Electronic Supplementary Material (ESI) for RSC Advances.

Synthesis and Fungicidal Activity of 3,4-Dichloroisothiazole Based Strobilurins as Potent Fungicide Candidates

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Supporting Information

1. Characterization of products

Data for (6a). Yellow crystal; yield, 59.1%; m.p.: 100-102°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.53(s,1H, C=CH), 7.42-7.36(m, 1H, Ph-H),7.31-7.23(m, 2H, Ph-H), 7.13-7.07(m, 1H, Ph-H), 5.20(s, 2H, Ph-CH_2), 3.72(s, 3H, O-CH_3), 3.59(s, 3H, O-CH_3), 2.45(s, 3H, C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ167.79, 160.21, 159.94, 148.28, 148.10, 143.93, 135.21, 132.08, 131.24, 129.05, 128.21, 128.02, 110.06, 75.84, 62.02, 51.69, 19.69. HRMS (m/z) calcd for $C_{17}H_{16}Cl_2N_2O_4S$ $(M+H)^+$: 415.0208, found: 415.0288.

Data for (6b). Yellow powder; yield, 71.4%; m.p.: 73-75°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.51(s, 1H, Ph-H), 7.47-7.43(m,2H, Ph-H), 7.24-7.20(m,1H, Ph-H), 5.23(s, 2H, Ph-CH_2), 4.06(s, 3H, O-CH_3), 3.83(s, 3H, O-CH_3), 2.52(s, 3H, N=C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ163.20, 149.09, 148.21, 144.33, 134.46, 130.02, 129.65, 129.40, 128.63, 128.42, 120.69, 75.56, 63.92, 53.03, 19.69. HRMS (m/z) calcd for $C_{16}H_{15}Cl_2N_3O_4S$ $(M+H)^+$: 416.0160, found: 416.0239.

Data for (6c). Yellow crystal; yield, 56.8%; m.p.: 61-63°C; ^{1}H NMR (400MHz, $CDCl_3$) δ8.10(s, 1H, O=C-H), 7.54(s, 1H, C=CH), 7.39(dd, *J*=5.4,3.6Hz, 1H, Ph-H), 7.28(dd, *J*=5.7,3.4Hz, 2H, Ph-H), 7.11(dd, *J*=5.4, 3.5Hz, 1H, Ph-H), 5.08(s, 2H, Ph-CH_2), 3.77(s, 3H, O-CH_3), 3.63(s, 3H, O-CH_3). ^{13}C NMR (400 MHz, $CDCl_3$) δ 167.82, 160.34, 147.52, 146.34, 135.91, 135.15, 132.22, 131.38, 129.07, 128.45, 128.14, 121.94, 110.05, 76.64, 62.11, 51.78. HRMS (m/z) calcd for $C_{16}H_{14}Cl_2N_2O_4S$ $(M+H)^+$: 401.0051, found: 401.0130.

Data for (6d). Yellow crystal; yield, 72.7%; m.p.: 88-90°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.74(s, 1H, N=C-H), 7.42(s, 1H, Ph-H), 7.37(dd, *J*=6.9, 2.9Hz, 2H, Ph-H), 7.15-7.12(m, 1H, Ph-H), 5.22(s, 2H, Ph-CH_2), 3.96(s, 3H, O-CH_3), 3.72(s, 3H, O-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ163.18, 152.66, 149.06, 147.56, 146.14, 139.42, 136.14, 134.33, 129.67, 129.35, 128.71, 128.58, 76.37, 63.93, 53.05. Anal. calcd for $C_{15}H_{13}Cl_2N_3O_4S$: C,44.79; H, 3.26; N, 10.45. Found: C, 44.53; H, 3.36; N, 10.32.

Data for (6e). Yellow solid; yield, 97.8%; m.p.: 105-107°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.61(s, 1H, C=CH-O), 7.48(dd, *J*=8.3, 4.9Hz, 1H, Ph-H), 7.37(dd, *J*=5.3, 3.8Hz, 2H, Ph-H), 7.22-7.18(m, 1H, Ph-H), 5.29(s, NH_2), 5.02(s, 2H, Ph-CH_2), 3.84(d, *J*=5.2Hz, 3H), 3.73(s, 3H). ^{13}C NMR (400MHz, $CDCl_3$) δ168.20, 159.89, 152.35, 148.49, 144.18, 135.99, 132.34, 131.06, 129.04, 128.06, 127.98, 110.43, 74.73, 61.99, 51.71. Anal. calcd for $C_{15}H_{13}Cl_2N_3O_4S$: C, 46.16; H, 3.63;

N, 10.09. Found: C, 45.78; H, 3.67; N, 10.07.

Data for (6f). Brown yellow crystal; yield, 43.0%; m.p.: 104-106°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.40-7.30(m, 3H, Ph-H), 7.13(d, *J*=6.4Hz, 1H, Ph-H), 5.18(s, 2H, NH_2), 4.91(s, 2H, Ph-CH_2), 3.97(s, 3H, O-CH_3), 3.79(s, 3H, O-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ163.69, 152.11, 149.67, 148.49, 144.26, 135.26, 130.23, 129.48, 129.20, 128.51, 128.17, 118.36, 74.95, 63.88, 53.11. Anal. calcd for $C_{15}H_{14}Cl_2N_4O_4S$: C, 43.18; H, 3.38; N, 13.43. Found: C, 42.46; H, 3.22; N, 13.21.

Data for (6g). White solid; yield, 40.0%; m.p.: 101-103°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.57(s, 1H, C=CH-O), 7.45(dd, *J*=7.3, 4.5Hz, 2H, CH=CH, Ph-H), 7.35-7.31(m, 2H, Ph-H), 7.19-7.15(m, 1H, Ph-H), 6.88(d, *J*=16.7Hz, 1H, CH=CH), 5.09(s, 2H, Ph-CH_2), 3.81(s, 3H, O-CH_3), 3.67(s, 3H, O-CH_3), 2.11(s, 3H, C=C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ167.90, 159.85, 158.19, 154.48, 149.11, 136.19, 133.54, 131.81, 131.05, 128.33, 127.93, 127.78, 120.14, 118.78, 110.31, 75.05, 61.96, 51.65, 10.18. HRMS (m/z) calcd for $C_{19}H_{18}Cl_2N_2O_4S$ $(M+H)^+$: 441.0364, found: 441.0441.

Data for (6h). white solid; yield, 60.0%; m.p.: 105-107°C; ^{1}HNMR (400MHz, $CDCl_3$) δ7.35(ddd, *J*=9.6, 6.1, 2.0Hz, 3H, Ph-H), 7.14-7.11(m, 1H, Ph-H), 6.75(d, *J*=5.1Hz, 2H, CH=CH), 5.02(s, 2H, Ph-CH_2), 3.97(s, 3H, O-CH_3), 3.79(s, 3H, N-CH_3), 1.97(s, 3H, C=C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ163.29, 158.06, 154.85, 149.50, 149.13, 135.49, 133.30, 129.93, 129.49, 128.87, 128.63, 128.02, 120.25, 119.06, 75.28, 63.86, 52.97, 10.12. HRMS (m/z) calcd for $C_{18}H_{17}Cl_2N_3O_4S$ $(M+H)^+$: 442.0317, found: 442.0392.

Data for (8a). White solid; yield, 99.0%; m.p.: 78-80°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.57-7.39(m, 3H, Ph-H), 7.22(dd, *J*=6.7, 1.9Hz, 1H, Ph-H), 7.11(s, 1H, Ph-H), 5.91(tdd, *J*=55.9, 8.6, 4.3Hz, 1H, CHF_2), 5.18(d, *J*=38.8Hz, 2H, Ph-CH_2), 4.00(d, *J*=13.8Hz, 3H, O-CH_3), 3.83-3.65(m, 2H, N-CH_2), 2.42(d, *J*=72.2Hz, 3H, N=C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ162.67, 156.76, 149.88, 148.58, 148.19, 134.84, 129.73, 129.36, 129.11, 128.98, 128.11, 113.53 (dd, *J*=243.1, 240.2 Hz), 75.78, 63.68, 41.73 (t, *J*=26.7 Hz), 19.65. HRMS (m/z) calcd for $C_{17}H_{16}Cl_2F_2N_4O_3S$ $(M+H)^+$: 465.0288, found: 465.0360.

Data for (8b). White solid; yield, 99.0%; m.p.: 120-122°C; ^{1} HNMR (400MHz, $CDCl_3$) δ7.50(s, 1H, Ph-H), 7.44(dd, *J*=9.6, 5.3Hz, 2H, Ph-H), 7.22(d, *J*=6.8Hz, 1H, Ph-H), 6.99(s, 1H, O=C-NH), 5.24(s, 2H, Ph-CH_2), 4.14(d, *J*=5.2Hz, 2H, N-CH_2), 3.98(s, 3H, O-CH_3), 2.42(d, *J*=70.7Hz, 3H, N=C-CH_3), 2.29(d, *J*=9.0Hz, 1H, C≡CH). ^{13}C NMR (400MHz, $CDCl_3$) δ 161.70, 156.85, 150.15,

148.54, 148.16, 134.83, 129.51, 129.31, 129.09, 128.94, 128.12, 120.60, 79.15, 75.79, 71.89, 63.57, 29.20, 19.69. Anal. calcd for $C_{18}H_{16}Cl_2N_4O_3S$: C,49.21; H, 3.67; N, 12.75. Found: C, 48.71; H, 3.73; N, 12.66.

Data for (8c). Colorless crystal; yield, 72.7%; m.p.: 115-117°C; ^{1}HNMR (400MHz, $CDCl_3$) δ7.50(d, *J*=7.0Hz, 1H, Ph-H), 7.42(dt, *J*=11.5, 8.0Hz, 2H, Ph-H), 7.22(d, *J*=6.7Hz, 1H, Ph-H), 6.87(s, 1H, O=C-NH), 5.24(s, 2H, Ph-CH_2), 3.93(s, 3H, O-CH_3), 2.78(d, *J*=3.6Hz, 1H, N-CH), 2.51(s, 3H, N=C-CH_3), 0.82(d, *J*=6.3Hz, 2H, cyclopropyl-CH_2), 0.59(s, 2H, cyclopropyl-CH_2). ^{13}C NMR (400MHz, $CDCl_3$) δ163.24, 156.87, 150.56, 148.44, 148.14, 134.81, 129.47, 129.37, 129.19, 128.99, 128.13, 120.57, 75.88, 63.37, 22.63, 19.68, 6.61. HRMS (m/z) calcd for $C_{18}H_{18}Cl_2N_4O_3S$ $(M+H)^+$: 441.0477, found: 441.0548.

Data for (8d). White solid; yield, 71.0%; m.p.: 79-81°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.52-7.44(m, 1H, Ph-H), 7.40(dd, *J*=9.4, 5.8Hz, 2H, Ph-H), 7.21(d, *J*=7.2Hz, 1H, Ph-H), 6.92(d, *J*=4.5Hz, 1H, O=C-NH), 5.25(s, 2H, Ph-CH_2), 3.91(s, 3H, O-CH_3), 2.84(d, *J*=4.9Hz, 3H, N-CH_3), 2.48(s, 3H, N=C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ 163.40, 157.59, 151.38, 149.15, 148.74, 135.50, 130.42, 130.13, 129.90, 129.71, 128.85, 121.22, 76.51, 64.04, 26.89, 20.34. HRMS (m/z) calcd for $C_{16}H_{16}Cl_2N_4O_3S$ $(M+H)^+$: 415.0320, found 415.0398.

Data for (8e). Yellow oil; yield, 36.8%; ^{1}HNMR (400MHz, $CDCl_3$) δ7.47(d, *J*=6.8Hz, 1H, Ph-H), 7.44-7.38(m, 2H, Ph-H), 7.23-7.19(m, 1H, Ph-H), 6.93(s, 1H, O=C-NH), 5.15(s, 2H, Ph-CH_2), 3.99(s, 3H, O-CH_3), 3.00(s, 2H, S-CH_2), 2.37(s, 3H, N=C-CH_3), 2.19(s, 3H, S-CH_3), 1.49(s, 6H, CH_3-C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ 161.46, 156.93, 151.32, 148.98, 148.42, 135.18, 129.60, 129.30, 129.01, 128.92, 127.94, 119.35, 75.87, 63.37, 54.72, 45.16, 26.69, 17.71, 13.26. HRMS (m/z) calcd for $C_{20}H_{24}Cl_2N_4O_3S_2$ $(M+H)^+$: 503.0667, found 503.0740.

Data for (8f). White solid; yield, 37.8%; m.p.: 35-37°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.44(dd, *J*=7.2, 4.1Hz, 1H, Ph-H), 7.42-7.37(m, 2H, Ph-H), 7.20(d, *J*=6.7Hz, 1H, Ph-H), 6.88(d, *J*=8.0Hz, 1H, O=C-NH), 5.13(s, 2H, Ph-CH_2), 4.24(dt, *J*=13.4, 6.6Hz, 1H, N-CH), 3.98(s, 3H, O-CH_3), 2.72(dd, *J*=13.5, 5.5Hz, 1H, S-CH_2), 2.63(dd, *J*=13.5, 6.4Hz, 1H, S-CH_2), 2.33(s, 3H, N=C-CH_3), 2.15(s, 3H, S-CH_3), 1.32(d, *J*=6.6Hz, 3H, N-C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ161.58, 156.88, 150.85, 148.98, 148.45, 135.20, 129.61, 129.37, 129.00, 128.97, 128.01, 119.37, 75.89, 63.45, 44.82, 40.65, 19.70, 16.37, 13.21. Anal. calcd for $C_{19}H_{22}Cl_2N_4O_3S_2$: C,46.63; H, 4.53; N,11.45. Found C, 46.70; H, 4.79; N, 11.24.

Data for (8g). White solid; yield, 53.6%; m.p.: 98-100°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.47-7.36(m, 4H, CH=CH, Ph-H), 7.21-7.16(m, 1H, Ph-H),7.07(d, *J*=5.8Hz, 1H, O=C-NH), 6.87(d, *J*=16.7Hz, 1H, CH=CH), 5.86(tt, *J*=55.9, 4.1Hz, 1H, CHF_2), 5.05(s, 2H, Ph-CH_2), 3.97(s, 3H, O-CH_3), 3.80-3.63(m, 2H, N-CH_2), 2.09(s, 3H, N=C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ162.79, 157.88, 151.05, 150.41, 149.26, 135.81, 133.28, 129.60, 128.87, 128.82, 127.88, 123.65, 121.83, 119.06, 113.53 (t, *J*=241.6 Hz), 74.96, 63.63, 41.75 (t, *J*=26.7 Hz), 16.56. HRMS (m/z) calcd for $C_{19}H_{18}Cl_2F_2N_4O_3S$ $(M+H)^+$: 491.0445, found: 491.0520.

Data for (8h). White solid; yield, 63.0%; m.p.: 92-93°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.47-7.35(m, 4H, CH=CH, Ph-H), 7.21-7.17(m, 1H, Ph-H), 7.00–6.91(m, 1H, O=C-NH), 6.82(d, *J*=3.7Hz, 1H, CH=CH), 5.05(s, 2H, Ph-CH_2), 4.17(s, 1H, N-CH_2), 4.12-4.09(m, 1H, N-CH_2), 3.97(s, 3H, O-CH_3), 2.26(dt, *J*=6.8, 2.6Hz, 1H, C≡CH), 2.05(s, 3H, N=C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ161.88, 158.00, 154.87, 151.05, 150.69, 135.79, 133.41, 129.49, 129.27, 128.82, 127.89, 123.71, 121.80, 118.99, 79.14, 75.10, 71.97, 63.51, 29.30, 16.59. HRMS (m/z) calcd for $C_{20}H_{18}Cl_2N_4O_3S$ $(M+H)^+$: 465.0477, found: 465.0555.

Data for (8i). White solid; yield,59.3%; m.p.: 95-97°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.50-7.36(m, 4H, CH=CH, Ph-H), 7.22(d, *J*=6.9Hz, 1H, Ph-H), 6.86(t, *J*=6.0Hz, 2H, O=C-NH, CH=CH), 5.11(s, 2H, Ph-CH_2), 3.97(s, 3H, O-CH_3), 2.07(s, 3H, N=C-CH_3), 0.84(d, *J*=5.6Hz, 2H, cyclopropyl-CH_2), 0.62(dd, *J*=3.7, 1.7Hz, 2H, cyclopropyl-CH_2). ^{13}C NMR (400MHz, $CDCl_3$) δ164.05, 158.83, 155.48, 151.66, 149.81, 136.31, 134.11, 130.06, 129.61, 129.40, 128.52, 124.58, 122.44, 119.66, 76.09, 64.04, 23.35, 10.90, 7.37. HRMS (m/z) calcd for $C_{20}H_{20}Cl_2N_4O_3S$ $(M+H)^+$: 467.0633, found: 467.0713.

Data for (8j). Colorless crystal; yield, 65.4%; m.p.: 137-139°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.48-7.35(m, 4H, CH=CH, Ph-H), 7.21-7.16(m, 1H, Ph-H), 6.81(d, *J*=3.7Hz, 1H, CH=CH), 6.77(s, 1H, O=C-NH), 5.09(s, 2H, Ph-CH_2), 3.96(s, 3H, O-CH_3), 2.93(d, *J*=5.0Hz, 3H, N-CH_3), 2.04(s, 3H, N=C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ162.83, 158.12, 154.79, 151.05, 149.11, 135.56 133.39, 129.37, 128.80, 128.75, 127.91, 123.79, 121.70, 118.96, 75.34, 63.35, 26.27, 10.12. Anal. calcd for $C_{18}H_{18}Cl_2N_4O_3S$: C, 48.99; H, 4.11; N, 12.69. Found: C, 47.39; H, 4.11; N, 12.14.

Data for (8k). Yellow oil; yield, 97.0%; ^{1}H NMR (400MHz, $CDCl_3$) δ7.47-7.34(m, 4H, CH=CH, Ph-H), 7.18(d, *J*=7.3Hz, 1H, Ph-H), 6.89(d, *J*=2.9Hz, 1H, O=C-NH), 6.83(s, 1H, CH=CH), 5.09(d, *J*=17.2Hz, 2H, Ph-CH_2), 3.97(s, 3H, O-CH_3), 2.98(s, 2H, S-CH_2), 2.16(s, 3H, S-CH_3), 2.07(s, 3H,

N=C-CH_3), 1.47(s, 6H, CH_3-C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ161.46, 158.15, 154.71, 151.37, 149.03, 135.69, 133.48, 129.28, 128.94, 128.54, 127.69, 123.90, 121.65, 118.87, 75.31, 63.34, 54.71, 45.14, 26.69, 17.75, 16.65. HRMS (m/z) calcd for $C_{22}H_{26}Cl_2N_4O_3S_2$ $(M+H)^+$: 529.0823, found: 529.0891.

Data for (8l). Yellow oil; yield, 84.6%; ^{1}H NMR (400MHz, $CDCl_3$) δ7.41-7.26(m, 4H, CH=CH, Ph-H), 7.12(dd, *J*=6.7, 2.0Hz, 1H, Ph-H), 6.81(d, *J*=4.5Hz, 1H, O=C-NH), 6.74(s, 1H, CH=CH), 5.03(s, 2H, Ph-CH_2), 4.16(dd, *J*=13.3, 6.6Hz, 1H, N-CH), 3.89(s, 3H, O-CH_3), 2.68–2.47(m, 2H, S-CH_2), 2.07(s, 3H, S-CH_3), 1.98(s, 3H, N=C-CH_3), 1.24(d, *J*=6.7Hz, 3H, N-C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ161.58, 158.14, 154.75, 150.92, 149.07, 135.66, 133.43, 129.36, 128.90, 128.64, 127.80, 123.86, 121.73, 118.93, 75.33, 63.40, 44.79, 40.67, 19.73, 16.43, 10.26. HRMS (m/z) calcd for $C_{21}H_{24}Cl_2N_4O_3S_2$ $(M+H)^+$: 515.0667, found: 515.0739.

Data for (8m). Colorless crystal; yield,76.6%; m.p.: 118-120°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.37(s,1H, Ph-H), 7.35-7.30(m, 2H, Ph-H),7.13-7.08(m, 1H, Ph-H),7.02(s, 1H, O=C-NH), 5.84(tt, *J*=55.9, 4.0Hz, 1H, CHF_2),5.18(s, 2H, NH_2), 4.88(s, 2H, Ph-CH_2), 3.92(s, 3H, O-CH_3), 3.73-3.60(m, 2H, N-CH_2). ^{13}C NMR (400MHz, $CDCl_3$) δ163.27, 152.17, 150.55, 148.54, 144.55, 135.26, 129.67, 129.52, 129.34, 128.63, 128.16, 118.45, 113.58(t, *J*=241.6Hz), 75.05, 63.64, 41.80(t, *J*=26.6Hz). Anal. calcd for $C_{16}H_{15}Cl_2F_2N_5O_3S$: C,41.21; H, 3.24; N, 15.02. Found: C, 41.23; H, 3.42; N, 15.00.

Data for (8n). White solid; yield, 71.4%; m.p.: 106-108°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.36(t, *J*=3.6Hz, 1H, Ph-H), 7.35–7.31(m, 2H, Ph-H), 7.10(dd, *J*=5.8, 3.0Hz, 1H, Ph-H), 6.92(s, 1H, O=C-NH), 5.21(s, 2H, NH_2), 4.88(s, 2H, Ph-CH_2), 4.08(dd, *J*=5.4, 2.5Hz, 2H, N-CH_3), 3.91(s, 3H, O-CH_3), 2.17(t, *J*=2.5Hz, 1H, C≡CH). ^{13}C NMR (400MHz, $CDCl_3$) δ162.40, 152.28, 150.82, 148.49, 144.57, 135.21, 129.96, 129.42, 129.35, 128.59, 128.18, 118.39, 79.19, 75.13, 71.86, 63.54, 29.26. HRMS (ESI) calcd for$C_{17}H_{15}Cl_2N_5O_3S$ $(M+H)^+$: 440.0273, found: 440.0349.

