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LETTERS

Synthesis of Indole-Oxadiazole coupled isoxazole hybrids as potent EGFR targeting anticancer agents

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Supplementary Information

EXPERIMENTAL SECTION

Chemistry:

All the reactants were purchased from the Aldrich chemical company. All the reagents and solvents were purchased from SD. Thin layer chromatography (TLC) was performed using Merck silica gel 60F254 precoated plates (0.25 mm), and silica gel was used for column chromatography. ^{1}H and ^{13}C NMR spectra were recorded on a 400-MHz instrument. ^{1}H-NMR and ^{13}C-NMR spectras were reported relative to Me_4Si and residual DMSO. Mass spectra were recorded on a Jeol JMC-300 spectrometer (ESI, 70 eV). Elemental analyses were performed on Carlo Erba 106 and PerkinElmer model 240 analyzers. Melting points were determined using a Cintex apparatus and are uncorrected.

Synthesis of 3-(3,5-dichloro-4-methoxyphenyl)-5-(1H-indol-3-yl)-1,2,4-oxadiazole (3): A mixture of 3,5-dichloro-4-methoxybenzonitrile (5g, 0.025 mol), $NH_2OH.HCl$ (0.025 mol) and triethylamine (5 mL) in dry DCM (50 mL) was stirred at room temperature for 8 hours. After the aromatic carboxylic acids (0.037 mol) and vilsmeier reagent (0.03 mol) were added and resulting mixture stirred for further 7 hours at same temperature. The completion of reaction was confirmed by TLC, then the reaction mixture was washed successively with saturated $NaHCO_3$ (50 ml) and brine (30 ml). The organic layer was dried (Na_2SO_4), filtered

and the solvent was removed to give the crude product, which 1,2,4-oxadiazoles **(3)** were purified by short column chromatography (petroleum ether/ethyl acetate 8:2). ^{1}H NMR (400 MHz, DMSO) δ 11.50 (s, 1H, -NH), 7.75 (d, *J*= 8.0Hz, 1H), 7.50 (d, *J*=8.0 Hz, 1H), 7.35 (s, 2H), 7.24-7.16 (m, 2H), 7.10-7.03 (m, 1H), 3.82 (s, 3H, -OCH_3); EI-MS m/z 360 [M+H].

Synthesis of 3-(3,5-dichloro-4-methoxyphenyl)-5-(1-(prop-2-yn-1-yl)-1H-indol-3-yl)-1,2,4-oxadiazole (4): A mixture of 3-(3,5-dichloro-4-methoxyphenyl)-5-(1H-indol-3-yl)-1,2,4-oxadiazole (**3**) (4g, 0.011 mol), K_2CO_3 (0.033 mol) and propargyl bromide (0.016 mol) in DMF (50 mL) was stirred at room temperature for 6h. The completion of the reaction as monitored by TLC, the mixture was diluted with water (40 mL) and extracted with ethyl acetate (2 × 30 mL). The combined organic layer was washed with brine (2 × 30 mL), then dried under anhydrous Na_2SO_4 and finally concentrated under vacuum to afford compound **(4)** (81%). ^{1}H NMR (400 MHz, DMSO) δ 7.73 (d, *J*= 8.0Hz, 1H), 7.55 (d, *J*=8.0 Hz, 1H), 7.38 (s, 2H), 7.26-7.22 (m, 1H), 7.16 (s, 1H), 7.11-7.05 (m, 1H), 4.15 (d, *J*=4.0 Hz, 2H, -CH_2), 3.81 (s, 3H, -OCH_3), 2.03 (t, *J*=4.0 Hz, 1H, -CH); EI-MS m/z 398 [M+H].

Synthesis of 3-(3,5-dichloro-4-methoxyphenyl)-5-(1-((3-(aryl)isoxazol-5-yl)methyl)-1H-indol-3-yl)-1,2,4-oxadiazole (**6a-6o**). Aldehyde (0.5g) was added to a solution of hydroxylamine hydrochloride (4.0 mmol) in 15 mL of 1:1 ^{t}BuOH : H_2O. To this was added NaOH (4.0 mmol), and the mixture was stirred for 30 min at ambient temperature. Chloramine-*T* trihydrate (4.0 mmol) was added in small portions over 10 min, followed by CuI (10mol %). 3-(3,5-dichloro-4-methoxyphenyl)-5-(1-(prop-2-yn-1-yl)-1H-indol-3-yl)-1,2,4-oxadiazole (0.5g) was added, pH was adjusted to 6 by addition of a few drops of 1M NaOH, and stirring was continued for 8-10h. The reaction mixture was poured into cold water (50 mL), and 5 mL of dilute NH_4OH were added to remove all copper salts. Isoxazole was collected by filtration, redissolved, and passed through a short plug of silica gel (35% ethyl acetate–hexane) affording pure product.

3-(3,5-dichloro-4-methoxyphenyl)-5-(1-((3-phenylisoxazol-5-yl)methyl)-1H-indol-3-yl)-1,2,4-oxadiazole (6a): ^{1}H NMR (400 MHz, DMSO) δ 7.75 (d, *J*= 8.0Hz, 1H), 7.56 (d, *J*=8.0 Hz, 1H),7.50-7.45 (m, 2H), 7.35 (s, 2H), 7.28-7.20 (m, 4H), 7.14 (s, 1H), 7.11-7.07 (m, 1H),

6.78 (s, 1H), 5.12 (s, 2H), 3.82 (s, 3H, -OCH_3); ^{13}C NMR (100 MHz, DMSO) δ 165.40, 161.66, 160.30, 159.04, 156.38, 135.22, 130.46, 129.51, 128.78(2C), 128.04(2C), 127.08(2C), 126.65, 126.12(2C), 123.78, 122.63, 122.08, 121.59, 120.83, 110.36, 98.72, 96.92, 56.20, 42.25; ESI-MS m/z: 517 [M+H]. Anal.Cal for $C_{27}H_{18}Cl_2N_4O_3$; C, 62.68; H, 3.51; N, 10.83; found C, 62.65; H, 3.53; N, 10.86.

3-(3,5-dichloro-4-methoxyphenyl)-5-(1-((3-(p-tolyl)isoxazol-5-yl)methyl)-1H-indol-3-yl)-1,2,4-oxadiazole (6b): ^{1}H NMR (400 MHz, DMSO) δ 7.73 (d, *J*= 8.0Hz, 1H), 7.61 (d, *J*= 8.0Hz, 2H), 7.53 (d, *J*=8.0 Hz, 1H), 7.40 (d, *J*= 8.0Hz, 2H), 7.31 (s, 2H), 7.26-7.22 (m, 1H), 7.13 (s, 1H), 7.10-7.07 5(m, 1H), 6.73 (s, 1H), 5.13 (s, 2H), 3.81 (s, 3H, -OCH_3), 2.37 (s, 3H, -CH_3); ^{13}C NMR (100 MHz, DMSO) δ 165.60, 161.40, 160.10, 159.19, 156.29, 139.59, 135.30, 130.42, 129.11(2C), 128.20(2C), 127.40(2C), 126.27, 125.59(2C), 123.30, 122.70, 122.16, 121.61, 120.29, 110.49, 98.70, 96.50, 56.43, 42.37, 21.54; ESI-MS m/z: 531 [M+H]. Anal.Cal for $C_{28}H_{20}Cl_2N_4O_3$; C, 63.29; H, 3.79; N, 10.54; found C, 63.33; H, 3.83; N, 10.57.

3-(3,5-dichloro-4-methoxyphenyl)-5-(1-((3-(m-tolyl)isoxazol-5-yl)methyl)-1H-indol-3-yl)-1,2,4-oxadiazole (6c): ^{1}H NMR (400 MHz, DMSO) δ 7.74 (d, *J*= 8.0Hz, 1H), 7.54 (d, *J*=8.0 Hz, 1H), 7.46-7.41(m, 2H), 7.35 (s, 2H), 7.28-7.22 (m, 3H), 7.13 (s, 1H), 7.10-7.04 (m, 1H), 6.79 (s, 1H), 5.13 (s, 2H), 3.81 (s, 3H, -OCH_3), 2.29 (s, 3H, -CH_3); ^{13}C NMR (100 MHz, DMSO) δ 13C NMR (125 MHz, Common NMR Solvents) δ 165.80, 161.36, 160.10, 159.09, 156.14, 137.22, 135.35, 132.30, 131.25, 129.76(2C), 128.97, 128.37, 127.27, 126.27(2C), 124.13, 123.58, 122.84, 122.20, 121.35, 120.29, 110.75, 98.24, 96.25, 56.53, 42.61, 21.13; ESI-MS m/z: 531 [M+H]. Anal.Cal for $C_{28}H_{20}Cl_2N_4O_3$; C, 63.29; H, 3.79; N, 10.54; found C, 63.32; H, 3.83; N, 10.58.

