Supplementary Material file

Design, synthesis, and bioactivity investigation of novel benzimidazole derivatives as potent urease inhibitors

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Content:

1. General procedure for the synthesis of intermediates and target compounds besides spectroscopic analysis
2. Copies of 1H-NMR, 13C-NMR, and MS of all intermediates **(3a-k)** and the target compounds **(5a-k)**



|  |  |
| --- | --- |
| compound | X |
| 3a, 5a | N-Me |
| 3b, 5b | N-Et |
| 3c, 5c | N-Bu |
| 3d, 5d | N-Hx |
| 3e, 5e | O |
| 3f, 5f | N-Ph |
| 3g, 5g | N-4-Me-Ph |
| 3h, 5h | N-4-OMe-Ph |
| 3i, 5i | N-4-F-Ph |
| 3j, 5j | N-3,4-DiCl-Ph |
| 3k, 5k | N-2-OMe-Ph |

Chemistry

All Chemical reagents and solvents were supplied from Merck (Darmstadt, Germany) and used without further purification. Melting points were determined on a Kofler hot-stage instrument (Reichert, Vienna, Austria). The 1H-NMR spectra were obtained on a Bruker FT-400 or 700 MHz spectrometers (Bruker, Darmstadt, Germany) and CDCl3, MeOH-d4 or DMSO-d6 were used as a solvent. 13C-NMR spectra were also recorded at 100 or 176 MHz. The spin multiplicities were written as s (singlet), d (doublet), t (triplet), and m (multiplet) and the Coupling constant (J) values are given in Hertz (Hz). EI-Mass spectra were done on an Agilent 5975B instrument (Agilent Technologies, Santa Clara, CA, USA) with a triple-axis detector. Elemental analyses were determined using a Perkin Elmer Model 240-C instrument (PerkinElmer, Hopkinton, MA, USA).

General procedure for the synthesis of benzaldehyde derivatives (3a-k)

To a solution of 4-F-Benzaldehyde 1 (10 mmol) and appropriate piperazine derivatives 2 (11 mmol) in DMF (10 mL) as a solvent, K2CO3 as a base (22 mmol) was added and the reaction mixture was stirred at 140 ℃ overnight. After completion of the reaction, detected by TLC, the reaction mixture was cooled to RT and then mixed with 100 mL cooled water. The mixture was extracted with DCM (3 × 50 mL). Then the organic layers were mixed and dried over Na2SO4 and concentrated using a rotary evaporator. The crude material was purified with column chromatography to obtain the pure product (3a-k).

4-(4-methylpiperazin-1-yl)benzaldehyde (3a)

Yellow solid. Yield 84%. M.p. 55℃. 1H NMR (700 MHz, Chloroform-*d*) δ 9.79 (s, 1H), 7.76 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 3.44 (dd, *J* = 6.3, 4.0 Hz, 4H), 2.58 (t, *J* = 5.1 Hz, 4H), 2.38 (s, 3H). 13C NMR (176 MHz, Chloroform-*d*) δ 190.45, 154.95, 131.83, 127.13, 113.59, 54.58, 46.95, 45.99. EI-Mass (m/z): calc mass: 204.1, found: 204.2 [M]+. Elemental analysis: C12H16N2O, calculated: C, 70.56; H, 7.90; N, 13.71. found: C, 70.71; H, 7.93; N, 13.75.

4-(4-ethylpiperazin-1-yl)benzaldehyde (3b)

Dark orange liquid. Yield 70%.1H NMR (700 MHz, Chloroform-*d*) δ 9.73 (s, 1H), 7.62 – 7.36 (m, 2H), 6.97 – 6.63 (m, 2H), 3.37 (dq, *J* = 14.8, 4.9 Hz, 4H), 2.69 – 2.33 (m, 4H), 2.43 (dt, *J* = 11.3, 7.1 Hz, 2H), 1.35 – 1.00 (m, 3H). 13C NMR (176 MHz, Chloroform-*d*) δ 190.25, 154.93, 131.74, 126.90, 113.37, 52.26, 52.16, 46.88, 11.83. EI-Mass (m/z): calc mass: 218.14, found: 218.2 [M]+. Elemental analysis: C13H18N2O, calculated: C, 71.53; H, 8.31; N, 12.83. found: C, 71.64; H, 8.34; N, 12.88.

