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Novel indole based hybrid oxadiazole scaffolds with *N*-(substituted-phenyl)butanamides: synthesis, lineweaver-burk plot evaluation and binding analysis of potent urease inhibitors

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Structural Characterization of Compounds

Ethyl 4-(1*H*-indol-3-yl)butanoate (2)

^{1}H-NMR (600 MHz, DMSO-d_6, δ, ppm): 10.76 (s, 1H, NH-1), 7.49 (br.d, *J* = 7.8 Hz, 1H, H-7), 7.32 (br.d, *J* = 8.1 Hz, 1H, H-4), 7.10 (dist.d, *J* = 1.8 Hz, 1H, H-2), 7.05 (br.dt, *J* = 0.96, 8.0 Hz, 1H, H-6), 6.96 (br.dt, *J* = 0.90, 7.8 Hz, 1H, H-5), 4.04 (q, *J* = 7.1 Hz, 2H, CH_2-1''), 2.69 (t, *J* = 7.6 Hz, 2H, CH_2-4'), 2.33 (m, 2H, CH_2-2'), 1.89 (quintet, *J* = 7.5 Hz, 2H, CH_2-3'), 1.16 (t, *J* = 7.1 Hz, 3H, CH_3-2''). ^{13}C-NMR (150 MHz, DMSO-d_6, δ, ppm): 172.83 (C-4'), 136.28 (C-8), 127.09 (C-9), 122.31 (C-2), 120.79 (C-6), 118.19 (C-7), 118.09 (C-5), 113.66 (C-3), 111.30 (C-4), 59.60 (C-1''), 32.99 (C-2'), 25.30 (C-4'), 23.97 (C-3'), 14.08 (C-2''). EI-MS (*m/z*): 231 [M; $C_{14}H_{17}NO_2$] $^{+}$, 186 $(C_{12}H_{12}NO)^{+}$, 143 $(C_{10}H_9N)^{+}$, 130 $(C_9H_8N)^{+}$, 116 $(C_8H_6N)^{+}$, 115 $(C_6H_{11}O_2)^{+}$, 91 $(C_6H_5N)^{+}$, 77 $(C_6H_5)^{+}$.

4-(1*H*-indol-3-yl)butanohydrazide (3)

^{1}H-NMR (600 MHz, DMSO-d_6, δ, ppm): 10.70 (s, 1H, NH-1), 9.90 (s, 1H, CONH), 8.96 (s, 2H, CONH-NH_2), 7.49 (br.d, *J* = 7.5 Hz, 1H, H-7), 7.32 (br.d, *J* = 8.0 Hz, 1H, H-4), 7.09 (s, 1H, H-2), 7.05 (br.t, *J* = 7.6 Hz, 1H, H-6), 6.95 (br.t, *J* = 7.3 Hz, 1H, H-5), 2.65 (t, *J* = 7.6 Hz, 2H, CH_2-4'), 2.08 (t, *J* = 7.4 Hz, 2H, CH_2-2'), 1.86 (quintet, *J* = 7.5 Hz, 2H, CH_2-3'). ^{13}C-NMR (150 MHz, DMSO-d_6, δ, ppm): 171.57 (C-1'), 136.23 (C-8), 127.11 (C-9), 122.17 (C-2), 120.76 (C-6), 118.24 (C-7), 118.03 (C-5), 114.02 (C-3), 111.26 (C-4), 33.28 (C-2'), 26.03 (C-4'), 24.31 (C-3'). EI-MS (*m/z*): 217 (M; $C_{12}H_{15}N_3O$] $^{+}$, 186 $(C_{12}H_{12}NO)^{+}$, 143 $(C_{10}H_9N)^{+}$, 130 $(C_9H_8N)^{+}$, 116 $(C_8H_6N)^{+}$, 91 $(C_6H_5N)^{+}$, 77 $(C_6H_5)^{+}$.

5-[3-(1*H*-indol-3-yl)propyl]-1,3,4-oxadiazole-2-thiol (4)

^{1}H-NMR (600 MHz, DMSO-d_6, δ, ppm): 10.81 (s, 1H, NH-1), 7.52 (br.d, *J* = 7.8 Hz, 1H, H-7), 7.35 (br.d, *J* = 8.1 Hz, 1H, H-4), 7.15 (dist.d, *J* = 1.9 Hz, 1H, H-2), 7.07 (br.t, *J* = 7.3 Hz, 1H, H-6), 6.98 (br.t, *J* = 7.2 Hz, 1H, H-5), 2.79 (t, *J* = 7.4 Hz, 2H, CH_2-3'), 2.76 (t, *J* = 7.4 Hz, 2H, CH_2-1'), 2.02 (quintet, *J* = 7.3 Hz, 2H, CH_2-2'). ^{13}C-NMR (150 MHz, DMSO-d_6, δ, ppm): 177.70 (C-2''), 164.15 (C-5''), 136.31 (C-8), 127.01 (C-9), 122.49 (C-2), 120.89 (C-6), 118.18 (C-7), 118.04 (C-5), 113.20 (C-3), 111.36 (C-4), 25.81 (C-1'), 24.53 (C-3'), 23.73 (C-2'). EI-MS (*m/z*): 259 [M; $C_{13}H_{13}N_3SO$] $^{+}$, $(M)^{+}$, 200 $(C_{12}H_{12}N_2O)$ $^{+}$, 186 $(C_{12}H_{12}NO)^{+}$, 184 $(C_{12}H_{12}N_2)$ $^{+}$, 156 $(C_{11}H_{10}N)$ $^{+}$, 143 $(C_{10}H_9N)^{+}$, 130 $(C_9H_8N)^{+}$, 116 $(C_8H_6N)^{+}$, 77 $(C_6H_5)^{+}$.

***N*-(4-Ethoxyphenyl)-4-({5-[3-(1*H*-indol-3-yl)propyl]-1,3,4-oxadiazol-2-yl}sulfanyl)butanamide (8a)**. Light brown sticky liquid; Yield: 69%; Mol. Formula: $C_{25}H_{28}N_4SO_3$; Mol. Weight: 464 g/mol; *υ* 3227 (N-H str.), 2939 (C-H str. of aromatic ring), 1668 (C=O str.), 1654 (C=N Str.), 1589 (C=C aromatic str.), 1526, 1482, 1417 (Str. for Oxadiazole), 1160 (C-O-C Str.), 645 (C-S str.) cm^{-1}; ^{1}H-NMR (600 MHz, DMSO-d_6, δ, ppm): 10.77 (s, 1H, NH-1), 7.93 (s, 1H, CONH), 7.49 (dist.d, *J* = 8.2 Hz, 3H, H-7, H-2"" & H-6""), 7.34 (br.d, *J* = 9.6 Hz, 1H, H-4), 7.13 (dist.d, *J* = 2.4 Hz, 1H, H-2), 7.07 (br.dt, *J* = 0.9, 8.5 Hz, 1H, H-6), 6.96 (br.dt, *J* = 0.7, 8.5 Hz, 1H, H-5), 6.88 (dist.d, *J* = 8.4 Hz, 2H, H-3"" & H-5""), 3.96 (q, *J* = 8.3 Hz, 2H, 4""-O$\underline{CH_2}CH_3$), 2.92-2.87 (m, 4H, CH_2-3' & CH_2-4'"), 2.76-2.72 (m, 2H, CH_2-1'), 2.43 (t, *J* = 9.5 Hz, 2H, CH_2-2'"), 2.05-1.98 (m, 4H, CH_2-2' & CH_2-3'"), 1.28 (t, *J* = 8.3 Hz, 3H, 4""-OCH$_2\underline{CH_3}$). ^{13}C-NMR (150 MHz, DMSO-d_6, δ/ppm): 173.91 (C-1'"), 164.52 (C-5"), 162.90 (C-2"), 155.46 (C-4""), 136.78 (C-8), 133.07 (C-1""), 127.50 (C-9), 122.87 (C-2), 121.63 (C-2"" & C-6""), 121.33 (C-6), 118.63 (C-7), 118.58 (C-5), 114.66 (C-3"" & C-5""), 113.77 (C-3), 111.78 (C-4), 63.59 (4""-O$\underline{CH_2}CH_3$), 36.18 (C-2'"), 32.43 (C-4'"), 31.12 (C-1'), 26.42 (C-3'"), 24.95 (C-3'), 24.14 (C-2'), 14.92 (4""-OCH$_2\underline{CH_3}$); Anal. Calc. for $C_{25}H_{28}N_4SO_3$ (464.19): C, 64.63; H, 6.07; N, 12.06. Found: C, 64.60; H, 6.03; N, 12.01. EI-MS (*m/z*): 464 $[M]^+$ 259 $(C_{13}H_{13}N_3SO)^+$, 206 $(C_{12}H_{16}N_2O)^+$, 200 $(C_{12}H_{12}N_2O)^+$, 186 $(C_{12}H_{12}NO)^+$, 184 $(C_{12}H_{12}N_2)^+$, 156 $(C_{11}H_{10}N)^+$, 149 $(C_9H_{11}NO)^+$, 143 $(C_{10}H_9N)^+$, 130 $(C_9H_8N)^+$, 91 $(C_6H_5N)^+$, 77 $(C_6H_5)^+$.

