

Synthesis, characterizations, anti-diabetic and molecular modeling approaches of hybrid indole-oxadiazole linked thiazolidinone derivatives

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S.1. Spectral Analysis

3-(4-Chlorophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one) 1 (Compound 1)

¹H NMR (600MHz, DMSO-*d*₆): δ 12.07 (s, 1H, H-Indole), 8.83 (dd, J = 7.26, 2.43 Hz, 1H, H-Indole), 8.56 (m, J = 6.5-7.5 Hz, 1H, H-Indole), 8.27 (d, J = 7.56 Hz, 2H, Ar-H), 7.84 (dd, J = 7.41, 2.81 Hz, 1H, H-Indole), 7.73 (d, J = 7.41 Hz, 2H, Ar-H), 7.49 (s, 1H, H-Indole), 7.29 (m, J = 6.3-7.3 Hz, 1H, H-Indole), 3.62 (t, J = 4.5 Hz, 1H, H-Aliphatic), 2.18 (s, 2H, H-Thiazolidinone), 2.02 (d, J = 4.3 Hz, 2H, H-Aliphatic); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 181.3, 164.0, 153.5, 151.8, 151.3, 151.1, 143.5, 141.0, 139.9, 136.5, 134.3, 130.7, 126.6, 124.5, 123.3, 121.0, 50.2, 34.4, 25.2; HREI MS : m/z calcd for C₂₂H₁₅ClF₃N₅O₂S [M]⁺ 505.90 Found 505.38

3-(3,5-Dichloro-2-hydroxyphenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one) (Compound 2)

¹H NMR (600MHz, DMSO-*d*₆): δ 12.73 (s, 1H, H-Indole), 9.53 (s, 1H, H-OH), 7.55 (dd, J = 7.26, 2.43 Hz, 1H, H-Indole), 7.53 (s, 1H, Ar-H), 7.37 (dd, J = 7.41, 2.81 Hz, 1H, H-Indole), 7.14 (s, 1H, H-Indole), 7.12 (s, 1H, Ar-H), 7.10 (m, J = 6.5-7.5 Hz, 1H, H-Indole), 7.07 (m, J = 6.3-7.3 Hz, 1H, H-Indole), 4.27 (t, J = 4.5 Hz, 1H, H-Aliphatic), 3.13 (s, 2H, H-Thiazolidinone), 2.25 (d, J = 4.3 Hz, 2H, H-Aliphatic); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 172.3, 163.7, 163.5, 155.7, 147.3, 136.2, 128.5, 127.5, 127.4, 126.4, 125.5, 123.5, 121.5, 121.3, 119.5, 118.5, 117.5, 113.5, 111.4, 50.4, 33.7, 19.3; HREI MS : m/z calcd for C₂₂H₁₄Cl₂F₃N₅O₃S [M]⁺ 556.34 Found 556.11

3-(2-Nitrophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one (Compound 3)

¹H NMR (600MHz, DMSO-*d*₆): δ 10.73 (s, 1H, H-Indole), 8.37 (dd, *J* = 7.41, 2.81 Hz, 1H, Ar-H), 7.95 (dd, *J* = 7.26, 2.43 Hz, 1H, Ar-H), 7.85 (m, *J* = 6.5-7.5 Hz, 1H, Ar-H), 7.75 (m, *J* = 6.3-7.3 Hz, 1H, Ar-H), 7.53 (dd, *J* = 7.26, 2.43 Hz, 1H, H-Indole), 7.37 (dd, *J* = 7.41, 2.81 Hz, 1H, H-Indole), 7.14 (s, 1H, H-Indole), 7.11 (m, *J* = 6.5-7.5 Hz, 1H, H-Indole), 7.07 (m, *J* = 6.3-7.3 Hz, 1H, H-Indole), 4.27 (t, *J* = 4.5 Hz, 1H, H-Aliphatic), 2.99 (s, 2H, H-Thiazolidinone), 2.25 (d, *J* = 4.3 Hz, 2H, H-Aliphatic); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 172.3, 163.7, 163.5, 155.7, 142.1, 136.2, 135.3, 135.1, 128.1, 127.4, 125.5, 125.3, 123.5, 122.3, 121.3, 119.5, 118.5, 113.5, 111.4, 50.4, 33.7, 19.3; HREI MS :*m/z* calcd for C₂₂H₁₅F₃N₆O₄S [M]⁺ 516.46 Found 516.12

3-(2-Methyl-5-nitrophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one (Compound 4)

¹H NMR (600MHz, DMSO-*d*₆): δ 11.93 (s, 1H, H-Indole), 8.52 (s, 1H, Ar-H), 7.94 (d, *J* = 7.41 Hz, 1H, Ar-H), 7.55 (dd, *J* = 7.26, 2.43 Hz, 1H, H-Indole), 7.54 (d, *J* = 7.56 Hz, 1H, Ar-H), 7.37 (dd, *J* = 7.41, 2.81 Hz, 1H, H-Indole), 7.14 (s, 1H, H-Indole), 7.10 (m, *J* = 6.5-7.5 Hz, 1H, H-Indole), 7.07 (m, *J* = 6.3-7.3 Hz, 1H, H-Indole), 3.99 (t, *J* = 4.5 Hz, 1H, H-Aliphatic), 3.21 (s, 2H, H-Thiazolidinone), 1.25 (d, *J* = 4.3 Hz, 2H, H-Aliphatic), 2.15 (s, 3H, H-Aliphatic); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 172.3, 163.7, 163.5, 155.7, 145.3, 140.3, 139.5, 136.2, 131.5, 130.4, 128.5, 127.5, 123.5, 121.5, 119.5, 118.5, 114.7, 113.5, 111.4, 50.4, 33.7, 19.3, 17.5; HREI MS :*m/z* calcd for C₂₃H₁₇F₃N₆O₄S [M]⁺ 530.48 Found 530.11

3-(4-Bromophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one (Compound 5)

¹H NMR (600MHz, DMSO-*d*₆): δ 11.98 (s, 1H, H-Indole), 7.67 (d, *J* = 7.41 Hz, 2H, Ar-H), 7.64 (d, *J* = 7.56 Hz, 2H, Ar-H), 7.55 (dd, *J* = 7.26, 2.43 Hz, 1H, H-Indole), 7.37 (dd, *J* = 7.41, 2.81 Hz, 1H, H-Indole), 7.14 (s, 1H, H-Indole), 7.10 (m, *J* = 6.5-7.5 Hz, 1H, H-Indole), 7.07 (m, *J* = 6.3-7.3 Hz, 1H, H-Indole), 4.28 (t, *J* = 4.5 Hz, 1H, H-Aliphatic), 2.98 (s, 2H, H-Thiazolidinone), 2.65 (d, *J* = 4.3 Hz, 2H, H-Aliphatic); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 178.2, 161.6, 150.8, 150.4, 150.3, 149.2, 141.5, 139.0, 137.9, 132.9, 129.2, 128.7, 125.0, 123.8, 122.3, 50.2, 33.5, 20.7; HREI MS :*m/z* calcd for C₂₂H₁₅BrF₃N₅O₂S [M]⁺ 550.35 Found 550.11

3-(4-Nitrophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one (Compound 6)

¹H NMR (600MHz, DMSO-*d*₆): δ 12.24 (s, 1H, H-Indole), 8.36 (d, *J* = 7.41 Hz, 2H, Ar-H), 8.28 (d, *J* = 7.56 Hz, 2H, Ar-H), 8.07 (dd, *J* = 7.26, 2.43 Hz, 1H, H-Indole), 7.83 (dd, *J* = 7.41, 2.81 Hz, 1H, H-Indole), 7.07 (s, 1H, H-Indole), 6.94 (m, *J* = 6.5-7.5 Hz, 2H, H-Indole), 3.57 (t, *J* = 4.5 Hz, 1H, H-Aliphatic), 2.35 (s, 2H, H-Thiazolidinone), 1.92 (d, *J* = 4.3 Hz, 2H, H-Aliphatic); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 172.1, 163.5, 162.1, 154.5, 152.5, 151.7, 137.3, 131.5, 129.3, 127.8, 122.8, 121.6, 121.3, 112.5, 111.2, 109.7, 104.1, 54.9, 33.7, 21.1; HREI MS :*m/z* calcd for C₂₂H₁₅F₃N₆O₄S [M]⁺ 516.46 Found 516.11

