

Supporting Information

Reductive Bromine Atom Transfer Reaction

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General Information.

Thin layer chromatography (TLC) was performed on Merck precoated plates (silica gel 60 F254, Art 5715, 0.25 mm) and were visualized by fluorescence quenching under UV light or by staining with p-anisaldehyde/AcOH/H₂SO₄/EtOH, or 12MoO₃.H₃PO₄/EtOH. The products were purified by flash chromatography on silica gel (Kanto Chem. Co. Silica Gel 60N (spherical, neutral, 40-50 μ m)) and, if necessary, were further purified by recycling preparative HPLC (Japan Analytical Industry Co. Ltd., LC-918) equipped with GPC columns (JAIGEL-1H + JAIGEL-2H columns) using CHCl₃ as eluent. ¹H NMR spectra were recorded with a JEOL JNM-ECS400 (400 MHz) spectrometer and referenced to the solvent peak at 7.26 ppm. ¹³C NMR spectra were recorded with a JEOL JNM-ECS400 (100 MHz) spectrometer and referenced to the solvent peak at 77.00 ppm. Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Infrared spectra were recorded on a JASCO FT/IR-4100 spectrometer and are reported as wavenumber (cm⁻¹). Conventional and high-resolution mass spectra were recorded with a JEOL MS700 spectrometer. Benzene, hexane and MeCN were distilled over calcium hydride.

Typical procedure for the synthesis of ethyl caprylate (4a)

A magnetic stirring bar, **1a** (54.1 mg, 0.25 mmol), **2a** (92.9 mg, 2.5 mmol), hexane (10 mL), and H₂O (100 mL) were placed in a quartz tube and then the tube was irradiated by 6 W low-pressure mercury lamp with stirring for 6 h. The reaction mixture was concentrated in vacuo. The resulting residue was subjected to silica gel column chromatography using hexane/EtOAc (150/1) as eluent affording **4a** (45.8 mg, 77%).

Procedure for the synthesis of ethyl 2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)acetate (5)

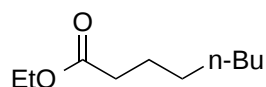
A magnetic stirring bar, **1a** (85.1 mg, 0.51 mmol), **2a** (420.1 mg, 5.0 mmol), C₆H₆ (10 mL), and TEMPO (90.8 mg, 0.58 mmol) were placed in quartz tube and then the tube was irradiated by 6 W low-pressure mercury lamp with stirring for 6 h. The reaction mixture was concentrated in vacuo. The resulting residue was subjected to silica gel column chromatography using hexane/EtOAc (150/1) as eluent affording **5** (90.1 mg, 69%).

Procedure for the deuterium-labeling experiments

A magnetic stirring bar, **1a** (46.4 mg, 0.28 mmol), **2a** (212.0 mg, 2.5 mmol), hexane (10 mL) and D₂O (100 mL) were placed in quartz tube and then the tube was irradiated by 6 W low-pressure

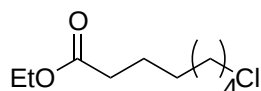
mercury lamp with stirring for 6 h. The reaction mixture was concentrated in vacuo. The resulting residue was subjected to silica gel column chromatography using hexane/EtOAc (150/1) as eluent affording **4a-D** (32.1 mg, 67%). D/H ratio (90:10) was determined by MS spectrum.

Ethyl caprylate (**4a**)



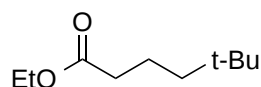
This compound is commercially available [CAS No. = 106-32-1]. ¹H NMR (CDCl₃, 400 MHz) δ 4.11 (q, *J* = 7.1 Hz, 2H), 2.28 (t, *J* = 7.6 Hz, 2H), 1.63-1.59 (m, 2H), 1.32-1.21 (m, 11H), 0.78 (t, *J* = 6.6 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.05, 14.23, 22.57, 24.97, 28.91, 29.08, 31.63, 34.37, 60.13, 173.93.

Ethyl 8-chlorooctanoate (**4b**)¹



¹H NMR (CDCl₃, 400 MHz) δ 4.12 (q, *J* = 7.2 Hz, 2H), 3.53 (t, *J* = 6.8 Hz, 2H), 2.29 (t, *J* = 7.4 Hz, 2H), 1.79-1.71 (m, 2H), 1.66-1.56 (m, 2H), 1.47-1.40 (m, 2H), 1.36-1.31 (m, 4H), 1.25 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.21, 24.80, 26.64, 28.49, 28.89, 32.49, 34.25, 60.17, 173.76.

