Supporting Information

Iridium-Catalyzed Asymmetric Hydrogenation of 5-Hydroxypicolinate Pyridinium Salts under Batch and Flow: Stereodefined Access to *Cis*-Configurated Hydroxypiperidine Esters

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Table of Contents

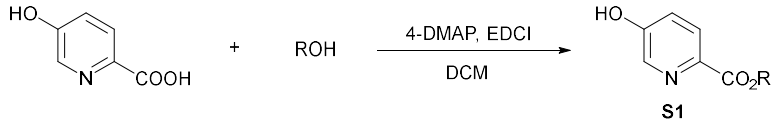
1. General Information

All commercially available reagents were used without further purification. Tetrahydrofuran and toluene were dried with sodium chips and indicated by benzophenone, other anhydrous solvents were purchased from Aladdin. Chromatography was conducted by using 300−400 mesh silica gel. All new compounds were characterized by NMR spectroscopy, high resolution mass spectrometry (HRMS) and melting point (if solids). NMR spectra were recorded on a 400 MHz NMR spectrometer. Reference values for residual solvents were taken as δ = 7.26 ($CDCl_3$) ppm, δ = 2.50 (DMSO-d_6) ppm for ^{1}H NMR and δ = 77.16 ($CDCl_3$) ppm, δ = 39.52 (DMSO-d_6) ppm for ^{13}C NMR. Coupling constants (*J*) were given in Hz and multiplicities for coupled signals were denoted as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad and dd = double doublet etc. Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum Two FT-IR spectrometer. High-resolution mass spectra (HRMS) were recorded on a Bruker microTOF Q III by the ESI method. Melting points (m.p.) were recorded on an SRS-optic melting point apparatus. Chiral HPLC was performed using a Daicel Chiralcel AD-H column, OJ-H column, IC column and OD-H column.

2. Experimental Procedures

2.1 General Procedures for 5-hydroxypicolinate esters

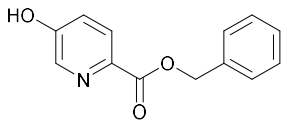
Picolinic acid esters were synthesized from 5-hydroxypicolinic acid with the corresponding alcohols via esterification. Methyl-5-hydroxypiperidine-2-carboxylate **S1m** was commercially available.

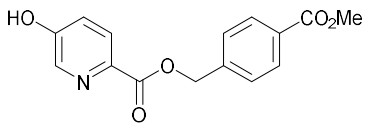


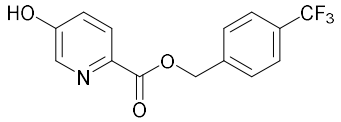
S1

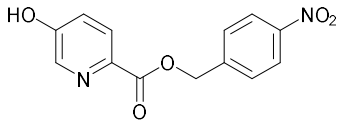
5-hydroxypicolinic acid (500.0 mg, 3.6 mmol, 1.0 equiv.), 4-DMAP (219.6 mg, 1.8 mmol, 0.5 equiv.) and EDCI (1.0 g, 5.4 mmol, 1.5 equiv.) were dissolved in dichloromethane (15 mL) and stirred at 0 °C for 15 min. Alcohol (4.0 mmol, 1.1 equiv.) was added to the reaction mixture that was then stirred at room temperature for 12 h. Water was added and the solution was extracted with dichloromethane. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (dichloromethane/methanol = 100:1) to give the desired products (81% – 95% yields).

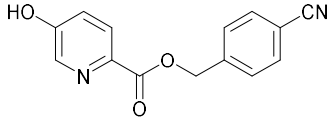
benzyl 5-hydroxypicolinate (S1a): 758.0 mg, 92% yield, white solid, m.p. = 171.1 – 171.9 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.84 (s, 1H), 8.23 (d, *J* = 2.8 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.48 – 7.31 (m, 5H), 7.27 (dd, *J* = 8.4, 2.8 Hz, 1H), 5.32 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.3, 156.9, 138.4, 138.2, 136.2, 128.5, 128.2, 128.1, 126.9, 122.1, 66.1. HRMS (ESI) m/z calcd for $C_{13}H_{11}NNaO_3$ $[M + Na]^+$: 252.0631, found: 252.0630.

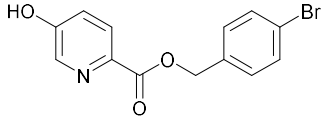


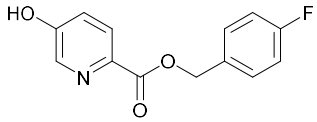
4-(methoxycarbonyl)benzyl 5-hydroxypicolinate (S1b): 918.9 mg, 89% yield, white solid, m.p. = 133.3 – 134.8 ℃.  ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.88 (s, 1H), 8.24 (d, J = 2.8 Hz, 1H), 7.99 (m, 3H), 7.58 (d, J = 8.0 Hz, 2H), 7.28 (dd, J = 8.8, 2.8 Hz, 1H), 5.40 (s, 2H), 3.85 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.0, 164.2, 157.0, 141.7, 138.5, 138.0, 129.4, 129.2, 127.9, 127.0, 122.1, 65.4, 52.2. HRMS (ESI) m/z calcd for $C_{15}H_{13}NNaO_5$ [M + Na]$^+$: 310.0686, found: 310.0689.

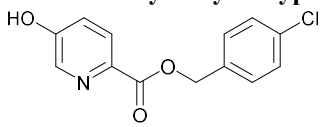
4-(trifluoromethyl)benzyl 5-hydroxypicolinate (S1c): 918.7 mg, 86% yield, white solid, m.p. = 158.7 – 159.6 ℃.  ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.90 (s, 1H), 8.24 (d, J = 2.8 Hz, 1H), 8.00 (d, J = 8.8 Hz, 1H), 7.80 – 7.65 (m, 4H), 7.28 (dd, J = 8.8, 2.8 Hz, 1H), 5.42 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 157.1, 141.0, 138.5, 138.0, 128.7 (q, J = 31.7 Hz), 128.4, 126.9, 125.3 (q, J = 3.6 Hz), 124.2 (q, J = 270.4 Hz), 122.1, 65.2. HRMS (ESI) m/z calcd for $C_{14}H_{10}F_3NNaO_3$ [M + Na]$^+$: 320.0505, found: 320.0504.

4-nitrobenzyl 5-hydroxypicolinate (S1d): 877.2 mg, 89% yield, white solid, m.p. = 211.7 – 213.0 ℃.  ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.92 (s, 1H), 8.29 – 8.21 (m, 3H), 8.01 (d, J = 8.4 Hz, 1H), 7.71 (d, J = 8.8 Hz, 2H), 7.28 (dd, J = 8.4, 2.8 Hz, 1H), 5.47 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.1, 157.1, 147.1, 144.0, 138.5, 137.8, 128.6, 127.0, 123.7, 122.1, 64.9. HRMS (ESI) m/z calcd for $C_{13}H_{10}N_2NaO_5$ [M + Na]$^+$: 297.0482, found: 297.0480.

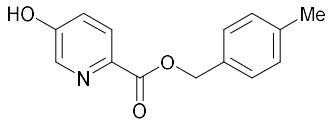
4-cyanobenzyl 5-hydroxypicolinate (S1e): 840.7 mg, 92% yield, white solid, m.p. = 208.6 – 209.5 ℃.  ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.90 (s, 1H), 8.24 (d, J = 2.8 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 8.0 Hz, 2H), 7.28 (dd, J = 8.8, 3.2 Hz, 1H), 5.41 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.1, 157.1, 141.9, 138.5, 137.9, 132.5, 128.4, 127.0, 122.1, 118.7, 110.7, 65.2. HRMS (ESI) m/z calcd for $C_{14}H_{10}N_2NaO_3$ [M + Na]$^+$: 277.0584, found: 277.0577.

4-bromobenzyl 5-hydroxypicolinate (S1f): 996.7 mg, 90% yield, white solid, m.p. = 163.0 – 164.2 ℃.  ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.87 (s, 1H), 8.22 (d, J = 2.8 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.4 Hz, 2H), 7.27 (dd, J = 8.4, 2.8 Hz, 1H), 5.29 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 157.0, 138.4, 138.1, 135.7, 131.4, 130.3, 126.9, 122.1, 121.3, 65.3. HRMS (ESI) m/z calcd for $C_{13}H_{10}BrNNaO_3$ [M + Na]$^+$: 329.9736, found: 329.9741.

4-fluorobenzyl 5-hydroxypicolinate (S1g): 854.6 mg, 91% yield, white solid, m.p. = 160.4 – 161.8 ℃.  ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.86 (s, 1H), 8.22 (d, J = 2.8 Hz, 1H), 7.97 (d, J = 8.8 Hz, 1H), 7.56 – 7.46 (m, 2H), 7.30 – 7.16 (m, 3H), 5.30 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.3, 162.0 (d, J = 242.6 Hz) 156.9, 138.4, 138.2, 132.5 (d, J = 3.0 Hz), 130.6 (d, J = 8.3 Hz), 126.9, 122.1, 115.3 (d, J = 21.4 Hz), 65.4. HRMS (ESI) m/z calcd for $C_{13}H_{10}FNNaO_3$ [M + Na]$^+$: 270.0537, found: 270.0537.

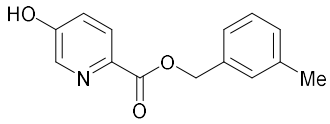
4-chlorobenzyl 5-hydroxypicolinate (S1h): 843.4 mg, 89% yield, white solid, m.p. = 154.8 – 155.2 ℃.  ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.87 (s, 1H), 8.23 (d, J = 2.8 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.52 – 7.42 (m, 4H), 7.27 (dd, J = 8.8, 2.8 Hz, 1H), 5.31 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 157.0, 138.4, 138.1, 135.3, 132.8, 130.0, 128.5, 126.9, 122.1, 65.3. HRMS (ESI) m/z calcd for $C_{13}H_{10}ClNNaO_3$ [M + Na]$^+$: 286.0241, found: 286.0243.

4-methylbenzyl 5-hydroxypicolinate (S1i): 795.6 mg, 91% yield, white solid, m.p. = 167.7 – 169.2 ℃.



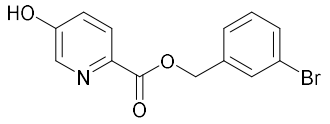
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.85 (s, 1H), 8.23 (d, J = 2.8 Hz, 1H), 7.96 (d, J = 8.4 Hz, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.26 (dd, J = 8.8, 2.8 Hz, 1H), 7.18 (d, J = 8.0 Hz, 2H), 5.27 (s, 2H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.3, 156.9, 138.4, 138.3, 137.5, 133.2, 129.0, 128.4, 126.8, 122.1, 66.0, 20.8. HRMS (ESI) m/z calcd for $C_{14}H_{13}NNaO_3$ [M + Na]$^+$: 266.0788, found: 266.0789.

3-methylbenzyl 5-hydroxypicolinate (S1j): 813.1 mg, 93% yield, white solid, m.p. = 161.0 – 162.5 ℃.



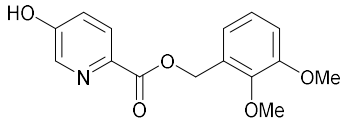
^{1}H NMR (400 MHz, DMSO-d_6) δ 10.85 (s, 1H), 8.23 (d, J = 2.8 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.34 – 7.19 (m, 4H), 7.15 (d, J = 7.6 Hz, 1H), 5.27 (s, 2H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.3, 156.9, 138.4, 138.2, 137.7, 136.1, 128.8, 128.8, 128.4, 126.8, 125.3, 122.1, 66.1, 21.0. HRMS (ESI) m/z calcd for $C_{14}H_{13}NNaO_3$ [M + Na]$^+$: 266.0788, found: 266.0787.

3-bromobenzyl 5-hydroxypicolinate (S1k): 1.0 g, 92% yield, white solid, m.p. = 148.0 – 149.5 ℃. ^{1}H



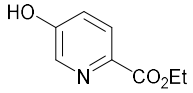
NMR (400 MHz, DMSO-d_6) δ 10.89 (s, 1H), 8.23 (d, J = 2.8 Hz, 1H), 7.98 (d, J = 8.8 Hz, 1H), 7.66 (t, J = 1.2 Hz, 1H), 7.56 – 7.53 (m, 1H), 7.48 – 7.45 (m, 1H), 7.36 (t, J = 8.0 Hz, 1H), 7.27 (dd, J = 8.4, 2.8 Hz, 1H), 5.31 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 157.0, 139.0, 138.5, 138.0, 131.0, 130.8, 130.7, 127.1, 126.9, 122.1, 121.7, 65.2. HRMS (ESI) m/z calcd for $C_{13}H_{10}BrNNaO_3$ [M + Na]$^+$: 329.9736, found: 329.9749.

2,3-dimethoxybenzyl 5-hydroxypicolinate (S1l): 883.7 mg, 85% yield, white solid, m.p. = 137.2 –



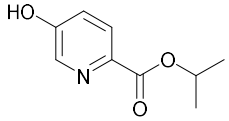
138.9 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.84 (s, 1H), 8.22 (d, J = 2.8 Hz, 1H), 7.96 (d, J = 8.8 Hz, 1H), 7.26 (dd, J = 8.4, 2.8 Hz, 1H), 7.12 – 6.98 (m, 3H), 5.30 (s, 2H), 3.82 (s, 3H), 3.76 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 156.9, 152.4, 147.0, 138.4, 138.3, 129.5, 126.8, 124.1, 122.1, 121.4, 113.3, 61.7, 60.5, 55.7. HRMS (ESI) m/z calcd for $C_{15}H_{15}NNaO_5$ [M + Na]$^+$: 312.0842, found: 312.0844.

ethyl 5-hydroxypicolinate (S1n): 570.7 mg, 95% yield, white solid, m.p. = 162.0 – 163.3 ℃. ^{1}H NMR



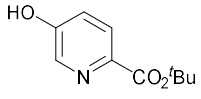
(400 MHz, DMSO-d_6) δ 10.81 (s, 1H), 8.22 (d, J = 2.8 Hz, 1H), 7.92 (d, J = 8.8 Hz, 1H), 7.25 (dd, J = 8.8, 2.8 Hz, 1H), 4.27 (q, J = 7.2 Hz, 2H), 1.28 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.5, 156.8, 138.5, 138.3, 126.6, 122.1, 60.6, 14.2. HRMS (ESI) m/z calcd for $C_8H_9NNaO_3$ [M + Na]$^+$: 190.0475, found: 190.0475.

isopropyl 5-hydroxypicolinate (S1o): 527.5mg, 81% yield, white solid, m.p. = 157.2 – 158.7 ℃. ^{1}H



NMR (400 MHz, DMSO-d_6) δ 10.79 (s, 1H), 8.21 (d, J = 2.8 Hz, 1H), 7.91 (d, J = 8.8 Hz, 1H), 7.25 (dd, J = 8.4, 2.8 Hz, 1H), 5.15 – 5.06 (m, 1H), 1.29 (d, J = 6.4 Hz, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.0, 156.7, 138.8, 138.2, 126.5, 122.0, 67.9, 21.7. HRMS (ESI) m/z calcd for $C_9H_{11}NNaO_3$ [M + Na]$^+$: 204.0631, found: 204.0630.

***tert*-butyl 5-hydroxypicolinate (S1p):** 610.4 mg, 87% yield, white solid, m.p. = 173.5 – 174.6 ℃. ^{1}H



NMR (400 MHz, DMSO-d_6) δ 10.71 (s, 1H), 8.20 (d, J = 2.8 Hz, 1H), 7.87 (d, J = 8.8 Hz, 1H), 7.23 (dd, J = 8.8, 2.9 Hz, 1H), 1.52 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.6, 156.5, 139.7, 138.1, 126.3, 122.0, 80.4, 27.9. HRMS (ESI) m/z calcd for $C_{10}H_{13}NNaO_3$ [M + Na]$^+$: 218.0788, found: 218.0793.

cyclopropylmethyl 5-hydroxypicolinate (S1q): 618.0 mg, 89% yield, white solid, m.p. = 133.7 – 134.5 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.82 (s, 1H), 8.22 (d, J = 2.8 Hz, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.26 (dd, J = 8.8, 2.8 Hz, 1H), 4.07 (d, J = 7.6 Hz, 2H), 1.26 – 1.13 (m, 1H), 0.60 – 0.50 (m, 2H), 0.32 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.6, 156.8, 138.5, 138.3, 126.7, 122.1, 69.2, 9.9, 3.2. HRMS (ESI) m/z calcd for $C_{10}H_{11}NNaO_3$ [M + Na]$^+$: 216.0631, found: 216.0634.

cyclopentylmethyl 5-hydroxypicolinate (S1r): 723.6 mg, 91% yield, white solid, m.p. = 119.8 – 122.1 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.80 (s, 1H), 8.23 (d, J = 2.8 Hz, 1H), 7.92 (d, J = 8.4 Hz, 1H), 7.26 (dd, J = 8.8, 2.8 Hz, 1H), 4.11 (d, J = 7.2 Hz, 2H), 2.32 – 2.17 (m, 1H), 1.71 (m, 2H), 1.63 – 1.44 (m, 4H), 1.28 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.5, 156.7, 138.5, 138.4, 126.6, 122.0, 68.2, 38.2, 28.9, 24.9. HRMS (ESI) m/z calcd for $C_{12}H_{15}NNaO_3$ [M + Na]$^+$: 244.0944, found: 244.0946.

cyclohexylmethyl 5-hydroxypicolinate (S1s): 786.4 mg, 93% yield, white solid, m.p. = 145.8 – 146.9 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.80 (s, 1H), 8.23 (d, J = 2.8 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.26 (dd, J = 8.4, 2.8 Hz, 1H), 4.05 (d, J = 6.0 Hz, 2H), 1.81 – 1.55 (m, 6H), 1.30 – 0.90 (m, 5H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.4, 156.7, 138.5, 138.3, 126.6, 122.0, 69.3, 36.7, 29.1, 25.9, 25.2. HRMS (ESI) m/z calcd for $C_{13}H_{17}NNaO_3$ [M + Na]$^+$: 258.1101, found: 258.1104.

2.2 General Procedures for the synthesis of pyridinium salts[1]

A mixture of 5-hydroxypicolinate ester (1.0 mmol), benzyl bromide (1.2 mmol) and acetone （10.0 mL）was stirred at 50 ℃ for 24 h. Ether was added, the resulting precipitate was collected and rinsed with ethyl acetate to give the solid product which was directly used for the hydrogenation. If the desired product was not precipitated, the reaction mixture was purified by column chromatography on silica gel using CH_2Cl_2/MeOH (20:1) to give the desired products (86%–98% yields).

1-benzyl-2-((benzyloxy)carbonyl)-5-hydroxypyridin-1-ium (1a): 392.3 mg, 98% yield, white solid, m.p. = 134.6 – 136.0 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.97 (d, J = 9.6 Hz, 1H), 7.90 (d, J = 2.8 Hz, 1H), 7.34 – 7.32 (m, 8H), 7.19 (dd, J = 7.6, 2.4 Hz, 2H), 6.89 (dd, J = 9.6, 2.8 Hz, 1H), 5.97 (s, 2H), 5.23 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.6, 160.2, 141.6, 135.6, 135.6, 131.9, 130.2, 128.8, 128.5, 128.3, 128.2, 128.1, 127.0, 116.7, 66.6, 60.8. HRMS (ESI) m/z calcd for $C_{20}H_{18}NO_3$ [M – Br]$^+$: 320.1281, found: 320.1280.

1-benzyl-5-hydroxy-2-(((4-(methoxycarbonyl)benzyl)oxy)carbonyl)pyridin-1-ium (1b): 403.3 mg, 88% yield, white solid, m.p. = 115.7 – 117.3 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.02 (d, J = 2.4 Hz, 1H), 8.51 (d, J = 8.8 Hz, 1H), 8.15 (dd, J = 8.8, 2.4 Hz, 1H), 7.94 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 7.6 Hz, 2H), 7.41 – 7.23 (m, 5H), 6.18 (s, 2H), 5.43 (s, 2H), 3.85 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.9, 159.3, 139.8, 138.3, 134.2, 132.4, 132.3, 131.3, 129.6, 129.3, 129.0, 128.8, 128.3, 127.7, 67.7, 62.1, 52.3. HRMS (ESI) m/z calcd for $C_{22}H_{20}NO_5$ [M – Br]$^+$: 378.1336, found: 378.1336.

1-benzyl-5-hydroxy-2-(((4-(trifluoromethyl)benzyl)oxy)carbonyl)pyridin-1-ium (1c): 416.8 mg, 89% yield, white solid, m.p. = 151.4 – 152.7 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (d, J = 2.4 Hz, 1H), 8.50 (d, J = 8.8 Hz, 1H), 8.10 (dd, J = 9.2, 2.8 Hz, 1H), 7.74 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 8.0 Hz, 2H), 7.43 – 7.18 (m, 5H), 6.16 (s, 2H), 5.44 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.6, 159.2, 139.2, 138.3, 134.2, 132.3, 132.0, 131.2, 128.90 (q, J = 31.7 Hz), 128.88 (2C), 128.7, 127.6, 125.3 (q, J = 3.9 Hz), 124.1 (q, J = 270.6 Hz), 67.5, 62.1. HRMS (ESI) m/z calcd for $C_{21}H_{17}F_3NO_3$ [M – Br]$^+$: 388.1155, found: 388.1154.

1-benzyl-5-hydroxy-2-(((4-nitrobenzyl)oxy)carbonyl)pyridin-1-ium (1d): 423.0mg, 95% yield, white solid, m.p. = 147.9 – 149.9 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20 (d, J = 8.0 Hz, 2H), 8.05 (d, J = 9.2 Hz, 1H), 7.92 (t, J = 2.4 Hz, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.40 – 7.28 (m, 3H), 7.18 (d, J = 6.8, 2H), 6.90 (dd, J = 11.6, 2.8 Hz, 1H), 5.96 (s, 2H), 5.37 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.7, 159.9, 147.1, 143.3, 141.9, 135.5, 132.0, 130.1, 128.8, 128.6, 128.2, 126.9, 123.5, 116.2, 65.3, 60.9. HRMS (ESI) m/z calcd for C20H17N2O5 [M – Br]$^+$: 365.1132, found: 365.1128.

1-benzyl-2-(((4-cyanobenzyl)oxy)carbonyl)-5-hydroxypyridin-1-ium (1e): 399.8 mg, 94% yield, white solid, m.p. = 144.1 – 145.2 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (d, J = 2.4 Hz, 1H), 8.51 (d, J = 8.9 Hz, 1H), 8.11 (dd, J = 9.0, 2.6 Hz, 1H), 7.85 (d, J =8.0 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H), 7.44 – 7.21 (m, 5H), 6.16 (s, 2H), 5.43 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.5, 159.2, 140.1, 138.3, 134.2, 132.5, 132.4, 132.1, 131.2, 129.0, 128.8 (2C), 127.6, 118.6, 111.1, 67.4, 62.2. HRMS (ESI) m/z calcd for $C_{21}H_{17}N_2O_3$ [M – Br]$^+$: 345.1234, found: 345.1234.

1-benzyl-2-(((4-bromobenzyl)oxy)carbonyl)-5-hydroxypyridin-1-ium (1f): 431.3 mg, 90% yield, white solid, m.p. = 135.7 – 137.2 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.96 (d, J = 2.8 Hz, 1H), 8.44 (d, J = 8.8 Hz, 1H), 8.08 (dd, J = 8.8, 2.4 Hz, 1H), 7.59 – 7.23 (m, 9H), 6.15 (s, 2H), 5.31 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.6, 160.1, 141.7, 135.6, 135.1, 131.9, 131.4, 130.23, 130.16, 128.8, 128.2, 126.9, 121.4, 116.5, 65.8, 60.8. HRMS (ESI) m/z calcd for $C_{20}H_{17}BrNO_3$ [M – Br]$^+$: 398.0386, found: 398.0386.

1-benzyl-2-(((4-fluorobenzyl)oxy)carbonyl)-5-hydroxypyridin-1-ium (1g): 401.5 mg, 96% yield, white solid, m.p. = 136.1 – 137.7 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.00 (d, J = 2.4 Hz, 1H), 8.43 (d, J = 8.8 Hz, 1H), 8.10 (dd, J = 8.8, 2.4 Hz, 1H), 7.44 – 7.21 (m, 9H), 6.16 (s, 2H), 5.32 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2 (d, J = 243.5 Hz), 159.4, 159,3, 138.2, 134.2, 132.3, 132.2, 131.2, 131.0 (d, J = 8.4 Hz), 130.7 (d, J = 3.1 Hz,), 128.9, 128.8, 127.7, 115.4 (d, J = 21.4 Hz), 67.8, 62.1. HRMS (ESI) m/z calcd for $C_{20}H_{17}FNO_3$ [M – Br]$^+$: 338.1187, found: 338.1184.

1-benzyl-2-(((4-chlorobenzyl)oxy)carbonyl)-5-hydroxypyridin-1-ium (1h): 391.2 mg, 90% yield, white solid, m.p. = 136.9 – 138.3 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.97 (d, J = 9.6 Hz, 1H), 7.91 (d, J = 2.8 Hz, 1H), 7.48 – 7.28 (m, 7H), 7.22 – 7.14 (m, 2H), 6.89 (dd, J = 9.2, 2.8 Hz, 1H), 5.96 (s, 2H), 5.22 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.5, 160.1, 141.7, 135.6, 134.6, 132.9, 131.9, 130.2, 130.0, 128.8, 128.5, 128.2, 126.9, 116.6, 65.8, 60.8. HRMS (ESI) m/z calcd for $C_{20}H_{17}ClNO_3$ [M – Br]$^+$: 354.0891, found: 354.0894.

1-benzyl-5-hydroxy-2-(((4-methylbenzyl)oxy)carbonyl)pyridin-1-ium (1i): 401.9 mg, 97% yield, white solid, m.p. = 122.8 – 124.1 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.93 (d, J = 9.6 Hz, 1H), 7.89 (d, J = 2.8 Hz, 1H), 7.39 – 7.30 (m, 3H), 7.26 – 7.14 (m, 6H), 6.88 (dd, J = 9.6, 2.8 Hz, 1H), 5.96 (s, 2H), 5.18 (s, 2H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.5, 160.2, 141.5, 137.6, 135.6, 132.5, 131.8, 130.2, 129.0, 128.8, 128.5, 128.2, 127.0, 116.8, 66.6, 60.7, 20.8. HRMS (ESI) m/z calcd for $C_{21}H_{20}NO_3$ $[M - Br]^+$: 334.1438, found: 334.1434.

1-benzyl-5-hydroxy-2-(((3-methylbenzyl)oxy)carbonyl)pyridin-1-ium (1j): 389.4 mg, 94% yield, white solid, m.p. = 97.8 – 99.2 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.95 (d, J = 9.2 Hz, 1H), 7.90 (d, J = 2.8 Hz, 1H), 7.40 – 7.09 (m, 9H), 6.88 (dd, J = 9.6, 2.8 Hz, 1H), 5.97 (s, 2H), 5.19 (s, 2H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.5, 160.2, 141.6, 137.7, 135.6, 135.5, 131.9, 130.2, 128.9, 128.8, 128.7, 128.4, 128.2, 127.0, 125.2, 116.7, 66.6, 60.8, 20.9. HRMS (ESI) m/z calcd for $C_{21}H_{20}NO_3$ $[M - Br]^+$: 334.1438, found: 334.1437.

1-benzyl-2-(((3-bromobenzyl)oxy)carbonyl)-5-hydroxypyridin-1-ium (1k): 436.0 mg, 91% yield, white solid, m.p. = 127.8 – 129.2 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.98 (d, J = 9.6 Hz, 1H), 7.91 (d, J = 2.8 Hz, 1H), 7.59 (t, J = 1.6 Hz, 1H), 7.54 (dt, J = 7.2, 2.0 Hz, 1H), 7.33 (m, 5H), 7.24 – 7.14 (m, 2H), 6.89 (dd, J = 9.6, 2.8 Hz, 1H), 5.96 (s, 2H), 5.22 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.6, 160.1, 141.7, 138.3, 135.6, 132.0, 131.1, 130.8, 130.7, 130.2, 128.8, 128.3, 127.1, 126.9, 121.7, 116.4, 65.7, 60.8. HRMS (ESI) m/z calcd for $C_{20}H_{17}BrNO_3$ $[M - Br]^+$: 398.0386, found: 398.0392.

1-benzyl-2-(((2,3-dimethoxybenzyl)oxy)carbonyl)-5-hydroxypyridin-1-ium (1l): 395.9 mg, 86% yield, white solid, m.p. = 129.7 – 131.1 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.94 – 7.89 (m, 2H), 7.37 – 7.31 (m, 3H), 7.22 – 7.17 (m, 2H), 7.08 – 7.02 (m, 2H), 6.91 – 6.86 (m, 2H), 5.97 (s, 2H), 5.22 (s, 2H), 3.81 (s, 3H), 3.68 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.4, 160.1, 152.3, 146.9, 141.5, 135.5, 131.8, 130.2, 128.8, 128.7, 128.2, 127.0, 124.0, 121.3, 116.8, 113.4, 62.1, 60.7, 60.4, 55.7. HRMS (ESI) m/z calcd for $C_{22}H_{22}NO_5$ $[M - Br]^+$: 380.1492, found: 380.1492.

1-benzyl-5-hydroxy-2-(methoxycarbonyl)pyridin-1-ium (1m): 314.4 mg, 97% yield, white solid, m.p. = 125.2- – 126.5 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.93 (d, J = 9.2 Hz, 1H), 7.87 (d, J = 2.8 Hz, 1H), 7.39 – 7.33 (m, 3H), 7.26 – 7.19 (m, 2H), 6.89 (dd, J = 9.2, 2.8 Hz, 1H), 5.95 (s, 2H), 3.74 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.4, 160.8, 141.4, 135.7, 131.8, 130.2, 128.8, 128.3, 127.0, 116.9, 60.8, 52.5. HRMS (ESI) m/z calcd for $C_{14}H_{14}NO_3$ $[M - Br]^+$: 244.0968, found: 244.0967.

1-benzyl-2-(ethoxycarbonyl)-5-hydroxypyridin-1-ium (1n): 321.3mg, 95% yield, white solid, m.p. = 126.0 – 126.9 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.92 (d, J = 9.2 Hz, 1H), 7.87 (d, J = 2.8 Hz, 1H), 7.39 – 7.32 (m, 3H), 7.22 – 7.20 (m, 2H), 6.89 (dd, J = 9.6, 2.8 Hz, 1H), 5.95 (s, 2H), 4.18 (q, J = 7.2 Hz, 2H), 1.19 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.5, 160.4, 141.3, 135.7, 131.7, 130.3, 128.8, 128.2, 127.0, 117.1, 61.3, 60.7, 13.9. HRMS (ESI) m/z calcd for $C_{15}H_{16}NO_3$ $[M - Br]^+$: 258.1125, found: 258.1122.

1-benzyl-5-hydroxy-2-(isopropoxycarbonyl)pyridin-1-ium (1o): 313.5 mg, 89% yield, white solid, m.p. = 122.9 – 124.3 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (d, J = 2.8 Hz, 1H), 8.36 (d, J = 9.2Hz, 1H), 8.07 (dd, J = 8.8, 2.8Hz, 1H), 7.46 – 7.19 (m, 5H), 6.13 (s, 2H), 5.07 (m, 1H), 1.18 (d, J = 6.4 Hz, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.5, 160.0, 141.1, 135.7, 131.6, 130.3, 128.8, 128.2, 126.9, 117.5, 69.1, 60.8, 21.3. HRMS (ESI) m/z calcd for $C_{16}H_{18}NO_3$ [M – Br]$^+$: 272.1281, found: 272.1281.

1-benzyl-2-(*tert*-butoxycarbonyl)-5-hydroxypyridin-1-ium (1p): 333.3 mg, 91% yield, white solid, m.p. = 136.3 – 137.2 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.88 (d, J = 2.8 Hz, 1H), 8.33 (d, J = 8.8 Hz, 1H), 8.01 (dd, J = 8.8, 2.4 Hz, 1H), 7.40 (m, 3H), 7.26 – 7.18 (m, 2H), 6.10 (s, 2H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.3, 160.0, 140.7, 135.7, 131.6, 130.4, 128.8, 128.3, 127.0, 118.6, 82.5, 60.7, 27.5. HRMS (ESI) m/z calcd for $C_{17}H_{20}NO_3$ [M – Br]$^+$: 286.1438, found: 286.1433.

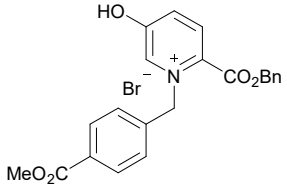
1-benzyl-2-((cyclopropylmethoxy)carbonyl)-5-hydroxypyridin-1-ium (1q): 331.5 mg, 91% yield, white solid, m.p. = 125.9 – 127.4 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.99 (d, J = 2.8 Hz, 1H), 8.40 (d, J = 8.8 Hz, 1H), 8.13 (dd, J = 8.8, 2.8 Hz, 1H), 7.44 – 7.24 (m, 5H), 6.15 (s, 2H), 4.11 (d, J = 7.2 Hz, 2H), 1.09 (m, 1H), 0.57 – 0.45 (m, 2H), 0.29 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.7, 159.1, 138.0, 134.2, 133.0, 131.9, 131.3, 129.0, 128.8, 127.8, 72.0, 62.1, 9.2, 3.3. HRMS (ESI) m/z calcd for $C_{17}H_{18}NO_3$ [M – Br]$^+$: 284.1281, found: 284.1280.

1-benzyl-2-((cyclopentylmethoxy)carbonyl)-5-hydroxypyridin-1-ium (1r): 364.8 mg, 93% yield, white solid, m.p. = 147.8 – 148.5 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.00 (d, J = 2.8 Hz, 1H), 8.39 (d, J = 8.8 Hz, 1H), 8.14 (dd, J = 8.8, 2.4 Hz, 1H), 7.43 – 7.22 (m, 5H), 6.16 (s, 2H), 4.14 (d, J = 7.2 Hz, 2H), 2.18 – 2.07 (m, 1H), 1.67 – 1.41 (m, 6H), 1.21 – 1.08 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.6, 159.1, 138.1, 134.2, 132.8, 131.9, 131.3, 128.9, 128.8, 127.7, 70.6, 62.1, 37.6, 28.6, 24.8. HRMS (ESI) m/z calcd for $C_{19}H_{22}NO_3$ [M – Br]$^+$: 312.1594, found: 312.1597.

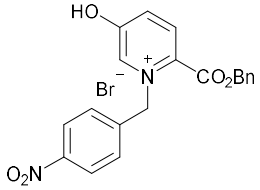
1-benzyl-2-((cyclohexylmethoxy)carbonyl)-5-hydroxypyridin-1-ium (1s): 386.0 mg, 95% yield, white solid, m.p. = 147.4 – 148.9 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.98 (d, J = 2.4 Hz, 1H), 8.40 (d, J = 9.2 Hz, 1H), 8.11 (dd, J = 8.4, 2.4 Hz, 1H), 7.44 – 7.20 (m, 5H), 6.15 (s, 2H), 4.07 (d, J = 6.0 Hz, 2H), 1.69 – 1.50 (m, 6H), 1.14 (m, 3H), 0.97 – 0.79 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.5, 159.3, 138.2, 134.3, 132.5, 132.0, 131.3, 128.9, 128.7, 127.5, 71.7, 62.1, 36.2, 28.7, 25.7, 25.1. HRMS (ESI) m/z calcd for $C_{20}H_{24}NO_3$ [M – Br]$^+$: 326.1751, found: 326.1752.

2-((benzyloxy)carbonyl)-1-(4-cyanobenzyl)-5-hydroxypyridin-1-ium (1t): 399.8 mg, 94% yield, white solid, m.p. = 139.7 – 142.6 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.02 (s, 1H), 8.49 (d, J = 8.8 Hz, 1H), 8.13 (d, J = 9.2 Hz, 1H), 7.82 (d, J = 7.6 Hz, 2H), 7.41 – 7.32 (m, 7H), 6.25 (s, 2H), 5.31 (s, 2H) ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.7, 159.1, 139.9, 138.9, 134.4, 132.6, 132.5, 132.2, 131.5, 128.6, 128.5, 128.5, 128.0, 118.4, 111.1, 68.5, 61.9. HRMS (ESI) m/z calcd for $C_{21}H_{17}N_2O_3$ [M – Br]$^+$: 345.1234, found: 345.1232.

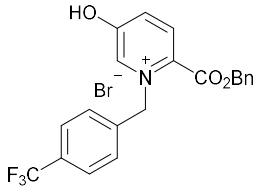
2-((benzyloxy)carbonyl)-5-hydroxy-1-(4-(methoxycarbonyl)benzyl)pyridin-1-ium (1u): 412.5 mg, 90% yield, white solid, m.p. = 114.8 – 116.1 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (d, J = 2.8 Hz, 1H), 8.44 (d, J = 9.2 Hz, 1H), 8.05 (dd, J = 9.2, 2.4 Hz, 1H), 7.91 (d, J = 8.0 Hz, 2H), 7.34 (m, 7H), 6.21 (s, 2H), 5.29 (s, 2H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.7, 160.0, 159.2, 139.6, 138.9, 134.4, 132.3, 131.7, 131.4, 129.6, 128.6, 128.5, 128.5, 127.5 (2C), 68.4, 62.0, 52.3. HRMS (ESI) m/z calcd for $C_{22}H_{20}NO_5$ [M + Na]$^+$: 378.1336, found: 378.1344.



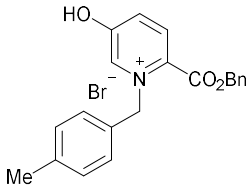
2-((benzyloxy)carbonyl)-5-hydroxy-1-(4-nitrobenzyl)pyridin-1-ium (1v): 427.5 mg, 96% yield, white solid, m.p. = 141.6 – 143.4 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.08 (d, J = 2.8 Hz, 1H), 8.52 (d, J = 9.2 Hz, 1H), 8.16 (m, 3H), 7.47 (d, J = 8.4 Hz, 2H), 7.32 (m, 5H), 6.32 (s, 2H), 5.30 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.9, 159.1, 147.2, 141.9, 139.1, 134.4, 132.5, 132.0, 131.6, 128.5, 128.5, 128.4, 128.3, 123.7, 68.5, 61.8. HRMS (ESI) m/z calcd for $C_{20}H_{17}N_2O_5$ [M – Br]$^+$: 365.1132, found: 365.1132.



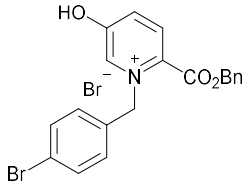
2-((benzyloxy)carbonyl)-5-hydroxy-1-(4-(trifluoromethyl)benzyl)pyridin-1-ium (1w): 416.8 mg, 89% yield, white solid, m.p. = 132.9 – 134.6 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.00 (d, J = 2.4 Hz, 1H), 8.48 (d, J = 9.2 Hz, 1H), 8.11 (dd, J = 9.2, 2.8 Hz, 1H), 7.72 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 8.0 Hz, 2H), 7.35 (m, 5H), 6.25 (s, 2H), 5.32 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.8, 159.2, 139.1, 138.9, 134.4, 132.4, 132.0, 131.5, 128.9 (q, J = 32.0 Hz), 128.6, 128.5 (2C), 128.1, 125.7 (q, J = 3.8 Hz), 124.0 (q, J = 270.5 Hz), 68.5, 61.8. HRMS (ESI) m/z calcd for $C_{21}H_{17}F_3NO_3$ [M – Br]$^+$: 388.1155, found: 388.1154.



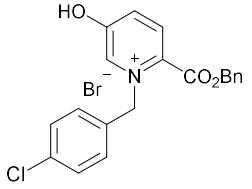
2-((benzyloxy)carbonyl)-5-hydroxy-1-(4-methylbenzyl)pyridin-1-ium (1x): 372.9 mg, 90% yield, white solid, m.p. = 135.8 – 137.3 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.96 (d, J = 2.4 Hz, 1H), 8.41 (d, J = 8.8 Hz, 1H), 8.07 (dd, J = 8.8, 2.4 Hz, 1H), 7.38 (m, 5H), 7.17 (m, 4H), 6.10 (s, 2H), 5.34 (s, 2H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.5, 159.3, 138.4, 138.0, 134.4, 132.4, 132.0, 131.1, 131.1, 129.5, 128.6, 128.5 (2C), 128.0, 68.6, 61.9, 20.7. HRMS (ESI) m/z calcd for $C_{21}H_{20}NO_3$ [M – Br]$^+$: 334.1438, found: 334.1443.



2-((benzyloxy)carbonyl)-1-(4-bromobenzyl)-5-hydroxypyridin-1-ium (1y): 460.0 mg, 96% yield, white solid, m.p. = 122.5 – 124.0 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.96 (d, J = 2.8 Hz, 1H), 8.44 (d, J = 8.8 Hz, 1H), 8.08 (dd, J = 9.2, 2.8 Hz, 1H), 7.57 (d, J = 8.4 Hz, 2H), 7.41 – 7.31 (m, 5H), 7.22 (d, J = 8.2 Hz, 2H), 6.12 (s, 2H), 5.34 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.5, 159.3, 138.5, 134.4, 133.7, 132.2, 132.1, 131.8, 131.3, 129.9, 128.6, 128.5, 128.5, 122.1, 68.5, 61.6. HRMS (ESI) m/z calcd for $C_{20}H_{17}BrNO_3$ [M – Br]$^+$: 398.0386, found: 398.0395.



2-((benzyloxy)carbonyl)-1-(4-chlorobenzyl)-5-hydroxypyridin-1-ium (1z): 400.0 mg, 92% yield, white solid, m.p. = 128.4 – 129.7 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.99 (d, J = 2.4 Hz, 1H), 8.44 (d, J = 8.8 Hz, 1H), 8.10 (dd, J = 8.8, 2.4 Hz, 1H), 7.47 – 7.25 (m, 9H), 6.15 (s, 2H), 5.34 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.6, 159.3, 138.5, 134.4, 133.5, 133.2, 132.3, 132.0, 131.3, 129.7, 128.9, 128.6, 128.5, 128.5, 68.5, 61.5. HRMS (ESI) m/z calcd for $C_{20}H_{17}ClNO_3$ [M – Br]$^+$: 354.0891, found: 354.0889.

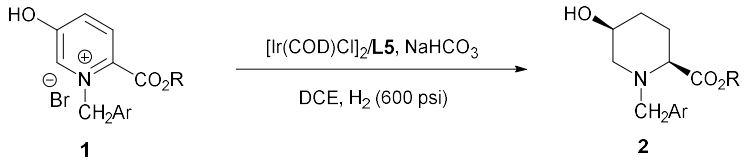


2-((benzyloxy)carbonyl)-1-(2-bromobenzyl)-5-hydroxypyridin-1-ium (1aa): 440.8 mg, 92% yield, white solid, m.p. = 124.7 – 125.9 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.85 (s, 1H), 8.53 (dd, *J* = 9.2, 2.8 Hz, 1H), 8.12 (d, *J* = 8.8 Hz, 1H), 7.75 – 7.72 (m, 1H), 7.37 – 7.31 (m, 7H), 6.74 (q, *J* = 4.0 Hz, 1H), 6.16 (s, 2H), 5.29 (s, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 159.9, 158.9, 140.3, 138.9, 134.4, 134.2, 132.9, 132.5, 132.2, 131.8, 130.1, 128.54, 128.51, 128.3, 127.3, 121.3, 68.4, 62.9. HRMS (ESI) m/z calcd for $C_{20}H_{17}BrNO_3$ $[M - Br]^+$: 398.0386, found: 398.0390.

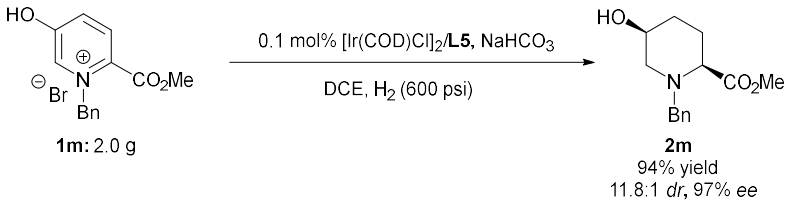
2-((benzyloxy)carbonyl)-1-(3,5-dimethylbenzyl)-5-hydroxypyridin-1-ium (1ab): 389.8 mg, 91% yield, white solid, m.p. = 132.4 – 133.9 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.96 (d, *J* = 9.2 Hz, 1H), 7.88 – 7.81 (d, *J* = 2.8 Hz, 1H), 7.35 (m, 5H), 6.95 (s, 1H), 6.88 (dd, *J* = 9.2, 2.4 Hz, 1H), 6.80 (s, 2H), 5.89 (s, 2H), 5.25 (s, 2H), 2.20 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.5, 160.3, 141.5, 137.9, 135.6, 135.5, 131.9, 130.2, 129.7, 128.5, 128.2, 128.0, 124.7, 116.7, 66.6, 60.6, 20.8. HRMS (ESI) m/z calcd for $C_{22}H_{22}NO_3$ $[M - Br]^+$: 348.1594, found: 348.1592.

2-((benzyloxy)carbonyl)-1-(3,5-dimethoxybenzyl)-5-hydroxypyridin-1-ium (1ac): 437.3 mg, 95% yield, white solid, m.p. = 123.2 – 125.1 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.90 (d, *J* = 2.8 Hz, 1H), 8.44 (d, *J* = 8.8 Hz, 1H), 8.08 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.38 (m, 5H), 6.52 (d, *J* = 2.4 Hz, 1H), 6.46 (d, *J* = 2.4 Hz, 2H), 6.08 (s, 2H), 5.37 (s, 2H), 3.71 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.9, 159.5, 159.4, 138.0, 136.2, 134.5, 132.2, 132.0, 131.3, 128.6, 128.5, 128.4, 106.1, 100.1, 68.5, 61.8, 55.4. HRMS (ESI) m/z calcd for $C_{22}H_{22}NO_5$ $[M - Br]^+$: 380.1492, found: 380.1492.

2.3 General Procedure for Hydrogenation of pyridinium salts

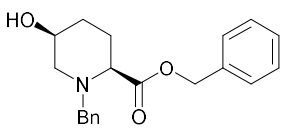


A mixture of $[Ir(COD)Cl]_2$ (0.7 mg, 1.0 μmol, 1.0 mol%) and (*S*)-ZhaoPhos (**L5**) (1.8 mg, 2.0 μmol, 2.0 mol%) were dissolved in degassed solvent (2.0 mL) at argon atmosphere, and the resulting solution was allowed to stirred for 20 min, followed by the addition of the substrate **1** (0.1 mmol, 1.0 equiv.) and $NaHCO_3$ (8.4 mg, 0.1 mmol, 1.0 equiv.). The resulting mixture was transferred to an autoclave, which was purged (3 × 50 psi) and charged with H_2 (600 psi), then the reaction mixtures were stirred at room temperature for 48 h. After careful release of the hydrogen gas, the reaction mixture was filtrated and concentrated in vacuo. Flash chromatography on silica gel using petroleum ether/ethyl acetate as the eluent gave the products. The enantiomeric excesses were determined by chiral HPLC.

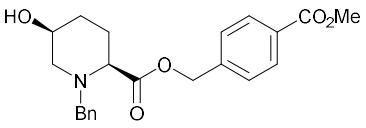


Asymmetric hydrogenation of 2-methyl ester-5-hydroxypyridinium salt (**1m**) at gram scale: A mixture of $[Ir(COD)Cl]_2$ (4.1 mg, 6.2 μmol, 0.1 mol%) and (*S*)-ZhaoPhos (**L5**) (10.8 mg, 12.4 μmol, 0.2 mol%) were dissolved in degassed solvent (80.0 mL) at argon atmosphere, and the resulting solution was allowed to stirred for 20 min, followed by the addition of the substrate **1m** (2.0 g, 6.2 mmol, 1.0 equiv.) and $NaHCO_3$ (520.9 mg, 6.2 mmol, 1.0 equiv.). The resulting mixture was transferred to an autoclave, which was purged (3 × 50 psi) and charged with H_2 (600 psi), then the reaction mixtures were stirred at room temperature for 48 h. After careful release of the hydrogen gas, the reaction mixture was filtrated and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (petroleum ether/ethyl acetate = 20:1) to give compound **2m** (1.45 g, 94% yield, 11.8:1 *dr*, 97% *ee*) as a colorless oil.

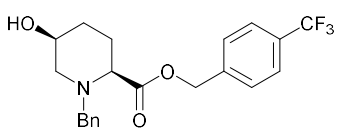
benzyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2a): 31.2 mg, 96% yield, 16.7:1 *dr*, 95% *ee*, $[\alpha]_D^{25}$ = –58.9 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.19 (m, 10H), 5.17 (s, 2H), 3.81 (d, *J* = 13.2 Hz, 1H), 3.77 – 3.72 (m, 1H), 3.51 (d, *J* = 13.6 Hz, 1H), 3.25 (dd, *J* = 7.2, 4.4 Hz, 1H), 2.87 (dd, *J* = 11.6, 6.8 Hz, 1H), 2.49 (s, 1H), 2.45 (dd, *J* = 11.2, 3.2 Hz, 1H), 2.13 – 2.00 (m, 1H), 1.86 – 1.72 (m, 1H), 1.72 – 1.53 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.0, 137.9, 135.8, 129.1, 128.7, 128.4, 128.4, 128.4, 127.3, 66.4, 65.9, 62.8, 59.7, 55.7, 30.1, 25.5. HRMS (ESI) m/z calcd for $C_{20}H_{23}NNaO_3$ $[M + Na]^+$: 348.1570, found: 348.1566. HPLC: Chiralcel AD-H column, 254 nm, 30 ℃, *n*-hexane/ethanol = 90/10, flow = 0.5 mL/min, retention time 15.6 min (maj) and 18.9 min.



4-(methoxycarbonyl)benzyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2b): 36.0 mg, 94% yield, 15.1:1 *dr*, 95% *ee*, $[\alpha]_D^{25}$ = –49.7 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.03 (d, *J* = 7.2 Hz, 2H), 7.42 (d, *J* = 7.6 Hz, 2H), 7.28 – 7.23 (m, 5H), 5.21 (s, 2H), 3.91 (s, 3H), 3.81 (d, *J* = 13.2 Hz, 1H), 3.78 – 3.70 (m, 1H), 3.54 (d, *J* = 13.2 Hz, 1H), 3.30 (t, *J* = 5.6 Hz, 1H), 2.88 (dd, *J* = 11.2, 6.4 Hz, 1H), 2.56 – 2.41 (m, 2H), 2.14 – 2.03 (m, 1H), 1.85 – 1.78 (m, 1H), 1.74 – 1.53 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.8, 166.7, 140.9, 137.9, 130.1, 130.0, 129.0, 128.4, 127.9, 127.4, 66.0, 65.5, 62.5, 59.7, 55.7, 52.3, 30.1, 25.6. HRMS (ESI) m/z calcd for $C_{22}H_{25}NNaO_5$ $[M + Na]^+$: 406.1625, found: 406.1624. HPLC: Chiralcel IA-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 21.3 min (maj) and 27.0 min.



4-(trifluoromethyl)benzyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2c): 35.4 mg, 90% yield, 13.6:1 *dr*, 94% *ee*, $[\alpha]_D^{25}$ = –46.4 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.30 – 7.21 (m, *J* = 6.0, 5.4 Hz, 5H), 5.21 (s, 2H), 3.81 (d, *J* = 13.2 Hz, 1H), 3.79 – 3.72 (m, 1H), 3.53 (d, *J* = 13.2 Hz, 1H), 3.29 (dd, *J* = 6.8, 4.4 Hz, 1H), 2.88 (dd, *J* = 11.2, 6.4 Hz, 1H), 2.50 – 2.46 (m, 2H), 2.12 – 2.03 (m, 1H), 1.87 – 1.77 (m, 1H), 1.73 – 1.54 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.8, 139.9, 137.9, 130.6 (q, *J* = 32.4 Hz), 129.0, 128.43, 128.39, 127.4, 125.7 (q, *J* = 3.6 Hz), 124.7 (q, *J* = 270.5 Hz), 65.9, 65.4, 62.7, 59.7, 55.8, 30.1, 25.6. HRMS (ESI) m/z calcd for $C_{21}H_{22}F_3NNaO_3$ $[M + Na]^+$: 416.1444,



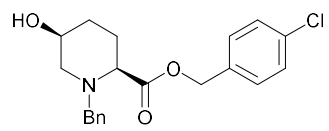
found: 416.1439. HPLC: Chiralcel IA-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 12.4 min (maj) and 15.7 min.

4-nitrobenzyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2d): 34.4 mg, 93% yield, 14.2:1 *dr*, 94% *ee*, $[\alpha]_D^{25}$ = –61.3 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.37 – 7.33 (m, 5H), 5.22 – 5.13 (m, 2H), 3.89 – 3.92 (m, 1H), 3.81 – 3.73 (m, 1H), 3.65 – 3.61 (m, 1H), 3.37 – 3.28 (m, 1H), 2.84 (dd, *J* = 11.6, 6.4 Hz, 1H), 2.53 – 2.50 (m, 1H), 2.24 (s, 1H), 2.18 – 2.07 (m, 1H), 1.92 – 1.79 (m, 1H), 1.79 – 1.69 (m, 1H), 1.60 – 1.51 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.6, 147.4, 135.7, 129.4, 128.8, 128.6, 128.5, 123.7, 66.6, 66.2, 62.5, 59.0, 55.8, 30.0, 25.7. HRMS (ESI) m/z calcd for $C_{20}H_{22}N_2NaO_5$ $[M + Na]^+$: 393.1421, found: 393.1418. HPLC: Chiralcel IA-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 66.9 min (maj) and 89.9 min.

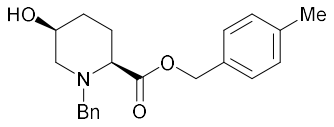
4-cyanobenzyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2e): 31.9 mg, 91% yield, 12.6:1 *dr*, 95% *ee*, $[\alpha]_D^{25}$ = –51.3 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.65 (d, *J* = 7.6 Hz, 2H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.31 – 7.25 (m, 5H), 5.20 (s, 2H), 3.80 (d, *J* = 13.6 Hz, 1H), 3.77 – 3.74 (m, 1H), 3.53 (d, *J* = 13.2 Hz, 1H), 3.30 (t, *J* = 6.0 Hz, 1H), 2.88 (dd, *J* = 11.6, 6.4 Hz, 1H), 2.51 – 2.43 (m, 2H), 2.17 – 2.02 (m, 1H), 1.86 – 1.80 (m, 1H), 1.72 – 1.69 (m, 1H), 1.68 – 1.54 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.7, 141.1, 137.8, 132.5, 128.9, 128.5, 128.4, 127.4, 118.5, 112.3, 65.9, 65.1, 62.6, 59.7, 55.7, 30.0, 25.6. HRMS (ESI) m/z calcd for $C_{21}H_{22}N_2NaO_3$ $[M + Na]^+$: 373.1523, found: 373.1520. HPLC: Chiralcel IA-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 95/5, flow = 0.7 mL/min, retention time 70.6 min (maj) and 92.3 min.

4-bromobenzyl (2S,5S)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2f): 35.6 mg, 88% yield, 15.4:1 *dr*, 94% *ee*, $[\alpha]_D^{25}$ = –59.6 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 – 7.47 (m, 2H), 7.33 – 7.18 (m, 7H), 5.10 (s, 2H), 3.79 (d, *J* = 13.2 Hz, 1H), 3.76 – 3.72 (m, 1H), 3.51 (d, *J* = 13.6 Hz, 1H), 3.25 (dd, *J* = 6.8, 4.4 Hz, 1H), 2.86 (dd, *J* = 11.2, 6.8 Hz, 1H), 2.49 (s, 1H), 2.46 (dd, *J* = 11.2, 3.3 Hz, 1H), 2.12 – 2.01 (m, 1H), 2.09 – 2.01 (m, 1H), 1.73 – 1.50 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.9, 137.9, 134.9, 131.8, 130.1, 129.0, 128.4, 127.4, 122.5, 65.9, 65.5, 62.7, 59.7, 55.7, 30.0, 25.5. HRMS (ESI) m/z calcd for $C_{20}H_{23}BrNO_3$ $[M + H]^+$: 404.0856, found: 404.0857. HPLC: Chiralcel IA-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 18.8 min (maj) and 23.7 min.

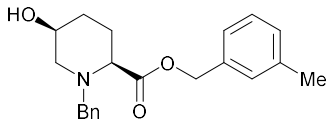
4-fluorobenzyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2g): 28.5 mg, 83% yield, 13.8:1 *dr*, 96% *ee*, $[\alpha]_D^{25}$ = –44.8 (c = 0.5, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.21 (m, 7H), 7.06 – 7.02 (m, 2H), 5.13 (s, 2H), 3.79 (d, *J* = 13.2 Hz, 1H), 3.76 – 3.73 (m, 1H), 3.50 (d, *J* = 13.2 Hz, 1H), 3.24 (dd, *J* = 7.2, 4.4 Hz, 1H), 2.87 (dd, *J* = 11.2, 6.4 Hz, 1H), 2.47 (s, 1H), 2.45 (dd, *J* = 11.2, 3.2 Hz, 1H), 2.12 – 1.98 (m, 1H), 1.79 (m, 1H), 1.71 – 1.53 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.9, 162.8 (d, *J* = 245.6 Hz), 137.8, 131.7 (d, *J* = 3.3 Hz), 130.5 (d, *J* = 8.2 Hz), 129.0, 128.4, 127.4, 115.7 (d, *J* = 21.5 Hz), 65.9, 65.7, 62.8, 59.7, 55.8, 30.1, 25.5. HRMS (ESI) m/z calcd for $C_{20}H_{22}FNNaO_3$ $[M + Na]^+$: 366.1476, found: 366.1477. HPLC: Chiralcel IA-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 95/5, flow = 0.5 mL/min, retention time 30.9 min (maj) and 41.9 min.

4-chlorobenzyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2h): 32.4 mg, 90% yield, 

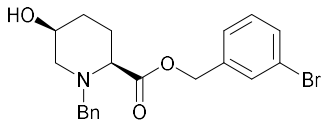
11.6:1 *dr*, 94% *ee*, $[\alpha]_D^{25}$ = –52.1 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.15 (m, 9H), 5.12 (s, 2H), 3.79 (d, *J* = 13.6 Hz, 1H), 3.75 – 3.72 (m, 1H), 3.51 (d, *J* = 13.2Hz, 1H), 3.25 (dd, *J* = 7.2, 4.4 Hz, 1H), 2.86 (dd, *J* = 11.6, 6.8 Hz, 1H), 2.52 (s, 1H), 2.46 (dd, *J* = 11.6, 3.6 Hz, 1H), 2.12 – 1.99 (m, 1H), 1.86 – 1.72 (m, 1H), 1.71 – 1.51 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.9, 137.9, 134.4, 134.3, 129.8, 129.0, 128.9, 128.4, 127.3, 65.9, 65.5, 62.7, 59.7, 55.7, 30.0, 25.5. HRMS (ESI) m/z calcd for $C_{20}H_{22}ClNNaO_3$ $[M + Na]^+$: 382.1180, found: 382.1185. HPLC: Chiralcel AD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 95/5, flow = 0.5 mL/min, retention time 49.4 min (maj) and 67.1 min.

4-methylbenzyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2i): 31.2 mg, 92% yield, 

14.2:1 *dr*, 97% *ee*, $[\alpha]_D^{25}$ = –59.6 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.13 (m, 9H), 5.12 (s, 2H), 3.80 (d, *J* = 13.2 Hz, 1H), 3.75 – 3.70 (m, 1H), 3.51 (d, *J* = 13.6 Hz, 1H), 3.23 (dd, *J* = 7.2, 4.4 Hz, 1H), 2.86 (dd, *J* = 11.2, 6.4 Hz, 1H), 2.50 (s, 1H), 2.44 (dd, *J* = 11.6, 3.6 Hz, 1H), 2.33 (s, 3H), 2.14 – 1.99 (m, 1H), 1.85 – 1.71 (m, 1H), 1.71 – 1.53 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.0, 138.3, 138.0, 132.9, 129.3, 129.1, 128.5, 128.3, 127.3, 66.3, 66.0, 62.8, 59.7, 55.7, 30.1, 25.5, 21.3. HRMS (ESI) m/z calcd for $C_{21}H_{25}NNaO_3$ $[M + Na]^+$: 362.1727, found: 362.1725. HPLC: Chiralcel OD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 95/5, flow = 0.5 mL/min, retention time 25.9 min (maj) and 28.0 min.

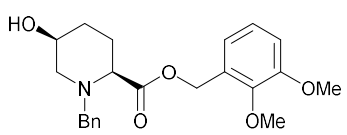
3-methylbenzyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2j): 31.6 mg, 93% yield, 

12.8:1 *dr*, 96% *ee*, $[\alpha]_D^{25}$ = –56.2 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 – 7.19 (m, 6H), 7.21 – 7.12 (m, 3H), 5.13 (s, 2H), 3.82 (d, *J* = 13.2 Hz, 1H), 3.77 – 3.72 (m, 1H), 3.51 (d, *J* = 13.2 Hz, 1H), 3.25 (t, *J* = 6.0 Hz, 1H), 2.88 (dd, *J* = 11.6, 6.4 Hz, 1H), 2.55 (s, 1H), 2.44 (dd, *J* = 11.2, 3.2 Hz, 1H), 2.34 (s, 3H), 2.12 – 2.03 (m, 1H), 1.85 – 1.75 (m, 1H), 1.68 – 1.59(m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.0, 138.4, 137.9, 135.7, 129.2, 129.1, 129.1, 128.6, 128.4, 127.3, 125.5, 66.5, 65.9, 62.9, 59.7, 55.8, 30.1, 25.5, 21.4. HRMS (ESI) m/z calcd for $C_{21}H_{25}NNaO_3$ $[M + Na]^+$: 362.1727, found: 362.1730. HPLC: Chiralcel IA-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 95/5, flow = 0.7 mL/min, retention time 16.1 min (maj) and 20.6 min.

3-bromobenzyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2k): 34.3 mg, 85% yield, 

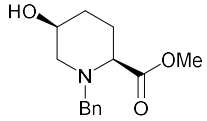
16.7:1 *dr*, 95% *ee*, $[\alpha]_D^{25}$ = –43.2 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 (t, *J* = 2.0 Hz, 1H), 7.46 – 7.43 (m, 1H), 7.33 – 7.18 (m, 7H), 5.11 (s, 2H), 3.80 (d, *J* = 13.2 Hz, 1H), 3.77 – 3.71 (m, 1H), 3.52 (d, *J* = 13.6 Hz, 1H), 3.27 (dd, *J* = 7.2, 4.4 Hz, 1H), 2.87 (dd, *J* = 11.6, 6.8 Hz, 1H), 2.48 (dd, *J* = 11.6, 3.6 Hz, 1H), 2.43 (s, 1H), 2.13 – 2.02 (m, 1H), 1.85 – 1.74 (m, 1H), 1.74 – 1.53 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.8, 138.1, 137.9, 131.5, 131.3, 130.3, 129.0, 128.4, 127.4, 126.8, 122.7, 66.0, 65.3, 62.6, 59.7, 55.8, 30.1, 25.6. HRMS (ESI) m/z calcd for $C_{20}H_{23}BrNO_3$ $[M + H]^+$: 404.0856, found: 404.0856. HPLC: Chiralcel AD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 17.6 min (maj) and 25.0 min.

2,3-dimethoxybenzyl (2S,5S)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2l): 33.2 mg, 86% yield,



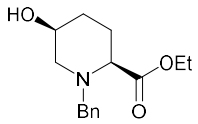
8.4:1 *dr*, 93% *ee*, $[\alpha]_D^{25}$ = –72.1 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.19 – 7.15 (m, 5H), 6.99 – 6.95 (m, 1H), 6.90 – 6.83 (m, 2H), 5.16 (s, 2H), 3.87 – 3.75 (m, 7H), 3.67 – 3.65 (m, 1H), 3.43 (d, *J* = 13.2 Hz, 1H), 3.16 (dd, *J* = 8.0, 4.4 Hz, 1H), 2.80 (t, *J* = 9.6 Hz, 1H), 2.36 (d, *J* = 11.2 Hz, 1H), 2.25 (s, 1H), 2.05 – 1.96 (m, 1H), 1.79 – 1.66 (m, 1H), 1.62 – 1.48 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.1, 152.8, 147.7, 138.1, 129.7, 129.1, 128.4, 127.3, 124.2, 121.8, 113.0, 66.0, 63.1, 61.7, 61.1, 59.7, 55.9, 55.8, 30.2, 25.5. HRMS (ESI) m/z calcd for $C_{22}H_{27}NNaO_5$ $[M + H]^+$: 408.1781, found: 408.1779. HPLC: Chiralcel AD-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 22.4 min (maj) and 24.4 min.

methyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2m): 23.2 mg, 93% yield, 11.8:1 *dr*, 97%



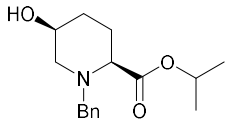
ee, $[\alpha]_D^{25}$ = –59.2 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.20 (m, 5H), 3.80 (d, *J* = 13.2 Hz, 1H), 3.76 – 3.73 (m, 1H), 3.71 (s, 3H), 3.51 (d, *J* = 13.2 Hz, 1H), 3.23 (dd, *J* = 7.2, 4.4 Hz, 1H), 2.85 (dd, *J* = 11.2, 6.4 Hz, 1H), 2.66 (s, 1H), 2.45 (dd, *J* = 11.2, 3.2 Hz, 1H), 2.12 – 1.99 (m, 1H), 1.84 – 1.72 (m, 1H), 1.72 – 1.54 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.8, 138.0, 129.0, 128.3, 127.3, 65.9, 62.8, 59.7, 55.6, 51.6, 30.0, 25.5. HRMS (ESI) m/z calcd for $C_{14}H_{19}NNaO_3$ $[M + Na]^+$: 272.1257, found: 272.1259. HPLC: Chiralcel AD-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 11.9 min (maj) and 14.2 min.

ethyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2n): 24.8 mg, 94% yield, 11.4:1 *dr*, 94%



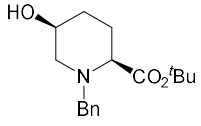
ee, $[\alpha]_D^{25}$ = –80.3 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.20 (m, 5H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.82 (d, *J* = 13.6 Hz, 1H), 3.78 – 3.69 (m, 1H), 3.50 (d, *J* = 13.6 Hz, 1H), 3.19 (dd, *J* = 7.6, 4.4 Hz, 1H), 2.86 (dd, *J* = 11.2, 6.4 Hz, 1H), 2.66 (s, 1H), 2.43 (dd, *J* = 11.2, 2.8 Hz, 1H), 2.10 – 2.02 (m, 1H), 1.82 – 1.75 (m, 1H), 1.68 – 1.58 (m, 2H), 1.29 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.3, 138.0, 129.0, 128.3, 127.3, 65.9, 63.1, 60.5, 59.7, 55.7, 30.1, 25.6, 14.4. HRMS (ESI) m/z calcd for $C_{15}H_{21}NNaO_3$ $[M + Na]^+$: 286.1414, found: 286.1415. HPLC: Chiralcel AD-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 11.3 min (maj) and 16.4 min.

isopropyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2o)： 23.6 mg, 85% yield, 13.8:1 *dr*,



92% *ee*, $[\alpha]_D^{25}$ = –69.1 (c = 1.0, $CHCl_3$) colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.19 (m, 5H), 5.13 – 5.04 (m, 1H), 3.83 (d, *J* = 13.6 Hz, 1H), 3.76 – 3.72 (m, 1H), 3.49 (d, *J* = 13.2 Hz, 1H), 3.15 (dd, *J* = 7.6, 4.4 Hz, 1H), 2.86 (dd, *J* = 11.2, 6.4 Hz, 1H), 2.64 (s, 1H), 2.41 (dd, *J* = 11.2, 2.8 Hz, 1H, 2.09 – 2.00 (m, 1H), 1.83 – 1.71 (m, 1H), 1.68 – 1.60 (m, 2H), 1.28 (d, *J* = 6.4 Hz, 3H), 1.26 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.8, 138.1, 129.0, 128.3, 127.3, 68.0, 65.9, 63.2, 59.6, 55.7, 30.1, 25.4, 22.0, 21.9. HRMS (ESI) m/z calcd for $C_{16}H_{23}NNaO_3$ $[M + Na]^+$: 300.1570, found: 300.1568. HPLC: Chiralcel AD-H column, 254 nm, 30 ℃, *n*-hexane/ethanol = 95/5, flow = 0.7 mL/min, retention time 15.5 min (maj) and 23.4 min.

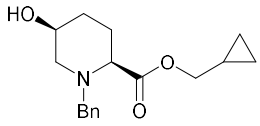
***tert*-butyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2p):** 26.5 mg, 91% yield, 19.3:1 *dr*,



94% *ee*, $[\alpha]_D^{25}$ = –59.6 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.20 (m, 5H), 3.86 (d, *J* = 13.2 Hz, 1H), 3.73 (m, 1H), 3.48 (d, *J* = 13.6 Hz, 1H), 3.06 (dd, *J* = 7.6, 4.4 Hz, 1H), 2.85 (dd, *J* = 11.6, 6.4 Hz, 1H), 2.68 (s, 1H), 2.38 (dd, *J* = 11.6, 3.2 Hz, 1H), 2.08 – 2.00 (m, 1H), 1.82 – 1.69 (m, 1H), 1.63 (m, 2H), 1.49 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.7, 138.3, 129.0, 128.4, 127.3,

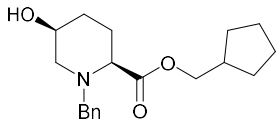
81.1, 65.9, 63.9, 59.6, 55.7, 30.1, 28.2, 25.5. HRMS (ESI) m/z calcd for $C_{17}H_{25}NNaO_3$ $[M + Na]^+$: 314.1727, found: 314.1731. HPLC: Chiralcel IA-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 95/5, flow = 0.5 mL/min, retention time 14.3 min (maj) and 16.6 min.

cyclopropylmethyl (2S,5S)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2q): 25.8 mg, 89% yield,



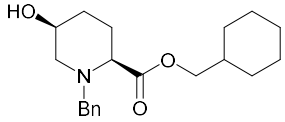
17.8:1 *dr*, 96% *ee*, $[\alpha]_D^{25}$ = –58.6 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.20 (m, 5H), 4.04 – 3.92 (m, 2H), 3.84 (d, *J* = 13.6 Hz, 1H), 3.78 – 3.73 (m, 1H), 3.52 (d, *J* = 13.2 Hz, 1H), 3.22 (dd, *J* = 7.6, 4.0 Hz, 1H), 2.87 (dd, *J* = 11.2, 6.4 Hz, 1H), 2.65 (s, 1H), 2.44 (dd, *J* = 11.6, 3.2 Hz, 1H), 2.15 – 2.01 (m, 1H), 1.85 – 1.74 (m, 1H), 1.70 – 1.58 (m, 2H), 1.22 – 1.10 (m, 1H), 0.62 – 0.52 (m, 2H), 0.35 – 0.26 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.4, 138.0, 129.1, 128.3, 127.3, 69.3, 65.9, 63.1, 59.7, 55.7, 30.1, 25.5, 10.0, 3.43, 3.41. HRMS (ESI) m/z calcd for $C_{17}H_{23}NNaO_3$ $[M + Na]^+$: 312.1570, found: 312.1572. HPLC: Chiralcel AD-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 95/5, flow = 0.7 mL/min, retention time 19.1 min (maj) and 36.1 min.

cyclopentylmethyl (2S,5S)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2r): 29.2 mg, 92% yield,



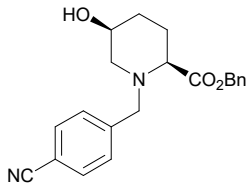
13.8:1 *dr*, 96% *ee*, $[\alpha]_D^{25}$ = –48.2 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.20 (m, 5H), 4.04 (d, *J* = 6.4 Hz, 2H), 3.83 (d, *J* = 13.6 Hz, 1H), 3.77 – 3.72 (m, 1H), 3.54 (d, *J* = 13.2 Hz, 1H), 3.22 (dd, *J* = 8.0, 3.6 Hz, 1H), 2.86 (dd, *J* = 11.6, 6.8 Hz, 1H), 2.48 – 2.44 (m, 2H), 2.25 (m, 1H), 2.13 – 2.01 (m, 1H), 1.83 – 1.80 (m, 3H), 1.68 – 1.52 (m, 6H), 1.31 – 1.22 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.4, 138.2, 129.0, 128.4, 127.3, 68.6, 66.1, 62.9, 59.7, 55.7, 38.7, 30.2, 29.6, 25.7, 25.5. HRMS (ESI) m/z calcd for $C_{19}H_{27}NNaO_3$ $[M + Na]^+$: 340.1883, found: 340.1887. HPLC: Chiralcel AS-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 95/5, flow = 0.5 mL/min, retention time 20.0 min (maj) and 23.5 min.

cyclohexylmethyl (2*S*,5*S*)-1-benzyl-5-hydroxypiperidine-2-carboxylate (2s): 30.8 mg, 93% yield,

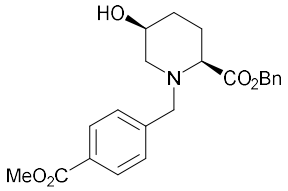


13.7:1 *dr*, 93% *ee*, $[\alpha]_D^{25}$ = –55.1 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.18 (m, 5H), 3.95 (d, *J* = 6.4 Hz, 2H), 3.83 (d, *J* = 13.2 Hz, 1H), 3.77 – 3.72 (m, 1H), 3.53 (d, *J* = 13.6 Hz, 1H), 3.22 (dd, *J* = 7.6, 4.4 Hz, 1H), 2.86 (dd, *J* = 11.6, 6.8 Hz, 1H), 2.54 – 2.36 (m, 2H), 2.16 – 2.00 (m, 1H), 1.87 – 1.53 (m, 9H), 1.33 – 1.12 (m, 3H), 1.04 – 0.95 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.4, 138.2, 129.0, 128.4, 127.3, 69.8, 66.0, 63.0, 59.7, 55.8, 37.3, 30.2, 29.9, 26.4, 25.8, 25.7. HRMS (ESI) m/z calcd for $C_{20}H_{29}NNaO_3$ $[M + Na]^+$: 354.2040, found: 354.2035. HPLC: Chiralcel AS-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 95/5, flow = 0.5 mL/min, retention time 18.1 min (maj) and 21.2 min.

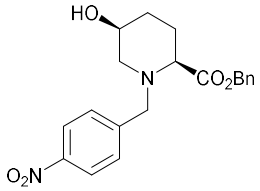
benzyl (2*S*,5*S*)-1-(4-cyanobenzyl)-5-hydroxypiperidine-2-carboxylate (2t): 31.2 mg, 89% yield,



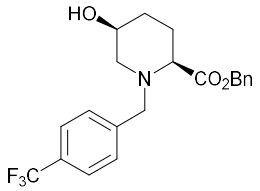
13.0:1 *dr*, 90% *ee*, $[\alpha]_D^{25}$ = –55.9 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 (d, *J* = 7.6 Hz, 2H), 7.31 – 7.27 (m, 7H), 5.13 – 5.05 (m, 2H), 3.78 (d, *J* = 14.0 Hz, 1H), 3.67 – 3.65 (m, 1H), 3.49 (d, *J* = 14.0 Hz, 1H), 3.22 (t, *J* = 5.6 Hz, 1H), 2.79 – 2.70 (m, 1H), 2.42 – 2.38 (m, 1H), 2.22 (s, 1H), 2.05 – 1.98 (m, 1H), 1.81 – 1.70 (m, 1H), 1.67 – 1.62 (m, 1H), 1.52 – 1.42 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.7, 144.2, 135.7, 132.2, 129.3, 128.7, 128.6, 128.4, 119.0, 111.1, 66.5, 66.1, 62.5, 59.3, 55.7, 30.0, 25.6. HRMS (ESI) m/z calcd for $C_{21}H_{22}N_2NaO_3$ $[M + Na]^+$: 373.1523, found: 373.1521. HPLC: Chiralcel AD-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 45.9 min (maj) and 52.4 min.

benzyl (2*S*,5*S*)-5-hydroxy-1-(4-(methoxycarbonyl)benzyl)piperidine-2-carboxylate (2u): 36.4 mg, 95% yield, 13.7:1 *dr*, 95% *ee*, $[\alpha]_D^{25}$ = –80.7 (c = 1.0, $CHCl_3$), colorless oil. 

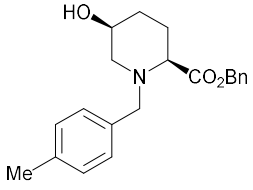
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.94 (d, *J* = 7.6 Hz, 2H), 7.35 – 7.26 (m, 7H), 5.24 – 5.10 (m, 2H), 3.89 (s, 3H), 3.85 (d, *J* = 14.0 Hz, 1H), 3.75 – 3.73 (m, 1H), 3.56 (d, *J* = 14.0 Hz, 1H), 3.33 – 3.23 (m, 1H), 2.89 – 2.79 (m, 1H), 2.47 (d, *J* = 11.2 Hz, 1H), 2.39 – 2.31 (m, 1H), 2.11 – 2.05 (m, 1H), 1.85 – 1.77 (m, 1H), 1.73 – 1.66 (m, 1H), 1.61 – 1.53 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.9, 167.1, 143.7, 135.8, 129.7, 129.2, 128.8, 128.7, 128.5, 128.4, 66.4, 66.1, 62.7, 59.4, 55.8, 52.1, 30.0, 25.6. HRMS (ESI) m/z calcd for $C_{22}H_{25}NNaO_5$ $[M + Na]^+$: 406.1625, found: 406.1620. HPLC: Chiralcel IA-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 26.3 min (maj) and 31.6 min.

benzyl (2*S*,5*S*)-5-hydroxy-1-(4-nitrobenzyl)piperidine-2-carboxylate (2v): 32.6 mg, 88% yield, 12.5:1 *dr*, 91% *ee*, $[\alpha]_D^{25}$ = –59.2 (c = 1.0, $CHCl_3$), colorless oil. 

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.34 – 7.33 (m, 5H), 5.22 – 5.13 (m, 2H), 3.91 (d, *J* = 14.4 Hz, 1H), 3.81 – 3.73 (m, 1H), 3.63 (d, *J* = 14.4 Hz, 1H), 3.32 t, *J* = 5.6 Hz, 1H), 2.84 (dd, *J* = 11.2, 6.4 Hz, 1H), 2.52 (dd, *J* = 10.8, 3.2 Hz, 1H), 2.25 (s, 1H), 2.18 – 2.07 (m, 1H), 1.92 – 1.79 (m, 1H), 1.79 – 1.69 (m, 1H), 1.61 – 1.52 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.6, 147.4, 146.2, 135.7, 129.4, 128.8, 128.6, 128.5, 123.7, 66.6, 66.2, 62.5, 59.0, 55.8, 30.0, 25.7. HRMS (ESI) m/z calcd for $C_{20}H_{22}N_2NaO_5$ $[M + Na]^+$: 393.1421, found: 393.1425. HPLC: Chiralcel AD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 53.0 min (maj) and 56.7 min.

benzyl (2*S*,5*S*)-5-hydroxy-1-(4-(trifluoromethyl)benzyl)piperidine-2-carboxylate (2w): 35.8 mg, 91% yield, 14.5:1 *dr*, 88% *ee*, $[\alpha]_D^{25}$ = –69.7 (c = 1.0, $CHCl_3$), colorless oil. 

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 8.0 Hz, 2H), 7.52 – 7.36 (m, 7H), 5.19 – 5.17 (m, 2H), 3.86 (d, *J* = 14.0 Hz, 1H), 3.76 – 3.74 (m, 1H), 3.56 (dd, *J* = 13.6, 2.4 Hz, 1H), 3.31 – 3.27 (m, 1H), 2.91 – 2.80 (m, 1H), 2.53 – 2.43 (m, 1H), 2.29 (s, 1H), 2.18 – 2.04 (m, 1H), 1.86 – 1.79 (m, 1H), 1.75 – 1.66 (m, 1H), 1.63 – 1.54 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.9, 142.5, 135.8, 129.6 (q, *J* = 32.1 Hz), 129.1, 128.8, 128.6, 128.5, 125.3 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 270.3 Hz), 66.5, 66.1, 62.8, 59.2, 55.8, 30.1, 25.6. HRMS (ESI) m/z calcd for $C_{21}H_{22}F_3NNaO_3$ $[M + Na]^+$: 416.1444, found: 416.1438. HPLC: Chiralcel AD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 10.8 min (maj) and 12.1 min.

benzyl (2*S*,5*S*)-5-hydroxy-1-(4-methylbenzyl)piperidine-2-carboxylate (2x): 30.9 mg, 91% yield, 16.5:1 *dr*, 97% *ee*, $[\alpha]_D^{25}$ = –51.7 (c = 1.0, $CHCl_3$), colorless oil. 

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.30 (m, 5H), 7.17 – 7.02 (m, 4H), 5.17 (s, 2H), 3.78 – 3.72 (m, 2H), 3.47 (dd, *J* = 12.8, 2.0 Hz, 1H), 3.25 – 3.21 (m, 1H), 2.91 – 2.82 (m, 1H), 2.54 – 2.39 (m, 2H), 2.31 (s, 3H), 2.09 – 2.02 (m, 1H), 1.82 – 1.74 (m, 1H), 1.67 – 1.53 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.1, 136.9, 135.9, 134.7, 129.1, 129.0, 128.7, 128.4 (2C), 66.3, 65.9, 62.8, 59.4, 55.7, 30.1, 25.5, 21.2. HRMS (ESI) m/z calcd for $C_{21}H_{25}NNaO_3$ $[M + Na]^+$: 362.1727, found: 362.1733. HPLC: Chiralcel AD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 15.0 min (maj) and 20.9 min.

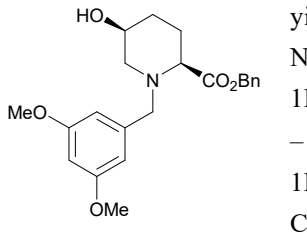
benzyl (*2S*,5*S*)-1-(4-bromobenzyl)-5-hydroxypiperidine-2-carboxylate (2y): 36.0 mg, 89% yield, 15.7:1 *dr*, 91% *ee*, $[\alpha]_D^{25}$ = –71.9 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 – 7.23 (m, 7H), 7.12 (d, *J* = 8.0 Hz, 2H), 5.16 (s, 2H), 3.76 – 3.73 (m, 2H), 3.45 (d, *J* = 13.6 Hz, 1H), 3.24 (t, *J* = 6.0 Hz, 1H), 2.84 (dd, *J* = 11.2, 6.4 Hz, 1H), 2.44 (d, *J* = 11.6 Hz, 1H), 2.36 (s, 1H), 2.14 – 1.99 (m, 1H), 1.83 – 1.76 (m, 1H), 1.74 – 1.52 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.9, 137.1, 135.8, 131.5, 130.7, 128.7, 128.54, 128.47, 121.2, 66.5, 66.0, 62.7, 59.0, 55.7, 30.0, 25.5. HRMS (ESI) m/z calcd for $C_{20}H_{23}BrNO_3$ $[M + H]^+$: 404.0856, found: 404.0853. HPLC: Chiralcel AD-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 20.9 min (maj) and 24.5 min.

benzyl (2*S*,5*S*)-1-(4-chlorobenzyl)-5-hydroxypiperidine-2-carboxylate (2z): 33.5 mg, 93% yield, 15.4:1 *dr*, 93% *ee*, $[\alpha]_D^{25}$ = –70.1 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.24 (m, 5H), 7.26 – 7.14 (m, 4H), 5.16 (s, 2H), 3.80 – 3.68 (m, 2H), 3.48 (dd, *J* = 13.6, 2.4 Hz, 1H), 3.25 (t, *J* = 6.0 Hz, 1H), 2.84 (dd, *J* = 11.6, 6.4 Hz, 1H), 2.51 – 2.36 (m, 2H), 2.11 – 2.01 (m, 1H),1.83 – 1.76 (m, 1H), 1.70 – 1.66 (m, 1H), 1.59 – 1.54 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.9, 136.6, 135.8, 133.0, 130.3, 128.7, 128.52 (2C), 128.45, 66.4, 66.0, 62.6, 59.0, 55.7, 30.1, 25.6. HRMS (ESI) m/z calcd for $C_{20}H_{22}ClNNaO_3$ $[M + Na]^+$: 382.1180, found: 382.1189. HPLC: Chiralcel AD-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 19.1 min (maj) and 22.7 min.

benzyl (2*S*,5*S*)-1-(2-bromobenzyl)-5-hydroxypiperidine-2-carboxylate (2aa): 34.4 mg, 85% yield, 11.9:1 *dr*, 90% *ee*, $[\alpha]_D^{20}$ = –57.7 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.28 – 7.26 (m, 5H), 7.21 – 7.14 (m, 1H), 7.04 – 7.00 (m, 1H), 5.15 – 5.05 (m, 2H), 3.76 (d, *J* = 14.4 Hz, 1H), 3.71 – 3.59 (m, 2H), 3.35 – 3.31 (m, 1H), 2.80 (t, *J* = 10.0 Hz, 1H), 2.53 – 2.49 (m, 1H), 2.12 – 1.93 (m, 2H), 1.79 – 1.64 (m, 2H), 1.49 – 1.42 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.0, 137.8, 135.9, 132.9, 130.8, 128.7, 128.7, 128.5, 128.4, 127.4, 124.7, 66.50, 66.46, 62.6, 59.1, 55.4, 30.2, 25.8. HRMS (ESI) m/z calcd for $C_{20}H_{23}BrNO_3$ $[M + H]^+$: 404.0856, found: 404.0854. HPLC: Chiralcel AD-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 18.9 min (maj) and 24.1 min.

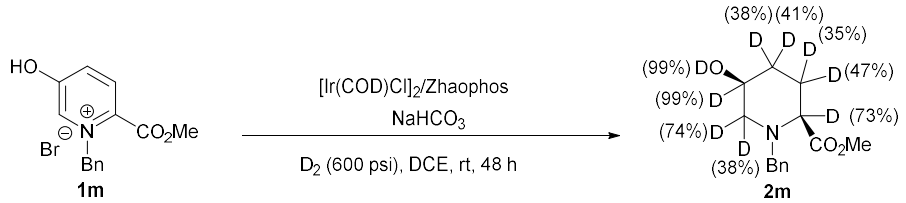
benzyl (2*S*,5*S*)-1-(3,5-dimethylbenzyl)-5-hydroxypiperidine-2-carboxylate (2ab): 32.2 mg, 91% yield, 13.6:1 *dr*, 94% *ee*, $[\alpha]_D^{25}$ = –65.1 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.35 (m, 5H), 6.93 – 6.83 (m, 3H), 5.19 (s, 2H), 3.77 –3.73 (m, 2H), 3.42 (d, *J* = 13.2 Hz, 1H), 2.91 – 2.88 (m, 1H), 2.94 – 2.84 (m, 1H), 243 – 2.27 (m, 2H), 2.27 (s, 6H), 2.11 – 2.06 (m, 1H), 1.88 – 1.75 (m, 1H), 1.64 (q, *J* = 6.3, 5.6 Hz, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.2, 137.8, 137.7, 135.9, 129.0, 128.7, 128.5 (2C), 127.0, 66.4, 65.9, 63.2, 59.7, 55.9, 30.2, 25.5, 21.4. HRMS (ESI) m/z calcd for $C_{22}H_{27}NNaO_3$ $[M + Na]^+$: 376.1883, found: 376.1878. HPLC: Chiralcel IA-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 95/5, flow = 0.5 mL/min, retention time 21.3 min (maj) and 29.7 min.

