procedure I, the reaction of (*R*)-**9b** (229.4 mg, 1.0 mmol, 98% ee), $Cu(NO_3)_2$•$3H_2O$ (24.1 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.5 mg, 0.1 mmol) in DCE (4 mL) afforded (*R*)-**10b**[53] (238.8 mg, 98%, 99% ee) [eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to 3/1 (~200 mL), then 2/1 (~150 mL)] as light yellow solid; m.p. 108.0-109.0 ºC (petroleum ether/dichloromethane); HPLC conditions: AD-H column, hexane/*i*-PrOH = 95/5, 1.0 mL/min, λ = 214 nm, t_R (major) = 9.2 min, t_R (minor) = 12.6 min; $[\alpha]_D^{27}$ = -45.57 (*c* = 0.98, $CHCl_3$) (reported:[53] $[\alpha]_D^{25}$ = -46.0 (*c* = 0.90, $CHCl_3$)); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 10.73 (br, 1 H, COOH), 7.52 (d, *J* = 7.6 Hz, 2 H, Ar-H), 7.47-7.26 (m, 4 H, Ar-H), 7.20-7.04 (m, 2 H, Ar-H), 3.77 (q, *J* = 7.1 Hz, 1 H, CH), 1.55 (d, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 180.4, 159.7 (d, *J* = 247.3 Hz), 140.9 (d, *J* = 7.9 Hz), 135.4, 130.9 (d, *J* = 4.0 Hz), 128.9 (d, *J* = 3.1 Hz), 128.4, 128.1 (d, *J* = 14.2 Hz), 127.7, 123.7 (d, *J* = 3.2 Hz), 115.4 (d, *J* = 23.7 Hz), 44.8, 17.9; **^{19}F NMR** (376 MHz, $CDCl_3$):

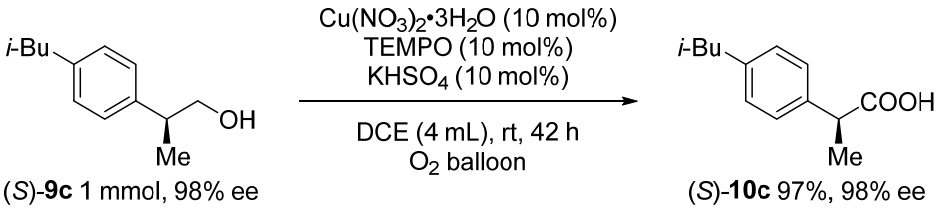
δ = -117.9; **IR** (neat, cm^{-1}): 3400-2800, 1728, 1692, 1482, 1417, 1390, 1174, 1141; **MS** (70 eV, EI) *m*/*z* (%): 244 (M^+, 51.67), 199 (100).

(51) Preparation of 2-(4-isobutylphenyl)propionic acid (Ibuprofen) (10c, yyb-3-142)



Following Typical Procedure I, the reaction of **9c** (192.7 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.1 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.8 mg, 0.1 mmol) in DCE (4 mL) afforded **10c**[52] (201.6 mg, 98%) [eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to 4/1 (~250 mL)] as light yellow oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 10.82 (br, 1 H, COOH), 7.21 (d, *J* = 7.6 Hz, 2 H, Ar-H), 7.09 (d, *J* = 7.6 Hz, 2 H, Ar-H), 3.69 (q, *J* = 6.9 Hz, 1 H, CH), 2.44 (d, *J* = 6.8 Hz, 2 H, CH_2), 1.84 (hept, *J* = 6.6 Hz, 1 H, CH), 1.48 (d, *J* = 6.8 Hz, 3 H, CH_3), 0.89 (d, *J* = 6.8 Hz, 6 H, 2 x CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 181.2, 140.7, 136.9, 129.3, 127.2, 45.0, 30.1, 22.3, 18.0; **IR** (neat, cm^{-1}): 3300-2350, 1710, 1458, 1419, 1229, 1183, 1070; **MS** (70 eV, EI) *m*/*z* (%): 206 (M^+, 50.21), 161 (100).