3-(3,5-dichloro-4-methoxyphenyl)-5-(1-((3-(4-methoxyphenyl)isoxazol-5-yl)methyl)-1H-indol-3-yl)-1,2,4-oxadiazole (6d): ^{1}H NMR (400 MHz, DMSO) δ 7.75 (d, *J*= 8.0Hz, 1H), 7.69 (d, *J*=8.0 Hz, 2H), 7.53 (d, *J*=8.0 Hz, 1H), 7.32 (s, 2H), 7.21-7.10 (m, 2H), 7.09-7.03 (m, 1H), 6.99 (d, *J*=8.0 Hz, 2H), 6.72 (s, 1H), 5.13 (s, 2H), 3.87 (s, 3H, -OCH_3), 3.81 (s, 3H, -OCH_3); ^{13}C NMR (100 MHz, DMSO) δ 13C NMR (101 MHz, DMSO) δ 165.67, 161.44, 160.15, 159.70, 159.15, 156.13, 135.32, 129.67(2C), 128.91(2C), 126.64, 126.11(2C), 123.82, 122.95, 122.08, 121.65, 121.13, 120.22, 114.60(2C), 110.68, 98.55, 96.82, 56.47, 55.27, 42.50; ESI-MS m/z: 547 [M+H]. Anal.Cal for $C_{28}H_{20}Cl_2N_4O_4$; C, 61.44; H, 3.68; N, 10.24; found C, 61.48; H, 3.71; N, 10.21.

5-(1-((3-(4-chlorophenyl)isoxazol-5-yl)methyl)-1H-indol-3-yl)-3-(3,5-dichloro-4-methoxyphenyl)-1,2,4-oxadiazole (6e): ^{1}H NMR (400 MHz, DMSO) δ 7.75 (d, *J*= 8.0Hz, 1H), 7.65 (d, *J*= 8.0Hz, 2H), 7.53 (d, *J*=8.0 Hz, 1H), 7.41 (d, *J*= 8.0Hz, 2H), 7.32 (s, 2H), 7.25-7.15(m, 2H), 7.10-7.03 (m, 1H), 6.77 (s, 1H), 5.13 (s, 2H), 3.81 (s, 3H, -OCH_3); ^{13}C NMR (100 MHz, DMSO) δ 165.39, 161.72, 160.18, 159.11, 156.20, 135.73, 135.17, 129.95, 129.07(2C), 128.21(2C), 127.33(2C), 126.39, 126.00(2C), 123.57, 122.58, 122.07, 121.44, 120.67, 110.34, 98.83, 96.64, 56.19, 42.47; ESI-MS m/z: 551 [M+H]. Anal.Cal for $C_{27}H_{17}Cl_3N_4O_3$; C, 58.77; H, 3.11; N, 10.15; found C, 58.75; H, 3.14; N, 10.17.

5-(1-((3-(4-bromophenyl)isoxazol-5-yl)methyl)-1H-indol-3-yl)-3-(3,5-dichloro-4-methoxyphenyl)-1,2,4-oxadiazole (6f): ^{1}H NMR (400 MHz, DMSO) δ 7.75 (d, *J*= 8.0Hz, 1H), 7.56 (d, *J*=8.0 Hz, 1H),7.48-7.43 (m, 4H), 7.35 (s, 2H), 7.23-7.19 (m, 1H), 7.14 (s, 1H), 7.10-7.05 (m, 1H), 6.76 (s, 1H), 5.13 (s, 2H), 3.81 (s, 3H, -OCH_3); ^{13}C NMR (100 MHz, DMSO) δ 165.60, 161.56, 160.29, 159.01, 156.09, 135.34, 131.44(2C), 129.17(2C), 127.44, 126.65(2C), 126.27, 125.83(2C), 124.80, 123.68, 122.69, 122.16, 121.39, 120.74, 110.47, 98.49, 96.33, 56.56, 42.47; ESI-MS m/z: 594 [M+H] & 596 [M+3H]. Anal.Cal for $C_{27}H_{17}BrCl_2N_4O_3$; C, 54.39; H, 2.87; N, 9.40; found C, 54.35; H, 2.82; N, 9.45.

3-(3,5-dichloro-4-methoxyphenyl)-5-(1-((3-(4-fluorophenyl)isoxazol-5-yl)methyl)-1H-indol-3-yl)-1,2,4-oxadiazole (6g): ^{1}H NMR (400 MHz, DMSO) δ 7.99 (d, *J*= 8.0Hz, 2H), 7.75 (d, *J*= 8.0Hz, 1H), 7.65 (d, *J*= 8.0Hz, 2H), 7.52 (d, *J*=8.0 Hz, 1H), 7.33 (s, 2H), 7.24-7.20 (m, 1H), 7.15 (s, 1H), 7.10-7.05 (m, 1H), 6.81 (s, 1H), 5.13 (s, 2H), 3.82 (s, 3H, -OCH_3); ^{13}C NMR (100 MHz, DMSO) δ 165.60, 161.72, 161.08, 160.11, 159.09, 156.09, 135.46, 130.27(2C), 129.76(2C), 127.96, 126.63, 126.27(2C), 123.35, 122.75, 122.16, 121.53, 120.75, 115.53(2C), 110.52, 98.91, 96.49, 56.48, 42.46; ESI-MS m/z: 535 [M+H]. Anal.Cal for $C_{27}H_{17}Cl_2FN_4O_3$; C, 60.57; H, 3.20; N, 10.47; found C, 60.54; H, 3.24; N, 10.45.

3-(3,5-dichloro-4-methoxyphenyl)-5-(1-((3-(4-nitrophenyl)isoxazol-5-yl)methyl)-1H-indol-3-yl)-1,2,4-oxadiazole (6h): ^{1}H NMR (400 MHz, DMSO) δ 8.40 (d, *J*= 8.0Hz, 2H), 8.20 (d, *J*= 8.0Hz, 2H), 7.75 (d, *J*= 8.0Hz, 1H), 7.55 (d, *J*=8.0 Hz, 1H), 7.36 (s, 2H), 7.26-7.20 (m, 2H), 7.12-7.05 (m, 1H), 6.82 (s, 1H), 5.13 (s, 2H), 3.81 (s, 3H, -OCH_3); ^{13}C NMR (100 MHz, DMSO) δ 165.38, 161.67, 160.16, 159.05, 156.24, 149.70, 136.35, 135.66, 129.62(2C), 128.01, 127.21(2C), 126.70(2C), 126.19, 125.70(2C), 125.20, 123.29, 122.61, 122.09, 121.57, 120.79, 110.74, 98.77, 96.46, 56.20, 42.64; ESI-MS m/z: 562 [M+H]. Anal.Cal for

$C_{27}H_{17}Cl_2N_5O_5$; C, 57.67; H, 3.05; N, 12.45; found C, 57.69; H, 3.02; N, 12.48.

3-(3,5-dichloro-4-methoxyphenyl)-5-(1-((3-(3,5-dimethylphenyl)isoxazol-5-yl)methyl)-1H-indol-3-yl)-1,2,4-oxadiazole (6i): ^{1}H NMR (400 MHz, DMSO) δ 7.74 (d, *J*= 8.0Hz, 1H), 7.59 (s, 2H), 7.52 (d, *J*=8.0 Hz, 1H), 7.35 (s, 2H), 7.29-7.20 (m, 2H), 7.18-7.06 (m, 2H), 6.72 (s, 1H), 5.15 (s, 2H), 3.82 (s, 3H, -OCH_3), 2.34 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, DMSO) δ 165.56, 161.54, 160.12, 159.51, 156.22, 137.04(2C), 135.36, 132.00, 131.12, 129.74(2C), 126.66, 126.13(2C), 125.57(2C), 123.88, 122.91, 122.09, 121.53, 120.23, 110.59, 98.69, 96.77, 56.11, 42.49, 21.30(2C), ESI-MS m/z: 545 [M+H]. Anal.Cal for $C_{29}H_{22}Cl_2N_4O_3$; C, 63.86; H, 4.07; N, 10.27; found C, 63.89; H, 4.03; N, 10.30.

