Supporting Information

Synthesis, antiviral, antibacterial activities and action mechanism of penta-1,4-dien-3-one oxime ether derivatives containing quinoxaline moiety

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Content

1. Biological activities tests

1.1 Antiviral activities *in vivo*

1.1.1 Curative activity of the target compounds against TMV *in vivo*

As the test subjects selecting Growing *N. tabacum* L. leaves of the same age ,the whole leaves that had beforehand were scattered with silicon carbide, was dipped and inoculated containing solution of the TMV virus. The leaves were washed with water after about 30 min and desiccation. The compound solution and the solvent were smeared on the left and right side of the leaf, respectively. After about 3-4 d, the local lesion numbers were counted and recorded. Each compound was tested three times.

1.1.2 Protection activity of the target compounds against TMV *in vivo*

The compound solution and the solvent were smeared on the left and right side of the leaf, respectively. After 12 h, the whole leaves that had beforehand were scattered with silicon carbide, was dipped and inoculated containing solution of the TMV virus. The leaves were washed with water after about 30 min and desiccation. After about 3-4 d, the local lesion numbers were counted and recorded. Each compound was tested three times.

1.1.3 Inactivation activity of the target compounds against TMV *in vivo*

the whole leaves had beforehand were scattered with silicon carbide,The TMV virus was mixed with a compound solution of the same volume for 30 min. The mixed solution and the untreated virus solution were smeared on the left and right side of the leaf, respectively. After about 3-4 d, the local lesion numbers were counted and recorded. Each compound was tested three times.

1.2 Antibacterial activities *in vitro*

Antibacterial activities were evaluated against there pathogenic bacteria (Xac, Xoo and Rs) in vitro with turbidimeter test. The mother liquor of two concentrations of 100 and 50 μg/mL was prepared by dissolving the title compound in dimethyl sulfoxide (150 μL) and 0.1% (v/v) Tween-20. In the 15ml tube, added to 1ml of mother liquor and 4 mL of nutrient broth (NB, 3 g of beef extract, 1 g of yeast powder,10 g of glucose, 5 g of peptone, and 1000 mL of distilled water, pH 7.0 to 7.2). after that, 40 μLof NB including Xac, Xoo or Rs was added. The inoculated test tubes were incubated at (28±1) °C under continuous shaking at 180/min for 24-48 h. when the optical density at 595 nm (OD_{595}), growth of the cultures was controlled spectrophotometrically and given by corrected turbidity.The relative inhibitory rate (I %) were calculated as below, C_{tur} expressed the corrected turbidity value(OD_{595}) of bacterial growth on undisposed NB; T_{tur} expressed the corrected turbidity value(OD_{595}) of bacterial growth on disposed NB.

$$I\% = (C_{tur} - T_{tur})/C_{tur} \times 100\%$$

five concentrations were at 100, 50, 25, 12.5, and 6.25 μg/mL, EC50 values of some title compounds were obtained against Xac Xoo and Rs.Each experiment was computed at least three times.

1.3 Expression and purification of TMV CP

The expression vector, pET28a-TMV CP, containing the full-length TMV CP gene, was stored at -80°C in our lab. A freshly transformed overnight culture of *Escherichia coli* strain *BL21(DE3)* containing the plasmid pET28a-TMV CP was transferred to 1 L Luria broth. The cells were grown at 37 °C in Luria-Bertani medium supplemented with 50 μg/ml kanamycin, and with an OD_{600} of 0.8. The cells were shaken at 200 rpm. Then protein expression was induced with 0.8 mM IPTG at 16 °C overnight. The cells were harvested by centrifugation and then stored at -80 °C. When analyzed, the cells were resuspended in lysis buffer (20 mM PB, 500 mM NaCl, 30 mM imidazole, 5 mM β-mercaptoethanol and 5% glycerol, pH 7.2) and then lysed at 4 °C by sonication. The lysate was clarified by centrifugation at 12, 000 g for 30 min at 4 °C, the soluble supernatants were loaded onto a 5 ml Ni-NTA column (GE Healthcare, USA), and the protein was eluted with a linear gradient of 30-350 mM imidazole (pH 7.2). The crude protein was performed at 4 °C using a desalting column (GE Healthcare, USA) attached to an AKTA purifier protein liquid chromatography system (GE Healthcare, USA), and the fractions containing target protein with His-tags were pooled, concentrated to a suitable concentration by ultrafiltration (10 kDa cut-off). The dealt protein concentration was determined using a Genequant100 (GE Healthcare, USA), and stored at -80 °C until further analysis.

1.4 Interaction studies between 6g, 6i and TMV CP

Using traditional method, the binding was calculated for MST Monolith NT.115(Nano Temper Technologies, Germany). According to NT-647 dye (Nano Temper Technologies,Germany), 0.5 μM purified recombinant proteins and a serise of ligands from 0 to 5 μM was incubated for about 5 min, final concentration of 20 nM was used in the thermophoresis experiment, The selected compounds dissolution of in DMSO were made into a sixteen point dilution series. sixteen point dilution series were successively transferred to protein solutions at 10 mM Tris-HCl and 100 mM sodium chloride pH 7.5, 0.05% Tween-20. The marked TMV CP with each dilution point was incubated about 15 min at indoor temperature, samples were added to standard capillaries (NanoTemper Technologies, Germany). under a setting of 20% light emitting diode and 40% infrared laser, using microscale thermophoresis system was measure. Laster on and off time were set at 30 and 5s, Using the mass action equation in the NT. 115, the Kd values were calculated from the average of three replicates experiment .

1.5 Scanning electron microscope sample preparation of 6k

The mechanism antibacterial action of compound against xac was analyzed by scanning electron microscopy (SEM). 1.5 mL *Xac* cells were centrifuged and washed 3 times with PBS (pH = 7.1) incubated in the logarithmic phase, and re-suspended in 1.5 mL of PBS (pH = 7.1). Subsequently, the *Xac* was incubated with compound **6k** that at concentrations of 50 μg/mL and 100 μg/mL, and an equivalent volume of DMSO for (28±1) °C, under continuous shaking at 180/min for 8-10 h. After incubation, these samples were washed 3 times with PBS (pH = 7.1). Whereafter, the bacterial cells were fixed with 2.5% glutaraldehyde at 4°C for 8 h, and then dehydrated with different concentrations of ethanol series about 10 min/time. Following dehydration, the samples were freezing dried and coated with gold, and visualized using Nova Nano SEM 450.

2 . ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS spectrum of the title compounds

*(1E,3Z,4E)-1-(2-((2-chlorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-quinoxalin-2-yl oxime (**6a**):* White solid (51%), m.p. 180-181 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1H, Py-6-H), 8.66 (d, *J* = 5.6 Hz, 1H, Qu-3-H), 8.10 (d, *J* = 8.3 Hz, 1H, Qu-5-H), 8.00 (d, *J* = 8.3 Hz, 1H, Ar(2-Cl)-3-H), 7.82 (d, *J* = 16.8 Hz, 1H, Qu-6-H), 7.79 – 7.75 (m, 1H, Qu-8-H), 7.74 – 7.69 (m, 2H, Ar(2-O)-6-H, Qu-7-H), 7.70 – 7.63 (m, 3H, Py-3,4,5-H), 7.54 (d, *J* = 7.7 Hz, 1H, Ar(2-Cl)-4-H), 7.48 (s, 1H, Ar(2-O)-4-H), 7.42 (d, *J* = 9.1 Hz, 2H, Ar(2-Cl)-5,6-H), 7.37 – 7.32 (m, 2H, Py-CH=, Ar--CH=), 7.18 (td, *J* = 7.7, 1.6 Hz, 1H, Ar(2-O)-3-H), 7.10 – 7.03 (m, 2H, Ar(2-O)-5-H, Py-C=CH), 7.00 (d, *J* = 8.2 Hz, 1H, Ar-C=CH), 5.25 (s, 2H, CH_2).^{13}C NMR (101 MHz, $CDCl_3$) δ 159.87, 157.96, 156.66, 154.26, 149.96, 140.25, 140.13, 137.17, 137.07, 136.73, 135.43, 134.35, 132.45, 131.11, 130.61, 129.39, 129.03, 128.99, 128.60, 127.98, 127.95, 127.60, 127.03, 125.01, 124.94, 123.28, 121.48, 116.95, 112.74, 67.64. HRMS calcd for $C_{31}H_{24}O_2N_4Cl$ $[M+H]^+$ 519.1582, found 519.1568.

*(1E,3Z,4E)-1-(2-((2,4-dichlorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-quinoxalin-2-yl oxime (**6b**)* :White solid (47%), m.p. 193-195 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (s, 1H, Py-6-H), 8.68 (t, *J* = 7.6 Hz, 1H, Qu-3-H), 8.11 (d, *J* = 7.4 Hz, 1H, Qu-5-H), 8.02 – 7.98 (m, 1H, Ar(2,4-di-Cl)-3-H), 7.83 – 7.76 (m, 2H, Qu-6,8-H), 7.76 – 7.66 (m, 3H, Ar(2-O)-6-H, Qu-7-H, Py-3-H), 7.66 – 7.61 (m, 2H, Py-4,5-H), 7.51 – 7.38 (m, 3H, Ar(2,4-di-Cl)-5,6-H, Ar(2-O)-4-H), 7.35 (dd, *J* = 4.3, 1.8 Hz, 2H, Py-CH=, Ar-CH=), 7.28 (dd, *J* = 4.9, 4.1 Hz, 1H, Ar(2-O)-3-H), 7.10 – 7.02 (m, 2H, Ar(2-O)-5-H, Py-C=CH), 6.98 (d, *J* = 8.2 Hz, 1H, Ar-C=CH), 5.19 (s, 2H, CH_2).^{13}C NMR (101 MHz, $CDCl_3$) δ 159.72, 157.99, 156.42, 154.20, 150.00, 140.25, 140.17, 137.09, 137.06, 136.76, 135.21, 134.15, 133.07, 133.03, 131.13, 130.63, 129.51, 129.22, 129.05, 127.96, 127.85, 127.62, 127.44, 125.06, 124.85, 123.39, 123.26, 121.70, 116.97, 112.69, 67.14. HRMS calcd for $C_{31}H_{23}O_2N_4Cl_2$ $[M+H]^+$ 553.1193, found 553.1174.

*(1E,3Z,4E)-1-(2-((3-chlorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-quinoxalin-2-yl oxime (**6c**):* White solid (59%), m.p. 172-173 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H, Py-6-H), 8.67 (d, *J* = 4.7 Hz, 1H, Qu-3-H), 8.05 (ddd, *J* = 41.8, 8.3, 1.0 Hz, 2H, Qu-5,6-H), 7.79 – 7.75 (m, 1H, Qu-8-H), 7.74 (dd, *J* = 4.2, 1.8 Hz, 2H, Ar(2-O)-6-H, Qu-7-H), 7.71 (dd, *J* = 7.7, 1.7 Hz, 1H, Py-3-H), 7.66 (dt, *J* = 3.9, 1.9 Hz, 2H, Py-4,5-H), 7.63 (dd, *J* = 4.5, 2.8 Hz, 1H, Ar(3-Cl)-4-H), 7.42 (d, *J* = 15.9 Hz, 1H, Ar(3-Cl)-5-H), 7.39 – 7.32 (m, 4H, Ar(3-Cl)-2,6-H, Ar(2-O)-4-H, Py-CH=), 7.29 – 7.26 (m, 1H, Ar-CH=), 7.21 (d, *J* = 8.4 Hz, 2H, Ar(2-O)-3,5-H), 7.05 (t, *J* = 7.5 Hz, 1H, Py-C=CH), 6.96 (d, *J* = 8.1 Hz, 1H, Ar-C=CH), 5.10 (s, 2H, CH_2).^{13}C NMR (101 MHz, $CDCl_3$) δ 159.78, 157.98, 156.75, 154.20, 149.99, 140.26, 140.17, 137.10, 137.09, 136.75, 135.41, 135.15, 133.74, 131.03, 130.60, 129.06, 128.80, 128.60, 127.98, 127.96, 127.59, 125.01, 124.87, 123.36, 123.19, 121.44, 116.95, 112.58, 69.70. HRMS calcd for $C_{31}H_{24}O_2N_4Cl$ $[M+H]^+$ 519.1582, found 519.1573.

*(1E,3Z,4E)-1-(2-((2-fluorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-quinoxalin-2-yl oxime (**6d**):* White solid (55%), m.p. 155-156 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H, Py-6-H), 8.58 (d, *J* = 4.0 Hz, 1H, Qu-3-H), 8.02 (dd, *J* = 8.2, 1.0 Hz, 1H, Qu-5-H), 7.92 (dd, *J* = 8.3, 0.8 Hz, 1H, Ar(2-F)-4-H), 7.68 (d, *J* = 10.2 Hz, 1H, Qu-6-H), 7.66 – 7.62 (m, 2H, Qu-8-H, Ar(2-O)-6-H), 7.62 – 7.53 (m, 4H, Ar(2-F)-3-H, Qu-7-H, Py-3,4-H), 7.40 (dt, *J* = 28.9, 11.7 Hz, 2H, Py-5-H, Ar(2-O)-4-H), 7.31 – 7.25 (m, 2H, Ar(2-F)-6-H, Py-CH=), 7.19 – 7.15 (m, 1H, Ar(2-F)-5-H), 7.15 – 7.10 (m, 1H, Ar-CH=), 7.00 – 6.92 (m, 3H, Ar(2-O)-3,5-H, Py-C=CH), 6.91 – 6.86 (m, 1H, Ar-C=CH), 5.14 (s, 2H, CH_2).^{13}C NMR (101 MHz, $CDCl_3$) δ 158.85, 156.91, 155.74, 153.25, 148.89, 139.22, 139.09, 136.13, 136.02, 135.63, 134.46, 129.99, 129.52, 128.65, 128.56, 128.40, 128.36, 127.98, 127.06, 126.93, 126.51, 124.04, 123.92, 123.28, 122.17, 120.42, 115.98, 114.37, 114.16, 111.67, 63.30. ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.53. HRMS calcd for $C_{31}H_{24}O_2N_4F$ $[M+H]^+$ 503.1878, found 503.1864.

*(1E,3Z,4E)-1-(2-((2-chlorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-(6-chloroquinoxalin-2-yl) oxime (**6e**):* Pink solid (52%), m.p. 198-199 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H, Py-6-H), 8.66 (s, 1H, Qu-3-H), 8.09 (s, 1H, Ar(2-Cl)-3-H), 7.93 (d, *J* = 8.5 Hz, 1H, Ar(2-O)-6-H), 7.79 (dd, *J* = 23.1, 11.9 Hz, 2H, Py-3,4-H), 7.67 (d, *J* = 15.2 Hz, 3H, Py-5-H, Ar(2-Cl)-4-H, Ar(2-O)-4-H), 7.54 (dd, *J* = 31.5, 24.6 Hz, 2H, Ar(2-Cl)-5,6-H), 7.39 (dd, *J* = 18.7, 10.7 Hz, 3H, Py-CH=, Qu-5,7-H), 7.26 (s, 2H, Qu-8-H, Ar-CH=), 7.18 (s, 1H, Ar(2-O)-3-H), 7.07 (d, *J* = 5.4 Hz, 2H, Ar(2-O)-5-H, Py-C=CH), 7.01 (d, *J* = 7.6 Hz, 1H, Ar-C=CH), 5.25 (s, 2H, CH_2).^{13}C NMR (101 MHz, $CDCl_3$) δ 160.15, 158.05, 156.72, 154.20, 149.98, 140.32, 138.86, 138.15, 137.24, 136.72, 135.71, 134.34, 133.10, 132.52, 131.43, 131.17, 129.41, 129.12, 129.02, 128.64, 128.06, 128.00, 127.01, 124.97, 124.77, 123.32, 123.30, 121.50, 116.86, 112.79, 67.70. HRMS calcd for $C_{31}H_{23}O_2N_4Cl_2$ $[M+H]^+$ 553.1193, found 553.1183.

*(1E,3Z,4E)-1-(2-((2,4-dichlorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-(6-chloroquinoxalin-2-yl) oxime (**6f**):* Pink solid (42%), m.p. 197-199 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H, Py-6-H), 8.68 (dd, *J* = 10.7, 4.4 Hz, 1H, Qu-3-H), 8.09 (d, *J* = 2.3 Hz, 1H, Ar(2,4-di-Cl)-3-H), 7.93 (d, *J* = 8.9 Hz, 1H, Ar(2-O)-6-H), 7.84 – 7.70 (m, 3H, Py-3,4,5-H), 7.70 – 7.58 (m, 3H, Ar(2,4-di-Cl)-5,6-H, Ar(2-O)-4-H), 7.51 – 7.38 (m, 3H, Py-CH=, Qu-5,7-H), 7.37 – 7.32 (m, 2H, Qu-8-H, Ar-CH=), 7.31 – 7.27 (m, 1H, Ar(2-O)-3-H), 7.11 – 7.01 (m, 2H, Ar(2-O)-5-H, Py-C=CH), 6.98 (d, *J* = 8.2 Hz, 1H, Ar-C=CH), 5.19 (s, 2H, CH_2).^{13}C NMR (101 MHz, $CDCl_3$) δ 160.01, 158.04, 156.46, 154.09, 150.01, 140.31, 138.82, 138.06, 137.21, 136.80, 135.50, 134.18, 133.16, 133.12, 133.00, 131.48, 131.22, 129.53, 129.24, 129.09, 128.05, 127.89, 127.43, 124.96, 124.66, 123.46, 123.31, 121.71, 116.83, 112.70, 67.16.HRMS calcd for $C_{31}H_{24}O_2N_4Cl$ $[M+H]^+$ 587.0803, found 587.0775.

*(1E,3Z,4E)-1-(2-((3-chlorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-(6-chloroquinoxalin-2-yl) oxime (**6g**):* White solid (49%), m.p. 153-155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H, Py-6-H), 8.67 (d, *J* = 4.0 Hz, 1H, Qu-3-H), 8.09 (d, *J* = 2.2 Hz, 1H, Ar(2-O)-6-H), 7.93 (d, *J* = 8.9 Hz, 1H, Py-3-H), 7.78 – 7.72 (m, 3H, Py-4,5-H, Ar(3-Cl)-4-H), 7.71 – 7.59 (m, 3H, Ar(3-Cl)-5,6-H, Ar(2-O)-4-H), 7.45 – 7.39 (m, 1H, Ar(3-Cl)-2-H), 7.36 (t, *J* = 8.8 Hz, 4H, Py-CH=, Qu-5,7,8-H), 7.28 (dd, *J* = 5.8, 3.0 Hz, 1H, Ar-CH=), 7.21 (d, *J* = 8.4 Hz, 2H, Ar(2-O)-3,5-H), 7.06 (t, *J* = 7.5 Hz, 1H, Py-C=CH), 6.97 (d, *J* = 8.2 Hz, 1H, Ar-C=CH), 5.11 (s, 2H, CH_2).^{13}C NMR (101 MHz, $CDCl_3$) δ 160.08, 158.04, 156.80, 154.10, 150.01, 140.32, 138.84, 138.08, 137.25, 136.78, 135.70, 135.12, 133.76, 133.12, 131.46, 131.12, 129.10, 128.81, 128.62, 128.07, 124.91, 124.67, 123.43, 123.24, 121.44, 116.84, 112.57, 69.70. HRMS calcd for $C_{31}H_{23}O_2N_4Cl_2$ $[M+H]^+$ 553.1193, found 553.1187.