4-(4-butylpiperazin-1-yl)benzaldehyde (3c)

Light orange liquid. Yield 76%.1H NMR (400 MHz, Chloroform-*d*) δ 9.65 (s, 1H), 7.63 (d, *J* = 8.9 Hz, 2H), 6.79 (d, *J* = 8.9 Hz, 2H), 3.42 – 3.20 (m, 4H), 2.54 – 2.39 (m, 4H), 2.37 – 2.17 (m, 2H), 1.48 – 1.35 (m, 2H), 1.32 – 1.18 (m, 2H), 0.83 (t, *J* = 7.3 Hz, 3H). 13C NMR (101 MHz, Chloroform-*d*) δ 190.36, 155.08, 131.86, 126.97, 113.44, 58.36, 52.84, 47.02, 28.96, 20.72, 14.11. ESI-MS: calc mass: 246.17, found [2M+Na]+: 593.20. Elemental analysis: C15H22N2O, calculated: C, 73.13; H, 9.00; N, 11.37. found: C, 73.25; H, 9.04; N, 11.39.

4-(4-hexylpiperazin-1-yl)benzaldehyde (3d)

Light orange liquid. Yield 79%. 1H NMR (400 MHz, Chloroform-*d*) δ 9.71 (dd, *J* = 3.5, 1.5 Hz, 1H), 7.77 – 7.55 (m, 2H), 6.93 – 6.76 (m, 2H), 3.35 (q, *J* = 4.7, 4.2 Hz, 4H), 2.53 (q, *J* = 4.7 Hz, 4H), 2.33 (dtd, *J* = 8.9, 4.9, 2.3 Hz, 2H), 1.58 – 1.39 (m, 2H), 1.36 – 1.14 (m, 6H), 0.84 (dt, *J* = 7.2, 3.2 Hz, 3H). 13C NMR (101 MHz, Chloroform-*d*) δ 190.48, 155.10, 131.92, 127.14, 113.54, 58.76, 52.88, 47.08, 31.82, 27.26, 26.79, 22.67, 14.12. ESI-MS: calc mass: 274.20, found [M+H]+: 275.05. Elemental analysis: C17H26N2O, calculated: C, 74.41; H, 9.55; N, 10.21. found: C, 74.53; H, 9.59; N, 10.24.

4-morpholinobenzaldehyde (3e)

Yellow solid. Yield 81%. M.p. 70-2℃. 1H NMR (400 MHz, Chloroform-*d*) δ 9.79 (s, 1H), 7.82 – 7.67 (m, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 3.94 – 3.76 (m, 4), 3.42 – 3.18 (m, 4H). 13C NMR (101 MHz, Chloroform-*d*) δ 190.59, 154.98, 131.90, 128.05, 113.81, 66.51, 47.61. Elemental analysis: C11H13NO2, calculated: C, 69.09; H, 6.85; N, 7.32. found: C, 69.22; H, 6.89; N, 7.35.

4-(4-phenylpiperazin-1-yl)benzaldehyde (3f)

Yellow solid. Yield 72%. M.p. 129-31℃. 1H NMR (700 MHz, Chloroform-*d*) δ 9.83 (s, 1H), 8.01 – 7.75 (m, 2H), 7.47 – 7.22 (m, 2H), 7.09 – 6.86 (m, 5H), 3.66 – 3.53 (m, 4H), 3.46 – 3.28 (m, 4H). 13C NMR (176 MHz, Chloroform-*d*) δ 190.53, 154.91, 150.86, 131.91, 129.30, 127.38, 120.37, 116.33, 113.68, 49.01, 47.21. EI-Mass (m/z): calc mass: 266.14, found: 266.1 [M]+. Elemental Analysis: C17H18N2O. C, 76.66; H, 6.81; N, 10.52. found: C, 76.75; H, 6.83; N, 10.57.

