Supporting Information

P_4O_{10}/TfOH Assisted One Pot Access to 8-Oxoprotoberbines[#]

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1. Experimental section

The reagents used for the experiments were purchased from commercial sources and used without any purification. Reactions were monitored by Thin Layer Chromatography, using silica gel 60 F_{254} plates (Merck). Melting points were recorded by an open capillary tube method and are uncorrected. Infrared spectra were recorded on the Shimadzu FTIR Spectrophotometer. ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) were recorded on Bruker AVANCE III instrument using TMS as an internal standard and $CDCl_3$ as the solvent. HRMS was achieved through Bruker Impact II UHR-TOF Mass Spectrometer System. LCMS studies were performed using Agilent 6460 Triple Quadrupole LC/MS system.

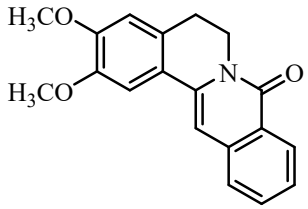
2. General Procedures for the Preparation of Compounds 3a-3m.

Aryl ethylamines **1** (2.2 mmol, 1.2 equiv.) and homophthalic acid **2** (2 mmol, 1 equiv.) was placed in a sealed tube and heated at 185 ^{o}C for 30 minutes. After cooling, DCM (2-5 mL) was added followed by the addition of 8.3 wt% P_4O_{10}/TfOH (45 mg of P_4O_{10} dissolved in 0.3 ml TfOH) *via* glass dropper at 0 °C. Reaction mixture was stirred at room temperature. Upon completion of reaction, ice cold water was added dropwise and the organic phase was extracted in DCM (20 mL). Organic layer was washed with brine (10.0 mL X 2), dried over anhydrous sodium sulfate, and filtered. The solvent was removed by a rotary evaporator, and the residue was purified by a flash column chromatography on silica gel (with 30:70 Ethyl acetate and Petroleum ether as eluent) to obtain products **3a-3l**.

3. General Procedures for the Preparation of Compounds 4a-4l.

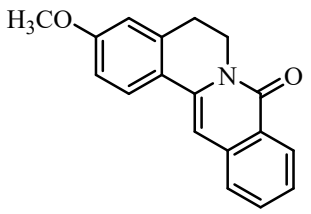
Aryl ethylamines **1** (2.2 mmol, 1.2 equiv) and homopthalic acid **2** (2 mmol, 1 equiv) was placed in a sealed tube and heated at 185 ^{o}C for 30 minutes. After cooling, DCM (20 mL) was added and organic layer was washed with water (20.0 mL X 2) and brine (10.0 mL X 2), dried over anhydrous sodium sulfate, and filtered. The solvent was removed by a rotary evaporator, and the residue was purified by a flash column chromatography on silica gel (with 20:80 Ethyl acetate and Petroleum ether as eluent) to obtain products **4a-4l**.

4. Characterization data of compounds 3a-3m.

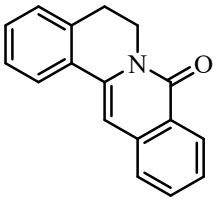


2,3-dimethoxy-5,6-dihydro-8H-isoquinolino[3,2-a]isoquinolin-8-one, ***(3a)*** 3a was prepared **1a** (398 mg, 2.2 mmol) and **2a** (360 mg, 2 mmol) according to the general procedure. Pale yellow solid, (0.565 g, 92 % yield). R_f = 0.3; (petroleum ether/EtOAc = 1:1); Mp 186-188 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.44 (d, J = 8 Hz, 1H), 7.65 (t, J = 7.2 Hz, 1H), 7.58 (d, J = 7.6

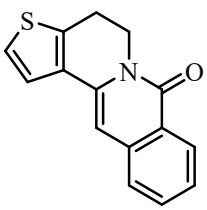
Hz, 1H), 7.46 (t, J = 7.2 Hz, 1H), 7.30 (s, 1H), 6.91 (s, 1H), 6.77 (s, 1H), 4.39 (t, J = 6 Hz, 2H), 4.02 (s, 3H), 3.97 (s, 3H), 2.97 (t, J = 6 Hz 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 162.3, 150.4, 148.5, 137.4, 136.7, 132.3, 128.8, 128.0, 126.2, 125.9, 124.6, 122.3, 110.5, 108.0, 101.5, 56.3, 56.1, 39.8, 28.1. IR (cm^{-1}): 1641, 1591, 1510, 1259, 1152, 1007, 805, 681.



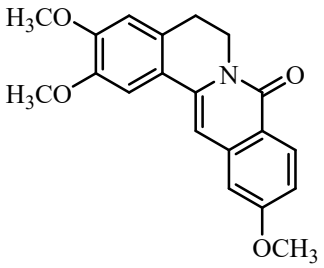
*3-methoxy-5,6-dihydro-8H-isoquinolino[3,2-a]isoquinolin-8-one (**3b**)* 3b was prepared from **1b** (333 mg, 2.2 mmol) and **2a** (360 mg, 2 mmol) according to the general procedure. White solid (0.490 mg, 88 % yield); R_f = 0.5; (petroleum ether/EtOAc = 1:1); Mp 144-146 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.44 (d, J = 8 Hz, 1H), 7.77 (d, J = 8.8 Hz, 1H), 7.61 (dt, J = 8.2, 1.2 Hz, 1H), 7.56 (d, J = 7.6 Hz, 1H), 7.45 (dt, J = 8, 1.2 Hz, 1H), 6.93 (s, 1H), 6.92-6.90 (m, 1H), 6.80 (d, J = 2.8 Hz, 1H), 4.40-4.37 (m, 2H), 3.88 (s, 3H), 3.01-2.99 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 162.2, 160.5, 137.5, 137.1, 136.8, 132.2, 128.0, 126.7, 126.1, 126.0, 124.5, 122.9, 113.7, 112.6, 101.4, 55.4, 39.6, 28.9. IR (cm^{-1}): 1641, 1588, 1504, 1441, 1343, 1242, 1158, 1028, 804, 752, 685.



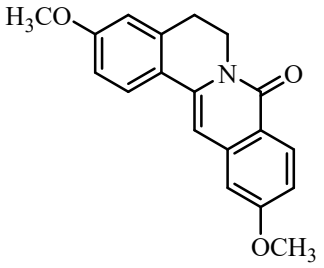
*5,6-dihydro-8H-isoquinolino[3,2-a]isoquinolin-8-one (**3c**)* 3c was prepared from **1c** (266 mg, 2.2 mmol) and **2a** (360 mg, 2 mmol) according to the general procedure. White solid (0.396 mg, 80 % yield); R_f = 0.6; (petroleum ether/EtOAc = 1:1); Mp 80-82 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.46 (d, J = 8 Hz, 1H), 7.84-7.83 (m, 1H), 7.66-7.63 (m, 1H), 7.58 (d, J = 7.5 Hz, 1H), 7.47 (dt, J = 7.2, 1.2 Hz, 1H), 7.39-7.35 (m, 2H), 7.29-7.27 (m, 1H), 7.03 (s, 1H), 4.40-4.38 (m, 2H), 3.02 (t, J = 6 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 162.2, 137.4, 136.6, 135.4, 132.3, 130.2, 129.3, 128.0, 128.0, 127.5, 126.6, 126.3, 125.0, 125.0, 102.9, 39.7, 28.6. IR (cm^{-1}): 3061, 2928, 1641, 1581, 1483, 1455, 1343, 1245, 1158, 759, 692.



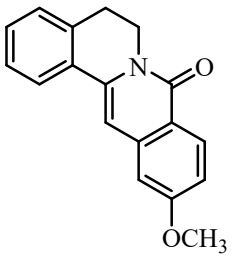
*4,5-dihydro-7H-thieno[3',2':3,4]pyrido[1,2-b]isoquinolin-7-one (**3d**)* 3d was prepared from **1d** (279 mg, 2.2 mmol) and **2a** (360 mg, 2 mmol) according to the general procedure. White solid (0.340 mg, 67 % yield); R_f = 0.6; (petroleum ether/EtOAc = 1:1); Mp 160-162 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.29 (d, *J* = 8 Hz, 1H), 7.50-7.47 (m, 1H), 7.38 (d, *J* = 8 Hz, 1H), 7.33-7.28 (m, 1H), 7.20 (d, *J* = 5.2 Hz, 1H), 7.10 (d, *J* = 5.2 Hz, 1H), 6.62 (s, 1H), 4.37 (t, *J* = 6.4 Hz, 2H), 3.00 (t, *J* = 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 162.5, 137.0, 136.7, 134.7, 132.4, 131.4, 128.1, 126.3, 125.9, 124.9, 124.5, 123.5, 101.6, 40.4, 23.7. IR (cm^{-1}): 1644, 1598, 1333, 1147, 1011, 752, 682.



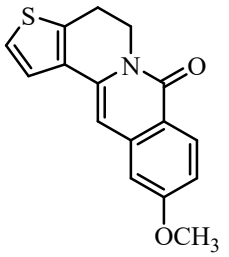
*2,3,11-trimethoxy-5,6-dihydro-8H-isoquinolino[3,2-a]isoquinolin-8-one (**3e**)* 3e was prepared from **1a** (398 mg, 2.2 mmol) and **2b** (420 mg, 2 mmol) according to the general procedure. White solid (596 mg, 88 % yield); R_f = 0.3; (petroleum ether/EtOAc = 1:1); Mp 226-228 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.33 (d, *J* = 8.8 Hz, 1H), 7.26 (s, 1H), 7.01 (dd, *J* = 9, 2.4 Hz, 1H), 6.92 (d, *J* = 2.4 Hz, 1H), 6.82 (s, 1H), 6.74 (s, 1H), 4.34 (t, *J* = 6 Hz, 2H), 3.99 (s, 3H), 3.94 (s, 3H), 3.91(s, 3H), 2.93 (t, *J* = 6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 162.7, 162.0, 150.3, 148.4, 138.7, 138.0, 130.0, 128.8, 122.3, 118.5, 116.0, 110.4, 107.7, 106.4, 101.4, 56.2, 56.1, 55.5, 39.6, 28.1. IR (cm^{-1}): 1611, 1577, 1524, 1378, 1249, 1162, 1110, 1028, 777, 679. HRMS (ESI) (m/z) $[M+H]^+$: calcd. for $C_{20}H_{20}NO_4$: 338.1392, found: 338.1391.



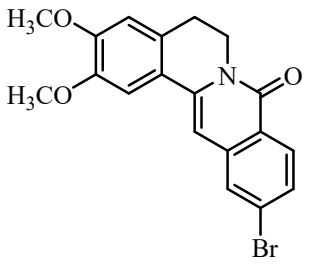
*3,11-dimethoxy-5,6-dihydro-8H-isoquinolino[3,2-a]isoquinolin-8-one (**3f**)* 3f was prepared from **1b** (333 mg, 2.2 mmol) and **2b** (420 mg, 2 mmol) according to the general procedure. White solid (498 mg, 81 % yield); R_f = 0.4; (petroleum ether/EtOAc = 1:1); Mp 138-140 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.34 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.75 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.03-7.00 (m, 1H), 6.91-6.90 (m, 2H), 6.86 (d, *J* = 2 Hz, 1H), 6.79 (s, 1H), 4.35 (t, *J* = 5.2 Hz, 2H), 3.92 (s, 3H), 3.87 (s, 3H), 2.98 (t, *J* = 5.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 162.7, 161.9, 160.5, 138.8, 138.1, 137.2, 130.0, 126.6, 122.9, 118.5, 115.9, 113.6, 112.6, 106.5, 101.3, 55.5, 39.4, 28.9. IR (cm^{-1}): 1637, 1588, 1255, 1227, 1145, 1032, 873, 805, 685. HRMS (ESI) (m/z) $[M+H]^+$: calcd. for $C_{19}H_{18}NO_3$: 308.1286, found: 308.1283.



11-methoxy-5,6-dihydro-8H-isoquinolino[3,2-a]isoquinolin-8-one ***(3g)*** 3g was prepared from **1c** (266 mg, 2.2 mmol) and **2b** (420 mg, 2 mmol) according to the general procedure. White solid (382 mg, 69 % yield); R_f = 0.6; (petroleum ether/EtOAc = 1:1); Mp 72-74^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.27 (d, *J* = 8.8 Hz, 1H), 7.75 (dd, *J* = 5.6, 3.6 Hz, 1H), 7.30-7.28 (m, 2H), 7.24-7.19 (m, 1H), 6.97 (dd, *J* = 2.4 Hz, 1H), 6.90 (s, 1H), 6.87 (d, *J* = 2.4 Hz, 1H), 4.29 (t, *J* = 6 Hz, 2H), 3.86 (s, 3H), 2.94 (t, *J* = 6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 162.8, 161.9, 138.6, 138.0, 135.5, 130.2, 130.0, 129.4, 128.0, 127.4, 125.0, 118.9, 116.4, 106.8, 102.8, 55.5, 39.5, 28.6. IR (cm^{-1}): 1637, 1581, 1462, 1401, 1231, 1164, 1023, 760. HRMS (ESI) (m/z) [M+ H]$^{+}$: calcd. for $C_{18}H_{16}NO_2$: 278.1175, found:278.1173.

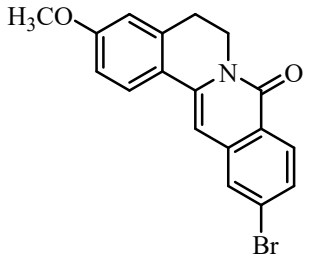


10-methoxy-4,5-dihydro-7H-thieno[3',2':3,4]pyrido[1,2-b]isoquinolin-7-one ***(3h)*** 3h was prepared from **1d** (279 mg, 2.2 mmol) and **2b** (420 mg, 2 mmol) according to the general procedure. Pale yellow solid (360 mg, 64 % yield); R_f = 0.4; (petroleum ether/EtOAc = 1:1); Mp 162-164 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.32 (d, *J* = 8.8 Hz, 1H), 7.33 (d, *J* = 5.2 Hz, 1H), 7.23 (d, *J* = 5.2 Hz, 1H), 7.00 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.88 (d, *J* = 2.8 Hz, 1H), 6.70 (s, 1H), 4.48 (t, *J* = 6.4 Hz, 2H), 3.91 (s, 3H), 3.13 (t, *J* = 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 162.8, 162.2, 138.7, 137.2, 135.3, 131.4, 130.2, 124.4, 123.5, 118.9, 115.9, 106.6, 101.4, 55.5, 40.2, 23.7. IR (cm^{-1}): 1642, 1585, 1488, 1427, 1362, 1226, 1172, 1030, 874, 732. HRMS (ESI) (m/z) [M+ H]$^{+}$: calcd. for $C_{16}H_{13}NO_2S$: 284.0739, found: 284.0738.

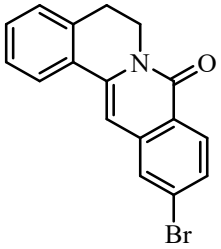


11-bromo-2,3-dimethoxy-5,6-dihydro-8H-isoquinolino[3,2-a]isoquinolin-8-one ***(3i)*** 3i was prepared from **1a** (398 mg, 2.2 mmol) and **2c** (518 mg, 2 mmol) according to the general procedure. White solid (684 mg, 89% yield); R_f = 0.4; (petroleum ether/EtOAc = 1:1); Mp 222-

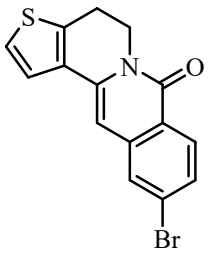
224 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.27 (d, *J* = 8.8 Hz, 1H), 7.74 (d, *J* = 1.6 Hz, 1H), 7.51 (dd, *J* = 8.6, 1.6 Hz,1H), 7.24 (s, 1H), 6.79 (s, 1H), 6.76 (s, 1H), 4.34 (t, *J* = 6 Hz, 2H), 4.00 (s, 3H), 3.96 (s, 3H), 2.96 (t, *J* = 6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.9, 150.6, 148.5, 138.8, 138.2, 129.9, 129.3, 128.9, 128.2, 127.3, 123.1, 121.9, 110.4, 107.8, 100.2, 56.2, 56.1, 39.8, 28.0. IR (cm^{-1}): 1641, 1595, 1513, 1262, 1152, 1018, 855, 773, 681. HRMS (ESI) (m/z) $[M+H]^+$: calcd. for $C_{19}H_{17}NO_3Br$: 386.0386, found: 386.0382.



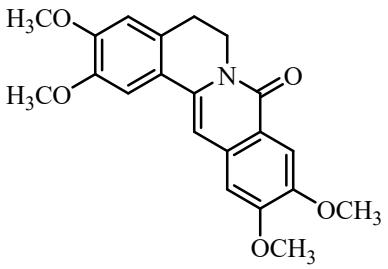
11-bromo-3-methoxy-5,6-dihydro-8H-isoquinolino[3,2-a]isoquinolin-8-one ***(3j)*** 3j was prepared from **1b** (333 mg, 2.2 mmol) and **2c** (518 mg, 2 mmol) according to the general procedure. White solid (590 mg, 83% yield); R_f = 0.5; (petroleum ether/EtOAc = 1:1); Mp 170-172 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.18 (d, *J* = 8.8 Hz, 1H), 7.65 (d, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 1.6 Hz, 1H), 7.42 (dd, *J* = 8.6, 1.6 Hz, 1H), 6.83 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.72 (s, 1H), 6.71-6.70 (m, 1H), 4.26 (t, *J* = 6 Hz, 2H), 3.80 (s, 3H), 2.91 (t, *J* = 6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.8, 160.8, 138.9, 138.3, 137.3, 129.8, 129.3, 128.2, 127.3, 126.8, 123.0, 122.5, 113.8, 112.7, 100.1, 55.5, 39.6, 28.7. IR (cm^{-1}): 1637, 1591, 1251, 1149, 873, 805, 770. HRMS (ESI) (m/z) $[M+H]^+$: calcd. for $C_{18}H_{14}BrNO_2$: 356.0280, found: 356.0275.



11-bromo-5,6-dihydro-8H-isoquinolino[3,2-a]isoquinolin-8-one ***(3k)*** 3k was prepared from **1c** (266 mg, 2.2 mmol) and **2c** (518 mg, 2 mmol) according to the general procedure. White solid (375mg, 58 % yield); R_f = 0.7; (petroleum ether/EtOAc = 1:1); Mp 216-218 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.21 (d, *J* = 8.4 Hz, 1H), 7.74 (m, 1H), 7.68 (s, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.31 (t, *J* = 4.4 Hz, 2H), 7.23-7.21 (m, 1H), 6.86 (s, 1H), 4.29 (t, *J* = 6 Hz, 2H), 2.95 (t, *J* = 6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.8, 138.8, 138.0, 135.5, 129.9, 129.8, 129.8, 128.6, 128.1, 127.6, 127.4, 125.2, 123.5, 101.7, 39.7, 28.4. IR (cm^{-1}): 1641, 1588, 1488, 1308, 1227, 1169, 1031, 876, 734. HRMS (ESI) (m/z) $[M+H]^+$: calcd. for $C_{17}H_{12}BrNO$: 326.0174, found: 326.0172.

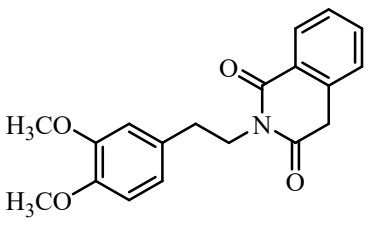


10-bromo-4,5-dihydro-7H-thieno[3',2':3,4]pyrido[1,2-b]isoquinolin-7-one ***(3l)*** 3l was prepared from **1d** (279 mg, 2.2 mmol) and **2c** (518 mg, 2 mmol) according to the general procedure. White solid (440 mg, 66 % yield); R_f = 0.8; (petroleum ether/EtOAc = 1:1); Mp 236-238 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.27 (d, *J* = 8.8 Hz, 1H), 7.70 (d, *J* = 1.6 Hz, 1H), 7.52 (dd, *J* = 8.8, 2 Hz, 1H), 7.34 (d, *J* = 5.2 Hz, 1H), 7.26 (d, *J* = 5.2 Hz, 1H), 6.68 (s, 1H), 4.50 (t, *J* = 6.4 Hz, 1H), 3.17 (t, *J* = 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 162.1, 138.2, 137.6, 136.0, 131.0, 130.0, 129.5, 128.2, 127.5, 124.7, 123.5, 123.5, 100.3, 40.4, 23.6. IR (cm^{-1}): 1641, 1587, 1425, 1227, 1169, 871, 827, 731. HRMS (ESI) (m/z) [M+ H]$^{+}$: calcd. for $C_{15}H_{10}BrNOS$: 331.9739, found: 331.9736.

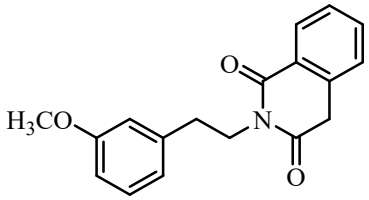


2,3,10,11-tetramethoxy-5,6-dihydro-8H-isoquinolino[3,2-a]isoquinolin-8-one ***(3m)*** 3m was prepared prepared from **1a** (398 mg, 2.2 mmol) and **2d** (480 mg, 2 mmol) according to the general procedure. Pale yellow solid (396 mg, 56 % yield); R_f = 0.4; (petroleum ether/EtOAc = 1:1); Mp 198-200 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.80 (s, 1H), 7.24 (s, 1H), 6.94 (s, 1H), 6.84 (s, 1H), 6.74 (s, 1H), 4.36 (t, *J* = 6 Hz, 2H), 4.02 (s, 3H), 4.01 (s, 3H), 3.99 (s, 3H), 3.94 (s, 3H), 2.94 (t, *J* = 6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.5, 153.5, 150.0, 149.0, 148.4, 136.1, 132.2, 128.4, 122.5, 118.5, 110.5, 107.8, 107.6, 105.9, 101.3, 56.2, 56.2, 56.0, 39.8, 28.1; IR (cm^{-1}): 1642, 1599, 1506, 1461, 1353, 1259, 1170, 1094, 753.

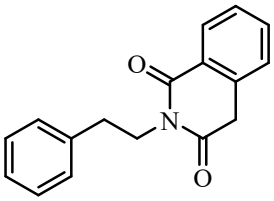
5. Characterization data of compounds 4a-4m.



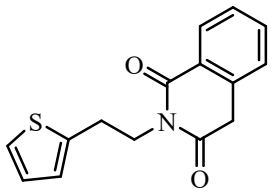
*2-(3,4-dimethoxyphenethyl)isoquinoline-1,3(2H,4H)-dione (**4a**)* 4a was prepared from **1a** (398 mg, 2.2 mmol) and **2a** (360 mg, 2 mmol) according to the general procedure. Pale yellow solid (557 mg, 86 % yield); R_f = 0.3; (petroleum ether/EtOAc = 2:1); Mp 146-148 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.13 (d, *J* = 7.6 Hz, 1H), 7.50 (td, *J* = 7.6, 1.2 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 6.78-6.71 (m, 3H), 4.14-4.09 (m, 2H), 3.94 (s, 2H), 3.78 (s, 3H), 3.77 (s, 3H), 2.81-2.77 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.8, 164.8, 148.9, 147.6, 134.1, 133.6, 131.1, 129.1, 127.8, 127.1, 125.4, 121.0, 112.1, 111.3, 55.9, 55.8, 41.6, 36.4, 33.7. IR (cm^{-1}): 1703, 1658, 1514, 1346, 1250, 1143, 1014, 741.



*2-(3-methoxyphenethyl)isoquinoline-1,3(2H,4H)-dione (**4b**)* 4b was prepared from **1b** (333 mg, 2.2 mmol) and **2a** (360 mg, 2 mmol) according to the general procedure. White solid (0.496 mg, 84 % yield); R_f = 0.4; (petroleum ether/EtOAc = 2:1); Mp 88-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.23 (d, *J* = 8 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.23 (t, *J* = 8 Hz, 1H), 6.92 (d, *J* = 7.2 Hz, 1H), 6.87 (s, 1H), 6.78 (d, *J* = 8 Hz, 1H), 4.22 (t, *J* = 8 Hz 2H), 4.03 (s, 2H), 3.80 (s, 3H), 2.91 (t, *J* = 8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.8, 164.7, 159.7, 140.2, 134.1, 133.6, 129.5, 129.1, 127.7, 127.1, 125.4, 121.3, 114.4, 112.2, 55.2, 41.4, 36.4, 34.2. IR (cm^{-1}): 1707, 1661, 1333, 1252, 1140, 745, 689. HRMS (ESI) (m/z) [M+ H]$^+$: calcd. for $C_{18}H_{17}NO_3$: 296.1281, found: 296.1278.

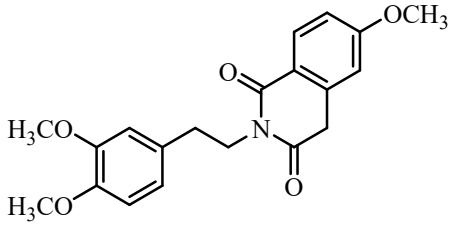


*2-phenethylisoquinoline-1,3(2H,4H)-dione (**4c**)* 4c was prepared from **1c** (266 mg, 2.2 mmol) and **2a** (360 mg, 2 mmol) according to the general procedure. White solid (0.480 mg, 90 % yield); R_f = 0.5; (petroleum ether/EtOAc = 2:1); Mp 126-128 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.14 (dd, *J* = 8, 0.8 Hz, 1H), 7.51 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.37 (t, *J* = 8 Hz, 1H), 7.23-7.14 (m, 6H), 4.16-4.11 (m, 2H), 3.94 (s, 2H), 2.86-2.82 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.8, 164.7, 138.6, 134.1, 133.6, 129.1, 129.0, 128.5, 127.8, 127.2, 126.5, 125.4, 41.5, 36.4, 34.2. IR (cm^{-1}): 1700, 1651, 1350, 1262, 1136, 1000, 734, 692.

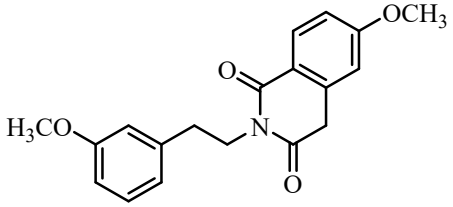


*2-(2-(thiophen-2-yl)ethyl)isoquinoline-1,3(2H,4H)-dione (**4d**)* 4d was prepared from **1d** (279 mg, 2.2 mmol) and **2a** (360 mg, 2 mmol) according to the general procedure. White solid (0.434

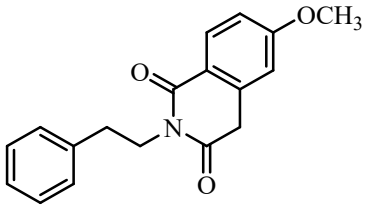
mg, 80 % yield); R_f = 0.6; (petroleum ether/EtOAc = 2:1); Mp 106-108 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.13 (d, *J* = 7.6 Hz, 1H), 7.52 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.20 (d, *J* = 8.8 Hz, 1H), 7.07 (dd, *J* = 4.8, 1.2 Hz, 1H), 6.87-6.82 (m, 2H), 4.21-4.17 (m, 2H), 3.96 (s, 2H), 3.10-3.06 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.8, 164.7, 140.6, 134.1, 133.7, 129.2, 127.8, 127.2, 126.9, 125.5, 125.3, 123.9, 41.4, 36.4, 28.1. IR (cm^{-1}): 1708, 1658, 1347, 1230, 989, 745, 690. HRMS (ESI) (m/z) $[M+H]^+$: calcd. for $C_{15}H_{13}NO_2S$: 272.0745, found: 272.0748.



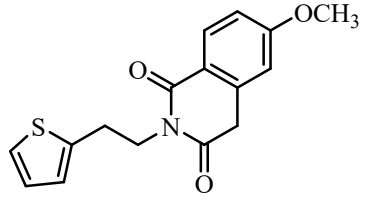
*2-(3,4-dimethoxyphenethyl)-6-methoxyisoquinoline-1,3(2H,4H)-dione (**4e**)* 4e was prepared from **1a** (398 mg, 2.2 mmol) and **2b** (420 mg, 2 mmol) according to the general procedure. White solid (588 mg, 83 % yield); R_f = 0.3; (petroleum ether/EtOAc = 2:1); Mp 172-174 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.13 (d, *J* = 8.5 Hz, 1H), 6.96 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.85-6.79 (m, 3H), 6.70 (d, *J* = 2.5 Hz, 1H), 4.18-4.15 (m, 2H), 3.97 (s, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 2.85 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 169.9, 164.4, 163.8, 148.8, 147.6, 136.4, 131.2, 120.9, 118.2, 114.4, 112.1, 111.2, 55.9, 55.8, 55.6, 41.5, 36.6, 33.8. IR (cm^{-1}): 1712, 1651, 1591, 1513, 1340, 1230, 1142, 1021, 759. HRMS (ESI) (m/z) $[M+H]^+$: calcd. for $C_{20}H_{22}NO_5$: 356.1453, found: 356.1458.