*(1E,3Z,4E)-1-(4-((2-chlorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-quinoxalin-2-yl oxime (**6h**):* White solid (54%), m.p. 160-161 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H, Py-6-H), 8.68 (dd, *J* = 5.7, 4.9 Hz, 1H, Qu-3-H), 8.05 (dd, *J* = 41.1, 8.3 Hz, 2H, Qu-5-H, Ar(2-Cl)-3-H), 7.77 – 7.70 (m, 2H, Ar(4-O)-2,6-H), 7.68 – 7.63 (m, 2H, Qu-6,8-H), 7.60 (d, *J* = 8.7 Hz, 2H, Qu-7-H, Py-3-H), 7.58 – 7.51 (m, 2H, Py-4,5-H), 7.46 (d, *J* = 4.3 Hz, 1H, Ar(2-Cl)-4-H), 7.44 – 7.40 (m, 2H, Ar(2-Cl)-6-H, Ar(2-Cl)-5-H), 7.33 – 7.27 (m, 3H, Py-CH=, Ar(2-O)-3,5-H), 7.26 – 7.22 (m, 1H, Ar-CH=), 7.03 (d, *J* = 8.7 Hz, 2H, Py-C=CH, Ar-C=CH), 5.23 (s, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.89, 159.07, 158.03, 154.11, 149.94, 140.23, 140.12, 139.88, 137.09, 136.80, 136.51, 134.24, 132.62, 130.59, 129.53, 129.45, 129.15, 129.02, 128.77, 128.71, 127.93, 127.57, 127.02, 124.36, 123.49, 123.35, 115.21, 114.56, 67.18.HRMS calcd for $C_{31}H_{24}O_2N_4Cl$ $[M+H]^+$ 519.1582, found 519.1565.

*(1E,3Z,4E)-1-(4-((4-chlorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-quinoxalin-2-yl oxime (**6i**):* White solid (47%), m.p. 161-163 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H, Py-6-H), 8.69 (d, *J* = 4.0 Hz, 1H, Qu-3-H), 8.09 (dd, *J* = 8.2, 1.1 Hz, 1H, Qu-5-H), 8.00 (dd, *J* = 17.6, 8.8 Hz, 2H, Ar(4-O)-2,6-H), 7.74 (qd, *J* = 7.5, 1.6 Hz, 2H,

Qu-6,8-H), 7.67 – 7.62 (m, 1H, Qu-7-H), 7.53 (t, *J* = 8.5 Hz, 3H, Py-3,4,5-H), 7.37 (d, *J* = 5.7 Hz, 4H, Ar(4-Cl)-2,3,5,6-H), 7.34 – 7.27 (m, 2H, Py-CH=, Ar(4-O)-3-H), 7.00 (dd, *J* = 12.4, 10.9 Hz, 3H, Ar-CH=, Py-C=CH, Ar-C=CH), 5.08 (s, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.06, 159.45, 157.73, 153.94, 150.08, 140.25, 140.09, 138.93, 138.16, 137.20, 136.82, 135.14, 133.93, 130.61, 129.11, 129.00, 128.93, 128.85, 128.80, 127.99, 127.59, 123.78, 123.34, 120.98, 118.85, 115.21, 69.30. HRMS calcd for $C_{31}H_{23}O_2N_4Cl$ $[M+H]^+$ 519.1588, found 519.1582.

*(1E,3Z,4E)-1-(4-((2,4-dichlorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-quinoxalin-2-yl oxime (**6j**):* Yellow solid (43%), m.p. 128-129 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1H, Py-6-H), 8.60 (d, *J* = 4.4 Hz, 1H, Qu-3-H), 7.98 (dd, *J* = 42.4, 8.2 Hz, 2H, Qu-5-H, Ar(2,4-Cl)-3-H), 7.70 – 7.63 (m, 2H, Ar(4-O)-2,6-H), 7.61 – 7.55 (m, 2H, Qu-6,8-H), 7.54 – 7.48 (m, 2H, Qu-7-H, Py-3-H), 7.46 – 7.41 (m, 2H, Py-4,5-H), 7.39 (d, *J* = 3.5 Hz, 1H, Ar(2,4-Cl)-5-H), 7.38 – 7.34 (m, 2H, Ar(2,4-Cl)-6-H, Py-CH=), 7.25 – 7.20 (m, 2H, Ar(4-O)-3,5-H), 7.17 (d, *J* = 4.9 Hz, 1H, Ar-CH=), 6.94 (d, *J* = 8.7 Hz, 2H, Py-C=CH, Ar-C=CH), 5.10 (s, 2H, CH_2).^{13}C NMR (101 MHz, $CDCl_3$) δ 159.62, 159.04, 158.05, 154.12, 149.97, 140.24, 140.15, 139.79, 137.09, 136.84, 136.55, 134.33, 133.22, 132.96, 130.64, 129.61, 129.58, 129.31, 129.05, 128.94, 127.94, 127.62, 127.40, 124.36, 123.52, 123.39, 115.19, 114.74, 66.65. HRMS calcd for $C_{31}H_{23}O_2N_4Cl_2$ $[M+H]^+$ 553.1193, found 553.1171.

*(1E,3Z,4E)-1-(4-((2-fluorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-quinoxalin-2-yl oxime (**6k**):* White solid (45%), m.p. 144-146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 9.03 (s, 1H, Py-6-H), 8.60 (d, *J* = 4.0 Hz, 1H, Qu-3-H), 8.07 – 7.89 (m, 2H, Qu-5-H, Ar(2-F)-4-H), 7.69 – 7.63 (m, 2H, Ar(4-O)-2,6-H), 7.60 – 7.55 (m, 2H, Qu-6,8-H), 7.52 (d, *J* = 8.7 Hz, 2H, Ar(2-F)-3-H, Qu-7-H), 7.49 – 7.41 (m, 2H, Py-3,4-H), 7.39 (d, *J* = 4.5 Hz, 1H, Py-5-H), 7.36 (d, *J* = 3.4 Hz, 1H, Ar(2-F)-6-H), 7.27 (dd, *J* = 10.3, 4.5 Hz, 1H, Py-CH=), 7.21 – 7.16 (m, 2H, Ar(2-F)-5-H, Ar(4-O)-3-H), 7.10 (dd, *J* = 10.9, 4.1 Hz, 1H, Ar(4-O)-5-H), 7.06 – 7.01 (m, 1H, Ar-CH=), 6.95 (d, *J* = 8.7 Hz, 2H, Py-C=CH, Ar-C=CH), 5.11 (s, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 159.96, 159.07, 158.06, 154.13, 149.96, 140.25, 140.14, 139.92, 137.11, 136.82, 136.51, 130.61, 129.96, 129.88, 129.70, 129.54, 129.04, 128.67, 127.94, 127.59, 124.38, 124.34, 123.51, 123.37, 115.54, 115.33, 115.17, 114.54, 63.76. ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.55. HRMS calcd for $C_{31}H_{24}O_2N_4F$ $[M+H]^+$ 503.1878, found 503.1863.

*(1E,3Z,4E)-1-(4-((2-chlorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-(6-chloroquinoxalin-2-yl) oxime (**6l**):* Yellow solid (51%), m.p. 129-131 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H, Py-6-H), 8.67 (d, *J* = 4.0 Hz, 1H, Qu-3-H), 8.09 (t, *J* = 3.7 Hz, 1H, Ar(2-Cl)-3-H), 7.93 (d, *J* = 8.9 Hz, 1H, Ar(4-O)-2-H), 7.73 (td, *J* = 7.7, 1.7 Hz, 1H, Ar(4-O)-6-H), 7.67 (dt, *J* = 13.7, 5.8 Hz, 2H, Py-3,4-H), 7.63 – 7.56 (m, 3H, Py-5-H, Ar(2-Cl)-4,6-H), 7.56 – 7.52 (m, 1H, Ar(2-Cl)-5-H), 7.46 (dd, *J* = 10.7, 7.9 Hz, 2H, Py-CH=, Qu-5-H), 7.44 – 7.39 (m, 2H, Qu-7,8-H), 7.34 – 7.28 (m, 3H, Ar(4-O)-3,5-H, Ar-CH=), 7.03 (d, *J* = 8.7 Hz, 2H, Py-C=CH, Ar-C=CH), 5.22 (s, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ

159.98, 159.37, 158.11, 154.04, 149.96, 140.28, 140.18, 138.83, 138.08, 136.87, 136.66, 134.24, 133.12, 132.65, 131.47, 129.59, 129.48, 129.19, 129.07, 128.98, 128.79, 128.65, 128.04, 127.05, 124.21, 123.57, 123.44, 115.25, 114.41, 77.38, 77.27, 77.06, 76.74, 67.21. HRMS calcd for $C_{31}H_{23}O_2N_4Cl_2$ $[M+H]^+$ 553.1193, found 553.1174.

*(1E,3Z,4E)-1-(4-((4-chlorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-(6-chloroquinoxalin-2-yl) oxime (**6m**):* White solid (50%), m.p. 165-167 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H, Py-6-H), 8.69 (d, *J* = 4.7 Hz, 1H, Qu-3-H), 8.11 – 7.91 (m, 3H, Ar(4-O)-2,6-H, Py-3-H), 7.75 (td, *J* = 7.7, 1.8 Hz, 1H, Py-4-H), 7.67 (dd, *J* = 8.9, 2.3 Hz, 1H, Py-5-H), 7.52 (dd, *J* = 8.2, 3.8 Hz, 3H, Ar(4-Cl)-2,3,5-H), 7.37 (d, *J* = 5.3 Hz, 4H, Ar(4-Cl)-6-H, Py-CH=, Qu-5,7-H), 7.36 – 7.27 (m, 3H, Qu-8-H, Ar(4-O)-3,5-H), 6.99 (dd, *J* = 12.5, 5.9 Hz, 3H, Ar-CH=, Py-C=CH, Ar-C=CH), 5.08 (s, 2H, CH_2).^{13}C NMR (101 MHz, $CDCl_3$) δ 160.32, 159.49, 157.81, 153.84, 150.11, 140.28, 139.09, 138.84, 138.35, 138.20, 136.80, 135.12, 133.93, 133.07, 131.40, 129.13, 129.02, 128.95, 128.85, 128.79, 128.04, 123.82, 123.43, 120.82, 118.66, 115.20, 69.28. HRMS calcd for $C_{31}H_{23}O_2N_4Cl_2$ $[M+H]^+$553.1193, found 553.1166.

*(1E,3Z,4E)-1-(4-((2,4-dichlorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-(6-chloroquinoxalin-2-yl) oxime (**6n**): Gray* solid (56%), m.p. 158-159 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H, Py-6-H)), 8.68 (d, *J* = 4.0 Hz, 1H, Qu-3-H), 8.10 (d, *J* = 2.2 Hz, 1H, Ar(2,4-di-Cl)-3-H), 7.93 (d, *J* = 8.9 Hz, 1H, Ar(4-O)-2-H), 7.76 – 7.71 (m, 1H, Ar(4-O)-6-H), 7.70 – 7.65 (m, 2H, Py-3,4-H), 7.63 – 7.57 (m, 3H, Py-5-H, Ar(2,4-di-Cl)-5,6-H), 7.52 (d, *J* = 8.9 Hz, 1H, Py-CH=), 7.49 (s, 1H, Qu-5-H), 7.47 – 7.42 (m, 3H, Qu-7,8-H, Ar(4-O)-3-H), 7.33 – 7.30 (m, 1H, Ar(4-O)-5-H), 7.28 (d, *J* = 2.1 Hz, 1H, Ar-CH=), 7.01 (d, *J* = 8.7 Hz, 2H, Py-C=CH, Ar-C=CH), 5.17 (s, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.69, 159.35, 158.12, 154.04, 149.98, 140.32, 140.06, 138.83, 138.08, 136.87, 136.71, 134.35, 133.23, 133.15, 132.93, 131.49, 129.61, 129.32, 129.08, 129.00, 128.86, 128.06, 127.41, 124.20, 123.57, 123.46, 115.22, 114.59, 66.66. HRMS calcd for $C_{31}H_{22}O_2N_4Cl_3$ $[M+H]^+$ 587.0803, found 587.0892.

*(1E,3Z,4E)-1-(4-((2-fluorobenzyl)oxy)phenyl)-5-(pyridin-2-yl)penta-1,4-dien-3-one O-(6-chloroquinoxalin-2-yl) oxime (**6o**):* Pink solid (41%), m.p. 154-155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H, Py-6-H), 8.67 (d, *J* = 4.0 Hz, 1H, Qu-3-H), 8.11 – 7.91 (m, 2H, Ar(2-F)-4-H, Ar(4-O)-2-H), 7.73 (td, *J* = 7.7, 1.7 Hz, 1H, Ar(4-O)-6-H), 7.65 (ddd, *J* = 31.9, 12.5, 5.5 Hz, 4H, Ar(2-F)-3-H, Py-3,4-H), 7.54 – 7.49 (m, 2H, Py-5-H, Ar(4-Cl)-6-H), 7.44 (dd, *J* = 11.8, 3.9 Hz, 2H, Ar(2-F)-6-H, Py-CH=), 7.31 (ddd, *J* = 13.6, 12.2, 3.9 Hz, 2H, Qu-5,7-H), 7.18 (t, *J* = 7.5 Hz, 1H, Qu-8-H), 7.14 – 7.08 (m, 1H, Ar-CH=), 7.03 (d, *J* = 8.7 Hz, 2H, Py-C=CH, Ar-C=CH), 5.19 (s, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.70, 160.03, 159.37, 158.13, 154.05, 149.97, 140.30, 140.18, 138.84, 138.09, 136.84, 136.67, 133.11, 131.46, 129.98, 129.74, 129.57, 129.09, 128.59, 128.05, 124.38, 124.21, 123.56, 123.43, 115.56, 115.35, 115.19, 114.39, 63.81. ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.78. HRMS calcd for $C_{31}H_{23}O_2N_4ClF$ $[M+H]^+$ 537.1488, found 537.1472.

^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS spectrum of the title compounds

