Supplementary Information (SI) for Organic & Biomolecular Chemistry.

Supplementary Information

Halogenation-Enabled Intramolecular Deaminative Cyclization

Wenbo Wang,[a] Gang He*[ab]

[a]State Key Laboratory and Institute of Elemento-Organic Chemistry, College of Chemistry,
Nankai University, Tianjin 300071, China
[b]Frontiers Science Center for New Organic Matter, Nankai University, Tianjin 300071, China

Table of Contents

1. General Information

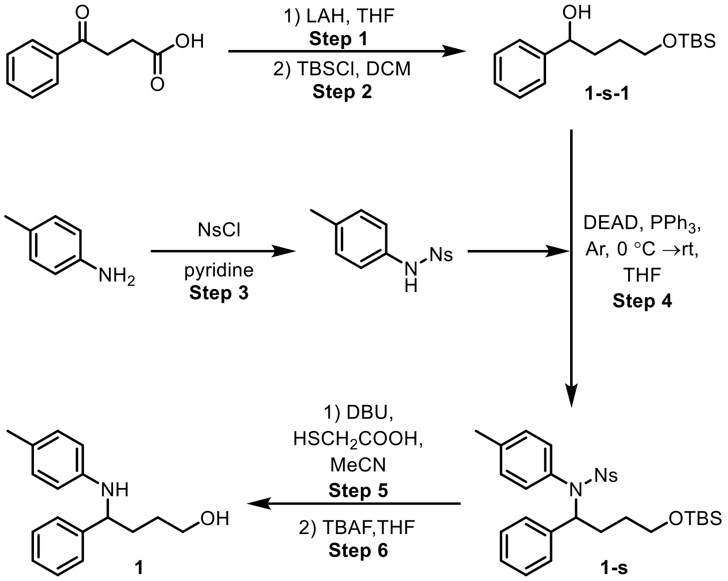
1.1 Reagents

All commercial materials were used as received unless otherwise noted. MeCN, DMSO and THF were purchased from J&K Chemical (dried by 4Å MS). DCM (dried by 4Å MS) were purchased from Energy Chemical. TLC were performed on silica gel Huanghai HSGF254 plates and visualization of the developed chromatogram was performed by fluorescence quenching of UV fluorescence (λmax = 254 nm). Flash chromatography was performed using Silica gel (200-300 mesh) purchased from Qingdao Haiyang Chemical Co. NBS (98%) and NCS (97%) were purchased from Bide pharm. Benzoylpropionic acids were purchased from Shanghai Bide pharm, Adamas-beta®, Macklin, Shanghai Haohong ScientificCo.Ltd, and others.

1.2 Instruments

NMR spectra were recorded on Bruker AVANCE AV 600 or AV 400 instruments and all NMR experiments were reported in units, parts per million (ppm), using residual solvent peaks [$CDCl_3$: 7.26 ppm or 0.00 ppm (TMS) for ^1H NMR and 77.16 ppm for ^{13}C NMR; CD_3OD: 3.31 ppm for ^1H NMR and 49.00 ppm for ^{13}C NMR; acetone-D_6: 2.05 ppm for for ^1H NMR and 29.84 ppm for ^{13}C NMR]. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, td = triplet of doublets, m = multiplet. The HRMS data were collected on a Thermo Q Exactive^{TM} Focus instrument with Quadrupole-Orbitrap^{TM} mass analyzer. Reactions carried out at elevated temperature were heated using heating blocks.

2. Synthesis of substrates



Step 1: $LiAlH_4$ (759.0 mg, 20.0 mmol, 4.0 equiv) was suspended in THF, and the mixture was cooled to 0 °C. Benzoylpropionic acid (5.0 mmol, 1.0 equiv) in THF was added dropwise. The reaction mixture was stirred overnight, allowing to warm to room temperature. After 12 h, the reaction mixture was cooled to 0 °C and quenched by successive dropwise addition of H_2O, 15% NaOH (aq), and H_2O. The resulting mixture was stirred at room temperature for 1 h, then $MgSO_4$ was added, and the mixture was filtered through a plug of celite (washing with THF). The filtrate was concentrated under reduced pressure to give a clear oil that solidified upon standing. A white solid was isolated and carried forward without purification.

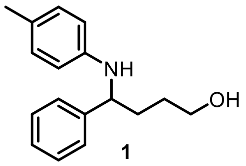
Step 2: Imidazole (816.8 mg, 12.0 mmol, 1.2 equiv) and TBSCl (1.8 g, 11.0 mmol, 1.1 equiv) were added to a solution of the product obtained in the **step 1** (1.7g, 10.0 mmol, 1.0 equiv) in CH_2Cl_2 (50 mL) at room temperature. After 9 h, the reaction was quenched by addition of saturated NH_4Cl solution (50 mL). The reaction mixture was extracted with CH_2Cl_2. The organic extracts were dried over Na_2SO_4 and concentrated. Purification of the residue by flash column chromatography gave TBS ether **1-s-1** as a colorless oil (2.0 g, 71%).

Step 3: Under nitrogen atmosphere, the mixture of p-toluidine (1.1 g, 10 mmol, 1.0 equiv) in pyridine (0.25 M) was stirred at 0 °C. 4-Nitrobenzenesulfonyl chloride (2.7 g, 12 mmol, 1.2 equiv) was added slowly, and then the mixture was stirred for 8 h at room temperature. The reaction solution was diluted with EtOAc (100 mL), and washed with 1N HCl (three times). The organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude material was purified by flash column chromatography to afford the desired product 4-nitro-N-(p-tolyl)benzenesulfonamide in quantitative yields (2.9 g).

Step 4: An oven-dried, three-necked round-bottomed flask was equipped with a Teflon-coated magnetic stir bar, an internal thermometer, a pressure-equalizing dropping funnel sealed with a rubber septum, and fitted with nitrogen gas inlet adaptor. The flask is evacuated and refilled with nitrogen three times, then charged with 4-nitro-N-(p-tolyl)benzenesulfonamide (2.3 g, 7.7 mmol, 1.1 equiv), triphenylphosphine (2.4 g, 9.1 mmol, 1.3 equiv), and THF (30 mL). **1-s-1** (2.0 g, 7.0 mmol, 1.0 equiv) was added and the solution was stirred in an ice bath for 10 min. Diethyl azodicarboxylate (1.5 g, 8.4 mmol, 1.2 equiv) was added dropwise from dropping funnel over 20 min, such that the internal temperature does not exceed 0 °C. The solution becomes cloudy during the addition. The mixture was stirred at 0 °C overnight, then the solution is evaporated. *n*-Hexane was added at room temperature and the white solid that precipitates was removed in a sintered-glass Büchner funnel (diameter 80 mm) using suction filtration and washed with *n*-hexane, and the filtrate was evaporated to give of the crude product as a clear, yellow oil. This material was purified by silica gel column chromatography to give the desired product **1-s** (2.4 g, 70%).

Step 5: Thioglycolic acid (736.9 mg, 8.0 mmol, 2.0 equiv) was added to a solution of **1-s** (2.2 g, 4.0 mmol, 1.0 equiv) and 1,8-diazabicyclo(5.4.0)undec-7-ene (2.4 g, 16.0 mmol, 4.0 equiv) in MeCN (20 mL). The solution was stirred at rt for 2 h and concentrated *in vacuo*. Then DCM (20 mL) and 10% aqueous solution of Na_2CO_3 (20 mL) were added. The organic layer was separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$, filtered and evaporated under vacuum. A yellow solid was isolated and carried forward without purification.

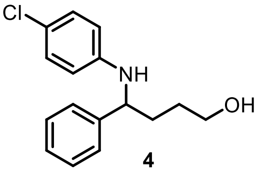
Step 6: To a stirred solution of the product obtained in the step 5 (1.0 equiv) in dry THF (20 mL) was added tetrabutylammonium fluoride (TBAF, 5.0 g, 16 mmol, 4.0 equiv) at room temperature, and the resulting mixture was stirred for 9 h. The reaction mixture was quenched with water and extracted with EtOAc. The organic extract was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography gave the desired product **1** (868.2 mg, 85%).



1

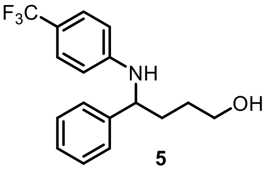
White solid. (R_f = 0.24, hexane/ethyl acetate = 3/1).
Compound 1 was synthesized following a reported procedure, and the spectra data are consistent with those reported in literature[1].
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 4H), 7.24 – 7.17 (m, 1H), 6.89 (d, J = 8.1 Hz, 2H), 6.44 (d, J = 8.4 Hz, 2H), 4.30 (t, J = 6.7 Hz, 1H), 3.65 (t, J = 6.3 Hz, 2H), 2.17 (s, 3H), 1.93 – 1.82 (m, 2H), 1.76 – 1.65 (m, 1H), 1.65 – 1.54 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 145.1, 144.2, 129.7, 128.7, 127.1, 126.7, 126.5, 113.7, 62.8, 58.6, 35.4, 29.7, 20.5.

HRMS: calculated for $C_{17}H_{22}NO^+$ [M+H$^+$]: 256.1696; **found**: 256.1700.



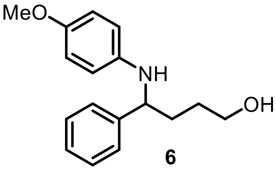
4

White solid. (R_f = 0.24, hexane/ethyl acetate = 3/1).
Compound **3** was synthesized following the procedure of synthesis of **1**.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 4H), 7.26 – 7.18 (m, 1H), 7.00 (d, *J* = 8.9 Hz, 2H), 6.41 (d, *J* = 8.9 Hz, 2H), 4.27 (t, *J* = 6.8 Hz, 1H), 3.69 – 3.57 (m, 2H), 1.91 – 1.80 (m, 2H), 1.71 – 1.62 (m, 1H), 1.62 – 1.54 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 146.0, 143.5, 129.0, 128.8, 127.3, 126.4, 121.9, 114.5, 62.6, 58.3, 35.2, 29.4.
HRMS: calculated for $C_{16}H_{19}ClNO^+$ [M+H$^+$]: 276.1150; **found**: 276.1151.



5

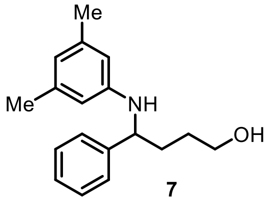
White solid. (R_f = 0.27, hexane/ethyl acetate = 3/1).
Compound **5** was synthesized following the procedure of synthesis of **1**.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 6H), 7.25 – 7.21 (m, 1H), 6.51 (d, *J* = 8.5 Hz, 2H), 4.36 (t, *J* = 6.8 Hz, 1H), 3.68 (td, *J* = 6.3, 1.8 Hz, 2H), 1.99 – 1.85 (m, 2H), 1.76 – 1.66 (m, 1H), 1.65 – 1.55 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 149.9, 143.1, 128.9, 127.5, 126.6 (q, *J* = 3.7 Hz), 126.4, 112.6, 62.6, 58.0, 35.1, 29.3.
^{19}F NMR (376 MHz, $CDCl_3$) δ -61.0.
HRMS: calculated for $C_{17}H_{19}F_3NO^+$ [M+H$^+$]: 310.1413; **found**: 310.1414.



6

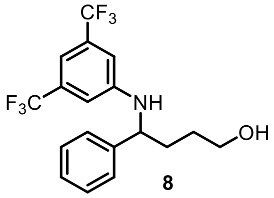
White solid. (R_f = 0.29, hexane/ethyl acetate = 3/1).
Compound **6** was synthesized following the procedure of synthesis of **1**.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 4H), 7.24 – 7.18 (m, 1H), 6.68 (d, *J* = 9.0 Hz, 2H), 6.49 (d, *J* = 8.9 Hz, 2H), 4.26 (t, *J* = 6.7 Hz, 1H), 3.68 (s, 3H), 3.66 (td, *J* = 6.3, 1.3 Hz, 2H), 2.79 (s, 1H), 1.96 – 1.82 (m, 2H), 1.73 – 1.66 (m, 1H), 1.65 – 1.57 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 152.2, 144.2, 141.5, 128.7, 127.1, 126.6, 115.0, 114.9, 62.8, 59.3, 55.9, 35.4, 29.7.

HRMS: calculated for $C_{17}H_{22}NO_2^+$ [M+H$^+$]: 272.1645; **found**: 272.1645.



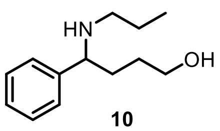
7

White solid. (R_f = 0.26, hexane/ethyl acetate = 3/1).
Compound **7** was synthesized following the procedure of synthesis of **1**.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 4H), 7.24 – 7.17 (m, 1H), 6.31 (s, 1H), 6.17 (s, 2H), 4.32 (t, J = 6.8 Hz, 1H), 3.65 (t, J = 6.3 Hz, 2H), 2.15 (s, 6H), 1.91 – 1.83 (m, 2H), 1.74 – 1.67 (m, 1H), 1.66 – 1.60 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 147.5, 144.2, 138.9, 128.7, 127.1, 126.5, 119.6, 111.5, 62.8, 58.2, 35.3, 29.7, 21.6.
HRMS: calculated for $C_{18}H_{24}NO^+$ [M+H$^+$]: 270.1852; **found**: 270.1854.



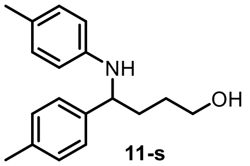
8

White solid. (R_f = 0.20, hexane/ethyl acetate = 3/1).
Compound **8** was synthesized following the procedure of synthesis of **1**.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 4H), 7.28 – 7.22 (m, 1H), 7.07 (s, 1H), 6.85 (d, J = 1.4 Hz, 2H), 4.86 (s, 1H), 4.36 (t, J = 6.8 Hz, 1H), 3.78 – 3.60 (m, 2H), 2.06 – 1.86 (m, 2H), 1.77 – 1.59 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 148.0, 142.2, 132.0 (q, J = 32.6 Hz), 129.0, 127.7, 126.4, 125.0, 122.3, 112.5 (d, J = 3.8 Hz), 112.5, 112.5, 110.2 (dt, J = 7.9, 4.0 Hz), 77.2, 62.5, 58.2, 34.9, 29.1.
^{19}F NMR (376 MHz, $CDCl_3$) δ -63.3.
HRMS: calculated for $C_{18}H_{18}F_6NO^+$ [M+H$^+$]: 378.1287; **found**: 378.1288.



10

White solid. (R_f = 0.27, hexane/ethyl acetate = 3/1).
Compound **10** was synthesized following the procedure of synthesis of **1**.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.29 (m, 5H), 4.97 (s, 2H), 3.72 – 3.64 (m, 2H), 3.63 – 3.54 (m, 1H), 2.44 (t, J = 7.5 Hz, 2H), 2.02 – 1.88 (m, 2H), 1.68 – 1.45 (m, 4H), 0.85 (t, J = 7.4 Hz, 3H).



11-s

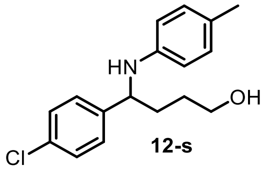
White solid. (R_f = 0.21, hexane/ethyl acetate = 3:1).

Compound **11-s** was synthesized following the procedure of synthesis of **1**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.1 Hz, 2H), 7.10 (d, *J* = 7.8 Hz, 2H), 6.88 (d, *J* = 8.2 Hz, 2H), 6.44 (d, *J* = 8.4 Hz, 2H), 4.27 (t, *J* = 6.7 Hz, 1H), 3.69 – 3.59 (m, 2H), 2.30 (s, 3H), 2.17 (s, 3H), 1.92 – 1.79 (m, 2H), 1.74 – 1.63 (m, 1H), 1.63 – 1.52 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2, 141.1, 136.6, 129.7, 129.4, 126.6, 126.4, 113.7, 62.8, 58.2, 35.3, 29.7, 21.2, 20.5.

HRMS: calculated for $C_{18}H_{24}NO^+$ [M+H$^+$]: 270.1852; **found**: 270.1855.



12-s

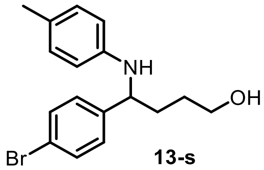
White solid. (R_f = 0.23, hexane/ethyl acetate = 3:1).

Compound **12-s** was synthesized following the procedure of synthesis of **1**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 5.4 Hz, 4H), 6.89 (d, *J* = 8.2 Hz, 2H), 6.44 – 6.37 (m, 2H), 4.27 (t, *J* = 6.7 Hz, 1H), 3.70 – 3.60 (m, 2H), 2.18 (s, 3H), 1.90 – 1.80 (m, 2H), 1.74 – 1.63 (m, 1H), 1.63 – 1.53 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 142.8, 132.6, 129.8, 128.9, 127.9, 127.0, 113.7, 62.6, 58.0, 35.3, 29.5, 20.5.

HRMS: calculated for $C_{17}H_{21}ClNO^+$ [M+H$^+$]: 290.1306; **found**: 290.1302.



13-s

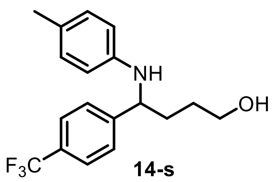
White solid. (R_f = 0.21, hexane/ethyl acetate = 3:1).

Compound **13-s** was synthesized following the procedure of synthesis of **1**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.1 Hz, 2H), 6.40 (d, *J* = 8.4 Hz, 2H), 4.25 (t, *J* = 6.7 Hz, 1H), 3.75 – 3.41 (m, 2H), 2.17 (s, 3H), 1.90 – 1.77 (m, 2H), 1.73 – 1.62 (m, 1H), 1.62 – 1.53 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 143.4, 131.8, 129.8, 128.3, 126.9, 120.7, 113.7, 62.6, 58.0, 35.3, 29.4, 20.5.

HRMS: calculated for $C_{17}H_{21}BrNO^+$ [M+H$^+$]: 334.0801; **found**: 334.0803.



14-s

White solid. (R_f = 0.29, hexane/ethyl acetate = 3:1).

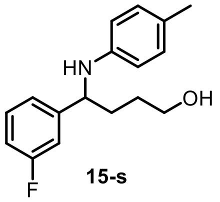
Compound **14-s** was synthesized following the procedure of synthesis of **1**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.1 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 8.1 Hz, 2H), 6.40 (d, *J* = 8.4 Hz, 2H), 4.35 (t, *J* = 6.7 Hz, 1H), 3.86 – 3.54 (m, 2H), 2.17 (s, 3H), 1.94 – 1.79 (m, 2H), 1.76 – 1.52 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 148.6, 144.7, 129.8, 129.3 (q, *J* = 32.2 Hz), 127.0, 126.8, 125.7 (q, *J* = 3.7 Hz), 123.0, 113.6, 62.5, 58.2, 35.3, 29.4, 20.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.3.

HRMS: calculated for $C_{18}H_{21}F_3NO^+$ [M+H$^+$]: 324.1570; **found**: 274.1569.



15-s

White solid. (R_f = 0.28, hexane/ethyl acetate = 3:1).

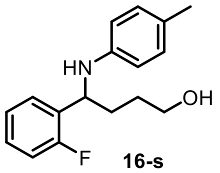
Compound **15-s** was synthesized following the procedure of synthesis of **1**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.22 (m, 1H), 7.11 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.07 – 7.02 (m, 1H), 6.95 – 6.83 (m, 3H), 6.42 (d, *J* = 8.4 Hz, 2H), 4.29 (t, *J* = 6.7 Hz, 1H), 3.71 – 3.59 (m, 2H), 2.18 (s, 3H), 1.92 – 1.79 (m, 2H), 1.76 – 1.54 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.6, 162.2, 147.3 (d, *J* = 3.3 Hz), 144.9, 130.2 (d, *J* = 8.2 Hz), 129.8, 127.0, 122.2 (d, *J* = 8.2 Hz), 114.0 (d, *J* = 21.3 Hz), 113.7, 113.3 (d, *J* = 21.6 Hz), 77.2, 62.6, 58.2, 35.3, 29.5, 20.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -113.0.

HRMS: calculated for $C_{17}H_{21}FNO^+$ [M+H$^+$]: 274.1602; **found**: 274.1598.



16-s

White solid. (R_f = 0.25, hexane/ethyl acetate = 3:1).

Compound **16-s** was synthesized following the procedure of synthesis of **1**.

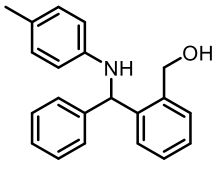
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 1H), 7.22 – 7.13 (m, 1H), 7.08 – 6.97 (m, 2H), 6.90 (d, *J* = 8.1 Hz, 2H), 6.47 (d, *J* = 8.3 Hz, 2H), 4.66 (t, *J* = 6.8 Hz, 1H), 3.72 – 3.62 (m, 2H), 2.17 (s, 3H), 1.97 – 1.86 (m, 2H), 1.80 – 1.68 (m, 1H), 1.68 – 1.56 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 159.6, 144.5, 130.8 (d, *J* = 13.4 Hz), 129.8, 128.5(d, *J* = 8.3 Hz), 12147.98.0, 127.9, 127.2, 114724.5 (d, *J* = 3.4 Hz), 115.7 (d, *J* =

22.1 Hz), 113.8, 62.7, 52.6, 52.5, 33.9, 29.7, 20.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -119.9.

HRMS: calculated for $C_{17}H_{21}FNO^+$ [M+H$^+$]: 274.1602; **found**: 274.1599.



20-s

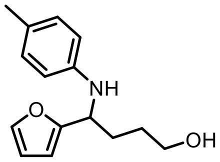
White solid. (R$_f$ = 0.21, hexane/ethyl acetate = 3:1).

Compound **20-s** was synthesized following the procedure of synthesis of **1**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 1H), 7.34 – 7.29 (m, 4H), 7.29 – 7.21 (m, 4H), 6.92 (d, *J* = 8.2 Hz, 2H), 6.49 (d, *J* = 8.4 Hz, 2H), 5.86 (s, 1H), 4.79 (d, *J* = 12.6 Hz, 1H), 4.60 (d, *J* = 12.6 Hz, 1H), 2.20 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 141.9, 140.8, 138.6, 129.8, 129.3, 128.8, 128.4, 128.2, 128.0, 127.9, 127.5, 127.4, 113.9, 63.3, 59.2, 20.5.

HRMS: calculated for $C_{21}H_{22}NO^+$ [M+H$^+$]: 304.1696; **found**: 304.1694.



21-s

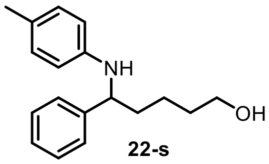
Colorless oil. (R$_f$ = 0.29, hexane/ethyl acetate = 3/1).

Compound **21-s** was synthesized following the procedure of synthesis of **1**.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (s, 1H), 6.95 (d, *J* = 7.8 Hz, 2H), 6.55 (d, *J* = 7.8 Hz, 2H), 6.26 (s, 1H), 6.14 (s, 1H), 4.79 (s, 1H), 4.46 (t, *J* = 6.9 Hz, 1H), 3.67 (t, *J* = 6.4 Hz, 2H), 2.21 (s, 3H), 2.07 – 1.97 (m, 1H), 1.97 – 1.88 (m, 1H), 1.75 – 1.61 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 156.2, 144.7, 141.5, 129.7, 127.3, 113.9, 110.1, 106.0, 62.6, 52.3, 31.7, 29.3, 20.4.

HRMS: calculated for $C_{15}H_{19}NNaO_2^+$ [M+Na$^+$]: 268.1308; **found**: 268.1309.



22-s

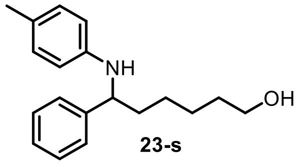
White solid. (R$_f$ = 0.28, hexane/ethyl acetate = 3:1).

Compound **22-s** was synthesized following the procedure of synthesis of **1**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 4H), 7.23 – 7.17 (m, 1H), 6.88 (d, *J* = 8.1 Hz, 2H), 6.43 (d, *J* = 8.4 Hz, 2H), 4.27 (t, *J* = 6.8 Hz, 1H), 3.60 (t, *J* = 6.4 Hz, 2H), 2.17 (s, 3H), 1.90 – 1.69 (m, 2H), 1.63 – 1.52 (m, 2H), 1.52 – 1.45 (m, 1H), 1.43 – 1.32 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2, 144.3, 129.7, 128.7, 127.0, 126.5, 113.5, 62.8, 58.5, 38.7, 32.6, 22.7, 20.5.

HRMS: calculated for $C_{18}H_{24}NO^+$ [M+H$^+$]: 270.1852; **found**: 270.1856.



23-s

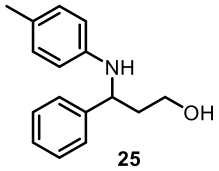
White solid. (R$_f$ = 0.24, hexane/ethyl acetate = 3:1).

Compound **23-s** was synthesized following the procedure of synthesis of **1**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 4H), 7.23 – 7.17 (m, 1H), 6.88 (d, *J* = 8.1 Hz, 2H), 6.43 (d, *J* = 8.4 Hz, 2H), 4.26 (t, *J* = 6.8 Hz, 1H), 3.60 (t, *J* = 6.5 Hz, 2H), 2.17 (s, 3H), 1.90 – 1.70 (m, 2H), 1.60 – 1.49 (m, 2H), 1.48 – 1.31 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2, 144.4, 129.7, 128.6, 127.0, 126.5, 113.5, 63.0, 58.6, 39.0, 32.7, 26.3, 25.8, 20.5.

HRMS: calculated for $C_{19}H_{25}NNaO^+$ [M+Na$^+$]: 306.1828; **found**: 306.1839.



25

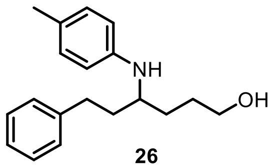
Colorless oil. (R$_f$ = 0.29, hexane/ethyl acetate = 3/1).

Compound **25** was synthesized following the procedure of synthesis of **1**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 4H), 7.24 – 7.17 (m, 1H), 6.89 (d, *J* = 8.2 Hz, 2H), 6.47 (d, *J* = 8.4 Hz, 2H), 4.53 (t, *J* = 6.7 Hz, 1H), 3.85 – 3.70 (m, 2H), 2.17 (s, 3H), 2.02 (td, *J* = 6.5, 4.7 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0, 143.8, 129.7, 128.8, 127.1, 127.0, 126.4, 114.1, 61.0, 57.4, 40.8, 20.5.

HRMS: calculated for $C_{16}H_{20}NO^+$ [M+H$^+$]: 242.1539; **found**: 242.1537.



26

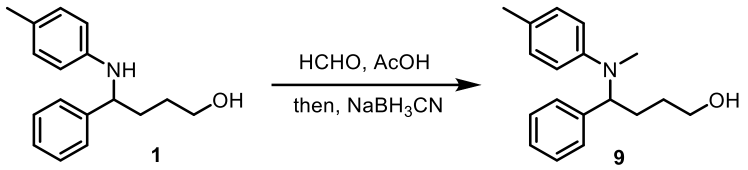
White solid. (R$_f$ = 0.26, hexane/ethyl acetate = 3/1).

Compound **26** was synthesized following the procedure of synthesis of **1**.

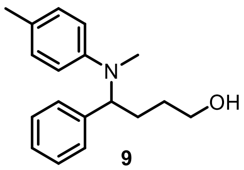
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.22 (m, 2H), 7.21 – 7.11 (m, 3H), 6.95 (d, *J* = 8.1 Hz, 2H), 6.46 (d, *J* = 8.3 Hz, 2H), 3.60 (t, *J* = 6.0 Hz, 2H), 3.40 – 3.30 (m, 1H), 2.76 – 2.64 (m, 2H), 2.58 (s, 2H), 2.22 (s, 3H), 1.90 – 1.76 (m, 2H), 1.75 – 1.59 (m, 3H), 1.58 – 1.44 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.4, 142.1, 129.9, 128.5, 126.6, 126.0, 113.7, 63.0, 52.9, 36.9, 32.4, 31.6, 29.4, 20.5.

HRMS: calculated for $C_{19}H_{26}NO^+$ [M+H$^+$]: 284.2009; **found**: 284.2017.

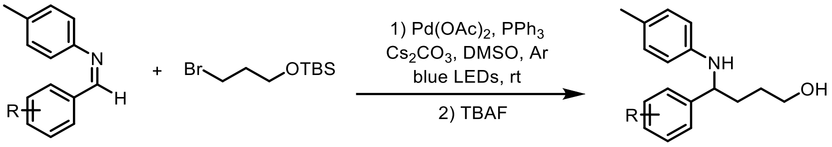


Compound **1** (153.2 mg, 0.6 mmol, 1.0 equiv)was dissolved in glacial acetic acid (2 mL) at rt. Aqueous formaldehyde solution (37% by weight, 180 mg, 6.0 mmol, 10 equiv) was added. The mixture was stirred at ambient temperature for 45 minutes. Sodium cyanoborohydride (113.0 mg, 1.8 mmol, 3.0 equiv) was added portionwise during 5 minutes and the mixture was stirred at ambient temperature for 30 minutes. The mixture was poured onto a mixture of ice and water (10 ml) and extracted with ethyl acetate. The organic phase was dried ($MgSO_4$) and evaporated. The residue was purified by column chromatography gave the desired product **9** (130.0 mg, 80%).



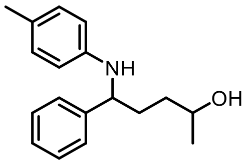
9

White solid. (R_f = 0.29, hexane/ethyl acetate = 3:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.25 (m, 2H), 7.25 – 7.18 (m, 3H), 7.04 (d, *J* = 8.3 Hz, 2H), 6.75 (d, *J* = 8.6 Hz, 2H), 4.89 (dd, *J* = 9.6, 5.6 Hz, 1H), 3.68 (t, *J* = 6.3 Hz, 2H), 2.64 (s, 3H), 2.25 (s, 3H), 2.19 – 1.97 (m, 2H), 1.74 – 1.62 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 148.7, 141.4, 129.9, 128.4, 127.4, 127.1, 126.3, 113.8, 63.0, 62.1, 32.0, 30.5, 28.3, 20.4.
HRMS: calculated for $C_{18}H_{24}NO^+$ [$M+H^+$]: 270.1852; **found**: 270.1855.



Step 1: A clean, oven-dried screw cap reaction tube equipped with a PTFE-coated stir–bar was charged with imine (1.0 equiv), $Pd(OAc)_2$ (10 mol%), PPh_3 (1.0 equiv), Cs_2CO_3 (2.0 equiv, added inside glove box), and alkyl bromide (2.0 equiv), capped with Teflon septum and parafilmed. The reaction tube was then purged with argon followed by the addition of anhydrous DMSO (0.1 M) under argon. The reaction tube was then stirred well for 10 min to generate yellow color which is then irradiated using 34 W blue LEDs while stirring at room temperature (under fan cooling). After 48 hours, the reaction mixture was treated with water and then extracted with ethyl acetate. The organic layer was collected, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a clear oil and carried forward without purification.
Step 2: To a stirred solution of step 1 product (1.0 equiv) in dry THF was added tetrabutylammonium fluoride (TBAF, 4.0 equiv) at room temperature, and stirring was continued for 9 h. The reaction mixture was quenched with water and extracted with EtOAc. The organic extract was washed with brine, dried over $MgSO_4$, and evaporated

in vacuo. The residue was purified by silica gel column chromatography gave the desired product.



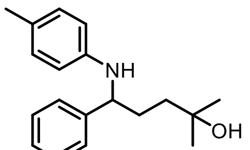
17-s

White solid. (R_f = 0.23, hexane/ethyl acetate = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.26 (m, 4H), 7.23 – 7.17 (m, 1H), 6.88 (d, *J* = 8.1 Hz, 2H), 6.43 (d, *J* = 7.5 Hz, 2H), 4.32 – 4.25 (m, 1H), 3.87 – 3.75 (m, 1H), 2.17 (s, 3H), 1.98 – 1.87 (m, 1H), 1.87 – 1.78 (m, 1H), 1.63 – 1.54 (m, 1H), 1.53 – 1.43 (m, 1H), 1.16 (dd, *J* = 6.2, 1.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2, 145.1, 144.3, 144.2, 129.7, 128.7, 127.0, 126.6, 126.5, 126.5, 113.7, 113.6, 68.1, 67.9, 58.7, 58.6, 36.1, 35.9, 35.3, 34.9, 23.9, 23.8, 20.5.

HRMS: calculated for $C_{18}H_{24}NO^+$ [M+H$^+$]: 270.1852; **found**: 270.1852.



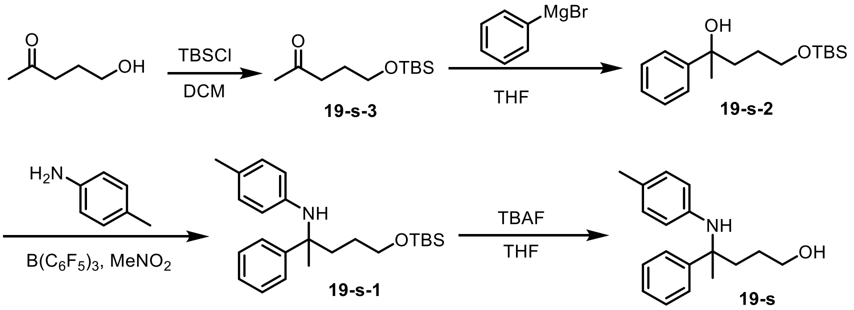
18-s

White solid. (R_f = 0.26, hexane/ethyl acetate = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.25 (m, 4H), 7.23 – 7.16 (m, 1H), 6.88 (d, *J* = 8.4 Hz, 2H), 6.43 (d, *J* = 8.4 Hz, 2H), 4.25 (t, *J* = 6.7 Hz, 1H), 2.16 (s, 3H), 1.91 – 1.79 (m, 2H), 1.68 – 1.57 (m, 1H), 1.51 – 1.42 (m, 1H), 1.18 (s, 3H), 1.17 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2, 144.3, 129.7, 128.7, 127.0, 126.5, 126.4, 113.5, 70.8, 59.0, 40.3, 33.6, 29.6, 29.3, 20.4.

HRMS: calculated for $C_{19}H_{26}NO^+$ [M+H$^+$]: 284.2009; **found**: 284.2014.



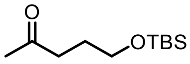
Step 1: To a solution of 5-hydroxypentan-2-one (1.0 g, 10.0 mmol, 1.0 equiv) and imidazole (816.8 mg, 12.0 mmol, 1.2 equiv) in CH_2Cl_2 was added TBSCl (1.7 g, 11.0 mmol, 1.1 equiv). The reaction mixture was stirred at room temperature overnight and then quenched with water, extracted twice with CH_2Cl_2. The combine organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness. The crude residue was purified by flash chromatography on silica gel to give

product **19-s-3** (1.8 g, 83%) as a colorless oil.

Step 2: To a solution of ketone (10 mmol) in THF (1.0 M) was added a solution of PhMgBr in THF (5 mL, 15 mmol, 3 M, 1.5 equiv) dropwise at 0 °C. The reaction mixture was stirred at room temperature for overnight. The reaction was quenched slowly with aqueous solution of NH_4Cl at 0 °C, and extracted with ethyl acetate (30 mL × 2). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel to give the resulting alcohol **19-s-2** (2.3 g, 78%).

Step 3: To a 25ml Schlenk tube was added alcohol (0.2 mmol, 1.0 equiv) and p-Toluidine (49.2 mg, 0.4 mmol) and $B(C_6F_5)_3$ (11.0 mg, 0.1 equiv), then 1ml CH_3NO_2 was added. The mixture was stirred at 85 ℃ until the alcohol was disappeared (monitored by TLC). Then the solvent was removed and the residue was purified by silica gel column chromatography to afford product **19-s-1** (15.3 mg, 20%).

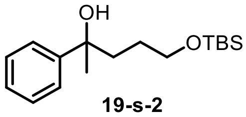
Step 4: To a stirred solution of step 3 product (1.0 equiv) in dry THF was added tetrabutylammonium fluoride (TBAF, 4.0 equiv) at room temperature, and stirring was continued for 9 h. The reaction mixture was quenched with water and extracted with EtOAc. The organic extract was washed with brine, dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by silica gel column chromatography gave the desired product **19-s** (40.0 mg, 75%).



19-s-3

colorless oil. (R_f = 0.30, hexane/ethyl acetate = 10:1).

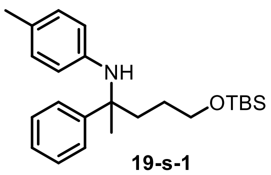
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.61 (t, J = 6.1 Hz, 2H), 2.51 (t, J = 7.2 Hz, 2H), 2.15 (s, 3H), 1.86 – 1.71 (m, 2H), 0.89 (s, 9H), 0.04 (s, 6H).



19-s-2

colorless oil. (R_f = 0.20, hexane/ethyl acetate = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.41 (m, 2H), 7.32 (dd, J = 8.5, 6.9 Hz, 2H), 7.25 – 7.17 (m, 1H), 3.68 – 3.54 (m, 2H), 3.43 (s, 1H), 2.12 – 2.00 (m, 1H), 1.93 – 1.83 (m, 1H), 1.53 (s, 3H), 1.51 – 1.39 (m, 2H), 0.89 (s, 9H), 0.04 (s, 6H).

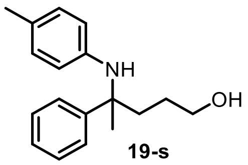


19-s-1

White solid. (R_f = 0.30, hexane/ethyl acetate = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 2H), 7.35 – 7.29 (m, 2H), 7.25 – 7.17 (m, 1H), 6.81 (d, J = 8.6 Hz, 2H), 6.25 (d, J = 8.3 Hz, 2H), 3.98 (s, 1H), 3.52 (t, J = 6.1

Hz, 2H), 2.16 (s, 3H), 1.99 – 1.81 (m, 2H), 1.63 (s, 3H), 1.52 – 1.38 (m, 2H), 0.87 (s, 9H), 0.00 (s, 6H).



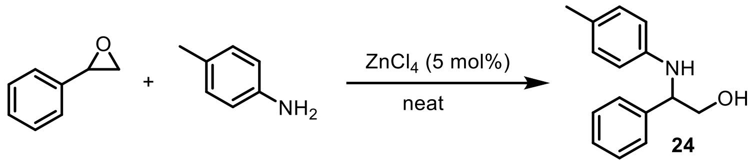
19-s

White solid. (R_f = 0.21, hexane/ethyl acetate = 3:1).

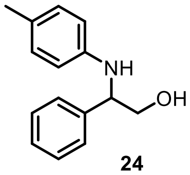
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.43 (m, 2H), 7.35 – 7.28 (m, 2H), 7.24 – 7.19 (m, 1H), 6.80 (d, *J* = 8.3 Hz, 2H), 6.25 (d, *J* = 8.4 Hz, 2H), 3.54 (t, *J* = 6.4 Hz, 2H), 2.15 (s, 3H), 2.03 – 1.85 (m, 2H), 1.63 (s, 3H), 1.56 – 1.42 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 146.5, 143.5, 129.4, 128.5, 126.5, 126.3, 115.7, 63.1, 58.3, 40.2, 27.2, 26.3, 20.4.

HRMS: calculated for $C_{18}H_{24}NO^+$ [M+H$^+$]: 270.1852; **found**: 270.1850.



$ZrCl_4$ (29.1 mg, 5 mol%) was added to a magnetically stirred mixture of styrene oxide (300.4 mg, 2.5 mmol, 1.0 equiv) and p-Toluidine (267.9 mg, 2.5 mmol, 1.0 equiv) at room temperature under nitrogen. After completion of the reaction (15 min, TLC), the reaction mixture was diluted with Et_2O (15 mL) and the precipitated catalyst was separated by decantation of the supernatant ethereal solution. The catalyst was washed with Et_2O (10 mL) and the combined ethereal solutions were dried (Na_2SO_4) and concentrated in vacuo to afford compound **24** (562.6 mg ,99%).



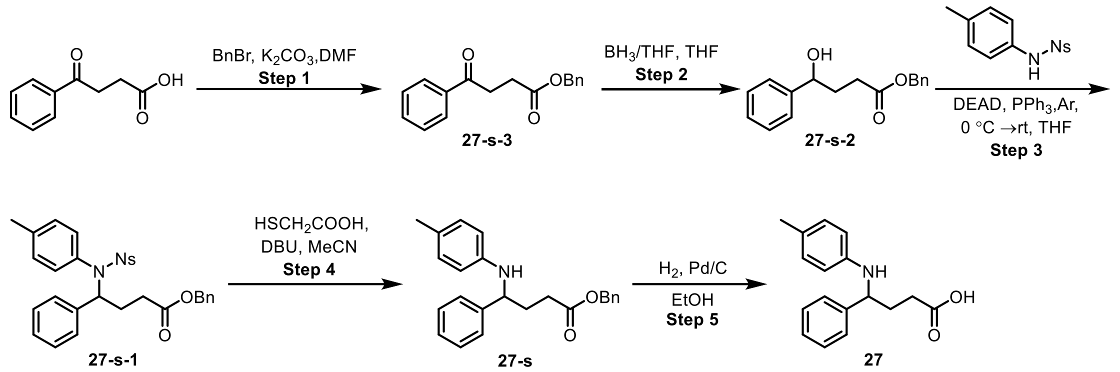
24

Colorless oil. (R_f = 0.24, hexane/ethyl acetate = 3/1).

Compound **24** was synthesized following a reported procedure, and the spectra data are consistent with those reported in literature^6.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 4H), 7.28 – 7.23 (m, 1H), 6.91 (d, *J* = 8.0 Hz, 2H), 6.50 (d, *J* = 8.5 Hz, 2H), 4.48 (dd, *J* = 7.2, 4.3 Hz, 1H), 4.35 (s, 1H), 3.93 (dd, *J* = 11.1, 4.2 Hz, 1H), 3.74 (dd, *J* = 11.1, 7.1 Hz, 1H), 2.19 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0, 140.4, 129.8, 128.9, 127.6, 127.2, 126.8, 114.2, 67.5, 60.3, 20.5.



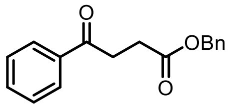
Step 1: Add K_2CO_3 (2.1 g, 15 mmol, 1.5 equiv) and benzyl bromide (2.6 g, 15 mmol, 1.5 equiv) to a solution of 3-benzoylpropionic acid (1.8 g, 10.0 mmol, 1.0 equiv) in 15 mL of DMF. The mixture was then stirred at 25 °C for 2 h. Water was added and the mixture was extracted with EtOAc. The combined organic layers were concentrated under reduced pressure and purified by silica gel column chromatography to obtain **27-s-3** (2.4 g, 89%).

Step 2: To a 1 M solution of BH_3 in THF (1.0 mL, 1.0 mmol, 0.5 equiv.) at 0 °C was added Compound **27-s-3** (2.0 mmol) was dissolved in THF (5 mL) drop wise. The reaction was completed after 3 h stirring at the same temperature (TLC). A saturated solution of NH_4Cl (25 mL) was added and solution was stirred for 15 min at rt. The reaction mixture was extracted with EtOAc (3×25 mL), washed with brine, dried over $MgSO_4$. The combined organic layer was concentrated under reduced pressure and purified by silica gel column chromatography to obtain **27-s-2** (486.6 mg, 90%).

Step 3: An oven-dried, three-necked round-bottomed flask was equipped with a Teflon-coated magnetic stir bar, an internal thermometer, a pressure-equalizing dropping funnel sealed with a rubber septum, and fitted with nitrogen gas inlet adaptor. The flask is evacuated and refilled with nitrogen three times, then charged with 4-nitro-N-(p-tolyl)benzenesulfonamide(321.5 mg, 1.1 mmol, 1.1 equiv), triphenylphosphine (367.2 mg, 1.4 mmol, 1.4 equiv), and THF (5 mL). **27-s-2** (270 mg, 1.0 mmol, 1.0 equiv) was added and the solution was stirred in an ice bath for 10 min. Diethyl azodicarboxylate (226.9 mg, 1.3 mmol, 1.3 equiv) was added dropwise from dropping funnel over 20 min, such that the internal temperature does not exceed 0 °C. The solution becomes cloudy during the addition. The mixture was stirred at 0 °C overnight, then the solution is evaporated. *n*-Hexane was added at room temperature and the white solid that precipitates was removed in a sintered-glass Büchner funnel (diameter 80 mm) using suction filtration and washed with *n*-hexane, and the filtrate was evaporated to give of the crude product as a clear, yellow oil. This material was purified by silica gel column chromatography to give the desired product **27-s-1** (239.6 g, 44%).

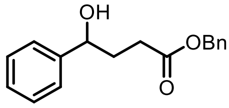
Step 4: Thioglycolic acid (18.4 mg, 0.2 mmol, 2.0 equiv) was added to a solution of **27-s-1** (54.5 mg, 0.1 mmol, 1.0 equiv) and 1,8-diazabicyclo(5.4.0)undec-7-ene (60.9 mg, 0.4 mmol, 4.0 equiv) in MeCN (2 mL). The solution was stirred at rt for 2 h and concentrated *in vacuo*. Then DCM (20 mL) and 10% aqueous solution of Na_2CO_3 (20 mL) were added. The organic layer was separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$, filtered and evaporated under vacuum. This material was purified by silica gel column chromatography to give the desired product **27-s** (29.8 g, 83%).

Step 5: To a MeOH (1 mL) solution of the **27-s** (35.9 mg, 0.1 mmol) was added Pd/C (10%; 3.5 mg) and the resulting black suspension was flushed with N_2 and placed under 1 atm of H_2. The mixture was stirred at room temperature overnight and filtered though a microfiber filter to remove the catalyst. The resulting clear solution was then concentrated under reduced pressure to obtain **27** (24.5 mg, 91%).



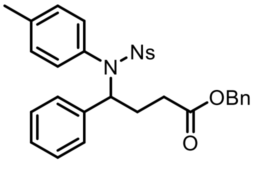
27-s-3

Colorless oil. (R*f* = 0.27, hexane/ethyl acetate = 10:1).
Compound **27-s-3** was synthesized following a reported procedure, and the spectra data are consistent with those reported in literature[3].
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 7.94 (m, 2H), 7.61 – 7.54 (m, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.39 – 7.26 (m, 5H), 5.15 (s, 2H), 3.34 (t, *J* = 6.6 Hz, 2H), 2.83 (t, *J* = 6.6 Hz, 2H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 198.2, 172.9, 136.7, 136.0, 133.4, 128.8, 128.7, 128.4, 128.2, 66.7, 33.5, 28.4.



27-s-2

Colorless oil. (R*f* = 0.22, hexane/ethyl acetate = 3:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.23 (m, 10H), 5.11 (s, 2H), 4.75 (t, *J* = 6.2 Hz, 1H), 2.49 (t, *J* = 7.2 Hz, 2H), 2.18 (s, 1H), 2.14 – 2.04 (m, 2H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 173.8, 144.1, 136.0, 128.7, 128.7, 128.4, 127.8, 125.9, 73.7, 66.5, 33.9, 30.8.

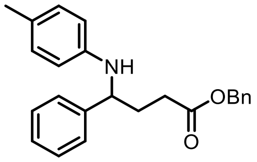


27-s-1

Colorless oil. (R*f* = 0.22, hexane/ethyl acetate = 3:1).
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.42 – 7.31 (m, 5H), 7.25 – 7.18 (m, 3H), 6.98 (d, *J* = 7.6 Hz, 4H), 6.42 (d, *J* = 7.7 Hz, 2H), 5.58 (t, *J* = 7.9 Hz, 1H), 5.13 (s, 2H), 2.45 – 2.38 (m, 2H), 2.32 (s, 3H), 2.24 – 2.15 (m, 1H), 2.14 – 2.07 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 172.6, 149.9, 146.7, 139.6, 137.6, 135.9, 132.5, 131.2, 129.7, 128.9, 128.8, 128.8, 128.7, 128.6, 128.5, 128.5, 124.0, 66.7, 62.5, 31.2, 27.7, 21.3.

HRMS: calculated for $C_{30}H_{28}N_2NaO_6S^+$ [M+Na$^+$]: 567.1560; **found**: 567.1561.



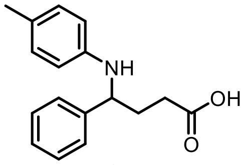
27-s

Colorless oil. (R_f = 0.22, hexane/ethyl acetate = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.17 (m, 10H), 6.87 (d, *J* = 8.1 Hz, 2H), 6.41 (d, *J* = 8.4 Hz, 2H), 5.10 (s, 2H), 4.34 (t, *J* = 6.8 Hz, 1H), 4.08 (s, 1H), 2.46 (t, *J* = 7.2 Hz, 2H), 2.17 (s, 3H), 2.16 – 2.04 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.5, 145.0, 143.4, 135.9, 129.7, 128.8, 128.7, 128.5, 128.4, 127.3, 126.7, 126.5, 113.6, 66.6, 58.0, 33.4, 31.5, 20.5.

HRMS: calculated for $C_{24}H_{26}NO_2^+$ [M+H$^+$]: 360.1958; **found**: 360.1956.



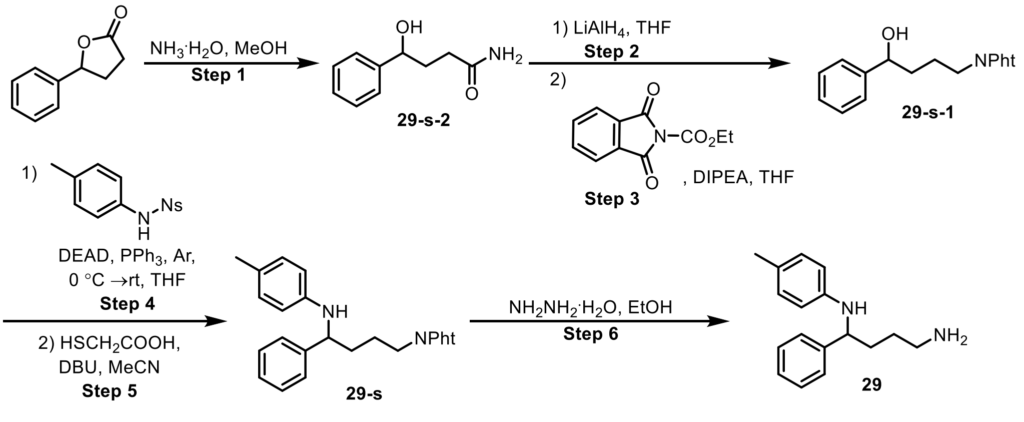
27

Colorless oil. (R_f = 0.22, DCM/MeOH = 10:1).

^{1}H NMR (400 MHz, MeOD) δ 7.35 (dd, *J* = 7.1, 1.5 Hz, 2H), 7.25 (t, *J* = 7.6 Hz, 2H), 7.18 – 7.11 (m, 1H), 6.77 (d, *J* = 8.3 Hz, 2H), 6.42 (d, *J* = 8.4 Hz, 2H), 4.28 (t, *J* = 6.8 Hz, 1H), 2.29 – 2.23 (m, 1H), 2.23 – 2.17 (m, 1H), 2.10 (s, 3H), 2.08 – 1.89 (m, 2H).

^{13}C NMR (101 MHz, MeOD) δ 182.2, 147.2, 146.2, 130.1, 129.3, 127.7, 127.5, 126.4, 114.7, 59.7, 36.3, 36.0, 20.4.

HRMS: calculated for $C_{17}H_{20}NO_2^+$ [M+H$^+$]: 270.1489; **found**: 270.1489.



Step 1: To a solution of 4-phenylbutyrolactone(1.95 g, 12 mmol, 1.0 eq) in MeOH (100 mL) was added dropwise ammonia water (50 mL), then the mixture was stirred at room temperature for 12 h. After the reaction is over, the MeOH is concentrated in vacuo.

The mixture was extracted with EtOAc, and the extract was dried over anhydrous Na_2SO_4, and concentrated in vacuo to yield the crude product. The crude product was purification by chromatography on silica gel gave **29-s-2** as a white solid (1.72 g, 80%).

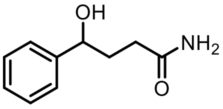
Step 2: $LiAlH_4$ (151.2 mg, 4.0 mmol, 4.0 equiv) was suspended in THF, and the mixture was cooled to 0 ℃. Compuond **29-s-2** (179.2 mg, 1.0 mmol, 1.0 equiv) in THF was added dropwise. The reaction mixture was stirred overnight, allowing to warm to room temperature. After 12 h, the reaction mixture was cooled to 0 ℃ and quenched by successive dropwise addition of H_2O, 15% NaOH (aq), and H_2O. The resulting mixture was stirred at room temperature for 1 h, then $MgSO_4$ was added, and the mixture was filtered through a plug of celite (washing with THF). The filtrate was concentrated under reduced pressure to give a clear oil that solidified upon standing. A white solid was isolated and carried forward without purification.