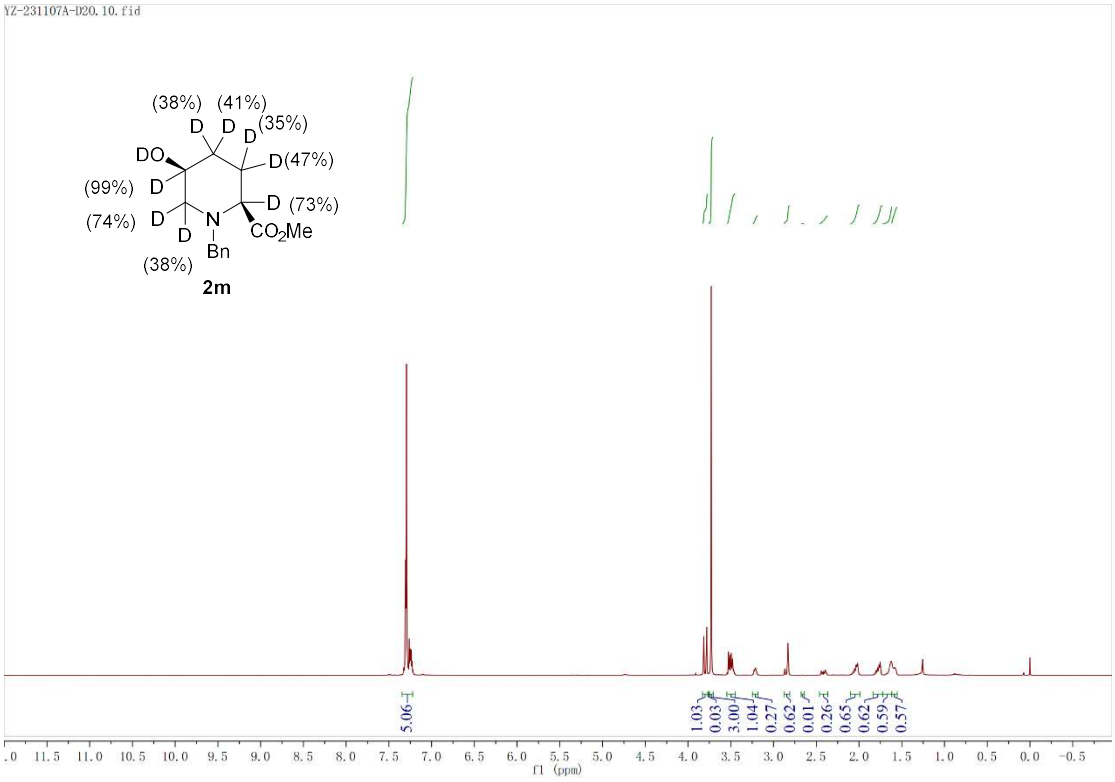
benzyl (2*S*,5*S*)-1-(3,5-dimethoxybenzyl)-5-hydroxypiperidine-2-carboxylate (2ac): 35.8 mg, 93% yield, >20:1 *dr*, 95% *ee*, $[\alpha]_D^{25}$ = –49.1 (c = 1.0, $CHCl_3$), colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 – 7.17 (m, 5H), 6.36 (s, 2H), 6.26 (s, 1H), 5.08 (s, 2H), 3.73 – 3.60 (m, 8H), 3.39 (dd, *J* = 13.2, 2.0 Hz, 1H), 3.25 – 3.15 (m, 1H), 2.84 – 2.74 (m, 1H), 2.40 – 2.38 (m, 2H), 2.06 – 1.96 (m, 1H), 1.78 – 1.67 (m, 1H), 1.65 – 1.44 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.1, 160.8, 140.6, 135.9, 128.7, 128.42, 128.36, 106.7, 99.3, 66.4, 66.1, 62.6, 59.8, 55.7, 55.3, 30.1, 25.6. HRMS (ESI) m/z calcd for $C_{22}H_{27}NNaO_5$ $[M + Na]^+$: 408.1781, found: 408.1790 HPLC: Chiralcel AD-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 15.9 min (maj) and 27.7 min.



2.4 Result of deuterium labeling experiments

Following standard hydrogenation procedure, deuterium labeling experiment was conducted with specific modification.





2.5 General procedure for asymmetric hydrogenation under continuous flow

All process parts, including fittings, tubes, valves and junctions that hold pressure were purchased from SHENZHEN INSFTECH CO,. Ltd. The specification of the reaction coil is 0.5 ml/m. The information of other main components is summarized in Table S1.

Table S1 Components details of reactor system

Name	Information
Pump	Sanotac high pressure HPLC pump AP0030 (0-10 mL/min; 20 MPa)
MFC	SHENZHEN INSFTECH CO,. Ltd. FCM-1050 (0-500 sccm,10 MPa)
BPR	SHENZHEN INSFTECH CO,. Ltd. FAV-1500B (0-500 mL/min, 10 MPa)
Mixer	Shanghai X-tec Fluid technology CO,. Ltd. SS-CUT-K1FF

A mixture of $[Ir(COD)Cl]_2$ (1.0 mol%) and Zhaophos (2.0 mol%) was dissolved in a degassed solvent DCE at argon atmosphere, and the resulting solution was allowed to be stirred at room temperature for 30.0 min. Then, 2-methyl ester-5-hydroxypyridinium salt **1m** (1.0 equiv.) and Et_3N (1.0 equiv.) were added. The process was washed by DCE at a liquid flow rate of 5 mL/min and gas flow rate of 10.0 sccm (avoid back flow of liquid to gas flow meter) for 10.0 minutes and then pressurized the BPR. After the reactor was pressurized to 8.0 MPa, the aforehand reaction medium was pumped instead of solvent. Liquid flow rate was set at 0.5 mL/min and gas flow rate was keeping 40.0 sccm. The liquid holding capacity of the reaction coil can be adjusted according to the needs. When reaction finished, system was depressurized by releasing the gas slowly, and washed the whole system by pumping ethanol for 10.0 minutes. The reaction mixture was filtrated and concentrated in vacuo. The residue was purified by silica gel flash column chromatography (CH_2Cl_2/MeOH = 100:1) to give the desired product **2m** (95% yield, 13.1:1 *dr*, 93% *ee*) as a pale-yellow oil.

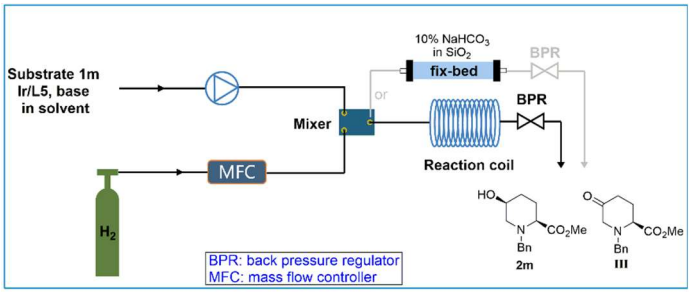
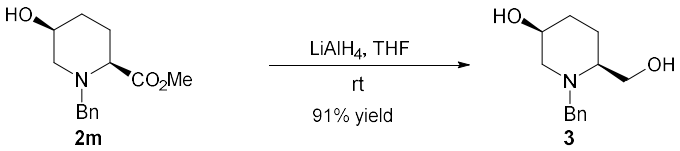


Figure S1 AH of **1m** under continuous flow.

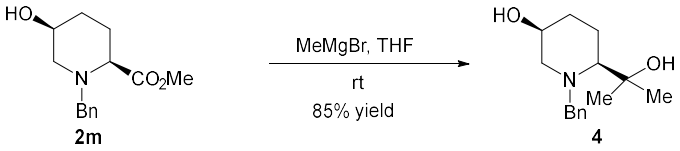
Figure S2 Set-up for asymmetric hydrogenation under continuous flow in a fix-bed.

Figure S3 Set-up for asymmetric hydrogenation under continuous flow in a coil.

2.6 General Procedures for Products Transformations

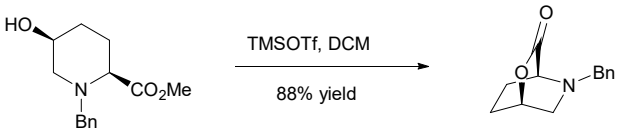


A solution of the methyl ester **2m** (100.0 mg, 0.40 mmol, 1.0 equiv.) in THF (2.5 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (22.9 mg, 0.60 mmol, 1.5 equiv.) in THF (2.5 mL) at 0 °C under an argon atmosphere. The resulting mixture was stirred at room temperature for 8 h and then 2 M NaOH(aq) (1 μL per 1 mg of $LiAlH_4$), Et_2O (5 mL) and Na_2SO_4 were carefully added. The solids were removed by filtration through Celite and evaporated under reduced pressure to give the crude product. The residue was purified by silica gel flash column chromatography (CH_2Cl_2/MeOH = 50:1) to give compound **3** (80.8 mg, 91% yield, 96% *ee*) as a pale-yellow oil. $[\alpha]_D^{25}$ = –35.1 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.22 (m, 5H), 4.11 (d, *J* = 13.6 Hz, 1H), 3.89 – 3.85 (m, 2H), 3.64 (dd, *J* = 11.2, 4.4 Hz, 1H), 3.44 (d, *J* = 13.2 Hz, 1H), 2.86 (dd, *J* = 12.4, 5.2 Hz, 1H), 2.51 – 2.46 (m, 1H), 2.38 (dd, *J* = 12.4, 2.4 Hz, 1H), 2.30 (s, 2H), 1.99 – 1.89 (m, 1H), 1.82 – 1.75 (m, 1H), 1.73 – 1.58 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 138.6, 128.9, 128.6, 127.4, 64.7, 62.8, 61.3, 58.2, 56.7, 30.5, 23.1. HRMS (ESI) m/z calcd for $C_{13}H_{20}NO_2$ $[M + H]^+$: 222.1489, found: 222.1492. HPLC: Chiralcel OJ-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 90/10, flow = 0.5 mL/min, retention time 28.5 min and 30.9 min (maj).



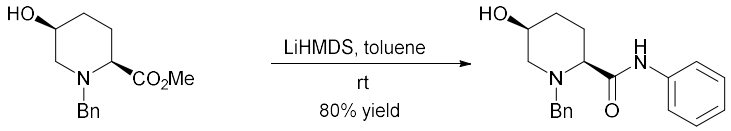
To a solution of the methyl ester **2m** (100.0 mg, 0.4 mmol, 1.0 equiv.) in anhydrous THF (5.0 mL) was added methyl magnesium bromide (1.0 M in THF, 1.2 ml, 1.2 mmol, 3.0 equiv.) dropwise under argon atmosphere at 0 °C. The resulting mixture was stirred at room temperature for 7 h and then quenched with aqueous NH_4Cl solution, extracted with ethyl acetate. Organic phases were combined and dried over

anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (CH_2Cl_2/MeOH = 50:1) to give compound **4** (84.8 mg, 85% yield, 95% *ee*) as a pale-yellow oil. $[\alpha]_D^{25}$ = –23.4 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.20 (m, 5H), 4.13 (d, *J* = 13.6 Hz, 1H), 3.95 – 3.90 (m, 1H), 3.69 (d, *J* = 13.2 Hz, 1H), 2.70 – 2.61 (m, 2H), 2.47 (t, *J* = 6.0 Hz, 1H), 1.82 – 1.68 (m, 4H), 1.29 (s, 3H), 1.21 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 139.7, 128.7, 128.6, 127.3, 73.3, 67.5, 63.2, 61.2, 53.6, 30.9, 29.6, 26.0, 20.4. HRMS (ESI) m/z calcd for $C_{15}H_{24}NO_2$ $[M + H]^+$: 250.1802, found: 250.1804. HPLC: Chiralcel OD-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.5 mL/min, retention time 16.6 min and 20.0 min (maj).



2m **5**

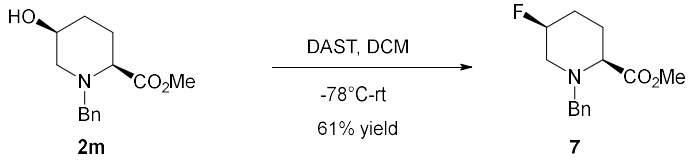
To a stirred solution of the methyl ester **2m** (100.0 mg, 0.4 mmol, 1.0 equiv.) in dry DCM (5.0 mL) was added TMSOTf (144.8 μL, 0.8 mmol, 2.0 equiv.). The resulting mixture was stirred overnight at room temperature, then quenched with aqueous NH_4Cl solution, extracted with ethyl acetate. Organic phases were combined and dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/ethyl acetate = 50:1) to give compound **5** (76.5 mg, 88% yield, 96% *ee*) as a pale-yellow oil. $[\alpha]_D^{25}$ = –21.7 (c = 0.3, $CHCl_3$). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.24 (m, 5H), 4.70 – 4.67 (m, 1H), 3.78 (d, *J* = 12.8 Hz, 1H), 3.61 (d, *J* = 13.2 Hz, 1H), 3.32 – 3.30 (m, 1H), 3.16 (dd, *J* = 11.6, 1.2 Hz, 1H), 2.70 – 2.65 (m, 1H), 2.25 – 2.14 (m, 1H), 1.98 – 1.86 (m, 2H), 1.79 – 1.69 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.9, 137.8, 129.0, 128.6, 127.6, 74.7, 62.1, 56.0, 54.7, 24.7, 23.5. HRMS (ESI) m/z calcd for $C_{13}H_{16}NO_2$ $[M + H]^+$: 218.1176, found: 218.1175. HPLC: Chiralcel IC-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.5 mL/min, retention time 13.7 min and 15.2 min (maj).



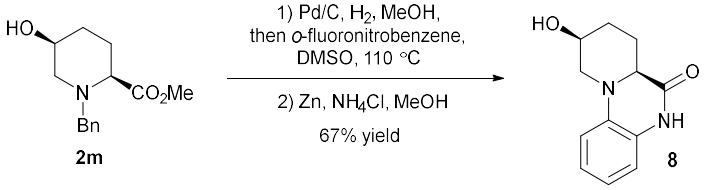
2m **6**

An oven-dried vial equipped with a stir bar was charged with the methyl ester **2m** (100.0 mg, 0.4 mmol, 1.0 equiv.), aniline (45.6 μL, 0.5 mmol, 1.2 equiv.) placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles. Toluene (5.0 mL) and LiHMDS (1.0 M in THF, 0.8 mL, 0.8 mmol, 2.0 equiv.) were sequentially added with vigorous stirring at room temperature, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was quenched with aqueous NH_4Cl solution, diluted with ethyl acetate (5.0 mL), the organic layer was washed with water, brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (CH_2Cl_2/MeOH = 100:1) to give compound **6** (99.3 mg, 80% yield, 95% *ee*) as a white solid, m.p. = 154.6 – 155.9 ℃. $[\alpha]_D^{25}$ = –55.1 (c = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.97 (s, 1H), 7.56 – 7.54 (m, 2H), 7.34 – 7.21 (m, 7H), 7.10 – 7.06 (m, 1H), 3.98 – 3.88 (m, 2H), 3.36 (d, *J* = 13.2 Hz, 1H), 3.03 (dd, *J* = 9.6, 4.0 Hz, 1H), 2.89 (dd, *J* = 12.8, 4.8 Hz, 1H), 2.72 (s, 1H), 2.34 (dd, *J* = 12.8, 2.8 Hz, 1H), 2.21 – 2.11 (m, 1H), 1.94 – 1.88 (m, 1H), 1.81 – 1.70 (m, 1H), 1.67 – 1.60 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.0, 137.9, 137.3, 129.1, 128.9, 128.7, 127.7, 124.3, 119.8, 66.8, 64.3, 60.5, 56.4, 30.2, 23.6. HRMS (ESI) m/z calcd for

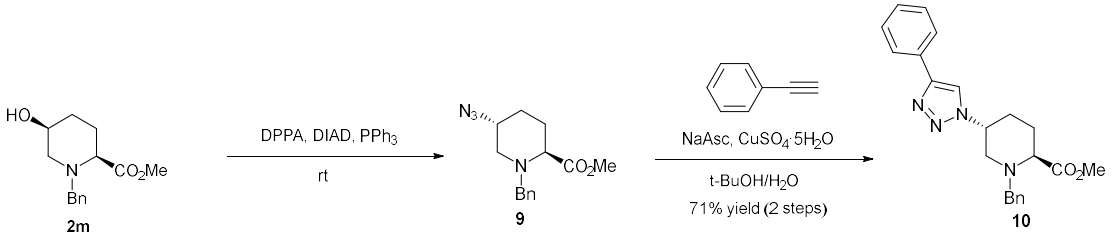
$C_{19}H_{23}N_2O_2$ [M + H]$^+$: 311.1754, found: 311.1759. HPLC: Chiralcel OD-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0. 5 mL/min, retention time 18.5 min and 19.7 min (maj).



Under nitrogen atmosphere, to a stirred solution of **2m** (100.0 mg, 0.4 mmol, 1.0 equiv.) in dichloromethane (5.0 mL) was added (*N*,*N*-diethylamino)sulfurtrifluoride (95.1 μL, 0.72 mmol, 1.8 equiv.) at –78 ℃, and the resulted mixture was slowly warmed to rt. Then, the reaction was quenched with saturated sodium bicarbonate solution and extracted with ethyl acetate. Organic phases were combined and dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/ethyl acetate = 30:1) to give compound **7** (61.3 mg, 61% yield, 97% *ee*) as a pale-yellow oil. $[\alpha]_D^{25}$ = –55.9 (c = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.25 (m, 5H), 4.67 – 4.50 (m, 1H), 3.84 (d, *J* = 13.6 Hz, 1H), 3.74 – 3.70 (m, 4H), 3.36 – 3.34 (m, 1H), 3.09 – 3.02 (m, 1H), 2.82 – 2.67 (m, 1H), 2.17 – 2.10 (m, 1H), 1.96 – 1.85 (m, 1H), 11.85 – 1.75 (m, 1H), 1.75 – 1.63 (m, 1H). ^{13}C NMR (100 MHz, Methanol-d_4) δ 173.3, 138.2, 128.9, 128.5, 127.4, 87.8 (d, *J* = 171.8 Hz), 60.7, 59.7, 52.2 (d, *J* = 24.7 Hz), 51.6, 27.8 (d, *J* = 19.5 Hz), 25.5 (d, *J* = 8.7 Hz). HRMS (ESI) m/z calcd for $C_{14}H_{19}FNO_2$ [M + H]$^+$: 252.1394, found: 252.1398. HPLC: Chiralcel AD-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.5 mL/min, retention time 14.0 min and 15.4 min (maj).

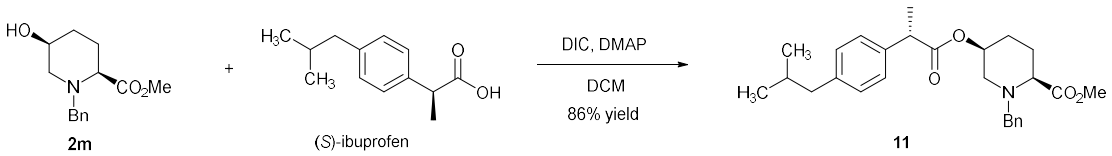


To a stirred solution of the methyl ester **2m** (100.0 mg, 0.4 mmol, 1.0 equiv.) in MeOH (5.0 mL) were added 10% Pd/C (10.0 mg, 10.0 wt%). The resulting mixture was stirred overnight at room temperature under H_2 (1 atm, balloon) and then filtered, washed with MeOH and concentrated under reduced pressure. The crude was dissolved in DMSO, *o*-fluoronitrobenzene (21.1 μL, 0.20 mmol, 0.5 equiv.) was added. The mixture was heated to 110 ℃ overnight. After cooled to room temperature, The mixture was extracted with ethyl acetate, the combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was next dissolved in methanol (5.0 mL), zinc powder (392.3 mg, 6.0 mmol, 15.0 equiv.) and ammonium chloride (320.9 mg, 6.0 mmol, 15.0 equiv.) was added to this solution, and the mixture was stirred at room temperature overnight. The mixture solution was then filtered, concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (CH_2Cl_2/MeOH = 100:1) to give compound **8** (58.5 mg, 67% yield over 3 steps, 95% *ee*) as a white solid, m.p. = 198.3 – 200.4 ℃. $[\alpha]_D^{25}$ = –12.3 (c = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, Methanol-d_4) δ 6.98 – 6.74 (m, 4H), 4.12 – 4.09 (m, 1H), 3.80 – 3.75 (m, 1H), 3.45 – 3.38 (m, 1H), 2.80 (dd, *J* = 12.4, 2.0 Hz, 1H), 2.15 – 2.07 (m, 2H), 2.01 – 1.94 (m, 1H), 1.78 – 1.68 (m, 1H). ^{13}C NMR (100 MHz, Methanol-d_4) δ 170.8, 137.9, 128.3, 124.9, 120.7, 116.2, 113.4, 65.0, 59.6, 53.1, 30.5, 22.4. HRMS (ESI) m/z calcd for $C_{12}H_{15}N_2O_2$ [M + H]$^+$: 219.1128, found: 219.1129. HPLC: Chiralcel OD-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.7 mL/min, retention time 14.9 min and 16.6 min (maj).

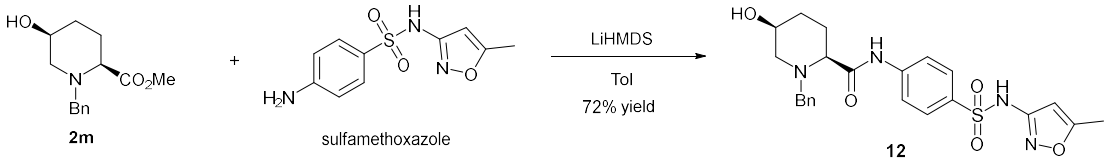


To a solution of compound **2m** (100.0 mg, 0.4 mmol, 1.0 equiv.) and triphenylphosphine (161.8 mg, 0.8 mmol, 2.0 equiv.) in THF (5.0 mL) were added DIAD (158.6 μL, 0.8 mmol, 2.0 equiv.) and DPPA (103.4 μL, 0.48 mmol, 1.2 equiv.) at 0 ℃. The reaction mixture was stirred for 7 h at room temperature and extracted with ethyl acetate. Organic phases were combined and dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/ethyl acetate = 50:1) to give compound **9** as a yellow oil.

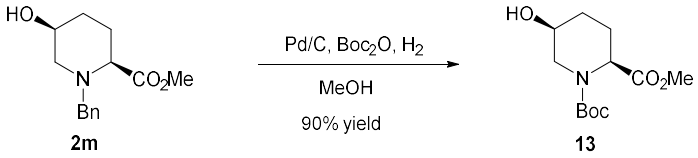
To a solution of $CuSO_4{\cdot}5H_2O$ (1.0 mg, 4.0 μmol, 1.0 mol%) and sodium ascorbate (1.6 mg, 8.0 μmol, 2.0 mol%) in *t*-BuOH/H_2O (1:1 by v/v, 6.0 mL) was added a mixture of phenylethyne (43.9 mg, 0.4 mmol, 1.0 equiv.) and **9** (109.7 mg, 0.4 mmol, 1.0 equiv.) at room temperature. The resultant mixture was stirred continuously overnight. Then CH_2Cl_2 was added to dissolve the crude product. The organic layer was washed with H_2O and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent yielded a residue, which was purified by silica gel flash column chromatography (petroleum ether/ethyl acetate = 40:1) to give compound **10** (106.9 mg, 71% yield, 96% *ee*) as a white solid, m.p. = 178.4 – 180.2 ℃. $[\alpha]_D^{25}$ = 93.73 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.94 (s, 1H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.45 – 7.23 (m, 8H), 4.79 – 4.73 (m, 1H), 3.94 – 3.66 (m, 5H), 3.53 (t, *J* = 4.4 Hz, 1H), 3.37 (dd, *J* = 116, 9.2 Hz, 1H), 2.98 (dd, *J* = 11.6, 4.4 Hz, 1H), 2.20 – 1.93 (m, 4H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.2, 147.4, 138.0, 130.9, 128.9 (2C), 128.6, 128.1, 127.6, 125.7, 118.6, 60.4, 59.8, 56.8, 52.3, 51.6, 27.9, 26.5. HRMS (ESI) m/z calcd for $C_{22}H_{25}N_4O_2$ $[M + H]^+$: 377.1972, found: 377.1966. HPLC: Chiralcel IA-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.5 mL/min, retention time 18.6 min (maj) and 25.2 min.



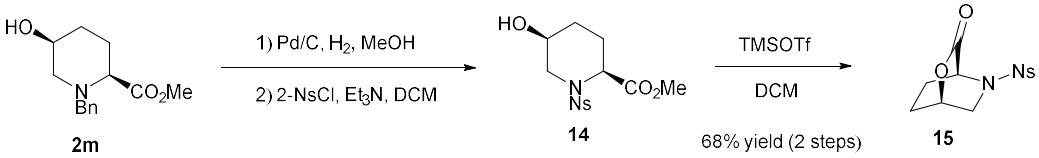
To a solution of **2m** (100.0 mg, 0.4 mmol, 1.0 equiv.) and (S)-ibuprofen (99.0 mg, 0.48 mmol, 1.2 equiv.) in CH_2Cl_2 (7.0 mL) were added DMAP (4.9 mg, 0.04 mmol, 10.0% mmol) and DIC (74.3 μL, 0.48 mmol, 1.2 equiv.). The resulting suspension was stirred at rt overnight. After adding H_2O, the reaction mixture was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, and concentrated under reduced pressure to give the residue, which was purified by flash column chromatography (petroleum ether/ethyl acetate = 50:1) to afford compound **11** (106.9 mg, 86% yield, >20:1 *dr*, 95% *ee*) as a pale-yellow oil. $[\alpha]_D^{25}$ = –1.5 (c = 2.0, $CHCl_3$). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.25 – 7.04 (m, 9H), 4.80 – 4.70 (m, 1H), 3.75 – 3.57 (m, 6H), 3.33 – 3.29 (m, 1H), 2.84 (dd, *J* = 11.2, 8.4 Hz, 1H), 2.53 (dd, *J* = 11.6, 4.4 Hz, 1H), 2.43 (d, *J* = 7.2 Hz, 2H), 2.03 – 1.97 (m, 1H), 1.88 – 1.72 (m, 3H), 1.55 – 1.46 (m, 1H), 1.40 (d, *J* = 7.2 Hz, 3H), 0.87 (d, *J* = 6.4 Hz, 6H). ^{13}C NMR (100 MHz, Methanol-d_4) δ 175.6, 174.5, 141.5, 139.5, 139.2, 130.3, 129.7, 129.3, 128.20, 128.17, 70.8, 61.5, 60.4, 52.3, 51.8, 46.4, 46.0, 31.4, 27.6, 26.8, 22.8, 18.9. HRMS (ESI) m/z calcd for $C_{27}H_{36}NO_4$ $[M + H]^+$: 438.2639, found: 438.2644. HPLC: Chiralcel OD-H column, 254 nm, 30 ℃, *n*-hexane/*i*-propanol = 90/10, flow = 0.5 mL/min, retention time 24.4 min (maj) and 31.9 min.



An oven-dried vial equipped with a stir bar was charged with the methyl ester **2m** (100.0 mg, 0.4 mmol, 1.0 equiv.), sulfamethoxazole (121.6 mg, 0.48 mmol, 1.2 equiv.) placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles. Toluene (5.0 mL) and LiHMDS (1.0 M in THF, 0.8 mL, 0.8 mmol, 2.0 equiv.) were sequentially added with vigorous stirring at room temperature, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was quenched with aqueous NH_4Cl solution, diluted with ethyl acetate (5.0 mL), the organic layer was washed with water, brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/ethyl acetate = 20:1) to give compound **12** (135.5 mg, 72% yield, 96% *ee*) as a yellow oil. $[\alpha]_D^{25} = -30.51$ (c = 0.3, $CHCl_3$). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.88 – 7.78 (m, 4H), 7.37 – 7.21 (m, 5H), 6.13 (s, 1H), 3.90 – 3.86 (m, 1H), 3.84 – 3.81 (m, 1H), 3.34 – 3.32 (m, 1H), 3.01 (dd, *J* = 10.0, 3.6 Hz, 1H), 2.94 (dd, *J* = 12.4, 4.4 Hz, 1H), 2.30 – 2.26 (m, 4H), 2.13 – 2.02 (m, 1H), 1.88 – 1.71 (m, 2H), 1.69 – 1.58 (m, 1H). ^{13}C NMR (100 MHz, Methanol-d_4) δ 175.4, 172.1, 159.3, 144.3, 138.4, 135.5, 130.3, 129.5, 129.4, 128.4, 120.4, 96.5, 68.7, 65.5, 61.6, 57.0, 30.6, 25.3, 12.3. HRMS (ESI) m/z calcd for $C_{23}H_{27}N_4O_5S$ $[M + H]^+$: 471.1697, found: 471.1695. HPLC: Chiralcel AD-H column, 254 nm, 30 °C, *n*-hexane/*i*-propanol = 95/5, flow = 0.7 mL/min, retention time 14.6 min (maj) and 21.4 min.



To a stirred solution of the methyl ester **2m** (100.0 mg, 0.4 mmol, 1.0 equiv.) and Boc_2O (104.8 mg, 0.48 mmol, 1.2 equiv.) in MeOH (5.0 mL) were added 10% Pd/C (10.0 mg, 10.0 wt%). The resulting mixture was stirred overnight at room temperature under H_2 (50 psi) and then filtered, washed with MeOH and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/ethyl acetate = 10:1) to give compound **13** (93.3 mg, 90% yield) as a pale-yellow oil. $[\alpha]_D^{20} = -19.7$ (c = 1.0, MeOH) [Lit.[2] $[\alpha]_D^{20} = -17.7$ (c = 1.3, MeOH), Lit.[3] $[\alpha]_D^{20} = -20.4$ (c = 1.0, MeOH)].



To a stirred solution of the methyl ester **2m** (100.0 mg, 0.4 mmol, 1.0 equiv.) in MeOH (5.0 mL) were added 10% Pd/C (10.0 mg, 10.0 wt%). The resulting mixture was stirred for 6 h at room temperature under H_2 (1 atm, balloon) and then filtered, washed with MeOH and concentrated under reduced pressure. The crude was dissolved in DCM, 2-Nitrobenzenesulfonyl chloride and Et_3N were added. The resultant mixture was stirred for 3 h, then extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, and concentrated under reduced pressure to give the residue, which was purified by flash column chromatography (petroleum ether/ethyl acetate = 50:1) to afford compound **14** as a yellow oil. ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.10 – 8.04 (m, 1H), 7.84 – 7.73 (m, 3H), 4.69 – 4.67 (m, 1H), 3.94 – 3.89 (m, 1H), 3.59 (s, 3H), 3.58 – 3.50 (m, 1H), 2.99 (dd, *J* = 12.4, 10.8 Hz, 1H), 2.33 – 2.25 (m, 1H), 1.98 –

1.80 (m, 2H), 1.23 – 1.10 (m, 1H). ^{13}C NMR (100 MHz, Methanol-d_4) δ 171.9, 149.1, 135.3, 133.8, 133.1, 131.7, 125.4, 67.1, 56.2, 52.8, 50.0, 30.6, 27.3. HRMS (ESI) m/z calcd for $C_{13}H_{17}N_2O_7S$ $[M + H]^+$: 345.0751, found: 345.0755.

To a stirred solution of the methyl ester **14** (137.7 mg, 0.4 mmol, 1.0 equiv.) in dry DCM (6.0 mL) was added TMSOTf (144.8 μL, 0.8 mmol, 2.0 equiv.). The resulting mixture was stirred overnight at room temperature, then quenched with aqueous NH_4Cl solution, extracted with ethyl acetate. Organic phases were combined and dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The residue was purified by silica gel flash column chromatography (petroleum ether/ethyl acetate = 50:1) to give compound **15** (85.2 mg, 68% yield over 2 steps) as a white crystal, m.p. = 130.6 – 132.5 ℃.

3. References

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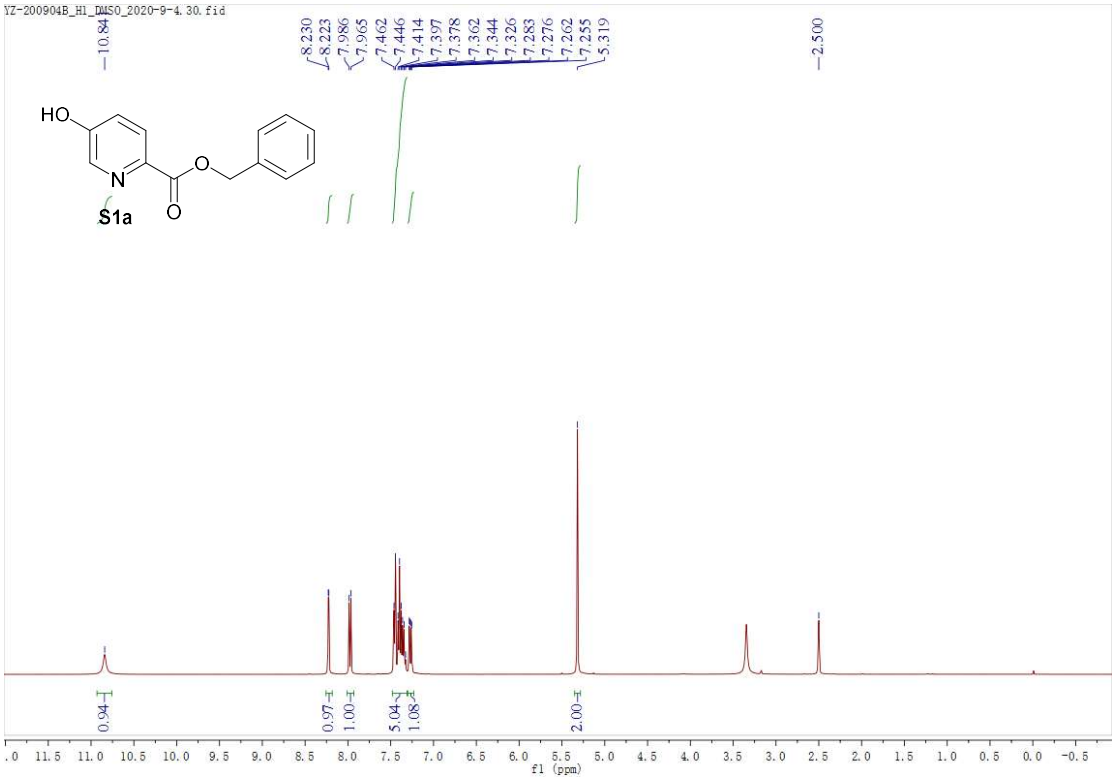
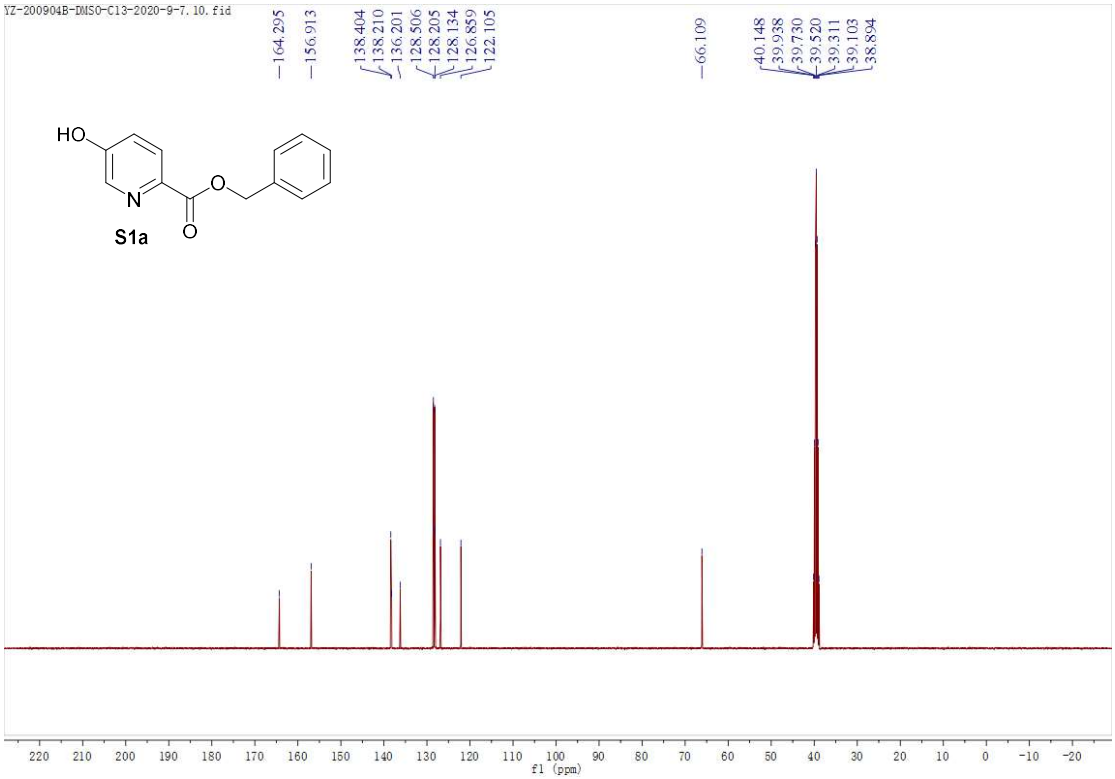
3. Z. Yang, Y. Chen, L. Wan, X. Cen, P. Tang, F. Chen, *Chem. Commun*. **2022**, *58*, 10869–10872.

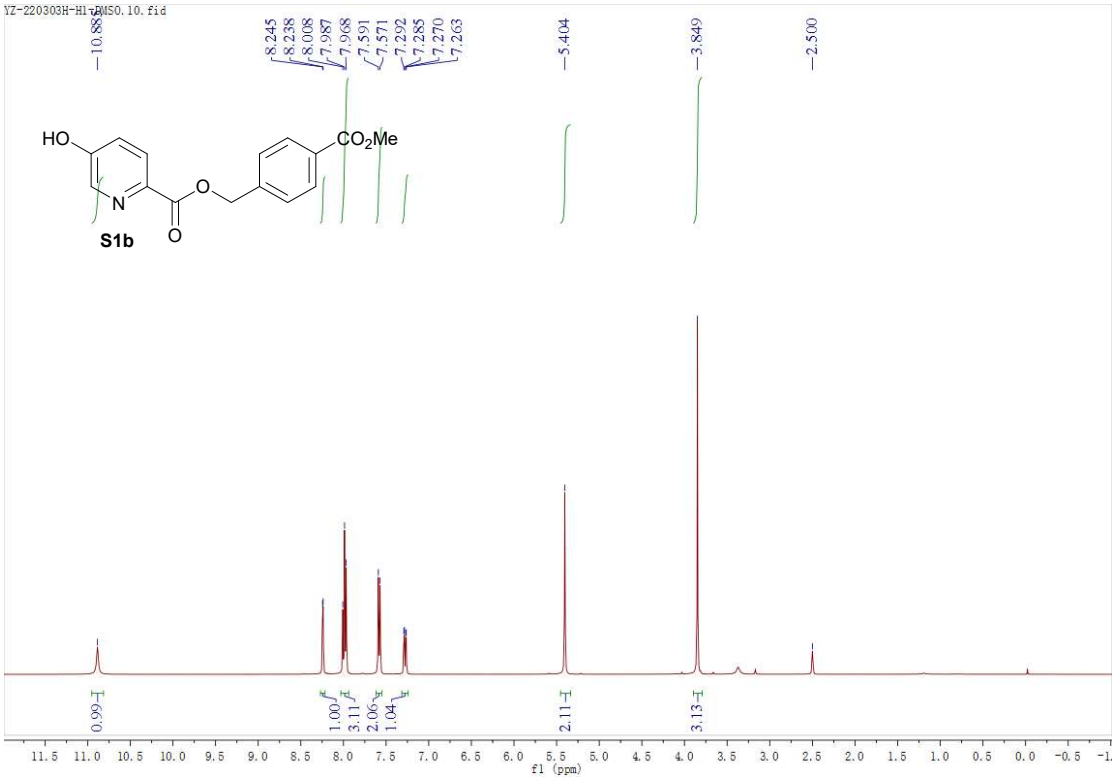
4. NMR Spectra



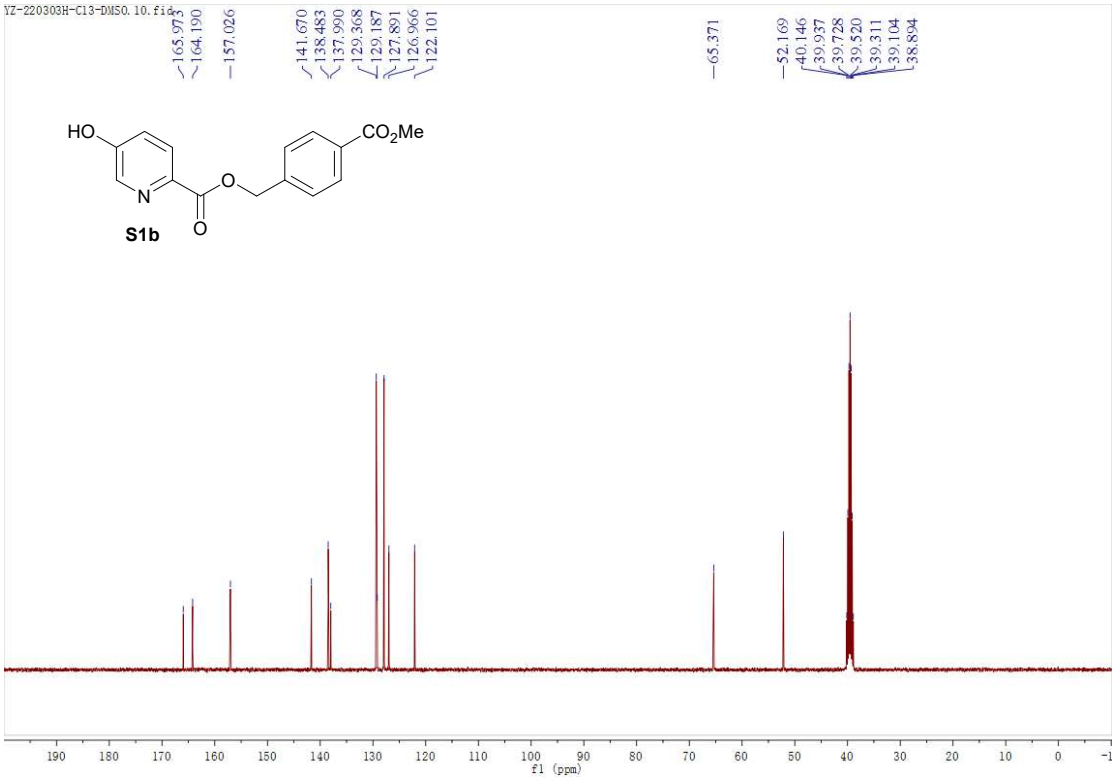
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1a



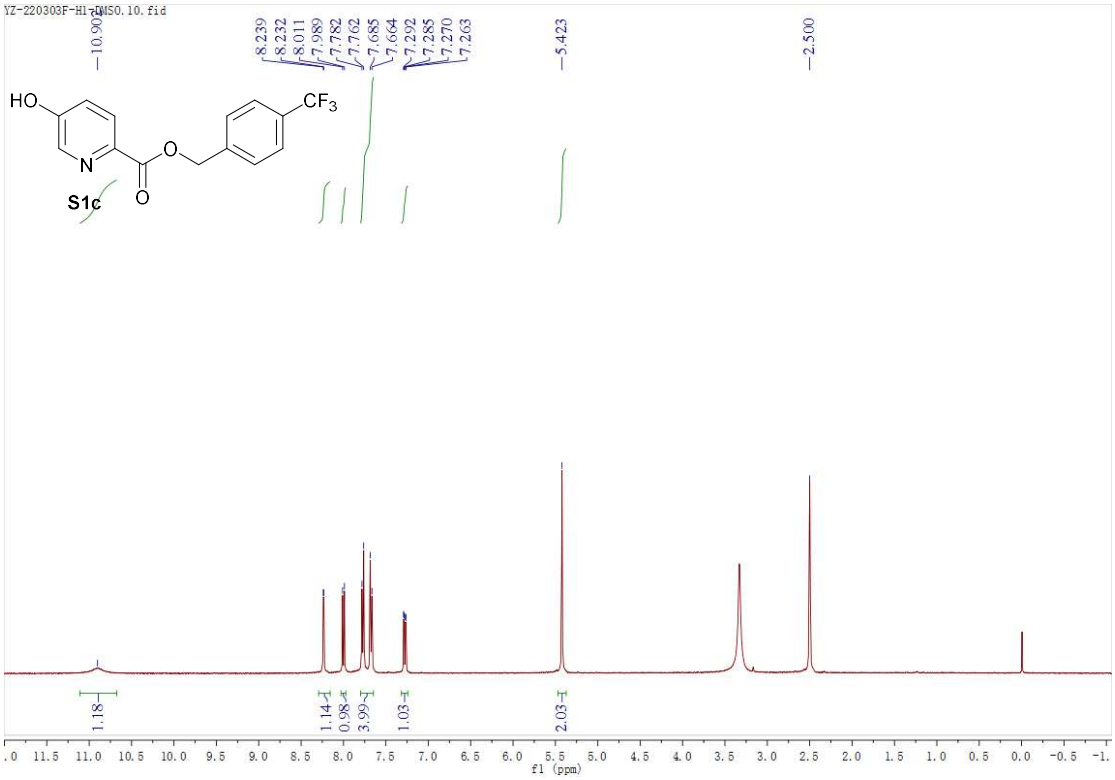
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1a



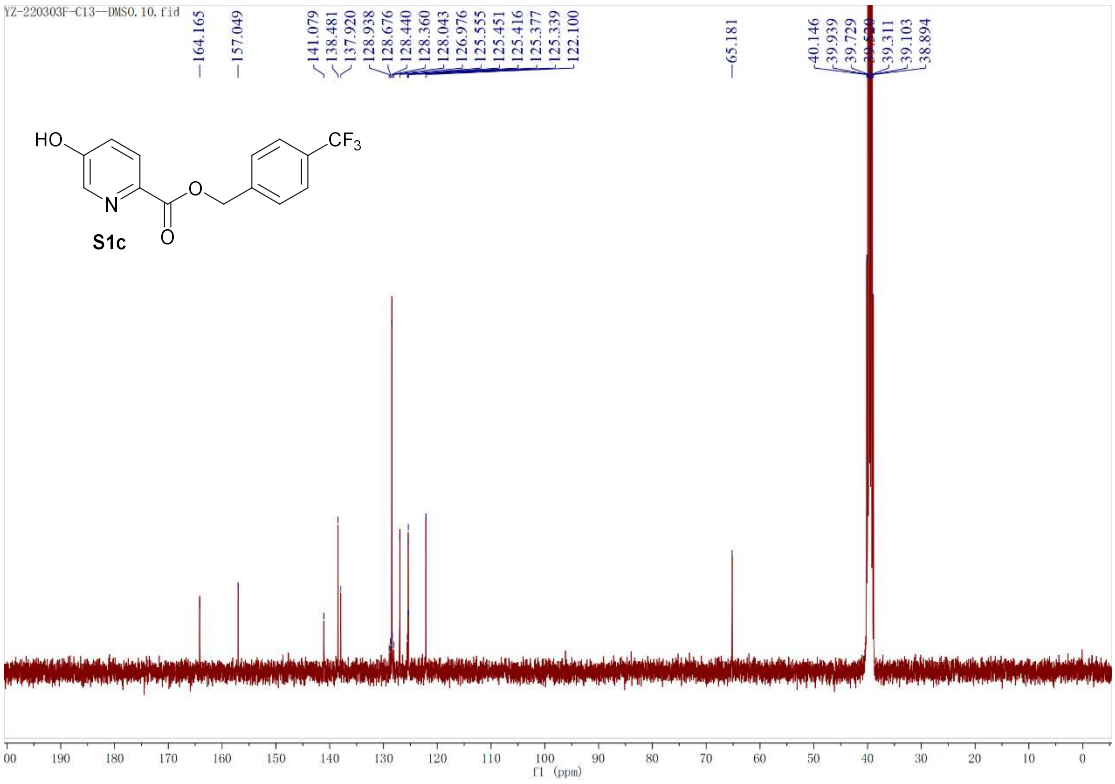
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1b



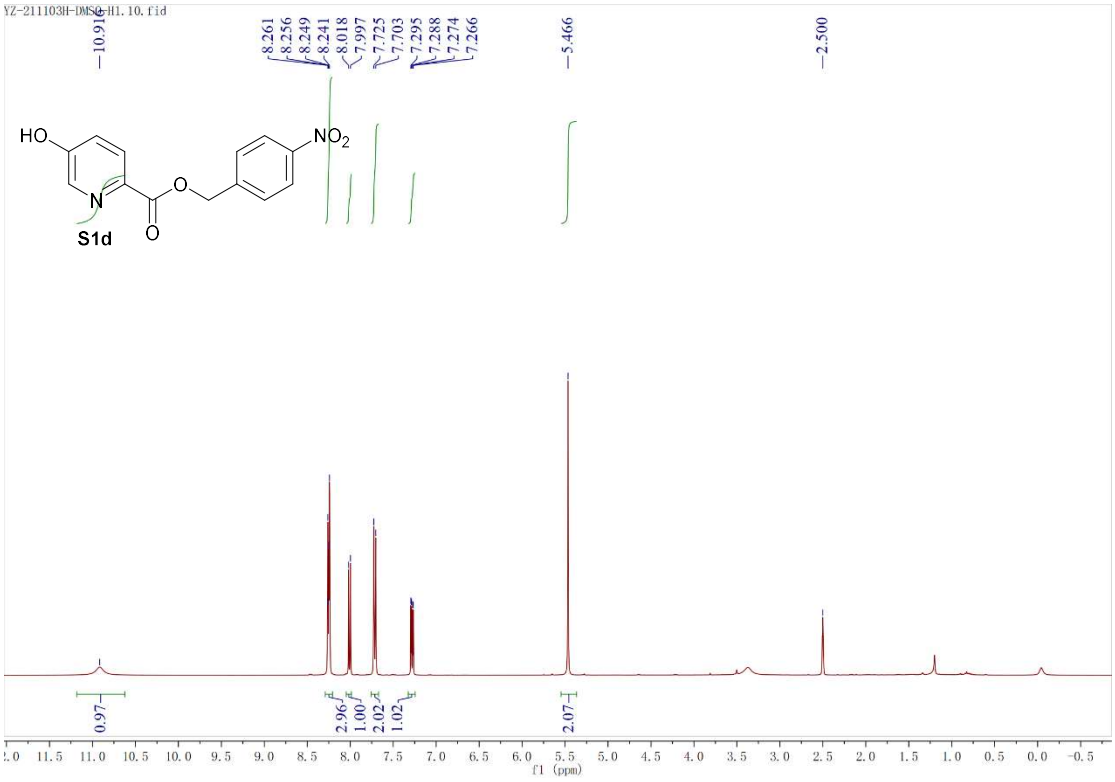
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1b



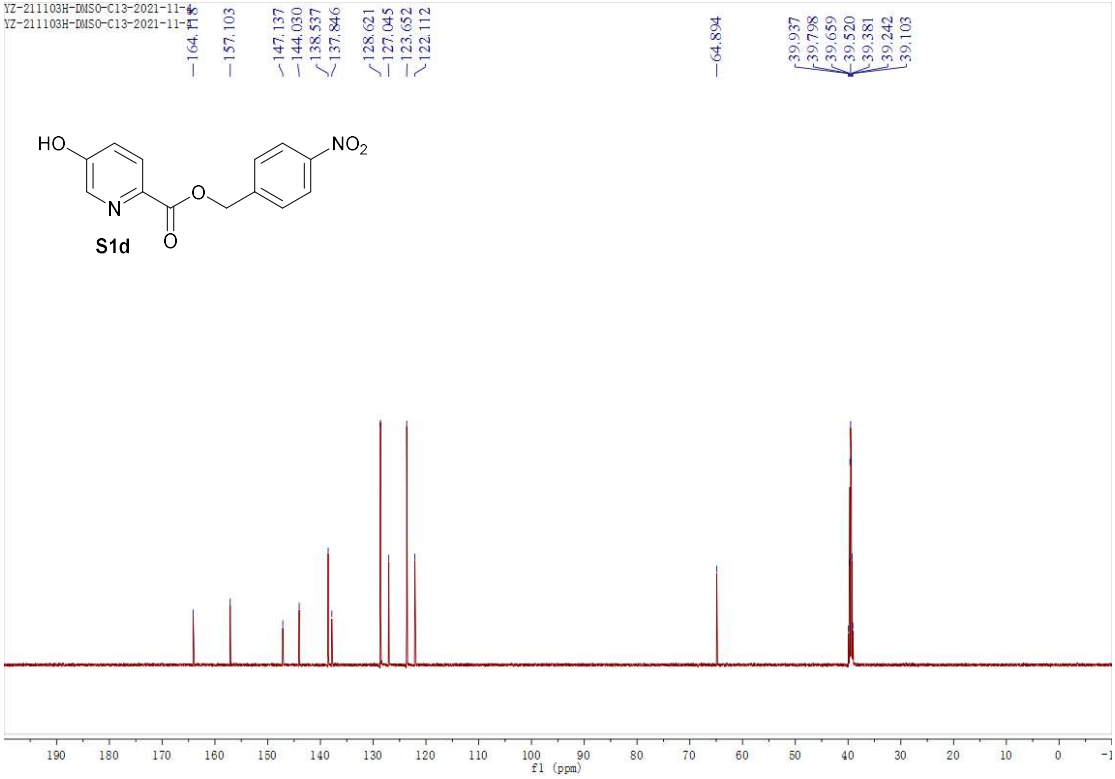
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1c



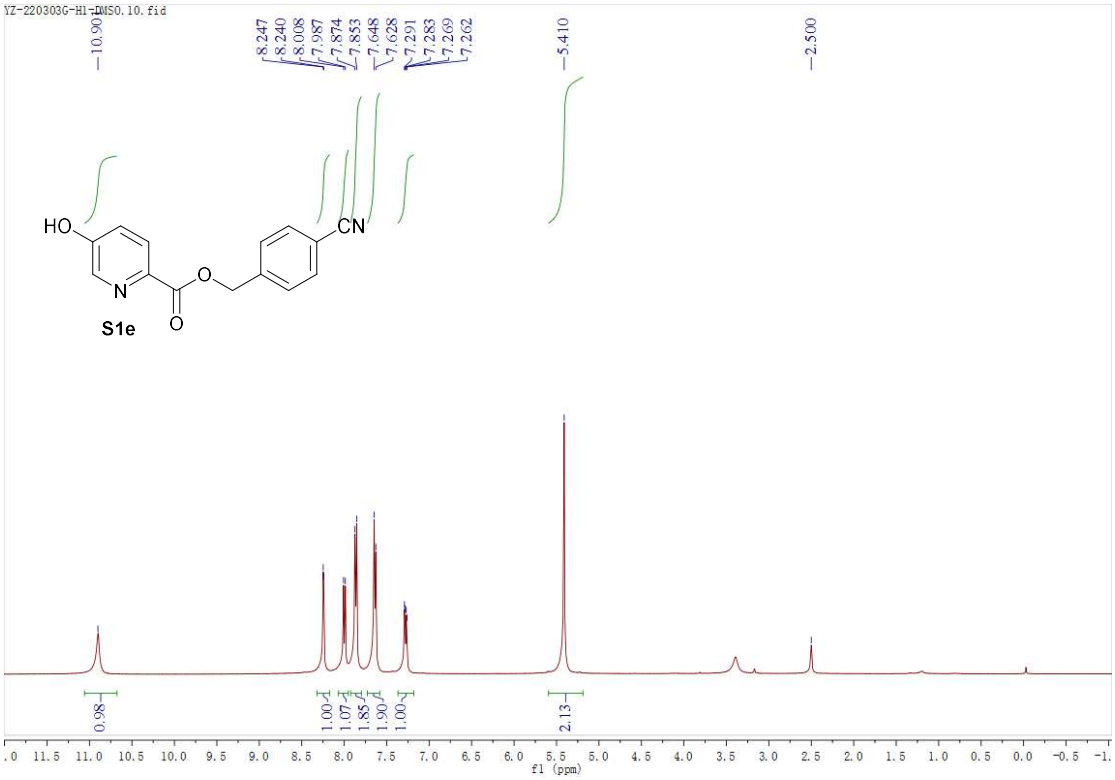
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1c



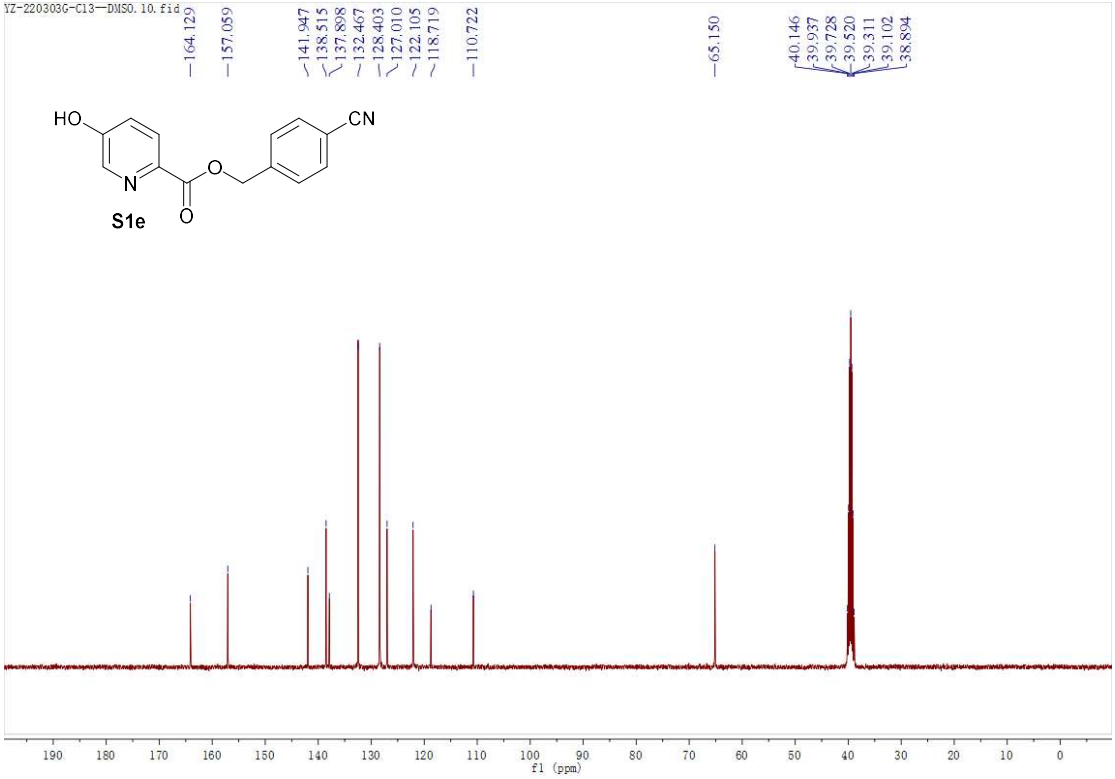
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1d



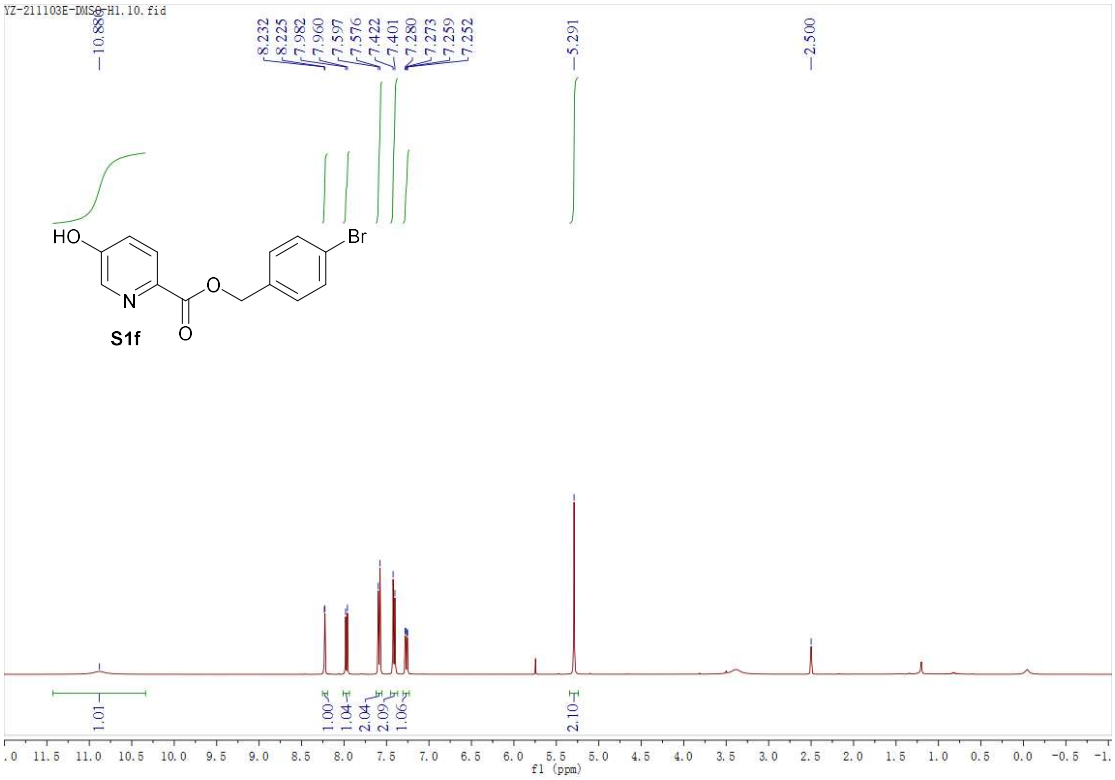
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1d



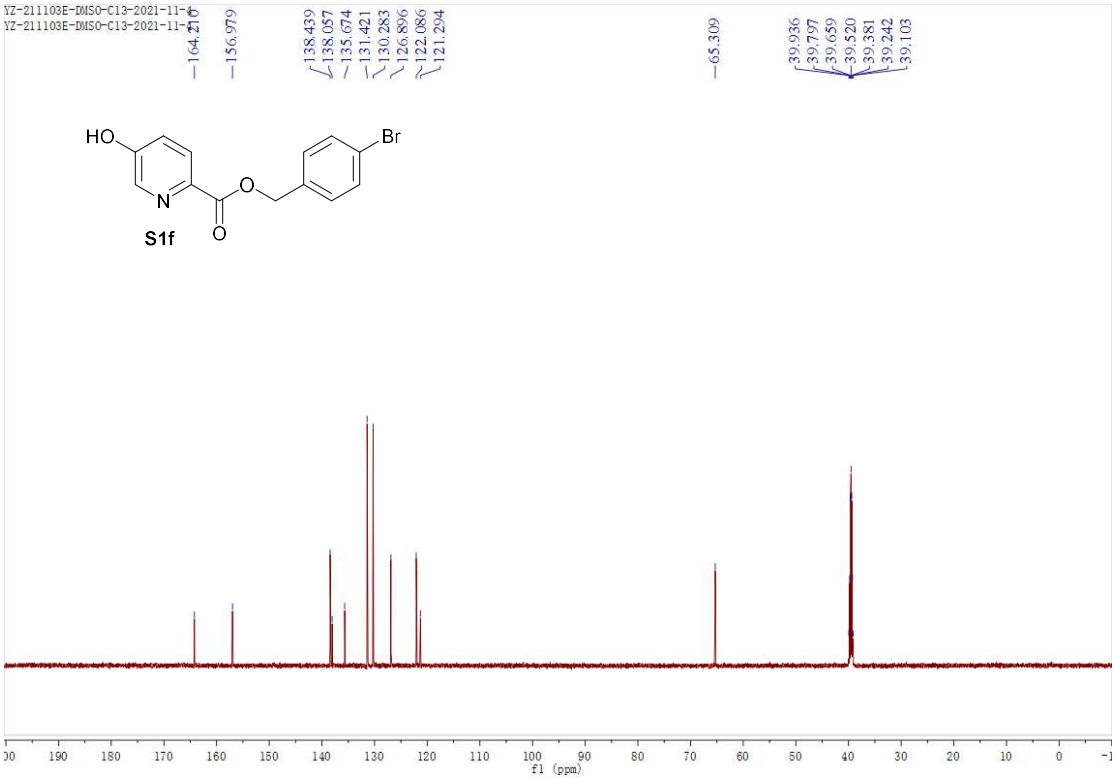
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1e



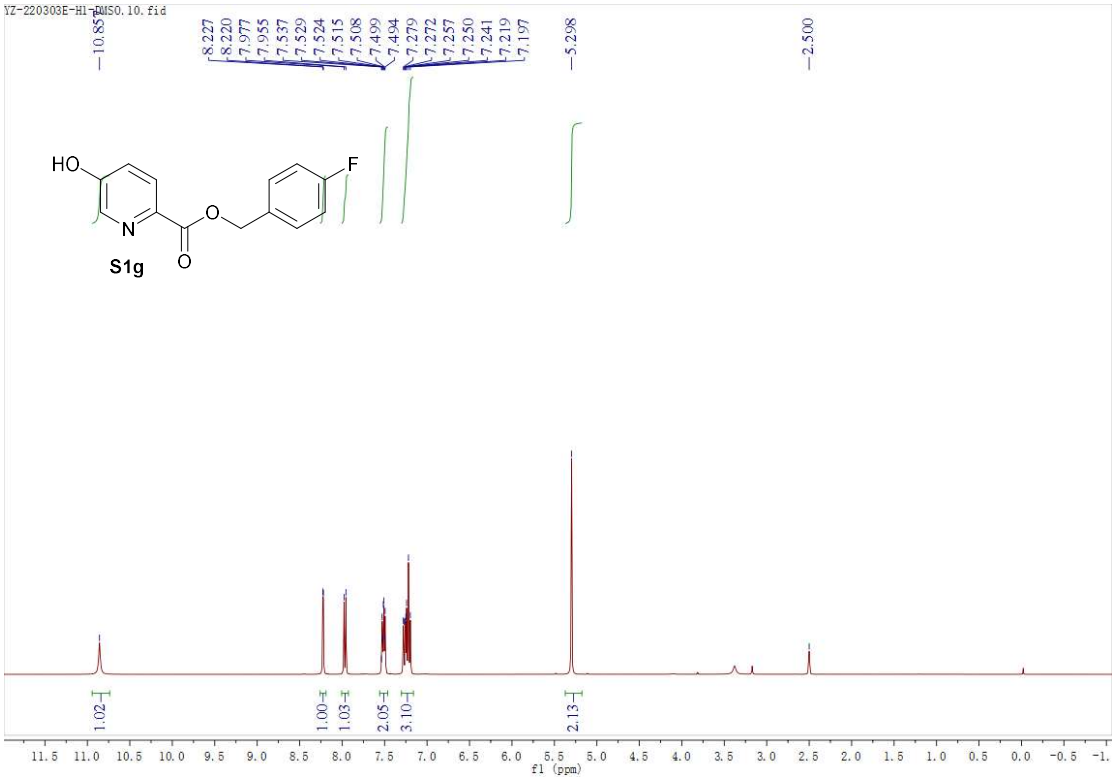
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1e



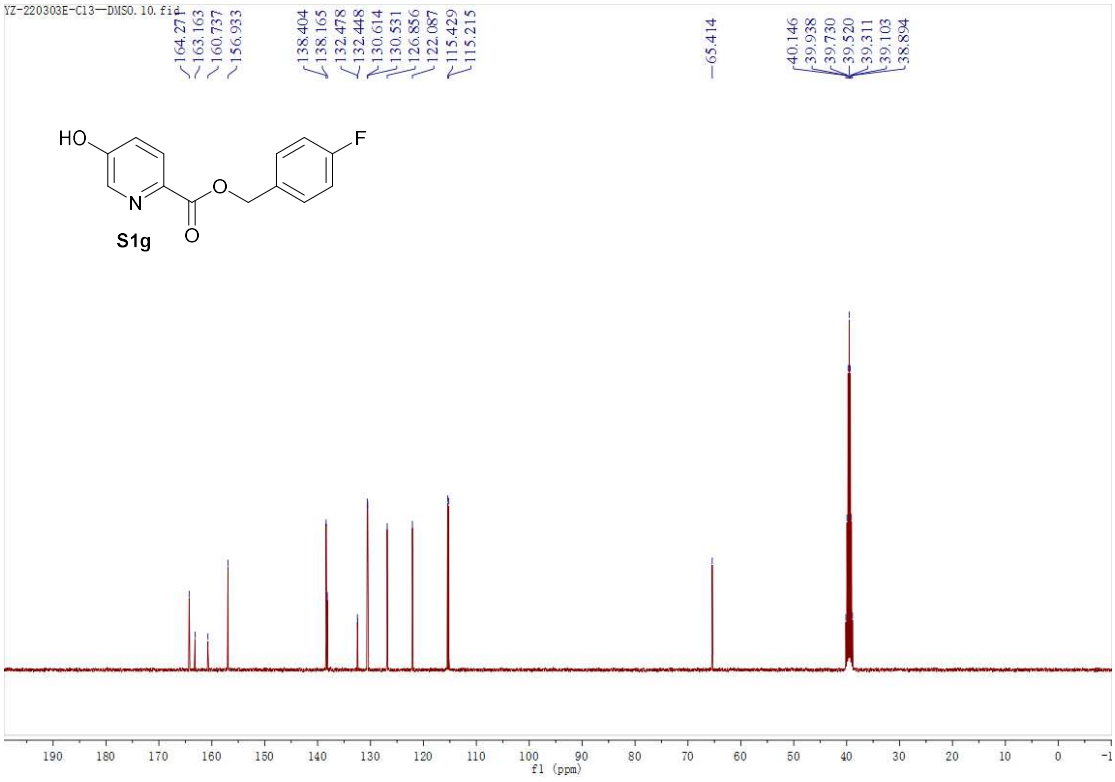
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1f



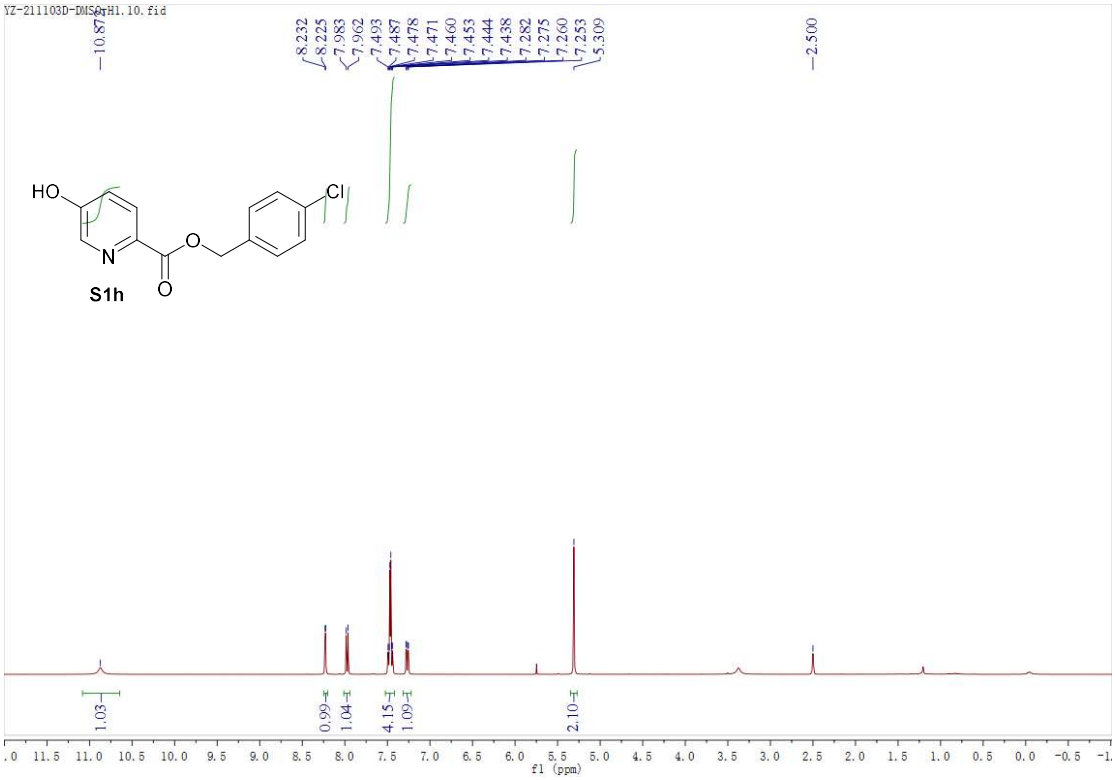
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1f



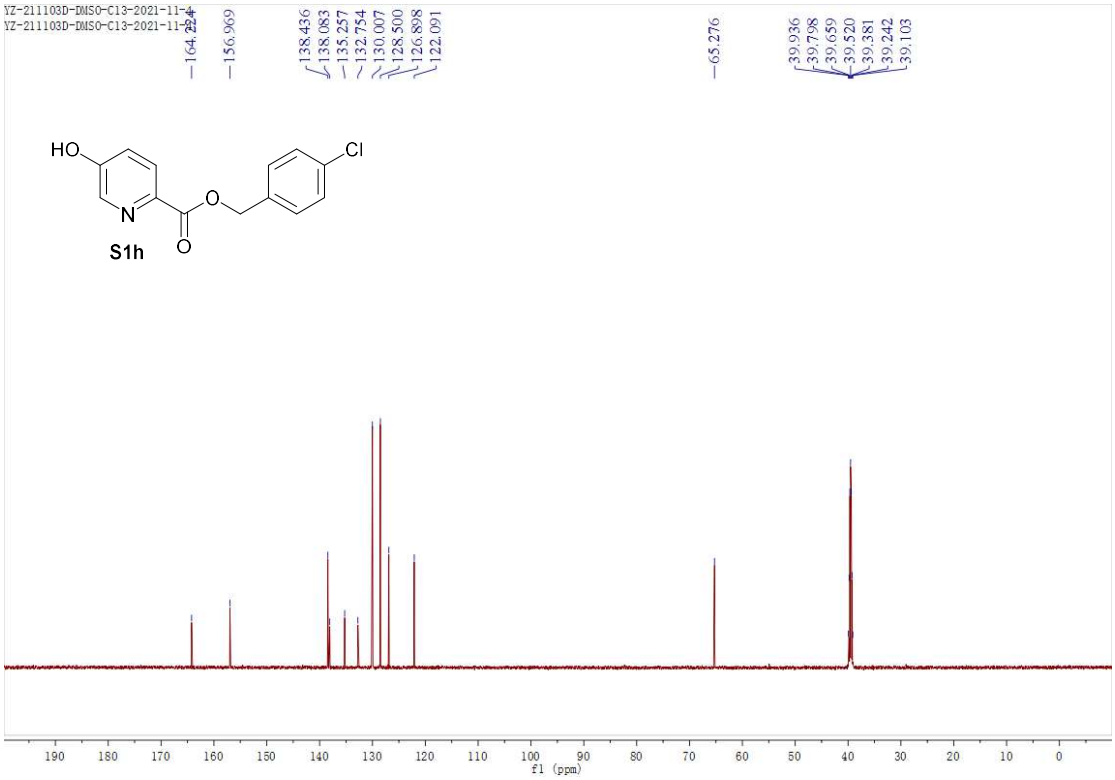
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1g



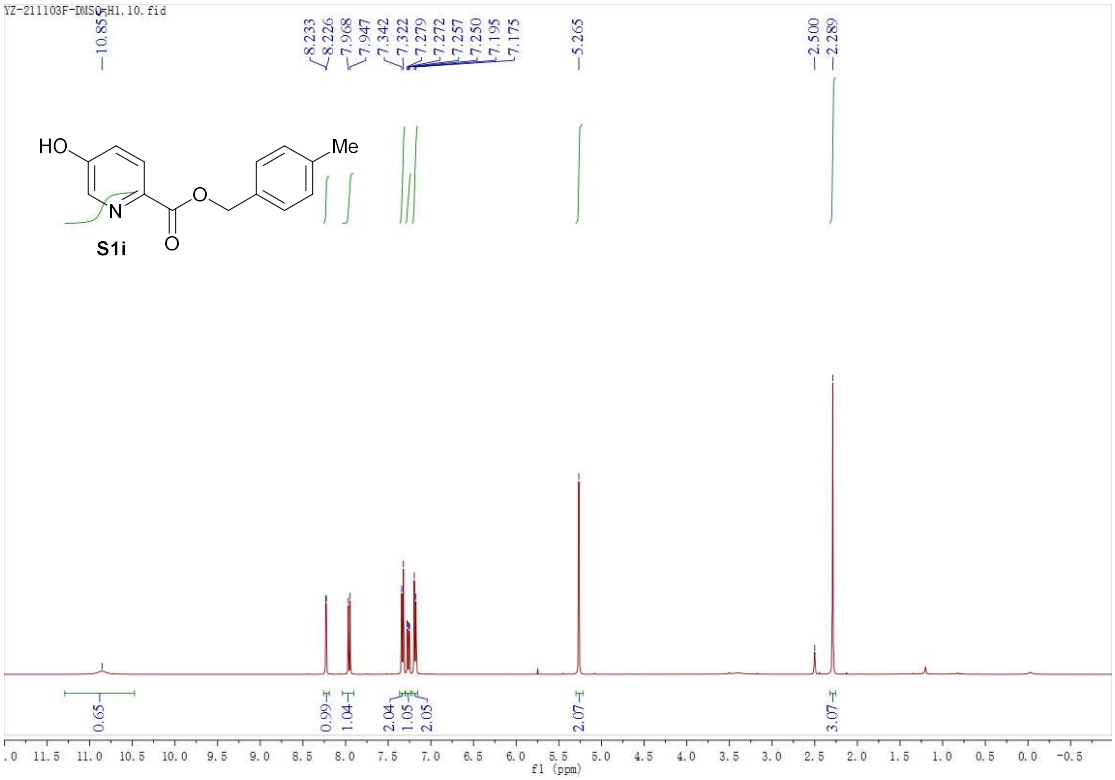
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1g



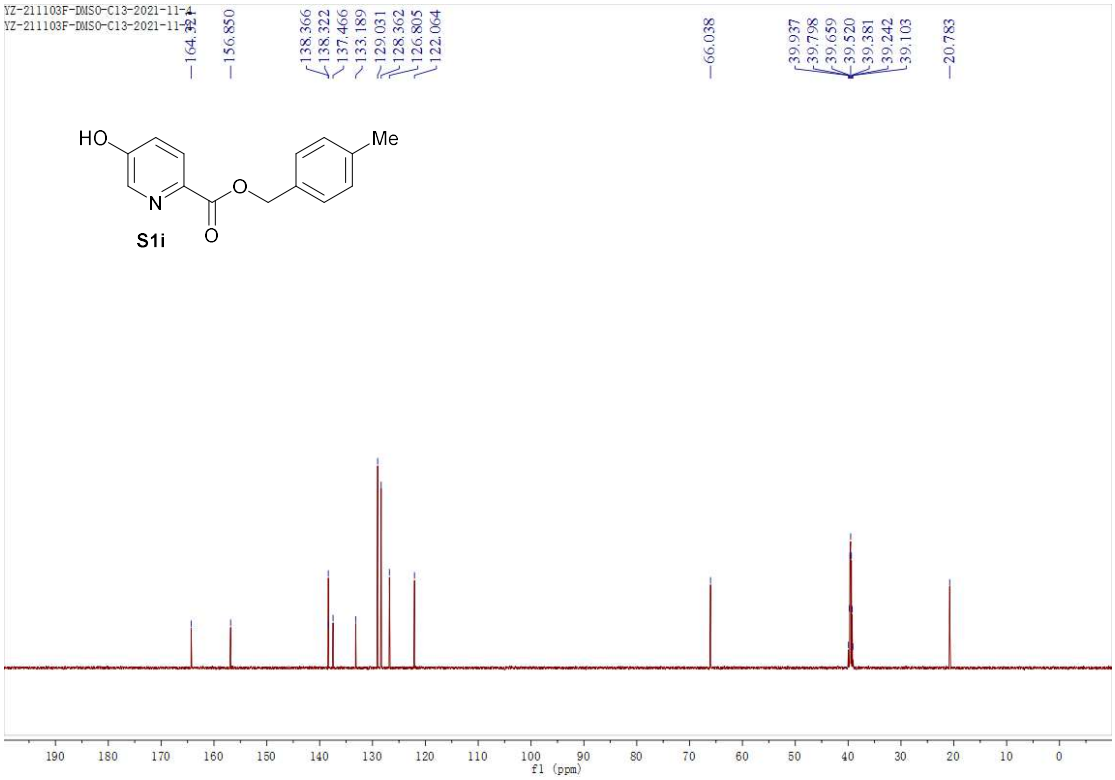
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1h



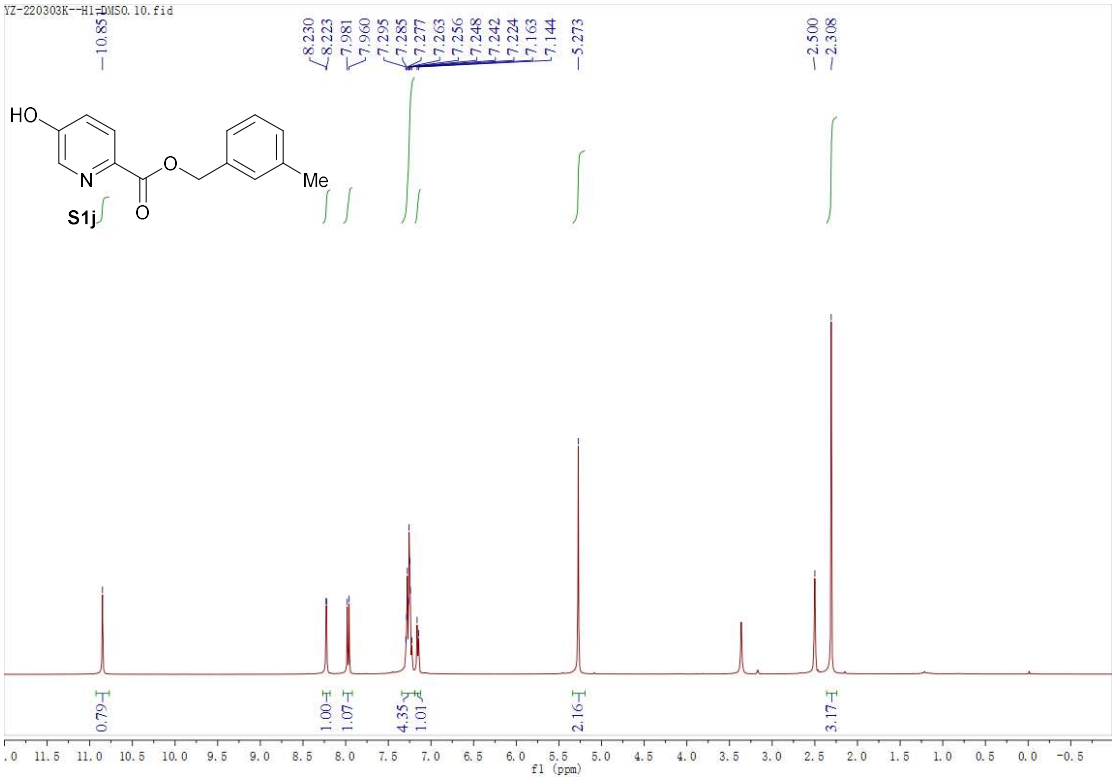
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1h



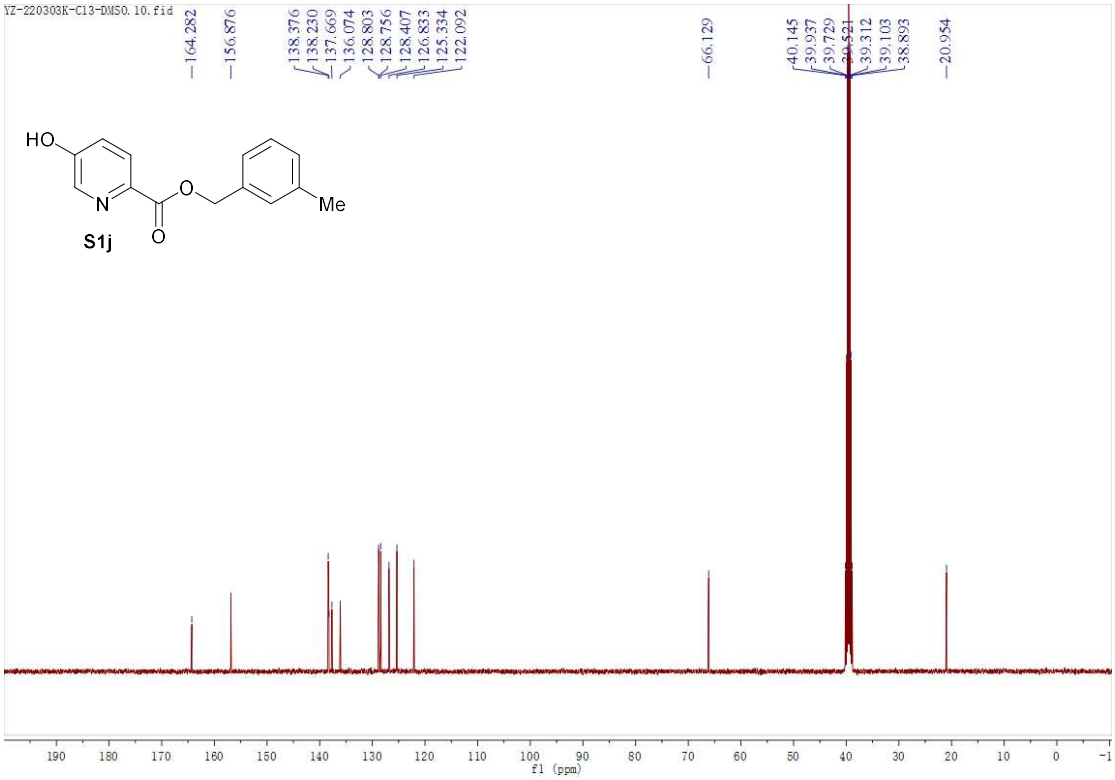
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1i



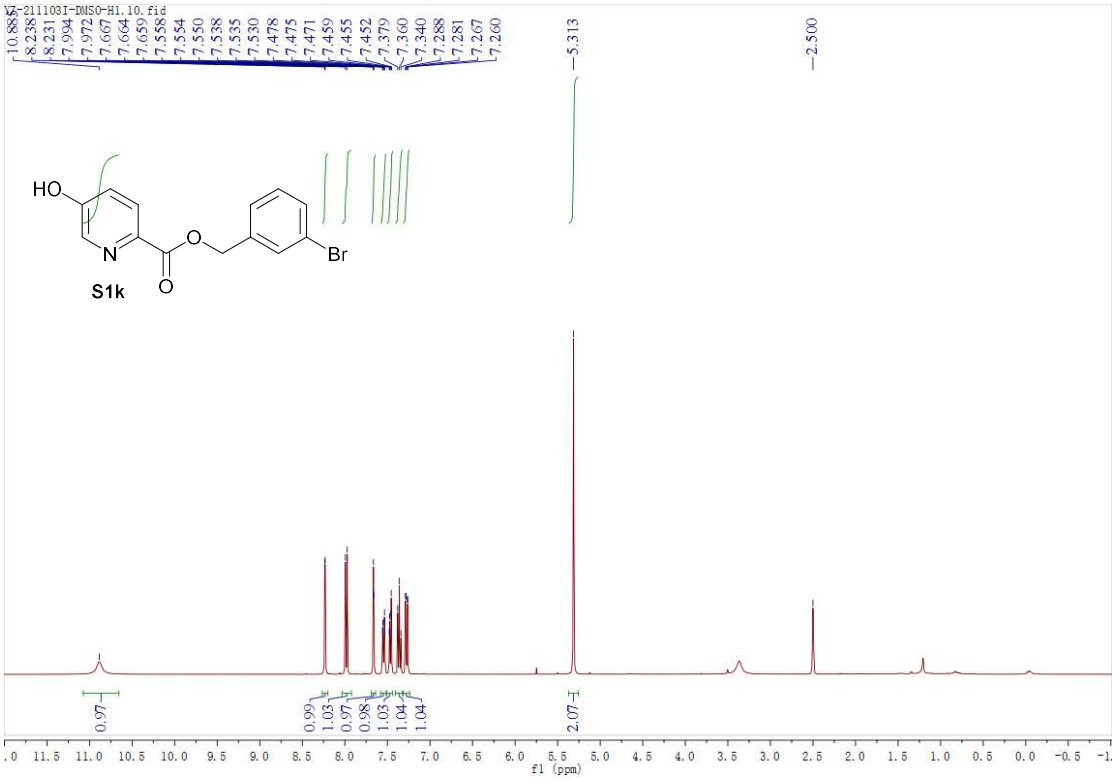
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1i