3-(4-Fluorophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one (Compound 7)

¹H NMR (600MHz, DMSO-*d*₆): δ 10.73 (s, 1H, H-Indole), 7.55 (dd, *J* = 7.26, 2.43 Hz, 1H, H-Indole), 7.53 (d, *J* = 7.41 Hz, 2H, Ar-H), 7.45 (d, *J* = 7.56 Hz, 2H, Ar-H), 7.37 (dd, *J* = 7.41, 2.81 Hz, 1H, H-Indole), 7.14 (s, 1H, H-Indole), 7.10 (m, *J* = 6.5-7.5 Hz, 1H, H-Indole), 7.07 (m, *J* = 6.3-7.3 Hz, 1H, H-Indole), 4.08 (t, *J* = 4.5 Hz, 1H, H-Aliphatic), 2.95 (s, 2H, H-Thiazolidinone), 2.34 (d, *J* = 4.3 Hz, 2H, H-Aliphatic); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 175.7, 161.3, 161.2, 160.2, 147.5, 141.5, 139.3, 137.8, 132.8, 128.6, 123.8, 122.3, 121.6, 120.6, 114.3, 113.8, 52.8, 35.1, 23.7; HREI MS :*m/z* calcd for C₂₂H₁₅F₄N₅O₂S [M]⁺ 489.45 Found 489.11

3-(4-Methoxyphenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one (Compound 8)

¹H NMR (600MHz, DMSO-*d*₆): δ 11.73 (s, 1H, H-Indole), 7.55 (dd, *J* = 7.26, 2.43 Hz, 1H, H-Indole), 7.37 (dd, *J* = 7.41, 2.81 Hz, 1H, H-Indole), 7.17 (d, *J* = 7.41 Hz, 2H, Ar-H), 7.14 (s, 1H, H-Indole), 7.12 (m, *J* = 6.5-7.5 Hz, 1H, H-Indole), 7.09 (d, *J* = 7.56 Hz, 2H, Ar-H), 7.07 (m, *J* = 6.3-7.3 Hz, 1H, H-Indole), 3.21 (t, *J* = 4.5 Hz, 1H, H-Aliphatic), 2.30 (s, 2H, H-Thiazolidinone), 1.85 (s, 3H, H-Aliphatic), 1.75 (d, *J* = 4.3 Hz, 2H, H-Aliphatic); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 172.3, 163.7, 163.5, 158.5, 155.7, 136.3, 129.6, 128.6, 128.5, 128.3, 127.5, 123.5, 121.5, 119.5, 118.5, 114.5, 114.3, 113.5, 111.4, 55.5, 50.4, 33.7, 19.3; HREI MS :*m/z* calcd for C₂₃H₁₈F₃N₅O₃S [M]⁺ 501.48 Found 501.11

3-(3-Chloro-2,5-dihydroxyphenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one (Compound 9)

¹H NMR (600MHz, DMSO-*d*₆): δ 11.84 (s, 1H, H-Indole), 9.54 (s, 1H, H-OH), 9.43 (s, 1H, H-OH), 7.55 (dd, *J* = 7.26, 2.43 Hz, 1H, H-Indole), 7.37 (dd, *J* = 7.41, 2.81 Hz, 1H, H-Indole), 7.14 (s, 1H, H-Indole), 7.12 (m, *J* = 6.5-7.5 Hz, 1H, H-Indole), 7.07 (m, *J* = 6.3-7.3 Hz, 1H, H-Indole), 7.05 (s, 1H, Ar-H), 7.03 (s, 1H, Ar-H), 4.27 (t, *J* = 4.5 Hz, 1H, H-Aliphatic), 3.56 (s, 2H, H-Thiazolidinone), 2.25 (d, *J* = 4.3 Hz, 2H, H-Aliphatic); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 172.3, 163.7, 163.5, 158.5, 155.7, 136.3, 129.6, 128.6, 128.5, 128.3, 127.5, 123.5, 121.5, 119.5, 118.5, 114.5, 114.3, 113.5, 111.4, 55.5, 50.4, 33.7, 19.3; HREI MS :*m/z* calcd for C₂₂H₁₅ClF₃N₅O₄S [M]⁺ 537.90 Found 537.41

3-(5-Chloro-2-methylphenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one (Compound 10)

¹H NMR (600MHz, DMSO-*d*₆): δ 12.03 (s, 1H, H-Indole), 7.85 (s, 1H, Ar-H), 7.55 (dd, *J* = 7.26, 2.43 Hz, 1H, H-Indole), 7.37 (dd, *J* = 7.41, 2.81 Hz, 1H, H-Indole), 7.25 (d, *J* = 7.41 Hz, 1H, Ar-H), 7.17 (d, *J* = 7.56 Hz, 1H, Ar-H), 7.14 (s, 1H, H-Indole), 7.12 (m, *J* = 6.5-7.5 Hz, 1H, H-Indole), 7.07 (m, *J* = 6.3-7.3 Hz, 1H, H-Indole), 4.27 (t, *J* = 4.5 Hz, 1H, H-Aliphatic), 4.02 (s, 2H, H-Thiazolidinone), 1.92 (d, *J* = 4.3 Hz, 2H, H-Aliphatic); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 172.3, 163.7, 163.5, 155.7, 139.3, 136.3, 132.7, 131.3, 130.2, 128.6, 127.5, 124.7, 123.5, 121.5, 121.3, 119.5, 118.5, 113.5, 111.4, 50.4, 33.7, 19.3, 17.3; HREI MS :*m/z* calcd for C₂₃H₁₇ClF₃N₅O₂S [M]⁺ 519.93 Found 519.41

3-(2,5-Dinitrophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one (Compound 11)

¹H NMR (600MHz, DMSO-*d*₆): δ 12.73 (s, 1H, H-Indole), 8.82 (s, 1H, Ar-H), 8.52 (d, *J* = 7.41 Hz, 1H, Ar-H), 8.25 (d, *J* = 7.56 Hz, 1H, Ar-H), 7.55 (dd, *J* = 7.26, 2.43 Hz, 1H, H-Indole), 7.37 (dd, *J* = 7.41, 2.81 Hz, 1H, H-Indole), 7.14 (s, 1H, H-Indole), 7.12 (m, *J* = 6.5-7.5 Hz, 1H, H-Indole), 7.07 (m, *J* = 6.3-7.3 Hz, 1H, H-Indole), 3.27 (t, *J* = 4.5 Hz, 1H, H-Aliphatic), 2.13 (s, 2H, H-Thiazolidinone), 1.82 (d, *J* = 4.3 Hz, 2H, H-Aliphatic); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 172.3, 163.7, 163.5, 155.7, 154.5, 148.3, 136.3, 136.1, 128.6, 127.5, 125.7, 123.5, 121.3, 120.5,

119.5, 118.5, 115.6, 113.5, 111.4, 50.4, 33.7, 19.3; HREI MS: m/z calcd for $C_{22}H_{14}F_3N_7O_6S [M]^+$ 561.45 Found 561.13

3-(3-Nitrophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one (Compound 12)

