

SUPPLEMENTARY MATERIAL TO

**Synthesis of novel {[4-(2-methoxyphenyl)piperazin-1-yl]alkyl}-1H-benzo[d]imidazoles
and assessment of their interactions with the D2 dopamine receptor**

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ANALYTICAL AND SPECTRAL DATA FOR THE SYNTHESIZED COMPOUNDS

Methyl 2-[4-(2-methoxyphenyl)piperazin-1-yl]acetate (3a):

Yield: 95.3 %; orange crystals m.p. 50 °C; IR (ATR, cm⁻¹): 2820.2, 1724.3, 1500.9, 1451.7,
1241.4, 1027.1, 751.3; ¹H-NMR (200 MHz, CDCl₃) δ: 2.75-2.80 (m, 4H, piperazine), 3.12-3.17
(m, 4H, piperazine), 3.29 (s, 2H, CH₂), 3.74 (s, 3H, -COCH₃), 3.85 (s, 3H, OCH₃), 6.84-7.01 (m,
4H, ArH); ¹³C-NMR (50 MHz, CDCl₃) δ: 50.22, 51.56, 53.20, 55.16, 59.43, 111.01, 118.11,
120.86, 122.86, 141.03, 152.10, 170.64; MS: m/z [M+H]⁺ calculated for C₁₄H₂₀N₂O₃ 265.15467,
found 265.15493.

Ethyl 3-[4-(2-methoxyphenyl)piperazin-1-yl]propanoate (3b):

Yield: 84.2 %; oil; IR (ATR, cm⁻¹): 2818.6, 1734.0, 1501.0, 1452.7, 1241.3, 1026.5, 749.6; ¹H-
NMR (200 MHz, CDCl₃) δ: 1.28 (t, 3H, J=7.4 Hz, CH₃), 2.51-2.59 (m, 2H, CH₂), 2.66-2.71 (m,
4H, piperazine), 2.75-2.83 (m, 2H, CH₂), 3.08-3.10 (m, 4H, piperazine), 3.86 (s, 3H, OCH₃), 4.16

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(q, J=7.4 Hz, J=11.4 Hz, 2H, COCH₂), 6.84-7.03 (m, 4H, ArH); ¹³C-NMR (50 MHz, CDCl₃) δ: 14.04, 32.13, 50.39, 52.94, 53.45, 55.13, 60.17, 110.99, 118.00, 120.80, 122.73, 141.12, 152.08, 172.35; MS: m/z [M+H]⁺ calculated for C₁₆H₂₄N₂O₃, 293.18597, found 293.18584.

Ethyl 4-[4-(2-methoxyphenyl)piperazin-1-yl]butanoate (3c):

Yield: 86.6 %; oil; IR (ATR, cm⁻¹): 2817.0, 1732.8, 1501.1, 1452.5, 1241.3, 1028.1, 750.6; ¹H-NMR (200 MHz, CDCl₃) δ: 1.26 (t, 3H, J= 7.4 Hz, CH₃), 1.78-1.93 (m, 2H, CH₂), 2.33-2.47 (m, 4H, CH₂), 2.63-2.66 (m, 4H, piperazine), 3.09 (s, 4H, piperazine), 3.86 (s, 3H, OCH₃), 4.13 (q, 2H, J= 6.6 Hz, J= 7.4 Hz, COCH₂), 6.83-7.04 (m, 4H, ArH); ¹³C-NMR (50 MHz, CDCl₃) δ: 14.11, 22.03, 32.19, 50.52, 53.23, 55.18, 57.64, 60.12, 111.01, 118.03, 120.84, 122.73, 141.25, 152.16, 173.49; MS: m/z [M+H]⁺ calculated for C₁₇H₂₆N₂O₃ 307.20162, found 307.20152.