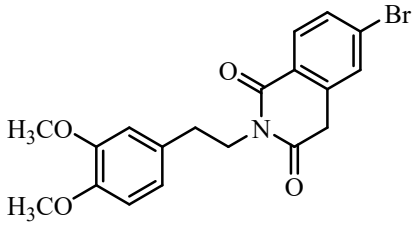
*6-methoxy-2-(3-methoxyphenethyl)isoquinoline-1,3(2H,4H)-dione (**4f**)* 4f was prepared from **1b** (360 mg, 2.2 mmol) and **2b** (420 mg, 2 mmol) according to the general procedure. White solid (546 mg, 84 % yield); R_f = 0.4; (petroleum ether/EtOAc = 2:1); Mp 128-130 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.15 (d, *J* = 9 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 6.97 (dd, *J* = 9, 2.5 Hz, 1H), 6.92 (d, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 2.5 Hz, 1H), 6.78 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.71 (d, *J* = 2.5 Hz, 1H), 4.20 (m, 2H), 3.99 (s, 2H), 3.89 (s, 3H), 3.80 (s, 3H), 2.90 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 169.8, 164.4, 163.8, 159.7, 140.3, 136.4, 131.3, 129.4, 121.4, 118.2, 114.4, 114.3, 112.2, 111.2, 55.6, 55.2, 41.3, 36.7, 34.3. IR (cm^{-1}): 1712, 1658, 1580, 1333, 1248, 1142, 1043, 989, 756, 678. HRMS (ESI) (m/z) $[M+H]^+$: calcd. for $C_{19}H_{20}NO_4$: 326.1386, found: 326.1387.



*6-methoxy-2-phenethylisoquinoline-1,3(2H,4H)-dione (**4g**)* 4g was prepared from **1c** (266 mg, 2.2 mmol) and **2b** (420 mg, 2 mmol) according to the general procedure. White solid (485 mg, 82 % yield); R_f = 0.5; (petroleum ether/EtOAc = 2:1); Mp 126-128 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.17 (d, *J* = 8.8 Hz, 1H), 7.33-7.30 (m, 4H), 7.26-7.22 (m, 1H), 6.98 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.73 (d, *J* = 2.4 Hz, 1H), 4.23-4.19 (m, 2H), 3.99 (s, 2H), 3.90 (s, 3H), 2.95-2.91 (m, 2H).^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 169.9, 164.4, 163.8, 138.7, 136.4, 131.3, 129.0, 128.5, 126.4, 118.2, 114.4, 111.2, 55.6, 41.4, 36.7, 34.2. IR (cm^{-1}): 1701, 1648, 1602, 1336, 1259, 1131, 1025, 844, 741, 688. HRMS (ESI) (m/z) [M+ H]$^{+}$: calcd. for $C_{18}H_{18}NO_3$: 296.1281, found: 296.1277.

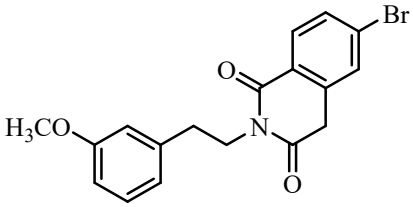


*6-methoxy-2-(2-(thiophen-2-yl)ethyl)isoquinoline-1,3(2H,4H)-dione (**4h**)* 4h was prepared from **1d** (279 mg, 2.2 mmol) and **2b** (420 mg, 2 mmol) according to the general procedure. Pale yellow solid (476 mg, 79 % yield); R_f = 0.4; (petroleum ether/EtOAc = 2:1); Mp 102-104 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.13 (d, *J* = 8.8 Hz, 1H), 7.14 (dd, *J* = 4.8, 0.8 Hz, 1H), 6.95 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.93-6.91 (m, 1H), 6.89 (d, *J* = 2.8 Hz, 1H), 6.70 (d, *J* = 2 Hz, 1H), 4.24 (t, *J* = 8 Hz, 2H), 3.98 (s, 2H), 3.88 (s, 3H), 3.14 (t, *J* = 8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.9, 164.3, 163.9, 140.7, 136.3, 131.3, 126.9, 125.5, 123.8, 118.2, 114.4, 111.3, 55.6, 41.2, 36.7, 28.1. IR (cm^{-1}): 1704, 1658, 1602, 1383, 1344, 1272, 1032, 989, 759, 695. HRMS (ESI) (m/z) [M+ H]$^{+}$: calcd. for $C_{16}H_{16}NO_3S$: 302.0845, found: 302.0836.

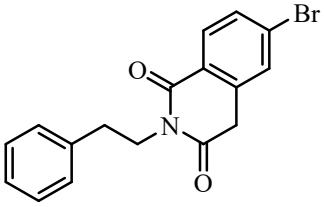


*6-bromo-2-(3,4-dimethoxyphenethyl)isoquinoline-1,3(2H,4H)-dione (**4i**)* 4i was prepared from **1a** (298 mg, 2.2 mmol) and **2c** (518 mg, 2 mmol) according to the general procedure. Yellow solid (630 mg, 78 % yield); R_f = 0.4; (petroleum ether/EtOAc = 2:1); Mp 154-156 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.07 (d, *J* = 8.4 Hz, 1H), 7.59 (dd, *J* = 8.4, 2 Hz, 1H), 7.46 (s, 1H), 6.84-6.79 (m, 3H), 4.20-4.16 (m, 2H), 4.00 (s, 2H), 3.87 (s, 3H), 3.86 (s, 3H), 2.88-2.84 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.0, 164.0, 148.9, 147.7, 135.7, 131.3, 130.9, 130.6, 130.1, 128.8, 124.3, 121.0, 112.2, 111.3, 55.9, 55.9, 41.7, 36.0, 33.6 IR (cm^{-1}): 1710,

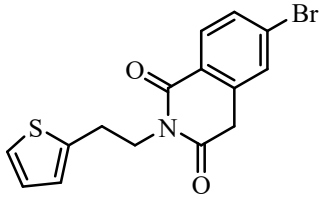
1654, 1592, 1517, 1344, 1235, 1142, 1024, 764. HRMS (ESI) (m/z) $[M+H]^+$: calcd. for $C_{19}H_{19}NO_4Br$: 404.0491, found: 404.0489.



*6-bromo-2-(3-methoxyphenethyl)isoquinoline-1,3(2H,4H)-dione (**4j**)* 4j was prepared from **1b** (360 mg, 2.2 mmol) and **2c** (518 mg, 2 mmol) according to the general procedure. White solid (612 mg, 82 % yield); R_f = 0.6; (petroleum ether/EtOAc = 2:1); Mp 116-118 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.07 (d, J = 8.4 Hz, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.46 (s, 1H), 7.22 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 7.6 Hz, 1H), 6.84 (s, 1H), 6.77 (dd, J = 8, 2.4 Hz, 1H), 4.21-4.18 (m, 2H), 4.00 (s, 2H), 3.79 (s, 3H), 2.90-2.87 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.0, 164.0, 159.7, 140.0, 135.7, 131.3, 130.7, 130.1, 129.5, 128.8, 124.3, 121.3, 114.4, 112.2, 55.2, 41.5, 36.0, 34.1. IR (cm^{-1}): 1711, 1659, 1592, 1583, 1435, 1379, 1338, 1252, 1143, 1041, 755. HRMS (ESI) (m/z) $[M+H]^+$: calcd. for $C_{18}H_{17}NO_3Br$: 374.0386, found: 374.0389.

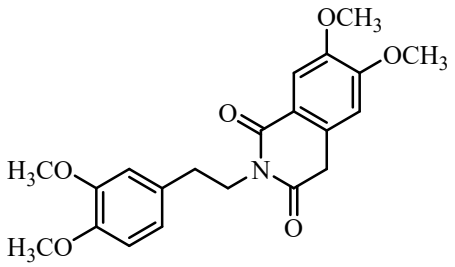


*6-bromo-2-phenethylisoquinoline-1,3(2H,4H)-dione, (**4k**)* 4k was prepared from **1c** (266 mg, 2.2 mmol) and **2c** (518 mg, 2 mmol) according to the general procedure. White solid (570 mg, 83 % yield); R_f = 0.6; (petroleum ether/EtOAc = 2:1); Mp 128-130 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.09 (d, J = 8.4 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H), 7.47 (s, 1H), 7.34-7.31 (m, 4H), 7.27-7.23 (m, 1H), 4.24-4.20 (m, 2H), 4.01 (s, 2H), 2.95-2.91 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.0, 164.0, 138.4, 135.7, 131.3, 130.7, 130.2, 129.0, 128.8, 128.8, 128.7, 128.5, 126.6, 124.3, 41.6, 36.0, 34.1. IR (cm^{-1}): 1710, 1654, 1591, 1339, 1262, 1143, 990, 762, 692. HRMS (ESI) (m/z) $[M+H]^+$: calcd. for $C_{17}H_{15}NO_2Br$: 344.0280, found: 344.0276.



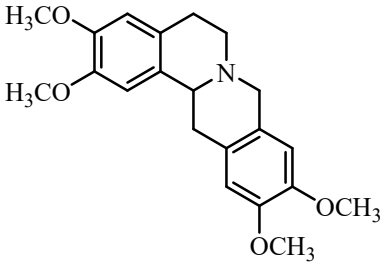
*6-bromo-2-(2-(thiophen-2-yl)ethyl)isoquinoline-1,3(2H,4H)-dione (**4l**)* 4l was prepared from **1d** (279 mg, 2.2 mmol) and **2c** (518 mg, 2 mmol) according to the general procedure. Pale yellow solid (591 mg, 84 % yield); R_f = 0.7; (petroleum ether/EtOAc = 2:1); Mp 118-120 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.98 (d, J = 8.4 Hz, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.39 (s, 1H), 7.07 (d, J = 4.8 Hz, 1H), 6.86-6.84 (m, 1H), 6.81 (d, J = 3.2 Hz, 1H), 4.18 (t, J = 7.6

Hz, 2H), 3.93 (s, 2H), 3.08 (t, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 169.0, 164.0, 140.4, 135.7, 131.4, 130.7, 130.2, 128.9, 127.0, 125.6, 124.2, 124.0, 41.5, 36.0, 28.0. IR (cm^{-1}): 1712, 1658, 1584, 1336, 1237, 1135, 989, 759, 699. HRMS (ESI) (m/z) $[M+H]^+$: calcd. for $C_{15}H_{12}BrNO_2S$: 349.9844, found: 349.9846.



2-(3,4-dimethoxyphenethyl)-6,7-dimethoxyisoquinoline-1,3(2H,4H)-dione ***(4m)*** 4m was prepared from **1a** (398 mg, 2.2 mmol) and **2d** (480 mg, 2 mmol) according to the general procedure. Pale yellow solid (0.508 mg, 66 % yield); R_f = 0.4; (petroleum ether/EtOAc = 1:1); Mp 152-154°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.66 (s, 1H), 6.87-6.81 (m, 3H), 6.68 (s, 1H), 4.20 (t, J = 8 Hz, 2H), 3.99 (s, 3H), 3.98 (s, 3H), 3.97 (s, 2H), 3.89 (s, 3H), 3.88 (s, 3H), 2.90-2.86 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 170.1, 164.6, 153.9, 148.9, 147.6, 131.2, 128.3, 120.9, 118.0, 112.2, 111.3, 110.1, 108.6, 56.3, 56.2, 55.9, 55.8, 41.5, 36.2, 33.8. IR (cm^{-1}): 1707, 1651, 1514, 1262, 1231, 1140, 1018, 762. HRMS (ESI) (m/z) $[M+H]^+$: calcd. for $C_{21}H_{23}NO_6$: 386.1598, found: 386.1597.

6. Characterization data of xylopinine



Xylopinine ***(5)*** 5 was prepared from **3m** (367 mg, 1 mmol) according to reported procedure.[1] White solid (209 mg), *Rf* = 0.3; (petroleum ether/EtOAc = 1:1); Mp 176-178 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.74 (s,1H), 6.67 (s, 1H), 6.62 (s, 1H), 6.58 (s, 1H), 3.95 (d, J = 14.4 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.86 (s, 3H), 3.86 (s, 3H), 3.68 (d, J = 14.4 Hz, 1H), 3.60 (dd, J = 11 Hz, 1H), 3.26 (dd, J = 16 Hz, 1H), 3.18-3.10 (m, 2H), 2.87-2.81 (m, 1H), 2.71-2.59 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.6, 147.5, 147.4, 147.4, 129.7, 126.7, 126.3, 126.3, 111.3, 111.3, 109.0, 108.5, 59.6, 58.3, 56.0, 55.9, 55.9, 55.8, 51.4, 36.4, 29.0. IR (cm^{-1}): 2928, 2833, 1610, 1514, 1461, 1354, 1257, 1142, 1101, 1022, 856, 730.

Compounds 3a, 3b, 3c, 3d, 3m, 4a, 4c and 5 are known compounds and the high resolution mass spectroscopy (HRMS) data is available in literature.[2,3,4]

7. Copies of NMR spectra.

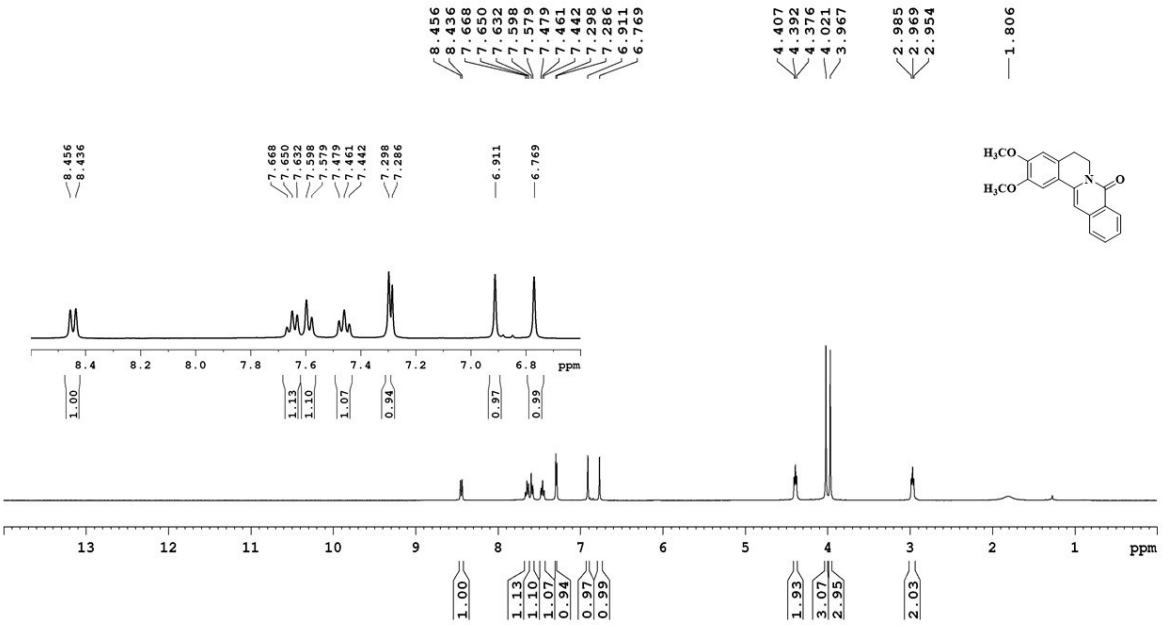


Figure S1: ^{1}H NMR spectra of 3a (400 MHz, $CDCl_3$).

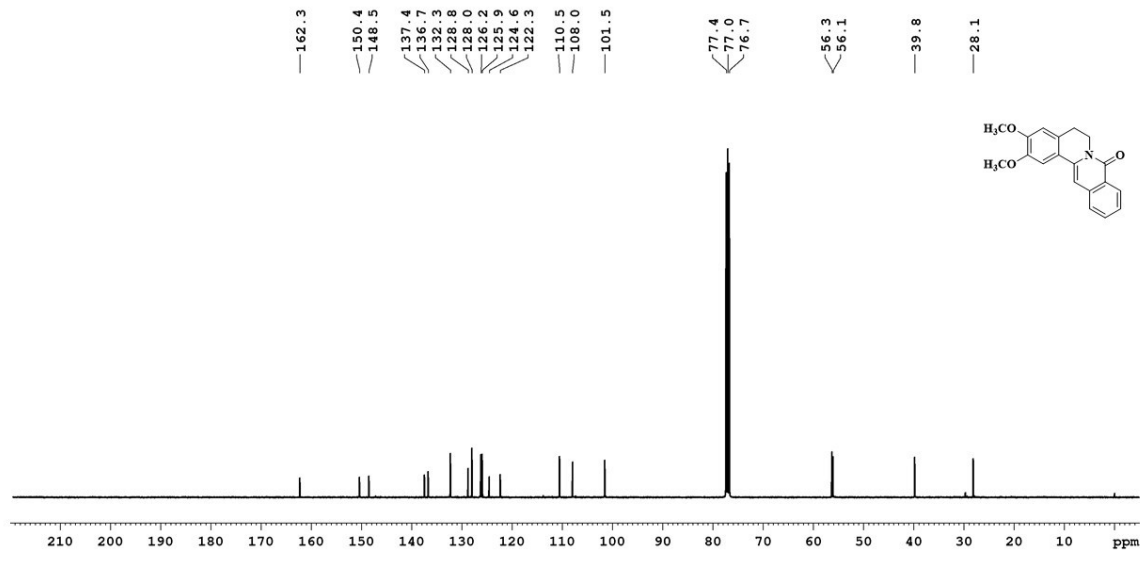


Figure S2: ^{13}C NMR spectra of 3a (100 MHz, $CDCl_3$).

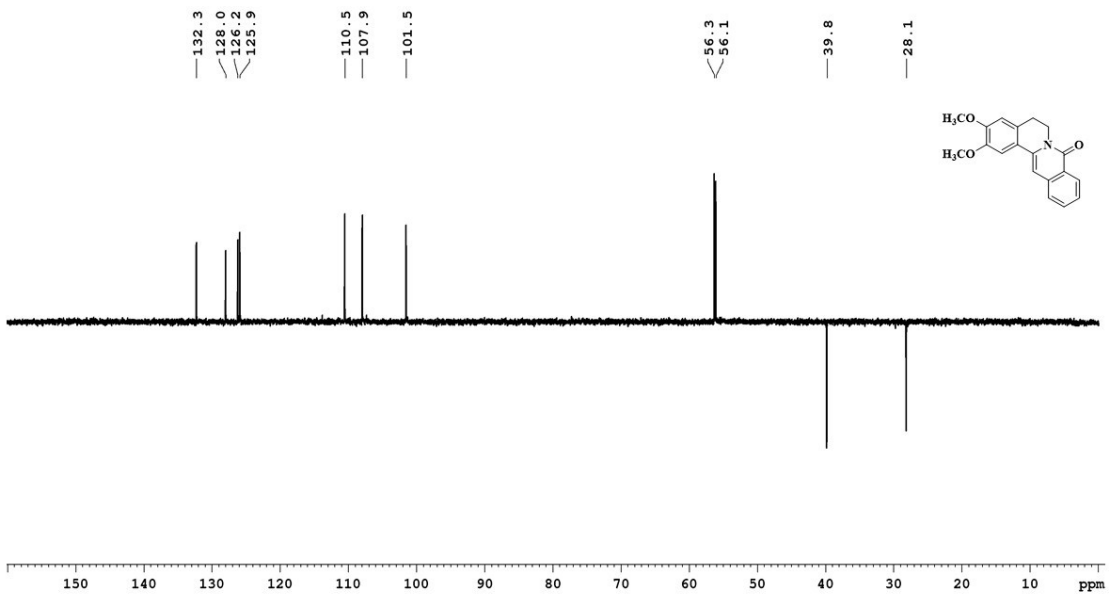


Figure S3: DEPT spectra of 3a (100 MHz, $CDCl_3$).

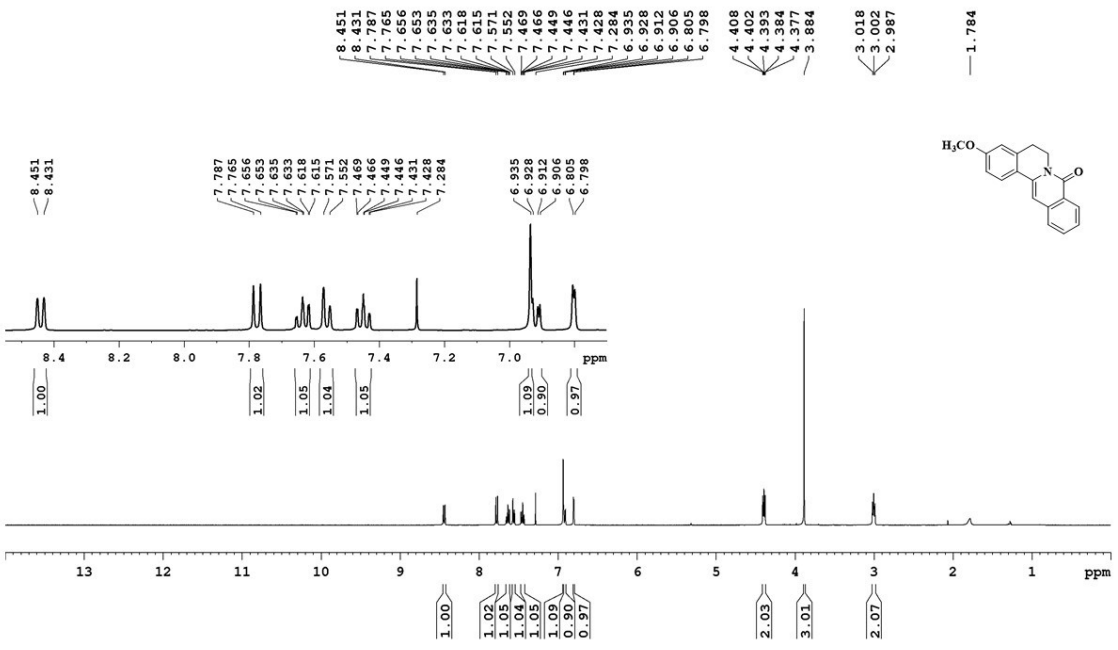


Figure S4: ^1H NMR spectra of 3b (400 MHz, $CDCl_3$).

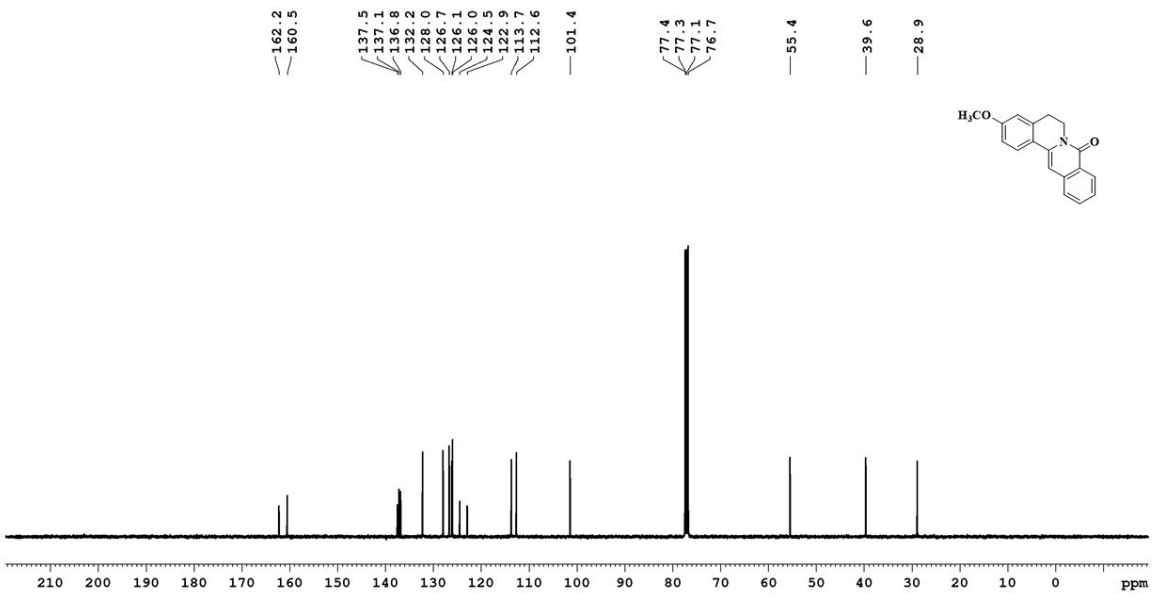


Figure S5: ^{13}C NMR spectra of 3b (100 MHz, $CDCl_3$).

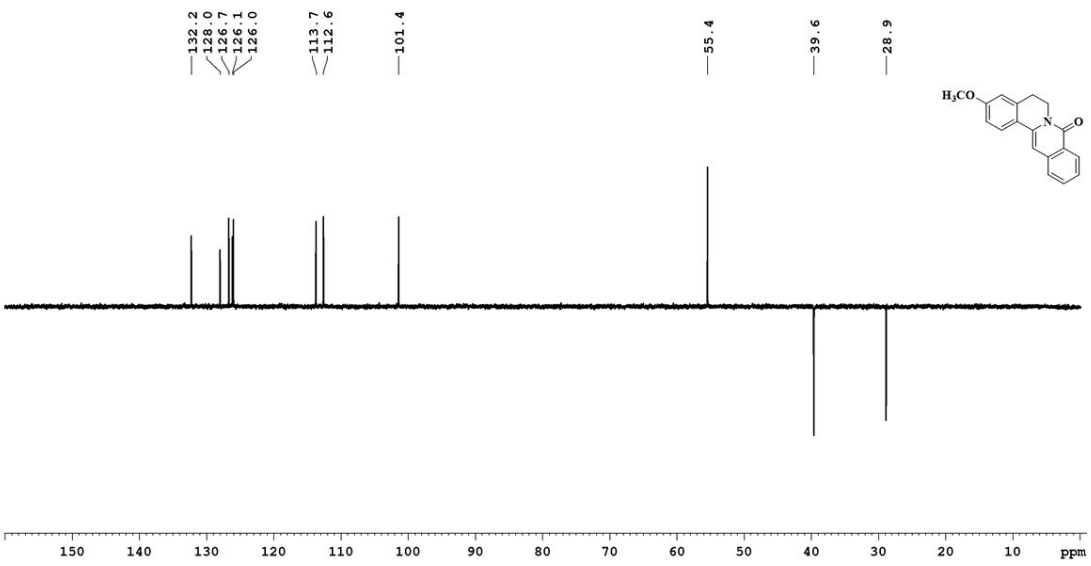


Figure S6: DEPT spectra of 3b (100 MHz, $CDCl_3$).