Figure S1. ^{1}H NMR spectrum of compound **6a**

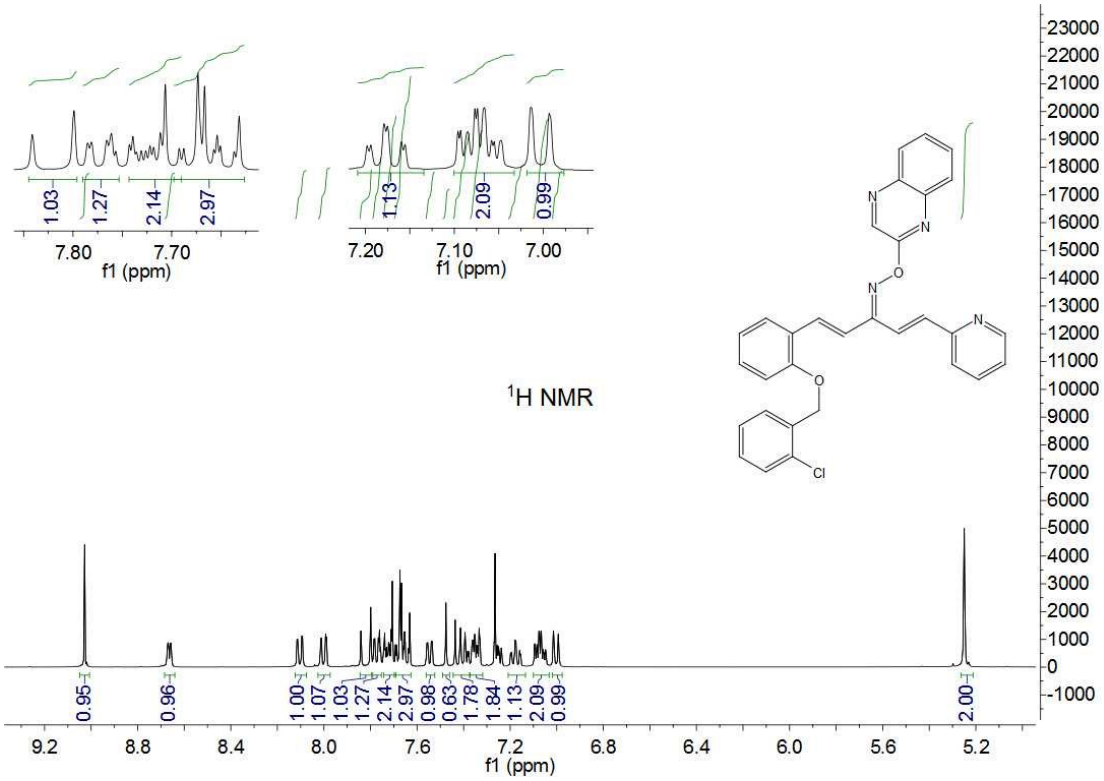

Figure S2. ^{13}C NMR spectrum of compound **6a**

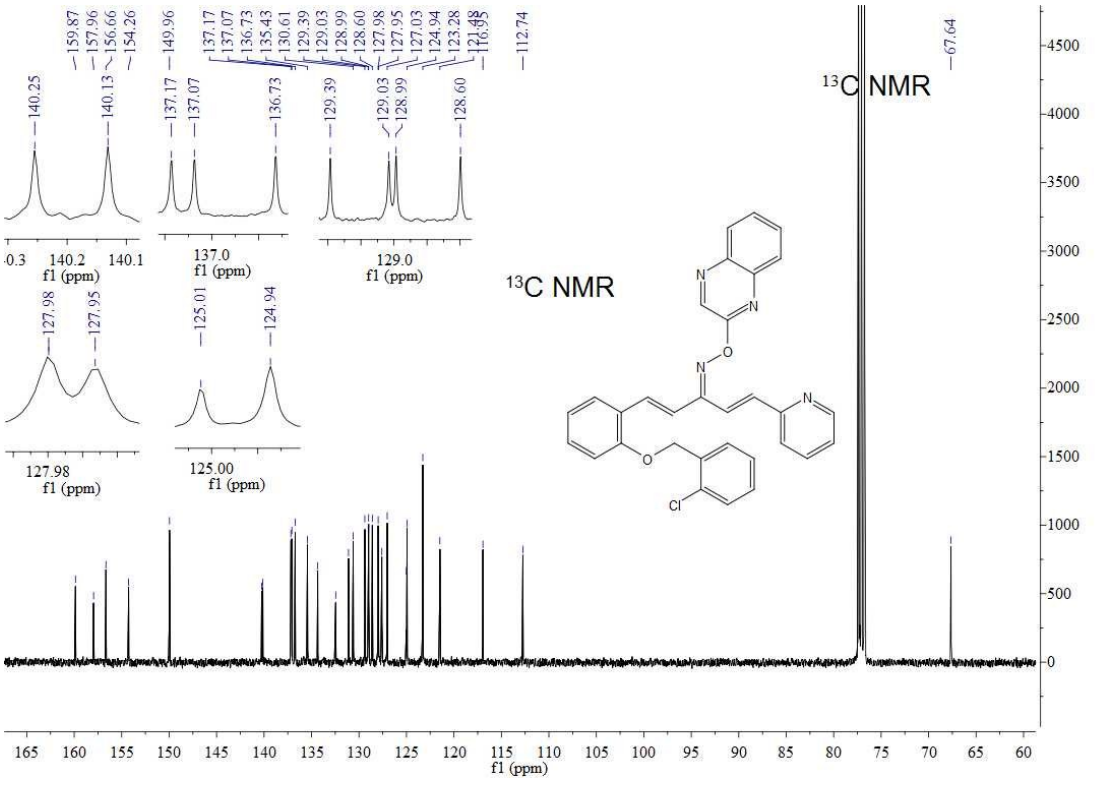

Figure S3. HRMS spectrum of compound **6a**

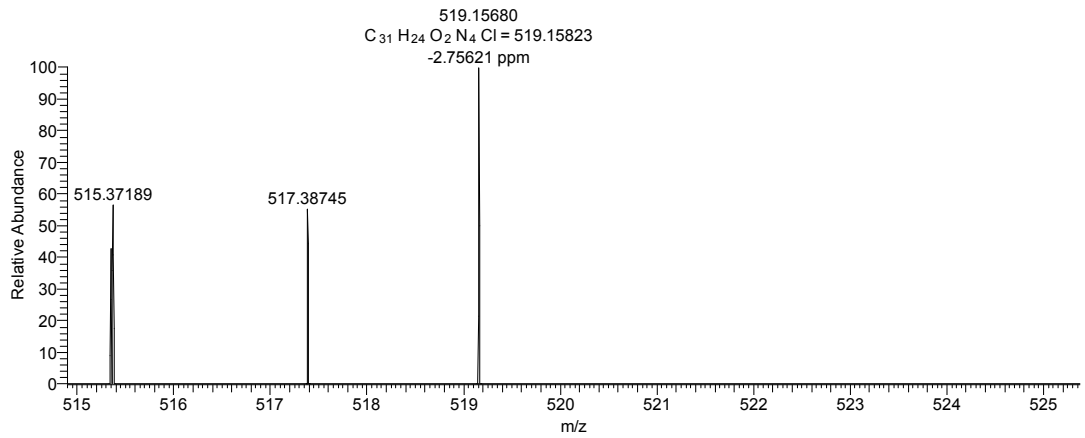

Figure S4. ^{1}H NMR spectrum of compound **6b**

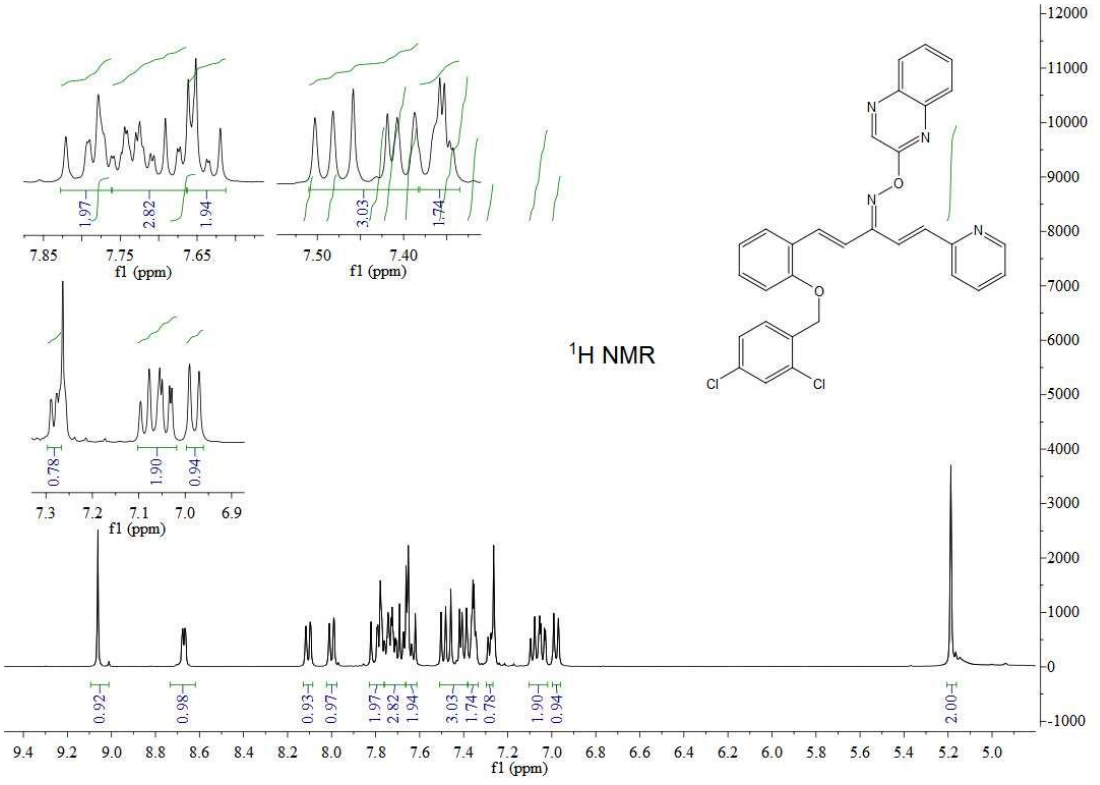

Figure S5. ^{13}C NMR spectrum of compound **6b**

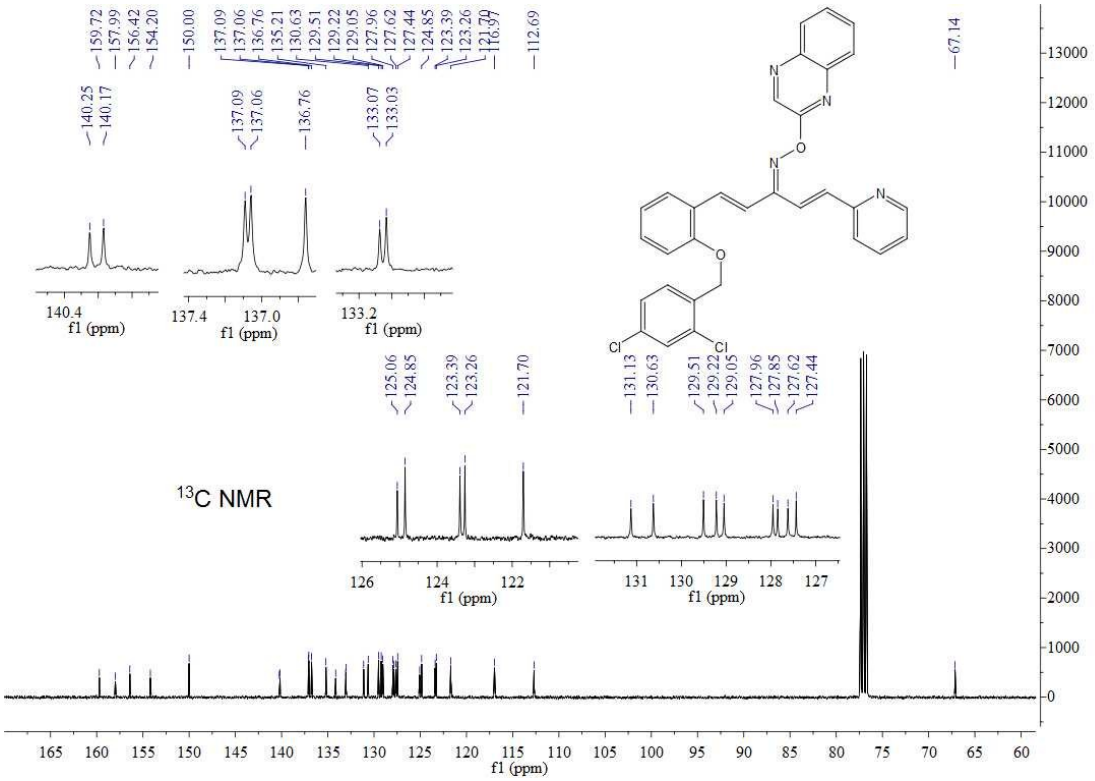

Figure S6. HRMS spectrum of compound **6b**

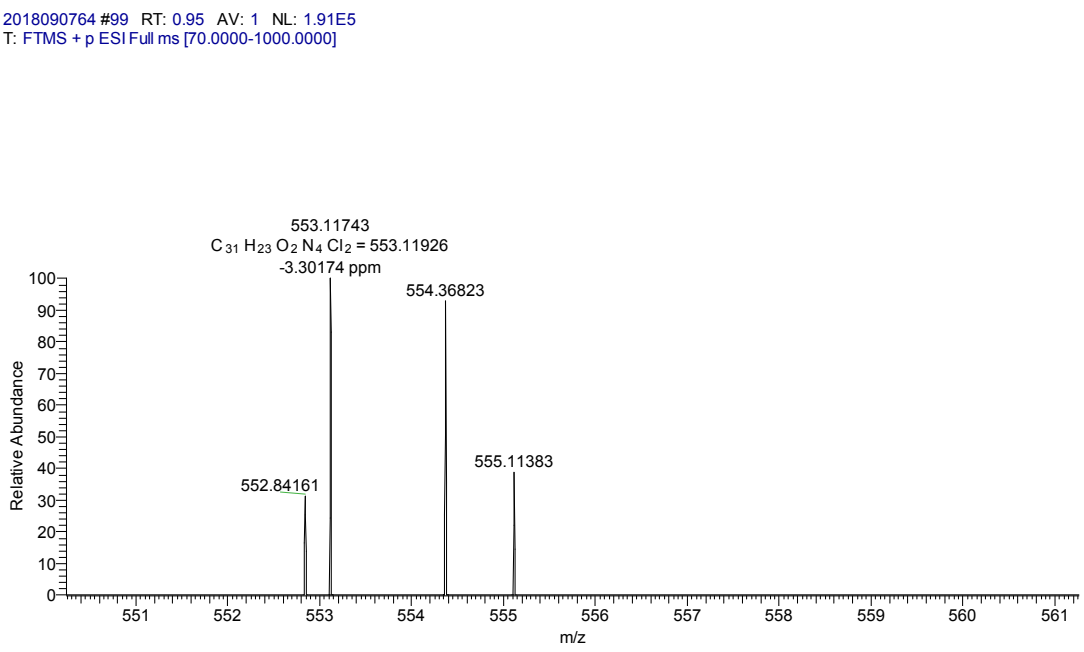

Figure S7. ^{1}H NMR spectrum of compound **6c**

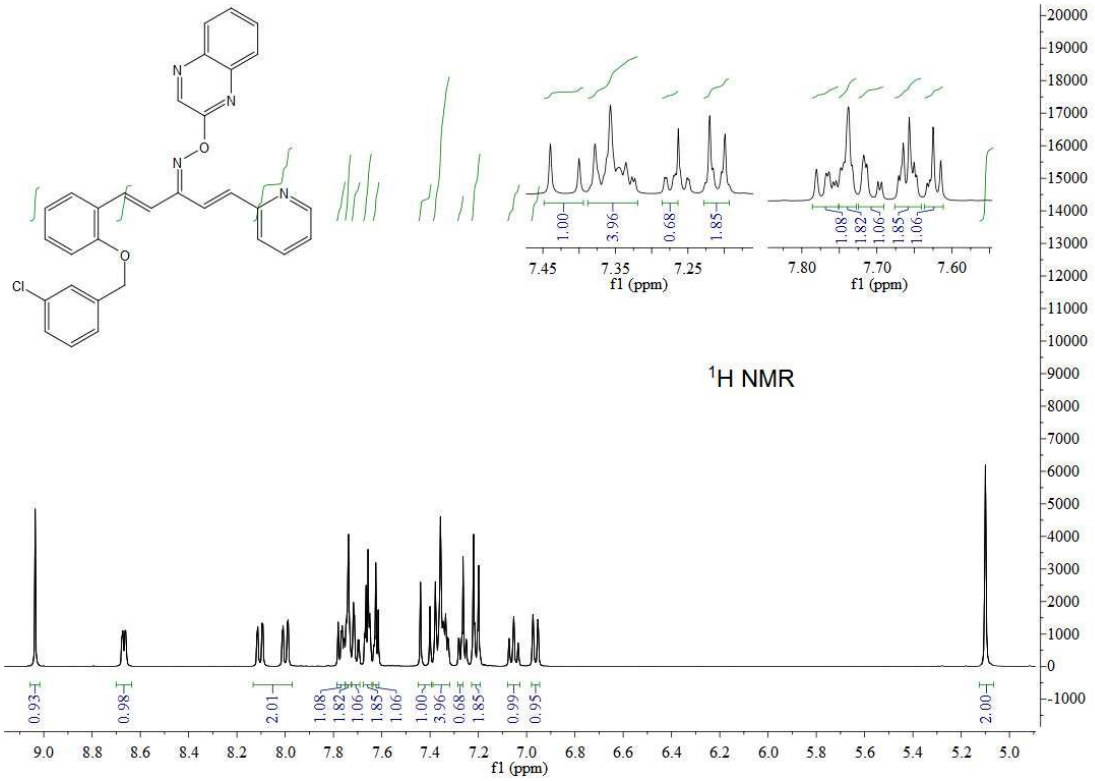

Figure S8. ^{13}C NMR spectrum of compound **6c**

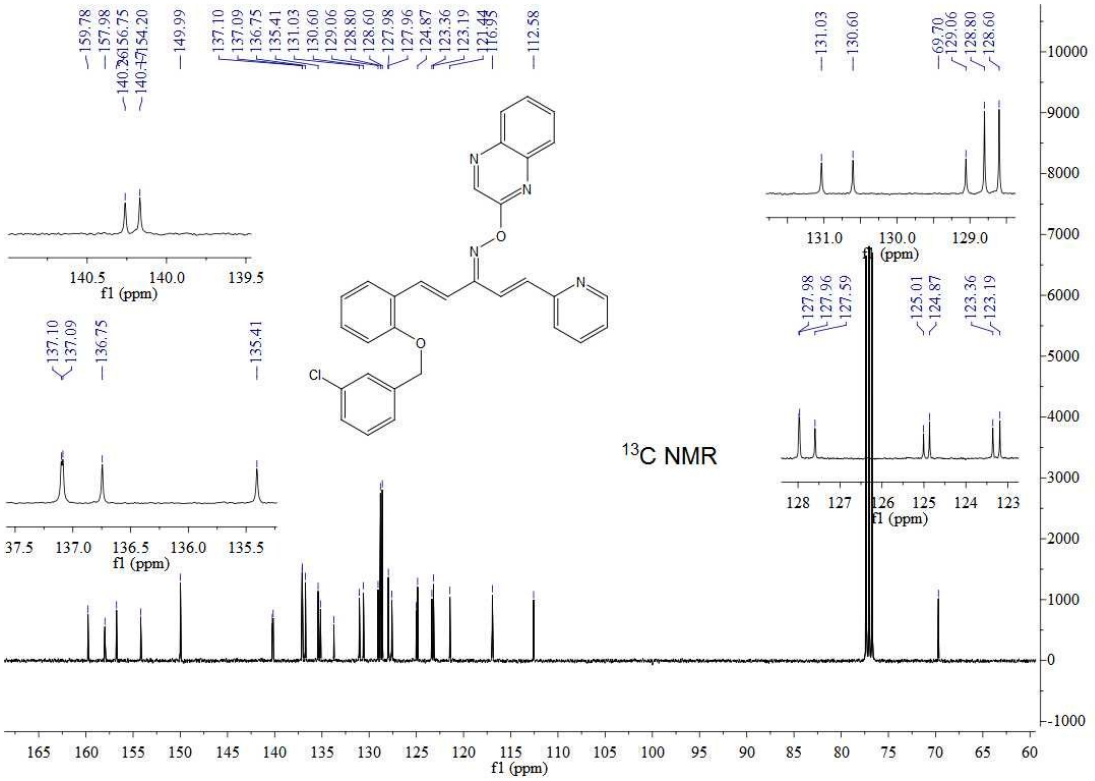