Step 3: A solution of the product obtained in the step 2(1.0 mmol, 1.0 equiv), N-(ethoxycarbonyl)phthalimide (328.8 mg, 1.5 mmol, 1.5 equiv), and DIPEA (193.9 mg, 1.5 mmol, 1.5 equiv) in dry THF (10 mL) was refluxed for 12 h. The volatile components were then removed under reduced pressure, and the residue was dissolved in EtOAc (50 mL), washed with 1N HCl and brine, and dried over $MgSO_4$, and concentrated in vacuo to yield the crude product. The crude product was purification by chromatography on silica gel gave **29-s-1** as a white solid (472.0 mg, 89%).

Step 4: An oven-dried, three-necked round-bottomed flask was equipped with a Teflon-coated magnetic stir bar, an internal thermometer, a pressure-equalizing dropping funnel sealed with a rubber septum, and fitted with nitrogen gas inlet adaptor. The flask is evacuated and refilled with nitrogen three times, then charged with 4-nitro-N-(p-tolyl)benzenesulfonamide (321.5 g, 1.1 mmol, 1.1 equiv), triphenylphosphine (367.2 mg, 1.4 mmol, 1.4 equiv), and THF (10 mL). **29-s-1** (295.3 mg, 1.0 mmol, 1.0 equiv) was added and the solution was stirred in an ice bath for 10 min. Diethyl azodicarboxylate (226.9 mg, 1.3 mmol, 1.3 equiv) was added dropwise from dropping funnel over 20 min, such that the internal temperature does not exceed 0 °C. The solution becomes cloudy during the addition. The mixture was stirred at 0 °C overnight, then the solution is evaporated. *n*-Hexane was added at room temperature and the white solid that precipitates was removed in a sintered-glass Büchner funnel (diameter 80 mm) using suction filtration and washed with *n*-hexane, and the filtrate was evaporated to give of the crude product as a clear, yellow oil and carried forward without purification.

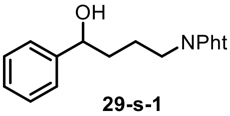
Step 5: Thioglycolic acid (18.4 mg, 0.2 mmol, 2.0 equiv) was added to a solution of the product obtained in the step 4 (57.0 mg, 0.1 mmol, 1.0 equiv) and 1,8-diazabicyclo(5.4.0)undec-7-ene (60.9 mg, 0.4 mmol, 4.0 equiv) in MeCN (2 mL). The solution was stirred at rt for 2 h and concentrated *in vacuo*. Then DCM (20 mL) and 10% aqueous solution of Na_2CO_3 (20 mL) were added. The organic layer was separated and the aqueous layer was extracted with DCM. The combined organic layers were dried over $MgSO_4$, filtered and evaporated under vacuum. The crude product was purification by chromatography on silica gel gave **29-s** as a white solid (19.2 mg, 50%, two steps).

Step 6: Add hydrazine monohydrate (101.1 mg, 2.0 mmol, 2.0 equiv) to a solution of **28-s** (384.5 mg, 1.0 mmol, 1.0 equiv) in EtOH (15.0 mL) at rt. Stir the reaction mixture for 12 h. Evaporate the solvent in vacuo. The crude product was purification by chromatography on silica gel gave **29** as a colorless oil (178.1 mg, 70%).



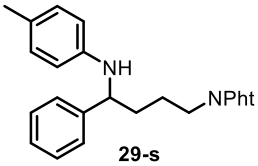
29-s-2

White solid. (R_f = 0.27, hexane/ethyl acetate = 3:1).
Compound **29-s-2** was synthesized following a reported procedure, and the spectra data are consistent with those reported in literature[4].
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 4H), 7.31 – 7.23 (m, 1H), 5.64 (s, 2H), 4.79 (dd, J = 7.7, 4.6 Hz, 1H), 3.40 (s, 1H), 2.44 – 2.32 (m, 2H), 2.15 – 2.00 (m, 2H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 176.1, 144.4, 128.6, 127.6, 125.9, 73.7, 34.1, 32.2.



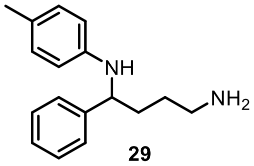
29-s-1

White solid. (R_f = 0.21, hexane/ethyl acetate = 3:1).
Compound **29-s-1** was a known compound, and the spectra data are consistent with those reported in literature[5].
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, J = 5.4, 3.1 Hz, 2H), 7.69 (dd, J = 5.5, 3.1 Hz, 2H), 7.37 – 7.29 (m, 4H), 7.28 – 7.21 (m, 1H), 4.72 (dd, J = 7.3, 4.9 Hz, 1H), 3.88 – 3.57 (m, 2H), 2.30 (s, 1H), 1.90 – 1.78 (m, 2H), 1.77 – 1.63 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 144.6, 134.0, 132.2, 128.6, 127.7, 125.9, 123.3, 74.1, 37.8, 36.1, 25.2.



29-s

White solid. (R_f = 0.39, hexane/ethyl acetate = 3:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 5.5, 3.1 Hz, 2H), 7.69 (dd, J = 5.5, 3.0 Hz, 2H), 7.36 – 7.24 (m, 4H), 7.18 (t, J = 6.9 Hz, 1H), 6.86 (d, J = 8.0 Hz, 2H), 6.42 (d, J = 8.0 Hz, 2H), 4.33 (t, J = 6.3 Hz, 1H), 4.02 (s, 1H), 3.70 (t, J = 5.1 Hz, 2H), 2.15 (s, 3H), 1.93 – 1.65 (m, 4H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 168.6, 145.0, 143.9, 134.1, 132.2, 129.7, 128.7, 127.1, 126.5, 123.4, 113.5, 58.1, 37.9, 35.8, 25.7, 20.4.
HRMS: calculated for $C_{25}H_{25}N_2O_2^+$ [M+H$^+$]: 385.1911; **found**: 385.1913.



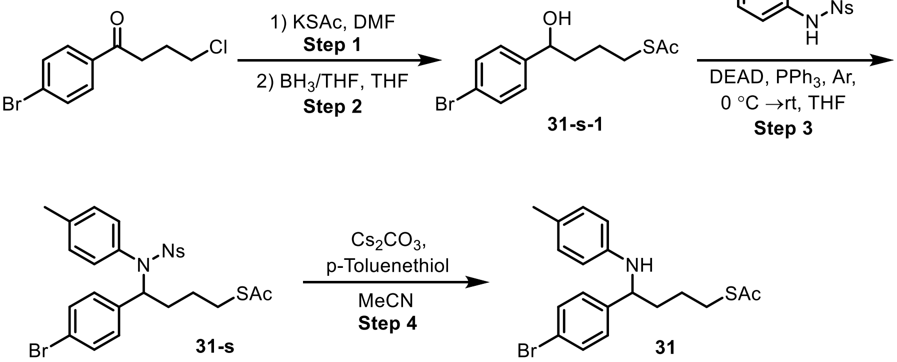
29

Colorless oil. (R_f = 0.17, DCM/MeOH = 10:1 with 0.5% Et_3N).

^{1}H NMR (400 MHz, MeOD) δ 7.33 (d, *J* = 7.1 Hz, 2H), 7.25 (t, *J* = 7.6 Hz, 2H), 7.15 (t, *J* = 7.3 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 2H), 6.45 (d, *J* = 8.4 Hz, 2H), 4.27 (t, *J* = 6.8 Hz, 1H), 2.65 (t, *J* = 7.2 Hz, 2H), 2.11 (s, 3H), 1.88 – 1.78 (m, 1H), 1.78 – 1.68 (m, 1H), 1.66 – 1.56 (m, 1H), 1.54 – 1.41 (m, 1H).

^{13}C NMR (151 MHz, MeOD) δ 147.0, 146.1, 130.2, 129.3, 127.8, 126.7, 114.9, 59.4, 42.3, 36.9, 30.3, 20.4.

HRMS: calculated for $C_{17}H_{23}N_2^+$ [M+H$^+$]: 255.1856; **found**: 255.1856.

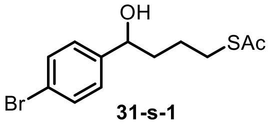


Step 1: To a solution of KSAc (1.5 equiv.) in DMF (25 ml) was added 4-chloro-1-arylbutan-1-one (10 mmol) dropwise at 0 °C. The reaction was run at rt for 10 h. After completion of the reaction (TLC), the solvent was evaporated; the residue was extracted with EtOAc (3×50 mL) and washed with water (2×50 mL) and Brine (1×50 mL). The combined organic phase was dried over $MgSO_4$ and the solvent was removed in reduced pressure to obtain pure desired product in analytically pure forms which were used directly for the next synthetic steps without further purifications.

Step 2: To a 1 M solution of BH_3 in THF (0.5 equiv.) at 0°C was added the product obtained in the step 1 (8 mmol) was dissolved in THF (12 mL) drop wise. The reaction was completed after 3 h stirring at the same temperature (TLC). A saturated solution of NH_4Cl (25 mL) was added and solution was stirred for 15 min at rt. The reaction mixture was extracted with EtOAc (3×50 mL), washed with brine, dried over $MgSO_4$. The combined organic layer was concentrated under reduced pressure and purified by silica gel column chromatography to obtain **31-s-1**.

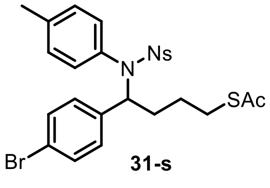
Step 3: An oven-dried, three-necked round-bottomed flask was equipped with a Teflon-coated magnetic stir bar, an internal thermometer, a pressure-equalizing dropping funnel sealed with a rubber septum, and fitted with nitrogen gas inlet adaptor. The flask is evacuated and refilled with nitrogen three times, then charged with 4-nitro-N-(p-tolyl)benzenesulfonamide (2.3 g, 7.7 mmol, 1.1 equiv), triphenylphosphine (2.4 g, 9.1 mmol, 1.3 equiv), and THF (30 mL). **31-s-1** (7.0 mmol, 1.0 equiv) was added and the solution was stirred in an ice bath for 10 min. Diethyl azodicarboxylate (1.5 g, 8.4 mmol, 1.2 equiv) was added dropwise from dropping funnel over 20 min, such that the internal temperature does not exceed 0 °C. The solution becomes cloudy during the addition. The mixture was stirred at 0 °C overnight, then the solution is evaporated. *n*-Hexane was added at room temperature and the white solid that precipitates was removed in a sintered-glass Büchner funnel (diameter 80 mm) using suction filtration and washed with *n*-hexane, and the filtrate was evaporated to give of the crude product as a clear, yellow oil. This material was purified by silica gel column chromatography to give the desired product **31-s**.

Step 4: To a solution of **31-s** in MeCN(0.862 mL) was added K_2CO_3 (46.82 mg, 0.34 mmol) and p-Toluenethiol (0.03 mL, 0.250 mmol). The mixture was then stirred at 25 °C for 2 h. Water was added and the mixture was extracted with EtOAc. The combined organic layers were concentrated under reduced pressure and purified by silica gel column chromatography to obtain compound **31**.



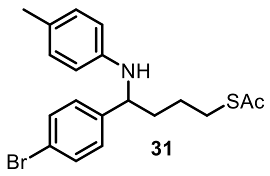
31-s-1

Colorless oil. (R*f* = 0.28, hexane/ethyl acetate = 3:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 4.64 (t, *J* = 6.1 Hz, 1H), 2.87 (t, *J* = 6.9 Hz, 2H), 2.37 (s, 1H), 2.30 (s, 3H), 1.85 – 1.64 (m, 3H), 1.63 – 1.51 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 196.2, 143.6, 131.6, 127.6, 121.4, 73.3, 37.9, 30.7, 28.9, 25.9.



31-s

Colorless oil. (R*f* = 0.35, hexane/ethyl acetate = 3:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.8 Hz, 2H), 7.79 (d, *J* = 8.8 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.02 (d, *J* = 7.8 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.45 (d, *J* = 7.8 Hz, 2H), 5.46 (t, *J* = 7.7 Hz, 1H), 2.93 – 2.77 (m, 2H), 2.33 (s, 3H), 2.31 (s, 3H), 1.93 – 1.83 (m, 1H), 1.82 – 1.73 (m, 1H), 1.68 – 1.57 (m, 1H), 1.57 – 1.48 (m, 1H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 195.7, 150.0, 146.5, 139.8, 137.3, 132.5, 131.7, 130.9, 130.4, 129.8, 128.9, 124.1, 122.6, 62.1, 31.6, 30.8, 28.6, 27.0, 21.3.
HRMS: calculated for $C_{25}H_{25}BrN_2NaO_5S_2^+$ [M+Na$^+$]: 599.0280; **found**: 599.0283.



31

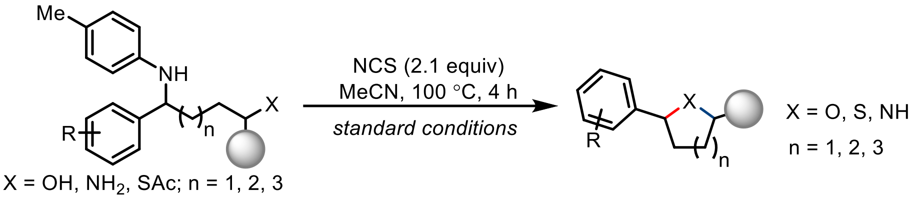
Colorless oil. (R_f = 0.47, hexane/ethyl acetate = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.1 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.90 (d, *J* = 7.9 Hz, 2H), 6.40 (d, *J* = 8.0 Hz, 2H), 4.26 (t, *J* = 6.7 Hz, 1H), 3.93 (s, 1H), 2.89 (t, *J* = 7.1 Hz, 2H), 2.33 (s, 3H), 2.19 (s, 3H), 1.90 – 1.76 (m, 2H), 1.74 – 1.54 (m, 2H).

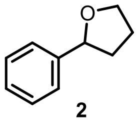
^{13}C NMR (101 MHz, $CDCl_3$) δ 195.9, 144.7, 143.1, 131.8, 129.8, 128.2, 126.9, 120.8, 113.5, 57.6, 37.7, 30.8, 28.8, 26.5, 20.5.

HRMS: calculated for $C_{19}H_{23}BrNOS^+$ [M+H$^+$]: 392.0678; **found**: 392.0681.

3. General procedure for deaminative cyclization.



General conditions : The amino alcohol substrates (0.2 mmol, 1.0 equiv) was dissolved in MeCN (2 mL, 0.1 M) in an in an 8 mL glass vial. To the solution was added NCS (74.8mg, 0.42 mmol, 2.1 equiv). The mixture was stirred at 100 °C under air atmosphere and monitored by TLC analysis. After being cooled to room temperature, the reaction mixture was concentrated under reduced pressure. The resulting residue was subjected to silica gel chromatography to give the desired product.



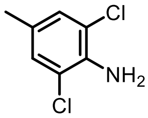
2

Colorless oil. (R_f = 0.24, hexane/ethyl acetate = 30/1)

Compound **2** is a known compound, and was obtained in 90% yield (26.7 mg) under the general procedure. The spectral data are consistent with those reported in literature[7].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 4H), 7.28 – 7.19 (m, 1H), 4.89 (t, *J* = 7.2 Hz, 1H), 4.14 – 4.04 (m, 1H), 3.98 – 3.88 (m, 1H), 2.38 – 2.25 (m, 1H), 2.05 – 1.95 (m, 2H), 1.87 – 1.74 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 128.4, 127.2, 125.8, 80.8, 68.8, 34.7, 26.2.



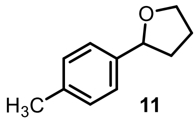
3

White solid. (R_f = 0.33, hexane/ethyl acetate = 30/1)

Compound **3** is a known compound, and was obtained in 92% yield (32.4 mg). The spectral data are consistent with those reported in literature[16].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (s, 2H), 4.28 (s, 2H), 2.21 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 137.7, 128.4, 119.6, 29.9, 20.2.



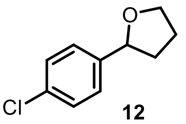
11

Colorless oil. (R_f = 0.21, hexane/ethyl acetate = 30/1)

Compound **11** is a known compound, and was synthesized in 90% yield (29.1 mg) under the general procedure. The spectra data are consistent with those reported in literature[7].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 7.9 Hz, 2H), 4.85 (t, *J* = 7.2 Hz, 1H), 4.08 (dt, *J* = 8.2, 6.8 Hz, 1H), 3.97 – 3.87 (m, 1H), 2.33 (s, 3H), 2.32 – 2.24 (m, 1H), 2.07 – 1.93 (m, 2H), 1.85 – 1.73 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.5, 136.8, 129.1, 125.7, 80.7, 68.7, 34.7, 26.2, 21.2.



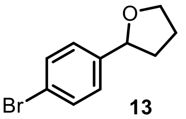
12

Colorless oil. (R*f* = 0.26, hexane/ethyl acetate = 30/1)

Compound **12** is a known compound, and was synthesized in 90% yield (33.0 mg) under the general procedure. The spectra data are consistent with those reported in literature[7].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.20 (m, 4H), 4.85 (t, *J* = 7.2 Hz, 1H), 4.14 – 4.02 (m, 1H), 3.98 – 3.87 (m, 1H), 2.38 – 2.25 (m, 1H), 2.07 – 1.93 (m, 2H), 1.82 – 1.67 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.2, 132.8, 128.5, 127.1, 80.1, 68.8, 34.8, 26.1.



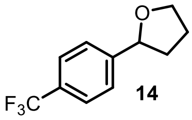
13

Colorless oil. (R*f* = 0.27, hexane/ethyl acetate = 30/1)

Compound **13** is a known compound, and was synthesized in 91% yield (41.3 mg) under the general procedure. The spectra data are consistent with those reported in literature[7].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 4.84 (t, *J* = 7.2 Hz, 1H), 4.14 – 4.03 (m, 1H), 3.98 – 3.86 (m, 1H), 2.39 – 2.26 (m, 1H), 2.06 – 1.91 (m, 2H), 1.82 – 1.68 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.7, 131.5, 127.5, 120.9, 80.2, 77.2, 68.9, 34.8, 26.1.



14

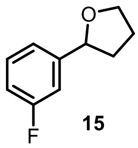
Colorless oil. (R*f* = 0.21, hexane/ethyl acetate = 30/1)

Compound **14** is a known compound, and was synthesized in 75% yield (32.3 mg) under the general procedure. The spectra data are consistent with those reported in literature[7].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.1 Hz, 2H), 7.44 (d, *J* = 8.1 Hz, 2H), 4.94 (t, *J* = 7.2 Hz, 1H), 4.18 – 4.04 (m, 1H), 4.01 – 3.87 (m, 1H), 2.51 – 2.25 (m, 1H), 2.16 – 1.90 (m, 2H), 1.86 – 1.65 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 147.9 (q, *J* = 1.3 Hz), 129.5, 129.2, 128.9, 125.3(q, *J* = 3.8 Hz), 123.0, 80.1, 69.0, 34.8, 26.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.4.



15

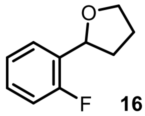
Colorless oil. (R_f = 0.23, hexane/ethyl acetate = 30/1)

Compound **15** is a known compound, and was synthesized in 80% yield (26.5 mg) under the general procedure. The spectra data are consistent with those reported in literature[8].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 1H), 7.12 – 7.03 (m, 2H), 6.97 – 6.88 (m, 1H), 4.89 (t, J = 7.1 Hz, 1H), 4.16 – 4.04 (m, 1H), 3.99 – 3.89 (m, 1H), 2.41 – 2.28 (m, 1H), 2.07 – 1.92 (m, 2H), 1.85 – 1.70 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 146.6 (d, J = 6.8 Hz), 129.9 (d, J = 8.1 Hz), 121.3, 121.2, 114.0(d, J = 21.3 Hz), 112.6 (d, J = 22.0 Hz), 80.1, 68.9, 34.8, 26.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -113.4.



16

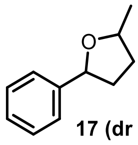
Colorless oil. (R_f = 0.22, hexane/ethyl acetate = 30/1)

Compound **16** is a known compound, and was synthesized in 82% yield (27.2 mg) under the general procedure. The spectra data are consistent with those reported in literature[9].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.41 (m, 1H), 7.24 – 7.18 (m, 1H), 7.17 – 7.08 (m, 1H), 7.04 – 6.96 (m, 1H), 5.14 (t, J = 7.1 Hz, 1H), 4.16 – 4.05 (m, 1H), 4.00 – 3.87 (m, 1H), 2.47 – 2.35 (m, 1H), 2.06 – 1.94 (m, 2H), 1.85 – 1.73 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.9 (d, J = 245.4 Hz), 131.1 (d, J = 13.4 Hz), 129.4, 128.6, 128.5, 127.0 (d, J = 4.7 Hz, 124.1 (d, J = 3.5 Hz), 115.2 (d, J = 21.3 Hz), 75.2, 75.2, 68.8, 33.6, 33.6, 26.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -118.7.



17 (dr = 1.2:1)

Colorless oil. (R_f = 0.25, hexane/ethyl acetate = 30/1)

Compound **17** is a known compound, and were synthesized in 90% yield (29.2 mg) (dr = 1: 1.2) under the general procedure as an inseparable mixture of anomers. The spectra data are consistent with those reported in literature[10].

***Cis*-isomer:**

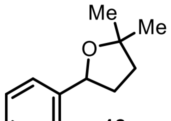
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 4H), 7.28 – 7.21 (m, 1H), 4.88 (t, J = 7.3 Hz, 1H), 4.22 – 4.12 (m, 1H), 2.34 – 2.24 (m, 1H), 2.12 – 2.04 (m, 1H), 1.69 – 1.59 (m, 2H), 1.37 (d, J = 6.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 128.4, 127.2, 125.7, 81.2, 34.8, 33.2, 21.5.

***Trans*-isomer**:

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 4H), 7.28 – 7.21 (m, 1H), 5.04 (dd, *J* = 8.2, 6.5 Hz, 1H), 4.43 – 4.29 (m, 1H), 2.44 – 2.33 (m, 1H), 2.22 – 2.13 (m, 1H), 1.96 – 1.77 (m, 2H), 1.32 (d, *J* = 6.1 Hz, 3H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 144.1, 128.4, 127.3, 126.0, 80.4, 35.8, 34.4, 21.7.



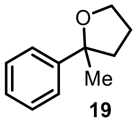
18

Colorless oil. (R_f = 0.26, hexane/ethyl acetate = 30/1)

Compound **18** is a known compound, and was synthesized in in 71% yield (25.1 mg) under the general procedure with the addition of 1.0 equiv aq. HBr (48% in water). The spectra data are consistent with those reported in literature[11].

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 4H), 7.25 – 7.20 (m, 1H), 5.05 – 4.91 (m, 1H), 2.41 – 2.24 (m, 1H), 1.94 – 1.83 (m, 3H), 1.39 (s, 3H), 1.35 (s, 3H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 143.8, 128.4, 127.2, 125.9, 81.5, 80.6, 39.2, 35.8, 29.2, 28.5.



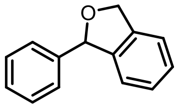
19

Colorless oil. (R_f = 0.29, hexane/ethyl acetate = 30/1)

Compound **19** is a known compound, and was synthesized in 77% yield (25.1 mg) under the general procedure. The spectra data are consistent with those reported in literature[7].

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.43 – 7.37 (m, 2H), 7.35 – 7.29 (m, 2H), 7.26 – 7.17 (m, 1H), 4.09 – 3.98 (m, 1H), 3.96 – 3.87 (m, 1H), 2.26 – 2.15 (m, 1H), 2.07 – 1.92 (m, 2H), 1.88 – 1.74 (m, 1H), 1.53 (s, 3H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 148.3, 128.2, 126.5, 124.8, 84.4, 67.7, 39.6, 29.9, 25.9.



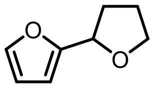
20

Colorless oil. (R_f = 0.21, hexane/ethyl acetate = 30/1)

Compound **20** is a known compound, and was synthesized in 92% yield (36.1 mg) under the general procedure. The spectra data are consistent with those reported in literature[12].

^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.30 – 7.24 (m, 4H), 7.24 – 7.19 (m, 3H), 7.17 – 7.11 (m, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.09 (s, 1H), 5.27 (dd, *J* = 12.1, 2.6 Hz, 1H), 5.14 (dd, *J* = 12.1, 1.9 Hz, 1H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 142.3, 142.1, 139.2, 128.7, 128.2, 127.8, 127.6, 127.1, 122.4, 121.1, 86.4, 73.4.



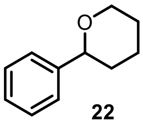
21

Colorless oil. (R_f = 0.22, hexane/ethyl acetate = 30/1)

Compound **21** is a known compound, and was synthesized in 68% yield (18.8 mg) under the general procedure. The spectra data are consistent with those reported in literature[17].

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (s, 1H), 6.32 (s, 1H), 6.25 (s, 1H), 4.92 (t, *J* = 6.7 Hz, 1H), 3.99 (q, *J* = 7.2, 6.7 Hz, 1H), 3.88 (q, *J* = 7.2 Hz, 1H), 2.26 – 2.15 (m, 1H), 2.15 – 2.04 (m, 2H), 2.04 – 1.93 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 155.1, 142.3, 110.1, 106.6, 73.9, 68.3, 30.3, 26.0.



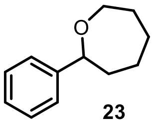
22

Colorless oil. (R_f = 0.28, hexane/ethyl acetate = 30/1)

Compound **22** is a known compound, and was synthesized in 61% yield (19.9 mg) under the general procedure, and 92% yield (30.0 mg) when NBS was used instead of NCS. The spectra data are consistent with those reported in literature[7].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 4H), 7.27 – 7.21 (m, 1H), 4.31 (dd, 1H), 4.18 – 4.07 (m, 1H), 3.61 (td, *J* = 11.5, 2.5 Hz, 1H), 1.97 – 1.90 (m, 1H), 1.86 – 1.78 (m, 1H), 1.71 – 1.54 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4, 128.4, 127.4, 125.9, 80.2, 69.1, 34.1, 26.0, 24.1.



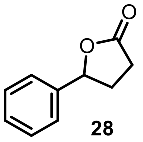
23

Colorless oil. (R_f = 0.29, hexane/ethyl acetate = 30/1)

Compound **23** is a known compound, and was synthesized in 58% yield (20.5 mg) under the general procedure when the reaction time was extended to 72 h. The spectra data are consistent with those reported in literature[10].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 4H), 7.27 – 7.19 (m, 1H), 4.57 (dd, *J* = 9.2, 3.9 Hz, 1H), 4.04 – 3.91 (m, 1H), 3.80 – 3.66 (m, 1H), 2.14 – 2.03 (m, 1H), 1.91 – 1.79 (m, 3H), 1.79 – 1.71 (m, 2H), 1.71 – 1.61 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 128.4, 127.0, 125.8, 81.5, 68.9, 38.0, 31.2, 26.9, 26.1.



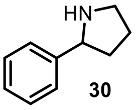
28

Colorless oil. (R_f = 0.21, hexane/ethyl acetate = 4/1)

Compound **28** is a known compound, and was synthesized in 78% yield (25.3 mg) under the general procedure. The spectra data are consistent with those reported in literature[14].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.25 (m, 5H), 5.50 (dd, *J* = 8.0, 6.0 Hz, 1H), 2.75 – 2.57 (m, 3H), 2.30 – 2.09 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 177.0, 139.5, 128.8, 128.5, 125.4, 81.3, 31.0, 29.0.



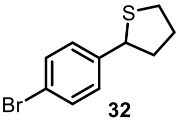
30

Colorless oil. (R_f = 0.21, DCM/MeOH = 20/1, 0.5% Et_3N)

Compound **30** is a known compound, and was synthesized in 31% yield (9.1 mg) under the general procedure. The spectra data are consistent with those reported in literature[15].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.34 (m, 2H), 7.34 – 7.29 (m, 2H), 7.25 – 7.20 (m, 1H), 4.12 (t, *J* = 7.8 Hz, 1H), 3.28 – 3.13 (m, 1H), 3.09 – 2.92 (m, 1H), 2.59 (s, 1H), 2.29 – 2.10 (m, 1H), 2.01 – 1.79 (m, 2H), 1.76 – 1.60 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.5, 128.5, 127.0, 126.7, 62.8, 47.0, 34.4, 25.7.



32

Colorless oil. (R_f = 0.31, hexane/ethyl acetate = 30/1)

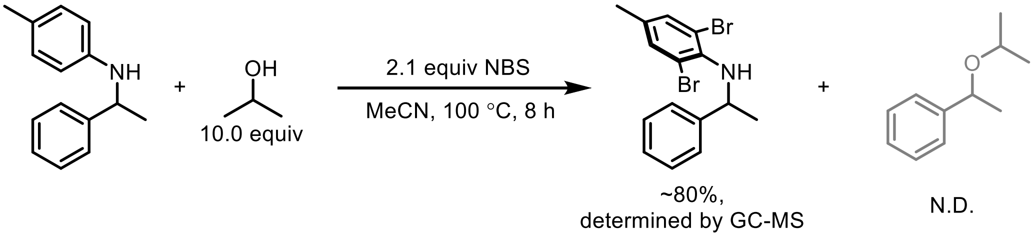
Compound **32** was synthesized in 91% yield (44.3 mg) under the general procedure.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 4.46 (dd, *J* = 8.6, 6.2 Hz, 1H), 3.21 – 3.09 (m, 1H), 3.07 – 2.95 (m, 1H), 2.43 – 2.32 (m, 1H), 2.30 – 2.19 (m, 1H), 2.04 – 1.94 (m, 1H), 1.93 – 1.82 (m, 1H).

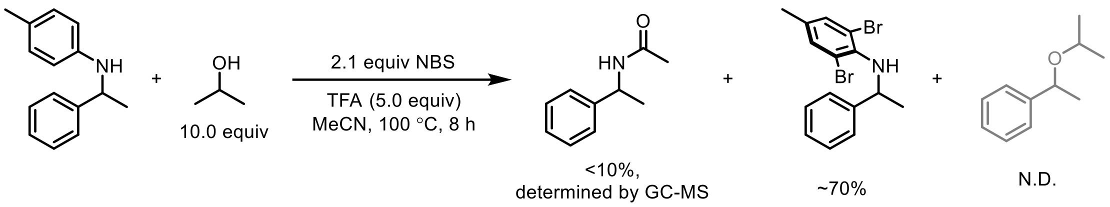
^{13}C NMR (151 MHz, $CDCl_3$) δ 142.3, 131.5, 129.5, 120.8, 52.2, 40.7, 33.7, 31.1.

HRMS: calculated for $C_{10}H_{11}BrS$ [M]: 241.9765; **found**: 241.9757.

Note: To verify whether this halogenation-induced substitution can proceed in an intermolecular fashion, the following experiments were conducted.



Under standard conditions, only dihalogenated products were obtained, with no observation of intermolecular substitution products.



When acid was added to promote the reaction, the dihalogenated product remained predominant, with minor formation of solvent-substituted byproducts (Ritter reaction), while no intermolecular substitution products were observed. This indicates that the halogenation-induced substitution reaction cannot proceed via an intermolecular pathway under the current reaction conditions.

4. References

[1] W. Wang, J. Wu, K. Jiang, M. Zhou and G. He, *Chem. Sci.*, 2025, **16**, 410-417.

[2] A. Bunrit, C. Dahlstrand, S. K. Olsson, P. Srifa, G. Huang, A. Orthaber, P. J. R. Sjöberg, S. Biswas, F. Himo and J. S. M. Samec, *J. Am. Chem. Soc.*, 2015, **137**, 4646-4649.

[3] J. Y. Mayorova, S. L. Nikitenko, P. A. Troshin, S. M. Peregudova, A. S. Peregudov, M. G. Kaplunov and R. N. Lyubovskaya, *Mendeleev Commun.*, 2007, **17**, 175-177.

[4] Z. Nie, M.-F. Chiou, J. Cui, Y. Qu, X. Zhu, W. Jian, H. Xiong, Y. Li and H. Bao, *Angew. Chem. Int. Ed.*, 2022, **61**, e202202077.

[5] S. Kamijo, Y. Amaoka and M. Inoue, *Tetrahedron Lett.*, 2011, **52**, 4654-4657.

[6] A. K. Chakraborti and A. Kondaskar, *Tetrahedron Lett.*, 2003, **44**, 8315-8319.

[7] H. A. Maashi, A. H. Husayni, K. M, M. E. Reid, J. Harnedy, E. C. Herneman, M. Pera-Titus and L. C. Morrill, *Org. Lett.*, 2024, **26**, 9051-9055.

[8] D. Rosas Vargas and S. P. Cook, *Tetrahedron*, 2018, **74**, 3314-3317.

[9] S. K. Rodrigo and H. Guan, *J. Org. Chem.*, 2012, **77**, 8303-8309.

[10] H. Im, D. Kang, S. Choi, S. Shin and S. Hong, *Org. Lett.*, 2018, **20**, 7437-7441.

[11] A. R. Rivero, P. Fodran, A. Ondrejková and C.-J. Wallentin, *Org. Lett.*, 2020, **22**, 8436-8440.

[12] K. M. Arendt and A. G. Doyle, *Angew. Chem. Int. Ed.*, 2015, **54**, 9876-9880.

[13] X. Si, L. Zhang and A. S. K. Hashmi, *Org. Lett.*, 2019, **21**, 6329-6332.

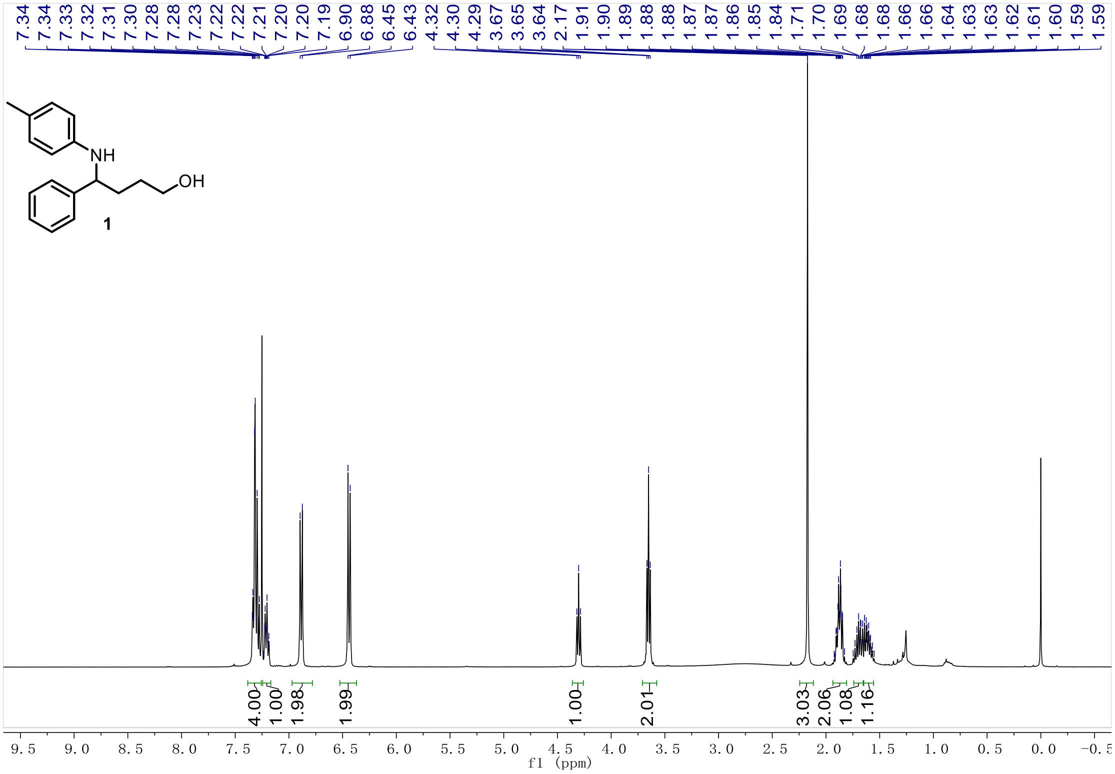
[14] Z. Zhang, Y. Deng, M. Hou, X. Lai, M. Guan, F. Zhang, R. Qi and G. Qiu, *Chem. Commun.*, 2022, **58**, 13644-13647.

[15] L. M. Bernhard, K. Zelenska, M. Takashima, M. Arisawa, K. Murai and H. Gröger, *J. Org. Chem.*, 2024, **89**, 8513-8520.

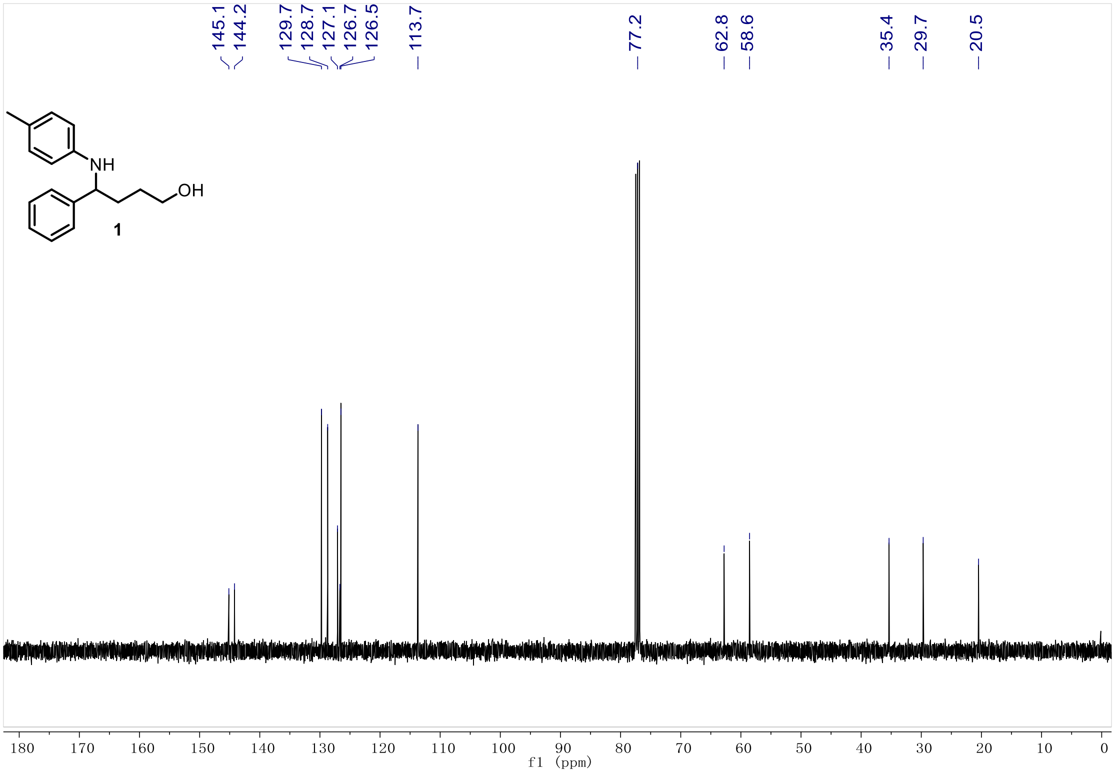
[16] Z. Lu, Q. Li, M. Tang, P. Jiang, H. Zheng and X. Yang, *Chem. Commun.*, 2015, **51**, 14852-14855.

[17] S. Dhiman and S. S. V. Ramasastry, *Org. Biomol. Chem.*, 2013, **11**, 4299-4303.

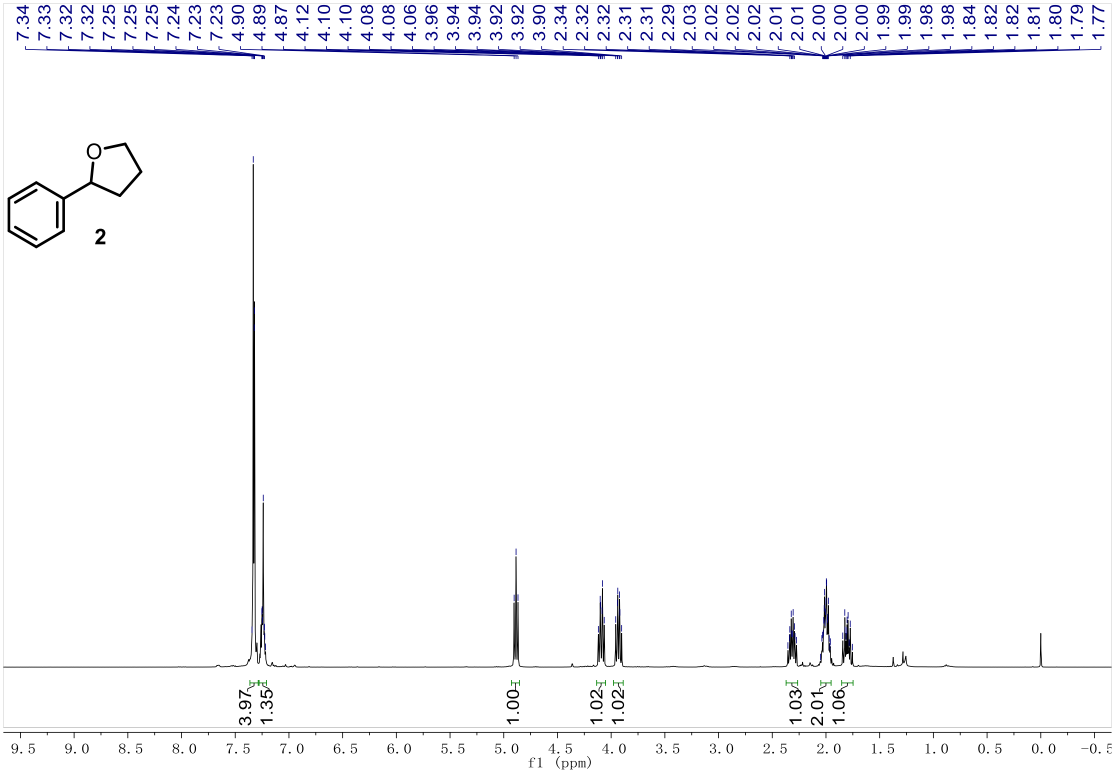
5. NMR spectrum



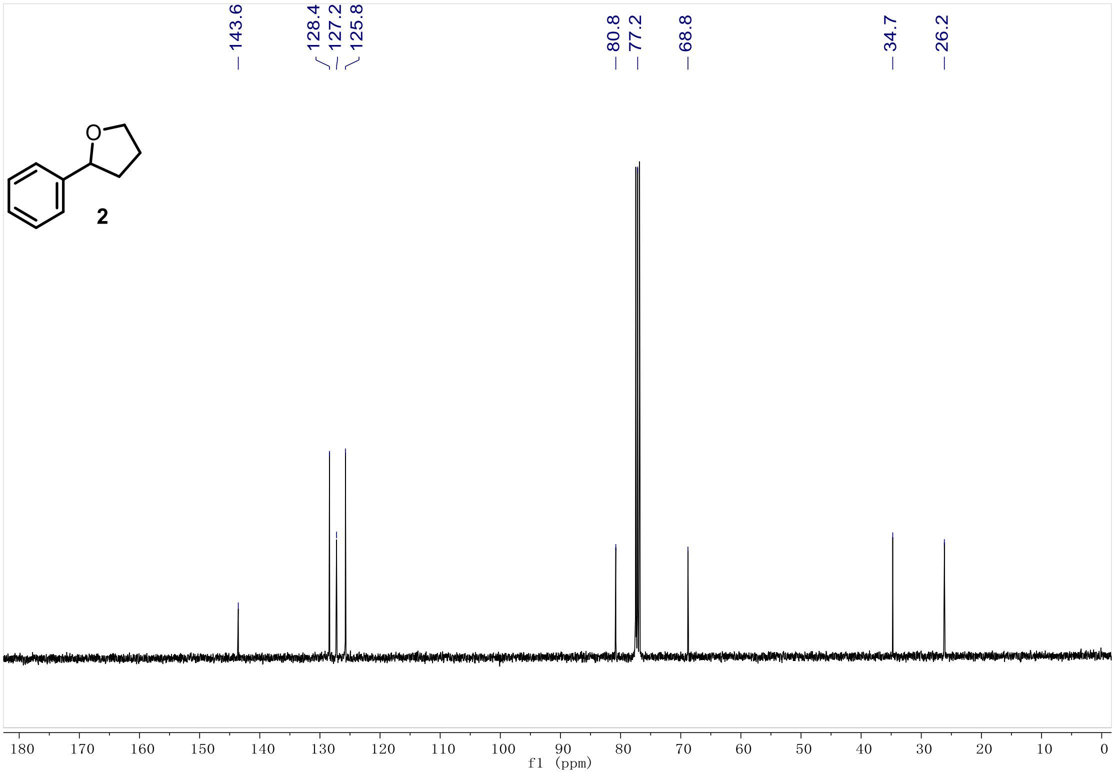
^{1}H NMR of compound **1**(400 MHz, CDCl$_3$)



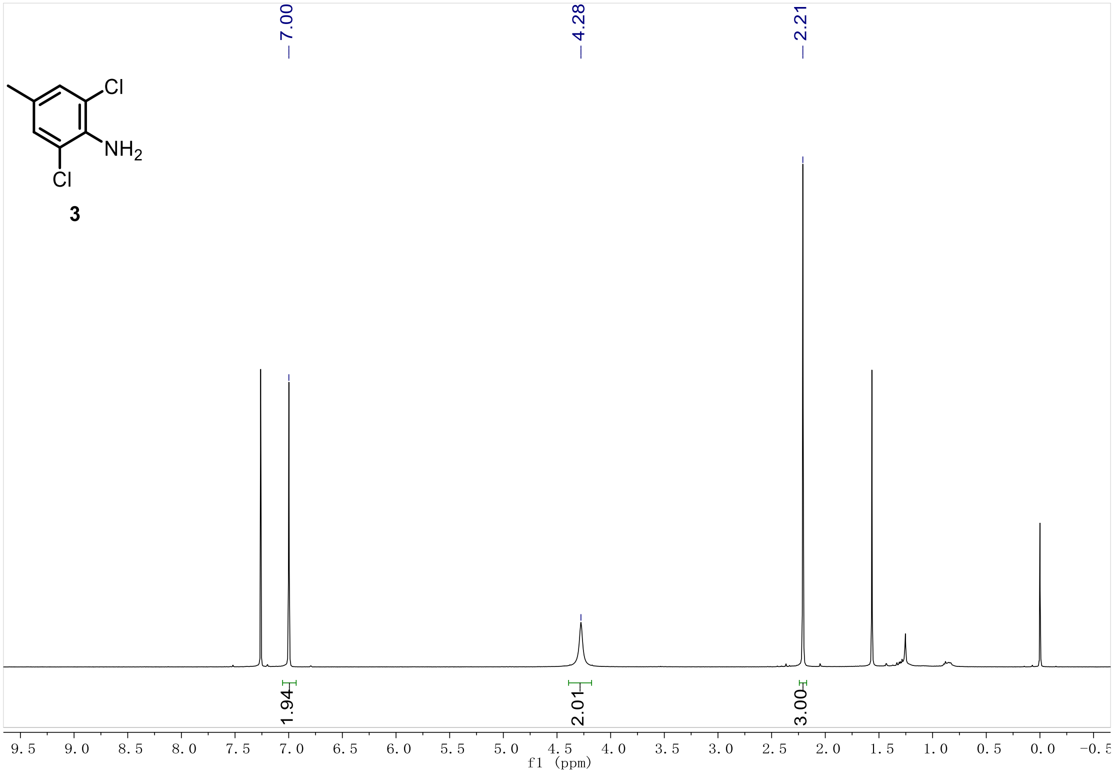
^{13}C NMR of compound **1** (101 MHz, CDCl$_3$)



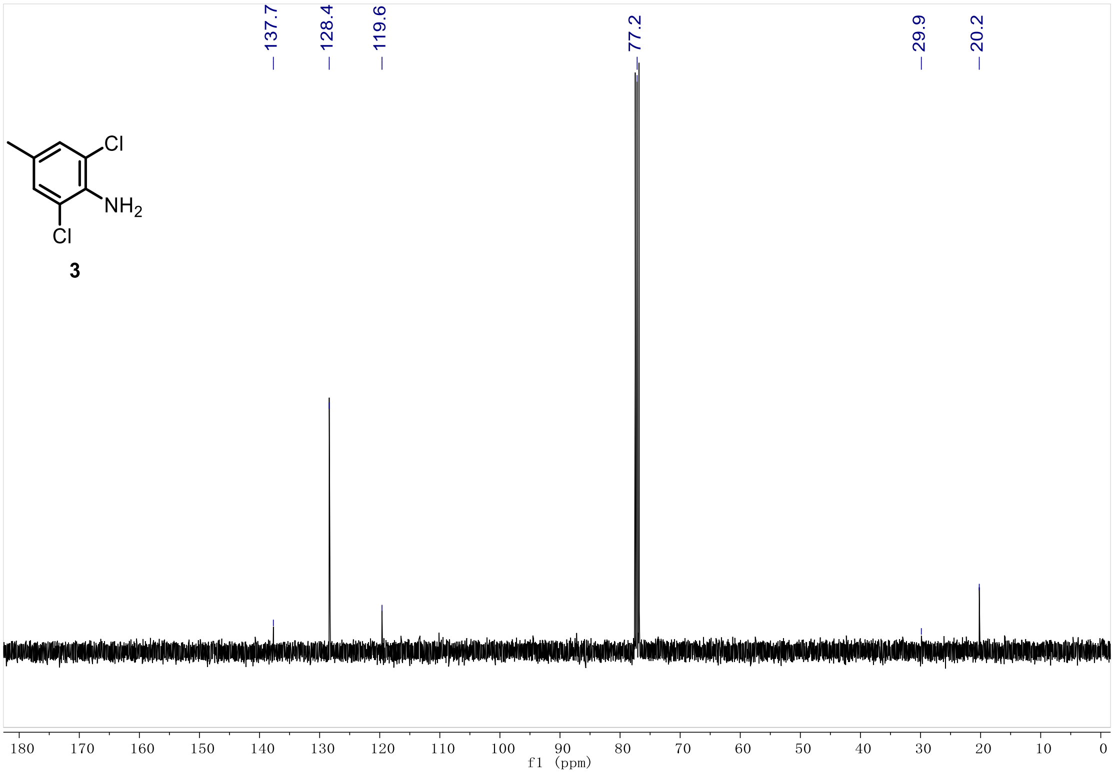
^{1}H NMR of compound **2** (400 MHz, CDCl$_3$)



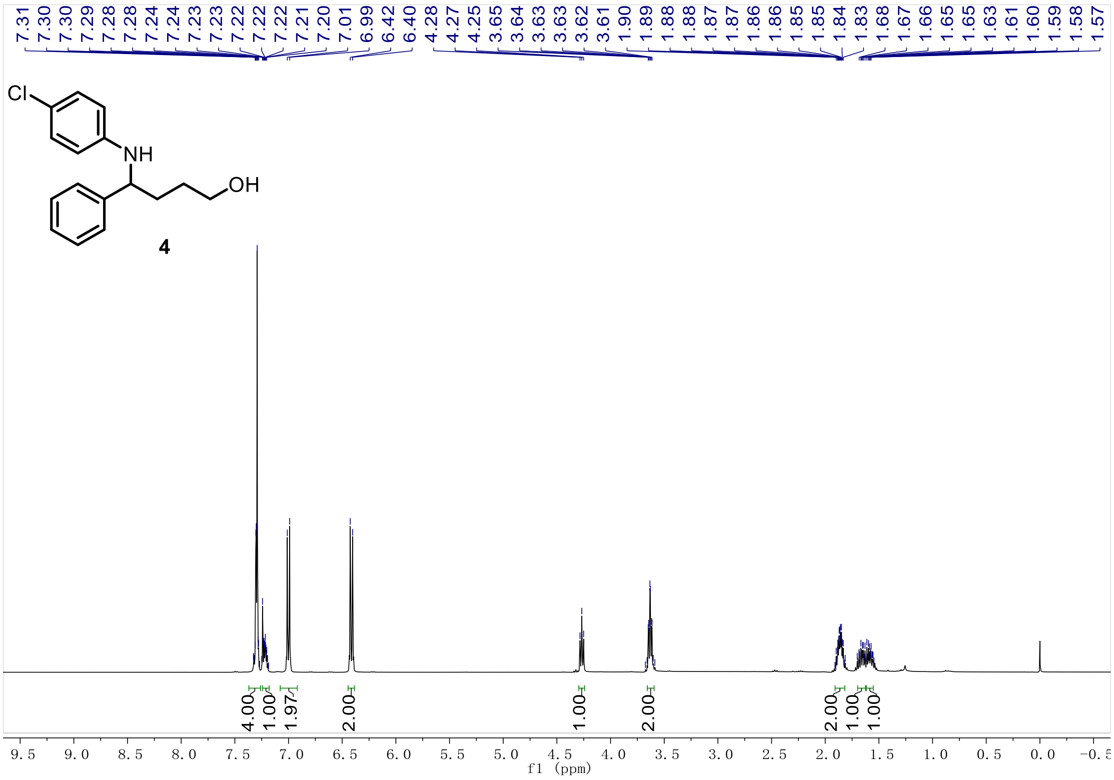
^{13}C NMR of compound **2** (101 MHz, CDCl$_3$)