Ethyl 5,5-dimethylhexanoate (**4c**)

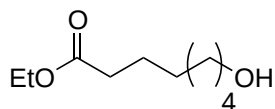


¹H NMR (CDCl₃, 400 MHz) δ 4.12 (q, *J* = 7.2 Hz, 2H), 2.26 (t, *J* = 7.6 Hz, 2H), 1.60-1.55 (m, 2H), 1.26 (t, *J* = 6.8 Hz, 2H), 1.20-1.16 (m, 2H), 0.88 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.26, 20.28, 29.28, 35.13, 43.58, 60.16, 173.92; IR (neat) 2958 cm⁻¹, 1737 cm⁻¹, 1366 cm⁻¹; MS (relative intensity) *m/z* 157 ([M-Me]⁺, 13), 127 (21), 115 (30), 111 (36), 88 (100), 57 (97); HRMS (CI) *m/z* calcd for C₁₀H₂₁O₂ 173.1463, found 173.1537.

Ethyl 8-hydroxyoctanoate (**4d**)²

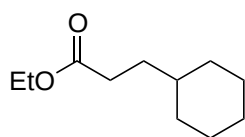
¹ Novartis AG; Novartis Pharma GmbH; Beranhard, R.; Ulrich M. Patent: WO200663821 A1, **2006**.

² Kudo, F.; Asou, Y.; Watanabe, M.; Kitayama, T.; Eguchi, T. *Synlett*, **2012**, 23, 1843.



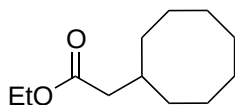
^1H NMR (CDCl_3 , 400 MHz) δ 4.11 (q, $J = 7.0$ Hz, 2H), 3.64 (t, $J = 6.4$ Hz, 2H), 2.29 (t, $J = 7.6$ Hz, 2H), 1.64-1.51 (m, 6H), 1.37-1.28 (m, 5H), 1.25 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.24, 24.85, 25.51, 29.01, 29.05, 32.66, 34.31, 60.18, 62.96, 173.87.

Ethyl 3-cyclohexylpropanoate (4e)³



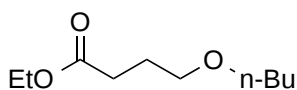
^1H NMR (CDCl_3 , 400 MHz) δ 4.11 (q, $J = 7.2$ Hz, 2H), 2.31-2.28 (m, 2H), 1.72-1.61 (m, 5H), 1.55-1.49 (m, 2H), 1.27-1.16 (m, 7H), 0.95-0.82 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.23, 26.21, 26.52, 31.96, 32.35, 32.94, 37.22, 60.16, 174.25.

Ethyl 2-cyclooctylacetate (4f)⁴



^1H NMR (CDCl_3 , 400 MHz) δ 4.12 (q, $J = 7.2$ Hz, 2H), 2.10 (d, $J = 7.2$ Hz, 2H), 2.12-2.00 (m, 1H), 1.69-1.41 (m, 12H), 1.33-1.25 (m, 2H), 1.25 (t, $J = 7.2$ Hz, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.28, 25.21, 26.14, 27.03, 32.14, 34.54, 42.91, 60.05, 173.42.

Ethyl 4-butoxybutanoate (4g)



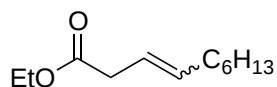
^1H NMR (CDCl_3 , 400 MHz) δ 4.12 (q, $J = 7.2$ Hz, 2H), 3.42 (t, $J = 6.4$ Hz, 2H), 3.39 (t, $J = 6.4$ Hz, 2H), 2.38 (t, $J = 7.4$ Hz, 2H), 1.88 (tt, $J = 6.7$ Hz, 2H), 1.56-1.49 (m, 2H), 1.37-1.33 (m, 2H), 1.25 (t, $J = 7.2$ Hz, 3H), 0.90 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.90, 14.21, 19.31, 25.07, 31.77, 60.24, 69.57, 70.64, 173.58; IR (neat) 2959 cm^{-1} , 1738 cm^{-1} , 1372 cm^{-1} , 1116 cm^{-1} ; MS (relative intensity) m/z 131 ($[\text{M}-\text{Bu}]^+$, 26), 115 (11), 101 (15), 87 (100), 57 (68); HRMS (CI) m/z

³ Ryu, I.; Uehara, S.; Hirao, H.; Fukuyama, T. *Org. Lett.* **2008**, *10*, 1005.

⁴ Yokohama, S.; Miwa, T.; Aibara, S.; Fujiwara, H.; Matsumoto, H.; Nakayama, K.; Iwamoto, T.; Mori, M.; Moroi, R.; Tsukada, W.; Isoda, S. *Chem. Pharm. Bull.* **1992**, *40*, 2391.