Figure S9. HRMS spectrum of compound **6c**

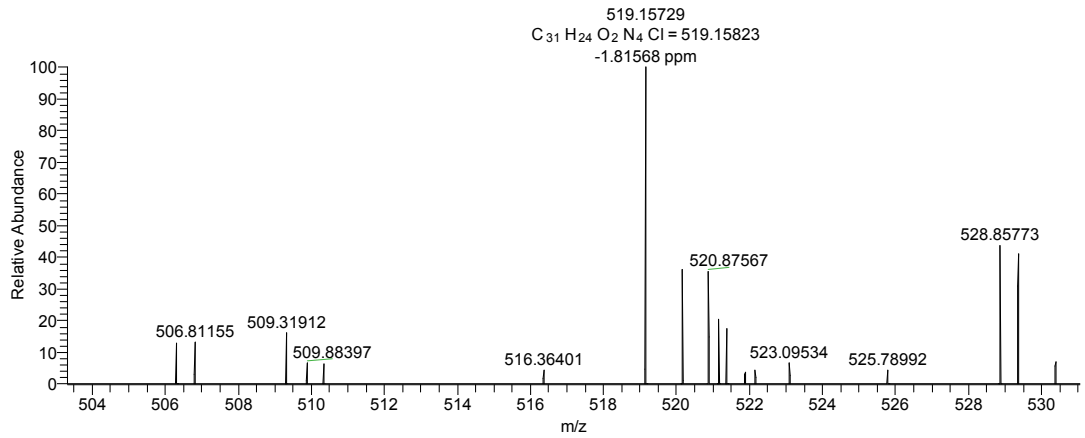

Figure S10. ^{1}H NMR spectrum of compound **6d**

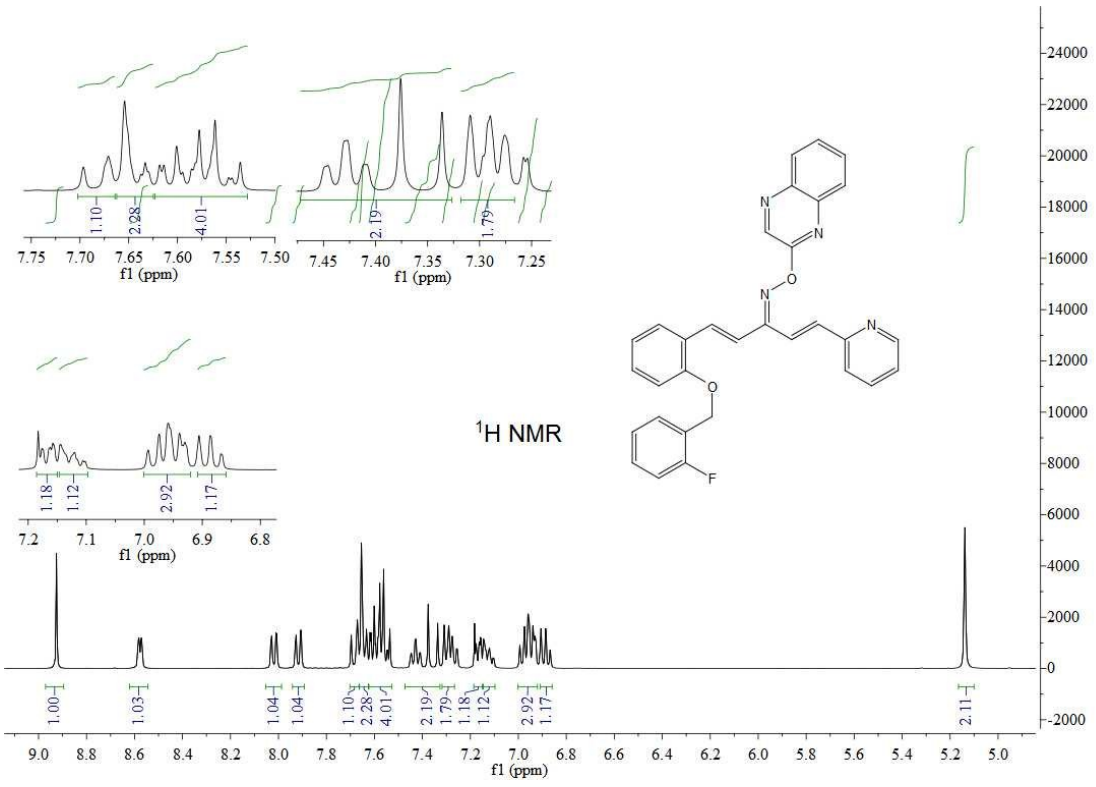

Figure S11. ^{13}C NMR spectrum of compound **6d**

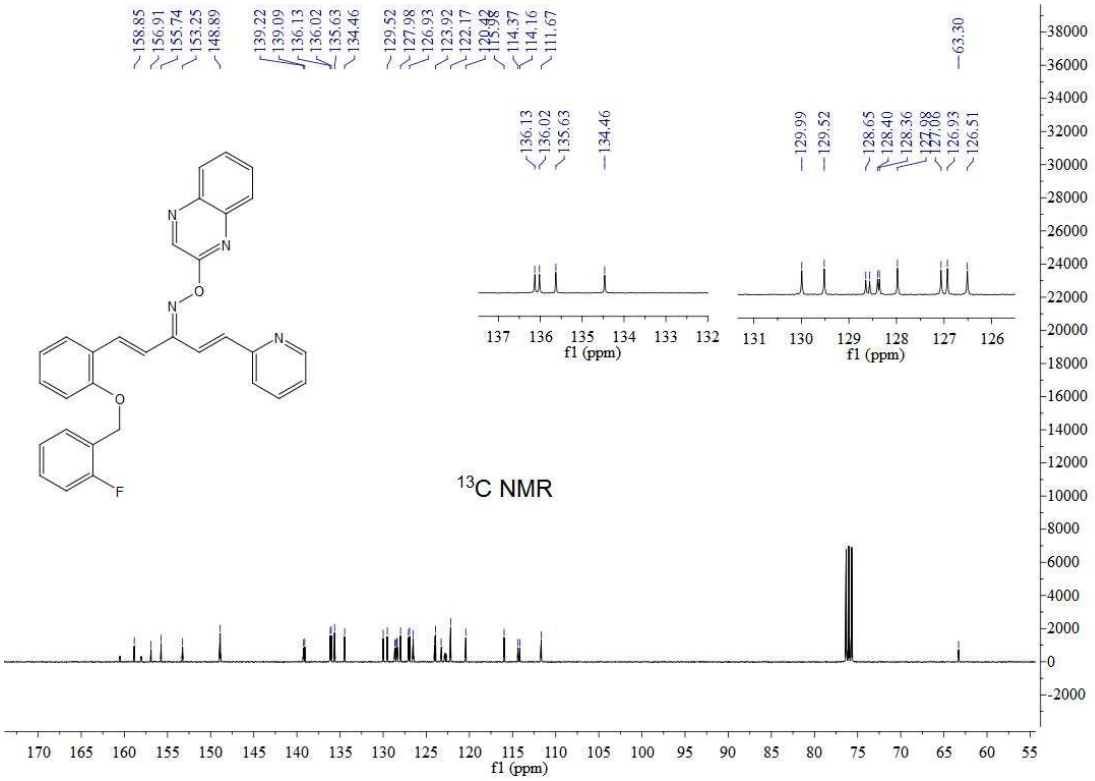

Figure S12. ^{19}F NMR spectrum of compound **6d**

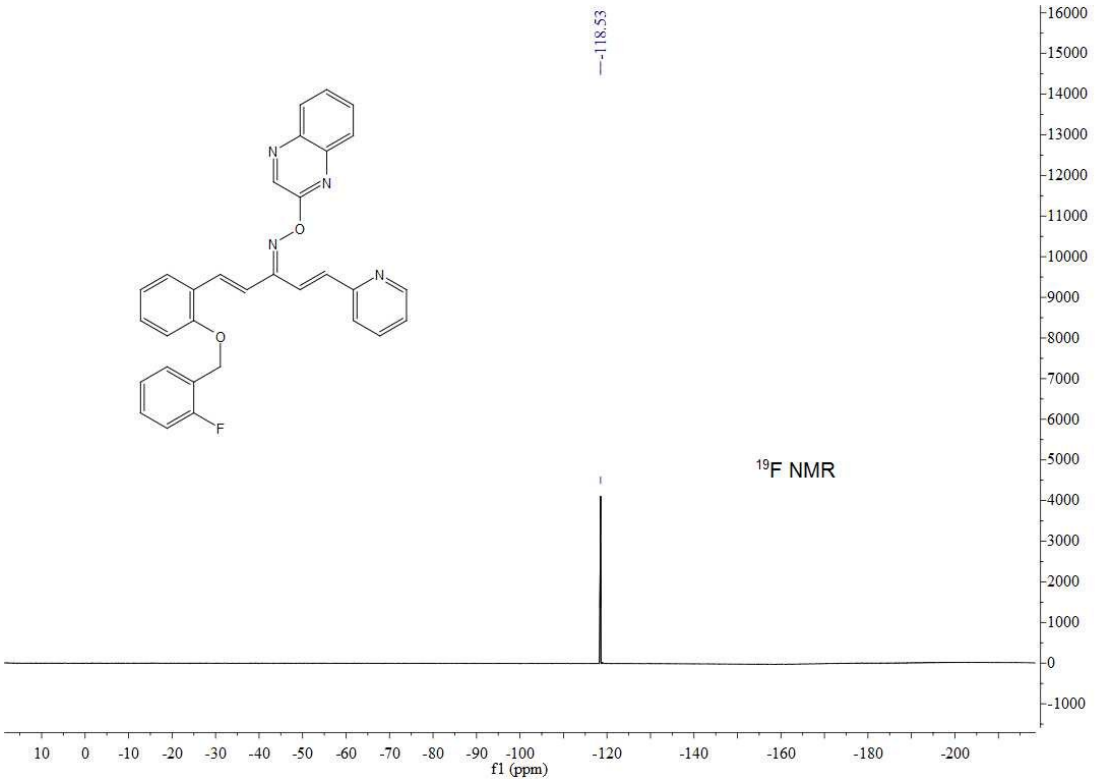

Figure S13. HRMS spectrum of compound6**d**

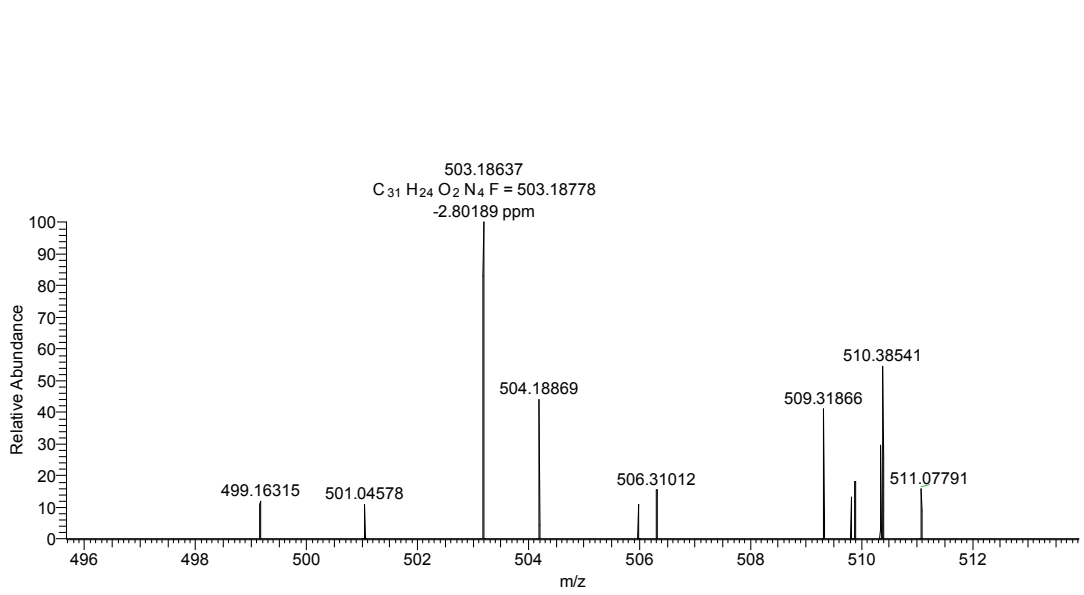

Figure S14. ^{1}H NMR spectrum of compound **6e**

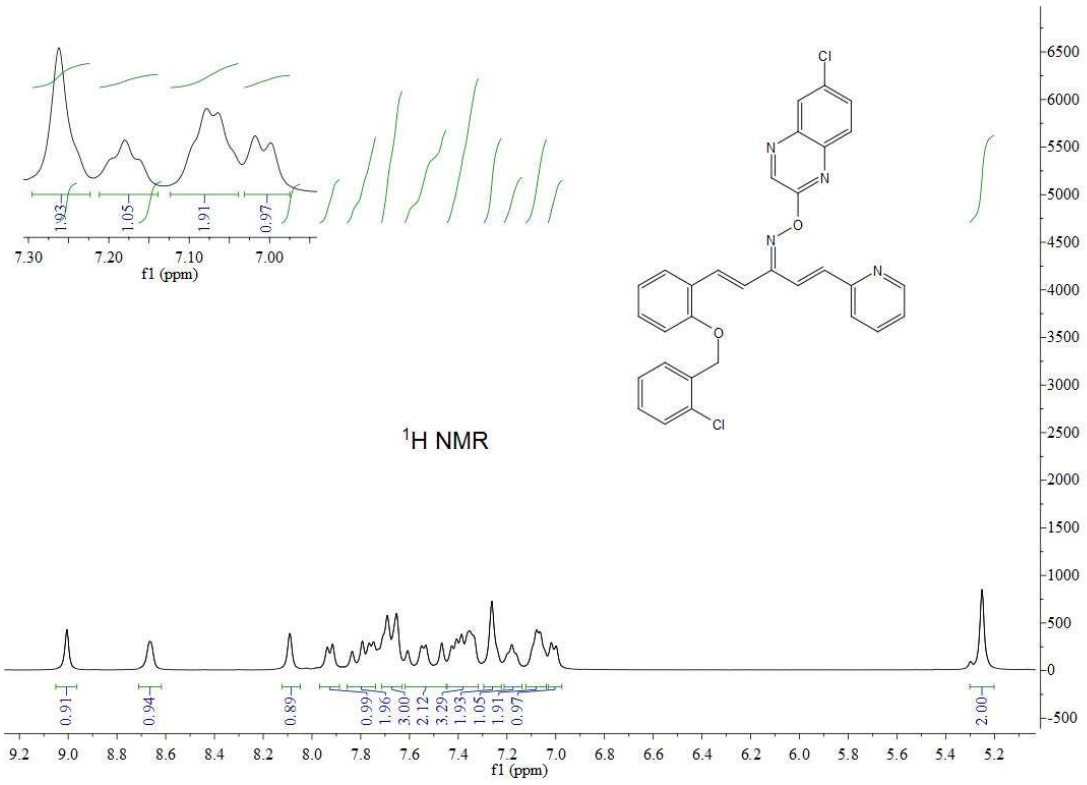

Figure S15. ^{13}C NMR spectrum of compound **6e**

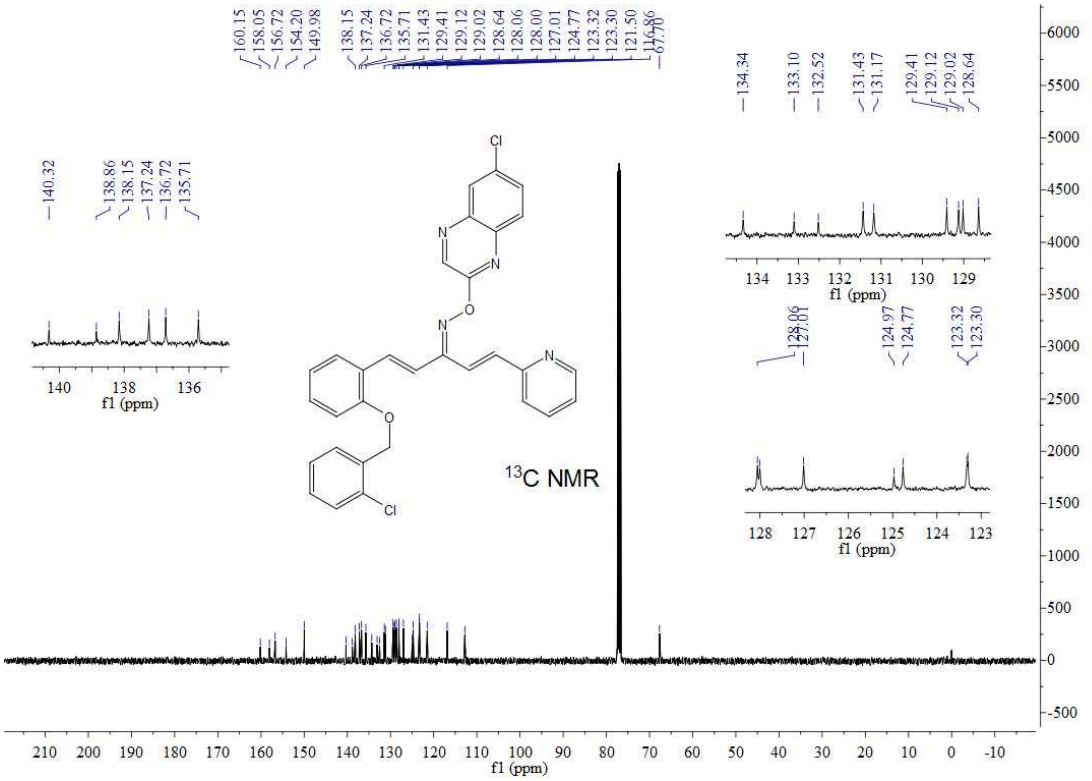

Figure S16. HRMS spectrum of compound **6e**

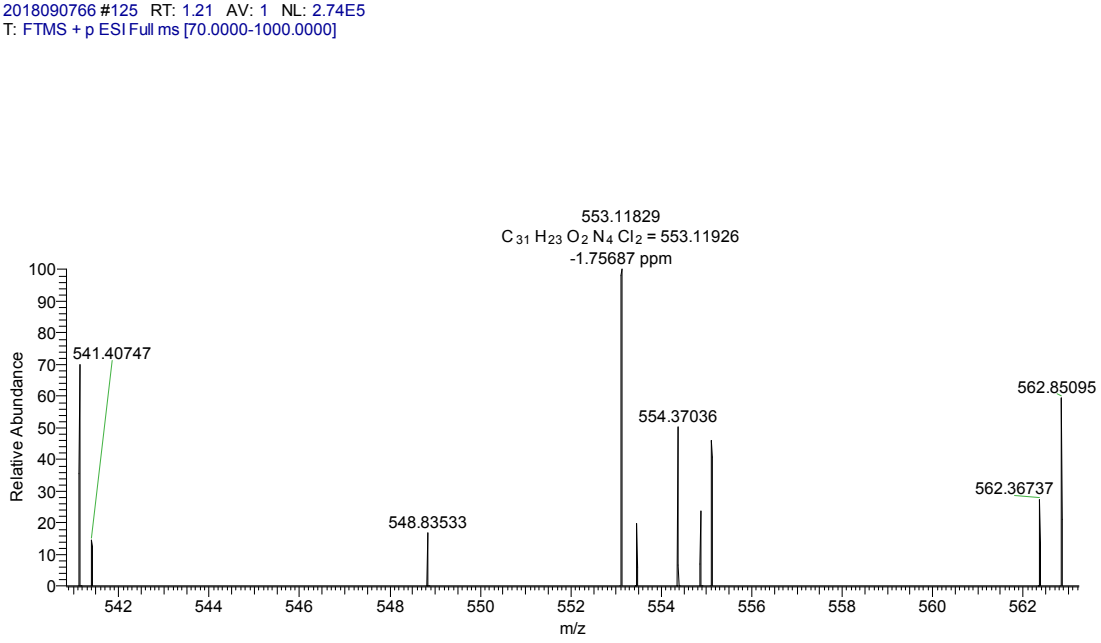

