Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Accessing Chiral 2,2-Disubstituted Morpholines via Organocatalytic Enantioselective Chlorocycloetherification

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GENERAL METHODS

General Procedures

All reactions were generally performed open air or in dried glassware under an atmosphere of dry N_2. Reaction mixtures were stirred magnetically unless otherwise indicated and monitored by thin layer chromatography (TLC) on Merck precoated glass-backed silica gel 60 F-254 0.25 mm plates with visualization by fluorescence quenching at 254 nm. TLC plates were stained using potassium permanganate. Chromatography purification of products (flash column chromatography) was performed on silica gel 60 (70-230 mesh, Merck) using a forced flow of eluent at 0.3-0.5 bar. Concentration of reaction product solutions and chromatography fractions under reduced pressure was performed by rotary evaporation at 35-45^{o}C at the appropriate pressure and then at rt, ca. 10 mmHg (vacuum pump) unless otherwise indicated.

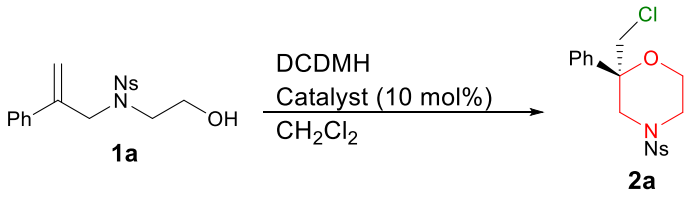
Materials

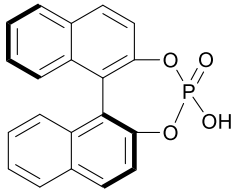
All chemicals, including dry solvents were purchased from Aldrich, Fluka, Acros, TCI, Merck, Strem, or Alfa Aesar and used as such unless stated otherwise. Yields given refer to chromatographically purified compounds unless otherwise demonstrated.

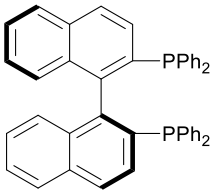
Instrumentation

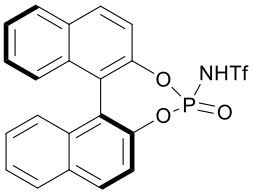
Melting points were determined on a Sinoinstructment melting point apparatus. ^{1}H NMR spectra were recorded on Bruker 300 MHz or Bruker 400 MHz spectrometer. ^{13}C NMR spectra were recorded on Bruker 75 MHz or Bruker 100 MHz spectrometer. ^{13}C NMR chemical shifts are expressed in parts per million (δ) downfield from tetramethylsilane (with the central peak of $CHCl_3$ at 77.16 ppm used as standard). ^{1}H NMR chemical shifts are expressed in parts per million (δ) downfield from tetramethylsilane (with the peak of $CHCl_3$ at 7.26 ppm used as standard; with the peak of benzene at 7. 36 ppm used as standard). All ^{13}C spectra were measured with complete proton decoupling. NMR coupling constants (J) are reported in Hertz (Hz), and splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; dd, doublet of doublet; ddd, doublet of doublet of doublet; dt, doublet of triplet; t, triplet; q, quartet; m, multiplet. High resolution mass spectrometric measurements (HRMS) were performed by the AB SCIEX, Triple TOF 5600+. Enantiomeric excesses were determined by HPLC analysis on Shimadzu HPLC units, including the following instruments: pump, LC-16; detector, SPD-16; column, Daicel Chiralpak AD-H, OD-H, OJ-H, and IC.

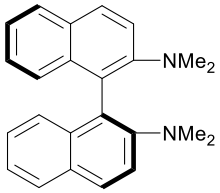
Scheme 1. Catalyst screening[a]

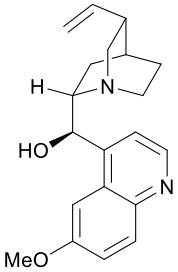


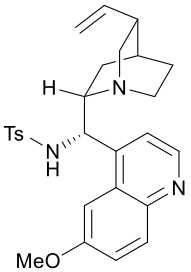

(82% yield, 9% *ee*)

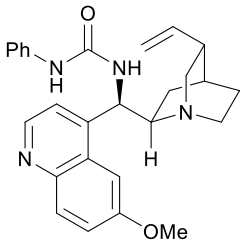

(89% yield, 11% *ee*)

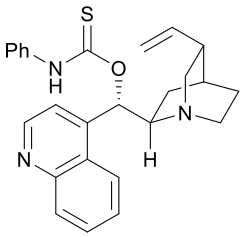

(89% yield, 17% *ee*)


(81% yield, 10% *ee*)


(80% yield, 12% *ee*)


(83% yield, 15% *ee*)


(91% yield, 24% ee)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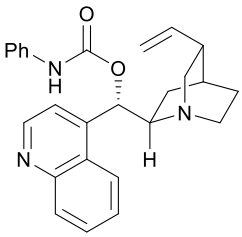
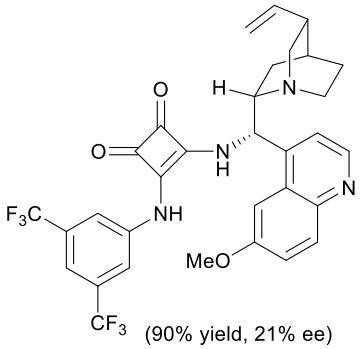
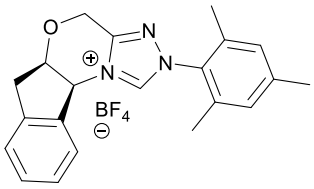
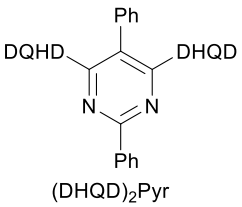
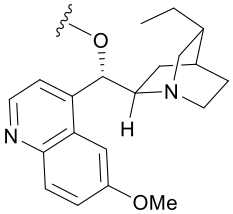
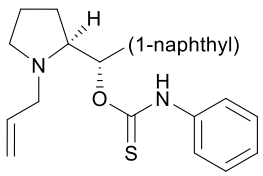

(93% yield, 22% ee)

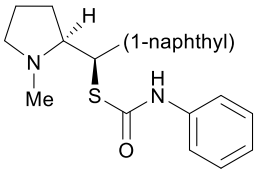

(90% yield, 21% ee)

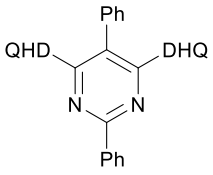

(70% yield, 3% *ee*)

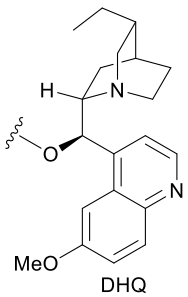

(DHQD)$_2$Pyr
(93% yield, 59% *ee*)


DHQD


(77% yield, 4% *ee*)


(75% yield, 6% *ee*)


(DHQ)$_2$Pyr
(93% yield, 47% *ee*)


DHQ

[a] Reactions were carried out with substrate **1a** (0.1 mmol), catalyst (0.01 mmol), and DCDMH (0.12 mmol) in CH_2Cl_2 (4 mL). The yield was isolated yield and the ee was determined by chiral HPLC.

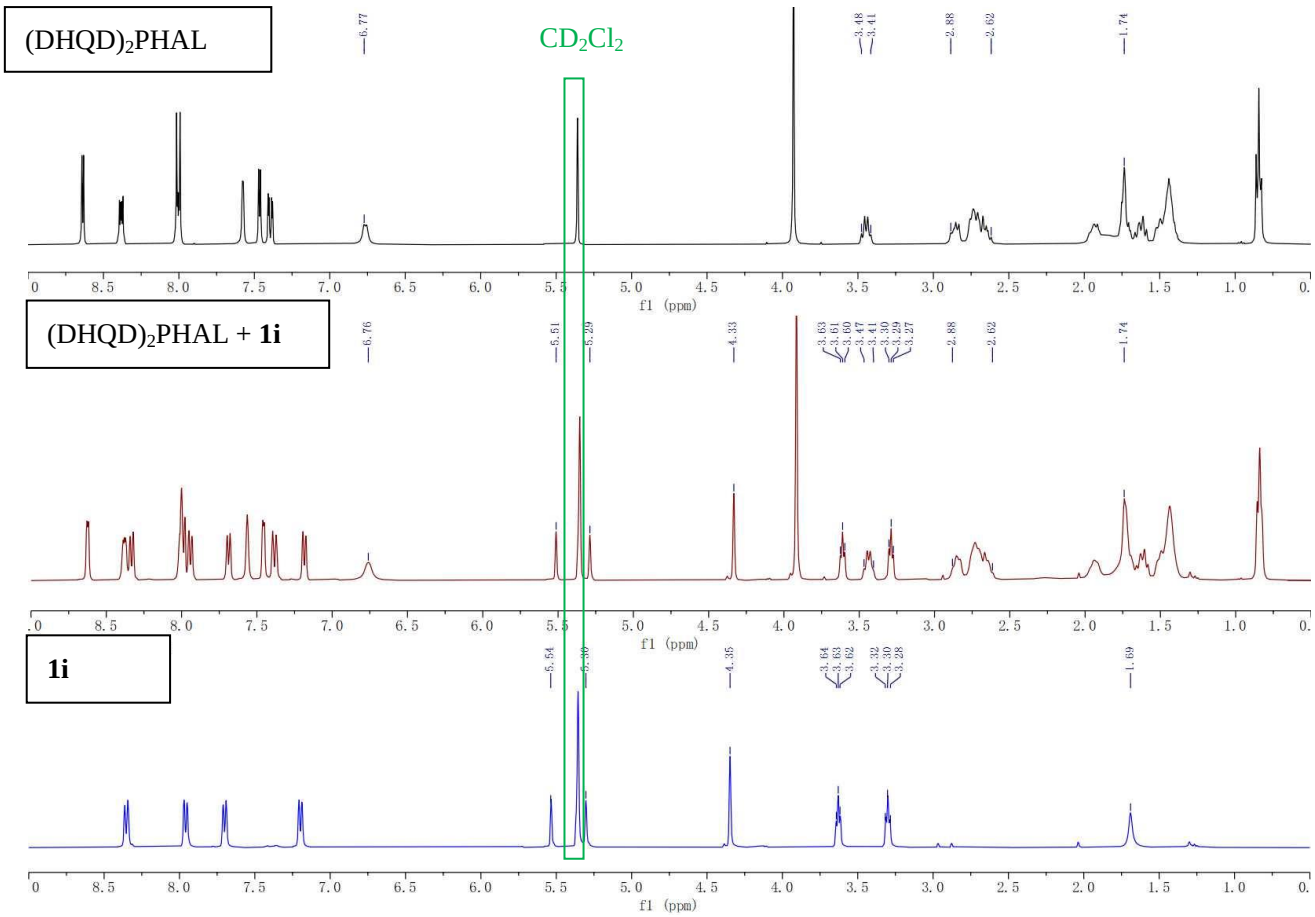


Figure 1. ^{1}H-NMR analysis of $(DHQd)_2PHAL$ and **1i**

Evaluation of antibacterial activity.

The compounds were diluted in 10% DMSO and 2μL of the dilution was added to a 200μl reaction so that the final concentration of DMSO is 0.1% in all of reactions. Minimum inhibitory concentrations (MIC) for compounds were determined following Luria-Bertani broth dilution guidelines . MIC values were determined as the lowest concentration of inhibitor to prevent visible *Staphylococcus aureus* growth after 18 h of incubation at 37 ℃. OD_{550nm} absorbance signal was measured using a multi-well spectrophotometer (Molecular Devices SpectraMax M5 microplate reader).

The compounds were diluted in 10% DMSO and 2μL of the dilution was added to a 200μl reaction so that the final concentration of DMSO is 0.1% in all of reactions. Minimum inhibitory concentrations (MIC) for compounds were determined following Luria-Bertani broth dilution guidelines. MIC values were determined as the lowest concentration of inhibitor to prevent visible *Staphylococcus aureus* (MRSA) growth after 18 h of incubation at 37 ℃. OD_{550nm} absorbance signal was measured using a multi-well spectrophotometer (Molecular Devices SpectraMax M5 microplate reader).

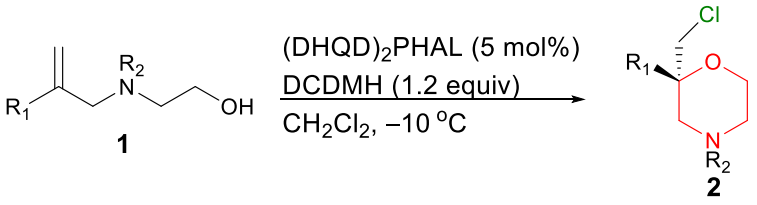
***Staphylococcus aureus* MIC results table**

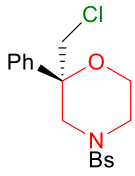
Compound	MIC
2h	1000 μg/ml
4	33 μg/ml
PhSSPh	>1000 μg/ml
Benzylpenicilin sodium	0.003 μg/ml

***Staphylococcus aureus* (MRSA) MIC results table**

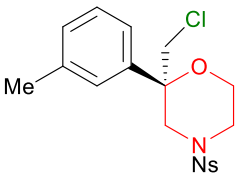
Compound	MIC
2h	1000 μg/ml
4	33 μg/ml
Benzylpenicilin sodium	0.1 μg/ml

Table 1 Substrate Scope[a]

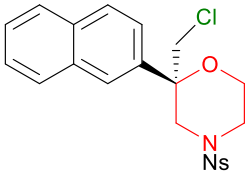




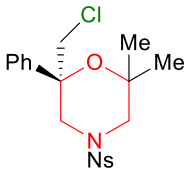
2r
(95% yield, 73% *ee*)



2s
(94% yield, 79% *ee*)



2t
(94% yield, 77% *ee*)

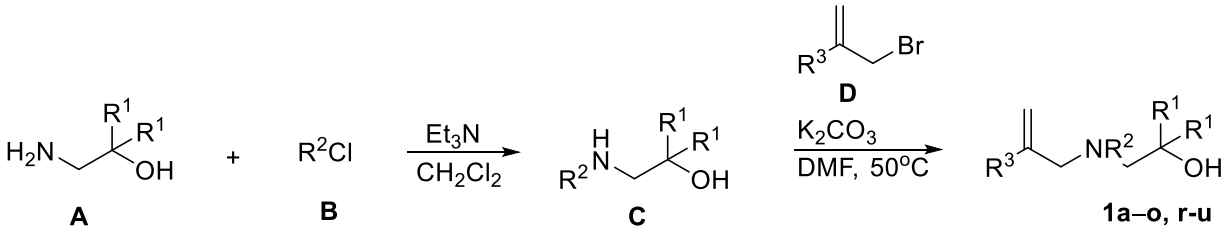


2u
(97% yield, 67% *ee*)

[a] Reactions were carried out with substrate **1** (0.1 mmol), $(DHQD)_2PHAL$ (0.005 mmol), and DCDMH (0.12 mmol) in CH_2Cl_2 (4 mL) at −10 °C. The yield is isolated yield and the ee was determined by chiral HPLC.

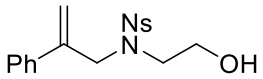
SYNTHESIS OF ALKENOL SUBSTRATES AND ASYMMETRIC CHLOROCYCLOETHERIFICATION REACTIONS

General Procedure for the Synthesis of Alkenol Substrates.



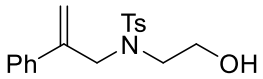
To a solution of **A** (2.0 mmol, 1.0 equiv) and Et_3N (202.2 mg, 2.0 mmol, 1.0 equiv) in CH_2Cl_2 (5.0 mL) was added **B** (2.0 mmol, 1.0 equiv) at room temperature. The mixture was then stirred for 2 h at room temperature. Water (10.0 mL) and EtOAc (15.0 mL) were added. The organic layer was washed with water, and dried over magnesium sulfate. Concentration of the organic layer offered the crude product **C**, which was used without further purification.

To a solution of **C** (1.0 mmol, 1.0 equiv) and K_2CO_3 (138.0 mg, 1.0 mmol, 1.0 equiv) in DMF (2.0 mL) was added **D** (1.0 mmol, 1.0 equiv) at room temperature. The mixture was then stirred for 24 h at 50°C. Water (10.0 mL) and EtOAc (15.0 mL) were added. The organic layer was washed with water, and dried over magnesium sulfate. Concentration of the organic layer offered the crude product that was further purified by flash column chromatography (hexane/EtOAc) to give the pure alkenol substrates **1a**－**t**.



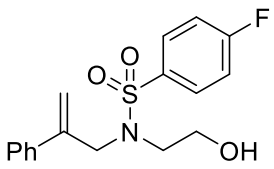
1a

322.2 mg, 89%, yellow solid; MP 146－147 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.30 (d, *J* = 12.0 Hz, 2H), 7.92 (d, *J* = 8.0 Hz, 2H), 7.39-7.31 (m, 5H), 5.49 (s, 1H), 5.25 (s, 1H), 4.39 (s, 2H), 3.68 (t, *J* = 4.0 Hz, 2H), 3.32 (t, *J* = 4.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.0, 144.9, 142.5, 137.9, 128.7, 128.5, 128.4, 126.5, 124.3, 117.5, 60.5, 52.9, 49.5; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{18}N_2O_5S$ 363.1755; found 363.1756.



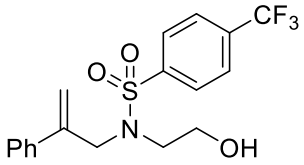
1b

304.5 mg, 92%, yellow solid; MP 113－114 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.71-7.32 (m, 9H), 5.52 (s, 1H), 5.25 (s, 1H), 4.27 (s, 2H), 3.60 (t, *J* = 4.0 Hz, 2H), 3.20 (t, *J* = 4.0 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.7, 143.1, 137.8, 135.2, 129.8, 128.6, 128.3, 127.6, 126.5, 116.8, 61.0, 53.7, 50.2, 21.6; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{18}H_{21}NO_3S$ 332.4927; found 332.4928.



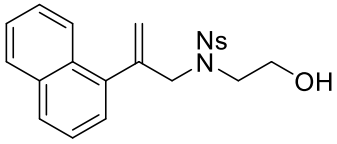
1c

304.9 mg, 91%, white solid; MP 109－110 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.81-7.16 (m, 9H), 5.51 (s, 1H), 5.25 (s, 1H), 4.30 (s, 2H), 3.63 (t, *J* = 4.0 Hz, 2H), 3.23 (t, *J* = 8.0 Hz, 2H), 2.11 (s, broad, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.4 (d, *J* = 253.0 Hz), 142.9, 137.9, 134.6, 130.2 (d, *J* = 10.0 Hz), 128.6 (d, *J* = 29.0 Hz), 126.5, 117.0, 116.5 (d, *J* = 22.0 Hz), 60.8, 53.3, 49.9 ; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{18}FNO_3S$ 336.7719; found 336.7720.



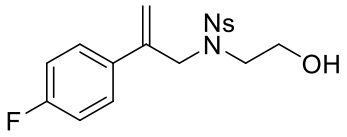
1d

365.8 mg, 94%, white solid; MP 122－123 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.89-7.31 (m, 9H), 5.49 (s, 1H), 5.26 (s, 1H), 4.35 (s, 2H), 3.66 (t, *J* = 4.0 Hz, 2H), 3.29 (t, *J* = 8.0 Hz, 2H), 2.06 (s, broad, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ142.7, 137.9, 128.6, 128.4, 127.9, 126.5, 126.3 (q, *J* = 40.0 Hz), 117.4, 60.7, 53.2, 49.7; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{18}H_{18}F_3NO_3S$ 386.4971; found 386.4972.



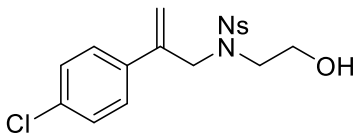
1e

362.6 mg, 88%, yellow solid; MP 168－169 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.78-7.13 (m, 11H), 5.65 (s, 1H), 5.32 (s, 1H), 4.45 (s, 2H), 3.91 (t, *J* = 4.0 Hz, 2H), 3.61 (t, *J* = 4.0 Hz, 2H), 2.52 (s, broad, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.0, 145.1, 142.3, 137.2, 133.6, 130.8, 128.4, 128.2, 127.4, 126.4, 126.1, 125.8, 125.2, 124.6, 123.4, 121.5, 60.5, 54.0, 48.4; HRMS (TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{20}N_2O_5S$ 413.7411; found 413.7412.



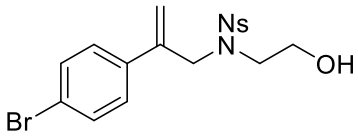
1f

330.6 mg, 87%, yellow solid; MP 130－131 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.34 (d, *J* = 8.0 Hz, 2H), 7.97 (d, *J* = 8.0 Hz, 2H), 7.42-7.01 (m, 4H), 5.46 (s, 1H), 5.23 (s, 1H), 4.34 (s, 2H), 3.65 (t, *J* = 4.0 Hz, 2H), 3.30 (t, *J* = 4.0 Hz, 2H), 1.94 (s, broad, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 164.0 (d, *J* = 247.0 Hz), 164.0, 150.1, 144.8, 141.6, 133.8, 128.6, 128.3 (d, *J* = 8.0 Hz), 124.3, 117.3, 115.7 (d, *J* = 21.0 Hz), 60.6, 53.2, 49.7; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{17}FN_2O_5S$ 381.5014; found 381.5015.



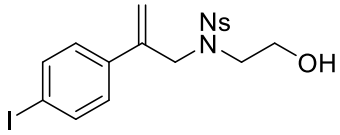
1g

352.4 mg, 89%, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.35 (d, *J* = 8.0 Hz, 2H), 7.97 (d, *J* = 8.0 Hz, 2H), 7.37-7.28 (m, 4H), 5.50 (s, 1H), 5.27 (s, 1H), 4.35 (s, 2H), 3.67 (t, *J* = 4.0 Hz, 2H), 3.31 (t, *J* = 4.0 Hz, 2H), 1.82 (s, broad, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.1, 144.8, 141.6, 136.2, 134.5, 128.8, 128.5, 127.8, 124.3, 117.8, 60.7, 53.1, 49.6; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{17}ClN_2O_5S$ 397.4425; found 397.4426.



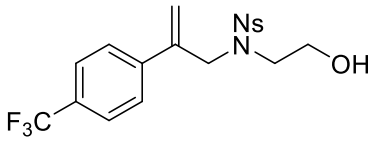
1h

378.4 mg, 86%, yellow solid; MP 161－162 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.34 (d, *J* = 8.0 Hz, 2H), 7.97 (d, *J* = 8.0 Hz, 2H), 7.61-7.53 (m, 4H), 5.59 (s, 1H), 5.8 (s, 1H), 4.40 (s, 2H), 3.67 (t, *J* = 4.0 Hz, 2H), 3.33 (t, *J* = 4.0 Hz, 2H), 1.90 (s, broad, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.1, 144.8, 141.6, 141.4, 128.5, 126.9, 125.6 (t, *J* = 4.0 Hz), 124.3, 119.1, 60.6, 52.9, 49.6; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{17}BrN_2O_5S$ 441.2986; found 441.2987.



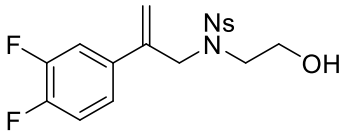
1i

434.3 mg, 89%, yellow solid; MP 192－193 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.35 (dd, J_1 = 8.0 Hz, J_1 = 160.0 Hz, 4H), 7.68(dd, J_1 = 8.0 Hz, J_1 = 204.0 Hz, 4H), 5.51 (s, 1H), 5.32 (s, 1H), 4.34 (s, 2H), 3.67 (t, *J* = 4.0 Hz, 2H), 3.31 (t, *J* = 8.0 Hz, 2H), 1.83 (s, broad, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.1, 144.7, 137.8, 137.3, 128.5, 128.3, 124.4, 118.0, 94.3, 60.6, 53.0, 49.6; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{17}IN_2O_5S$ 489.3044; found 489.3045.



1j

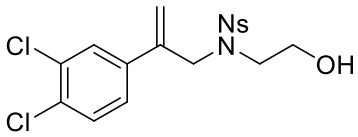
374.1 mg, 87%, yellow solid; MP 147－148 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.34 (d, *J* = 8.0 Hz, 2H), 7.97 (d, *J* = 8.0 Hz, 2H), 7.61-7.53 (m, 4H), 5.59 (s, 1H), 5.38 (s, 1H), 4.40 (s, 2H), 3.67 (t, *J* = 4.0 Hz, 2H), 3.33 (t, *J* = 4.0 Hz, 2H), 1.90 (s, broad, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.1, 144.8, 141.6, 141.4, 128.5, 126.9, 125.6 (d, *J* = 4.0 Hz), 124.3, 119.1, 60.6, 52.9, 49.6; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{18}H_{17}F_3N_2O_5S$ 431.4750; found 431.4751.



1k

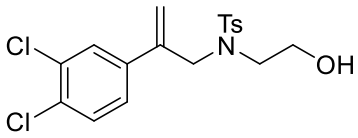
350.2 mg, 88%, yellow solid; MP 147－148 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.83 (d, *J* = 12.0 Hz, 2H), 8.01 (d, *J* = 8.0 Hz, 2H), 7.28-7.11 (m, 3H), 5.50 (s, 1H), 5.29 (s, 1H), 4.31 (s, 2H), 3.66 (t, *J* =

4.0 Hz, 2H), 3.31 (t, *J* = 4.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 151.5 (d, *J* = 240.0 Hz), 150.1, 149.0, 144.7, 140.7, 134.8, 128.6, 124.4, 122.7, 122.6, 118.2, 117.6 (d, *J* = 18.0 Hz), 115.6 (d, *J* = 18.0 Hz), 60.7, 53.1, 49.7; HRMS (TOF) m/z: [M＋H]$^+$Calcd for $C_{17}H_{16}F_2N_2O_5S$ 399.2945; found 399.2946.



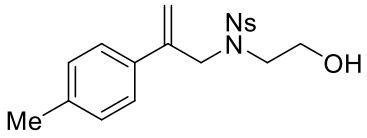
1l

387.0 mg, 90%, yellow solid; MP 155－156 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.35 (d, *J* = 8.0 Hz, 2H), 7.97 (d, *J* = 8.0 Hz, 2H), 7.43-7.26 (m, 3H), 5.53 (s, 1H), 5.33 (s, 1H), 4.33 (s, 2H), 3.70 (t, *J* = 4.0 Hz, 2H), 3.34 (t, *J* = 4.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.1, 144.8, 140.6, 137.9, 132.8, 132.6, 130.6, 128.5, 128.4, 125.8, 124.4, 118.9, 60.6, 52.8, 49.6; HRMS (TOF) m/z: [M＋H]$^+$ Calcd for $C_{17}H_{16}Cl_2N_2O_5S$ 431.5090; found 431.5089.



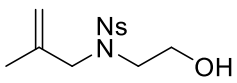
1m

363.1 mg, 91%, yellow solid; MP 126－127 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.69-7.31 (m, 7H), 5.51 (s, 1H), 5.32 (s, 1H), 4.22 (s, 2H), 3.62 (t, *J* = 4.0 Hz, 2H), 3.21 (t, *J* = 4.0 Hz, 2H), 2.46 (s, 3H), 2.08 (s, broad, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.0, 141.1, 138.0, 135.3, 132.7, 132.3, 130.5, 130.0, 128.4, 127.4, 127.1, 125.9, 118.4; HRMS (TOF) m/z: [M＋H]$^+$Calcd for $C_{18}H_{19}Cl_2NO_3S$ 400.6237; found 400.6238.



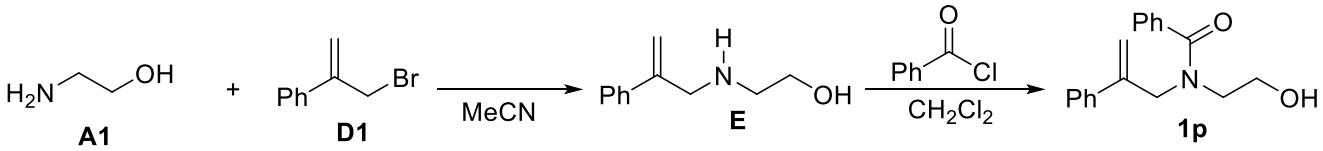
1n

349.7 mg, 93%, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.24 (d, *J* = 12.0 Hz, 2H), 7.91 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 12.0 Hz, 2H), 7.09 (d, *J* = 32.0 Hz, 2H), 5.42 (s, 1H), 5.19 (s, 1H), 4.34 (s, 2H), 3.65 (t, *J* = 4.0 Hz, 2H), 3.33 (t, *J* = 4.0 Hz, 2H), 2.55 (s, 1H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.8, 145.0, 142.3, 138.3, 135.1, 129.3, 128.5, 126.3, 124.3, 116.7, 60.4, 52.8, 49.4, 21.1; HRMS (TOF) m/z: [M＋H]$^+$Calcd for $C_{18}H_{20}N_2O_5S$ 377.4129; found 377.4130.



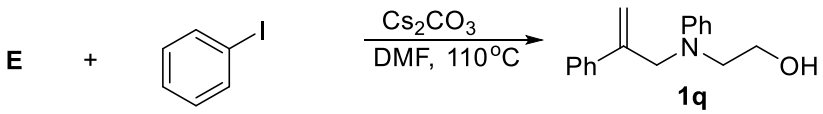
1o

249.0 mg, 83%, white solid; MP 93－94 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.38 (d, *J* = 8.0 Hz, 2H), 8.06 (d, *J* = 8.0 Hz, 2H), 4.96 (s, 1H), 4.89 (s, 1H), 3.84 (s, 2H), 3.74 (t, *J* = 4.0 Hz, 2H), 3.34 (t, *J* = 4.0 Hz, 2H), 1.71 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.0, 145.4, 139.9, 128.5, 124.4, 115.3, 60.6, 55.4, 50.0, 19.8; HRMS (TOF) m/z: [M＋H]$^+$Calcd for $C_{12}H_{16}N_2O_5S$ 301.6912; found 301.6913.

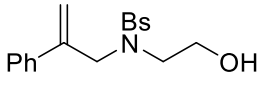


To a solution of **A1** (610.1 mg, 10.0 mmol, 3.3 equiv) in MeCN (10.0 mL) was added **D1** (588.0 mg, 3.0 mmol, 1.0 equiv) at room temperature. The mixture was then stirred for 2 h at room temperature. After removal of MeCN, water (30.0 mL) and EtOAc (50.0 mL) were added. The organic layer was washed with water, and dried over magnesium sulfate. Concentration of the organic layer offered the crude product that was further purified by flash column chromatography (hexane/EtOAc) to give the pure alkenol substrates **E**. 318.6 mg, 60%, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.45-7.29 (m, 5H), 5.43 (s, 1H), 5.34 (s, 1H), 5.26 (s, 1H), 3.71 (s, 2H), 3.64 (t, *J* = 4.0 Hz, 2H), 2.81 (t, *J* = 4.0 Hz, 2H), 2.16 (s, 1H, contains H_2O); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.1, 139.6, 128.5, 127.8, 126.2, 113.8, 60.8, 52.9, 50.2; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{11}H_{15}NO$ 178.6154; found 178.6153.

To a solution of **E** (137.0 mg, 1.0 mmol, 1.0 equiv) in CH_2Cl_2 (4.0 mL) was added benzoyl chloride (140.7 mg, 1.0 mmol, 1.0 equiv) at room temperature. The mixture was then stirred for 2 h at room temperature. After removal of CH_2Cl_2, water (10.0 mL) and EtOAc (15.0 mL) were added. The organic layer was washed with water, and dried over magnesium sulfate. Concentration of the organic layer offered the crude product that was further purified by flash column chromatography (hexane/EtOAc) to give the pure alkenol substrates **1p**. 267.0 mg, 95%, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.61-7.27 (m, 10H), 6.49 (s, broad, 1H), 5.56 (s, 1H), 5.34 (s, 1H), 4.46 (s, 2H), 3.66-3.63 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.4, 144.0, 138.3, 134.4, 131.4, 128.5, 128.0, 127.0, 126.1, 115.3, 73.1, 68.4, 39.7; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{18}H_{19}NO_2$ 282.4761; found 282.4762.

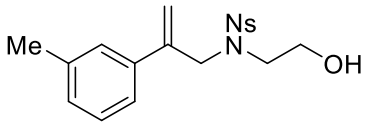


To a solution of **E** (137.0 mg, 1.0 mmol, 1.0 equiv) and Cs_2CO_3 (651.6 mg, 2.0 mmol, 2.0 equiv) in DMF (2.0 mL) was added iodobenzene (408.0 mg, 2.0 mmol, 2.0 equiv) at room temperature. The mixture was then stirred for 8 h at 110°C. Water (10.0 mL) and EtOAc (15.0 mL) were added. The organic layer was washed with water, and dried over magnesium sulfate. Concentration of the organic layer offered the crude product that was further purified by flash column chromatography (hexane/EtOAc) to give the pure alkenol substrates **1q**. 179.6 mg, 71%, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.49-6.88 (m, 10H), 5.46 (s, 1H), 5.32 (s, 1H), 4.12 (t, *J* = 4.0 Hz, 2H), 3.78 (s, 2H), 3.08 (m, 4H), 1.96 (s, broad, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.8, 146.1, 139.8, 129.5, 128.5, 127.8, 126.2, 120.8, 114.5, 113.6, 67.1, 53.3, 48.0; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{19}NO$ 254.7139; found 254.7140.



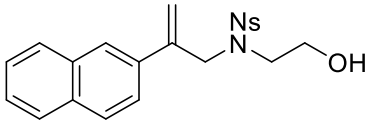
1r

288.5 mg, 91%, yellow solid; MP 104－105 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.82-7.32 (m, 10H), 5.51 (s, 1H), 5.25 (s, 1H), 4.29 (s, 2H), 3.61 (t, *J* = 4.0 Hz, 2H), 3.22 (t, *J* = 4.0 Hz, 2H), 2.05 (s, broad, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.0, 138.3, 137.8, 132.9, 129.2, 128.6, 128.3, 127.5, 126.5, 116.9,60.9, 53.6, 50.1; HRMS (TOF) m/z: [M＋H]$^+$Calcd for $C_{17}H_{19}NO_3S$ 318.5124; found 318.5123.



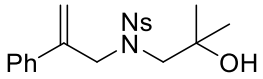
1s

349.7 mg, 93%, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.26 (d, *J* = 12.0 Hz, 2H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.21-7.11 (m, 4H), 5.44 (s, 1H), 5.21 (s, 1H), 4.37 (s, 2H), 3.69 (t, *J* = 4.0 Hz, 2H), 3.34 (t, *J* = 4.0 Hz, 2H), 3.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.9, 145.1, 142.6, 138.3, 138.0, 129.1, 128.5, 127.2, 124.2, 123.6, 117.2, 60.4, 52.8, 49.5, 21.4; HRMS (TOF) m/z: [M＋H]$^+$Calcd for $C_{18}H_{20}N_2O_5S$ 377.4129; found 377.4128.



1t

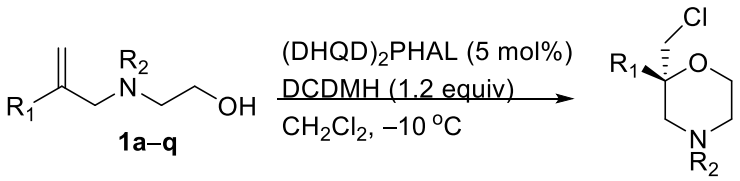
370.8 mg, 90%, yellow solid; MP 161－162 ℃; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05-7.45 (m, 11H), 5.59 (s, 1H), 5.35 (s, 1H), 4.49 (s, 2H), 3.72 (t, *J* = 4.0 Hz, 2H), 3.39 (t, *J* = 4.0 Hz, 2H), 2.28 (s, broad, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.6, 145.1, 142.5, 135.3, 133.0, 128.3, 128.2, 128.1, 127.6, 126.6, 125.5, 124.5, 124.0, 118.3, 60.5, 52.9, 49.3; HRMS (TOF) m/z: [M＋H]$^+$Calcd for $C_{21}H_{20}N_2O_5S$ 413.7411; found 413.7410.



1u

354.9 mg, 91%, yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.26 (d, *J* = 12.0 Hz, 2H), 7.89 (d, *J* = 12.0 Hz, 2H), 7.29-7.22 (m, 5H), 5.39 (s, 1H), 5.18 (s, 1H), 4.52 (t, *J* = 4.0 Hz, 2H), 3.30 (s, 2H), 1.27 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 149.9, 145.3, 142.7, 138.7, 128.6, 128.5, 128.3, 126.5, 124.1, 117.5, 71.8, 58.1, 53.8, 27.9; HRMS (TOF) m/z: [M＋H]$^+$Calcd for $C_{19}H_{22}N_2O_5S$ 391.6274; found 391.6275.

General Procedure for the asymmetric chlorocycloetherification.

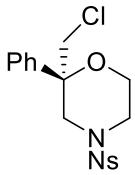


To a solution of **1a-o, r-u** (0.1 mmol, 1.0 equiv) and $(DHQD)_2PHAL$ (3.9 mg, 0.005 mmol, 0.05 equiv) in CH_2Cl_2 (4.0 mL) was added DCDMH (23.6 mg, 1.2 mmol, 1.2 equiv) at －10 °C. The mixture was then stirred for 2－3 days at －10 °C. The reaction was quenched with saturated Na_2SO_3 (1.0 mL) at －10 °C. The solution was diluted with water (3.0 mL) and extrated with EtOAc,

dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc) to yield the corresponding morpholines **2a−o, r-u**.

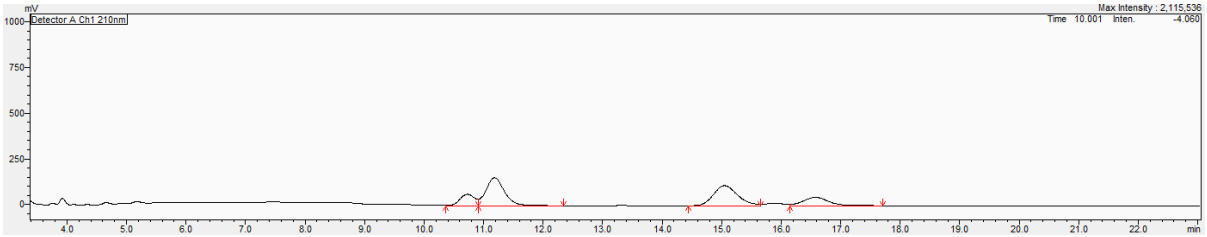
To a solution of **1a**,**b**, **l**, **r-u** (0.1 mmol, 1.0 equiv) and $(ECin)_2PHAL$ (3.6 mg, 0.005 mmol, 0.05 equiv) in CH_2Cl_2 (4.0 mL) was added DCDMH (23.6 mg, 1.2 mmol, 1.2 equiv) at −10 °C. The mixture was then stirred for 2−3 days at −10 °C. The reaction was quenched with saturated Na_2SO_3 (1.0 mL) at −10 °C. The solution was diluted with water (3.0 mL) and extrated with EtOAc, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc) to yield the corresponding morpholines *ent*-**2a**,**b**, **l**, **r-u**.

Representative Procedure for the asymmetric chlorocycloetherification (1.0 mmol scale).
To a solution of **1a** (362.1 mg, 1.0 mmol, 1.0 equiv) and $(DHQD)_2PHAL$ (39.0 mg, 0.05 mmol, 0.05 equiv) in CH_2Cl_2 (40.0 mL) was added DCDMH protionwise (236.2 mg, 1.2 mmol, 1.2 equiv) at −10 °C. The mixture was then stirred for 3 days at −10 °C. The reaction was quenched with saturated Na_2SO_3 (10.0 mL) at −10 °C. The solution was diluted with water (30.0 mL) and extrated with EtOAc, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc) to yield **2a**.
To a solution of **1a** (362.1 mg, 1.0 mmol, 1.0 equiv) and $(ECin)_2PHAL$ (36.0 mg, 0.05 mmol, 0.05 equiv) in CH_2Cl_2 (40.0 mL) was added DCDMH protionwise (236.2 mg, 1.2 mmol, 1.2 equiv) at −10 °C. The mixture was then stirred for 3 days at −10 °C. The reaction was quenched with saturated Na_2SO_3 (10.0 mL) at −10 °C. The solution was diluted with water (30.0 mL) and extrated with EtOAc, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc) to yield *ent*-**2a**.

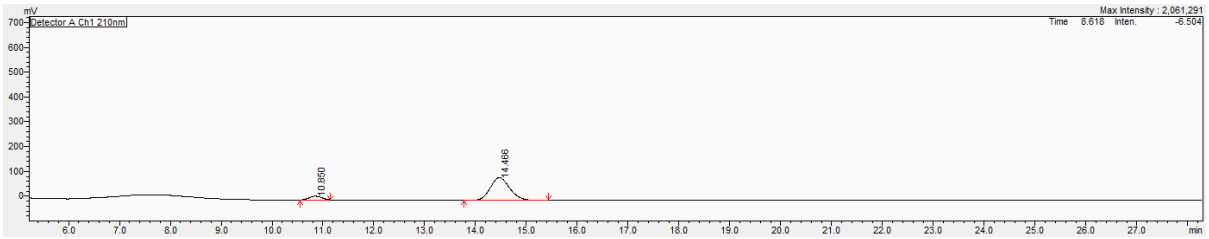


2a

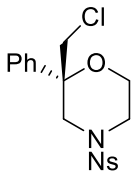
386.1 mg (1.0 mmol scale), 97%, yellow solid; MP 189−190 ℃; $[\alpha]_D^{25}$ = −19.2 (*c* 1.0, MeOH, 82% ee); ^1H NMR ($CDCl_3$, 400 MHz): δ 8.45 (d, *J* = 8.0 Hz, 2H), 8.00 (d, *J* = 12.0 Hz, 2H), 7.52-7.38 (m, 5H), 4.18-4.15 (m, 1H), 3.85-3.65 (m, 4H), 3.34-3.31 (m, 1H), 3.03 (d, *J* = 12.0 Hz, 1H), 2.85-2.75 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.5, 141.1, 137.5, 129.0, 128.6, 127.0, 124.6, 76.8, 60.9, 50.2, 49.1, 45.4; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{17}ClN_2O_5S$ 397.6944; found 397.6945; HPLC (Daicel Chiralcel AD-H, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 210 nm) t_1 = 10.9 min (minor), t_2 = 14.5 min (major).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	10.725	1110079	63240	V	12.129
2	11.185	3400306	153568	V	37.153
3	15.047	3183638	110982	V	34.785
4	16.574	1458250	46697	V	15.933
Total		9152273	374486		100.000

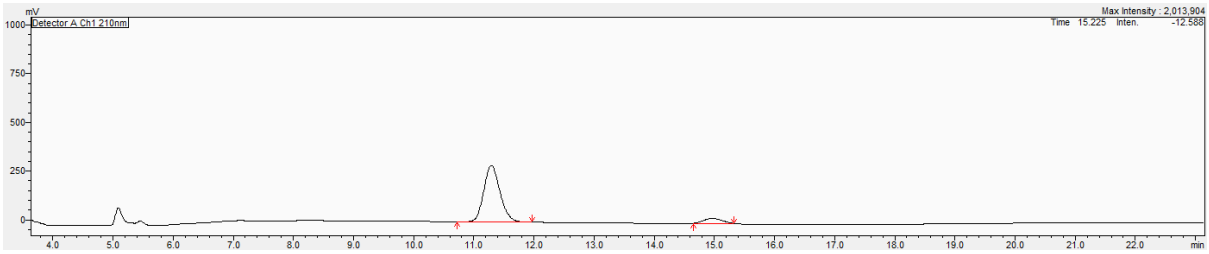


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	10.850	250331	14638	M	9.171
2	14.466	2479150	93072	M	90.829
Total		2729480	107710		100.000

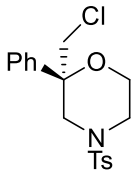


ent-**2a**

382.0 mg (1.0 mmol scale), 96%; $[\alpha]_D^{25}$= +18.9 (*c* 1.0, MeOH, 82% ee); HPLC (Daicel Chiralcel AD-H, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 254 nm) t_1 = 11.3 min (major), t_2 = 15.0 min (minor).

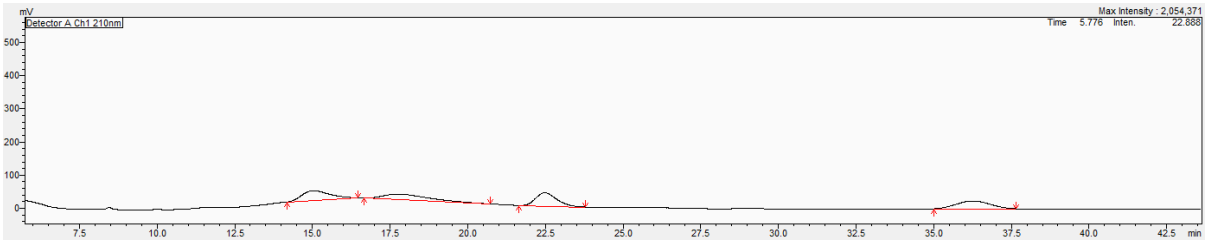


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	11.291	5440536	289201	M	91.073
2	14.965	533251	25167	M	8.927
Total		5973787	314368		100.000

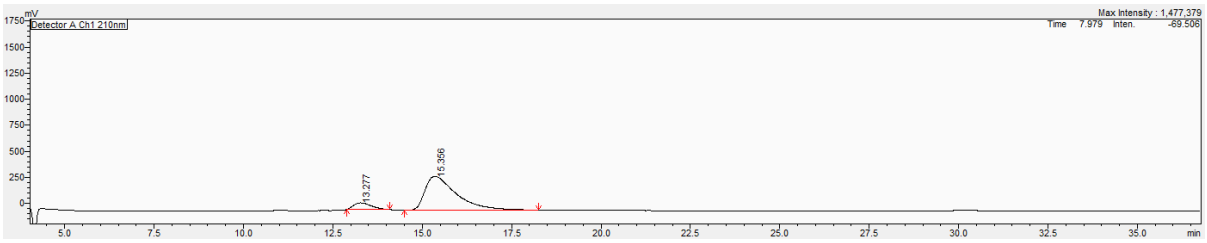


2b

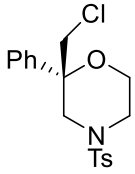
34.7 mg, 95%, yellow solid; MP 177－178 ℃; $[\alpha]_D^{25}$= －58.2 (*c* 1.0, MeOH, 80% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.69-7.34 (m, 9H), 4.03-4.00 (m, 1H), 3.83-3.68 (m, 4H), 3.23-3.20 (m, 1H), 3.00 (d, *J* = 12.0 Hz, 1H), 2.79-2.73 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.1, 138.2, 132.1, 129.9, 128.8, 128.3, 127.9, 127.0,76.7, 61.1, 50.0, 49.4, 45.5, 21.6; HRMS (TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{20}ClNO_3S$ 366.8199; found 366.8198; HPLC (Daicel Chiralcel OJ-H, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 210 nm) t_1 = 13.3 min (minor), t_2 = 15.4 min (major).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	15.038	1855689	29455	M	25.458
2	17.804	1751268	17209	M	24.025
3	22.477	1887734	39954		25.897
4	36.254	1794662	23717	M	24.620
Total		7289352	110335		100.000

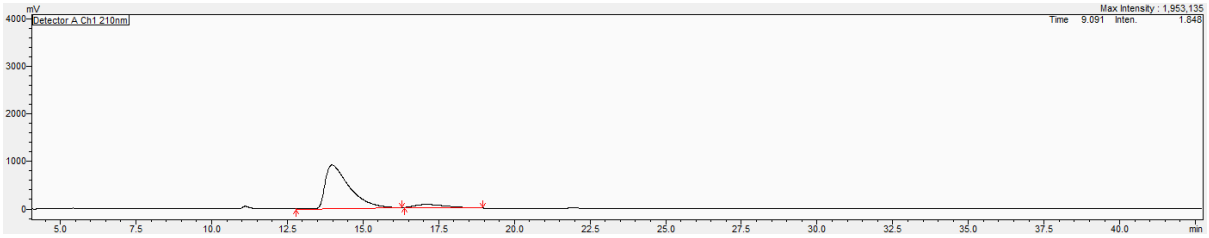


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	13.277	2181589	63580	M	9.915
2	15.356	19821288	324644	M	90.085
Total		22002877	388225		100.000

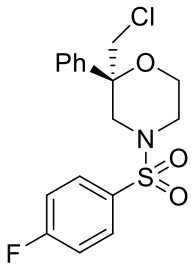


ent-**2b**

34.7 mg, 95%; $[\alpha]_D^{25}$= +57.6 (*c* 1.0, MeOH, 83% ee); HPLC (Daicel Chiralcel OJ-H, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 210 nm) t_1 = 14.0 min (major), t_2 = 17.1 min (minor).

