Supporting Information for

Recyclable NaHSO₄ Catalyed Alkylation of *tert***-Enamides** with Indoles and Amines in Water: Construction of pharmaceutically active 2-oxo-1-pyrrolidine analogues

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General Information

Melting points were recorded on an Electrothermal digital melting point apparatus and were uncorrected. IR spectra were recorded on a Varian FT-1000 spectrophotometer using KBr optics. ¹H NMR and ¹³C NMR spectra were recorded on a Varian INOVA 300 or 400 MHz (¹H NMR) and 75 or 100 MHz (¹³C NMR) spectrumeter using CDCl₃ or DMSO-d₆ as solvent and TMS as internal standard. High resolution mass spectra were obtained using GCT-TOF instrument with EI or ESI source.

Typical procedure for the alkylation of indoles, anilines with enamides:

Nucleophile (0.5 mmol), NaHSO₄·H₂O (1 mol%), enamide (1 mmol) and water (1.5 ml) were added into a tube. Then the mixture was vigorously stirred at room temperature, until nucleophile was completely consumed as indicated by TLC analysis. Then the mixture was poured into H₂O and extracted with ethyl acetate (3×5 ml). The combined organic layer was washed with brine (2×3 ml), dried with anhyd MgSO₄, and evaporated under the reduced pressure. Finally, the residue was purified by flash column chromatography with EtOAc and PE as eluents to afford pure product.

Typical procedure for reuse of NaHSO₄ in water:

Indole **2a** (10 mmol), NaHSO₄·H₂O (5 mol%), 1-vinylpyrrolidin-2-one **1a** (12 mmol) and water (3 ml) were added into a flask. Then the mixture was vigorously stirred at room temperatureand and the progress of the reaction was monitored by TLC analysis. After completion of the reaction, 10 mL of deionized water was added into the reaction, the mixture was extracted with CH_2Cl_2 (3×10 ml), and the combined organic layer washed with deionized water (3×5 ml), the water layer was collected. Organic layers were dried with anhydrous MgSO₄, filtered, and concentrated under reduced pressure and the residue was purified by flash column chromatography. NaHSO₄ left in water was concentrated to 1ml under reduced pressure at 80 °Gror another cycle.

Analytical and spectral data for compounds



1-(1-(1H-indol-3-yl)ethyl)pyrrolidin-2-one (3aa):

White solid; m.p. 165-167 °C. IR (KBr): 3243, 3165, 3107, 2972, 2876, 1659, 1490, 1440, 1288, 1198, 751 cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): $\delta = 1.52$ (d, J = 7.0 Hz, 3H), 1.62-1.73 (m, 1H), 1.78-1.88 (m, 1H), 2.18-2.34 (m, 2H), 2.67-2.73 (m, 1H), 3.22-3.27 (m, 1H), 5.53 (q, J = 6.9 Hz, 1H), 6.97 (t, J = 7.4 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 7.32 (s, 1H), 7.37 (d, J = 8.1 Hz, 1H), 7.42 (d, J = 7.9 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): $\delta = 174.8$, 137.0, 126.9, 122.8, 122.6, 120.3, 119.9, 116.4, 111.6, 43.1, 42.7, 32.2, 18.2, 17.1. HRMS (EI): *m/z* calcd for C₁₄H₁₆N₂O: 228.1263; found: 228.1266.



1-(1-(1-methyl-1H-indol-3-yl)ethyl)pyrrolidin-2-one (3ab):

Yellow oil. IR (KBr): 3056, 2971, 2890, 1673, 1468, 1280, 1213, 1095, 745 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 1.58$ (d, J = 7.2 Hz, 3H), 1.78-1.93 (m, 2H), 2.40-2.46 (m, 2H), 2.85-2.93 (m, 1H), 3.23-3.31 (m, 1H), 3.77 (s, 3H), 5.73-5.80 (q, J = 6.9 Hz, 1H, CH), 6.97 (s, 1H), 7.07-7.12 (m, 1H), 7.21-7.30 (m, 2H), 7.61 (d, J = 8.1 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): $\delta = 174.4$, 137.4, 127.1, 127.0, 122.3, 119.9, 114.7, 109.5, 42.8, 42.5, 33.1, 32.0, 18.0, 17.0. HRMS (EI): m/z calcd for C₁₅H₁₈N₂O: 242.1419; found: 242.1418.



