Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

A Facile and Efficient [4 + 2] Cyclization Reaction of Sulfur Ylides: Access to N-Fused Benzimidazoles

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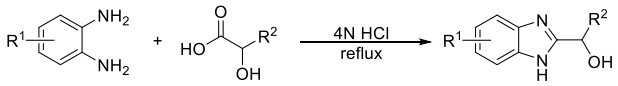
1. General information

Unless stated otherwise, all reactions for preparing compound **1a-w** were carried out under an air atmosphere and all reactions for providing compound **3a-w** were performed under argon atmosphere at room temperature. All reagents and solvents were of commercial quality and were used without further purification. Purification was carried out according to standard laboratory methods[1]. All reactions were monitored by TLC analysis with silica gel-coated plates with fluorescent indicator UV254. ^{1}H and ^{13}C NMR spectra were obtained on either a Bruker AV 300 at 300 MHz and 75 MHz, respectively. Chemical shifts are reported in ppm and coupling constants are reported in Hz with TMS at 0.0 ppm (^{1}H and ^{13}C) or $CDCl_3$ referenced at 7.26 (^{1}H) and 77.0 ppm (^{13}C) and DMSO-d_6 referenced at 2.50 (1H) and 39.5 (^{13}C). Mass spectra were measured with an Agilent Q-TOF 6520 mass spectrometer using ESI ionization.

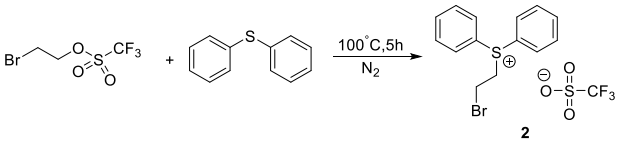
2. General procedure for the synthesis of 1a-w



1a-w

To a 50 mL round bottomed flask was added different substituted 1,2-phenylenediamine **1** (10 mmol, 1.0 equiv.), requisite acid 9 (15 mmol, 1.5 equiv.) and 4N hydrochloric acid (20 mL). The mixture was heated for 6 h under reflux. The reaction mixture was cooled to room temperature and ammonia solution was added and the mixture cooled in ice until precipitate formed. The resulting solid was recrystallised from aqueous ethanol to give compound **1a-w** as a solid[2].

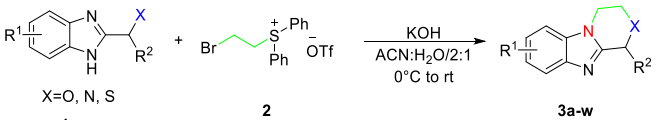
3. General procedure for the synthesis of 2



2

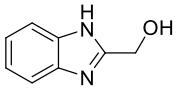
A solution of 2-bromoethyl trifluoromethanesulfonate[3] (4.12 g, 16.0 mmol) in anhydrous toluene (12 mL) was treated with phenyl sulfide (3.66 g, 19.2 mmol) at room temperature under argon with stirring. The reaction mixture was then heated at 100 °C under argon for 5 hours. The solution was allowed to cool to RT and diethyl ether (20 mL) was added to precipitate the product 9 which was isolated by filtration as a white to grey powder (3.22 g, 45%) after washing with Et_2O and used in the next step without further purification[4].

4. General procedure for the synthesis of 3a-w



In a 25 mL round bottomed flask compound **1a-w** (0.4 mmol, 1.0 equiv.) and bromoethylsulfonium salt **2** (0.2 mmol, 2.0 equiv.) was dissolved with acetonitrile: water (ACN: H_2O)/2:1 and was treated with KOH (1.6 mmol, 4.0 equiv.) at 0 °C under N_2 for 30 minutes. Then mixture was warmed to room temperature and was stirred for 12 hours until the reaction completed. After that, reaction system was quenched with saturated ammonium chloride solution (5 mL), and was extracted with DCM (3 x 30 mL). The combined organic layer washed with H_2O (2 x 10 mL), dried with anhydrous sodium sulfate. After concentration, product was purified using column chromatography on silica gel with suitable eluent.

5. Characterization of products

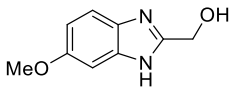


1*H*-benzimidazol-2-methanol (1a)[5]: White solid, 93% yield, mp 157-159 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 12.34 (brs, 1H), 7.48-7.51 (dd, *J* = 6.0, 3.2 Hz, 2H), 7.12-7.15 (dd, *J* = 6.0, 3.2 Hz, 2H), 5.76 (brs, 1H), 4.70 (s, 2H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 155.53, 138.95, 121.86, 115.26, 58.12.

HRMS (ESI-TOF) calcd for $C_8H_8N_2O$ [M+H] $^+$: 149.0709; found: 149.0717.

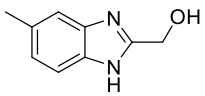


(5-Methoxy-1*H*-benzimidazol-2-yl)-methanol (1b)[6]: bright brown solid, 66% yield, mp 197-199 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 7.38 (d, *J* = 8.7 Hz, 1H), 7.00 (d, *J* = 2.3 Hz, 1H), 6.78 (dd, *J* = 8.7, 2.4 Hz, 1H), 5.56 (brs, 1H), 4.65 (s, 2H), 3.77 (s, 3H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 155.71, 155.02, 111.08, 58.16, 55.84.

HRMS (ESI-TOF) calcd for $C_9H_{10}N_2O_2$ [M+H] $^+$: 179.0815; found: 179.0819.

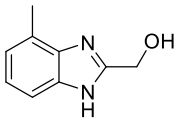


(5-Methyl-1*H*-benzimidazol-2-yl)-methanol (1c)[6]: pale creamy powdery solid, 68% yield, mp 176-178 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 7.38 (d, *J* = 8.1 Hz, 1H), 7.28 (s, 1H), 6.99 (dd, *J* = 8.2, 1.1 Hz, 1H), 5.94 (brs, 1H), 4.67 (s, 2H), 2.39 (s, 3H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 155.20, 138.59, 137.29, 131.01, 123.36, 115.16, 114.64, 58.04, 21.71.

HRMS (ESI-TOF) calcd for $C_9H_{10}N_2O$ [M+H] $^+$: 163.0866; found: 163.0862.

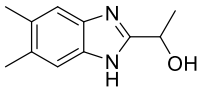


(4-Methyl-1*H*-benzimidazol-2-yl)-methanol (1d)[7]: brown crystalline, 89% yield, mp 196-198 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 7.31 (d, J = 7.9 Hz, 1H), 7.03 (t, J = 7.6 Hz, 1H), 6.99 (d, J = 7.2 Hz, 1H), 5.66 (brs, 1H), 4.69 (s, 2H), 2.50 (s, 3H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 154.81, 139.32, 137.77, 125.50, 122.18, 121.85, 112.10, 58.18, 17.23.

HRMS (ESI-TOF) calcd for $C_9H_{10}N_2O$ $[M+H]^+$: 163.0866; found: 163.0871.

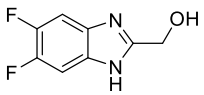


(5, 6-Dimethyl-1*H*-benzimidazol-2-yl)-methanol (1e)[8]: brick red solid, 60% yield, mp 243-246 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 7.26 (s, 2H), 5.74 (brs, 1H), 4.65 (s, 2H), 2.28 (s, 6H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 154.51, 137.50, 130.08, 115.37, 58.13, 20.41.

HRMS (ESI-TOF) calcd for $C_{10}H_{12}N_2O$ $[M+H]^+$: 177.1022; found: 177.1020.

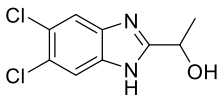


(5, 6-Difluoro-1*H*-benzimidazol-2-yl)-methanol (1f): black solid, 74% yield, mp 198-201 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 12.56 (brs, 1H), 7.51 (t, $J_{H\text{-}F}$= 9.2 Hz, 2H), 5.76 (s, 1H), 4.67 (s, 2H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 157.08, 145.11-148.50 (dd, $J_{C\text{-}F}$ = 16.9, 237.3 Hz), 102.88, 58.02.

HRMS (ESI-TOF) calcd for $C_8H_6F_2N_2O$ $[M+H]^+$: 185.0521; found: 185.0522.

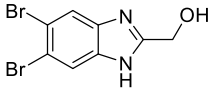


(5, 6-Dichloro-1*H*-benzimidazol-2-yl)-methanol (1g): red solid, 87% yield, mp 248-250 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 7.77 (s, 2H), 6.43 (brs, 1H), 4.74 (s, 2H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 158.46, 137.55, 124.95, 116.48, 57.62.

HRMS (ESI-TOF) calcd for $C_8H_6Cl_2N_2O$ $[M+H]^+$: 216.9930; found: 216.9928.

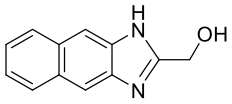


(5, 6-Dibromo-1*H*-benzimidazol-2-yl)-methanol (1h): rufous crystalline, 91% yield, mp 260-262 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 12.64 (brs, 1H), 7.87 (s, 2H), 5.83 (s, 1H), 4.71 (d, J = 4.7 Hz, 2H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 158.40, 115.90, 57.98.

HRMS (ESI-TOF) calcd for $C_8H_6Br_2N_2O$ [M+H] $^+$: 304.8920; found: 304.8929.

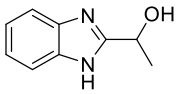


(1*H*-Naphth[2, 3-*d*]imidazol-2yl)-methanol (1i)[9]: pale brown crystalline, 57% yield, mp 257-259 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 12.45 (brs, 1H), 7.96-8.01 (m, 4H), 7.32-7.38 (m, 2H), 5.88 (t, *J* = 5.9 Hz, 1H), 4.81 (d, *J* = 4.8 Hz, 2H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 160.41, 139.34, 130.04, 128.15, 123.69, 111.17, 58.40.

HRMS (ESI-TOF) calcd for $C_{12}H_{10}N_2O$ [M+H] $^+$: 199.0866; found: 199.0868.

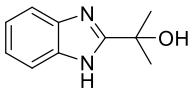


(1*H*-benzimidazole-2-yl)-ethanol (1j)[10]: white powder, 93% yield, mp 170-173 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 7.48-7.51 (dd, *J* = 5.9, 3.2 Hz, 2H), 7.12-7.14 (dd, *J* = 5.9, 3.1 Hz, 2H), 5.81 (brs, 1H), 4.96 (q, *J* = 6.5 Hz, 1H), 1.52 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 159.01, 138.84, 121.82, 115.28, 64.09, 23.41.

HRMS (ESI-TOF) calcd for $C_9H_{10}N_2O$ [M+H] $^+$: 163.0866; found: 163.0874.

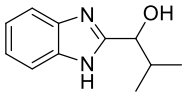


2-(α-Hydroxyisopropyl)-benzimidazole (1k)[11]: colorless crystalline, 59% yield, mp 221-223 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 12.13 (brs, 1H), 7.48 (m, 2H), 7.12 (dd, *J* = 6.0, 3.2 Hz, 2H), 5.59 (s, 1H), 1.57 (s, 6H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 161.74, 121.58, 69.28, 30.47.

HRMS (ESI-TOF) calcd for $C_{10}H_{12}N_2O$ [M+H] $^+$: 177.1022; found: 177.1030.

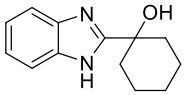


α-(1-Methylethyl)-1*H*-benzimidazol-2-methanol (1l): pale brown crystalline, 25% yield, mp 225-227 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 12.18 (brs, 1H), 7.47-7.50 (m, 2H), 7.08-7.13 (m, 2H), 5.76 (d, *J* = 4.7 Hz, 1H), 4.54 (t, *J* = 5.2 Hz, 1H), 2.15 (dq, *J* = 13.3, 6.7 Hz, 1H), 0.89 (dd, *J* = 11.5, 6.8 Hz, 6H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 157.80, 121.56, 73.06, 34.08, 19.21, 18.05.

HRMS (ESI-TOF) calcd for $C_{11}H_{14}N_2O$ [M+H] $^+$: 191.1179; found: 191.1196.

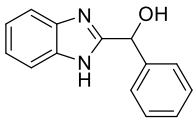


(1*H*-benzimidazol-2-yl)-cyclohexanol (1m): pale creamy powder, 49% yield, mp 229-232 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 7.49 (dd, J = 5.9, 3.2 Hz, 2H), 7.13 (dd, J = 6.0, 3.2 Hz, 2H), 5.38 (s, 1H), 4.54 (t, J = 5.2 Hz, 1H), 1.96-2.04 (m, 2H), 1.51-1.82 (m, 7H), 1.29-1.33 (m, 1H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 161.90, 121.69, 115.37, 70.31, 37.32, 25.62, 21.85.

HRMS (ESI-TOF) calcd for $C_{13}H_{16}N_2O$ [M+H] $^{+}$: 217.1335; found: 217.1340.

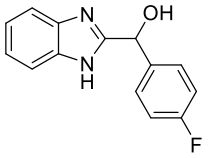


2-(α-Hydroxybenzyl)-benzimidazole (1n): pale creamy crystalline, 64% yield, mp 200-203 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 12.37 (brs, 1H), 7.47-7.52 (m, 4H), 7.32-7.37 (m, 2H), 7.23-7.28 (m, 1H), 7.13 (dd, J = 5.9, 3.1 Hz, 2H), 6.54 (d, J = 3.4 Hz, 1H), 5.94 (d, J = 2.5 Hz, 1H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 157.44, 142.87, 128.62, 127.88, 126.88, 121.94, 70.43.

HRMS (ESI-TOF) calcd for $C_{14}H_{12}N_2O$ [M+H] $^{+}$: 225.1022; found: 225.1037.

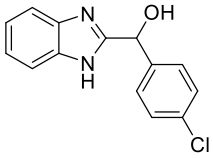


2-(α-Hydroxy-p-fluorobenzyl)-benzimidazole (1o): pale brown solid, 58% yield, mp 160-162 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 7.47-7.56 (m, 4H), 7.13-7.20 (m, 4H), 6.60 (s, 1H), 5.95 (s, 1H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 160.33-163.55 (d, $J_{C\text{-}F}$ = 241.5 Hz), 157.22, 139.08-139.11 (d, $J_{C\text{-}F}$ = 2.7 Hz), 128.85-128.96 (d, $J_{C\text{-}F}$ = 8.2 Hz), 121.98, 115.22-115.50 (d, $J_{C\text{-}F}$ = 41.2 Hz), 69.71.

HRMS (ESI-TOF) calcd for $C_{14}H_{11}FN_2O$ [M+H] $^{+}$: 243.0928; found: 243.0942.

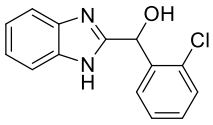


2-(α-Hydroxy-p-chlorobenzyl)-benzimidazole (1p): pale yellow solid, 63% yield, mp 155-158 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 12.40 (brs, 1H), 7.39-7.53 (m, 6H), 7.13 (dd, J = 6.0, 3.2 Hz, 2H), 6.59-6.67 (m, 1H), 5.94 (d, J = 4.2 Hz, 1H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 156.97, 141.87, 132.41, 128.76, 128.58, 121.93, 69.69.

HRMS (ESI-TOF) calcd for $C_{14}H_{11}ClN_2O$ [M+H] $^{+}$: 259.0633; found: 259.0636.



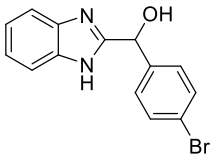
2-(α-Hydroxy-o-chlorobenzyl)-benzimidazole (1q): pale red powder, 46% yield, mp 211-214 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 12.43 (brs, 1H), 7.68 (dd, J = 7.5, 1.7 Hz, 1H), 7.30-7.50 (m, 5H),

7.12-7.16 (dd, *J* = 6.8, 3.6 Hz, 2H), 6.62 (d, *J* = 4.9 Hz, 1H), 6.24 (d, *J* = 4.7 Hz, 1H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 155.87, 140.24, 129.67, 129.56, 129.43, 127.69, 122.01, 67.17.

HRMS (ESI-TOF) calcd for $C_{14}H_{11}ClN_2O$ [M+H] $^+$: 259.0633; found: 259.0638.

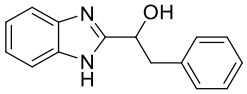


2-(α-Hydroxy-p-bromobenzyl)-benzimidazole (1r): brown solid, 89% yield, mp 249-252 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 7.44-7.57 (m, 6H), 7.10-7.16 (m, 2H), 6.68 (s, 1H), 5.94 (s, 1H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 156.89, 142.25, 131.50, 129.14, 122.04, 120.98, 69.64.

HRMS (ESI-TOF) calcd for $C_{14}H_{11}BrN_2O$ [M+H] $^+$: 303.0128; found: 303.0133.

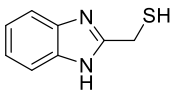


(1*H*-benzimidazol-2-yl)-phenylethanol (1s)[12]: pale red crystalline, 64% yield, mp 248-250 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 7.50 (dd, *J* = 6.0, 3.2 Hz, 2H), 7.12-7.24 (m, 7H), 5.92 (d, *J* = 3.8 Hz, 1H), 5.00 (d, *J* = 3.7 Hz, 1H), 3.28 (dd, *J* = 13.7, 4.9 Hz, 1H), 3.07 (dd, *J* = 13.7, 8.2 Hz, 1H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 157.79, 138.88, 129.89, 128.47, 126.53, 121.84, 115.29, 69.21, 42.91.

HRMS (ESI-TOF) calcd for $C_{15}H_{14}N_2O$ [M+H] $^+$: 239.1179; found: 239.1194.

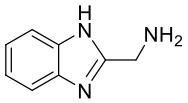


(1*H*-benzimidazol-2-yl)-methanethiol (1t)[13]: white powder, 96% yield, mp 155-157 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 12.40 (brs, 1H), 7.50 (dd, *J* = 6.0, 3.2 Hz, 2H), 7.15 (dd, *J* = 6.0, 3.2 Hz, 2H), 3.92 (s, 2H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 154.11, 122.29, 122.07, 115.25, 21.57.

HRMS (ESI-TOF) calcd for $C_8H_8N_2S$ [M+H] $^+$: 165.0481; found: 165.0476.

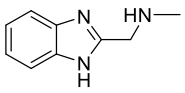


(1*H*-benzimidazol-2-yl)-methanamine (1u)[14]: brown solid, 79% yield, mp 101-103 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 7.51 (dd, *J* = 5.9, 3.2 Hz, 2H), 7.13 (dd, *J* = 6.0, 3.2 Hz, 2H), 5.53 (brs, 1H). 3.97 (s, 2H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 156.66, 139.07, 121.73, 115.11, 40.16.

HRMS (ESI-TOF) calcd for $C_8H_9N_3$ [M+H] $^+$: 148.0869; found: 148.0865.

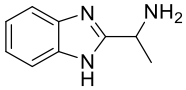


(1*H*-benzimidazol-2-yl)-*N*-methylmethanamine (1v)[15]: pale brown oily solid, 43% yield, mp 120-123 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56 (dd, *J* = 6.0, 3.2 Hz, 2H), 7.23 (dd, *J* = 6.1, 3.2 Hz, 2H), 4.15 (s, 2H), 2.53 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 151.90, 138.31, 122.59, 115.07, 48.84, 35.66.

HRMS (ESI-TOF) calcd for $C_9H_{11}N_3$ $[M+H]^+$: 162.1026; found: 162.1026.

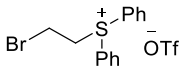


(1*H*-benzimidazol-2-yl)-ethylamine (1w)[16]: pale yellow solid, 62% yield, mp 203-205 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57 (dd, *J* = 6.0, 3.2 Hz, 2H), 7.23 (dd, *J* = 6.0, 3.2 Hz, 2H), 4.73 (brs, 2H), 4.46 (q, *J* = 6.7 Hz, 2H), 1.60 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 159.11, 151.62, 138.29, 122.58, 122.32, 114.98, 46.19, 23.74.

HRMS (ESI-TOF) calcd for $C_9H_{11}N_3$ $[M+H]^+$: 162.1026; found: 162.1023.

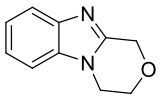


Bromoethylsulfonium salt (2)[3a]: grey powder, 45% yield, mp 85-87 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06-8.12 (m, 4H), 7.71-7.77 (m, 6H), 4.92 (t, *J* = 5.9 Hz, 2H), 3.73 (t, *J* = 5.9 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 135.3, 131.9, 131.1, 122.9, 48.2, 23.8.

HRMS (ESI-TOF) calcd for $C_{15}H_{14}BrF_3O_3S_2$ $[M-CF_3O_3S]^+$: 292.9994; found: 293.0007.

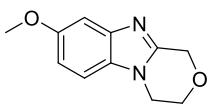


3, 4-Dihydro-1*H*- [1, 4] oxazino [4,3-*a*] benzimidazole (3a)[17]: pale yellow solid, 61 mg, 88% yield, mp 125-127 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.73-7.76 (m, 1H), 7.28-7.36 (m, 3H), 5.07 (s, 2H), 4.18-4.22 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 147.86, 142.55, 134.00, 122.69, 122.41, 119.45, 108.78, 65.49, 63.97, 42.02.

HRMS (ESI-TOF) calcd for $C_{10}H_{10}N_2O$ $[M+H]^+$: 175.0866; found: 175.0866.

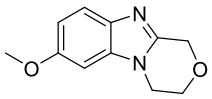


3, 4-Dihydro-8-methoxy-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3b$_1$): white solid, 34 mg, 41% yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.19-7.22 (m, 2H), 6.90 (m, 1H), 5.01 (s, 2H), 4.16-4.20 (m, 2H), 4.08-4.13 (m, 2H), 3.87 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 156.43, 148.04, 143.08, 128.49, 119.77, 112.30, 101.78, 65.28, 63.88, 55.86, 41.97.

HRMS (ESI-TOF) calcd for $C_{11}H_{12}N_2O_2$ [M+H] $^+$: 205.0972; found: 205.0971.

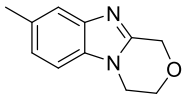


3, 4-Dihydro-7-methoxy-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3b$_2$): white solid, 39 mg, 46% yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 (d, *J* = 8.8 Hz, 1H), 6.92 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.78 (d, *J* = 2.3 Hz, 1H), 5.00 (s, 2H), 4.16-4.20 (m, 2H), 4.08-4.13 (m, 2H), 3.87 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 156.58, 146.98, 136.72, 134.52, 111.61, 109.12, 92.78, 65.46, 63.97, 55.92, 42.03.

HRMS (ESI-TOF) calcd for $C_{11}H_{12}N_2O_2$ [M+H] $^+$: 205.0792; found: 205.0790.

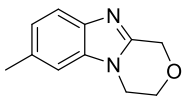


3, 4-Dihydro-8-methyl-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3c$_1$): white solid, 27 mg, 33% yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52 (m, 1H), 7.24 (d, *J* = 8.2 Hz, 1H), 7.09-7.13 (m, 1H), 5.03 (s, 2H), 4.18-4.21 (m, 2H), 4.12-4.15 (m, 2H), 2.50 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 147.41, 142.59, 134.18, 123.88, 119.17, 108.30, 65.39, 63.95, 41.99, 21.60.

HRMS (ESI-TOF) calcd for $C_{11}H_{12}N_2O$ [M+H] $^+$: 189.1022; found: 189.1021.

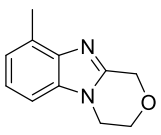


3, 4-Dihydro-7-methyl-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3c$_2$): white solid, 43 mg, 51% yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.8 Hz, 1H), 7.09-7.13 (m, 2H), 5.03 (s, 2H), 4.18-4.21 (m, 2H), 4.12-4.15 (m, 2H), 2.51 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 147.31, 140.41, 132.47, 124.25, 118.84, 108.78, 65.45, 63.99, 41.96, 21.74.

HRMS (ESI-TOF) calcd for $C_{11}H_{12}N_2O$ [M+H] $^+$: 189.1022; found: 189.1019.



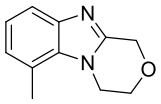
3, 4-Dihydro-9-methyl-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3d$_1$): pale yellow solid, 58 mg, 70%

yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.15-7.21 (m, 2H), 7.08-7.11 (m, 1H), 5.07 (s, 2H), 4.17-4.21 (m, 2H), 4.12-4.15 (m, 2H), 2.66 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 147.04, 141.77, 133.62, 129.41, 123.11, 122.32, 106.29, 65.59, 63.98, 42.08, 16.68.

HRMS (ESI-TOF) calcd for $C_{11}H_{12}N_2O$ $[M+H]^+$: 189.1022; found: 189.1020.

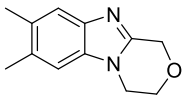


3, 4-Dihydro-6-methyl-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3d$_2$): pale yellow solid, 6 mg, 7% yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.2 Hz, 1H), 7.14 (d, *J* = 3.5 Hz, 1H), 6.97 (d, *J* = 7.3 Hz, 1H), 5.03 (s, 2H), 4.17-4.21 (m, 2H), 4.12-4.15 (m, 2H), 2.69 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 147.66, 140.74, 131.34, 122.50, 117.35, 65.72, 64.25, 44.85, 18.16.

HRMS (ESI-TOF) calcd for $C_{11}H_{12}N_2O$ $[M+H]^+$: 189.1022; found: 189.1018.

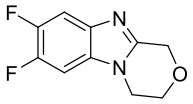


3, 4-Dihydro-7, 8-dimethyl-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3e): pale yellow solid, 59 mg, 73% yield, mp 185-187 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47 (s, 1H), 7.08 (s, 1H), 4.99 (s, 2H), 4.14-4.18 (m, 2H), 4.07-4.10 (m, 2H), 2.38 (d, *J* = 3.9 Hz, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 131.45, 131.40, 119.53, 109.06, 65.56, 64.03, 42.01, 20.49, 20.33.

HRMS (ESI-TOF) calcd for $C_{12}H_{14}N_2O$ $[M+H]^+$: 203.1179; found: 203.1176.

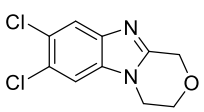


3, 4-Dihydro-7, 8-difluoro-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3f): pale red crystalline, 73 mg, 85% yield, mp 155-158 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49 (dd, $J_{H\text{-}F}$ = 10.5, 7.2 Hz, 1H), 7.12 (dd, $J_{H\text{-}F}$ = 9.5, 6.9 Hz, 1H), 5.01 (s, 2H), 4.19-4.23 (m, 2H), 4.10-4.13 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 149.40-149.66 (dd, $J_{C\text{-}F}$ = 1.1, 14.3 Hz), 146.24-146.48 (dd, $J_{C\text{-}F}$ = 2.6, 14.5 Hz), 137.64-137.79 (d, $J_{C\text{-}F}$ = 11.2 Hz), 129.30-129.35 (d, $J_{C\text{-}F}$ = 3.3 Hz), 106.78-107.06 (dd, $J_{C\text{-}F}$ = 0.9, 20.0 Hz), 96.79-97.10 (dd, $J_{C\text{-}F}$ = 0.8, 22.7 Hz), 65.37, 63.79, 42.22.

HRMS (ESI-TOF) calcd for $C_{10}H_8F_2N_2O$ $[M+H]^+$: 211.0677; found: 211.0678.

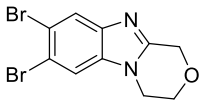


3, 4-Dihydro-7, 8-dichloro-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3g): pale yellow solid, 77 mg, 78% yield, mp 190-193 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.78 (s, 1H), 7.42 (s, 1H), 5.00 (s, 2H), 4.18-4.22 (m, 2H), 4.10-4.13 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 149.92, 142.00, 133.31, 126.63, 126.43, 120.68, 110.26, 65.32, 63.75, 42.22.

HRMS (ESI-TOF) calcd for $C_{10}H_8Cl_2N_2O$ $[M+H]^+$: 243.0086; found: 243.0081.

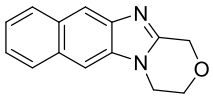


3, 4-Dihydro-7, 8-dibromo-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3g): pale brown crystalline, 98 mg, 73% yield, mp 202-205 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 (s, 1H), 7.63 (s, 1H), 5.02 (s, 2H), 4.20-4.23 (m, 2H), 4.12-4.15 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 149.78, 142.81, 134.18, 123.90, 117.95, 117.68, 113.48, 65.26, 63.73, 42.23.

HRMS (ESI-TOF) calcd for $C_{10}H_8Br_2N_2O$ $[M+H]^+$: 330.9076; found: 330.9077.

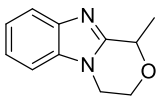


1*H*-naphth[2', 3': 4, 5]imidazo[2,1-*c*][1,4]oxazine (3i): sliver crystalline, 83 mg, 90% yield, mp 227-229 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19 (s, 1H), 7.98-8.08 (m, 1H), 7.88-7.97 (m, 1H), 7.63 (s, 1H), 7.38-7.51 (M, 2H), 5.06 (s, 2H), 4.17-4.20 (m, 2H), 4.10-4.14 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 152.06, 142.54, 134.76, 130.56, 130.16, 128.51, 127.45, 124.45, 123.68, 116.22, 104.58, 65.57, 63.97, 42.05.

HRMS (ESI-TOF) calcd for $C_{14}H_{12}N_2O$ $[M+H]^+$: 225.1022; found: 225.1016.

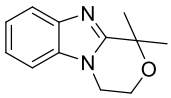


3, 4-Dihydro-1-methyl-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3j): pale yellow oily solid, 73 mg, 88% yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70-7.80 (m, 1H), 7.22-7.35 (m, 3H), 5.00 (q, *J* = 6.5 Hz, 1H), 4.38 (ddd, *J* = 11.6, 4.5, 1.8 Hz, 1H), 4.14-4.27 (m, 1H), 3.99-4.09 ((m, 2H), 1.76 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 151.93, 142.45, 134.15, 122.60, 122.47, 119.51, 108.93, 71.79, 63.06, 42.24, 19.22.

HRMS (ESI-TOF) calcd for $C_{11}H_{12}N_2O$ $[M+H]^+$: 189.1022; found: 189.1025.

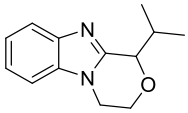


3, 4-Dihydro-1-dimethyl-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3k): colorless oil, 49 mg, 60% yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75-7.78 (m, 1H), 7.24-7.41 (m, 3H), 4.11-4.27 (m, 4H), 1.75 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 154.94, 142.50, 133.96, 122.58, 122.28, 119.49, 108.99, 74.69, 58.39, 42.46, 27.46

HRMS (ESI-TOF) calcd for $C_{12}H_{14}N_2O$ $[M+H]^+$: 203.1179; found: 203.1195.

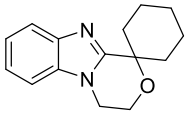


3, 4-Dihydro-1-isopropyl-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3l): pale yellow oil, 64 mg, 74% yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77-7.80 (m, 1H), 7.25-7.40 (m, 3H), 4.83 (d, *J* = 2.7 Hz, 1H), 4.43 (dd, *J* = 11.7, 4.4 Hz, 1H), 4.23 (td, *J* = 11.4, 4.5 Hz, 1H), 4.10 (dd, *J* = 11.7, 3.2 Hz, 1H), 3.98 (td, *J* = 11.4, 3.5 Hz, 1H), 2.73 (dtd, *J* = 13.9, 6.9, 2.8 Hz, 1H), 1.22 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 150.91, 142.75, 134.18, 122.46, 122.22, 119.59, 108.78, 79.81, 63.17, 42.27, 31.85, 19.04, 16.05.

HRMS (ESI-TOF) calcd for $C_{13}H_{16}N_2O$ $[M+H]^+$: 217.1335; found: 217.1349.

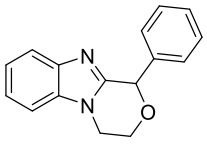


3, 4-Dihydro-1-spirocyclohexyl-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3m): red oil, 55 mg, 56% yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72-7.84 (m, 1H), 7.22-7.41 (m, 3H), 4.04-4.26 (m, 4H), 2.08-2.13 (m, 4H), 1.63-1.84 (m, 5H), 1.40-1.52 m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 155.37, 142.49, 134.02, 122.47, 122.16, 119.48, 108.92, 75.49, 57.70, 42.41, 34.72, 25.12, 21.02.

HRMS (ESI-TOF) calcd for $C_{15}H_{18}N_2O$ $[M+H]^+$: 243.1492; found: 243.1516.

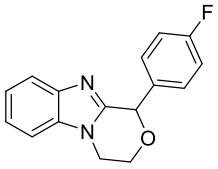


3, 4-Dihydro-1-phenyl-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3n): pale yellow solid, 86 mg, 86% yield, mp 156-158 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75-7.83 (m, 1H), 7.47-7.54 (m, 2H), 7.37-7.46 (m, 4H), 7.28-7.35 (m, 2H), 6.06 (s, 1H), 4.14-4.44 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 149.62, 142.38, 137.55, 128.93, 128.70, 128.28, 122.82, 122.72, 119.86, 109.00, 77.21, 61.89, 42.35.

HRMS (ESI-TOF) calcd for $C_{16}H_{14}N_2O$ [M+H] $^+$: 251.1179; found: 251.1186.

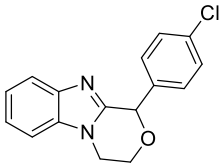


3, 4-Dihydro-1-(4-fluorophenyl)-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3o): grey solid, 93 mg, 86% yield, mp 144-147 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75-7.82 (m, 1H), 7.44-7.54 (m, 2H), 7.37-7.43 (m, 1H), 7.28-7.34 (m, 2H), 7.06-7.14 (m, 2H), 6.02 (s, 1H), 4.14-4.45 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 161.37-164.65 (d, $J_{C\text{-}F}$ = 246.0 Hz), 149.93, 142.64, 134.05, 133.55-133.59 (d, $J_{C\text{-}F}$ = 3.1 Hz), 130.10, 122.78, 122.74, 120.00, 115.48-115.77 (d, $J_{C\text{-}F}$ = 21.5 Hz), 108.99, 76.69, 62.15, 42.33.

HRMS (ESI-TOF) calcd for $C_{16}H_{13}FN_2O$ [M+H] $^+$: 269.1085; found: 269.1093.

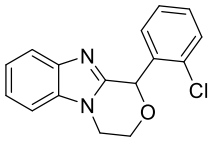


3, 4-Dihydro-1-(4-chlorophenyl)-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3p): colorless crystal, 104 mg, 92% yield, mp 108-111 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72-7.80 (m, 1H), 7.27-7.52 (m, 8H), 6.02 (s, 1H), 4.15-4.46 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 149.16, 142.62, 136.14, 134.78, 134.02, 129.58, 128.87, 122.81, 122.78, 120.00, 108.99, 76.56, 62.14, 42.31.

HRMS (ESI-TOF) calcd for $C_{16}H_{13}ClN_2O$ [M+H] $^+$: 285.0789; found: 285.0790.



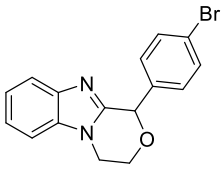
3, 4-Dihydro-1-(2-chlorophenyl)-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3q): pale yellow oil, 106 mg, 94% yield.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75-7.81 (m, 1H), 7.25-7.52 (m, 8H), 6.43 (s, 1H), 4.20-4.51 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 149.06, 142.74, 135.03, 134.60, 134.02, 130.87, 130.44, 130.25,

127.02, 122.73, 122.67, 120.05, 108.93, 75.06, 62.66, 42.27.

HRMS (ESI-TOF) calcd for $C_{16}H_{13}ClN_2O$ $[M+H]^+$: 285.0789; found: 285.0799.

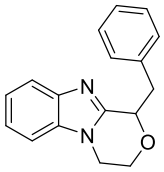


3, 4-Dihydro-1-(4-bromophenyl)-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3r): pale brown solid, 110 mg, 82% yield, mp 113-116 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75-7.80 (m, 1H), 7.52-7.55 (m, 2H), 7.30-7.45 (m, 5H), 6.00 (s, 1H), 4.15-4.44 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 149.08, 142.64, 136.66, 134.03, 134.02, 131.82, 129.87, 123.03, 122.81, 122.78, 120.02, 108.99, 76.60, 62.15, 42.31.

HRMS (ESI-TOF) calcd for $C_{16}H_{13}BrN_2O$ $[M+H]^+$: 329.0284; found: 329.0292.

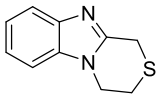


3, 4-Dihydro-1-benzyl-1*H*-[1, 4]oxazino[4,3-*a*]benzimidazole (3s): bright white solid, 88 mg, 84% yield, mp 115-117 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80-7.85 (m, 1H), 7.26-7.44 (m, 8H), 5.17 (dd, *J* = 9.6, 2.7 Hz, 1H), 4.34-4.44 (m, 1H), 4.15-4.27 (m, 1H), 4.06-4.13 (m, 1H), 3.93-4.05 (m, 1H), 3.79 (dd, *J* = 14.6, 2.7 Hz, 1H), 3.22 (dd, *J* = 14.6, 9.7 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 150.62, 142.58, 137.71, 134.30, 129.62, 128.34, 126.47, 122.68, 122.53, 119.64, 108.96, 76.28, 63.07, 42.23, 39.75.

HRMS (ESI-TOF) calcd for $C_{17}H_{16}N_2O$ $[M+H]^+$: 265.1335; found: 265.1359.

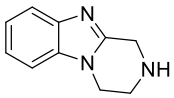


3, 4-Dihydro-1*H*-[1, 4]thiazino[4,3-*a*]benzimidazole (3t)[18]: yellow solid, 25 mg, 33% yield, mp 146-148 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59-7.64 (m, 1H), 7.15-7.22 (m, 3H), 4.14-4.24 (m, 2H), 3.99 (s, 2H), 2.99-3.08 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 146.76, 141.53, 134.84, 122.76, 122.46, 119.25, 108.81, 44.77, 26.66, 26.05.

HRMS (ESI-TOF) calcd for $C_{10}H_{10}N_2S$ $[M+H]^+$: 191.0637; found: 191.0632.

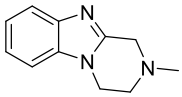


1, 2, 3, 4-Tetrahydropyrazino[1,2-*a*]benzimidazole (3u)[19]: pale yellow solid, 14 mg, 20% yield, mp 129-132 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 7.53-7.58 (m, 1H), 7.42-7.50 (m, 1H), 7.15-7.21 (m, 2H), 3.97-4.08 (m, 4H), 3.19 (t, J = 5.6 Hz, 2H), 1.67 (s, 1H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 150.58, 142.60, 134.80, 122.10, 121.71, 118.70, 109.86, 44.89, 43.16, 42.59.

HRMS (ESI-TOF) calcd for $C_{10}H_{11}N_3$ [M+H] $^+$: 174.1026; found: 174.1018.

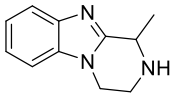


1, 2, 3, 4-Tetrahydro-2-methyl-pyrazino[1,2-*a*]benzimidazole (3v): white solid, 21 mg, 28% yield, mp 144-146 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 7.53-7.62 (m, 1H), 7.45-7.51 (m, 1H), 7.14-7.27 (m, 2H), 4.13 (t, J = 5.6 Hz, 2H), 3.76 (s, 2H), 2.93 (t, J = 5.6 Hz, 2H), 2.45 (s, 3H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 149.64, 142.94, 134.47, 122.19, 121.92, 118.87, 110.09, 53.77, 51.26, 45.36, 41.92.

HRMS (ESI-TOF) calcd for $C_{11}H_{13}N_3$ [M+H] $^+$: 188.1182; found: 188.1173.

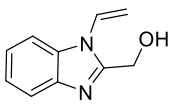


1, 2, 3, 4-Tetrahydro-1-methyl-pyrazino[1,2-*a*]benzimidazole (3v): white solid, 27 mg, 36% yield, mp 153-155 °C.

^{1}H NMR (300 MHz, DMSO-d_6): δ 7.55-7.60 (m, 1H), 7.38-7.49 (m, 1H), 7.12-7.26 (m, 2H), 4.07-4.19 (m, 2H), 3.89-4.05 (m, 1H), 3.30-3.40 (m, 1H), 3.04-3.20 (m, 1H), 1.50 (d, J = 6.7 Hz, 3H), 1.29-1.38 (m, 1H).

^{13}C NMR (75 MHz, DMSO-d_6): δ 154.28, 142.63, 134.91, 122.05, 121.83, 118.90, 110.02, 50.54, 43.27, 41.81, 19.80.

HRMS (ESI-TOF) calcd for $C_{11}H_{13}N_3$ [M+H] $^+$: 188.1182; found: 188.1176.



1-Ethenyl-1*H*-benzimidazole-2-methanol (4a): pale white solid, 32 mg, 45% yield, mp 110-112 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64-7.76 (m, 1H), 7.47-7.60 (m, 1H), 7.26-7.37 (m, 2H), 7.12-7.26 (m, 1H), 6.12 (s, 1H), 5.66 (d, J = 15.8 Hz, 1H), 5.33 (d, J = 8.9 Hz, 1H), 4.92 (s,2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 153.30, 141.58, 133.81, 128.34, 123.87, 123.19, 119.52, 111.25,

107.92, 56.96.

HRMS (ESI-TOF) calcd for $C_{10}H_{10}N_2O$ $[M+H]^+$: 175.0866; found: 175.0869.