Methyl 5-[4-(2-methoxyphenyl)piperazin-1-yl]pentanoate (3d):

Yield: 69.0 %; oil; IR (ATR, cm⁻¹): 2818.4, 1737.6, 1500.9, 1450.9, 1241.1, 1027.2, 751.1; ¹H-NMR (200 MHz, CDCl₃) δ: 1.67-1.71 (m, 4H, CH₂), 2.35-2.38 (m, 2H, CH₂), 2.51-2.54 (m, 2H, CH₂), 2.76 (s, 4H, piperazine), 3.17 (s, 4H, piperazine), 3.67 (s, 3H, CH₃), 3.86 (m, 3H, OCH₃), 6.85-7.02 (m, 4H, ArH); ¹³C-NMR (50 MHz, CDCl₃) δ: 22.41, 25.80, 33.35, 50.10, 50.90, 52.93, 54.78, 57.70, 110.64, 117.63, 120.47, 122.33, 140.85, 151.75, 173.40; MS: m/z [M+H]⁺ calculated for C₁₇H₂₆N₂O₃ 307.20162, found 307.20075.

Ethyl 6-[4-(2-methoxyphenyl)piperazin-1-yl]hexanoate (3e):

Yield: 91.0%; oil; IR (ATR, cm⁻¹): 2814.2, 1734.5, 1501.2, 1452.5, 1240.9, 1029.8, 748.0; ¹H-NMR (200 MHz, CDCl₃) δ: 1.22 (t, 3H, J=7.4 Hz, CH₃), 1.29-1.39 (m, 2H, CH₂), 1.45-1.71 (m, 4H, CH₂), 2.24-2.41 (m, 4H, CH₂), 2.61 (s, 4H, piperazine), 3.07 (s, 4H, piperazine), 3.82 (s, 3H, OCH₃), 4.09 (q, 2H, J=6 Hz, J= 8 Hz, COCH₂), 6.80-7.00 (m, 4H, ArH); ¹³C-NMR (50 MHz, CDCl₃) δ: 14.07, 24.72, 26.42, 26.96, 34.08, 50.47, 53.33, 55.13, 58.42, 60.01, 110.95, 118.00, 120.80, 122.70, 141.23, 152.10, 173.59; MS: m/z [M+H]⁺ calculated for C₁₉H₃₀N₂O₃ 335.23292, found 335.23342.

54

55 *Ethyl 7-[4-(2-methoxyphenyl)piperazin-1-yl]heptanoate (3f):*

56 Yield: 92.2%; oil; IR (ATR, cm^{-1}): 2818.4, 1734.5, 1501.4, 1450.3, 1240.1, 1028.6, 750.3; ^1H -
57 NMR (200 MHz, CDCl_3) δ : 1.20 (t, 3H, $J=7.4$ Hz, CH_3), 1.28-1.34 (m, 4H, CH_2), 1.46-1.63 (m,
58 4H, CH_2), 2.21-2.35 (m, 4H, CH_2), 2.60 (s, 4H, piperazine), 3.06 (s, 4H, piperazine), 3.80 (s, 3H,
59 OCH_3), 4.07 (q, 2H, $J=7.2$ Hz, $J=7.4$ Hz, COCH_2), 6.78-6.99 (m, 4H, ArH); ^{13}C -NMR (50 MHz,
60 CDCl_3) δ : 14.02, 24.65, 26.52, 27.03, 28.82, 34.03, 50.43, 53.29, 55.07, 58.53, 59.90, 110.90,
61 117.94, 120.75, 122.62, 141.19, 152.05, 173.55; MS: m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{20}\text{H}_{32}\text{N}_2\text{O}_3$
62 349.24857, found 349.24825.

