SUPPLEMENTARY MATERIAL TO

μ-Opioid/D_2 dopamine receptor pharmacophore containing ligands: Synthesis and pharmacological evaluation

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Contents

Isolated yields and spectroscopic data of synthesized compounds

*3-Bromo-1-(4-phenylpiperazin-1-yl)propan-1-one, (**3a**).* Yield: 0.99 g (96%); pale yellow oil. IR (ATR): 3486, 2914, 2823, 1646, 1598, 1498, 1441, 1231, 1025, 761, 695 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ =7.33 – 7.24 (m, 2H), 6.99 – 6.89 (m, 3H), 3.82 – 3.76 (m, 2H), 3.71 – 3.64 (m, 2H), 3.65 – 3.59 (m, 2H), 3.22 – 3.16 (m, 4H), 2.96 (t, J = 7.1 Hz, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 168.6, 150.9, 129.3, 120.7, 116.8, 49.8, 49.5, 45.5, 41.8, 36.4, 27.3 ppm.

*3-Bromo-1-(4-(2-methoxyphenyl)piperazin-1-yl) propan-1-one, (**3b**).* Yield: 1.09 g (95.8%); pale yellow oil. IR (ATR): 3485, 2915, 2824, 1644, 1591, 1468, 1442, 1233, 1027, 762, 696 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.08 – 7.00 (m, 1H), 6.96 – 6.85 (m, 3H), 3.88 (s, 3H), 3.82 (t, J = 5.0 Hz, 2H), 3.68 (t, J = 7.1 Hz, 2H, partially overlapped), 3.64 (t, J = 5.0 Hz, 2H, partially overlapped), 3.05 (dt, J = 17.5, 5.0 Hz, 4H), 2.96 (t, J = 7.1 Hz, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.0, 153.8, 142.1, 125.2, 122.6, 120.0, 112.9, 57.0, 52.5, 52.1, 47.3, 43.5, 37.9, 28.9 ppm.

*3-Bromo-1-(4-(2,3-dichlorophenyl)piperazin-1-yl) propan-1-one, (**3c**).* Yield: 1.20 g (94,2%); pale yellow oil. IR (ATR): 3487, 2917, 2825, 1647, 1578, 1446, 1236, 958, 784 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.21 – 7.14 (m, 2H), 6.90 (d, J = 1.8 Hz, 1H), 3.80 (t, J = 5.0 Hz, 2H), 3.66 (t, J = 7.1 Hz, 2H), 3.63 (t, J = 5.0 Hz, 2H), 3.04 – 2.97 (m, 4H), 2.95 (t, J = 7.1 Hz, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 168.8, 150.7, 150.7, 134.4, 128.3, 127.8, 127.6, 119.0, 51.3, 45.9, 36.5, 27.5 ppm.

*4-Bromo-1-(4-(2-methoxyphenyl)piperazin-1-yl)butan-1-one, (**3d**).* Yield: 1.14 g (96,0 %); pale yellow oil. IR (ATR): 3394, 2920, 2495, 1637, 1592, 1500, 1454, 1243, 1028, 746 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.03 – 6.92 (m, 1H), 6.89 – 6.76 (m, 3H), 3.80 (s, 3H), 3.76 – 3.66 (m, 2H), 3.65 – 3.55 (m, 4H), 2.96 (dt, *J* = 18.4, 5.1 Hz, 4H), 2.48 (t, *J* = 7.1 Hz, 2H), 2.13 – 2.03 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.2, 152.3, 140.7, 123.6, 121.1, 118.5, 111.4, 55.5, 51.0, 50.6, 45.8, 44.9, 41.9, 29.8, 28.0 ppm.

*5-Bromo-1-(4-phenylpiperazin-1-yl)pentan-1-one, (**3e**).* Yield: 1.11 g (97.9 %); pale yellow oil. IR (ATR): 3454, 2956, 1639, 1578, 1446, 1234, 1035, 775 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.33 – 7.27 (m, 2H), 6.98 – 6.89 (m, 3H), 3.82 – 3.77 (m, 2H), 3.69 – 3.62 (m, 2H), 3.59 (t, J = 6.2 Hz, 2H), 3.23 – 3.13 (m, 4H), 2.45 – 2.39 (m, 2H), 1.91 – 1.80 (m, 4H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.4, 152.5, 130.8, 122.1, 118.2, 51.3, 51.0, 47.1, 46.3, 43.1, 33.9, 33.7, 24.1 ppm.

*5-Bromo-1-(4-(2-methoxyphenyl)piperazin-1-yl) pentan-1-one, (**3f**).* Yield: 1.19 g (96.3 %); pale yellow oil. IR (ATR): 3453, 2954, 1630, 1577, 1448, 1236, 1036, 782 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.06 – 7.00 (m, 1H), 6.94 – 6.84 (m, 3H), 3.86 (s, 3H), 3.80 (s, 2H), 3.65 (s, 2H), 3.55 (t, J = 6.3 Hz, 2H), 3.04 (d, J = 17.3 Hz, 4H), 2.42 – 2.35 (m, 2H), 1.87 – 1.76 (m, 4H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.5, 153.8, 125.5, 122.7, 120.3, 113.0, 57.0, 52.6, 52.2, 47.3, 46.3, 43.2, 33.8, 33.7, 24.1 ppm.

*5-Bromo-1-(4-(2,3-dichlorophenyl)piperazin-1-yl) pentan-1-one, (**3g**).* Yield: 1.31 g (94.9 %); pale yellow oil. IR (ATR): 3451, 2957, 1619, 1579, 1449, 1235, 1035, 783 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.23 – 7.13 (m, 2H), 6.93 (dd, J = 7.8, 1.8 Hz, 1H), 3.80 (br. s, 2H), 3.66 (t, J =

5.0 Hz, 2H), 3.45 (t, J = 6.6 Hz, 2H), 3.02 (dt, J = 16.1, 5.0 Hz, 4H), 2.34 (t, J = 7.3 Hz, 2H), 1.86 – 1.75 (m, 4H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.3, 150.6, 134.2, 127.6, 125.3, 118.8, 51.2, 45.9, 33.5, 33.0, 32.1, 23.8 ppm.

*6-Bromo-1-(4-phenylpiperazin-1-yl)hexan-1-one, (**3h**).* Yield: 1.16 g (98.0 %); pale yellow oil. IR (ATR): 3444, 2938, 2911, 2825, 1646, 1593, 1497, 1442, 1232, 1024, 763, 696 cm-1. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 – 7.24 (m, 2H), 6.96 – 6.87 (m, 3H), 3.78 (t, J = 5.3 Hz, 2H), 3.62 (t, J = 5.2 Hz, 2H), 3.51 – 3.34 (m, 2H), 3.22 – 3.08 (m, 4H), 2.39 (t, J = 7.5 Hz, 2H), 1.98 – 1.79 (m, 2H), 1.76 – 1.62 (m, 2H), 1.57 – 1.41 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.3, 151.0, 129.3, 120.6, 116.7, 49.9, 49.5, 45.6, 41.6, 33.8, 33.0, 32.6, 28.0, 24.4 ppm.

*6-Bromo-1-(4-(2-methoxyphenyl)piperazin-1-yl) hexan-1-one, (**3i**).* Yield: 1.26 g (97.7 %); pale yellow oil. IR (ATR): 3454, 2939, 2918, 2824, 1647, 1597, 1494, 1441, 1233, 1025, 762, 696 cm-1. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.07 – 7.00 (m, 1H), 6.96 – 6.86 (m, 3H), 3.88 (s, 3H), 3.80 (t, J = 5.1 Hz, 2H), 3.65 (t, J = 4.9 Hz, 2H), 3.42 (t, J = 6.7 Hz, 2H), 3.10 – 2.97 (m, 4H), 2.39 (t, J = 7.5 Hz, 2H), 1.75 – 1.64 (m, 2H), 1.57 – 1.47 (m, 2H), 1.44 (t, J = 7.3 Hz, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.8, 153.8, 142.1, 125.1, 122.6, 120.0, 112.9, 57.0, 52.6, 52.1, 47.4, 43.3, 35.3, 34.5, 34.1, 29.5, 25.9 ppm.

*6-Bromo-1-(4-(2,3-dichlorophenyl) piperazin-1-yl)hexan-1-one, (**3j**).* Yield: 1.36 g (95.2 %); pale yellow oil. IR (ATR): 3467, 2938, 2862, 1645, 1450, 1236, 1032, 783, 736 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.22 – 7.11 (m, 2H), 6.93 (dd, J = 7.8, 1.9 Hz, 1H), 3.80 (br. s, 2H), 3.65 (t, J = 5.0 Hz, 2H), 3.43 – 3.37 (m, 2H), 3.01 (dt, J = 13.7, 5.1 Hz, 4H), 2.39 (t, J = 7.5 Hz, 2H), 1.96 – 1.89 (m, 2H), 1.79 – 1.68 (m, 2H), 1.56 – 1.51 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.4, 150.6, 134.2, 127.8, 127.6, 125.2, 118.8, 51.8, 51.2, 45.9, 41.8, 35.0, 33.8, 33.0, 28.0, 24.4 ppm.