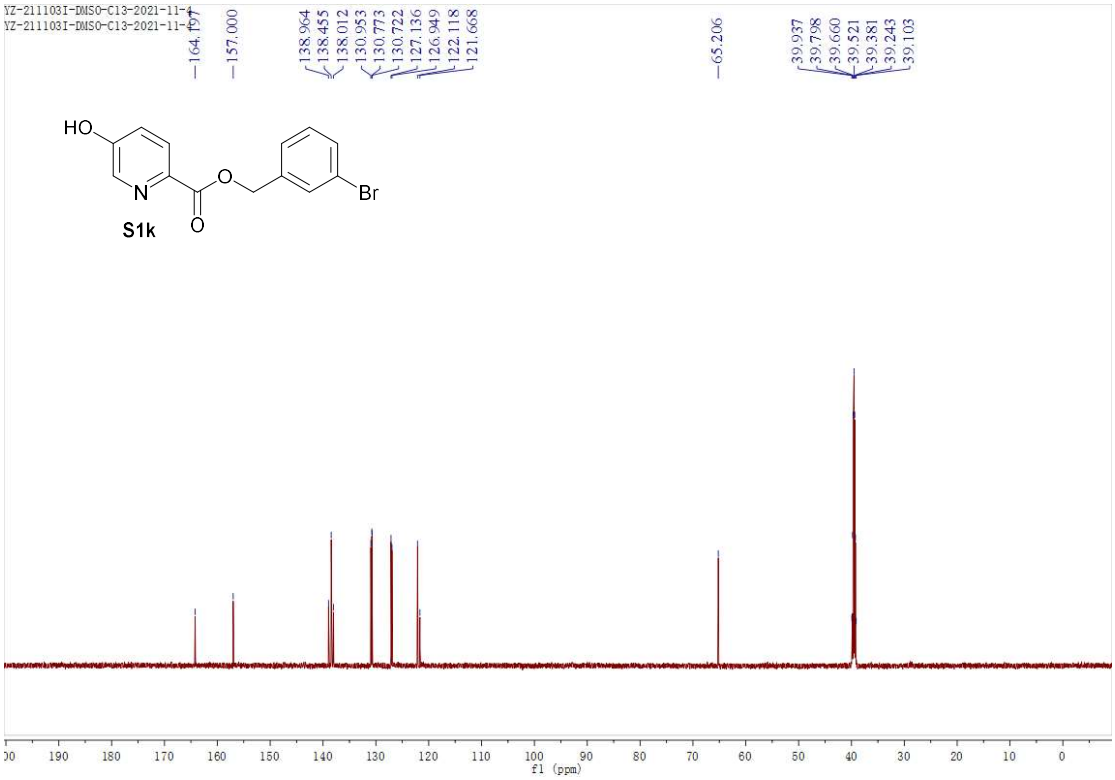
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1j



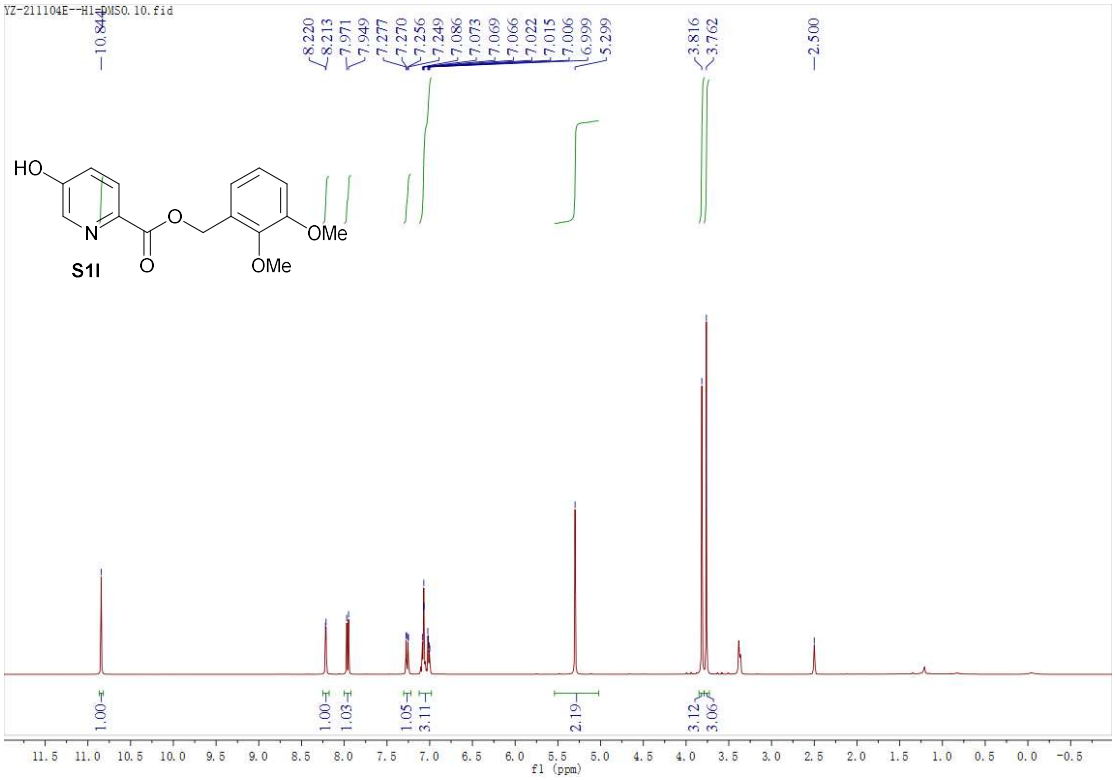
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1j



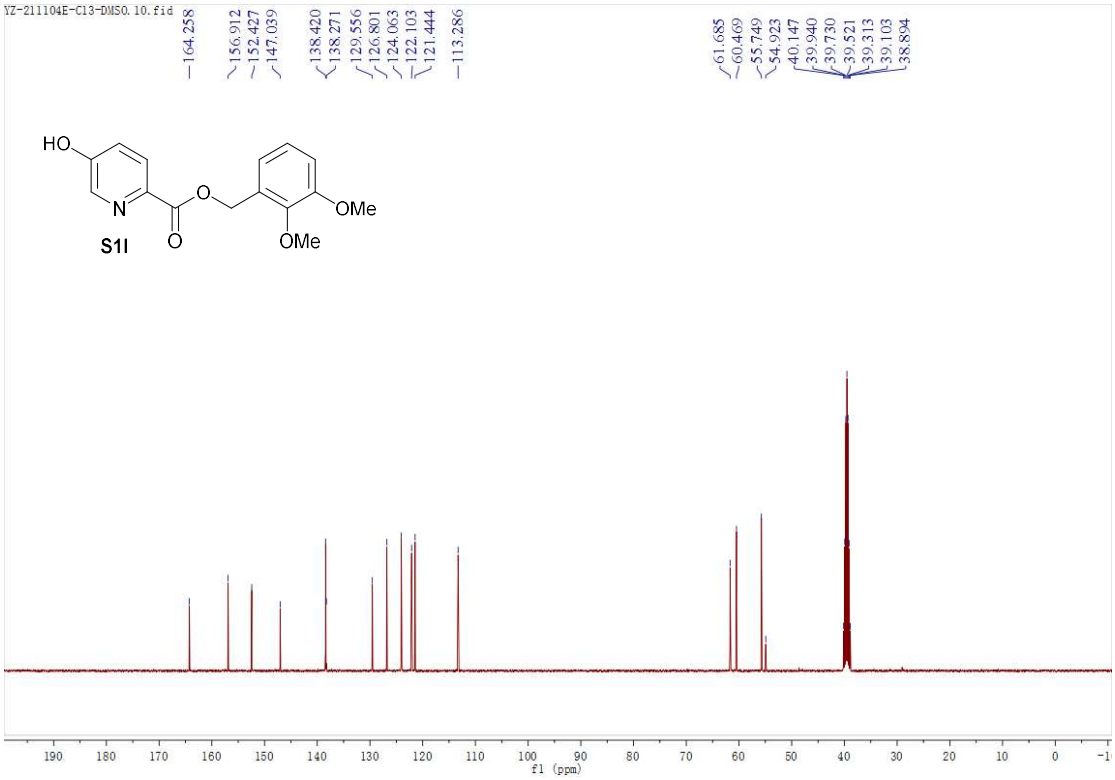
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1k



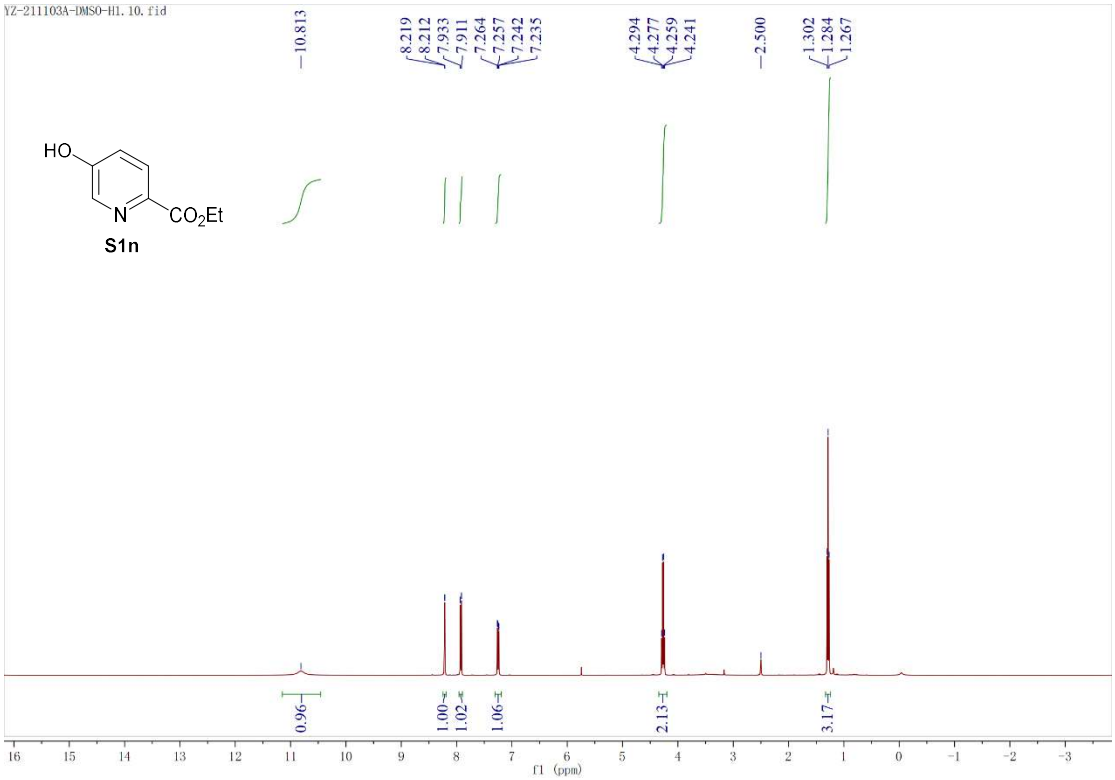
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1k



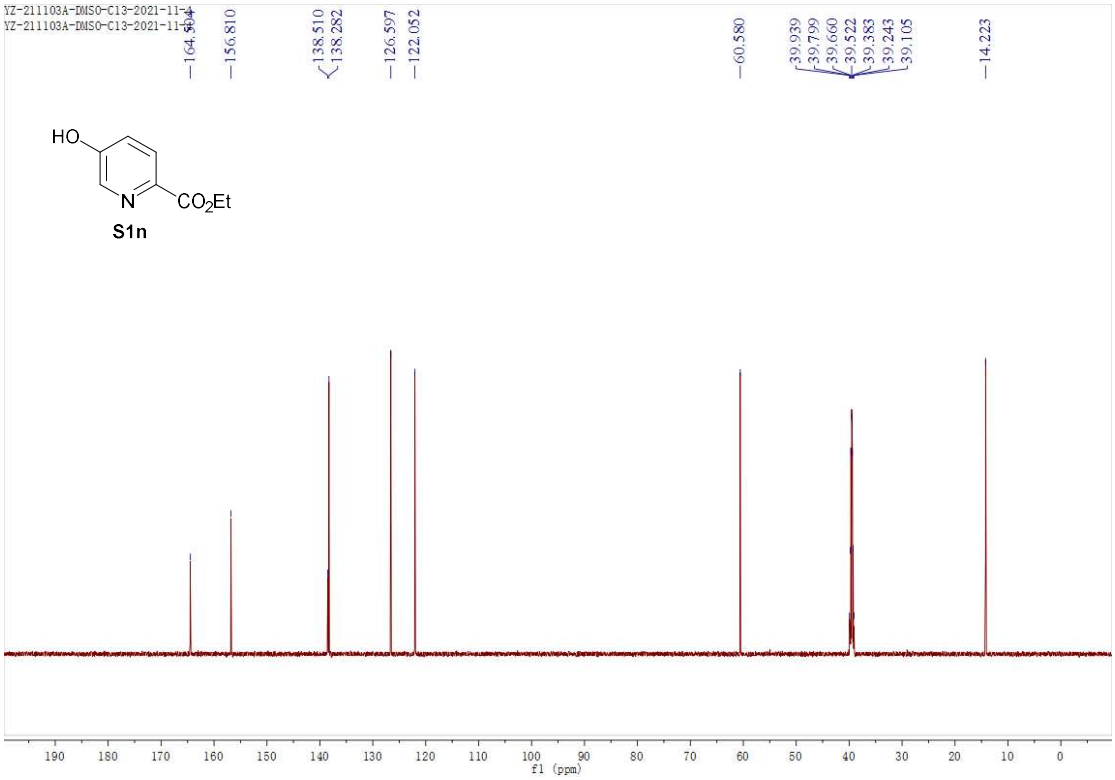
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1l



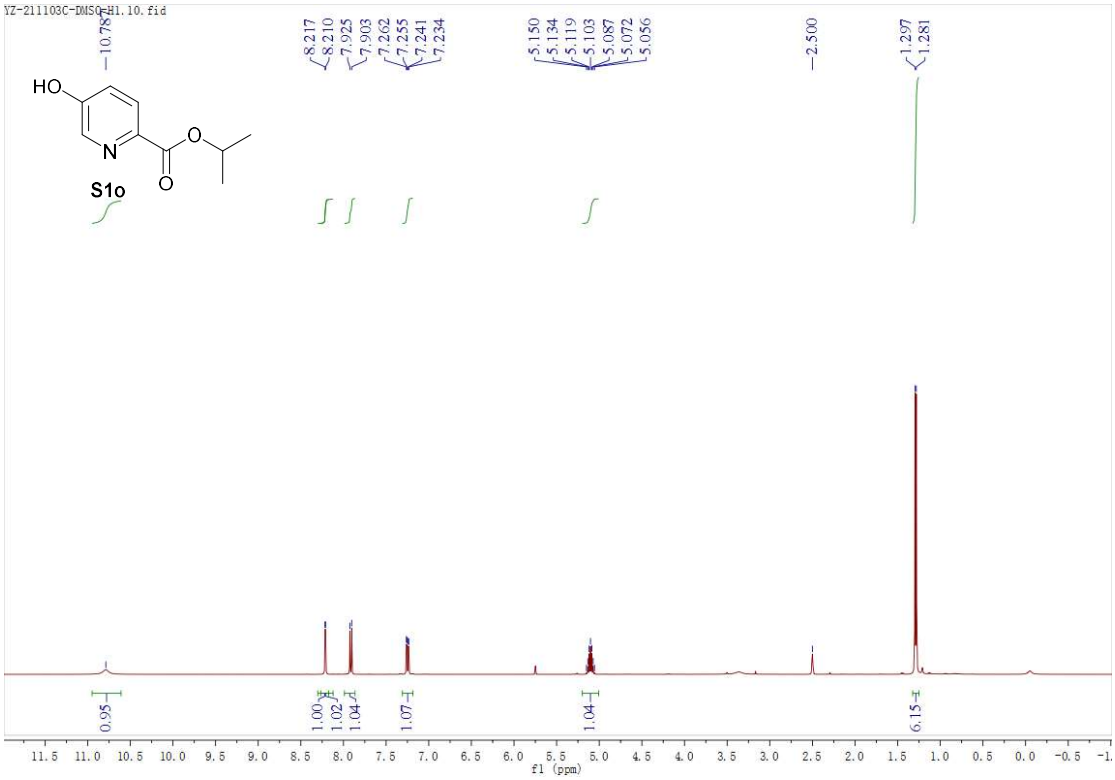
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1l



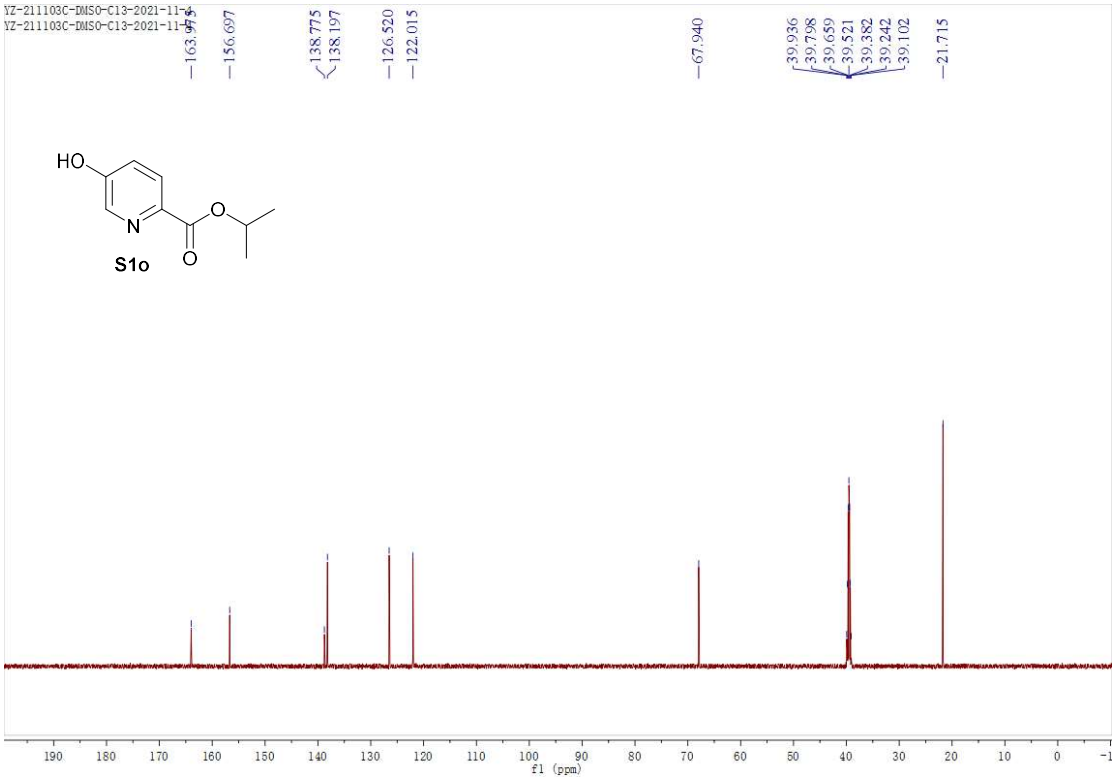
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1n



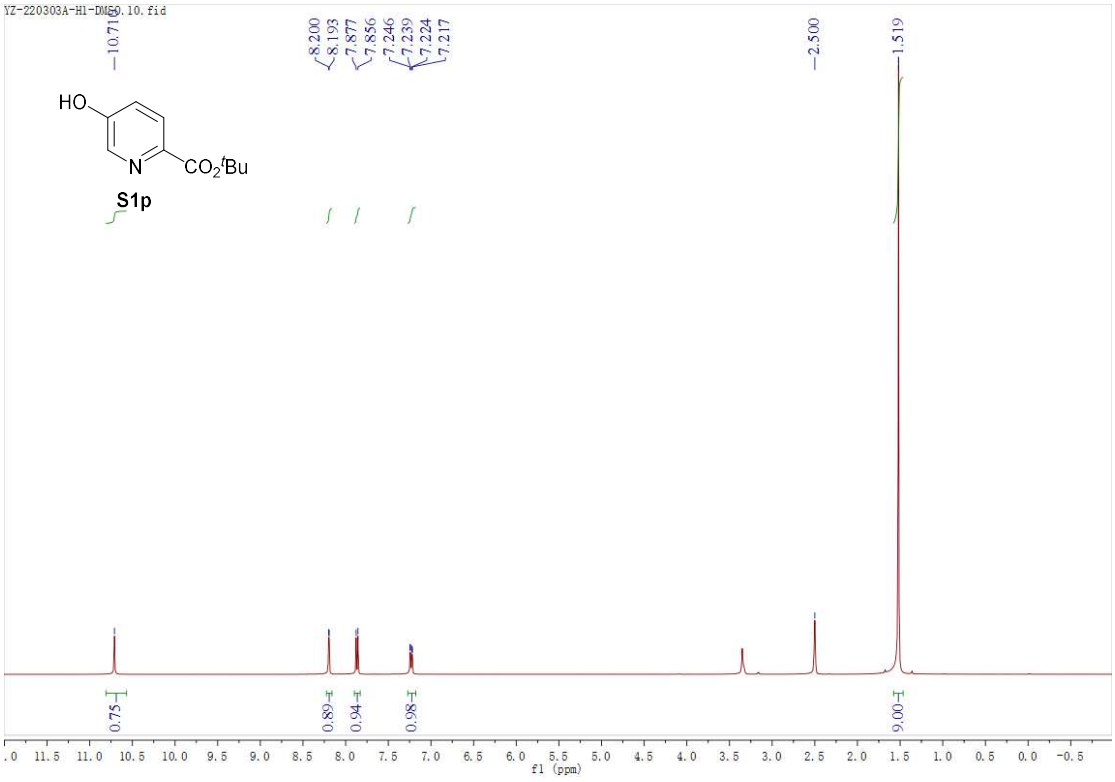
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1n



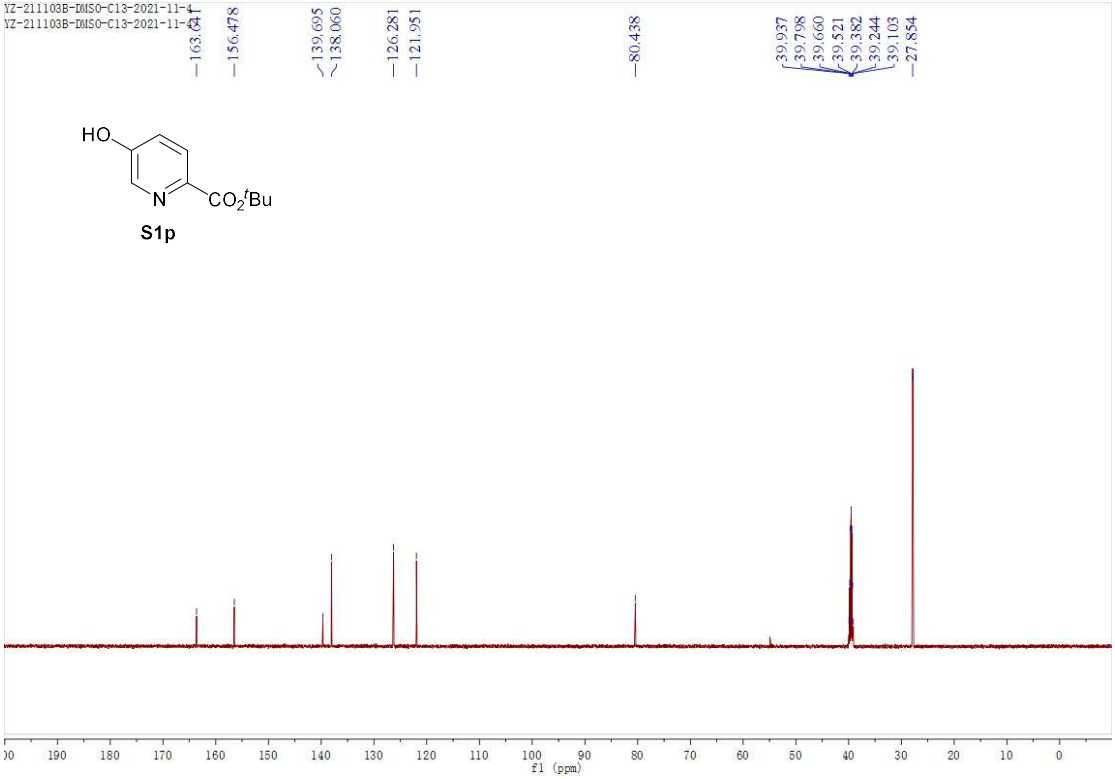
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1o



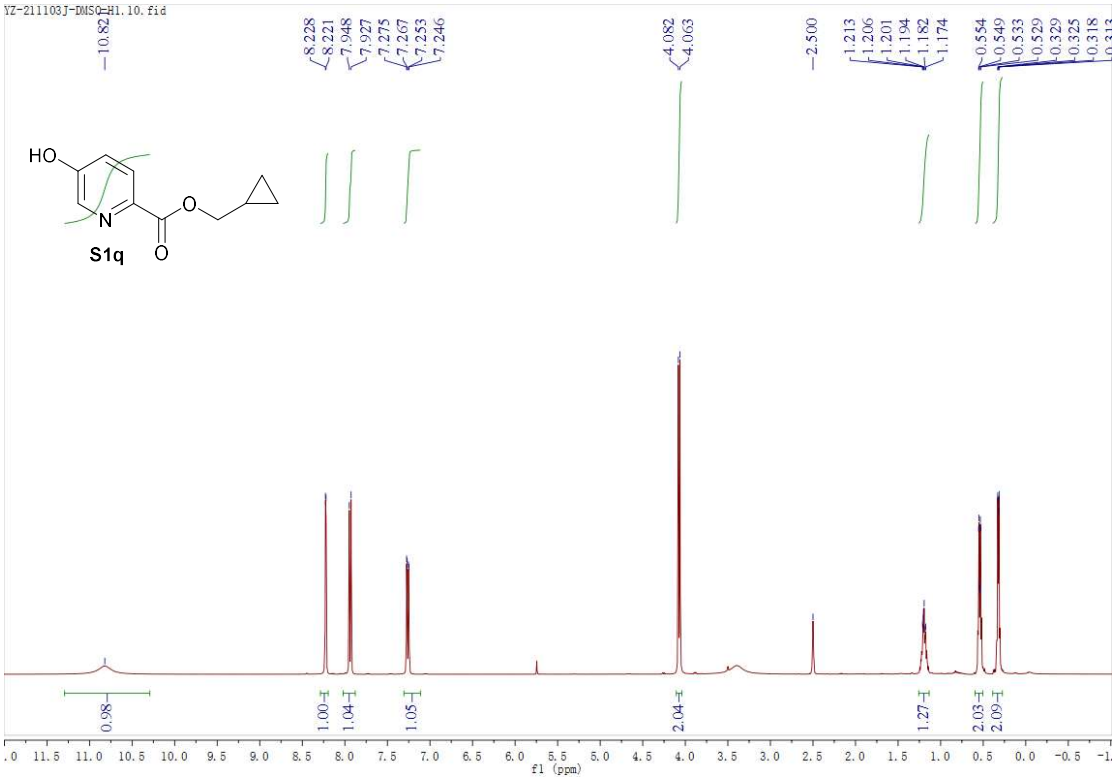
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1o



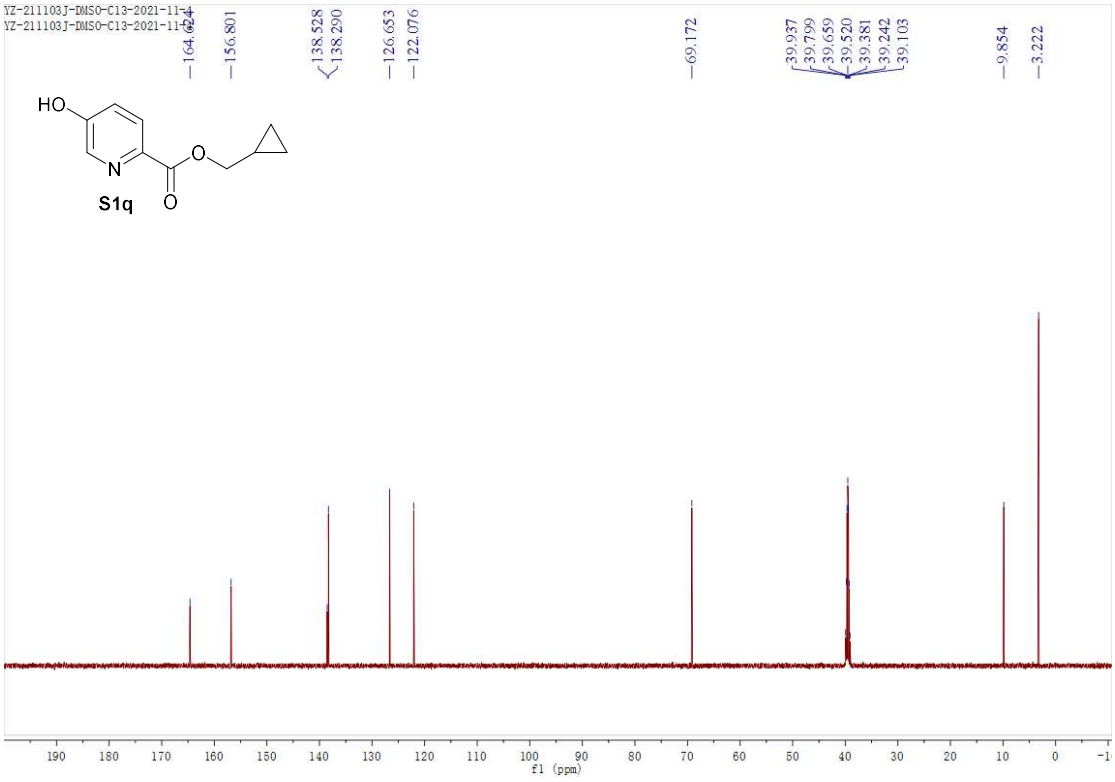
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1p



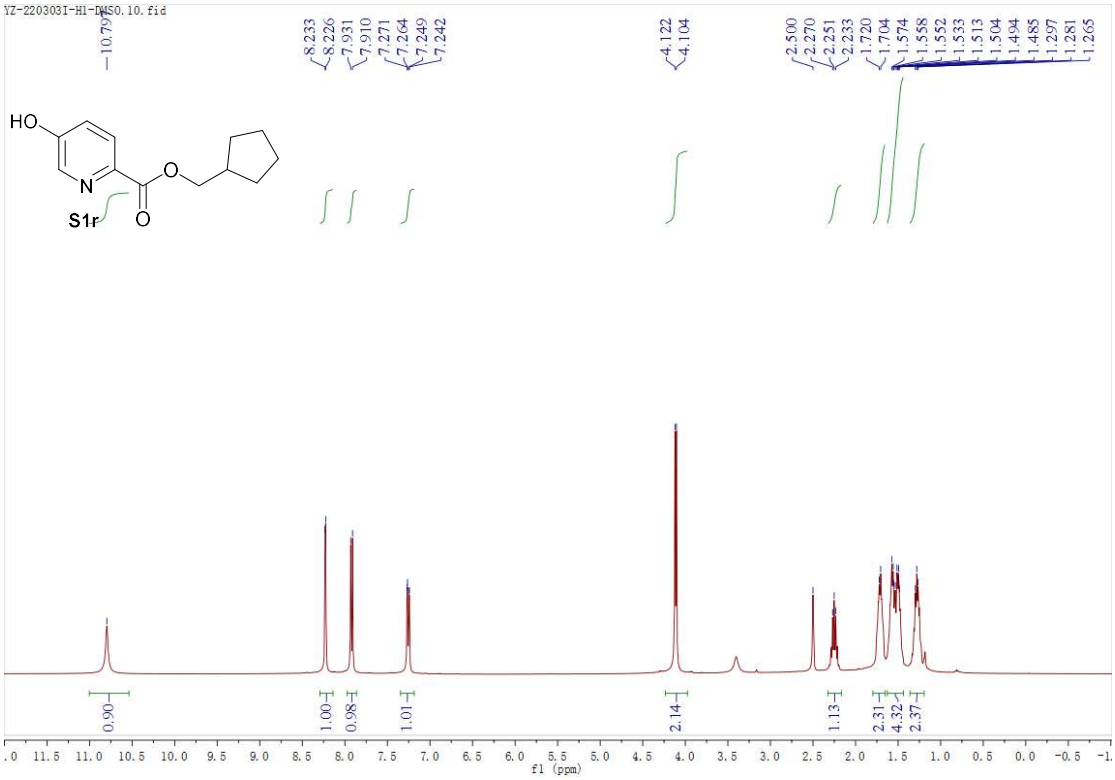
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1p



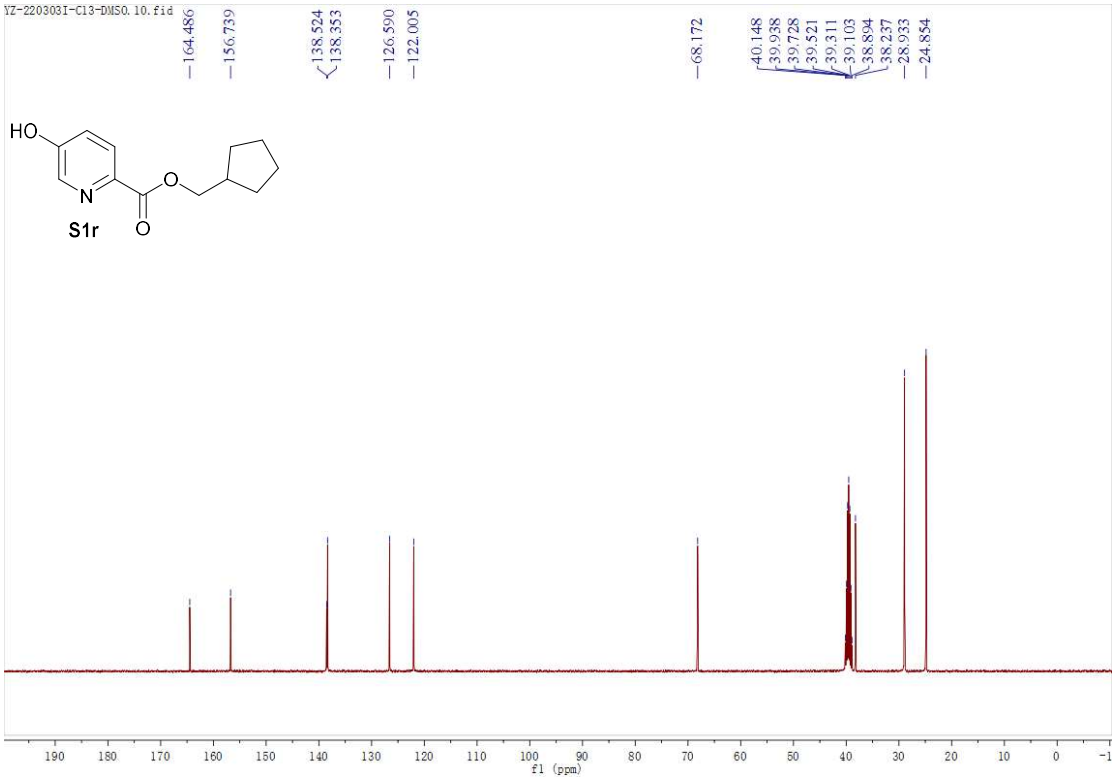
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1q



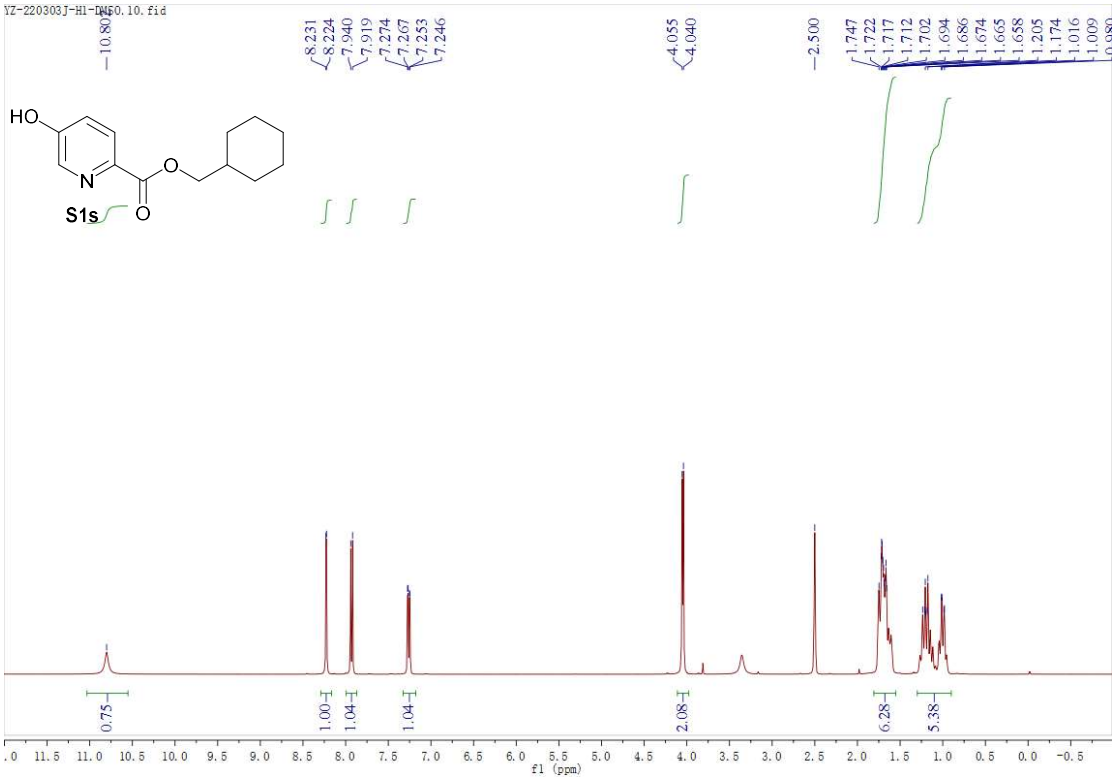
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1q



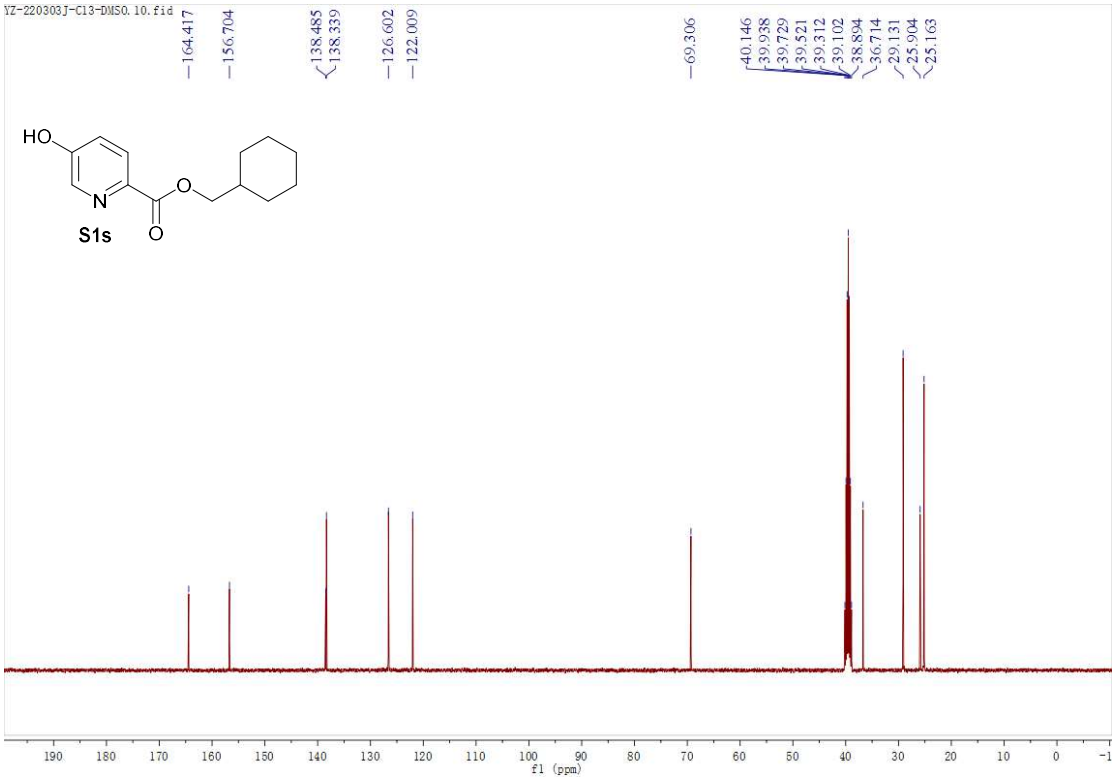
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1r



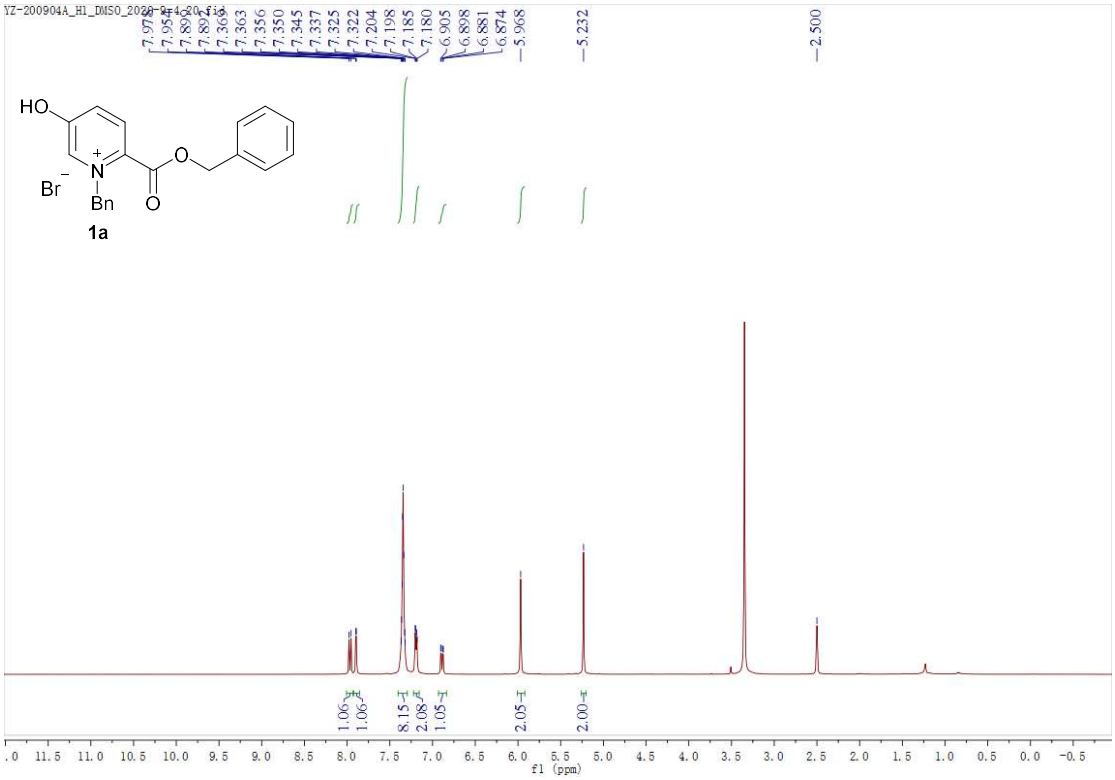
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1r



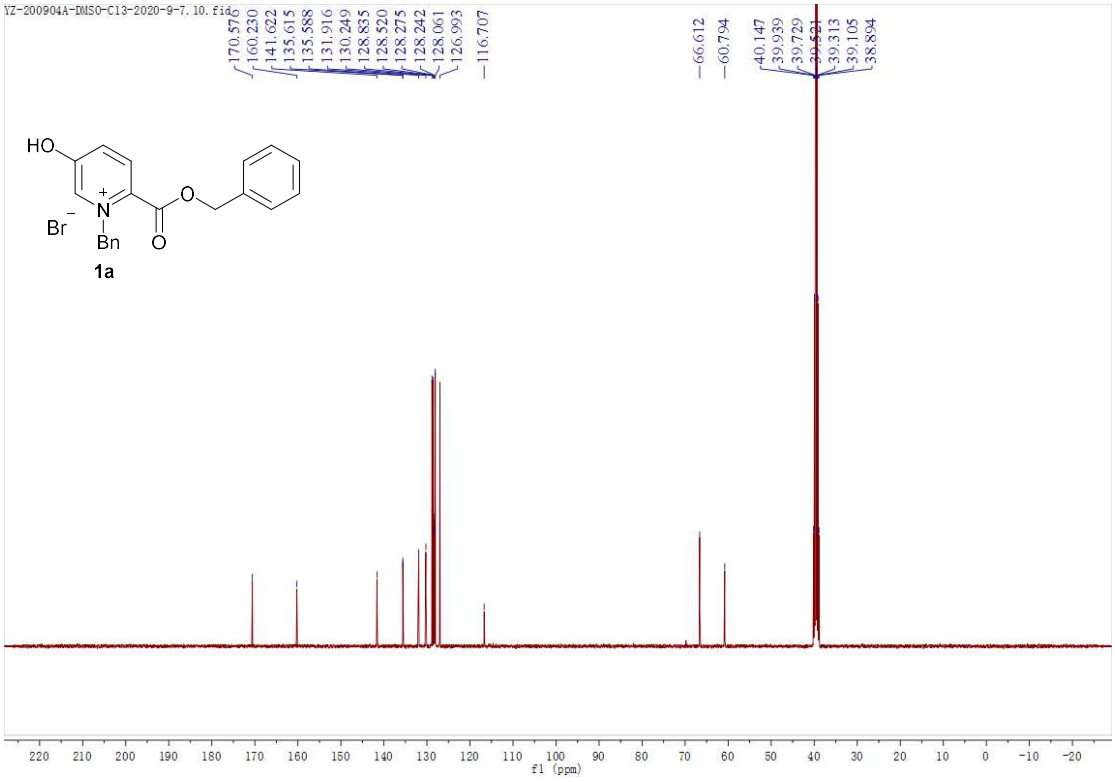
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound S1s



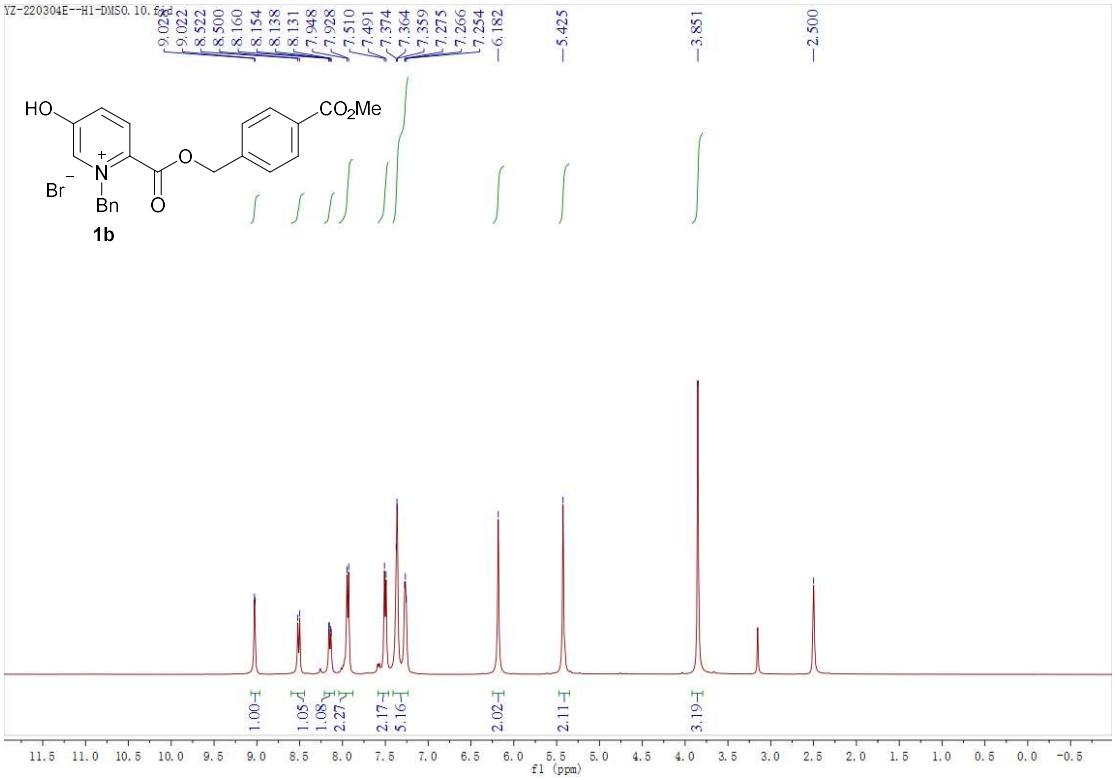
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound S1s



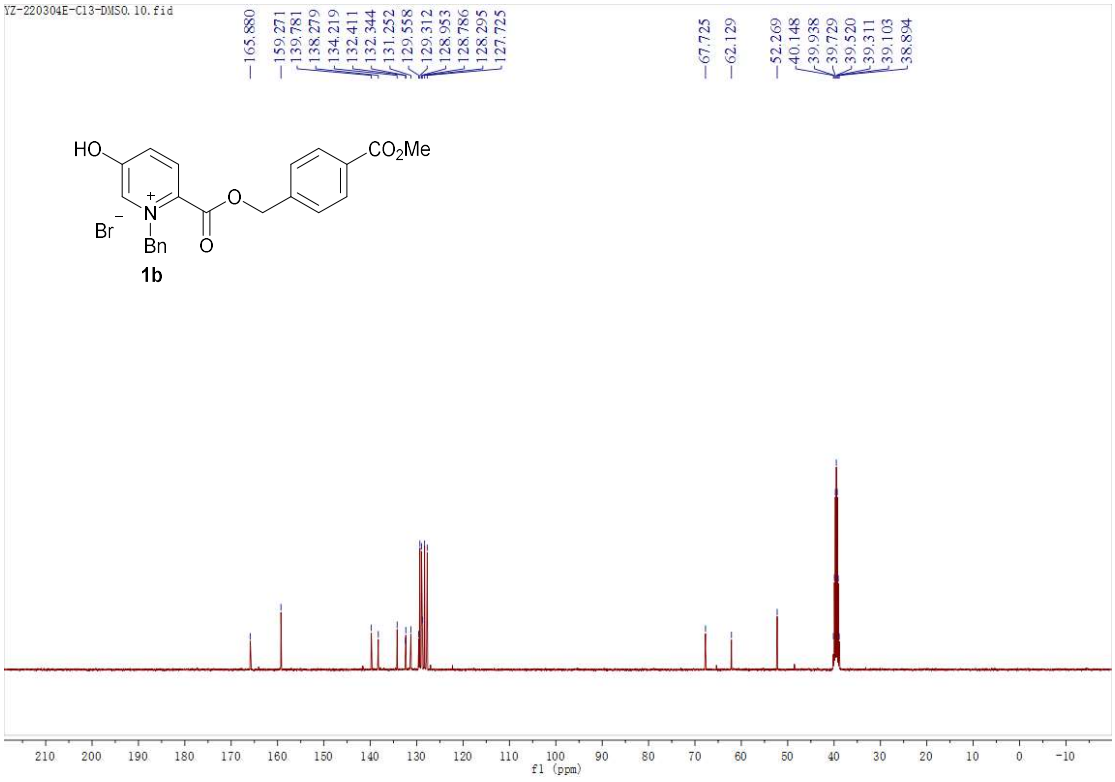
[1]H-NMR Spectrum (400 MHz, DMSO-*d*6) of Compound 1a



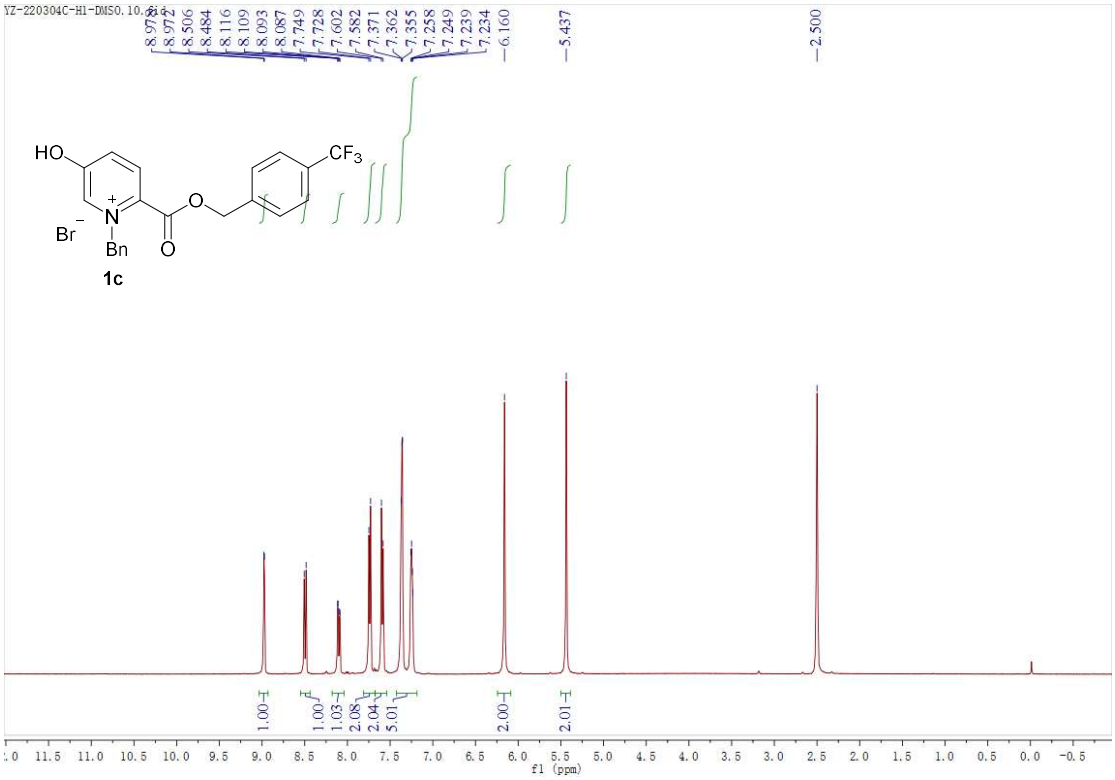
[13]C-NMR Spectrum (100 MHz, DMSO-*d*6) of Compound 1a



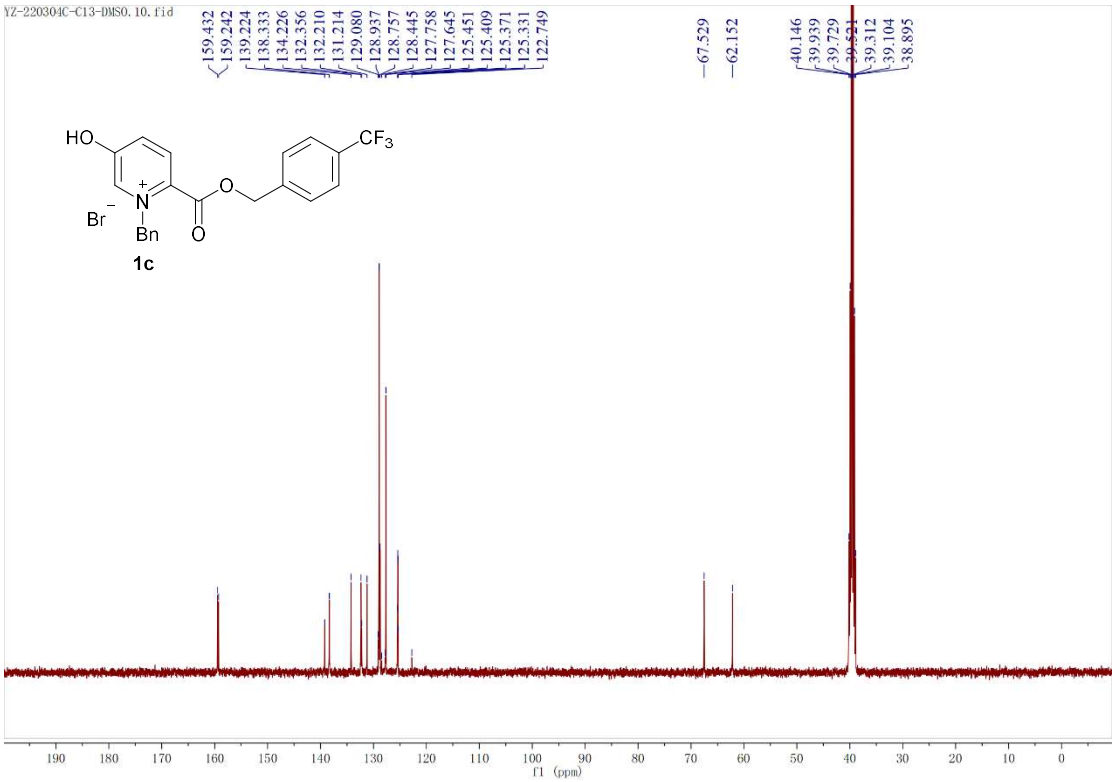
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1b



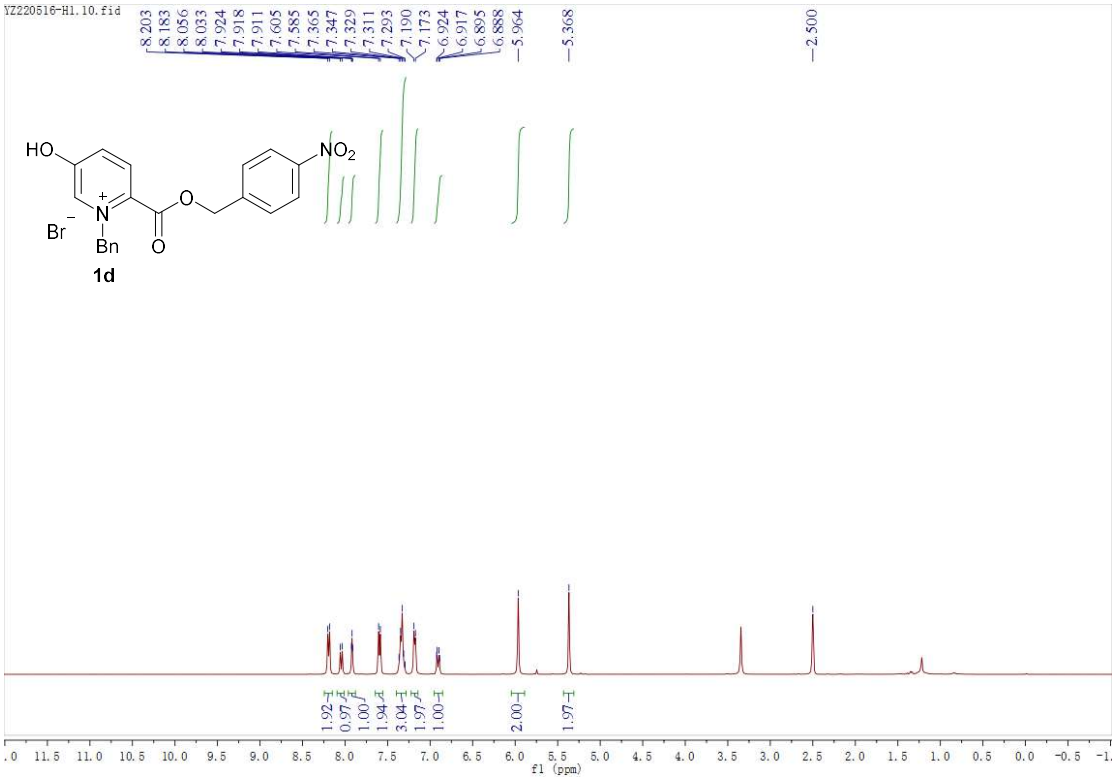
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1b



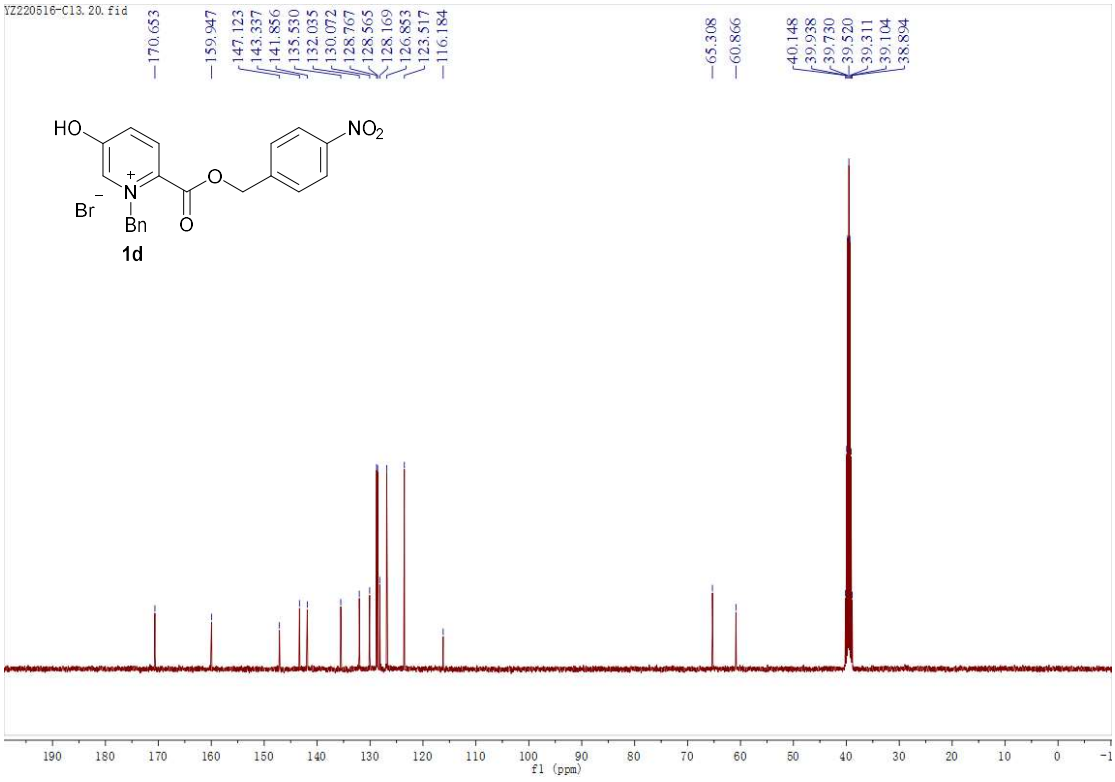
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1c



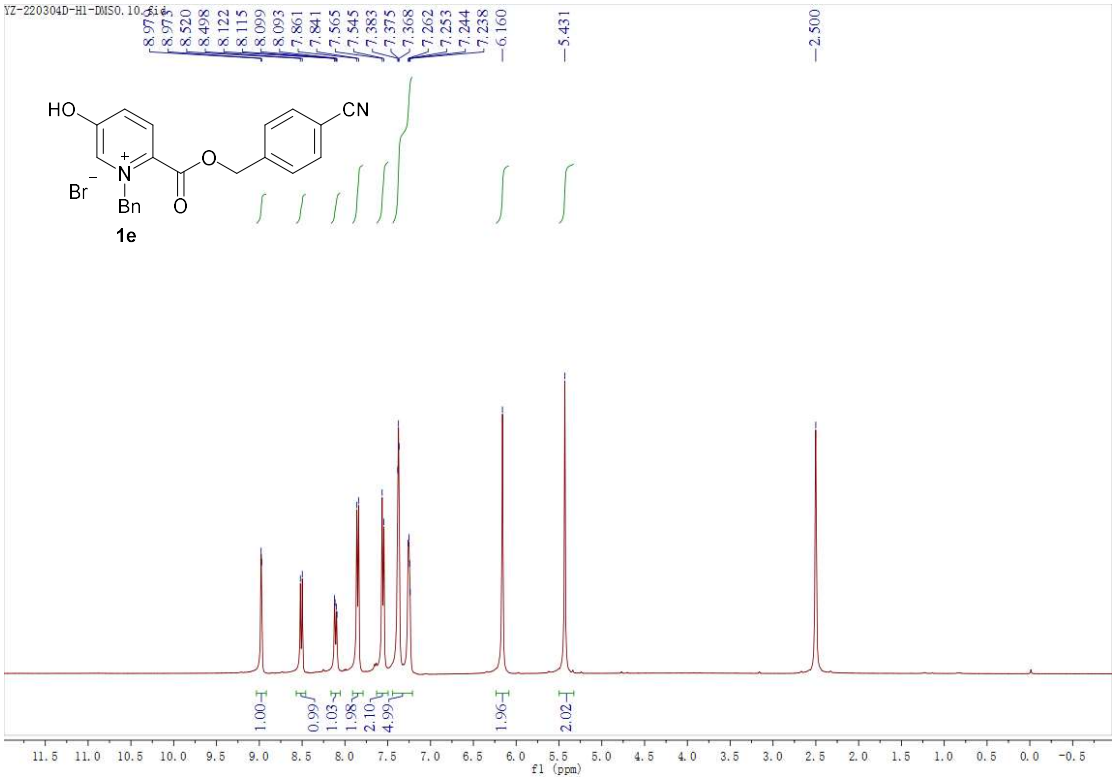
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1c



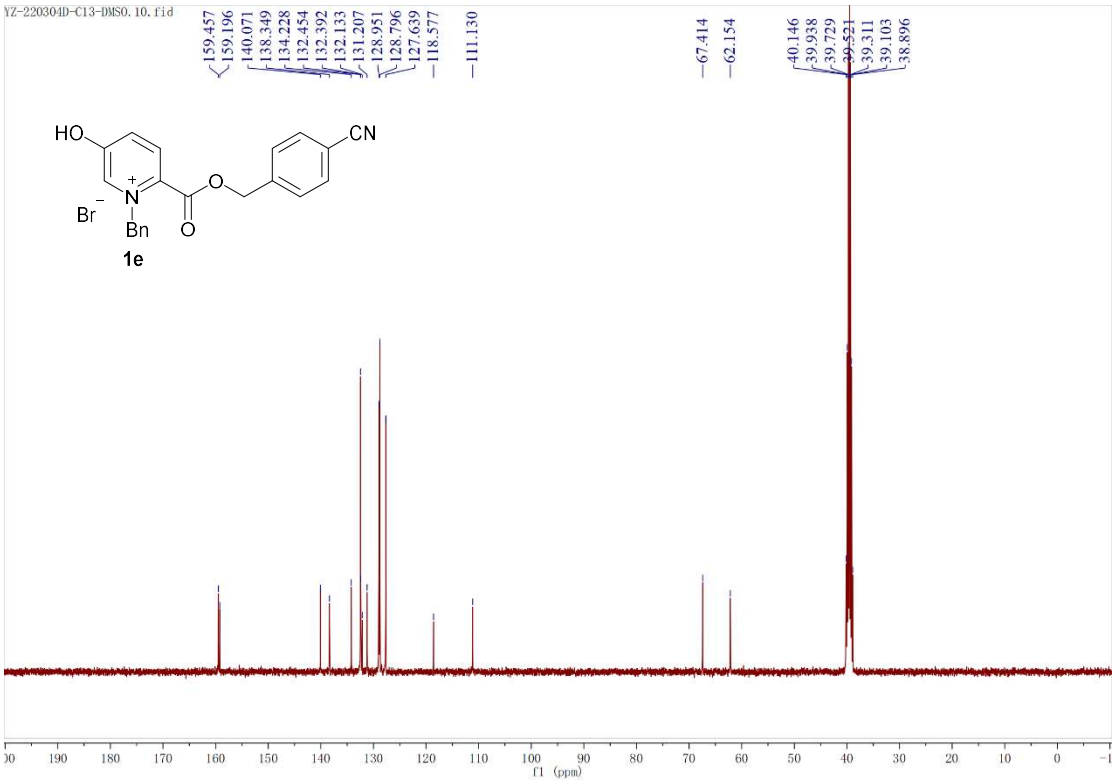
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1d



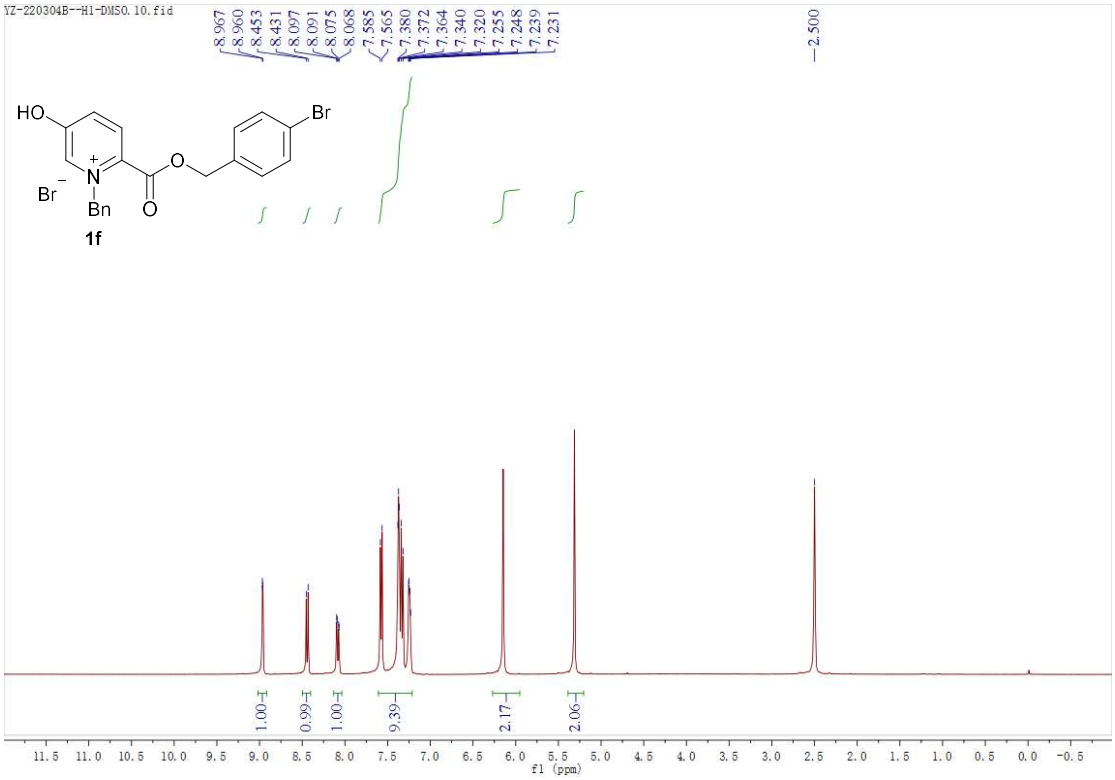
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1d



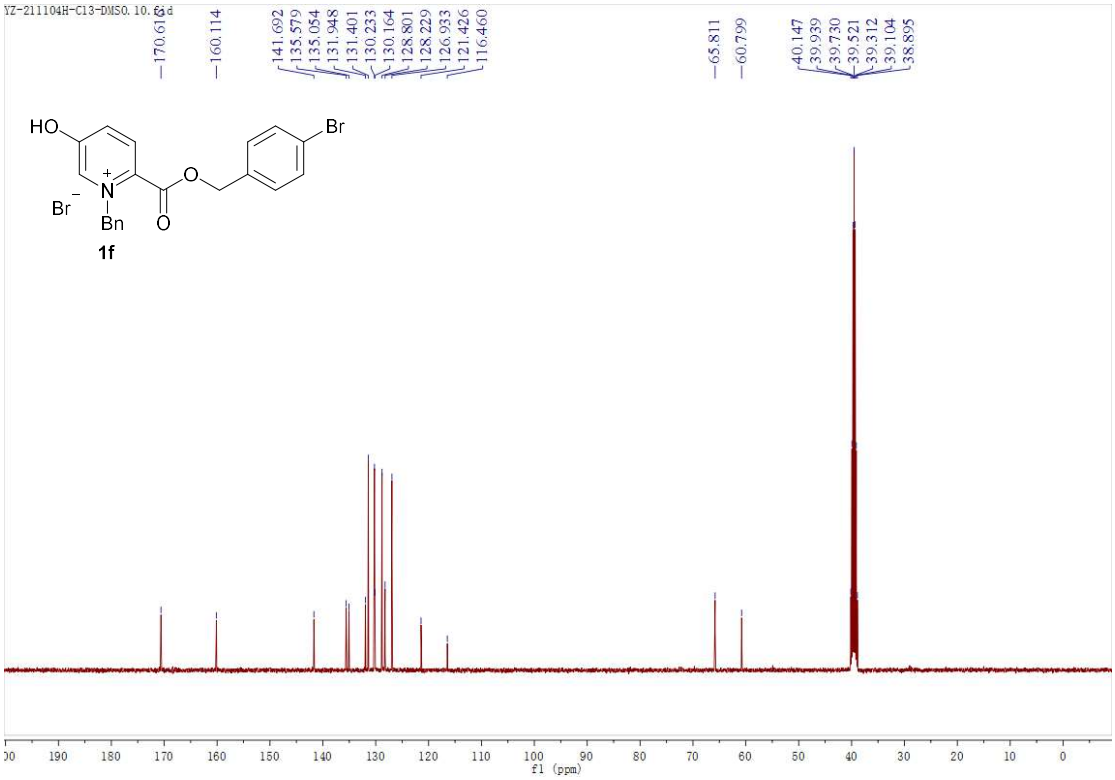
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1e



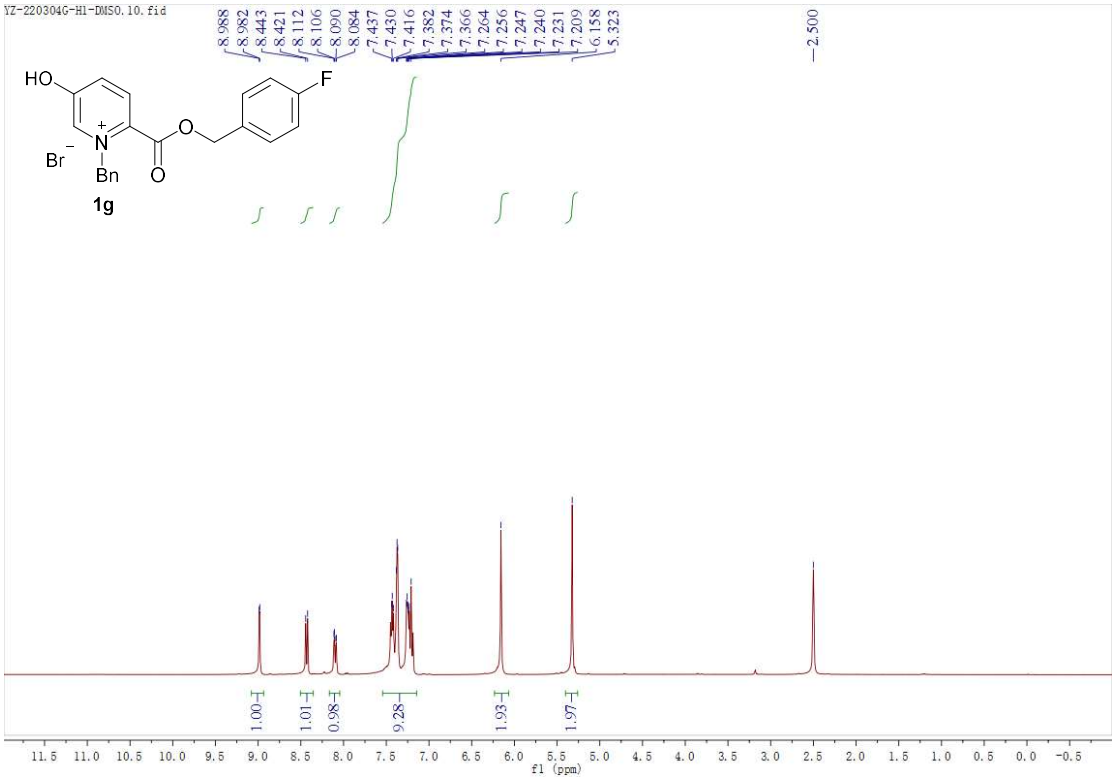
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1e



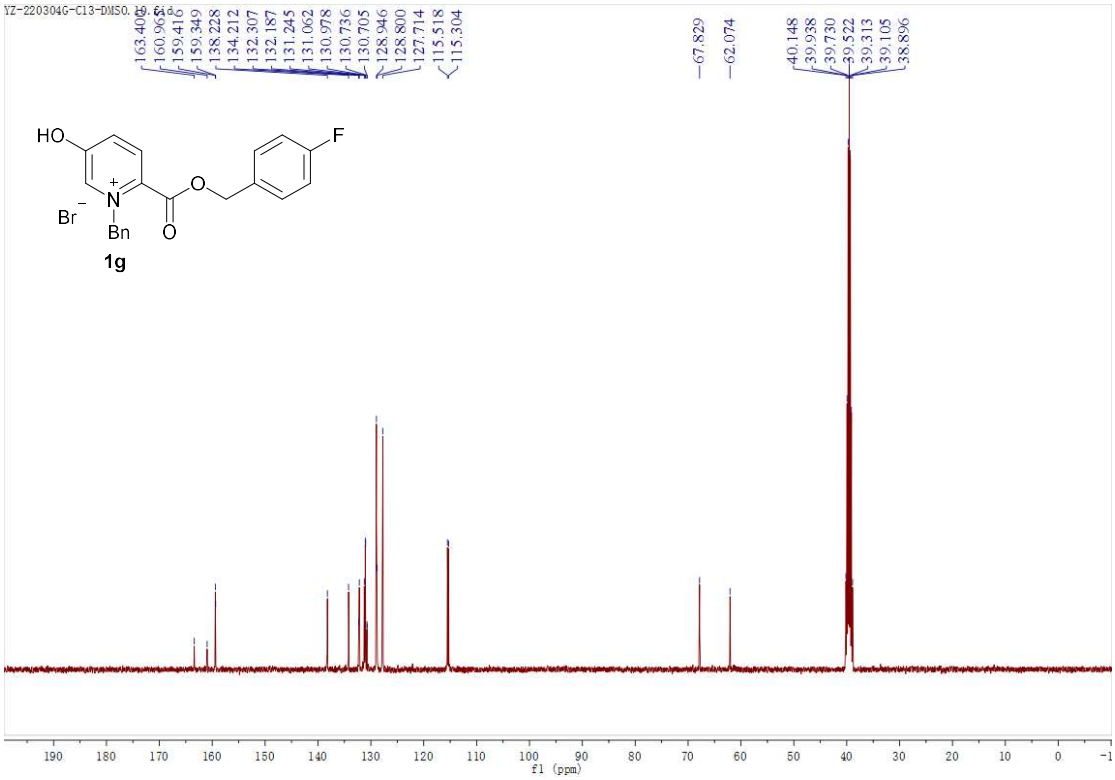
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1f



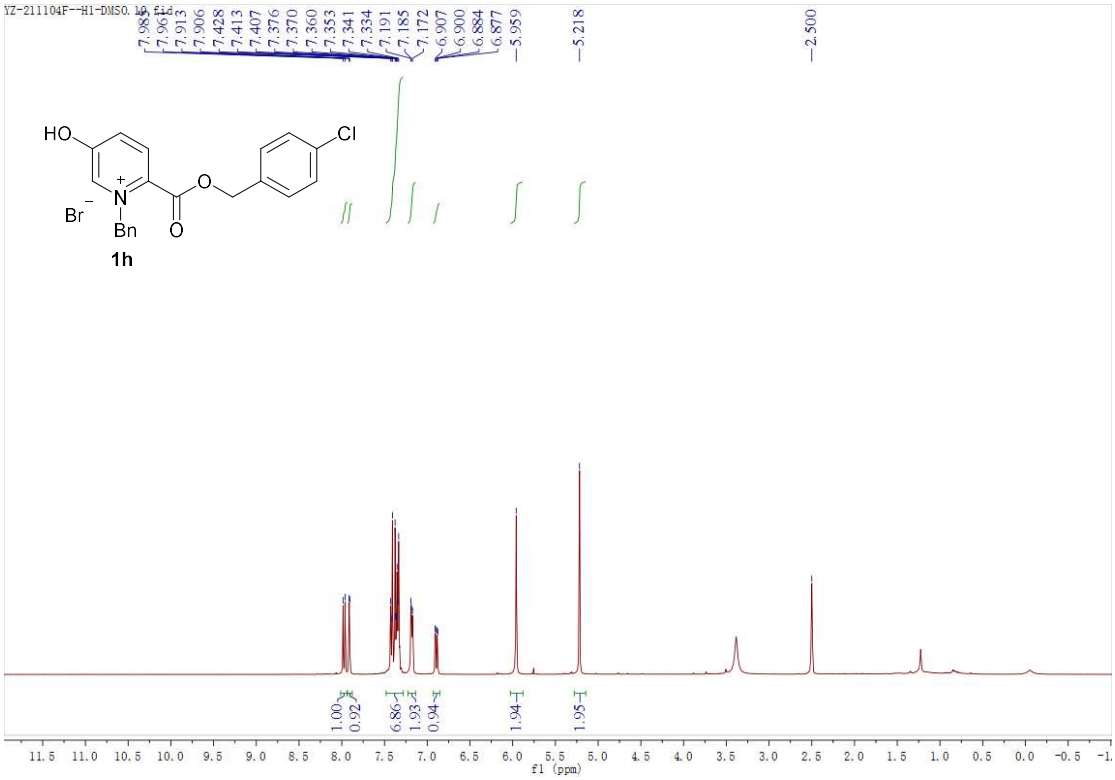
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1f



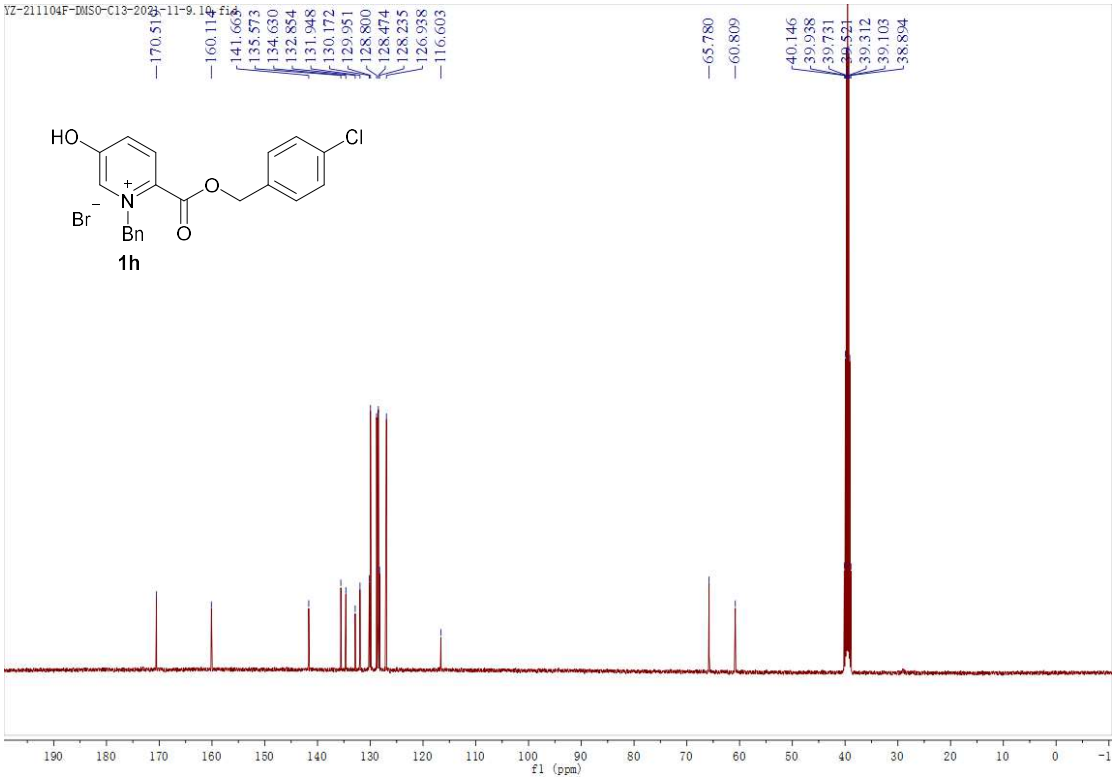
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1g



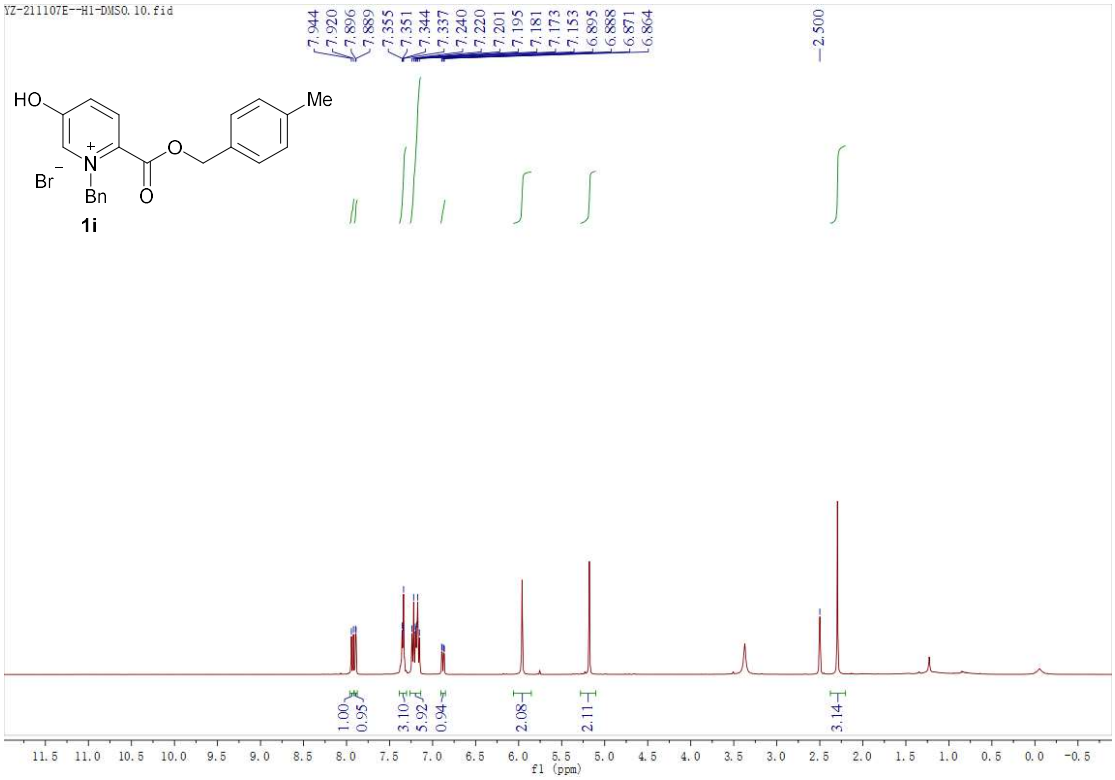
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1g



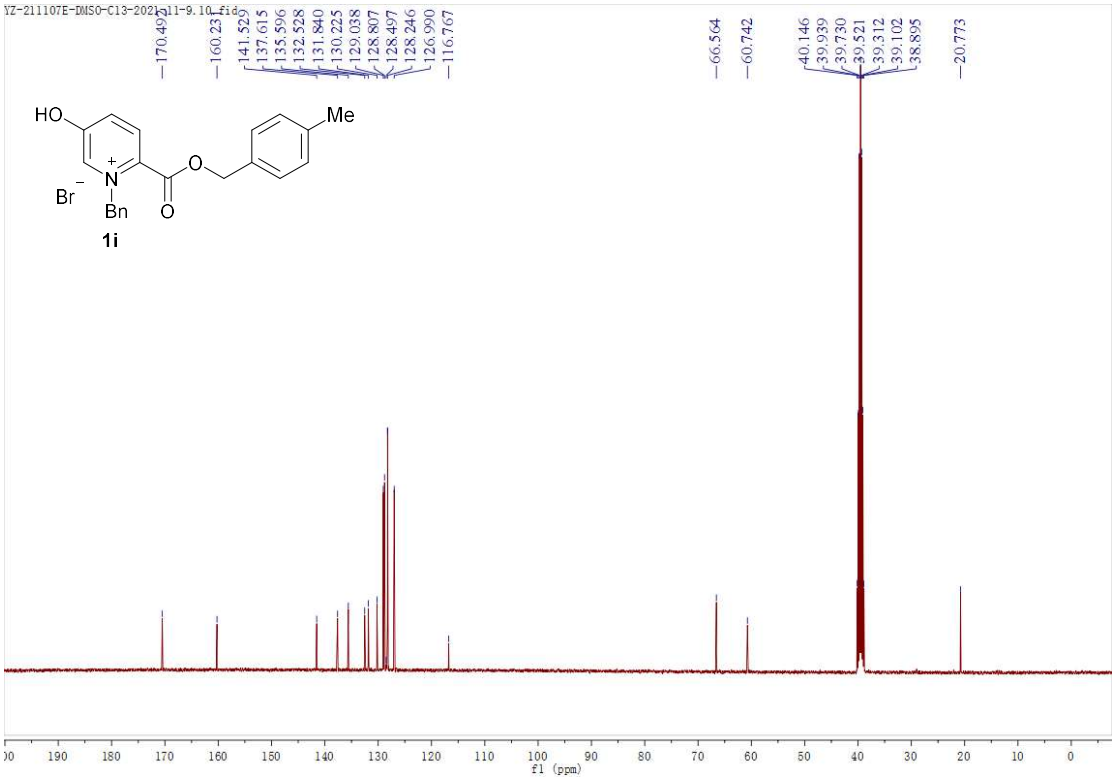
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1h



