SUPPORTING INFORMATION

Design and Synthesis of Novel Spirocyclic oxindole Based Hybrid Scaffolds: In silico Docking Approach Towards Therapeutic Target Exploration

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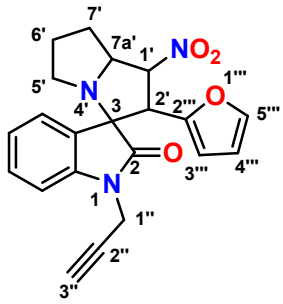
List of Contents

1. Characterization Data of the synthesized compounds:

2'-(Furan-2-yl)-1'-nitro-1-(prop-2-yn-1-yl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one. (6)



(6)

It was obtained as a brown solid with 90% Yield

Melting point: 130-132 ˚C

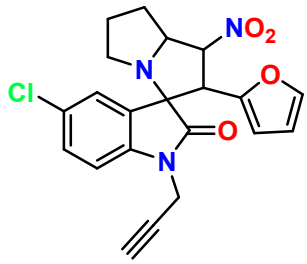
IR (KBr, cm^{-1}): 2950, 2351, 1616, 1490, 410

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88 (d, J = 6.3 Hz, 1H, *Fur- H*-5’’’), 7.48 – 7.33 (m, 2H, *Ar-H*), 7.15 (t, J = 7.6 Hz, 1H, *Ar-H*), 7.05 (d, J = 7.8 Hz, 1H, *Ar-H*), 6.20 (dd, J = 3.3, 1.8 Hz, 1H, *Fur-H-4’’’*), 6.19 – 6.10 (m, 1H, *Fur-H-3’’’*), 5.88 (d, J = 3.3 Hz, 1H, *CH-NO$_2$*), 4.78 (d, J = 10.6 Hz, 1H, *H-2’*), 4.65 – 4.55 (m, 1H, *H-7a’*), 4.41 (d, J = 5.2 Hz, 2H, *H-1’’*), 3.31 – 3.24 (m, 1H, *H-5’*), 3.21 (t, J = 2.4 Hz, 1H, *H-3’’*), 2.58 (t, J = 7.1 Hz, 1H, *H-5’*), 2.02 (m, 1H, *H-7’*) 1.95 – 1.84 (m, 1H, *H-6’*), 1.68 – 1.60 (m, 1H, *H-7’*), 1.41 – 1.31 (m, 1H, *H-6’*).

^{13}C NMR (100 MHz, DMSO-d_6) δ 174.74, 148.63, 143.34, 143.21, 130.72, 127.24, 124.60, 123.25, 111.05, 110.03, 107.71, 90.89, 77.96, 74.96, 72.79, 63.79, 51.01, 46.04, 28.96, 27.99, 25.65.

HRMS data: Calcd mass $(M+H)^{+}$: 378.1376, found, 378.1462

5-Chloro-2'-(furan-2-yl)-1'-nitro-1-(prop-2-yn-1-yl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one. (7).



(7)

It was obtained as a brown solid with 98% Yield.

Melting point: 135-137 ˚C

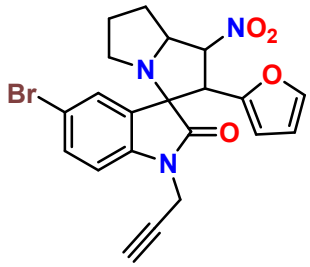
IR (KBr, cm^{-1}): 2940, 2363, 1611, 1489, 403

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.12 (d, 1H), 7.49 (d, J = 6.3 Hz, 1H), 7.39 (s, 1H), 7.07 (d, J = 8.4 Hz, 1H), 6.22 (d, J = 3.4 Hz, 1H), 6.16 (t, J = 10.0 Hz, 1H), 5.96 (d, J = 3.4 Hz, 1H), 4.89 (d, J = 10.6 Hz, 1H), 4.57 (m, 1H), 4.42 (d, J = 2.6 Hz, 2H), 3.31 (m, 1H), 3.21 (t, J = 5.0 Hz, 1H), 2.59 (t, J = 7.1 Hz, 1H), 1.99 (m, 1H), 1.89 (m, , 1H), 1.63 (m, 1H), 1.45 – 1.29 (m, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 174.44, 148.44, 143.33, 142.04, 130.55, 127.56, 127.51, 126.56, 111.36, 110.97, 107.83, 90.34, 77.54, 75.05, 72.81, 63.83, 50.83, 45.83, 29.05, 27.98, 25.62.

HRMS data: Calculated mass $(M+H)^+$:412.0986, found, 412.1051.

5-Bromo-2'-(furan-2-yl)-1'-nitro-1-(prop-2-yn-1-yl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one. (8)



(8)

It is obtained as dark brown solid with 92% Yield.

Melting point: 140-141 ˚C

IR (KBr, cm^{-1}): 2950, 2351, 1616, 1490, 409

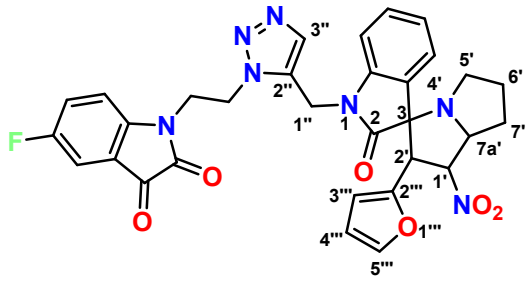
^{1}H NMR (400 MHz, DMSO-d_6) δ 8.24 (d, J = 1.9 Hz, 1H), 7.63 (dd, J = 8.4, 1.9 Hz, 1H), 7.50 – 7.28 (m, 1H), 7.03 (dd, J = 12.0, 7.6 Hz, 1H), 6.22 (dd, J = 8.1, 1.8 Hz, 1H), 6.18 – 6.11 (m, 1H), 5.94 (d, J = 3.3 Hz, 1H), 4.89 (d, J = 10.4 Hz, 1H), 4.64 – 4.50 (m, 1H), 4.41 (d, J =

4.5 Hz, 2H), 3.33 – 3.24 (m, 1H), 3.23 (t, 1H), 2.55 (t, *J* = 7.2 Hz, 1H), 1.98 (m, 1H), 1.89 (m, 1H), 1.69 – 1.55 (m, 1H), 1.36 (m, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 174.42, 148.55, 143.44, 142.54, 133.50, 130.30, 126.95, 115.26, 111.95, 111.05, 107.88, 90.33, 77.62, 75.18, 72.79, 63.86, 50.87, 45.81, 29.08, 28.04, 25.68.

HRMS data: Calcd mass $(M+H)^+$: 456.0481, found 456.0565.

5-Fluoro-1-(2-(5-((2'-(furan-2-yl)-1'-nitro-2-oxo-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-1-yl) methyl)-1*H*-1,2,3-triazol-1-yl) ethyl) indoline-2,3-dione. (11)



(11)

It is obtained as an orange solid with 80% Yield.

Melting point: 156-157˚C

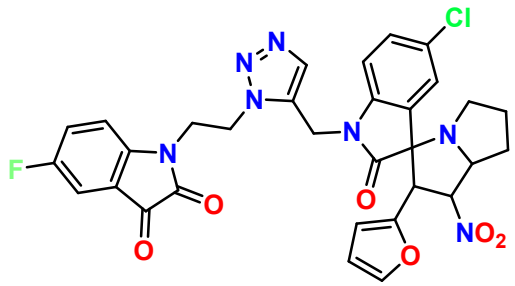
IR (KBr, cm^{-1}): 2940, 1737, 1611, 1489, 407

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.84 (d, 1H, *Fur- H-5'''*), 7.82 (s, 1H, *triazole-H*), 7.44 (dd, *J* = 7.0, 2.8 Hz, 1H, *Ar-H*), 7.35 (d, *J* = 7.8 Hz , 1H), 7.33 – 7.23 (m, 2H,), 7.10 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 6.78 (dd, *J* = 8.8, 3.8 Hz, 1H), 6.24 – 6.10 (m, 2H, *Fur- H-4''',H-3'''*), 5.83 (d, *J* = 3.4 Hz, 1H, *CH-NO_2*), 4.77 (d, *J* = 7.9 Hz, 1H, *H-2'*), 4.73 (t, *J* = 5.4 Hz, 2H, -*CH_2-CH_2-Isatin*), 4.63 (d, *J* = 7.8 Hz, 1H, *H-7a'*), 4.58 (t, *J* = 5.8 Hz, 2H, , -*CH_2-CH_2-Isatin*), 4.13 – 4.04 (m, 2H, *H-1''*), 3.27 (m, 1H, *H-5'*), 2.58 (t, *J* = 7.3 Hz, 1H, *H-5'*), 2.02 (dt, *J* = 14.3, 7.6 Hz, 1H, *H-7'*), 1.89 (m, *J* = 6.3 Hz, 1H, *H-6'*), 1.70 – 1.55 (m, 1H, *H-7'*), 1.41 – 1.29 (m, 1H, *H-6'*).

^{13}C NMR (100 MHz, DMSO-d_6) δ 181.72, 173.96, 158.99, 157.55, 156.58, 147.55, 145.83, 142.67, 142.14, 141.06, 129.51, 125.96, 123.46, 123.41, 123.22, 121.82, 117.54, 111.00, 110.76, 109.93, 108.84, 106.55, 89.76, 71.58, 62.70, 49.82, 46.29, 45.07, 33.71, 26.83, 24.51

HRMS data: Calcd mass $(M+H)^+$:612.1929, found, 612.2013.

1-(2-(5-((5-Chloro-2'-(furan-2-yl)-1'-nitro-2-oxo-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-1-yl) methyl)-1*H*-1,2,3-triazol-1-yl) ethyl)-5-fluoroindoline-2,3-dione. (12)



(12)

It is obtained as orange solid with 82% Yield.

Melting point: 156-156˚C

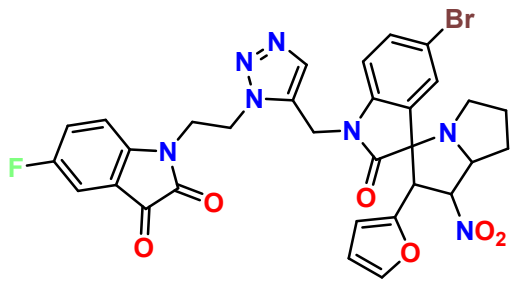
IR (KBr, cm^{-1}): 2940, 1740, 1606, 1488, 400

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.07 (d, J = 2.1 Hz, 1H), 7.85 (s, 1H), 7.44 (dd, J = 7.0, 2.8 Hz, 1H), 7.40 – 7.34 (m, 2H), 7.31 – 7.24 (m, 1H), 6.96 (d, J = 9.5 Hz, 1H), 6.80 (dd, J = 8.7, 3.7 Hz, 1H), 6.19 (d, J = 5.3 Hz, 1H), 6.15 (d, J = 9.5 Hz, 1H), 5.91 (d, J = 3.5 Hz, 1H), 4.85 (d, J = 10.6 Hz, 1H), 4.74 (t, J = 3.5 Hz, 2H), 4.62 (d, J = 8.5 Hz, 1H), 4.58 (t, J = 3.5 Hz, 2H), 4.09 (m, 2H), 3.33 – 3.26 (m, 1H), 2.58 (t, J = 7.4 Hz, 1H), 2.00 (m, J = 12.1, 7.8 Hz, 1H), 1.94 – 1.85 (m, 1H), 1.68 – 1.57 (m, 1H), 1.44 – 1.33 (m, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 182.75, 174.80, 160.05, 158.62, 157.65, 148.51, 146.89, 143.32, 142.63, 141.83, 130.44, 127.42, 127.20, 126.47, 124.56, 124.27, 118.62, 112.04, 111.34, 111.00, 107.78, 90.34, 79.64, 72.69, 63.83, 50.76, 47.37, 45.91, 34.84, 27.95, 25.61.

HRMS data: Calcd mass $(M+H)^+$: 646.1539, found, 646.1601.

1-(2-(5-((5-Bromo-2'-(furan-2-yl)-1'-nitro-2-oxo-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-1-yl) methyl)-1*H*-1,2,3-triazol-1-yl) ethyl)-5-fluoroindoline-2,3-dione. (13)



(13)

It was obtained as orange solid with 88% Yield.

Melting point: 165-167 ˚C

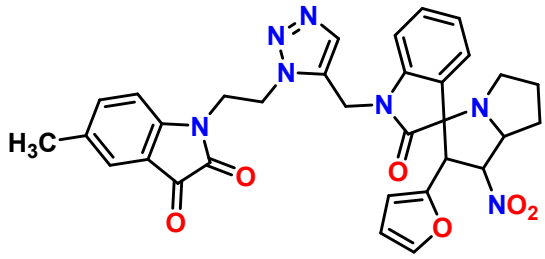
IR (KBr, cm^{-1}): 2937, 1741, 1606, 1488, 407

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.07 (d, J = 2.3 Hz, 1H), 7.84 (s, 1H), 7.45 – 7.41 (m, 1H), 7.39 – 7.34 (m, 2H), 7.30 – 7.23 (m, 1H), 6.96 (d, J = 8.5 Hz, 1H), 6.83 – 6.76 (m, 1H), 6.22 – 6.17 (m, 1H), 6.15 (d, J = 10.6 Hz, 1H), 5.90 (d, J = 3.4 Hz, 1H), 4.85 (d, J = 10.6 Hz, 1H), 4.73 (t, J = 4.0 Hz, 2H), 4.60 (s, 1H), 4.59 – 4.53 (m, 2H), 4.17 – 4.03 (m, 2H), 3.32 – 3.25 (m, 1H), 2.57 (t, J = 7.1 Hz, 1H), 2.05 – 1.95 (m, 1H), 1.89 (p, J = 6.3 Hz, 1H), 1.70 – 1.54 (m, 1H), 1.37 (m, J = 12.2, 6.1 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 182.78, 174.70, 160.04, 158.62, 157.65, 148.53, 146.89, 143.31, 143.05, 141.81, 133.31, 130.05, 126.80, 124.55, 124.27, 118.69, 118.62, 114.91, 112.05, 111.80, 111.00, 107.76, 90.30, 72.62, 63.82, 50.76, 47.37, 45.88, 34.81, 27.95, 25.62.

HRMS data: Calcd mass $(M+H)^+$:690.1034, found, 690.1121.

1-(2-(5-((2'-(Furan-2-yl)-1'-nitro-2-oxo-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-1-yl) methyl)-1*H*-1,2,3-triazol-1-yl) ethyl)-5-methylindoline-2,3-dione. (14)



(14)

It is obtained as Orange Solid with 78% Yield.

Melting point: 166-168 ˚C

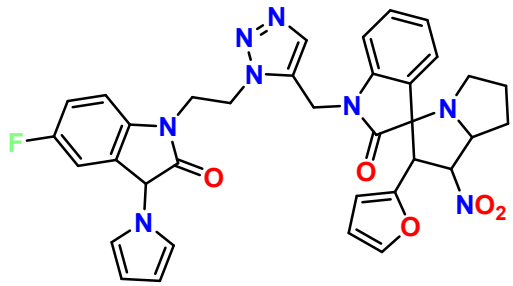
IR (KBr, cm^{-1}): 2974, 1730, 1635, 1484, 410.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.83 (d, J = 7.5 Hz, 1H), 7.78 (s, 1H), 7.34 (d, J = 5.0 Hz, 2H), 7.30 (d, J = 7.8 Hz, 1H), 7.23 (d, J = 9.9 Hz, 1H), 7.11 (t, J = 7.5 Hz, 1H), 6.93 (d, J = 7.9 Hz, 1H), 6.69 (d, J = 8.1 Hz, 1H), 6.25 – 6.09 (m, 2H), 5.82 (d, J = 3.4 Hz, 1H), 4.75 (s, 1H), 4.73 (d, J = 3.3 Hz, 2H), 4.63 (d, J = 7.9 Hz, 1H), 4.58 (t, J = 5.8 Hz, 2H), 4.05 (q, J = 5.6 Hz, 2H), 3.26 (q, J = 8.3 Hz, 1H), 2.57 (t, J = 7.3 Hz, 1H), 2.23 (s, 3H), 2.07 – 1.97 (m, 1H), 1.89 (p, J = 6.4 Hz, 1H), 1.62 (m, J = 13.3, 6.6 Hz, 1H), 1.44 – 1.29 (m, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 183.57, 175.06, 158.62, 148.59, 148.52, 143.72, 143.19, 142.13, 138.85, 133.15, 130.61, 127.00, 125.21, 124.48, 124.28, 122.90, 117.71, 111.01, 110.48, 109.90, 107.63, 90.82, 72.65, 63.78, 50.89, 47.37, 46.14, 34.83, 27.89, 25.57, 20.46.

HRMS data: Calcd mass $(M+H)^+$: 608.2179, found, 608.2273.

1-((1-(2-(5-Fluoro-2-oxo-3-(1*H*-pyrrol-1-yl) indolin-1-yl) ethyl)-1*H*-1,2,3-triazol-5-yl) methyl)-2'-(furan-2-yl)-1'-nitro-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one. (15)



(15)

It was obtained as a white solid with 70% Yield.