*7-Bromo-1-(4-phenylpiperazin-1-yl)heptan-1-one, (**3k**).* Yield: 1.19 g (97.1 %); pale yellow oil. IR (ATR): 3485, 2933, 2857, 1645, 1597, 1498, 1437, 1231, 1027, 760, 695 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 – 7.21 (m, 2H), 7.02 – 6.85 (m, 3H), 3.85 – 3.72 (m, 2H), 3.62 (t, J = 5.3 Hz, 2H), 3.48 – 3.32 (m, 2H), 3.16 (dt, J = 13.5, 5.3 Hz, 4H), 2.37 (t, J = 7.6 Hz, 2H), 1.93 – 1.79 (m, 2H), 1.75 – 1.58 (m, 2H), 1.55 – 1.43 (m, 2H), 1.46 – 1.31 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.6, 151.0, 129.3, 120.6, 116.7, 49.9, 49.5, 45.6, 41.6, 34.0, 33.1, 32.6, 28.6, 28.0, 25.1 ppm.

*7-Bromo-1-(4-(2-methoxyphenyl)piperazin-1-yl)heptan-1-one, (**3l**).* Yield: 1.30 g (97.3 %); pale yellow oil. IR (ATR): 3441, 2935, 2858, 1643, 1501, 1460, 1242, 1029, 735 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.08 – 6.99 (m, 1H), 6.94 – 6.85 (m, 3H), 3.87 (s, 3H), 3.79 (t, J = 5.1 Hz, 2H), 3.64 (t, J = 5.1 Hz, 2H), 3.44 – 3.37 (m, 2H), 3.02 (dt, J = 16.2, 5.1 Hz, 4H), 2.37 (t, J = 7.6 Hz, 2H), 1.91 – 1.82 (m, 2H), 1.71 – 1.62 (m, 2H), 1.52 – 1.41 (m, 2H, partially overlapped), 1.43 – 1.32 (m, 2H, partially overlapped) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.6, 152.3, 140.7, 123.6, 121.1, 118.5, 111.4, 55.5, 51.2, 50.7, 46.0, 41.9, 34.0, 33.9, 33.2, 32.7, 32.6, 28.6, 28.0, 25.2 ppm.

*7-Bromo-1-(4-(2,3-dichlorophenyl)piperazin-1-yl)heptan-1-one, (**3m**).* Yield: 1.40 g (94.7 %); pale yellow oil. IR (ATR): 3460, 2935, 2859, 1646, 1578, 1450, 1236, 783, 735 cm^{-1}. ^{1}H NMR

(500 MHz, $CDCl_3$): δ = 7.16 – 7.03 (m, 2H), 6.93 – 6.75 (m, 1H), 3.72 (br. s, 2H), 3.59 – 3.52 (m, 2H), 3.35 – 3.31 (m, 2H), 2.93 (dt, J = 12.8, 5.0 Hz, 4H), 2.30 (t, J = 7.6 Hz, 2H), 1.89 – 1.74 (m, 2H), 1.66 – 1.50 (m, 2H), 1.48 – 1.34 (m, 2H, partially overlapped), 1.36 – 1.23 (m, 2H, partially overlapped). ^{13}C NMR (126 MHz, $CDCl_3$): δ =171.6, 150.7, 134.3, 129.3, 127.7, 125.3, 116.7, 51.8, 51.3, 45.9, 41.8, 34.0, 33.2, 32.6, 28.6, 28.0, 25.1 ppm.

*3-(4-(Phenylamino)piperidin-1-yl)-1-(4-phenylpiperazin-1-yl)propan-1-one, (**5a**).* Yield: 0.48 g (62 %); pale yellow oil. IR (ATR): 3385, 2924, 2829, 1601, 1501, 1439, 1313, 1233, 1104, 754, 691 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.36 – 7.27 (m, 3H), 7.24 – 7.17 (m, 2H), 7.02 – 6.91 (m, 3H), 6.73 (t, J = 7.3 Hz, 1H), 6.63 (d, J = 7.9 Hz, 2H), 3.82 (t, J = 5.2 Hz, 2H), 3.69 (t, J = 5.1 Hz, 2H), 3.38 (dt, J = 10.1, 5.6 Hz, 1H), 3.27 – 3.16 (m, 4H), 3.09 (br. s, 1H, partially overlapped), 2.98 (d, J = 10.5 Hz, 2H), 2.85 (t, J = 7.5 Hz, 2H), 2.68 (t, J = 7.5 Hz, 2H), 2.32 (t, J = 11.0 Hz, 2H), 2.18 – 2.09 (m, 2H), 1.62 – 1.50 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 151.0, 147.1, 129.5, 129.4, 120.7, 117.5, 116.8, 113.4, 54.2, 52.7, 49.9, 49.5, 45.7, 41.7, 32.4, 31.2 ppm.

*1-(4-(2-Methoxyphenyl)piperazin-1-yl)-3-(4-(phenylamino)piperidin-1-yl)propan-1-one, (**5b**).* Yield: 0.49 g (59 %); pale yellow oil. IR (ATR): 3345, 2939, 2815, 1637, 1602, 1501, 1318, 1241, 1118, 1026, 749, 697 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.21 – 7.14 (m, 2H), 7.09 – 7.02 (m, 1H), 6.98 – 6.87 (m, 3H), 6.70 (t, J = 7.3 Hz, 1H), 6.61 (d, J = 8.0 Hz, 2H), 3.89 (s, 3H), 3.82 (t, J = 5.2 Hz, 2H), 3.68 (t, J = 5.0 Hz, 2H), 3.34 (dt, J = 10.2, 5.8 Hz, 1H), 3.05 (dt, J = 15.3, 5.1 Hz, 4H), 3.01 – 2.89 (m, 2H), 2.80 (dd, J = 8.7, 6.6 Hz, 2H), 2.63 (dd, J = 8.7, 6.6 Hz, 2H), 2.26 (td, J = 11.5, 2.6 Hz, 2H), 2.14 – 2.02 (m, 2H), 1.60 – 1.40 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.7, 153.8, 148.6, 142.2, 130.9, 125.2, 122.6, 120.0, 118.8, 114.8, 112.9, 57.0, 55.7, 54.1, 52.6, 52.1, 51.3, 47.4, 43.4, 34.0, 32.7 ppm.

*1-(4-(2,3-Dichlorophenyl)piperazin-1-yl)-3-(4-(phenylamino)piperidin-1-yl)propan-1-one, (**5c**).* Yield: 0.58 g (63.4 %); pale yellow oil. IR (ATR): 3365, 2933, 2813, 1636, 1602, 1502, 1318, 1241, 1110, 1023, 781, 752, 695 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.25 – 7.12 (m, 4H), 6.94 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.70 (t, *J* = 7.3 Hz, 1H), 6.61 (d, *J* = 7.9 Hz, 2H), 3.86 – 3.78 (m, 2H), 3.68 (d, *J* = 4.9 Hz, 2H), 3.34 (tt, *J* = 10.2, 4.3 Hz, 1H), 3.10 – 2.97 (m, 4H), 2.93 (d, *J* = 12.1 Hz, 2H), 2.84 – 2.74 (m, 2H), 2.66 – 2.59 (m, 2H), 2.26 (td, *J* = 11.4, 2.6 Hz, 2H), 2.15 – 2.02 (m, 2H), 1.56 – 1.42 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.9, 152.1, 148.6, 135.8, 130.9, 129.3, 129.1, 126.8, 120.3, 118.8, 114.8, 55.7, 54.2, 53.3, 52.7, 51.3, 47.4, 43.3, 34.0, 32.9 ppm.

*1-(4-(2-Methoxyphenyl)piperazin-1-yl)-4-(4-(phenylamino)piperidin-1-yl)butan-1-one, (**5d**).* Yield: 0.54 g (62.5 %); pale yellow oil. IR (ATR): 3342, 2935, 1638, 1502, 1440, 1246, 1023, 765 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.21 – 7.11 (m, 2H), 7.10 – 6.99 (m, 1H), 6.96 – 6.86 (m, 3H), 6.74 – 6.62 (m, 1H), 6.60 – 6.55 (m, 2H), 3.88 (s, 3H), 3.82 – 3.77 (m, 2H), 3.71 – 3.60 (m, 2H), 3.51 (br. s, 1H), 3.33 – 3.24 (m, 1H), 3.01 – 2.96 (m, 4H), 2.89 (d, J = 11.0 Hz, 2H, 2H), 2.46 – 2.36 (m, 4H), 2.14 (t, J = 11.0 Hz, 2H), 2.03 (d, J = 11.8 Hz, 2H), 1.93 – 1.78 (m, 2H), 1.58 – 1.31 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.3, 152.2, 147.1, 140.7, 129.3, 123.5, 121.0, 118.4, 117.1, 113.2, 111.3, 57.9, 55.5, 52.4, 51.1, 50.6, 49.9, 45.9, 41.8, 32.6, 31.0, 22.7 ppm.