***N*-(2-Ethylphenyl)-4-({5-[3-(1*H*-indol-3-yl)propyl]-1,3,4-oxadiazol-2-yl}sulfanyl)butanamide (8b)**. Light yellow colored amorphous powder; Yield: 91%; m.p: 101-102 °C; Mol. Formula: $C_{25}H_{28}N_4SO_2$; Mol. Weight: 448 g/mol; IR (KBr, cm^{-1}): *υ* 3229 (N-H str.), 2940 (C-H str. of aromatic ring), 1671 (C=O str.), 1651 (C=N Str.), 1584 (C=C aromatic str.), 1521, 1477, 1413 (Str. for Oxadiazole), 1157 (C-O-C Str.), 643 (C-S str.) cm^{-1}; ^{1}H-NMR (600 MHz, DMSO-d_6, δ, ppm): 10.80 (s, 1H, NH-1), 9.34 (s, 1H, CONH), 7.51 (br.d, *J* = 7.6 Hz, 1H, H-7), 7.34 (dist.d, *J* = 8.0 Hz, 1H, H-4), 7.31 (dist.d, *J* = 7.3 Hz, 1H, H-6""), 7.22 (dist.d, *J* = 6.0 Hz, H-3""), 7.14 (m, 3H, H-2, H-4"" & H-5""), 7.07 (br.t, *J* = 7.4 Hz, 1H, H-6), 6.97 (br.t, *J* = 7.3 Hz, 1H, H-5), 3.28 (t, *J* = 6.7 Hz, 2H, CH_2-4'"), 2.88 (t, *J* = 7.2 Hz, 2H, CH_2-3'), 2.77 (t, *J* = 7.0 Hz, 2H, CH_2-1'), 2.56 (q, *J* = 7.3 Hz, 2H, 2""-$\underline{CH_2}CH_3$), 2.49 (m merge in DMSO-d_6, 2H, CH_2-2'"), 2.05-2.04 (m, 4H, CH_2-2' & CH_2-3'"), 1.09 (t, *J* = 7.4 Hz, 3H, 2""-CH$_2\underline{CH_3}$). ^{13}C-NMR (150 MHz, DMSO-d_6, δ, ppm): 170.88 (C-1'"), 168.32 (C-5"), 163.36 (C-2"), 138.46 (C-1""), 136.81 (C-8), 136.05 (C-5""), 128.88 (C-3""), 127.52 (C- 9), 126.29 (C-2""), 126.13 (C-4""), 126.09 (C-6""), 122.98 (C-2), 121.35 (C-6), 118.66

(C-5 & C-7), 113.77 (C-3), 111.84 (C-4), 34.61 (C-2'''), 32.14 (C-4'''), 27.02 (C-1'), 25.63 (C-3'''), 24.77 (C-3'), 24.30 (C-2'), 24.21 (2''''-$\underline{CH_2}CH_3$), 14.65 (2''''-$CH_2\underline{CH_3}$); Anal. Calc. for $C_{25}H_{28}N_4SO_2$ (448.19): C, 66.94; H, 6.29; N, 12.49. Found: C, 66.90; H, 6.23; N, 12.44. EI-MS (*m/z*): 448 $[M]^+$, 259 $(C_{13}H_{13}N_3SO)^+$, 200 $(C_{12}H_{12}N_2O)^+$, 190 $(C_{12}H_{16}NO)^+$, 186 $(C_{12}H_{12}NO)^+$, 184 $(C_{12}H_{12}N_2)^+$, 156 $(C_{11}H_{10}N)^+$, 143 $(C_{10}H_9N)^+$, 130 $(C_9H_8N)^+$, 91 $(C_6H_5N)^+$, 77 $(C_6H_5)^+$.

***N*-(4-Ethylphenyl)-4-({5-[3-(1*H*-indol-3-yl)propyl]-1,3,4-oxadiazol-2-yl}sulfanyl)butanamide (8c)**. Light yellow colored amorphous powder; Yield: 91%; m.p: 101-102 °C; Mol. Formula: $C_{25}H_{28}N_4SO_2$; Mol. Weight: 448 g/mol; IR (KBr, cm^{-1}): υ 3227 (N-H str.), 2938 (C-H str. of aromatic ring), 1669 (C=O str.), 1648 (C=N Str.), 1583 (C=C aromatic str.), 1521, 1478, 1417 (Str. for Oxadiazole), 1157 (C-O-C Str.), 641 (C-S str.) cm^{-1}; ^{1}H-NMR (600 MHz, DMSO-d_6, δ, ppm): 10.80 (s, 1H, NH-1), 10.38 (s, 1H, CONH), 7.51 (br.d, *J* = 7.8 Hz, 1H, H-7), 7.47 (br.d, *J* = 8.3 Hz, 2H, H-2'''' & H-6''''), 7.34 (br.d, *J* = 7.8 Hz, 1H, H-4), 7.16-7.14 (m, 3H, H-2, H-3'''' & H-5''''), 7.07 (dist.t, *J* = 6.9 Hz, 1H, H-6), 6.98 (m, 1H, H-5), 2.91-2.87 (m, 4H, CH_2-3' & CH_2-4'''), 2.79-2.77 (m, 4H, CH_2-1' & CH_2-2'''), 2.55 (q, *J* = 7.5 Hz, 2H, 4''''-$\underline{CH_2}CH_3$), 2.09-2.04 (m, 4H, CH_2-2' & CH_2-3'''), 1.15 (t, *J* = 7.5 Hz, 3H, 4''''-$CH_2\underline{CH_3}$). ^{13}C-NMR (150 MHz, DMSO-d_6, δ, ppm): 169.12 (C-1'''), 168.62 (C-5''), 164.26 (C-2''), 142.30 (C-4''''), 139.70 (C-1''''), 136.80 (C-8), 128.51 (C-3'''' & C-5''''), 127.52 (C-9), 122.98 (C-2), 121.36 (C-6), 119.81 (C-2'''' & C-6''''), 118.69 (C-7), 118.66 (C-5), 113.74 (C-3), 111.84 (C-4), 28.03 (C-2''' & 4''''-$\underline{CH_2}CH_3$), 27.21 (C-4'''), 26.97 (C-1' & C-3'''), 24.78 (C-3'), 24.30 (C-2'), 16.08 (4''''-$CH_2\underline{CH_3}$); Anal. Calc. for $C_{25}H_{28}N_4SO_2$ (448.19): C, 66.94; H, 6.29; N, 12.49. Found: C, 66.92; H, 6.24; N, 12.43. EI-MS (*m/z*): 448 $[M]^+$, 259 $(C_{13}H_{13}N_3SO)^+$, 200 $(C_{12}H_{12}N_2O)^+$, 190 $(C_{12}H_{16}NO)^+$, 186 $(C_{12}H_{12}NO)^+$, 184 $(C_{12}H_{12}N_2)^+$, 156 $(C_{11}H_{10}N)^+$, 143 $(C_{10}H_9N)^+$, 130 $(C_9H_8N)^+$, 91 $(C_6H_5N)^+$, 77 $(C_6H_5)^+$.