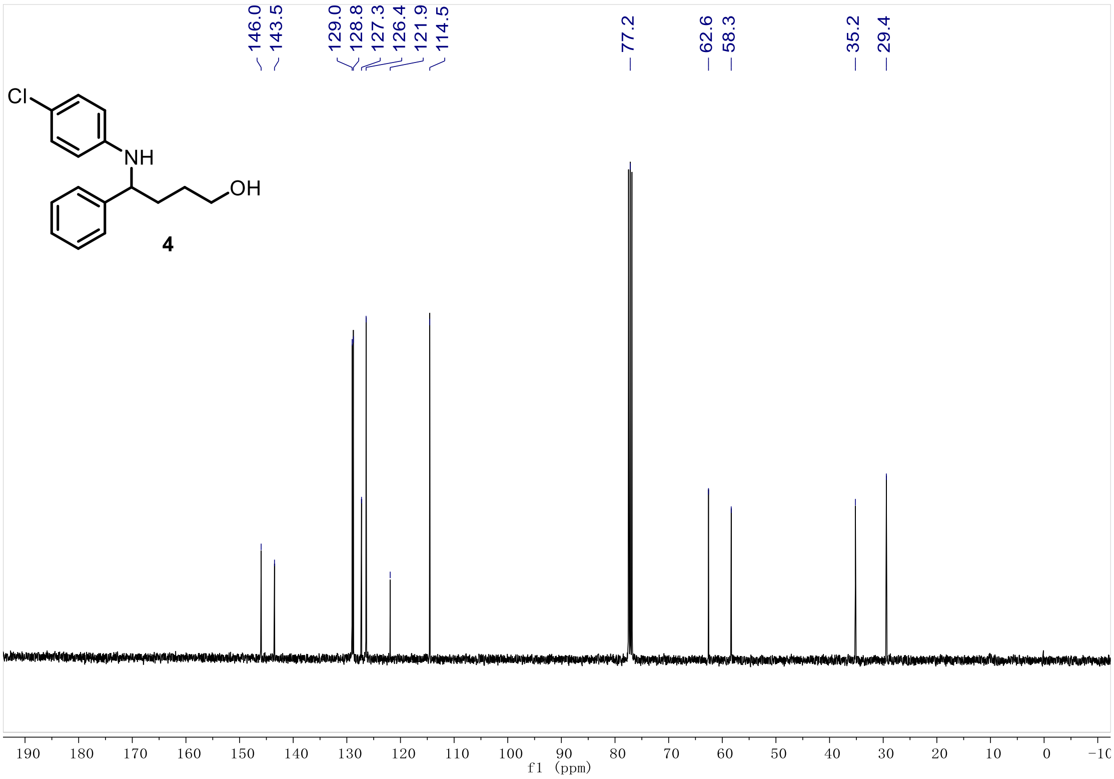
^{1}H NMR of compound **3** (400 MHz, CDCl$_3$)



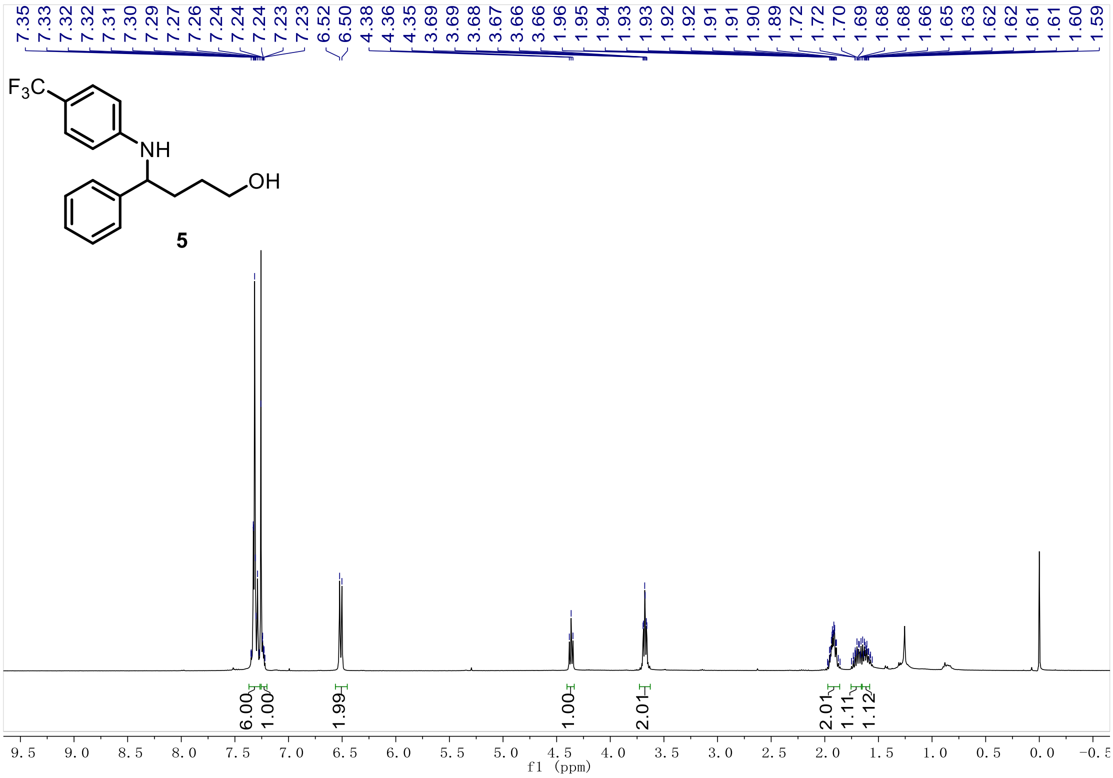
^{13}C NMR of compound **3** (101 MHz, CDCl$_3$)



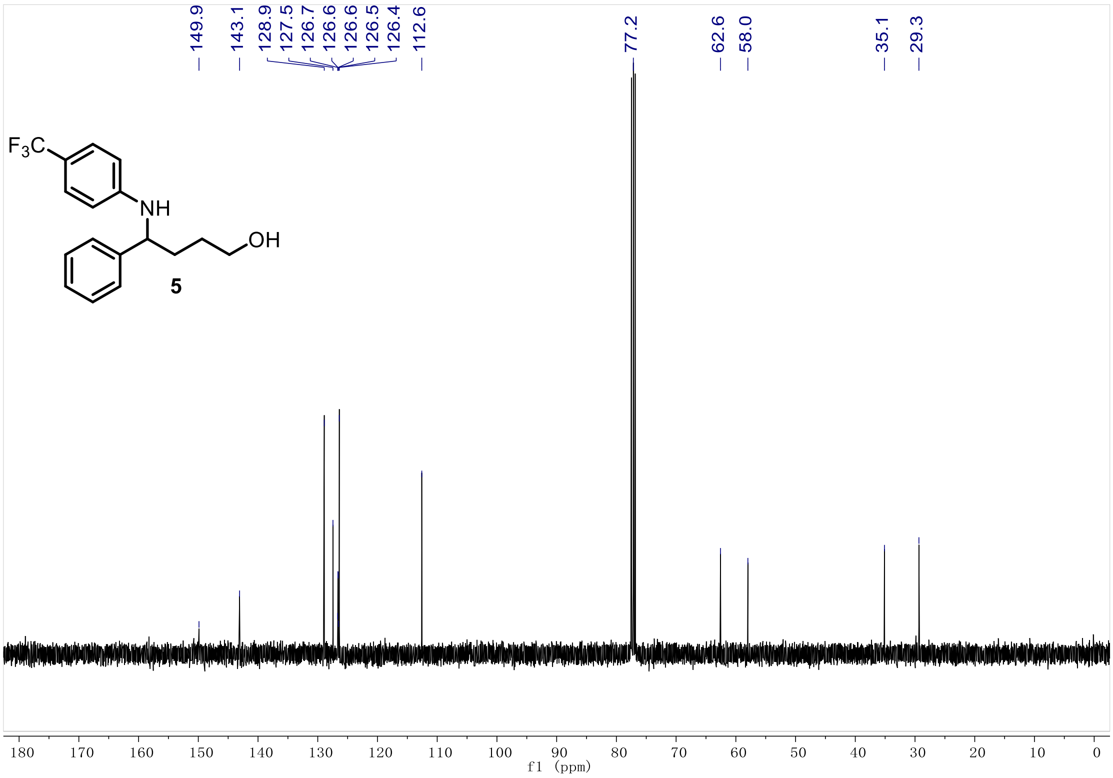
^{1}H NMR of compound **4** (400 MHz, CDCl$_3$)



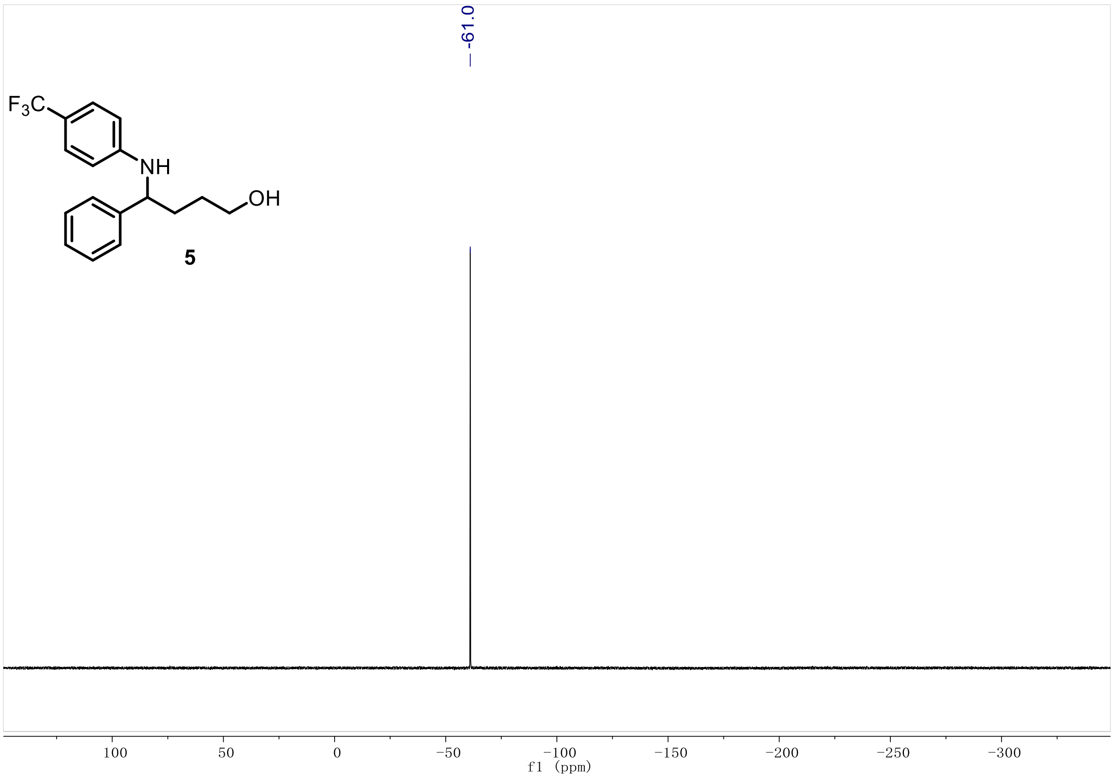
^{13}C NMR of compound **4** (101 MHz, CDCl$_3$)



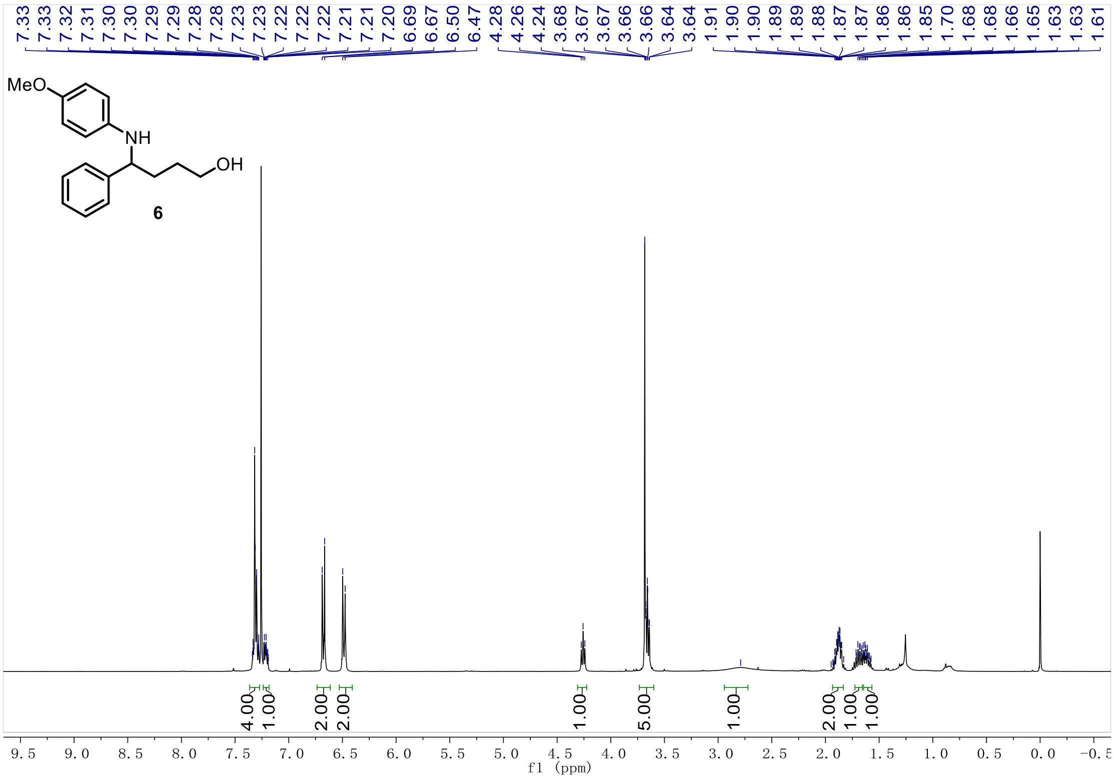
^{1}H NMR of compound **5** (400 MHz, CDCl$_3$)



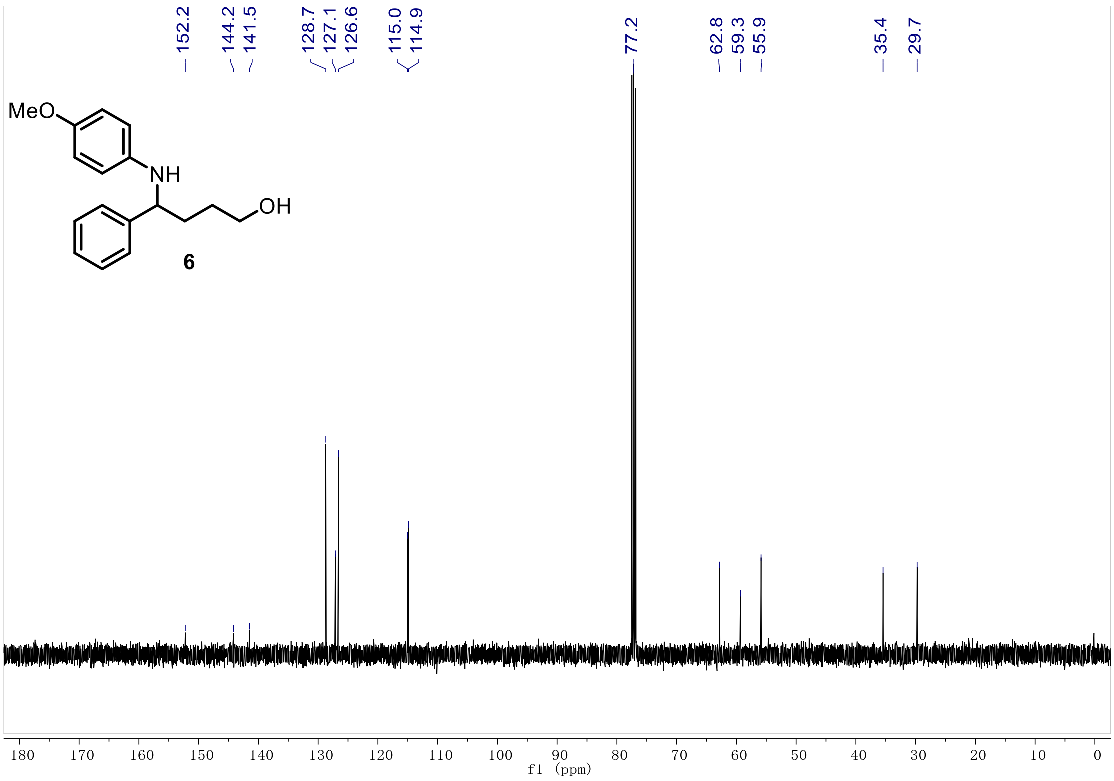
^{13}C NMR of compound **5** (101 MHz, CDCl$_3$)



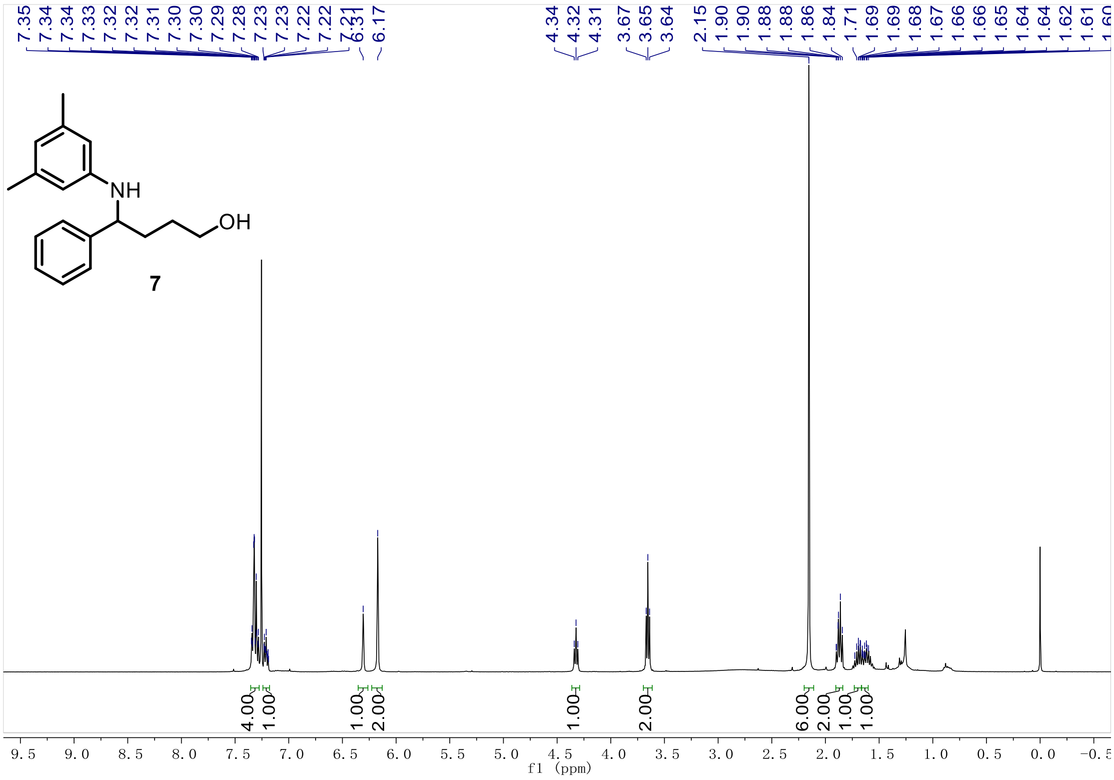
^{19}F NMR of compound **5** (376 MHz, CDCl$_3$)



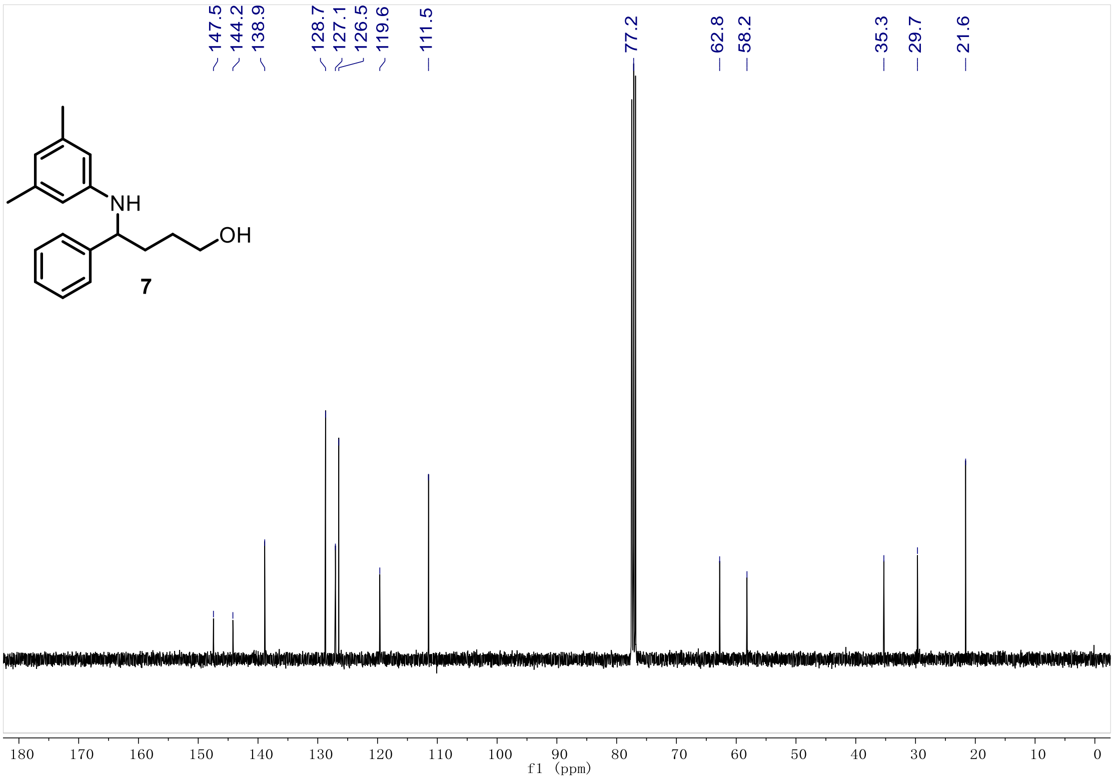
^{1}H NMR of compound **6** (400 MHz, CDCl$_3$)



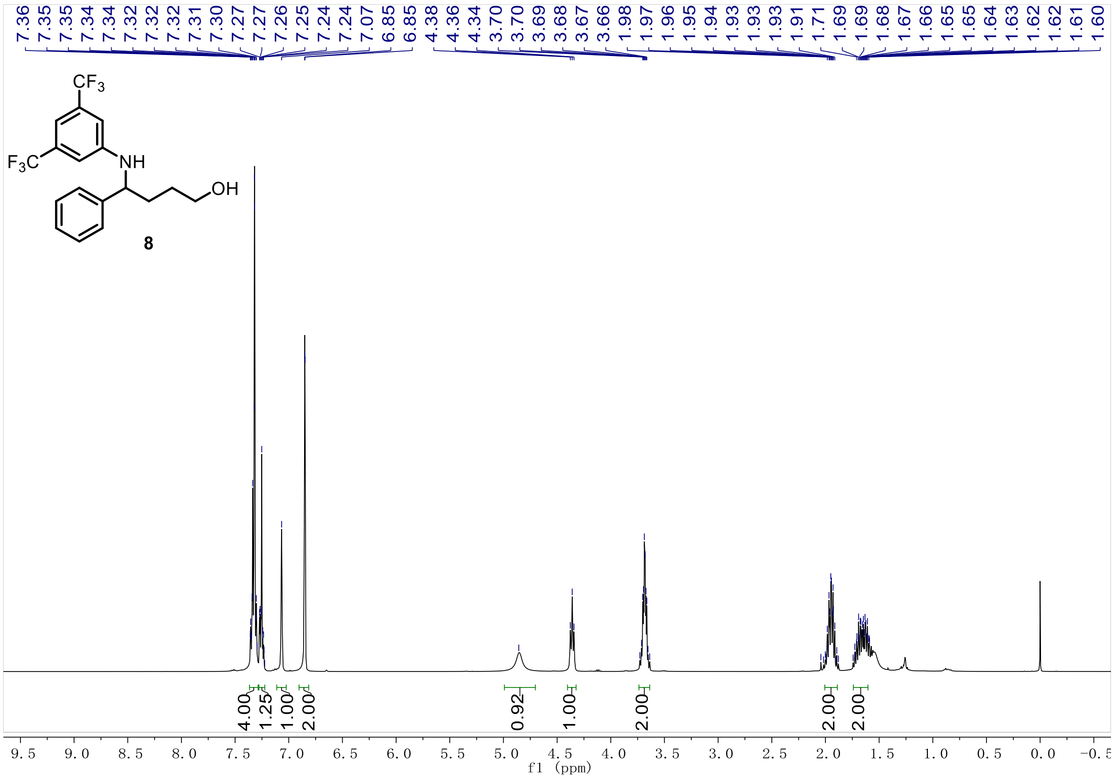
^{13}C NMR of compound **6** (101 MHz, CDCl$_3$)



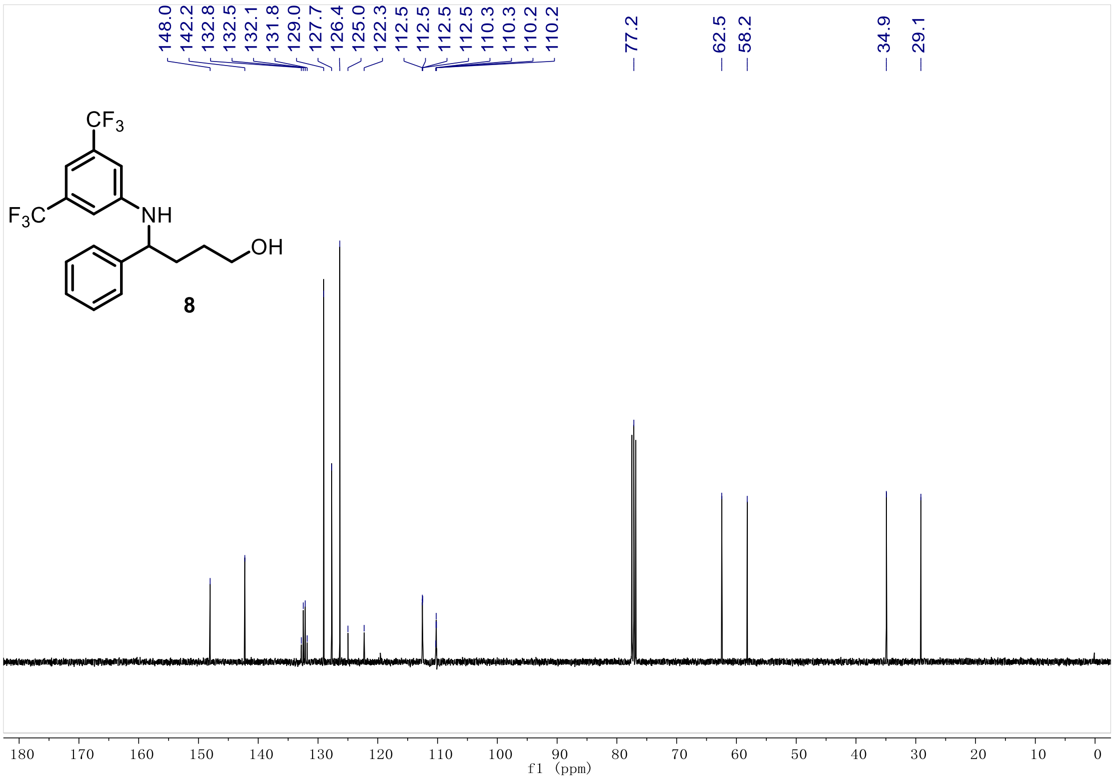
^{1}H NMR of compound **7** (400 MHz, CDCl$_3$)



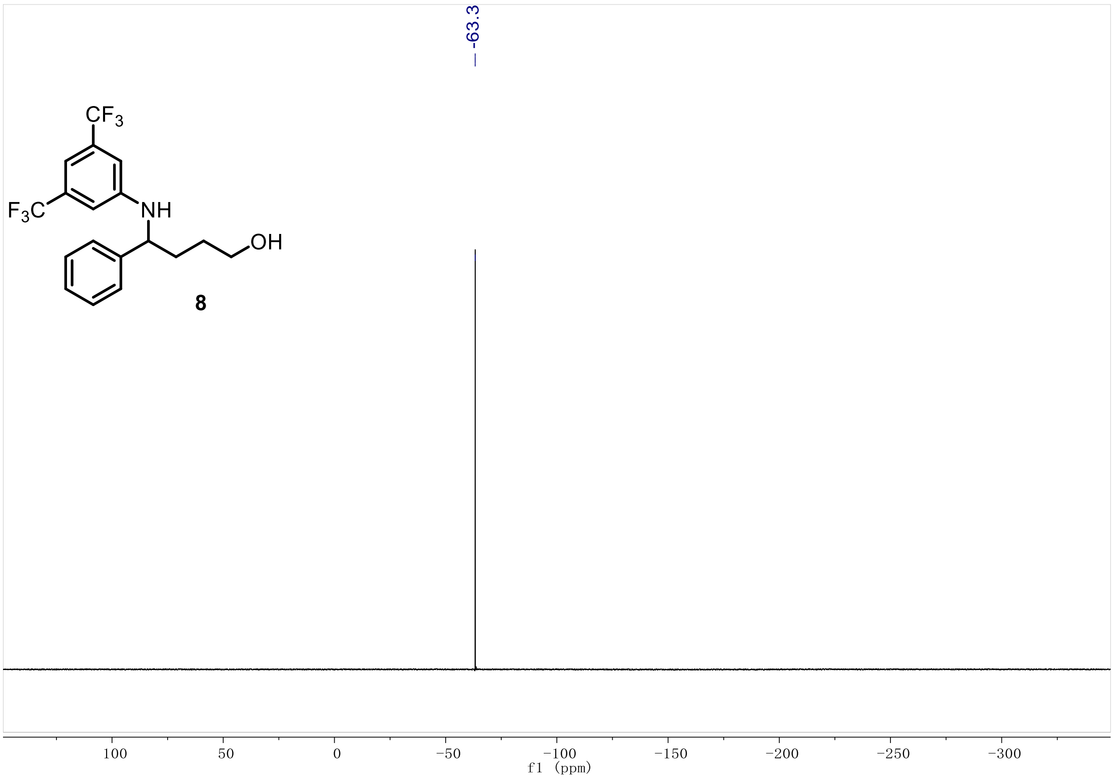
^{13}C NMR of compound **7** (101 MHz, CDCl$_3$)



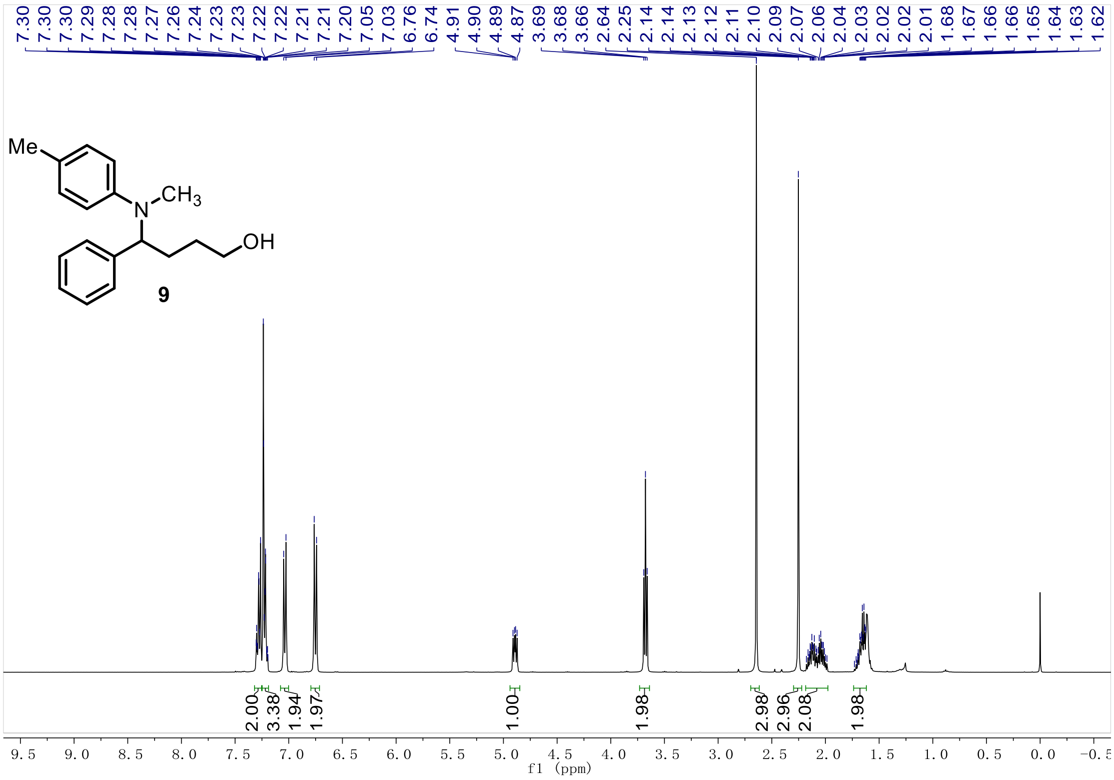
^{1}H NMR of compound **8** (400 MHz, CDCl$_3$)



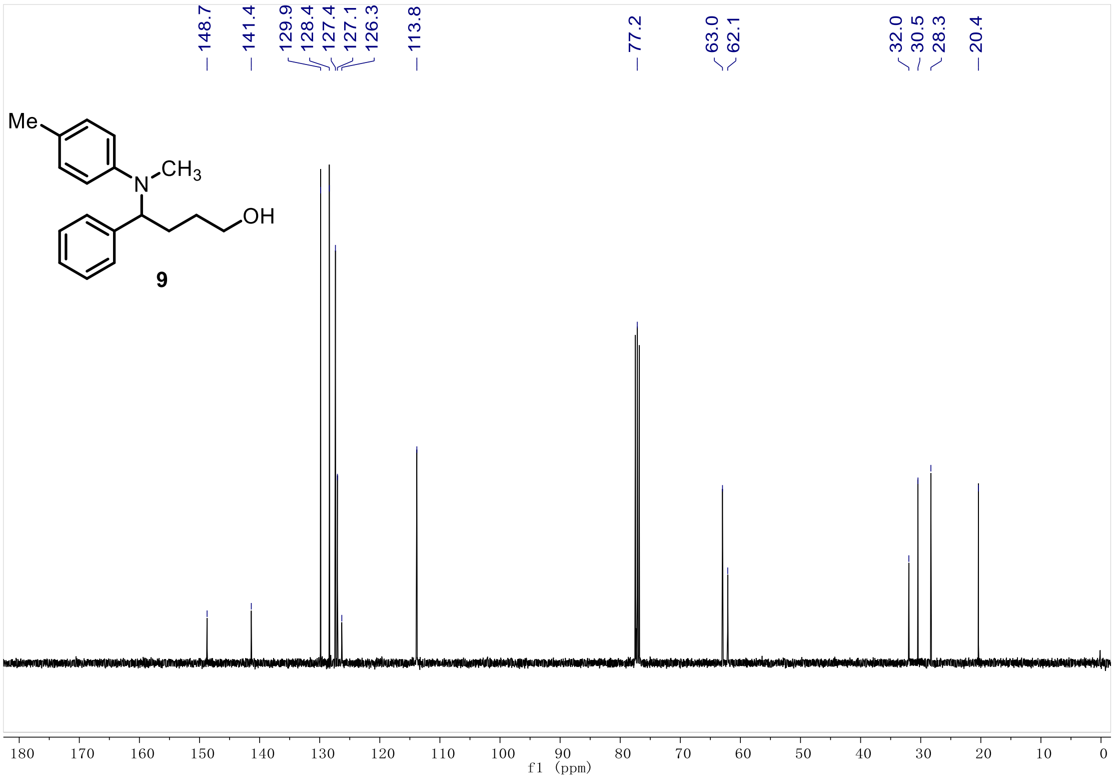
^{13}C NMR of compound **8** (101 MHz, CDCl$_3$)



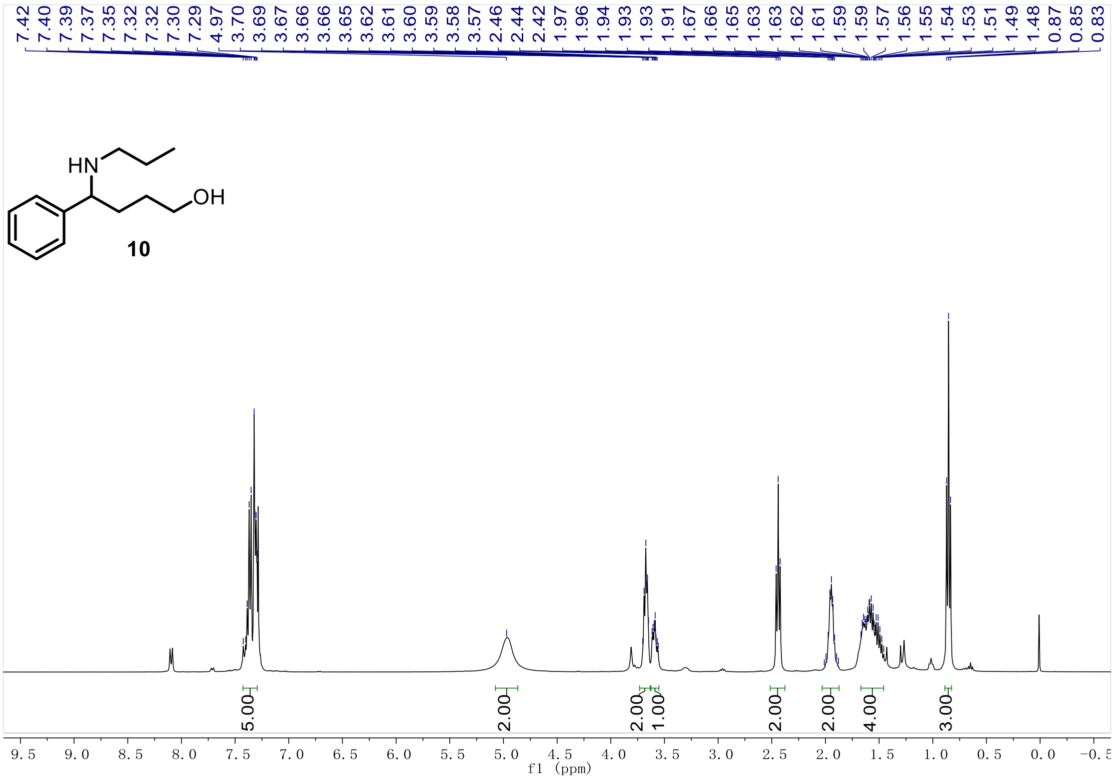
^{19}F NMR of compound **8** (376 MHz, CDCl$_3$)



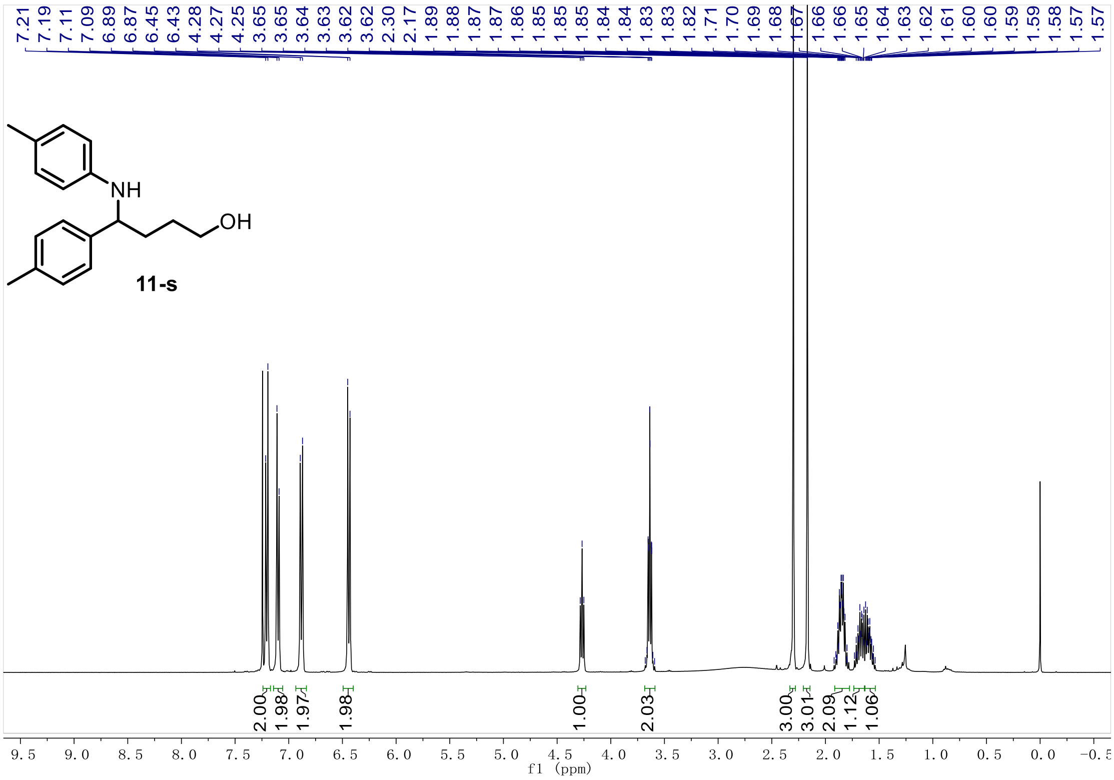
^{1}H NMR of compound **9** (400 MHz, CDCl$_3$)



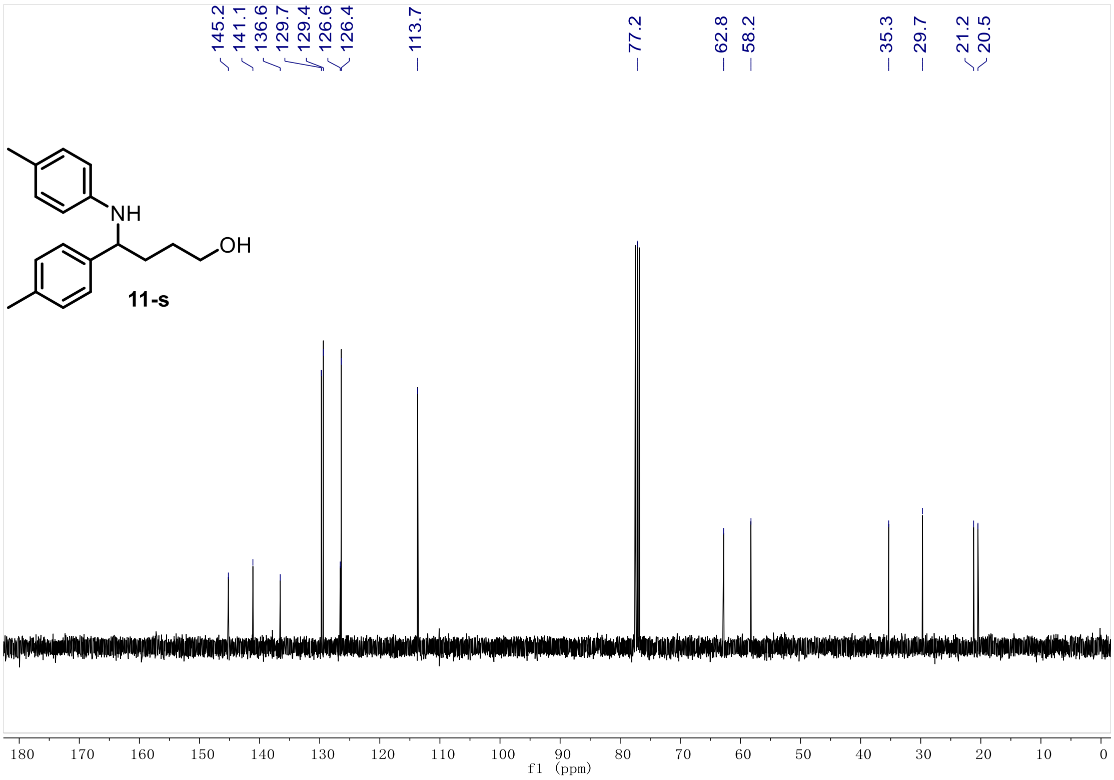
^{13}C NMR of compound **9** (101 MHz, CDCl$_3$)



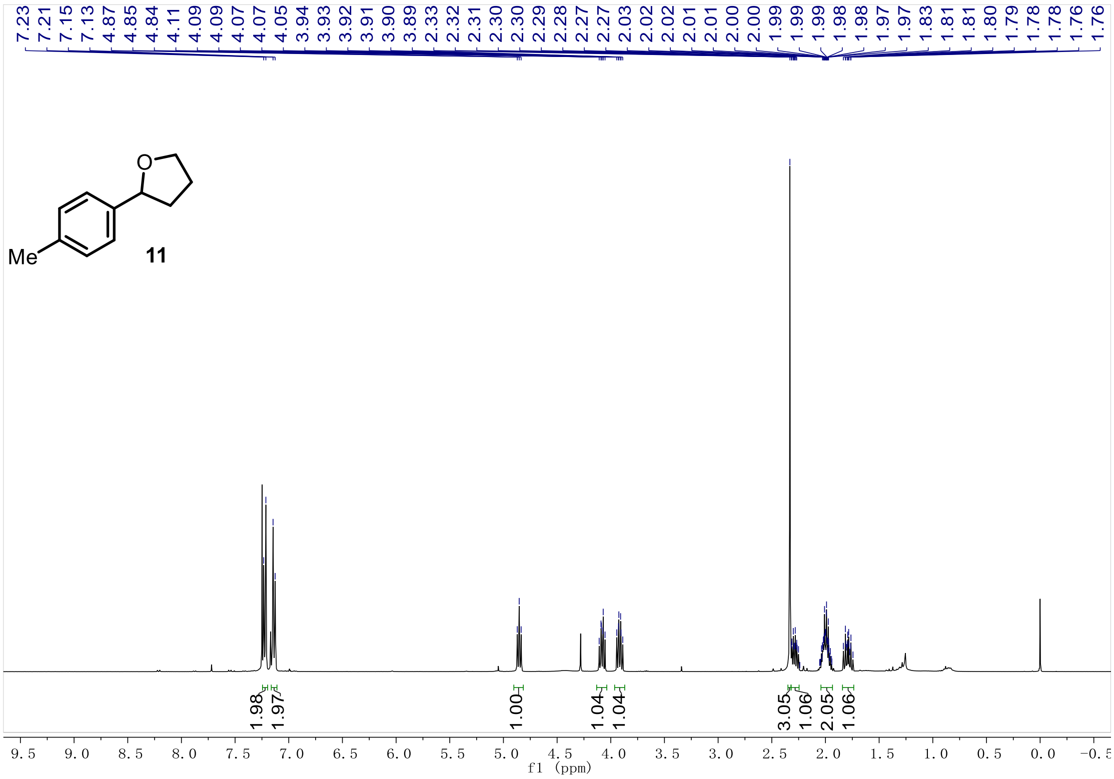
^{1}H NMR of compound **10** (400 MHz, CDCl$_3$)



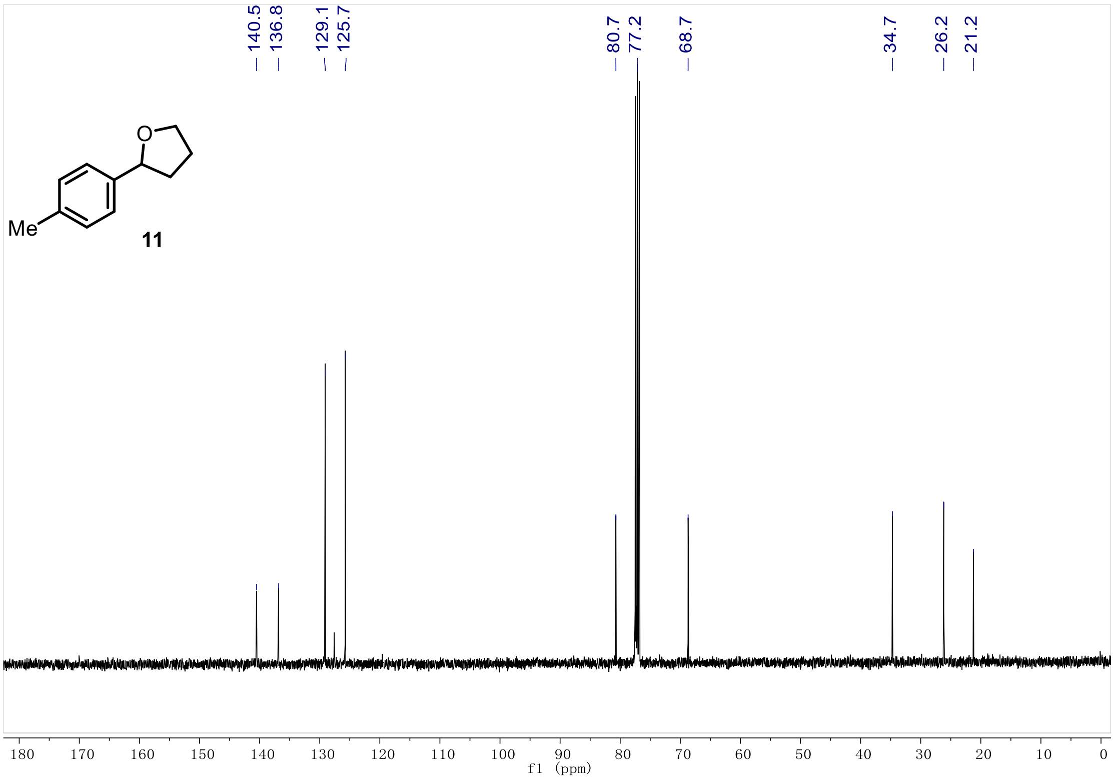
^{1}H NMR of compound **11-s** (400 MHz, CDCl$_3$)



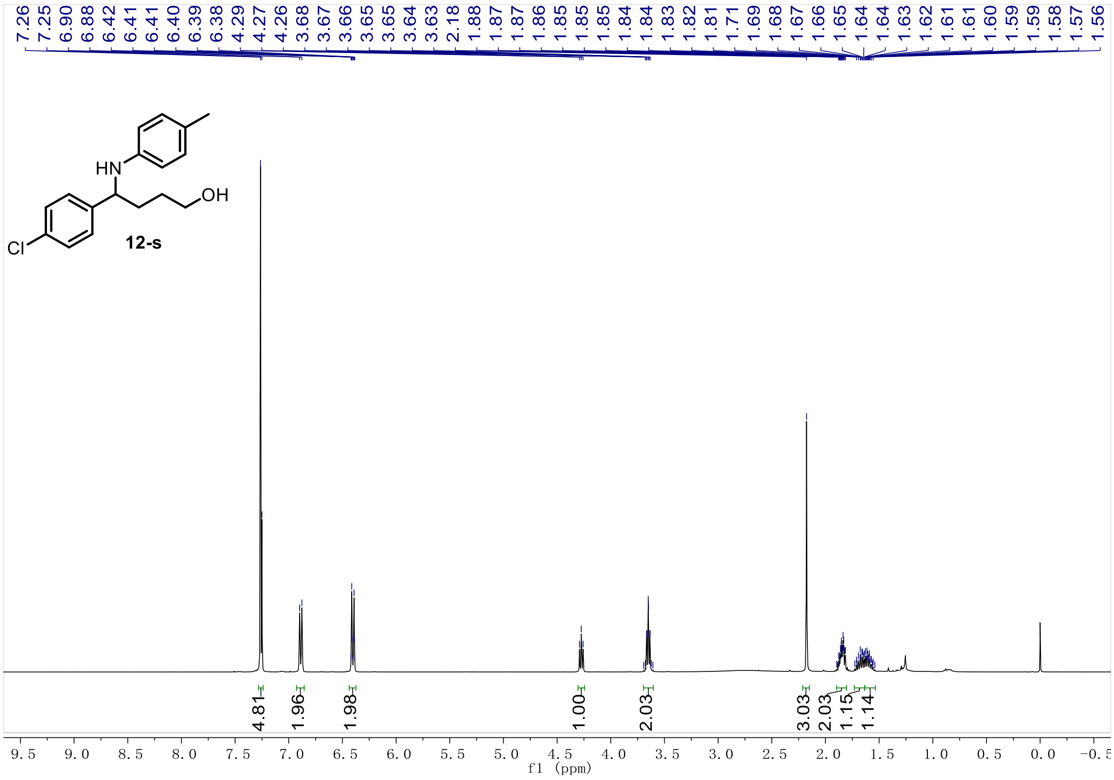
^{13}C NMR of compound **11-s** (101 MHz, CDCl$_3$)