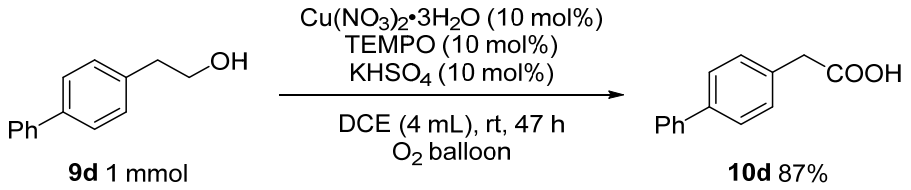
(52) Preparation of (2*S*)-2-(4-isobutylphenyl)propionic acid ((*S*)-(+)-Ibuprofen) ((*S*)-10c, yyb-3-131)



Following Typical Procedure I, the reaction of (*S*)-**9c** (193.9 mg, 1.0 mmol, 98% ee), $Cu(NO_3)_2$•$3H_2O$ (24.6 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.6 mg, 0.1 mmol) in DCE (4 mL) afforded (*S*)-**10c**[15] (201.1 mg, 97%, 98% ee) [eluent: petroleum ether/ethyl acetate = 15/1 (~160 mL) to 4/1 (~250 mL)] as light yellow oil; HPLC conditions: OJ-H column, hexane/*i*-PrOH = 98/2, 1.0 mL/min, λ =

214 nm, t_R (major) = 10.2 min, t_R (minor) = 9.5 min; $[\alpha]_D^{25}$ = +55.07 (*c* = 1.14, $CHCl_3$) (reported:[54] $[\alpha]_D^{20}$ = +54.7 (*c* = 0.68, $CHCl_3$)); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.36 (br, 1 H, COOH), 7.21 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.09 (d, *J* = 8.0 Hz, 2 H, Ar-H), 3.69 (q, *J* = 7.1 Hz, 1 H, CH), 2.44 (d, *J* = 7.2 Hz, 2 H, CH_2), 1.84 (hept, *J* = 6.7 Hz, 1 H, CH), 1.49 (d, *J* = 7.2 Hz, 3 H, CH_3), 0.89 (d, *J* = 6.8 Hz, 6 H, 2 x CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 181.2, 140.8, 136.9, 129.3, 127.2, 44.96, 44.94, 30.1, 22.3, 18.0; **IR** (neat, cm^{-1}): 3250-2350, 1702, 1450, 1418, 1282, 1229, 1184, 1070; **MS** (70 eV, EI) *m*/*z* (%): 206 (M^+, 49.01), 161 (100).

(53) Preparation of (4-biphenylyl)acetic acid (Felbinac) (10d, yyb-3-120)

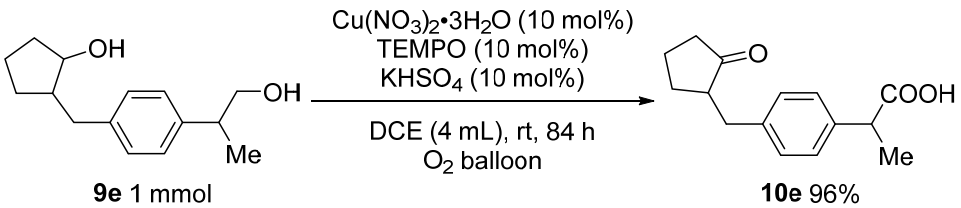


9d 1 mmol **10d** 87%

Following Typical Procedure I, the reaction of **9d** (199.2 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.4 mg, 0.1 mmol), TEMPO (16.3 mg, 0.1 mmol), and $KHSO_4$ (13.5 mg, 0.1 mmol) in DCE (4 mL) afforded **10d** (185.7 mg, 87%) [eluent: petroleum ether/ethyl acetate = 3/1 (~200 mL) to 1/1 (~200 mL)] as white solid;

10d:[52] m.p. 162.9-163.5 °C (petroleum ether/ethyl acetate); **^{1}H NMR** (400 MHz, DMSO-d_6) δ = 12.38 (br, 1 H, COOH), 7.65 (d, *J* = 7.6 Hz, 2 H, Ar-H), 7.61 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.46 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.40-7.30 (m, 3 H, Ar-H), 2.62 (s, 2 H, CH_2); **^{13}C NMR** (100 MHz, DMSO-d_6): δ = 172.7, 140.0, 138.6, 134.3, 130.0, 129.0, 127.4, 126.62, 126.60, 40.3; **IR** (neat, cm^{-1}): 3250-2300, 1683, 1487, 1412, 1345, 1249, 1204, 1036; **MS** (70 eV, EI) *m*/*z* (%): 212 (M^+, 44.47), 167 (100).

