Supporting Information

Solvent-Controlled Halohydroxylation or C3-C2 Coupling of Pyridinium Salts through an Interrupted Dearomative Reduction

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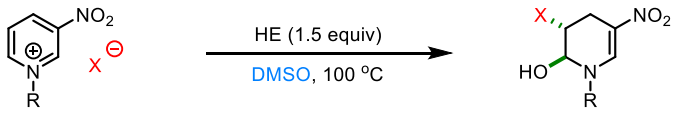
Table of Contents

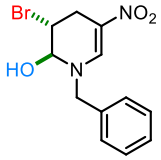
1. General methods

NMR spectra were recorded with tetramethylsilane as the internal standard. ^{1}H NMR spectra were recorded at 400 MHz, and ^{13}C NMR spectra were recorded at 100 MHz (Bruker Avance). ^{1}H NMR chemical shifts (δ) are reported in ppm relative to tetramethylsilane (TMS) with the solvent signal as the internal standard ($CDCl_3$ at 7.26 ppm, $(CD_3)_2SO$ at 2.50 ppm). ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ at 77.00 ppm, $(CD_3)_2SO$ at 39.52 ppm). Data are given as: s (singlet), d (doublet), t (triplet), q (quartet), dd (double of doublet), br (broad) or m (multiplets), coupling constants (Hz) and integration. Flash column chromatography was carried out using silica gel eluting with ethyl acetate and petroleum ether. High resolution mass spectra were obtained with the Q-TOF-Premier mass spectrometer. Reactions were monitored by TLC and visualized with ultraviolet light. IR spectra were recorded on a Thermo Fisher Nicolet Avatar 360 FTIR spectrometer on a KBr beam splitter. All the solvents were used directly without any purification.

2. Experimental data for the formation of products 2-17



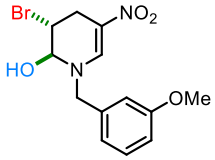
General procedure： To a 5.0 mL vial were successively added pyridinium or quinolinium salts (0.2 mmol), Hantzsch ester (0.3 mmol, 1.5 equiv) and 1.0 mL of DMSO. The resulting mixture was stirred at 100 °C until the complete consumption of pyridinium or quinolinium salts as monitored by thin layer chromatography. After cooling down to room temperature, water was added, and the reaction mixture was extracted with CH_2Cl_2 (3 × 2.0 mL). The combined organic layers were washed with brine, dried over Na_2SO_4. After removal of the solvent, the residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent to produce compounds **2-14**.



1-Benzyl-3-bromo-5-nitro-1,2,3,4-tetrahydropyridin-2-ol (**2**)

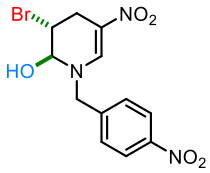
Purple solid obtained by column chromatography (petroleum ether/ethyl acetate = 4:1 to 3:1); 55.0 mg, 59% yield; dr > 20:1; reaction time = 5 min; mp 139.6-140.4 °C; ^{1}H NMR (400 MHz,

DMSO-d_6) δ 8.46 (s, 1H), 7.43-7.31 (m, 5H), 7.17 (d, J = 4.0 Hz, 1H), 4.80 (d, J = 16.0 Hz, 1H), 4.69 (d, J = 4.0 Hz, 1H), 4.63 (d, J = 16.0 Hz, 1H), 4.47-4.45 (m, 1H), 3.14-3.03 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 143.6, 135.8, 128.8, 128.6, 128.1, 118.2, 79.0, 55.9, 39.9, 25.9. IR (KBr) ν 3270, 1622, 1403, 1302, 1204, 1185, 744 cm^{-1}. HRMS (ESI) calcd for $C_{12}H_{13}N_2O_3NaBr$ $[M+Na]^+$: 335.0007, found: 335.0009.



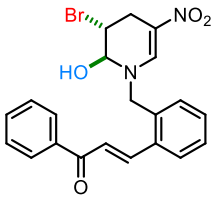
3-Bromo-1-(3-methoxybenzyl)-5-nitro-1,2,3,4-tetrahydropyridin-2-ol (**3**)

Purple solid obtained by column chromatography (petroleum ether/ethyl acetate = 5:1 to 4:1); 70.0 mg, 68% yield; dr > 20:1; reaction time = 5 min; mp 109.3-110.3 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.44 (s, 1H), 7.30 (t, J = 8.0 Hz, 1H), 7.17 (d, J = 4.0 Hz, 1H), 7.00-6.97 (m, 2H), 6.90 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 4.76 (d, J = 16.0 Hz, 1H), 4.71 (d, J = 4.0 Hz, 1H), 4.61 (d, J = 16.0 Hz, 1H), 4.48-4.47 (m, 1H), 3.75 (s, 3H), 3.15-3.04 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.4, 143.6, 137.3, 129.6, 120.9, 118.3, 114.2, 113.6, 79.0, 55.8, 55.1, 39.9, 25.8. IR (KBr) ν 3274, 1610, 1312, 1186, 1049, 741 cm^{-1}. HRMS (ESI) calcd for $C_{13}H_{15}N_2O_4NaBr$ $[M+Na]^+$: 365.0113, found: 365.0113.



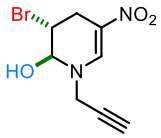
3-Bromo-5-nitro-1-(4-nitrobenzyl)-1,2,3,4-tetrahydropyridin-2-ol (**4**)

Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 3:1 to 2:1); 74.0 mg, 69% yield; dr > 20:1; reaction time = 5 min; mp 149.6-150.5 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.53 (s, 1H), 8.24 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 8.0 Hz, 1H), 4.92 (d, J = 16.0 Hz, 1H), 4.82 (d, J = 16.0 Hz, 1H), 4.69 (d, J = 4.0 Hz, 1H), 4.46-4.45 (m, 1H), 3.15-3.03 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.2, 144.0, 143.6, 129.8, 123.6, 118.9, 79.4, 55.1, 39.9, 25.8. IR (KBr) ν 3314, 1615, 1519, 1309, 1046, 957, 745 cm^{-1}. HRMS (ESI) calcd for $C_{12}H_{12}N_3O_5NaBr$ $[M+Na]^+$: 379.9858, found: 379.9854.



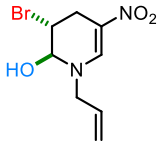
(*E*)-3-(2-((3-Bromo-2-hydroxy-5-nitro-3,4-dihydropyridin-1(2*H*)-yl)methyl)phenyl)-1-phenylprop-2-en-1-one (**5**)

Grey solid obtained by column chromatography (petroleum ether/ethyl acetate = 3:1 to 2:1); 108.0 mg, 82% yield; dr > 20:1; reaction time = 5 min; mp 154.3-155.1 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.34 (s, 1H), 8.12 (d, J = 4.0 Hz, 2H), 8.07-8.04 (m, 2H), 7.80 (d, J = 16.0 Hz, 1H), 7.66 (t, J = 8.0 Hz, 1H), 7.58-7.46 (m, 5H), 7.22 (d, J = 4.0 Hz, 1H), 5.05 (d, J = 16.0 Hz, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.65 (d, J = 4.0 Hz, 1H), 4.45 (d, J = 4.0 Hz, 1H), 3.17-3.02 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 189.2, 143.0, 140.3, 137.5, 134.8, 134.5, 133.2, 130.6, 130.4, 128.9, 128.8, 128.6, 127.8, 124.8, 118.8, 78.9, 53.2, 39.9, 25.9. IR (KBr) ν 3231, 1609, 1297, 1217, 1042, 750 cm^{-1}. HRMS (ESI) calcd for $C_{21}H_{19}N_2O_4NaBr$ [M+Na]$^+$: 465.0426, found: 465.0433.



3-Bromo-5-nitro-1-(prop-2-yn-1-yl)-1,2,3,4-tetrahydropyridin-2-ol (**6**)

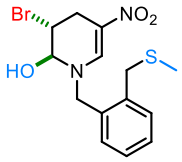
Light brown solid obtained by column chromatography (petroleum ether/ethyl acetate = 5:1 to 4:1); 40.0 mg, 51% yield; dr > 20:1; reaction time = 5 min; mp 115.8-116.7 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.39 (s, 1H), 7.13 (d, J = 4.0 Hz, 1H), 4.91 (d, J = 4.0 Hz, 1H), 4.54-4.49 (m, 2H), 3.36 (dd, J_1 = 20.0 Hz, J_2 = 4.0 Hz, 1H), 3.52 (s, 1H), 3.12-3.02 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 142.4, 118.8, 79.1, 77.9, 77.4, 44.2, 41.9, 25.7. IR (KBr) ν 3270, 1616, 1358, 1227, 1181, 1049, 748 cm^{-1}. HRMS (ESI) calcd for $C_8H_9N_2O_3NaBr$ [M+Na]$^+$: 282.9694, found: 282.9688.



1-Allyl-3-bromo-5-nitro-1,2,3,4-tetrahydropyridin-2-ol (**7**)

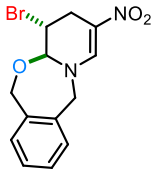
Grey solid obtained by column chromatography (petroleum ether/ethyl acetate = 5:1 to 4:1); 48.0

mg, 61% yield; dr > 20:1; reaction time = 5 min; mp 112.4-113.2 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.31 (s, 1H), 7.07 (d, J = 8.0 Hz, 1H), 5.91-5.81 (m, 1H), 5.39 (dd, J_1 = 16.0 Hz, J_2 = 4.0 Hz, 1H), 5.27 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 4.77 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 4.49 (q, J = 4.0 Hz, 1H), 4.22-4.07 (m, 2H), 3.13-3.02 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 143.3, 133.3, 119.5, 118.1, 79.0, 55.3, 44.5, 25.8. IR (KBr) ν 3425, 3301, 1614, 1287, 1213, 747 cm^{-1}. HRMS (ESI) calcd for $C_8H_{11}N_2O_3NaBr$ [M+Na]$^+$: 284.9851, found: 284.9847.



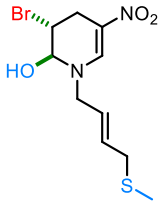
3-Bromo-1-(2-((methylthio)methyl)benzyl)-5-nitro-1,2,3,4-tetrahydropyridin-2-ol (**8**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 5:1 to 4:1); 22.0 mg, 17% yield; dr > 20:1; reaction time = 5 min; mp 122.6-123.7 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.29 (s, 1H), 7.45-7.43 (m, 1H), 7.36-7.31 (m, 3H), 7.22 (d, J = 4.0 Hz, 1H), 4.83 (q, J = 16.0 Hz, 2H), 4.70 (s, 1H), 4.49-4.48 (m, 1H), 3.85-3.78 (m, 2H), 3.17-3.04 (m, 2H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 143.1, 136.8, 133.5, 130.5, 130.4, 128.2, 127.4, 118.5, 79.3, 52.9, 39.9, 34.5, 25.9, 14.6. IR (KBr) ν 3225, 1615, 1306, 1214, 1044 cm^{-1}. HRMS (ESI) calcd for $C_{14}H_{17}N_2O_3NaSBr$ [M+Na]$^+$: 395.0041, found: 395.0038.



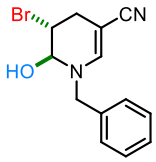
4-Bromo-2-nitro-4,4a,6,11-tetrahydro-3*H*-benzo[e]pyrido[2,1-*b*][1,3]oxazepine (**9**)

Grey solid obtained by column chromatography (petroleum ether/ethyl acetate = 5:1 to 4:1); 26.0 mg, 24% yield; dr > 20:1; reaction time = 5 min; mp 187.2-187.7 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.35 (s, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.33-7.27 (m, 3H), 5.31 (s, 1H), 5.26 (d, J = 16.0 Hz, 1H), 5.02 (d, J = 16.0 Hz, 1H), 4.86 (t, J = 12.0 Hz, 2H), 4.73 (s, 1H), 3.07-2.93 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 142.3, 139.6, 137.8, 129.2, 128.3, 128.0, 127.9, 120.0, 90.1, 73.5, 57.5, 39.9, 26.4. IR (KBr) ν 1626, 1427, 1308, 1209, 1047 cm^{-1}. HRMS (ESI) calcd for $C_{13}H_{13}N_2O_3NaBr$ [M+Na]$^+$: 347.0007, found: 347.0012.



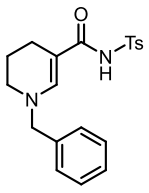
3-Bromo-1-((*E*)-4-(methylthio)but-2-en-1-yl)-5-nitro-1,2,3,4-tetrahydropyridin-2-ol (**10**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 4:1 to 3:1); 23.0 mg, 21% yield; dr > 20:1; reaction time = 5 min; mp 90.6-91.4 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.32 (s, 1H), 7.10 (d, J = 8.0 Hz, 1H), 5.79-5.75 (m, 1H), 5.73-5.55 (m, 1H), 4.76 (d, J = 4.0 Hz, 1H), 4.49 (d, J = 4.0 Hz, 1H), 4.19 (dd, J_1 = 16.0 Hz, J_2 = 8.0 Hz, 1H), 4.09 (dd, J_1 = 16.0 Hz, J_2 = 8.0 Hz, 1H), 3.11 (d, J = 4.0 Hz, 2H), 3.06 (s, 2H), 1.97 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 143.2, 131.4, 127.1, 118.0, 78.9, 54.2, 44.6, 34.4, 25.8, 13.9. IR (KBr) ν 3289, 1618, 1295, 1184, 1047 cm^{-1}. HRMS (ESI) calcd for $C_{10}H_{16}N_2O_3SBr$ [M+H]$^+$: 323.0065, found: 323.0064.



1-Benzyl-5-bromo-6-hydroxy-1,4,5,6-tetrahydropyridine-3-carbonitrile (**11**)

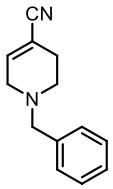
Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 8:1 to 7:1); 34.1 mg, 39% yield; dr > 20:1; reaction time = 10 min; mp 110.8-111.5 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.56 (d, J = 8.0 Hz, 1H), 7.38-7.30 (m, 6H), 4.71 (d, J = 8.0 Hz, 1H), 4.45 (d, J = 16.0 Hz, 2H), 3.36 (d, J = 4.0 Hz, 1H), 2.96 (d, J = 16.0 Hz, 1H), the hydrogen for OH was missing; ^{13}C NMR (100 MHz, DMSO-d_6) δ 145.3, 136.4, 128.7, 128.5, 127.9, 127.8, 120.8, 82.5, 72.4, 63.6, 55.3. IR (KBr) ν 3263, 2198, 1625, 1425, 1196, 752 cm^{-1}. HRMS (ESI) calcd for $C_{13}H_{13}N_2ONaBr$ [M+Na]$^+$: 315.0109, found: 315.0112.



1-Benzyl-*N*-tosyl-1,4,5,6-tetrahydropyridine-3-carboxamide (**12**)

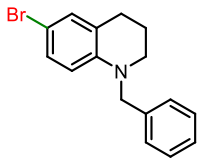
Yellow oil obtained by column chromatography (petroleum ether/ethyl acetate = 3:1 to 2:1); 13.2 mg, 14% yield; reaction time = 7 h; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (br, 1H), 7.98 (d, J = 8.0

Hz, 2H), 7.60 (s, 1H), 7.30-7.27 (m, 5H), 7.15-7.13 (m, 2H), 4.24 (s, 2H), 2.99 (s, 1H), 2.96 (t, *J* = 8.0 Hz, 1H), 2.40 (s, 3H), 2.18 (t, *J* = 8.0 Hz, 2H), 1.79-1.73 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 147.0, 144.0, 136.9, 136.1, 129.3, 128.8, 128.3, 127.9, 127.5, 60.1, 45.1, 42.6, 21.6, 20.8, 19.6. IR (KBr) ν 2930, 1610, 1139, 1058 cm^{-1}. HRMS (ESI) calcd for $C_{20}H_{22}N_2O_3NaS$ $[M+Na]^+$: 393.2249, found: 393.1252.



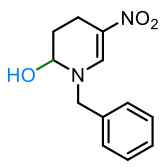
1-Benzyl-1,2,3,6-tetrahydropyridine-4-carbonitrile (**13**)

Yellow oil obtained by column chromatography (petroleum ether/ethyl acetate = 25:1 to 20:1); 16.3 mg, 27% yield; reaction time = 1 h; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.28 (m, 5H), 6.55 (s, 1H), 3.61 (s, 2H), 3.13-3.11 (m, 2H), 2.62 (t, *J* = 5.0 Hz, 2H), 2.37-2.36 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.3, 137.4, 129.0, 128.4, 127.4, 118.8, 110.8, 62.2, 52.4, 48.3, 27.6. IR (KBr) ν 2924, 2810, 1725, 1448, 742 cm^{-1}. HRMS (ESI) calcd for $C_{13}H_{15}N_2$ $[M+H]^+$: 199.1235, found: 199.1239.



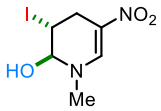
1-Benzyl-6-bromo-1,2,3,4-tetrahydroquinoline (**14**)

Colorless oil obtained by column chromatography (petroleum ether/ethyl acetate = 150:1 to 120:1); 67.9 mg, 75% yield; reaction time = 30 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (q, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 3H), 7.22-7.21 (m, 1H), 7.18-7.15 (m, 1H), 6.50-6.47 (m, 1H), 4.58 (s, 2H), 3.49 (t, *J* = 8.0 Hz, 2H), 2.91 (t, *J* = 8.0 Hz, 2H), 2.12 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.3, 138.1, 131.1, 129.5, 128.5, 126.8, 126.3, 124.2, 112.3, 107.2, 54.9, 49.6, 27.9, 21.9. IR (KBr) ν 3455, 1592, 1500, 1294, 791 cm^{-1}. HRMS (ESI) calcd for $C_{16}H_{17}NBr$ $[M+H]^+$: 302.0544, found: 302.0543.



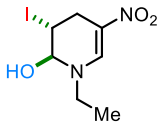
1-Benzyl-5-nitro-1,2,3,4-tetrahydropyridin-2-ol (**15**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 4:1 to 3:1); 27.0 mg, 38% yield; reaction time = 48 h; mp 99.4-99.9 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.36 (s, 1H), 7.39-7.31 (m, 5H), 6.53 (d, J = 8.0 Hz, 1H), 4.76-4.64 (m, 3H), 2.70 (d, J = 12.0 Hz, 1H), 2.51-2.42 (m, 1H), 1.91 (d, J = 12.0 Hz, 1H), 1.53-1.52 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 145.0, 136.8, 128.8, 127.9, 127.8, 120.7, 75.7, 55.5, 27.2, 16.2. IR (KBr) ν 3439, 3286, 1618, 1318, 1205 cm^{-1}. HRMS (ESI) calcd for $C_{12}H_{14}N_2O_3Na$ [M+Na]$^+$: 257.0902, found: 257.0899.



3-Iodo-1-methyl-5-nitro-1,2,3,4-tetrahydropyridin-2-ol (**16**)

Red solid obtained by column chromatography (petroleum ether/ethyl acetate = 10:1 to 9:1); 43.0 mg, 51% yield; dr > 20:1; reaction time = 3.5 h; mp 119.2-120.3 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.03 (s, 1H), 6.04 (d, J = 8.0 Hz, 1H), 5.27-5.25 (m, 1H), 3.29 (s, 2H), 3.15 (s, 3H), the hydrogen was missing for O-H; ^{13}C NMR (100 MHz, DMSO-d_6) δ 142.5, 128.8, 119.9, 110.0, 40.9, 23.5. IR (KBr) ν 3450, 1672, 1293, 1204 cm^{-1}. HRMS (ESI) calcd for $C_6H_9N_2O_3NaI$ [M+Na]$^+$: 306.9556, found: 306.9558.

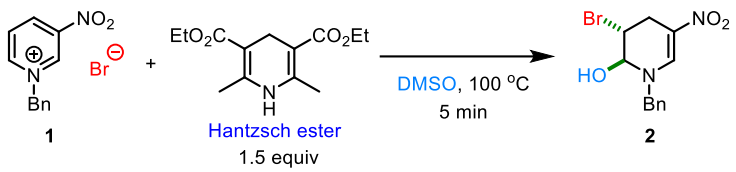


1-Ethyl-3-iodo-5-nitro-1,2,3,4-tetrahydropyridin-2-ol (**17**)

Red solid obtained by column chromatography (petroleum ether/ethyl acetate = 15:1 to 10:1); 47.0 mg, 53% yield; dr > 20:1; reaction time = 3.5 h; mp 78.4-79.2 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.08 (d, J = 4.0 Hz, 1H), 6.16-6.13 (m, 1H), 5.30-5.26 (m, 1H), 3.45 (q, J = 8.0 Hz, 2H), 3.32 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 2H), 1.16 (t, J = 8.0 Hz, 1H), the hydrogen was missing for O-H; ^{13}C NMR (100 MHz, DMSO-d_6) δ 141.4, 127.4, 120.0, 110.2, 48.7, 23.8, 14.9. IR (KBr) ν 3454, 1673, 1593, 1255, 1186 cm^{-1}. HRMS (ESI) calcd for $C_7H_{11}N_2O_3NaI$ [M+Na]$^+$: 320.9712, found: 320.9710.

3. Optimization of conditions

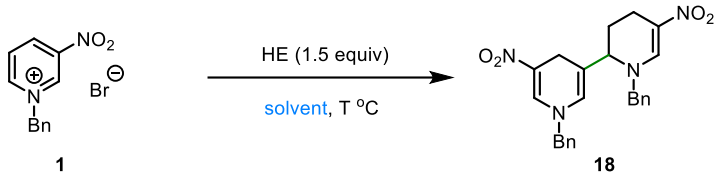
Table S1 Optimization of reaction conditions for the formation of **2**[a]



Entry	Variation from above	Yield (%)[b]
1	none	59
2	Stirring at 120 °C for 5 min	46
3	Stirring at 80 °C for 10 min	53
4	Stirring at 60 °C for 30 min	48
5	Stirring at 25 °C for 1 h	22
6	LiBr (2.0 equiv) as additive	53

[a] Unless otherwise noted, the reactions were performed using pyridinium salt **1** (0.2 mmol) and Hantzsch ester (0.3 mmol) in DMSO (1.0 mL) at 100 °C for 5 min. [b] Isolated yield obtained by silica gel column chromatography.

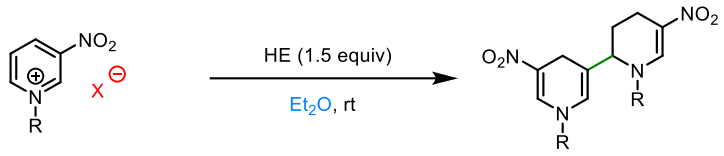
Table S2 Optimization of conditions for the formation of **18**[a]



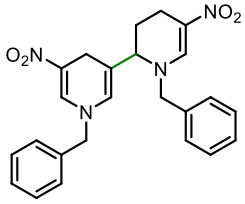
entry	solvent	temperature	time	Yield (%)[b]
1	toluene	100	10 min	14
2	$CHCl_3$	70	5 min	40
3	*i*-PrOH	80	5 min	37
4	CH_3CO_2Et	70	5 min	19
5	THF	80	10 min	46
6	Et_2O	25	36 h	74

[a] Unless otherwise noted, the reactions were performed using pyridinium salt **1** (0.2 mmol), and Hantzsch ester (0.3 mmol) in solvent (1.0 mL). [b] Isolated yield obtained by silica gel column chromatography.

4. Experimental data for the formation of products 18-26

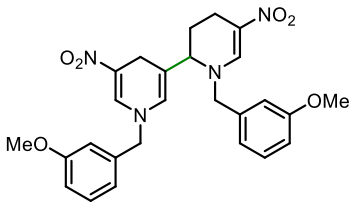


General procedure: To a 5.0 mL vial were successively added pyridinium salts (0.3 mmol), Hantzsch ester (0.45 mmol) and 1.0 mL of Et_2O. The resulting mixture was stirred at room temperature until the complete consumption of the pyridinium salts as monitored by thin layer chromatography. After removal of the solvent, the residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent to produce compounds **18-26**.



1,1'-Dibenzyl-5,5'-dinitro-1,1',2,3,4,4'-hexahydro-2,3'-bipyridine (**18**)

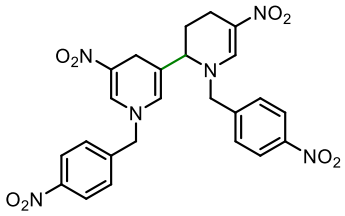
Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 3:1 to 2:1); 47.0 mg, 74% yield; reaction time = 36 h; mp 182.8-183.5 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.52 (s, 1H), 8.25 (s, 1H), 7.38-7.31 (m, 8H), 7.26 (d, J = 8.0 Hz, 2H), 5.96 (s, 1H), 4.74-4.65 (m, 3H), 4.37 (d, J = 16.0 Hz, 1H), 3.82 (s, 1H), 3.18 (q, J = 20.0 Hz, 1H), 2.64 (d, J = 12.0 Hz, 2H), 2.15-2.02 (m, 2H), 1.57-1.51 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 146.5, 140.7, 136.8, 136.1, 128.8, 128.8, 128.1, 128.0, 128.0, 127.5, 124.9, 121.3, 119.7, 118.2, 57.2, 56.9, 56.5, 24.3, 21.8, 17.7. IR (KBr) ν 3426, 1609, 1281, 1191, 1087 cm^{-1}. HRMS (ESI) calcd for $C_{24}H_{24}N_4O_4Na$ $[M+Na]^+$: 455.1695, found: 455.1692.



1,1'-Bis(3-methoxybenzyl)-5,5'-dinitro-1,1',2,3,4,4'-hexahydro-2,3'-bipyridine (**19**)

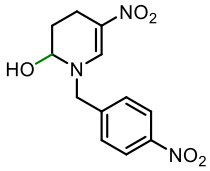
Red solid obtained by column chromatography (petroleum ether/ethyl acetate = 3:1 to 2:1); 38.0 mg, 59% yield; reaction time = 57 h; mp 152.2-153.3 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.52 (s, 1H), 8.23 (s, 1H), 7.30-7.25 (m, 2H), 6.91-6.82 (m, 6H), 5.98 (s, 1H), 4.71-4.64 (m, 3H), 4.35 (d, J = 12.0 Hz, 1H), 3.85 (s, 1H), 3.74 (s, 6H), 3.19 (q, J = 20.0 Hz, 2H), 2.66 (d, J = 16.0 Hz,

1H), 2.15-1.98 (m, 2H), 1.57-1.51 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.6, 159.6, 146.5, 140.7, 138.4, 137.7, 130.0, 129.9, 124.9, 121.4, 120.1, 119.7, 119.5, 118.2, 113.7, 113.5, 113.4, 113.1, 57.2, 56.9, 56.5, 55.1, 55.1, 24.4, 21.8, 17.7. IR (KBr) ν 3068, 1608, 1299, 1190, 1090 cm^{-1}. HRMS (ESI) calcd for $C_{26}H_{28}N_4O_6Na$ [M+Na]$^+$: 515.1907, found: 515.1912.