Data for (8o). White powder; yield, 48.7%; m.p.: 126-128°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.38–7.35(m, 1H, Ph-H), 7.34–7.30(m, 2H, Ph-H), 7.11-7.08(m, 1H, Ph-H), 6.80(s, 1H, O=C-NH), 5.27(s, 2H, NH_2), 4.87(s, 2H, Ph-CH_2), 3.87(s, 3H, O-CH_3), 2.77-2.70(m, 1H, N-CH), 0.73(dd, *J*=7.0, 5.4Hz,2H, cyclopropyl-CH_2), 0.55-0.50(m, 2H, cyclopropyl-CH_2). ^{13}C NMR (400MHz, $CDCl_3$) δ163.98, 152.32, 151.26, 148.50, 144.71, 135.09, 130.24, 129.30, 129.28, 128.56, 128.10, 118.41, 75.04, 63.35, 22.72, 6.62. HRMS (m/z) calcd for $C_{17}H_{17}Cl_2N_5O_3S$ $(M+H)^+$:

442.0429, found: 442.0507.

Data for (8p). White powder; yield, 39.4%; m.p.: 122-124°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.37(d, *J*=5.7Hz, 1H, Ph-H), 7.32(dd, *J*=6.0, 3.1Hz, 2H, Ph-H), 7.12-7.08(m, 1H, Ph-H), 6.73(d, *J*=3.8Hz, 1H, O=C-NH), 5.25(s, 2H, NH_2), 4.88(s, 2H, Ph-CH_2), 3.88(s, 3H, O-CH_3), 2.84(d, *J*=5.0Hz, 3H, N-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ163.43, 152.26, 151.30, 148.53, 144.69, 135.00, 130.47, 129.40, 129.34, 128.42, 128.24, 118.39, 75.05, 63.40, 26.34. HRMS (m/z) calcd for $C_{15}H_{15}Cl_2N_5O_3S$ $(M+H)^+$: 446.0273, found: 446.0340.

Data for (8q). Yellow crystal; yield, 58.1%; m.p.: 28-30°C; ^{1}H NMR (400MHz, $CDCl_3$) δ7.44(dd, *J*=5.9, 3.3Hz, 1H, Ph-H), 7.40-7.36(m, 2H, Ph-H), 7.16(dd, *J*=5.6, 3.3Hz, 1H, Ph-H), 6.91(s, 1H, O=C-NH), 5.35(s, 2H, NH_2), 4.96(s, 2H, Ph-CH_2), 3.96(s, 3H, O-CH_3), 2.98(s, 2H, S-CH_2), 2.16(s, 3H, S-CH_3), 1.46(s, 6H, CH_3-C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ161.92, 152.32, 151.65, 148.48, 144.68, 135.28, 130.04, 129.27, 129.21, 128.61, 128.03, 118.33, 74.92, 63.39, 54.75, 45.10, 26.70, 17.72. HRMS (ESI) calcd for $C_{19}H_{23}Cl_2N_5O_3S_2$ $(M+H)^+$: 504.0619, found: 504.0698.

Data for (8r). Yellow oil; yield, 44.2%; ^{1}H NMR (400MHz, $CDCl_3$) δ7.44(dd, *J*=3.9, 1.9Hz, 1H, Ph-H), 7.41-7.38(m, 2H, Ph-H), 7.20-7.16(m, 1H, Ph-H), 6.91(d, *J*=8.2Hz, 1H, O=C-NH), 5.34(s, 2H, NH_2), 4.96(s, 2H, Ph-CH_2), 4.29-4.21(m, 1H, N-CH), 3.97(s, 3H, O-CH_3), 2.73(dd, *J*=13.5, 5.5Hz, 1H, S-CH_2), 2.64(dd, *J*=13.5, 6.4Hz, 1H, S-CH_2), 2.15(s, 3H, S-CH_3), 1.32(d, *J*=6.6Hz, 3H, N-C-CH_3). ^{13}C NMR (400MHz, $CDCl_3$) δ162.11, 152.28, 151.19, 148.52, 144.67, 135.12, 130.19, 129.34, 128.57, 128.15, 118.37, 75.01, 63.46, 44.86, 40.67, 19.76, 16.45. HRMS (m/z) calcd for $C_{18}H_{21}Cl_2N_5O_3S_2$ $(M+H)^+$: 490.0463, found: 490.0534.

Figure 1. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **6a**.

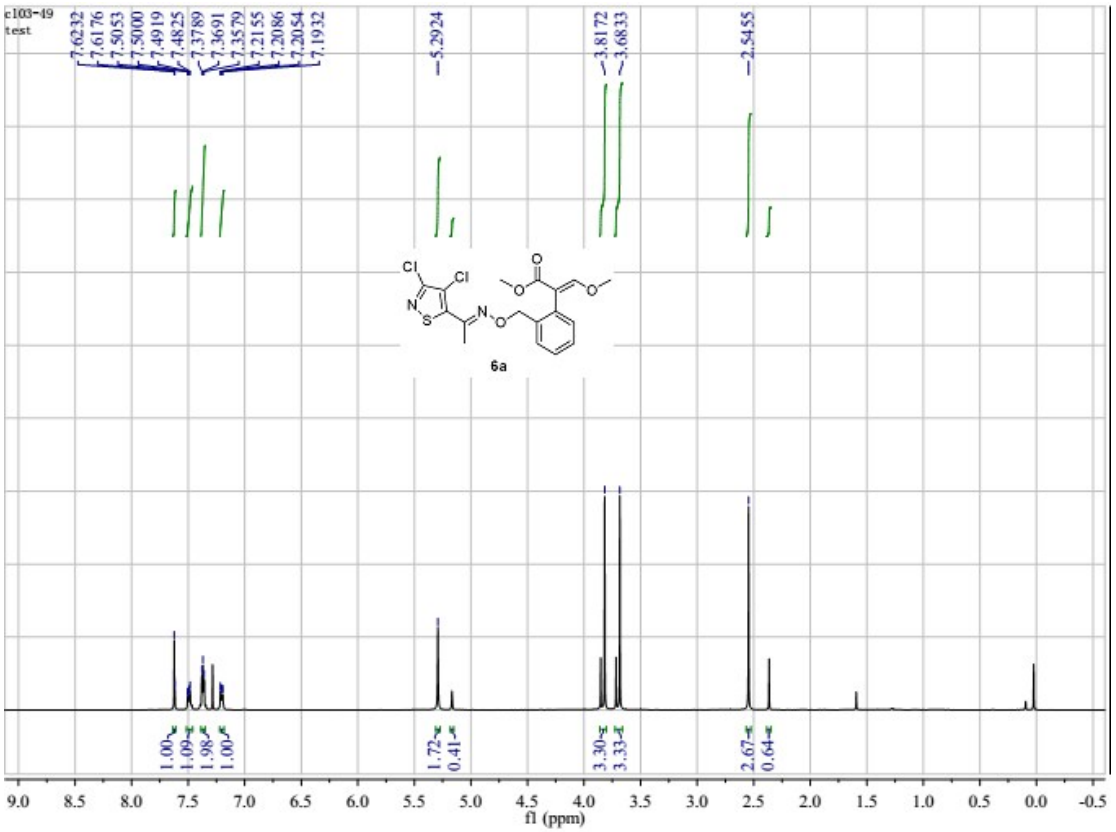

Figure 2. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **6a**.