1H NMR (600MHz, DMSO- d_6): δ 12.28 (s, 1H, H-Indole), 8.46 (s, 1H, Ar-H), 7.87 (dd, $J = 7.41$, 2.34 Hz, 1H, Ar-H), 7.74 (dd, $J = 7.56$, 2.37 Hz, 1H, Ar-H), 7.62 (dd, $J = 7.13$, 2.42 Hz, 1H, Ar-H), 7.47 (dd, $J = 7.26$, 2.43 Hz, 1H, H-Indole), 7.08 (dd, $J = 7.41$, 2.81 Hz, 1H, H-Indole), 6.85 (s, 1H, H-Indole), 6.72 (m, $J = 6.5$ -7.5 Hz, 1H, H-Indole), 7.72 (m, $J = 6.3$ -7.3 Hz, 1H, H-Indole), 3.53 (t, $J = 4.5$ Hz, 1H, H-Aliphatic), 2.34 (s, 2H, H-Thiazolidinone), 2.08 (d, $J = 4.3$ Hz, 2H, H-Aliphatic); ^{13}C NMR (125 MHz, DMSO- d_6): δ 172.2, 167.6, 165.7, 157.5, 151.8, 148.3, 146.8, 136.8, 129.6, 126.5, 124.7, 121.7, 121.5, 112.3, 108.2, 106.6, 104.1, 51.2, 34.3, 21.7; HREI MS: m/z calcd for $C_{22}H_{15}F_3N_6O_4S [M]^+$ 516.46 Found 516.13

3-(3-Methoxyphenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one (Compound 13)

1H NMR (600MHz, DMSO- d_6): δ 12.73 (s, 1H, H-Indole), 7.55 (dd, $J = 7.26$, 2.43 Hz, 1H, H-Indole), 7.36 (dd, $J = 7.41$, 2.34 Hz, 1H, Ar-H), 7.32 (dd, $J = 7.41$, 2.81 Hz, 1H, H-Indole), 7.17 (s, 1H, H-Indole), 7.16 (dd, $J = 7.13$, 2.42 Hz, 1H, Ar-H), 7.12 (m, $J = 6.5$ -7.5 Hz, 1H, H-Indole), 7.07 (m, $J = 6.3$ -7.3 Hz, 1H, H-Indole), 7.05 (s, 1H, Ar-H), 7.01 (dd, $J = 7.56$, 2.37 Hz, 1H, Ar-H), 3.27 (t, $J = 4.5$ Hz, 1H, H-Aliphatic), 2.99 (s, 2H, H-Thiazolidinone), 1.74 (s, 3H, H-Aliphatic), 2.25 (d, $J = 4.3$ Hz, 2H, H-Aliphatic); ^{13}C NMR (125 MHz, DMSO- d_6): δ 172.3, 163.7, 163.5, 160.5, 155.7, 136.3, 136.1, 129.3, 128.6, 127.5, 123.5, 121.3, 120.1, 119.5, 118.5, 116.7, 113.5, 111.4, 104.4, 55.5, 50.4, 33.7, 19.3; HREI MS: m/z calcd for $C_{23}H_{18}F_3N_5O_3S [M]^+$ 501.48 Found 501.13

3-(3-Phenoxyphenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one (Compound 14)

1H NMR (600MHz, DMSO- d_6): δ 10.73 (s, 1H, H-Indole), 7.55 (dd, $J = 7.26$, 2.43 Hz, 1H, H-Indole), 7.45 (dd, $J = 7.26$, 2.43 Hz, 1H, Ar-H), 7.41 (dd, $J = 7.64$, 2.32 Hz, 2H, Ar-H), 7.37 (dd, $J = 7.41$, 2.81 Hz, 1H, H-Indole), 7.19 (m, $J = 6.5$ -7.5 Hz, 1H, Ar-H), 7.17 (dd, $J = 7.66$, 2.73 Hz, 1H, Ar-H), 7.14 (s, 1H, H-Indole), 7.10 (m, $J = 6.5$ -7.5 Hz, 1H, H-Indole), 7.09 (s, 1H, Ar-

H), 7.07 (m, $J = 6.3$ - 7.3 Hz, 1H, H-Indole), 7.06 (dd, $J = 7.56$, 2.18 Hz, 2H, Ar-H), 7.04 (dd, $J = 7.64$, 2.32 Hz, 1H, Ar-H), 3.40 (t, $J = 4.5$ Hz, 1H, H-Aliphatic), 2.96 (s, 2H, H-Thiazolidinone), 2.35 (d, $J = 4.3$ Hz, 2H, H-Aliphatic); ^{13}C NMR (125 MHz, DMSO- d_6): δ 172.3, 163.7, 163.5, 157.5, 157.3, 155.7, 136.2, 135.5, 128.7, 128.5, 128.3, 128.1, 127.5, 123.5, 121.7, 121.5, 121.3, 119.5, 118.5, 118.3, 118.1, 114.5, 113.5, 111.4, 107.5, 50.4, 33.7, 19.3; HREI MS : m/z calcd for $\text{C}_{28}\text{H}_{20}\text{F}_3\text{N}_5\text{O}_3\text{S}$ $[\text{M}]^+$ 563.56 Found 563.11

3-(2,5-Difluorophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one (Compound 15)

^1H NMR (600MHz, DMSO- d_6): δ 12.19 (s, 1H, H-Indole), 8.83 (s, 1H, Ar-H), 8.57 (s, 1H, H-Indole), 8.07 (dd, $J = 7.26$, 2.43 Hz, 1H, H-Indole), 7.85 (dd, $J = 7.41$, 2.81 Hz, 1H, H-Indole), 7.72 (d, $J = 7.41$, Hz, 1H, Ar-H), 7.49 (d, $J = 7.13$ Hz, 1H, Ar-H), 7.27 (m, $J = 6.5$ - 7.5 Hz, 1H, H-Indole), 7.22 (m, $J = 6.3$ - 7.3 Hz, 1H, H-Indole), 3.70 (t, $J = 4.5$ Hz, 1H, H-Aliphatic), 2.28 (s, 2H, H-Thiazolidinone), 1.54 (d, $J = 4.3$ Hz, 2H, H-Aliphatic); ^{13}C NMR (125 MHz, DMSO- d_6): δ 172.7, 161.9, 159.1, 158.1, 149.6, 141.5, 138.9, 137.9, 133.0, 132.9, 131.6, 131.0, 130.4, 129.2, 128.7, 122.7, 121.1, 54.1, 34.6, 20.6; HREI MS: m/z calcd for $\text{C}_{22}\text{H}_{14}\text{F}_5\text{N}_5\text{O}_2\text{S}$ $[\text{M}]^+$ 507.44 Found 507.13

S.2 Alpha-Glucosidase Activity Assay:

The inhibitory potential of Alpha-glucosidase was assessed using a well-established method [39]. Briefly, a 96-well plate was utilized, and each well received 35 μL of phosphate buffer, 31 μL of the tested compound solution (concentration range: 50-250 $\mu\text{g/mL}$), and 18 μL of [4-nitrophenyl- α -D glucopyranoside(p-NPG)] substrate. This mixture was then incubated at 37 $^\circ\text{C}$ for 5 minutes. Subsequently, 16 μL of α -glucosidase (0.15 U/mL) dissolved in sodium phosphate was introduced into each well, resulting in a total volume of 100 μL . The reaction was initiated by adding 100 μL of sodium carbonate (200 mM). The absorbance at 405 nm was measured using a microplate reader. This experimental procedure was conducted in triplicate, and a control group without the tested compound was included for comparison. Acarbose served as the standard reference drug. The percentage inhibition was calculated using the following equation, where "Abs" represents absorbance."

$$\% \text{ inhibition} = \frac{(\text{Abs control} - \text{Abs sample})}{\text{Abs control}} \times 100$$

S.3 Alpha-Amylase Activity Assay:

The inhibitory potential of α -Amylase enzyme was evaluated through the standard methodology [40]. A test tube containing (250 μ L) of the compound being tested at various concentrations (50 - 250 μ g/mL), (250 μ L) of [1% (w/v)] starch solution, and (250 μ L) of (1U/mL) alpha-amylase solution was prepared. Post-incubation at 20°C for 3 minutes, the enzymatic process was halted by adding (500 μ L) of dinitro salicylic acid (color Reagent). Following this, (250 μ L) of α -amylase was immediately introduced after heating the mixture in hot water. The mixture was subsequently subjected to heating at 85°C for duration of 15 minutes, followed by a 5-minute incubation period at room temperature. (4500 μ L) of distilled water was added, resulting in a final volume of (6000 μ L). Spectrophotometric analysis at 540 nm was conducted to determine absorbance. A control sample devoid of the test substance was prepared, and Acarbose served as the reference drug. The % inhibition equation is used for calculation.

