Supporting Information

for

Design and synthesis of novel *N*-benzyl-2,5-dihydro-1*H*-pyrrole linked benzopyrimidines conjugates as antimicrobial agents: study combining *in vitro* and *in silico*

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I. General remarks

All reactions were monitored by TLC using aluminum sheets of Merck silica gel 60 F254, 0.2 mm. Melting temperatures were determined on an electrothermal 9002 apparatus and were reported uncorrected. All purifications were performed using an automated purification system Büchi C-815 puriflash, using 200-800 nm UV scan and ELSD as a detector. NMR spectra were recorded on a Bruker AC-300 spectrometer at 300 MHz (^{1}H) and 75 MHz (^{13}C). Chemical shifts are reported in parts per million (δ).

Chromatographic separations were achieved on silica gel columns (Kieselgel 60, 40–63 µm, Merck) typically using a cyclohexane/ethyl acetate eluent system. In all cases, distilled solvents were used as eluents for column chromatography.

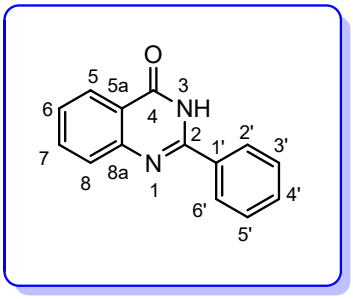
Solvents (CH_3CN, DMF, THF) were distilled before use, taking care to exclude moisture. All reactions were carried out under an inert argon atmosphere. All glass apparatus was oven-dried and cooled under vacuum before use. The infrared spectra (IR) were recorded on a Perkin-Elmer FT-IR Paragon 1000 spectrometer.

Mass spectra (GC-MS) were obtained on a ThermoFinniganAutomass III spectrometer coupled with a gas chromatograph Trace GC 2000. High-resolution mass spectra (HRMS) were measured on an Agilent 6530 Q-Tof MS system.

II. General procedure for the synthesis of 2-aryl-benzopyrimidinone 2

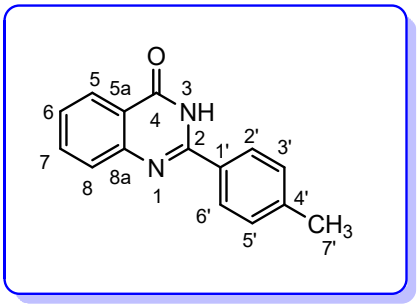
To a mixture of 2-aminobenzamide **1** (5 mmol) and various arylaldehydes (5 mmol) in dry acetonitrile (50 mL), molecular iodine (5 mmol) was added. After the reaction was completed, the mixture was cooled to room temperature. A solution of sodium thiosulphate (5%) was added and the resulting solid was filtered off and washed with water. The crude product was recrystallized from ethanol.

2a : 2-phenylbenzopyrimidin-4(3H)-one



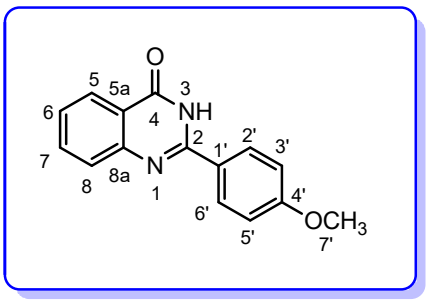
White solid; yield: 55%; mp: 250-252 °C; IR (ATR, cm^{-1}) *v*: 1660.82 (C=O); R_f (cyclohexane/ EtOAc: 6/4) = 0.5. ^1H NMR (300MHz,DMSO-d_6): δ (ppm) = 7.56 (m, 4H, H_{arom}), 7.74 (d, 1H, H_8, *J* = 7.5 Hz), 7.82 (td, 1H, H_7, *J* = 8.1Hz, *J* = 1.5 Hz), 8.18 (m, 3H, H_{arom}), 12.47 (s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) = 121.9 (C_{5a}), 125.8, (C_{arom}), 126.4 (C_{arom}), 127.3 (C_{arom}), 127.7 ($2C_{arom}$), 128.5 ($2C_{arom}$), 131.2 (C_{arom}), 132.7 (C_{arom}), 134.4 ($C_{1'}$), 148.6 (C_{8a}), 152.5 (C_2), 162.2 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{14}H_{11}N_2O)^+$: 223.0871, found: 223.0880.

2b: 2-(p-tolyl)benzopyrimidin-4(3H)-one



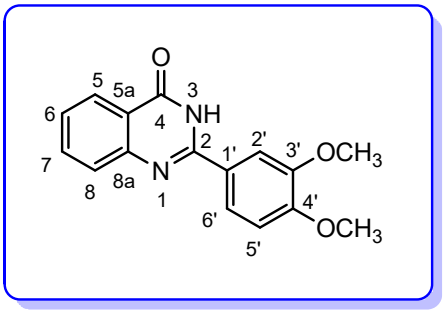
White solid; yield: 82%; mp: 253-255 °C; IR (ATR, cm^{-1}) *v*: 1656.30 (C=O); R_f (cyclohexane/ EtOAc: 6/4) = 0.48. ^1H NMR (300 MHz, DMSO-d_6): δ (ppm) = 2.39 (s, 3H, $H_{7'}$), 7.34 (d, 2H, $H_{3',5'}$, *J* = 8.1 Hz), 7.48 (t, 1H, H_6, *J* = 7.9 Hz), 7.71 (d, 1H, H_8, *J* = 7.9 Hz), 7.80 (t, 1H, H_7, *J* = 7.6 Hz), 8.09 (d, 2H, $H_{2',6'}$, *J* = 8.2 Hz), 8.14 (d, 1H, H_5, *J* = 6.9 Hz), 12.44 (s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) = 21.4 ($C_{7'}$), 121.3 (C_{5a}), 126.3 (C_{arom}), 126.8 (C_{arom}), 127.8 (C_{arom}), 128.1 ($2C_{arom}$), 129.6 ($2C_{arom}$), 130.1 ($C_{1'}$), 135.0 (C_{arom}), 141.9 ($C_{4'}$), 149.2 (C_{8a}), 152.7 (C_2), 162.8 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{15}H_{13}N_2O)^+$: 237.0983, found: 237.1034.

2c: 2-(4-methoxyphenyl)benzopyrimidinone



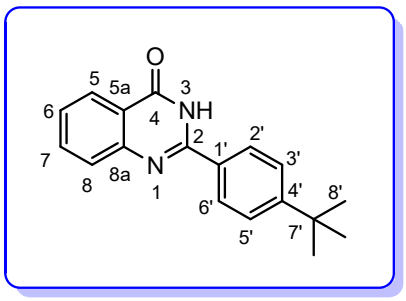
White solid; yield: 60%; mp: 240-242 °C; IR (ATR, cm^{-1}) *v*: 1660.01 (C=O); R_f (cyclohexane/ EtOAc: 6/4) = 0.45). ^1H NMR(300MHz, DMSO-d_6) : δ (ppm) = 3.77 (s, 3H, $H_{1'}$), 7.00 (d, 2H, $H_{3',5'}$, *J* = 8.7 Hz), 7.40 (t, 1H, H_6, *J* = 7.8 Hz), 7.60 (d, 1H, H_8, *J* = 8.1 Hz), 7.72 (td, 1H, H_7, *J* = 8.1 Hz, *J* = 1.2 Hz), 8.06 (dd, 1H, H_5, *J* = 8.1 Hz, *J* = 0.9 Hz), 8.12 (d, 2H, $H_{2',6'}$, *J* = 8.7 Hz), 12.26 (s, 1H, NH). ^{13}CNMR (75 MHz, DMSO-d_6): δ (ppm) = 55.4 ($C_{7'}$), 113.9 ($2C_{arom}$), 120.6(C_{arom}), 124.8($C_{1'}$), 125.7(C_{arom}), 126.0 (C_{arom}), 127.1 (C_{arom}), 129.4 ($2C_{arom}$), 134.4 (C_{arom}), 148.8 (C_{8a}), 151.9 (C_2), 161.9 (C_4), 162.3 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{15}H_{13}N_2O_2)^+$: 253.0977, found: 253.0981.

2d: 2-(3,4-dimethoxyphenyl)benzopyrimidin-4(3H)-one



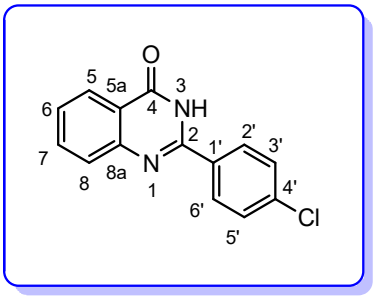
White solid; yield: 70%; mp: 244-246 °C; IR (ATR, cm^{-1}) *v*: 1572.33 (C=O); R_f (cyclohexane/ EtOAc: 6/4) = 0.51.^1H NMR(300 MHz, DMSO-d_6): δ (ppm) = 3.85 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 7.10 (d, 1H, $H_{5'}$, *J* = 8.6 Hz), 7.46 (t, 1H, H_6, *J* = 7.9 Hz), 7.70 (d, 1H, H_{arom}, *J* = 7.8 Hz), 7.79-7.89 (m, 3H, H_{arom}), 8.12 (d, 1H, H_5, *J* = 7.8 Hz), 12.44 (s, 1H, NH) . ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) = 56.1 ($2OCH_3$), 111.1 (C_{arom}), 111.8 (C_{arom}), 121.1 (C_{5a}), 121.6 (C_{arom}), 125.2 ($C_{1'}$), 126.3 (C_{arom}), 126.6 (C_{arom}), 127.8 (C_{arom}), 135.0 (C_{arom}), 149.0 (C_{8a}), 149.4 ($C_{3'}$), 152.0 ($C_{4'}$), 152.3 (C_2), 162.8(C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{16}H_{15}N_2O_3)^+$: 283.1038, found: 283.1092.

2e: 2-(4-(tert-butyl)phenyl)benzopyrimidin-4(3H)-one



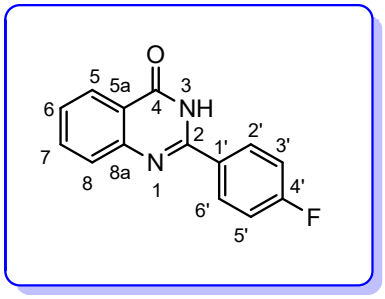
White solid; yield: 78%; mp: 222-224°C; IR (ATR, cm^{-1}) *v*: 1572.33 (C=O); R_f (cyclohexane/ EtOAc: 6/4) = 0.50.^1H NMR (300 MHz, DMSO-d_6): δ (ppm) = 1.32 (s, 9H, H_{15}), 7.48-7.57 (m, 3H, H_{arom}), 7.72 (d, 1H, H_8, *J* = 7.7 Hz), 7.81 (t, 1H, H_7, *J* = 7.6 Hz), 8.13-8.17 (m, 3H, H_{arom}), 12.48 (s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) = 31.3 ($C_{8'}$), 35.1 ($C_{7'}$), 121.4 (C_{5a}), 125.9 ($2C_{arom}$), 126.3 (C_{arom}), 126.8 (C_{arom}), 127.8 (C_{arom}), 128.0 ($2C_{arom}$), 130.4 ($C_{1'}$), 135.0 (C_{arom}), 149.4 (C_{8a}), 152.7 (C_2), 154.8 ($C_{4'}$), 162.8 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{18}H_{19}N_2O)^+$: 279.1453, found: 279.1503.

2f : 2-(4-chlorophenyl)benzopyrimidinone



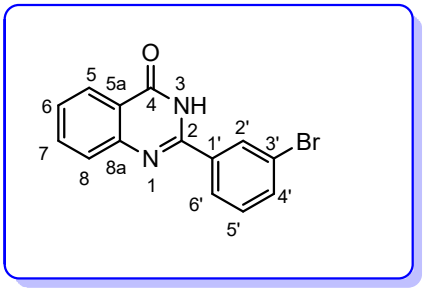
White solid; yield: 68%; mp>300 °C; IR (ATR, cm^{-1}) v: 1665.72 (C=O); R_f (cyclohexane/ EtOAc: 6/4) = 0.60. ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) = 7.75 (m, 5H, H_{arom}), 8.19 (d, 3H, H_{arom}, J = 6.6 Hz), 12.53 (s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) = 121.0 (C_{5a}), 125.8 (C_{arom}), 126.6 (C_{arom}), 127.3 (C_{arom}), 128.6 ($2C_{arom}$), 129.5 ($2C_{arom}$), 131.6 ($C_{1'}$), 134.5 (C_{arom}), 136.2 ($C_{4'}$), 148.5 (C_{8a}), 151.5 (C_2), 162.2 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{14}H_{10}ClN_2O)^+$: 257.0482, found: 257.0491.

2g: 2-(4-fluorophenyl)benzopyrimidin-4(3H)-one



White solid; yield: 80%, mp>300 °C; IR (ATR, cm^{-1}) *v*: 1661.33 (C=O). R_f (cyclohexane/ EtOAc: 6/4) = 0.60. ^{1}H NMR(300 MHz, DMSO-d_6): δ (ppm) = 7.37-7.43 (m, 2H, H_{arom}), 7.50 (t, 1H, H_6, J = 8.1 Hz), 7.73 (d, 1H, H_8, J = 7.6 Hz), 7.82-7.88 (m, 1H, H_7), 8.14 (dd, 1H, H_5, J_1 = 7.6 Hz, J_2 = 1.3 Hz), 8.24-8.28 (m, 2H, H_{arom}, J = 7.6 Hz), 12.59 (s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) = 116.0 (d, J = 22.0 Hz, $C_{3'}$ + $C_{5'}$),121.3 (C_{5a}), 126.3 (C_{arom}), 127.0 (C_{arom}), 127.9 (C_{arom}), 129.7 (d, J = 3.0 Hz, $C_{1'}$), 130.8 (d, J = 9.0 Hz, $C_{2'}$ + $C_{6'}$), 135.1 (C_{arom}), 149.0 (C_{8a}), 151.9 (C_2), 162.7 (C_4), 164.5 (d, J = 249.6 Hz, $C_{4'}$). ES-HRMS $[M+H]^+$ calcd. $(C_{14}H_{10}FN_2O)^+$: 241.0724, found: 241.0784.

2h: 2-(3-bromophenyl)benzopyrimidin-4(3H)-one

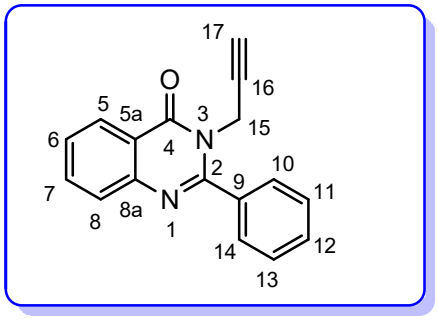


White solid; yield: 72%; mp>300 °C; IR (ATR, cm^{-1}) *v*: 1670.98 (C=O); R_f (cyclohexane/ EtOAc: 6/4) = 0.60. ^1H NMR (300 MHz, DMSO-d_6): δ (ppm) = 7.50-7.58 (m, 2H, H_{arom}), 7.56-7.89 (m, 3H, H_{arom}), 8.15-8.22 (m, 2H, H_{arom}), 8.39 (t, 1H, H_{10}, J = 1.7 Hz), 12.64 (s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) = 113.3 (C_{arom}), 115.2 (C_{arom}), 120.8 (C_{5a}), 123.2 ($C_{3'}$), 126.3 (C_{arom}), 127.3 (C_{arom}), 127.5 (C_{arom}), 129.6 (C_{arom}), 130.8 ($C_{1'}$), 131.2(C_{arom}), 133.4 (C_{arom}), 148.7 (C_{8a}), 152.3 (C_2), 161.0 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{14}H_{10}BrN_2O)^+$: 300.9934, found: 300.9994.

III. General procedure for *N*-propargylation of 2-aryl-benzopyrimidinone 2

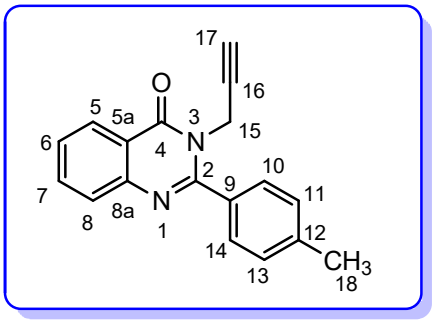
2-aryl-benzopyrimidinone **2** (1 mmol) was dissolved in dry DMF (15 mL) and (2 eq.) of sodium borohydride was added. The reaction mixture was stirred at room temperature for 1 h. Then, propargyl bromide (1.5 eq.) was added dropwise. The reaction was performed for 24 h at room temperature. The mixture was diluted with water. The precipitate formed was filtered, washed with water, dried and purified by silica gel flash column chromatography to afford to dialkylated products **3** and **4**.

3a: 2-phenyl-3-(prop-2-yn-1-yl)benzopyrimidin-4(3H)-one



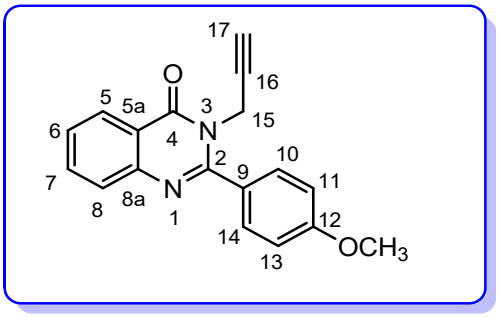
White solid; yield: 58%; mp: 178-180 °C; IR (ATR, cm^{-1}) *v*: 2121.50 (C≡C), 3247.71 (≡C–H), 1571.23 (C=O); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.36 (s, 1H, H_{17}), 4.70 (d, 2H, H_{15}, J = 1.4 Hz), 7.50-7.65 (m, 4H, H_{arom}), 7.70-7.84 (m, 4H, H_{arom}), 8.27 (d, 1H, H_5, J = 7.9 Hz). ^{13}C NMR(75 MHz, $CDCl_3$): δ (ppm) = 36.3 (C_{15}), 72.6 (C_{17}), 78.3 (C_{16}), 120.6 (C_{5a}), 126.9 (C_{arom}), 127.3 (C_{arom}), 127.6 (C_{arom}),128.1 ($2C_{arom}$), 128.9 ($2C_{arom}$), 130.4 (C_{arom}), 134.7 (C_{arom}), 134.8 (C_9), 147.1 (C_{8a}), 155.4 (C_2), 161.6 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{17}H_{13}N_2O)^+$: 261.0983, found: 261.1040.

3b: 3-(prop-2-yn-1-yl)-2-(p-tolyl)benzopyrimidin-4(3H)-one



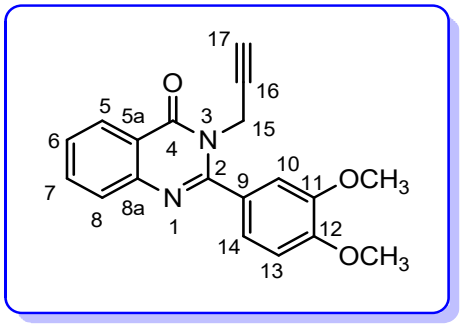
White solid; yield: 36%; mp: 166-168 °C; IR (ATR, cm^{-1}) *v*: 2121.70 (C≡C), 3247.09 (≡C–H), 1577.02 (C=O); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ(ppm) = 2.35-2.37 (m, 1H, H_{17}), 2.46 (s, 3H, H_{18}), 4.69 (d, 2H, H_{15}, *J* = 2.3 Hz), 7.34 (d, 2H, H_{arom}, *J* = 7.8 Hz), 7.49-7.55 (m, 1H, H_{arom}), 7.63-7.67 (m, 2H, H_{arom}), 7.74-7.81 (m, 2H, H_{arom}), 8.35 (d, 1H, H_5, *J* = 8.3 Hz). ^{13}C NMR(75 MHz,$CDCl_3$): δ (ppm) = 21.5 (C_{18}), 36.4 (C_{15}), 72.6 (C_{17}), 78.5 (C_{16}), 120.5 (C_{5a}), 126.9 (C_{arom}), 127.1 (C_{arom}), 127.6 (C_{arom}),128.0 ($2C_{arom}$), 129.5 ($2C_{arom}$), 131.9 (C_9), 134.6 (C_{arom}), 140.6 (C_{12}), 147.2 (C_{8a}), 155.6 (C_2), 161.7 (C_4). ES-HRMS $[M+H]^+$ calcd.$(C_{18}H_{15}N_2O)^+$: 275.1140, found: 275.1194.

3c: 2-(4-methoxyphenyl)-3-(prop-2-yn-1-yl)benzopyrimidin-4(3H)-one



White solid; yield: 55%; mp: 234-236 °C; IR (ATR, cm-1) *v*: 2119.95 (C≡C), 3245.43 (≡C–H), 1605.21 (C=O); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.38 (s, 1H, H_{17}), 3.91 (s, 3H, OCH_3), 4,72 (d, 2H, H_{15}, *J* = 1.8 Hz), 7.06 (d, 2H, H_{arom}, *J* = 8.6 Hz), 7.52 (t, 1H, H_6, *J* = 6.8 Hz), 7.73-7.82 (m, 4H, H_{arom}), 8.36 (d, 1H, H_5, *J* = 8.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 36.5 (C_{15}), 55.5 (OCH_3), 72.6 (C_{17}), 78.6 (C_{16}), 114.2 ($2C_{arom}$), 120.5 (C_{5a}), 126.9 (C_{arom}), 127.0 (C_9), 127.1 (C_{arom}), 127.5 (C_{arom}),129.8 ($2C_{arom}$), 134.6 (C_{arom}), 147.2 (C_{8a}), 155.4 (C_2), 161.2 (C_{12}), 161.9 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{18}H_{15}N_2O_2)^+$: 291.1089, found: 291.1144.

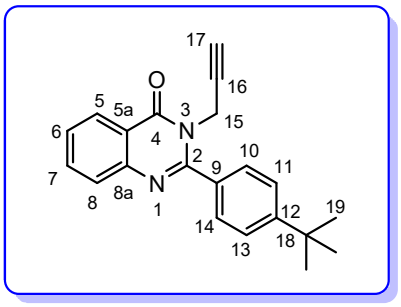
3d: 2-(3,4-dimethoxyphenyl)-3-(prop-2-yn-1-yl)benzopyrimidin-4(3H)-one



White solid; yield: 32%; mp: 157-159 °C; IR (ATR, cm^{-1}) *v*: 2121.49 (C≡C), 3221.04 (≡C–H), 1577.16 (C=O); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.40 (t, 1H, H_{17}, *J* = 2.2 Hz), 3.98 (s, 6H, $2OCH_3$), 4.72 (d, 2H, H_{15}, *J* = 2.2 Hz), 7.03 (d, 1H, H_{arom}, *J* = 8.2 Hz), 7.35-7.39 (m, 2H, H_{arom}), 7.50-7.55 (m, 1H, H_{arom}), 7.75-7.82 (m, 2H, H_{arom}), 8.36 (d, 1H, H_5, *J* = 8.1 Hz). ^{13}C NMR(75 MHz, $CDCl_3$): δ (ppm) = 36.7 (C_{15}), 56.0 (OCH_3), 56.1 (OCH_3), 72.6 (C_{17}), 79.0 (C_{16}), 111.1 (C_{arom}), 111.2 (C_{arom}), 120.5 (C_{5a}), 121.3 (C_{arom}), 126.9 (C_{arom}), 127.1 (C_9), 127.2 (C_{arom}), 127,5 (C_{arom}), 134.7 (C_{arom}), 147.1 (C_{8a}), 148.9 (C_{11}),

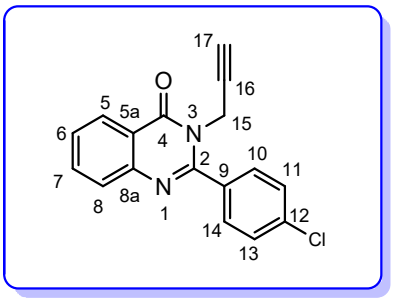
150.7 (C_{12}), 155.3 (C_2), 161.8 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{19}H_{17}N_2O_3)^+$: 321.1194, found: 321.1260.

3e: 2-(4-(tert-butyl)phenyl)-3-(prop-2-yn-1-yl)benzopyrimidin-4(3H)-one



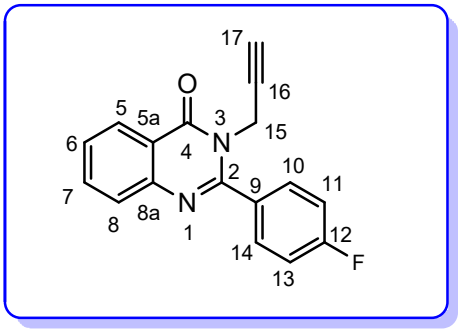
White solid; yield: 60%; mp: 220-222 °C; IR (ATR, cm^{-1}) *v*: 2120.73 (C≡C), 3246.61 (≡C–H), 1630.35 (C=O). R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^{1}HNMR (300 MHz, $CDCl_3$): δ (ppm) = 1.39 (s, 9H, H_{19}), 2.39 (t, 1H, H_{17}, J = 2.4 Hz), 4.72 (d, 2H, H_{15}, J = 2.4 Hz), 7.50-7.58 (m, 3H, H_{arom}), 7.69-7.81 (m, 4H, H_{arom}), 8.36 (d, 1H, H_5, J = 8.2 Hz). ^{13}CNMR (75 MHz, $CDCl_3$): δ (ppm) = 31.2 (C_{19}), 34.9 (C_{18}), 36.5 (C_{15}), 72.6 (C_{17}), 78.6 (C_{16}), 120.6 (C_{5a}), 125.8 ($2C_{arom}$), 126.9 (C_{arom}), 127.1 (C_{arom}), 127.6 (C_{arom}), 127.9 ($2C_{arom}$), 131.8 (C_9), 134.6 (C_{arom}), 147.2 (C_{8a}), 153.7 (C_{12}), 155.6 (C_2), 161.7 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{21}H_{21}N_2O)^+$: 317.1609, found: 317.1666.

3f: 2-(4-chlorophenyl)-3-(prop-2-yn-1-yl)benzopyrimidin-4(3H)-one



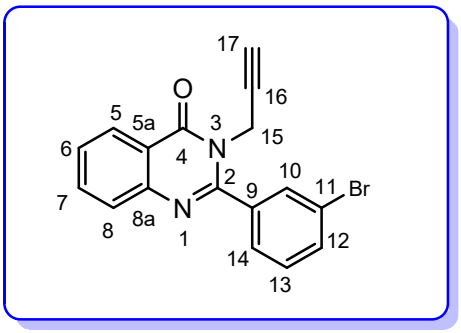
White solid; yield: 15%; mp: 159-161 °C; IR (ATR, cm^{-1}) *v*: 2121.96 (C≡C), 3248.47 (≡C–H), 1620.10 (C=O); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.38 (t, 1H, H_{17}, J = 2.3 Hz), 4.68 (d, 2H, H_{15}, J = 2.3 Hz), 7.55 (d, 3H, H_{arom}, J = 8.4 Hz), 7.72-7.84 (m, 4H, H_{arom}), 8.37 (d, 1H, H_5, J = 7.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 36.3 (C_{15}), 73.0 (C_{17}), 78.2 (C_{16}), 120.6 (C_{5a}), 127.0 (C_{arom}), 127.5 (C_{arom}), 127.6 (C_{arom}), 129.2 ($2C_{arom}$), 129.6 ($2C_{arom}$), 133.1 (C_9), 134.8 (C_{arom}), 136.7 (C_{12}), 147.0 (C_{8a}), 154.3 (C_2), 161.5 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{17}H_{12}ClN_2O)^+$: 294.0530, found: 294.0651.

3g: 2-(4-fluorophenyl)-3-(prop-2-yn-1-yl)benzopyrimidin-4(3H)-one



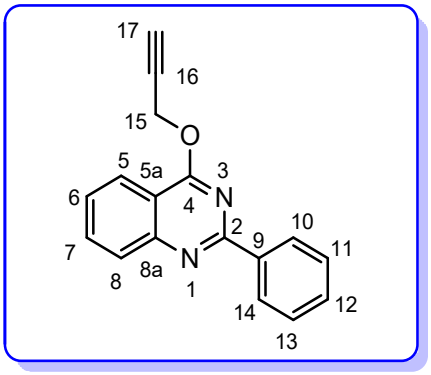
White solid; yield: 21%; mp: 190-192 °C; IR (ATR, cm^{-1}) *v*: 2124.82 (C≡C), 3246.49 (≡C–H), 1578.13 (C=O); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.38 (t, 1H, H_{17}, *J* = 2.4 Hz), 4.69 (d, 2H, H_{15}, *J* = 2.4 Hz), 7.23-7.29 (m, 2H, H_{arom}), 7.55-7.57 (m, 1H, H_{arom}), 7.74-7.84 (m, 4H, H_{arom}), 8.36 (d, 1H, H_5, *J* = 8.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 36.3 (C_{15}), 72.8 (C_{17}), 78.3 (C_{16}), 116.0 (d, *J* = 22.0 Hz, C_{11} + C_{13}), 120.6 (C_{5a}), 126.9 (C_{arom}), 127.4 (C_{arom}), 127.6 (C_{arom}), 130.4 (d, *J* = 8.6 Hz, C_{10} + C_{14}), 130.8 (d, *J* = 3.0 Hz, C_9), 134.8 (C_{arom}), 147.0 (C_{8a}), 154.5 (C_2), 161.6 (C_4), 163.8 (d, *J* = 251.3 Hz, C_{12}). ES-HRMS $[M+H]^+$ calcd. $(C_{17}H_{12}FN_2O)^+$: 279.0889, found: 279.0943.

3h: 2-(3-bromophenyl)-3-(prop-2-yn-1-yl)benzopyrimidin-4(3H)-one



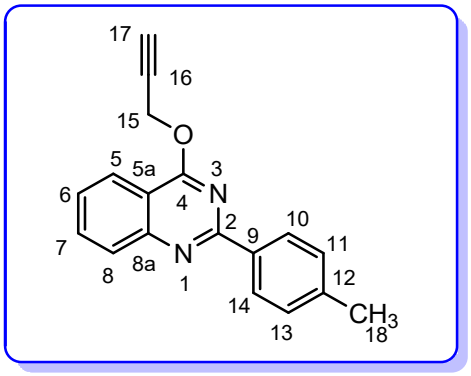
White solid; yield: 20%; mp: 174-176 °C; IR (ATR, cm^{-1}) *v*: 2134.15 (C≡C), 3245.66 (≡C–H), 1610.55 (C=O); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.40 (t, 1H, H_{17}, *J* = 2.4 Hz), 4.68 (d, 2H, H_{15}, *J* = 2.4 Hz), 7.44 (t, 1H, H_6,*J* = 7.9 Hz), 7.54 (t, 1H, H_7, *J* = 6.7 Hz), 7.70-7.84 (m, 4H, H_{arom}), 7.93 (t, 1H, H_{arom}, *J* = 1.6 Hz), 8.37 (d, 1H, H_5, *J* = 8.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 36.2 (C_{15}), 73.0 (C_{17}), 78.1 (C_{16}), 120.6 (C_{5a}), 122.9 (C_{11}), 126.6 (C_{arom}), 127.0 (C_{arom}), 127.6 (C_{arom}), 127.7 (C_{arom}), 130.3 (C_{arom}), 131.3 (C_{arom}), 133.5 (C_{arom}), 134.8 (C_{arom}), 136.4 (C_9), 146.9 (C_{8a}), 153.8 (C_2), 161.4 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{17}H_{12}BrN_2O)^+$: 339.0098, found: 338.0148.

4a: 2-phenyl-4-(prop-2-yn-1-yloxy)benzopyrimidine



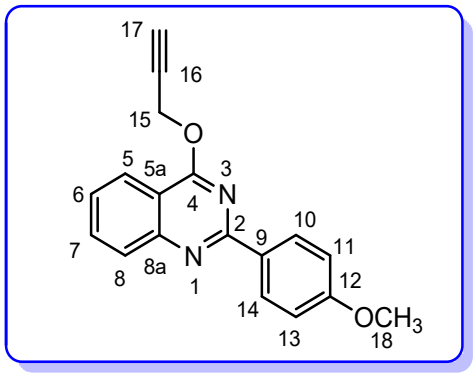
White solid; yield: 58%; mp: 140-142 °C; IR (ATR, cm^{-1}) *v*: 2126.35 (≡C–H), 3206.16 (≡C–H); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.59 (t, 1H, H_{17}, *J* = 2.4 Hz), 5.37 (d, 2H, H_{15}, *J* = 2.4 Hz), 7.53-7.59 (m, 4H, H_{arom}), 7.86 (t, 1H, H_7, *J* = 8.3 Hz), 8.03 (d, 1H, H_5, *J* = 8.4 Hz), 8.23 (d, 1H, H_8, *J* = 8.1 Hz), 8.60-8.64 (m, 2H, H_{arom}). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 54.2 (C_{15}), 75.1 (C_{17}), 78.2 (C_{16}), 114.9 (C_{5a}), 123.5 (C_{arom}), 126.6 (C_{arom}), 128.0 (C_{arom}), 128.4 ($2C_{arom}$), 128.5 ($2C_{arom}$), 130.6 (C_{arom}), 133.8 (C_{arom}), 137.8 (C_9), 152.1 (C_{8a}), 159.7 (C_2), 165.5 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{17}H_{13}N_2O)^+$: 261.0983, found: 261.1036.

4b: 4-(prop-2-yn-1-yloxy)-2-(p-tolyl)benzopyrimidine



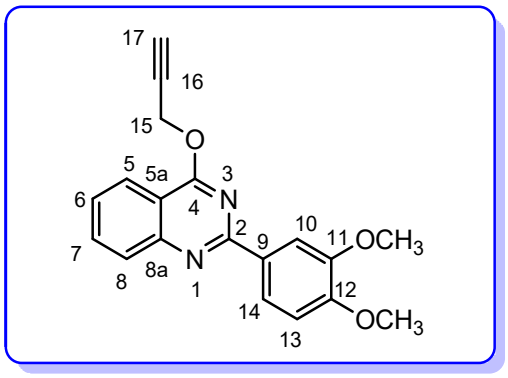
White solid; yield: 44%; mp: 160-162 °C; IR (ATR, cm^{-1}) *v*: 2126.65 (C≡C–H), 3199.32 (≡C–H); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.47 (s, 3H, H_{18}, *J* = 2.4 Hz), 2.59 (t, 1H, H_{17}, *J* = 2.4 Hz), 5.35 (d, 2H, H_{15}, *J* = 2.4 Hz), 7.34 (d, 2H, $H_{11\text{-}13}$, *J* = 8.0 Hz), 7.53 (t, 1H, H_6, *J* = 8.1 Hz), 7.81-7.87 (m, 1H, H_7), 8.01 (d, 1H, H_5, *J* = 8.4 Hz), 8.20 (d, 1H, H_8, *J* = 8.9 Hz), 8.50 (d, 2H, $H_{10\text{-}14}$, *J* = 8.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 21.3 (C_{18}), 54.0 (C_{15}), 75.0 (C_{17}), 78.3 (C_{16}), 114.8 (C_{5a}), 123.4 (C_{arom}), 126.4 (C_{arom}), 127.8 (C_{arom}), 128.5 ($2C_{arom}$), 129.2 ($2C_{arom}$), 133.7 (C_{arom}), 135.4 (C_9), 140.8 (C_{12}), 152.1 (C_{8a}), 159.8 (C_2), 165.4 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{18}H_{15}N_2O)^+$: 275.1140, found: 275.1194.