4-(4-(p-tolyl)piperazin-1-yl)benzaldehyde (3g)

Yellow solid. Yield 69%. M.p. 154-6℃. 1H NMR (400 MHz, Chloroform-*d*) δ 9.80 (s, 1H), 7.83 – 7.71 (m, 2H), 7.22 – 6.81 (m, 6H), 3.79 – 3.54 (m, 4H), 3.35 (s, 4H), 2.30 (s, 3H). 13C NMR (101 MHz, Chloroform-*d*) δ 190.55, 154.94, 132.18, 131.98, 129.98, 127.55, 119.47, 117.09, 113.87, 77.45, 77.33, 77.13, 76.81, 50.01, 47.21, 20.60. EI-Mass (m/z): calc mass: 280.15, found: 280.1 [M]+. Elemental Analysis: C18H20N2O. C, 77.11; H, 7.19; N, 9.99. found: C, 77.20; H, 7.23; N, 9.95.

4-(4-(4-methoxyphenyl)piperazin-1-yl)benzaldehyde (3h)

Yellow solid. Yield 77%. M.p. 156-8℃.1H NMR (400 MHz, Chloroform-*d*) δ 9.79 (s, 1H), 7.77 (d, *J* = 9.0 Hz, 2H), 7.06 – 6.62 (m, 6H), 3.77 (s, 3H), 3.67 – 3.48 (m, 4H), 3.24 (t, *J* = 5.2 Hz, 4H). 13C NMR (101 MHz, Chloroform-*d*) δ 190.56, 154.94, 131.98, 127.59, 119.15, 119.05, 114.73, 113.92, 55.68, 50.97, 47.29. ESI-MS: calc mass: 296.15, found [2M+H]+: 593.20. Elemental Analysis: C18H20N2O2. C, 72.95; H, 6.80; N, 9.45. found: C, 73.08; H, 6.83; N, 9.51.

4-(4-(4-fluorophenyl)piperazin-1-yl)benzaldehyde (3i)

Yellow solid. Yield 63%. M.p. 123-5℃.1H NMR (400 MHz, Chloroform-*d*) δ 9.79 (s, 1H), 7.85 – 7.65 (m, 6H), 7.14 – 6.89 (m, 6H), 3.57 (q, *J* = 5.4, 4.7 Hz, 6H), 3.25 (dt, *J* = 10.6, 5.3 Hz, 6H). 13C NMR (101 MHz, Chloroform-*d*) δ 190.56, 155.87 (d, J = 245.1 Hz), 155.05, 131.98, 129.57 (d, *J* = 8.5 Hz), 127.62, 119.28, 116.43(d, *J* = 22.3 Hz), 113.93, 50.42, 47.48. ESI-MS: calc mass: 284.13, found [2M+H]+: 569.30. Elemental Analysis: C17H17FN2O. C, 71.81; H, 6.03; N, 9.85. found: C, 71.90; H, 6.05; N, 9.89.

4-(4-(3,4-dichlorophenyl)piperazin-1-yl)benzaldehyde (3j)

Yellow solid. Yield 75%. M.p. 179-81℃.1H NMR (400 MHz, Chloroform-*d*) δ 9.80 (s, 1H), 7.78 (d, *J* = 8.9 Hz, 2H), 7.31 (dd, *J* = 8.8, 0.7 Hz, 1H), 7.02 (s, 1H), 6.98 – 6.92 (m, 2H), 6.81 (ddd, *J* = 8.9, 3.6, 1.9 Hz, 1H), 3.62 – 3.51 (m, 4H), 3.38 – 3.30 (m, 4H). 13C NMR (101 MHz, Chloroform-*d*) δ 190.55, 154.58, 149.81, 133.15, 131.98, 130.79, 127.86, 123.50, 117.80, 115.83, 114.00, 48.76, 47.02. ESI-MS: calc mass: 334.06, found [M+H]+: 335.20. Elemental Analysis: calculated: C17H16Cl2N2O. C, 60.91; H, 4.81; N, 8.36. found: C, 60.99; H, 4.84; N, 8.33.