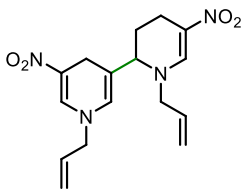
5,5'-Dinitro-1,1'-bis(4-nitrobenzyl)-1,1',2,3,4,4'-hexahydro-2,3'-bipyridine (**20**)

Red solid obtained by column chromatography (petroleum ether/ethyl acetate = 2:1 to 1:1); 23.0 mg, 29% yield; reaction time = 41 h; mp 230.7-231.4 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.55 (s, 1H), 8.29 (s, 1H), 8.22 (d, *J* = 8.0 Hz, 2H), 8.18 (d, *J* = 8.0 Hz, 2H), 7.58 (d, *J* = 4.0 Hz, 2H), 7.56 (d, *J* = 4.0 Hz, 2H), 5.94 (s, 1H), 4.90-4.79 (m, 3H), 4.57 (d, *J* = 16.0 Hz, 1H), 3.82 (s, 1H), 3.20 (q, *J* = 20.0 Hz, 2H), 2.66-2.62 (m, 1H), 2.16-2.05 (m, 2H), 1.63-1.57 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.1, 146.7, 144.7, 144.3, 140.7, 129.0, 128.6, 124.7, 124.0, 123.9, 123.7, 121.8, 120.2, 118.2, 57.0, 56.4, 55.6, 24.2, 21.7, 17.7. IR (KBr) ν 3079, 1612, 1521, 1297, 1184 cm^{-1}. HRMS (ESI) calcd for $C_{24}H_{22}N_6O_8Na$ [M+Na]$^+$: 545.1397, found: 545.1401.



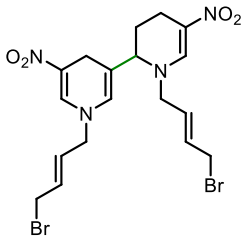
5-Nitro-1-(4-nitrobenzyl)-1,2,3,4-tetrahydropyridin-2-ol (**21**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 3:1 to 2:1); 11.0 mg, 13% yield; reaction time = 41 h; mp 159.5-160.6 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.41 (s, 1H), 8.23 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 2H), 6.54 (s, 1H), 4.86 (s, 2H), 4.71 (s, 1H), 2.74-2.68 (m, 1H), 2.53-2.43 (m, 1H), 1.98-1.90 (m, 1H), 1.66-1.57 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.0, 145.0, 129.0, 128.9, 123.8, 121.3, 76.2, 54.8, 27.2, 16.2. IR (KBr) ν 3317, 1617, 1518, 1299, 1207 cm^{-1}. HRMS (ESI) calcd for $C_{12}H_{14}N_3O_5$ [M+H]$^+$: 280.0933, found: 280.0935.



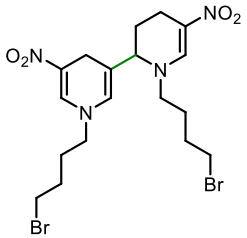
1,1'-Diallyl-5,5'-dinitro-1,1',2,3,4,4'-hexahydro-2,3'-bipyridine (**22**)

Red solid obtained by column chromatography (petroleum ether/ethyl acetate = 3:1 to 2:1); 42.0 mg, 84% yield; reaction time = 41 h; mp 157.1-157.9 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.35 (s, 1H), 8.07 (s, 1H), 5.88 (s, 2H), 5.81 (s, 1H), 5.24 (q, *J* = 16.0 Hz, 4H), 4.11 (s, 3H), 3.91 (s, 2H), 3.25 (q, *J* = 20.0 Hz, 2H), 2.69 (d, *J* = 12.0 Hz, 1H), 2.17-2.10 (m, 2H), 1.65 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 146.2, 140.8, 133.8, 133.3, 124.6, 121.0, 119.4, 119.1, 118.3, 117.8, 56.9, 56.4, 55.5, 24.5, 21.5, 17.6. IR (KBr) ν 3458, 1610, 1283, 1193 cm^{-1}. HRMS (ESI) calcd for $C_{16}H_{20}N_4O_4Na$ $[M+Na]^+$: 355.1382, found: 355.1386.



1,1'-Bis((*E*)-4-bromobut-2-en-1-yl)-5,5'-dinitro-1,1',2,3,4,4'-hexahydro-2,3'-bipyridine (**23**)

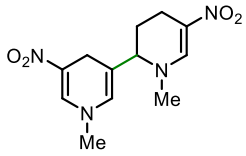
Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 2:1 to 1:1); 41.0 mg, 53% yield; reaction time = 49 h; mp 153.4-154.7 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.36 (s, 1H), 8.08 (s, 1H), 6.02-5.88 (m, 4H), 5.77 (s, 1H), 4.14-4.10 (m, 7H), 3.96-3.88 (m, 2H), 3.24 (q, *J* = 20.0 Hz, 2H), 2.70 (d, *J* = 16.0 Hz, 1H), 2.20-2.08 (m, 2H), 1.66-1.59 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 146.0, 140.6, 131.0, 130.3, 130.0, 129.9, 124.4, 121.1, 119.6, 118.5, 56.9, 54.9, 53.9, 32.8, 32.6, 24.5, 21.4, 17.6. IR (KBr) ν 3077, 1683, 1279, 1190, 973 cm^{-1}. HRMS (ESI) calcd for $C_{18}H_{22}N_4O_4NaBr_2$ $[M+Na]^+$: 538.9906, found: 538.9902.



1,1'-Bis(4-bromobutyl)-5,5'-dinitro-1,1',2,3,4,4'-hexahydro-2,3'-bipyridine (**24**)

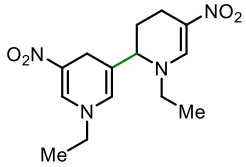
Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 3:1 to 2:1);

38.0 mg, 49% yield; reaction time = 44 h; mp 123.8-124.2 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.38 (s, 1H), 8.11 (s, 1H), 5.89 (s, 1H), 4.02 (s, 1H), 3.57-3.48 (m, 7H), 3.24 (s, 2H), 2.68 (d, *J* = 16.0 Hz, 1H), 2.20-2.10 (m, 2H), 1.79-1.63 (m, 10H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 146.6, 140.8, 124.2, 120.6, 119.1, 118.5, 56.8, 53.3, 52.7, 34.5, 34.3, 29.3, 28.8, 28.0, 27.2, 24.4, 21.6, 17.7. IR (KBr) ν 3456, 1611, 1276, 1178 cm^{-1}. HRMS (ESI) calcd for $C_{18}H_{26}N_4O_4NaBr_2$ [M+Na]$^+$: 543.0219, found: 543.0218.



1,1'-Dimethyl-5,5'-dinitro-1,1',2,3,4,4'-hexahydro-2,3'-bipyridine (**25**)

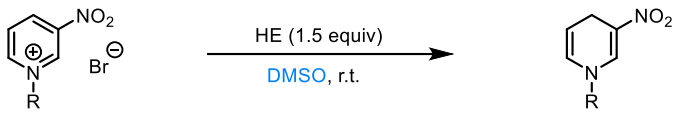
Red solid obtained by column chromatography (petroleum ether/ethyl acetate = 3:1 to 2:1); 38.0 mg, 90% yield; reaction time = 34 h; mp 146.9-147.7 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.38 (s, 1H), 8.07 (s, 1H), 5.86 (s, 1H), 3.92 (s, 1H), 3.21 (d, *J* = 4.0 Hz, 2H), 3.20 (s, 3H), 3.16 (s, 3H), 2.69-2.65 (m, 1H), 2.22-2.14 (m, 1H), 2.10-2.05 (m, 1H), 1.74-1.65 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.5, 141.6, 125.3, 120.2, 118.7, 118.1, 58.9, 39.9, 39.7, 24.3, 21.4, 17.4. IR (KBr) ν 3443, 1617, 1281, 1192 cm^{-1}. HRMS (ESI) calcd for $C_{12}H_{16}N_4O_4Na$ [M+Na]$^+$: 303.1069, found: 303.1068.



1,1'-Diethyl-5,5'-dinitro-1,1',2,3,4,4'-hexahydro-2,3'-bipyridine (**26**)

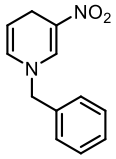
Red solid obtained by column chromatography (petroleum ether/ethyl acetate = 2:1 to 1:1); 20.0 mg, 43% yield; reaction time = 34 h; mp 191.9-192.4 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.38 (s, 1H), 8.10 (s, 1H), 5.92 (s, 1H), 4.05 (s, 1H), 3.57-3.43 (m, 3H), 3.29 (t, *J* = 8.0 Hz, 1H), 3.24 (s, 2H), 2.71-2.67 (m, 1H), 2.20-2.09 (m, 2H), 1.67-1.58 (m, 1H), 1.18 (t, *J* = 8.0 Hz, 3H), 1.11 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 146.3, 140.6, 124.0, 120.4, 119.0, 118.9, 56.6, 49.2, 48.9, 24.5, 21.7, 17.7, 15.1, 14.2. IR (KBr) ν 3453, 1617, 1302, 1244, 1186 cm^{-1}. HRMS (ESI) calcd for $C_{14}H_{20}N_4O_4Na$ [M+Na]$^+$: 331.1382, found: 331.1386.

5. Experimental data for the formation of 29 and 30



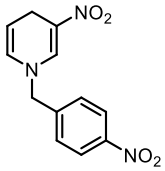
29, **30**

General procedure: To a 5.0 mL vial were successively added pyridinium salts (0.2 mmol), Hantzsch ester (0.3 mmol, 1.5 equiv) and 1.0 mL of DMSO. The resulting mixture was stirred at room temperature for 15 min. Then, water was added, and the reaction mixture was extracted with CH_2Cl_2 (3 × 2.0 mL). The combined organic layers were washed with brine, dried over Na_2SO_4. After removal of the solvent, the residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent to produce compounds **29** and **30**.



1-Benzyl-3-nitro-1,4-dihydropyridine (**29**)

Red solid obtained by column chromatography (petroleum ether/ethyl acetate = 12:1 to 10:1); 48.0 mg, 74% yield; reaction time = 15 min; mp 56.4-57.6 ℃; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.26 (s, 1H), 7.39-7.33 (m, 5H), 6.10 (d, J = 5.0 Hz, 1H), 5.24 (t, J = 5.0 Hz, 1H), 4.64 (s, 2H), 3.32 (s, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 141.6, 136.6, 128.8, 128.0, 127.8, 127.7, 120.7, 110.0, 56.5, 23.6. IR (KBr) ν 1673, 1591, 1282, 1215 cm^{-1}. HRMS (ESI) calcd for $C_{12}H_{12}N_2O_2Na$ $[M+Na]^+$: 239.0796, found: 239.0799.

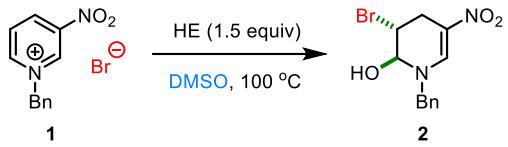


3-Nitro-1-(4-nitrobenzyl)-1,4-dihydropyridine (**30**)

Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 4:1 to 3:1); 43.0 mg, 55% yield; reaction time = 15 min; mp 153.1-154.4 ℃; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.29 (d, J = 5.0 Hz, 1H), 8.25 (d, J = 10.0 Hz, 2H), 7.62 (d, J = 10.0 Hz, 2H), 6.11 (dd, J_1 = 10.0 Hz, J_2 = 5.0 Hz, 1H), 5.28-5.25 (m, 1H), 4.81 (s, 2H), 3.33-3.32 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 147.2, 144.5, 141.6, 128.7, 127.7, 123.9, 121.3, 110.1, 55.6, 23.5. IR (KBr) ν 1672, 1599, 1522, 1332, 1216 cm^{-1}. HRMS (ESI) calcd for $C_{12}H_{12}N_3O_4$ $[M+H]^+$: 262.0828, found: 262.0829.

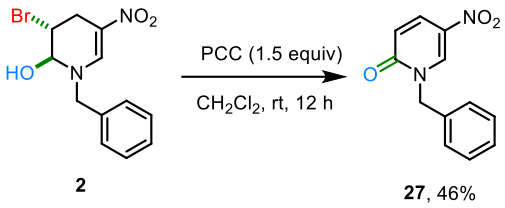
6. Methodology application

6.1 Scalable preparation of 2

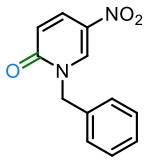


General procedure for scalable preparation of 2: To a solution of 3-nitropyridinium salt **1** (1.18 g, 4.0 mmol) in DMSO (13 mL) was added Hantzsch ester (1.52 g, 6.0 mmol) successively. The reaction went completion within 10 min with stirring at 100 °C. After cooling down to room temperature, water was added, and the reaction mixture was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4. After removal of the solvent, the residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (4:1 to 3:1) as the eluent to produce compound **2** in 57% yield (0.71 g).

6.2 Derivation of 2



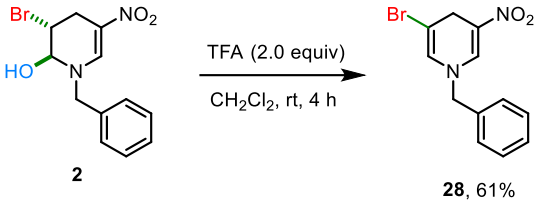
General procedure for the preparation of 27: To a 5.0 mL vial were successively added **2** (62.6 mg, 0.2 mmol), PCC (64.7 mg, 0.3 mmol) and 1.0 mL of CH_2Cl_2. Then, the resulting mixture was stirred at room temperature until complete consumption of **2** as monitored by thin layer chromatography. After 12 h, the reaction mixture was directly subjected to flash column chromatography on silica gel (petroleum ether/ ethyl acetate) to afford the corresponding product **27** in 46% yield.



1-Benzyl-5-nitropyridin-2(1*H*)-one (**27**)

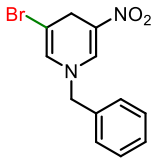
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 12:1 to 10:1); 21.0 mg, 46% yield; reaction time = 12 h; mp 104.2-104.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, J = 4.0 Hz, 1H), 8.04 (dd, J_1 = 12.0 Hz, J_2 = 4.0 Hz, 1H), 7.40-7.32 (m, 5H), 6.57 (d, J = 8.0

Hz, 1H), 5.17 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 139.0, 134.3, 133.0, 130.8, 129.2, 128.8, 128.4, 119.6, 53.1. IR (KBr) ν 3117, 1671, 1341, 1089 cm^{-1}. HRMS (ESI) calcd for $C_{12}H_{11}N_2O_3$ $[M+H]^+$: 231.0770, found: 231.0770.



2 **28**, 61%

General procedure for the preparation of 28: To a 5.0 mL vial were successively added **2** (62.6 mg, 0.2 mmol), TFA (29.7 μL, 0.4 mmol) and 1.0 mL of CH_2Cl_2. The resulting mixture was stirred at room temperature until complete consumption of **2** as monitored by thin layer chromatography. After 4 h, the reaction mixture was directly subjected to flash column chromatography on silica gel (petroleum ether/ ethyl acetate) to afford the corresponding product **28** in 61% yield.



1-Benzyl-3-bromo-5-nitro-1,4-dihydropyridine (**28**)

Yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 15:1 to 12:1); 36.0 mg, 61% yield; reaction time = 4 h; mp 98.7-99.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 4.0 Hz, 1H), 7.34-7.27 (m, 3H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.09 (d, *J* = 4.0 Hz, 1H), 4.38 (s, 2H), 3.68 (d, *J* = 4.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 134.4, 129.3, 128.9, 127.5, 127.3, 121.9, 107.0, 58.4, 33.2. IR (KBr) ν 3024, 1667, 1600, 1303, 1191, 1095 cm^{-1}. HRMS (ESI) calcd for $C_{12}H_{11}N_2O_2NaBr$ $[M+Na]^+$: 316.9902, found: 316.9903.

7. Crystal structures

7.1 Crystal structure of 3

Preparation of the single crystals of **3**: 15.0 mg of pure compound **3** was dissolved in the combined solvents of dichloromethane and methanol (2 mL, v/v = 1:1) at room temperature. The bottle was sealed by a piece of plastic film with several tiny holes, thus allowing slow evaporation of the solvents at room temperature. After about five days, several small particles were observed at the bottom of the bottle. The crystals were chosen and subjected to the single crystal X-ray diffraction analysis for the determination of the structure and relative configuration of **3**. The data

were collected by SuperNova, Dual, Cu at zero, AtlasS2 diffractometer at 220.00(10) K.

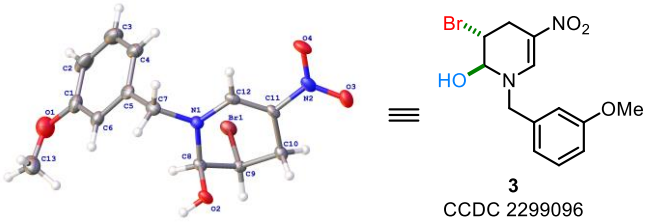


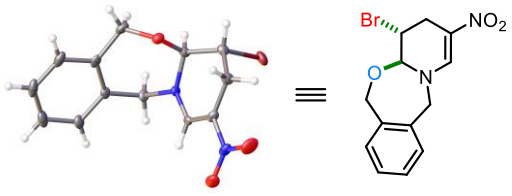
Table S2. Crystal data and structure refinement for 3.

Identification code	**3**
Empirical formula	$C_{13}H_{15}BrN_2O_4$
Formula weight	343.18
Temperature/K	220.00(10)
Crystal system	monoclinic
Space group	C2/c
a/Å	19.5005(19)
b/Å	7.9603(6)
c/Å	18.992(2)
α/°	90
β/°	110.951(13)
γ/°	90
Volume/Å^3	2753.2(5)
Z	8
ρ_{calc}g/cm^3	1.656
μ/mm^{-1}	3.001
F(000)	1392.0
Crystal size/mm^3	0.14 × 0.12 × 0.1
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.474 to 49.994
Index ranges	-17 ≤ h ≤ 23, -9 ≤ k ≤ 7, -22 ≤ l ≤ 22
Reflections collected	5471

Independent reflections	2432 [R_{int} = 0.0267, R_{sigma} = 0.0390]
Data/restraints/parameters	2432/0/183
Goodness-of-fit on F^2	1.069
Final R indexes [I>=2σ (I)]	R_1 = 0.0365, wR_2 = 0.0771
Final R indexes [all data]	R_1 = 0.0543, wR_2 = 0.0853
Largest diff. peak/hole / e $Å^{-3}$	0.65/-0.25

7.2 Crystal structure of 9

Preparation of the single crystals of **9**: 28.0 mg of pure compound **9** was dissolved in the combined solvents of dichloromethane and methanol (2.0 mL, v/v = 1:1) at room temperature. The bottle was sealed by a piece of plastic film with several tiny holes, thus allowing slow evaporation of the solvents at room temperature. After one day, several small particles were observed at the bottom of the bottle. The crystals were chosen and subjected to the single crystal X-ray diffraction analysis for the determination of the structure and relative configuration of **9**. The data were collected on a SuperNova, Dual, Cu at zero, AtlasS2 diffractometer. The crystal was kept at 150.00(10) K during data collection.



9
CCDC 2299098

Table S3. Crystal data and structure refinement for 9.

Identification code	**9**
Empirical formula	$C_{13}H_{13}BrN_2O_3$
Formula weight	325.16
Temperature/K	150.00(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	10.5757(3)

b/Å	12.8565(3)
c/Å	10.0965(3)
α/°	90
β/°	111.417(3)
γ/°	90
Volume/Å^3	1277.99(7)
Z	4
ρ_{calc}g/cm^3	1.690
μ/mm^{-1}	4.455
F(000)	656.0
Crystal size/mm^3	0.14 × 0.12 × 0.11
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.982 to 147.142
Index ranges	-8 ≤ h ≤ 12, -14 ≤ k ≤ 15, -12 ≤ l ≤ 9
Reflections collected	4547
Independent reflections	2498 [R_{int} = 0.0497, R_{sigma} = 0.0461]
Data/restraints/parameters	2498/0/172
Goodness-of-fit on F^2	1.038
Final R indexes [I>=2σ (I)]	R_1 = 0.0681, wR_2 = 0.2046
Final R indexes [all data]	R_1 = 0.0706, wR_2 = 0.2098
Largest diff. peak/hole / e Å^{-3}	1.34/-1.96

7.3 Crystal structure of 10

Preparation of the single crystals of **10**: 15.0 mg of pure compound **10** was dissolved in the combined solvents of dichloromethane and methanol (1.5 mL, v/v = 2:1) at room temperature. The bottle was sealed by a piece of plastic film with several tiny holes, thus allowing slow evaporation of the solvents at room temperature. After two days, several small particles were observed at the bottom of the bottle. The crystals were chosen and subjected to the single crystal X-ray diffraction analysis for the determination of the structure and relative configuration of **10**. The data were

collected on a SuperNova, Dual, Cu at zero, AtlasS2 diffractometer. The crystal was kept at 200.00(10) K during data collection.

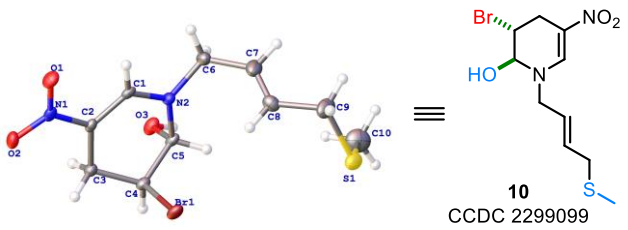


Table S4. Crystal data and structure refinement for 10.

Identification code	**10**
Empirical formula	$C_{10}H_{15}BrN_2O_3S$
Formula weight	323.21
Temperature/K	200.00(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	7.8851(8)
b/Å	16.802(2)
c/Å	10.6416(9)
α/°	90
β/°	111.647(11)
γ/°	90
Volume/Å^3	1310.4(3)
Z	4
ρ_{calc}g/cm^3	1.638
μ/mm^{-1}	3.295
F(000)	656.0
Crystal size/mm^3	0.14 × 0.13 × 0.1
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	4.778 to 49.998
Index ranges	$-9 \le h \le 9$, $-19 \le k \le 17$, $-10 \le l \le 12$

Reflections collected	6558
Independent reflections	2256 [R_{int} = 0.0297, R_{sigma} = 0.0374]
Data/restraints/parameters	2256/20/166
Goodness-of-fit on F^2	1.024
Final R indexes [I>=2σ (I)]	R_1 = 0.0342, wR_2 = 0.0705
Final R indexes [all data]	R_1 = 0.0505, wR_2 = 0.0762
Largest diff. peak/hole / e Å^{-3}	0.56/-0.30

7.4 Crystal structure of 18

Preparation of the single crystals of **18**: 28.0 mg of pure compound **18** was dissolved in the combined solvents of dichloromethane and methanol (2.0 mL, v/v = 1:1) at room temperature. The bottle was sealed by a piece of plastic film with several tiny holes, thus allowing slow evaporation of the solvents at room temperature. After about half a day, several small particles were observed at the bottom of the bottle. The crystals were chosen and subjected to the single crystal X-ray diffraction analysis for the determination of the structure and relative configuration of **18**. The data were collected by a Bruker D8 VENTURE PHOTON II CCD diffractometer at 149.99(10) K.

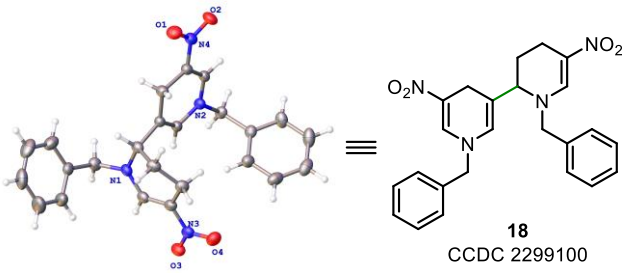


Table S5. Crystal data and structure refinement for 18.

Identification code	**18**
Empirical formula	$C_{24}H_{24}N_4O_4$
Formula weight	432.47
Temperature/K	149.99(10)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	8.7417(2)
b/Å	13.7590(2)

c/Å	9.4773(2)
α/°	90
β/°	112.031(2)
γ/°	90
Volume/Å^3	1056.67(4)
Z	2
ρ_{calc}g/cm^3	1.359
μ/mm^{-1}	0.772
F(000)	456.0
Crystal size/mm^3	0.14 × 0.12 × 0.1
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	10.068 to 147.04
Index ranges	-10 ≤ h ≤ 10, -12 ≤ k ≤ 16, -10 ≤ l ≤ 11
Reflections collected	4080
Independent reflections	2982 [R_{int} = 0.0195, R_{sigma} = 0.0279]
Data/restraints/parameters	2982/1/298
Goodness-of-fit on F^2	1.054
Final R indexes [I>=2σ (I)]	R_1 = 0.0315, wR_2 = 0.0833
Final R indexes [all data]	R_1 = 0.0320, wR_2 = 0.0838
Largest diff. peak/hole / e Å^{-3}	0.18/-0.18
Flack parameter	0.58(15)

7.5 Crystal structure of 27

Preparation of the single crystals of **27**: 21.0 mg of pure compound **27** was dissolved in the combined solvents of chloroform and methanol (1.5 mL, v/v = 2:1) at room temperature. The bottle was sealed by a piece of plastic film with several tiny holes, thus allowing slow evaporation of the solvents at room temperature. After about two days, several small particles were observed at the bottom of the bottle. The crystals were chosen and subjected to the single crystal X-ray diffraction analysis for the determination of the structure of **27**. The data were collected by

a XtaLAB AFC12 (RINC): Kappa single diffractometer at 100.00(10) K.