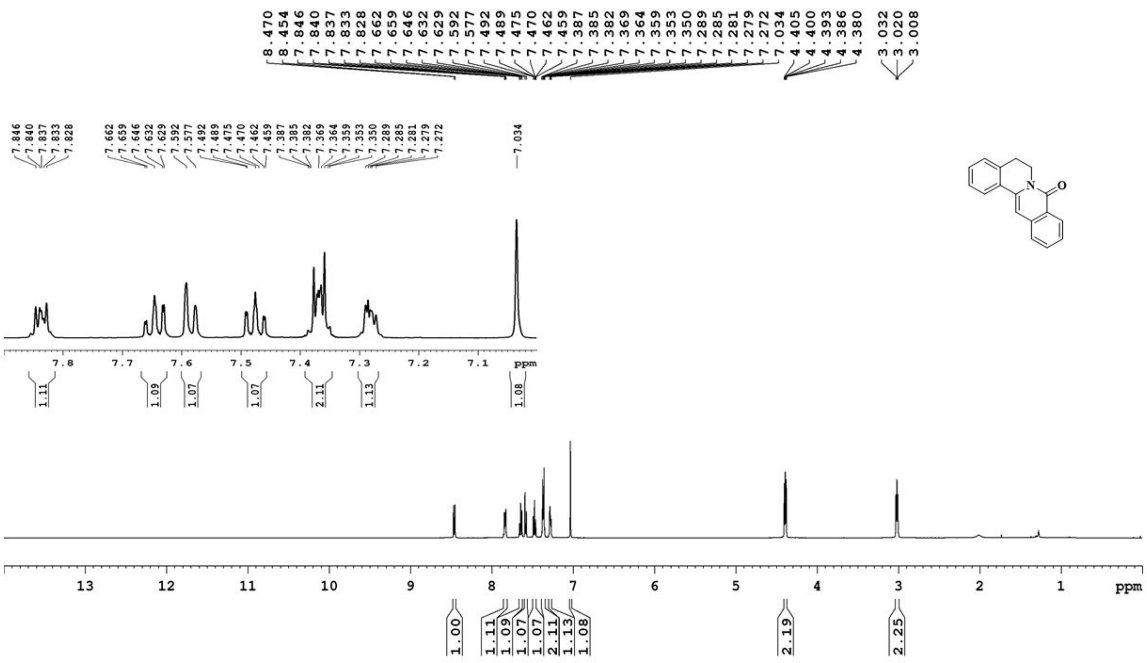


Figure S7: ^{1}H NMR spectra of 3c (500 MHz, $CDCl_3$).

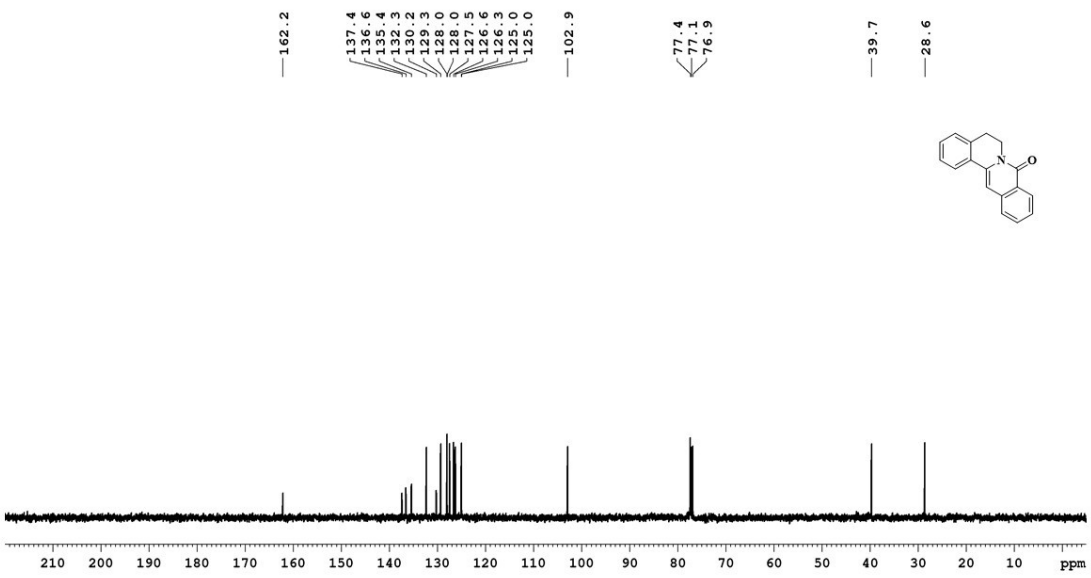


Figure S8: ^{13}C NMR spectra of 3c (125 MHz, $CDCl_3$).

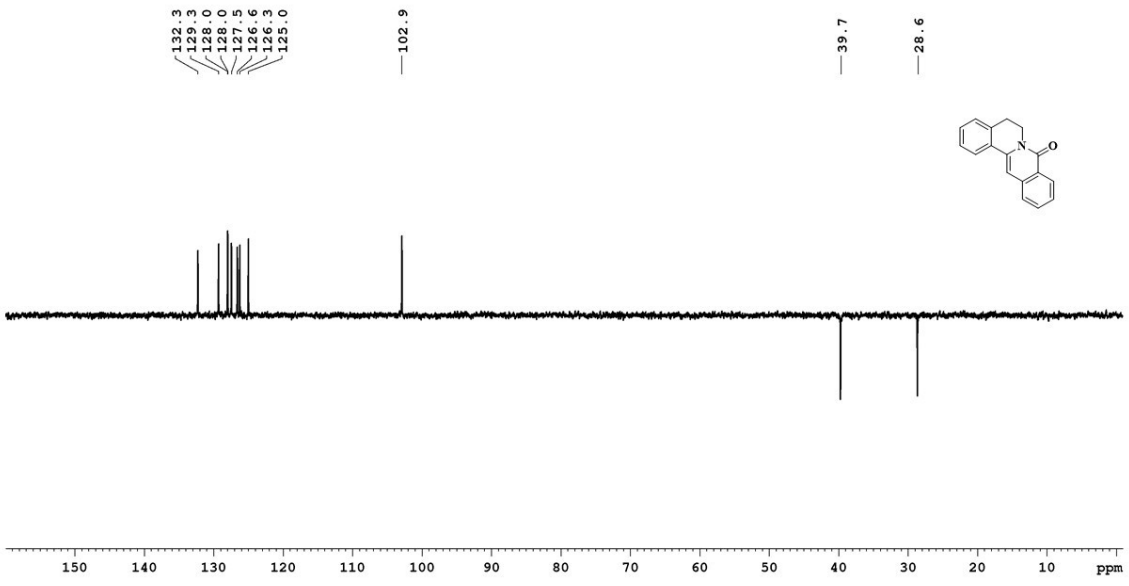


Figure S9: DEPT spectra of 3c (125 MHz, $CDCl_3$).

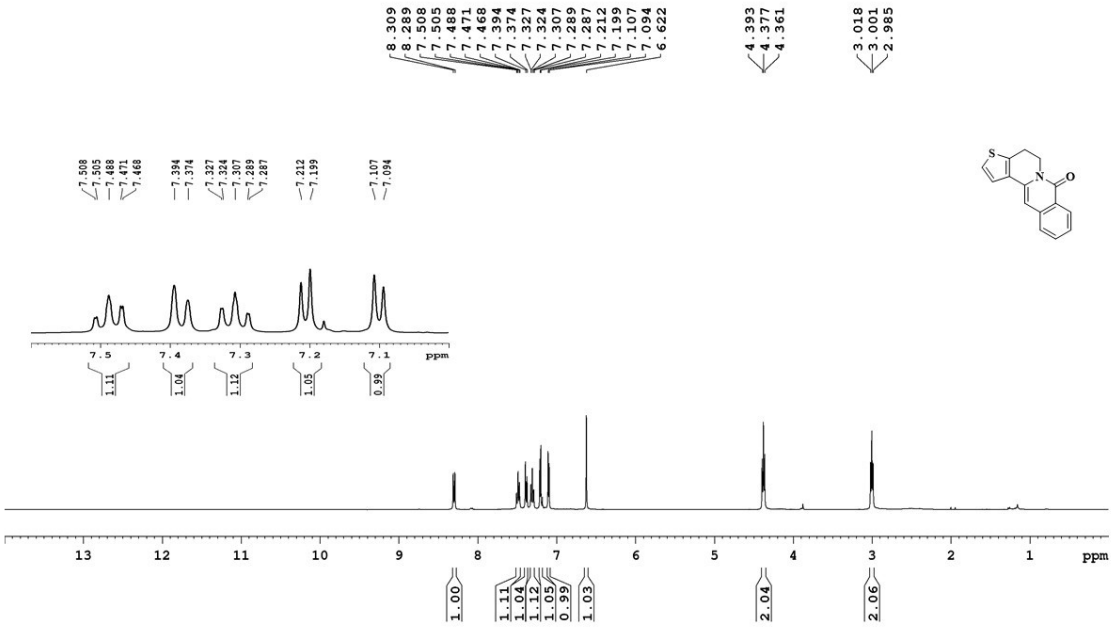


Figure S10: ^1H NMR spectra of 3d (400 MHz, $CDCl_3$).

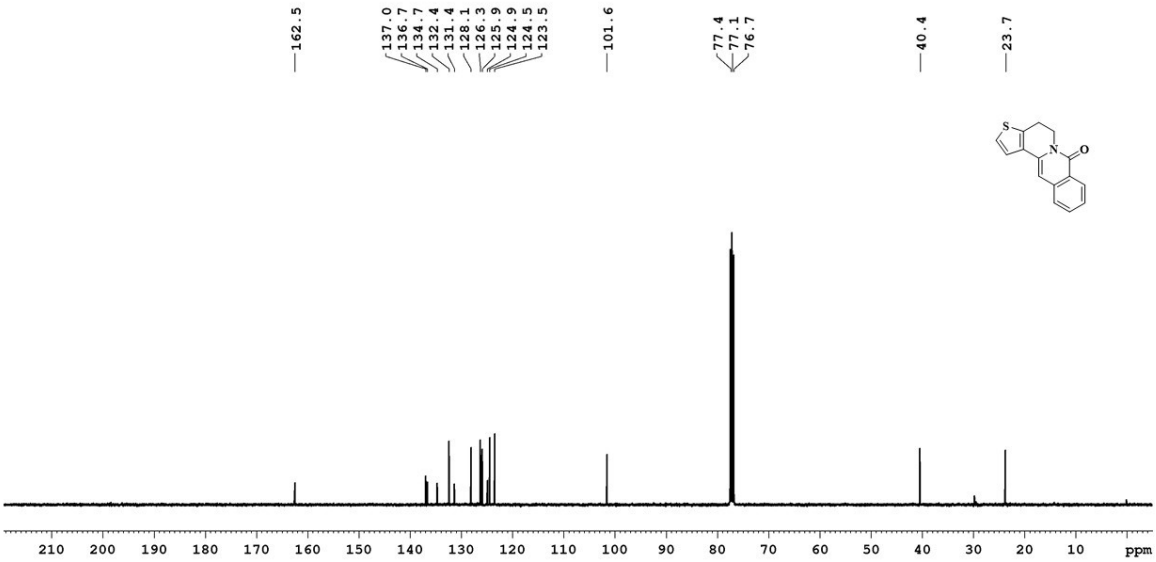


Figure S11: ^{13}C NMR spectra of 3d (100 MHz, $CDCl_3$).

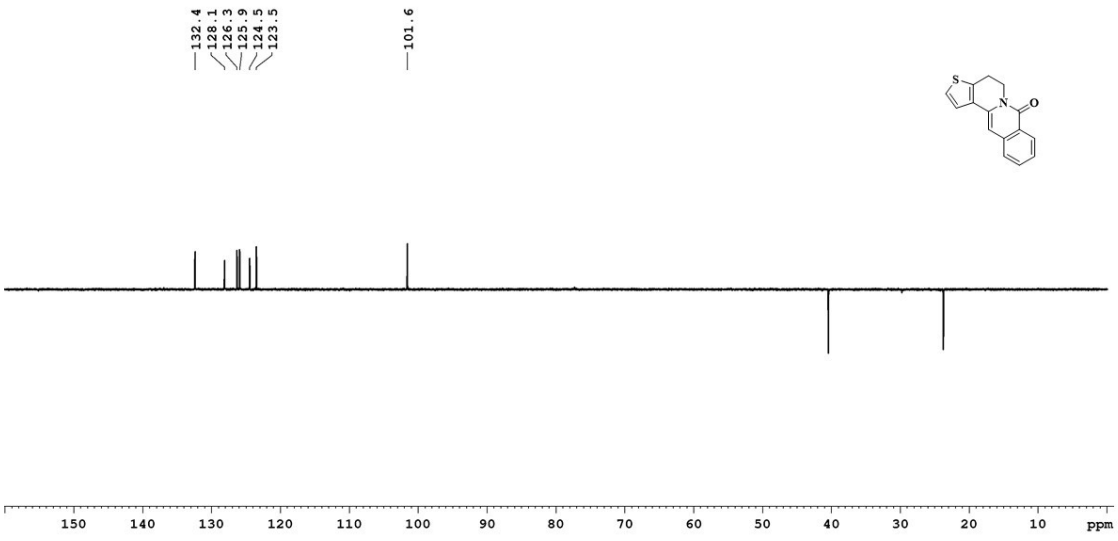


Figure S12: DEPT spectra of 3d (100 MHz, $CDCl_3$).

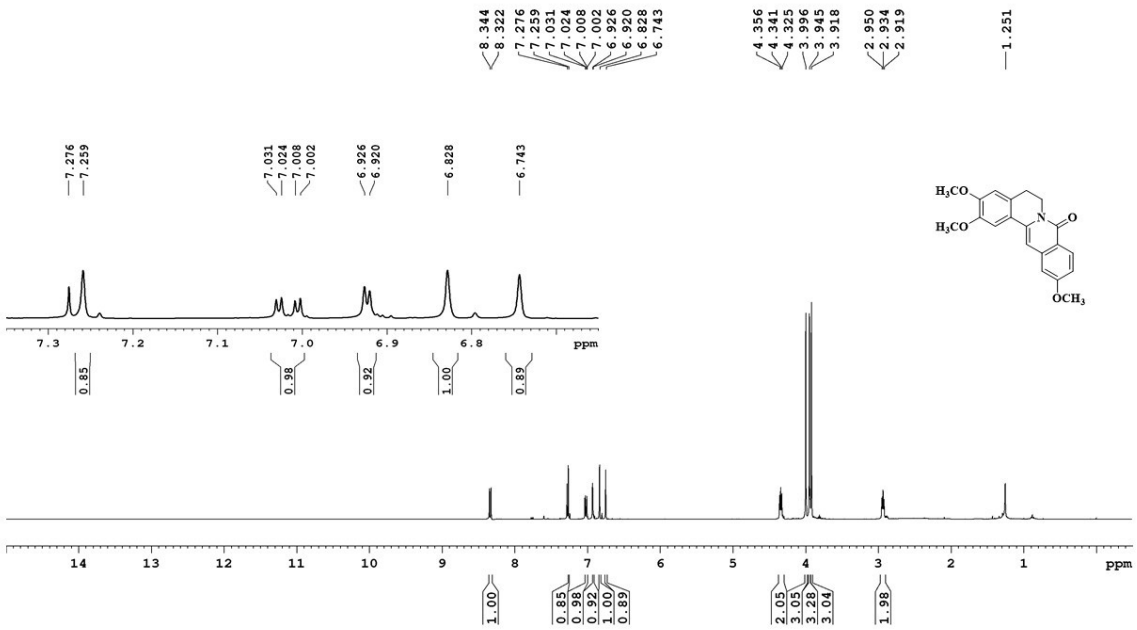


Figure S13: ^{1}H NMR spectra of 3e (400 MHz, $CDCl_3$).

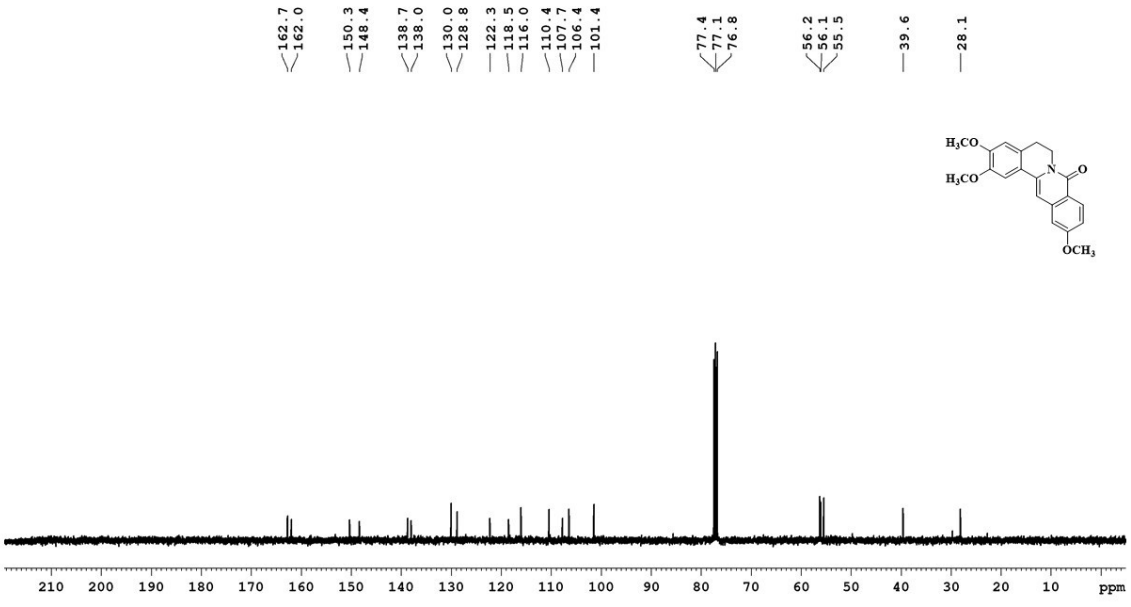


Figure S14: ^{13}C NMR spectra of 3e (100 MHz, $CDCl_3$).

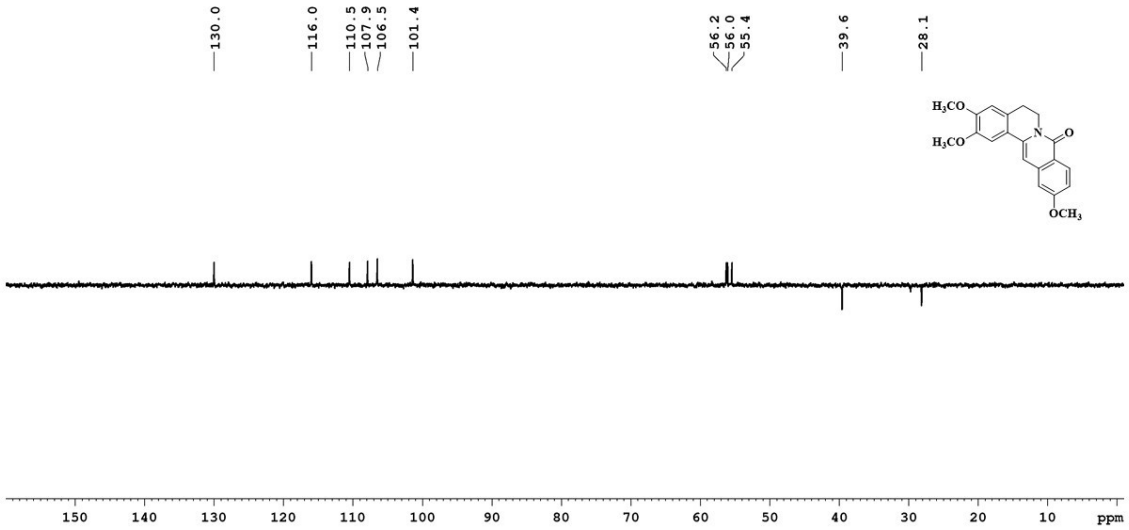


Figure S15: DEPT spectra of 3e (100 MHz, $CDCl_3$).

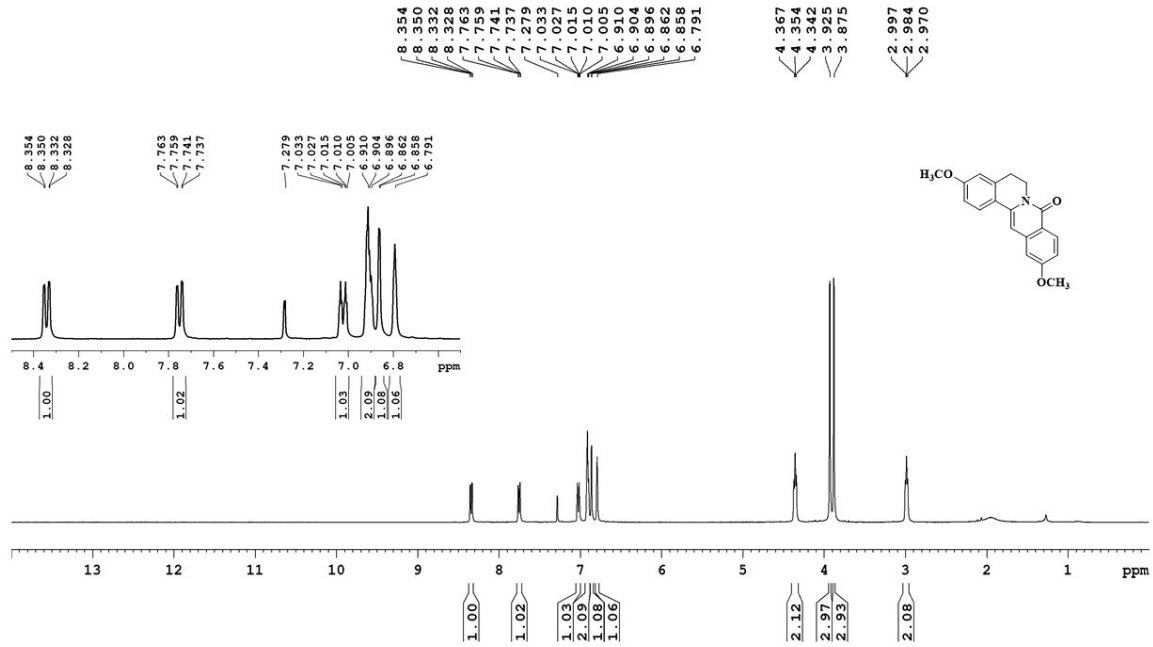


Figure S16: ^1H NMR spectra of 3f (400 MHz, $CDCl_3$).

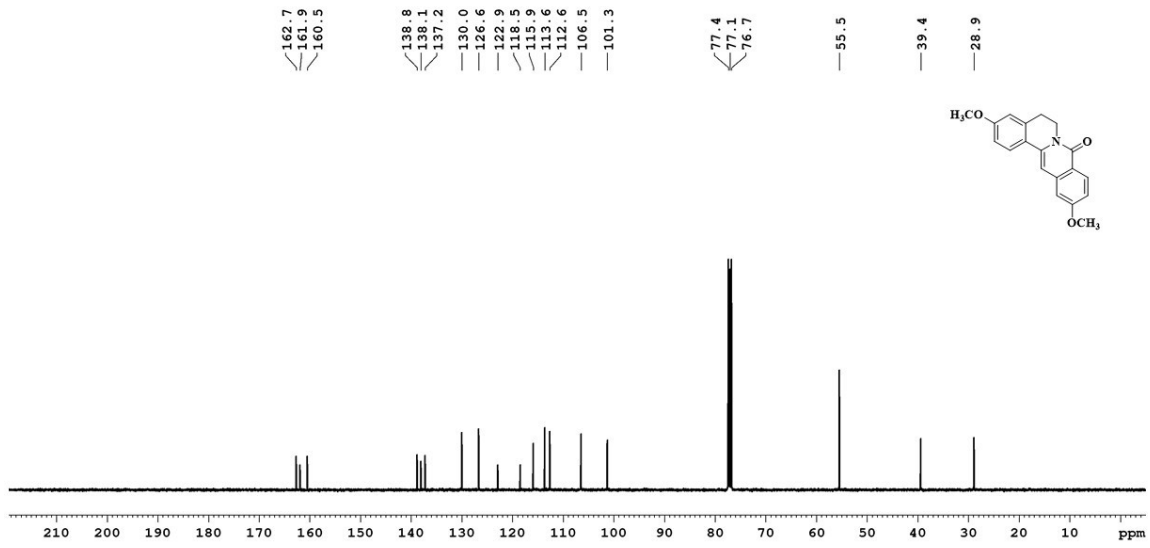


Figure S17: ^{13}C NMR spectra of 3f (100 MHz, $CDCl_3$).

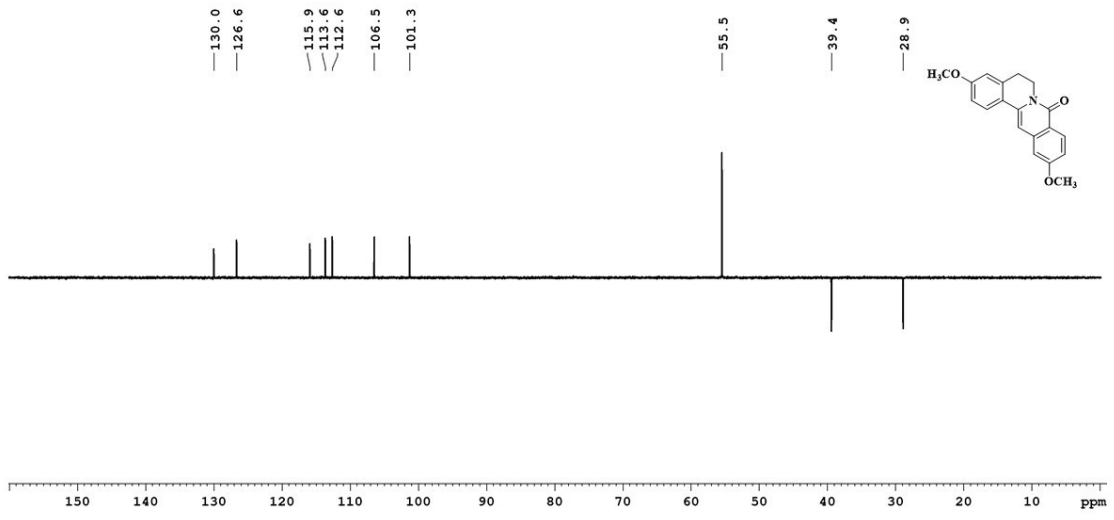


Figure S18: DEPT spectra of 3f (100 MHz, $CDCl_3$).

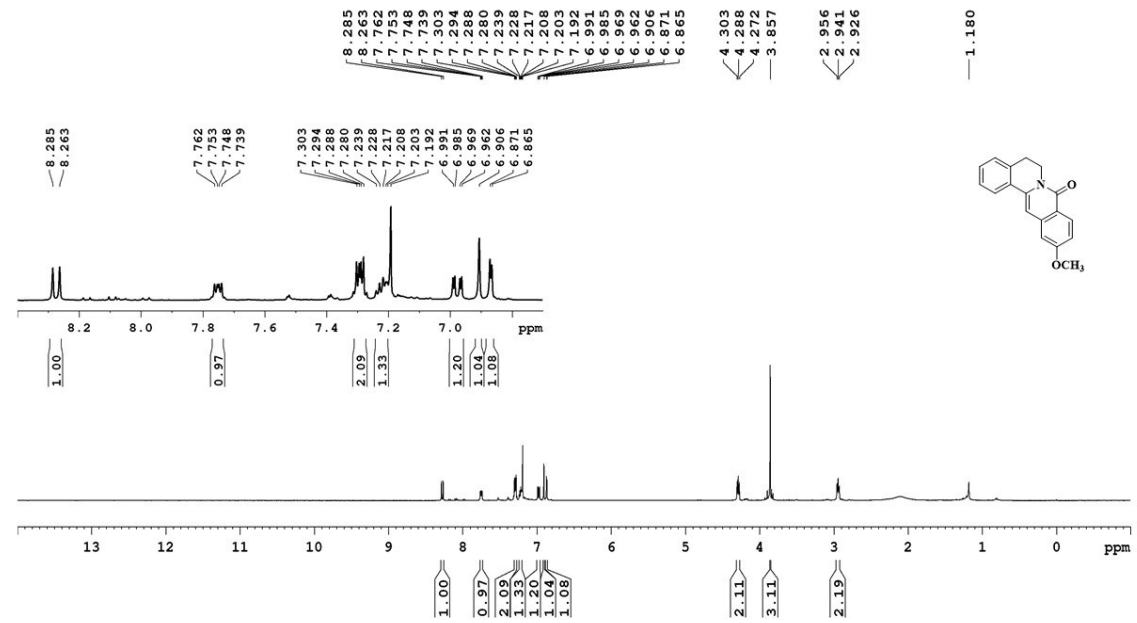


Figure S19: ^{1}H NMR spectra of 3g (400 MHz, $CDCl_3$).