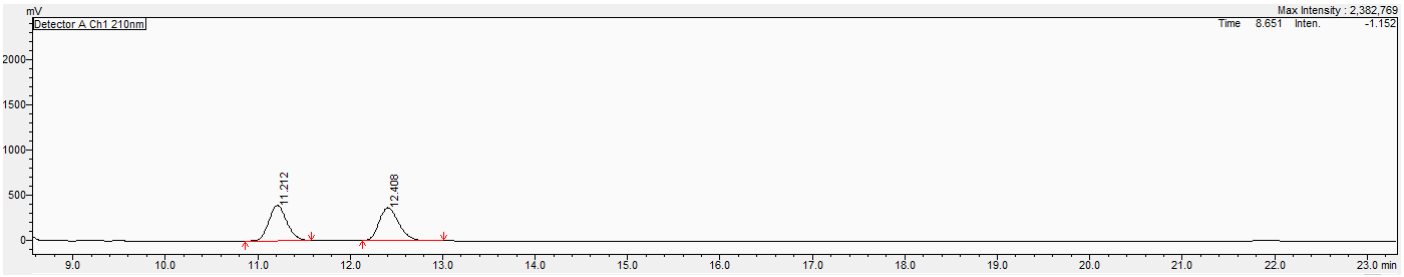


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	13.980	50906385	917707	M	91.413
2	17.091	4782089	65563	M	8.587
Total		55688474	983271		100.000

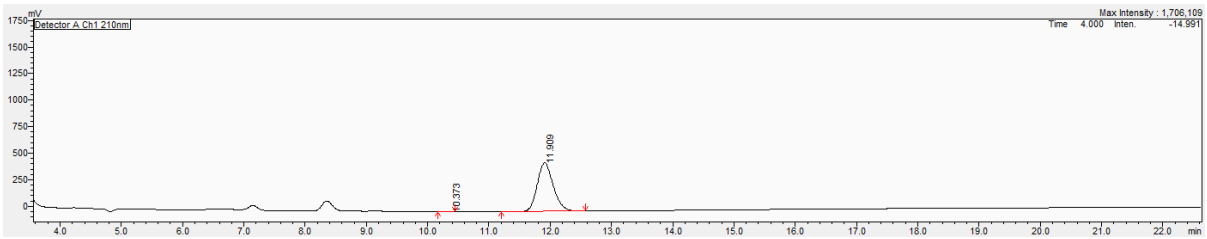


2c

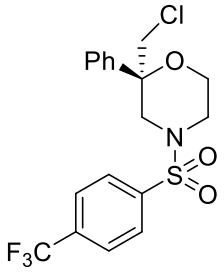
33.7 mg, 91%, yellow solid; MP 182－183 ℃; $[\alpha]_D^{25}$= +79.2 (*c* 1.0, MeOH, >99% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.83-7.25 (m, 9H), 4.08 (d, *J* = 12.0 Hz, 1H), 3.83-3.70 (m, 4H), 3.26-2.72 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.8 (d, *J* = 254.0 Hz), 137.9, 130.6 (d, *J* = 9.0 Hz), 128.9, 128.5, 127.0, 116.8 (d, *J* = 22.0 Hz), 76.8, 61.0, 50.1, 49.3, 45.5; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{17}ClFNO_3S$ 370.8264; found 370.8265; HPLC (Daicel Chiralcel AD-H, *i*-PrOH/Hexane = 1 /99, 1.0 mL/min, 210 nm) t_1 = 10.4 min (minor), t_2 = 11.9 min (major).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	11.212	5322769	392382	M	49.559
2	12.408	5417519	365960	M	50.441
Total		10740288	758342		100.000

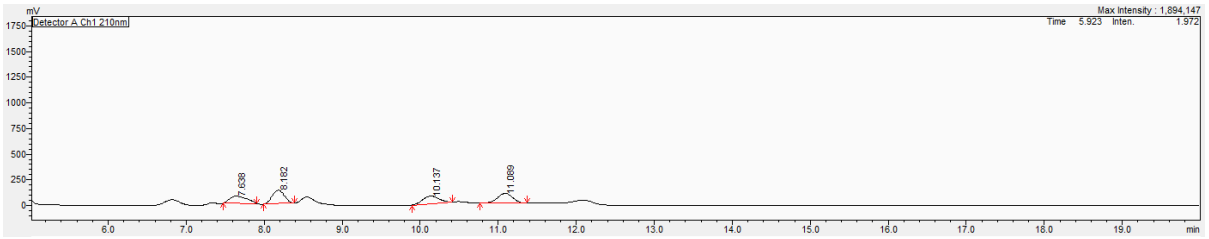


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	10.373	2611	209		0.032
2	11.909	8269794	456004	M	99.968
Total		8272405	456214		100.000

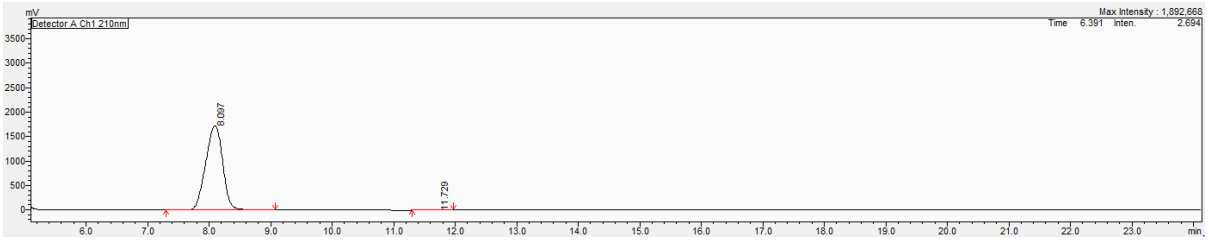


2d

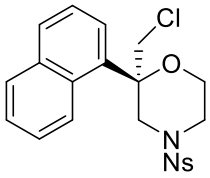
38.5 mg, 92%, yellow solid; MP 189－190 ℃; $[\alpha]_D^{25}$= +62.7 (*c* 1.0, MeOH, 99.5% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95-7.86 (m, 4H), 7.53-7.36 (m, 5H), 4.14 (d, *J* = 12.0 Hz, 1H), 3.84-3.70 (m, 4H), 3.03-2.76 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.9, 137.7, 135.1 (q, *J* = 32.0 Hz), 128.9, 128.5, 128.3, 127.0, 126.6, 126.5, 76.8, 60.9, 50.1, 49.2, 45.4; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{18}H_{17}ClF_3NO_3S$ 420.6102; found 420.6103; HPLC (Daicel Chiralcel IC, *i*-PrOH/Hexane = 10/90, 1.0 mL/min, 210 nm) t_1 = 10.4 min (minor), t_2 = 11.9 min (major).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	7.638	1070441	69783	M	21.961
2	8.182	1428180	130993	M	29.300
3	10.137	1028040	71994	M	21.091
4	11.089	1347605	97283	M	27.647
Total		4874265	370053		100.000

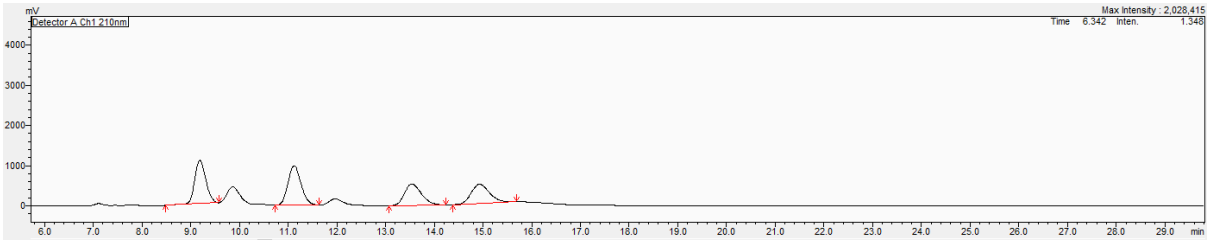


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	8.097	33107528	1716662	M	99.725
2	11.729	91312	4778	M	0.275
Total		33198840	1721440		100.000

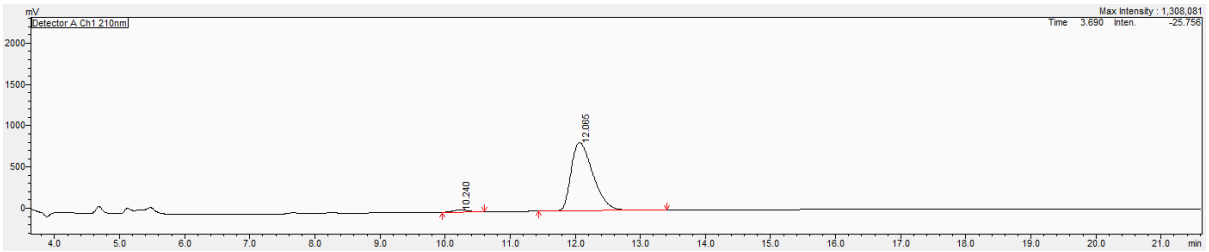


2e

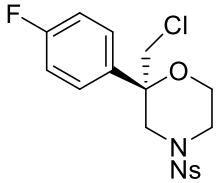
36.6 mg, 82%, yellow solid; MP 204－205 ℃; $[\alpha]_D^{25}$= －47.3 (*c* 1.0, MeOH, 96% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.74-8.71 (m, 1H), 8.50 (d, *J* = 12.0 Hz, 2H), 8.06 (d, *J* = 8.0 Hz, 2H), 7.91-7.50 (m, 6H), 4.74 (d, *J* = 12.0 Hz, 1H), 4.07 (dd, J_1 = 12.0 Hz, J_2 = 48.0 Hz, 2H), 3.83-3.49 (m, 3H), 2.91 (d, *J* = 12.0 Hz, 1H), 2.69-2.62 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.6, 141.1, 135.0, 131.2, 130.8, 130.4, 129.7, 129.6, 129.1, 126.5, 125.6, 125.1, 125.0, 124.6, 79.7,61.2, 50.2, 49.1, 45.3; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{21}H_{19}ClN_2O_5S$ 447.8358; found 447.8359; HPLC (Daicel Chiralcel AD-H, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 254 nm) t_1 = 10.2 min (minor), t_2 = 12.1 min (major).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	9.188	17300350	1083019	M	28.374
2	11.125	18210912	979773		29.868
3	13.543	12853486	534943		21.081
4	14.930	12607172	477917		20.677
Total		60971919	3075652		100.000

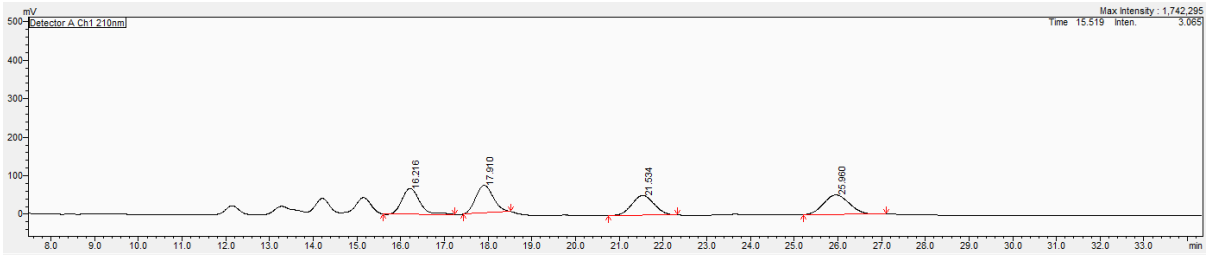


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	10.240	394902	25469	M	1.999
2	12.065	19359612	823628	M	98.001
Total		19754514	849097		100.000

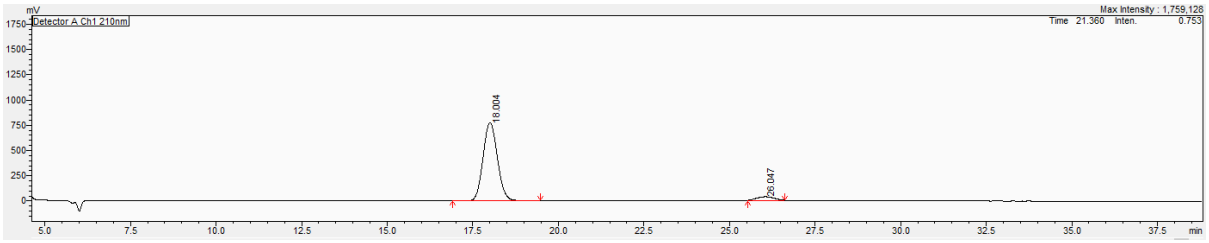


2f

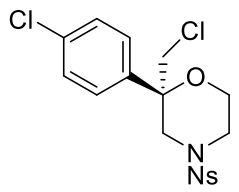
39.3 mg, 95%, yellow solid; MP 172－173 ℃; $[\alpha]_D^{25}$= +77.2 (*c* 1.0, MeOH, 90% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.43 (d, *J* = 12.0 Hz, 2H), 8.00 (d, *J* = 8.0 Hz, 2H), 7.52-7.12 (m, 4H), 4.17-3.69 (m, 3H), 3.66 (s, 2H), 3.36-2.94 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.9 (d, *J* = 248.0 Hz), 150.5, 141.1, 133.3 (d, *J* = 3.0 Hz), 129.1 (d, *J* = 9.0 Hz), 124.6, 116.0 (d, *J* = 22.0 Hz), 76.5, 60.9, 50.1, 49.3, 45.4; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{16}ClFN_2O_5S$ 415.3826; found 415.3827; HPLC (Daicel Chiralcel IC, *i*-PrOH/Hexane = 20/80, 1.0 mL/min, 210 nm) t_1 = 18.0 min (major), t_2 = 16.0 min (minor).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	16.216	1870215	67256	M	24.073
2	17.910	2004615	71928	M	25.803
3	21.534	1832932	51532	M	23.593
4	25.960	2061115	50608	M	26.530
Total		7768878	241323		100.000

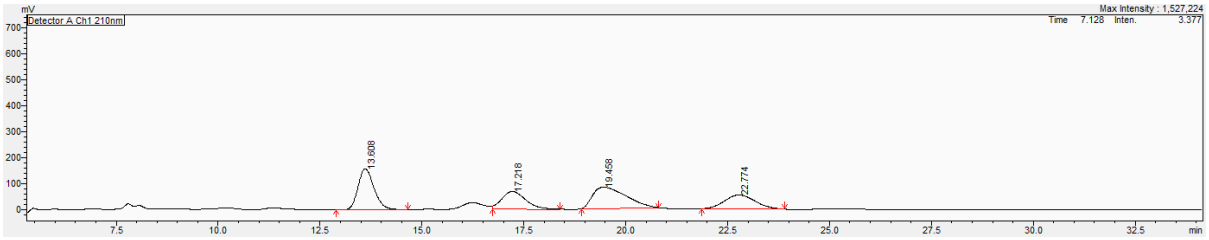


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	18.004	22463327	776354	M	94.762
2	26.047	1241760	35531	M	5.238
Total		23705087	811885		100.000

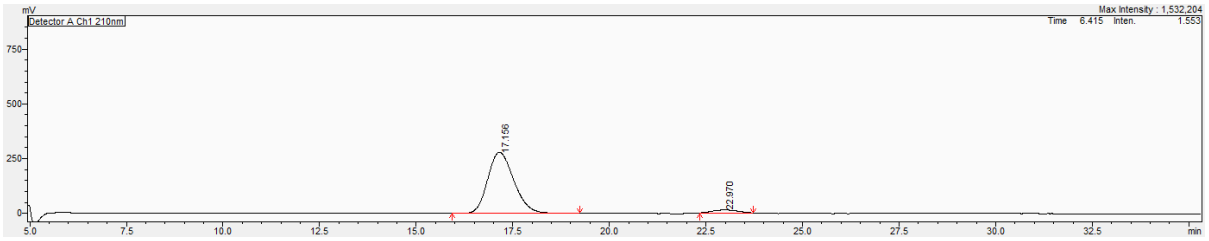


2g

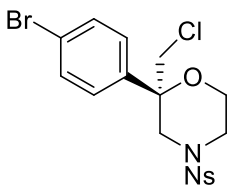
41.3 mg, 96%, yellow solid; MP 177－178 ℃; $[\alpha]_D^{25}$= +96.3 (*c* 1.0, MeOH, 91% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.46 (d, *J* = 8.0 Hz, 2H), 8.00 (d, *J* = 8.0 Hz, 2H), 7.47-7.42 (m, 4H), 4.17-3.85 (m, 3H), 3.65 (s, 2H), 3.37-2.73 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.5, 141.1, 136.1, 134.7, 129.0, 128.6, 124.6, 76.6, 61.0, 49.9, 49.2, 45.4; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{16}Cl_2N_2O_5S$ 431.5090; found 431.5089; HPLC (Daicel Chiralcel OD-H, *i*-PrOH/Hexane = 30/70, 1.0 mL/min, 210 nm) t_1 = 17.2 min (major), t_2 = 23.0 min (minor).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	13.608	4289135	157292	M	29.703
2	17.218	2763472	67768	M	19.138
3	19.458	4578086	81149	M	31.704
4	22.774	2809361	53842	M	19.455
Total		14440054	360051		100.000

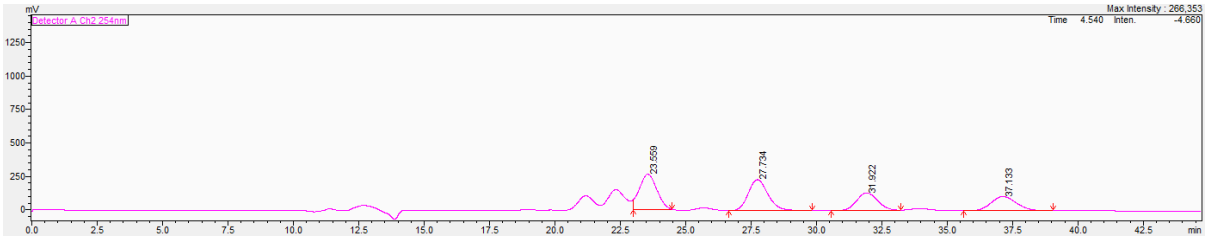


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	17.156	13100560	278986	M	95.491
2	22.970	618583	13522	M	4.509
Total		13719144	292508		100.000

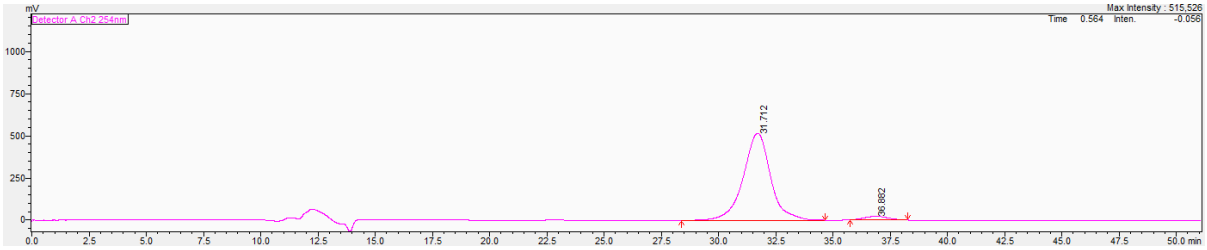


2h

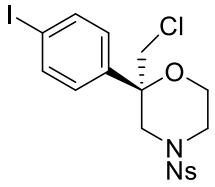
45.5 mg, 96%, yellow solid; MP 197－198 ℃; $[\alpha]_D^{25}$= +73.0 (*c* 1.0, MeOH, 94% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.46 (d, *J* = 12.0 Hz, 2H), 7.99 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 4.15-3.65 (m, 5H), 3.36-2.74 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.5, 141.0, 136.6, 132.1, 129.0, 128.9, 124.6, 122.9, 76.7, 61.0, 49.8, 49.2, 45.5; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{16}ClBrN_2O_5S$ 475.1367; found 475.1368; HPLC (Daicel Chiralcel IC, *i*-PrOH/Hexane = 30/70, 1.0 mL/min, 254 nm) t_1 = 31.7 min (major), t_2 = 36.9 min (minor).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	23.559	12378526	266120	M	31.888
2	27.734	12103191	231191		31.178
3	31.922	7226324	131519		18.615
4	37.133	7111194	105816		18.319
Total		38819235	734646		100.000

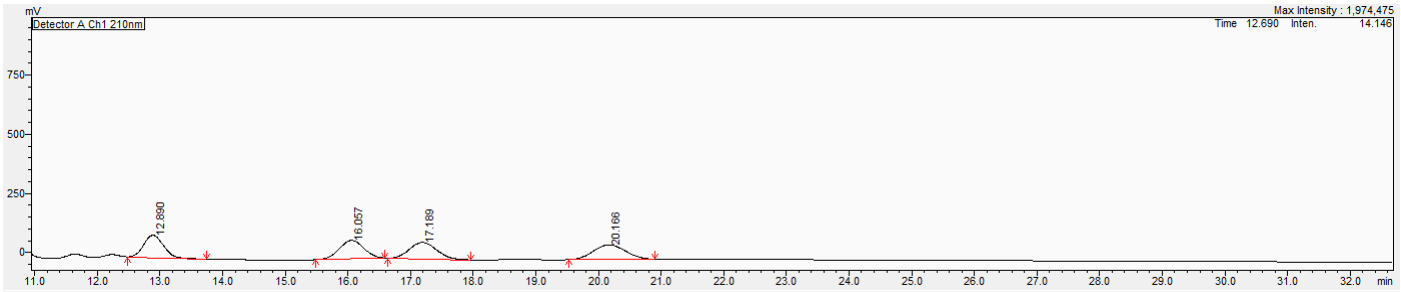


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	31.712	42575767	515916	M	96.926
2	36.882	1350465	20135	M	3.074
Total		43926232	536050		100.000

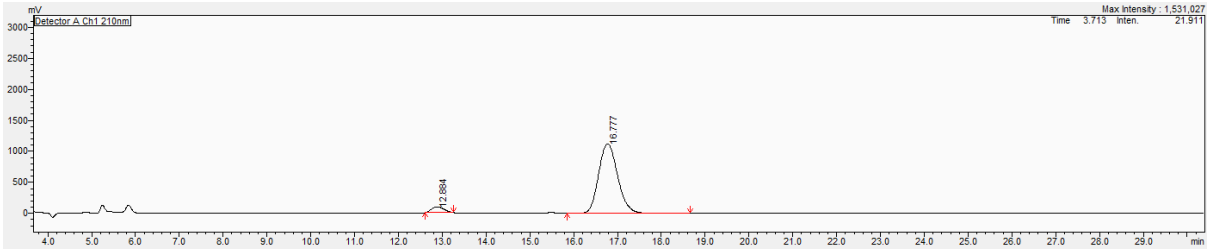


2i

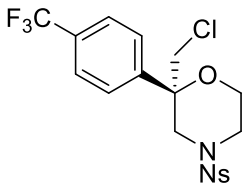
48.5 mg, 93%, yellow solid; MP 217－218 ℃; $[\alpha]_D^{25}$= +64.9 (*c* 1.0, MeOH, 90% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.45 (d, *J* = 8.0 Hz, 2H), 7.99 (d, *J* = 8.0 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 4.14-3.64 (m, 5H), 3.35-2.74 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.5, 141.0, 138.1, 137.3, 129.1, 129.0, 124.6, 94.7, 76.8, 61.0, 49.8, 49.1, 45.4; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{16}ClIN_2O_5S$ 523.7125; found 523.7126; HPLC (Daicel Chiralcel IC, *i*-PrOH/Hexane = 30/70, 1.0 mL/min, 210 nm) t_1 = 12.9 min (minor), t_2 = 16.8 min (major).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	12.890	2064815	94111		24.314
2	16.057	2116939	77879	M	24.928
3	17.189	2089055	69261		24.600
4	20.166	2221368	61995	M	26.158
Total		8492177	303246		100.000

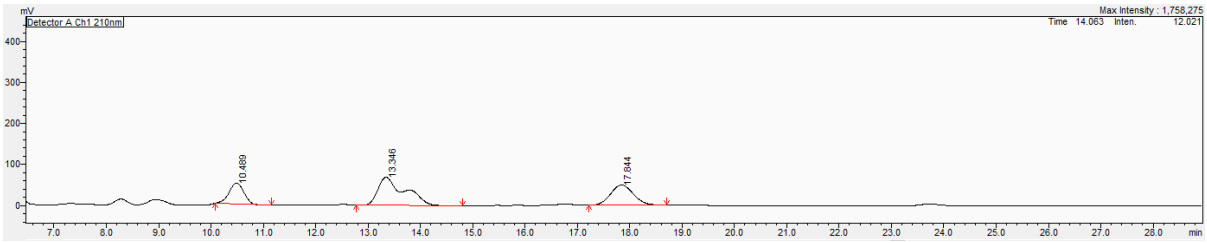


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	12.884	1882057	95670	M	5.283
2	16.777	33745753	1121907	M	94.717
Total		35627810	1217577		100.000

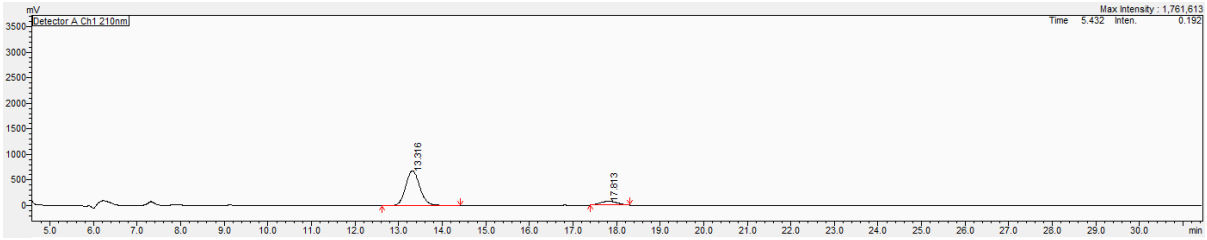


2j

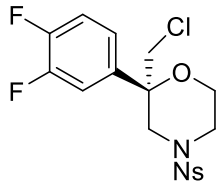
39.0 mg, 84%, yellow solid; MP 195－196 ℃; $[\alpha]_D^{25}$= +49.3 (*c* 1.0, MeOH, 77% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.46 (d, *J* = 8.0 Hz, 2H), 8.00 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 12.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 4.19-3.65 (m, 5H), 3.36-2.77 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.6, 141.7, 140.9, 131.0, 130.6, 129.0, 127.6, 125.9 (q, *J* = 4.0 Hz), 124.7, 76.7, 61.0, 49.6, 49.4, 45.4; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{18}H_{16}ClF_3N_2O_5S$ 465.8291; found 465.8292; HPLC (Daicel Chiralcel IC, *i*-PrOH/Hexane = 20/80, 1.0 mL/min, 210nm) t_1 = 13.3 min (major), t_2 = 17.8 min (minor).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	10.489	995506	50758	M	20.165
2	13.346	2413008	68459	M	48.878
3	17.844	1528302	49561	M	30.957
Total		4936816	168778		100.000

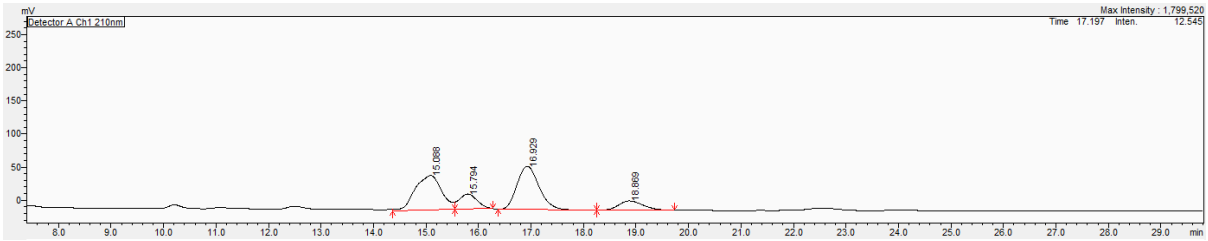


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	13.316	15314397	679367	M	88.284
2	17.813	2032304	74605	M	11.716
Total		17346701	753971		100.000

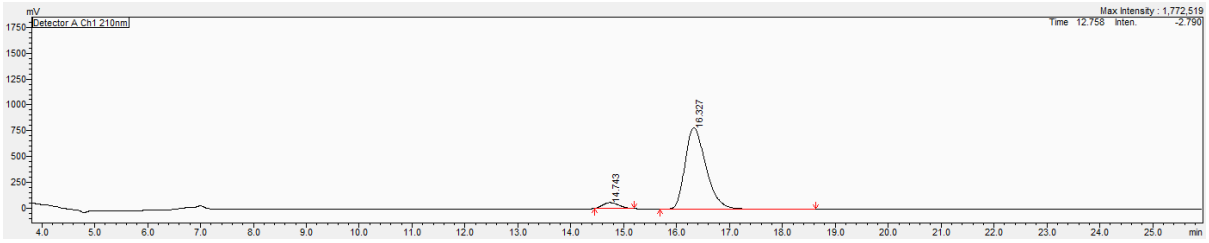


2k

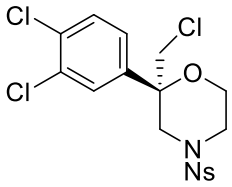
42.3 mg, 98%, yellow solid; MP 179－180 ℃; $[\alpha]_D^{25}$= +68.9 (*c* 1.0, MeOH, 90% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.47 (d, *J* = 12.0 Hz, 2H), 8.00 (d, *J* = 8.0 Hz, 2H), 7.40-7.24 (m, 3H), 4.10-3.61 (m, 5H), 3.37-2.93 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 151.8, 150.6, 149.5 (d, *J* = 12.0 Hz), 141.1, 134.8, 128.9, 124.6, 123.5, 117.8 (d, *J* = 18.0 Hz), 116.1 (d, *J* = 19.0 Hz), 76.3, 61.0, 49.6, 49.4, 45.5; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{17}H_{15}ClF_2N_2O_5S$ 433.7523; found 433.7524; HPLC (Daicel Chiralcel AD-H, *i*-PrOH/Hexane = 20/80, 1.0 mL/min, 210 nm) t_1 = 14.7 min (minor), t_2 = 16.3 min (major).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	15.088	1848711	52268	M	39.219
2	15.794	526300	22505	M	11.165
3	16.929	1882550	65088	S	39.937
4	18.869	456200	14075		9.678
Total		4713761	153937		100.000

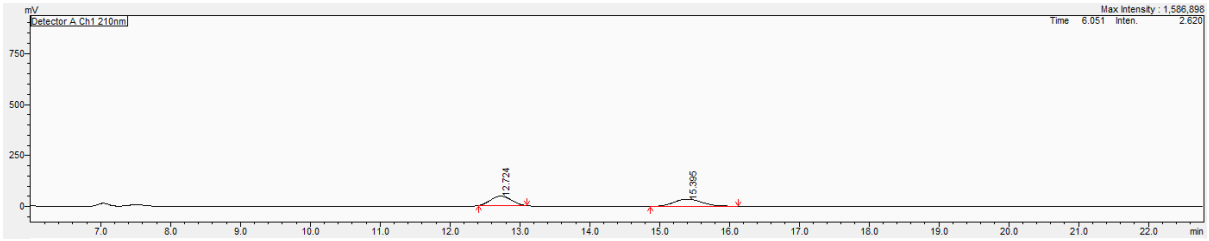


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	14.743	1187930	56393	M	5.246
2	16.327	21457002	782937	M	94.754
Total		22644933	839329		100.000

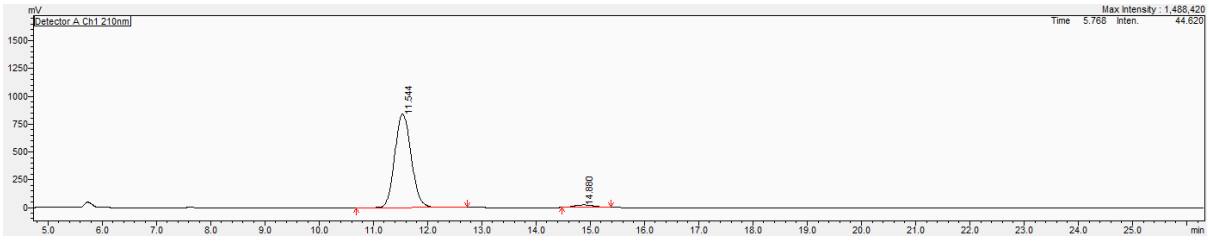


2l

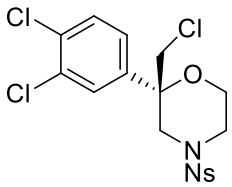
44.6 mg, 96%, yellow solid; MP 184－185 ℃; $[\alpha]_D^{25}$= +44.4 (*c* 1.0, MeOH, 94% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.46 (d, *J* = 8.0 Hz, 2H), 8.00 (d, *J* = 8.0 Hz, 2H), 7.60-7.35 (m, 3H), 4.07-3.62 (m, 5H), 3.35-2.80 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.6, 141.0, 138.0, 133.3, 133.0, 130.9, 129.2, 129.0, 126.6, 124.7, 76.4, 61.1, 49.4, 45.4, 22.5; HRMS (TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{15}Cl_3N_2O_5S$ 465.5796; found 465.5797; HPLC (Daicel Chiralcel IC, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 210 nm) t_1 = 11.5 min (major), t_2 = 14.9 min (minor).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	12.724	941783	46235	M	49.342
2	15.395	966905	35195	M	50.658
Total		1908688	81430		100.000

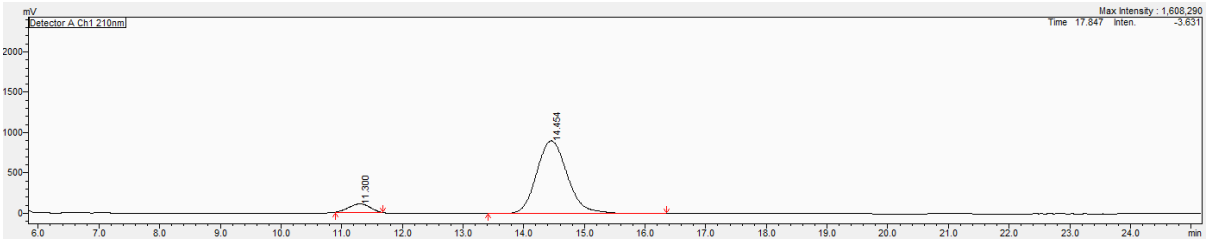


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	11.544	17747780	839929	M	96.803
2	14.880	586101	22744	M	3.197
Total		18333882	862673		100.000

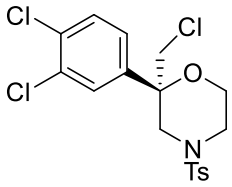


ent-**2l**

43.6 mg, 94%, $[\alpha]_D^{25}$= －29.7 (*c* 1.0, MeOH, 85% ee); HPLC (Daicel Chiralcel IC, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 210 nm) t_1 = 11.3 min (minor), t_2 = 14.5 min (major).

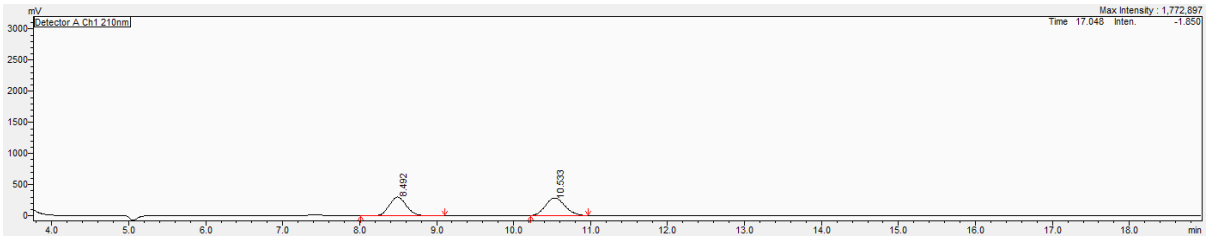


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	11.300	2502817	103545	M	7.297
2	14.454	31797959	900967	M	92.703
Total		34300776	1004512		100.000

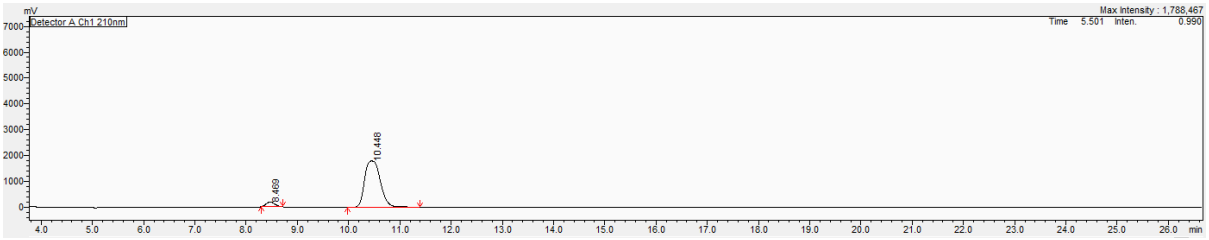


2m

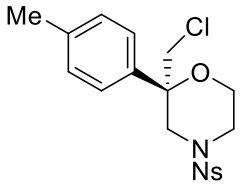
41.6 mg, 96%, yellow solid; MP 171－172 ℃; $[\alpha]_D^{25}$= +32.1 (*c* 1.0, MeOH, 89% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.68-7.34 (m, 7H), 3.92-3.61 (m, 5H), 3.24-2.76 (m, 3H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.4, 138.6, 133.1, 132.6, 131.9, 130.7, 130.0, 129.2, 127.8, 126.7, 76.3, 61.3, 49.7, 49.4, 45.5, 21.6; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{18}H_{18}Cl_3NO_3S$ 434.7022; found 434.7023; HPLC (Daicel Chiralcel AD-H, *i*-PrOH/Hexane = 20/80, 1.0 mL/min, 210 nm) t_1 = 8.5 min (minor), t_2 = 10.4 min (major).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	8.492	4640844	301855	M	47.988
2	10.533	5030030	282453	M	52.012
Total		9670873	584308		100.000

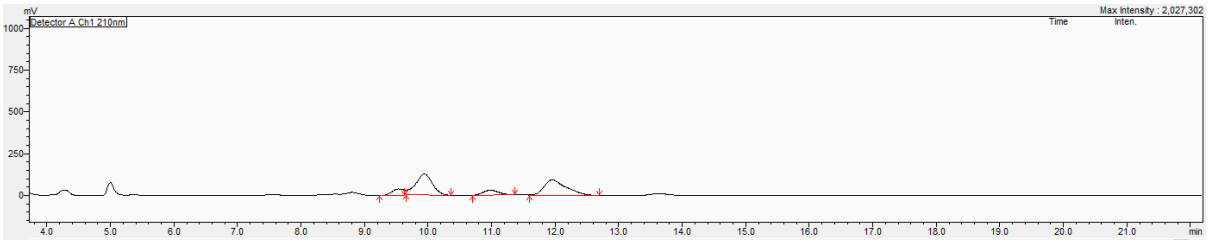


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	8.469	2213348	185482	M	5.447
2	10.448	38421710	1786880	M	94.553
Total		40635059	1972362		100.000

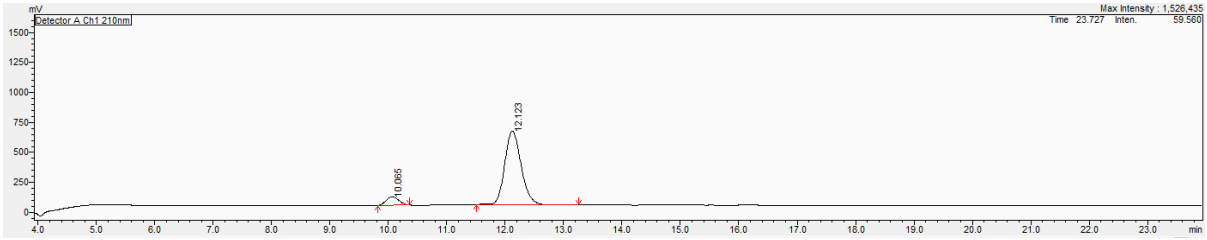


2n

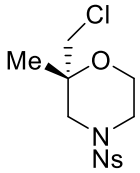
40.2 mg, 98%, yellow solid; MP 200－201 ℃; $[\alpha]_D^{25}$= +61.4 (*c* 1.0, MeOH, 84% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.45 (d, *J* = 8.0 Hz, 2H), 7.99 (d, *J* = 8.0 Hz, 2H), 7.40-7.25 (m, 4H), 4.16 (d, *J* = 12.0 Hz, 1H), 3.83-3.63 (m, 4H), 3.35-3.31 (m, 1H), 3.00 (d, *J* = 12.0 Hz, 1H), 2.79-2.74 (m, 1H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.5, 141.3, 138.5, 134.5, 129.7, 129.0, 126.9, 124.5, 76.7, 60.8, 50.3, 49.1, 45.4,21.9; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{18}H_{19}ClN_2O_5S$ 411.6972; found 411.6973; HPLC (Daicel Chiralcel AD-H, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 210 nm) t_1 = 10.0 min (minor), t_2 = 12.1 min (major).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	9.535	492893	37798	M	8.994
2	9.941	2285662	125523	M	41.708
3	10.982	504086	29453	M	9.198
4	11.955	2197474	91274		40.099
Total		5480114	284047		100.000

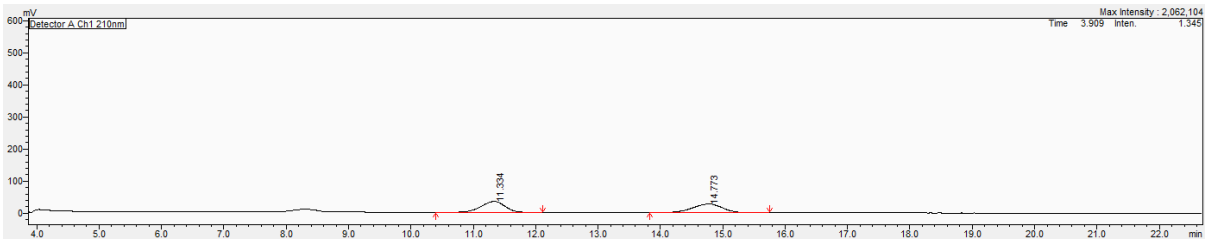


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	10.065	1042541	70660	M	8.028
2	12.123	11943692	614042	M	91.972
Total		12986233	684701		100.000

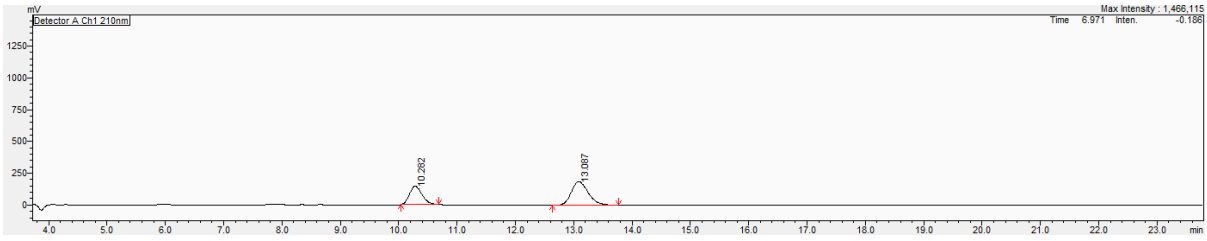


2o

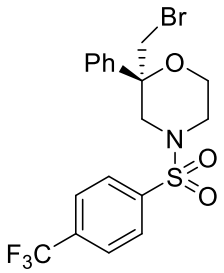
30.1 mg, 90%, yellow solid; MP 146－147 ℃; $[\alpha]_D^{25}$= +2.8 (*c* 1.0, MeOH, 26% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.45 (d, *J* = 12.0 Hz, 2H), 7.98 (d, *J* = 12.0 Hz, 2H), 3.91-3.55 (m, 4H), 3.12-2.90 (m, 4H), 1.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 152.2, 141.6, 128.9, 124.5, 72.7, 60.4, 51.4, 47.4, 45.3, 20.8; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{12}H_{15}ClN_2O_5S$ 335.6819; found 335.6820; HPLC (Daicel Chiralcel AD-H, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 210 nm) t_1 = 10.0 min (minor), t_2 = 13.1 min (major).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	11.334	960642	34590		50.604
2	14.773	937724	27278	V	49.396
Total		1898366	61867		100.000

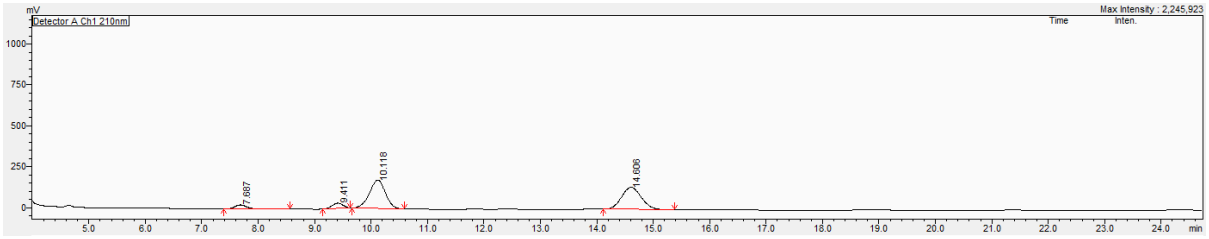


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	10.282	2157239	144492	M	36.855
2	13.087	3696137	184966	M	63.145
Total		5853376	329458		100.000