*5-(4-(Phenylamino)piperidin-1-yl)-1-(4-phenylpiperazin-1-yl)pentan-1-one, (**5e**).* Yield: 0.54 g (64.5 %); pale yellow oil. IR (ATR): 3340, 2940, 2814, 1639, 1602, 1500, 1441, 1325, 1232, 1027, 755, 696 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.18 (t, J = 7.9 Hz, 2H), 7.06 (t, J = 7.9 Hz, 2H), 6.86 – 6.79 (m, 3H), 6.58 (t, J = 7.3 Hz, 1H), 6.49 (d, J = 7.9 Hz, 2H), 3.69 – 3.63 (m, 2H), 3.59 – 3.42 (m, 3H), 3.21 (dd, J = 8.6, 4.9 Hz, 1H), 3.04 (dt, J = 10.5, 5.0 Hz, 4H), 2.83 (d, J = 11.5 Hz, 2H), 2.40 – 2.31 (m, 2H), 2.29 (t, J = 7.4 Hz, 2H), 2.09 (t, J = 10.8 Hz, 2H), 1.97 (d, J = 11.6 Hz, 2H), 1.64 – 1.55 (m, 2H), 1.56 – 1.48 (m, 2H), 1.48 – 1.37 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.2, 150.8, 147.0, 129.2, 129.1, 120.4, 117.1, 116.5, 113.1, 58.0, 52.2, 49.6, 49.3, 45.4, 41.3, 32.9, 32.0, 26.5, 23.1 ppm.

*1-(4-(2-Methoxyphenyl)piperazin-1-yl)-5-(4-(phenylamino)piperidin-1-yl)pentan-1-one, (**5f**).* Yield: 0.52 g (58.4 %); pale yellow oil. IR (ATR): 3319, 2909, 2822, 1641, 1600, 1499, 1443, 1241, 1029, 751, 696 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.18 – 7.12 (m, 2H), 7.07 – 6.99 (m, 1H), 6.95 – 6.86 (m, 3H), 6.70 – 6.65 (m, 1H), 6.63 – 6.56 (m, 2H), 3.87 (s, 3H), 3.79 (br. s, 2H, partially overlapped), 3.68 – 3.61 (m, 2H), 3.54 (s, 1H), 3.33 (dt, J = 9.8, 5.9 Hz, 1H), 3.03 (dt, J = 16.4, 5.0 Hz, 4H, partially overlapped), 2.96 (d, J = 11.7 Hz, 2H, partially overlapped), 2.51 – 2.44 (m, 2H), 2.40 (t, J = 7.3 Hz, 2H), 2.23 (t, J = 10.8 Hz, 2H), 2.13 – 2.04 (m, 2H), 1.74 – 1.61 (m, 4H), 1.60 – 1.51 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.3, 152.3, 147.0, 140.7, 129.4, 123.6, 121.1, 118.5, 117.4, 113.3, 111.4, 58.1, 55.5, 52.3, 51.1, 50.6, 49.6, 45.9, 41.8, 33.0, 32.0, 26.5, 23.2 ppm.

*1-(4-(2,3-Dichlorophenyl)piperazin-1-yl)-5-(4-(phenylamino)piperidin-1-yl)pentan-1-one, (**5g**).*

Yield: 0.61 g (62.3 %); pale yellow oil. IR (ATR): 3301, 2911, 2820, 1643, 1599, 1500, 1441, 1240, 1026, 786, 752, 694 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.19 – 7.08 (m, 4H), 6.88 (dd, J = 8.0, 1.7 Hz, 1H), 6.64 (t, J = 7.3 Hz, 1H), 6.56 (d, J = 7.9 Hz, 2H), 4.09 (s, 1H), 3.80 – 3.72 (m, 2H), 3.65 – 3.56 (m, 2H), 3.29 (tt, J = 9.5, 3.6 Hz, 1H), 3.02 – 2.95 (m, 4H, partially overlapped), 2.92 (d, J = 11.7 Hz, 2H, partially overlapped), 2.47 – 2.40 (m, 2H), 2.37 (t, J = 7.3 Hz, 2H), 2.18 (t, J = 10.8 Hz, 2H), 2.05 (d, J = 11.4 Hz, 2H), 1.70 – 1.55 (m, 4H), 1.55 – 1.46 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.5, 150.7, 147.1, 134.3, 129.4, 127.8, 127.6, 125.3, 118.8, 117.4, 113.3, 58.1, 52.3, 51.8, 51.2, 49.7, 45.9, 41.8, 33.1, 32.1, 26.5, 23.2 ppm.

*6-(4-(Phenylamino)piperidin-1-yl)-1-(4-phenylpiperazin-1-yl)hexan-1-one, (**5h**).* Yield: 0.57 g (65.1 %); pale yellow oil. IR (ATR): 3341, 2936, 2814, 1638, 1602, 1500, 1441, 1323, 754, 696 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36 – 7.21 (m, 2H), 7.15 (t, J = 7.8 Hz, 2H), 6.97 – 6.84 (m, 3H), 6.67 (t, J = 7.3 Hz, 1H), 6.59 (d, J = 8.0 Hz, 2H), 3.96 (br. s, 1H), 3.76 (t, J = 5.2 Hz, 2H), 3.60 (t, J = 5.0 Hz, 2H), 3.33 (dt, J = 10.1, 5.5 Hz, 1H), 3.22 – 3.08 (m, 4H), 2.97 (d, J = 10.8 Hz, 2H), 2.51 – 2.41 (m, 2H), 2.37 (t, J = 7.6 Hz, 2H), 2.23 (t, J = 11.6 Hz, 2H), 2.09 (d, J = 12.1 Hz, 2H), 1.68 (p, J = 7.6 Hz, 2H, partially overlapped), 1.64 – 1.50 (m, 4H, partially overlapped), 1.39 (p, J = 7.7 Hz, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.4, 151.0, 147.0, 129.4, 129.3, 120.5, 117.3, 116.6, 113.3, 58.4, 52.3, 49.8, 49.4, 45.5, 41.5, 33.1, 31.9, 27.3, 26.5, 25.0 ppm.

*1-(4-(2-Methoxyphenyl)piperazin-1-yl)-6-(4-(phenylamino)piperidin-1-yl)hexan-1-one, (**5i**).* Yield: 0.59 g (63.7 %); pale yellow oil. IR (ATR): 3313, 2928, 2818, 1652, 1602, 1453, 1236, 749, 694 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.17 (t, J = 7.8 Hz, 2H), 7.09 – 7.01 (m, 1H), 6.98 –

6.85 (m, 3H), 6.69 (t, J = 7.3 Hz, 1H), 6.61 (d, J = 8.0 Hz, 2H), 3.89 (s, 3H), 3.81 (t, J = 5.1 Hz, 2H), 3.65 (t, J = 5.0 Hz, 2H), 3.52 (br. s, 1H), 3.36 (td, J = 9.6, 4.8 Hz, 1H), 3.04 (dt, J = 15.0, 5.1 Hz, 4H, partially overlapped), 2.98 (d, J = 10.5 Hz, 2H, partially overlapped), 2.50 – 2.43 (m, 2H), 2.39 (t, J = 7.6 Hz, 2H), 2.24 (t, J = 11.5 Hz, 2H), 2.11 (d, J = 13.0 Hz, 2H), 1.70 (p, J = 7.6 Hz, 2H), 1.66 – 1.53 (m, 4H), 1.41 (p, J = 7.8 Hz, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.5, 152.4, 147.1, 140.8, 129.4, 123.6, 121.2, 118.5, 117.4, 113.4, 111.4, 58.5, 55.5, 52.4, 51.2, 50.7, 46.0, 41.9, 33.2, 32.1, 27.5, 26.6, 25.2 ppm.

*1-(4-(2,3-Dichlorophenyl)piperazin-1-yl)-6-(4-(phenylamino)piperidin-1-yl)hexan-1-one, **(5j)**.* Yield: 0.63g (63.4%); pale yellow oil. IR (ATR): 3312, 2934, 2819, 1637, 1603, 1500, 1446, 1240, 1028, 784, 751, 697 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.24 – 7.13 (m, 4H), 6.97 – 6.90 (m, 1H), 6.71 (t, J = 7.4 Hz, 1H), 6.64 (d, J = 7.9 Hz, 2H), 3.83 – 3.76 (m, 2H), 3.69 – 3.60 (m, 2H), 3.56 (br.s, 1H), 3.40 – 3.29 (m, 2H), 3.07 – 2.95 (m, 4H), 2.88 – 2.79 (m, 2H, partially overlapped), 2.76 (s, 1H, partially overlapped), 2.40 (t, J = 7.4 Hz, 2H), 2.27 (d, J = 11.0 Hz, 2H), 1.95 (d, J = 10.0 Hz, 2H), 1.88 – 1.79 (m, 2H), 1.76 – 1.66 (m, 3H), 1.48 – 1.38 (m, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.3, 150.7, 146.6, 134.2, 129.4, 127.8, 127.7, 125.3, 118.9, 117.9, 113.6, 57.5, 51.7, 51.3, 45.9, 41.9, 32.8, 29.8, 26.8, 24.5 ppm.