Melting point: 159-161˚C

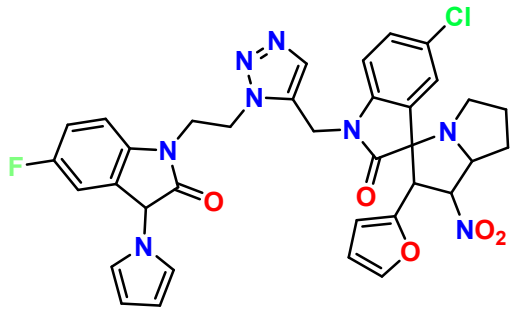
IR (KBr, cm^{-1}): 2940, 1606, 1488, 400

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.84 (d, J = 7.4 Hz, 1H), 7.76 (d, J = 33.9 Hz, 1H), 7.41 – 7.24 (m, 2H), 7.16 – 7.06 (m, 1H), 6.95 (d, J = 9.4 Hz, 2H), 6.93 – 6.83 (m, 1H), 6.80 – 6.72 (m, 1H), 6.67 (dd, J = 4.3, 2.1 Hz, 2H), 6.24 – 6.15 (m, 2H), 6.11 (s, 1H), 6.08 (s, 1H), 5.90 (s, 1H), 5.87 – 5.78 (m, 1H), 4.77 (s, 1H), 4.75 – 4.70 (m, 2H), 4.66 (d, J = 11.8 Hz, 1H), 4.62 (t, J = 6.5 Hz, 2H), 4.21 – 4.02 (m, 2H), 3.31 – 3.22 (m, 1H), 2.59 (t, J = 7.2 Hz, 1H), 2.02 (m, J = 13.3, 6.8 Hz, 1H), 1.88 (m, J = 6.1 Hz, 1H), 1.69 – 1.57 (m, 1H), 1.37 (m, J = 12.1, 6.1 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 173.98, 171.61, 158.99, 156.62, 147.55, 142.67, 142.64, 142.19, 142.14, 141.13, 138.02, 129.52, 126.56, 125.98, 123.44, 123.10, 122.99, 121.83, 119.94, 115.18, 114.95, 111.75, 111.48, 109.98, 109.94, 109.17, 109.09, 108.87, 108.10, 106.62, 106.57, 89.76, 89.71, 71.61, 62.71, 58.94, 49.82, 46.16, 45.08, 33.74, 26.85, 24.51.

HRMS data: Calcd mass $(M+H)^+$: 663.2401, found, 663.2481.

5-Chloro-1-((1-(2-(5-fluoro-2-oxo-3-(1*H*-pyrrol-1-yl) indolin-1-yl) ethyl)-1*H*-1,2,3-triazol-5-yl) methyl)-2'-(furan-2-yl)-1'-nitro-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one. (16)



(16)

It was obtained as a white solid with 73% Yield.

Melting point: 169-171˚C

IR (KBr, cm^{-1}): 2962, 1626, 1484, 393.

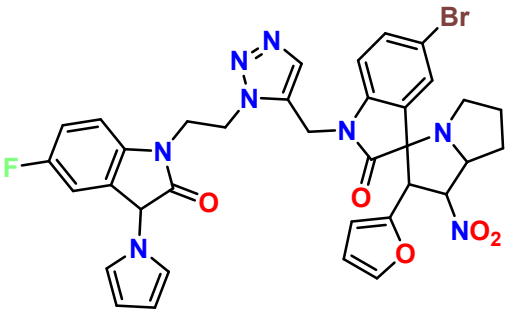
^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20 (d, 1H), 7.81 (s, 1H), 7.56 – 7.42 (m, 1H), 7.38 (dd, J = 12.0, 2.8 Hz, 1H), 7.03 – 6.91 (m, 2H), 6.88 (dd, J = 14.4, 8.5 Hz, 1H), 6.83 – 6.74 (m, 1H), 6.74 – 6.50 (m, 2H), 6.23 – 6.14 (m, 2H), 6.14 – 6.10 (m, 1H), 6.10 – 6.06 (m, 1H), 5.96 – 5.91

(m, 1H), 5.86 (td, J = 6.7, 3.3 Hz, 1H), 4.87 (d, J = 12.8 Hz, 1H), 4.85 – 4.70 (m, 2H), 4.68 (d, J = 4.0 Hz, 1H), 4.63 – 4.47 (m, 2H), 4.12 (m, 2H), 3.33 – 3.19 (m, 1H), 2.57 (t, J = 6.1 Hz, 1H), 1.99 (m, J = 7.1 Hz, 1H), 1.90 (m, 1H), 1.61 (m, 1H), 1.37 (m, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 174.82, 172.67, 160.07, 157.69, 148.53, 143.38, 142.63, 141.91, 139.07, 130.47, 127.42, 127.20, 126.49, 124.22, 124.10, 121.01, 116.22, 115.99, 112.78, 112.55, 111.39, 111.06, 110.25, 109.17, 107.86, 90.35, 72.72, 63.84, 60.02, 50.77, 47.24, 45.92, 34.89, 27.97, 25.60.

HRMS data: Calcd mass $(M+H)^+$:697.2012, found, 697.2074.

5-Bromo-1-((1-(2-(5-fluoro-2-oxo-3-(1*H*-pyrrol-1-yl) indolin-1-yl) ethyl)-1*H*-1,2,3-triazol-5-yl) methyl)-2'-(furan-2-yl)-1'-nitro-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one. (17)



(17)

It was obtained as a white solid with 72% Yield.

Melting point: 171-172˚C

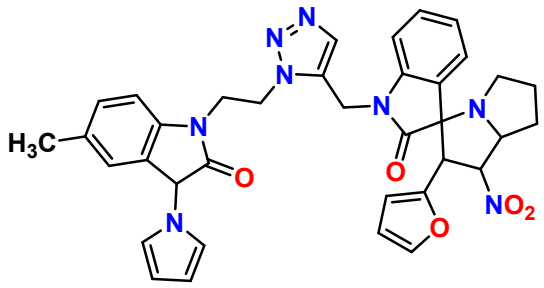
IR (KBr, cm^{-1}): 2966, 1624, 1484, 397.

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20 (d, 1H), 7.81 (s, 1H), 7.56 – 7.42 (m, 1H), 7.38 (dd, J = 12.0, 2.8 Hz, 1H), 7.03 – 6.91 (m, 2H), 6.88 (dd, J = 14.4, 8.5 Hz, 1H), 6.83 – 6.74 (m, 1H), 6.74 – 6.50 (m, 2H), 6.23 – 6.14 (m, 2H), 6.14 – 6.10 (m, 1H), 6.10 – 6.06 (m, 1H), 5.96 – 5.91 (m, 1H), 5.86 (td, J = 6.7, 3.3 Hz, 1H), 4.87 (d, J = 12.8 Hz, 1H), 4.85 – 4.70 (m, 2H), 4.68 (d, J = 4.0 Hz, 1H), 4.63 – 4.47 (m, 2H), 4.12 (m, J = 13.7, 6.3 Hz, 2H), 3.33 – 3.19 (m, 1H), 2.57 (t, J = 6.1 Hz, 1H), 1.99 (p, J = 7.1 Hz, 1H), 1.90 (t, J = 5.6 Hz, 1H), 1.61 (s, 1H), 1.37 (m, J = 11.8, 6.9 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 174.72, 172.67, 160.07, 157.69, 148.55, 143.37, 143.32, 143.05, 141.88, 139.07, 133.33, 130.05, 126.82, 124.10, 121.01, 116.23, 114.93, 111.89, 111.02, 110.25, 109.18, 107.84, 107.78, 90.32, 72.65, 63.83, 60.01, 50.76, 47.24, 45.90, 34.87, 27.97, 25.61.

HRMS data: Calcd mass $(M+H)^+$: 741.1507, found, 741.1591.

2'-(Furan-2-yl)-1-((1-(2-(5-methyl-2-oxo-3-(1*H*-pyrrol-1-yl) indolin-1-yl) ethyl)-1*H*-1,2,3-triazol-5-yl) methyl)-1'-nitro-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (18)



(18)

It was obtained as white solid with 68% Yield.

Melting point: 162-164˚C

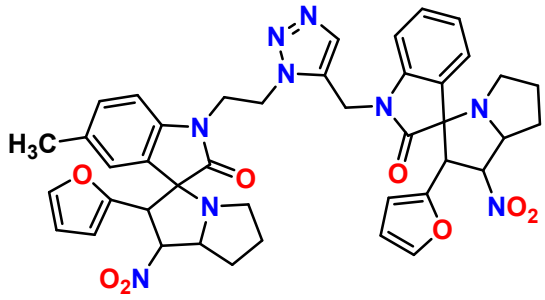
IR (KBr, cm^{-1}): 2974, 1635, 1484, 410.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.85 (d, J = 8.9 Hz, 1H), 7.75 (s, 1H), 7.41 – 7.24 (m, 2H), 7.12 (d, J = 7.6 Hz, 1H), 6.96 – 6.87 (m, 3H), 6.73 – 6.60 (m, 3H), 6.22 – 6.18 (m, 1H), 6.18 – 6.13 (m, 1H), 6.08 – 6.05 (m, 2H), 5.85 (d, J = 12.1 Hz, 1H), 5.82 (s, 1H), 4.77 (s, 1H), 4.76 – 4.70 (m, 2H), 4.66 (d, J = 13.0 Hz, 1H), 4.60 (d, J = 5.5 Hz, 2H), 4.18 – 4.00 (m, 2H), 3.32 – 3.21 (m, 1H), 2.58 (t, J = 7.5 Hz, 1H), 2.18 (d, J = 4.0 Hz, 3H), 2.06 – 1.99 (m, 1H), 1.92 – 1.84 (m, 1H), 1.67 – 1.55 (m, 1H), 1.35 (m, J = 18.8, 12.1, 7.4 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 175.06, 172.72, 148.62, 143.72, 143.26, 143.20, 142.19, 140.42, 140.39, 132.29, 130.62, 130.08, 127.06, 126.04, 125.36, 124.51, 124.02, 123.93, 122.91, 120.96, 111.06, 111.02, 109.95, 108.97, 107.69, 90.79, 72.68, 63.76, 60.01, 50.92, 47.27, 46.10, 34.86, 27.93, 25.59, 20.90.

HRMS data: Calcd mass $(M+H)^+$: 659.2652, found, 659.2741.

2'-(Furan-2-yl)-1-((1-(2-(2'-(furan-2-yl)-5-methyl-1'-nitro-2-oxo-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-1-yl) ethyl)-1*H*-1,2,3-triazol-5-yl) methyl)-1'-nitro-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one. (19)



(19)

It was obtained as white solid with 65% Yield.

Melting point: 178-180˚C

IR (KBr, cm^{-1}): 2971, 1642, 1555, 1484, 411.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.84 (d, J = 7.1 Hz, 1H), 7.65 (s, 1H), 7.44 – 7.37 (m, 1H), 7.36 – 7.26 (m, 2H), 7.11 (t, J = 7.6 Hz, 1H), 6.94 (dd, J = 17.1, 7.8 Hz, 2H), 6.56 – 6.43 (m, 1H), 6.26 – 6.06 (m, 4H), 5.91 – 5.77 (m, 2H), 4.79 – 4.66 (m, 4H), 4.67 – 4.48 (m, 3H), 4.36 (q, J = 6.2 Hz, 2H), 3.93 (d, J = 6.0 Hz, 2H), 3.27 – 3.15 (m, 2H), 2.58 (t, J = 7.3 Hz, 2H), 2.33 – 2.23 (m, 3H), 2.04 – 1.96 (m, 2H), 1.88 (m, 2H), 1.63 (m, 2H), 1.35 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 175.66, 175.04, 148.67, 148.59, 143.71, 143.28, 143.26, 143.22, 143.18, 142.09, 141.35, 132.01, 130.69, 130.56, 127.67, 127.06, 124.54, 124.35, 124.00, 123.90, 122.91, 111.14, 111.01, 109.86, 108.69, 107.59, 90.79, 72.67, 63.80, 50.89, 50.76, 47.33, 46.17, 34.78, 27.87, 25.56, 21.13.

HRMS data: Calcd mass $(M+H)^+$: 799.3078, found, 800.3166.

2. ^{1}H and ^{13}C NMR Spectra of the synthesized compounds:

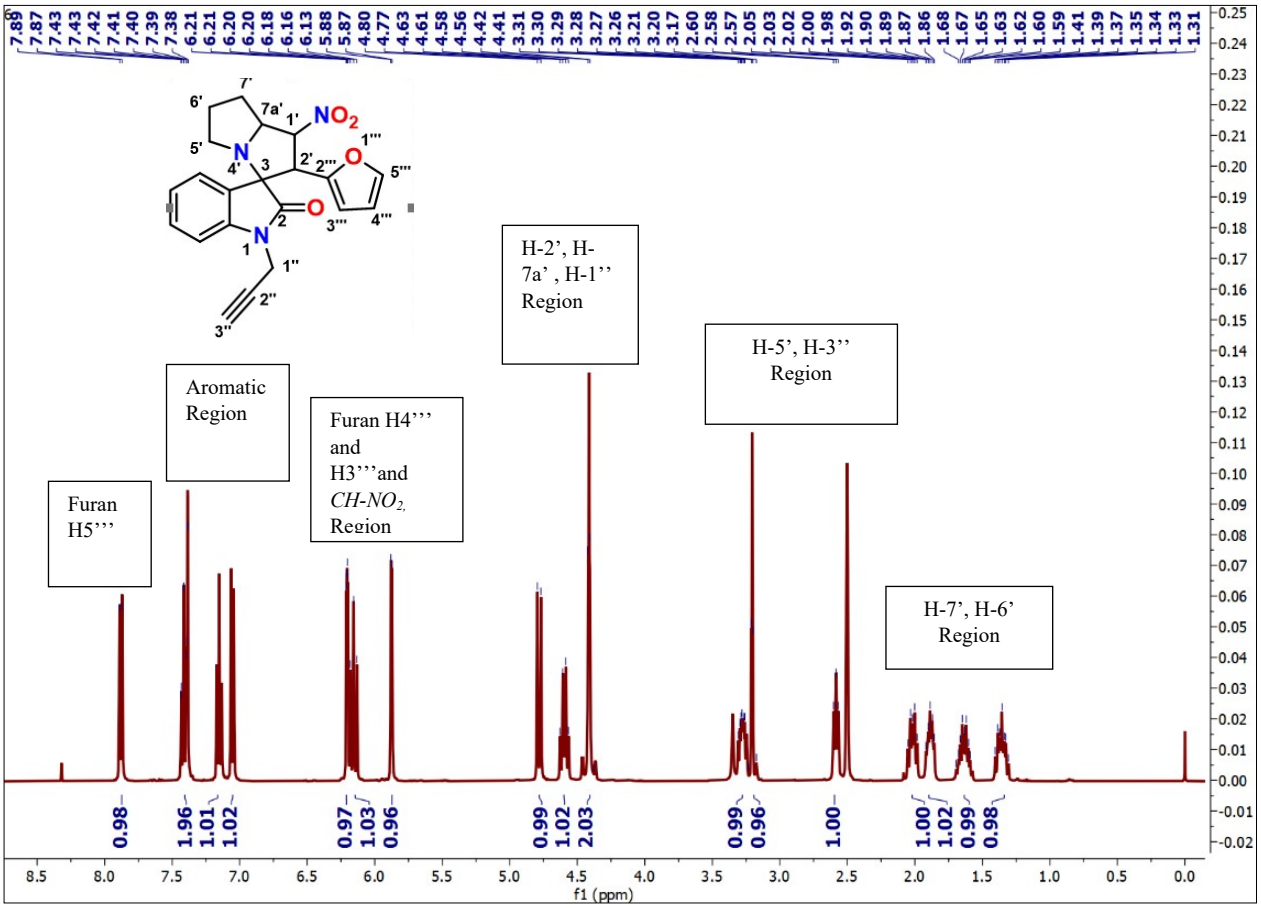


Figure S1. ^{1}H NMR spectrum of compound **6** (400 MHz, DMSO-d_6).