1-(1-(2-methyl-1H-indol-3-yl)ethyl)pyrrolidin-2-one (3ac):

White solid; m.p. 176-177 °C. IR (KBr): 3317, 2974, 2933, 2876, 1656, 1491, 1435, 1287, 1198, 1051, 749 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 1.72$ (d, J = 6.9 Hz, 3H), 1.82-2.00 (m, 2H), 2.32-2.41 (m, 2H), 2.48 (s, 3H), 3.11-3.19 (m, 1H), 3.53-3.61 (m, 1H), 5.75 (q, J = 7.2 Hz, 1H), 7.05-7.12 (m, 2H), 7.27 (t, J = 1.8 Hz, 1H), 7.70 (d, J = 7.5 Hz, 1H), 8.07 (br, s, 1H). ¹³C NMR (75 MHz, CDCl₃): $\delta = 174.3$, 135.6, 133.9,

128.3, 121.3, 119.9, 119.6, 111.0, 110.8, 44.0, 44.0, 31.9, 18.1, 18.0, 13.0. HRMS (EI): *m/z* calcd for C₁₅H₁₈N₂O: 242.1419; found: 242.1420.



1-(1-(2-phenyl-1H-indol-3-yl)ethyl)pyrrolidin-2-one (3ad):

White solid; m.p. 166-167 °C. IR (KBr): 3398, 3165, 2930, 2895, 1660, 1442, 1288, 1204, 778 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 1.62$ (d, J = 6.9 Hz, 3H), 1.79-2.00 (m, 2H), 2.36-2.43 (m, 2H), 3.24-3.31 (m, 1H), 3.58-3.66 (m, 1H), 5.62 (q, J = 7.2 Hz, 1H), 7.16-7.23 (m, 2H), 7.39-7.49 (m, 6H), 7.84 (d, J = 7.8 Hz, 1H), 8.21 (br, s, 1H). ¹³C NMR (100 MHz, CDCl₃): $\delta = 174.3$, 737.3, 136.3, 133.0, 129.5, 129.1, 128.8, 128.3, 122.5, 121.0, 120.3, 111.7, 111.5, 45.3, 44.9, 32.0, 18.7, 18.3. HRMS (EI): *m/z* calcd for C₂₀H₂₀N₂O: 304.1576; found: 304.1577.



1-(1-(4-methyl-1H-indol-3-yl)ethyl)pyrrolidin-2-one (3ae):

Yellow solid; m.p. 184-185 °C. IR (KBr): 3158, 3109, 3041, 2942, 2878, 1661, 1493, 1439, 1290, 750 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 1.58$ (d, J = 6.4 Hz, 3H), 1.82-1.93 (m, 2H), 2.43 (t, J = 7.9 Hz, 2H), 2.60 (s, 3H), 2.85-2.92 (m, 1H), 3.17-3.25 (m, 1H), 5.85 (q, J = 6.4 Hz, 1H), 6.86 (d, J = 6.8 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 7.21 (d, J = 12.7 Hz, 2H), 8.41 (br, s, 1H). ¹³C NMR (75 MHz, CDCl₃): $\delta = 174.1$, 137.2, 131.2, 125.5, 123.2, 122.4, 121.6, 115.9, 109.3, 44.4, 43.4, 32.4, 20.2, 17.9, 17.5. HRMS (EI): m/z calcd for C₁₅H₁₈N₂O: 242.1419; found: 242.1420.



1-(1-(5-methoxy-1H-indol-3-yl)ethyl)pyrrolidin-2-one (3af):

White solid; m.p. 134.5-135.4 °C. IR (KBr): 3433, 3235, 3050, 2935, 2826, 1647, 1489, 1440, 1289, 1216, 1028, 926, 800, 666 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 1.57$ (d, J = 6.9 Hz, 3H), 1.70-2.01 (m, 2H), 2.30-2.55 (m, 2H), 2.86 (dd, J = 8.9, 14.9 Hz, 1H), 3.26 (dd, J = 8.9, 14.5 Hz, 1H), 3.80 (s, 3H), 5.75 (q, J = 6.8 Hz, 1H), 6.84 (d, J = 8.7 Hz, 1H), 7.10 (s, 2H), 7.24 (d, J = 8.8 Hz, 1H), 8.61 (br, s, 1H). ¹³C NMR (100 MHz, CDCl₃): $\delta = 174.5$, 154.1, 146.4, 131.8, 126.9, 123.0, 115.5, 112.7, 112.2, 100.8, 55.9, 42.8, 42.3, 31.9, 17.8. HRMS (EI): *m/z* calcd for C₁₅H₁₈N₂O₂: 258.1368;

found: 258.1364.