6. Reference

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7. Copies of ^{1}H NMR and ^{13}C NMR Spectra

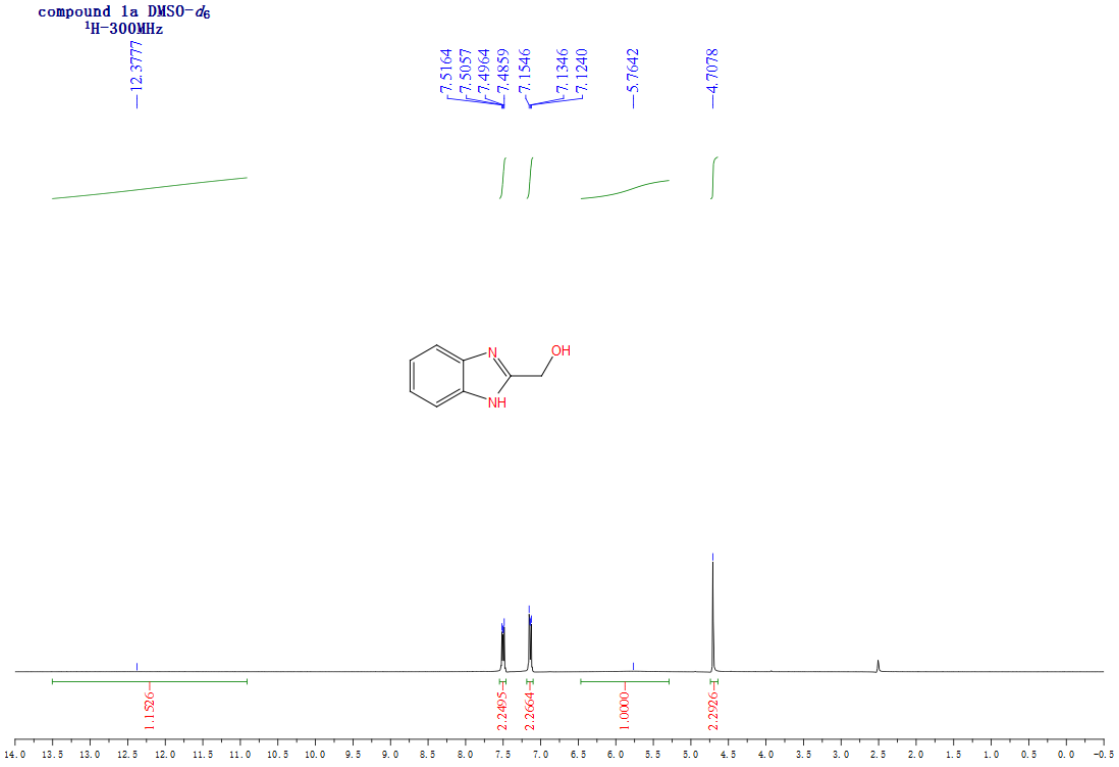

Figure S1. The ^{1}H NMR Spectrum of Compound **1a** in DMSO-d_6

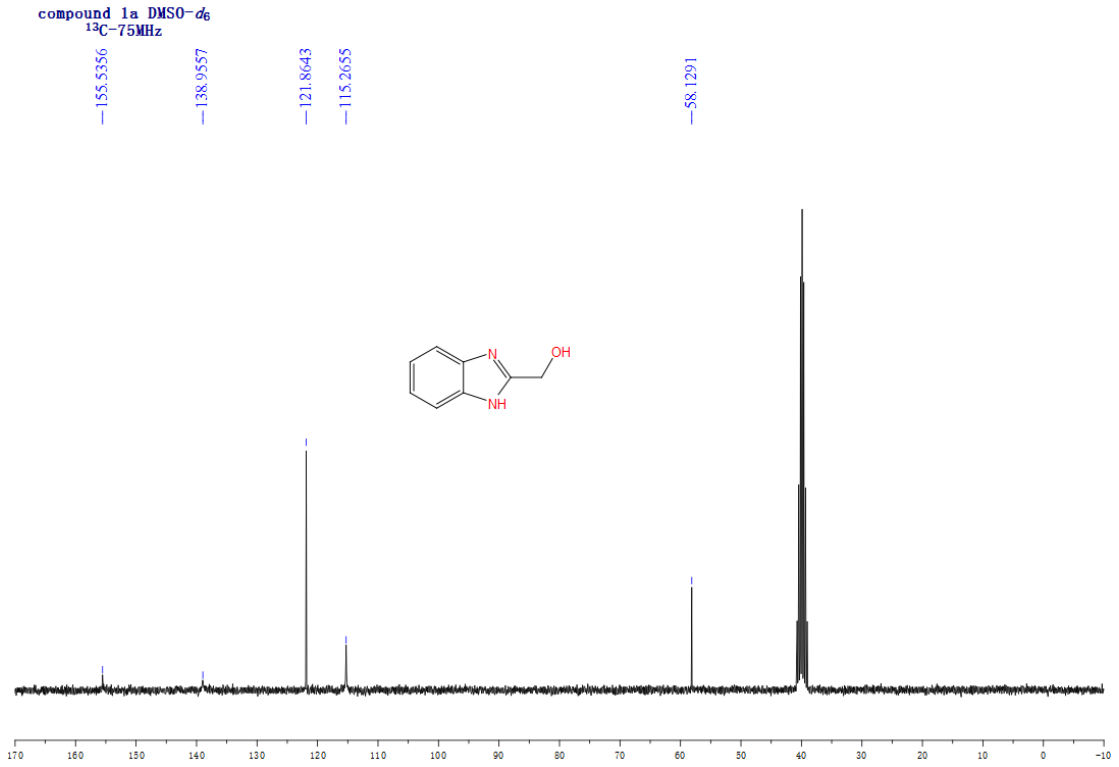

Figure S2. The ^{13}C NMR Spectrum of Compound **1a** in DMSO-d_6

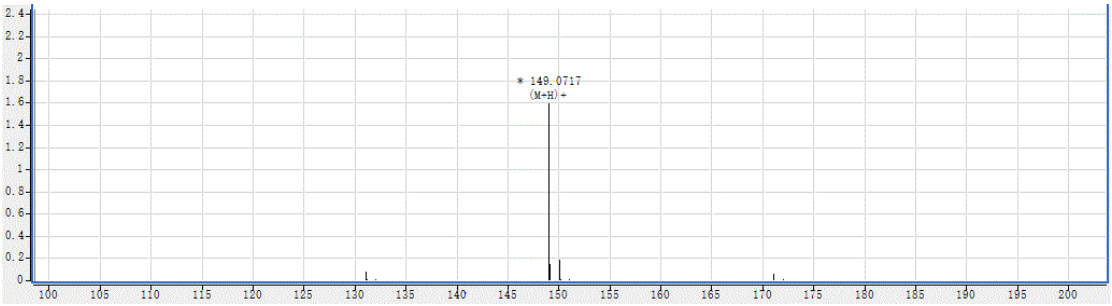

Figure S3. The HR-ESI-MS Spectrum of Compound **1a**

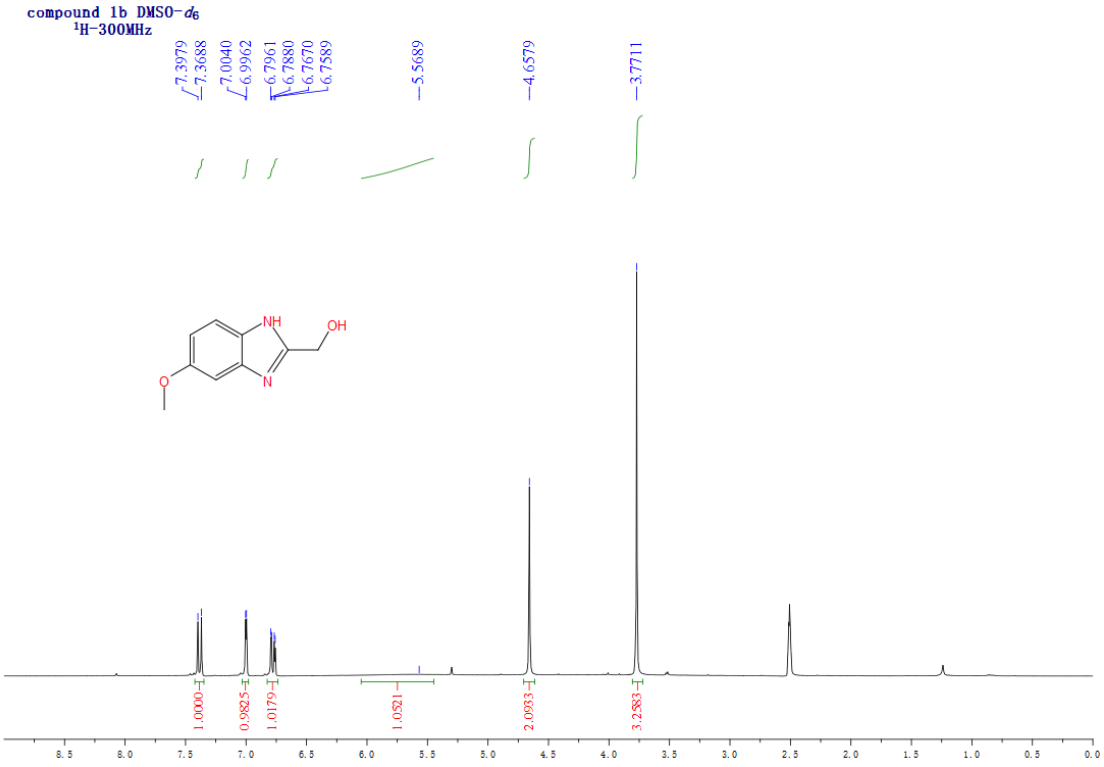

Figure S4. The ^{1}H NMR Spectrum of Compound **1b** in DMSO-d_6

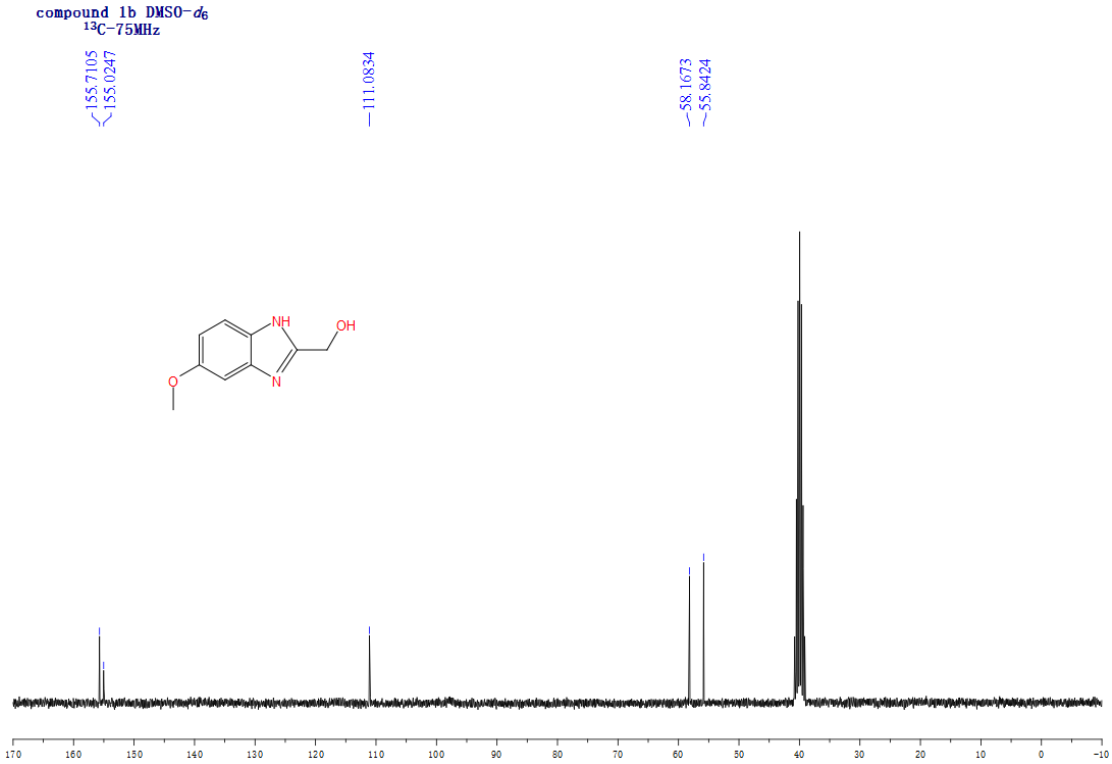

Figure S5. The ^{13}C NMR Spectrum of Compound **1b** in DMSO-d_6

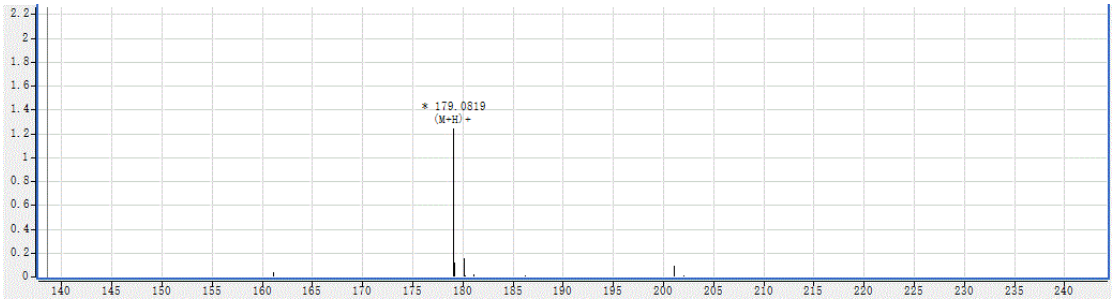

Figure S6. The HR-ESI-MS Spectrum of Compound **1b**

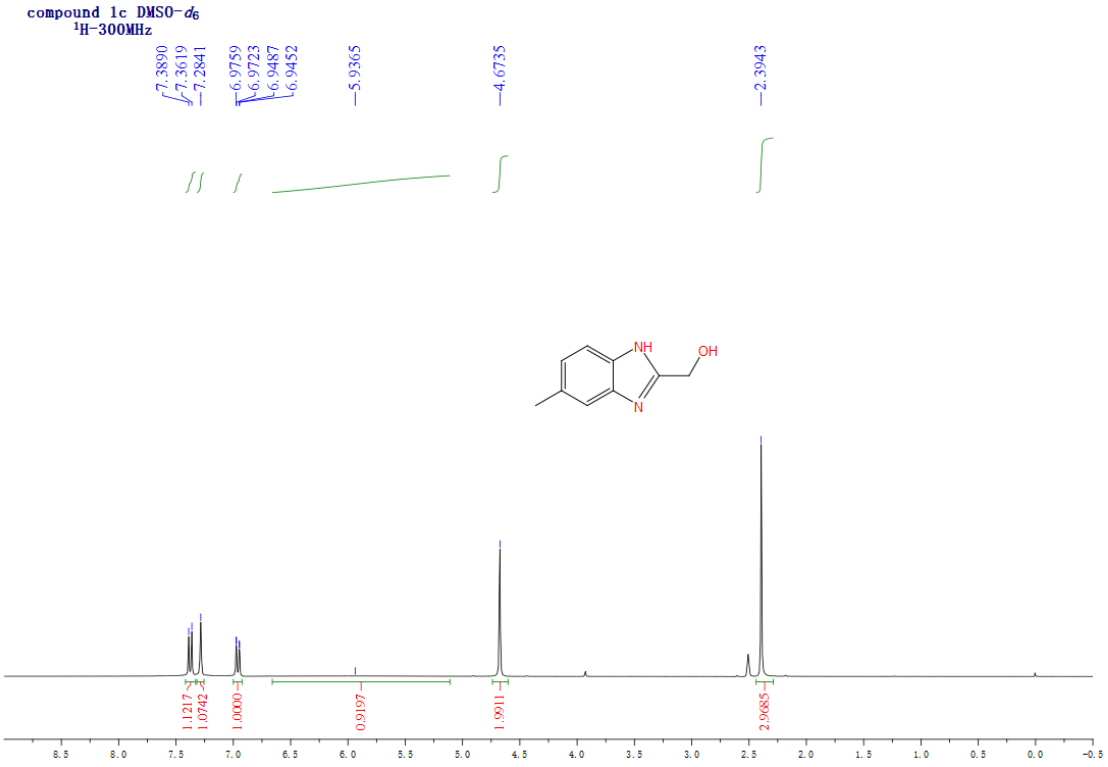

Figure S7. The ^{1}H NMR Spectrum of Compound **1c** in DMSO-d_6

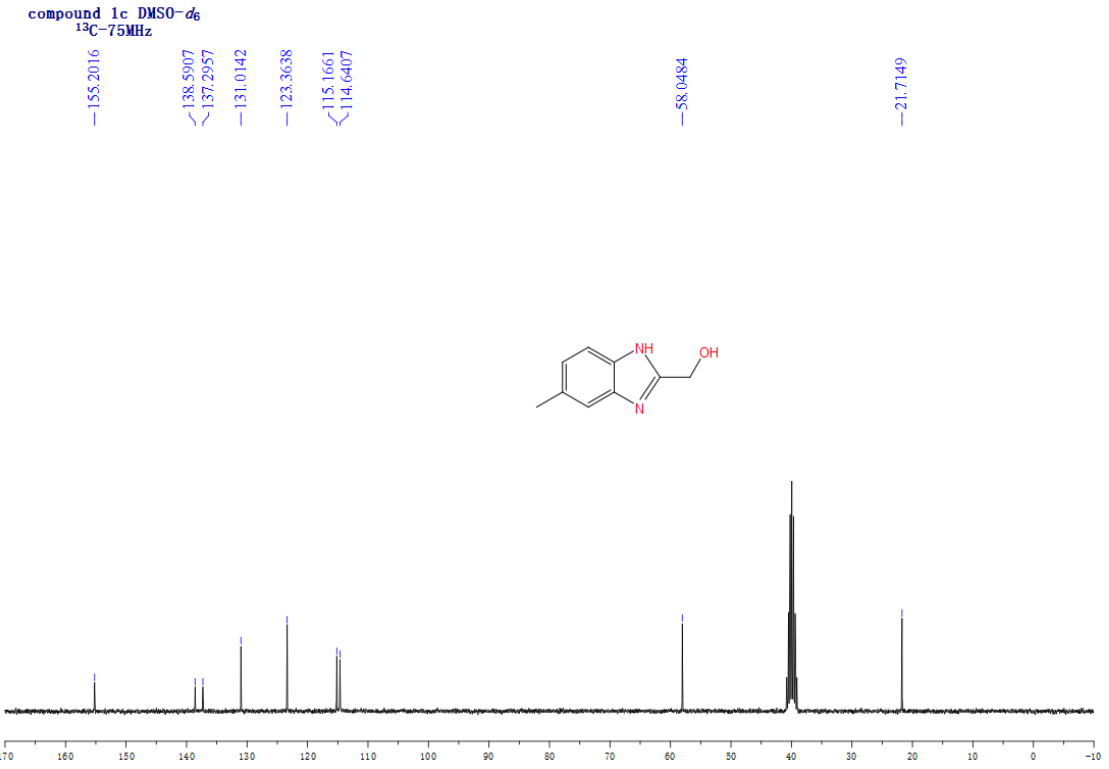

Figure S8. The ^{13}C NMR Spectrum of Compound **1c** in DMSO-d_6

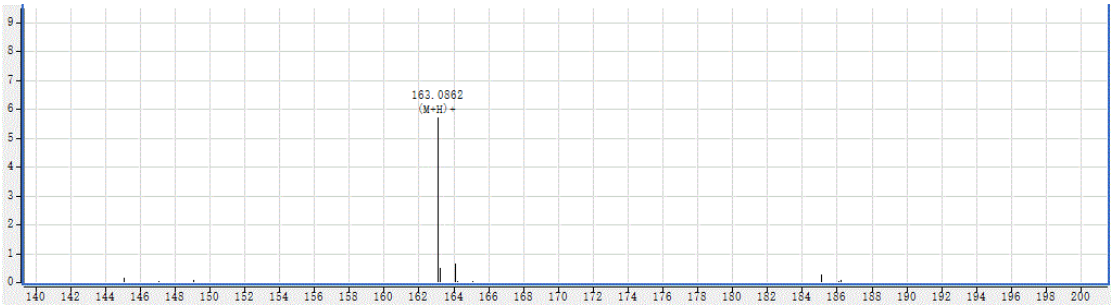

Figure S9. The HR-ESI-MS Spectrum of Compound **1c**

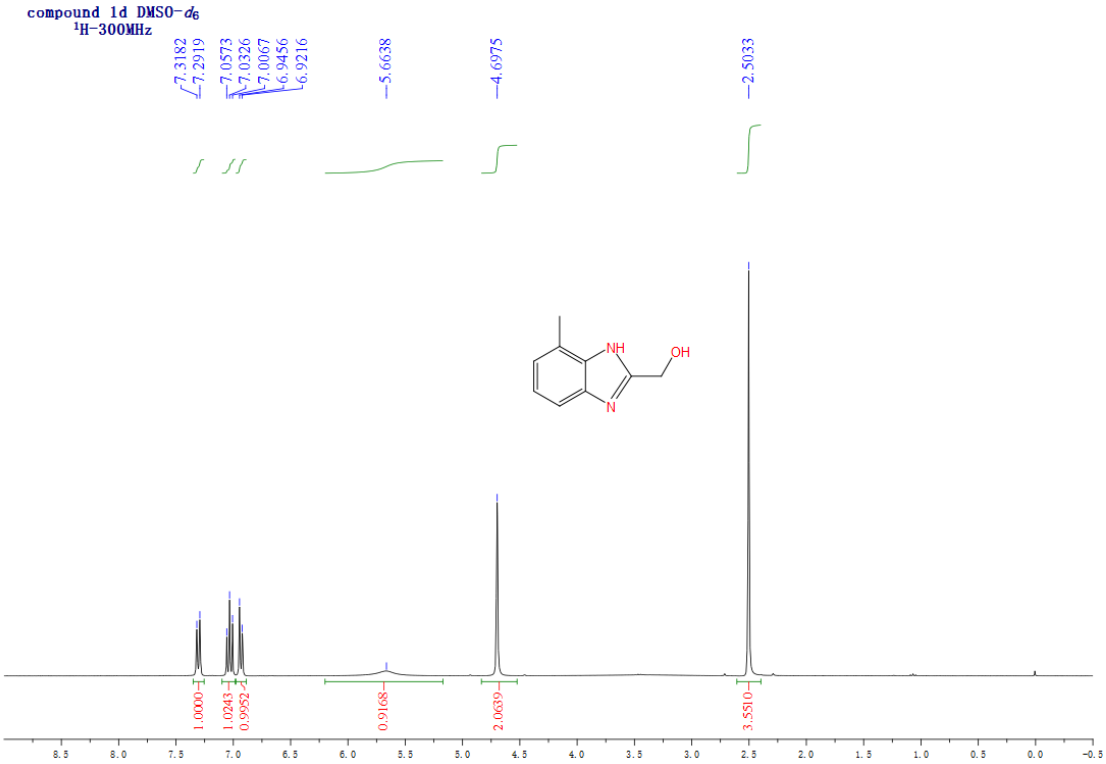

Figure S10. The ^{1}H NMR Spectrum of Compound **1d** in DMSO-d_6

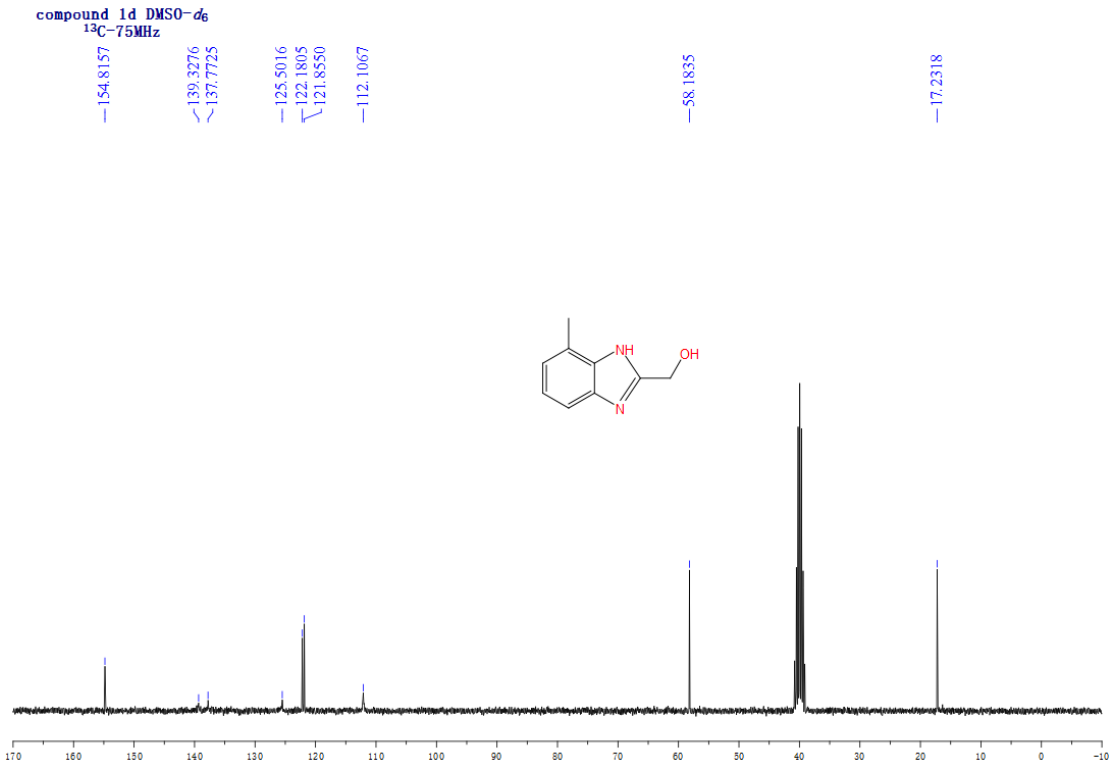

Figure S11. The ^{13}C NMR Spectrum of Compound **1d** in DMSO-d_6

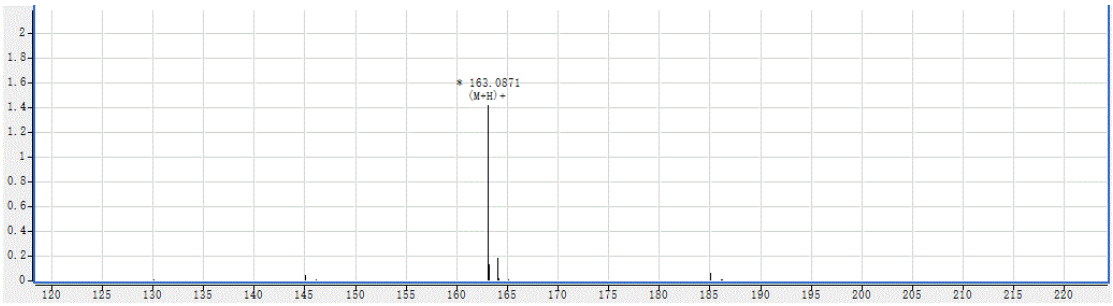

Figure S12. The HR-ESI-MS Spectrum of Compound **1d**

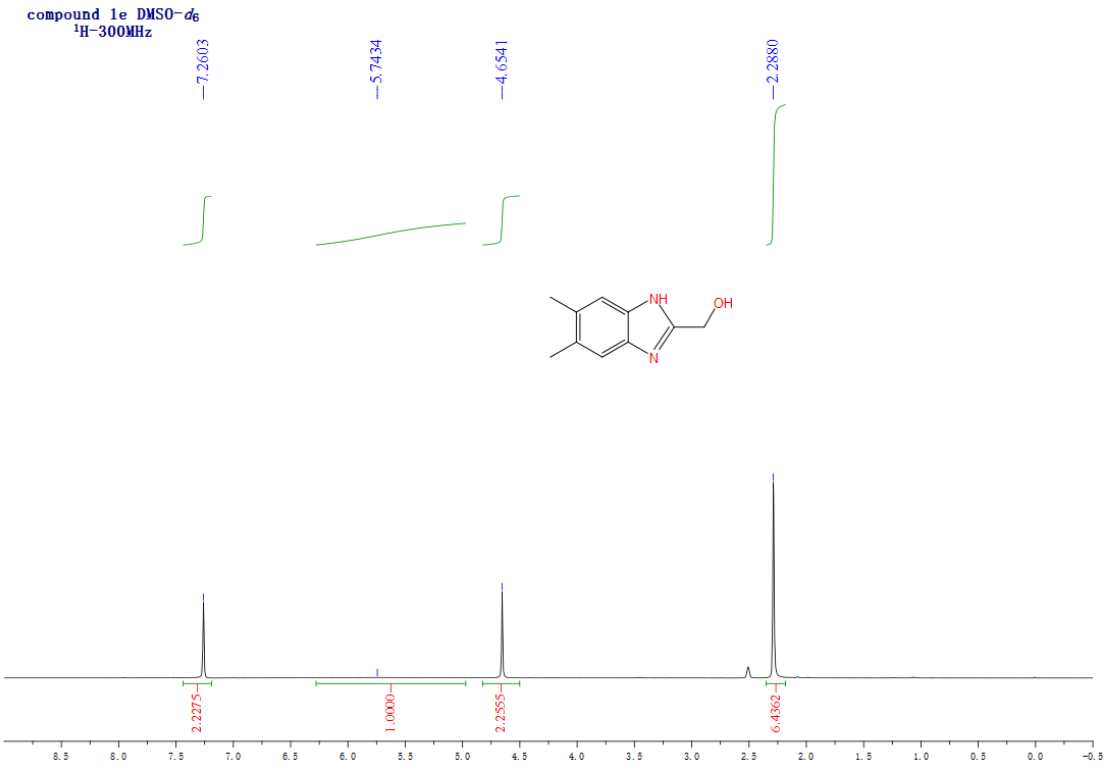

Figure S13. The ^{1}H NMR Spectrum of Compound **1e** in DMSO-d_6

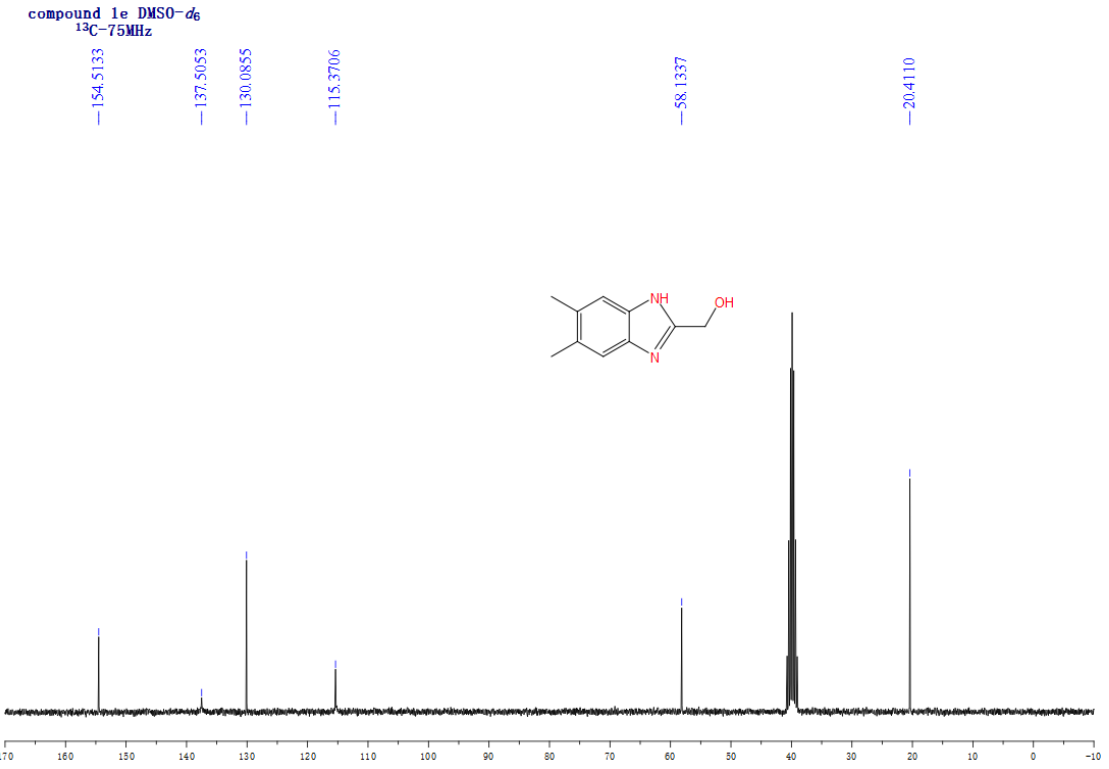

Figure S14. The ^{13}C NMR Spectrum of Compound **1e** in DMSO-d_6

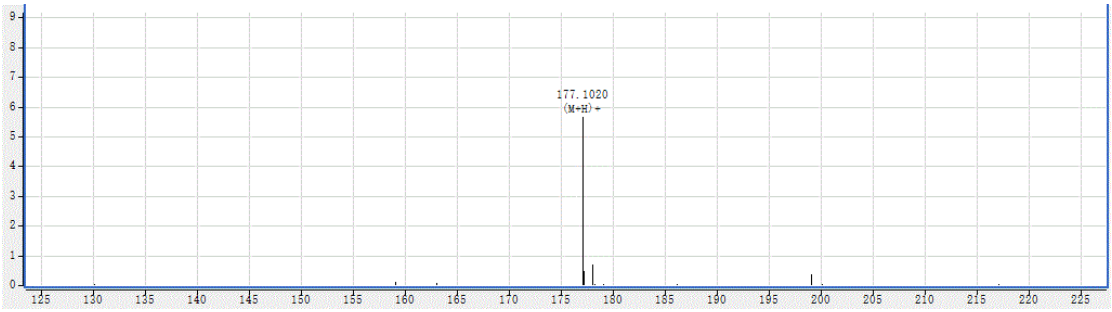

Figure S15. The HR-ESI-MS Spectrum of Compound **1e**

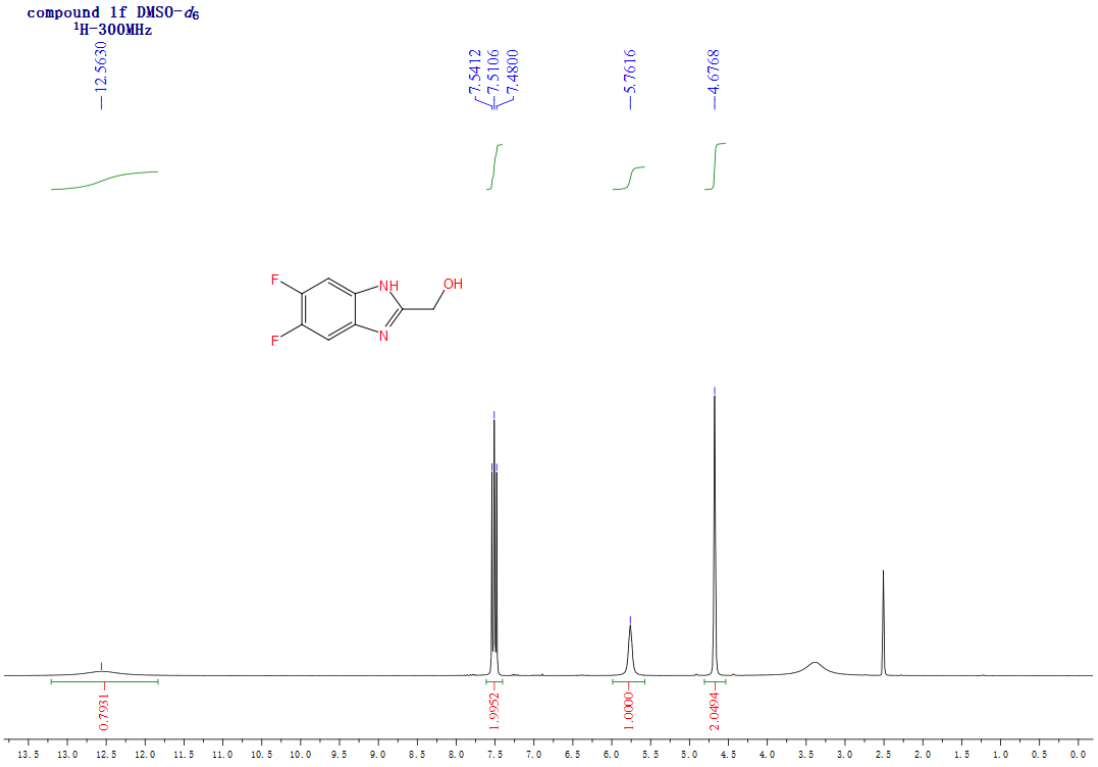

Figure S16. The ^{1}H NMR Spectrum of Compound **1f** in DMSO-d_6

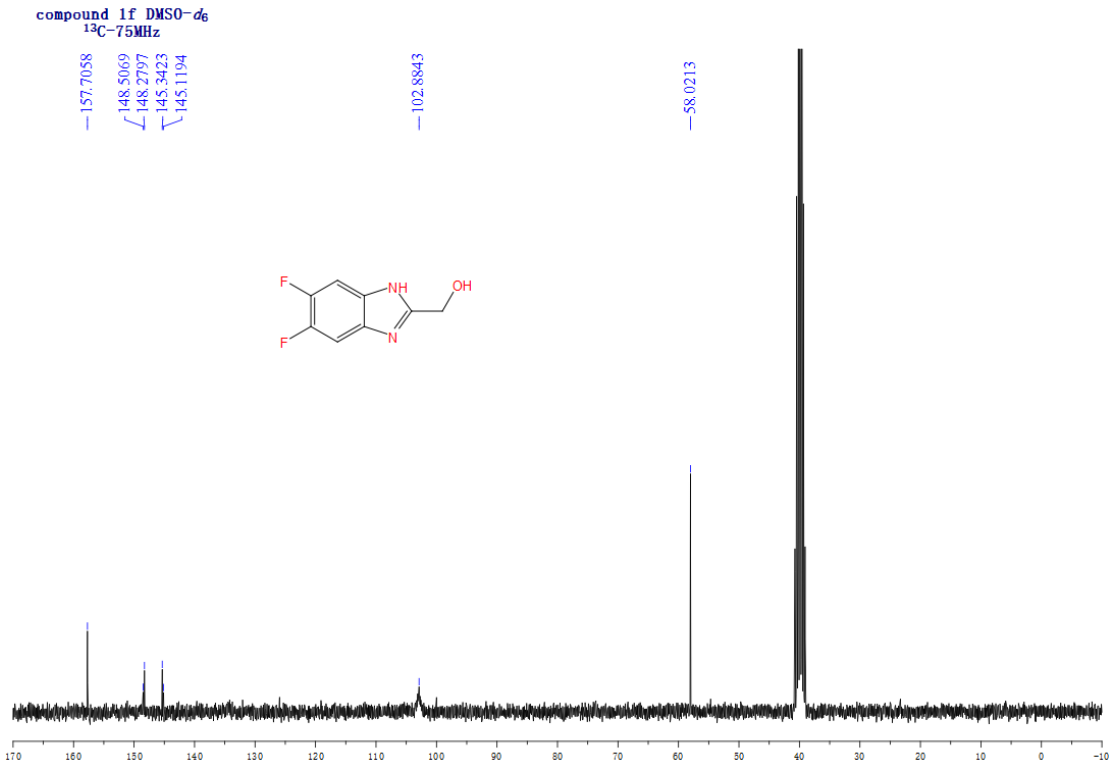

Figure S17. The ^{13}C NMR Spectrum of Compound **1f** in DMSO-d_6

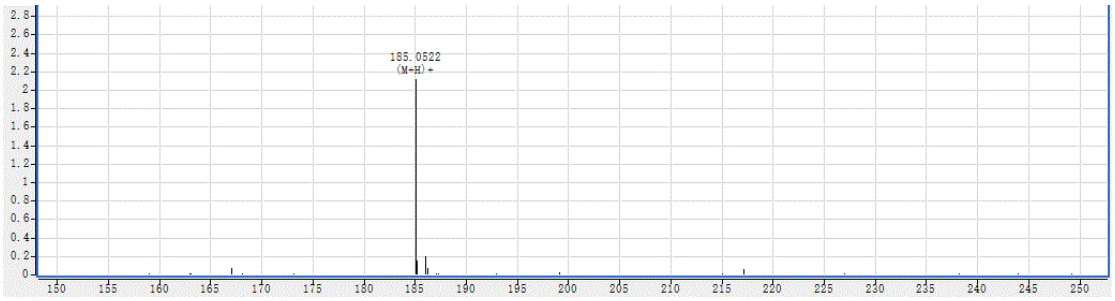

Figure S18. The HR-ESI-MS Spectrum of Compound **1f**

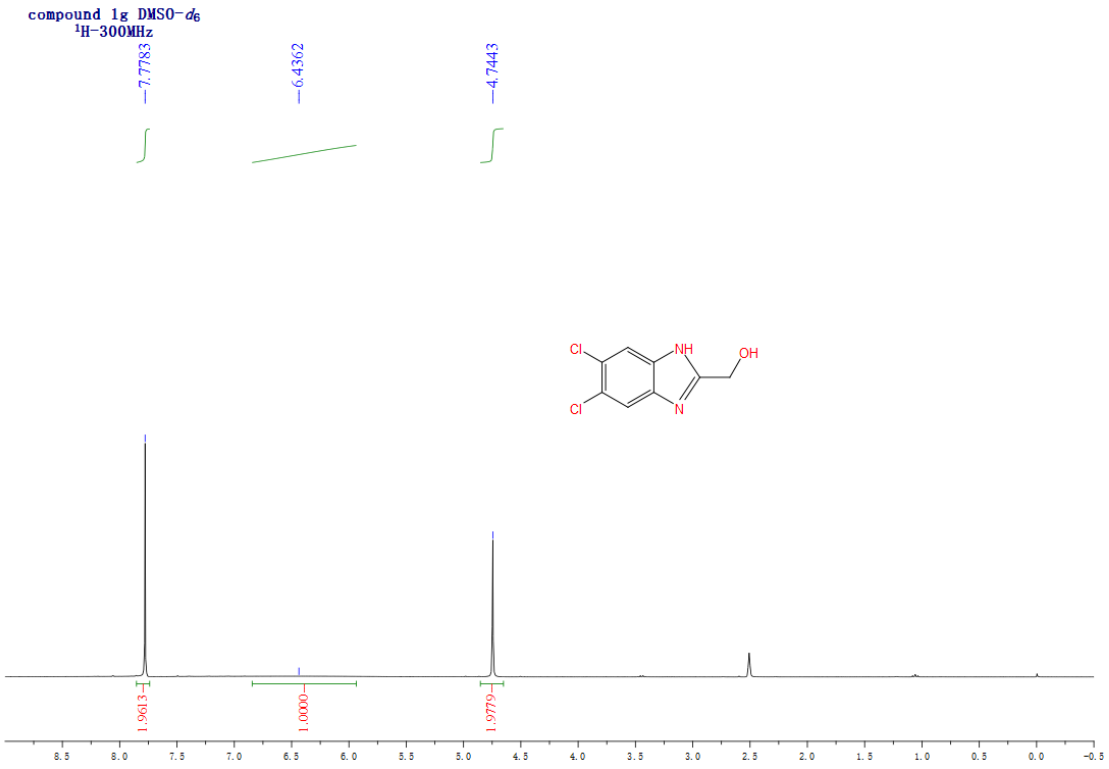

Figure S19. The ^{1}H NMR Spectrum of Compound **1g** in DMSO-d_6

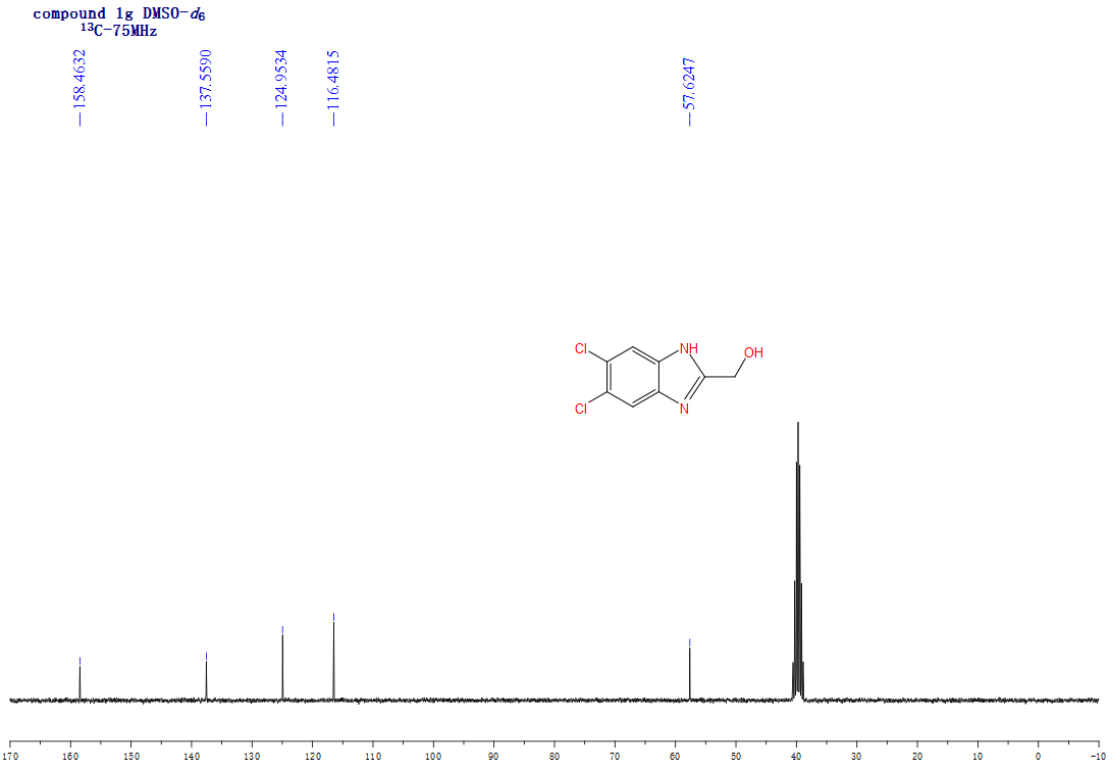

Figure S20. The ^{13}C NMR Spectrum of Compound **1g** in DMSO-d_6

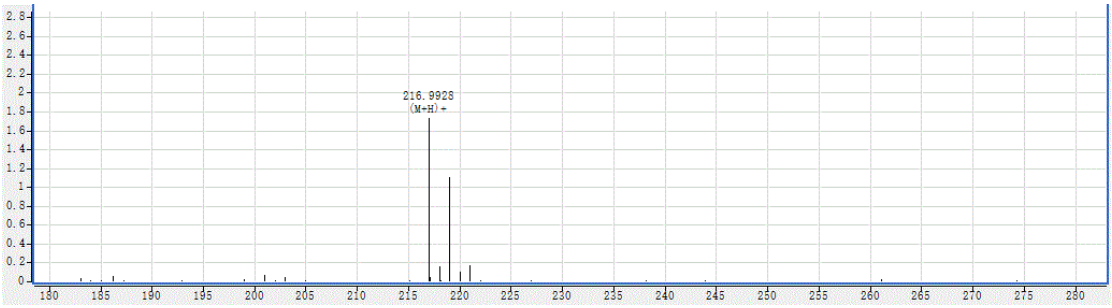