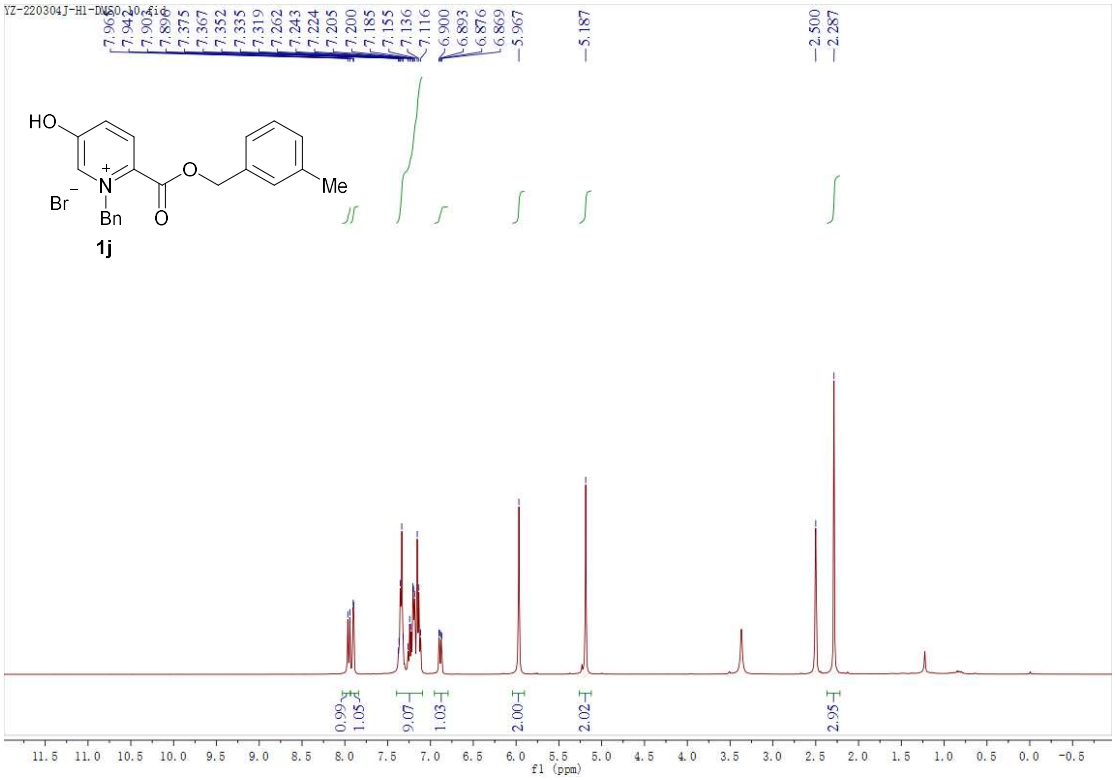
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1h



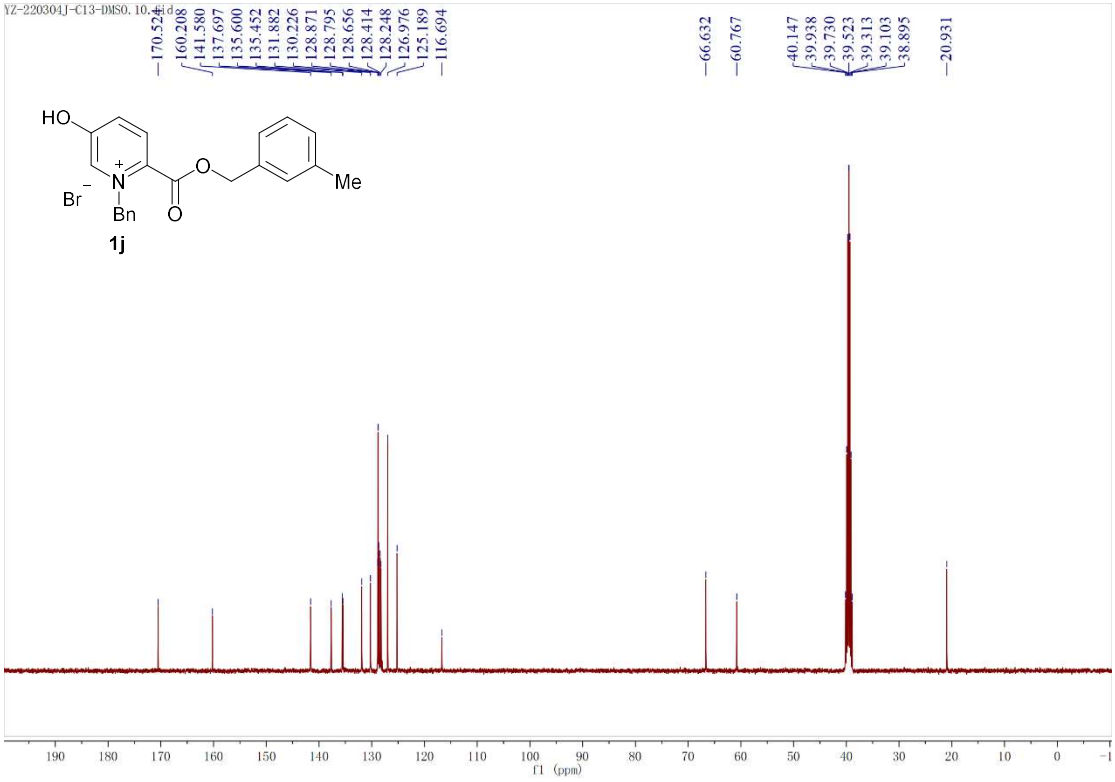
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1i



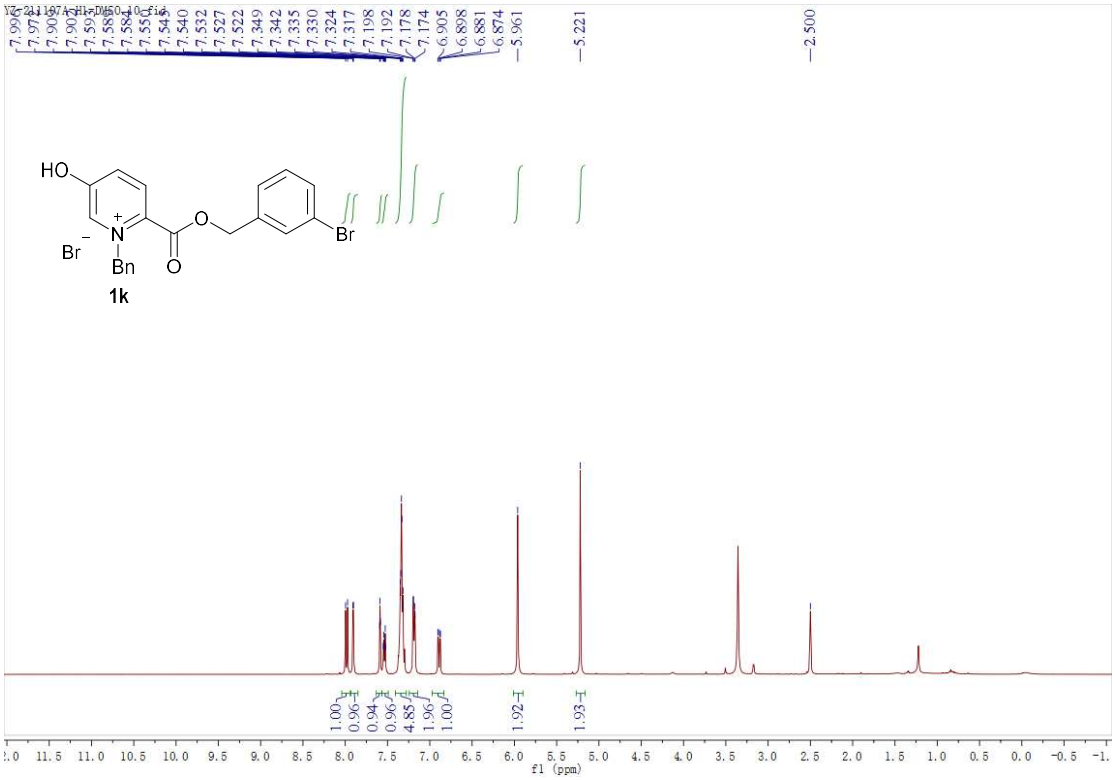
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1i



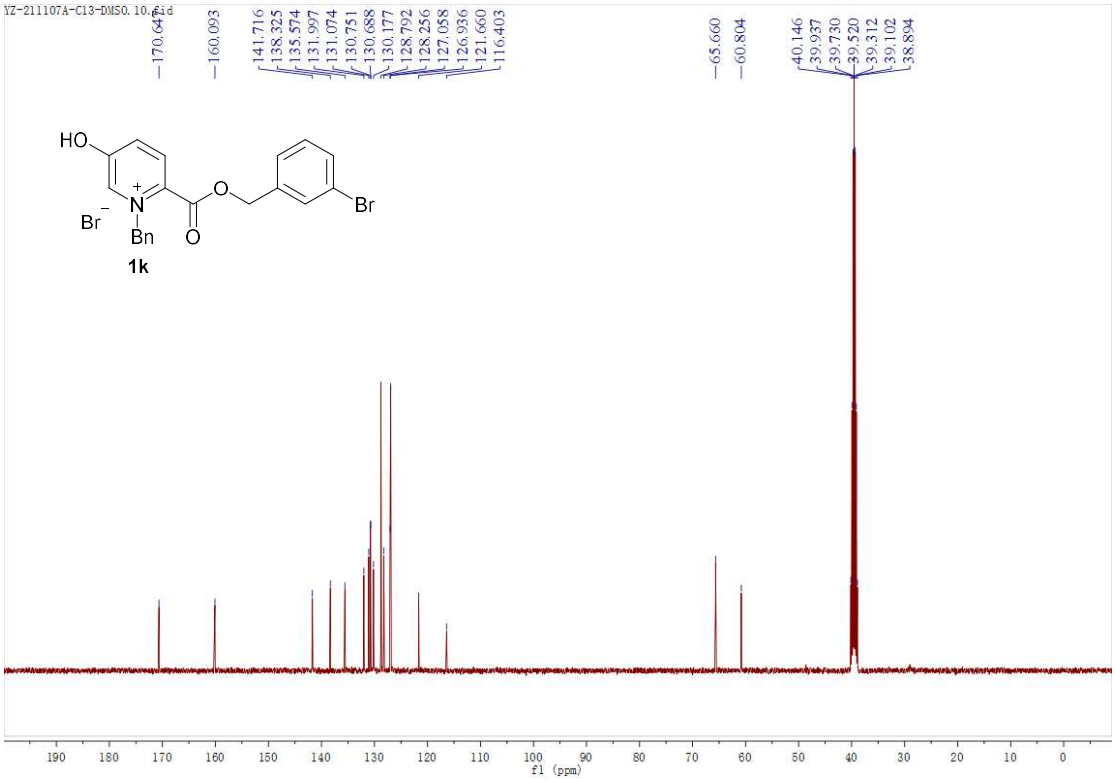
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1j



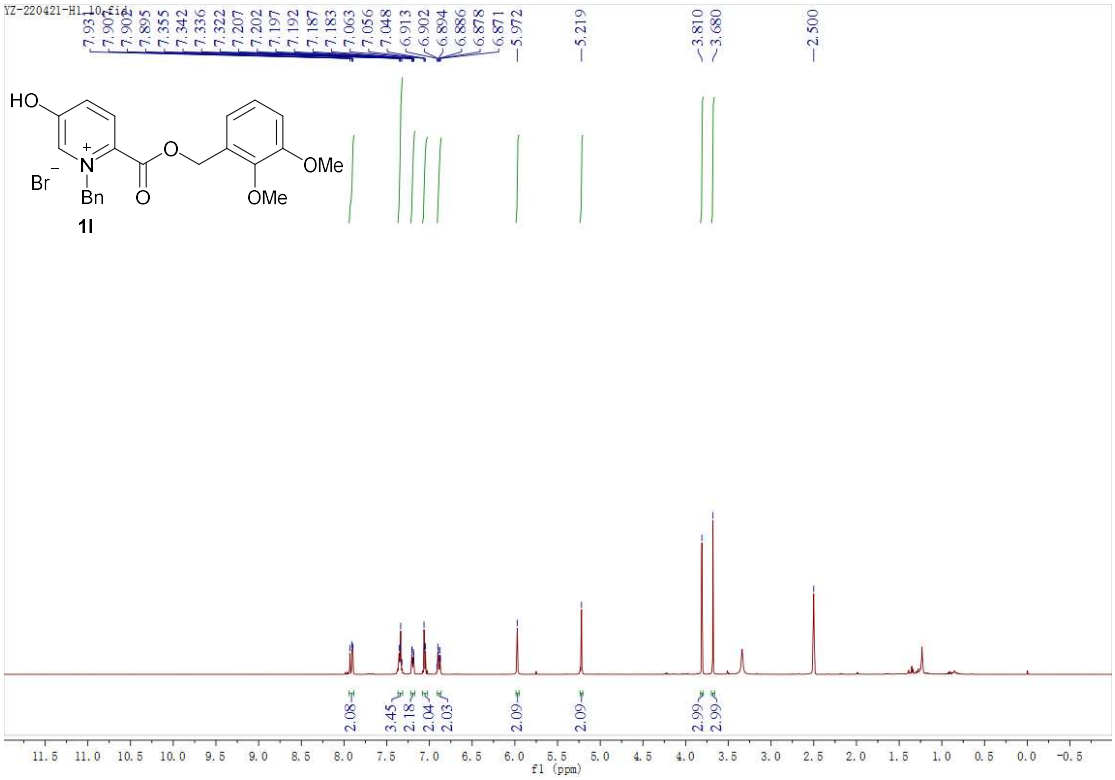
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1j



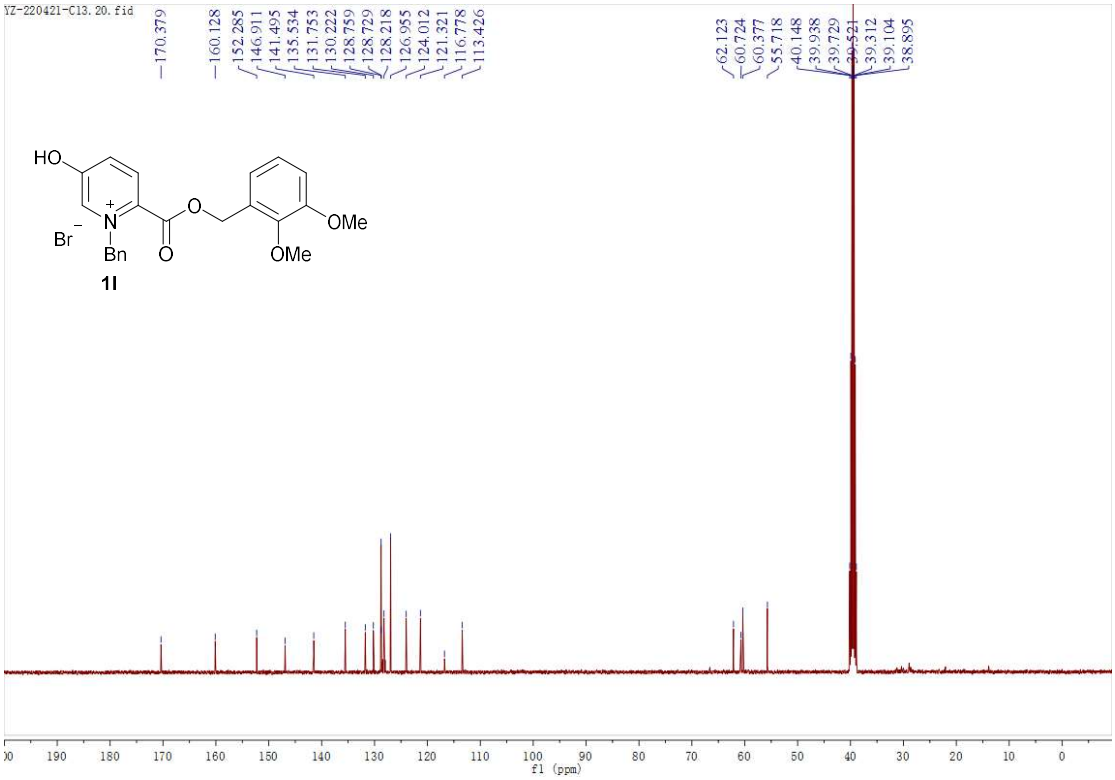
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1k



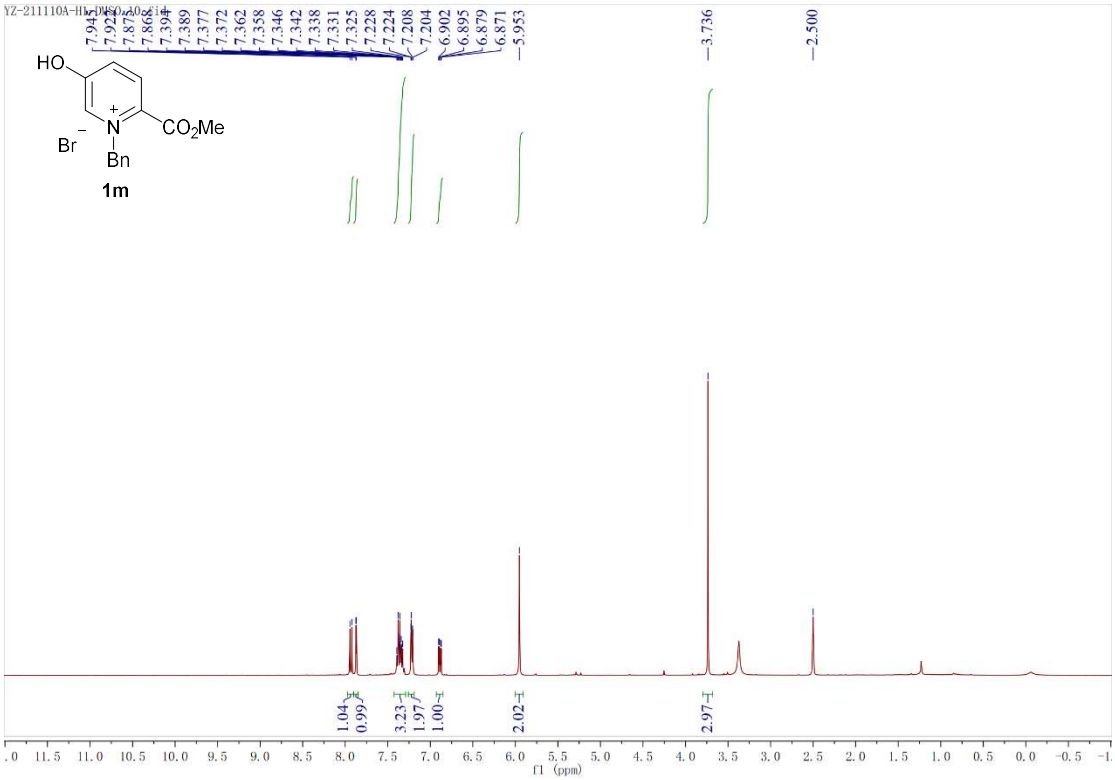
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1k



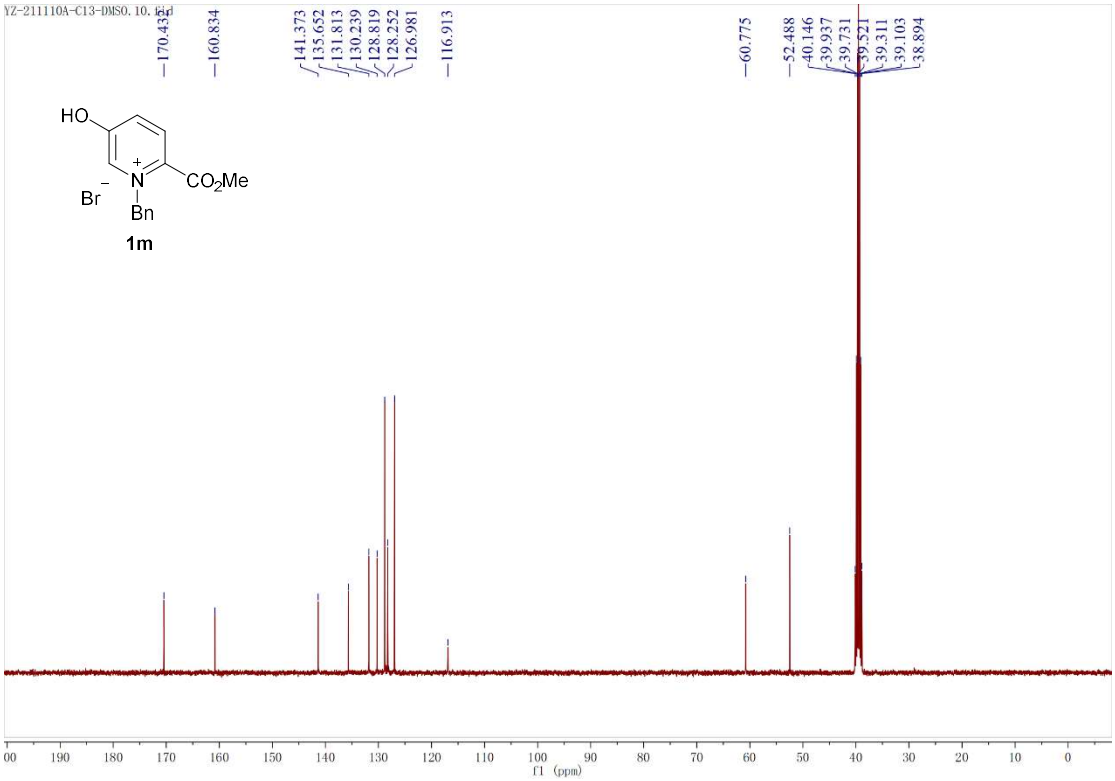
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1l



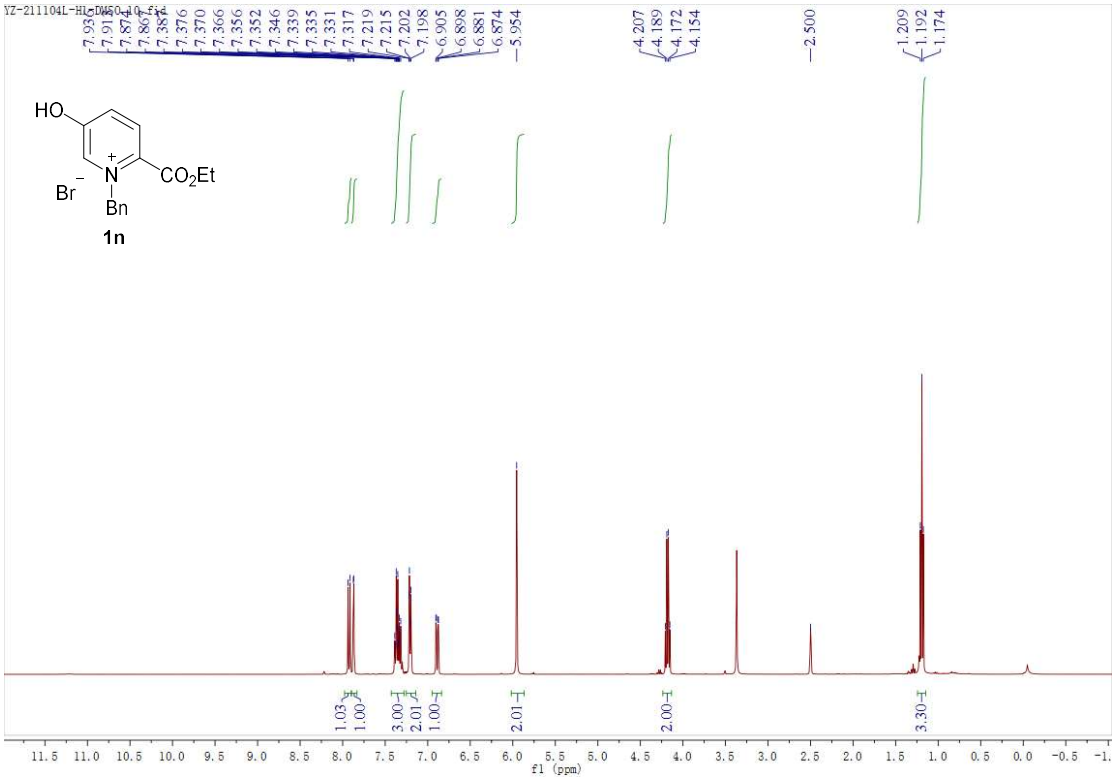
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1l



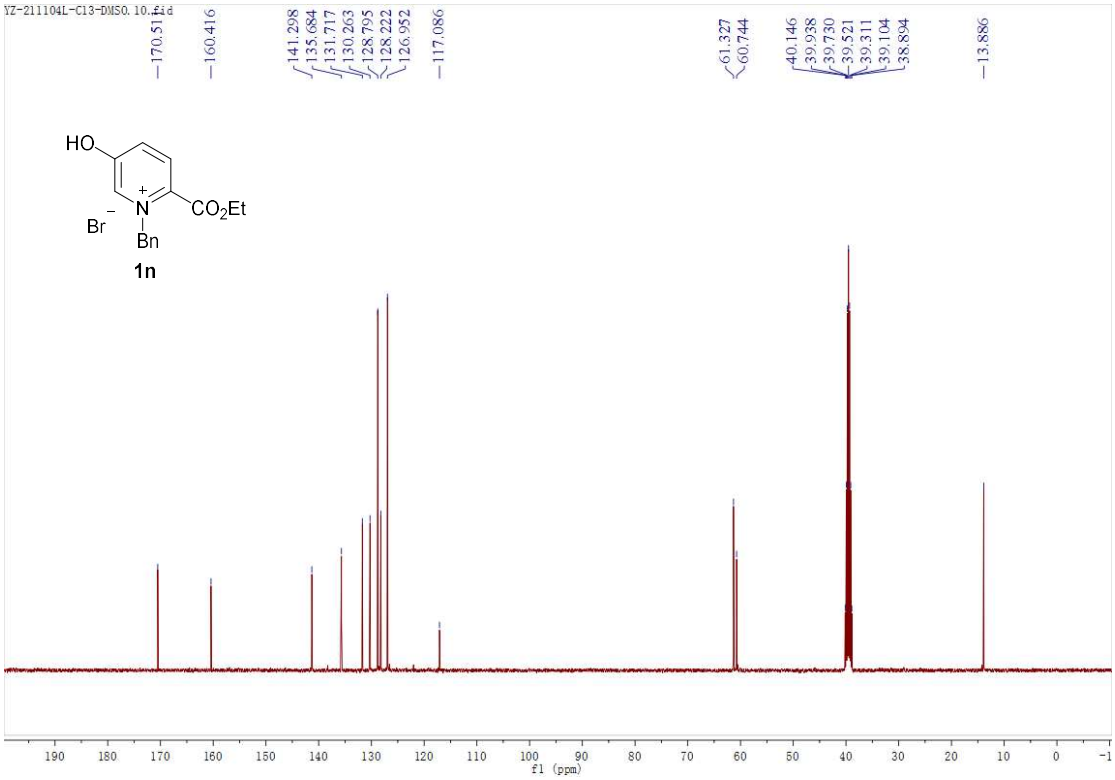
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1m



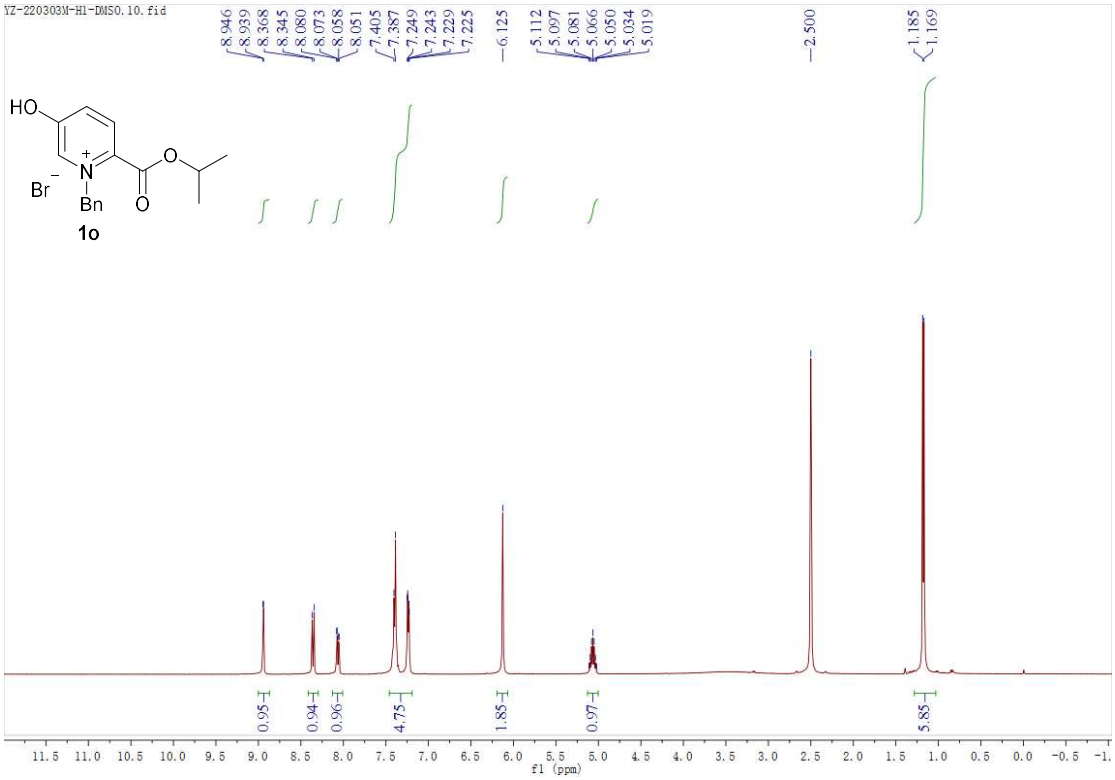
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1m



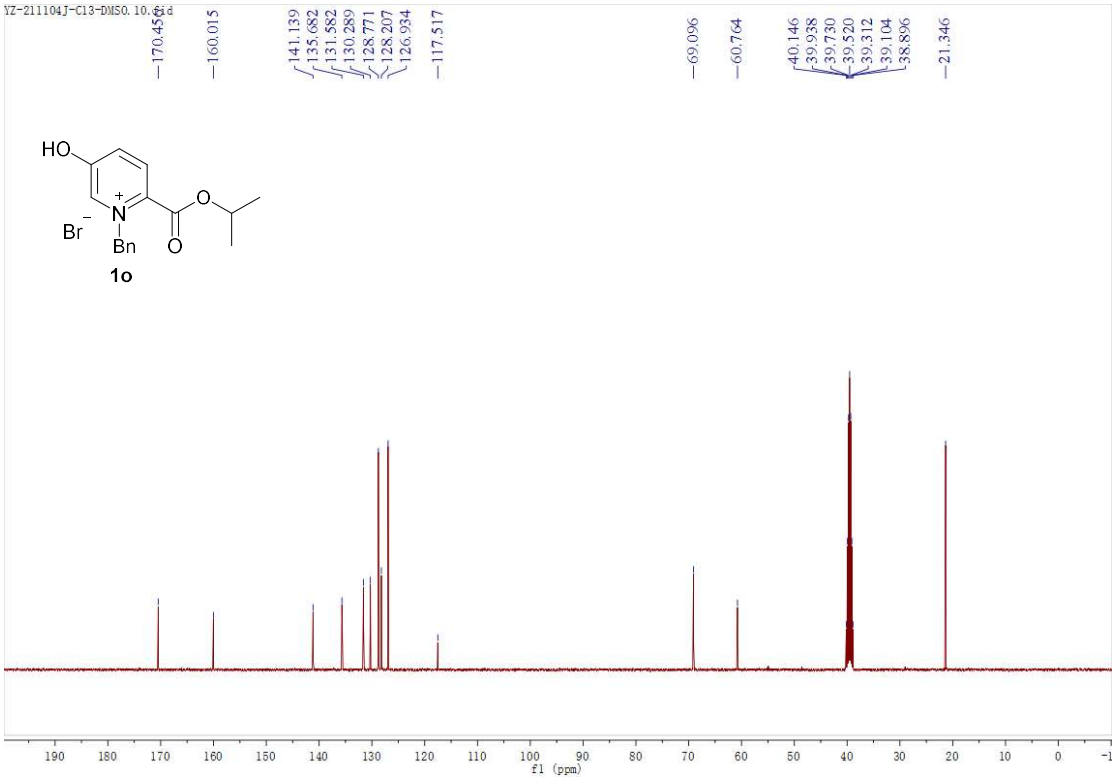
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1n



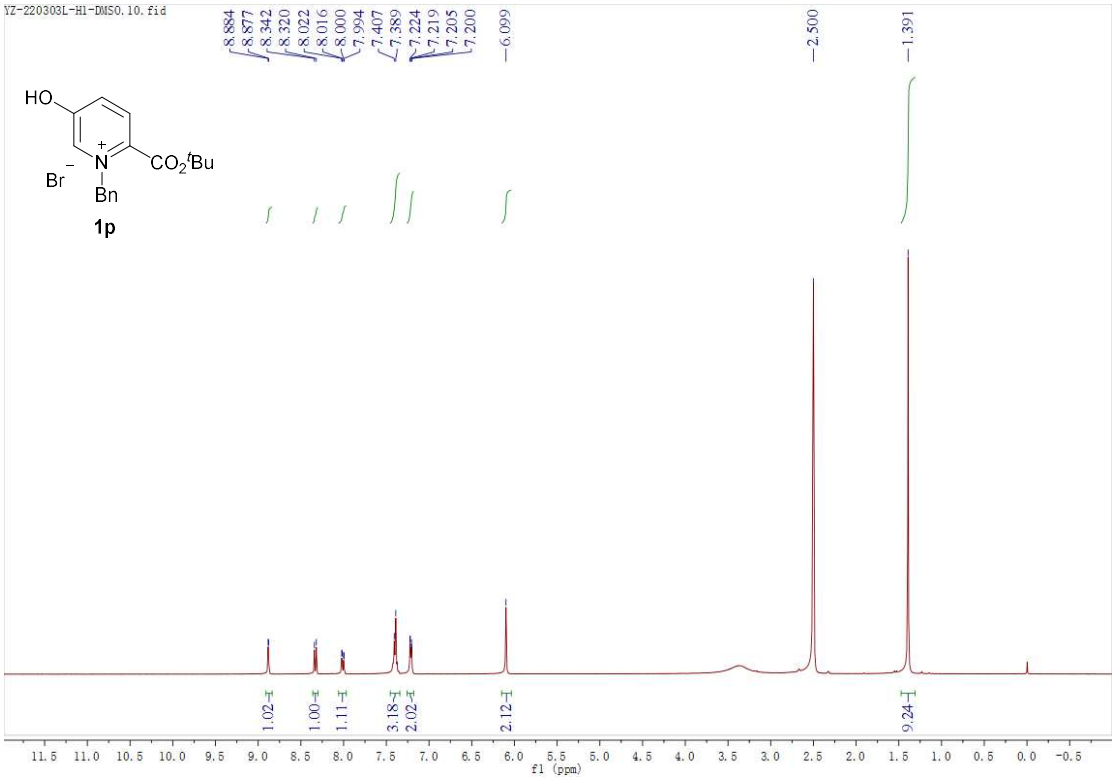
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1n



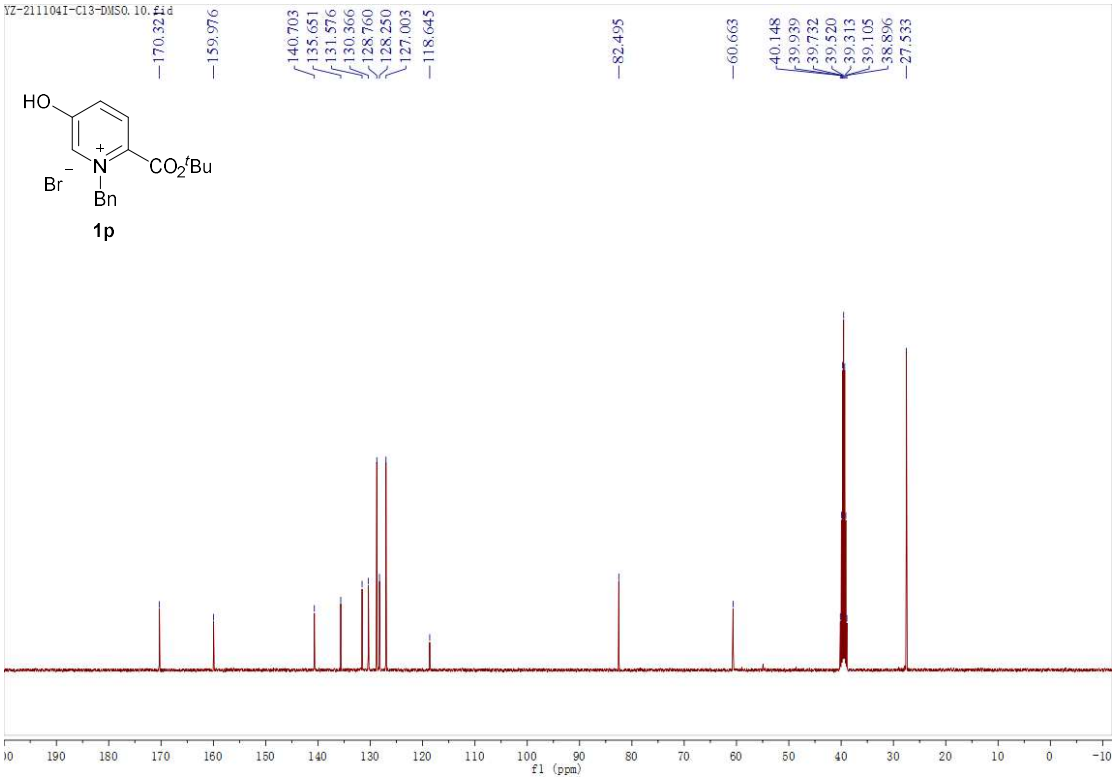
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1o



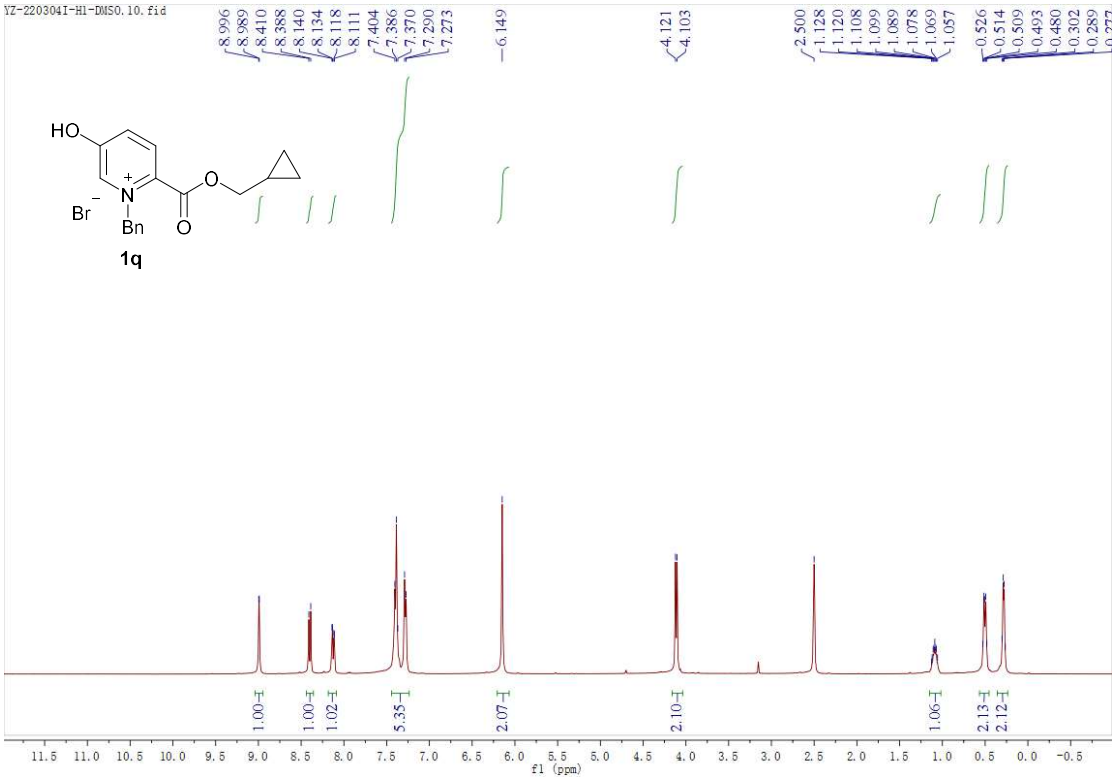
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1o



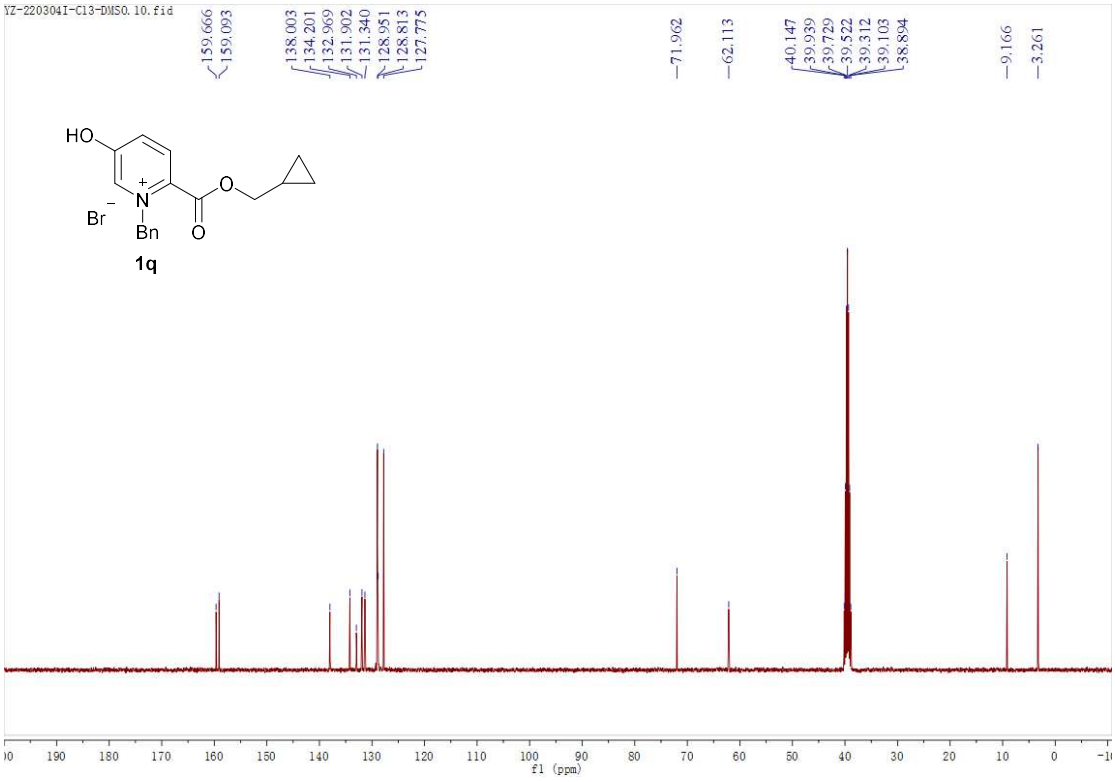
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1p



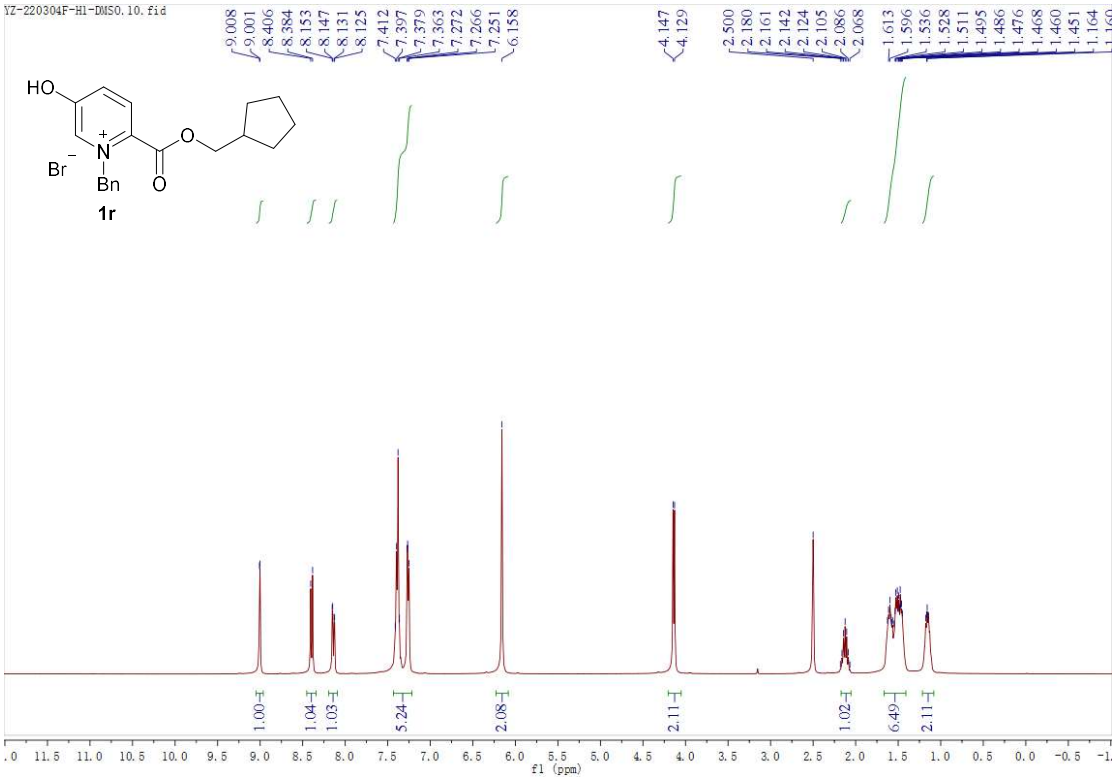
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1p



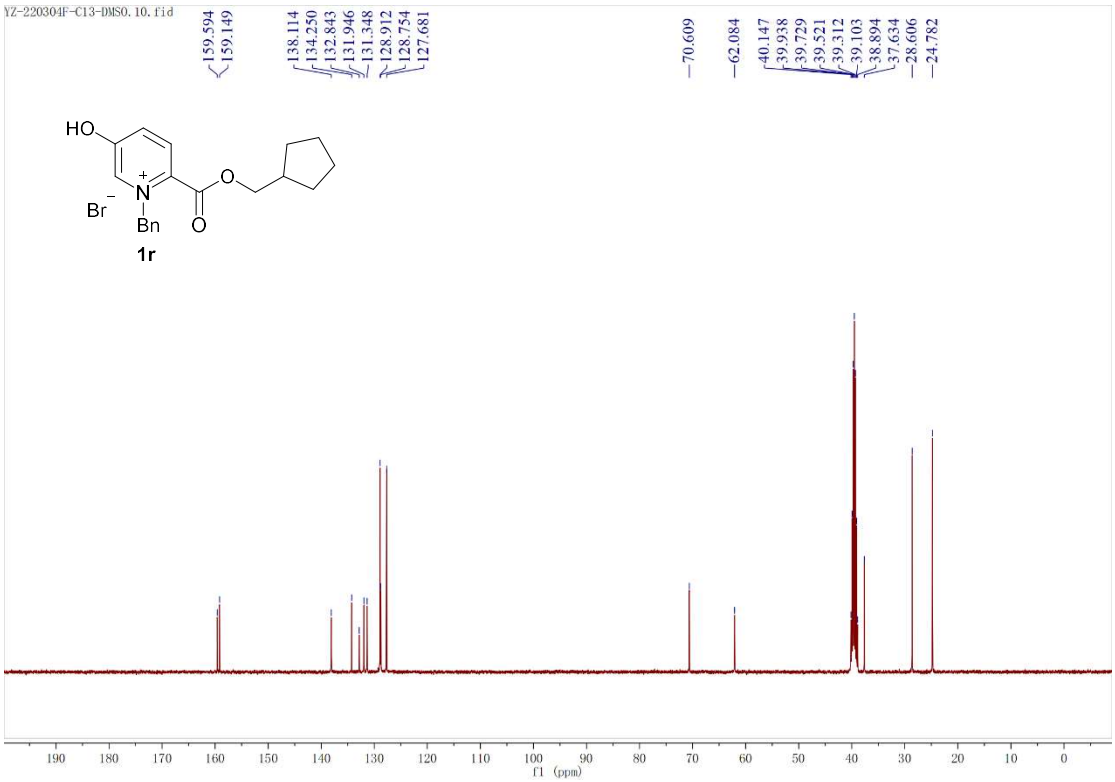
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1q



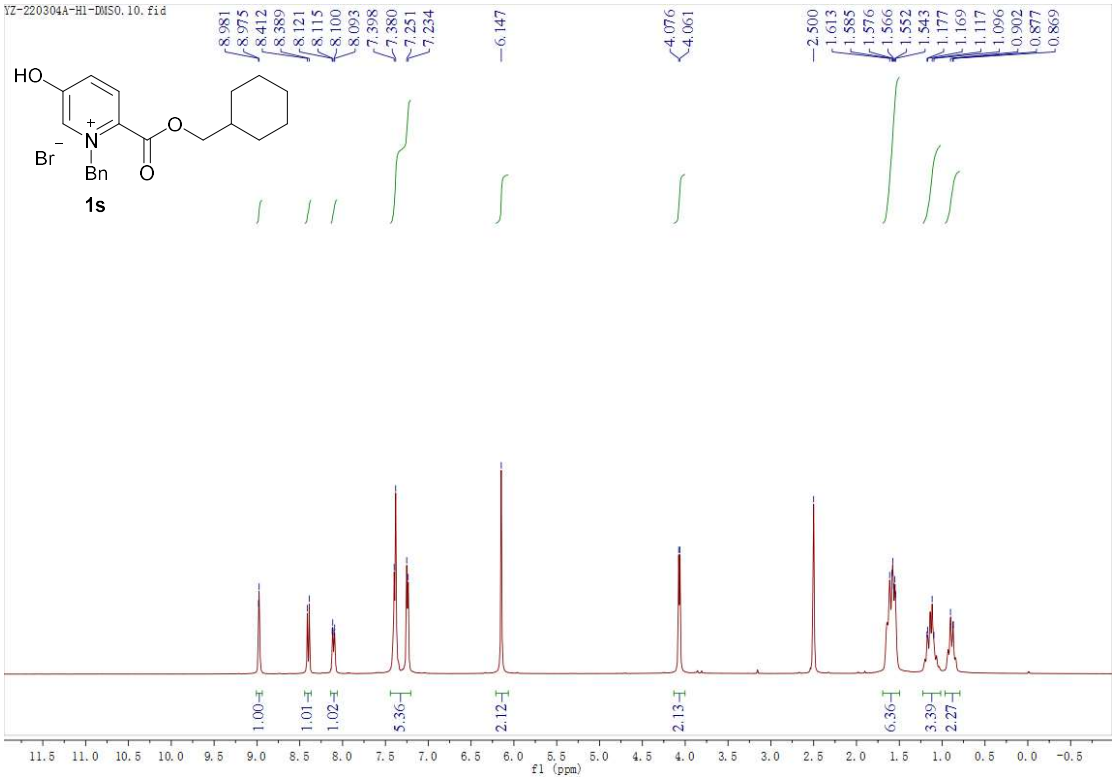
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1q



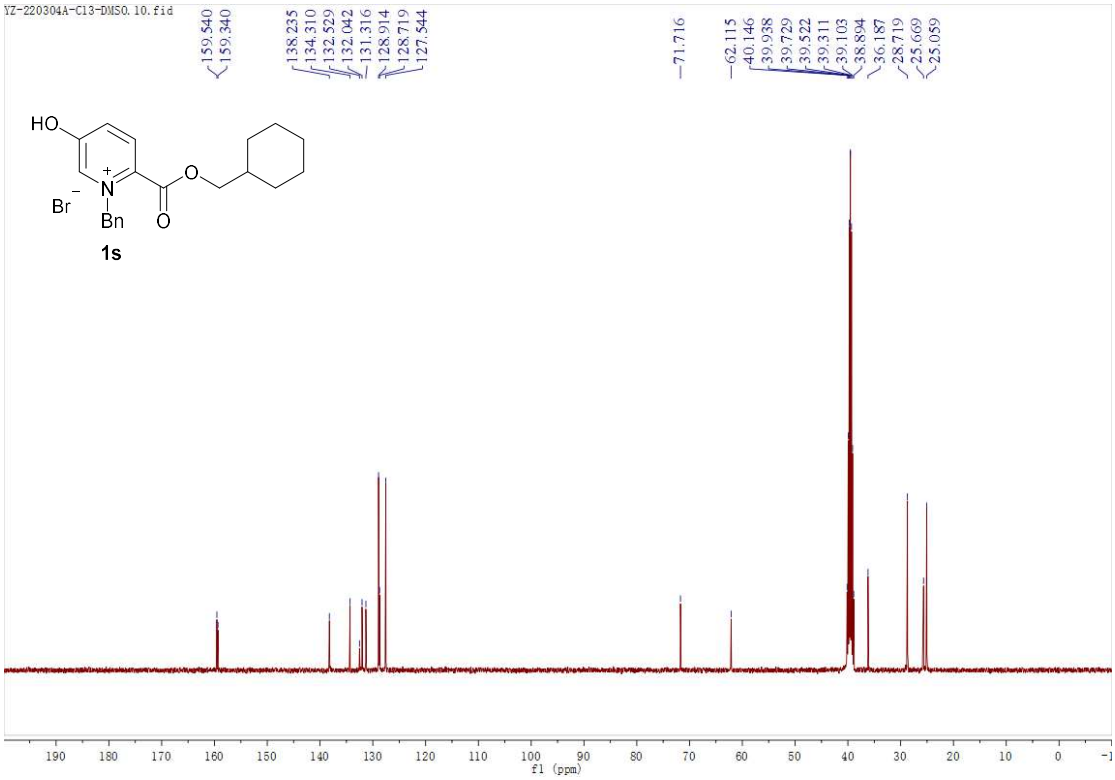
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1r



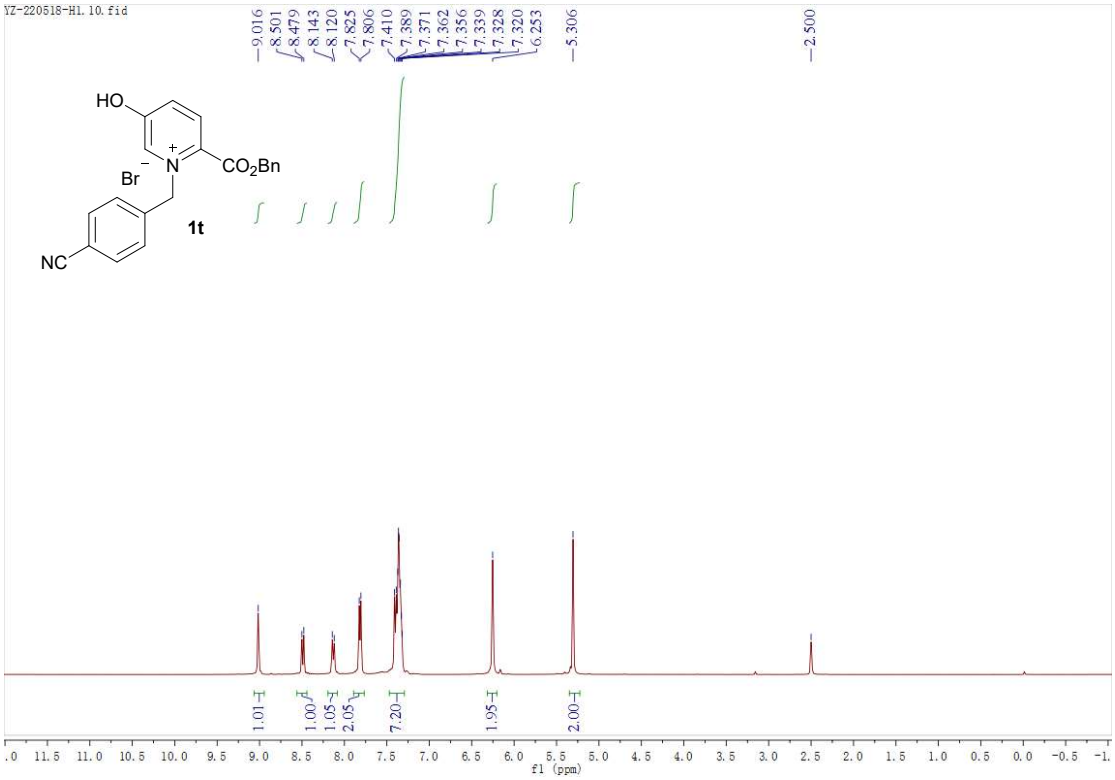
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1r



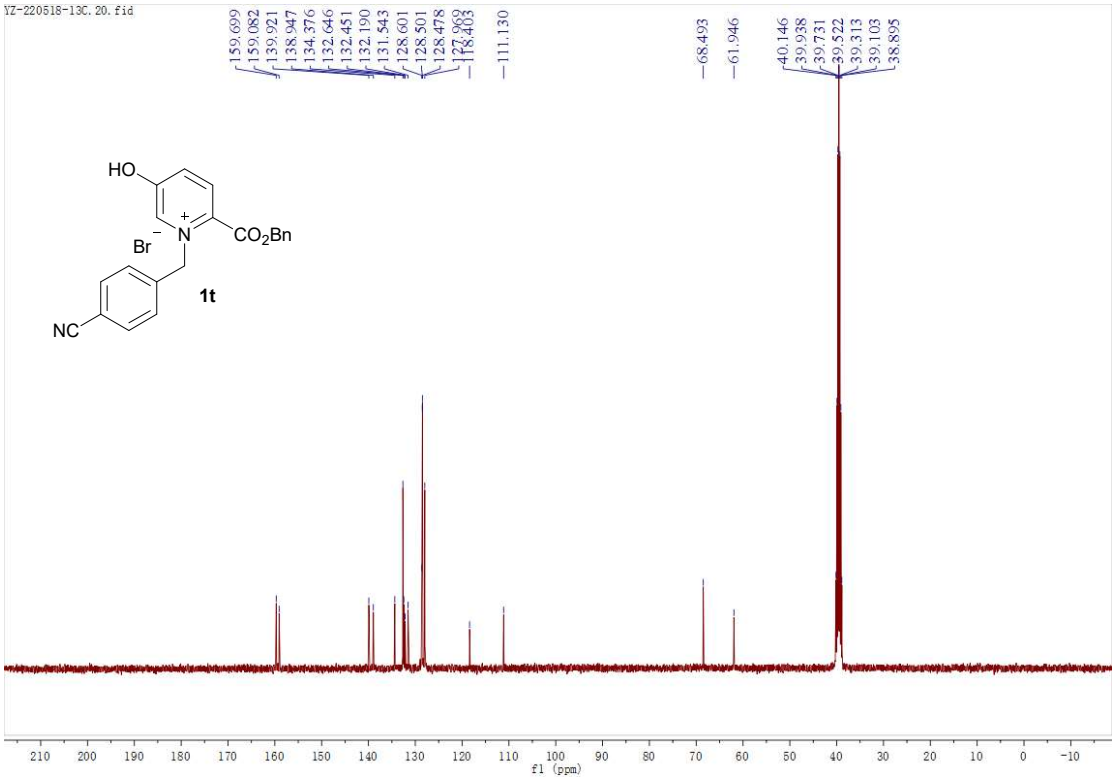
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1s



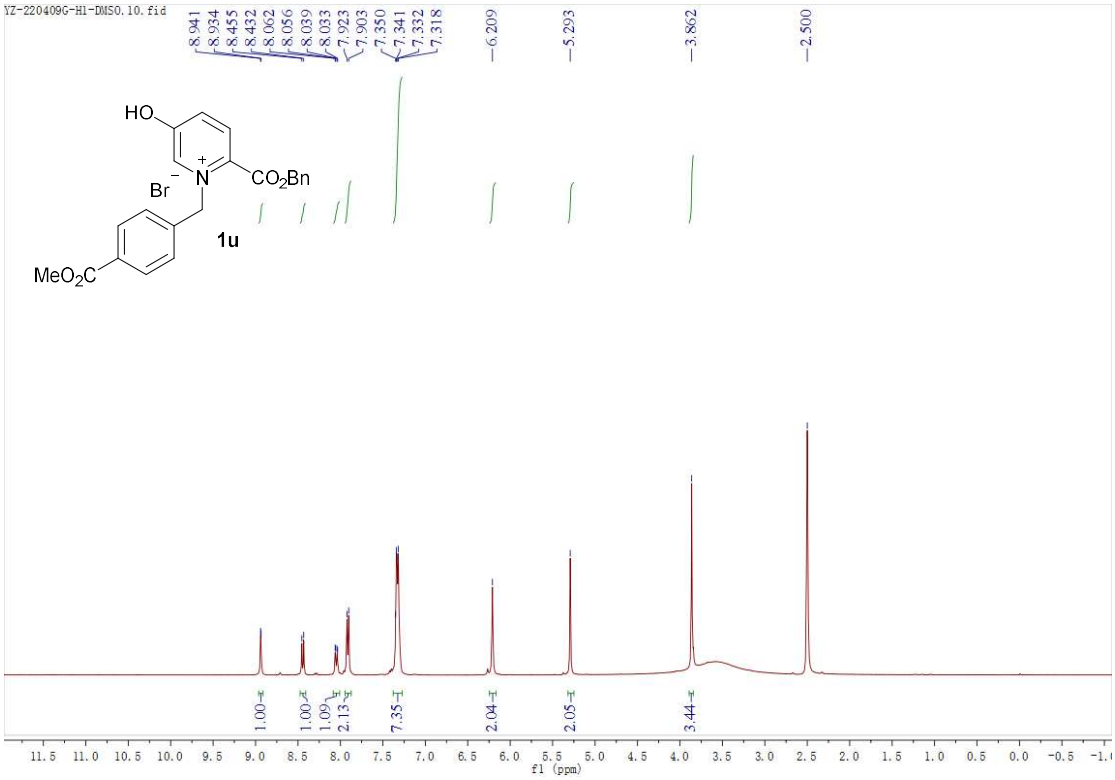
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1s



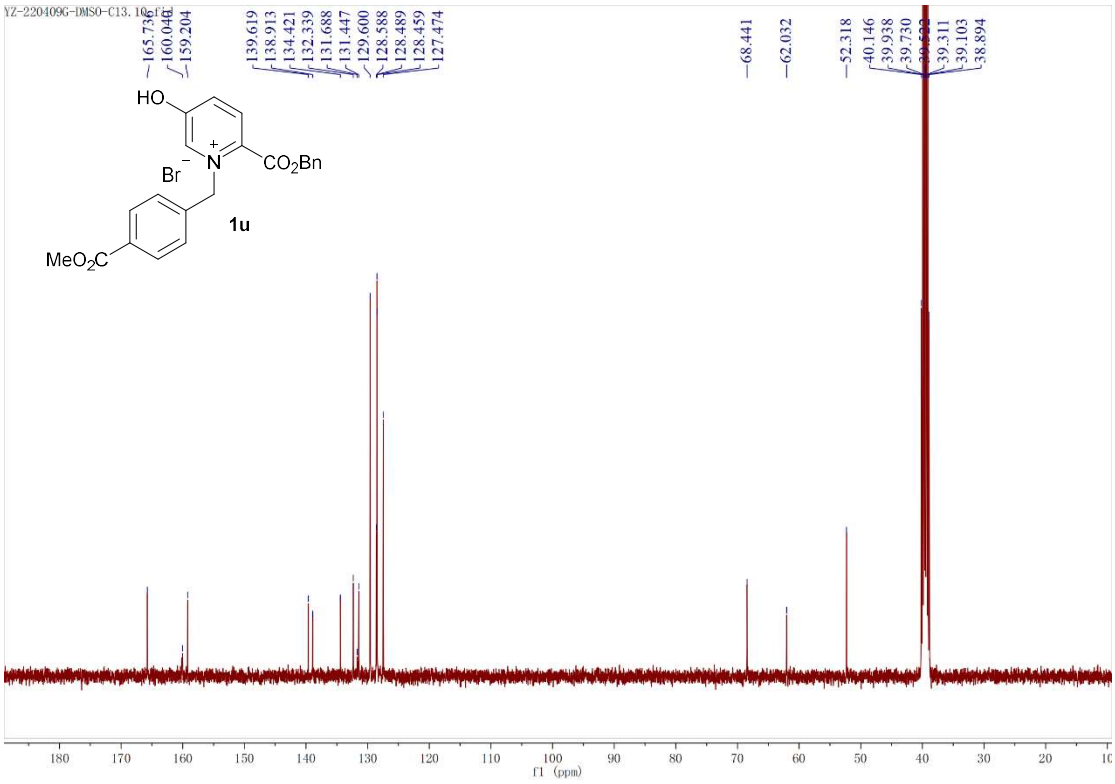
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1t



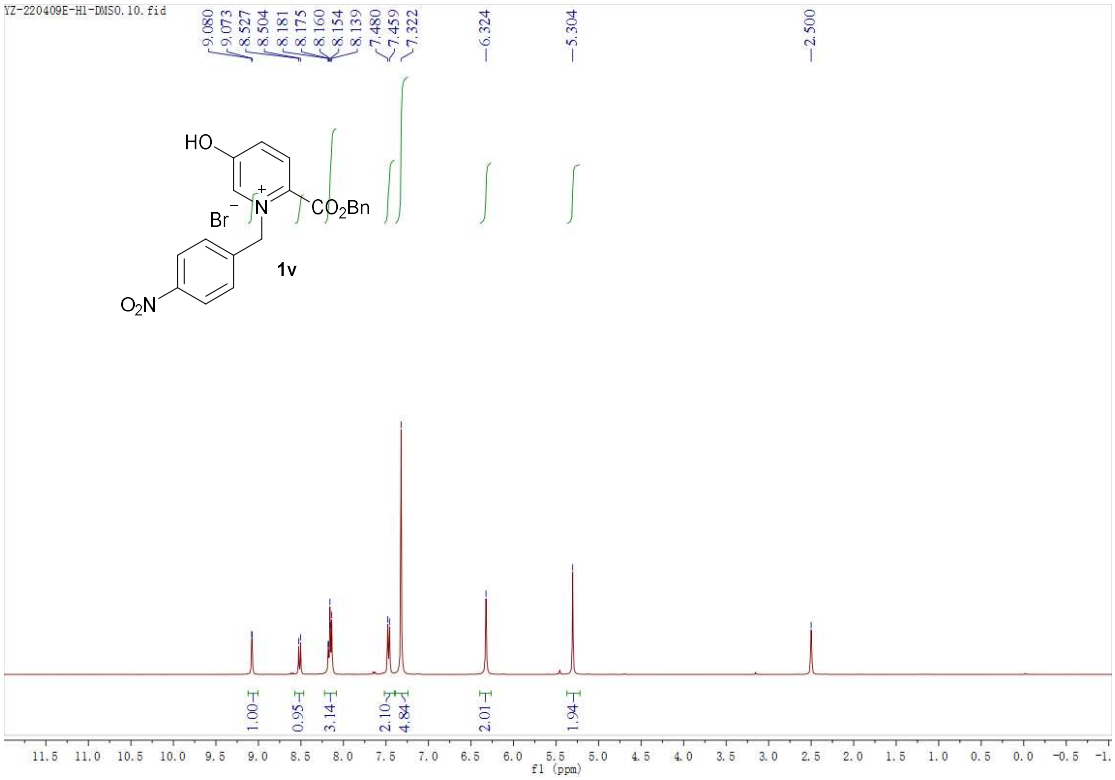
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1t



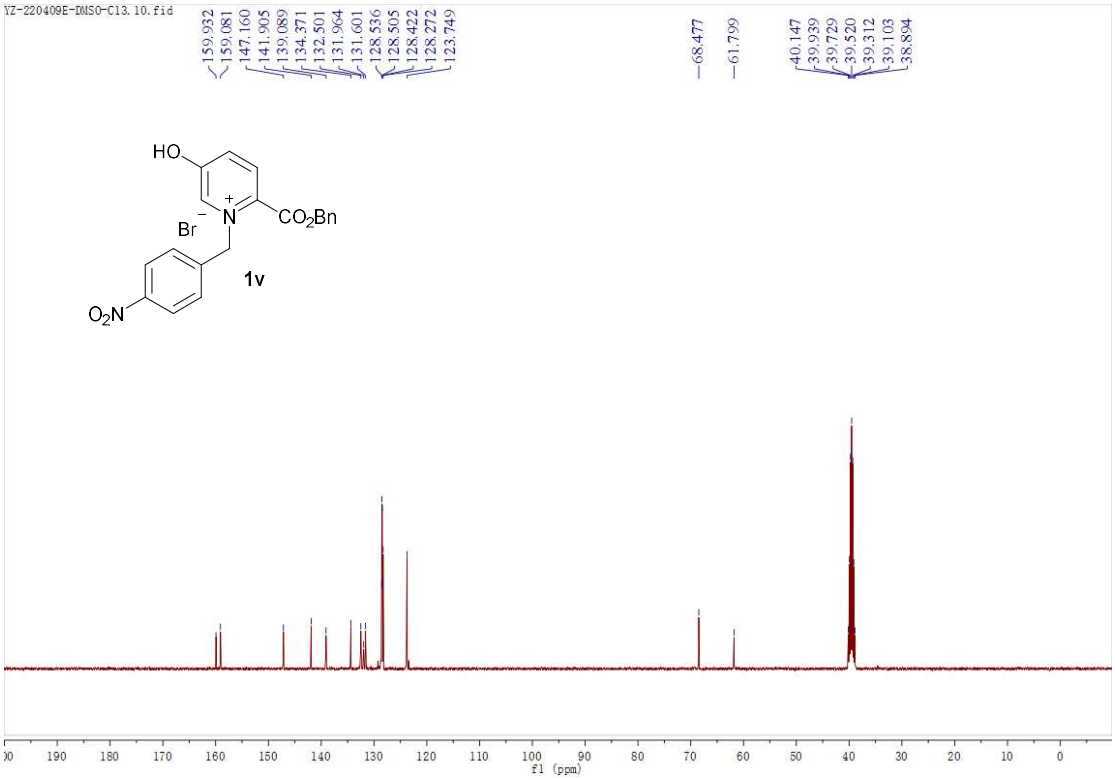
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1u



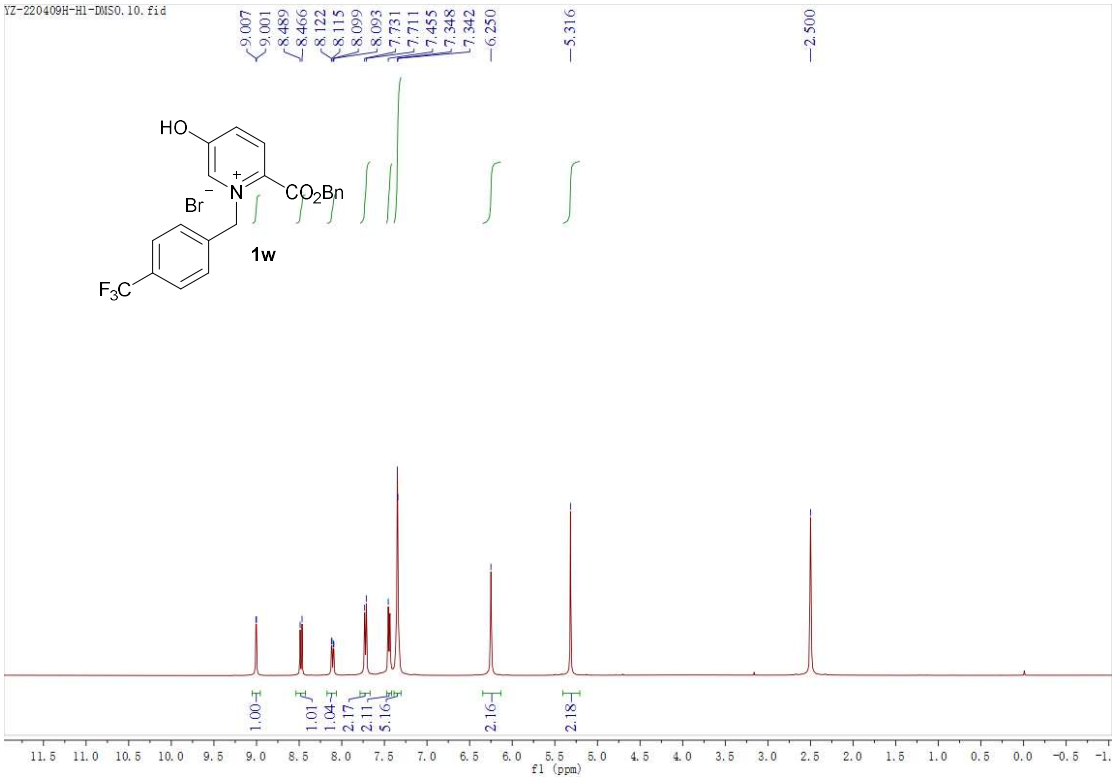
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1u



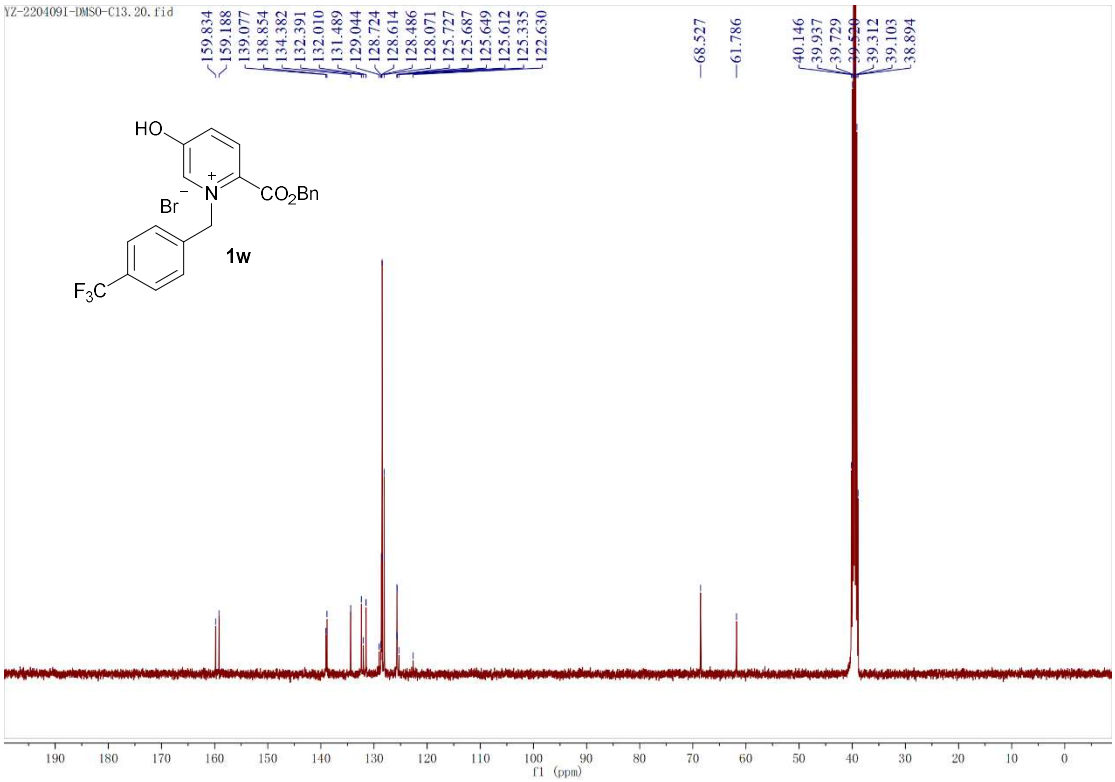
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1v



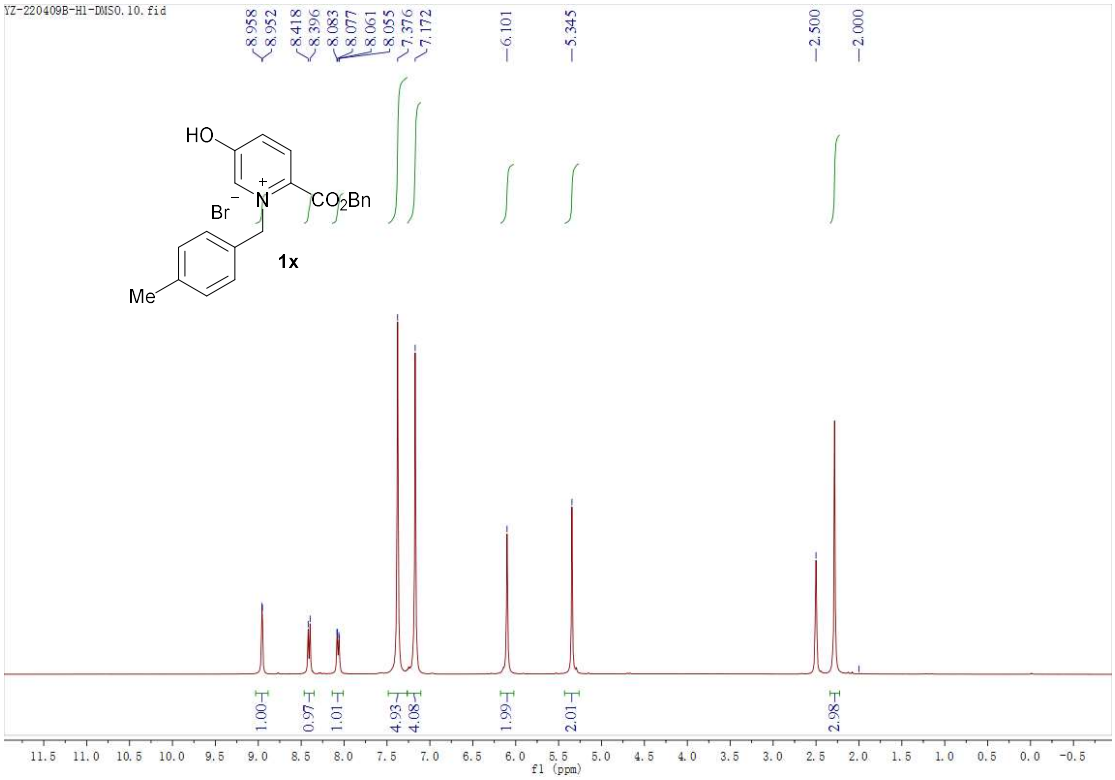
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1v



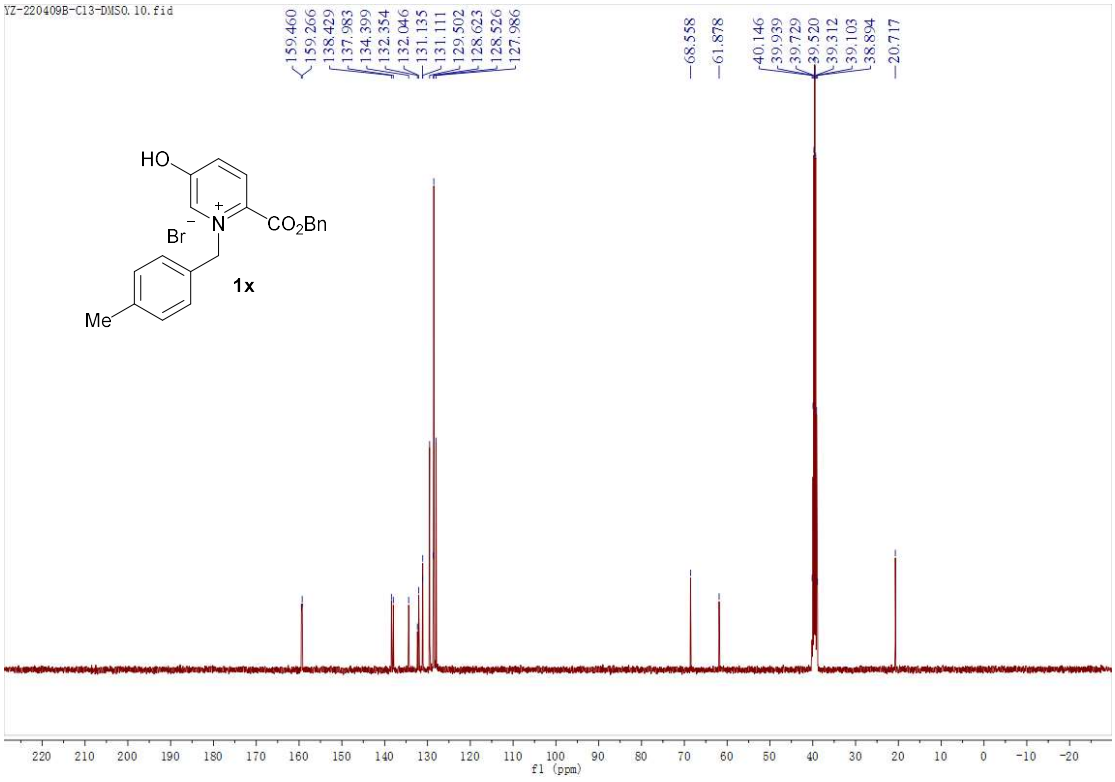
[1]H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1w



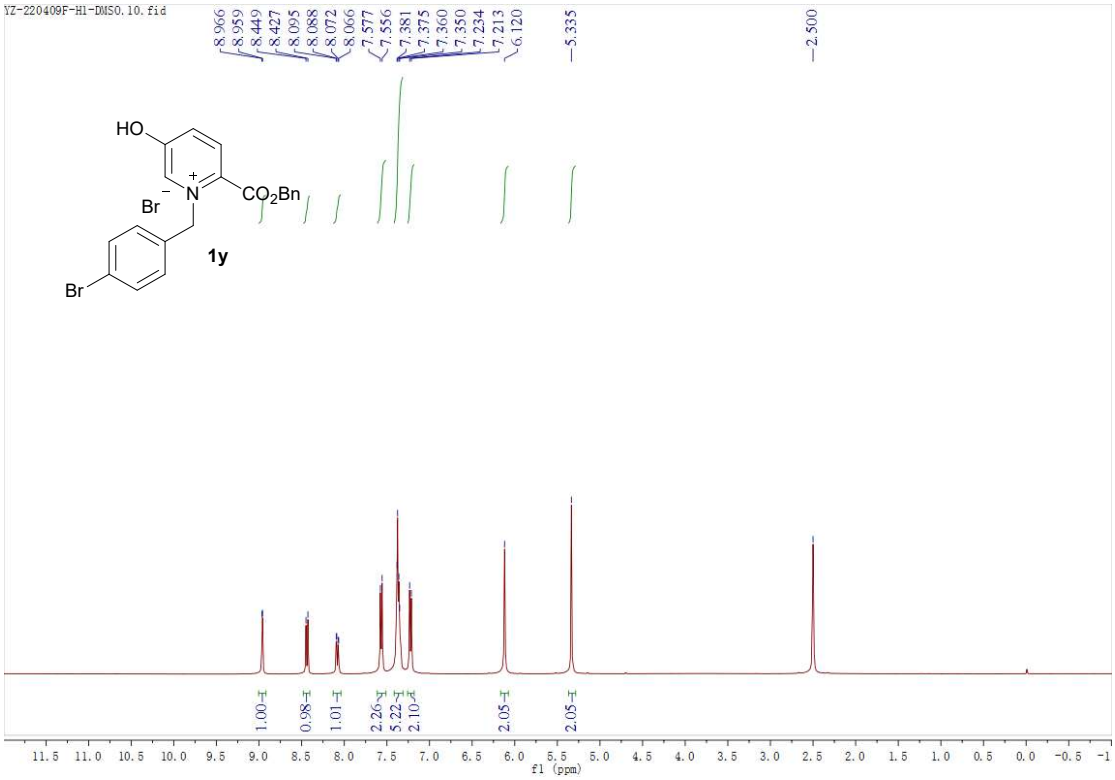
[13]C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1w



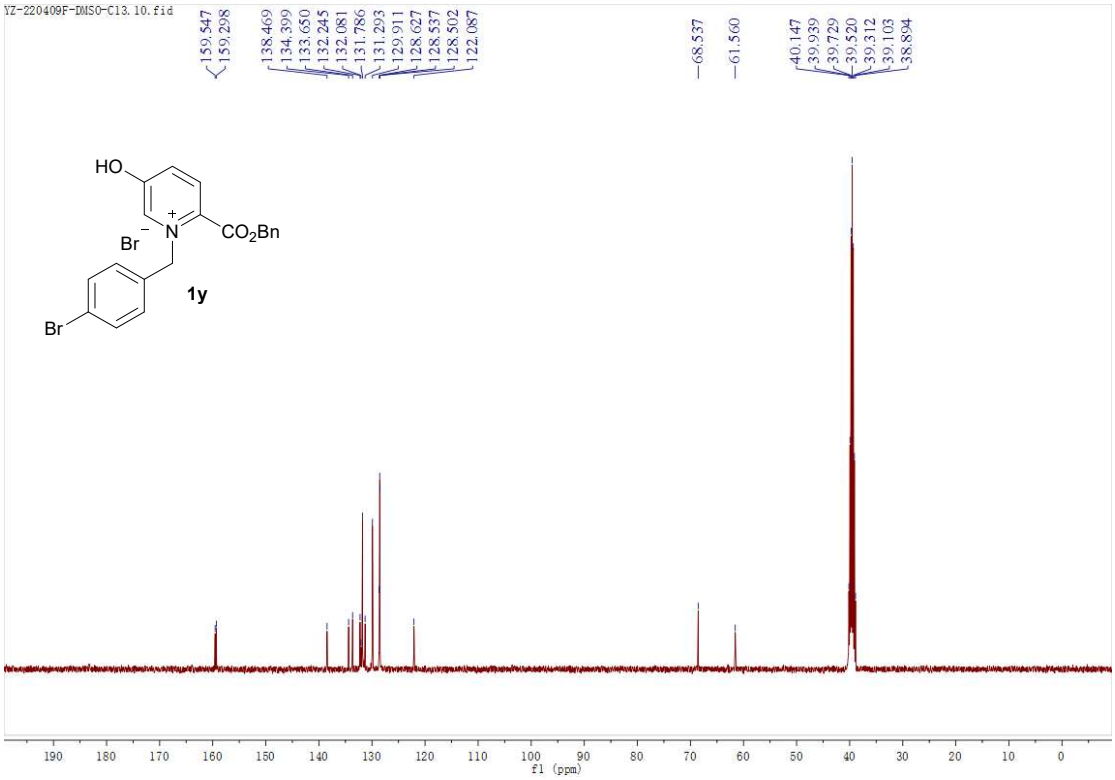
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1x



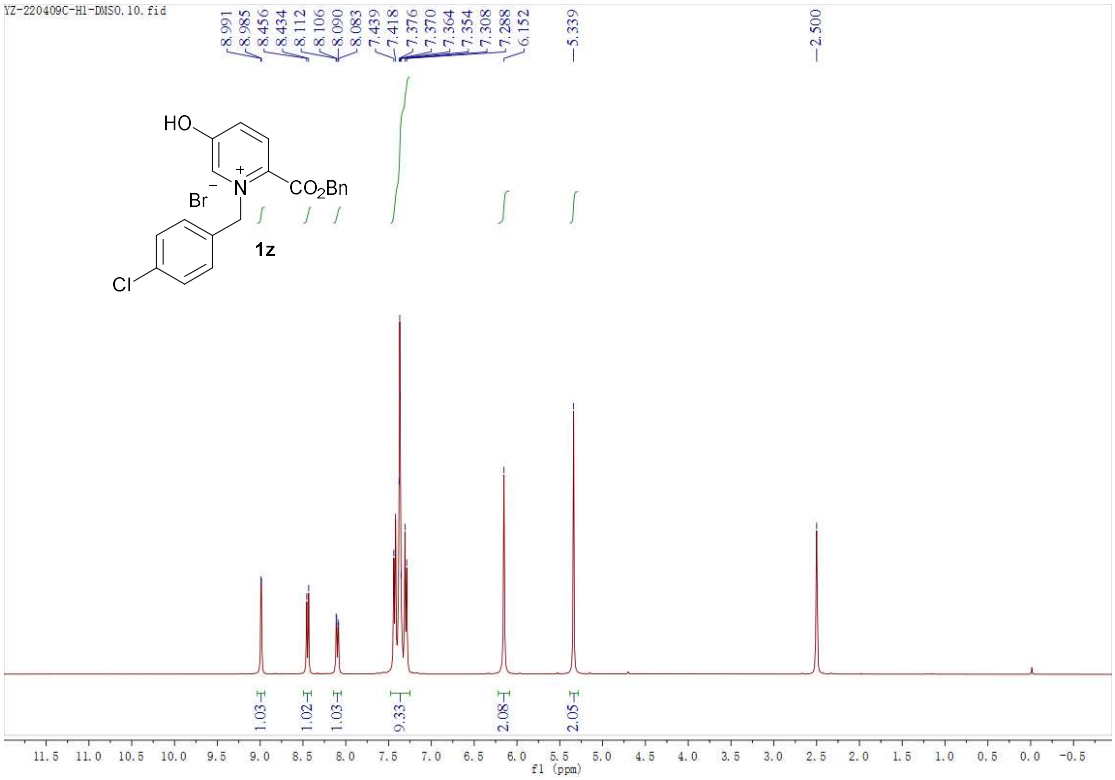
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1x