4c: 2-(4-methoxyphenyl)-4-(prop-2-yn-1-yloxy)benzopyrimidine



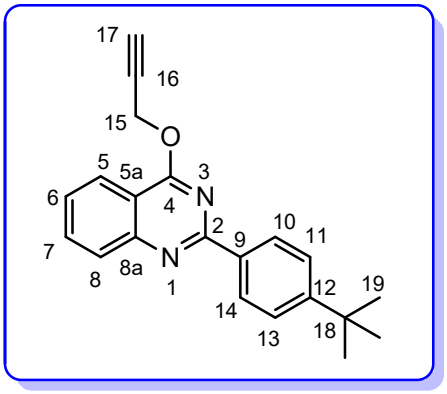
White solid; yield: 27%; mp: 137-139 °C; IR (ATR, cm^{-1}) *v*: 2127.11 (C≡C), 3185.15 (≡C–H); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.59 (t,1H, H_{17}, *J* = 1.9 Hz),3.91 (s, 3H, OCH_3), 5.35 (d, 2H, H_{15}, *J* = 2.2 Hz), 7.04 (d, 2H, $H_{11\text{-}13}$, *J* = 8.8 Hz), 7.51 (t, 1H, H_6, *J* = 7.5 Hz), 7.83 (t, 1H, H_7, *J* = 7.4 Hz), 7.98 (d, 1H, H_5, *J* = 8.4 Hz), 8.19 (d, 1H, H_8, *J* = 8.1 Hz), 8.56 (d, 2H, $H_{10\text{-}14}$, *J* = 8.8 Hz). ^{13}CNMR (75 MHz, $CDCl_3$): δ (ppm) = 54.1 (C_{15}), 55.4 (OCH_3), 75.0 (C_{17}), 78.3 (C_{16}), 113.8 ($2C_{arom}$), 114.7 (C_{5a}), 123.4 (C_{arom}), 126.2 (C_{arom}), 127.7 (C_{arom}), 130.1 ($2C_{arom}$), 130.5 (C_9), 133.7 (C_{arom}), 152.1 (C_{8a}), 159.5 (C_2), 161.8 (C_{12}), 165.3 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{18}H_{15}N_2O_2)^+$: 291.1089, found: 291.1145.

4d: 2-(3,4-dimethoxyphenyl)-4-(prop-2-yn-1-yloxy)benzopyrimidine



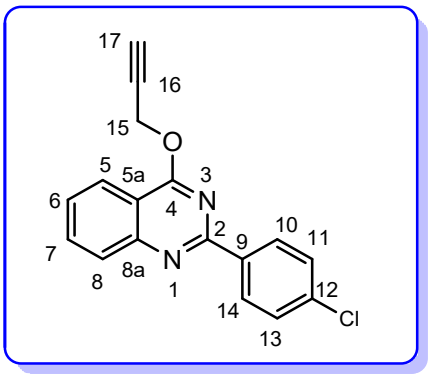
White solid; yield: 51%; mp: 143-145 °C; IR (ATR, cm^{-1}) *v*: 2117.35 (C≡C), 3271.64 (≡C–H); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^{1}H NMR(300 MHz, $CDCl_3$): δ (ppm) = 2.59 (t, 1H, H_{17}, *J* = 2.4 Hz), 3.99 (s, 3H, OCH_3), 4.07 (s, 3H, OCH_3), 5.32 (d, 2H, H_{15}, *J* = 2.4 Hz), 7.00 (d, 1H, H_{13}, *J* = 8.4 Hz), 7.49-7.54 (m, 1H, H_6), 7.80-7.85 (m, 1H, H_7), 7.98 (d, 1H, H_5, *J* = 8.4 Hz), 8.17-8.21 (m, 3H, H_{arom}). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 54.1 (C_{15}), 55.9 ($2OCH_3$), 75.0 (C_{17}), 78.3 (C_{16}), 110.6 (C_{arom}), 111.1 (C_{arom}), 114.7 (C_{5a}), 121.9 (C_{arom}), 123.4 (C_{arom}), 126.2 (C_{arom}), 127.7 (C_{arom}), 130.7 (C_9), 133.7 (C_{arom}), 148.9 (C_{12}), 151.4 (C_{11}), 152.1 (C_{8a}), 159.4 (C_2), 165.3 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{19}H_{17}N_2O_3)^+$: 321.1194, found: 321.1253.

4e: 2-(4-(tert-butyl)phenyl)-4-(prop-2-yn-1-yloxy)benzopyrimidine



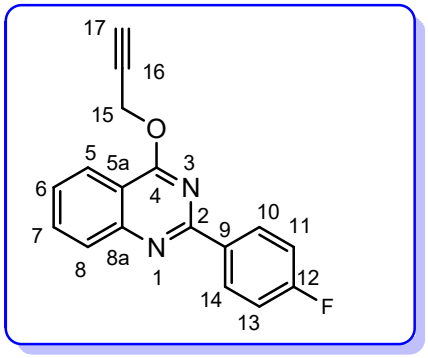
White solid; yield: 31%; mp: 120-122°C; IR (ATR, cm^{-1}) *v*: 2129.98 (C≡C), 32015.20 (≡C–H); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^{1}H NMR(300 MHz, $CDCl_3$): δ (ppm) = 1.42 (s, 9H, H_{19}), 2.59 (t, 1H, H_{17}, *J* = 2.4 Hz), 5.36 (d, 2H, H_{15}, *J* = 2.4 Hz), 7.52 (d,1H, H_6, *J* = 8.1Hz), 7.57 (d, 2H, $H_{11\text{-}13}$, *J* = 8.5Hz), 7.82-7.87 (m, 1H, H_7), 8.02 (d, 1H, H_5, *J* = 8.4 Hz), 8.21 (d, 1H, H_8, *J* = 9.0 Hz), 8.53 (d, 2H, $H_{10\text{-}14}$, *J* = 8.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 31.6 (C_{19}), 34.8 (C_{18}), 54.2 (C_{15}), 75.0 (C_{17}), 78.3 (C_{16}), 110.6 (C_{arom}), 111.1 (C_{arom}), 114.9 (C_{5a}), 123.4 (C_{arom}), 125.5 ($2C_{arom}$), 126.4 (C_{arom}), 127.9 (C_{arom}), 128.3 ($2C_{arom}$), 133.7 (C_{arom}), 135.2 (C_9), 152.4 (C_{11}), 152.1 (C_{8a}), 153.8 (C_{12}), 159.8 (C_2), 165.4 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{21}H_{21}N_2O)^+$: 317.1609, found: 317.1664.

4f: 2-(4-chlorophenyl)-4-(prop-2-yn-1-yloxy)benzopyrimidine



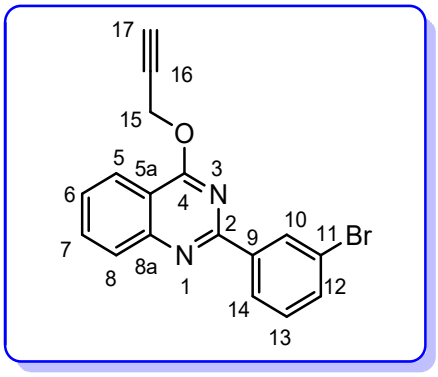
White solid; yield: 73%; mp: 198-200 °C; IR (ATR, cm^{-1}) *v*: 2124.10 (C≡C), 3208.15 (≡C–H); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.59 (t, 1H, H_{17}, *J* = 2.4 Hz), 5.35 (d, 2H, H_{15}, *J* = 2.4 Hz), 7.49 (d, 2H, $H_{10\text{-}14}$, *J* = 8.7Hz), 7.54-7.60 (m, 1H, H_6),7.84-7.90 (m, 1H, H_7), 8.01 (d, 1H, H_5, *J* = 8.4 Hz), 8.22 (d, 1H, H_8, *J* = 7.4 Hz), 8.56 (d, 2H, $H_{11\text{-}13}$, *J* = 6.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 54.3 (C_{15}), 75.2 (C_{17}), 78.1 (C_{16}), 114.9 (C_{5a}), 123.5 (C_{arom}), 126.8 (C_{arom}), 127.9 (C_{arom}), 128.6 ($2C_{arom}$), 129.8 ($2C_{arom}$), 133.9 (C_{arom}), 136.3 (C_9), 136.8 (C_{12}), 151.9 (C_{8a}), 159.6 (C_2), 165.6 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{17}H_{12}ClN_2O)^+$: 295.0644, found: 295.0684.

4g: 2-(4-fluorophenyl)-4-(prop-2-yn-1-yloxy)benzopyrimidine



White solid; yield: 65%; mp: 168-170°C; IR (ATR, cm^{-1}) *v*: 2127.348 (C≡C), 3196.48 (≡C–H); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.59 (t,1H, H_{17}, *J* = 2.4 Hz), 5.35 (d, 2H, H_{15}, *J* = 2.4 Hz), 7.21 (t, 2H, H_{arom}, *J* = 8.7 Hz), 7.56 (t, 1H, H_6, *J* = 7.6 Hz), 7.86 (t, 1H, H_7, *J* = 8.2 Hz), 8.00 (d, 1H, H_5, *J* = 8.4 Hz), 8.22 (d, 1H, H_8, *J* = 8.2Hz), 8.59-8.64 (m, 2H, H_{arom}). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 54.2 (C_{15}), 75.1 (C_{17}), 78.1 (C_{16}), 114.8 (C_{5a}), 115.4 (d, *J* = 21.6 Hz, C_{11} + C_{13}), 123.5 (C_{arom}), 126.6 (C_{arom}), 127.9 (C_{arom}), 130.6 (d, *J* = 8.6 Hz, C_{10} + C_{14}), 133.8 (C_{arom}), 134.0 (d, *J* = 3 Hz, C_9), 152.0 (C_{8a}), 158.7 (C_2), 164.6 (d, *J* = 249.0 Hz, C_{12}), 165.6 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{17}H_{12}FN_2O)^+$: 279.0889, found: 279.0944.

4h: 2-(3-bromophenyl)-4-(prop-2-yn-1-yloxy)benzopyrimidine

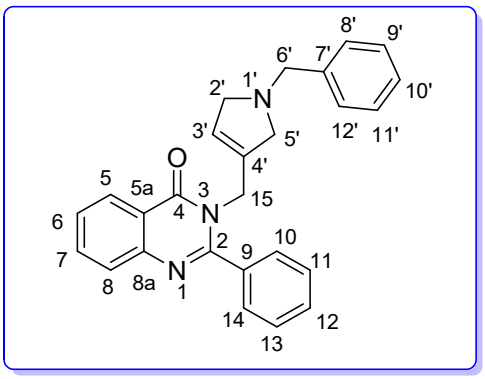


White solid; yield: 68%; mp: 152-154 °C; IR (ATR, cm^{-1}) *v*: 2134.15 (C≡C), 3293.32 (≡C–H); R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.61 (t, 1H, H_{17}, *J* = 2.4 Hz), 5.36 (d, 2H, H_{15}, *J* = 2.4 Hz), 7.41 (t, 1H, H_{arom}, *J* = 7.9 Hz), 7.56-7.66 (m, 2H, H_{arom}), 7.87-7.91 (m, 1H, H_{arom}), 8.02 (d, 1H, H_5, *J* = 8.3 Hz), 8.23 (d, 1H, H_8, *J* = 9.0 Hz), 8.53-8.56 (m, 1H, H_{arom}), 8.75 (t, 1H, H_{arom}, *J* = 1.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 54.4 (C_{15}), 75.2 (C_{17}), 78.0 (C_{16}), 115.1 (C_{5a}), 122.7 (C_{11}), 123.5 (C_{arom}), 127.0 (C_{arom}), 127.1 (C_{arom}), 128.0 (C_{arom}), 129.9 (C_{arom}), 131.4 (C_{arom}), 133.4 (C_{arom}), 133.9 (C_{arom}), 139.9 (C_9), 151.9 (C_{8a}), 158.2 (C_2), 165.6 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{17}H_{12}BrN_2O)^+$: 339.0097, found: 339.0147.

IV. General procedure for the synthesis of the cyclo-adducts 5a-h and 6a-h

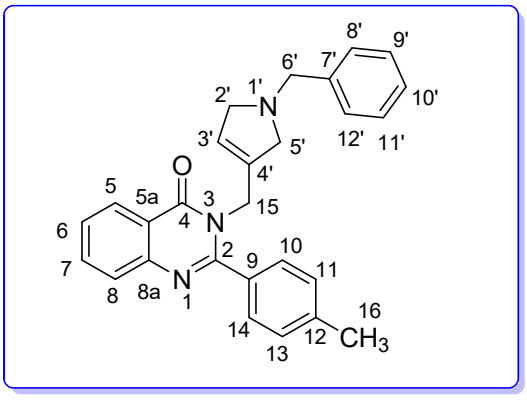
To a stirred solution of dipolarophiles **3** or **4 (**0.045 mmol) and trifluroroacetic acid (0.2 equiv.) in dry THF (3 mL), *N*-benzyl-*N*-methoxymethyl-(trimethylsilyl)methylamine (3 mmol) was added dropwise at room temperature for 3 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to give the pure cycloadducts **5** and **6**.

5a: 3-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)methyl)-2-phénylbenzopyrimidin-4(3H)-one



White solid; yield: 73%; mp: 99-101 °C; IR (ATR, cm^{-1}) *v*: 1666.88 (C=O); R_f (cyclohexane/ EtOAc: 7/3) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.24-3.28 (m, 2H, $H_{5'}$), 3.34-3.38 (m, 2H, $H_{2'}$), 3.67 (s, 2H, $H_{6'}$), 4.59 (s, 2H, H_{15}), 5.17-5.20 (m, 1H, $H_{3'}$), 7.13-7.24 (m, 5H, H_{arom}), 7.38-7.48 (m, 6H, H_{arom}), 7.67-7.75 (m, 2H, H_{arom}), 8.26 (d, 1H, H_5, *J* = 8.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 44.4 (C_{15}), 59.6-60.3 ($C_{5'}$+$C_{2'}$), 60.4 ($C_{6'}$), 120.6 (C_{5a}), 124.1 (C_{arom}), 126.9 (C_{arom}), 127.0 (C_{arom}), 127.1 (C_{arom}), 127.5 (C_{arom}),127.9 ($2C_{arom}$), 128.3 ($2C_{arom}$), 128.5 ($2C_{arom}$), 128.6 ($2C_{arom}$), 130.0 (C_{arom}), 134.5 ($C_{3'}$), 135.1 (C_9), 136.6 ($C_{7'}$), 139.2 ($C_{4'}$), 147.2 (C_{8a}), 156.1 (C_2), 162.0 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{26}H_{24}N_3O)^+$: 394.1875, found: 394.1933.

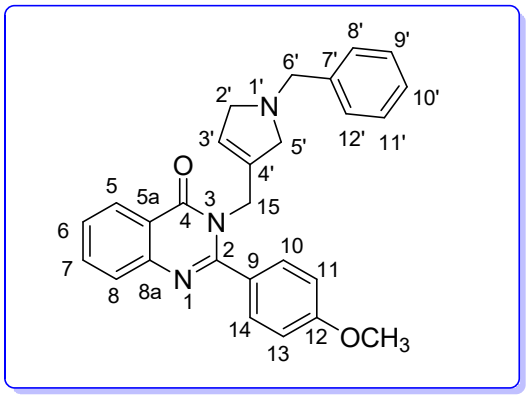
5b: 3-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)methyl)-2-(p-tolyl)benzopyrimidin-4(3H)-one



White solid; yield: 95%; mp: 94-96 °C; IR (ATR, cm^{-1}) *v*: 1671.31 (C=O); R_f (cyclohexane/ EtOAc: 7/3) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.35 (s, 3H, H_{16}), 3.25-3.29 (m, 2H, $H_{5'}$), 3.35-3.39 (m, 2H, $H_{2'}$), 3.67 (s, 2H, $H_{6'}$), 4.58 (s, 2H, H_{15}), 5.20-5.21 (m, 1H, $H_{3'}$), 7.13-7.23 (m, 7H, H_{arom}), 7.34 (d, 2H, H_{arom}, *J* = 8.0 Hz), 7.40-7.47 (m, 1H, H_{arom}), 7.63-7.71 (m, 2H, H_{arom}), 8.24 (d, 1H, H_5, *J* = 8.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 21.4 (C_{16}), 44.5 (C_{15}), 59.7-60.3 ($C_{5'}$+$C_{2'}$), 60.4 ($C_{6'}$), 120.6 (C_{5a}), 123.9 (C_{arom}), 126.9 (C_{arom}), 127.0

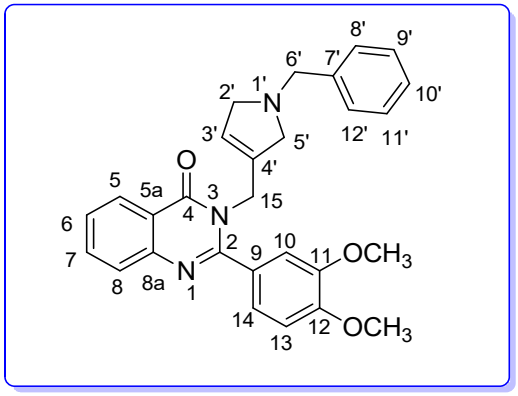
(C_{arom}), 127.5 (C_{arom}), 127.9 (2C_{arom}),128.3 (2C_{arom}), 128.5 (2C_{arom}), 129.2 (2C_{arom}), 132.3 (C_9), 134.4 ($C_{3'}$), 136.7 (C_{12}), 139.1 ($C_{7'}$), 140.1 ($C_{4'}$), 147.3 (C_{8a}), 156.3 (C_2), 162.0 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{27}H_{26}N_3O)^+$: 408.2031, found: 408.2092.

5c: 3-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)méthyl)-2-(4-methoxyphenyl)benzopyrimidin-4(3H)-one



Yellow oil; yield: 52%; IR (ATR, cm^{-1}) *v*: 1671.62 (C=O); R_f (cyclohexane/ EtOAc: 7/3) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.37-3.46 (m, 2H, $H_{5'}$), 3.47-3.50 (m, 2H, $H_{2'}$), 3.78 (s, 2H, $H_{6'}$), 3.89 (s, 3H, OCH_3), 4.69 (s, 2H, H_{15}), 5.30-5.33 (m, 1H, $H_{3'}$), 6.99 (d, 2H, H_{arom}, *J* = 8.8 Hz), 7.25-7.37 (m, 5H, H_{arom}), 7.50-7.55 (m, 3H, H_{arom}), 7.47-7.81 (m, 2H, H_{arom}), 8.33 (d, 1H, H_5, *J* = 8.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 44.6 (C_{15}), 55.4 (OCH_3), 59.7-60.3 ($C_{5'}$+$C_{2'}$), 60.4 ($C_{6'}$), 114.0 (2C_{arom}), 120.5 (C_{5a}), 123.8 (C_{arom}), 126.9 (C_{arom}), 126.9 (C_{arom}), 127.0 (C_{arom}), 127.5 (C_{arom}),127.6(C_9),128.3 (2C_{arom}), 128.6 (2C_{arom}), 129.6 (2C_{arom}), 134.4 ($C_{3'}$), 136.8 ($C_{7'}$), 139.1 ($C_{4'}$), 147.3 (C_{8a}), 156.0 (C_2), 160.8(C_{12}), 162.1 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{27}H_{26}N_3O_2)^+$: 424.1980, found: 424.2041.

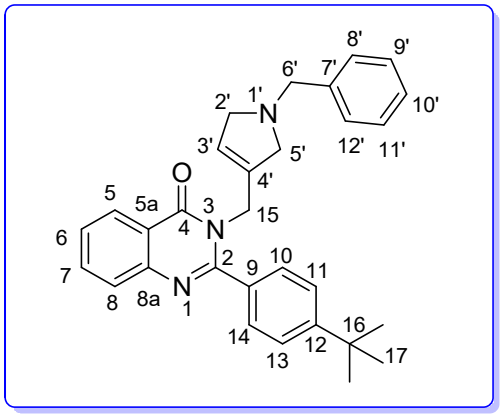
5d: 3-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)methyl)-2-(3,4-dimethoxyphenyl)benzopyrimidin-4(3H)-one



White solid; yield: 60%; mp: 140-142 °C; IR (ATR, cm^{-1}) *v*: 1671.83 (C=O); R_f (cyclohexane/ EtOAc: 7/3) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.37-3.40 (m, 2H, $H_{5'}$), 3.46-3.49 (m, 2H, $H_{2'}$), 3.77 (s, 2H, $H_{6'}$), 3.91 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 4.65 (s, 2H, H_{15}), 5.36-5.38 (m, 1H, $H_{3'}$), 6.96 (d, 1H, H_{arom}, *J* = 8.5 Hz), 7.11-7.17 (m, 2H, H_{arom}), 7.20-7.31 (m, 5H, H_{arom}), 7.48-7.54 (m, 1H, H_{arom}), 7.74-7.82 (m, 2H, H_{arom}), 8.32 (d, 1H, H_5, *J* = 6.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 45.0 (C_{15}), 55.9 (OCH_3), 56.0 (OCH_3), 59.7-60.2 ($C_{5'}$+$C_{2'}$),

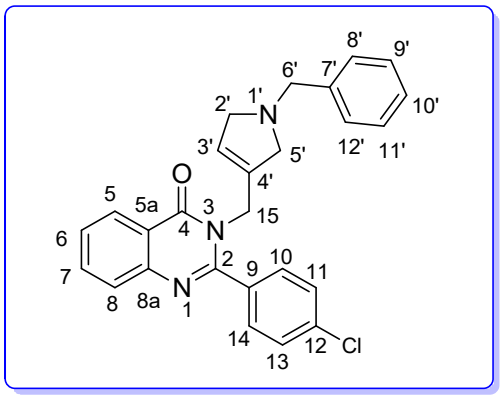
60.4 ($C_{6'}$), 110.9 (C_{arom}), 111.0 (C_{arom}), 120.5 (C_{5a}), 120.9 (C_{arom}), 123.7 (C_{arom}), 126.9 (C_{arom}), 127.0 (C_{arom}), 127.0 (C_{arom}), 127.5 (C_{arom}),127.6 (C_9), 128.3 ($2C_{arom}$), 128.5 ($2C_{arom}$), 134.4 ($C_{3'}$), 137.2 ($C_{7'}$), 139.2 ($C_{4'}$), 147.2 (C_{8a}), 148.8 (C_{11}), 150.4 (C_{12}), 156.0 (C_2), 162.1 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{28}H_{28}N_3O_3)^+$: 454.2086, found: 454.2146.

5e: 3-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)methyl)-2-(4-(tert-butyl)phenyl)quinazolin-4(3H)-one



White solid; yield: 73%; mp:179-181 °C; IR (ATR, cm^{-1}) *v*: 1666.02 (C=O); R_f (cyclohexane/ EtOAc: 7/3) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.18 (s, 9H, H_{17}), 3.15-3.25 (m, 2H, $H_{5'}$), 3.26-3.28 (m, 2H, $H_{2'}$), 3.57 (s, 2H, $H_{6'}$), 4.49 (s, 2H, H_{15}), 5.09-5.11 (m, 1H, $H_{3'}$), 7.02-7.12 (m, 5H, H_{arom}), 7.26-7.35 (m, 5H, H_{arom}), 7.55-7.61 (m, 2H, H_{arom}), 8.13 (d, 1H, H_5, J = 7.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 31.2 (C_{17}), 34.9 (C_{16}), 44.5 (C_{15}), 59.7-60.3 ($C_{5'}$+$C_{2'}$), 60.5 ($C_{6'}$), 120.6 (C_{5a}), 123.8 (C_{arom}), 125.6 ($2C_{arom}$), 126.9 (C_{arom}), 127.0 (C_{arom}), 127.0 (C_{arom}), 127.5 (C_{arom}), 127.7 ($2C_{arom}$), 128.3 ($2C_{arom}$), 128.6 ($2C_{arom}$), 132.2 (C_9), 134.4 ($C_{3'}$), 136.8 ($C_{7'}$), 139.2 ($C_{4'}$), 147.3 (C_{8a}), 153.3 (C_{12}), 156.3 (C_2), 162.0 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{30}H_{32}N_3O)^+$: 450.2501, found:450.2552.

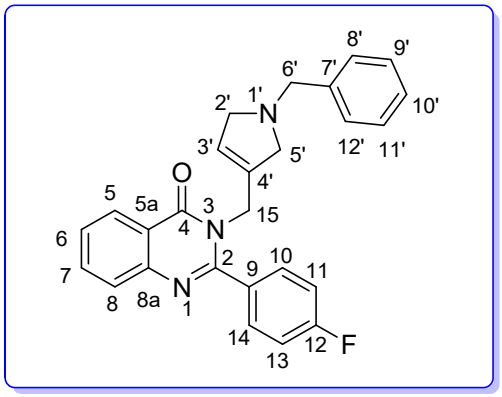
5f: 3-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)methyl)-2-(4-chlorophenyl)benzopyrimidin-4(3H)-one



White solid; yield: 62%; mp: 127-129 °C; IR (ATR, cm^{-1}) *v*: 1667.94 (C=O); R_f (cyclohexane/ EtOAc: 7/3) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.51-3.54 (m, 2H, $H_{5'}$), 3.55-3.63 (m, 2H, $H_{2'}$), 3.68 (s, 2H, $H_{6'}$), 5.20 (s, 2H, H_{15}), 5.87-5.89 (m, 1H, $H_{3'}$), 7.19-7.31 (m, 5H, H_{arom}), 7.38 (d, 2H, J = 7.4 Hz, H_{arom}), 7.42-7.47 (m, 1H, H_{arom}), 7.72-7.78 (m, 1H, H_{arom}), 7.89 (d, 1H, J = 8.2 Hz, H_{arom}), 8.08 (d, 1H, J = 8.2 Hz, H_{arom}), 8.42 (d, 2H, J = 7.4 Hz, H_{arom}). ^{13}C

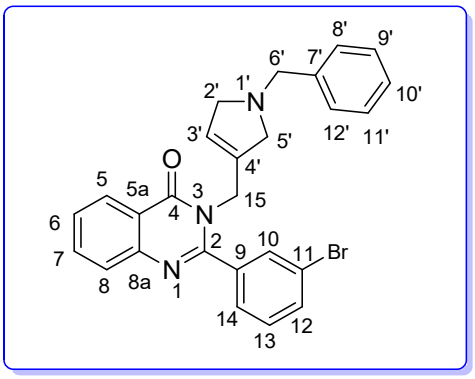
NMR (75 MHz, $CDCl_3$): δ (ppm) = 59.8 (C_{15}), 60.2 ($C_{5'}$), 60.4 ($C_{6'}$), 63.7 ($C_{2'}$), 115.2 (C_{5a}), 123.5 (C_{arom}), 125.8 (C_{arom}), 126.6 (C_{arom}), 127.1 (C_{arom}), 127.9 (C_{arom}),128.4 ($2C_{arom}$), 128.6 ($2C_{arom}$), 128.7 ($2C_{arom}$), 129.7 ($2C_{arom}$), 133.7 (C_9), 136.5 ($C_{3'}$), 136.6 (C_{12}), 136.7 ($C_{7'}$), 139.1 ($C_{4'}$), 151.8 (C_{8a}), 158.8 (C_2), 166.3 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{26}H_{23}ClN_3O)^+$: 428.1496, found: 428.1546.

5g: 3-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)méthyl)-2-(4-fluorophényl)benzopyrimidin-4(3H)-one



White solid; yield: 93%; mp: 124-126 °C; IR (ATR, cm^{-1}) *v*: 1665,83 (C=O); R_f (cyclohexane/ EtOAc: 7/3) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.35-3.38 (m, 2H, $H_{5'}$), 3.45-3.48 (m, 2H, $H_{2'}$), 3.37 (s, 2H, $H_{6'}$), 4.65 (s, 2H, H_{15}), 5.28-5.31 (m, 1H, $H_{3'}$), 7.17-7.33 (m, 7H, H_{arom}), 7 52-7.59 (m, 3H, H_{arom}), 7.74-7.83 (m, 2H, H_{arom}), 8.35 (d, 1H, H_5, J = 8.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 44.5 (C_{15}), 59.7 ($C_{5'}$ or $C_{2'}$), 60.3 ($C_{5'}$ or $C_{2'}$), 60.4 ($C_{6'}$), 115.8 (d, J = 22.0 Hz, $C_{11} + C_{13}$), 120.6 (C_{5a}), 124.1 (C_{arom}), 127.0 (C_{arom}), 127.1 (C_{arom}), 127.3 (C_{arom}), 127.5 (C_{arom}), 128.4 ($2C_{arom}$), 128.6 ($2C_{arom}$), 130.2 (d, J = 8.5 Hz, $C_{10} + C_{14}$), 131.2 (d, J = 3.6 Hz, C_9), 134.6 ($C_{3'}$), 136.7 ($C_{4'}$), 139.1 ($C_{7'}$), 147.1 (C_{8a}), 155.2 (C_2), 161.9 (C_4), 163.5 (d, J = 250.0 Hz, C_{12}). ES-HRMS $[M+H]^+$ calcd. $(C_{26}H_{23}FN_3O)^+$: 412.1780, found :412.1833.

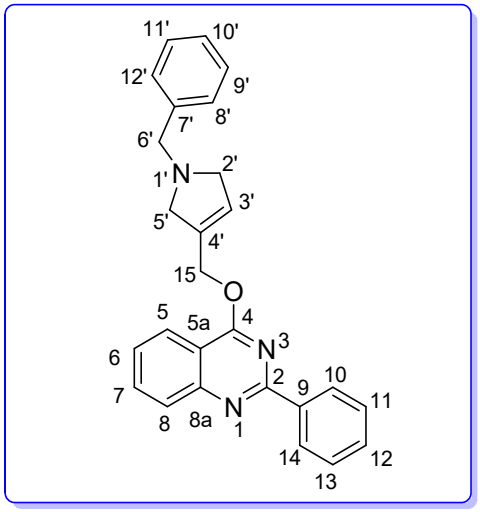
5h: 3-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)methyl)-2-(3-bromophenyl)benzopyrimidin-4(3H)-one



White solid; yield: 80%; mp: 107-109 °C; IR (ATR, cm^{-1}) *v*: 1667.90 (C=O); R_f (cyclohexane/ EtOAc: 7/3) = 0.5. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.36-3.39 (m, 2H, $H_{5'}$), 3.47-3.49 (m, 2H, $H_{2'}$), 3.78 (s, 2H, $H_{6'}$), 4.64 (s, 2H, H_{15}), 5.30-5.31 (m, 1H, $H_{3'}$), 7.24-7.36 (m, 6H, H_{arom}), 7.39-7.41 (m, 1H, H_{arom}), 7.49-7.58 (m, 2H, H_{arom}), 7.66-7.84 (m, 4H, H_{arom}), 8.36 (d, 1H, H_5, J = 8.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 44.5 (C_{15}), 59.6 ($C_{5'}$)-60.3 ($C_{2'}$),

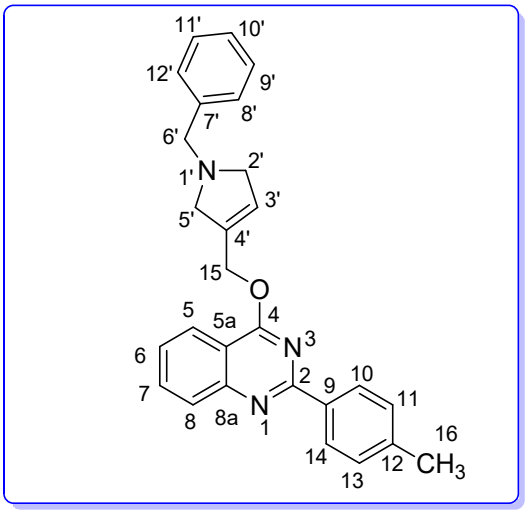
60.4 ($C_{6'}$), 120.7 (C_{5a}), 122.6 (C_{11}), 124.5 (C_{arom}), 126.5 (C_{arom}), 127.0 ($2C_{arom}$), 127.4 (C_{arom}), 127.6 (C_{arom}), 128.3 ($2C_{arom}$), 128.5 ($2C_{arom}$), 130.2 (C_{arom}), 131.2 (C_{arom}), 133.1 (C_{arom}), 134.7 ($C_{3'}$), 136.6 (C_9), 136.8 ($C_{7'}$), 139.1 ($C_{4'}$), 147.0 (C_{8a}), 154.5 (C_2), 161.8 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{26}H_{23}BrN_3O)^+$: 472.0971, found: 472.1021.

6a: 4-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)methoxy)-2-phenylbenzopyrimidine



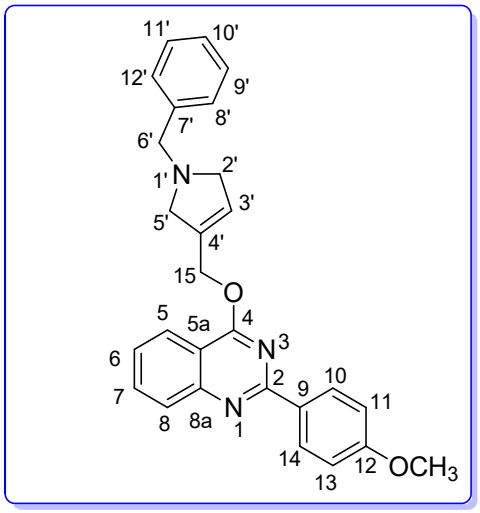
White solid; yield: 85%; mp: 97-99 °C; R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.53-3.56 (m, 2H, $H_{5'}$), 3.62-3.79 (m, 2H, $H_{2'}$), 3.79 (s, 2H, $H_{6'}$), 5.23 (s, 2H, H_{15}), 5.87-5.89 (m, 1H, $H_{3'}$), 7.16-7.32 (m, 4H, H_{arom}), 7.43-7.47 (m, 4H, H_{arom}), 7.72-7.78 (M, 1H, H_6), 7.92 (d, 1H, H_7, J = 8.3 Hz), 8.09 (d, 1H, H_5, J = 7.8 Hz), 8.48-8.51 (m, 2H, H_{arom}).^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 59.8 ($C_{5'}$), 60.2 ($C_{2'}$), 60,4 ($C_{6'}$), 63.6 (C_{15}), 115.2 (C_{5a}), 123.5 (C_{arom}), 125.6 (C_{arom}), 126.5 (C_{arom}), 127.1 (C_{arom}), 128.0 (C_{arom}), 128.4 ($2C_{arom}$), 128.5 ($4C_{arom}$), 128.7 ($2C_{arom}$), 130.5 (C_{arom}), 133.6 ($C_{3'}$), 136.8 ($C_{7'}$), 138.0 (C_9), 139.0 ($C_{4'}$), 151.9 (C_{8a}), 159.9 (C_2), 166.3 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{26}H_{24}N_3O)^+$: 394.1875, found: 394.1926.

6b: 4-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)methoxy)-2-(p-tolyl)benzopyrimidine



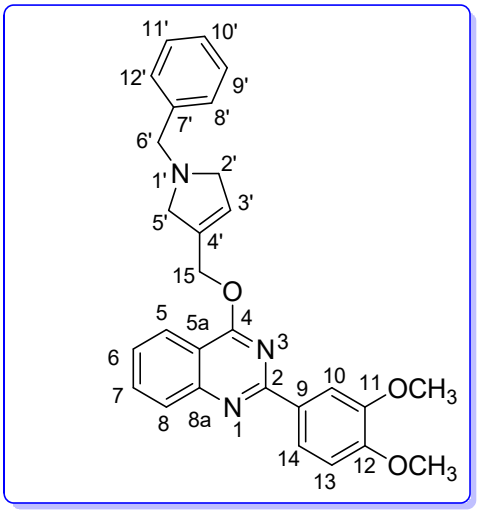
White solid; yield: 87%; mp: 104-106 °C; R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 2.37 (s, 3H, H_{16}), 3.53-3.54 (m, 2H, $H_{5'}$), 3.61-3.64 (m, 2H, $H_{2'}$), 3.79 (s, 2H, $H_{6'}$), 5.23 (s, 2H, H_{15}), 5.88-5.89 (m, 1H), 7.19-7.32 (m, 7H, H_{arom}), 7.43 (t, 1H, H_6, J = 7.4 Hz), 7.74 (t, 1H, H_7, J = 7.2 Hz), 7.90 (d, 1H, H_5, J = 8.4 Hz), 8.08 (d, 1H, H_8, J = 8.1 Hz), 8.38 (d, 2H, H_{arom}, J = 8.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 21.5 (C_{16}), 59.8 ($C_{5'}$), 60.2 ($C_{2'}$), 60.4 ($C_{6'}$), 63.6 (C_{15}), 115.1 (C_{5a}), 123.4 (C_{arom}), 125.6 (C_{arom}), 126.2 (C_{arom}), 127.1 (C_{arom}), 127.8 (C_{arom}), 128.4 (4C_{arom}), 128.7 (2C_{arom}), 129.2 (2C_{arom}), 133.5 ($C_{3'}$), 135.5 (C_9), 136.8 (C_{12}), 139.2 ($C_{7'}$), 140.7($C_{4'}$), 152.0 (C_{8a}), 160.0 (C_2), 166.2 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{27}H_{26}N_3O)^+$: 408.2031, found: 408.2092.