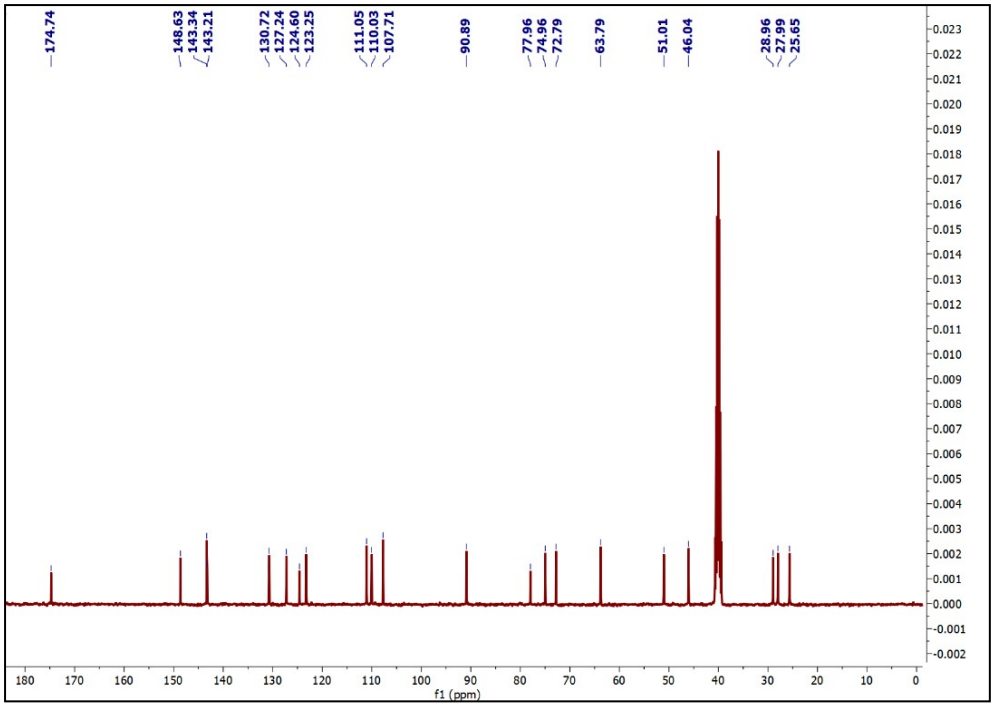


Figure S2. ^{13}C NMR spectrum of compound **6** (100 MHz, DMSO-d_6)

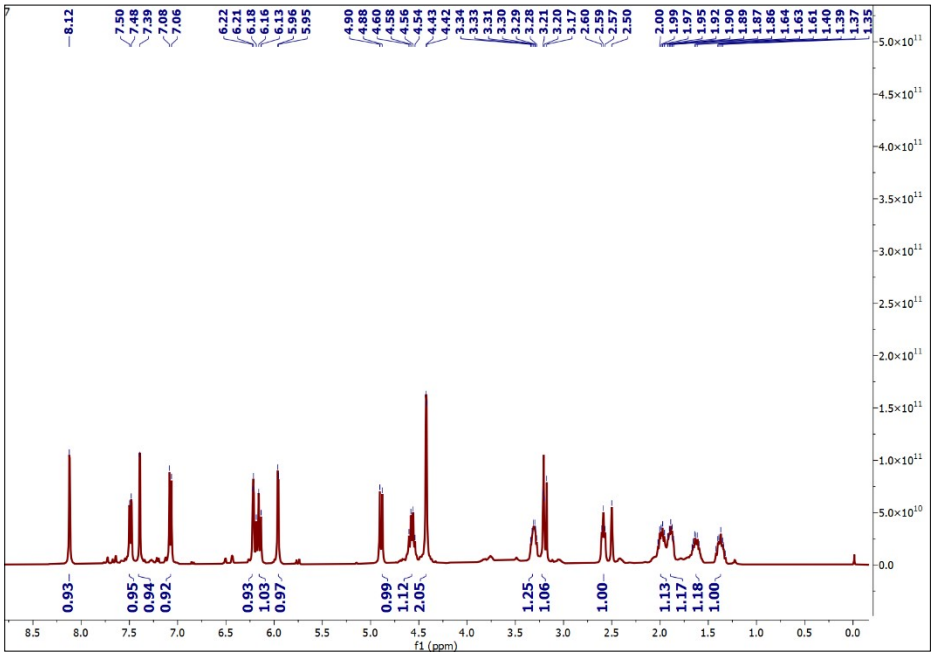


Figure S3. ^{1}H NMR spectrum of compound **7** (400 MHz, DMSO-d_6).

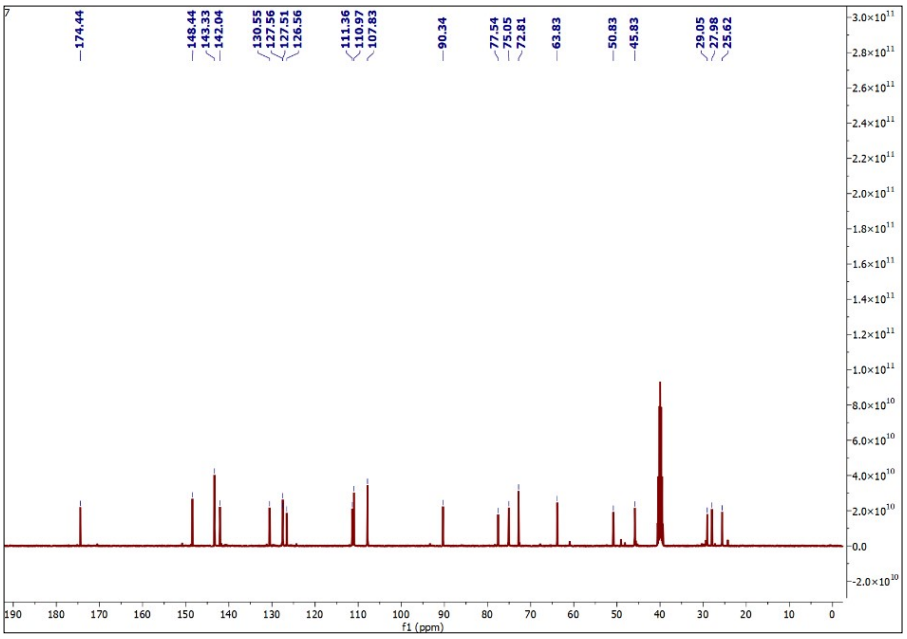


Figure S4. ^{13}C NMR spectrum of compound **7** (100 MHz, DMSO-d_6).

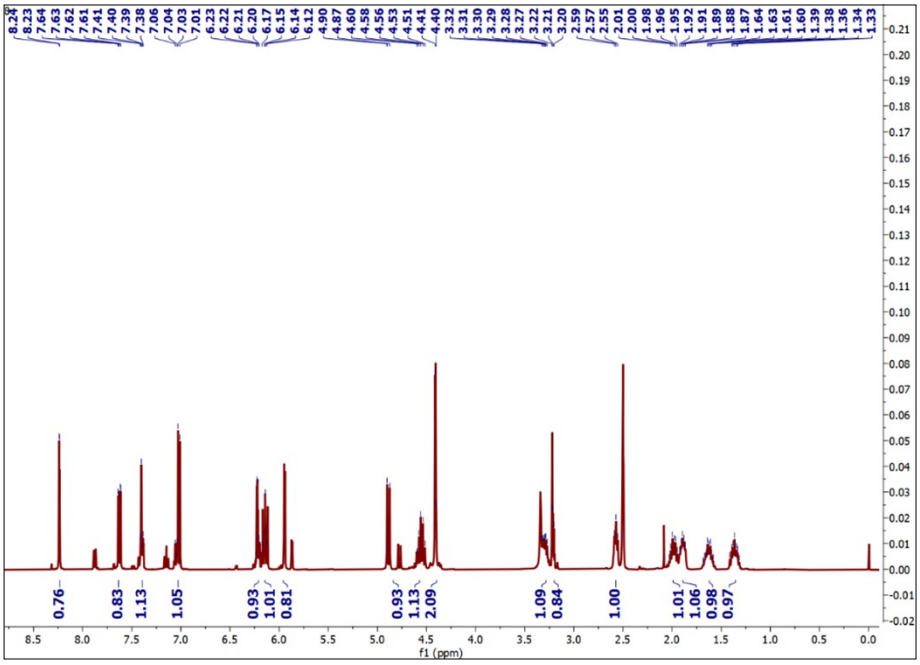


Figure S5. ^{1}H NMR spectrum of compound **8** (400 MHz, DMSO-d_6)

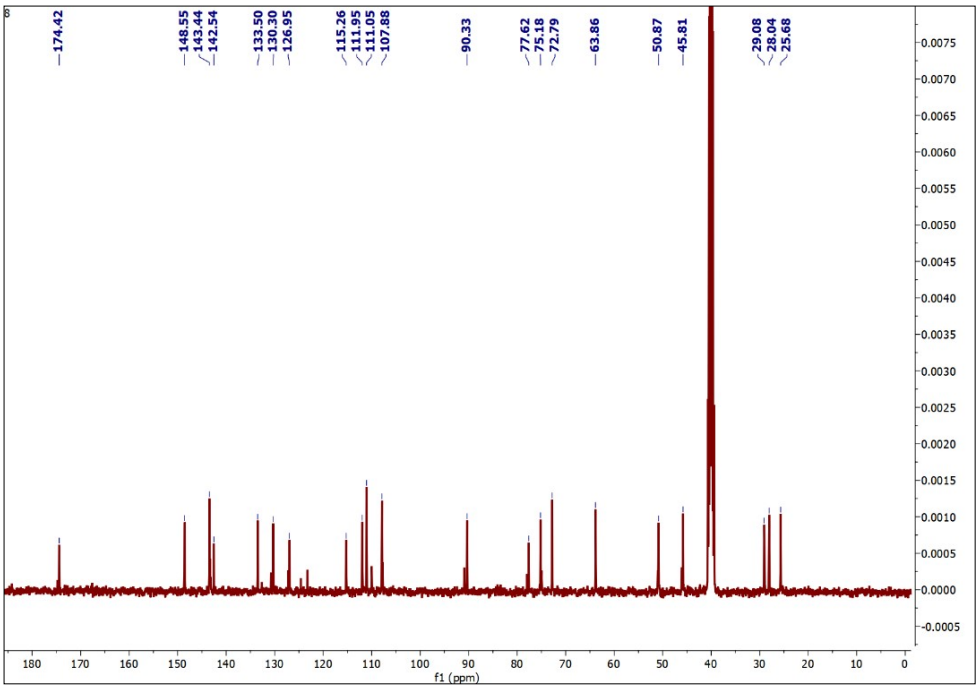


Figure S6. ^{13}C NMR spectrum of compound **8** (100 MHz, DMSO-d_6).

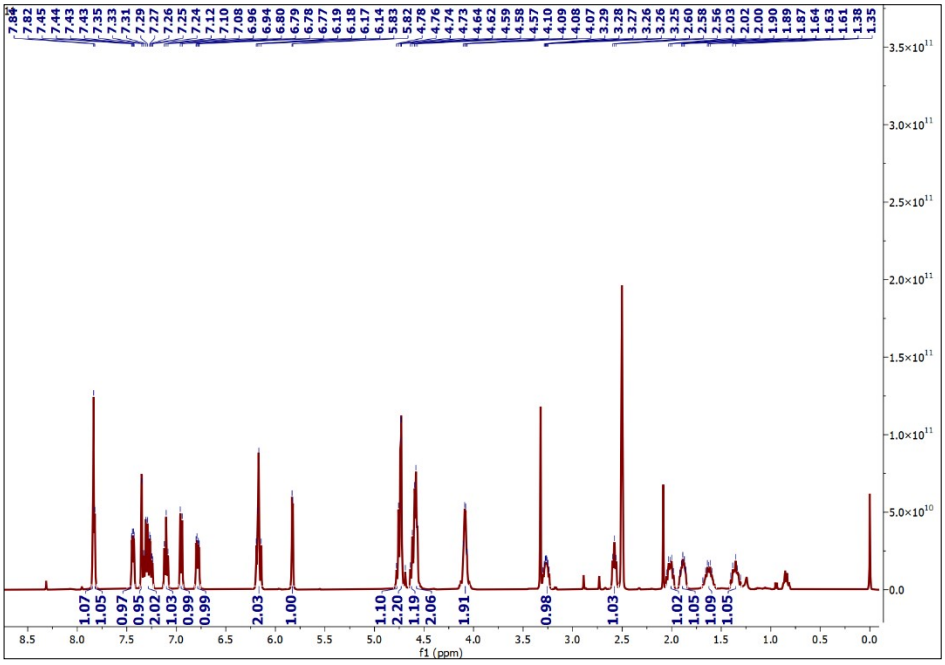


Figure S7. ^{1}H NMR spectrum of compound **11** (400 MHz, DMSO-d_6).

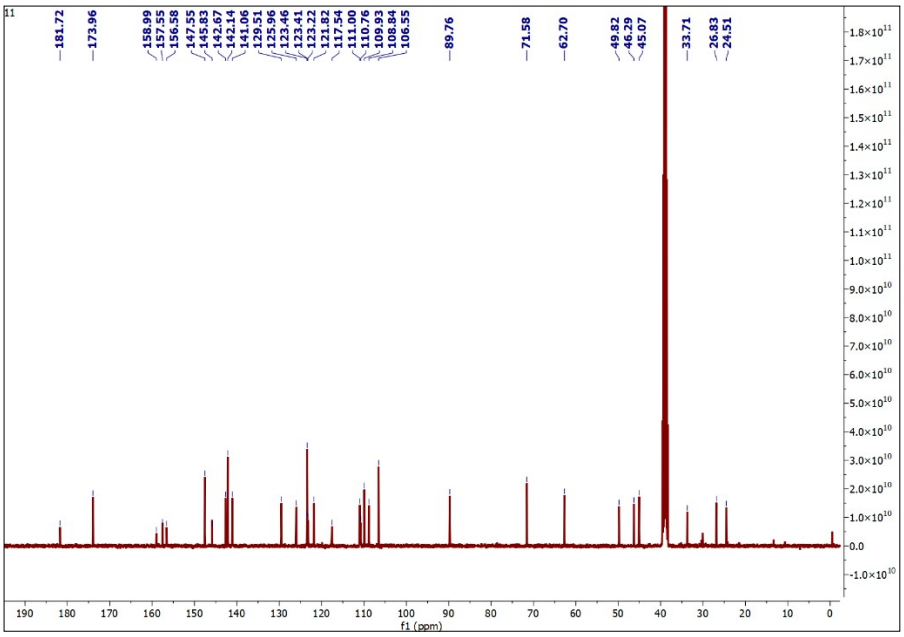


Figure S8. ^{13}C NMR spectrum of compound **11** (100 MHz, DMSO-d_6).

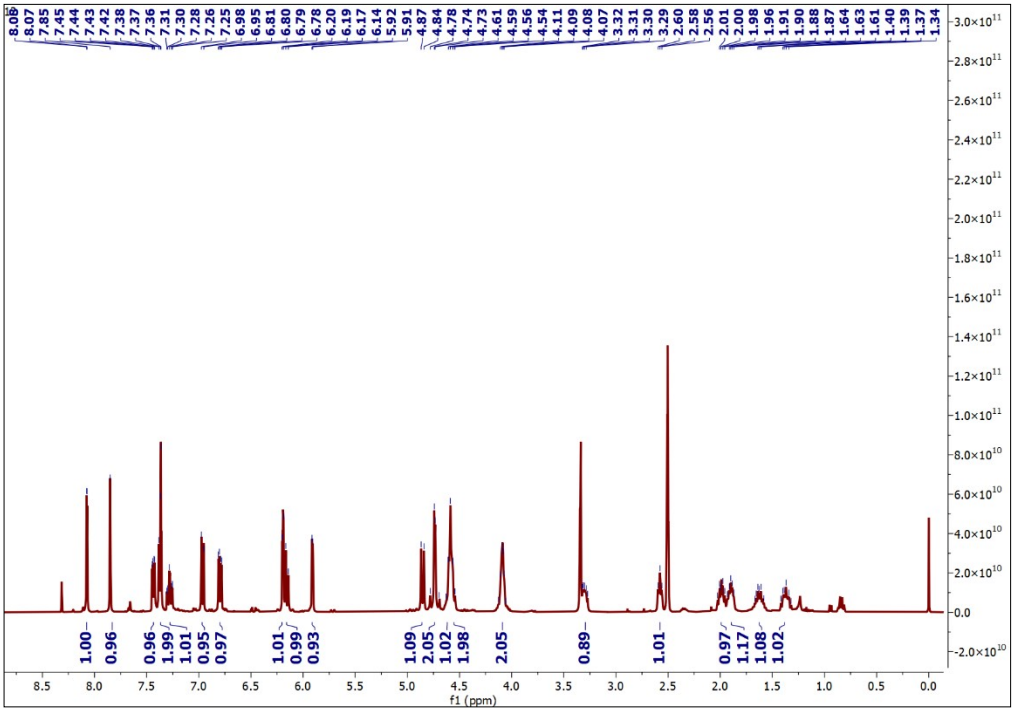


Figure S9. ^{1}H NMR spectrum of compound **12** (400 MHz, DMSO-d_6)

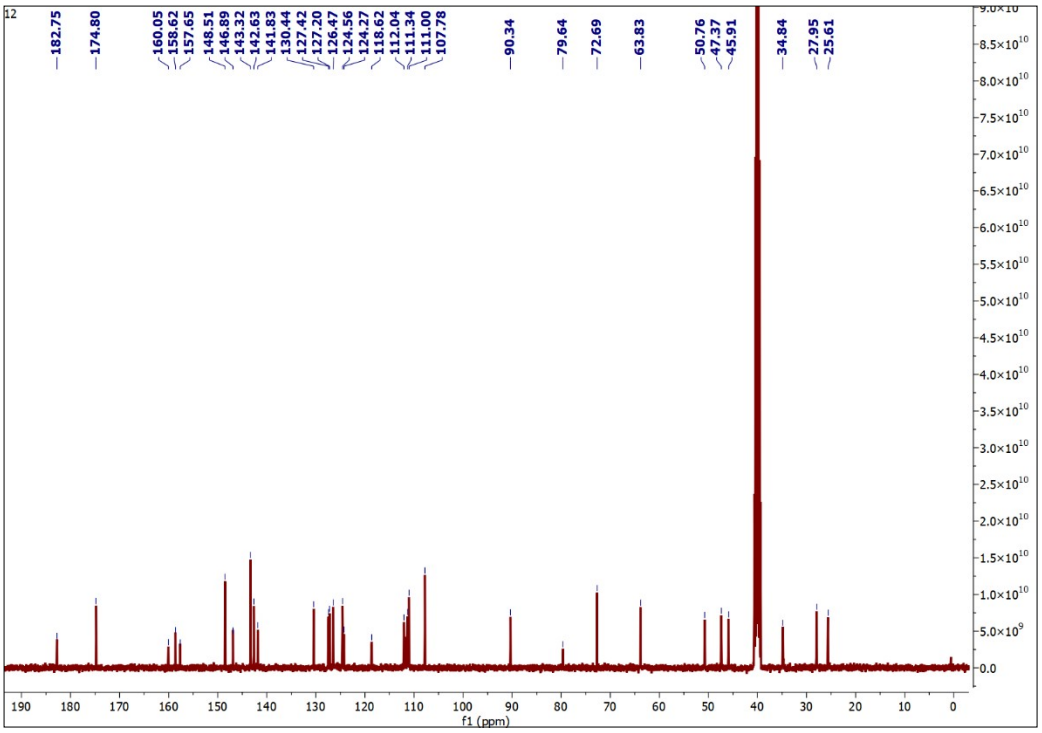


Figure S10. ^{13}C NMR spectrum of compound **12** (400 MHz, DMSO-d_6).