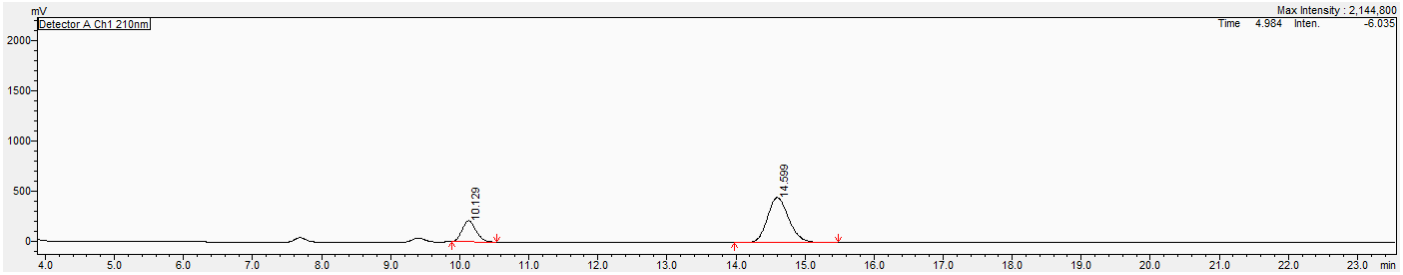


2d-Br

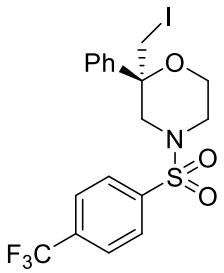
44.9 mg, 97%, white solid; MP 197－198 ℃; $[\alpha]_D^{25}$= +9.4 (*c* 1.0, MeOH, 54% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.94-7.86 (m, 4H), 7.52-7.37 (m, 5H), 4.07 (d, *J* = 12.0 Hz, 1H), 3.85-3.57 (m, 4H), 3.25-2.81 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.9, 137.9, 135.1, 134.8, 128.9, 128.5, 128.3, 126.8, 126.5 (q, *J* = 30.0 Hz), 128.9, 128.5, 128.3, 127.0, 126.6, 126.5, 76.8, 60.9, 50.1, 49.2, 45.4; HRMS (TOF) m/z: [M＋H]$^+$Calcd for $C_{18}H_{17}BrF_3NO_3S$ 464.5912; found 464.5913; HPLC (Daicel Chiralcel AD-H, *i*-PrOH/Hexane = 10/90, 1.0 mL/min, 210 nm) t_1 = 10.1 min (minor), t_2 = 14.6 min (major).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	7.687	368595	24349		4.885
2	9.411	442340	32230	M	5.863
3	10.118	3426041	173555		45.408
4	14.606	3307995	135140		43.844
Total		7544971	365275		100.000

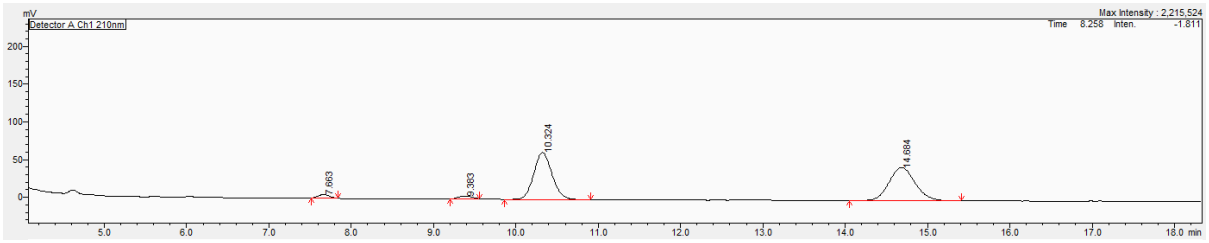


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	10.129	2898955	208782	M	23.238
2	14.599	9575923	448602	M	76.762
Total		12474878	657384		100.000

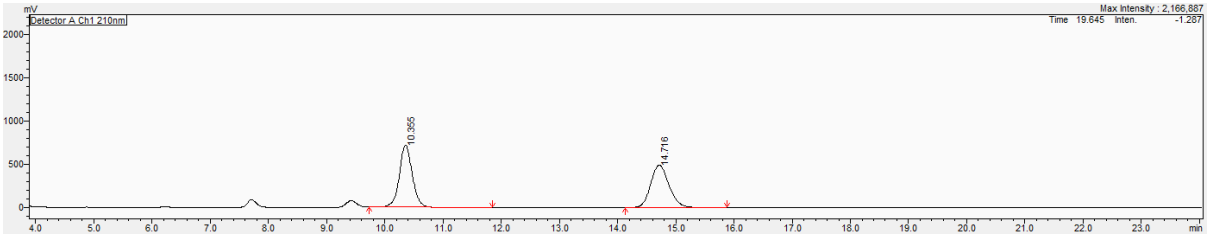


2d-I

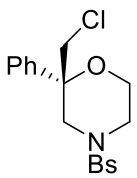
48.5 mg, 95%, yellow solid; MP 225－226 ℃; $[\alpha]_D^{25}$ = 0 (*c* 1.0, MeOH, 2% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.93-7.85 (m, 4H), 7.49-7.35 (m, 5H), 3.87-3.75 (m, 3H), 3.65 (d, *J* = 8.0 Hz, 1H), 3.48 (d, *J* = 8.0 Hz, 1H), 3.21-2.92 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.9, 138.6, 135.1, 134.8, 128.8, 128.3, 126.6 (q, *J* = 30.0 Hz), 126.4, 75.0, 61.1, 51.4, 45.3, 13.8; HRMS (TOF) m/z: [M＋H]$^+$ Calcd for $C_{18}H_{17}IF_3NO_3S$ 512.4077; found 512.4076; HPLC (Daicel Chiralcel AD-H, *i*-PrOH/Hexane = 10/90, 1.0 mL/min, 210 nm) t_1 = 10.1 min (minor), t_2 = 14.6 min (major).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	7.663	45690	4633	M	2.257
2	9.383	43192	3817	M	2.133
3	10.324	969095	62371		47.863
4	14.684	966729	43899	M	47.747
Total		2024707	114720		100.000

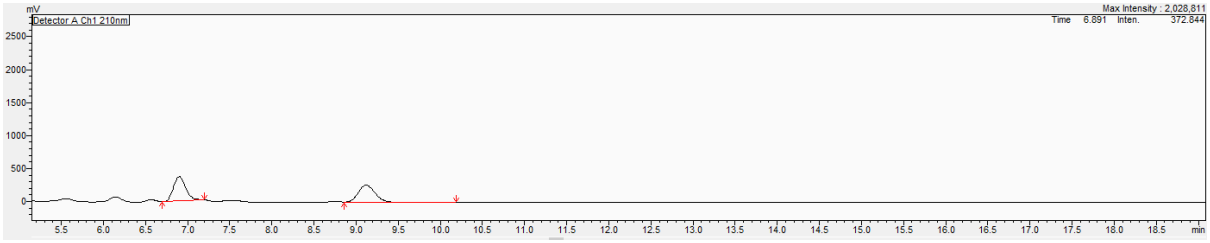


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	10.355	11049054	715308	S	50.985
2	14.716	10622053	488247		49.015
Total		21671106	1203556		100.000

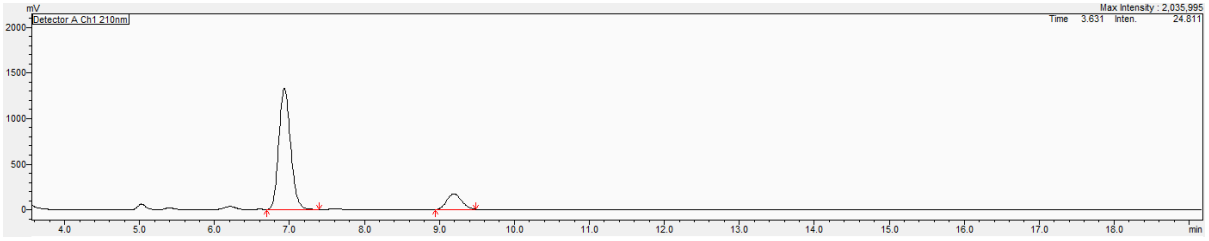


ent-**2r**

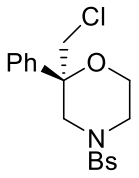
33.0 mg, 94%, yellow solid; MP 165－166 ℃; $[\alpha]_D^{25}$=－65.1 (*c* 1.0, MeOH, 73% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.81-7.35 (m, 10H), 4.07 (d, *J* = 12.0 Hz,1H), 3.84-3.68 (m, 4H), 3.26-3.23 (m, 1H), 3.01 (d, *J* = 12.0 Hz, 1H), 2.79-2.73 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.0, 135.0, 133.3, 129.3, 128.8, 128.4, 127.8, 127.0, 76.7, 61.0, 50.1, 49.4, 45.5; HRMS (TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}ClN_2O_3S$ 352.9033; found 352.9034; HPLC (Daicel Chiralcel AD-H, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 210 nm) t_1 = 6.9 min (major), t_2 = 9.2 min (minor).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	6.901	3702749	366892	M	49.957
2	9.119	3709183	262611	V	50.043
Total		7411932	629503		100.000

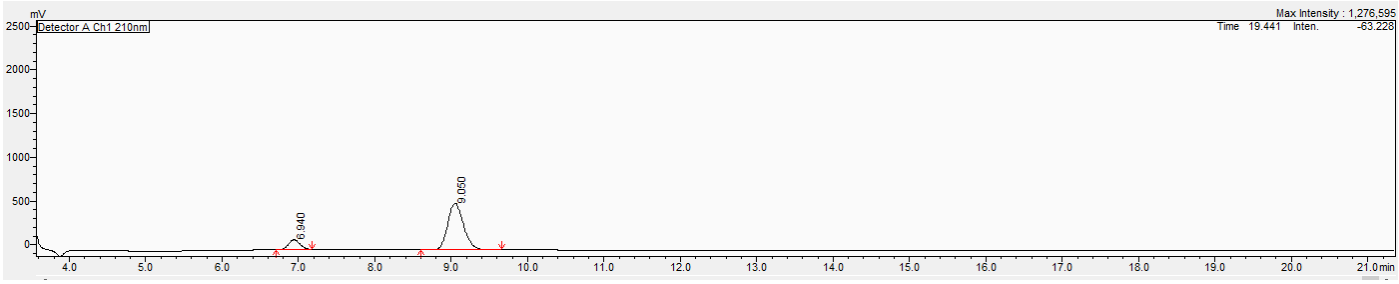


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	6.931	14731685	1332202	V	86.359
2	9.191	2327023	171384	M	13.641
Total		17058708	1503587		100.000

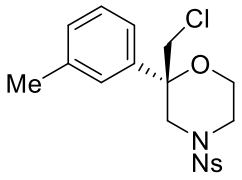


2r

33.3 mg, 95%, $[\alpha]_D^{25}$= +61.2 (*c* 1.0, MeOH, 73% ee); HPLC (Daicel Chiralcel AD-H, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 210 nm) t_1 = 6.9 min (minor), t_2 = 9.1 min (major).

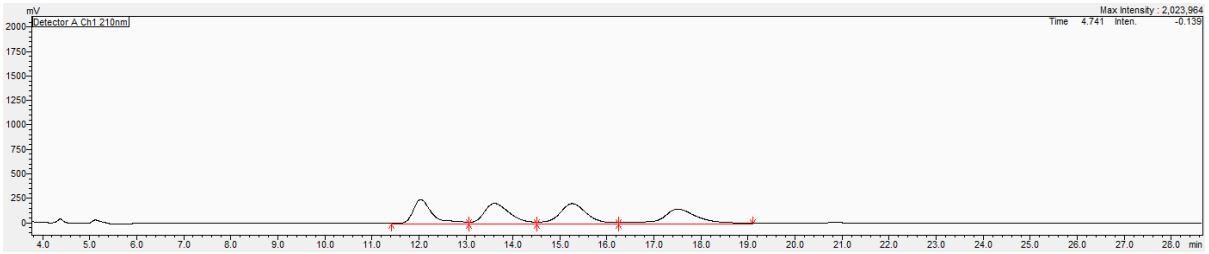


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	6.940	1196097	112979	M	13.504
2	9.050	7661372	533246	M	86.496
Total		8857470	646225		100.000

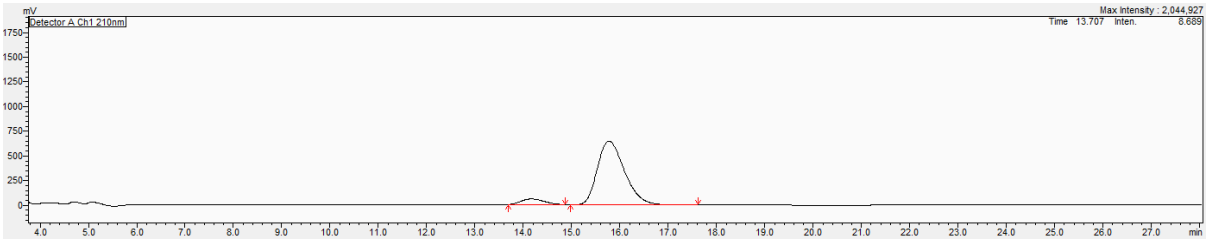


ent-**2s**

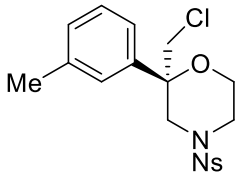
40.2 mg, 98%, yellow solid; MP 186－187 ℃; $[\alpha]_D^{25}$= +65.3 (*c* 1.0, MeOH, 86% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.45 (d, *J* = 8.0 Hz, 2H), 7.99 (d, *J* = 8.0 Hz, 2H), 7.36-7.19 (m, 4H), 4.11 (d, *J* = 12.0 Hz, 1H), 3.80-3.75 (m, 4H), 3.32-3.30 (m, 1H), 3.05 (d, *J* = 12.0 Hz, 1H), 2.84-2.78 (m, 1H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.5, 141.2, 138.6, 137.5, 129.4, 129.0, 128.8, 127.5, 127.6, 124.0, 76.7, 60.9, 50.0, 49.2, 45.4, 21.7; HRMS (TOF) m/z: [M ＋ H]$^+$ Calcd for $C_{18}H_{19}ClN_2O_5S$ 411.6972; found 411.6971; HPLC (Daicel Chiralcel OD-H, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 210 nm) t_1 = 14.2 min (minor), t_2 = 15.8 min (major).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	12.040	7546957	251348	V	23.295
2	13.609	8249933	210207	V	25.465
3	15.261	8551472	207424	V	26.396
4	17.507	8048486	150348	V	24.843
Total		32396847	819327		100.000

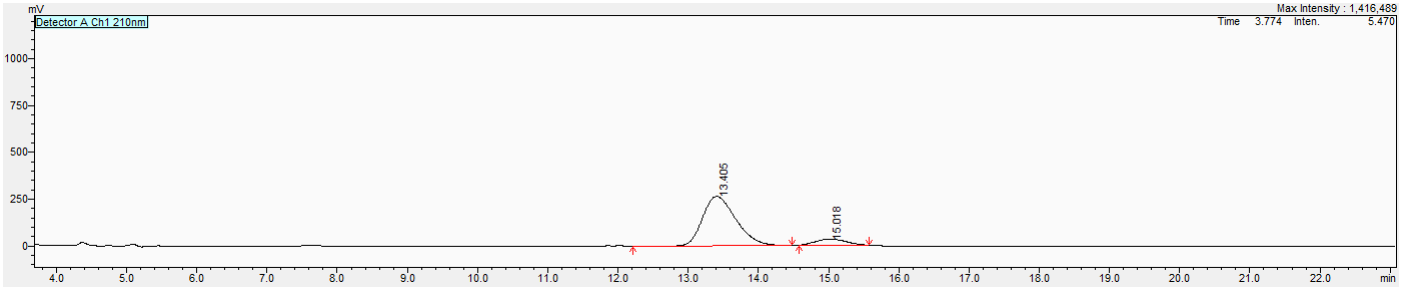


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	14.167	1954742	57715	M	7.189
2	15.774	25236485	647060	M	92.811
Total		27191226	704775		100.000

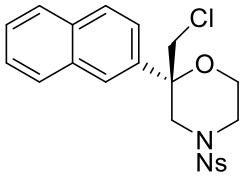


2s

38.5 mg, 94%, $[\alpha]_D^{25}$ = －59.6 (*c* 1.0, MeOH, 79% ee); HPLC (Daicel Chiralcel OD-H, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 210 nm) t_1 = 13.4 min (major), t_2 = 15.0 min (minor).

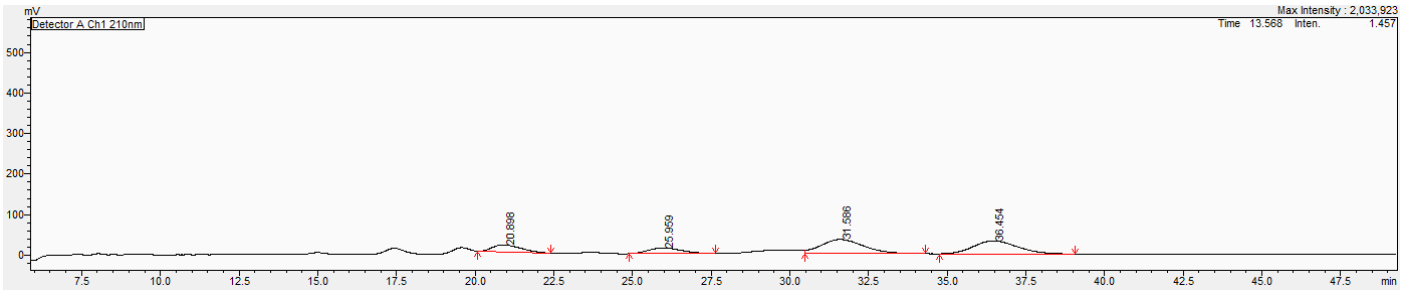


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	13.405	8592296	262582	M	89.615
2	15.018	995734	32939	M	10.385
Total		9588030	295521		100.000

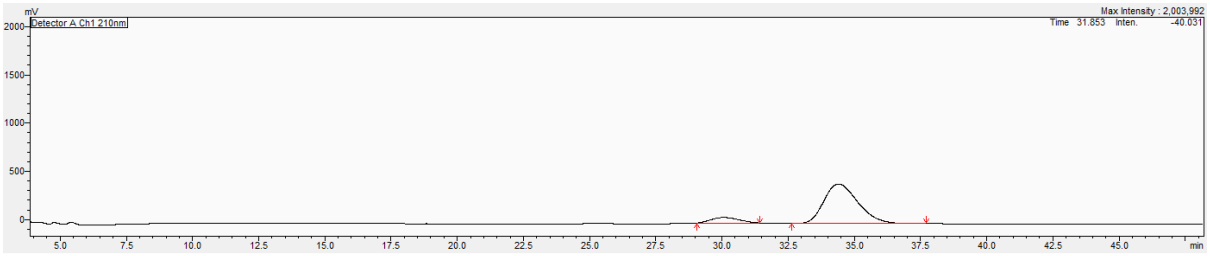


ent-**2t**

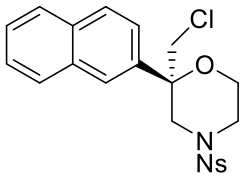
41.5 mg, 93%, yellow solid; MP 198－199 ℃; $[\alpha]_D^{25}$= －55.8 (*c* 1.0, MeOH, 80% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.42-7.54 (m, 11H), 4.32-3.75 (m, 5H), 3.36 (d, *J* = 8.0 Hz, 1H), 3.12 (d, *J* = 16.0 Hz, 1H), 2.86-2.81 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.5, 141.4, 134.8, 133.2, 133.1, 128.9, 128.5, 127.6, 127.4, 126.8, 126.5, 124.5, 123.7, 77.0, 61.1, 50.0, 49.3, 45.4; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{21}H_{19}ClN_2O_5S$ 447.8358; found 447.8357; HPLC (Daicel Chiralcel OD-H, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 210 nm) t_1 = 30.1 min (minor), t_2 = 34.4 min (major).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	20.898	1124285	17507	M	13.327
2	25.959	1033088	14105	M	12.246
3	31.586	3108271	33861	M	36.846
4	36.454	3170256	32240	V	37.581
Total		8435900	97714		100.000

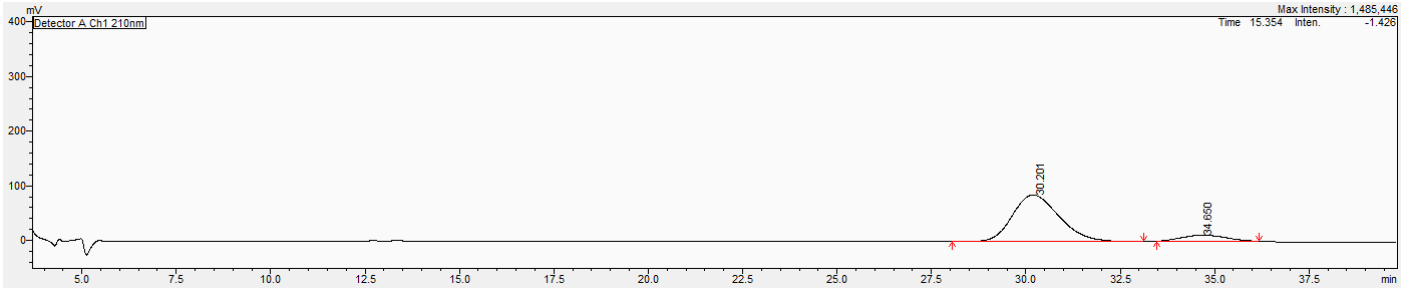


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	30.055	4181386	57084	M	10.162
2	34.404	36967724	411610	M	89.838
Total		41149110	468694		100.000

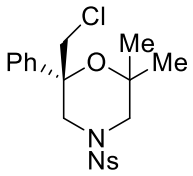


2t

41.9 mg, 94%, $[\alpha]_D^{25}$= +52.9 (*c* 1.0, MeOH, 78% ee); HPLC (Daicel Chiralcel OD-H, *i*-PrOH/Hexane = 35/65, 1.0 mL/min, 210 nm) t_1 = 30.2 min (major), t_2 = 34.6 min (minor).



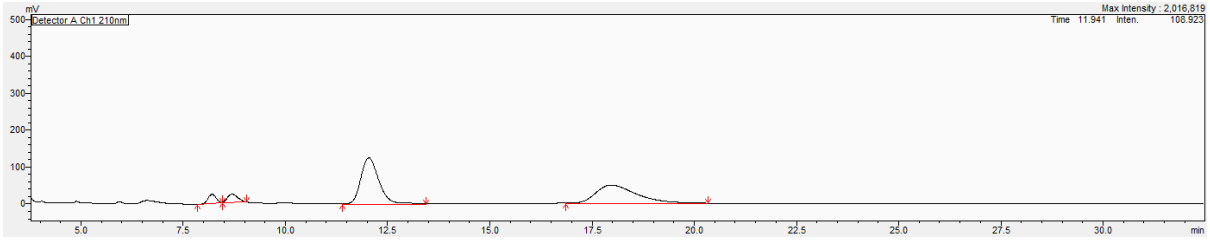
Peak#	Ret. Time	Area	Height	Mark	Conc.
1	30.201	7300560	85142	M	88.971
2	34.650	905018	11213	M	11.029
Total		8205578	96355		100.000



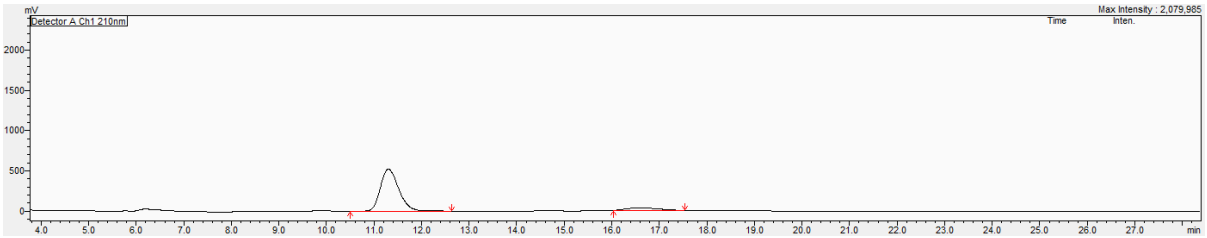
ent-**2u**

40.7 mg, 96%, yellow solid; MP 185－186 ℃; $[\alpha]_D^{25}$= －67.3 (*c* 1.0, MeOH, 81% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.47 (d, *J* = 8.0 Hz, 2H), 8.03 (d, *J* = 8.0 Hz, 2H), 7.59-7.33 (m, 5H), 4.33 (d, *J*

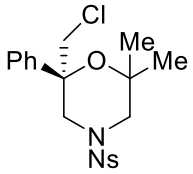
= 12.0 Hz, 1H), 3.68 (dd, J_1 = 12.0 Hz, J_2 = 32.0 Hz, 2H), 3.21 (d, J = 12.0 Hz, 1H), 2.91 (d, J = 16.0 Hz, 1H), 2.50 (d, J = 12.0 Hz, 1H), 1.28 (s, 3H), 0.83 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.5, 141.6, 140.5, 128.9, 128.4, 128.3, 126.8, 124.6, 75.4, 73.5, 55.1, 52.1, 48.8, 28.2, 26.5; HRMS (TOF) m/z: $[M+H]^+$Calcd for $C_{19}H_{21}ClN_2O_5S$ 425.7761; found 425.7763; HPLC (Daicel Chiralcel OD-H, *i*-PrOH/Hexane = 30/70, 1.0 mL/min, 210 nm) t_1 = 11.3 min (major), t_2 = 16.6 min (minor).



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	8.207	319485	24027	M	3.836
2	8.692	383772	21883	M	4.607
3	12.039	3844212	125333	V	46.151
4	17.969	3782088	51170	V	45.406
Total		8329557	222414		100.000

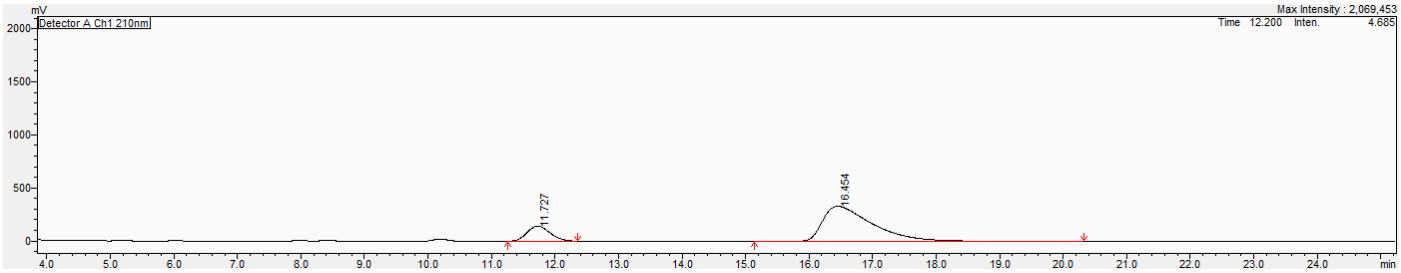


Peak#	Ret. Time	Area	Height	Mark	Conc.
1	11.304	13897456	522009	M	90.286
2	16.593	1495206	31831	M	9.714
Total		15392662	553840		100.000



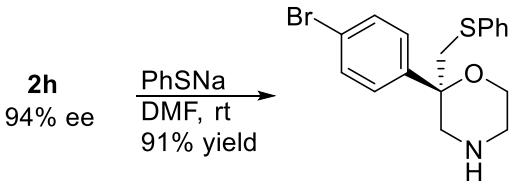
2u

41.1 mg, 97%, $[\alpha]_D^{25}$ = −67.3 (*c* 1.0, MeOH, 81% ee); HPLC (Daicel Chiralcel OD-H, *i*-PrOH/Hexane = 30/70, 1.0 mL/min, 210 nm) t_1 = 11.7 min (minor), t_2 = 16.5 min (major).



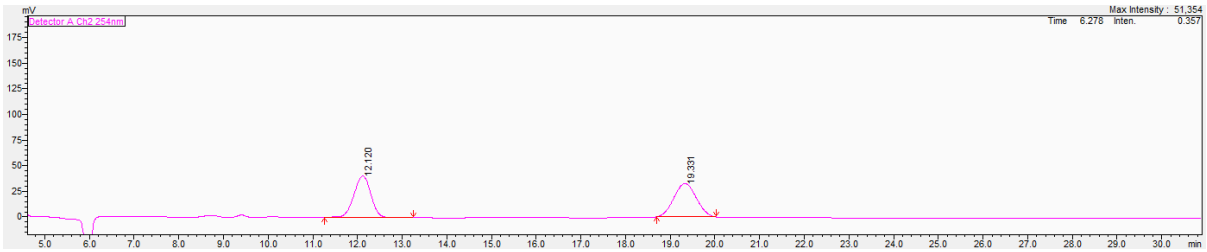
Peak#	Ret. Time	Area	Height	Mark	Conc.
1	11.727	3579575	142737	M	16.707
2	16.454	17846049	329170	M	83.293
Total		21425624	471907		100.000

Synthesis of 4

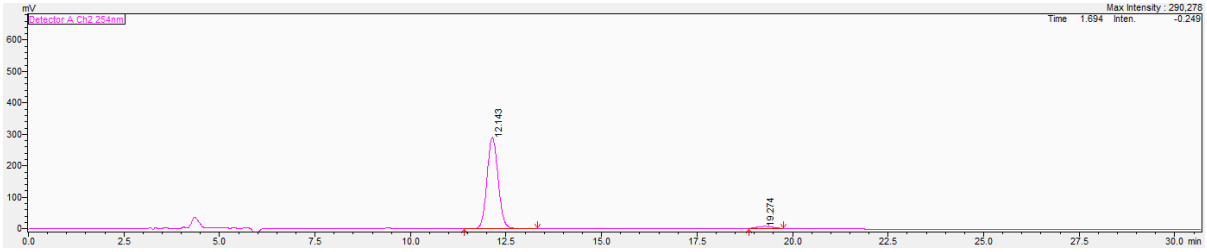


4

To a solution of **2h** (47.5 mg, 0.1 mmol, 1.0 equiv) in DMF (1.0 mL), was added sodium thiophenolate (132.0 mg, 1.0 mmol, 10.0 equiv) at room temperature. The mixture was then stirred for 12 h at room temperature. Then water and EtOAc were added. The organic layer was washed with water, and dried over magnesium sulfate. Concentration of the organic layer offered the crude product that was further purified by flash column chromatography (hexane/EtOAc) to give the corresponding **4** as yellow oil, 30.0 mg, 91%;$[\alpha]_D^{25}$= +32.7 (*c* 1.0, MeOH, 94% ee); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.61-7.25 (m, 9H), 4.00-3.62 (m, 6H), 3.24-2.71 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.5, 137.1, 134.7, 132.0, 131.4, 130.7, 130.0, 129.5, 128.9, 128.2, 127.1, 122.7, 76.6, 61.1, 49.8, 49.4, 45.4; HRMS (TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{19}BrNOS$ 364.1977; found 364.1978; HPLC (Daicel Chiralcel IC, *i*-PrOH/Hexane = 20/80, 1.0 mL/min, 254 nm) t_1 = 12.1 min (major), t_2 = 19.3 min (minor).



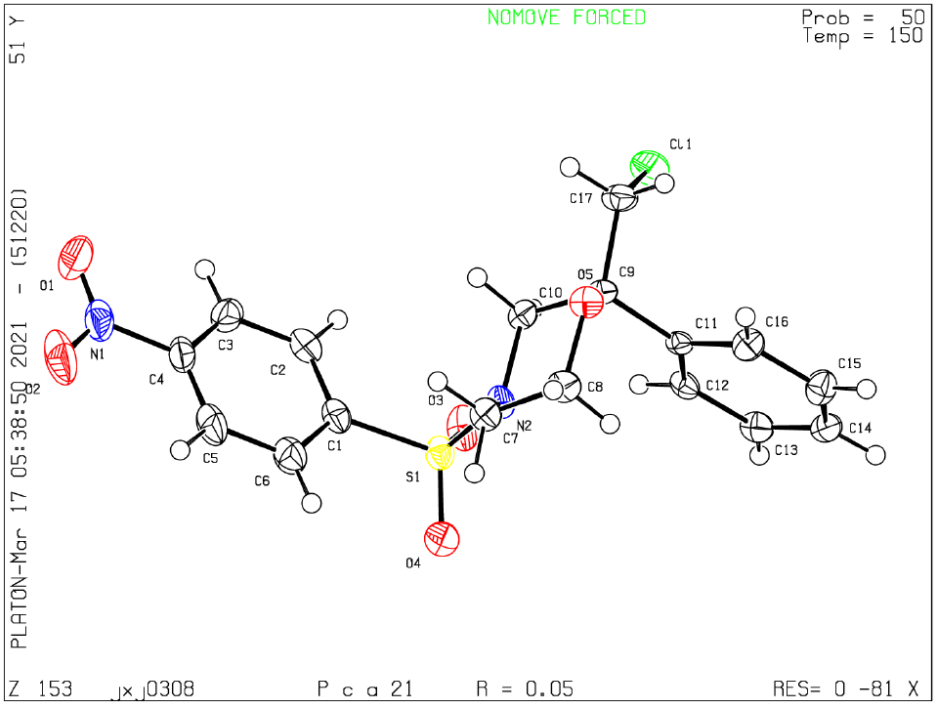
Peak#	Ret. Time	Area	Height	Mark	Conc.
1	12.120	1046833	40136	M	48.802
2	19.331	1098216	32081	M	51.198
Total		2145049	72216		100.000



Peak#	Ret. Time	Area	Height	Mark	Conc.
1	12.143	5849053	289584	M	96.927
2	19.274	185456	6532	M	3.073
Total		6034509	296116		100.000

X-ray of *ent*-2a

Sample preparation for crystal growth: Compound ***ent*-2a** (20 mg) was dissolved in EtOAc/Hexane (v/v = 1 mL / 2 mL), while slow evaporation of solvent at room temperature white crystals were grown.



Thermal ellipsoids are shown at 50% probability.

Bond precision: C-C = 0.0067 A Wavelength=1.54184

Cell: a=15.0862(5) b=9.1161(4) c=12.7347(6)
alpha=90 beta=90 gamma=90
Temperature: 150 K

	Calculated	Reported
Volume	1751.37(13)	1751.37(13)
Space group	P c a 21	P c a 21
Hall group	P 2c -2ac	P 2c -2ac
Moiety formula	C17 H17 Cl N2 O5 S	C17 H17 Cl N2 O5 S
Sum formula	C17 H17 Cl N2 O5 S	C17 H17 Cl N2 O5 S
Mr	396.84	396.83
Dx,g cm-3	1.505	1.505
Z	4	4
Mu (mm-1)	3.338	3.338
F000	824.0	824.0
F000'	829.16	
h,k,lmax	18,11,15	18,11,15
Nref	3546[1859]	3034
Tmin,Tmax	0.658,0.693	0.133,1.000
Tmin'	0.597	

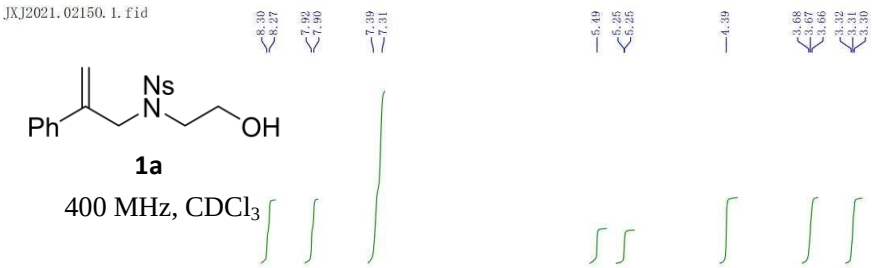
Correction method= # Reported T Limits: Tmin=0.133 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.63/0.86 Theta(max)= 73.762

R(reflections)= 0.0546(2947) wR2(reflections)= 0.1497(3034)