6c: 4-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)methoxy)-2-(p-tolyl)benzopyrimidine



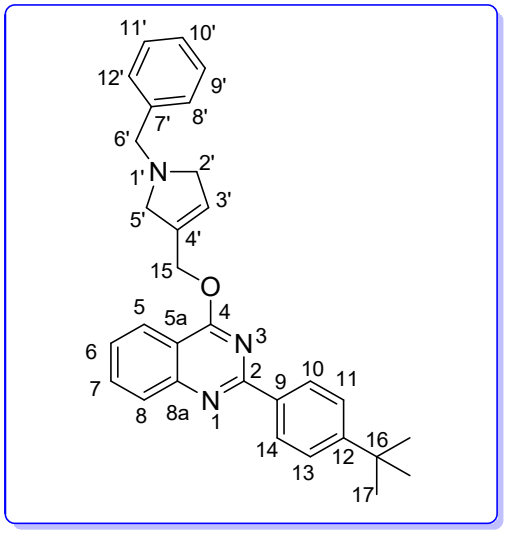
Yellow oil; yield: 63%; R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.47-3.50 (m, 2H, $H_{5'}$), 3.57-3.60 (m, 2H, $H_{2'}$), 3.74 (s, 2H, $H_{6'}$), 3.78 (s, 3H, OCH_3), 5.16 (s, 2H, H_{15}), 5.82-5.84 (m, 1H, $H_{3'}$), 6.89 (d, 2H, H_{arom}, J = 7.4 Hz), 7.12-7.28 (m, 5H, H_{arom}), 7.33-7.35 (m, 1H, $H_{6,}$), 7.65-7.70 (m, 1H, H_7), 7.83 (d, 1H, H_5, J = 8.4 Hz), 8.00-8.03 (m, 1H, H_8), 8.38-8.43 (m, 2H, H_{arom}). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 55.4 (OCH_3), 59.8- ($C_{5'}$), 60.2 ($C_{2'}$), 60.4 ($C_{6'}$), 63.5 (C_{15}), 113.7 (2C_{arom}), 114.9 (C_{5a}), 123.5 (C_{arom}), 125,6 (C_{arom}), 126.0 (C_{arom}), 127.1 (C_{arom}), 127.7 (C_{arom}), 128.4 (2C_{arom}), 128.7 (2C_{arom}), 130.1 (2C_{arom}), 130.7 (C_9), 133.5 ($C_{3'}$), 136.9 (C_7), 139.1 ($C_{4'}$), 152.1 (C_{8a}), 159.7 (C_2), 161.7 (C_{12}), 166.1 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{27}H_{26}N_3O_2)^+$: 424.1980, found: 424.2041.

6d: 4-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)methoxy)-2(3,4dimethoxyphenyl)benzopyrimidine



White solid; yield: 65%; mp: 102-104 °C; R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.54-3.57 (m, 2H, $H_{5'}$), 3.62-3.65 (m, 2H, $H_{2'}$), 3.79 (s, 2H, $H_{6'}$), 3.90 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 5.21 (s, 2H, H_{15}), 5.87-5.88 (m, 1H, $H_{3'}$), 6.89 (d, 1H, H_{arom}, J = 8.4 Hz), 7.20-7.32 (m, 5H, H_{arom}), 7.38-7.43 (m, 1H, H_6), 7.70-7.75 (m, 1H, H_7), 7.88 (d, 1H, H_5, J = 8.3 Hz), 8.05-8.12 (m, 3H, H_{arom}). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 55.9 (OCH_3), 56.0 (OCH_3), 59.8- ($C_{5'}$), 60.2 ($C_{2'}$), 60.3 ($C_{6'}$), 63.4 (C_{15}), 110.6 (C_{arom}), 111.0 (C_{arom}), 114.9 (C_{5a}), 121.9 (C_{arom}), 123.4 (C_{arom}), 125.6 (C_{arom}), 126.1 (C_{arom}), 127.2 (C_{arom}), 127.7 (C_{arom}), 128.4 ($2C_{arom}$), 128.7 ($2C_{arom}$), 130.9 (C_9), 133.5 ($C_{3'}$), 136.8 ($C_{7'}$), 138.8 ($C_{4'}$), 148.9 (C_{12}), 151.3 (C_{11}), 152.0 (C_{8a}), 159.6 (C_2), 166.1 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{26}H_{28}N_3O)^+$: 454.2086, found: 454.2139.

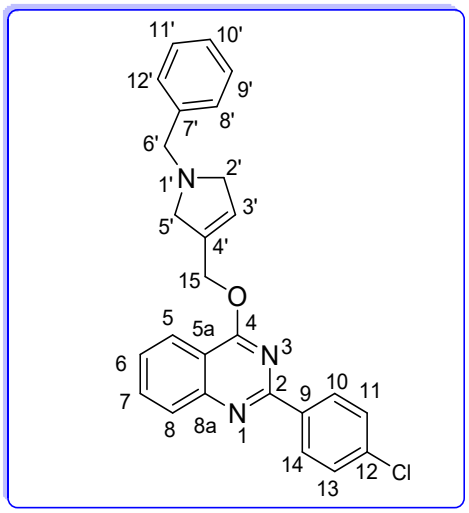
6e: 4-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)methoxy)-2-(4-(tert-butyl)phenyl)benzopyrimidine



Yellow oil; yield: 59%; R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 1.32 (s, 9H, H_{17}), 3.55 (s, 2H, $H_{5'}$), 3.64 (d, 2H, $H_{2'}$, J = 6.1 Hz), 3.80 (s, 2H, $H_{6'}$), 5.23

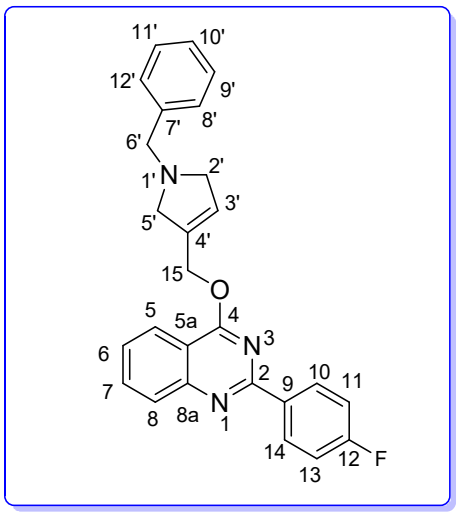
(s, 2H, H_{15}), 5.88 (t, 1H, $H_{3'}$, J = 6.1 Hz), 7.21-7.33 (m, 5H, H_{arom}), 7.41-7.47 (m, 3H, H_{arom}), 7.72-7.77 (m, 1H, H_7), 7.91 (d, 1H, H_5, J = 8.4 Hz), 8.07-8.10 (m, 1H, H_8), 8.38-8.42 (m, 2H, H_{arom}). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 31.2 (C_{17}), 34.8 (C_{16}), 59.8-60.2 ($C_{5'}$+$C_{2'}$), 60.3 ($C_{6'}$), 63.5 (C_{15}), 115.1 (C_{5a}), 123.4 (C_{arom}), 125.4 (2C_{arom}), 125.6 (C_{arom}), 126.2 (C_{arom}), 127.1 (C_{arom}), 127.9 (C_{arom}), 128.2 (2C_{arom}), 128.4 (2C_{arom}), 128.7 (2C_{arom}), 133.5 ($C_{3'}$), 135.4 (C_9), 136.9 ($C_{7'}$), 138.8 ($C_{4'}$), 152.1 (C_{8a}), 153.8 (C_{12}), 160.0 (C_2), 166.2 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{30}H_{32}N_3O)^+$: 450.2501, found: 450.2552.

6f: 4-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)methoxy)-2-(4-chlorophenyl)benzopyrimidine



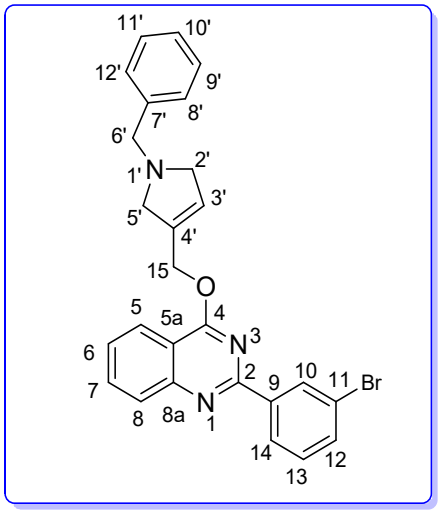
White solid; yield: 65%; mp: 123-125 °C; R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.52-3.55 (m, 2H, $H_{5'}$), 3.60-3.63 (m, 2H, $H_{2'}$), 3.78 (s, 2H, $H_{6'}$), 5.20 (s, 2H, H_{15}), 5.87-5.88 (m, 1H, $H_{3'}$), 7.19-7.31 (m, 5H, H_{arom}), 7.37-7.47 (m, 3H, H_{arom}), 7.72-7.78 (m, 1H, H_7), 7.89 (d, 1H, H_5, J = 8.4 Hz), 8.08 (d, 1H, H_8, J = 8.1 Hz), 8.41-8.45 (m, 2H, H_{arom}). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 59.8 ($C_{5'}$), 60.2 ($C_{2'}$), 60.4 ($C_{6'}$), 63.7 (C_{15}), 115.2 (C_{5a}), 123.5 (C_{arom}), 125.8 (C_{arom}), 126.7 (C_{arom}), 127.1 (C_{arom}), 127.9 (C_{arom}), 128.4 (2C_{arom}), 128.6 (2C_{arom}), 128.7 (2C_{arom}), 129.7 (2C_{arom}), 133.7 ($C_{3'}$), 136.5 (C_9), 136.6 (C_{12}), 136.7 ($C_{7'}$), 139.1 ($C_{4'}$), 151.8 (C_{8a}), 158.8 (C_2), 166.3 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{26}H_{23}ClN_3O)^+$: 428.1484, found: 428.1534.

6g: 4-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)methoxy)-2-(4-fluorophenyl)benzopyrimidine



White solid; yield: 81%; mp: 96-98 °C; R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.53-3.55 (m, 2H, $H_{5'}$), 3.60-3.63 (m, 2H, $H_{2'}$), 3.79 (s, 2H, $H_{6'}$), 5.21 (s, 2H, H_{15}), 5.87-5.88 (m, 1H, $H_{3'}$), 7.09 (t, 2H, H_{arom}, J = 8.7 Hz), 7.18-7.31 (m, 5H, H_{arom}), 7.41-7.44 (m, 1H, H_6), 7.72-7.77 (m, 1H, H_7), 7.88 (d, 1H, H_5, J = 8.3 Hz), 8.07-8.10 (m, 1H, H_8), 8.46-8.51 (m, 2H, H_{arom}). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 59.8($C_{5'}$ or $C_{2'}$), 60.2 ($C_{5'}$ or $C_{2'}$), 60.4 ($C_{6'}$), 63.7 (C_{15}), 115.0 (C_{arom}), 115.3 (d, J = 21.6 Hz, C_{11} + C_{13}), 123.5 (C_{arom}), 125.8 (C_{arom}), 126.5 (C_{arom}), 127.1 (C_{arom}), 127.8 (C_{arom}), 128.4 (2C_{arom}), 128.7 (2C_{arom}), 130.5 (d, J = 8.6 Hz, C_{10} + C_{14}), 133.7 (C_{arom}), 134.2 (d, J = 3 Hz, C_9), 136.8 ($C_{4'}$), 139.0 (C_{arom}), 151.9 (C_{8a}), 158.9 (C_2), 164.6 (d, J = 250.2 Hz, C_{12}), 166.3 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{26}H_{23}FN_3O)^+$: 412.1780, found: 412.1833.

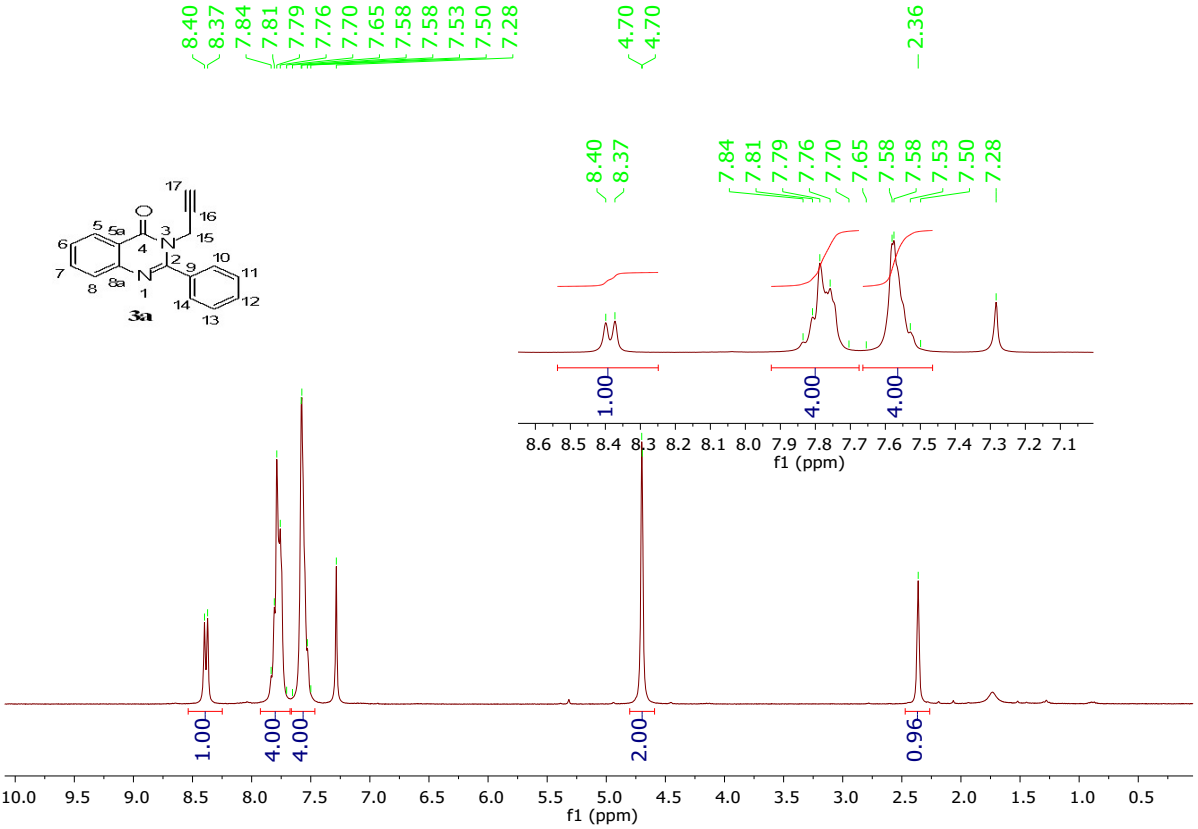
6h: 4-((1-benzyl-2,5-dihydro-1H-pyrrol-3-yl)methoxy)-2-(3-bromophenyl)benzopyrimidine



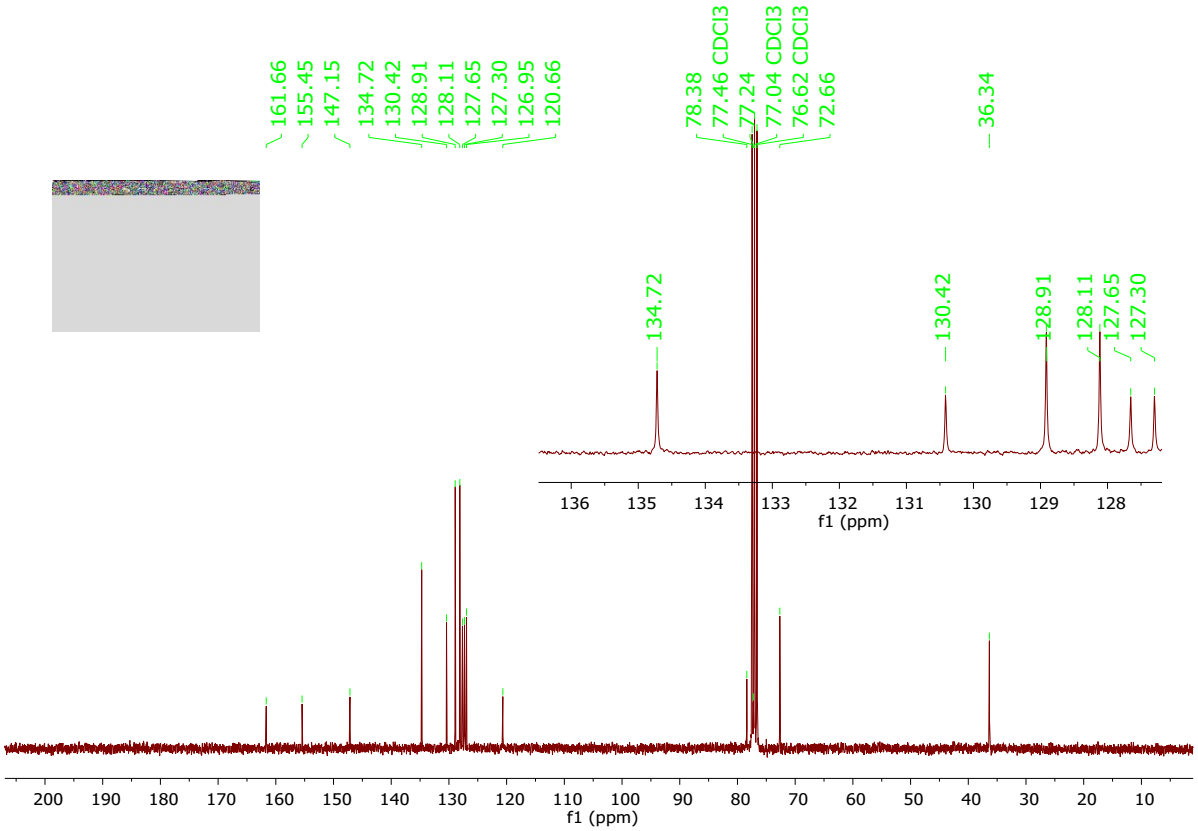
White solid; yield: 70%; mp: 99-101 °C; R_f (cyclohexane/ EtOAc: 9/1) = 0.5. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.54-3.56 (m, 2H, $H_{5'}$), 3.61-3.64 (m, 2H, $H_{2'}$), 3.80 (s, 2H, $H_{6'}$), 5.22 (s, 2H, H_{15}), 5.88-5.89 (m, 1H, $H_{3'}$), 7.21-7.33 (m, 6H, H_{arom}), 7.44-7.50 (m, 1H, H_6), 7.53-7.56 (m, 1H, H_7), 7.74-7.80 (m, 1H, H_{arom}), 7.92 (d, 1H, H_5, J = 8.3 Hz), 8.09-8.12 (m, 1H, H_8), 8.41-8.45 (m, 1H, H_{arom}), 8.64 (t, 1H, H_{10}, J = 1.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) = 59.8 ($C_{5'}$), 60.1 ($C_{2'}$), 60.4 ($C_{6'}$), 63.8 (C_{15}), 115.3 (C_{5a}), 122.7 (C_{11}), 123.5 (C_{arom}), 125.8 (C_{arom}), 126.8 (C_{arom}), 126.9 (C_{arom}),127.1 (C_{arom}), 128.0 (C_{arom}), 128.4 (2C_{arom}), 128.7 (2C_{arom}), 129.9

(C_{arom}), 131.4 (C_{arom}), 133.3 (C_{arom}), 133.7 ($C_{3'}$), 136.7 (C_9), 139.1 ($C_{7'}$), 140.1 ($C_{4'}$), 151.8 (C_{8a}), 158.4 (C_2), 166.4 (C_4). ES-HRMS $[M+H]^+$ calcd. $(C_{26}H_{23}BrN_3O)^+$: 472.0971, found: 472.1021.