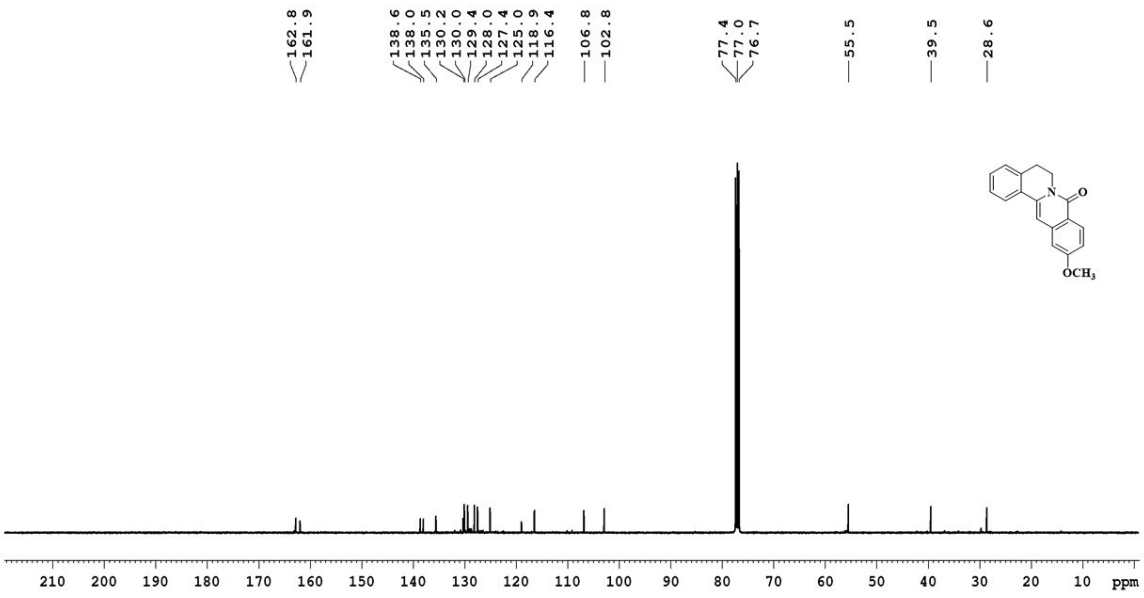


Figure S20: ^{13}C NMR spectra of 3g (100 MHz, $CDCl_3$).

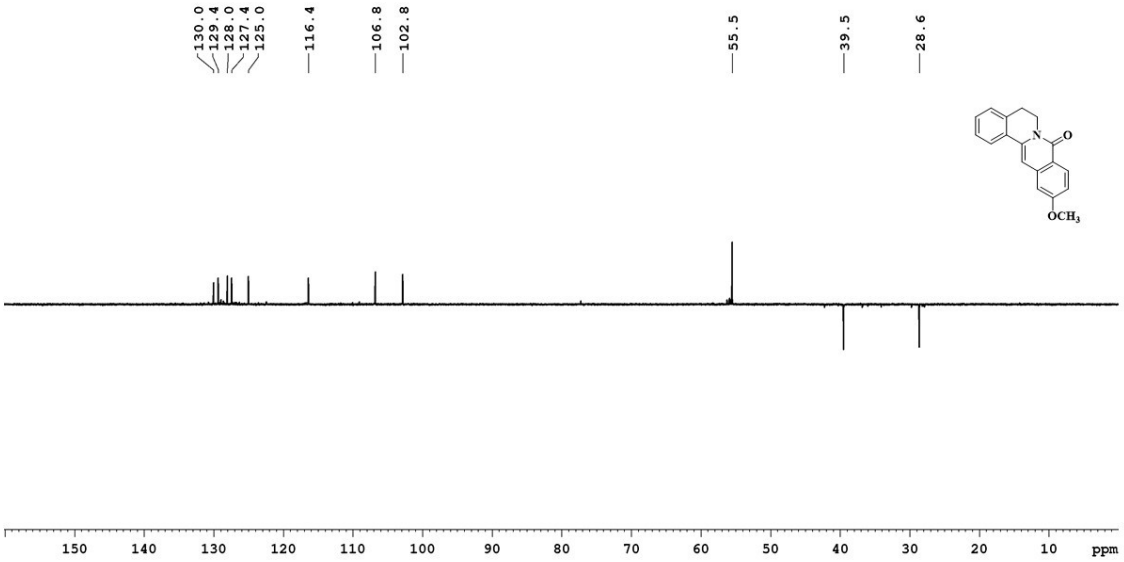


Figure S21: DEPT spectra of 3g (100 MHz, $CDCl_3$).

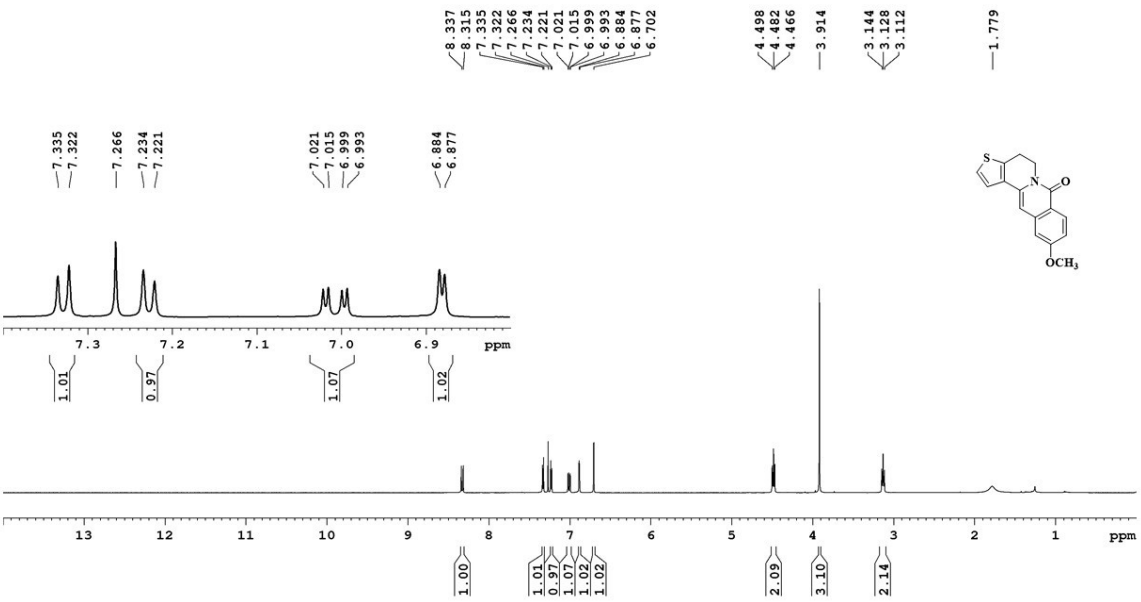


Figure S22: ^1H NMR spectra of 3h (400 MHz, $CDCl_3$).

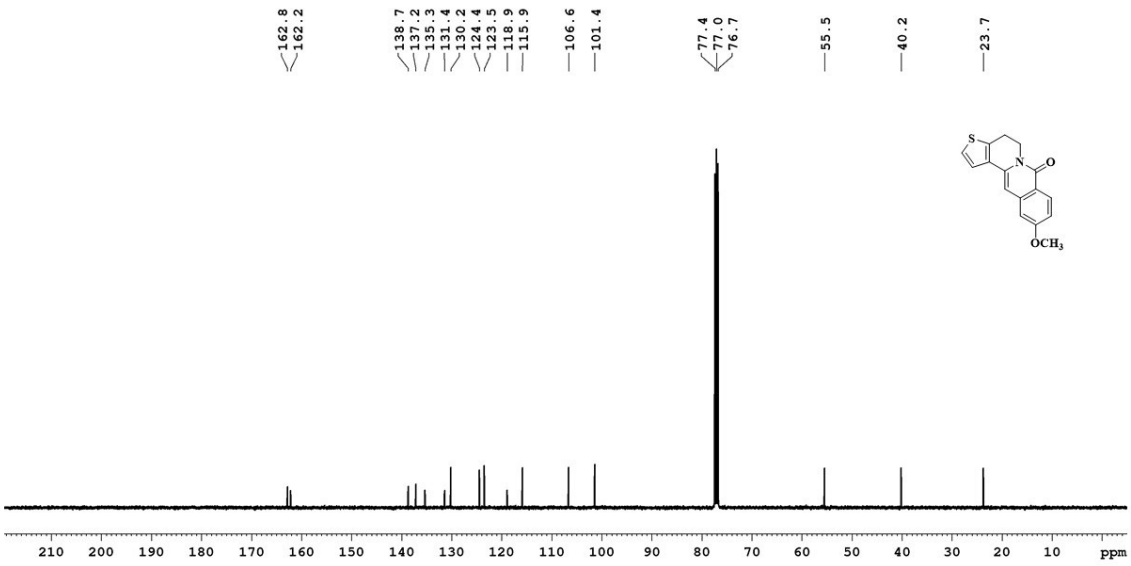


Figure S23: ^{13}C NMR spectra of 3h (100 MHz, $CDCl_3$).

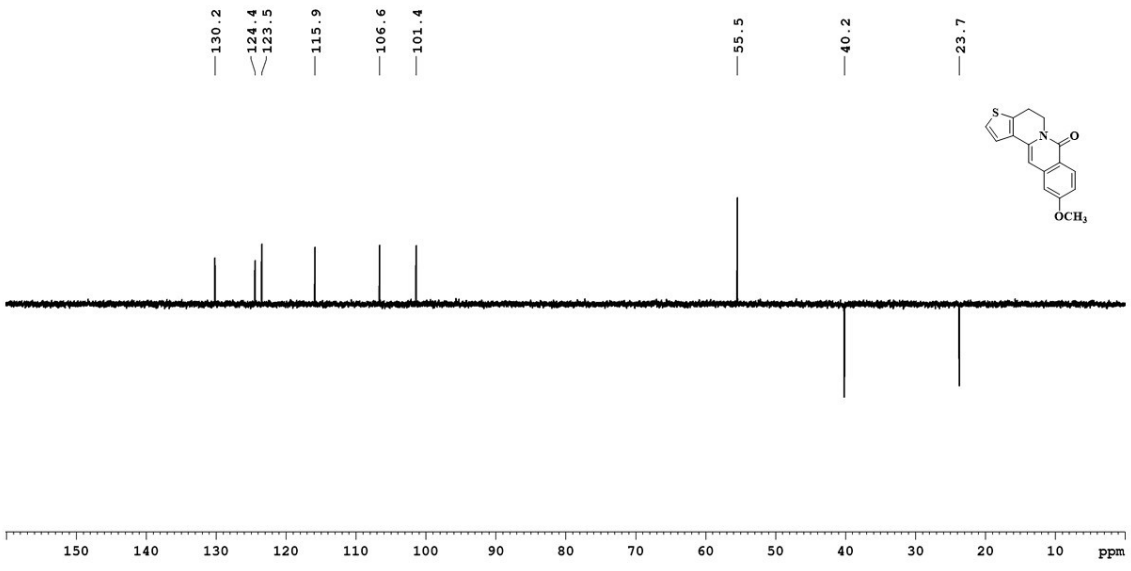


Figure S24: DEPT spectra of 3h (100 MHz, $CDCl_3$).

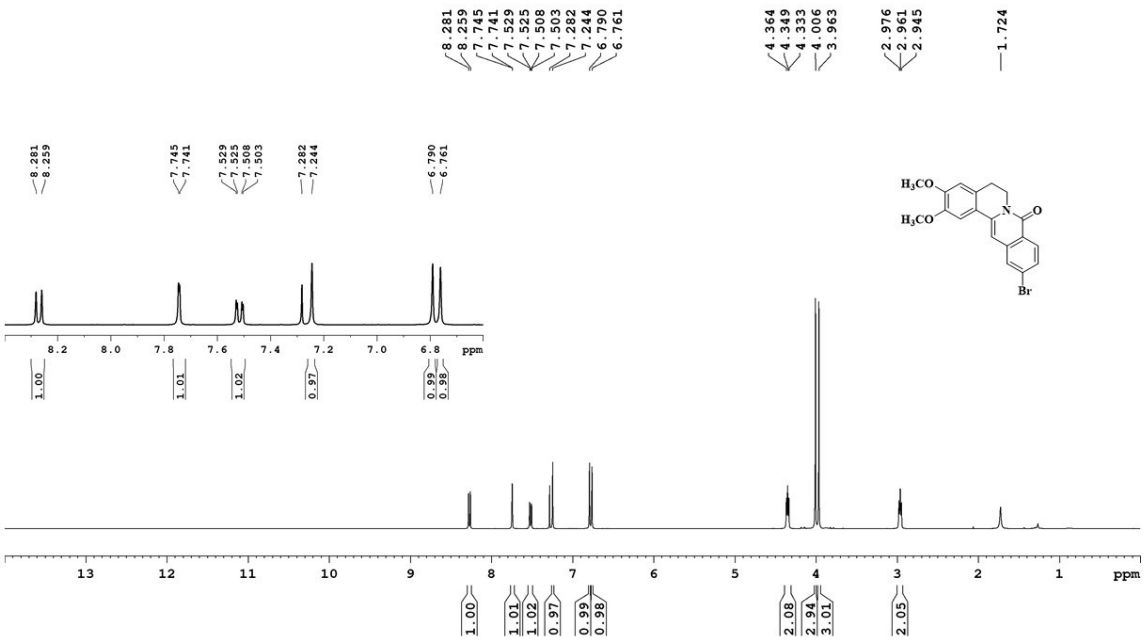


Figure S25: ^{1}H NMR spectra of 3i (400 MHz, $CDCl_3$).

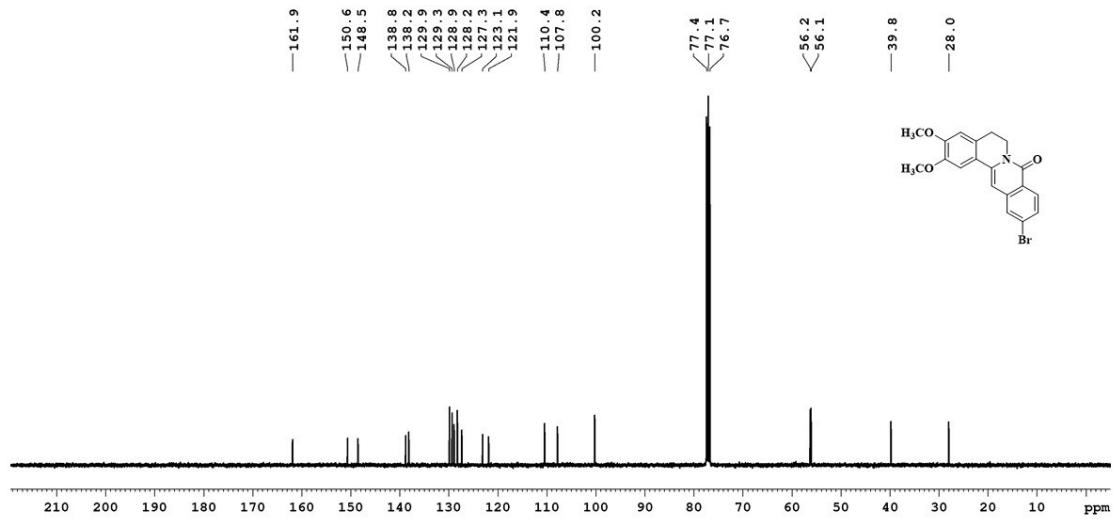


Figure S26: ^{13}C NMR spectra of 3i (100 MHz, $CDCl_3$).

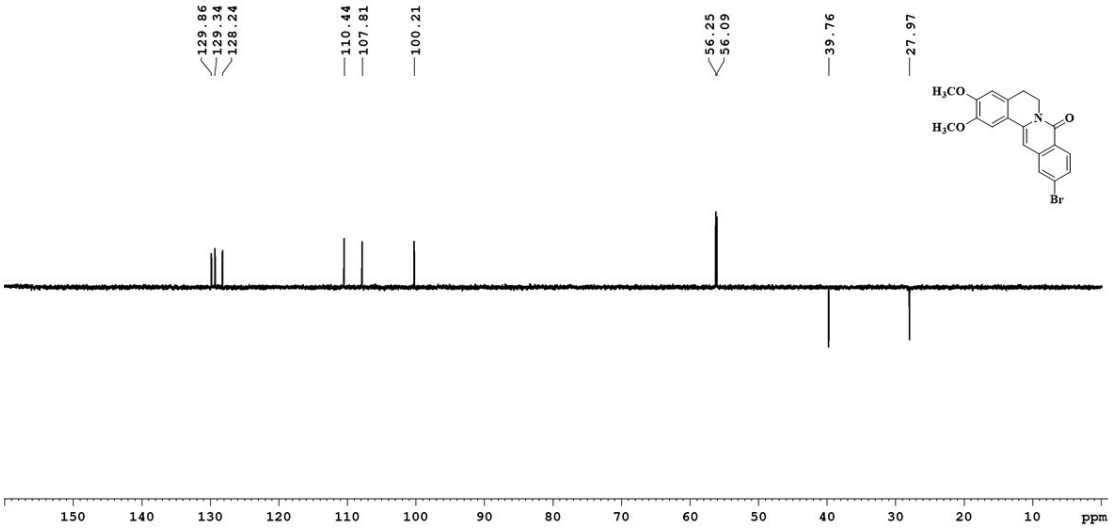


Figure S27: DEPT spectra of 3i (100 MHz, $CDCl_3$).

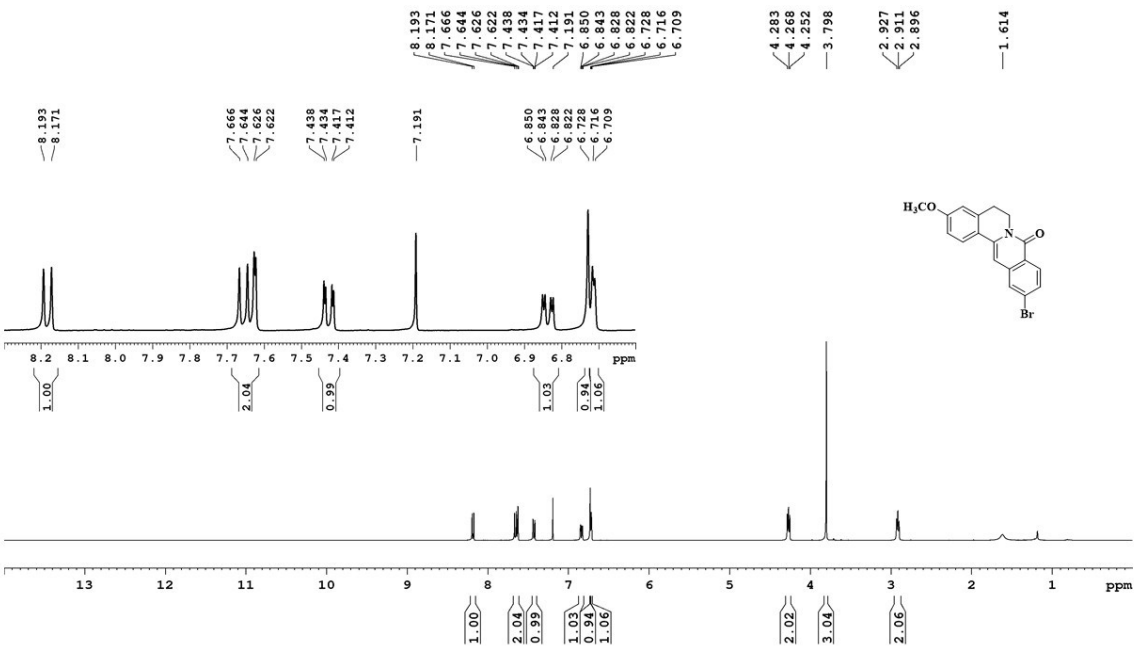


Figure S28: ^1H NMR spectra of 3j (400 MHz, $CDCl_3$).

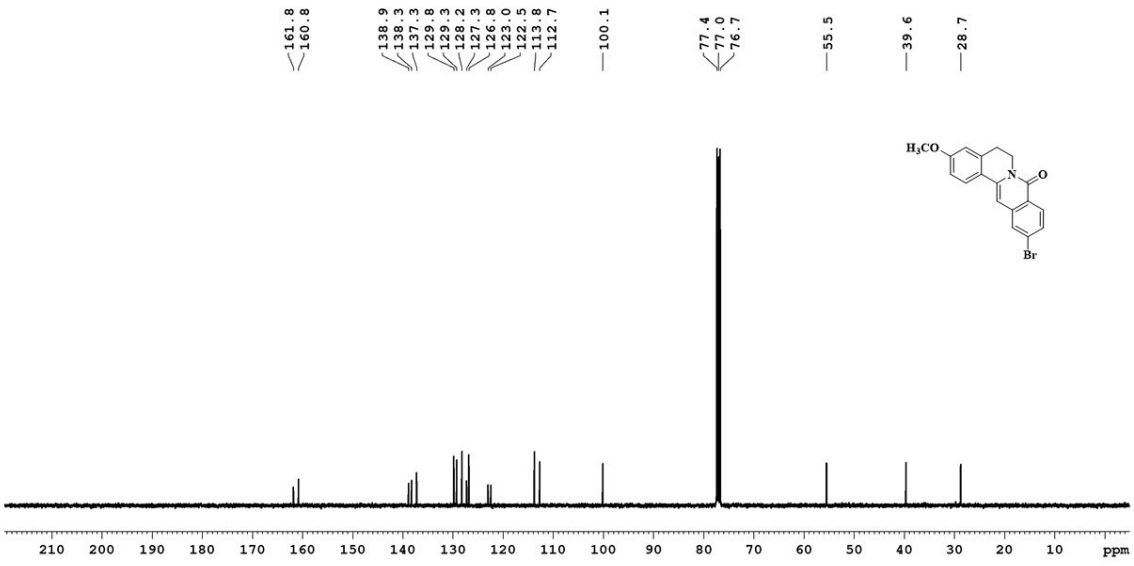


Figure S29: ^{13}C NMR spectra of 3j (100 MHz, $CDCl_3$).

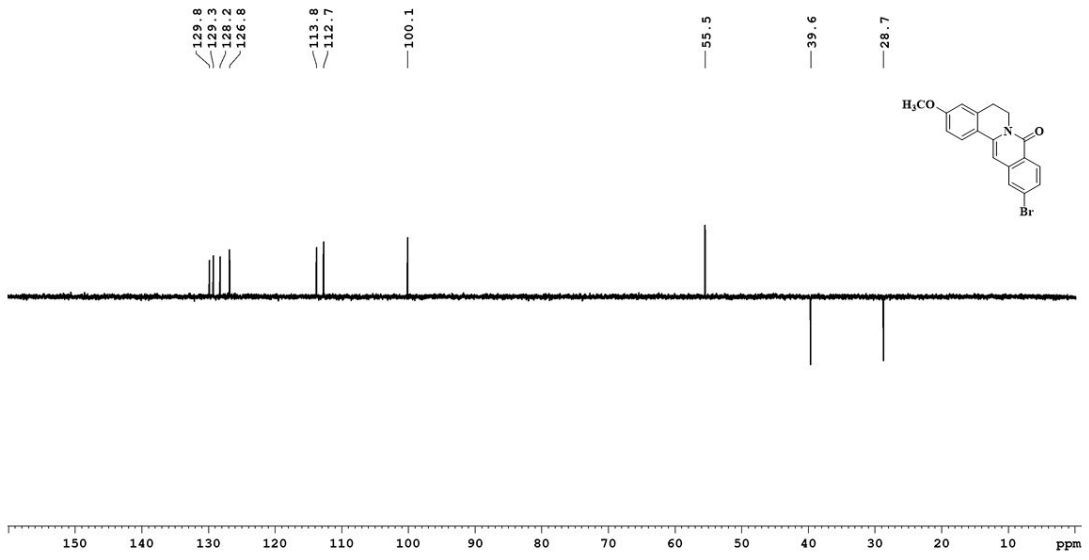


Figure S30: DEPT spectra of 3j (100 MHz, $CDCl_3$).

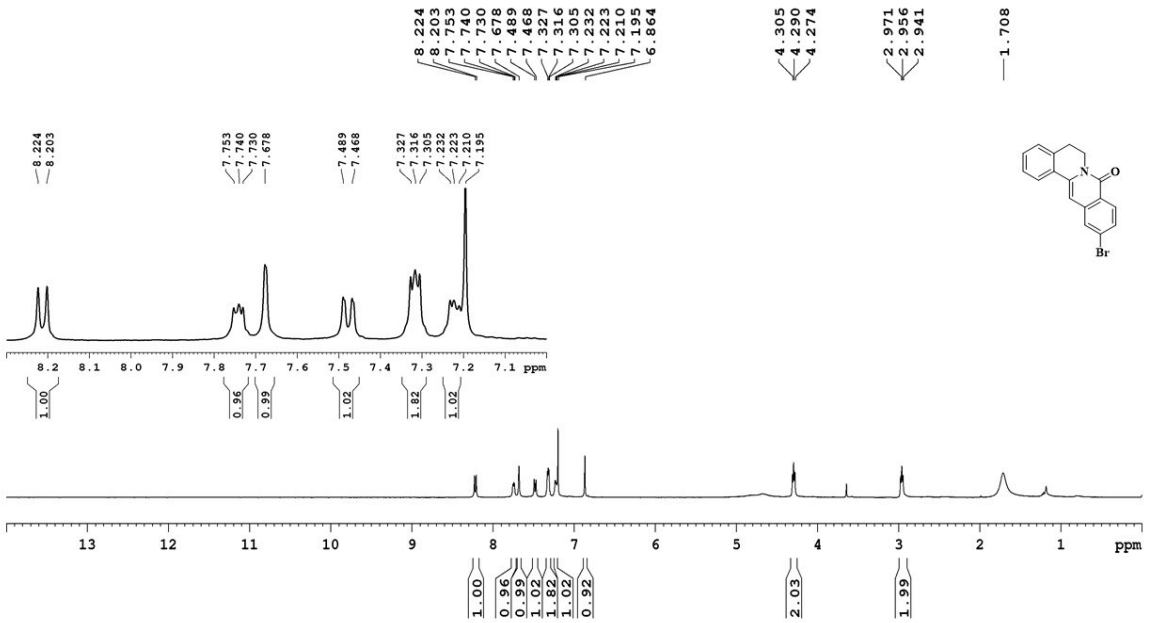


Figure S31: ^{1}H NMR spectra of 3k (400 MHz, $CDCl_3$).

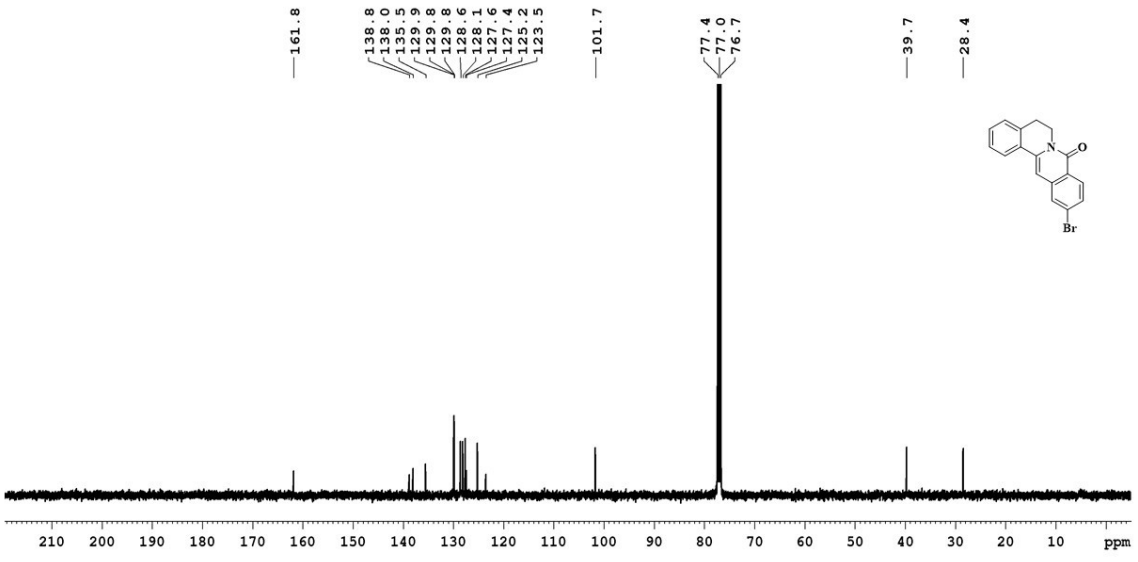


Figure S32: ^{13}C NMR spectra of 3k (100 MHz, $CDCl_3$).