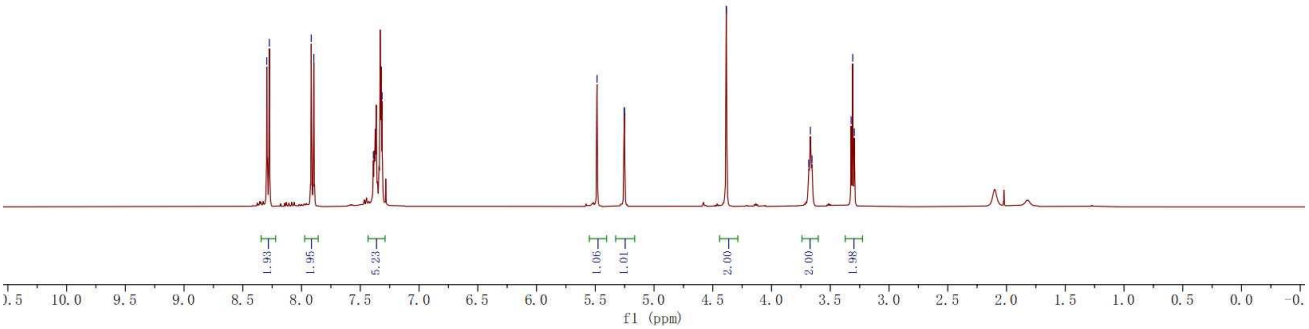
S = 1.034 Npar= 235

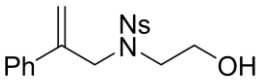
$^{1}H/^{13}C$ Spectra



1a

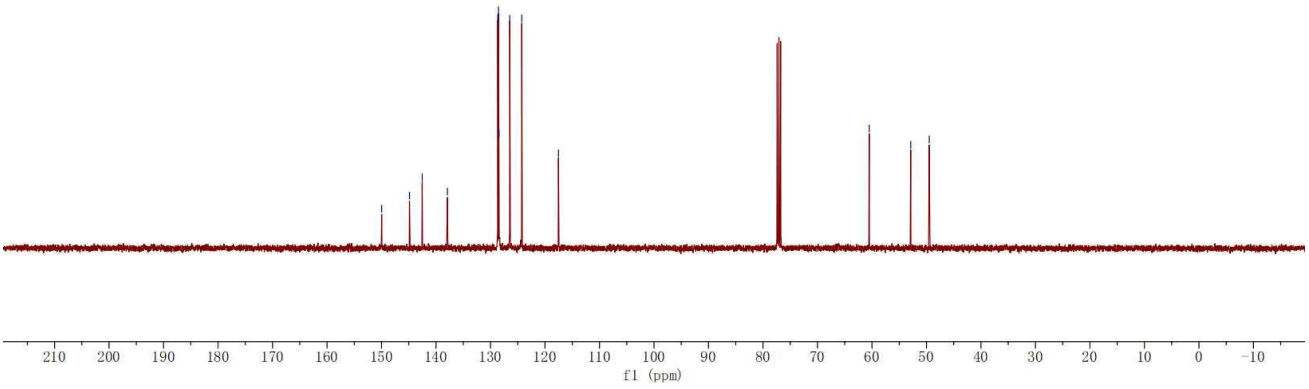
400 MHz, $CDCl_3$



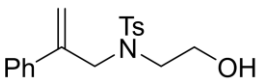


1a

100 MHz, $CDCl_3$

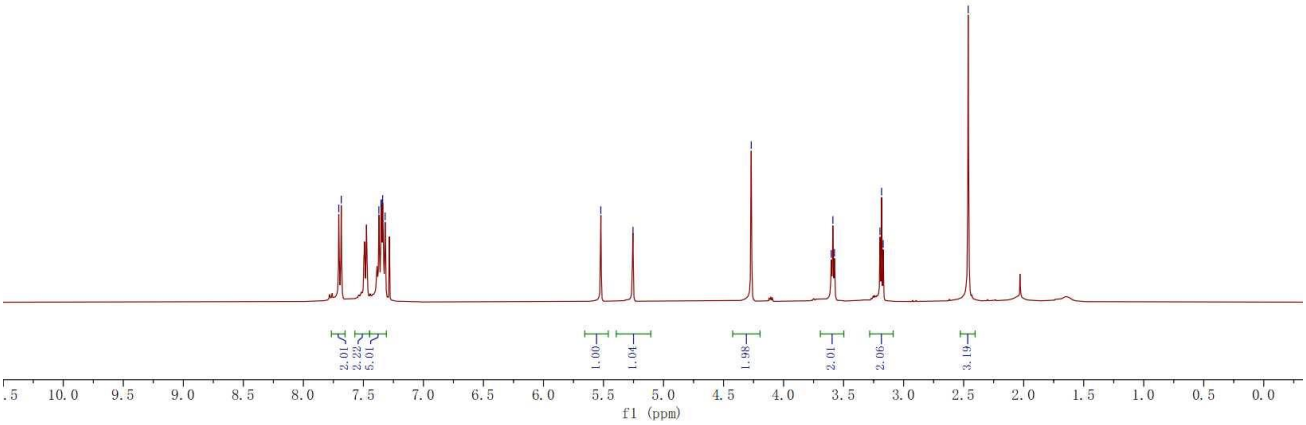


JXJ2021.0123B.1.fid

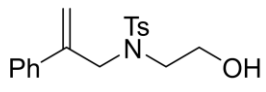


1b

400 MHz, $CDCl_3$

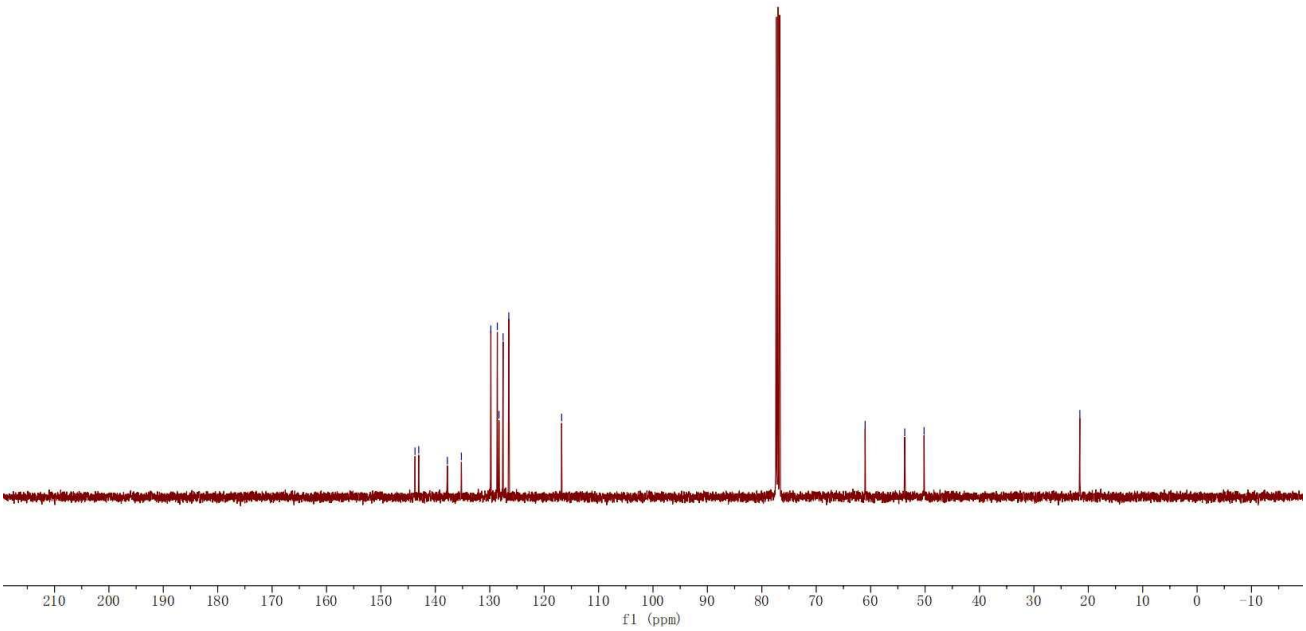


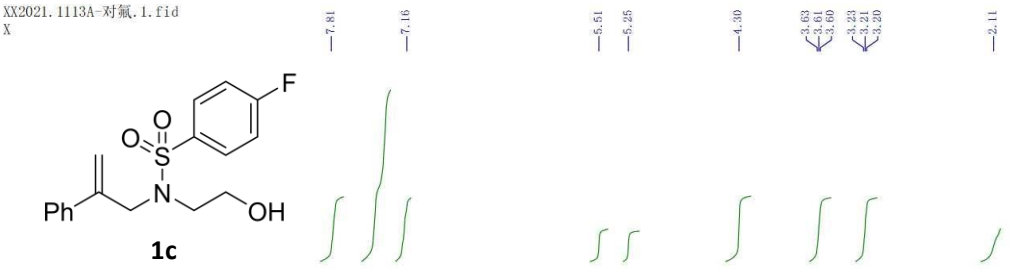
JXJ2021.0123B.2.fid



1b

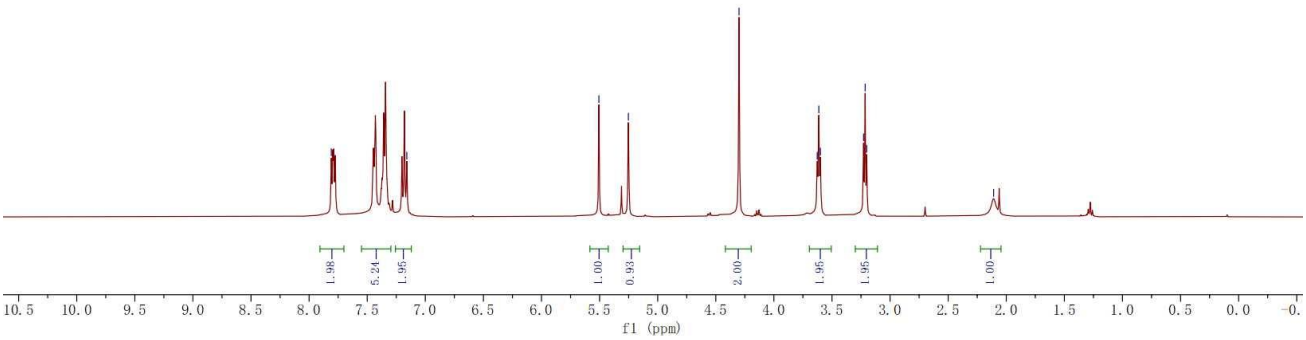
100 MHz, $CDCl_3$

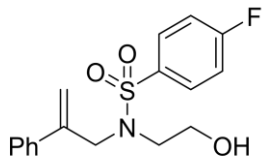




1c

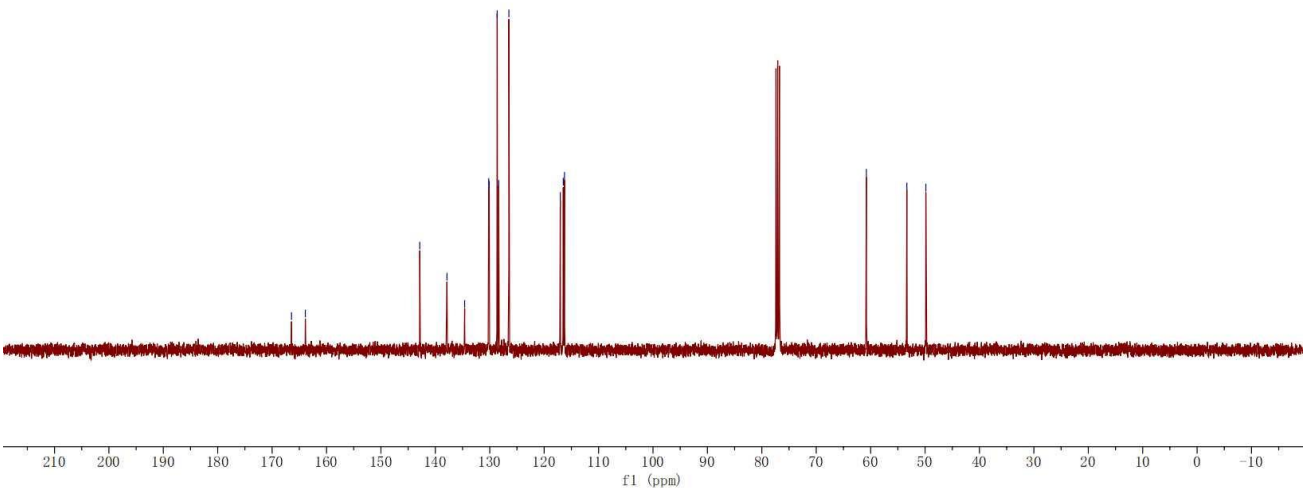
400 MHz, $CDCl_3$

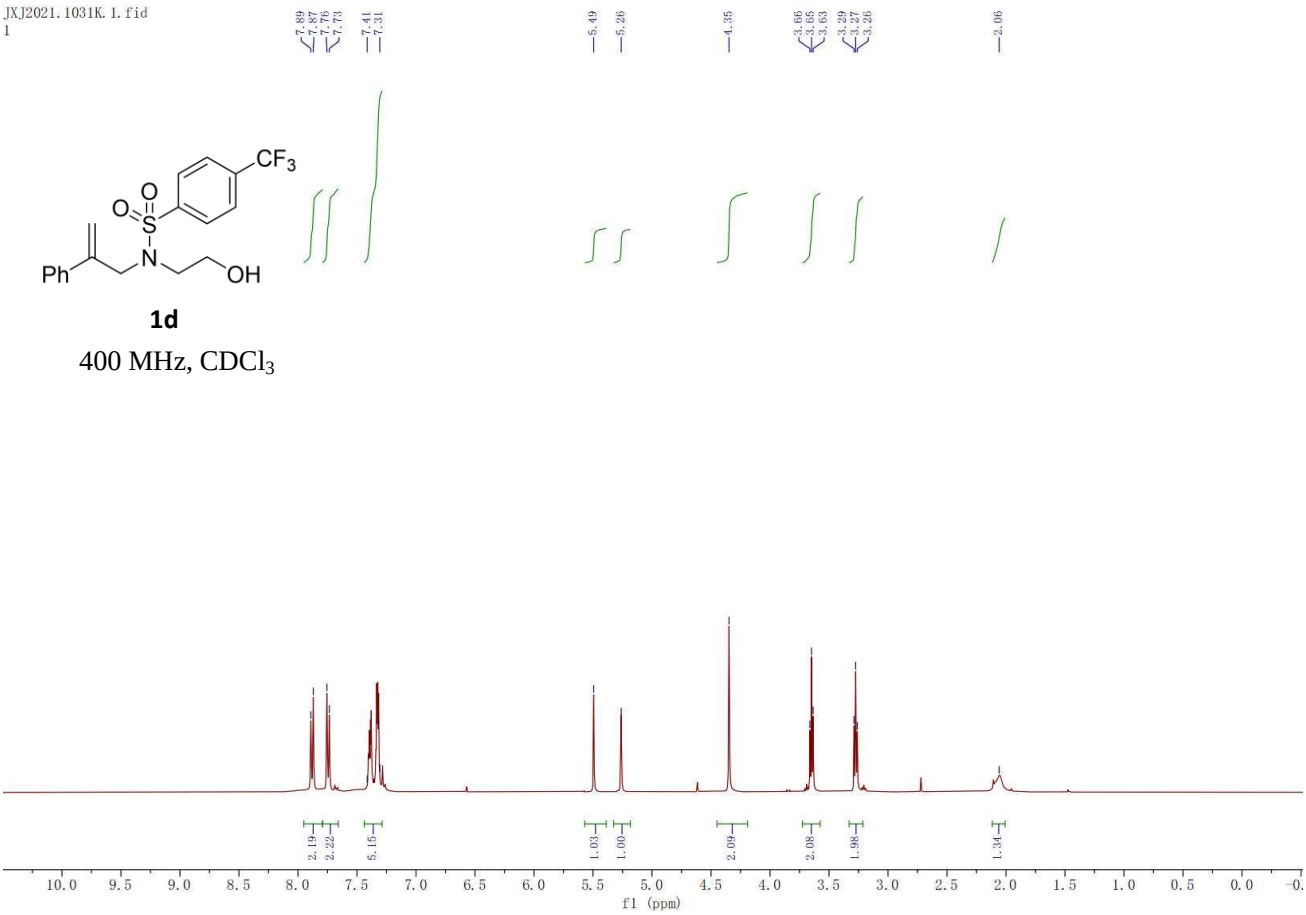




1c

100 MHz, $CDCl_3$





1d

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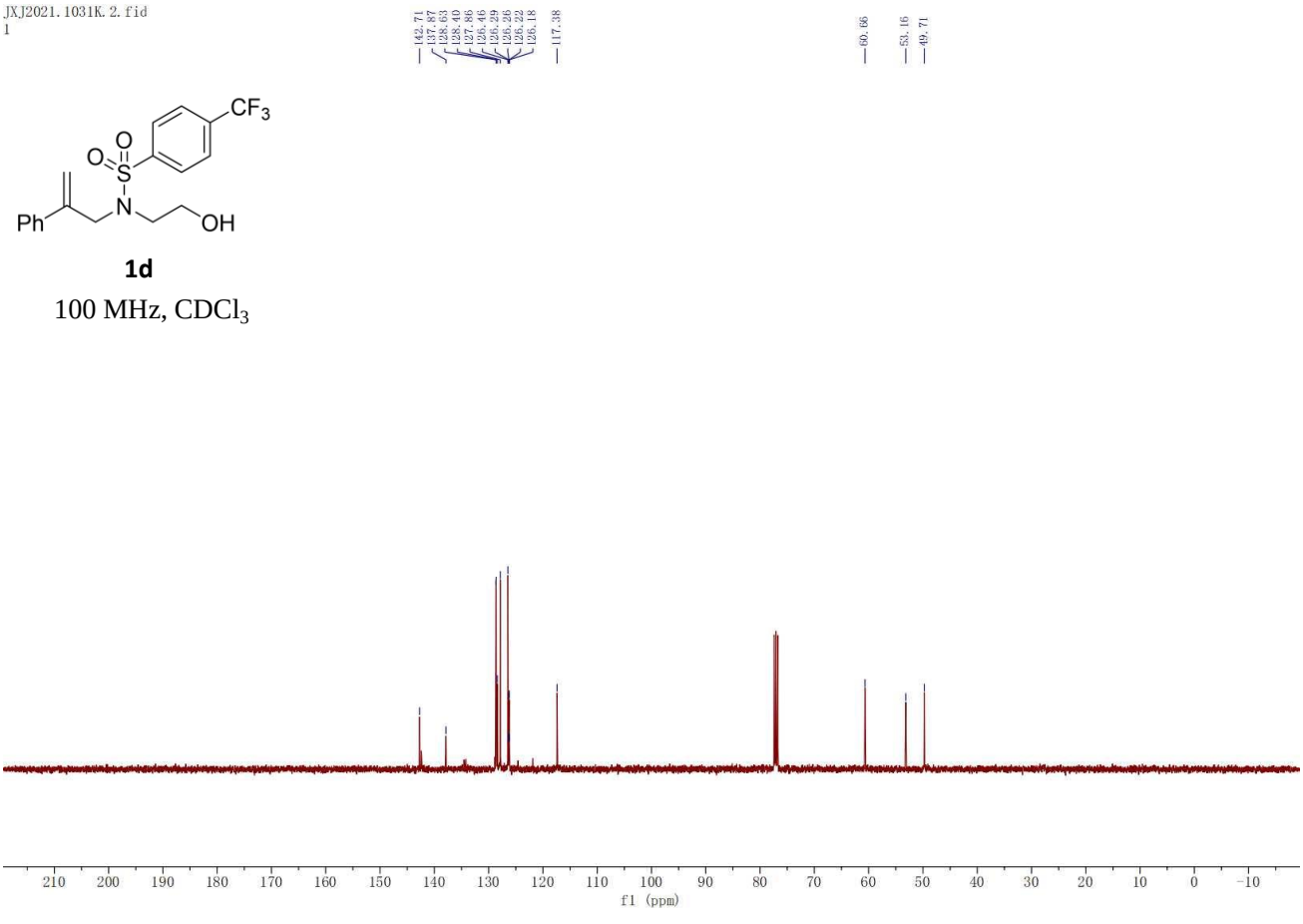
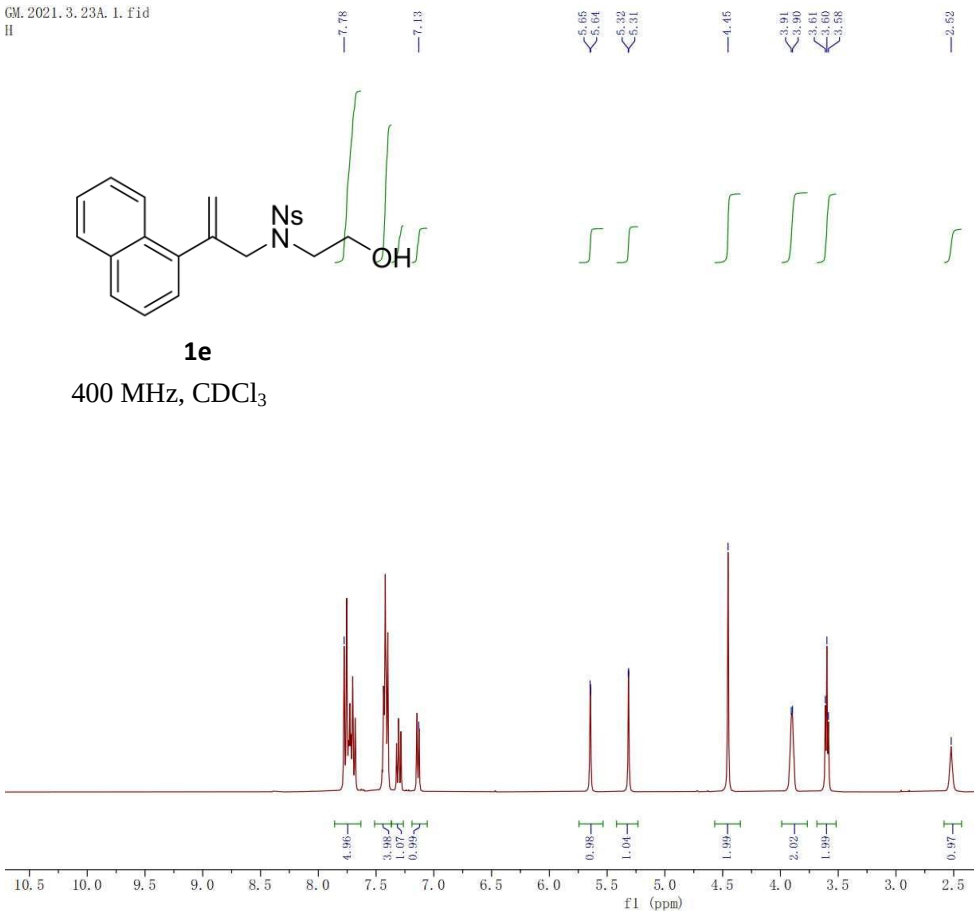