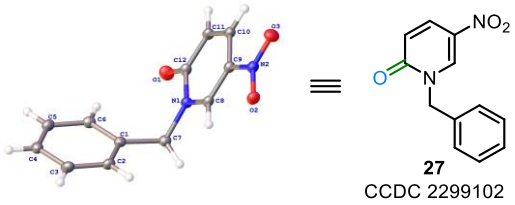


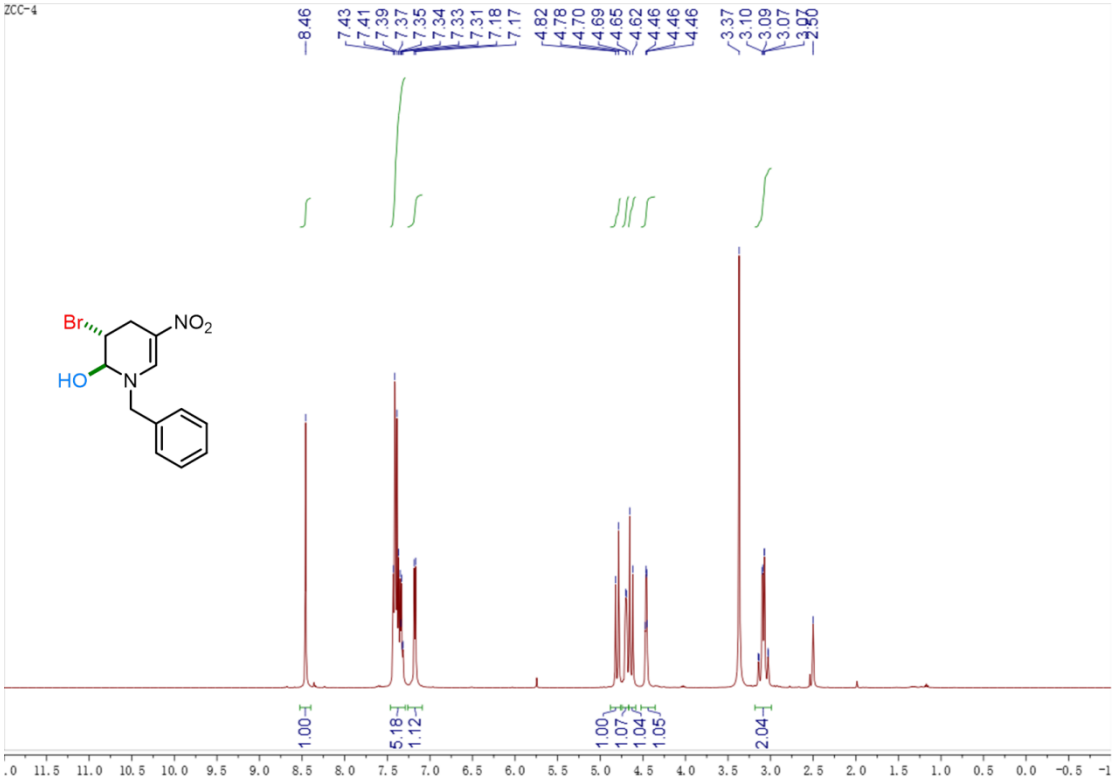
Table S6. Crystal data and structure refinement for 27.

Identification code	**27**
Empirical formula	$C_{24}H_{20}N_4O_6$
Formula weight	460.44
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	12.1802(2)
b/Å	11.8247(2)
c/Å	14.6931(3)
α/°	90
β/°	90.067(2)
γ/°	90
Volume/Å^3	2116.21(7)
Z	4
ρ_{calc}g/cm^3	1.445
μ/mm^{-1}	0.886
F(000)	960.0
Crystal size/mm^3	0.14 × 0.12 × 0.11
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.258 to 143.812
Index ranges	-14 ≤ h ≤ 14, -14 ≤ k ≤ 14, -17 ≤ l ≤ 12
Reflections collected	18367

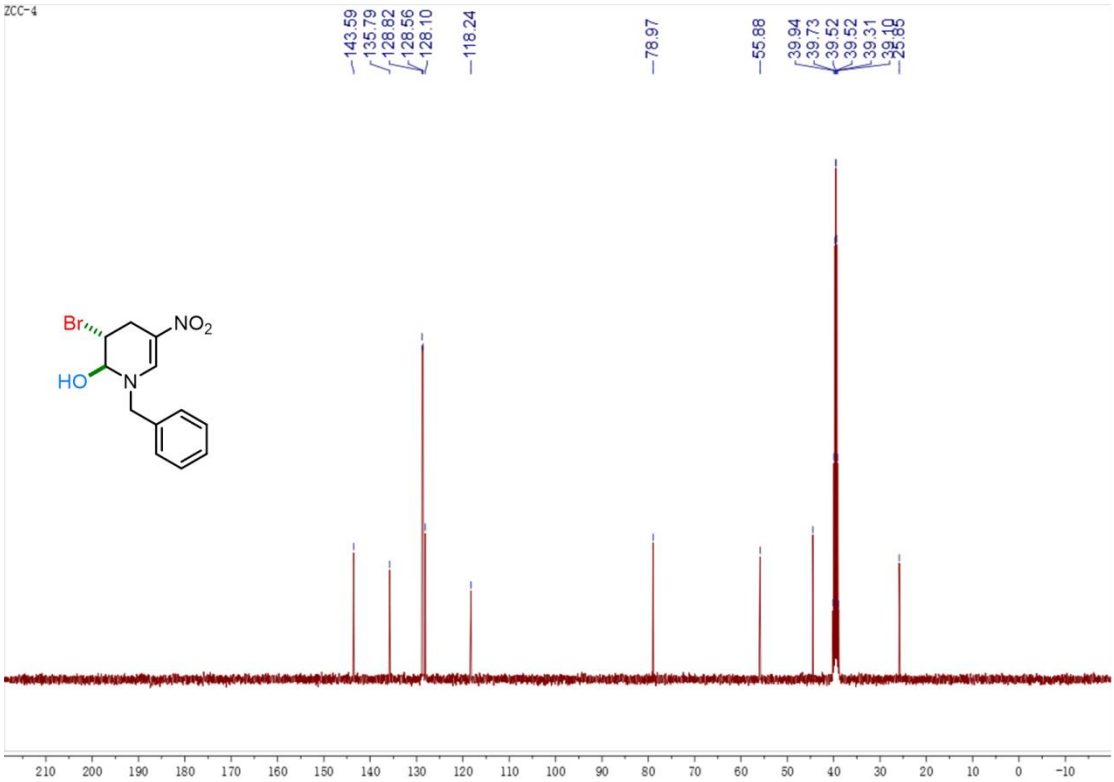
Independent reflections	4023 [R_{int} = 0.0535, R_{sigma} = 0.0464]
Data/restraints/parameters	4023/0/307
Goodness-of-fit on F^2	1.053
Final R indexes [I>=2σ (I)]	R_1 = 0.0410, wR_2 = 0.1063
Final R indexes [all data]	R_1 = 0.0482, wR_2 = 0.1115
Largest diff. peak/hole / e $Å^{-3}$	0.19/-0.25

8. NMR spectra

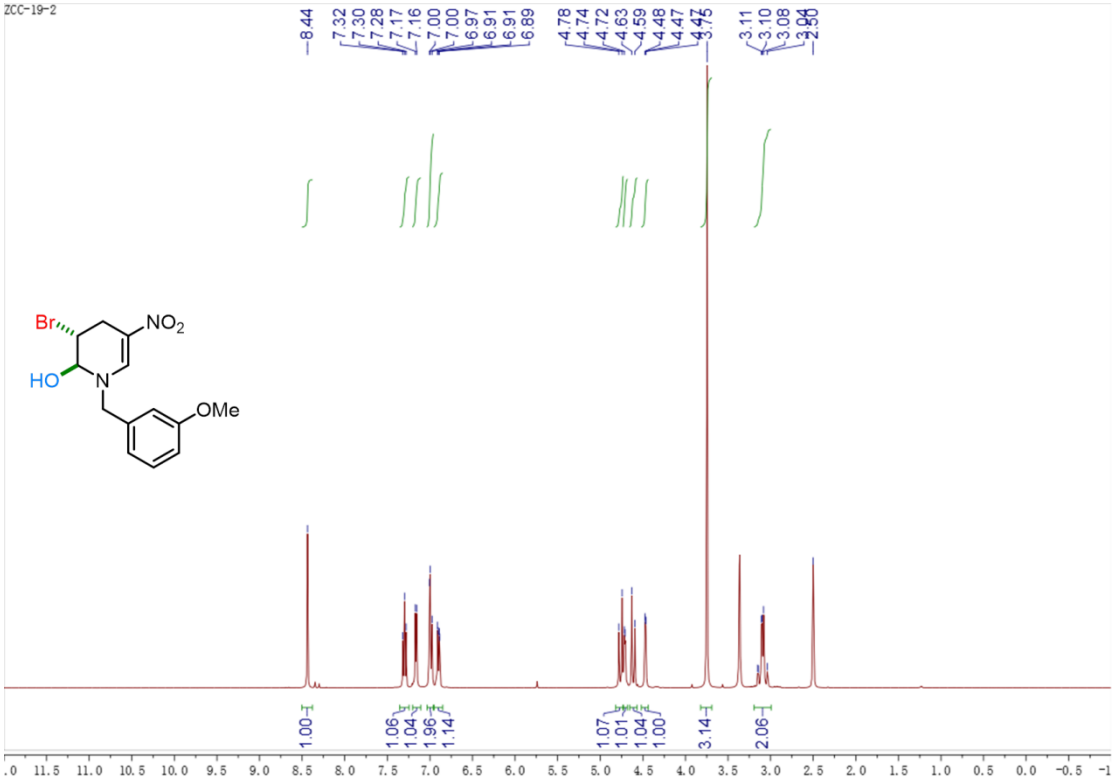
^{1}H NMR spectrum of **2** (400 MHz, DMSO-d_6)



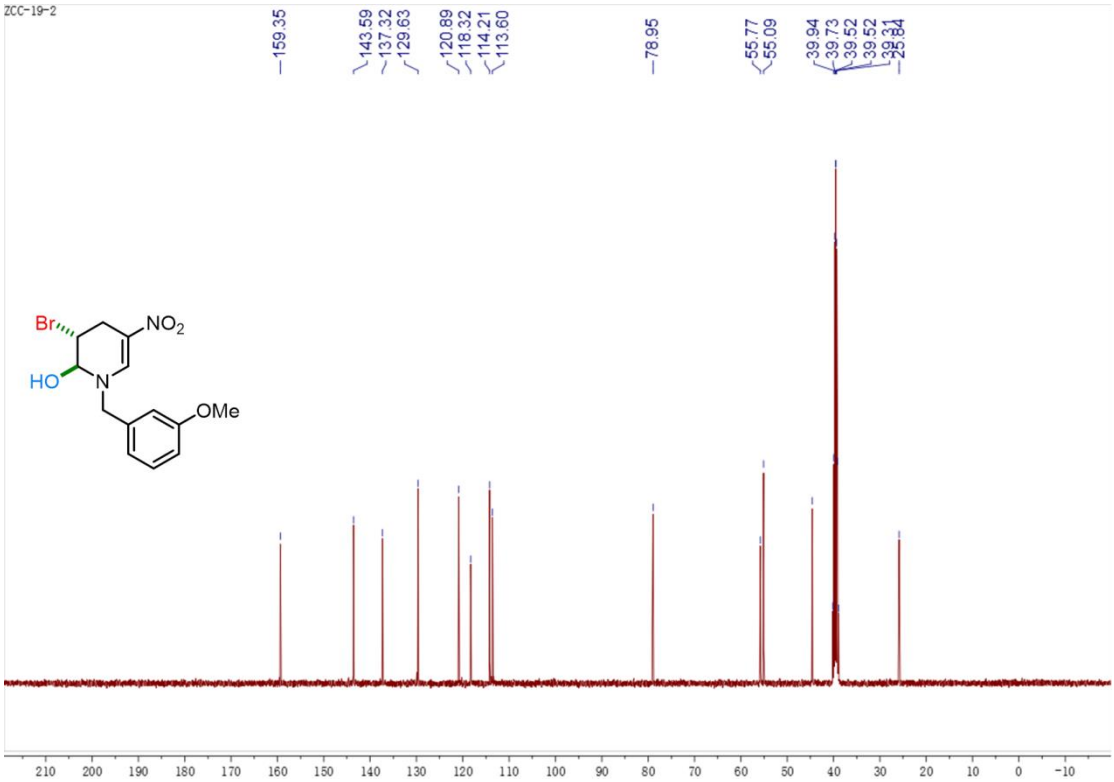
^{13}C NMR spectrum of **2** (100 MHz, DMSO-d_6)



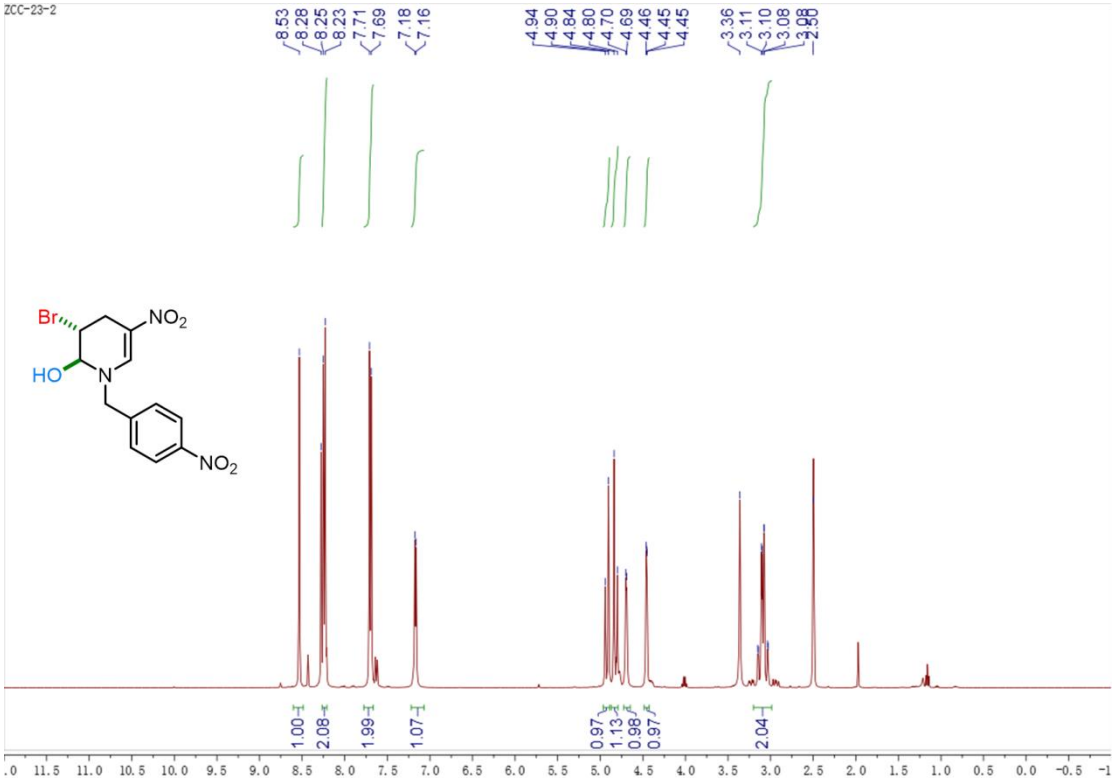
^{1}H NMR spectrum of **3** (400 MHz, DMSO-d_6)



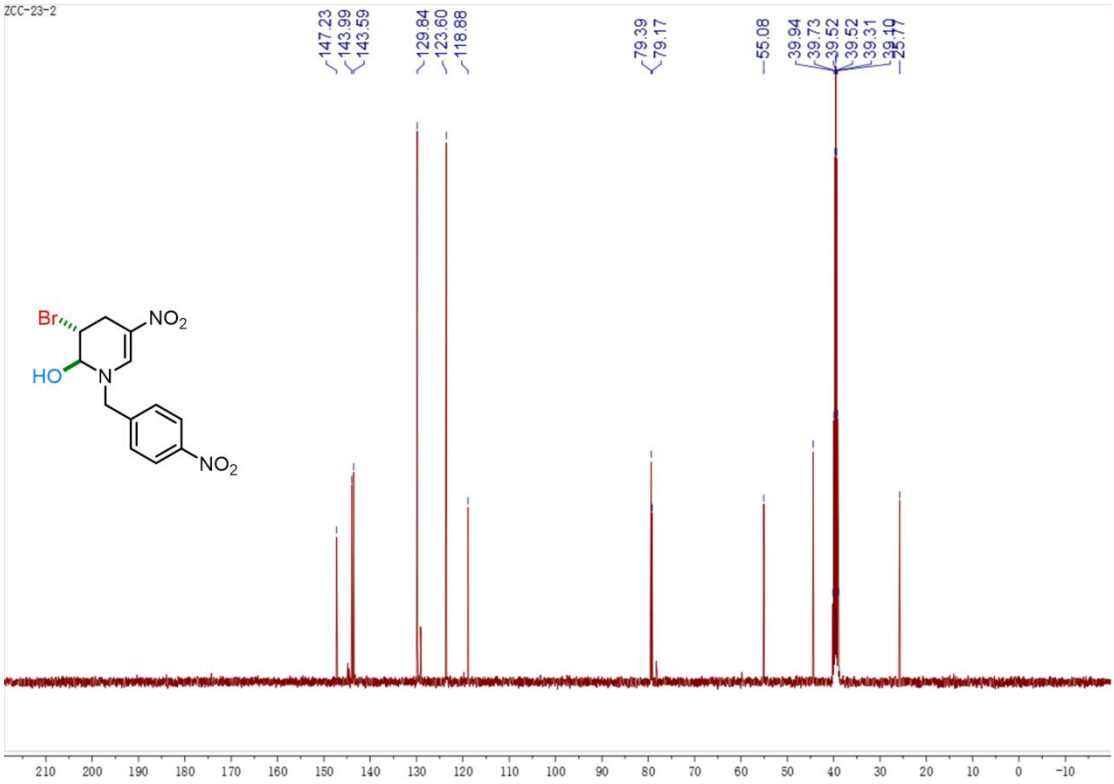
^{13}C NMR spectrum of **3** (100 MHz, DMSO-d_6)



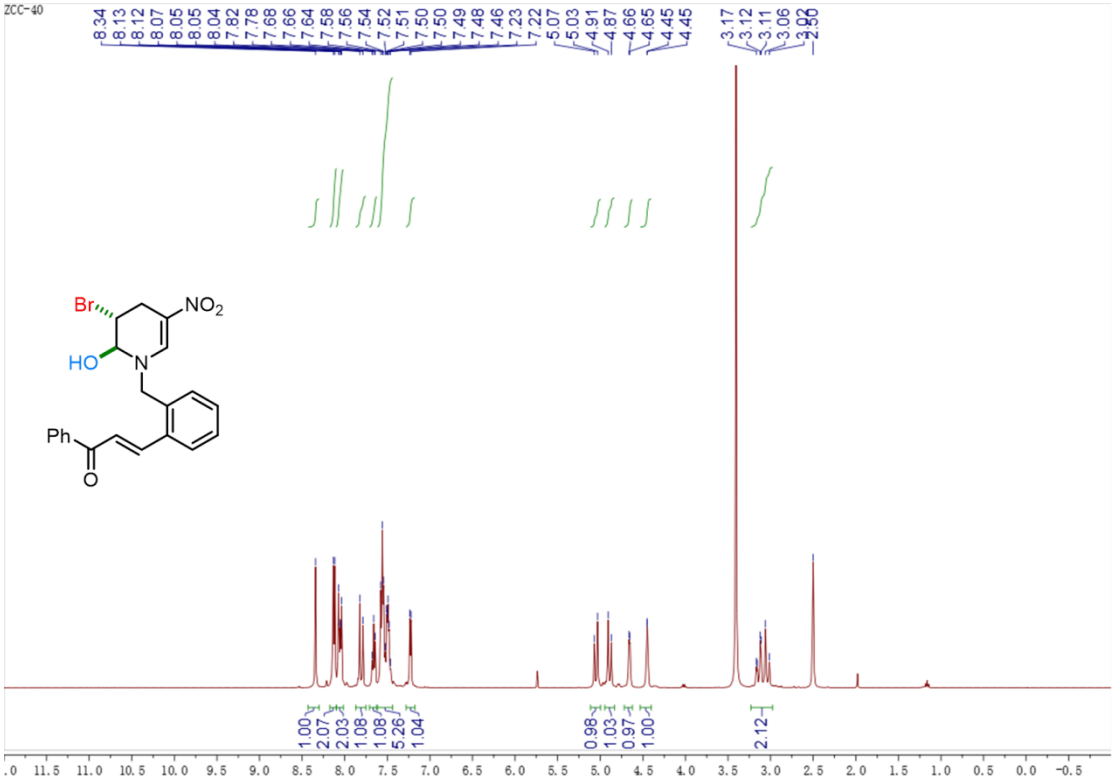
^{1}H NMR spectrum of **4** (400 MHz, DMSO-d_6)



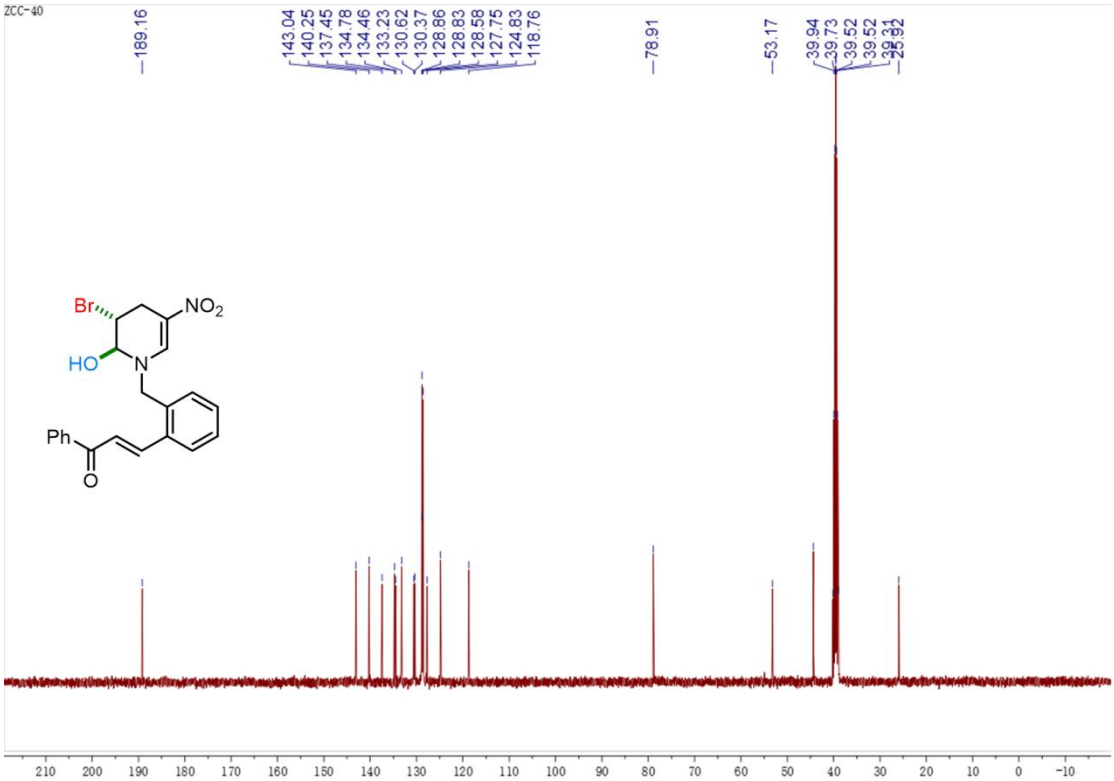
^{13}C NMR spectrum of **4** (100 MHz, DMSO-d_6)



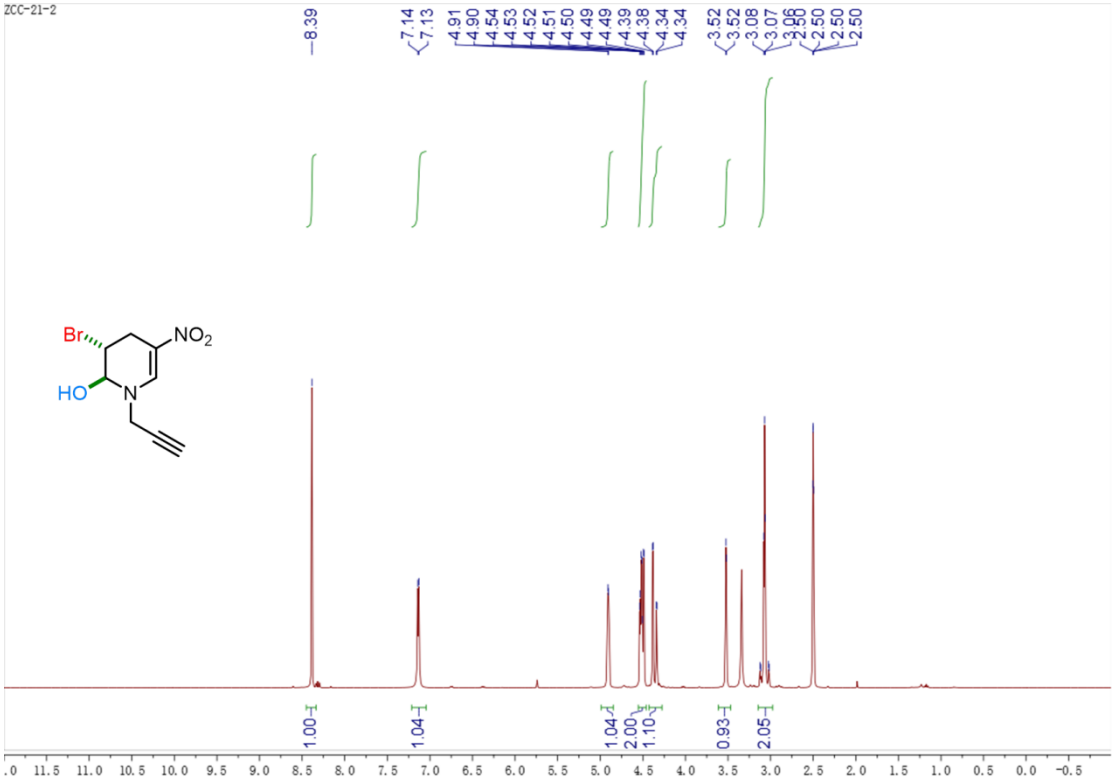
^{1}H NMR spectrum of **5** (400 MHz, DMSO-d_6)