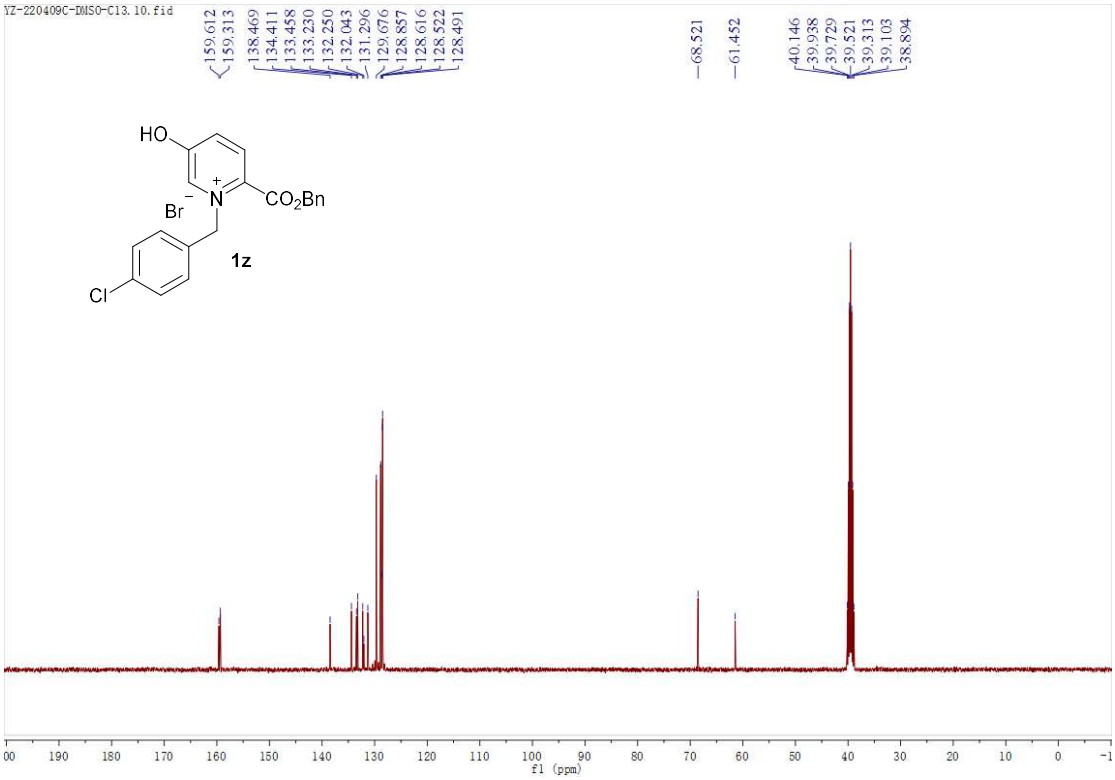
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1y



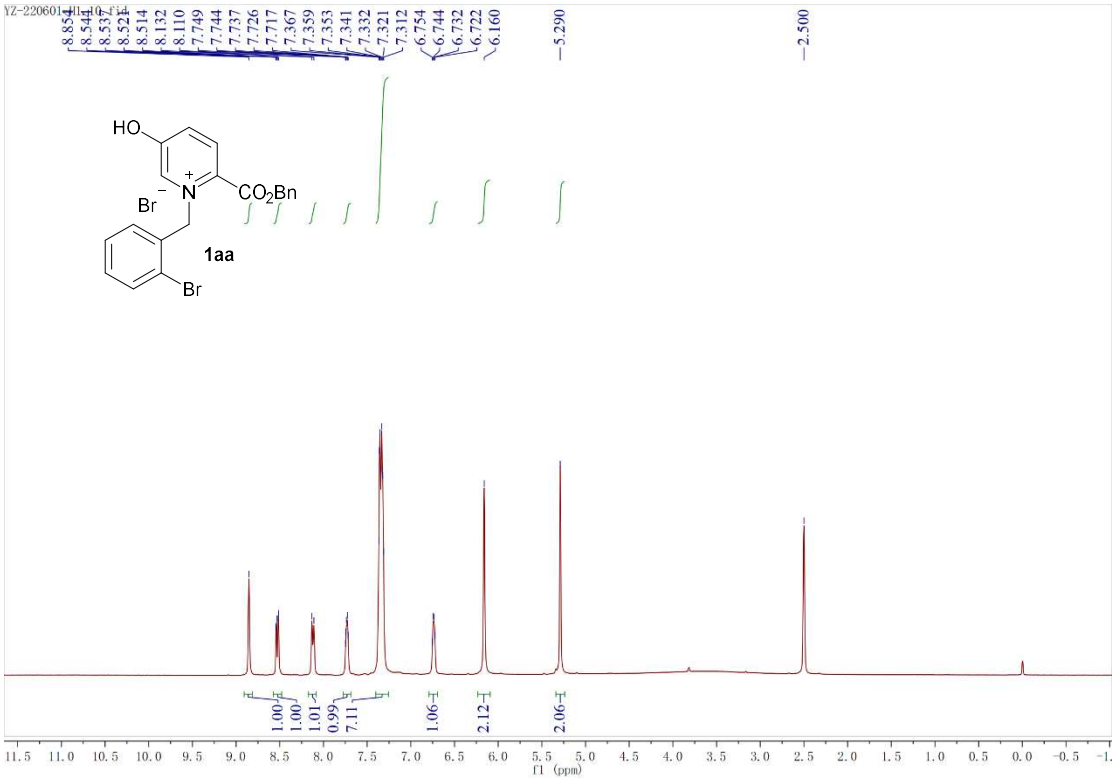
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1y



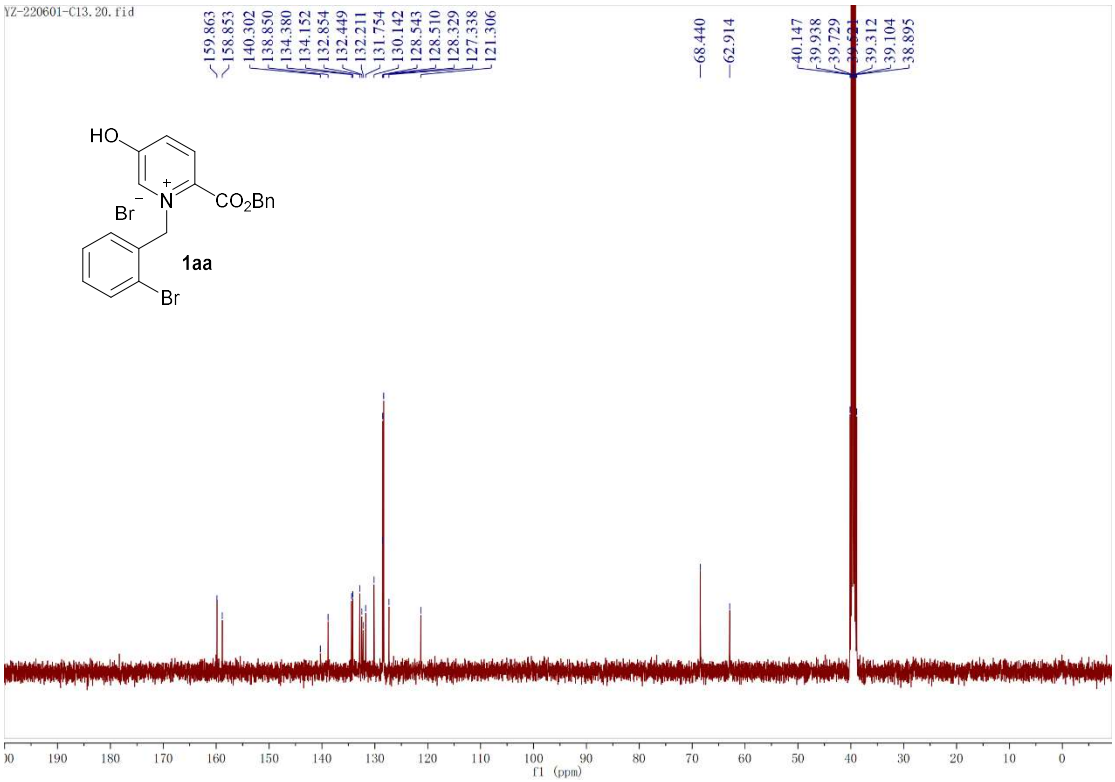
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1z



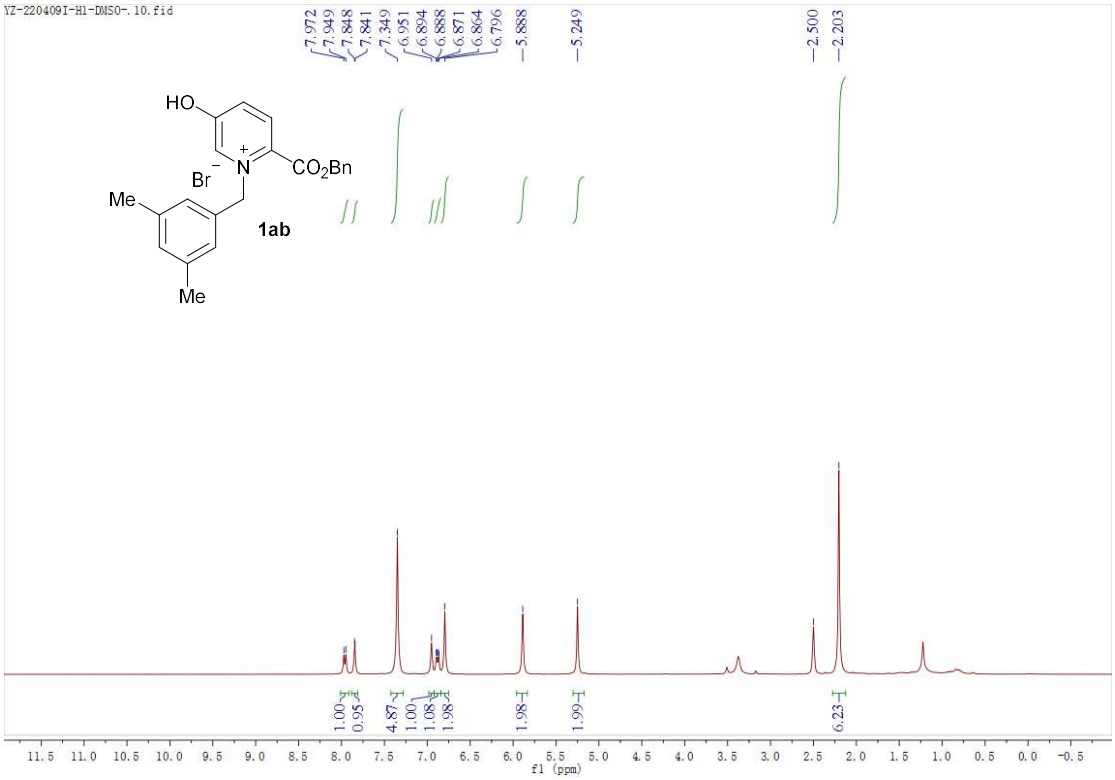
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1z



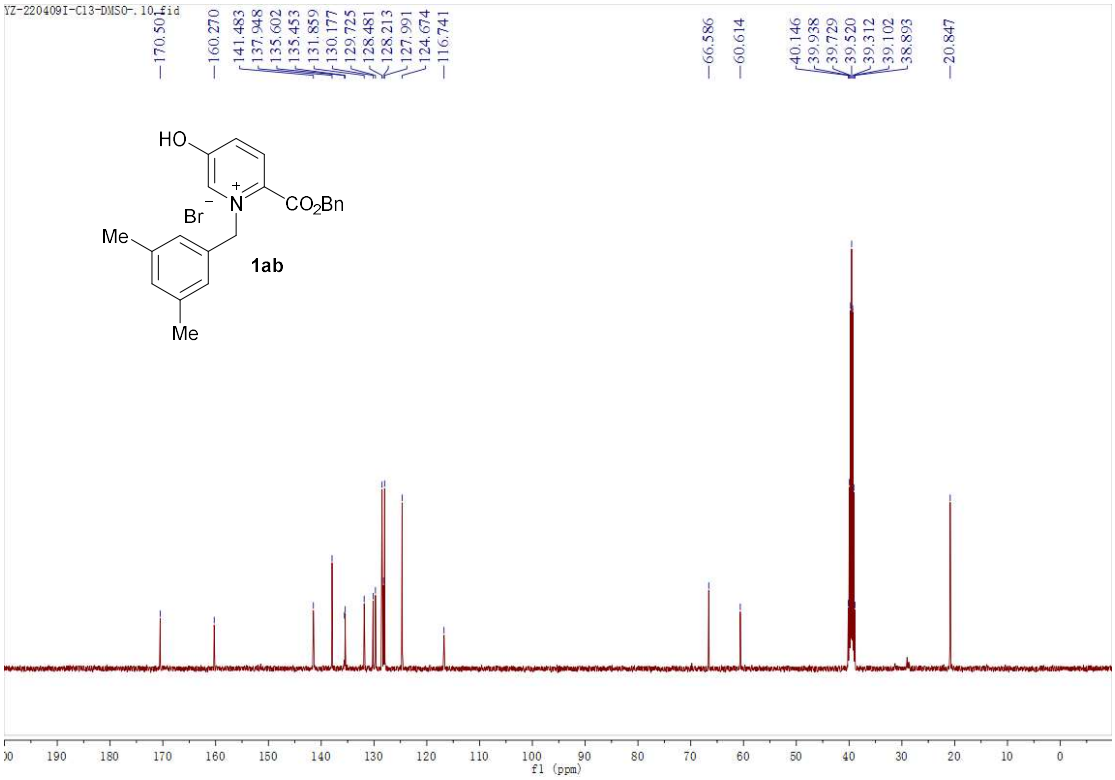
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1aa



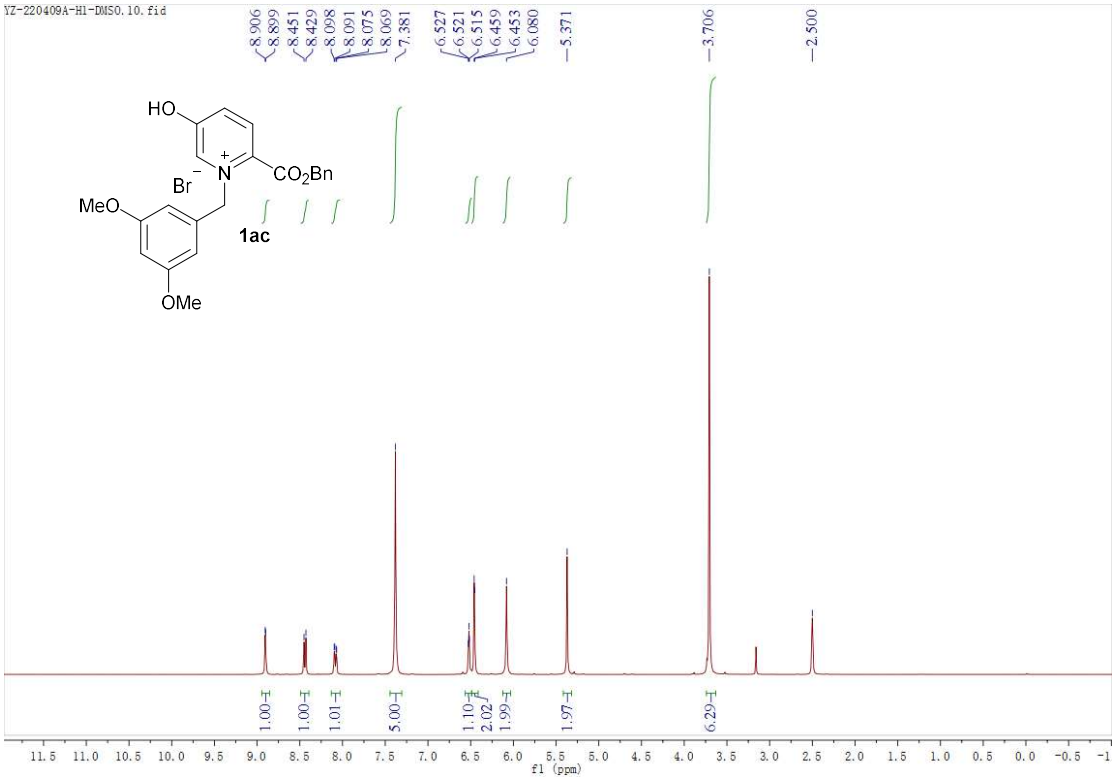
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1aa



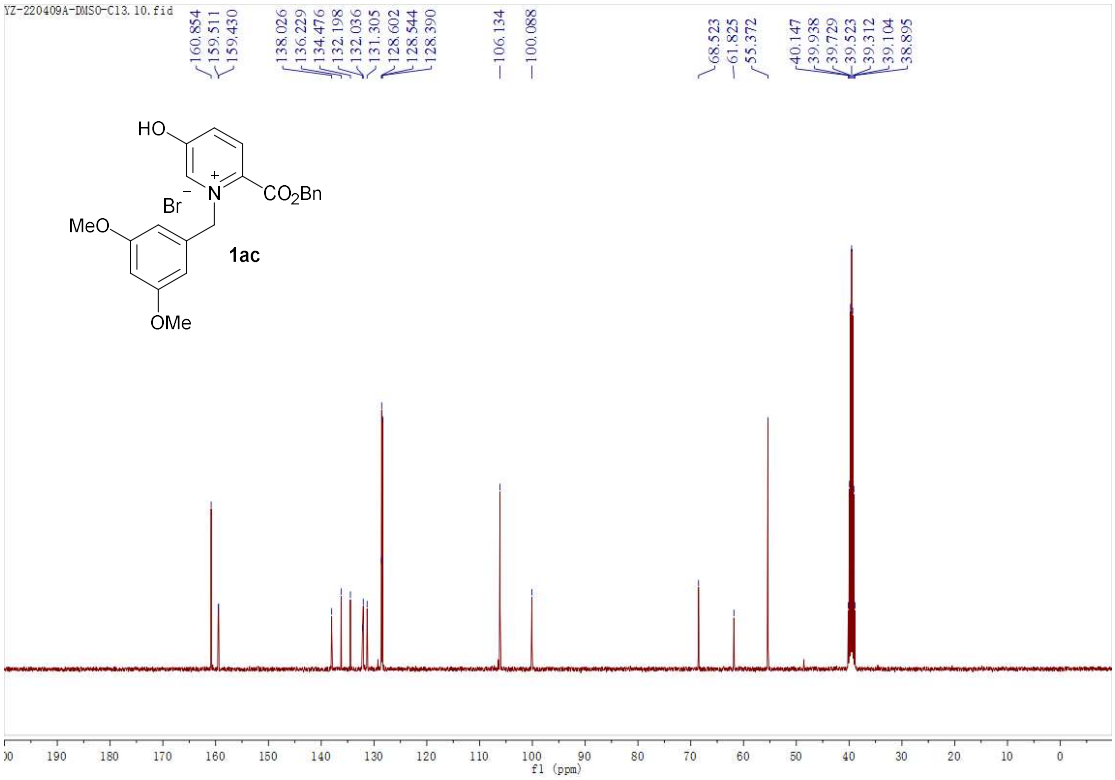
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1ab



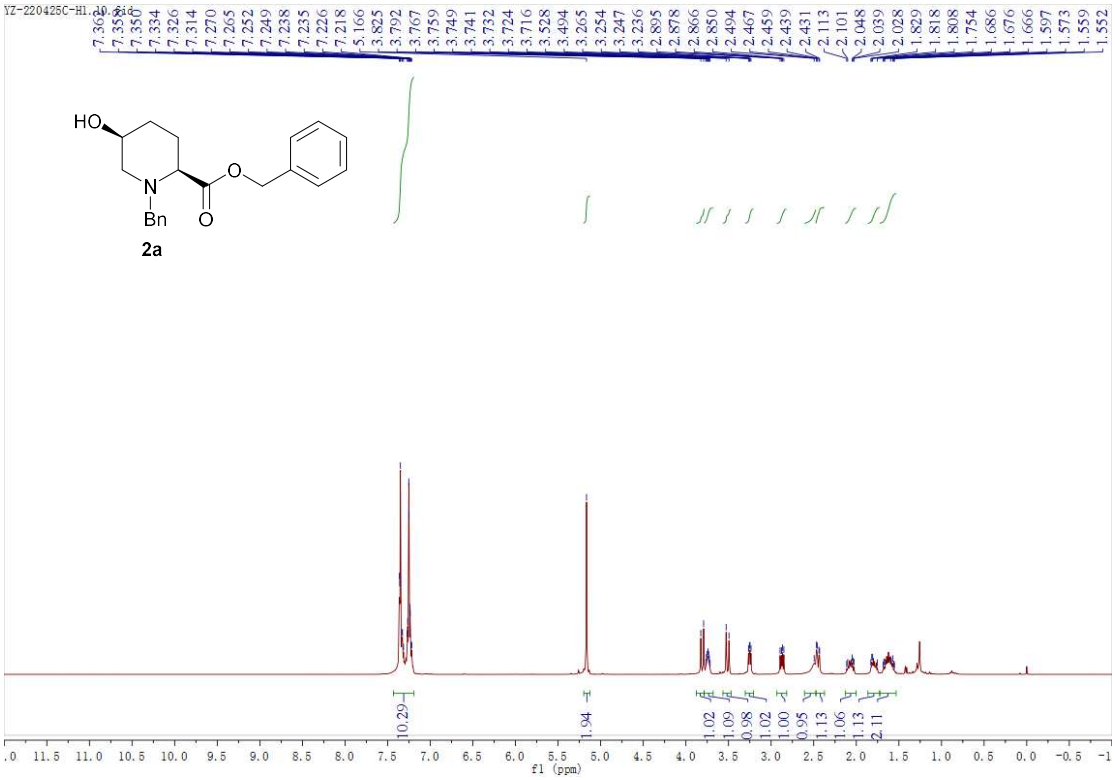
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1ab



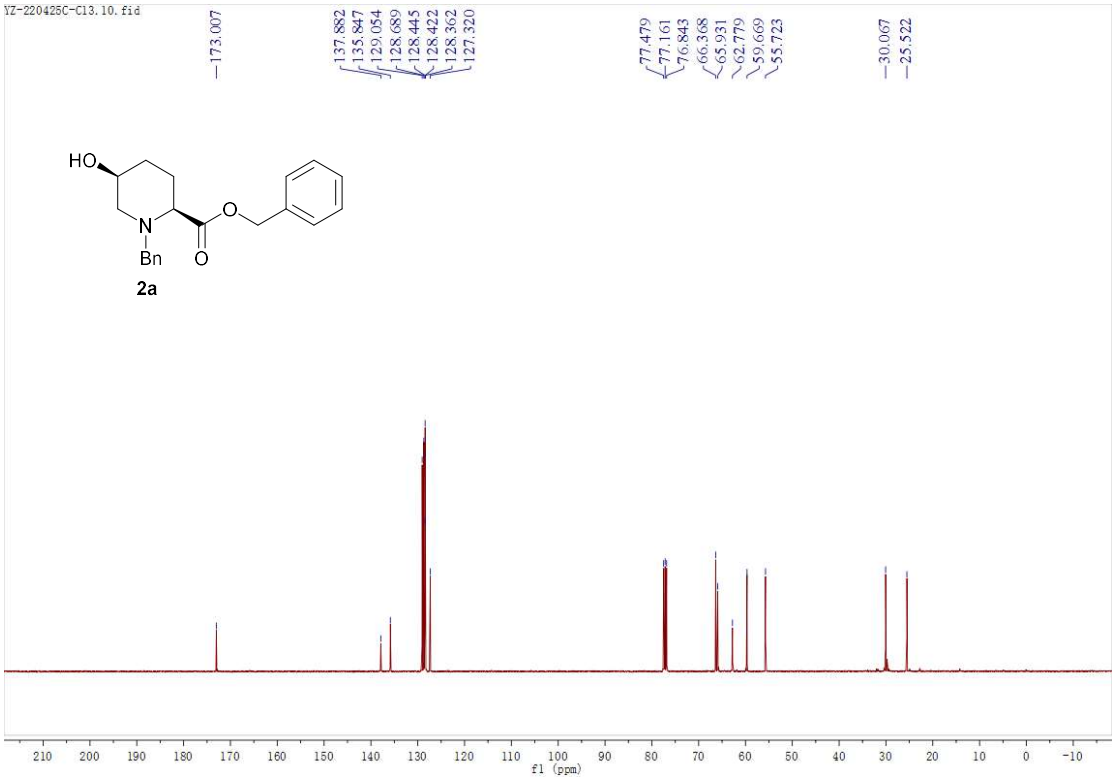
^{1}H-NMR Spectrum (400 MHz, DMSO-d_6) of Compound 1ac



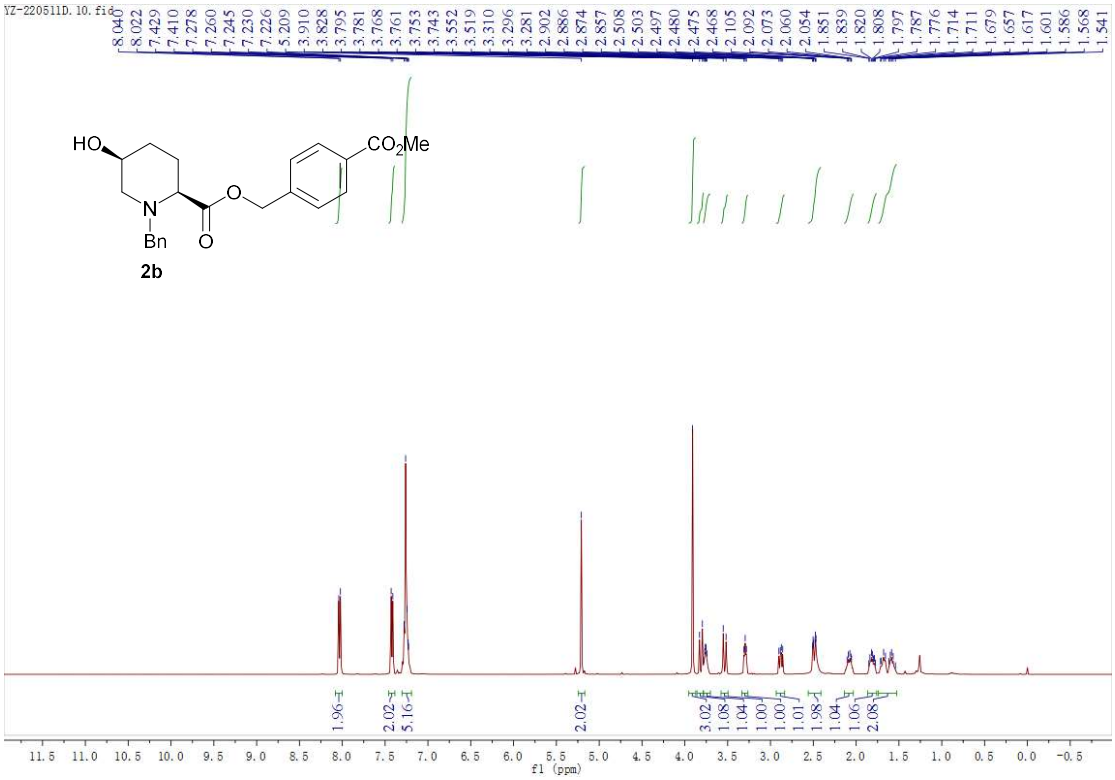
^{13}C-NMR Spectrum (100 MHz, DMSO-d_6) of Compound 1ac



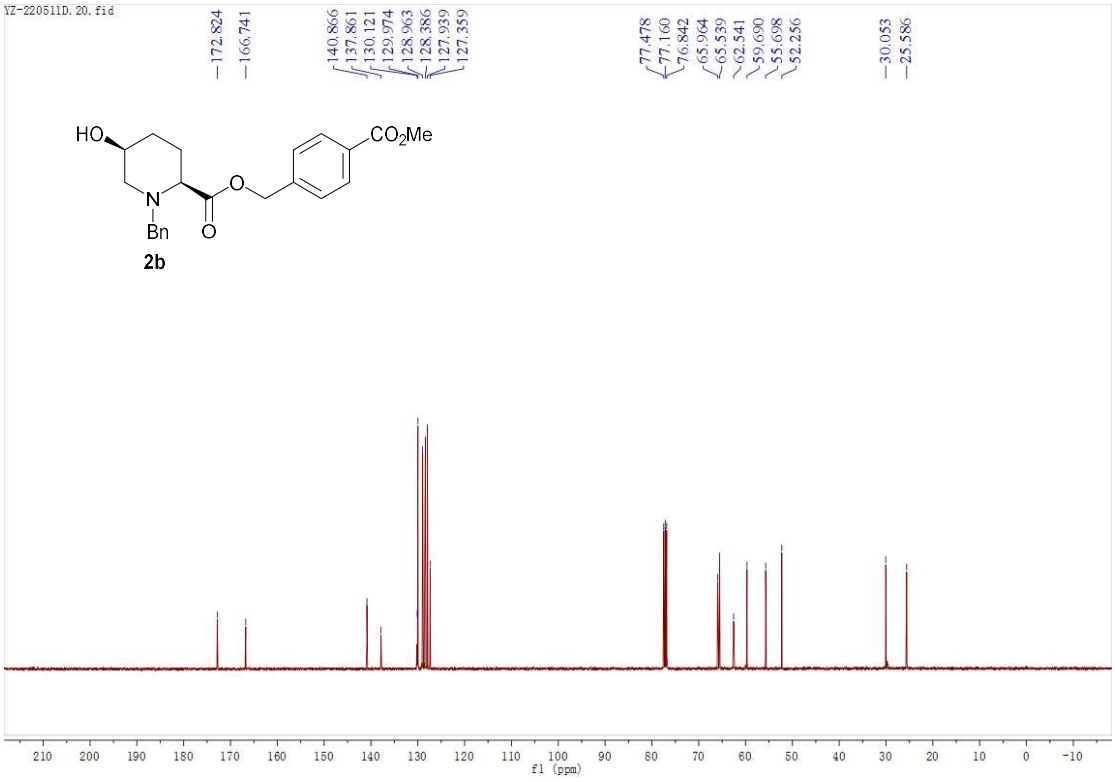
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2a



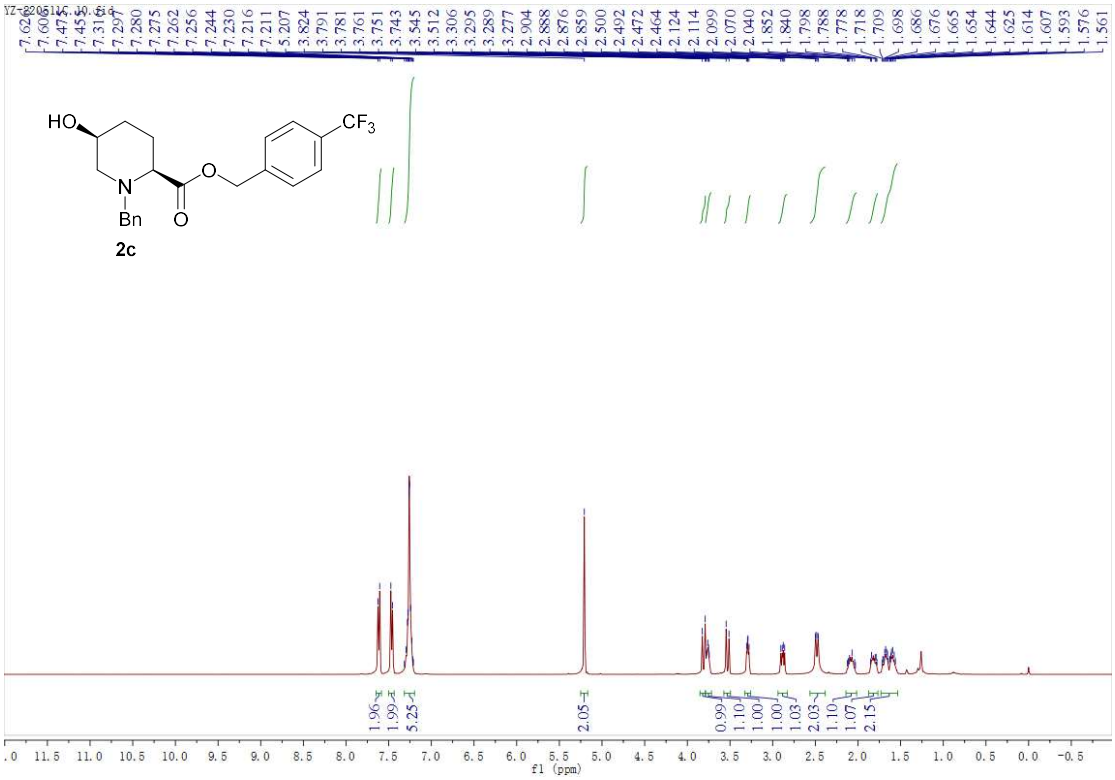
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2a



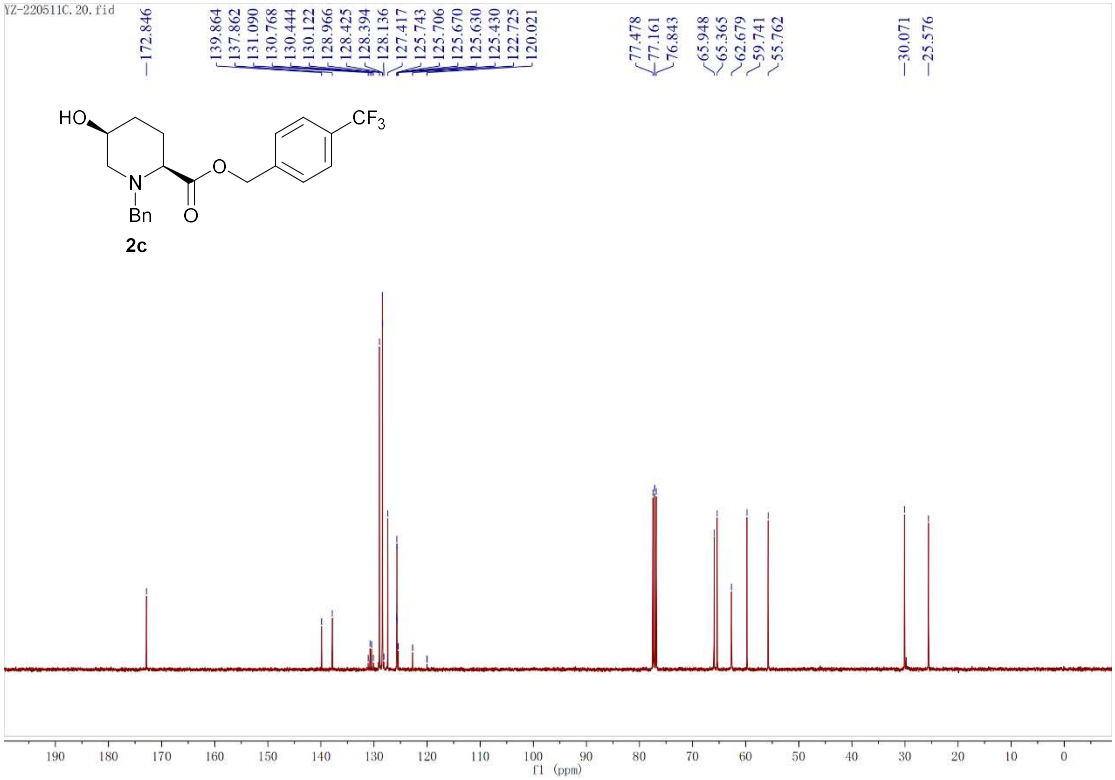
[1]H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2b



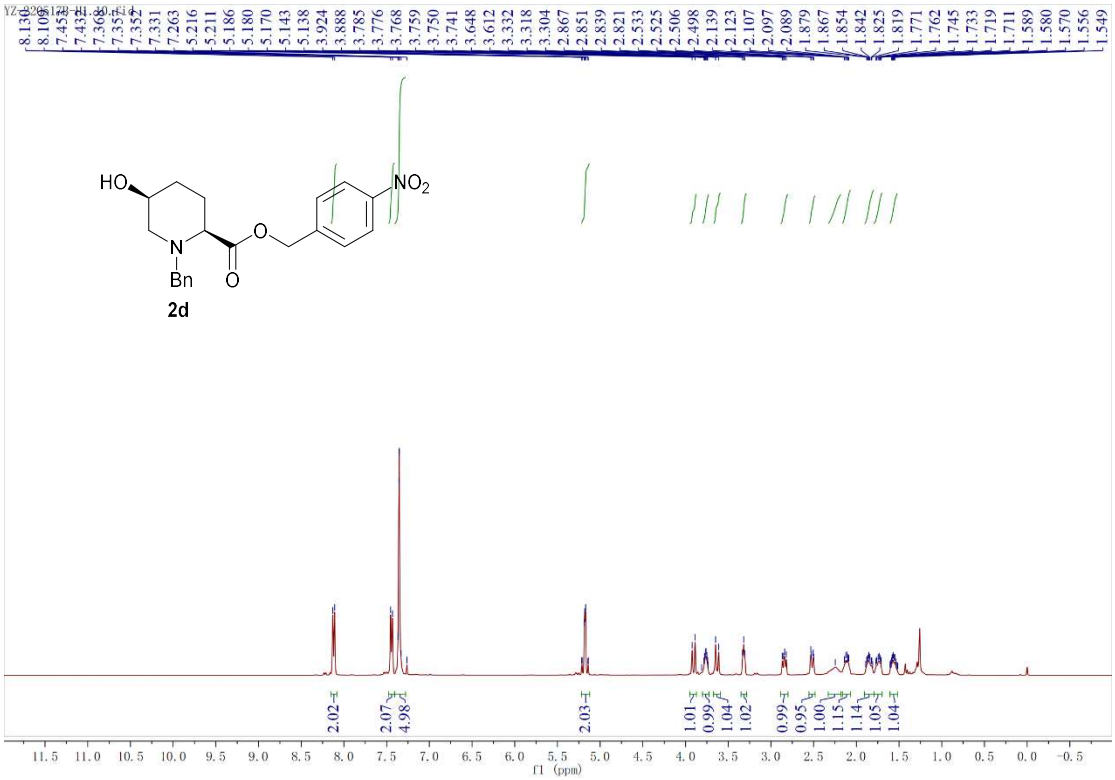
[13]C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2b



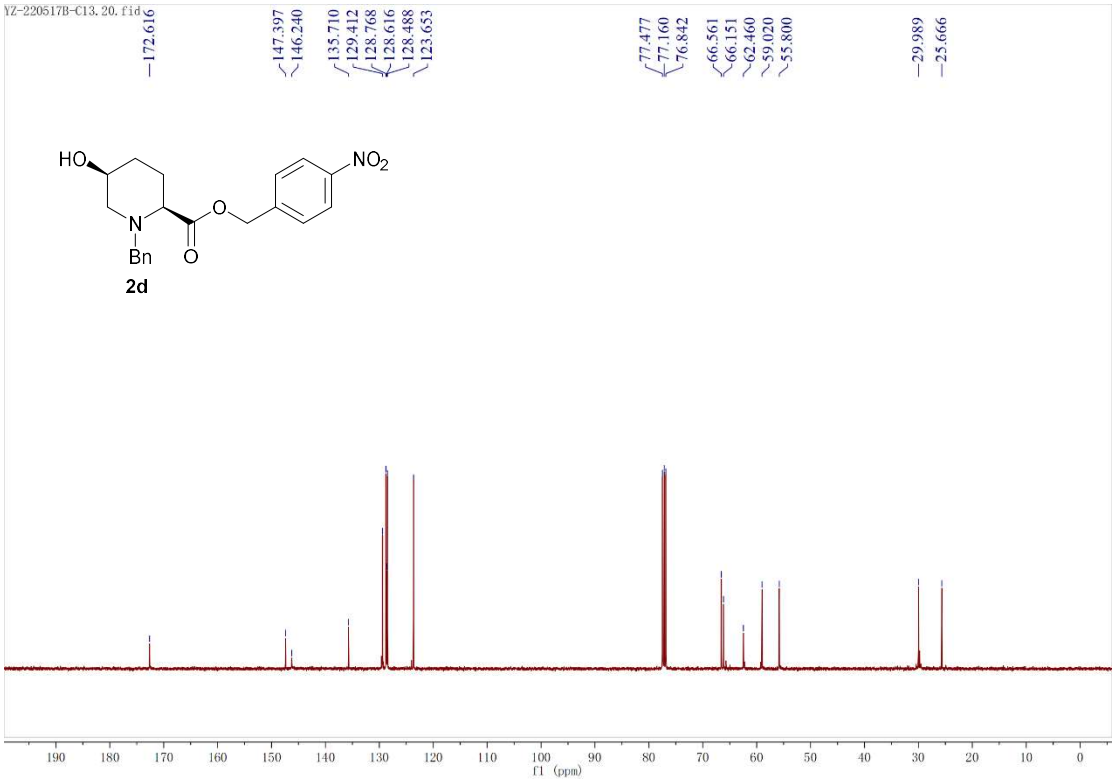
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2c



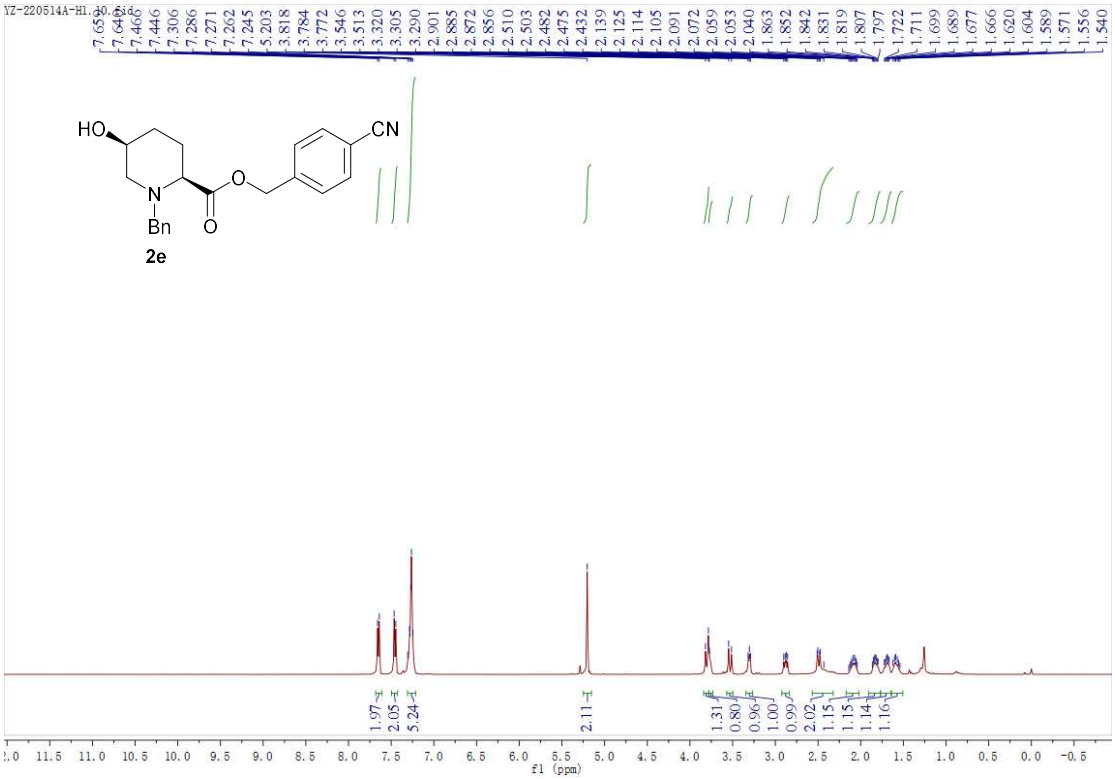
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2c



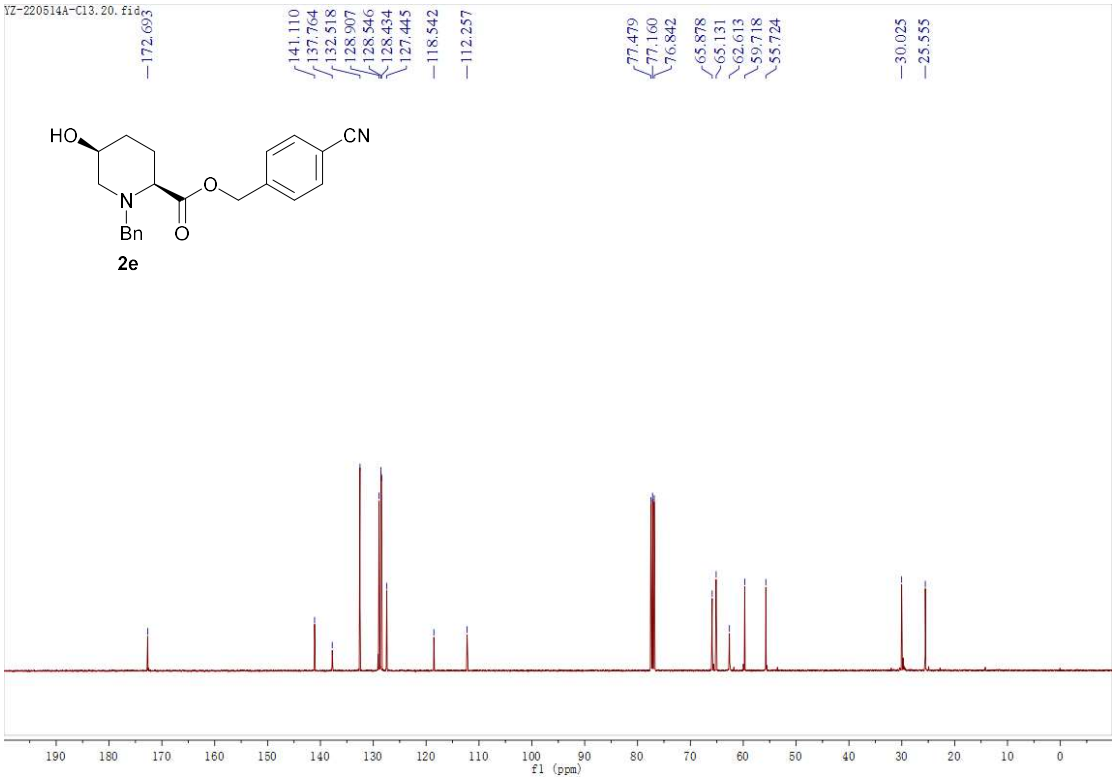
[1]H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2d



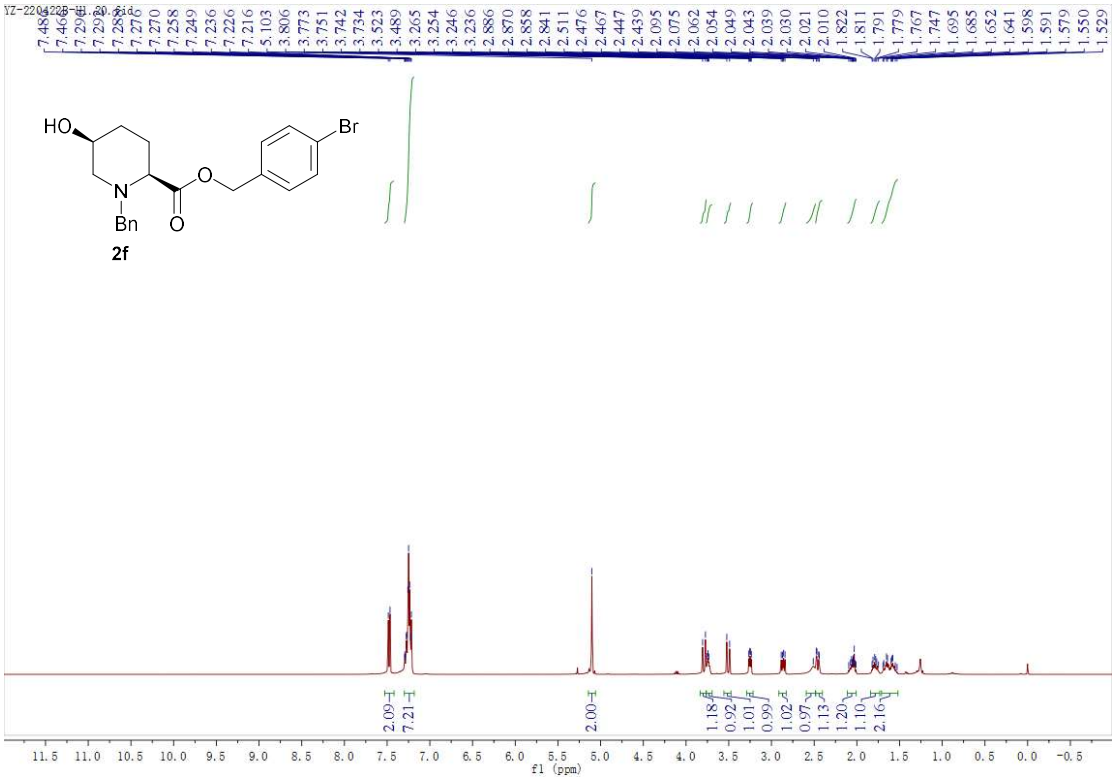
[13]C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2d



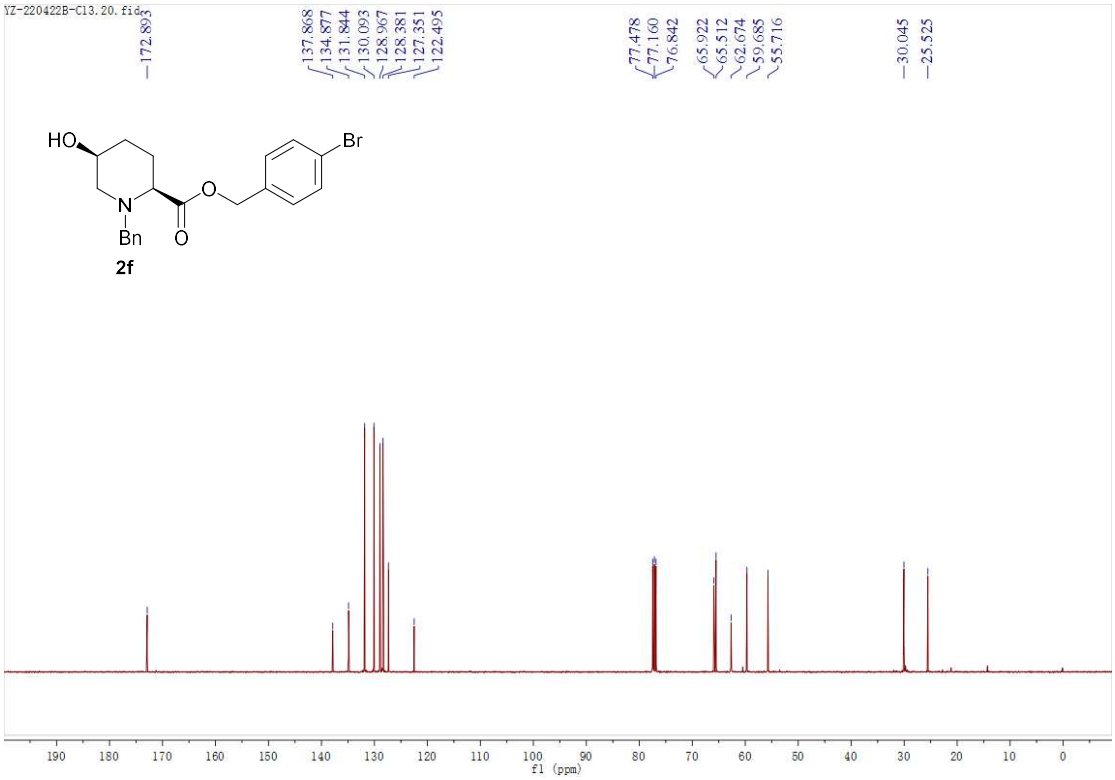
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2e



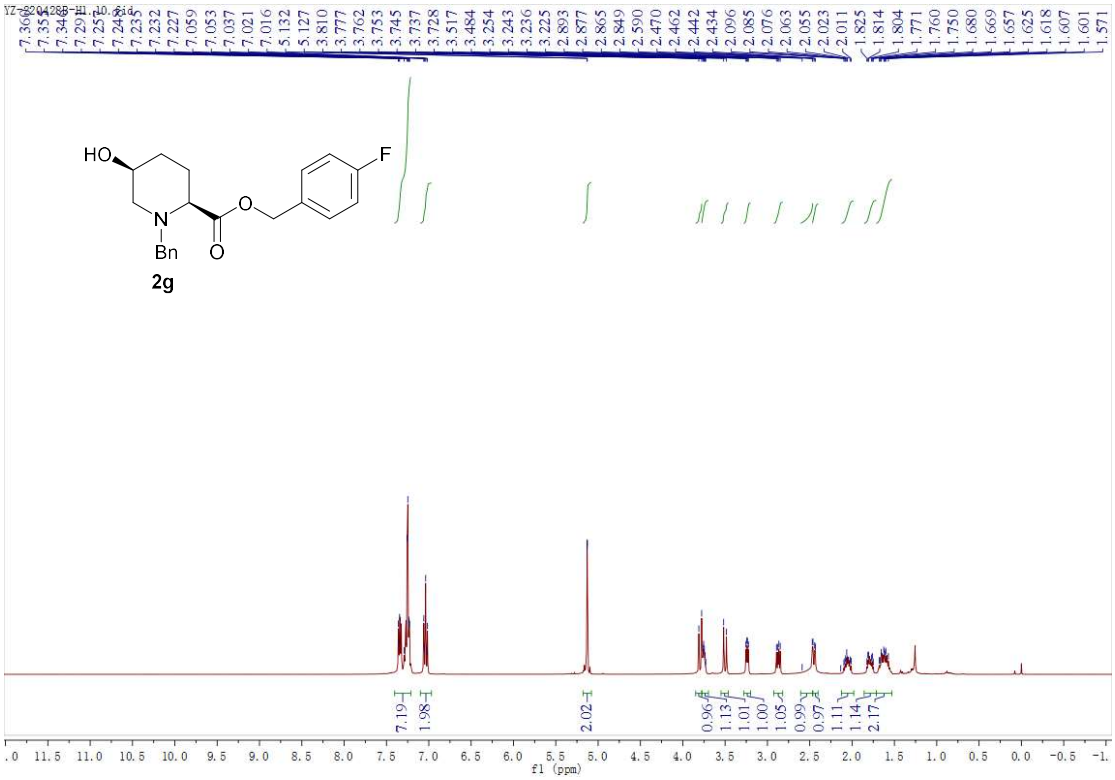
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2e



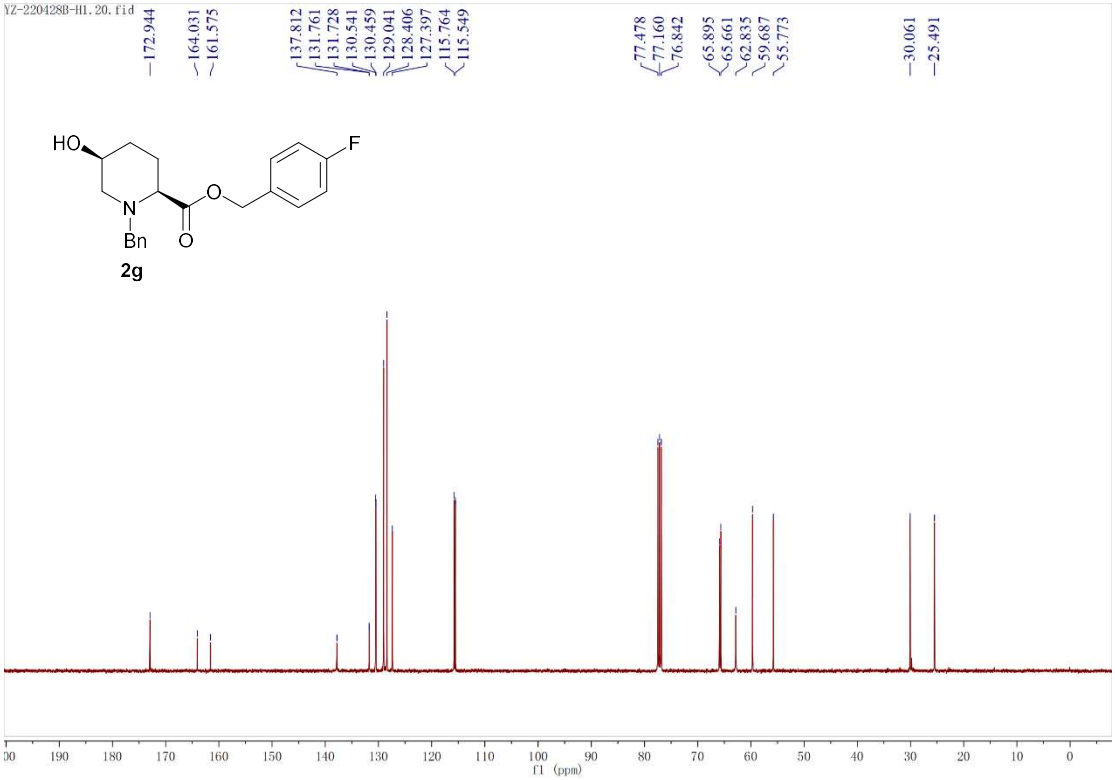
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2f



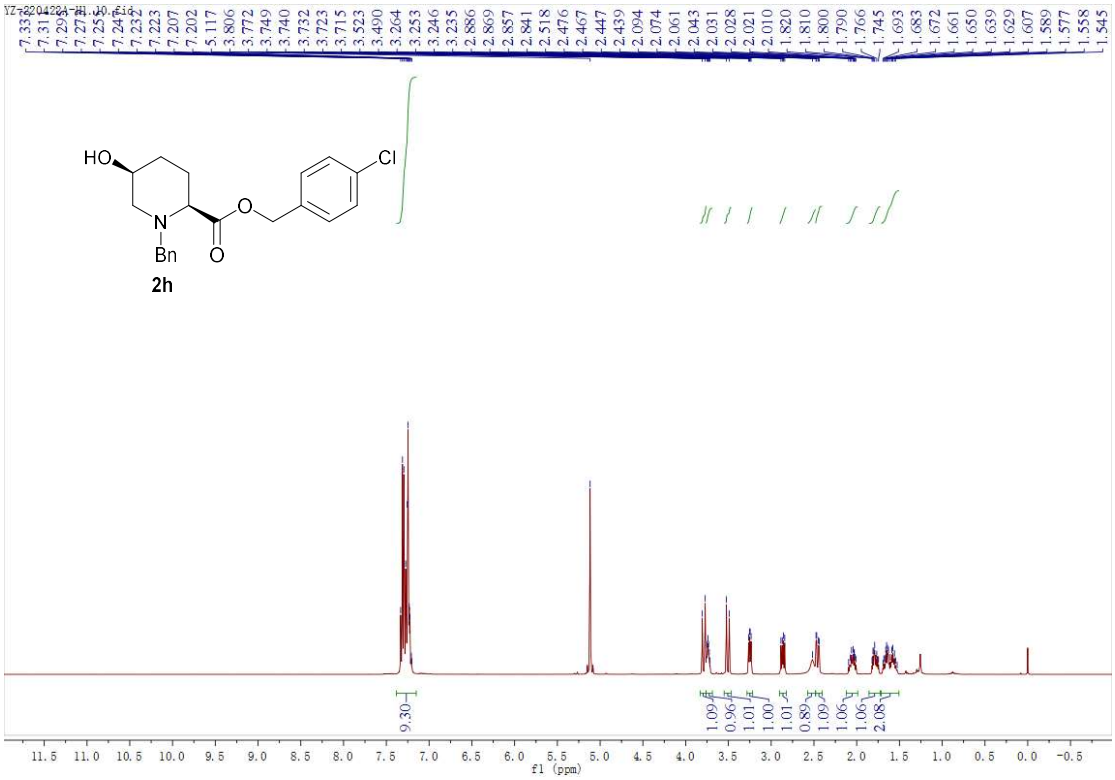
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2f



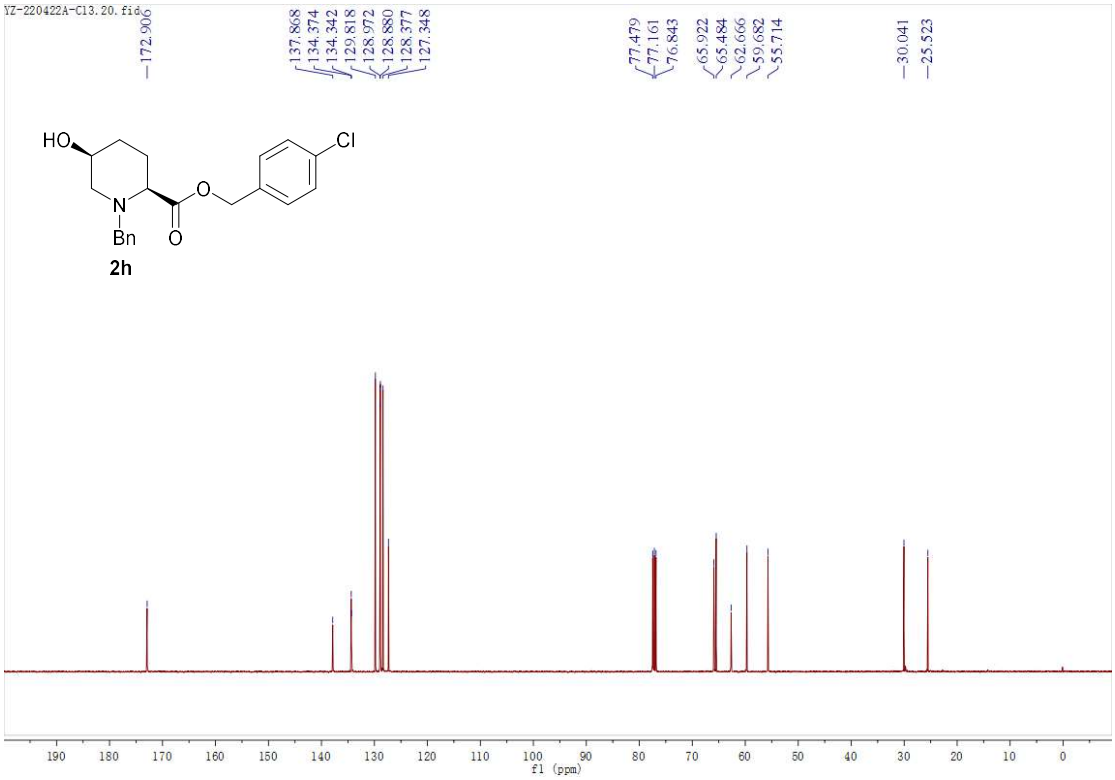
[1]H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2g



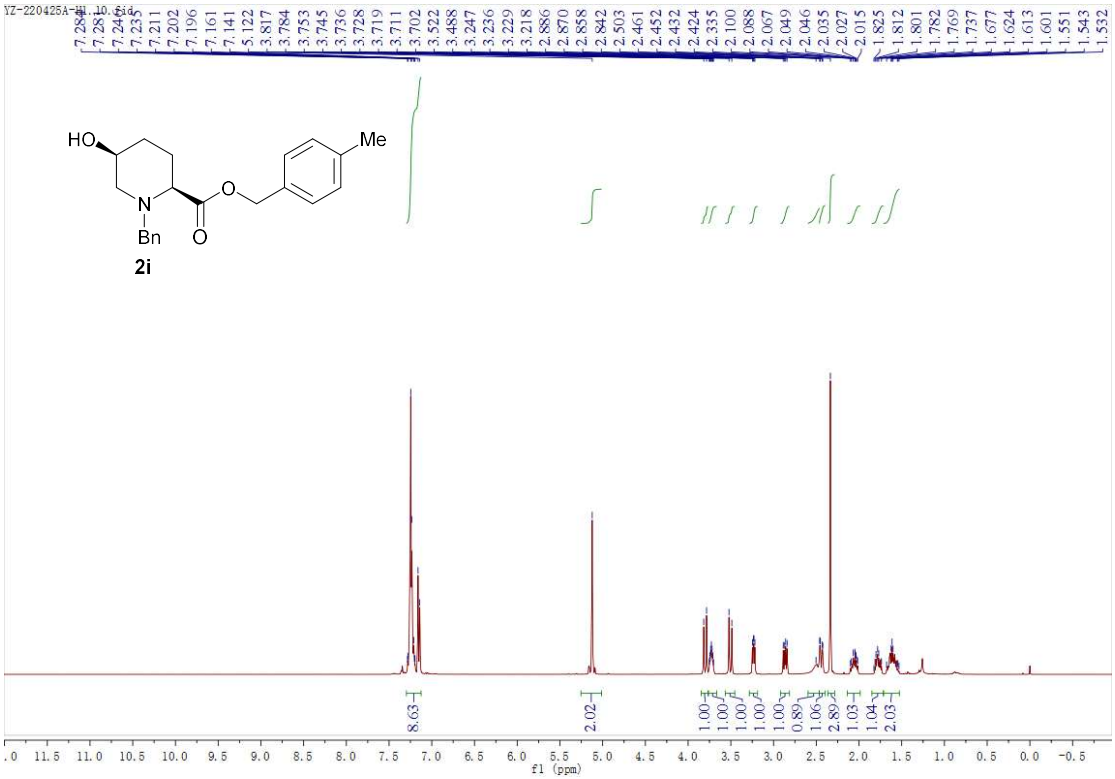
[13]C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2g



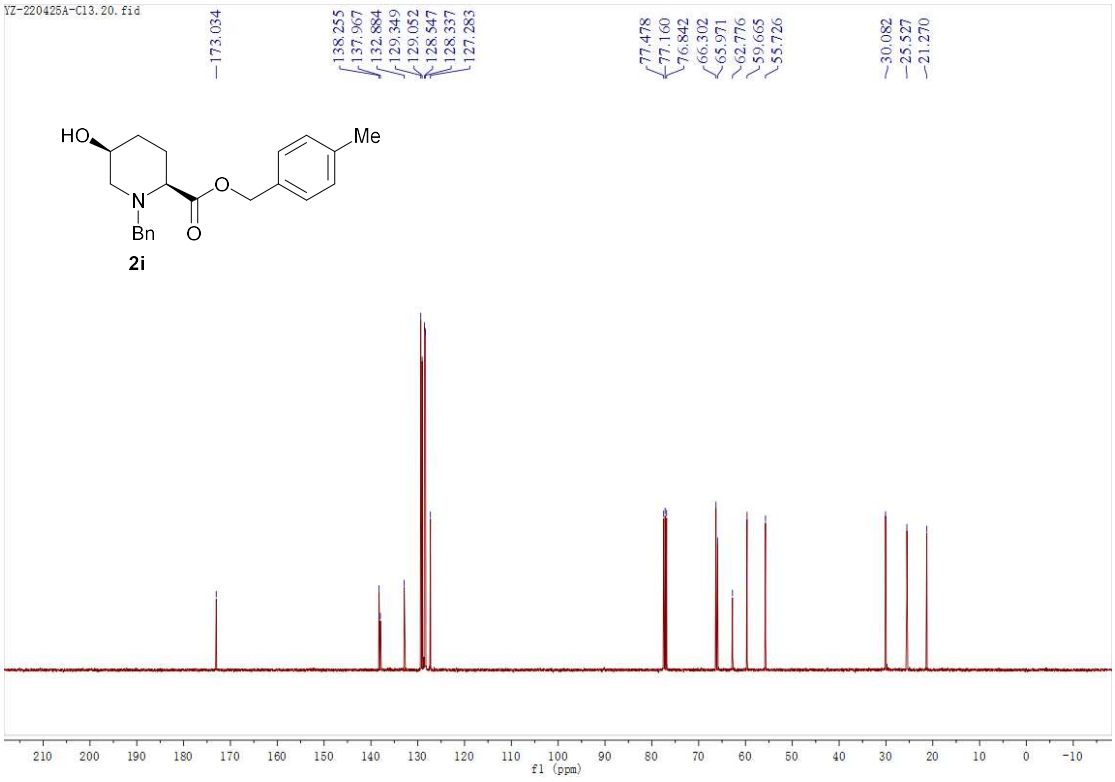
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2h



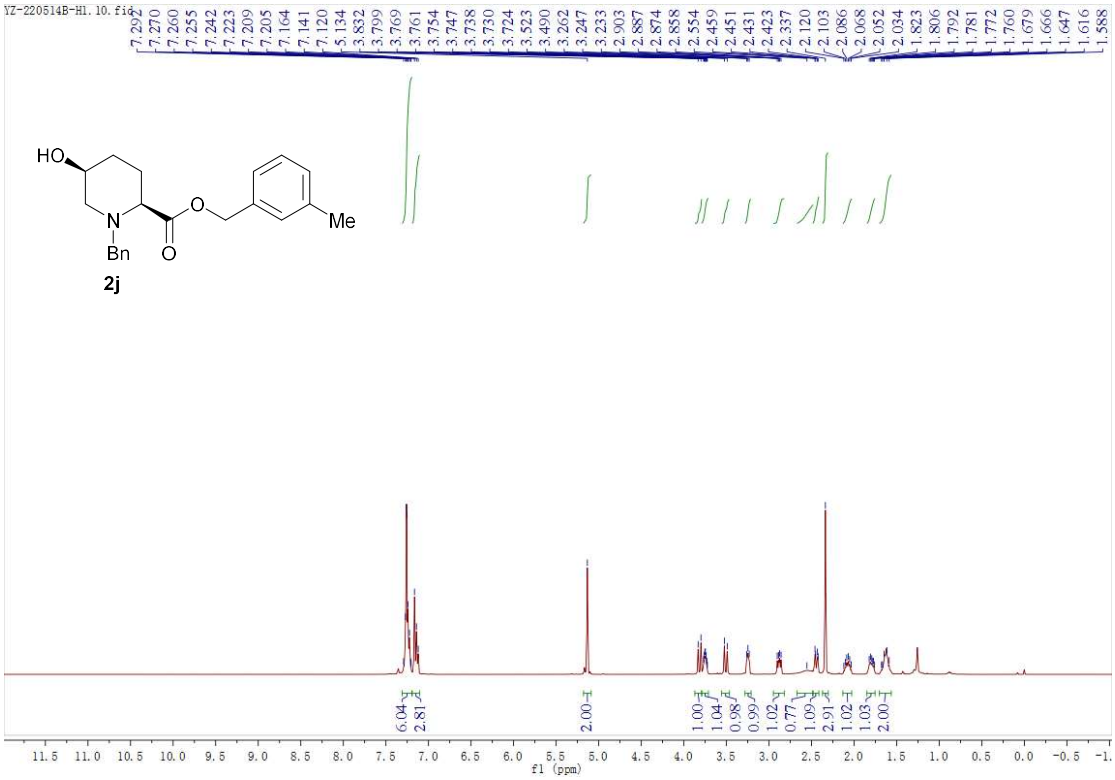
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2h



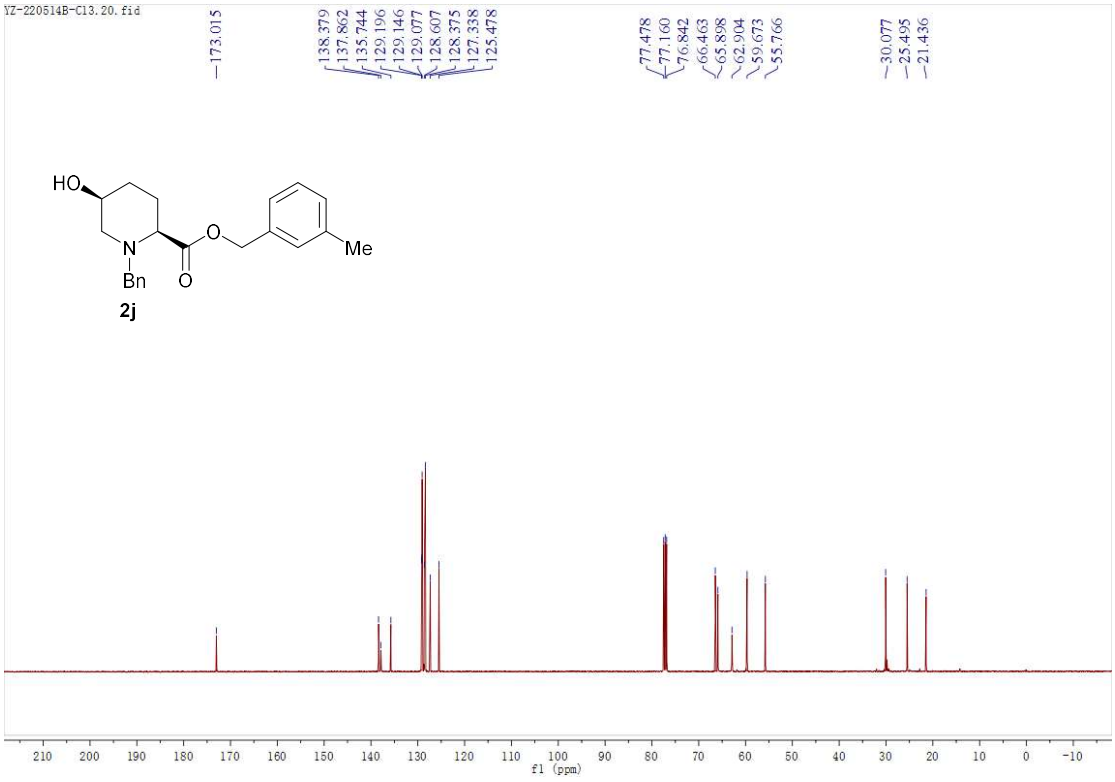
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2i



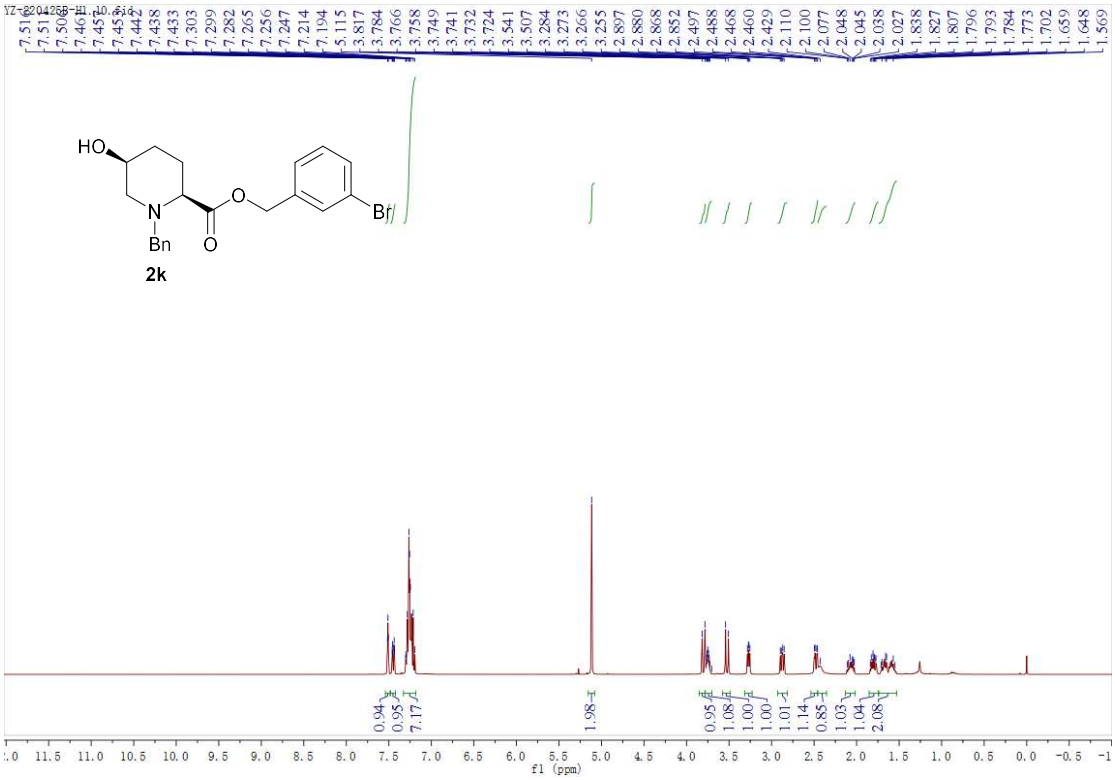
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2i



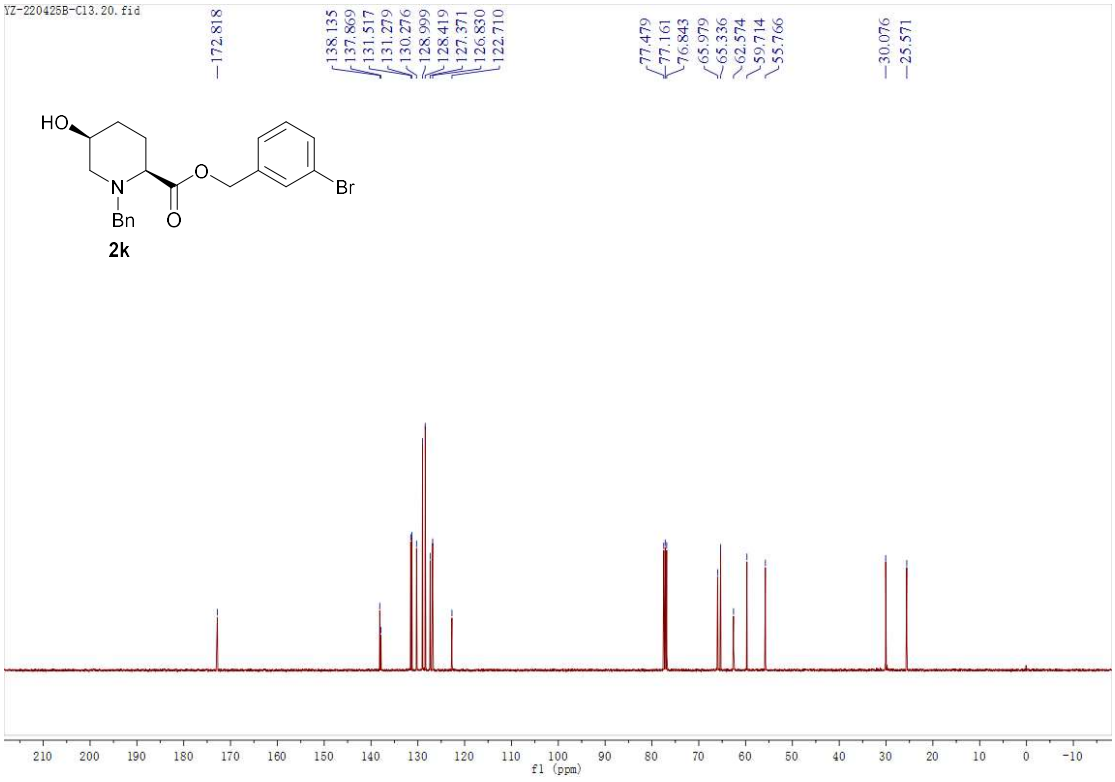
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2j



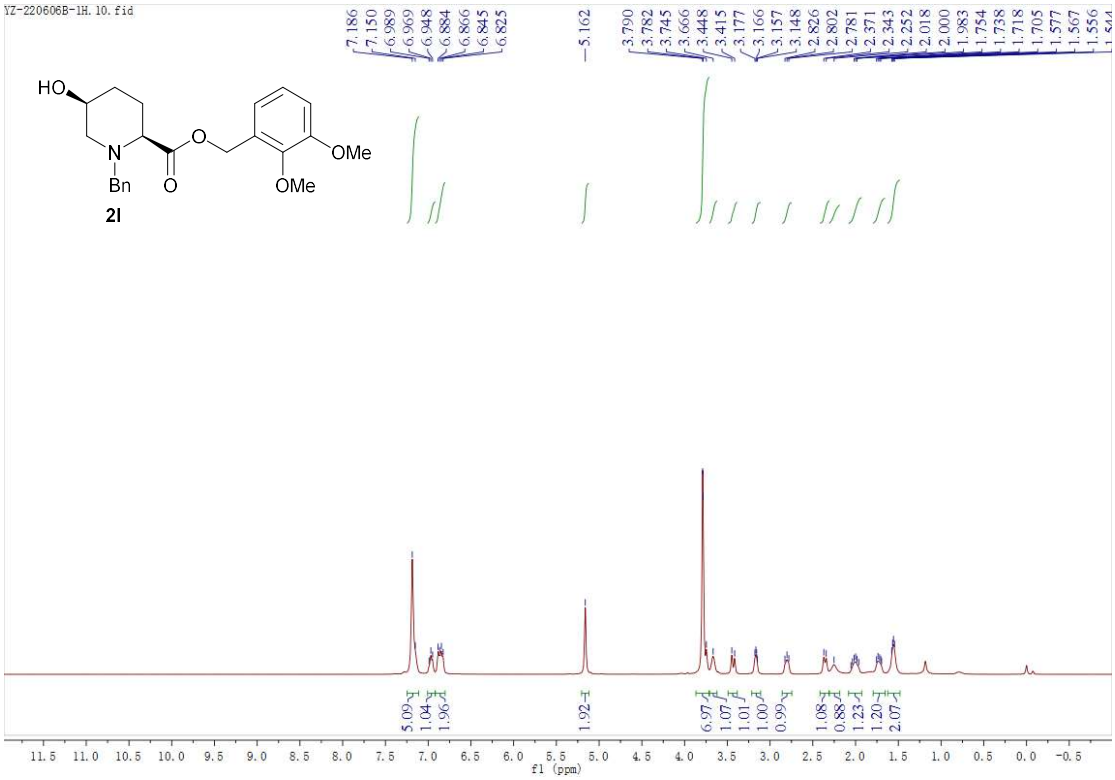
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2j



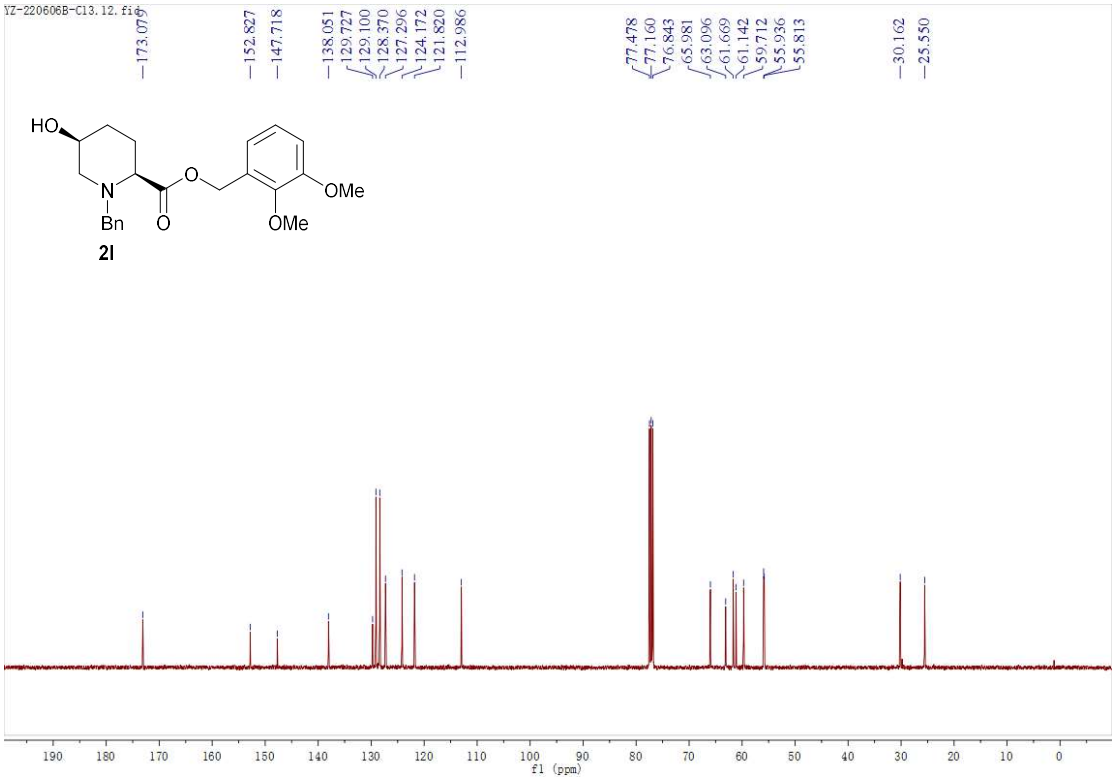
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2k



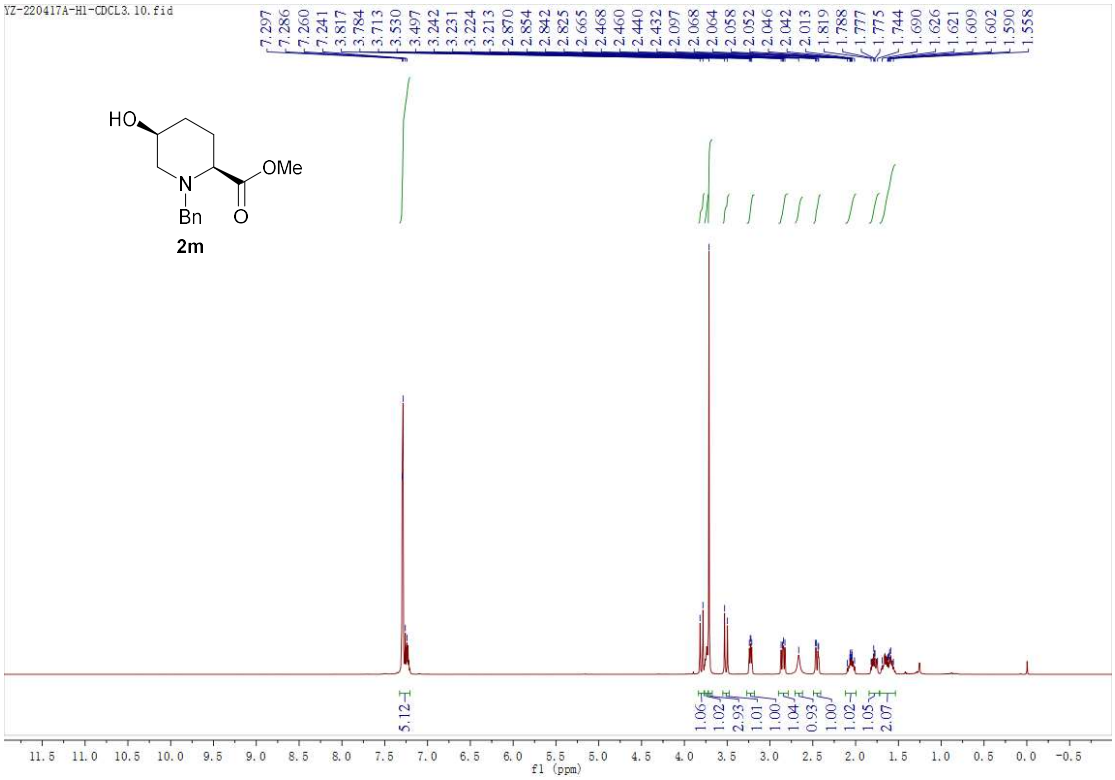
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2k