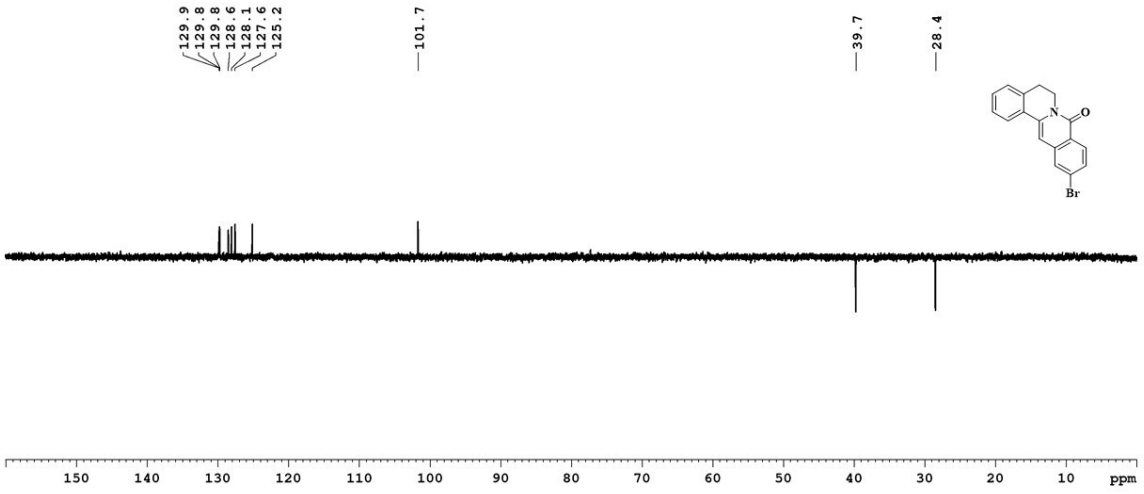


Figure S33: DEPT spectra of 3k (100 MHz, $CDCl_3$).

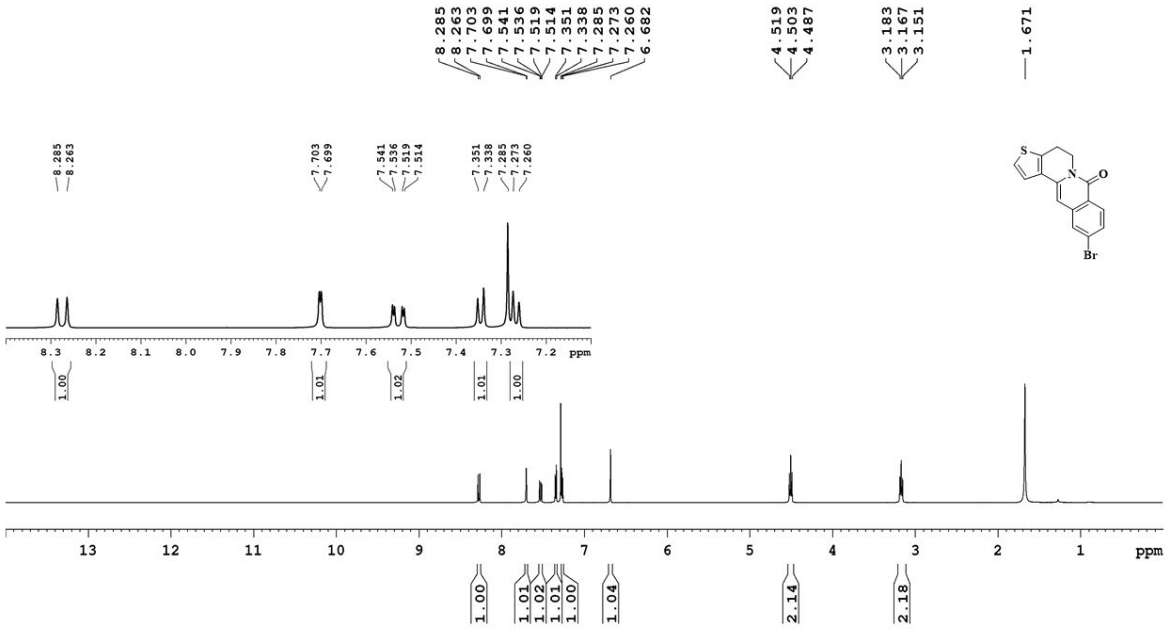


Figure S34: ^1H NMR spectra of 3l (400 MHz, $CDCl_3$).

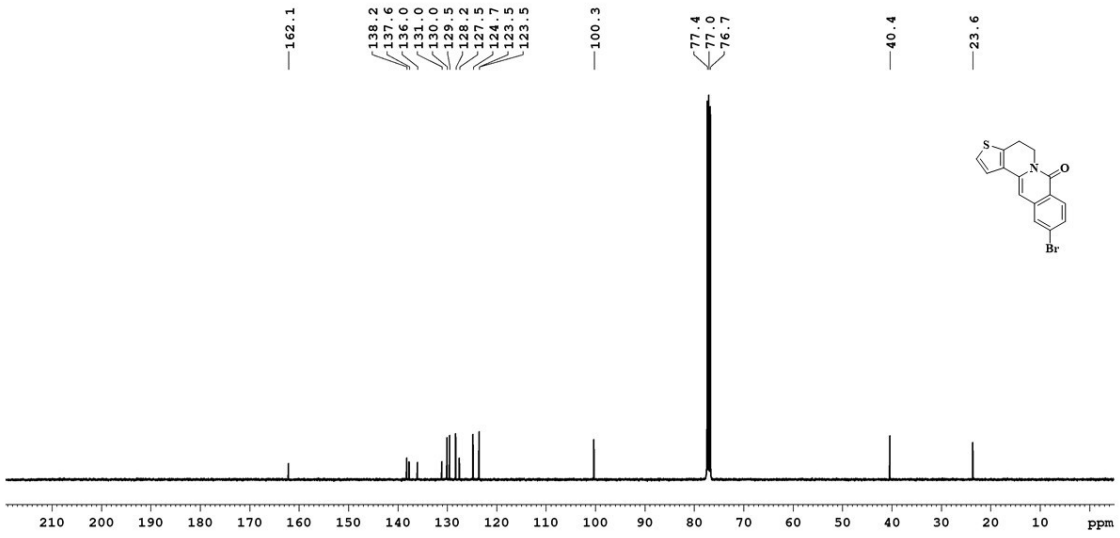


Figure S35: ^{13}C NMR spectra of 3l (100 MHz, $CDCl_3$).

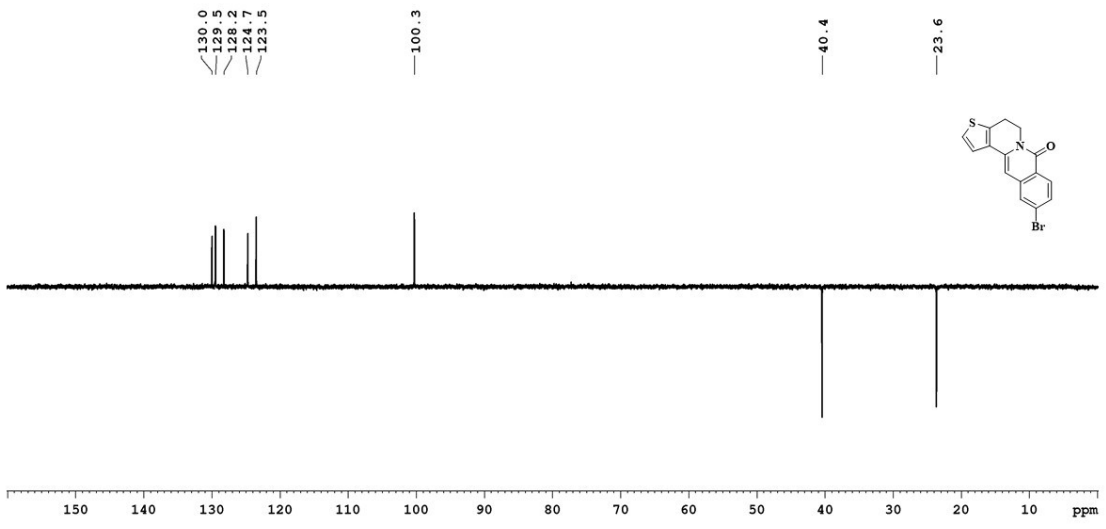


Figure S36: DEPT spectra of 3l (100 MHz, $CDCl_3$).

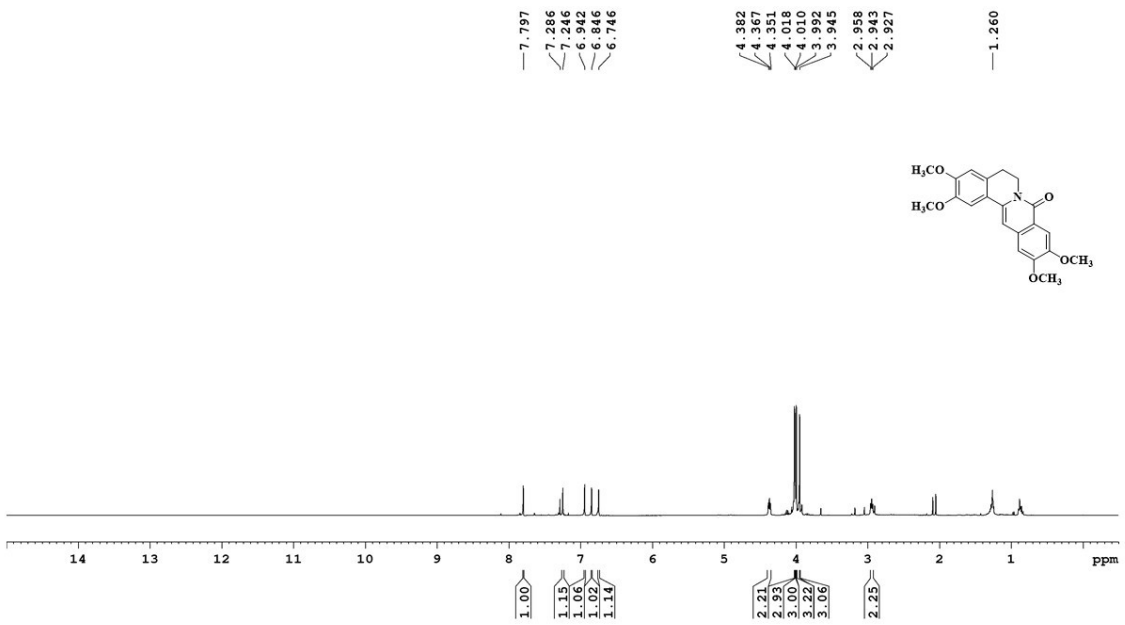


Figure S37: ^{1}H NMR spectra of 3m (400 MHz, $CDCl_3$).

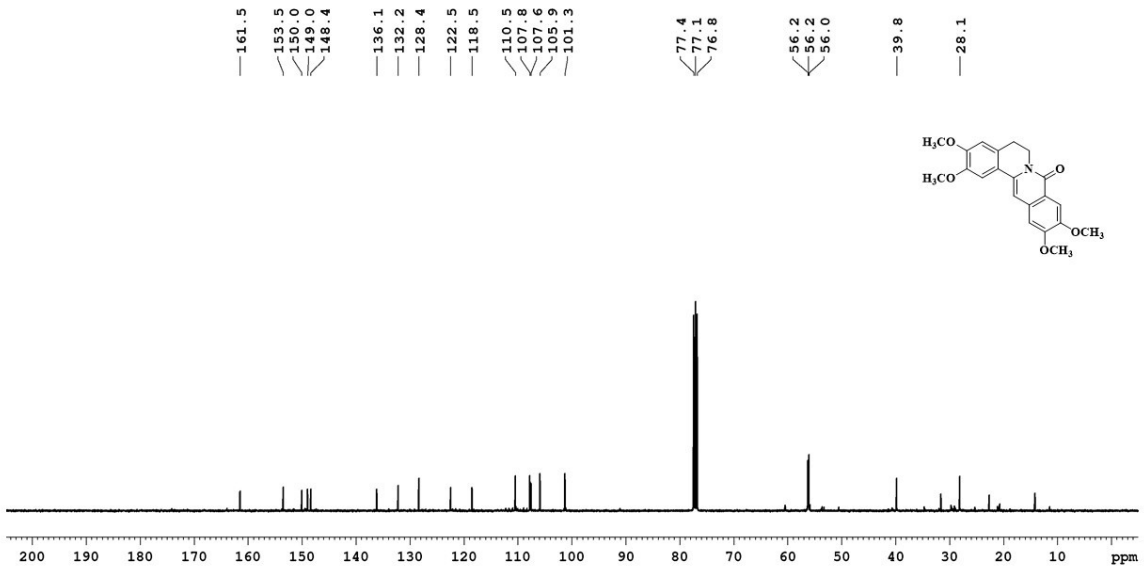


Figure S38: ^{13}C NMR spectra of 3m (100 MHz, $CDCl_3$).

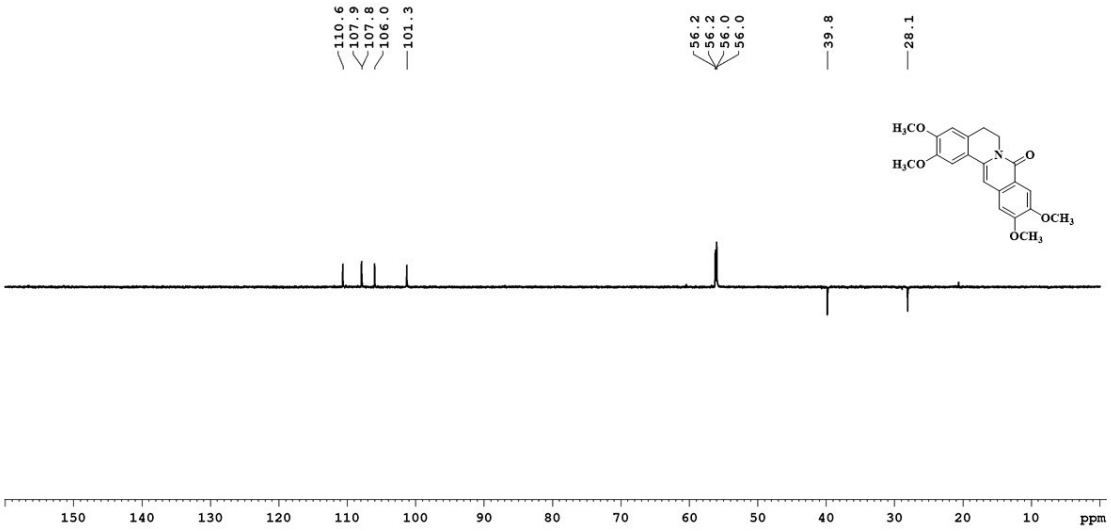


Figure S39: DEPT spectra of 3m (100 MHz, $CDCl_3$).

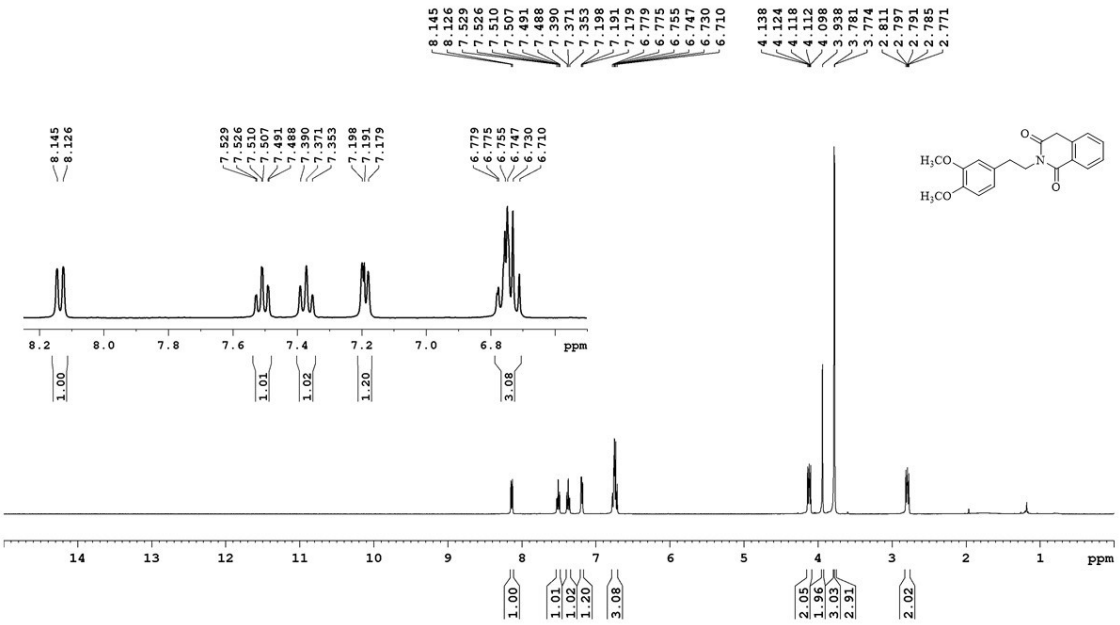


Figure S40: ^1H NMR spectra of 4a (400 MHz, $CDCl_3$).

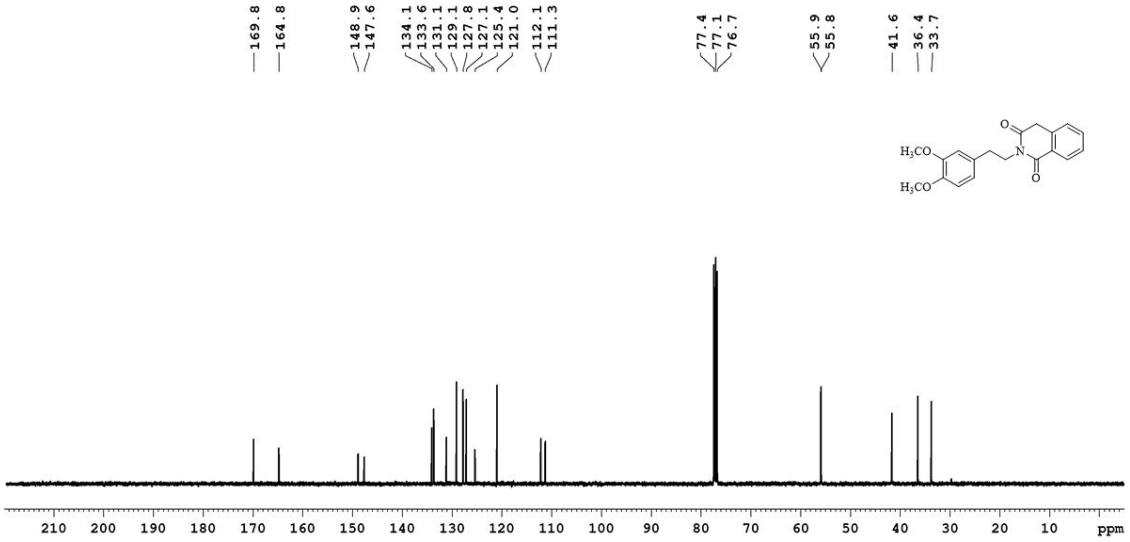


Figure S41: ^{13}C NMR spectra of 4a (100 MHz, $CDCl_3$).

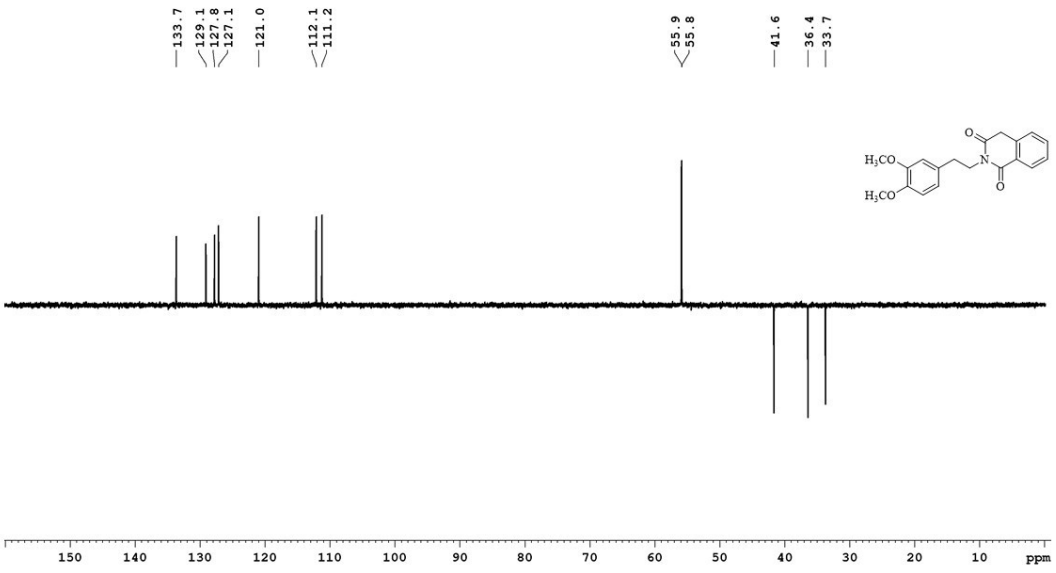


Figure S42: DEPT spectra of 4a (100 MHz, $CDCl_3$).

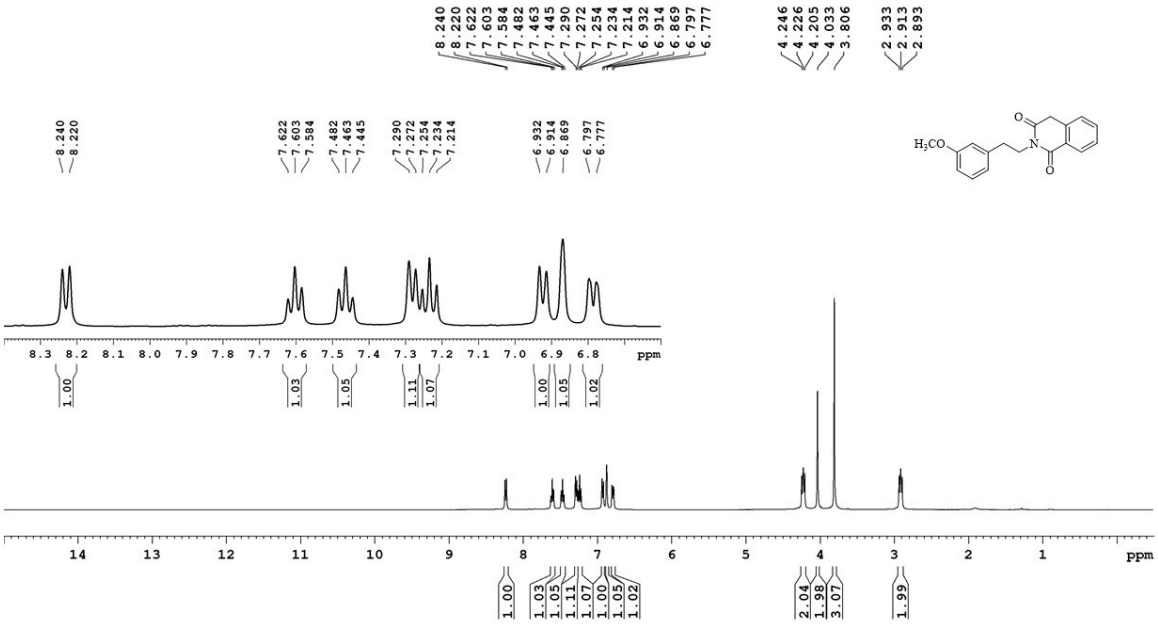


Figure S43: ^{1}H NMR spectra of 4b (400 MHz, $CDCl_3$).

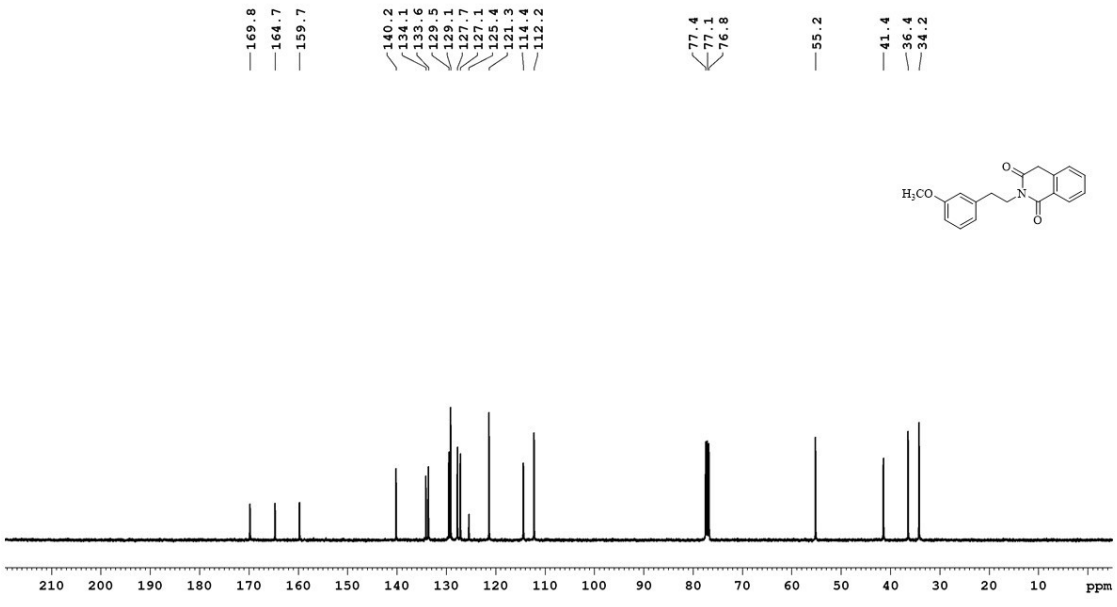


Figure S44: ^{13}C NMR spectra of 4b (100 MHz, $CDCl_3$).

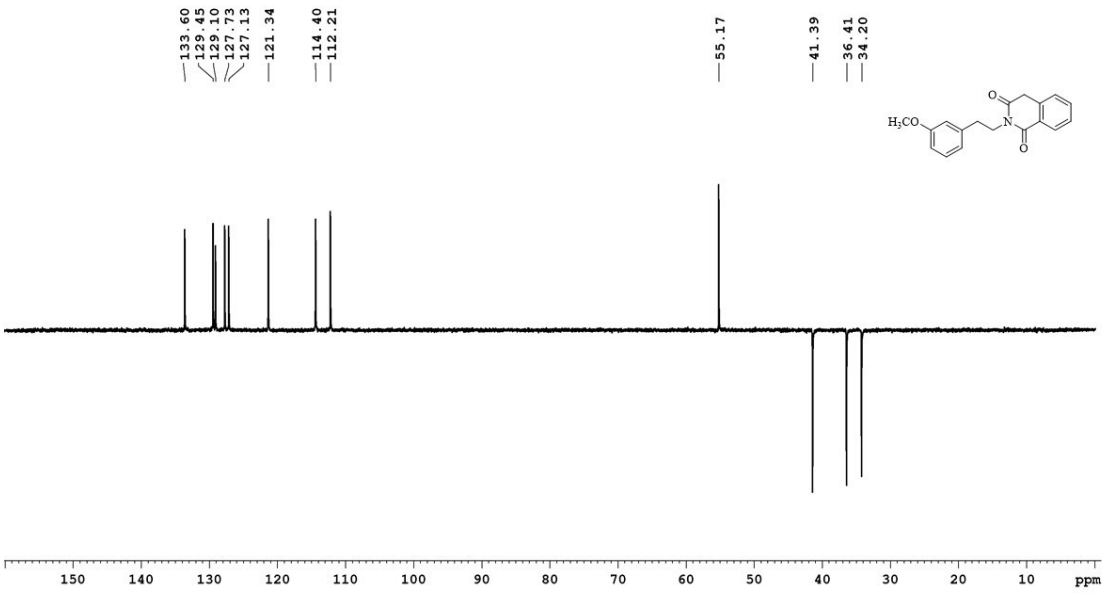


Figure S45: DEPT spectra of 4b (100 MHz, $CDCl_3$).