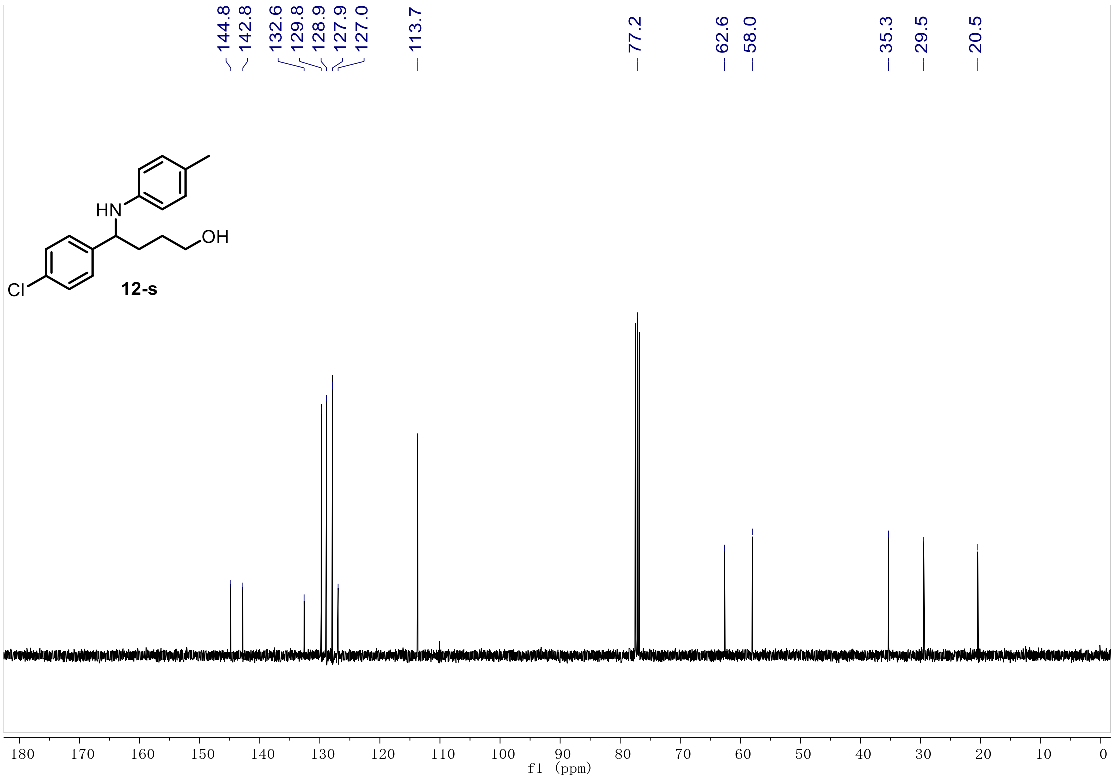
^{1}H NMR of compound **11** (400 MHz, CDCl$_3$)



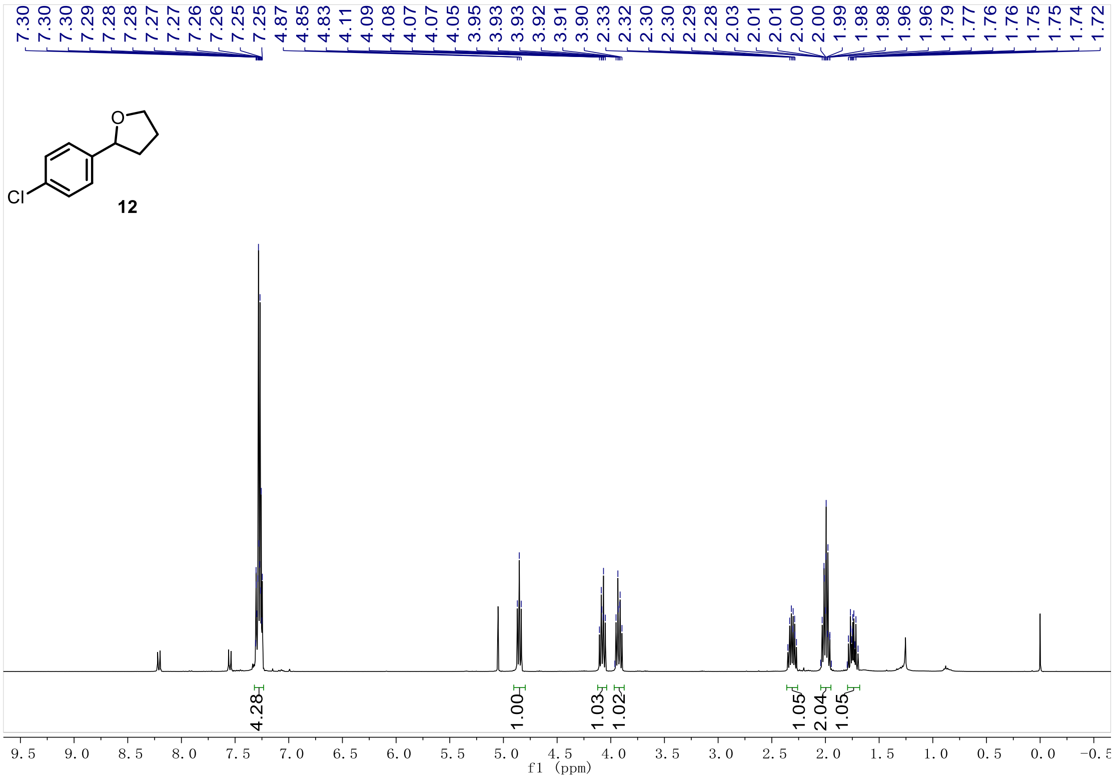
^{13}C NMR of compound **11** (101 MHz, CDCl$_3$)



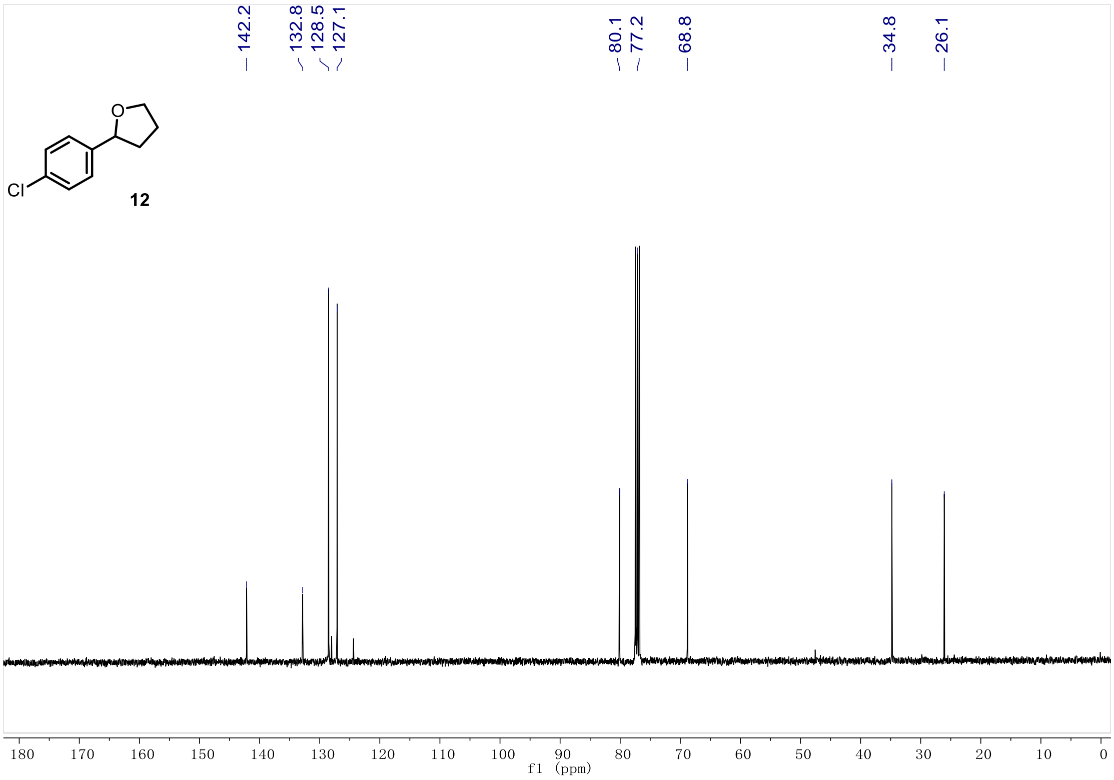
^{1}H NMR of compound **12-s** (400 MHz, CDCl$_3$)



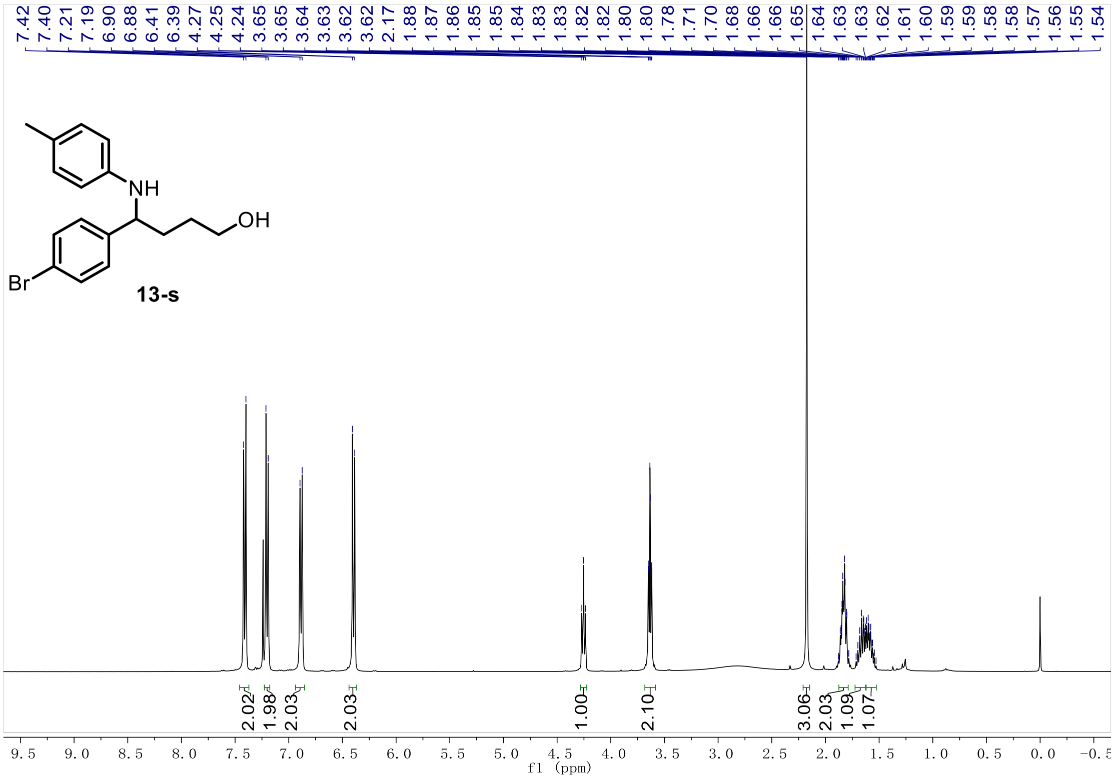
^{13}C NMR of compound **12-s** (101 MHz, $CDCl_3$)



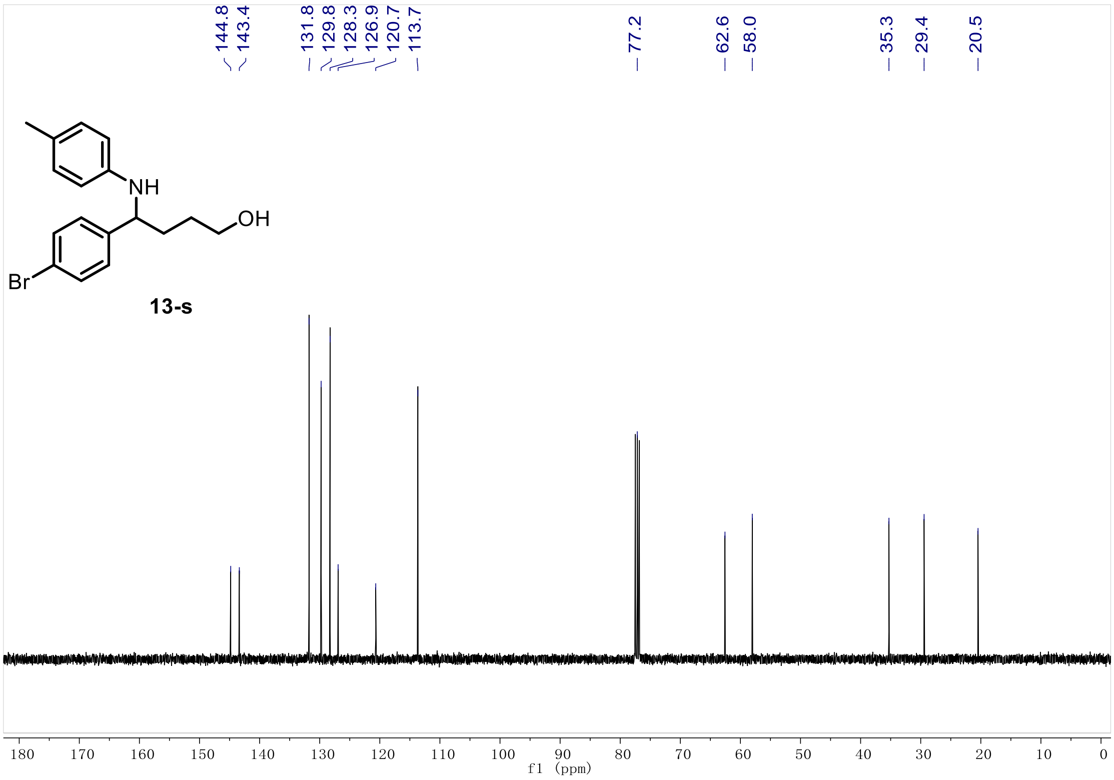
^{1}H NMR of compound **12** (400 MHz, $CDCl_3$)



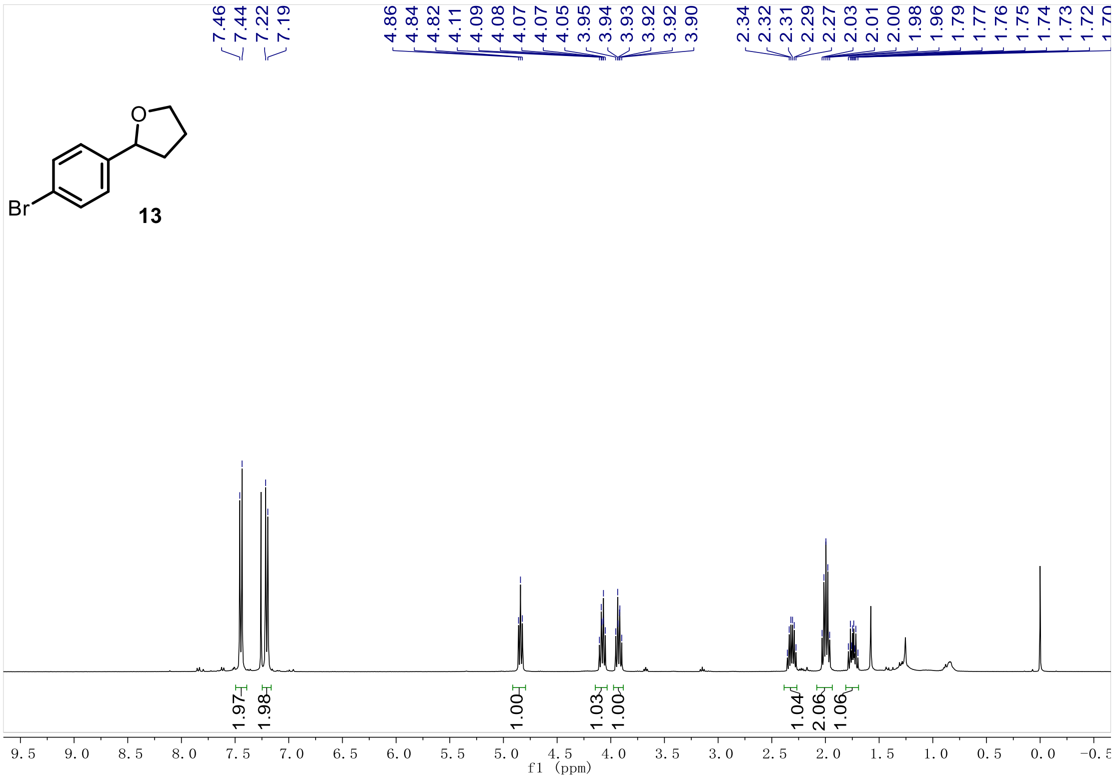
^{13}C NMR of compound **12** (101 MHz, CDCl$_3$)



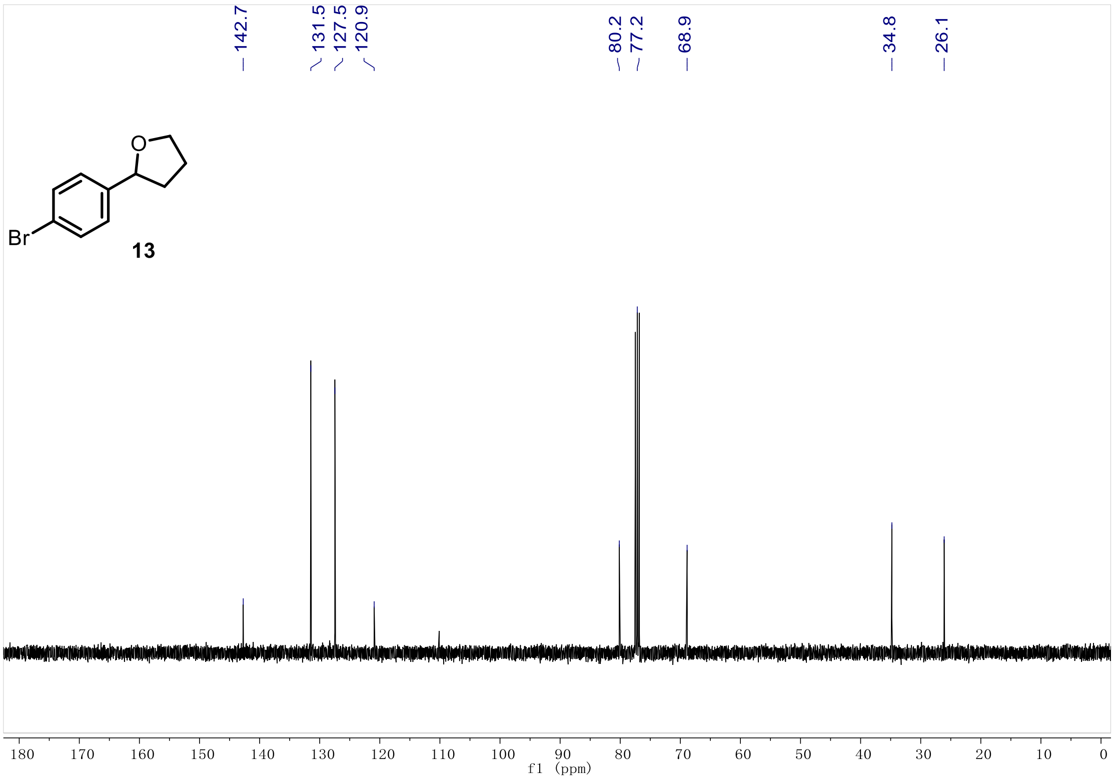
^{1}H NMR of compound **13-s** (400 MHz, CDCl$_3$)



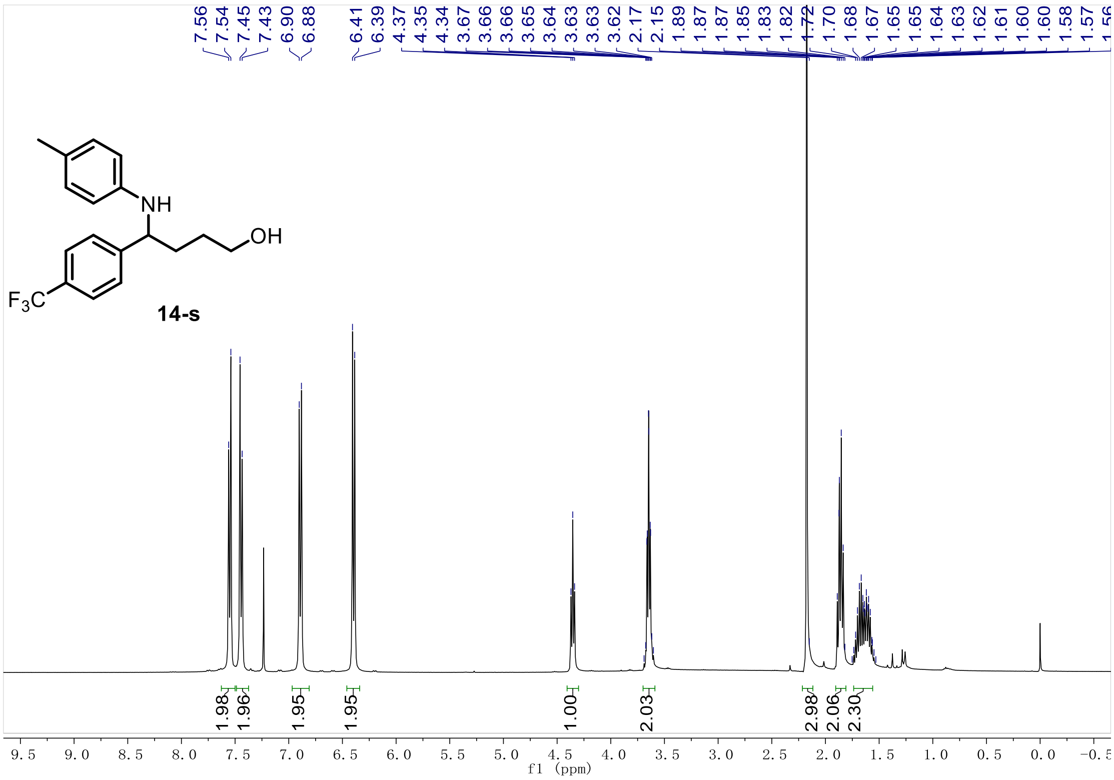
^{13}C NMR of compound **13-s** (101 MHz, $CDCl_3$)



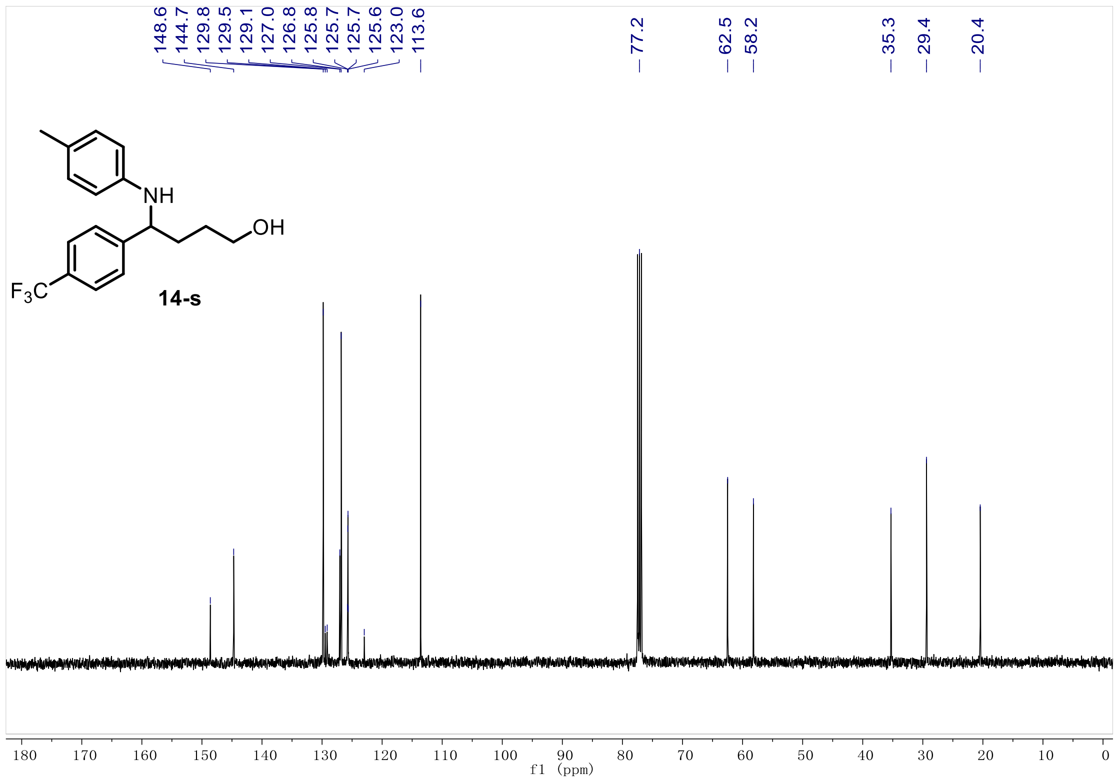
^{1}H NMR of compound **13** (400 MHz, $CDCl_3$)



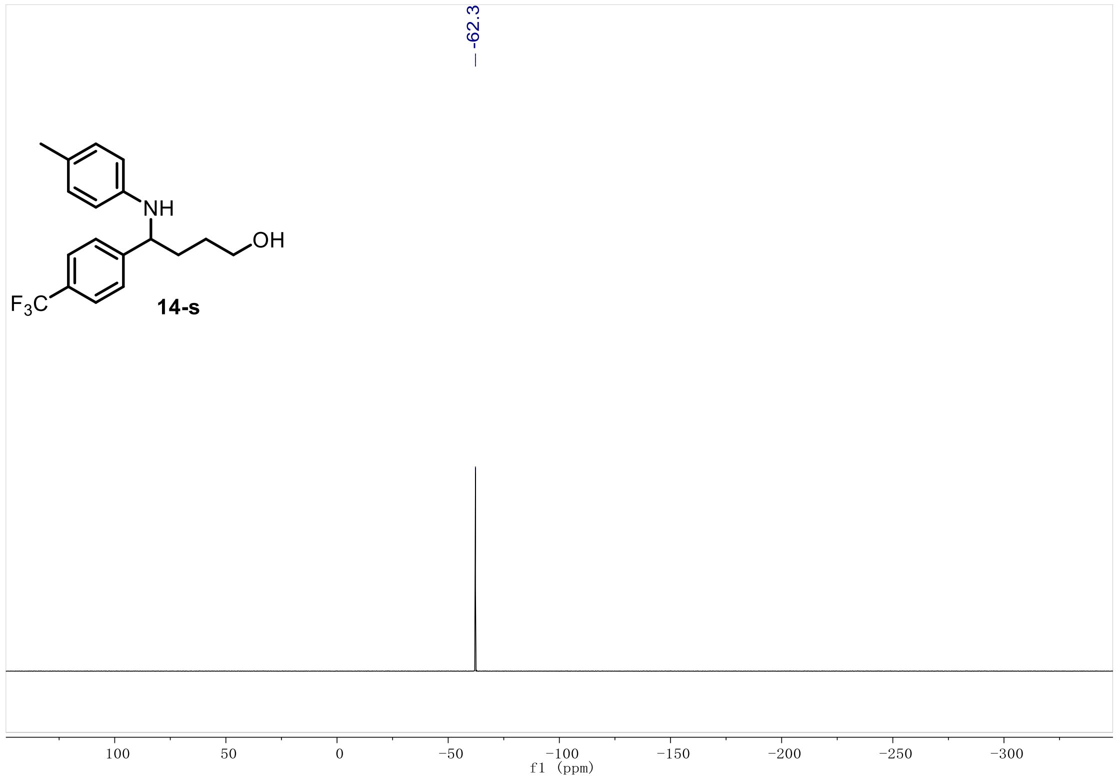
^{13}C NMR of compound **13** (101 MHz, CDCl$_3$)



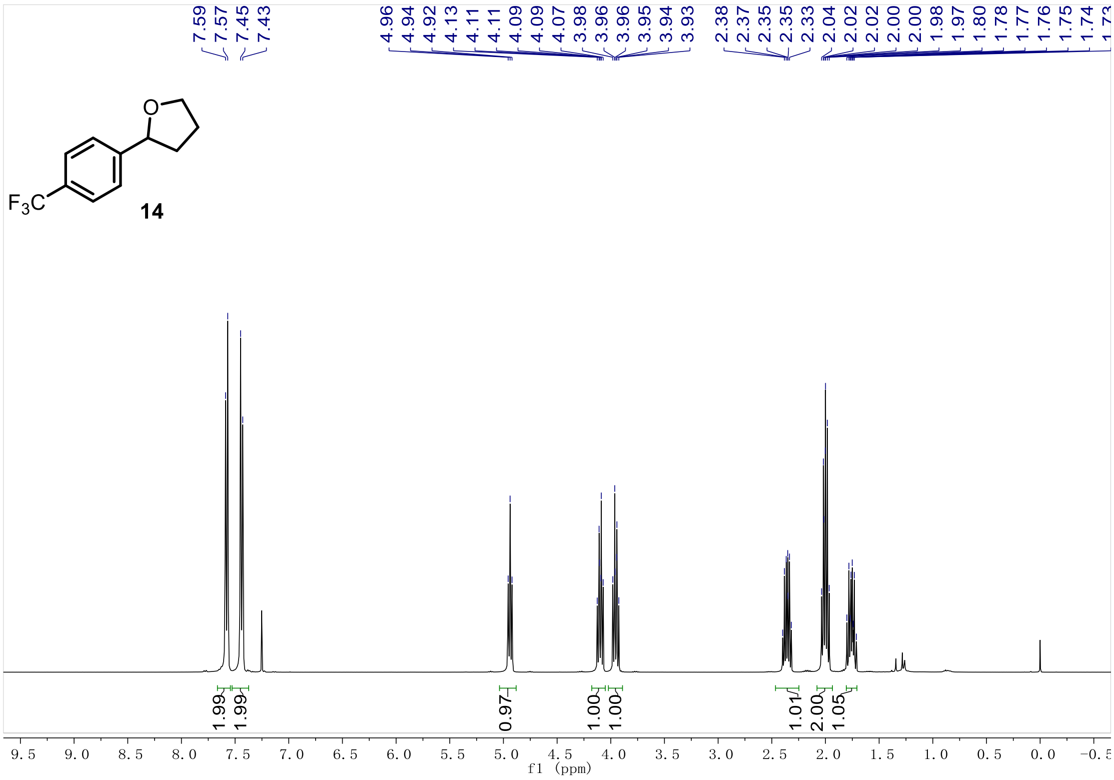
^{1}H NMR of compound **14-s** (400 MHz, CDCl$_3$)



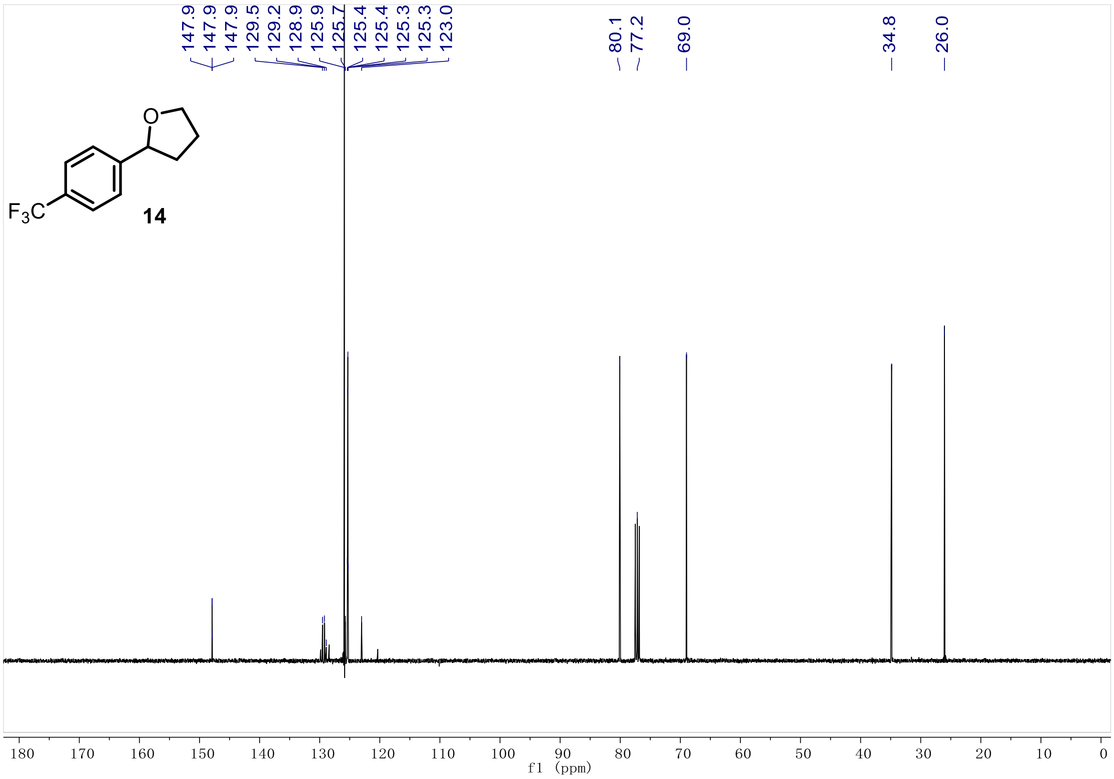
^{13}C NMR of compound **14-s** (101 MHz, CDCl$_3$)



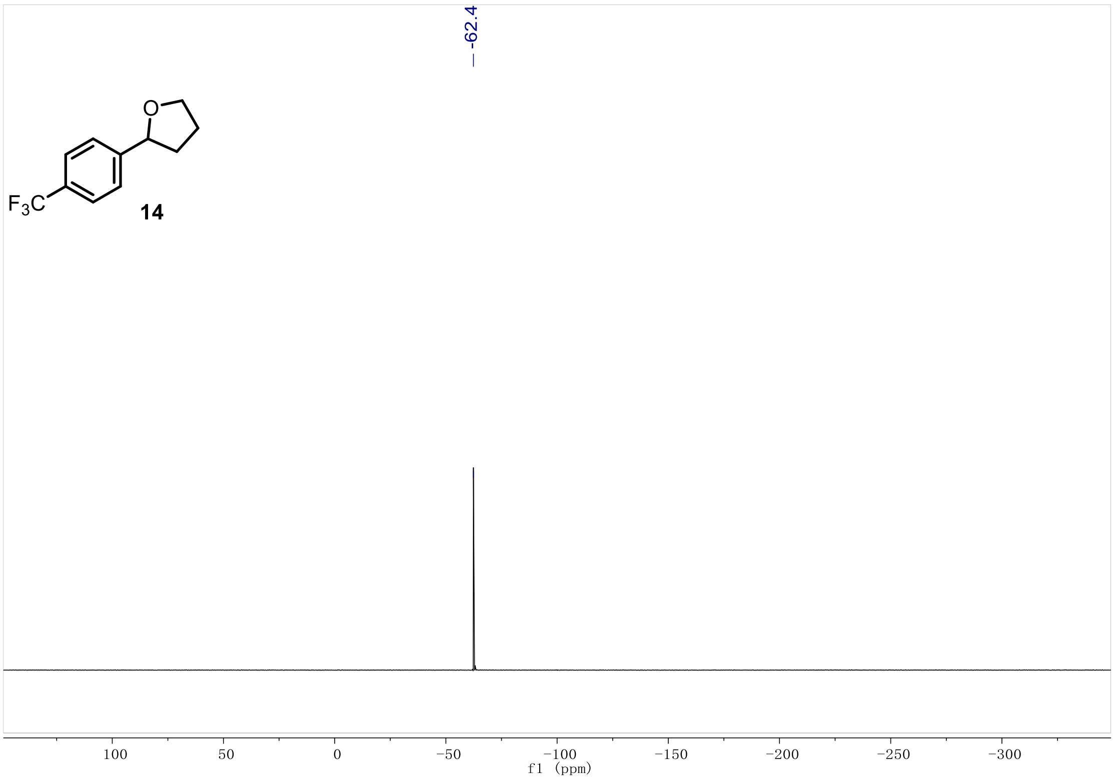
^{19}F NMR of compound **14-s** (376 MHz, CDCl$_3$)



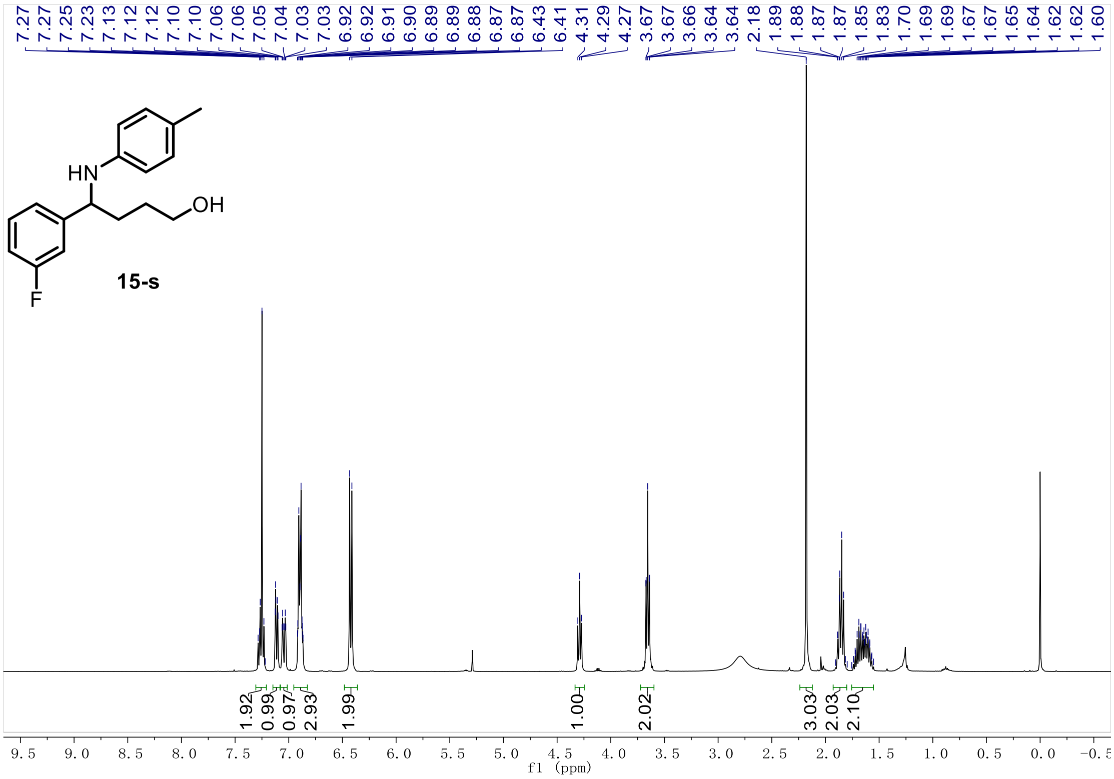
^{1}H NMR of compound **14** (400 MHz, $CDCl_3$)



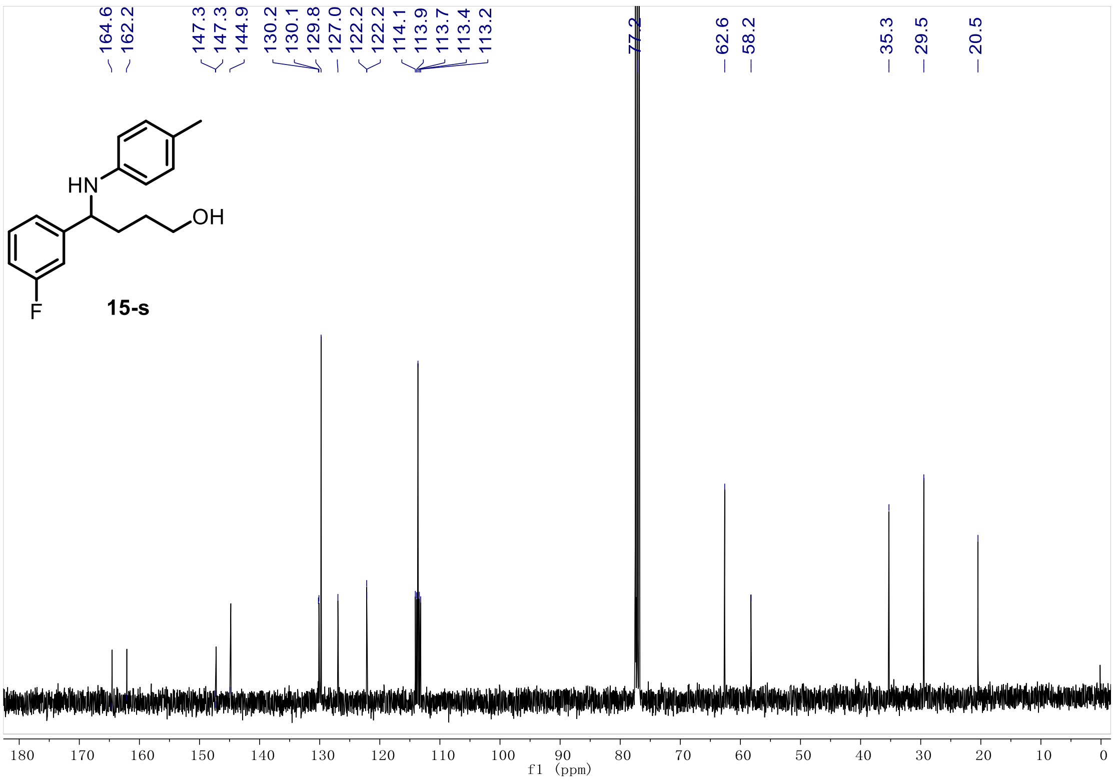
^{13}C NMR of compound **14** (101 MHz, $CDCl_3$)



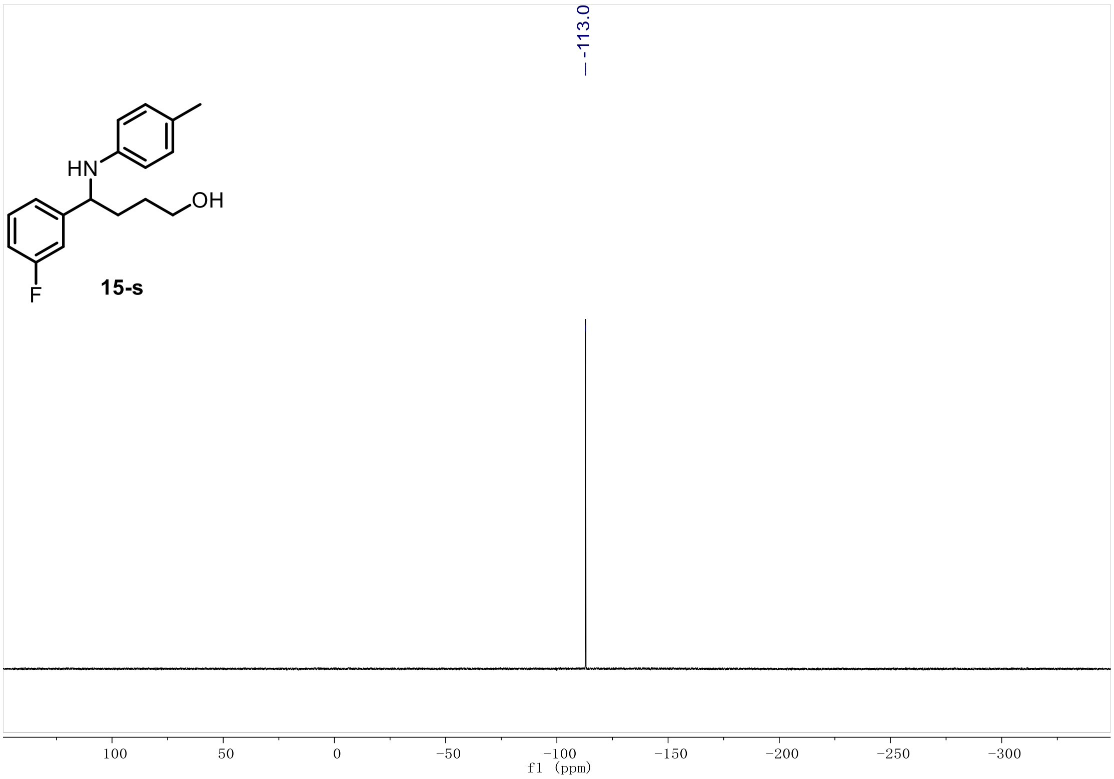
^{19}F NMR of compound **14** (376 MHz, CDCl$_3$)



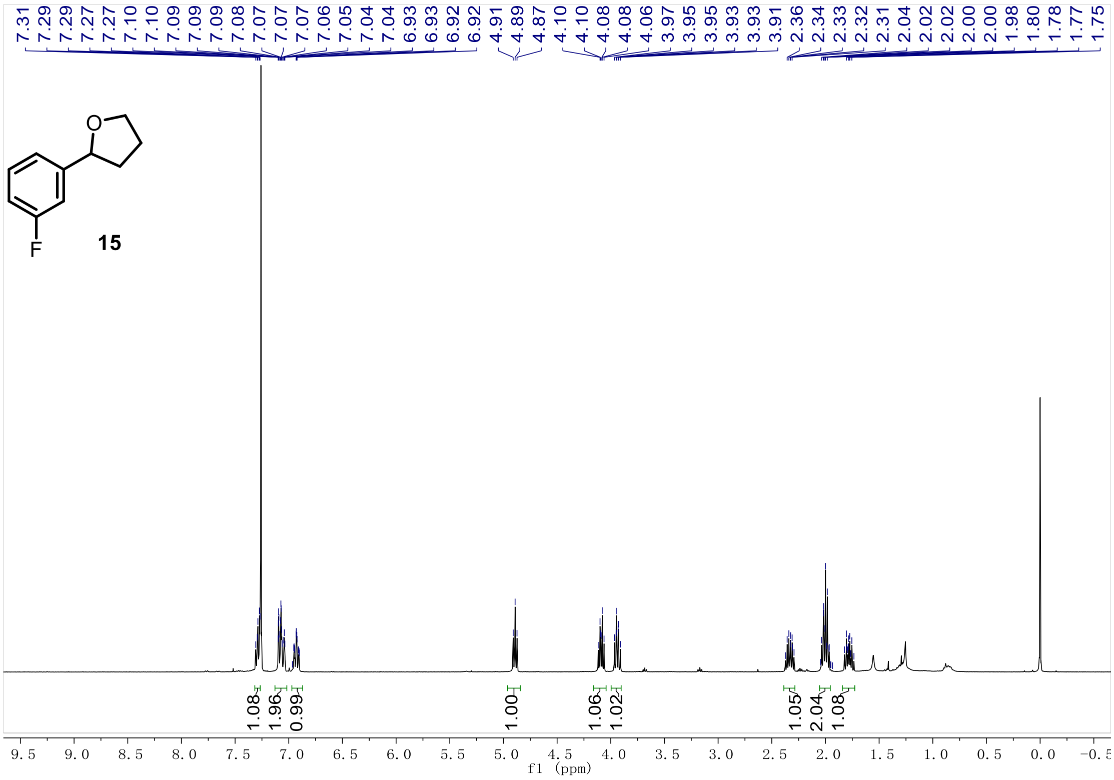
^{1}H NMR of compound **15-s** (400 MHz, CDCl$_3$)



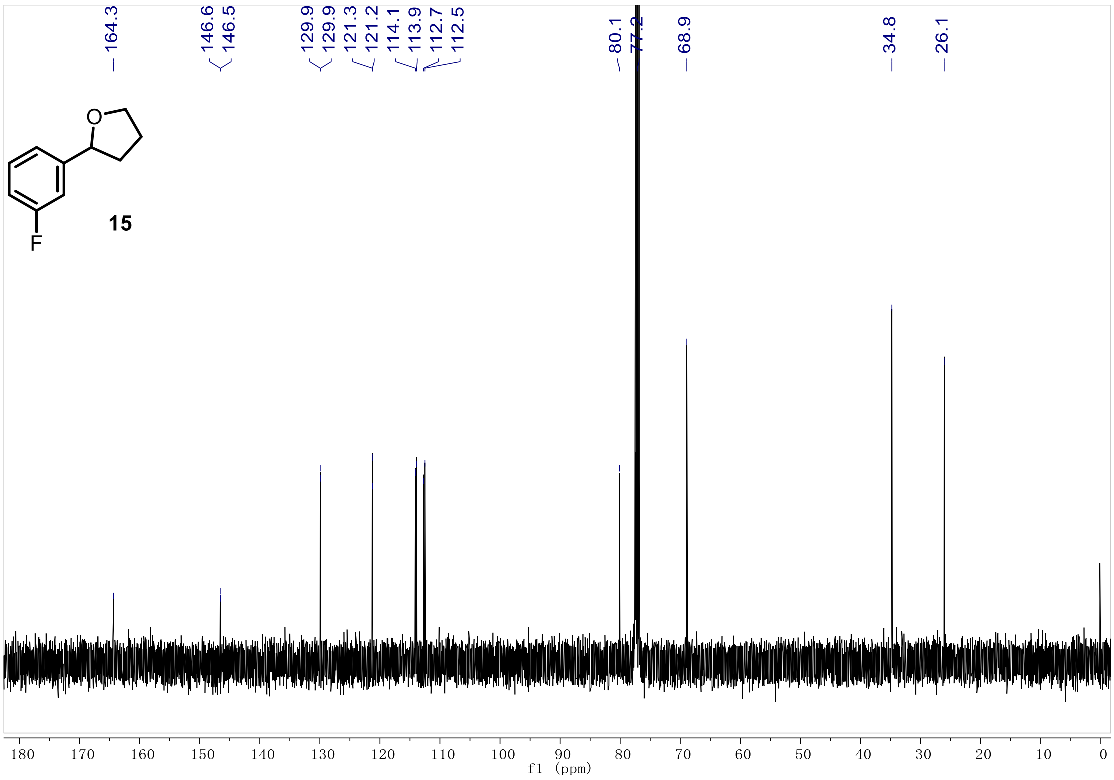
^{13}C NMR of compound **15-s** (101 MHz, CDCl$_3$)



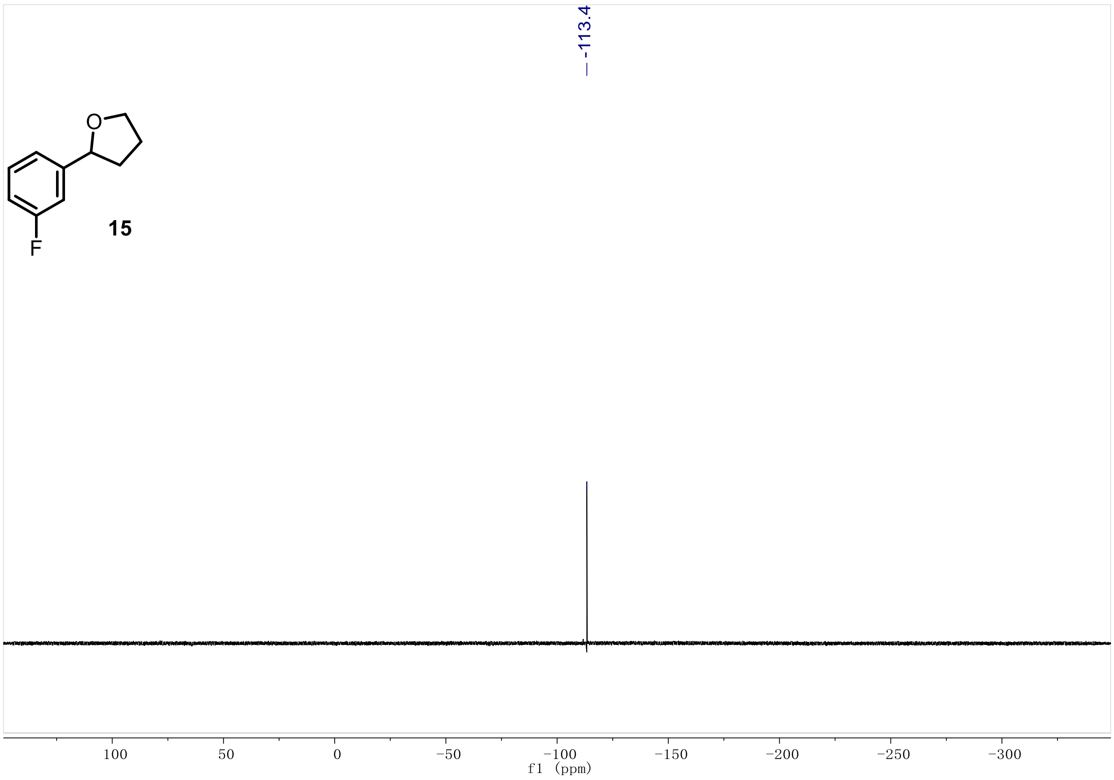
^{19}F NMR of compound **15-s** (376 MHz, CDCl$_3$)