Figure S21. The HR-ESI-MS Spectrum of Compound **1g**

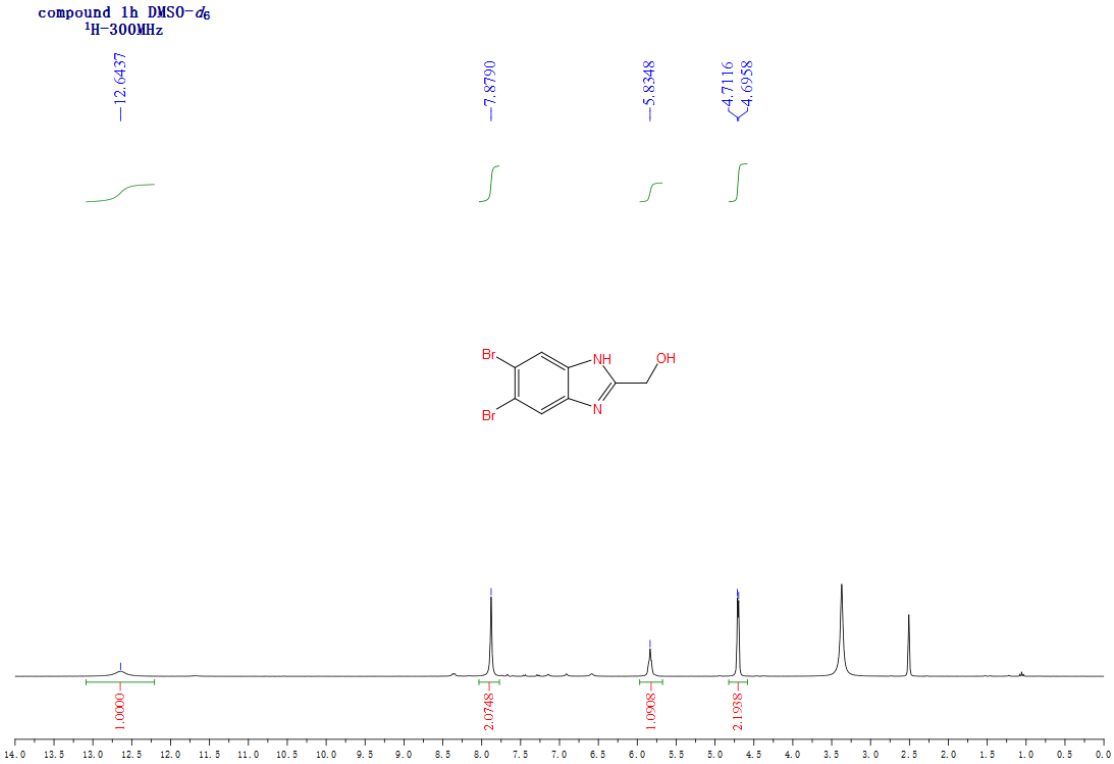

Figure S22. The ^{1}H NMR Spectrum of Compound **1h** in DMSO-d_6

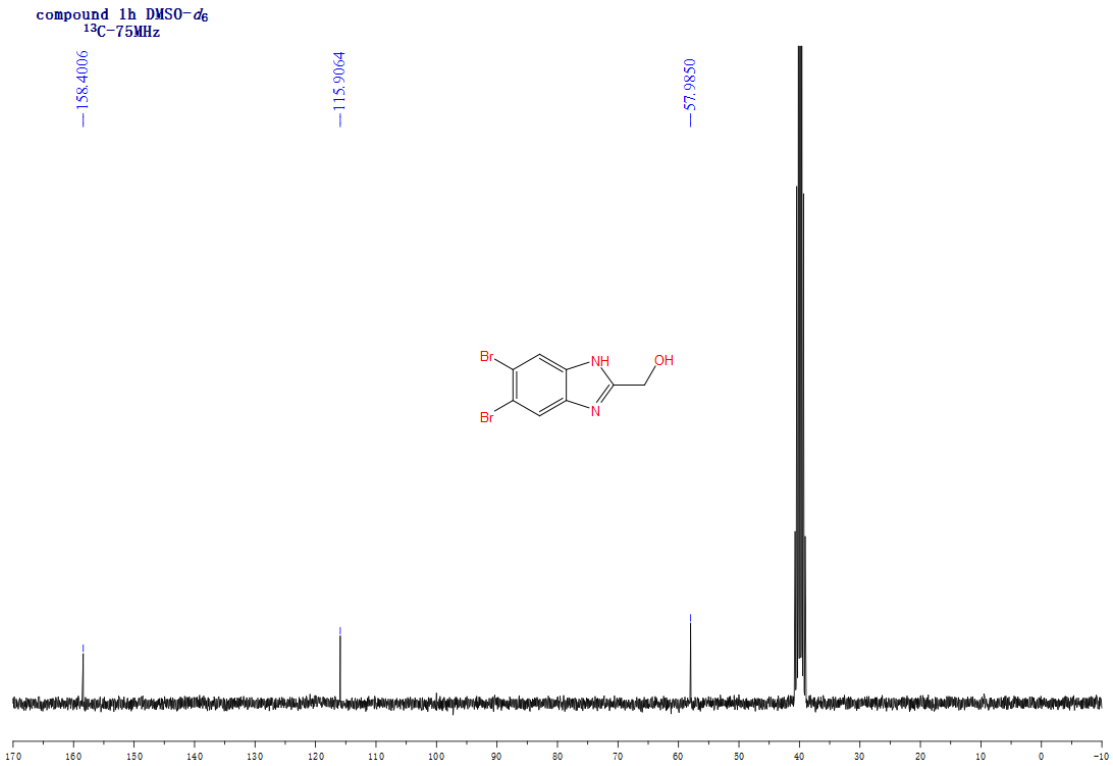

Figure S23. The ^{13}C NMR Spectrum of Compound **1h** in DMSO-d_6

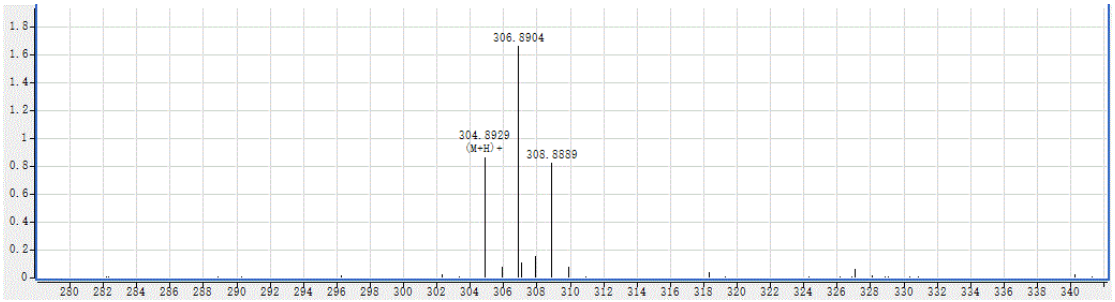

Figure S24. The HR-ESI-MS Spectrum of Compound **1h**

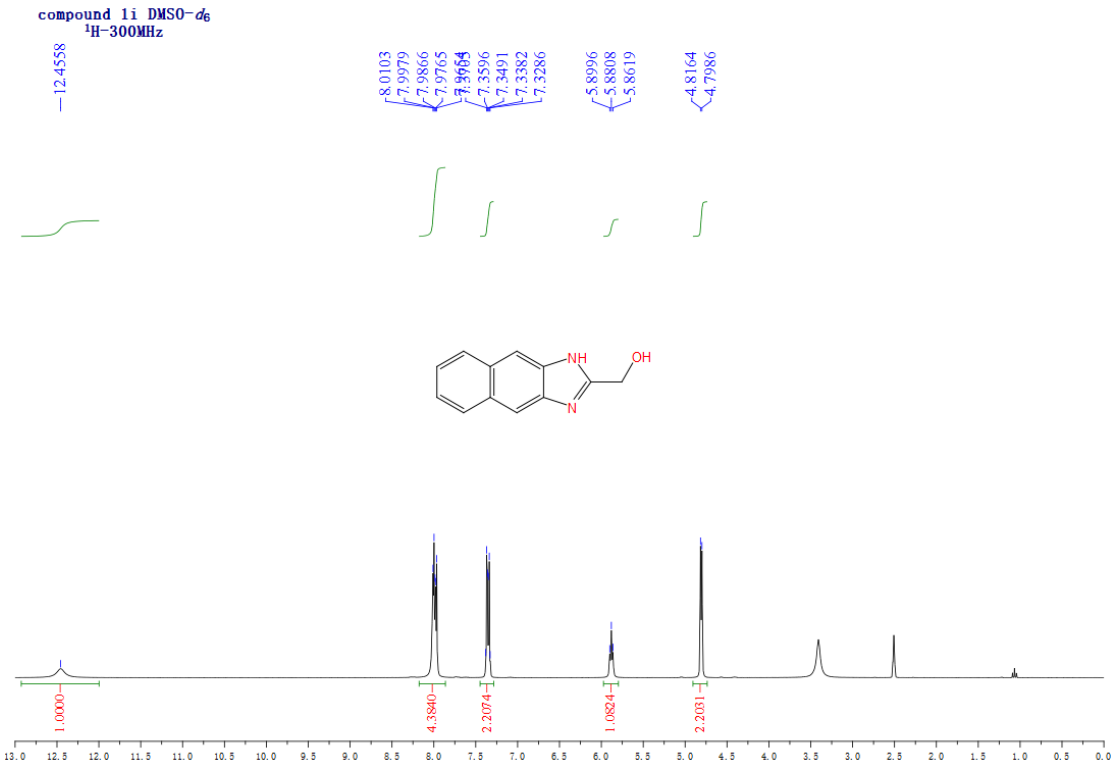

Figure S25. The ^{1}H NMR Spectrum of Compound **1i** in DMSO-d_6

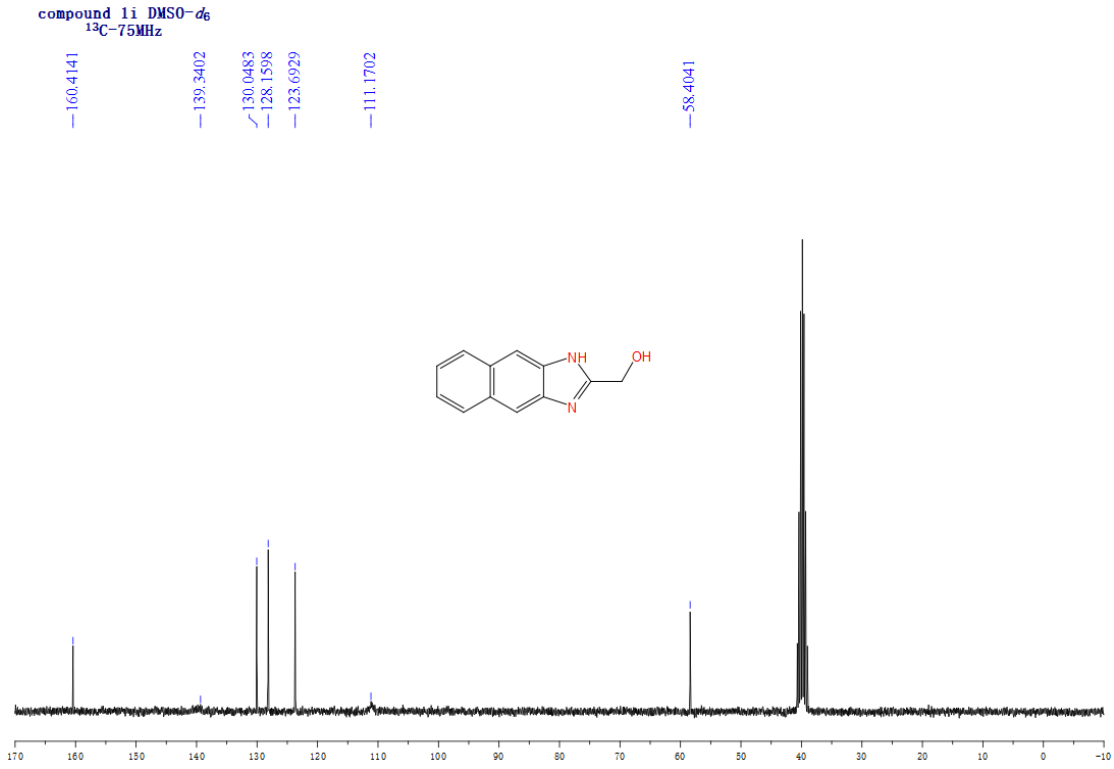

Figure S26. The ^{13}C NMR Spectrum of Compound **1i** in DMSO-d_6

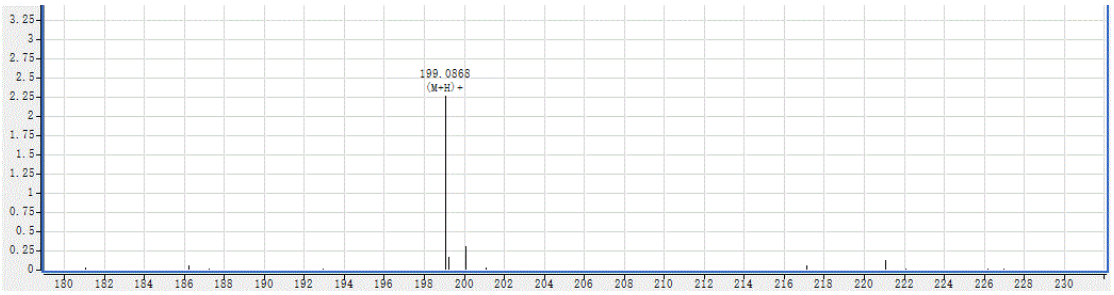

Figure S27. The HR-ESI-MS Spectrum of Compound **1i**

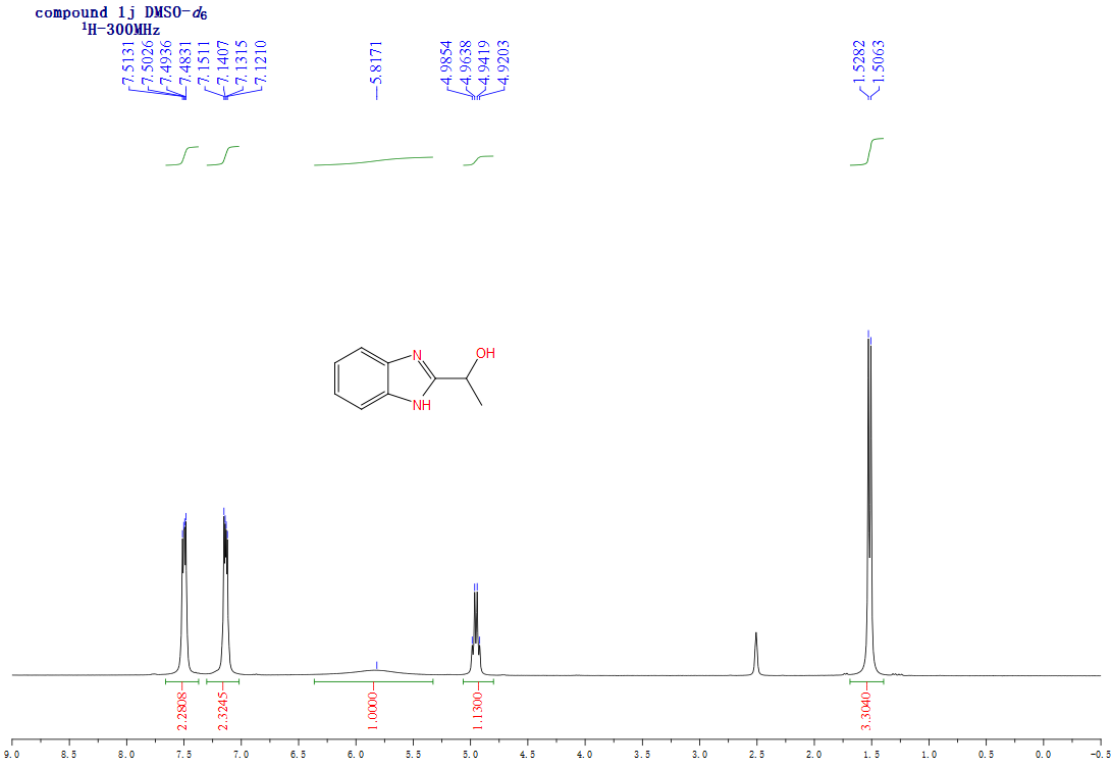

Figure S28. The ^{1}H NMR Spectrum of Compound **1j** in DMSO-d_6

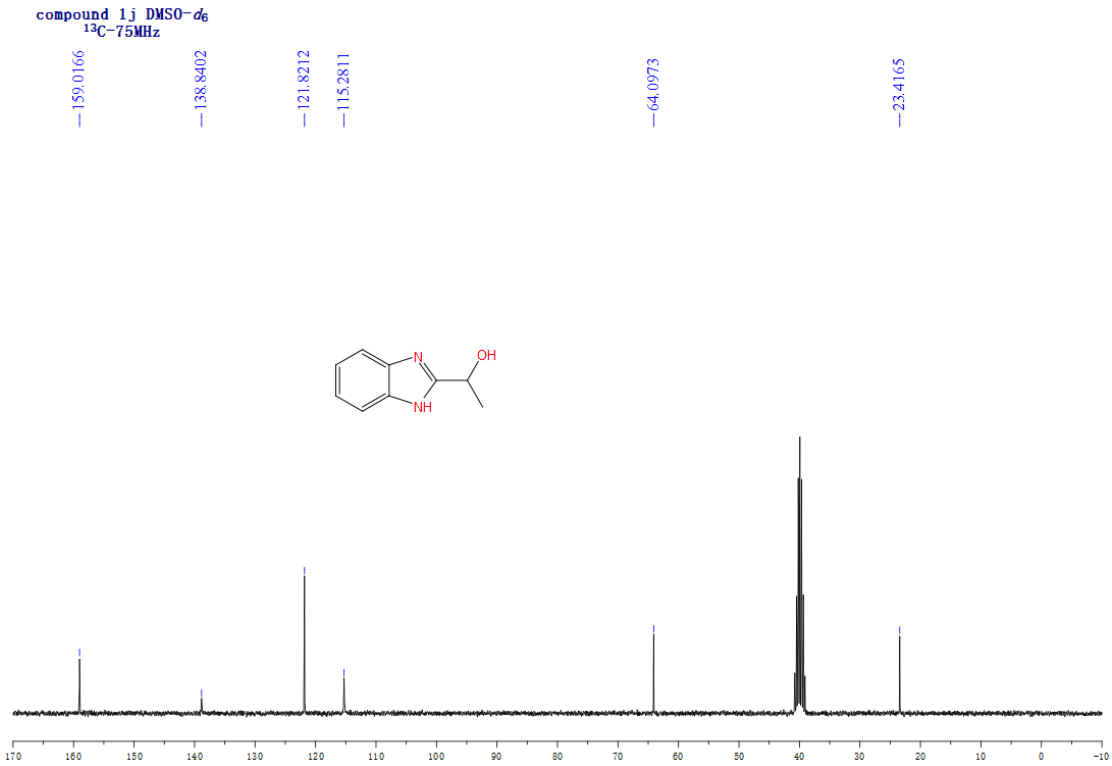

Figure S29. The ^{13}C NMR Spectrum of Compound **1j** in DMSO-d_6

Figure S30. The HR-ESI-MS Spectrum of Compound **1j**

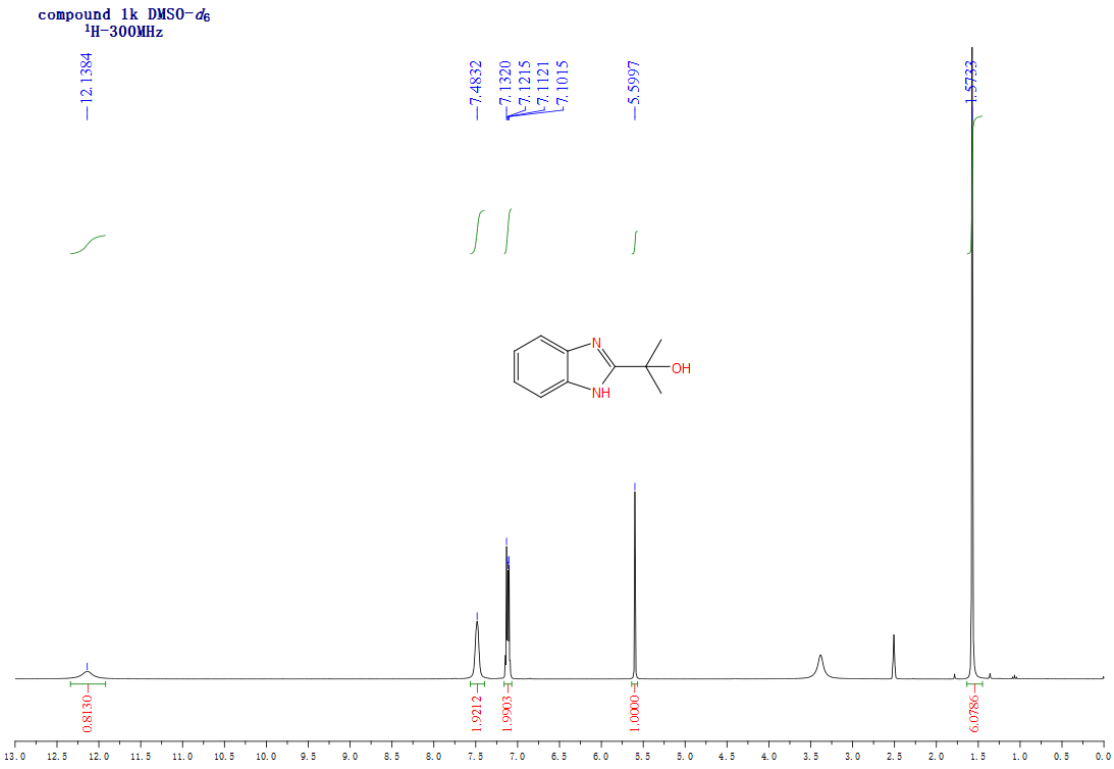

Figure S31. The ^{1}H NMR Spectrum of Compound **1k** in DMSO-d_6

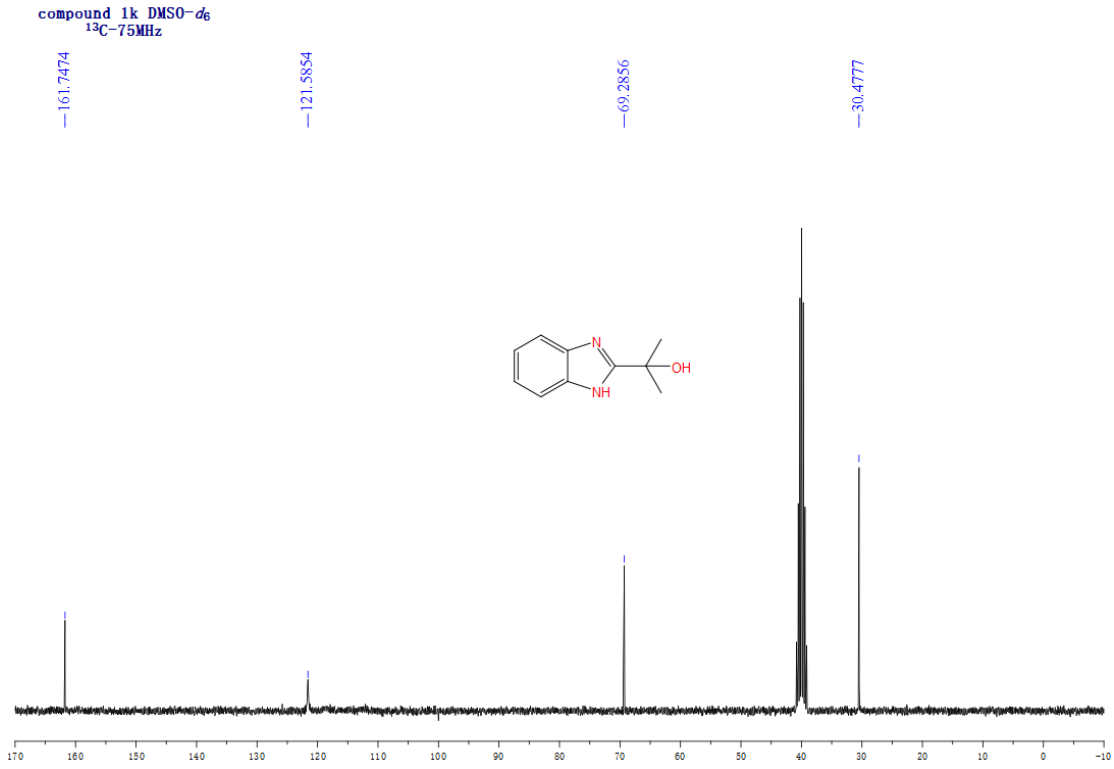

Figure S32. The ^{13}C NMR Spectrum of Compound **1k** in DMSO-d_6

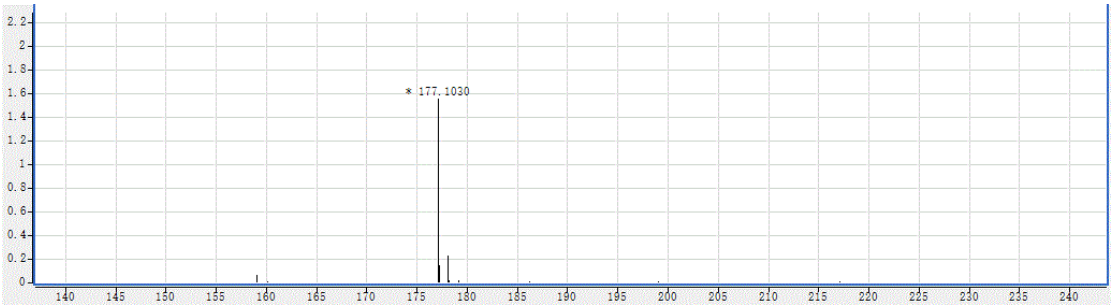

Figure S33. The HR-ESI-MS Spectrum of Compound **1k**

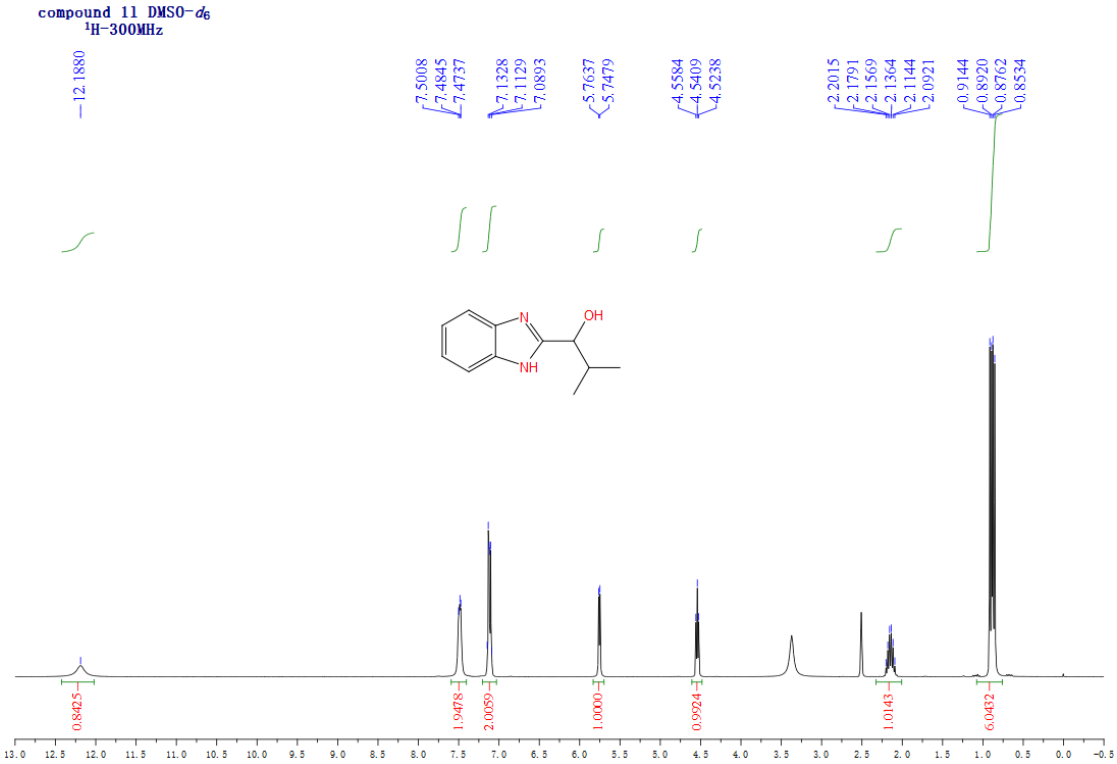

Figure S34. The ^{1}H NMR Spectrum of Compound **1l** in DMSO-d_6

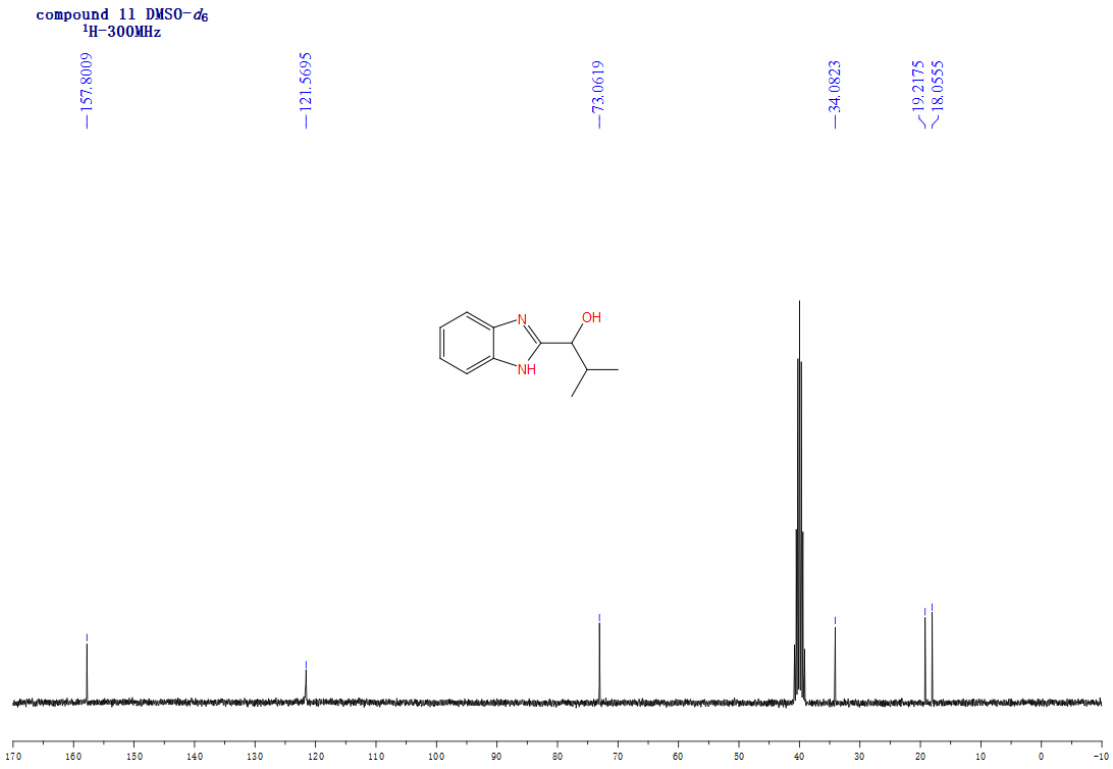

Figure S35. The ^{13}C NMR Spectrum of Compound **1l** in DMSO-d_6

Figure S36. The HR-ESI-MS Spectrum of Compound **1l**

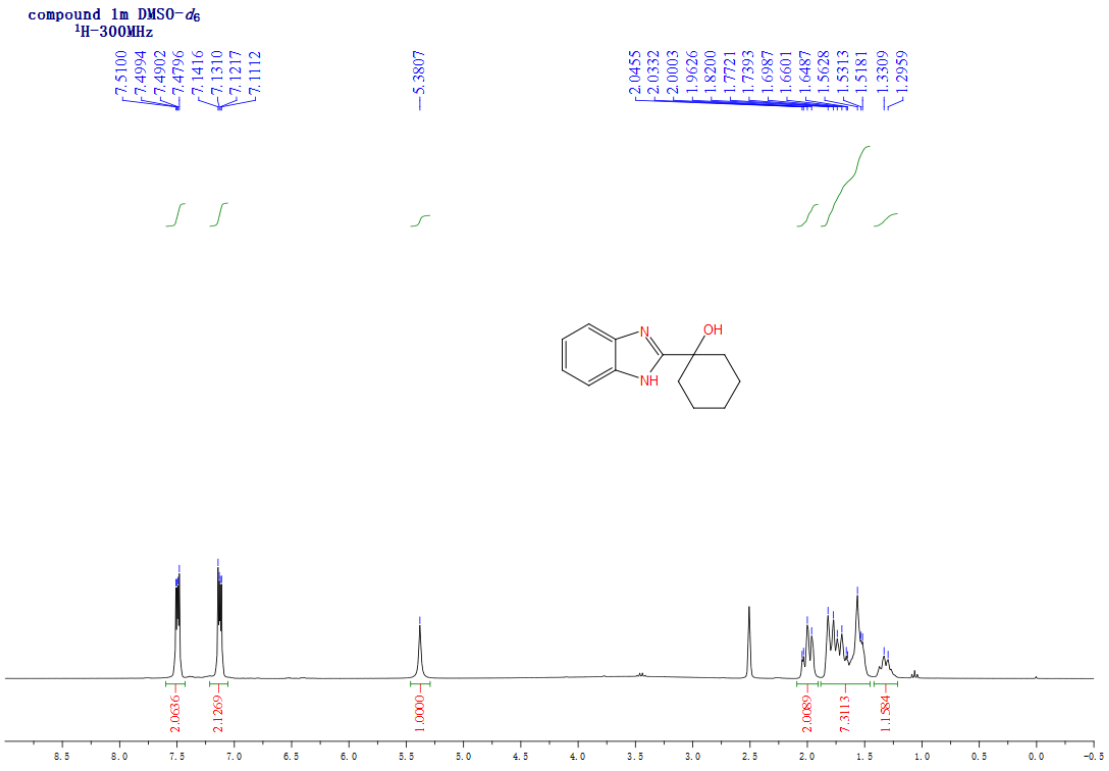

Figure S37. The ^{1}H NMR Spectrum of Compound **1m** in DMSO-d_6

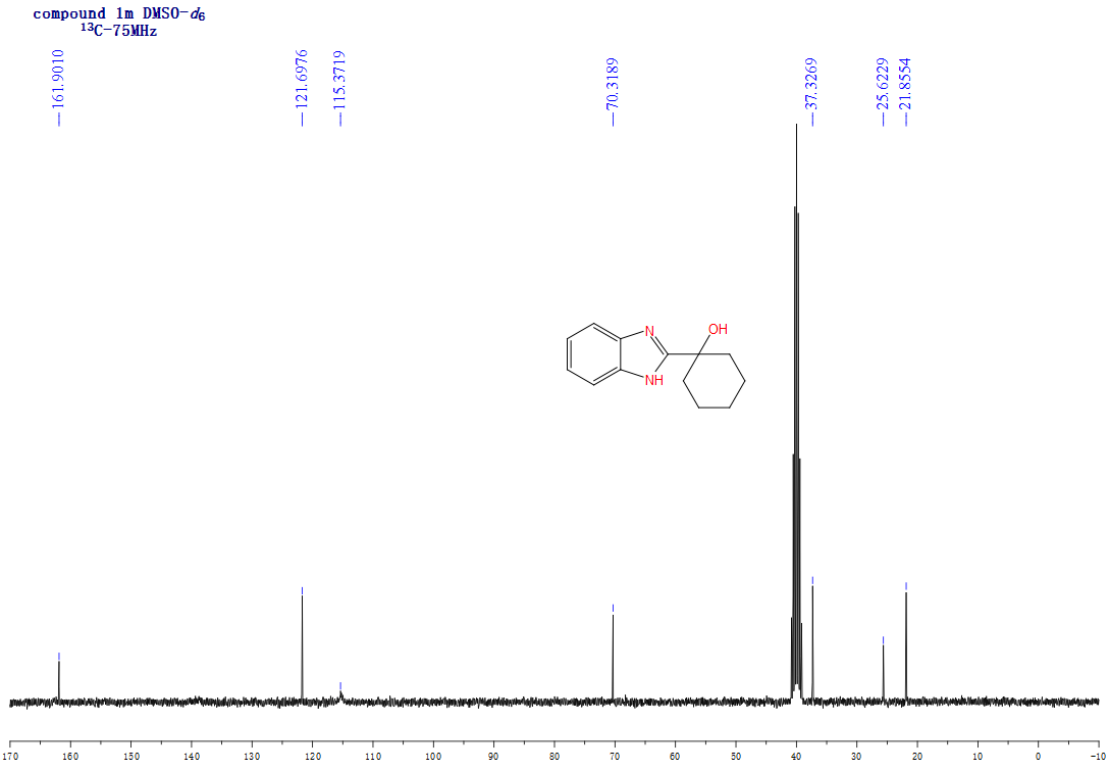

Figure S38. The ^{13}C NMR Spectrum of Compound **1m** in DMSO-d_6

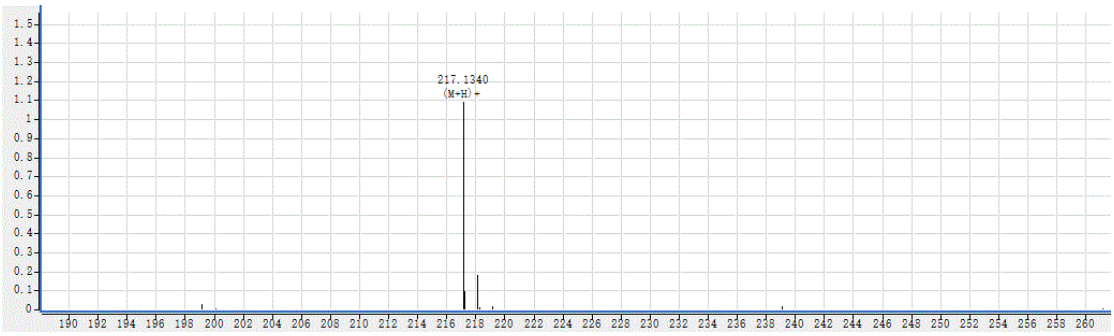

Figure S39. The HR-ESI-MS Spectrum of Compound **1m**

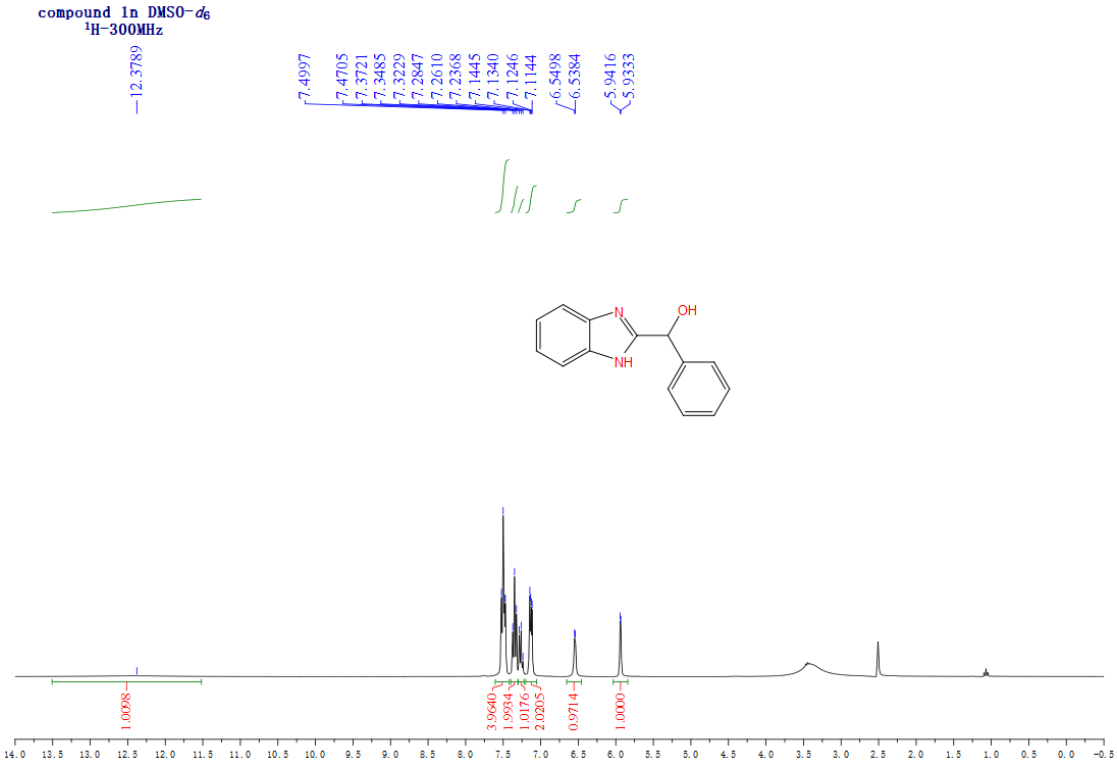

Figure S40. The ^{1}H NMR Spectrum of Compound **1n** in DMSO-d_6

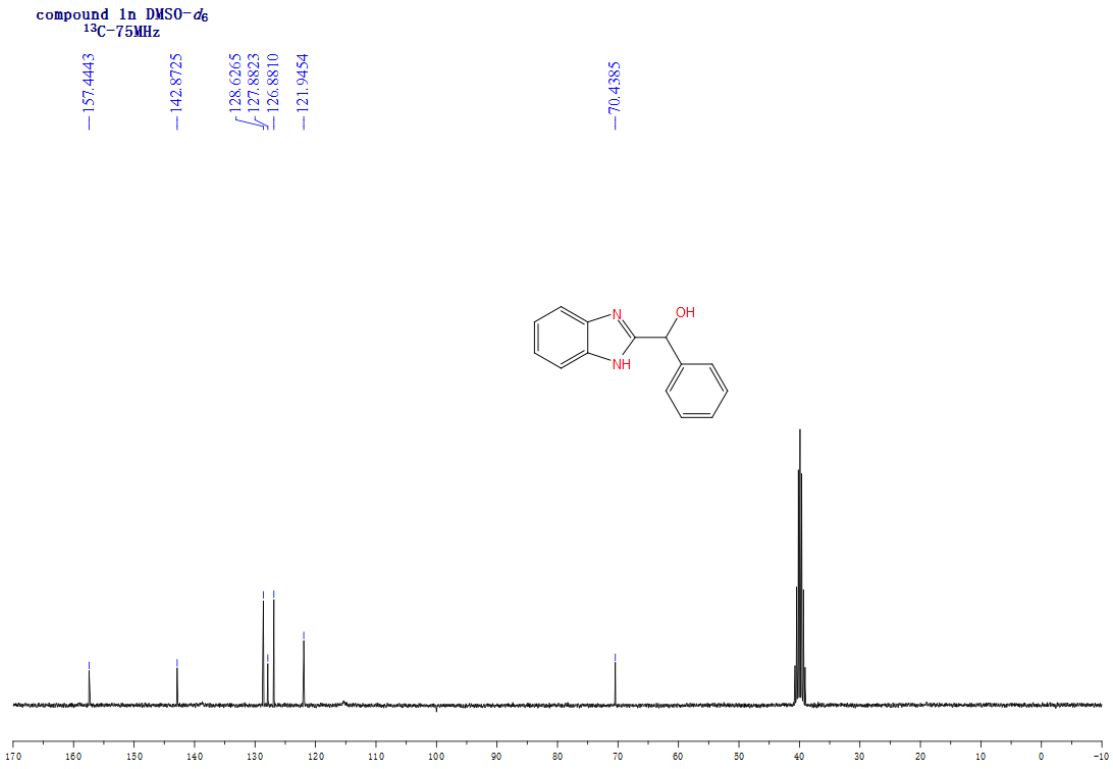

Figure S41. The ^{13}C NMR Spectrum of Compound **1n** in DMSO-d_6

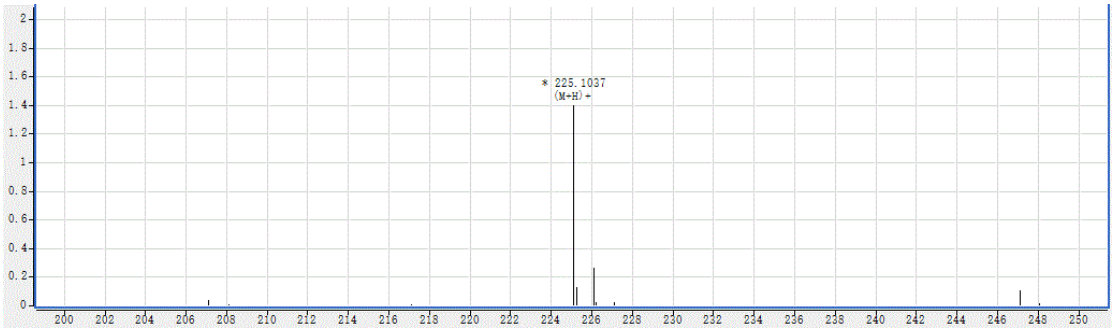

Figure S42. The HR-ESI-MS Spectrum of Compound **1n**

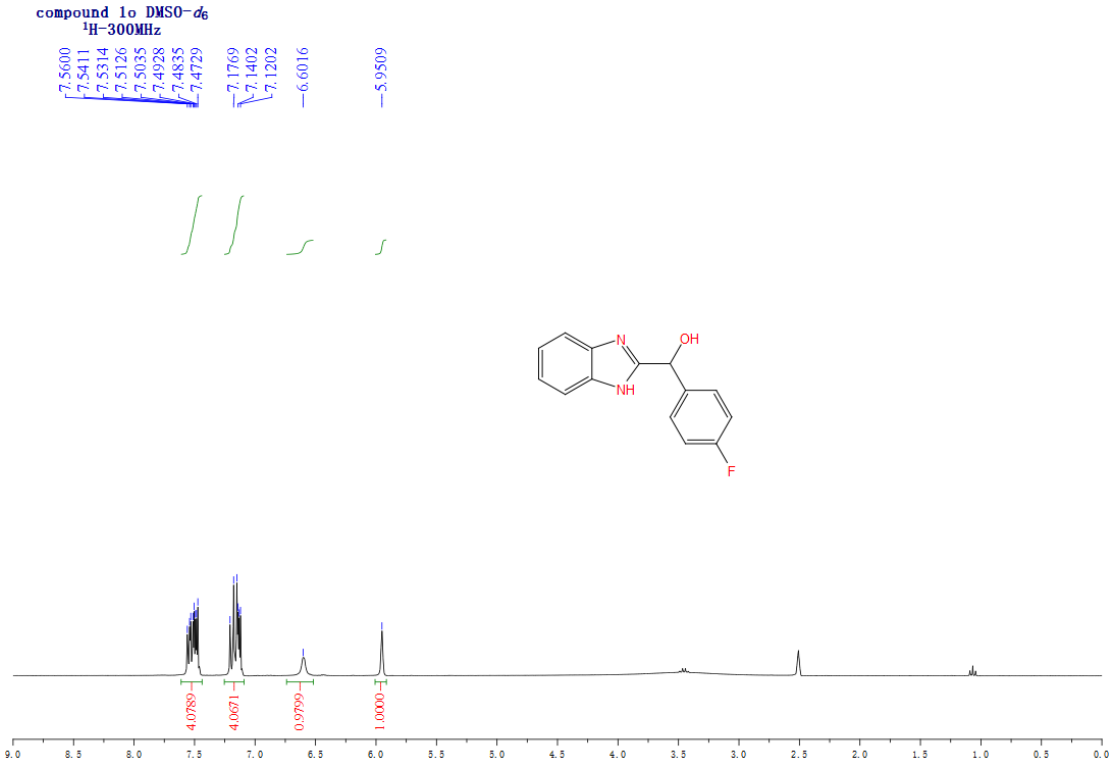

Figure S43. The ^{1}H NMR Spectrum of Compound **1o** in DMSO-d_6