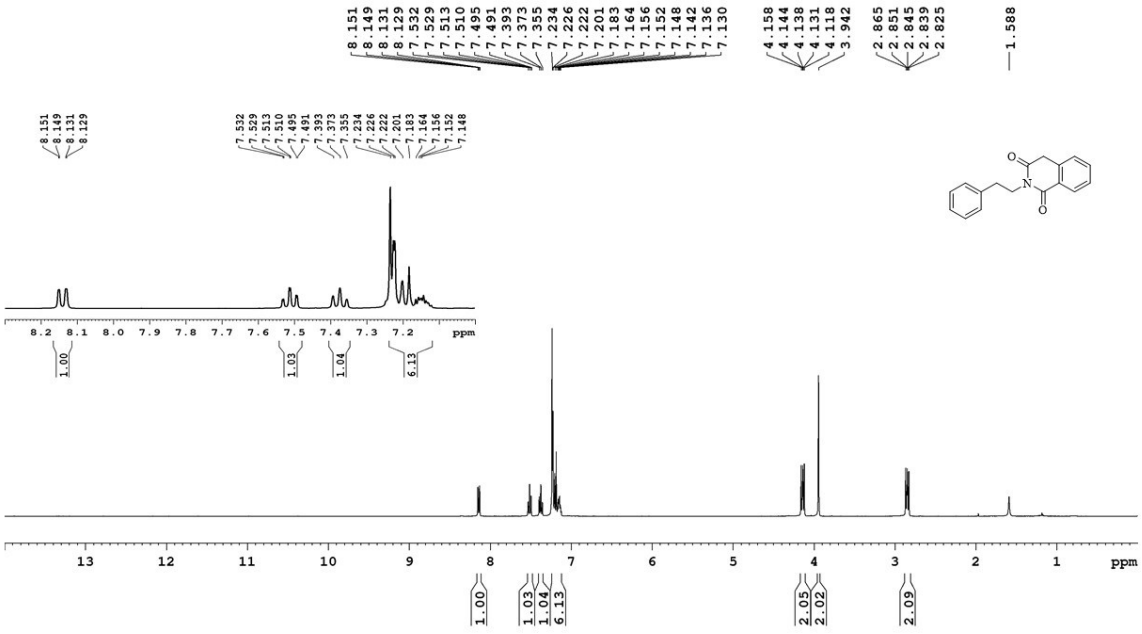


Figure S46: ^1H NMR spectra of 4c (400 MHz, $CDCl_3$).

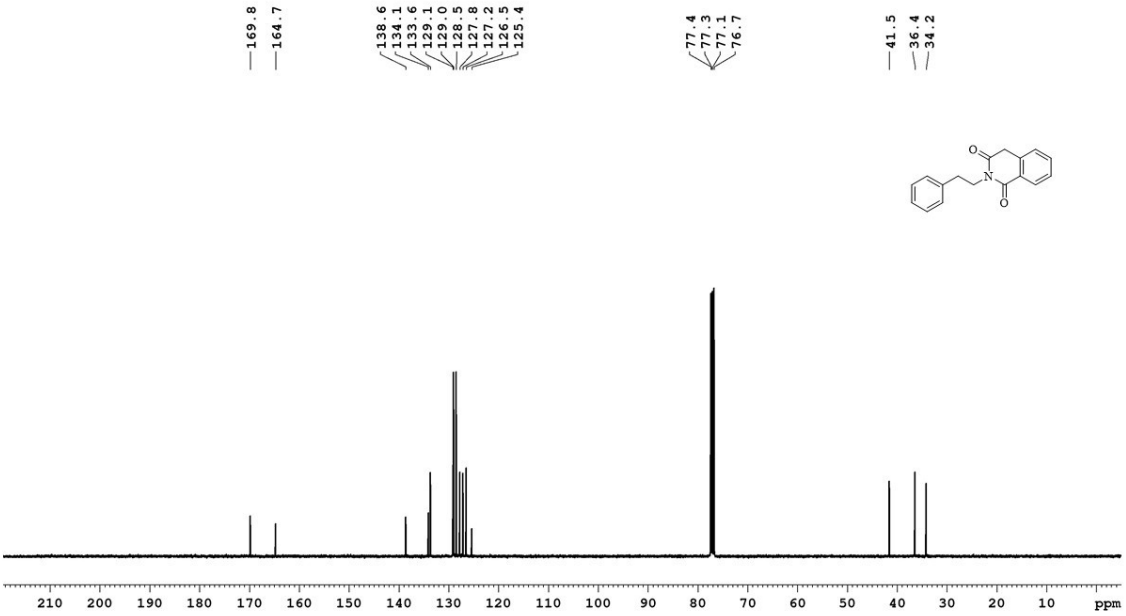


Figure S47: ^{13}C NMR spectra of 4c (100 MHz, $CDCl_3$).

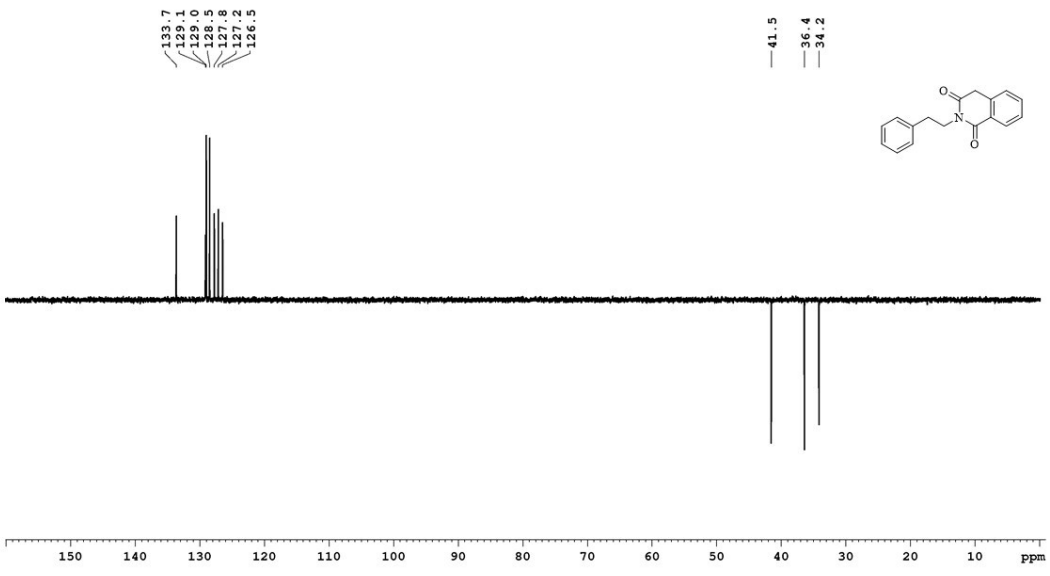


Figure S48: DEPT spectra of 4c (100 MHz, $CDCl_3$).

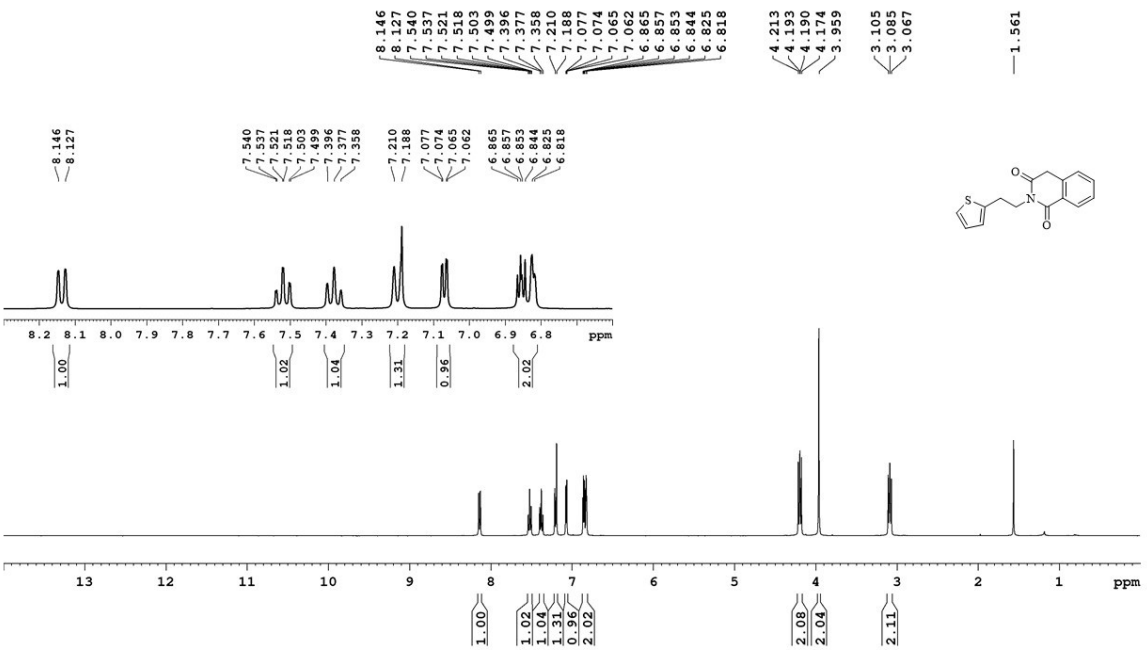


Figure S49: ^{1}H NMR spectra of 4d (400 MHz, $CDCl_3$).

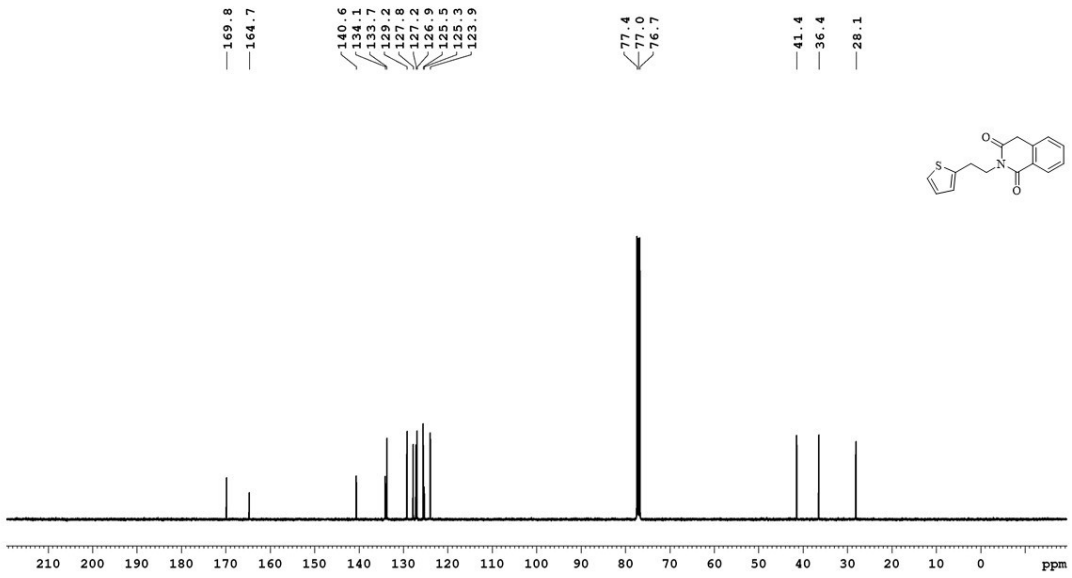


Figure S50: ^{13}C NMR spectra of 4d (100 MHz, $CDCl_3$).

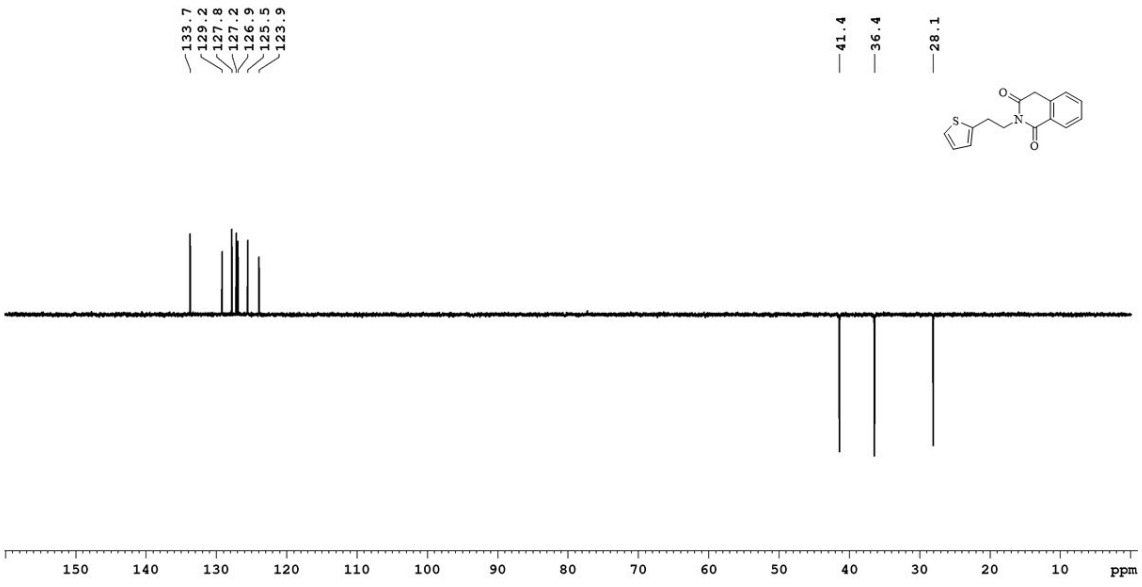


Figure S51: DEPT spectra of 4d (100 MHz, $CDCl_3$).

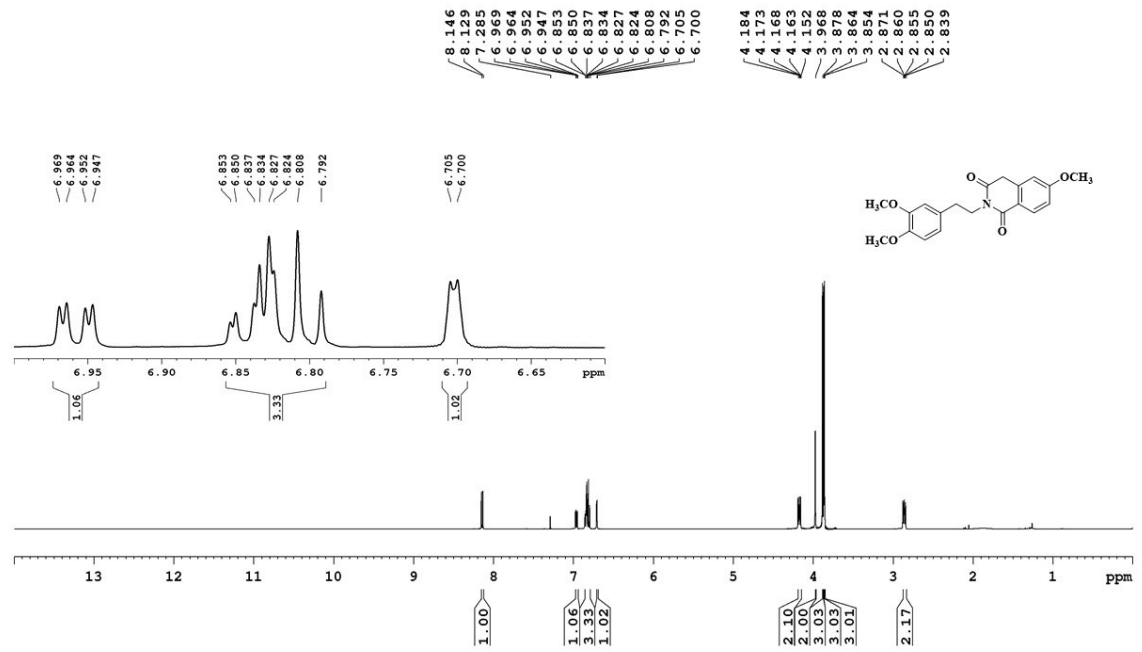


Figure S52: ^1H NMR spectra of 4e (500 MHz, $CDCl_3$).

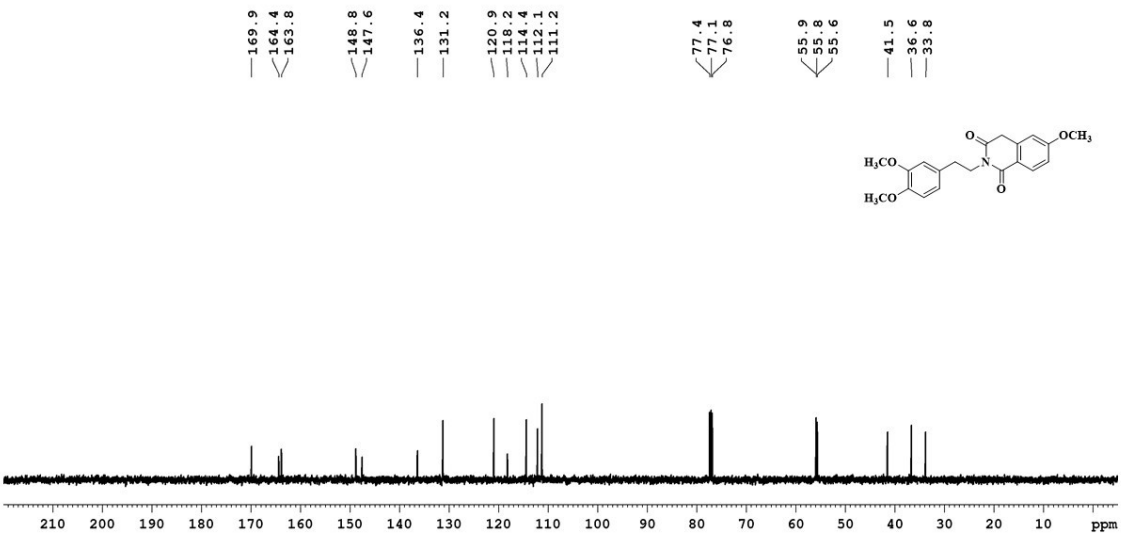


Figure S53: ^{13}C NMR spectra of 4e (125 MHz, $CDCl_3$).

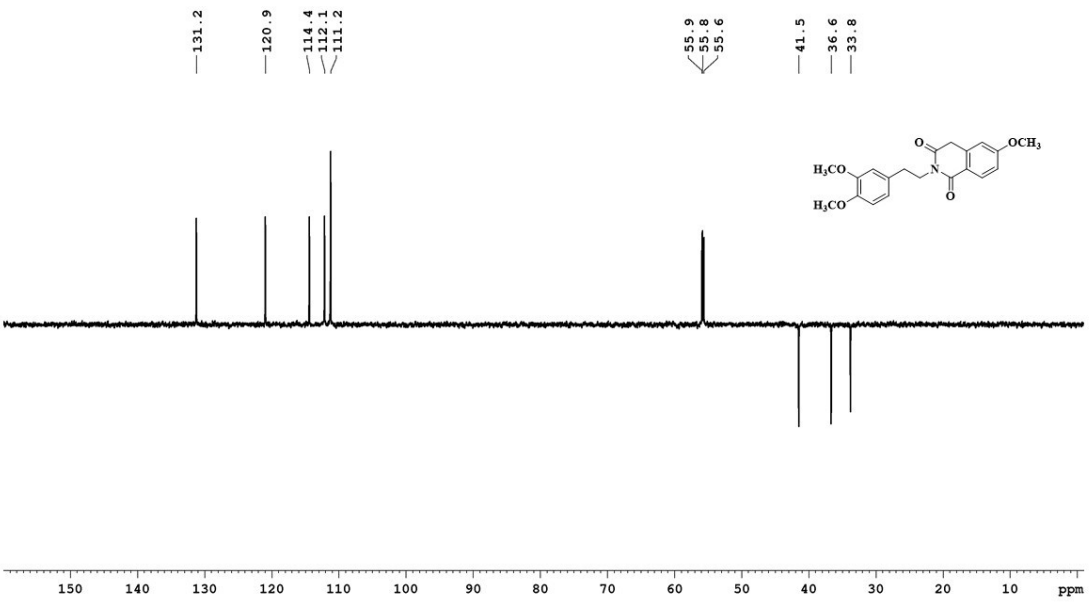


Figure S54: DEPT spectra of 4e (125 MHz, $CDCl_3$).

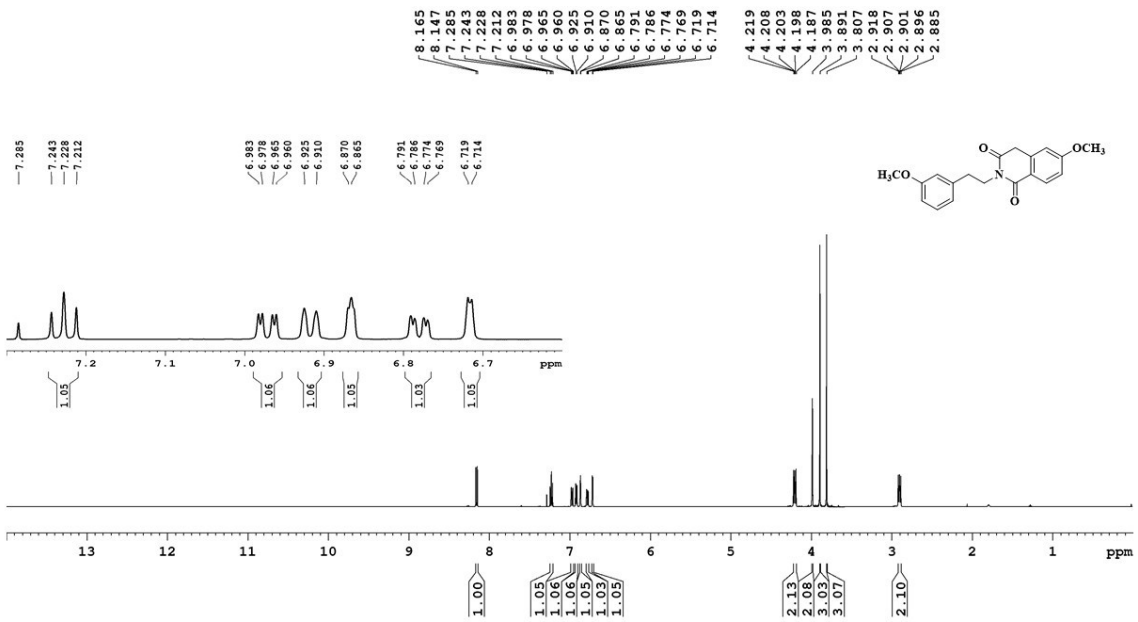


Figure S55: ^{1}H NMR spectra of 4f (500 MHz, $CDCl_3$).

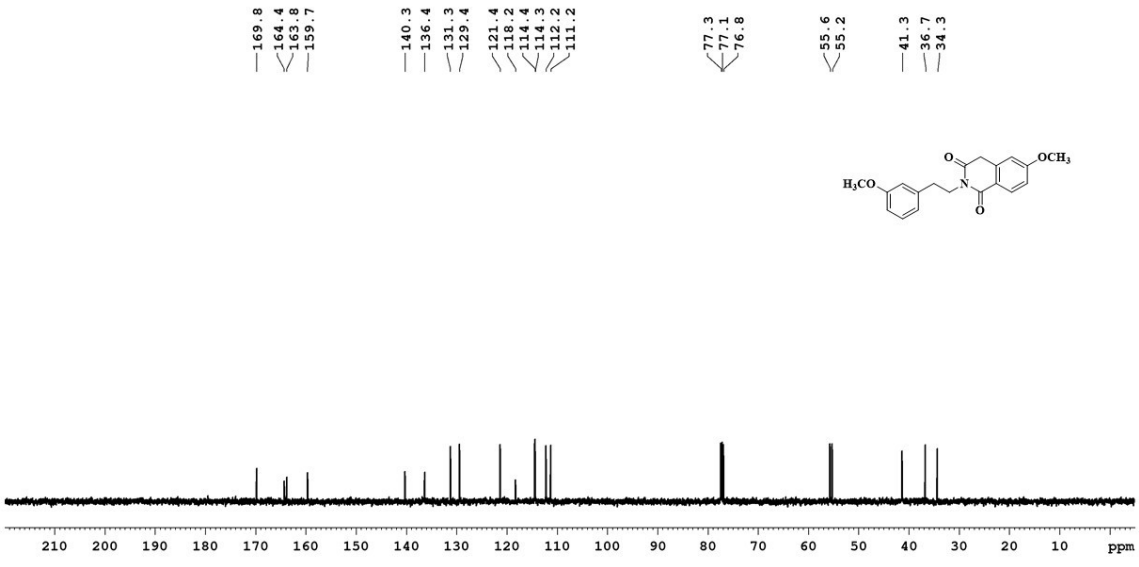


Figure S56: ^{13}C NMR spectra of 4f (125 MHz, $CDCl_3$).

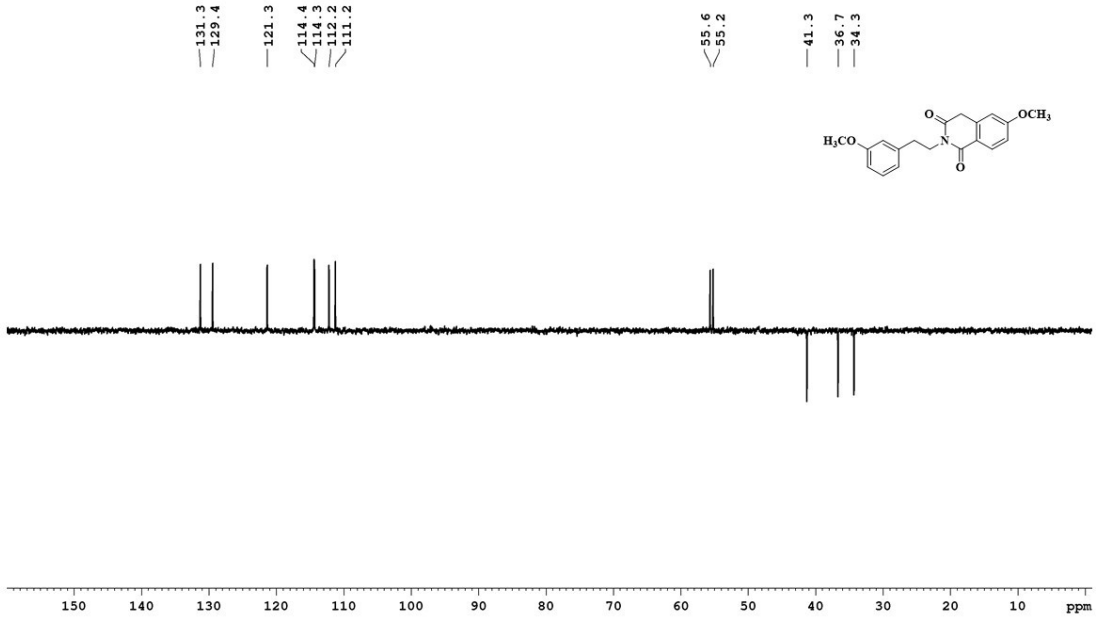


Figure S57: DEPT spectra of 4f (125 MHz, $CDCl_3$).

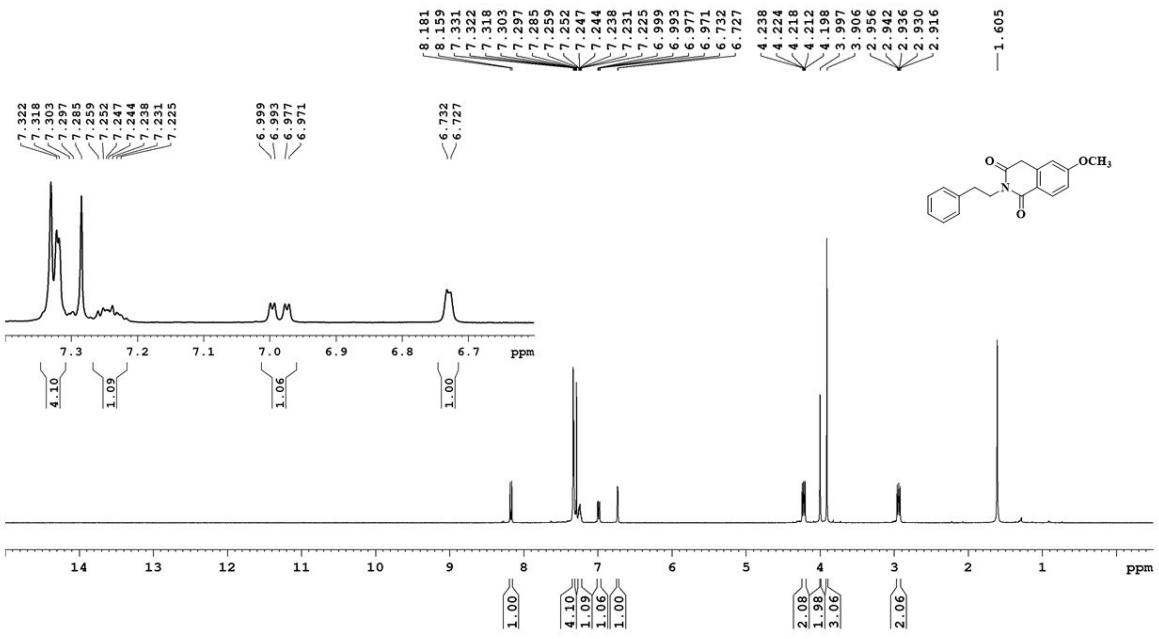


Figure S58: ^1H NMR spectra of 4g (400 MHz, $CDCl_3$).