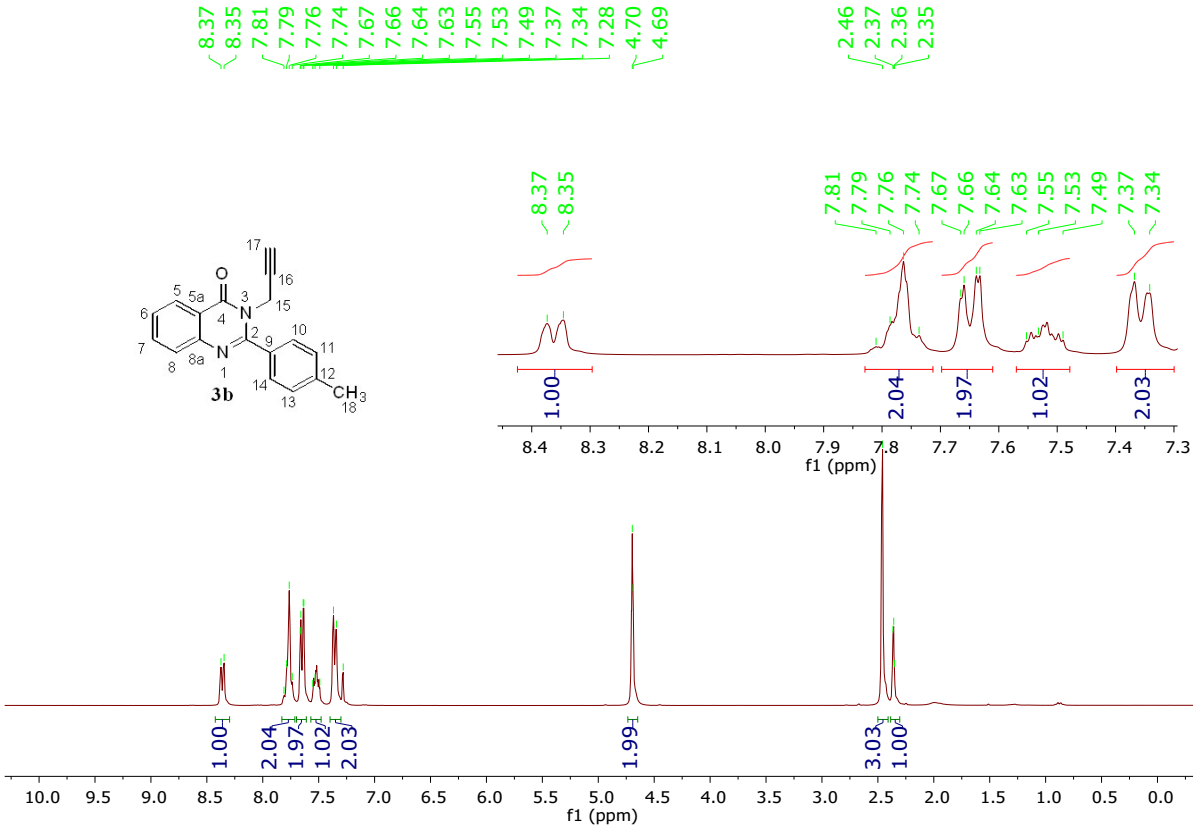
V. Copies of NMR spectra



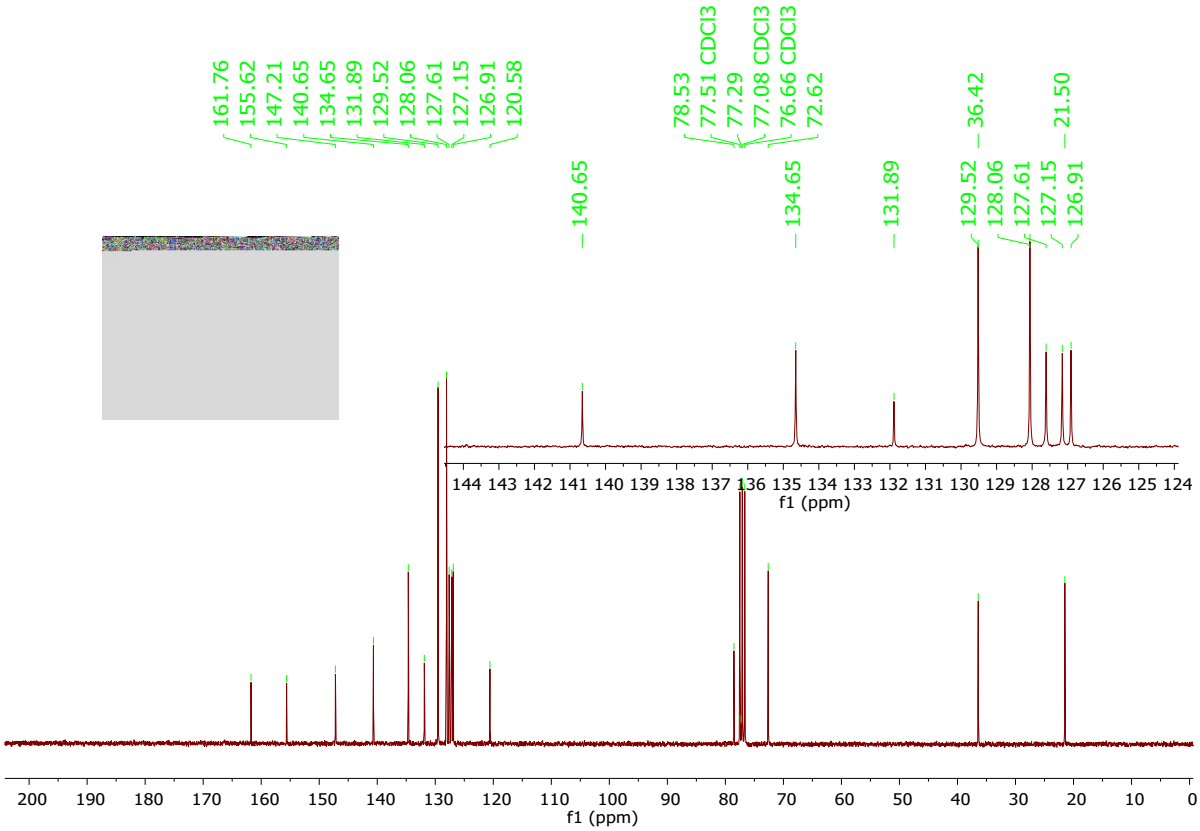
^{1}H NMR spectrum of compound 3a



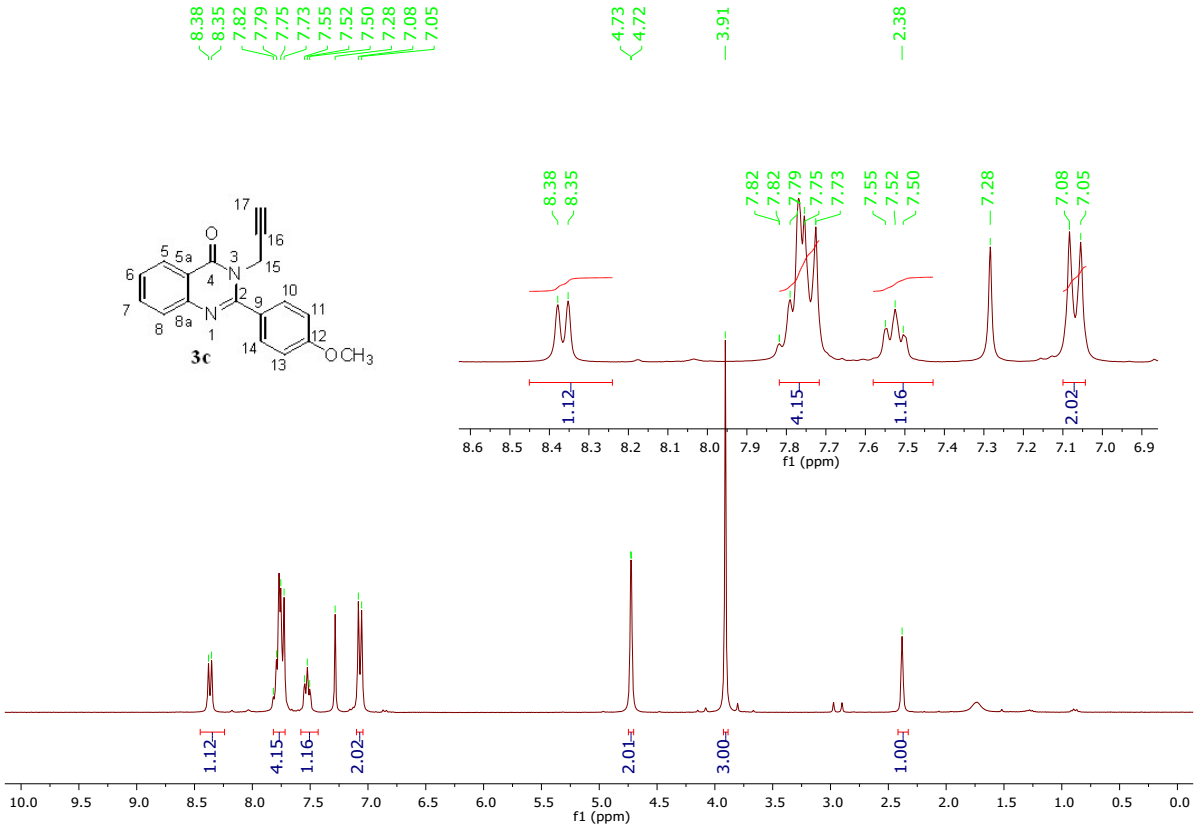
^{13}C NMR spectrum of compound 3a



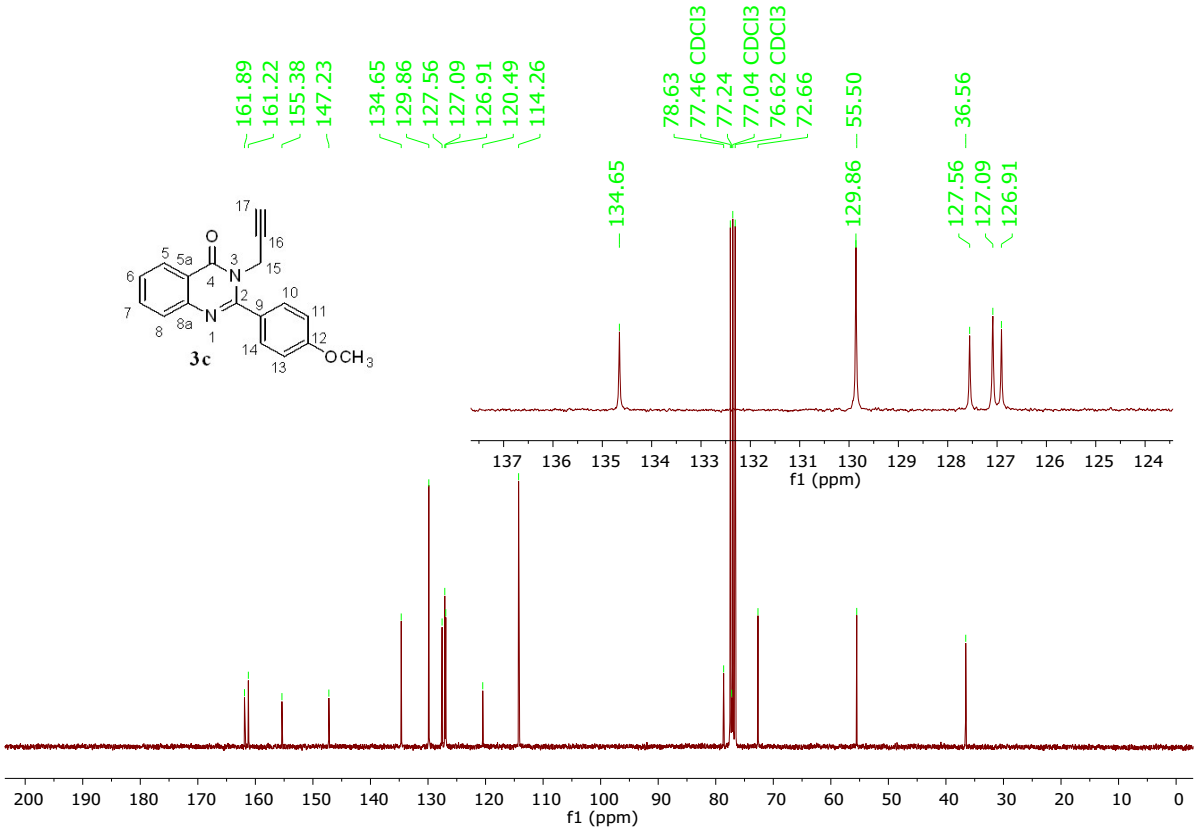
^{1}H NMR spectrum of compound 3b



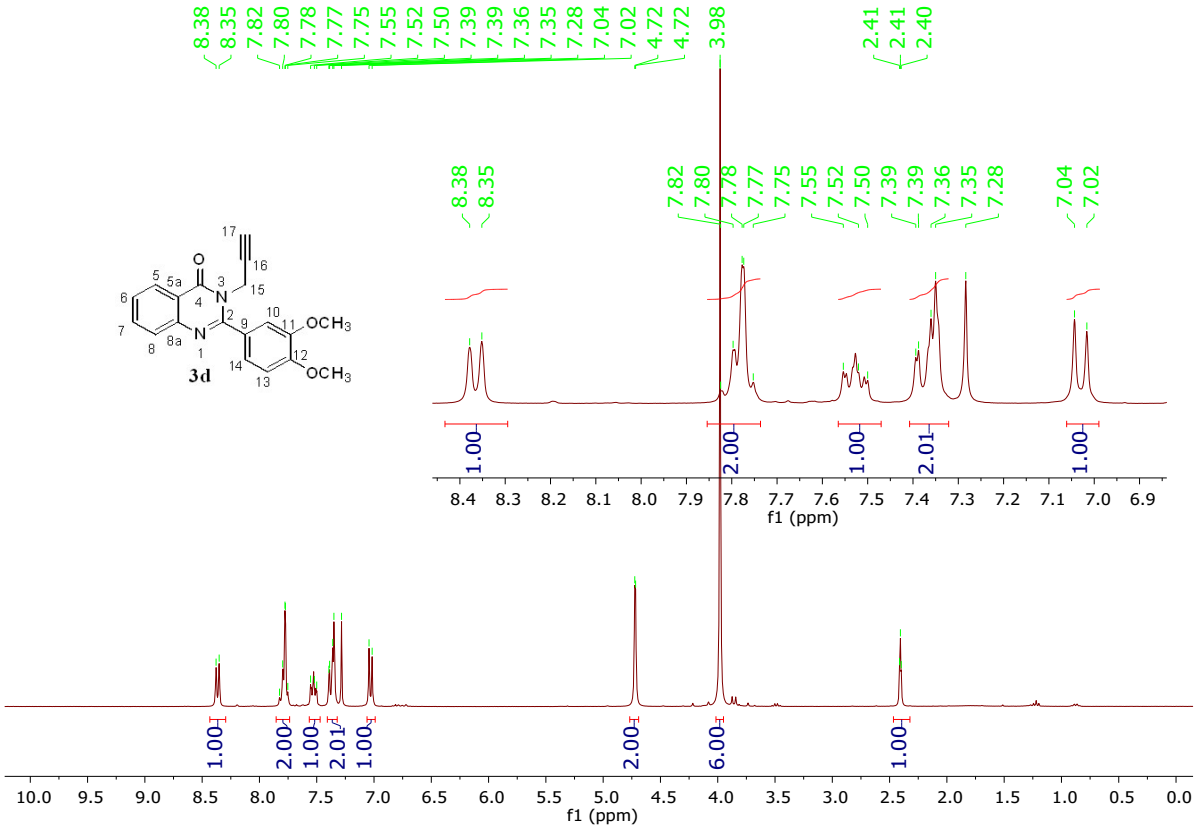
^{13}C NMR spectrum of compound 3b



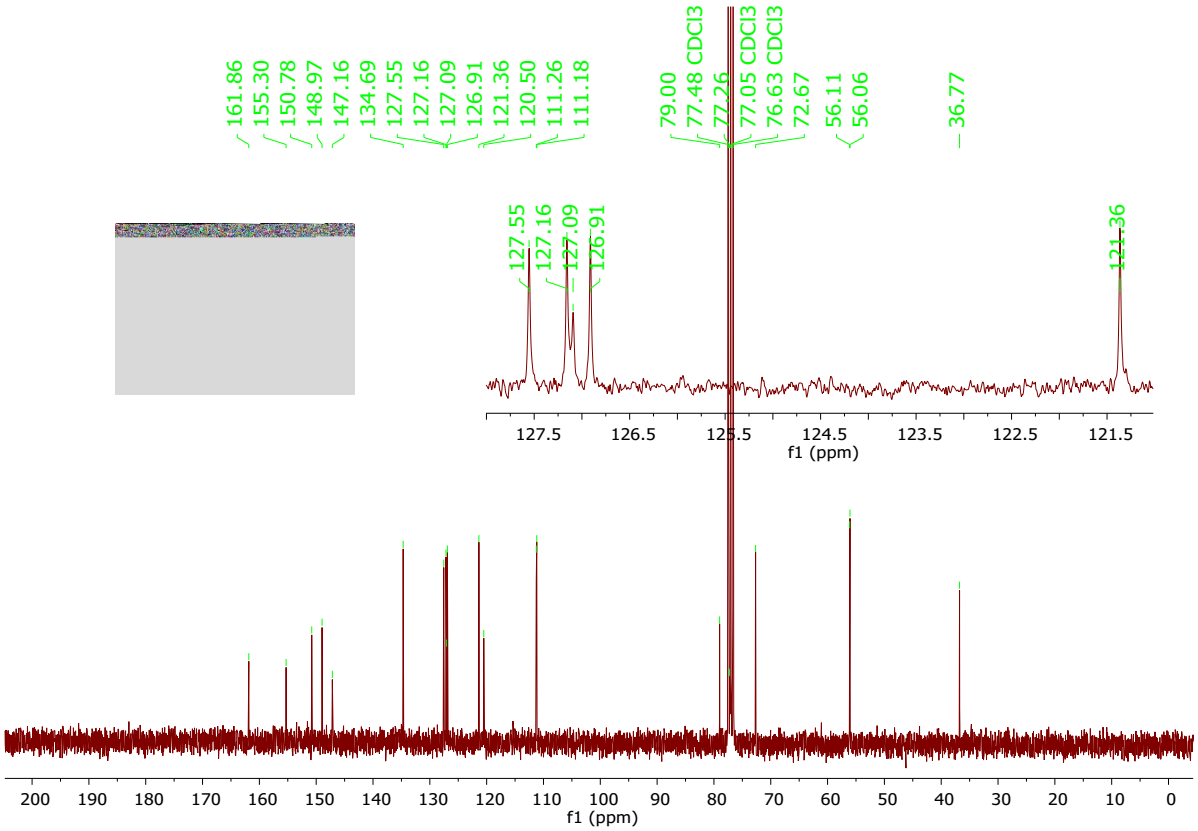
^{1}H NMR spectrum of compound 3c



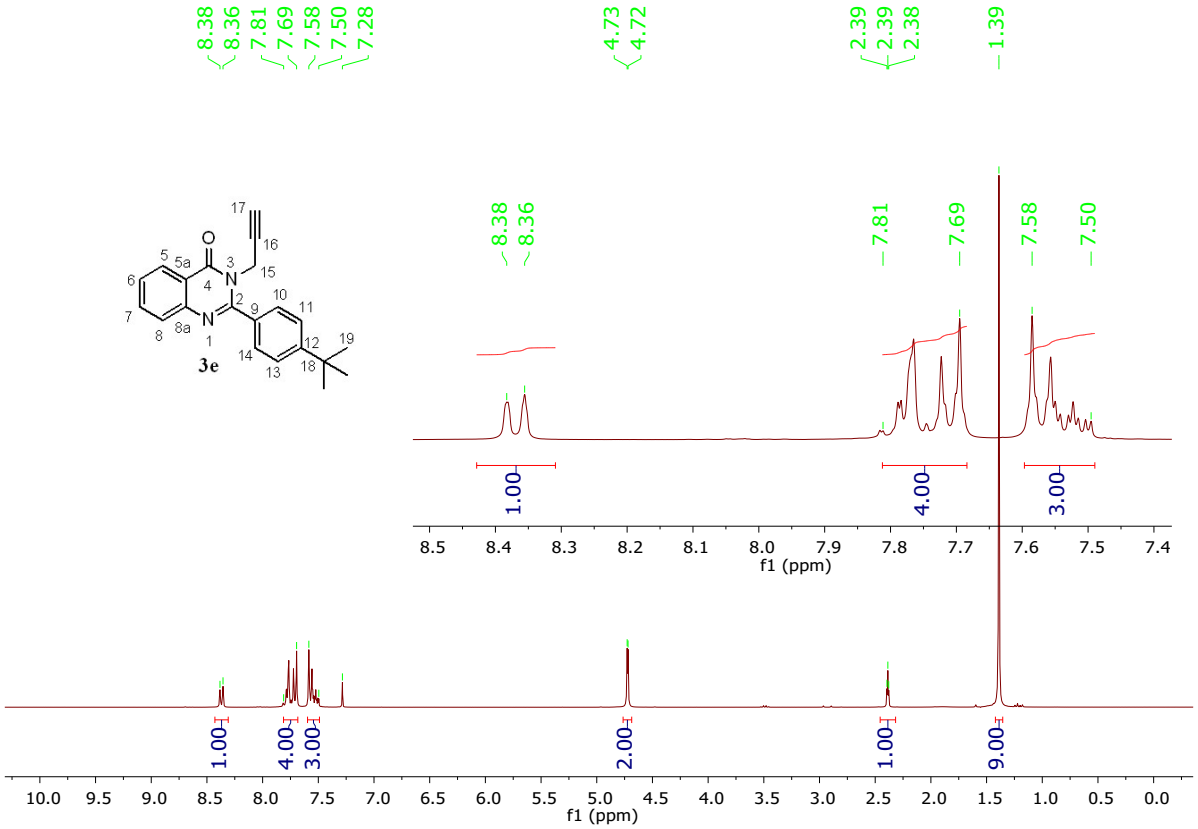
^{13}C NMR spectrum of compound 3c



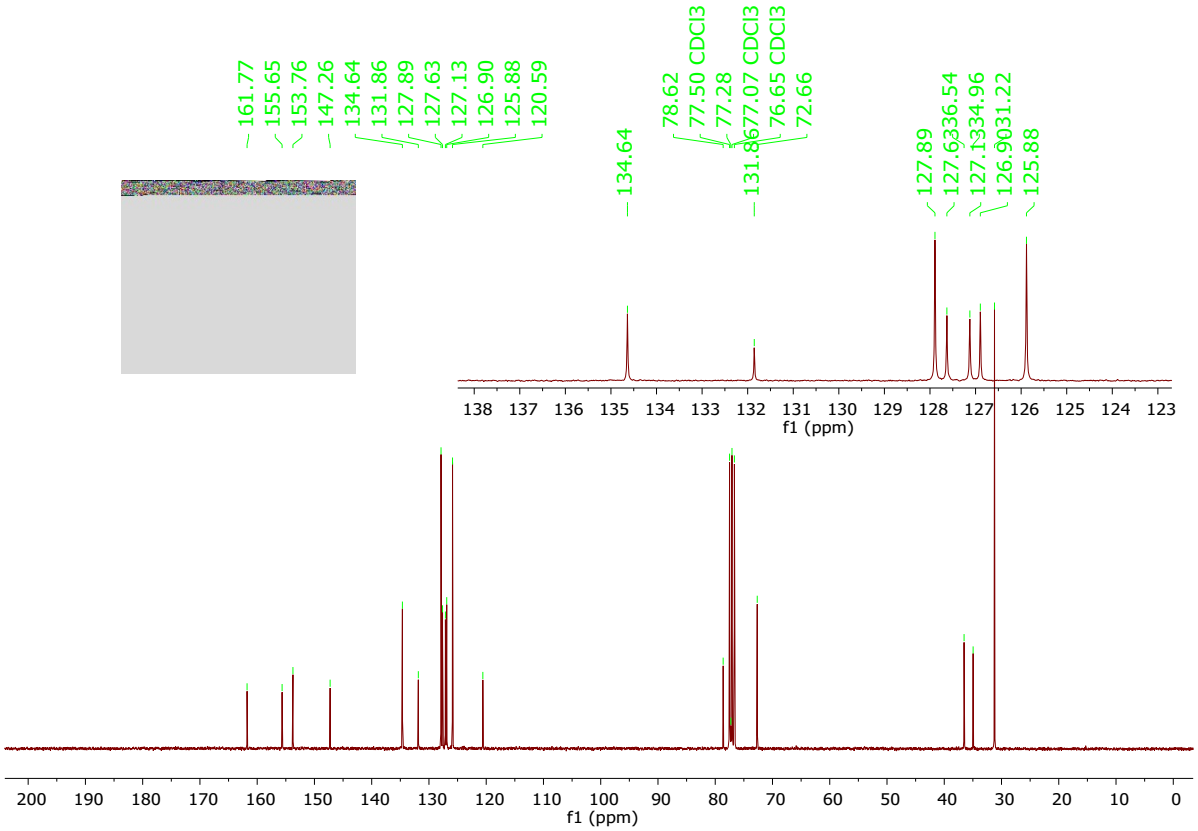
^{1}H NMR spectrum of compound 3d



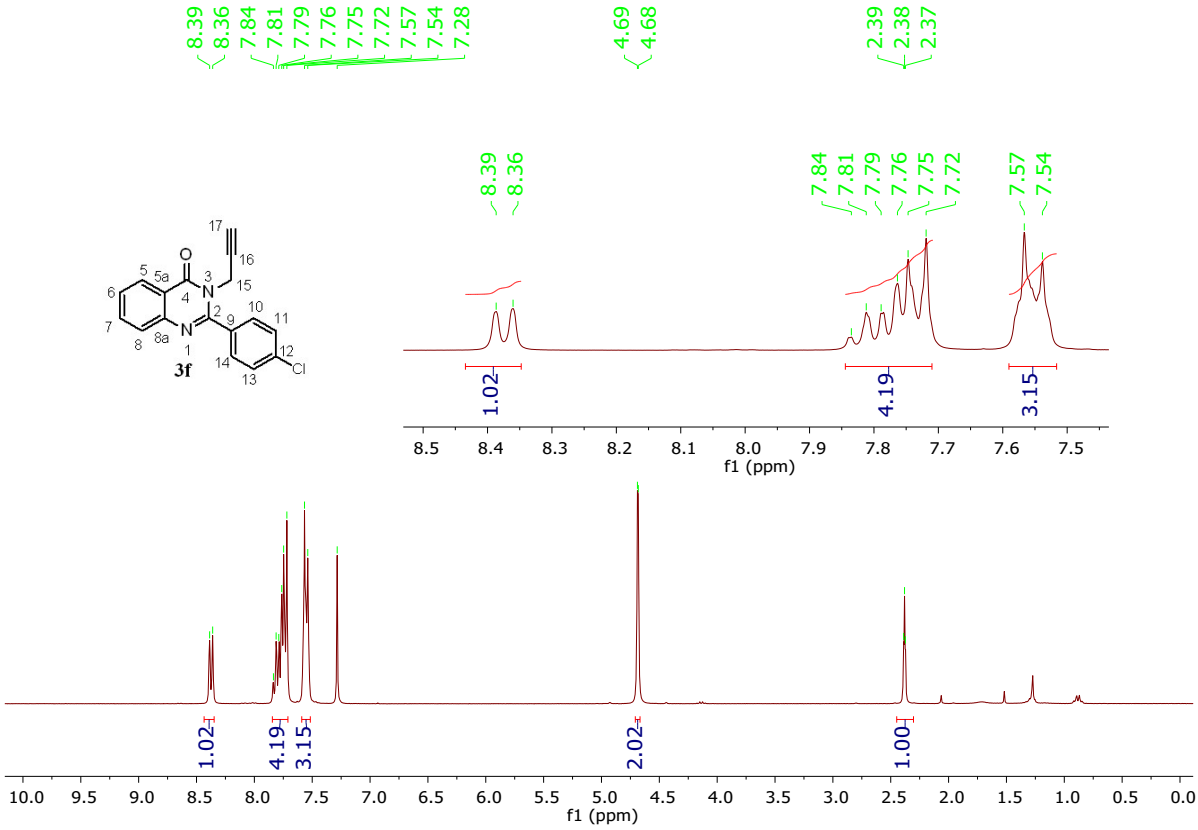
^{13}C NMR spectrum of compound 3d



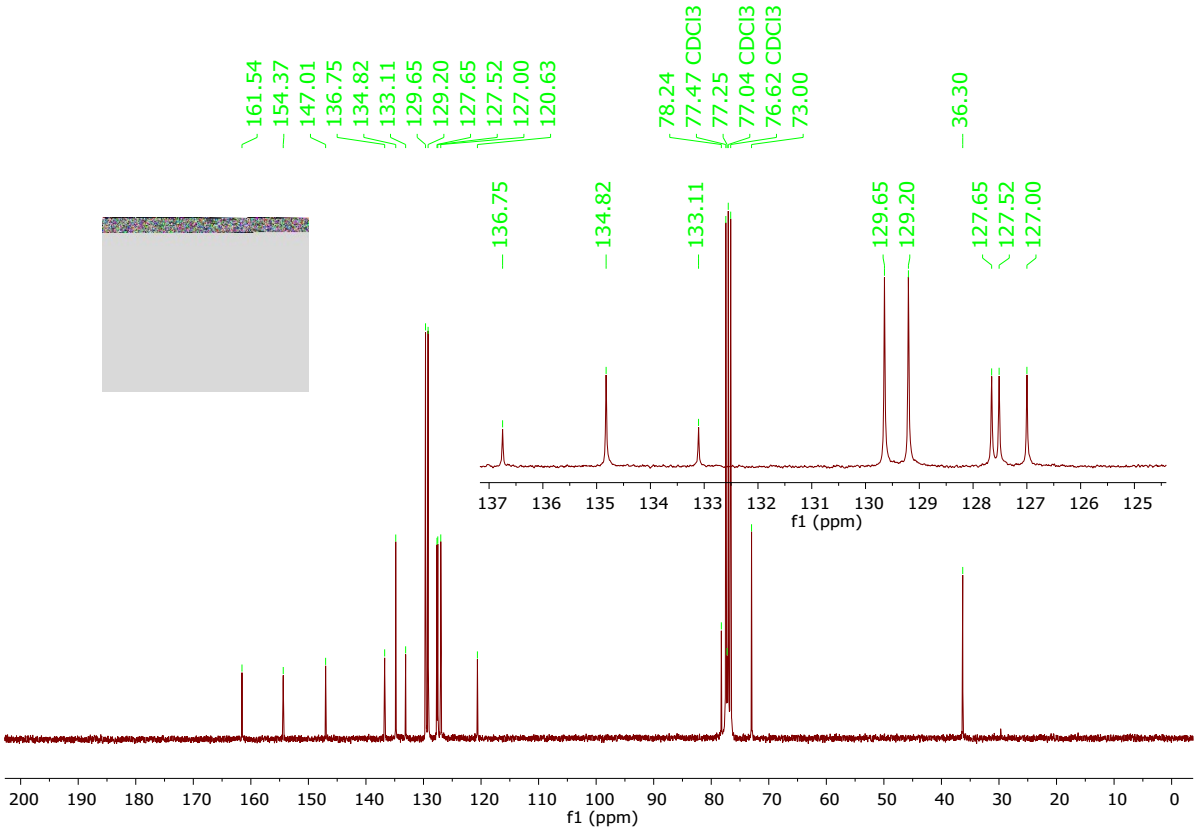
^{1}H NMR spectrum of compound 3e



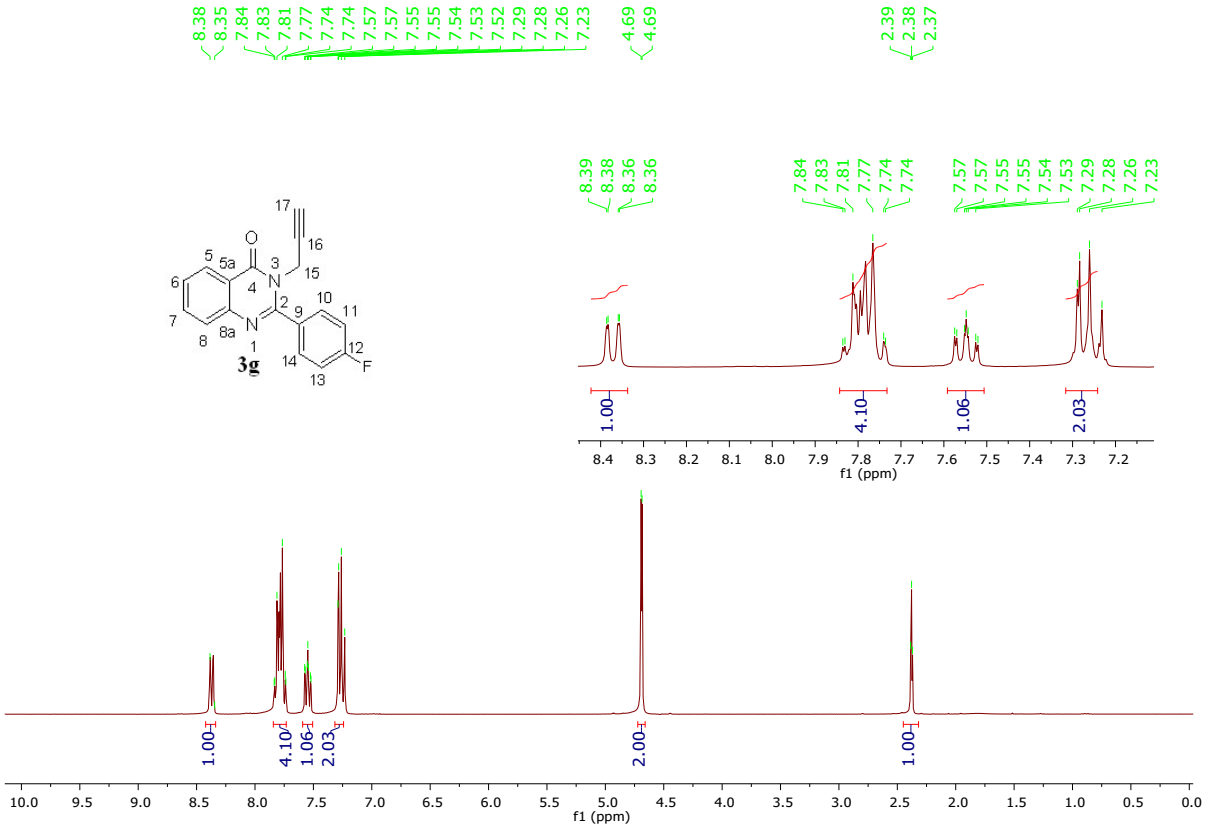
^{13}C NMR spectrum of compound 3e



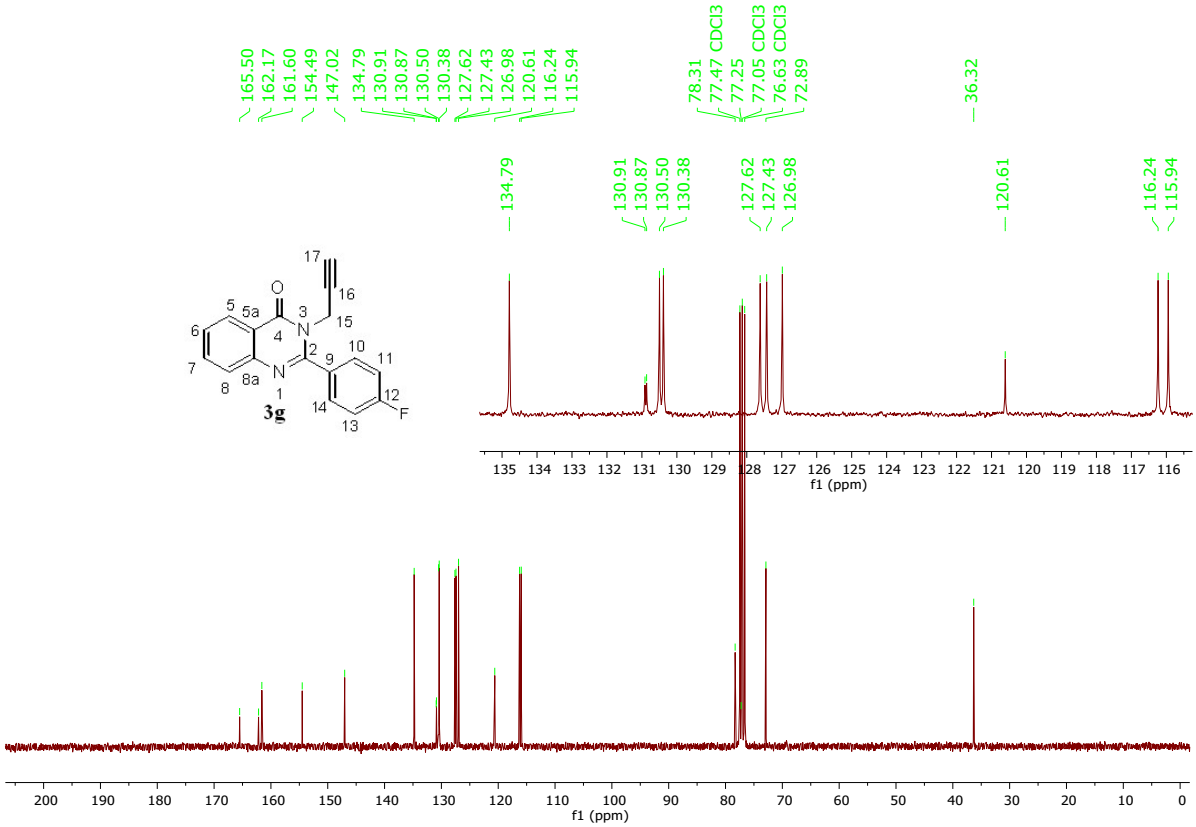
^{1}H NMR spectrum of compound 3f



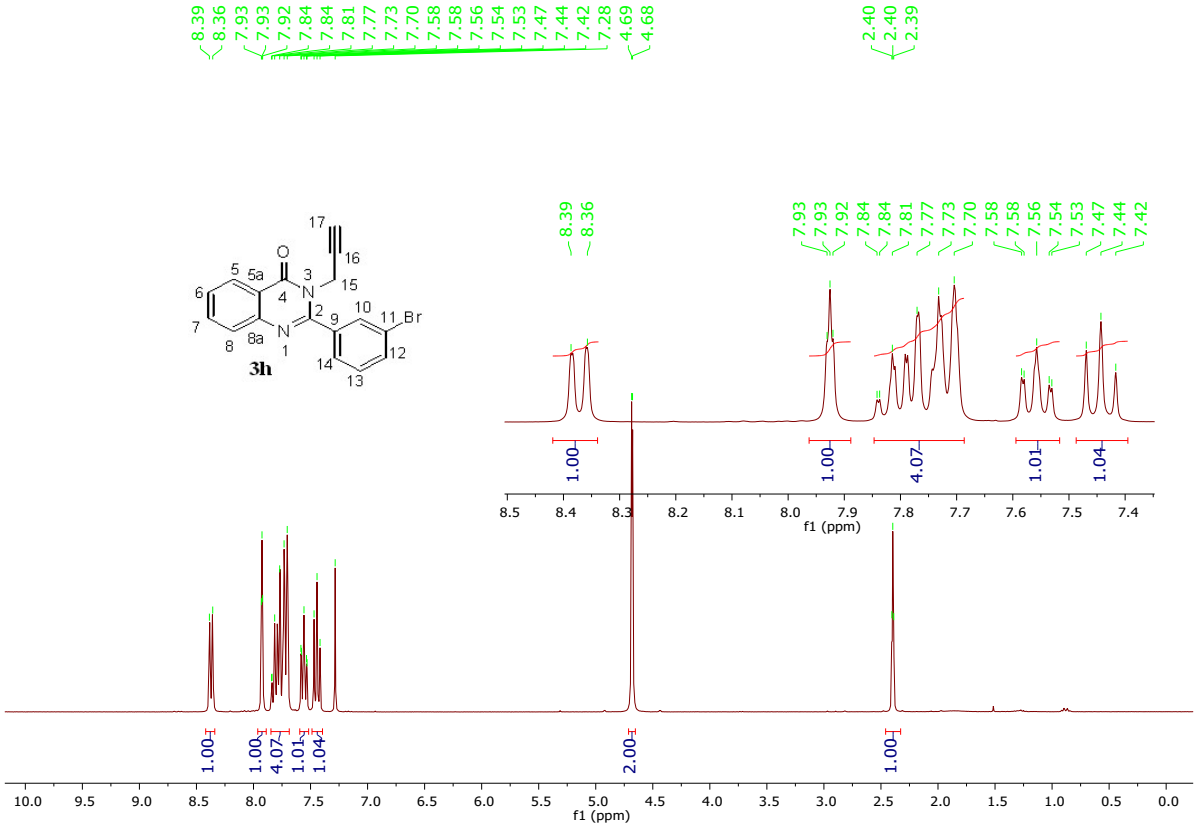
^{13}C NMR spectrum of compound 3f