S.4 Docking protocol

Protein data bank (PDB) was used a medium for retrieval of crystalline structure, optimizing the structure by the removal water molecules, co-factors and hetero-atoms and computing hydrogen bonds, charges and the missing atoms. Benzothiazole based sulfonamide derivatives used for docking studies were prepared and then optimized by the use of built and Ligand Preparation module implemented in Discovery Studio 2018 (Dassault Systemes BIOVIA, USA). Gold docking tool was used for docking analysis, Ligand preparation involves generating varied tautomer's, bond order assigning and stereochemistry. Furthermore, amylase active site was surrounded by the receptor grid choosing centroid of complexed ligand (Montbretin A). Radius of 12 Å around the Montbretin A binding site was defined for enzyme active site. Accomplishment of docking calculations was achieved using Chem PLP scoring function [41].

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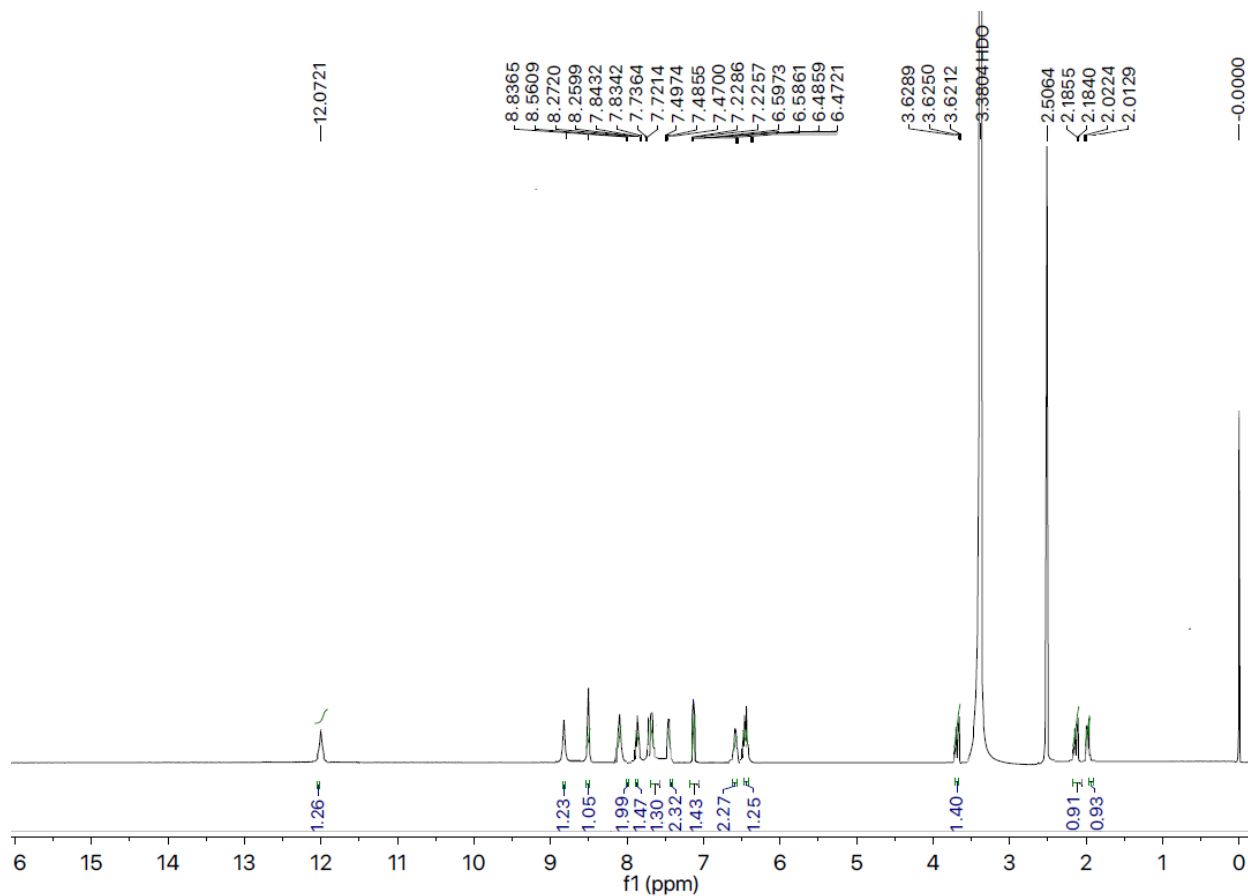


Figure S1. ¹H NMR for the compound **1** 3-(4-chlorophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one)

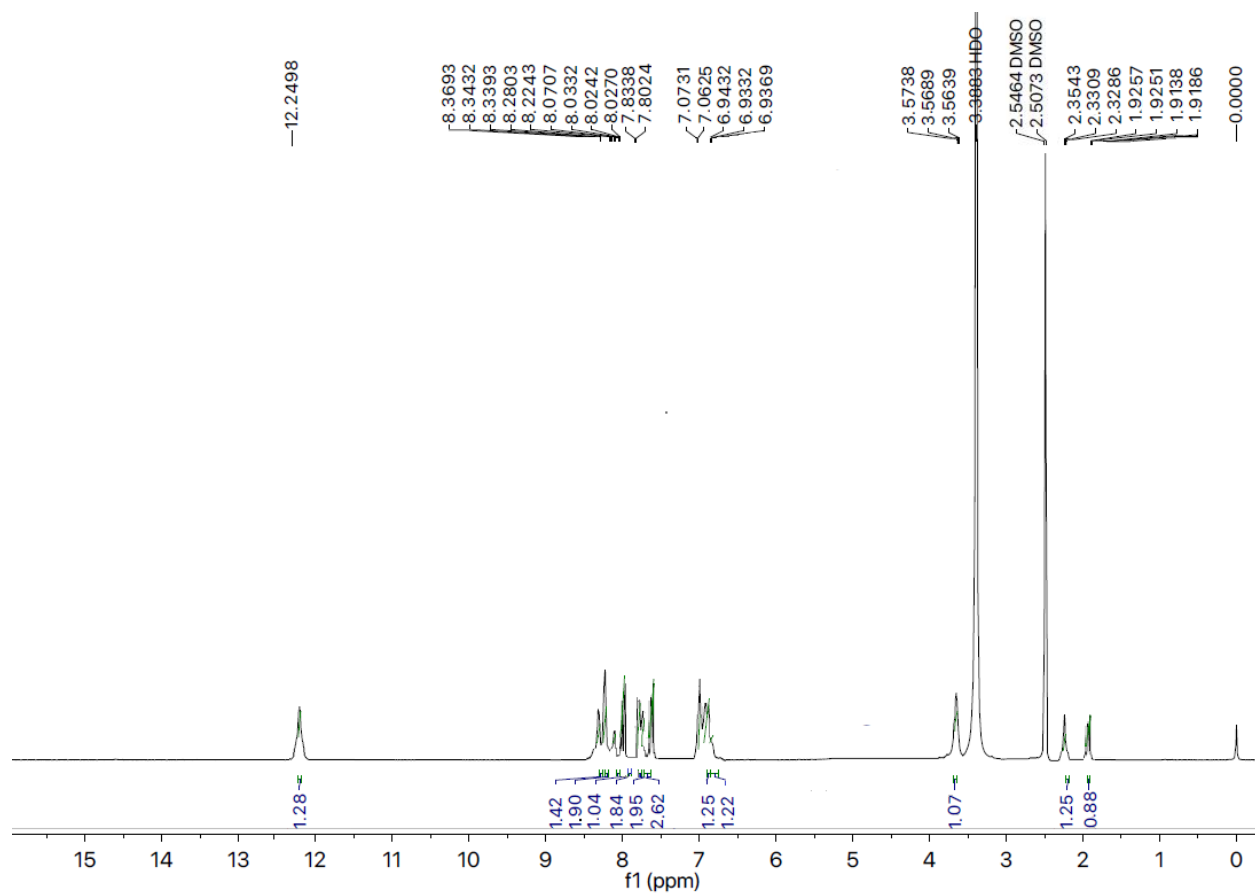


Figure S2. ^1H NMR for the compound **2** 3-(4-nitrophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one)