(54) Preparation of 2-(4-((2-oxocyclopentyl)methyl)phenyl)propanoic acid (Loxoprofen) (10e, yyb-3-167)

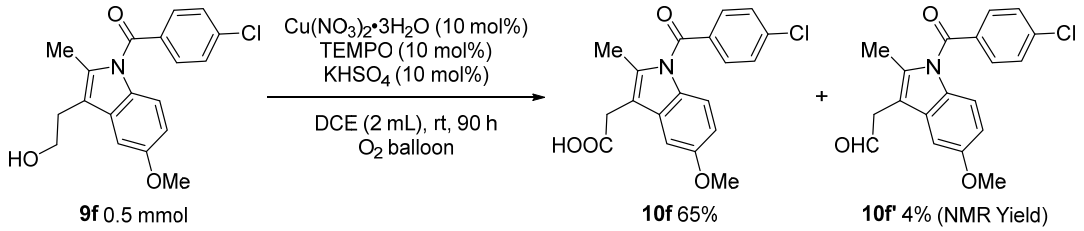


9e 1 mmol **10e** 96%

Following Typical Procedure I, the reaction of **9e** (236.0 mg, 1.0 mmol),

$Cu(NO_3)_2$•$3H_2O$ (24.0 mg, 0.1 mmol), TEMPO (16.2 mg, 0.1 mmol), and $KHSO_4$ (13.5 mg, 0.1 mmol) in DCE (4 mL) afforded **10e**[55] (236.9 mg, 96%) [eluent: petroleum ether/ethyl acetate = 5/1 (~180 mL) to 2/1 (~300 mL)] as light yellow oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 10.12 (br, 1 H, COOH), 7.22 (d, *J* = 7.2 Hz, 2 H, Ar-H), 7.11 (d, *J* = 7.6 Hz, 2 H, Ar-H), 3.70 (q, *J* = 7.1 Hz, 1 H, CH), 3.11 (dd, J_1 = 14.0 Hz, J_2 = 4.0 Hz, 1 H, one proton of CH_2), 2.50 (dd, J_1 = 13.6 Hz, J_2 = 9.6 Hz, 1 H, one proton of CH_2), 2.42-2.25 (m, 2 H, CH_2), 2.19-2.00 (m, 2 H, CH and one proton of CH_2), 2.00-1.87 (m, 1 H, one proton of CH_2), 1.80-1.63 (m, 1 H, one proton of CH_2), 1.61-1.41 (m, 4 H, CH_3 and one proton of CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 220.5, 180.3, 139.0, 137.6, 129.0, 127.5, 50.8, 44.8, 38.0, 35.0, 29.0, 20.4, 18.0; **IR** (neat, cm^{-1}): 3400-2250, 1734, 1703, 1512, 1454, 1378, 1156, 1072; **MS** (70 eV, EI) *m*/*z* (%): 246 (M^+, 86.3), 201 (100).

(55) Preparation of 2-(1-(4-chlorobenzoyl)-2-methyl-1*H*-indol-3-yl)acetic acid (Indometacin) (10f, yyb-3-156-1)

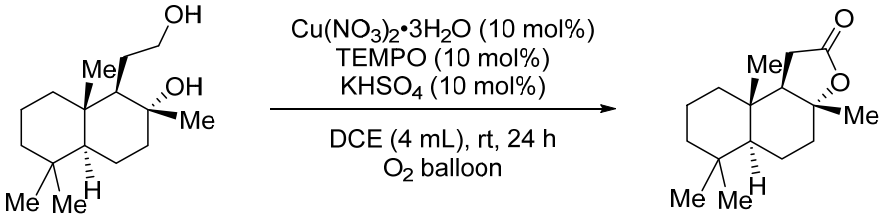


9f 0.5 mmol **10f** 65% **10f'** 4% (NMR Yield)