Figure S17. ^{1}H NMR spectrum of compound **6f**

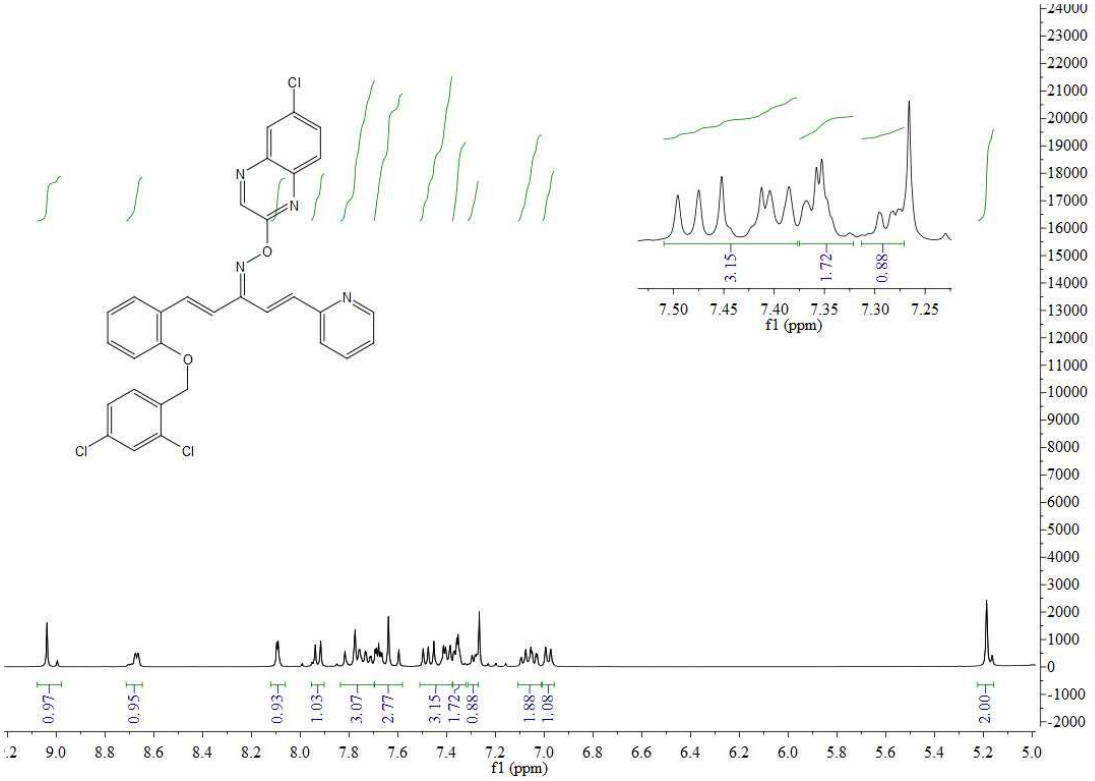

Figure S18. ^{13}C NMR spectrum of compound **6f**

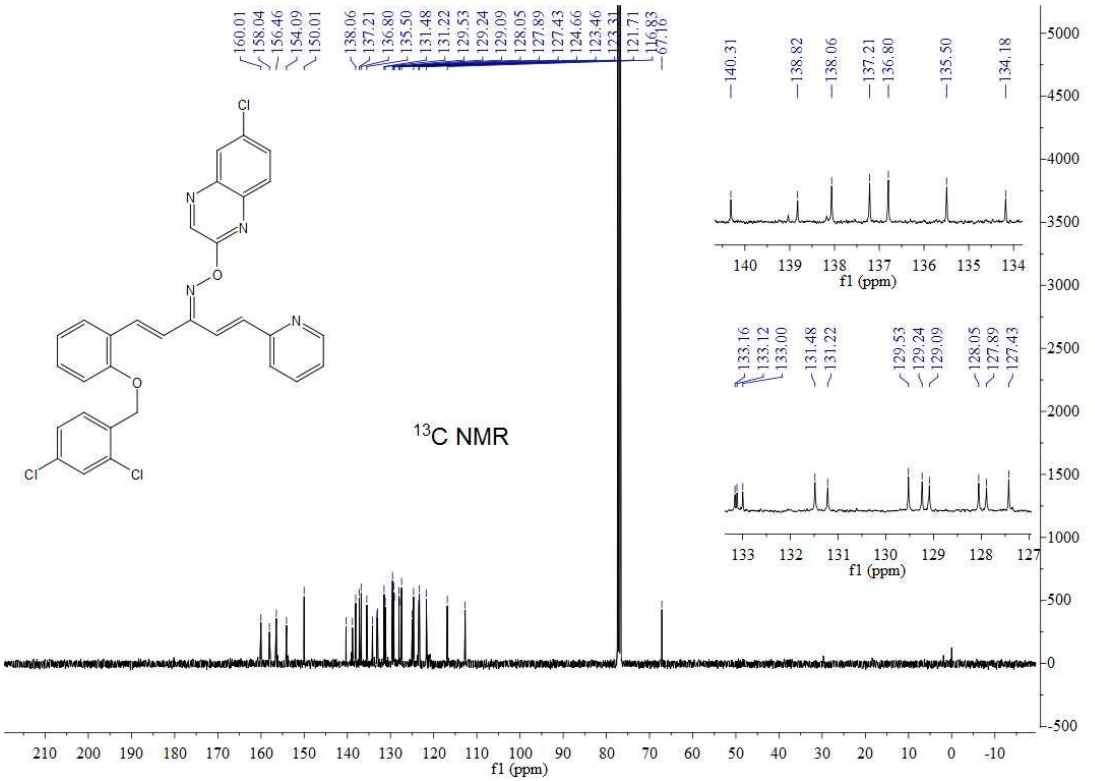

Figure S19. HRMS spectrum of compound **6f**

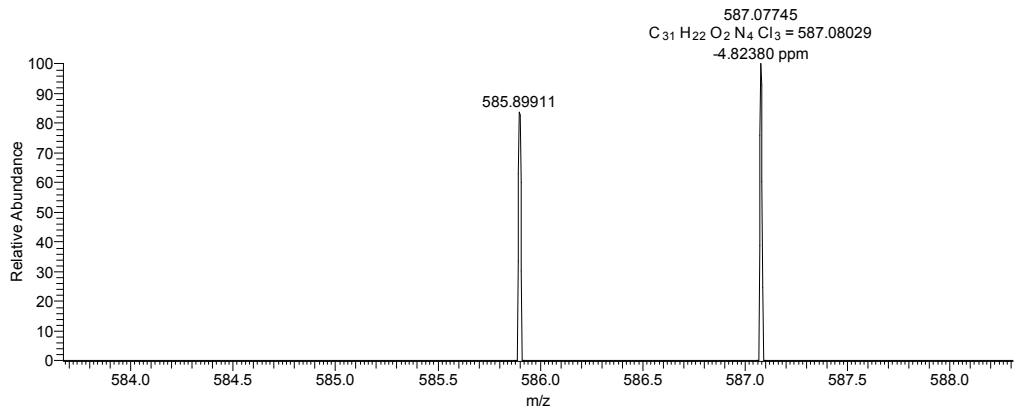

Figure S20. ^{1}H NMR spectrum of compound **6g**

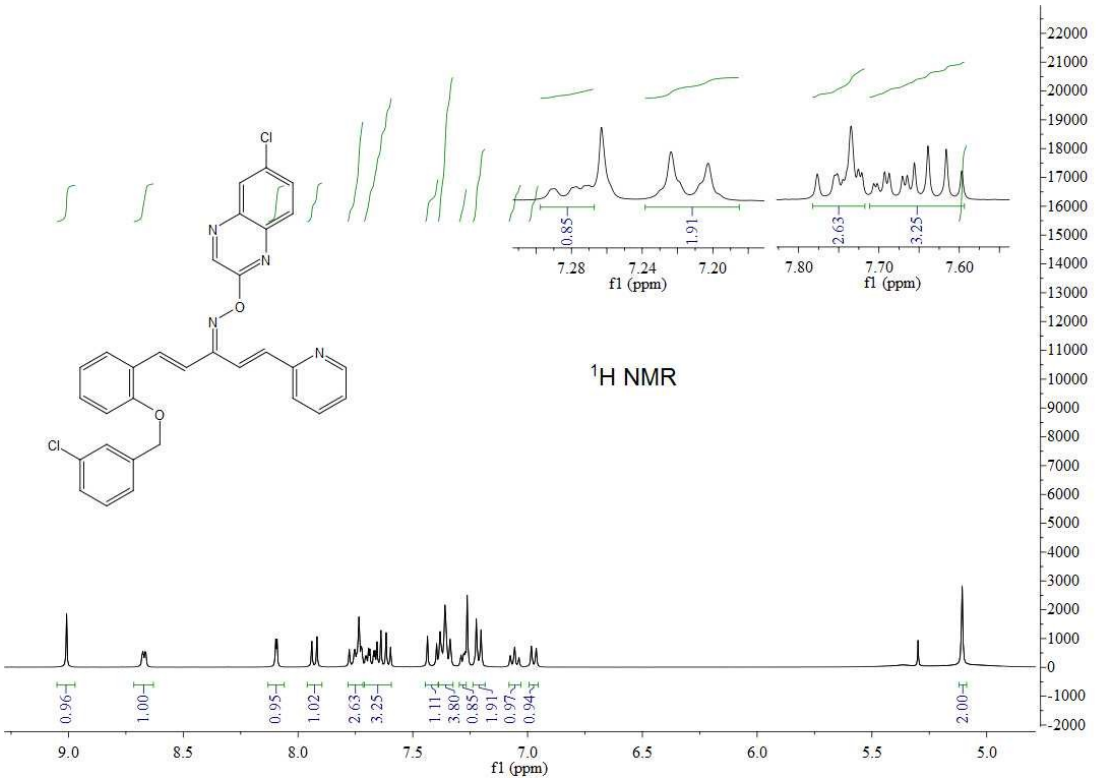

Figure S21. ^{13}C NMR spectrum of compound **6g**

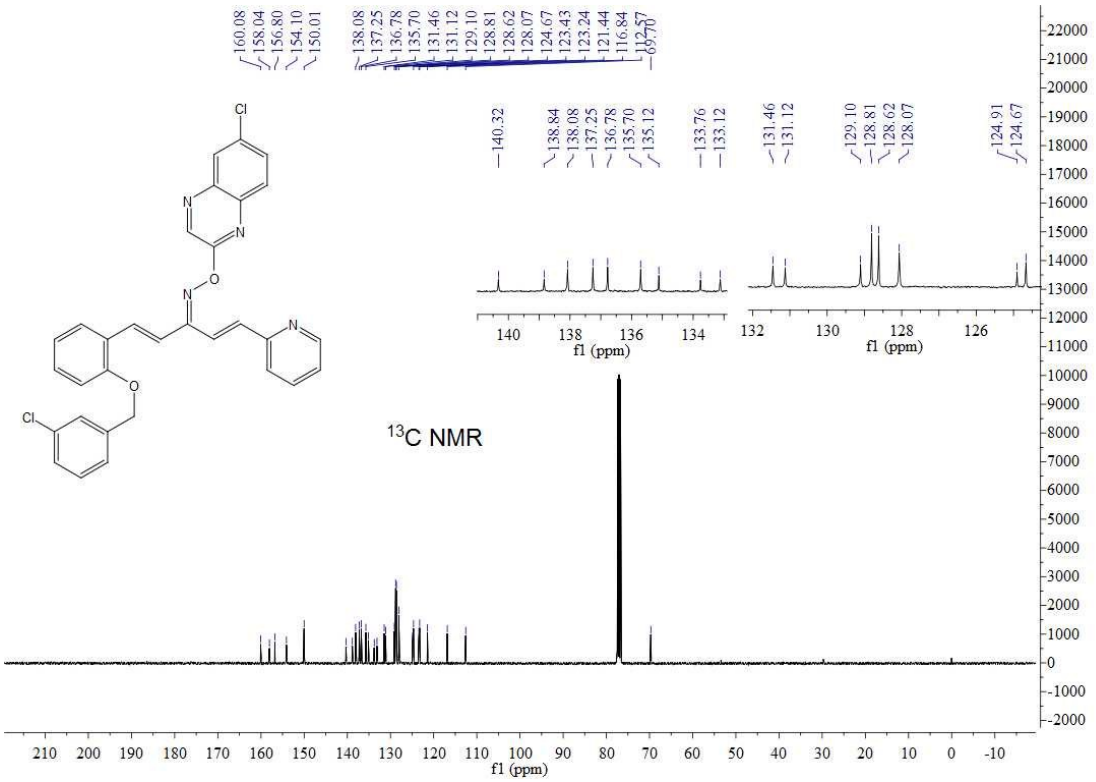

Figure S22. HRMS spectrum of compound **6g**

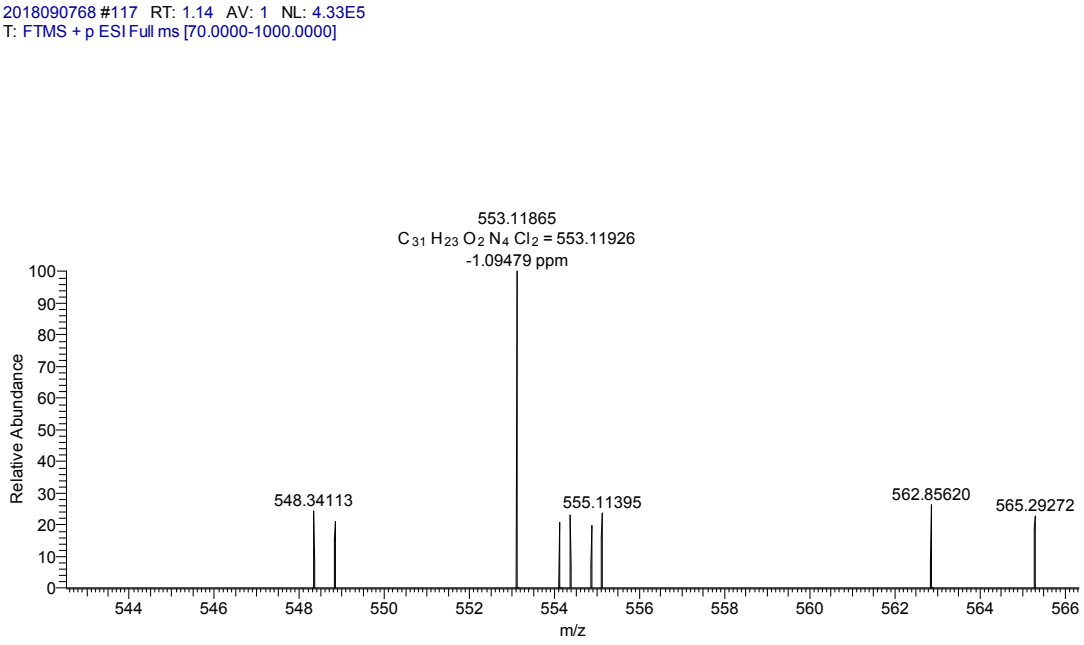

Figure S23. ^{1}H NMR spectrum of compound **6h**

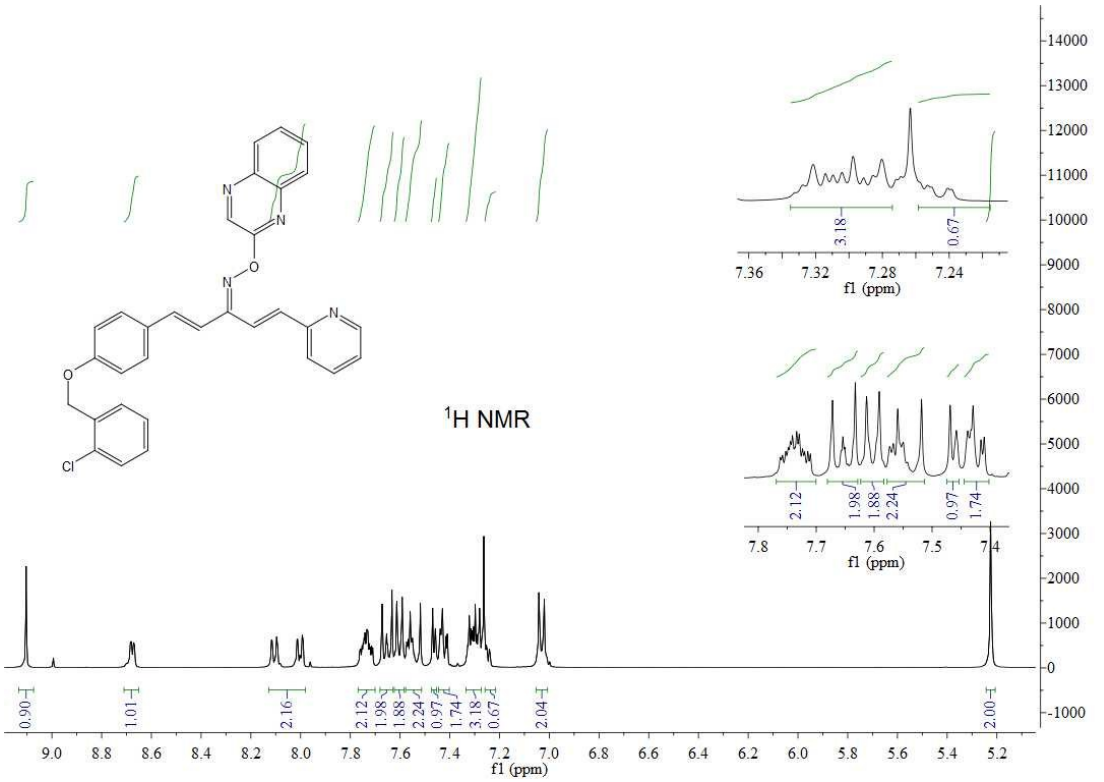

Figure S24. ^{13}C NMR spectrum of compound **6h**

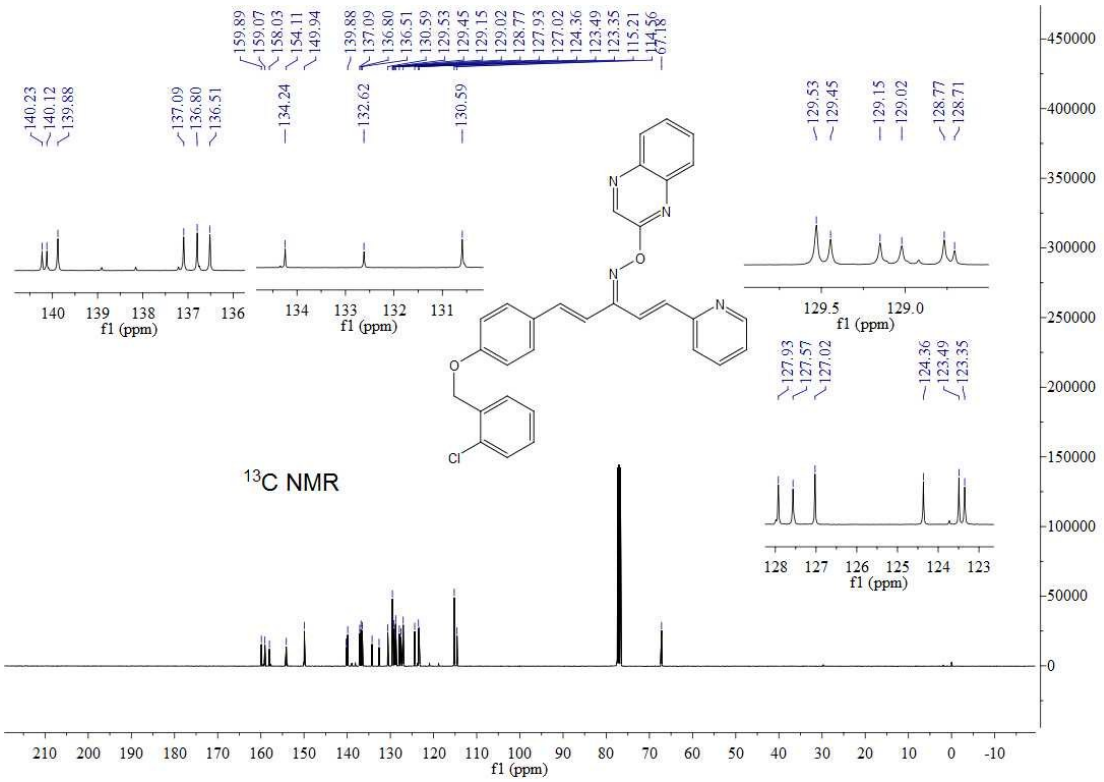

Figure S25. HRMS spectrum of compound **6h**