1-(1-(5-bromo-1H-indol-3-yl)ethyl)pyrrolidin-2-one (3ag):

White solid; m.p. 154-156 °C. IR (KBr): 3157, 3080, 2982, 1650, 1439, 1288, 1194, 885, 790 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 1.58$ (d, J = 7.2 Hz, 3H), 1.79-1.98 (m, 2H), 2.45 (t, J = 8.1 Hz, 2H), 2.82-2.90 (m, 1H), 3.24-3.31 (m, 1H), 5.70 (q, J = 6.9 Hz, 1H), 7.14-7.31 (m, 3H), 7.74 (s, 1H), 8.25 (br, s, 1H). ¹³C NMR (100 MHz, CDCl₃): $\delta = 174.9$, 135.7, 128.6, 125.7, 123.9, 122.3, 116.1, 113.6, 113.2, 43.0, 42.7, 32.2, 18.2, 17.2. HRMS (EI): m/z calcd for C₁₄H₁₅BrN₂O: 308.0347(⁸¹Br); found: 308.0343.



1-(1-(5-nitro-1H-indol-3-yl)ethyl)pyrrolidin-2-one (3ah):

Yellow solid; m.p. 241-242 °C. IR (KBr): 3379, 2968, 1660, 1522, 1295 cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): $\delta = 1.54$ (d, J = 6.8 Hz, 3H), 1.70-1.74 (m, 1H), 1.86-1.90 (m, 1H), 2.20-2.36 (m, 2H), 2.70-2.76 (m, 1H), 3.27-3.34 (m, 1H), 5.56-5.61 (m, 1H), 7.54 (d, J = 9.2 Hz, 1H), 7.64 (s, 1H), 8.00 (d, J = 8.4 Hz, 1H), 8.45 (s, 1H). ¹³C NMR (100 MHz, DMSO-d₆): $\delta = 173.1$, 140.5, 139.6, 127.2, 125.4, 117.6, 116.8, 115.7, 112.0, 41.4, 41.3, 31.0, 17.3, 16.7. HRMS (EI): m/z calcd for C₁₄H₁₅N₃O₃: 273.1113; found: 273.1112.



1-(1-(5-methyl-1H-indol-3-yl)ethyl)pyrrolidin-2-one (3ai):

White solid; m.p. 173-174 °C. IR (KBr): 3154, 2928, 2890, 1652, 1490, 1441, 1290, 792 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 1.58 (d, *J* = 6.9 Hz, 3H), 1.77-1.91 (m, 2H), 2.42-2.46 (m, 5H, CH2), 2.88-2.90 (m, 1H), 3.27-3.28 (m, 1H), 5.75 (q, *J* = 6.6 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 7.09 (s, 1H), 7.24-7.27 (m, 1H), 7.39 (s, 1H), 8.26 (br, s, 1H). ¹³C NMR (100 MHz, CDCl₃): δ = 174.7, 135.3, 129.5, 127.1, 124.4, 122.8, 119.3, 115.8, 111.3, 43.2, 42.8, 32.2, 22.0, 18.2, 17.2. HRMS (EI): *m/z* calcd for C₁₅H₁₈N₂O: 242.1419; found: 242.1420.



1-(1-(6-methyl-1H-indol-3-yl)ethyl)pyrrolidin-2-one (3aj):

white solid; m.p. 135-136 °C. IR (KBr): 3213, 3100, 2980, 2879, 1662, 1610, 1493, 1440, 1289, 1119 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): $\delta = 1.57$ (d, J = 7.0 Hz, 3H), 1.74–1.81 (m, 1H), 1.87–1.93 (m, 1H), 2.41–2.46 (m, 5H), 2.84–2.89 (m, 1H), 3.23–3.29 (m, 1H), 5.73–5.78 (q, J = 7.0 Hz, 1H), 6.93 (d, J = 8.0 Hz, 1H), 7.04 (s, 1H), 7.16 (s, 1H), 7.49 (d, J = 8.0 Hz, 1H), 8.36 (br, s, 1H). ¹³C NMR (75 MHz, CDCl₃): $\delta = 174.50$, 137.19, 132.19, 124.40, 121.84, 121.59, 119.07, 115.64, 111.38, 42.91, 42.39, 31.94, 21.80, 17.83, 16.80. HRMS (EI): m/z calcd for C₁₅H₁₈N₂O: 242.1419; found: 242.1416.