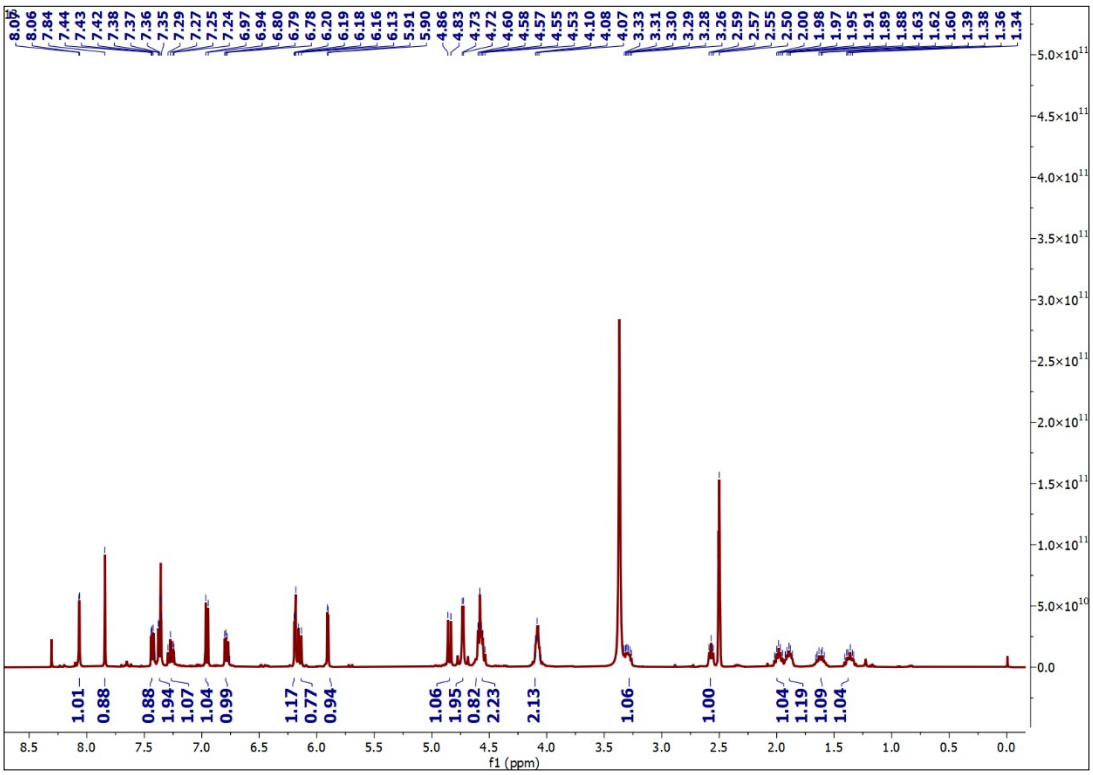


Figure S11. ^{1}H NMR spectrum of compound **13** (400 MHz, DMSO-d_6)

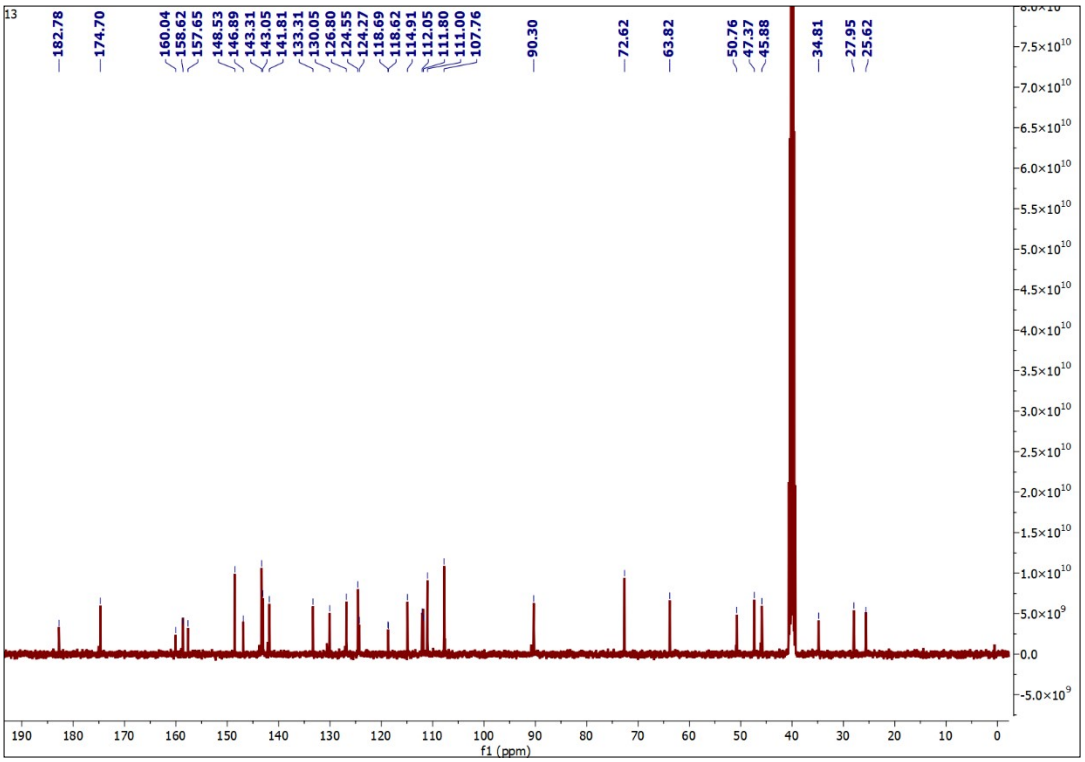


Figure S12. ^{13}C NMR spectrum of compound **13** (400 MHz, DMSO-d_6).

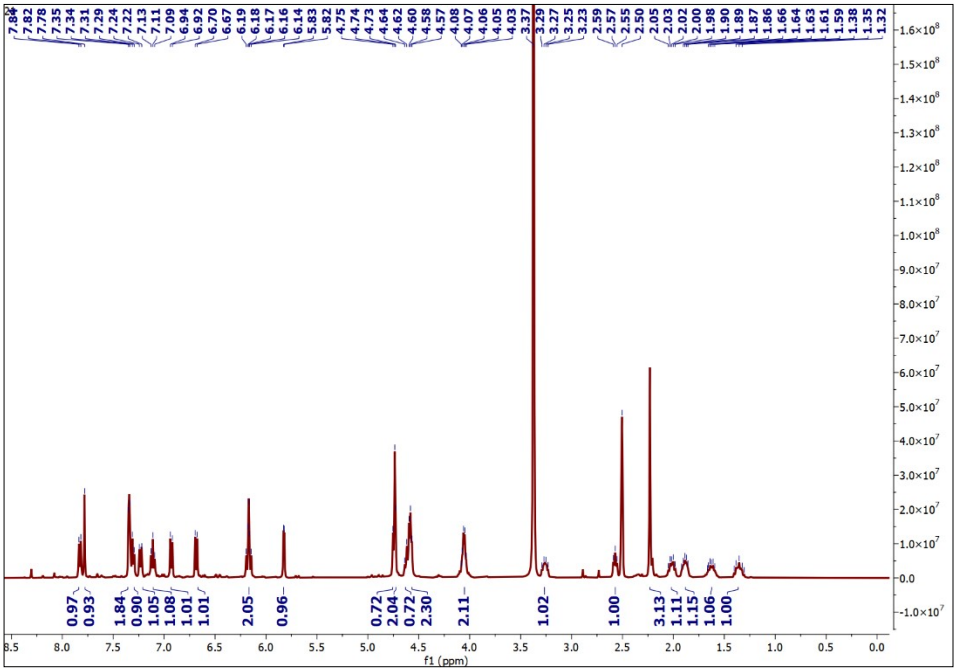


Figure S13. ^{1}H NMR spectrum of compound **14** (400 MHz, DMSO-d_6).

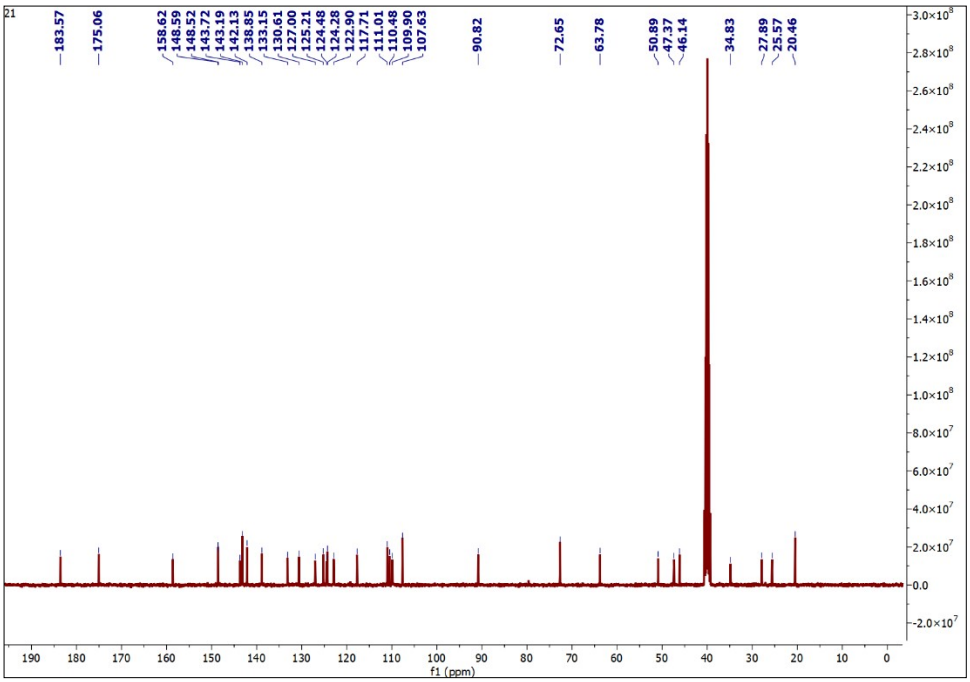


Figure S14. ^{13}C NMR spectrum of compound **14** (100 MHz, DMSO-d_6).

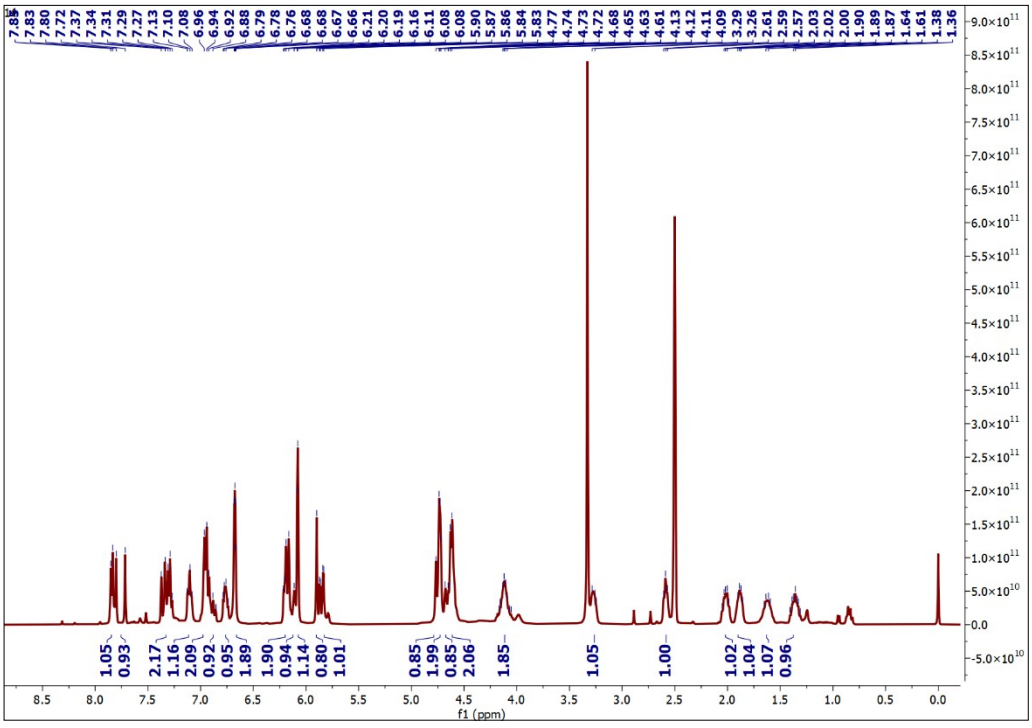


Figure S15. ^{1}H NMR spectrum of compound **15** (400 MHz, DMSO-d_6)

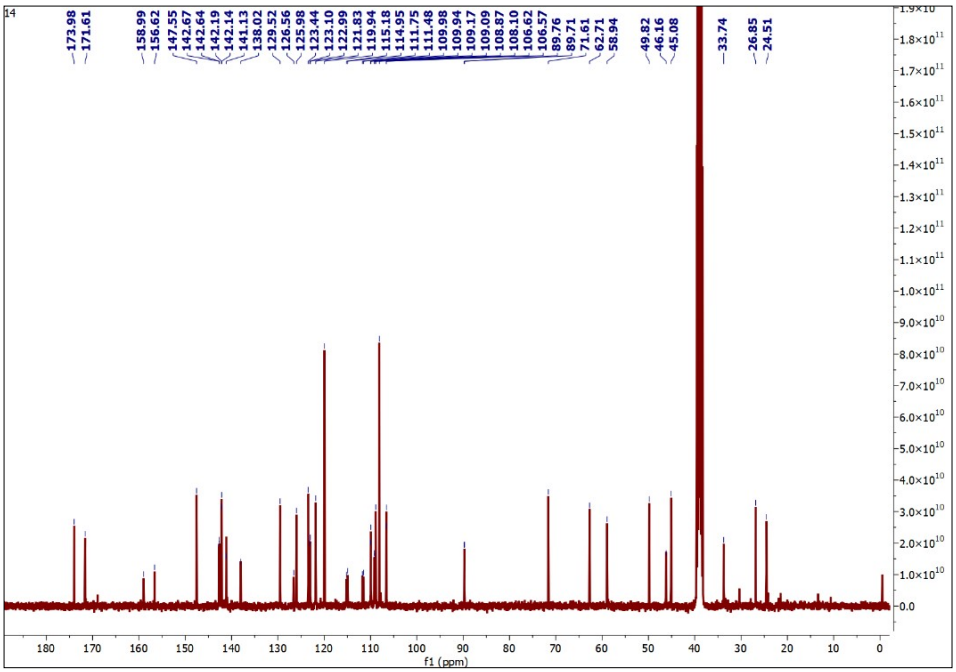


Figure S16. ^{13}C NMR spectrum of compound **15** (400 MHz, DMSO-d_6).