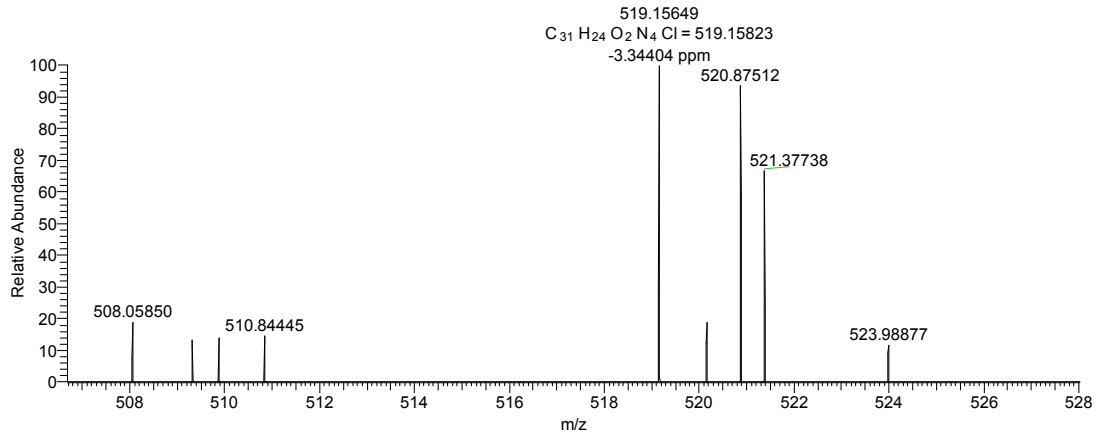

Figure S26. ^{1}H NMR spectrum of compound **6i**

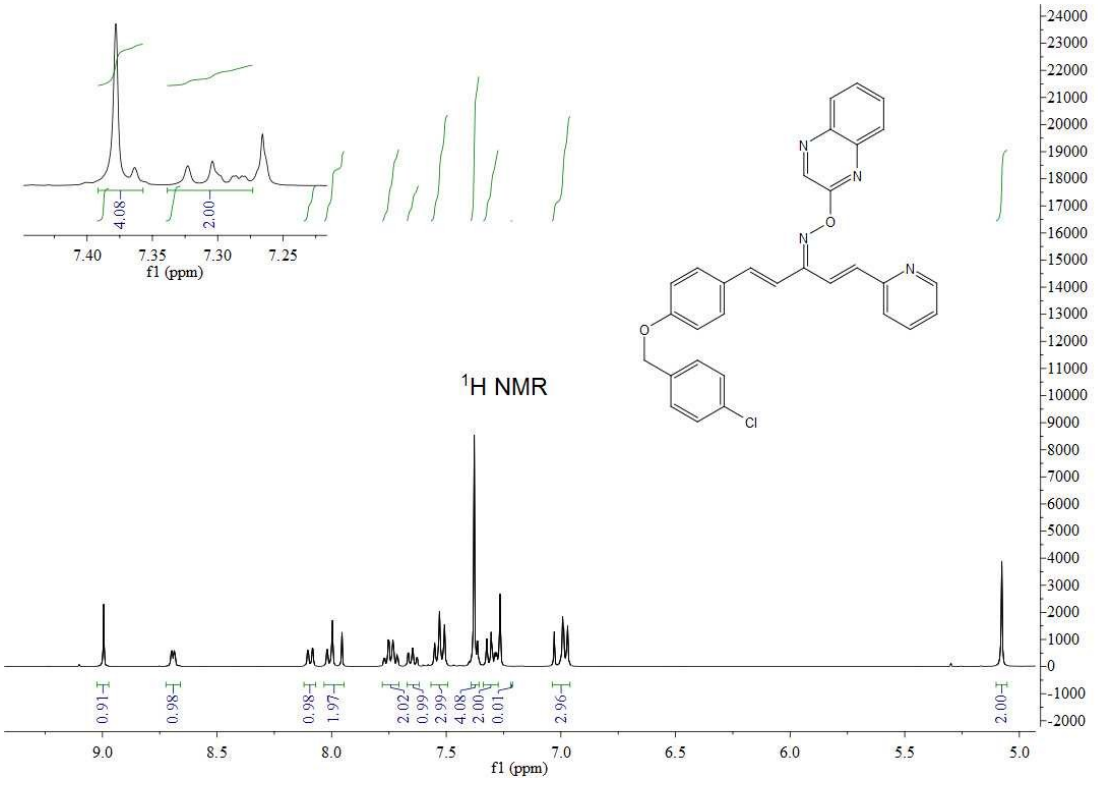

Figure S27. ^{13}C NMR spectrum of compound **6i**

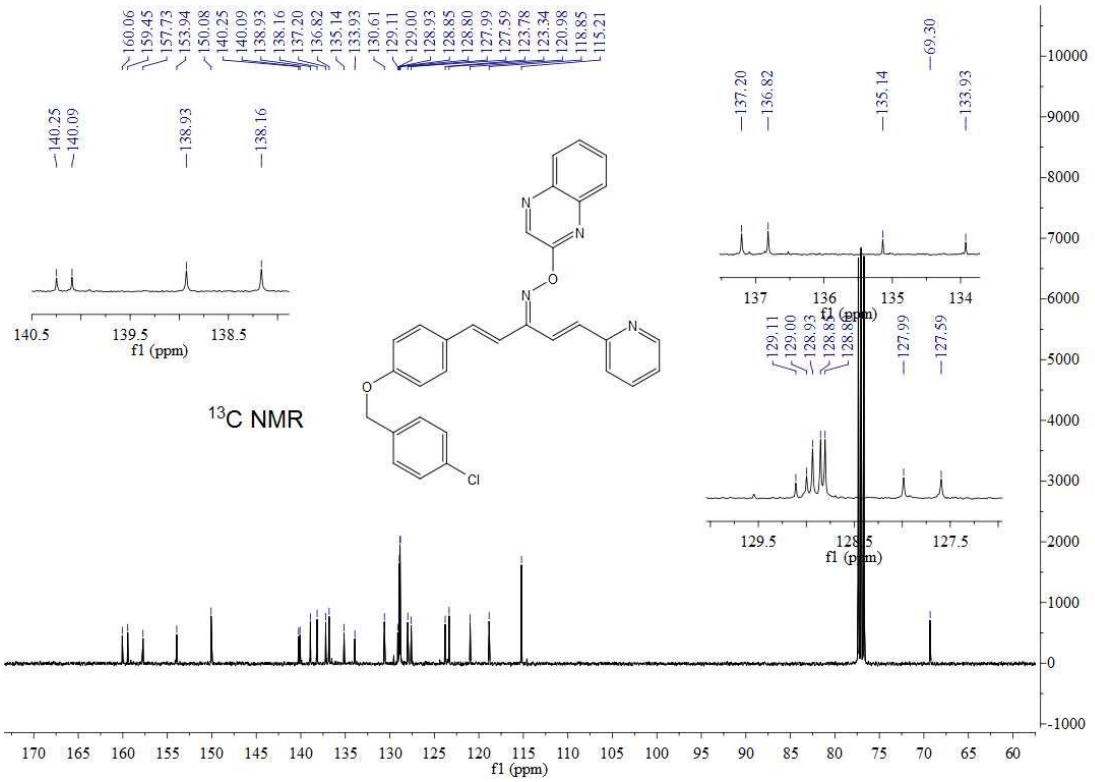

Figure S28. HRMS spectrum of compound **6i**

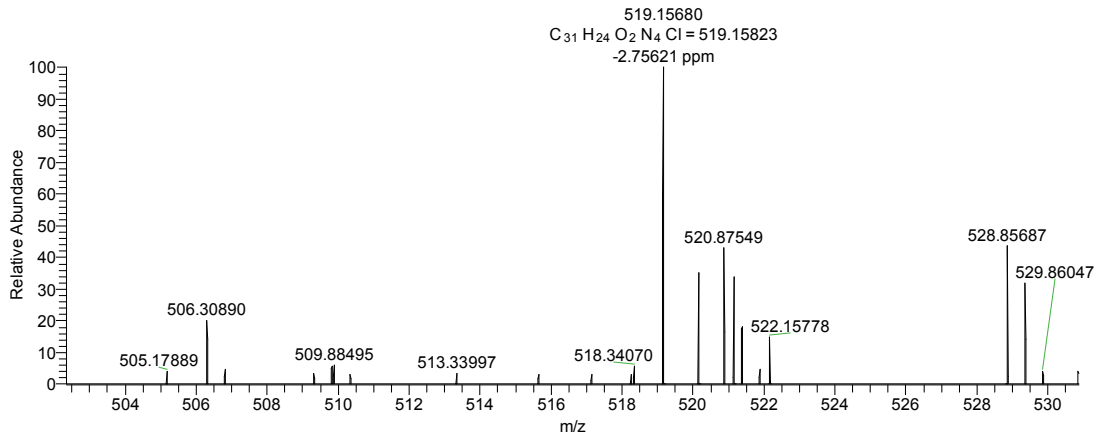

Figure S29. ^{1}H NMR spectrum of compound **6j**

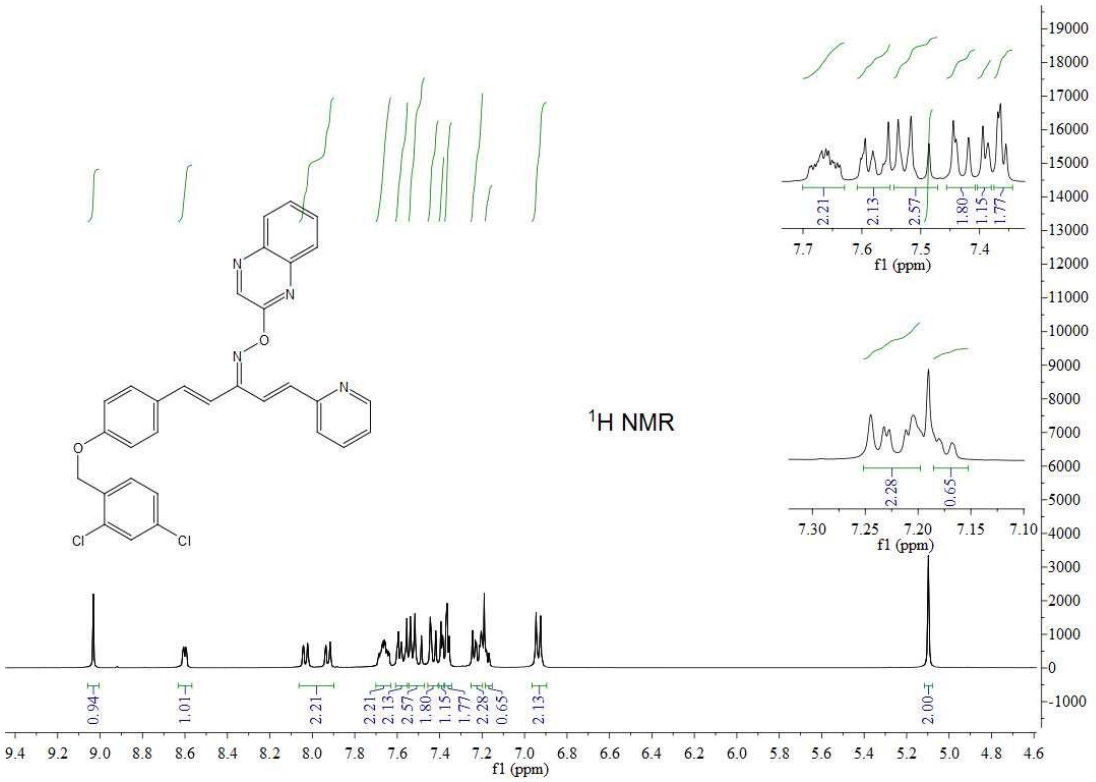

Figure S30. ^{13}C NMR spectrum of compound **6j**

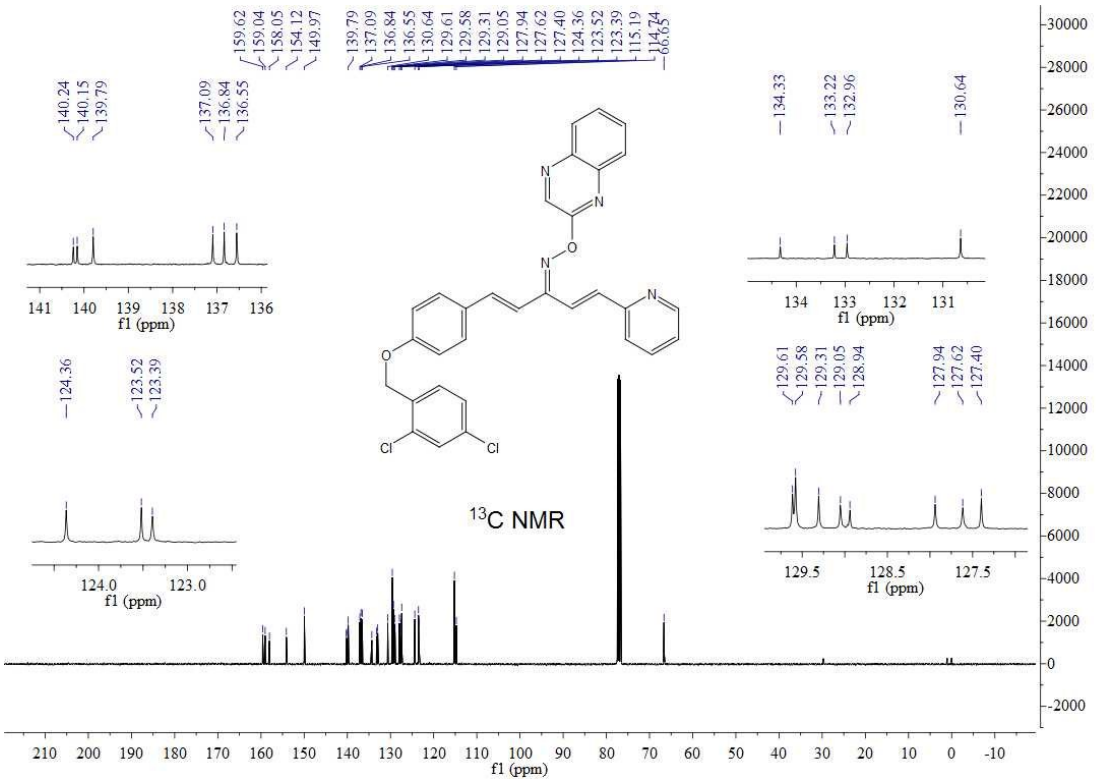

Figure S30. HMNR spectrum of compound **6j**

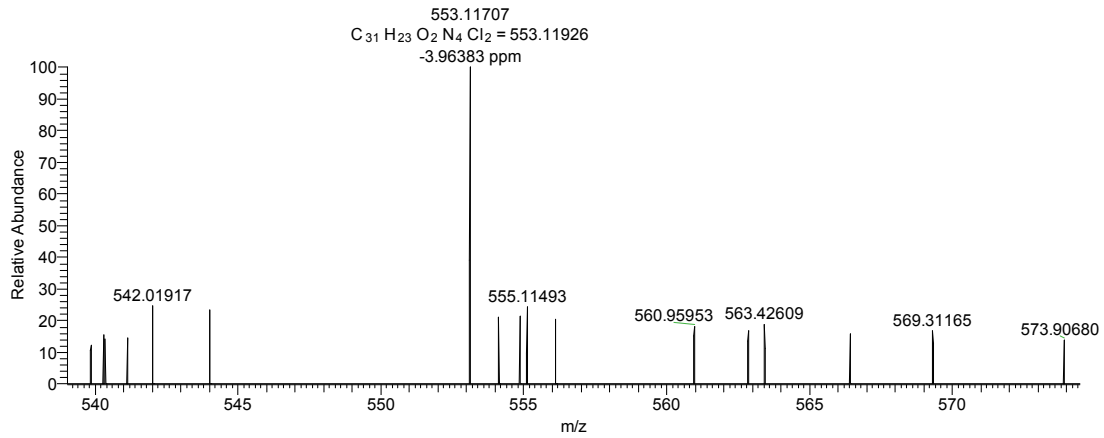

Figure S32. ^{1}H NMR spectrum of compound **6k**

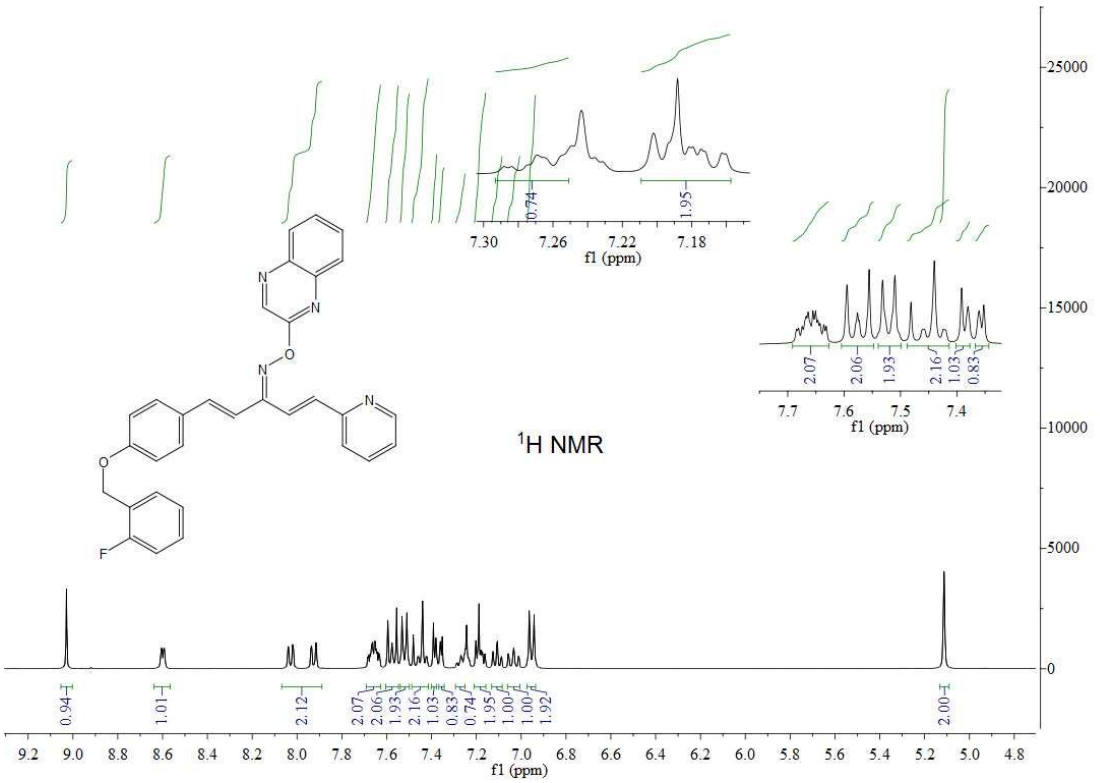

Figure S33. ^{13}C NMR spectrum of compound **6k**