1-(1-(7-methyl-1H-indol-3-yl)ethyl)pyrrolidin-2-one (3ak):

White solid; m.p. 166-168 °C. IR (KBr): 3222, 3113, 2971, 2933, 2873, 1650, 1614, 1498, 1444, 1298, 1201, 1123, 788 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 1.59$ (d, J = 6.9 Hz, 3H), 1.78-1.91 (m, 2H), 2.40-2.46 (m, 2H), 2.49 (s, 3H), 2.83-2.91 (m, 1H), 3.23-3.31 (m, 1H), 5.77 (q, J = 6.6 Hz, 1H), 7.02-7.06 (m, 2H), 7.13(s, 1H), 7.46-7.49 (m, 1H), 8.11 (br, s, 1H). ¹³C NMR (100 MHz, CDCl₃): $\delta = 174.7$, 136.6, 126.4, 123.2, 122.4, 120.9, 120.4, 117.5, 116.7, 43.2, 42.7, 32.2, 18.2, 17.1, 17.1. HRMS (EI): m/z calcd for C₁₅H₁₈N₂O: 242.1419; found: 242.1417.



1-(1-(1H-indol-3-yl)ethyl)azepan-2-one (3ba):

White solid; m.p. 125-126 °C. IR (KBr): 3482, 3182, 2930, 1607, 1483, 1178, 744 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 1.12-1.32 (m, 3H), 1.52 (d, *J* = 6.9 Hz, 3H), 1.57-1.70 (m, 3H), 2.59-2.62 (m, 2H), 3.01-3.19 (m, 2H), 6.29 (q, *J* = 6.9 Hz, 1H), 7.07-7.22 (m, 3H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 8.26 (br, s, 1H). ¹³C NMR (100 MHz, DMSO-d₆): δ = 173.8, 136.4, 126.4, 123.5, 121.2, 118.7, 118.5, 115.2, 111.4, 43.9, 41.8, 37.0, 29.2, 28.6, 23.0, 17.0. HRMS (EI): *m*/*z* calcd for C₁₆H₂₀N₂O: 256.1576; found: 256.1577.



1-(1-(5-methyl-1H-indol-3-yl)ethyl)azepan-2-one (3bi):

White solid; m.p. 75-76 °C. IR (KBr): 3464, 3184, 3159, 2932, 1585, 1486, 1446, 1174 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 1.12$ -1.30 (m, 3H), 1.50 (d, J = 6.9 Hz, 3H), 1.57-1.72 (m, 3H), 2.42 (s, 3H), 2.59-2.63 (m, 2H), 3.01-3.19 (m, 2H), 6.24 (q, J = 6.9 Hz, 1H), 7.01-7.10 (m, 2H), 7.23-7.26 (m, 1H), 7.35 (s, 1H), 8.13 (br, s, 1H). ¹³C NMR (100 MHz, CDCl₃): $\delta = 176.0$, 135.3, 129.2, 127.3, 124.3, 123.3, 119.6, 116.3, 111.2, 45.6, 43.3, 38.2, 30.5, 29.3, 23.8, 21.9, 17.6. HRMS (EI): *m/z* calcd for C₁₇H₂₂N₂O: 270.1732; found: 270.1732.



1-(1-(5-bromo-1H-indol-3-yl)ethyl)azepan-2-one (3bg):

White solid; m.p. 73-74 °C. IR (KBr): 3484, 3006, 2973, 2934, 1584, 1486, 1377, 1113 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): $\delta = 1.07$ -1.35 (m, 3H), 1.50 (d, J = 6.9 Hz, 3H), 1.57-1.71 (m, 3H), 2.60-2.64 (m, 2H), 3.00-3.17 (m, 2H), 6.22 (q, J = 6.9 Hz, 1H), 7.14 (s, 1H), 7.21-7.37 (m, 2H), 7.71 (s, 1H), 8.32 (br, s, 1H). ¹³C NMR (75 MHz, CDCl₃): $\delta = 176.0$, 136.9, 127.1, 123.1, 123.0, 122.7, 120.1, 117.1, 117.1, 111.6, 45.4, 43.4, 38.2, 30.5, 29.4, 23.9, 17.5. HRMS (EI): m/z calcd for C₁₆H₁₉BrN₂O: 336.0660(⁸¹Br); found: 336.0645.