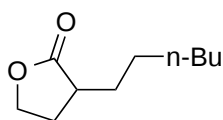
calcd for C₁₀H₂₁O₃ 189.1485, found 189.1492.

Ethyl dec-3-enoate (4h)⁵



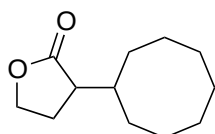
Obtained as a *E/Z* isomer mixture in a 71/29 ratio, as determined by ¹H NMR analysis: ¹H NMR (CDCl₃, 400 MHz) δ 5.56-5.51 (m, 2H), 4.17-4.12 (m, 2H), 3.08 (d, *J* = 3.6 Hz, 0.48H), 3.01 (d, *J* = 6.0 Hz, 1.19H), 2.03-1.99 (m, 2H), 1.35-1.22 (m, 11H), 0.88-0.84 (m, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.09 (*E* and *Z*, 2 lines superimposed), 14.19 (*E* and *Z*, 2 lines superimposed), 22.61 (*E* and *Z*, 2 lines superimposed), 28.80 (*E*), 28.90 (*Z*), 29.11 (*E*), 29.27 (*Z*), 31.69 (*E* and *Z*, 2 lines superimposed), 32.74 (*E*), 33.01 (*Z*), 38.18 (*E* and *Z*, 2 lines superimposed), 60.49(*E*), 60.57 (*Z*), 120.76 (*Z*), 121.50 (*E*), 133.50 (*Z*), 134.85 (*E*), 172.27 (*E* and *Z*, 2 lines superimposed).

3-Hexyl-dihydro-furan-2-one (4i)



This product is commercially available [CAS No. = 18436-37-8]. ¹H NMR (CDCl₃, 400 MHz) δ 4.36-4.30 (m, 1H), 4.22-4.15 (m, 1H), 2.55-2.46 (m, 1H), 2.41-2.35 (m, 1H), 2.00-1.85 (m, 2H), 1.51-1.21 (m, 9H), 0.88 (m, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.02, 22.54, 27.26, 28.60, 28.97, 30.29, 31.58, 66.48, 179.63.

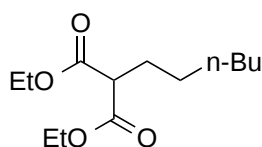
2,2-Heptamethylen-butylolacton (4j)



¹H NMR (CDCl₃, 400 MHz) δ 4.31 (dt, *J* = 2.8, 9.2 Hz, 1H), 4.15 (dt, *J* = 7.2, 9.2 Hz, 1H), 2.55 (ddd, *J* = 4.4, 9.2, 10.4 Hz, 1H), 2.29-2.01 (m, 3H), 1.81-1.21 (m, 14H); ¹³C NMR (CDCl₃, 100 MHz) δ 24.44, 25.26, 25.96, 26.50, 26.58, 29.37, 32.50, 36.69, 46.59, 66.46, 178.98; IR (neat) 2926 cm⁻¹, 1773 cm⁻¹, 1764 cm⁻¹, 1449 cm⁻¹, 1301 cm⁻¹; MS (relative intensity) *m/z* 196 (M⁺, 10), 125 (12), 86 (100); HRMS (EI) *m/z* calcd for C₁₂H₂₀O₂ 196.1463, found 196.1459.

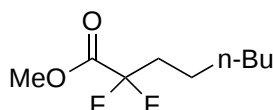
Diethyl 2-hexylmalonate (4k)⁶

⁵ Deng, M.-Z.; Li, N.-S.; Huang, Y.-Z. *J. Org. Chem.* **1992**, *57*, 4017.



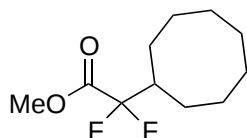
^1H NMR (CDCl_3 , 400 MHz) δ 4.18 (q, J = 7.2 Hz, 4H), 3.31 (t, J = 7.4 Hz, 1H), 1.91-1.87 (m, 2H), 1.31-1.24 (m, 14H), 0.87 (t, J = 6.6 Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.01, 14.07, 22.50, 27.25, 28.72, 28.85, 31.48, 52.05, 61.23, 169.62.

Methyl 2,2-difluorooctanoate (4l)⁷



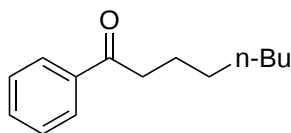
^1H NMR (CDCl_3 , 400 MHz) δ 3.87 (s, 3H), 2.10-1.95 (m, 2H), 1.49-1.21 (m, 8H), 0.88 (t, J = 7.0 Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 13.97, 21.35 (t, J_{CF} = 7.6 Hz), 22.39, 28.69, 31.38, 34.51 (t, J_{CF} = 22.9 Hz), 116.45, 164.94.