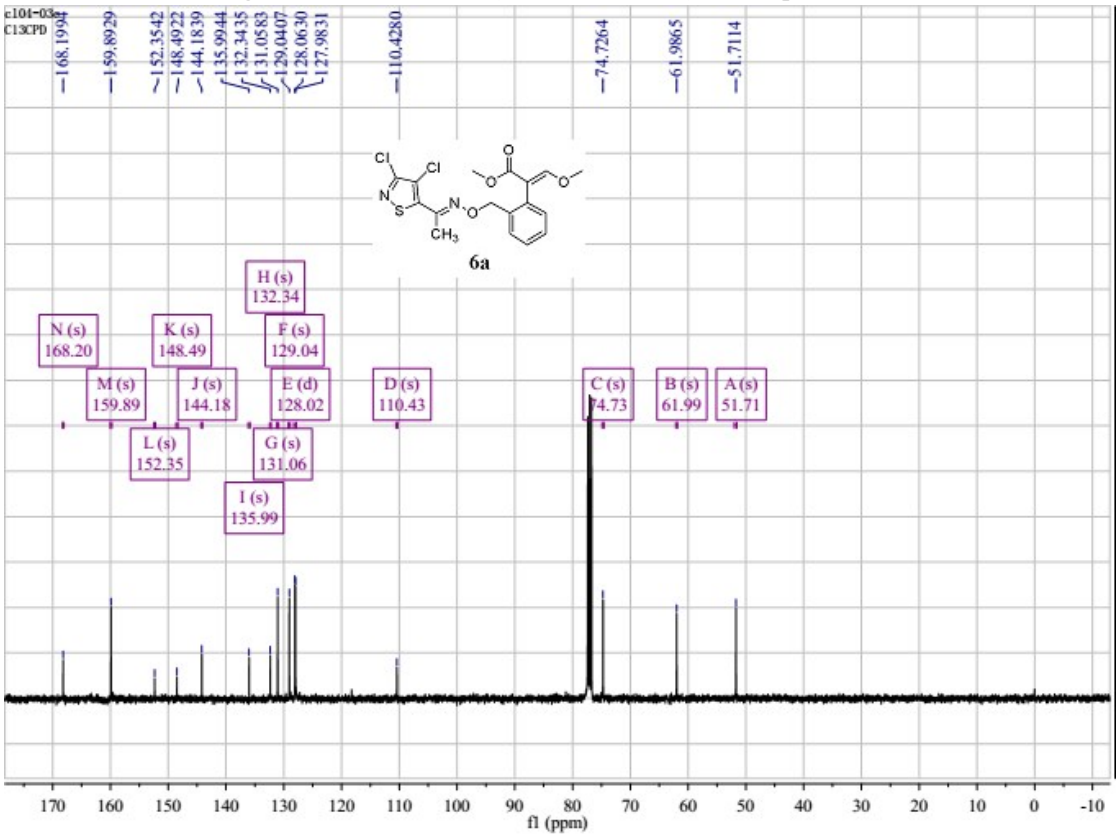

Figure 3. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **6b**

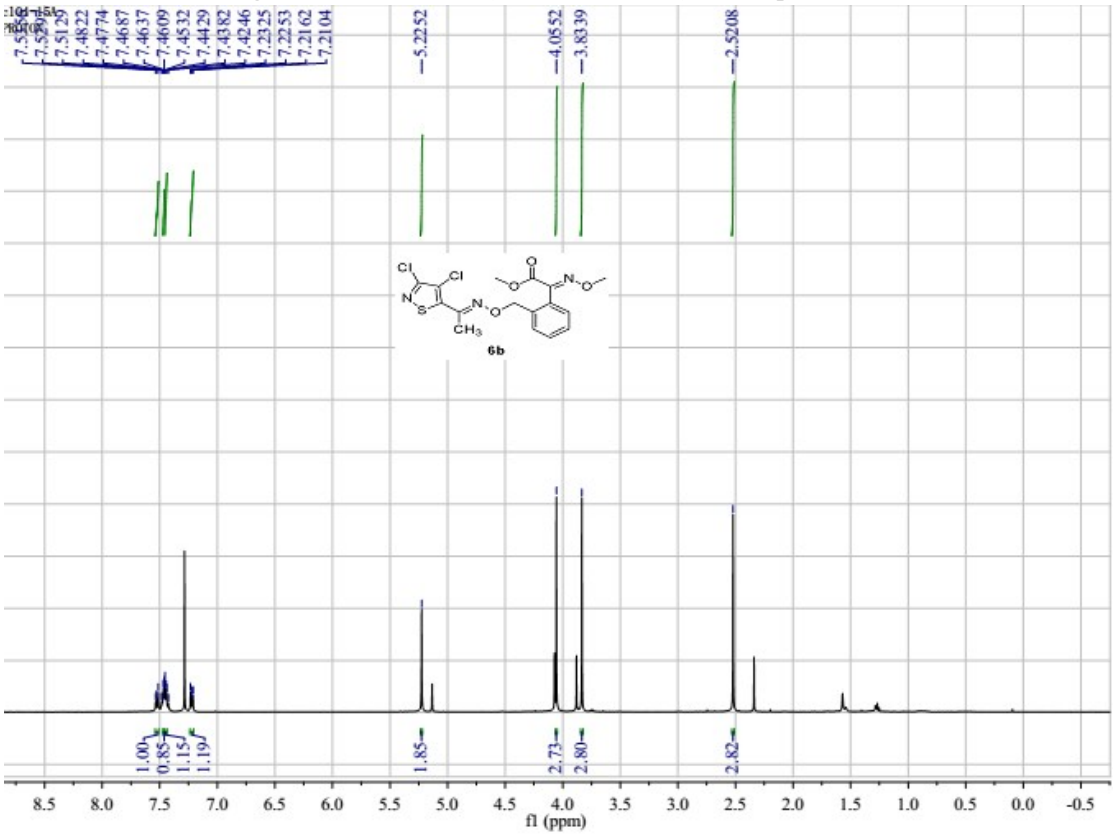

Figure 4. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **6b**

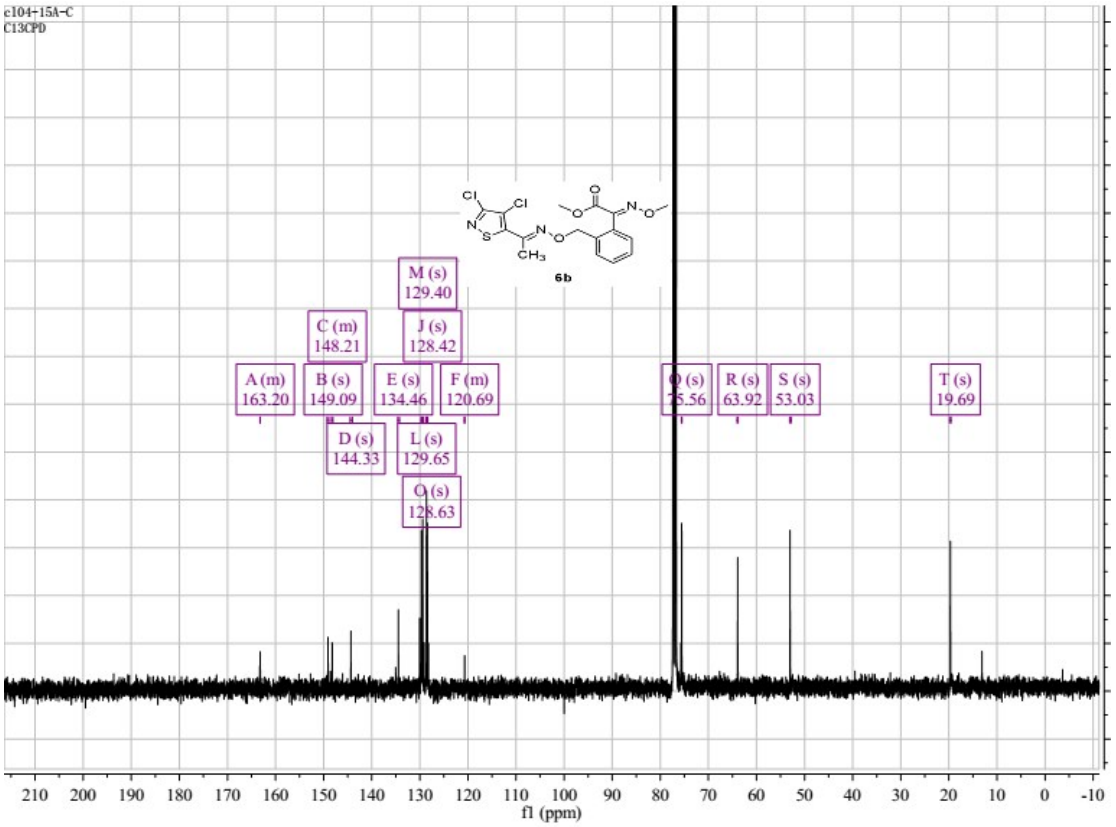

Figure 5. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **6c**

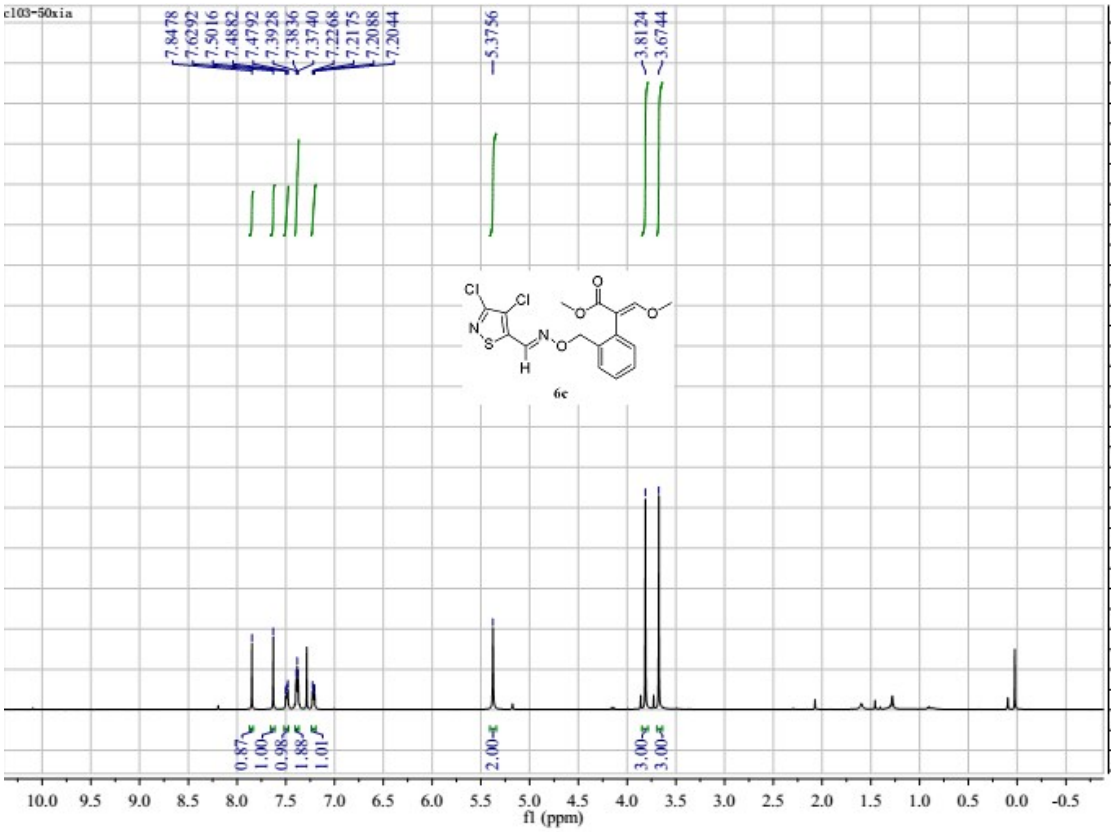

Figure 6. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **6c**

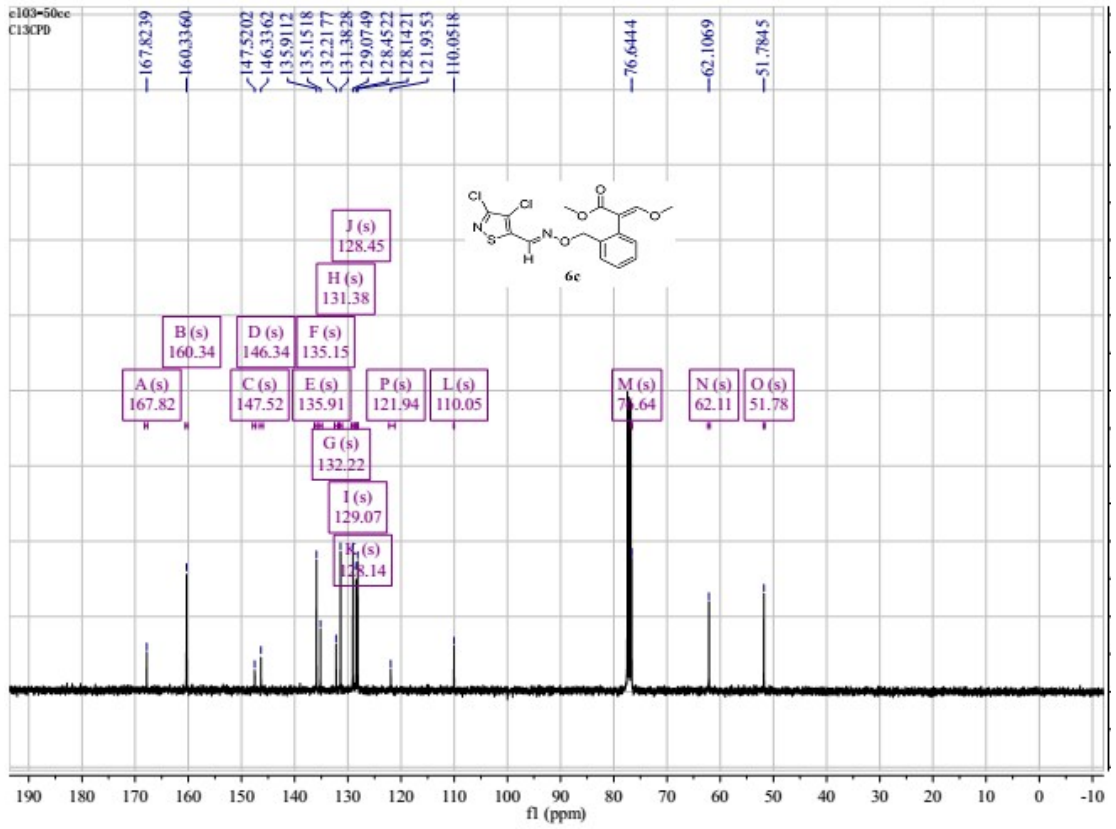

Figure 7. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **6d**

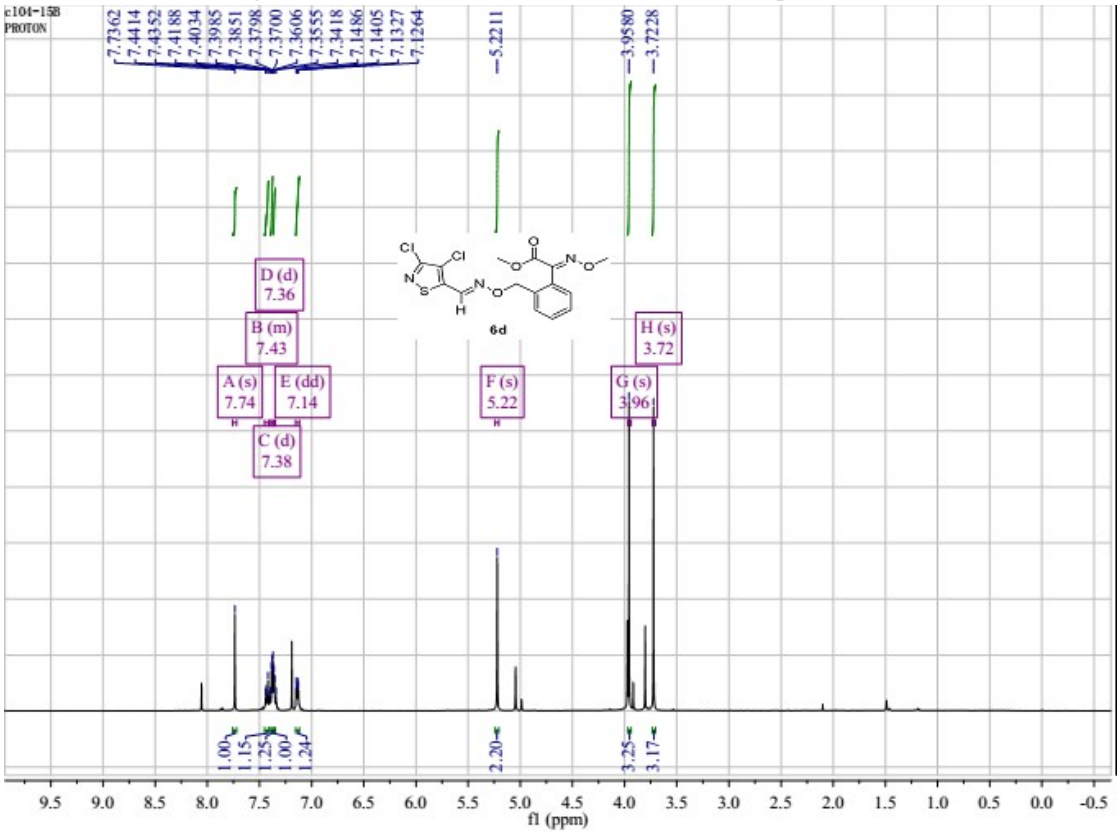

Figure 8. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **6d**

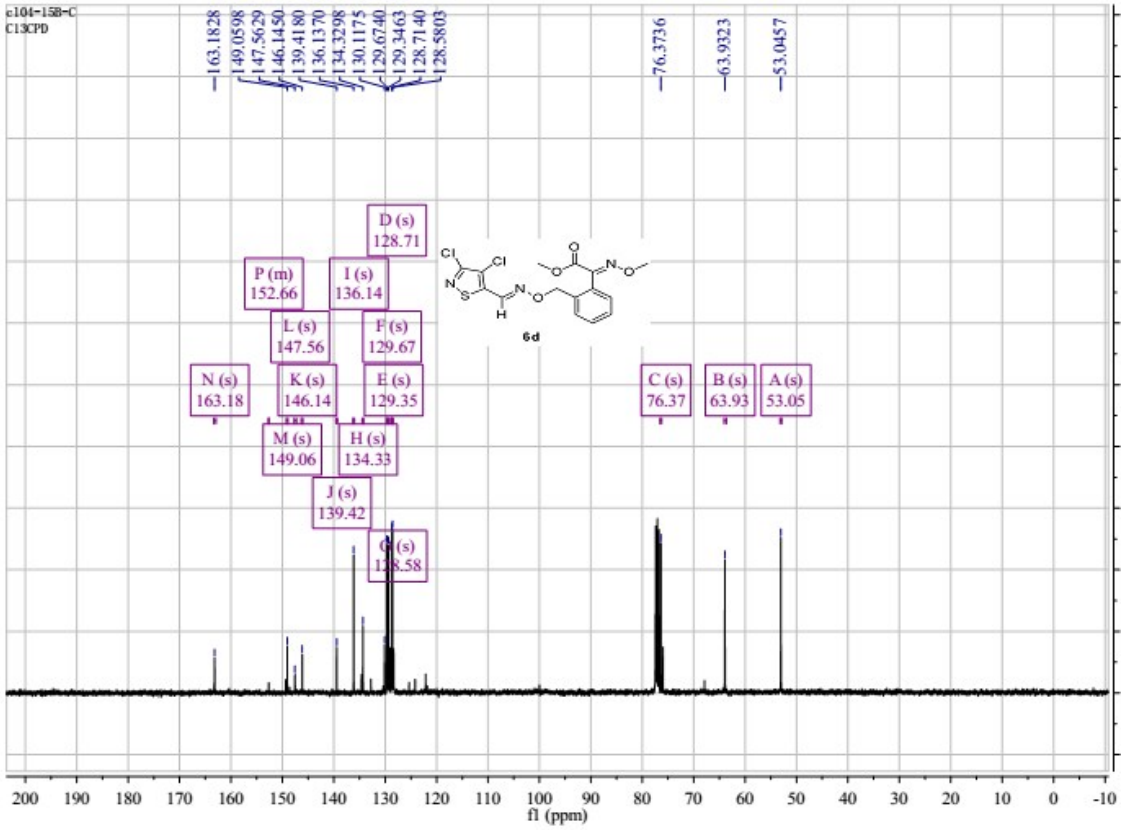

Figure 9. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **6e**

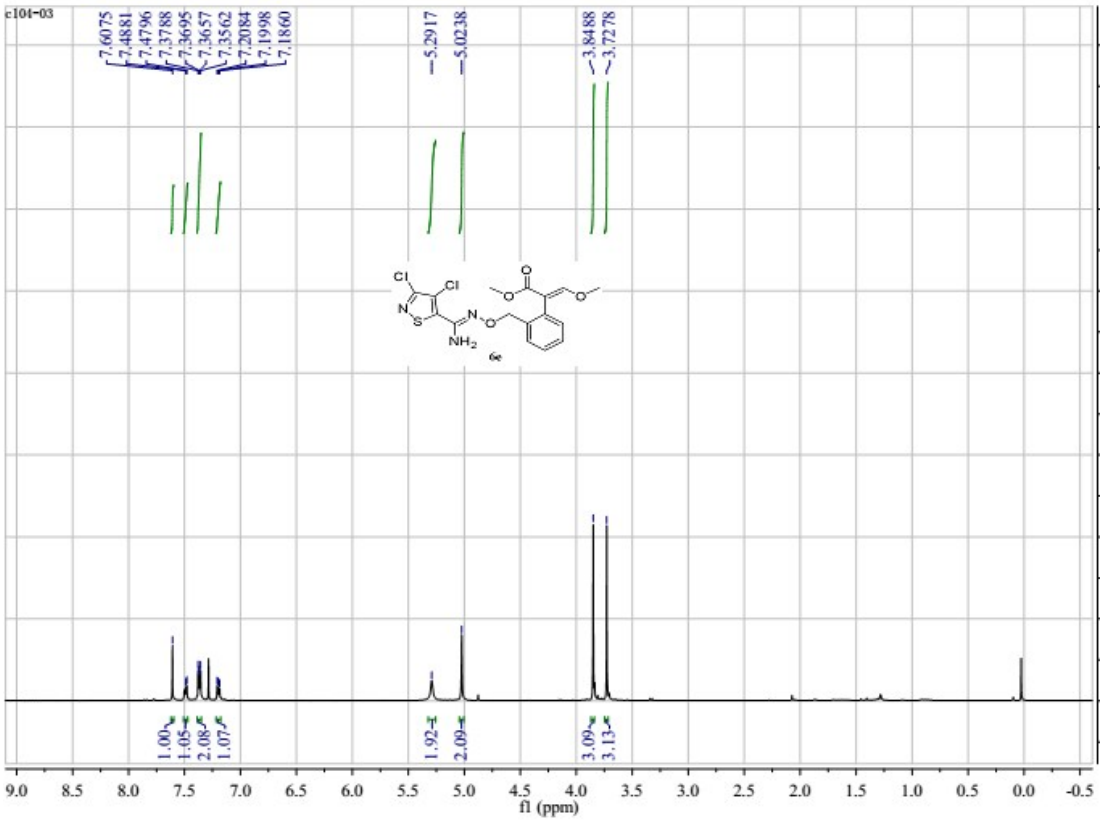

Figure 10. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **6e**

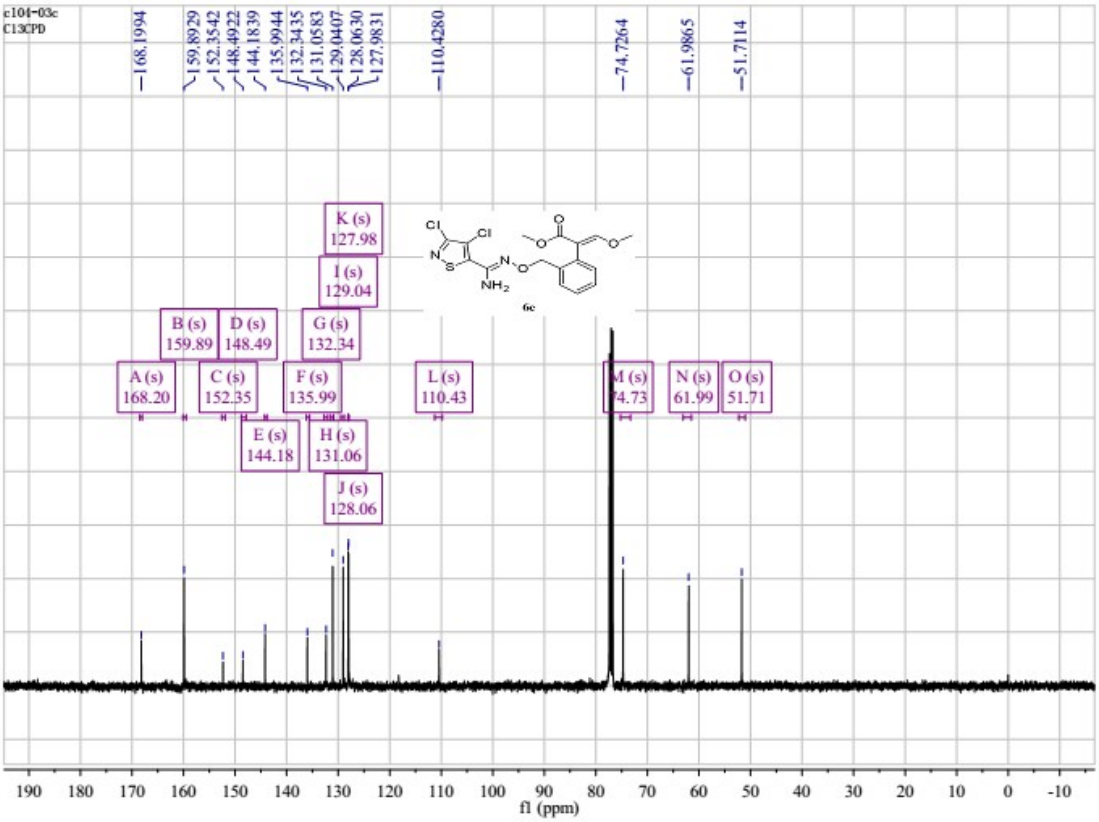