Following Typical Procedure I, the reaction of **9f** (171.8 mg, 0.5 mmol), $Cu(NO_3)_2$•$3H_2O$ (12.4 mg, 0.05 mmol), TEMPO (8.1 mg, 0.05 mmol), and $KHSO_4$ (7.1 mg, 0.05 mmol) in DCE (2 mL) afforded **10f**[56] (116.6 mg, 65%) (4% NMR yield of corresponding aldehyde was formed based on ^{1}H NMR analysis of the crude product) [eluent: petroleum ether/ethyl acetate = 5/1 (~600 mL) to 3/1 (~200 mL), then 1/1 (~200 mL). The impure product was further purified by washing with aq. Na_2CO_3 (pH 9-10). The aqueous layer was separated and acidified to pH 6-7 with 3M HCl (aq.), then extracted with ethyl acetate (3 x 10 mL), the solvent was removed under reduced pressure] as yellow solid; m.p. 149.0-149.9 °C (petroleum ether/dichloromethane) (reported:[56] m.p. 159-161 °C (ethyl acetate)); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.66 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.46 (d, *J* = 8.4 Hz, 2 H, Ar-H), 6.95 (d, *J* = 2.0 Hz, 1 H, Ar-

H), 6.85 (d, J = 9.2 Hz, 1 H, Ar-H), 6.67 (dd, J_1 = 9.0 Hz, J_2 = 2.2 Hz, 1 H, Ar-H), 3.82 (s, 3 H, OCH_3), 3.69 (s, 2 H, CH_2), 2.38 (s, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 176.6, 168.3, 156.1, 139.3, 136.2, 133.8, 131.2, 130.8, 130.5, 129.1, 115.0, 111.8, 111.7, 101.2, 55.7, 30.0, 13.3; **IR** (neat, cm^{-1}): 3200-2250, 1695, 1676, 1607, 1474, 1354, 1326, 1218, 1150; **MS** (70 eV, EI) *m/z* (%): 359 ($M(^{37}Cl)^+$, 2.74), 357 ($M(^{35}Cl)^+$, 6.87), 84 (100).

(56) Preparation of (3a*R*,5a*S*,9a*S*,9b*R*)-3a,6,6,9a tetramethyldecahydro-naphtho[2,1-b]furan-2(1*H*)-one ((+)-Sclareolide) (12, yyb-3-136)

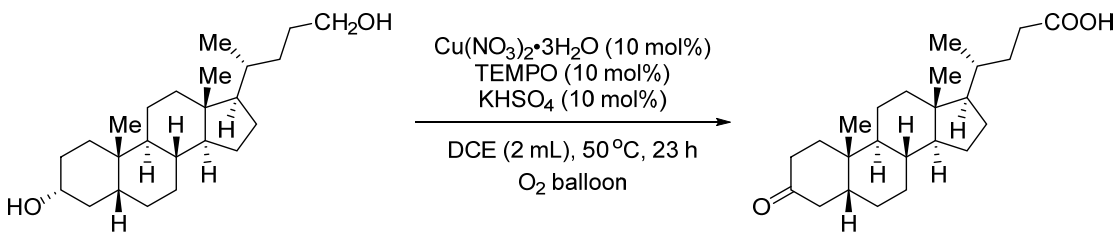


11a 1 mmol

12 98%, dr > 20:1

Following Typical Procedure I, the reaction of **11a** (254.1 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.1 mg, 0.1 mmol), TEMPO (16.0 mg, 0.1 mmol), and $KHSO_4$ (13.9 mg, 0.1 mmol) in DCE (4 mL) afforded **12**[7] (244.2 mg, 98%) [eluent: petroleum ether/ethyl acetate =25/1 (~260 mL) to 10/1 (~220 mL)] as white solid; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.41 (t, J = 15.4 Hz, 1 H, one proton of CH_2), 2.23 (dd, J_1 = 16.2 Hz, J_2 = 6.2 Hz, 1 H, one proton of CH_2), 2.08 (d, J = 11.6 Hz, 1 H), 1.97 (dd, J_1 = 14.8 Hz, J_2 = 6.0 Hz, 1 H), 1.88 (d, J = 14.0 Hz, 1 H), 1.77-1.56 (m, 2 H), 1.54-1.26 (m, 7 H), 1.26-1.12 (m, 1 H), 1.12-0.96 (m, 2 H), 0.92 (s, 3 H, CH_3), 0.89 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 176.7, 86.2, 59.0, 56.5, 42.0, 39.4, 38.6, 35.9, 33.04, 32.98, 28.6, 21.4, 20.8, 20.4, 17.9, 14.9.