4-(4-(2-methoxyphenyl)piperazin-1-yl)benzaldehyde (3k)

Yellow solid. Yield 78%. M.p. 120-2℃.1H NMR (400 MHz, Chloroform-*d*) δ 9.78 (s, 1H), 7.76 (d, *J* = 8.9 Hz, 2H), 7.11 – 6.72 (m, 6H), 3.88 (s, 3H), 3.65 – 3.40 (m, 4H), 3.32 – 3.03 (m, 4H). 13C NMR (101 MHz, Chloroform-*d*) δ 190.62, 155.27, 152.39, 140.81, 132.00, 127.26, 123.63, 121.17, 118.38, 113.68, 111.45, 77.45, 77.33, 77.13, 76.81, 55.56, 50.50, 47.52. ESI-MS: calc mass: 296.15, found [2M+H]+: 593.20. Elemental Analysis: calculated: C18H20N2O2. C, 72.95; H, 6.80; N, 9.45. found: C, 72.99; H, 6.82; N, 9.40.

General procedure for the synthesis of target compounds (5a-k)

A mixture of benzaldehyde derivative 3 (1 mmol), 2-aminobenzimidazole 4 (1mmol), and triethylamine (2 mmol) in ethanol as a solvent was stirred at 50 ℃ overnight. After completion of the reaction, detected by TLC, the precipitates were collected using suction filtration and the collected solid was recrystallized in ethanol to get the pure product (5a-k).

(E)-N-(1H-benzo[d]imidazol-2-yl)-1-(4-(4-methylpiperazin-1-yl)phenyl)methanimine (5a)

Yellow solid; yield 77%; M.p. 296-8℃. IR (KBr): ʋ cm–1 = 3300, 3043, 2903, 1600, 1539, 1426, 1299.1H NMR (400 MHz, DMSO-*d*6) δ 9.21 (s, 1H), 7.88 – 7.80 (m, 2H), 7.69 – 7.25 (m, 2H), 7.12 – 6.97 (m, 4H), 3.36 – 3.33 (m, 4H), 2.40 (q, *J* = 5.0 Hz, 4H), 2.18 (d, *J* = 5.6 Hz, 3H). 13C NMR (176 MHz, DMSO-*d*6) δ 191.28, 150.71, 131.54, 129.44, 127.69, 123.45, 116.74, 114.42, 111.03, 51.83, 50.63, 44.47. EI-Mass (m/z): calc mass: 319.18, found: 319.3 [M]+. Elemental analysis: C19H21N5, calculated: C, 71.45; H, 6.63; N, 21.93. found: C, 71.56; H, 6.68; N, 22.01.

(E)-N-(1H-benzo[d]imidazol-2-yl)-1-(4-(4-ethylpiperazin-1-yl)phenyl)methanimine (5b)

Yellow solid; yield 72%; M.p. 256-8℃. IR (KBr): ʋ cm–1 = 3310, 3055, 2892, 1606, 1530, 1434, 1283.1H NMR (700 MHz, Methanol-*d*4) δ 9.73 (s, 1H), 7.87 – 6.92 (m, 8H), 4.15 (d, *J* = 14.0 Hz, 1H), 3.89 (d, *J* = 11.0 Hz, 1H), 3.71 (dd, *J* = 22.6, 11.1 Hz, 2H), 3.39 – 3.25 (m, 5H), 3.19 (td, *J* = 12.4, 3.3 Hz, 1H), 1.41 (t, *J* = 7.3 Hz, 3H). 13C NMR (176 MHz, DMSO-*d*6 ) δ 191.28, 150.71, 131.54, 129.44, 127.69, 123.45, 116.74, 114.42, 111.03, 51.83, 50.63, 44.47, 8.22. EI-Mass (m/z): calc mass: 333.2, found: 333.3 [M]+. Elemental analysis: C20H23N5, calculated: C, 72.04; H, 6.95; N, 21.00. found: C, 72.15; H, 6.99; N, 21.07.