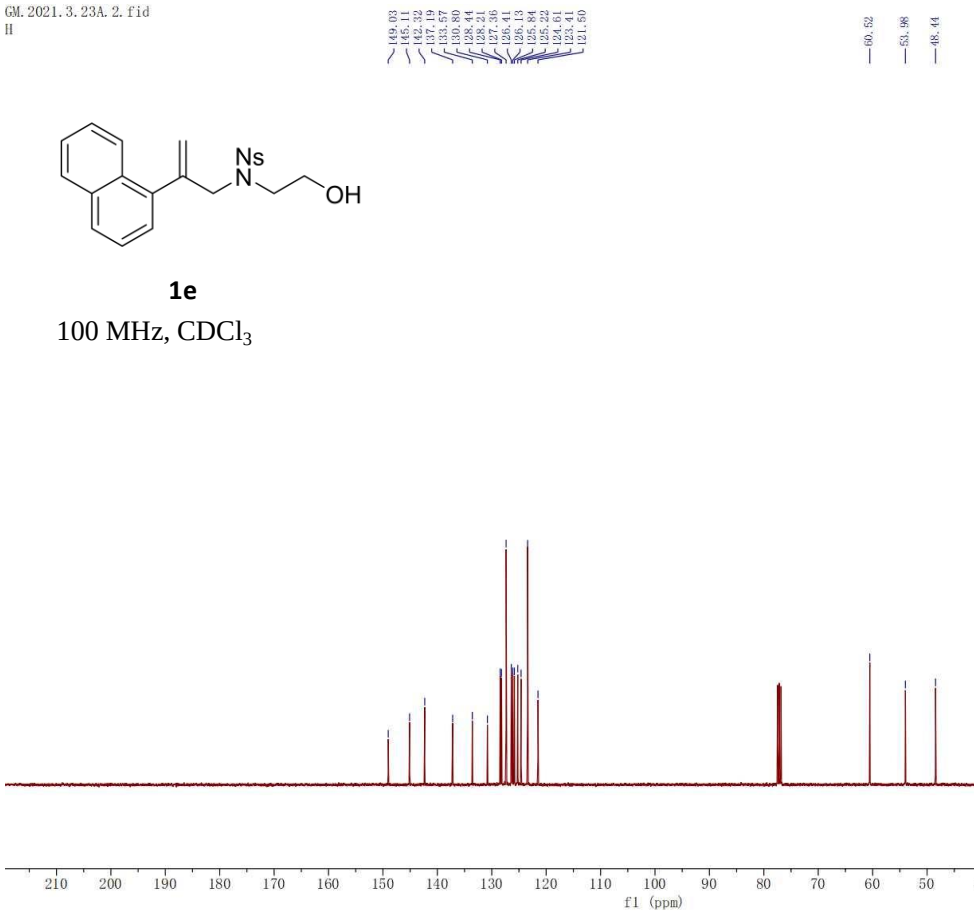
1d

100 MHz, $CDCl_3$



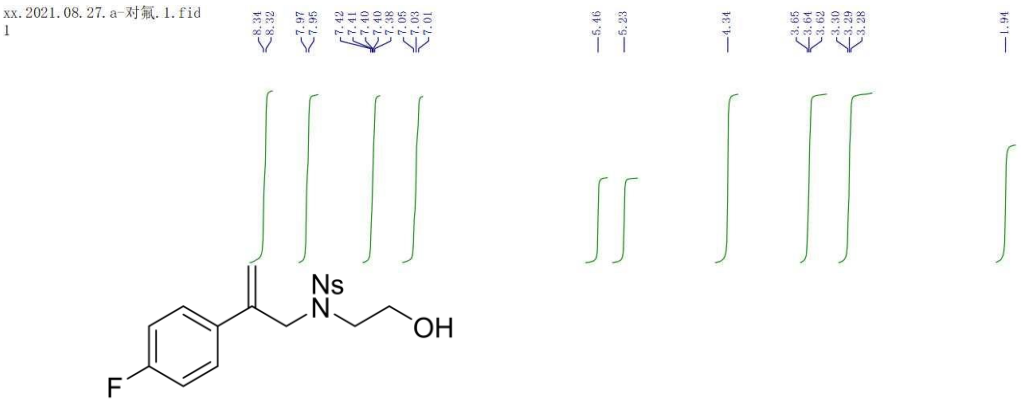
1e

400 MHz, $CDCl_3$



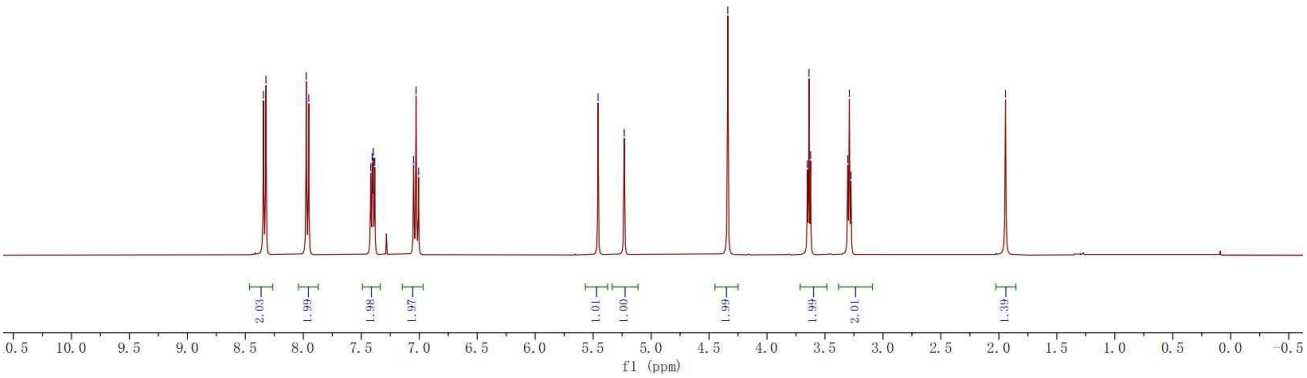
1e

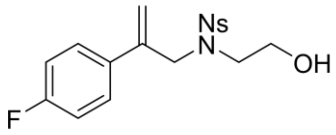
100 MHz, $CDCl_3$



1f

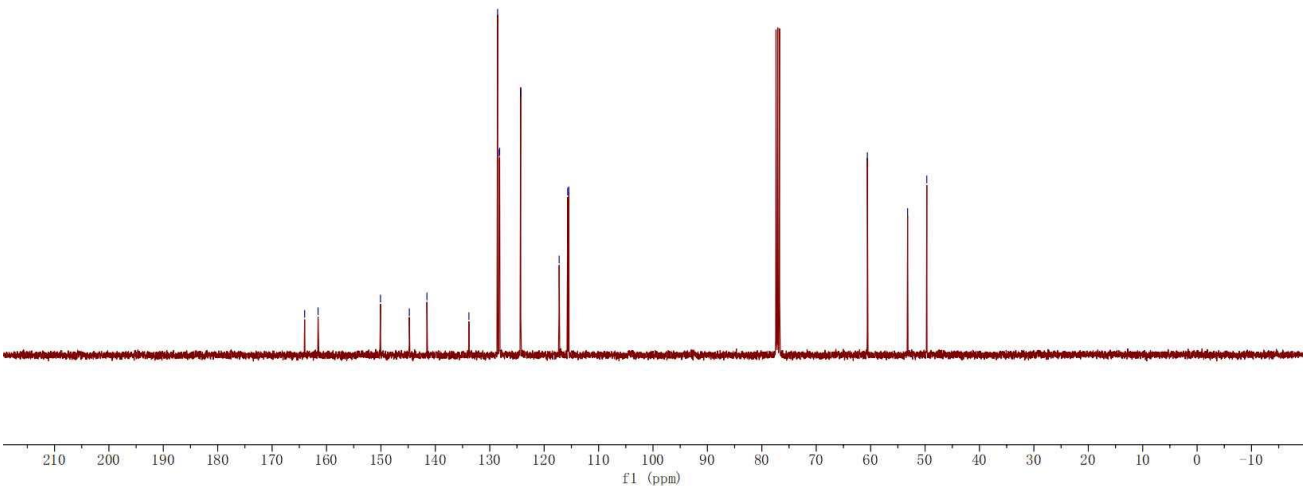
400 MHz, $CDCl_3$

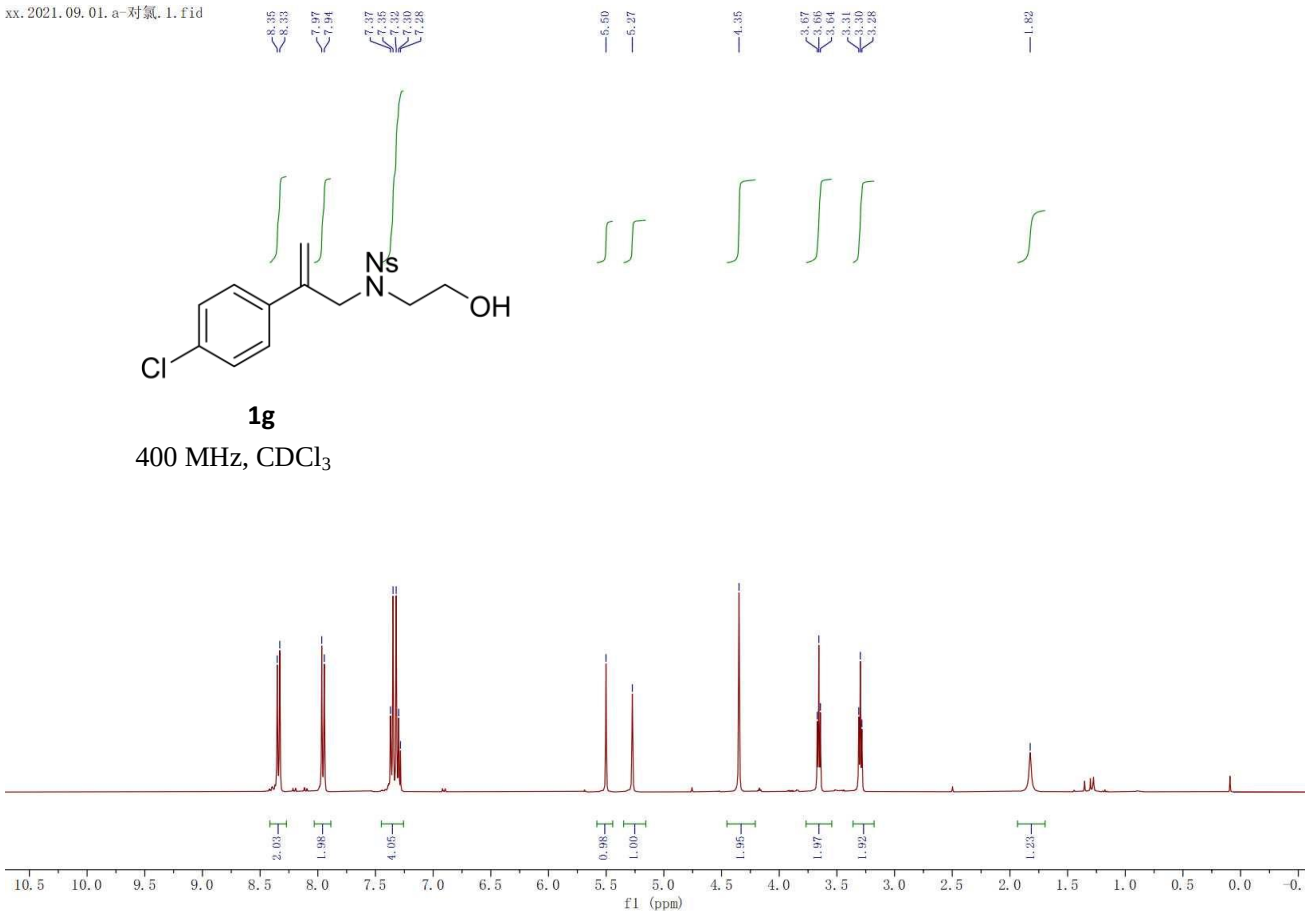




1f

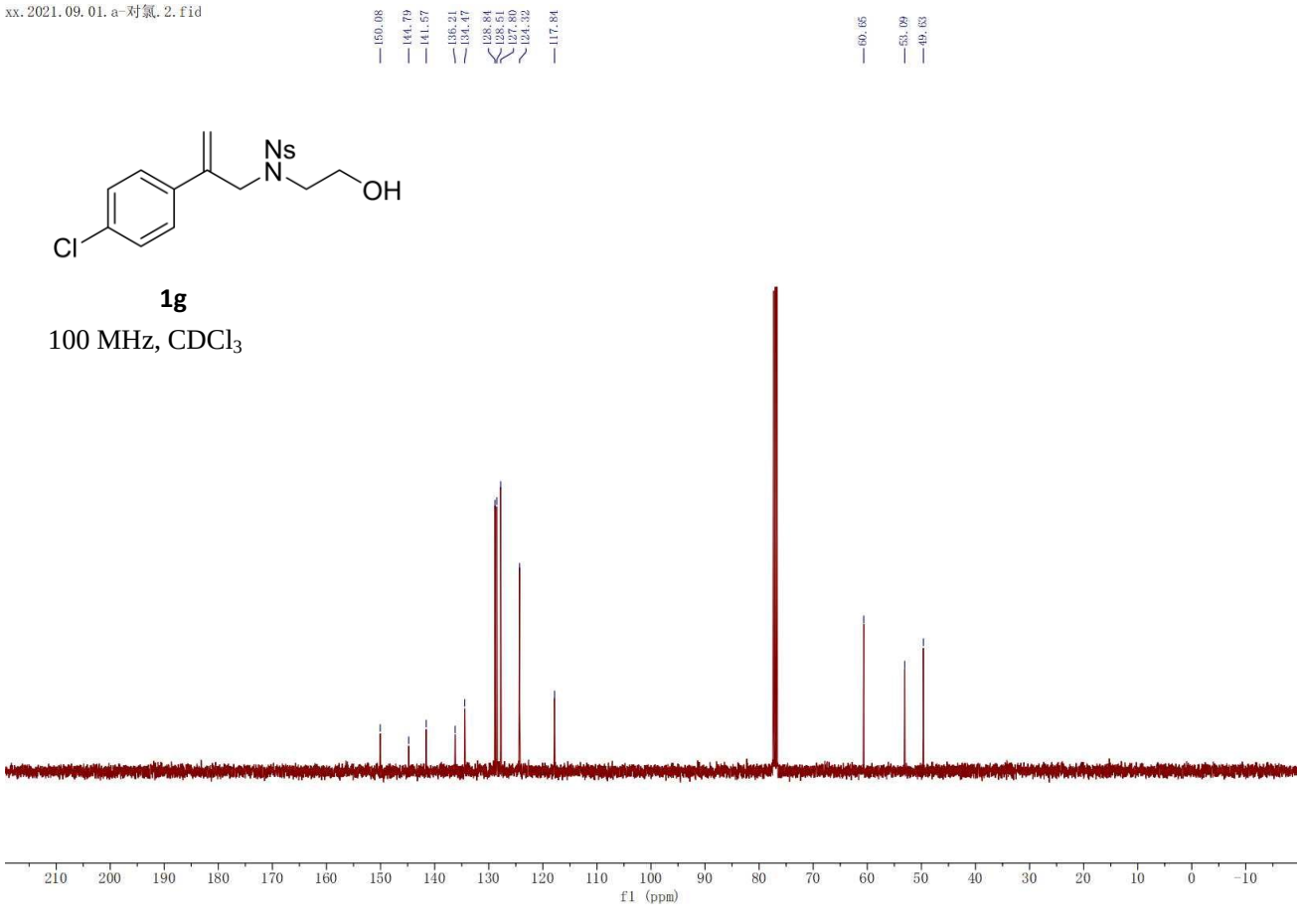
100 MHz, $CDCl_3$





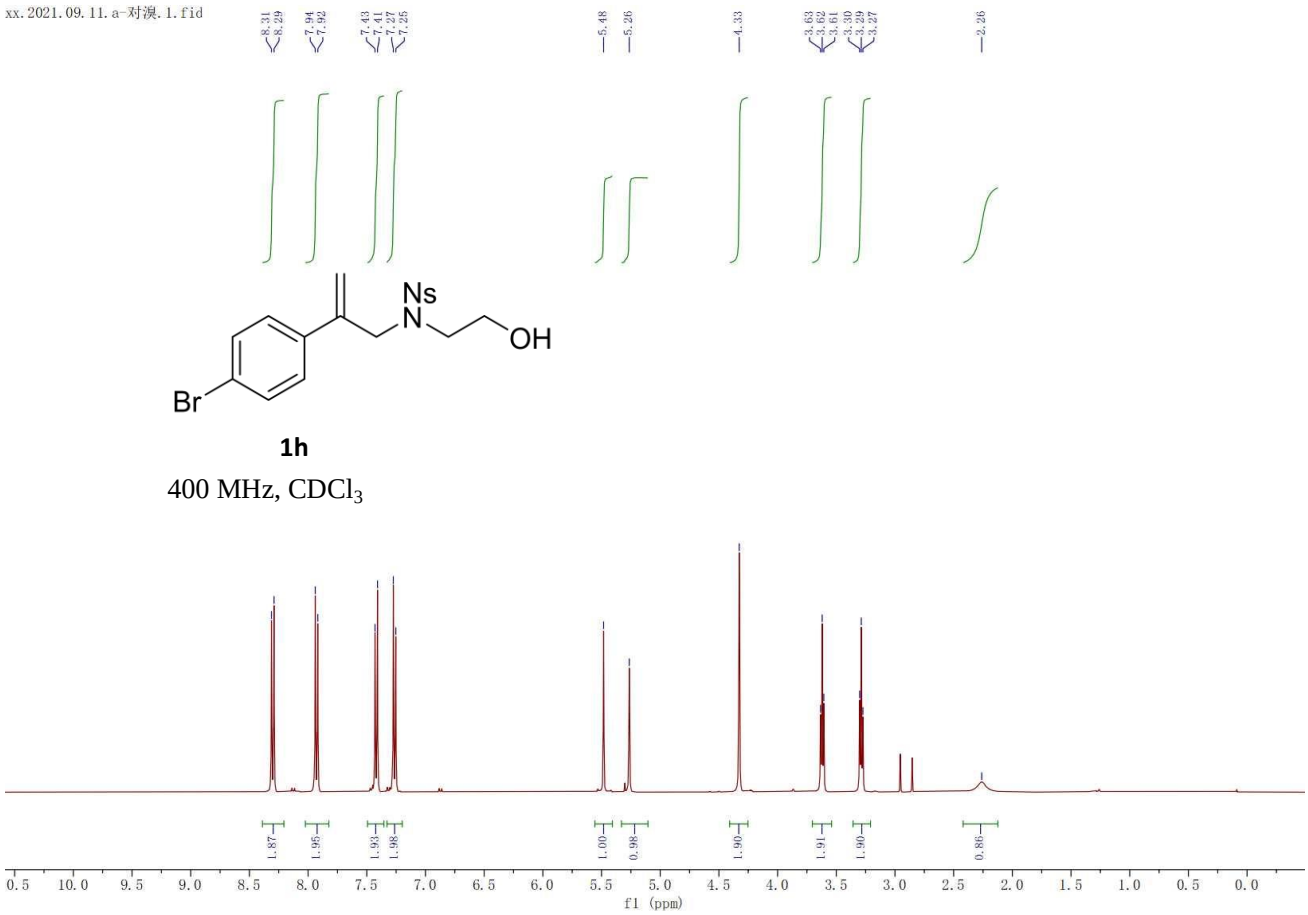
1g

400 MHz, $CDCl_3$



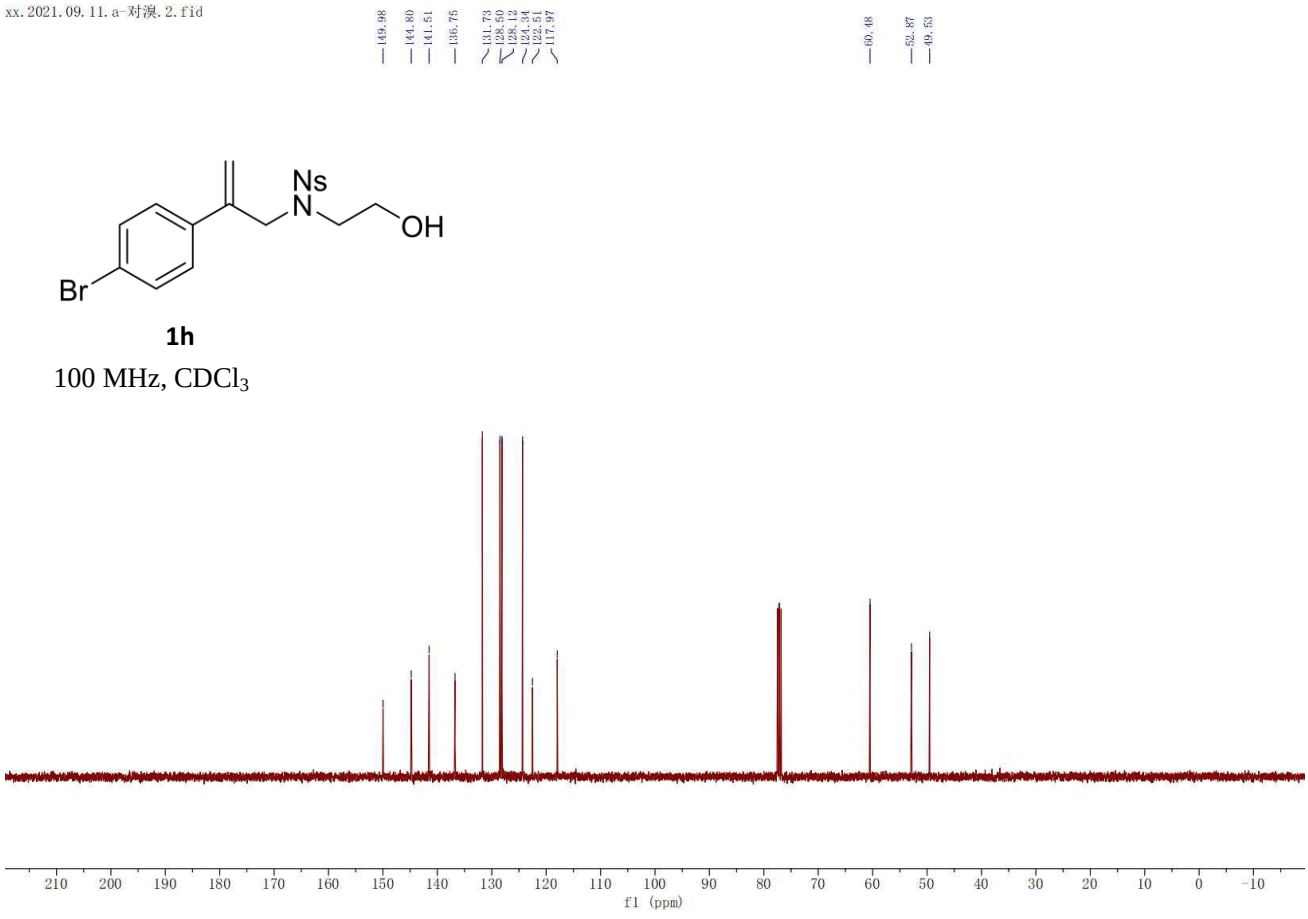
1g

100 MHz, $CDCl_3$



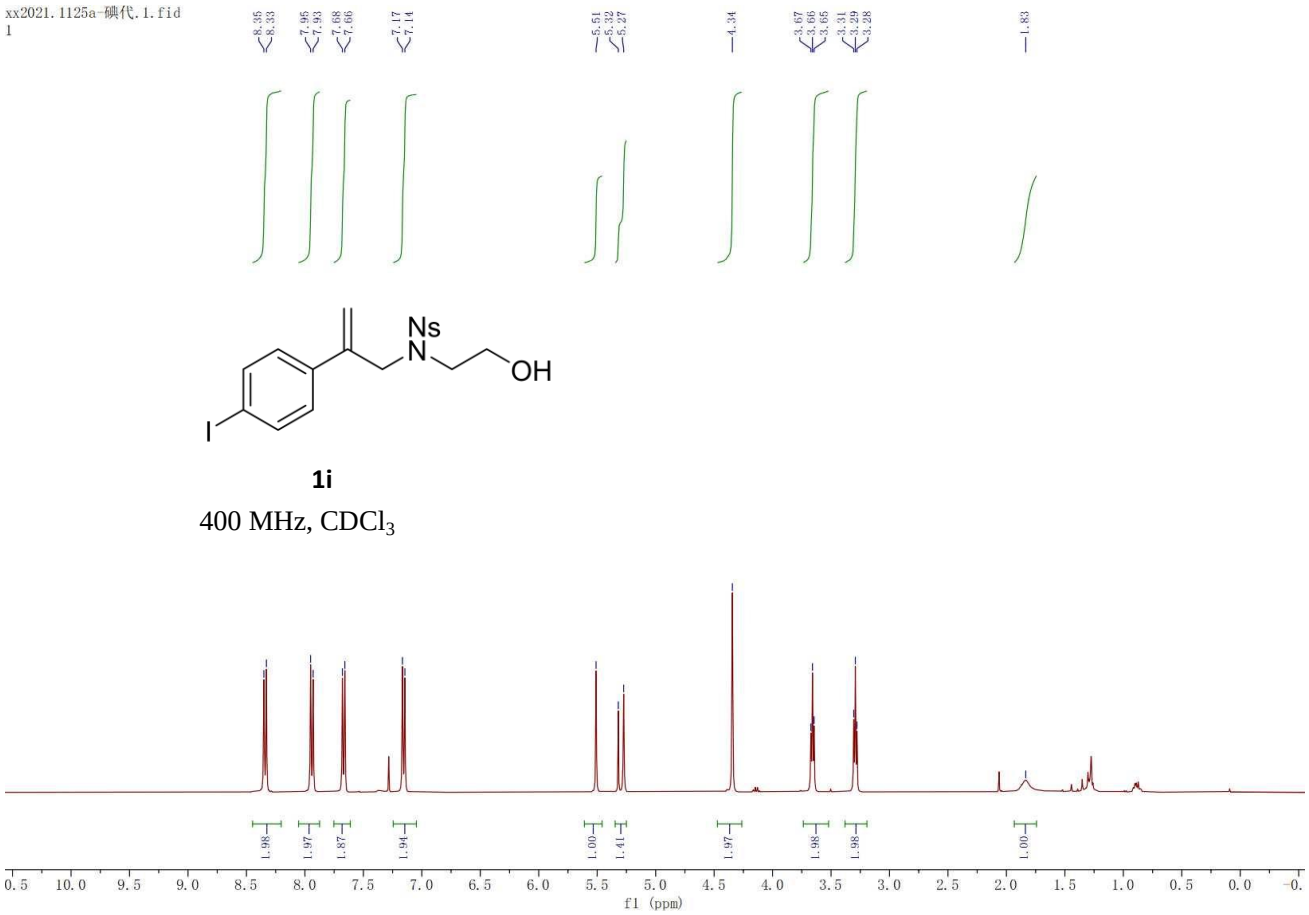
1h

400 MHz, $CDCl_3$



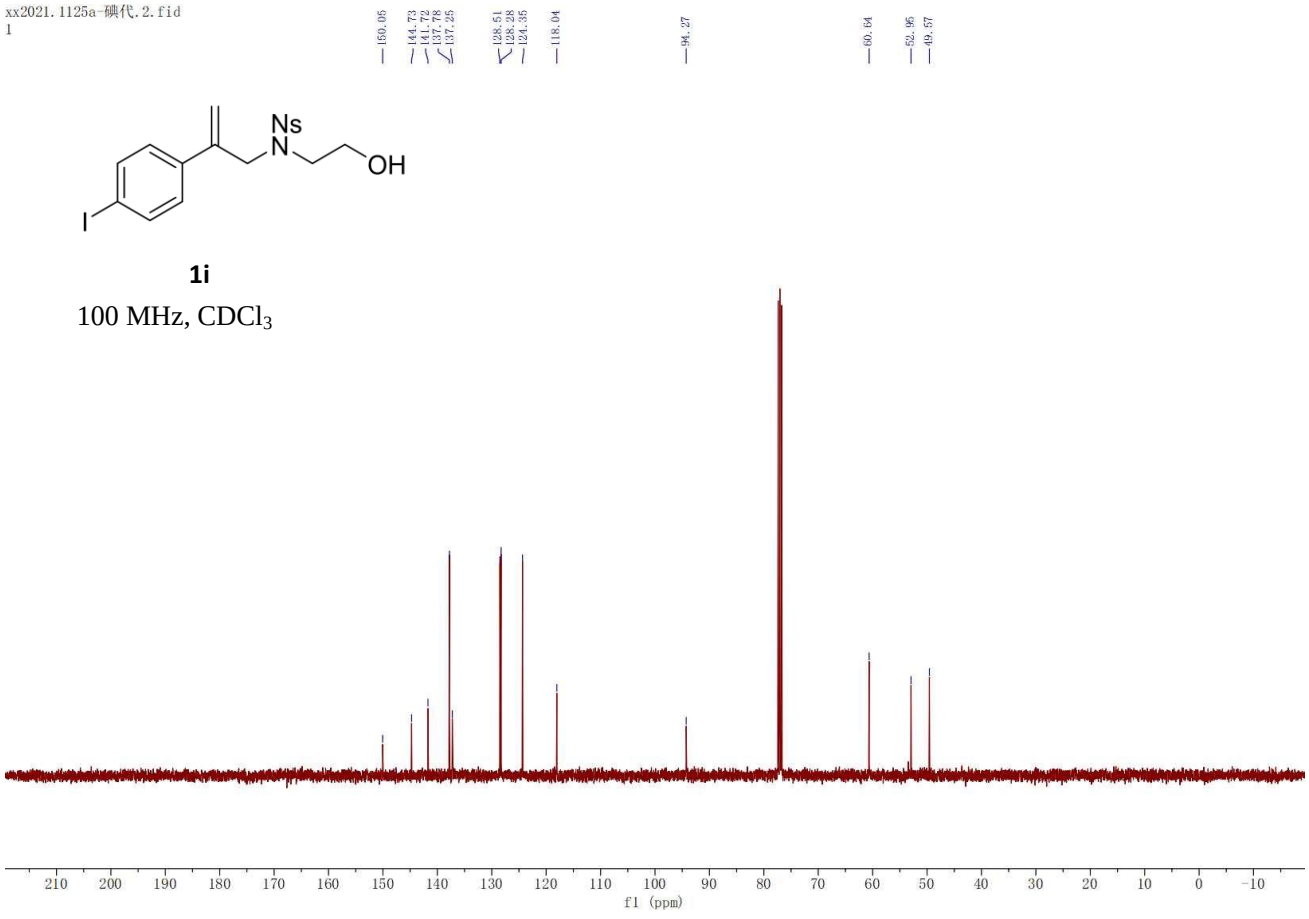
1h

100 MHz, $CDCl_3$



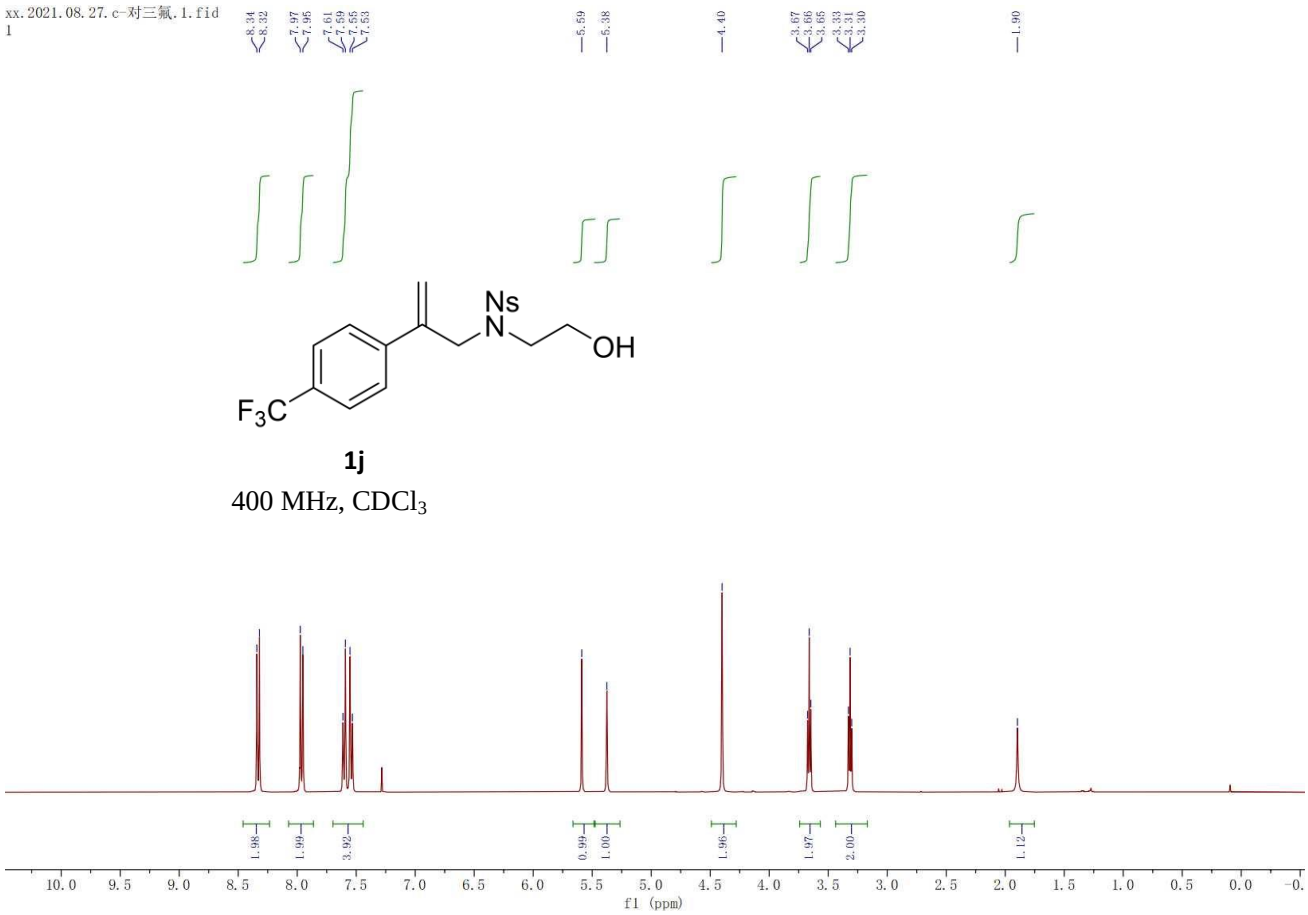
1i

400 MHz, $CDCl_3$



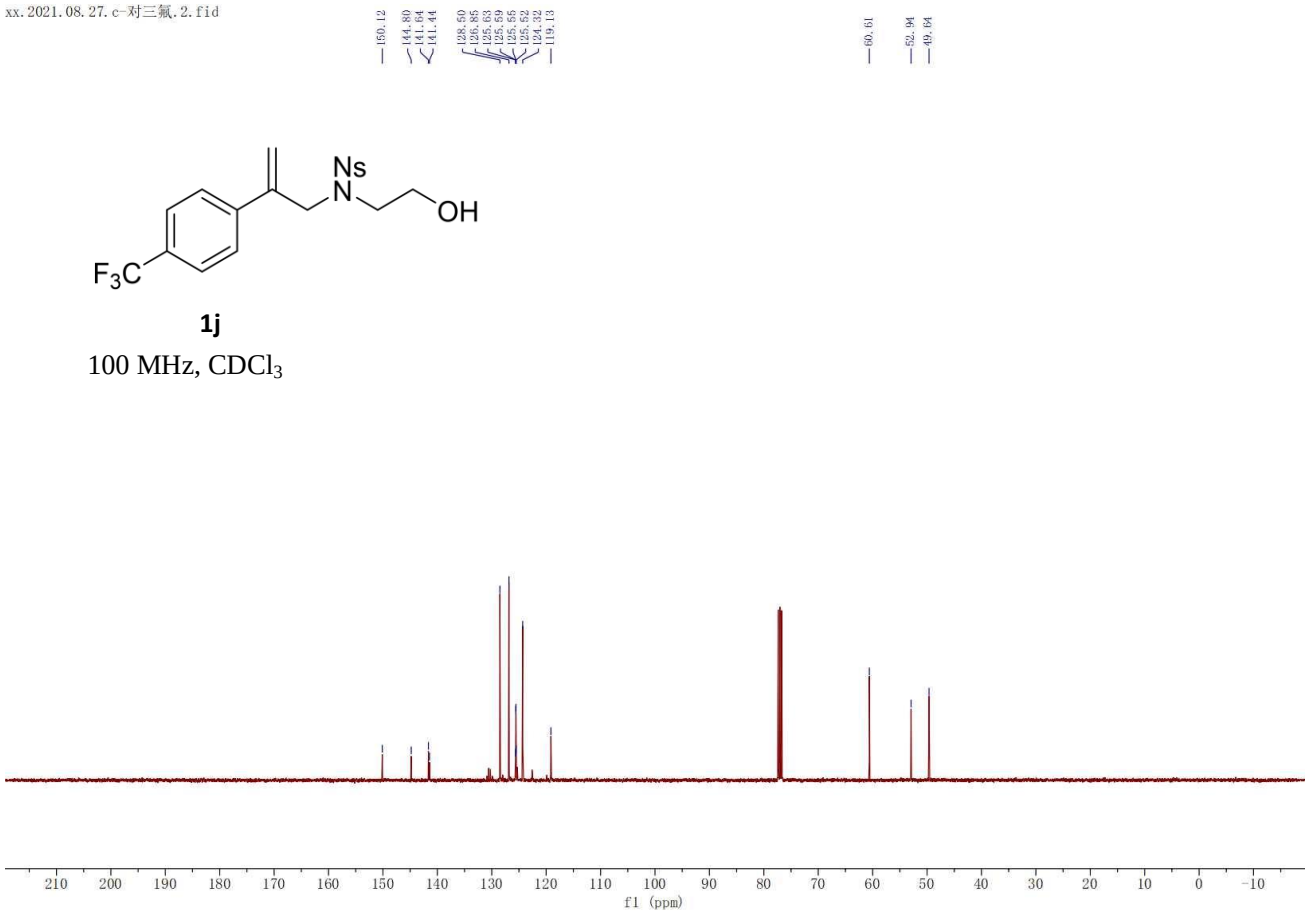
1i

100 MHz, $CDCl_3$



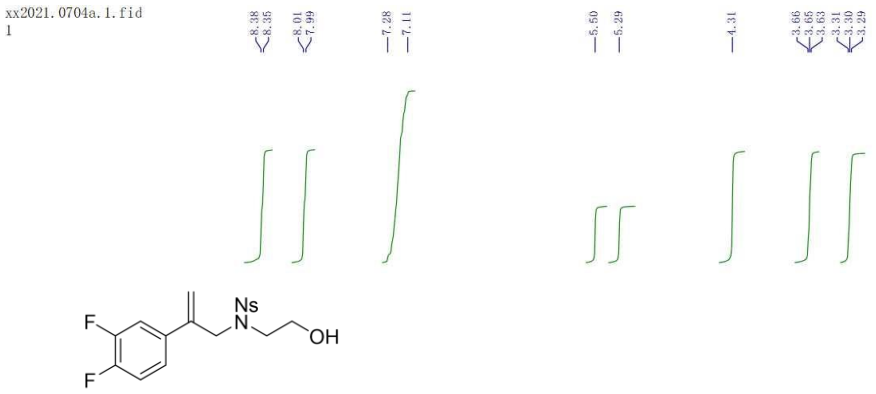
1j

400 MHz, $CDCl_3$



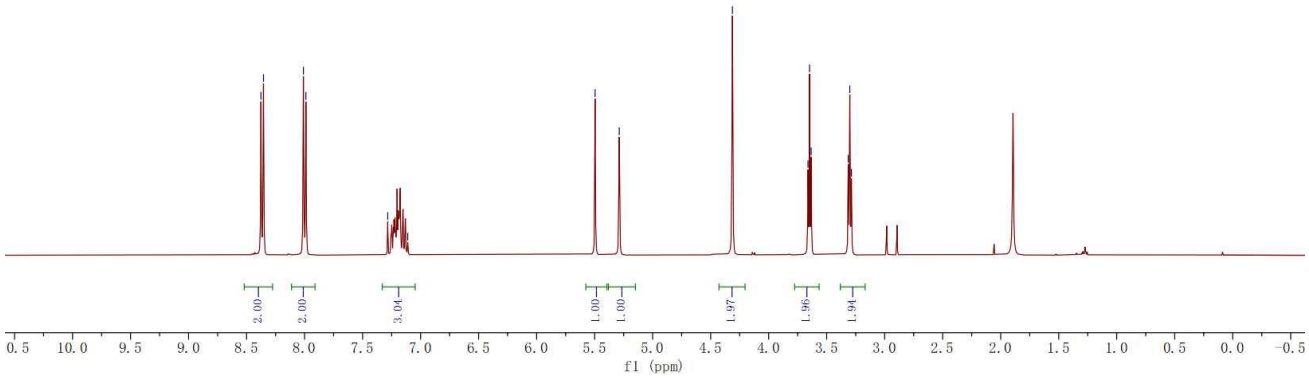
1j

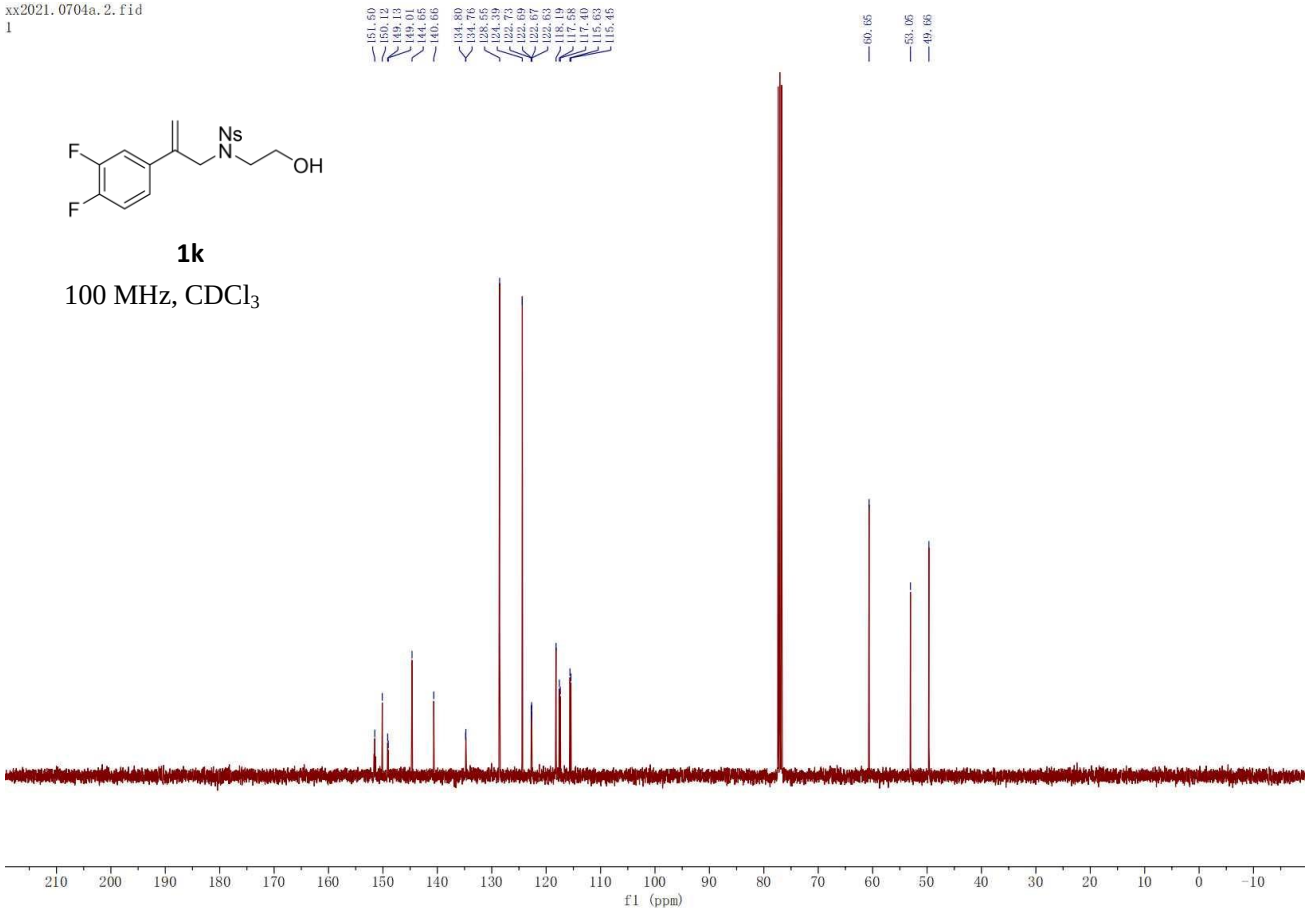
100 MHz, $CDCl_3$



1k

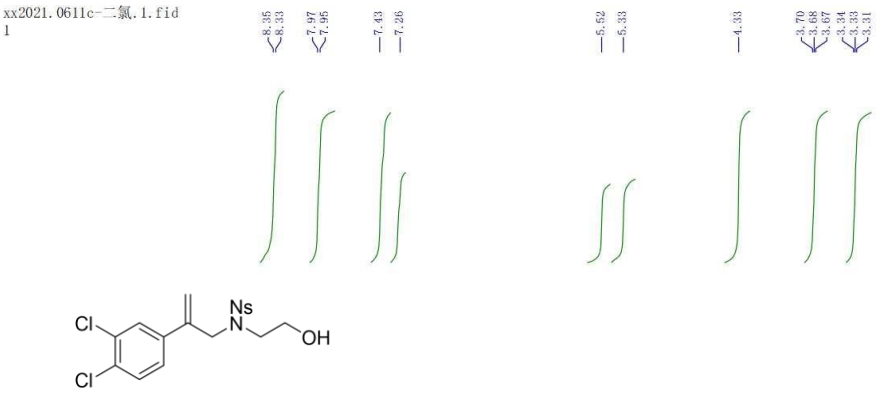
400 MHz, $CDCl_3$





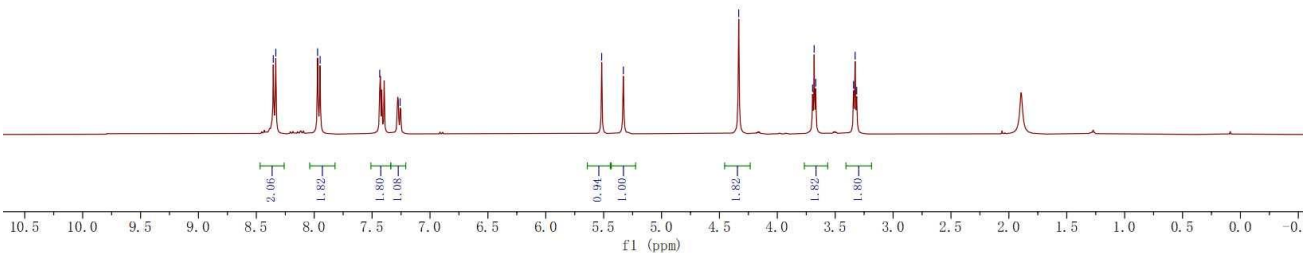
1k

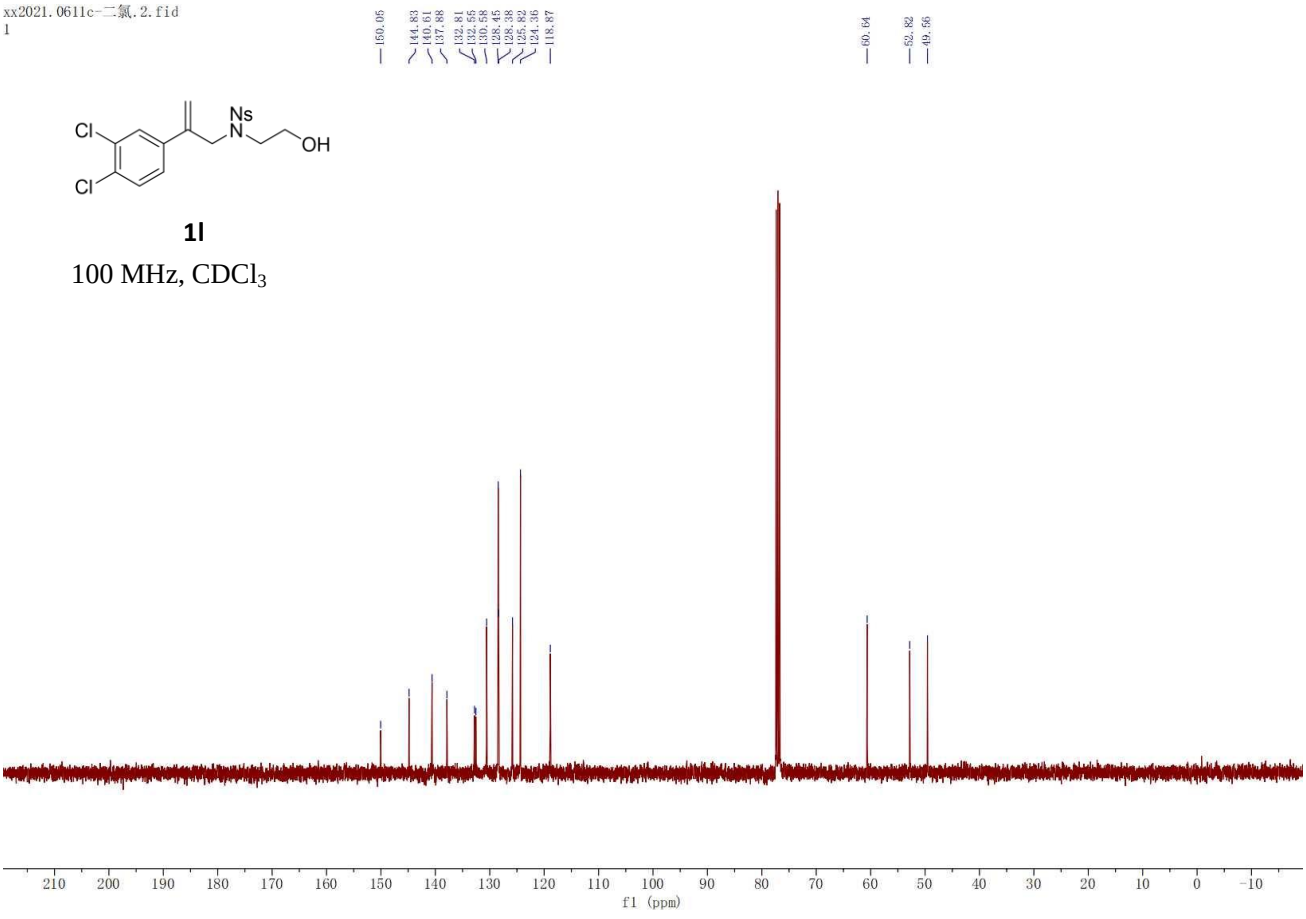
100 MHz, $CDCl_3$



1l

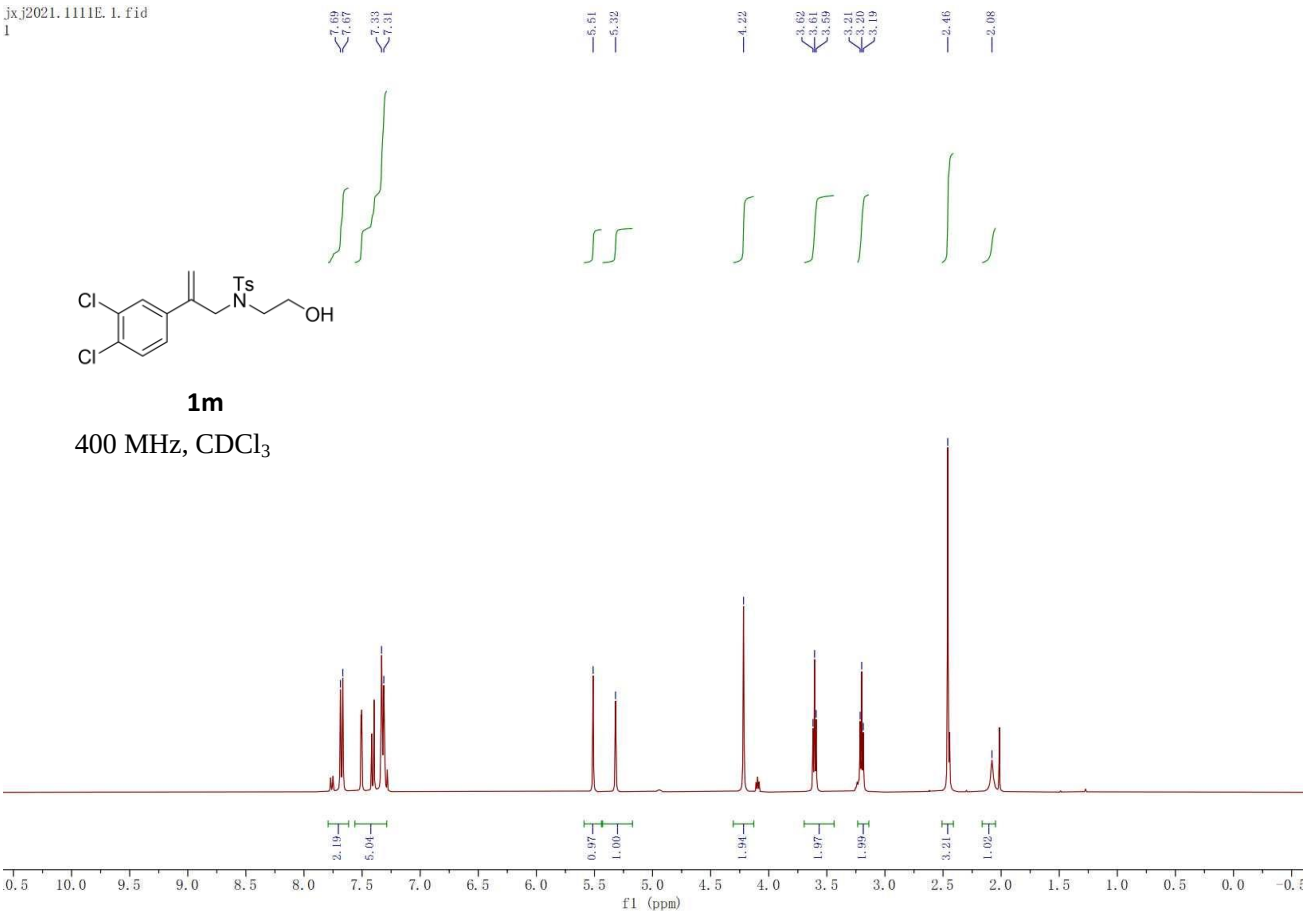
400 MHz, $CDCl_3$





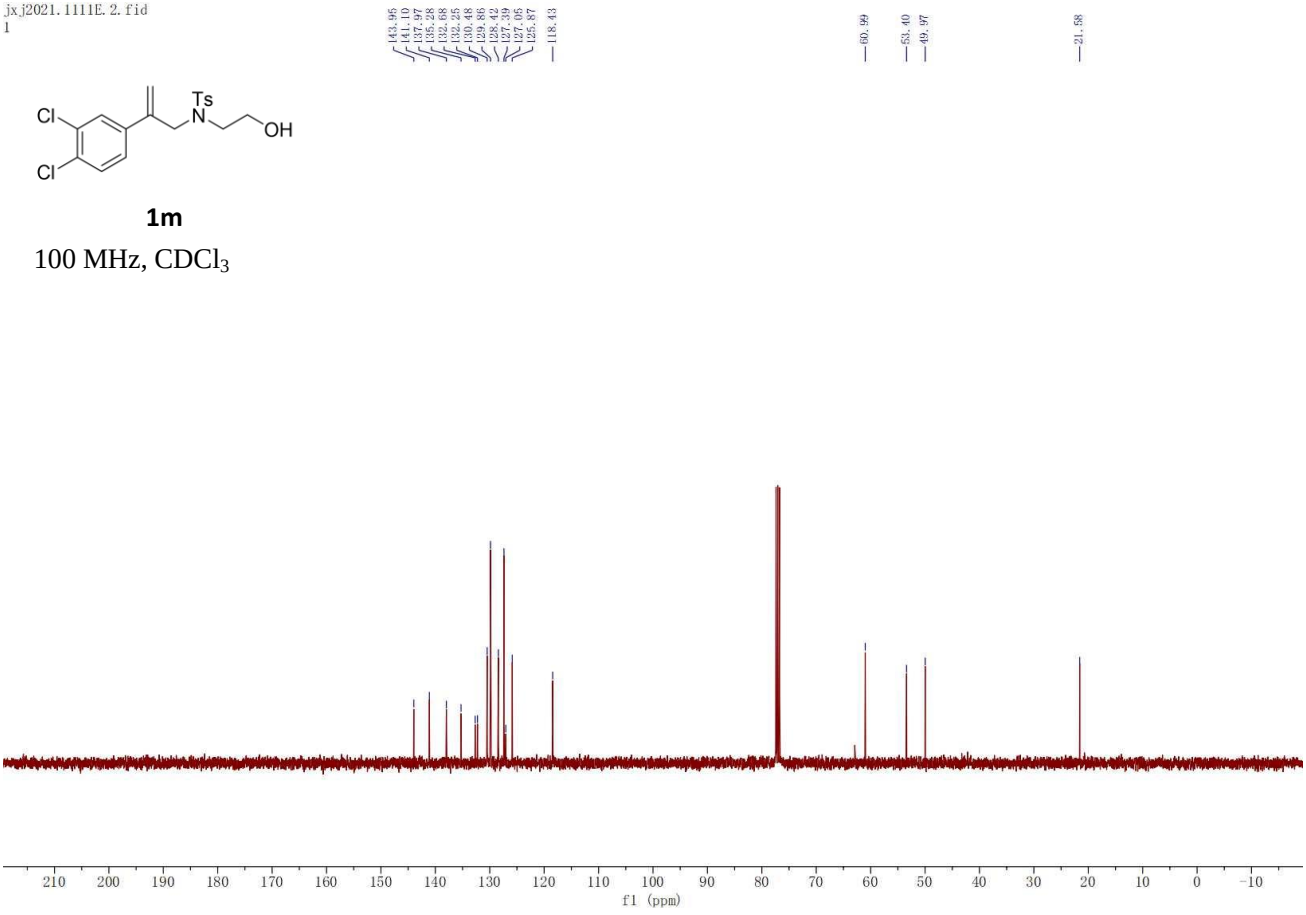
1l

100 MHz, $CDCl_3$



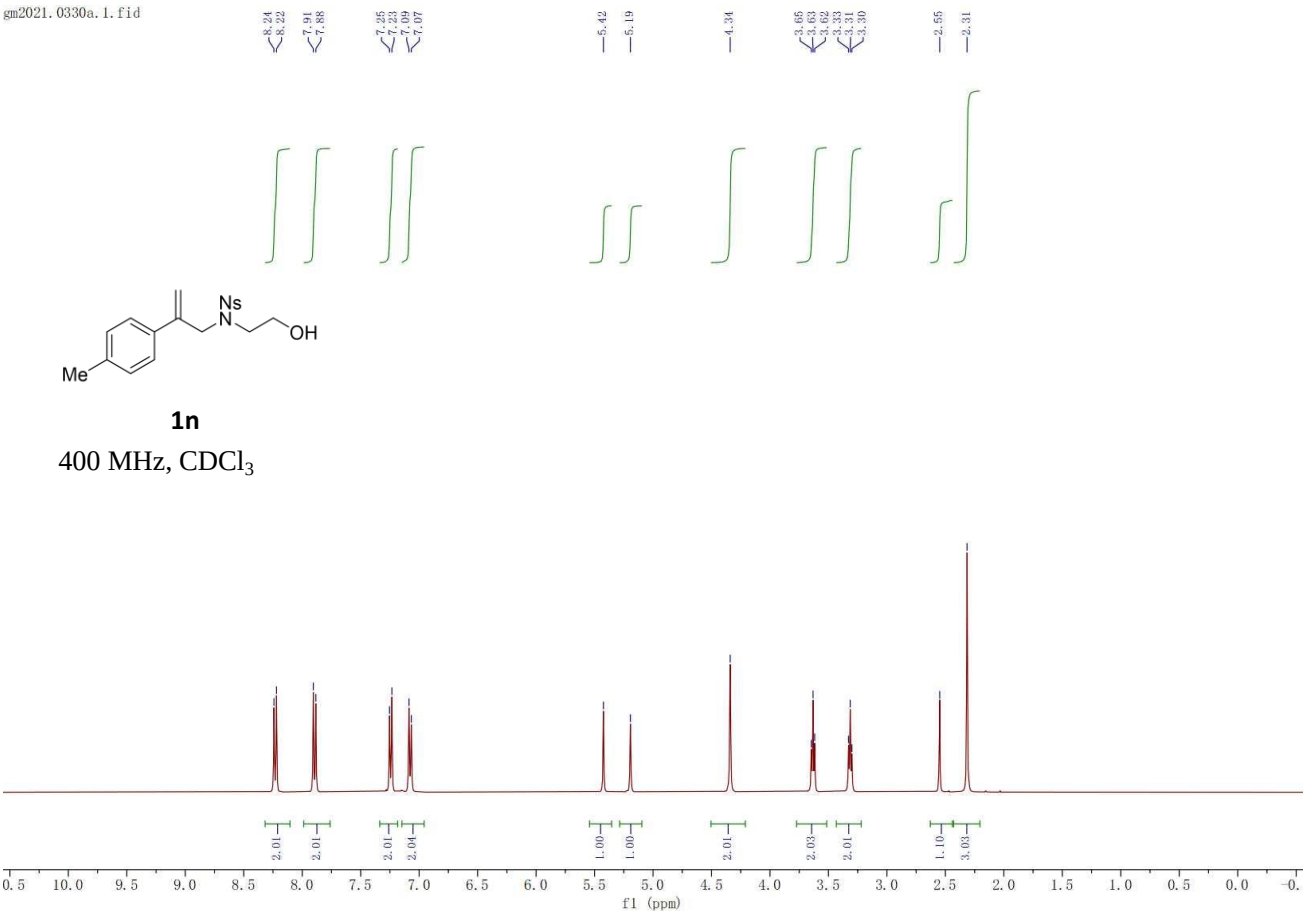