3-(3,5-dichloro-4-methoxyphenyl)-5-(1-((3-(2,3-dimethylphenyl)isoxazol-5-yl)methyl)-1H-indol-3-yl)-1,2,4-oxadiazole (6j): ^{1}H NMR (400 MHz, DMSO) δ 7.74 (d, *J*= 8.0Hz, 1H), 7.54 (d, *J*=8.0 Hz, 1H), 7.48-7.40 (m, 1H), 7.33 (s, 2H), 7.24-7.20 (m, 4H), 7.10-7.04 (m, 1H), 6.77 (s, 1H), 5.15 (s, 2H), 3.81 (s, 3H, -OCH_3), 2.30 (s, 3H, -CH_3), 1.98 (s, 3H, -CH_3); ^{13}C NMR (100 MHz, DMSO) δ 165.59, 161.87, 160.41, 159.13, 156.16, 137.50, 136.90, 135.10, 133.22, 131.30, 129.27(2C), 126.64, 126.11(2C), 125.36, 123.67, 122.95, 122.08, 121.13, 120.22, 110.66, 98.68, 96.90, 56.42, 42.47, 19.46, 16.24; ESI-MS m/z: 545 [M+H]. Anal.Cal for $C_{29}H_{22}Cl_2N_4O_3$; C, 63.86; H, 4.07; N, 10.27; found C, 63.89; H, 4.04; N, 10.29.

3-(3,5-dichloro-4-methoxyphenyl)-5-(1-((3-(3-nitrophenyl)isoxazol-5-yl)methyl)-1H-indol-3-yl)-1,2,4-oxadiazole (6k): ^{1}H NMR (400 MHz, DMSO) δ 8.48 (s, 1H), 8.23-8.19 (m, 3H), 7.76 (d, *J*= 8.0Hz, 1H), 7.55 (d, *J*=8.0 Hz, 1H), 7.32 (s, 2H), 7.25-7.20 (m, 1H), 7.13 (s, 1H), 7.09-7.05 (m, 1H), 6.81 (s, 1H), 5.13 (s, 2H), 3.82 (s, 3H, -OCH_3); ^{13}C NMR (100 MHz, DMSO) δ 13C NMR (101 MHz, DMSO) δ 165.78, 161.70, 160.50, 159.22, 156.44, 147.48, 135.76, 134.46, 132.11, 129.58(2C), 128.36, 127.69, 126.65, 126.11(2C), 124.80, 123.82, 122.76, 122.07, 121.35, 120.72, 110.58, 98.33, 96.71, 56.28, 42.62; ESI-MS m/z: 562 [M+H]. Anal.Cal for $C_{27}H_{17}Cl_2N_5O_5$; C, 57.67; H, 3.05; N, 12.45; found C, 57.63; H, 3.07; N, 12.48.

5-(1-((3-(3-chlorophenyl)isoxazol-5-yl)methyl)-1H-indol-3-yl)-3-(3,5-dichloro-4-methoxyphenyl)-1,2,4-oxadiazole (6l): ^{1}H NMR (400 MHz, DMSO) δ 7.82 (s, 1H), 7.75 (d, *J*= 8.0Hz, 1H), 7.56 (d, *J*=8.0 Hz, 1H),7.49-7.43 (m, 2H), 7.35 (s, 2H), 7.28-7.23 (m, 2H), 7.13 (s, 1H), 7.09-7.04 (m, 1H), 6.79 (s, 1H), 5.13 (s, 2H), 3.81 (s, 3H, -OCH_3); ^{13}C NMR (100 MHz, DMSO) δ 165.42, 161.55, 160.42, 159.28, 156.27, 135.52, 132.71, 132.21, 129.40,

128.67(2C), 128.06, 126.27(2C), 125.54, 124.52, 123.06, 122.65, 122.16, 121.29, 120.29, 110.62, 98.49, 96.69, 56.21, 42.31; ESI-MS m/z: 551 [M+H]. Anal.Cal for $C_{27}H_{17}C_{l3}N_4O_3$; C, 58.77; H, 3.11; N, 10.15; found C, 58.72; H, 3.15; N, 10.18.

3-(3,5-dichloro-4-methoxyphenyl)-5-(1-((3-(3,5-dichlorophenyl)isoxazol-5-yl)methyl)-1H-indol-3-yl)-1,2,4-oxadiazole (6m): ^{1}H NMR (400 MHz, DMSO) δ 7.75 (d, *J*= 8.0Hz, 1H), 7.70 (s, 2H), 7.56 (d, *J*=8.0 Hz, 1H), 7.43(s, 1H), 7.35 (s, 2H), 7.28-7.20 (m, 1H), 7.15 (s, 1H), 7.10-7.05 (m, 1H), 6.79 (s, 1H), 5.13 (s, 2H), 3.81 (s, 3H, -OCH_3); ^{13}C NMR (100 MHz, DMSO) δ 13C NMR (101 MHz, DMSO) δ 165.55, 161.77, 160.54, 159.18, 156.35, 135.64, 133.65(2C), 131.97, 130.74, 129.58(2C), 126.65, 126.00(2C), 125.15(2C), 123.02, 122.54, 122.15, 121.09, 120.56, 110.85, 98.70, 96.60, 56.56, 42.47; ESI-MS m/z: 584 [M+H]. Anal.Cal for $C_{27}H_{16}Cl_4N_4O_3$; C, 55.32; H, 2.75; N, 9.56; found C, 55.35; H, 2.77; N, 9.52.

3-(3,5-dichloro-4-methoxyphenyl)-5-(1-((3-(3,5-dinitrophenyl)isoxazol-5-yl)methyl)-1H-indol-3-yl)-1,2,4-oxadiazole (6n): ^{1}H NMR (400 MHz, DMSO) δ 8.48 (s, 2H), 8.21 (s, H), 7.77 (d, *J*= 8.0Hz, 1H), 7.57 (d, *J*=8.0 Hz, 1H), 7.34 (s, 2H), 7.25-7.20 (m, 1H), 7.15 (s, 1H), 7.10-7.06 (m, 1H), 6.80 (s, 1H), 5.13 (s, 2H), 3.83 (s, 3H, -OCH_3); ^{13}C NMR (100 MHz, DMSO) δ 13C NMR (101 MHz, DMSO) δ 165.74, 161.51, 160.21, 159.35, 156.09, 146.31(2C), 135.69, 132.89(2C), 131.15, 129.30(2C), 126.65, 126.12(2C), 123.78, 122.58, 122.08, 121.86, 121.29, 120.22, 110.53, 98.49, 96.77, 56.74, 42.47; ESI-MS m/z: 607 [M+H]. Anal.Cal for $C_{27}H_{16}Cl_2N_6O_7$; C, 53.39; H, 2.66; N, 13.84; found C, 53.35; H, 2.62; N, 13.87.

4-(5-((3-(3-(3,5-dichloro-4-methoxyphenyl)-1,2,4-oxadiazol-5-yl)-1H-indol-1-yl) methyl)isoxazol-3-yl)benzonitrile (6o): ^{1}H NMR (400 MHz, DMSO) δ 7.75 (d, *J*= 8.0Hz, 1H), 7.72 (d, *J*=8.0 Hz, 2H), 7.56 (d, *J*=8.0 Hz, 1H), 7.43 (d, *J*=8.0 Hz, 2H), 7.32 (s, 2H), 7.25-7.20 (m, 1H), 7.13 (s, 1H), 7.08-7.02 (m, 1H), 6.79 (s, 1H), 5.13 (s, 2H), 3.81 (s, 3H, -OCH_3); ^{13}C NMR (100 MHz, DMSO) δ 165.49, 161.56, 160.39, 159.34, 156.26, 135.93, 135.09, 132.54(2C), 129.55(2C), 128.40(2C), 126.64, 126.08(2C), 123.64, 122.95, 122.08, 121.22, 120.22, 119.08, 114.75, 110.40, 98.62, 96.72, 56.38, 42.52; ESI-MS m/z: 542 [M+H]. Anal.Cal for $C_{28}H_{17}Cl_2N_5O_3$; C, 62.01; H, 3.16; N, 12.91; found C, 62.04; H, 3.12; N, 12.95.