Figure 11. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **6f**

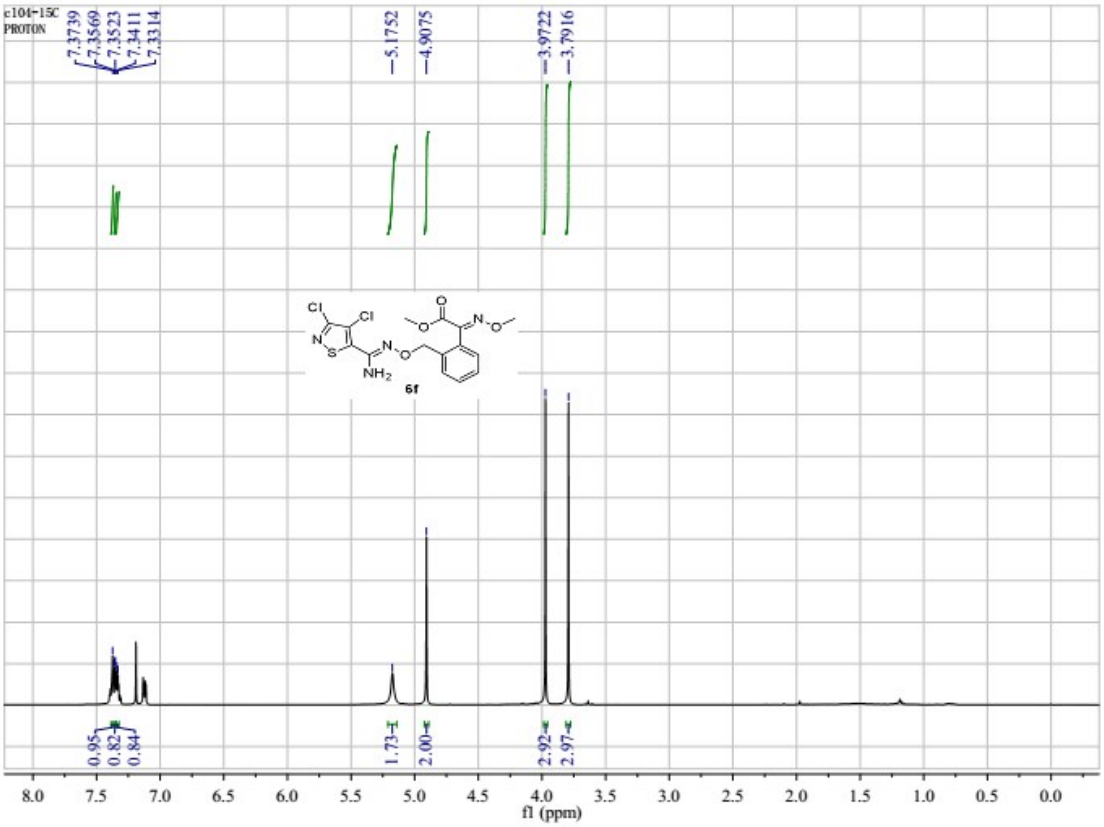

Figure 12. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **6f**

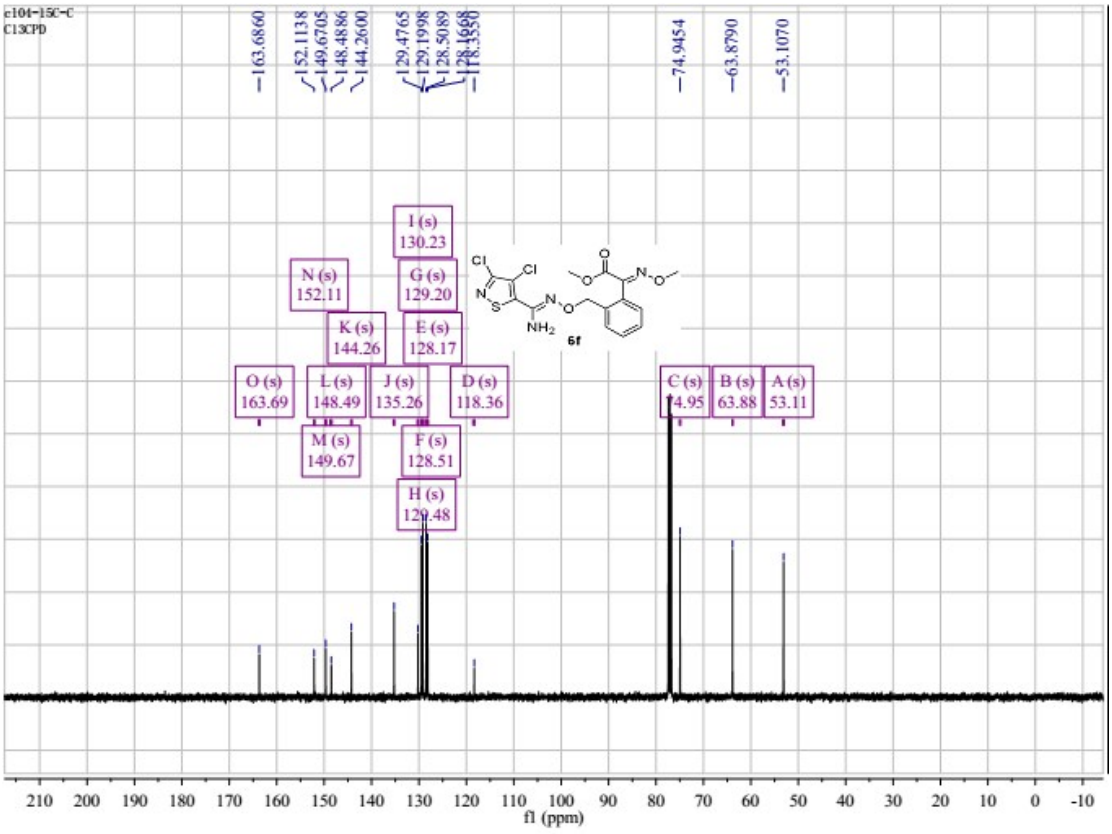

Figure 13. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **6g**

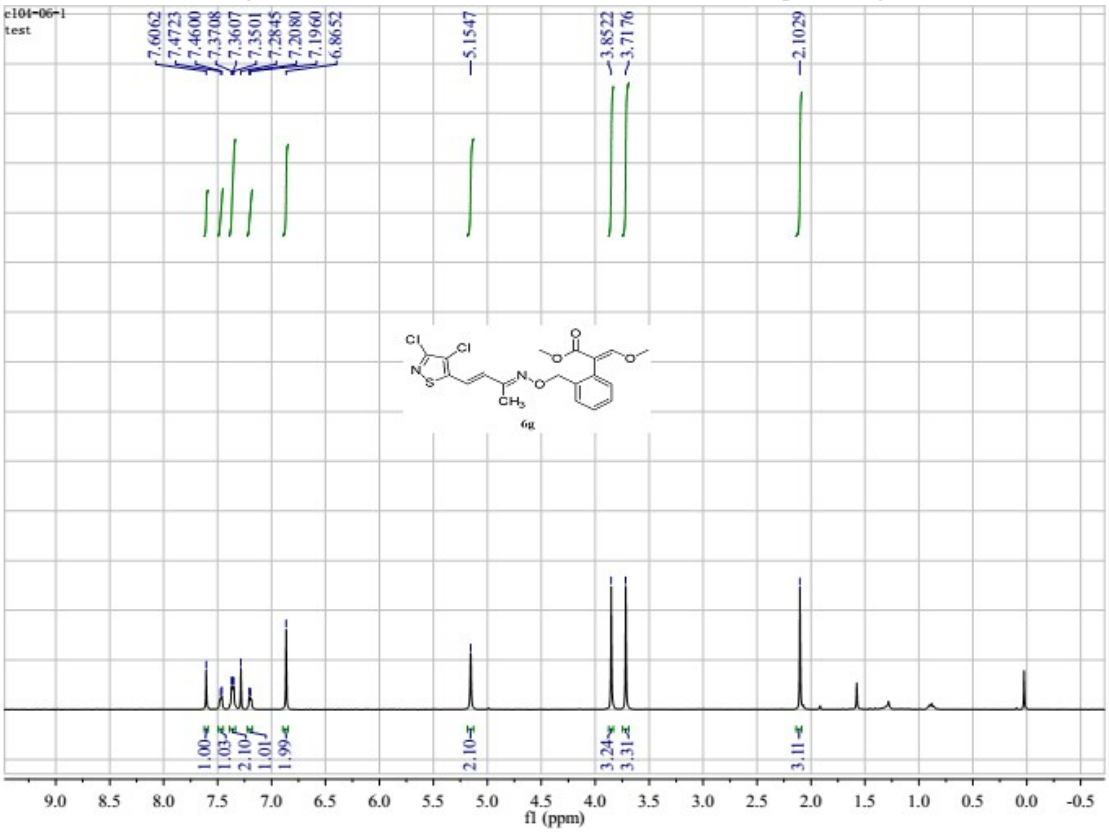

Figure 14. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **6g**

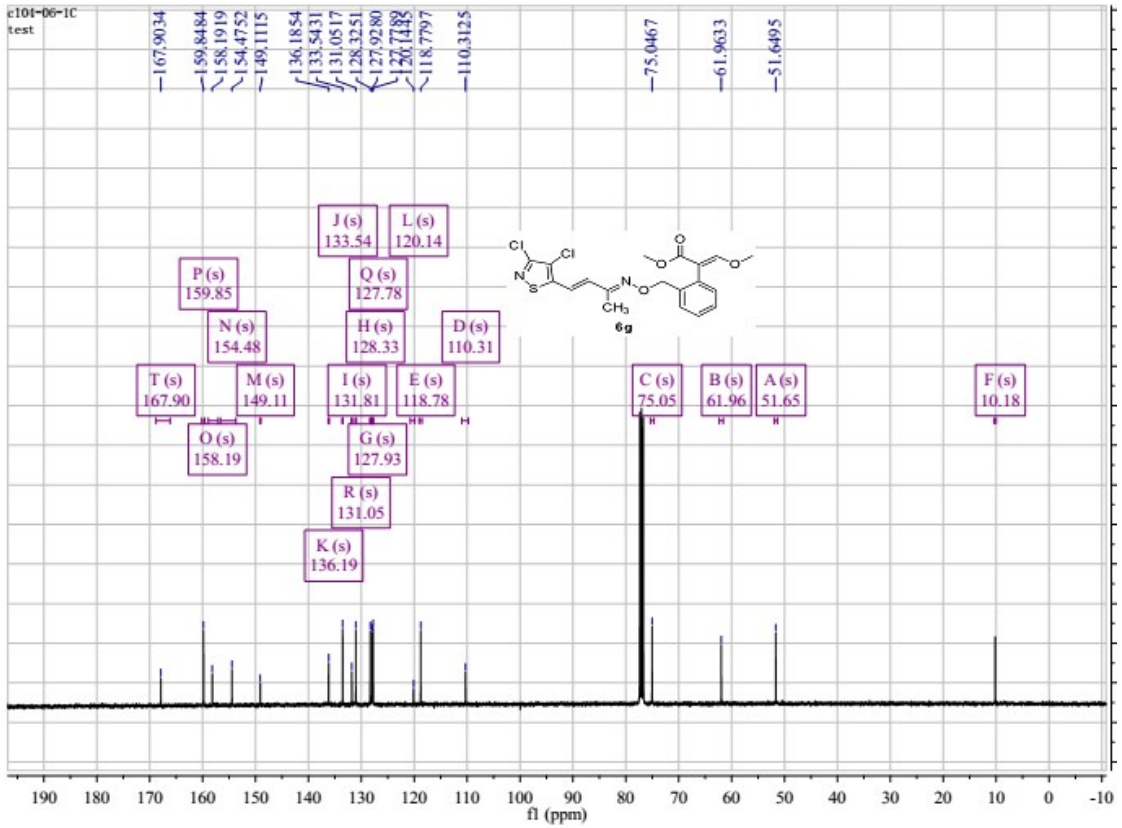

Figure 15. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **6h**

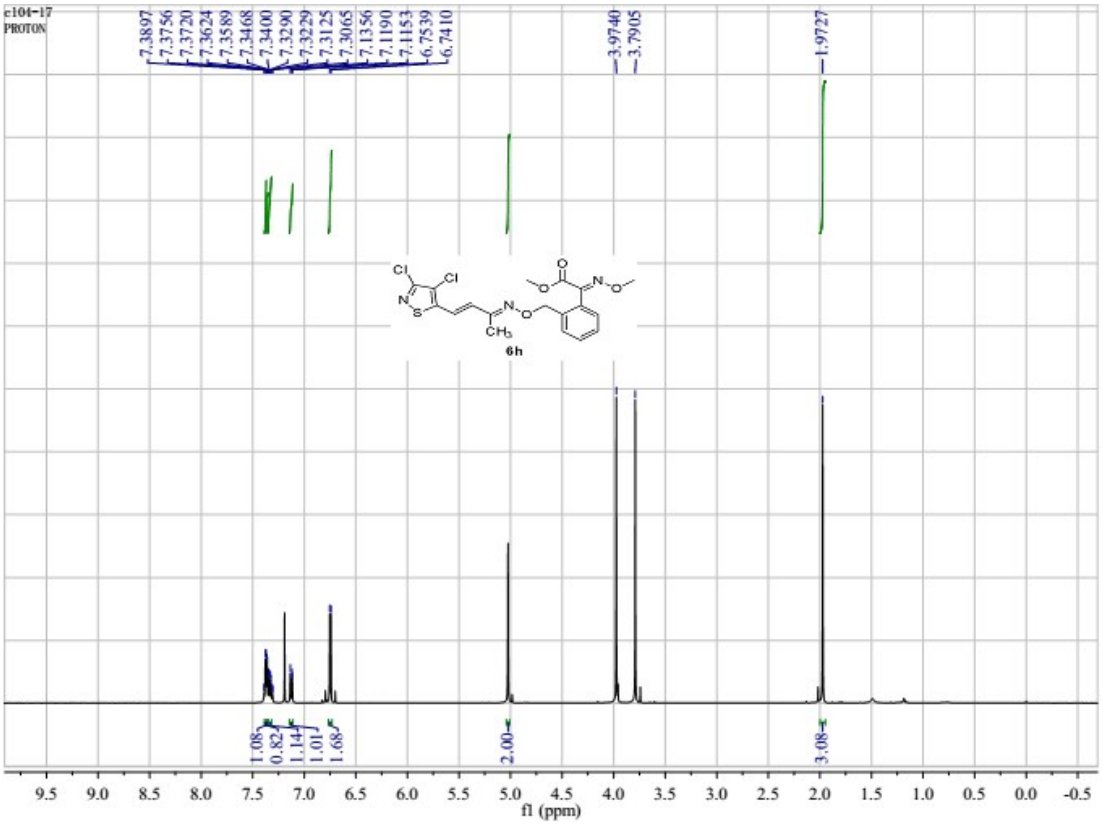

Figure 16. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **6h**

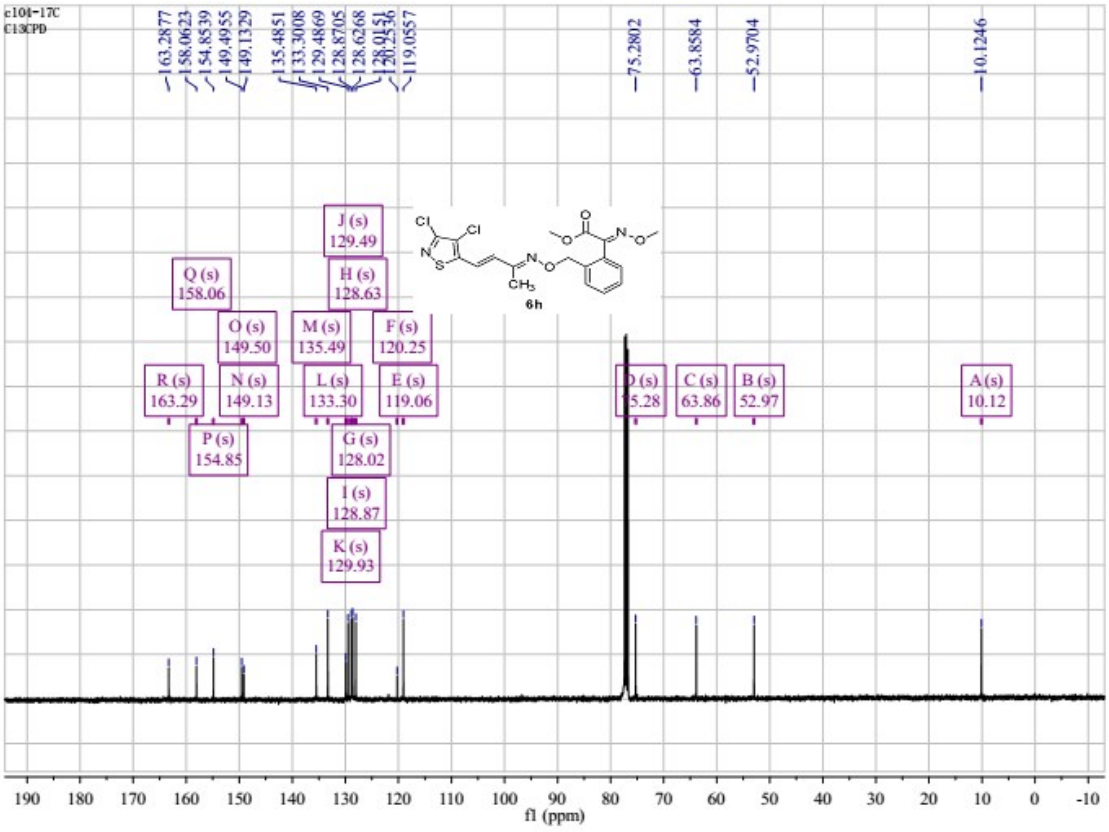

Figure 17. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8a**

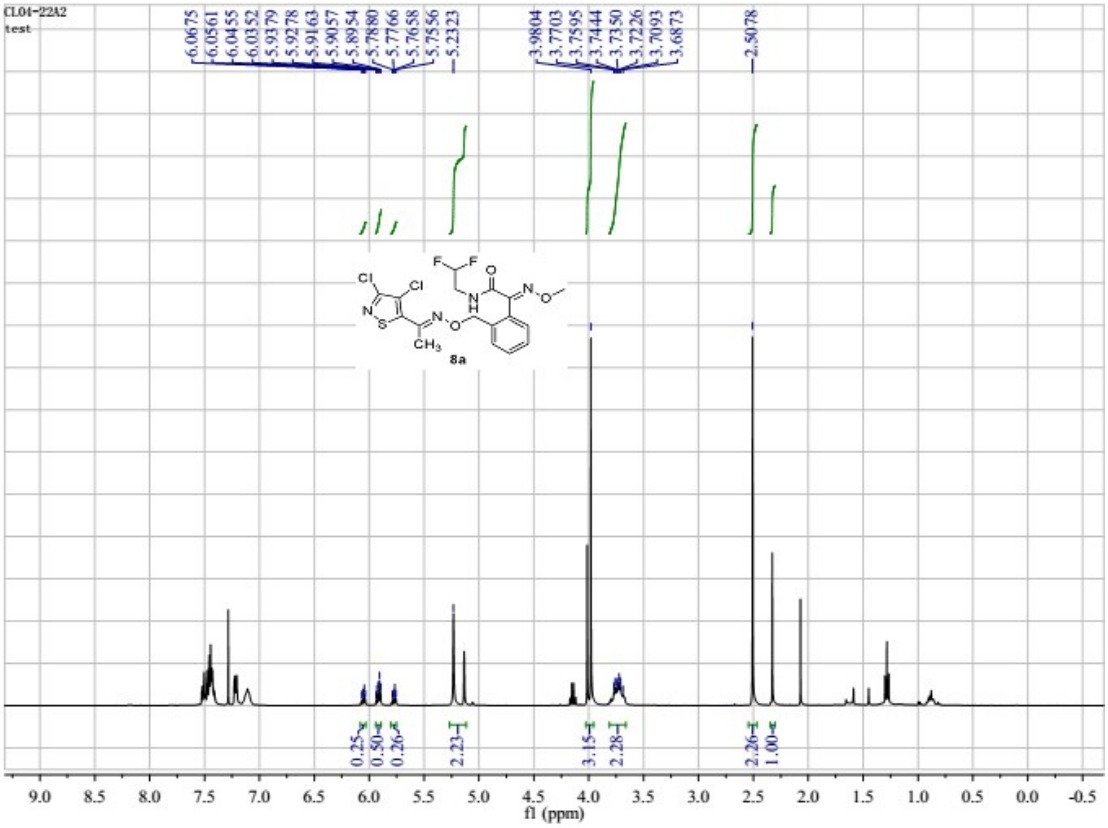

Figure 18. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8a**

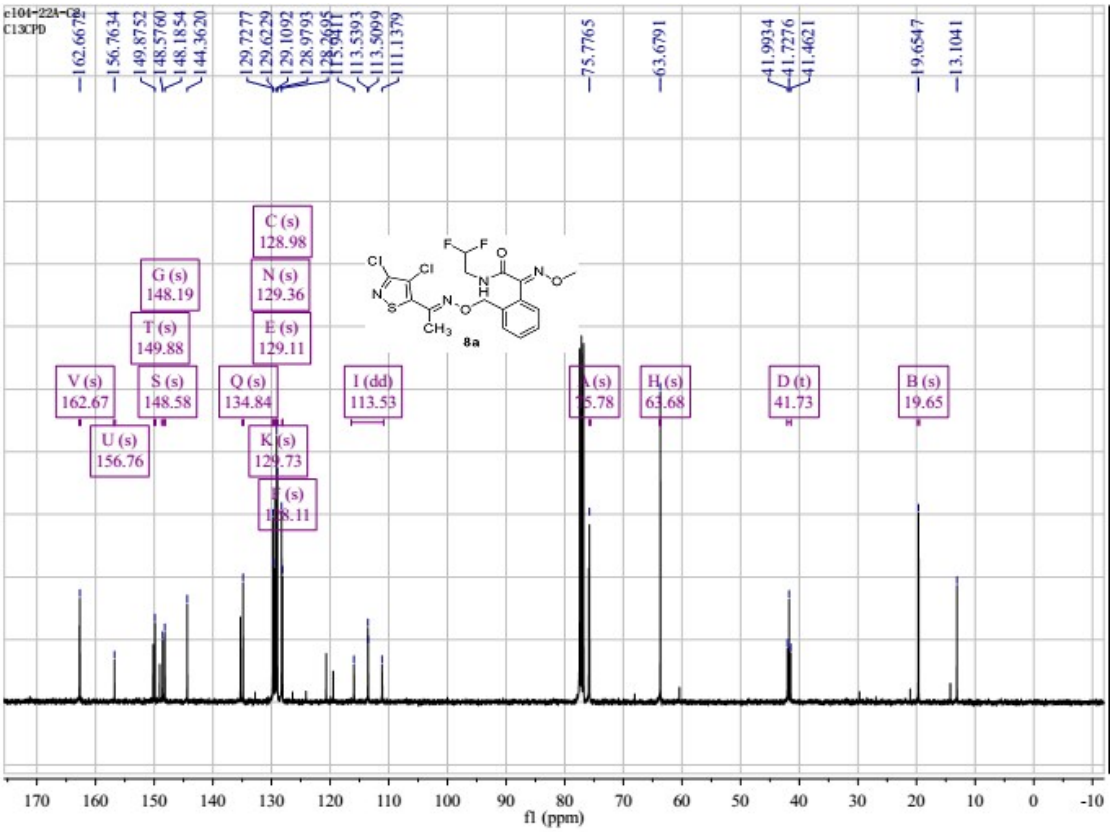