4-({5-[3-(1*H*-Indol-3-yl)propyl]-1,3,4-oxadiazol-2-yl}sulfanyl)-*N*-(2-methylphenyl)butanamide (8d). Light Brown colored amorphous powder; Yield: 78%; m.p: 58-59 °C; Mol. Formula: $C_{24}H_{26}N_4SO_2$; Mol. Weight: 434 g/mol; IR (KBr, cm^{-1}): υ 3222 (N-H str.), 2943 (C-H str. of aromatic ring), 1674 (C=O str.), 1649 (C=N Str.), 1583 (C=C aromatic str.), 1520, 1478, 1416 (Str. for Oxadiazole), 1165 (C-O-C Str.), 646 (C-S str.) cm^{-1}; ^{1}H-NMR (600 MHz, DMSO-d_6, δ, ppm): 10.80 (s, 1H, NH-1), 9.33 (s, 1H, CONH), 7.51 (br.d, *J* = 9.2 Hz, 1H, H-7), 7.38 (dist.d, *J* = 9.4 Hz, 1H, H-6''''), 7.35 (dist.d, *J* = 9.7 Hz, 1H, H-4), 7.20 (br.d, *J* = 8.5 Hz, 1H, H-3''''), 7.14 (m, 2H, H-2 & H-5''''), 7.07 (m, 2H, H-6 & H-

4""), 6.97 (br.t, *J* = 8.6 Hz, 1H, H-5), 3.29 (t, *J* = 8.3 Hz, 2H, CH_2-4'"), 2.88 (t, *J* = 8.8 Hz, 2H, CH_2-3'), 2.78 (t, *J* = 8.6 Hz, 2H, CH_2-1'), 2.49 (m merge in DMSO-d_6, 2H, CH_2-2'"), 2.18 (s, 3H, 2""-CH_3), 2.08-2.04 (m, 4H, CH_2-2' & CH_2-3'"). ^{13}C-NMR (150 MHz, DMSO-d_6, δ, ppm): 170.59 (C-1'"), 168.33 (C-5"), 163.38 (C-2"), 136.81 (C-8), 136.78 (C-1""), 132.24 (C-2""), 130.64 (C-3""), 127.53 (C-9), 126.30 (C-5""), 125.64 (C-4""), 125.57 (C-6""), 122.97 (C-2), 121.36 (C-6), 118.67 (C-5 & C-7), 113.79 (C-3), 111.84 (C-4), 34.68 (C-2'"), 32.11 (C-4'"), 27.02 (C-1'), 25.66 (C-3'"), 24.78 (C-3'), 24.31 (C-2'), 18.31 (2""-CH_3); Anal. Calc. for $C_{24}H_{26}N_4SO_2$ (434.18): C, 66.33; H, 6.03; N, 12.89. Found: C, 66.30; H, 6.00; N, 12.86. EI-MS (*m/z*): 434 $[M]^+$, 291 $(C_{14}H_{17}N_3SO_2)^+$, 259 $(C_{13}H_{13}N_3SO)^+$, 200 $(C_{12}H_{12}N_2O)^+$, 186 $(C_{12}H_{12}NO)^+$, 184 $(C_{12}H_{12}N_2)^+$, 176 $(C_{11}H_{14}NO)^+$, 156 $(C_{11}H_{10}N)^+$, 143 $(C_{10}H_9N)^+$, 130 $(C_9H_8N)^+$, 91 $(C_6H_5N)^+$, 77 $(C_6H_5)^+$.

4-({5-[3-(1*H*-Indol-3-yl)propyl]-1,3,4-oxadiazol-2-yl}sulfanyl)-*N*-(3-methylphenyl)butanamide (8e). Light yellow colored amorphous powder; Yield: 94%; m.p: 98-99 °C; Mol. Formula: $C_{24}H_{26}N_4SO_2$; Mol. Weight: 434 g/mol; IR (KBr, cm^{-1}): *υ* 3224 (N-H str.), 2939 (C-H str. of aromatic ring), 1672 (C=O str.), 1652 (C=N Str.), 1583 (C=C aromatic str.), 1521, 1477, 1413 (Str. for Oxadiazole), 1162 (C-O-C Str.), 644 (C-S str.) cm^{-1}; ^{1}H-NMR (600 MHz, DMSO-d_6, δ, ppm): 10.80 (s, 1H, NH-1), 9.87 (s, 1H, CONH), 7.51 (br.d, *J* = 7.8 Hz, 1H, H-7), 7.44 (s, 1H, H-2""), 7.37 (br.d, *J* = 8.1 Hz, 1H, H-6""), 7.34 (br.d, *J* = 8.1 Hz, 1H, H-4), 7.16 (br.t, *J* = 7.8 Hz, 1H, H-5""), 7.14 (dist.d, *J* = 1.98 Hz, 1H, H-2), 7.06 (br.dt, *J* = 0.6 & 7.8 Hz, 1H, H-6), 6.97 (br.t, 0.5 & 7.6 Hz, 1H, H-5), 6.85 (br.d, 1H, *J* = 7.4 Hz, H-4""), 3.27 (t, *J* = 7.2 Hz, 2H, CH_2-4'"), 2.86 (t, *J* = 7.4 Hz, 2H, CH_2-3'), 2.77 (t, *J* = 7.4 Hz, 2H, CH_2-1'), 2.46 (t, *J* = 7.2 Hz, 2H, CH_2-2'"), 2.26 (s, 3H, 3""-CH_3), 2.06-2.01 (m, 4H, CH_2-2' & CH_2-3'"). ^{13}C-NMR (150 MHz, DMSO-d_6, δ, ppm): 170.56 (C-1'"), 168.31 (C-5"), 163.36 (C-2"), 139.55 (C-3""), 138.24 (C-1""), 136.79 (C-8), 128.92 (C-5""), 127.25 (C-9), 124.21 (C-4""), 122.97 (C-2), 121.35 (C-6), 120.14 (C-2""), 118.67 (C-7), 118.66 (C-5), 116.79 (C-6""), 113.77 (C-3), 111.84 (C-4), 35.18 (C-2'"), 32.10 (C-4'"), 27.00 (C-1'), 25.41 (C-3'"), 24.76 (C-3'), 24.31 (C-2'), 21.63 (3""-CH_3); Anal. Calc. for $C_{24}H_{26}N_4SO_2$ (434.18): C, 66.33; H, 6.03; N, 12.89. Found: C, 66.28; H, 5.97; N, 12.82. EI-MS (*m/z*): 434 $[M]^+$, 291 $(C_{14}H_{17}N_3SO_2)^+$, 259 $(C_{13}H_{13}N_3SO)^+$, 200 $(C_{12}H_{12}N_2O)^+$, 186 $(C_{12}H_{12}NO)^+$, 184 $(C_{12}H_{12}N_2)^+$, 176 $(C_{11}H_{14}NO)^+$, 156 $(C_{11}H_{10}N)^+$, 143 $(C_{10}H_9N)^+$, 130 $(C_9H_8N)^+$, 91 $(C_6H_5N)^+$, 77 $(C_6H_5)^+$.