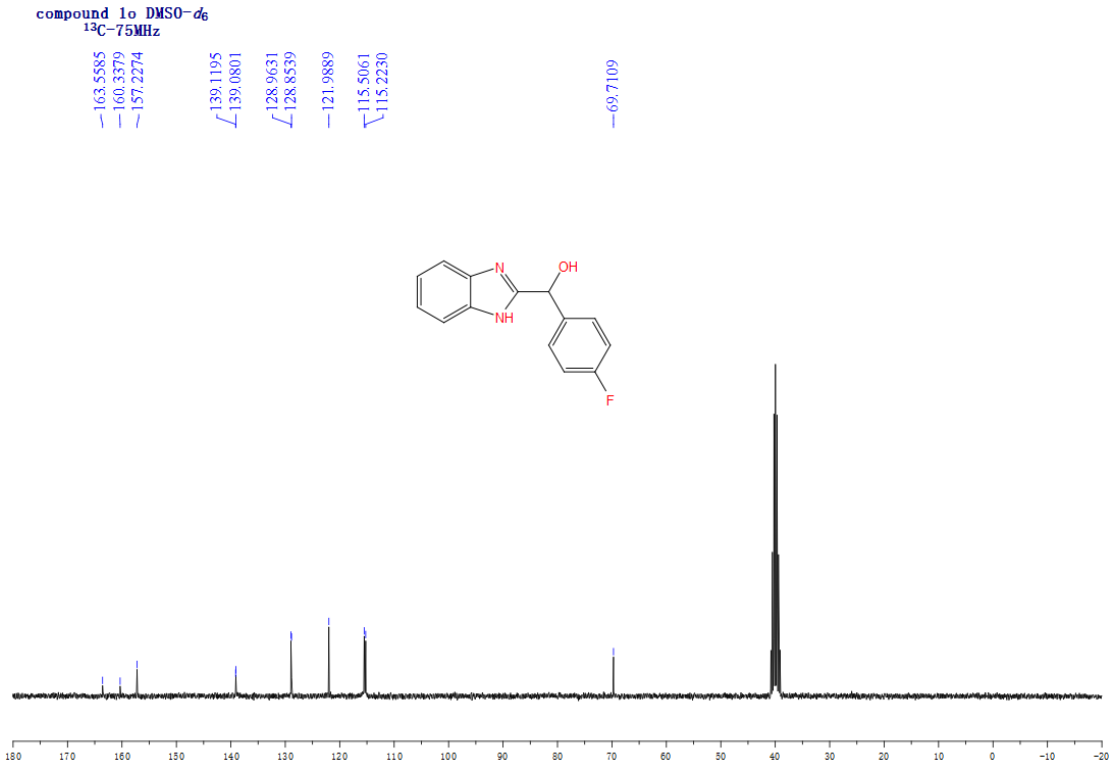

Figure S44. The ^{13}C NMR Spectrum of Compound **1o** in DMSO-d_6

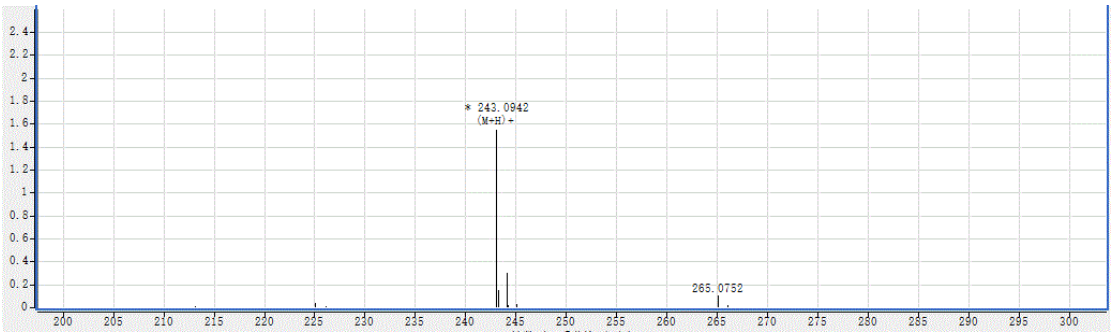

Figure S45. The HR-ESI-MS Spectrum of Compound **1o**

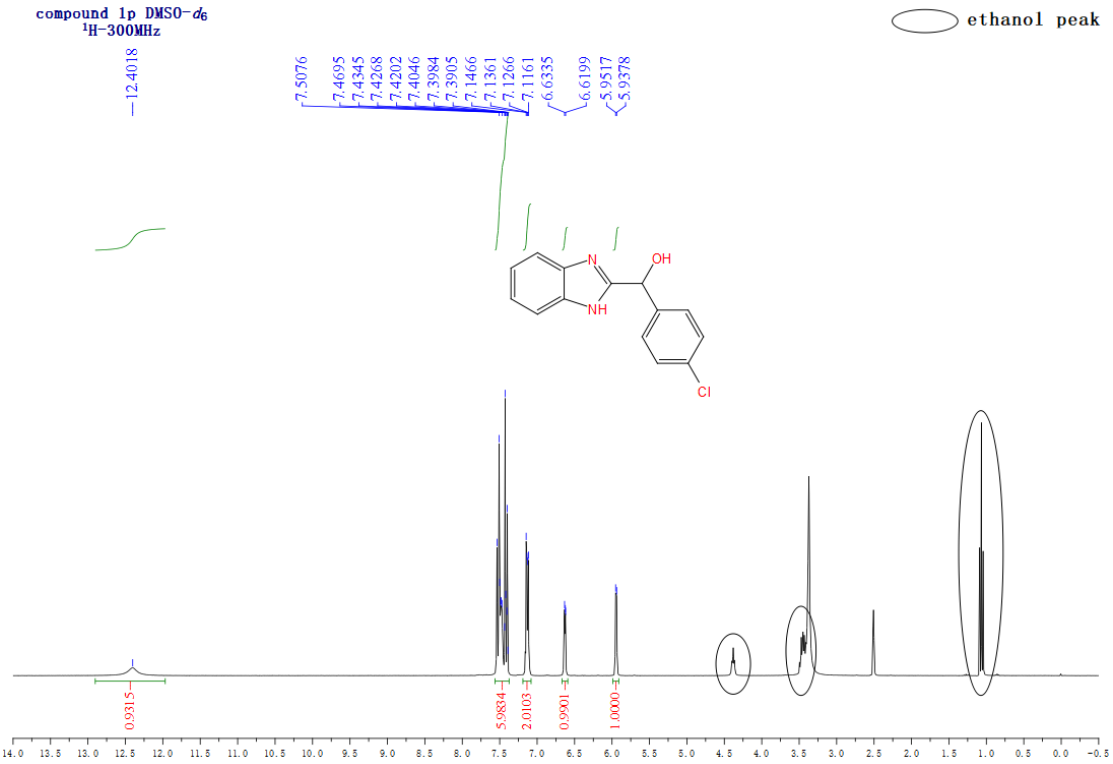

Figure S46. The ^{1}H NMR Spectrum of Compound **1p** in DMSO-d_6

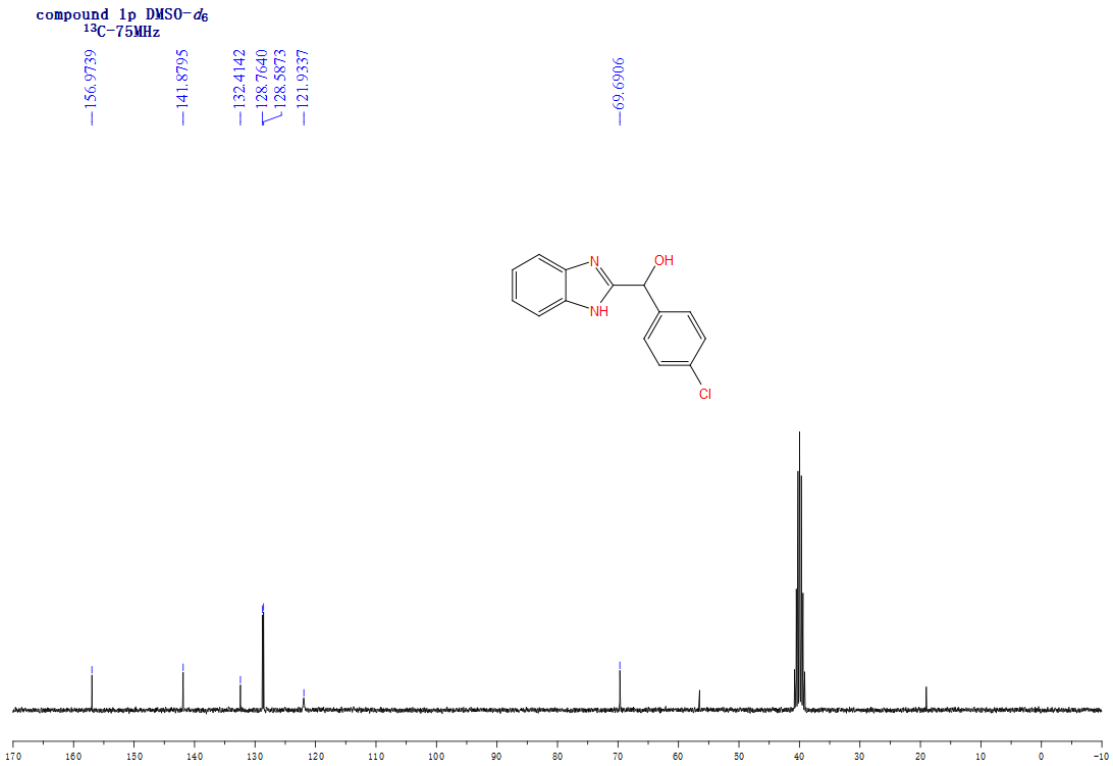

Figure S47. The ^{13}C NMR Spectrum of Compound **1p** in DMSO-d_6

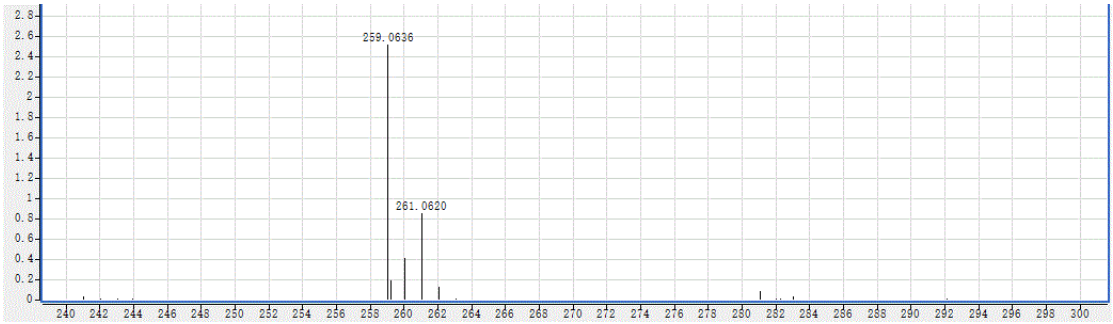

Figure S48. The HR-ESI-MS Spectrum of Compound **1p**

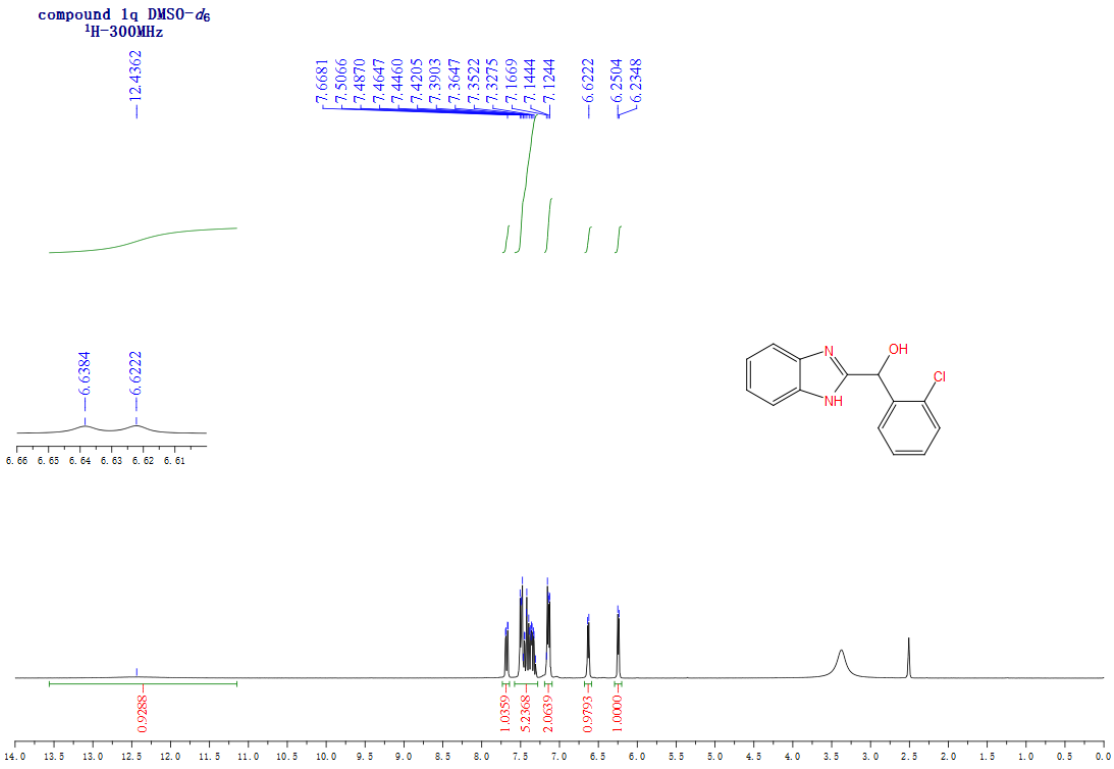

Figure S49. The ^{1}H NMR Spectrum of Compound **1q** in DMSO-d_6

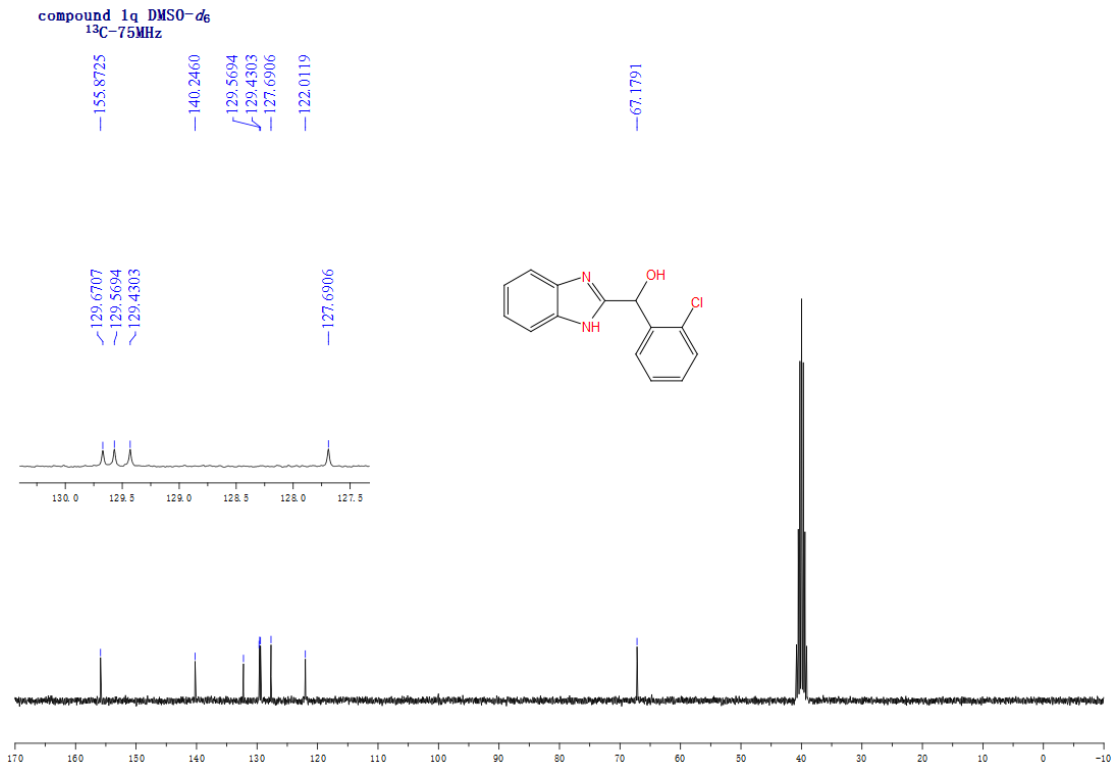

Figure S50. The ^{13}C NMR Spectrum of Compound **1q** in DMSO-d_6

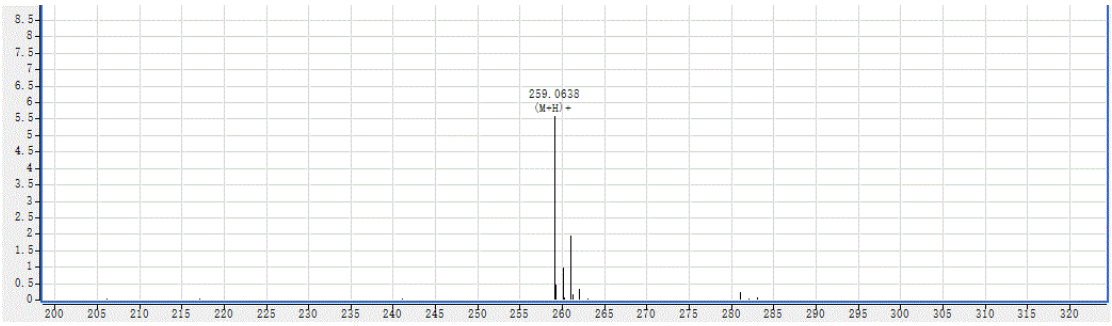

Figure S51. The HR-ESI-MS Spectrum of Compound **1q**

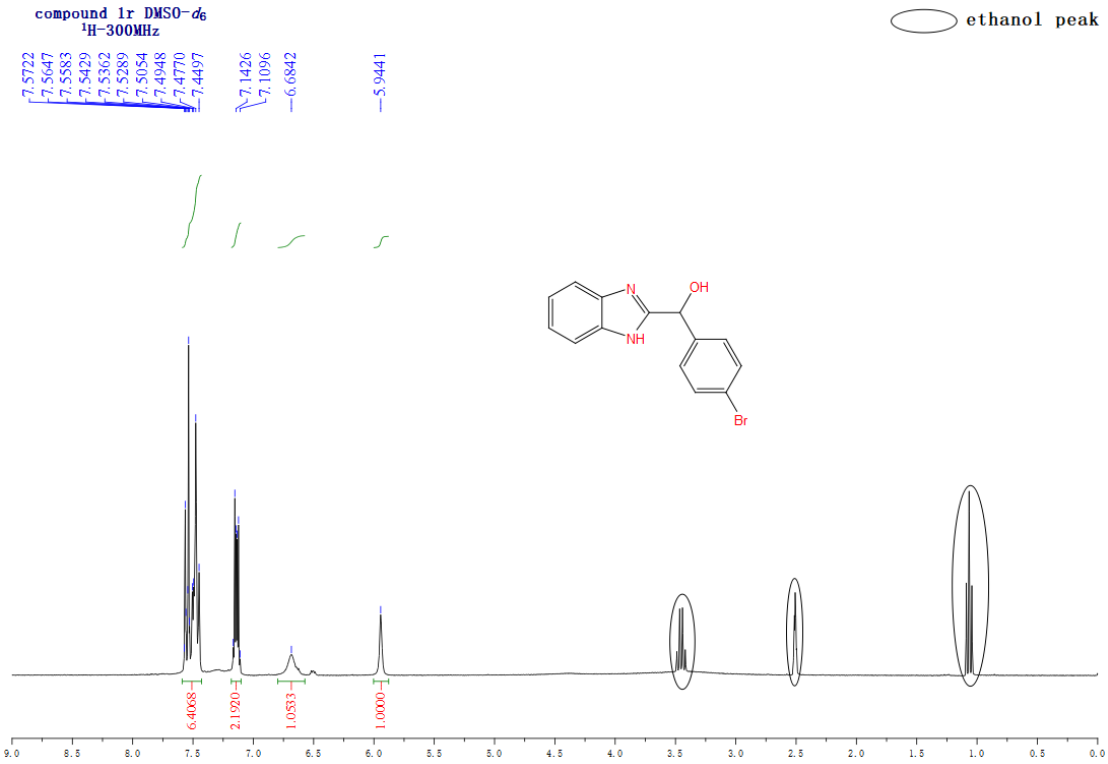

Figure S52. The ^{1}H NMR Spectrum of Compound **1r** in DMSO-d_6

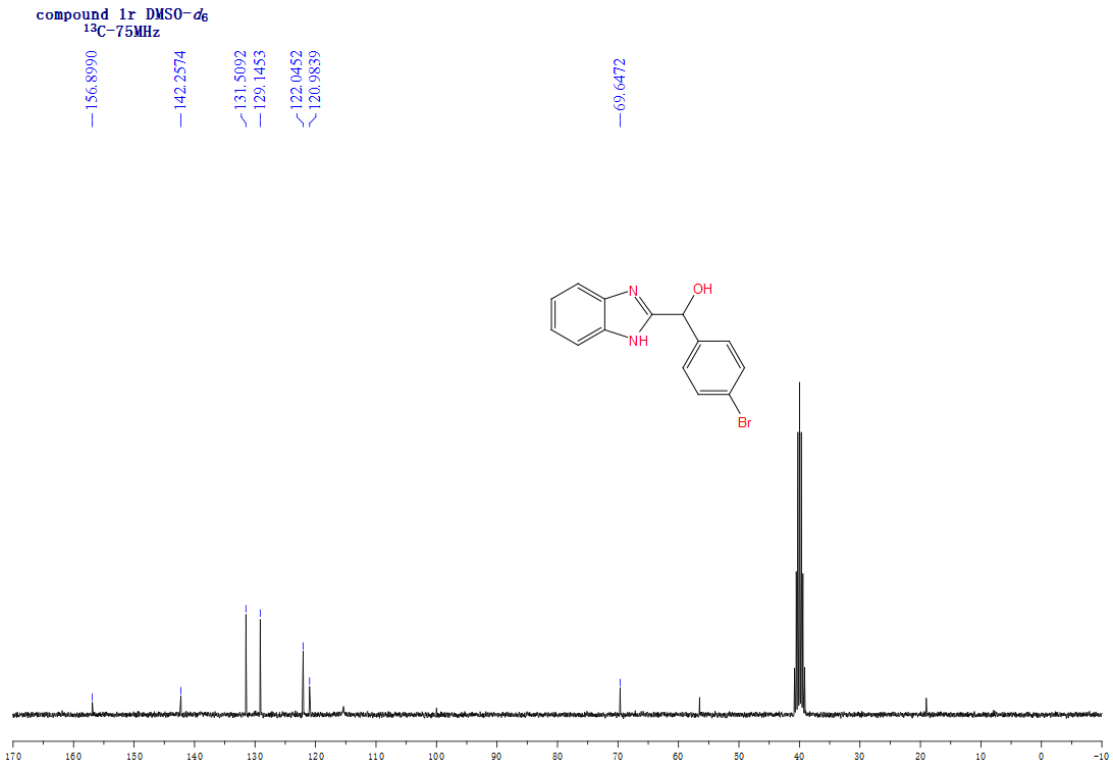

Figure S53. The ^{13}C NMR Spectrum of Compound **1r** in DMSO-d_6

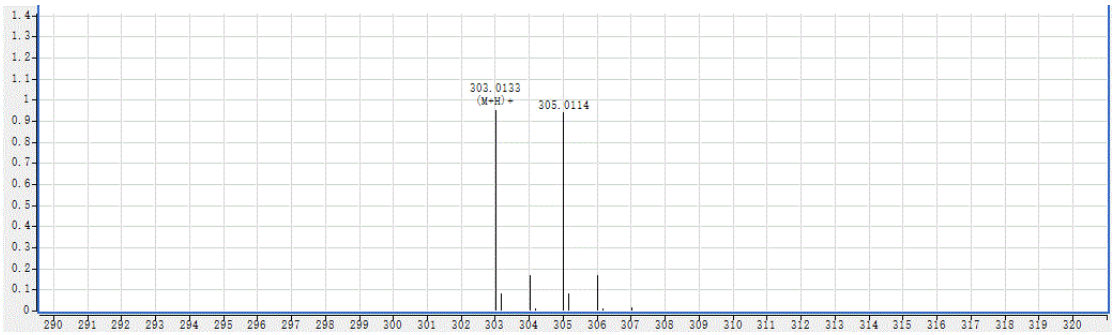

Figure S54. The HR-ESI-MS Spectrum of Compound **1r**

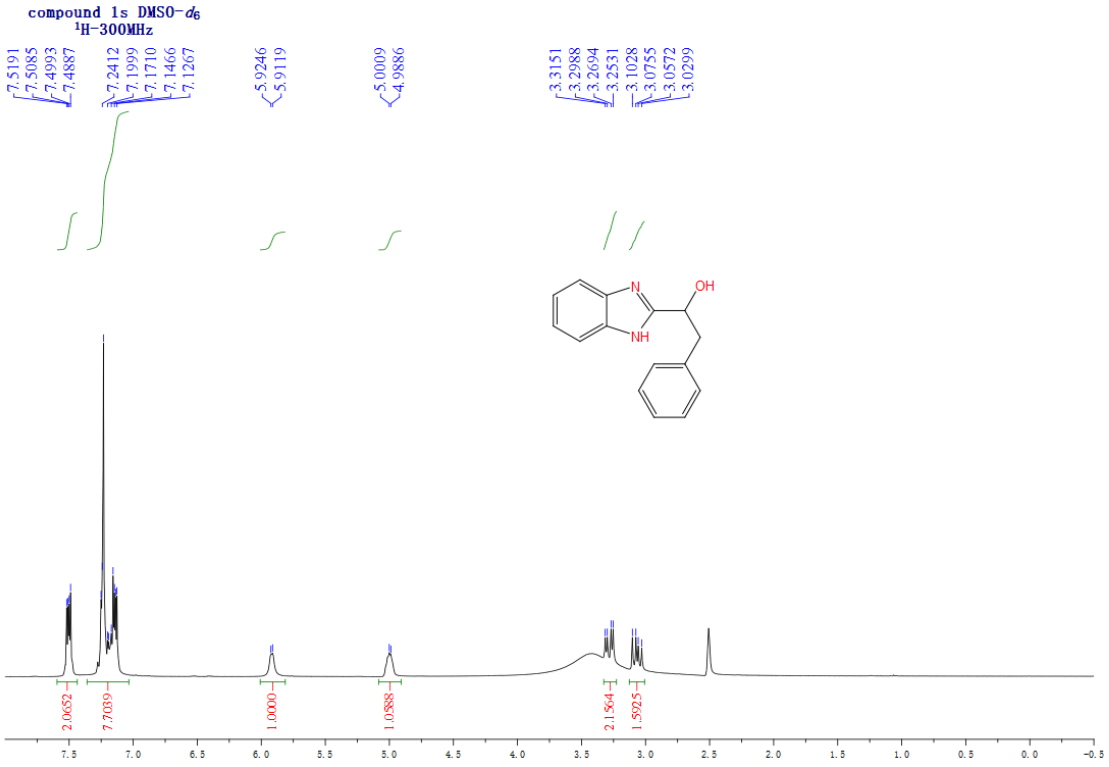

Figure S55. The ^{1}H NMR Spectrum of Compound **1s** in DMSO-d_6

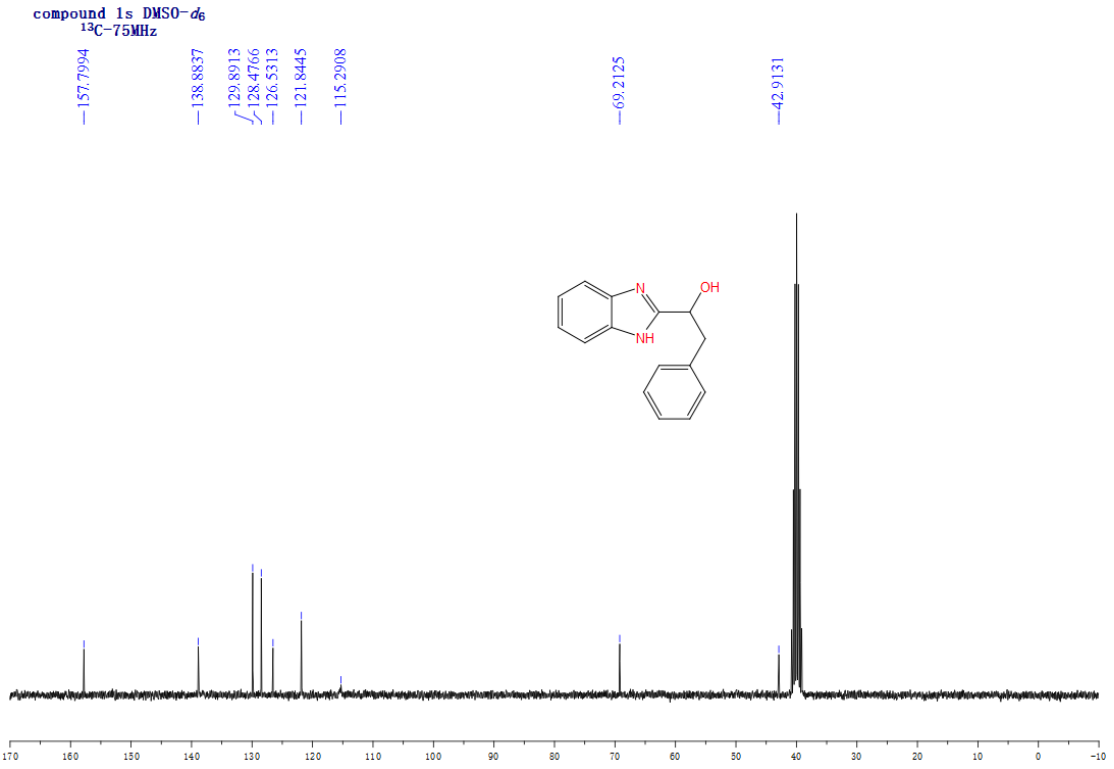

Figure S56. The ^{13}C NMR Spectrum of Compound **1s** in DMSO-d_6

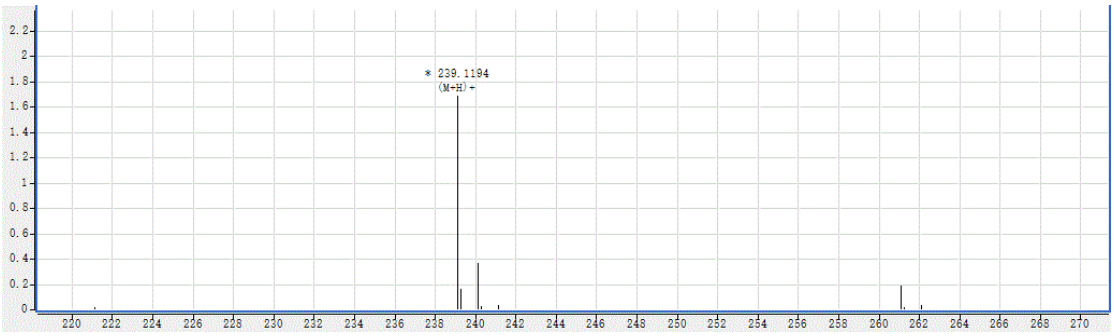

Figure S57. The HR-ESI-MS Spectrum of Compound **1s**

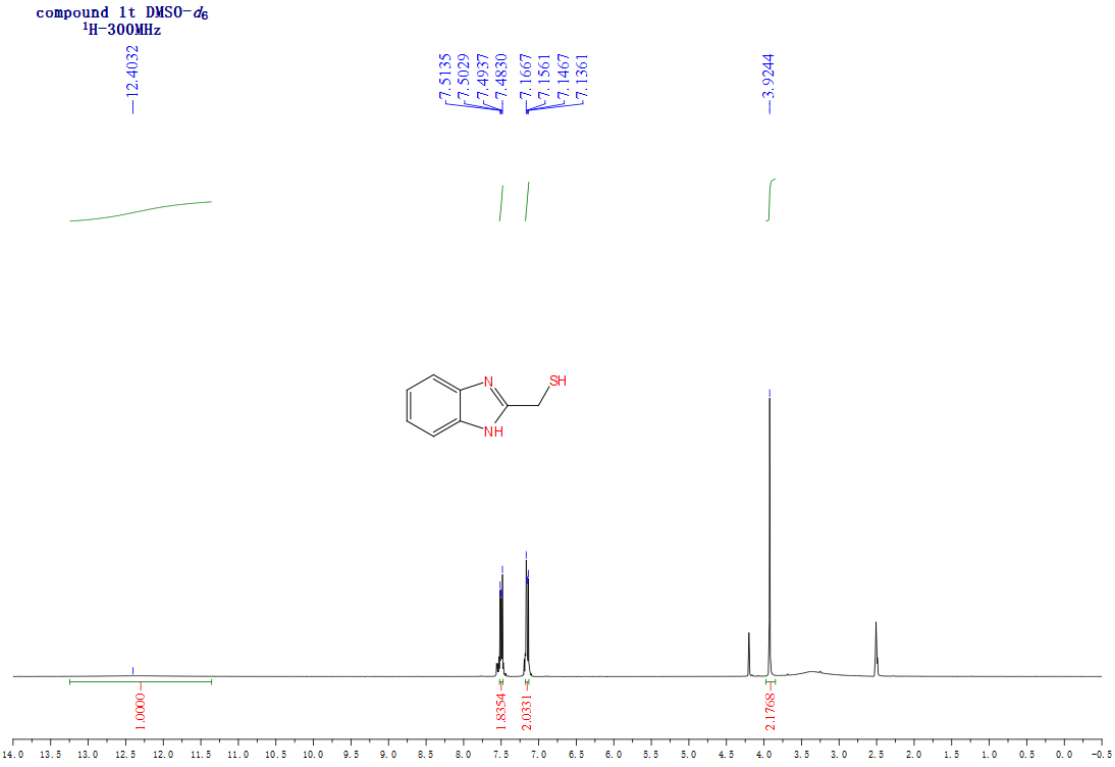

Figure S58. The ^{1}H NMR Spectrum of Compound **1t** in DMSO-d_6

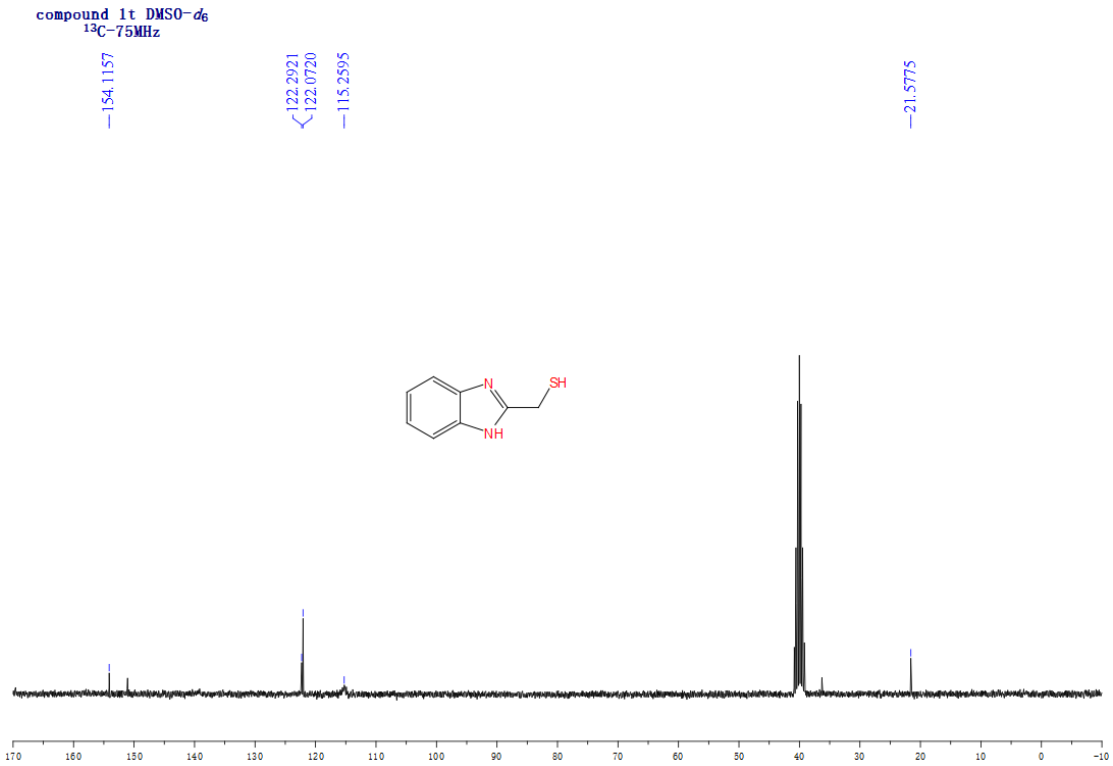

Figure S59. The ^{13}C NMR Spectrum of Compound **1t** in DMSO-d_6

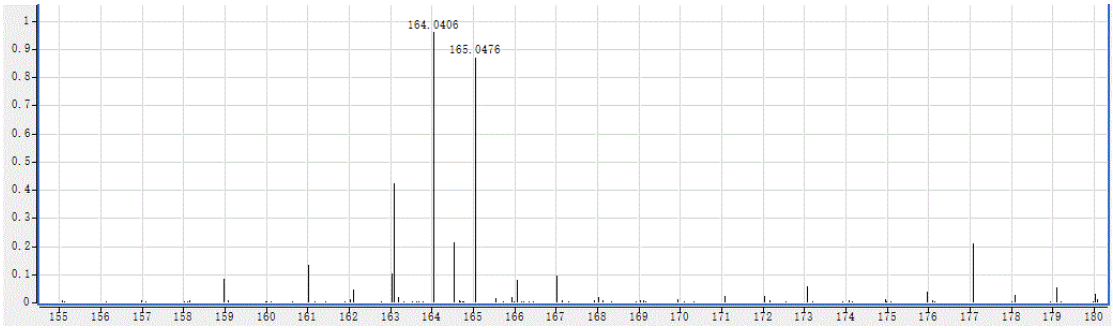

Figure S60. The HR-ESI-MS Spectrum of Compound **1t**

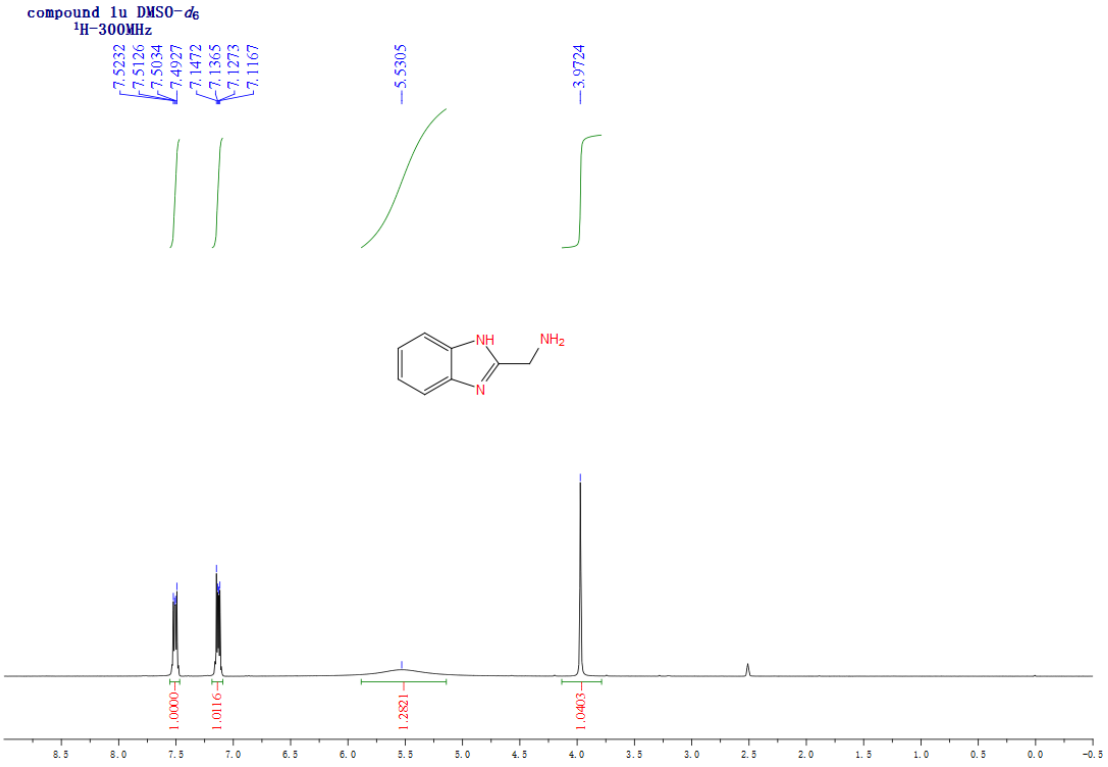

Figure S61. The ^{1}H NMR Spectrum of Compound **1u** in DMSO-d_6

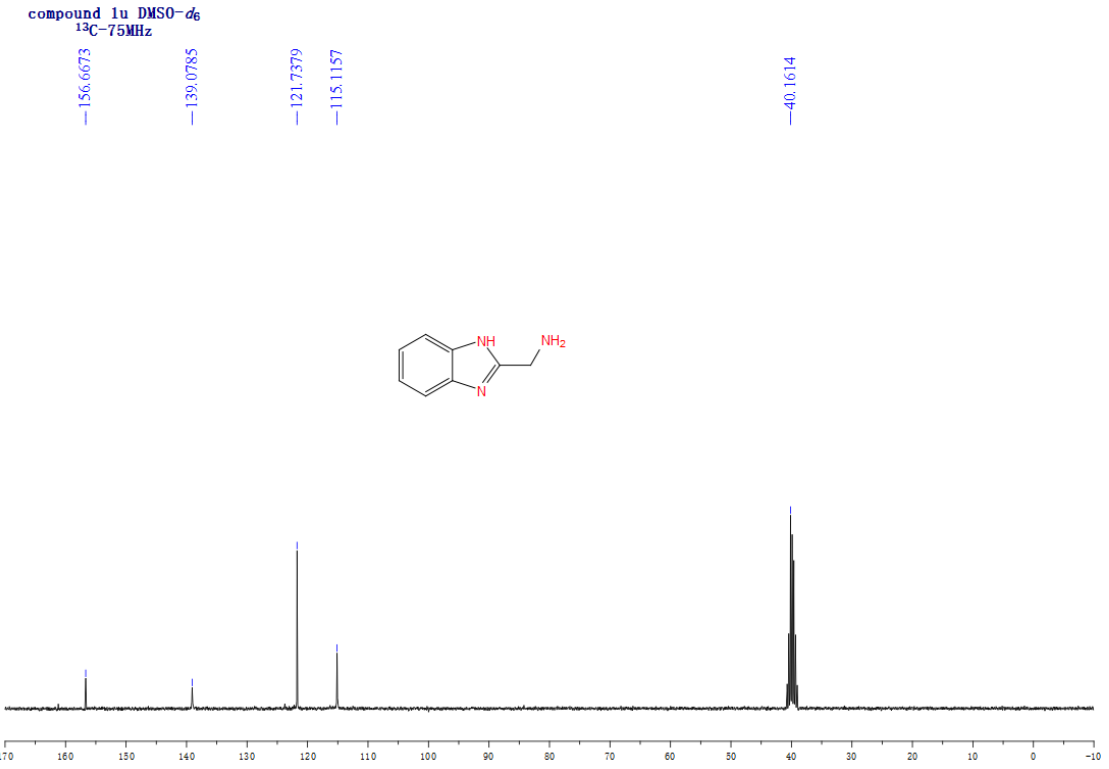

Figure S62. The ^{13}C NMR Spectrum of Compound **1u** in DMSO-d_6

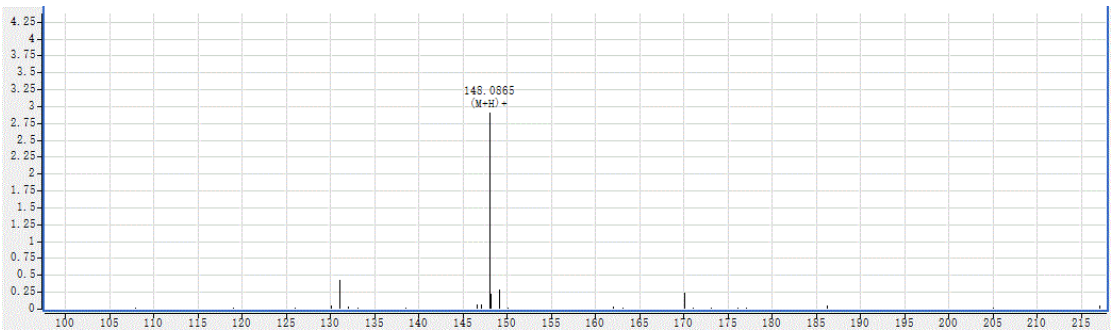

Figure S63. The HR-ESI-MS Spectrum of Compound **1u**

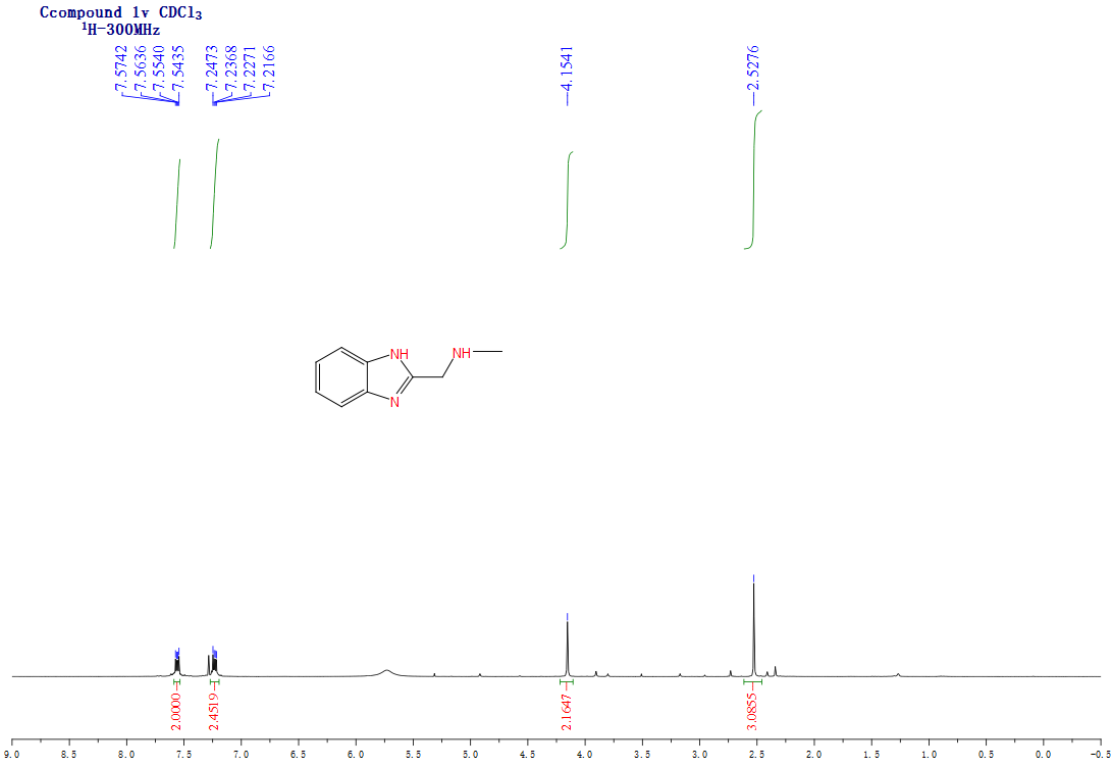

Figure S64. The ^{1}H NMR Spectrum of Compound **1v** in $CDCl_3$

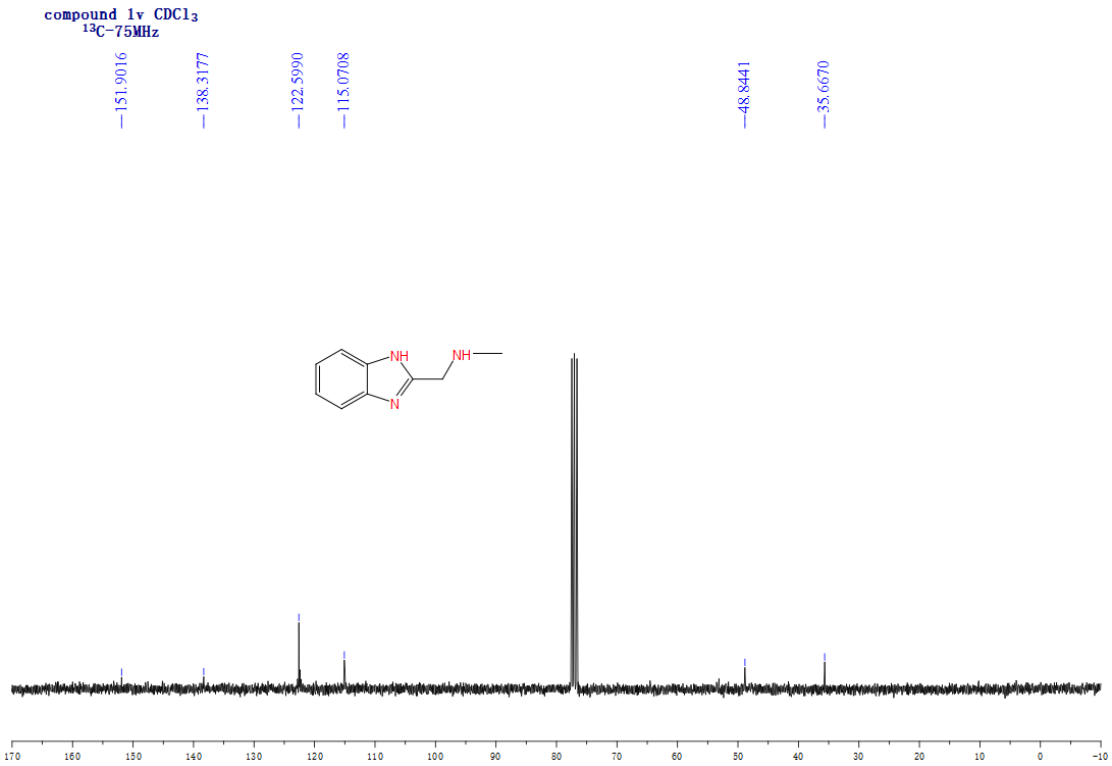

Figure S65. The ^{13}C NMR Spectrum of Compound **1v** in $CDCl_3$

