*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**

JELENA Z. PENJIŠEVIĆa, DEANA B. ANDRIĆb, VLADIMIR B. ŠUKALOVIĆa, GORAN M. ROGLIĆb, VUKIĆ ŠOŠKIĆc and SLAĐANA V. KOSTIĆ-RAJAČIĆa[[1]](#footnote-1)\*

*a ICTM-Department of Chemistry, University of Belgrade, Njegoševa 12 11000 Belgrade, Serbia*

*b Faculty of Chemistry, University of Belgrade, Studentski trg 12-16, 11000 Belgrade, Serbia*

*c Orgentec GmbH, Carl-Zeiss-Str. 49, 55129 Mainz, Germany*

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, piprazine), 3.86 (s, 3H, OCH3), 4.16 (q, 2H, J=7.4 Hz, 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= 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 (s, 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= 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, found335.23342.

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

Yield: 92.2%; oil; IR (ATR, cm-1): 2818.4, 1734.5, 1501.4, 1450.3, 1240.1, 1028.6, 750.3; 1H-NMR (200 MHz, CDCl3) δ:1.20 (t, 3H, J=7.4 Hz, CH3), 1.28-1.34 (m, 4H, CH2), 1.46-1.63 (m, 4H, CH2), 2.21-2.35 (m, 4H, CH2), 2.60 (s, 4H, piperazine), 3.06 (s, 4H, piperazine), 3.80 (s, 3H, OCH3), 4.07 (q, 2H, J=7.4 Hz, COCH2), 6.78-6.99 (m, 4H, ArH);13C-NMR (50 MHz, CDCl3) 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, 117.94, 120.75, 122.62, 141.19, 152.05, 173.55; MS: m/z [M+H]+calculated for C20H32N2O3 349.24857, found 349.24825.

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

Yield: 82.8 %; oil; IR (ATR, cm-1): 2828.2, 1754.6, 1521.4, 1448.8, 1236.3, 1025.6, 755.4; 1H NMR (200 MHz, CDCl3) δ: 1.26-1.32 (m, 6H, CH2 ), 1.53-1.66 (m, 4H, CH2), 2.27-2.43 (m, 4H, CH2), 2.65-2.67 (m, 4H,piperazine), 3.11 (s, 4H, piperazine), 3.67 (s, OCH3), 3.86 (s, 3H, OCH3), 6.84-7.04 (m, 4H, ArH); 13C NMR (50 MHz, CDCl3) δ: 24.79, 26.74, 27.34, 29.09, 33.97, 50.56 , 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 [M+H]+ calculated for C20H32N2O3 349.24857, found 349.24849.

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

Yield: 16 %; oil; IR (ATR, cm-1): 2817.2, 1502.0, 1455.7, 1240.3, 1026.5, 743.0; 1H NMR (200 MHz, CDCl3) δ:2.75-2.80 (m, 4H, piperazine), 3.08-3.13 (m, 4H, piperazine), 3.84 (s, 3H, OCH3), 3.91 (s, 2H, CH2), 6.84-7.06 (m, 4H, ArH), 7.20-7.27 (m, 2H, ArH), 7.57-7.60 (m, 2H, ArH); 13C NMR (50 MHz, CDCl3) δ:50.41 , 53.64, 55.31, 56.46, 111.23, 118.14, 120.93, 122.02, 122.40, 123.11, 140.90, 151.90, 152.23; MS: m/z [M+H]+ calculated for C19H22N4O 323.18664, found 323.18515.