4-({5-[3-(1*H*-Indol-3-yl)propyl]-1,3,4-oxadiazol-2-yl}sulfanyl)-*N*-(4-methylphenyl)butanamide (8f). Light yellow colored amorphous powder; Yield: 74%; m.p: 81-82 °C; Mol. Formula: $C_{24}H_{26}N_4SO_2$; Mol. Weight: 434 g/mol; IR (KBr, cm^{-1}): υ 3225 (N-H str.), 2940 (C-H str. of aromatic ring), 1671 (C=O str.), 1647 (C=N Str.), 1585 (C=C aromatic str.), 1520, 1480, 1414 (Str. for Oxadiazole), 1155 (C-O-C Str.), 641 (C-S str.) cm^{-1}; ^{1}H-NMR (600 MHz, DMSO-d_6, δ, ppm): 10.81 (s, 1H, NH-1), 7.95 (s, 1H, CONH), 7.5 (br.d, *J* = 10.2 Hz, 3H, H-7, H-2"" & H-6""), 7.35 (br.d, *J* = 9.7 Hz, 1H, H-4), 7.16-7.14 (m, 3H, H-2, H-3"" & H-5""), 7.07 (br.t, *J* = 8.5, 1H, H-6), 6.98 (br.t, 8.5 Hz, 1H, H-5), 3.77 (t, *J* = 8.4 Hz, 2H, CH_2-4'"), 2.88 (br,s, 2H, CH_2-3'), 2.77 (t, *J* = 8.8 Hz, 2H, CH_2-1'), 2.46 (t, *J* = 9.4 Hz, 2H, CH_2-2'"), 2.26 (s, 3H, 4""-CH_3), 2.04-1.99 (m, 4H, CH_2-2' & CH_2-3'"). ^{13}C-NMR (150 MHz, DMSO-d_6, δ, ppm): 174.00 (C-1'"), 164.50 (C-5"), 162.78 (C-2"), 137.62 (C-1""), 136.82 (C-8), 133.35 (C-4""), 129.42 (C-3"" & C-5""), 127.51 (C-9), 122.92 (C-2), 121.36 (C-6), 119.89 (C-2"" & C-6""), 118.66 (C-7), 118.65 (C-5), 113.77 (C-3), 111.83 (C-4), 36.21 (C-2'"), 32.68 (C-4'"), 27.18 (C-1'), 25.04 (C-3'"), 24.62 (C-3'), 24.31 (C-2'), 20.80 (4""-CH_3); Anal. Calc. for $C_{24}H_{26}N_4SO_2$ (434.18): C, 66.33; H, 6.03; N, 12.89. Found: C, 66.26; H, 5.98; N, 12.83. EI-MS (*m/z*): 434 $[M]^+$, 291 $(C_{14}H_{17}N_3SO_2)^+$, 259 $(C_{13}H_{13}N_3SO)^+$, 200 $(C_{12}H_{12}N_2O)^+$, 186 $(C_{12}H_{12}NO)^+$, 184 $(C_{12}H_{12}N_2)^+$, 176 $(C_{11}H_{14}NO)^+$, 156 $(C_{11}H_{10}N)^+$, 143 $(C_{10}H_9N)^+$, 130 $(C_9H_8N)^+$, 91 $(C_6H_5N)^+$, 77 $(C_6H_5)^+$.

***N*-(2,4-Dimethylphenyl)-4-({5-[3-(1*H*-indol-3-yl)propyl]-1,3,4-oxadiazol-2-yl}sulfanyl)butanamide (8g)**. Brown sticky liquid; Yield: 71%; Mol. Formula: $C_{25}H_{28}N_4SO_2$; Mol. Weight: 448 g/mol; υ 3226 (N-H str.), 2942 (C-H str. of aromatic ring), 1673 (C=O str.), 1648 (C=N Str.), 1585 (C=C aromatic str.), 1520, 1477, 1415 (Str. for Oxadiazole), 1159 (C-O-C Str.), 644 (C-S str.) cm^{-1}; ^{1}H-NMR (600 MHz, DMSO-d_6, δ, ppm): 10.80 (s, 1H, NH-1), 9.25 (s, 1H, CONH), 7.51 (br.d, *J* = 7.8 Hz, 1H, H-7), 7.34 (br.d, *J* = 8.1 Hz, 1H, H-4), 7.21 (br.d, *J* = 7.9 Hz, 1H, H-7), 7.14 (dist.d, *J* = 1.8 Hz, 1H, H-2), 7.06 (br.t, *J* = 7.2 Hz, 1H, H-6), 7.00 (s, 1H, H-3""), 6.97 (br.t, *J* = 7.2 Hz, 1H, H-5), 6.94 (br.d, *J* = 7.7 Hz, 1H, H-5""), 3.27 (t, *J* = 7.1 Hz, 2H, CH_2-4'"), 2.87 (t, *J* = 7.4 Hz, 2H, CH_2-3'), 2.77 (t, *J* = 7.3 Hz, 2H, CH_2-1'), 2.47 (t, *J* = 7.2 Hz, 2H, CH_2-2'"), 2.23 (s, 3H, 4""-CH_3), 2.12 (s, 3H, 2""-CH_3), 2.06-2.01 (m, 4H, CH_2-2' & CH_2-3'"). ^{13}C-NMR (150 MHz, DMSO-d_6, δ, ppm): 170.51 (C-1'"), 168.32 (C-5"), 163.36 (C-2"), 136.79 (C-8), 134.63 (C-1""), 134.18 (C-2""), 132.22 (C-4""), 131.17 (C-5""), 127.50 (C-9), 126.80 (C-3""), 125.71 (C-6""), 122.97 (C-2), 121.35 (C-6), 118.66 (C-5 & C-7), 113.78 (C-3), 111.83 (C-4), 34.62 (C-2'"), 32.15 (C-4'"), 27.02 (C-1'), 25.68 (C-3'"), 24.77 (C-3'), 24.31 (C-2'), 20.91 (4""-CH_3), 18.20 (2""-

CH_3); Anal. Calc. for $C_{25}H_{28}N_4SO_2$ (448.19): C, 66.94; H, 6.29; N, 12.49. Found: C, 66.90; H, 6.26; N, 12.43. EI-MS (*m/z*): 448 $[M]^+$, 259 $(C_{13}H_{13}N_3SO)^+$, 200 $(C_{12}H_{12}N_2O)^+$, 190 $(C_{12}H_{16}NO)^+$, 186 $(C_{12}H_{12}NO)^+$, 184 $(C_{12}H_{12}N_2)^+$, 156 $(C_{11}H_{10}N)^+$, 143 $(C_{10}H_9N)^+$, 130 $(C_9H_8N)^+$, 91 $(C_6H_5N)^+$, 77 $(C_6H_5)^+$.