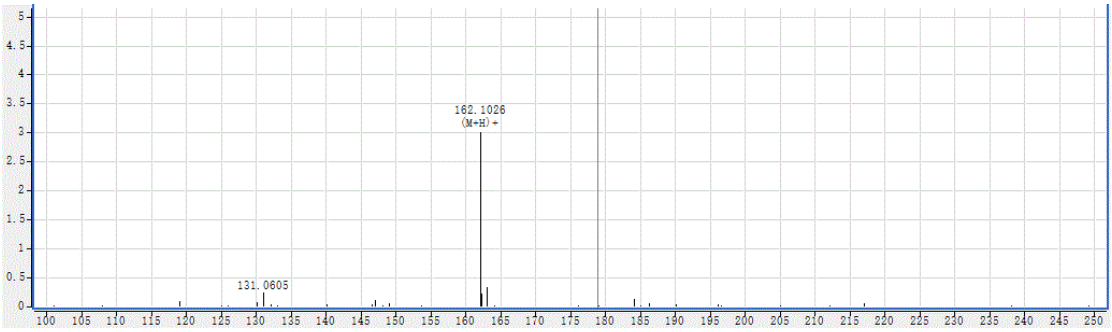

Figure S66. The HR-ESI-MS Spectrum of Compound **1v**

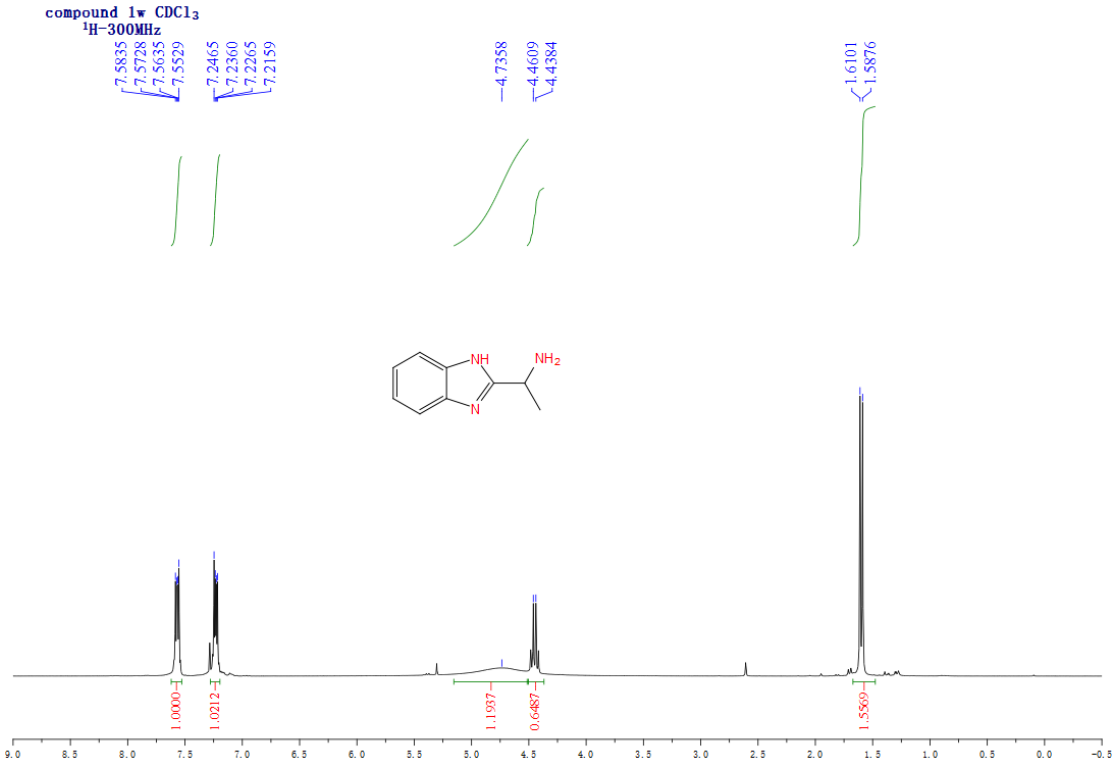

Figure S67. The ^{1}H NMR Spectrum of Compound **1w** in $CDCl_3$

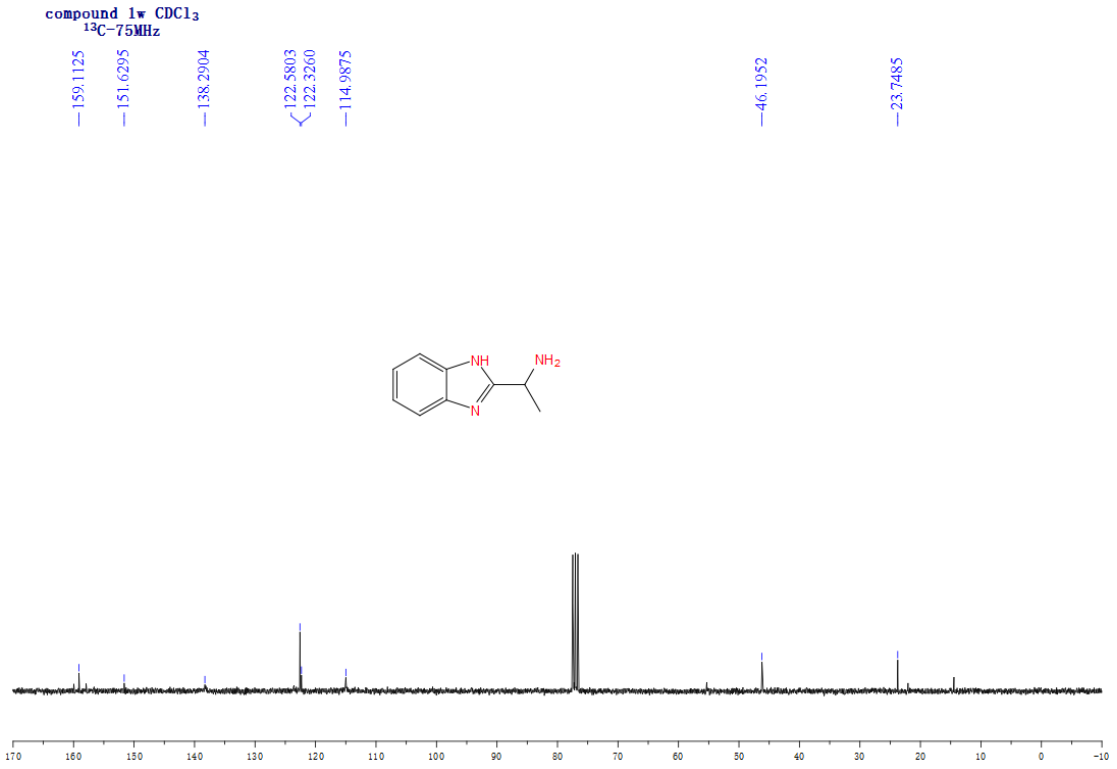

Figure S68. The ^{13}C NMR Spectrum of Compound **1w** in $CDCl_3$

Figure S69. The HR-ESI-MS Spectrum of Compound **1w**

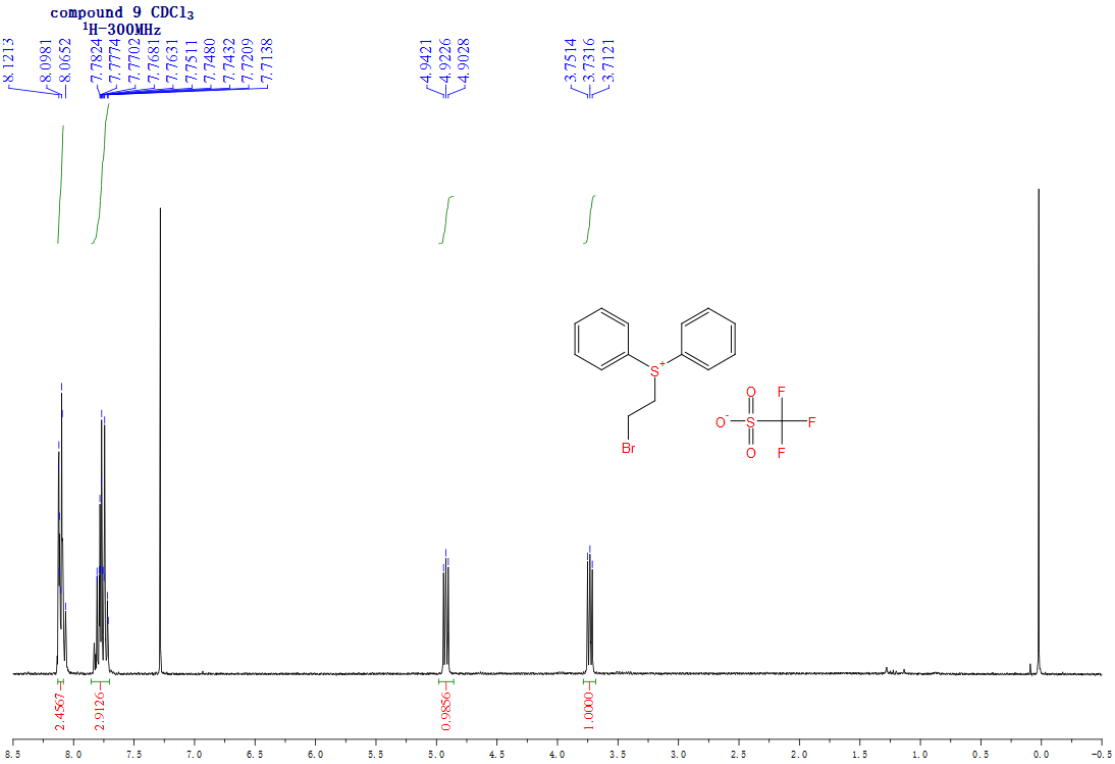

Figure S70. The ^{1}H NMR Spectrum of Compound **2** in $CDCl_3$

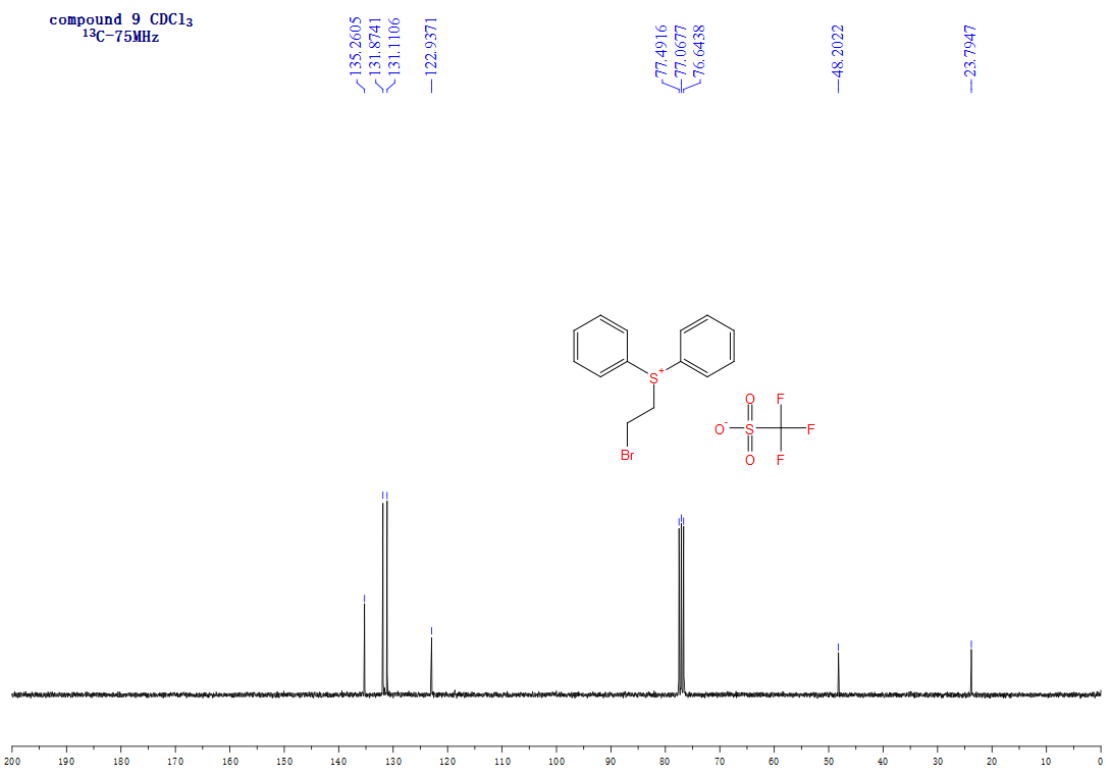

Figure S71. The ^{13}C NMR Spectrum of Compound **2** in $CDCl_3$

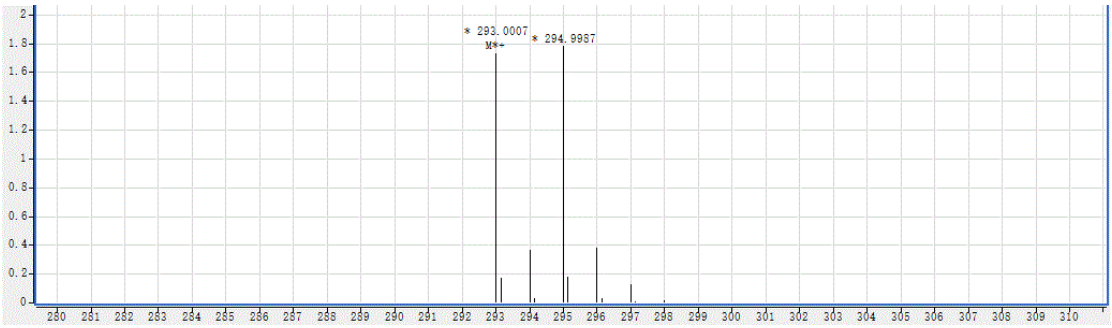

Figure S72. The HR-ESI-MS Spectrum of Compound **2**

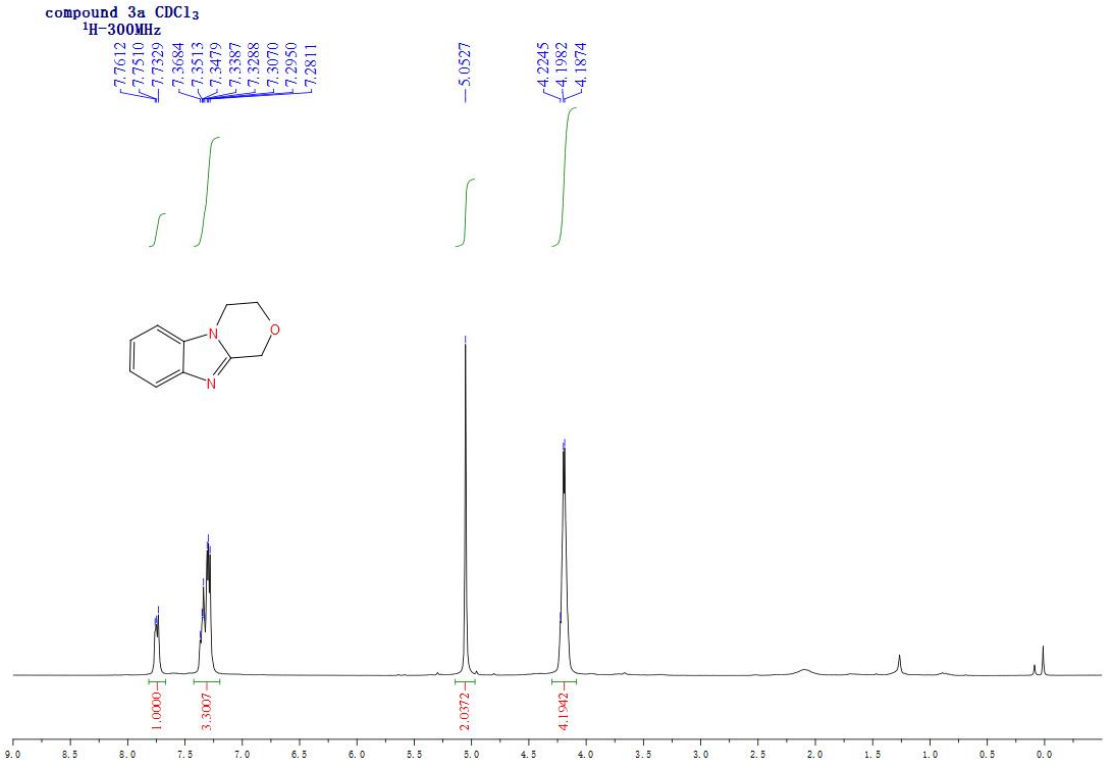

Figure S73. The ^{1}H NMR Spectrum of Compound **3a** in $CDCl_3$

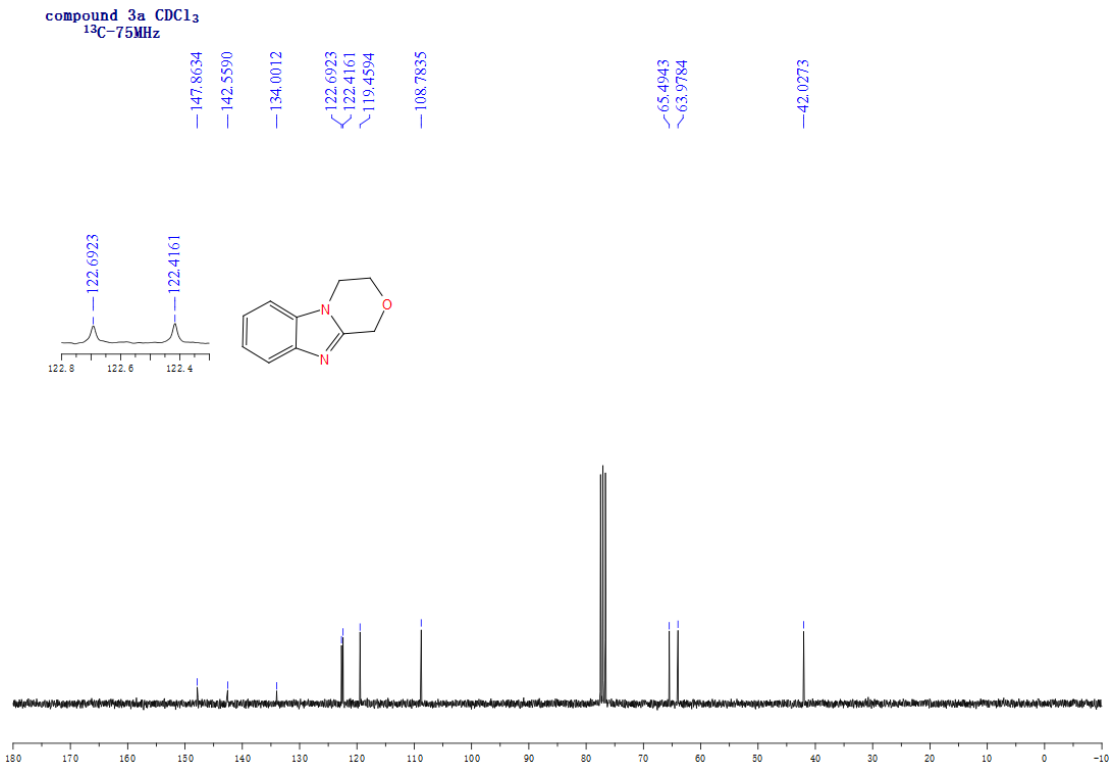

Figure S74. The ^{13}C NMR Spectrum of Compound **3a** in $CDCl_3$

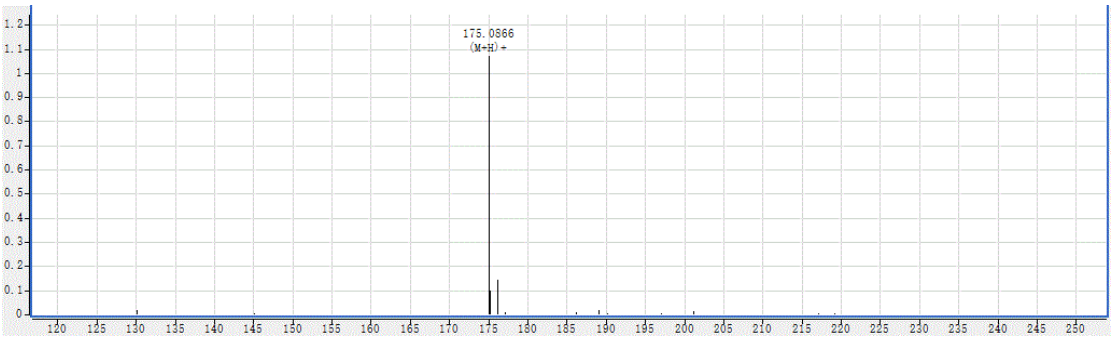

Figure S75. The HR-ESI-MS Spectrum of Compound **3a**

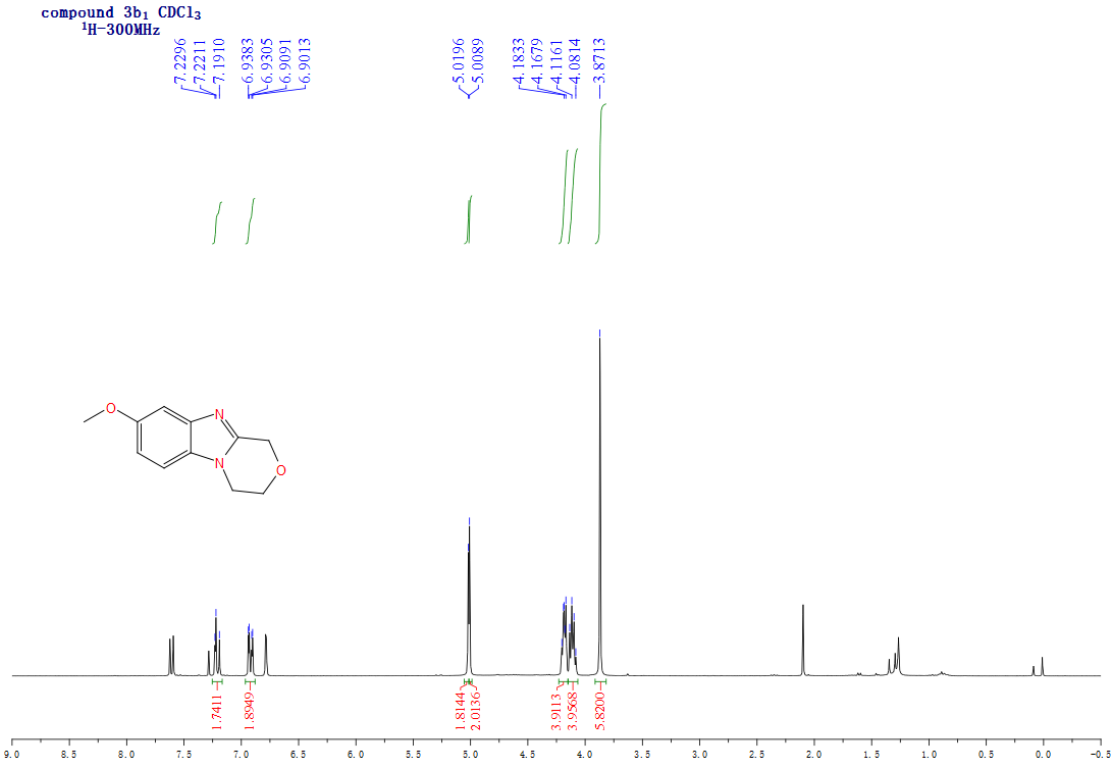

Figure S76. The ^{1}H NMR Spectrum of Compound **3b$_1$** in $CDCl_3$

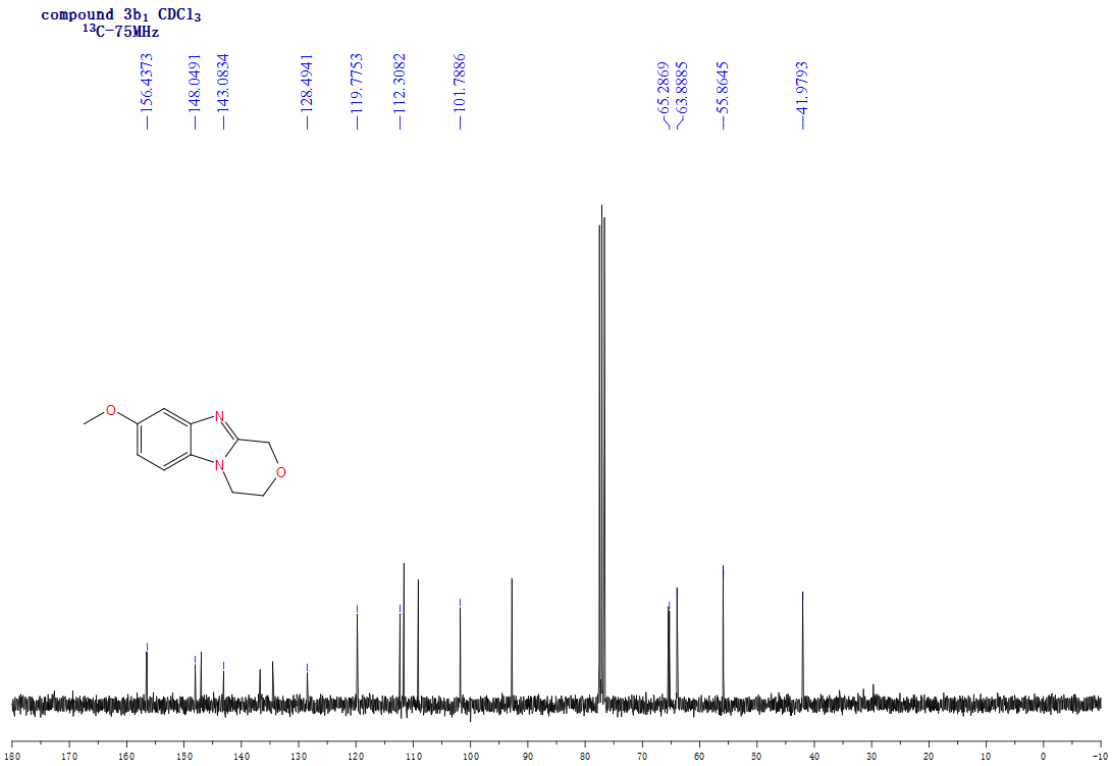

Figure S77. The ^{13}C NMR Spectrum of Compound **3b1** in $CDCl_3$

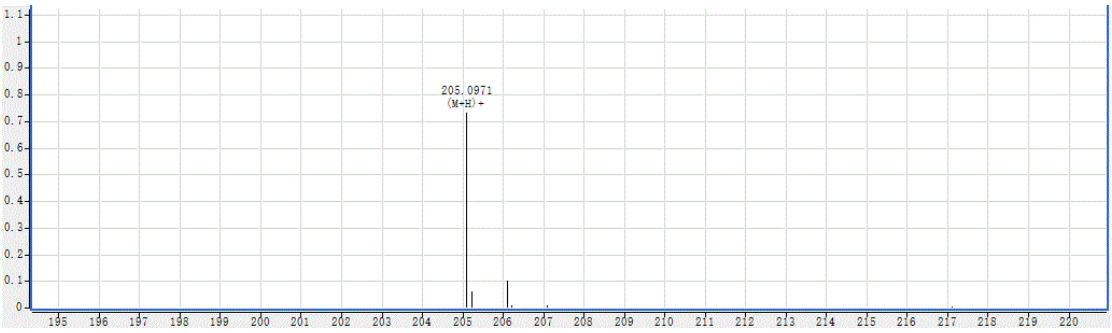

Figure S78. The HR-ESI-MS Spectrum of Compound **3b1**

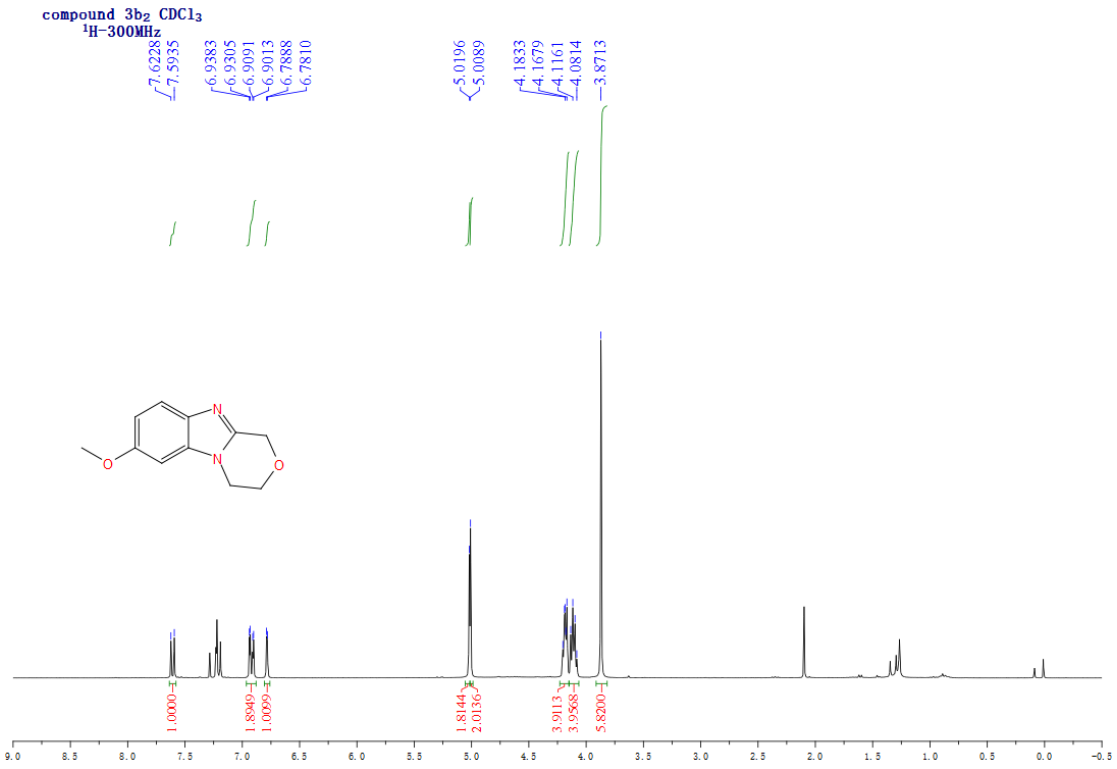

Figure S79. The ^{1}H NMR Spectrum of Compound **3b₂** in $CDCl_3$

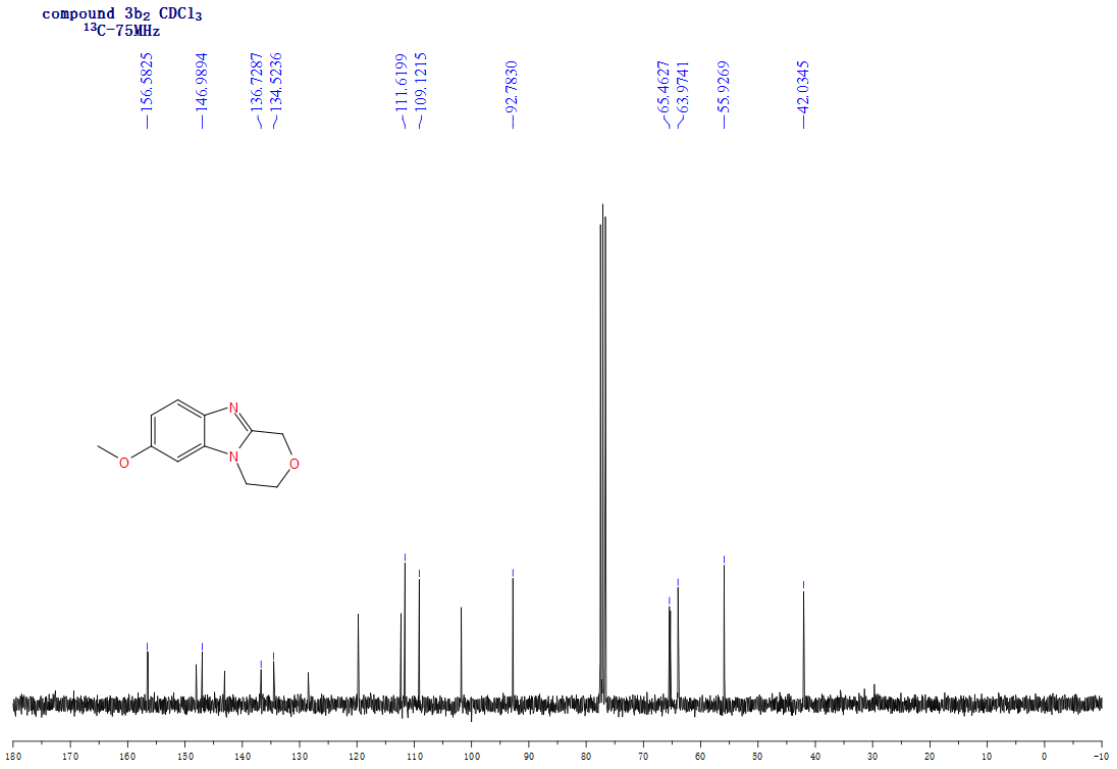

Figure S80. The ^{13}C NMR Spectrum of Compound **3b₂** in $CDCl_3$

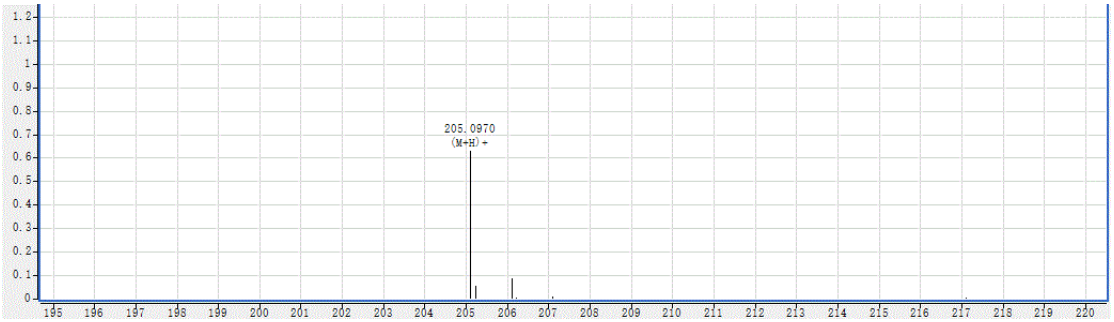

Figure S81. The HR-ESI-MS Spectrum of Compound **3b2**

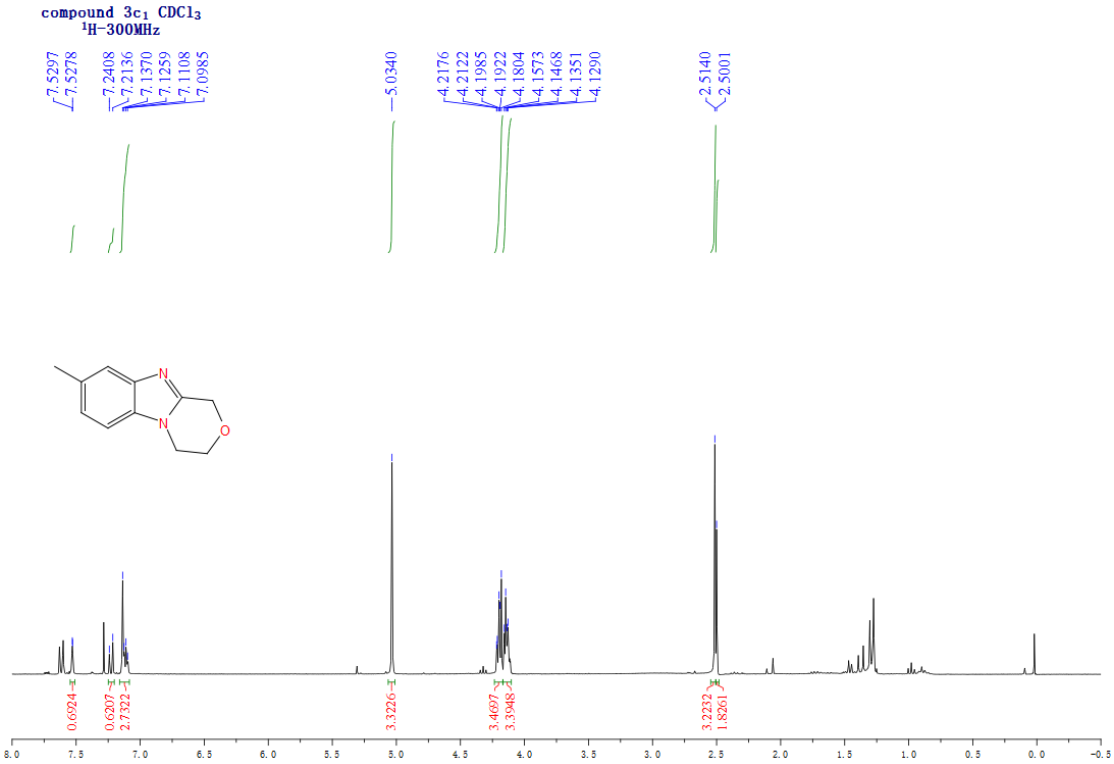

Figure S82. The ^{1}H NMR Spectrum of Compound **3c1** in $CDCl_3$

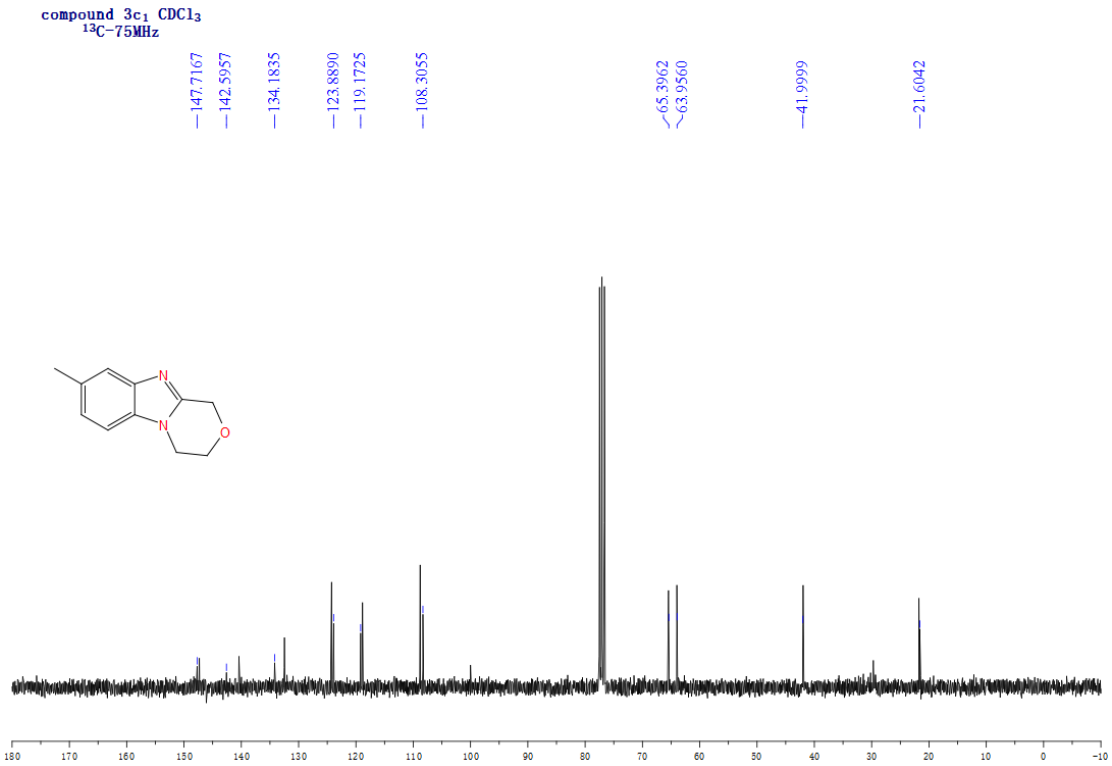

Figure S83. The ^{13}C NMR Spectrum of Compound **3c1** in $CDCl_3$

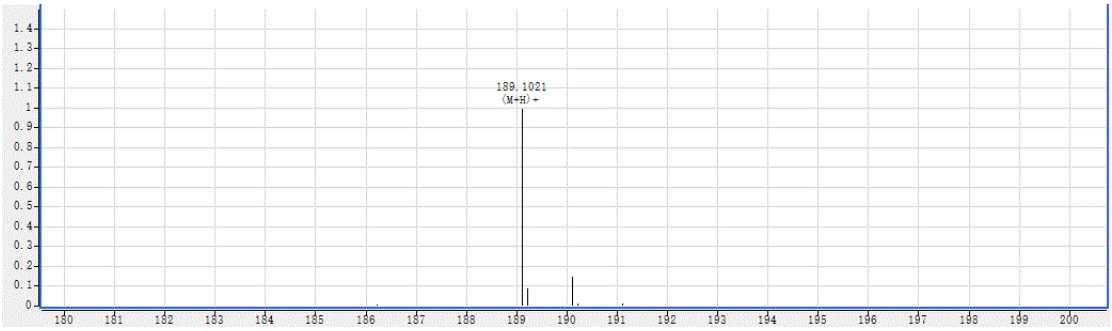

Figure S84. The HR-ESI-MS Spectrum of Compound **3c1**

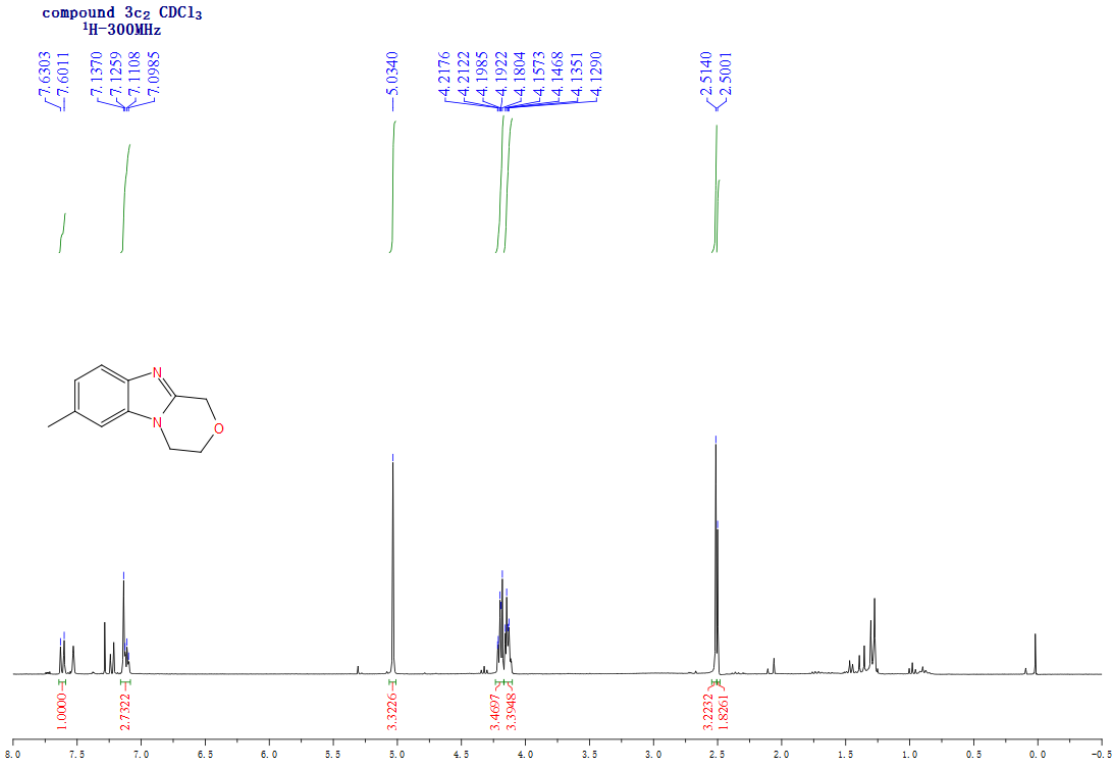

Figure S85. The ^{1}H NMR Spectrum of Compound **3c$_2$** in $CDCl_3$

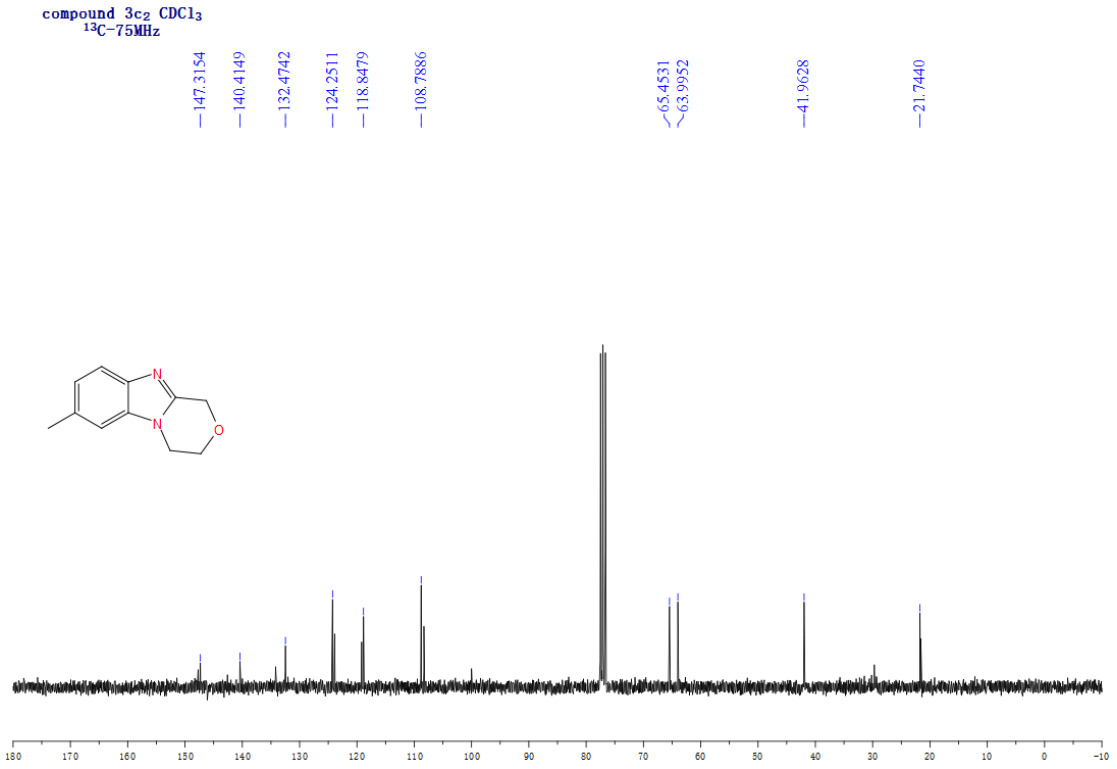

Figure S86. The ^{13}C NMR Spectrum of Compound **3c$_2$** in $CDCl_3$

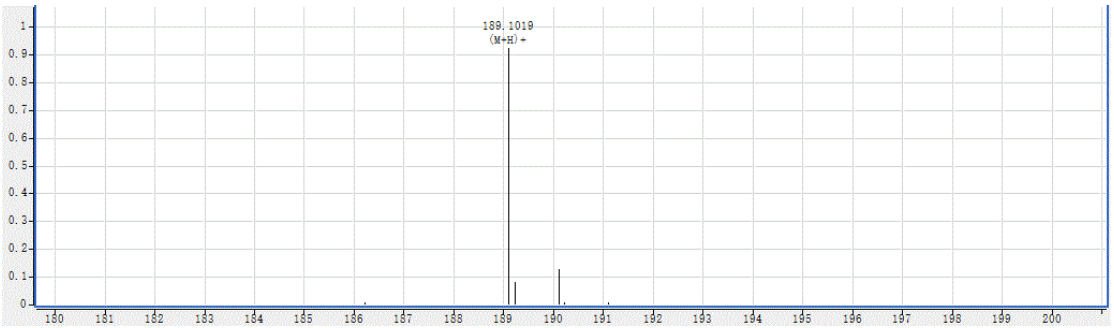

Figure S87. The HR-ESI-MS Spectrum of Compound **3c₂**