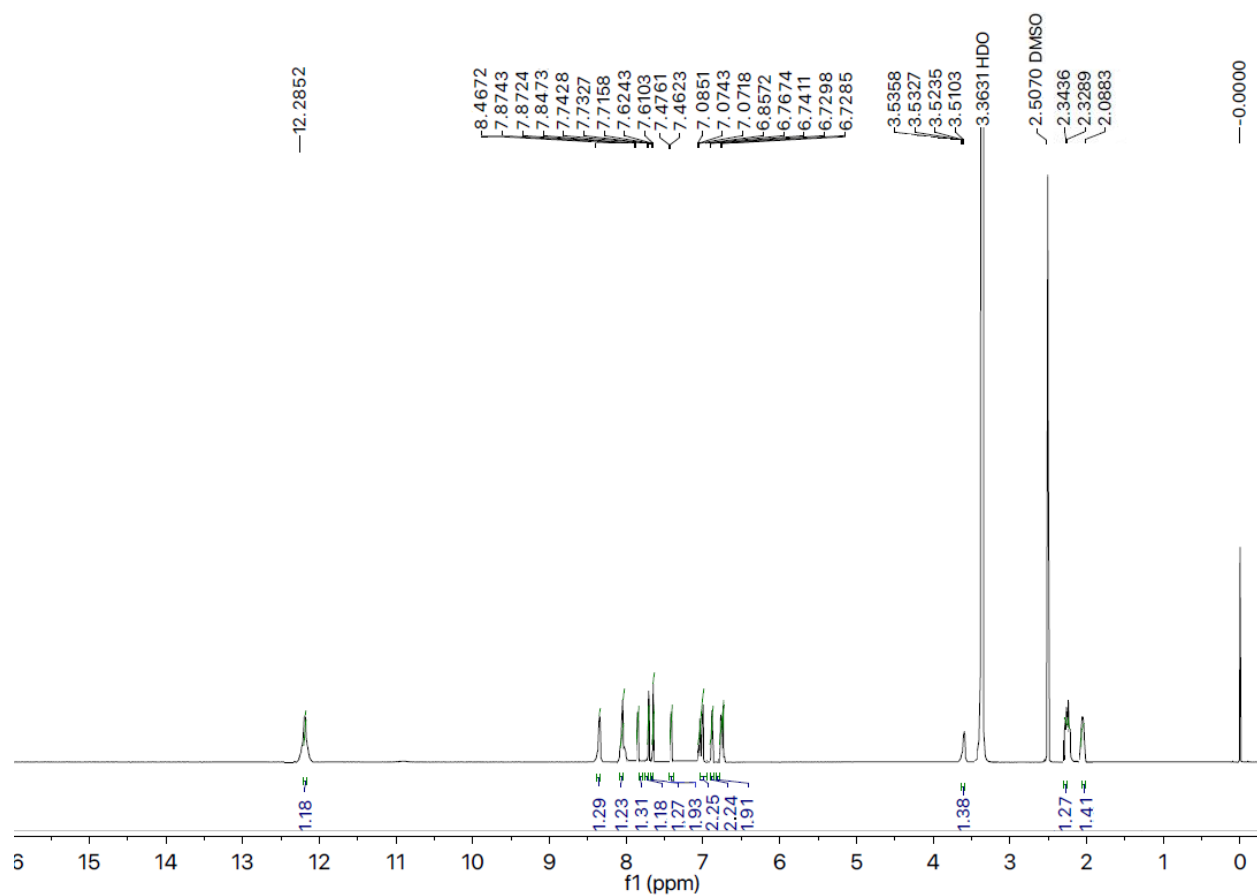


Figure S3. ¹H NMR for the compound **12** 3-(3-nitrophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one)

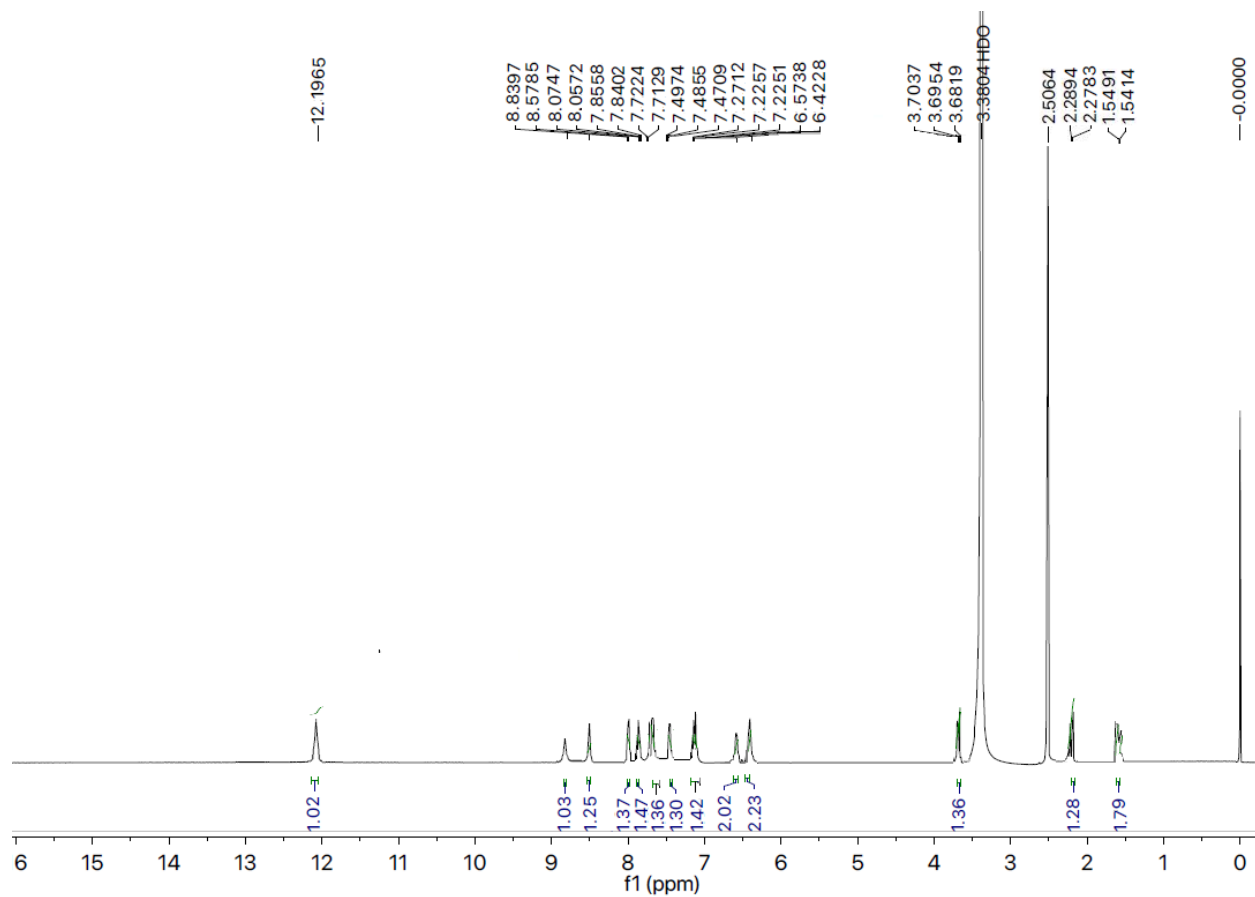


Figure S4. ¹H NMR for the compound **15** 3-(2,5-difluorophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one)