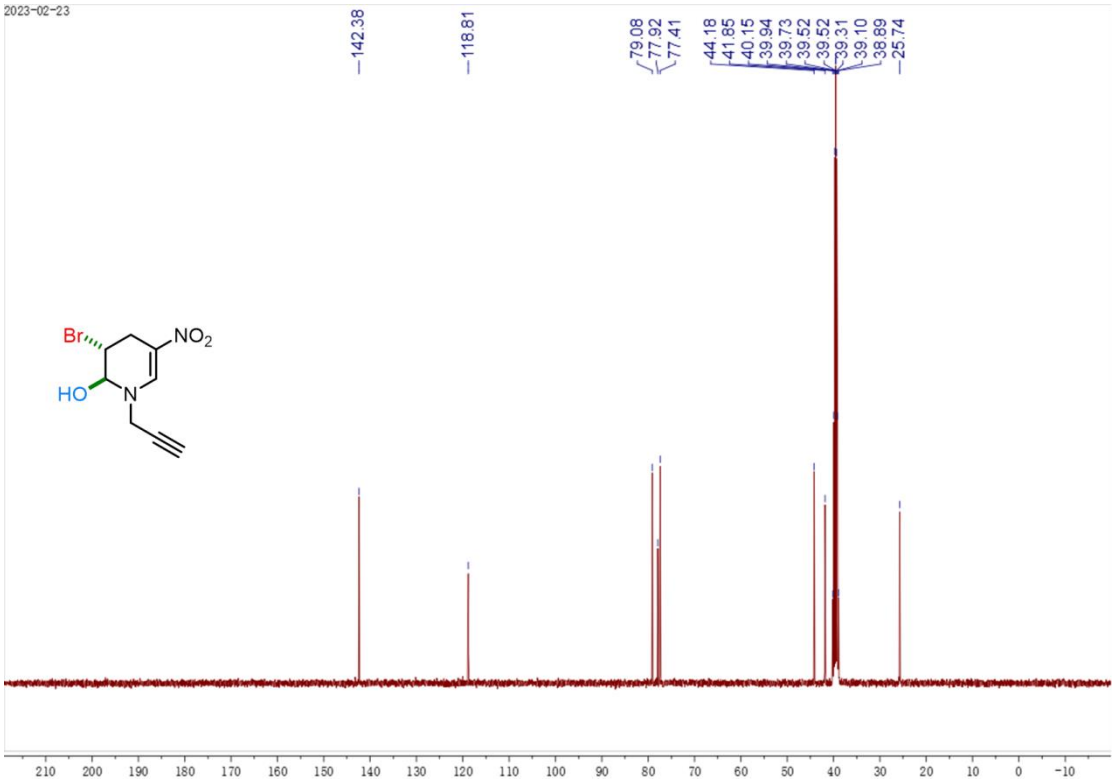
^{13}C NMR spectrum of **5** (100 MHz, DMSO-d_6)



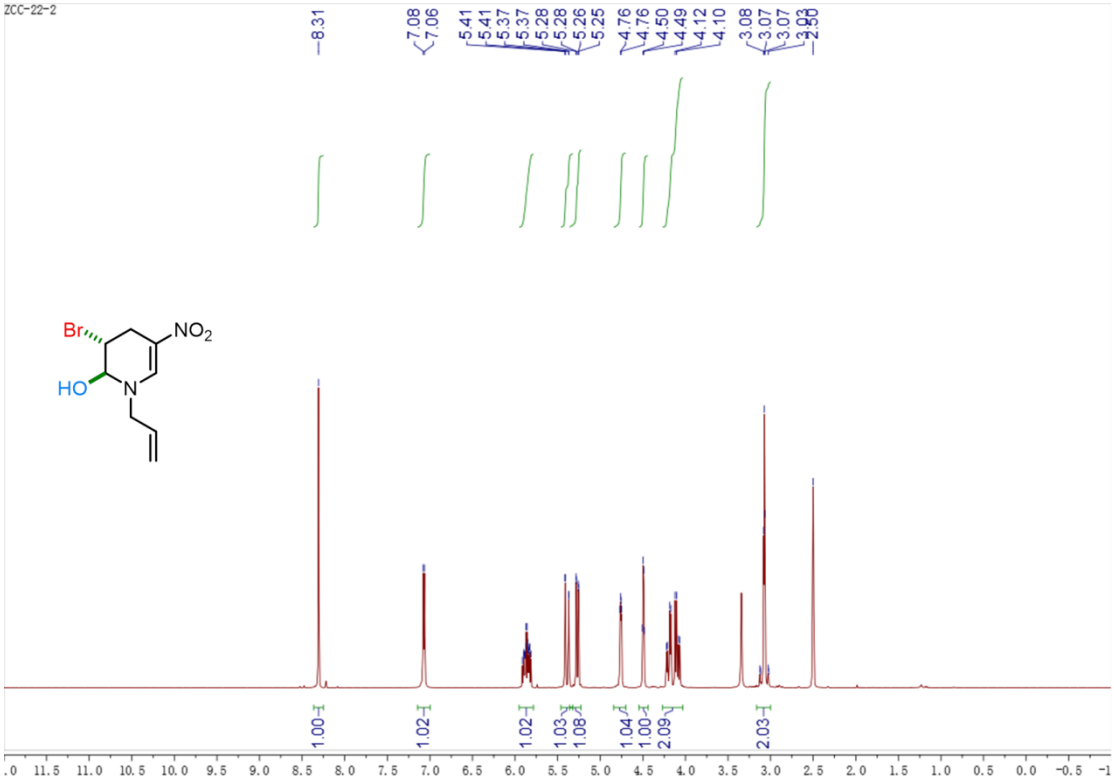
^{1}H NMR spectrum of **6** (400 MHz, DMSO-d_6)



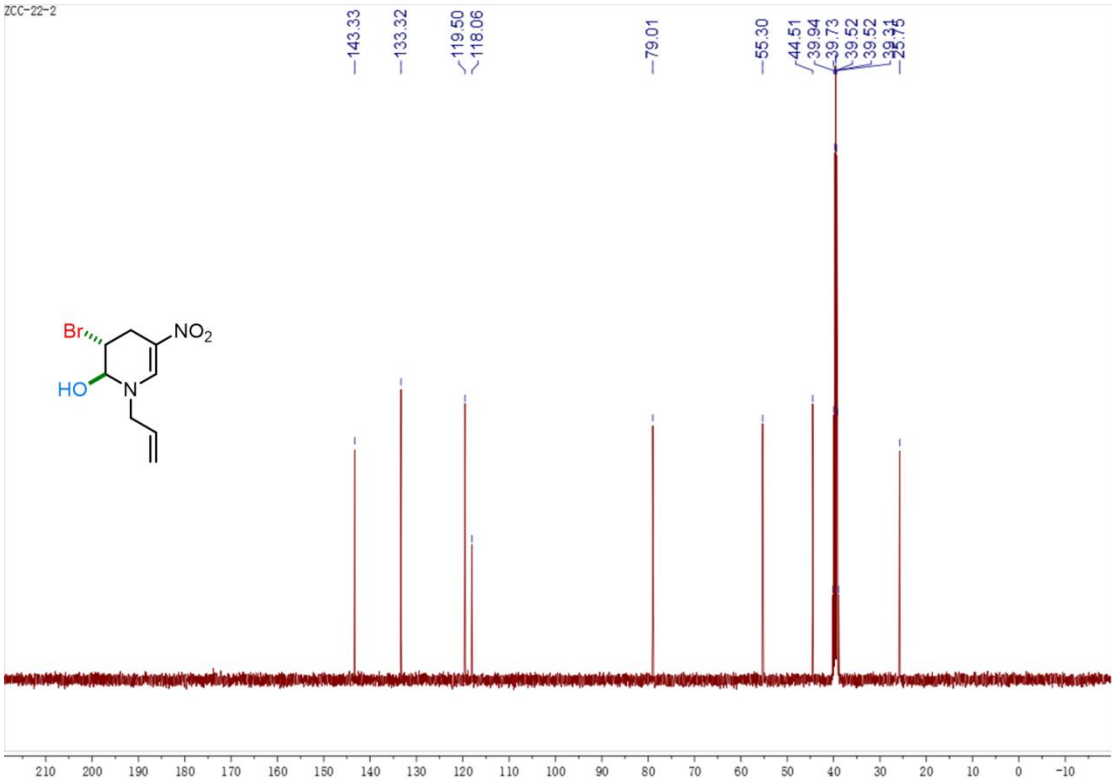
^{13}C NMR spectrum of **6** (100 MHz, DMSO-d_6)



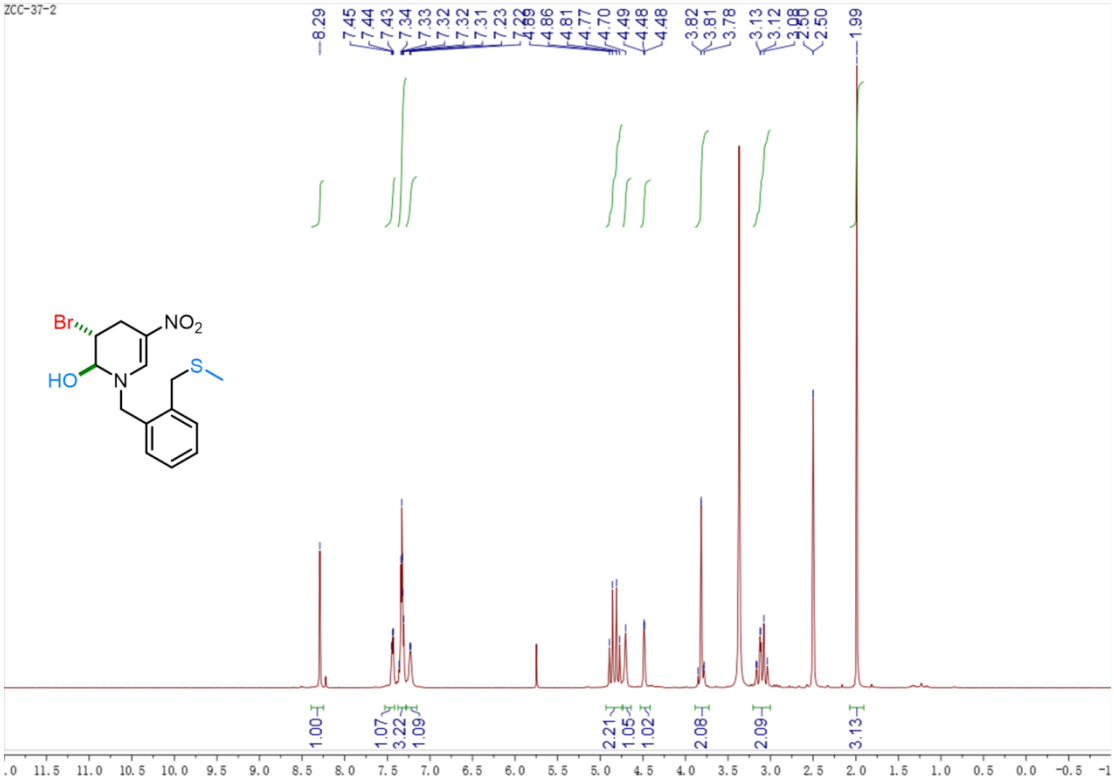
^{1}H NMR spectrum of **7** (400 MHz, DMSO-d_6)



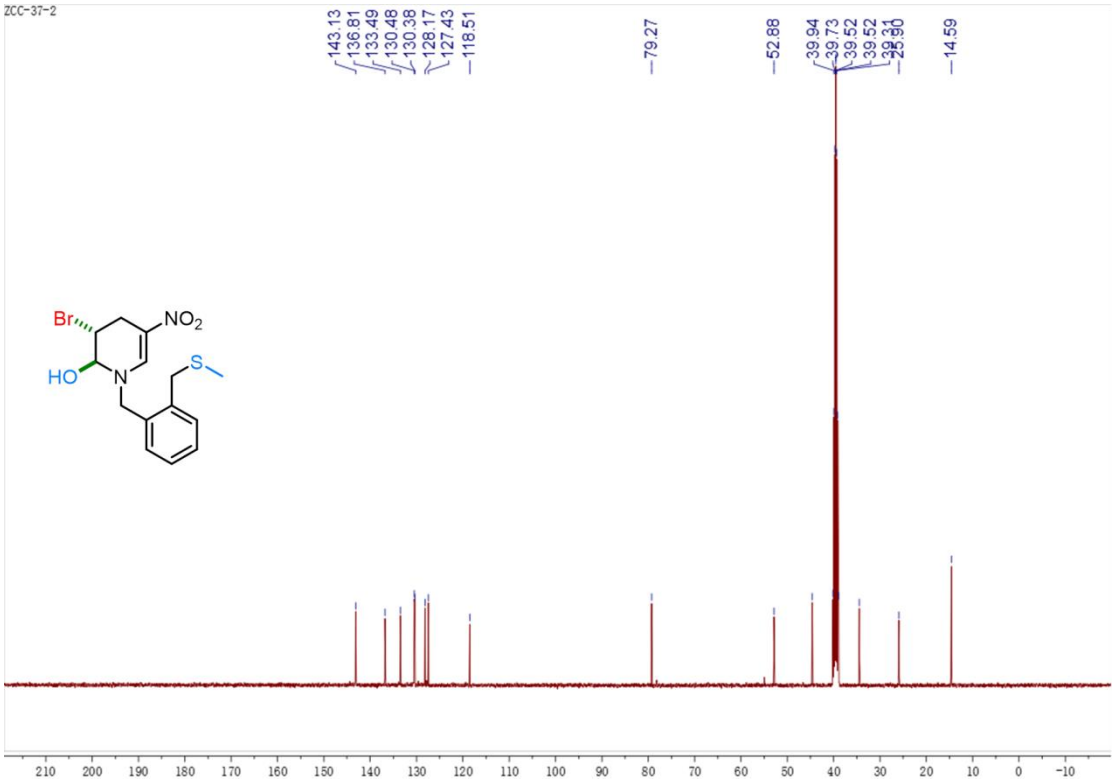
^{13}C NMR spectrum of **7** (100 MHz, DMSO-d_6)



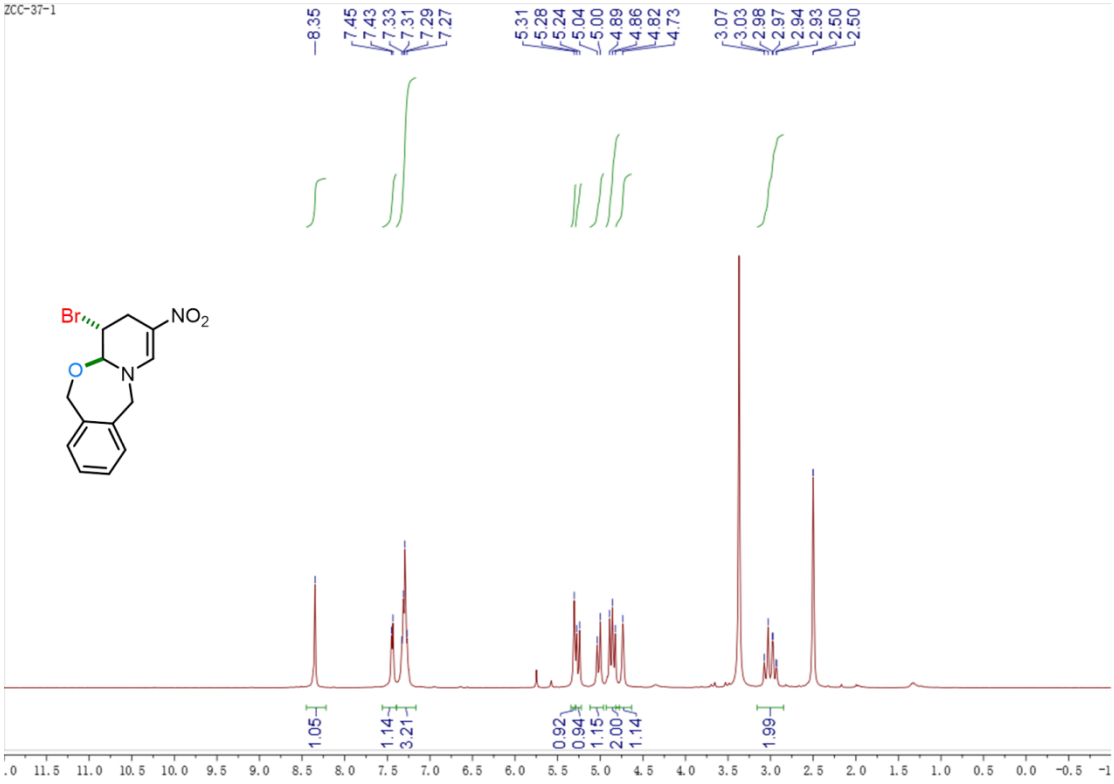
^{1}H NMR spectrum of **8** (400 MHz, DMSO-d_6)



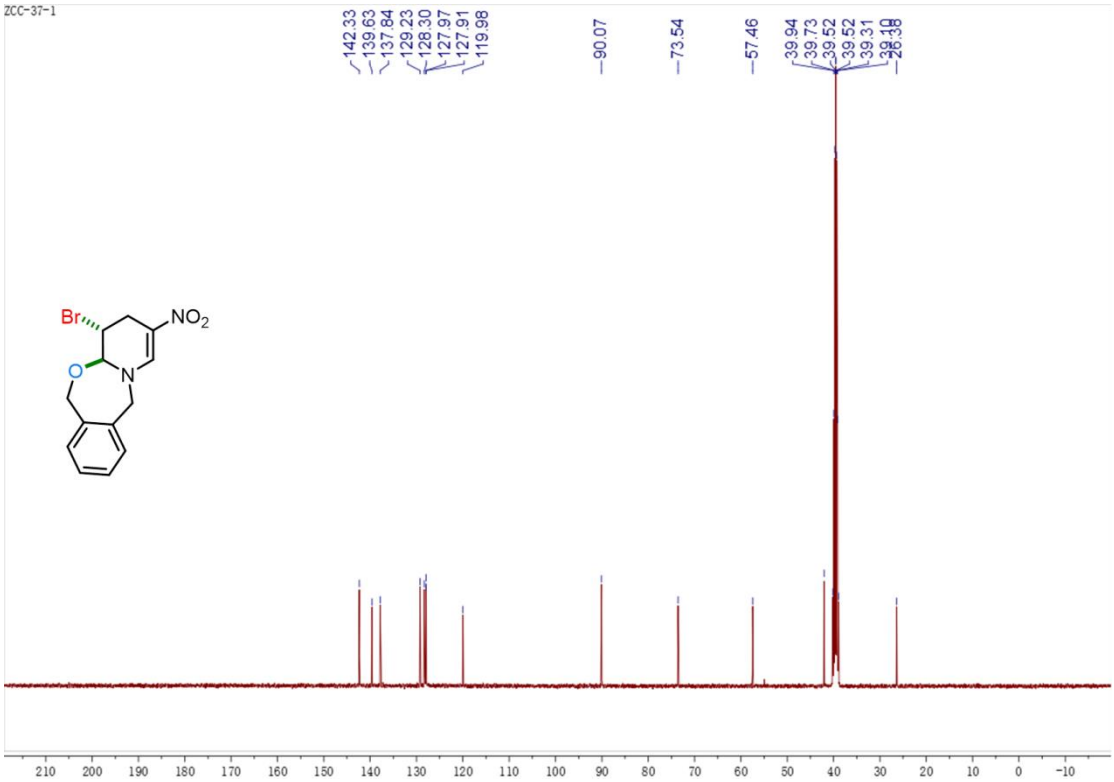
^{13}C NMR spectrum of **8** (100 MHz, DMSO-d_6)



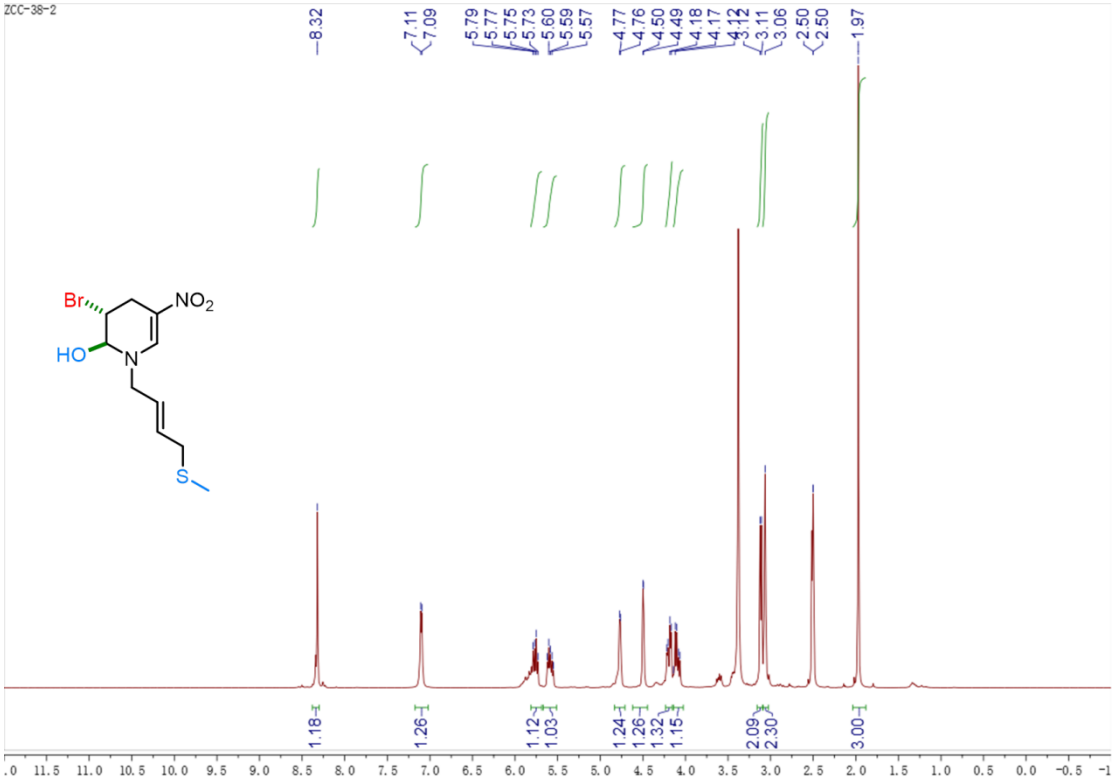
^{1}H NMR spectrum of **9** (400 MHz, DMSO-d_6)



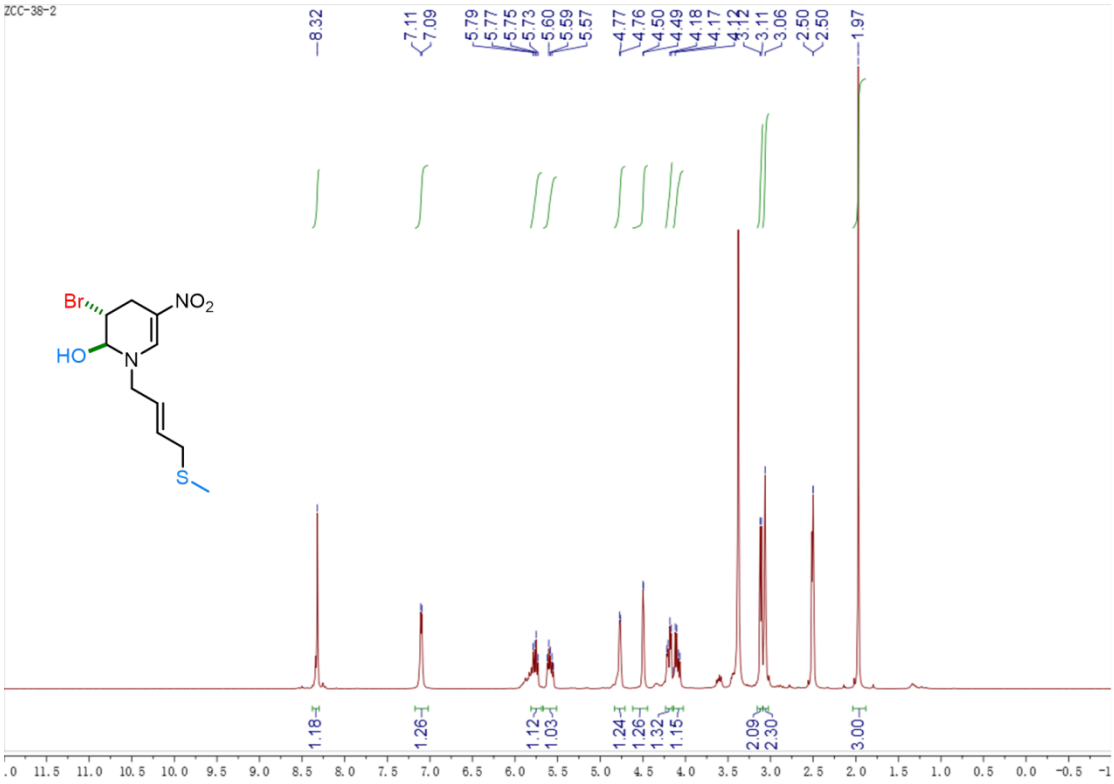
^{13}C NMR spectrum of **9** (100 MHz, DMSO-d_6)



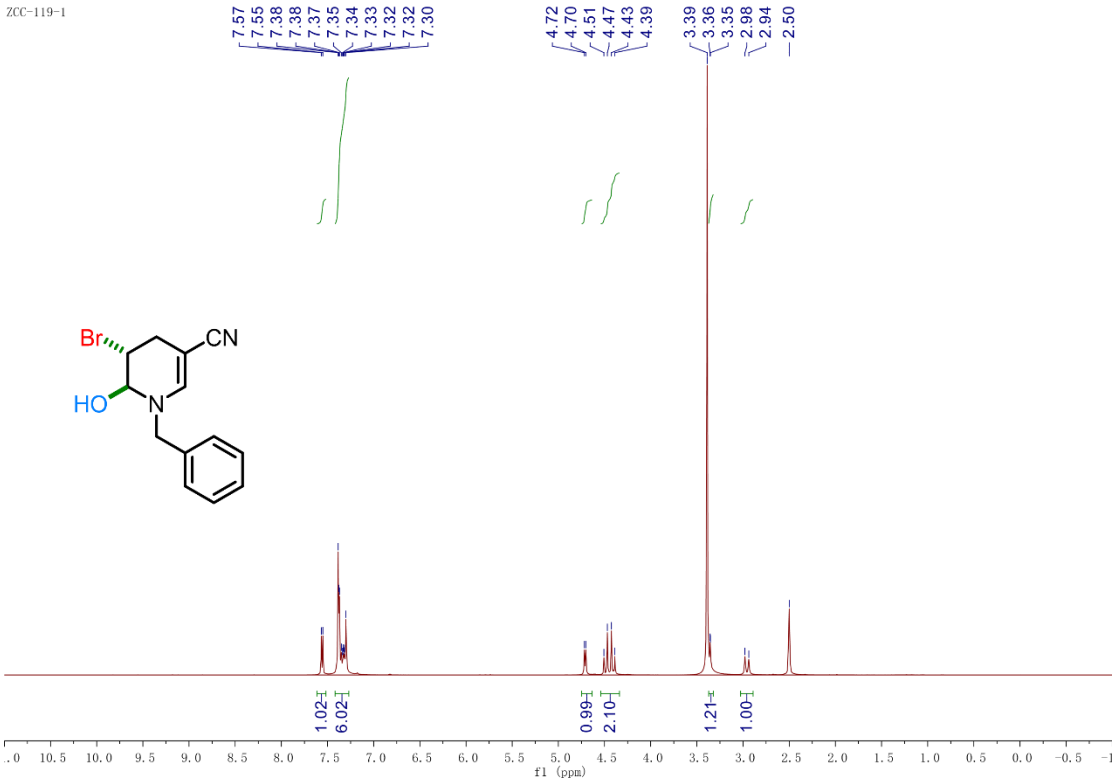
^{1}H NMR spectrum of **10** (400 MHz, DMSO-d_6)