*7-(4-(Phenylamino)piperidin-1-yl)-1-(4-phenylpiperazin-1-yl)heptan-1-one, **(5k)**.* Yield: 0.57 g (64.8 %); pale yellow oil. IR (ATR): 3300, 2934, 2858, 2808, 2729, 1648, 1624, 1600, 1498, 1451, 1227, 1023, 755, 693 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 – 7.28 (m, 2H), 7.23 – 7.15 (m, 2H), 6.99 – 6.89 (m, 3H), 6.72 (t, J = 7.3 Hz, 1H), 6.64 (d, J = 8.0 Hz, 2H), 3.80 (t, J = 5.2 Hz, 2H), 3.74 (br. s, 1H), 3.65 (t, J = 5.1 Hz, 2H), 3.44 (dt, J = 9.8, 5.2 Hz, 1H), 3.19 (dt, J = 15.3, 5.0 Hz, 4H), 3.12 (d, J = 11.4 Hz, 2H), 2.62 – 2.55 (m, 2H), 2.48 – 2.41 (m, 2H, partially overlapped), 2.40 (t, J = 7.6 Hz, 2H, partially overlapped), 2.18 (d, J = 9.8 Hz, 2H), 1.79 – 1.62 (m, 6H), 1.48 – 1.35 (m, 4H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.5, 151.0, 146.9, 129.4, 129.3, 120.5, 117.5, 116.6, 113.4, 58.2, 52.0, 49.8, 49.4, 45.6, 41.5, 33.1, 31.2, 29.2, 27.2, 25.9, 25.1 ppm.

*1-(4-(2-Methoxyphenyl)piperazin-1-yl)-7-(4-(phenylamino)piperidin-1-yl)heptan-1-one, **(5l)**.* Yield: 0.57 g (59.7 %); pale yellow oil. IR (ATR): 3318, 2937, 2857, 2814, 1638, 1603, 1501, 1462, 1242, 1029, 751, 697 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.19 – 7.12 (m, 2H), 7.07 – 6.99 (m, 1H), 6.96 – 6.85 (m, 3H), 6.69 (tt, J = 7.5, 1.1 Hz, 1H), 6.64 – 6.58 (m, 2H), 3.88 (s, 3H), 3.79 (t, J = 5.1 Hz, 2H, partially overlapped), 3.75 (br.s, 1H, partially overlapped), 3.67 – 3.61 (m, 2H), 3.47 (s, 1H), 3.18 (d, J = 11.7 Hz, 2H), 3.03 (dt, J = 17.5, 5.1 Hz, 4H), 2.70 – 2.61 (m, 2H), 2.55 (s, 2H), 2.40 – 2.32 (m, 2H), 2.20 (d, J = 10.3 Hz, 2H), 1.81 (td, J = 13.2, 9.5 Hz, 2H), 1.75 – 1.61 (m, 4H), 1.44 – 1.32 (m, 4H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.5, 152.3, 146.8, 140.7, 129.4, 123.6, 121.1, 118.5, 117.7, 113.5, 111.4, 58.0, 55.5, 51.7, 51.1, 50.7, 48.5, 45.9, 41.8, 33.1, 30.6, 29.1, 27.1, 25.4, 25.1 ppm.

*1-(4-(2,3-Dichlorophenyl)piperazin-1-yl)-7-(4-(phenylamino)piperidin-1-yl)heptan-1-one, **(5m)**.* Yield: 0.68 g (66.5 %); pale yellow oil. IR (ATR): 3319, 2941, 2855, 2821, 1636, 1602, 1498, 1444, 1236, 784, 751, 695 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.20 – 7.09 (m, 4H), 6.89 (dd, J = 7.9, 1.8 Hz, 1H), 6.65 (t, J = 7.3 Hz, 1H), 6.57 (d, J = 7.9 Hz, 2H), 3.81 – 3.71 (m, 2H), 3.64 – 3.58 (m, 2H, partially overlapped), 3.57 (br. s, 1H, partially overlapped), 3.31 (dt, J = 10.3, 5.5 Hz, 1H), 3.04 – 2.88 (m, 6H), 2.44 – 2.37 (m, 2H), 2.38 – 2.31 (m, 2H), 2.19 (t, J = 11.1 Hz, 2H), 2.06

(d, J = 12.7 Hz, 2H), 1.65 (p, J = 7.5 Hz, 2H), 1.60 – 1.47 (m, 4H), 1.42 – 1.29 (m, 4H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.7, 150.6, 147.0, 134.2, 129.3, 127.7, 127.6, 125.2, 118.8, 117.3, 113.3, 58.5, 52.3, 51.7, 51.2, 49.6, 45.8, 41.7, 33.2, 32.0, 29.3, 27.4, 26.6, 25.2 ppm.

*N-Phenyl-1-(3-(4-phenylpiperazin-1-yl)propyl)piperidin-4-amine, (**6a**).* Yield: 0.30 g (79%); pale yellow oil. IR (ATR): 3393, 2943, 2808, 2772, 1602, 1505, 1448, 1323, 1239, 751, 691 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41 – 7.34 (m, 2H), 7.32 – 7.24 (m, 2H), 7.04 (d, J = 8.2 Hz, 2H), 6.96 (t, J = 7.2 Hz, 1H), 6.79 (t, J = 7.3 Hz, 1H), 6.71 (d, J = 7.9 Hz, 2H), 3.62 (br. s, 1H), 3.42 (dt, J = 10.3, 5.8 Hz, 1H), 3.36 – 3.29 (m, 4H), 3.01 (d, J = 11.2 Hz, 2H), 2.77 – 2.69 (m, 4H), 2.53 (q, J = 8.6 Hz, 4H), 2.24 (t, J = 11.0 Hz, 2H, partially overlapped), 2.18 (d, J = 12.3 Hz, 2H, partially overlapped), 1.92 – 1.80 (m, 2H), 1.67 – 1.54 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 151.4, 147.2, 129.4, 129.2, 119.7, 117.3, 116.1, 113.3, 56.8, 53.4, 52.6, 49.2, 32.6, 24.7 ppm.

*1-(3-(4-(2-Methoxyphenyl)piperazin-1-yl)propyl)-N-phenylpiperidin-4-amine, (**6b**).* Yield: 0.33 g (81.0 %); pale yellow oil. IR (ATR): 3296, 3208, 2817, 2773, 1601, 1499, 1324, 1241, 1147, 1026, 748, 695 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.08 (t, J = 7.9 Hz, 2H), 6.95 – 6.88 (m, 1H), 6.90 – 6.81 (m, 2H), 6.78 (d, J = 7.9 Hz, 1H), 6.59 (t, J = 7.3 Hz, 1H), 6.51 (d, J = 7.8 Hz, 2H), 3.78 (s, 3H), 3.43 (br. s, 1H), 3.22 (dt, J = 10.3, 5.7 Hz, 1H), 3.03 (s, 4H), 2.81 (d, J = 11.1 Hz, 2H), 2.58 (s, 4H), 2.43 – 2.29 (m, 4H), 2.13 – 2.02 (m, 2H, partially overlapped), 1.98 (d, J = 12.2 Hz, 2H, partially overlapped), 1.68 (p, J = 7.7 Hz, 2H), 1.53 – 1.32 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 152.3, 147.2, 141.4, 129.4, 122.9, 121.0, 118.3, 117.2, 113.3, 111.2, 56.9, 56.8, 55.4, 53.6, 52.6, 50.7, 50.0, 32.6, 24.7 ppm.

*1-(3-(4-(2,3-Dichlorophenyl)piperazin-1-yl)propyl)-N-phenylpiperidin-4-amine, (**6c**).* Yield: 0.36 g (83.0 %); pale yellow oil. IR (ATR): 3322, 2943, 2817, 1602, 1503, 1449, 1374, 1243, 1142, 961, 781, 750, 695 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.30 – 7.19 (m, 4H), 7.11 – 7.01 (m, 1H), 6.77 (t, J = 7.3 Hz, 1H), 6.69 (d, J = 7.8 Hz, 2H), 3.61 (br. s, 1H), 3.40 (dt, J = 10.2, 5.4 Hz, 1H), 3.23 – 3.14 (m, 4H), 3.00 (d, J = 11.5 Hz, 2H), 2.74 (br. s, 4H), 2.53 (dt, J = 21.0, 7.7 Hz, 4H), 2.23 (t, J = 11.5 Hz, 2H, partially overlapped), 2.20 – 2.12 (m, 2H, partially overlapped), 1.90 – 1.77 (m, 2H), 1.65 – 1.49 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 151.4, 147.2, 134.1, 129.4, 127.6, 127.5, 124.7, 118.7, 117.3, 113.4, 56.8, 53.4, 52.7, 52.6, 51.4, 50.0, 46.3, 32.6, 24.8 ppm.