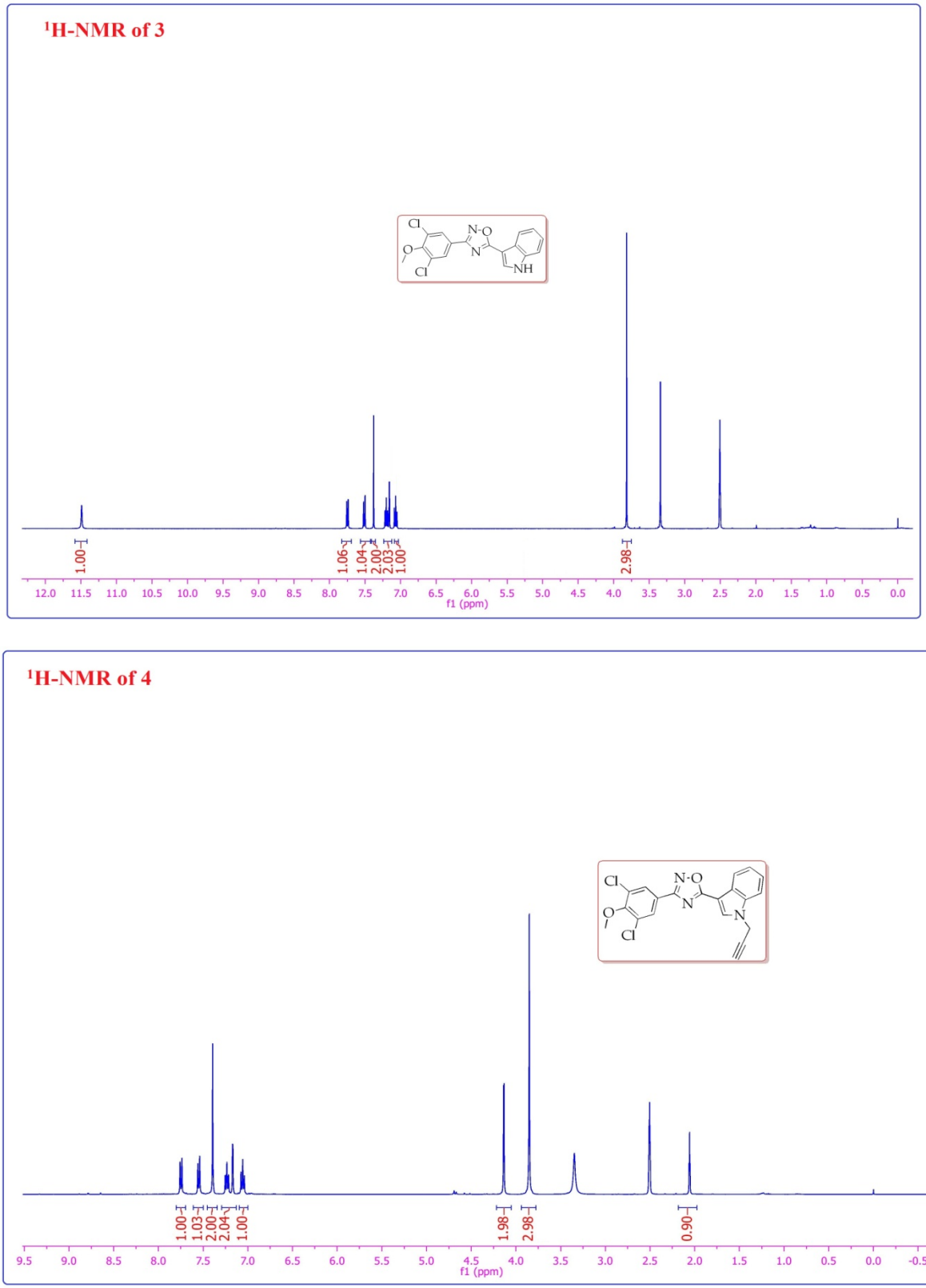


Figure S_1: [1]H-NMR of 3 and 4.

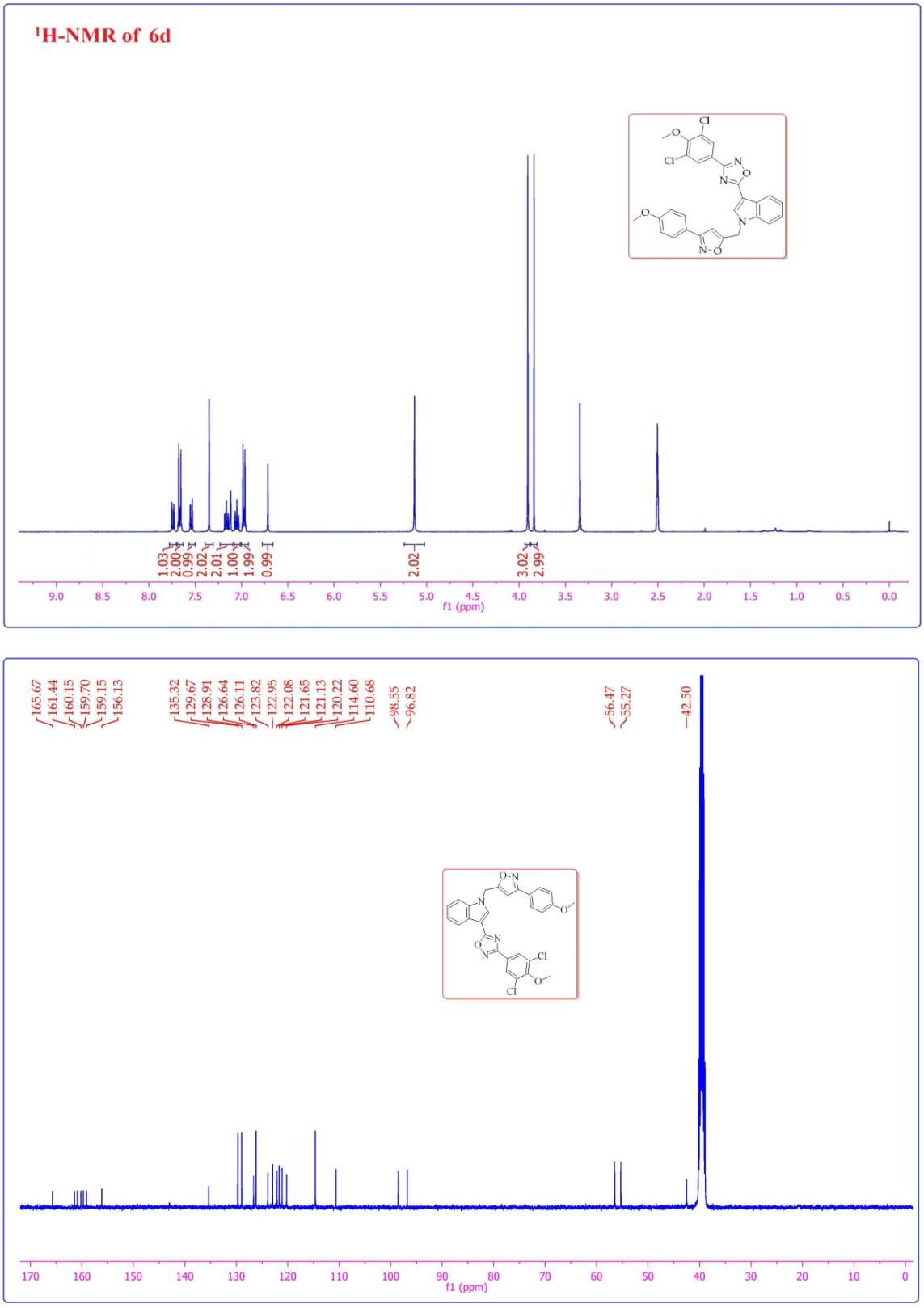


Figure S_2: ^{1}H-NMR and ^{13}C-NMR of 6d.

