**Additional File 1**

**Chemical Synthesis and Characterization of Vilazodone Metabolite M17**

All reactions were performed under an Ar or N2 atmosphere and all glassware was dried in an oven at 125 °C overnight, unless otherwise noted. THF and CH2Cl2 were purified using an alumina filtration system. Methyl magnesium bromide, 5-bromoindole, ZnCl2, methyl 4-chloro-4-oxobutanoate, AlCl3, NaBH4, BF3·OEt2, CuCN, NMP and LiOH·H2O were purchased from Sigma-Aldrich or Fisher Scientific and were used without further purification. Reactions were monitored by TLC analysis (EM Science pre-coated silica gel 60 F254 plates, 250 μm layer thickness) and visualization was accomplished with a 254 nm UV light and by staining with a KMnO4 solution (1.5 g of KMnO4, 10 g of K2CO3, and 1.25 mL of a 10% NaOH solution in 200 mL of water). Reactions were also monitored by LC-MS (Shimadzu LC-MS 2020 with Kinetex 2.6 μm C18 50 x 2.10 mm). Flash chromatography on SiO2 was used to purify the crude reaction mixtures and performed on a Biotage Isolera utilizing Biotage cartridges and linear gradients. Infrared spectra were determined on a Jasco FT/IR-4100 spectrometer. 1H, 13C spectra were obtained on a Varian Mercury-VX 300, a Varian Mercury-VX 400, or a Varian Mercury-Plus 300 instrument in CDCl3 unless otherwise noted. Chemical shifts were reported in parts per million with the residual solvent peak used as an internal standard (CDCl3 = 7.26 ppm for 1H and 77.23 ppm for 13C). 1H NMR spectra were run at 300 or 400 MHz and are tabulated as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, bs = broad singlet, dt = doublet of triplet, ddd = doublet of doublet of doublet, qd = quartet of doublets), number of protons, and coupling constant(s). 13C NMR spectra were run at 100 MHz using a proton-decoupled pulse sequence with a d1 of 1 second unless otherwise noted and are tabulated by observed peak. High-resolution mass spectra were obtained on a Thermo Fisher Scientific, Exactive Plus mass spectrometer using Heated Electrospray Ionization.

**Methyl 4-(5-bromo-1*H*-indol-3-yl)-4-oxobutanoate (1):** To a solution of 5-bromoindole (3.47 g, 17.7 mmol) and ZnCl2 (2.80 g, 18.6 mmol) in dry CH2Cl2, MeMgBr (3 M in diethyl ether, 6.20 mL, 18.6 mmol) was added dropwise under an inert atmosphere over 20 minutes at 0 °C. The reaction mixture was then warmed to room temperature and allowed to stir for 30 minutes before the addition of methyl 4-chloro-4-oxobutanoate (2.80 g, 2.29 mL, 18.6 mmol). AlCl3 (1.18 g, 8.85 mmol) was slowly added and the reaction was monitored by TLC. Upon full consumption of 5-bromoindole, the reaction was quenched with saturated NH4Cl (aq) (50 mL) and transferred to a separatory funnel containing H2O (20 mL) and CH2Cl2 (50 mL). The aqueous layer was further extracted with CH2Cl2 (4 x 100 mL), the organic layers combined, washed (sat. aq. NaHCO3, 50 mL), brine (50 mL) and dried (Na2SO4). The crude solution was then concentrated *in vacuo* and purified by recrystallization (CH2Cl2) to yield **1** as a colorless solid (1.23 g, 21%): 1H NMR (300 MHz, DMSO) δ 12.20 (brs, 1 H), 8.44 (s, 1 H), 8.27 (s, 1 H), 7.45 (d, 1 H, *J* = 8.6 Hz), 7.34 (d, 1 H, *J* = 8.57 Hz), 3.59 (s, 3 H), 3.18 (t, 2 H, *J* = 6.5 Hz ), 2.64 (t, 2 H, *J* = 6.5 Hz); 13C NMR (100 MHz, DMSO) δ 193.7, 173.5, 135.7, 135.4, 127.5, 125.8, 123.8, 114.9, 114.7, 51.8, 33.9, 28.2; ESIMS *m/z* 310 [M+H]+.