(E)-N-(1H-benzo[d]imidazol-2-yl)-1-(4-(4-butylpiperazin-1-yl)phenyl)methanimine (5c)

Yellow solid; yield 76%; M.p. 253-5℃. IR (KBr): ʋ cm–1 = 3354, 3081, 2910, 1607, 1541, 1419.1H NMR (700 MHz, DMSO-*d*6) δ 9.75 (s, 1H), 7.77 (d, *J* = 8.3 Hz, 2H), 7.47 – 7.02 (m, 6H), 3.60 – 3.45 (m, 4H), 3.30 (t, *J* = 13.1 Hz, 2H), 3.09 (t, *J* = 8.4 Hz, 4H), 1.68 (q, *J* = 8.0, 7.5 Hz, 2H), 1.32 (q, *J* = 7.5 Hz, 2H), 0.90 (t, *J* = 7.4 Hz, 3H). 13C NMR (176 MHz, DMSO-*d*6) δ 191.41, 154.05, 150.87, 132.00, 129.92, 127.81, 123.61, 114.58, 111.80, 55.83, 50.78, 44.18, 25.49, 19.82, 13.90. EI-Mass (m/z): calc mass: 361.23, found: 361.3 [M]+. Elemental analysis: C22H27N5, calculated: C, 73.10; H, 7.53; N, 19.37. found: C, 73.19; H, 7.56; N, 19.44.

(E)-N-(1H-benzo[d]imidazol-2-yl)-1-(4-(4-hexylpiperazin-1-yl)phenyl)methanimine (5d)

Yellow solid; yield 81%; M.p. 247-9℃. IR (KBr): ʋ cm–1 = 3060, 2881, 1600, 1539, 1428, 1274.1H NMR (700 MHz, DMSO-*d*6) δ 9.74 (s, 1H), 7.81 – 7.65 (m, 2H), 7.36 (dd, *J* = 5.9, 3.2 Hz, 2H), 7.21 (dd, *J* = 5.9, 3.2 Hz, 2H), 7.16 – 7.05 (m, 2H), 4.09 (d, *J* = 13.8 Hz, 2H), 3.55 (d, *J* = 12.3 Hz, 2H), 3.31 (d, *J* = 13.3 Hz, 2H), 3.16 – 3.00 (m, 4H), 1.77 – 1.65 (m, 2H), 1.35 – 1.18 (m, 6H), 0.93 – 0.77 (m, 3H). 13C NMR (176 MHz, DMSO-*d*6) δ 189.32, 151.99, 148.80, 129.93, 127.83, 125.73, 121.53, 112.49, 109.72, 53.97, 48.69, 42.10, 29.00, 24.02, 21.33, 20.20, 12.20. EI-Mass (m/z): calc mass: 389.26, found: 389.4 [M]+. Elemental analysis: C24H31N5, calculated: C, 74.00; H, 8.02; N, 17.98. found: C, 74.12; H, 8.06; N, 17.93.

(E)-N-(1H-benzo[d]imidazol-2-yl)-1-(4-morpholinophenyl)methanimine (5e)

Yellow solid; yield 30%; M.p. 230℃ (Decomposed). IR (KBr): ʋ cm–1 = 3320, 2990, 2900, 1628, 1587, 1436. 1H NMR (400 MHz, Methanol-*d*4) δ 9.66 (s, 1H), 7.85 – 7.58 (m, 2H), 7.17 (dt, *J* = 5.8, 3.5 Hz, 2H), 7.08 – 6.87 (m, 4H), 3.91 – 3.64 (m, 4H), 3.34 – 3.30 (m, 4H). 13C NMR (101 MHz, Methanol-*d*4) δ 191.29, 155.76, 131.65, 127.25, 122.12, 120.48, 113.78, 113.23, 111.43, 66.30, 47.01. EI-Mass (m/z): calc mass: 306.15, found: 306.3 [M]+. Elemental analysis: C18H18N4O, calculated: C, 70.57; H, 5.92; N, 18.29. found: C, 70.69; H, 5.98; N, 18.35.