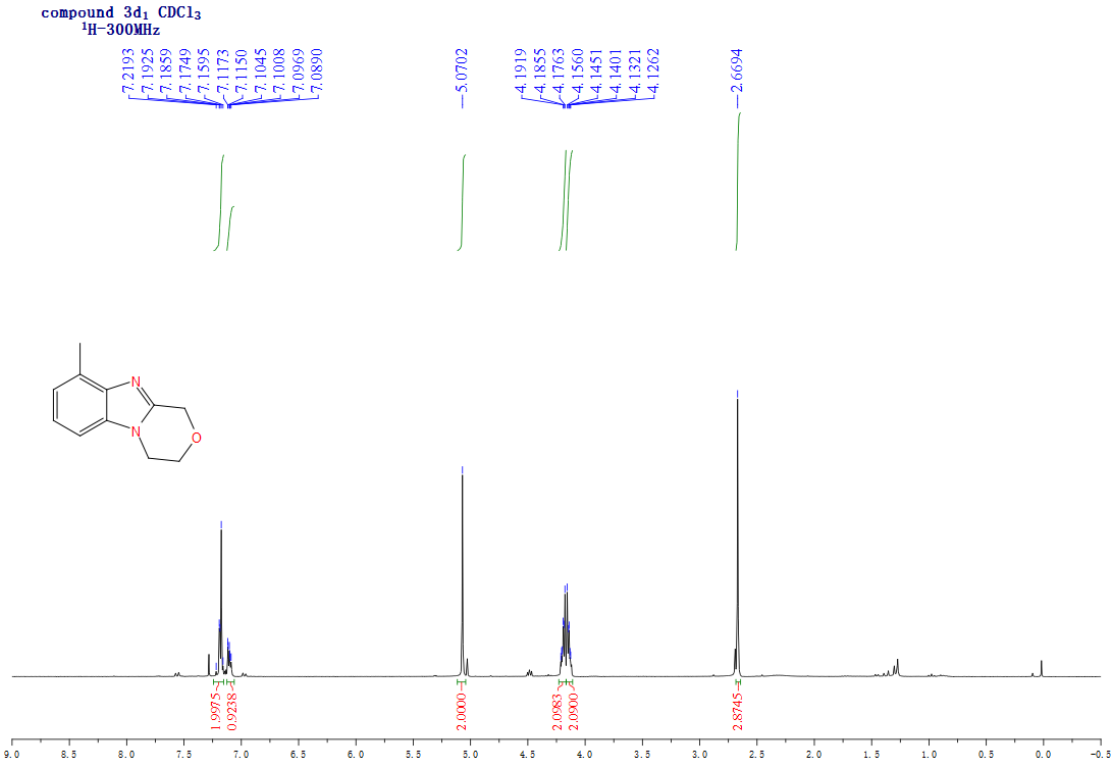

Figure S88. The ^{1}H NMR Spectrum of Compound **3d₁** in $CDCl_3$

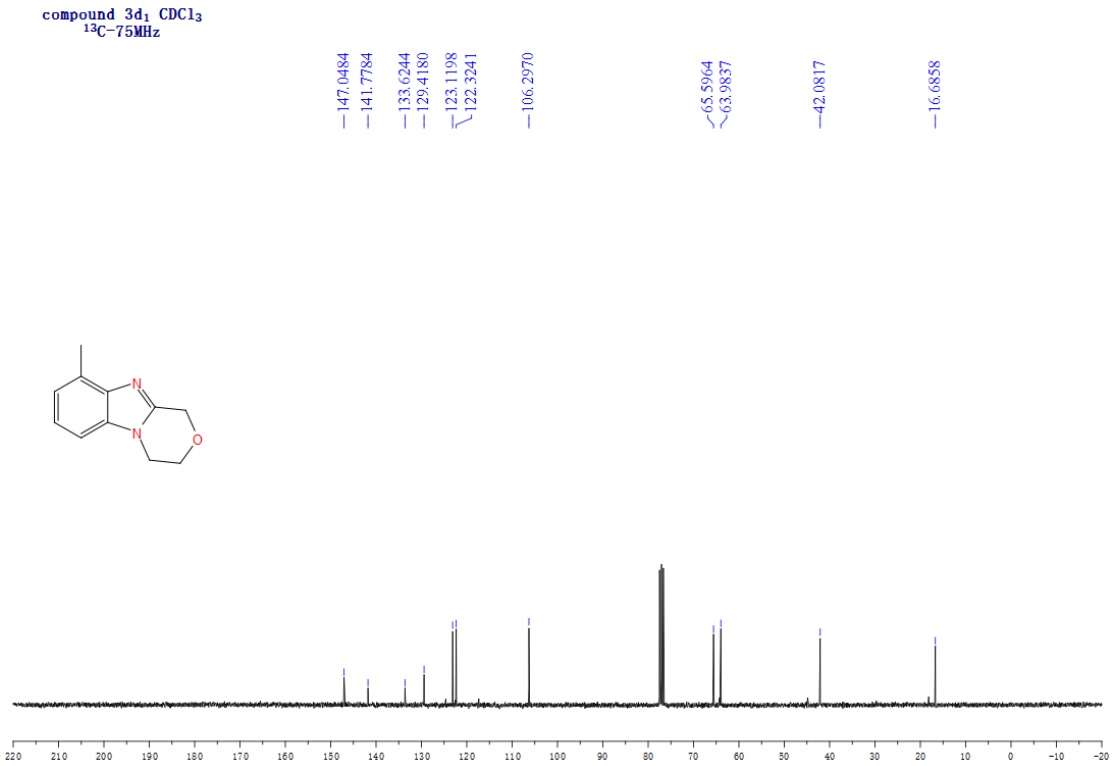

Figure S89. The ^{13}C NMR Spectrum of Compound **3d1** in $CDCl_3$

Figure S90. The HR-ESI-MS Spectrum of Compound **3d1**

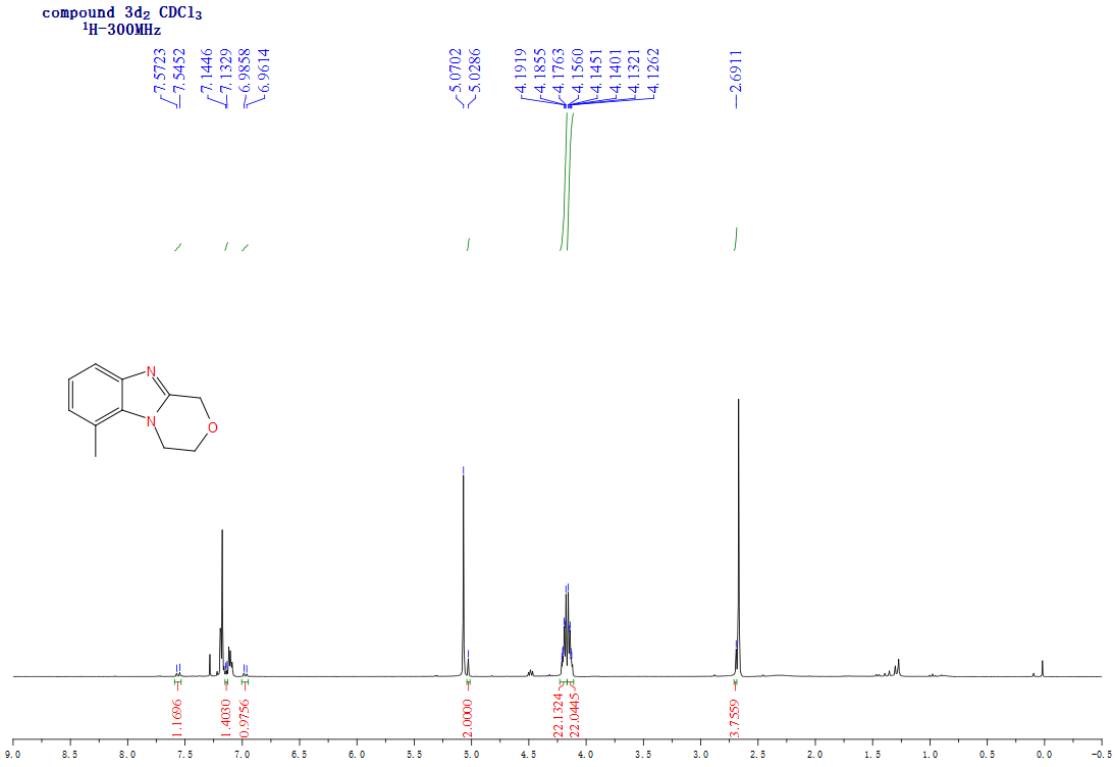

Figure S91. The ^{1}H NMR Spectrum of Compound **3d$_2$** in $CDCl_3$

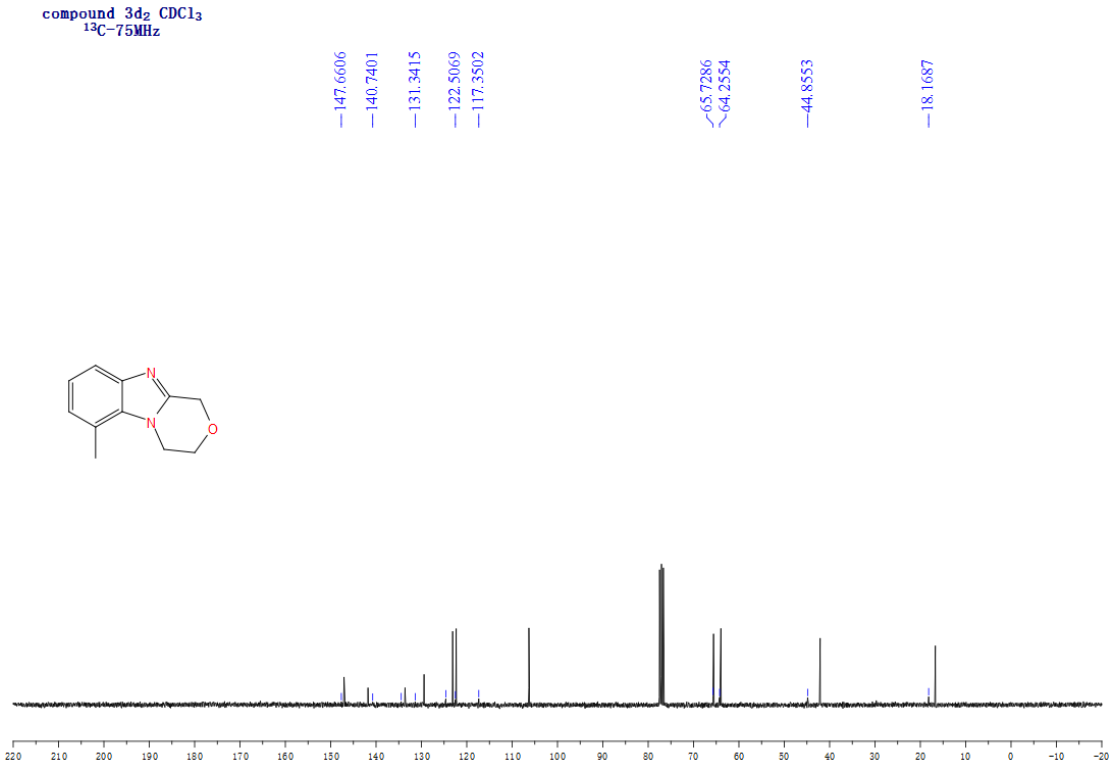

Figure S92. The ^{13}C NMR Spectrum of Compound **3d$_2$** in $CDCl_3$

Figure S93. The HR-ESI-MS Spectrum of Compound **3d₂**

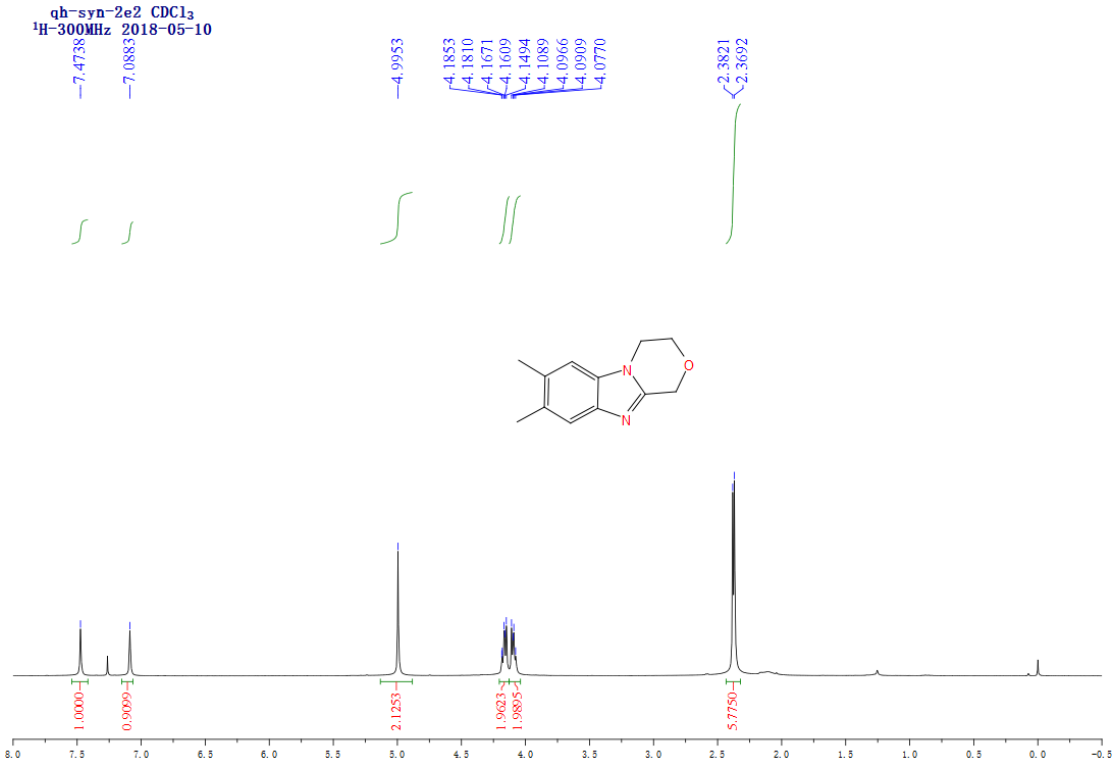

Figure S94. The ^{1}H NMR Spectrum of Compound **3e** in $CDCl_3$

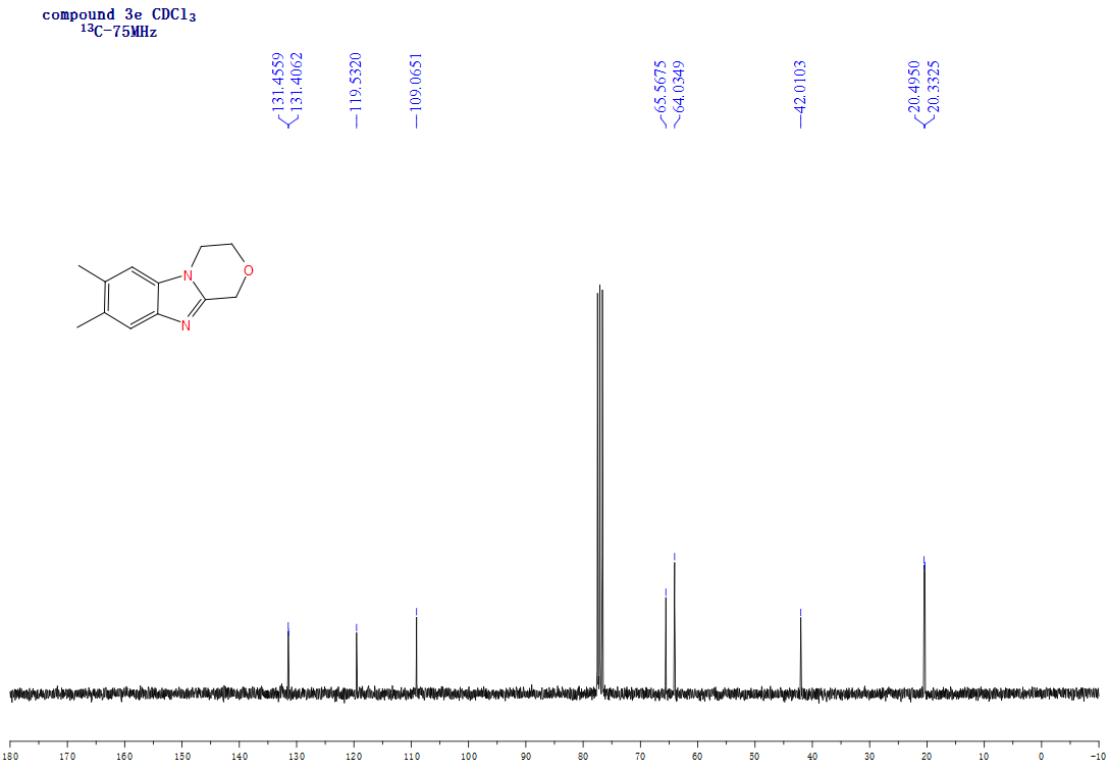

Figure S95. The ^{13}C NMR Spectrum of Compound **3e** in $CDCl_3$

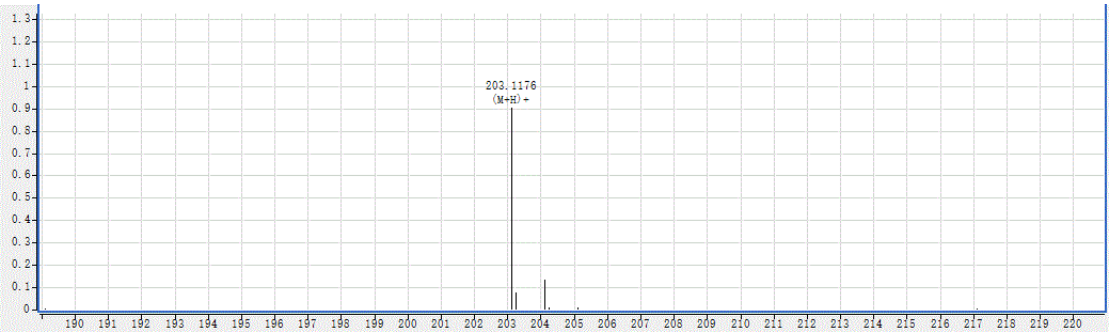

Figure S96. The HR-ESI-MS Spectrum of Compound **3e**

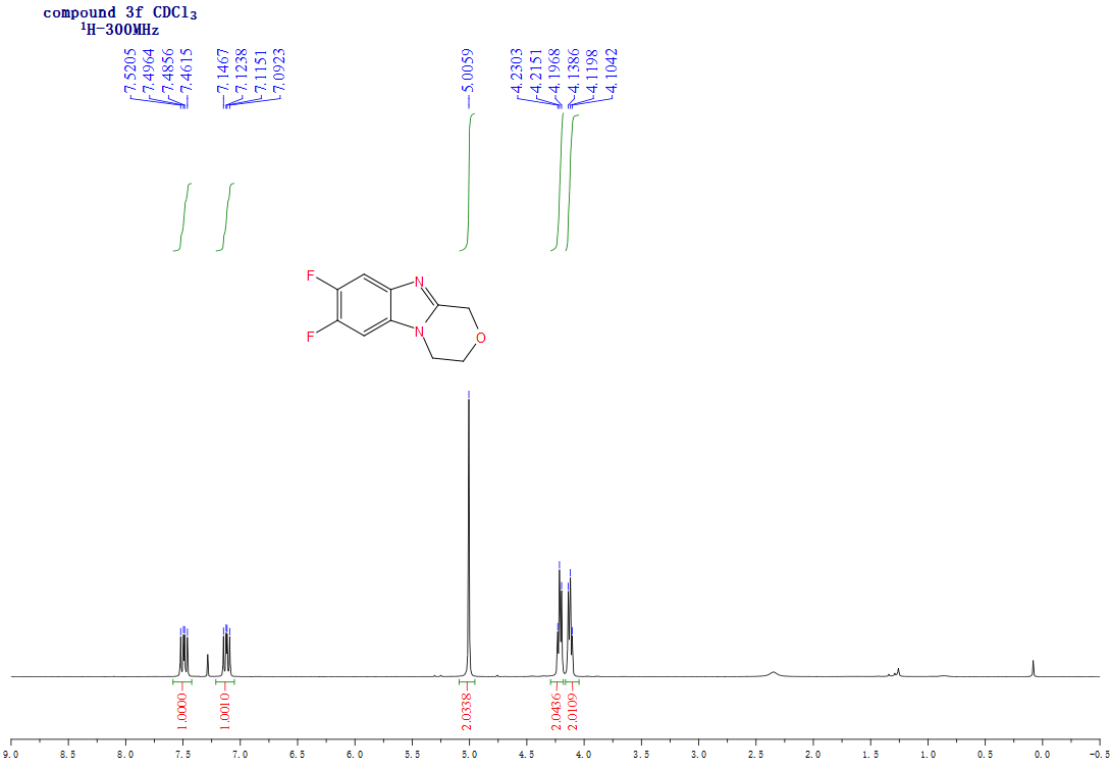

Figure S97. The ^{1}H NMR Spectrum of Compound **3f** in $CDCl_3$

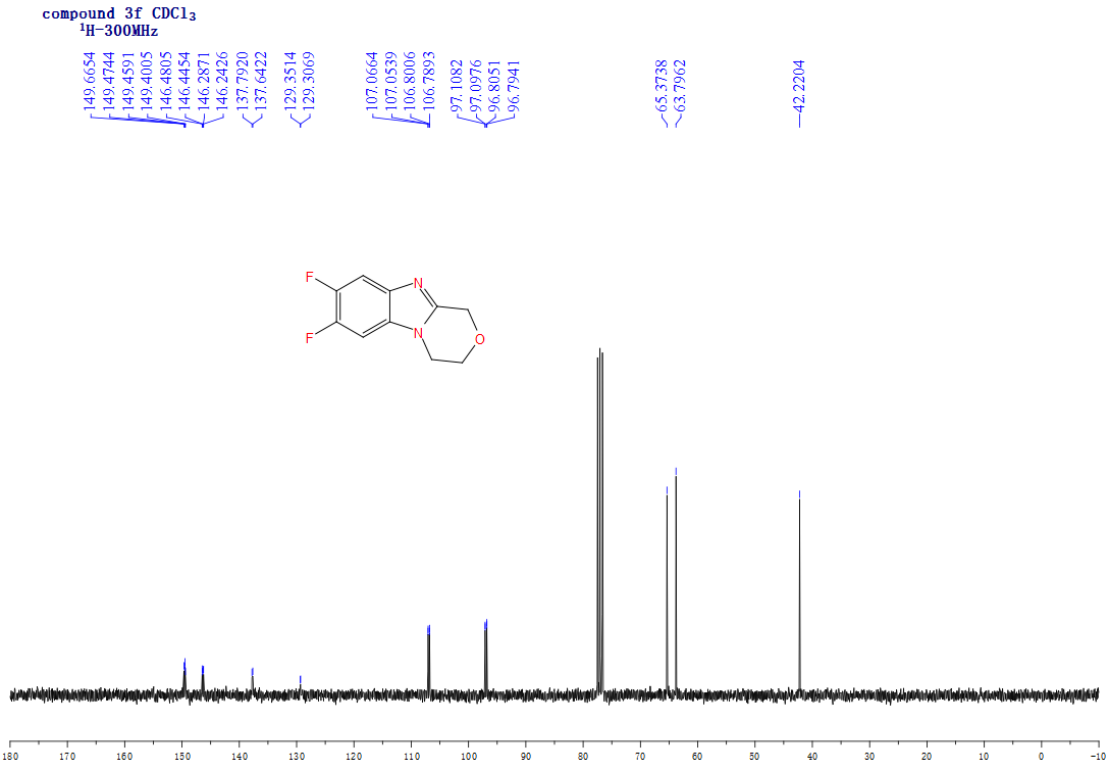

Figure S98. The ^{13}C NMR Spectrum of Compound **3f** in $CDCl_3$

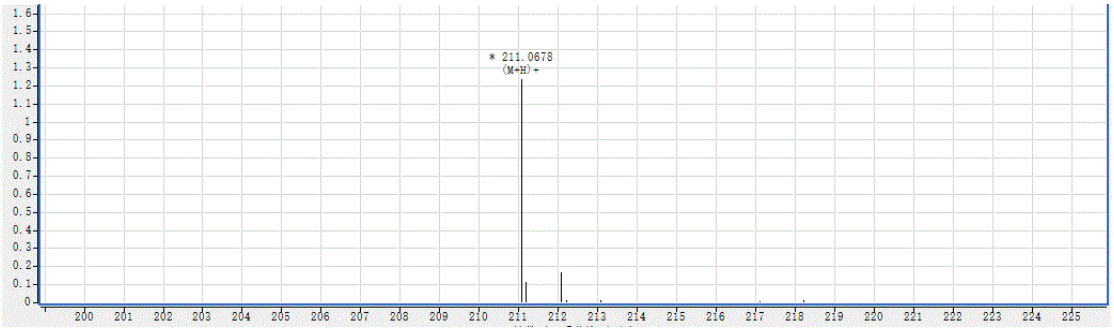

Figure S99. The HR-ESI-MS Spectrum of Compound **3f**

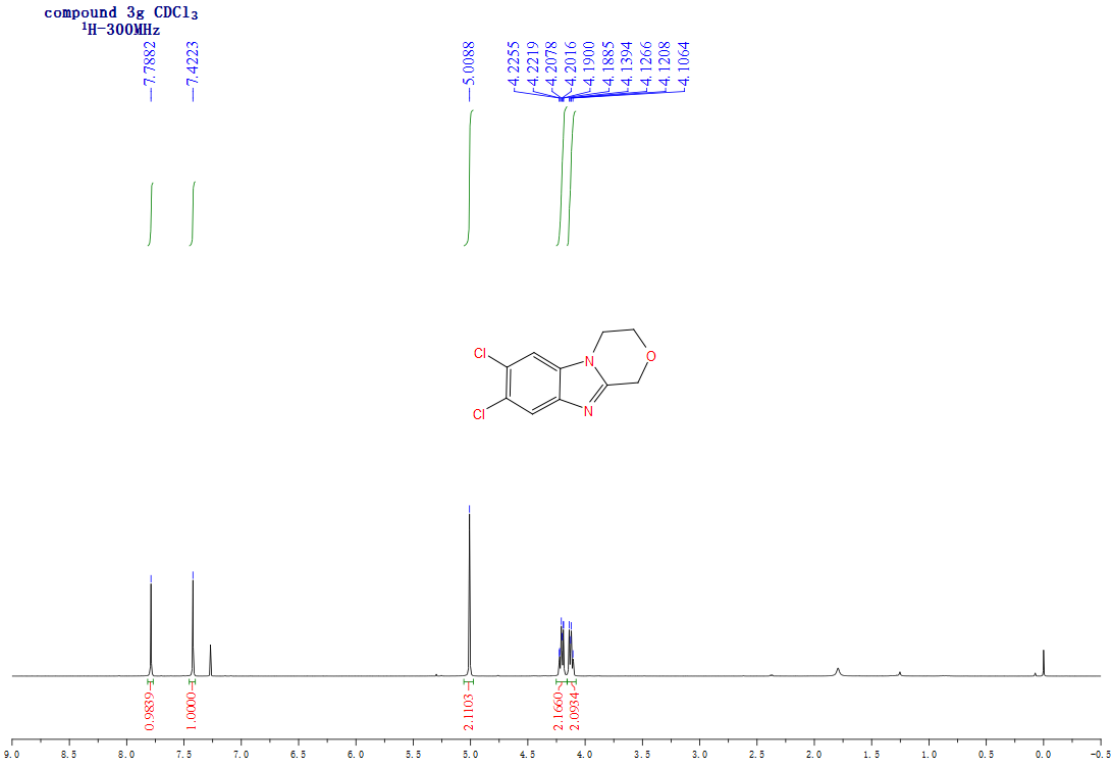

Figure S100. The ^{1}H NMR Spectrum of Compound **3g** in $CDCl_3$

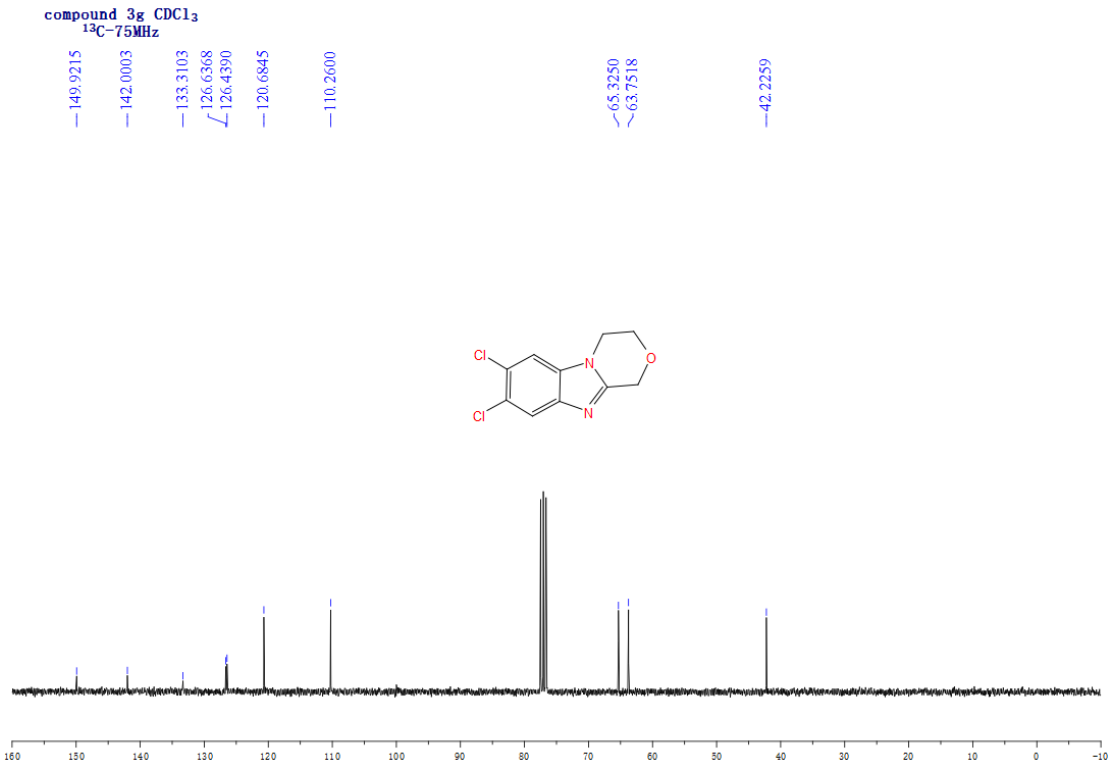

Figure S101. The ^{13}C NMR Spectrum of Compound **3g** in $CDCl_3$

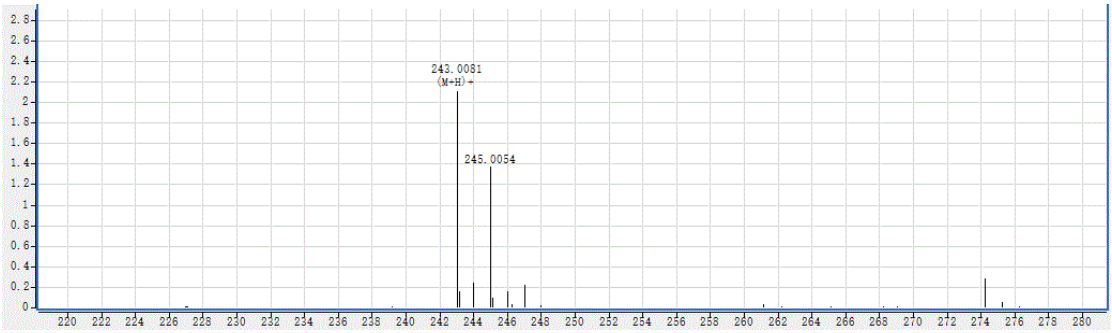

Figure S102. The HR-ESI-MS Spectrum of Compound **3g**

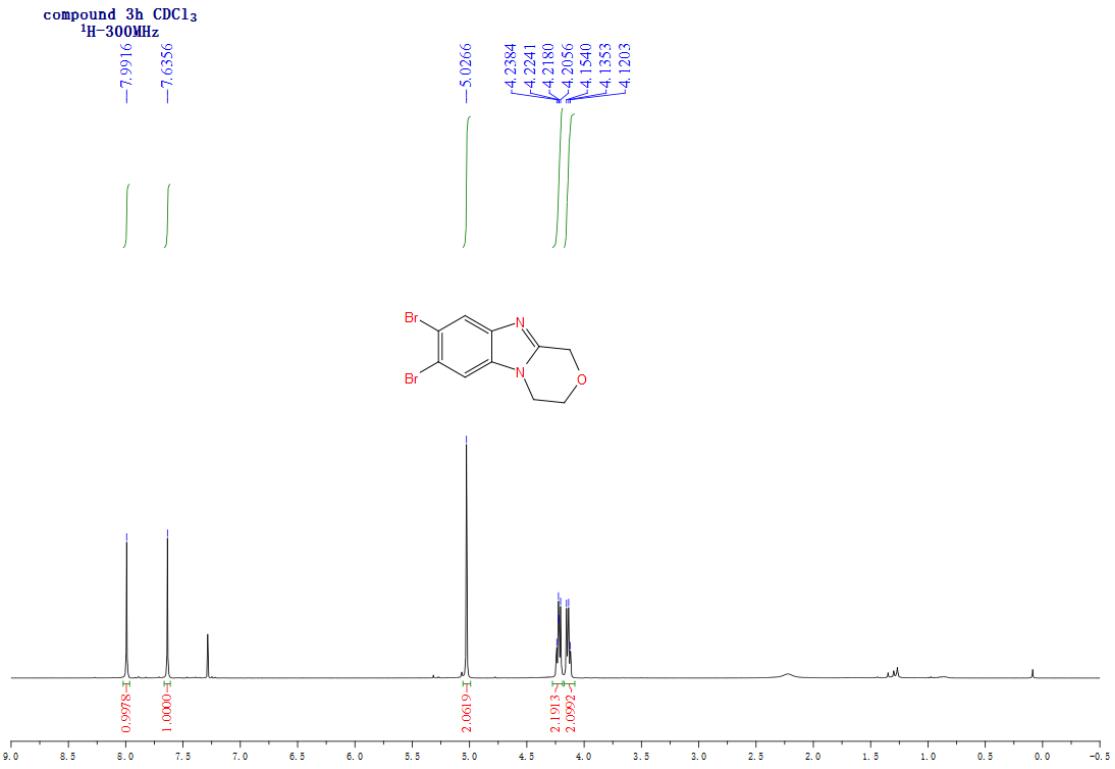

Figure S103. The ^{1}H NMR Spectrum of Compound **3h** in $CDCl_3$

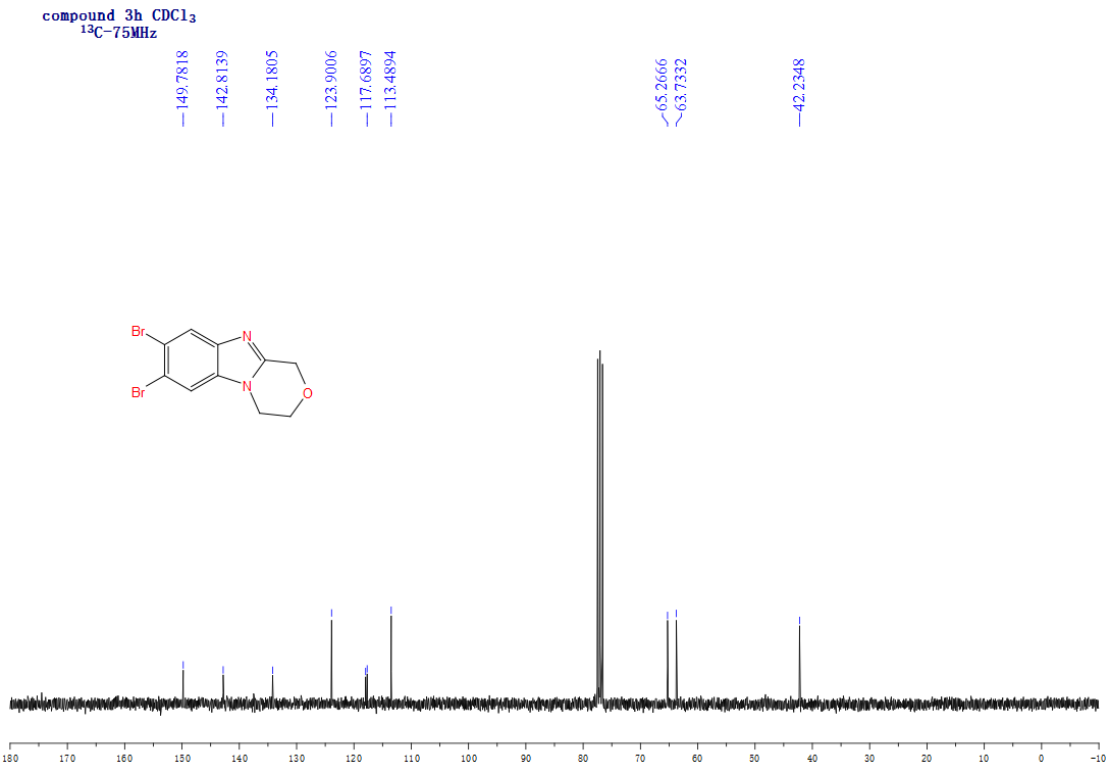

Figure S104. The ^{13}C NMR Spectrum of Compound **3h** in $CDCl_3$

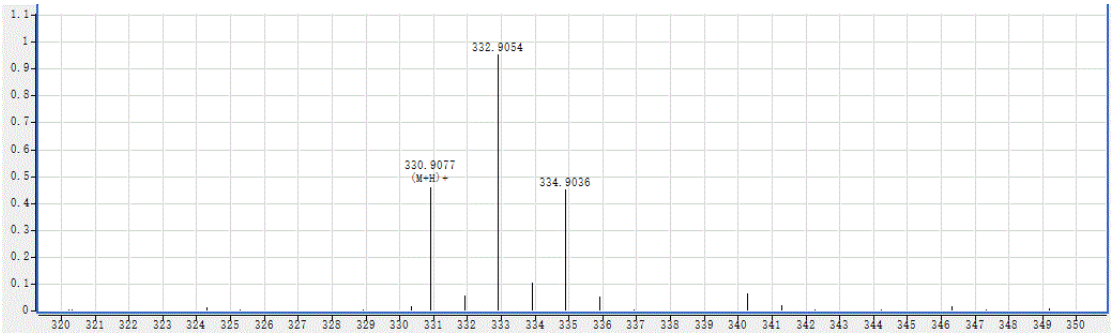

Figure S105. The HR-ESI-MS Spectrum of Compound **3h**

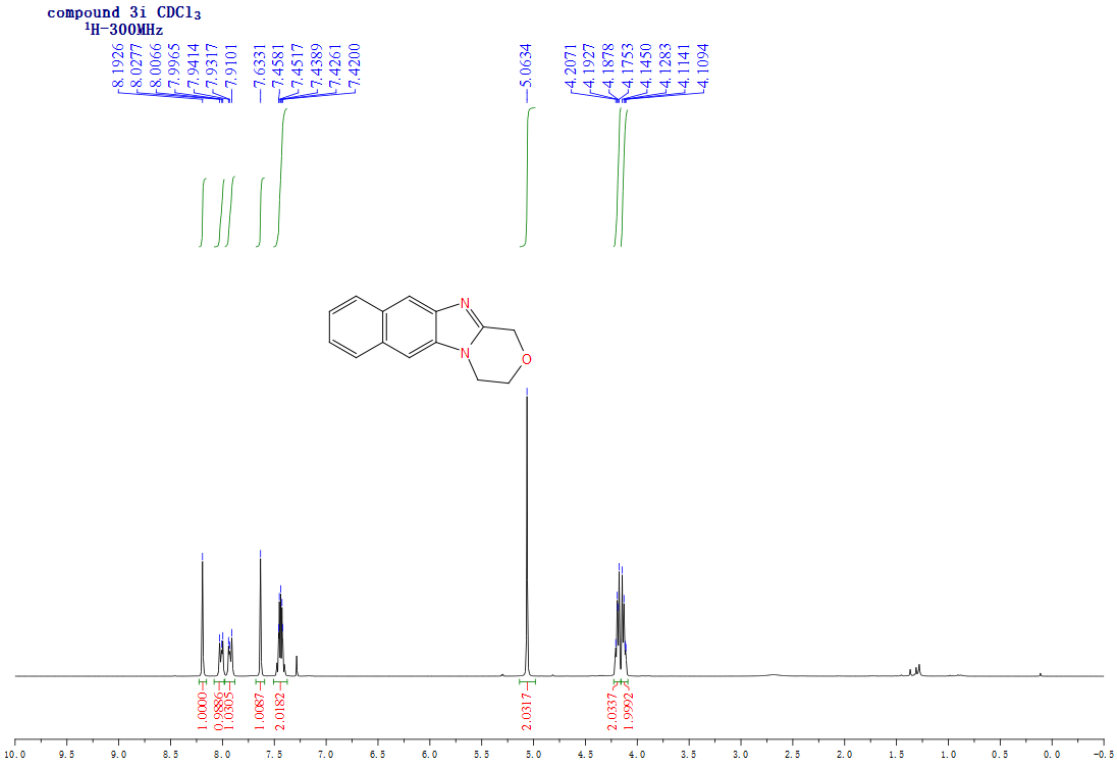

Figure S106. The ^{1}H NMR Spectrum of Compound **3i** in $CDCl_3$

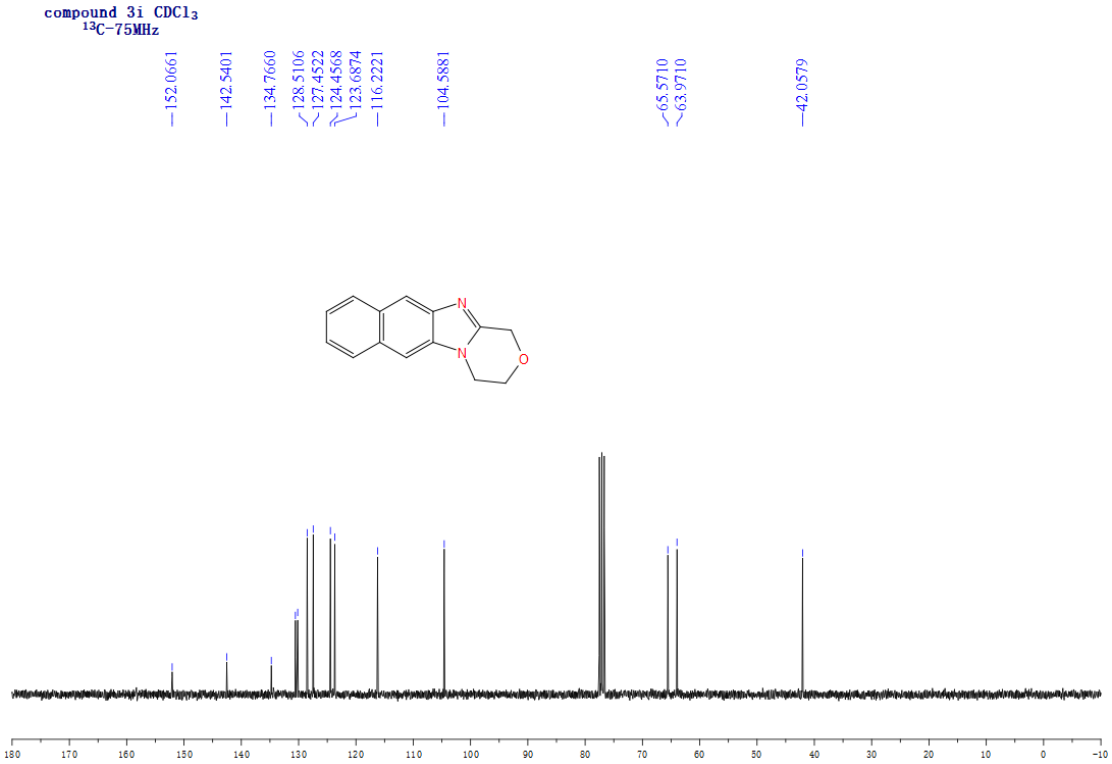

Figure S107. The ^{13}C NMR Spectrum of Compound **3i** in $CDCl_3$

Figure S108. The HR-ESI-MS Spectrum of Compound **3i**

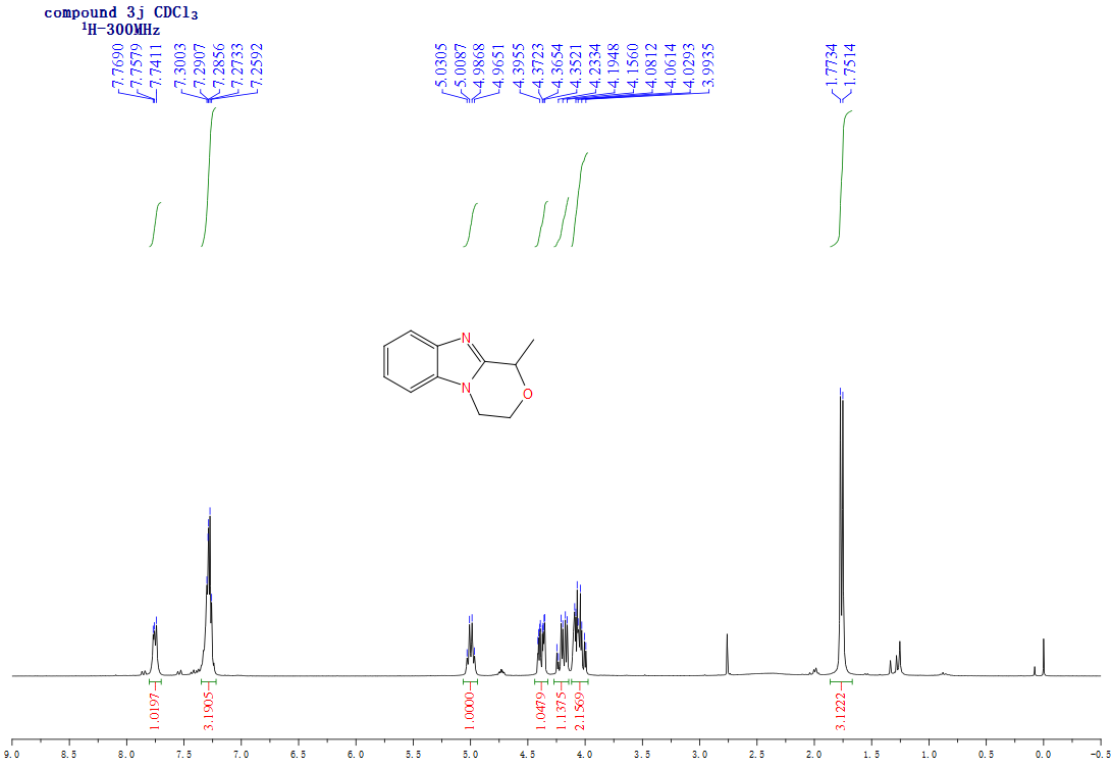

Figure S109. The ^{1}H NMR Spectrum of Compound **3j** in $CDCl_3$

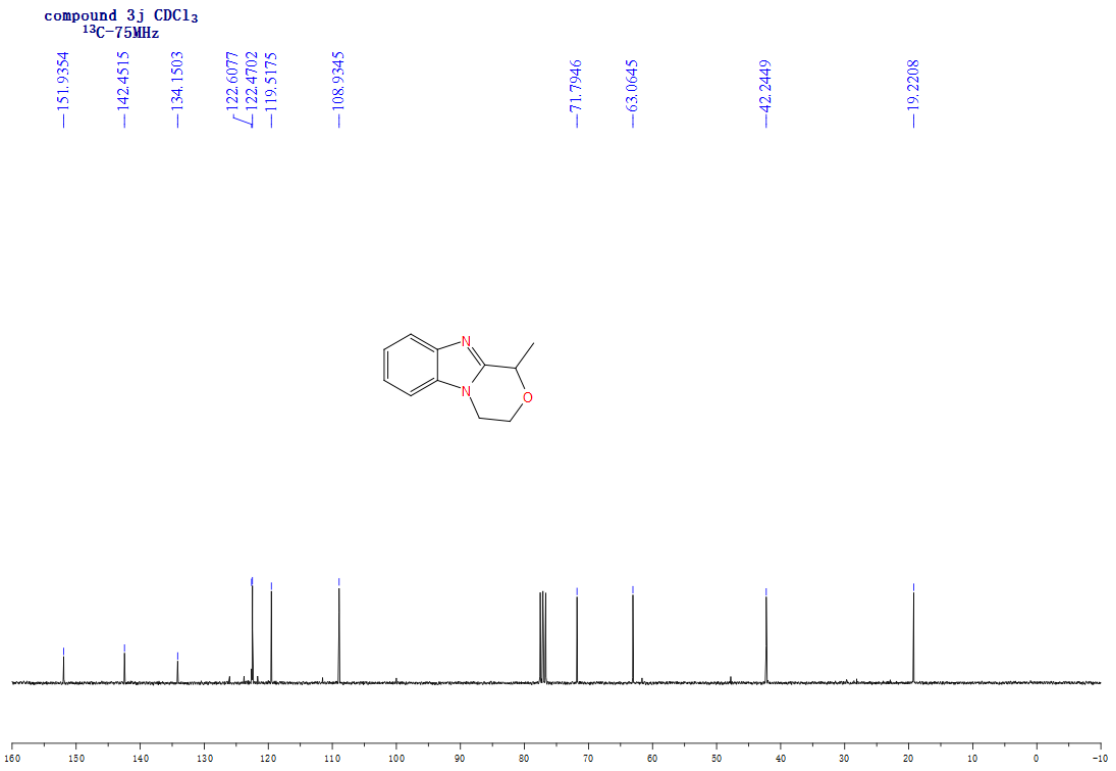