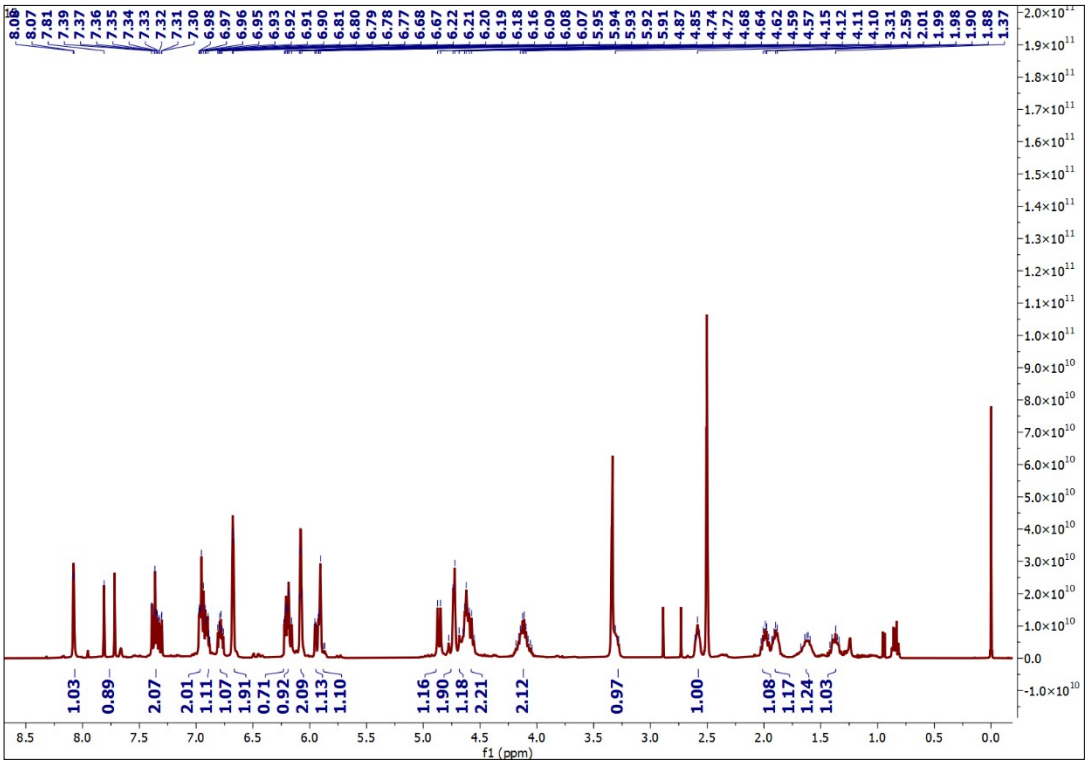


Figure S17. ^{1}H NMR spectrum of compound **16** (400 MHz, DMSO-d_6)

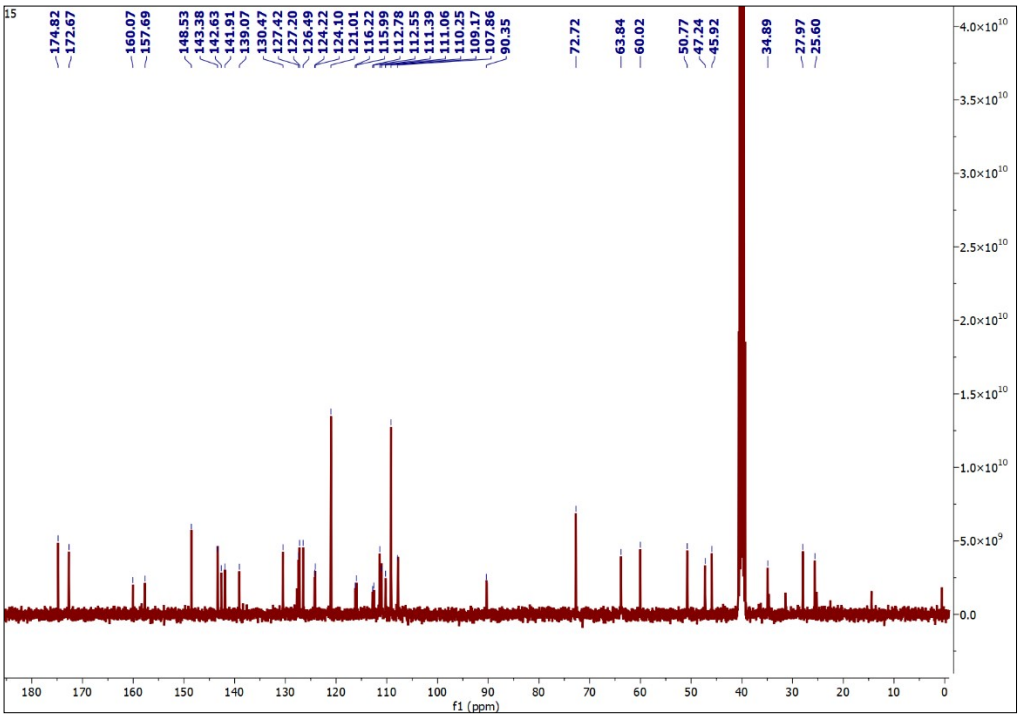


Figure S18. ^{13}C NMR spectrum of compound **16** (400 MHz, DMSO-d_6).

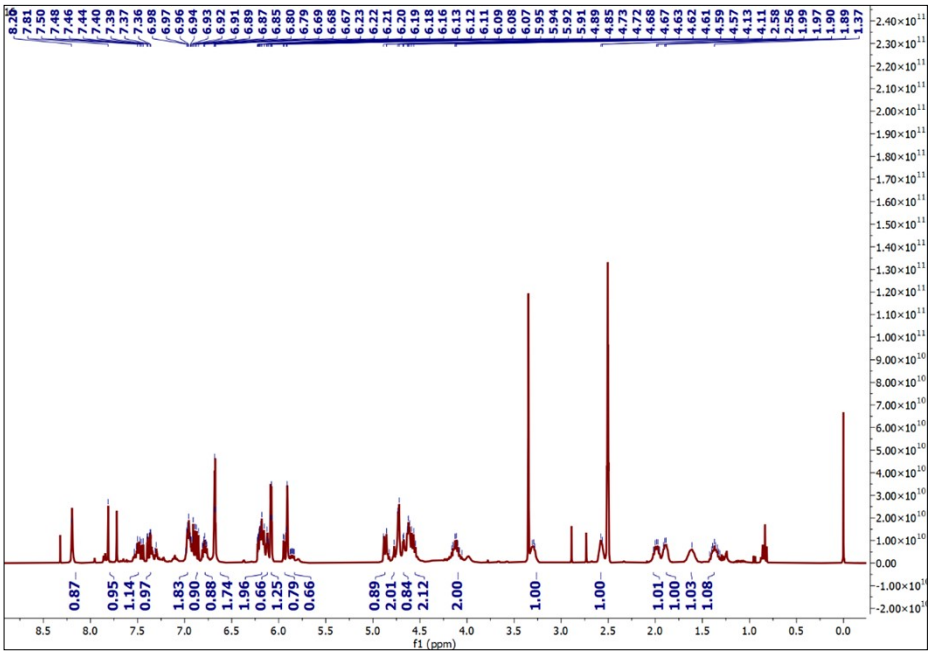


Figure S19. ^{1}H NMR spectrum of compound **17** (400 MHz, DMSO-d_6).

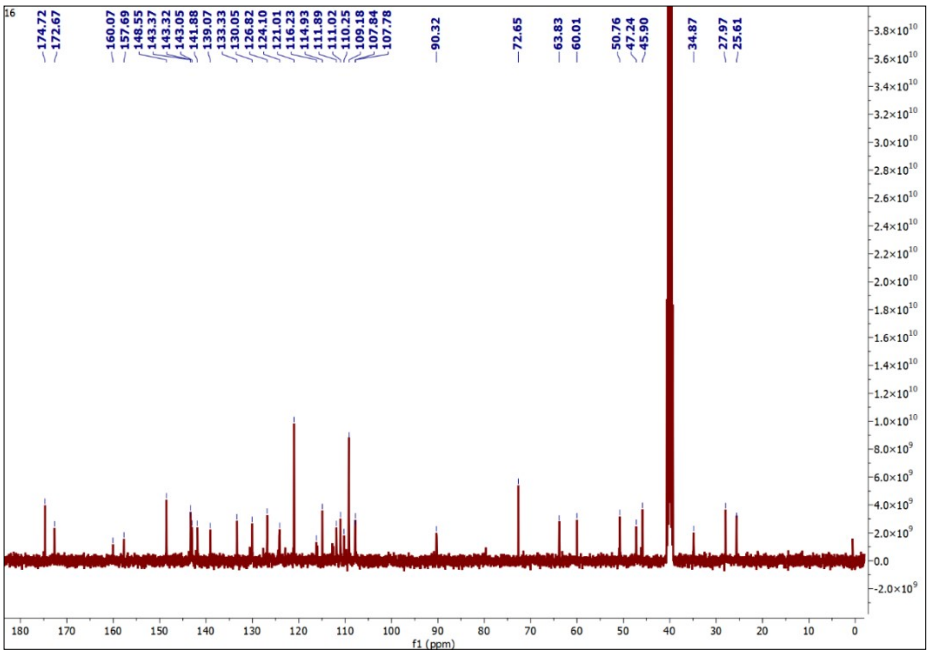


Figure S20. ^{13}C NMR spectrum of compound **17** (400 MHz, DMSO-d_6).

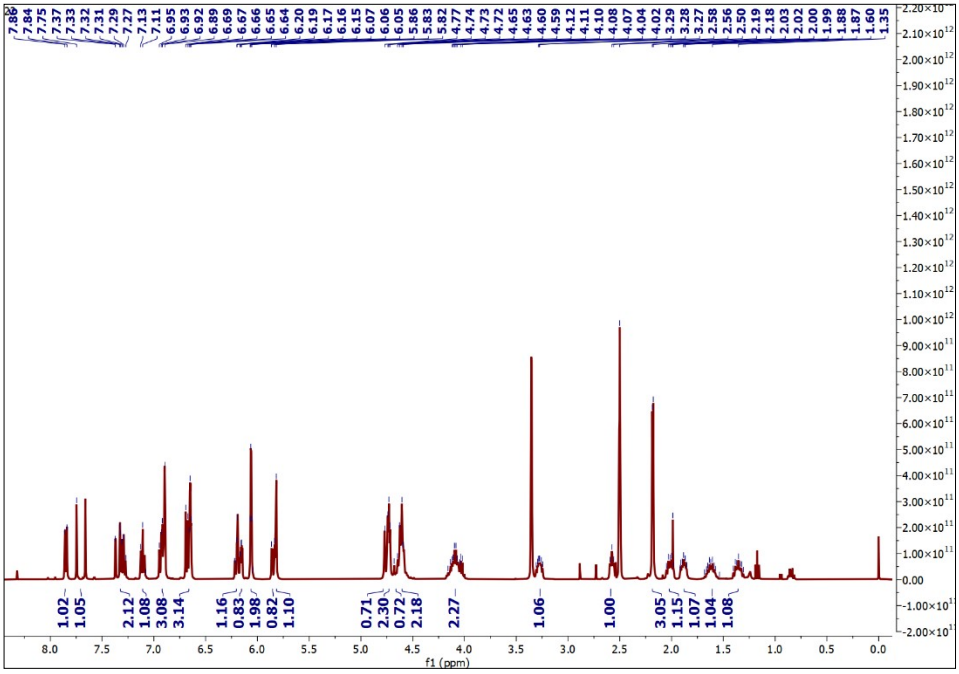


Figure S21. ^{1}H NMR spectrum of compound **18** (400 MHz, DMSO-d_6).

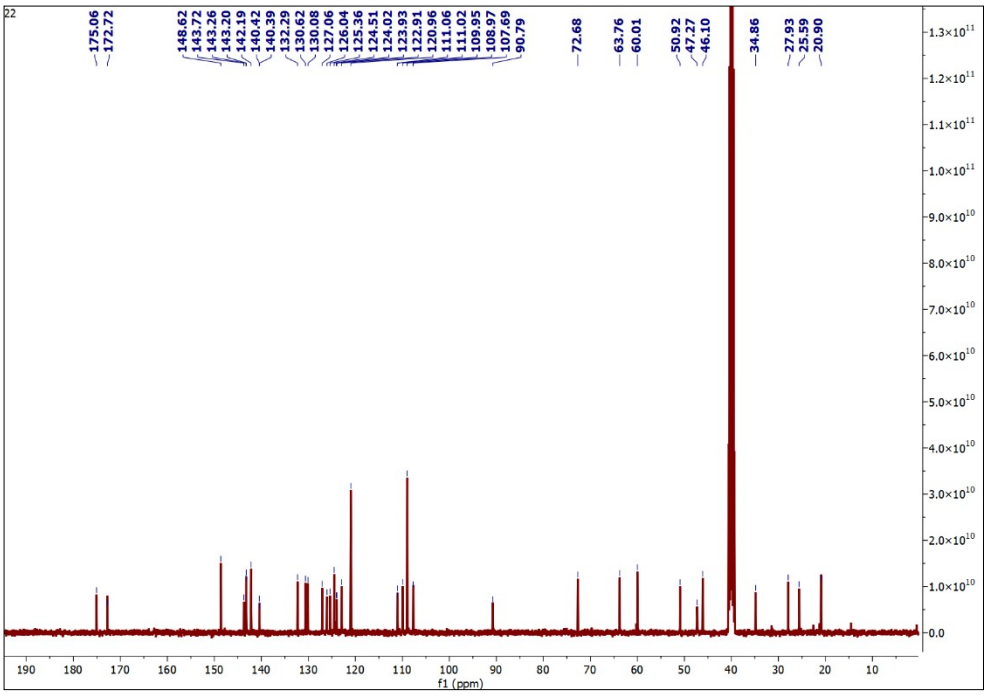


Figure S22. ^{13}C NMR spectrum of compound **18** (100 MHz, DMSO-d_6).

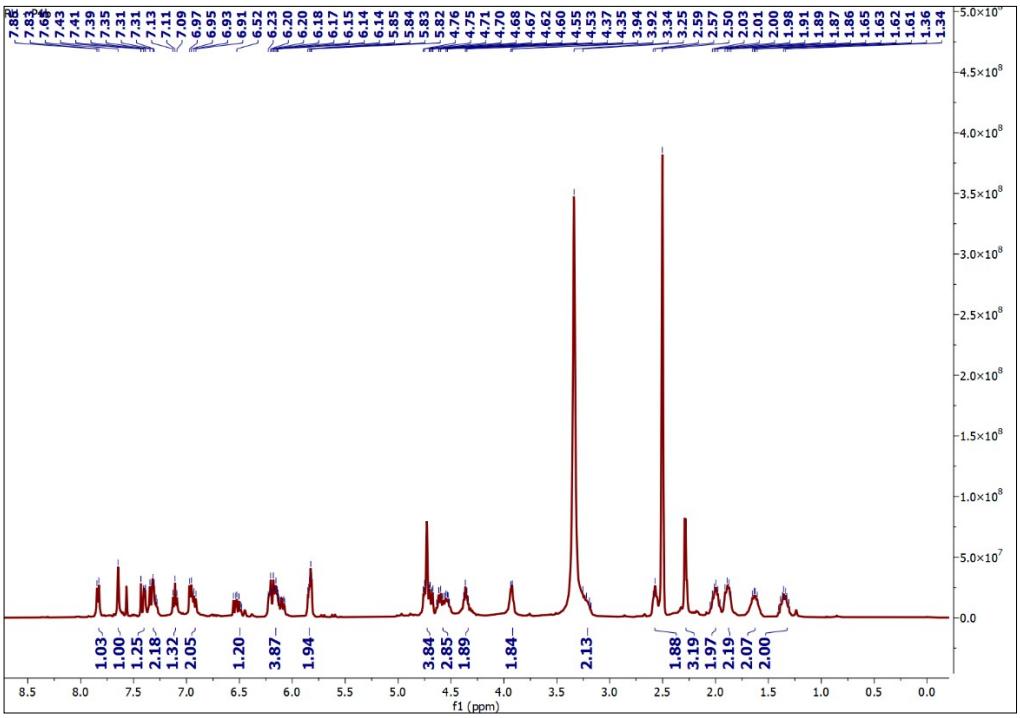


Figure S23. ^{1}H NMR spectrum of compound **19** (400 MHz, DMSO-d_6).

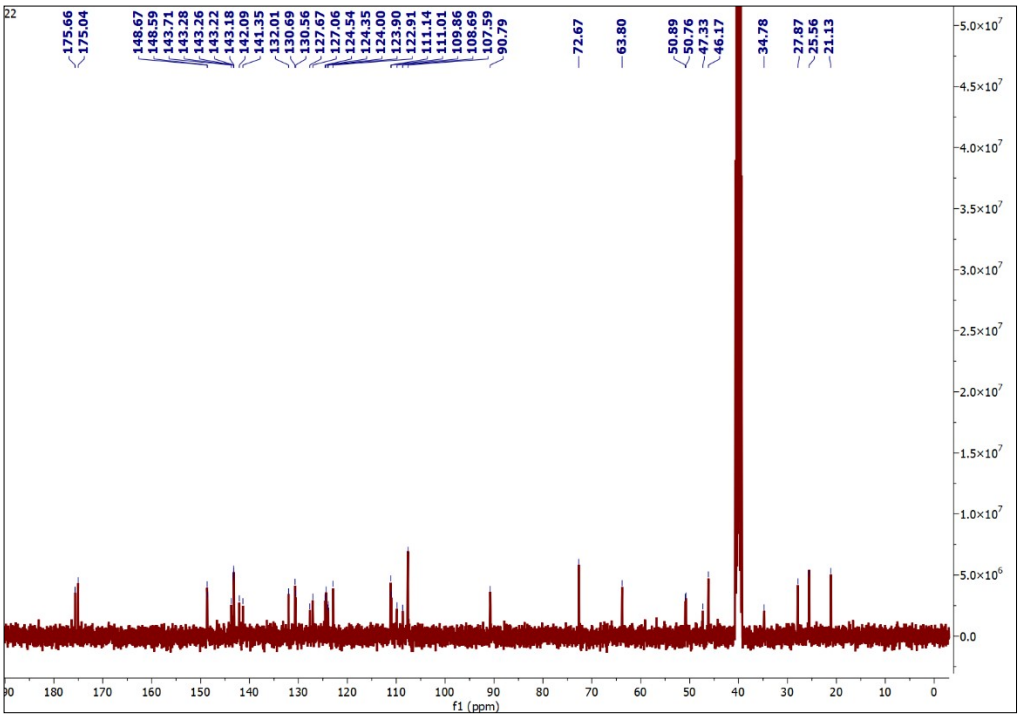


Figure 24. ^{13}C NMR spectrum of compound **19** (100 MHz, DMSO-d_6).