(57) Preparation of 3-oxo-5β-cholan-24-oic acid (13, yyb-2-068)



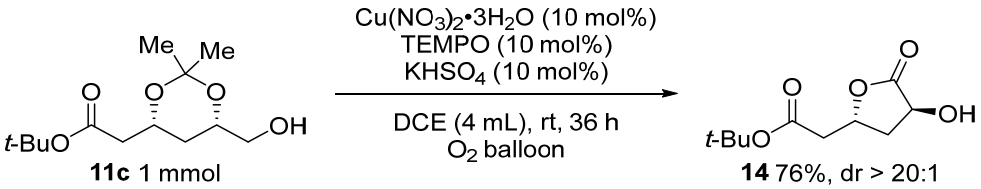
11b 1 mmol

13 71%, dr > 20:1

Following Typical Procedure II, the reaction of **11b** (362.7 mg, 1.0 mmol),

$Cu(NO_3)_2$•$3H_2O$ (24.4 mg, 0.1 mmol), TEMPO (16.1 mg, 0.1 mmol), and $KHSO_4$ (13.9 mg, 0.1 mmol) in DCE (2 mL) afforded **13**[7] (267.7 mg, 71%) [eluent: petroleum ether/ethyl acetate = 4/1 (~250 mL) to 1/1 (~200 mL)] as white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 10.15 (br, 1 H, COOH), 2.70 (t, *J* = 14.2 Hz, 1 H, one proton of CH_2), 2.50-2.21 (m, 3 H), 2.21-2.10 (m, 1 H), 2.09-1.96 (m, 3 H), 1.95-1.74 (m, 4 H), 1.69-1.55 (m, 1 H), 1.55-1.05 (m, 15 H), 1.02 (s, 3 H, CH_3), 0.94 (d, *J* = 6.0 Hz, 3 H, CH_3), 0.69 (s, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 213.7, 180.1, 56.3, 55.8, 44.2, 42.6, 42.2, 40.6, 39.9, 37.0, 36.9, 35.4, 35.1, 34.7, 30.9, 30.6, 28.0, 26.5, 25.6, 24.0, 22.5, 21.1, 18.1, 11.9.

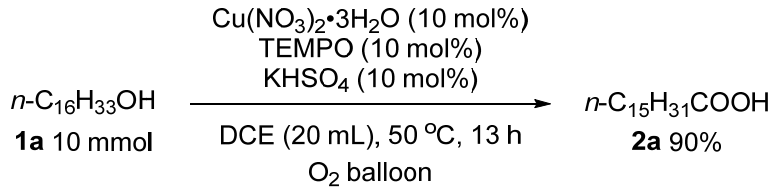
(58) Preparation of tert-butyl ((2*R*,4*S*)-4-hydroxy-5-oxotetrahydrofuran-2-yl)acetate (14, yyb-3-186)



Following Typical Procedure I, the reaction of **11c** (259.5 mg, 1.0 mmol), $Cu(NO_3)_2$•$3H_2O$ (24.2 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), and $KHSO_4$ (13.6 mg, 0.1 mmol) in DCE (4 mL) afforded **14** (163.6 mg, 76%) [eluent: petroleum ether/ethyl acetate = 2/1 (~300 mL) to 1/1 (~200 mL)] as light yellow oil; $[\alpha]_D^{23}$ = -59.06 (*c* =1.00, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 5.12-4.90 (m, 1 H, CH), 4.60 (t, *J* = 7.6 Hz, 1 H, CH), 4.40 (s, 1 H, OH), 2.67 (dd, J_1 = 16.0 Hz, J_2 = 6.8 Hz, 1 H, one proton of CH_2), 2.58 (dd, J_1 = 16.0 Hz, J_2 = 6.4 Hz, 1 H, one proton of CH_2), 2.48-2.27 (m, 2 H, CH_2), 1.46 (s, 9 H, $C(CH_3)_3$); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 177.3, 168.7, 81.7, 74.5, 67.0, 40.9, 35.1, 27.8; **IR** (neat, cm^{-1}): 3433, 2979, 2932, 1777, 1723, 1368, 1256, 1147, 1120; **MS** (ESI) *m/z*: 234 $(M+NH_4)^+$, 239 $(M+Na)^+$; **HRMS** calcd *m/z* for $C_{10}H_{16}O_5Na$ $[M+Na]^+$: 239.0890, found 239.0884.