Figure 19. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8b**

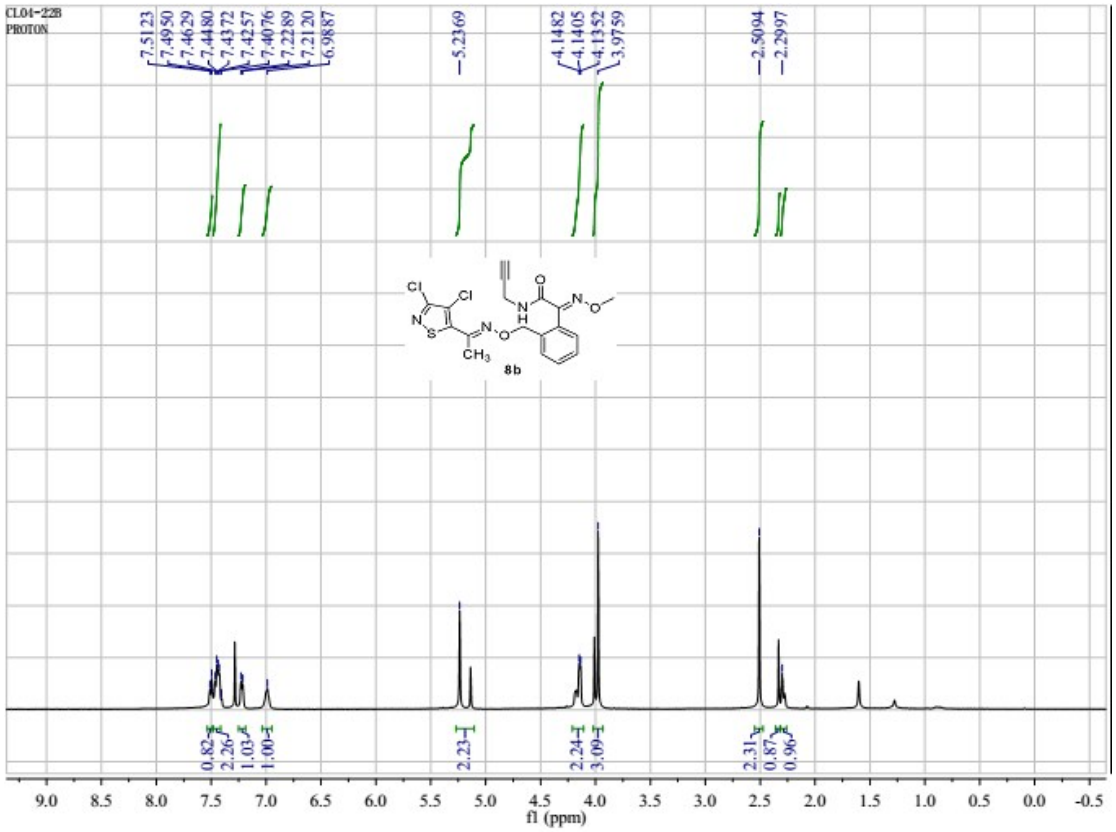

Figure 20. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8b**

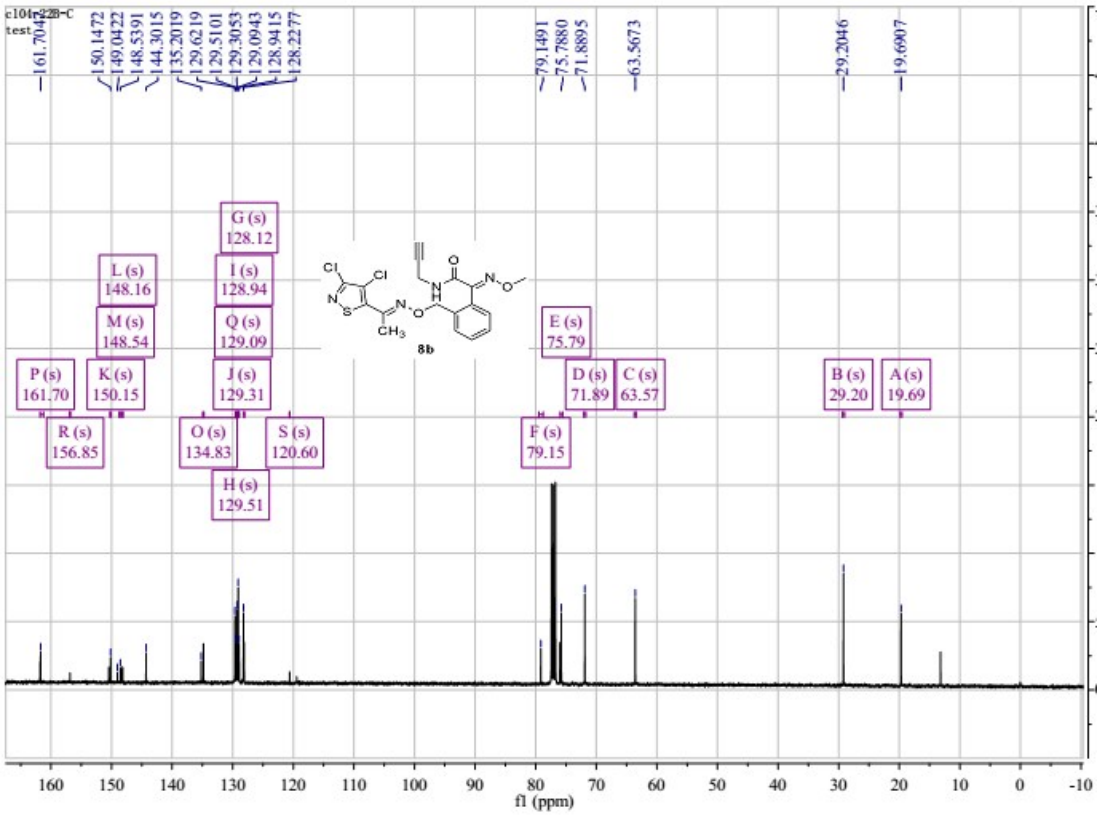

Figure 21. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8c**

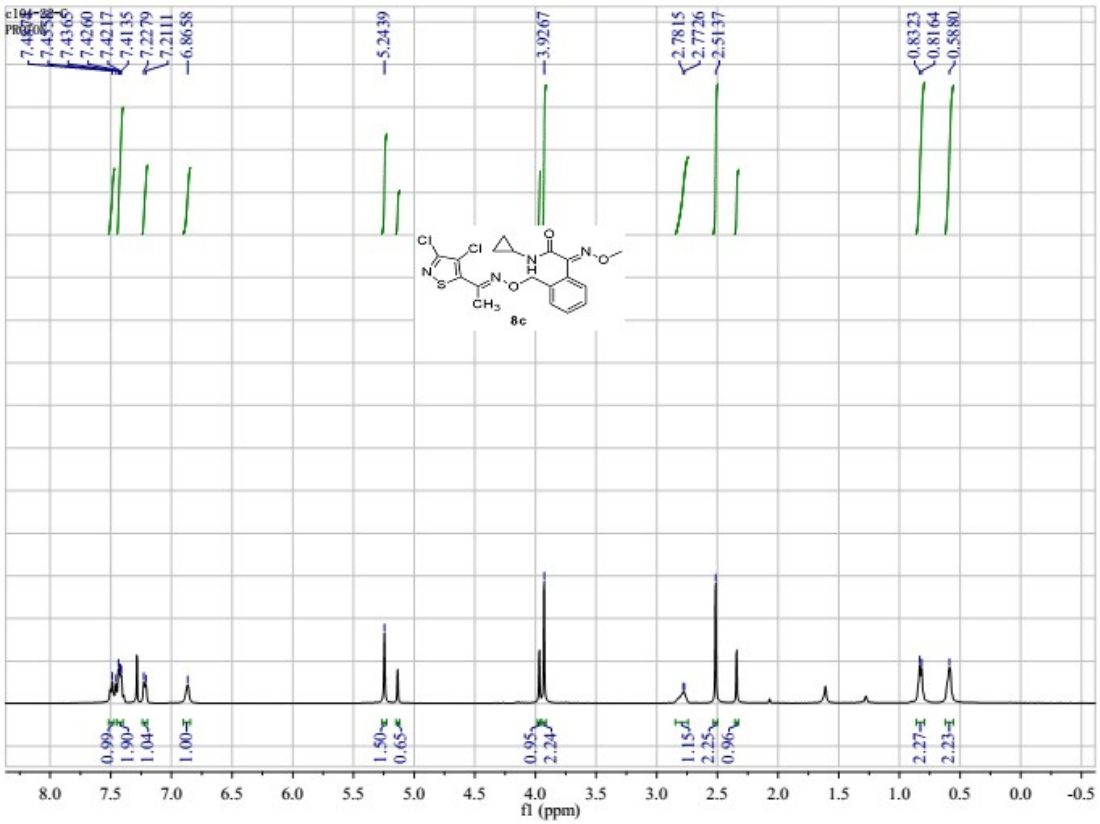

Figure 22. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8c**

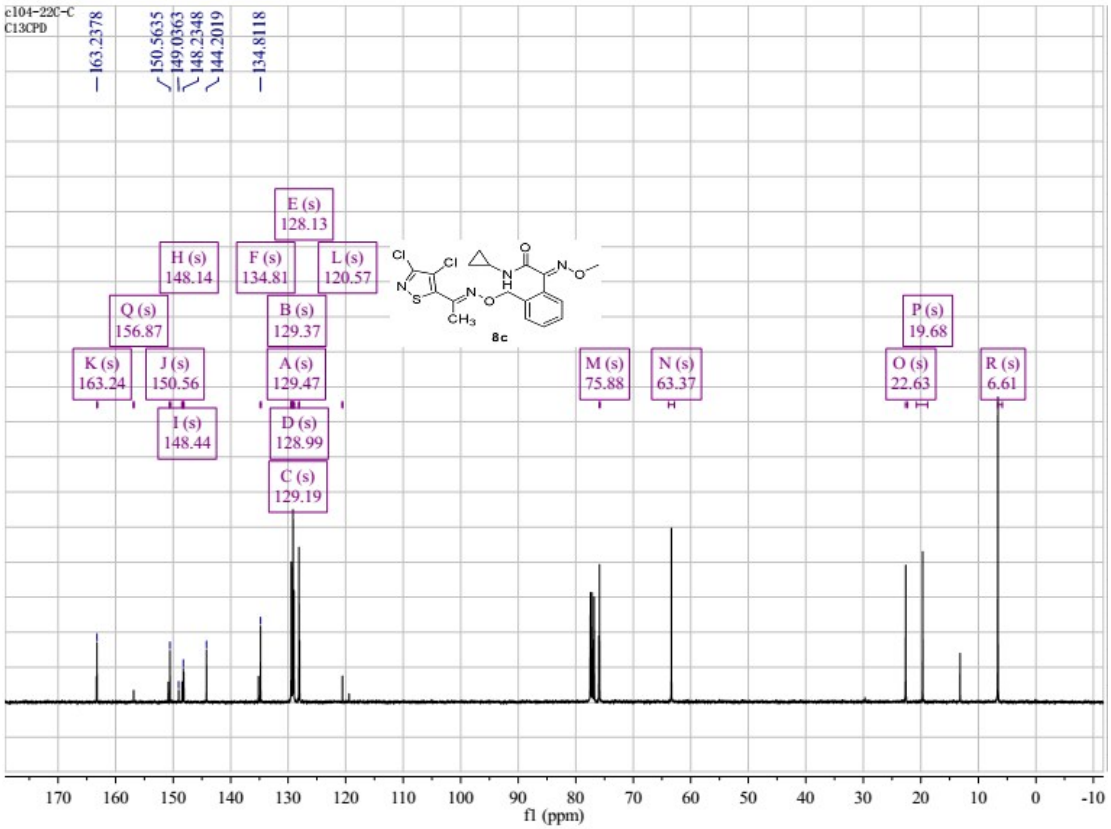

Figure 23. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8d**

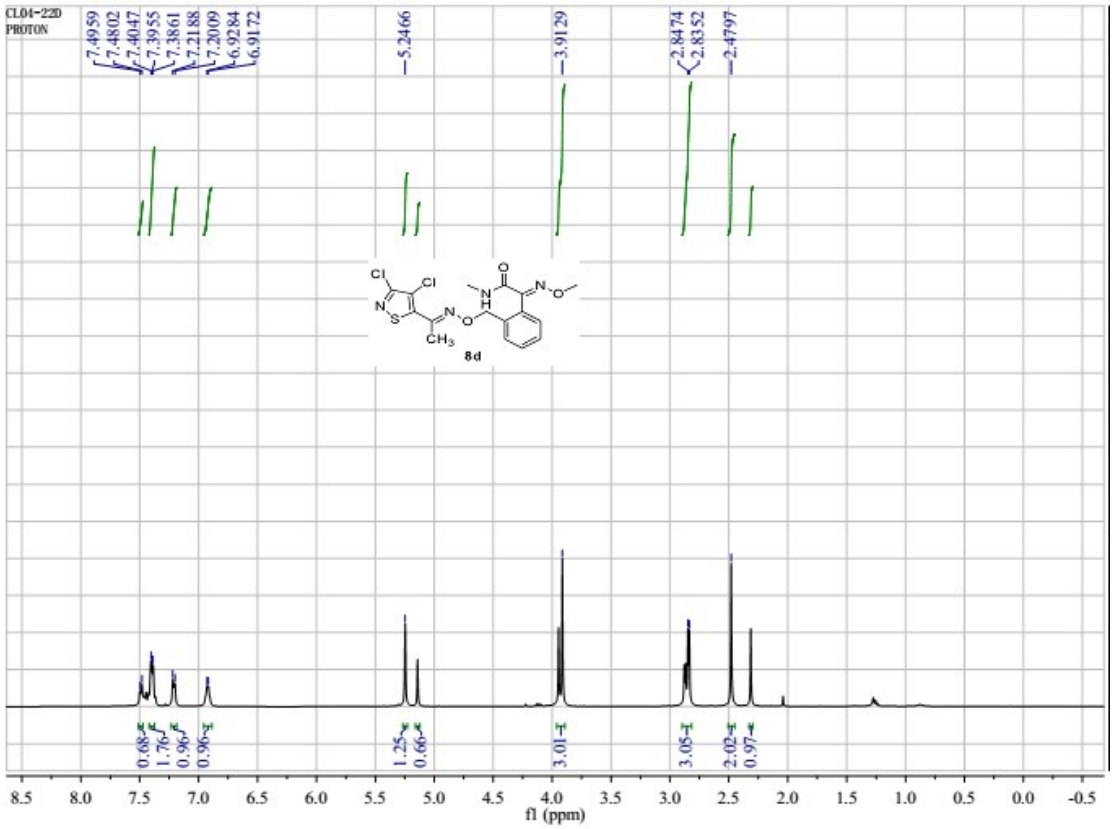

Figure 24. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8d**

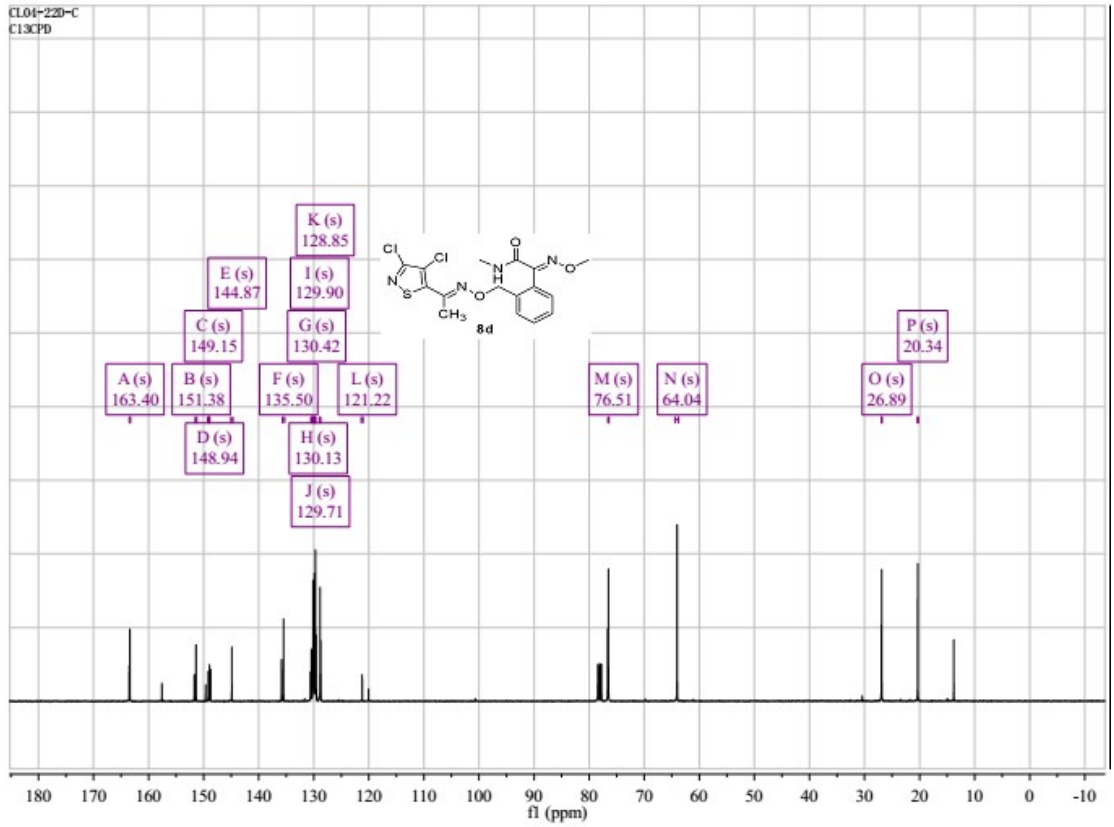

Figure 25. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8e**

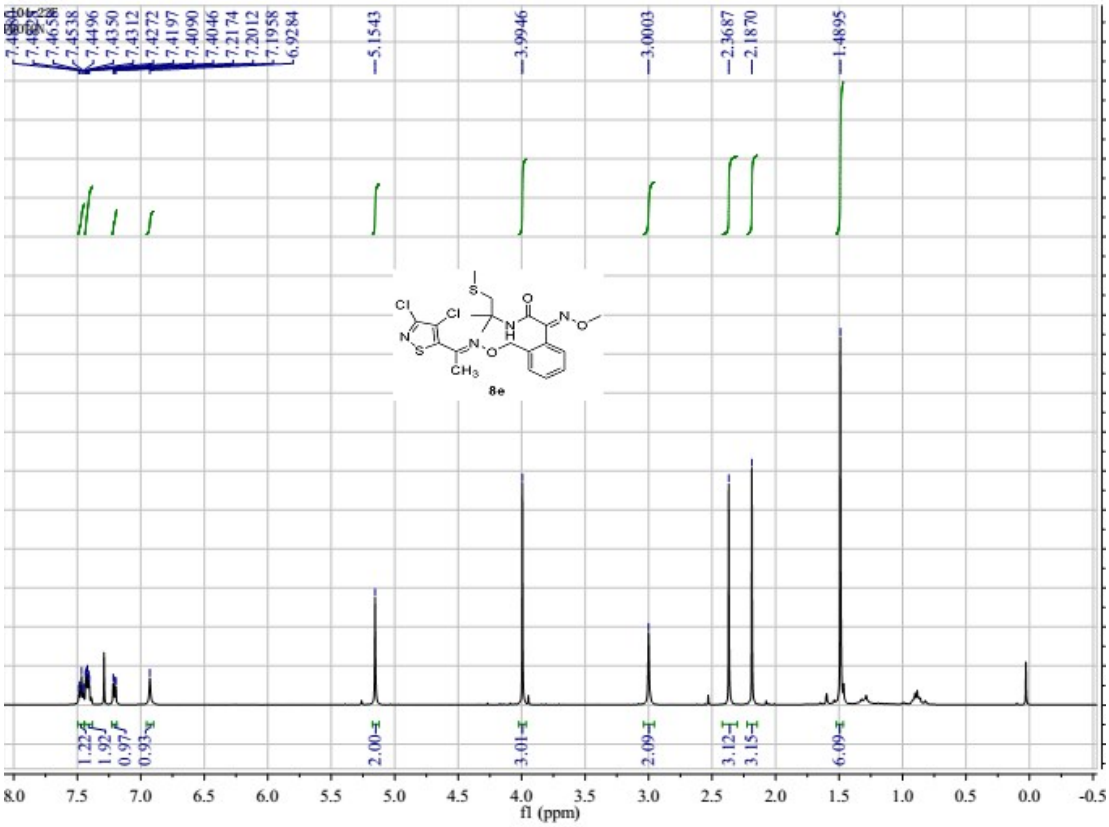

Figure 26 The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8e**

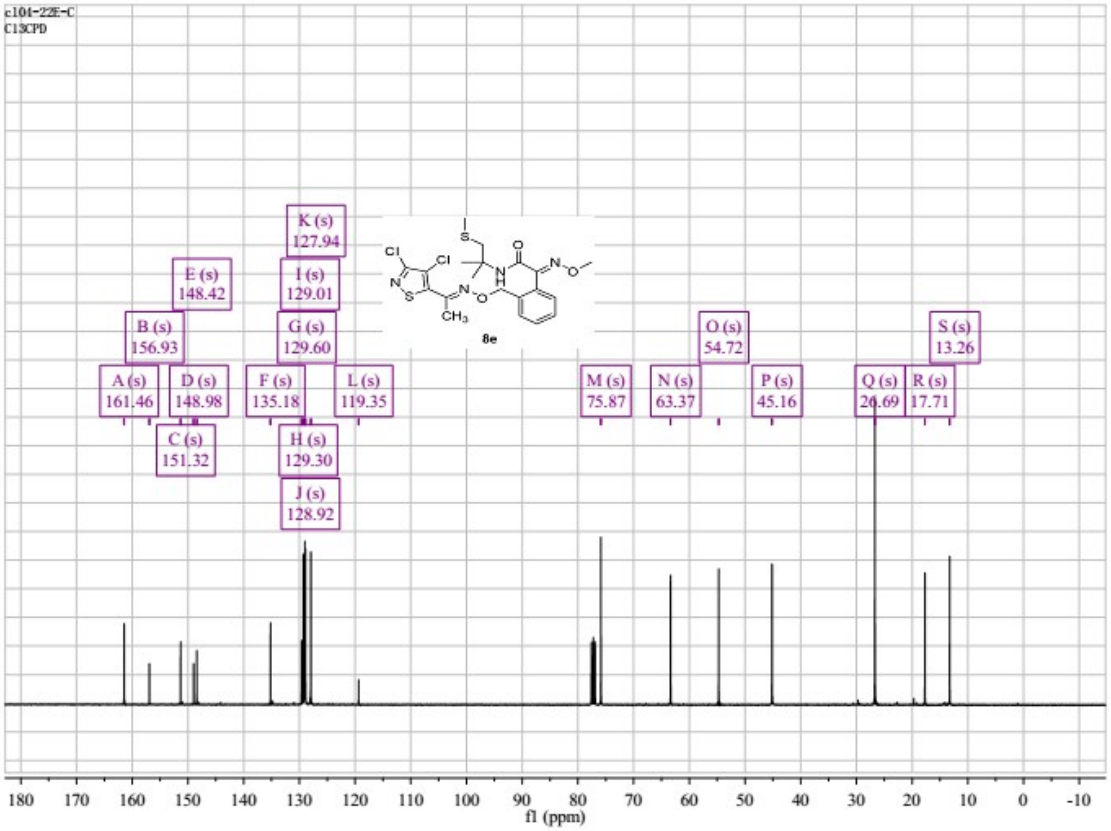

Figure 27. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8f**