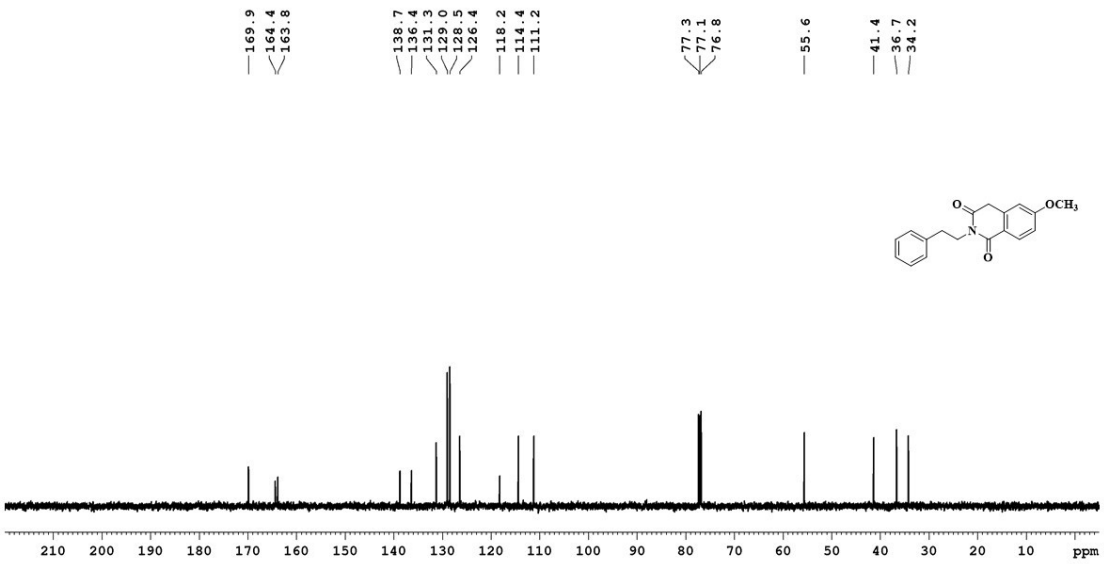


Figure S59: ^{13}C NMR spectra of 4g (100 MHz, $CDCl_3$).

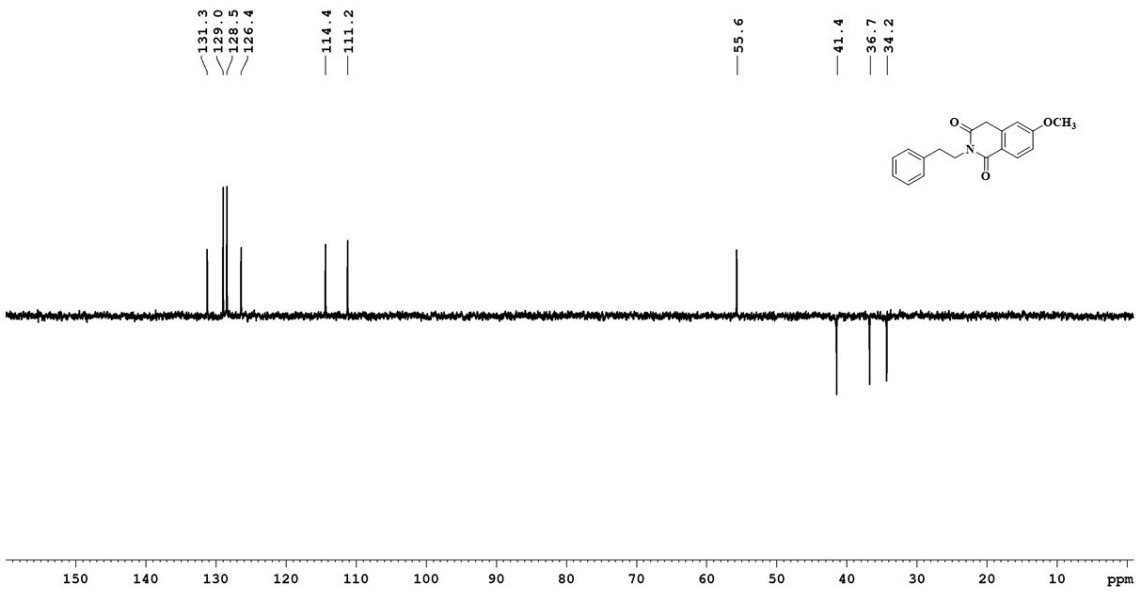


Figure S60: DEPT spectra of 4g (100 MHz, $CDCl_3$).

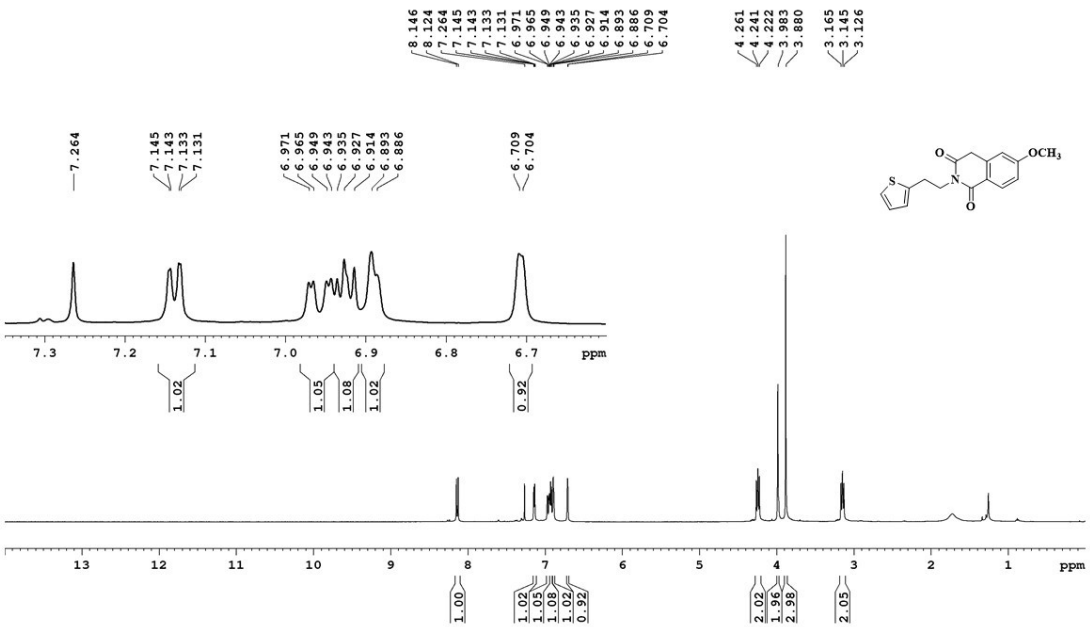


Figure S61: ^{1}H NMR spectra of 4h (400 MHz, $CDCl_3$).

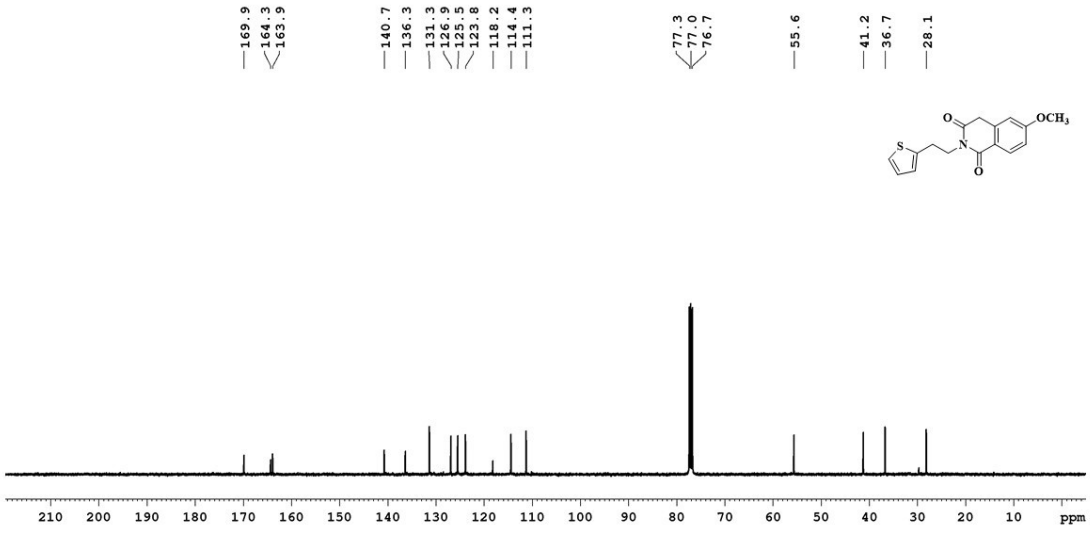


Figure S62: ^{13}C NMR spectra of 4h (100 MHz, $CDCl_3$).

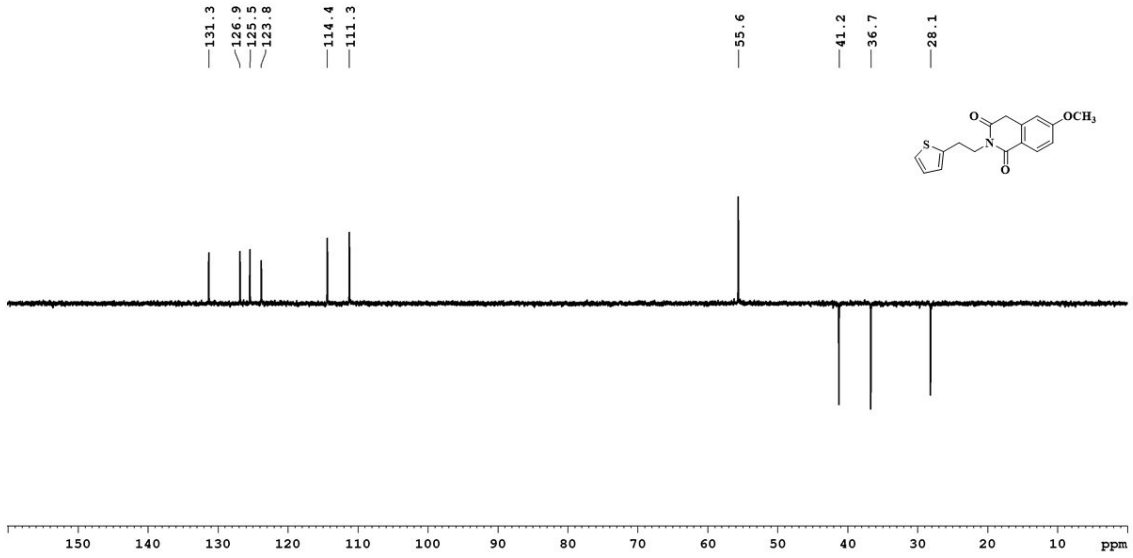


Figure S63: DEPT spectra of 4h (100 MHz, $CDCl_3$).

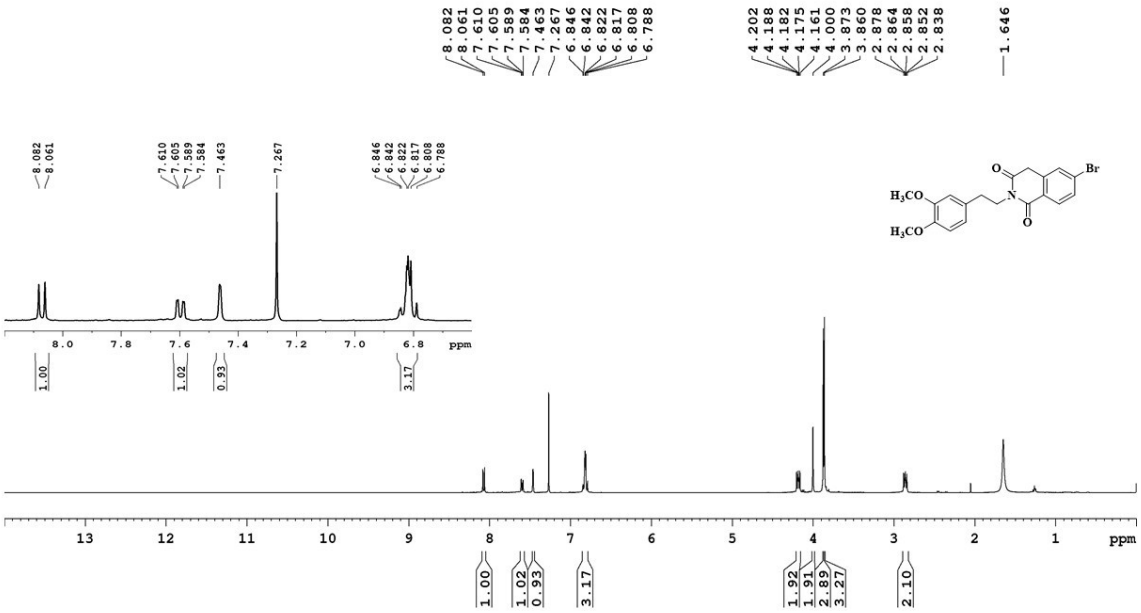


Figure S64: ^1H NMR spectra of 4i (400 MHz, $CDCl_3$).

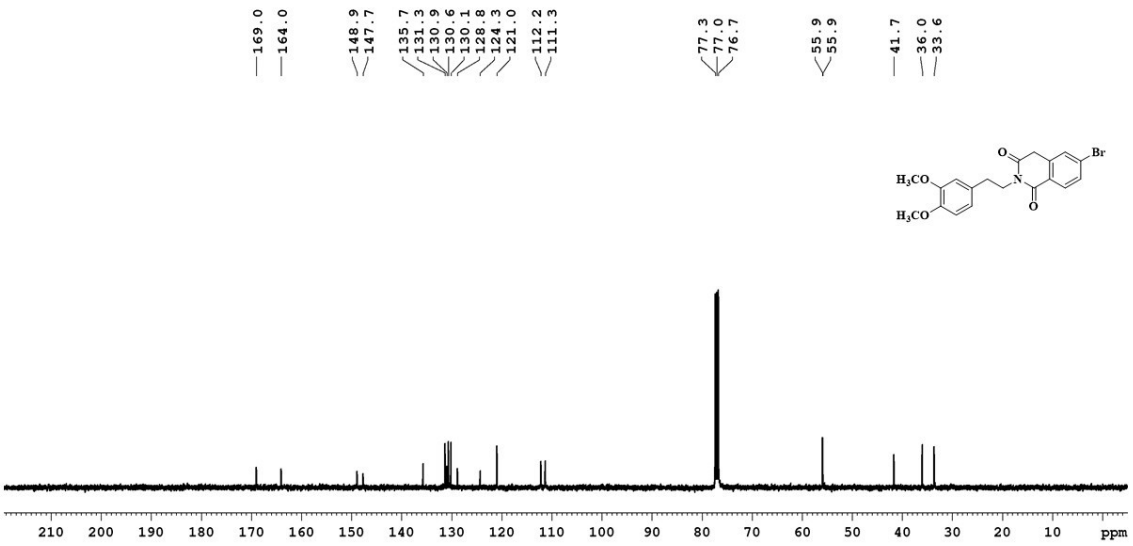


Figure S65: ^{13}C NMR spectra of 4i (100 MHz, $CDCl_3$).

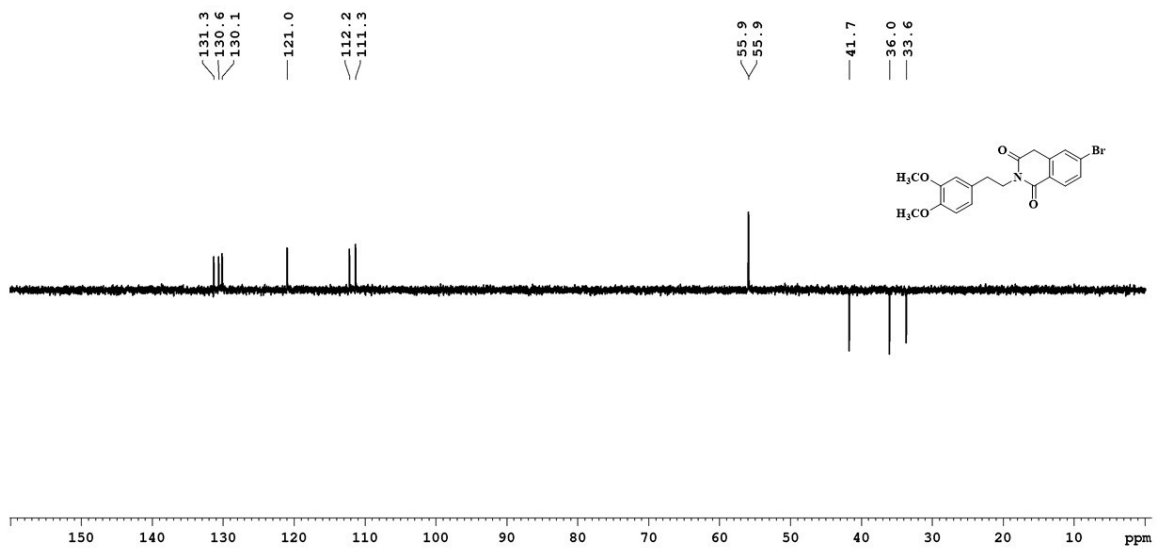


Figure S66: DEPT spectra of 4i (100 MHz, $CDCl_3$).

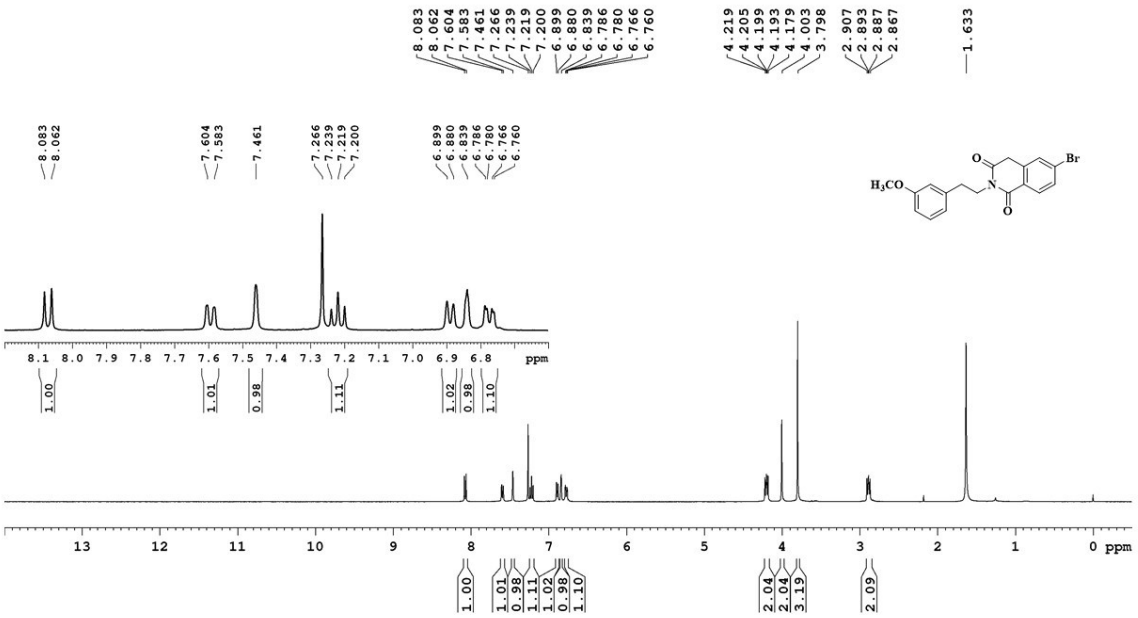


Figure S67: ^{1}H NMR spectra of 4j (400 MHz, $CDCl_3$).

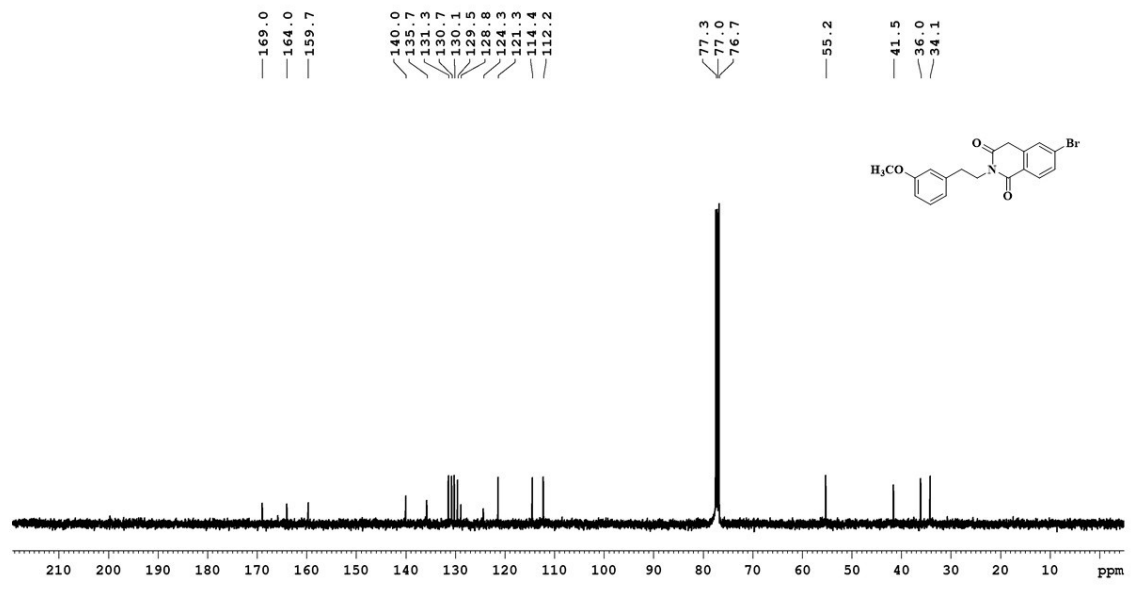


Figure S68: ^{13}C NMR spectra of 4j (100 MHz, $CDCl_3$).

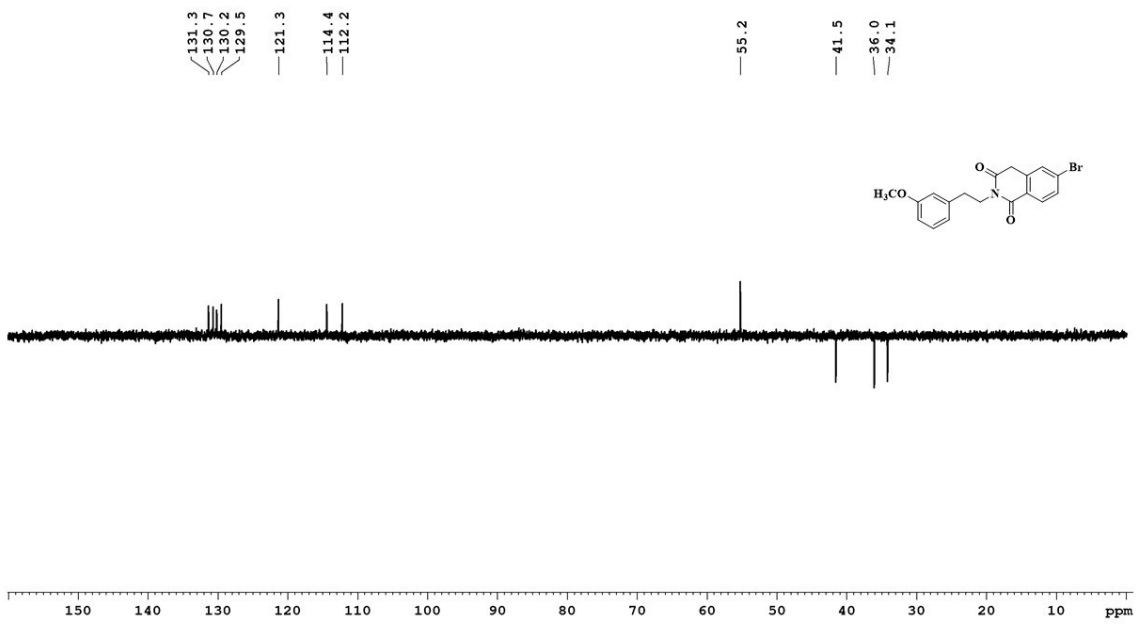


Figure S69: DEPT spectra of 4j (100 MHz, $CDCl_3$).

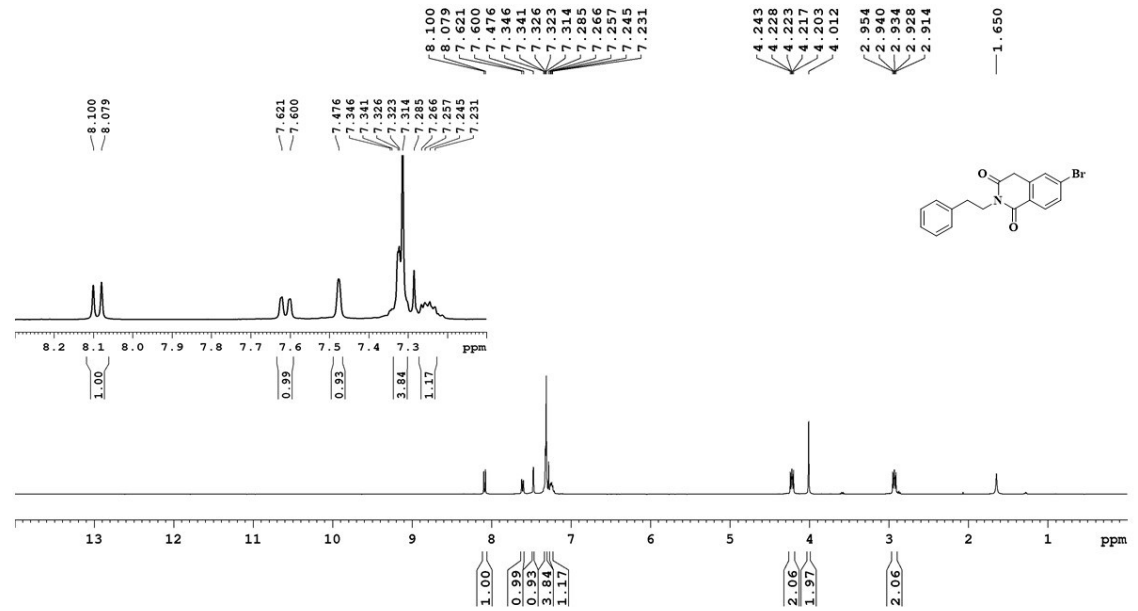


Figure S70: ^1H NMR spectra of 4k (400 MHz, $CDCl_3$).