1m

400 MHz, $CDCl_3$



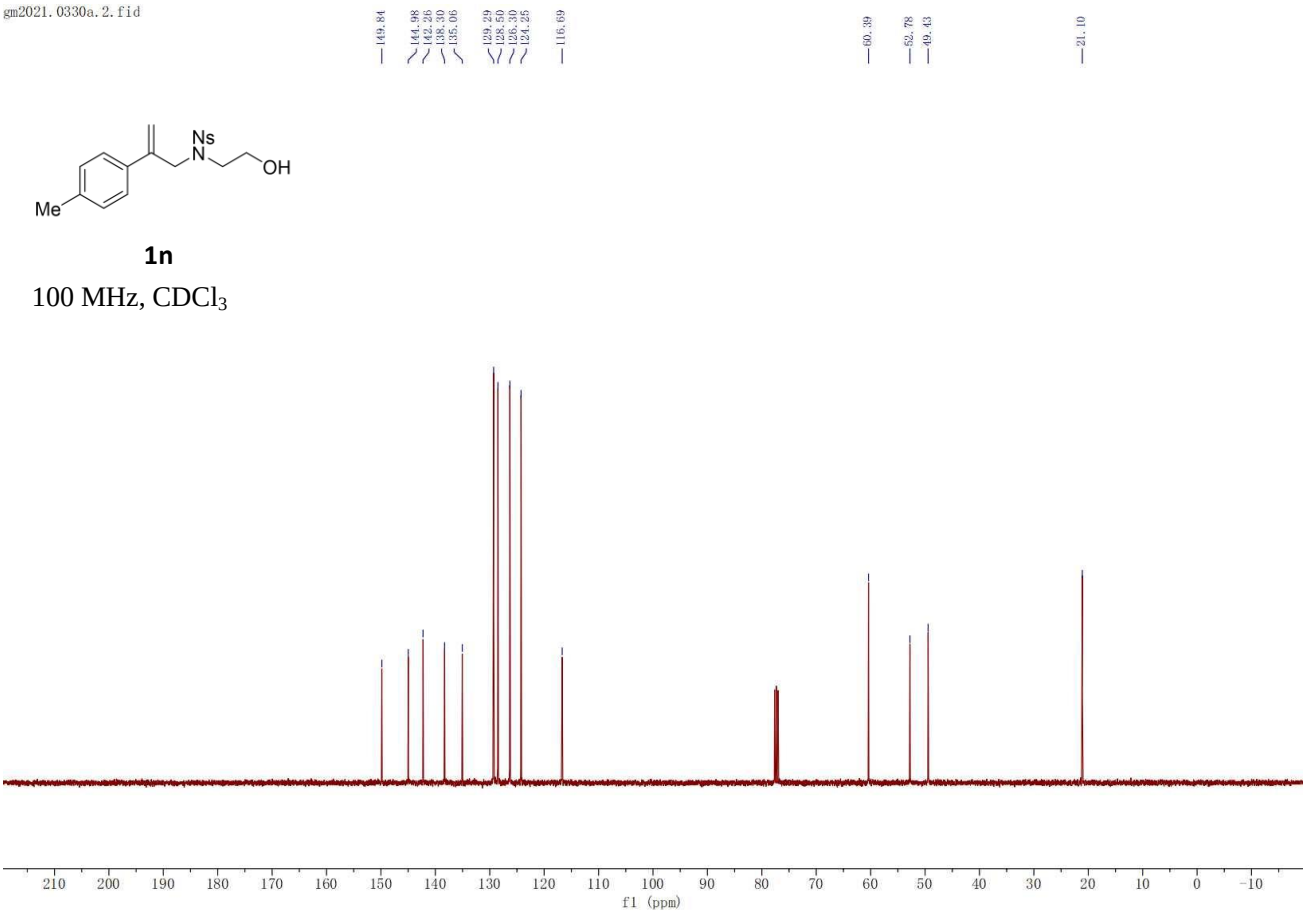
1m

100 MHz, $CDCl_3$



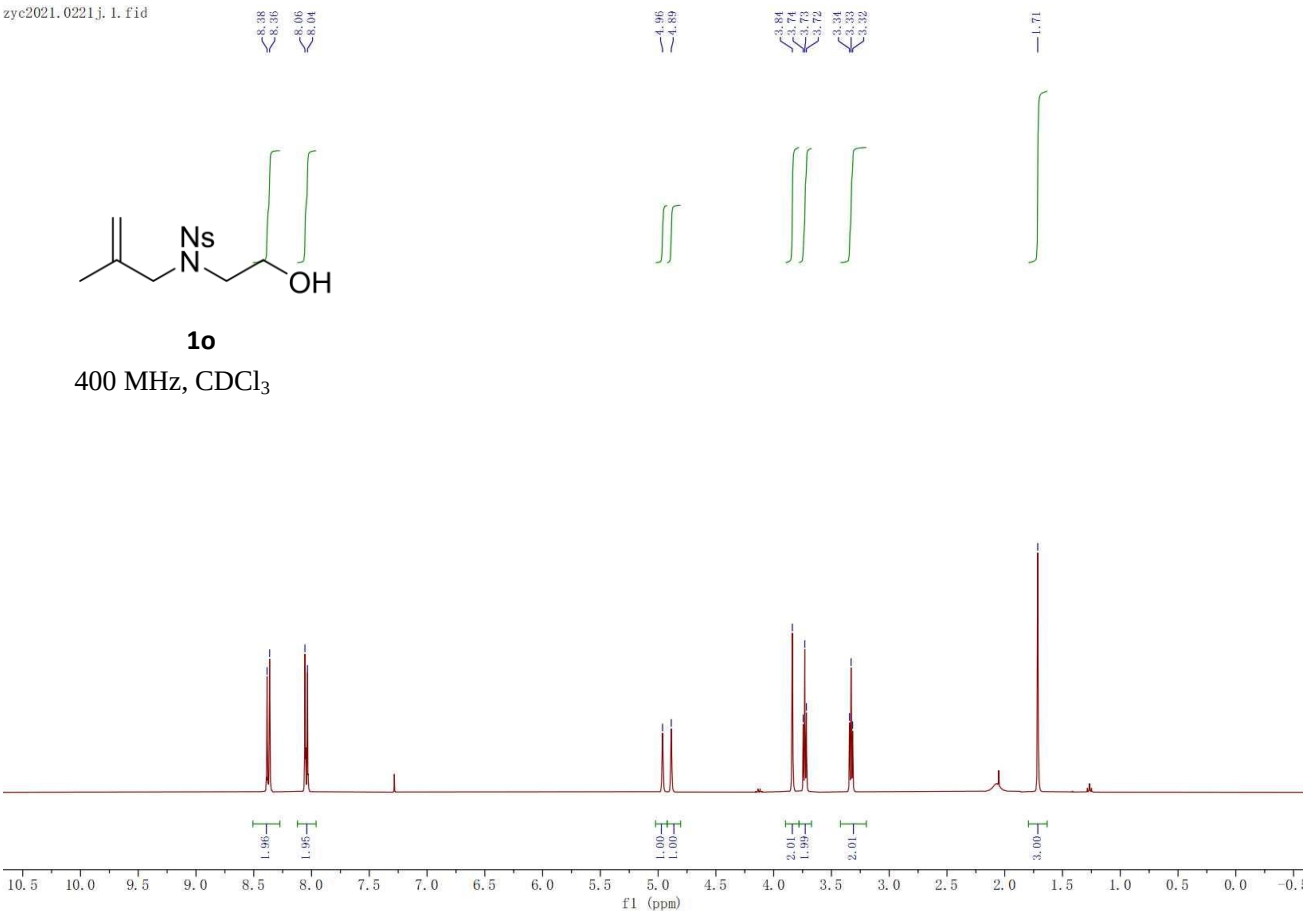
1n

400 MHz, $CDCl_3$



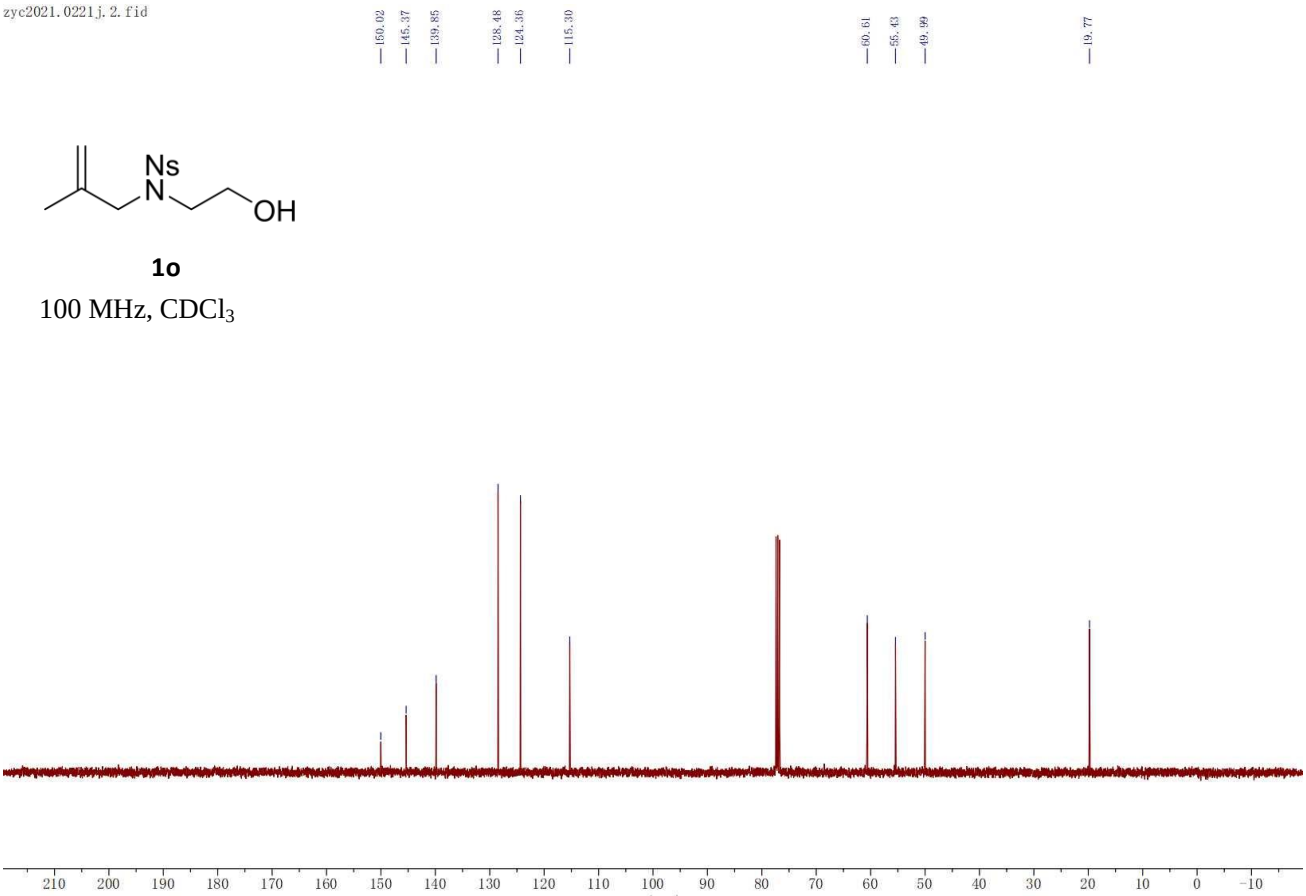
1n

100 MHz, $CDCl_3$



1o

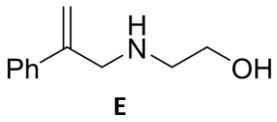
400 MHz, $CDCl_3$



1o

100 MHz, $CDCl_3$

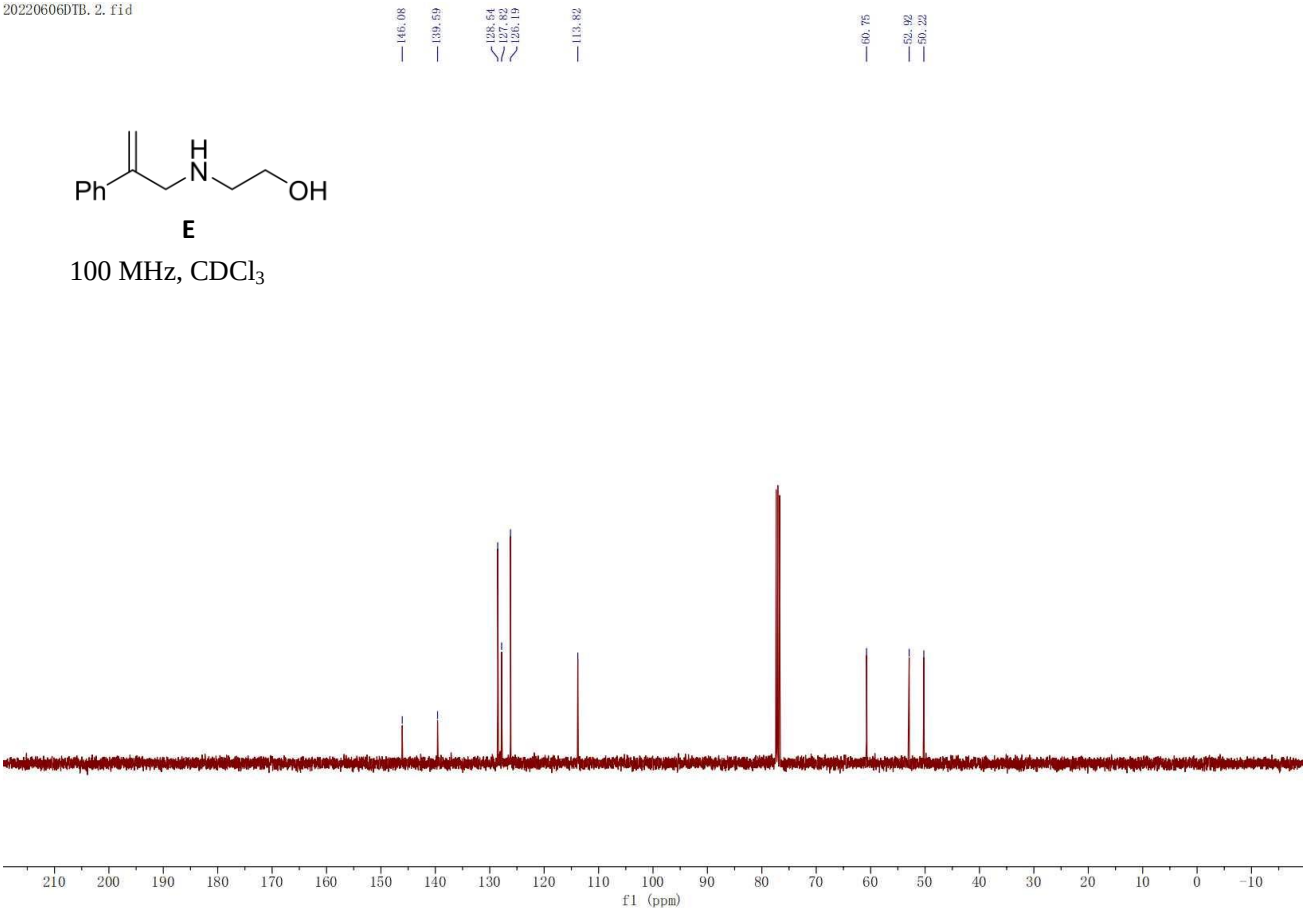
20220606DTB. 1. fid



E

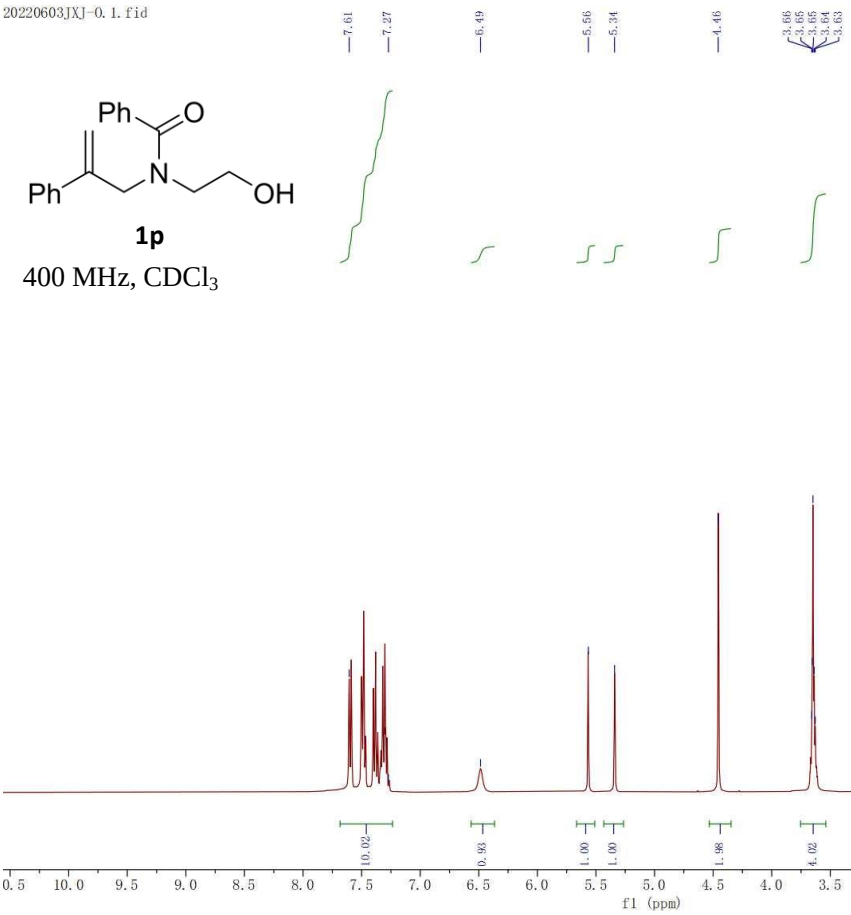
400 MHz, $CDCl_3$

20220606DTB. 2. fid



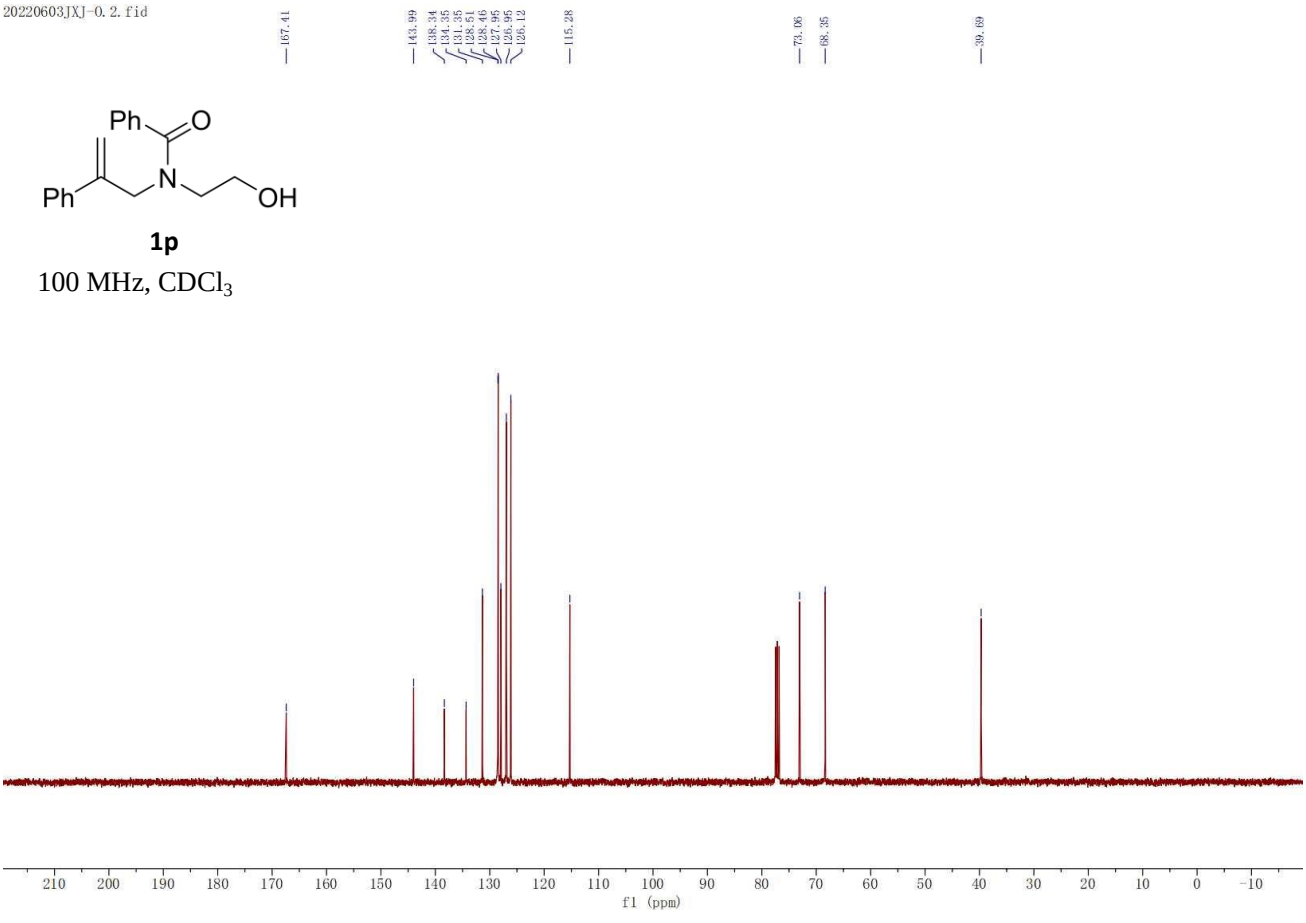
E

100 MHz, $CDCl_3$



1p

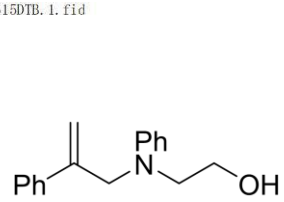
400 MHz, $CDCl_3$



1p

100 MHz, $CDCl_3$

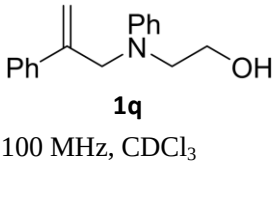
20220615DTB. 1. fid



1q

400 MHz, $CDCl_3$

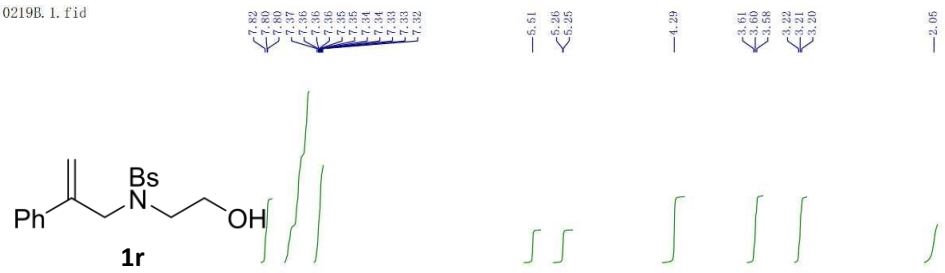
20220615DTB. 2. fid



1q

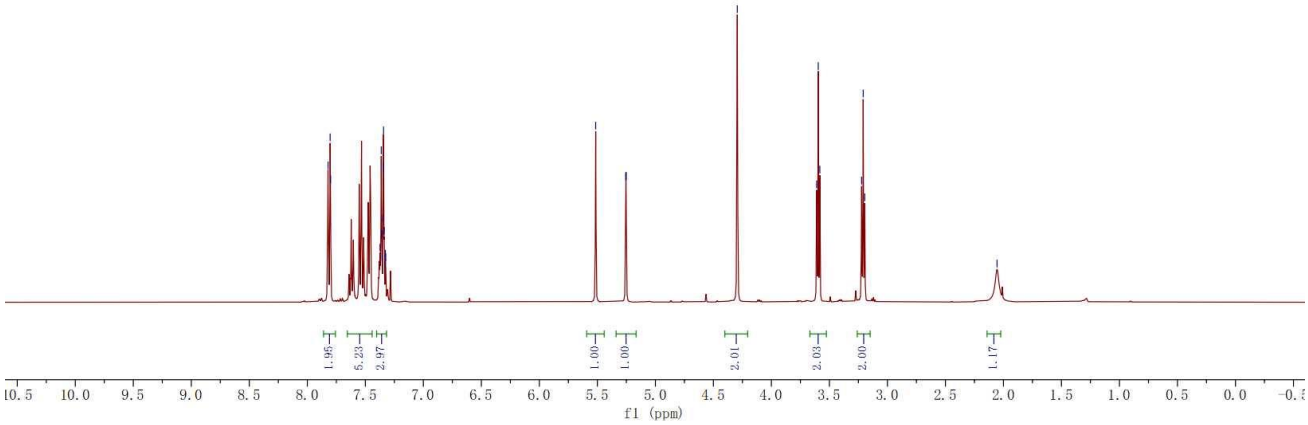
100 MHz, $CDCl_3$

JXJ2021.0219B.1.fid

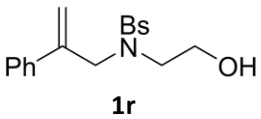


1r

400 MHz, $CDCl_3$

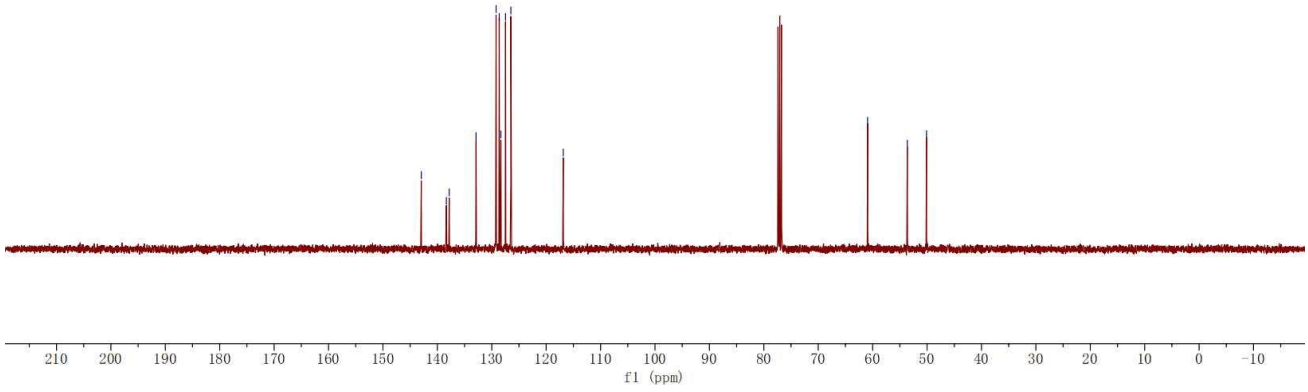


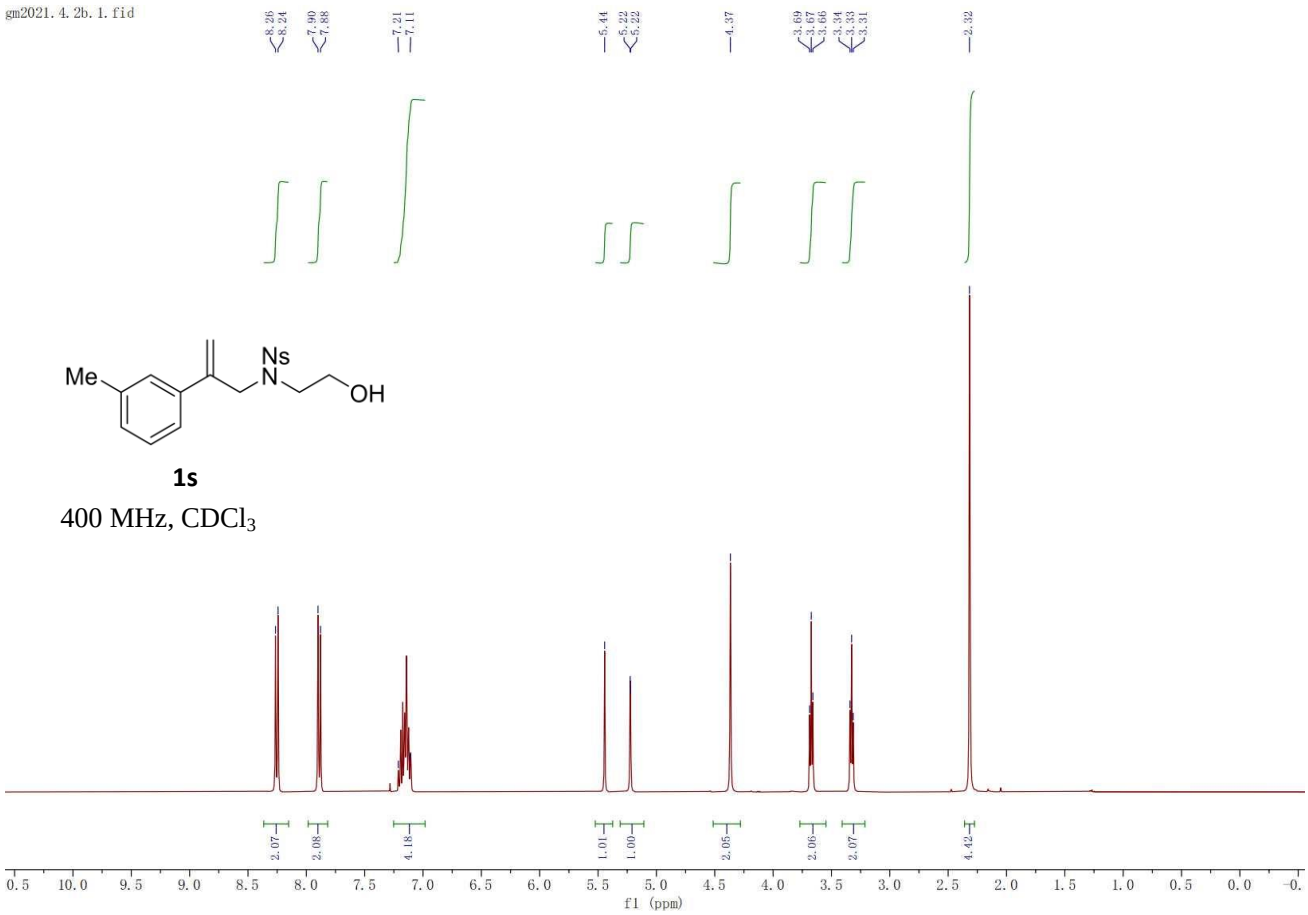
JXJ2021.0219B.2.fid



1r

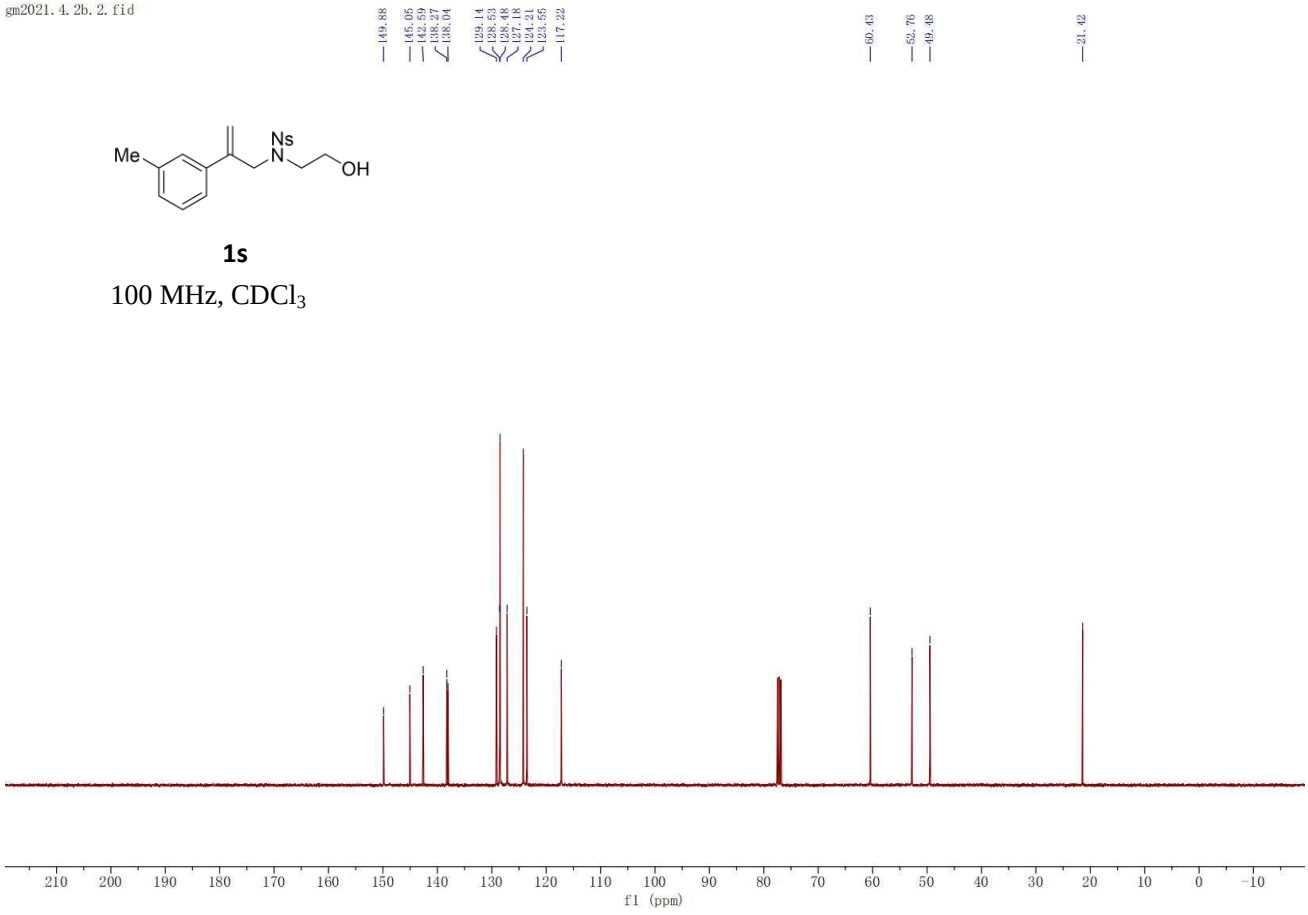
100 MHz, $CDCl_3$





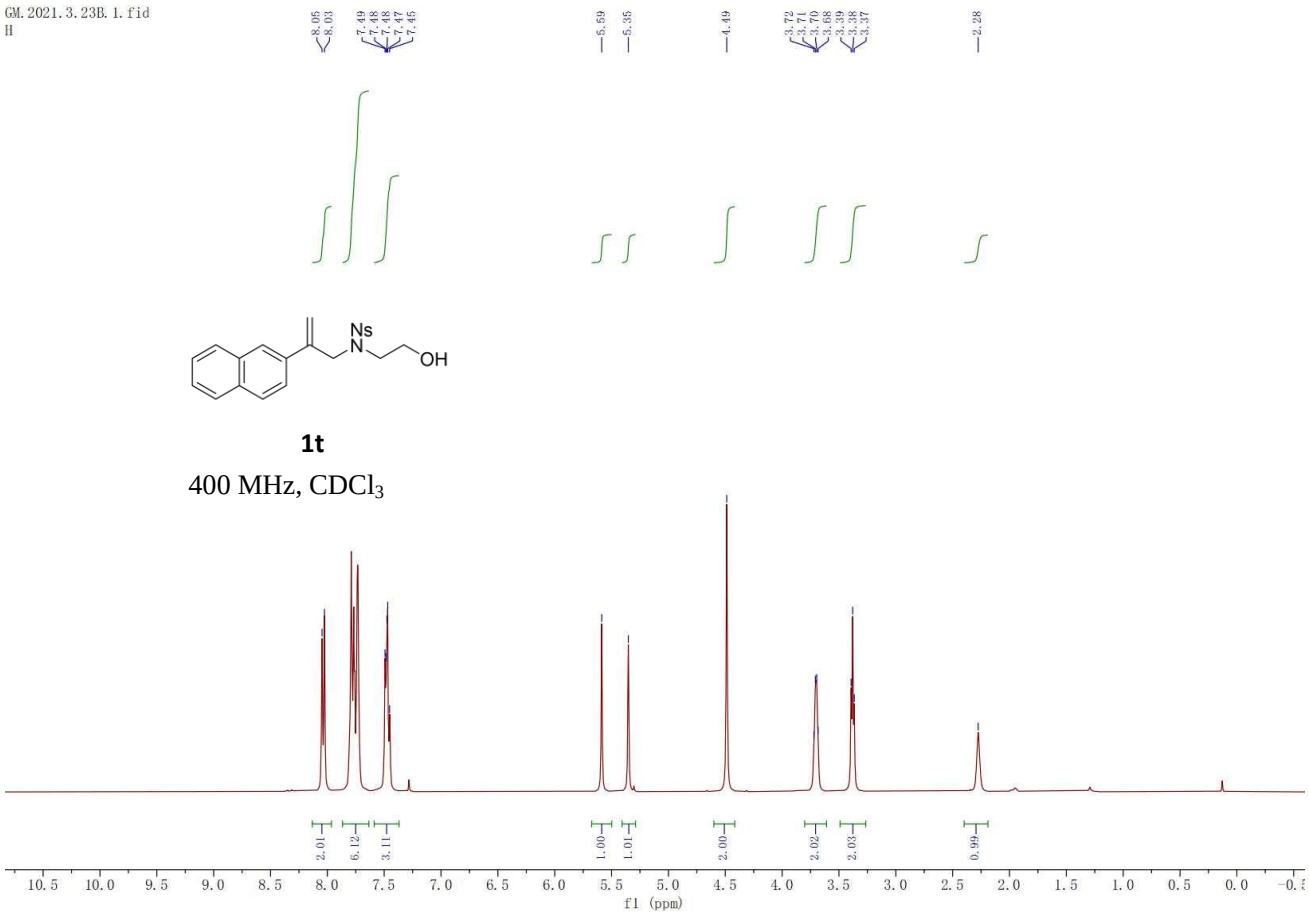
1s

400 MHz, $CDCl_3$



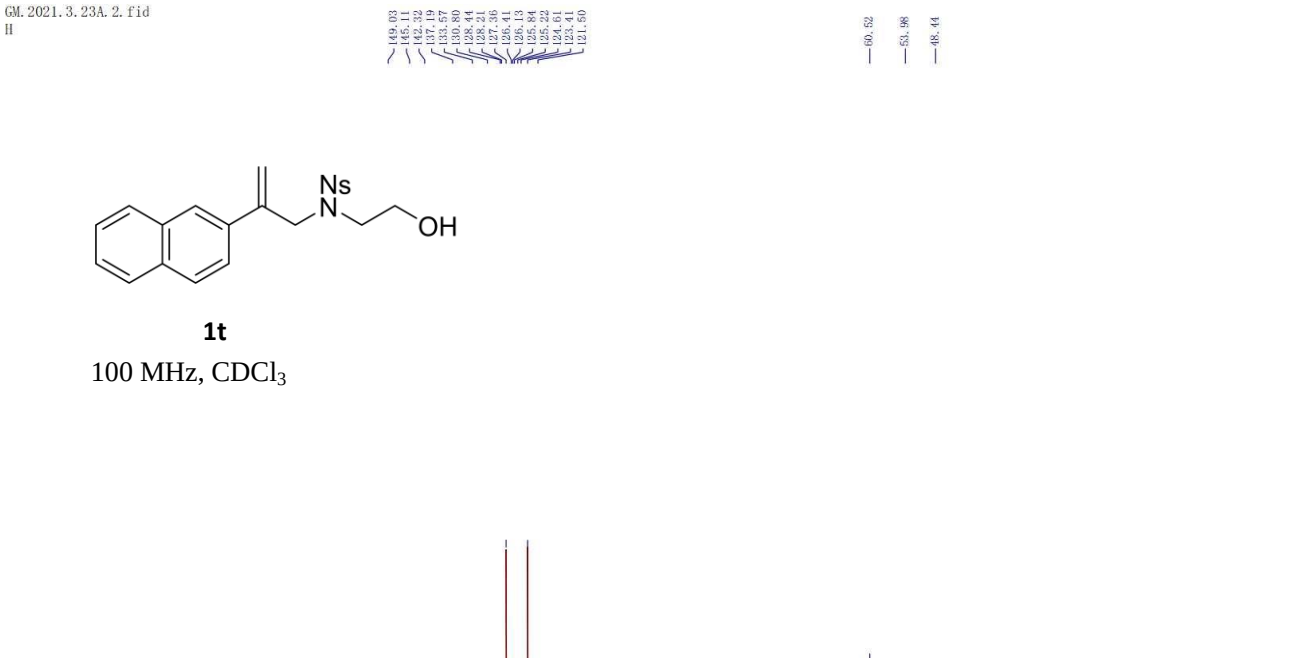
1s

100 MHz, $CDCl_3$



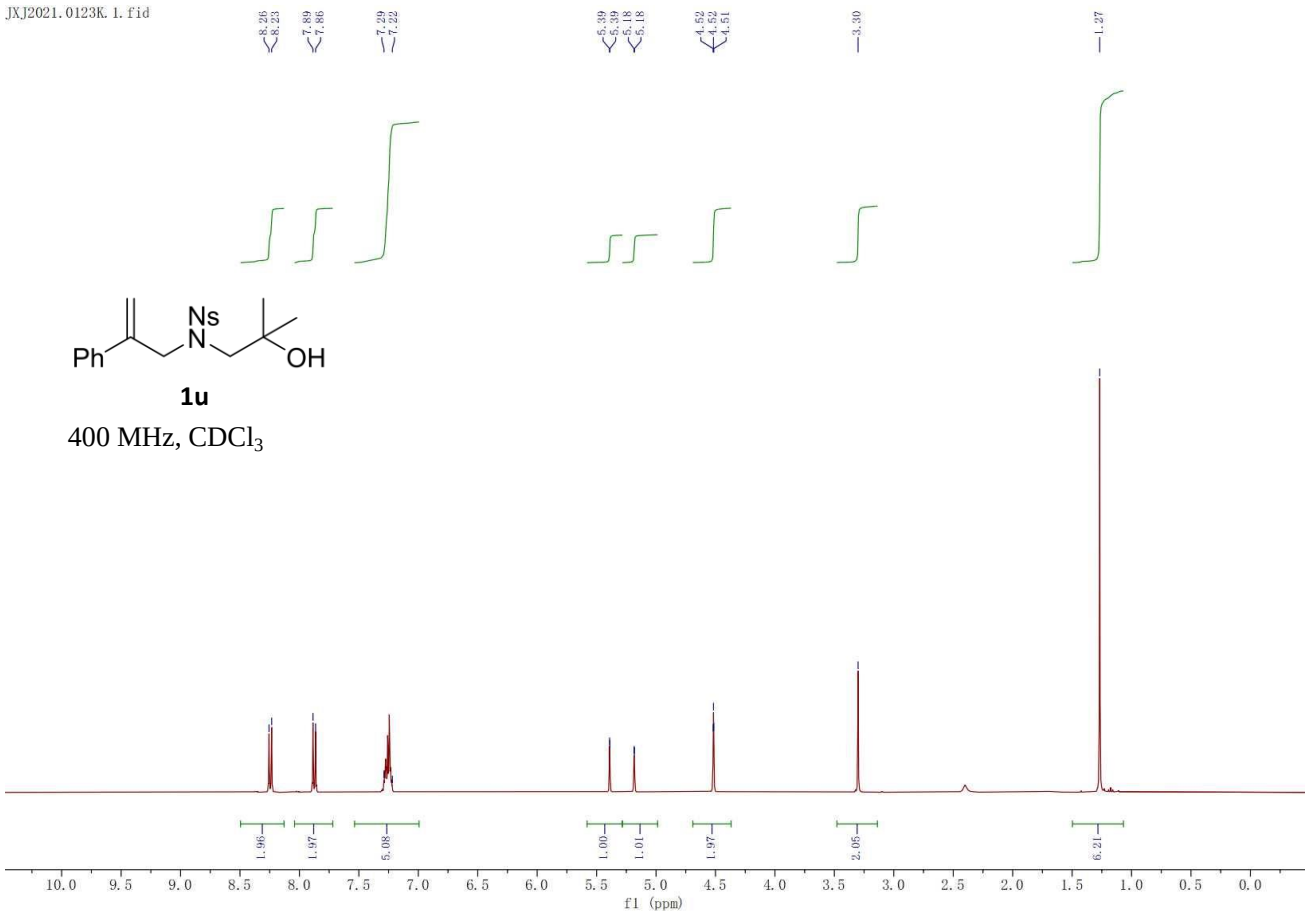
1t

400 MHz, $CDCl_3$



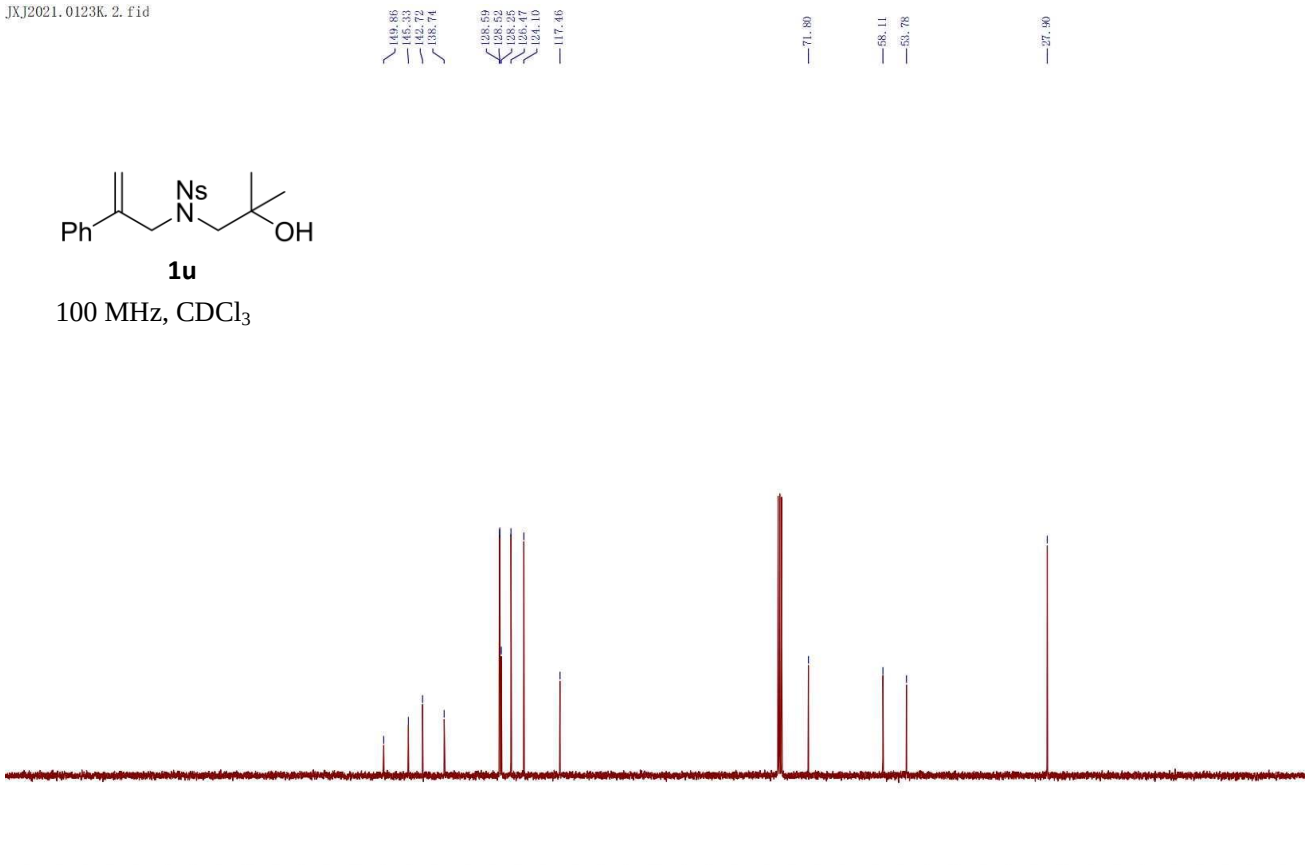