*1-(4-(4-(2-Methoxyphenyl)piperazin-1-yl)butyl)-N-phenylpiperidin-4-amine, (**6d**).* Yield: 0.34 g (80.0 %); pale yellow oil. IR (ATR): 3301, 2934, 2819, 1600, 1503, 1456, 1316, 1240, 1117, 745, 696 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.19 – 7.12 (m, 2H), 7.03 – 6.94 (m, 1H), 6.97 – 6.90 (m, 2H), 6.88 – 6.83 (m, 1H), 6.72 – 6.64 (m, 1H), 6.63 – 6.55 (m, 2H), 3.86 (3H s,), 3.54 (br. s, 1H), 3.41 – 3.25 (m, 1H), 3.10 (br. s, 4H), 2.91 (d, *J* = 11.2 Hz, 2H), 2.66 (br. s, 4H), 2.47 – 2.36 (m, 4H), 2.15 (t, *J* = 11.0 Hz, 2H), 2.07 (d, *J* = 11.8 Hz, 2H), 1.57 (br. s, 4H), 1.56 – 1.45 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 152.4, 147.2, 141.4, 129.4, 123.0, 121.1, 118.3, 117.3, 113.3, 111.3, 58.6, 55.4, 53.5, 52.5, 50.7, 49.9, 32.4, 25.1, 25.0 ppm.

*N-Phenyl-1-(5-(4-phenylpiperazin-1-yl)pentyl)piperidin-4-amine, (**6e**).* Yield: 0.36 g (83.0 %); pale yellow oil. IR (ATR): 3291, 2938, 2848, 1600, 1500, 1454, 1322, 1242, 1118, 743, 694 cm-1. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.30 – 7.22 (m, 2H), 7.20 – 7.13 (m, 2H), 6.94 (d, J = 8.1 Hz,

2H), 6.85 (t, J = 7.3 Hz, 1H), 6.68 (t, J = 7.3 Hz, 1H), 6.60 (d, J = 7.9 Hz, 2H), 3.51 (br. s, 1H), 3.30 (dt, J = 10.9, 5.9 Hz, 1H), 3.26 – 3.18 (m, 4H), 2.88 (d, J = 12.0 Hz, 2H), 2.64 – 2.55 (m, 4H), 2.43 – 2.37 (m, 2H, partially overlapped), 2.37 – 2.33 (m, 2H, partially overlapped), 2.16 – 2.01 (m, 4H), 1.61 – 1.49 (m, 4H, partially overlapped), 1.51 – 1.42 (m, 2H, partially overlapped), 1.41 – 1.31 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 151.5, 147.2, 129.4, 129.2, 119.7, 117.3, 116.1, 113.3, 58.9, 58.8, 53.4, 52.7, 50.1, 49.2, 32.7, 27.3, 26.9, 25.8 ppm.

*1-(5-(4-(2-Methoxyphenyl)piperazin-1-yl)pentyl)-N-phenylpiperidin-4-amine, **(6f)**.* Yield: 0.35 g (82 %); pale yellow oil. IR (ATR): 3324, 2937, 2813, 1601, 1501, 1452, 1315, 1241, 1028, 749, 696 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.19 – 7.10 (m, 2H), 7.03 – 6.97 (m, 1H), 6.96 – 6.89 (m, 2H), 6.88 – 6.82 (m, 1H), 6.67 (t, J = 7.3 Hz, 1H), 6.58 (d, J = 8.0 Hz, 2H), 3.85 (s, 3H), 3.30 (ddd, J = 10.1, 5.9, 4.0 Hz, 1H), 3.11 (d, J = 7.4 Hz, 5H), 2.90 (d, J = 11.5 Hz, 2H), 2.65 (s, 4H), 2.46 – 2.34 (m, 4H), 2.13 (t, J = 11.8 Hz, 2H), 2.06 (d, J = 12.2 Hz, 2H), 1.61 – 1.45 (m, 6H), 1.39 – 1.29 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 152.3, 147.1, 141.4, 129.3, 122.9, 121.0, 118.2, 117.2, 113.3, 111.2, 58.7, 58.7, 55.4, 55.4, 53.5, 52.5, 50.6, 49.8, 45.8, 32.4, 27.0, 26.7, 25.7 ppm.

*1-(5-(4-(2,3-Dichlorophenyl)piperazin-1-yl)pentyl)-N-phenylpiperidin-4-amine, **(6g)**.* Yield: 0.38 g (81.3 %); pale yellow oil. IR (ATR): 3321, 2920, 2850, 1601, 1500, 1448, 1373, 1241, 1095, 804, 747, 695 cm-1. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.18 – 7.10 (m, 4H), 6.94 (dd, J = 7.0, 2.5 Hz, 1H), 6.66 (t, J = 7.3 Hz, 1H), 6.58 (d, J = 7.8 Hz, 2H), 3.52 (br. s, 1H), 3.29 (tt, J = 9.9, 4.2 Hz, 1H), 3.11 – 3.02 (m, 4H), 2.87 (d, J = 10.6 Hz, 2H), 2.62 (s, 4H), 2.44 – 2.37 (m, 2H, partially overlapped), 2.38 – 2.29 (m, 2H, partially overlapped), 2.15 – 2.00 (m, 4H), 1.60 – 1.42 (m, 6H), 1.34 (p, J = 7.6 Hz, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 151.4, 147.2, 134.1, 129.4, 127.5, 127.5, 124.6, 118.7, 117.2, 113.3, 58.8, 58.7, 53.4, 52.8, 52.6, 51.4, 50.0, 46.3, 32.6, 27.2, 26.9, 25.7 ppm.

*N-Phenyl-1-(6-(4-phenylpiperazin-1-yl)hexyl)piperidin-4-amine, **(6h)**.* Yield: 0.31 g (74.6 %); pale yellow oil. IR (ATR): 3329, 2913, 2814, 1602, 1502, 1452, 1317, 1236, 1133, 753, 693 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.30 (d, J = 8.5 Hz, 2H), 7.19 (t, J = 7.7 Hz, 2H), 6.96 (d, J = 8.1 Hz, 2H), 6.88 (t, J = 7.3 Hz, 1H), 6.71 (t, J = 7.3 Hz, 1H), 6.63 (d, J = 7.9 Hz, 2H), 3.53 (br. s, 1H), 3.34 (dt, J = 10.4, 5.6 Hz, 1H), 3.24 (t, J = 5.0 Hz, 4H), 2.93 (d, J = 11.4 Hz, 2H), 2.63 (t, J = 5.0 Hz, 4H), 2.48 – 2.32 (m, 4H), 2.23 – 2.01 (m, 4H), 1.69 – 1.48 (m, 6H), 1.44 – 1.32 (m, 4H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 151.5, 147.2, 129.5, 129.2, 119.8, 117.4, 116.2, 113.4, 58.9, 53.5, 52.7, 50.1, 49.3, 32.6, 27.8, 27.7, 27.2, 27.0 ppm.

*1-(6-(4-(2-Methoxyphenyl)piperazin-1-yl)hexyl)-N-phenylpiperidin-4-amine, **(6i)**.* Yield: 0.34 g (77 %); pale yellow oil. IR (ATR): 3389, 2940, 2823, 1599, 1503, 1451, 1320, 1237, 1154, 752, 691 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.18 (t, J = 7.9 Hz, 2H), 7.05 – 6.90 (m, 3H), 6.88 (d, J = 7.9 Hz, 1H), 6.69 (t, J = 7.3 Hz, 1H), 6.61 (d, J = 7.7 Hz, 2H), 3.88 (br. s, 3H), 3.53 (br. s, 1H), 3.32 (br. s, 1H), 3.13 (br. s, 4H), 2.90 (d, J = 10.8 Hz, 2H), 2.67 (s, 4H), 2.46 – 2.40 (m, 2H), 2.39 – 2.34 (m, 2H), 2.18 – 2.01 (m, 4H), 1.62 – 1.45 (m, 6H), 1.42 – 1.32 (m, 4H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 152.4, 147.2, 141.5, 129.4, 122.9, 121.1, 118.3, 117.2, 113.3, 111.2, 58.9, 55.4, 53.6, 52.6, 50.7, 50.1, 32.6, 27.7, 27.7, 27.2, 27.0 ppm.