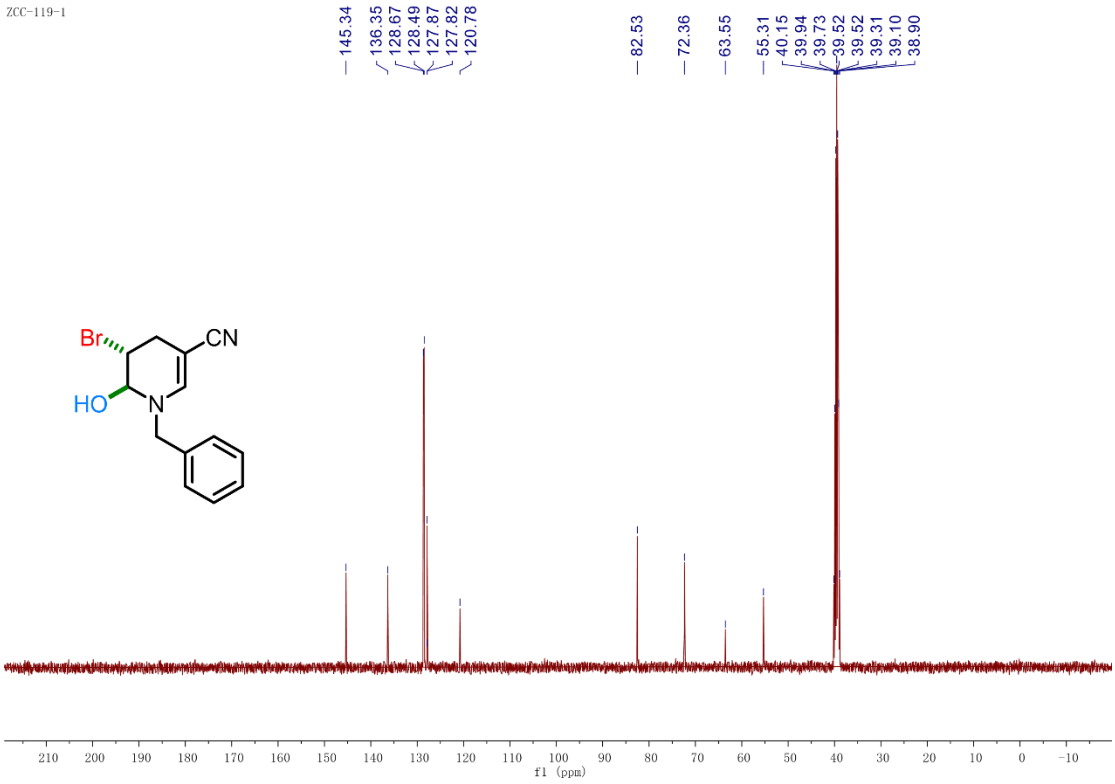
^{13}C NMR spectrum of **10** (100 MHz, DMSO-d_6)



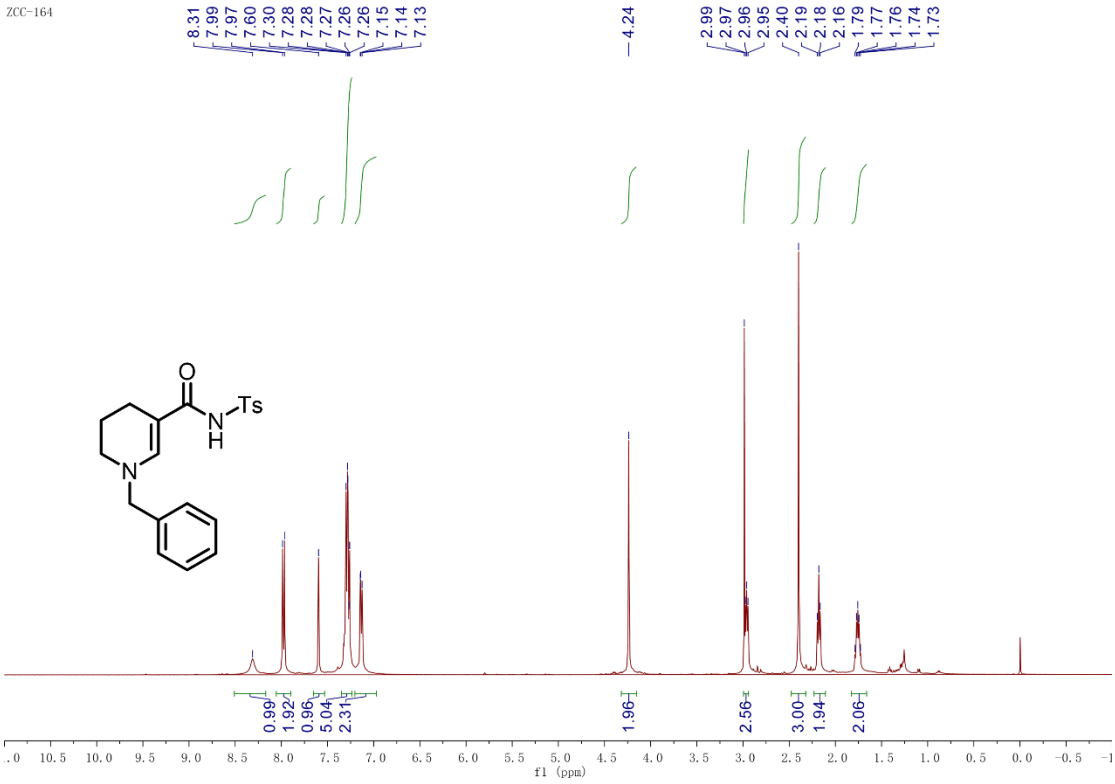
^{1}H NMR spectrum of **11** (400 MHz, $CDCl_3$)



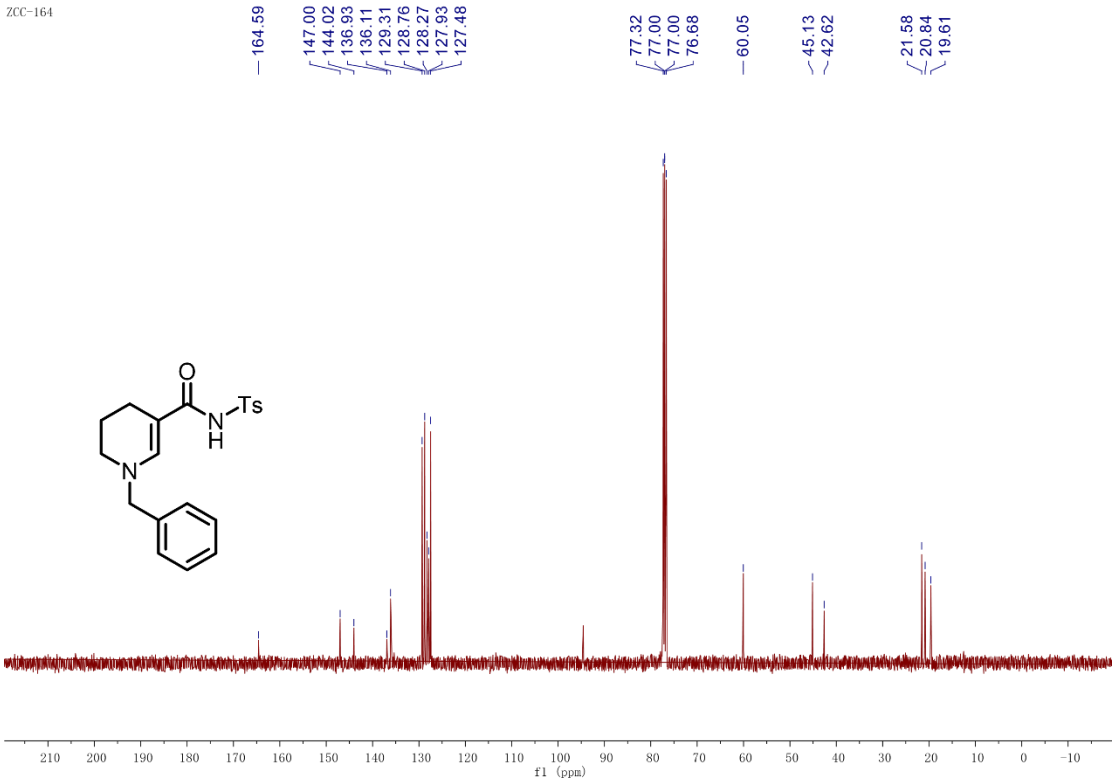
^{13}C NMR spectrum of **11** (100 MHz, $CDCl_3$)



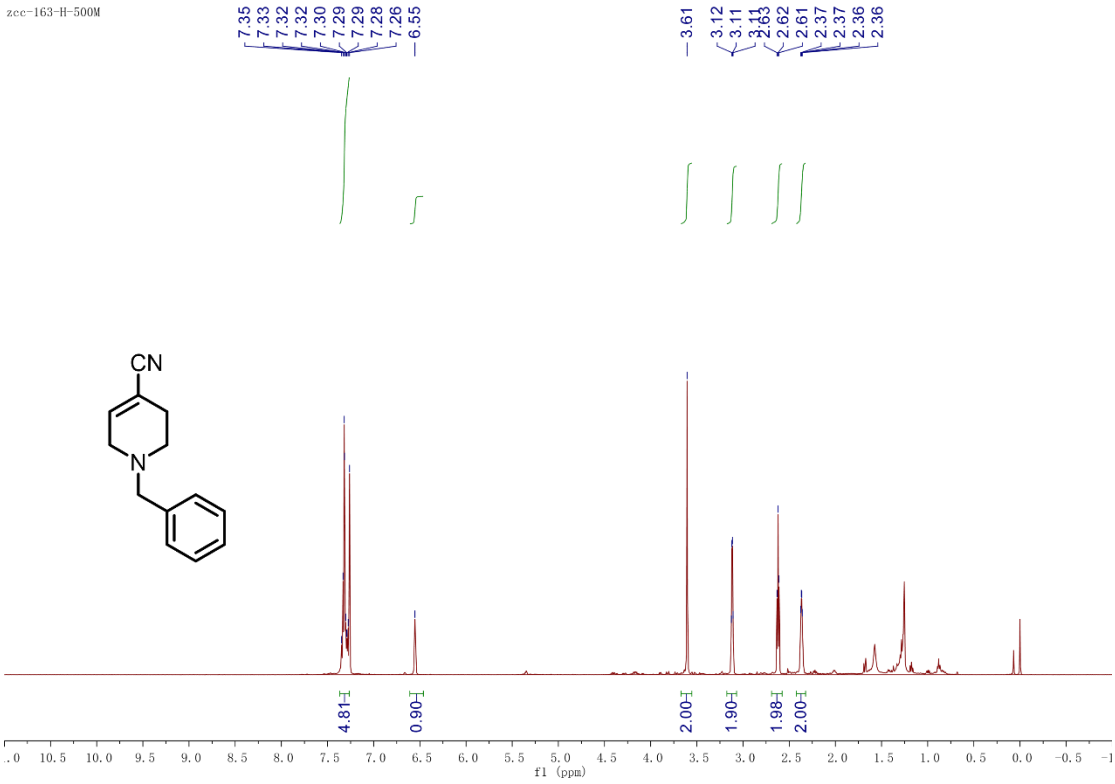
^{1}H NMR spectrum of **12** (400 MHz, $CDCl_3$)



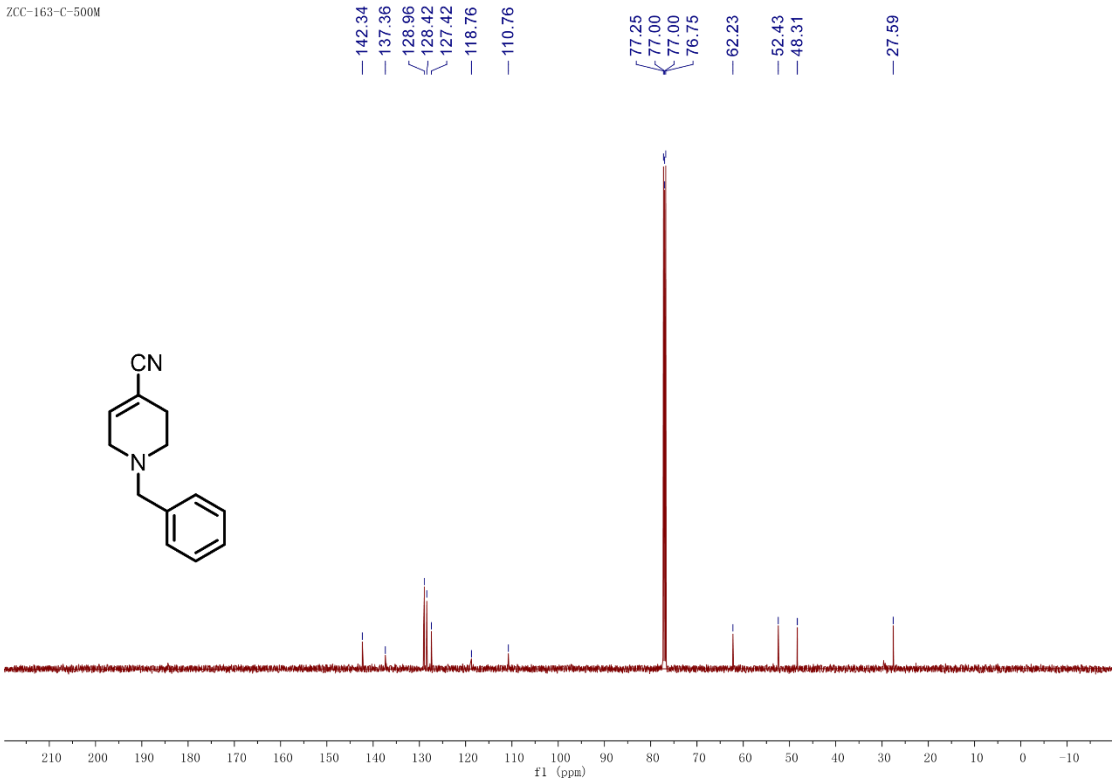
^{13}C NMR spectrum of **12** (100 MHz, $CDCl_3$)



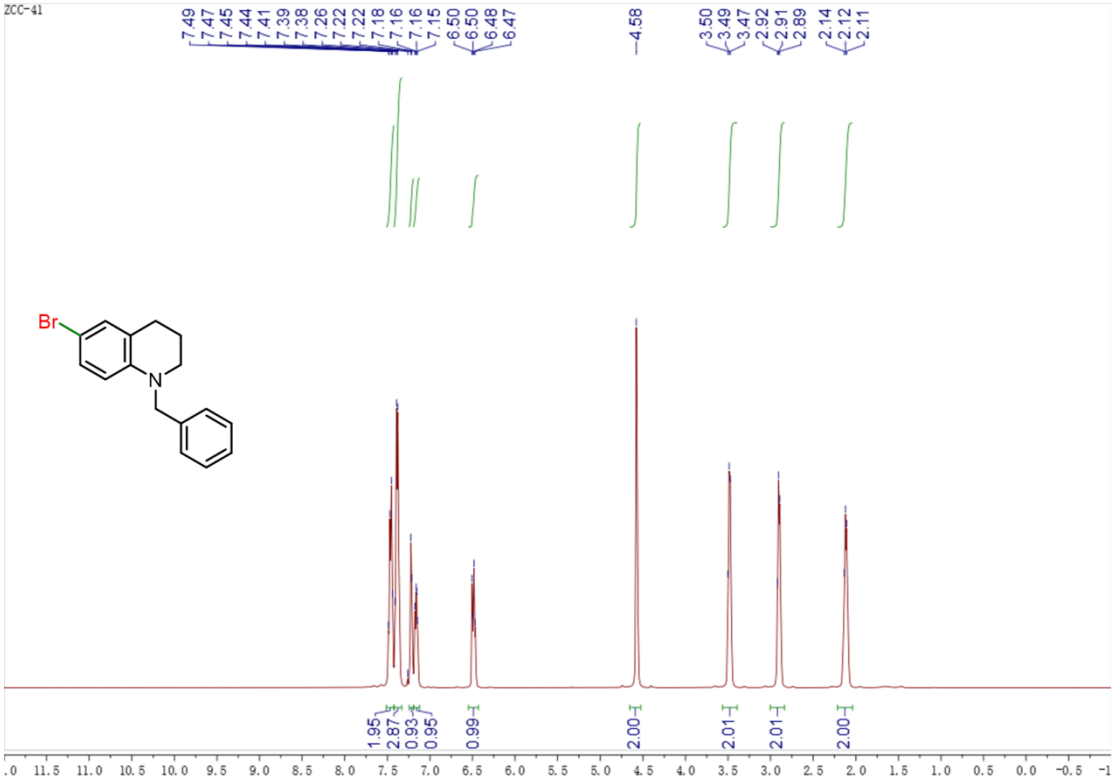
^{1}H NMR spectrum of **13** (500 MHz, $CDCl_3$)



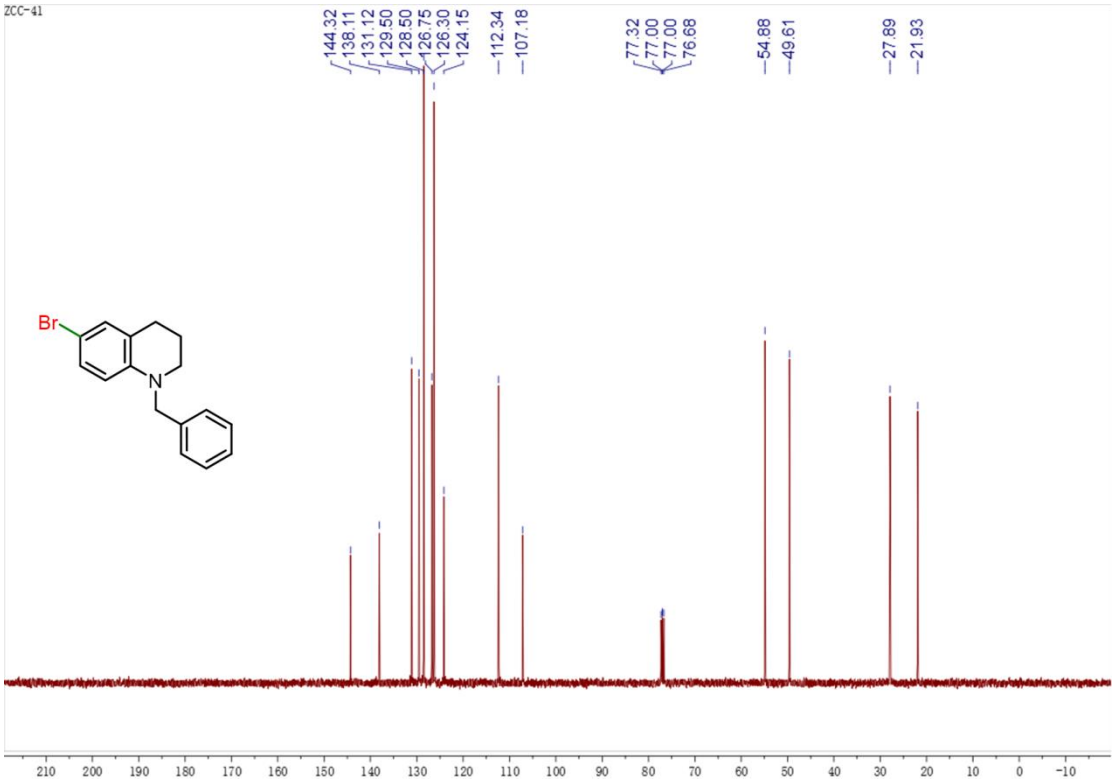
^{13}C NMR spectrum of **13** (125MHz, $CDCl_3$)



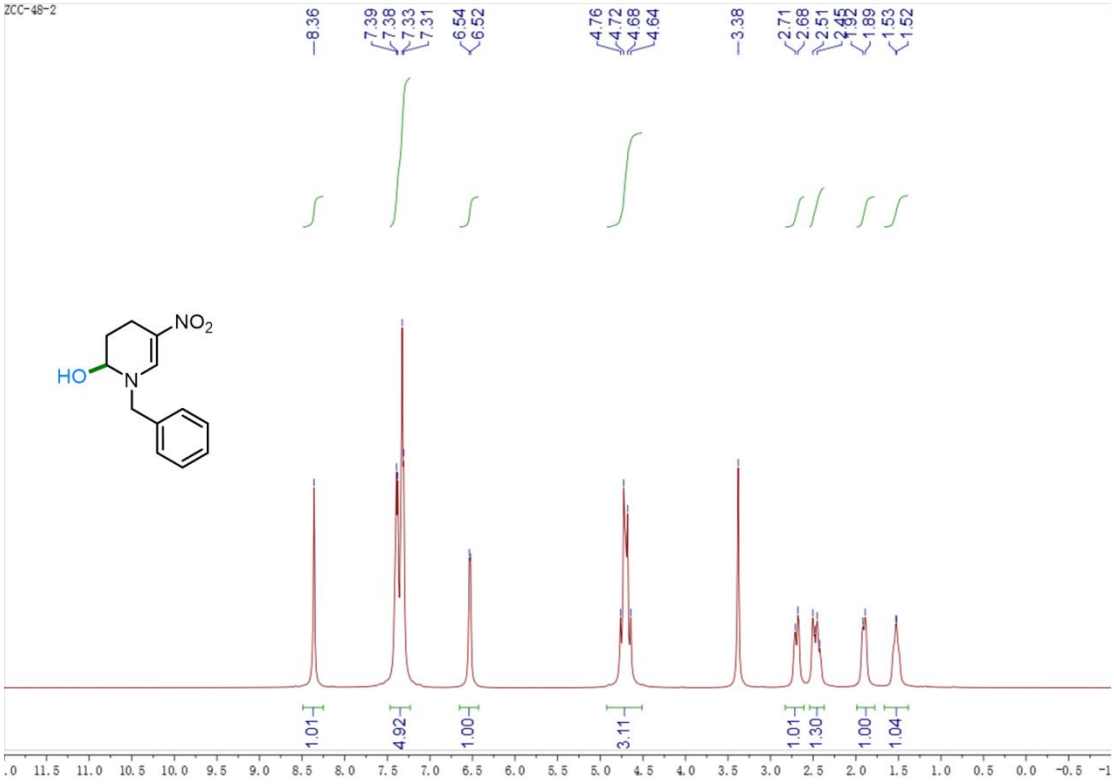
^{1}H NMR spectrum of **14** (400 MHz, $CDCl_3$)



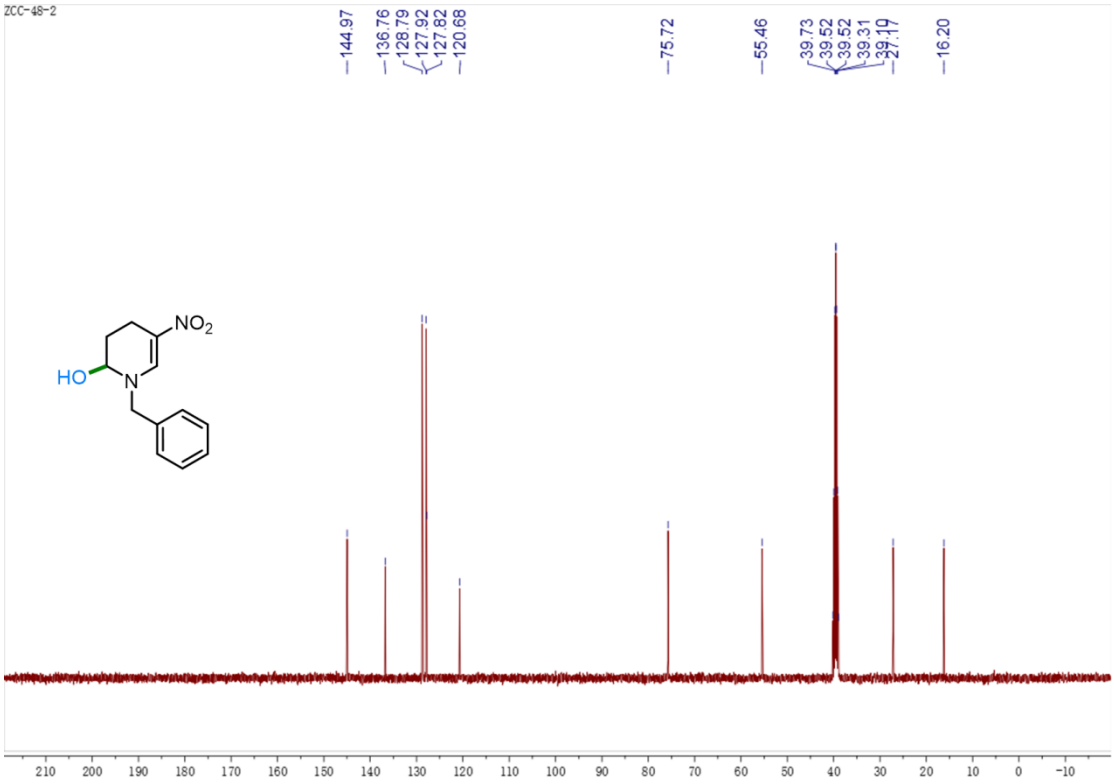
^{13}C NMR spectrum of **14** (100 MHz, $CDCl_3$)



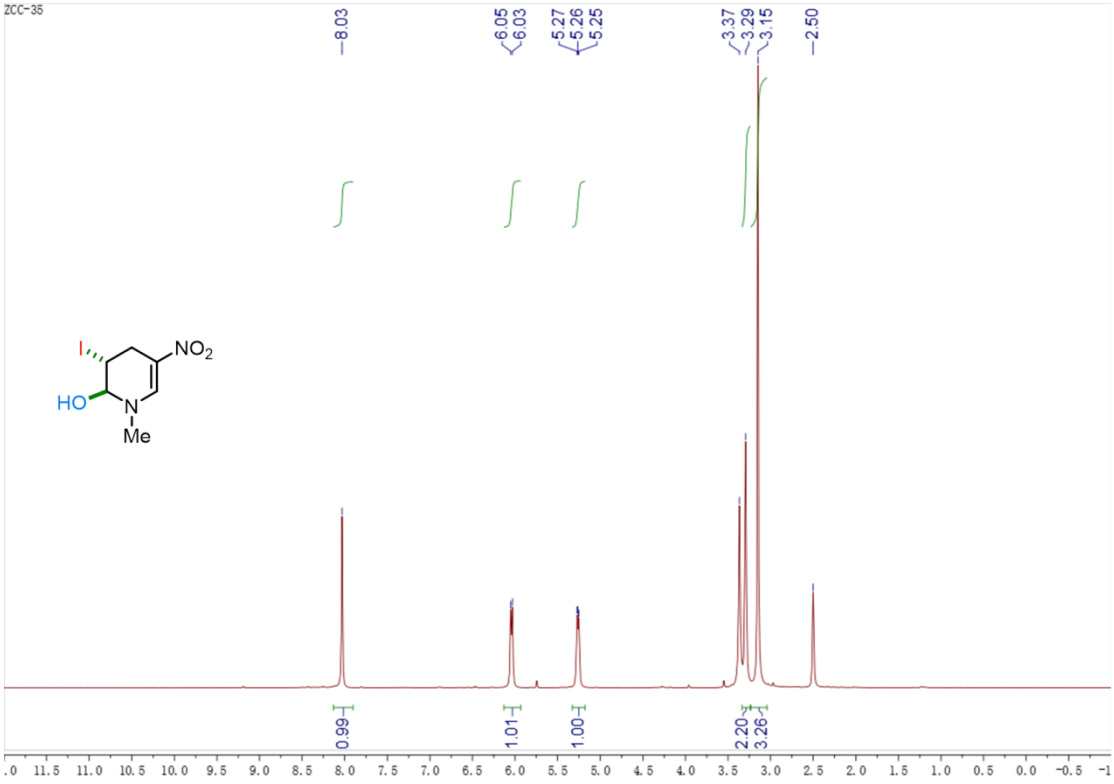
^{1}H NMR spectrum of **15** (400 MHz, DMSO-d_6)