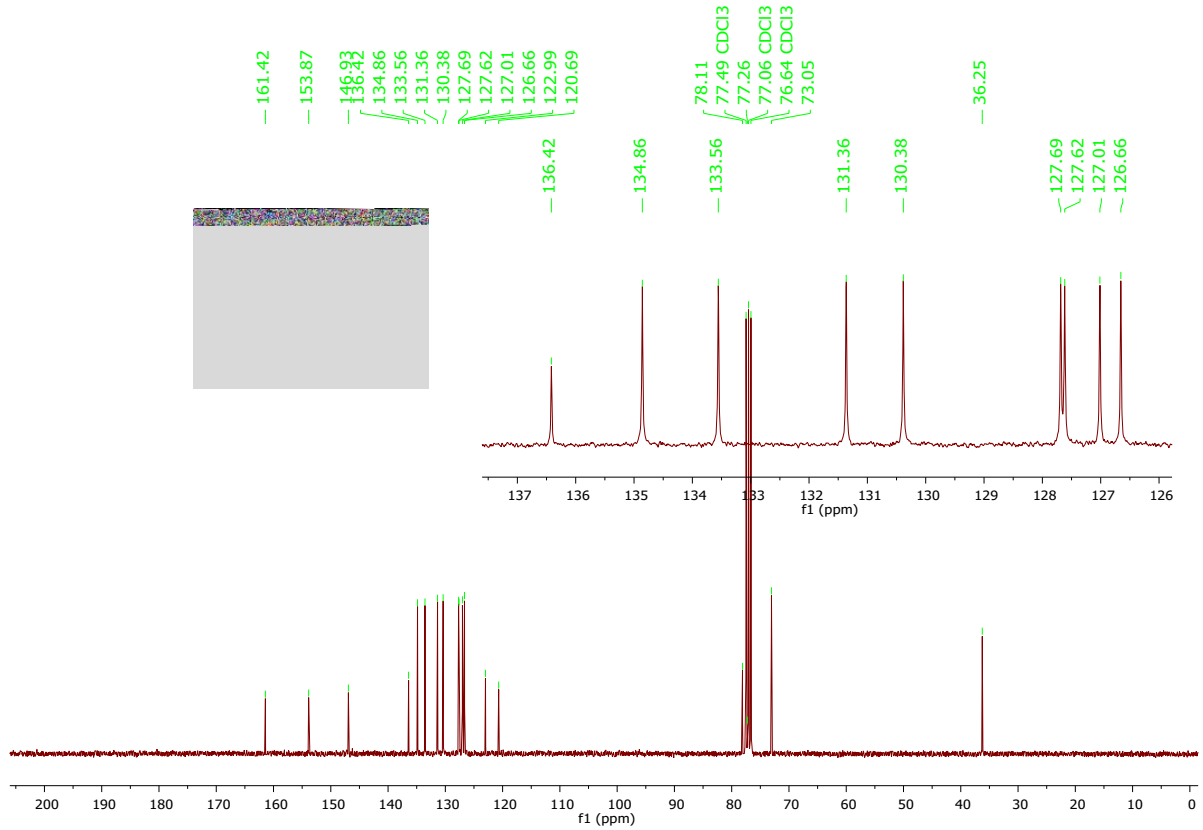
^{1}H NMR spectrum of compound 3g



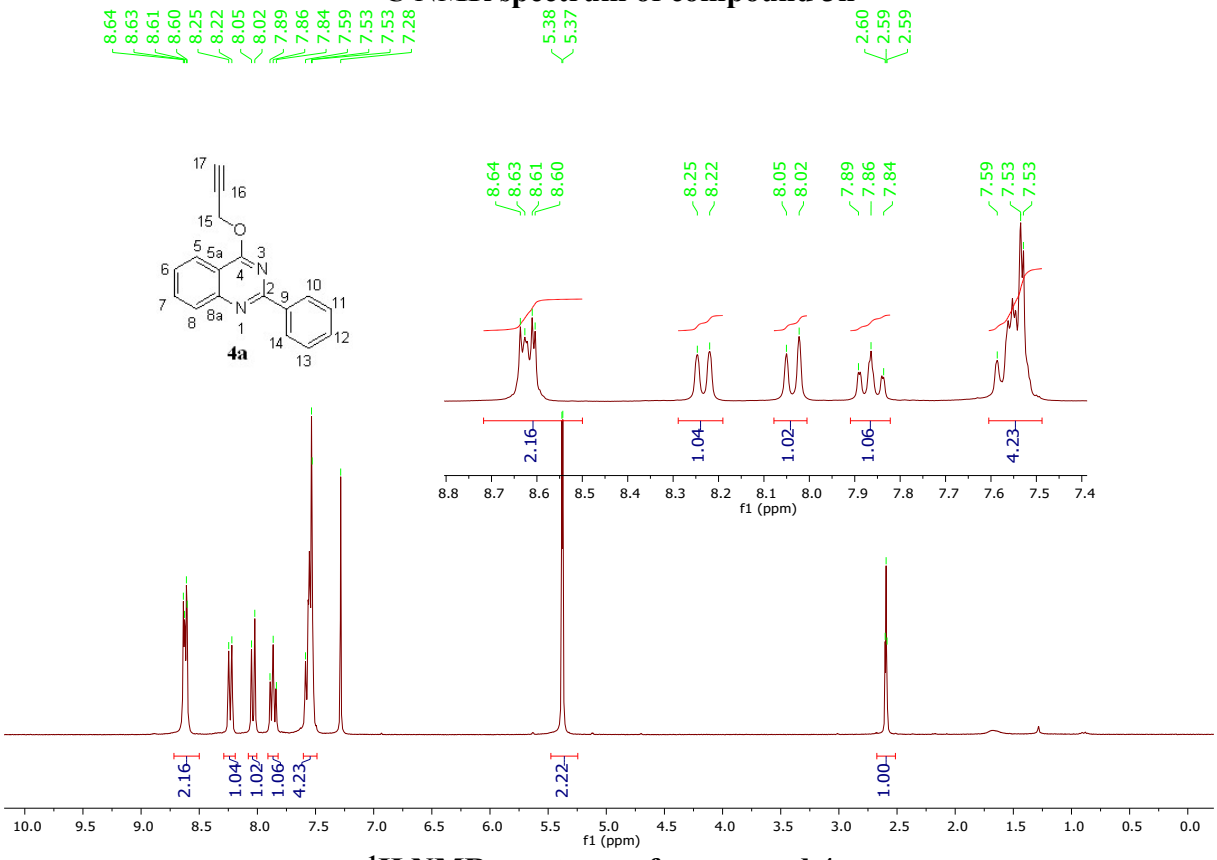
^{13}C NMR spectrum of compound 3g



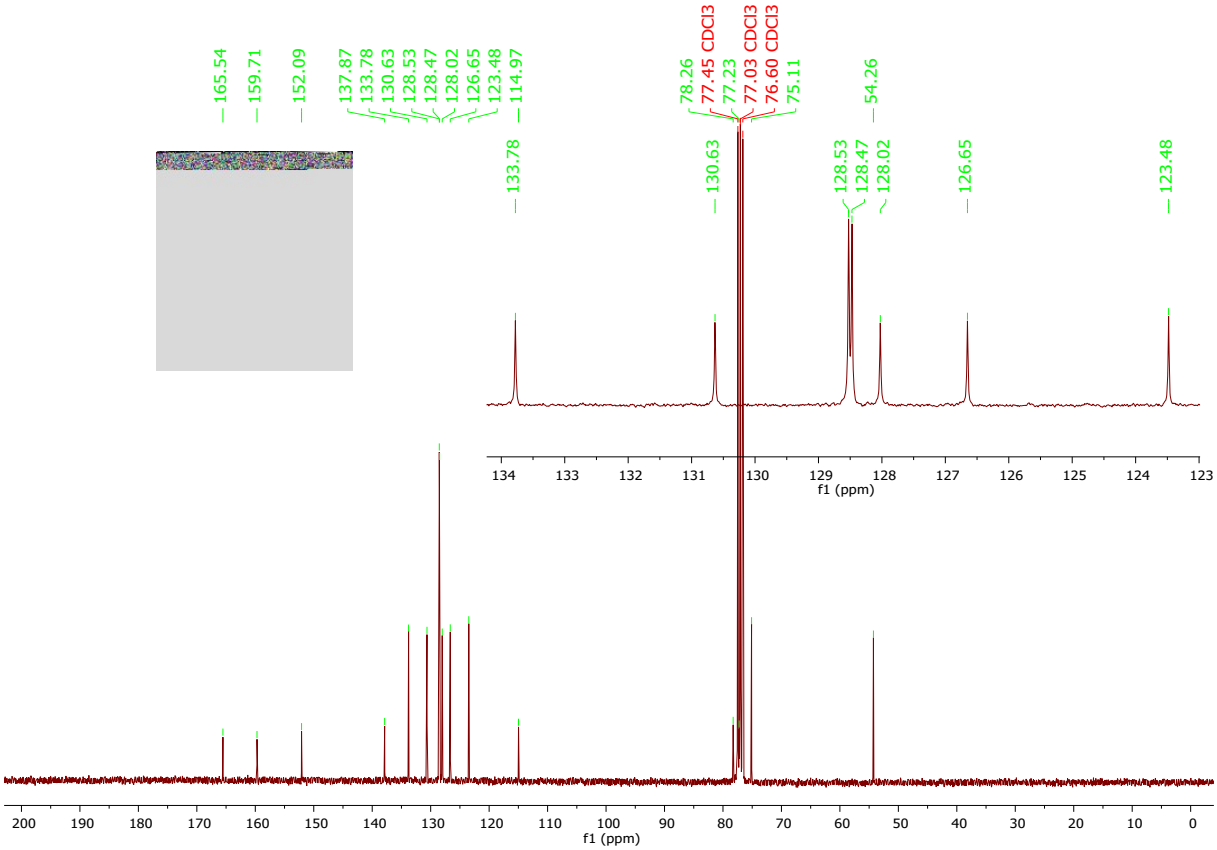
^{1}H NMR spectrum of compound 3h



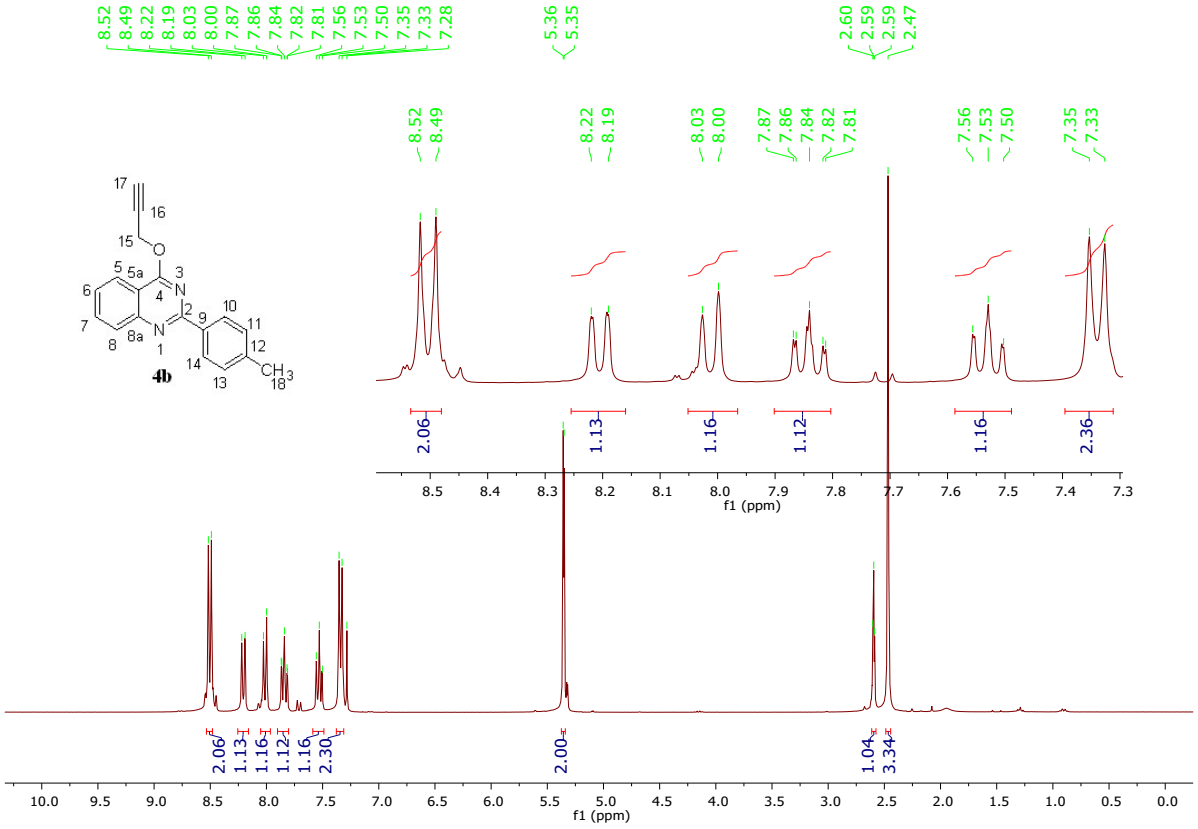
^{13}C NMR spectrum of compound 3h



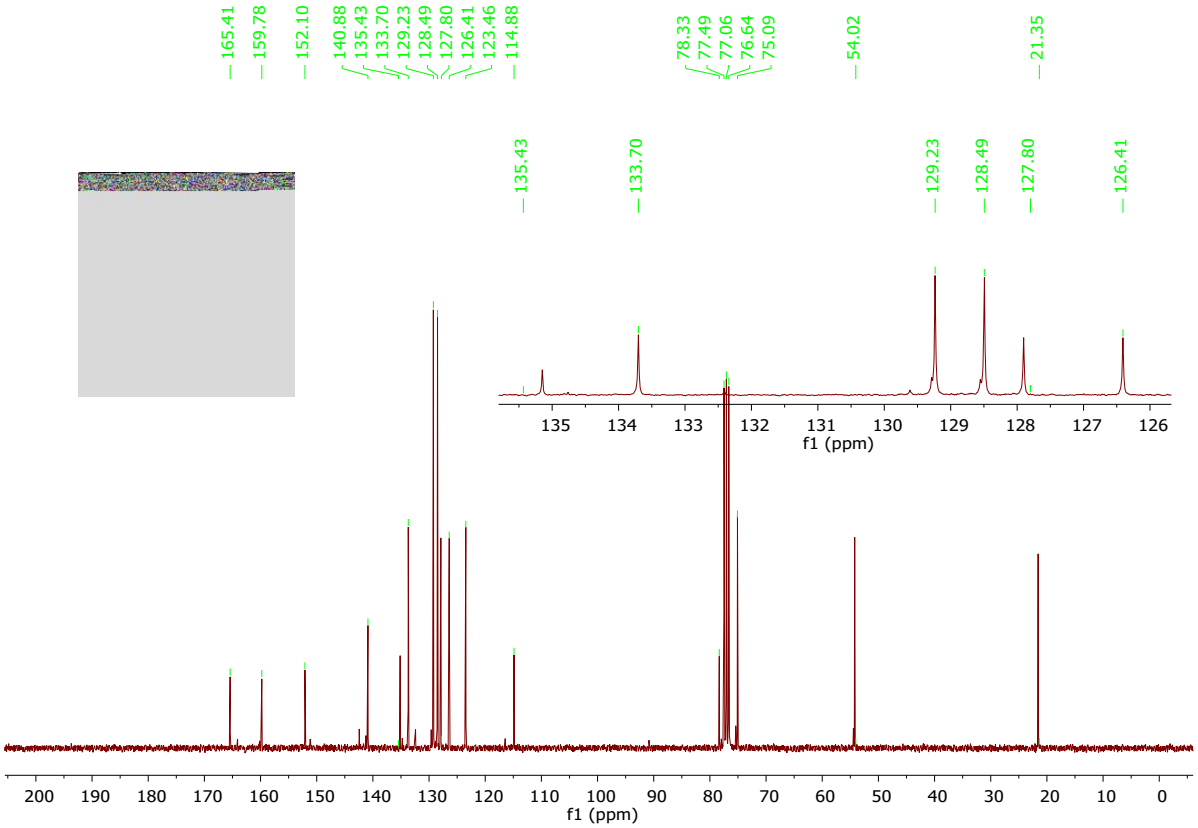
^{1}H NMR spectrum of compound 4a



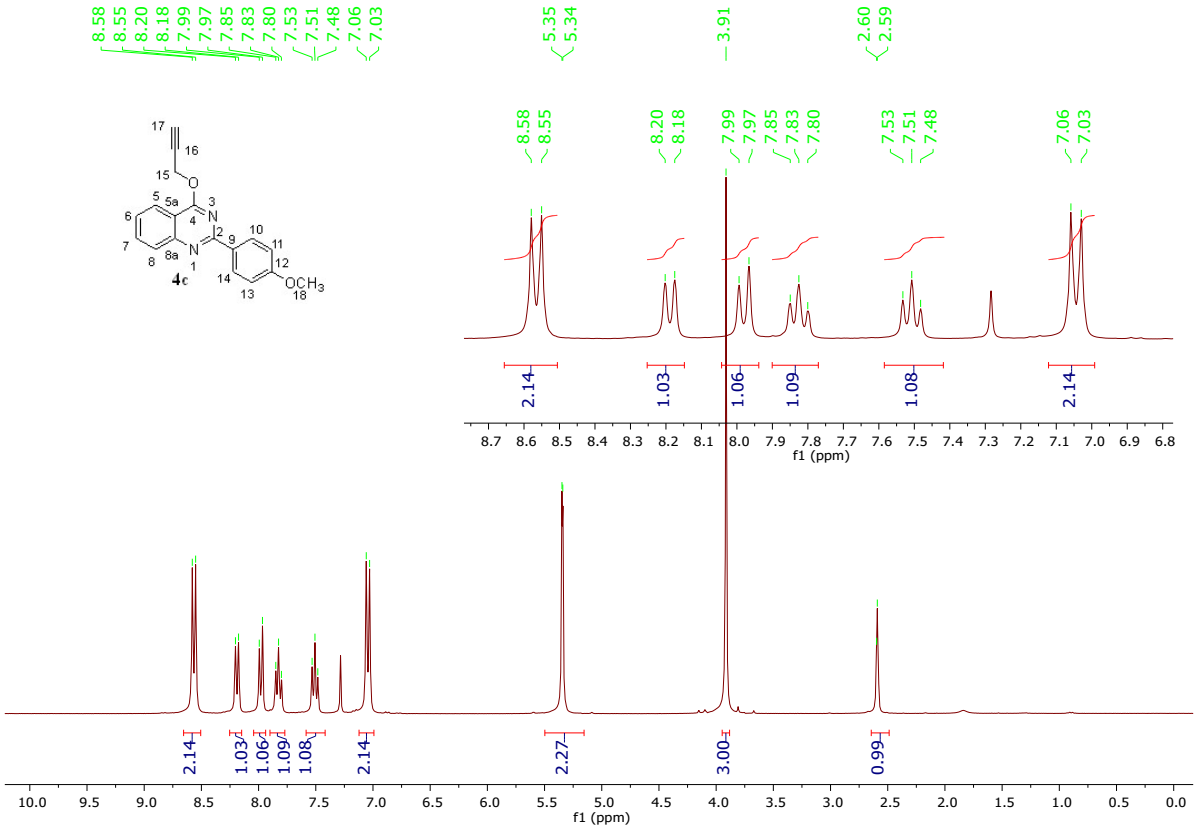
^{13}C NMR spectrum of compound 4a



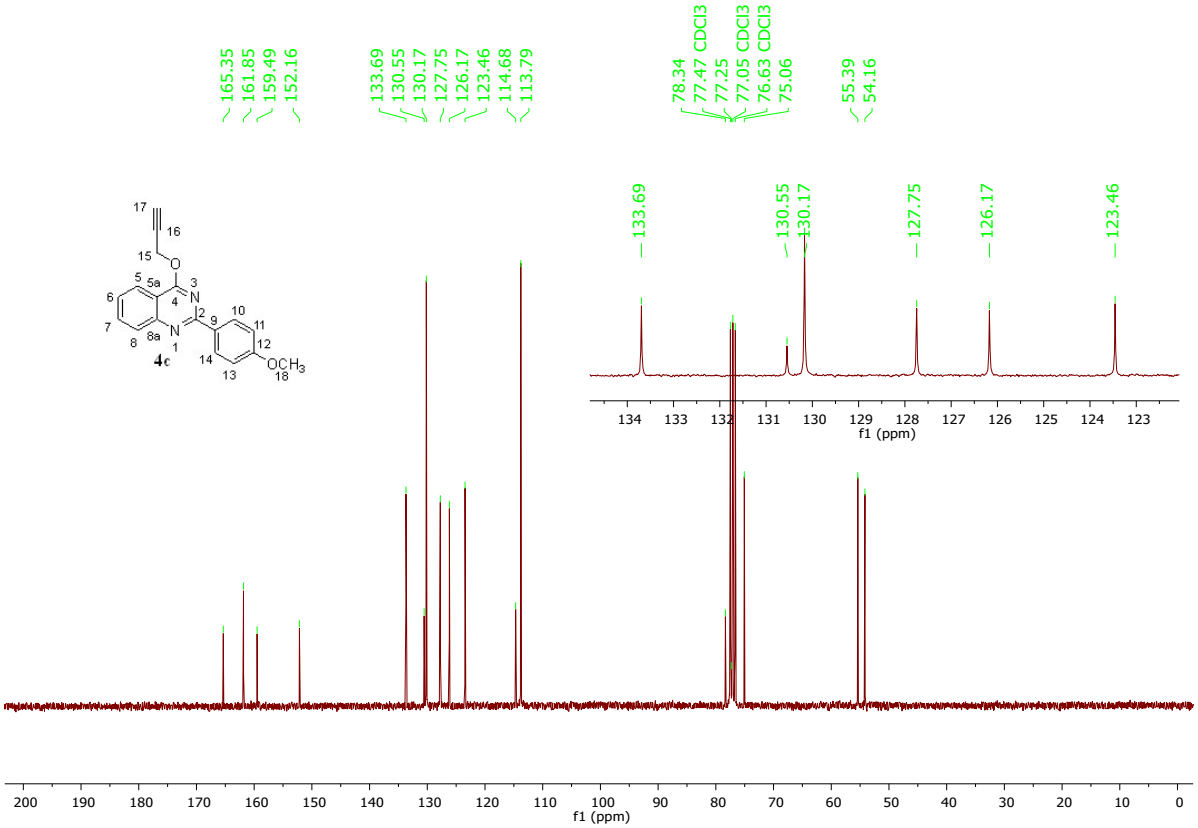
^{1}H NMR spectrum of compound 4b



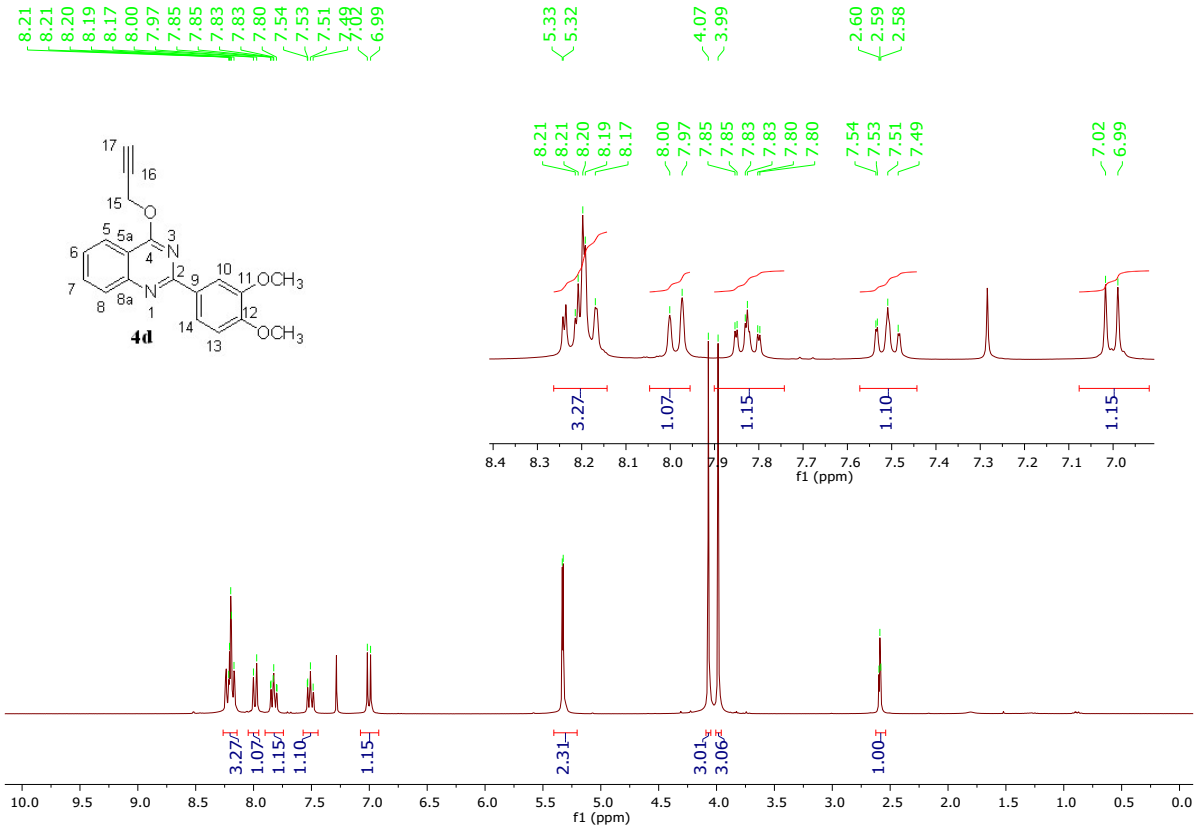
^{13}C NMR spectrum of compound 4b



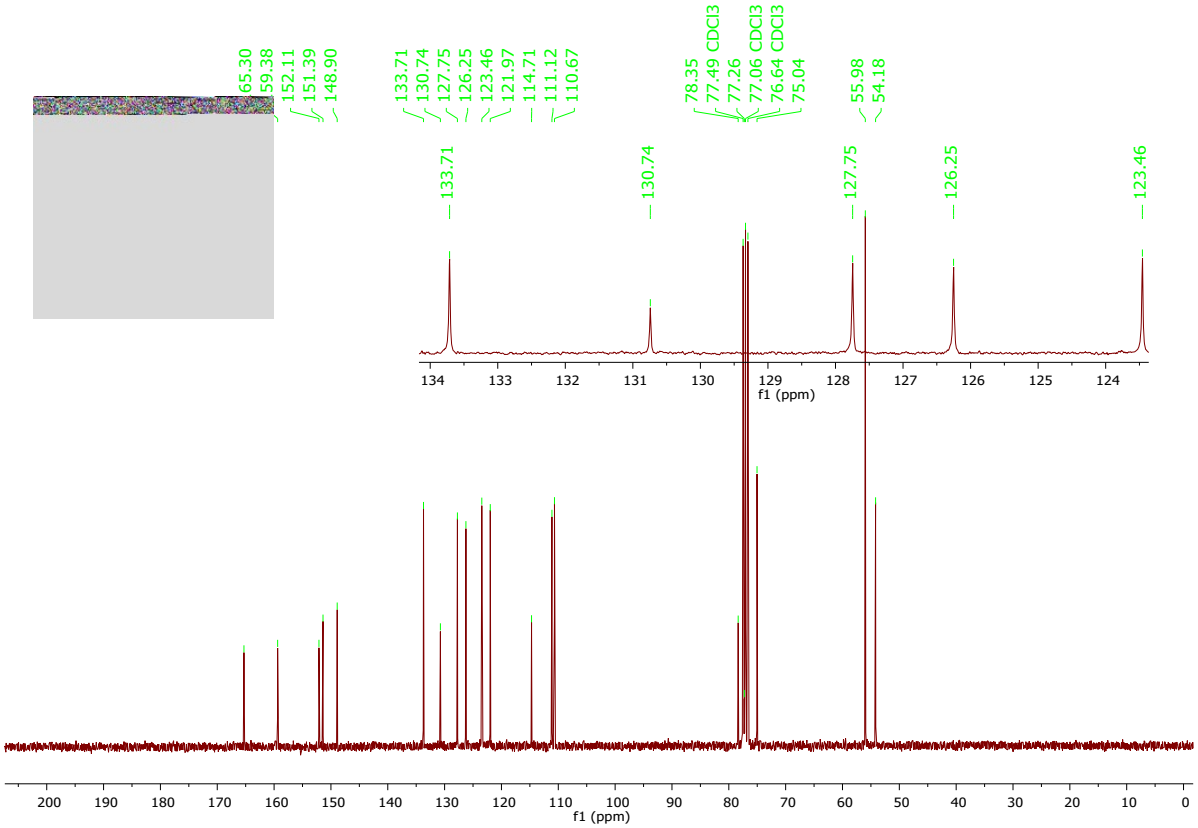
^{1}H NMR spectrum of compound 4c



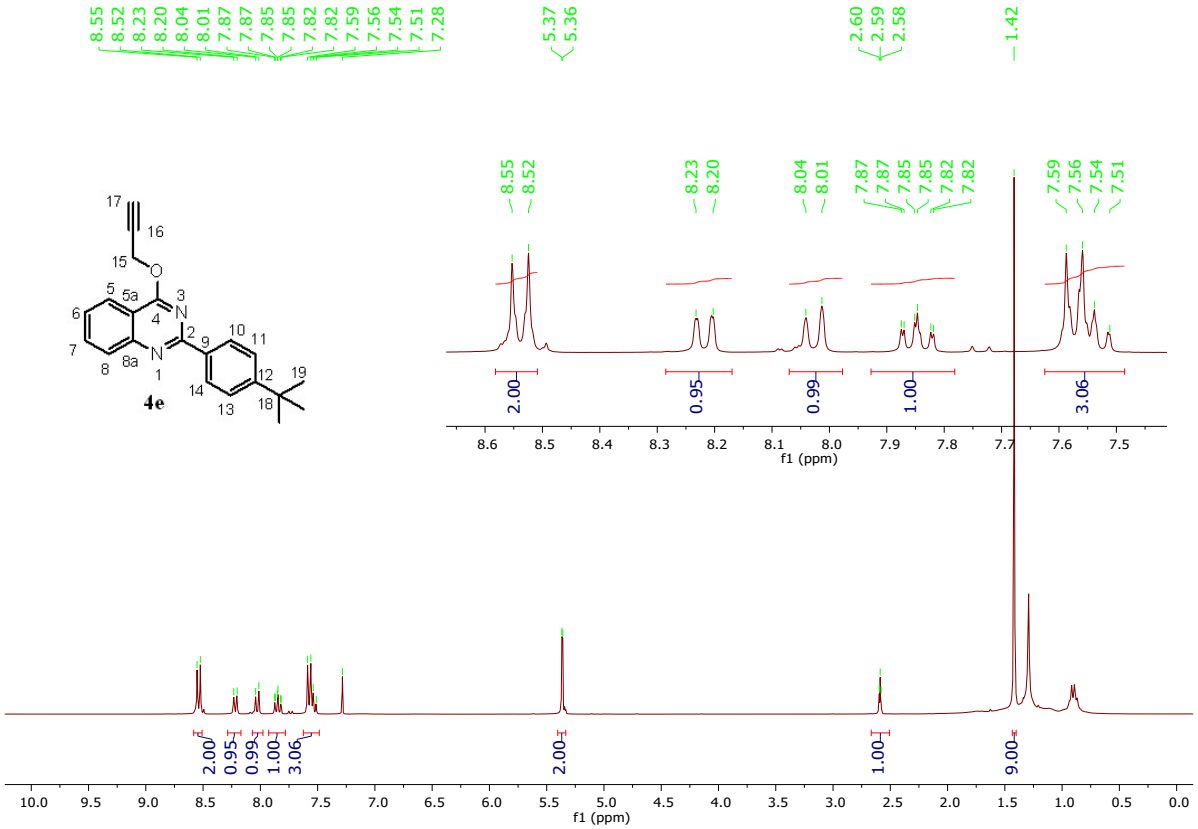
^{13}C NMR spectrum of compound 4c



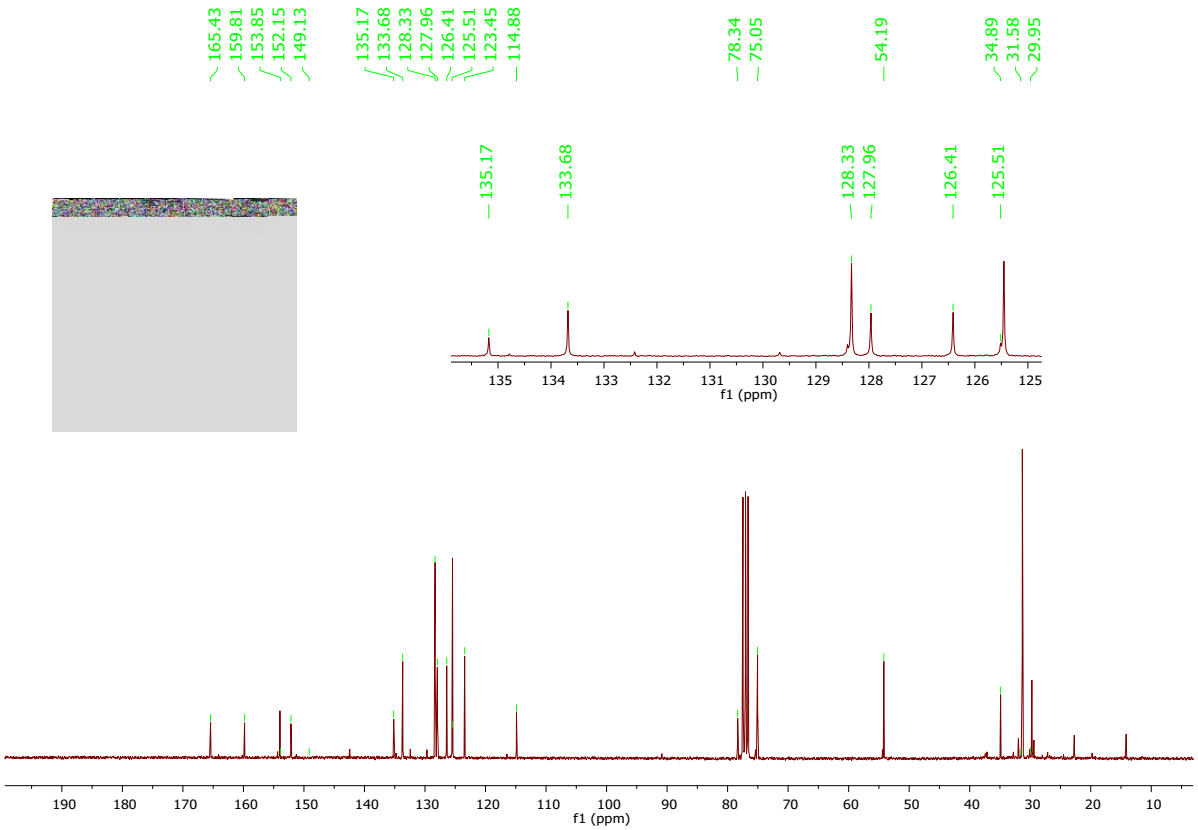
^{1}H NMR spectrum of compound 4d



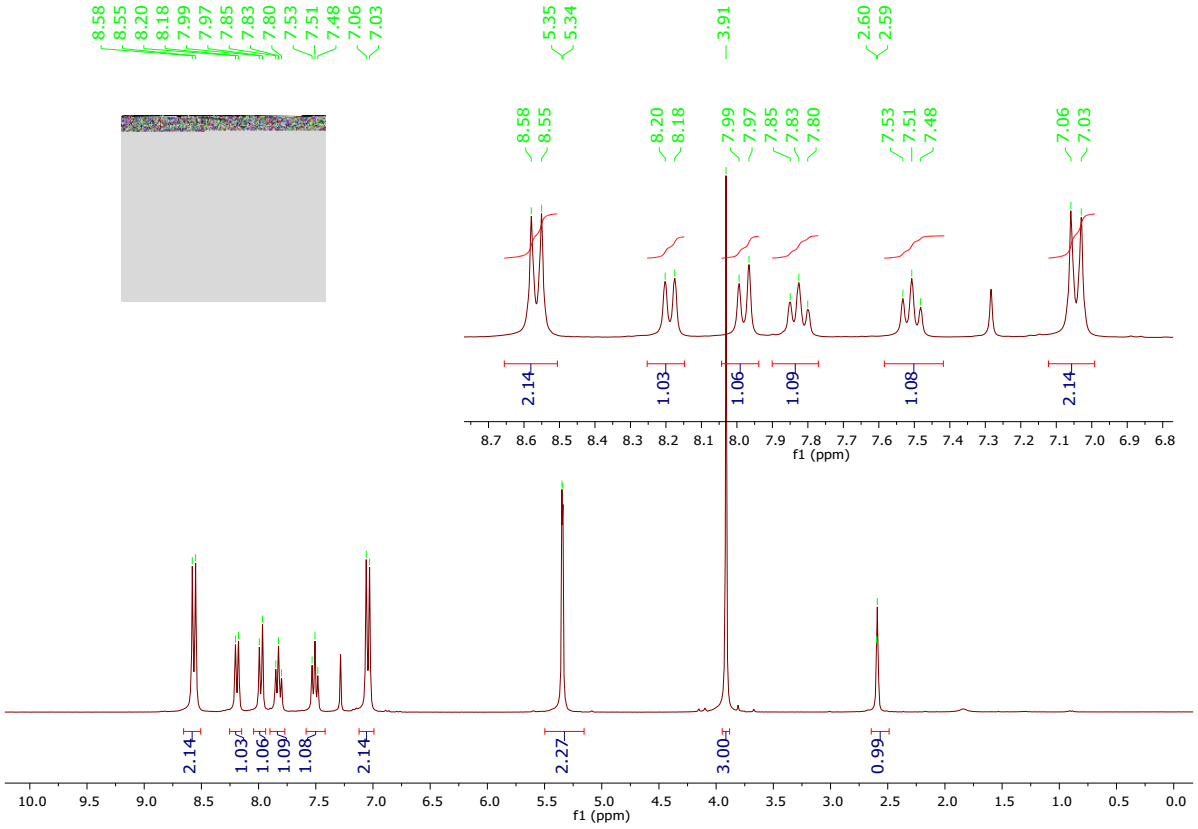
^{13}C NMR spectrum of compound 4d



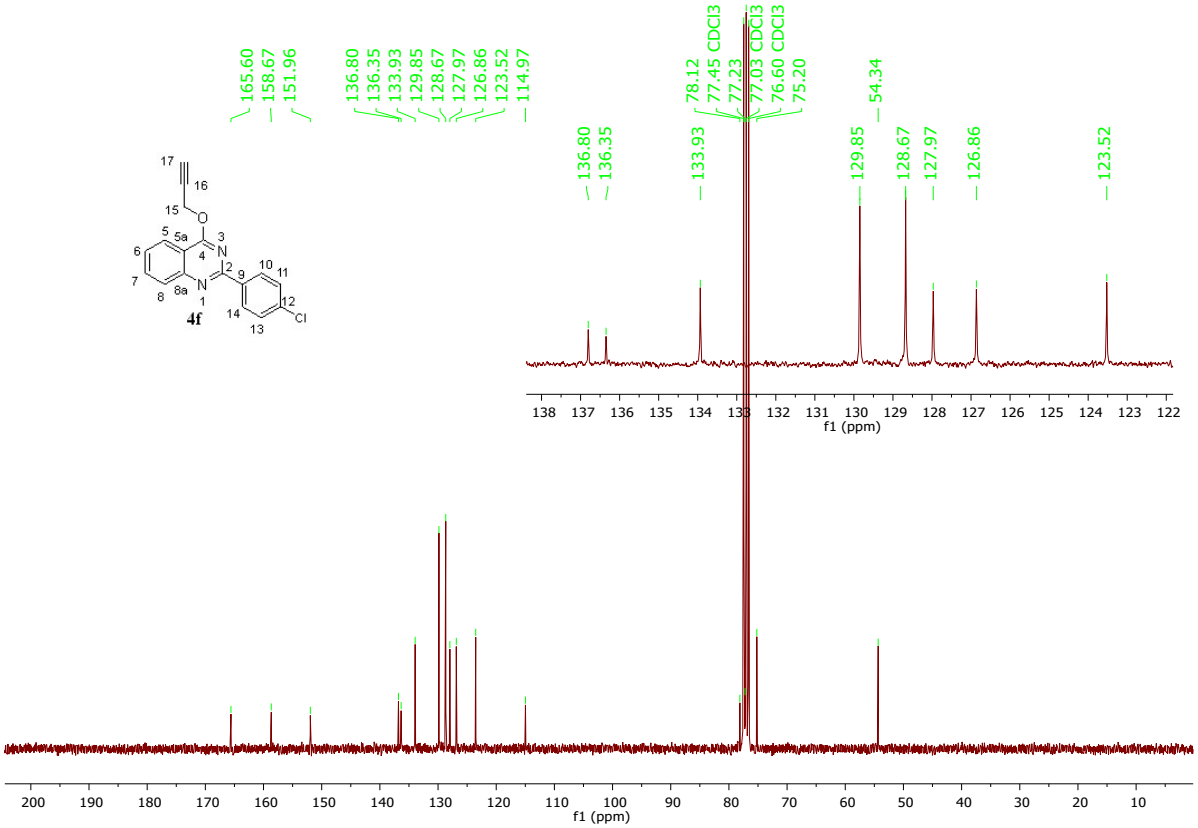