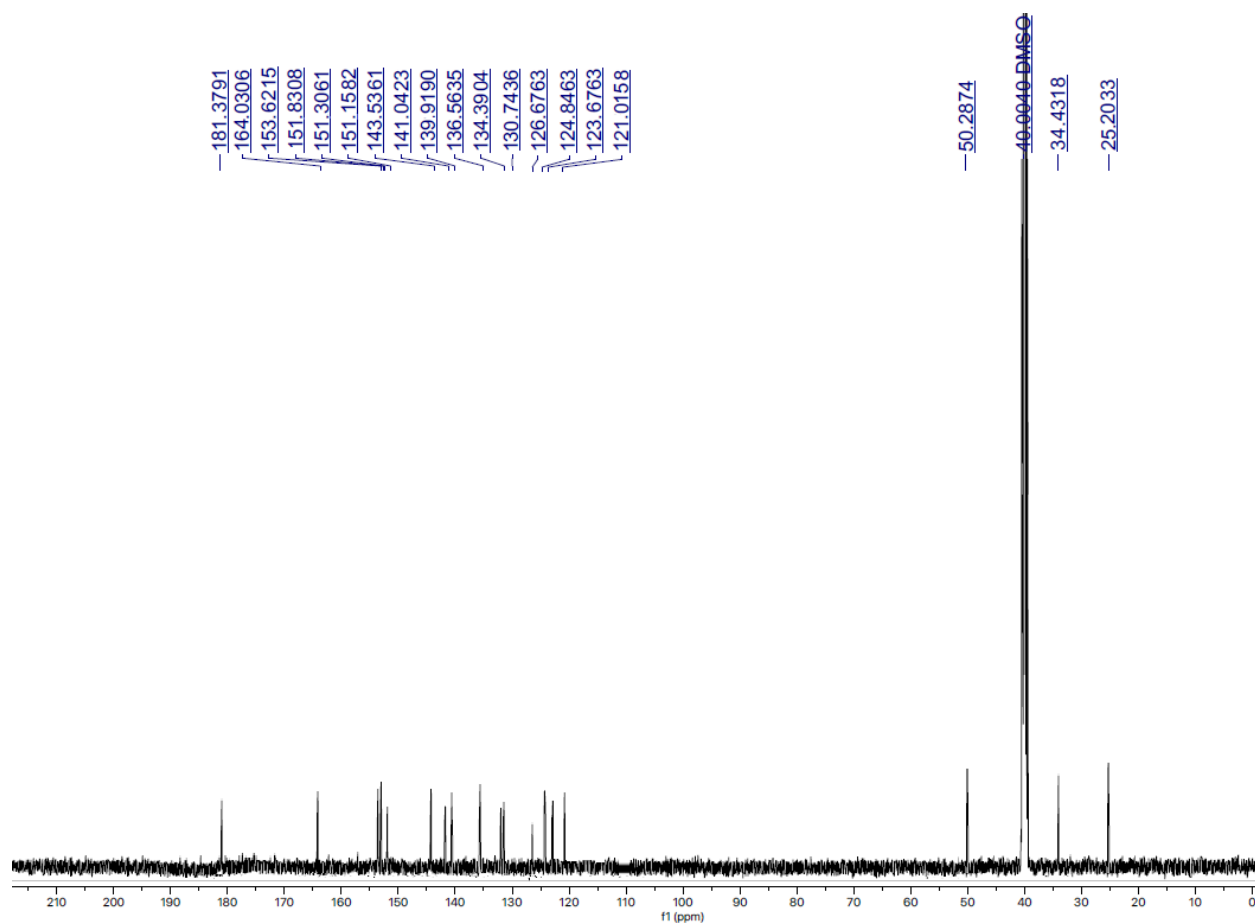


Figure S5. ^{13}C NMR for the compound **1** *3-(4-chlorophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one*

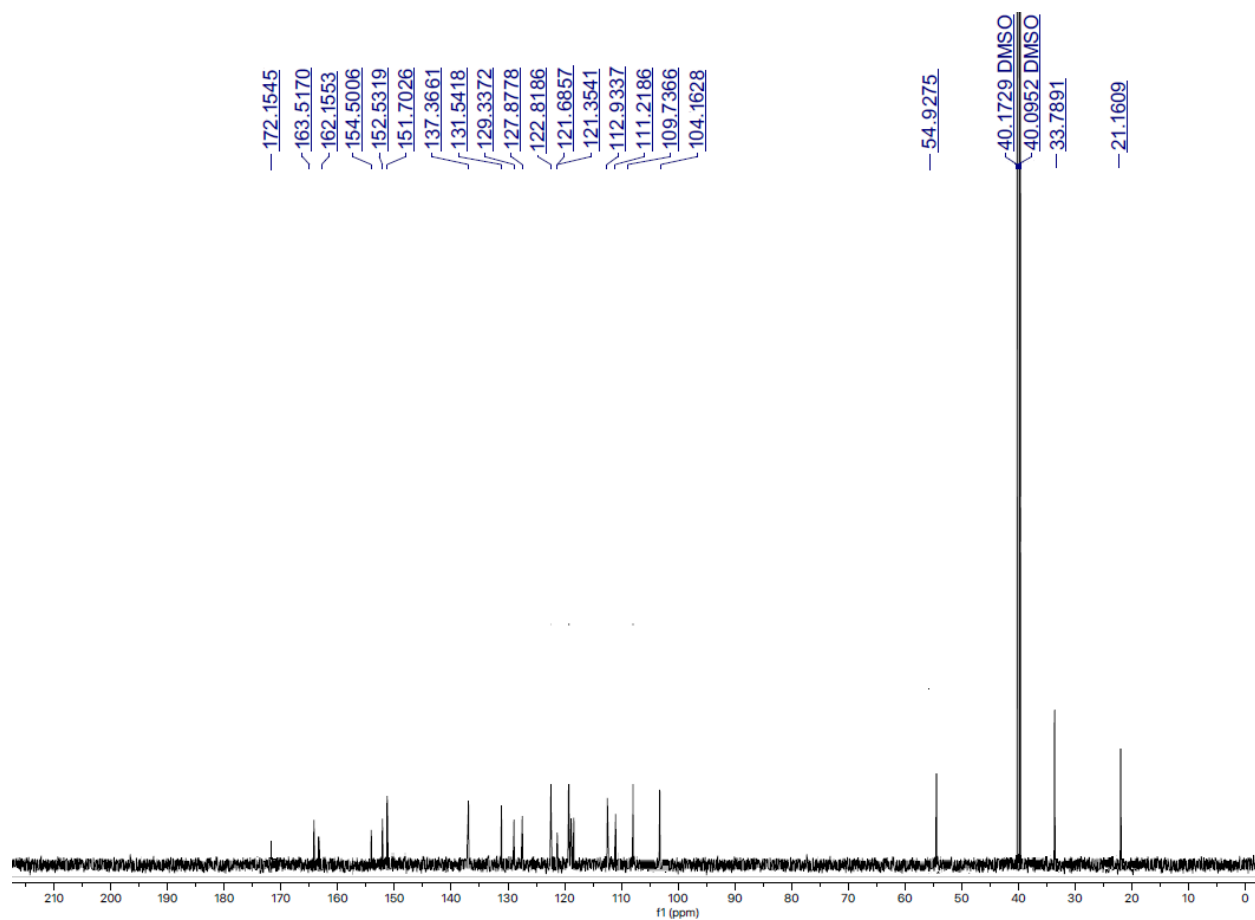


Figure S6. ^{13}C NMR for the compound **6** *3-(4-nitrophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one*