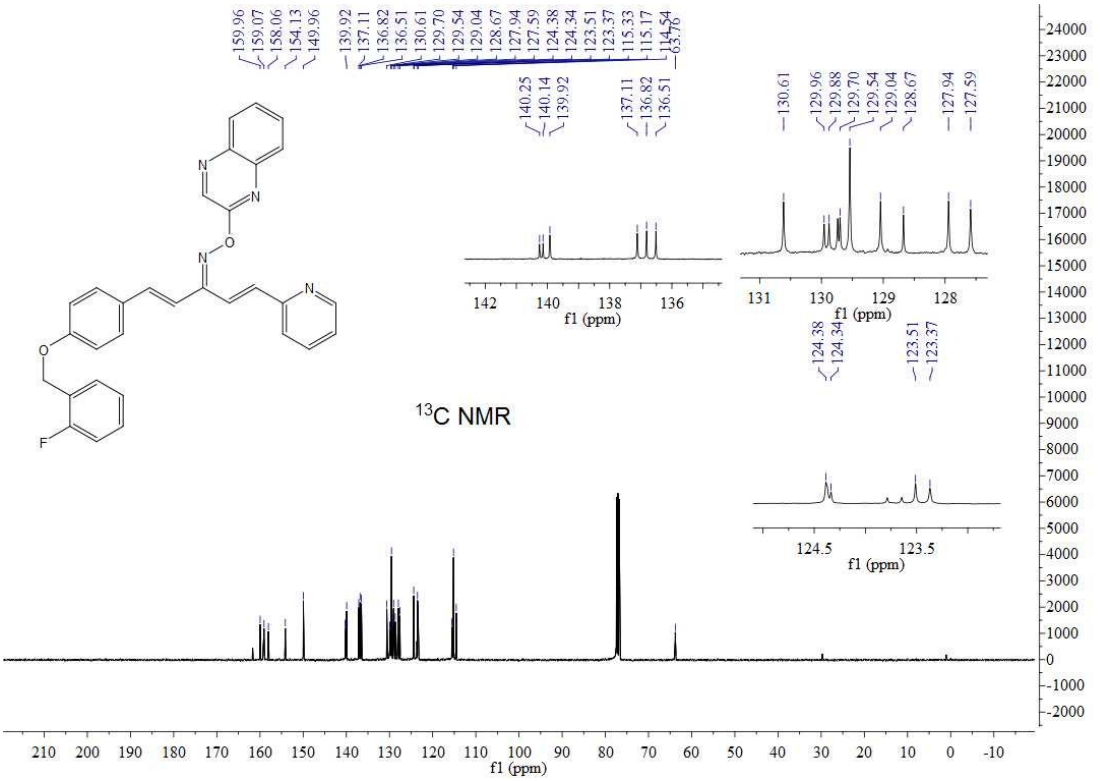

Figure S34. ^{19}F NMR spectrum of compound **6k**

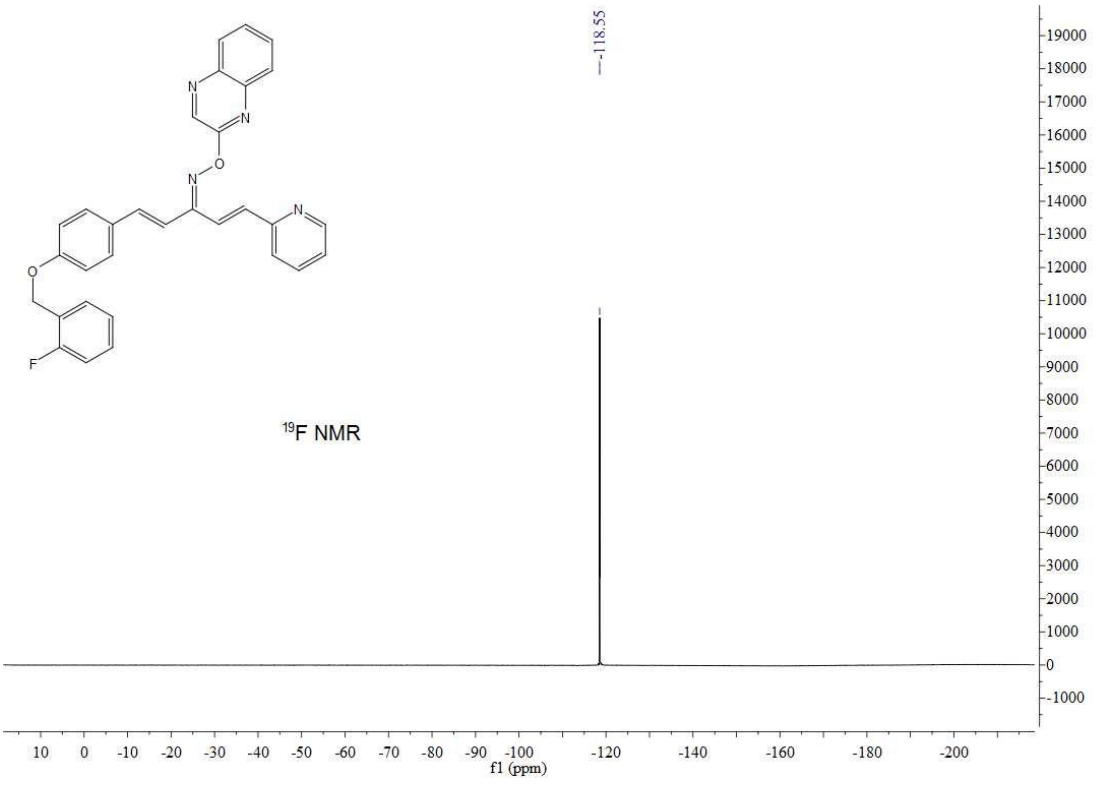

Figure S35. HRMS spectrum of compound **6k**

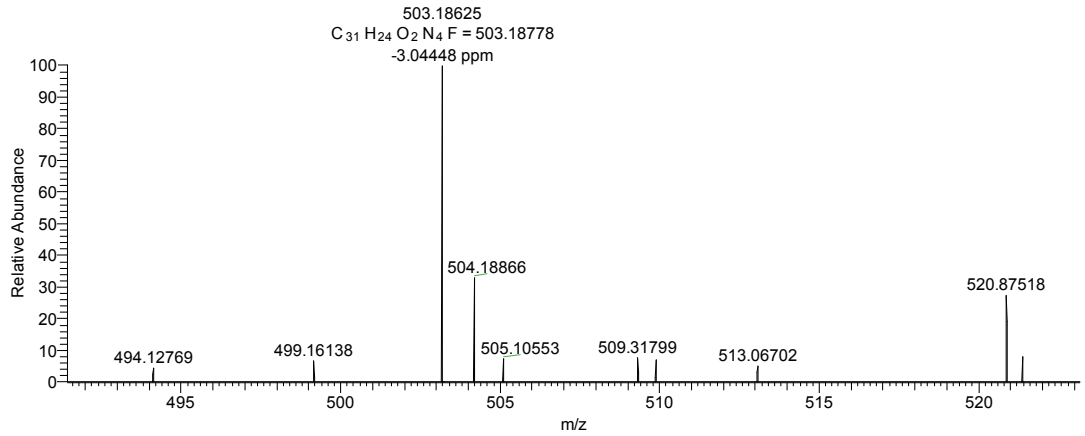

Figure S36. ^{1}H NMR spectrum of compound **6l**

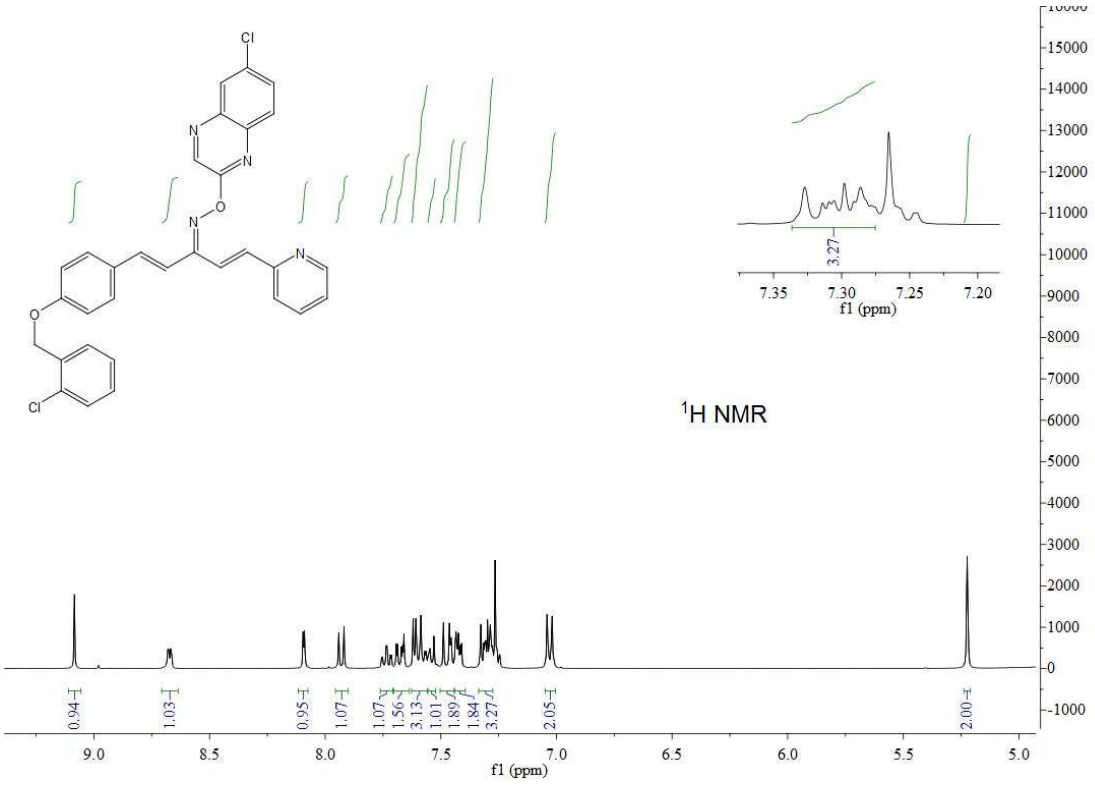

Figure S37. ^{13}C NMR spectrum of compound **6l**

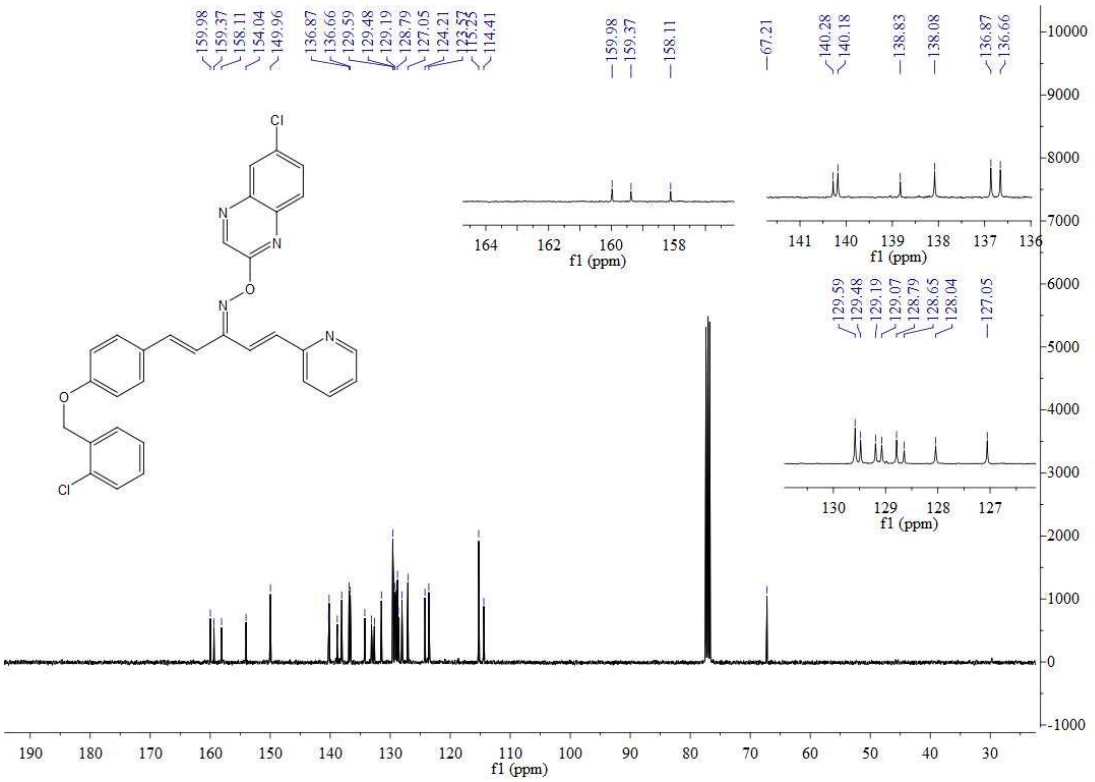

Figure S38. HRMS spectrum of compound **6l**

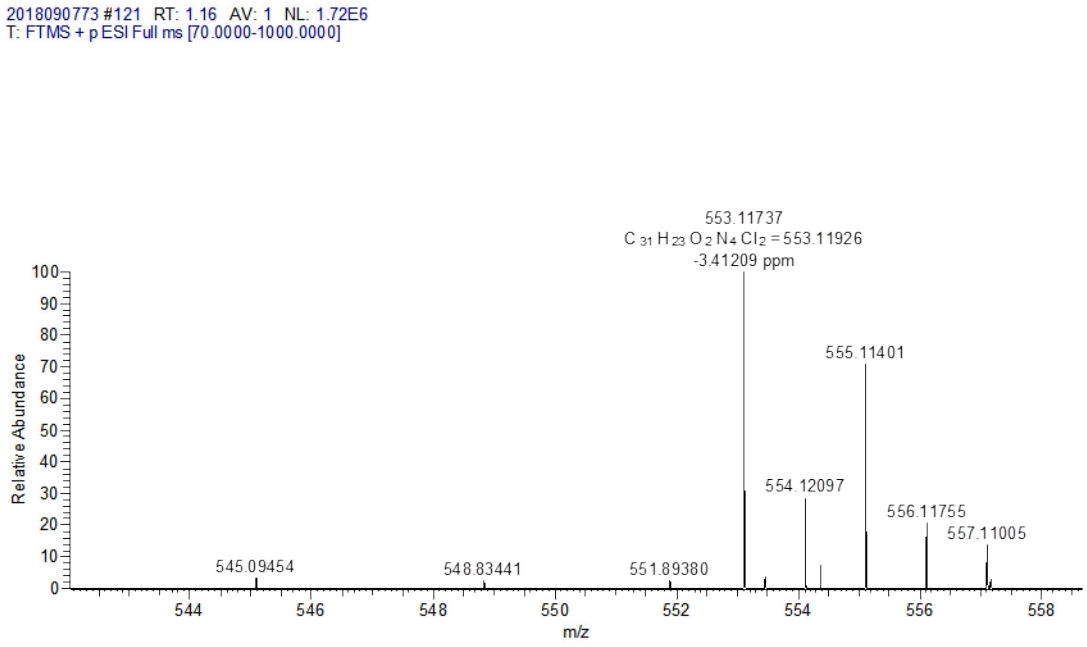

Figure S39. ^{1}H NMR spectrum of compound **6m**

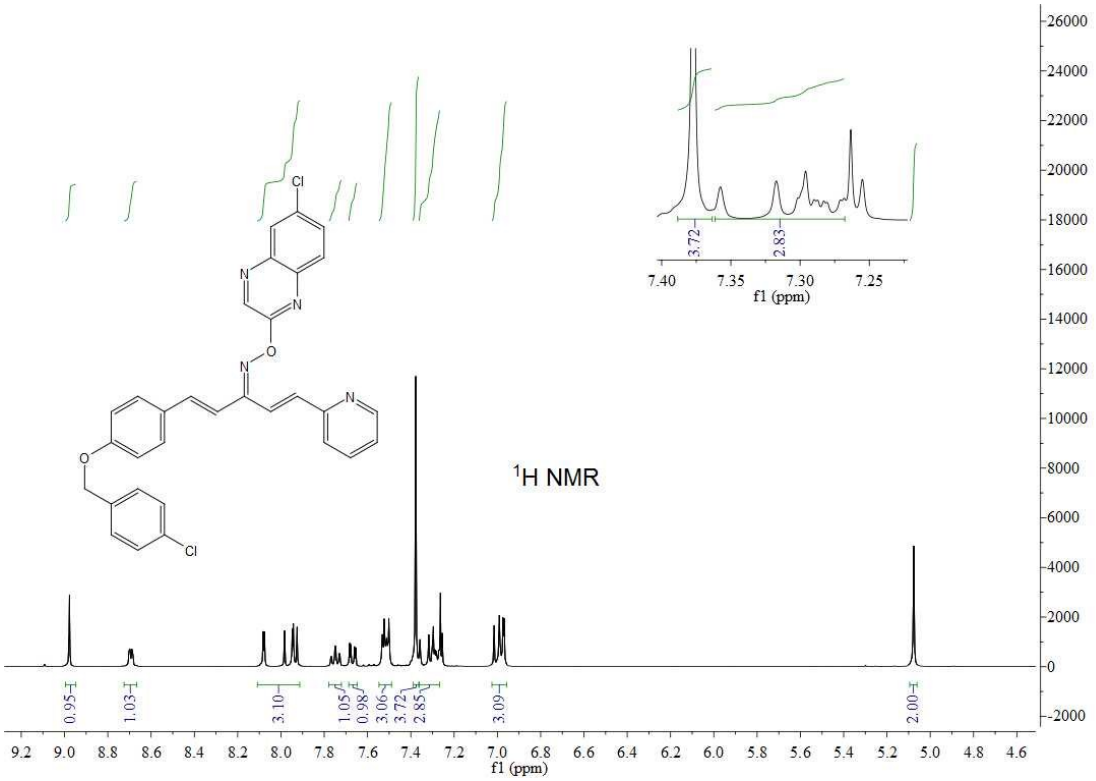

Figure S40. ^{13}C NMR spectrum of compound **6m**

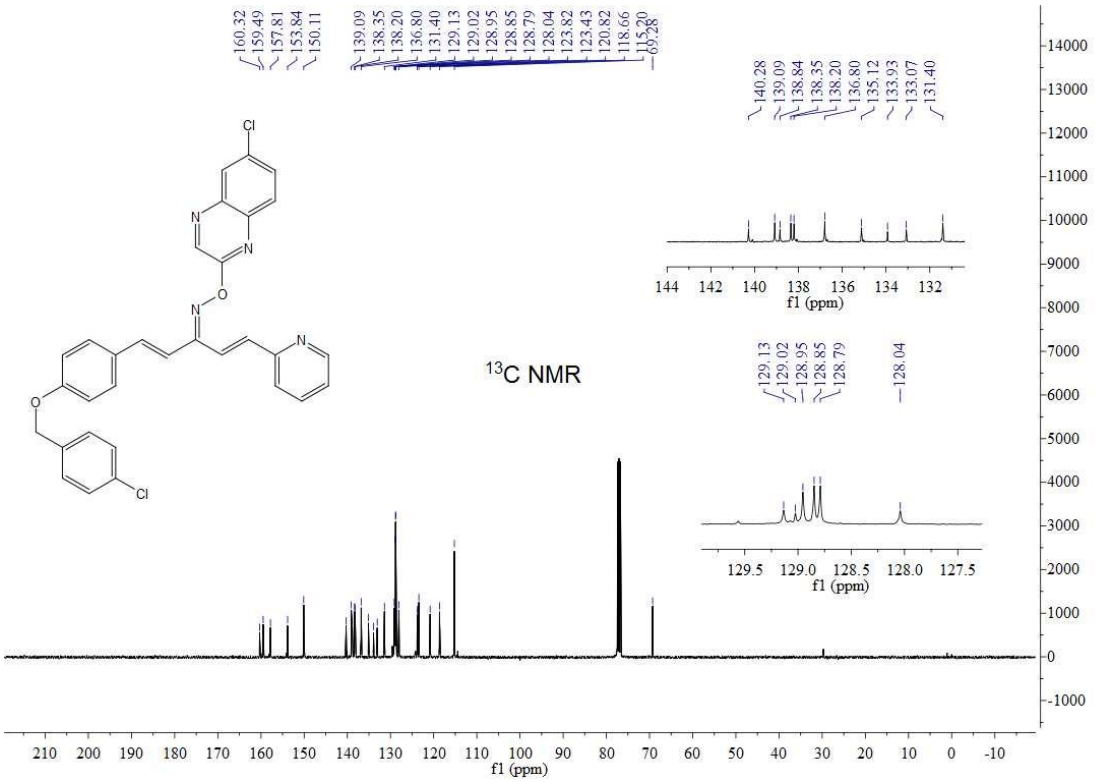

Figure S41. HRMS spectrum of compound **6m**