63

64 *Methyl 8-(4-(2-methoxyphenyl)piperazin-1-yl)octanoate (3g):*

65 Yield: 82.8 %; oil; IR (ATR, cm^{-1}): 2828.2, 1754.6, 1521.4, 1448.8, 1236.3, 1025.6, 755.4; ^1H -
66 NMR (200 MHz, CDCl_3) δ : 1.26-1.32 (m, 6H, CH_2), 1.53-1.66 (m, 4H, CH_2), 2.27-2.43 (m, 4H,
67 CH_2), 2.65-2.67 (m, 4H, piperazine), 3.11 (s, 4H, piperazine), 3.67 (s, OCH_3), 3.86 (s, 3H, OCH_3),
68 6.84-7.04 (m, 4H, ArH); ^{13}C NMR (50 MHz, CDCl_3) δ : 24.79, 26.74, 27.34, 29.09, 33.97, 50.56 ,
69 51.33, 53.43, 55.25, 58.76, 111.06, 118.12, 120.91, 122.79, 141.33, 152.22, 174.24; MS: m/z
70 $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{20}\text{H}_{32}\text{N}_2\text{O}_3$ 349.24857, found 349.24849.

71

72 *2-([4-(2-methoxyphenyl)piperazin-1-yl]methyl)-1H-benzo[d]imidazole (5a):*

73 Yield: 16 %; oil; IR (ATR, cm^{-1}): 2817.2, 1502.0, 1455.7, 1240.3, 1026.5, 743.0; ^1H NMR (200
74 MHz, CDCl_3) δ : 2.75-2.80 (m, 4H, piperazine), 3.08-3.13 (m, 4H, piperazine), 3.84 (s, 3H, OCH_3),
75 3.91 (s, 2H, CH_2), 6.84-7.06 (m, 4H, ArH), 7.20-7.27 (m, 2H, ArH), 7.57-7.60 (m, 2H, ArH); ^{13}C
76 NMR (50 MHz, CDCl_3) δ : 50.41 , 53.64, 55.31, 56.46, 111.23, 118.14, 120.93, 122.02, 122.40,
77 123.11, 140.90, 151.90, 152.23; MS: m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{19}\text{H}_{22}\text{N}_4\text{O}$ 323.18664, found
78 323.18515.

79

80 *2-{2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl}-1H-benzo[d]imidazole (5b):*

Yield: 36.5 %; oil; IR (ATR, cm^{-1}): 2818.4, 1500.6, 1456.7, 1240.0, 1026.3, 745.2; ^1H NMR (200 MHz, CDCl_3) δ : 2.77-2.92 (m, 6H, 4H piperazine and CH_2), 3.11-3.18 (m, 6H, 4H piperazine and CH_2) 3.87 (s, 3H, OCH_3), 6.87-7.04 (m, 4H, ArH), 7.17-7.25 (m, 2H, ArH), 7.52-7.57 (m, 2H, ArH); ^{13}C NMR (50 MHz, CDCl_3) δ : 25.03, 50.76, 52.94, 55.33, 58.06, 111.23, 114.67, 118.13, 120.95, 122.02, 123.24, 140.78, 152.21, 154.52; MS: m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{20}\text{H}_{24}\text{N}_4\text{O}$ 337.20229, found 337.20205.

2-{3-[4-(2-methoxyphenyl)piperazin-1-yl]propyl}-1H-benzo[d]imidazole (5c):

Yield: 55.7 %; oil; IR (ATR, cm^{-1}): 2825.5, 1500.7, 1452.9, 1241.4, 1026.5, 746.5; ^1H NMR (200, MHz, CDCl_3) δ : 1.96-2.08 (m, 2H, CH_2), 2.64 (t, 2H, $J=5.6$ Hz, CH_2), 2.72 (s, 4H, piperazine), 3.06-3.16 (m, 6H, 4H piperazine and CH_2), 3.85 (s, 3H, OCH_3), 6.86-7.05 (m, 4H, ArH), 7.16-7.18 (m, 2H, ArH), 7.52-7.57 (m, 2H, ArH); ^{13}C NMR (50 MHz, CDCl_3) δ : 23.61, 28.90, 50.49, 53.25, 55.24, 58.72, 111.18, 114.46, 118.03, 120.98, 121.66, 123.18, 140.77, 152.18, 155.58; MS: m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{21}\text{H}_{26}\text{N}_4\text{O}$ 351.21794, found 351.21682.