N-(1-(1*H*-indol-3-yl)ethyl)-*N*-methylacetamide (3ca):

White solid; m.p. 95–98 °C. IR (KBr): 3243, 3050, 2957, 1650, 1497, 1456 cm⁻¹. ¹H NMR (300 MHz, CDCl₃, δ = 1.51 (d, J = 6.9 Hz, 3H), 1.65 (d, J = 6.5 Hz, 1H), 2.15 (s, 3H), 2.40 (s, 1H), 2.62 (s, 3H), 2.64 (s, 1H), 5.33 (q, J = 6.6 Hz, 0.35 H), 6.33 (q, J = 6.9 Hz, 1H), 7.05–7.19 (m, 4H), 7.35–7.44 (m, 1.7H), 7.57 (d, J = 7.9 Hz, 1H), 8.17 (s, 1H), 8.90 (s, 0.35H) ppm. ¹³C NMR (75 MHz, DMSO–d₆): δ = 169.2, 169.0, 136.6, 136.5, 126.3, 126.0, 123.6, 123.6, 121.4, 121.3, 118.9, 118.7, 118.6, 118.4, 114.9, 114.6, 111.7, 111.5, 49.8, 43.5, 29.1, 26.7, 22.2, 21.8, 17.9, 16.5 ppm. HRMS (EI):

m/z Calcd for C₁₃H₁₆N₂O: 216.1263; Found, 216.1268.



1-(1-(1*H*-Indol-3-yl)-2-phenylethyl)pyrrolidin-2-one (3ad):

White solid; m.p. 190.8–191.7 °C. IR (KBr): 3280, 2942, 2359, 1655, 1438, 1283, 741 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ = 1.82–1.72 (m, 2H), 2.29–2.19 (m, 2H), 2.97–2.91 (m, 1H), 3.39–3.27 (m, 2H), 3.44–3.40 (m, 1H), 6.02–5.98 (m, 1H), 7.11 (t, *J*=7.4 Hz, 1H), 7.22–7.19 (m, 2H), 7.31–7.26 (m, 5H), 7.36 (d, *J*=8.1 Hz, 1H), 7.71 (d, *J*=7.9 Hz, 1H), 8.31 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ =174.7, 138.2, 138.6, 129.1, 128.6, 126.7, 122.8, 122.6, 120.1, 119.8, 114.7, 111.5, 48.1, 42.8, 37.1, 31.7, 18.0 ppm. HRMS (EI): *m/z* calcd for C₂₀H₂₀N₂ONa: [M+Na]+ 327.1473; found, 327.1468.



4-(1-(2-oxopyrrolidin-1-yl)ethylamino)benzonitrile (5aa):

White solid; m.p. 185–186 °C. IR (KBr): 3305, 2983, 2218, 1664, 1612, 1531, 1285, 1161 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ = 1.48 (d, *J* = 6.4 Hz, 3H), 1.88–2.05 (m, 2H), 2.39–2.44 (m, 2H), 3.15–3.21 (m, 1H), 3.30–3.36 (m, 1H), 4.51 (br s, 1H, NH), 5.70–5.75 (m, 1H), 6.67 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 2H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 174.97, 148.93, 133.83, 120.30, 113.17, 99.97, 56.39, 40.86, 31.60, 19.08, 17.82 ppm. HRMS (EI): *m*/*z* Calcd for C₁₃H₁₅N₃O: 229.1215; Found, 229.1213.



ethyl 4-(1-(2-oxopyrrolidin-1-yl)ethylamino)benzoate (5ab): White solid; m.p. 91–92°C. IR (KBr): 3503, 2977, 1708, 1439, 1281, 1103, 844, 770

cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ = 1.36 (t, *J* = 7.1 Hz, 3H), 1.47 (d, *J* = 6.3 Hz, 3H), 1.86–1.99 (m, 2H), 2.40 (t, *J* = 8.0 Hz, 2H), 3.14–3.20 (m, 1H), 3.29–3.34 (m, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 5.75 (q, *J* = 6.2 Hz, 1H), 6.64 (d, *J* = 8.5 Hz, 2H), 7.88 (d, *J* = 8.5 Hz, 2H) ppm. ¹³C NMR (75 MHz, DMSO–d₆): δ = 173.6, 165.7, 150.4, 130.9, 117.7, 111.8, 59.7, 55.6, 40.3, 18.5, 17.4, 14.3 ppm. HRMS (EI): *m/z* Calcd for C₁₅H₂₀N₂O₃: 276.1474; Found, 276.1473.



1-(1-(4-nitrophenylamino)ethyl)pyrrolidin-2-one (5ac):

Yellow solid; m.p. 204–205°C. IR (KBr): 3271, 3072, 2928, 1665, 1484, 1323, 1161, 832 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): $\delta = 1.51$ (d, J = 6.4 Hz, 3H), 1.90–2.05 (m, 2H), 2.40–2.45 (m, 2H), 3.16–3.22 (m, 1H), 3.32–3.38 (m, 1H), 4.77 (d, J = 6.9 Hz, 1H), 5.75–5.81 (m, 1H, CH), 6.67 (d, J = 9.0 Hz, 2H), 8.09 (d, J = 9.0 Hz, 2H) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 175.15$, 150.75, 126.53, 112.45, 56.69, 41.02, 31.62, 19.31, 17.98 ppm. HRMS (EI): m/z Calcd for C₁₂H₁₅N₃O₃: 249.1113; Found, 249.1108.