*1-(6-(4-(2,3-Dichlorophenyl)piperazin-1-yl)hexyl)-N-phenylpiperidin-4-amine, **(6j)**.* Yield: 0.39 g (80.0 %); pale yellow oil. IR (ATR): 3322, 2929, 2853, 1600, 1501, 1450, 1375, 1242, 1098, 806, 748, 695 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.12 – 7.04 (m, 3H), 6.91 – 6.84 (m, 1H), 6.59 (t, J = 7.4 Hz, 1H), 6.52 (d, J = 8.0 Hz, 2H), 3.35 (s, 1H), 3.27 – 3.15 (m, 1H), 3.00 (s, 4H), 2.80 (d, J = 11.4 Hz, 2H), 2.56 (s, 4H), 2.37 – 2.29 (m, 2H), 2.26 (dd, J = 9.2, 6.2 Hz, 2H), 2.10 – 1.91 (m, 4H), 1.52 – 1.34 (m, 6H), 1.26 (s, 5H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 151.4, 147.2, 134.1, 129.4, 127.5, 124.6, 122.9, 121.1, 118.7, 117.2, 113.3, 58.9, 58.8, 53.6, 53.4, 52.6, 51.4, 50.7, 45.1, 32.6, 27.7, 27.7, 27.2, 26.9 ppm.

*N-Phenyl-1-(7-(4-phenylpiperazin-1-yl)heptyl)piperidin-4-amine, **(6k)**.* Yield: 0.36 g (83.1 %); pale yellow oil. IR (ATR): 3387, 2931, 2821, 1600, 1502, 1449, 1237, 1102, 805, 753, 692 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28 (t, J = 7.9 Hz, 2H), 7.18 (t, J = 7.8 Hz, 2H), 6.95 (d, J = 8.0 Hz, 2H), 6.87 (t, J = 7.2 Hz, 1H), 6.70 (t, J = 7.3 Hz, 1H), 6.61 (d, J = 7.8 Hz, 2H), 3.57 (br. s, 1H), 3.39 – 3.29 (m, 1H), 3.28 – 3.16 (m, 4H), 2.98 (d, J = 10.7 Hz, 2H), 2.68 – 2.58 (m, 4H), 2.50 – 2.36 (m, 4H), 2.23 (t, J = 10.2 Hz, 2H), 2.11 (d, J = 11.6 Hz, 2H), 1.66 – 1.49 (m, 6H), 1.36 (br. s, 6H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 151.4, 147.1, 129.4, 129.2, 119.7, 117.4, 116.1, 113.4, 58.8, 58.7, 53.4, 52.4, 49.7, 49.2, 32.1, 29.5, 27.6, 26.9, 26.8 ppm.

*1-(7-(4-(2-Methoxyphenyl)piperazin-1-yl)heptyl)-N-phenylpiperidin-4-amine, **(6l)**.* Yield: 0.39 g (85.0 %); pale yellow oil. IR (ATR): 3365, 2934, 2812, 1601, 1502, 1451, 1311, 1240, 1104, 749, 694 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.18 – 7.11 (m, 2H), 7.02 – 6.87 (m, 3H), 6.85 (d, J = 7.9 Hz, 1H), 6.66 (t, J = 7.3 Hz, 1H), 6.58 (d, J = 8.0 Hz, 2H), 3.85 (s, 3H), 3.48 – 3.39 (m, 1H), 3.29 (dt, J = 10.1, 5.6 Hz, 1H), 3.10 (br. s, 4H), 2.87 (d, J = 11.4 Hz, 2H), 2.65 (br. s, 4H), 2.45 – 2.36 (m, 2H), 2.36 – 2.29 (m, 2H), 2.15 – 2.00 (m, 4H), 1.58 – 1.40 (m, 6H), 1.38 – 1.25 (m, 6H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 152.3, 147.2, 141.4, 129.4, 122.9, 121.1, 118.3, 117.2, 113.3, 111.2, 59.0, 55.4, 53.6, 52.6, 50.7, 50.0, 32.5, 29.6, 27.7, 27.6, 27.2, 26.9 ppm.

*1-(7-(4-(2,3-Dichlorophenyl)piperazin-1-yl)heptyl)-N-phenylpiperidin-4-amine, **(6m)**.* Yield: 0.36 g (73.2 %); pale yellow oil. IR (ATR): 3315, 2937, 2854, 1600, 1449, 1319, 1139, 964, 780, 743, 693 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.12 – 7.02 (m, 4H), 6.88 (dd, J = 7.0, 2.6 Hz, 1H), 6.59 (t, J = 7.3 Hz, 1H), 6.51 (d, J = 8.0 Hz, 2H), 3.44 – 3.32 (m, 1H), 3.22 (tt, J = 9.8, 4.1 Hz, 1H), 3.00 (br. s, 4H), 2.80 (d, J = 10.4 Hz, 2H), 2.56 (br. s, 4H), 2.40 – 2.31 (m, 2H), 2.30 – 2.21 (m, 2H), 2.07 – 1.93 (m, 4H), 1.52 – 1.33 (m, 6H), 1.33 – 1.19 (m, 6H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 151.2, 147.0, 133.9, 129.2, 127.3, 124.4, 118.5, 117.1, 113.2, 58.8, 58.7, 53.2, 52.4, 51.2, 49.9, 32.4, 29.4, 27.5, 27.4, 27.0, 26.7 ppm.

*N-Phenyl-N-(1-(3-(4-phenylpiperazin-1-yl)propyl)piperidin-4-yl)propionamide, **(1a)**.* Yield: 0.18 g (89.1 %); pale yellow oil. IR (ATR): 3058, 2938, 2817, 1654, 1598, 1497, 1379, 1265, 1239, 1152, 759, 705 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42 – 7.33 (m, 3H), 7.29 – 7.21 (m, 2H), 7.10 – 7.04 (m, 2H), 6.91 (d, J = 8.1 Hz, 2H), 6.84 (t, J = 7.3 Hz, 1H), 4.66 (tt, J = 12.2, 3.9 Hz, 1H), 3.18 (t, J = 4.9 Hz, 4H), 3.03 – 2.91 (m, 2H), 2.57 (t, J = 5.0 Hz, 4H), 2.43 – 2.32 (m, 4H), 2.19 – 2.04 (m, 2H), 1.92 (q, J = 7.4 Hz, 2H), 1.85 – 1.74 (m, 2H), 1.75 – 1.62 (m, 2H), 1.42 (qd, J = 12.5, 3.8 Hz, 2H), 1.01 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.7, 151.4, 138.9, 130.5, 129.4, 129.2, 128.4, 119.8, 116.1, 77.4, 77.2, 76.9, 56.6, 56.5, 53.3, 53.2, 52.2, 49.1,

30.4, 28.6, 24.4, 9.7 ppm. HRMS-Heated ESI-Orbitrap: calcd. for $C_{27}H_{38}N_4O$ $[M+H]^+$ 435.31184; found 435.31227.

*N-(1-(3-(4-(2-Methoxyphenyl)piperazin-1-yl)propyl)piperidin-4-yl)-N-phenylpropionamide, **(1b)**.* Yield: 0.21 g (94.0 %); pale yellow oil. IR (ATR): 3059, 2939, 2812, 1657, 1594, 1499, 1453, 1377, 1242, 1150, 749, 707cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.42 – 7.33 (m, 3H), 7.07 (d, J = 7.0 Hz, 2H), 7.01 – 6.96 (m, 1H), 6.95 – 6.88 (m, 2H), 6.84 (d, J = 7.7 Hz, 1H), 4.66 (ddd, J = 12.2, 8.5, 3.9 Hz, 1H), 3.85 (br. s, 3H), 3.07 (s, 4H), 2.92 (d, J = 11.3 Hz, 2H), 2.61 (br. s, 4H), 2.34 (dt, J = 21.8, 7.7 Hz, 4H), 2.07 (t, J = 11.3 Hz, 2H), 1.92 (q, J = 7.4 Hz, 2H), 1.78 (d, J = 11.7 Hz, 2H), 1.72 – 1.58 (m, 2H), 1.39 (qd, J = 12.1, 3.2 Hz, 2H), 1.01 (t, J = 7.4 Hz, 3H) ppm.^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.6, 152.4, 141.5, 139.0, 130.5, 129.4, 128.3, 122.9, 121.1, 118.3, 111.3, 56.9, 56.7, 55.4, 53.5, 53.3, 52.3, 50.7, 30.6, 28.6, 24.7, 9.7 ppm. HRMS-Heated ESI-Orbitrap: calcd. for $C_{28}H_{40}N_4O_2$ $[M+H]^+$ 465.32240; found 465.32221.