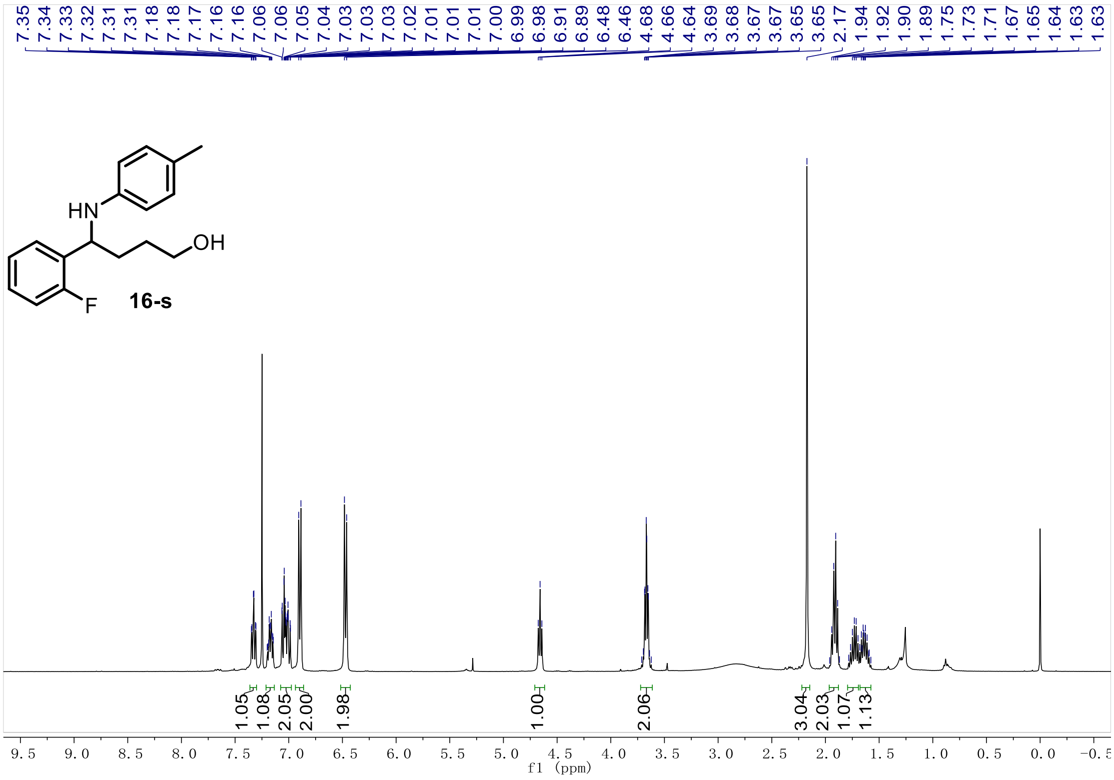
^{1}H NMR of compound **15** (400 MHz, $CDCl_3$)



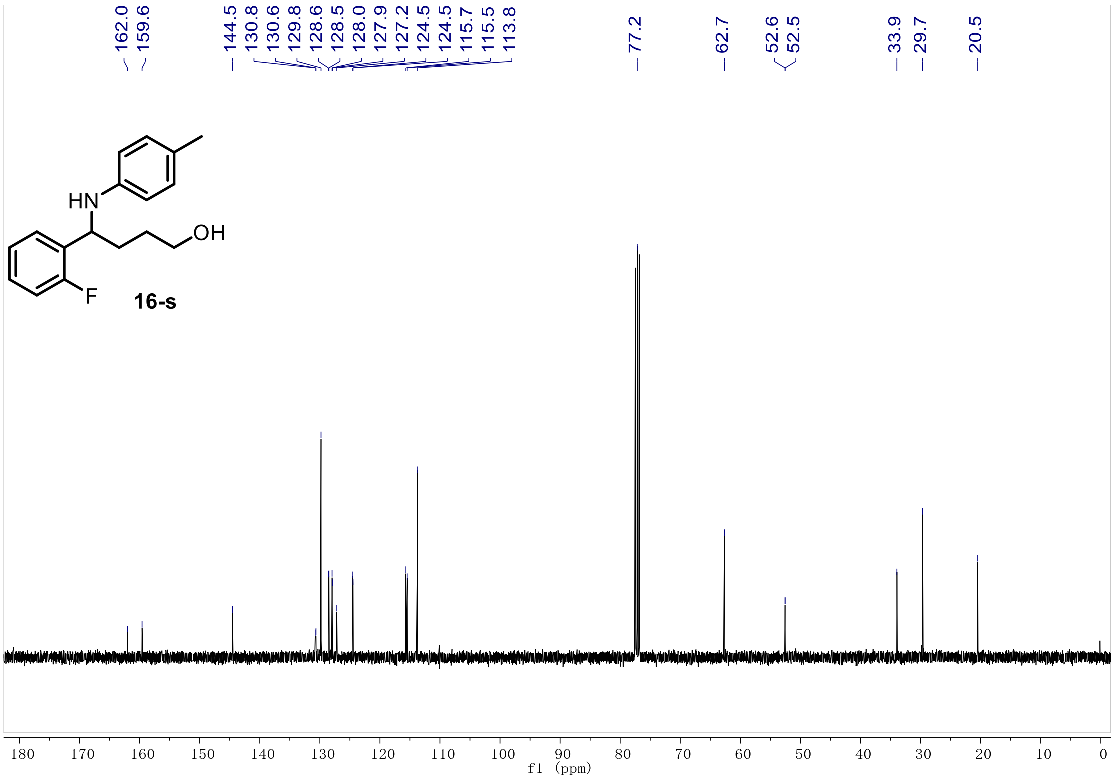
^{13}C NMR of compound **15** (101 MHz, $CDCl_3$)



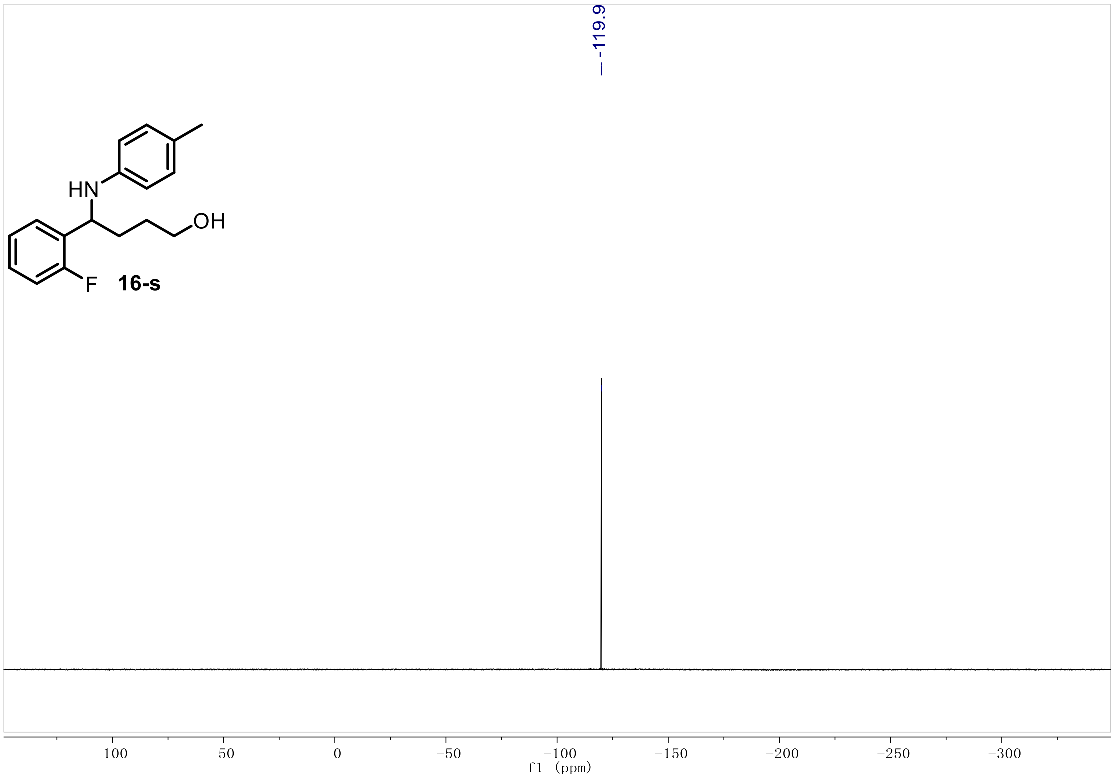
^{19}F NMR of compound **15** (376 MHz, CDCl$_3$)



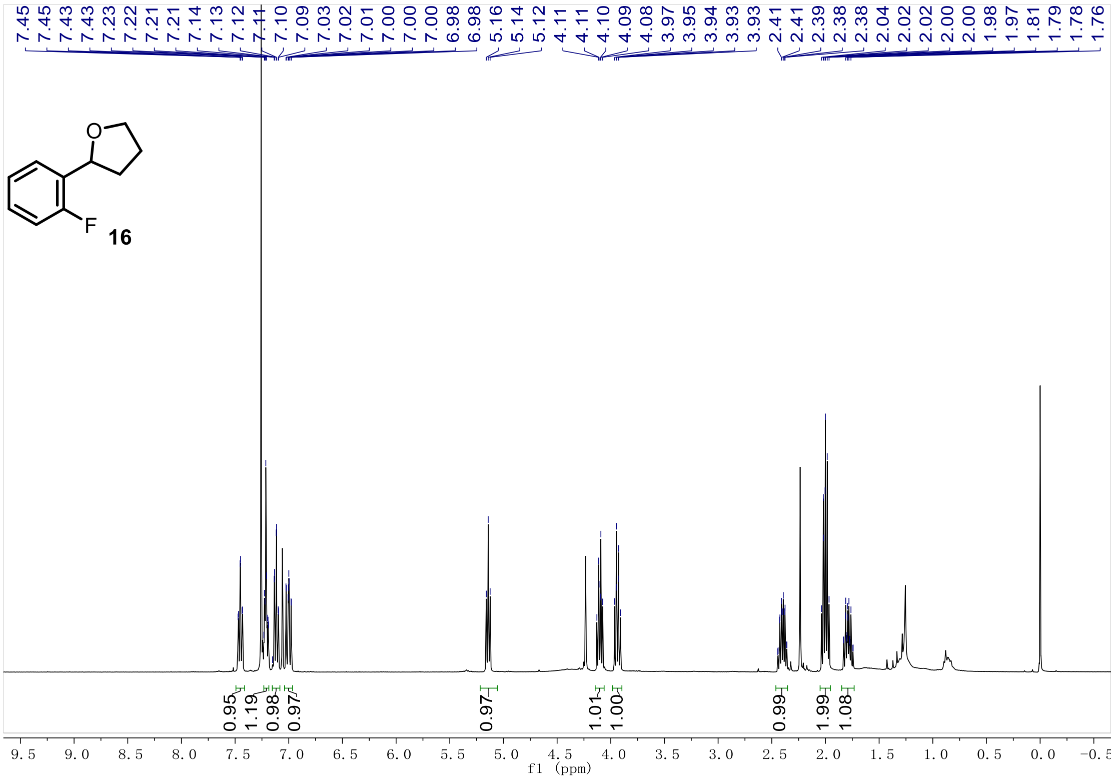
^{1}H NMR of compound **16-s** (400 MHz, CDCl$_3$)



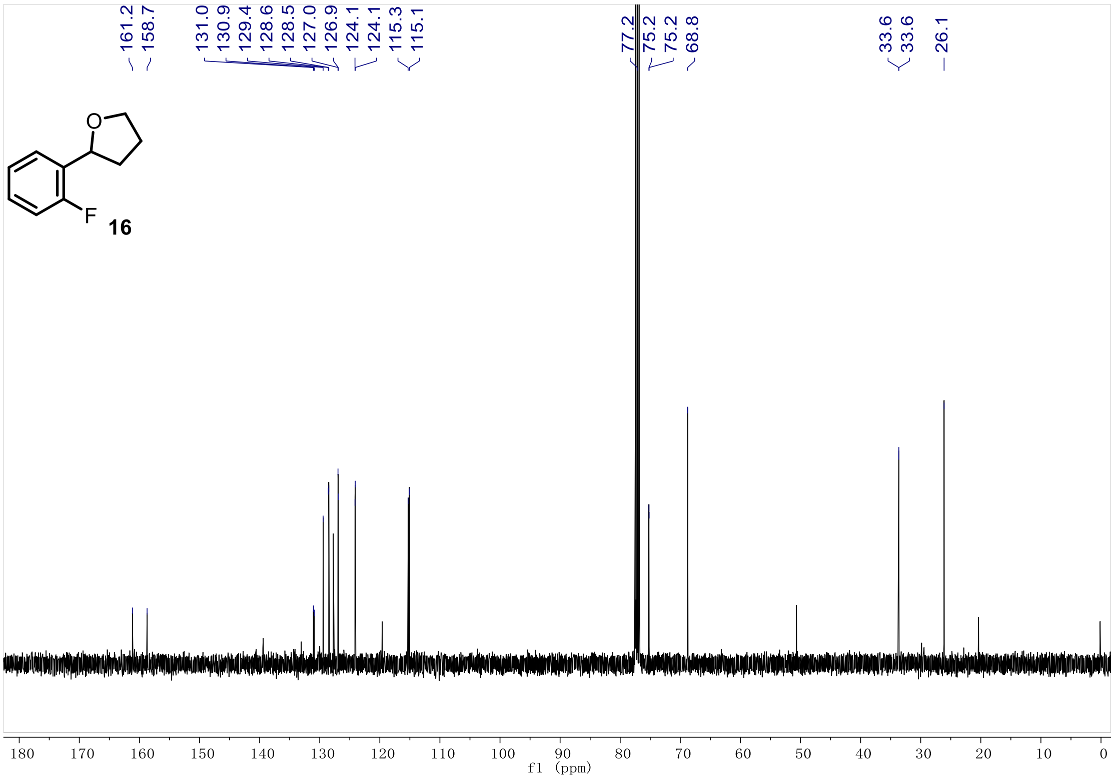
^{13}C NMR of compound **16-s** (101 MHz, CDCl$_3$)



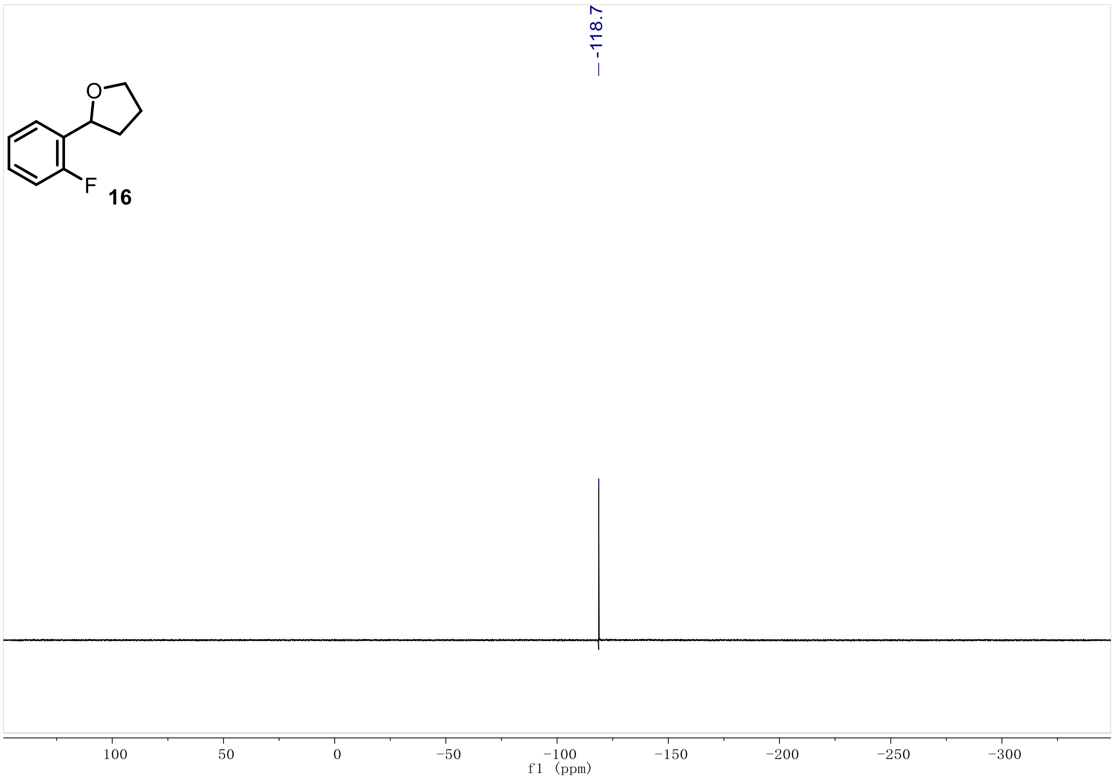
^{19}F NMR of compound **16-s** (376 MHz, CDCl$_3$)



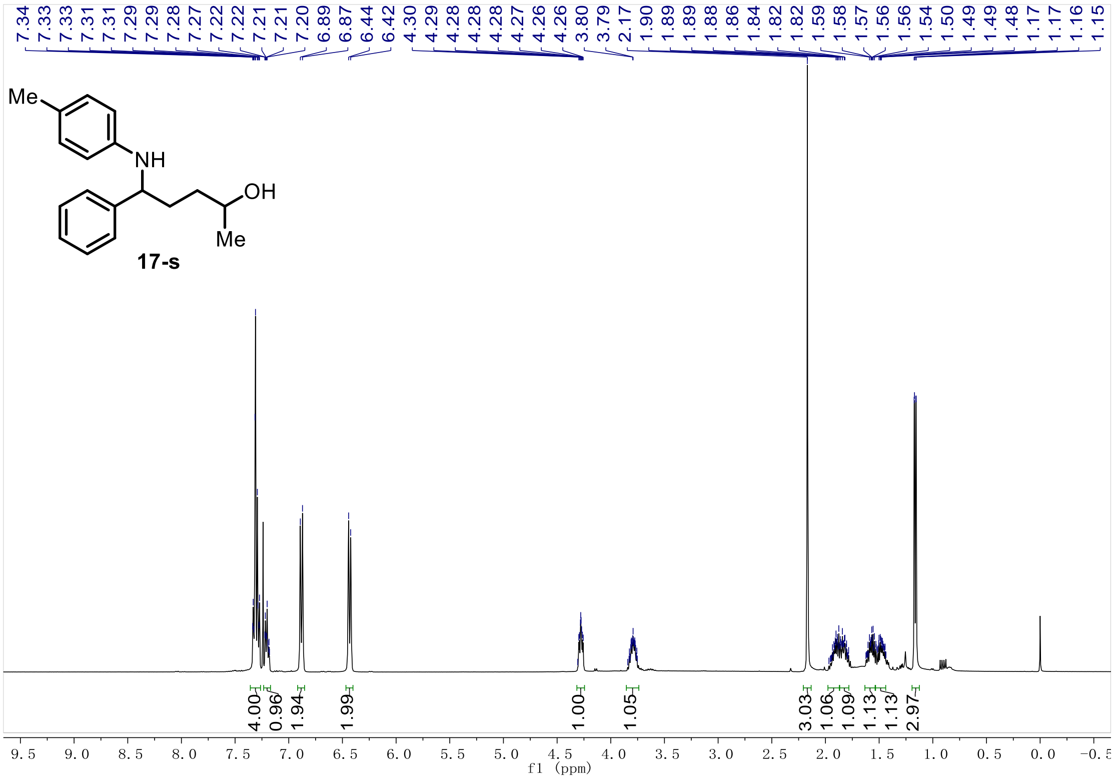
^{1}H NMR of compound **16** (400 MHz, CDCl$_3$)



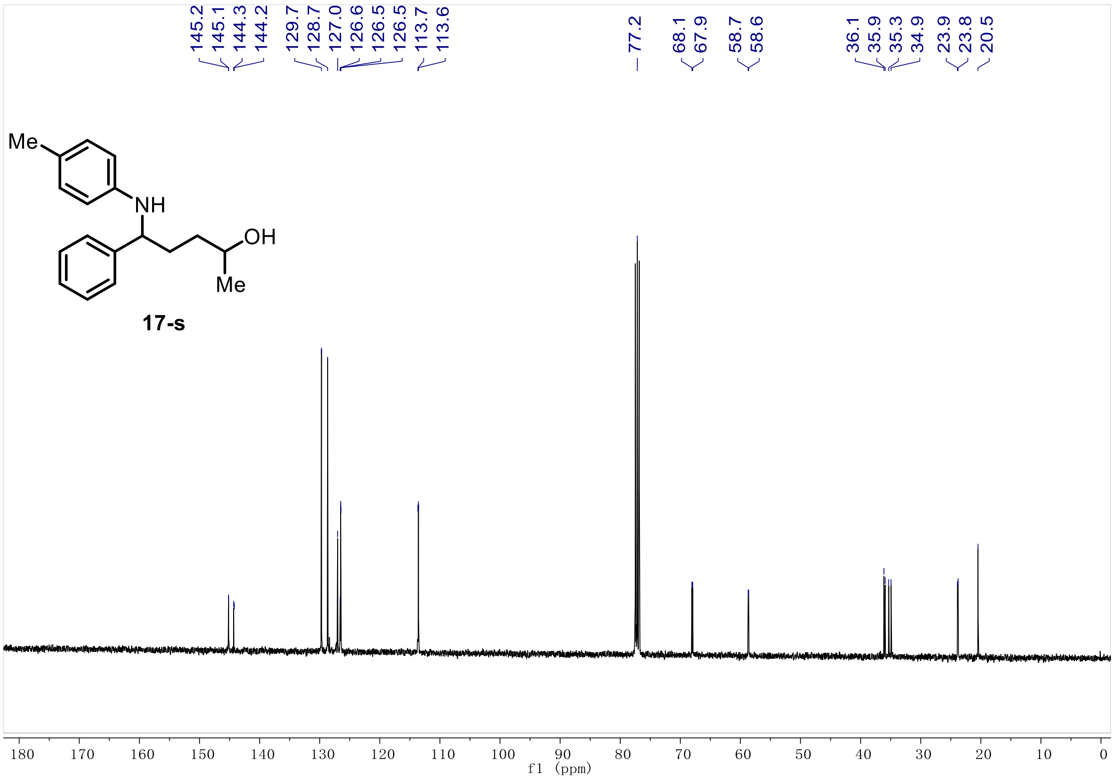
^{13}C NMR of compound **16** (101 MHz, CDCl$_3$)



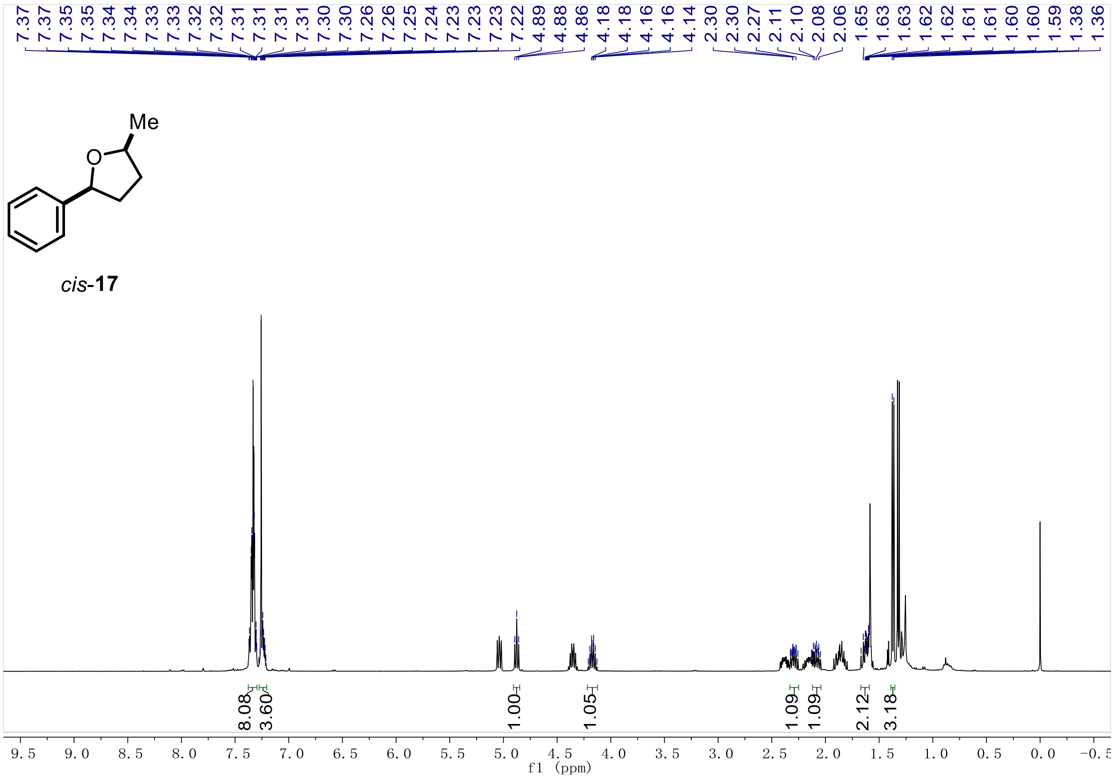
^{19}F NMR of compound **16** (376 MHz, CDCl$_3$)



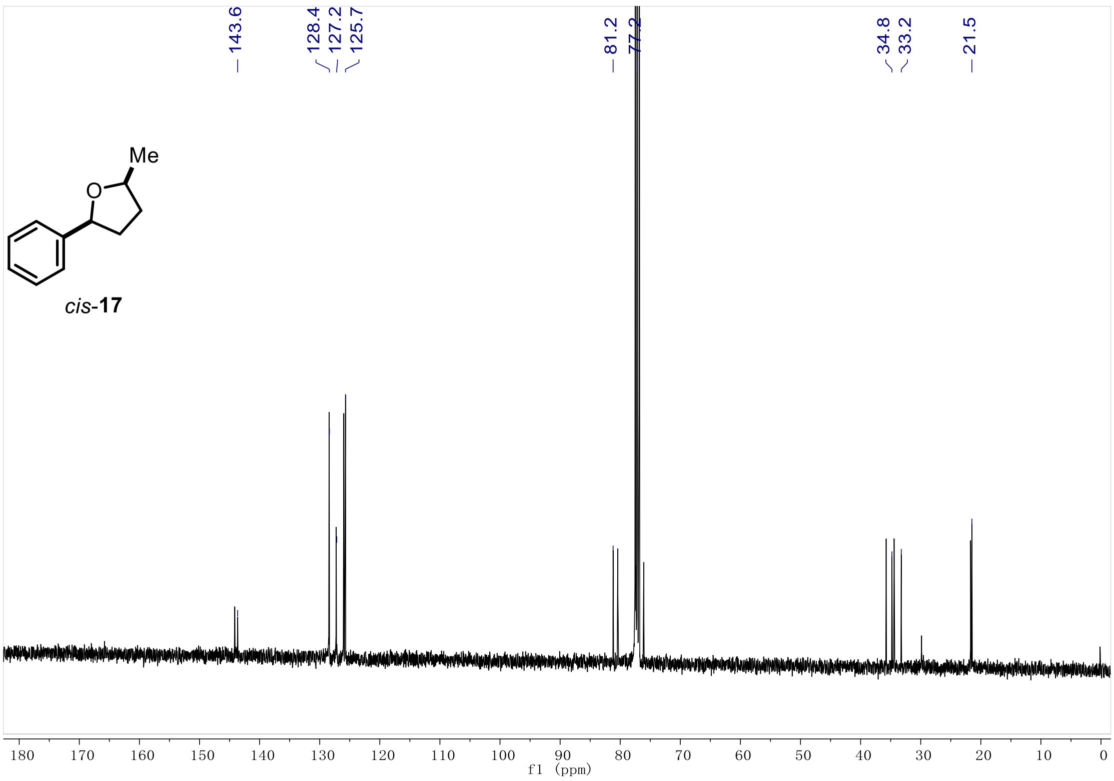
^{1}H NMR of compound **17-s** (400 MHz, CDCl$_3$)



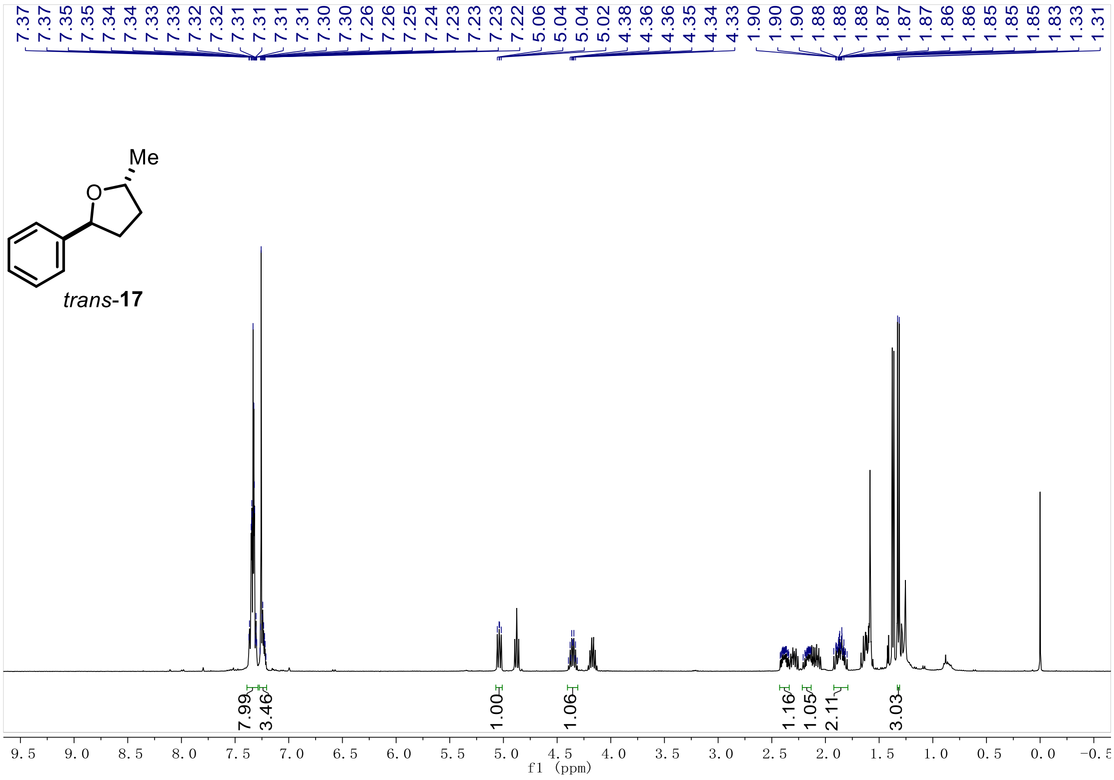
^{13}C NMR of compound **17-s** (101 MHz, $CDCl_3$)



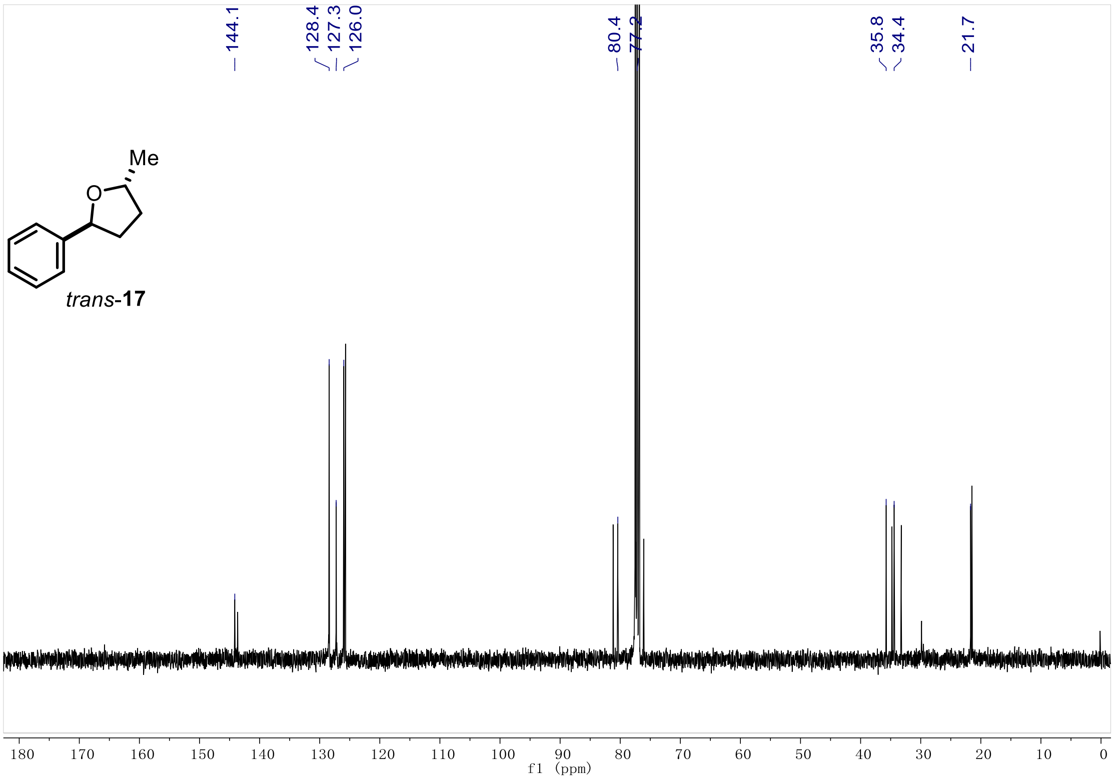
^{1}H NMR of compound *cis*-**17** (400 MHz, $CDCl_3$)



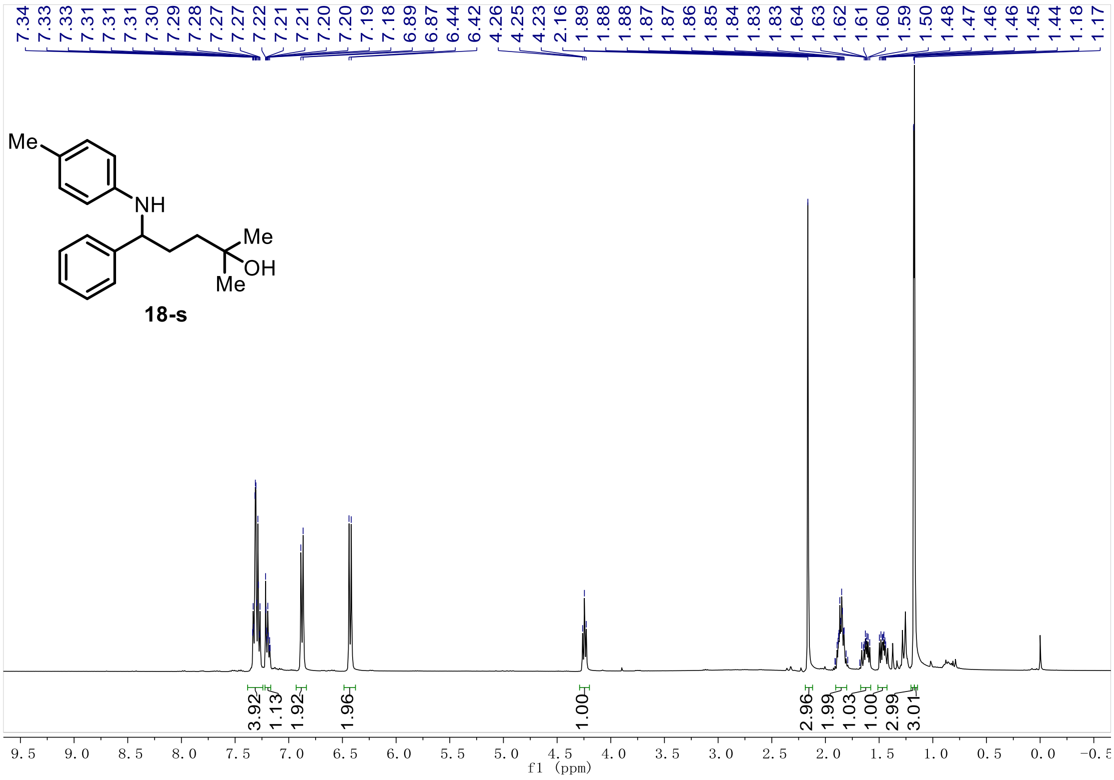
^{13}C NMR of compound *cis*-**17** (101 MHz, CDCl$_3$)



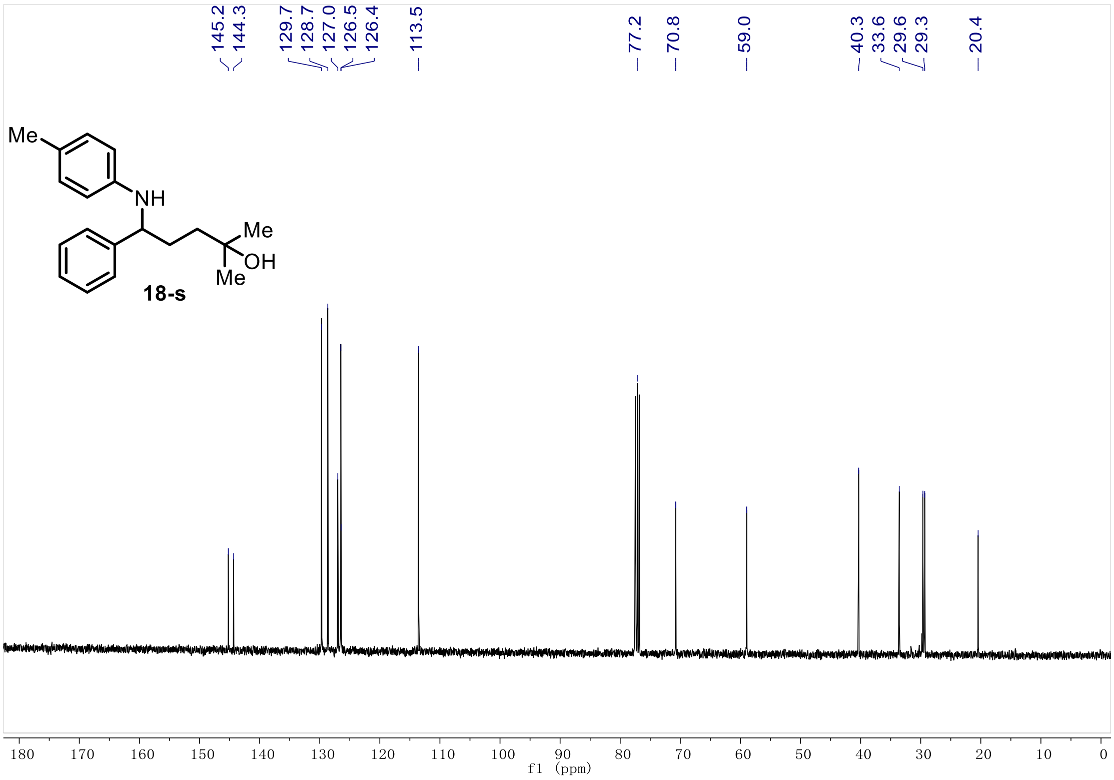
^{1}H NMR of compound *trans*-**17** (400 MHz, CDCl$_3$)



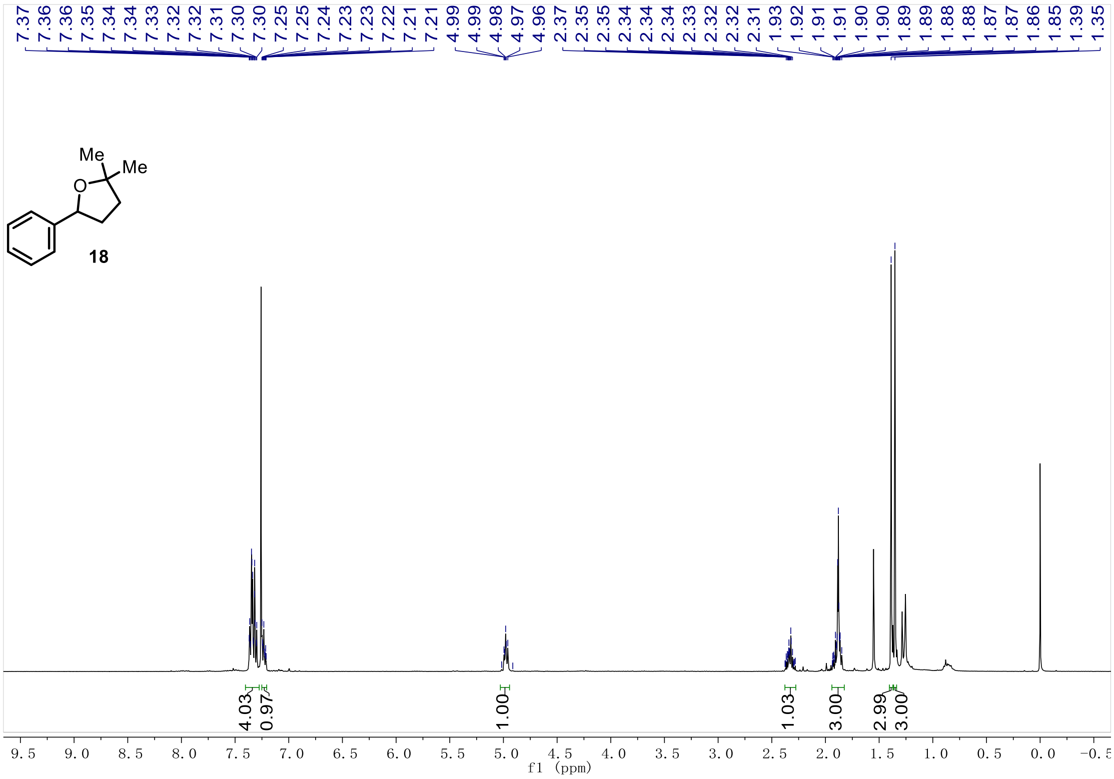
^{13}C NMR of compound *trans*-**17** (101 MHz, CDCl$_3$)



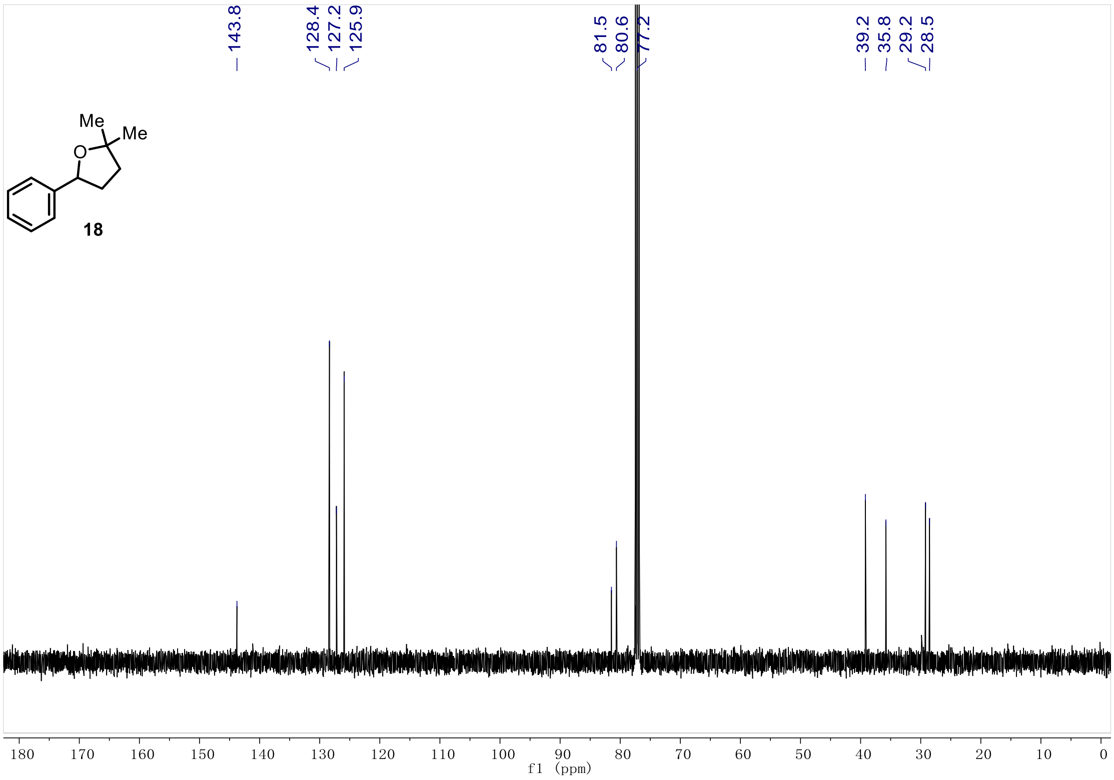
^{1}H NMR of compound **18-s** (400 MHz, CDCl$_3$)



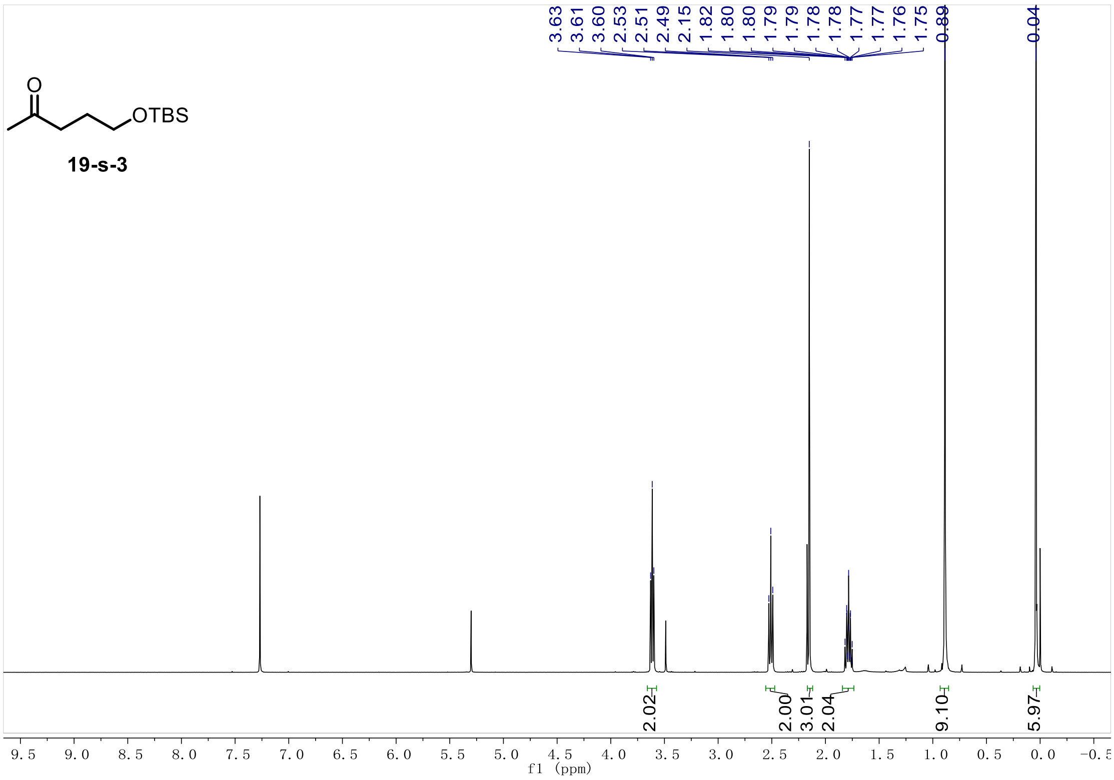
^{13}C NMR of compound **18-s** (101 MHz, CDCl$_3$)



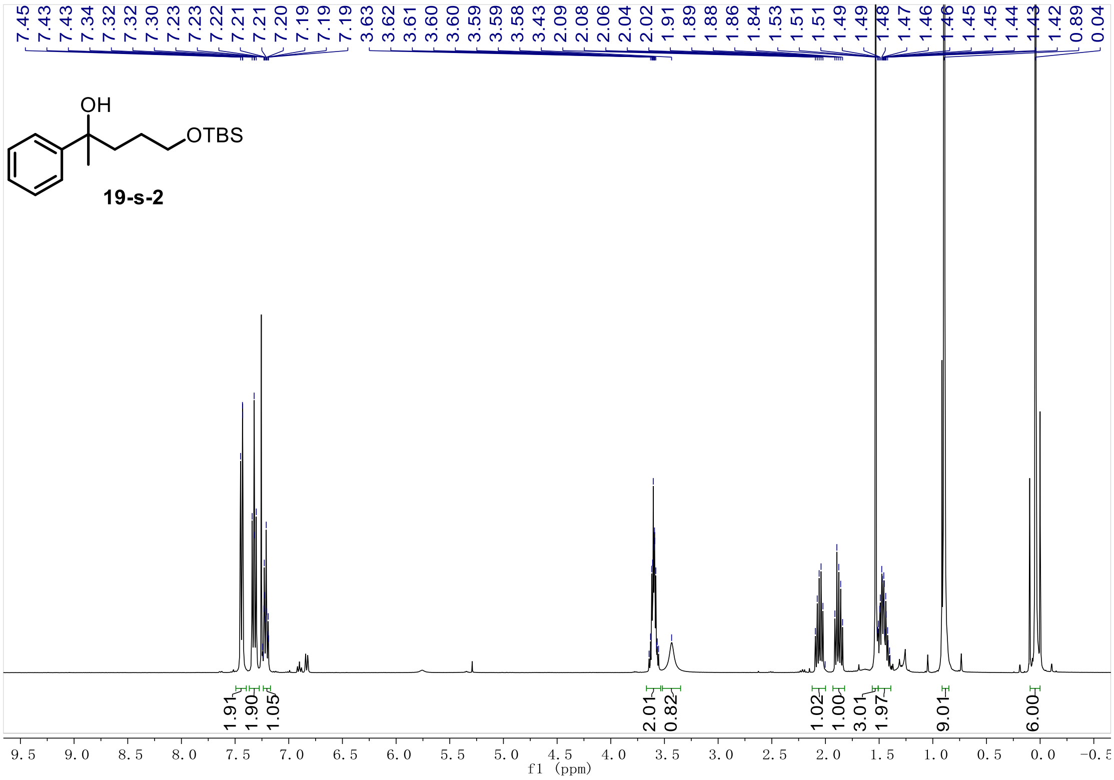
^{1}H NMR of compound **18** (400 MHz, CDCl$_3$)



