Supporting Information

A Short Synthesis of Lennoxamine Using a Radical Cascade

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***N*-Ethenyl-*N*-[2-(5-iodobenzo[*d*][1,3]dioxol-6-yl)ethyl]-2,3-dimethoxybenzamide (**7**).** To a stirred suspension of **5** (0.55 g, 1.9 mmol) and molecular sieves 4 Å (2 g) in THF (5 mL) was added a solution of acetaldehyde (0.13 mL, 2.3 mmol) in THF (1 mL) at -10 °C. After stirring for 5 h at the same temperature, triethylamine (1.05 mL, 7.52 mmol) and a solution of 2,3-dimethoxybenzoyl chloride (0.57 g, 2.8 mmol) were added to the mixture. After further stirring for 30 min at the same temperature, a saturated aqueous solution of NaHCO₃ was added, and then the sieves were filtered off. The filtrate was extracted with CHCl₃, washed with brine, dried (MgSO₄), and concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane-AcOEt, 2:1) to give **7** (0.49 g, 54%) as colorless crystals, mp 98.5-99.5 °C (hexane). IR (CHCl₃) 1660, 1620 cm⁻¹; Rotamers of **7** were observed by ¹H NMR and ¹³C NMR. ¹H NMR (270 MHz, CDCl₃) δ 2.81-2.88 (1/3 x 2 H, m), 3.05 (2/3 x 2 H, t-like, *J* = 7.9 Hz), 3.52-3.62 (1/3 x 2 H, m), 3.85 (3 H, s), 3.89 (3 H, s), 3.98 (2/3 x 2 H, t-like, *J* = 7.6 Hz), 4.12 (1/3 H, d *J* = 9.2 Hz), 4.15 (2/3 H, dd, *J* = 9.2, 1.0 Hz), 4.69 (2/3 x 1 H, dd, *J* = 15.5, 1.0 Hz), 4.88 (1/3 x 1 H, d, *J* = 15.5 Hz), 5.91 (1/3 x 2 H, s), 5.96 (2/3 x 2 H, s), 6.32 (1/3 H, s), 6.45 (2/3 x 1 H, dd, *J* = 15.5, 9.2 Hz), 6.63 (1/3 H, d, *J* = 7.6 Hz), 6.79 (2/3 H, dd, *J* = 7.6, 1.3 Hz), 6.91 (2/3 H, s), 6.97 (2/3 H, d, *J* = 7.3 Hz), 7.05-7.15 (4/3 H, m), 7.24 (2/3 H, s), 7.61 (1/3 H, dd, *J* = 15.5, 9.2 Hz); ¹³C NMR (67.5 MHz, CDCl₃) δ 37.5, 37.8, 41.7, 41.9, 55.7, 55.9, 61.3, 61.5, 87.6, 93.3, 101.2, 101.5, 101.9, 109.6, 109.7, 110.1, 113.4, 118.3, 118.5, 119.0, 119.2, 124.5, 124.6, 130.5, 130.7, 130.9, 131.1, 134.2, 134.6, 135.1, 145.3, 147.2, 148.6, 152.7, 168.0, 168.2. Anal. Calcd for C₂₀H₂₀INO₅: C, 49.91; H, 4.19; N, 2.91. Found: C, 49.63; H, 4.22; N, 2.87.

Lennoxamine (1) and 2,3,4,5-Tetrahydro-3-[(2,3-dimethoxy)benzoyl]-1*H*-3-(7,8-methylenedioxy)benzoazepine (9); (a) Table 1, Entry 1. To a boiling solution of **7** (150 mg, 0.31 mmol) and V-40 (137 mg, 0.56 mmol) in toluene (25 mL) was added a solution of Bu₃SnH (120 mg, 0.37 mmol) and V-40 (15.2 mg, 0.062 mmol) in toluene (25 mL) for 3 h by using a syringe-pump, and the mixture was further heated at reflux for 2 h. After evaporation of the solvent, the residue was chromatographed on silica gel containing KF (10%)¹ (hexane-AcOEt, 2:1 → 1:1) to give **1** (17.6 mg, 16%) as a white solid and **9** (35.5 mg, 32%) as a white solid. **1**: mp 227-228 °C (MeOH),