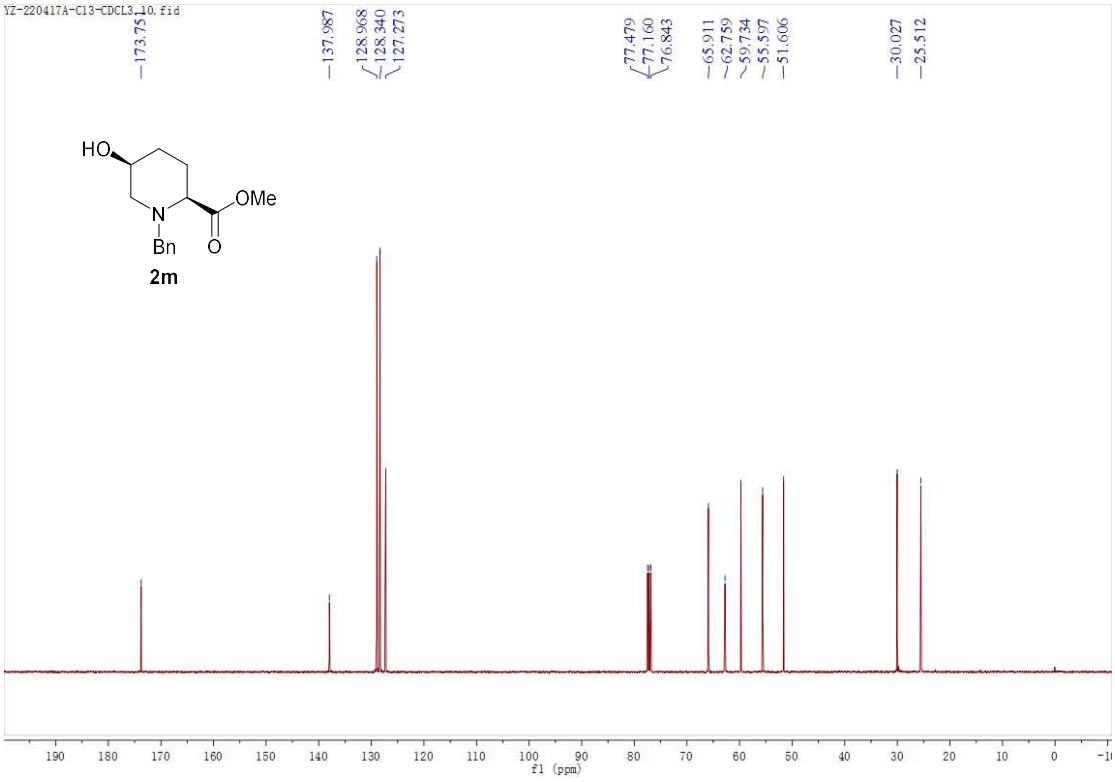
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2l



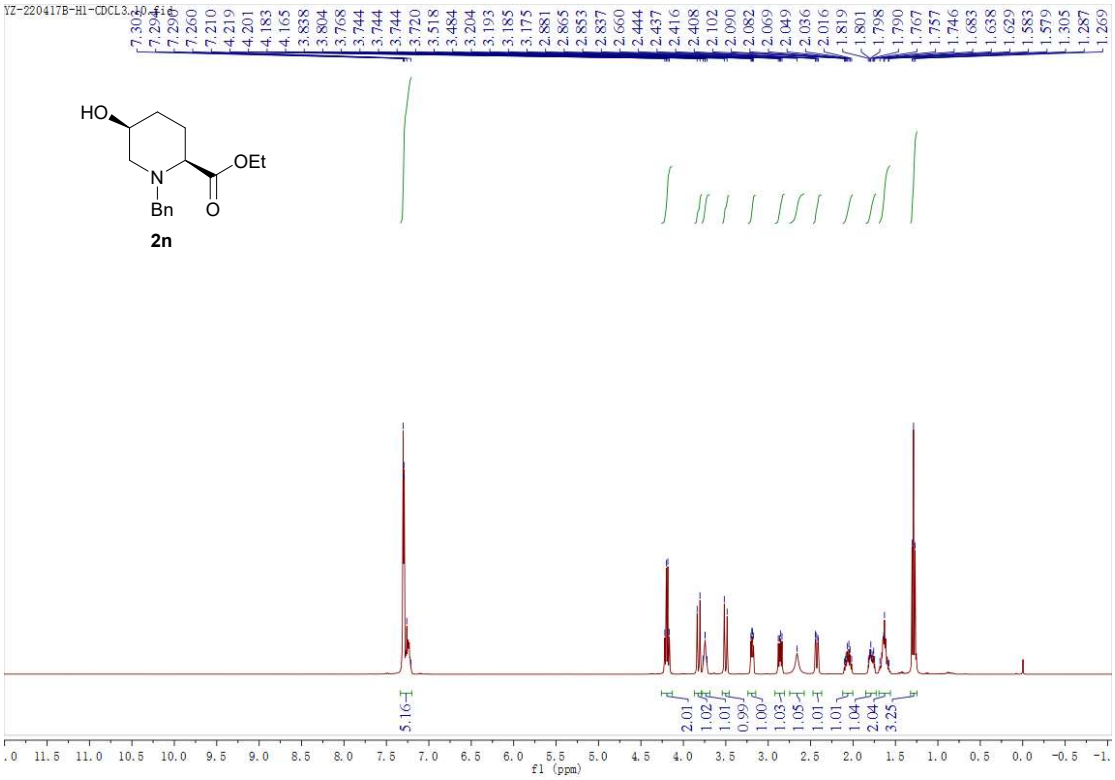
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2l



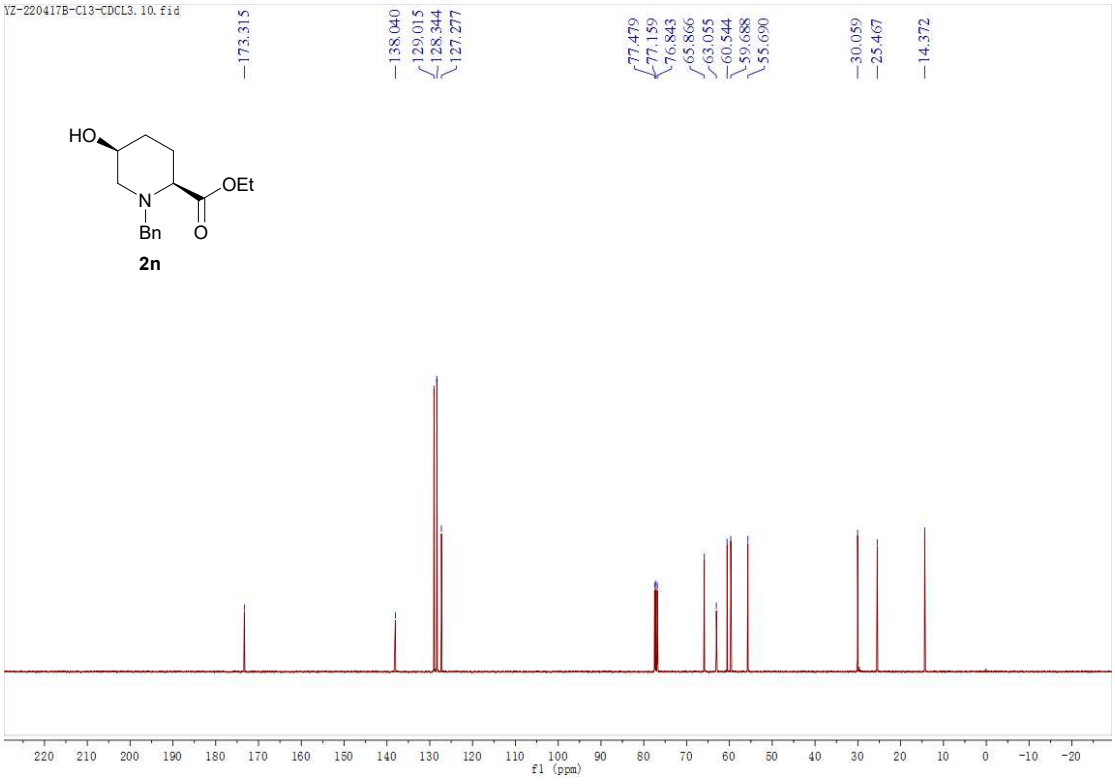
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2m



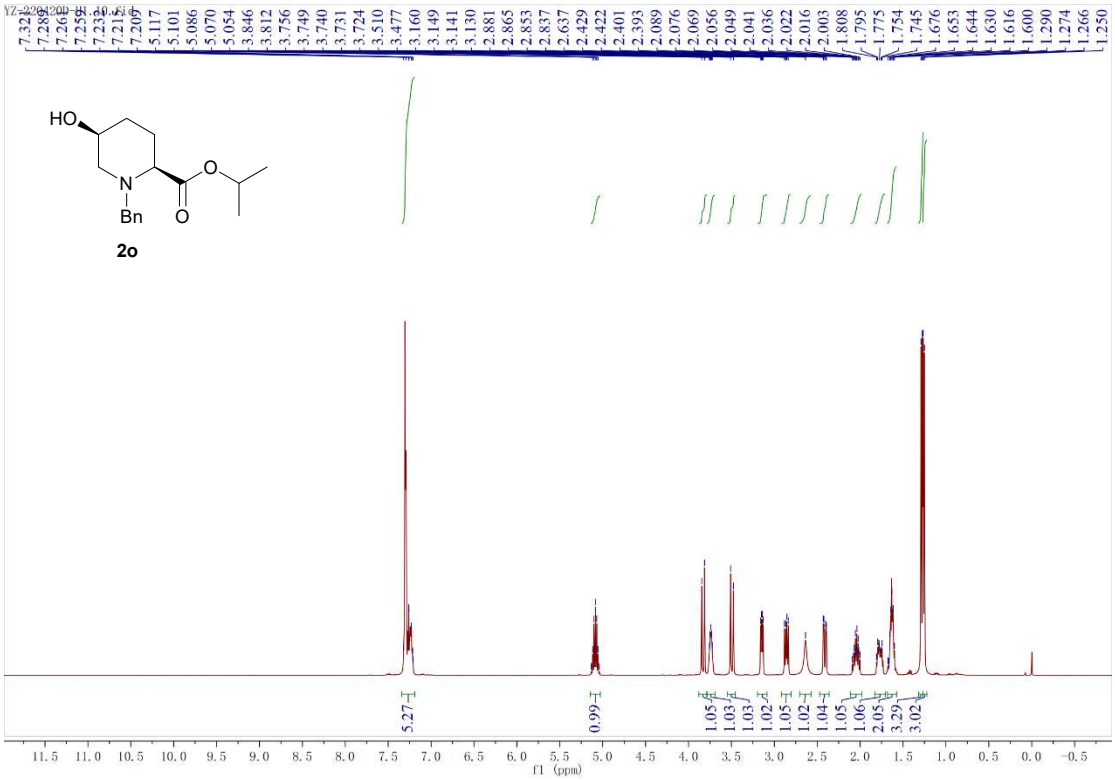
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2m



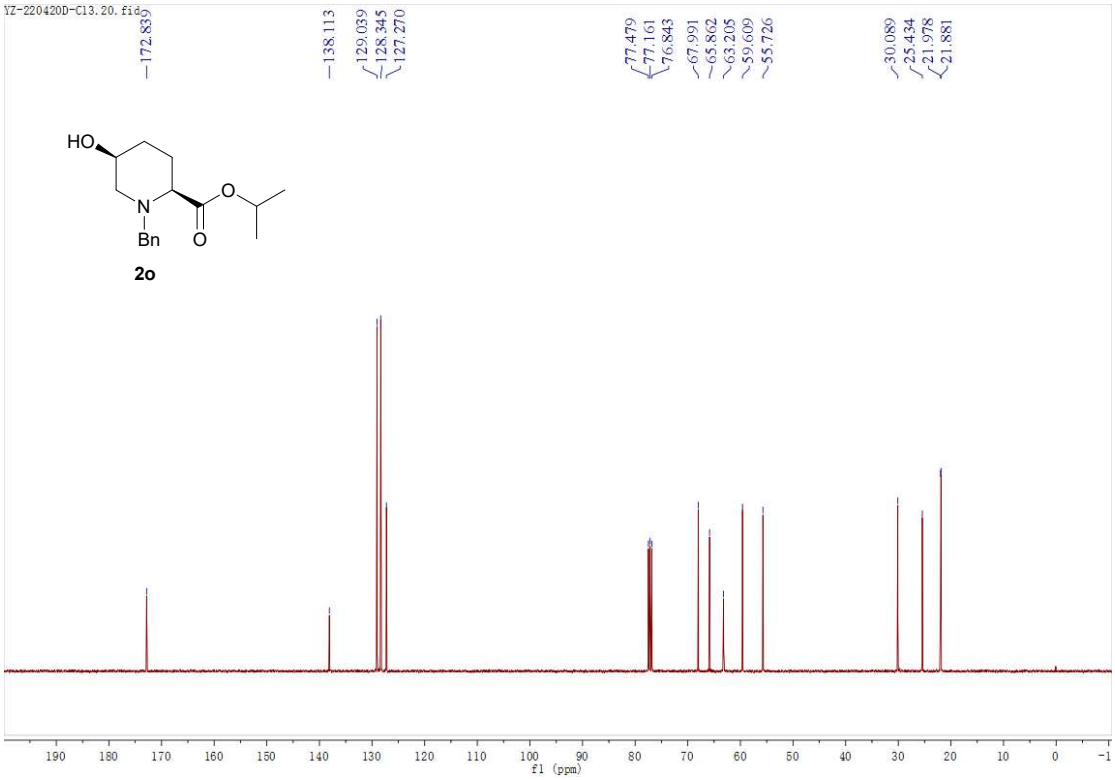
[1]H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2n



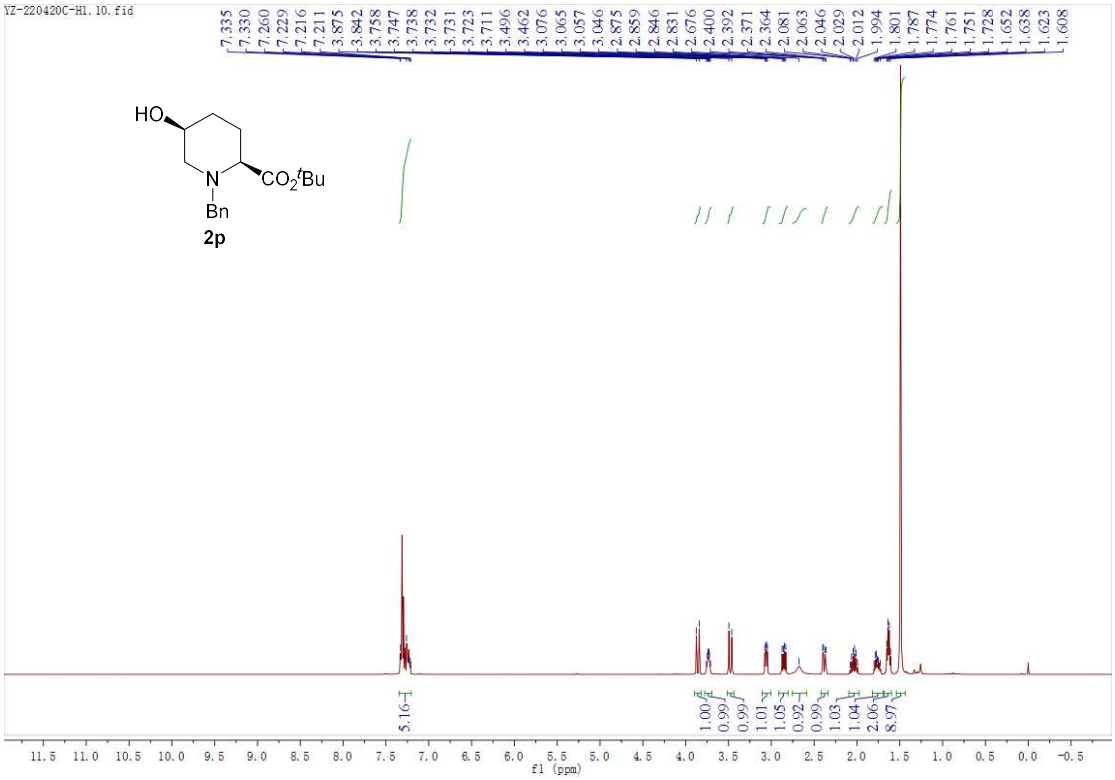
[13]C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2n



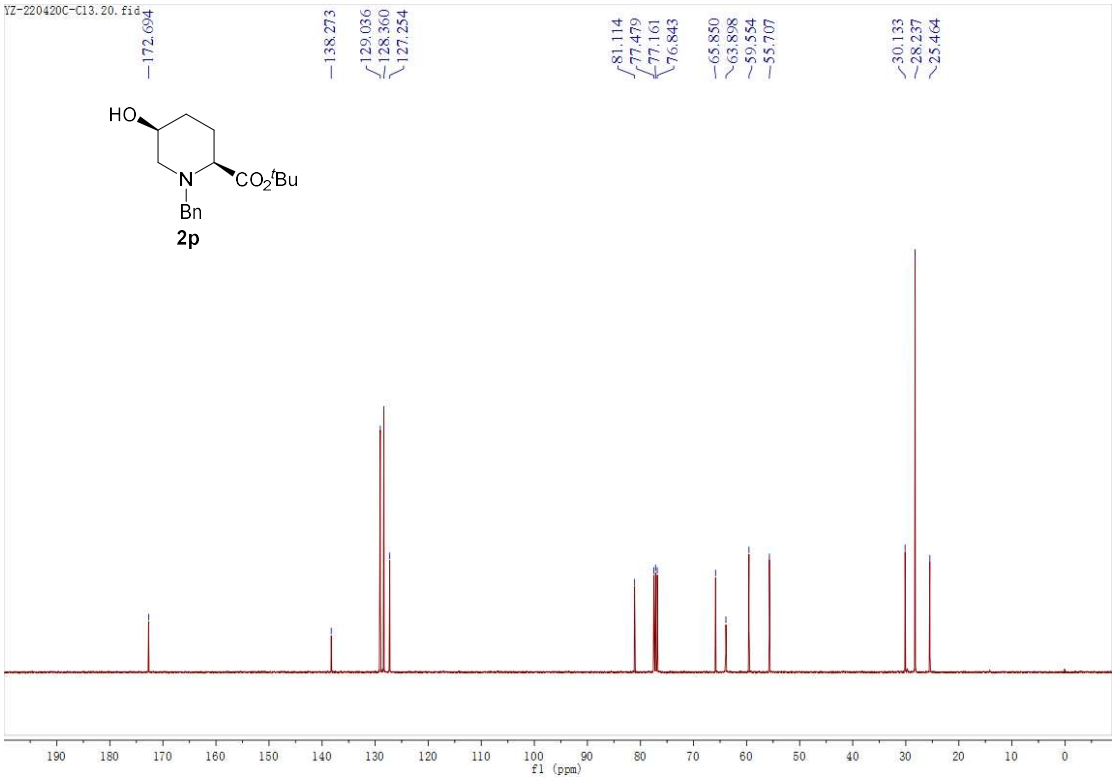
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2o



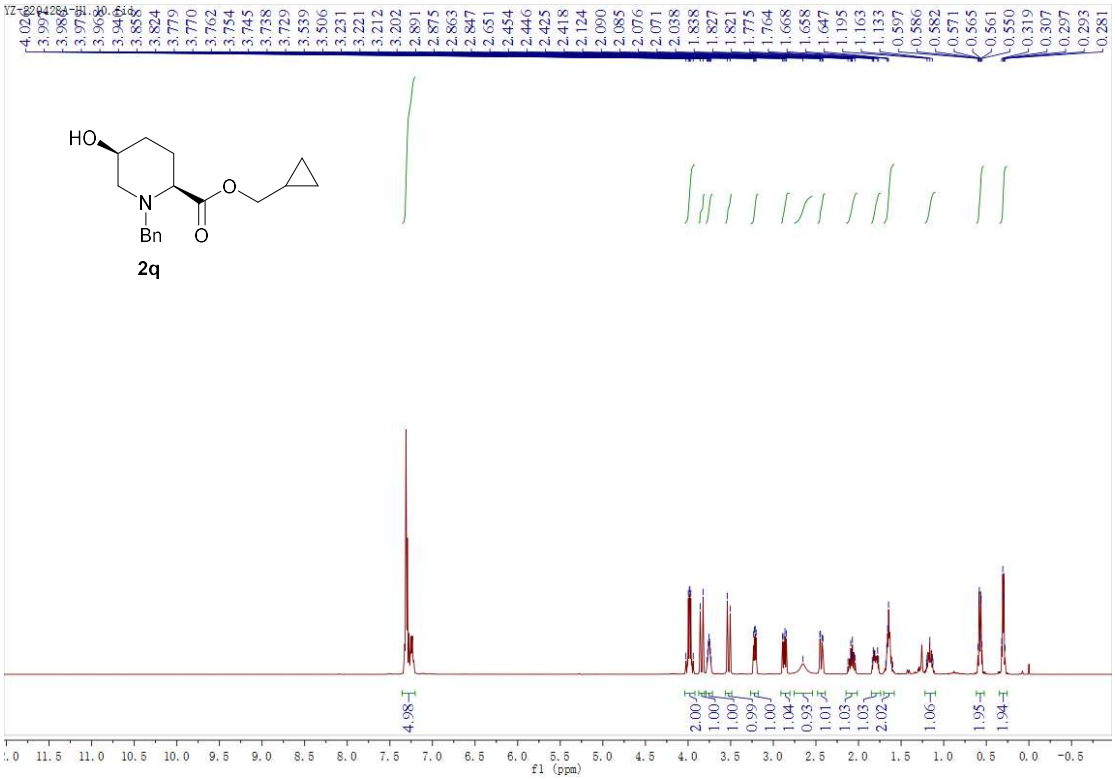
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2o



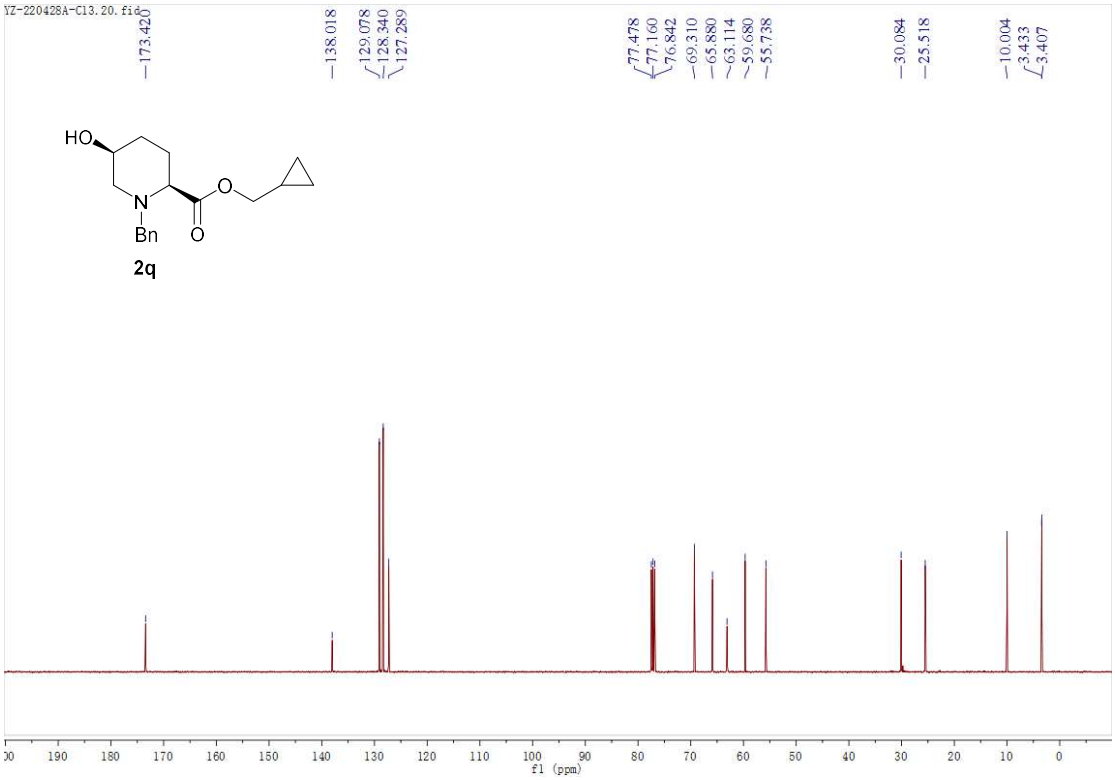
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2p



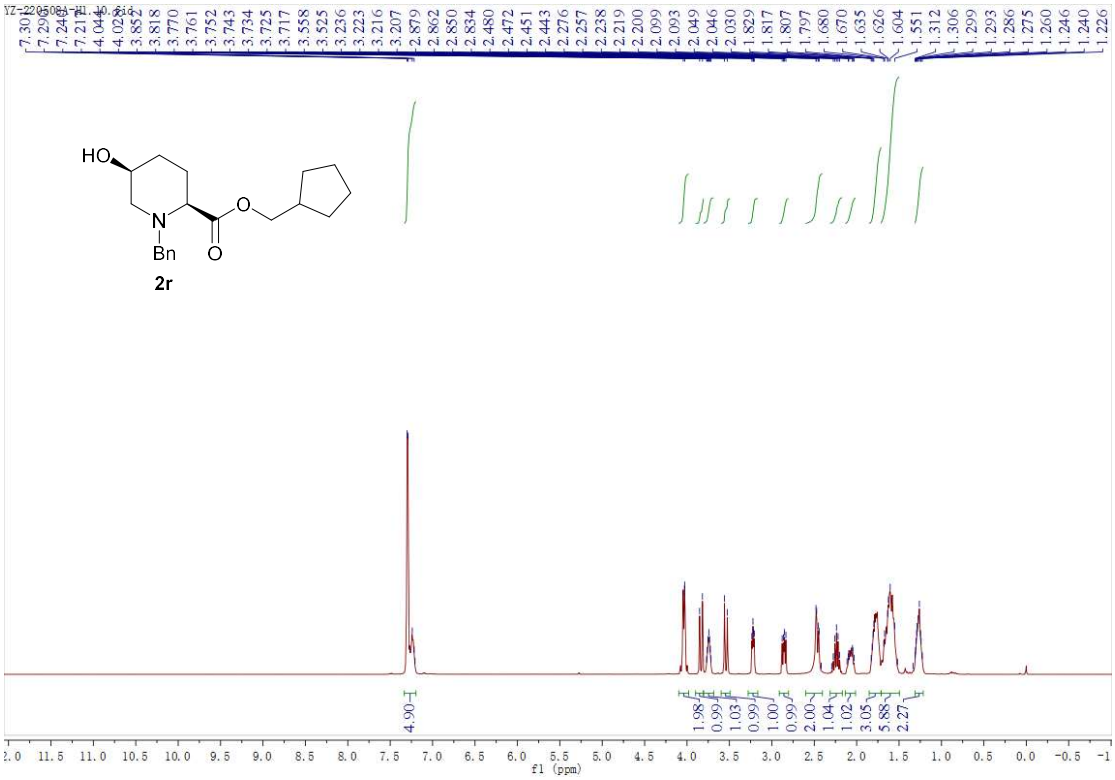
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2p



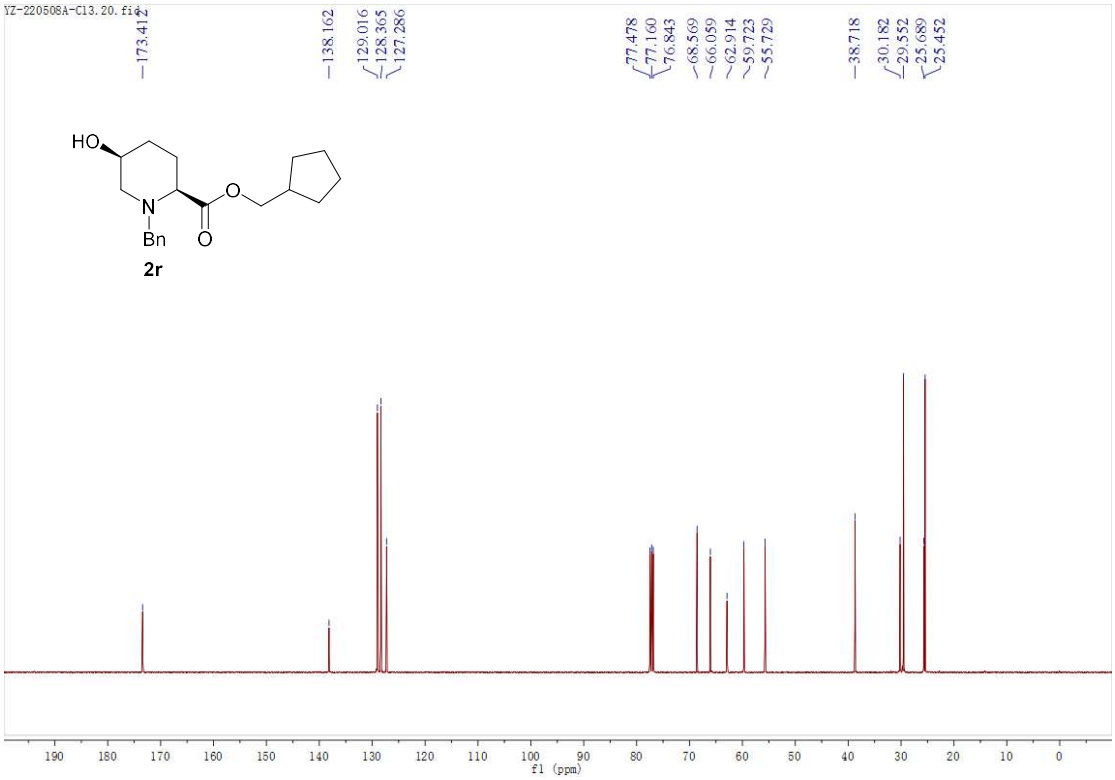
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2q



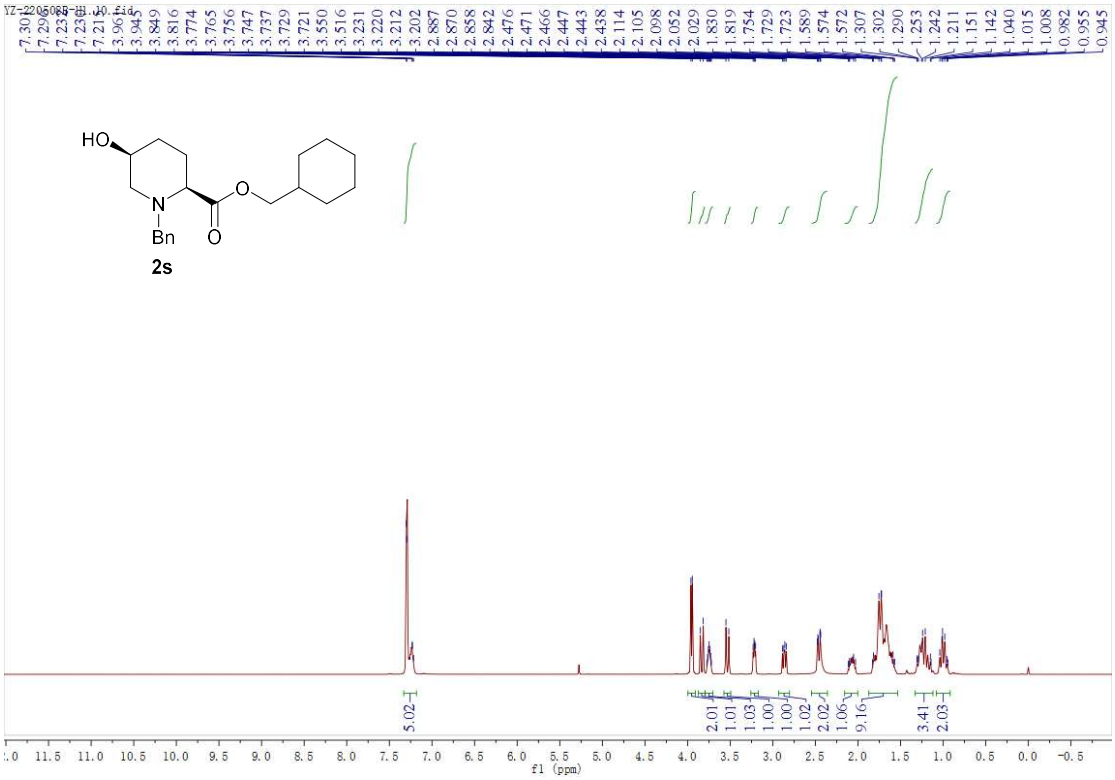
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2q



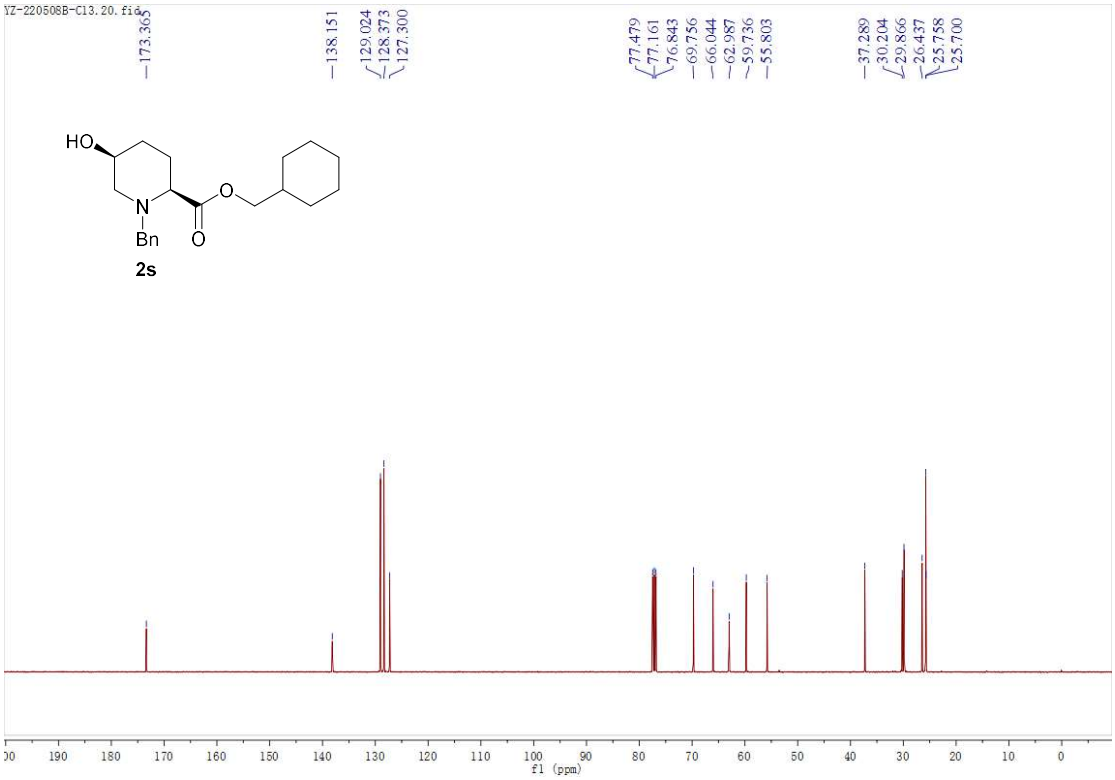
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2r



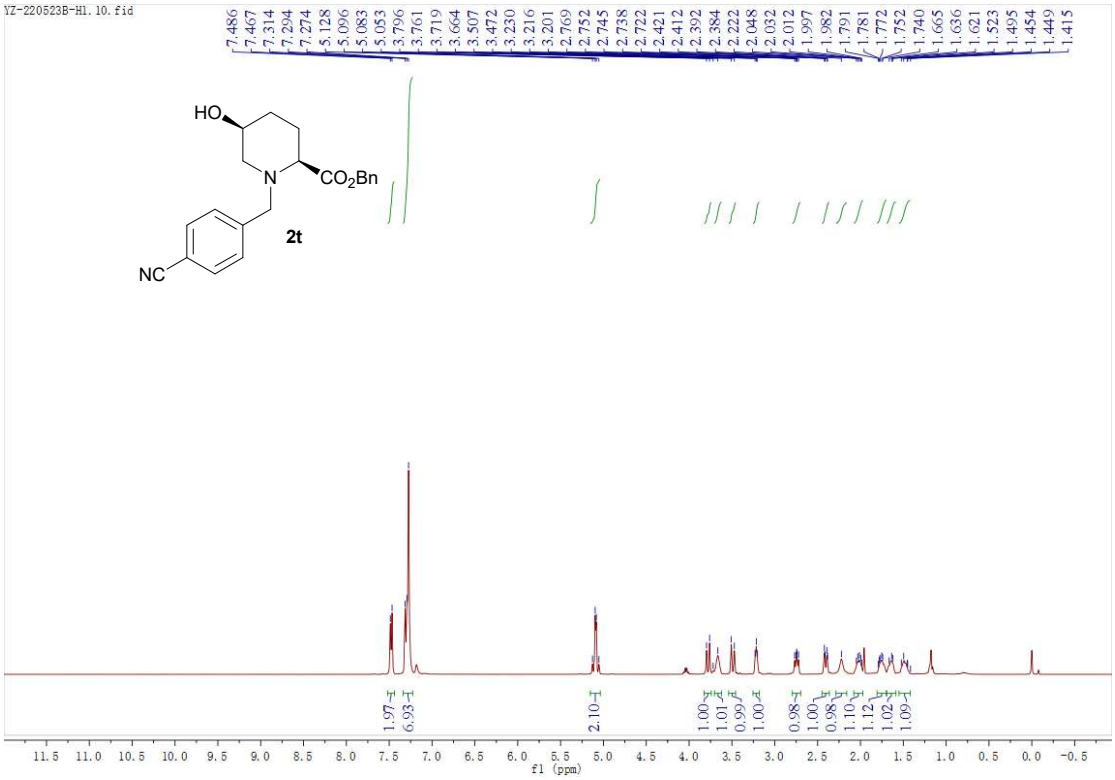
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2r



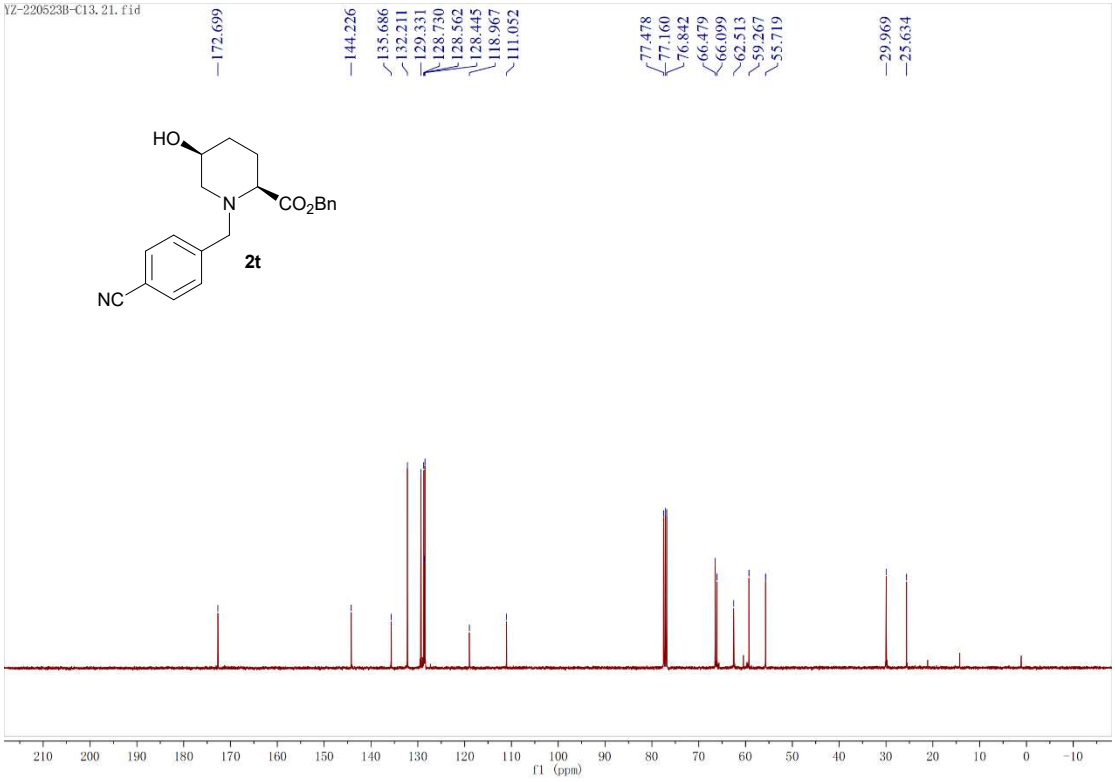
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2s



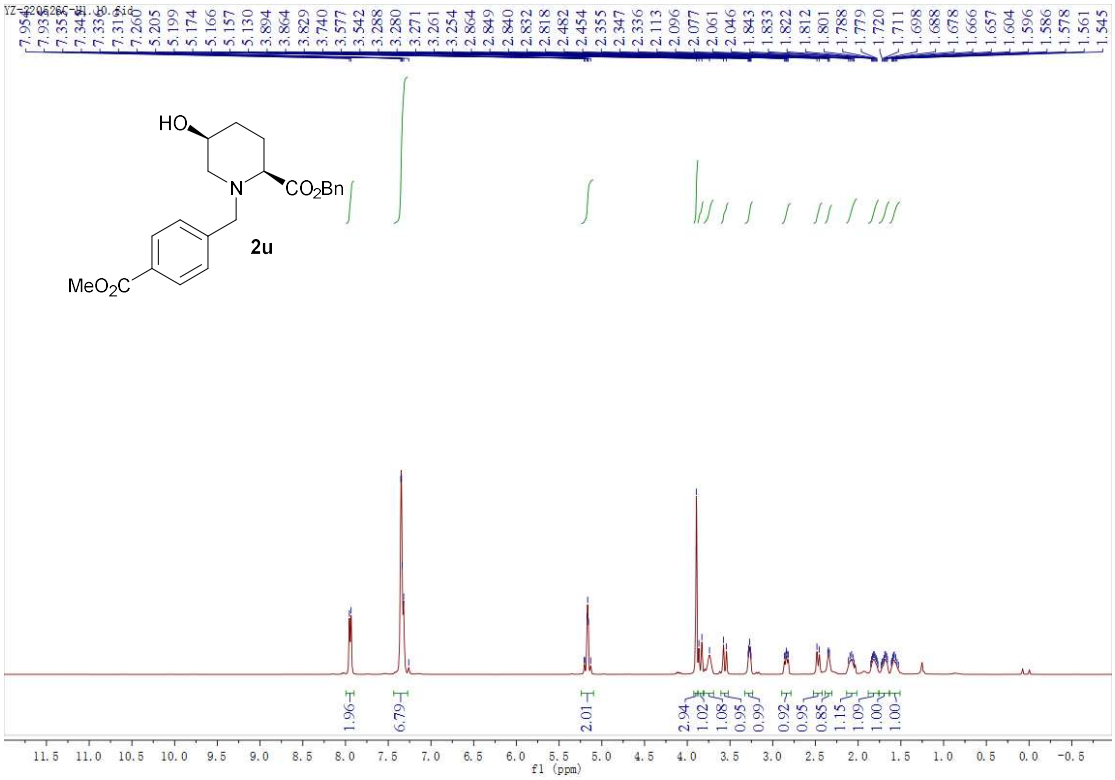
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2s



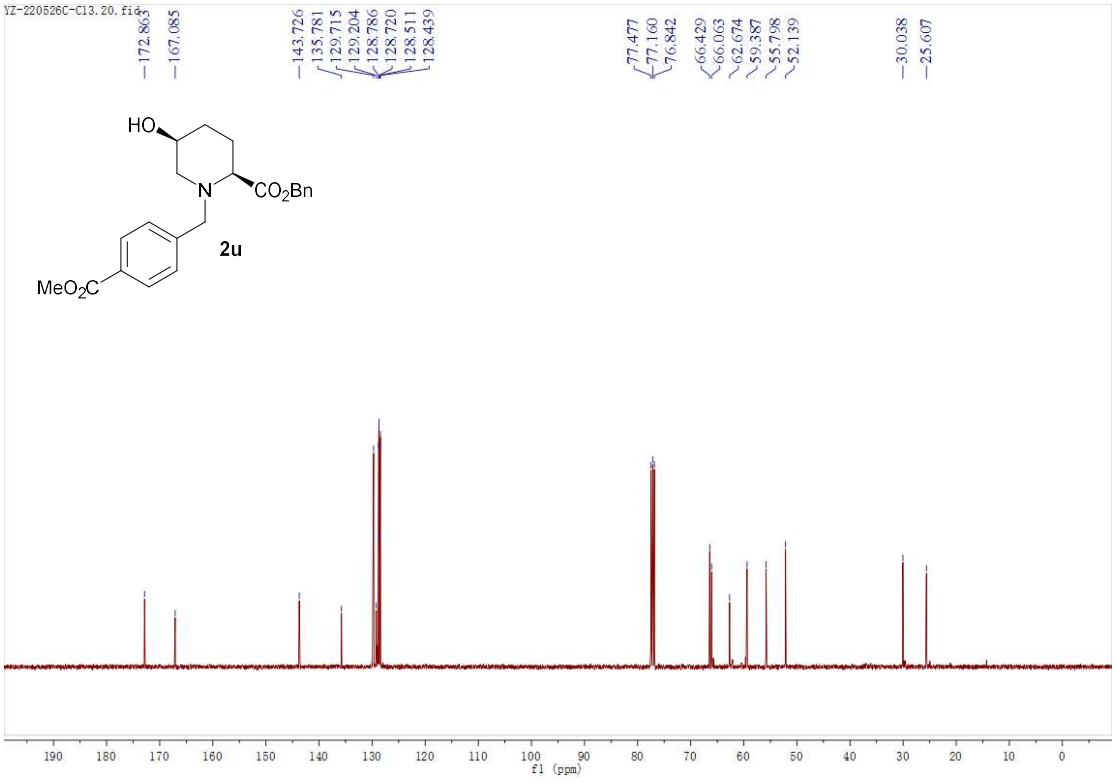
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2t



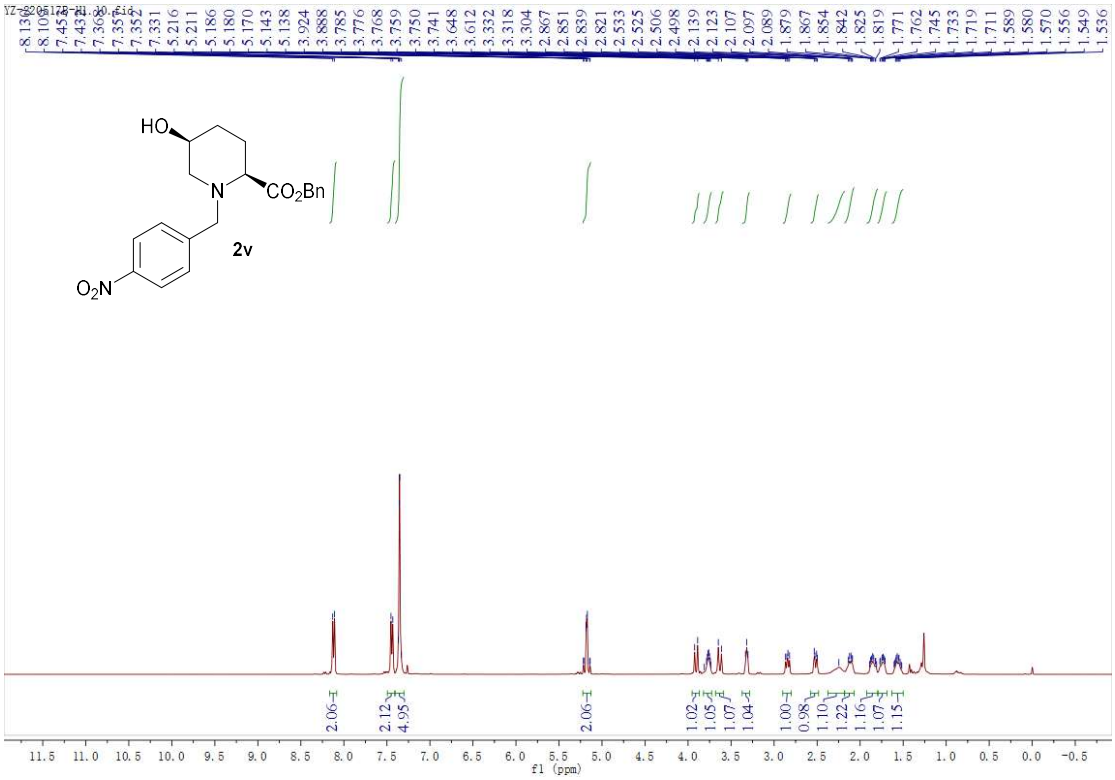
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2t



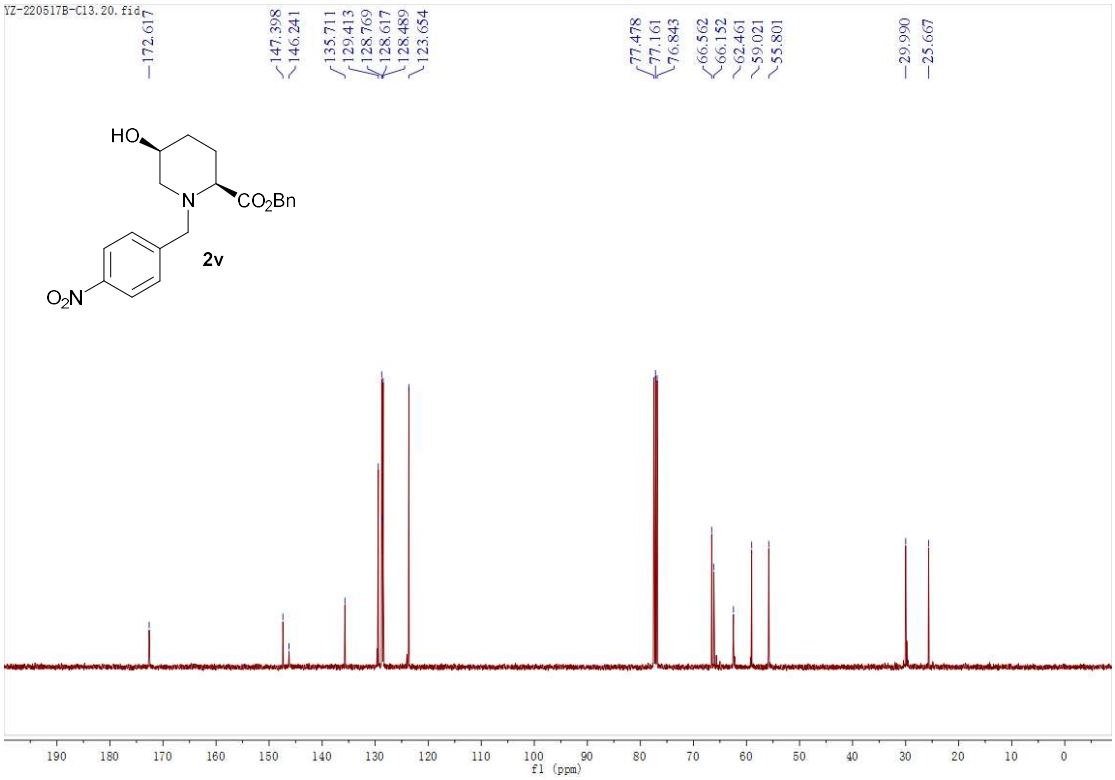
[1]H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2u



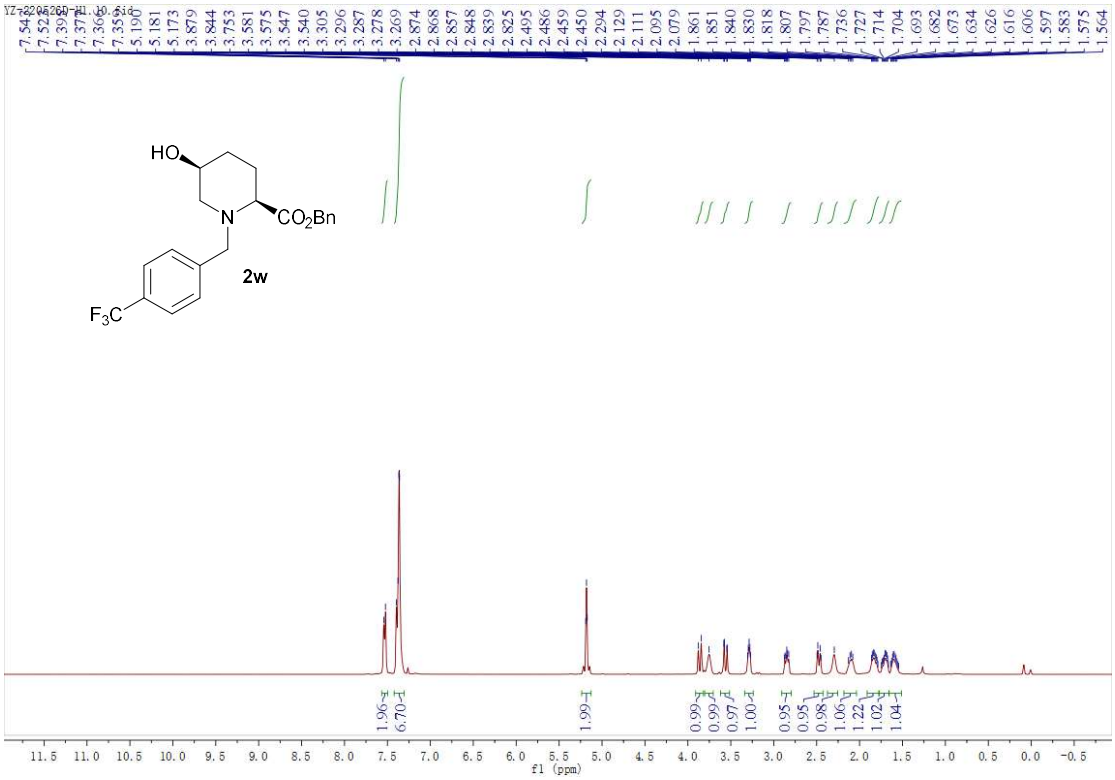
[13]C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2u



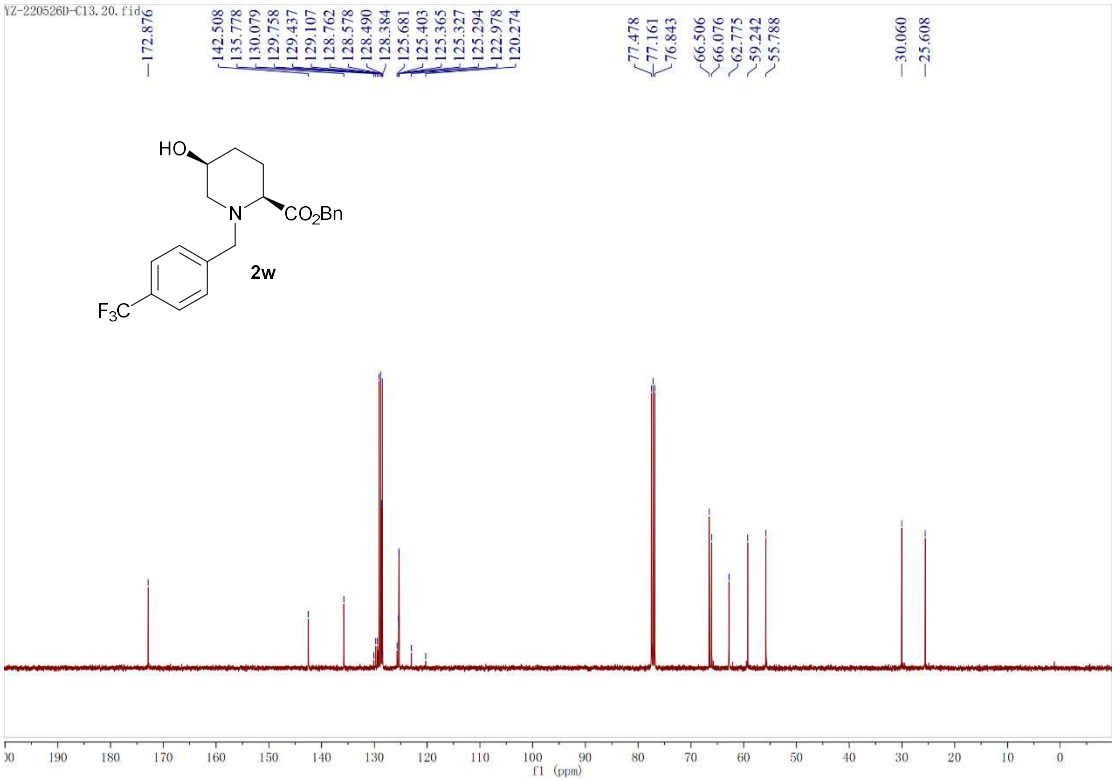
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2v



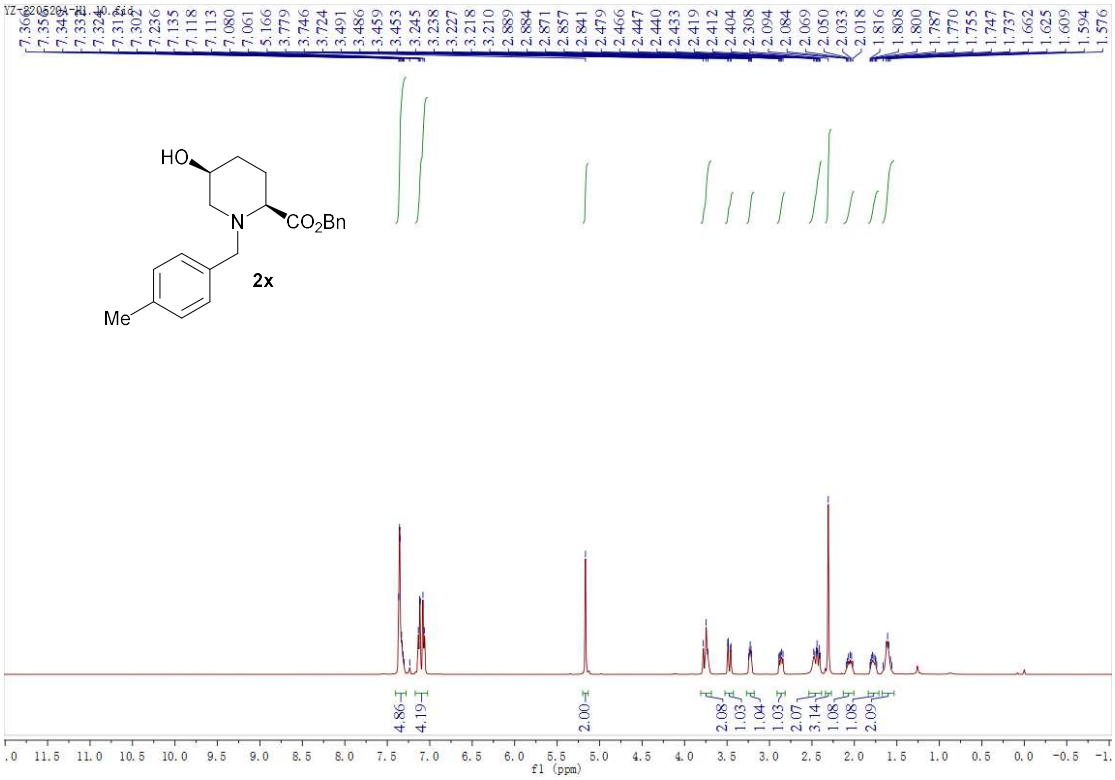
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2v



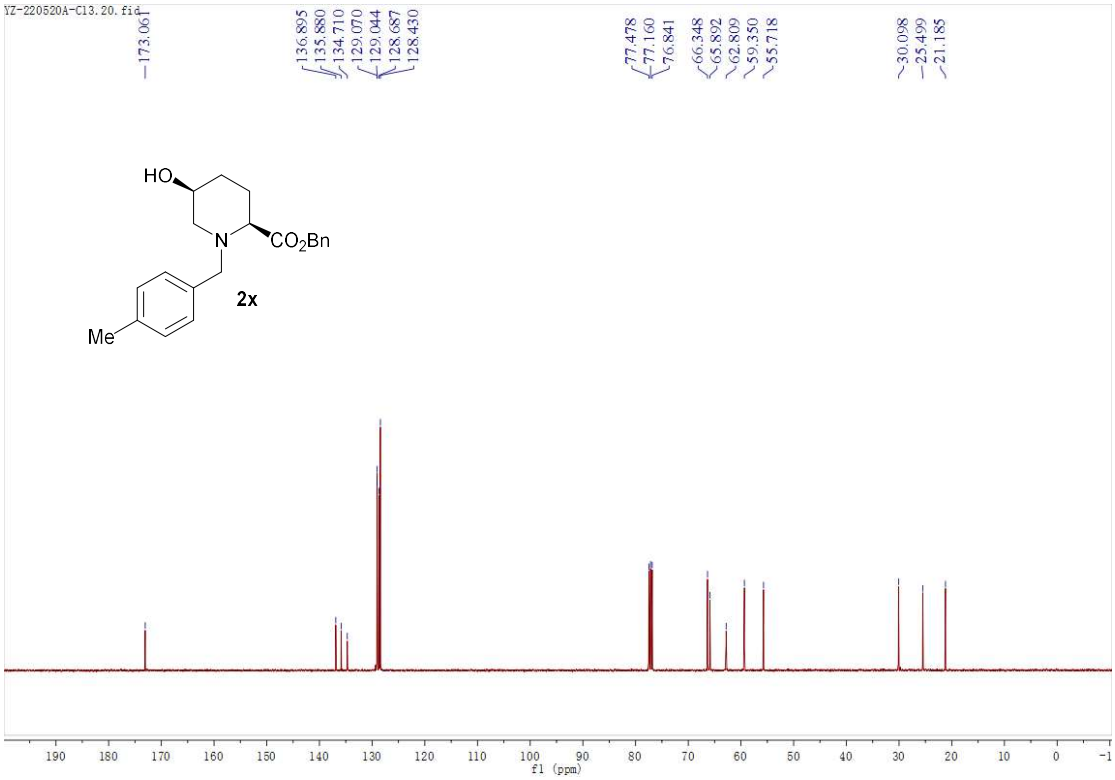
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2w



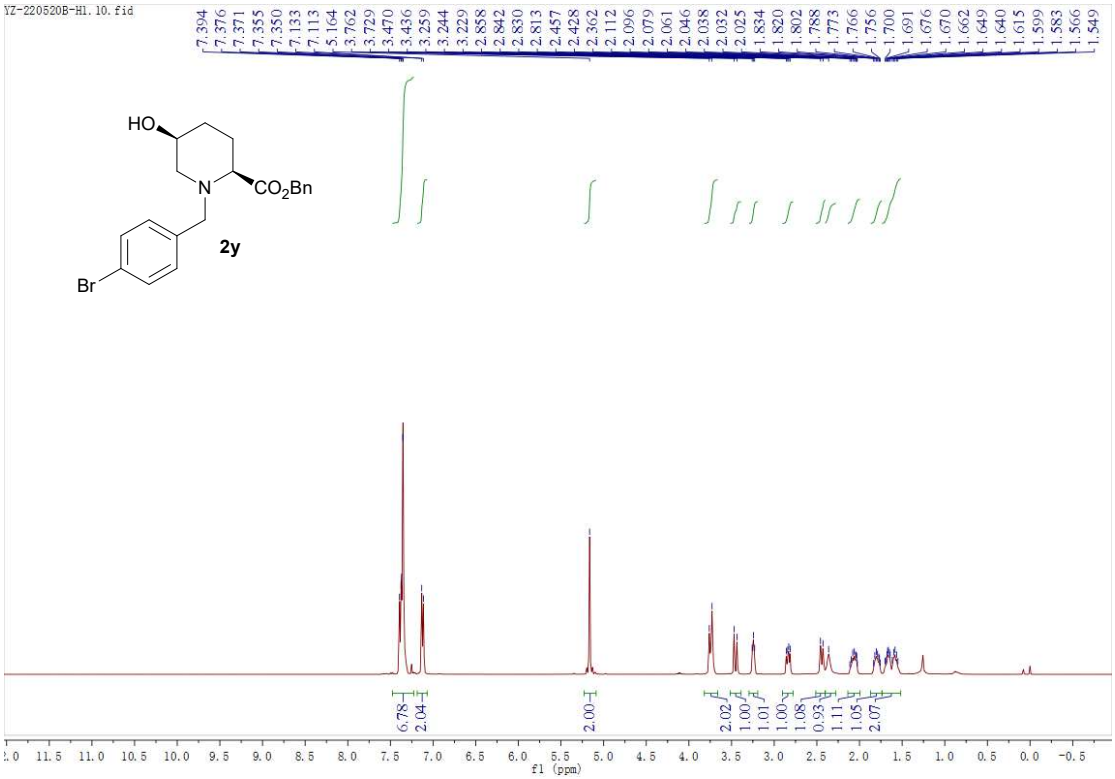
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2w



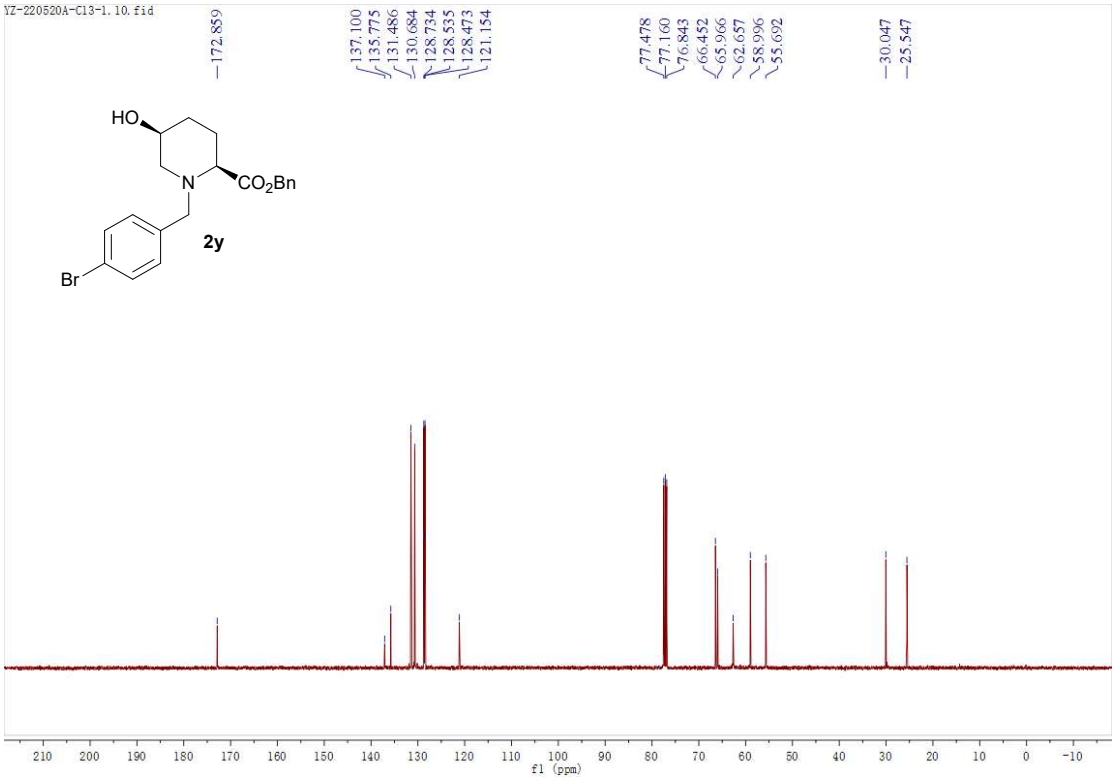
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2x



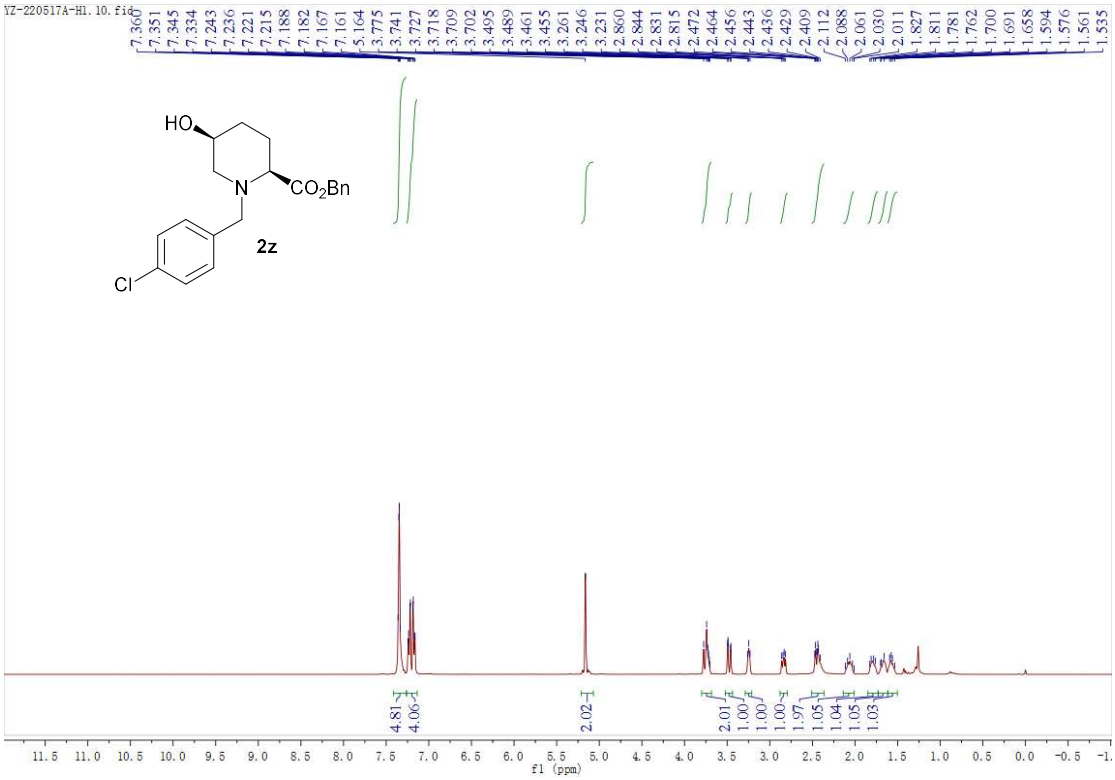
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2x



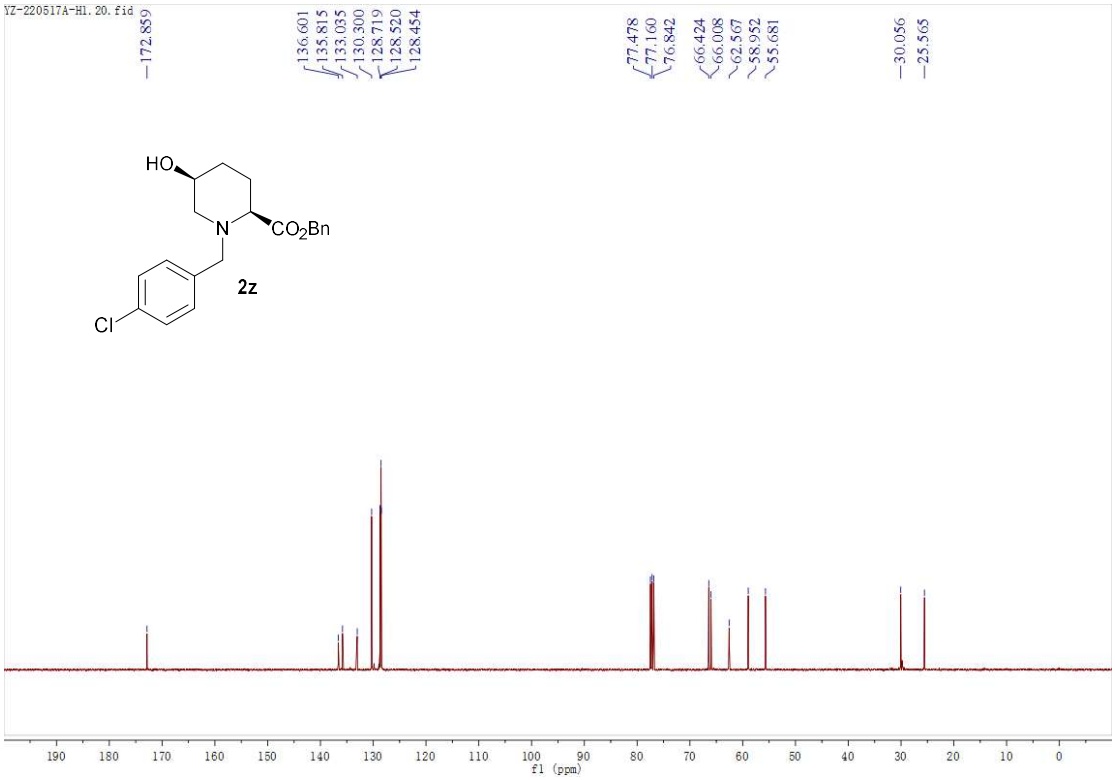
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2y



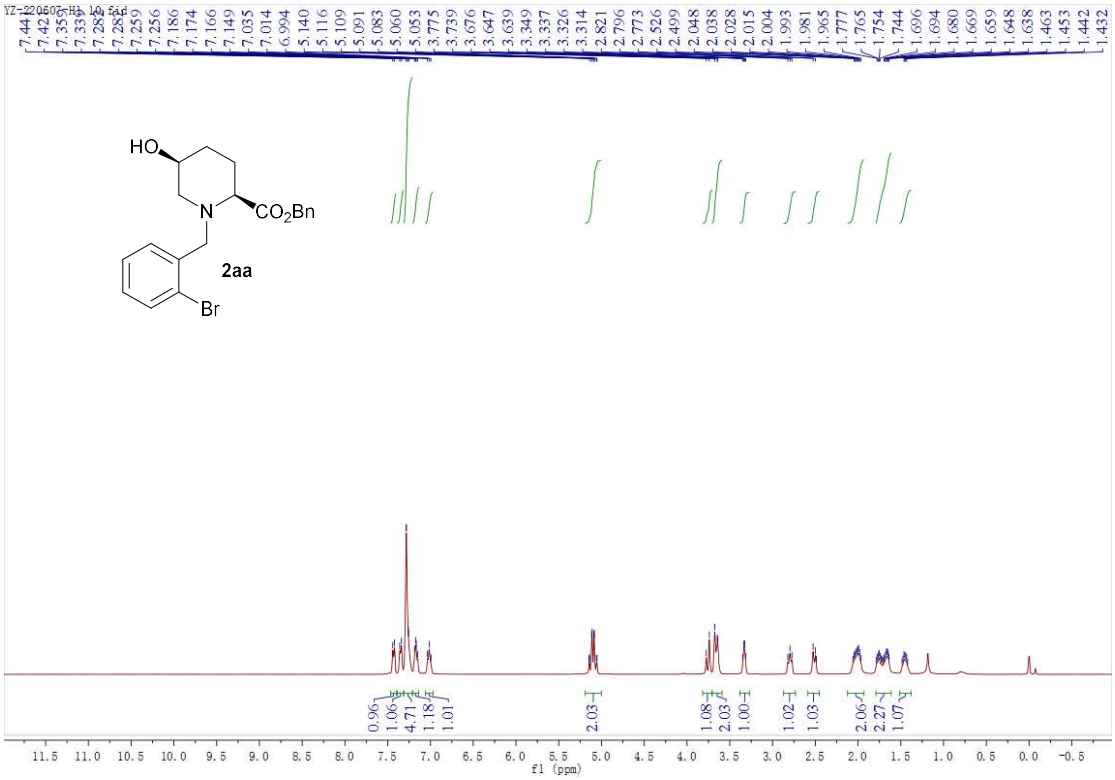
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2y



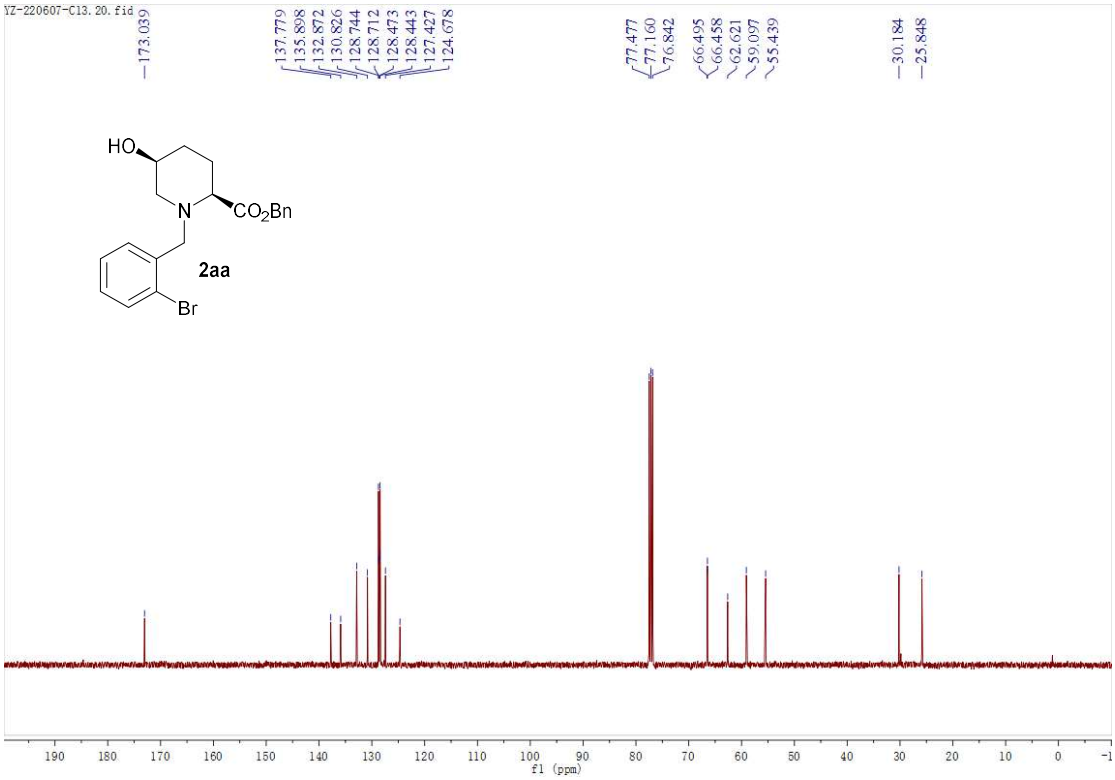
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2z



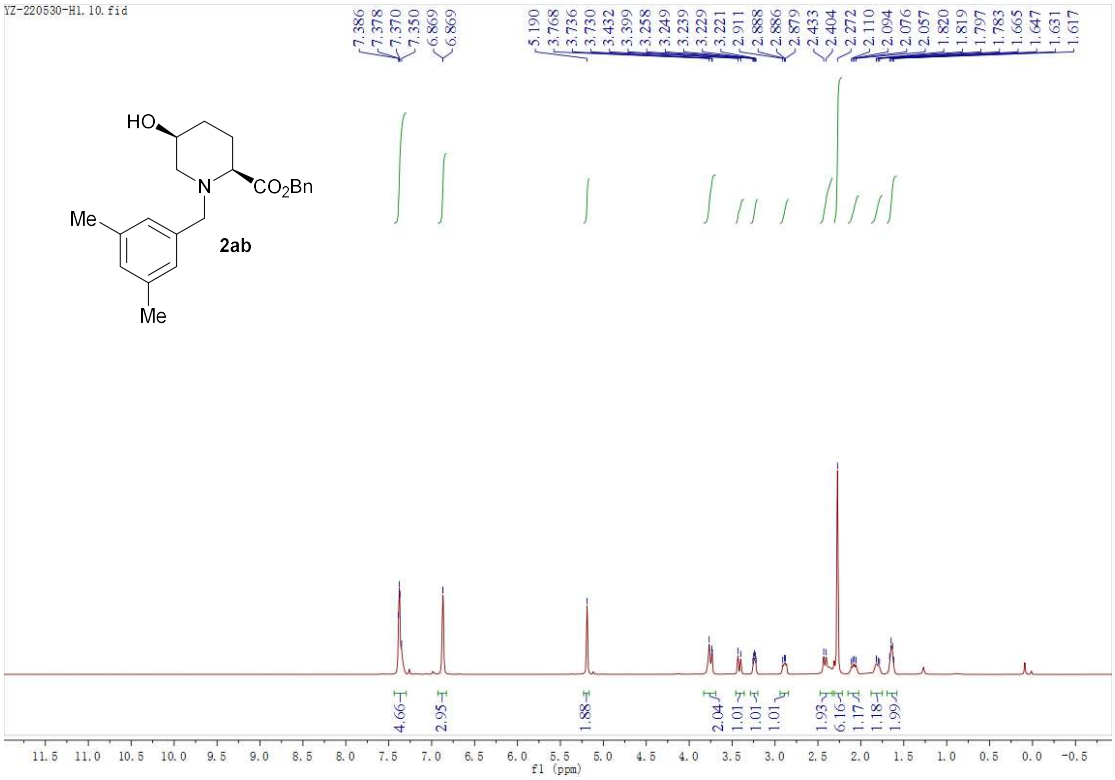
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2z



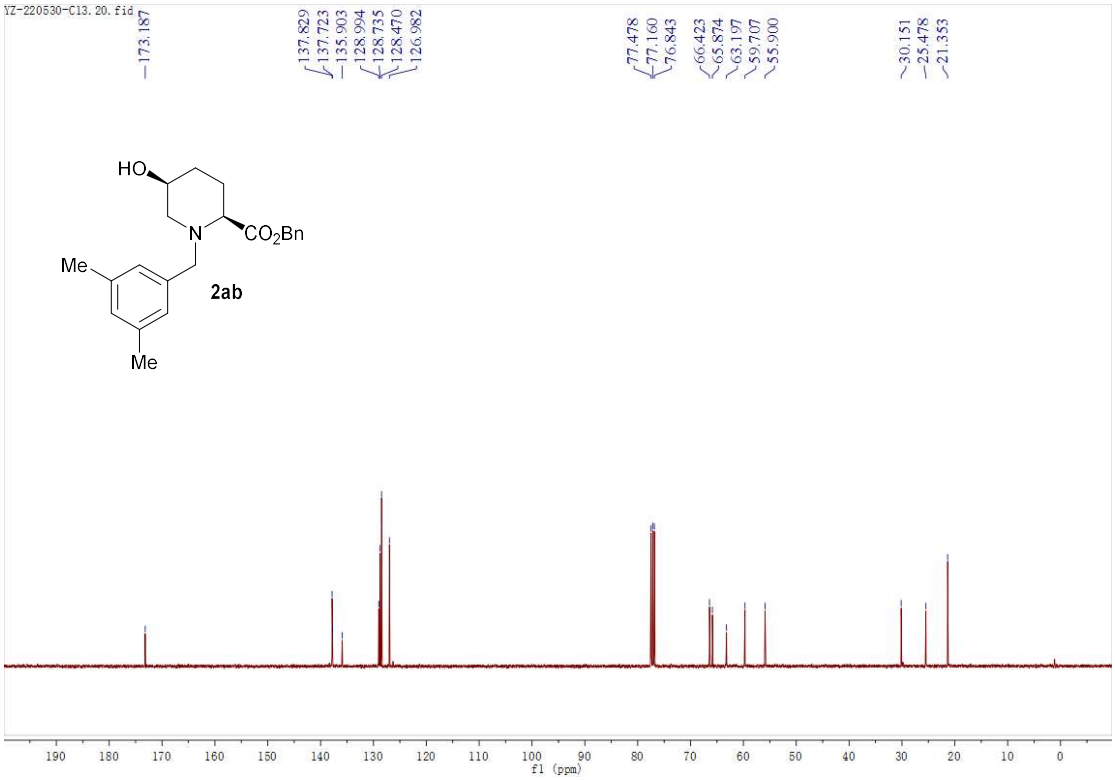
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2aa



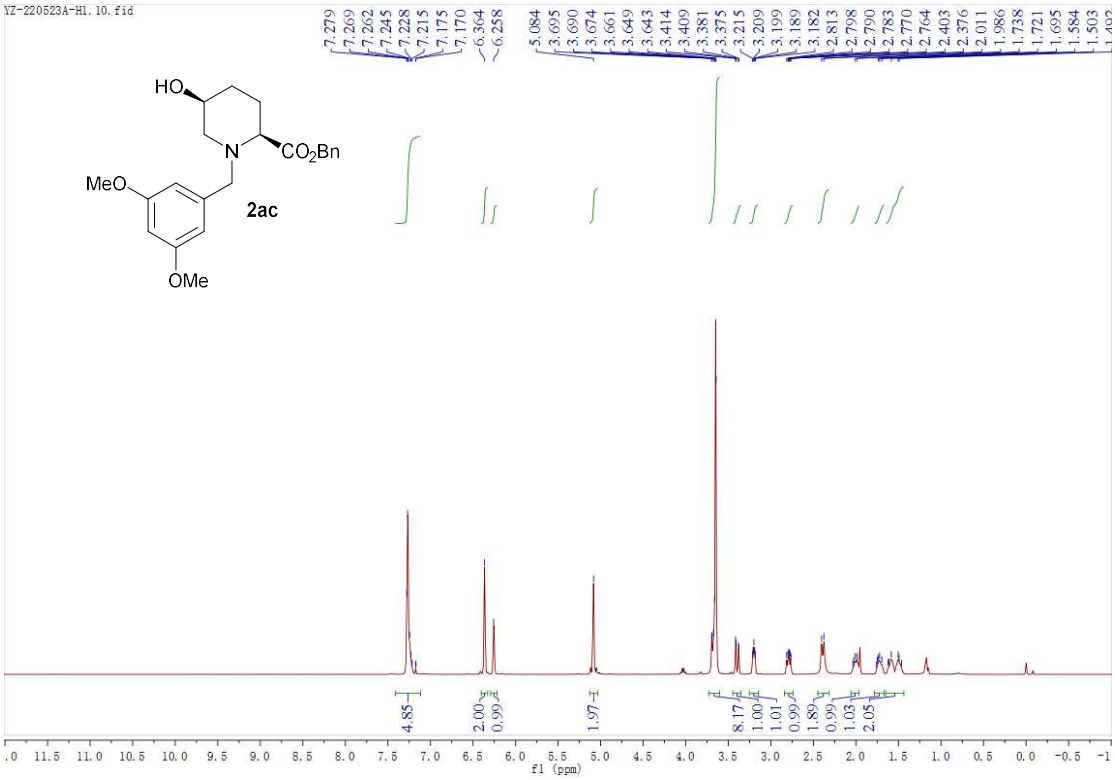
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2aa



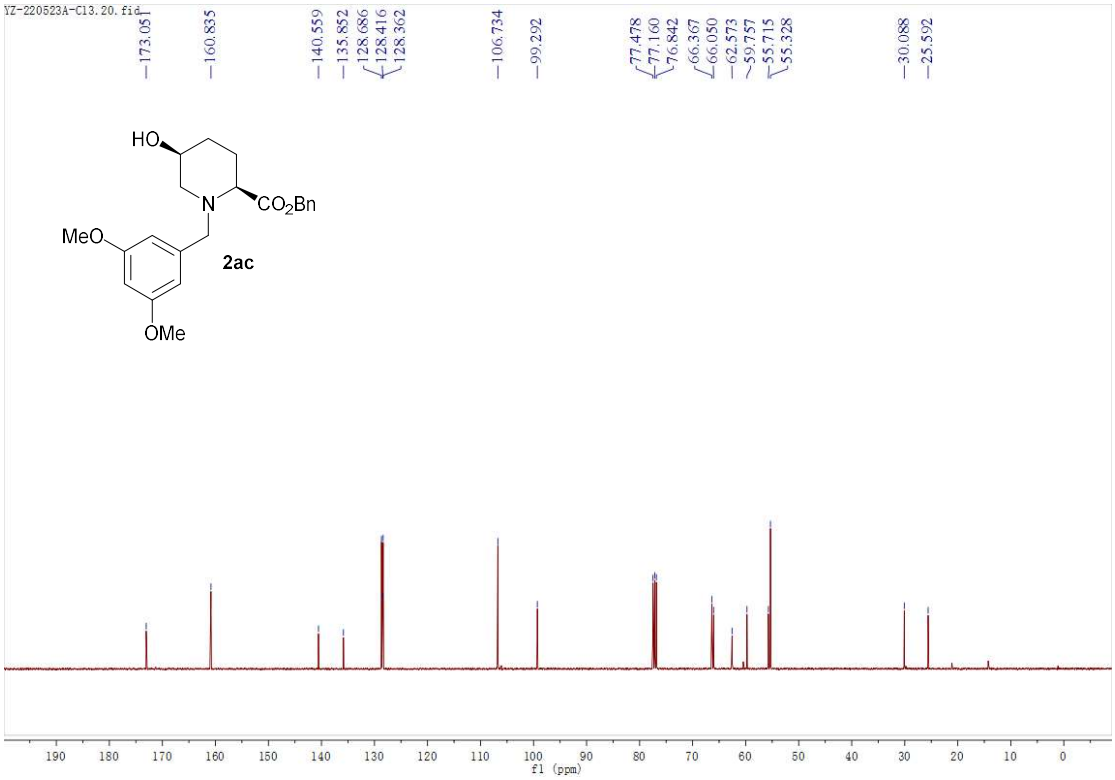
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2ab