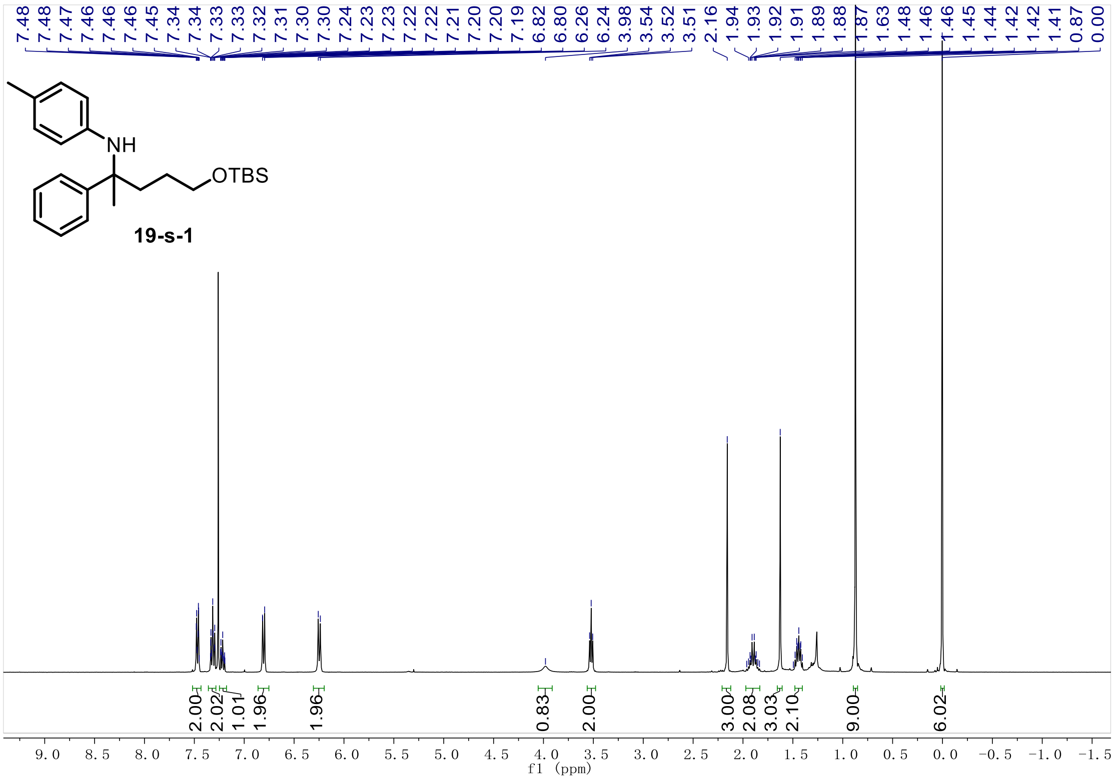
^{13}C NMR of compound **18** (101 MHz, $CDCl_3$)



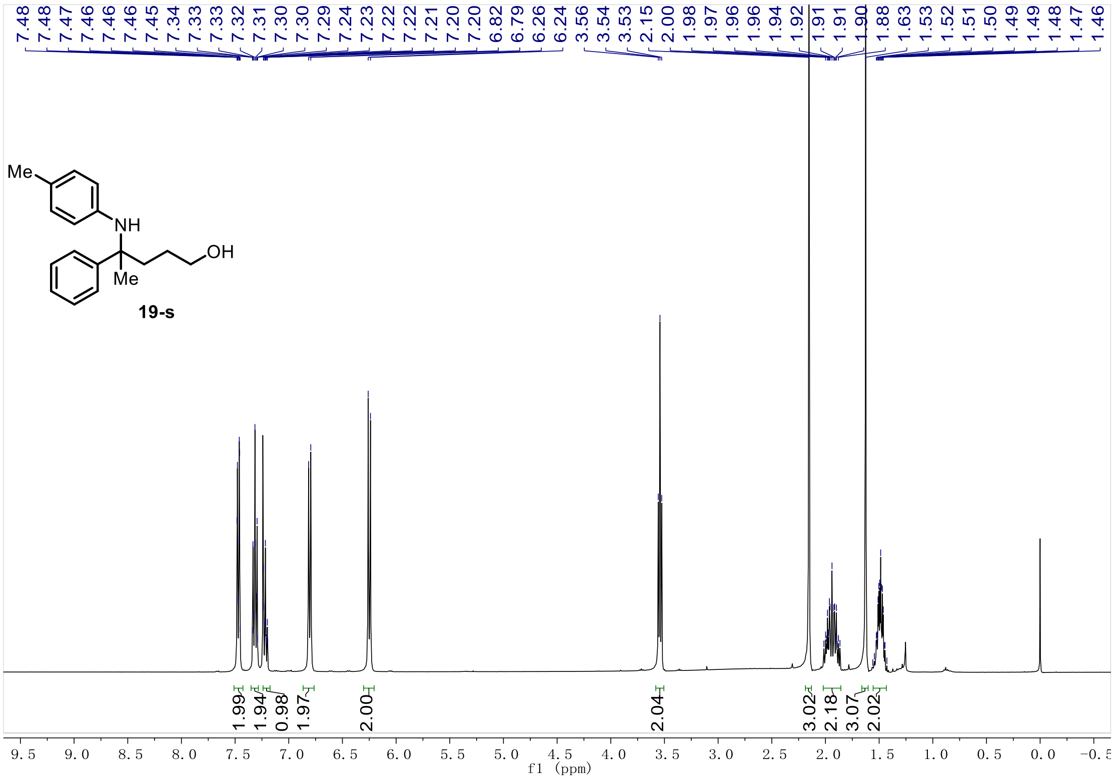
^{1}H NMR of compound **19-s-3** (400 MHz, $CDCl_3$)



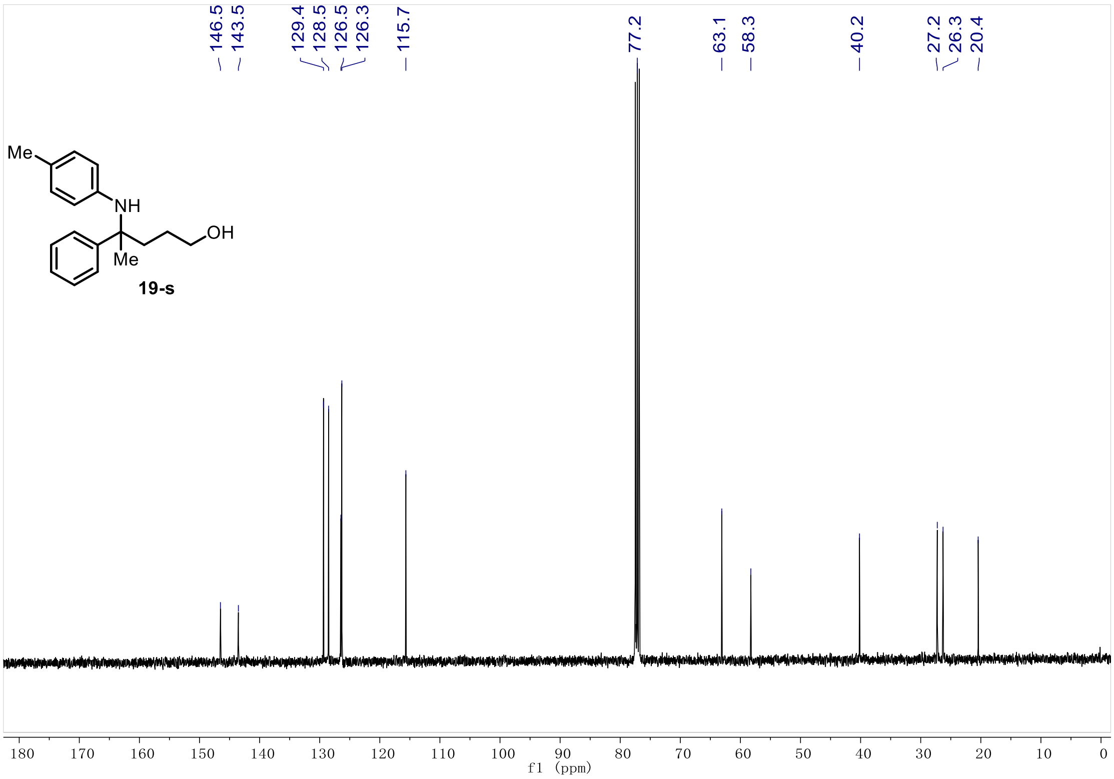
^{1}H NMR of compound **19-s-2** (400 MHz, $CDCl_3$)



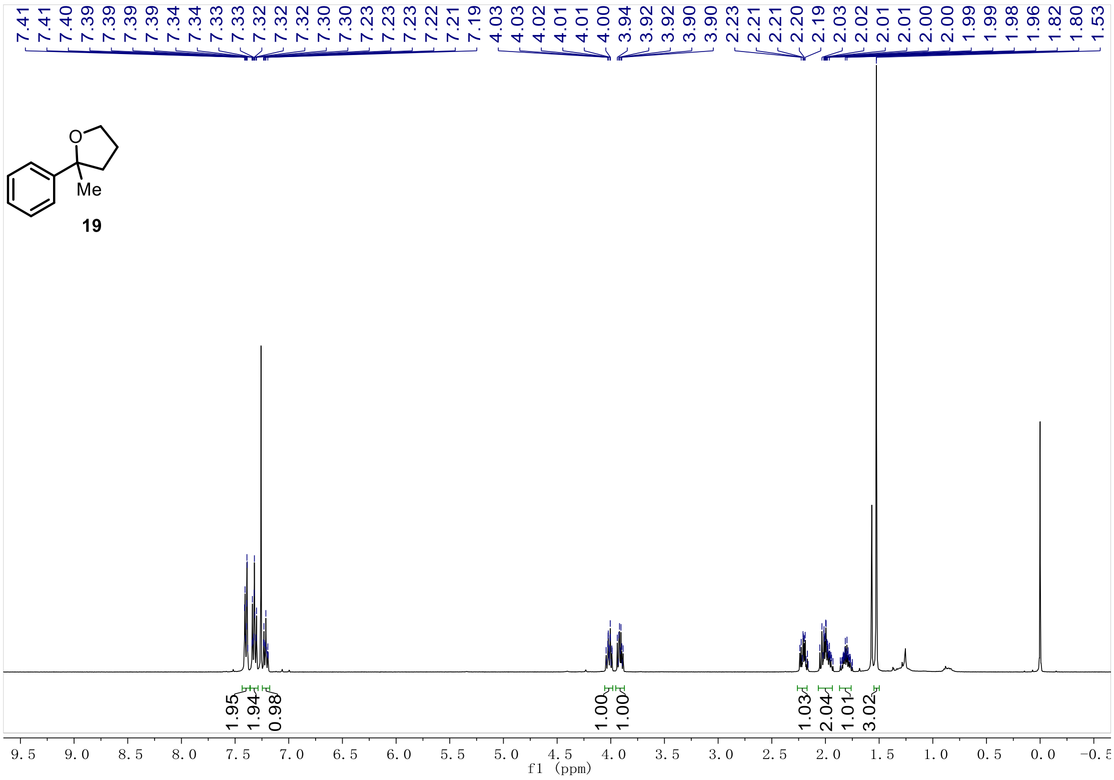
^{1}H NMR of compound **19-s-1** (400 MHz, $CDCl_3$)



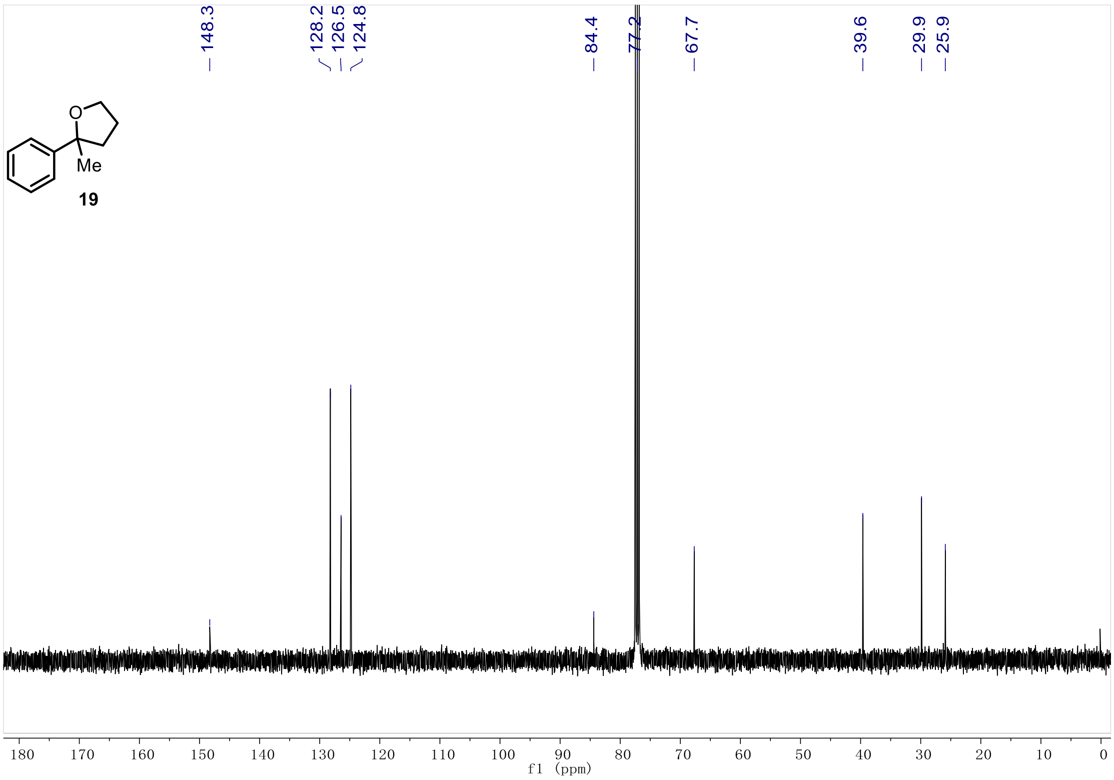
^{1}H NMR of compound **19-s** (400 MHz, CDCl$_3$)



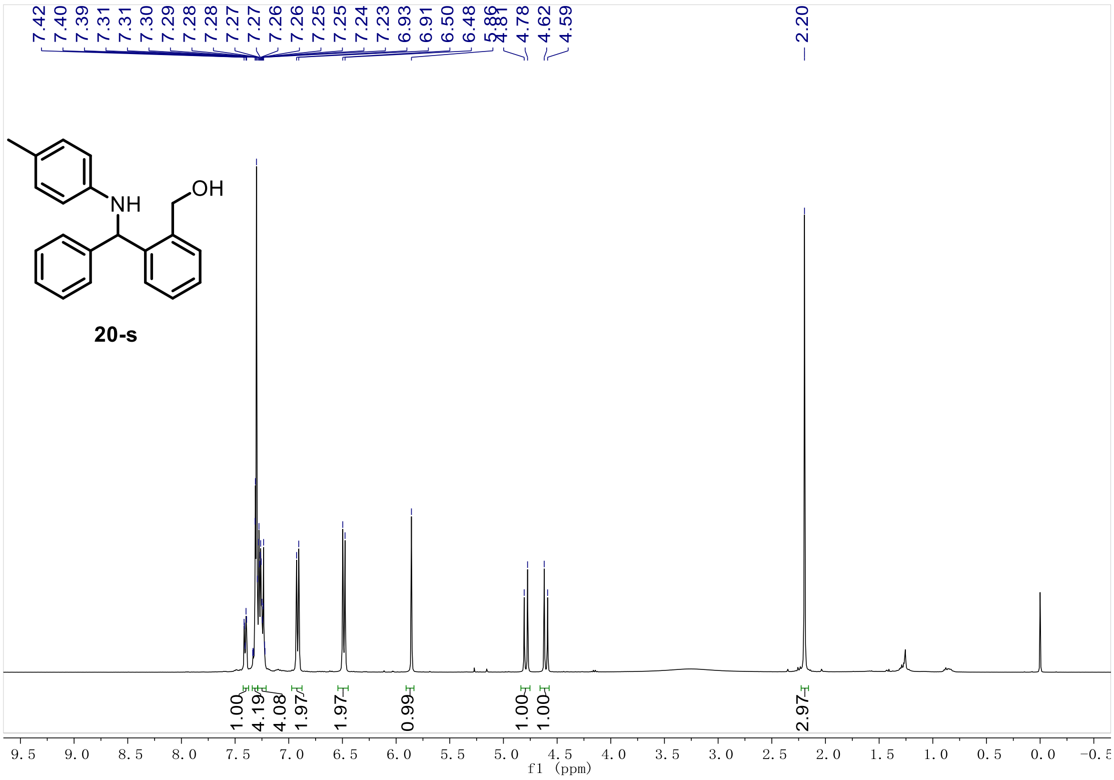
^{13}C NMR of compound **19-s** (101 MHz, CDCl$_3$)



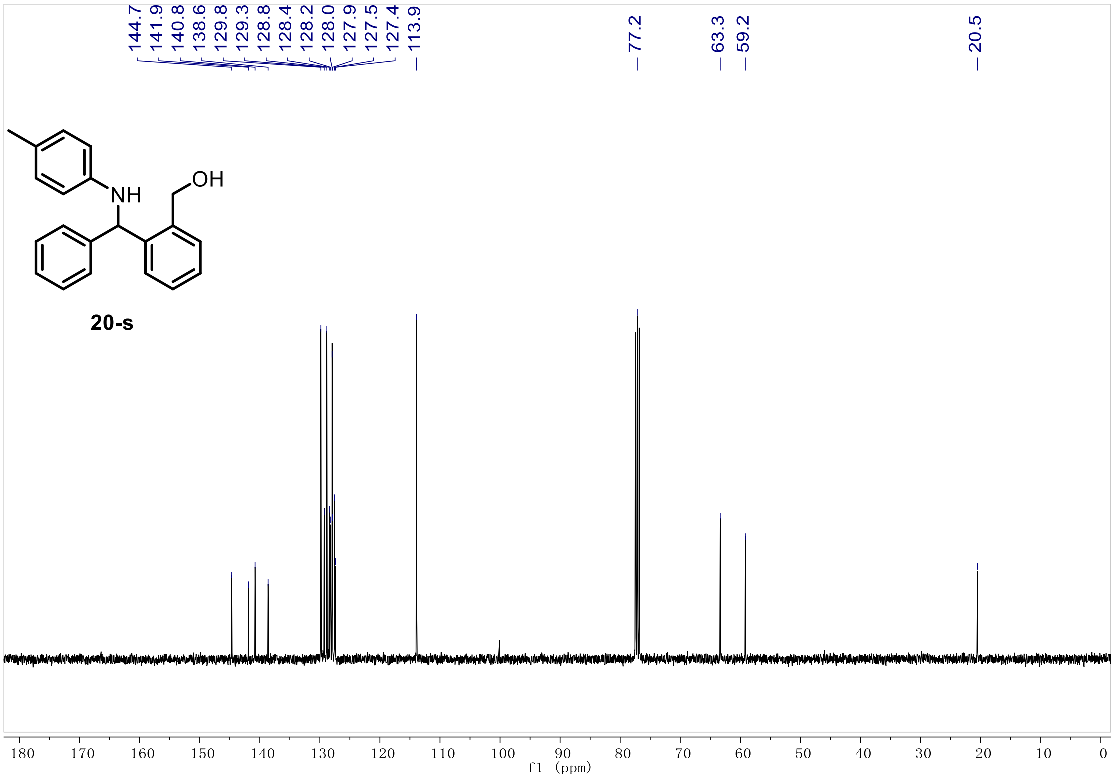
^{1}H NMR of compound **19** (400 MHz, CDCl$_3$)



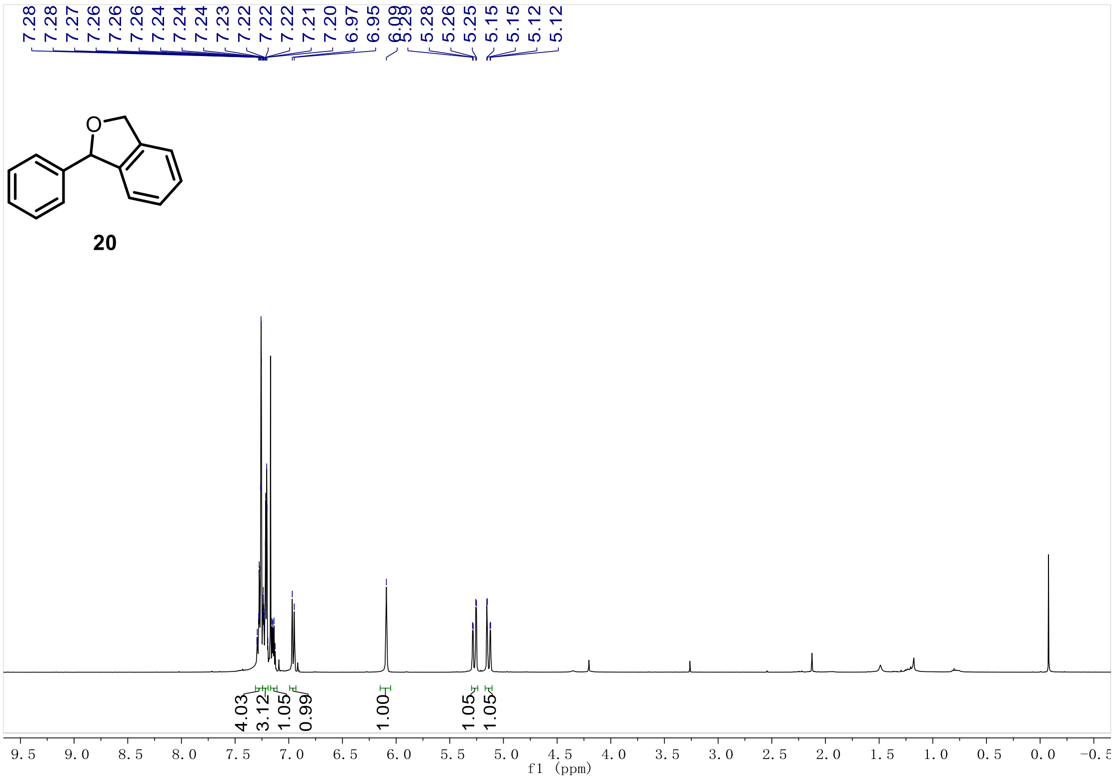
^{13}C NMR of compound **19** (101 MHz, CDCl$_3$)



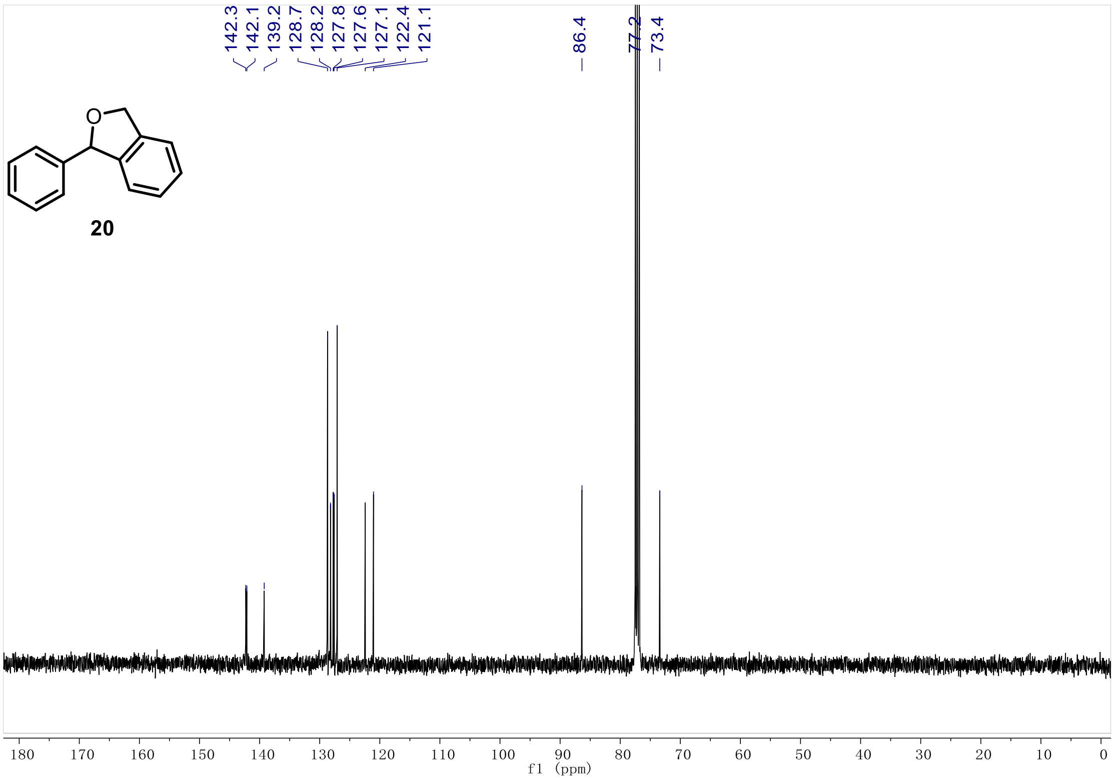
^{1}H NMR of compound **20-s** (400 MHz, CDCl$_3$)



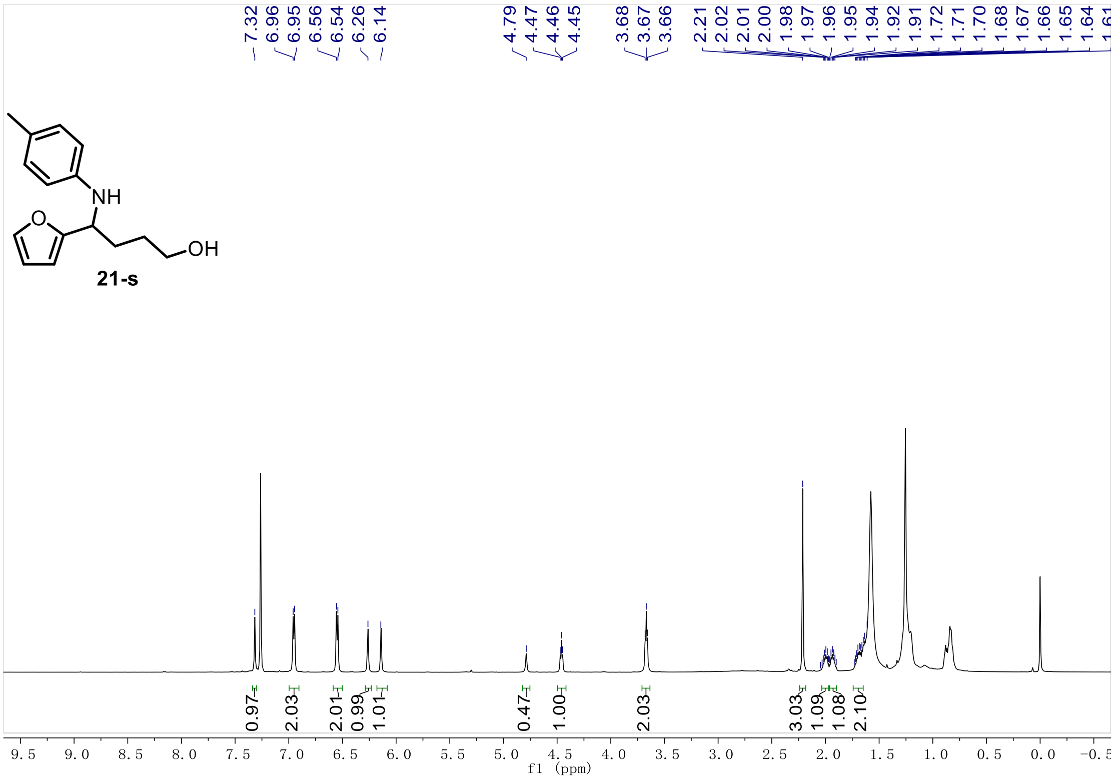
^{13}C NMR of compound **20-s** (101 MHz, CDCl$_3$)



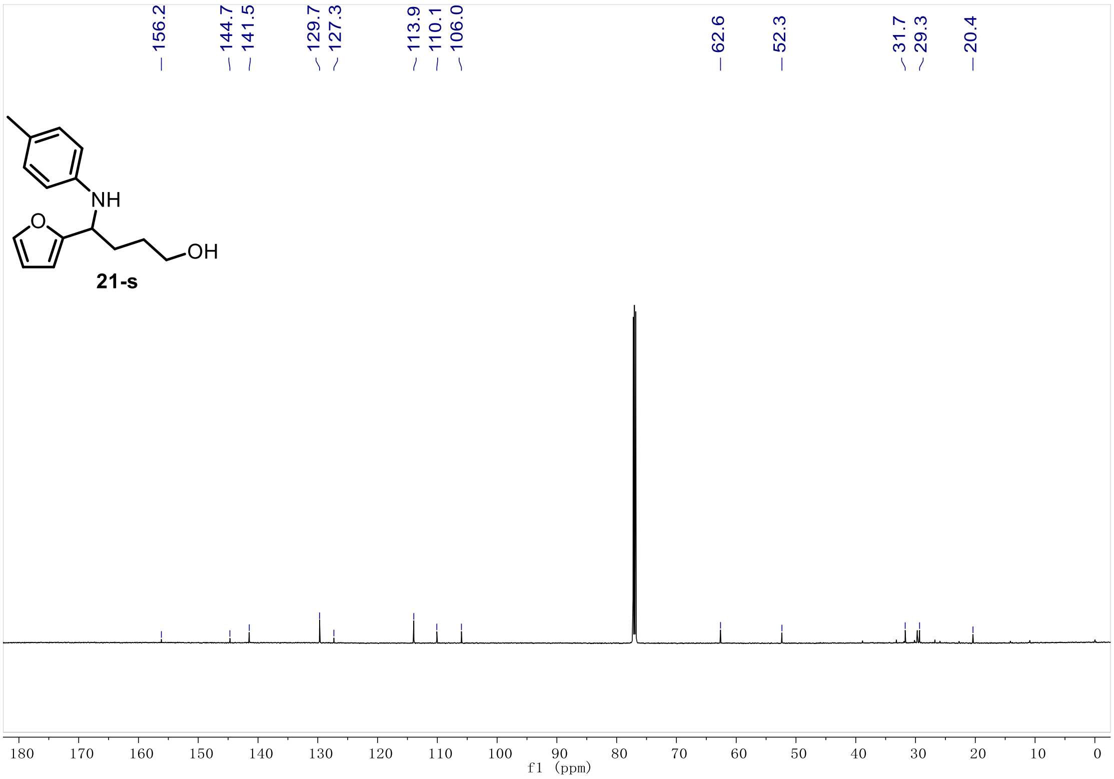
^{1}H NMR of compound **20** (400 MHz, CDCl$_3$)



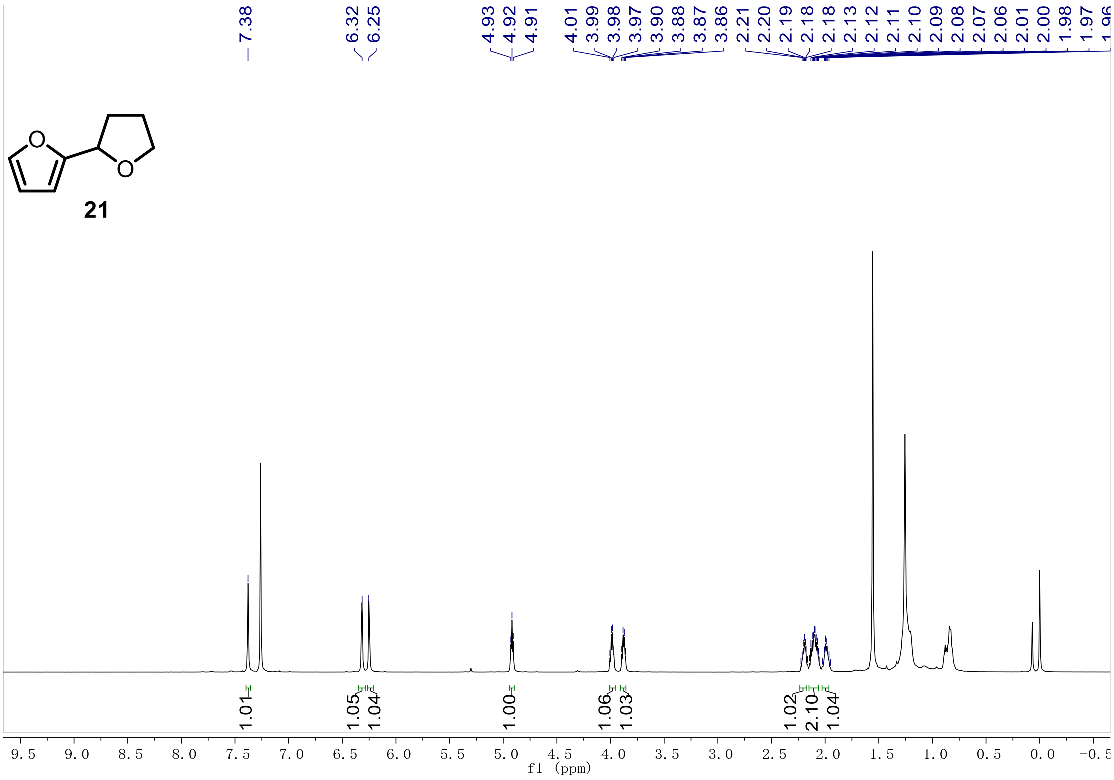
^{13}C NMR of compound **20** (101 MHz, CDCl$_3$)



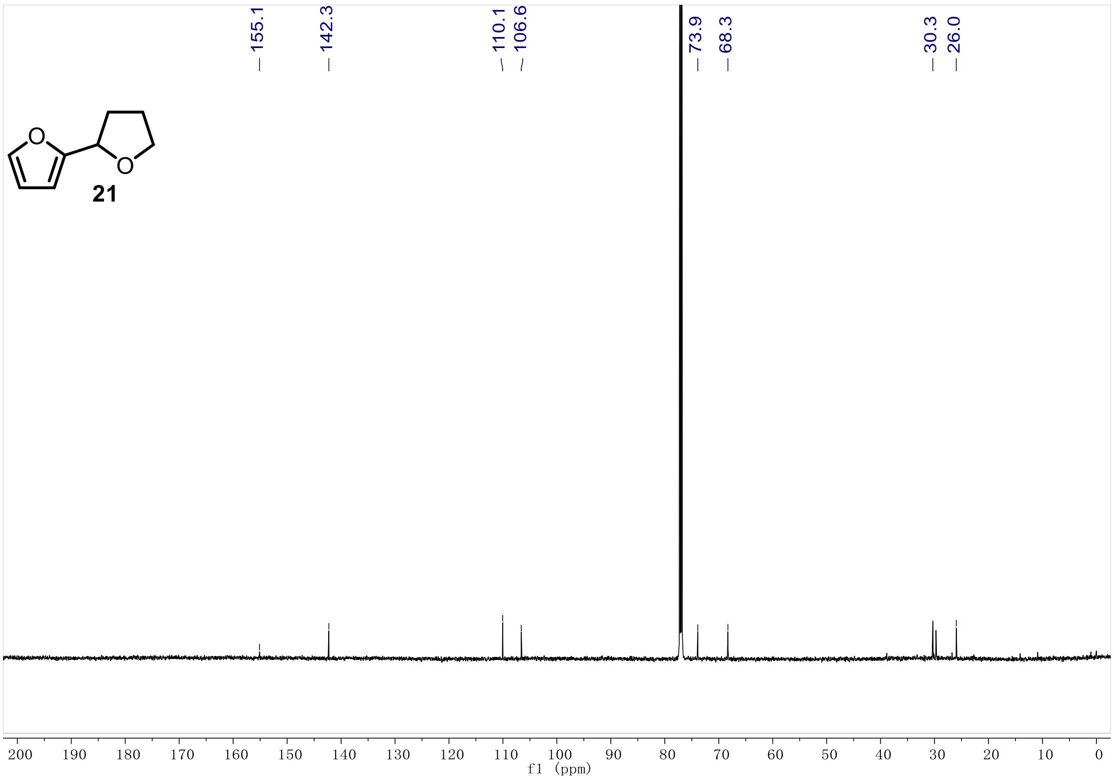
^{1}H NMR of compound **21-s** (600 MHz, $CDCl_3$)



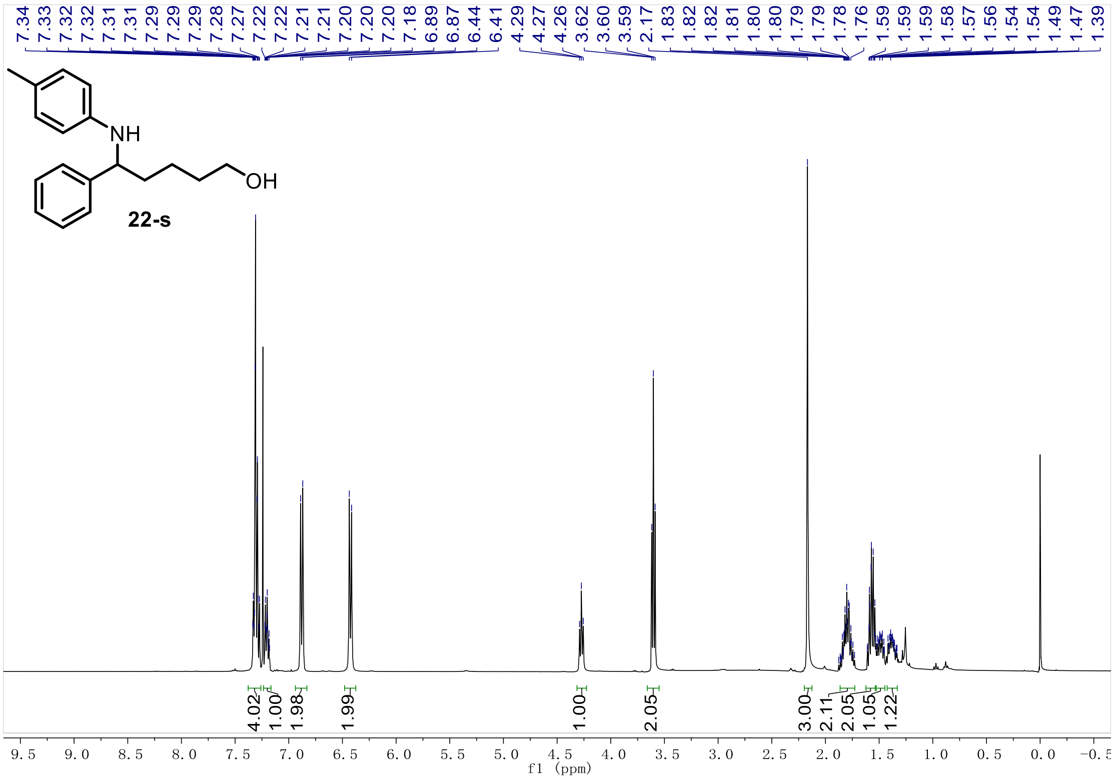
^{13}C NMR of compound **21-s** (151 MHz, $CDCl_3$)



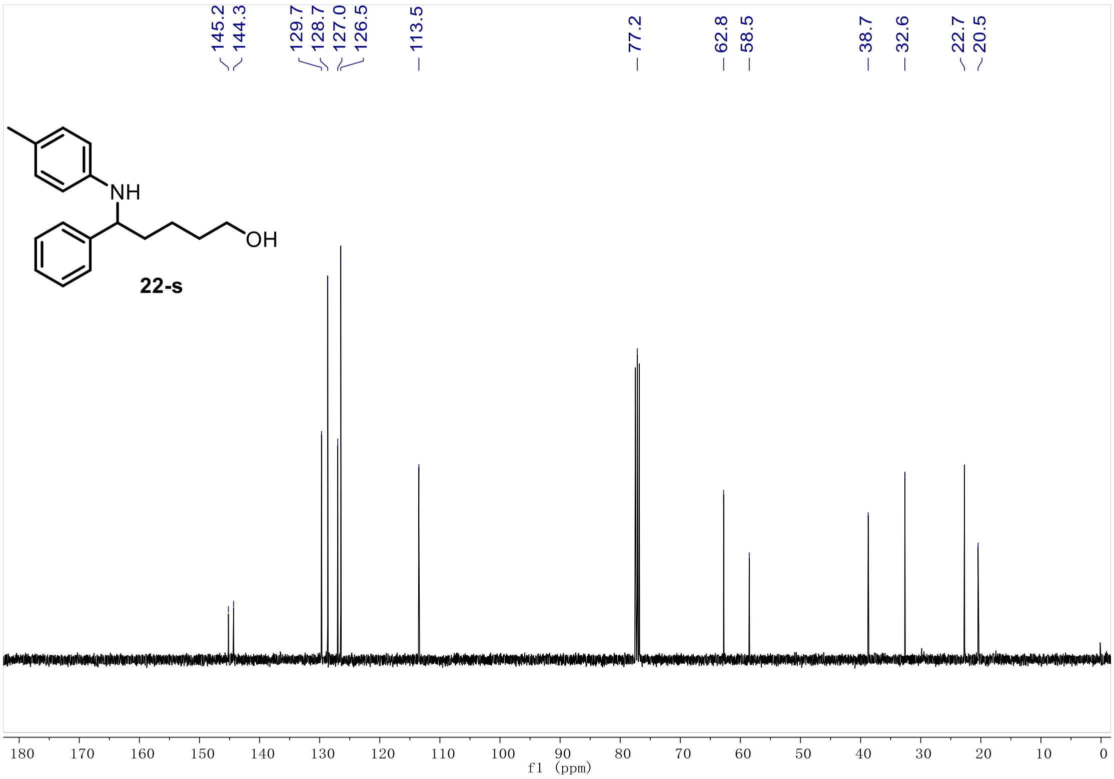
^{1}H NMR of compound **21** (600 MHz, $CDCl_3$)



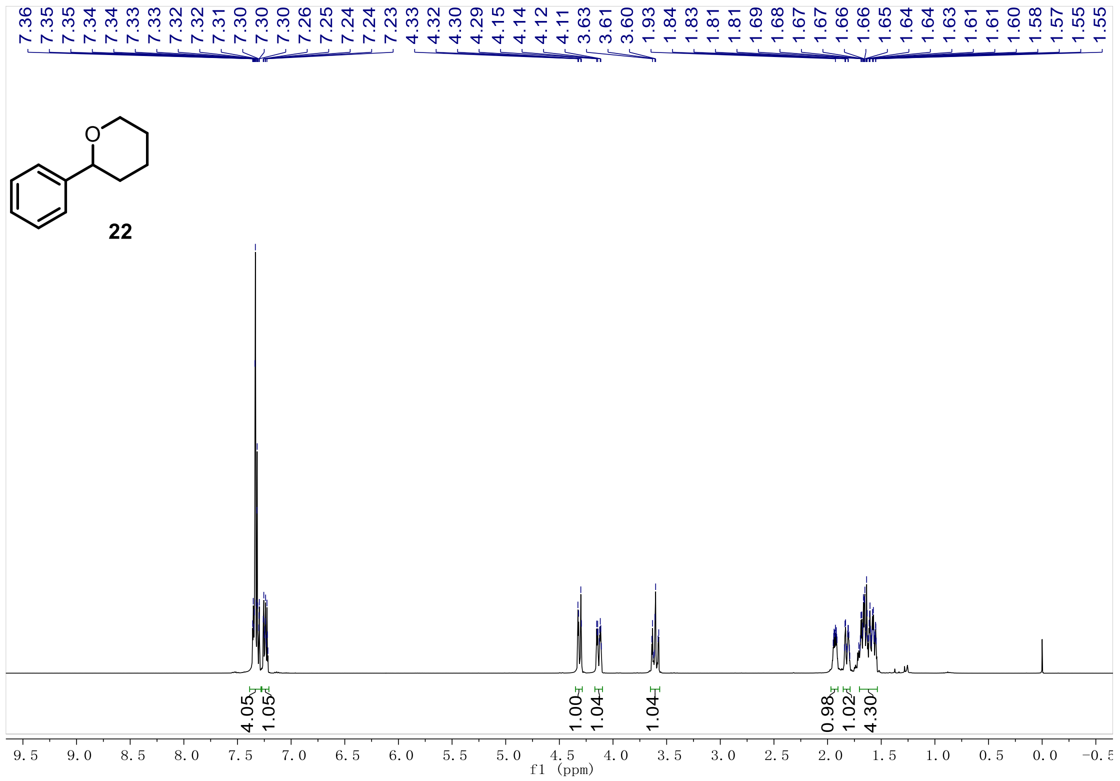
^{13}C NMR of compound **21** (151 MHz, $CDCl_3$)



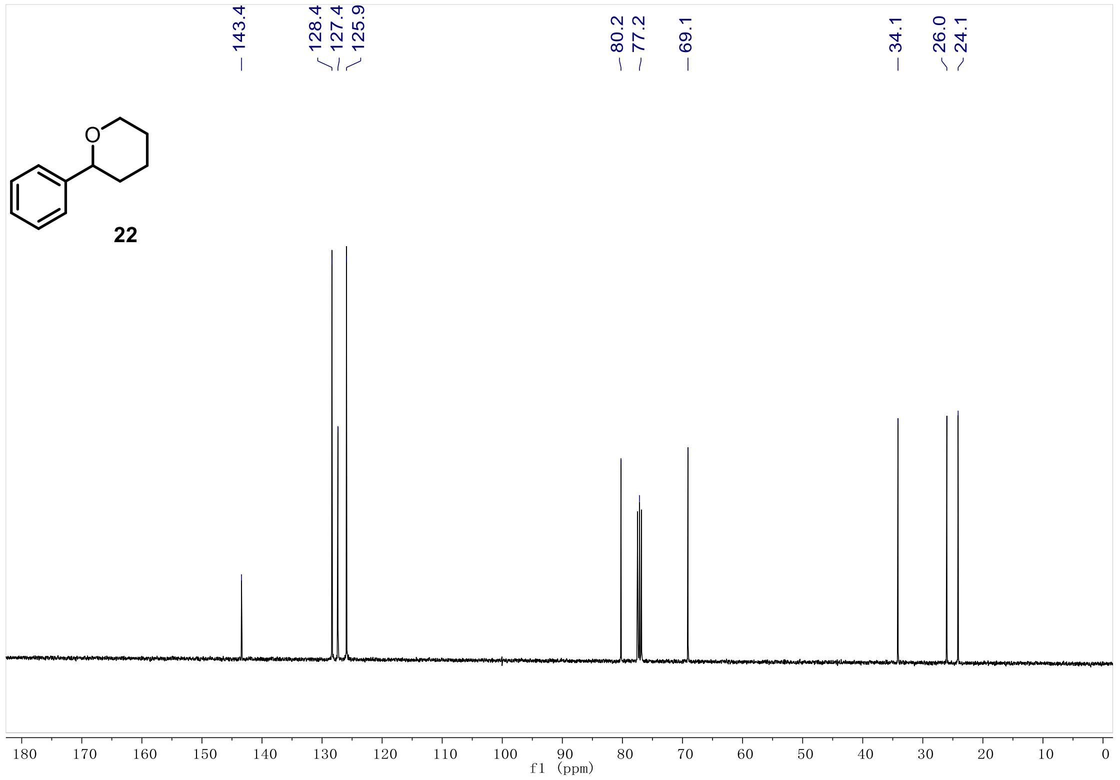
^{1}H NMR of compound **22-s** (400 MHz, $CDCl_3$)



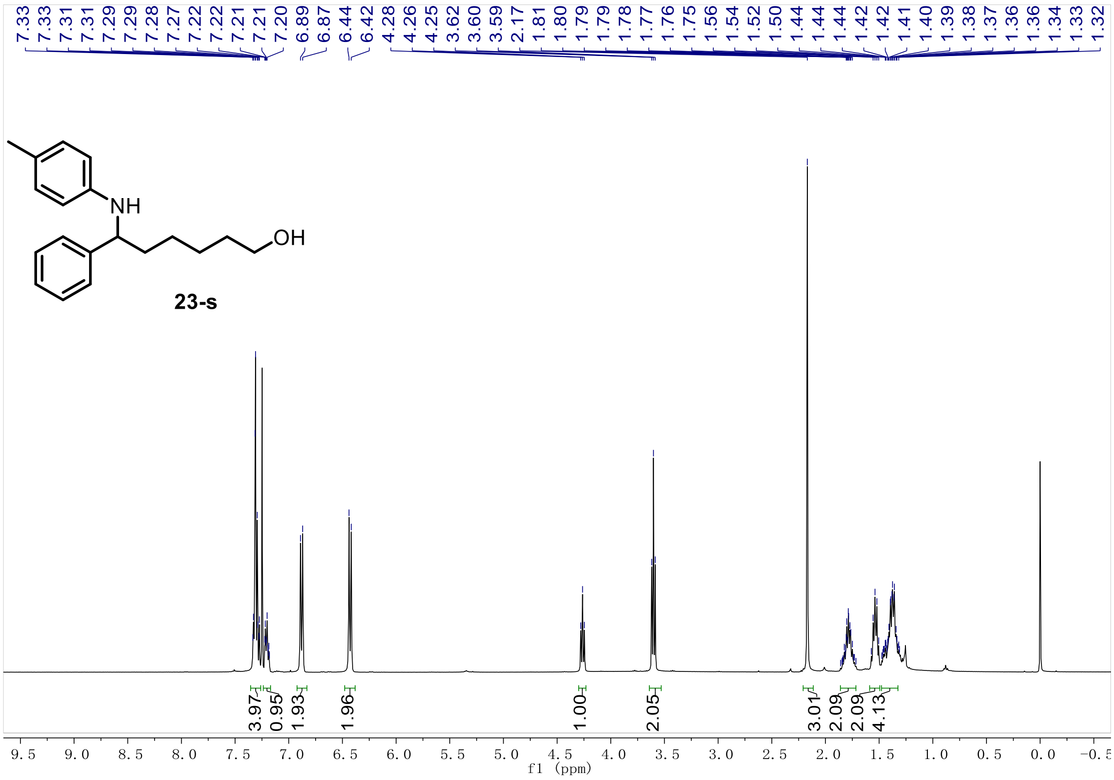
^{13}C NMR of compound **22-s** (101 MHz, $CDCl_3$)



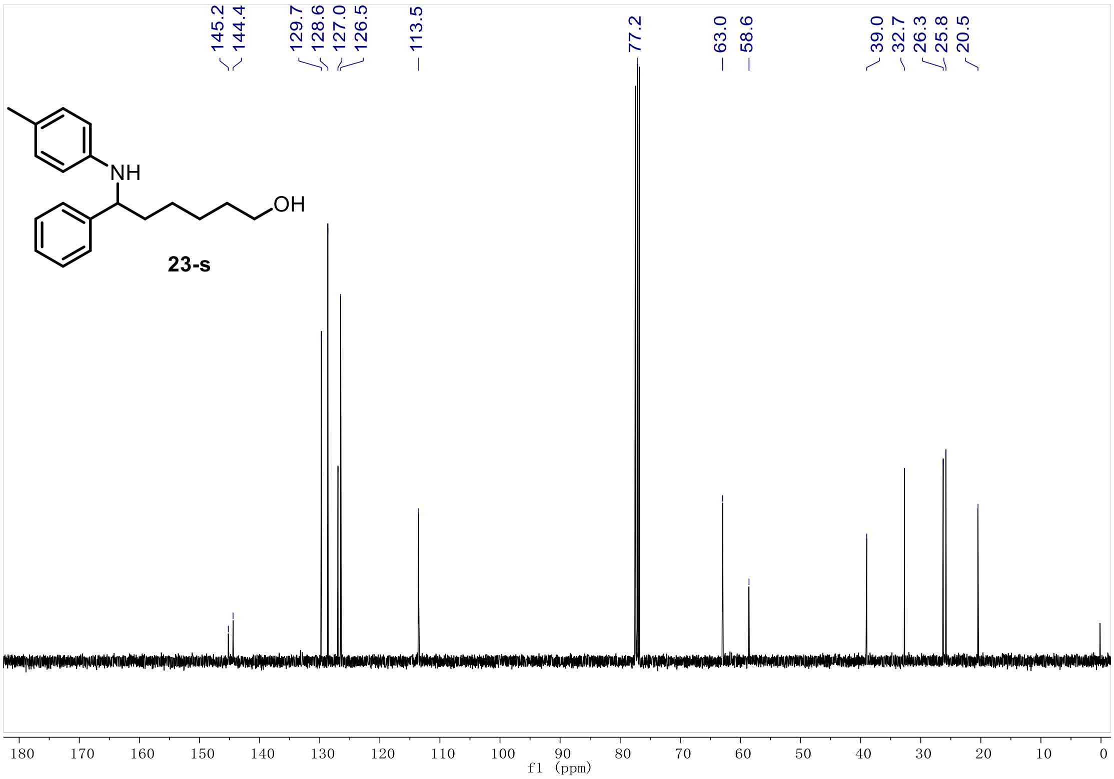
^{1}H NMR of compound **22** (400 MHz, $CDCl_3$)