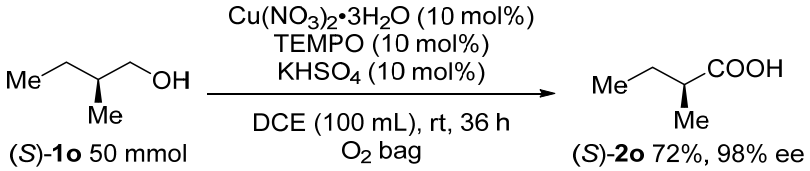
3. Large-Scale Reactions with O_2 or Air:

(59) Preparation of hexadecanoic acid (2a, yyb-2-063)



Following Typical Procedure II, to a 100 mL Schlenk tube were added $Cu(NO_3)_2$•$3H_2O$ (241.5 mg, 1.0 mmol), TEMPO (160.1 mg, 1.0 mmol), $KHSO_4$ (137.0 mg, 1.0 mmol), **1a** (2.4349 g, 10.0 mmol), and DCE (20 mL) sequentially. The reaction was then conducted at room temperature until the completion of the reaction as monitored by TLC (petroleum ether/ethyl acetate = 5/1) (36 h). The reaction mixture was filtrated through a short column of silica gel eluted with ethyl acetate (3 x 50 mL). After evaporation, the residue was purified by recrystallization to afford **2a**[7] (2.3126 g, 90%) [petroleum ether/chloroform = 10/1 for the first round to get 1.6826 g of **2a**, petroleum ether/chloroform = 20/1 for the second round after evaporation of the filtrate to get 0.5185 g of **2a**, and petroleum ether/chloroform = 20/1 for the third round after evaporation of the filtrate to get 0.1115 g of **2a**] as white solid; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 11.48 (br, 1 H, COOH), 2.34 (t, *J* = 7.6 Hz, 2 H, CH_2), 1.63 (quintet, *J* = 7.3 Hz, 2 H, CH_2), 1.47-1.16 (m, 24 H, 12 x CH_2), 0.88 (t, *J* = 6.6 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 180.6, 34.1, 31.9, 29.68, 29.66, 29.6, 29.43, 29.36, 29.2, 29.1, 24.7, 22.7, 14.1.

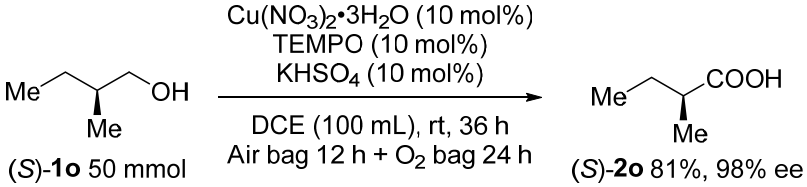
(60) Preparation of (*S*)-2-methylbutanoic acid ((*S*)-2o, yyb-4-025)



Following Typical Procedure I, to a 500 mL three-neck flask were added $Cu(NO_3)_2$•$3H_2O$ (1.2102 g, 5.0 mmol), TEMPO (796.9 mg, 5.0 mmol), $KHSO_4$ (679.3 mg, 5.0 mmol), (*S*)-**1o** (5.5 mL, d = 0.811 g/mL, 98% purity, 50.0 mmol), and DCE (100 mL) sequentially. The reaction was then conducted at room temperature until the completion of the reaction as monitored by NMR analysis (36 h). The crude mixture was filtrated through a short column of silica gel eluted with diethyl ether (200 mL) and

the filtrate was concentrated through evaporation under atmospheric pressure. The residue was distilled under reduced pressure (the main fraction was collected at 90-110 ℃ (0.013MPa) to get (*S*)-**2o** (2.6172 g), the residual solution was transferred to a 25 mL flask and distilled to get 1.0097 g of (*S*)-**2o**[57] (86-102 ℃, 0.01MPa)) to afford (*S*)-**2o** (3.6269 g, 72%, 98% ee) as yellow oil. HPLC conditions: OJ-H column, hexane/*i*-PrOH = 99/1, 0.5 mL/min, λ = 214 nm, t_R (major) = 16.7 min, t_R (minor) = 15.8 min; $[\alpha]_D^{25}$ = +18.36 (*c* = 1.205, $CHCl_3$) (reported:[57] $[\alpha]_D^{23}$ = +19.2 (*c* = 1.15, $CHCl_3$)); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 10.70 (br, 1 H, COOH), 2.40 (sextet, *J* = 7.0 Hz, 1 H, CH), 1.72 (hept, *J* = 7.2 Hz, 1 H, one proton of CH_2), 1.50 (hept, *J* = 7.1 Hz, 1 H, one proton of CH_2), 1.18 (d, *J* = 7.2 Hz, 3 H, CH_3), 0.95 (t, *J* = 7.4 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 183.3, 40.7, 26.3, 16.1, 11.3; **IR** (neat, cm^{-1}): 3300-2450, 1702, 1464, 1417, 1383, 1227, 1157, 1089; **MS** (ESI) *m/z*: 101 $(M-H)^-$.