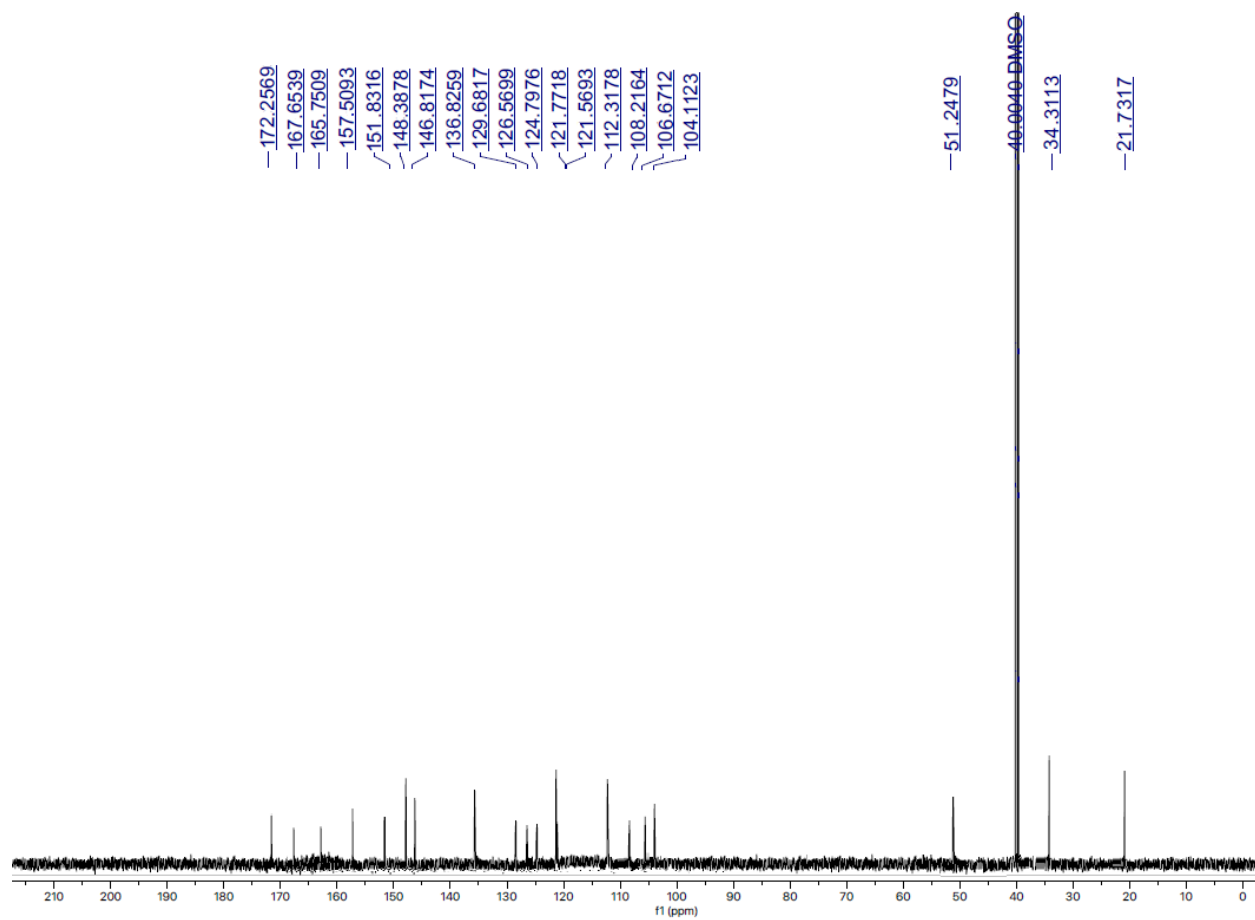


Figure S7. ^{13}C NMR for the compound **12** *3-(3-nitrophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one)*

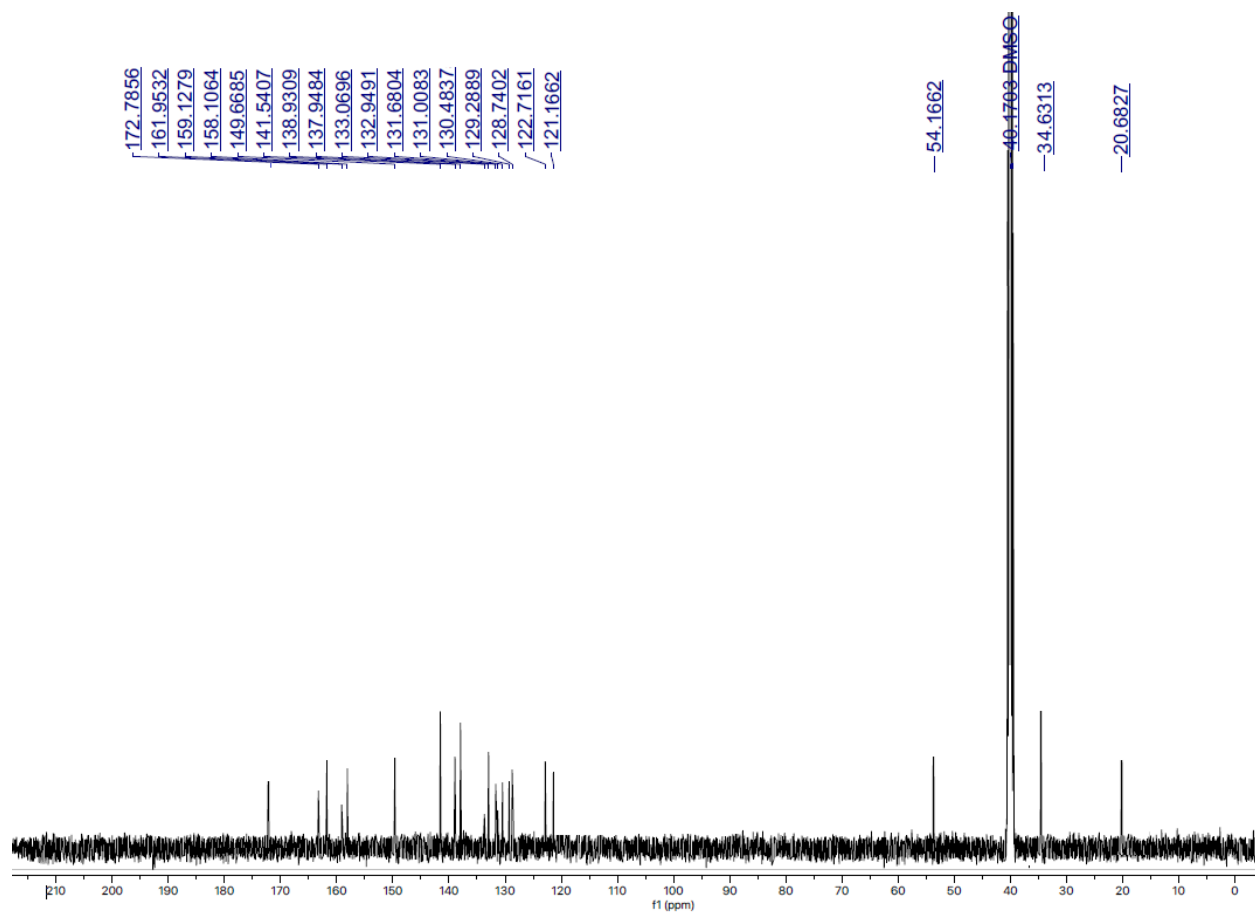


Figure S8. ¹³CNMR for the compound **15** 3-(2,5-difluorophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one)

