

Supplementary Information Data S1

Chemical synthesis of *O*-(*N,N*-dimethylaminopropyl)-coccoline **84**, related to STAR Methods

To a suspension of NaH (90 %) (11.7 mg, 0.44 mmol, 5.0 eq.) in dry DMF (1.0 mL) was added coccoline (50 mg, 88 μ mol, 1.0 eq.) in dry DMF (2.0 mL) at 0 °C and was stirred for 30 min at RT. To the reaction mixture 3-dimethylaminopropylchloride hydrochloride (41.9 mg, 0.26 mmol, 3.0 eq.) and a crystal of KI (1.0 mg) was added and stirred at 80 °C overnight.. The reaction mixture was quenched by drops of a saturated solution of NaHCO₃ and the volatiles were removed under reduced pressure. The residue was partitioned between ethyl acetate and a saturated solution of NaHCO₃. The organic layer was separated and the aqueous layer was extracted 3 times with EtOAc. The combined organic layers were dried over Na₂SO₄ and the solvent was removed under reduced pressure. The residue was purified by silica gel flash chromatography using a linear gradient of ammonia 1N in methanol (0 to 20 %) in dichloromethane to afford **84** as a yellow solid. (41 mg, 63 μ mol, 72 %).

¹H NMR (DMSO-*d*₆, 500 MHz) δ 7.62 (d, 1H, *J* = 10 Hz), 7.25-7.19 (m, 2H), 6.89-6.88 (m, 1H), 6.67 (s, 1H), 6.53 (s, 1H), 6.47 (s, 1H), 6.01 (s, 1H), 4.12 (t, 2H, *J* = 5 Hz), 3.96 (s br, 1H), 3.81 (s, 3H), 3.35 (s, br, 2H), 3.28 (d, 1H, *J* = 15 Hz), 3.09 (s, br, 1H), 3.06-3.02 (m, 1H), 2.90-2.79 (m, 4H), 2.64-2.59 (m, 4H), 2.44 (t, 3H, *J* = 5 Hz), 2.53-2.50 (m, 4H), 2.31 (s, 6H), 2.19 (s, 3H), 1.96-1.91 (m, 2H).

¹³C NMR (DMSO-*d*₆, 126 MHz) δ 156.4, 153.1, 149.0, 148.7, 142.9, 141.9, 141.9, 141.5, 138.6, 137.9, 134.2, 133.4, 131.6, 131.3, 131.0, 125.4, 124.8, 124.7, 123.3, 119.6, 116.5, 110.1, 70.4, 70.1, 62.7, 58.9, 58.8, 58.0, 52.9, 48.3, 47.8, 45.89, 44.70, 44.19, 30.63, 30.19, 26.64.

HRMS (ESI) (m/z) calculated for C₄₀H₄₆N₃O₅ [M+H]⁺: 648.3438; Found : 648.3453.