(61) Preparation of (*S*)-2-methylbutanoic acid ((*S*)-2o, yyb-4-039)

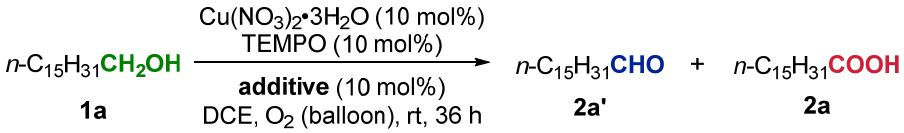


To a 500 mL three-neck flask were added $Cu(NO_3)_2$•$3H_2O$ (1.2033 g, 5.0 mmol), TEMPO (798.8 mg, 5.0 mmol), $KHSO_4$ (682.1 mg, 5.0 mmol), (*S*)-**1o** (5.5 mL, d = 0.811 g/mL, 98% purity, 50.0 mmol), and DCE (100 mL) sequentially. Then a 70 L air bag was connected to the flask. After stirring at room temperature for 12 h, a 2 L pure O_2 bag was connected to the flask to supply O_2 until the completion of the reaction as monitored by NMR analysis (24 h). The crude mixture was filtrated through a short column of silica gel eluted with diethyl ether (200 mL), and the filtrate was concentrated via evaporation under atmospheric pressure. The residue was distilled under reduced pressure, the main fraction was collected at 112-134 ℃ (0.032MPa) to afford (*S*)-**2o** (4.1961g, 81%, 98% purity, 98% ee) as yellow oil. HPLC conditions: OJ-H column, hexane/*i*-PrOH = 99/1, 0.5 mL/min, λ = 214 nm, t_R (major) = 16.5 min, t_R (minor) = 15.7 min; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 10.73 (br, 1 H, COOH), 2.40 (sextet, *J* = 6.9 Hz, 1 H,CH), 1.72 (hept, *J* = 7.2 Hz, 1 H, one proton of CH_2), 1.50 (hept, *J* = 7.1

Hz, 1 H, one proton of CH_2), 1.18 (d, J = 7.2 Hz, 3 H, CH_3), 0.95 (t, J = 7.4 Hz, 3 H, CH_3); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ = 183.1, 40.5, 26.1, 15.9, 11.0.

Optimization for the aerobic oxidation of 1a

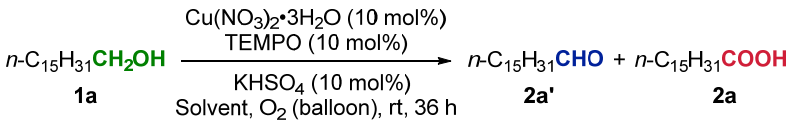
Table S1. Extra catalyst screening for the aerobic oxidation of **1a** [a]



Entry	**additive**	Recovery of **1a** (%)	NMR Yield of **2a'** (%)	NMR Yield of **2a** (%)
1	*none*	21	61	0
2	$KHCO_3$	95	5	0
3	K_2CO_3	93	5	0
4	K_3PO_4	94	6	0
5	K_2HPO_4	95	6	0
6	KCl	0	18	76
7	KBr	0	61	30
8	KI	67	31	0
9	K_2SO_4	48	35	0
10	KH_2PO_4	0	12	87
11	NaH_2PO_4	0	0	98
12	$NaHSO_4•H_2O$	0	0	99
13	**$KHSO_4$**	**0**	**0**	**100**
14	$SnCl_4$	0	80	13
15	$InCl_3$	0	14	67
16	$CuF_2•2H_2O$	0	5	71
17	$AlCl_3$	0	6	90
18	$ZnCl_2$	0	4	92
19	$Yb(OTf)_3$	87	5	0
20	$La(OTf)_3$	64	17	0
21	$Sc(OTf)_3$	54	5	0

[a] The reaction was conducted with 1.0 mmol of **1a**, 10 mol% each of $Cu(NO_3)_2•3H_2O$, TEMPO, and additive in 4 mL of DCE at rt for 36 h with an O_2 balloon. The NMR yield and recovery were determined by ^{1}H NMR analysis using dibromomethane as the internal standard.