1-(1-(3-nitrophenylamino)ethyl)pyrrolidin-2-one (5ad):

Yellow solid; m.p. 89–90°C. IR (KBr): 3297, 3094, 2979, 1663, 1572, 1339, 1156, 735 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ = 1.50 (d, *J* = 6.3 Hz, 3H), 1.90–2.20 (m, 2H), 2.39–2.44 (m, 2H), 3.20–3.24 (m, 1H), 3.32–3.38 (m, 1H), 4.44 (br s, 1H), 5.74 (q, *J* = 6.2 Hz, 1H), 6.99 (d, *J* = 6.2 Hz, 1H), 7.31 (t, *J* = 8.1 Hz, 1H), 7.56 (s, 1H), 7.57 (d, *J* = 7.9 Hz, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 175.2, 149.3, 146.3, 130.3, 118.6, 112.8, 108.2, 56.9, 41.0, 31.7, 19.2, 17.9 ppm. HRMS (EI): *m/z* Calcd for C₁₂H₁₅N₃O₃: 249.1113; Found, 249.1108.



1-(1-(2-nitrophenylamino)ethyl)pyrrolidin-2-one (5ae):

Yellow solid; m.p. 89–91°C. IR (KBr): 3361, 3091, 2976, 1687, 1504, 1421, 1041, 753 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): $\delta = 1.57$ (d, J = 6.3 Hz, 3H), 1.91–2.04 (m, 2H), 2.40–2.46 (m, 2H), 3.17–3.23 (m, 1H), 3.36-3.42 (m, 1H), 5.86–5.92 (m, 1H), 6.67 (t, J = 7.7 Hz, 1H), 7.04 (d, J = 8.6 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 8.09–8.19 (m, 2H) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 174.8$, 142.8, 136.7, 132.5, 126.6, 117.0, 115.3, 55.9, 40.7, 39.5, 19.3, 17.8 ppm. HRMS (EI): *m/z* Calcd for C₁₂H₁₅N₃O₃: 249.1113; Found, 249.1108.



1-(1-((4-chlorophenyl)amino)ethyl)pyrrolidin-2-one (5af):

White solid; m.p. 162–164°C. IR (KBr): 3302, 3105, 2981, 1602, 1493, 1428, 1258, 1160, 820 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 1.44 (d, *J* = 6.4 Hz, 3H), 1.85–2.06 (m, 2H), 2.39 (t, *J* = 8.2 Hz, 2H), 3.12–3.20 (m, 1H), 3.25-3.33 (m, 1H), 5.65 (q, *J* = 6.3 Hz, 1H), 6.57 (d, *J* = 8.8 Hz, 2H), 7.12 (d, *J* = 8.8 Hz, 2H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 175.1, 143.7, 129.4, 123.2, 114.5, 57.1, 40.9, 31.8, 19.5, 17.9 ppm. HRMS (EI): *m*/*z* Calcd for C₁₂H₁₅ClN₂O: 238.0873; Found, 238.0874.



1-(1-(2-iodophenylamino)ethyl)pyrrolidin-2-one (5ag):

Pale yellow oil. IR (KBr): 3231, 3067, 2978, 1680, 1498, 1418, 1121 cm^{-1} . ¹H NMR (400 MHz, CDCl₃): $\delta = 1.51$ (d, J = 6.4 Hz, 3H), 1.83–1.98 (m, 2H), 2.36–2.41 (m, 2H), 3.08–3.13 (m, 1H), 3.29–3.35 (m, 1H), 4.41 (br s, 1H), 5.75–5.79 (m, 1H, CH),

6.50 (t, J = 8.0 Hz, 1H), 6.70 (d, J = 8.2 Hz, 1H), 7.20 (t, J = 7.7 Hz, 1H), 7.65 (d, J = 7.8 Hz, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): $\delta = 174.93$, 144.24, 139.00, 129.90, 120.06, 112.43, 85.17, 56.96, 40.66, 31.69, 19.40, 17.78 ppm. HRMS (EI): m/z Calcd for C₁₂H₁₅IN₂O: 330.0229; Found: 330.0232.