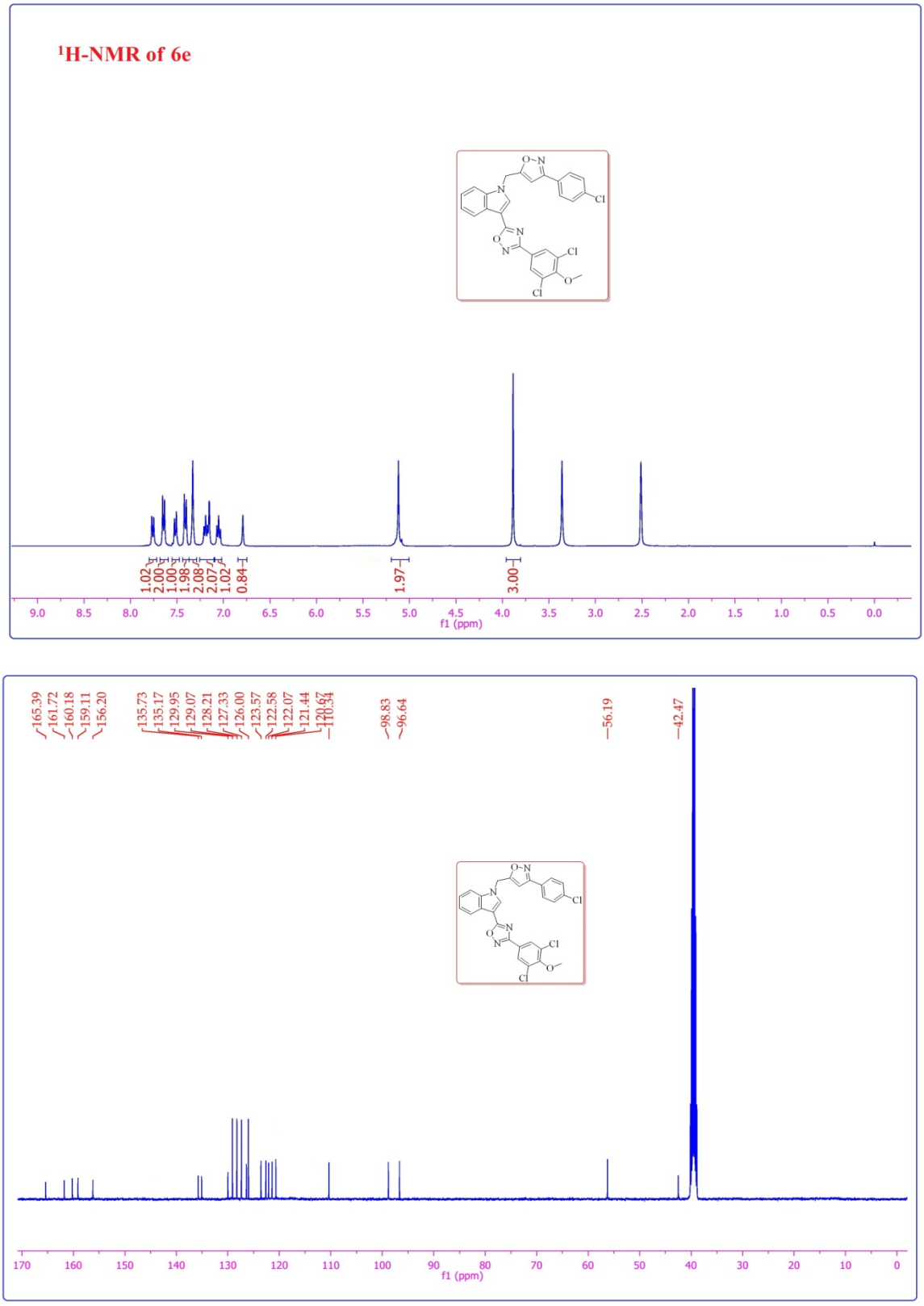


Figure S3: ^{1}H-NMR and ^{13}C-NMR of 6e.

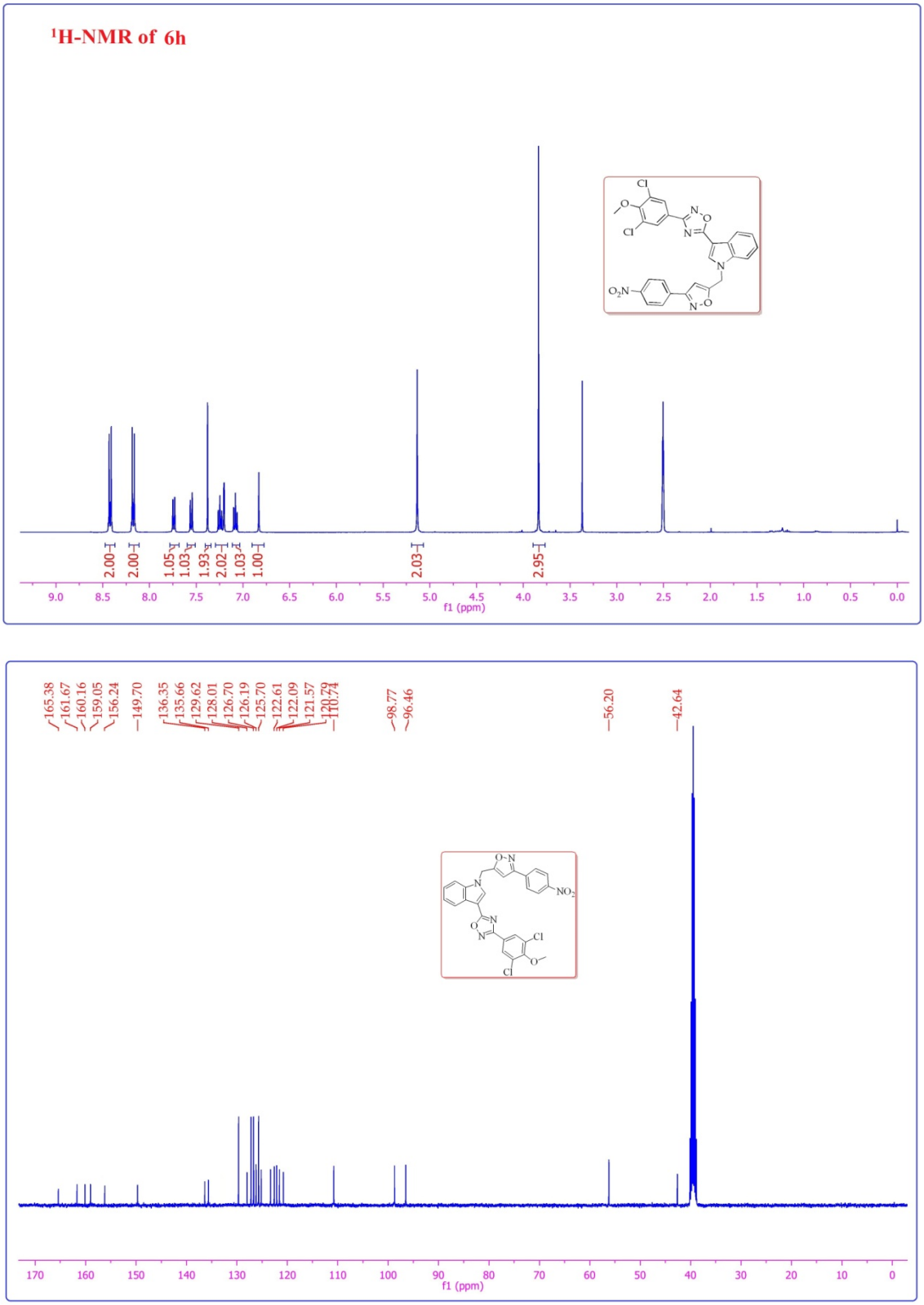
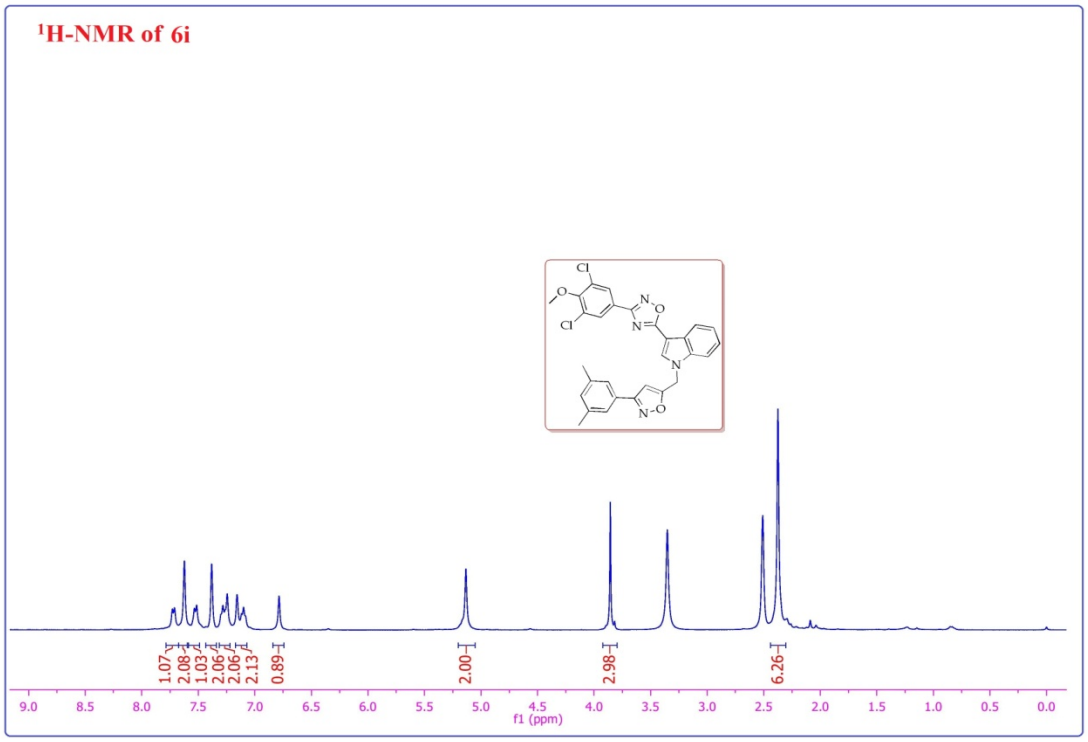