Table - S1: List of synthesised spiroindoline derivatives **6-19**.

S. N.	Compounds	R	Yields (%)	Melting Point (ºC)
1.	6	H	90	130-132
2.	7	Cl	98	135-137
3.	8	Br	92	140-141
4.	11	H	80	156-157
5.	12	Cl	82	161-163
6.	13	Br	88	165-167
7.	14	H	78	166-168
8.	15	H	70	159-161
9.	16	Cl	73	169-171
10.	17	Br	72	171-173
11.	18	H	68	162-164
12.	19	H	65	178-180

Note: Yields refer to isolated products obtained from single experiment under the specified reaction conditions

3. Molecular Docking Assessment

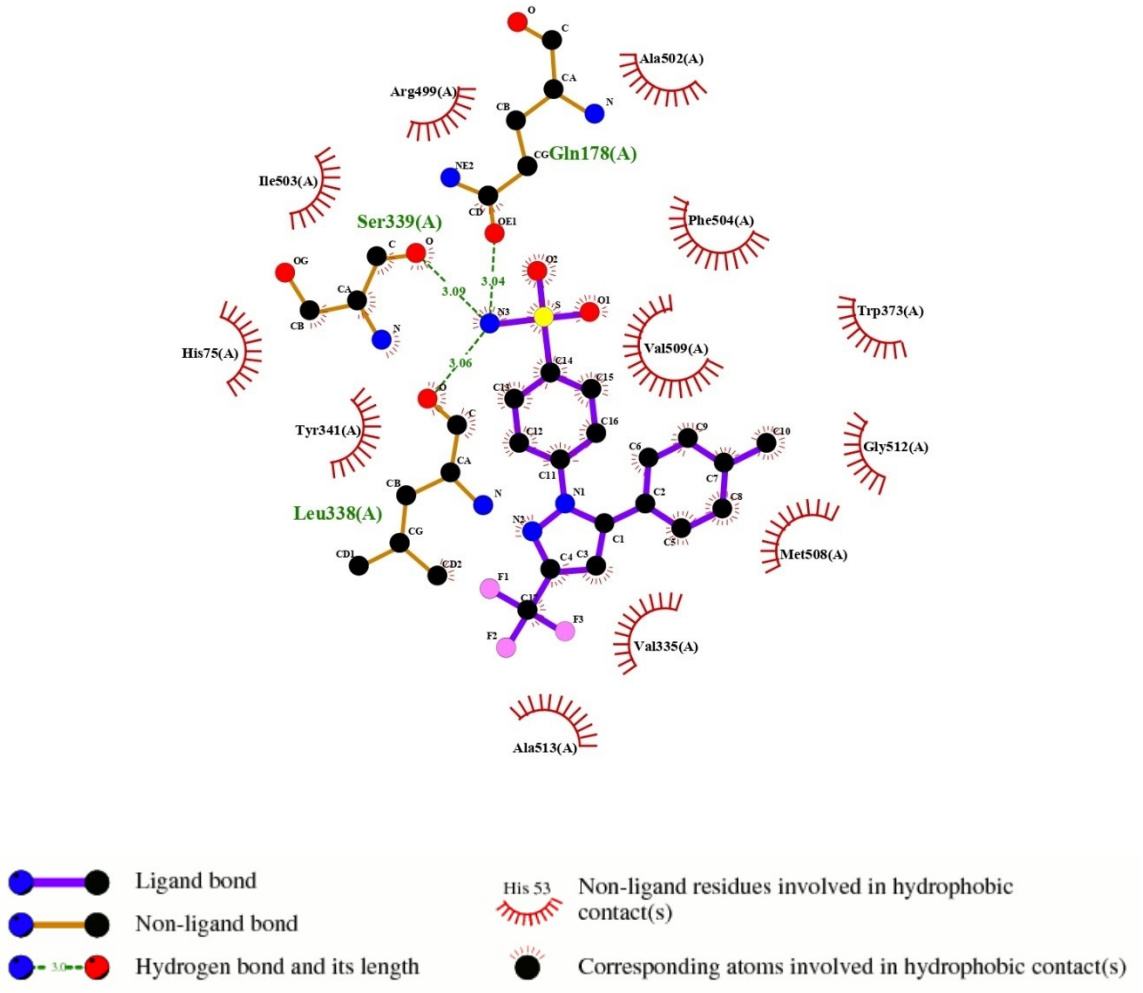
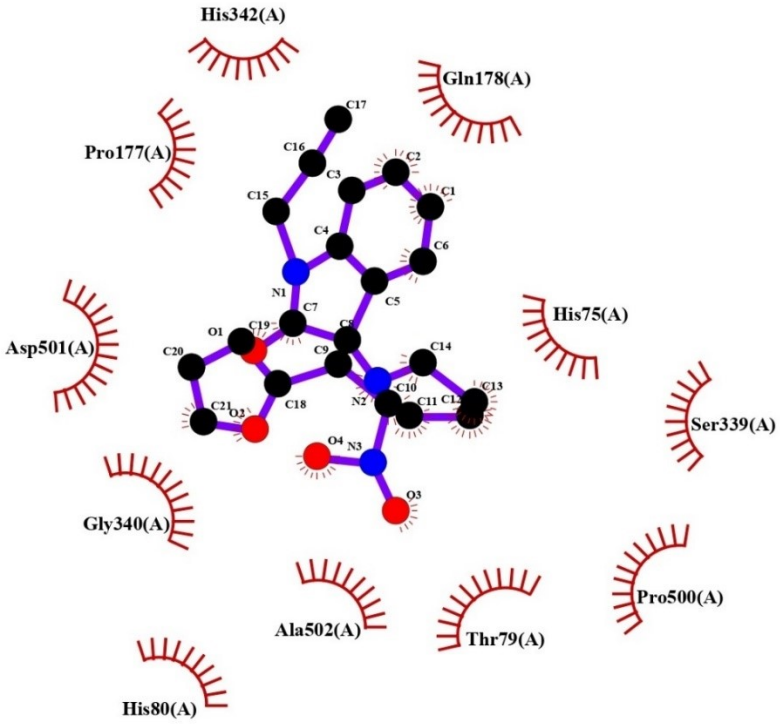


Figure S25. 2D and 3D image of Standard drug (**Celecoxib**) with target protein Cyclooxygenase (COX-2).



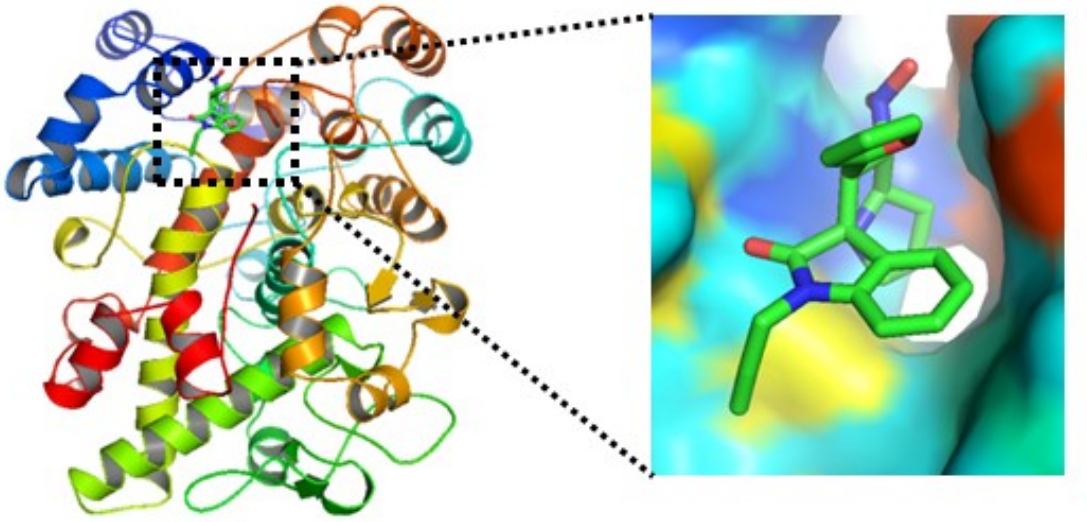
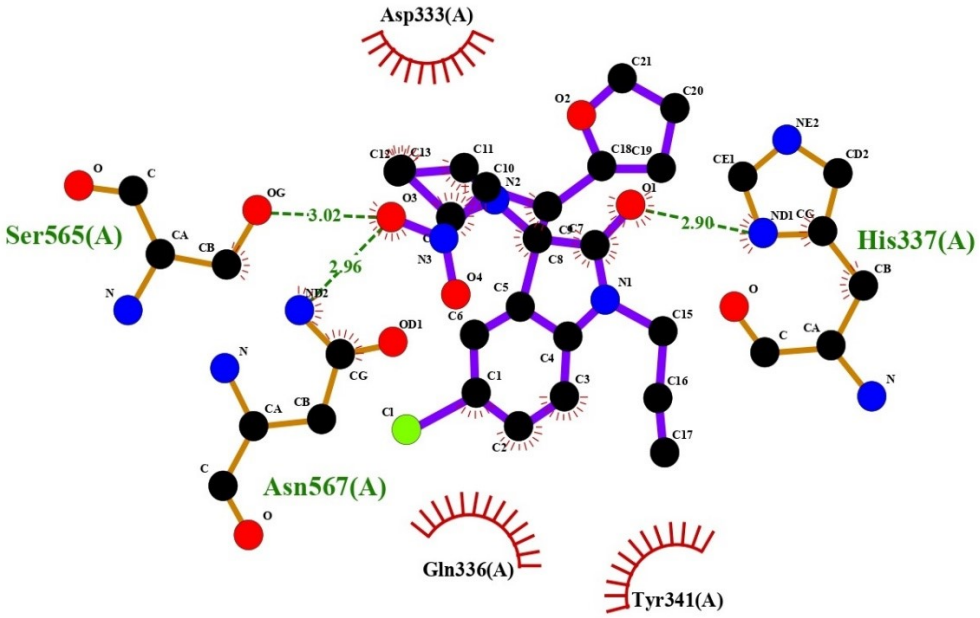


Figure S26. 2D and 3D image of compound **6** with target protein Cyclooxygenase (COX-2).



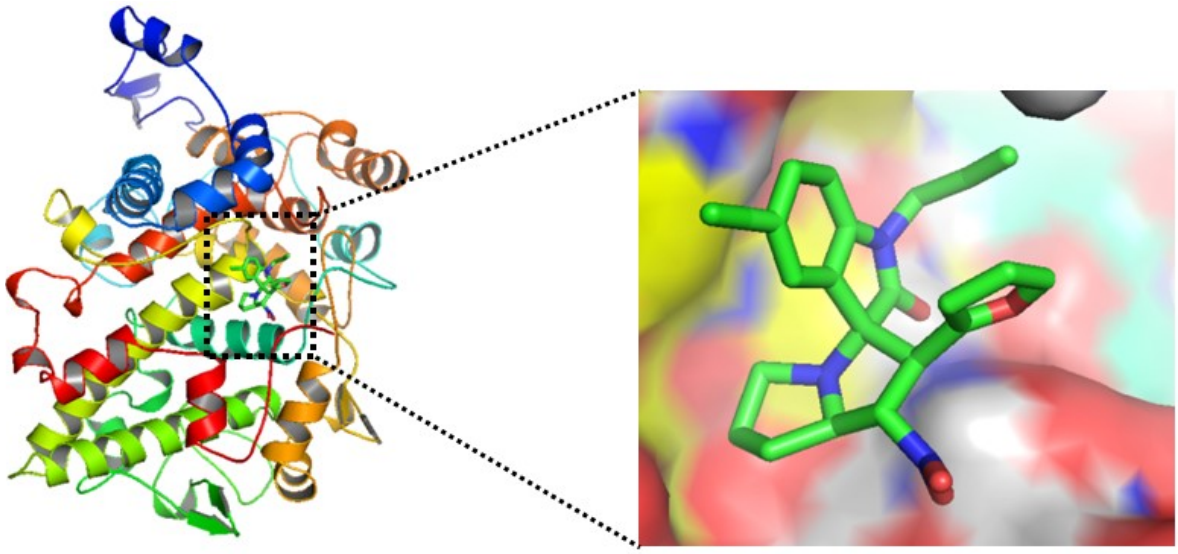


Figure S27. 2D and 3D image of compound **7** with target protein Cyclooxygenase (COX-2).

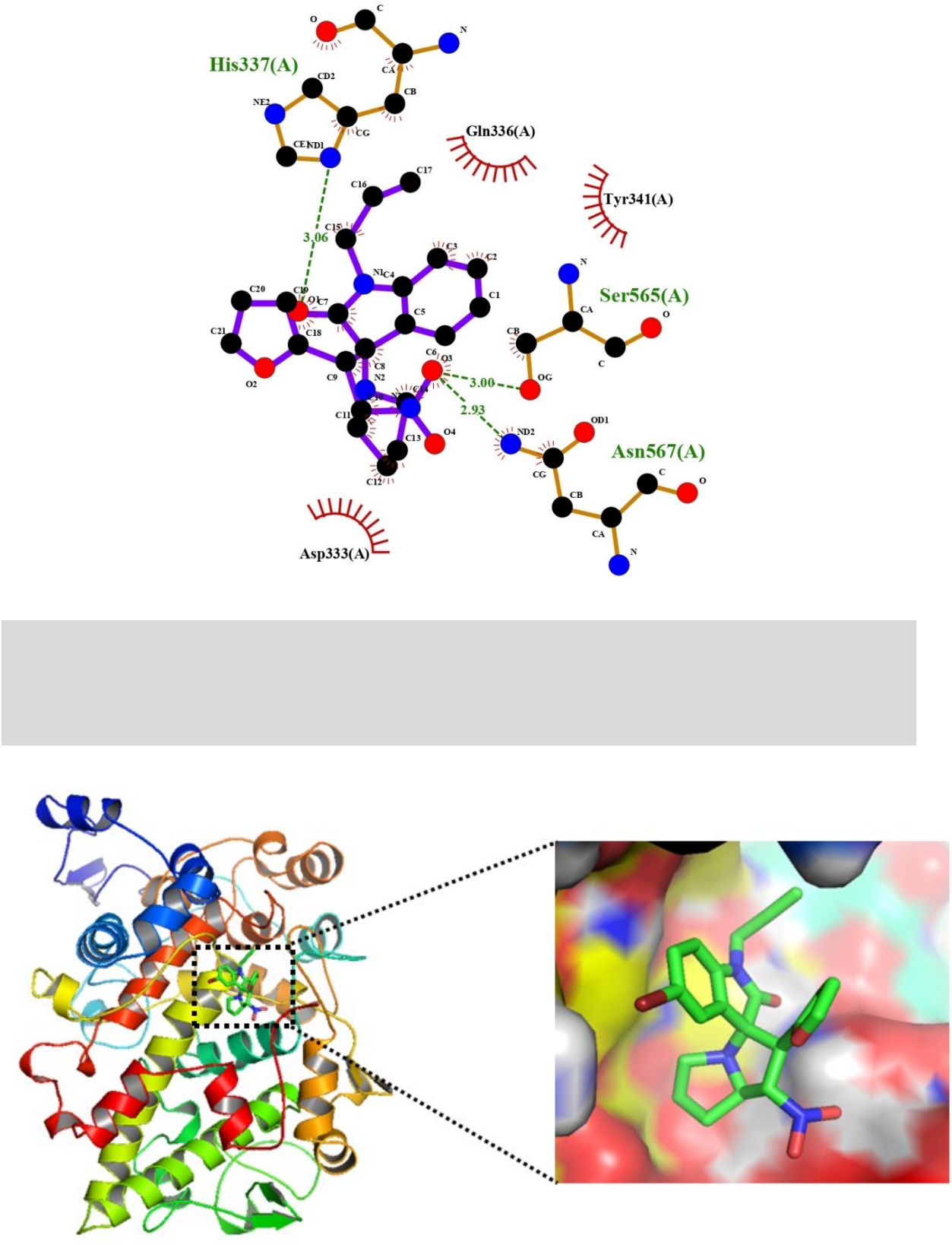


Figure S28. 2D and 3D image of compound **8** with target protein Cyclooxygenase (COX-2).