*N-(1-(3-(4-(2,3-Dichlorophenyl)piperazin-1-yl)propyl)piperidin-4-yl)-N-phenylpropionamide, **(1c)**.* Yield: 0.23 g (90.0 %); pale yellow oil. IR (ATR): 3059, 2941, 2815, 1654, 1579, 1450, 1376, 1264, 1143, 964, 783, 736, 708 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.45 – 7.33 (m, 3H), 7.19 – 7.10 (m, 2H), 7.08 (d, J = 6.9 Hz, 2H), 6.95 (dd, J = 7.0, 2.6 Hz, 1H), 4.68 (tt, J = 12.3, 4.0 Hz, 1H), 3.06 (br. s, 4H, partially overlapped), 2.98 (d, J = 11.2 Hz, 2H, partially overlapped), 2.63 (br. s, 4H), 2.48 – 2.34 (m, 4H), 2.20 – 2.07 (m, 2H), 1.93 (q, J = 7.3 Hz, 2H), 1.84 – 1.76 (m, 2H), 1.70 (h, J = 7.5, 6.4 Hz, 2H), 1.44 (qd, J = 12.3, 3.9 Hz, 2H), 1.02 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.7, 151.3, 138.9, 134.1, 130.5, 129.4, 128.4, 127.6, 127.5, 124.7, 118.7, 56.5, 56.5, 53.3, 53.1, 52.2, 51.2, 30.4, 28.6, 24.2, 9.7 ppm. HRMS-Heated ESI-Orbitrap: calcd. for $C_{27}H_{36}Cl_2N_4O$ $[M+H]^+$ 503.23389; found 503.23436.

*N-(1-(4-(4-(2-Methoxyphenyl)piperazin-1-yl)butyl)piperidin-4-yl)-N-phenylpropionamide, **(1d)**.* Yield: 0.25 g (88.0 %); pale yellow oil. IR (ATR): 3058, 2938, 2807, 1654, 1595, 1496, 1374, 1242, 747, 706 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.40 – 7.30 (m, 3H), 7.08 – 7.01 (m, 2H), 7.00 – 6.93 (m, 1H), 6.94 – 6.85 (m, 2H), 6.83 (d, J = 8.0 Hz, 1H), 4.64 (tt, J = 12.6, 3.9 Hz, 1H), 3.83 (s, 3H), 3.06 (br. s, 4H), 2.91 (d, J = 11.4 Hz, 2H), 2.61 (br. s, 4H), 2.37 (t, J = 7.2 Hz, 2H), 2.29 (t, J = 7.1 Hz, 2H), 2.11 – 1.98 (m, 2H), 1.90 (q, J = 7.3 Hz, 2H), 1.81 – 1.71 (m, 2H), 1.54 – 1.30 (m, 6H), 0.99 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 175.0, 153.8, 142.9, 140.4, 131.9, 130.8, 129.8, 124.4, 122.5, 119.7, 112.7, 60.0, 59.9, 56.9, 55.0, 54.7, 53.7, 52.1, 32.0, 30.1, 26.6, 26.4, 11.2 ppm. HRMS-HESI-Orbitrap: calcd. for $C_{29}H_{42}N_4O_2$ $[M+H]^+$ 479.33805; found 479.33825.

*N-Phenyl-N-(1-(5-(4-phenylpiperazin-1-yl)pentyl)piperidin-4-yl)propionamide, **(1e)**.* Yield: 0.21 g (92.1 %); pale yellow oil. IR (ATR):3059, 2937, 2813, 1656, 1598, 1498, 1378, 1238, 759, 705 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34 – 7.23 (m, 3H), 7.22 – 7.13 (m, 2H), 6.99 (d, J = 7.1 Hz, 2H), 6.85 (d, J = 8.1 Hz, 2H), 6.77 (t, J = 7.3 Hz, 1H), 4.59 (tt, J = 12.3, 4.1 Hz, 1H), 3.12 (t, J = 4.9 Hz, 4H), 2.86 (d, J = 11.3 Hz, 2H), 2.50 (t, J = 5.0 Hz, 4H), 2.35 – 2.25 (m, 2H), 2.26 – 2.17 (m, 2H), 2.00 (t, J = 11.8 Hz, 2H), 1.85 (q, J = 7.5 Hz, 2H), 1.75 – 1.65 (m, 2H), 1.53 – 1.29 (m, 6H), 1.26 – 1.15 (m, 2H), 0.94 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.6, 151.4, 138.9, 130.5, 129.4, 129.2, 128.3, 119.7, 116.1, 58.6, 58.6, 53.3, 53.2, 52.2, 49.2,

30.5, 28.6, 27.0, 26.8, 25.6, 9.7 ppm. HRMS-Heated ESI-Orbitrap: calcd. for $C_{29}H_{42}N_4O$ $[M+H]^+$ 463.34314; found 463.34340.

N-(1-(5-(4-(2-Methoxyphenyl)piperazin-1-yl)pentyl)piperidin-4-yl)-N-phenylpropionamide, (**1f**). Yield: 0.22 g (89.8 %); pale yellow oil. IR (ATR): 3056, 2937, 2812, 1652, 1594, 1499, 1377, 1241, 1026, 746, 706 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.43 – 7.33 (m, 3H), 7.07 (d, J = 6.7 Hz, 2H), 7.04 – 6.96 (m, 1H), 6.96 – 6.87 (m, 2H), 6.86 (d, J = 8.0 Hz, 1H), 4.68 (ddd, J = 12.4, 8.5, 3.9 Hz, 1H), 3.85 (s, 3H), 3.16 (br. s, 4H), 3.06 (d, J = 11.5 Hz, 2H), 2.78 (br. s, 4H), 2.51 (dd, J = 9.4, 6.3 Hz, 2H), 2.46 – 2.35 (m, 2H), 2.23 (t, J = 11.8 Hz, 2H), 1.93 (q, J = 7.1 Hz, 2H), 1.88 – 1.76 (m, 2H), 1.68 – 1.47 (m, 6H), 1.38 – 1.28 (m, 2H), 1.01 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.6, 152.2, 140.8, 138.6, 130.2, 129.4, 128.4, 123.2, 121.0, 118.3, 111.2, 58.1, 57.9, 55.4, 53.1, 52.8, 51.7, 49.8, 29.7, 28.5, 26.1, 25.8, 25.2, 9.6 ppm. HRMS-Heated ESI-Orbitrap: calcd. for $C_{30}H_{44}N_4O_2$ $[M+H]^+$ 493.35370; found 493.35412.

*N-(1-(5-(4-(2,3-Dichlorophenyl)piperazin-1-yl)pentyl)piperidin-4-yl)-N-phenylpropionamide, (**1g**).* Yield: 0.24 g (91.7 %); pale yellow oil. IR (ATR): 3060, 2937, 2814, 1654, 1579, 1450, 1376, 1241, 1142, 959, 783, 740, 709 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.40 – 7.31 (m, 3H), 7.16 – 7.10 (m, 2H), 7.06 (d, J = 7.8 Hz, 2H), 6.94 (dd, J = 6.7, 2.7 Hz, 1H), 4.66 (ddd, J = 12.2, 8.5, 3.9 Hz, 1H), 3.04 (br. s, 4H), 2.91 (d, J = 11.6 Hz, 2H), 2.60 (br. s, 4H), 2.44 – 2.31 (m, 2H), 2.33 – 2.20 (m, 2H), 2.04 (t, J = 11.4 Hz, 2H), 1.91 (q, J = 7.4 Hz, 2H), 1.77 (d, J = 11.8 Hz, 2H), 1.56 – 1.34 (m, 6H), 1.27 (p, J = 7.4 Hz, 2H), 1.00 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.6, 151.4, 139.0, 134.1, 130.5, 129.4, 128.3, 127.6, 127.5, 124.6, 118.7, 58.7, 53.4, 53.3, 52.4, 51.4, 30.7, 28.6, 27.2, 26.9, 25.7, 9.7 ppm. HRMS-Heated ESI-Orbitrap: calcd. for $C_{29}H_{40}Cl_2N_4O$ $[M+H]^+$ 531.26519; found 531.26545.

*N-Phenyl-N-(1-(6-(4-phenylpiperazin-1-yl)hexyl)piperidin-4-yl)propionamide, (**1h**).* Yield: 0.23 g (96 %); pale yellow oil. IR (ATR): 3059, 2933, 2810, 1657, 1598, 1497, 1377, 1237, 1137, 757, 704 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.42 – 7.32 (m, 3H), 7.29 – 7.21 (m, 2H), 7.07 (d, J = 7.2 Hz, 2H), 6.92 (d, J = 8.0 Hz, 2H), 6.84 (t, J = 7.2 Hz, 1H), 4.66 (ddd, J = 12.2, 8.1, 4.0 Hz, 1H), 3.25 – 3.14 (m, 4H), 2.91 (d, J = 11.5 Hz, 2H), 2.66 – 2.53 (m, 4H), 2.41 – 2.30 (m, 2H), 2.30 – 2.22 (m, 2H), 2.04 (t, J = 11.9 Hz, 2H), 1.92 (q, J = 7.3 Hz, 2H), 1.77 (d, J = 11.5 Hz, 2H), 1.61 – 1.44 (m, 2H, partially overlapped), 1.47 – 1.33 (m, 4H, partially overlapped), 1.35 – 1.22 (m, 4H, partially overlapped), 1.01 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.6, 151.5, 139.0, 130.6, 129.3, 129.2, 128.3, 119.7, 116.1, 58.8, 58.8, 53.4, 53.3, 52.4, 49.2, 30.7, 28.6, 27.7, 27.6, 27.2, 26.9, 9.7 ppm. HRMS-Heated ESI-Orbitrap: calcd. for $C_{30}H_{44}N_4O$ $[M+H]^+$ 477.35879; found 477.35880.