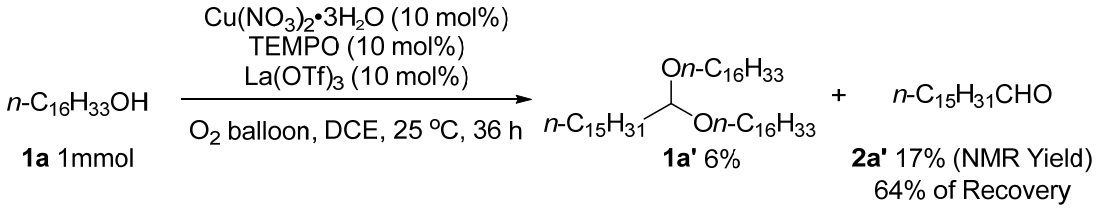
Table S2. The solvent effect.[a]



Entry	Solvent	Recovery of **1a** (%)	NMR Yield of **2a'** (%)	NMR Yield of **2a** (%)
1	toluene	66	22	0
2	DCM	22	60	0
3	$CHCl_3$	0	9	91
4	**DCE**	**0**	**0**	**100**
5[b]	**DCE**	**0**	**0**	**92**
6	MeCN	36	49	0
7[c]	MeCN/H_2O	100	0	0
8	DMF	92	0	0

[a] The reaction was conducted with 1.0 mmol of 1a, 10 mol% each of $Cu(NO_3)_2$•$3H_2O$, TEMPO, and $KHSO_4$ in 4 mL of solvent at rt for 36 h with an O_2 balloon. The NMR yield and recovery were determined by ^1H NMR analysis using dibromomethane as the internal standard. [b] The reaction was conducted in 2 mL of DCE at 50 °C for 12 h. [c] MeCN/H_2O = 2:1.

(1) Preparation of cetyladehyde dicetyl acetal (1a', yyb-4-189B-1)



A Schlenk tube was degassed to remove the air inside and refilled with O_2 using an O_2 balloon for three times. Then $Cu(NO_3)_2$•$3H_2O$ (24.0 mg, 0.1 mmol), TEMPO (15.9 mg, 0.1 mmol), $La(OTf)_3$ (60.0 mg, 0.1 mmol, 98% purity), **1a** (241.8 mg, 1.0 mmol), and DCE (4 mL) were added sequentially. The resulting mixture was stirred at room temperature for 36 h and filtrated through a short column of silica gel eluted with diethyl ether (3 x 25 mL). After evaporation, to the residue was added MeOH (2 mL) and $NaBH_4$ (39.8 mg, 1.0 mmol, 98% purity). The resulting mixture was stirred for 0.5 h, quenched with H_2O (5 mL), separated, and extracted with ethyl acetate (5 mL × 3). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4.

After filtration and evaporation, the residue was purified by chromatography on silica gel to afford **1a'** (42.4 mg, 6%) [eluent: petroleum ether/ethyl acetate = 40/1 (~200 mL)] as white solid; m.p. 44.4-46.6 °C (we were not able to obtain the crystal from the solvent tested, the m.p. of **1a'** was determined by using the solid right after evaporation of the eluent); **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 4.45 (t, *J* = 5.8 Hz, 1 H, CH), 3.59-3.51 (m, 2 H, OCH_2), 3.44-3.34 (m, 2 H, OCH_2), 1.65-1.52 (m, 6 H, 3 x CH_2), 1.45-1.17 (m, 78 H, 39 x CH_2), 1.31 (t, *J* = 6.8 Hz, 9 H, 3 x CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 103.1, 65.4, 33.5, 31.9, 29.9, 29.71, 29.66, 29.64, 29.59, 29.5, 29.4, 26.3, 24.8, 22.7, 14.1; **IR** (neat, cm^{-1}): 2955, 2915, 2849, 1468, 1383, 1349, 1125, 1027; **MS** (70 eV, EI) *m*/*z* (%): 495 ($(M-C_{15}H_{31})^+$, 9.64), 71 (100); **Anal. Calcd.** For $C_{48}H_{98}O_2$: C 81.51, H 13.97; found C 81.02, H 14.39.

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