1t

100 MHz, $CDCl_3$



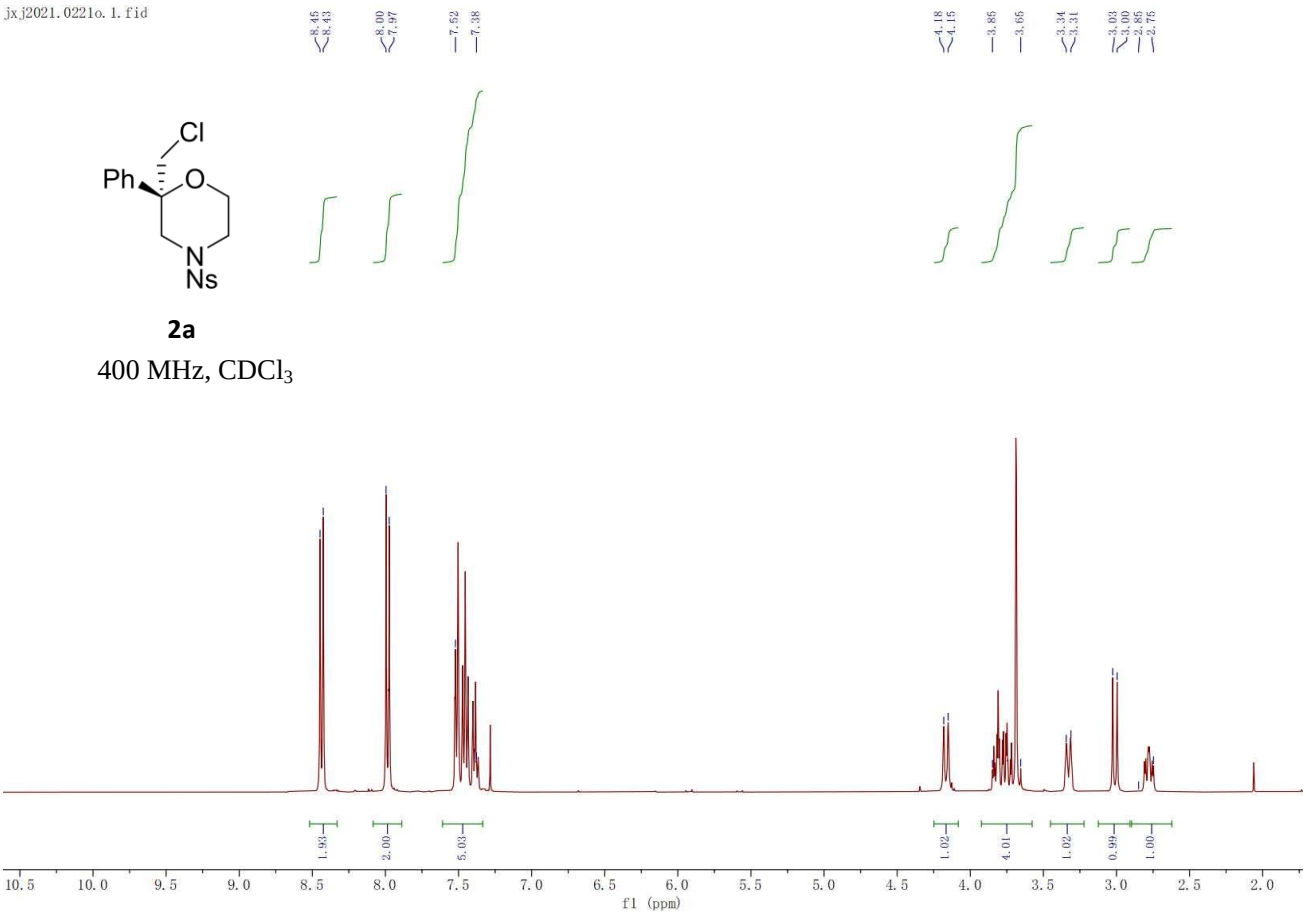
1u

400 MHz, $CDCl_3$



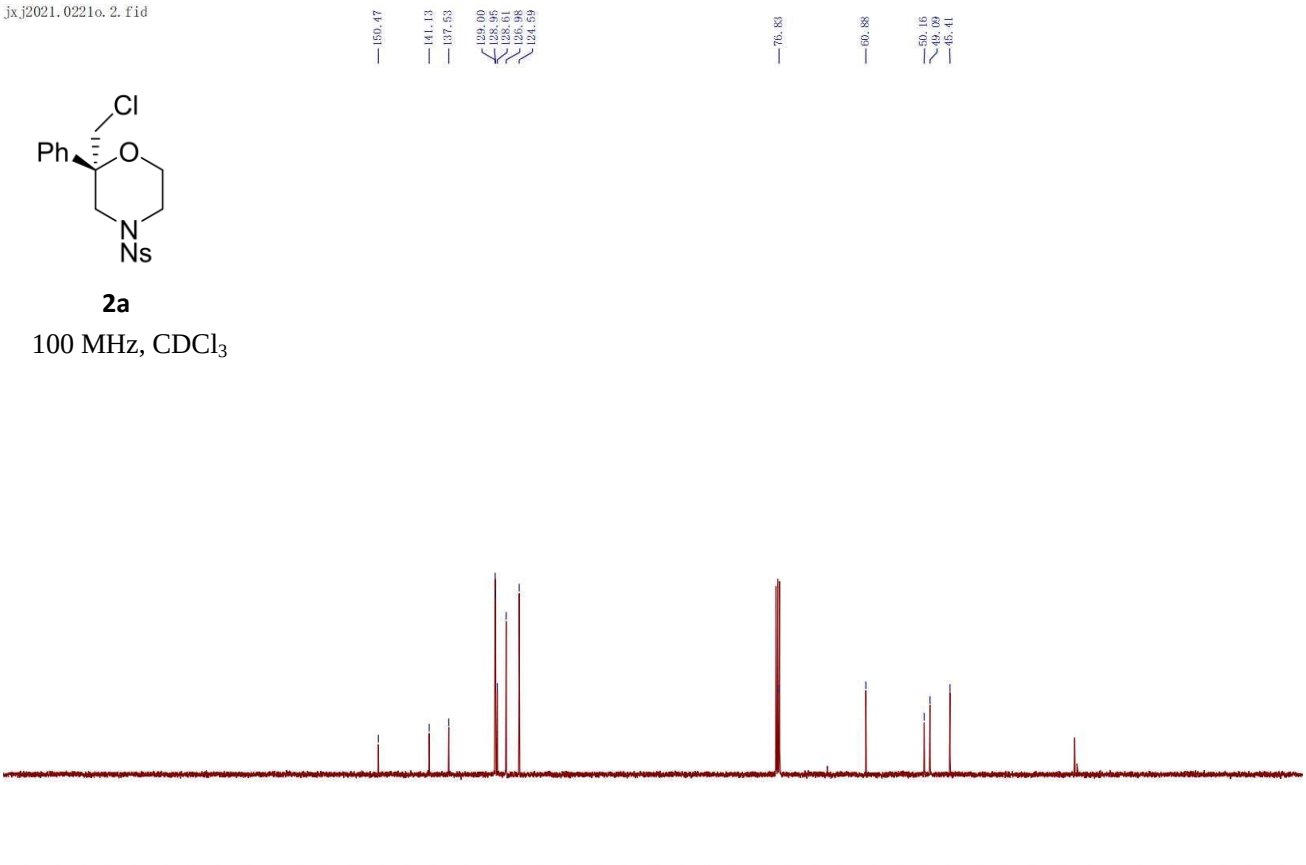
1u

100 MHz, $CDCl_3$



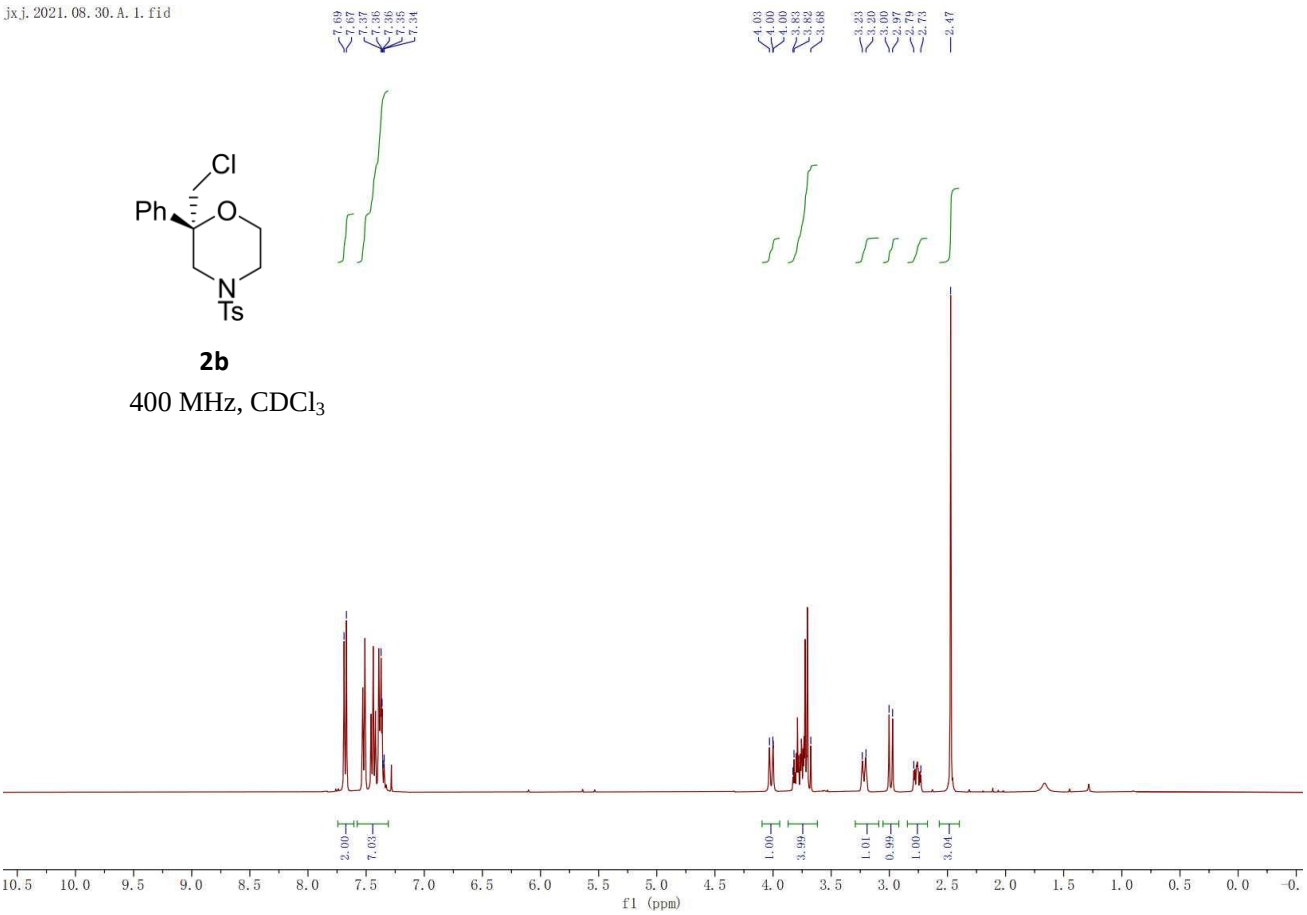
2a

400 MHz, $CDCl_3$



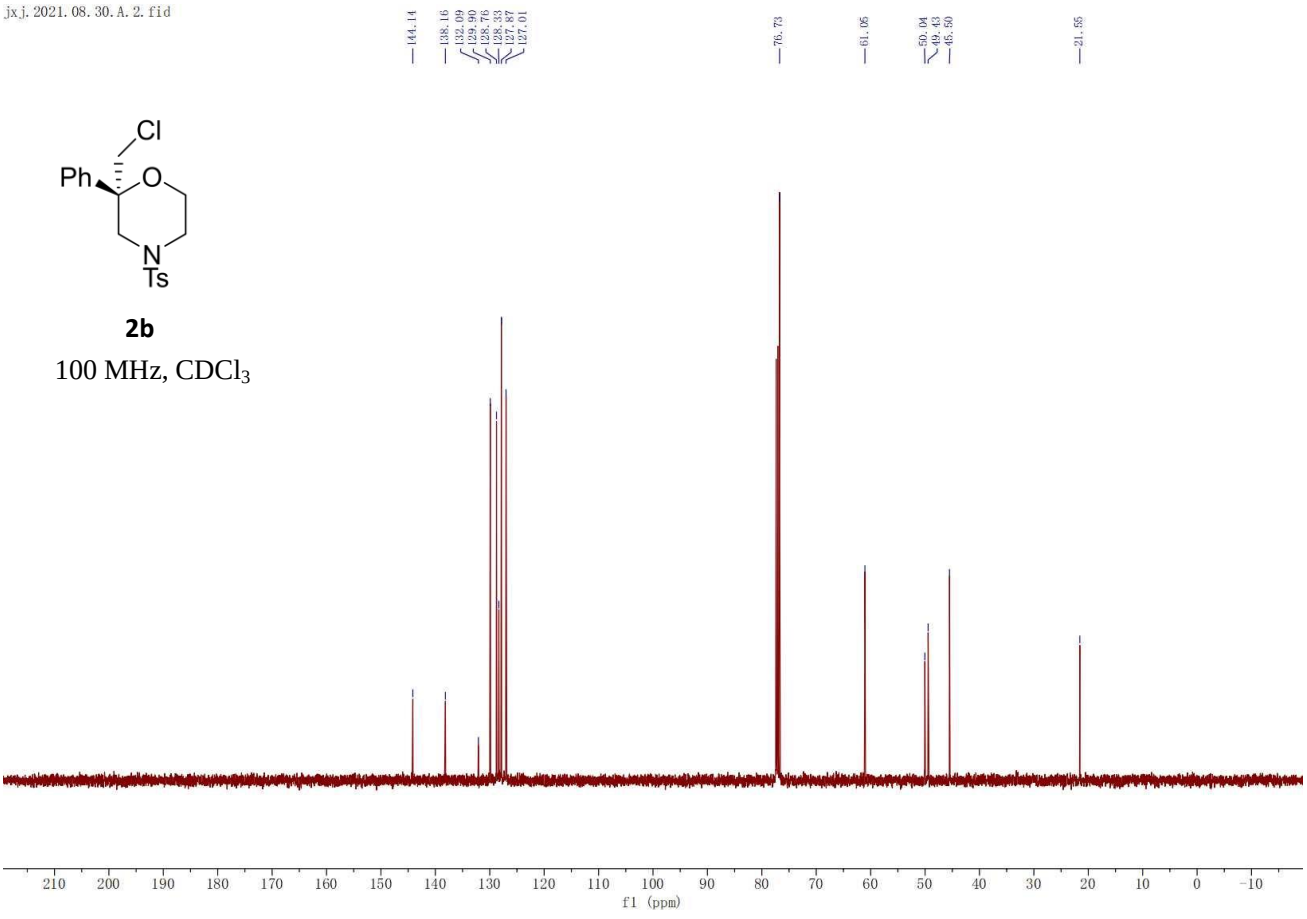
2a

100 MHz, $CDCl_3$



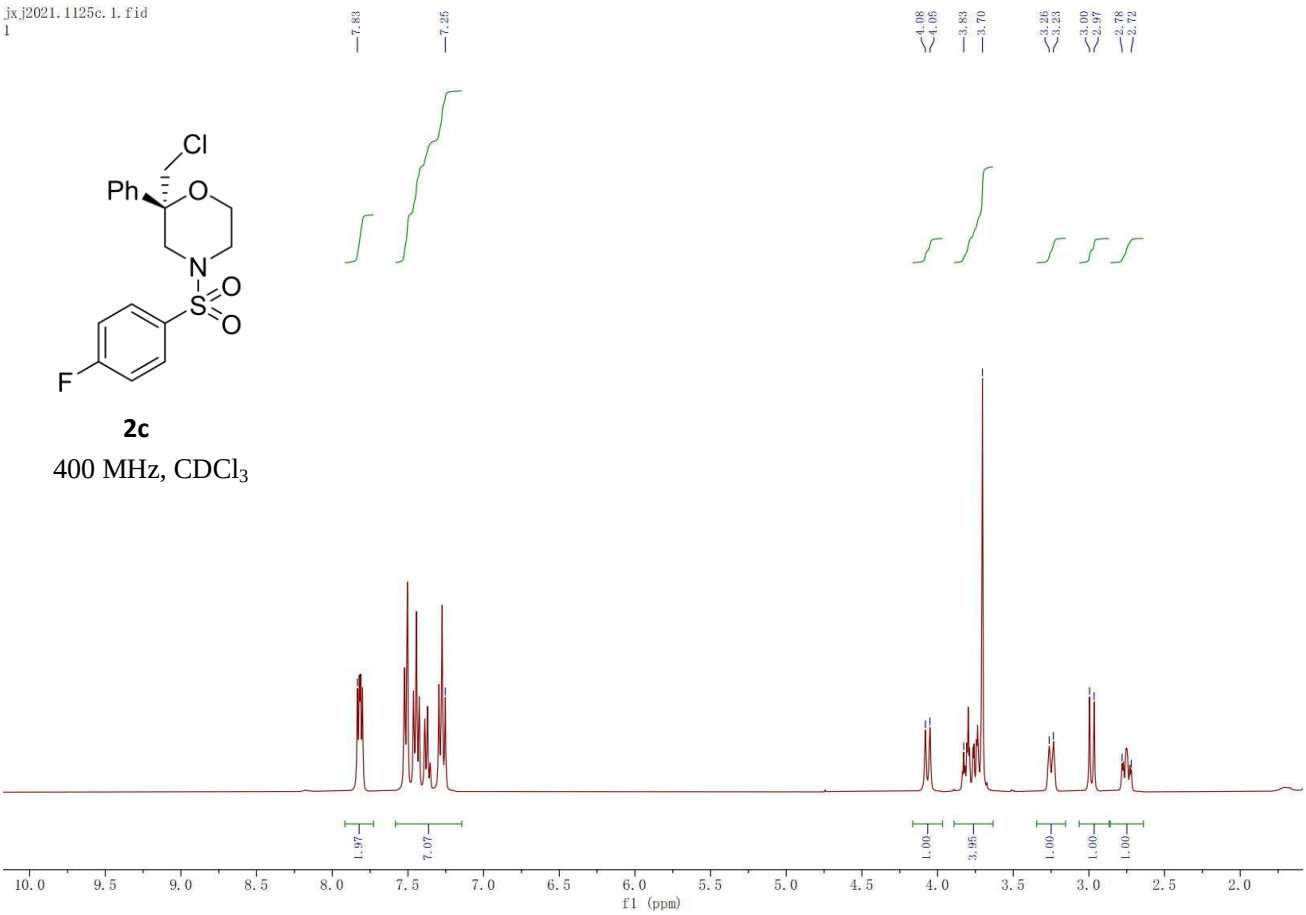
2b

400 MHz, $CDCl_3$



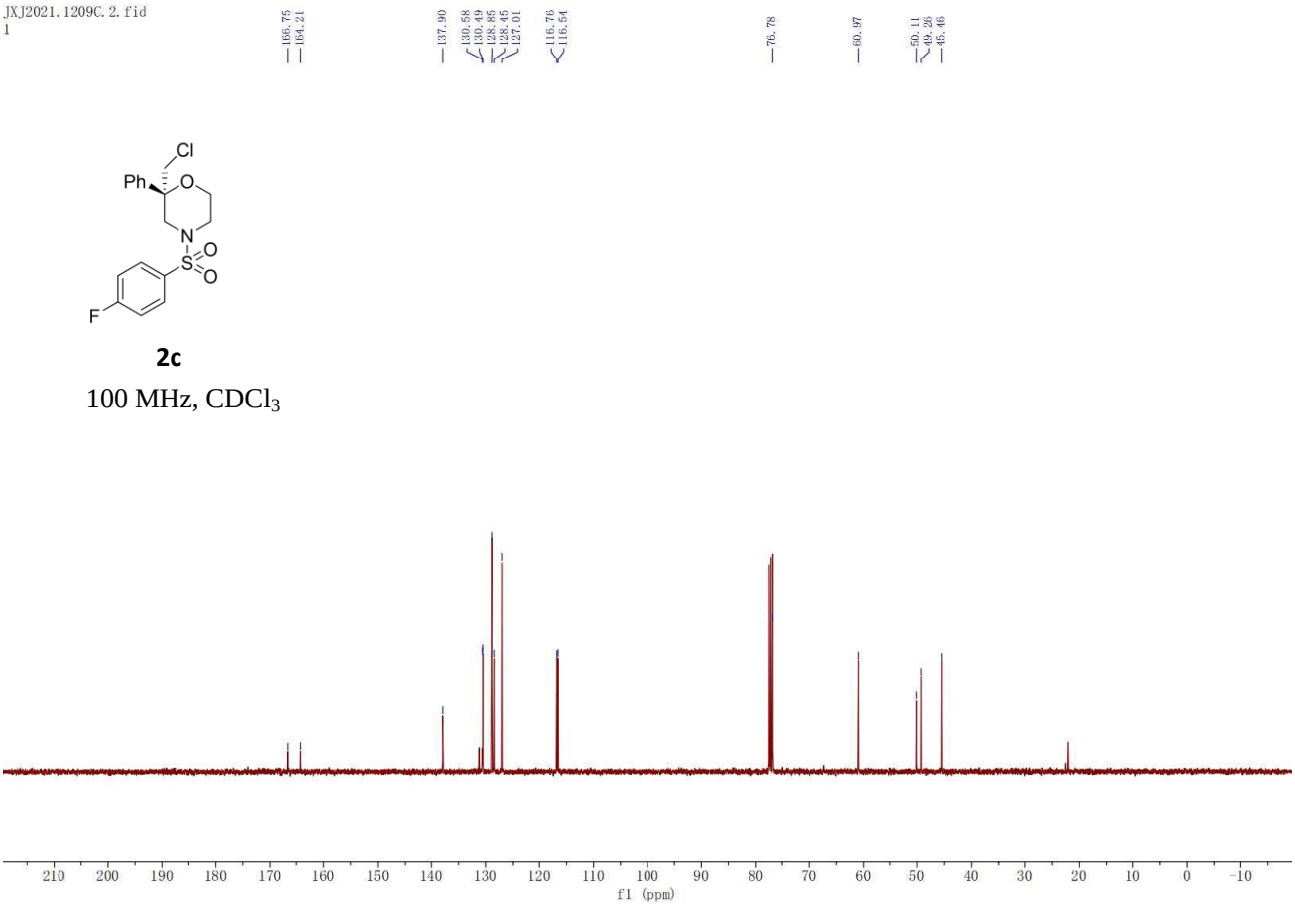
2b

100 MHz, $CDCl_3$



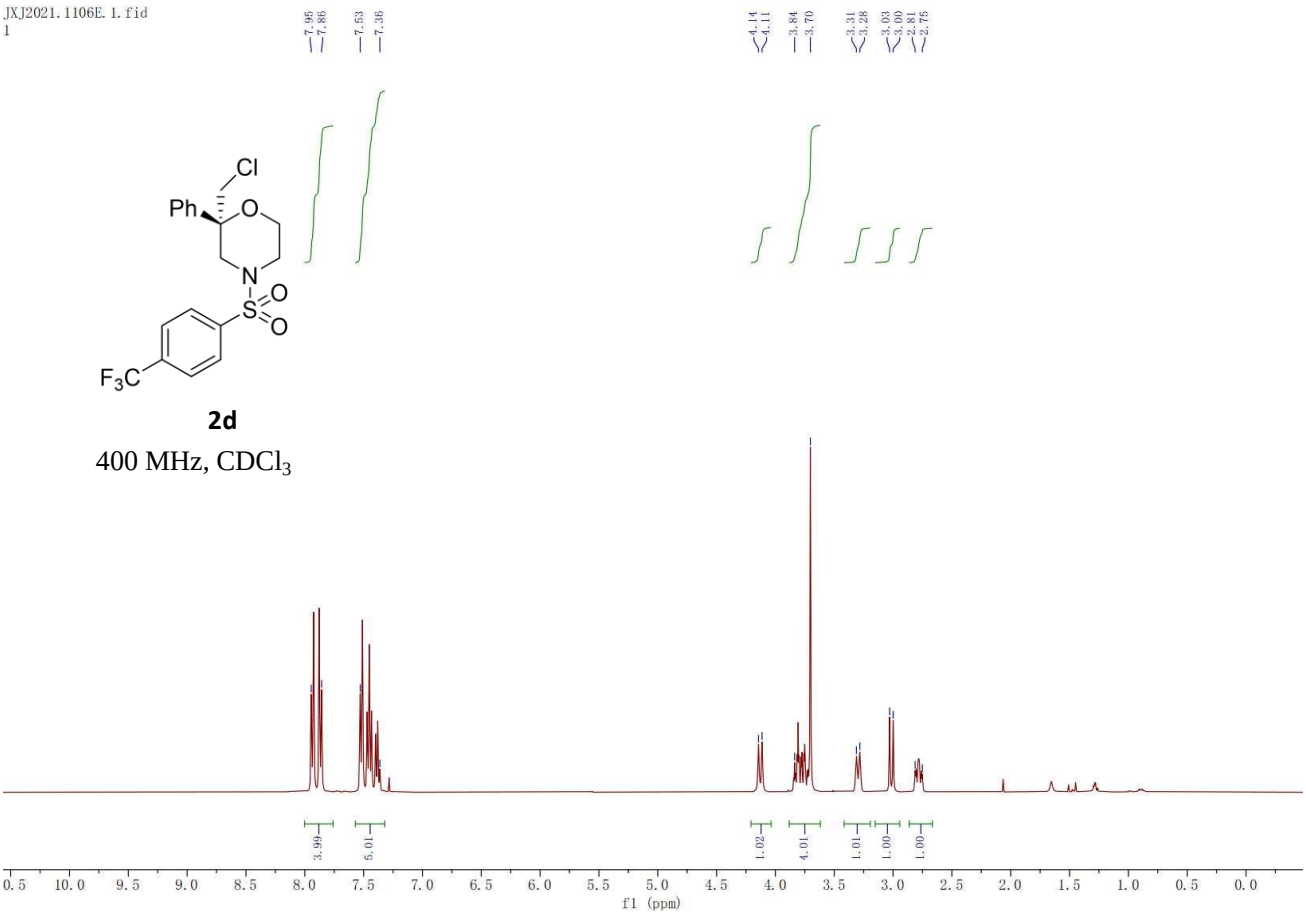
2c

400 MHz, $CDCl_3$



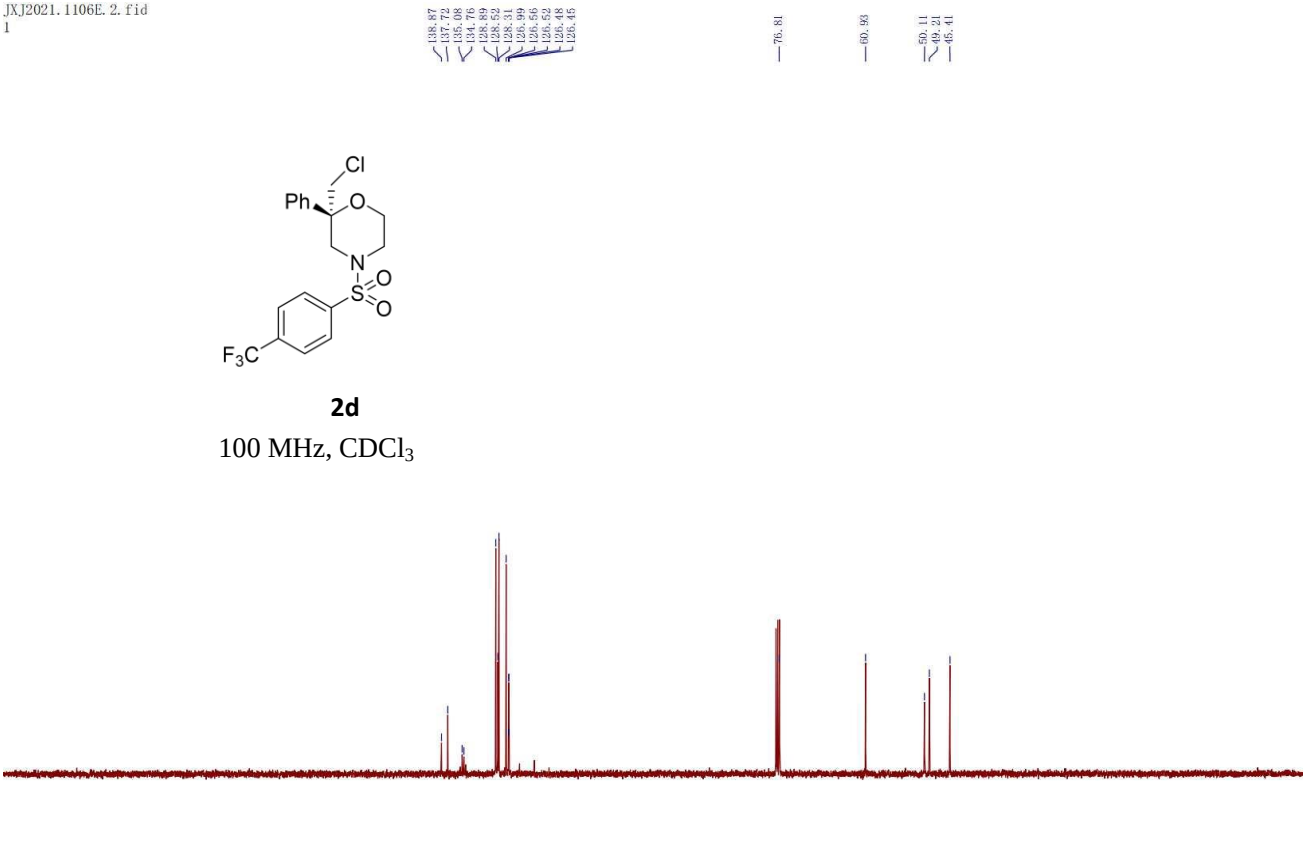
2c

100 MHz, $CDCl_3$



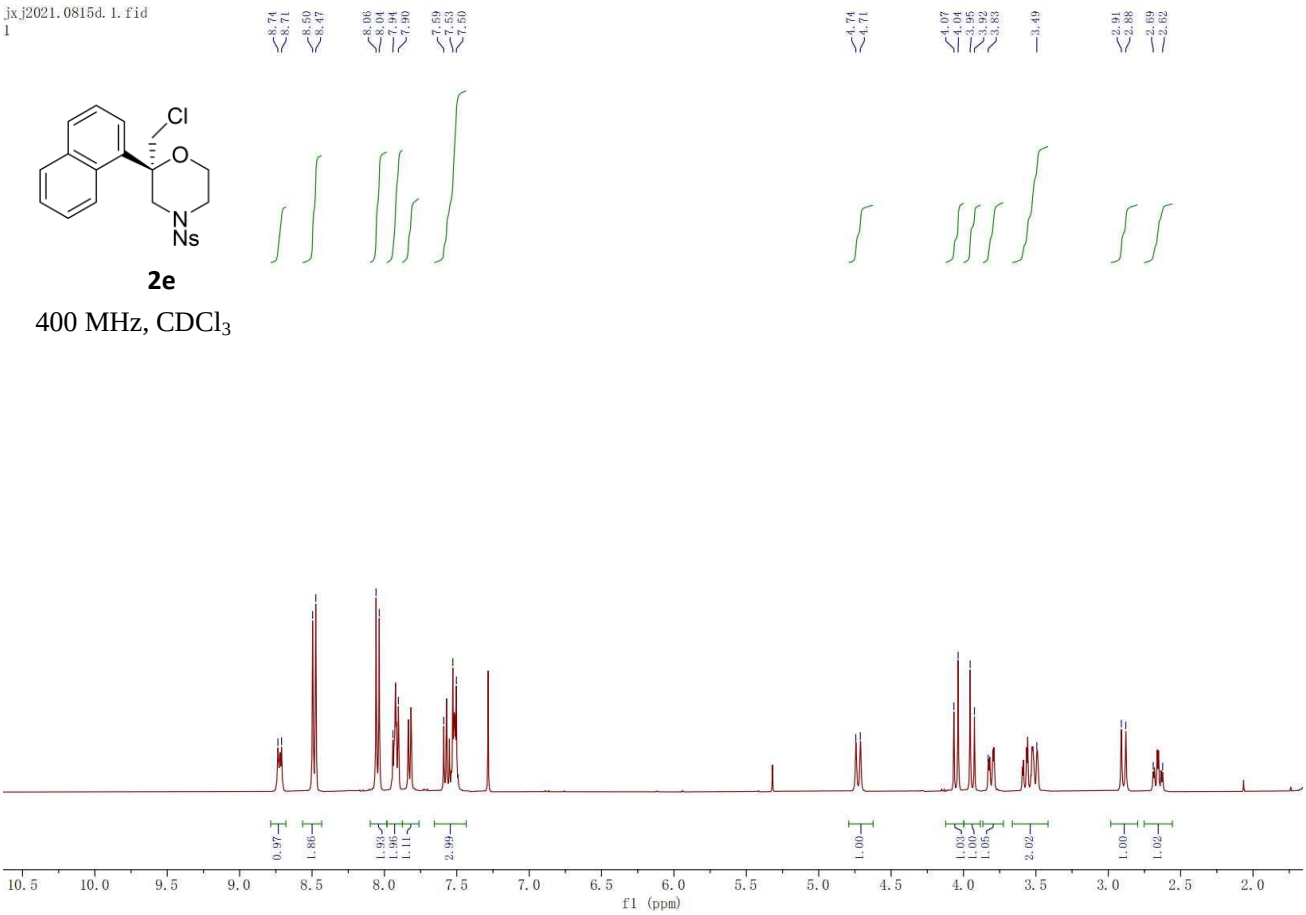
2d

400 MHz, $CDCl_3$



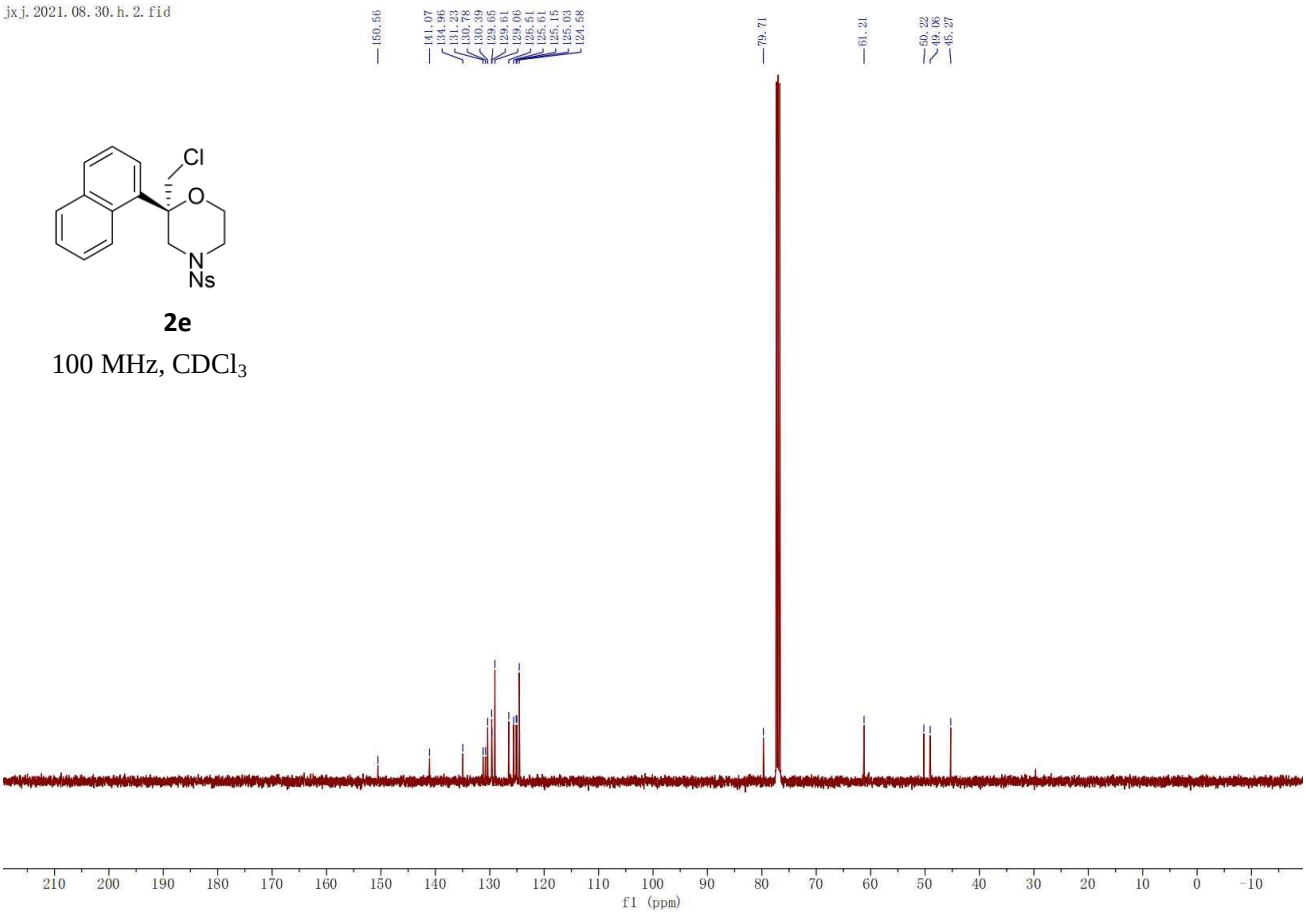
2d

100 MHz, $CDCl_3$



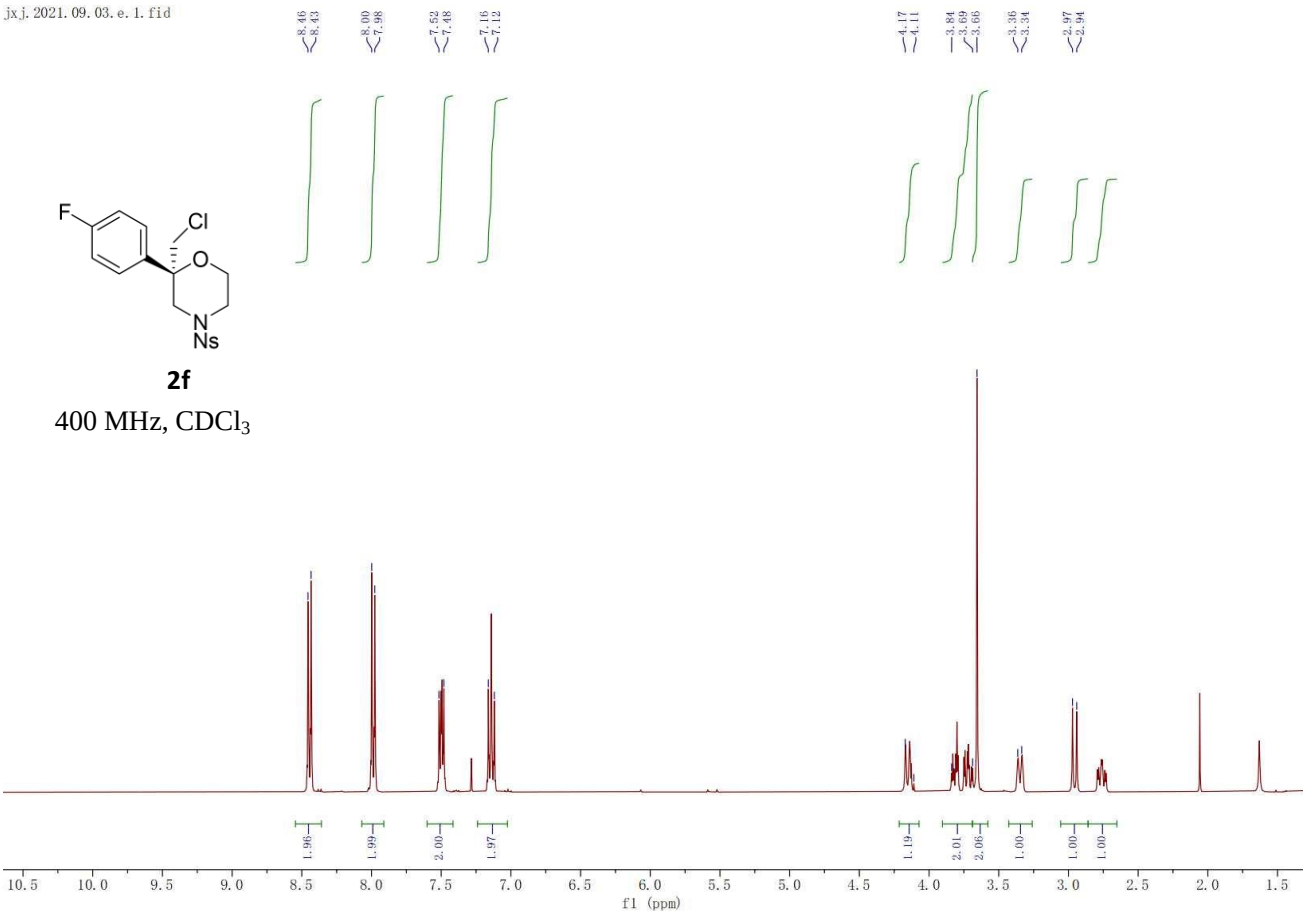
2e

400 MHz, $CDCl_3$



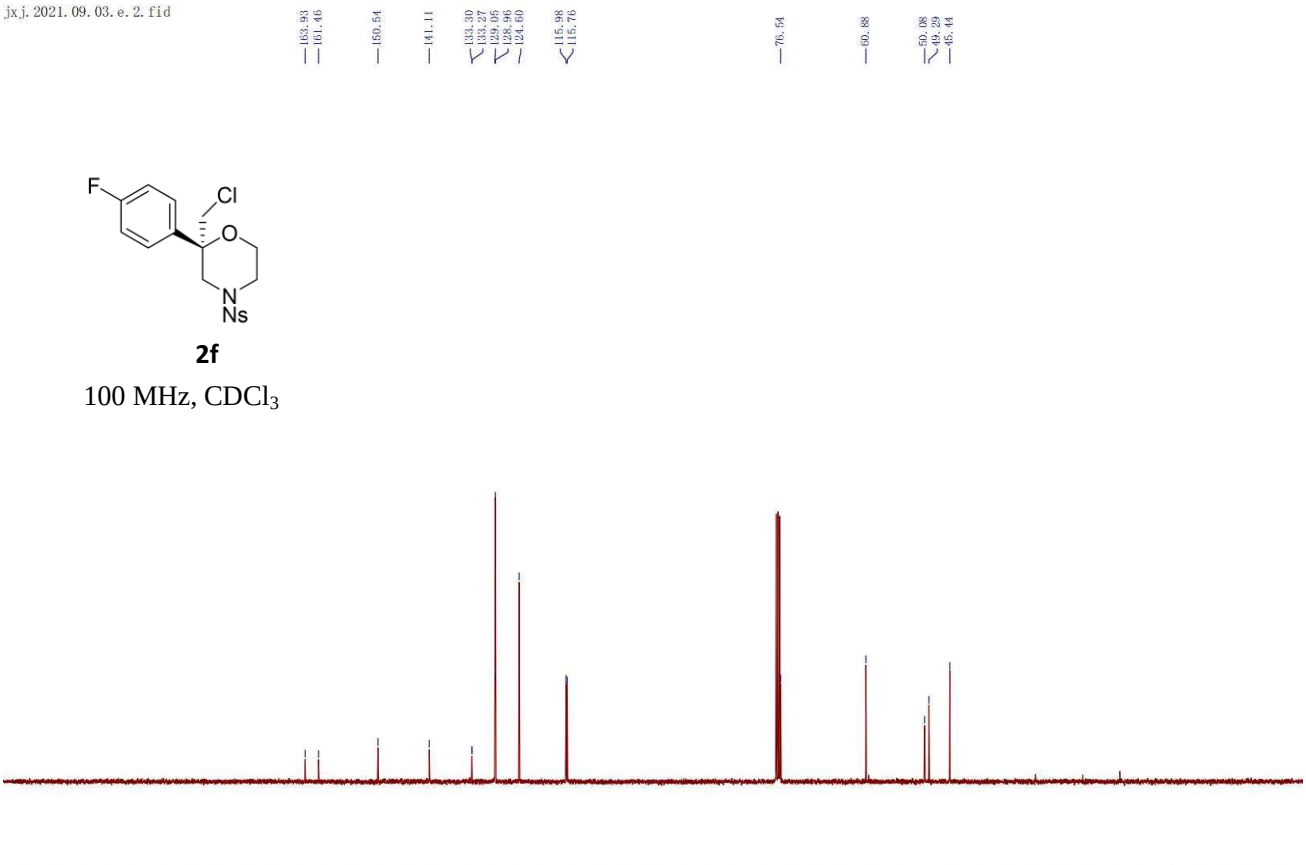
2e

100 MHz, $CDCl_3$



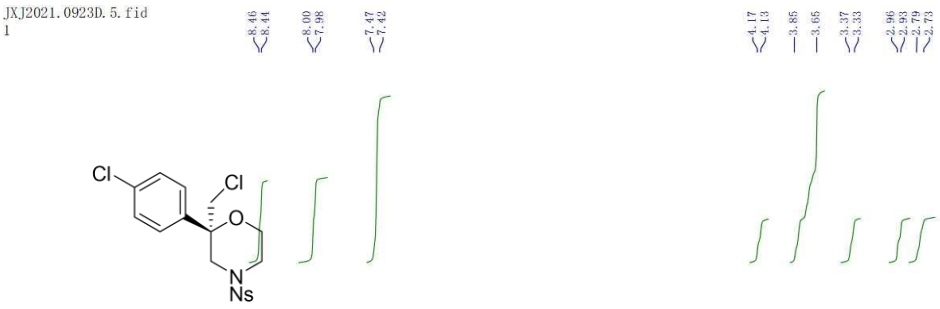
2f

400 MHz, $CDCl_3$



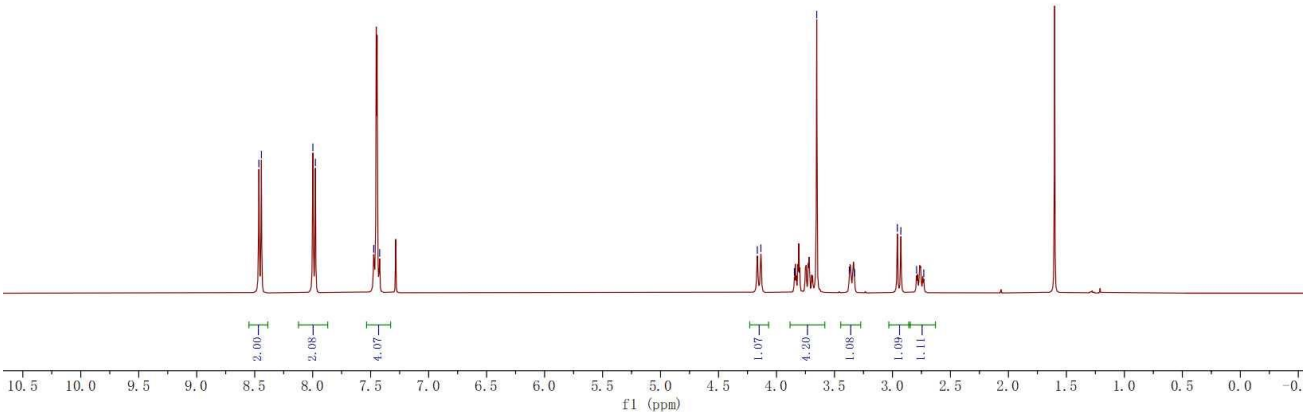
2f

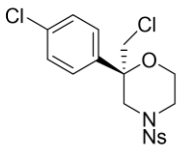
100 MHz, $CDCl_3$



2g

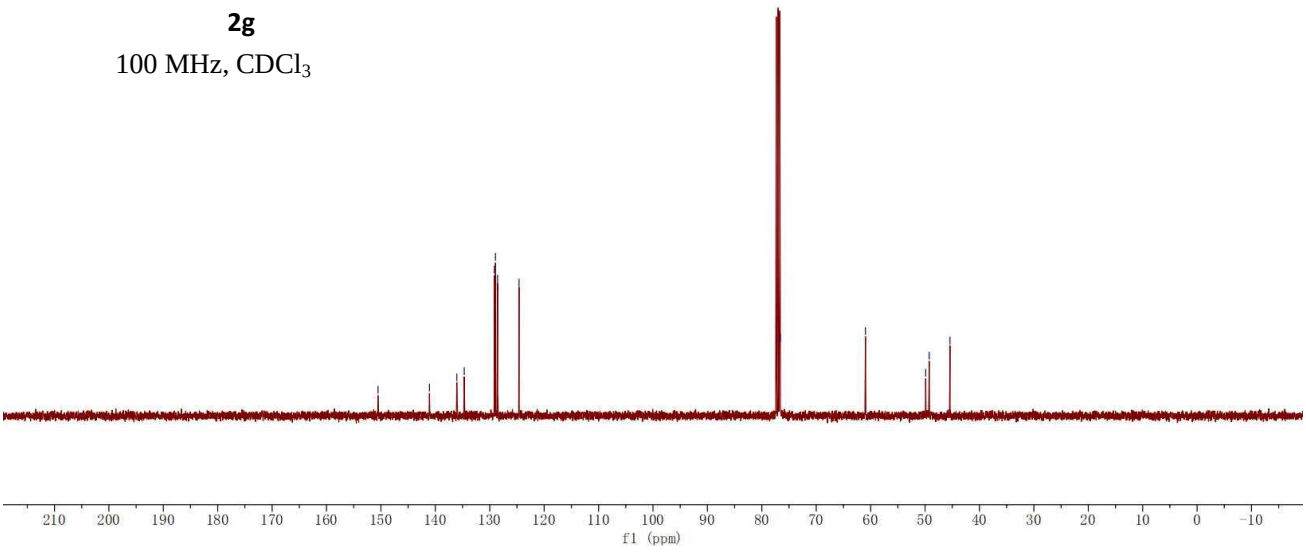
400 MHz, $CDCl_3$

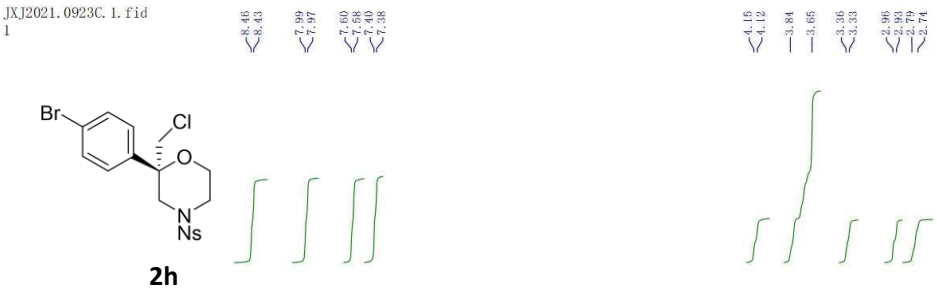




2g

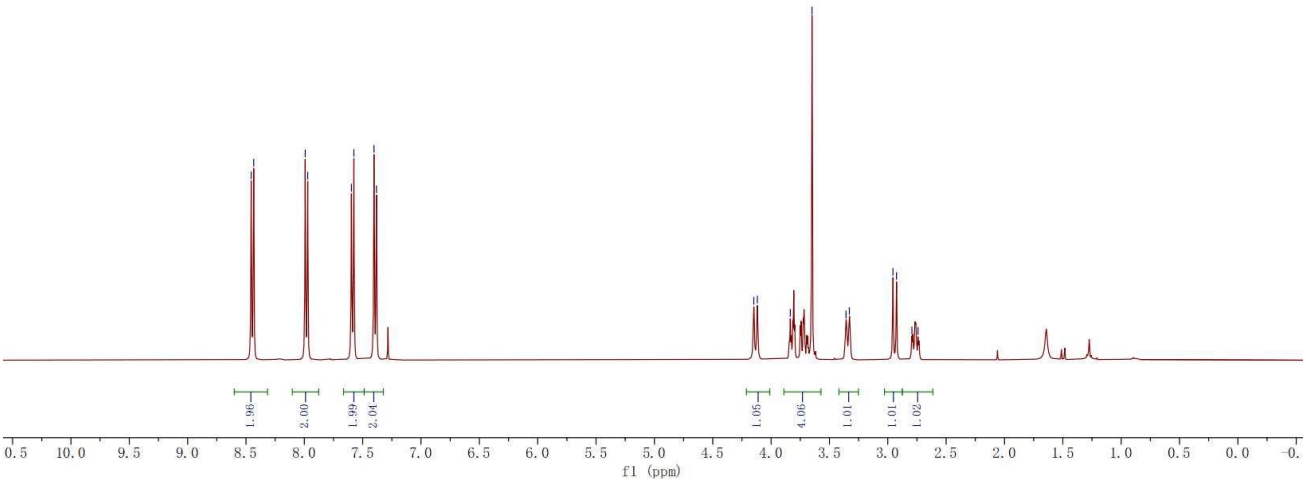
100 MHz, $CDCl_3$





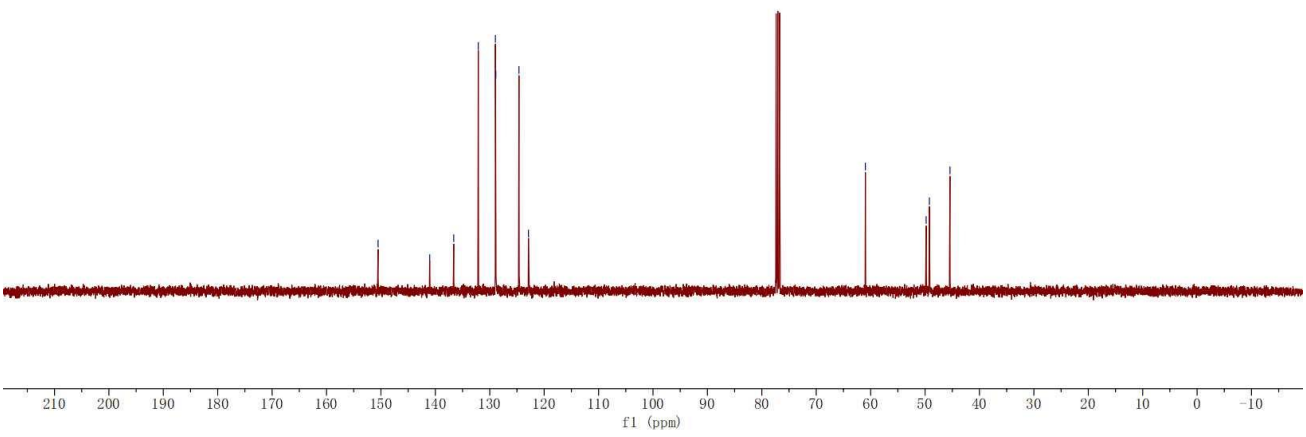
2h

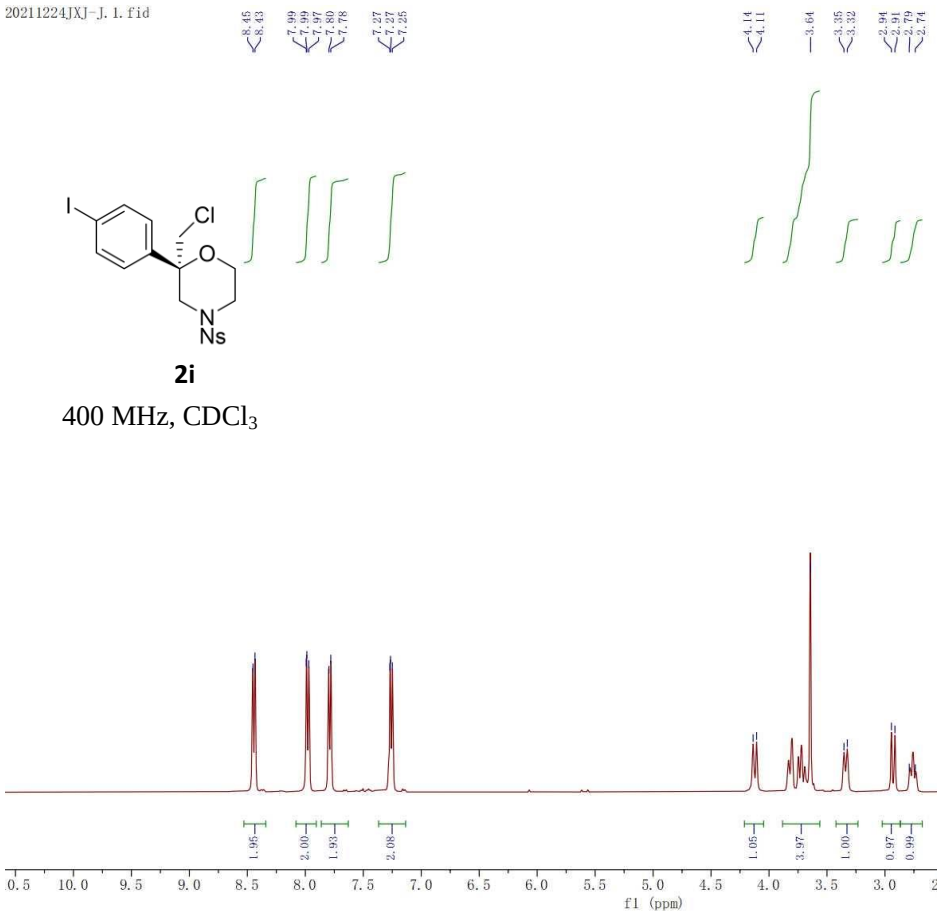
400 MHz, $CDCl_3$



2h

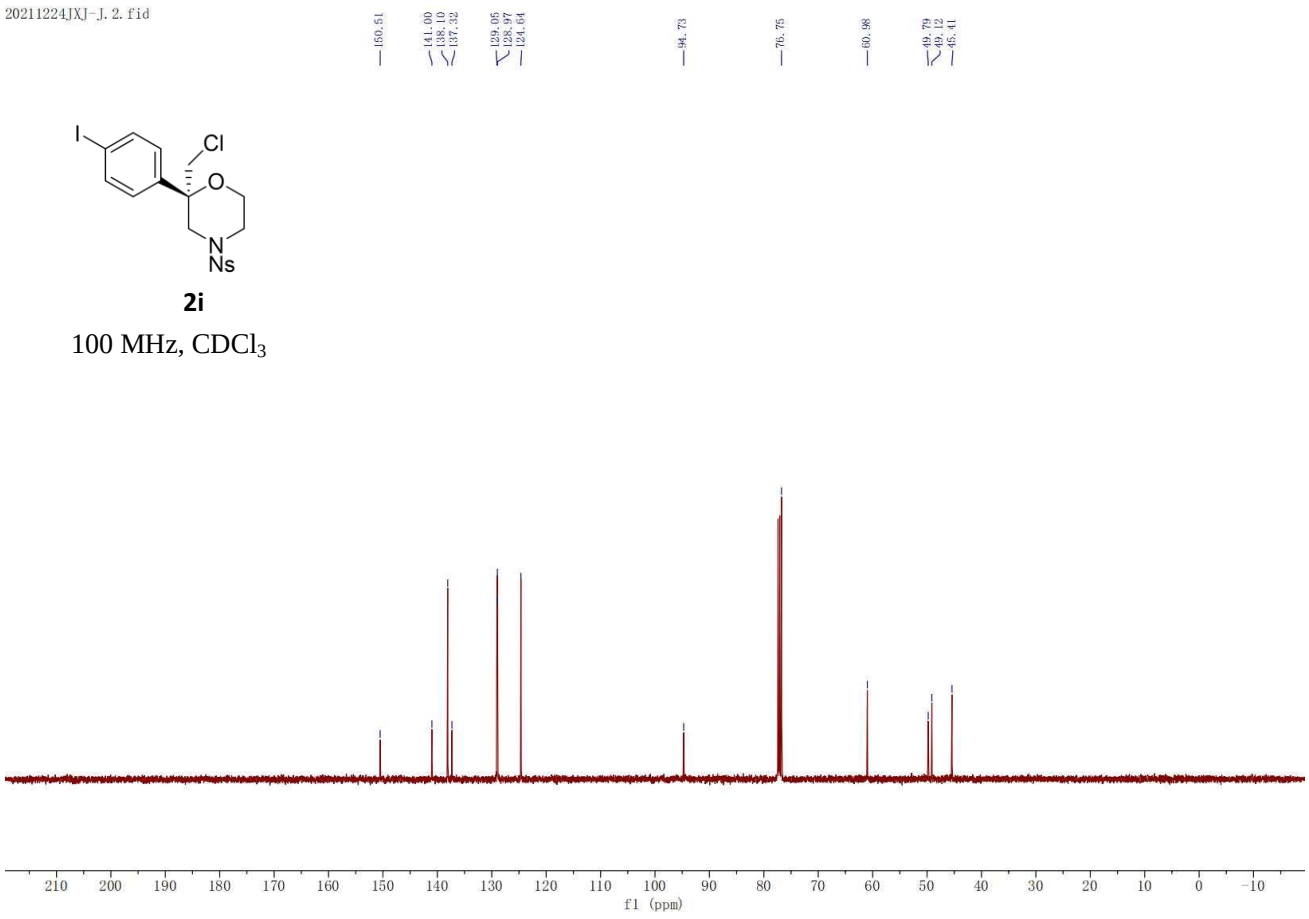
100 MHz, $CDCl_3$