*N-(1-(6-(4-(2-Methoxyphenyl)piperazin-1-yl)hexyl)piperidin-4-yl)-N-phenylpropionamide, (**1i**).* Yield: 0.23 g (93.4 %); pale yellow oil. IR (ATR): 3058, 2935, 2810, 1656, 1594, 1498, 1375, 1241, 1027, 805, 748, 707 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.42 – 7.32 (m, 3H), 7.07 (d, J = 6.9 Hz, 2H), 7.02 – 6.95 (m, 1H, partially overlapped), 6.97 – 6.89 (m, 2H, partially overlapped), 6.85 (d, J = 7.9 Hz, 1H), 4.66 (ddd, J = 12.1, 8.4, 4.0 Hz, 1H), 3.86 (br. s, 3H), 3.10 (s, 4H), 2.93 (d, J = 11.5 Hz, 2H), 2.64 (br. s, 4H), 2.44 – 2.35 (m, 2H), 2.33 – 2.24 (m, 2H), 2.06 (td, J = 12.2, 2.5 Hz, 2H), 1.92 (q, J = 7.5 Hz, 2H), 1.78 (d, J = 11.9 Hz, 2H), 1.57 – 1.46 (m, 2H, partially overlapped), 1.48 – 1.35 (m, 4H, partially overlapped), 1.36 – 1.24 (m, 4H, partially overlapped),

1.01 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.6, 152.3, 141.4, 138.9, 130.5, 129.3, 128.3, 122.9, 121.1, 118.3, 111.2, 58.8, 58.7, 55.4, 53.5, 53.3, 52.3, 50.6, 30.6, 28.6, 27.7, 27.6, 27.1, 26.8, 9.7 ppm. HRMS-Heated ESI-Orbitrap: calcd. for $C_{31}H_{46}N_4O_2$ $[M+H]^+$ 507.36935; found 507.36902.

*N-(1-(6-(4-(2,3-Dichlorophenyl)piperazin-1-yl)hexyl)piperidin-4-yl)-N-phenylpropionamide, **(1j)**.* Yield: 0.24 g (88.5 %); pale yellow oil. IR (ATR): 3060, 2932, 2817, 1656, 1578, 1449, 13 7 5, 1260, 1138, 783, 743, 708 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ =7.41 – 7.31 (m, 3H), 7.15 – 7.08 (m, 2H), 7.06 (d, J = 7.0 Hz, 2H), 6.98 – 6.90 (m, 1H), 4.65 (ddd, J = 12.2, 8.6, 3.9 Hz, 1H), 3.04 (br. s, 4H), 2.90 (d, J = 11.5 Hz, 2H), 2.59 (br. s, 4H), 2.39 – 2.33 (m, 2H), 2.30 – 2.19 (m, 2H), 2.03 (t, J = 11.4 Hz, 2H), 1.91 (q, J = 7.4 Hz, 2H), 1.76 (d, J = 11.8 Hz, 2H), 1.59 – 1.33 (m, 6H, partially overlapped), 1.32 – 1.20 (m, 4H, partially overlapped), 1.00 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.6, 151.4, 139.0, 134.1, 130.5, 129.3, 128.3, 127.5, 124.6, 118.7, 58.8, 53.4, 53.3, 52.4, 51.4, 30.7, 28.6, 27.7, 27.6, 27.2, 26.9, 9.7 ppm. HRMS-Heated ESI-Orbitrap: calcd. for $C_{30}H_{42}Cl_2N_4O$ $[M+H]^+$ 545.28084; found 545.28083.

*N-Phenyl-N-(1-(7-(4-phenylpiperazin-1-yl)heptyl)piperidin-4-yl)propionamide, **(1k)**.* Yield: 0.24 g (95 %); pale yellow oil. Yield: 0.22 g (83 %); pale yellow oil. IR (ATR): 3058, 2932, 2812, 1655, 1598, 1378, 1262, 1094, 805, 758, 703 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42 – 7.32 (m, 3H), 7.26 (t, J = 7.7 Hz, 2H), 7.08 (d, J = 7.2 Hz, 2H), 6.93 (d, J = 8.2 Hz, 2H), 6.85 (t, J = 7.2 Hz, 1H), 4.67 (tt, J = 12.3, 4.0 Hz, 1H), 3.27 – 3.15 (m, 4H), 2.97 (d, J = 10.9 Hz, 2H), 2.69 – 2.53 (m, 4H), 2.41 – 2.34 (m, 2H), 2.35 – 2.27 (m, 2H), 2.11 (t, J = 11.4 Hz, 2H), 1.93 (q, J = 7.4 Hz, 2H), 1.79 (d, J = 11.8 Hz, 2H), 1.57 – 1.40 (m, 6H), 1.34 – 1.22 (m, 6H), 1.02 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.6, 151.4, 138.9, 130.4, 129.4, 129.1, 128.4, 119.7, 116.1, 58.8, 58.6, 53.3, 53.2, 52.2, 49.1, 30.4, 29.5, 28.6, 27.6, 27.5, 26.9, 26.8, 9.7 ppm. HRMS-Heated ESI-Orbitrap: calcd. for $C_{31}H_{46}N_4O$ $[M+H]^+$ 491.37444; found 491.37464.

*N-(1-(7-(4-(2-Methoxyphenyl)piperazin-1-yl)heptyl)piperidin-4-yl)-N-phenylpropionamide, **(1l)**.* Yield: 0.24 g (91.2 %); pale yellow oil. IR (ATR): 3059, 2810, 1659, 1595, 1499, 1453, 1242, 1028, 807, 748, 707 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42 – 7.31 (m, 3H), 7.07 (d, J = 6.9 Hz, 2H), 7.03 – 6.95 (m, 1H, partially overlapped), 6.97 – 6.87 (m, 2H, partially overlapped), 6.85 (d, J = 8.0 Hz, 1H), 4.66 (tt, J = 12.2, 4.0 Hz, 1H), 3.85 (s, 3H), 3.10 (br. s, 4H), 2.93 (d, J = 12.0 Hz, 2H), 2.65 (br. s, 4H), 2.43 – 2.34 (m, 2H), 2.30 – 2.21 (m, 2H), 2.06 (td, J = 12.1, 2.3 Hz, 2H), 1.92 (q, J = 7.4 Hz, 2H), 1.77 (d, J = 12.3 Hz, 2H), 1.56 – 1.47 (m, 2H), 1.47 – 1.36 (m, 4H), 1.32 – 1.21 (m, 6H), 1.01 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): = δ 173.6, 152.4, 141.4, 138.9, 130.5, 129.3, 128.3, 123.0, 121.1, 118.3, 111.3, 58.9, 58.7, 55.4, 53.5, 53.2, 52.3, 50.6, 30.5, 29.5, 28.6, 27.6, 27.6, 27.1, 26.8, 9.7 ppm. HRMS-Heated ESI-Orbitrap: calcd. for $C_{32}H_{48}N_4O_2$ $[M+H]^+$ 521.38500; found 521.38566.

*N-(1-(7-(4-(2,3-Dichlorophenyl)piperazin-1-yl)heptyl)piperidin-4-yl)-N-phenylpropionamide, **(1m)**.* Yield: 0.26 g (93 %); pale yellow oil. IR (ATR): 3061, 2933, 2811, 1658, 1658, 1578, 1450, 1375, 1260, 1142, 783, 743, 708 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.43 – 7.33 (m, 3H), 7.18 – 7.12 (m, 2H), 7.07 (d, J = 7.3 Hz, 2H), 6.96 (dd, J = 6.7, 2.8 Hz, 1H), 4.76 – 4.54 (m, 1H), 3.07 (br. s, 4H), 2.93 (d, J = 11.5 Hz, 2H), 2.63 (br. s, 4H), 2.47 – 2.34 (m, 2H), 2.32 – 2.22 (m, 2H), 2.06 (t, J = 11.4 Hz, 2H), 1.92 (q, J = 7.4 Hz, 2H), 1.77 (d, J = 12.0 Hz, 2H), 1.62 – 1.46 (m, 2H,

partially overlaped), 1.49 – 1.34 (m, 4H, partially overlapped), 1.34 – 1.20 (m, 6H, partially overlapped), 1.01 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.6, 151.4, 139.0, 134.1, 130.5, 129.4, 128.3, 127.5, 124.6, 118.7, 58.8, 58.8, 53.4, 53.3, 52.3, 51.4, 30.6, 29.6, 28.6, 27.7, 27.6, 27.1, 26.9, 9.7 ppm. HRMS-Heated ESI-Orbitrap: calcd. for $C_{31}H_{44}Cl_2N_4O$ $[M+H]^+$ 559.29649; found 559.29701.