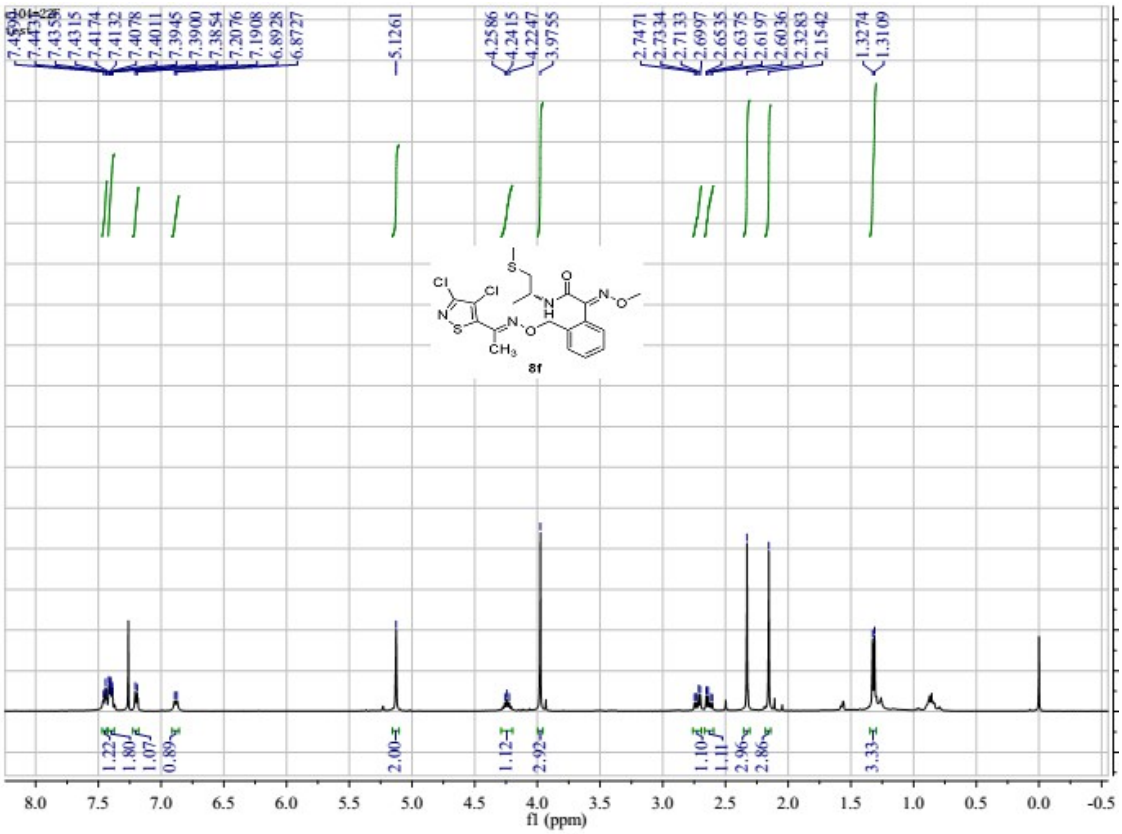

Figure 28. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8f**

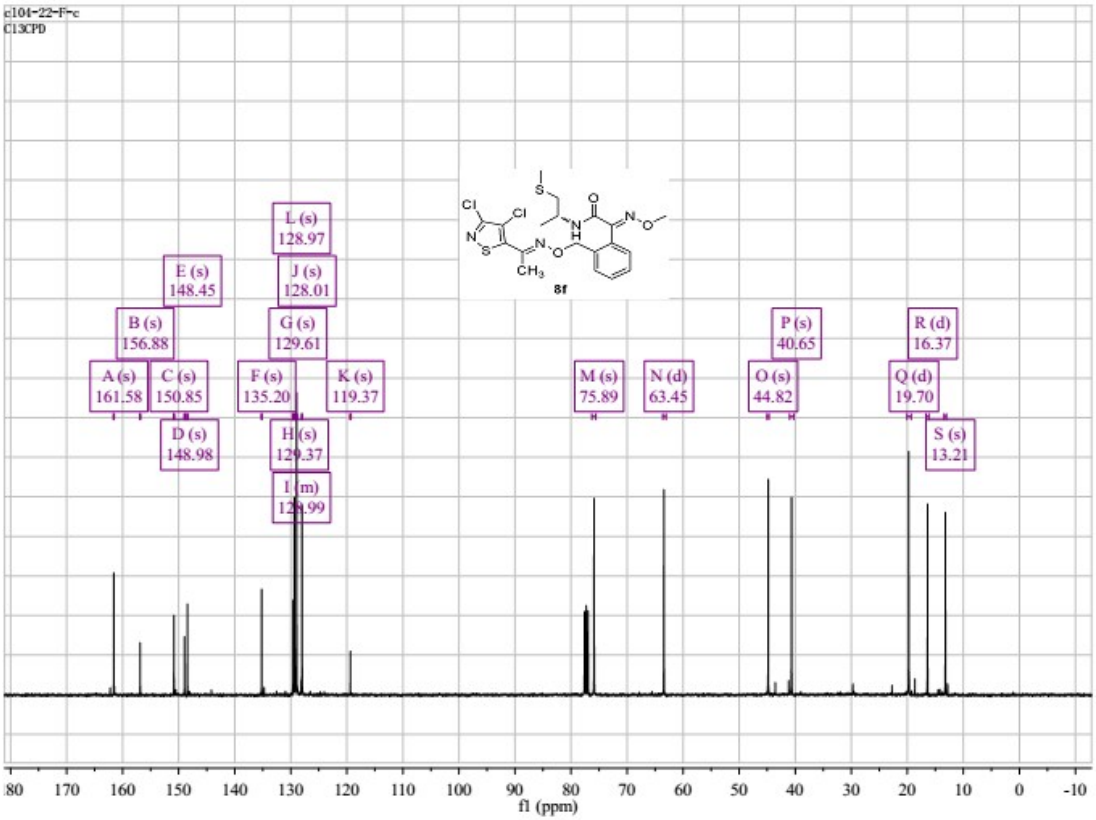

Figure 29. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8g**

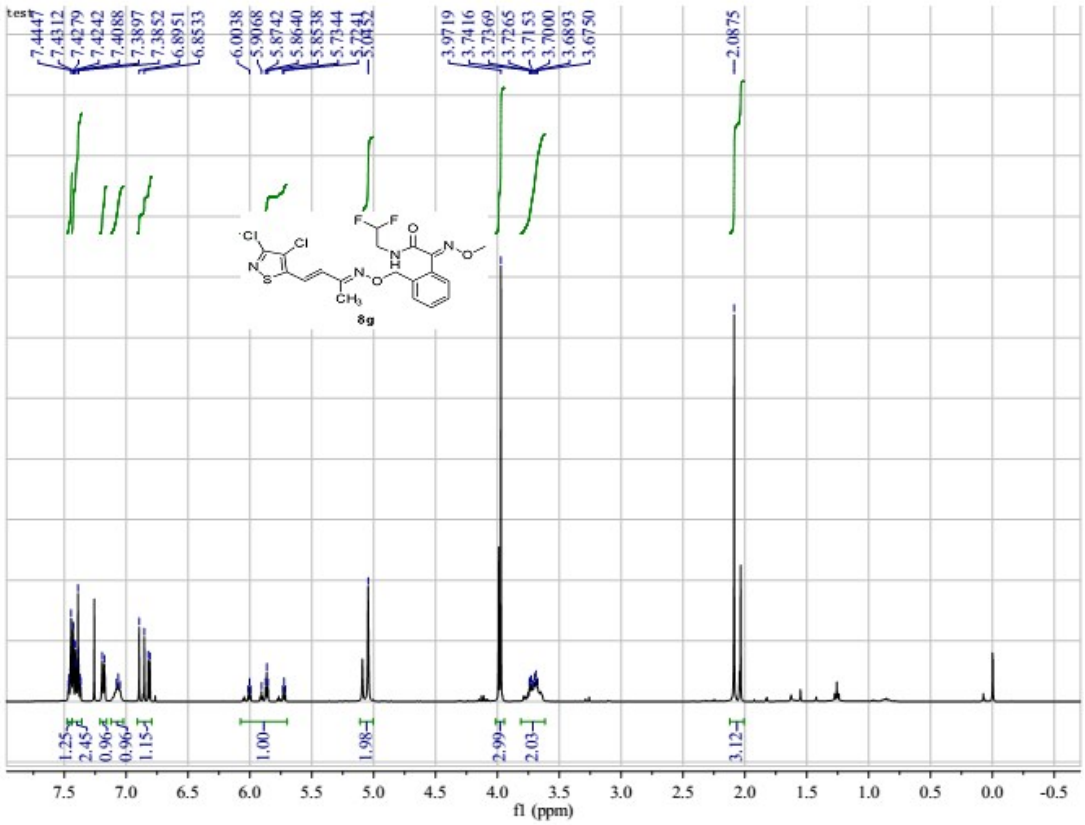

Figure 30. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8g**

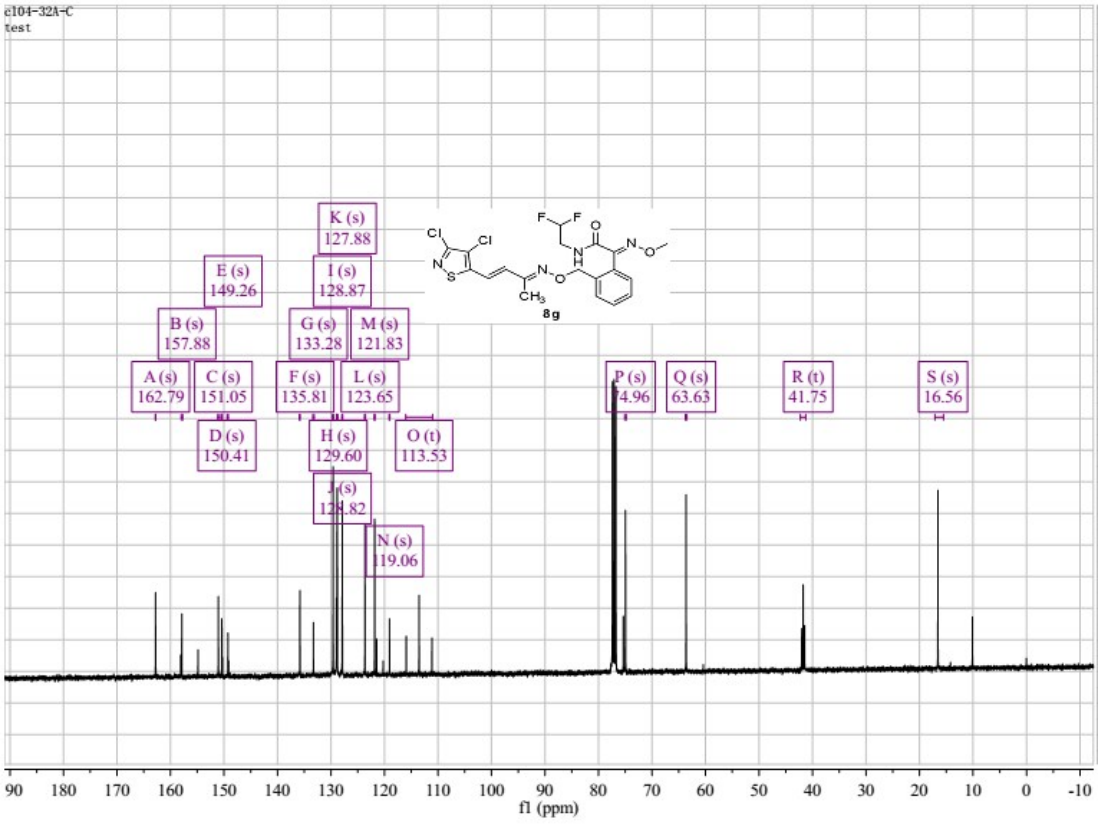

Figure 31. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8h**

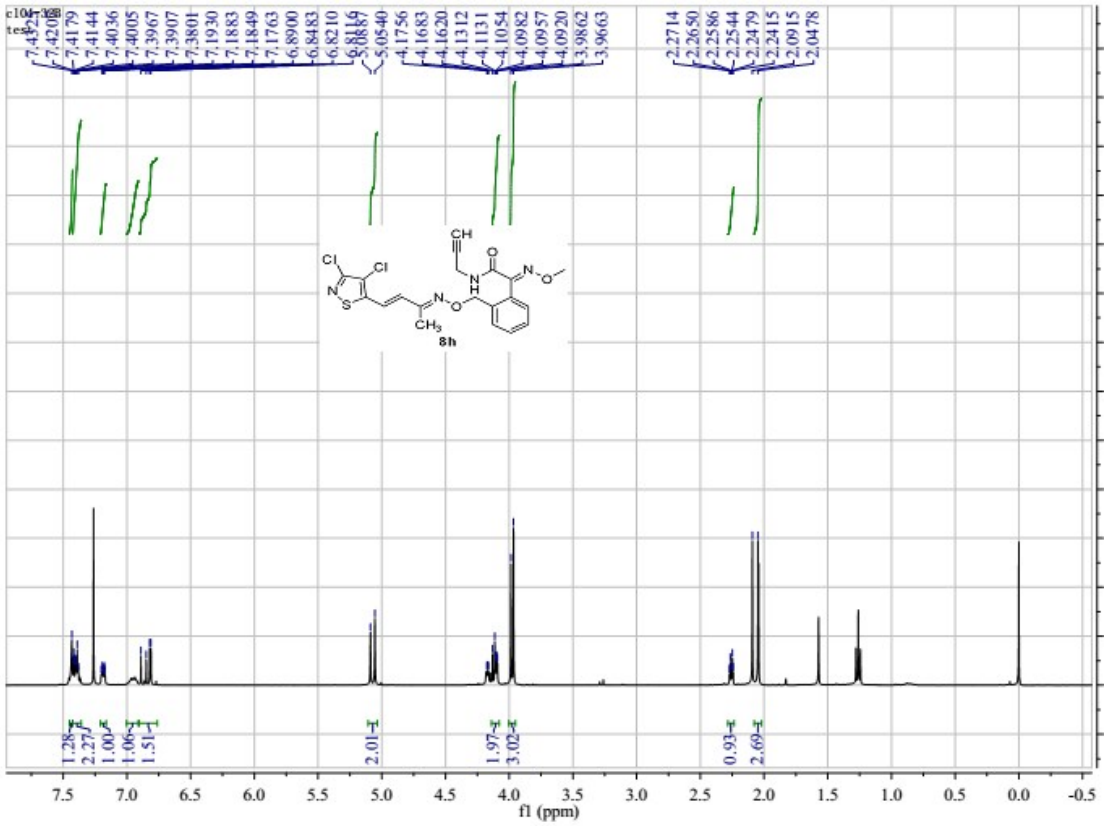

Figure 32. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8h**

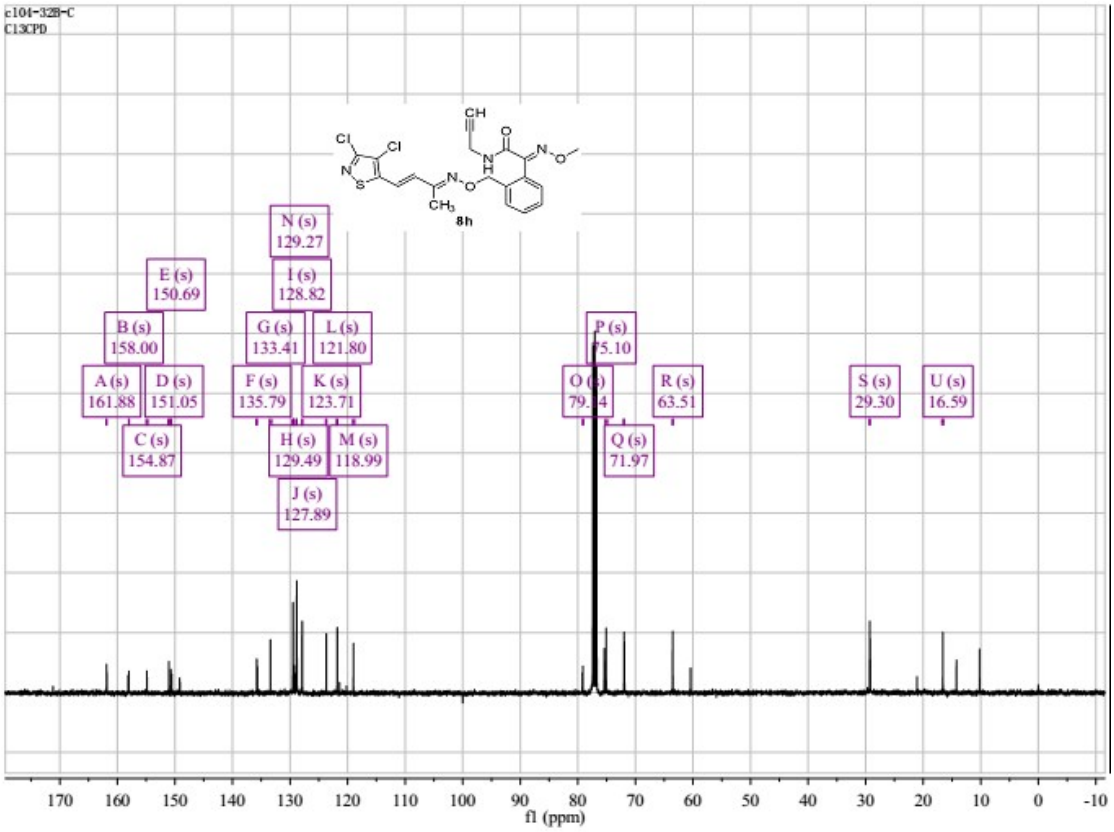

Figure 33. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8i**

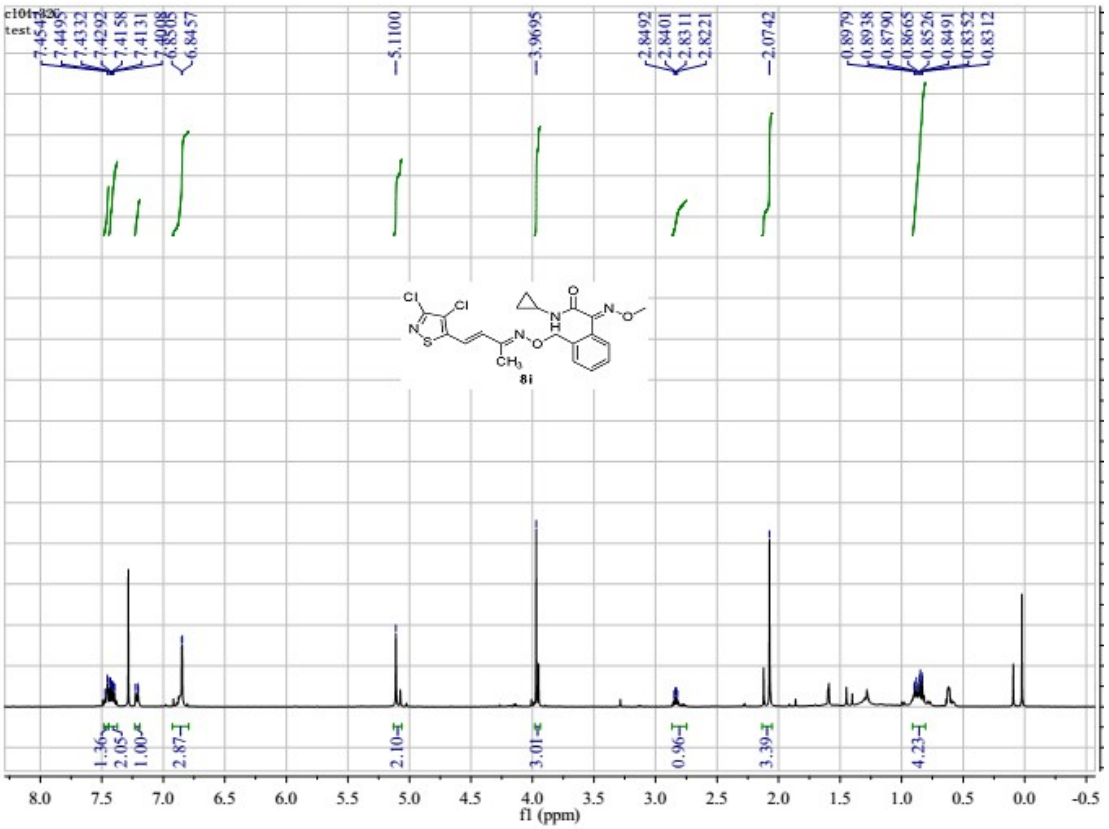

Figure 34. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8i**

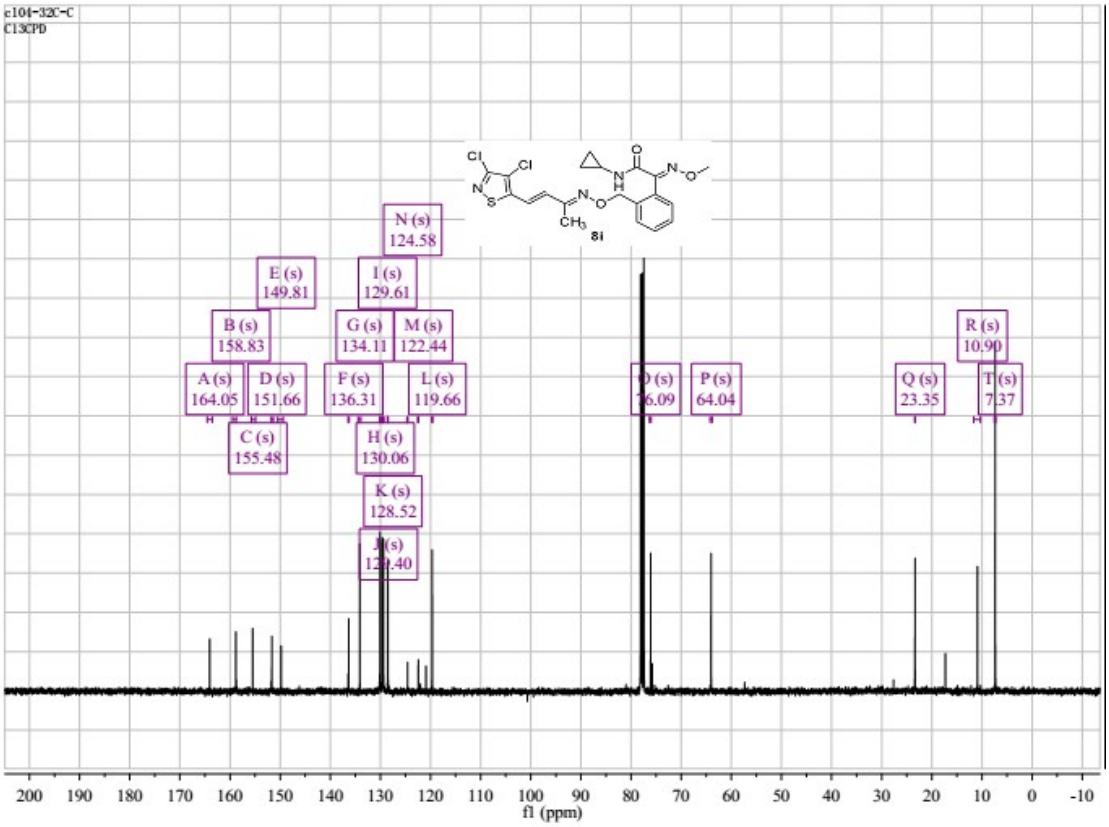

Figure 35. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8j**

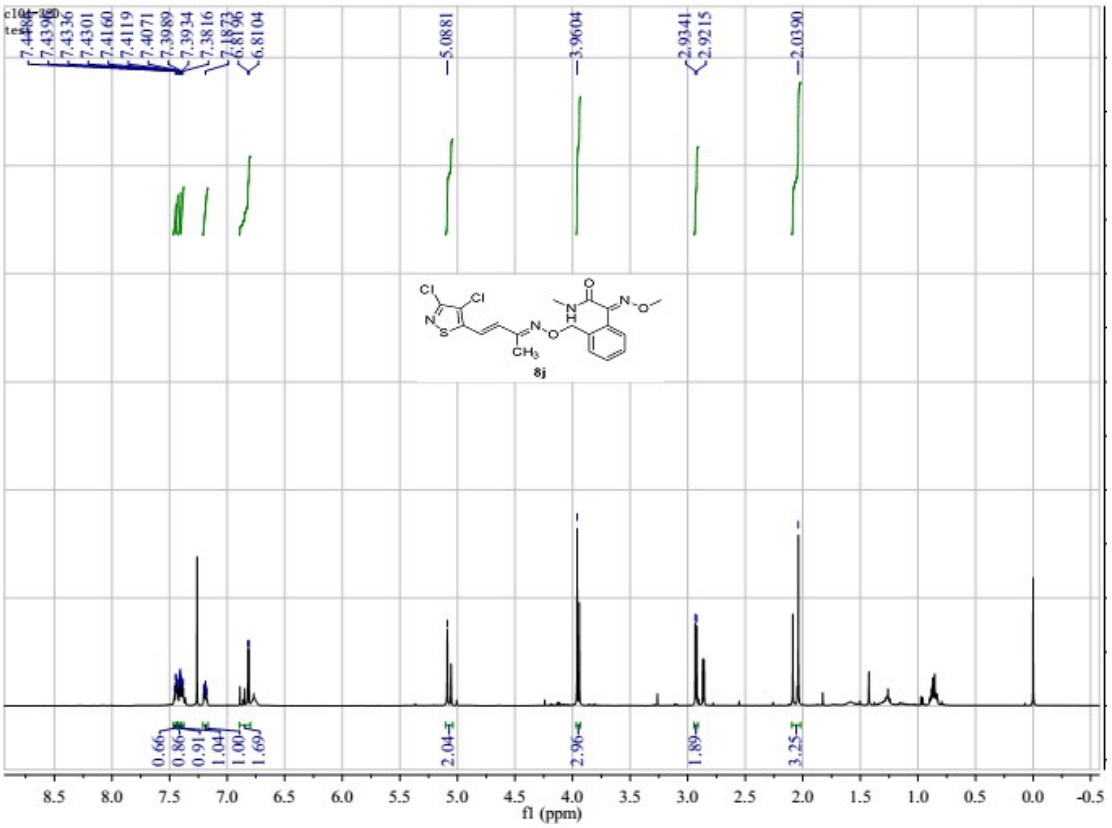