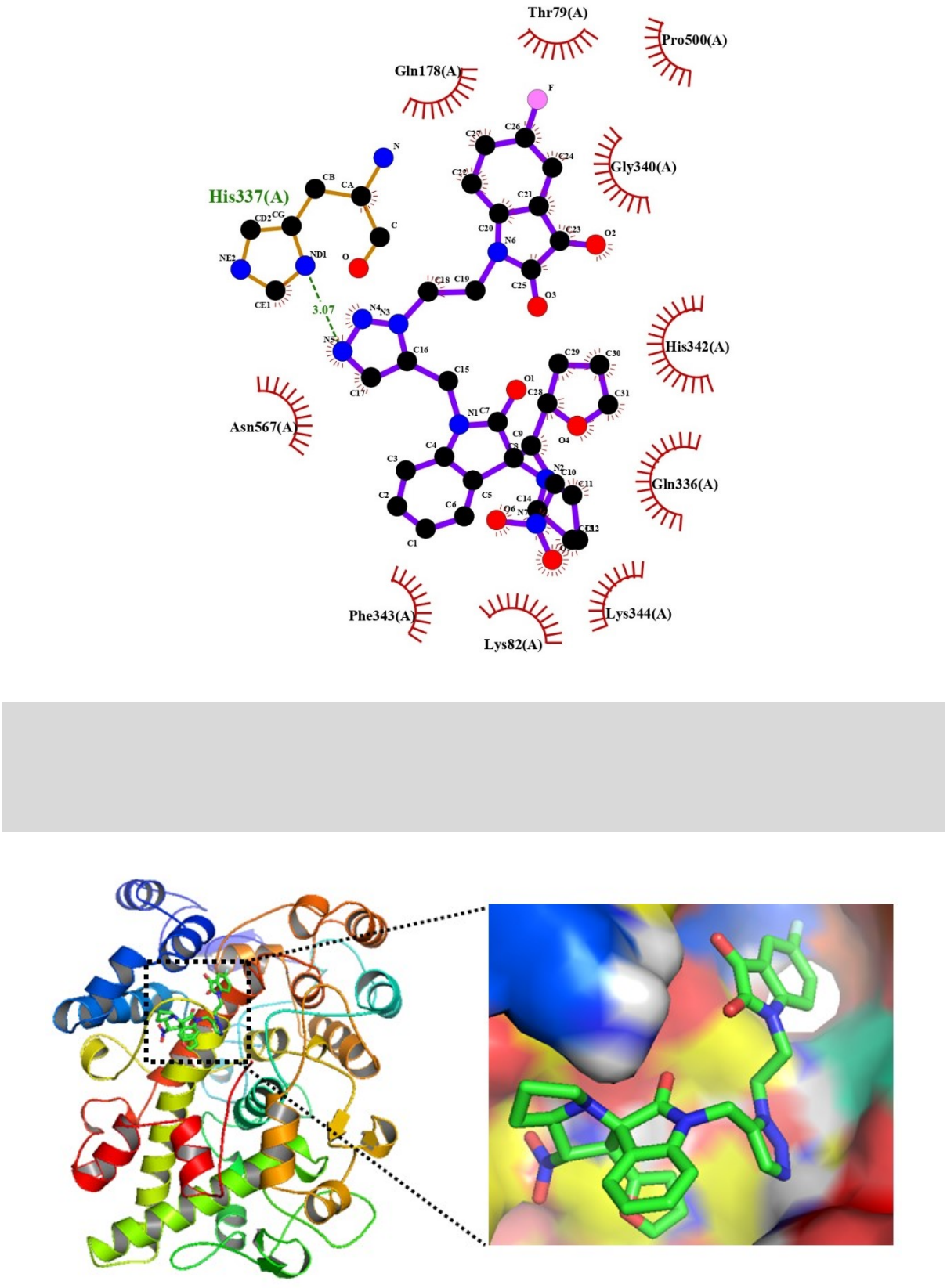


Figure S29. 2D and 3D image of compound **11** with target protein Cyclooxygenase (COX-2).

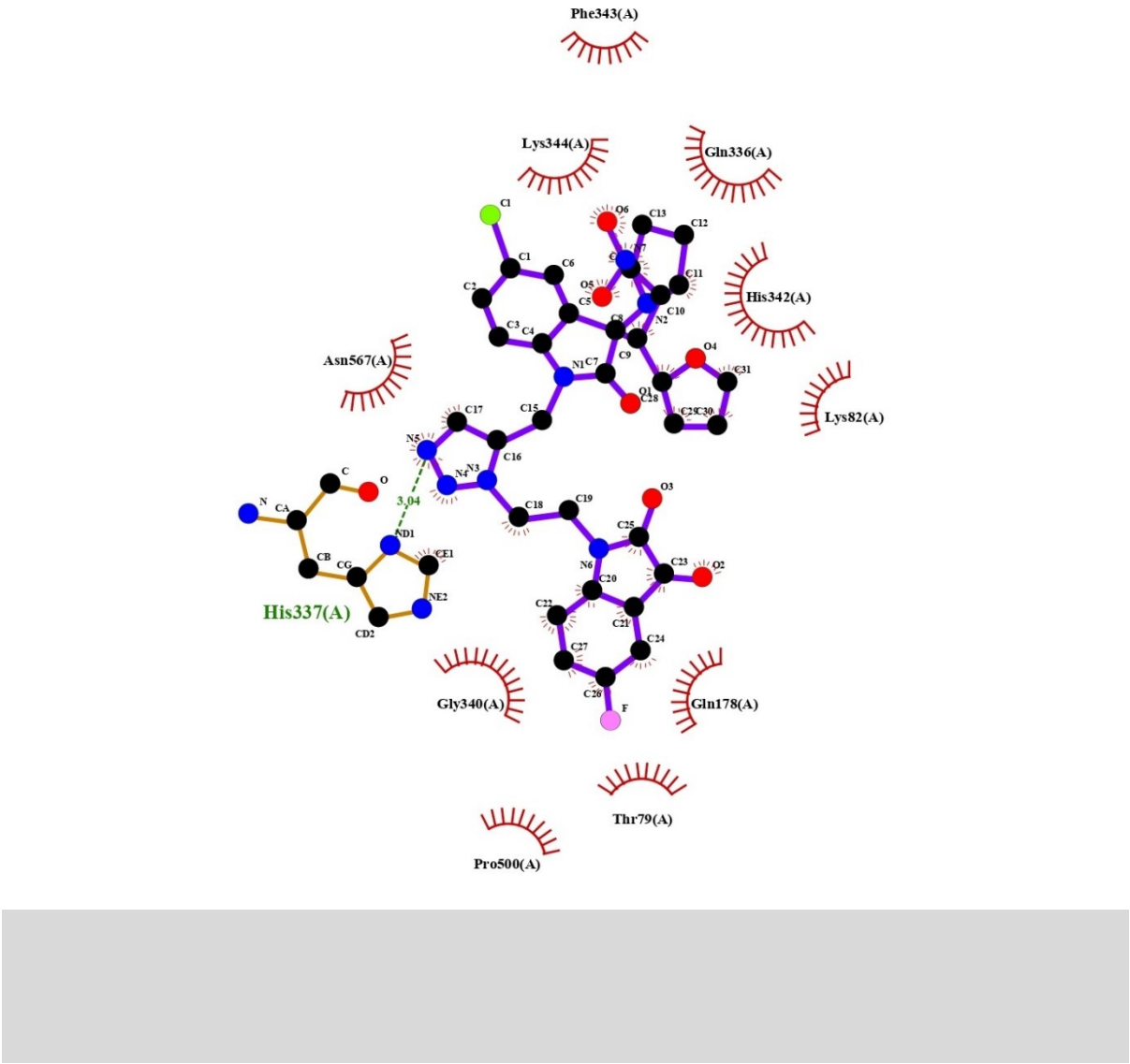


Figure S30. 2D and 3D image of compound **12** with target protein Cyclooxygenase (COX-2).

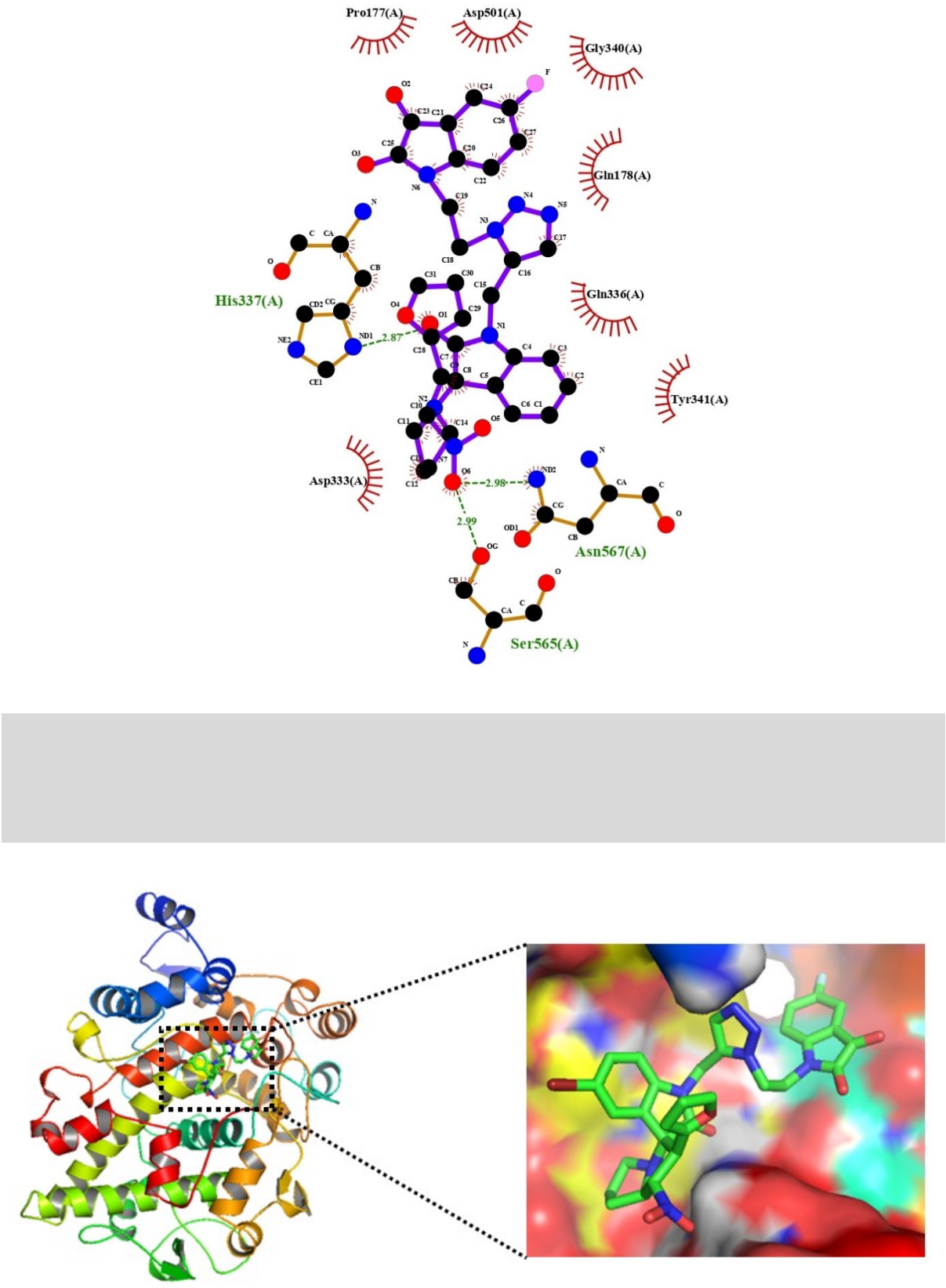


Figure S31. 2D and 3D image of compound **13** with target protein Cyclooxygenase (COX-2).

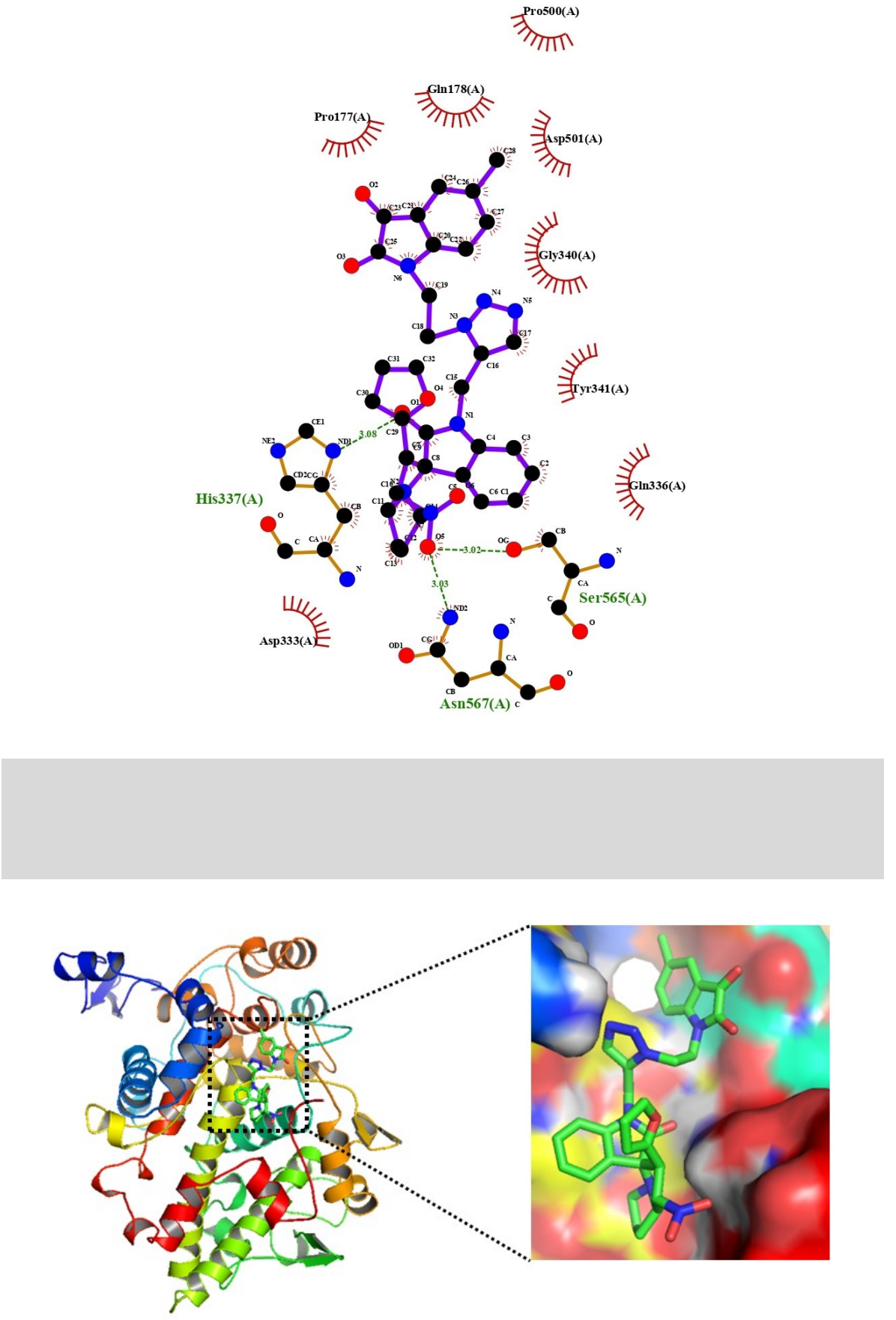


Figure S35. 2D and 3D image of compound **14** with target protein Cyclooxygenase (COX-2).