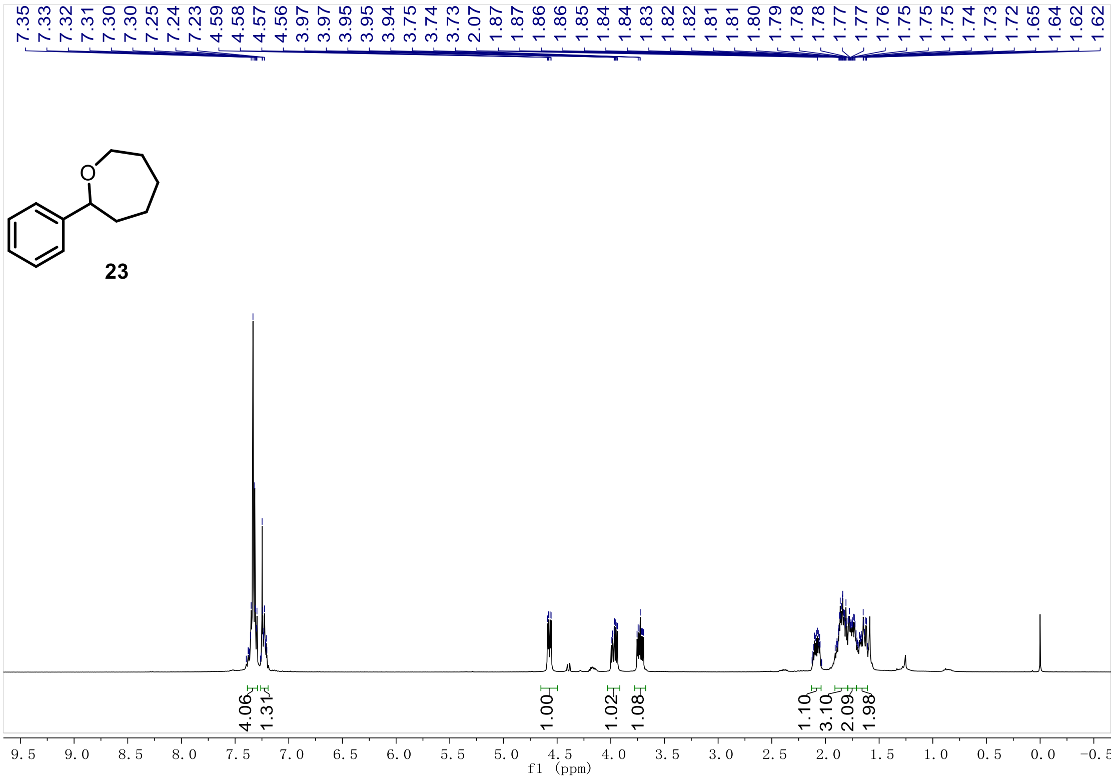
^{13}C NMR of compound **22** (101 MHz, $CDCl_3$)



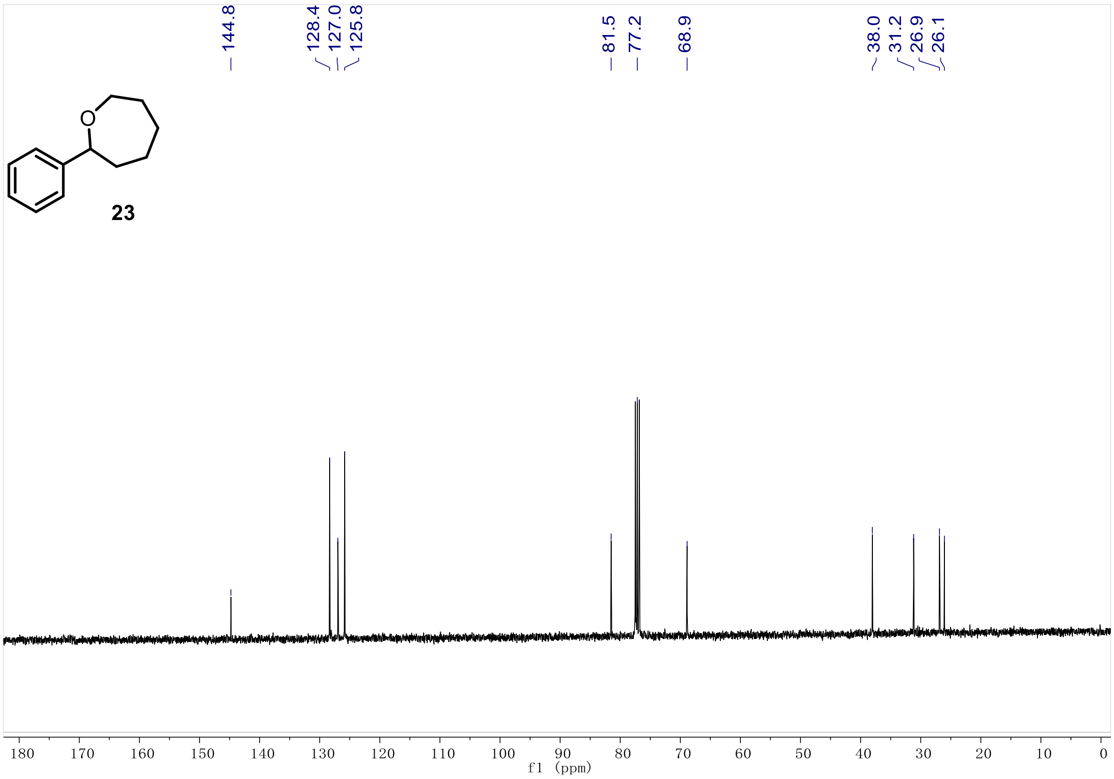
^{1}H NMR of compound **23-s** (400 MHz, $CDCl_3$)



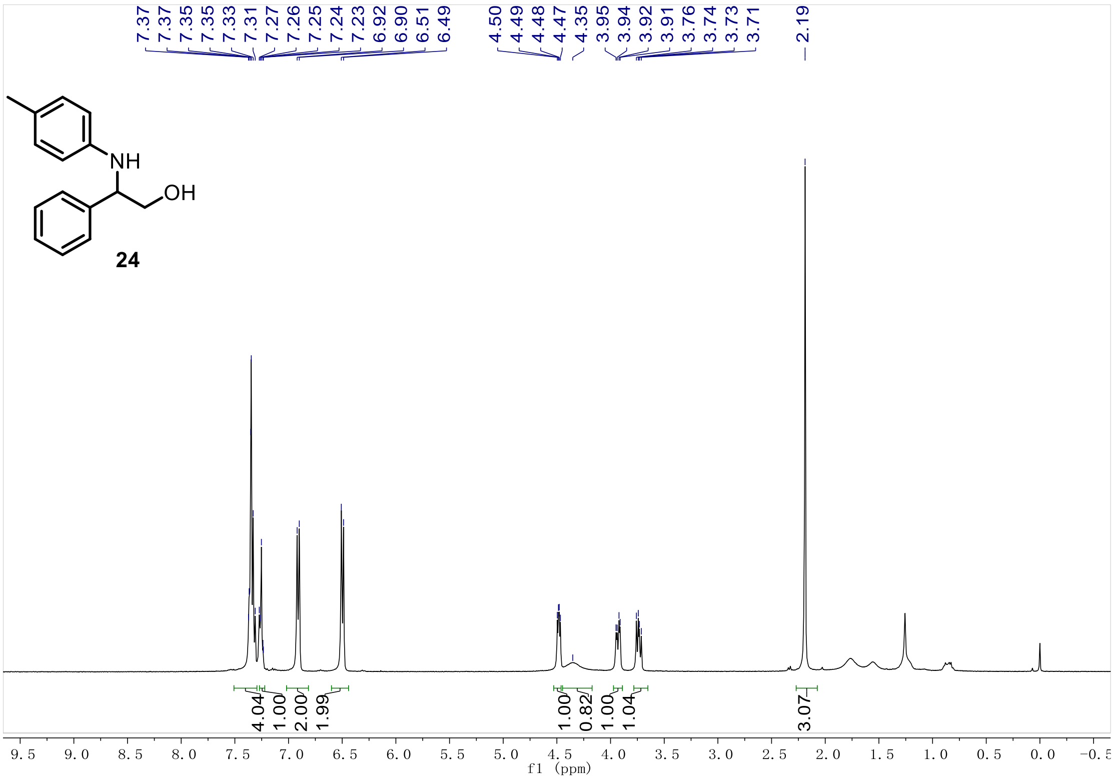
^{13}C NMR of compound **23-s** (101 MHz, $CDCl_3$)



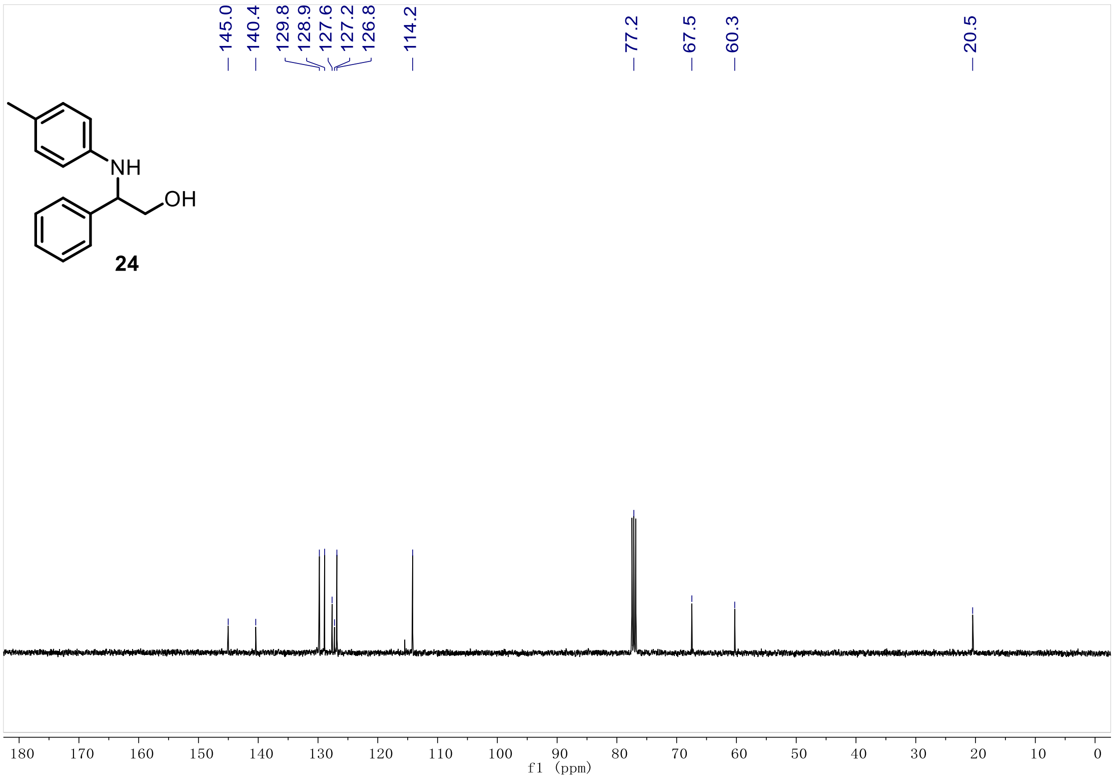
^{1}H NMR of compound **23** (400 MHz, $CDCl_3$)



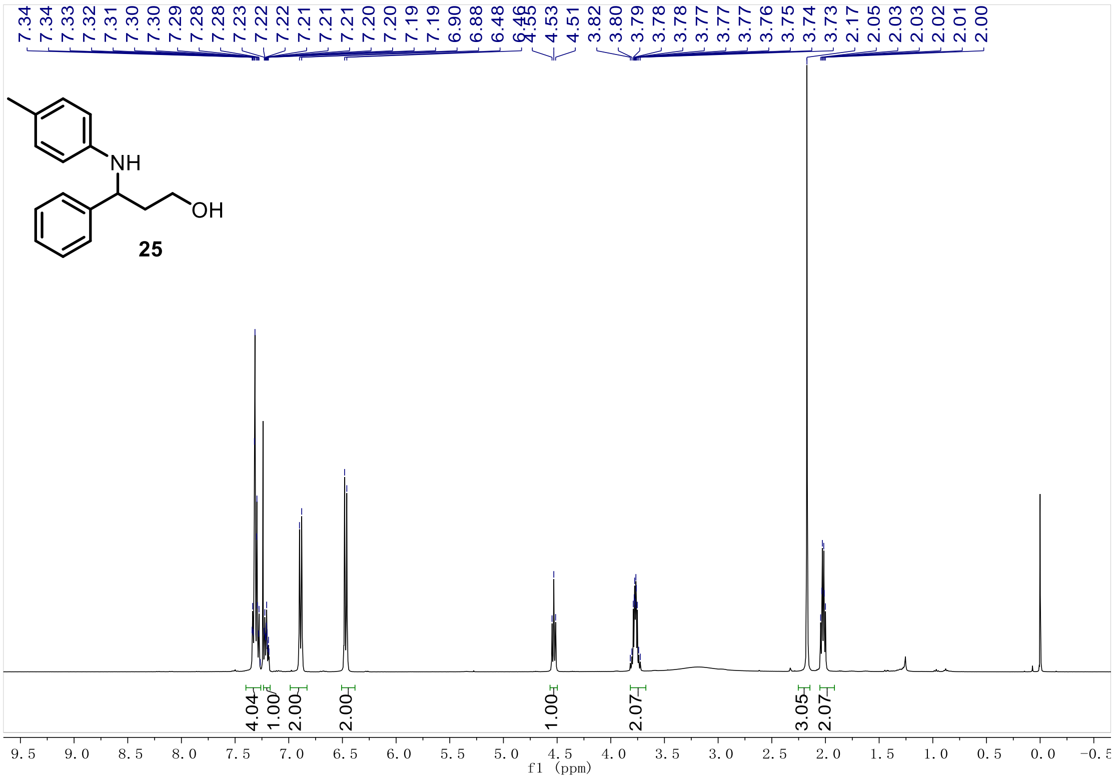
^{13}C NMR of compound **23** (101 MHz, $CDCl_3$)



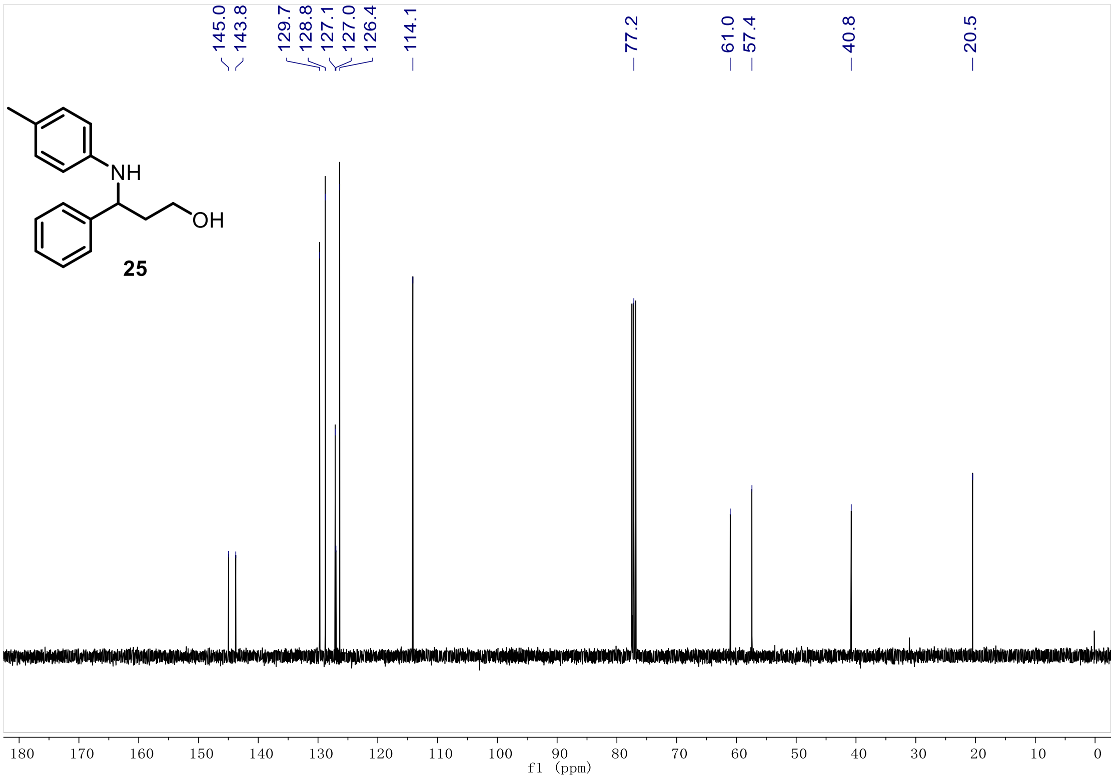
^{1}H NMR of compound **24** (400 MHz, CDCl$_3$)



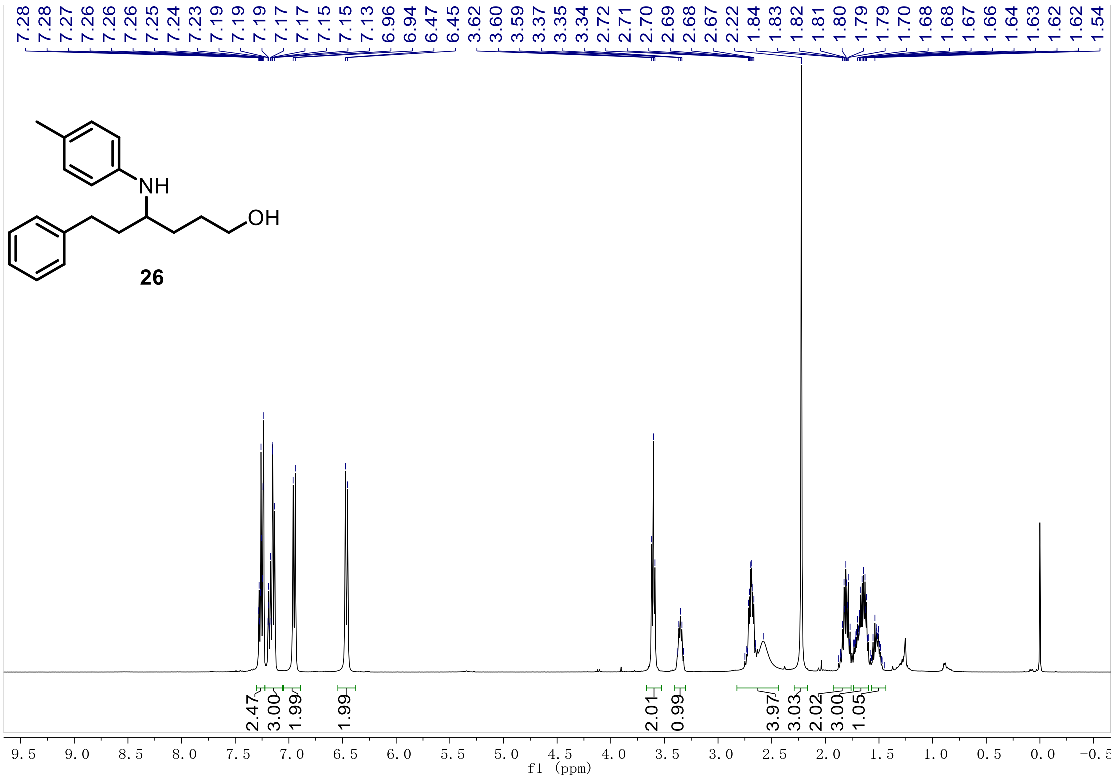
^{13}C NMR of compound **24** (101 MHz, CDCl$_3$)



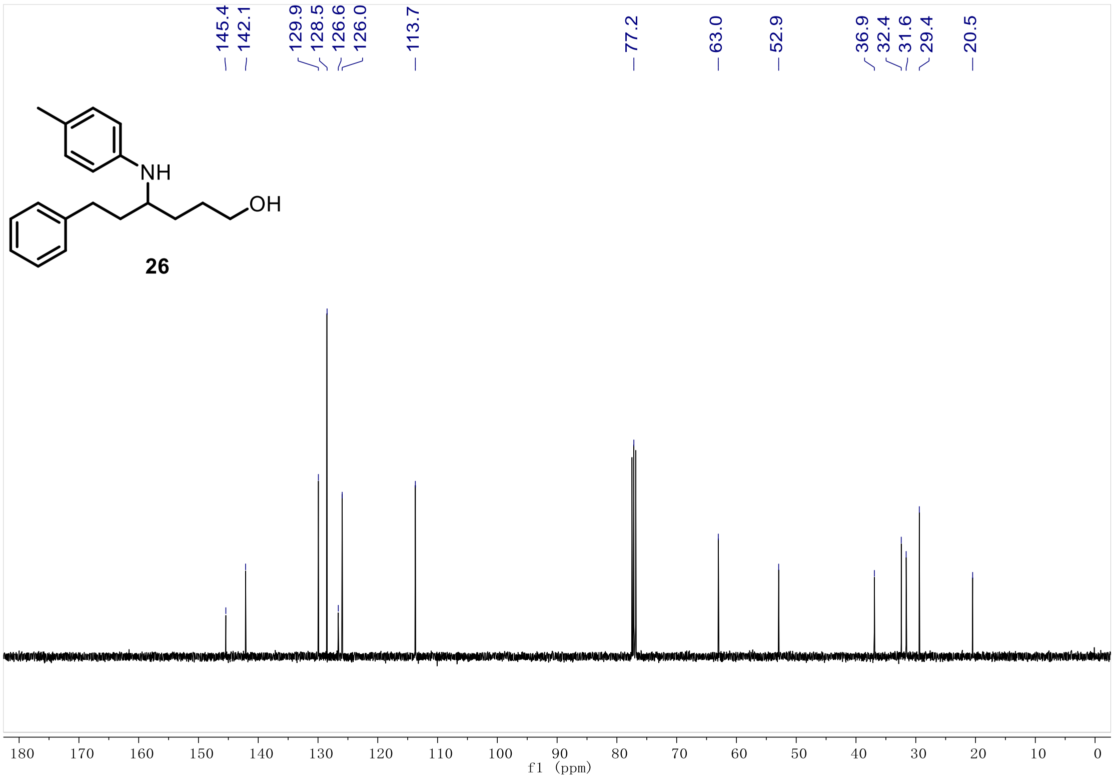
^{1}H NMR of compound **25** (400 MHz, $CDCl_3$)



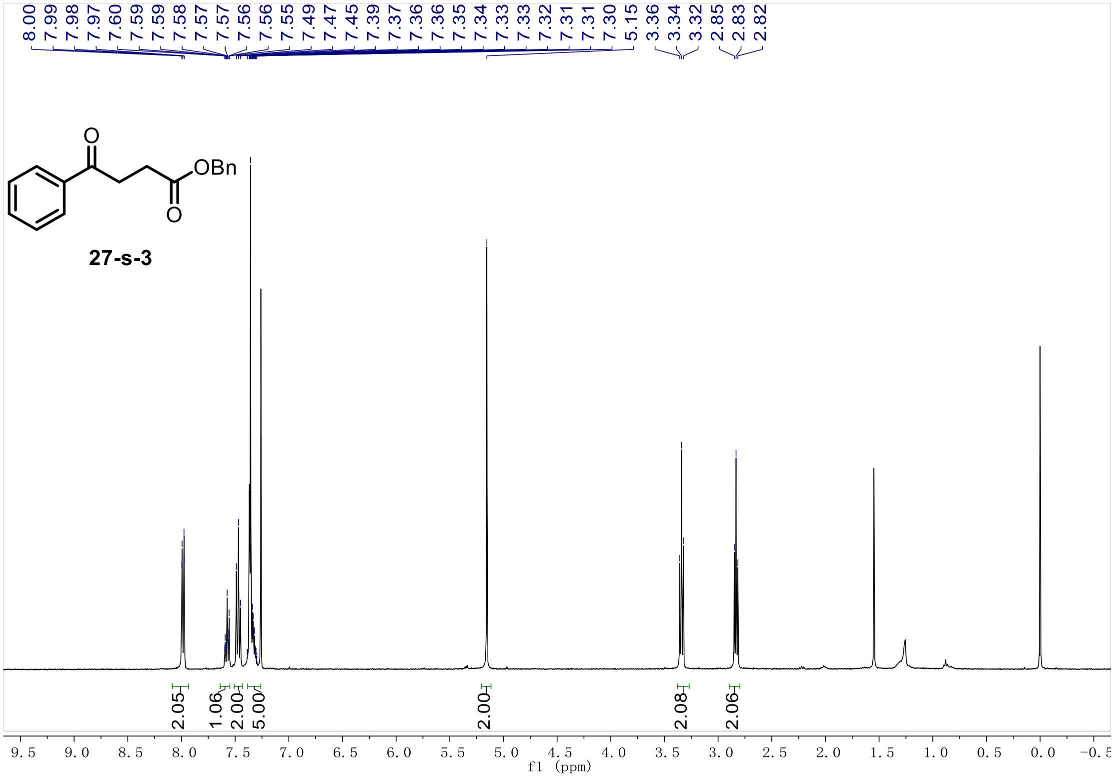
^{13}C NMR of compound **25** (101 MHz, $CDCl_3$)



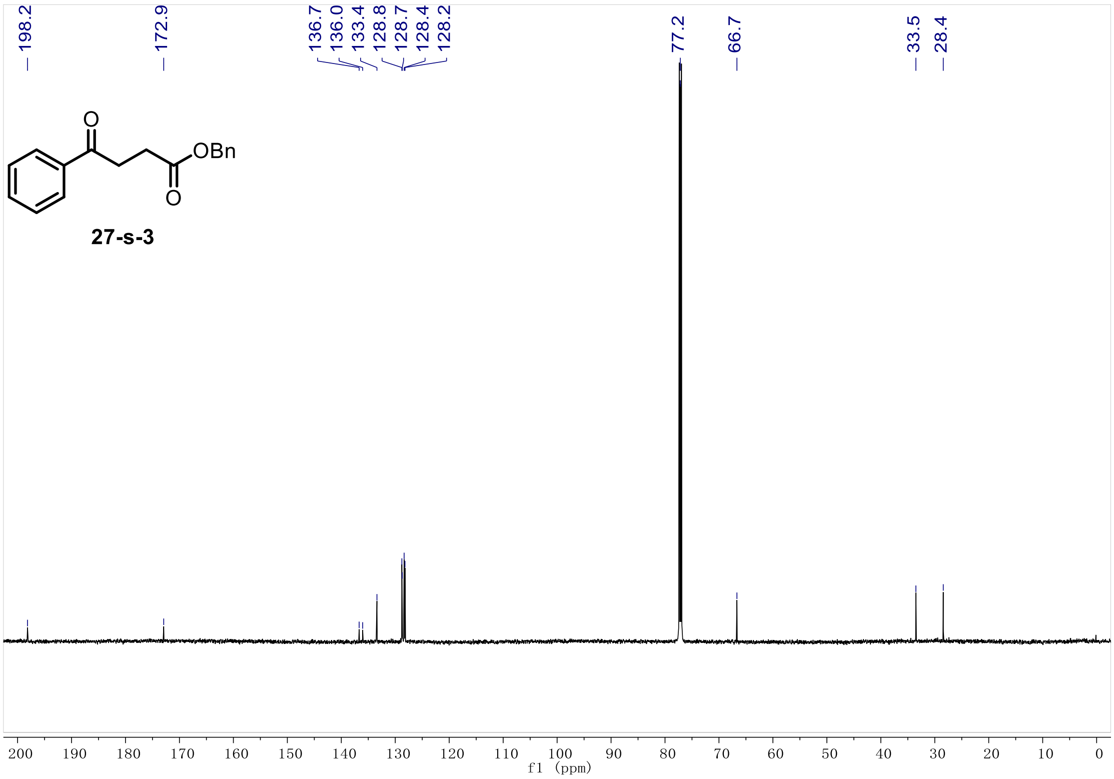
^{1}H NMR of compound **26** (400 MHz, CDCl$_3$)



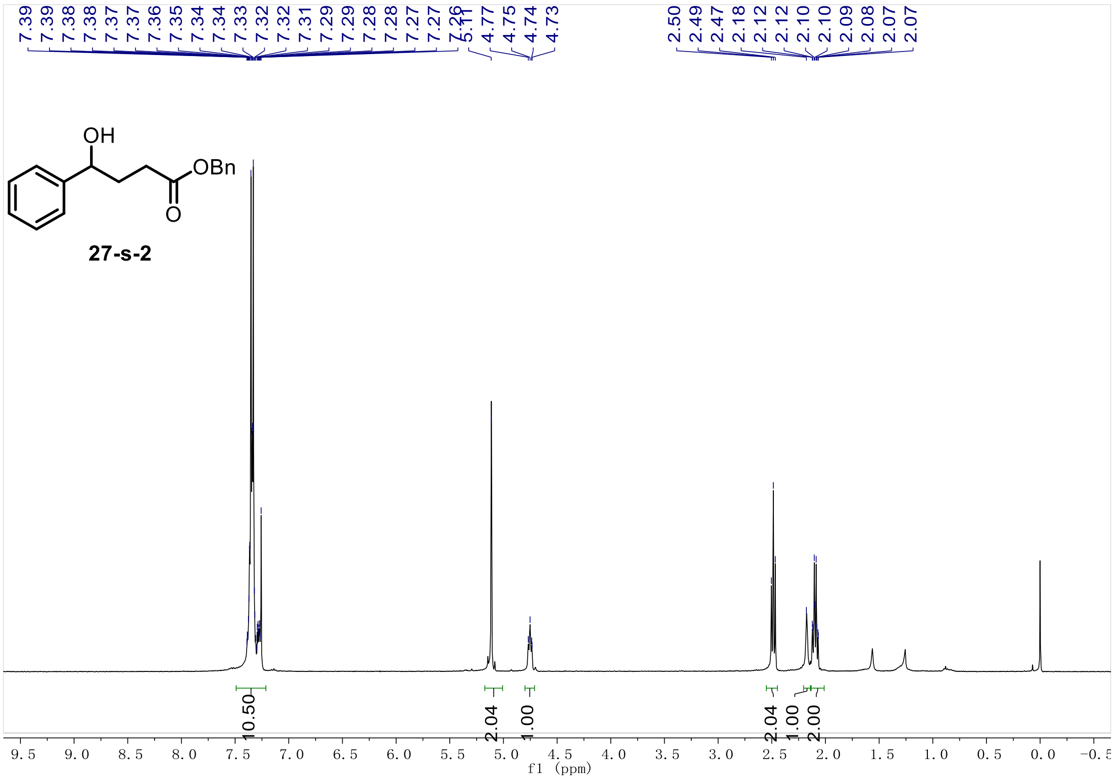
^{13}C NMR of compound **26** (101 MHz, CDCl$_3$)



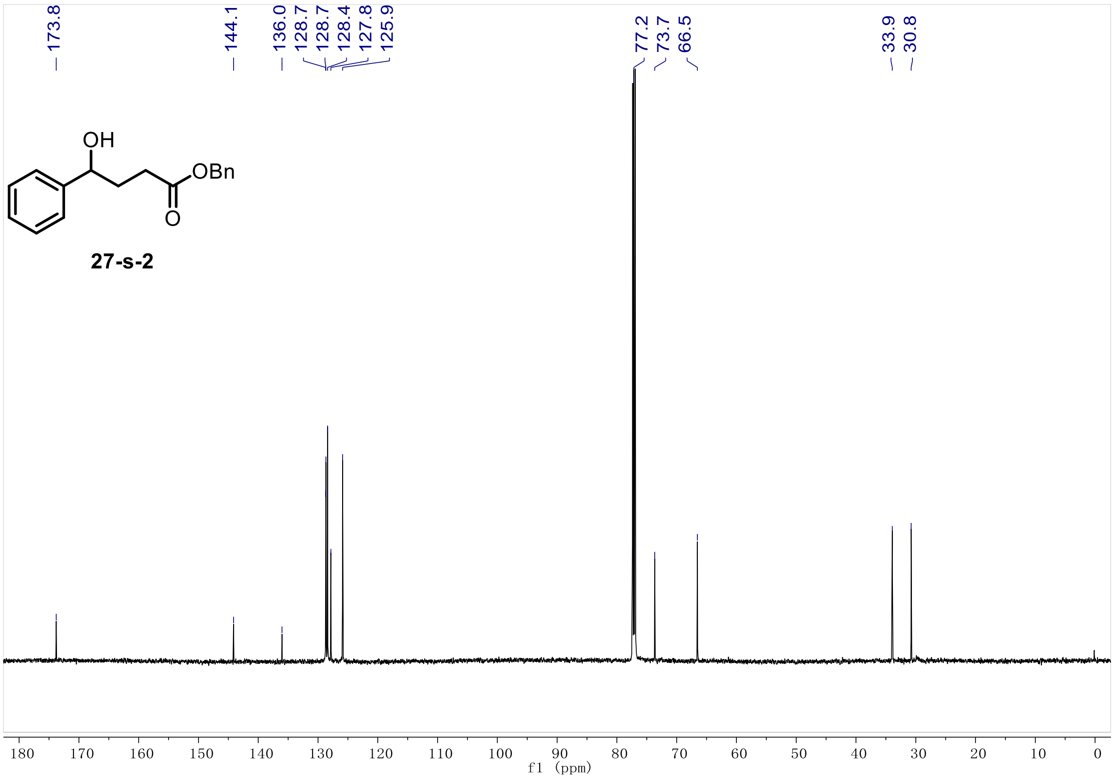
^{1}H NMR of compound **27-s-3** (400 MHz, $CDCl_3$)



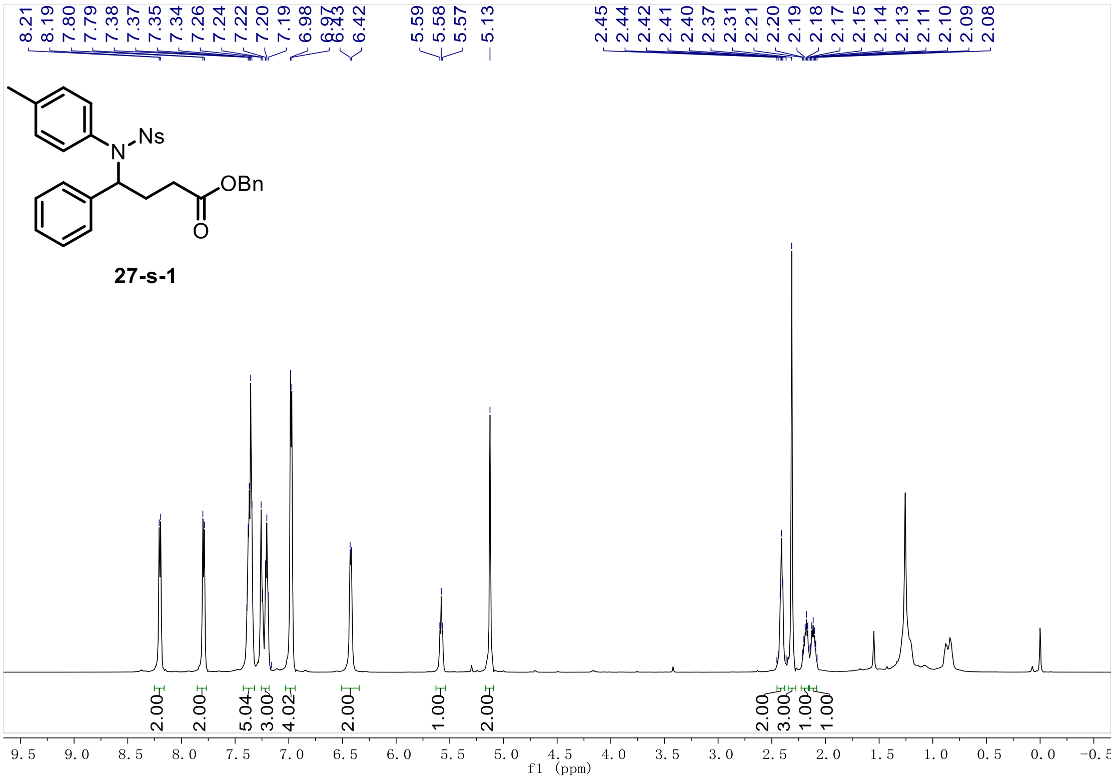
^{13}C NMR of compound **27-s-3** (151 MHz, $CDCl_3$)



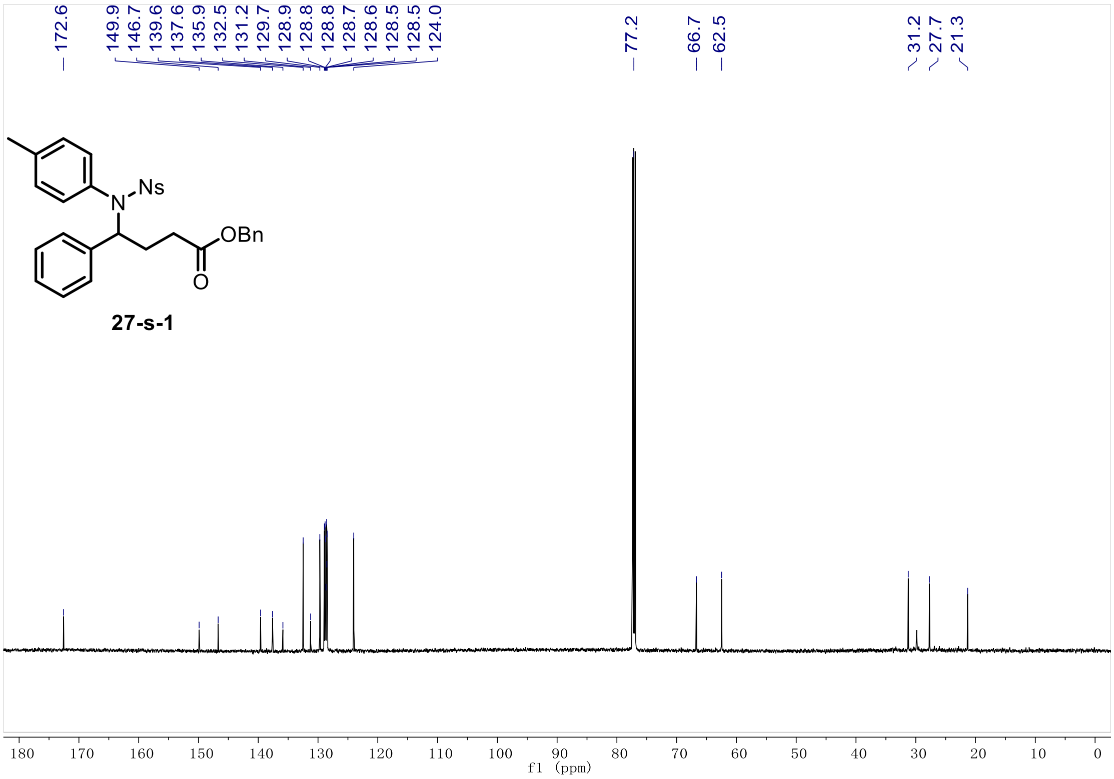
^{1}H NMR of compound **27-s-2** (400 MHz, $CDCl_3$)



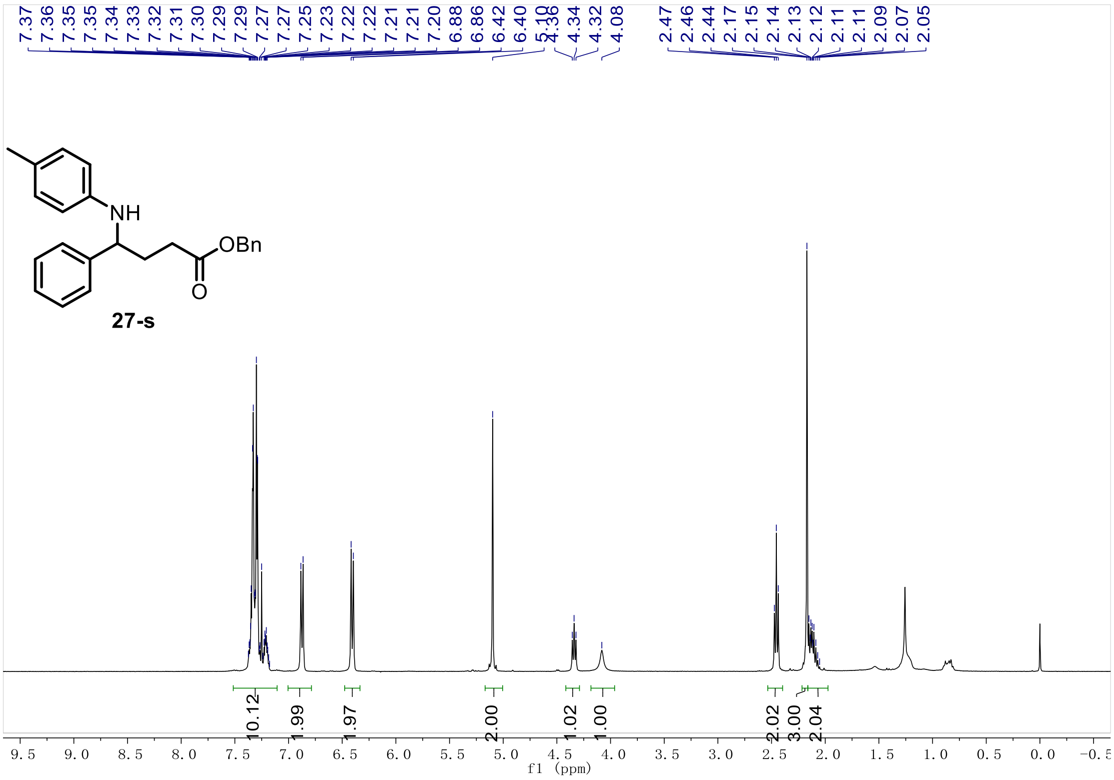
^{13}C NMR of compound **27-s-2** (151 MHz, $CDCl_3$)



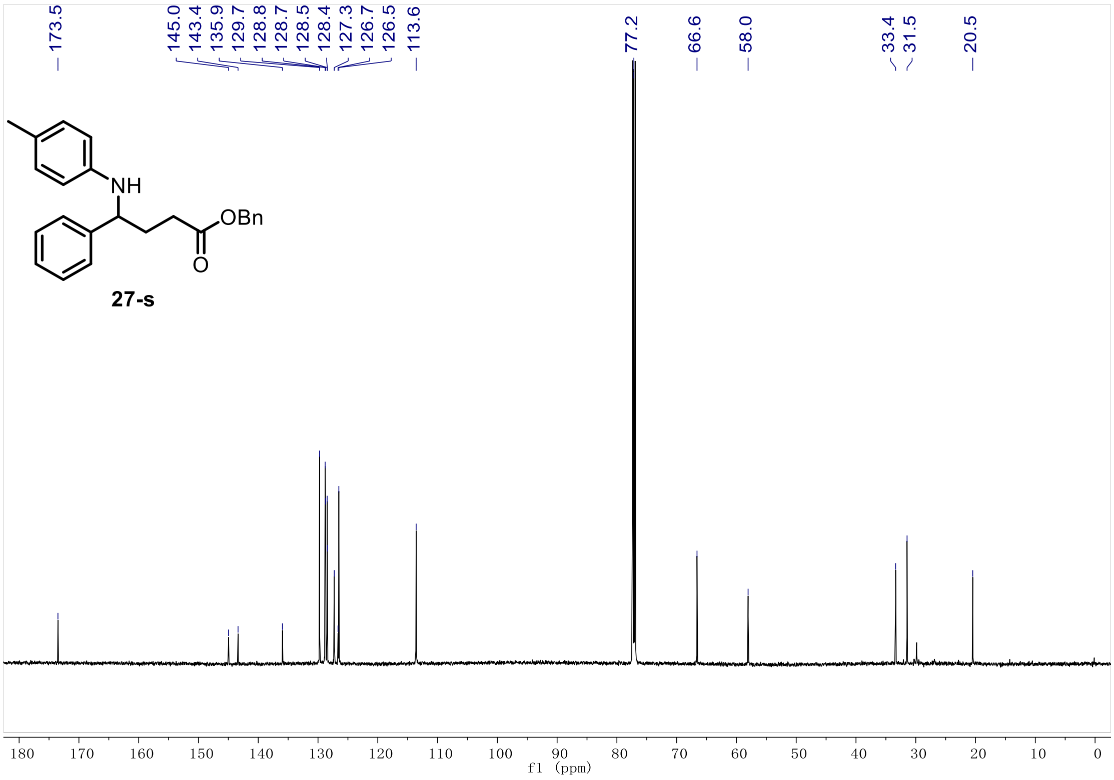
^{1}H NMR of compound **27-s-1** (600 MHz, $CDCl_3$)



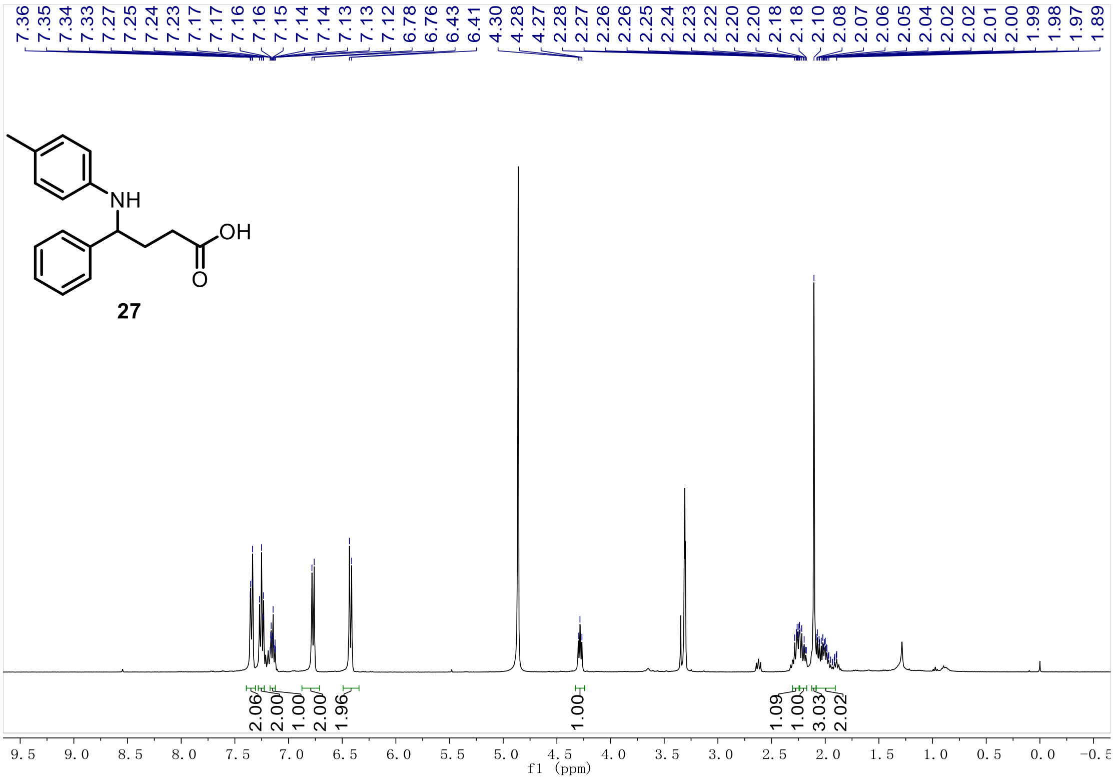
^{13}C NMR of compound **27-s-1** (151 MHz, $CDCl_3$)



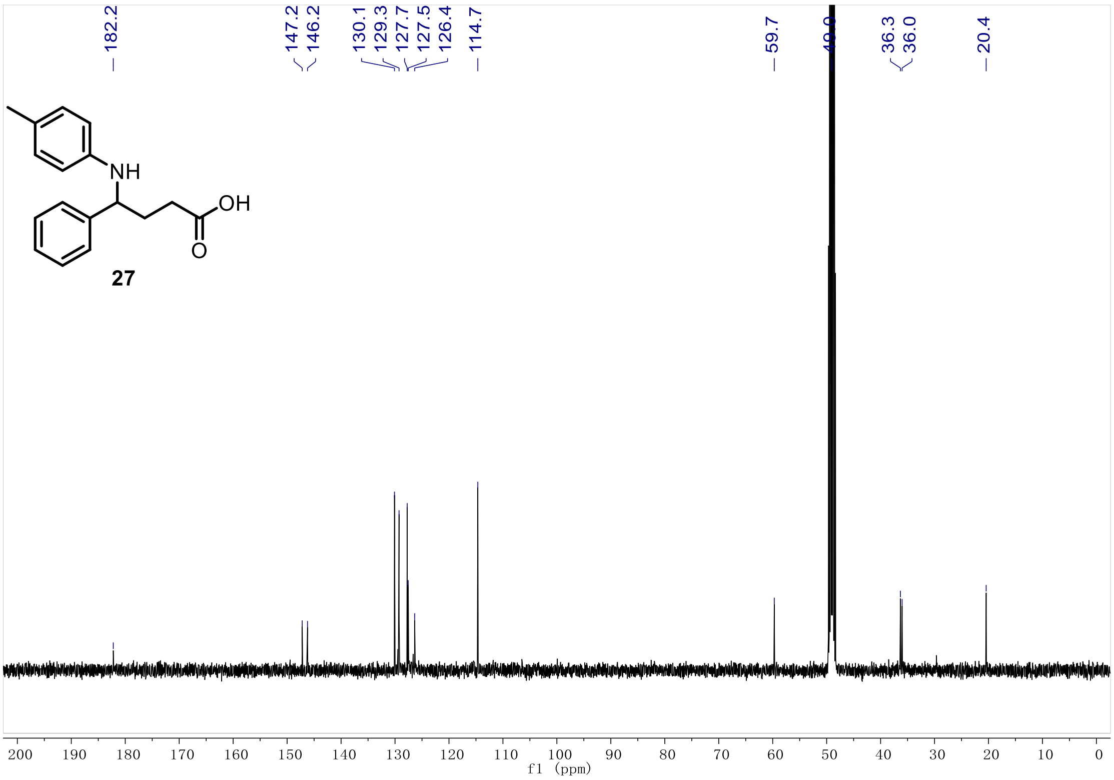
^{1}H NMR of compound **27-s** (400 MHz, $CDCl_3$)



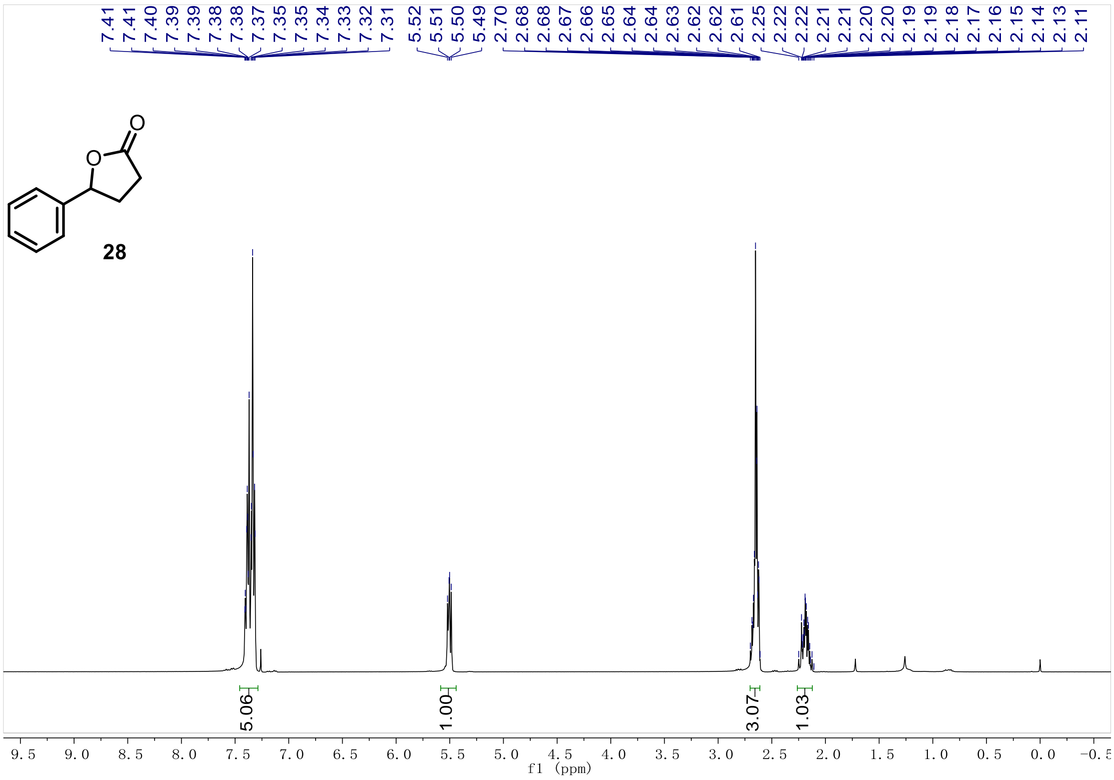
^{13}C NMR of compound **27-s** (151 MHz, $CDCl_3$)