Methyl 2-cyclooctyl-2,2-difluoroacetate (4m)



^1H NMR (CDCl_3 , 400 MHz) δ 3.86 (s, 3H), 2.39-2.21 (m, 1H), 1.73-1.42 (m, 14H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 25.33, 25.36 (t, J_{CF} = 3.8 Hz), 41.59 (t, J_{CF} = 20.5 Hz), 53.11, 118.36 (t, J_{CF} = 500.3 Hz), 165.18 (t, J_{CF} = 33.4 Hz); IR (neat) 2921 cm^{-1} , 1768 cm^{-1} , 1158 cm^{-1} , 1029 cm^{-1} ; MS (relative intensity) m/z 220 ($[\text{M}]^+$, 1), 189 (1), 143 (10), 111 (25), 74 (22), 69 (100); HRMS (CI) m/z calcd for $\text{C}_{11}\text{H}_{19}\text{F}_2\text{O}_2$ 221.1348, found 221.1346.

1-Phenyloctan-1-one (4n)



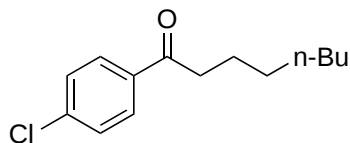
This compound is commercially available [CAS No. = 1674-37-9]. ^1H NMR (CDCl_3 , 400 MHz) δ 7.97-7.95 (m, 2H), 7.55-7.52 (m, 1H), 7.48-7.44 (m, 2H), 2.98-2.94 (m, 2H), 1.78-1.69 (m, 2H),

⁶ Marmillon, C.; Bompart, J.; Calas, M.; Escale, R; Bonnet, P.-A. *Heterocycles* **2000**, *53*, 1317.

⁷ Okano, T.; Takakura, N.; Nakano, Y.; Okajima, A.; Eguchi, S. *Tetrahedron* **1995**, *51*, 1903.

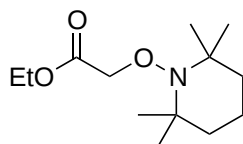
1.37-1.26 (m, 8H), 0.88 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.09, 22.62, 24.37, 29.14, 29.33, 31.70, 38.63, 128.04, 128.53, 132.85, 137.06, 200.64.

1-(4-Chlorophenyl)-5,5-dimethylhexan-1-one (4o)⁸



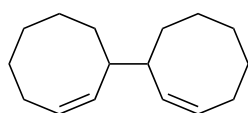
^1H NMR (CDCl_3 , 400 MHz) δ 7.91-7.87 (m, 2H), 7.44-7.42 (m, 2H), 2.93 (t, $J = 7.4$ Hz, 2H), 1.76-1.68 (m, 2H), 1.55-1.28 (m, 8H), 0.88 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.07, 22.60, 24.25, 29.10, 29.26, 31.67, 38.58, 128.83, 129.45, 135.32, 139.25, 199.32.

Ethyl 2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)acetate (5)



^1H NMR (CDCl_3 , 400 MHz) δ 4.43 (s, 2H), 4.20 (q, $J = 7.2$ Hz, 2H), 1.46-1.40 (m, 4H), 1.35-1.25 (m, 3H), 1.28 (t, $J = 7.2$ Hz, 2H), 1.15 (s, 12H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.18, 17.01, 20.05, 32.69, 29.66, 60.02, 60.46, 75.56, 169.83; IR (neat) 2933 cm^{-1} , 1760 cm^{-1} , 1375 cm^{-1} , 1195 cm^{-1} , 1095 cm^{-1} ; MS (relative intensity) m/z 244 ($\text{M}+1^+$, 2), 228 (100), 198 (5), 156 (28), 140 (8); HRMS (EI) m/z calcd for $\text{C}_{12}\text{H}_{23}\text{NO}_3$ 228.1600, found 228.1591.

3-(Cycloocten-3-yl)cyclooctene (6)



This compound is commercially available [CAS No. = 7123-80-0]. ^1H NMR (CDCl_3 , 400 MHz) δ 5.70-5.63 (m, 2H), 5.36-5.27 (m, 2H), 2.51-2.17 (m, 4H), 2.05-1.99 (m, 2H), 1.73-1.09 (m, 16H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 25.78, 25.88, 26.76, 27.09, 27.15, 29.53, 29.72, 34.26, 40.63, 40.98, 129.20, 129.40, 133.30, 134.43.

⁸ Dohi, S.; Moriyama, K.; Togo, H. *Tetrahedron* **2012**, *68*, 6557.