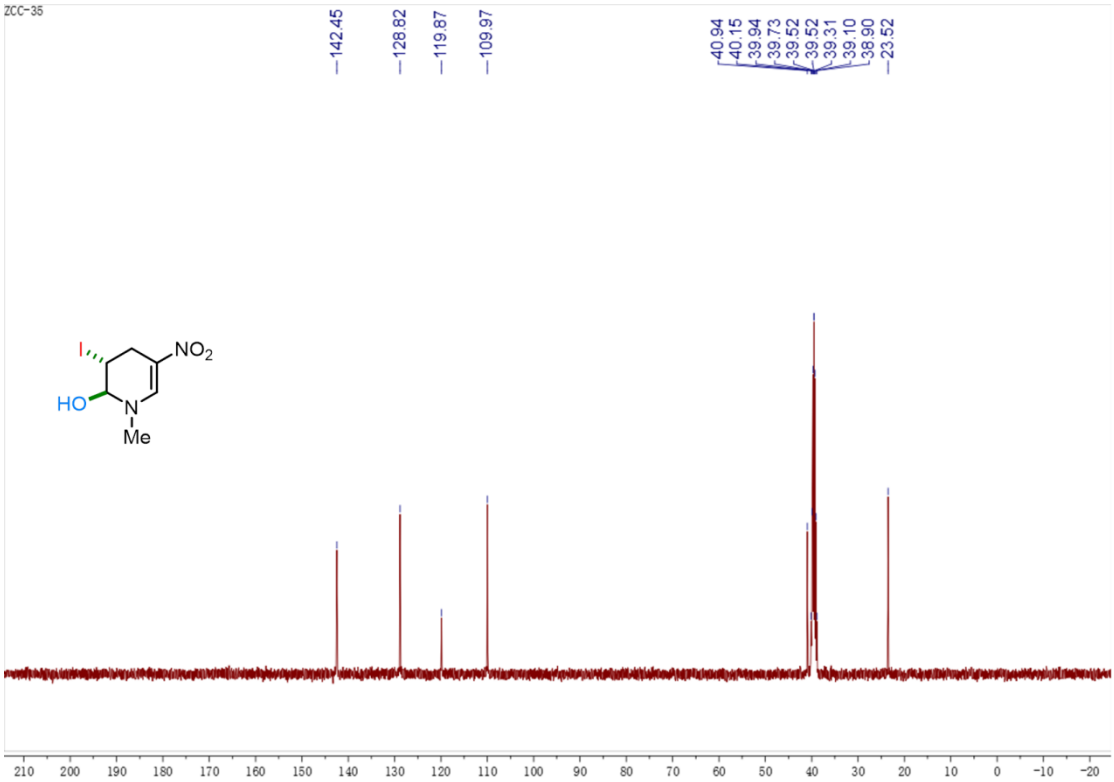
^{13}C NMR spectrum of **15** (100 MHz, DMSO-d_6)



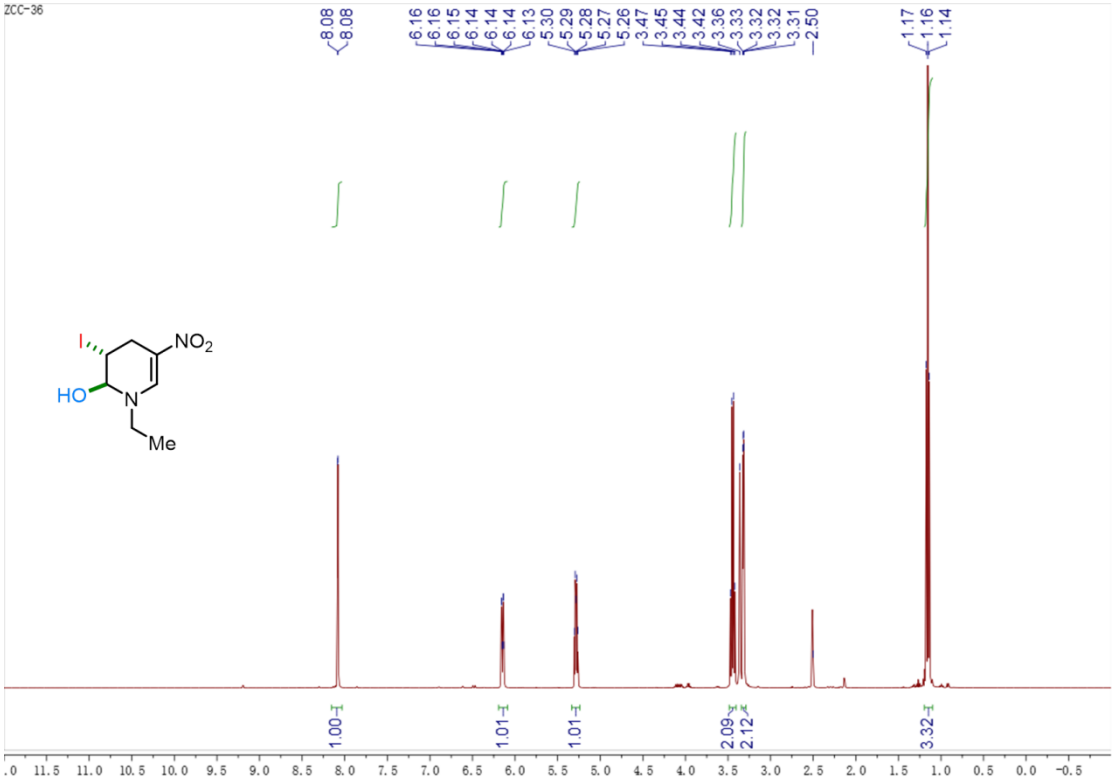
^{1}H NMR spectrum of **16** (400 MHz, DMSO-d_6)



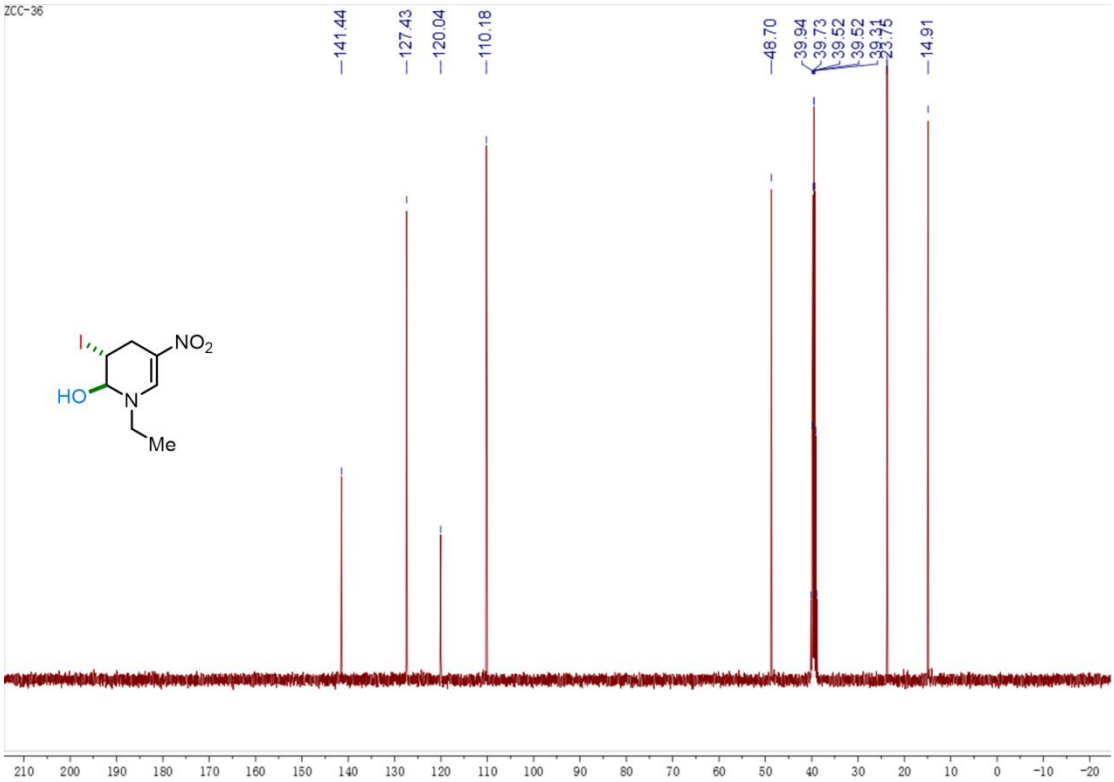
^{13}C NMR spectrum of **16** (100 MHz, DMSO-d_6)



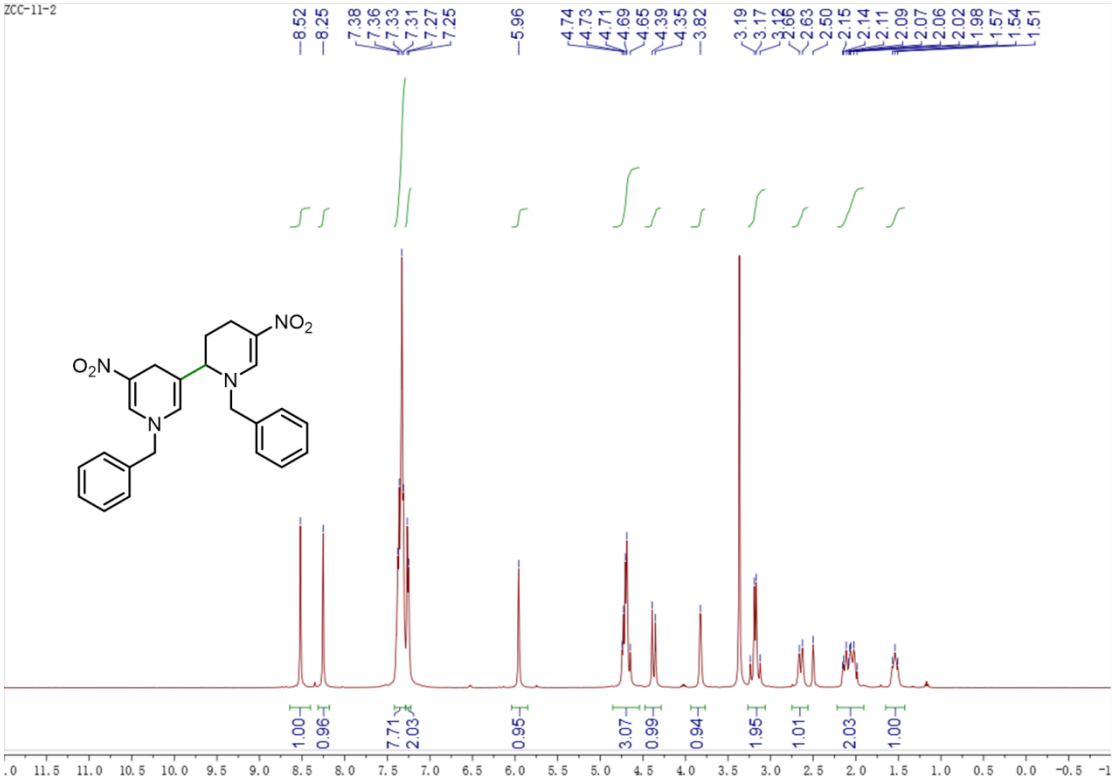
^{1}H NMR spectrum of **17** (400 MHz, DMSO-d_6)



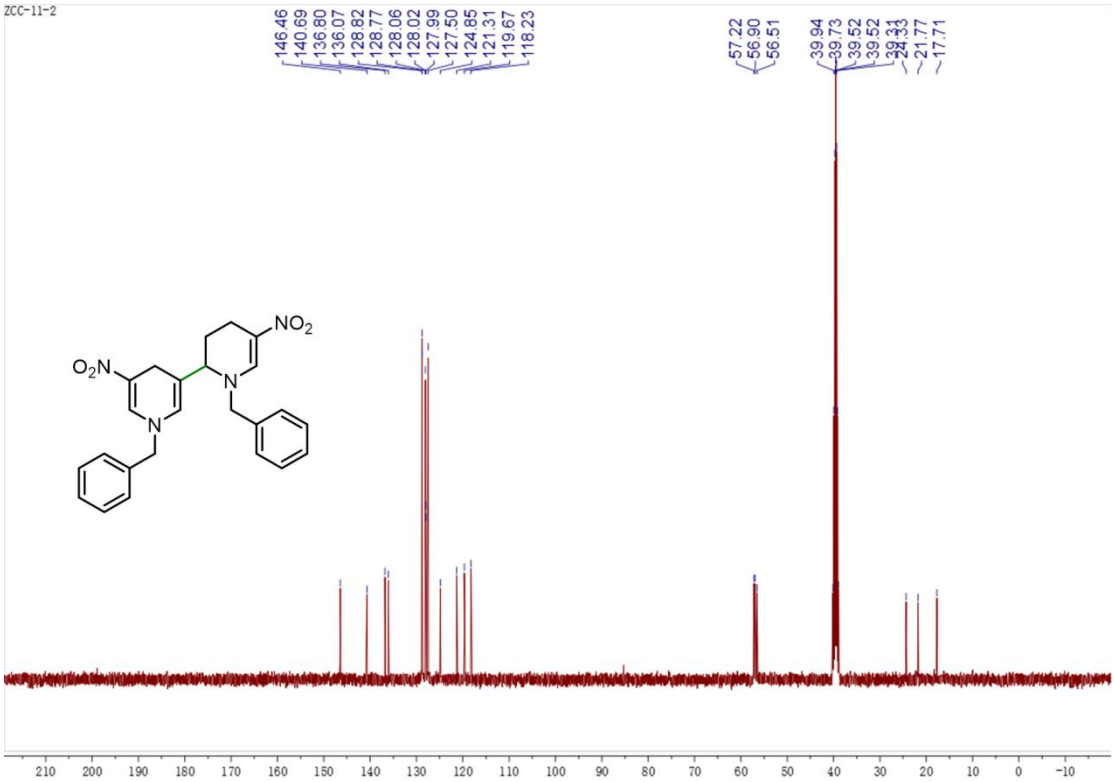
^{13}C NMR spectrum of **17** (100 MHz, DMSO-d_6)



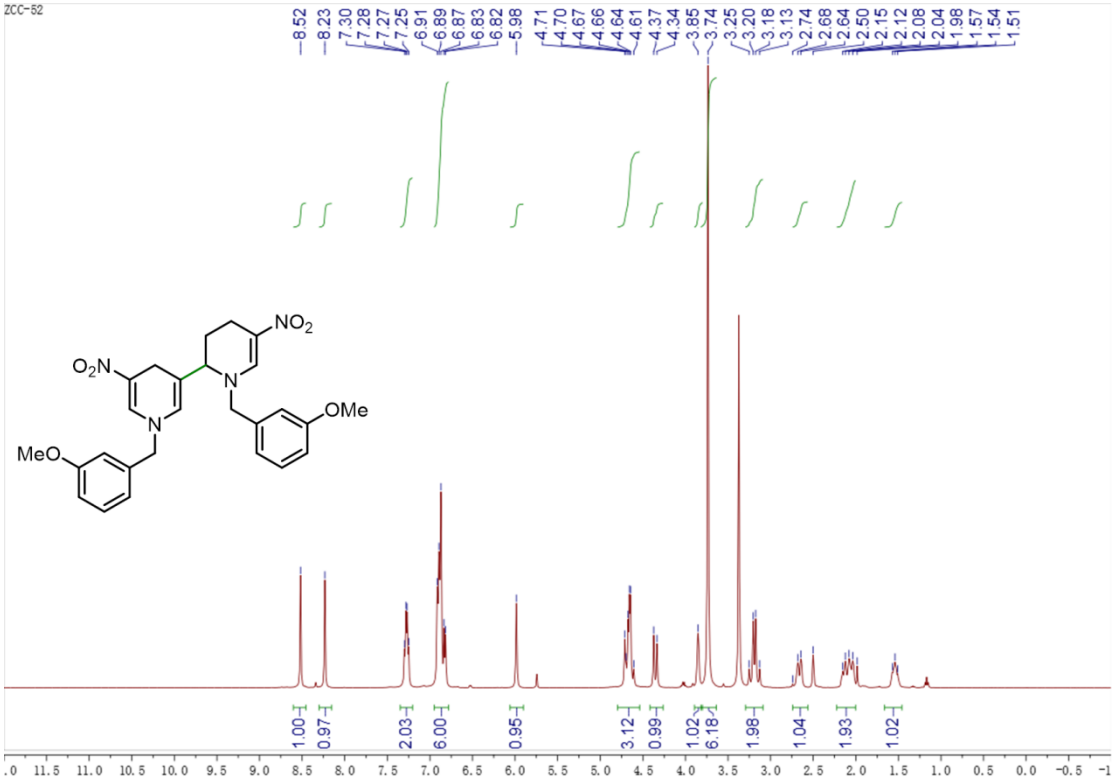
^{1}H NMR spectrum of **18** (400 MHz, DMSO-d_6)



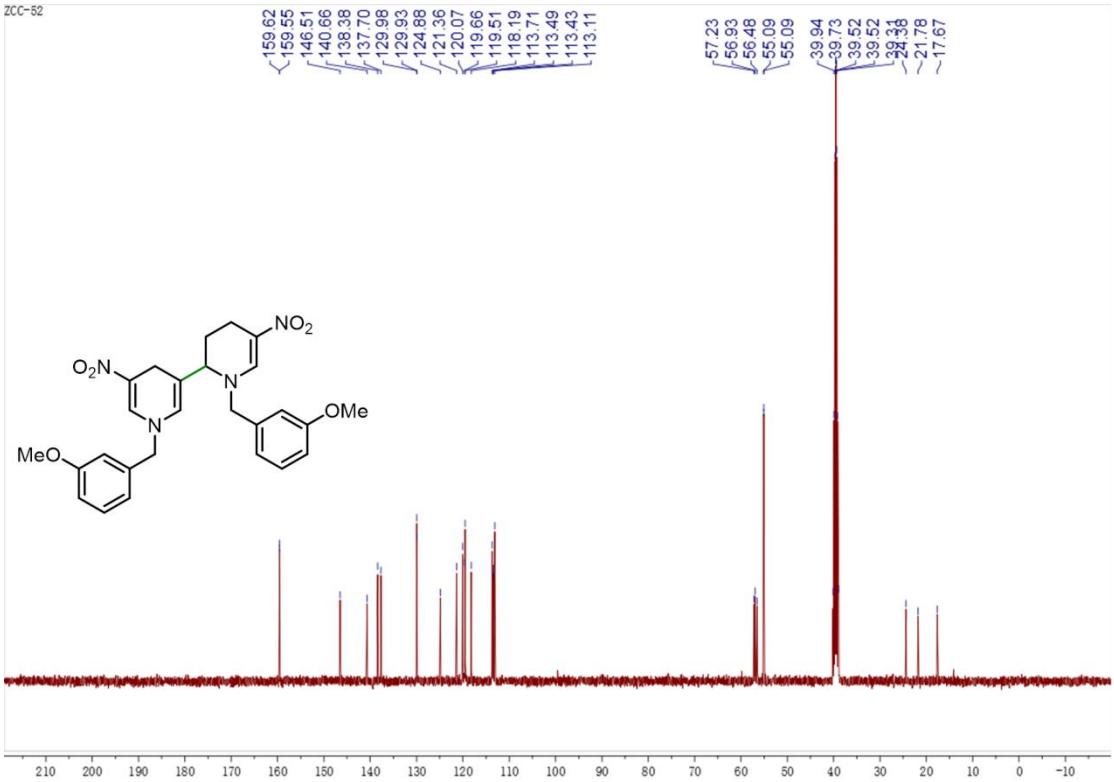
^{13}C NMR spectrum of **18** (100 MHz, DMSO-d_6)



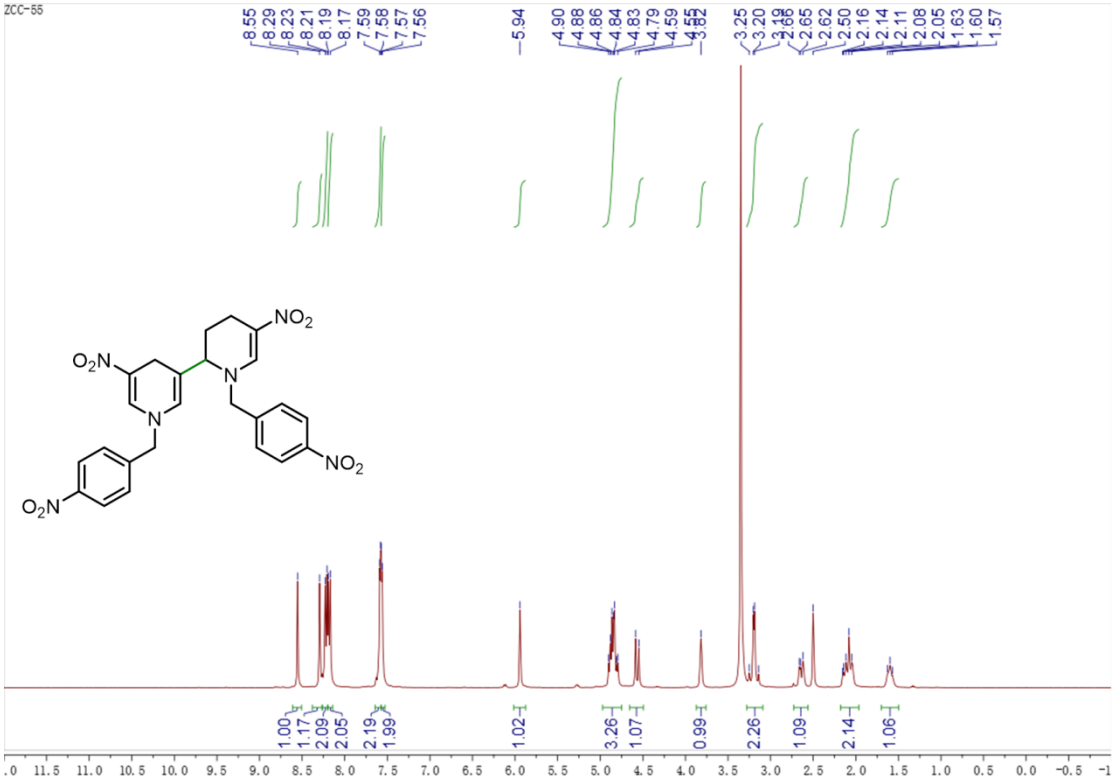
^{1}H NMR spectrum of **19** (400 MHz, DMSO-d_6)



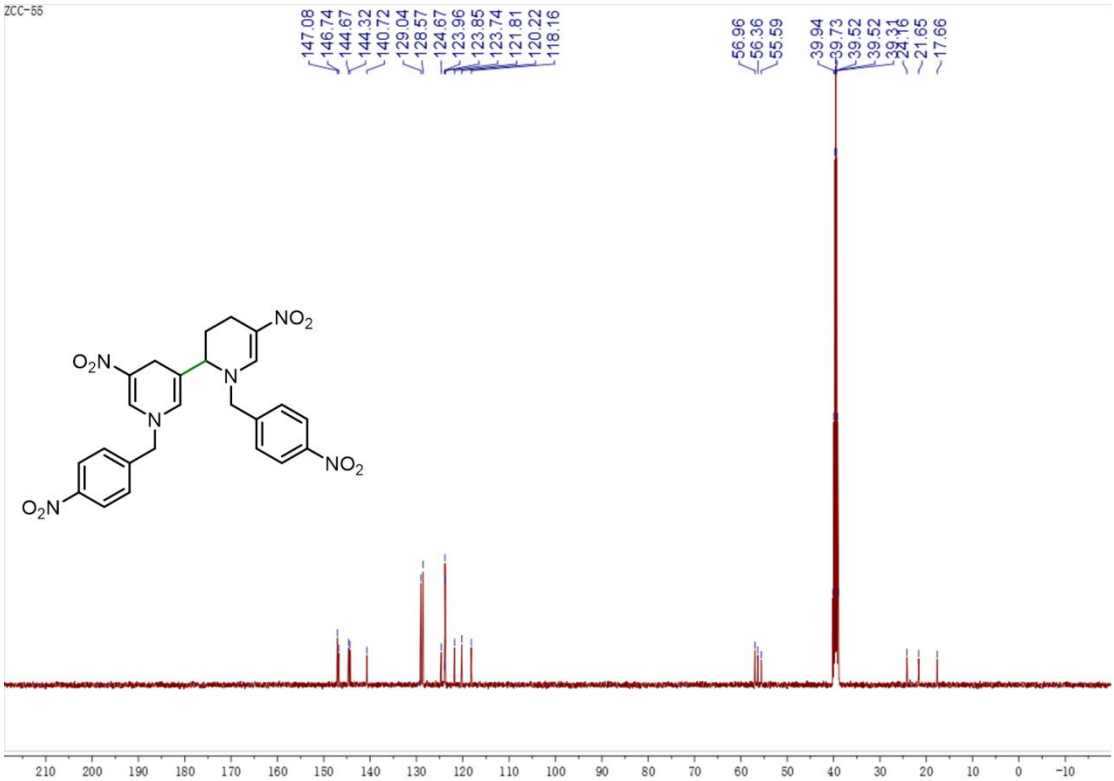
^{13}C NMR spectrum of **19** (100 MHz, DMSO-d_6)