lit² mp 226-227 °C; IR (CHCl₃) 1680 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 2.76-2.94 (4 H, m), 3.10 (1 H, dd, *J* = 13.8, 1.8 Hz), 3.91 (3 H, s), 4.10 (3 H, s), 4.29 (1 H, dd, *J* = 10.0, 1.8 Hz), 4.71-4.76 (1 H, m), 5.94 (1H, d, *J* = 1.4 Hz), 5.95 (1 H, d, *J* = 1.4 Hz), 6.70 (1 H, s), 6.77 (1 H, s), 7.12 (1 H, d, *J* = 8.1 Hz), 7.17 (1 H, d, *J* = 8.1 Hz); ¹³C NMR (67.5 MHz, CDCl₃) δ 35.9, 41.1, 42.7, 56.7, 60.1, 62.5, 101.0, 110.29, 110.32, 116.2, 117.0, 124.1, 130.9, 134.8, 138.2, 146.0, 146.3, 147.2, 152.6, 165.1. These spectral data were identical with those reported.³ **9**: mp 151-152 °C (Et₂O); IR (CHCl₃) 1620 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) δ 2.64 (1 H, dd, *J* = 13.9, 7.9 Hz), 2.82-3.01 (3H, m), 3.27 (1 H, dd, *J* = 13.9, 8.6 Hz), 3.42 (1 H, dd, *J* = 13.9, 7.6 Hz), 3.72 (1 H, dd, *J* = 13.9, 7.9 Hz), 3.87 (3 H, s), 3.90 (3 H, s), 3.98-4.08 (1H, m), 5.91 (2H, s), 6.54 (1 H, s), 6.68 (1 H, s), 6.80 (1 H, dd, *J* = 7.9, 1.3 Hz), 6.94 (1 H, d, *J* = 7.9 Hz), 7.10 (1 H, dd, *J* = 7.9, 1.0 Hz); ¹³C NMR (67.5 MHz, CDCl₃) δ 37.0, 37.6, 44.6, 49.9, 55.8, 61.5, 100.8, 110.1, 110.2, 112.7, 118.8, 124.7, 131.9, 133.6, 134.4, 144.9, 145.6, 145.8, 152.7 168.0. Anal. Calcd for C₂₀H₂₁NO₅: C, 67.59; H, 5.96; N, 3.94. Found: C, 67.29; H, 6.01; N, 3.93. **(b) Table 1, Entry 2.** A solution of **7** (100 mg, 0.21 mmol) and Bu₆Sn₂ (244 mg, 0.42 mmol) in toluene (30 mL) was irradiated with sun lamp (300 W) at reflux for 12h. After evaporation of the solvent, the residue was chromatographed on silica gel containing KF (10%) (hexane-AcOEt, 2:1 → 1:1) to give **1** (13.3 mg, 18%). **(c) Table 1, Entry 3.** A solution of **7** (140 mg, 0.29 mmol) and Bu₆Sn₂ (333 mg, 0.58 mmol) in chlorobenzene (40 mL) was irradiated with sun lamp (300 W) at reflux for 8h. After evaporation of the solvent, the residue was chromatographed on silica gel containing KF (10%) (hexane-AcOEt, 2:1 → 1:1) to give **1** (25.8 mg, 25%). **(d) Table 1, Entry 4.** A solution of **7** (140 mg, 0.29 mmol), Bu₆Sn₂ (333 mg, 0.58 mmol), and V-40 (142 mg, 0.58 mmol) in chlorobenzene (40 mL) was irradiated with sun lamp (300 W) at reflux for 8h. After evaporation of the solvent, the residue was chromatographed on silica gel containing KF (10%) (hexane-AcOEt, 2:1 → 1:1) to give **1** (26.6 mg, 26%). **(e) Table 1, Entry 5.** A solution of **7** (140 mg, 0.29 mmol) and Bu₆Sn₂ (333 mg, 0.58 mmol) in 1,2-dichlorobenzene (40 mL) was irradiated with sun lamp (300 W) at reflux for 4h. After evaporation of the solvent, the residue was chromatographed on silica gel containing KF (10%) (hexane-AcOEt, 2:1 → 1:1) to give **1** (40.6 mg, 40%). **(f) Table 1, Entry 6.** A solution of **7** (140 mg, 0.29 mmol) and Me₆Sn₂ (191 mg, 0.58 mmol) in 1,2-dichlorobenzene (40 mL) was irradiated with sun lamp (300 W) at reflux for 4h. After evaporation of the solvent, the residue was chromatographed on silica gel (hexane-AcOEt, 2:1 → 1:1) to give **1** (41.8 mg, 41%).

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 Tue May 24 22:32:57 2005

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 COMNT
 DATIM
 OBNUC
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1H
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 270.05 MHz
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 16
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 0.9340 sec
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 23.3 c
 CDCL3
 0.00 ppm
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