Figure S_3: ^{1}H-NMR and ^{13}C-NMR of 6h.



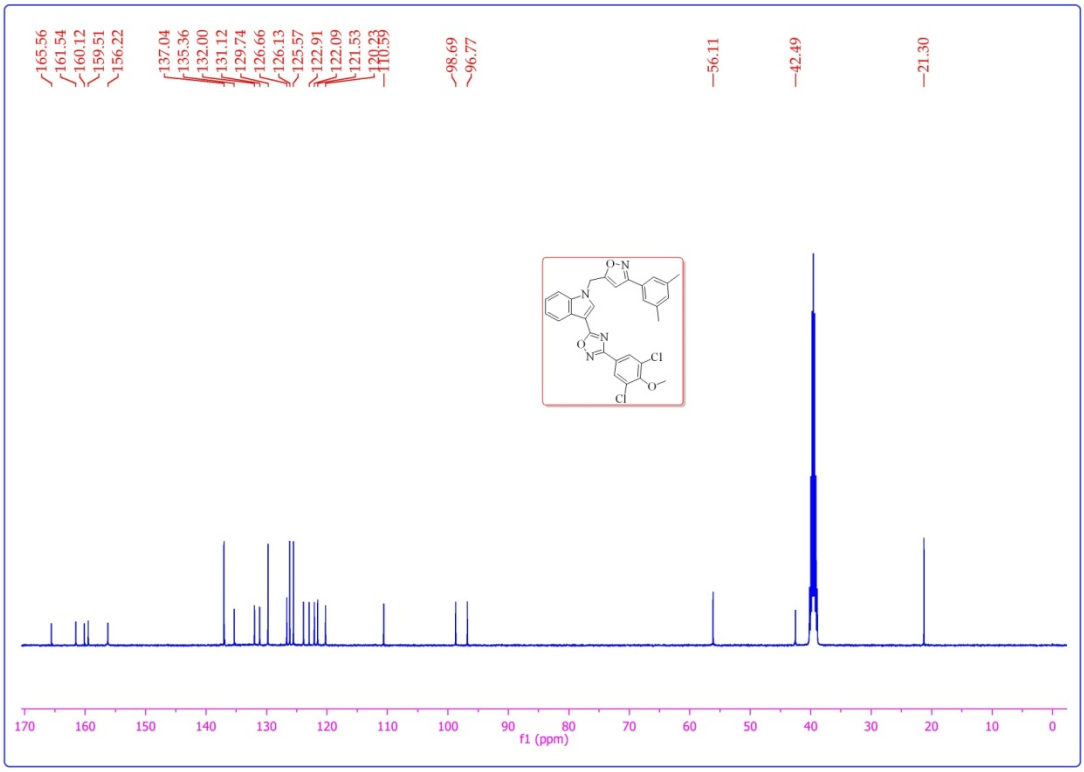


Figure S4: ^{1}H-NMR and ^{13}C-NMR of 6i.

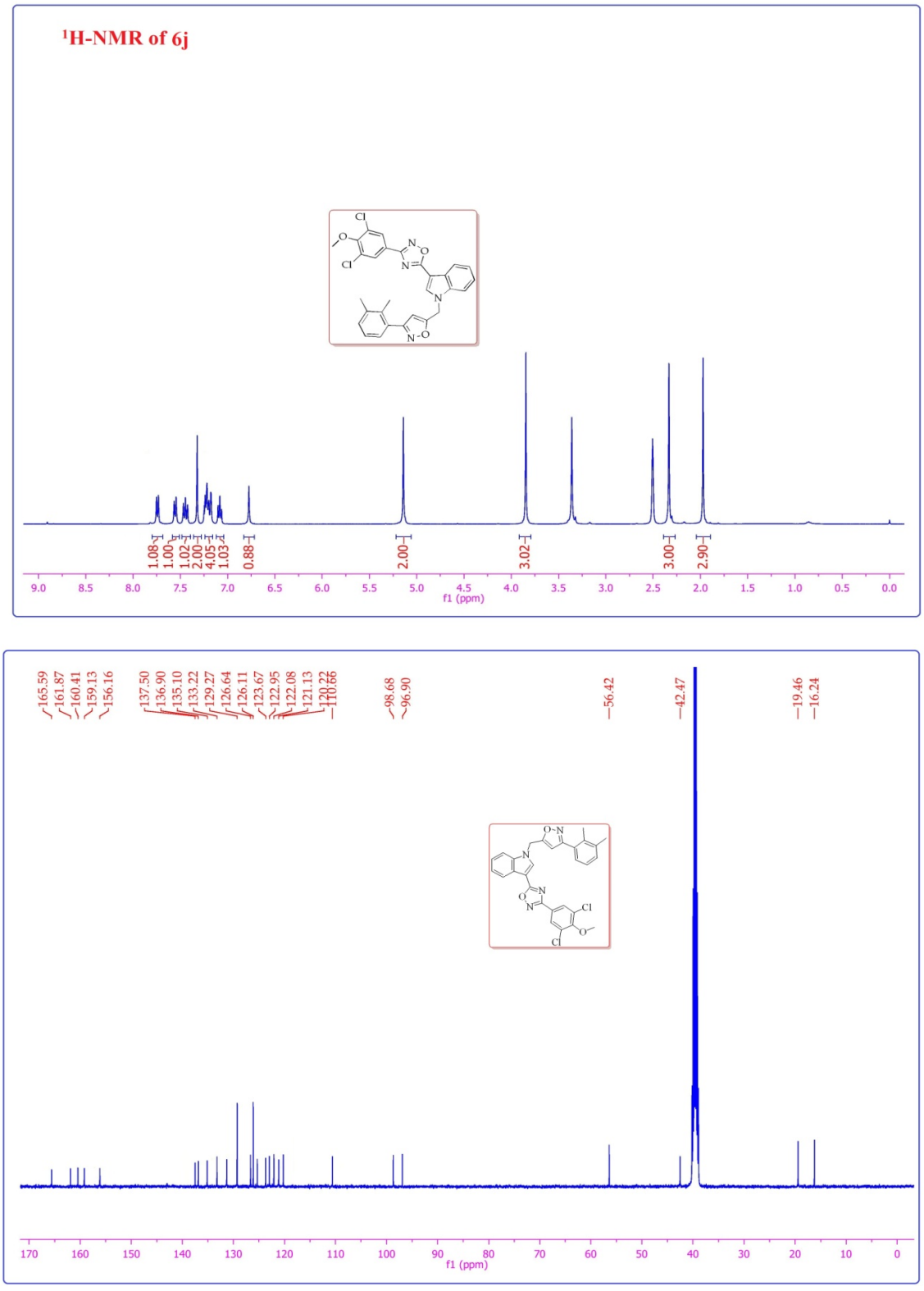


Figure S_5: ^{1}H-NMR and ^{13}C-NMR of 6j.