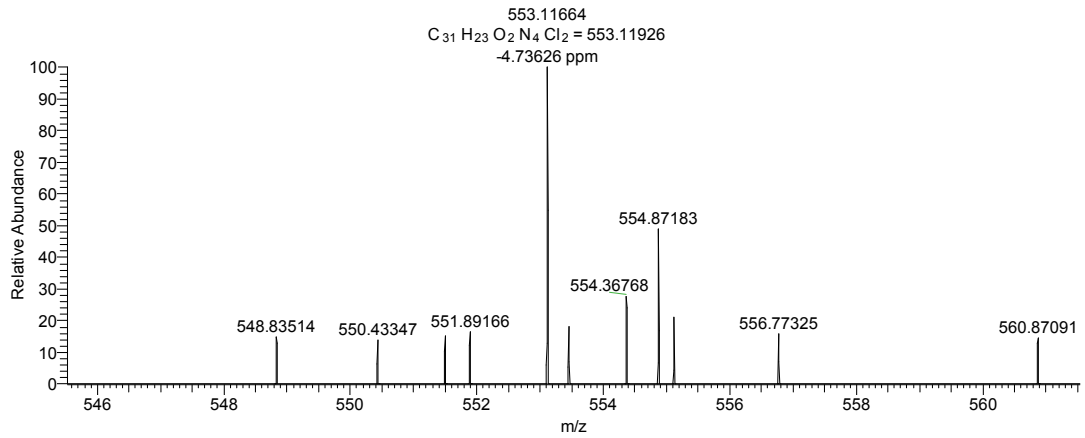

Figure S42. ^{1}H NMR spectrum of compound **6n**

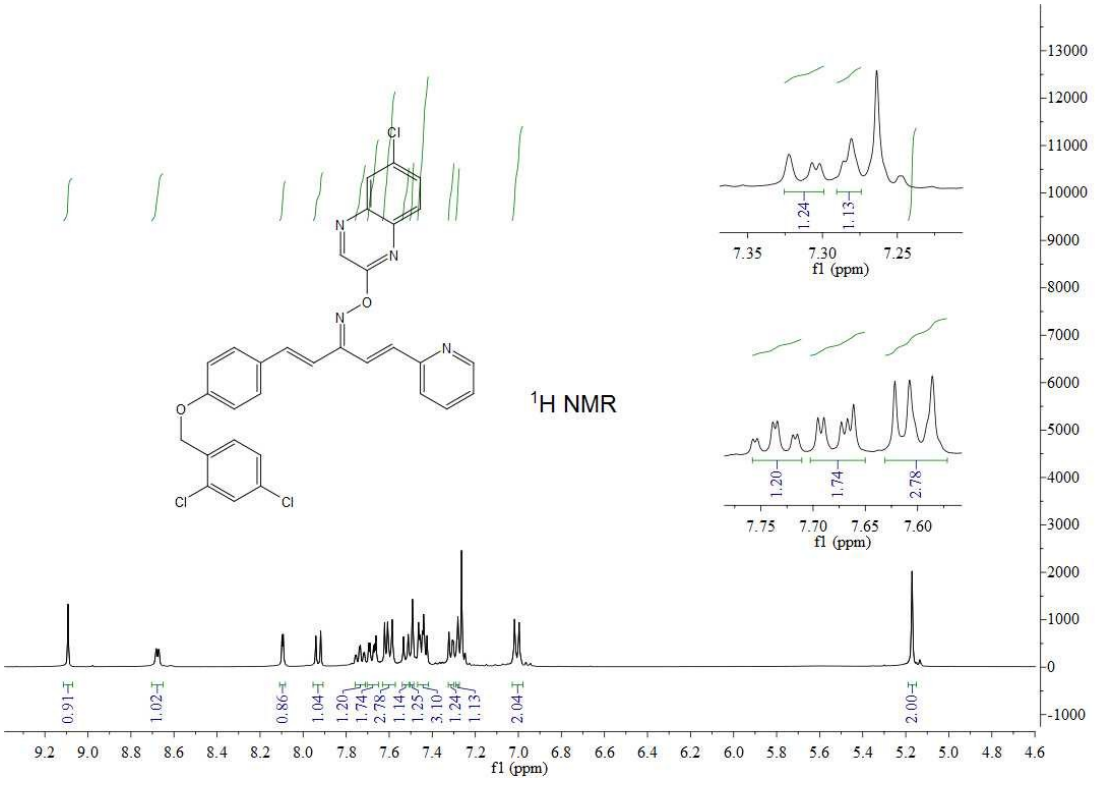

Figure S43. ^{13}C NMR spectrum of compound **6n**

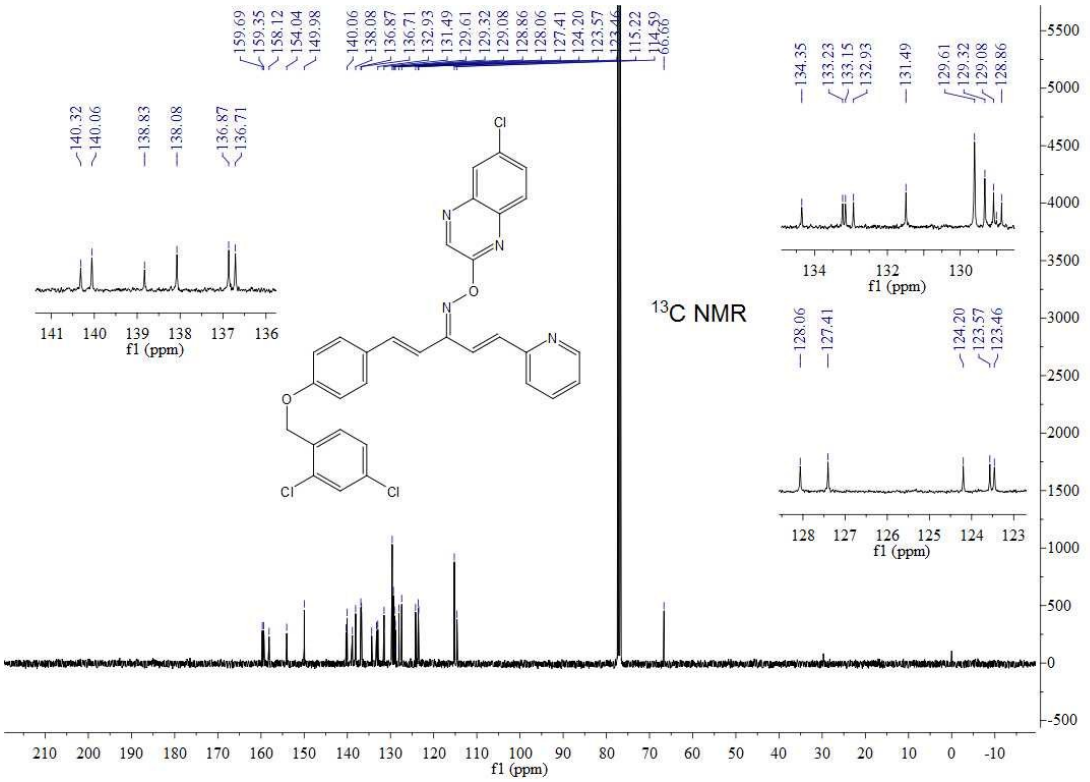

Figure S44. HRMS spectrum of compound **6n**

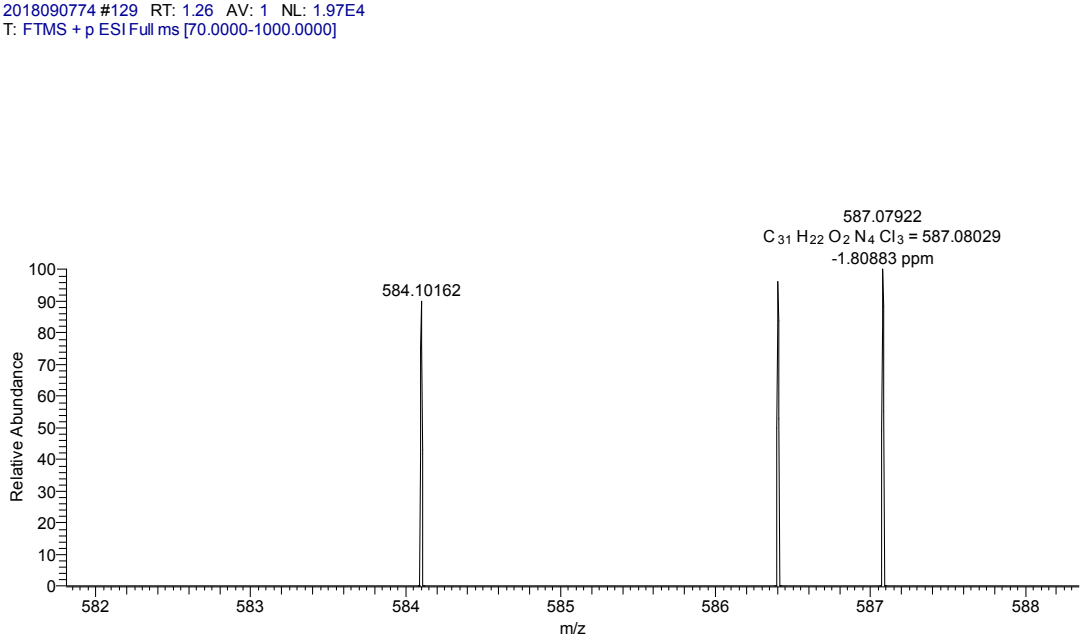

Figure S45. ^{1}H NMR spectrum of compound **6o**

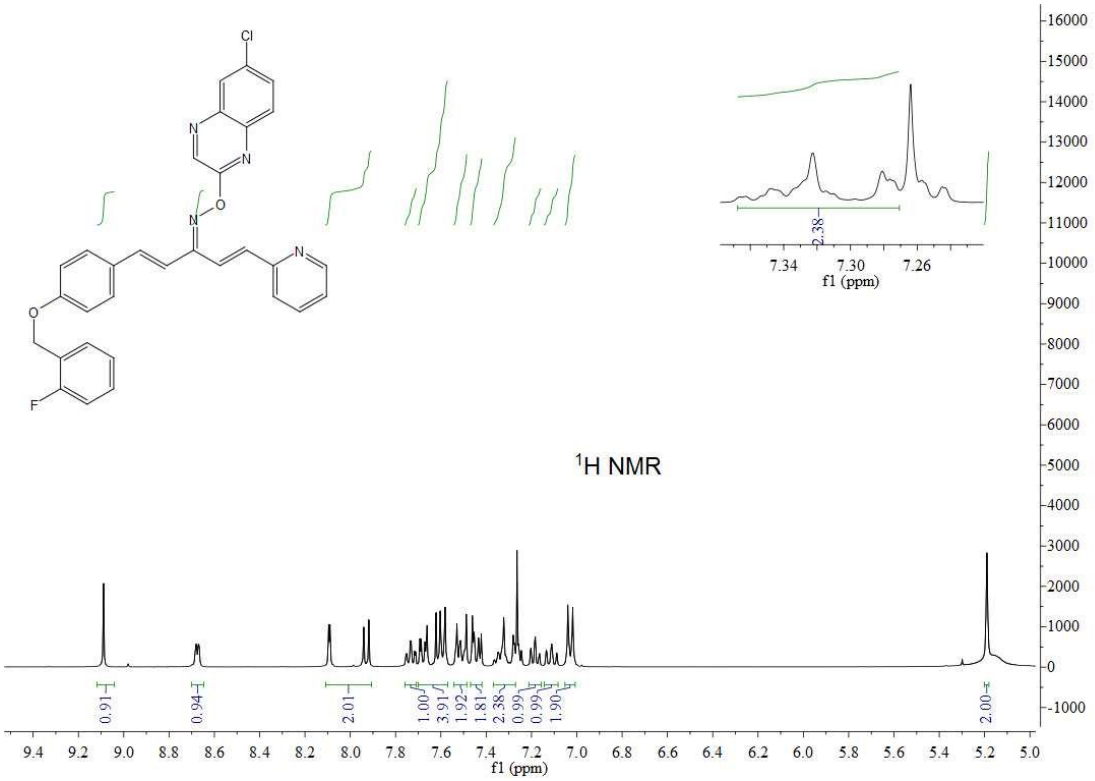

Figure S46. ^{13}C NMR spectrum of compound **6o**

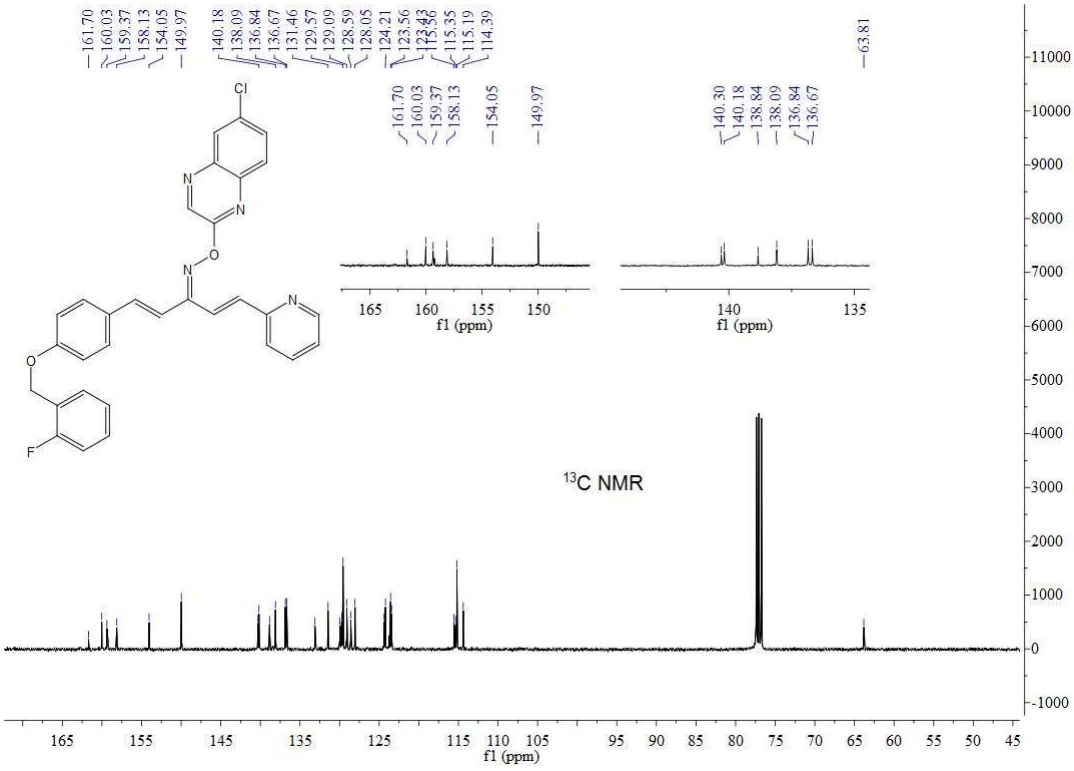

Figure S47. ^{19}F NMR spectrum of compound **6o**

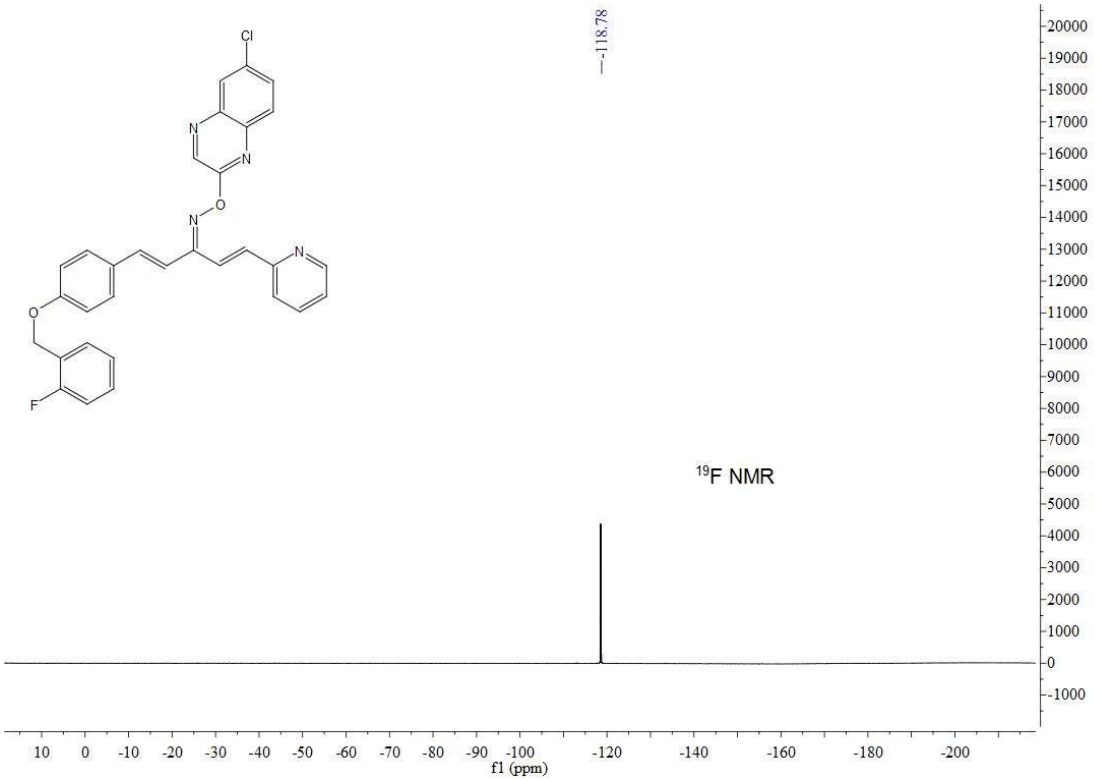

Figure S48. HRMS spectrum of compound **6o**

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T: FTMS + p ESI Full ms [70.0000-1000.0000]