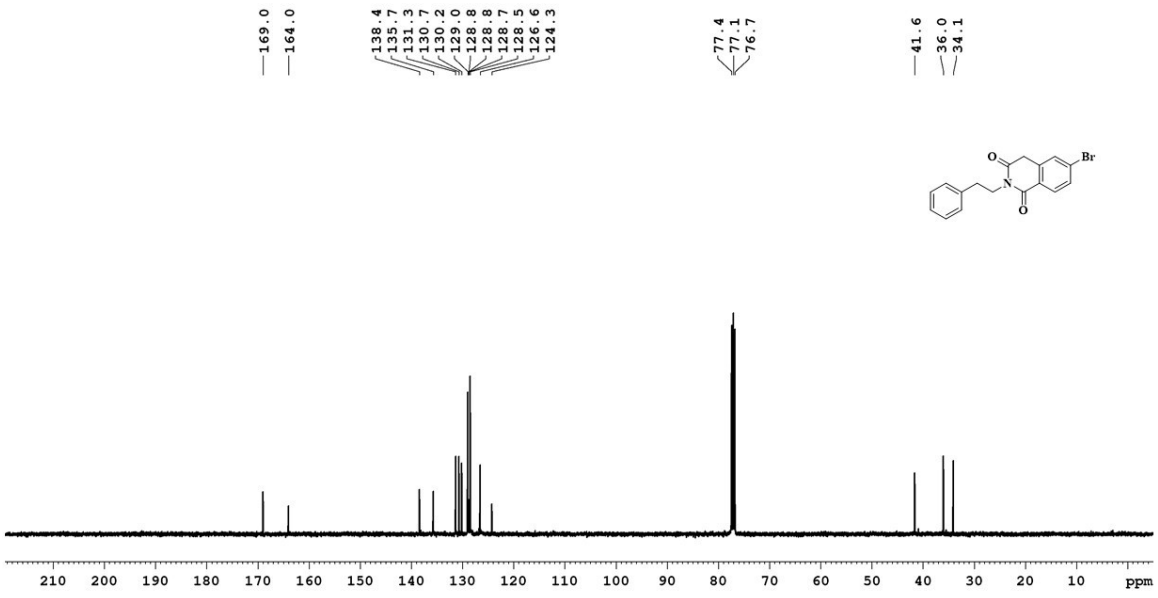


Figure S71: ^{13}C NMR spectra of 4k (100 MHz, $CDCl_3$).

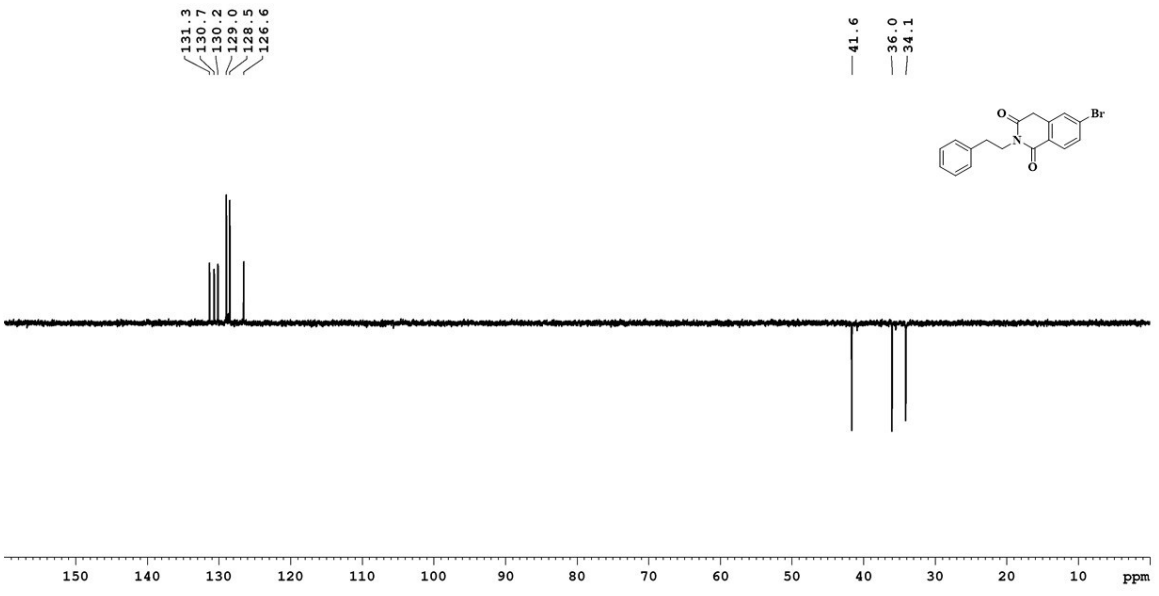


Figure S72: DEPT spectra of 4k (100 MHz, $CDCl_3$).

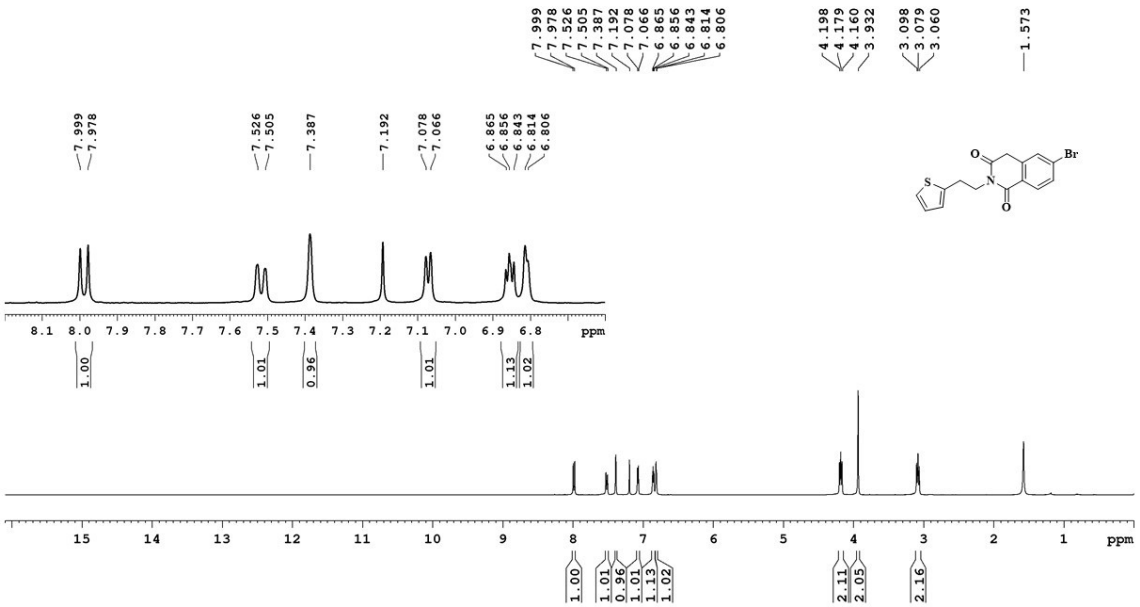


Figure S73: ^{1}H NMR spectra of 4l (400 MHz, $CDCl_3$).

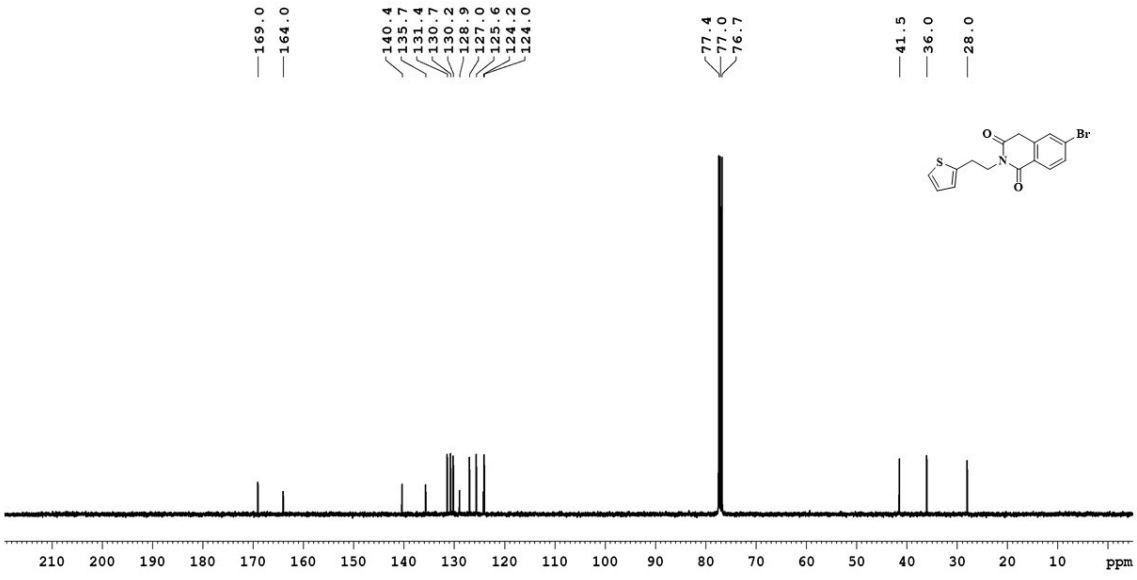


Figure S74: ^{13}C NMR spectra of 4l (100 MHz, $CDCl_3$).

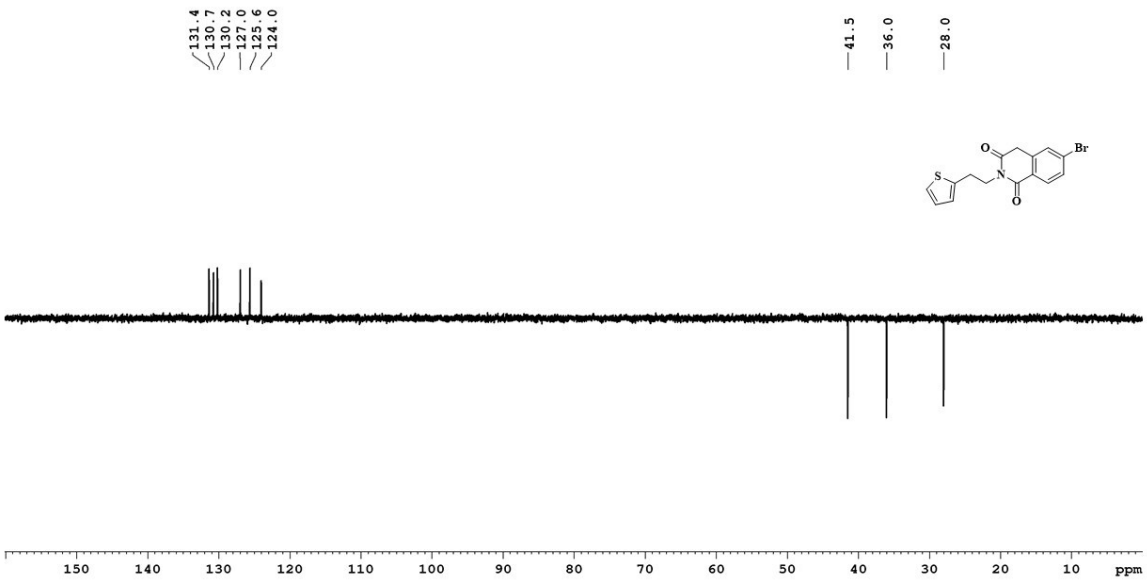


Figure S75: DEPT spectra of 4l (100 MHz, $CDCl_3$).

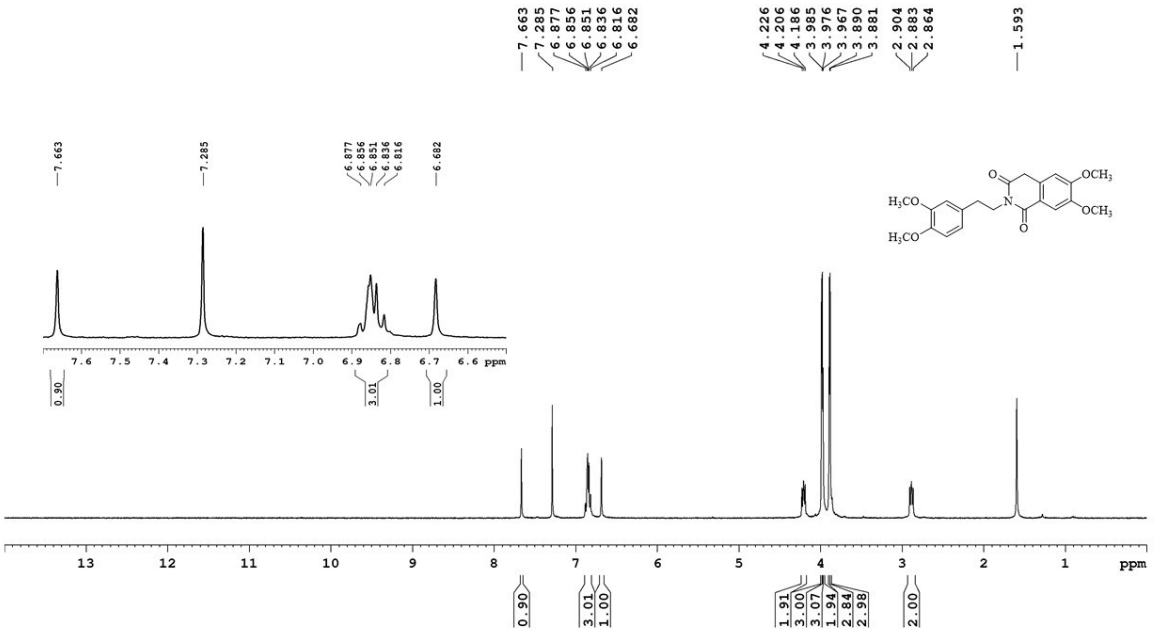


Figure S76: ^1H NMR spectra of 4m (400 MHz, $CDCl_3$).

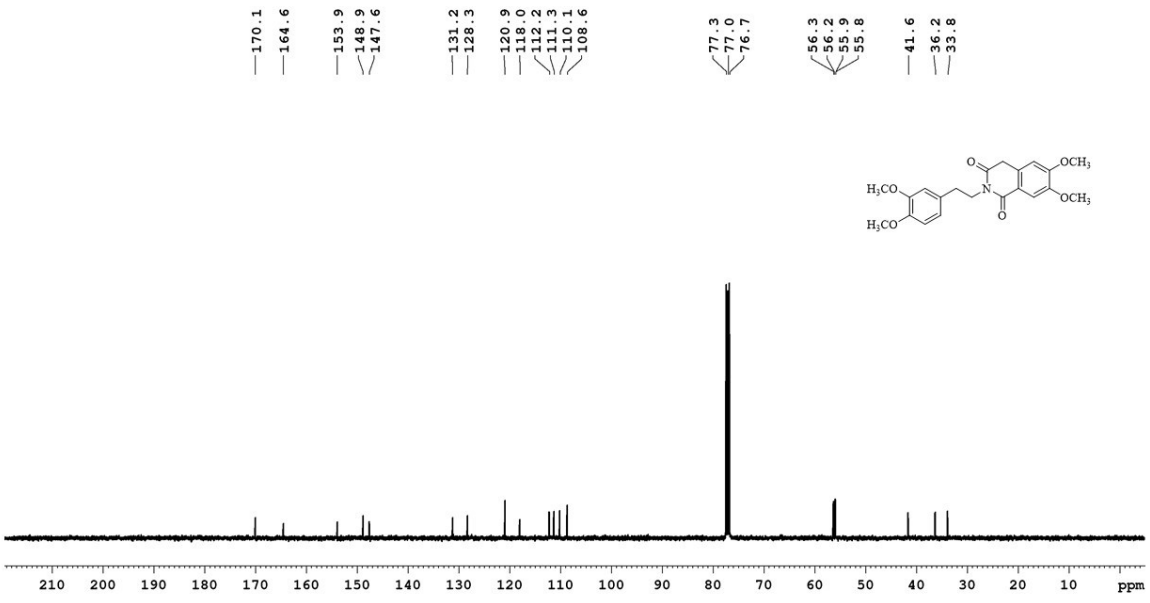


Figure S77: ^{13}C NMR spectra of 4m (100 MHz, $CDCl_3$).

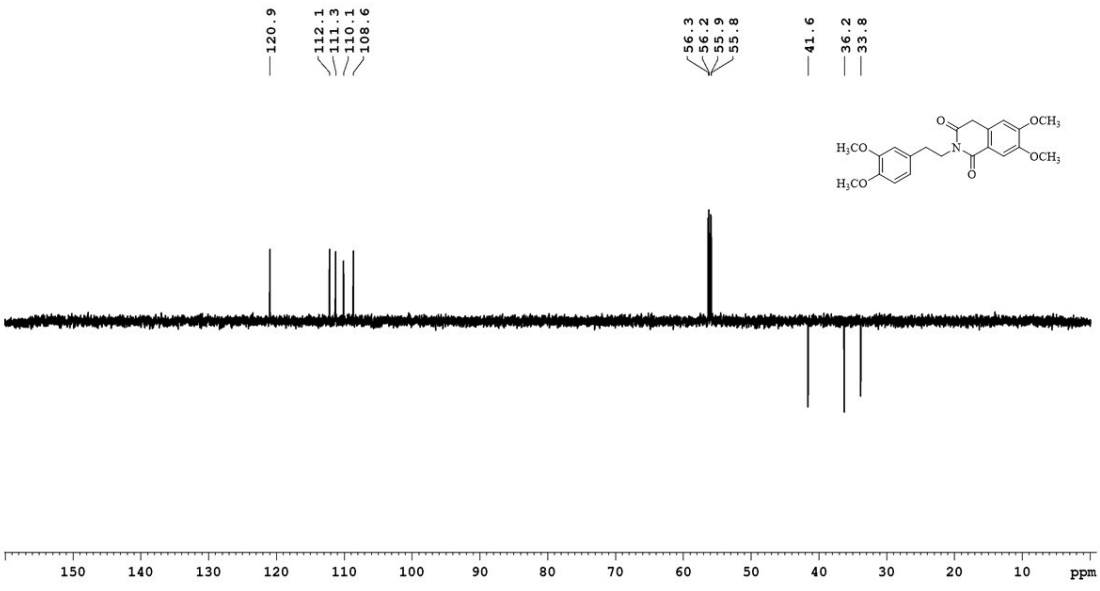


Figure S78: DEPT spectra of 4m (100 MHz, $CDCl_3$).

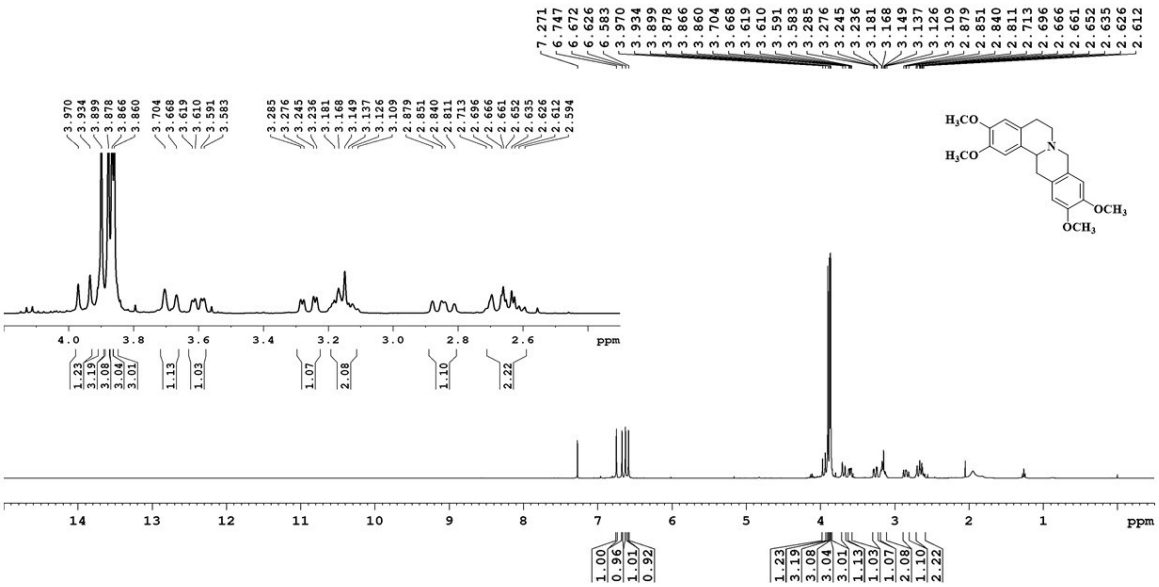


Figure S79: ^{1}H NMR spectra of 5 (400 MHz, $CDCl_3$).

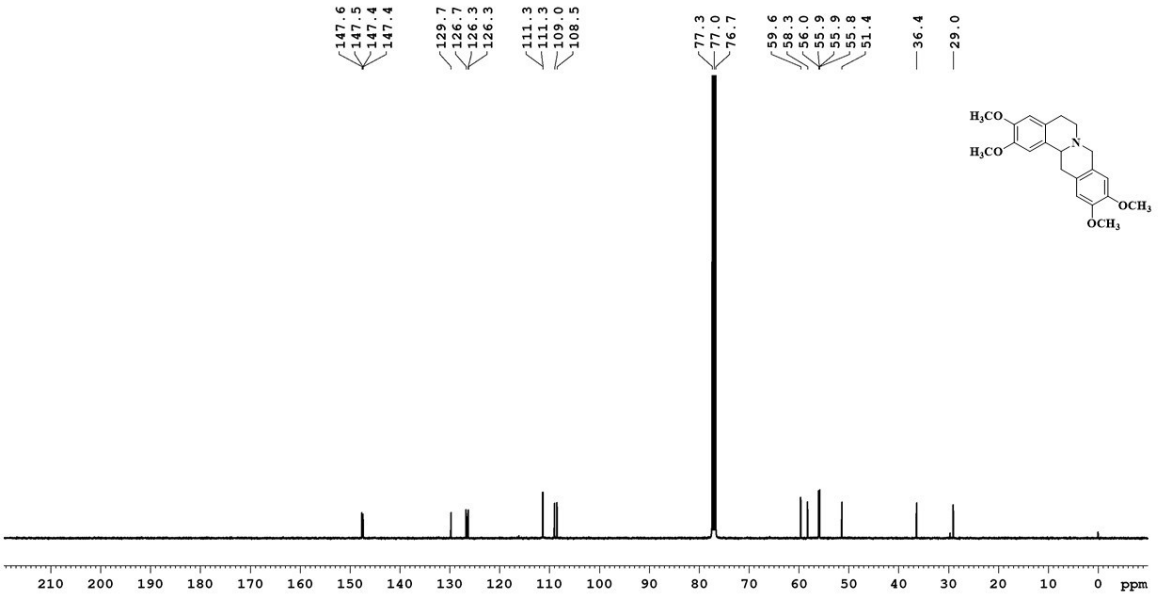


Figure S80: ^{13}C NMR spectra of 5 (100 MHz, $CDCl_3$).

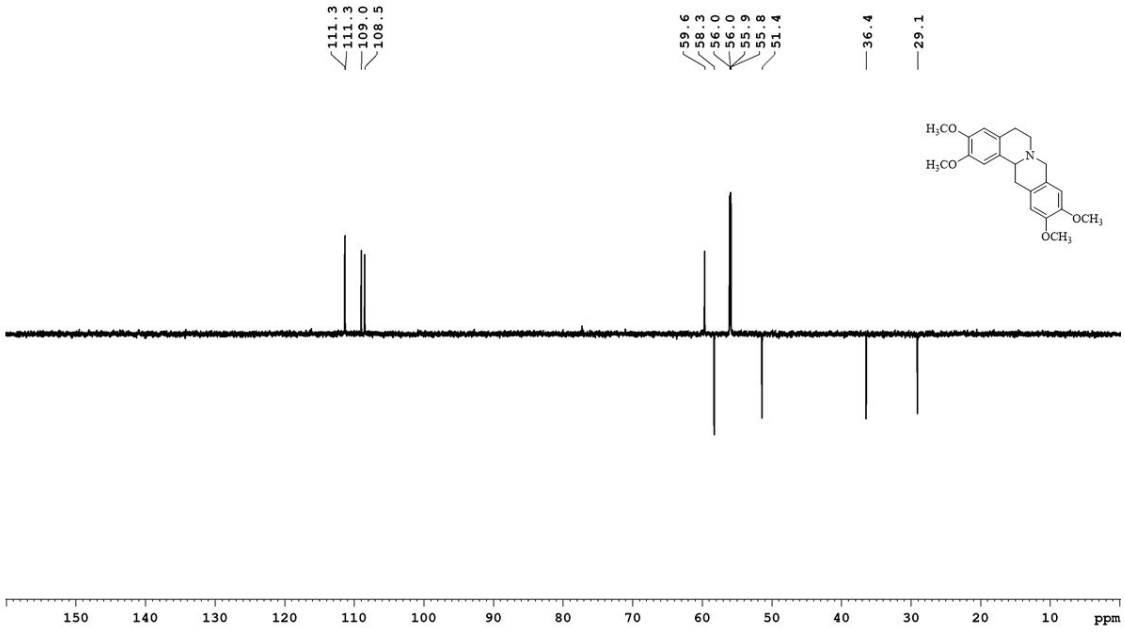
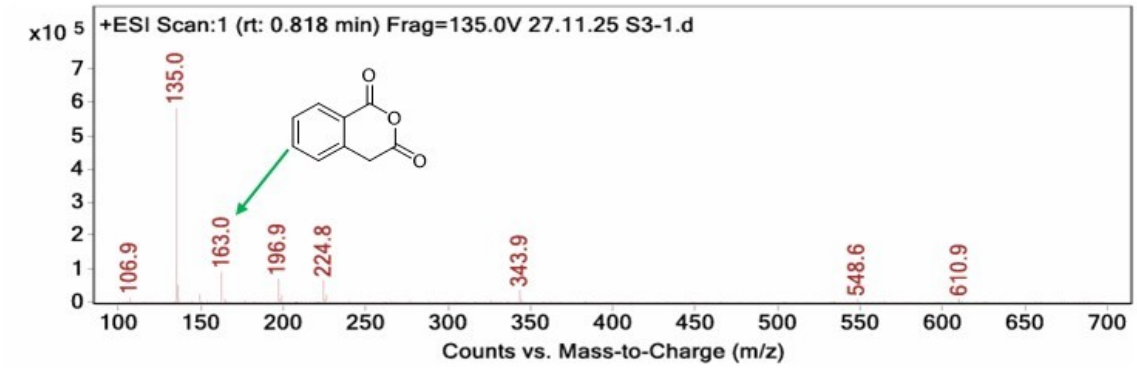


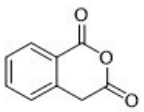
Figure S81: DEPT spectra of 5 (100 MHz, $CDCl_3$).

8. LCMS spectra of intermediates observed towards formation of compound 3a.



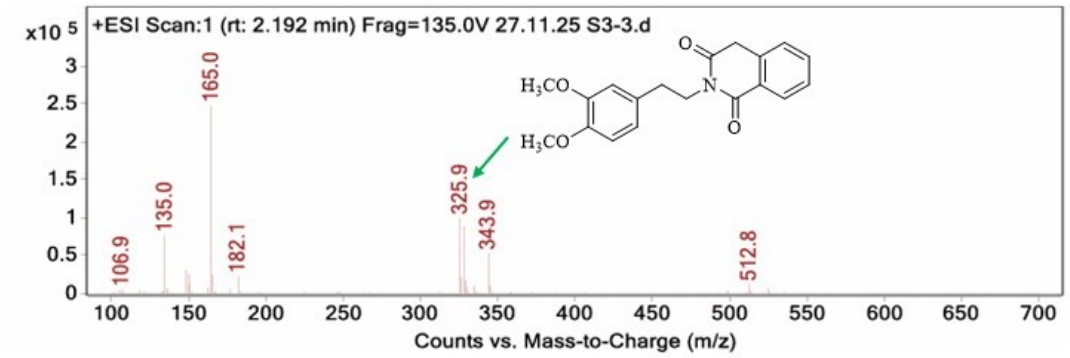
Peak List

m/z	z	Abund
106.9		13025.54
135	1	583350.56
136	1	51904.61
149		22871
163	1	89998.69
196.9	1	69247.28
198.9	1	21022.16
224.8	1	65347.3
226.8	1	22625.22
343.9	1	35732.2



Expected m/z = 163.0
Observed m/z (M+H) = 163.0

Figure S82: LCMS spectrum showing presence of intermediate D.



Peak List

m/z	z	Abund
135	1	76615.33
149		30702.46
151	1	25808.8
165	1	248260.25
166	1	25170.32
182.1	1	22697.06
325.9	1	100057.87
326.8	1	22052.56
327.9	1	89448.47
343.9	1	53269.29

Expected m/z = 326.1
Observed m/z (M+H) = 325.9

Figure S83: LCMS spectrum showing presence of intermediate 4a.

9. References

1) J.Yu, Z. Zhang, S. Zhou, W. Zhang and R. Tong, *Org. Chem. Front*. 2018, **5**, 242.
2) S.Li, H. Nie, M. Duan, W. Wang, C. Zhu, and C. Song, *Org. Lett*., 2021, **23**, 9631.
3) C. S. Lee, T. S. Yu, J. W. Luo, Y. Y. Cheng and C. P. Chuang, *Tetrahedron Lett*. 2009, **50**, 4558.
4) H. Heaney and M.O. Taha, *ARKIVOC*, 2000, **3**, 343.