Figure 36. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8j**

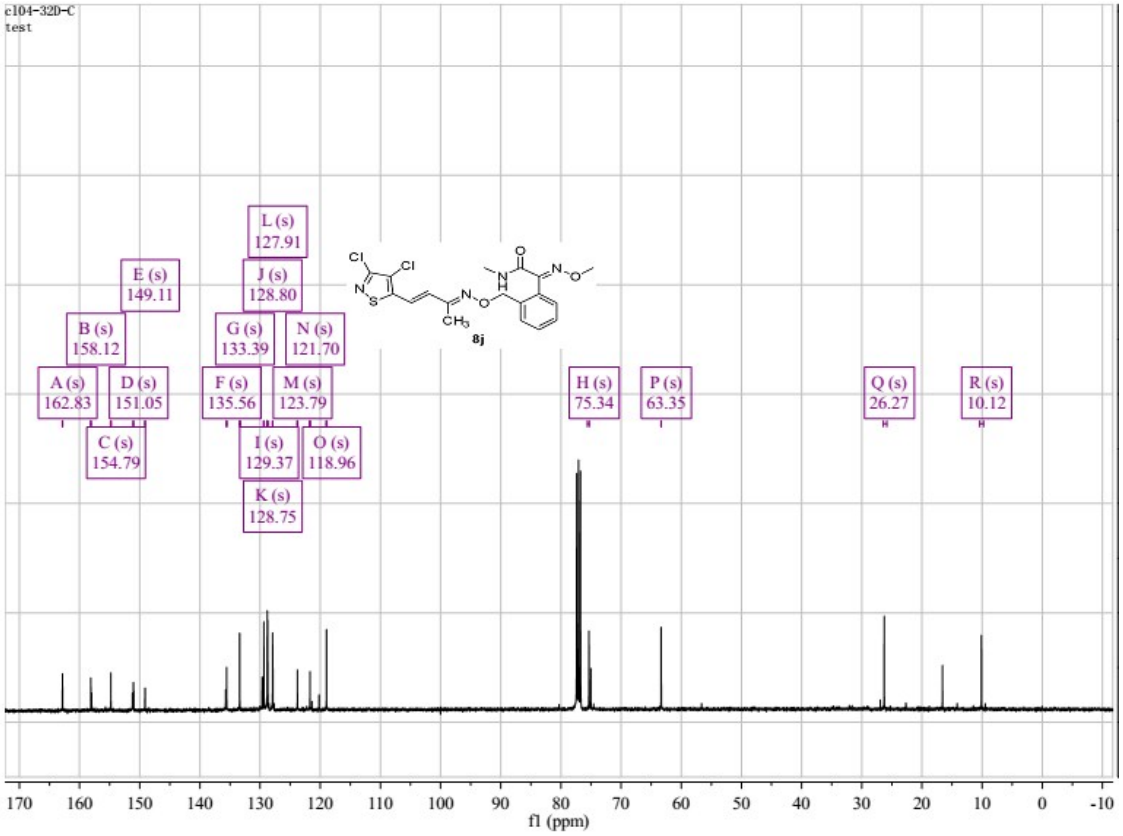

Figure 37. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8k**

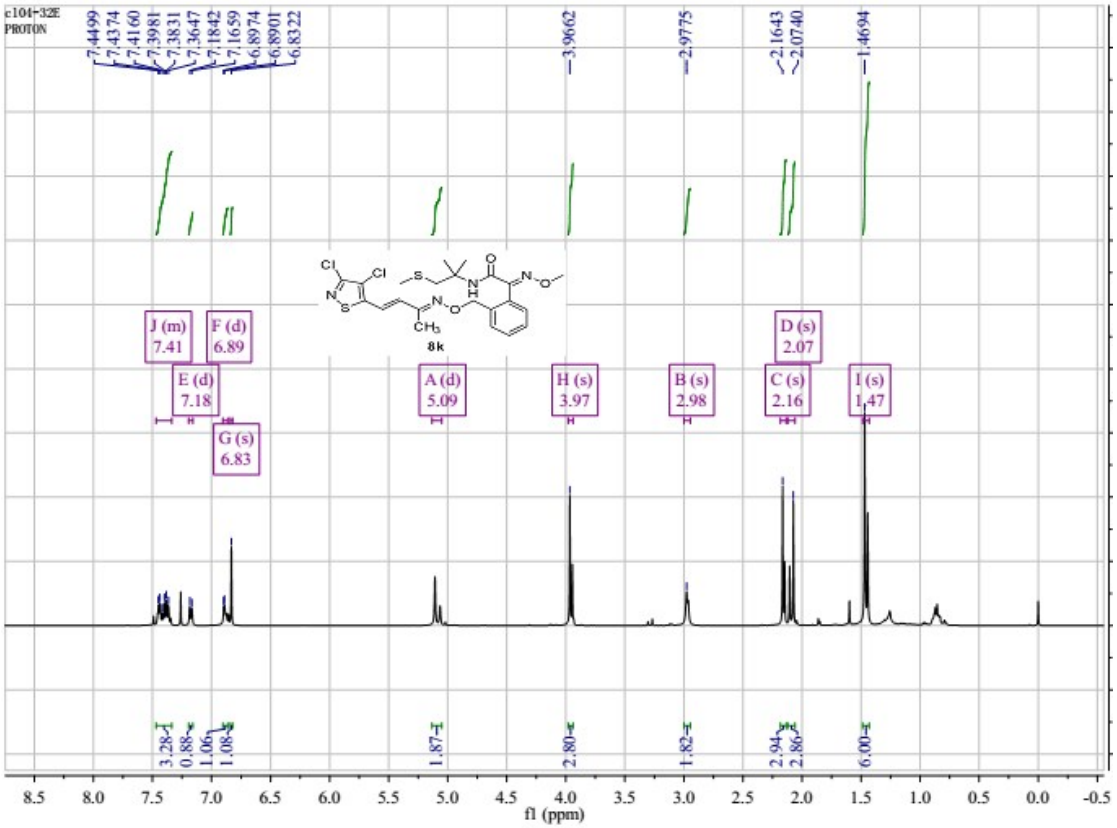

Figure 38. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8k**

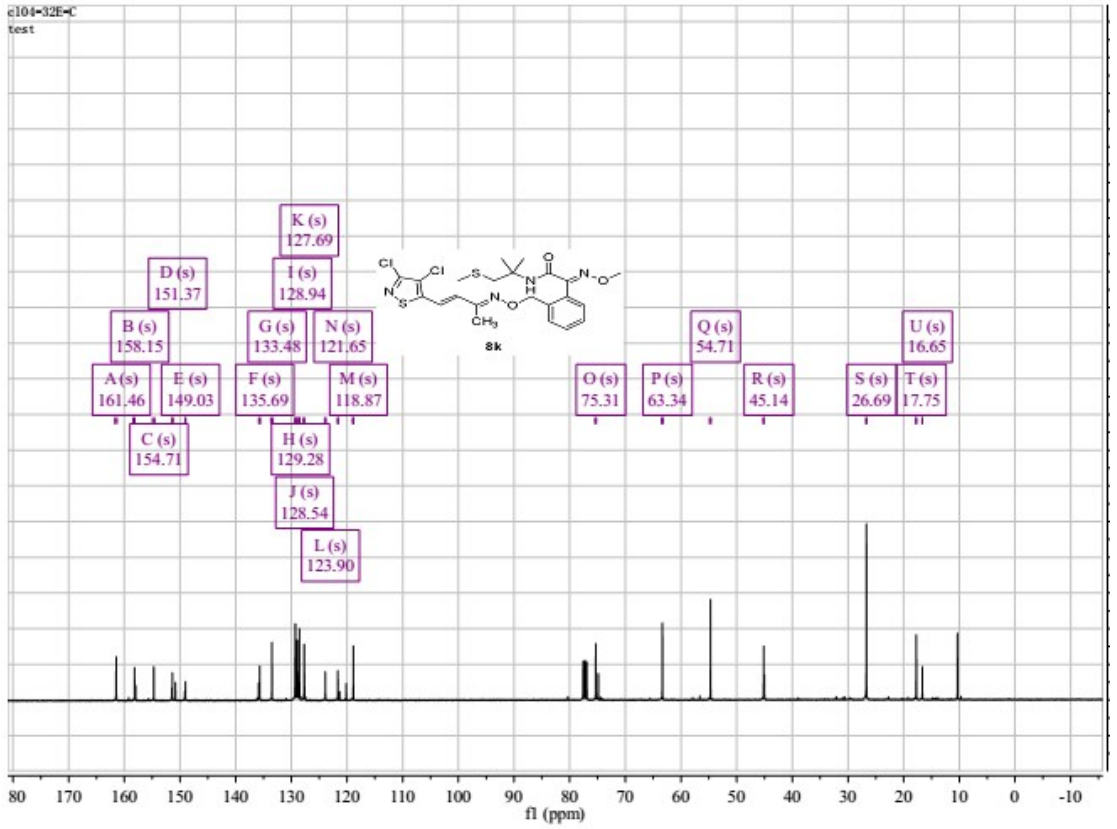

Figure 39. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8l**

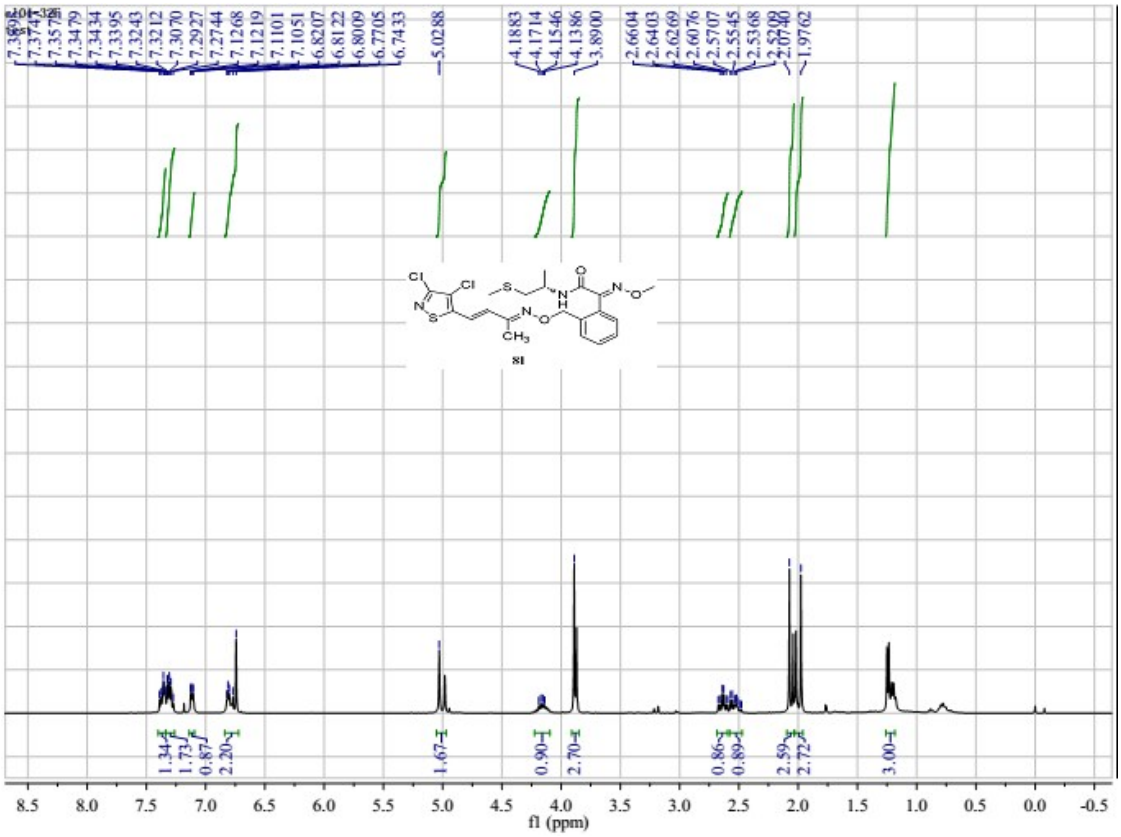

Figure 40. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8l**

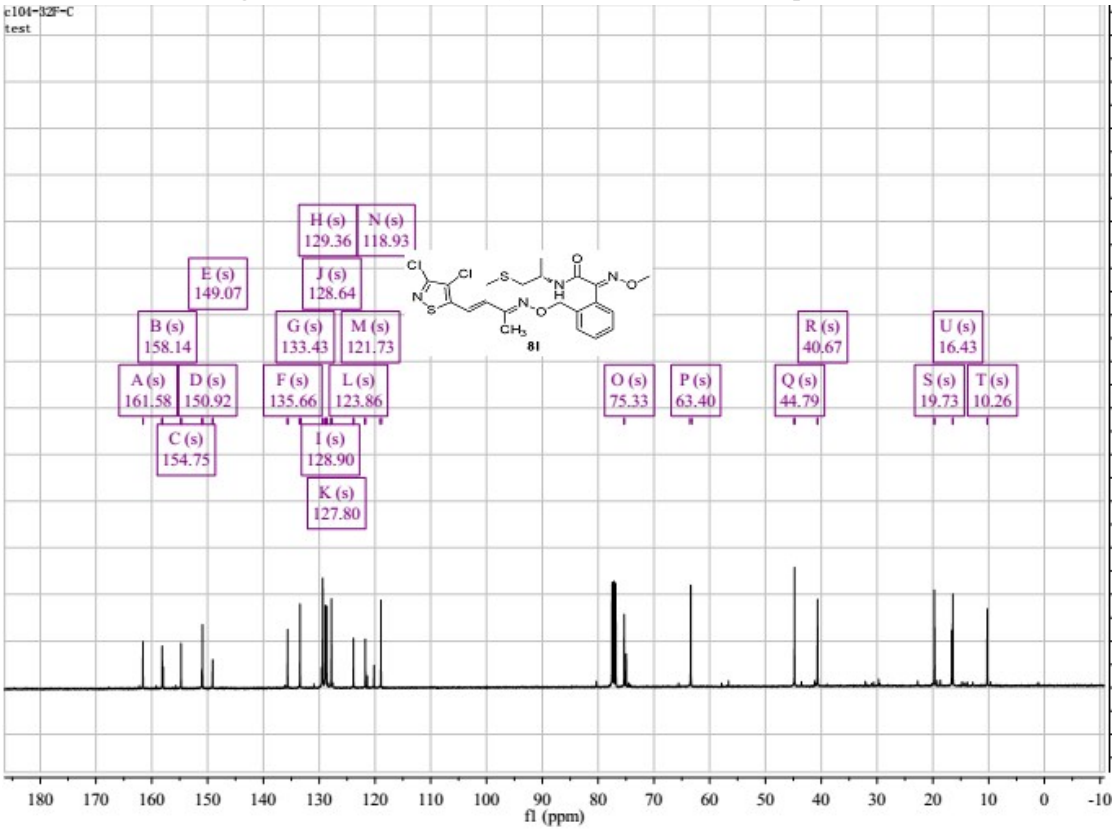

Figure 41. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8m**

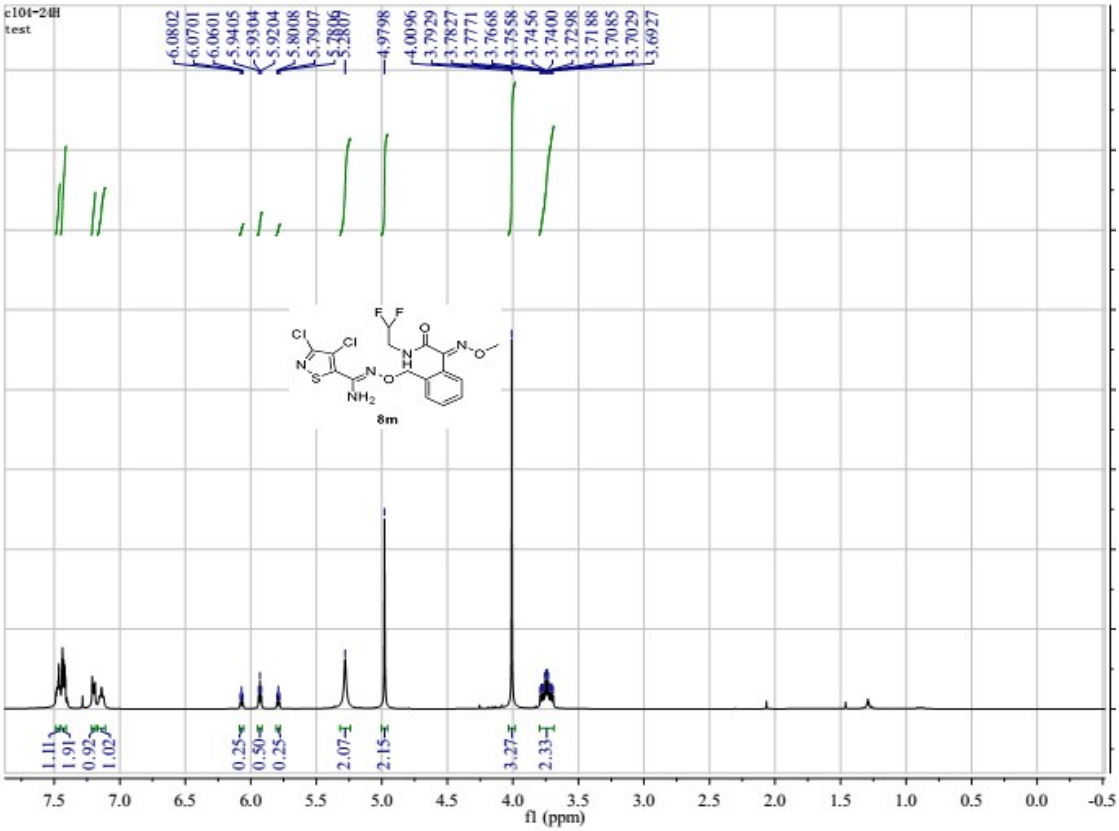

Figure 42. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8m**

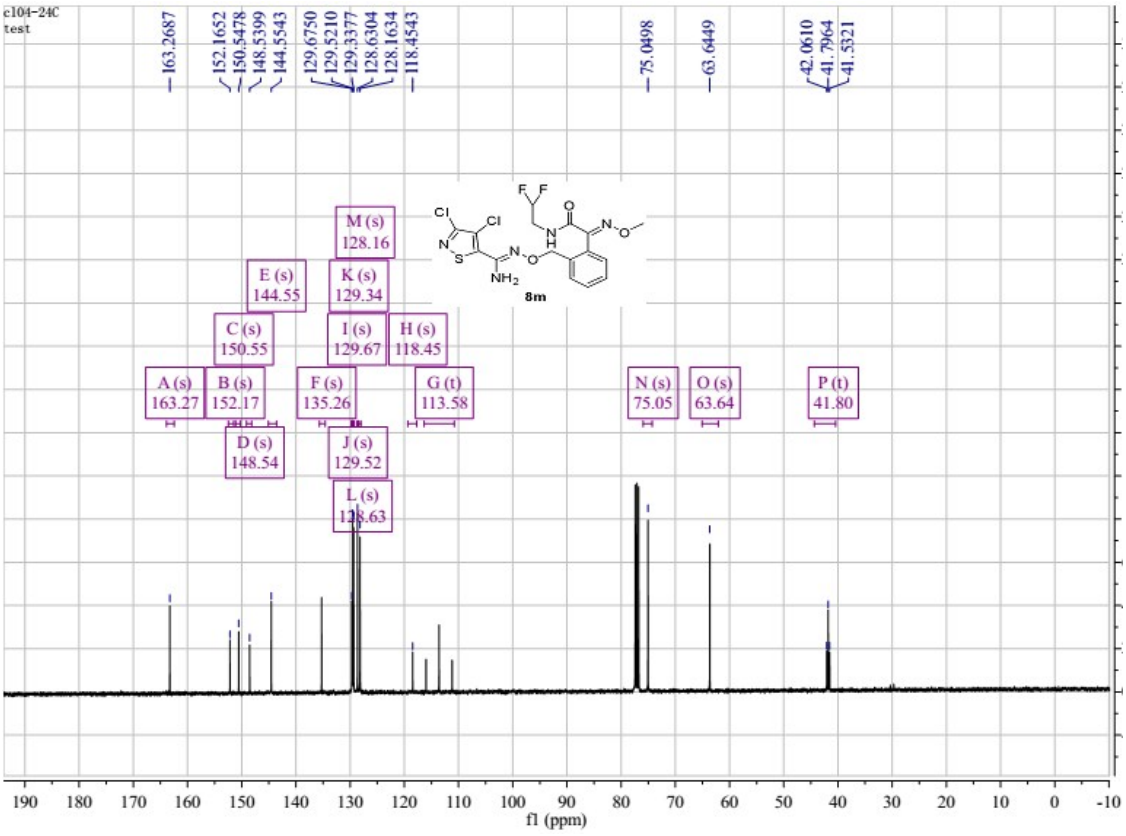

Figure 43. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8n**

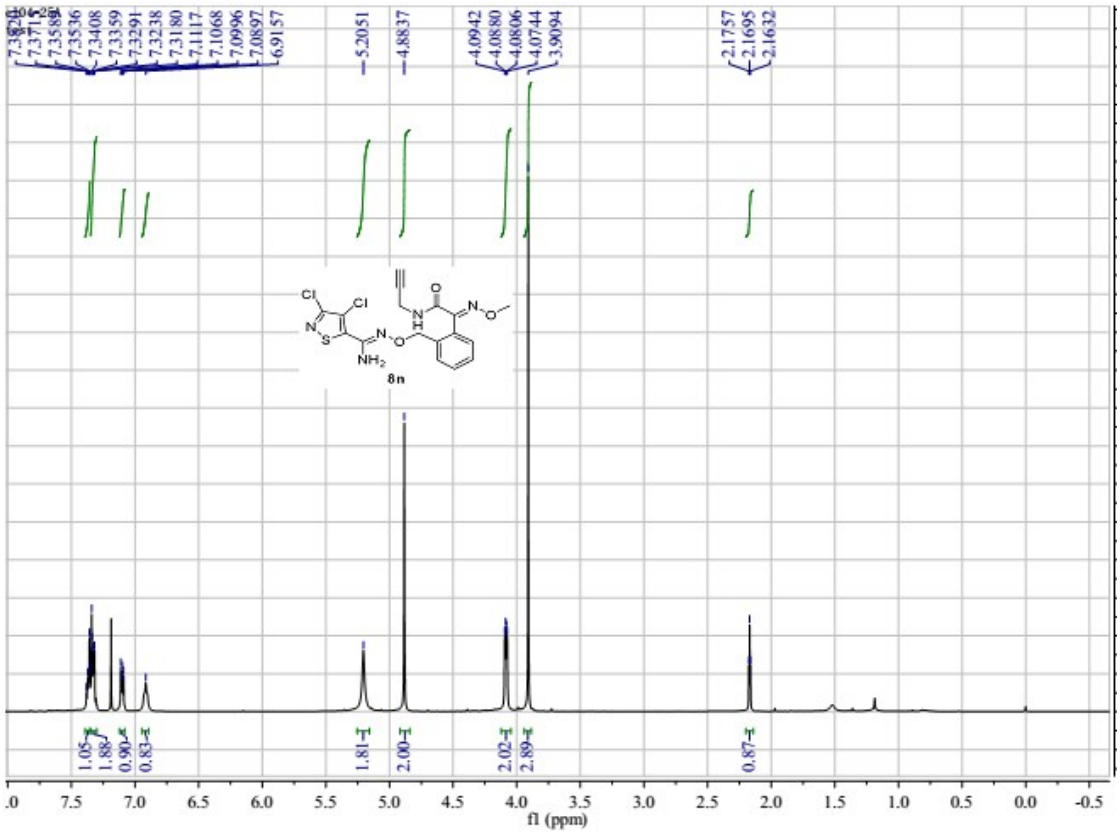