*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, CDCl3) δ:2.77-2.92 (m, 6H, 4H piperazine and CH2), 3.11-3.18 (m, 6H, 4H piperazine and CH2) 3.87 (s, 3H, OCH3), 6.87-7.04 (m, 4H, ArH), 7.17-7.25 (m, 2H, ArH), 7.52‑7.57 (m, 2H,ArH);13C NMR (50 MHz, CDCl3) 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 [M+H]+ calculated for C20H24N4O 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, CDCl3) δ:1.96-2.08 (m, 2H, CH2), 2.64 (t, 2H, J=5.6 Hz, CH2), 2.72 (s, 4H, piperazine), 3.06-3.16 (m, 6H, 4H piperazine and CH2), 3.85 (s, 3H, OCH3), 6.86-7.05 (m, 4H, ArH), 7.16-7.18 (m, 2H, ArH), 7.52-7.57 (m, 2H, ArH); 13C NMR (50 MHz, CDCl3) 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 [M+H]+ calculated for C21H26N4O 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, CDCl3) δ: 1.55-1.70 (m, 2H,CH2), 1.83-1.94 (m, 2H,CH2), 2.43 (t, 2H, J=6.8 Hz, CH2), 2.64 (s, 4H, piperazine), 2.98 (t, 2H, J=6.8 Hz, CH2), 3.12(s, 4H,piperazine), 3.84 (s, 3H, OCH3), 6.84-7.05 (m, 4H, ArH), 7.14-7.21 (m, 2H,ArH), 7.51-7.56 (m, 2H, ArH); 13C NMR (50 MHz, CDCl3) 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 [M+H]+ calculated for C22H28N4O 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, CDCl3) δ:1.33-1.48(m, 2H,CH2), 1.60-1.75 (m, 2H, CH2), 1.80-1.93 (m, 2H, CH2), 2.54-2.62 (m, 2H, CH2), 2.84-2.95 (m, 6H, CH2 and 4H piperazine), 3.17-3.19 (m, 4H, piperazine), 3.86 (s, 3H, OCH3), 6.85-7.06 (m, 4H, ArH), 7.19‑7.22 (m, 2H, ArH), 7.54-7.58 (m, 2H, ArH);13C NMR (50 MHz, CDCl3) 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 [M+H]+ calculated for C23H30N4O 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, CDCl3) δ:1.26-1.58 (m, 6H, CH2), 1.76-1.92 (m, 2H, CH2), 2.37 (t, 2H, J=7.4 Hz, CH2), 2.61-2.65 (m, 4H,piperazine), 2.90 (t, 2H, J=8 Hz, CH2), 3.11 (s, 4H, piperazine), 3.85 (s, 3H, OCH3), 6.84-7.04 (m, 4H, ArH), 7.18-7.27 (m, 2H, ArH), 7.51-7.58 (m, 2H, ArH); 13C NMR (50 MHz, CDCl3) 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 [M+H]+ calculated for C24H32N4O 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, CDCl3) δ: 1.26-1.49 (m, 8H, CH2), 1.79-1.86 (m, 2H, CH2), 2.38 (t, 2H, J=7.4 Hz, CH2), 2.68 (s, 4H, piperazine), 2.89 (t, 2H, J=8 Hz, CH2), 3.13 (s, 4H, piperazine), 3.85 (s, 3H, OCH3), 6.84-6.94 (m, 4H, ArH), 7.19-7.24 (m, 2H, ArH), 7.52-7.56 (m, 2H, ArH); 13C NMR (50 MHz, CDCl3) 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 [M+H]+ calculated for C25H34N4O 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, CDCl3) δ: 1.64-1.76 (m, 2H, CH2), 1.84-1.98 (m, 2H, CH2), 2.49 (t, 2H , J=7.4 Hz, CH2), 2.70 (s, 4H, piperazine), 2.96 (t, 2H, J=7.2 Hz, CH2), 3.16 (s, 4H, piperazine), 3.83 (s, 3H, OCH3,), 3.87 (s, 3H, OCH3), 6.81-7.08 (m, 7H, ArH); 13C NMR (50 MHz, CDCl3) 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 [M+H]+ calculated for C23H30 N4O2 395.24415, found 395.24331.

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

Yield: 73.0%; oil; IR (ATR, cm-1): 2832.2, 1500.2, 1455.8, 1242.6, 1027.7, 752.9; 1H NMR (200 MHz, CDCl3) δ**:** 1.38-1.45(m, 2H, CH2), 1.71-1.90 (m, 4H, CH2), 2.77-2.94 (m, 4H, CH2), 3.09 (s ,4H, piperazine), 3.28 (s, 4H,piperazine), 3.83 (s, 3H, OCH3), 3.87 (s, 3H, OCH3), 6.82-6.92 (m, 4H, ArH), 7.02-7.08 (m, 2H, ArH), 7.46 (d, 2H, J=8Hz, ArH); 13C NMR (50 MHz, CDCl3) 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, 118.51, 121.09, 123.92, 138.19, 139.72, 152.10, 154.72, 156.18; MS: m/z [M+H]+ calculated for C24H32N4O2  409.25980, found 409.26000.