***N*-(2,6-Dimethylphenyl)-4-({5-[3-(1*H*-indol-3-yl)propyl]-1,3,4-oxadiazol-2-yl}sulfanyl)butanamide (8h)**. White colored amorphous powder; Yield: 85%; m.p: 88 °C; Mol. Formula: $C_{25}H_{28}N_4SO_2$; Mol. Weight: 448 g/mol; υ 3224 (N-H str.), 2940 (C-H str. of aromatic ring), 1673 (C=O str.), 1651 (C=N Str.), 1587 (C=C aromatic str.), 1521, 1476, 1415 (Str. for Oxadiazole), 1158 (C-O-C Str.), 641 (C-S str.) cm^{-1}; ^{1}H-NMR (600 MHz, DMSO-d_6, δ, ppm): 10.80 (s, 1H, NH-1), 9.29 (s, 1H, CONH), 7.52 (br.d, *J* = 7.4 Hz, 1H, H-7), 7.34 (br.d, *J* = 8.0 Hz, 1H, H-4), 7.14 (s, 1H, H-2), 7.12-7.05 (m, 4H, H-6, H-3"", H-4"" & H-5""), 6.97 (br.t, *J* = 7.4 Hz, 1H, H-5), 3.29 (t, *J* = 7.0 Hz, 2H, CH_2-4'"), 2.87 (br.t, *J* = 7.3 Hz, 2H, CH_2-3'), 2.78 (t, *J* = 7.2 Hz, 2H, CH_2-1'), 2.49 (t, *J* = 7.2 Hz, 2H, CH_2-2'"), 2.11 (s, 6H, 2""-CH_3 & 6""-CH_3), 2.07-2.01 (m, 4H, CH_2-2' & CH_2-3'"). ^{13}C-NMR (150 MHz, DMSO-d_6, δ, ppm): 170.21 (C-1'"), 168.34 (C-5"), 163.34 (C-2"), 136.79 (C-8), 135.62 (C-1""), 135.58 (C-2"" & C-6""), 128.05 (C-3"" & C-5""), 127.52 (C-9), 126.77 (C-4""), 122.97 (C-2), 121.35 (C-6), 118.66 (C-5 & C-7), 113.77 (C-3), 111.84 (C-4), 36.26 (C-2'"), 32.18 (C-4'"), 27.02 (C-1'), 25.79 (C-3'"), 24.78 (C-3'), 24.31 (C-2'), 18.53 (2""-CH_3 & 6""-CH_3); Anal. Calc. for $C_{25}H_{28}N_4SO_2$ (448.19): C, 66.94; H, 6.29; N, 12.49. Found: C, 66.89; H, 6.27; N, 12.45. EI-MS (*m/z*): 448 $[M]^+$, 259 $(C_{13}H_{13}N_3SO)^+$, 200 $(C_{12}H_{12}N_2O)^+$, 190 $(C_{12}H_{16}NO)^+$, 186 $(C_{12}H_{12}NO)^+$, 184 $(C_{12}H_{12}N_2)^+$, 156 $(C_{11}H_{10}N)^+$, 143 $(C_{10}H_9N)^+$, 130 $(C_9H_8N)^+$, 91 $(C_6H_5N)^+$, 77 $(C_6H_5)^+$.

***N*-(3,5-Dimethylphenyl)-4-({5-[3-(1*H*-indol-3-yl)propyl]-1,3,4-oxadiazol-2-yl}sulfanyl)butanamide (8i)**. Light Brown colored amorphous powder; Yield: 88%; m.p: 110-111 °C; Mol. Formula: $C_{25}H_{28}N_4SO_2$; Mol. Weight: 448 g/mol; IR (KBr, cm^{-1}): υ 3228 (N-H str.), 2941 (C-H str. of aromatic ring), 1675 (C=O str.), 1653 (C=N Str.), 1587 (C=C aromatic str.), 1523, 1479, 1416 (Str. for Oxadiazole), 1160 (C-O-C Str.), 643 (C-S str.) cm^{-1}; ^{1}H-NMR (600 MHz, DMSO-d_6, δ, ppm): 10.79 (s, 1H, NH-1), 9.78 (s, 1H, CONH), 7.51 (br.d, *J* = 9.2 Hz, 1H, H-7), 7.34 (br.d, *J* = 9.6 Hz, 1H, H-4), 7.20 (br.s, 2H, H-2"" & H-6""), 7.13 (dist.d, *J* = 2.5 Hz, 1H, H-2), 7.06 (br.t, *J* = 8.5 Hz, 1H, H-6), 6.97 (br.t, *J* = 8.5 Hz, 1H, H-5), 6.67 (br.s, 1H, H-4""), 3.26 (t, *J* = 8.6 Hz, 2H, CH_2-4'"), 2.85 (t, *J* = 8.8 Hz, 2H, CH_2-3'), 2.76 (t, *J* = 8.8 Hz, 2H, CH_2-1'), 2.44 (t, *J* = 8.7 Hz, 2H, CH_2-2'"), 2.21 (s, 6H, 3""-CH_3 &

5""-CH_3), 2.07-1.99 (m, 4H, CH_2-2' & CH_2-3'"). ^{13}C-NMR (150 MHz, DMSO-d_6, δ, ppm): 170.49 (C-1'"), 168.32 (C-5"), 163.34 (C-2"), 138.01 (C-1"", C-3"" & C-5""), 136.80 (C-8), 127.52 (C-9), 125.05 (C-4""), 122.97 (C-2), 121.35 (C-6), 118.65 (C-5 & C-7), 117.41 (C-2"" & C-6""), 113.78 (C-3), 111.83 (C-4), 35.19 (C-2'"), 32.12 (C-4'"), 27.00 (C-1'), 25.44 (C-3'"), 24.76 (C-3'), 24.30 (C-2'), 21.53 (3""-CH_3 & 5""-CH_3); Anal. Calc. for $C_{25}H_{28}N_4SO_2$ (448.19): C, 66.94; H, 6.29; N, 12.49. Found: C, 66.91; H, 6.25; N, 12.46. EI-MS (*m/z*): 448 $[M]^+$, 259 $(C_{13}H_{13}N_3SO)^+$, 200 $(C_{12}H_{12}N_2O)^+$, 190 $(C_{12}H_{16}NO)^+$, 186 $(C_{12}H_{12}NO)^+$, 184 $(C_{12}H_{12}N_2)^+$, 156 $(C_{11}H_{10}N)^+$, 143 $(C_{10}H_9N)^+$, 130 $(C_9H_8N)^+$, 91 $(C_6H_5N)^+$, 77 $(C_6H_5)^+$.

***N*-(2-Ethyl-6-methylphenyl)-4-({5-[3-(1*H*-indol-3-yl)propyl]-1,3,4-oxadiazol-2-yl}sulfanyl)butanamide (8j)**. Red colored amorphous powder; Yield: 91%; Melting Point 98-99 °C; Mol. Formula: $C_{26}H_{30}N_4SO_2$; Mol. Weight: 462 g/mol; IR (KBr, cm^{-1}): υ 3286 (N-H str.), 2945 (C-H aromatic str.), 1672 (C=O str.), 1650 (C=N Str.), 1599 (C=C aromatic str.), 1517, 1478, 1441 (Str. for Oxadiazole), 1159 (C-O-C str.), 689 (C-S str.); ^{1}H-NMR (600 MHz, DMSO-d_6, δ, ppm): 10.80 (s, 1H, NH-1), 7.95 (s, 1H, CONH), 7.51 (br.d, *J* = 9.3 Hz, 1H, H-7), 7.34 (br.d, *J* = 9.7 Hz, 1H, H-4), 7.18 (dist.d, *J* = 8.9 Hz, 1H, H-5""), 7.14 (br.s, 1H, H-2), 7.12-7.11 (m, *J* = 2H, H-3"" & H-4""), 7.07 (br.t, *J* = 8.5 Hz, 1H, H-6), 6.97 (br.t, *J* = 8.5 Hz, 1H, H-5), 2.89-2.74 (m, 6H, CH_2-1', CH_2-3' & CH_2-4'"), 2.44 (q, *J* = 9.0 Hz, 2H, 2""-$\underline{CH_2}CH_3$), 2.42 (t, *J* = 9.7 Hz, 2H, CH_2-2'"), 2.15 (quintet, *J* = 8.8 Hz, 2H, CH_2-2'), 2.11 (s, 3H, 6""-CH_3), 2.01 (quintet, *J* = 8.9 Hz, 2H, CH_2-3'"), 1.12 (t, *J* = 9.0 Hz, 3H, 2""-$CH_2\underline{CH_3}$). ^{13}C-NMR (150 MHz, DMSO-d_6, δ, ppm): 174.21 (C-1'"), 164.54 (C-5"), 162.78 (C-2"), 142.20 (C-1""), 136.81 (C-8), 136.33 (C-2"" & C-6""), 128.51 (C-4""), 128.29 (C-5""), 127.51 (C-9), 126.80 (C-3""), 122.95 (C-2), 121.36 (C-6), 118.70 (C-7), 118.66 (C-5), 113.51 (C-3), 111.84 (C-4), 36.23 (C-2'"), 31.24 (C-4'"), 26.40 (C-1'), 25.04 (C-3'"), 24.23 (C-3'), 24.01 (C-2'), 22.83 (2""-$\underline{CH_2}CH_3$), 17.83 (6""-CH_3), 14.30 (2""-$CH_2\underline{CH_3}$); Anal. Calc. for $C_{26}H_{30}N_4SO_2$ (462.21): C, 67.50; H, 6.54; N, 12.11. Found: C, 67.47; H, 6.50; N, 12.07. EI-MS (*m/z*): 434 M]$^+$, 259 $(C_{13}H_{13}N_3SO)^+$, 204 $(C_{13}H_{18}NO)^+$, 200 $(C_{12}H_{12}N_2O)^+$, 186 $(C_{12}H_{12}NO)^+$, 184 $(C_{12}H_{12}N_2)^+$, 156 $(C_{11}H_{10}N)^+$, 143 $(C_{10}H_9N)^+$, 130 $(C_9H_8N)^+$, 91 $(C_6H_5N)^+$, 77 $(C_6H_5)^+$.