2-{4-[4-(2-methoxyphenyl)piperazin-1-yl]butyl}-1H-benzo[d]imidazole (5d):

Yield: 90.6 %; oil; IR (ATR, cm^{-1}): 2818.3, 1499.7, 1456.0, 1244.1, 1028.9, 793.3; ^1H NMR (200 MHz, CDCl_3) δ : 1.55-1.70 (m, 2H, CH_2), 1.83-1.94 (m, 2H, CH_2), 2.43 (t, 2H, $J=6.8$ Hz, CH_2), 2.64 (s, 4H, piperazine), 2.98 (t, 2H, $J=6.8$ Hz, CH_2), 3.12 (s, 4H, piperazine), 3.84 (s, 3H, OCH_3), 6.84-7.05 (m, 4H, ArH), 7.14-7.21 (m, 2H, ArH), 7.51-7.56 (m, 2H, ArH); ^{13}C NMR (50 MHz, CDCl_3) δ : 25.38, 25.81, 28.45, 50.34, 53.18, 55.24, 57.24, 111.19, 114.52, 118.16, 120.98, 121.88, 123.08, 138.57, 140.94, 152.19, 155.38; MS: m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{22}\text{H}_{28}\text{N}_4\text{O}$ 365.23359, found 365.23263.

2-{5-[4-(2-methoxyphenyl)piperazin-1-yl]pentyl}-1H-benzo[d]imidazole (5e):

Yield: 43.0 %; brown crystals m.p. 63°C ; IR (ATR, cm^{-1}): 2825.2, 1500.3, 1454.9, 1240.7, 1023.6, 752.8; ^1H NMR (200 MHz, CDCl_3) δ : 1.33-1.48 (m, 2H, CH_2), 1.60-1.75 (m, 2H, CH_2), 1.80-1.93 (m, 2H, CH_2), 2.54-2.62 (m, 2H, CH_2), 2.84-2.95 (m, 6H, CH_2 and 4H piperazine), 3.17-3.19 (m, 4H, piperazine), 3.86 (s, 3H, OCH_3), 6.85-7.06 (m, 4H, ArH), 7.19-7.22 (m, 2H, ArH),

7.54-7.58 (m, 2H, ArH); ^{13}C NMR (50 MHz, CDCl_3) δ : 25.54, 26.62, 27.82, 28.84, 49.94, 53.00, 55.20, 57.97, 111.15, 114.50, 118.18, 120.95, 121.88, 123.10, 138.52, 140.78, 152.12, 155.31; MS: m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{23}\text{H}_{30}\text{N}_4\text{O}$ 379.24924, found 379.24889.

2-{6-[4-(2-methoxyphenyl)piperazin-1-yl]hexyl}-1H-benzo[d]imidazole (5f):

Yield: 69.0 %; brown crystals m.p. 134 °C; IR (ATR, cm^{-1}): 2828.5, 1503.0; 1454.6, 1240.6, 1019.5, 750; ^1H NMR (200 MHz, CDCl_3) δ : 1.26-1.58 (m, 6H, CH_2), 1.76-1.92 (m, 2H, CH_2), 2.37 (t, 2H, $J=7.4$ Hz, CH_2), 2.61-2.65 (m, 4H, piperazine), 2.90 (t, 2H, $J=8$ Hz, CH_2), 3.11 (s, 4H, piperazine), 3.85 (s, 3H, OCH_3), 6.84-7.04 (m, 4H, ArH), 7.18-7.27 (m, 2H, ArH), 7.51-7.58 (m, 2H, ArH); ^{13}C NMR (50 MHz, CDCl_3) δ : 26.12, 26.94, 28.00, 28.96, 29.13, 50.29, 53.20, 55.22, 58.37, 111.13, 114.54, 118.18, 121.97, 121.89, 123.02, 138.55, 141.01, 152.17, 155.38; MS: m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{24}\text{H}_{32}\text{N}_4\text{O}$ 393.26489, found 393.26320.