Figure S110. The ^{13}C NMR Spectrum of Compound **3j** in $CDCl_3$

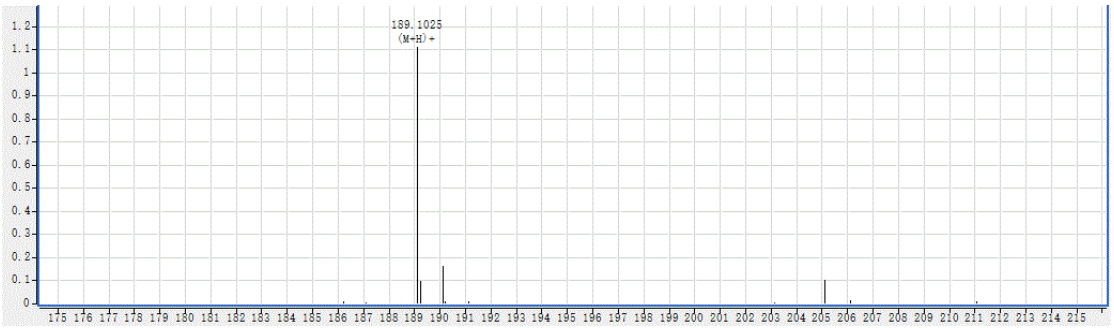

Figure S111. The HR-ESI-MS Spectrum of Compound **3j**

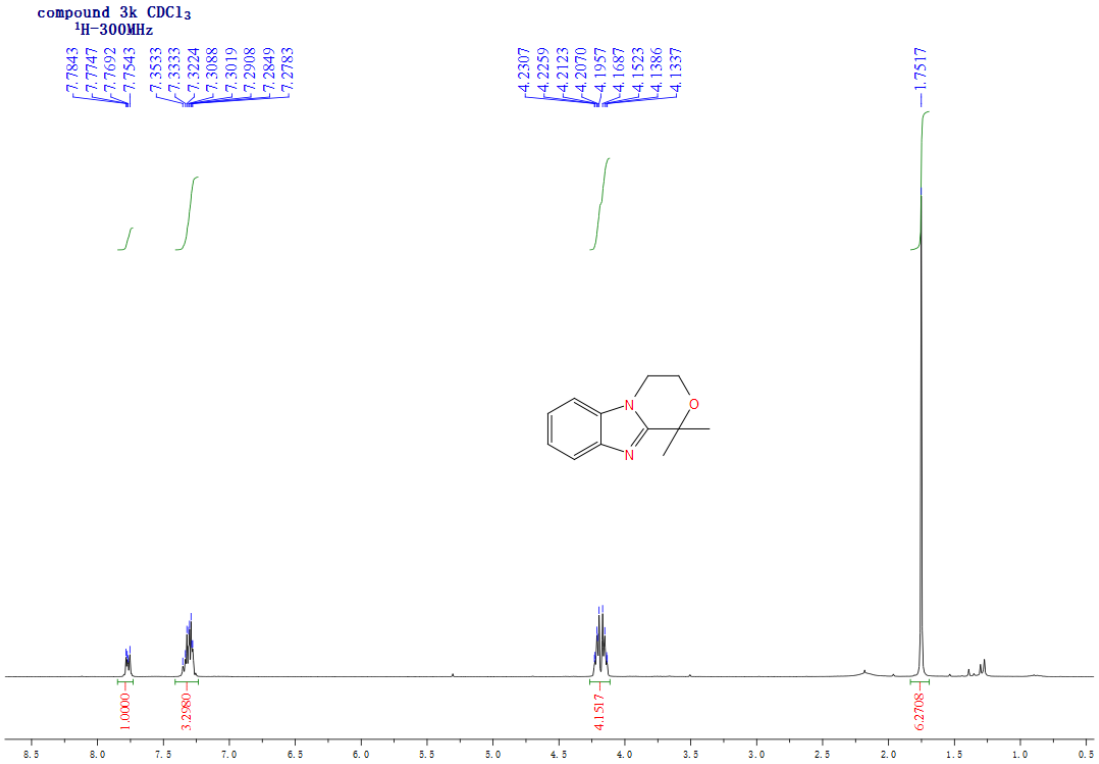

Figure S112. The ^{1}H NMR Spectrum of Compound **3k** in $CDCl_3$

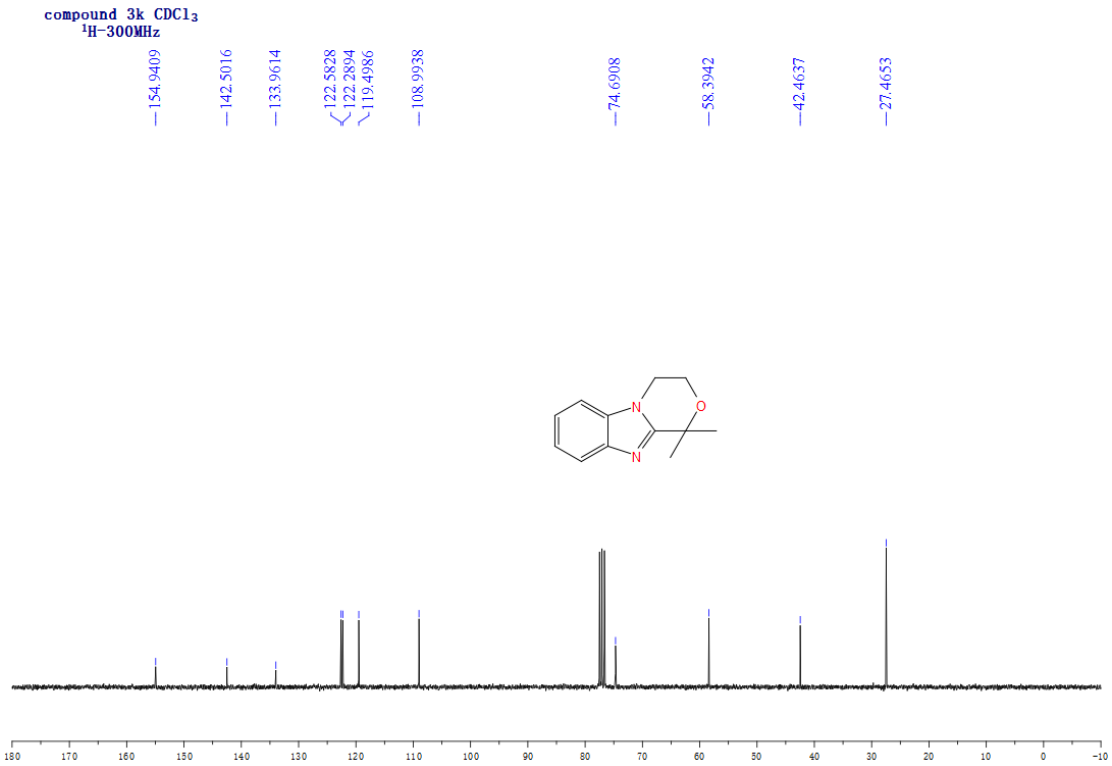

Figure S113. The ^{13}C NMR Spectrum of Compound **3k** in $CDCl_3$

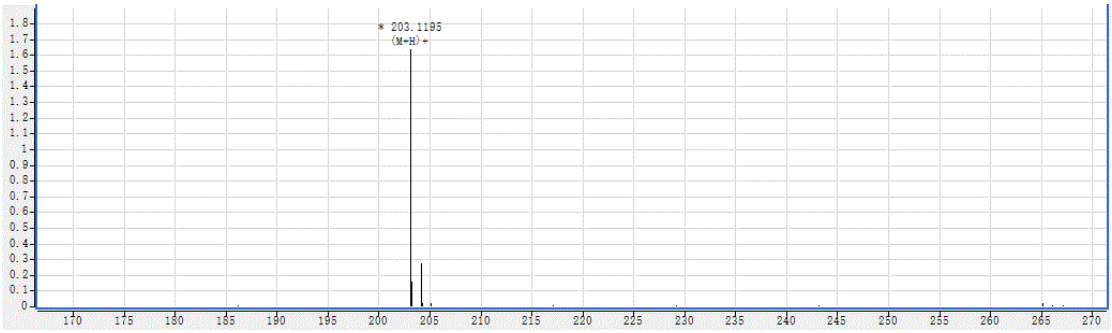

Figure S114. The HR-ESI-MS Spectrum of Compound **3k**

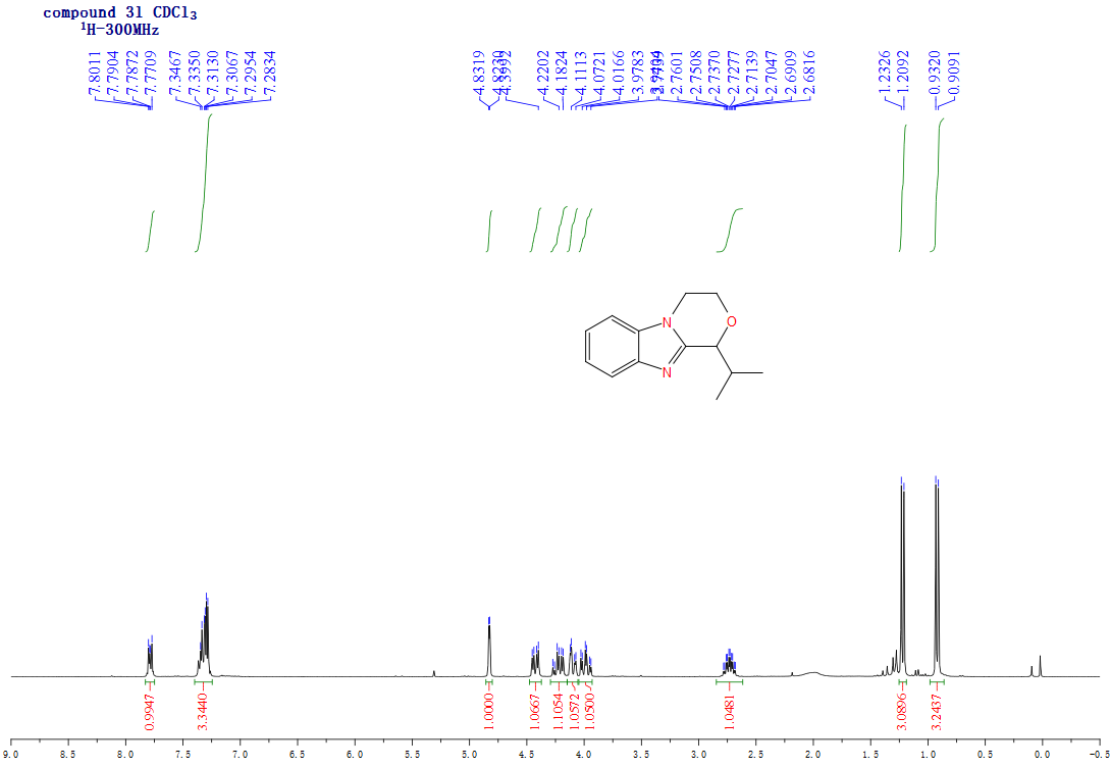

Figure S115. The ^{1}H NMR Spectrum of Compound **3l** in $CDCl_3$

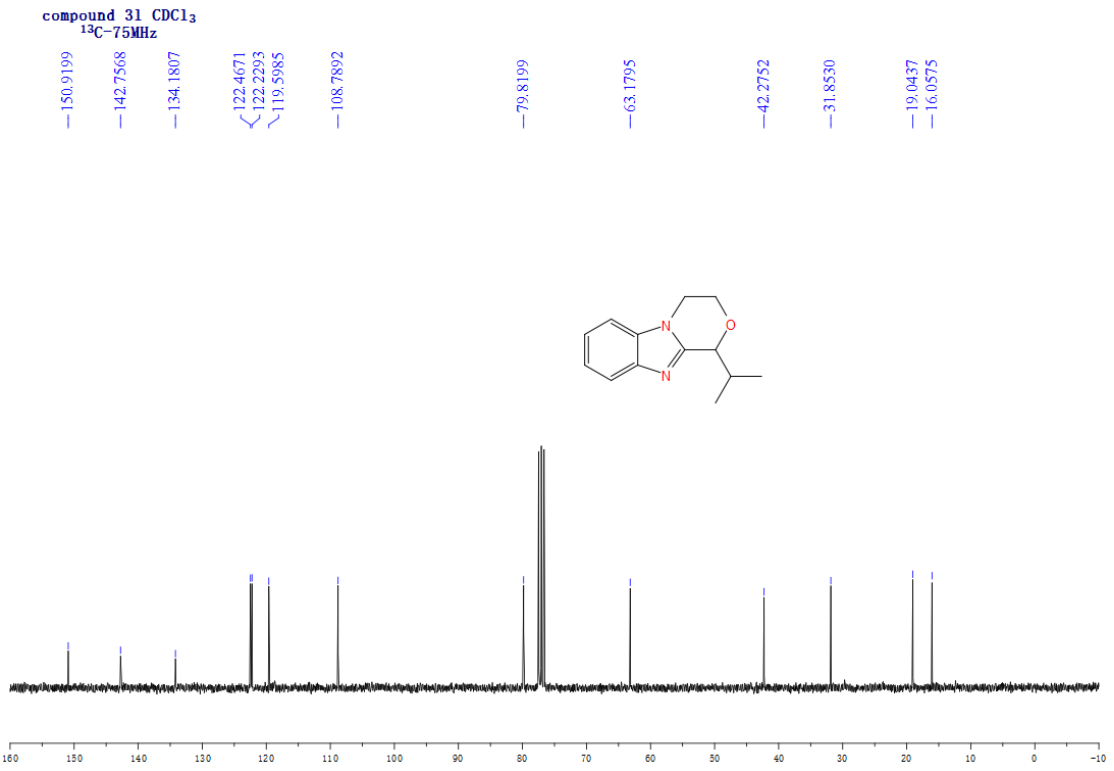

Figure S116. The ^{13}C NMR Spectrum of Compound **3l** in $CDCl_3$

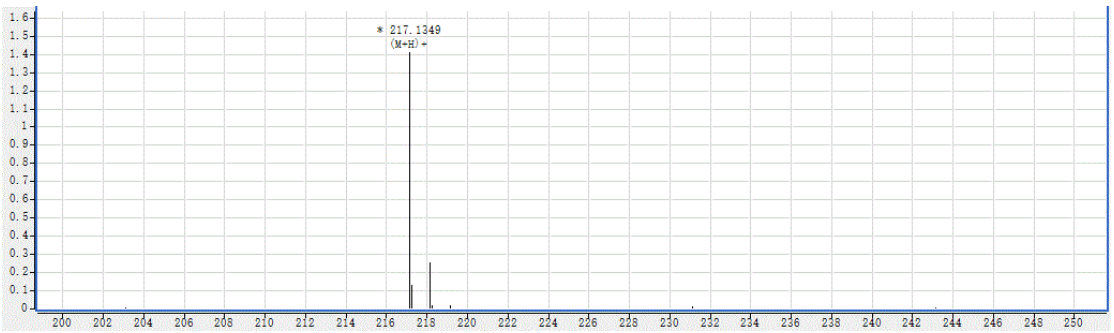

Figure S117. The HR-ESI-MS Spectrum of Compound **3l**

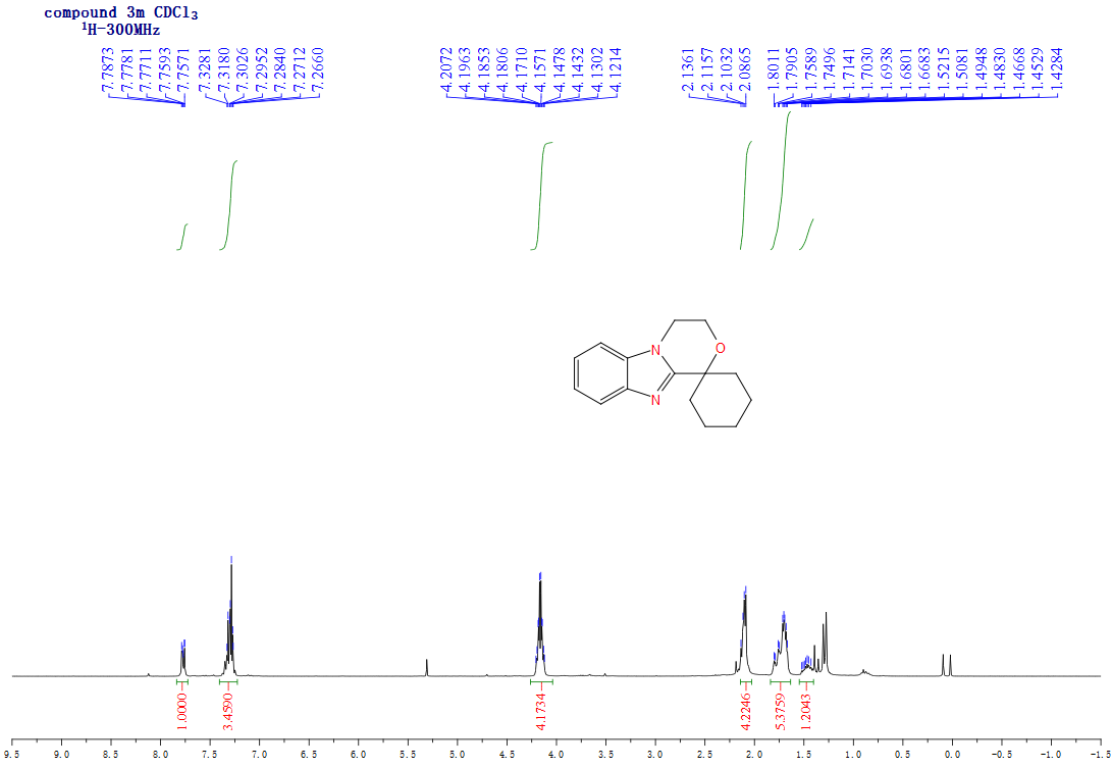

Figure S118. The ^{1}H NMR Spectrum of Compound **3m** in $CDCl_3$

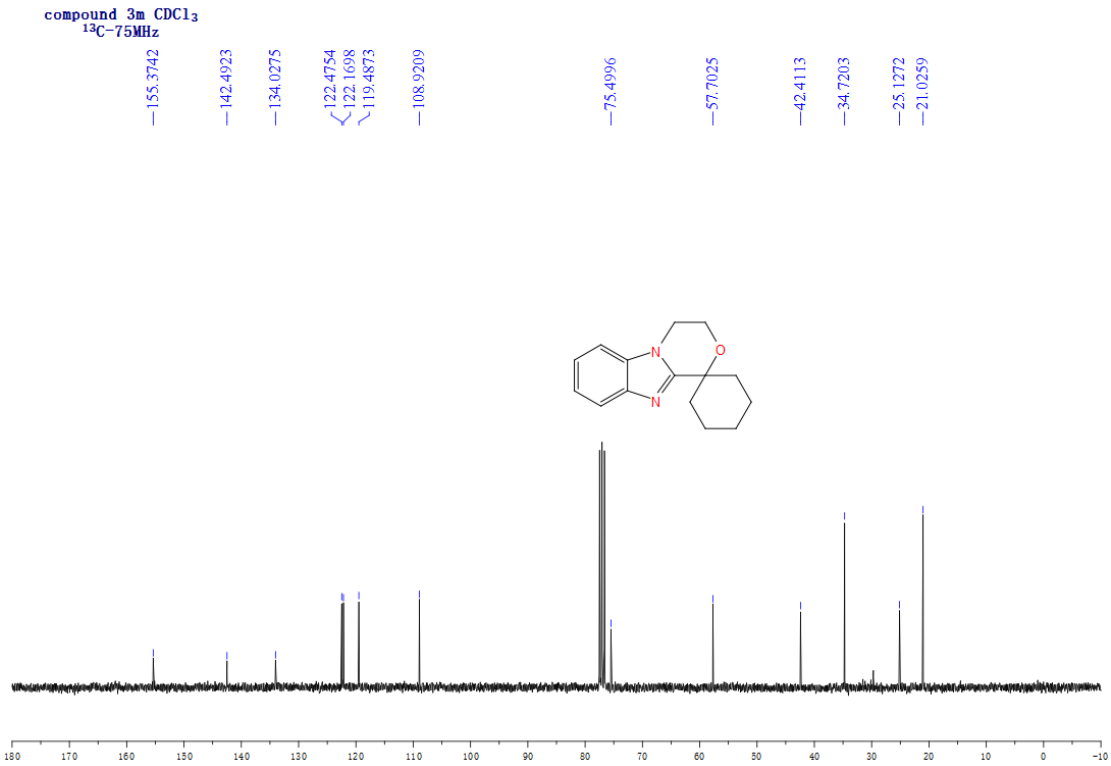

Figure S119. The ^{13}C NMR Spectrum of Compound **3m** in $CDCl_3$

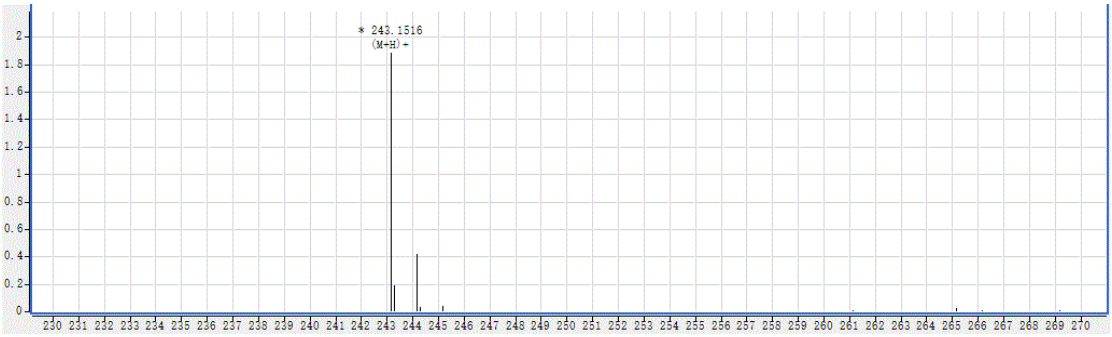

Figure S120. The HR-ESI-MS Spectrum of Compound **3m**

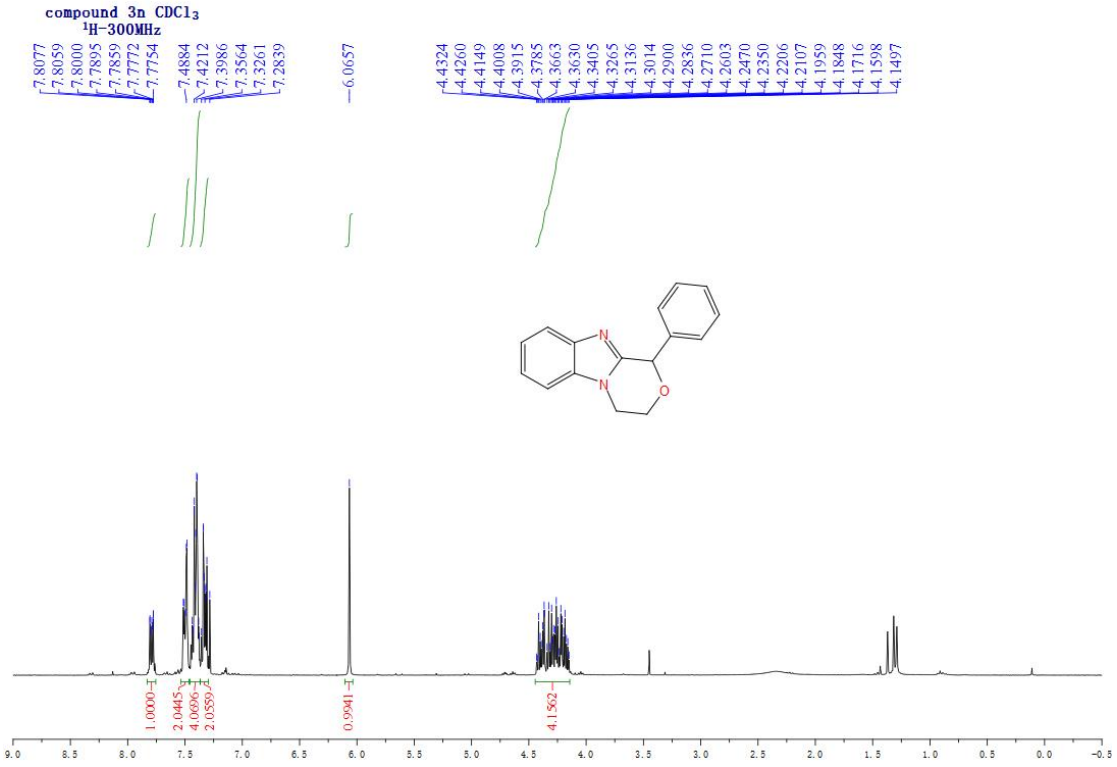

Figure S121. The ^{1}H NMR Spectrum of Compound **3n** in $CDCl_3$

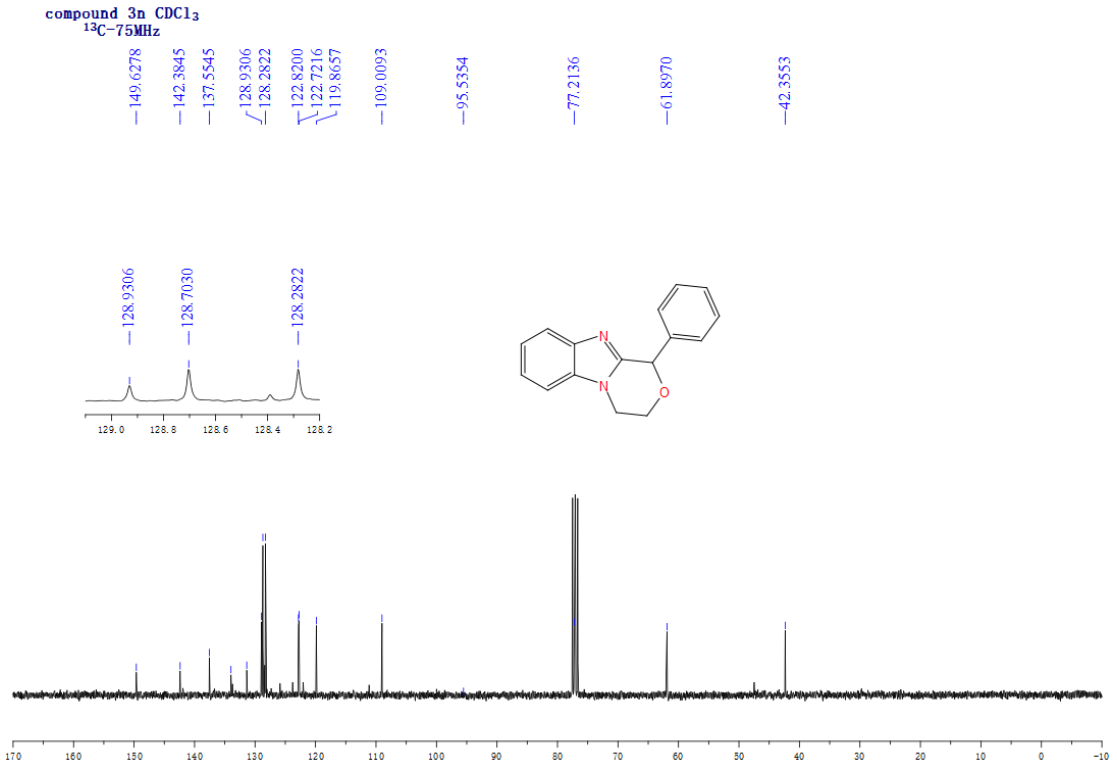

Figure S122. The ^{13}C NMR Spectrum of Compound **3n** in $CDCl_3$

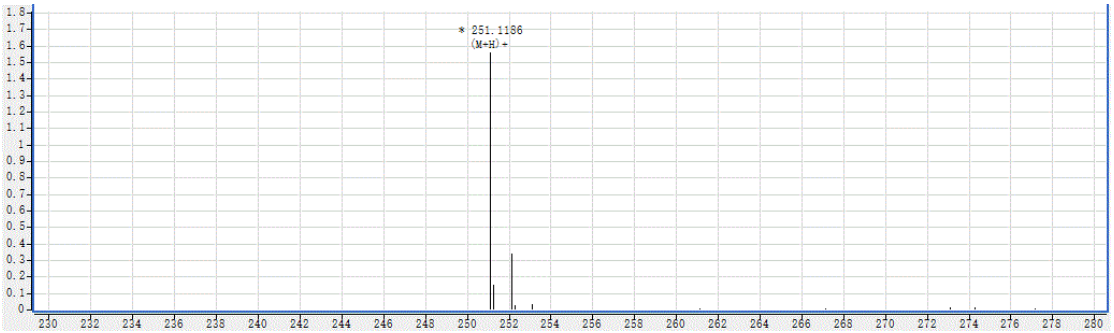

Figure S123. The HR-ESI-MS Spectrum of Compound **3n**

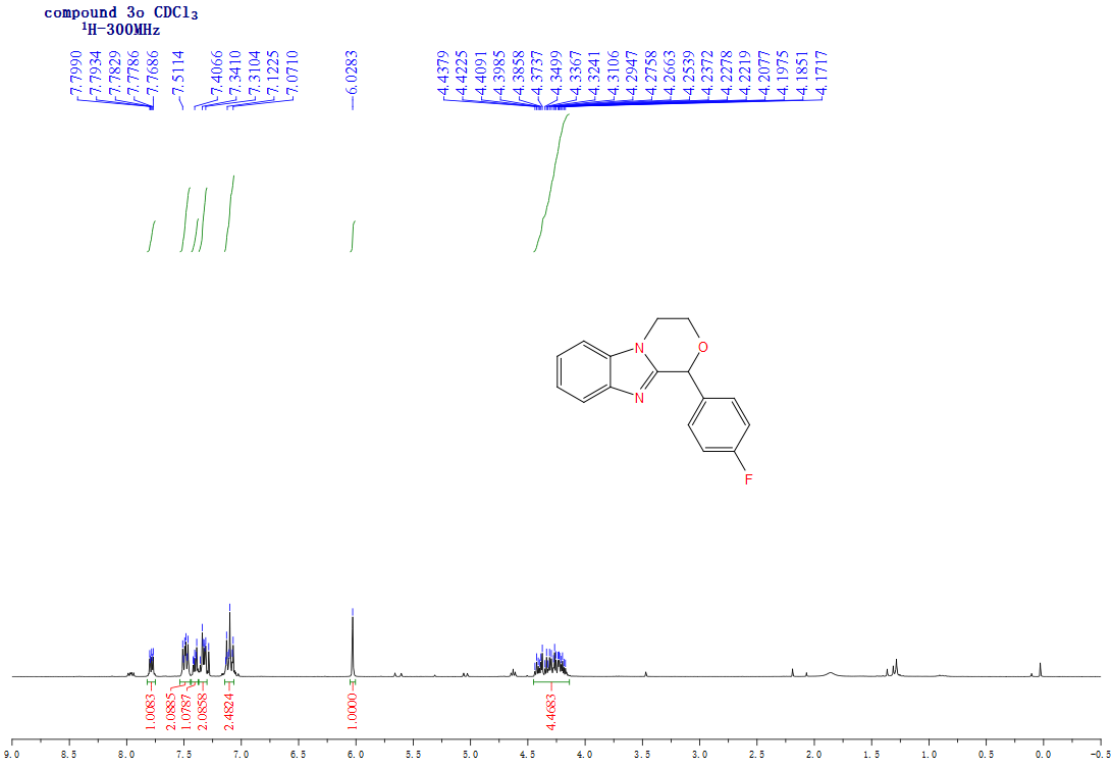

Figure S124. The ^{1}H NMR Spectrum of Compound **3o** in $CDCl_3$

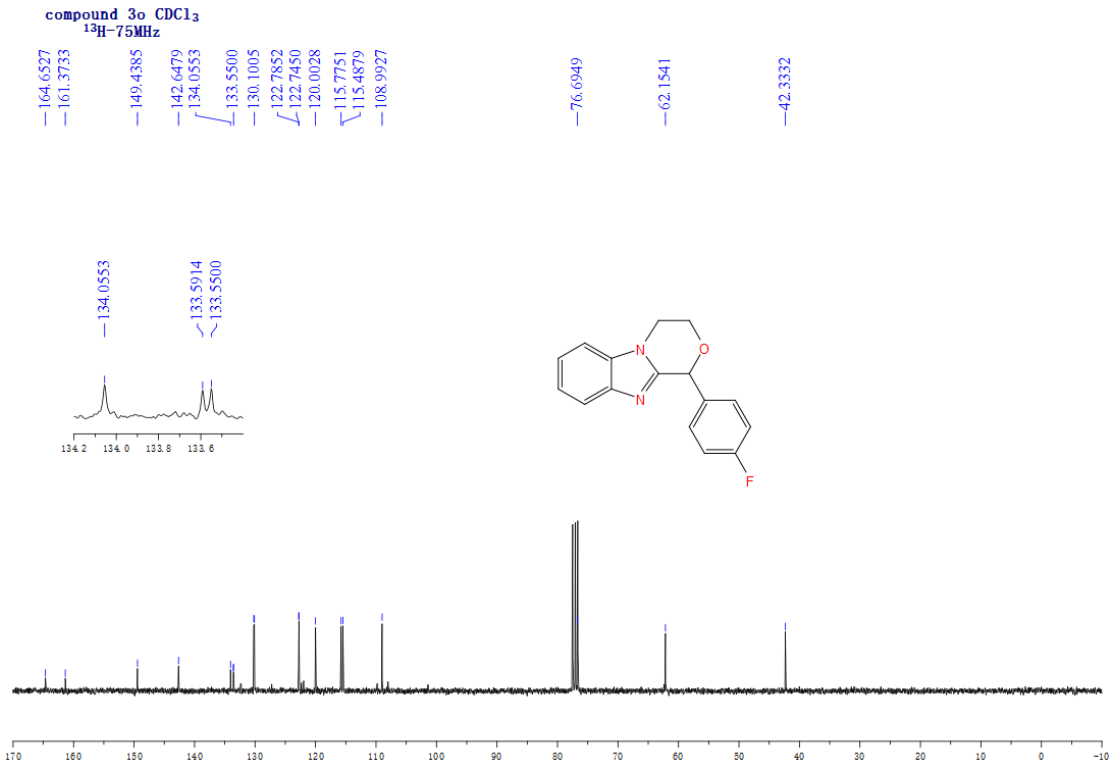

Figure S125. The ^{13}C NMR Spectrum of Compound **3o** in $CDCl_3$

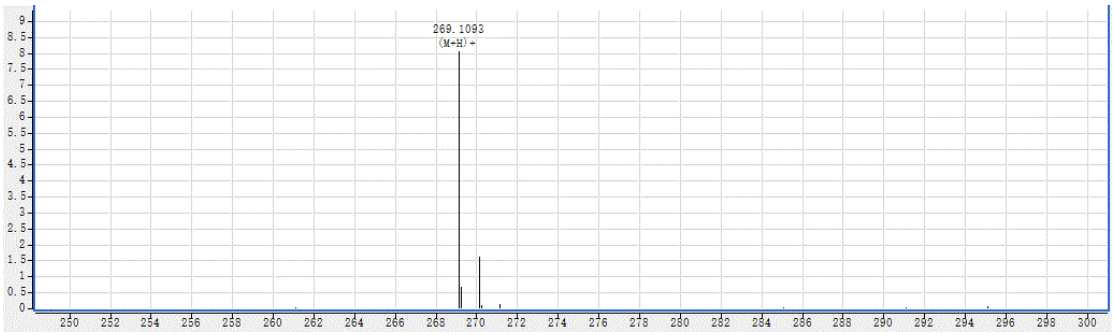

Figure S126. The HR-ESI-MS Spectrum of Compound **3o**

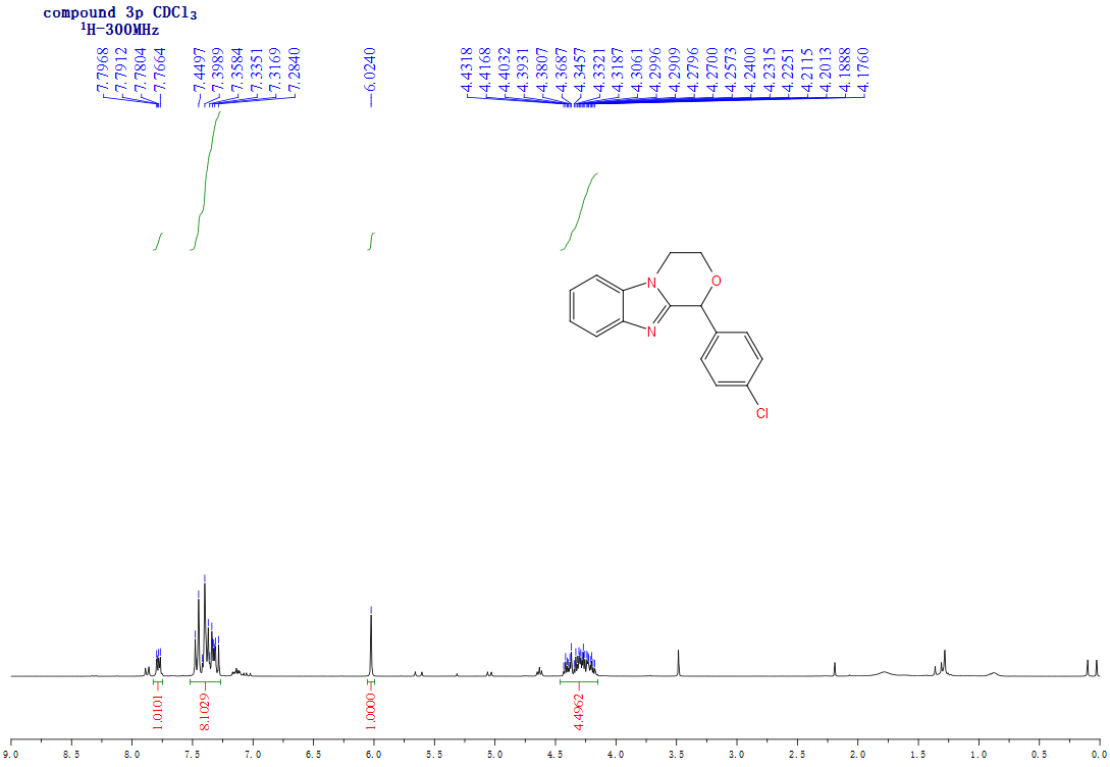

Figure S127. The ^{1}H NMR Spectrum of Compound **3p** in $CDCl_3$

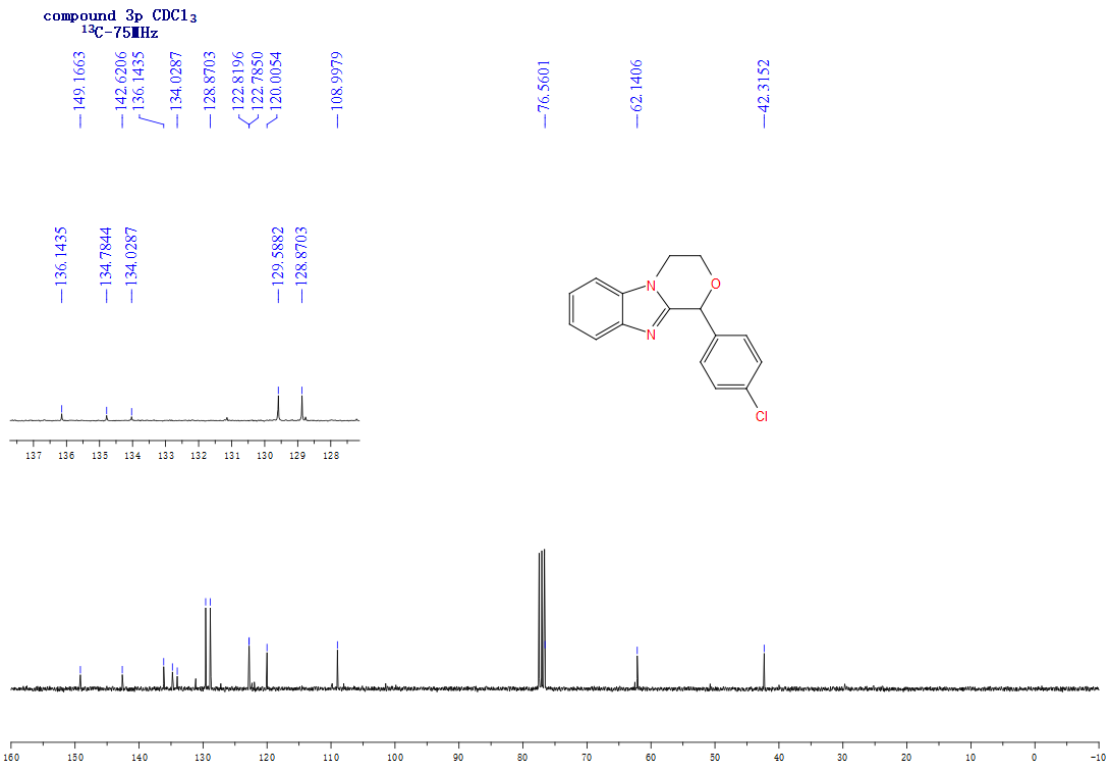

Figure S128. The ^{13}C NMR Spectrum of Compound **3p** in $CDCl_3$

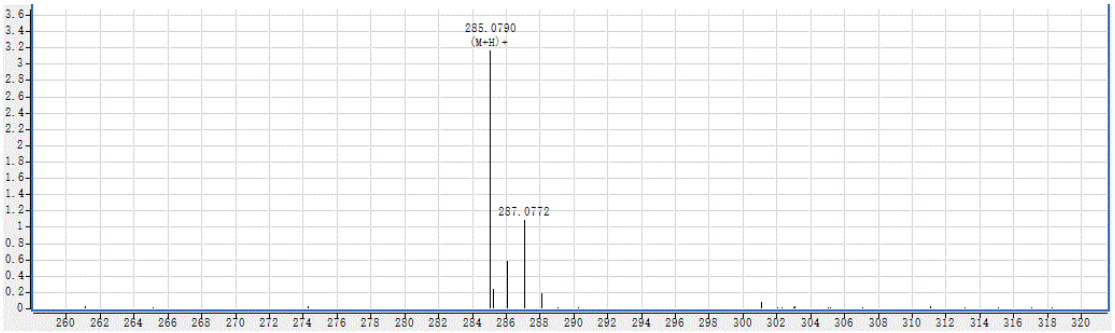

Figure S129. The HR-ESI-MS Spectrum of Compound **3p**

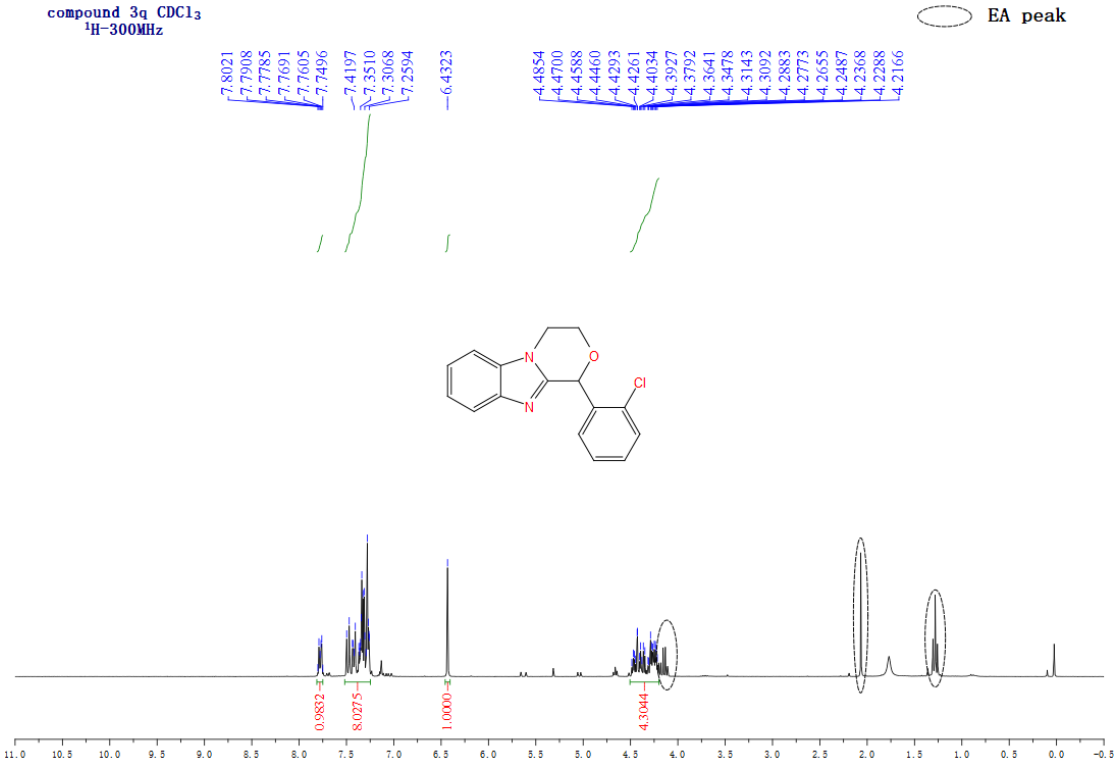

Figure S130. The ^{1}H NMR Spectrum of Compound **3q** in $CDCl_3$

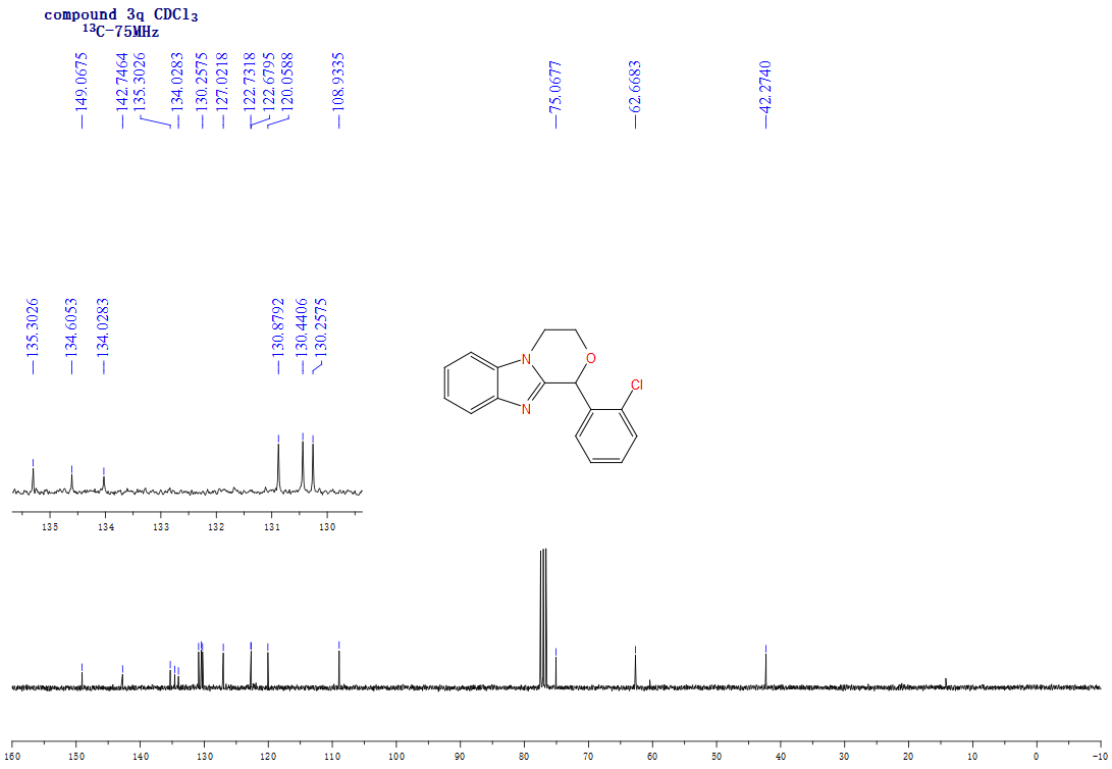

Figure S131. The ^{13}C NMR Spectrum of Compound **3q** in $CDCl_3$