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

Yield: 67.1%; oil; IR (ATR, cm-1): 2856.0, 1501.3, 1457.2, 1247.5, 1026.2, 753.3; 1H NMR (200 MHz, CDCl3) δ**:** 1.35-1.55(m, 4H,CH2), 1.63-1.88 (m, 2H,CH2), 2.41 (t,2H, J=8 Hz, CH2), 2.67-2.72 (m ,4H, piperazine), 2.85 (t, 2H, J=7.4 Hz, CH2), 3.10-3.15 (m, 4H, piperazine), 3.79 (s, 3H, OCH3), 3.85 (s, 3H, OCH3), 4.21-4.24 (m, 2H, CH2), 6.81-7.03 (m, 4H, ArH), 7.38-7.43 (m, 1H, ArH), 7.50‑7.55 (m, 1H, ArH), 7.67-7.74 (m, 1H, ArH); 13C NMR (50 MHz, CDCl3) δ: 22.85, 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, 120.95, 123.10, 130.85, 140.87, 152.14, 154.98, 155.91; MS: m/z [M+H]+ calculated for C25H34N4O2 423.27545, found 423.27570.

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

Yield: 62.3%; oil; IR (ATR, cm-1): 2927.7, 1501.3, 1499.0, 1453.5, 1240.3, 1026.6, 748.2; 1H NMR (200 MHz, CDCl3) δ: 1.58 (s, 6H, CH2), 2.16-2.23 (m, 2H, CH2), 2.53 (s, 2H, CH2), 2.85 (s, 6H, 4H piperazine and CH2), 3.15 (s, 6H, 4H piperazine and CH2), 3.81 (s, 3H, OCH3), 3.85 (s, 3H, OCH3), 6.84-7.01 (m 7H, ArH); 13C NMR (50 MHz, CDCl3) δ: 25.57, 27.13, 29.13, 49.53, 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; MS: m/z [M+H]+ calculated for C26H36N4O2 437.29110, found437.29115.

*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, CDCl3) δ: 1.59-1.69 (m, 2H, CH2), 1.82-1.96 (m, 2H,CH2), 2.39 (t, 2H, J=7.2 Hz, CH2), 2.65 (s, 4H, piperazine), 2.96 (t, 2H, J=6.6 Hz, CH2), 3.12 (s, 4H, piperazine), 3.84 (s, 3H, OCH3), 6.84-7.02 (m, 4H, ArH), 7.12-7.17 (m, 1H, ArH), 7.39-7.50 (m, 2H, ArH); 13C-NMR (50 MHz, CDCl3) 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 [M+H]+ calculated for C22H27ClN4O 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, CDCl3) δ:1.35-1.62(m, 4H, CH2), 1.77-1.91 (m, 2H, CH2), 2.39 (t, 2H, J=8 Hz, CH2), 2.64 (s, 4H, piperazine), 2.89 (t, 2H, J=8 Hz, CH2), 3.11 (s, 4H, piperazine), 3.85 (s, 3H, OCH3), 6.84-7.06 (m, 4H, ArH), 7.13-7.18 (m, 1H, ArH), 7.40‑7.50 (m, 2H, ArH); 13C NMR (50 MHz, CDCl3) 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 [M+H]+ calculated for C23H29ClN4O 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, CDCl3) δ:1.30-1.46 (m, 6H, CH2), 1.72-1.83 (m, 2H, CH2), 2.34 (t, 2H, J=8.6 Hz, CH2), 2.63 (s, 4H, piperazine), 2.86 (t, 2H, J=7.4 Hz, CH2), 3.09 (s, 4H, piperazine), 3.84 (s, 3H, OCH3), 6.84-7.06 (m, 4H, ArH), 7.12-7.18 (m, 1H, ArH), 7.38-7.48 (m, 2H, ArH); 13C NMR (50 MHz, CDCl3) 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 [M+H]+ calculated for C24H31ClN4O 427.22592, found 427.22408.

SUMMARY RESULTS OF MD SIMULATIONS

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

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 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.

1. \*Corresponding author. E-mail: srkostic@chem.bg.ac.rs [↑](#footnote-ref-1)