2-{7-[4-(2-methoxyphenyl)piperazin-1-yl]heptyl}-1H-benzo[d]imidazole (5g):

Yield: 72.0 %; oil; IR (ATR, cm^{-1}): 2962.9, 1497.9, 1449.6, 1261.7, 1026.4, 744.5; ^1H NMR (200 MHz, CDCl_3) δ : 1.26-1.49 (m, 8H, CH_2), 1.79-1.86 (m, 2H, CH_2), 2.38 (t, 2H, $J=7.4$ Hz, CH_2), 2.68 (s, 4H, piperazine), 2.89 (t, 2H, $J=8$ Hz, CH_2), 3.13 (s, 4H, piperazine), 3.85 (s, 3H, OCH_3), 6.84-6.94 (m, 4H, ArH), 7.19-7.24 (m, 2H, ArH), 7.52-7.56 (m, 2H, ArH); ^{13}C NMR (50 MHz, CDCl_3) δ : 26.45, 27.21, 28.11, 29.05, 29.29, 50.40, 53.35, 55.28, 58.65, 111.13, 114.64, 118.22, 120.98, 121.99, 123.01, 138.47, 141.11, 152.22, 155.26; MS: m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{25}\text{H}_{34}\text{N}_4\text{O}$ 407.28054, found 407.28007.

5-methoxy-2-{4-[4-(2-methoxyphenyl)piperazin-1-yl]butyl}-1H-benzo[d]imidazole (5h):

Yield: 88.0%; oil; IR (ATR, cm^{-1}): 2817.0, 1498.4, 1458.2, 1237.6, 1027, 751.2; ^1H NMR (200 MHz, CDCl_3) δ : 1.64-1.76 (m, 2H, CH_2), 1.84-1.98 (m, 2H, CH_2), 2.49 (t, 2H, $J=7.4$ Hz, CH_2), 2.70 (s, 4H, piperazine), 2.96 (t, 2H, $J=7.2$ Hz, CH_2), 3.16 (s, 4H, piperazine), 3.83 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 6.81-7.08 (m, 7H, ArH); ^{13}C NMR (50 MHz, CDCl_3) δ : 25.09, 25.87, 28.40, 50.54, 53.31, 55.33, 55.82, 57.09, 111.17, 118.18, 121.02, 123.17, 141.03, 152.26, 155.98; MS: m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{23}\text{H}_{30}\text{N}_4\text{O}_2$ 395.24415, found 395.24331.

139

140 *5-methoxy-2-{5-[4-(2-methoxyphenyl)piperazin-1-yl]pentyl}-1H-benzo[d]imidazole (5i):*

141 Yield: 73.0%; oil; IR (ATR, cm^{-1}): 2832.2, 1500.2, 1455.8, 1242.6, 1027.7, 752.9; ^1H NMR
142 (200 MHz, CDCl_3) δ : 1.38-1.45 (m, 2H, CH_2), 1.71-1.90 (m, 4H, CH_2), 2.77-2.94 (m, 4H, CH_2),
143 3.09 (s, 4H, piperazine), 3.28 (s, 4H, piperazine), 3.83 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 6.82-
144 6.92 (m, 4H, ArH), 7.02-7.08 (m, 2H, ArH), 7.46 (d, 2H, $J=8\text{Hz}$, ArH); ^{13}C NMR (50 MHz, CDCl_3)
145 δ : 22.59, 22.97, 25.21, 27.00, 48.25, 52.18, 55.38, 55.80, 56.82, 97.42, 111.26, 111.63, 115.19,
146 118.51, 121.09, 123.92, 138.19, 139.72, 152.10, 154.72, 156.18; MS: m/z $[\text{M}+\text{H}]^+$ calculated for
147 $\text{C}_{24}\text{H}_{32}\text{N}_4\text{O}_2$ 409.25980, found 409.26000.