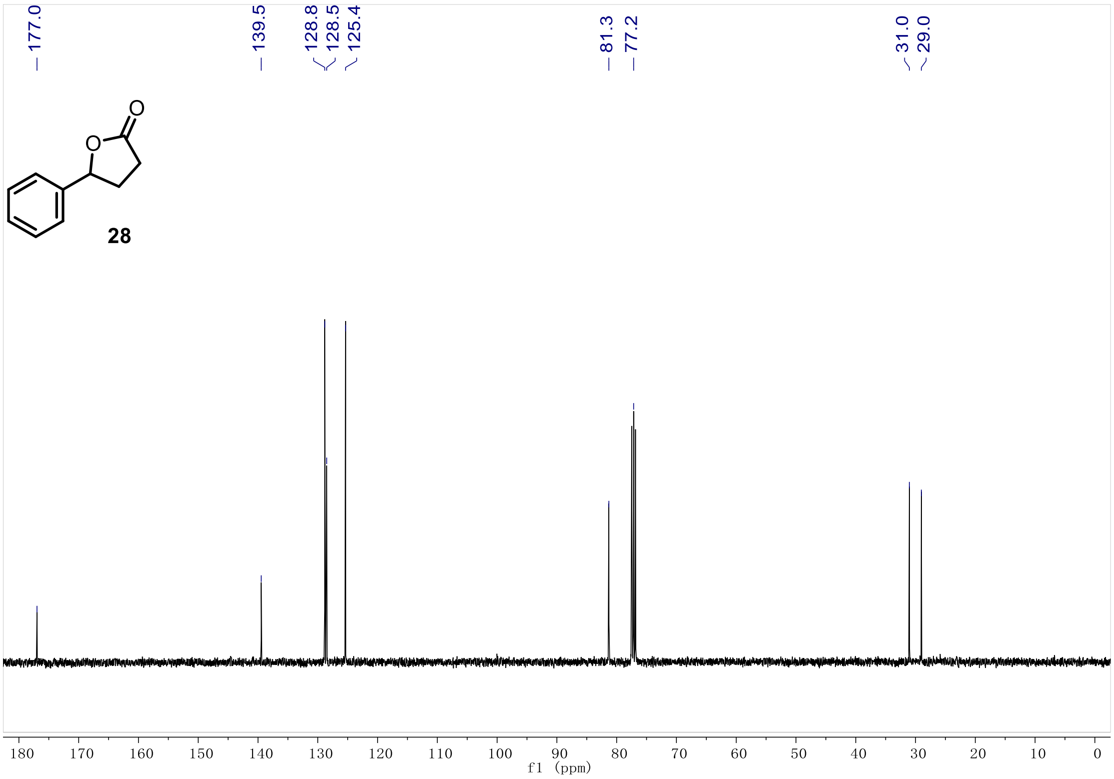
^{1}H NMR of compound **27** (400 MHz, $CDCl_3$)



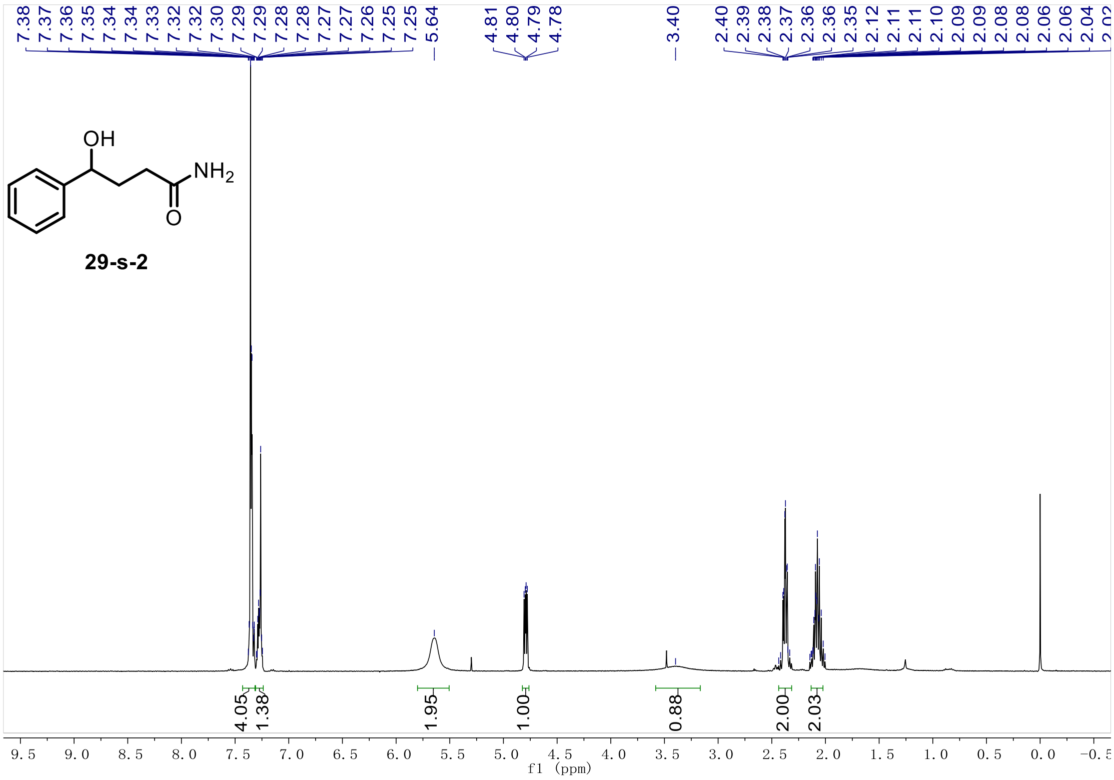
^{13}C NMR of compound **27** (101 MHz, $CDCl_3$)



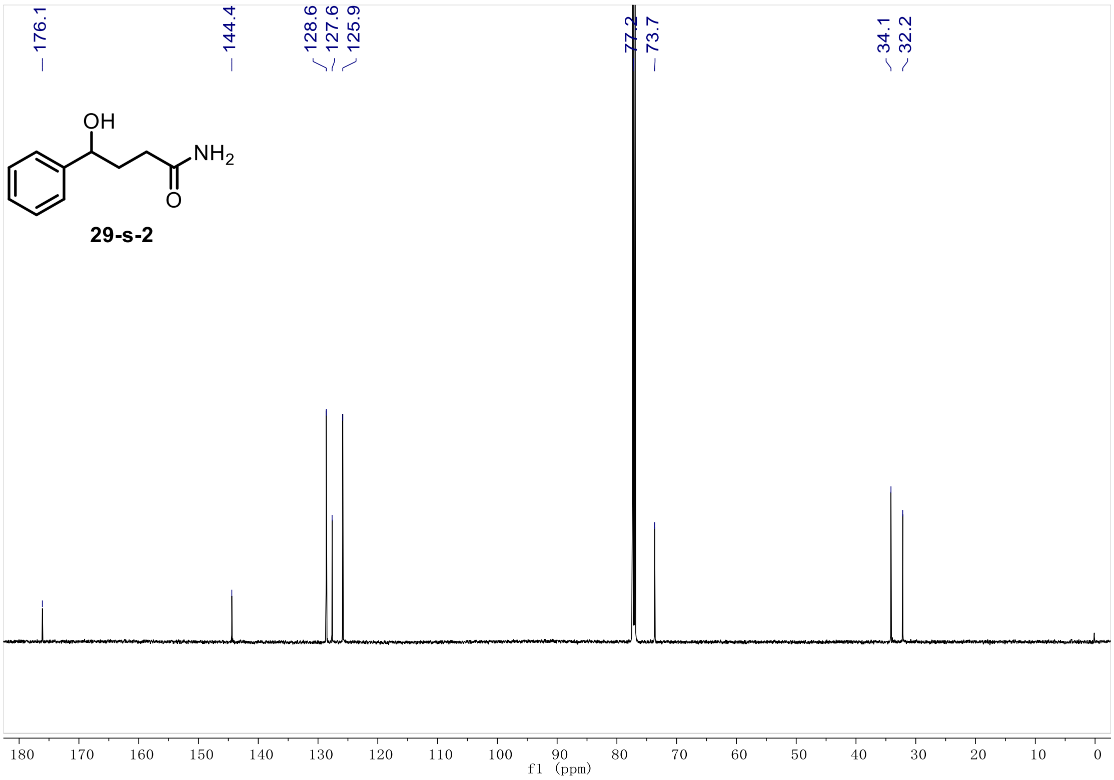
^{1}H NMR of compound **28** (400 MHz, CDCl$_3$)



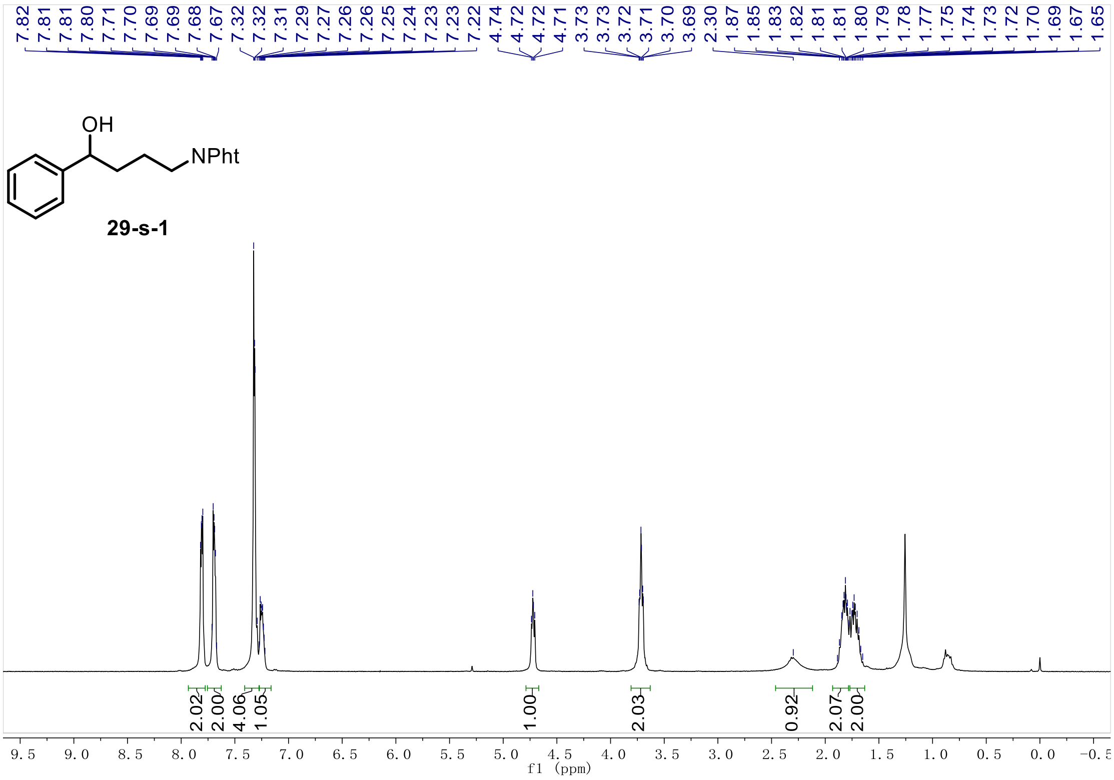
^{13}C NMR of compound **28** (101 MHz, CDCl$_3$)



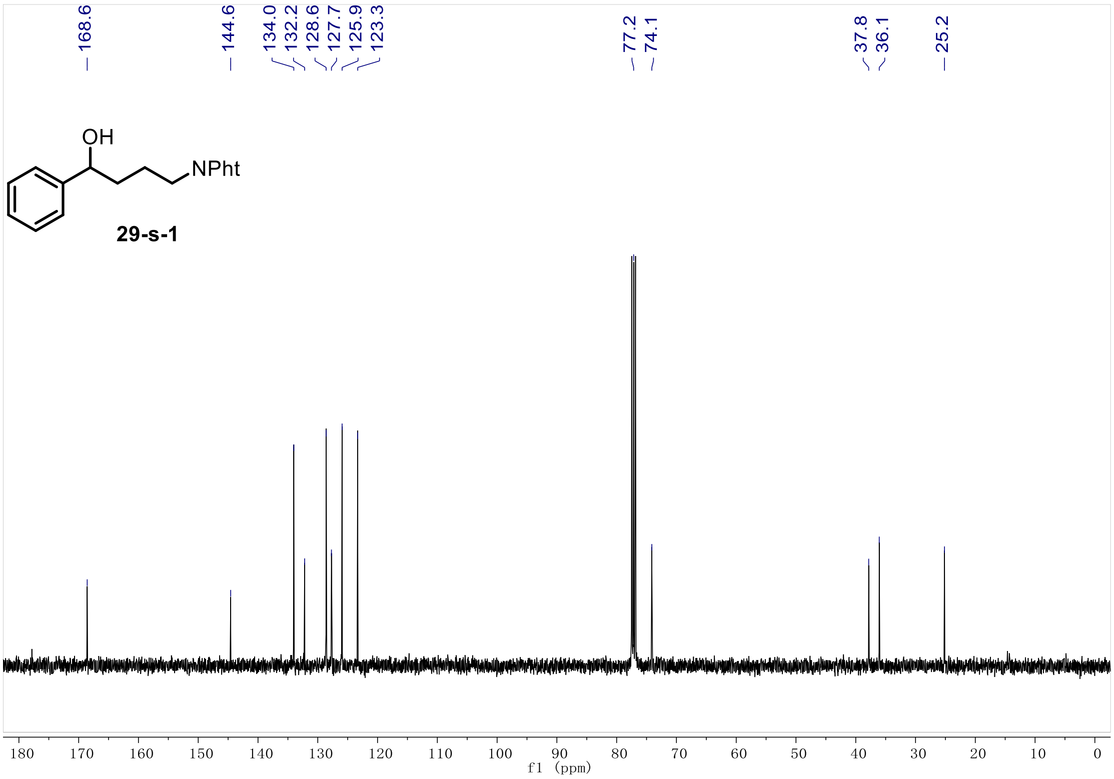
^{1}H NMR of compound **29-s-2** (400 MHz, CDCl$_3$)



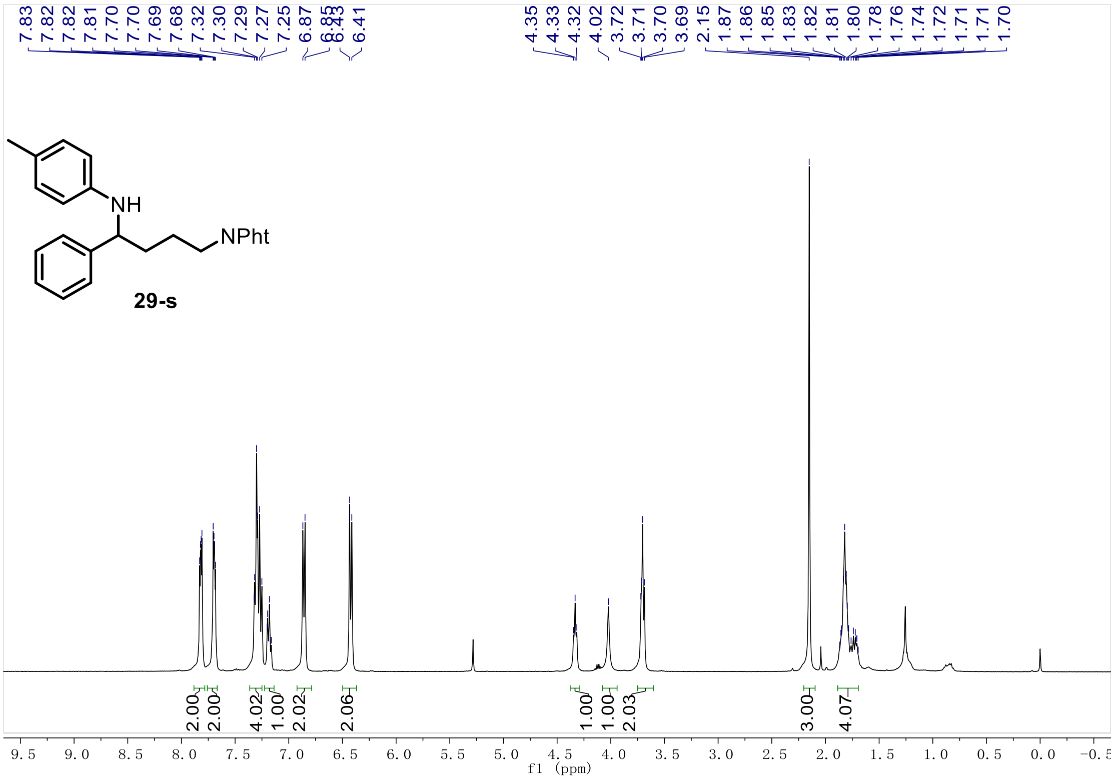
^{13}C NMR of compound **29-s-2** (151 MHz, CDCl$_3$)



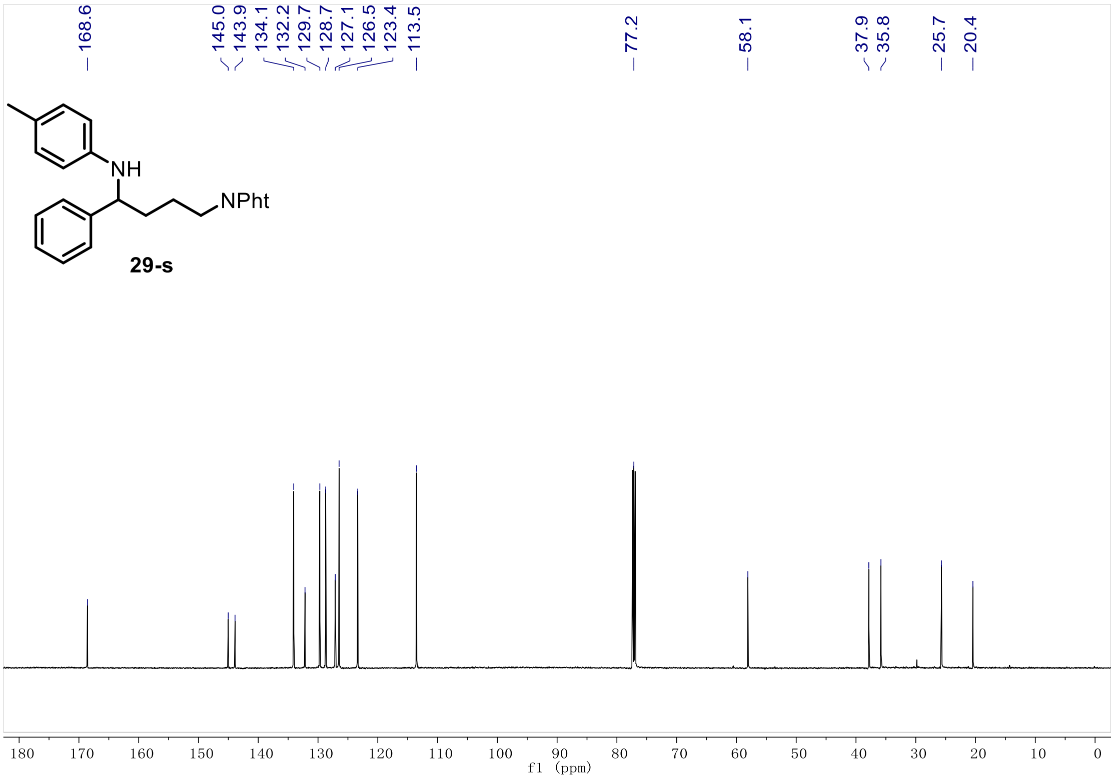
^{1}H NMR of compound **29-s-1** (400 MHz, CDCl$_3$)



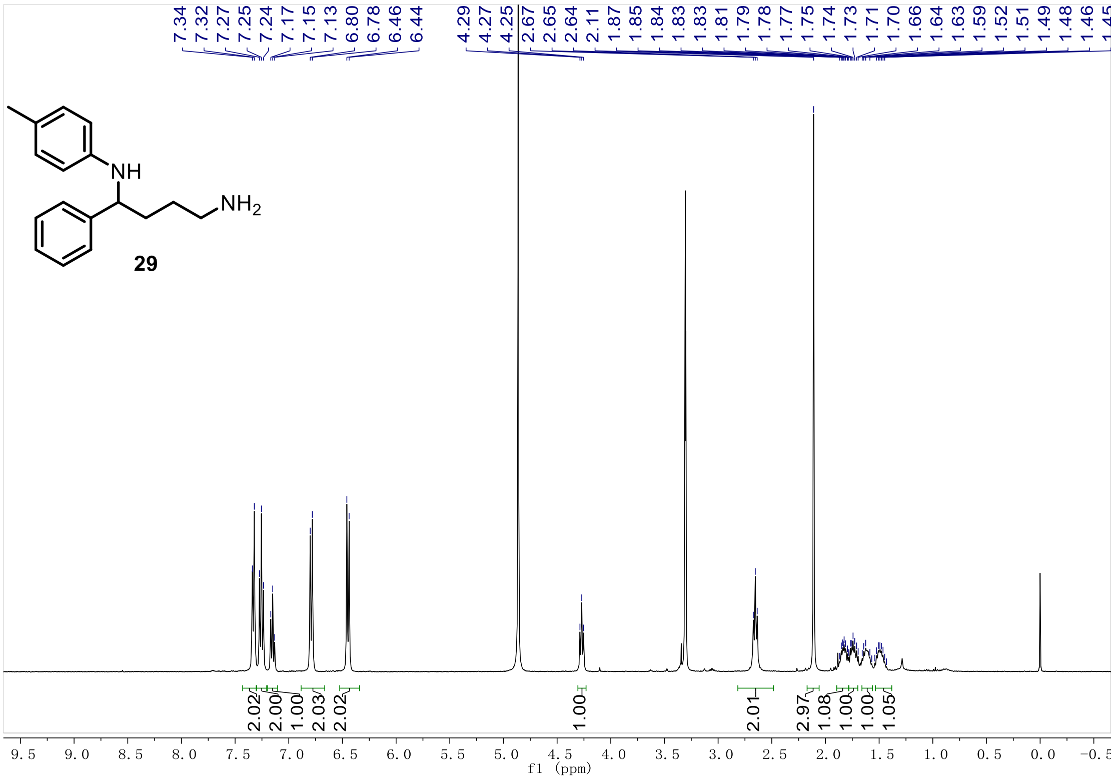
^{13}C NMR of compound **29-s-1** (101 MHz, CDCl$_3$)



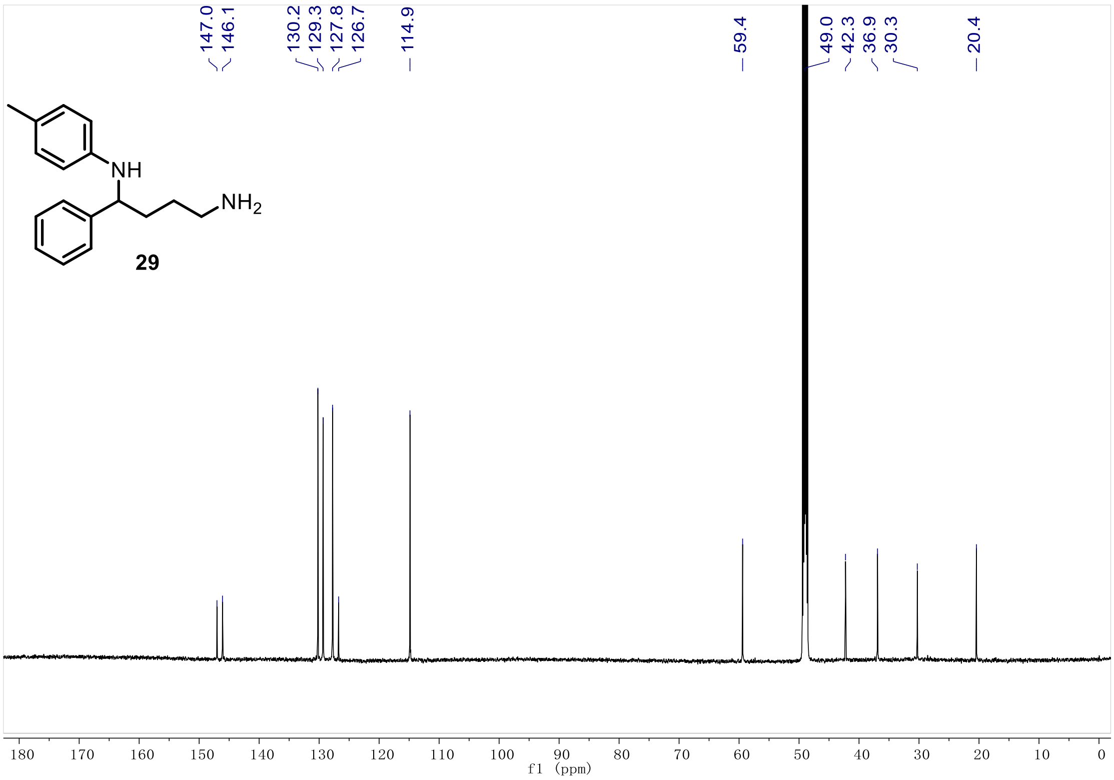
^{1}H NMR of compound **29-s** (400 MHz, CDCl$_3$)



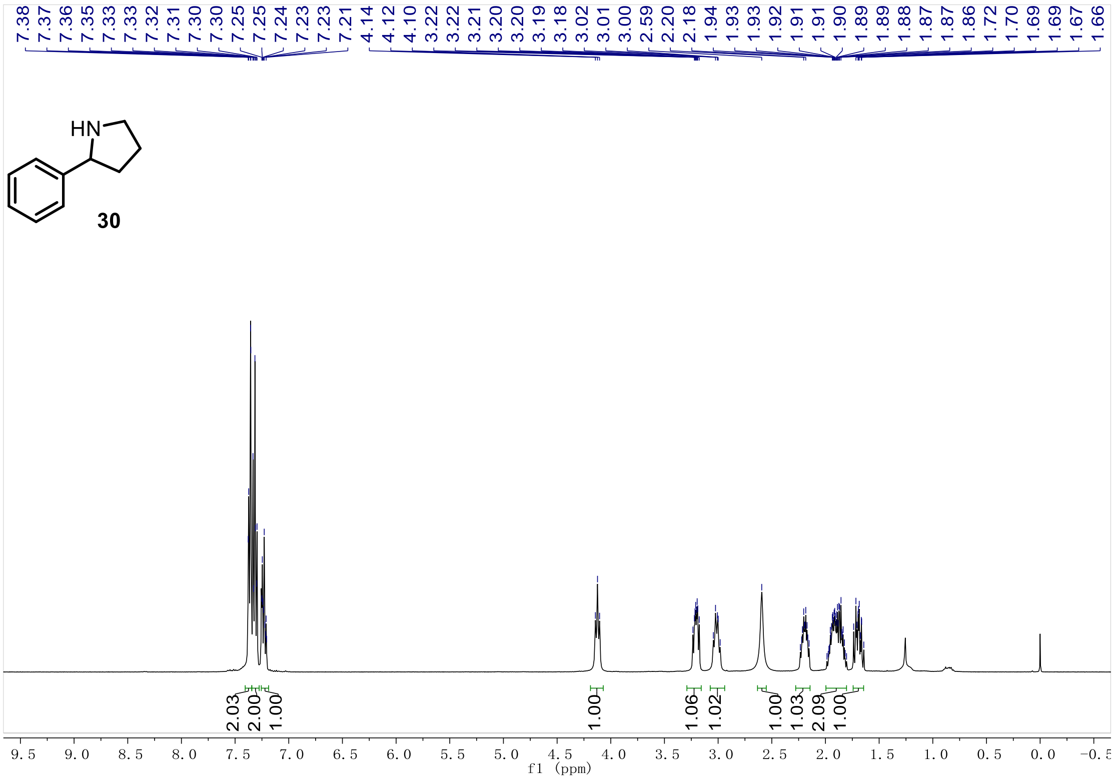
^{13}C NMR of compound **29-s** (151 MHz, CDCl$_3$)



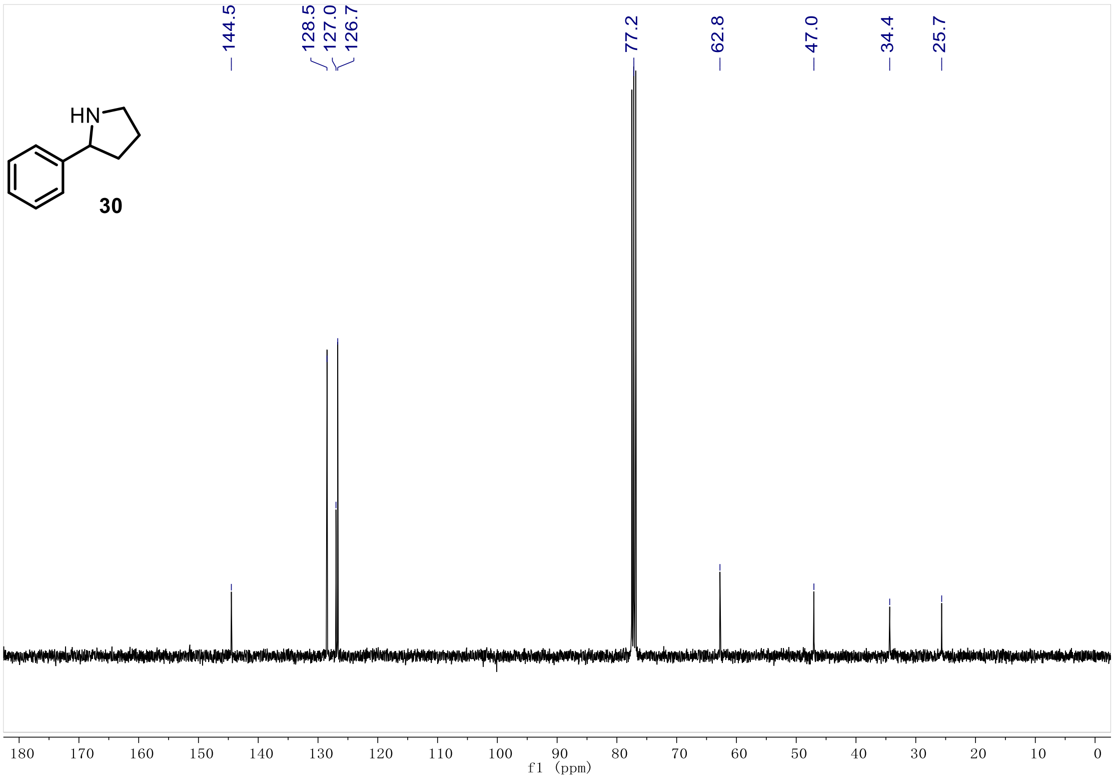
^{1}H NMR of compound **29** (400 MHz, MeOD)



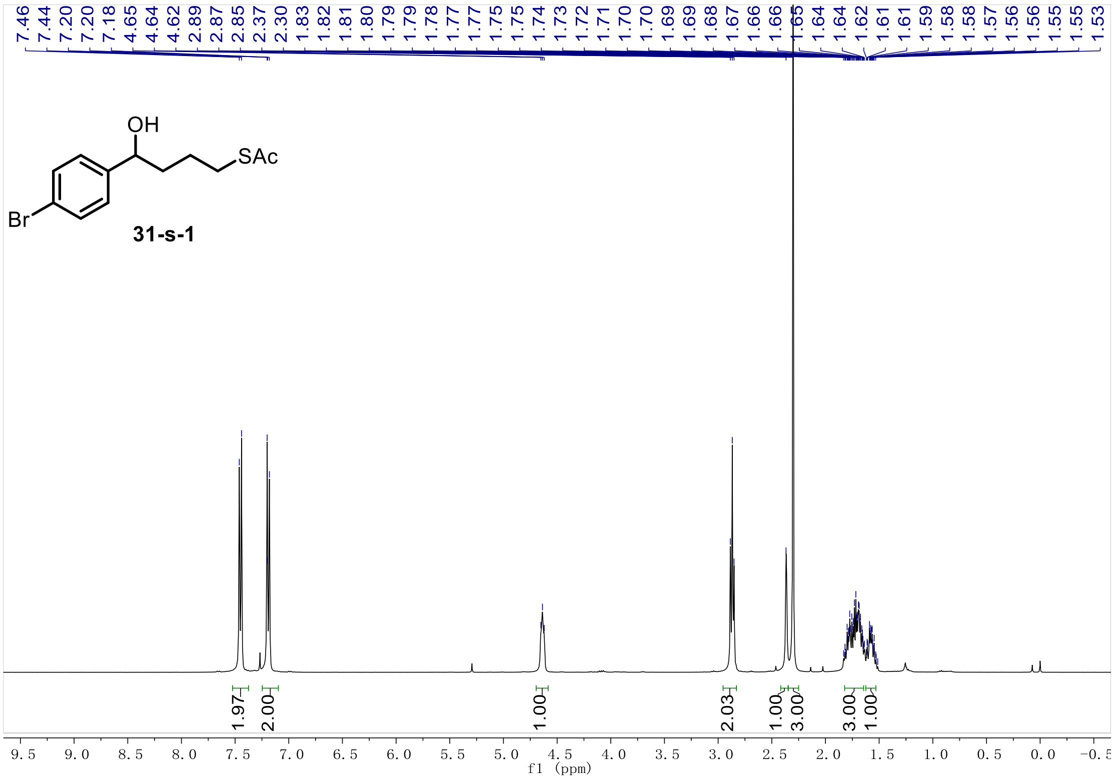
^{13}C NMR of compound **29** (151 MHz, MeOD)



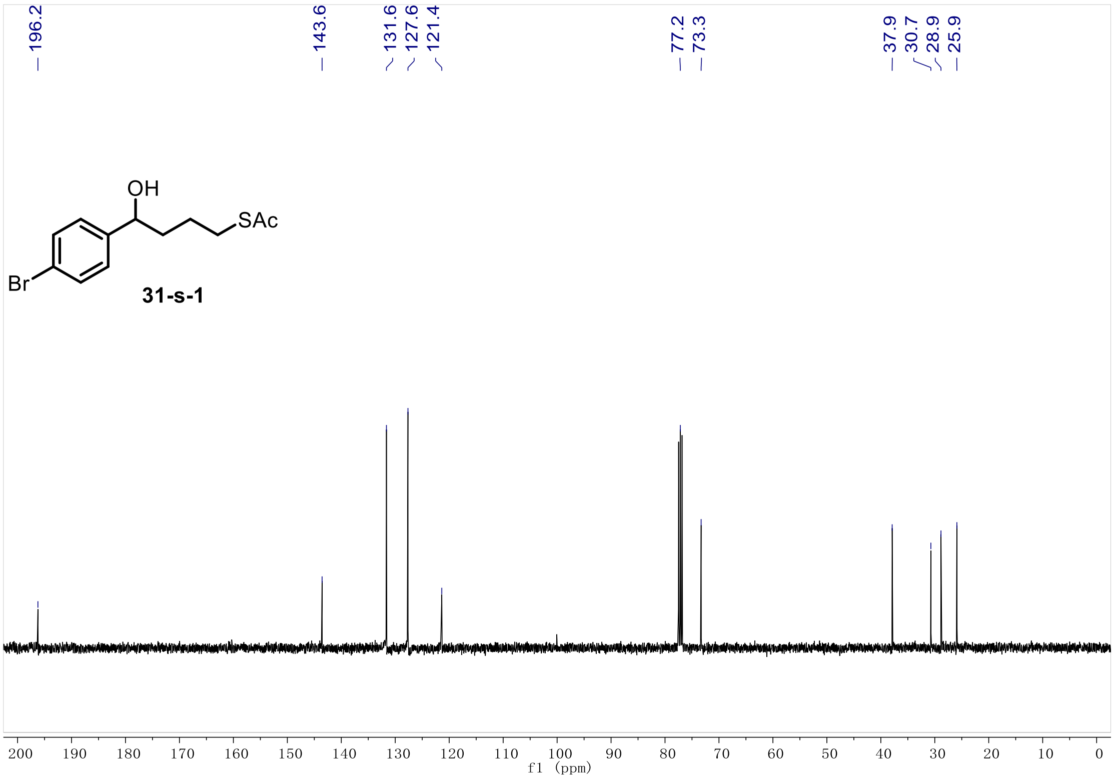
^{1}H NMR of compound **30** (400 MHz, $CDCl_3$)



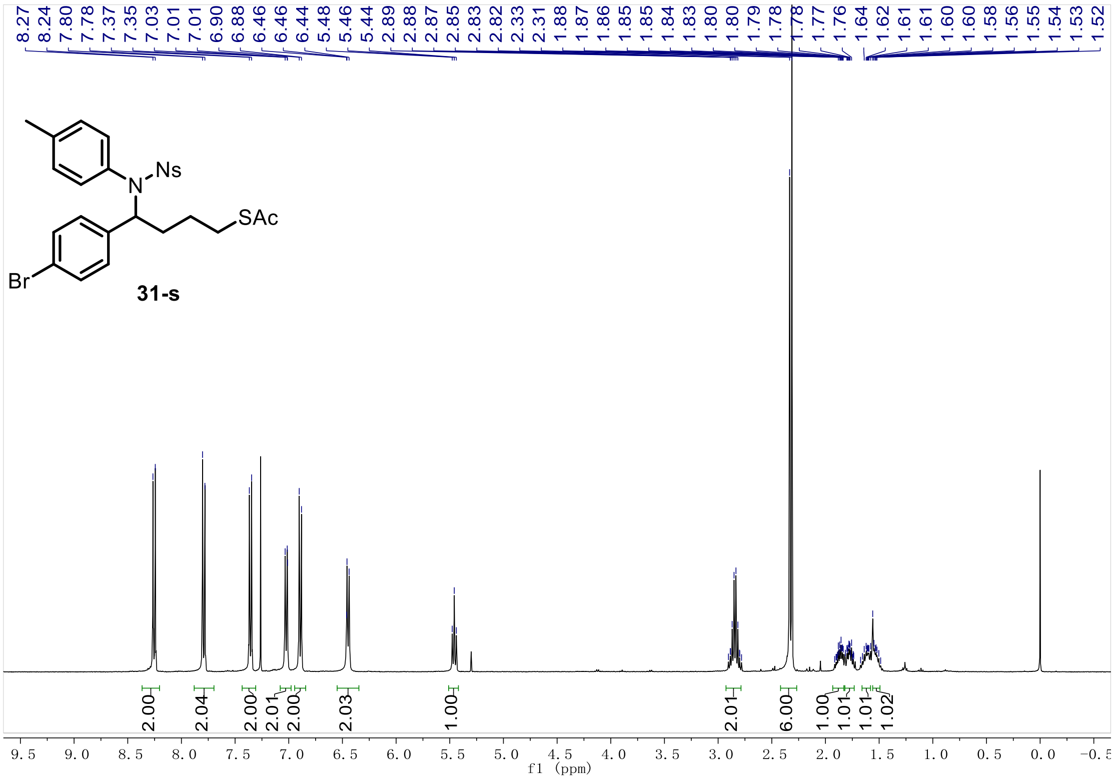
^{13}C NMR of compound **30** (101 MHz, $CDCl_3$)



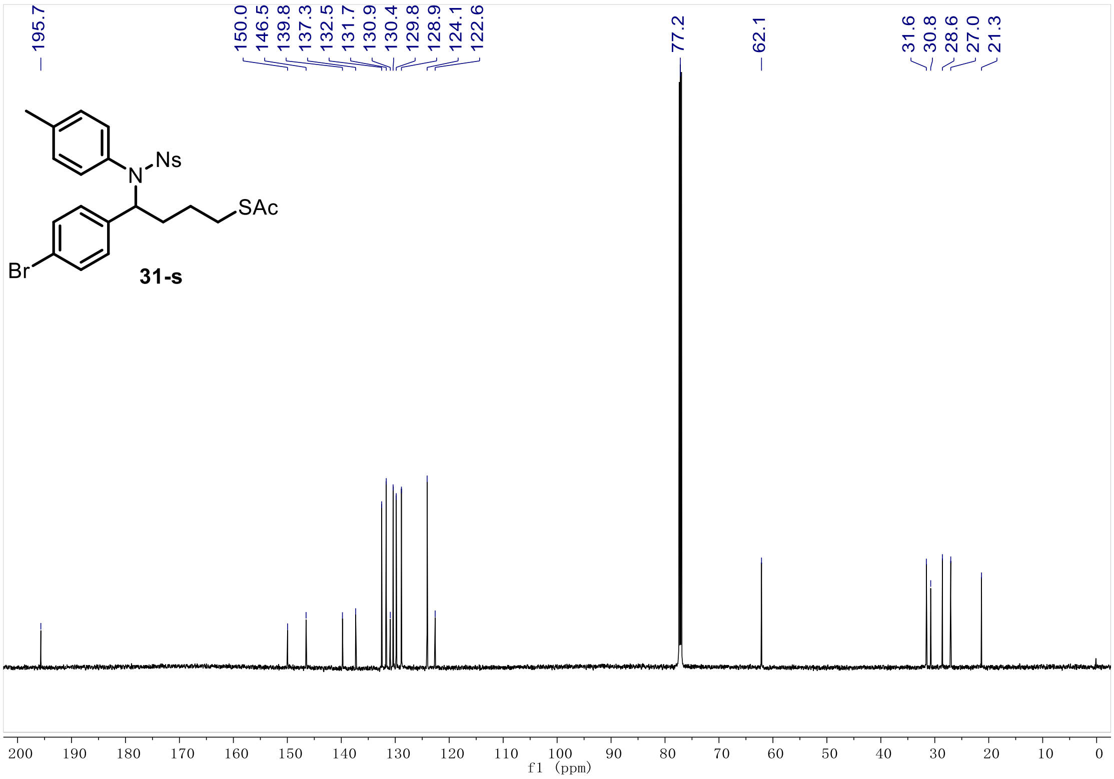
^{1}H NMR of compound **31-s-1** (400 MHz, CDCl$_3$)



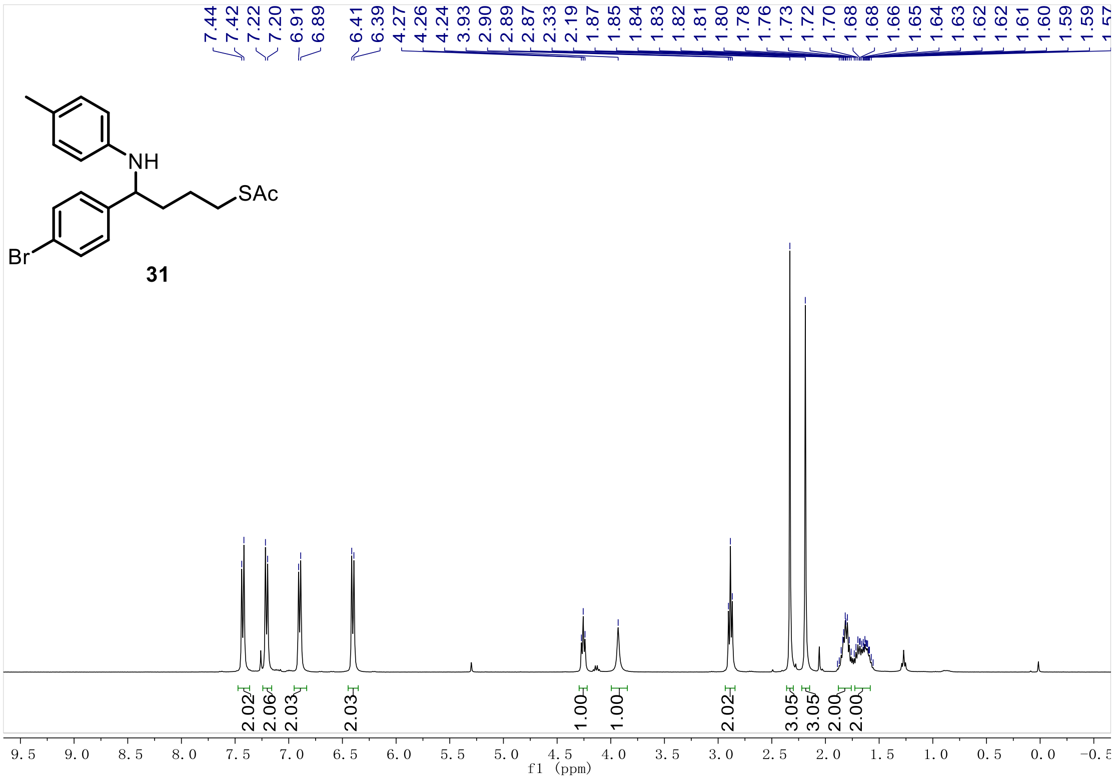
^{13}C NMR of compound **31-s-1** (101 MHz, CDCl$_3$)



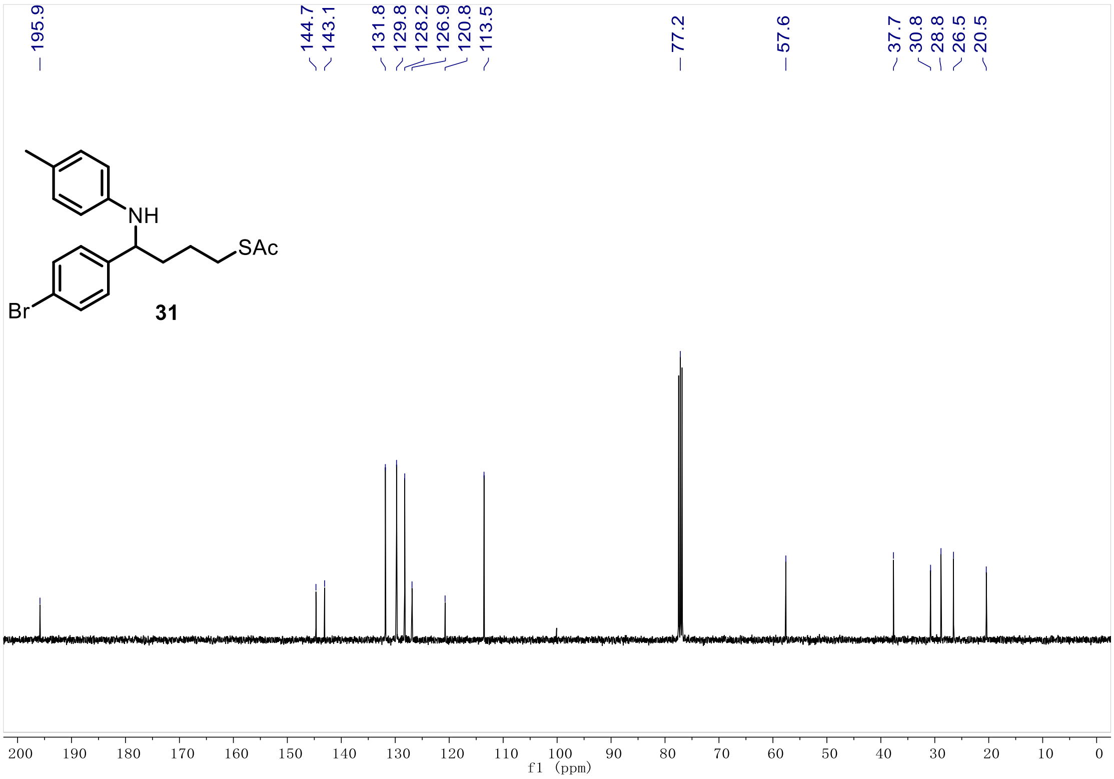
^{1}H NMR of compound **31-s** (400 MHz, CDCl$_3$)



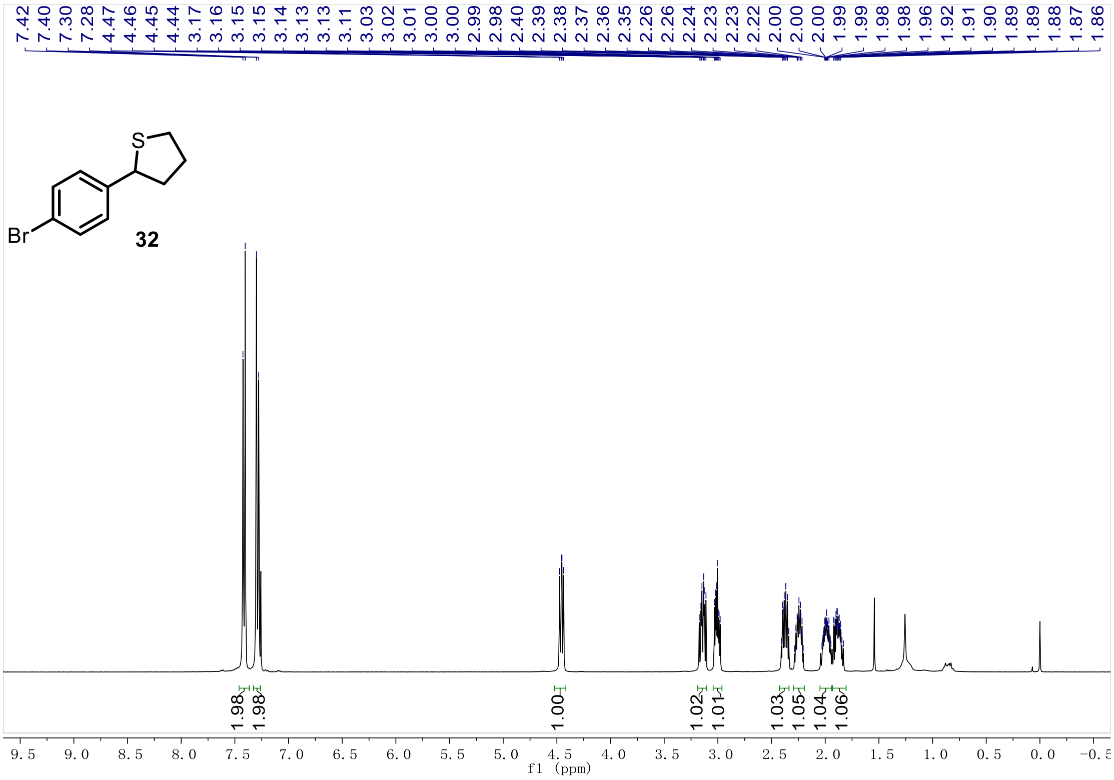
^{13}C NMR of compound **31-s** (151 MHz, CDCl$_3$)



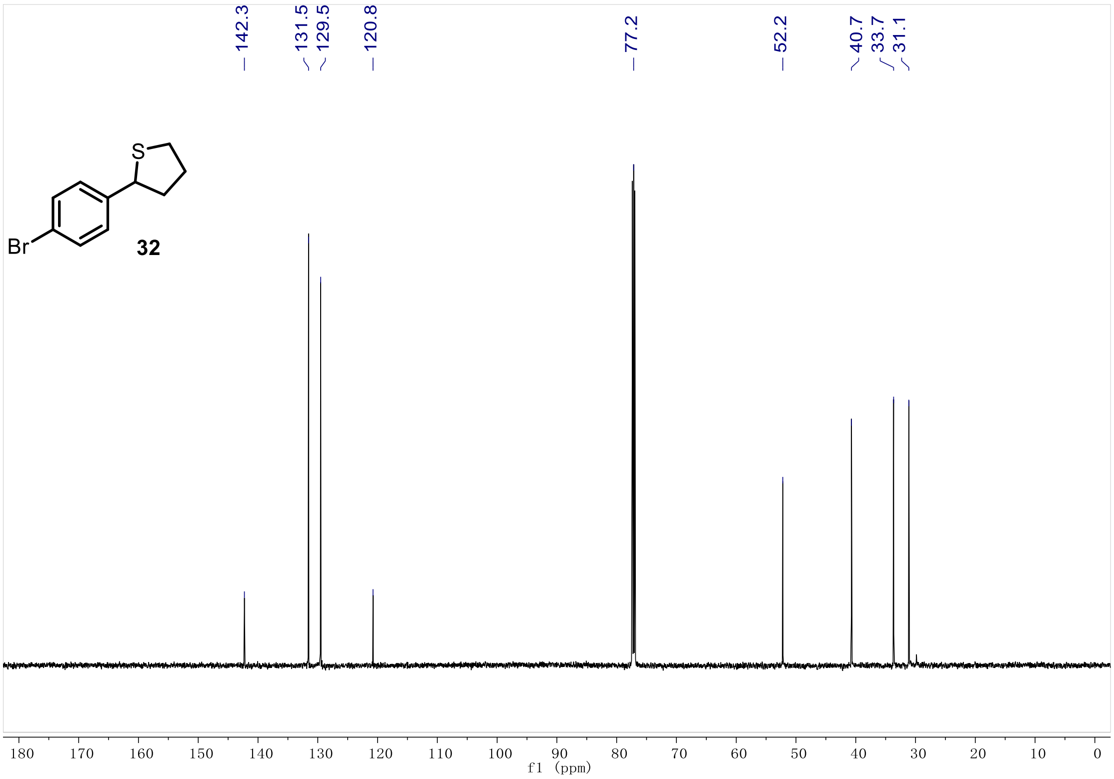
^{1}H NMR of compound **31** (400 MHz, $CDCl_3$)



^{13}C NMR of compound **31** (101 MHz, $CDCl_3$)



^{1}H NMR of compound **32** (400 MHz, $CDCl_3$)



^{13}C NMR of compound **32** (151 MHz, $CDCl_3$)