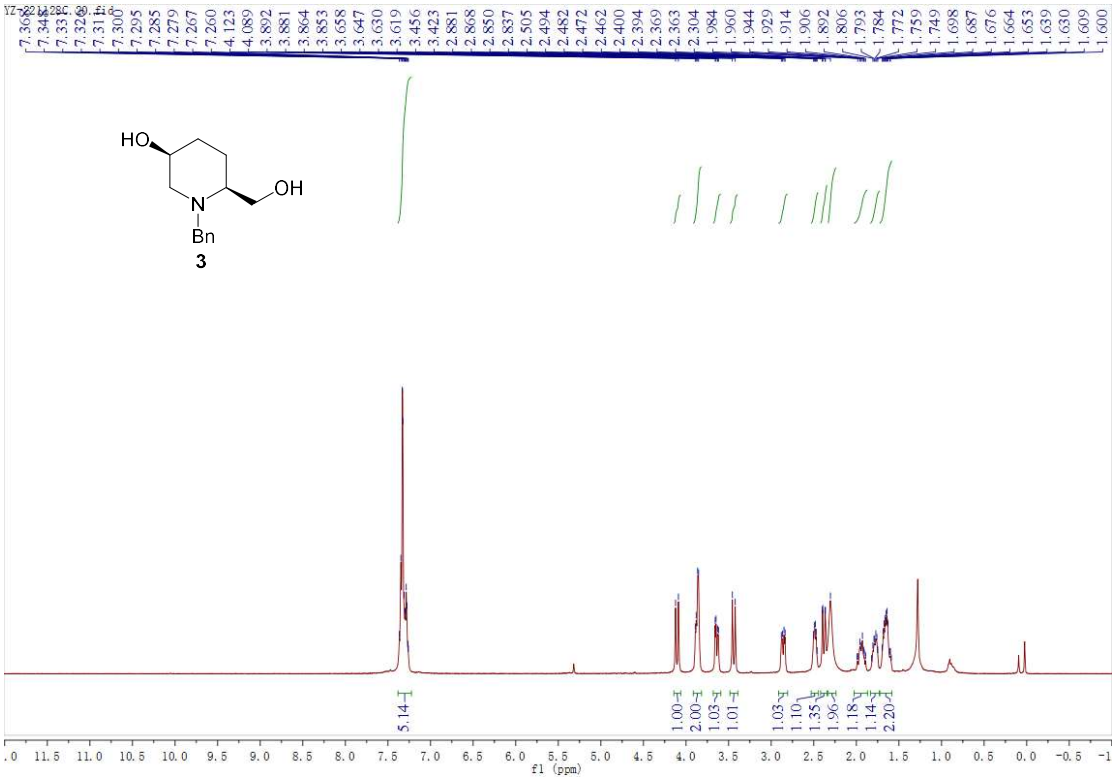
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2ab



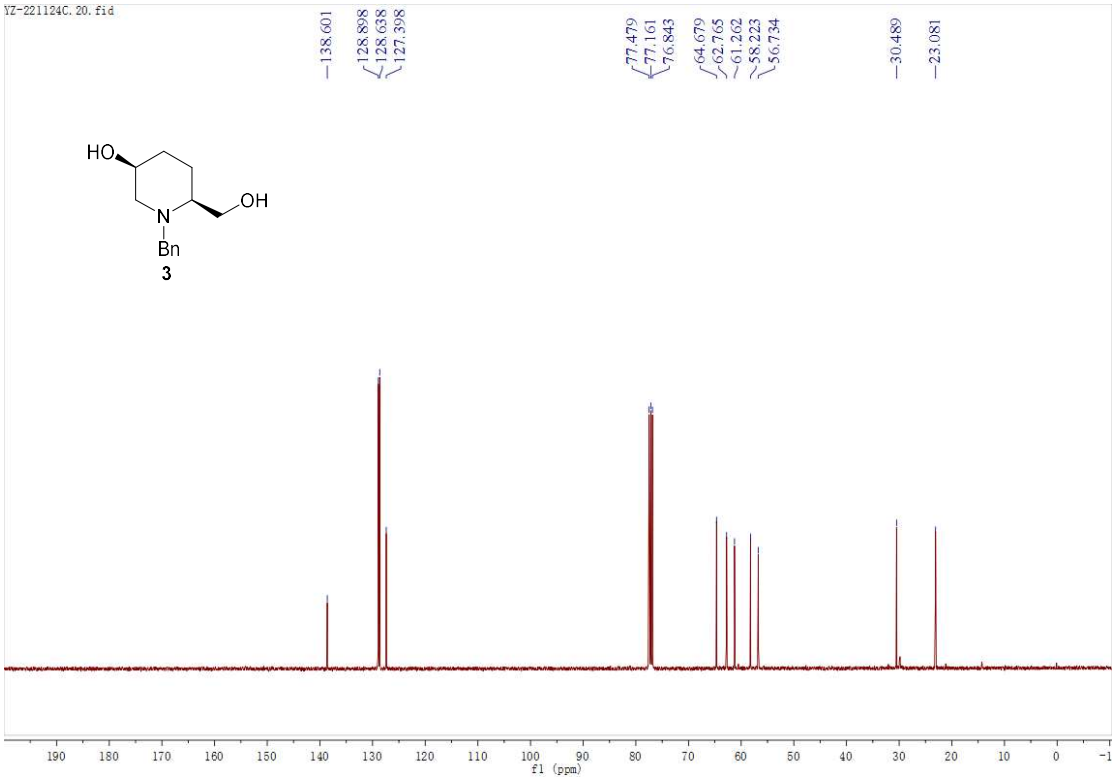
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 2ac



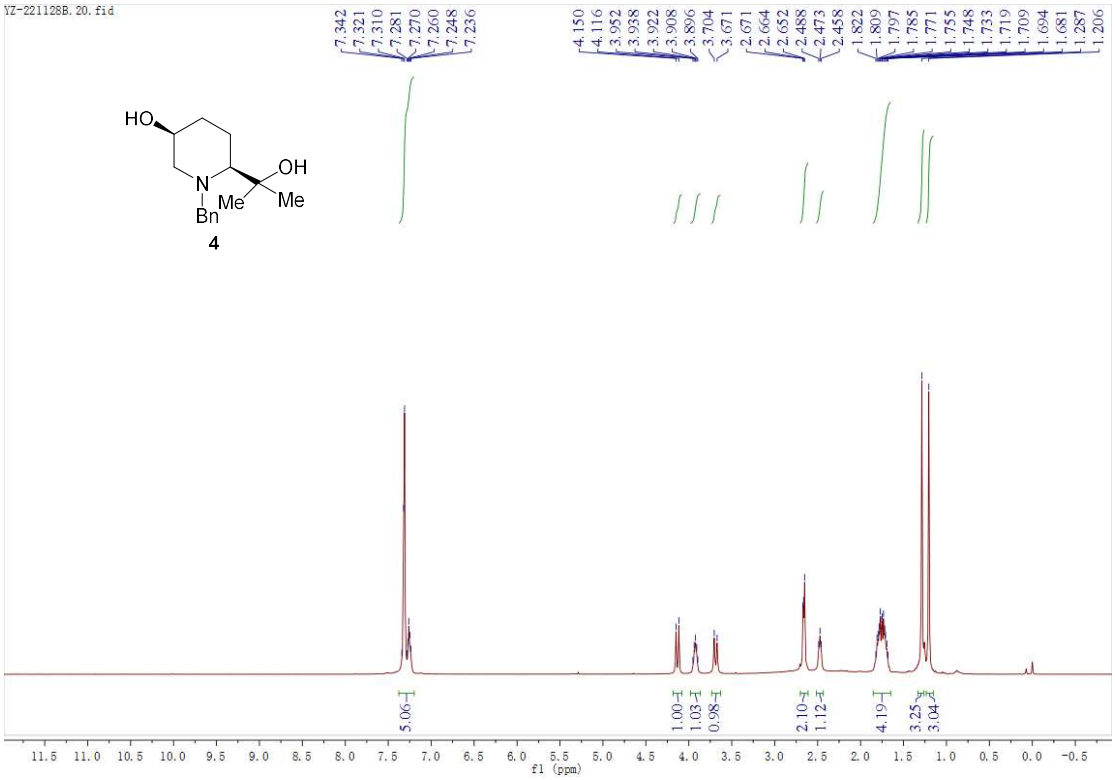
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 2ac



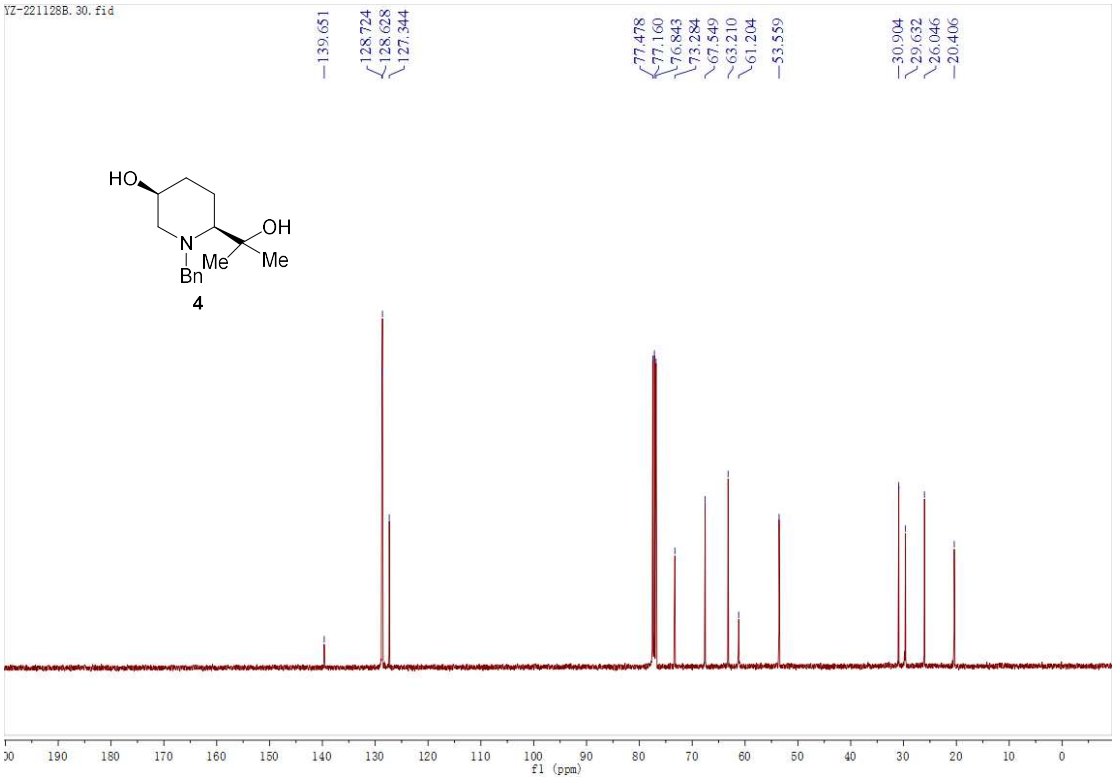
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 3



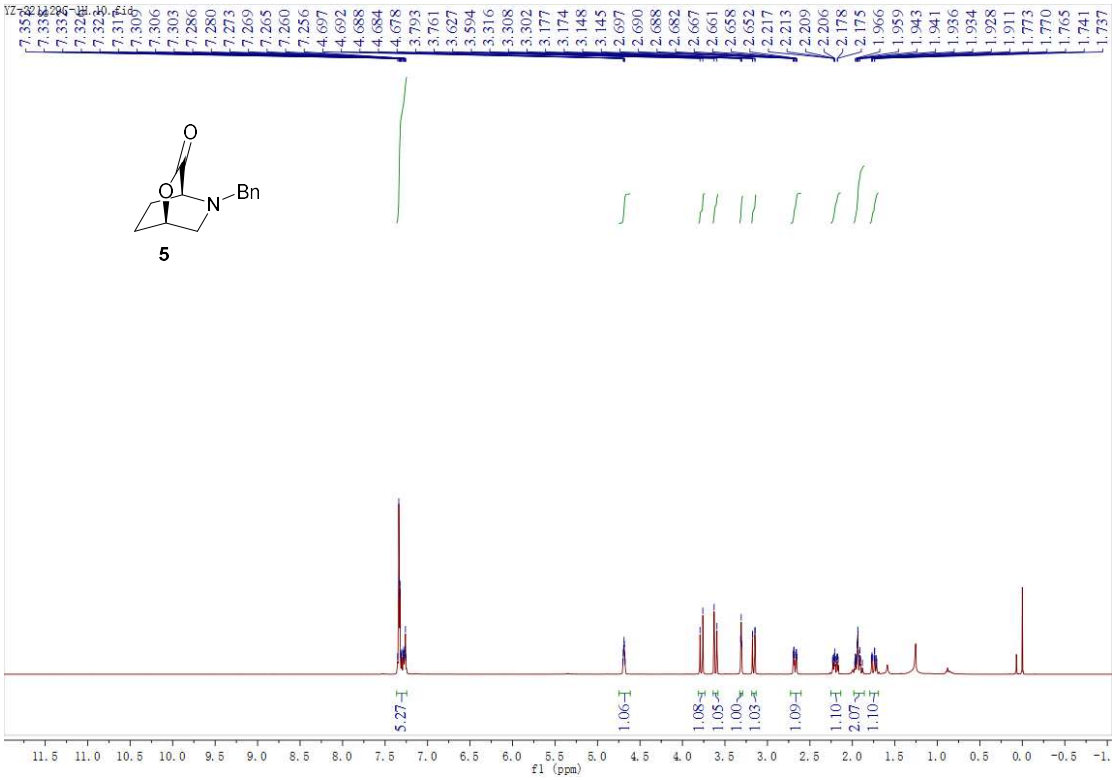
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 3



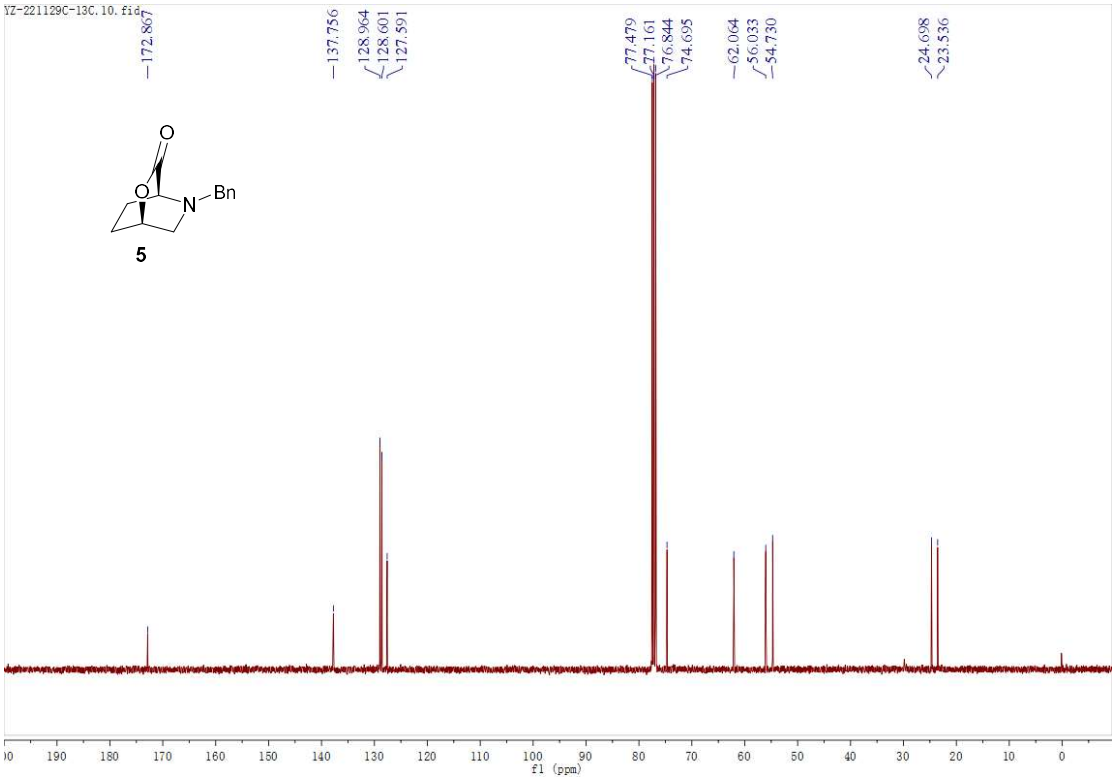
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 4



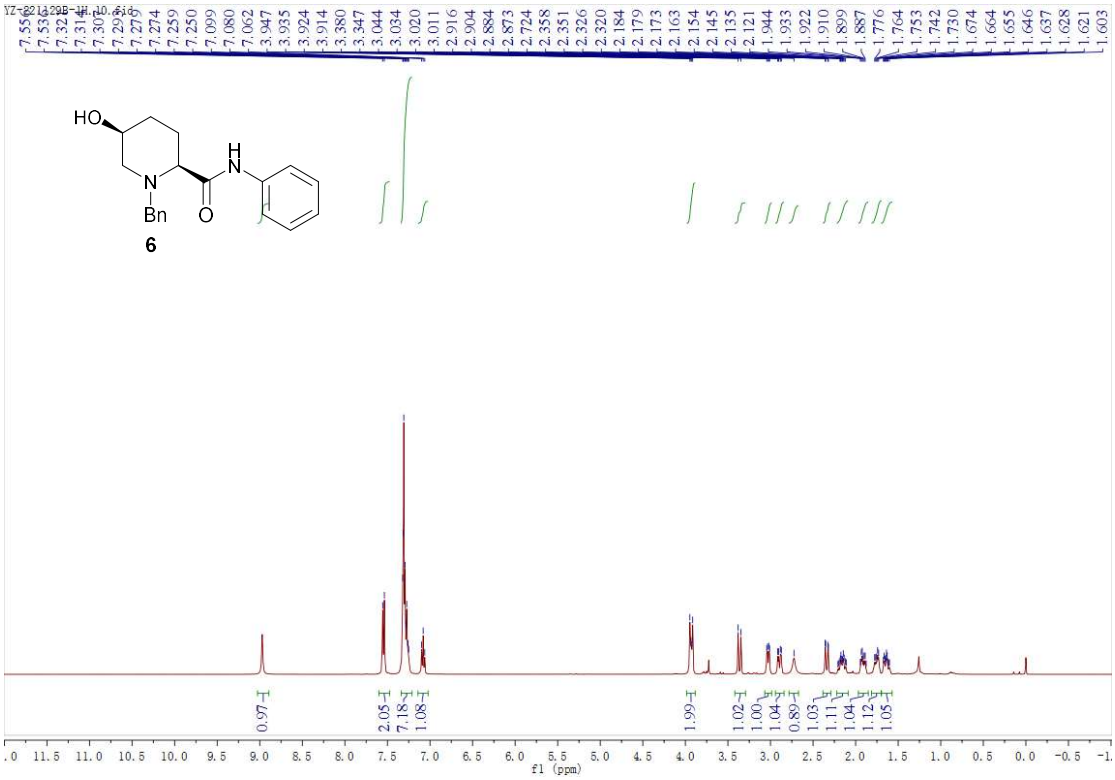
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 4



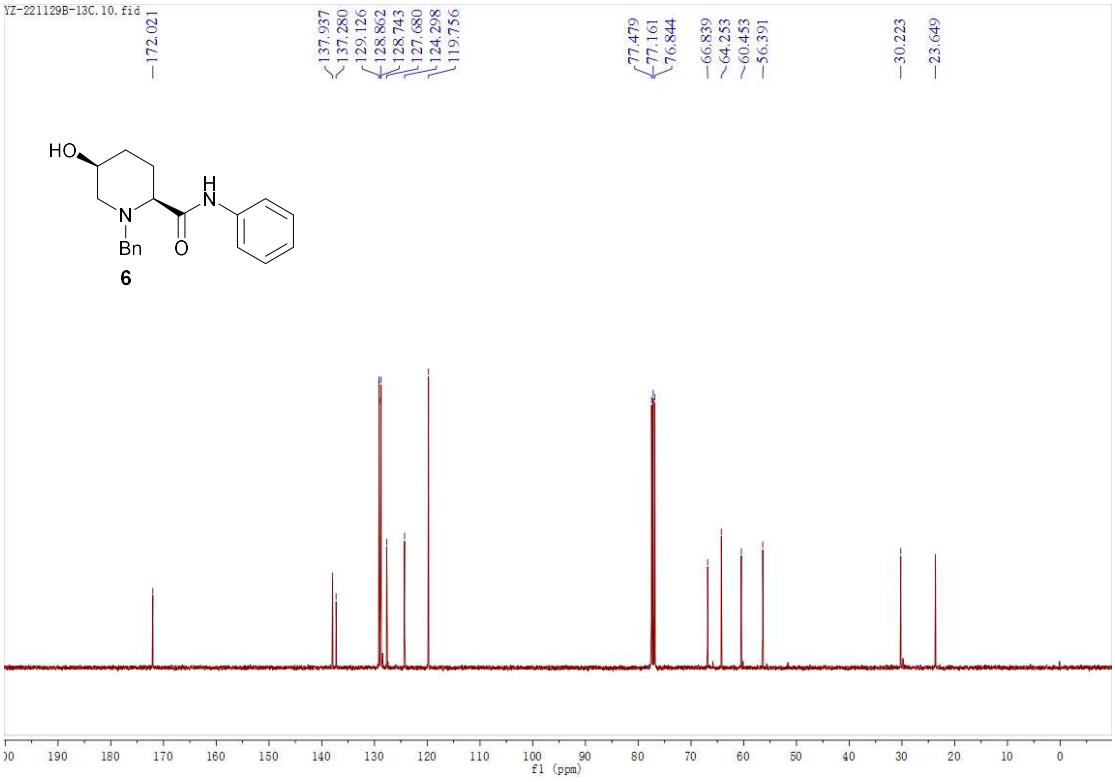
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 5



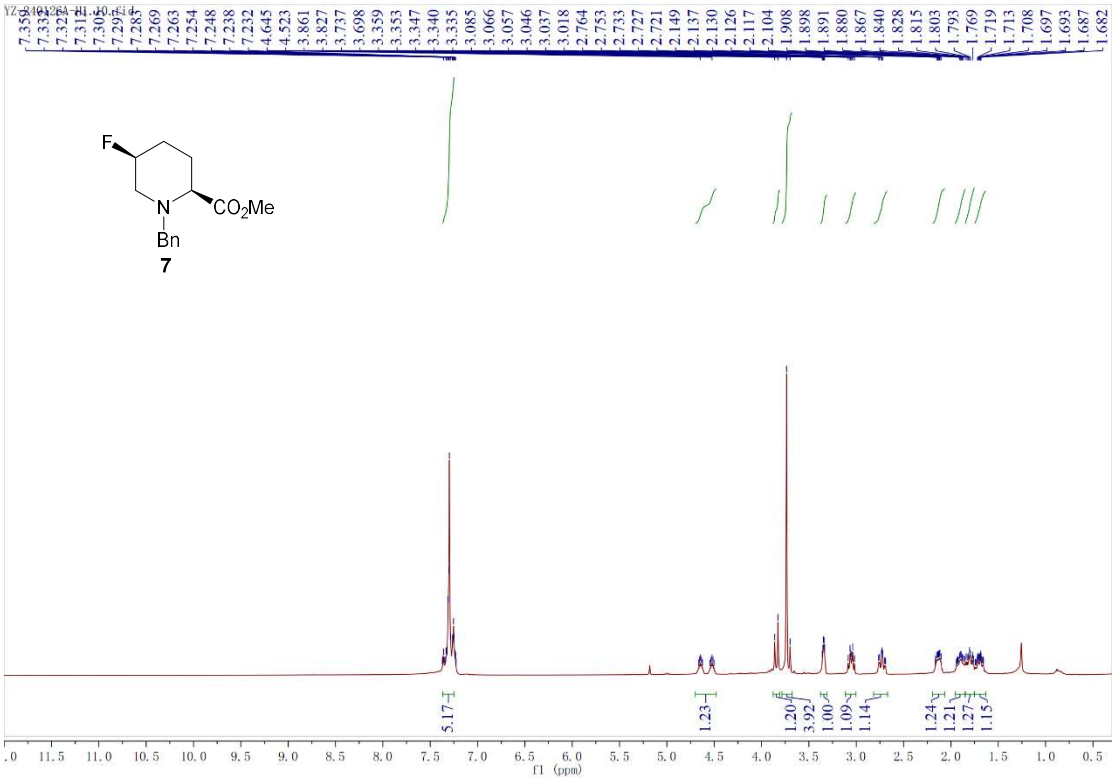
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 5



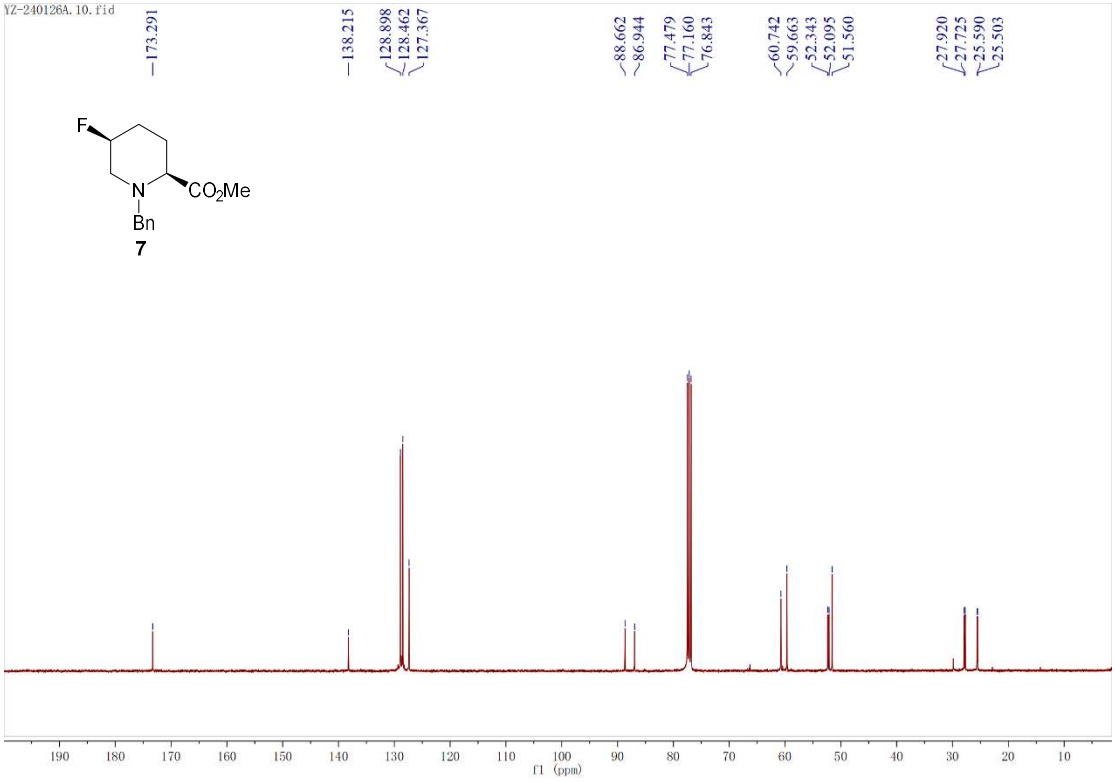
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 6



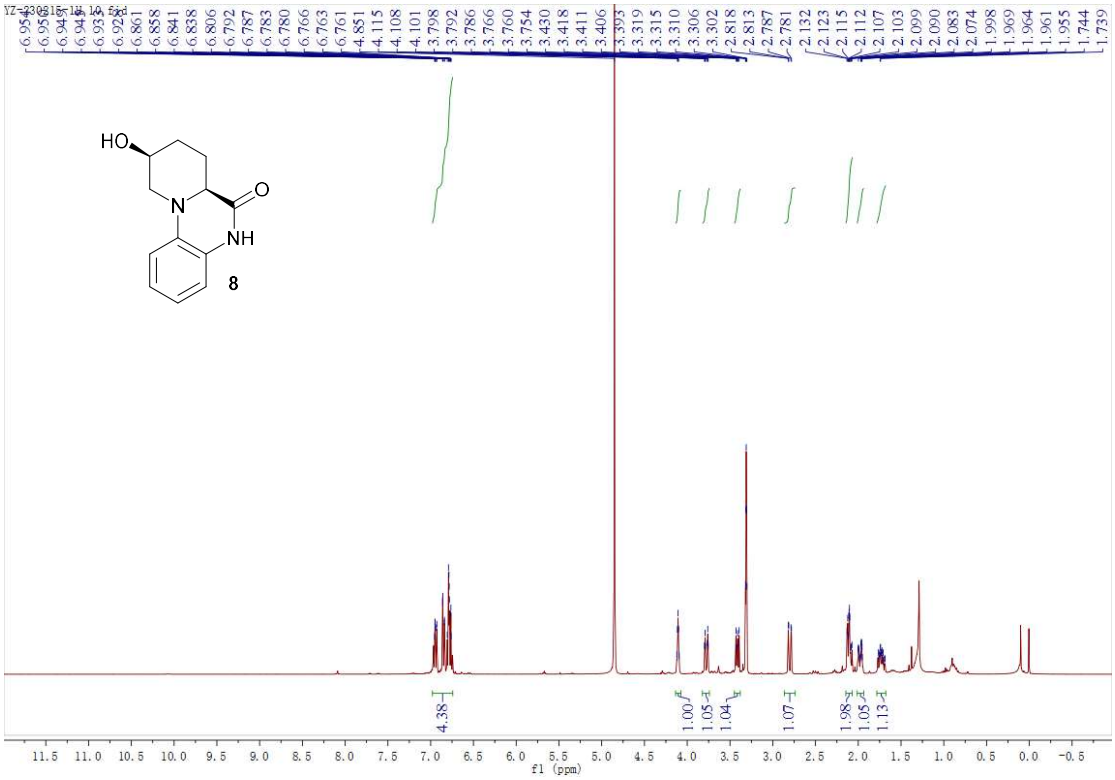
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 6



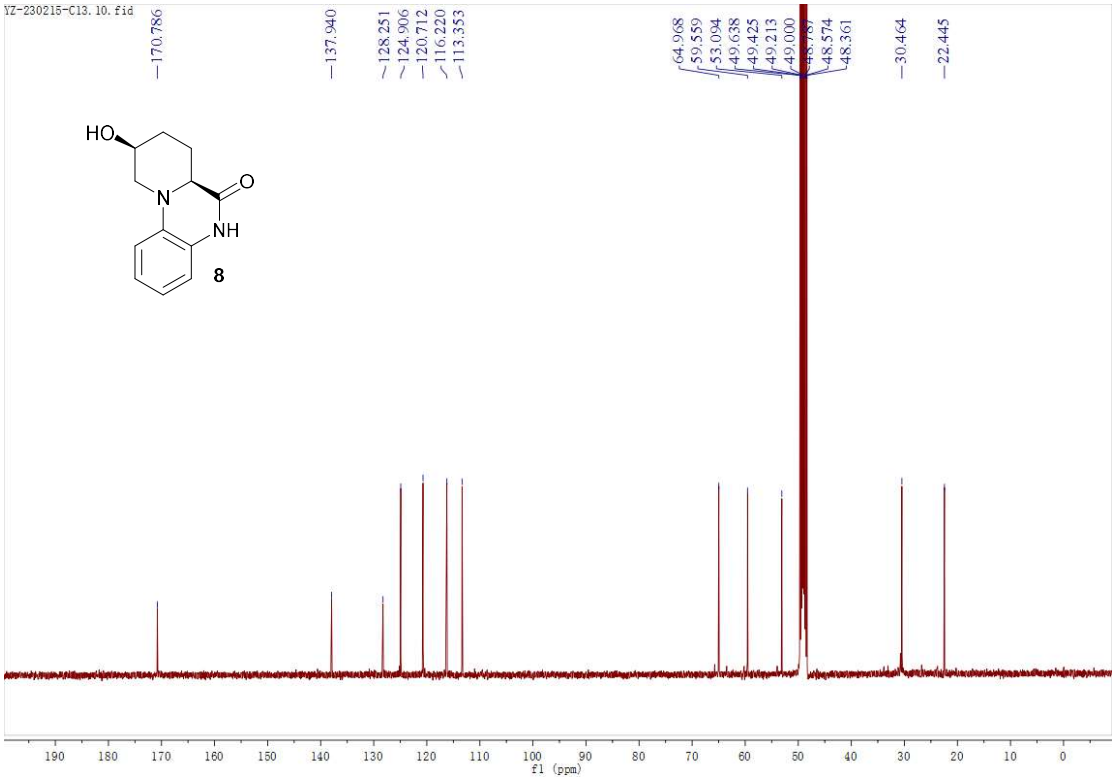
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 7



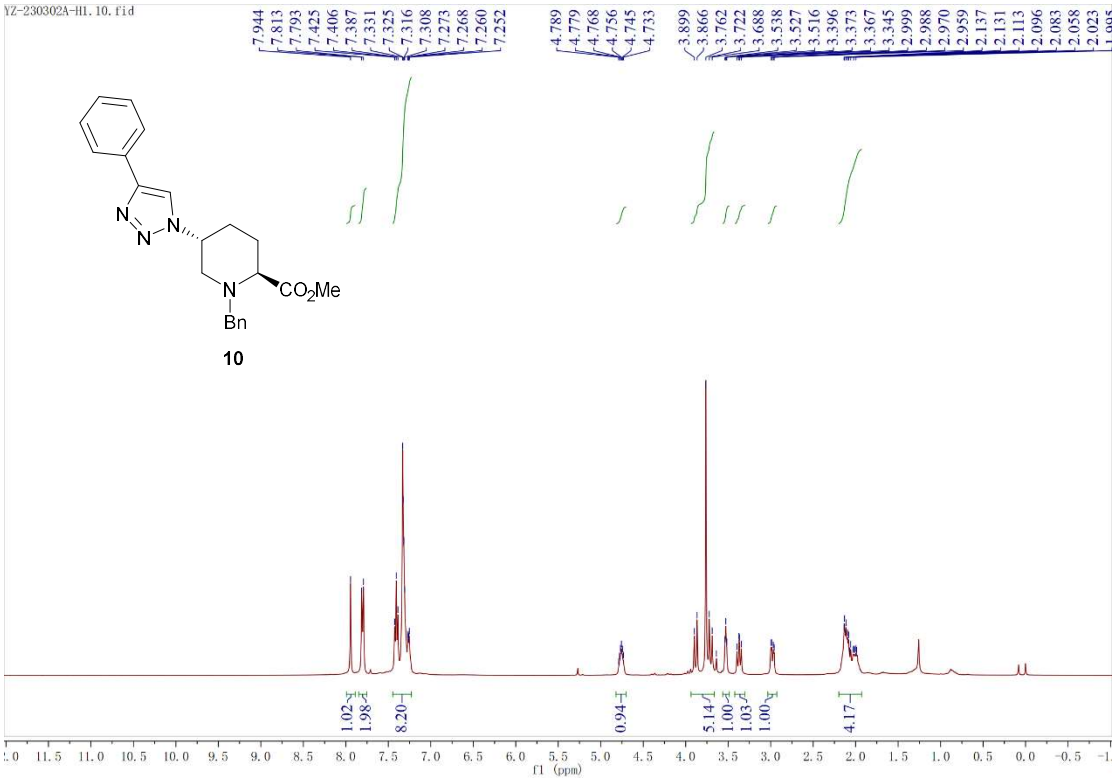
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 7



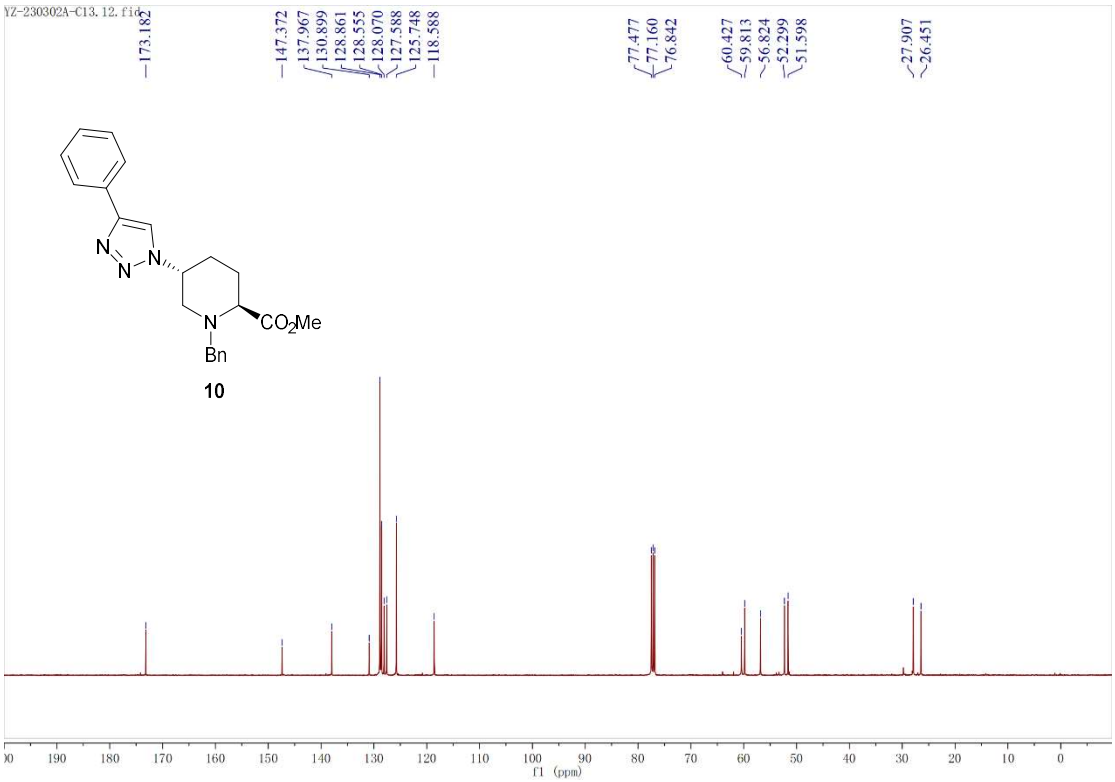
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 8



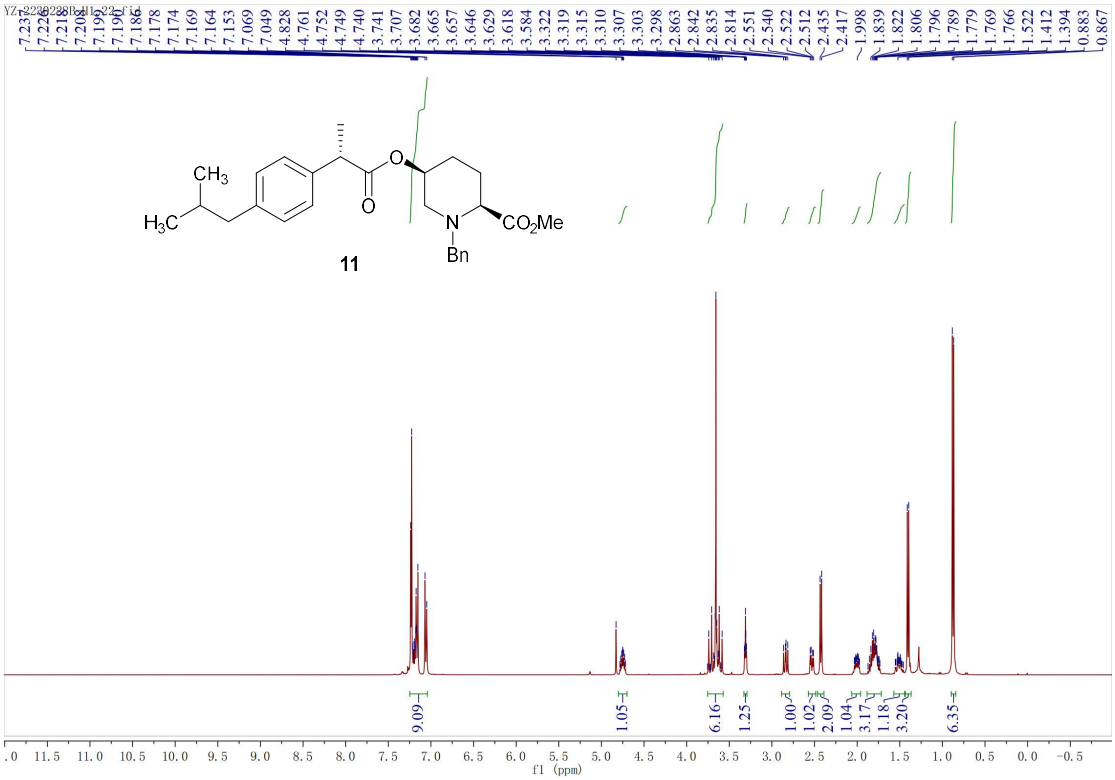
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 8



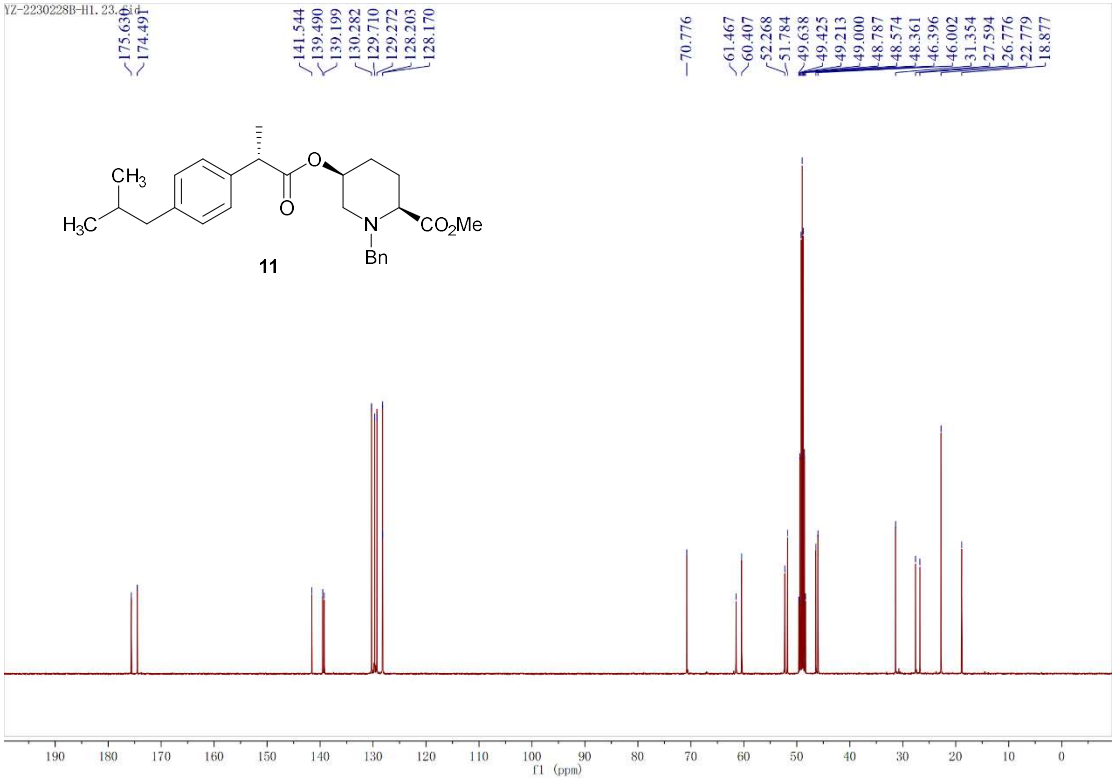
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 10



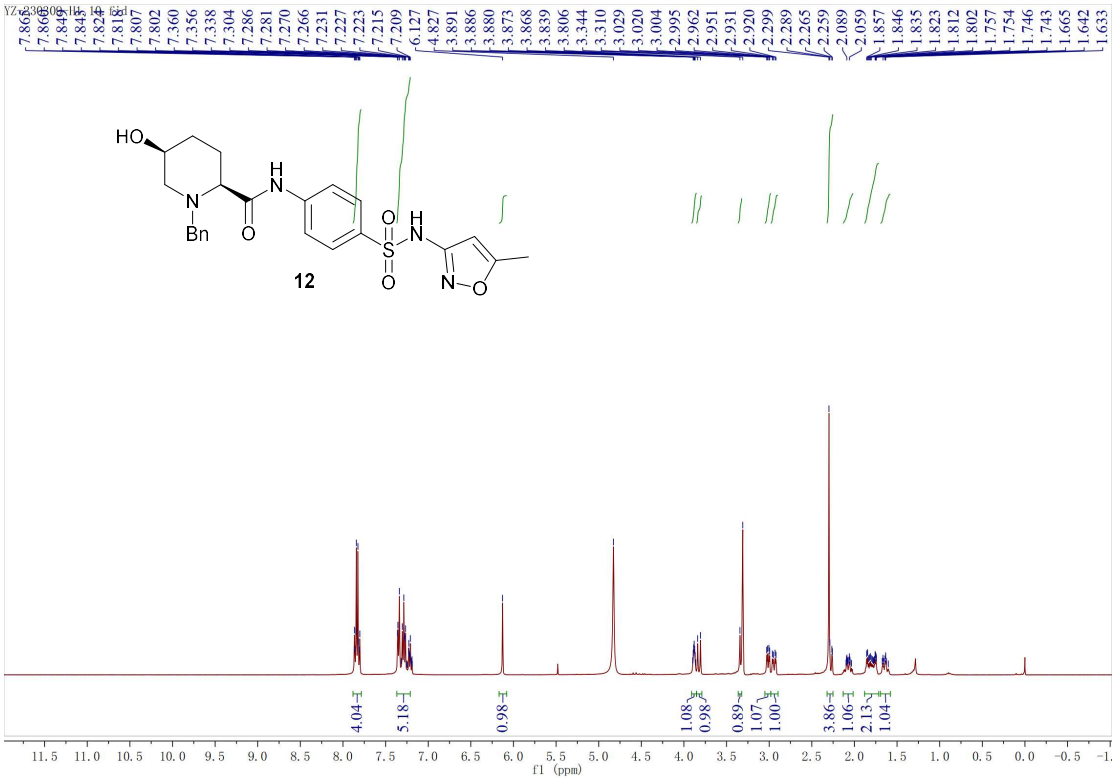
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 10



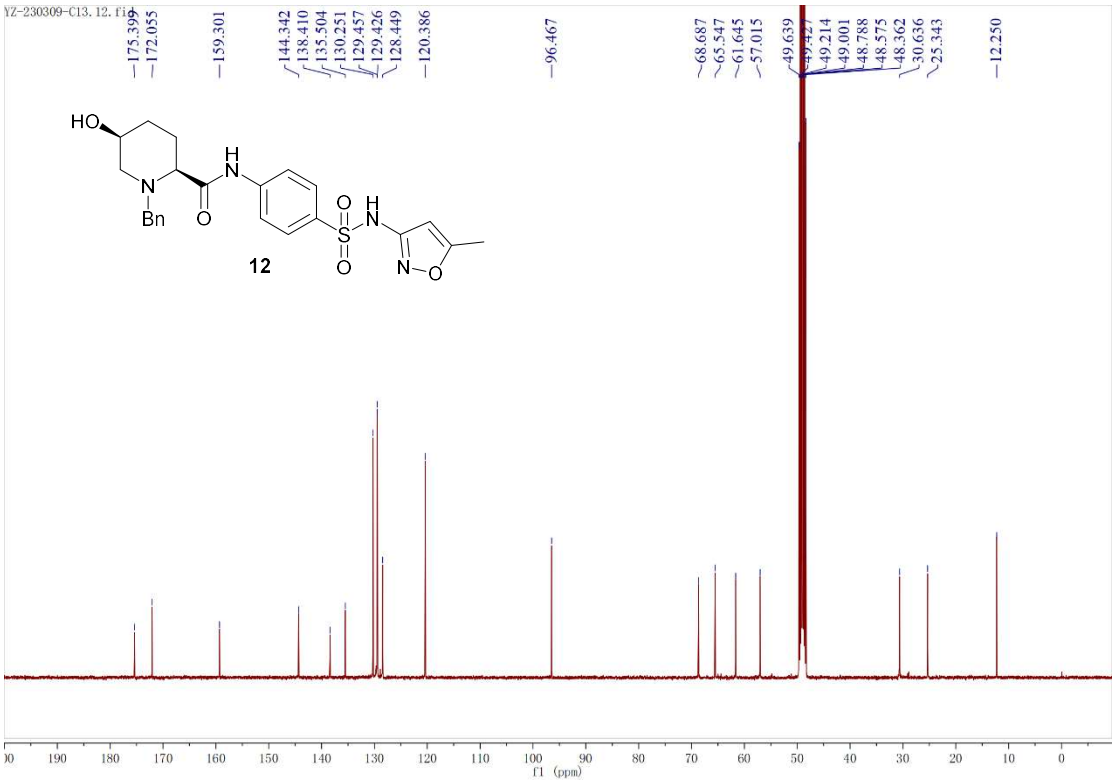
^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 11



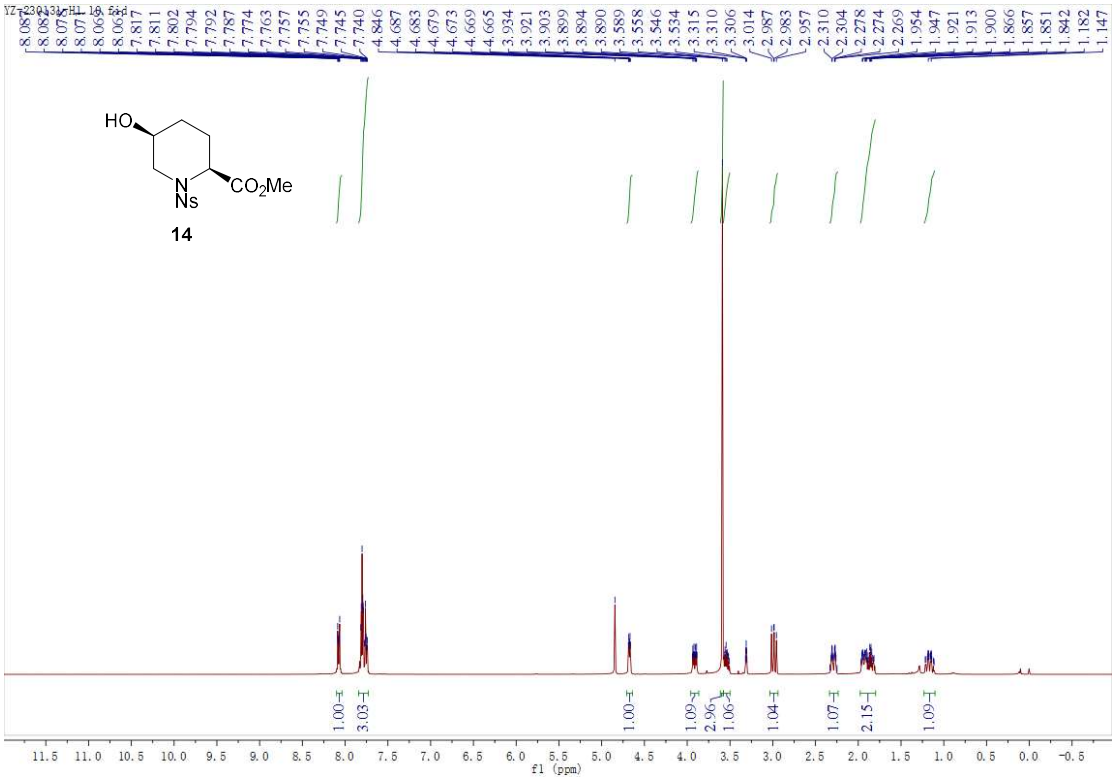
^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 11



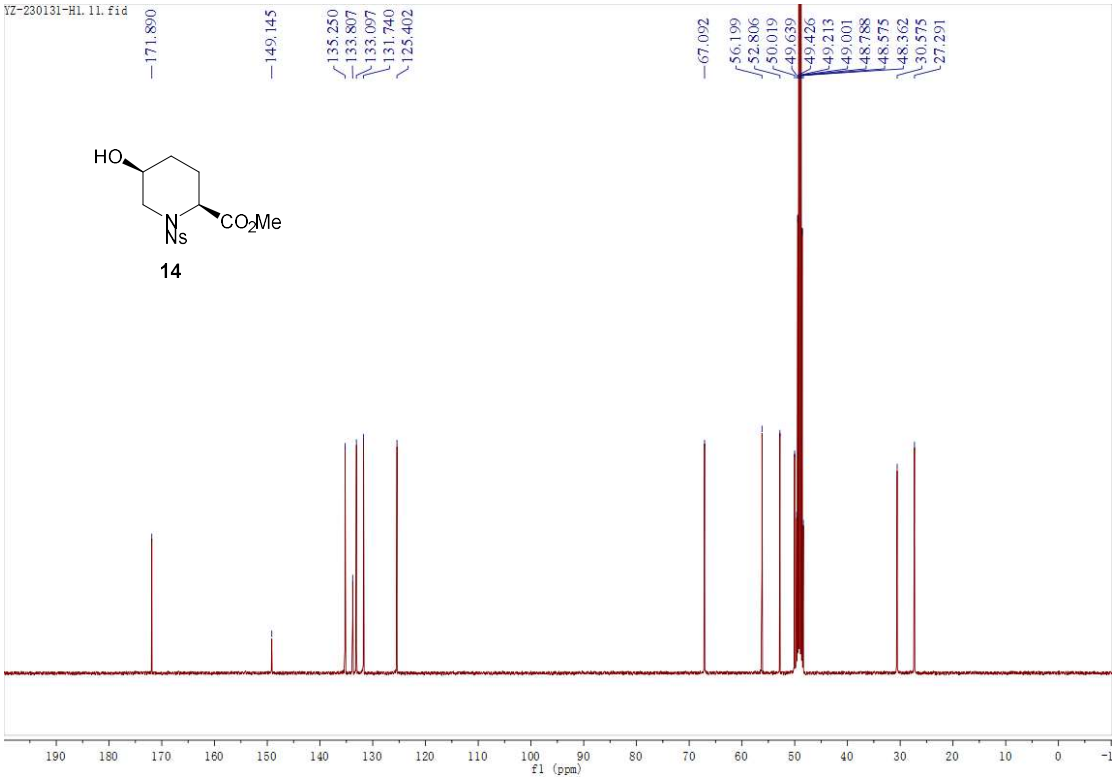
[1]H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 12



[13]C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 12

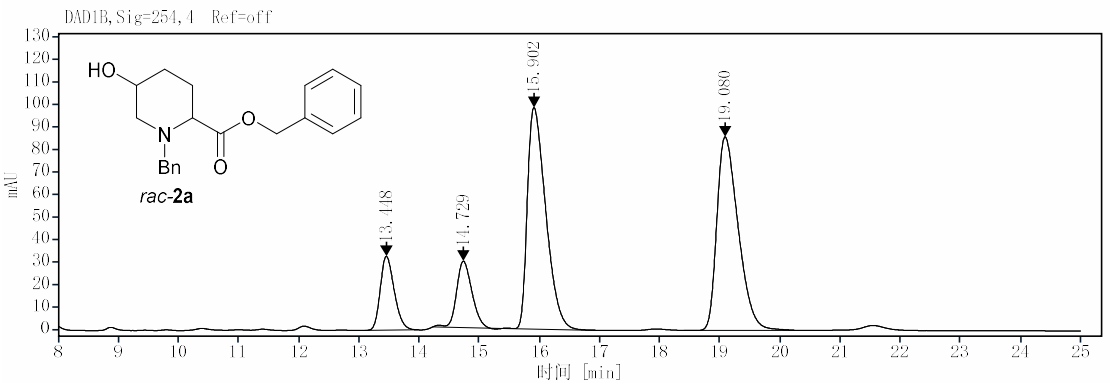


^{1}H-NMR Spectrum (400 MHz, Chloroform-*d*) of Compound 14

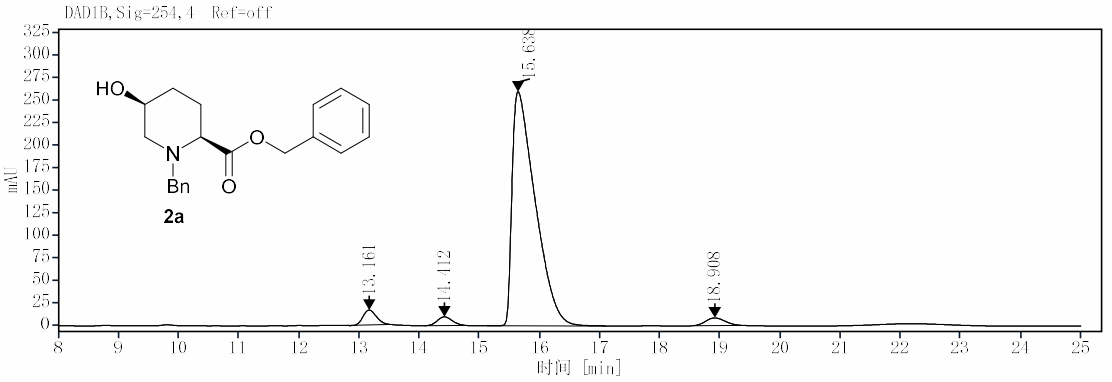


^{13}C-NMR Spectrum (100 MHz, Chloroform-*d*) of Compound 14

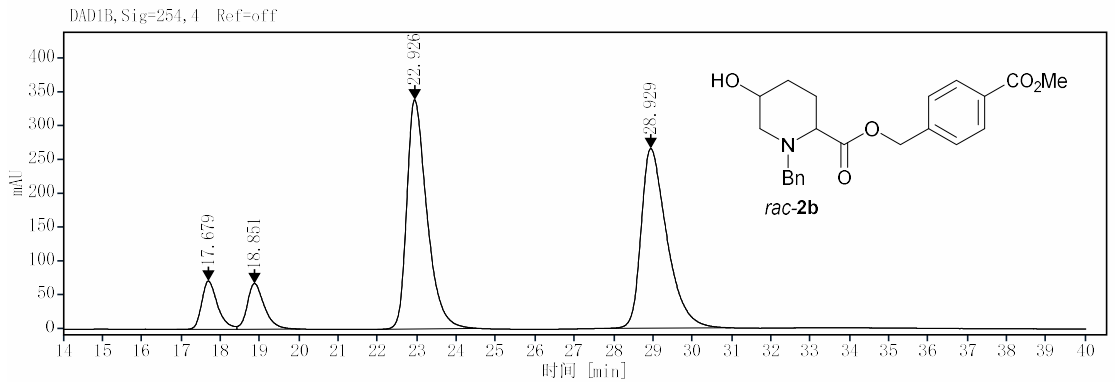
5. HPLC Spectra



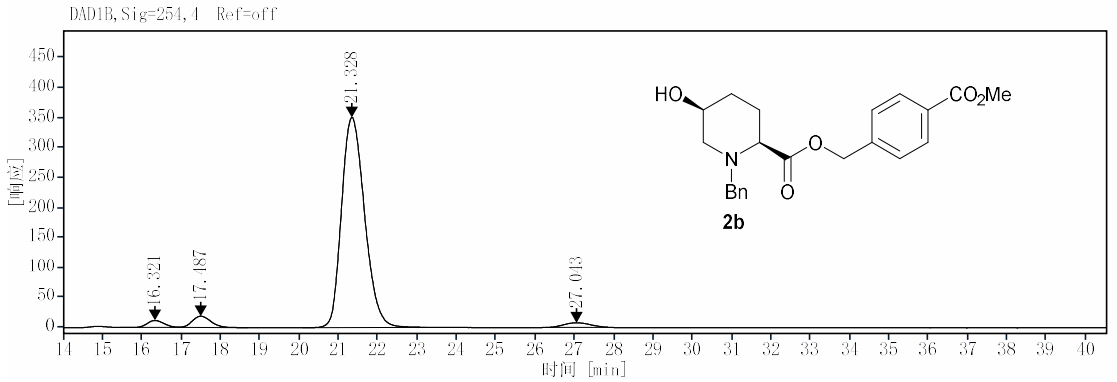
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
13.448	MM m	0.25	532.07	32.86	10.09
14.729	MM m	0.28	528.10	29.61	10.01
15.902	MM m	0.33	2096.13	98.52	39.75
19.080	MM m	0.38	2117.60	85.99	40.15



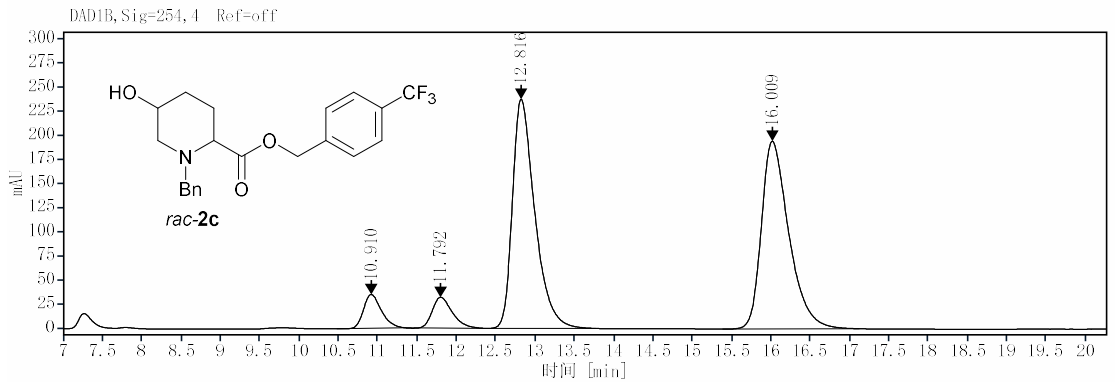
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
13.161	MM m	0.24	255.30	16.59	3.38
14.412	MM m	0.27	170.32	9.76	2.26
15.638	MM m	0.40	6931.59	260.14	91.89
18.908	MM m	0.34	186.06	8.47	2.47



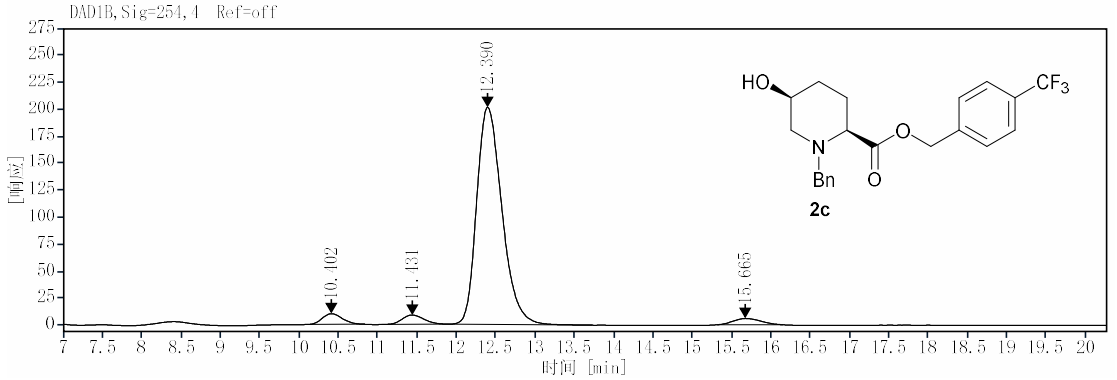
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
17.679	MM m	0.43	2006.84	71.59	7.10
18.851	MM m	0.45	2039.08	67.69	7.21
22.926	MM m	0.54	12089.23	339.59	42.75
28.929	MM m	0.69	12145.60	266.05	42.95



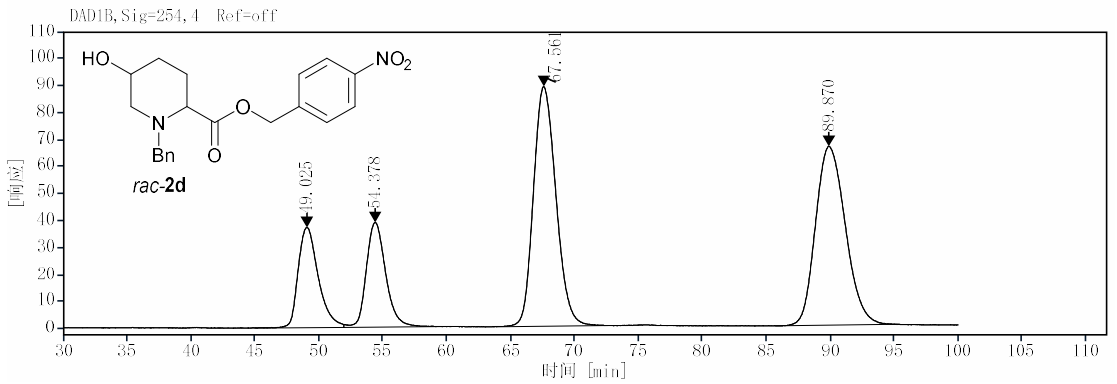
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.321	MM m	0.43	348.43	11.58	2.23
17.487	MM m	0.48	622.95	18.86	4.00
21.328	MM m	0.65	14267.48	350.20	91.51
27.043	MM m	0.55	352.89	7.68	2.26



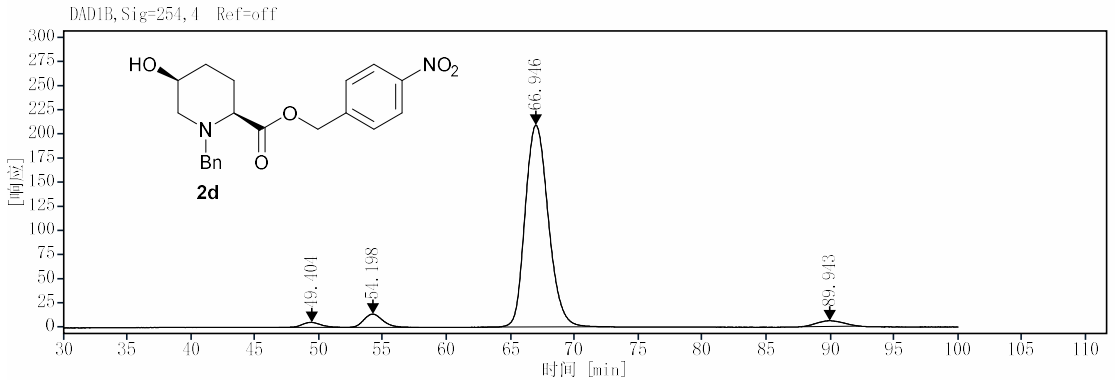
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
10.910	MM m	0.24	554.22	35.01	5.25
11.792	MM m	0.27	560.83	31.93	5.32
12.816	MM m	0.30	4703.55	237.69	44.59
16.009	MM m	0.37	4729.33	194.75	44.84



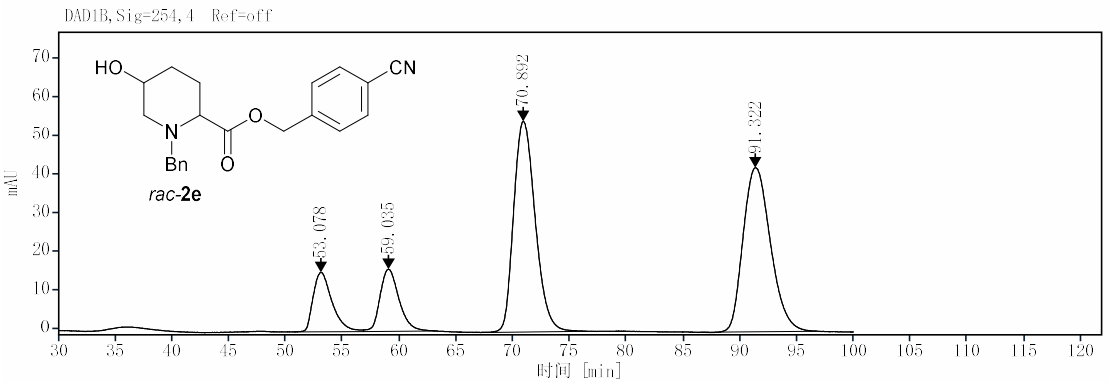
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
10.402	MM m	0.27	177.11	9.94	3.57
11.431	MM m	0.29	162.37	8.56	3.27
12.390	MM m	0.35	4483.85	200.91	90.29
15.665	MM m	0.31	142.97	5.85	2.88



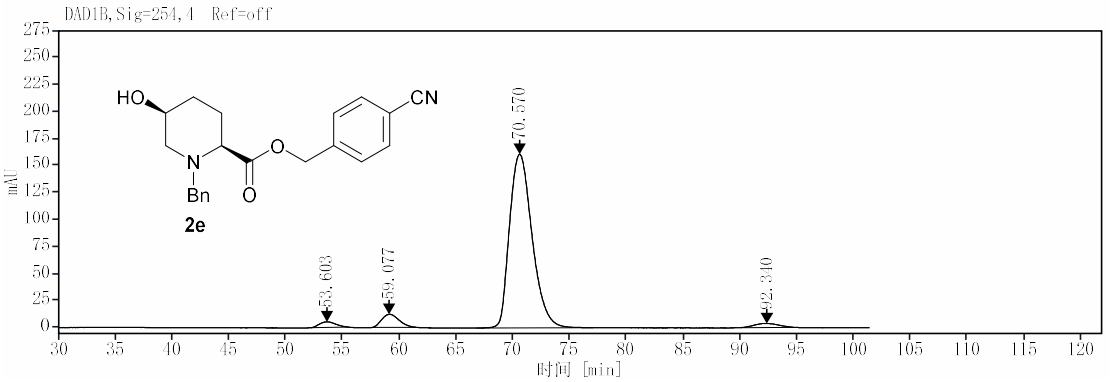
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
49.025	MM m	1.31	4054.57	37.13	13.63
54.378	MM m	1.24	4097.81	38.78	13.78
67.561	MM m	1.44	10843.72	88.78	36.45
89.870	MM m	1.90	10749.52	66.24	36.14



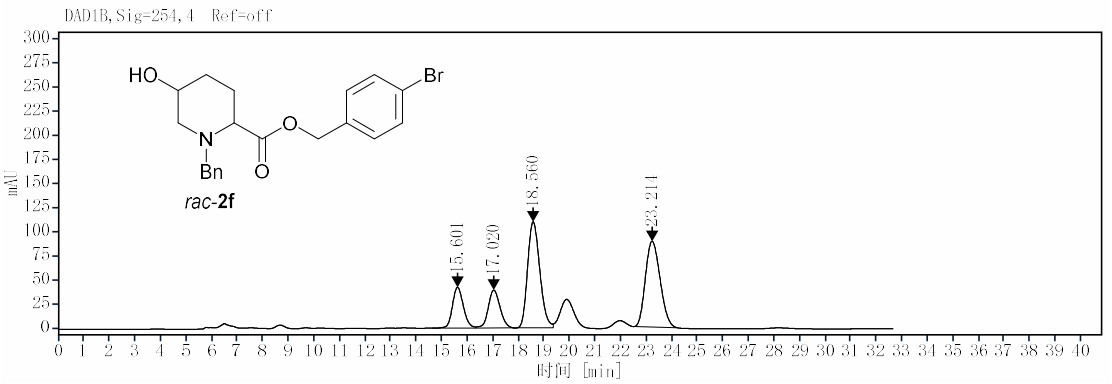
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
49.404	MM m	1.17	514.95	5.16	1.76
54.198	MM m	1.21	1404.86	13.73	4.81
66.946	MM m	1.58	26416.70	209.37	90.49
89.943	MM m	1.68	857.70	5.96	2.94



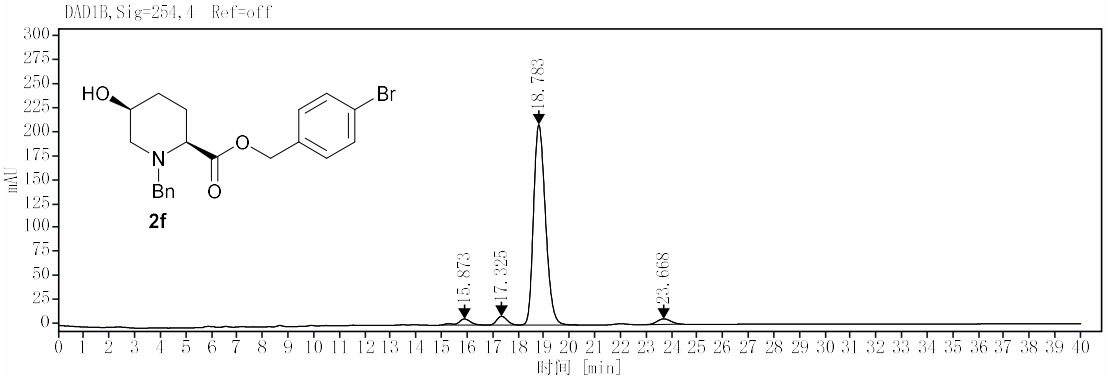
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
53.078	MM m	1.36	1776.60	15.37	9.88
59.035	MM m	1.38	1870.11	16.11	10.40
70.892	MM m	1.55	7210.49	54.60	40.10
91.322	MM m	1.98	7126.14	42.54	39.63



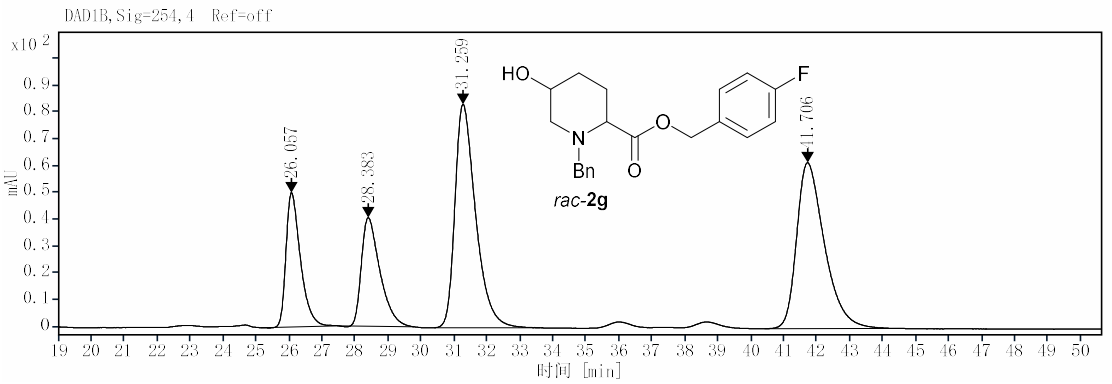
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
53.603	MM m	1.18	534.70	5.30	2.18
59.077	MM m	1.24	1262.80	12.03	5.15
70.570	MM m	1.73	22194.15	160.69	90.48
92.340	MM m	1.71	537.95	3.71	2.19



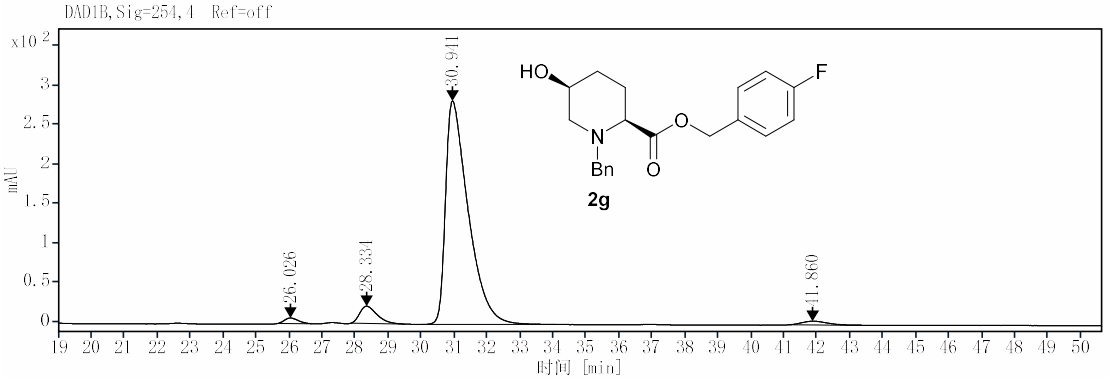
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
15.601	MM m	0.46	1253.46	42.28	12.87
17.020	MM m	0.50	1259.55	39.24	12.94
18.560	MM m	0.52	3659.21	109.94	37.59
23.214	MM m	0.63	3563.59	89.07	36.60



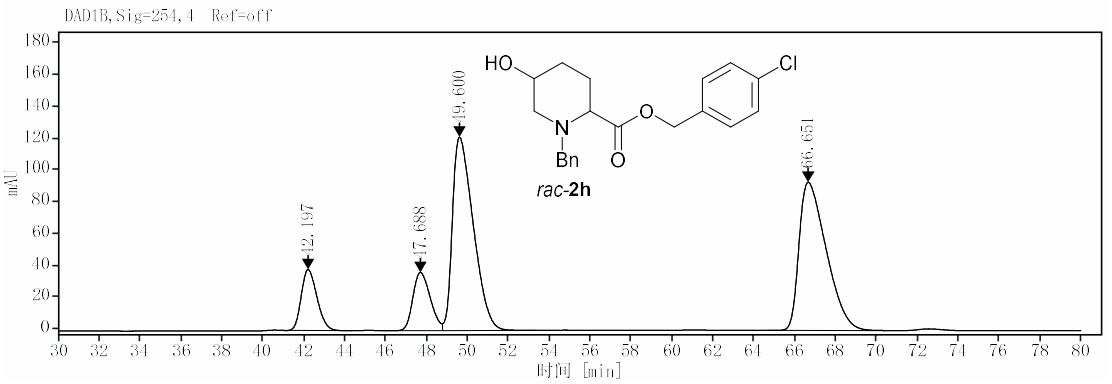
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
15.873	MM m	0.49	205.99	6.24	2.77
17.325	MM m	0.44	246.85	9.00	3.32
18.783	MM m	0.51	6772.57	208.95	91.06
23.668	MM m	0.56	211.68	5.71	2.85



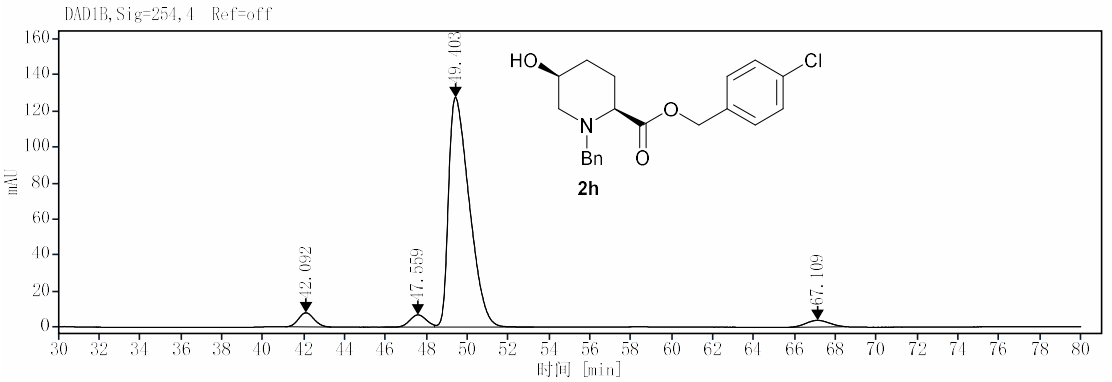
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
26.057	MM m	0.46	1524.28	50.05	14.70
28.383	MM m	0.59	1577.53	40.43	15.22
31.259	MM m	0.66	3640.61	83.21	35.12
41.706	MM m	0.86	3624.36	61.79	34.96



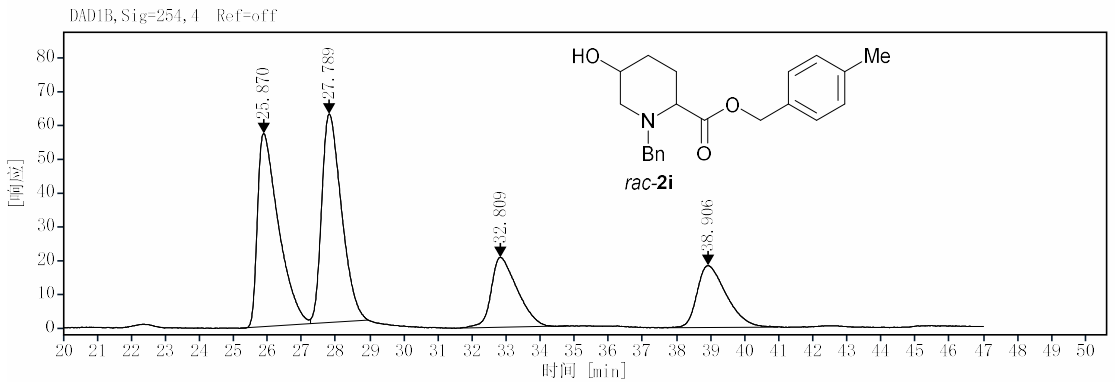
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
26.026	MM m	0.43	202.69	7.05	1.37
28.334	MM m	0.54	796.96	21.80	5.39
30.941	MM m	0.70	13525.76	282.51	91.52
41.860	MM m	0.62	253.68	4.78	1.72



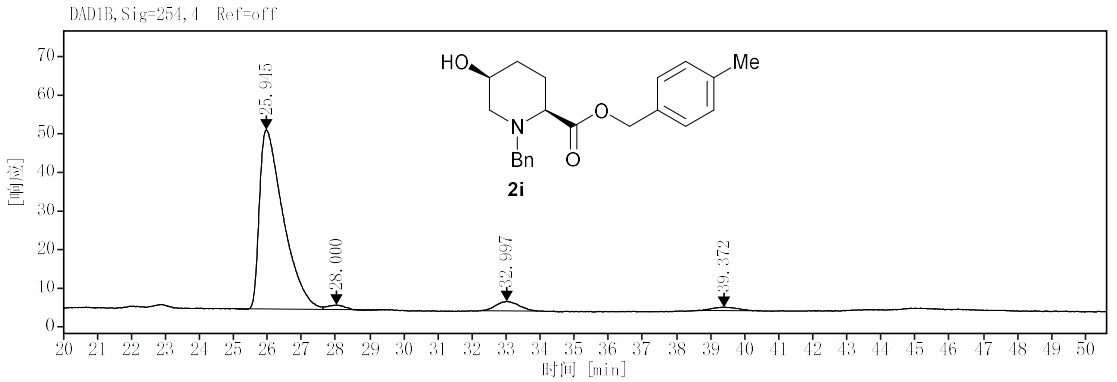
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
42.197	MM m	0.81	2040.05	38.30	9.51
47.688	MM m	0.89	2152.75	36.60	10.04
49.600	MM m	1.05	8637.66	121.72	40.27
66.651	MM m	1.35	8617.55	93.29	40.18



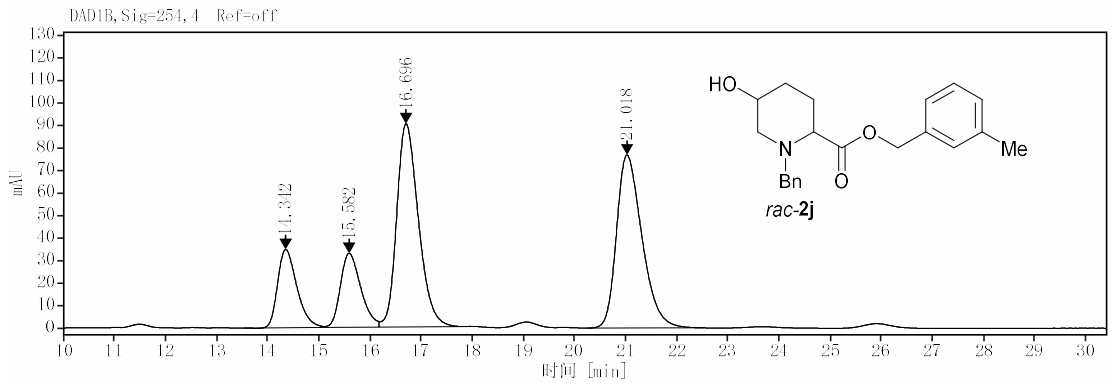
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
42.092	MM m	0.71	414.24	7.82	4.12
47.559	MM m	0.68	385.98	6.83	3.84
49.403	MM m	1.05	8968.91	127.56	89.12
67.109	MM m	0.94	294.22	3.69	2.92



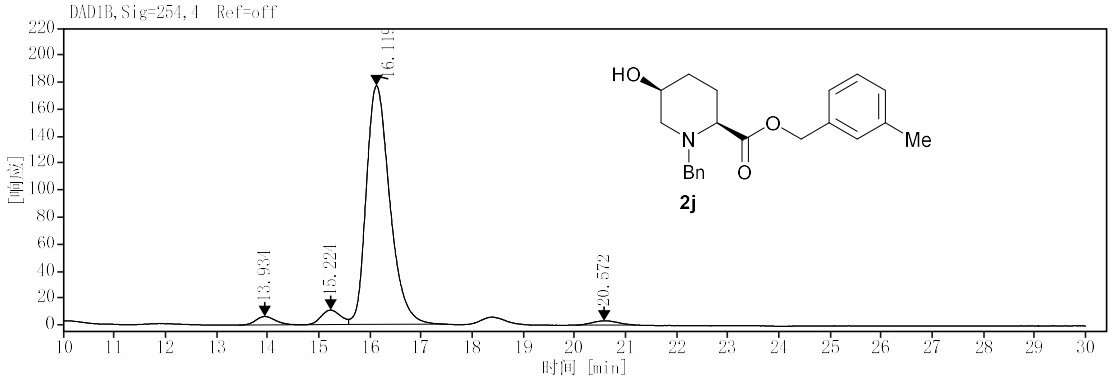
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
25.870	MM m	0.61	2468.37	57.24	34.49
27.789	MM m	0.59	2501.64	61.76	34.95
32.809	MM m	0.68	1094.38	20.66	15.29
38.906	MM m	0.71	1093.31	18.36	15.27



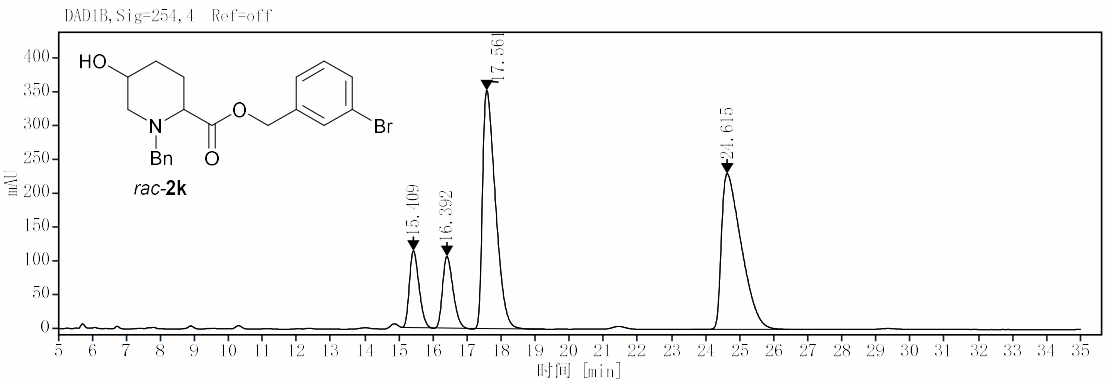
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
25.945	MM m	0.68	2248.26	46.36	91.99
28.000	MM m	0.36	34.91	1.14	1.43
32.997	MM m	0.57	115.18	2.43	4.71
39.372	MM m	0.60	45.68	0.90	1.87



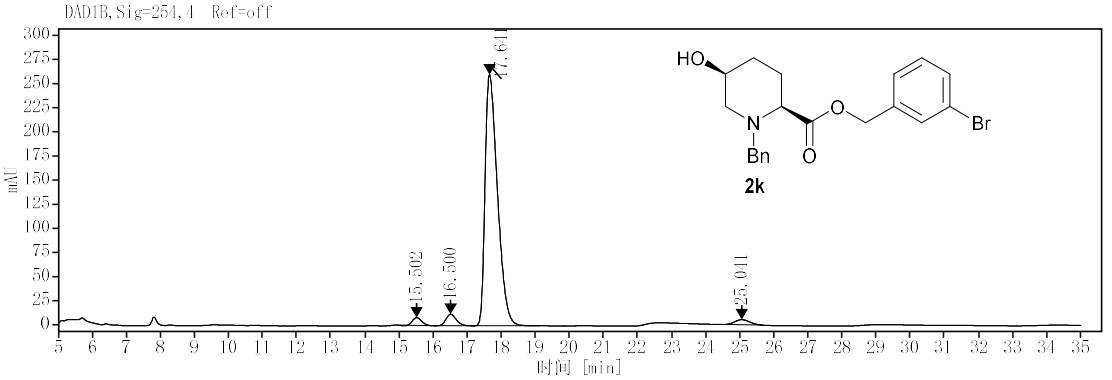
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
14.342	MM m	0.40	906.09	34.79	12.67
15.582	MM m	0.42	914.03	32.88	12.78
16.696	MM m	0.46	2673.15	90.34	37.37
21.018	MM m	0.53	2659.89	76.86	37.18