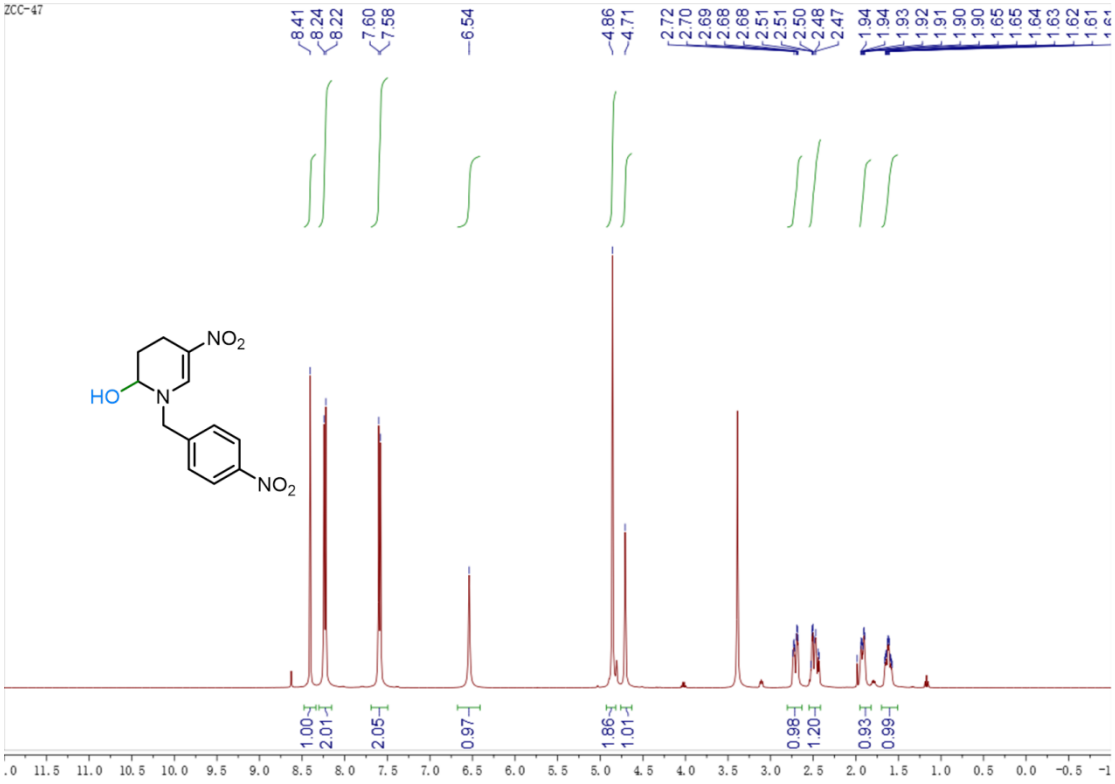
^{1}H NMR spectrum of **20** (400 MHz, DMSO-d_6)



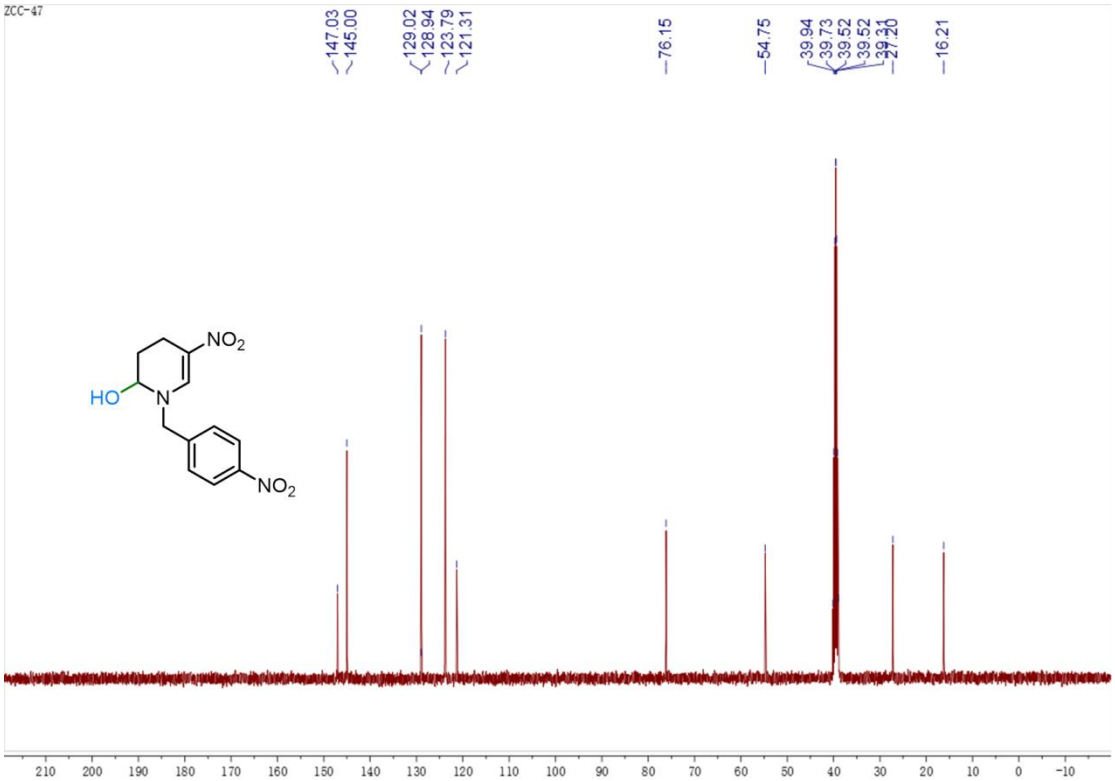
^{13}C NMR spectrum of **20** (100 MHz, DMSO-d_6)



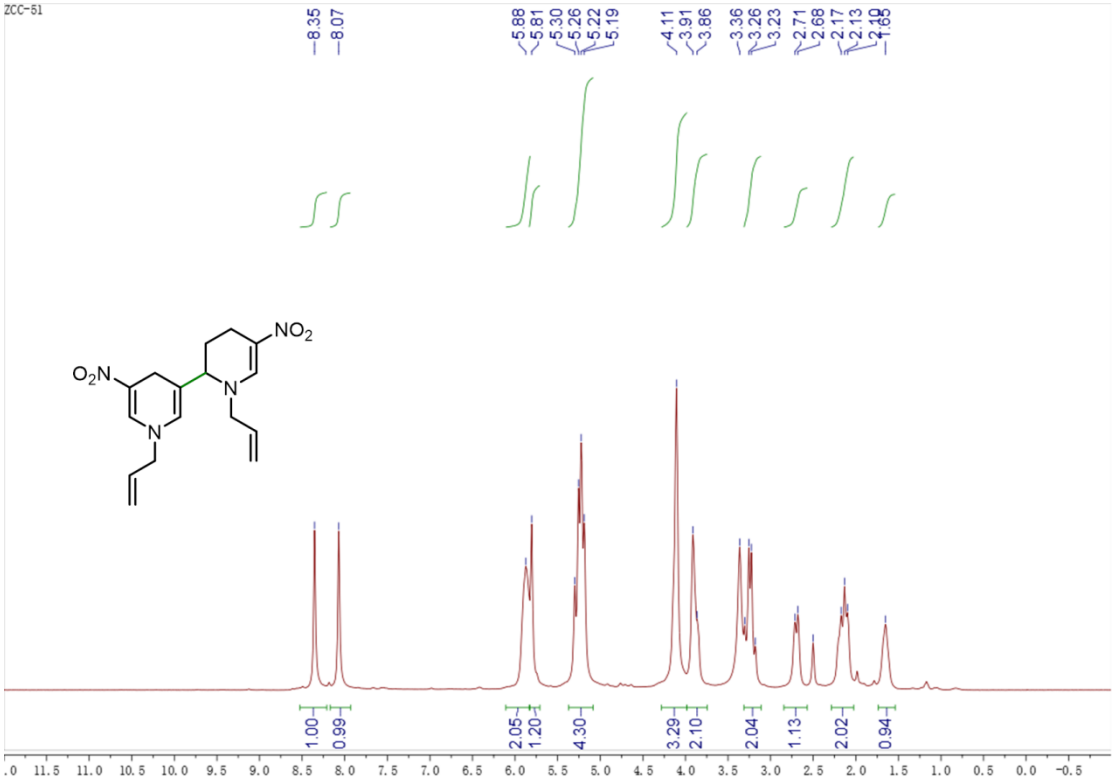
^{1}H NMR spectrum of **21** (400 MHz, DMSO-d_6)



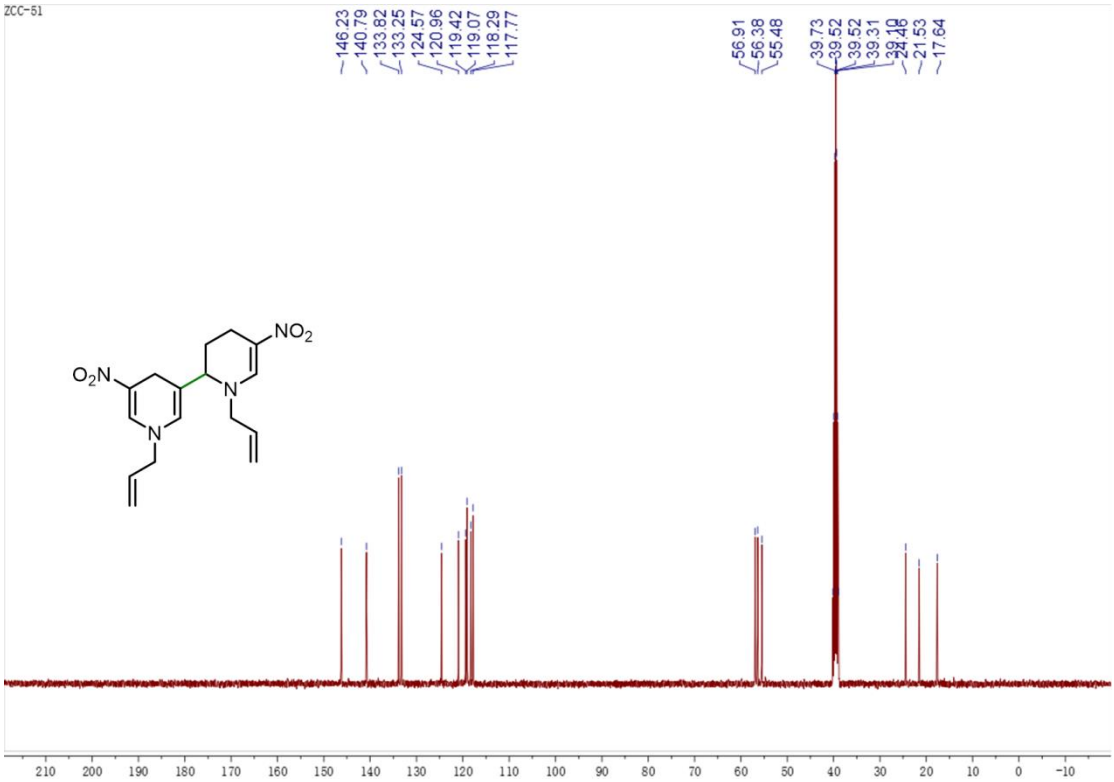
^{13}C NMR spectrum of **21** (100 MHz, DMSO-d_6)



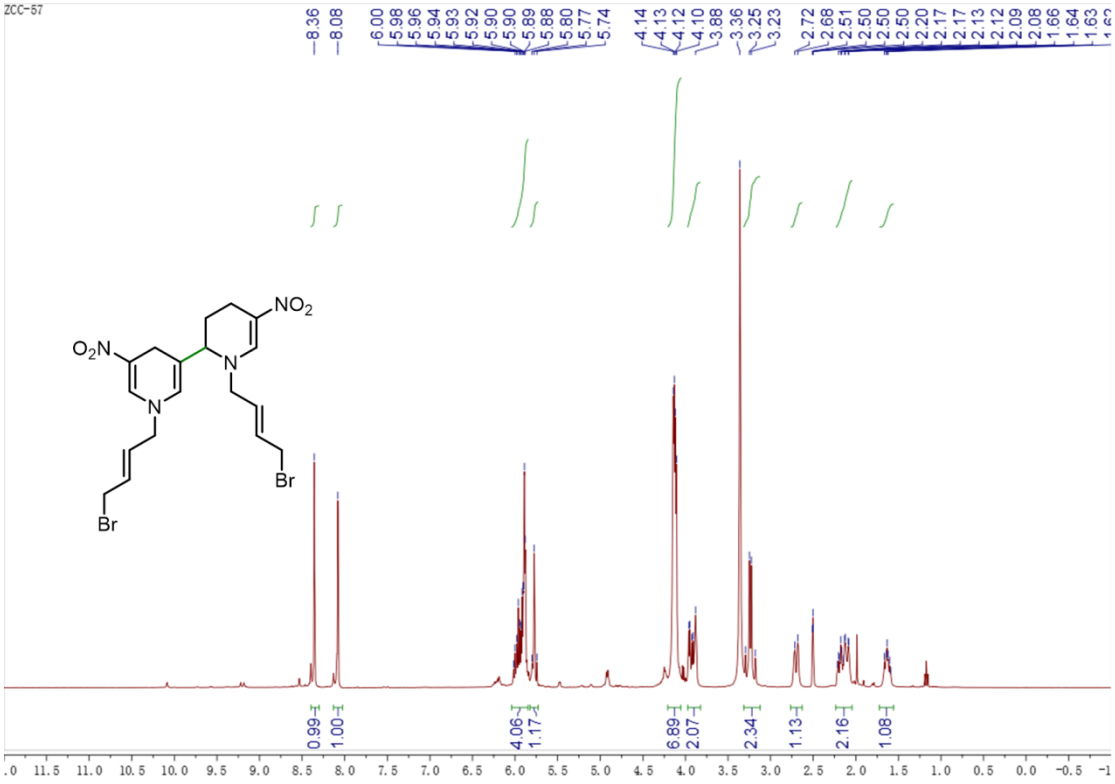
^{1}H NMR spectrum of **22** (400 MHz, DMSO-d_6)



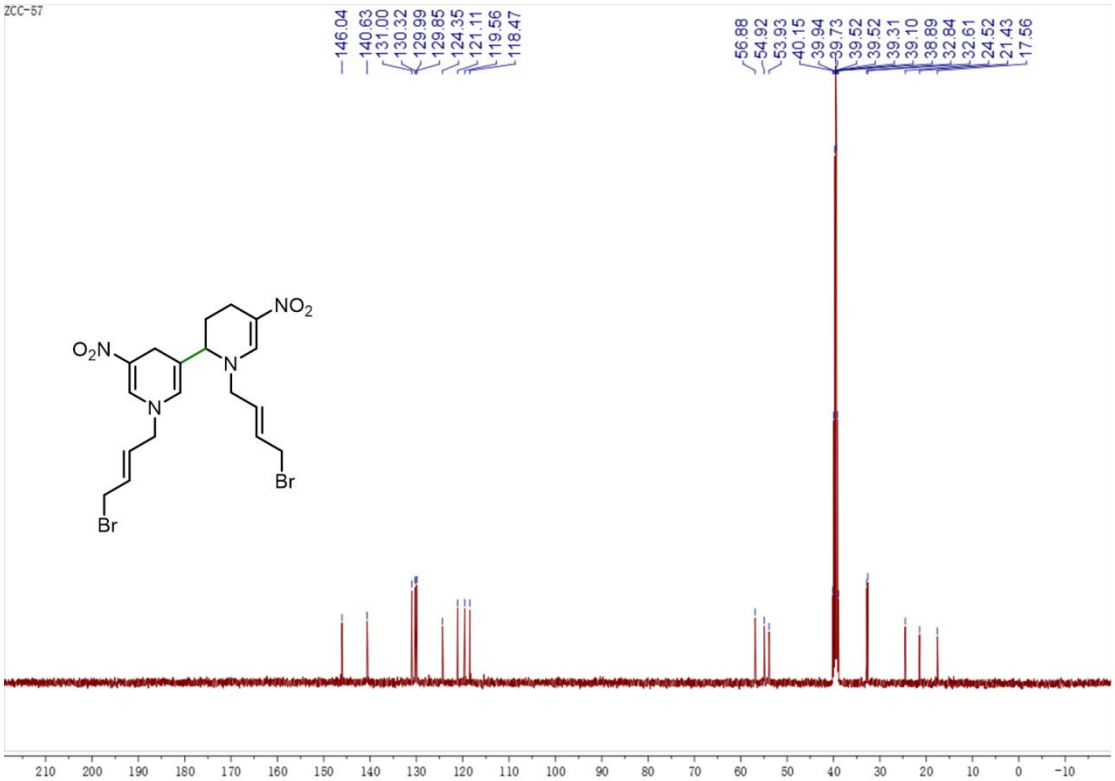
^{13}C NMR spectrum of **22** (100 MHz, DMSO-d_6)



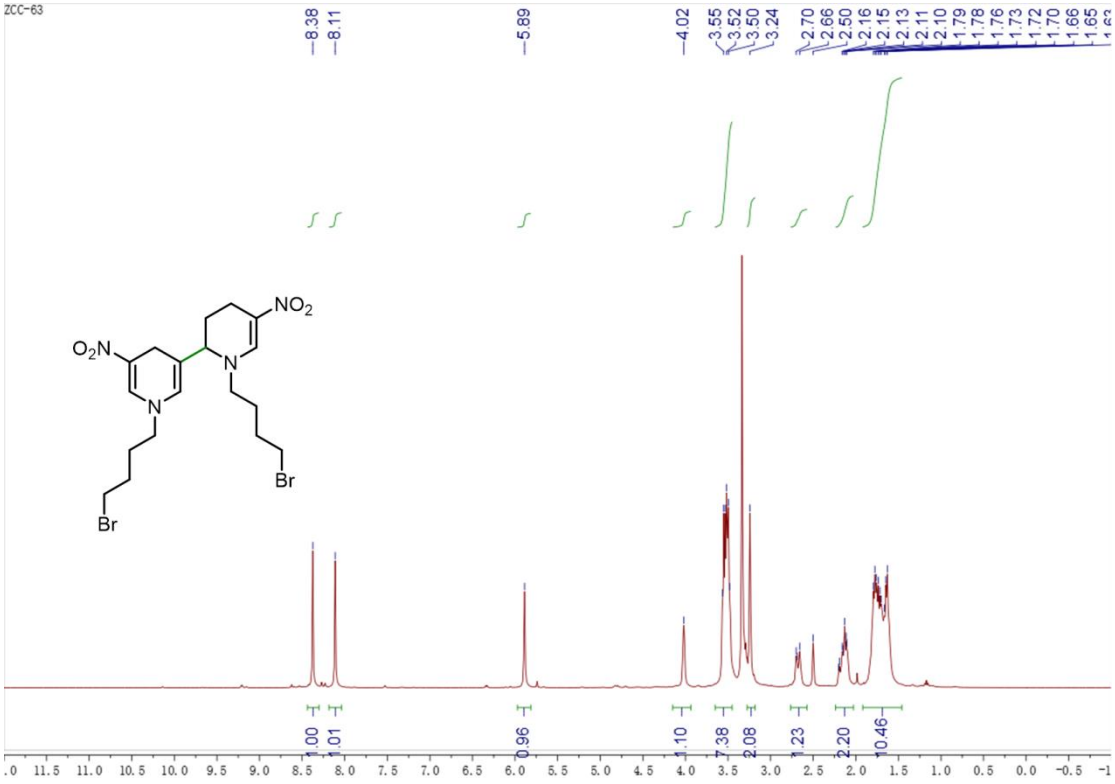
^{1}H NMR spectrum of **23** (400 MHz, DMSO-d_6)



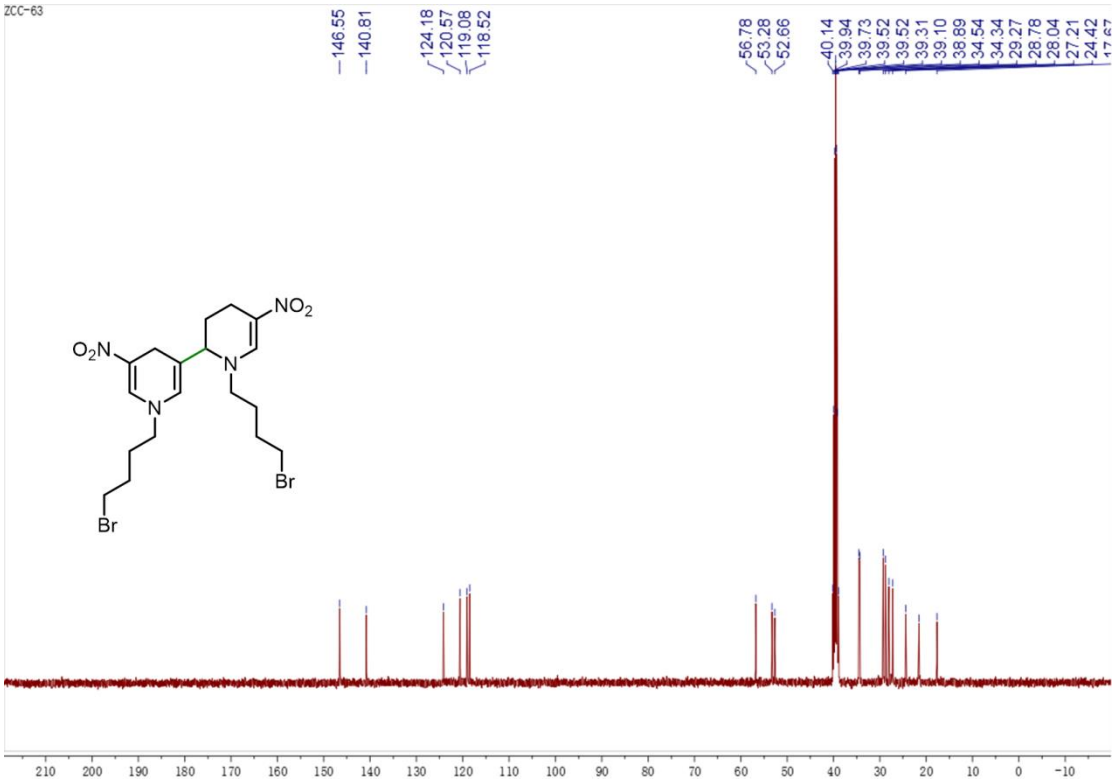
^{13}C NMR spectrum of **23** (100 MHz, DMSO-d_6)



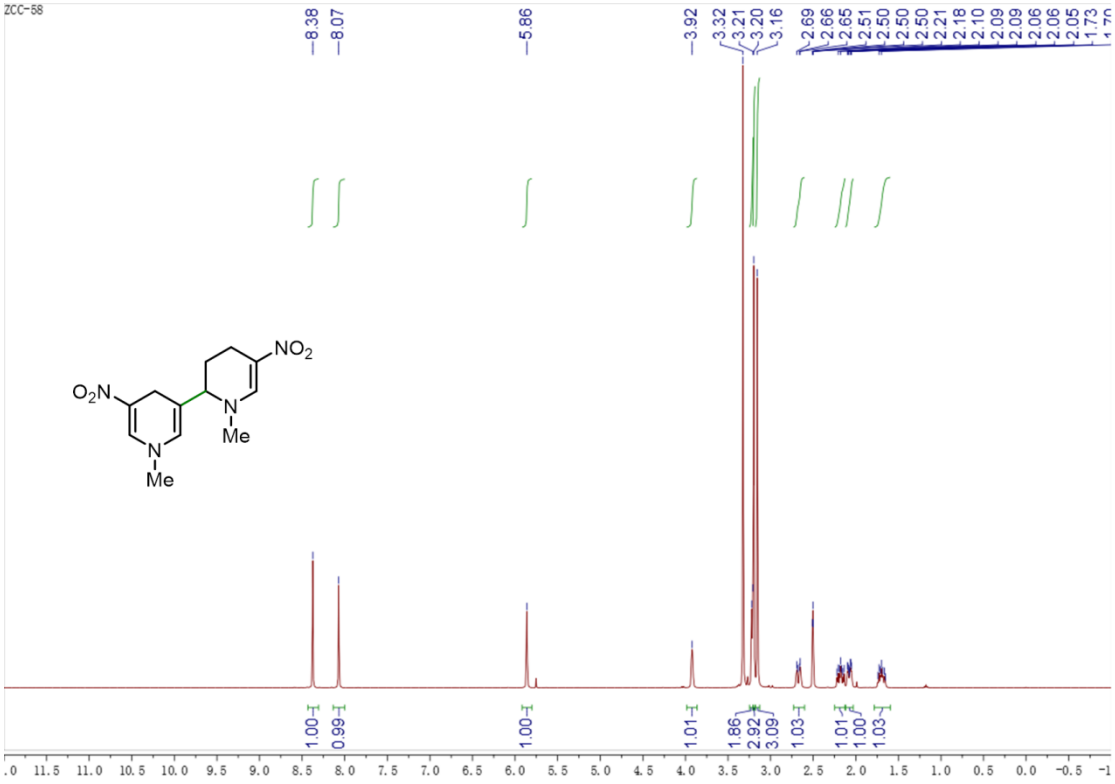
^{1}H NMR spectrum of **24** (400 MHz, DMSO-d_6)



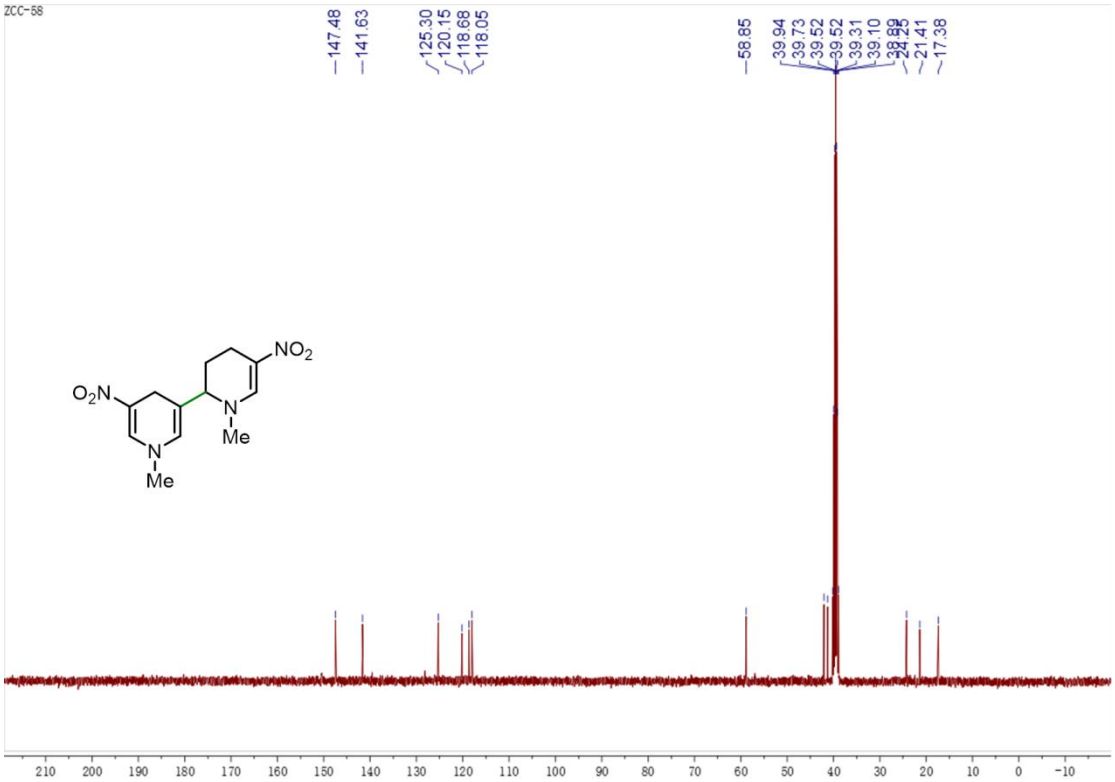
^{13}C NMR spectrum of **24** (100 MHz, DMSO-d_6)