148

149 *5-methoxy-2-{6-[4-(2-methoxyphenyl)piperazin-1-yl]hexyl}-1H-benzo[d]imidazole (5j):*

150 Yield: 67.1%; oil; IR (ATR, cm^{-1}): 2856.0, 1501.3, 1457.2, 1247.5, 1026.2, 753.3; ^1H NMR
151 (200 MHz, CDCl_3) δ : 1.35-1.55 (m, 4H, CH_2), 1.63-1.88 (m, 2H, CH_2), 2.41 (t, 2H, $J=8\text{ Hz}$, CH_2),
152 2.67-2.72 (m, 4H, piperazine), 2.85 (t, 2H, $J=7.4\text{ Hz}$, CH_2), 3.10-3.15 (m, 4H, piperazine), 3.79 (s,
153 3H, OCH_3), 3.85 (s, 3H, OCH_3), 4.21-4.24 (m, 2H, CH_2), 6.81-7.03 (m, 4H, ArH), 7.38-7.43 (m,
154 1H, ArH), 7.50-7.55 (m, 1H, ArH), 7.67-7.74 (m, 1H, ArH); ^{13}C NMR (50 MHz, CDCl_3) δ : 22.85,
155 23.59, 25.83, 26.78, 27.82, 50.05, 53.11, 55.24, 55.71, 58.22, 97.59, 111.12, 115.16, 118.18,
156 120.95, 123.10, 130.85, 140.87, 152.14, 154.98, 155.91; MS: m/z $[\text{M}+\text{H}]^+$ calculated for
157 $\text{C}_{25}\text{H}_{34}\text{N}_4\text{O}_2$ 423.27545, found 423.27570.

158

159 *5-methoxy-2-(7-(4-(2-methoxyphenyl)piperazin-1-yl)heptyl)-1H-benzo[d]imidazole (5k):*

160 Yield: 62.3%; oil; IR (ATR, cm^{-1}): 2927.7, 1501.3, 1499.0, 1453.5, 1240.3, 1026.6, 748.2; ^1H
161 NMR (200 MHz, CDCl_3) δ : 1.58 (s, 6H, CH_2), 2.16-2.23 (m, 2H, CH_2), 2.53 (s, 2H, CH_2), 2.85
162 (s, 6H, 4H piperazine and CH_2), 3.15 (s, 6H, 4H piperazine and CH_2), 3.81 (s, 3H, OCH_3), 3.85 (s,
163 3H, OCH_3), 6.84-7.01 (m 7H, ArH); ^{13}C NMR (50 MHz, CDCl_3) δ : 25.57, 27.13, 29.13, 49.53,
164 52.60, 55.31, 55.77, 57.9, 97.67, 111.11, 118.29, 120.99, 123.20, 140.74, 152.14, 154.93, 155.96;
165 MS: m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{26}\text{H}_{36}\text{N}_4\text{O}_2$ 437.29110, found 437.29115.

166

5-chloro-2-{4-[4-(2-methoxyphenyl)piperazin-1-yl]butyl}-1H-benzo[d]imidazole (5l):

Yield: 88,4%; oil; IR (ATR, cm^{-1}): 2811.0, 1501.1, 1447.5, 1239.6, 1027.4, 751.2; ^1H NMR (200 MHz, CDCl_3) δ : 1.59-1.69 (m, 2H, CH_2), 1.82-1.96 (m, 2H, CH_2), 2.39 (t, 2H, $J=7.2$ Hz, CH_2), 2.65 (s, 4H, piperazine), 2.96 (t, 2H, $J=6.6$ Hz, CH_2), 3.12 (s, 4H, piperazine), 3.84 (s, 3H, OCH_3), 6.84-7.02 (m, 4H, ArH), 7.12-7.17 (m, 1H, ArH), 7.39-7.50 (m, 2H, ArH); ^{13}C -NMR (50 MHz, CDCl_3) δ : 25.18, 25.83, 28.45, 50.38, 53.18, 55.24, 57.11, 111.12, 114.48, 115.19, 118.16, 120.97, 122.39, 123.17, 127.43, 140.79, 152.16, 156.67; MS: m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{22}\text{H}_{27}\text{ClN}_4\text{O}$ 399.19462, found 399.19367.