1-(1-(phenylamino)ethyl)pyrrolidin-2-one (5ah):

White solid; m.p.124–125°C. IR (KBr): 3311, 3053, 2934, 1661, 1496, 1280, 1168 cm⁻¹ ¹H NMR (400 MHz, CDCl₃): δ = 1.44 (d, *J* = 6.4 Hz, 3H), 1.84–1.91 (m, 2H), 2.39 (t, *J* = 8.1 Hz, 2H), 3.17–3.23 (m, 1H), 3.27–3.33 (m, 1H), 3.95 (s, 1H, NH), 5.69 (q, *J* = 6.0 Hz, 1H), 6.64 (d, *J* = 8.2 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 7.18 (d, *J* = 7.8 Hz, 2H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 175.0, 145.1, 129.6, 118.5, 113.3, 57.1, 41.0, 31.9, 19.5, 17.9 ppm. HRMS (EI): *m*/*z* Calcd for C₁₂H₁₆N₂O: 204.1263; Found, 204.1262.



1-(1-(p-tolylamino)ethyl)pyrrolidin-2-one (5ai):

White solid; m.p. 147–148 °C. IR (KBr): 3317, 3054, 2937, 1661, 1497, 1280, 1160 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ = 1.43 (d, *J* = 6.4 Hz, 3H), 1.82–1.96 (m, 2H), 2.23 (s, 3H), 2.38 (t, *J* = 8.0 Hz, 2H), 3.16–3.22 (m, 1H), 3.26–3.31 (m, 1H), 3.87 (br s, 1H), 5.66 (q, *J* = 6.4 Hz, 1H), 6.56 (d, *J* = 8.4 Hz, 2H,), 6.98 (d, *J* = 8.4 Hz, 2H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 174.9, 142.8, 130.0, 127.6, 113.3, 57.3, 41.0, 31.9, 20.5, 19.5, 17.9 ppm. HRMS (EI): *m*/*z* Calcd for C₁₃H₁₈N₂O: 218.1419; Found, 218.1417.



1-(1-(3, 4-dihydroquinolin-1(2H)-yl)ethyl)pyrrolidin-2-one (5aj):

Colorless Oil. IR (KBr): 2981, 2939, 1677, 1499, 1316, 1186 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 1.49 (d, J = 6.7 Hz, 3H), 1.91–1.98 (m, 4H), 2.35–2.40 (m, 2H), 2.78 (t, J = 5.8 Hz, 2H), 3.13–3.18 (m, 1H), 3.34–3.38 (m, 2H), 3.44–3.47 (m, 1H), 6.87 (q, J = 6.6 Hz, 1H), 6.63-6.68 (m, 2H), 6.98 (d, J = 6.9 Hz, 1H), 7.08 (t, J = 7.7 Hz, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 174.5, 143.8, 129.3, 127.8, 122.7, 117.1, 111.6, 61.3, 43.2, 42.4, 31.2, 28.5, 22.4, 18.0, 16.8 ppm. HRMS (EI): m/z Calcd for C₁₅H₂₁N₂O: [M+H]⁺ 245.1654; Foud, 245.1660.



1-(1-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)ethyl)pyrrolidin-2-one (5al):

White solid; m.p. 57–58°C. IR (KBr): 3451, 2972, 1685, 1422, 1268, 1241, 1049, 752 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ = 1.84–1.87 (m, 1H), 1.99–2.04 (m, 1H), 2.12 (d, J = 6.7 Hz, 3H), 2.27–2.36 (m, 1H), 2.42–2.48 (m, 1H), 3.08–3.14 (m, 1H), 3.60–3.66 (m, 1H), 7.00 (q, J = 6.6 Hz, 1H), 7.39 (t, J = 7.3 Hz, 1H), 7.54-7.47 (m, 1H), 7.83 (d, J = 8.1 Hz, 1H), 8.05 (d, J = 8.1 Hz, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 175.2, 145.9, 132.5, 127.9, 124.5, 119.7, 110.5, 60.0, 41.9, 31.0, 17.7, 17.1 ppm. HRMS (EI): m/z Calcd for C₁₂H₁₄N₄O: 230.1168; Found, 230.1168.