**Methyl 4-(5-bromo-1*H*-indol-3-yl)butanoate (2):** To a stirred solution of (**1)** (937 mg, 3.02 mmol) in dry THF (10 mL), NaBH4 (229 mg, 6.04 mmol) was added and the reaction was allowed to stir for 20 minutes under an inert atmosphere. BF3·OEt2 (1.29 g, 1.12 mL, 9.06 mmol) was slowly added and the reaction was monitored by HPLC-MS. Upon completion, the reaction was carefully quenched with H2O (10 mL) and extracted with EtOAc (3 x 25 mL). The combined organic layers were dried (Na2SO4) and concentrated *in vacuo*. The crude residue was purified by column chromatography (hexanes:EtOAc, 10 to 100%) to yield **2** as a colorless oil (725 mg, 81%): 1H NMR (300 MHz, CDCl3) δ 8.02 (brs, 1 H), 7.71 (s, 1 H), 7.20-7.27 (m, 2 H), 6.99 (s, 1 H), 3.67 (s, 3 H), 2.75 (t, 2 H, *J* = 7.4 Hz), 2.38 (t, 2 H, *J* = 7.4 Hz), 2.02 (p, 2 H, *J* = 7.9 Hz); 13C NMR (100 MHz, CDCl3) δ 174.2, 135.0, 129.2, 124.7, 122.7, 121.5, 115.3, 112.5, 112.4, 51.5, 33.6, 25.2, 24.3; ESIMS *m/z* 310 [M+H]+.

**Methyl 4-(5-cyano-1H-indol-3-yl)butanoate (3):** CuCN (39.5 mg, 0.441 mmol) and (**2**) (100 mg, 0.339 mmol) in 0.5 mL of NMP was submitted to microwave irradiation (200 ˚C, 150 W) for 15 minutes. The reaction mixture was then diluted with EtOAc (5 mL) and filtered before washing with H2O (3 x 5 mL). The organic layer was dried (MgSO4) and concentrated *in vacuo* to yield a crude residue which was purified by column chromatography (hexanes:EtOAc, 10 to 100%) to afford **3** as an light-yellow oil (47 mg, 59%): 1H NMR (300 MHz, CDCl3) δ 8.26 (brs, 1 H), 7.96 (s, 1 H), 7.41 (dd, 2 H, *J* = 8.4, 7.9 Hz), 7.12 (s, 1 H), 3.67 (s, 3 H), 2.89 (t, 2 H, *J* = 7.6 Hz), 2.39 (t, 2 H, *J* = 7.4 Hz), 2.04 (p, 2 H, *J* = 7.5 Hz); 13C NMR (100 MHz, CDCl3) δ 173.9, 137.9, 127.4, 125.0, 124.7, 123.5, 120.8, 116.8, 111.9, 102.5, 51.6, 33.5, 25.2, 24.2; HRMS m/z calculated for C14H14N2O2 [M+H]+ 243.11280, found 243.11217.

**4-(5-Cyano-1H-indol-3-yl)butanoic acid (4):** To a 1:1 THF/H2O (0.3 mL), ester **3** (13 mg, 0.054 mmol) and LiOH·H2O (33 mg, 0.81 mmol) was added. The mixture was stirred for 12 h before diluting with H2O (5 mL) and acidification with 3N HCl. Extraction with EtOAc (3 x 5 mL) and concentration *in vacuo* afforded **4** as a light-yellow oil (8 mg, 67%): 1H NMR (300 MHz, CD3OD) δ 7.98 (s, 1 H), 7.46 (d, 1 H, *J* = 8.5 Hz), 7.35 (d, 1 H, *J* = 10.0 Hz), 7.21 (s, 1 H), 2.81 (t, 2 H, *J* = 7.5 Hz), 2.35 (t, 2 H, *J* = 7.3 Hz), 1.99 (p, 2 H, *J* = 7.4 Hz); 13C NMR (100 MHz, CD3OD) δ 176.0, 138.5, 127.3, 124.3, 123.9, 123.6, 120.6, 115.7, 111.9, 100.6, 33.0, 25.4, 23.7; IR (neat) 3336, 2928, 2858, 2097, 1670, 1523 cm-1; HRMS m/z calculated for C13H12N2O2 [M+H]+ 229.09715, found 229.09707.