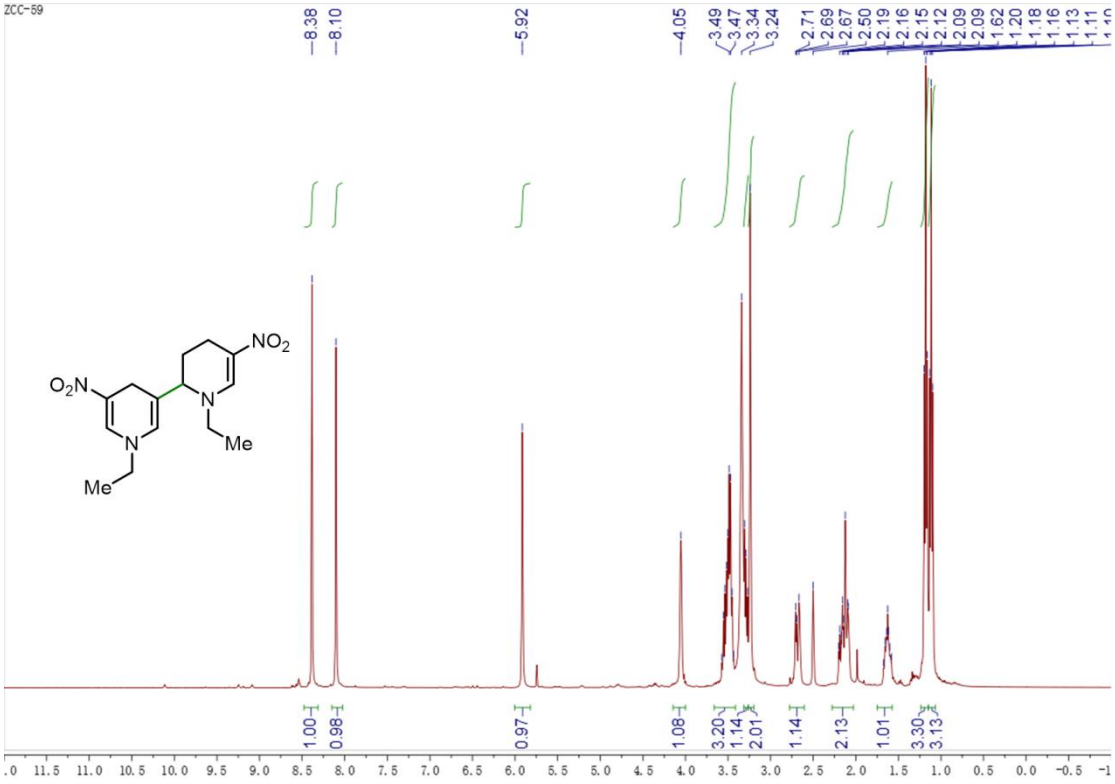
^{1}H NMR spectrum of **25** (400 MHz, DMSO-d_6)



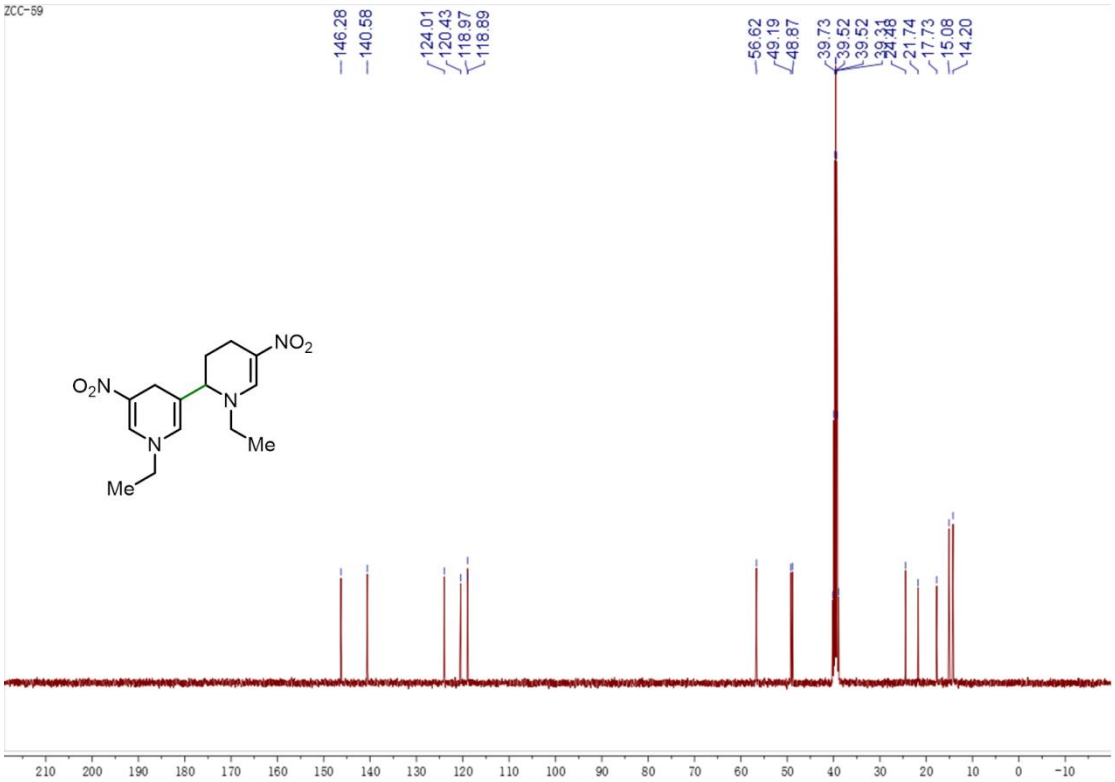
^{13}C NMR spectrum of **25** (100 MHz, DMSO-d_6)



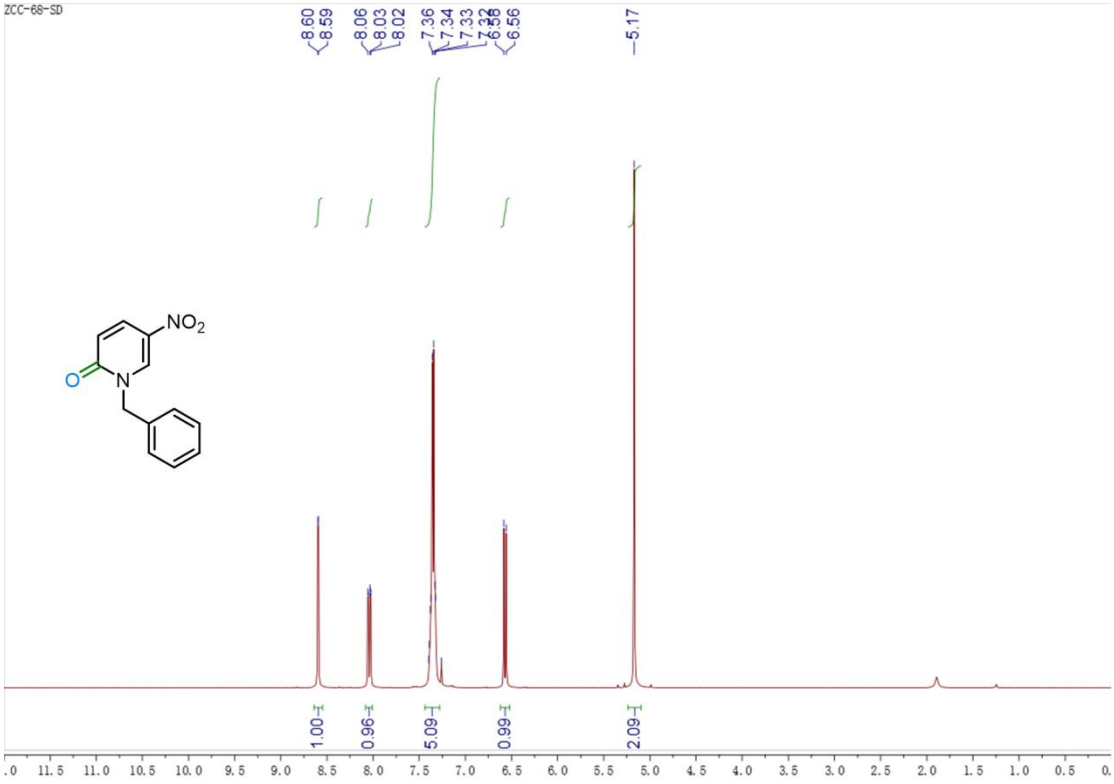
^{1}H NMR spectrum of **26** (400 MHz, DMSO-d_6)



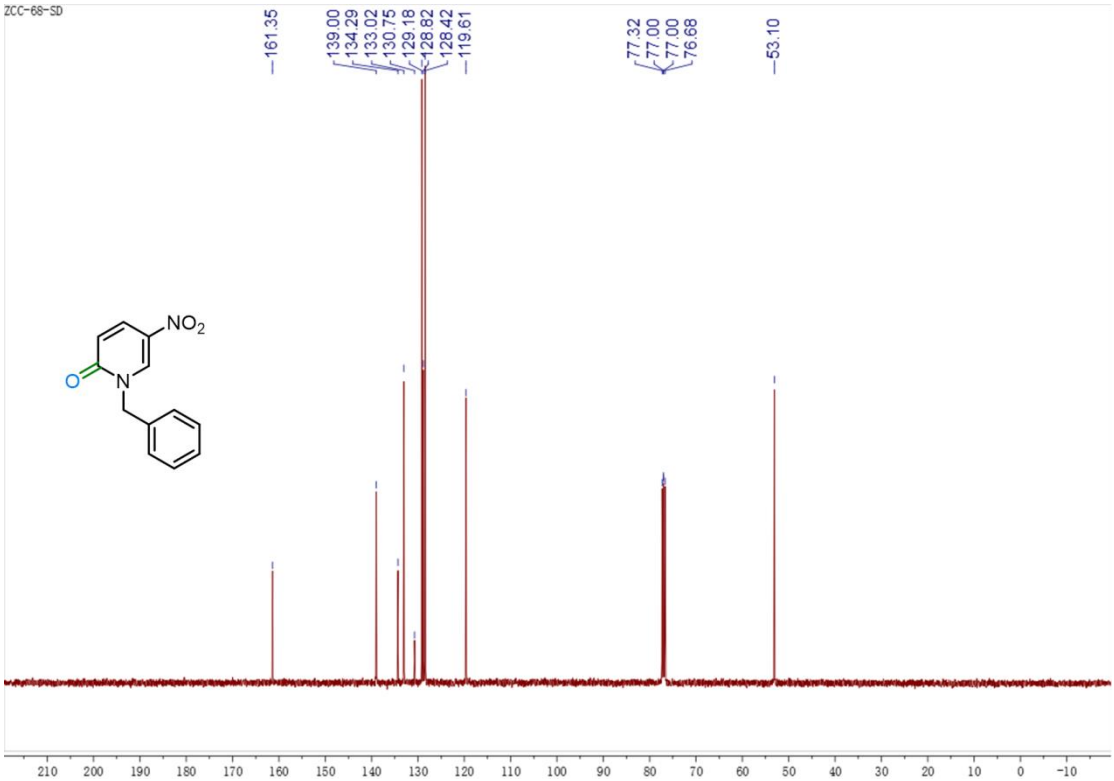
^{13}C NMR spectrum of **26** (100 MHz, DMSO-d_6)



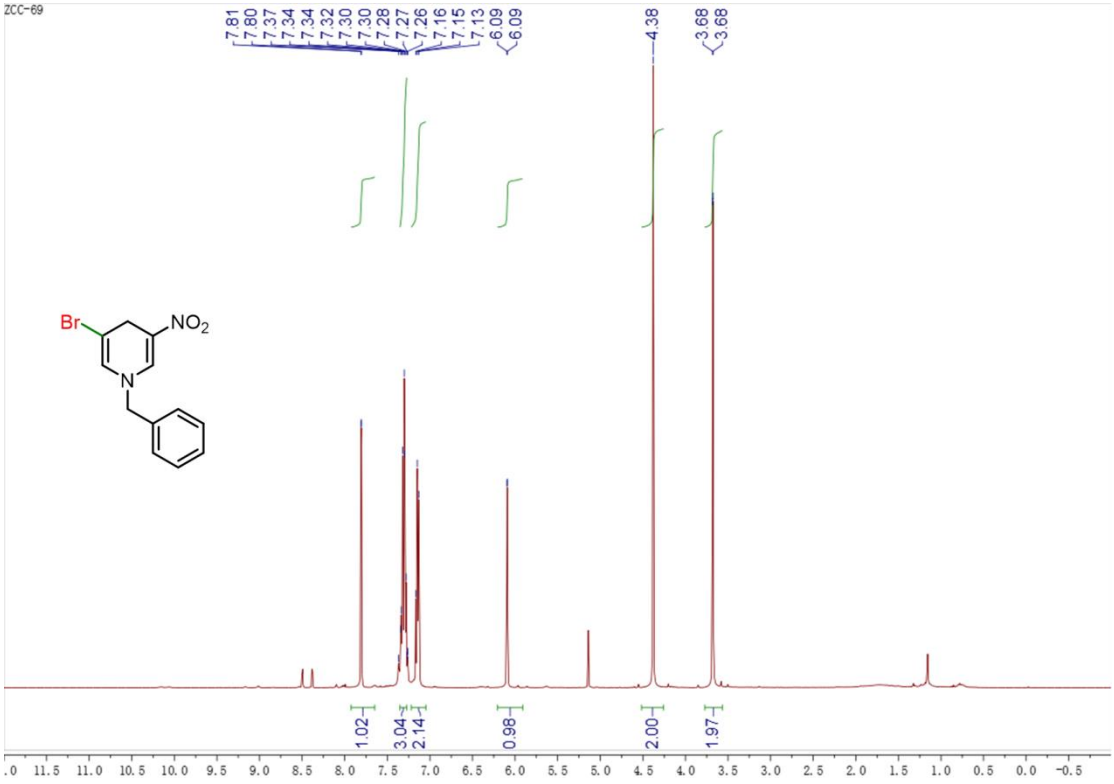
^{1}H NMR spectrum of **27** (400 MHz, $CDCl_3$)



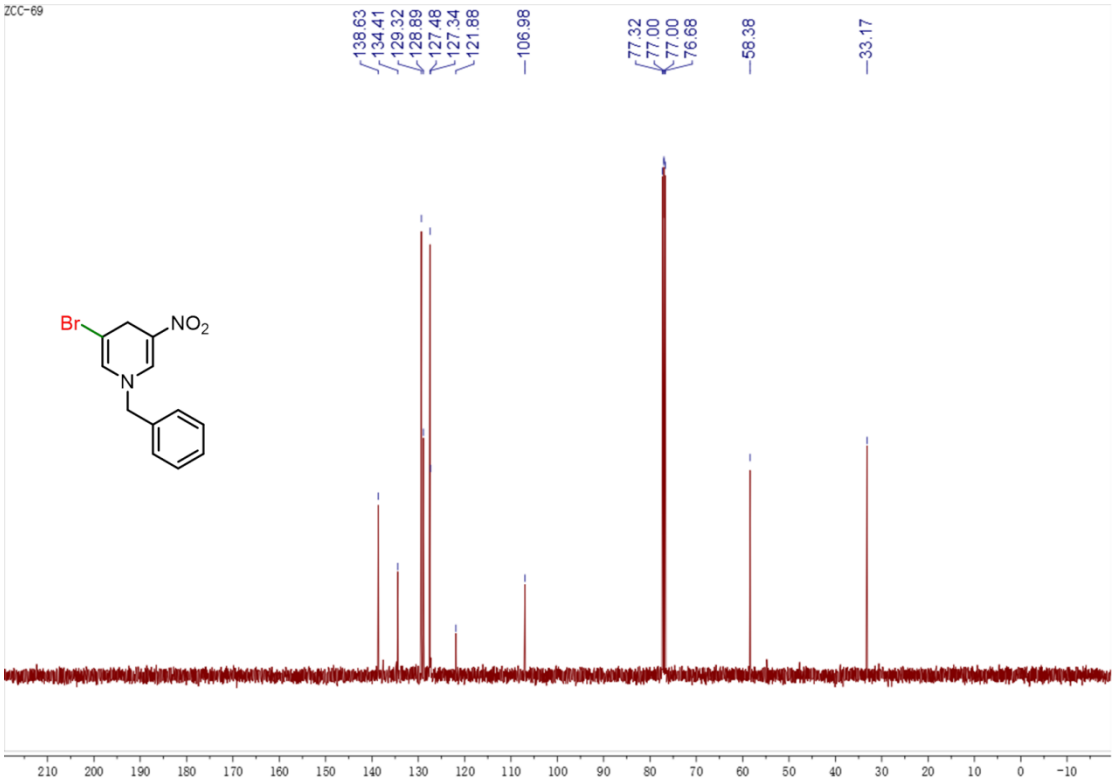
^{13}C NMR spectrum of **27** (100 MHz, $CDCl_3$)



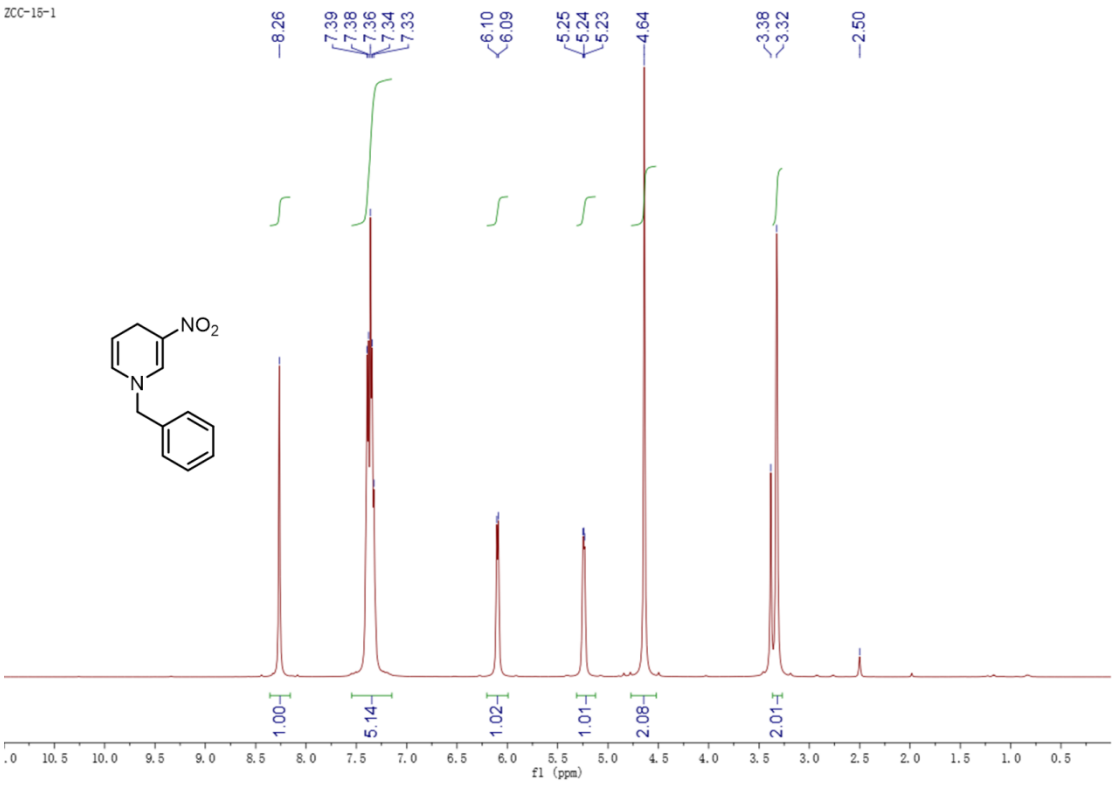
^{1}H NMR spectrum of **28** (400 MHz, $CDCl_3$)



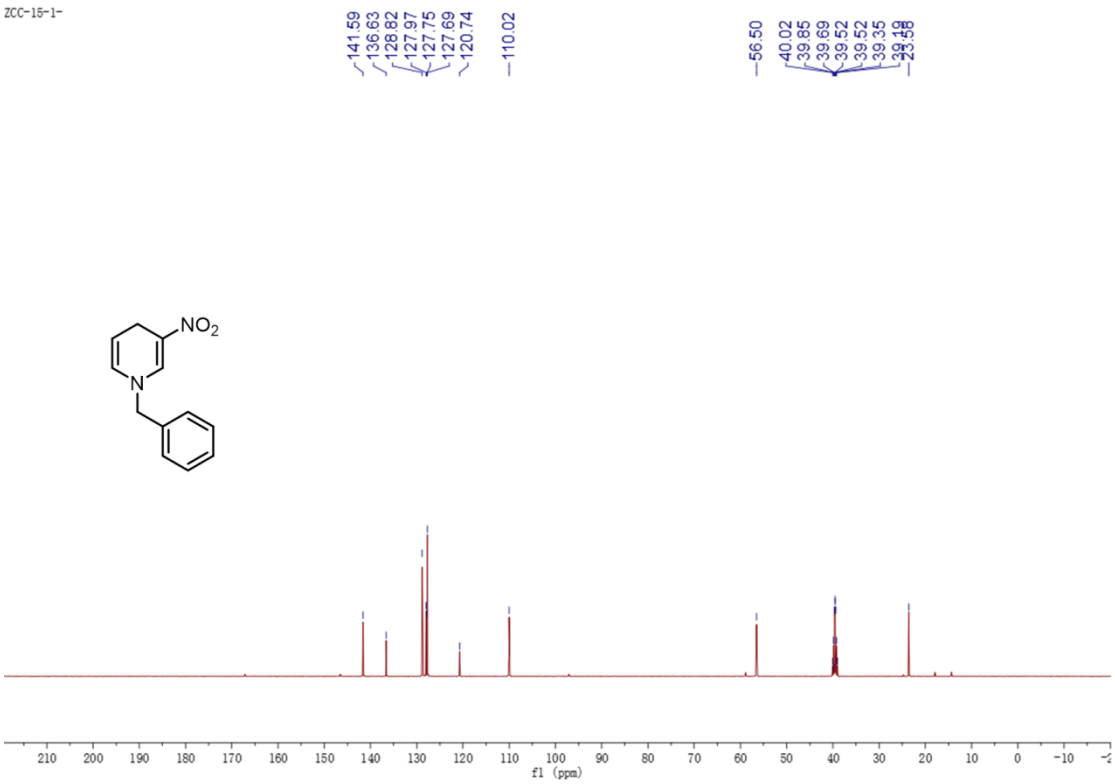
^{13}C NMR spectrum of **28** (100 MHz, $CDCl_3$)



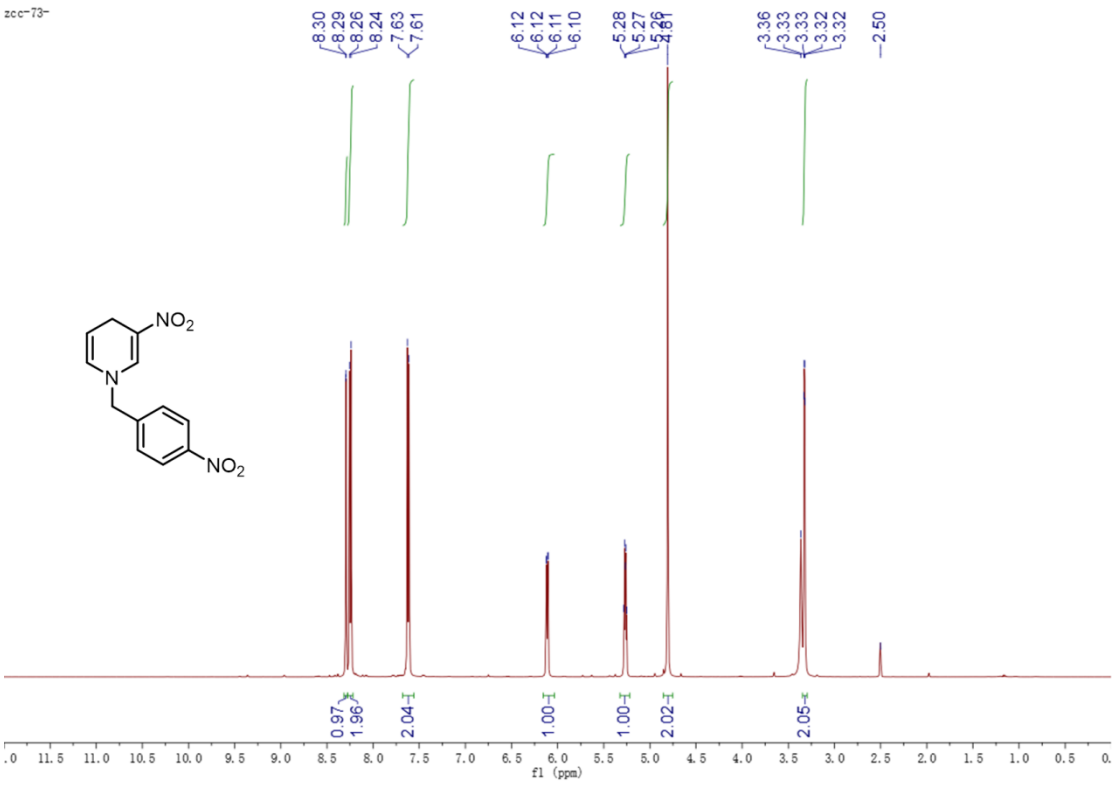
^{1}H NMR spectrum of **29** (500 MHz, DMSO-d_6)



^{13}C NMR spectrum of **29** (125 MHz, DMSO-d_6)



^{1}H NMR spectrum of **30** (500 MHz, DMSO-d_6)



^{13}C NMR spectrum of **30** (125 MHz, DMSO-d_6)