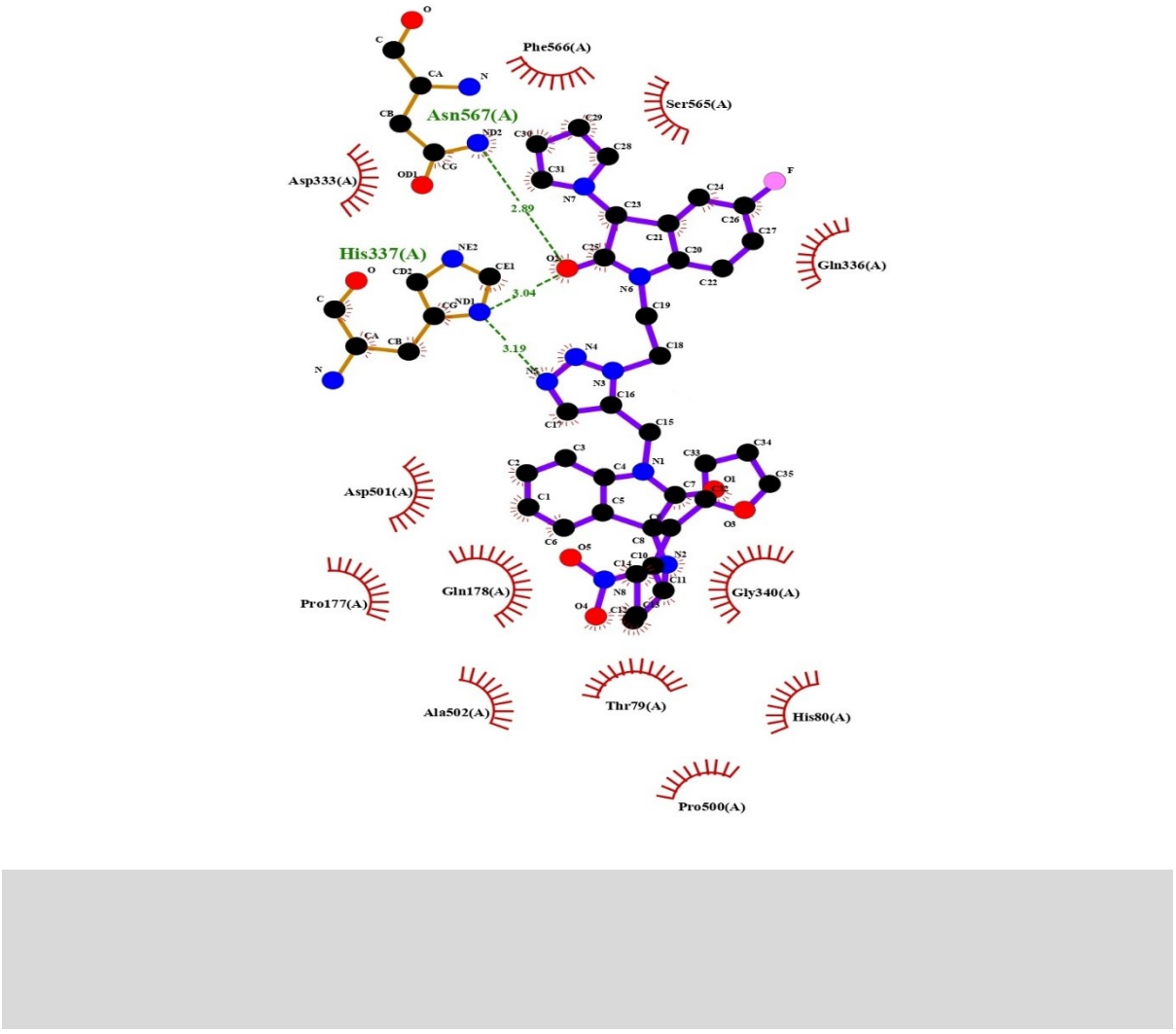


Figure S32. 2D and 3D image of compound **15** with target protein Cyclooxygenase (COX-2).

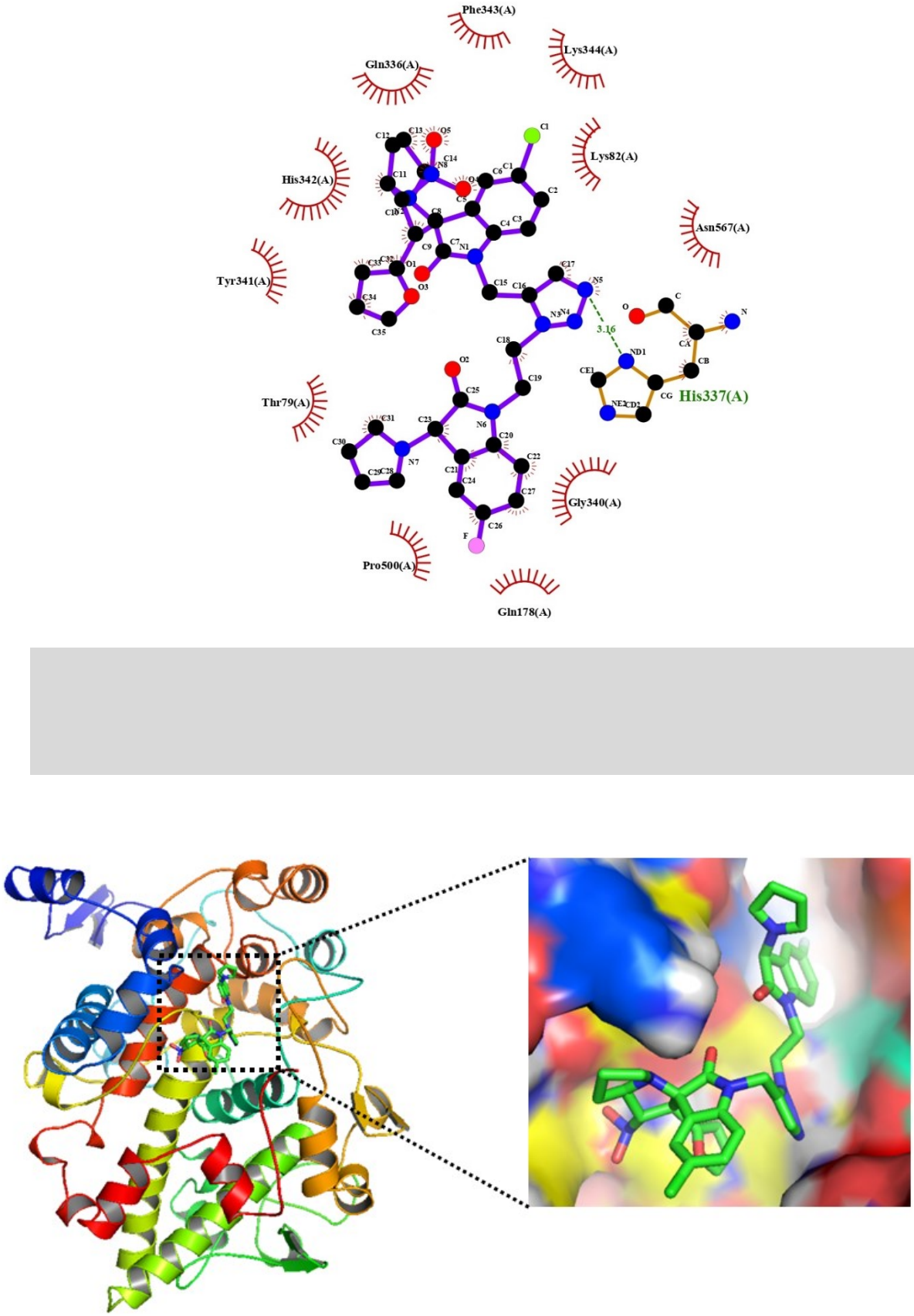


Figure S33. 2D and 3D image of compound **16** with target protein Cyclooxygenase (COX-2).

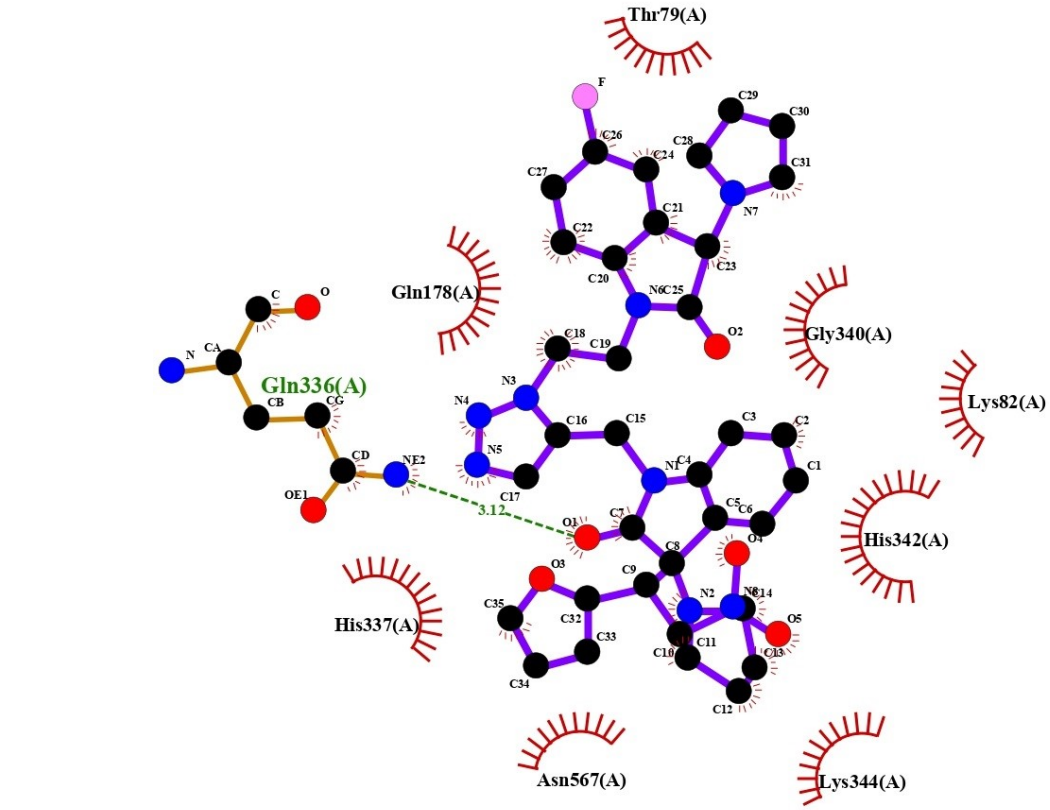


Figure S34. 2D and 3D image of compound **17** with target protein Cyclooxygenase (COX-2).

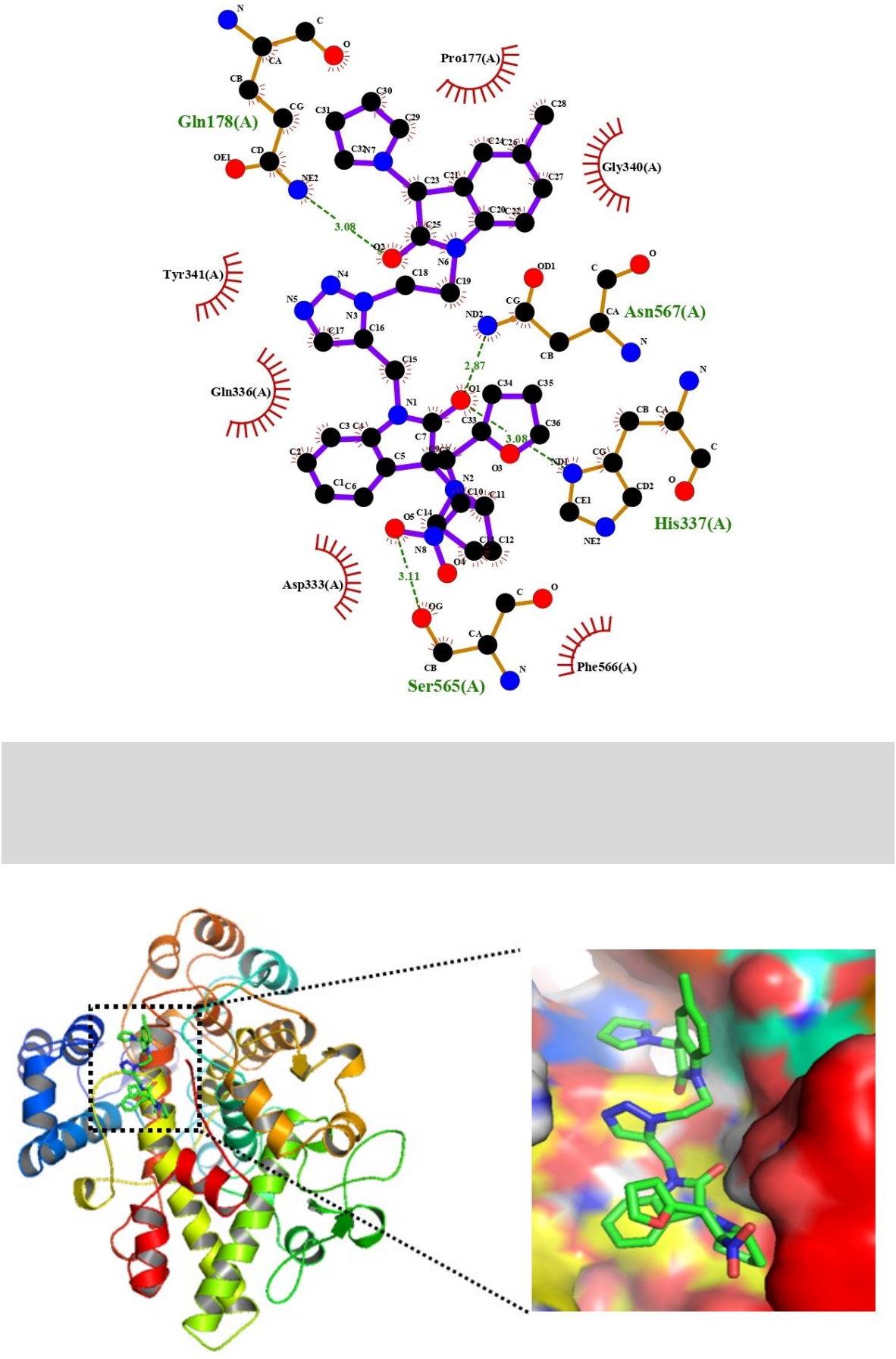


Figure S36. 2D and 3D image of compound **18** with target protein Cyclooxygenase (COX-2).

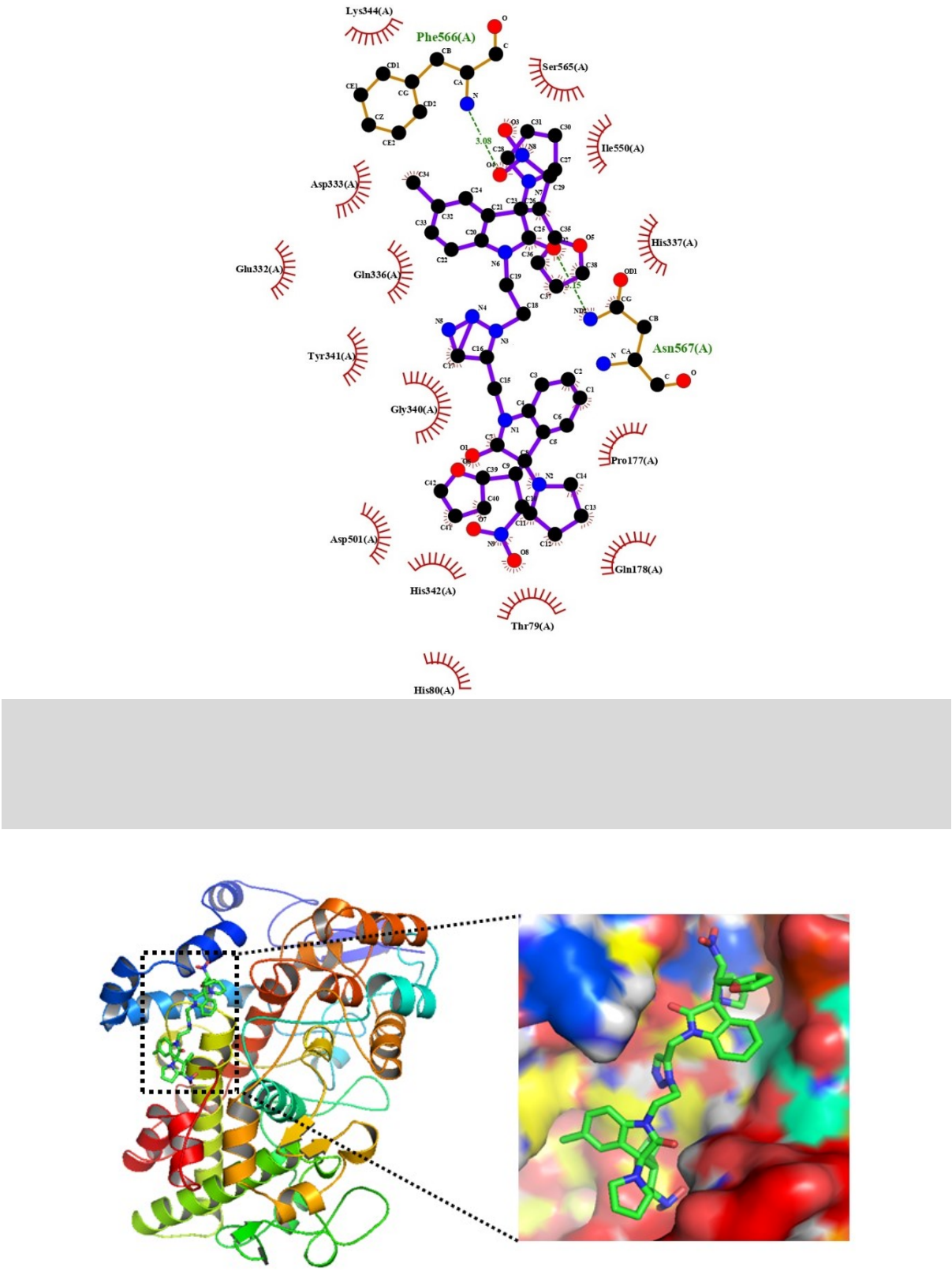


Figure S37. 2D and 3D image of compound **19** with target protein Cyclooxygenase (COX-2).