5-chloro-2-{5-[4-(2-methoxyphenyl)piperazin-1-yl]pentyl}-1H-benzo[d]imidazole (5m):

Yield: 65%; oil; IR (ATR, cm^{-1}): 2824.8, 1500.7, 1450.7, 1241.2, 1027.0, 749.9; ^1H NMR (200 MHz, CDCl_3) δ : 1.35-1.62 (m, 4H, CH_2), 1.77-1.91 (m, 2H, CH_2), 2.39 (t, 2H, $J=8$ Hz, CH_2), 2.64 (s, 4H, piperazine), 2.89 (t, 2H, $J=8$ Hz, CH_2), 3.11 (s, 4H, piperazine), 3.85 (s, 3H, OCH_3), 6.84-7.06 (m, 4H, ArH), 7.13-7.18 (m, 1H, ArH), 7.40-7.50 (m, 2H, ArH); ^{13}C NMR (50 MHz, CDCl_3) δ : 25.96, 26.63, 27.67, 28.98, 50.38, 53.33, 55.27, 58.22, 111.15, 118.20, 121.00, 122.50, 123.13, 127.58, 140.96, 152.19, 156.32; MS: m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{23}\text{H}_{29}\text{ClN}_4\text{O}$ 413.21027, found 413.20891.

5-chloro-2-{6-[4-(2-methoxyphenyl)piperazin-1-yl]hexyl}-1H-benzo[d]imidazole (5n):

Yield: 74%; oil; IR (ATR, cm^{-1}): 2825.8, 1500.6, 1451.2, 1241.8, 1027.6, 750.4; ^1H NMR (200 MHz, CDCl_3) δ : 1.30-1.46 (m, 6H, CH_2), 1.72-1.83 (m, 2H, CH_2), 2.34 (t, 2H, $J=8.6$ Hz, CH_2), 2.63 (s, 4H, piperazine), 2.86 (t, 2H, $J=7.4$ Hz, CH_2), 3.09 (s, 4H, piperazine), 3.84 (s, 3H, OCH_3), 6.84-7.06 (m, 4H, ArH), 7.12-7.18 (m, 1H, ArH), 7.38-7.48 (m, 2H, ArH); ^{13}C NMR (50 MHz, CDCl_3) δ : 26.27, 26.96, 27.91, 28.89, 29.09, 50.45, 53.27, 55.22, 58.42, 111.10, 118.16, 120.97, 122.46, 123.08, 127.52, 140.98, 152.14, 156.51; MS: m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{24}\text{H}_{31}\text{ClN}_4\text{O}$ 427.22592, found 427.22408.

SUMMARY RESULTS OF MD SIMULATIONS

Table 1. D2DR-ligand key interactions observed in 100 ns MD simulations.

Residue	Leu 94	Trp 100	Asp 114	Cys 118	Ile 184	Phe 382	Trp 386	Phe 389	Phe 390	Tyr 408	Thr 412	Tyr 416
Ligand												
5e		54	81	68	27		76	65	42	65	37	
5f	21	31	79	36	40		82	74	20	33	42	
5h		67	81	58			84	85	24	36		
5i	50	89	80	75			96	84	42	22	30	
5j	36	94	82	73	24	32	98	53	31	25		
5l		22	82	64	26		95	75	34	37		
5m		75	84	69			78	50	49	63	40	
5n	32	42	80	32			82	68	35	28		32

D2DR-ligand interactions presented in more than 20% of MS simulation time are shown. Numbers provided in the table refers to the percentage of the total simulation time one interaction observed to occur. Interacting residues in OBS are shaded in grey colour; residues found in EBP are white.