(E)-N-(1H-benzo[d]imidazol-2-yl)-1-(4-(4-phenylpiperazin-1-yl)phenyl)methanimine (5f)

Yellow solid; yield 64%; M.p. 300℃ ˂. IR (KBr): ʋ cm–1 =3363, 3050, 1626, 1568, 1452, 1265, 1210, 746. 1H NMR (700 MHz, DMSO-*d*6) δ 9.73 (s, 1H), 7.76 (d, *J* = 8.9 Hz, 2H), 7.49 – 7.39 (m, 4H), 7.36 (dd, *J* = 5.9, 3.2 Hz, 2H), 7.23 – 7.16 (m, 3H), 7.12 (d, *J* = 8.9 Hz, 2H), 3.78 – 3.69 (m, 4H), 3.54 – 3.47 (m, 4H). 13C NMR (176 MHz, DMSO-*d*6) δ 191.28, 154.52, 150.87, 146.37, 132.07, 130.13, 129.89, 127.36, 125.45, 123.60, 119.25, 114.25, 111.78, 51.64, 45.59. EI-Mass (m/z): calc mass: 381.20, found: 381.3 [M]+. Elemental analysis: C24H23N5, calculated: C, 75.56; H, 6.08; N, 18.36. found: C, 75.66; H, 6.11; N, 18.43.

(E)-N-(1H-benzo[d]imidazol-2-yl)-1-(4-(4-(p-tolyl)piperazin-1-yl)phenyl)methanimine (5g)

Yellow solid; yield 59%; M.p. 300℃ ˂. IR (KBr): ʋ cm–1 = 3063, 2874, 1602, 1531, 1420, 1283, 1170, 1039. 1H NMR (700 MHz, DMSO-*d*6) δ 9.80 (s, 1H), 8.00 – 6.90 (m, 12H), 3.99 (s, 4H), 3.69 (t, *J* = 5.2 Hz, 4H), 2.35 (s, 3H). 13C NMR (176 MHz, DMSO-*d*6) δ 191.12, 154.16, 150.95, 131.96, 130.77, 130.75, 129.99, 127.76, 123.38, 121.67, 114.49, 114.48, 111.83, 54.03, 44.62, 20.97. EI-Mass (m/z): calc mass: 395.21, found: 395.3 [M]+. Elemental analysis: C25H25N5, calculated: C, 75.92; H, 6.37; N, 17.71. found: C, 75.98; H, 6.34; N, 17.79.

(E)-N-(1H-benzo[d]imidazol-2-yl)-1-(4-(4-(4-methoxyphenyl)piperazin-1-yl)phenyl)methanimine (5h)

Yellow solid; yield 52%; M.p. 300℃ ˂. IR (KBr): ʋ cm–1 = 3300, 2840, 1630, 1560, 1420, 1250. 1H NMR (700 MHz, ) δ 9.76 (s, 1H), 7.86 – 7.67 (m, 4H), 7.43 – 7.00 (m, 8H), 3.91 (s, 4H), 3.78 (s, 3H), 3.68 (t, *J* = 5.2 Hz, 4H). 13C NMR (176 MHz, DMSO-*d*6) δ 191.39, 159.95, 154.14, 150.86, 135.40, 132.04, 129.89, 127.80, 123.60, 123.23, 115.52, 114.58, 111.79, 56.09, 54.56, 44.69. EI-Mass (m/z): calc mass: 411.21, found: 411.3 [M]+. Elemental analysis: C25H25N5O, calculated: C, 72.97; H, 6.12; N, 17.02. found: C, 72.90; H, 6.15; N, 17.09.