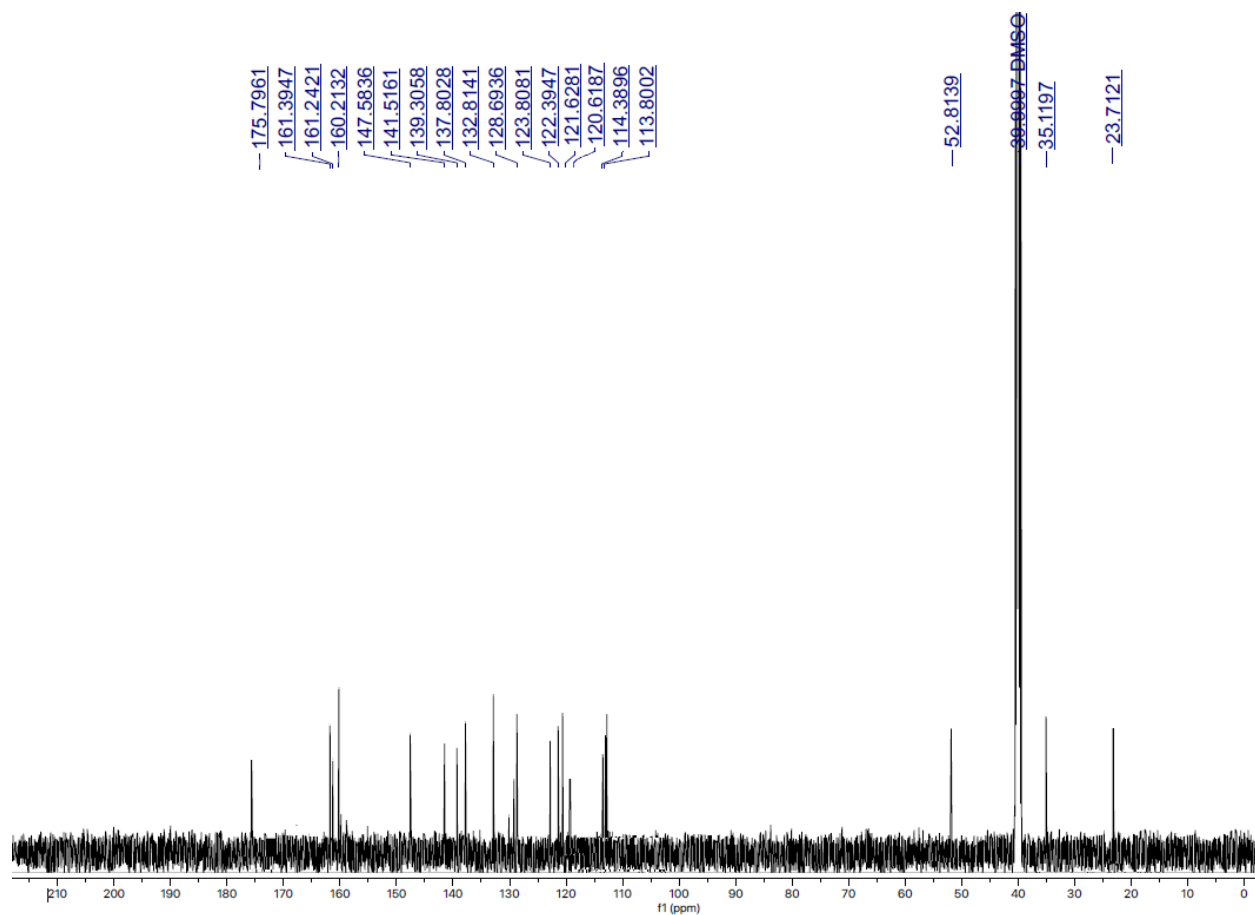


Figure S9. ^{13}C NMR for the compound **7** *3-(4-fluorophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one)*

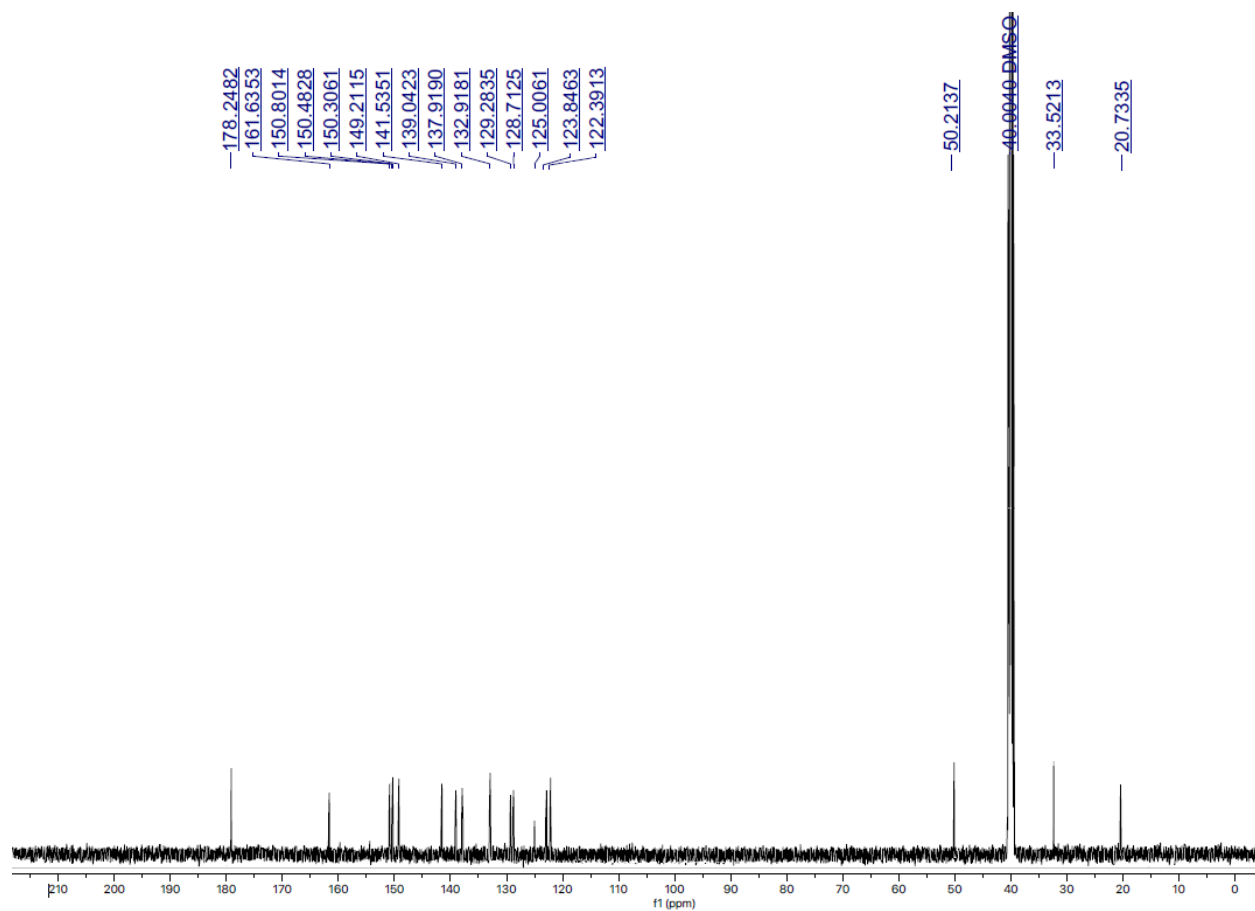


Figure S10. ¹³CNMR for the compound **5** *3-(4-bromophenyl)-2-((5-(3,3,3-trifluoro-2-(1H-indol-3-yl)propyl)-1,3,4-oxadiazol-2-yl)imino)thiazolidin-4-one)*