^{1}H NMR spectrum of compound 4e



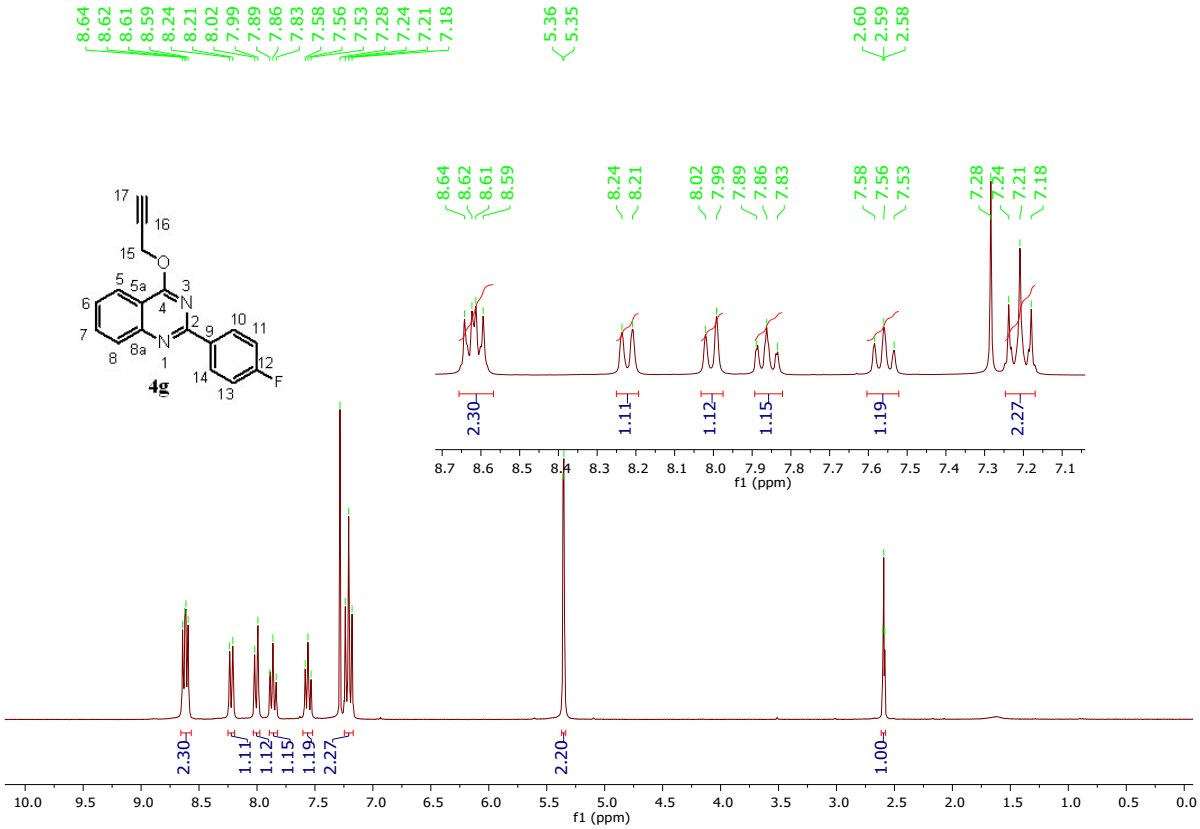
^{13}C NMR spectrum of compound 4e



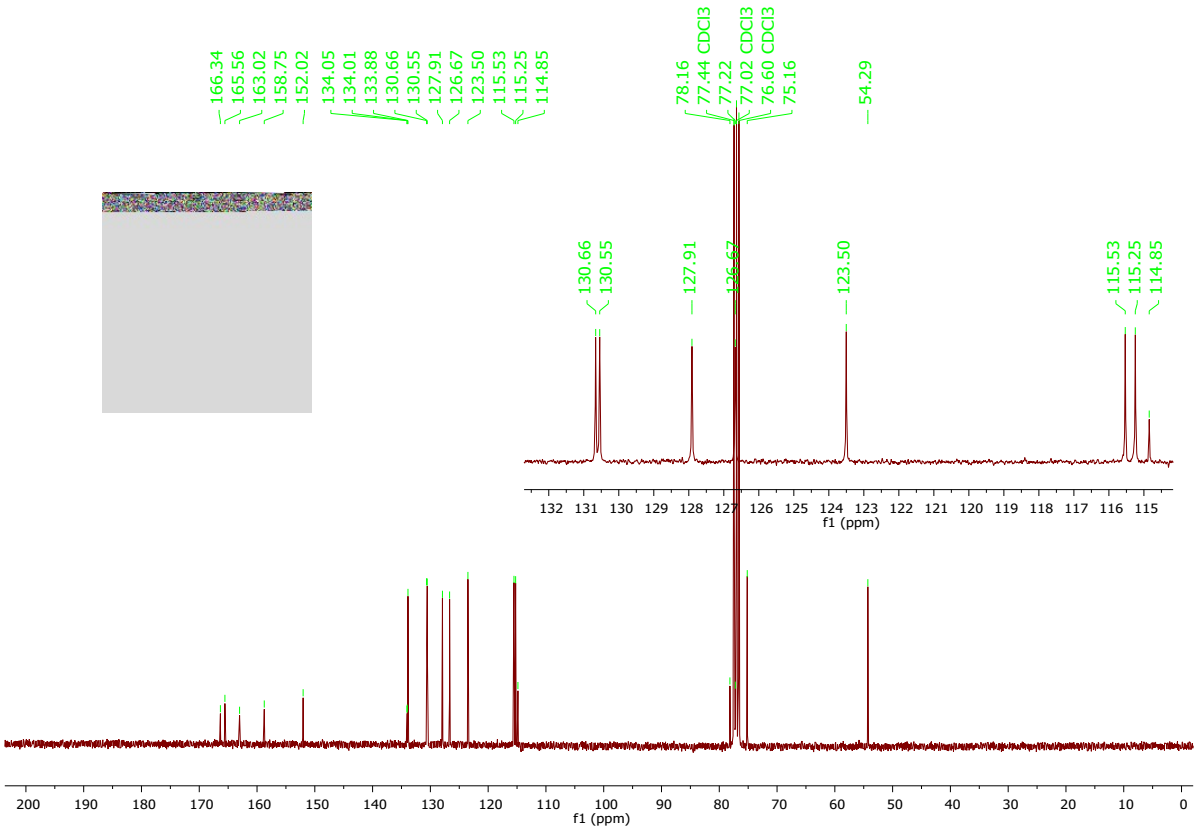
^{1}H NMR spectrum of compound 4f



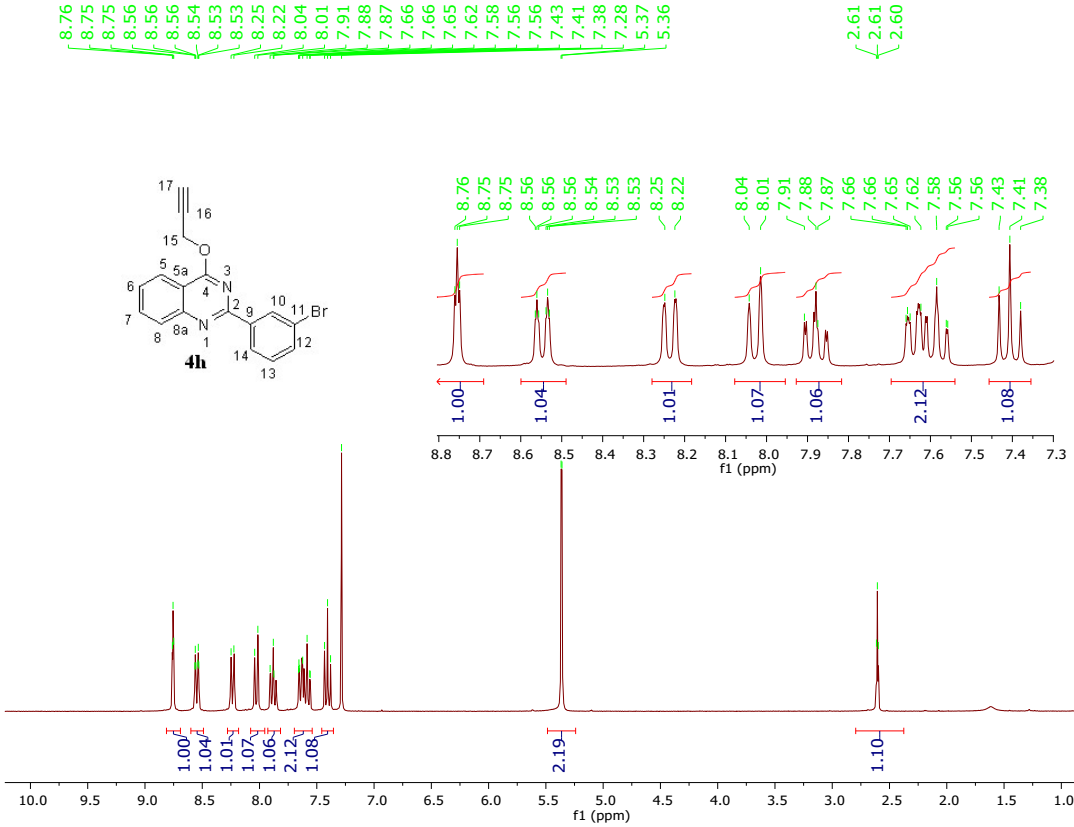
^{13}C NMR spectrum of compound 4f



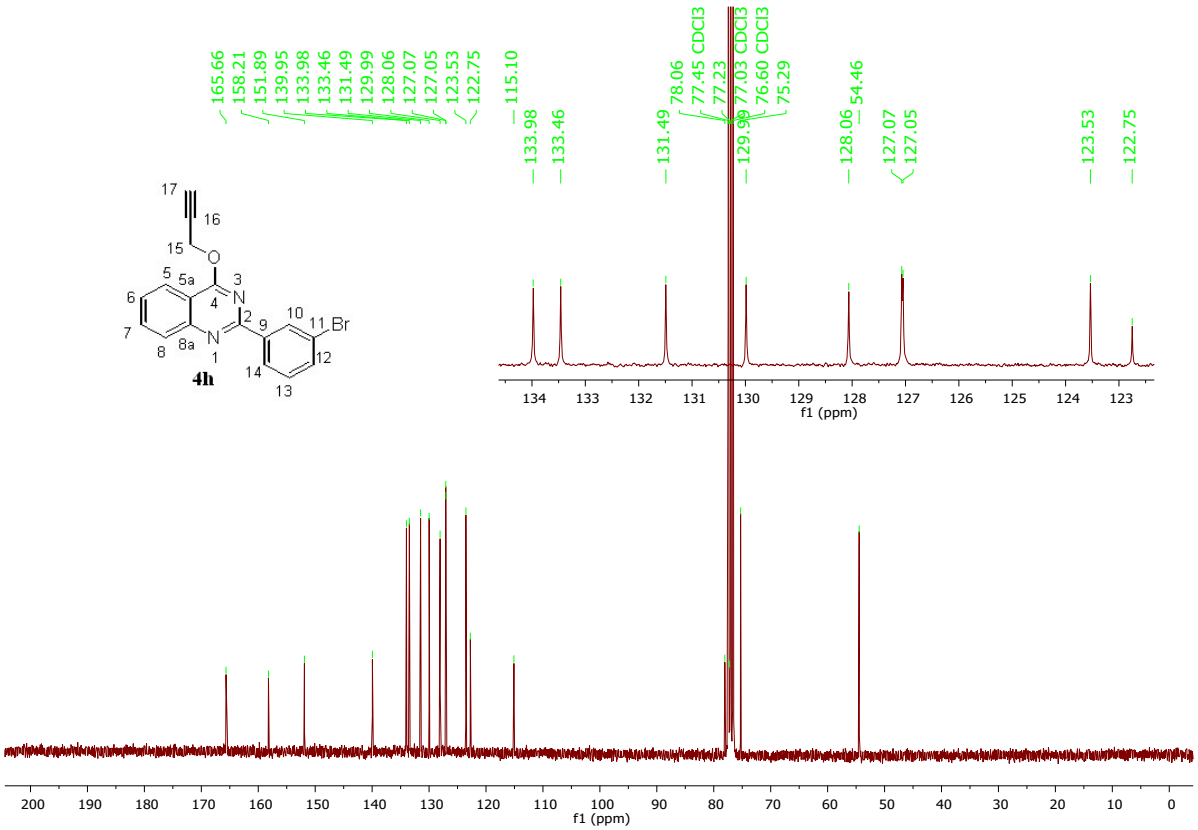
^{1}H NMR spectrum of compound 4g



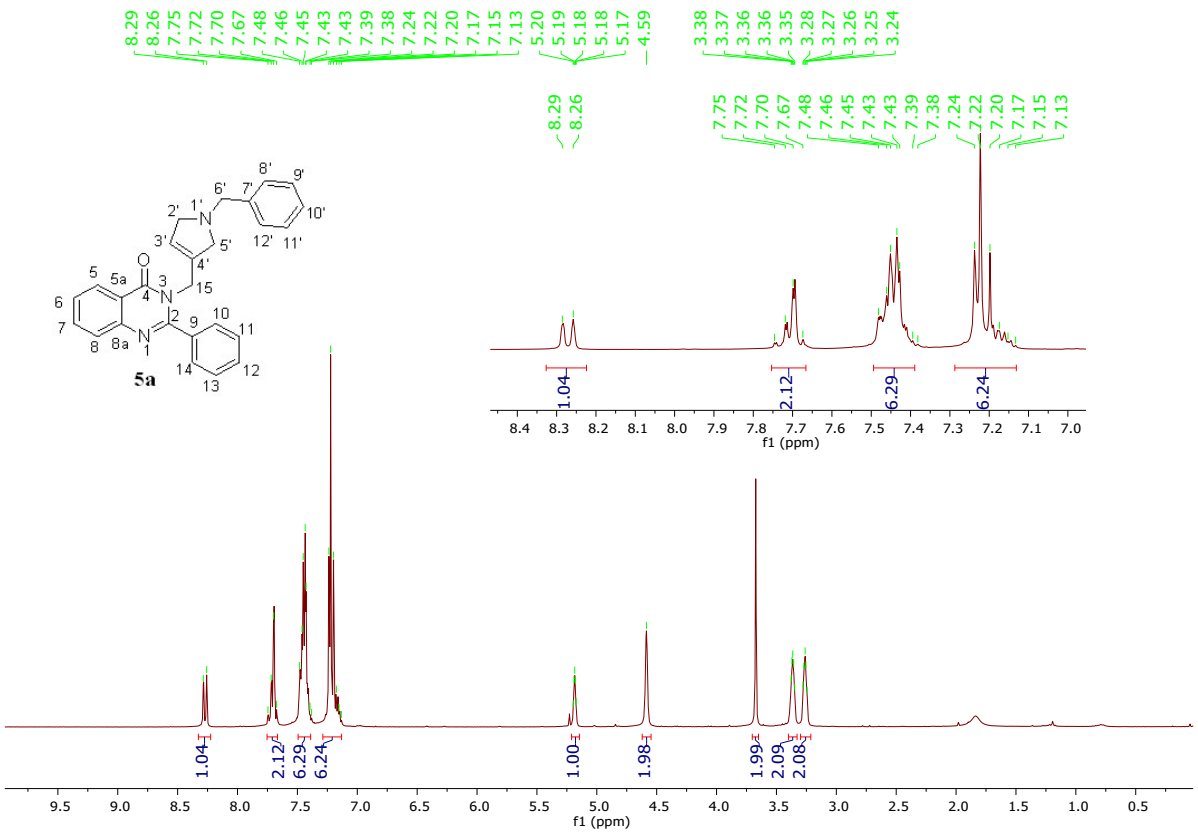
^{13}C NMR spectrum of compound 4g



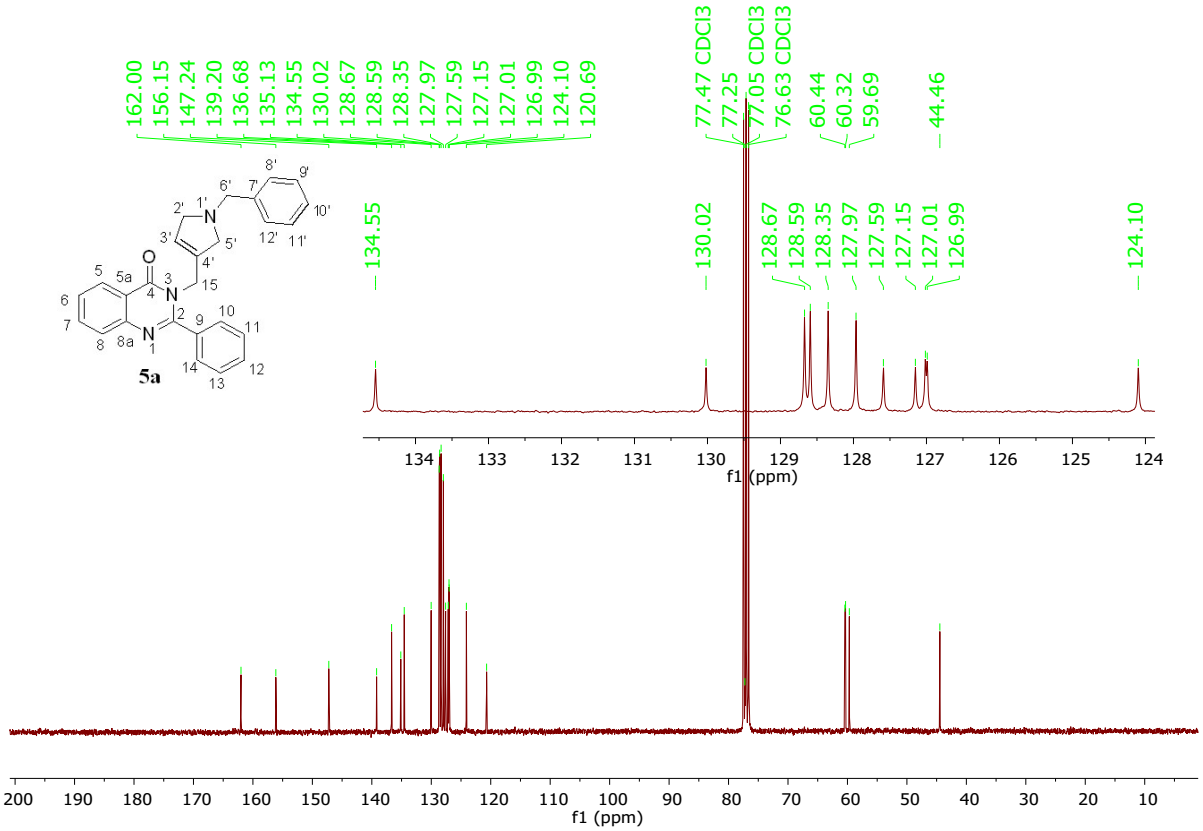
^{1}H NMR spectrum of compound 4h



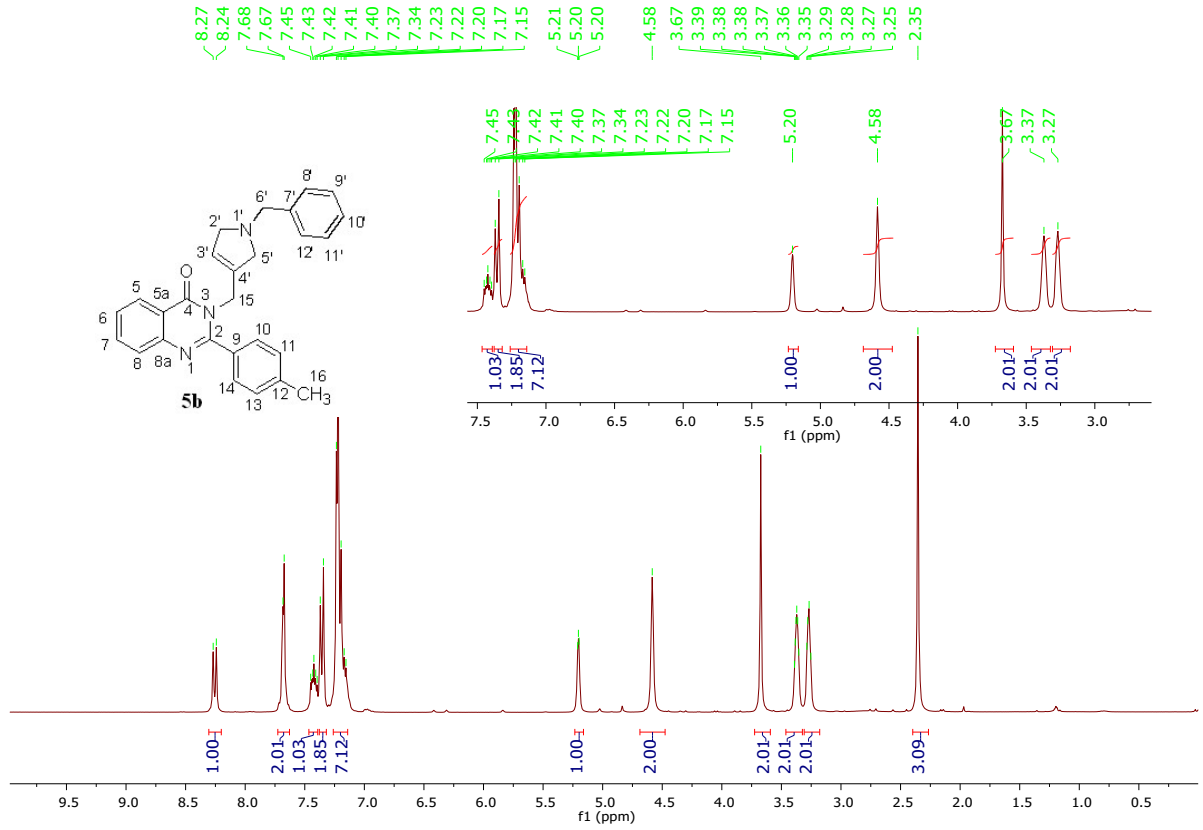
^{13}C NMR spectrum of compound 4h



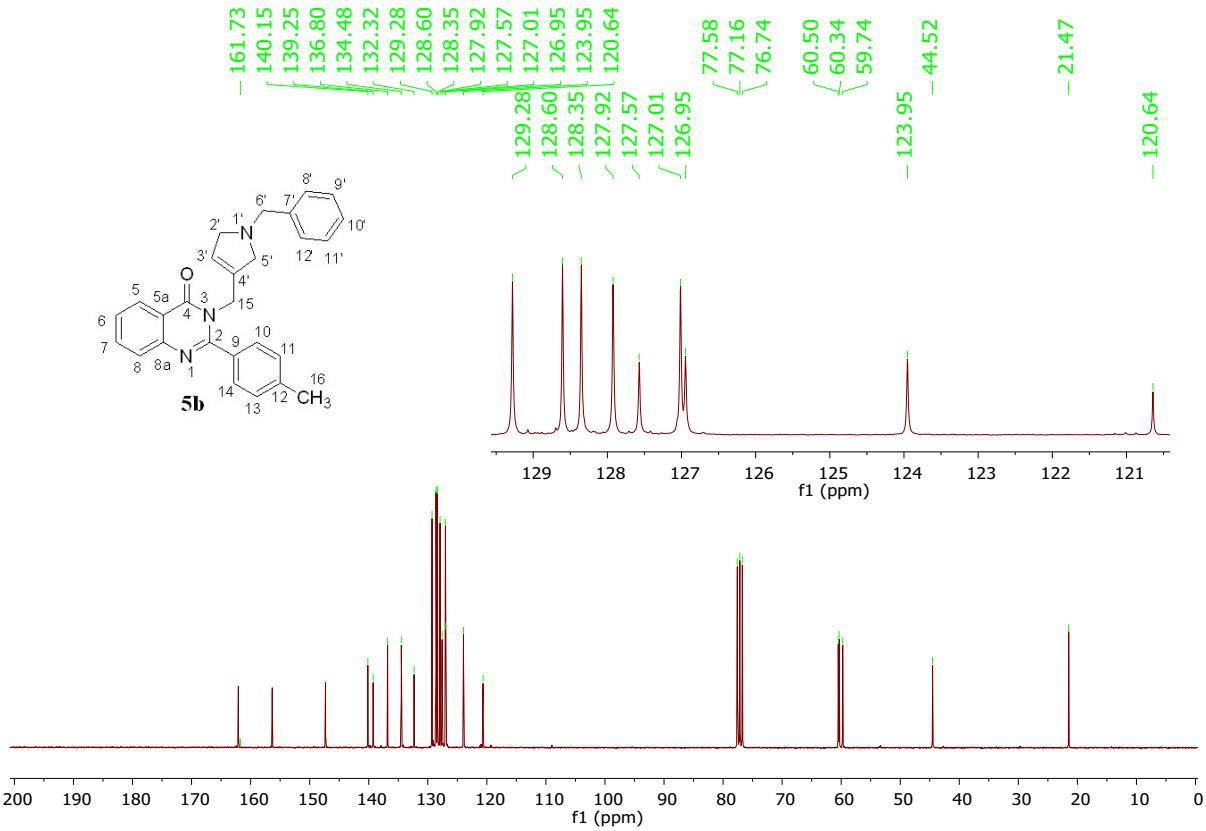
^{1}H NMR spectrum of compound 5a



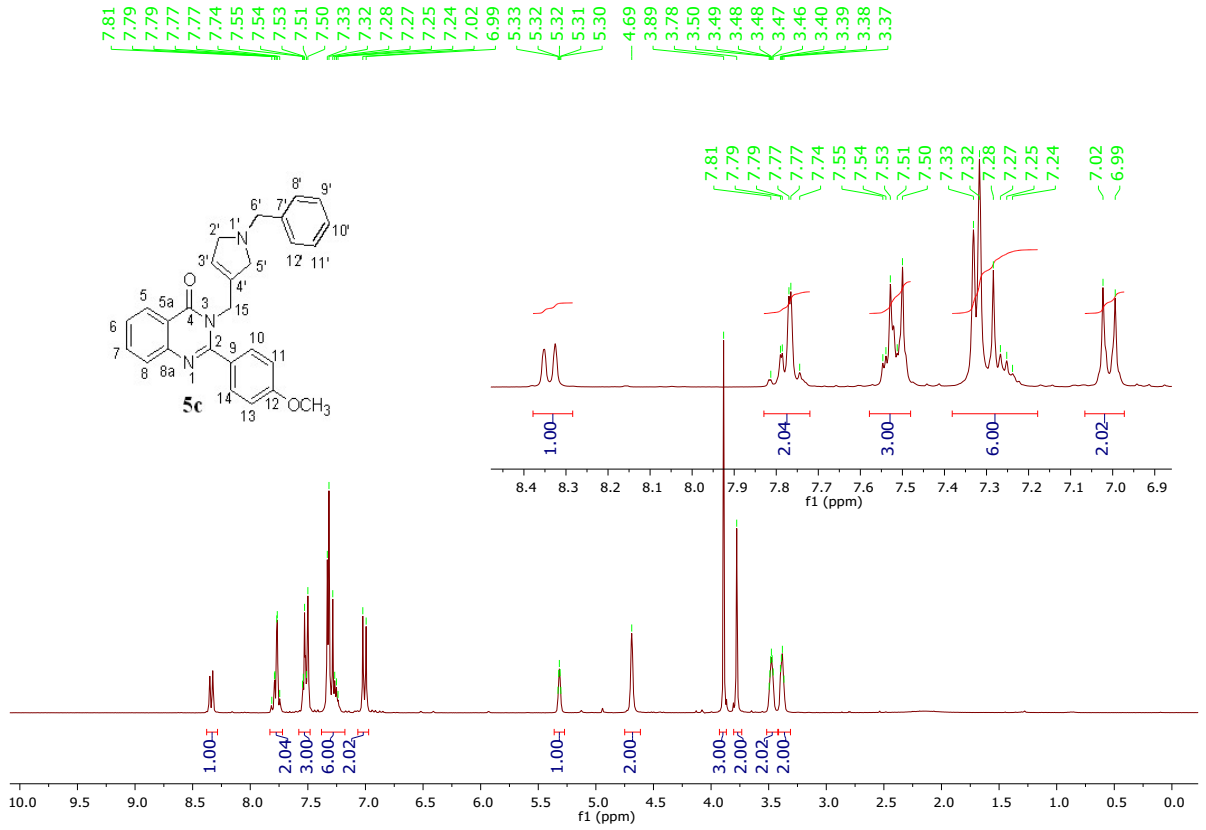
^{13}C NMR spectrum of compound 5a



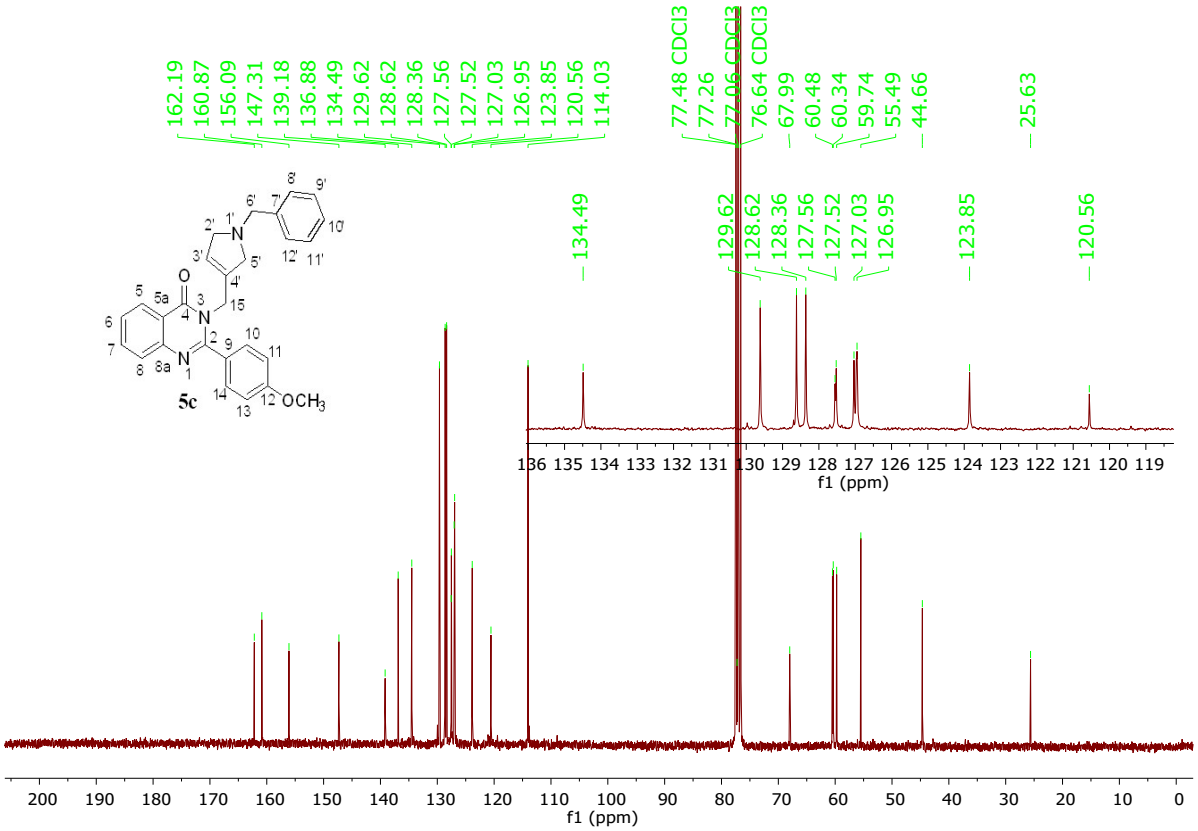
^{1}H NMR spectrum of compound 5b



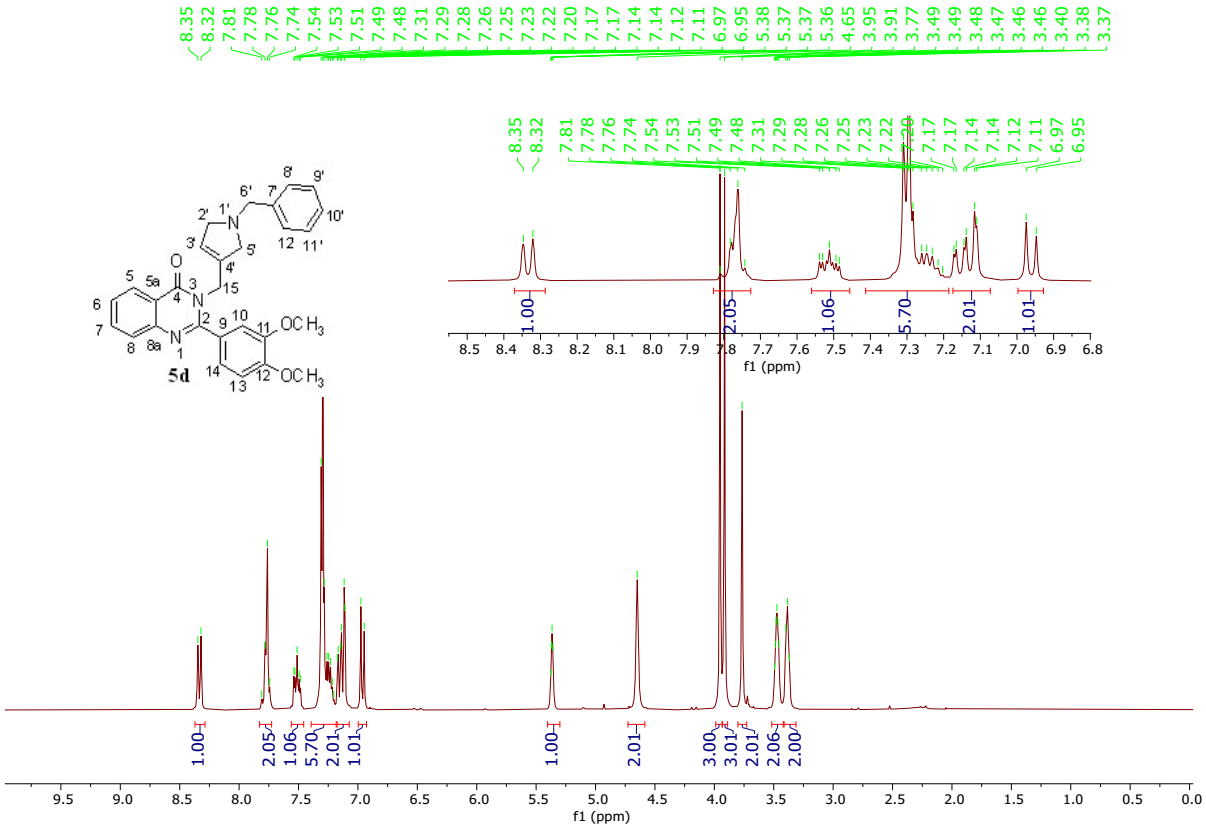
^{13}C NMR spectrum of compound 5b



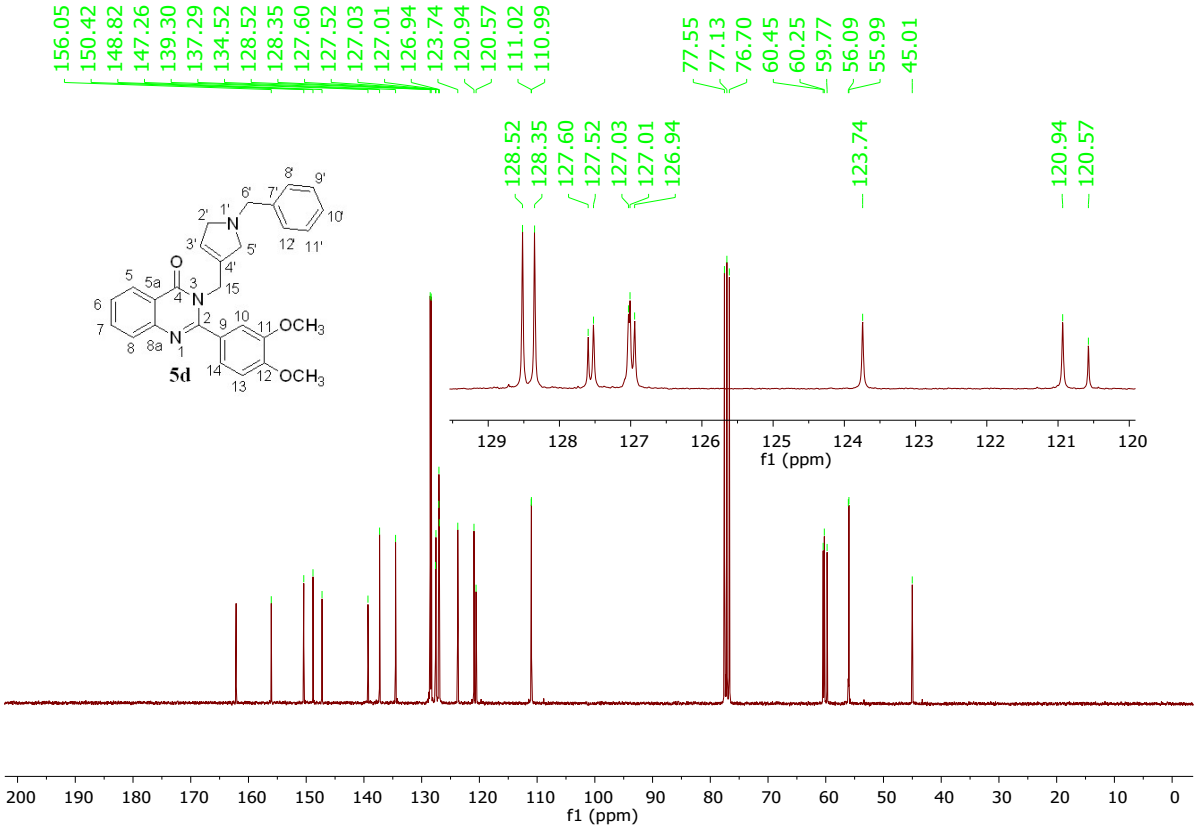
^{1}H NMR spectrum of compound 5c