(E)-N-(1H-benzo[d]imidazol-2-yl)-1-(4-(4-(4-fluorophenyl)piperazin-1-yl)phenyl)methanimine (5i)

Yellow solid; yield 61%; M.p. 300℃ ˂. IR (KBr): ʋ cm–1 = 3375, 3065, 2993, 1612, 1570, 1500, 1429, 1311, 1234, 1089, 821, 738. 1H NMR (700 MHz, ) δ 9.73 (s, 1H), 7.81 – 7.71 (m, 2H), 7.70 – 7.59 (m, 2H), 7.42 – 7.05 (m, 8H), 3.89 – 3.72 (m, 4H), 3.63 – 3.49 (m, 4H). 13C NMR (176 MHz, DMSO-*d*6) δ 191.30, 160.53 (d, *J* = 243.6 Hz), 154.35, 150.85, 141.63, 132.03, 129.87, 127.53, 123.58, 122.46 (d, *J* = 12.1 Hz), 116.92 (d, *J* = 25.3 Hz), 114.39, 111.78, 52.87, 45.32. EI-Mass (m/z): calc mass: 399.21, found: 399.3 [M]+. Elemental analysis: C24H22FN5, calculated: C, 72.16; H, 5.55; N, 17.53. found: C, 72.24; H, 5.57; N, 17.59.

(E)-1-(4-(4-(3,4-dichlorophenyl)piperazin-1-yl)phenyl)-N-(1H-indol-2-yl)methanimine (5j)

Yellow solid; yield 72%; 293-5℃. IR (KBr): ʋ cm–1 = 3400, 2880, 1640, 1560, 1420, 1300, 810. 1H NMR (700 MHz, ) δ 9.70 (s, 1H), 7.73 (d, *J* = 8.9 Hz, 2H), 7.41 (d, *J* = 9.0 Hz, 1H), 7.36 (dd, *J* = 5.9, 3.2 Hz, 2H), 7.21 (dd, *J* = 5.9, 3.2 Hz, 2H), 7.15 (d, *J* = 2.9 Hz, 1H), 7.07 (d, *J* = 8.8 Hz, 2H), 6.97 (dd, *J* = 9.0, 2.9 Hz, 1H), 3.58 – 3.48 (m, 4H), 3.38 – 3.28 (m, 4H). 13C NMR (176 MHz, DMSO-*d*6) δ 191.09, 154.83, 150.87, 150.64, 132.00, 131.03, 129.91, 126.81, 123.62, 123.61, 120.39, 116.71, 115.86, 113.80, 111.78, 47.54, 46.36. EI-Mass (m/z): calc mass: 449.12, found: 449.2 [M]+. Elemental analysis: C24H21Cl2N5, calculated: C, 64.01; H, 4.70; N, 15.55. found: C, 64.08; H, 4.73; N, 15.52.

(E)-N-(1H-benzo[d]imidazol-2-yl)-1-(4-(4-(2-methoxyphenyl)piperazin-1-yl)phenyl)methanimine (5k)

Yellow solid; yield 48%; M.p. 225-7℃. IR (KBr): ʋ cm–1 = 3300, 3105, 2900, 1620, 1600, 1580, 1430, 1275. 1H NMR (400 MHz, Methanol-*d*4) δ 9.67 (s, 1H), 7.96 – 7.68 (m, 2H), 7.50 – 6.83 (m, 10H), 3.89 – 3.82 (s, 3H), 3.56 (dq, *J* = 7.6, 3.0, 2.4 Hz, 4H), 3.15 (ddd, *J* = 10.3, 6.4, 3.6 Hz, 4H). 13C NMR (101 MHz, DMSO-*d*6) δ 190.42, 154.90, 151.82, 135.34, 130.92, 126.47, 126.07, 122.73, 120.07, 119.86, 117.39, 114.59, 112.56, 110.68, 110.57, 62.28, 53.83, 49.70. EI-Mass (m/z): calc mass: 411.21, found: 411.2 [M]+. Elemental analysis: C25H25N5O, calculated: C, 72.97; H, 6.12; N, 17.02. found: C, 72.93; H, 6.16; N, 17.05.