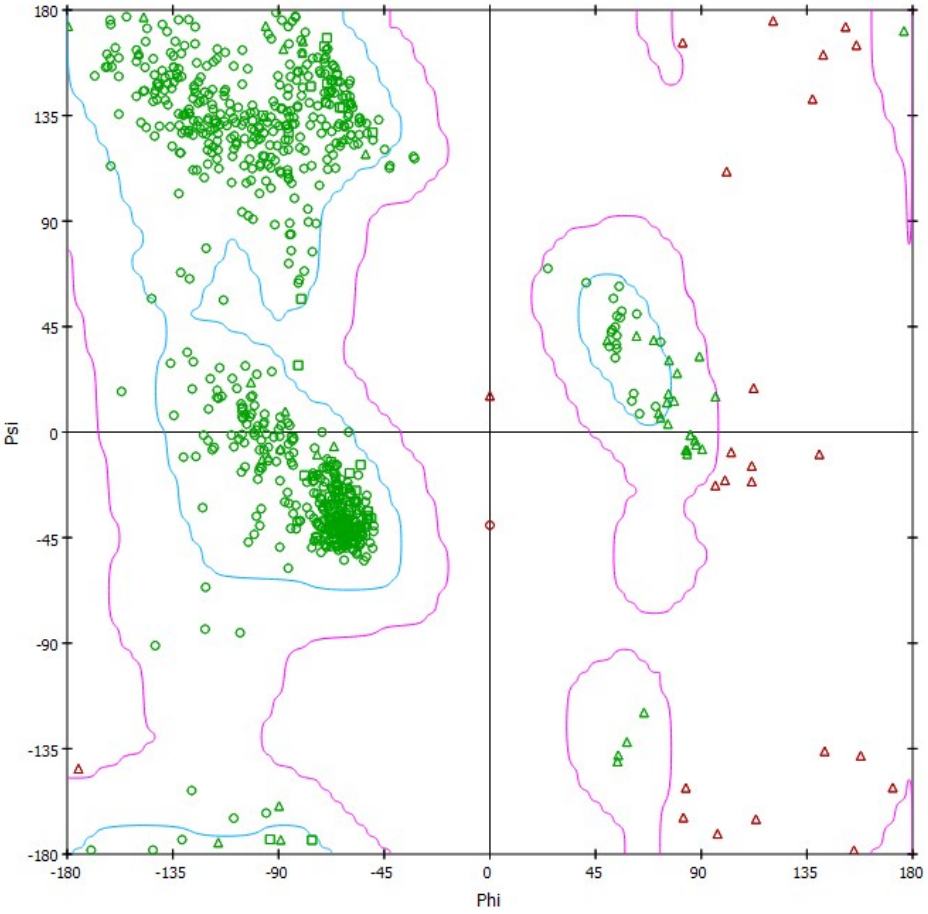

Figure S1. Ramachandran graph of jack bean urease. The region around cyan boundary is favoured region while around pink boundary is allowed region and outside pink boundary is dis-allowed part.

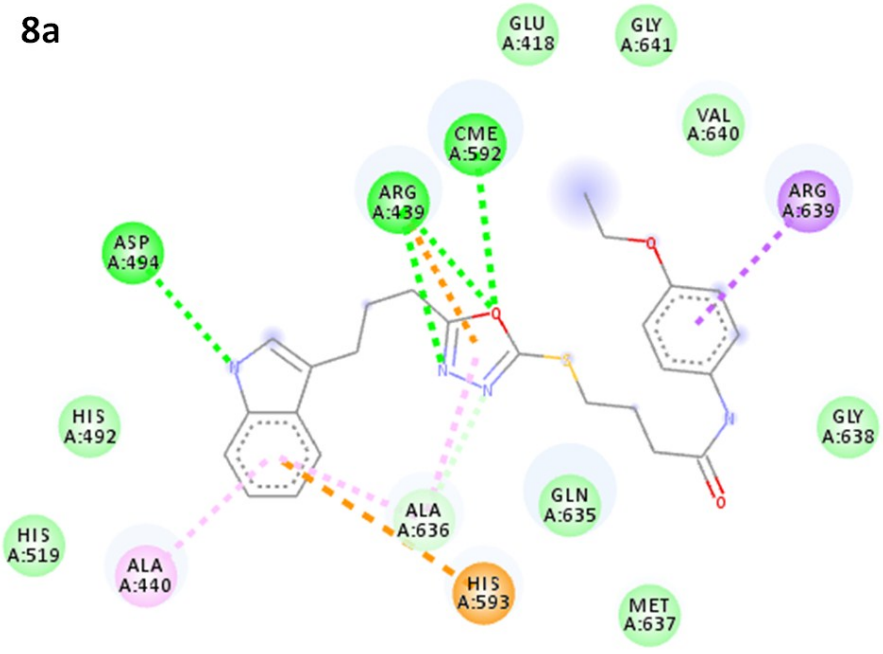

Figure S2: Docking complex of **8a** against urease.

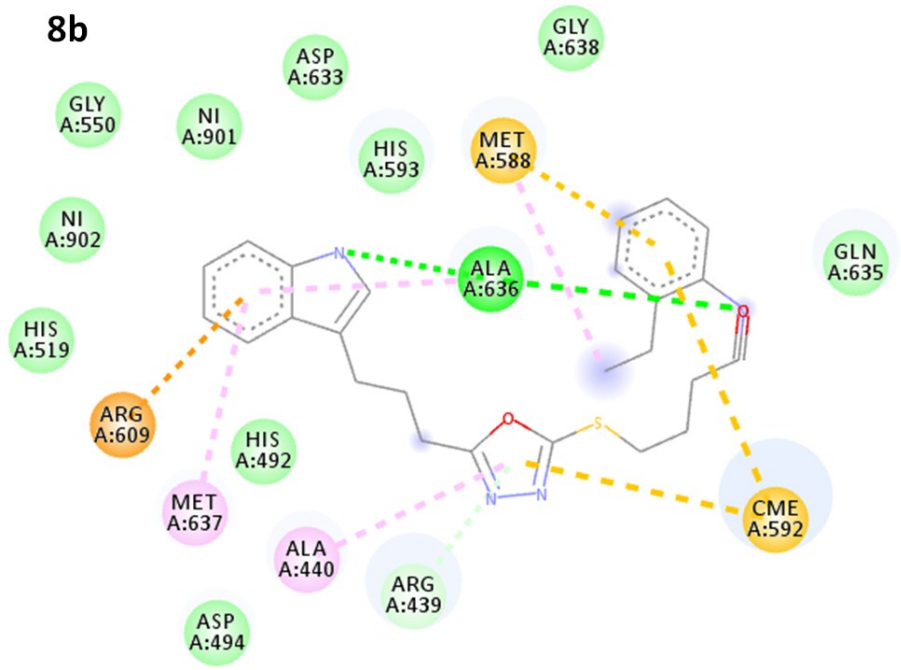

Figure S3: Docking complex of **8b** against urease.