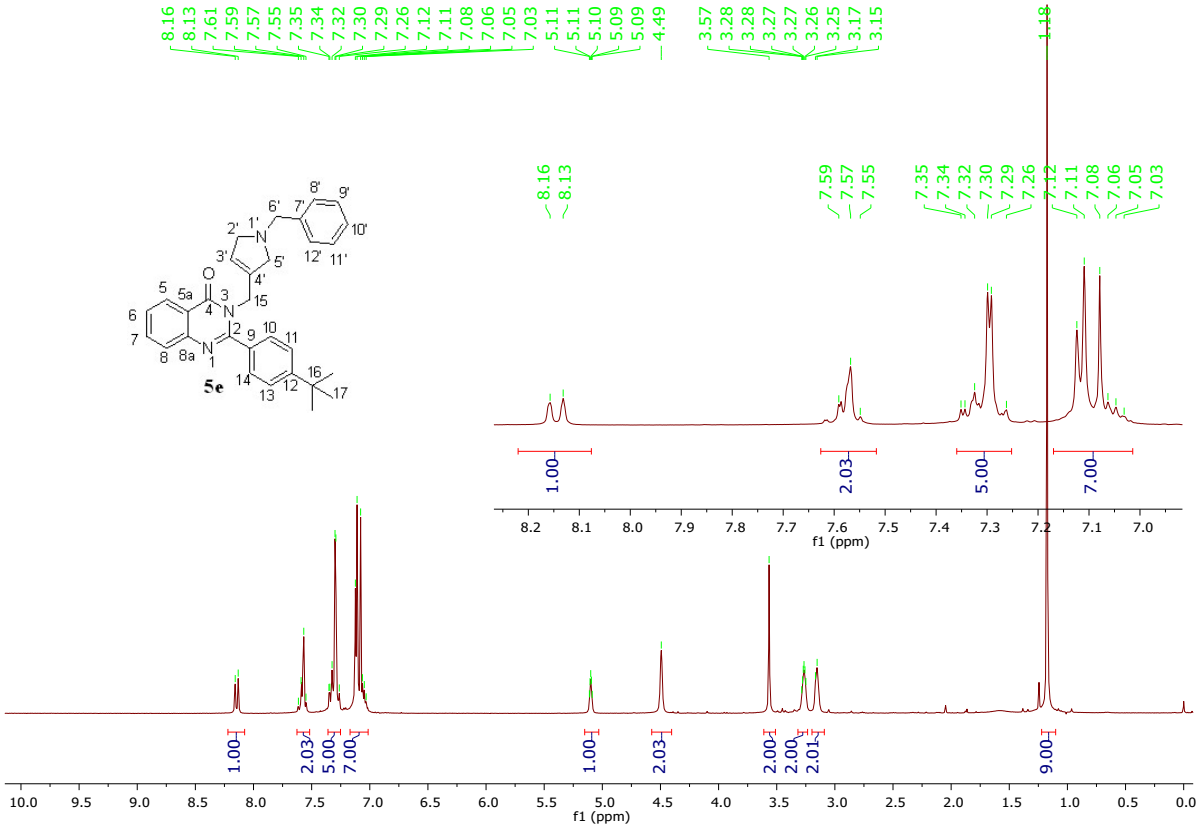
^{13}C NMR spectrum of compound 5c



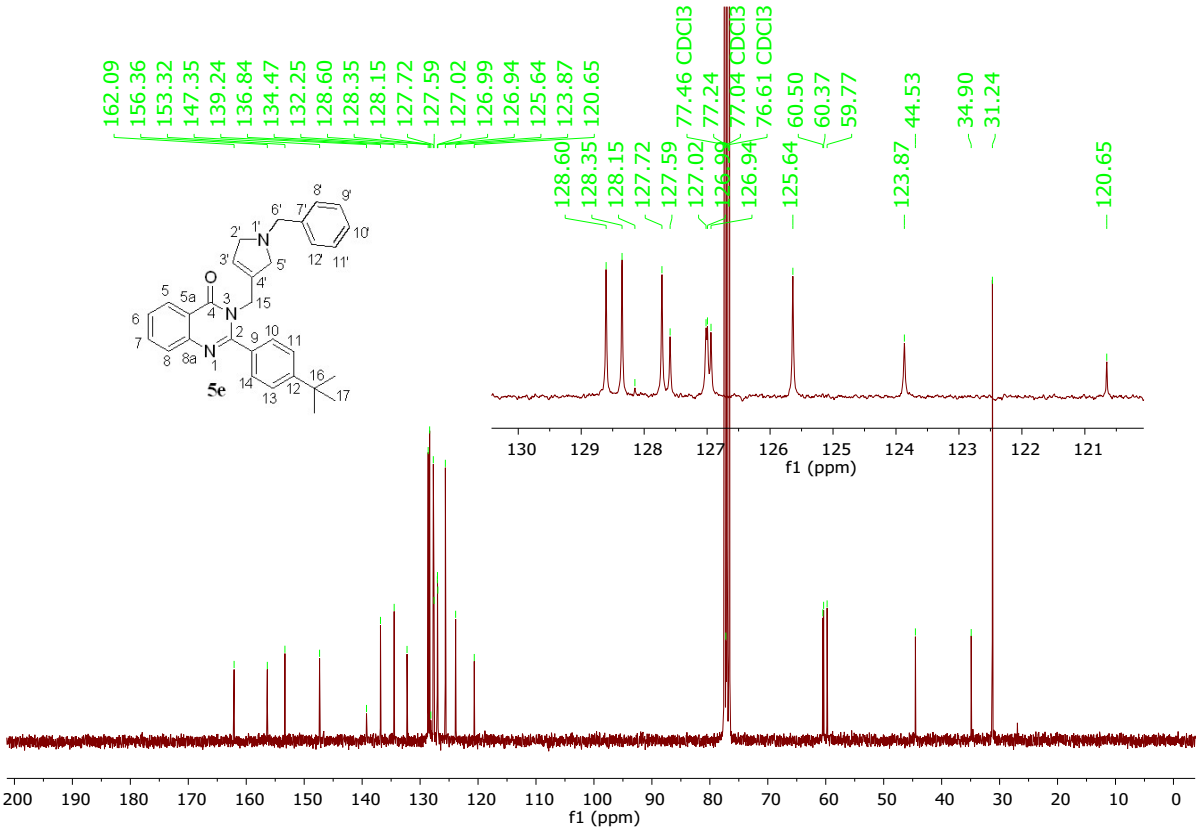
^{1}H NMR spectrum of compound 5d



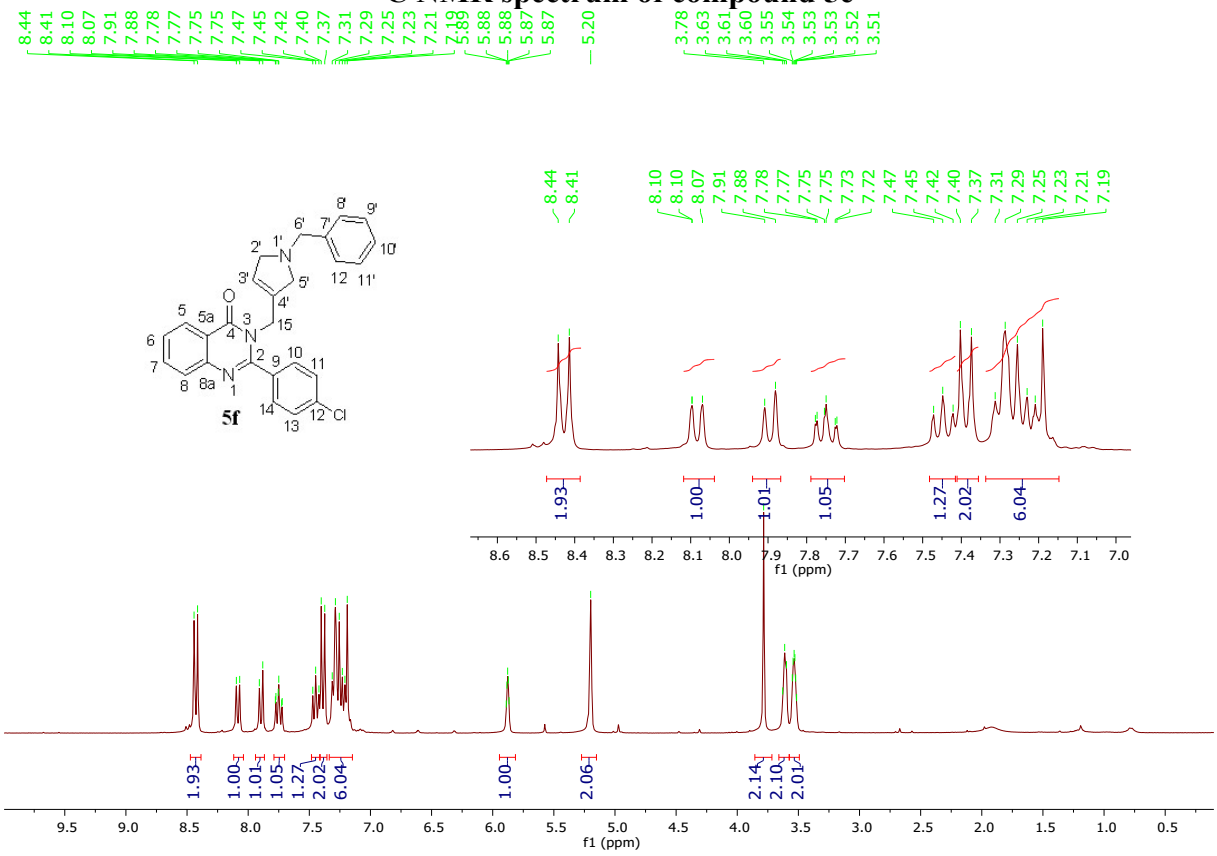
^{13}C NMR spectrum of compound 5d



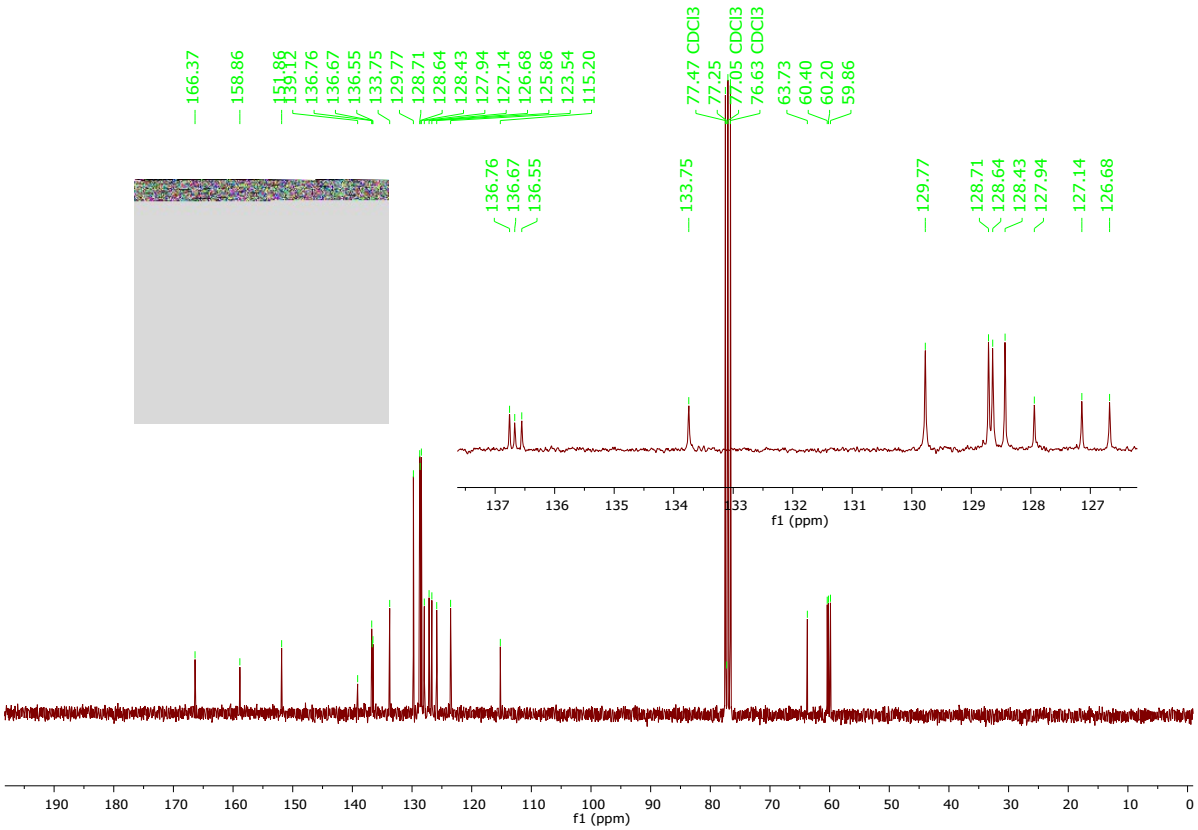
^{1}H NMR spectrum of compound 5e



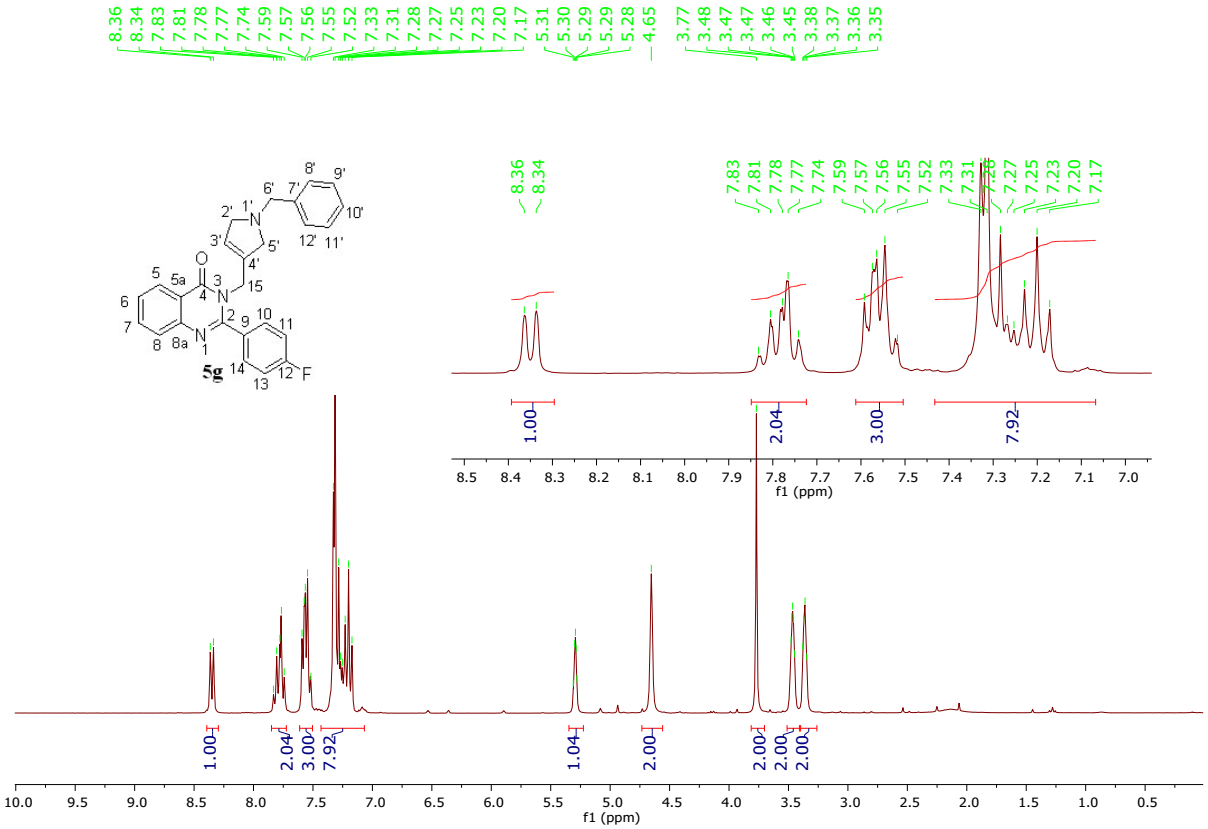
^{13}C NMR spectrum of compound 5e



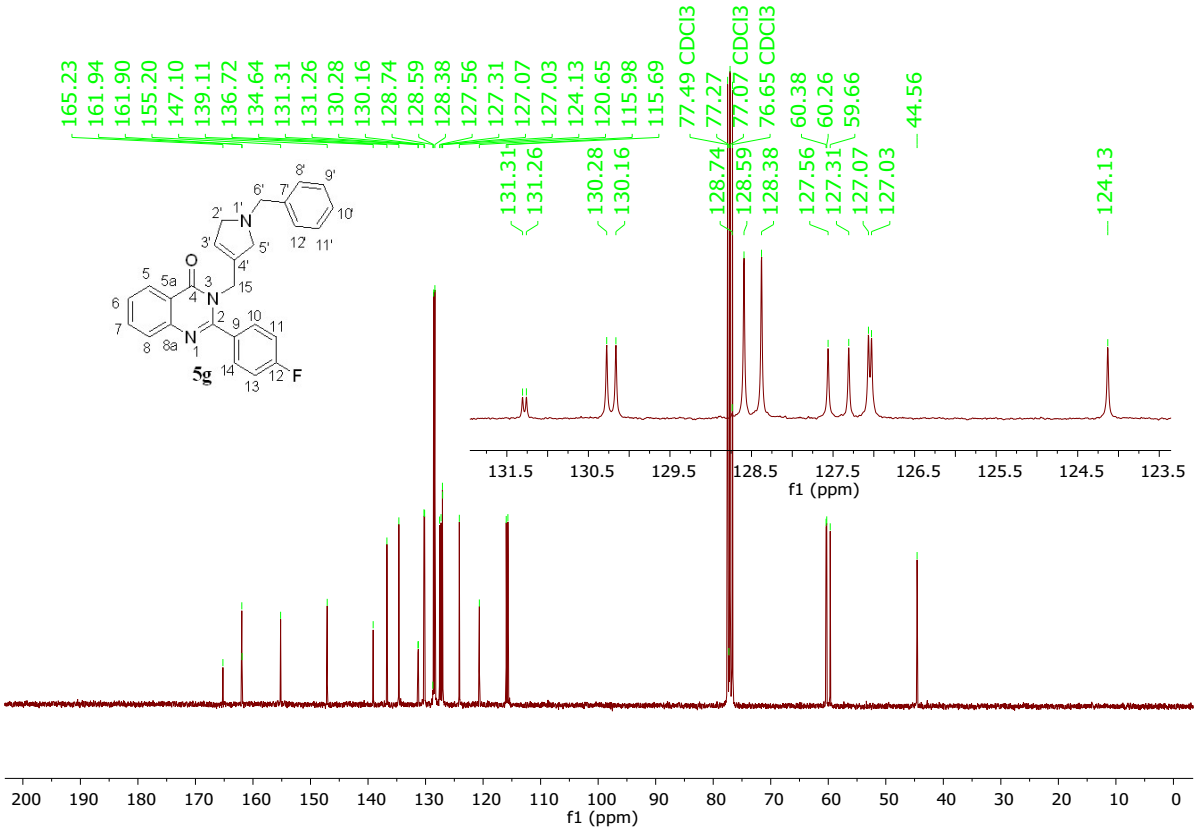
^{1}H NMR spectrum of compound 5f



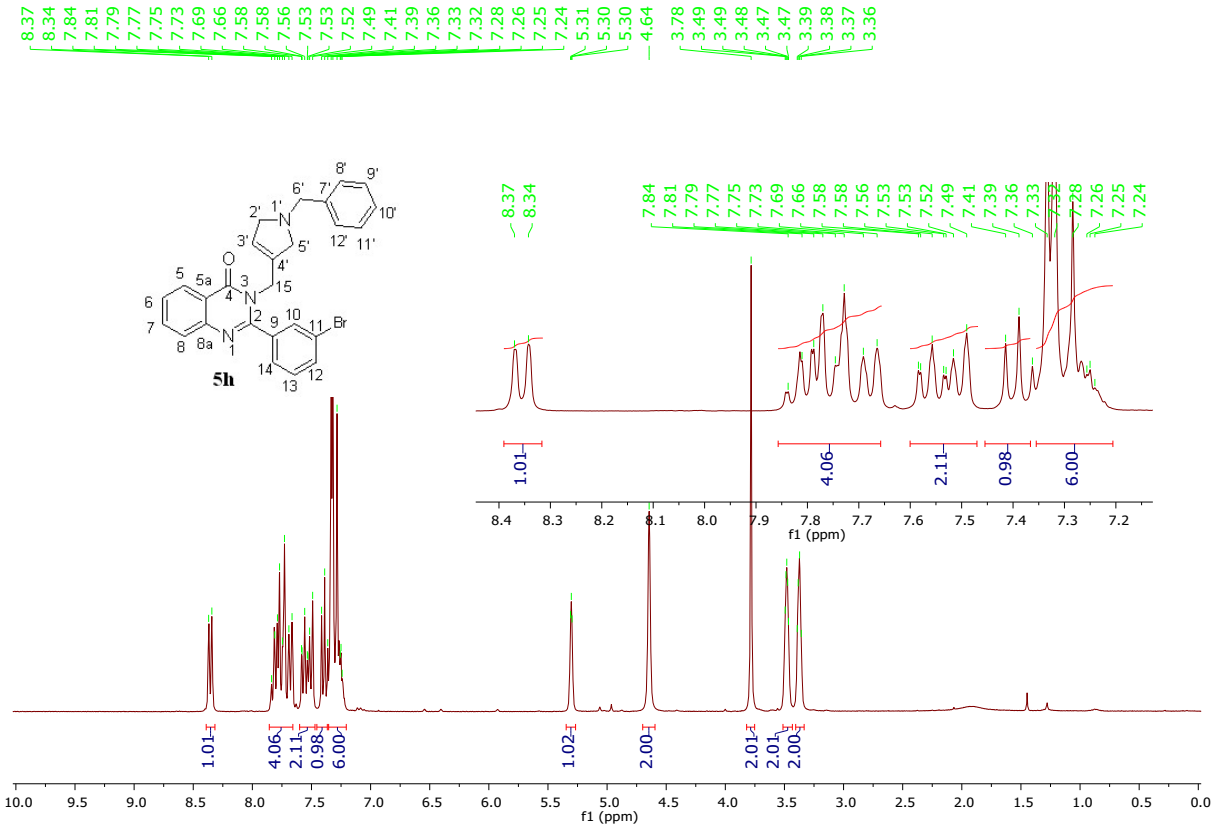
^{13}C NMR spectrum of compound 5f



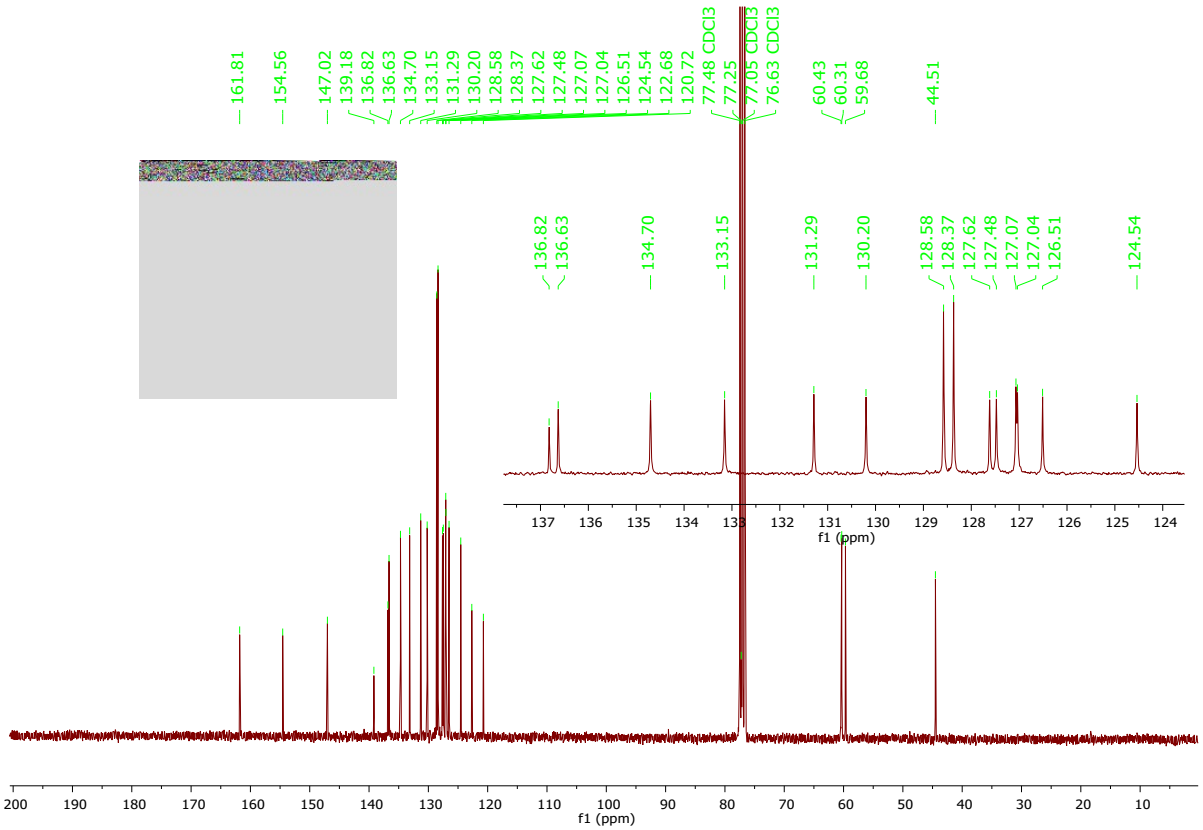
^{1}H NMR spectrum of compound 5g



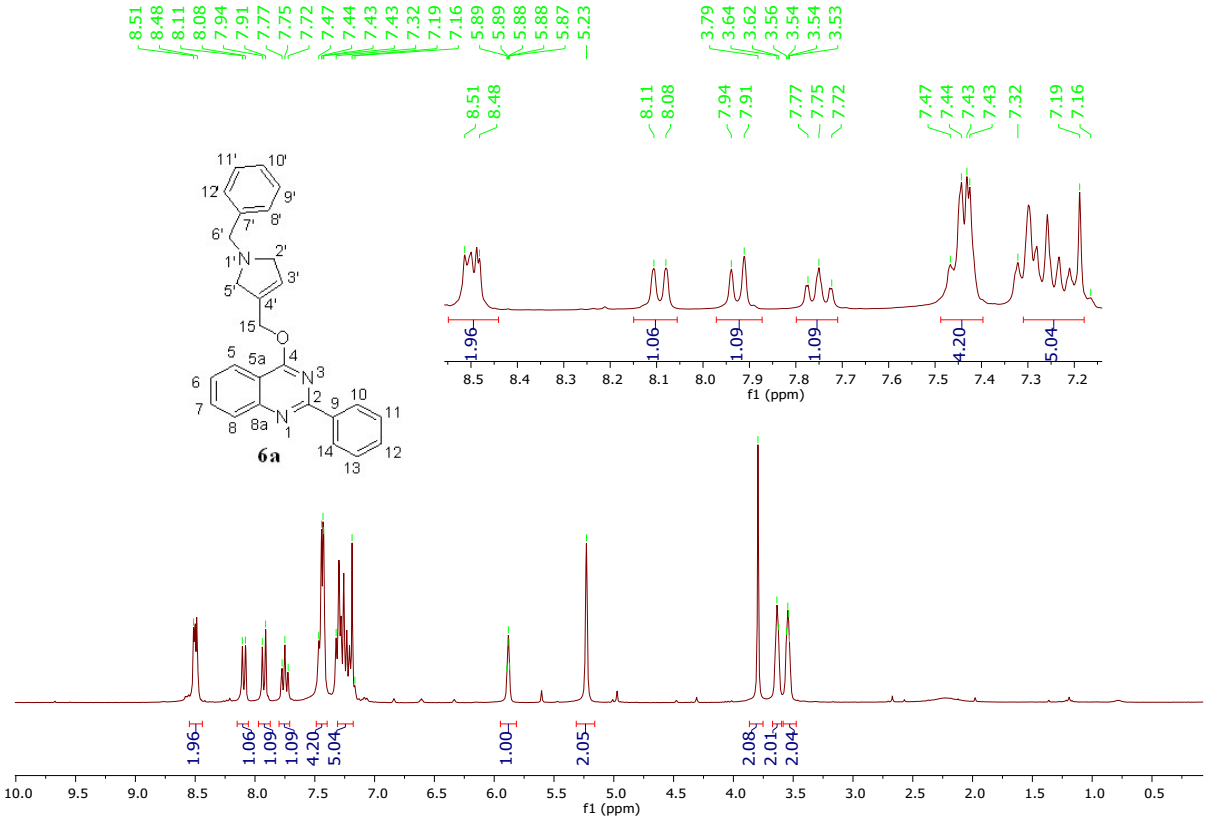
^{13}C NMR spectrum of compound 5g



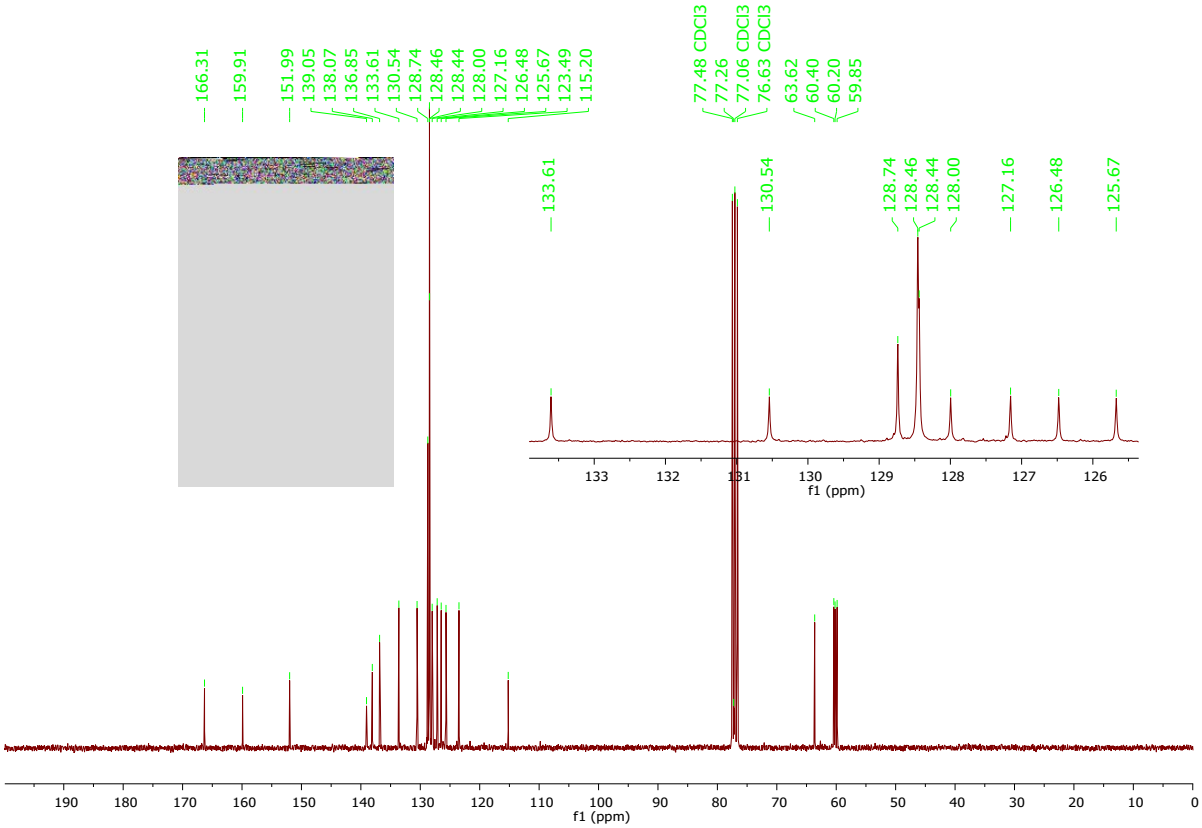
^{1}H NMR spectrum of compound 5h



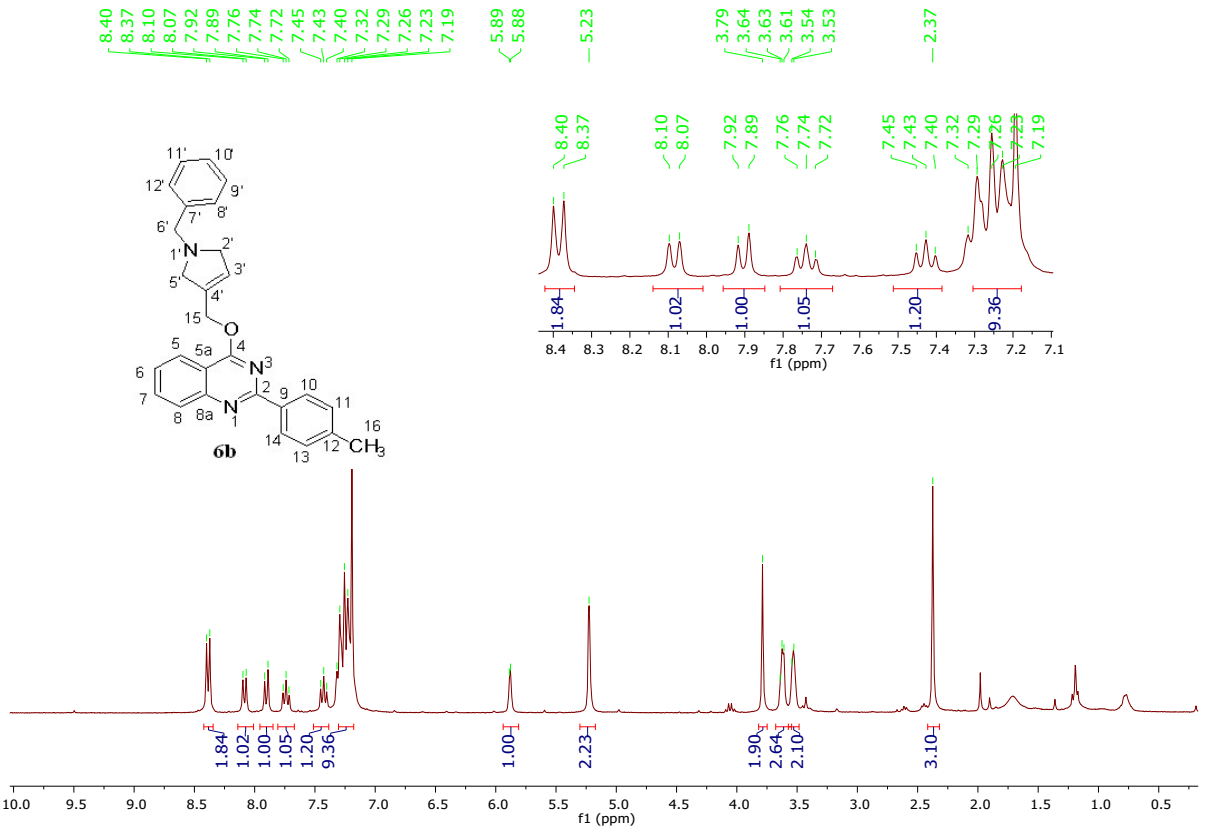
^{13}C NMR spectrum of compound 5h



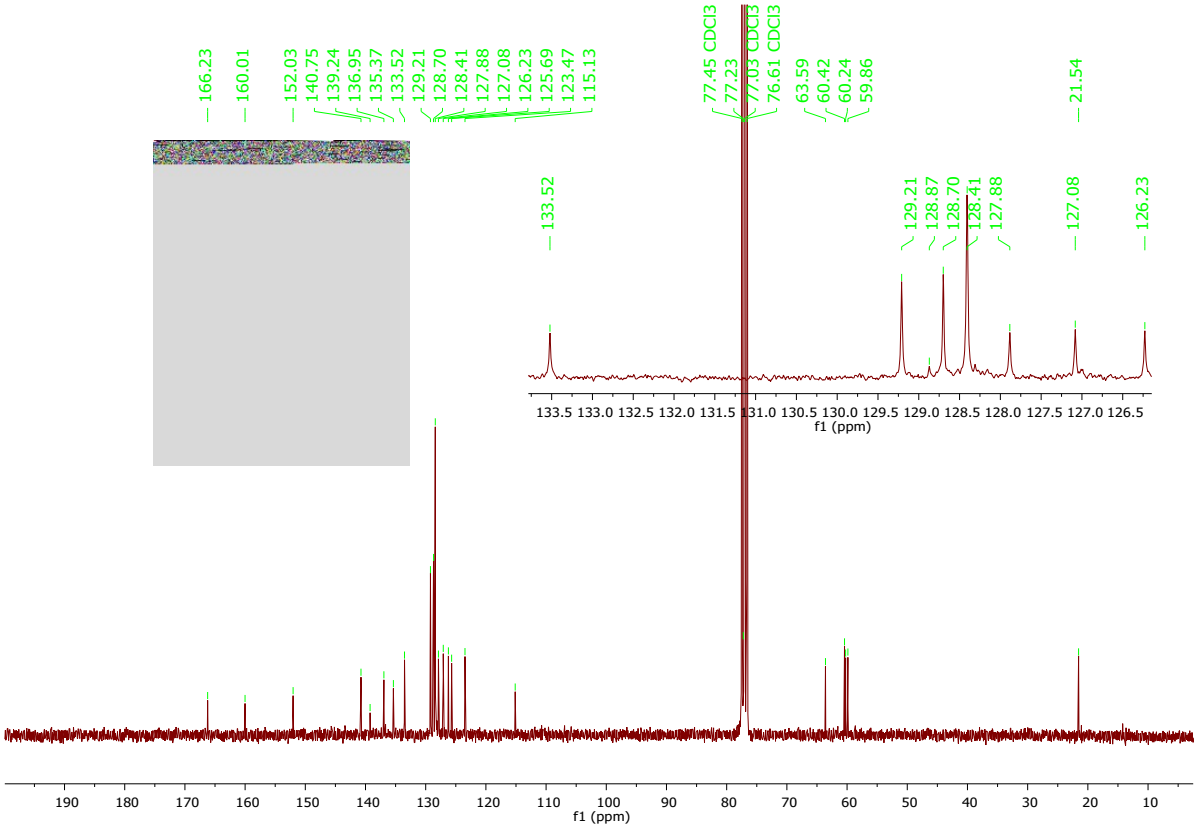
^{1}H NMR spectrum of compound 6a



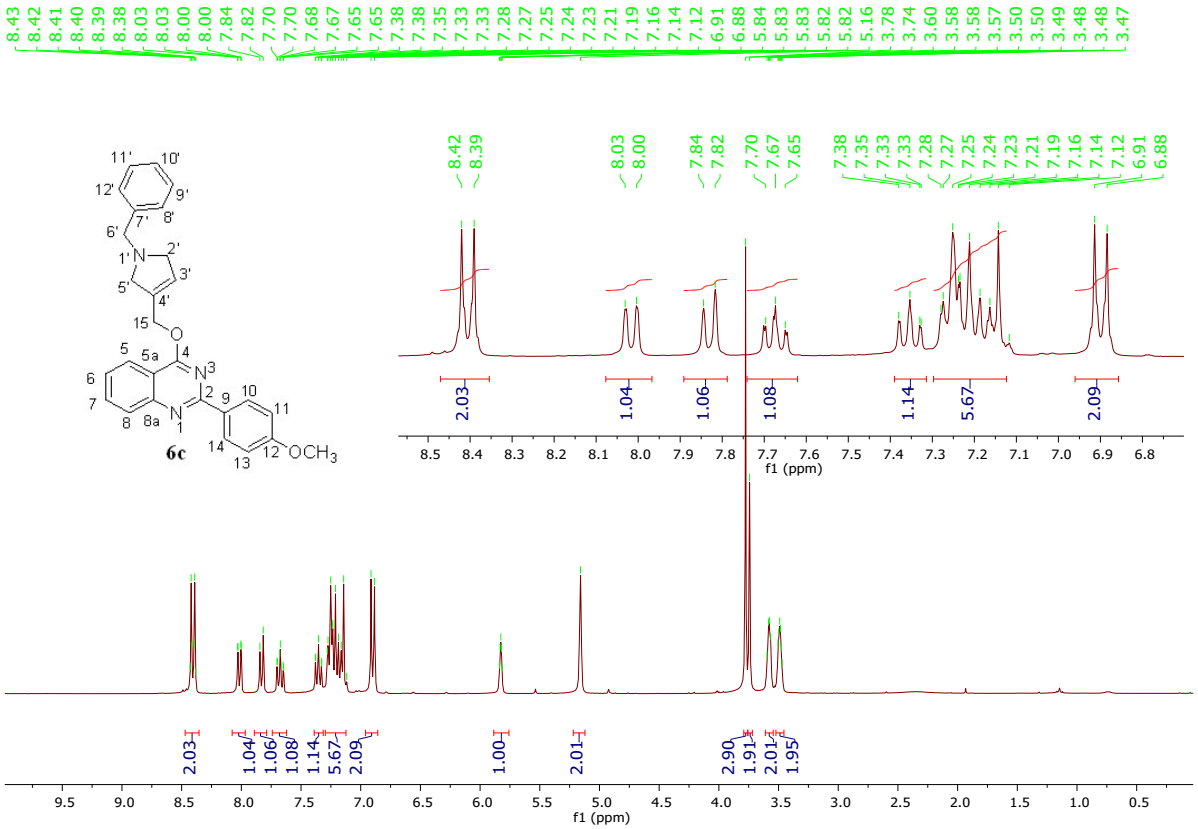