4-methyl-*N*-(1-(2-oxopyrrolidin-1-yl)ethyl)benzenesulfonamide (5am):

White solid; m.p. 113–115°C. IR (KBr): 3466, 3087, 1662, 1446, 1322, 1147, 1023, 878, 664 cm⁻¹. ¹H NMR (400 MHz, DMSO–d₆): $\delta = 1.17$ (d, J = 6.6 Hz, 3H), 1.59–2.03 (m, 2H), 1.95–2.03 (m, 1H), 2.38 (s, 3H), 2.74–2.78 (m, 1H), 2.97–3.03 (m, 1H), 3.34–3.37 (m, 1H), 5.39–5.42 (m, 1H), 7.37 (d, J = 7.8 Hz, 2H), 7.58 (d, J = 7.8 Hz, 2H) ppm. ¹³C NMR (100 MHz, DMSO–d₆): $\delta = 172.6$, 142.8, 138.1, 129.3, 126.4, 56.4, 56.3, 30.4, 21.0, 18.9, 16.6 ppm. HRMS (EI): m/z Calcd for C₁₃H₁₈N₂O₃S: 282.1038; Found, 282.1039.



4-(1-(2-oxoazepan-1-yl)ethylamino)benzonitrile (5ba):

White solid; m.p. 196–197 °C. IR (KBr): 3294, 3163, 2931, 2215, 1612, 1536, 1340, 1164, 1142, 817 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ = 1.40 (d, *J* = 6.4 Hz, 3H), 1.54–1.70 (m, 6H), 2.46–2.59 (m, 2H), 3.16–3.28 (m, 2H), 4.58 (br s, 1H), 6.15–6.20 (m, 1H), 6.63 (d, *J* = 8.7 Hz, 2H), 7.44 (d, *J* = 8.7 Hz, 2H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 176.10, 149.14, 133.86, 120.39, 113.27, 99.98, 58.38, 41.57, 37.96, 30.07, 29.04, 23.47, 19.51 ppm. HRMS (EI): *m*/*z* Calcd for C₁₅H₁₉N₃O: 257.1528; Found, 257.1512.



1-(1-(3-nitrophenylamino)ethyl)azepan-2-one (5bd):

Yellow solid; m.p. 115–117°C. IR (KBr): 3288, 3063, 2936, 1623, 1530, 1339, 1151, 982cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ = 1.25–1.26 (m, 1H), 1.41 (d, *J* = 6.2 Hz, 3H), 1.54–1.68 (m, 5H), 2.49–2.56 (m, 2H), 3.20–3.30 (m, 2H), 4.64 (br s, 1H), 6.16–6.18 (m, 1H), 6.49 (d, *J* = 7.2 Hz, 1H), 7.30 (t, *J* = 8.2 Hz, 1H), 7.46 (s, 1H), 7.55 (d, *J* = 7.6 Hz, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 176.3, 149.3, 146.6, 130.2, 118.7, 112.7, 108.1, 59.0, 41.6, 38.0, 30.1, 29.1, 23.5, 19.6 ppm. HRMS (EI): *m/z* Calcd for C₁₄H₁₉N₃O₃: 277.1426; Found, 277.1426.





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¹H NMR





¹H NMR





1-(1-(2-phenyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ad):



100

150

50





¹³C NMR

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1-(1-(5-methoxy-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3af): ¹H NMR





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1-(1-(5-nitro-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ah): ¹H NMR



S22



1-(1-(5-methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ai): ¹H NMR





¹H NMR





1-(1-(7-methyl-1*H*-indol-3-yl)ethyl)pyrrolidin-2-one (3ak):



S26

1-(1-(1*H*-indol-3-yl)ethyl)azepan-2-one (3ba): ¹H NMR









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1-(1-(5-bromo-1*H*-indol-3-yl)ethyl)azepan-2-one (3bg): ¹H NMR



S29





1-(1-(1*H*-Indol-3-yl)-2-phenylethyl)pyrrolidin-2-one (3ad): ¹H NMR





4-(1-(2-oxopyrrolidin-1-yl)ethylamino)benzonitrile (5aa):









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1-(1-(4-nitrophenylamino)ethyl)pyrrolidin-2-one (5ac): ¹H NMR

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1-(1-(3-nitrophenylamino)ethyl)pyrrolidin-2-one (5ad): ¹H NMR

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1-(1-(2-nitrophenylamino)ethyl)pyrrolidin-2-one (5ae): ¹H NMR

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1-(1-((4-chlorophenyl)amino)ethyl)pyrrolidin-2-one (5af): ¹H NMR



1-(1-(2-iodophenylamino)ethyl)pyrrolidin-2-one (5ag): ¹H NMR

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1-(1-(phenylamino)ethyl)pyrrolidin-2-one (5ah):



1-(1-(p-tolylamino)ethyl)pyrrolidin-2-one (5ai):













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4-(1-(2-oxoazepan-1-yl)ethylamino)benzonitrile (5ba): ¹H NMR

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1-(1-(3-nitrophenylamino)ethyl)azepan-2-one (5bd):

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