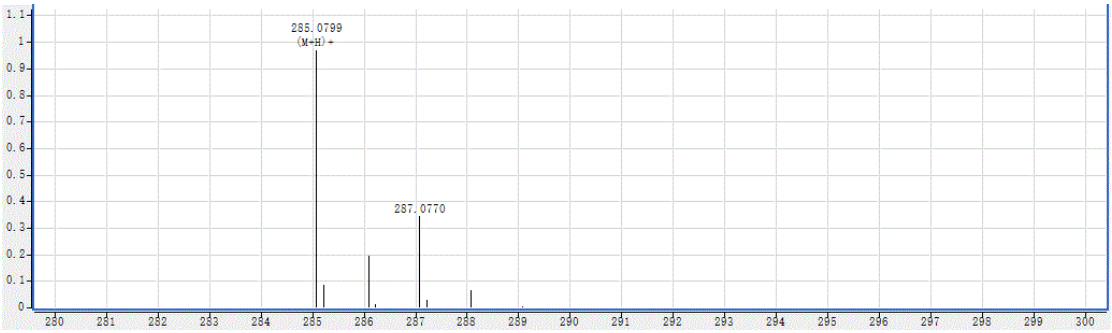

Figure S132. The HR-ESI-MS Spectrum of Compound **3q**

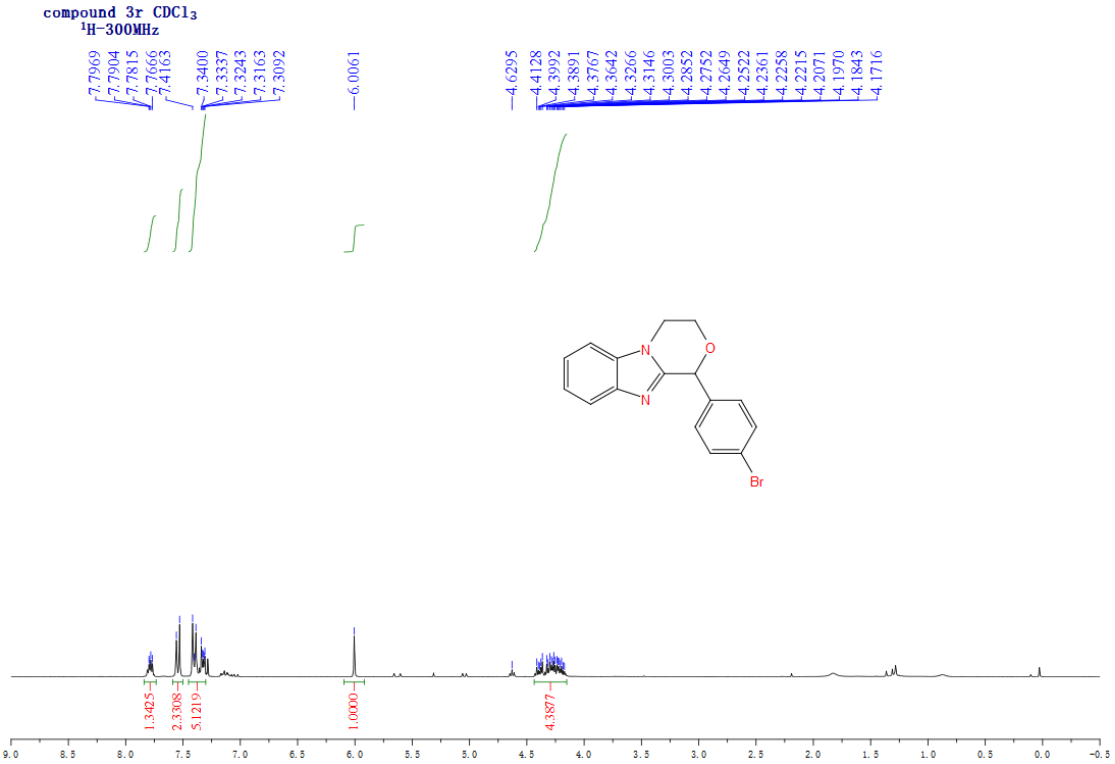

Figure S133. The ^{1}H NMR Spectrum of Compound **3r** in $CDCl_3$

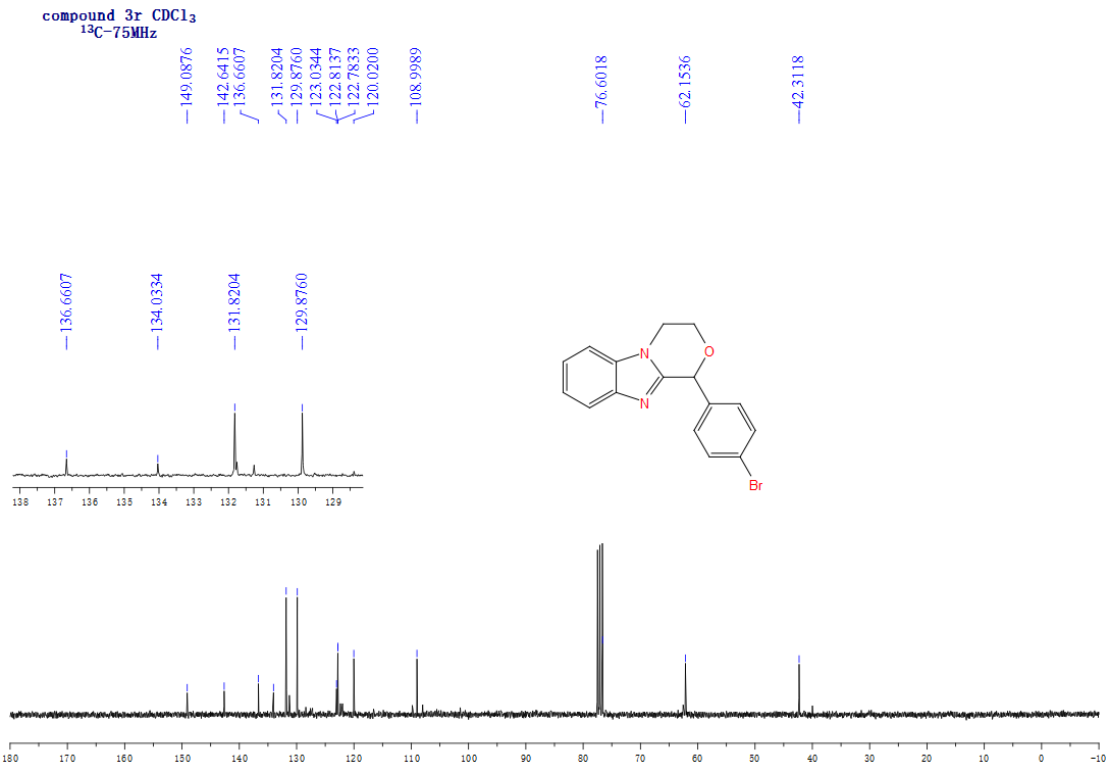

Figure S134. The ^{13}C NMR Spectrum of Compound **3r** in $CDCl_3$

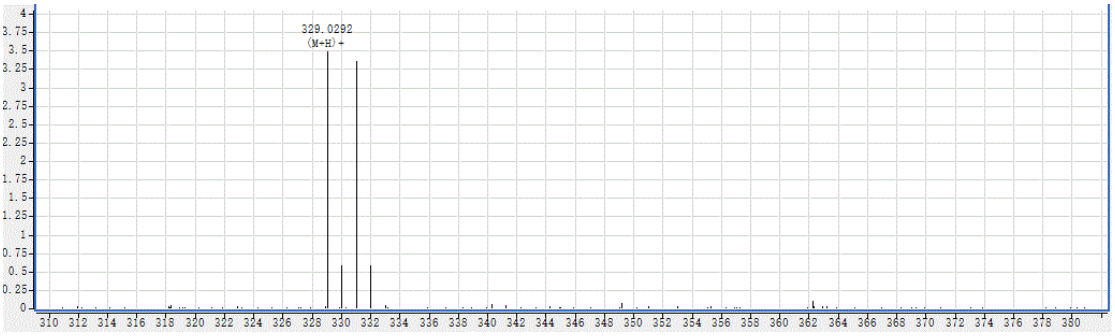

Figure S135. The HR-ESI-MS Spectrum of Compound **3r**

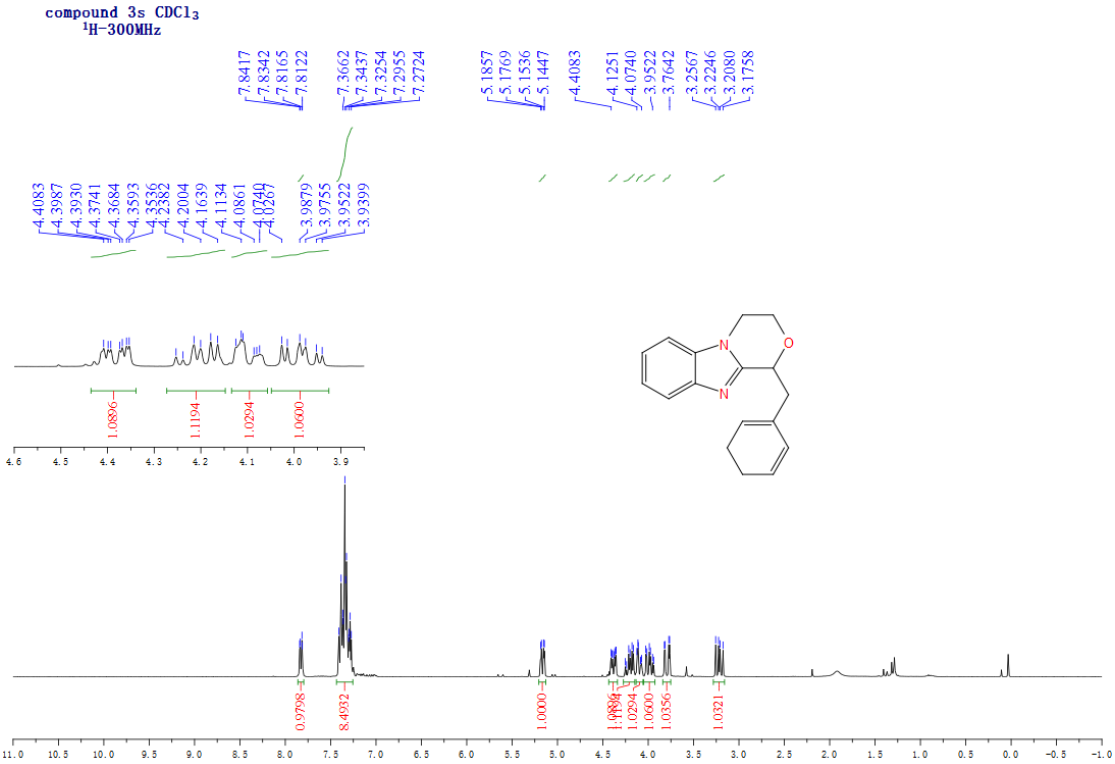

Figure S136. The ^{1}H NMR Spectrum of Compound **3s** in $CDCl_3$

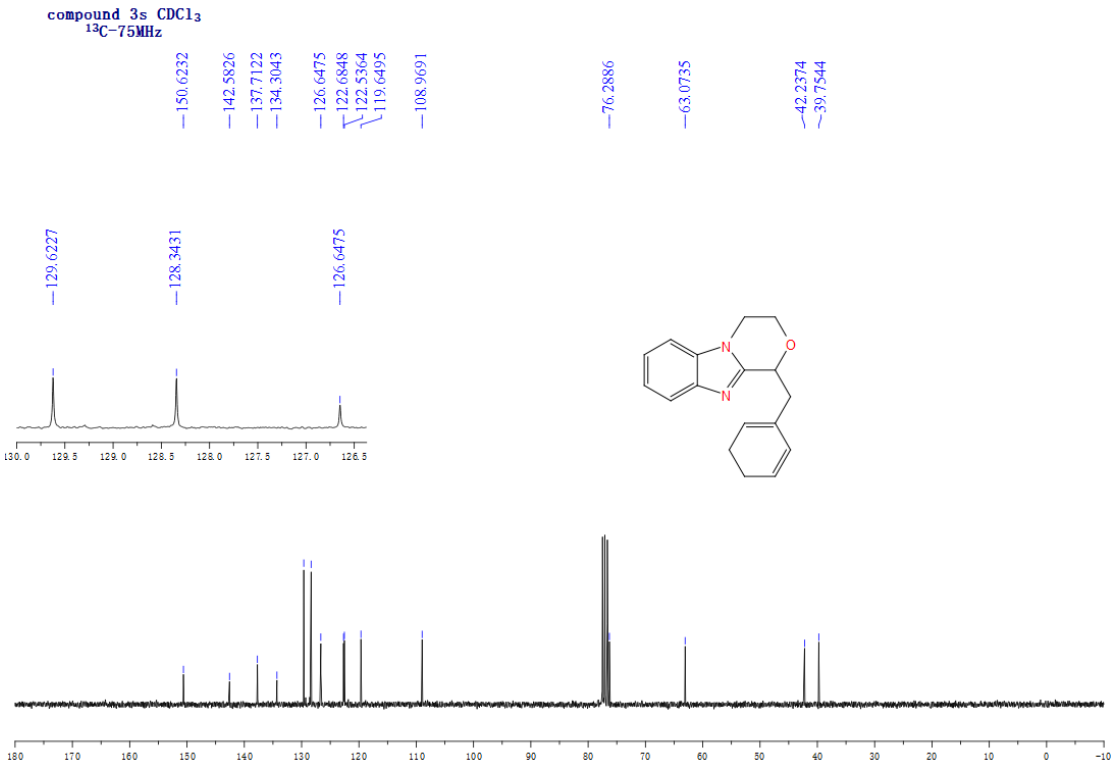

Figure S137. The ^{13}C NMR Spectrum of Compound **3s** in $CDCl_3$

Figure S138. The HR-ESI-MS Spectrum of Compound **3s**

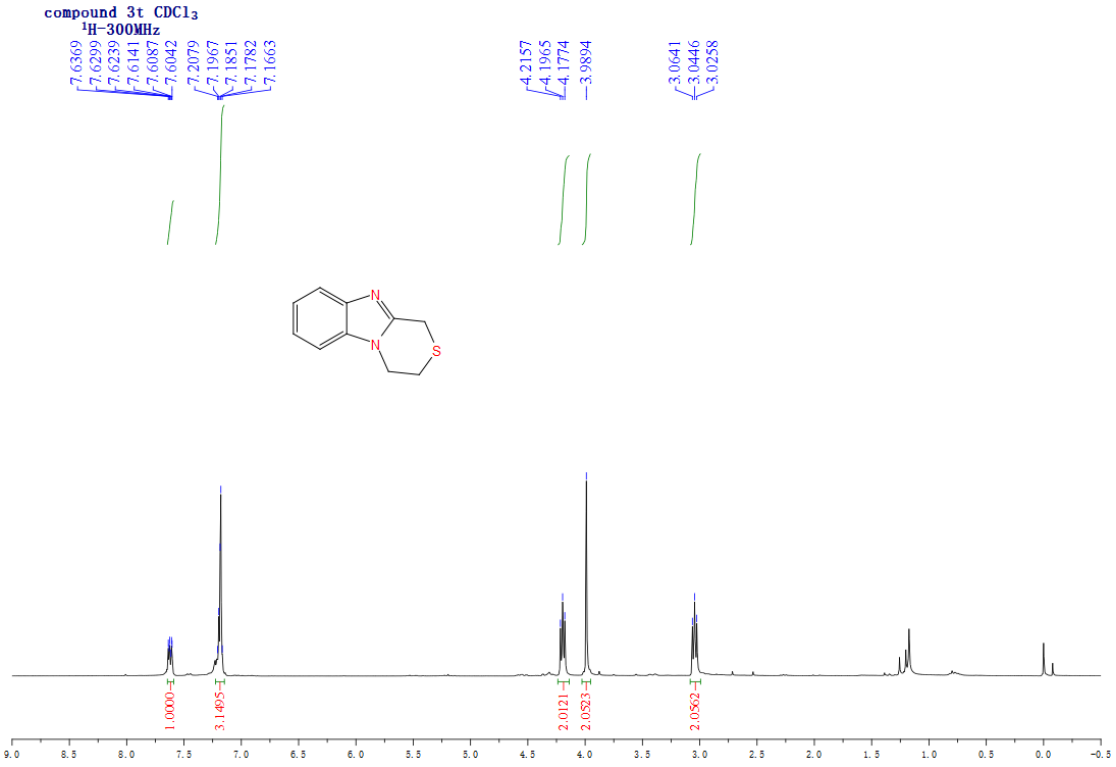

Figure S139. The ^{1}H NMR Spectrum of Compound **3t** in $CDCl_3$

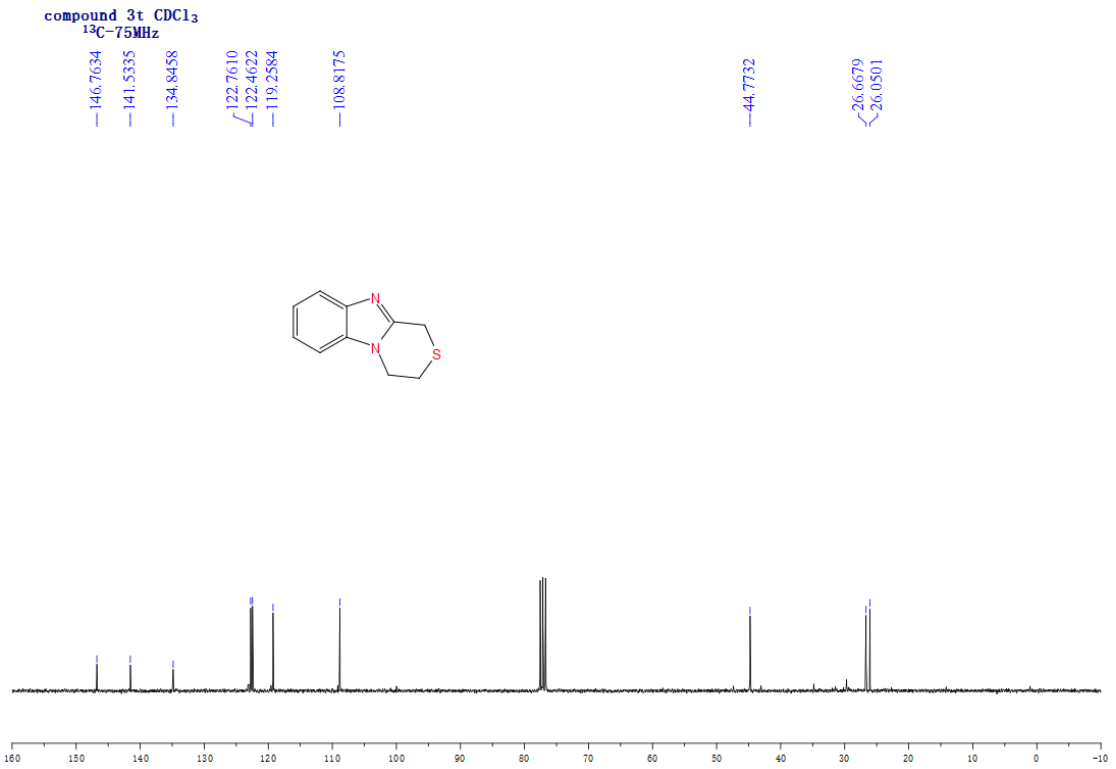

Figure S140. The ^{13}C NMR Spectrum of Compound **3t** in $CDCl_3$

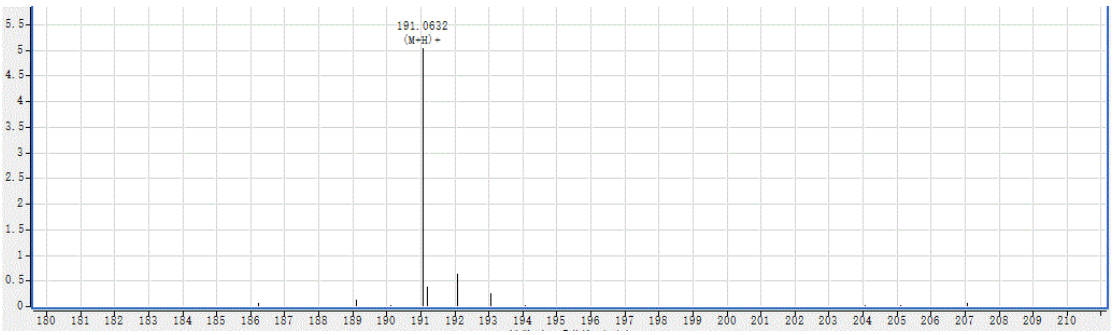

Figure S141. The HR-ESI-MS Spectrum of Compound **3t**

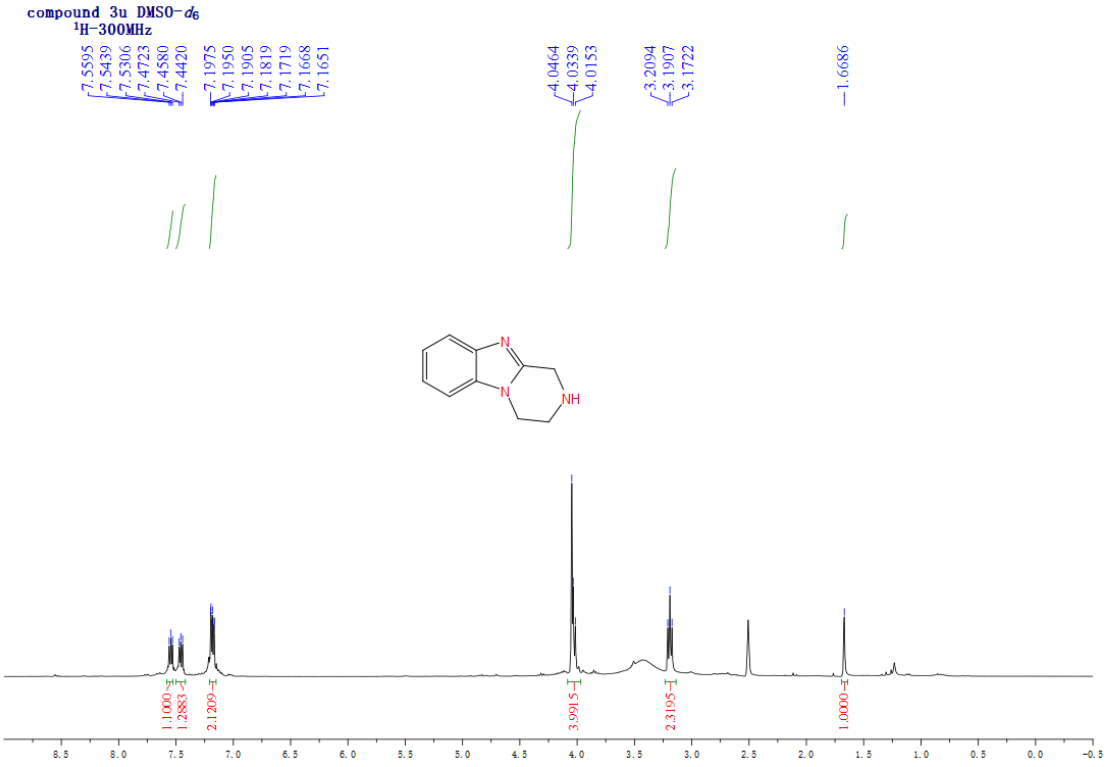

Figure S142. The ^{1}H NMR Spectrum of Compound **3u** in DMSO-d_6

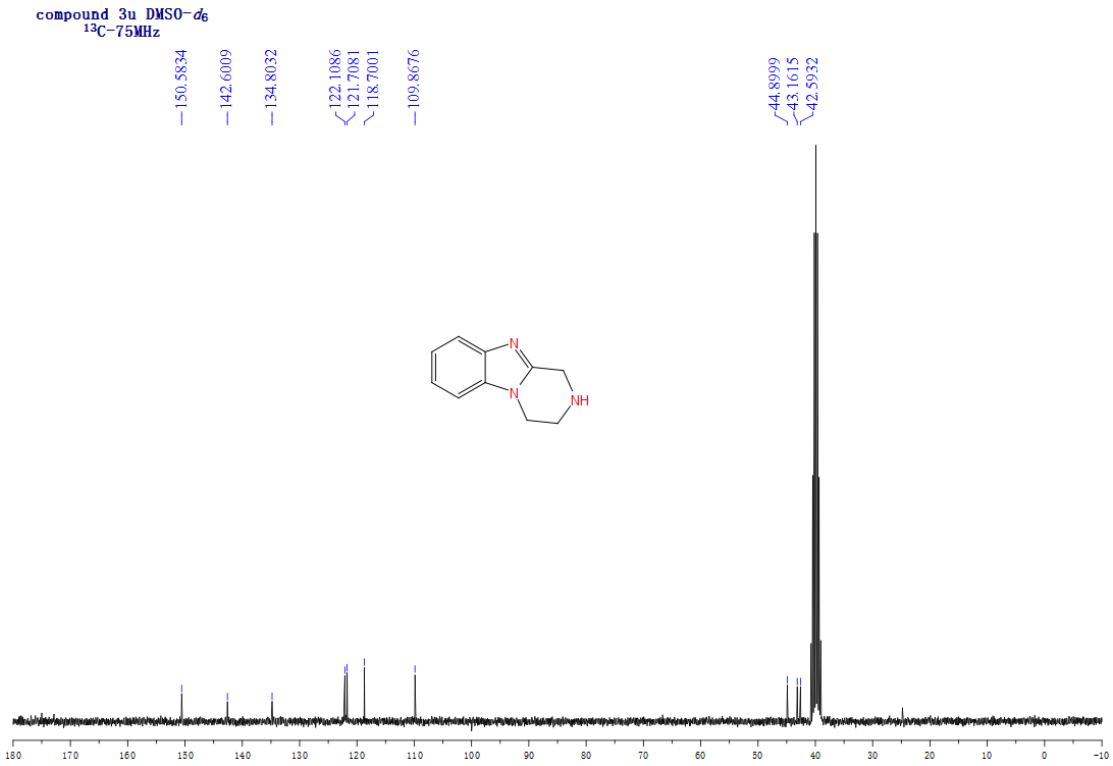

Figure S143. The ^{13}C NMR Spectrum of Compound **3u** in DMSO-d_6

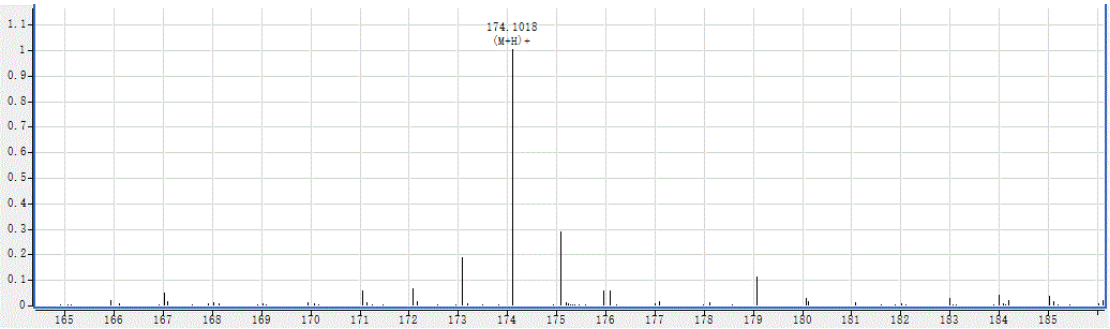

Figure S144. The HR-ESI-MS Spectrum of Compound **3u**

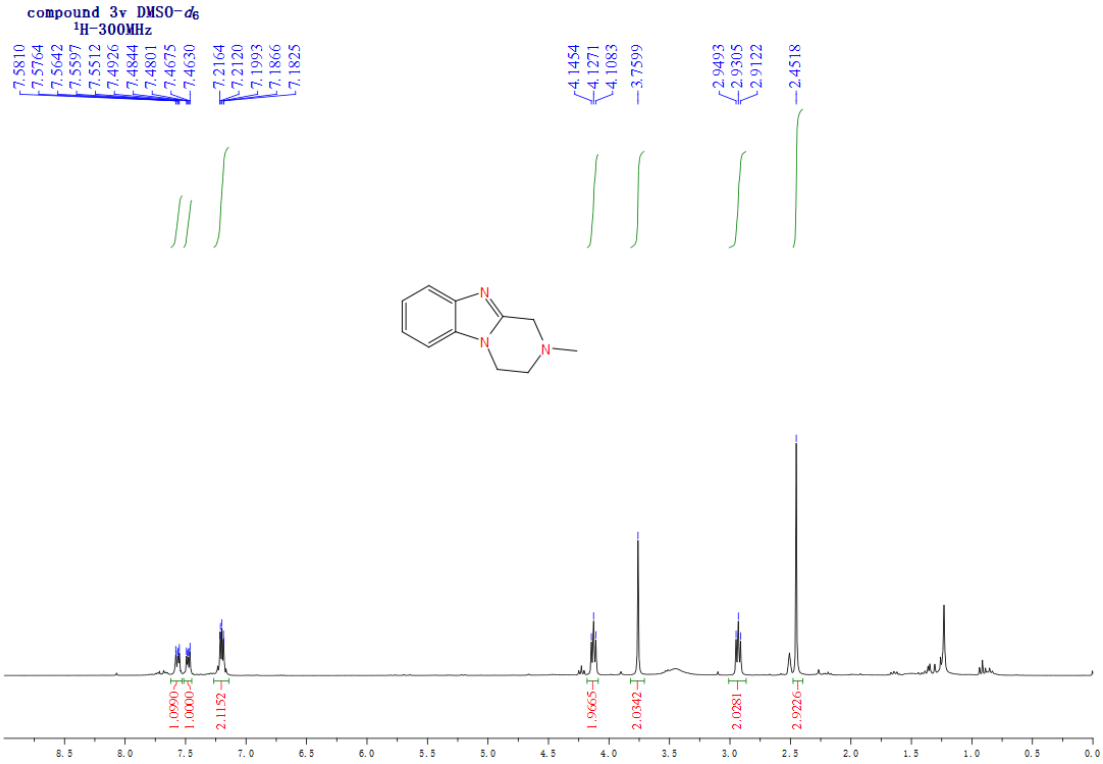

Figure S145. The ^{1}H NMR Spectrum of Compound **3v** in DMSO-d_6

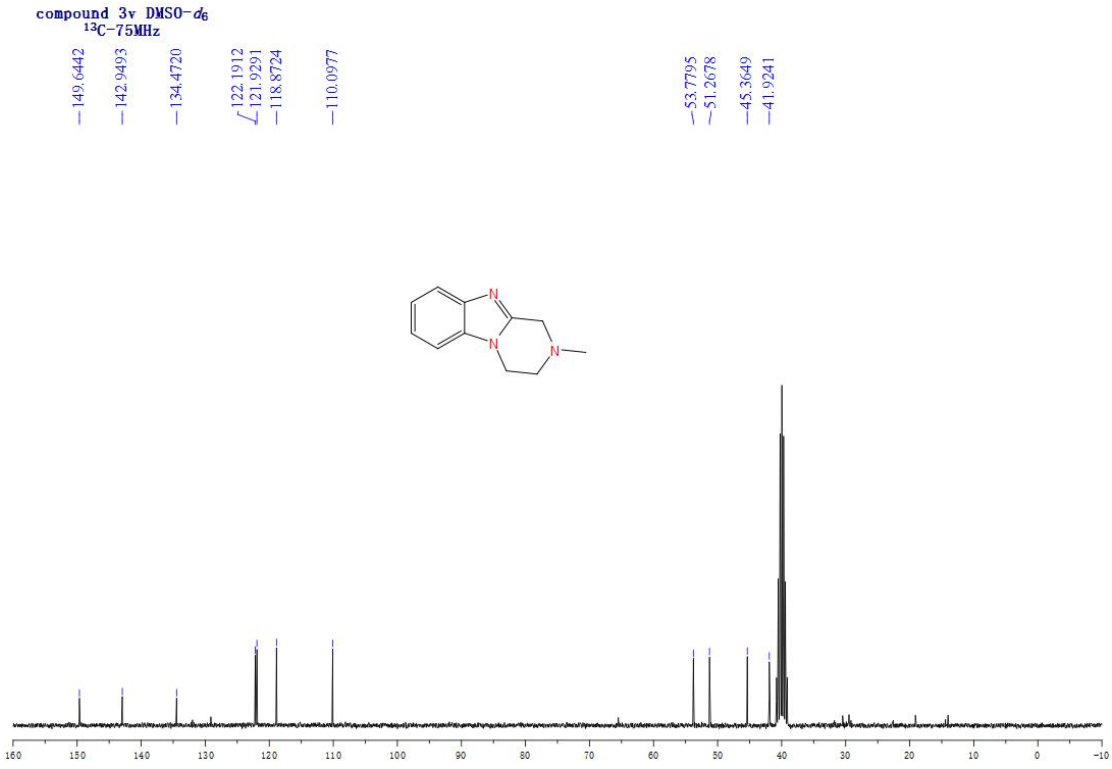

Figure S146. The ^{13}C NMR Spectrum of Compound **3v** in DMSO-d_6

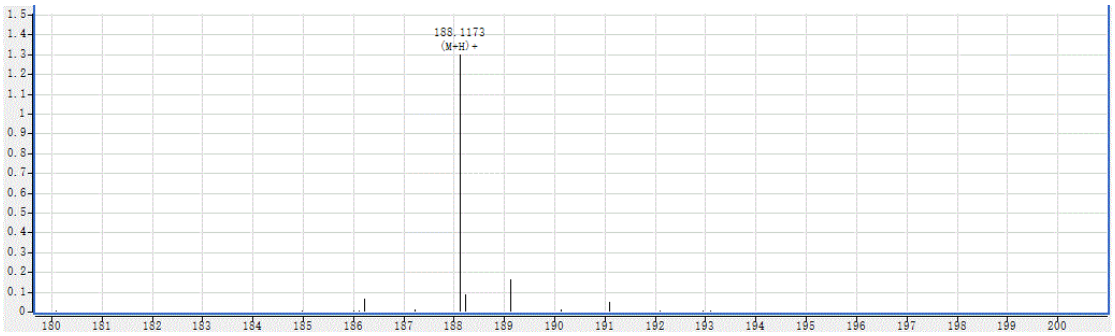

Figure S147. The HR-ESI-MS Spectrum of Compound **3v**

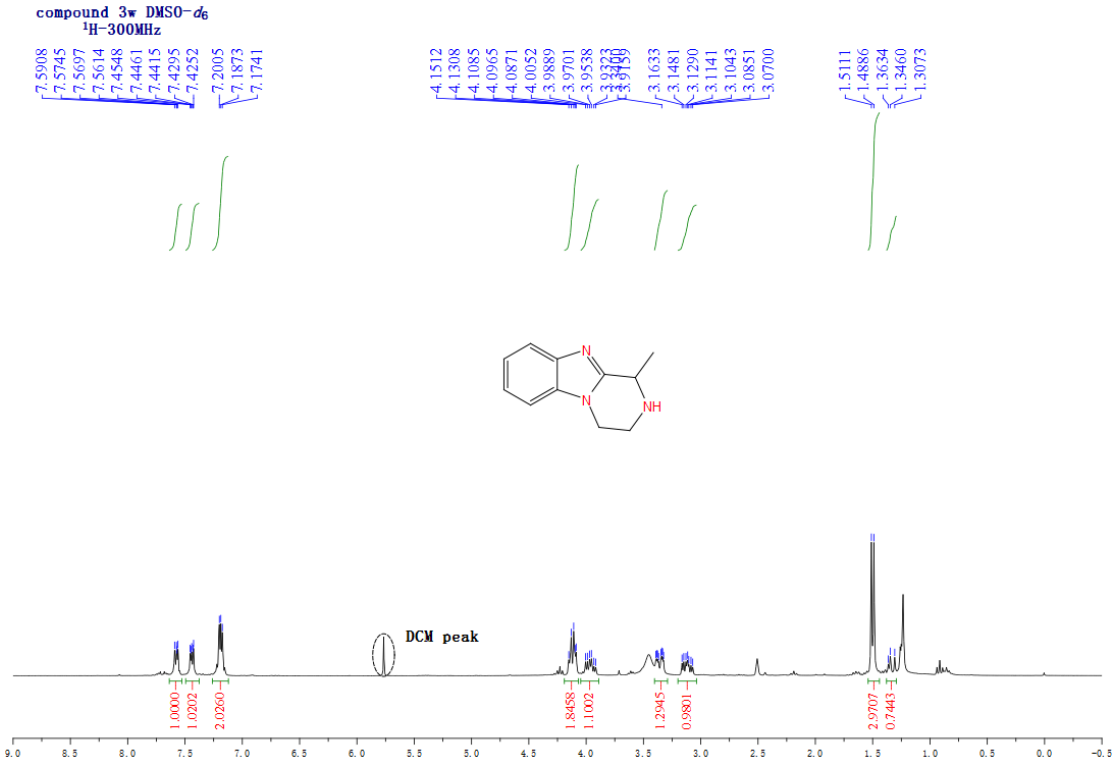

Figure S148. The ^{1}H NMR Spectrum of Compound **3w** in DMSO-d_6

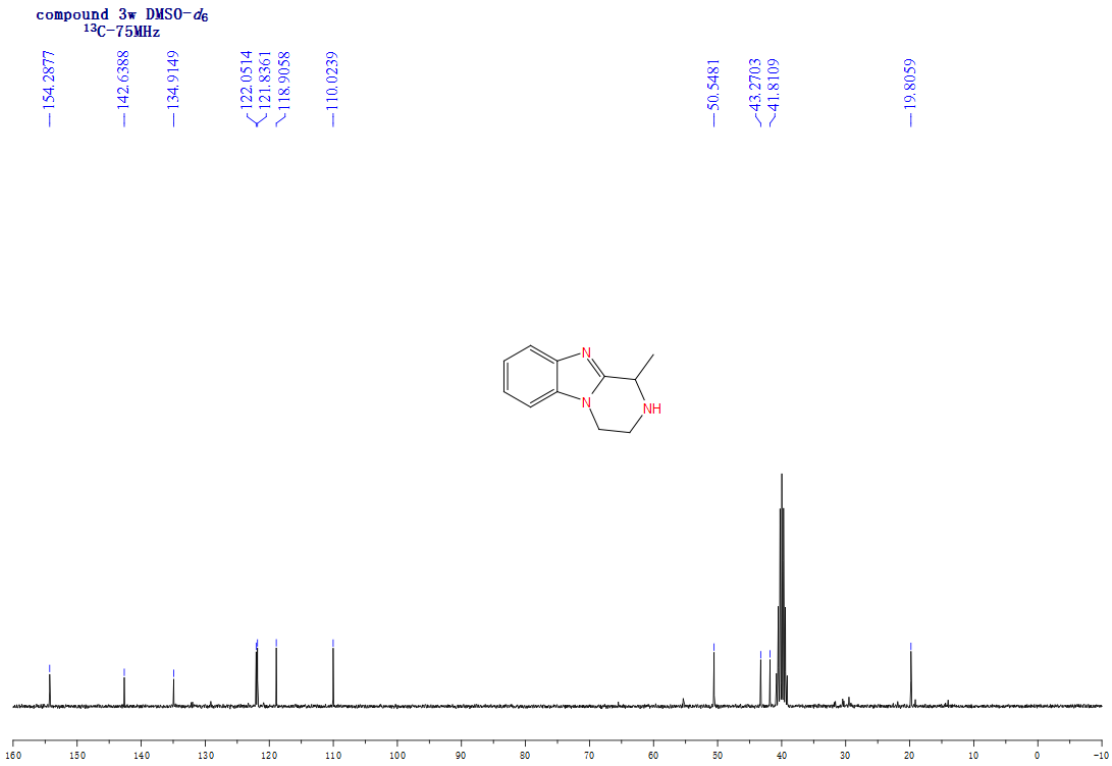

Figure S149. The ^{13}C NMR Spectrum of Compound **3w** in DMSO-d_6

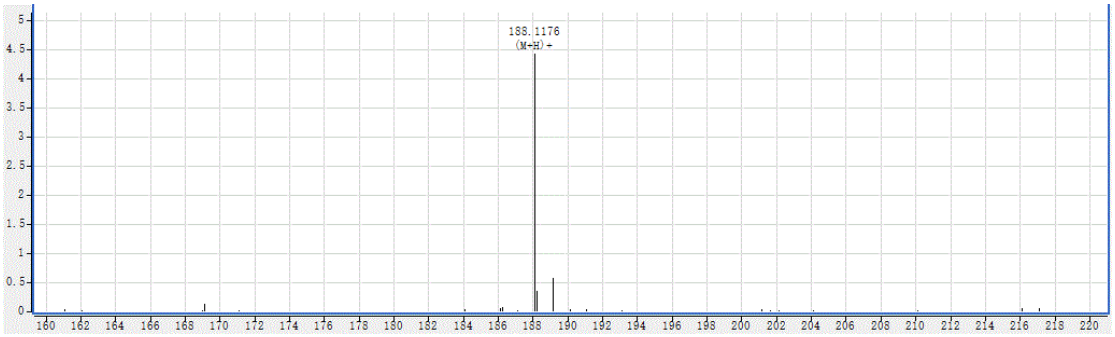

Figure S150. The HR-ESI-MS Spectrum of Compound **3w**

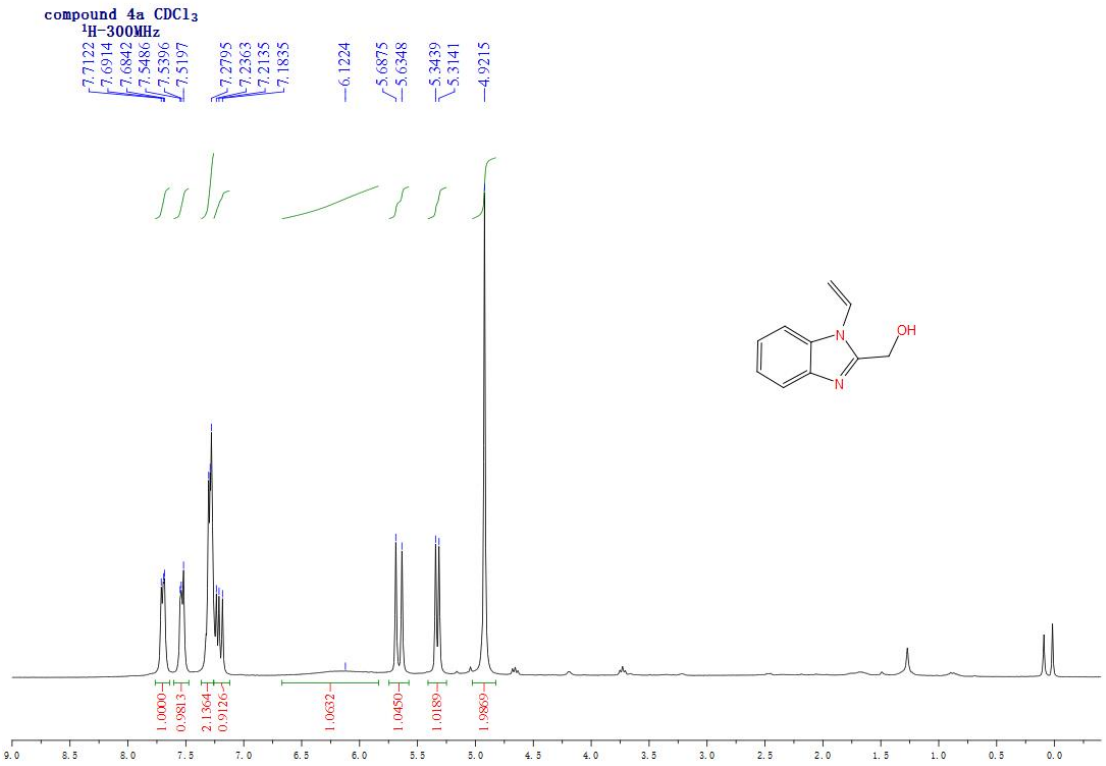

Figure S151. The ^{1}H NMR Spectrum of Compound **4a** in $CDCl_3$

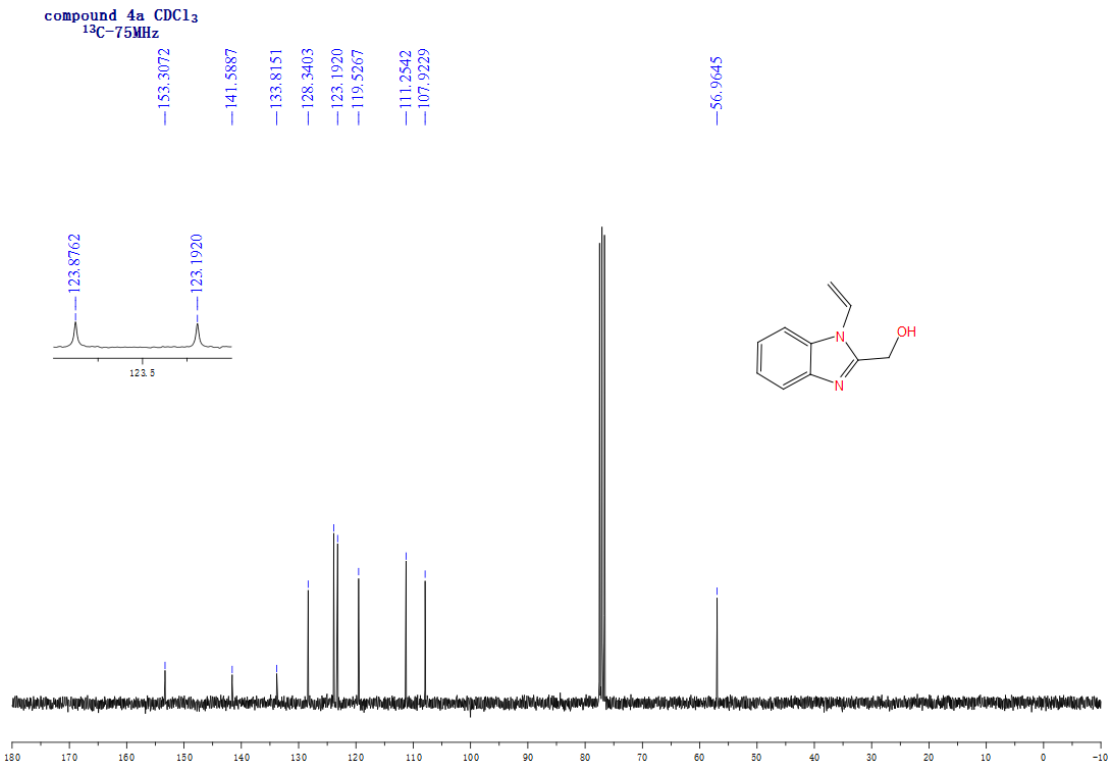

Figure S152. The ^{13}C NMR Spectrum of Compound **4a** in $CDCl_3$

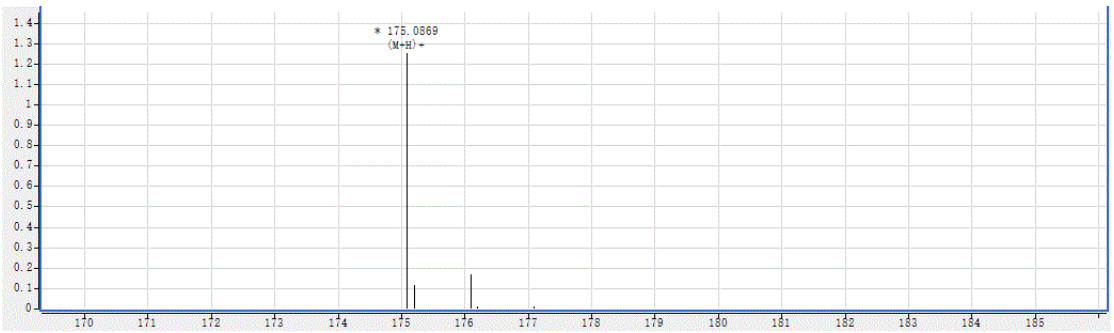

Figure S153. The HR-ESI-MS Spectrum of Compound **4a**