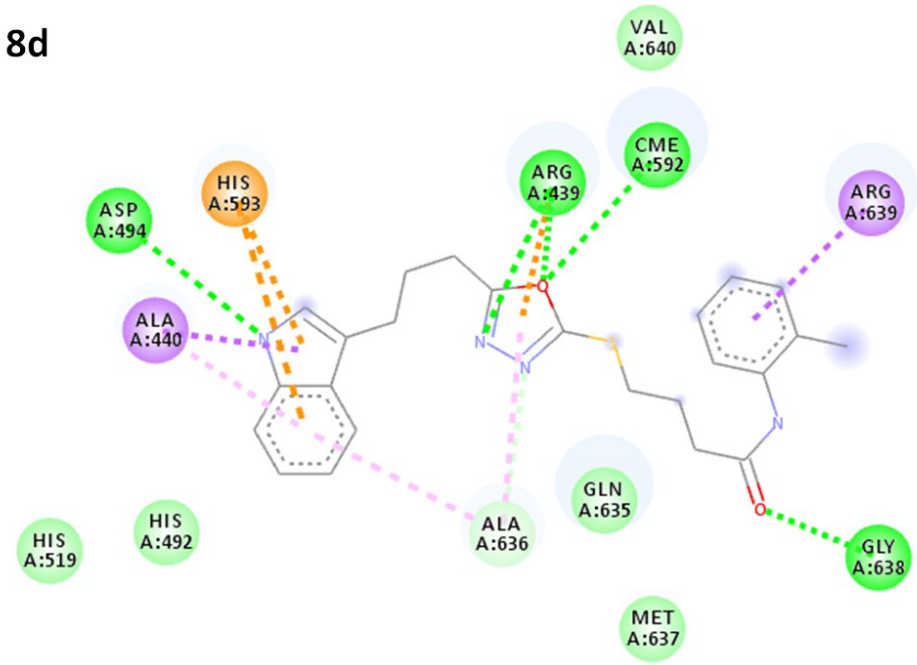

Figure S4: Docking complex of **8d** against urease.

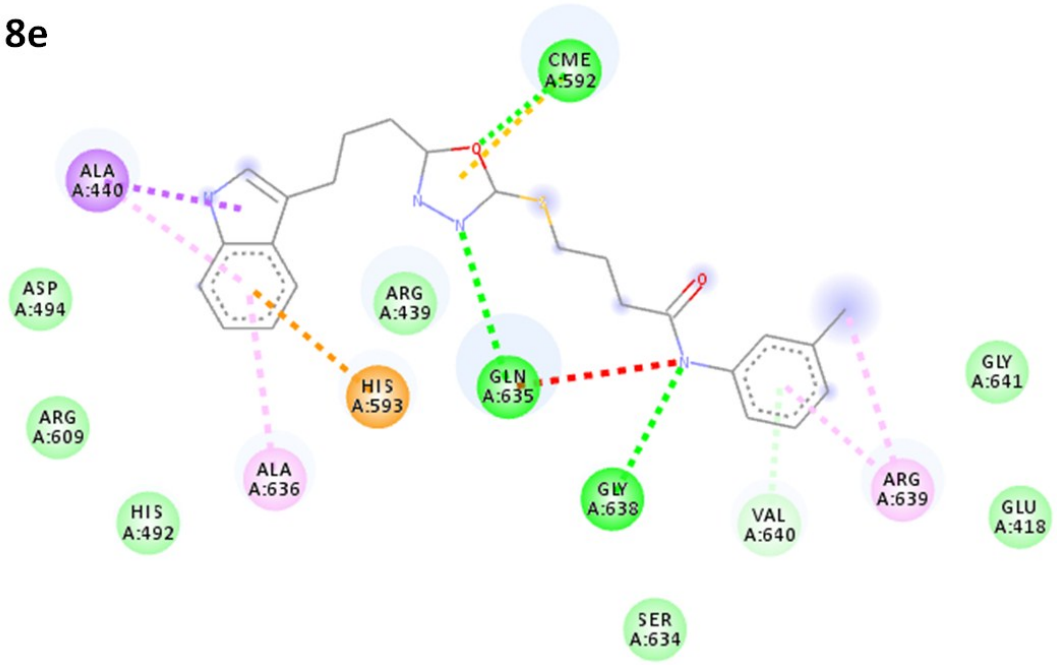

Figure S5: Docking complex of **8e** against urease.

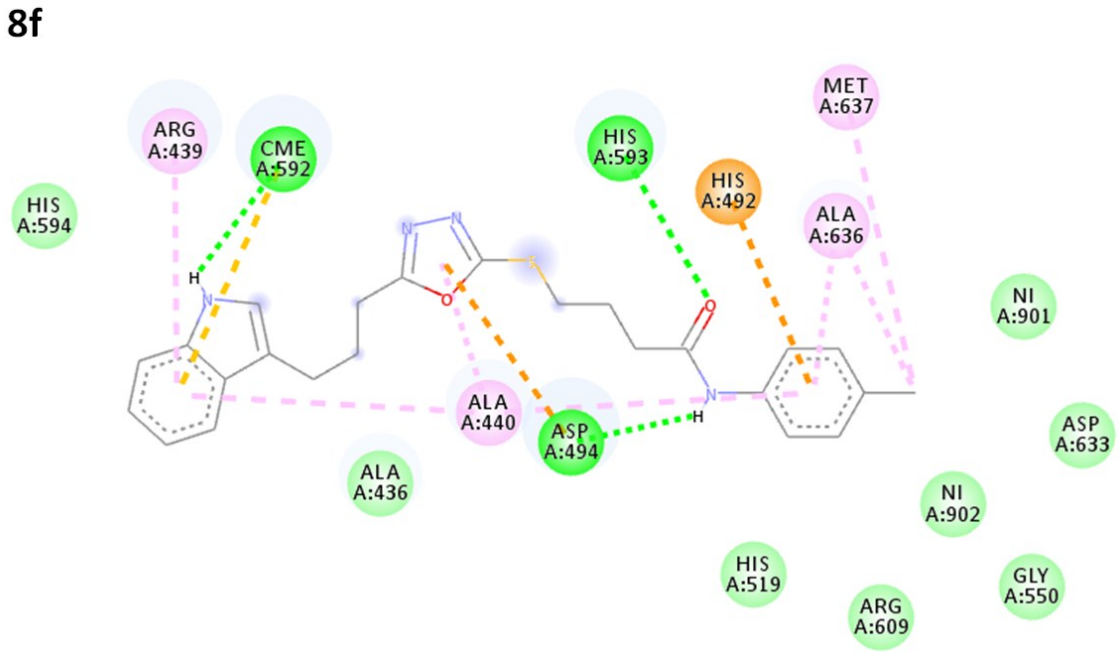

Figure S6: Docking complex of **8f** against urease.