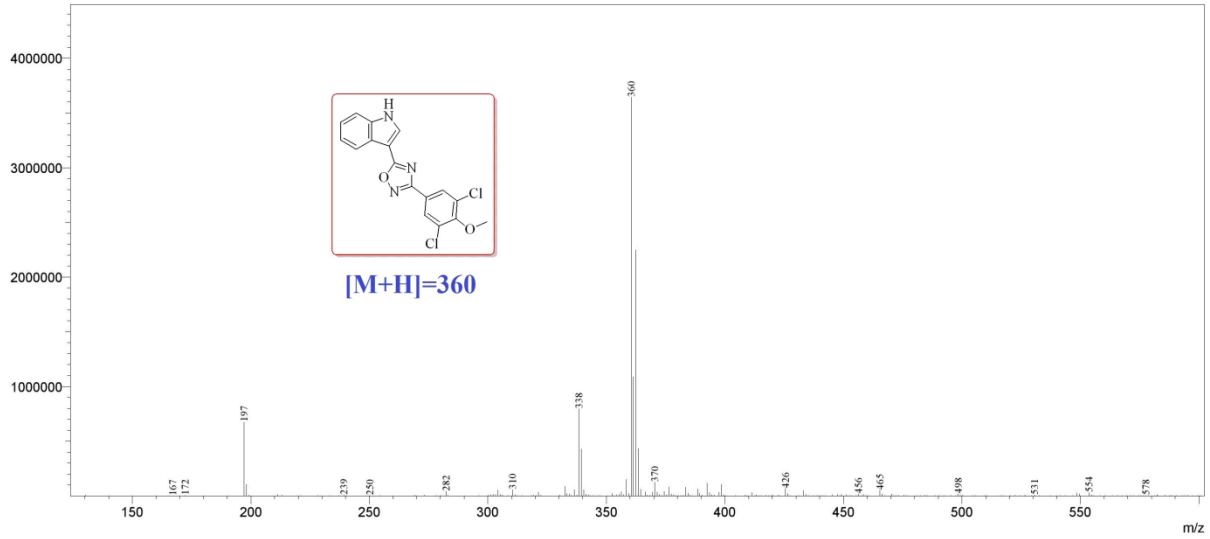


Figure S6: Mass spectrum of 3.

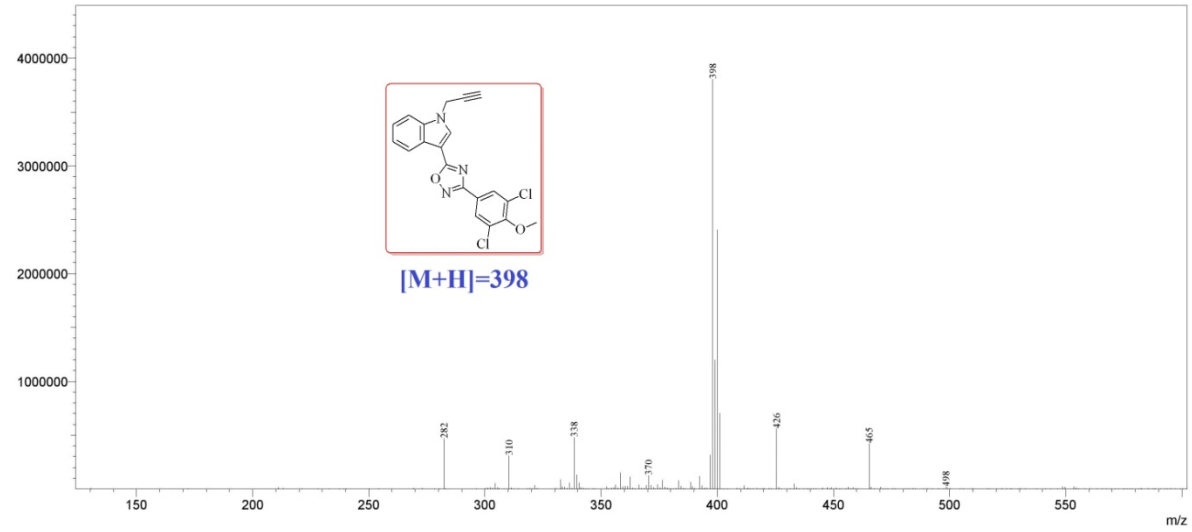


Figure S7: Mass spectrum of 4.

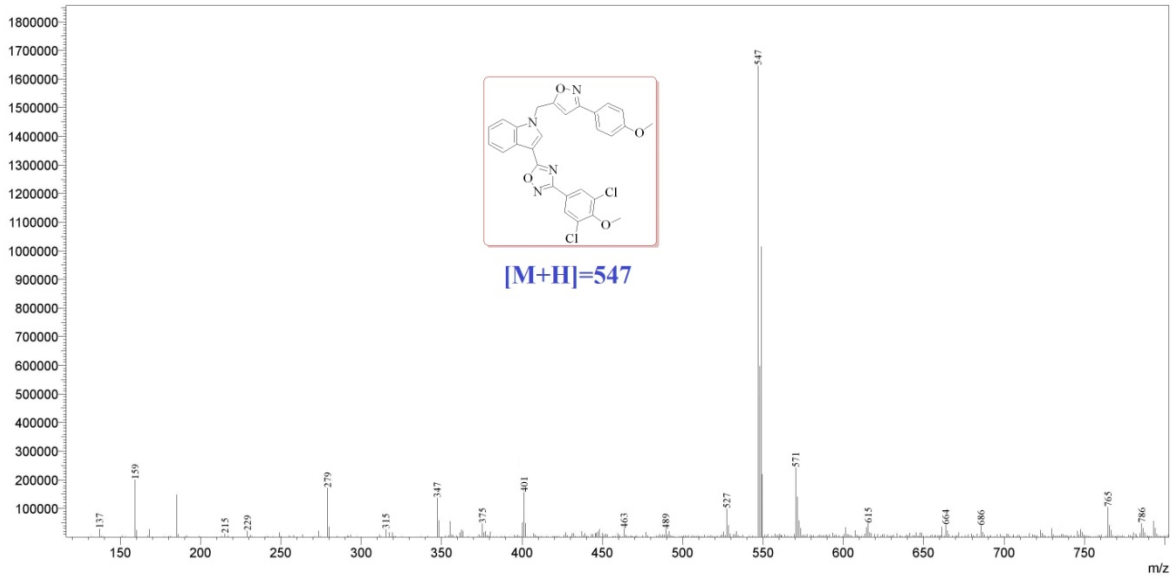


Figure S8: Mass spectrum of 6d.