Figure 44 The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8n**

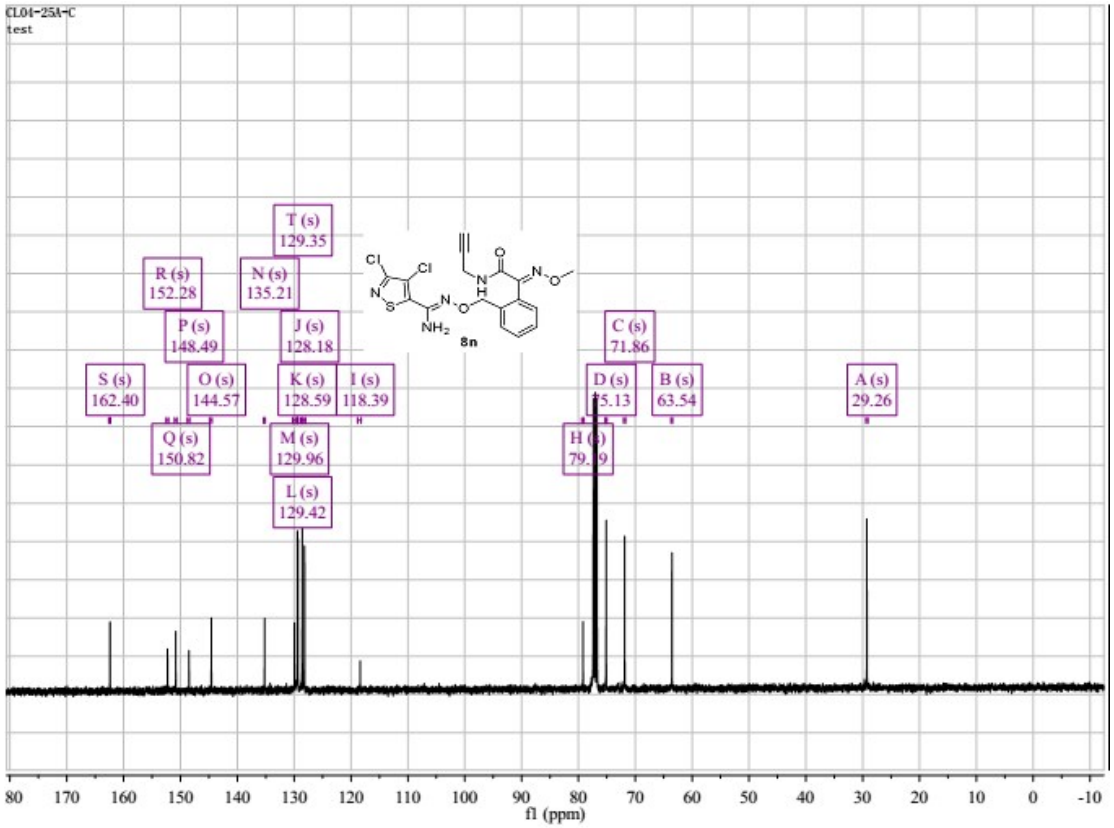

Figure 45. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8o**

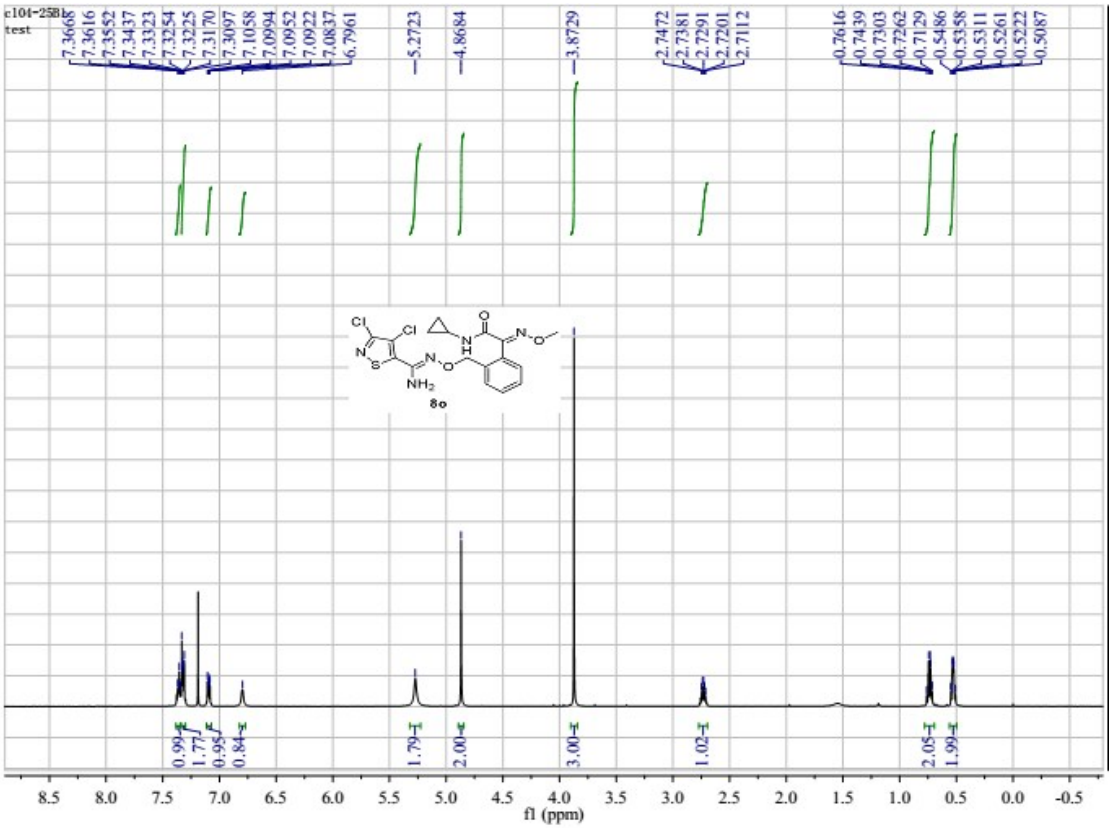

Figure 46. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8o**

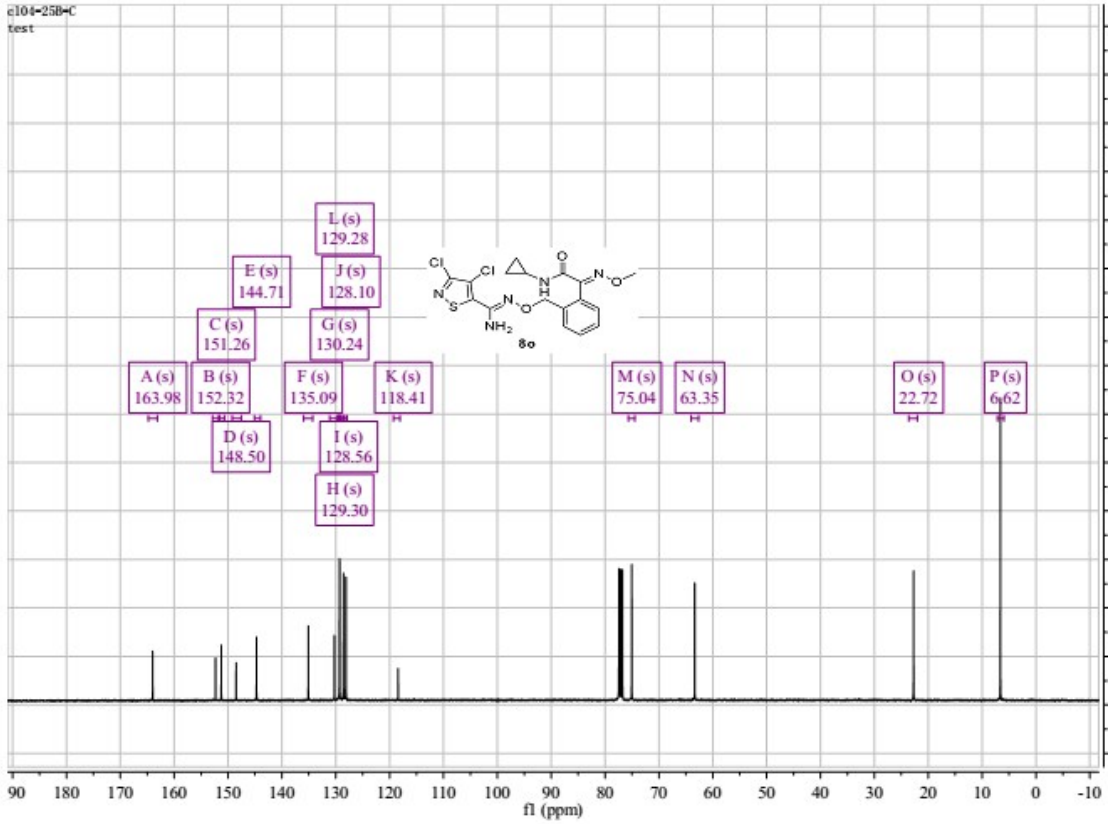

Figure 47. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8p**

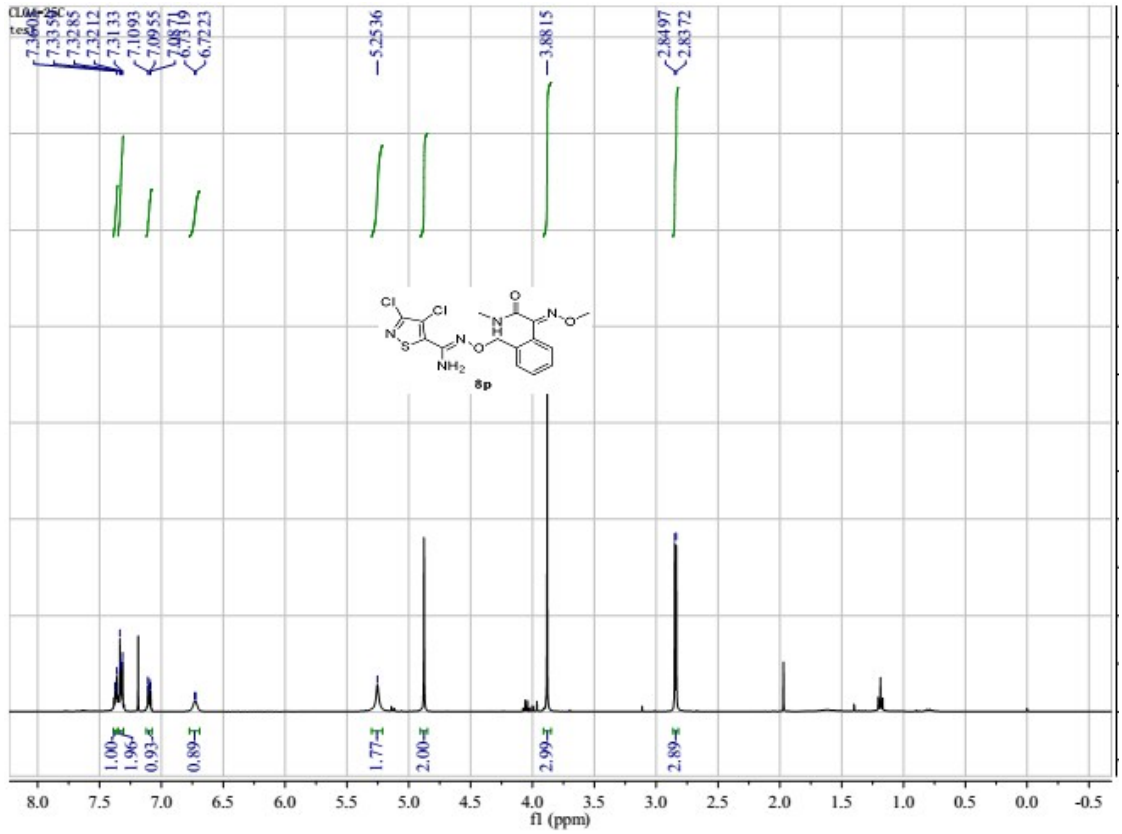

Figure 48. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8p**

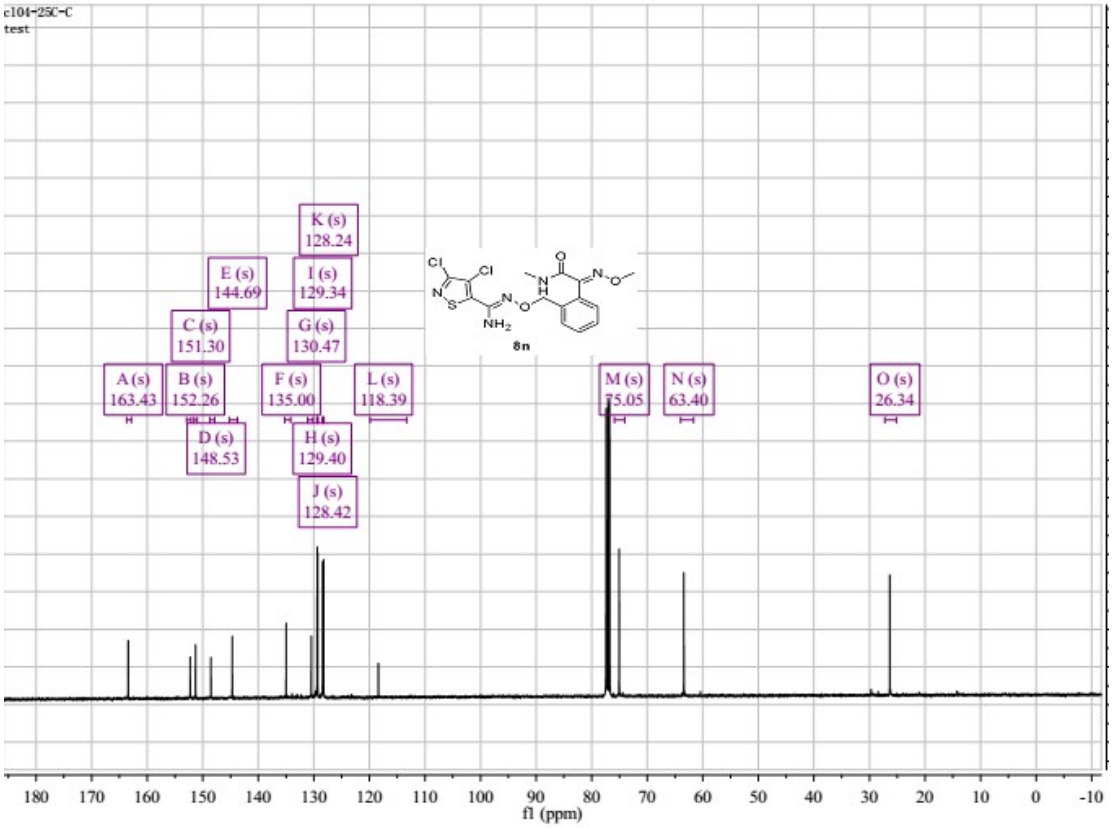

Figure 49. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8q**

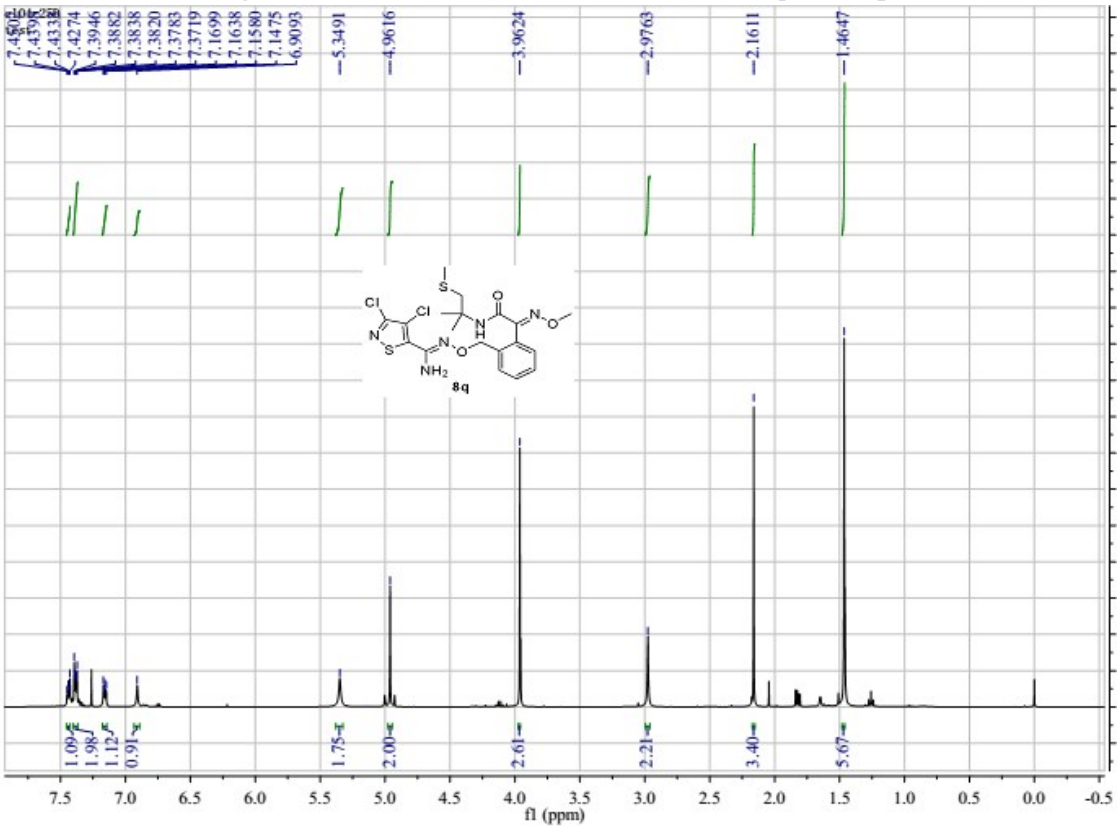

Figure 50. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8q**

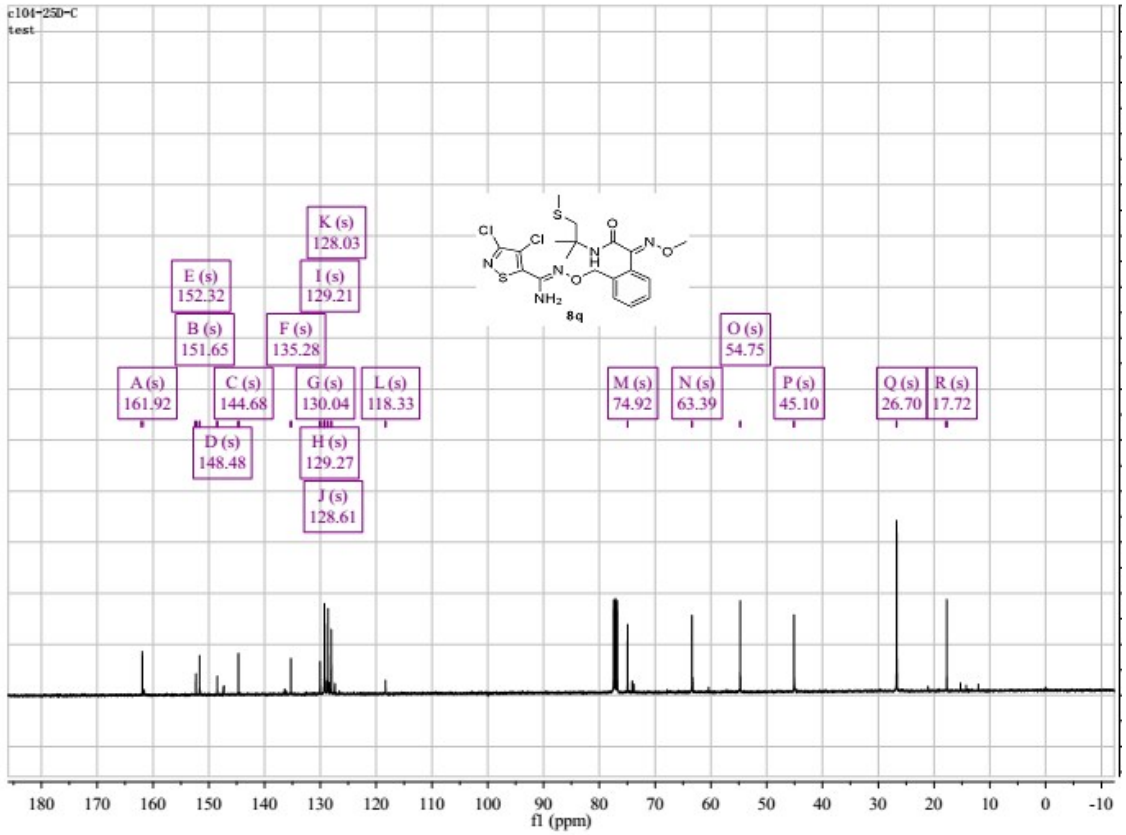

Figure 51. The ^{1}HNMR(400MHz, $CDCl_3$) of compound **8r**

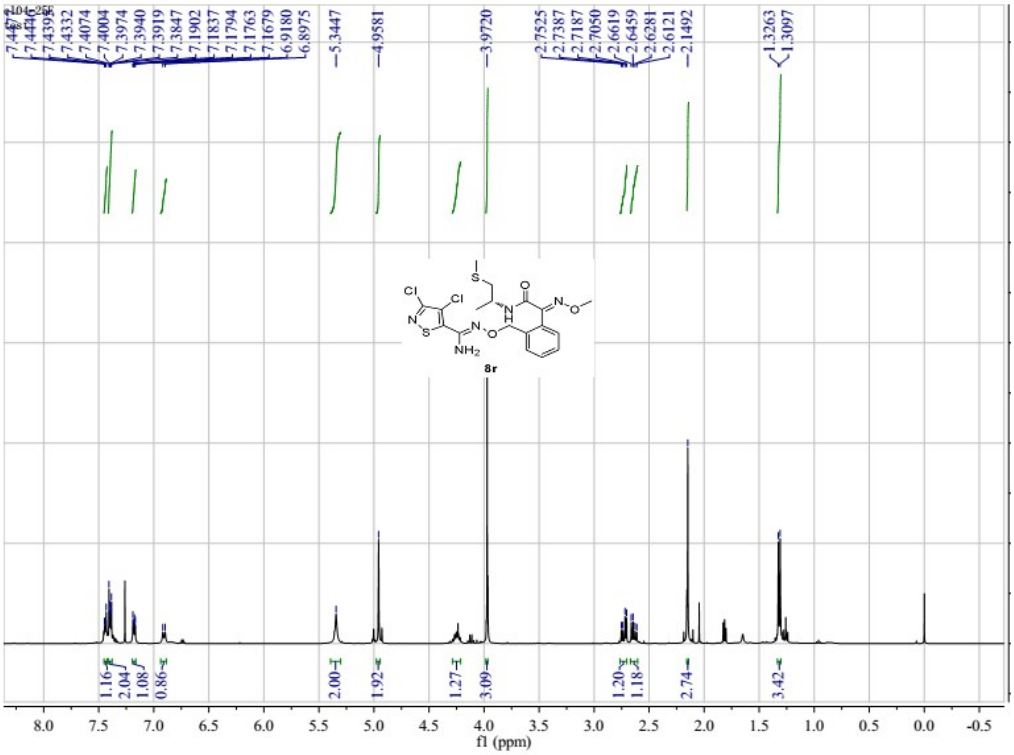

Figure 52. The ^{13}C NMR(400MHz, $CDCl_3$) of compound **8r**