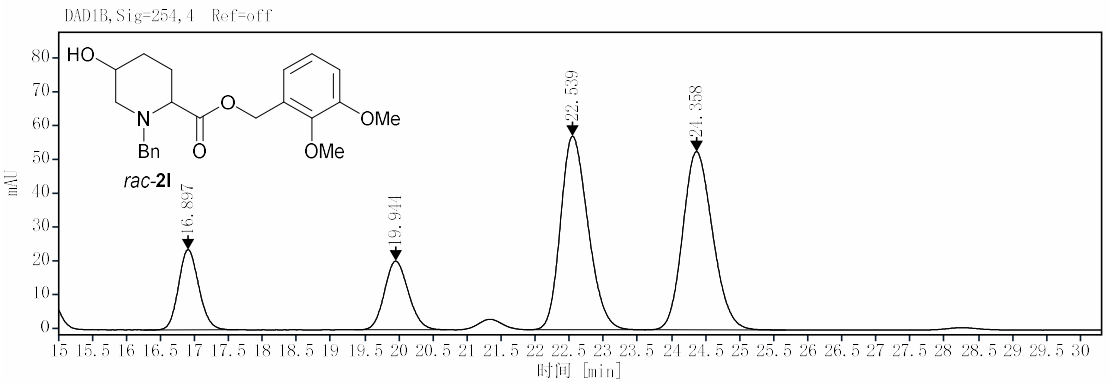
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
13.934	MM m	0.32	163.00	6.21	2.62
15.224	MM m	0.33	286.50	10.72	4.61
16.119	MM m	0.50	5660.57	176.83	91.07
20.572	MM m	0.42	105.41	3.02	1.70



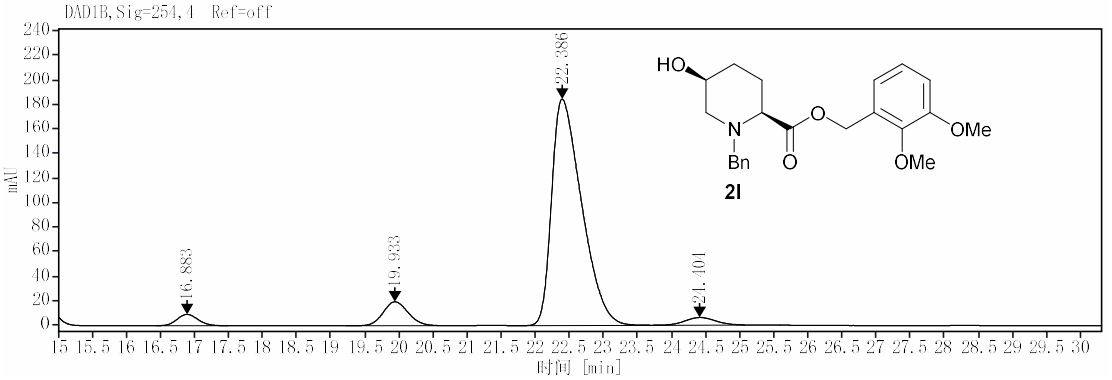
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
15.409	MM m	0.30	2227.17	113.65	9.63
16.392	MM m	0.33	2271.30	106.36	9.82
17.561	MM m	0.40	9284.10	352.86	40.14
24.615	MM m	0.62	9345.55	230.59	40.41



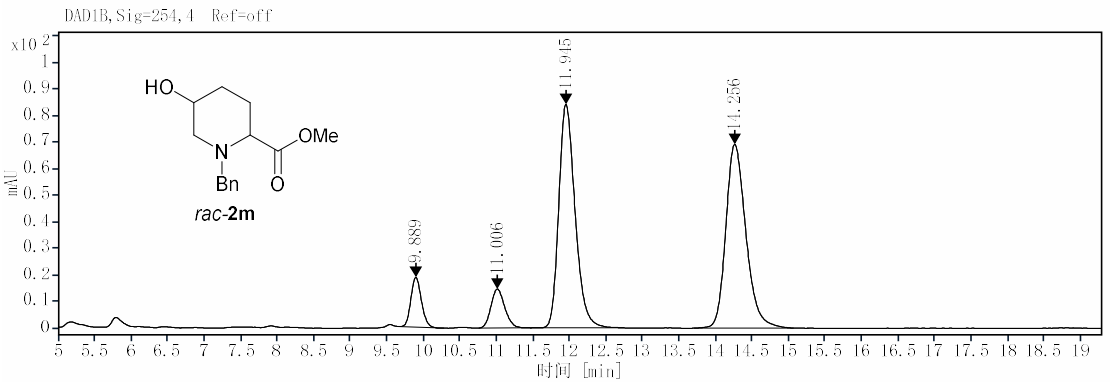
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
15.502	MM m	0.29	151.60	8.21	2.13
16.500	MM m	0.32	250.50	11.96	3.52
17.641	MM m	0.39	6558.90	260.25	92.10
25.041	MM m	0.45	160.71	5.27	2.26



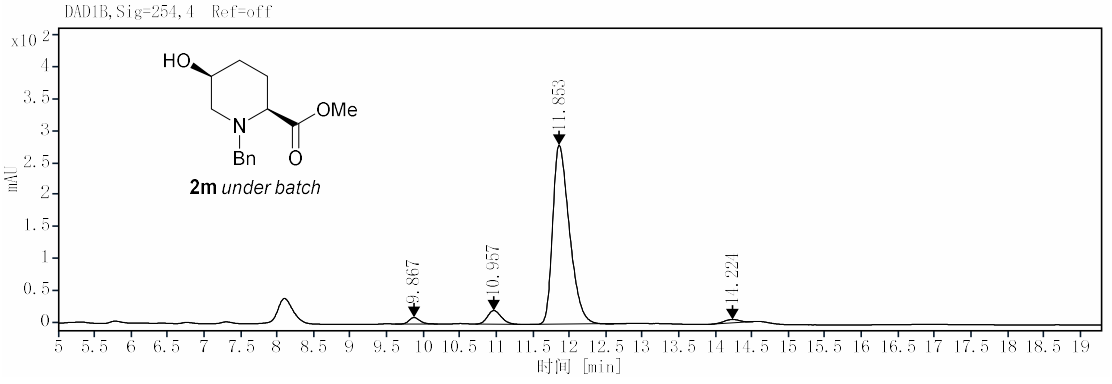
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.897	MM m	0.32	491.64	23.78	11.68
19.944	MM m	0.39	497.01	20.37	11.81
22.539	MM m	0.43	1608.13	57.35	38.21
24.358	MM m	0.47	1612.10	52.82	38.30



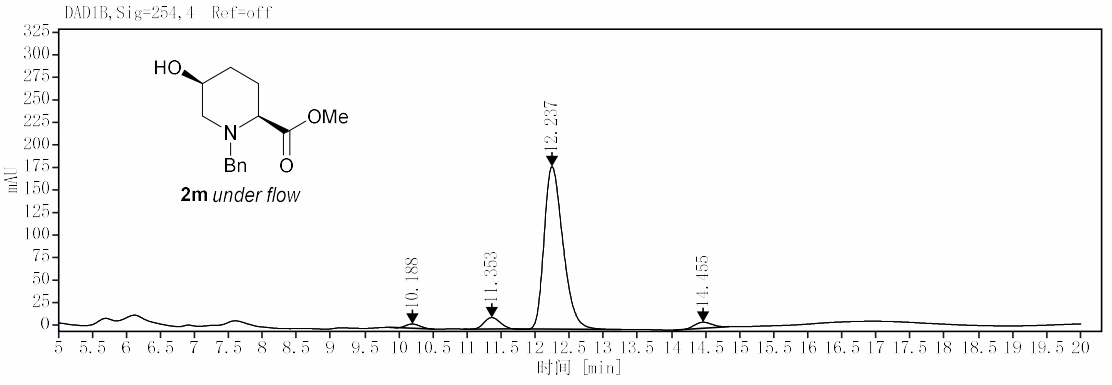
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.883	MM m	0.34	199.26	9.22	3.05
19.933	MM m	0.40	492.97	19.43	7.56
22.386	MM m	0.47	5641.28	184.44	86.47
24.404	MM m	0.46	190.58	6.18	2.92



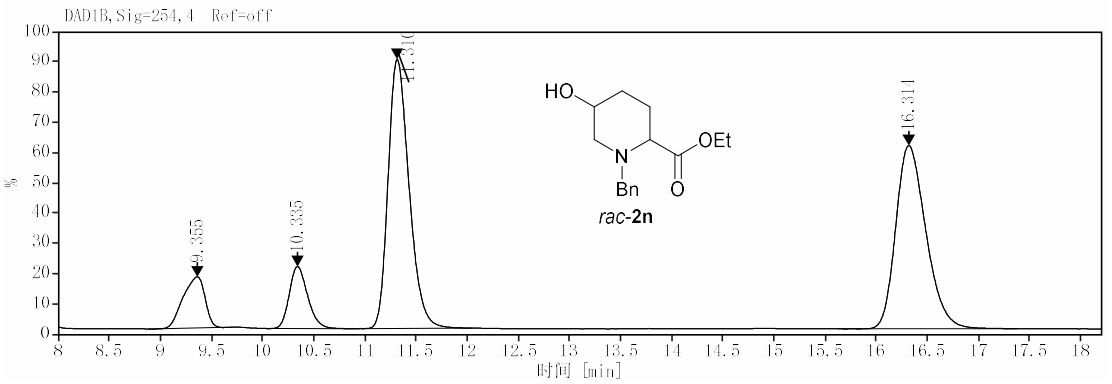
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
9.889	MM m	0.15	187.35	18.72	6.23
11.006	MM m	0.20	191.46	14.61	6.37
11.945	MM m	0.24	1304.70	84.03	43.40
14.256	MM m	0.29	1322.61	69.06	44.00



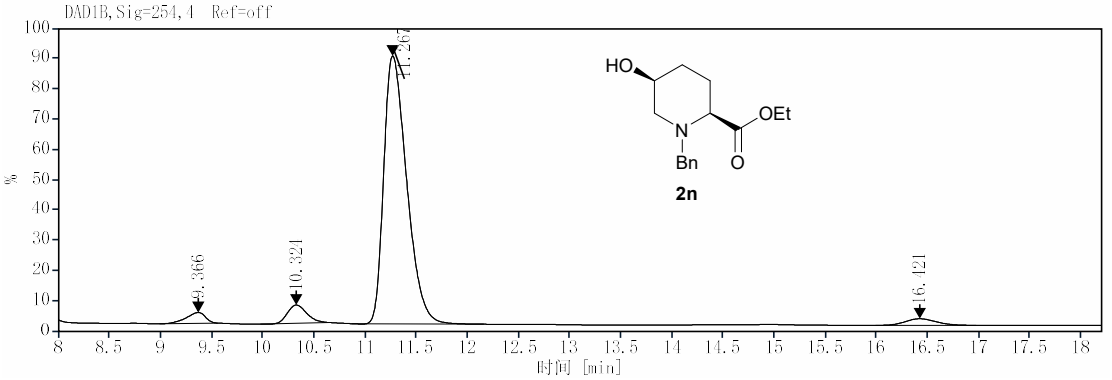
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
9.867	MM m	0.16	104.58	10.23	2.13
10.957	MM m	0.20	278.87	21.27	5.67
11.853	MM m	0.24	4459.27	279.88	90.67
14.224	MM m	0.23	75.44	5.29	1.53



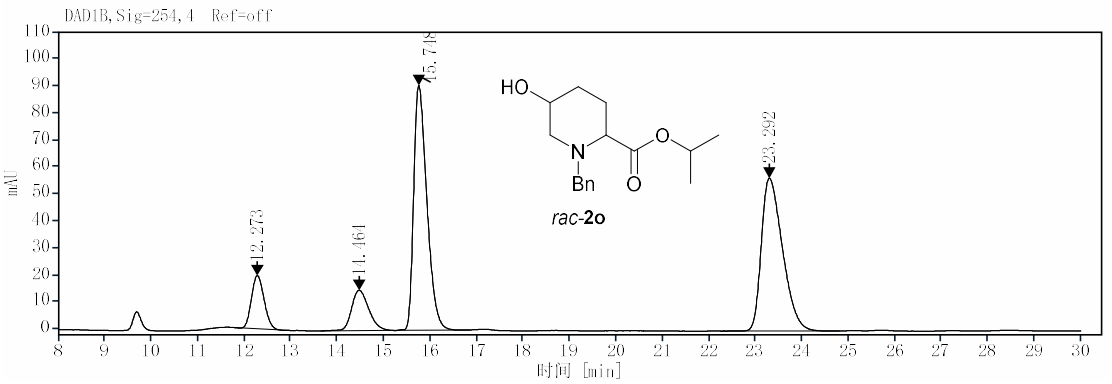
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
10.188	MM m	0.23	68.42	4.81	1.78
11.353	MM m	0.26	204.21	12.67	5.31
12.237	MM m	0.30	3458.96	180.46	89.90
14.455	MM m	0.27	116.06	6.68	3.02



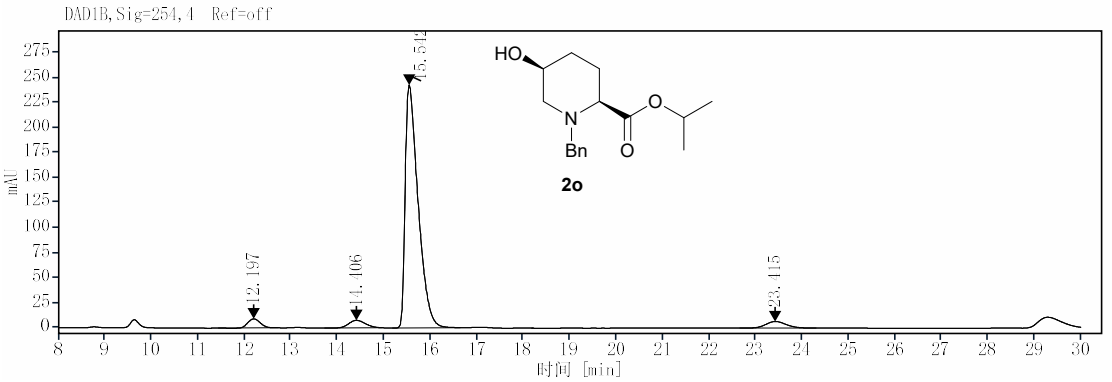
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
9.355	MM m	0.25	226.33	15.25	8.31
10.335	MM m	0.19	229.62	18.47	8.43
11.310	MM m	0.22	1146.44	80.30	42.10
16.314	MM m	0.32	1120.62	54.67	41.15



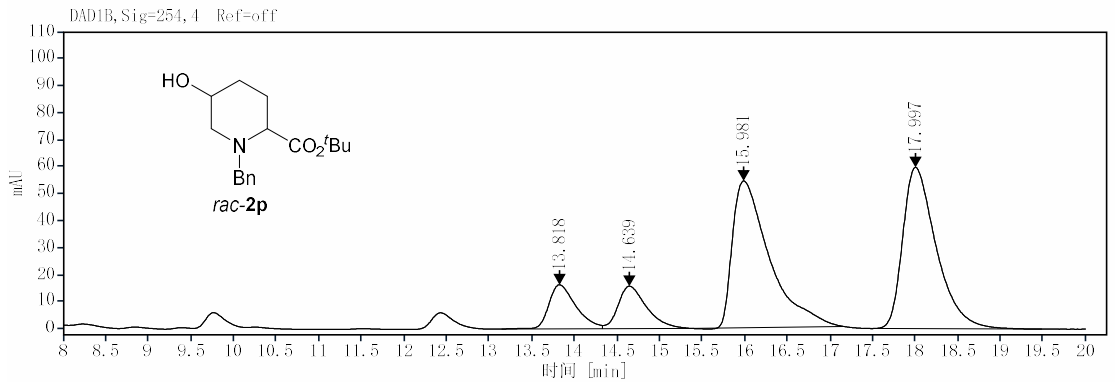
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
9.366	MM m	0.20	122.88	9.45	3.01
10.324	MM m	0.20	206.61	15.87	5.06
11.267	MM m	0.24	3634.41	232.67	89.01
16.421	MM m	0.32	119.20	5.71	2.92



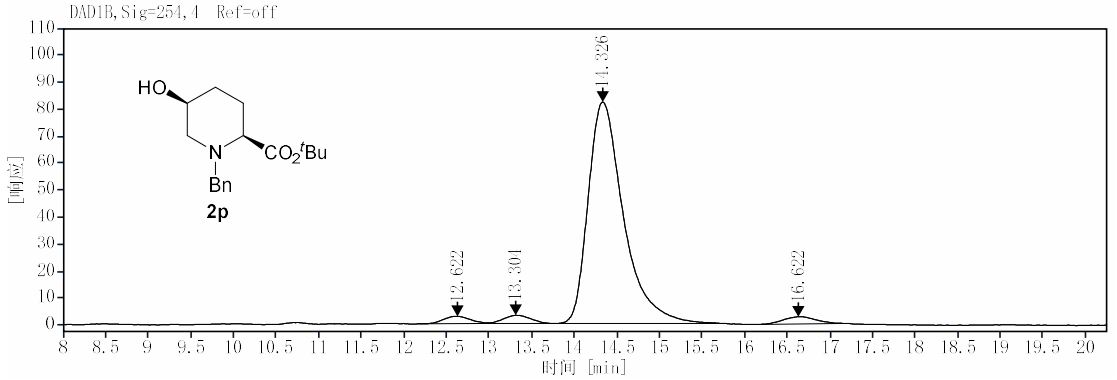
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
12.273	MM m	0.29	368.19	19.65	8.52
14.464	MM m	0.39	380.31	14.93	8.80
15.748	MM m	0.30	1781.21	90.62	41.23
23.292	MM m	0.49	1790.55	56.64	41.45



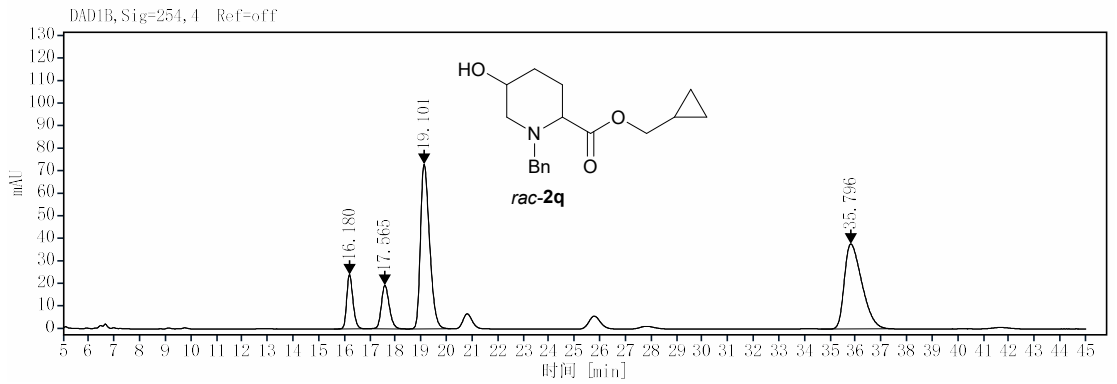
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
12.197	MM m	0.29	164.21	9.07	3.14
14.406	MM m	0.39	189.25	7.53	3.62
15.542	MM m	0.29	4673.32	242.88	89.38
23.415	MM m	0.46	201.65	6.58	3.86



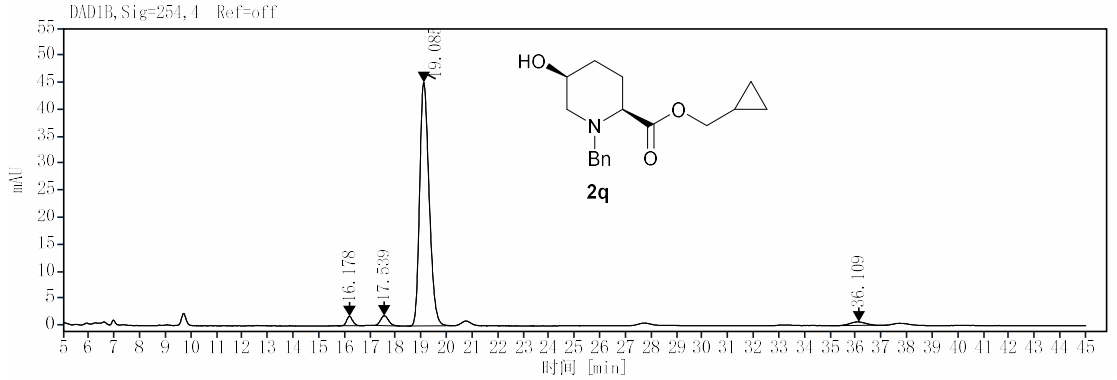
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
13.818	MM m	0.33	358.07	16.31	8.95
14.639	MM m	0.35	364.05	15.69	9.10
15.981	MM m	0.45	1643.38	54.37	41.07
17.997	MM m	0.41	1635.44	59.74	40.88



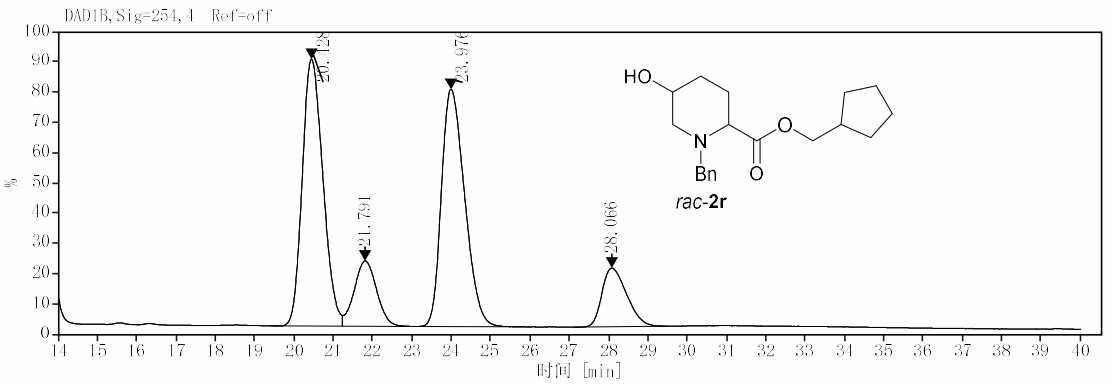
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
12.622	MM m	0.27	60.50	2.76	2.36
13.304	MM m	0.27	65.84	3.03	2.57
14.326	MM m	0.44	2364.38	81.98	92.37
16.622	MM m	0.32	69.03	2.66	2.70



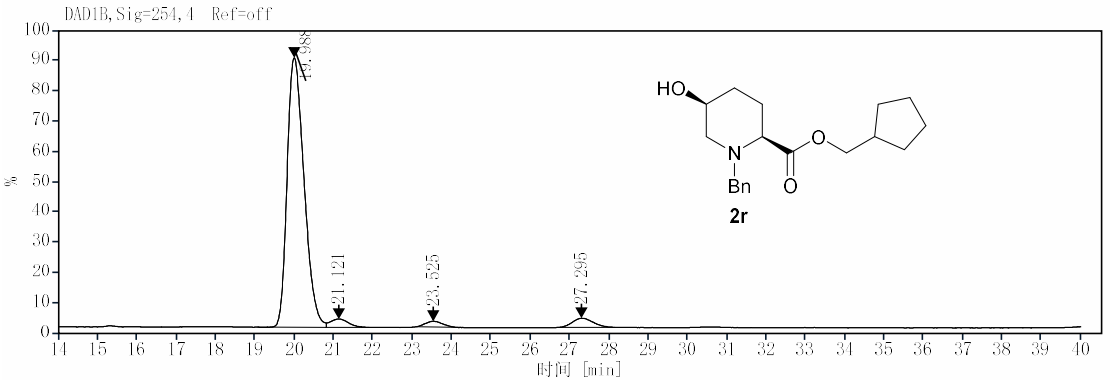
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.180	MM m	0.26	408.55	24.14	9.21
17.565	MM m	0.33	415.95	19.33	9.38
19.101	MM m	0.38	1809.51	73.12	40.81
35.796	MM m	0.72	1799.96	37.75	40.59



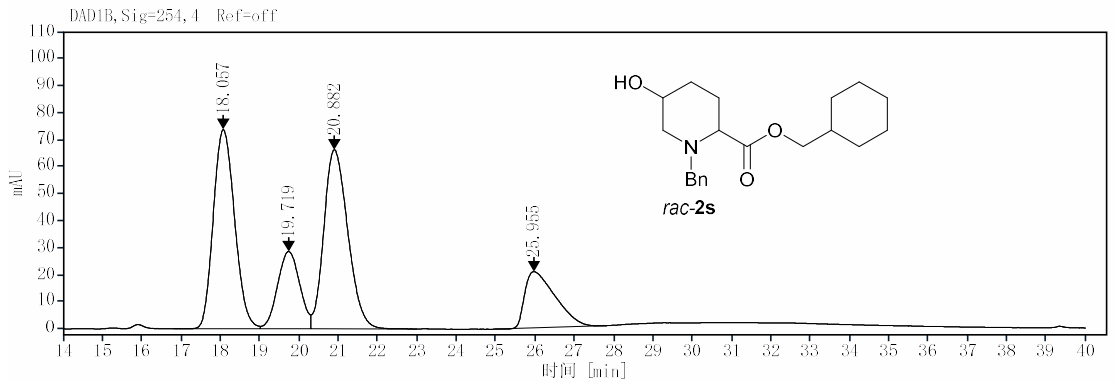
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.178	MM m	0.23	27.12	1.72	2.16
17.539	MM m	0.31	39.69	1.83	3.16
19.085	MM m	0.40	1162.67	45.06	92.58
36.109	MM m	0.49	26.42	0.65	2.10



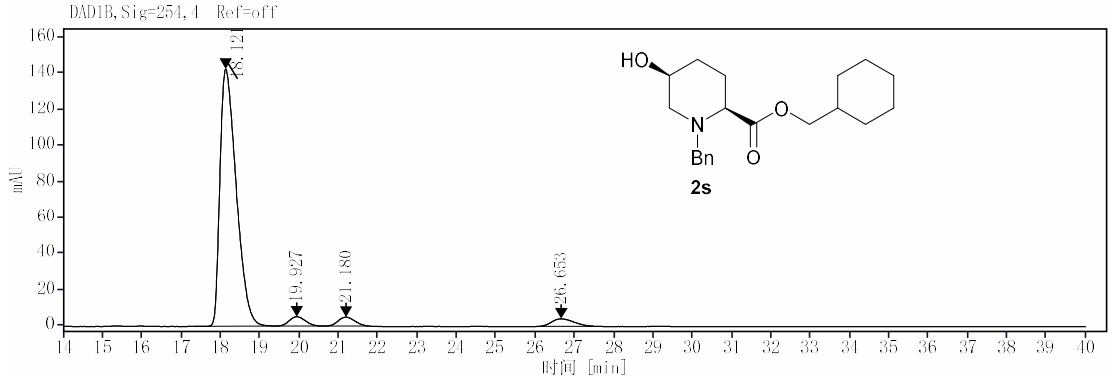
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
20.428	MM m	0.57	2482.85	67.84	39.59
21.791	MM m	0.60	660.02	16.62	10.52
23.976	MM m	0.62	2478.44	60.33	39.52
28.066	MM m	0.62	650.44	14.94	10.37



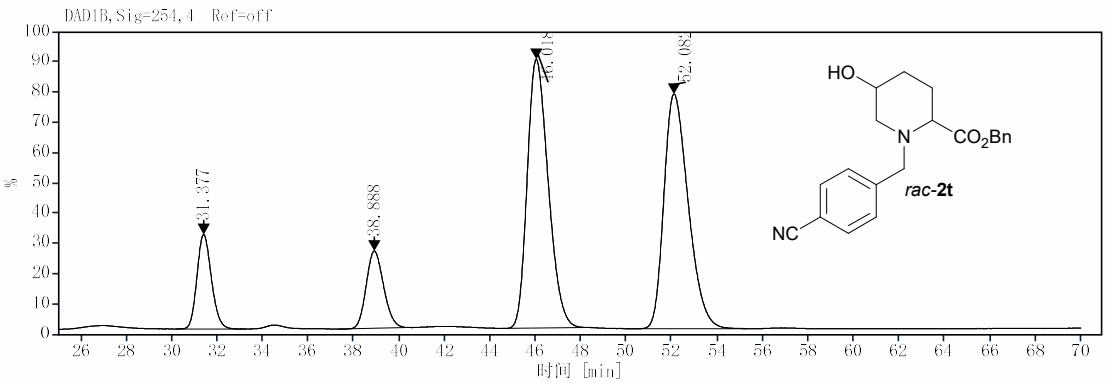
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
19.988	MM m	0.47	1845.08	61.73	91.25
21.121	MM m	0.38	60.34	1.90	2.98
23.525	MM m	0.36	40.06	1.34	1.98
27.295	MM m	0.44	76.59	2.09	3.79



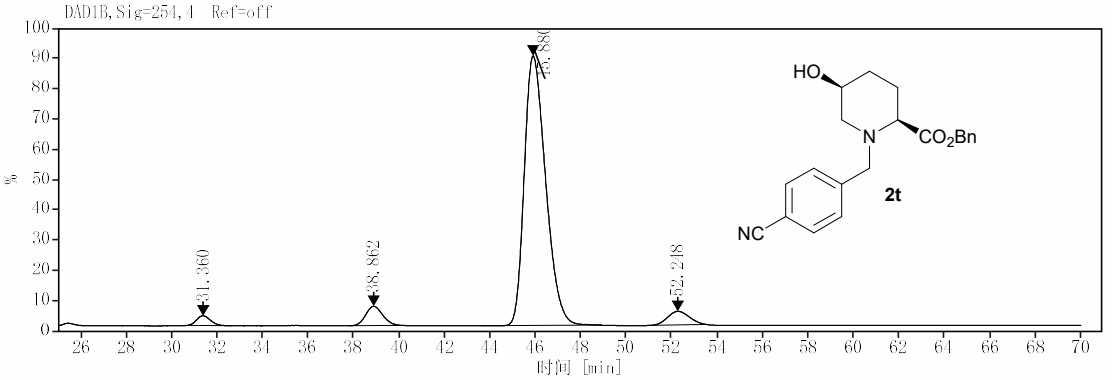
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
18.057	MM m	0.60	2775.62	73.84	35.50
19.719	MM m	0.60	1121.16	28.60	14.34
20.882	MM m	0.66	2810.35	66.33	35.95
25.955	MM m	0.74	1111.03	20.83	14.21



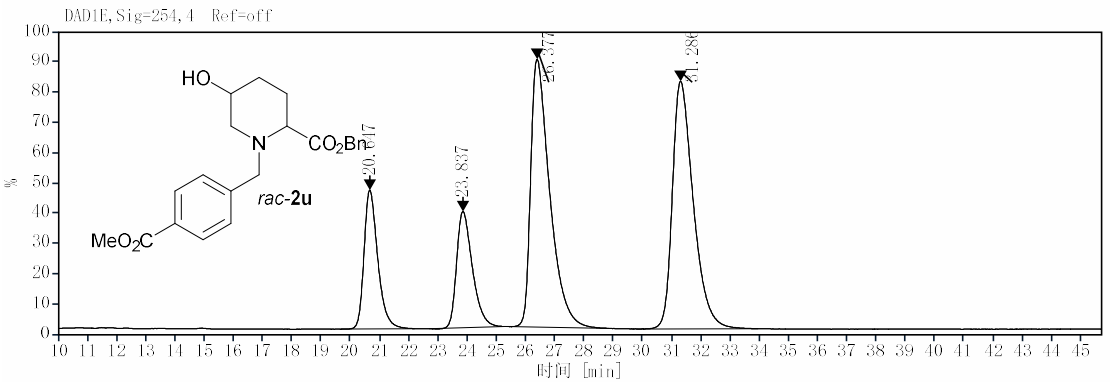
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
18.121	MM m	0.44	4093.80	142.88	90.02
19.927	MM m	0.42	144.72	5.17	3.18
21.180	MM m	0.40	145.55	4.96	3.20
26.653	MM m	0.48	163.64	4.18	3.60



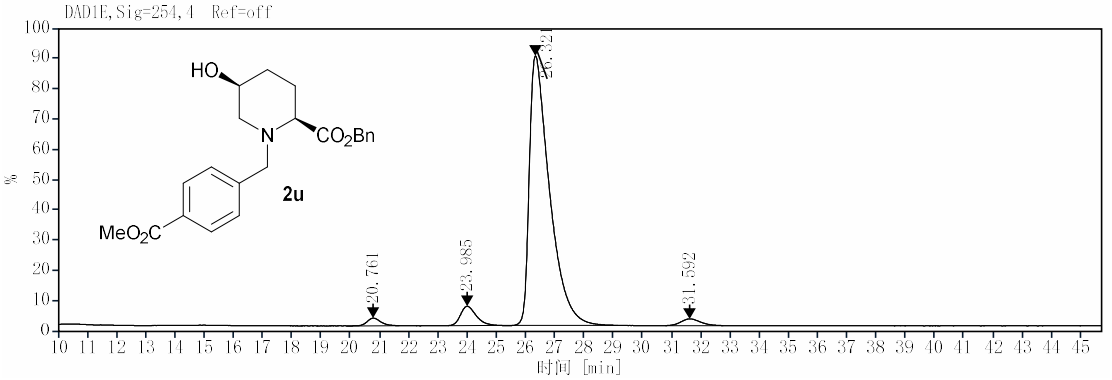
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
31.377	MM m	0.66	2080.10	47.08	9.71
38.888	MM m	0.78	2043.97	38.51	9.54
46.018	MM m	0.96	8611.10	133.97	40.19
52.082	MM m	1.10	8693.21	116.95	40.57



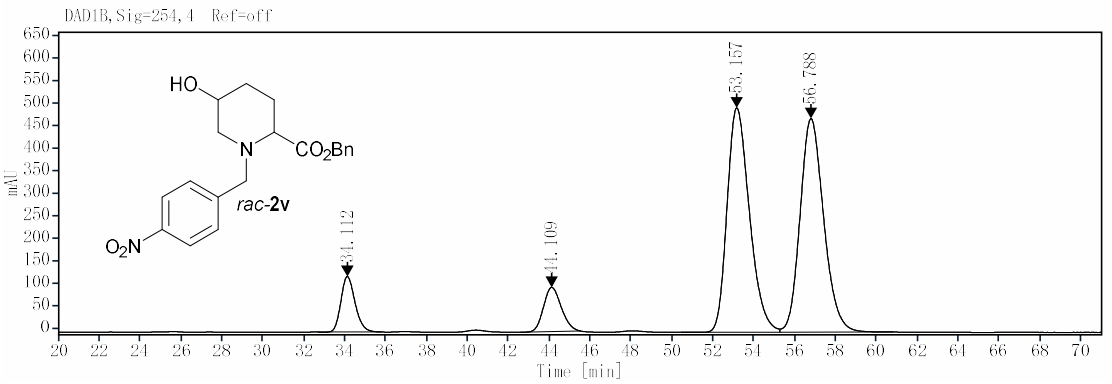
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
31.360	MM m	0.52	295.53	6.90	2.11
38.862	MM m	0.70	705.54	13.53	5.04
45.880	MM m	1.00	12351.36	188.80	88.28
52.248	MM m	0.79	638.54	9.57	4.56



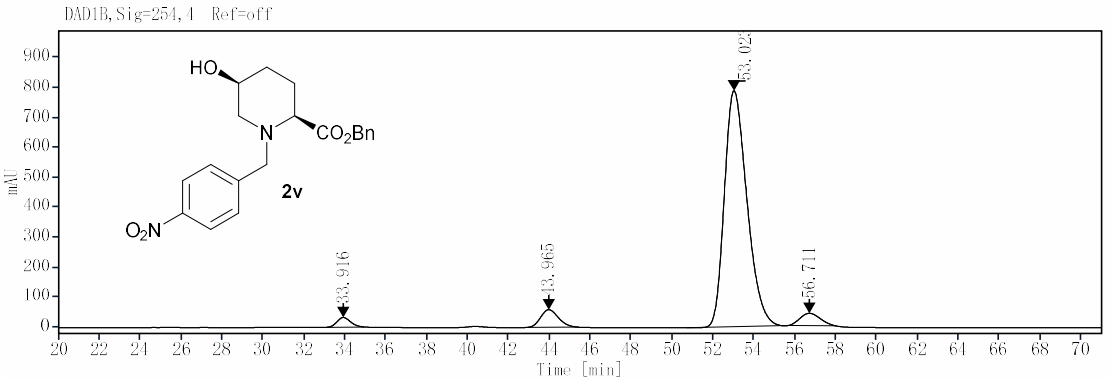
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
20.647	MM m	0.50	5252.59	160.76	13.61
23.837	MM m	0.57	5056.26	134.56	13.10
26.377	MM m	0.66	14057.19	309.79	36.41
31.286	MM m	0.73	14238.86	286.42	36.88



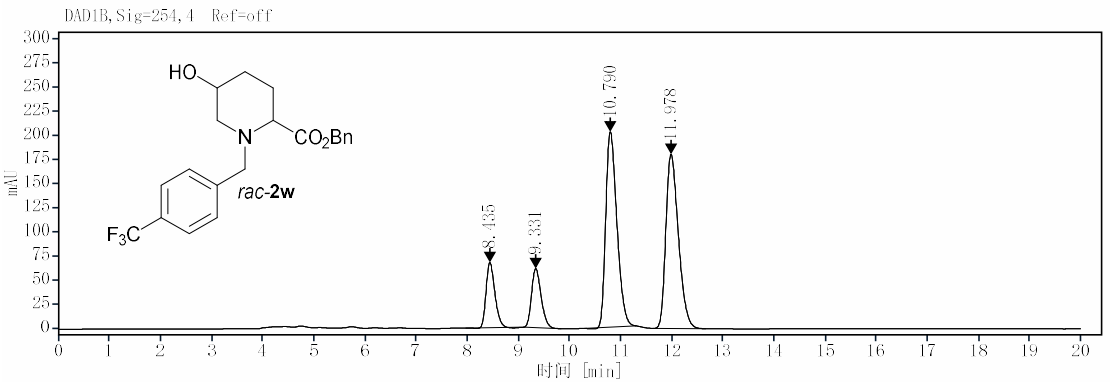
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
20.761	MM m	0.43	439.02	13.75	1.72
23.985	MM m	0.53	1296.10	34.74	5.06
26.321	MM m	0.71	23298.98	483.48	91.03
31.592	MM m	0.57	560.10	12.01	2.19



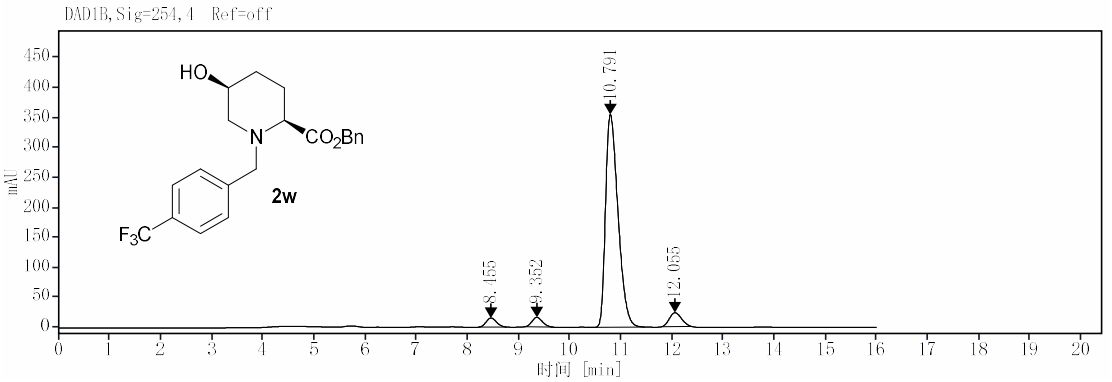
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
34.112	MM m	0.74	5960.83	123.84	6.76
44.109	MM m	0.93	5965.96	98.63	6.77
53.157	MM m	1.17	37994.58	499.56	43.10
56.788	MM m	1.23	38234.70	475.45	43.37



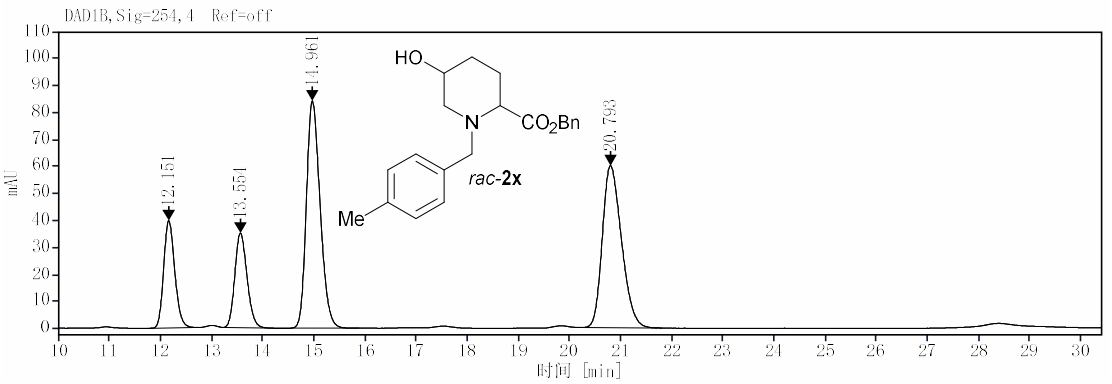
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
33.916	MM m	0.70	1462.28	32.06	2.15
43.965	MM m	0.92	3570.54	58.95	5.25
53.023	MM m	1.18	60151.14	786.98	88.44
56.711	MM m	1.08	2831.15	41.12	4.16



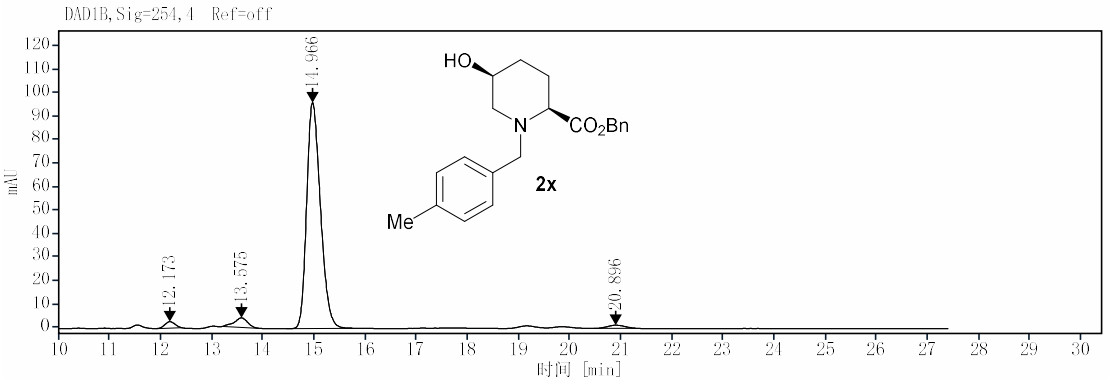
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
8.435	MM m	0.18	797.33	67.65	10.30
9.331	MM m	0.20	798.20	61.33	10.31
10.790	MM m	0.23	3060.92	202.62	39.54
11.978	MM m	0.27	3084.13	180.56	39.84



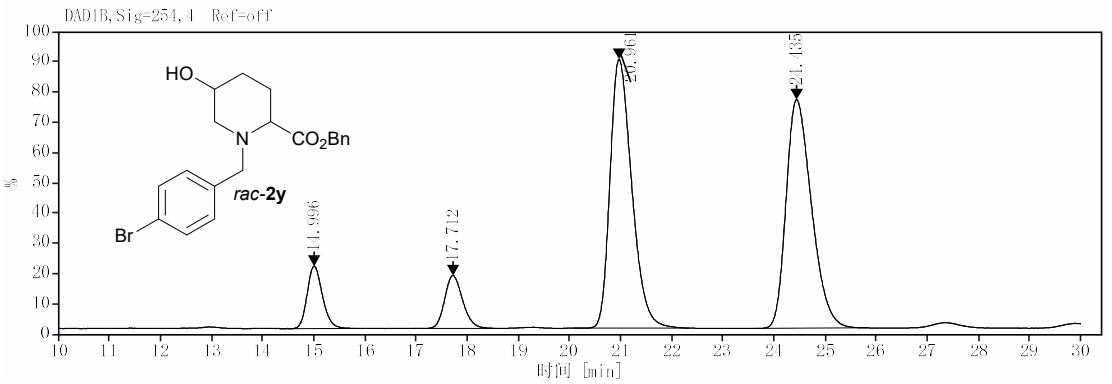
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
8.455	MM m	0.22	212.47	15.19	3.11
9.352	MM m	0.22	228.40	15.97	3.35
10.791	MM m	0.26	6007.08	354.27	88.01
12.055	MM m	0.26	377.78	23.01	5.53



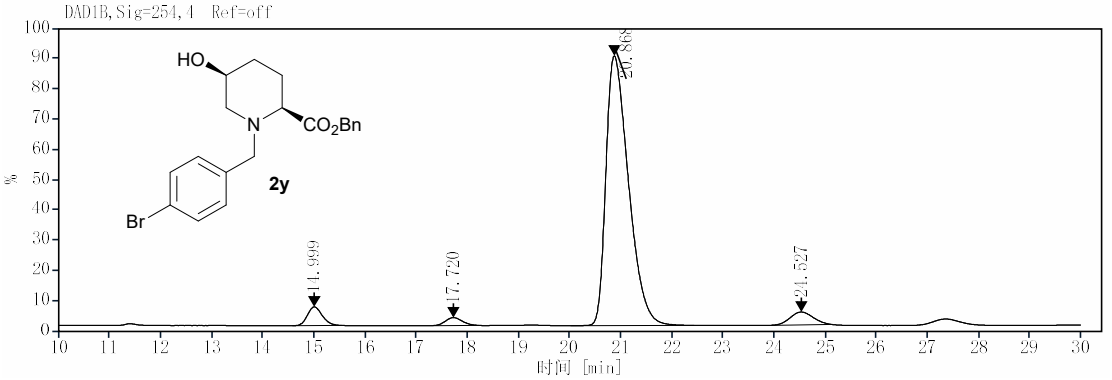
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
12.151	MM m	0.23	601.23	39.77	13.94
13.554	MM m	0.26	580.98	35.05	13.47
14.961	MM m	0.29	1568.85	84.10	36.38
20.793	MM m	0.40	1561.24	59.97	36.20



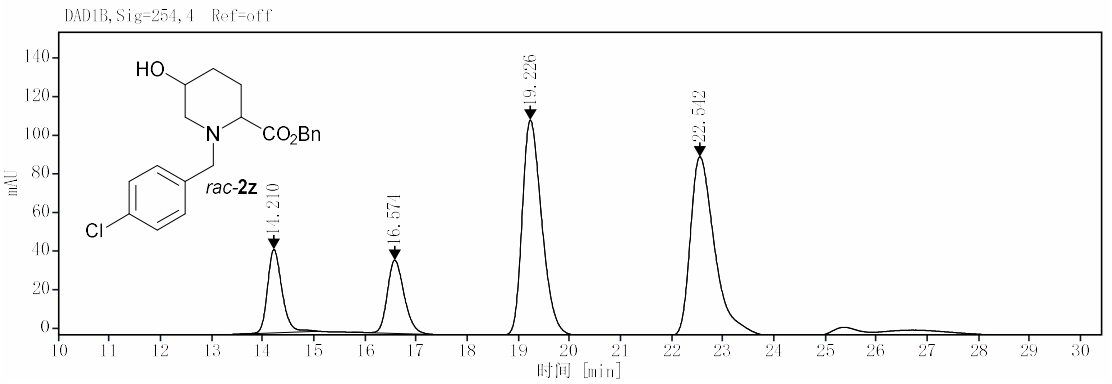
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
12.173	MM m	0.19	36.97	2.76	1.91
13.575	MM m	0.28	74.14	4.05	3.82
14.966	MM m	0.29	1798.66	96.22	92.71
20.896	MM m	0.29	30.43	1.34	1.57



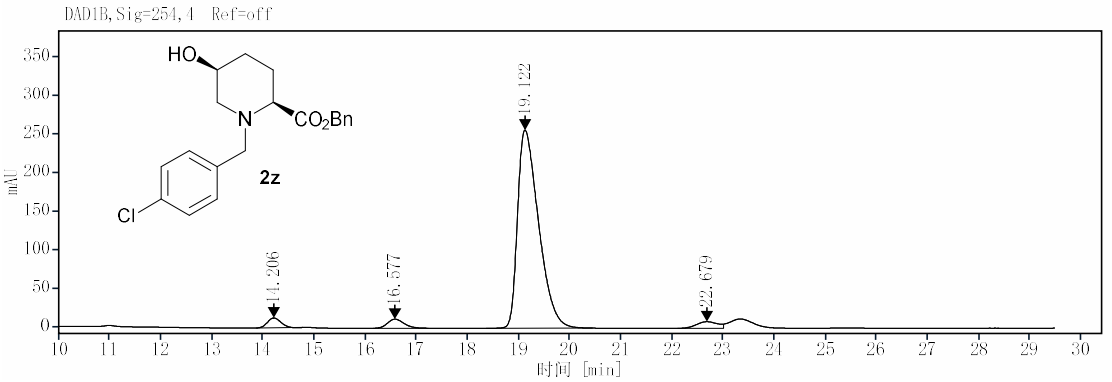
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
14.996	MM m	0.32	504.53	24.29	7.02
17.712	MM m	0.37	501.86	20.60	6.98
20.961	MM m	0.45	3101.72	104.72	43.13
24.435	MM m	0.53	3083.43	89.05	42.88



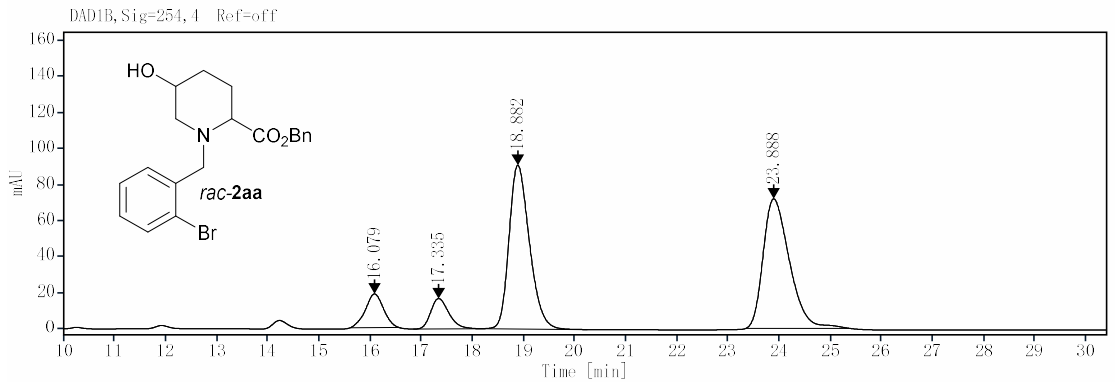
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
14.999	MM m	0.31	313.89	15.59	4.07
17.720	MM m	0.35	149.22	6.57	1.93
20.868	MM m	0.47	6917.10	225.16	89.63
24.527	MM m	0.45	336.77	10.74	4.36



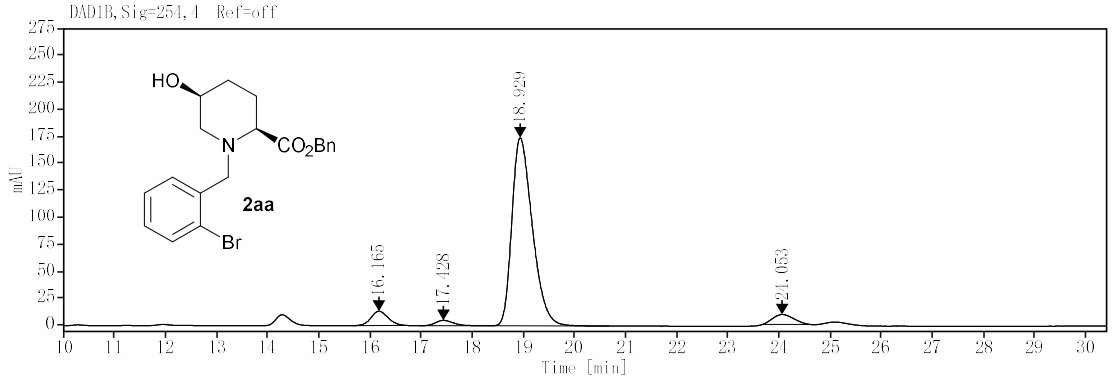
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
14.210	MM m	0.30	847.64	43.22	10.94
16.574	MM m	0.35	868.79	37.96	11.22
19.226	MM m	0.41	2982.11	111.81	38.50
22.542	MM m	0.50	3047.32	92.75	39.34



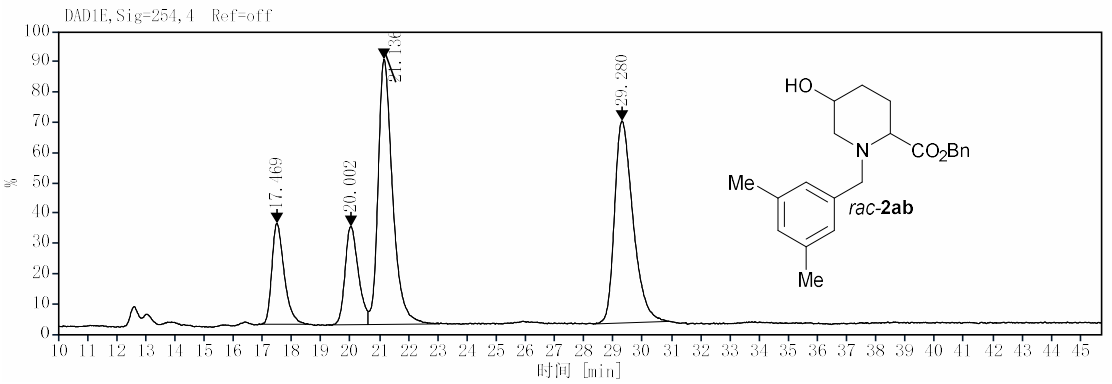
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
14.206	MM m	0.28	228.60	12.79	2.82
16.577	MM m	0.34	263.69	11.78	3.26
19.122	MM m	0.44	7349.28	256.89	90.82
22.679	MM m	0.43	250.98	8.52	3.10



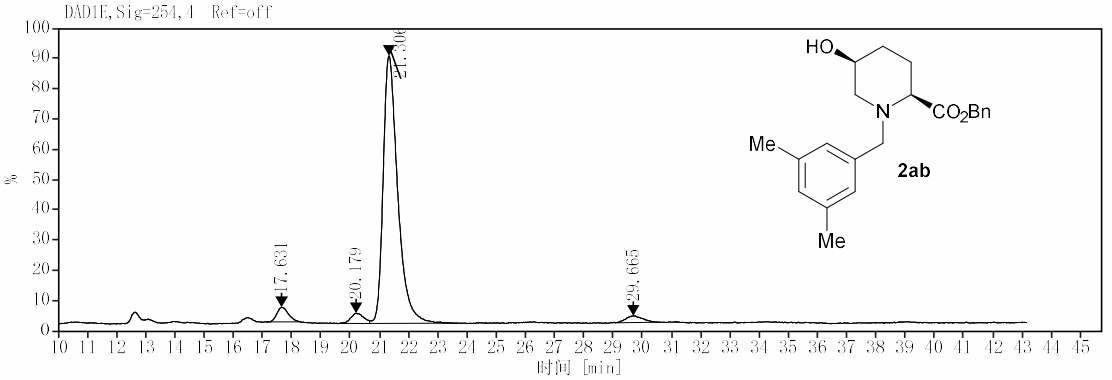
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.079	MM m	0.38	460.04	18.69	7.72
17.335	MM m	0.38	412.91	16.85	6.93
18.882	MM m	0.43	2518.27	91.01	42.27
23.888	MM m	0.55	2566.03	71.89	43.07



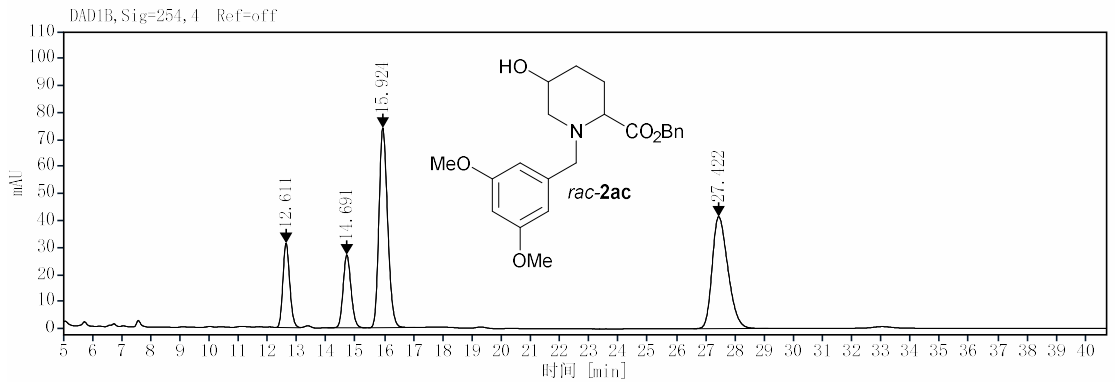
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.165	MM m	0.36	311.23	13.37	5.62
17.428	MM m	0.36	118.44	4.97	2.14
18.929	MM m	0.43	4843.40	174.05	87.50
24.053	MM m	0.46	262.21	9.19	4.74



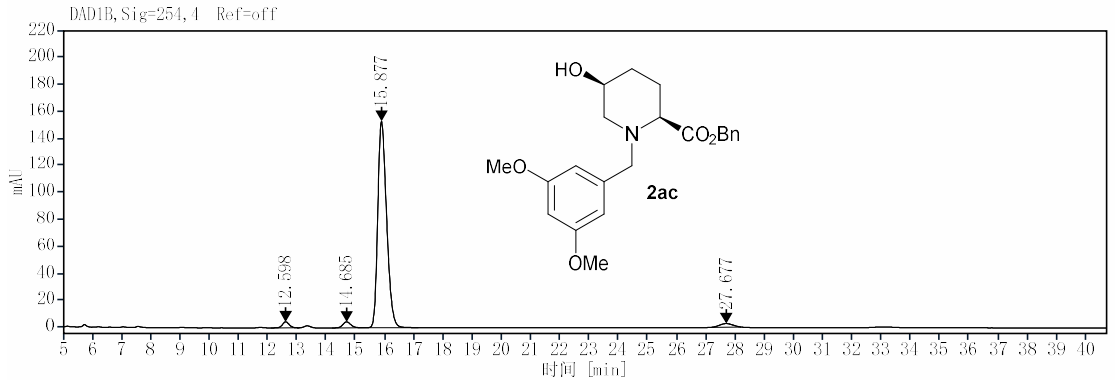
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
17.469	MM m	0.42	569.31	19.43	12.28
20.002	MM m	0.44	597.82	18.93	12.89
21.136	MM m	0.50	1763.07	51.09	38.02
29.280	MM m	0.63	1706.97	38.88	36.81



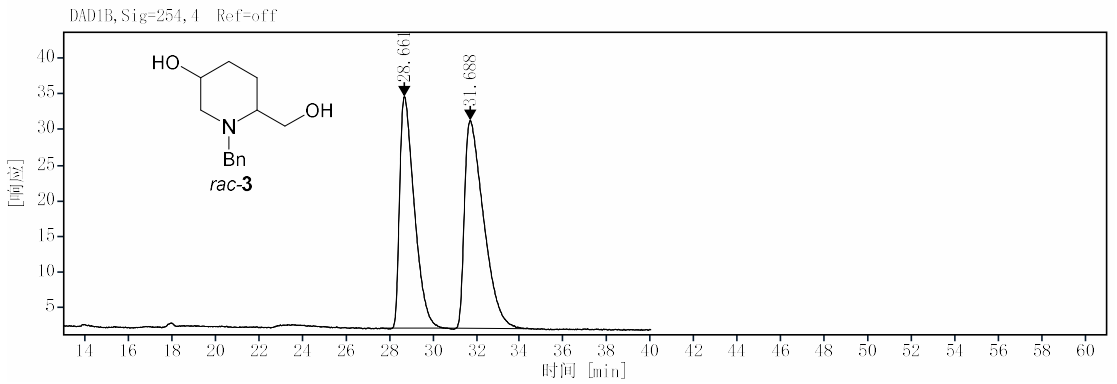
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
17.631	MM m	0.33	98.51	3.65	3.83
20.179	MM m	0.37	77.03	2.51	3.00
21.306	MM m	0.52	2329.00	67.24	90.60
29.665	MM m	0.46	66.12	1.71	2.57



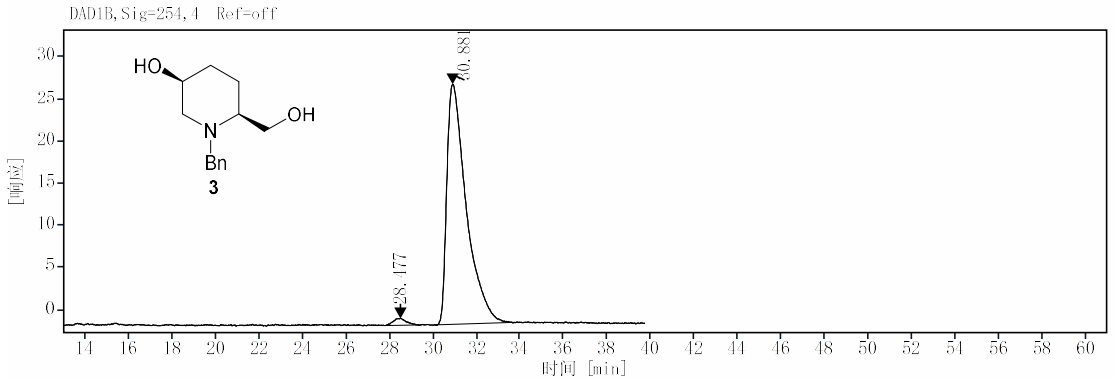
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
12.611	BV	0.88	510.27	31.24	12.43
14.691	BB	1.33	512.23	27.01	12.48
15.924	BB	1.61	1535.15	73.93	37.40
27.422	BB	2.56	1547.46	41.46	37.70



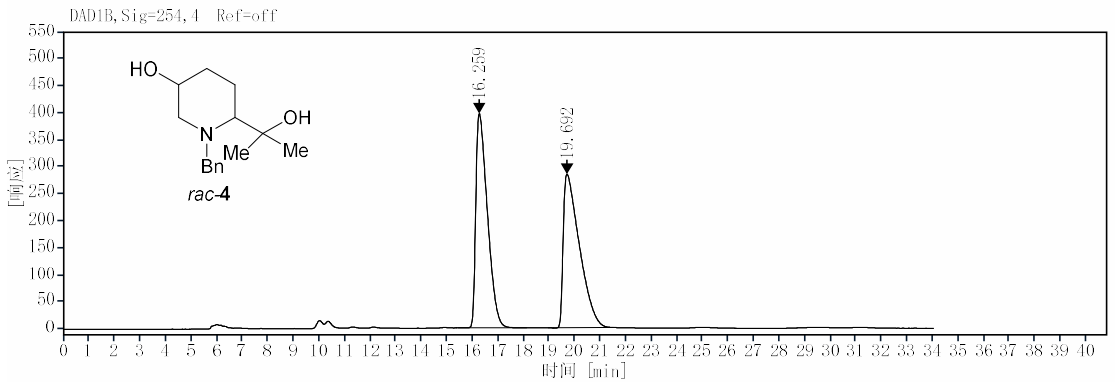
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
12.598	MM m	0.24	70.89	4.47	2.06
14.685	MM m	0.29	81.19	4.39	2.36
15.877	BB	1.79	3209.14	152.77	93.19
27.677	MM m	0.46	82.27	2.64	2.39



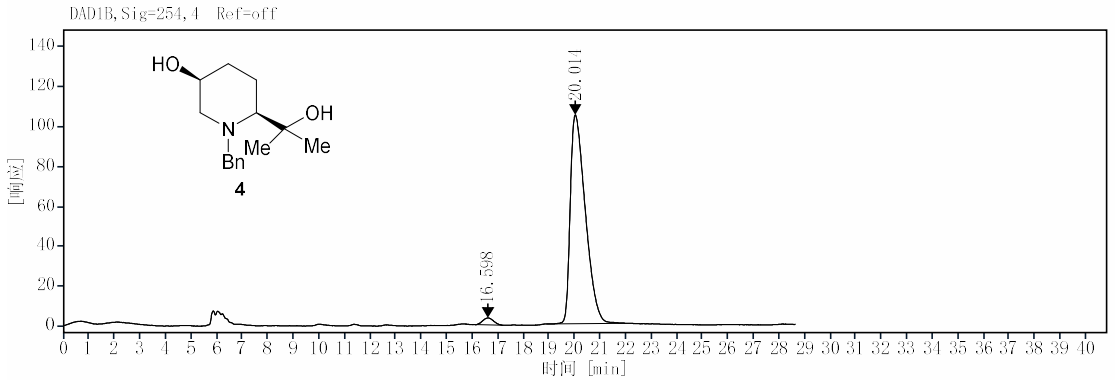
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
28.661	MM m	0.65	1715.80	32.57	49.08
31.688	MM m	0.73	1780.13	29.24	50.92



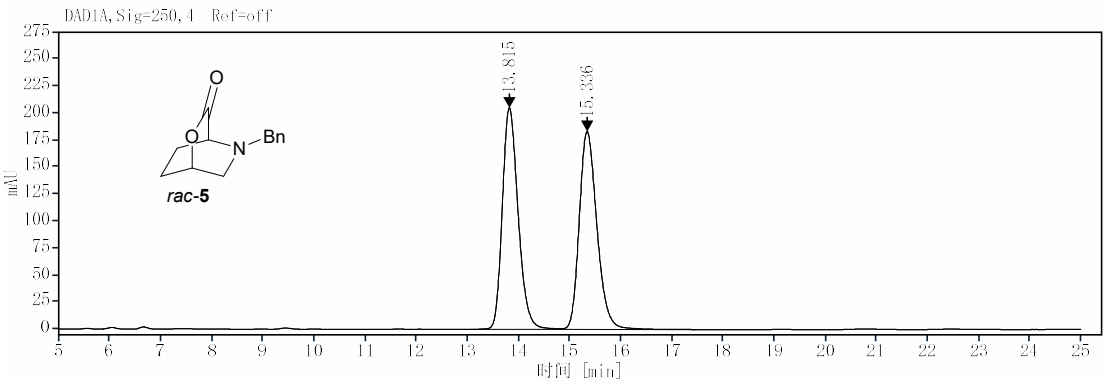
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
28.477	MM m	0.50	34.82	0.82	1.93
30.881	MM m	0.82	1766.92	28.47	98.07



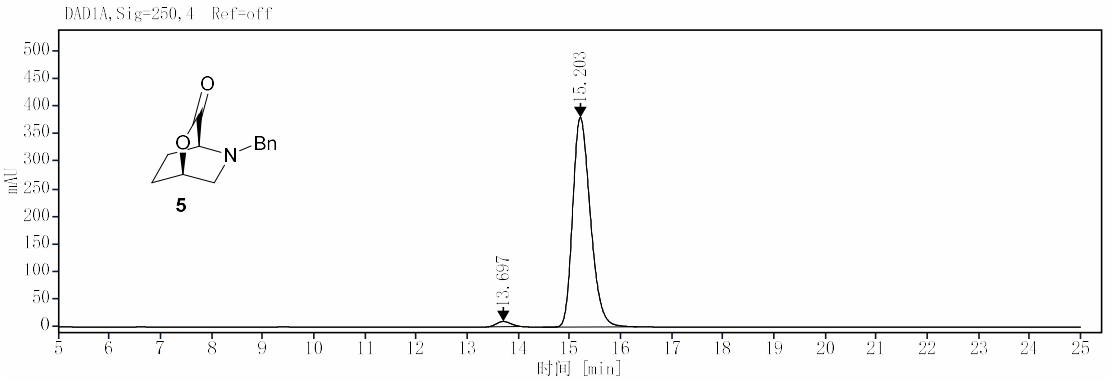
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.259	MM m	0.49	12474.32	396.57	49.97
19.692	MM m	0.64	12491.48	284.37	50.03



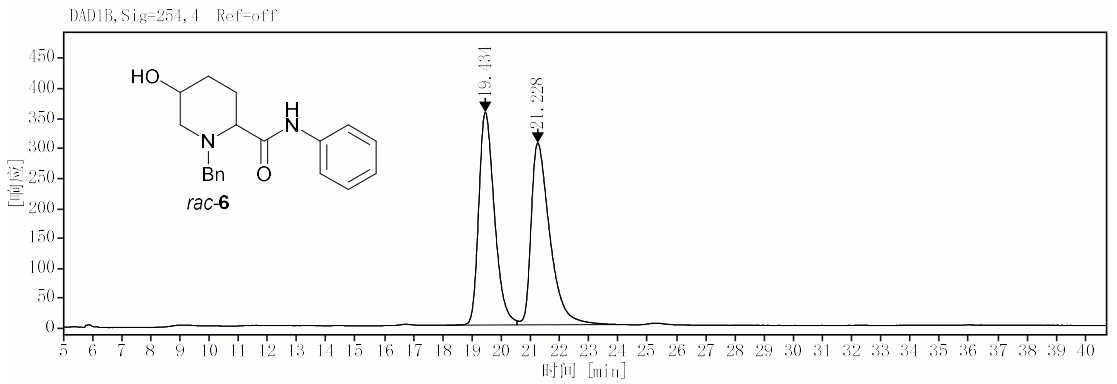
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.598	MM m	0.35	99.96	3.47	2.28
20.014	MM m	0.60	4276.06	104.37	97.72



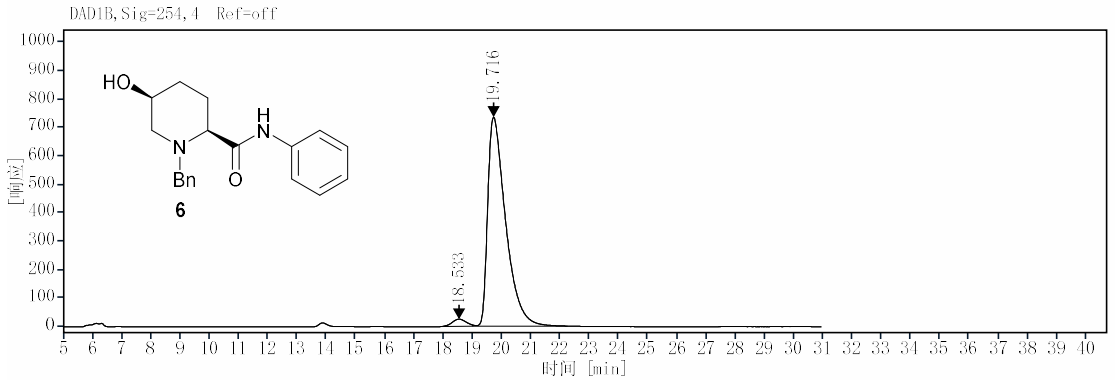
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
13.815	BV	1.73	4403.93	205.15	50.01
15.336	VB	2.65	4402.65	183.37	49.99



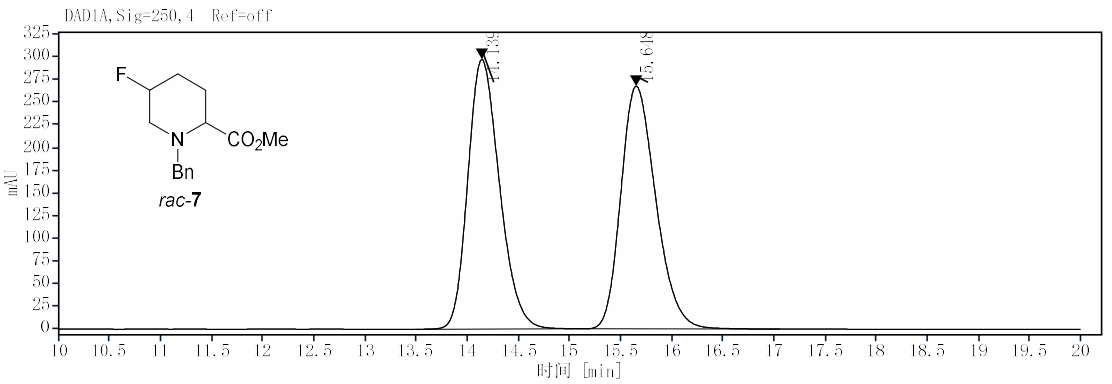
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
13.697	MM m	0.30	182.75	9.50	1.96
15.203	MM m	0.37	9132.80	380.10	98.04



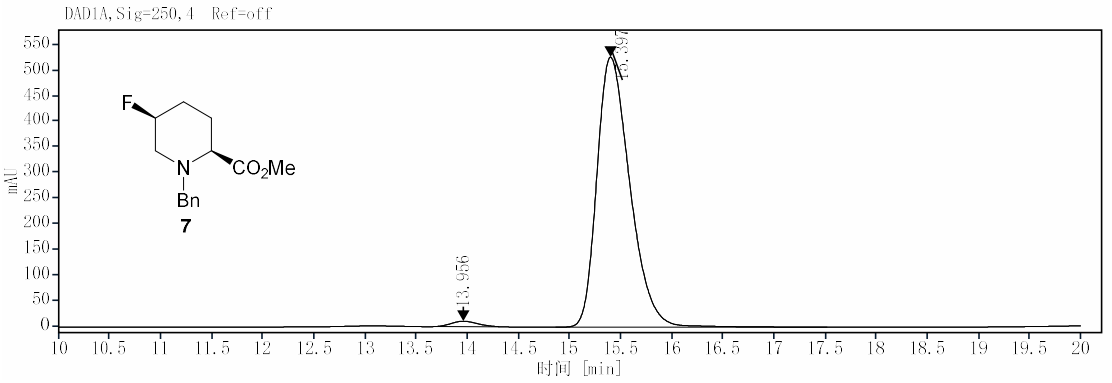
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
19.434	MM m	0.58	13248.74	354.33	49.53
21.228	MM m	0.67	13502.23	302.71	50.47



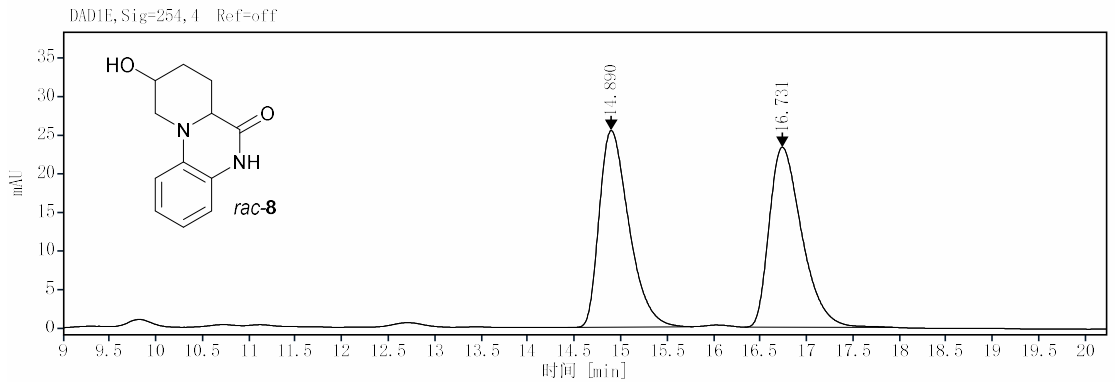
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
18.533	MM m	0.50	825.58	25.24	2.56
19.716	MM m	0.64	31370.24	736.04	97.44



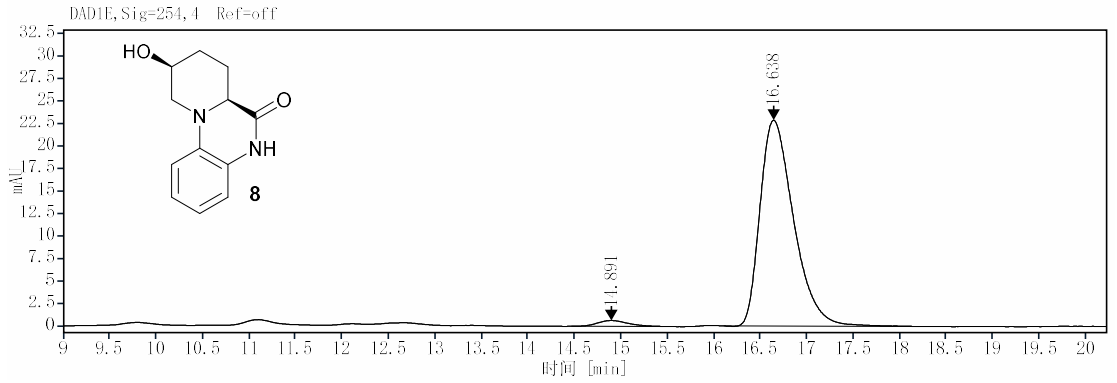
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
14.139	BB	1.63	6429.54	298.08	50.18
15.648	BB	1.93	6382.45	268.23	49.82



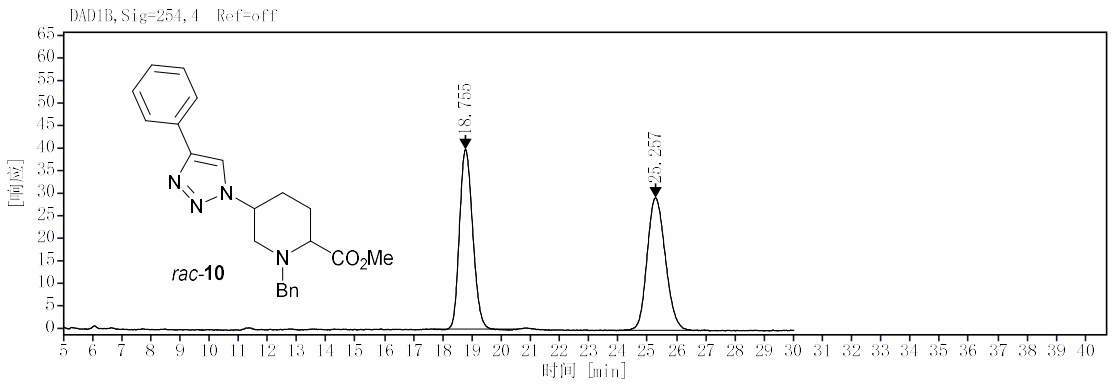
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
13.956	MM m	0.27	179.27	10.34	1.49
15.397	BB	2.66	11855.48	528.34	98.51



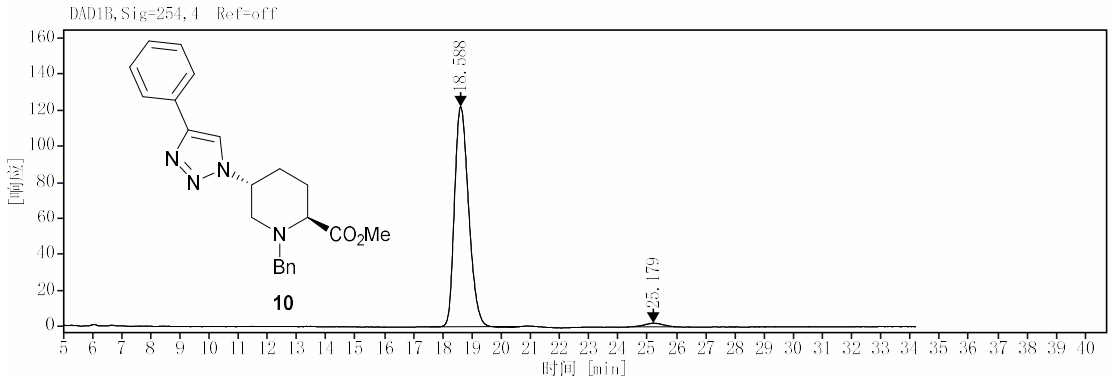
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
14.890	BB	1.34	566.23	25.51	49.86
16.731	BM m	0.37	569.32	23.34	50.14



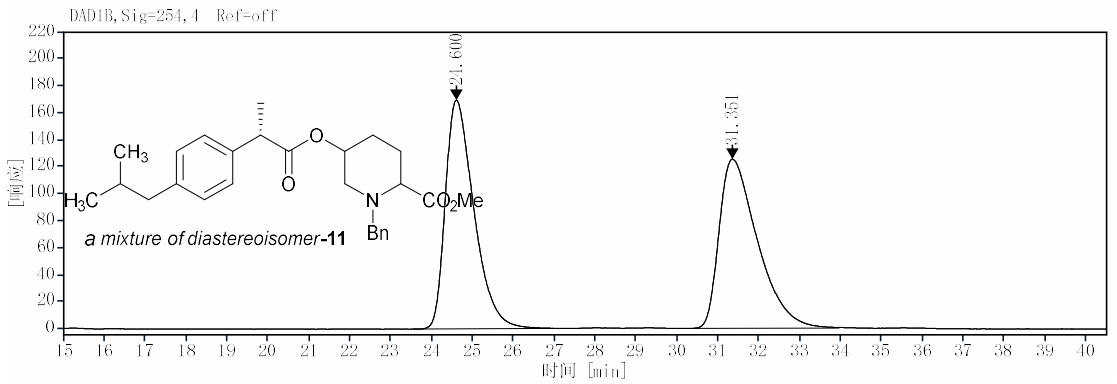
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
14.891	MM m	0.31	14.57	0.65	2.47
16.638	MM m	0.39	574.77	22.88	97.53



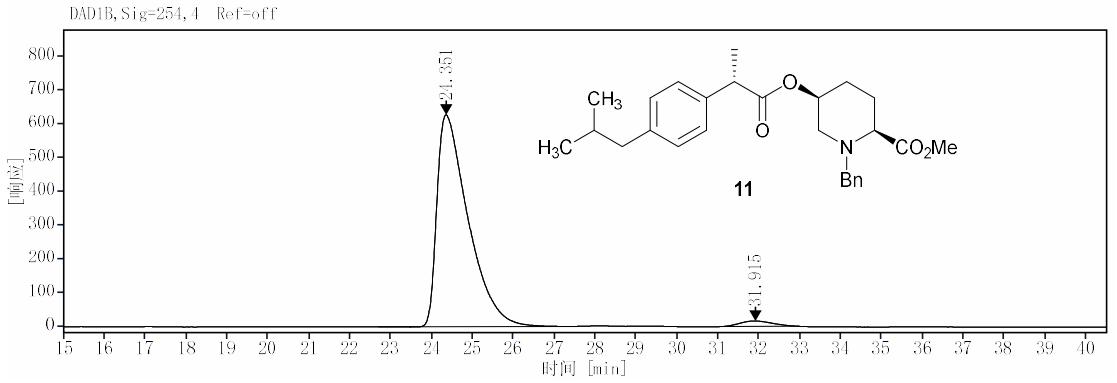
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
18.755	MM m	0.49	1242.84	39.90	49.23
25.257	MM m	0.60	1281.66	29.43	50.77



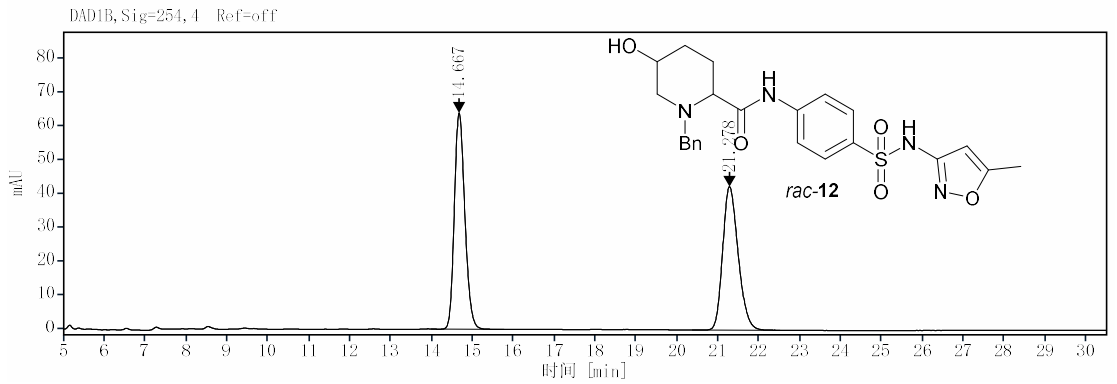
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
18.588	MM m	0.53	4089.28	122.21	97.99
25.179	MM m	0.50	84.08	2.01	2.01



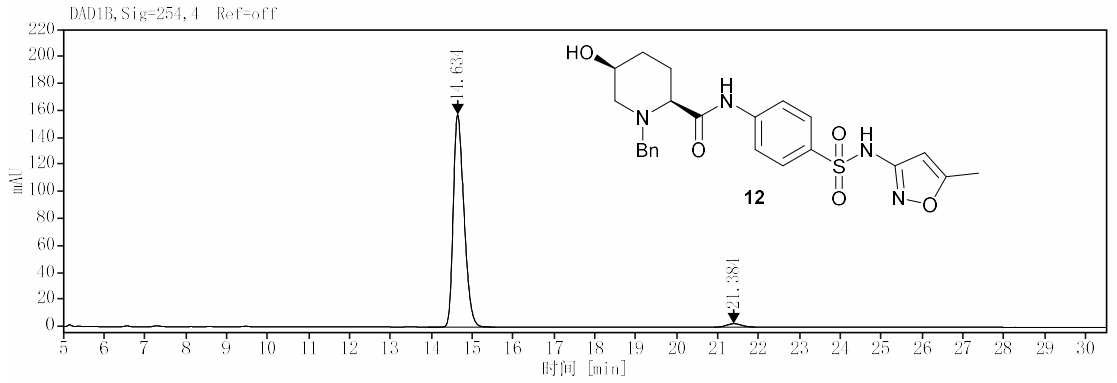
Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
24.600	BV	3.39	8259.47	169.54	50.22
31.351	VV	3.64	8188.42	125.30	49.78



Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
24.351	MV m	0.78	33232.71	627.61	97.34
31.915	MM m	0.67	908.81	16.29	2.66



Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
14.667	MM m	0.27	1134.19	64.07	50.34
21.278	MM m	0.40	1118.73	42.54	49.66



Ret Time [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
14.634	MM m	0.28	2858.60	157.27	97.84
21.384	MM m	0.39	63.12	2.52	2.16

6. Crystallographic Data

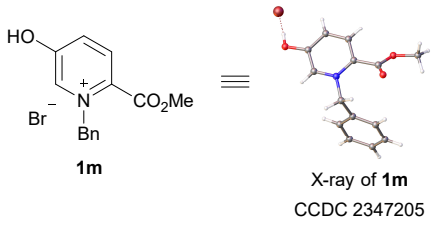


Figure S4. ORTEP of the molecular structure of **1m.**

Diffraction-quality crystal of compound **1m**was obtained in MeOH and DCM.

CCDC 2347205 contains the supplementary crystallographic data for compound **1m**.

Empirical formula	$C_{14}H_{14}BrNO_3$
Formula weight	324.17
Temperature/K	150.0
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	10.2580(8)
b/Å	12.5884(9)
c/Å	21.5327(18)
α/°	90
β/°	96.556(3)
γ/°	90
Volume/Å^3	2762.4(4)
Z	8
ρ_{calc}g/cm^3	1.559
μ/mm^{-1}	2.979
F(000)	1312.0
Crystal size/mm^3	0.38 × 0.26 × 0.12
Radiation	MoKα (λ = 0.71073)
2θ range for data collection/°	3.996 to 55.202
Index ranges	-13 ⩽ h ⩽ 13, -16 ⩽ k ⩽ 16, -28 ⩽ l ⩽ 23
Reflections collected	31343
Independent reflections	6314 [R_{int} = 0.1055, R_{sigma} = 0.0793]
Data/restraints/parameters	6314/0/347
Goodness-of-fit on F^2	1.007
Final R indexes [I>=2σ (I)]	R_1 = 0.0417, wR_2 = 0.0733
Final R indexes [all data]	R_1 = 0.1003, wR_2 = 0.0885
Largest diff. peak/hole / e Å^{-3}	0.35/-0.50