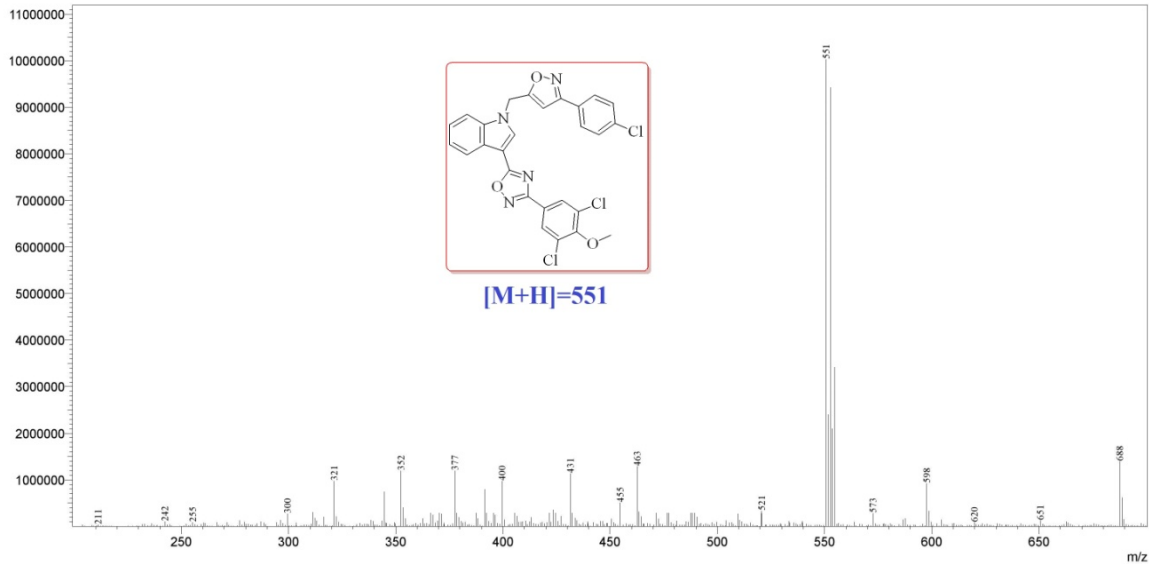


Figure S9: Mass spectrum of 6e.

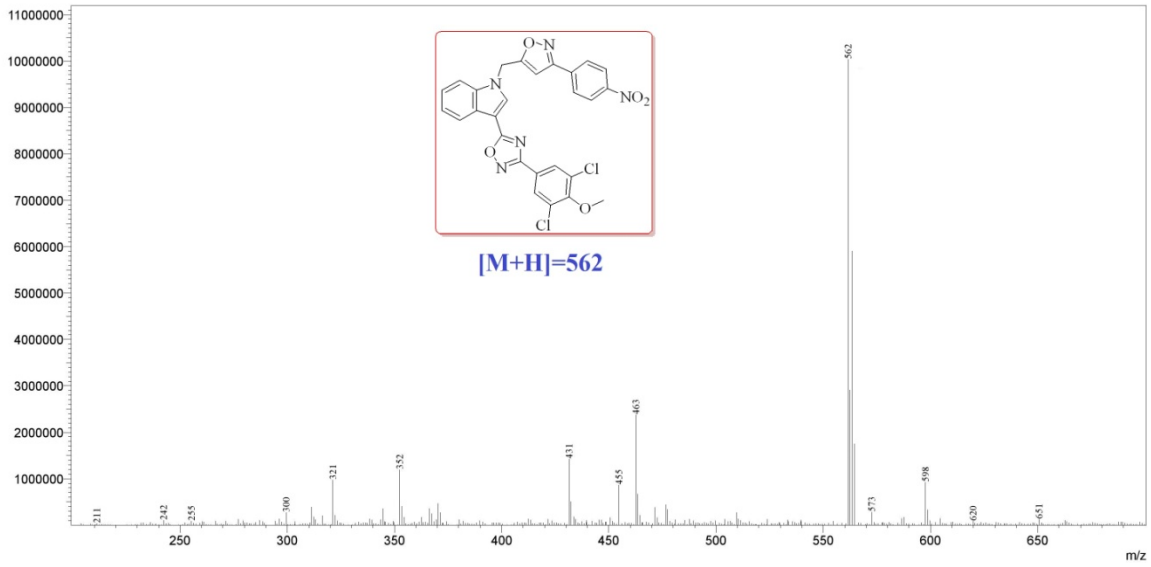


Figure S_{10}: Mass spectrum of 6h.

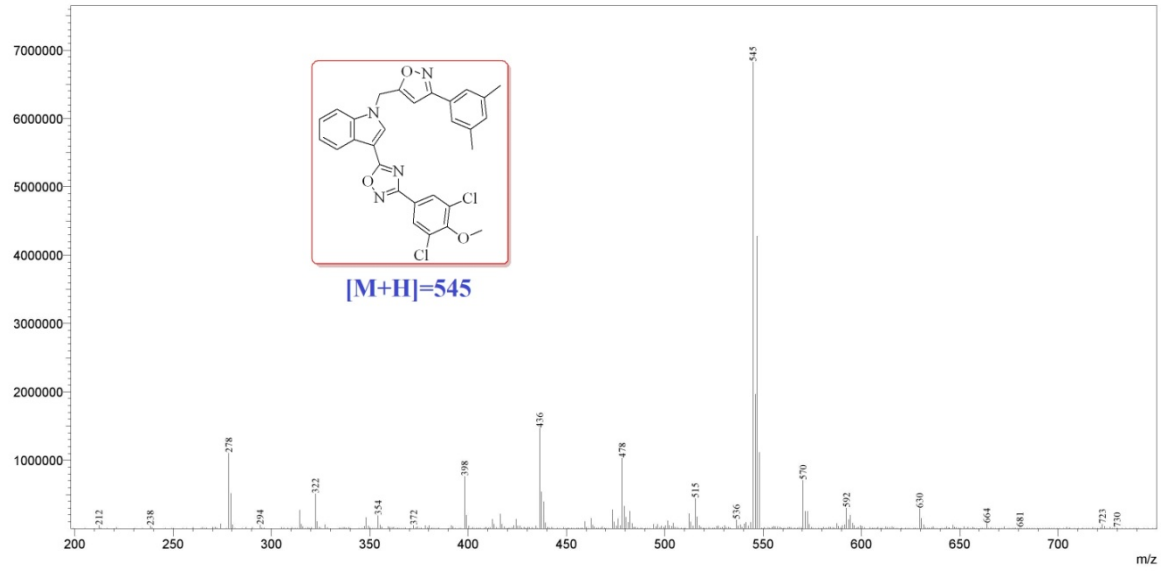


Figure S_{11}: Mass spectrum of 6i.

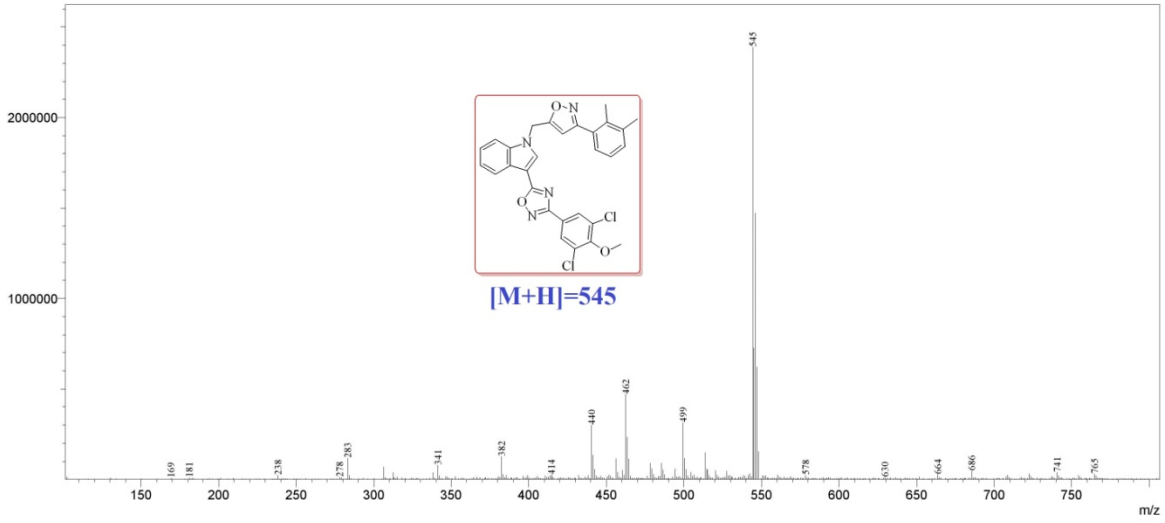


Figure S_{12}: Mass spectrum of 6j.