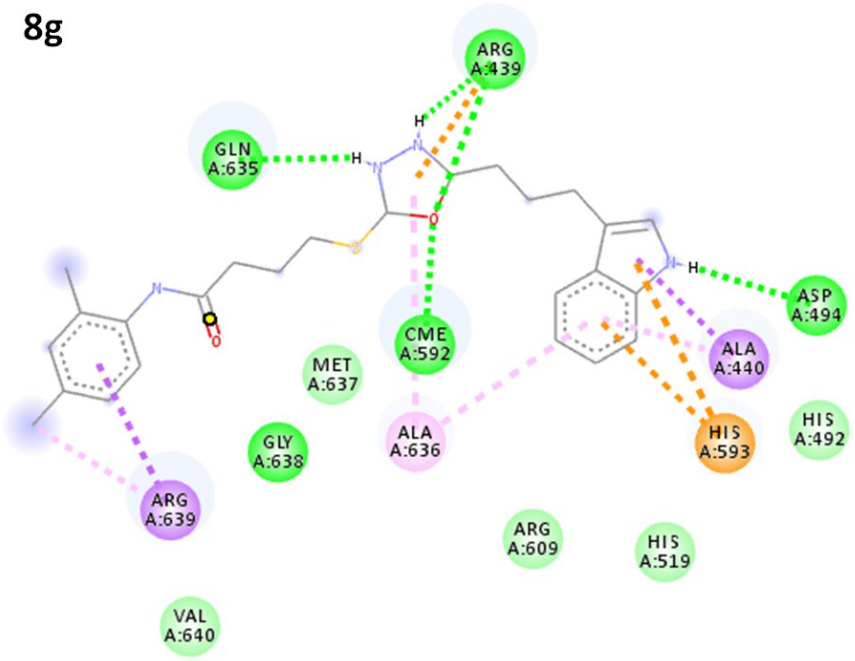

Figure S7: Docking complex of **8g** against urease.

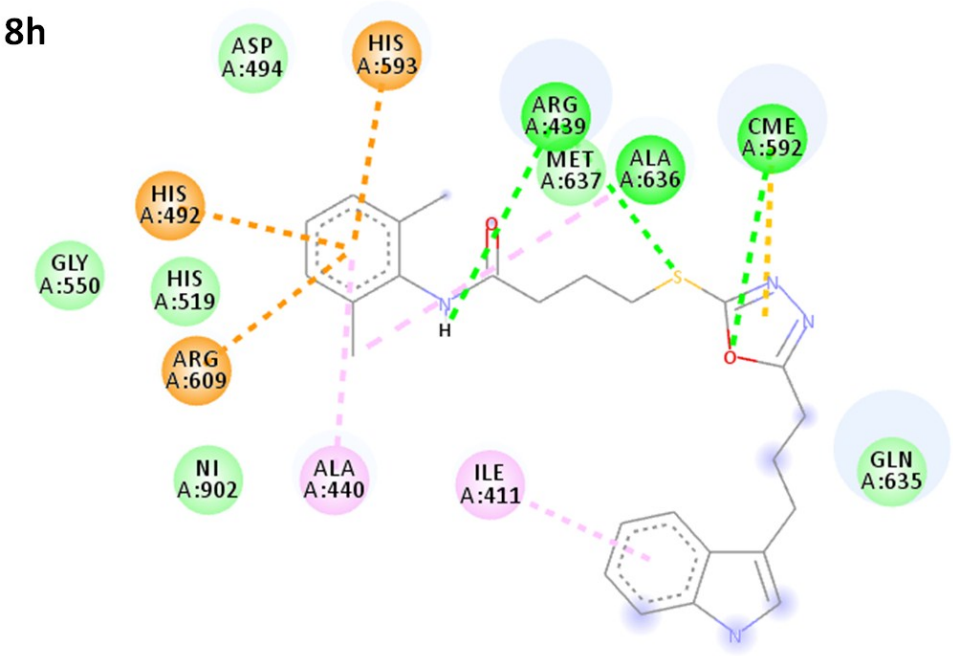

Figure S8: Docking complex of **8h** against urease.

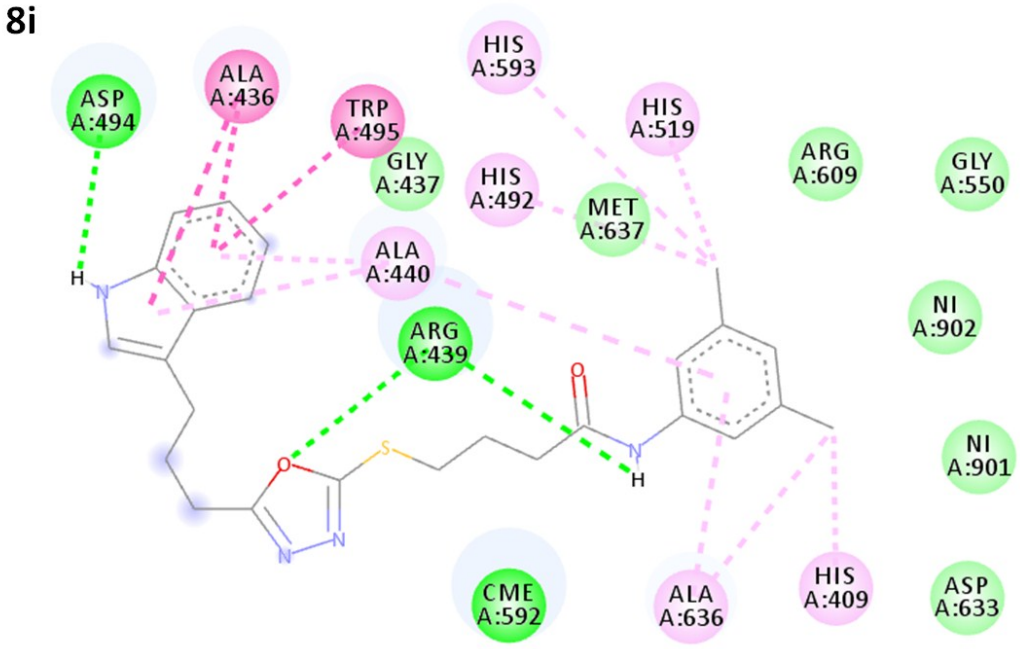

Figure S9: Docking complex of **8h** against urease.

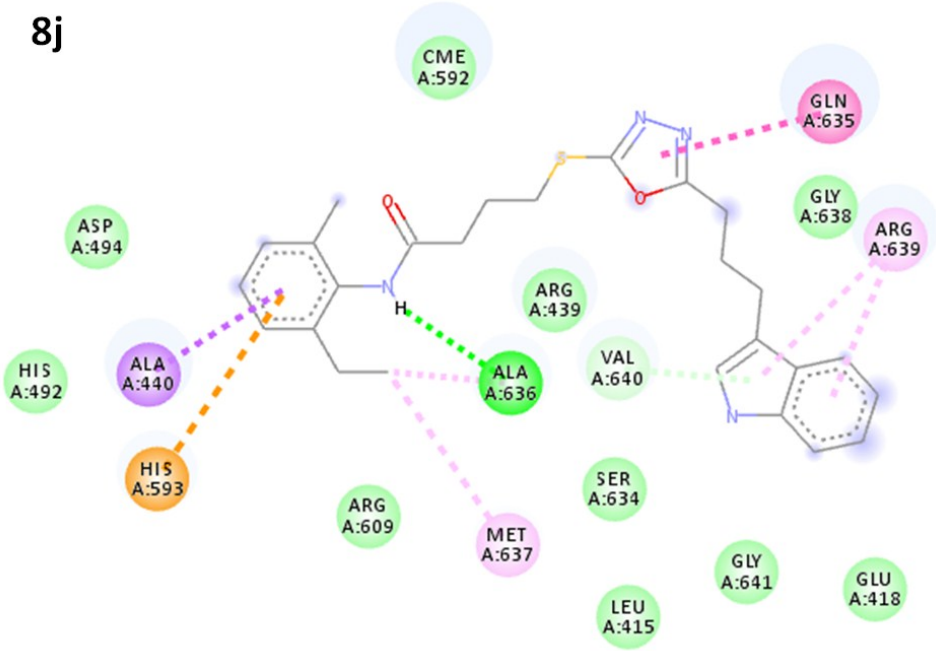

Figure S10: Docking complex of **8h** against urease.