^{13}C NMR spectrum of compound 6a



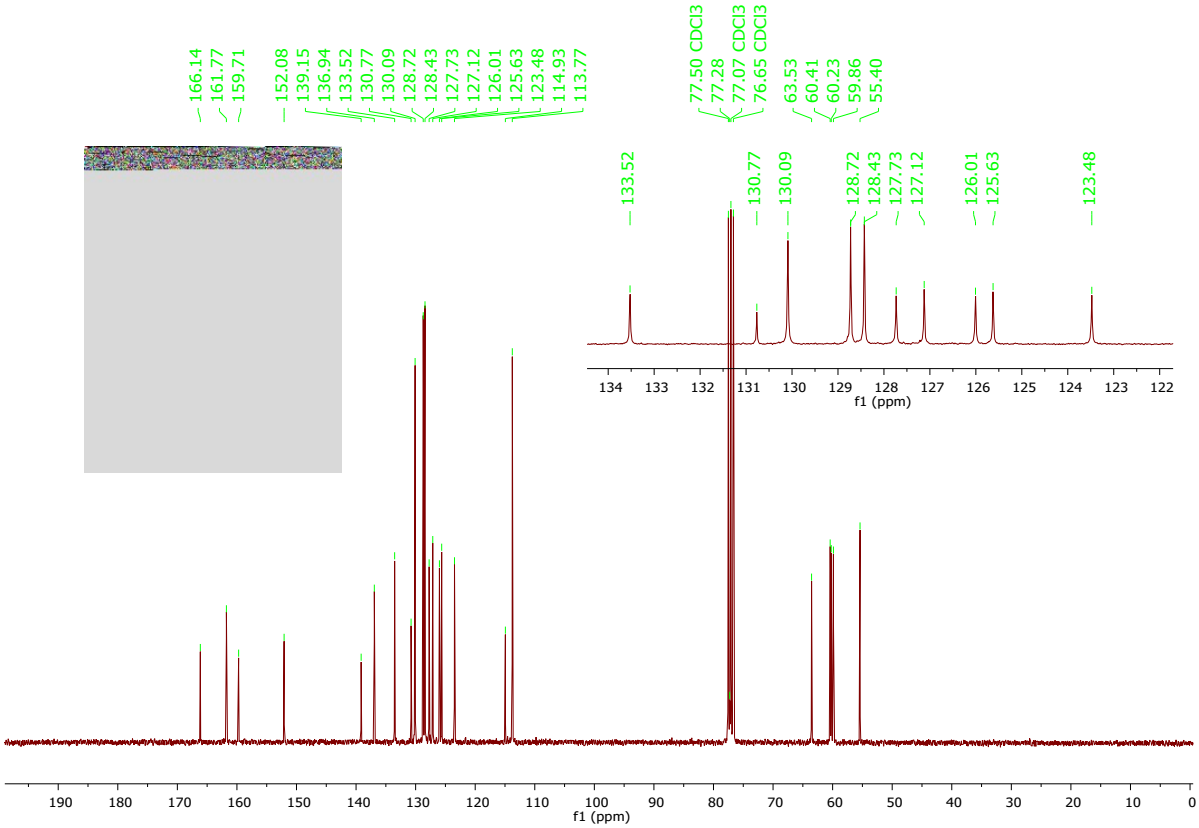
^{1}H NMR spectrum of compound 6b



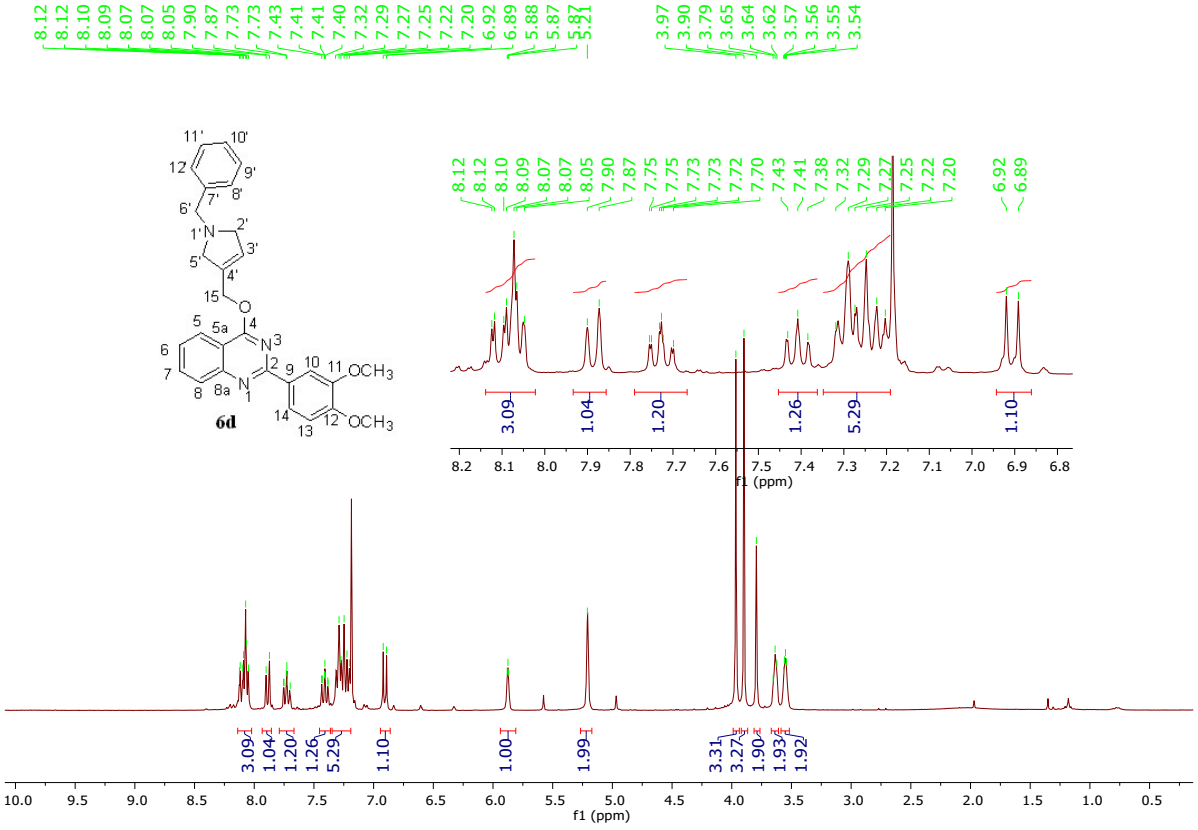
^{13}C NMR spectrum of compound 6b



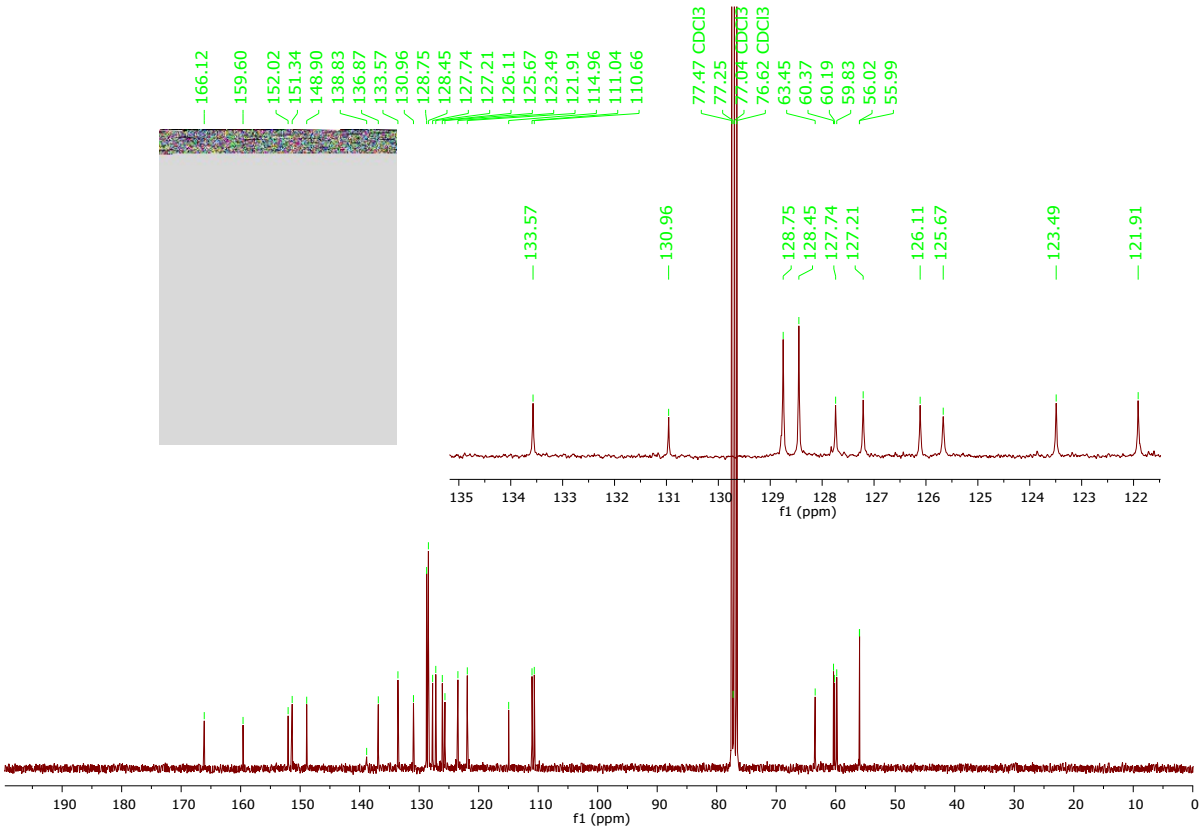
^{1}H NMR spectrum of compound 6c



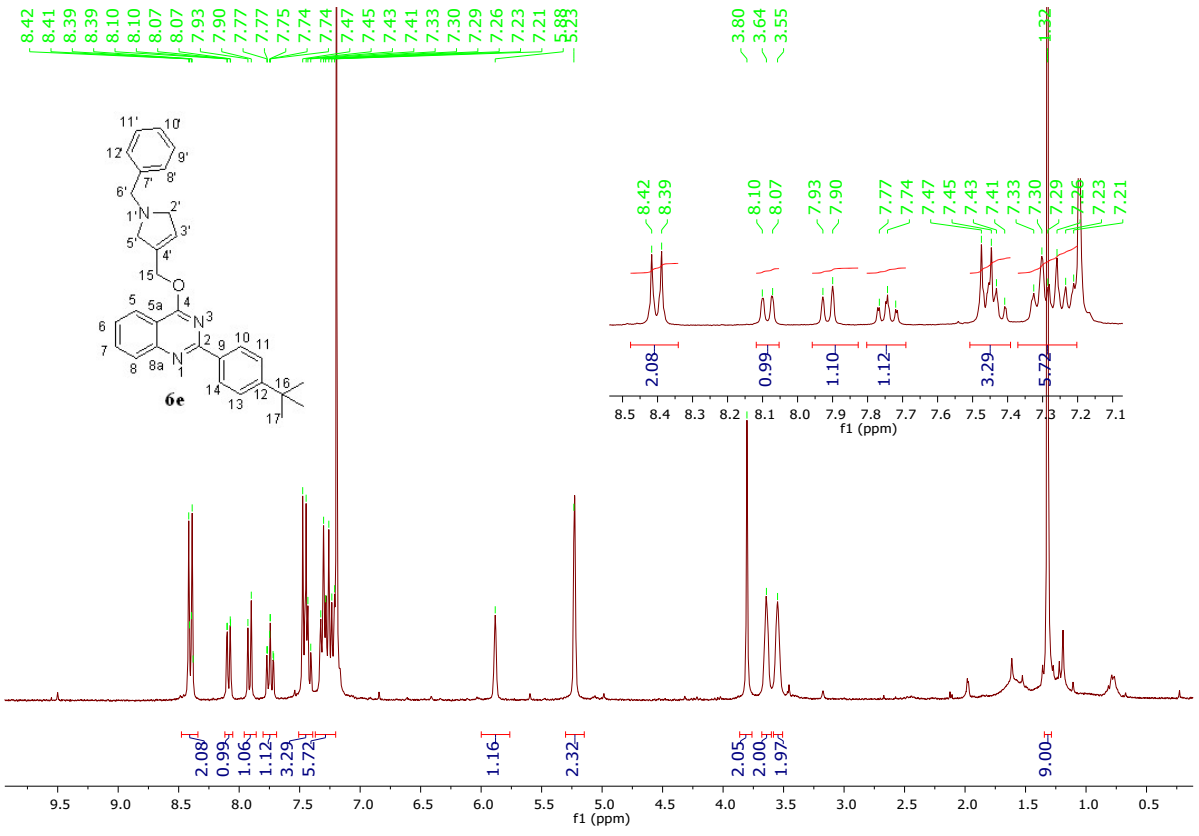
^{1}H NMR spectrum of compound 6c



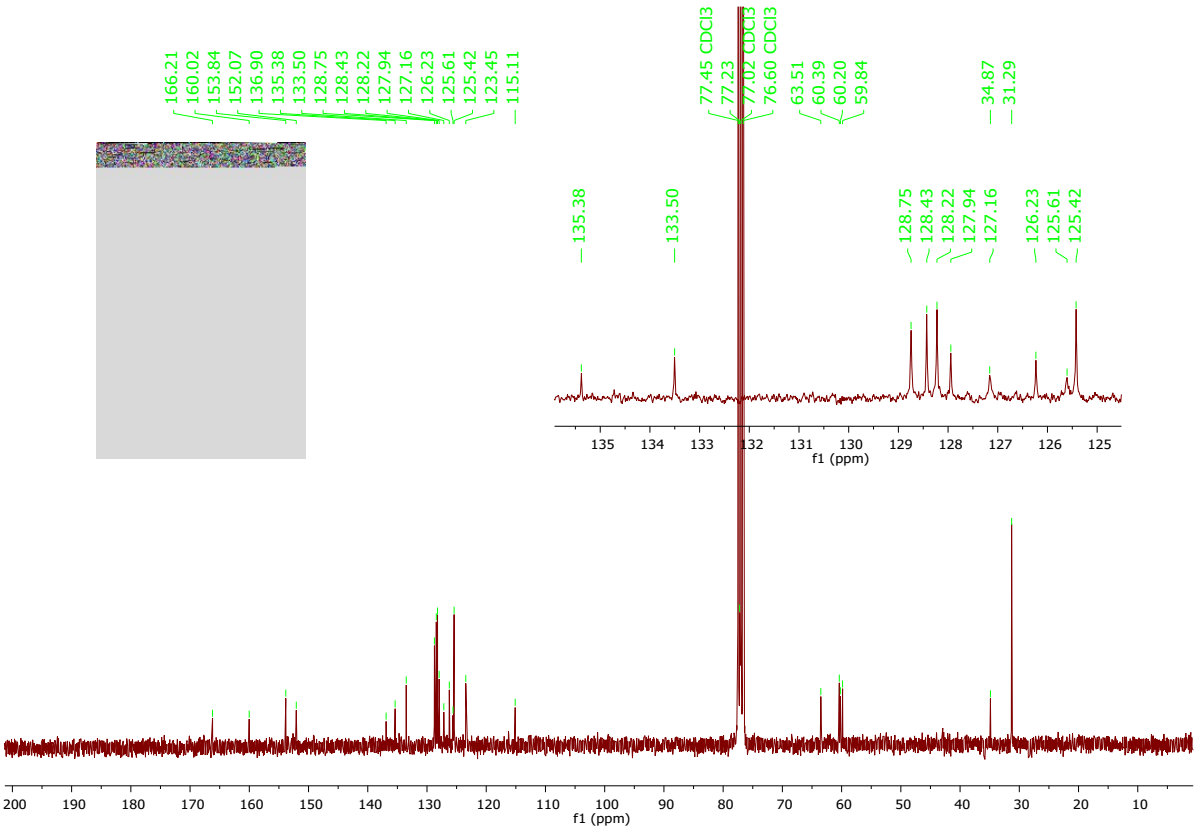
^{1}H NMR spectrum of compound 6d



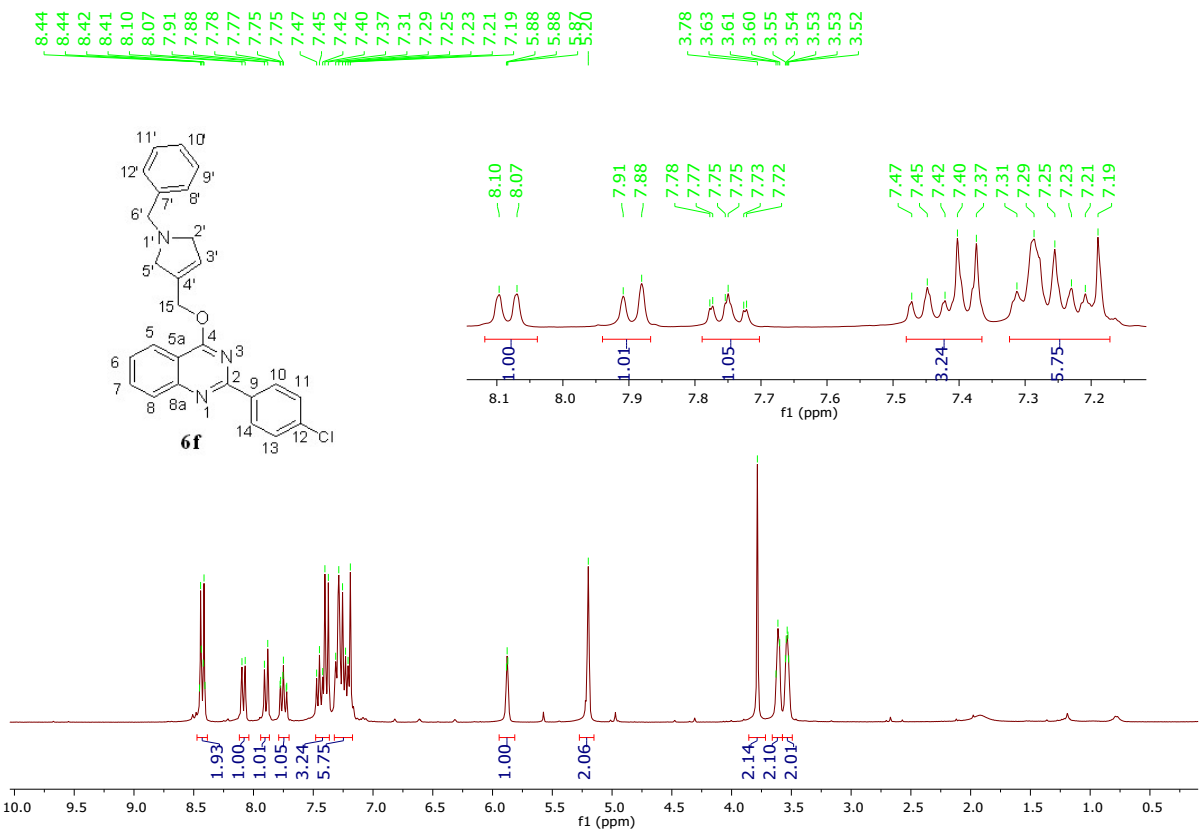
^{13}C NMR spectrum of compound 6d



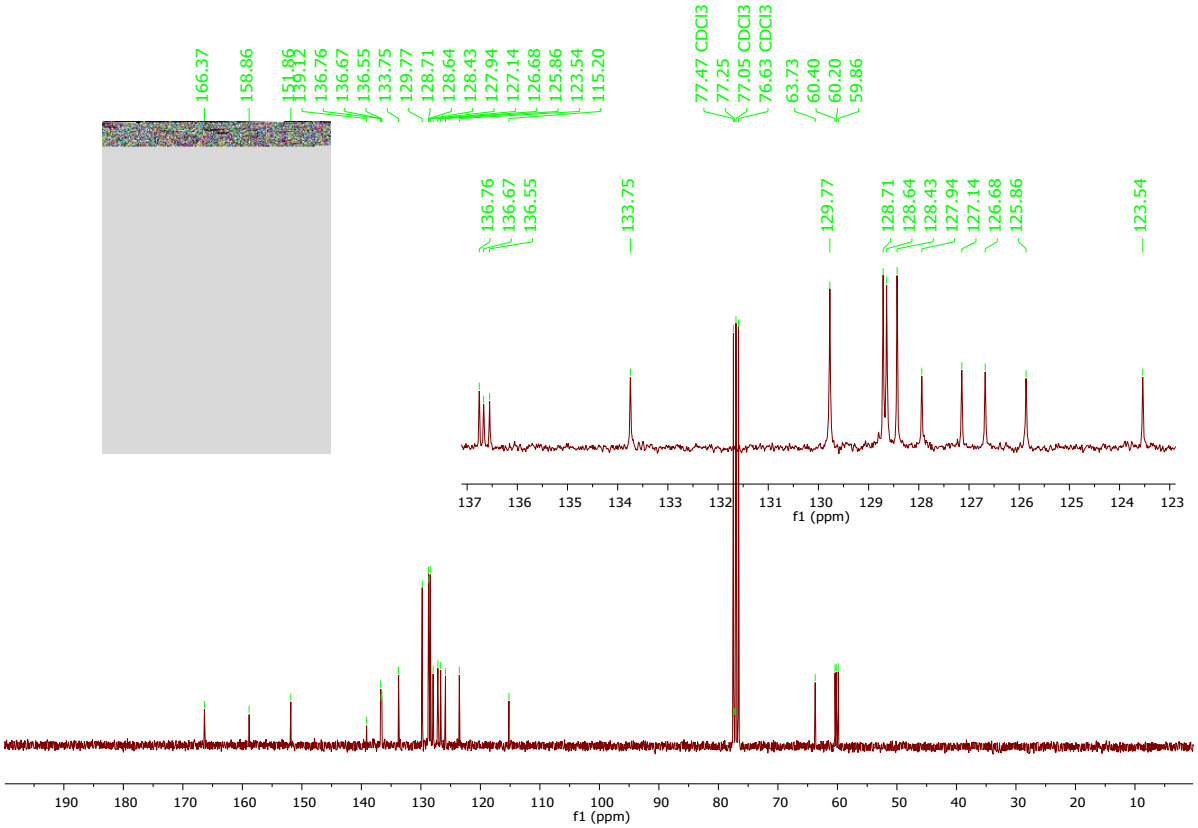
^{1}H NMR spectrum of compound 6e



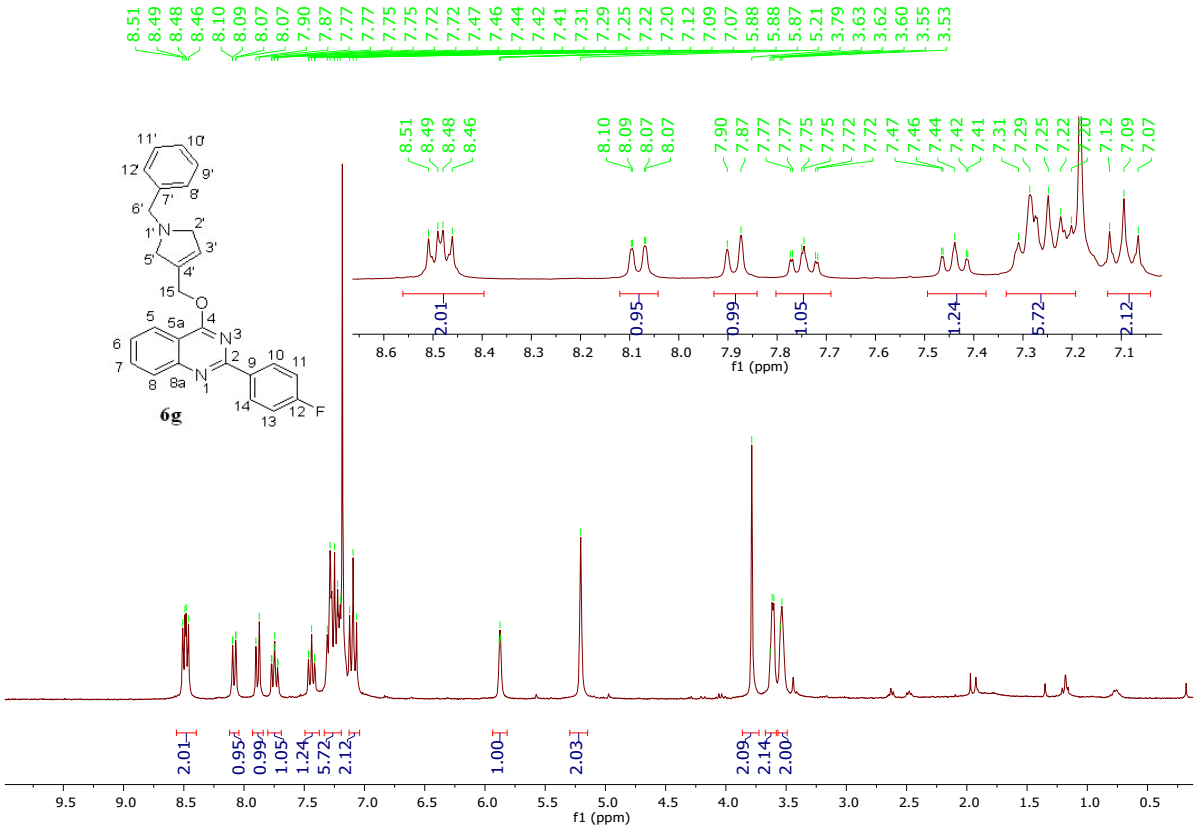
^{13}C NMR spectrum of compound 6e



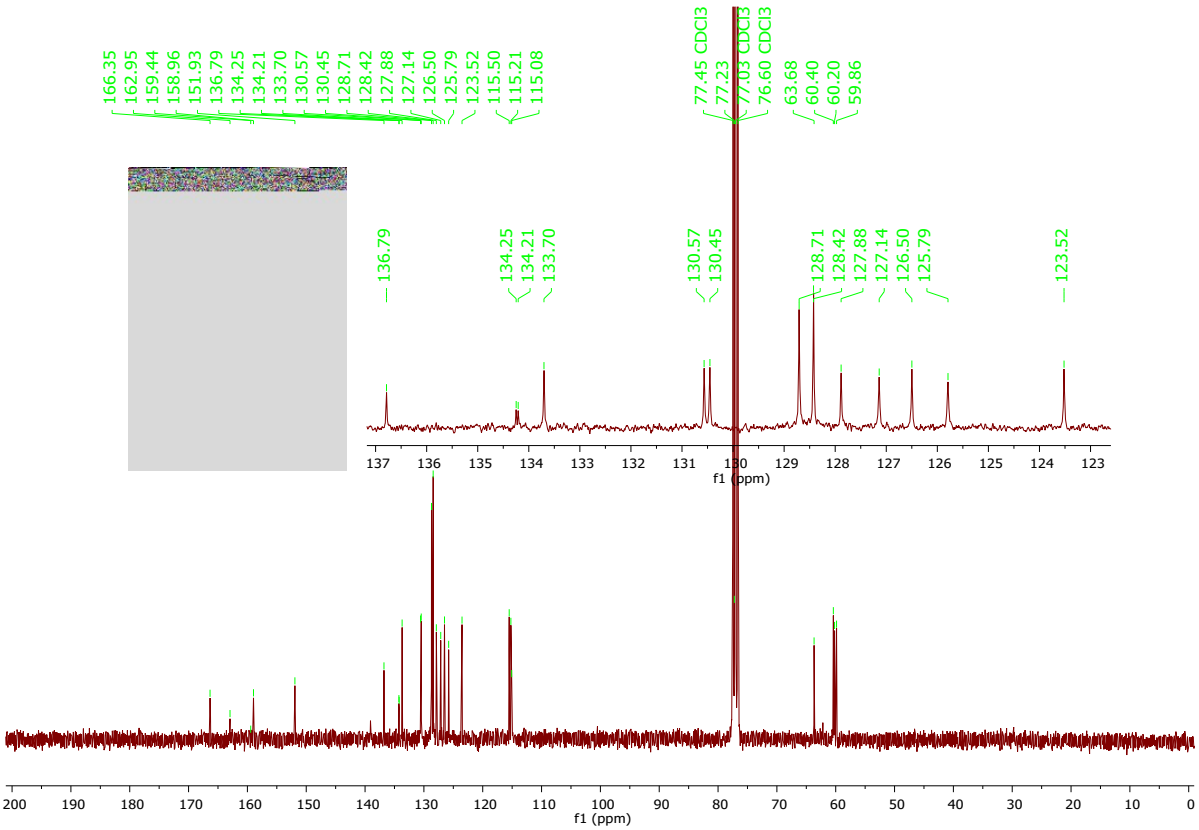
^{1}H NMR spectrum of compound 6f



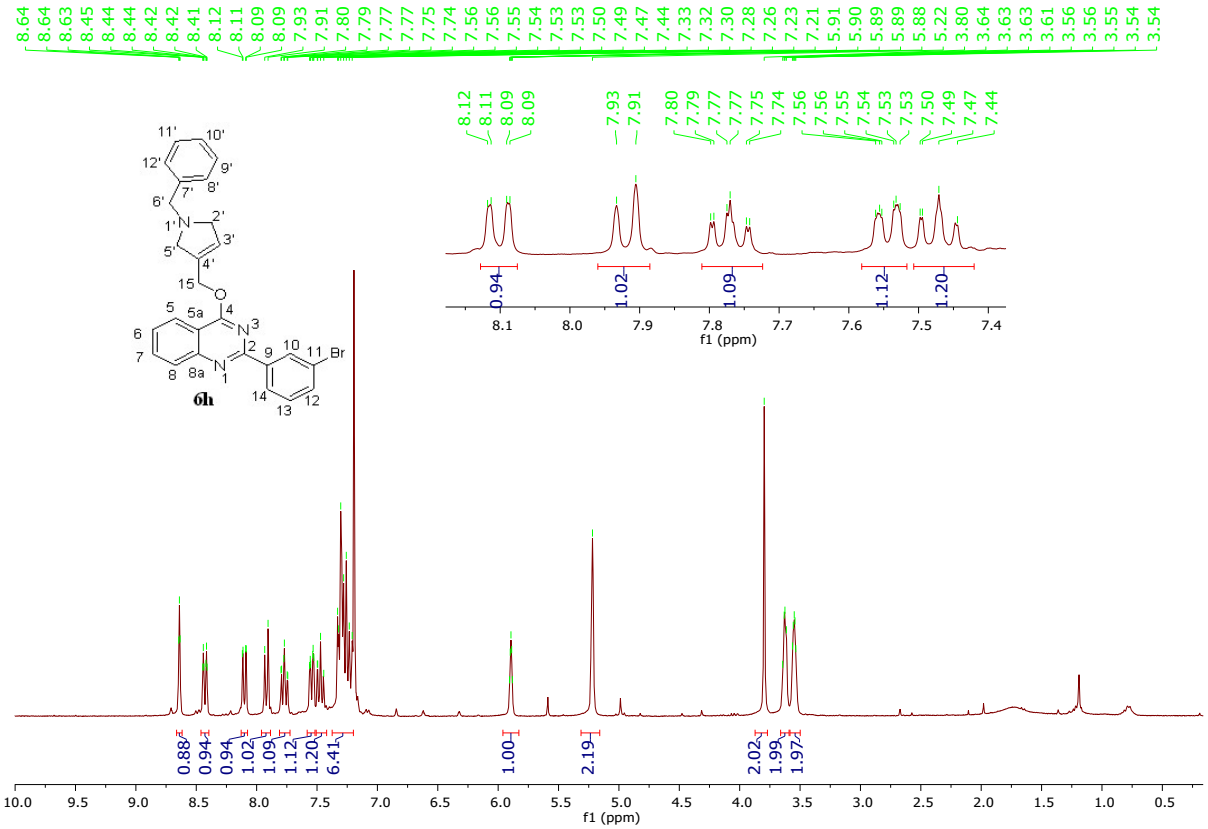
^{13}C NMR spectrum of compound 6f



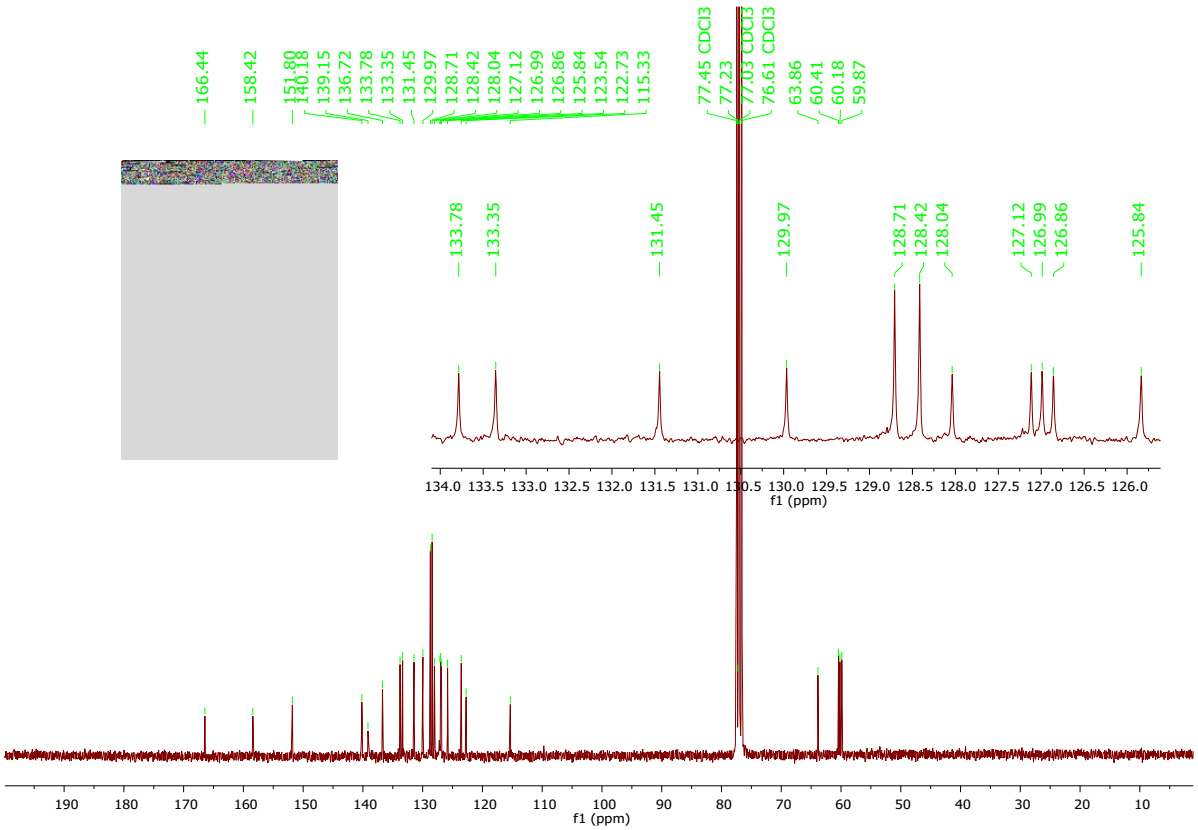
^{1}H NMR spectrum of compound 6g



^{13}C NMR spectrum of compound 6g



^{1}H NMR spectrum of compound 6h



^{13}C NMR spectrum of compound 6h