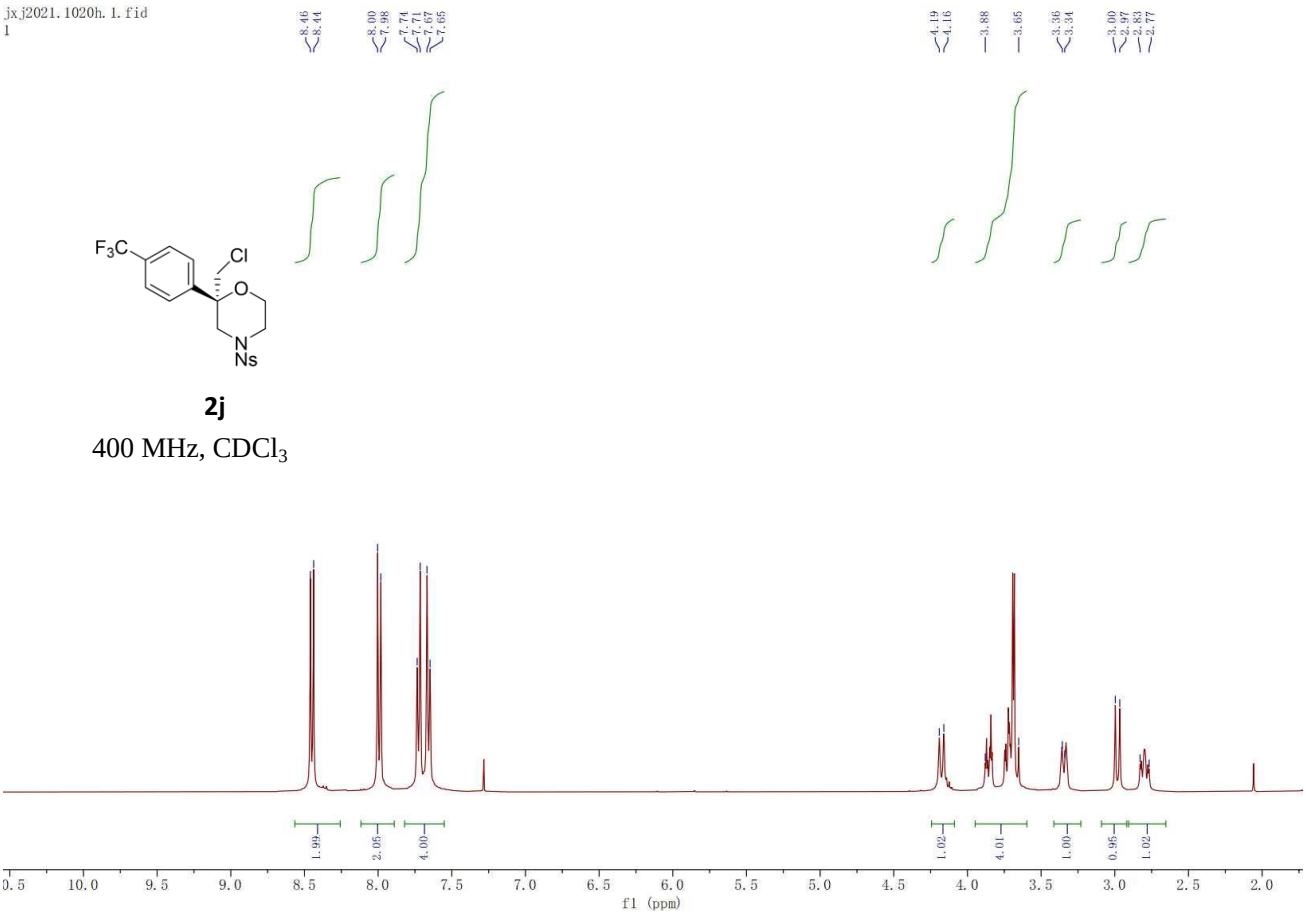
2i

400 MHz, $CDCl_3$



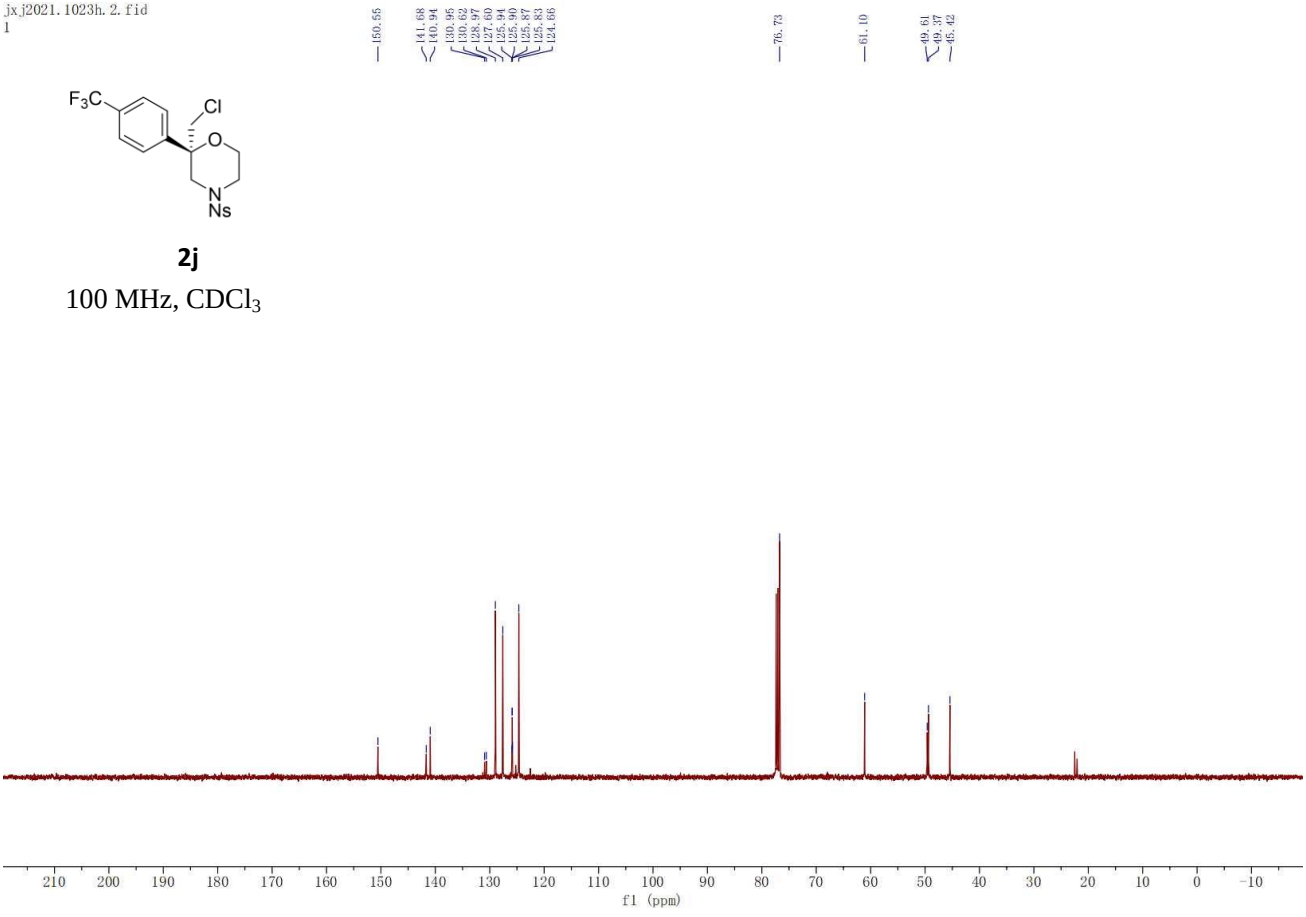
2i

100 MHz, $CDCl_3$



2j

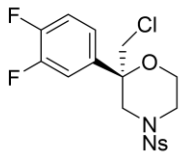
400 MHz, $CDCl_3$



2j

100 MHz, $CDCl_3$

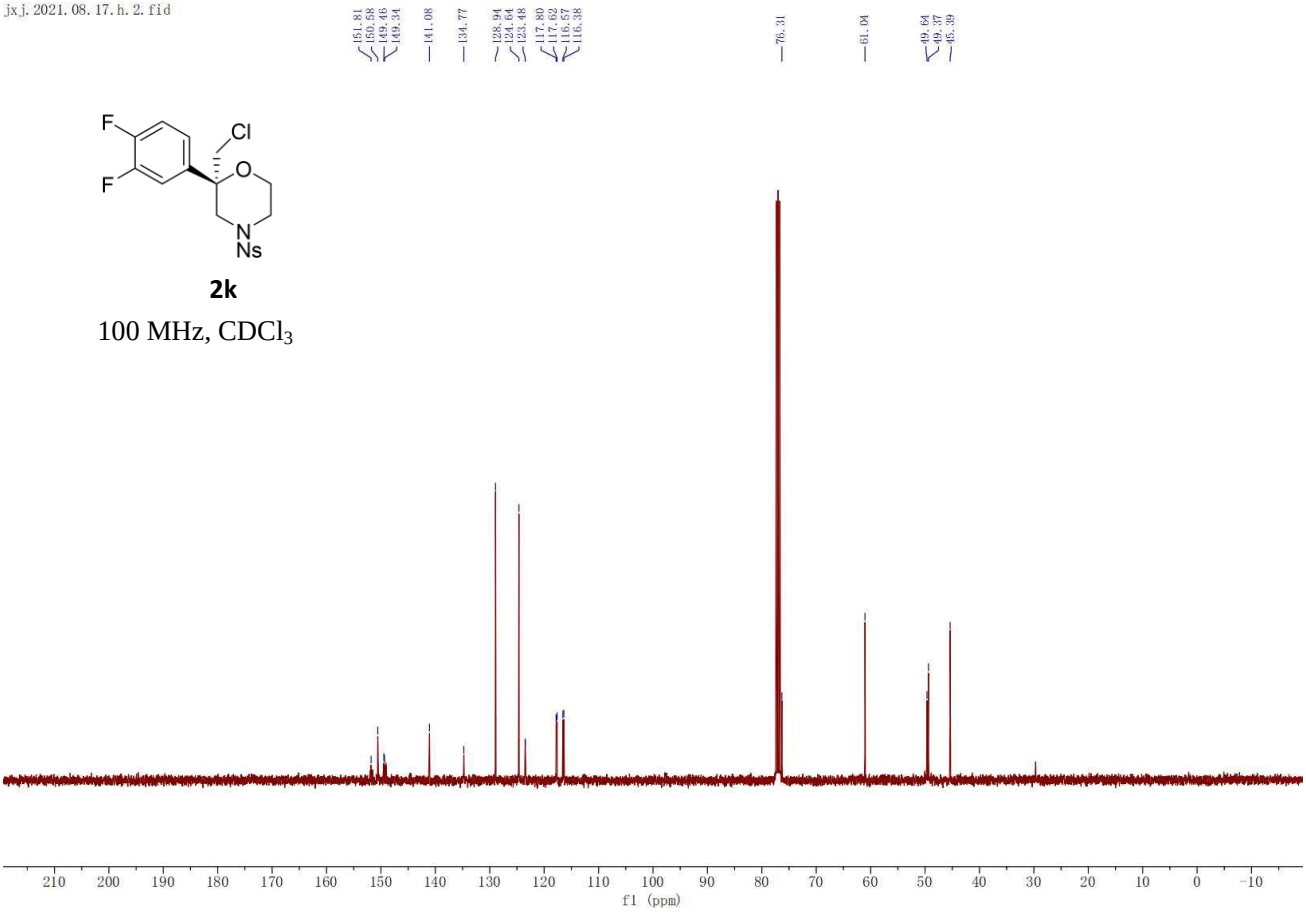
jxj. 2021. 08. 17. h. 1. fid



2k

400 MHz, $CDCl_3$

jxj. 2021. 08. 17. h. 2. fid



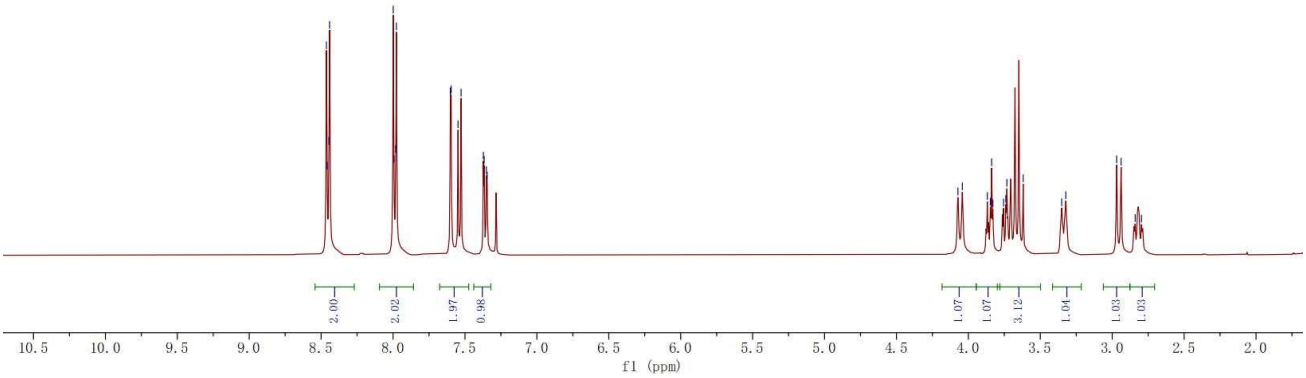
2k

100 MHz, $CDCl_3$

jxj2021.0625a.1.fid

2l

400 MHz, $CDCl_3$



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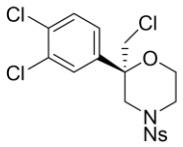
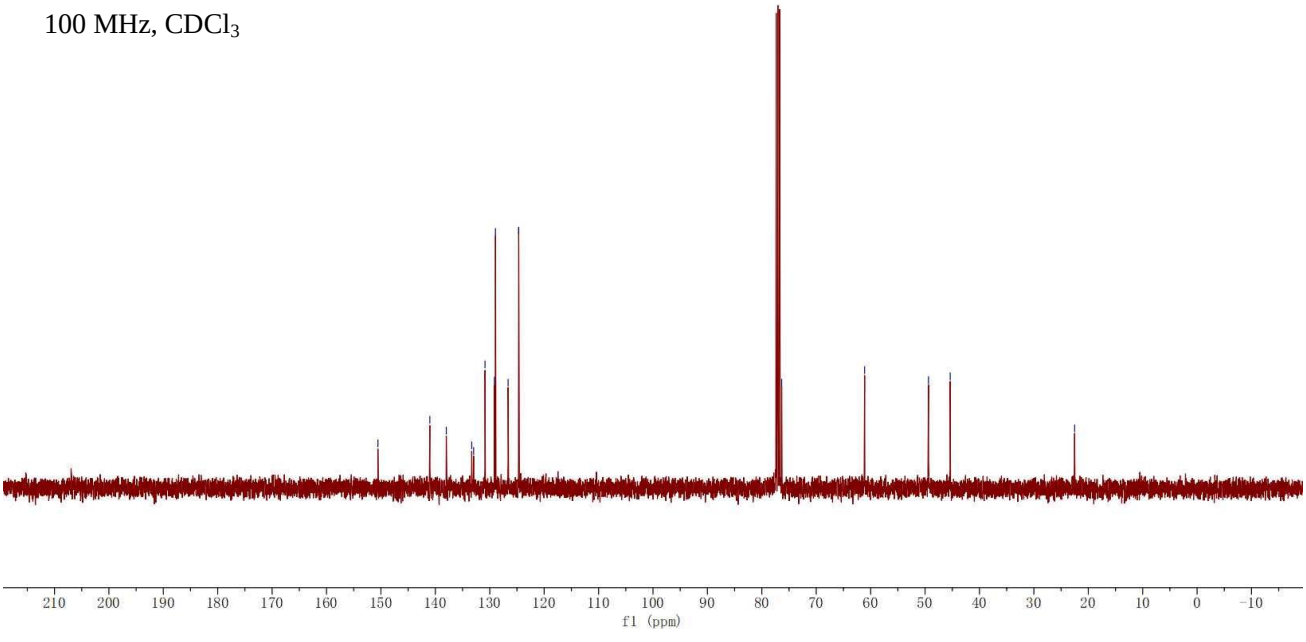
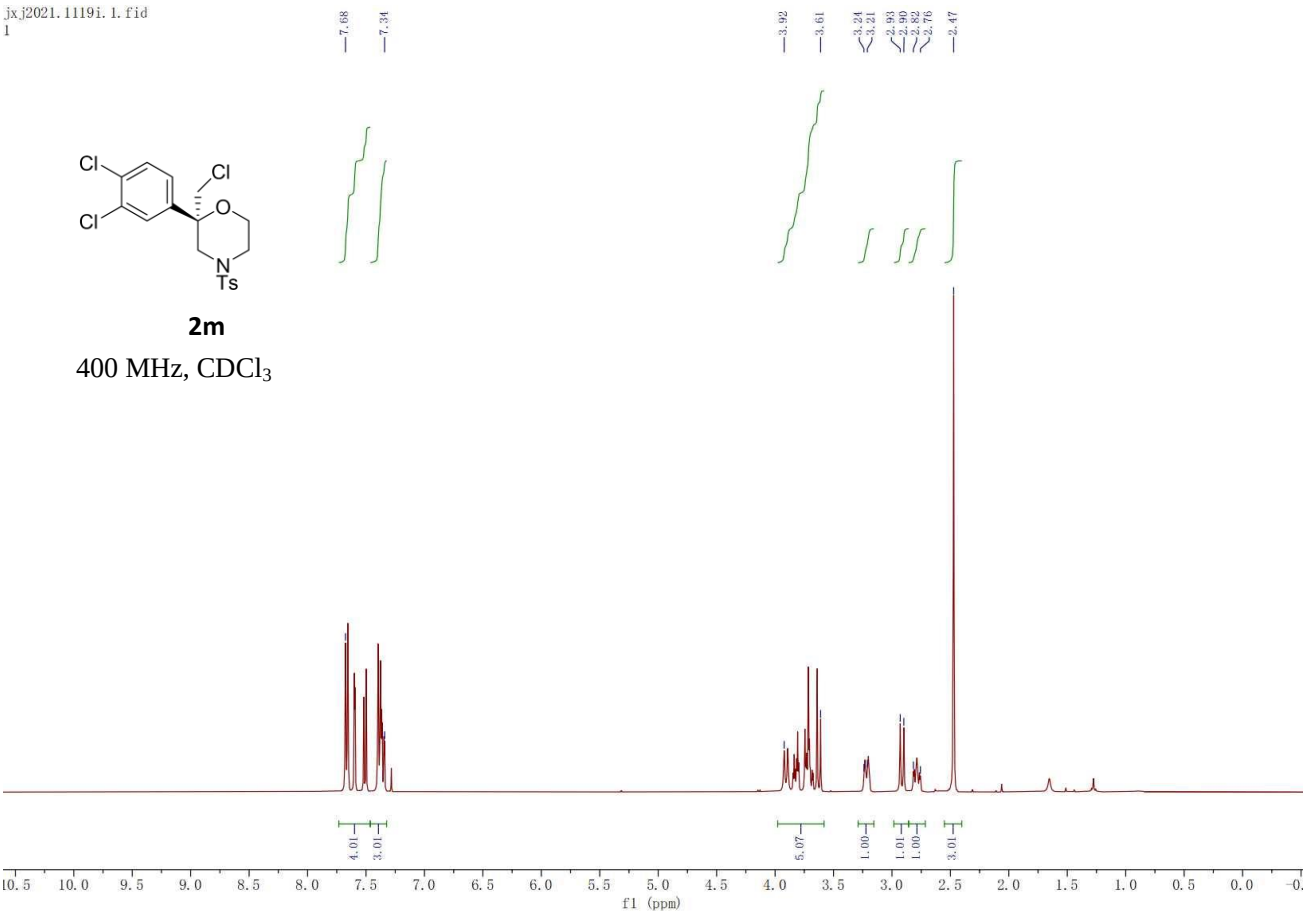


2l

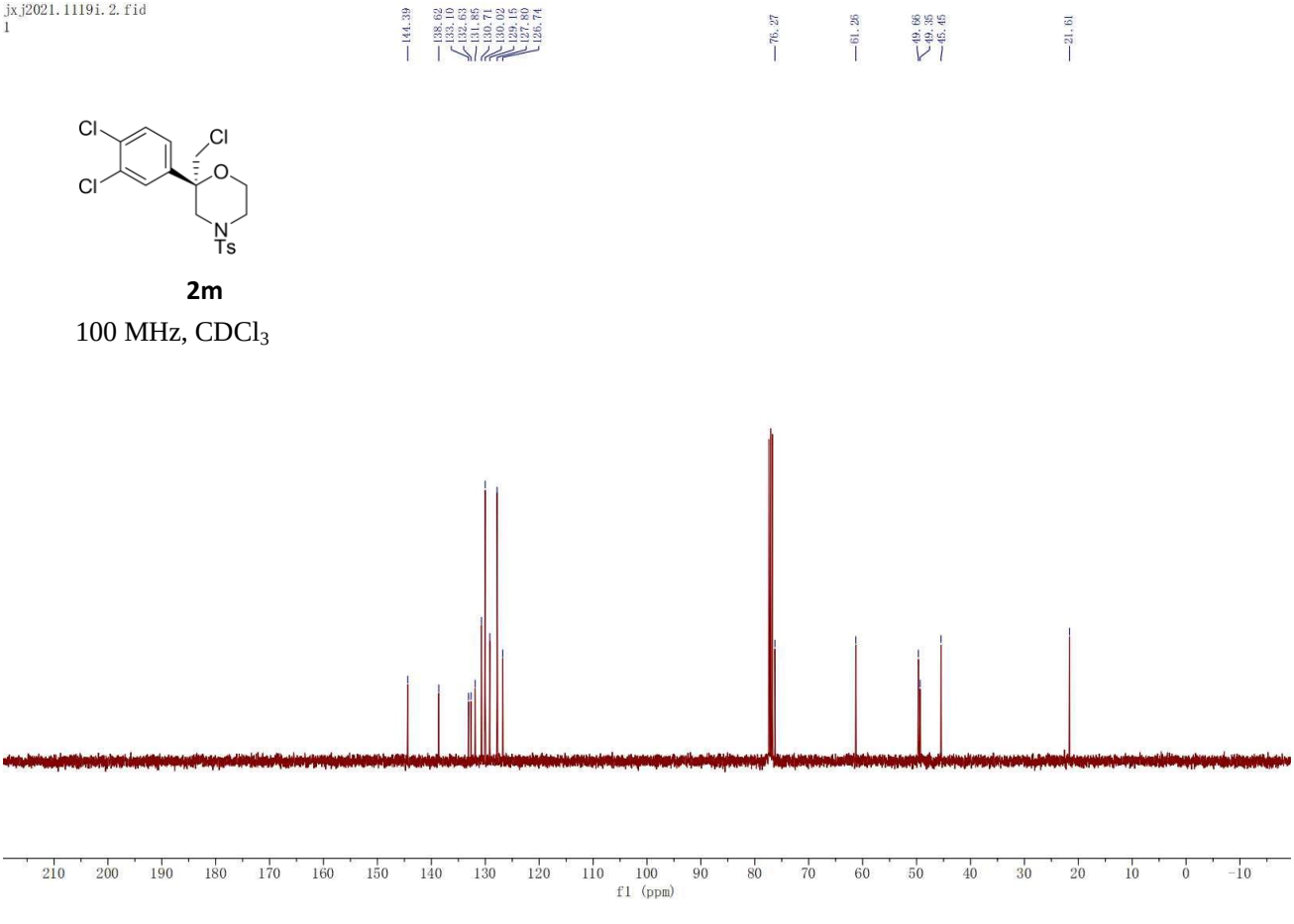
100 MHz, $CDCl_3$





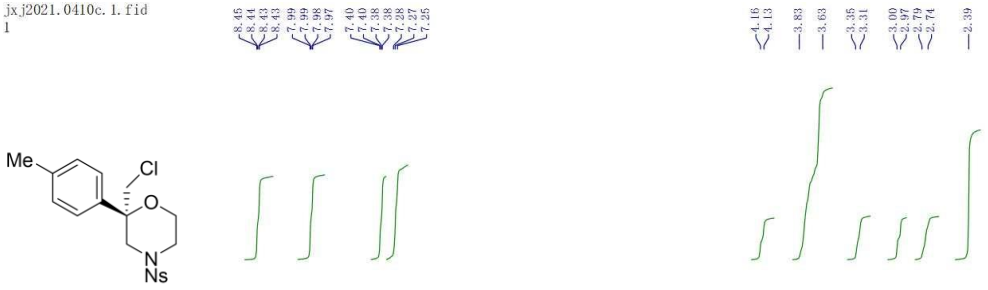
2m

400 MHz, $CDCl_3$



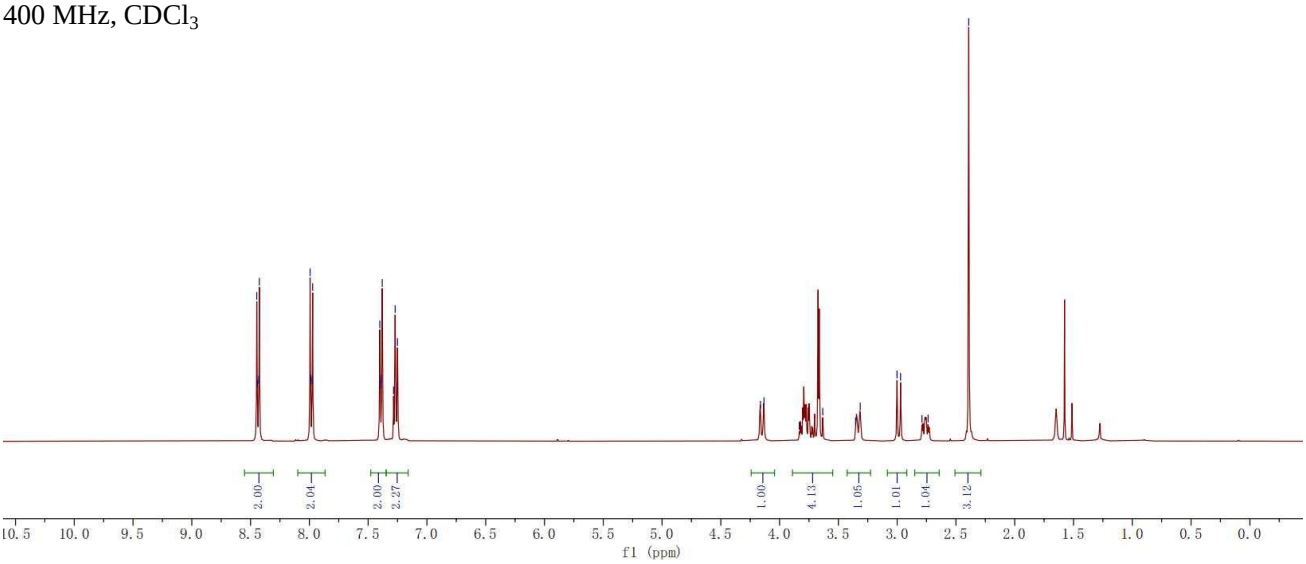
2m

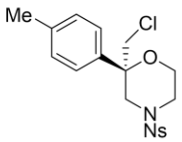
100 MHz, $CDCl_3$



2n

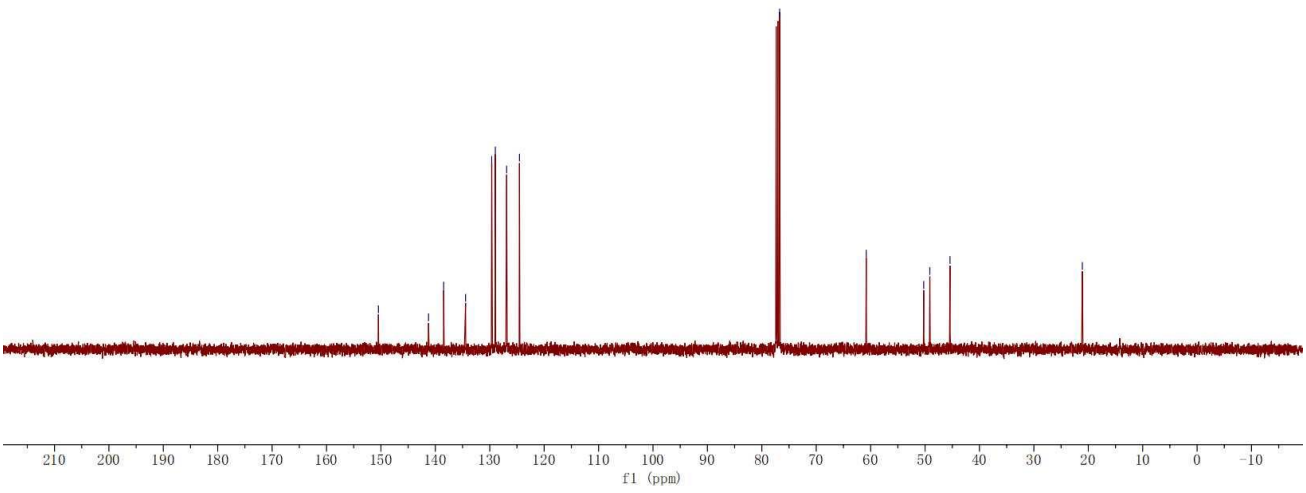
400 MHz, $CDCl_3$

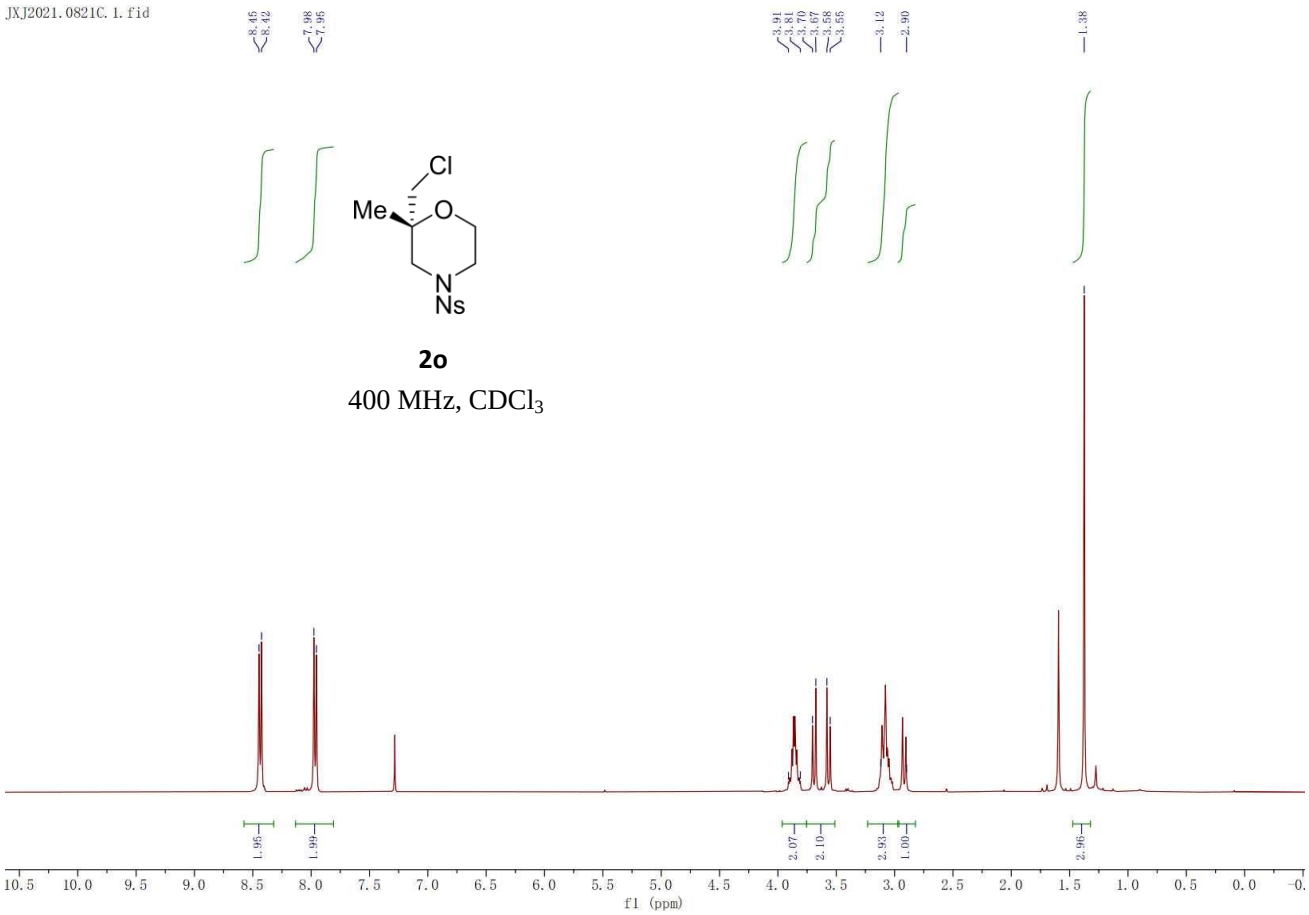




2n

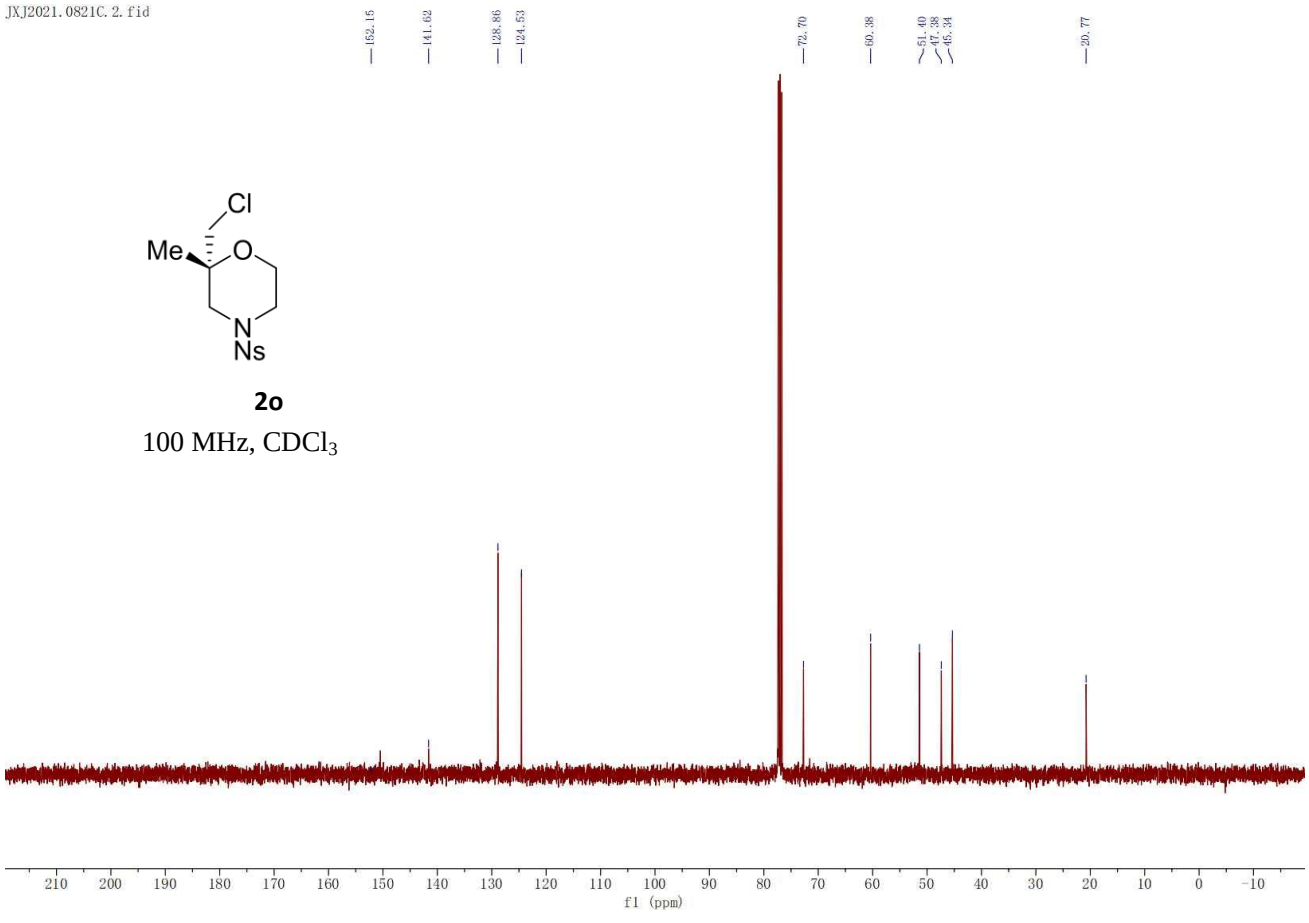
100 MHz, $CDCl_3$





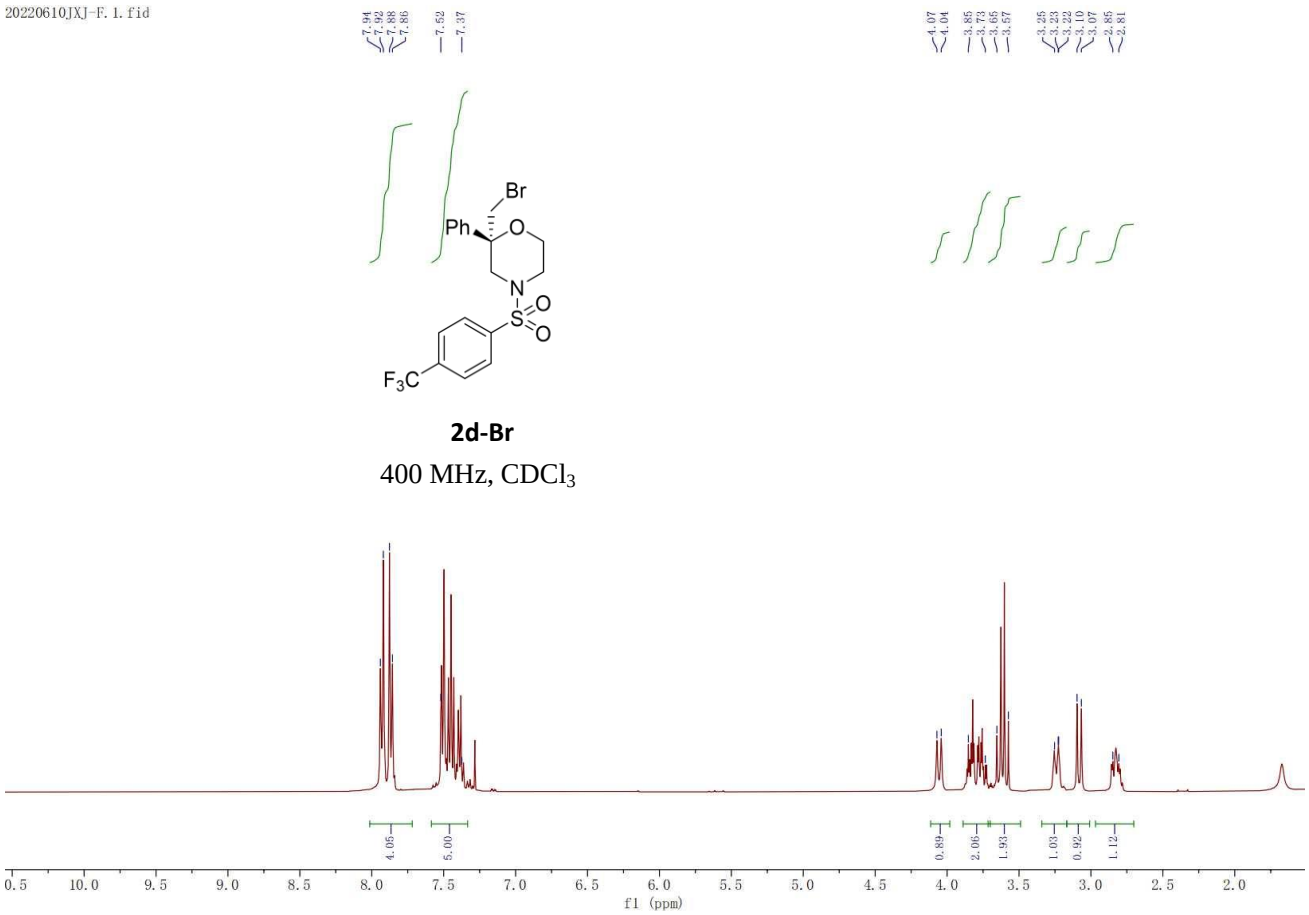
2o

400 MHz, $CDCl_3$



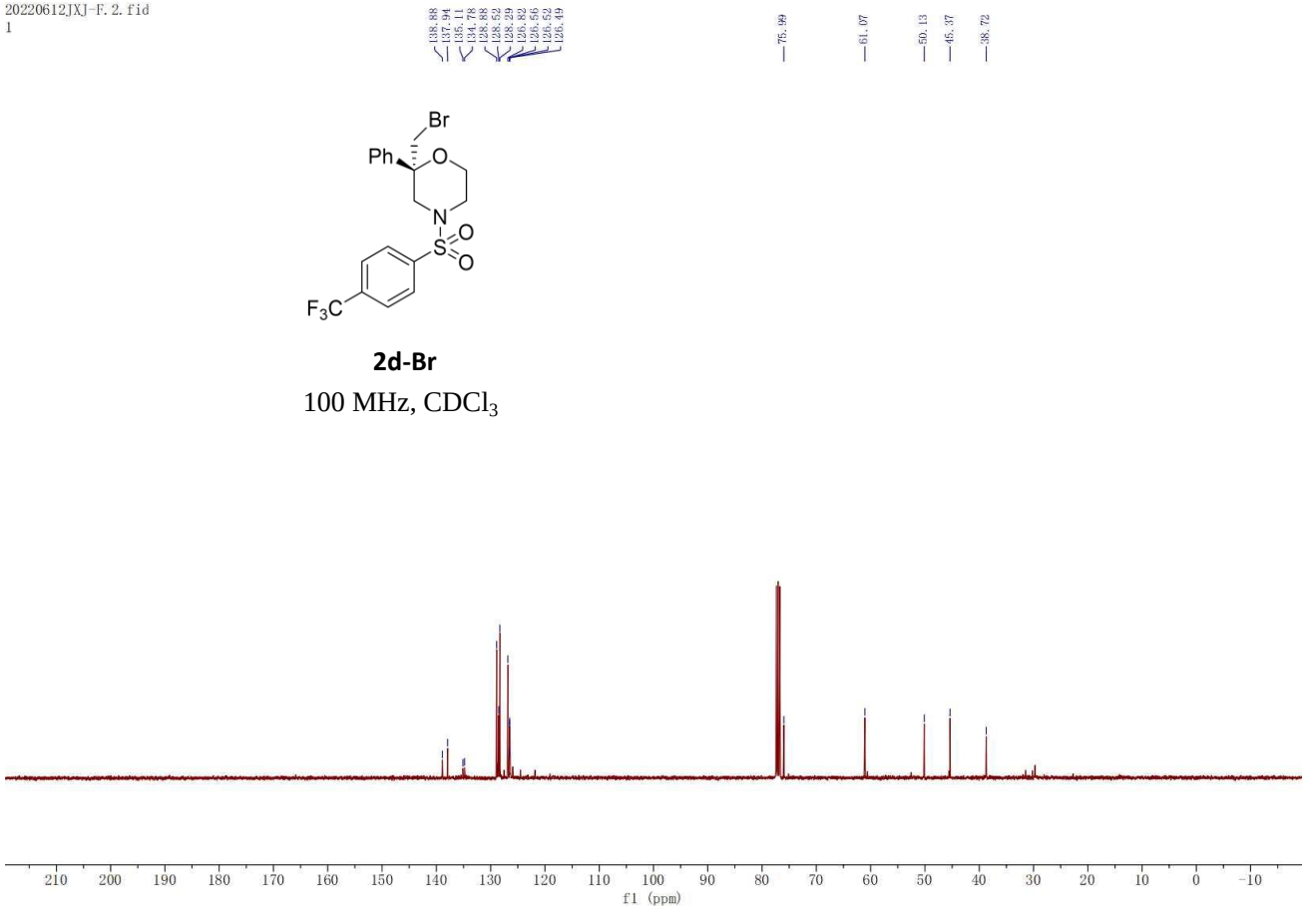
2o

100 MHz, $CDCl_3$



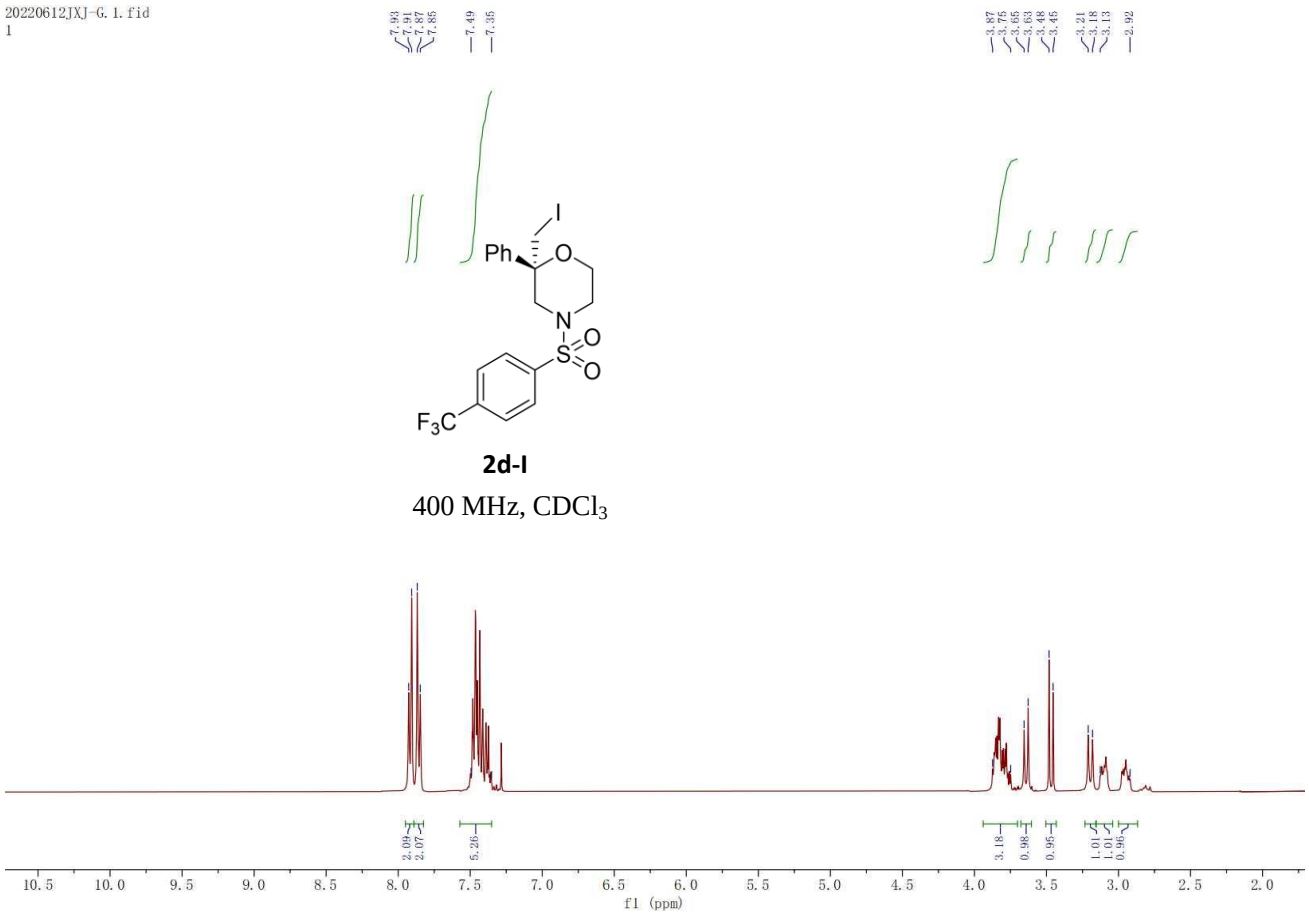
2d-Br

400 MHz, $CDCl_3$



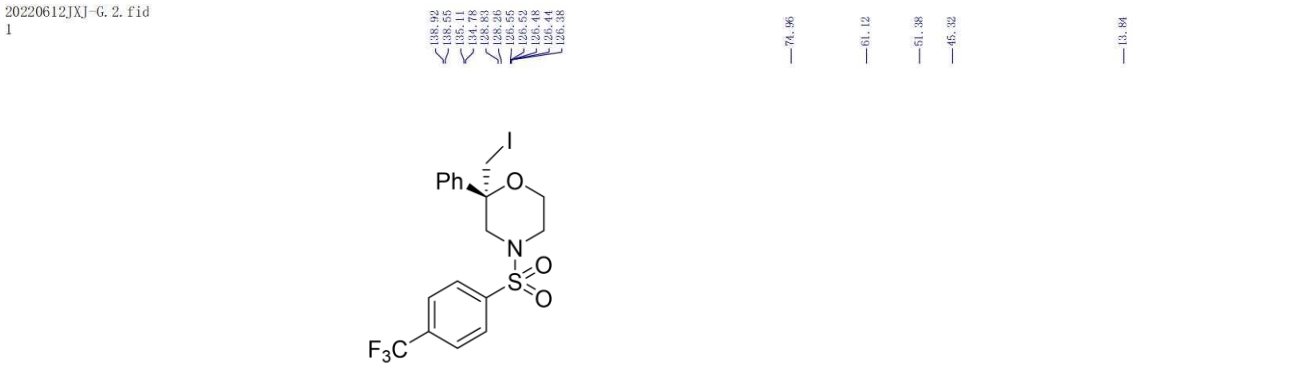
2d-Br

100 MHz, $CDCl_3$



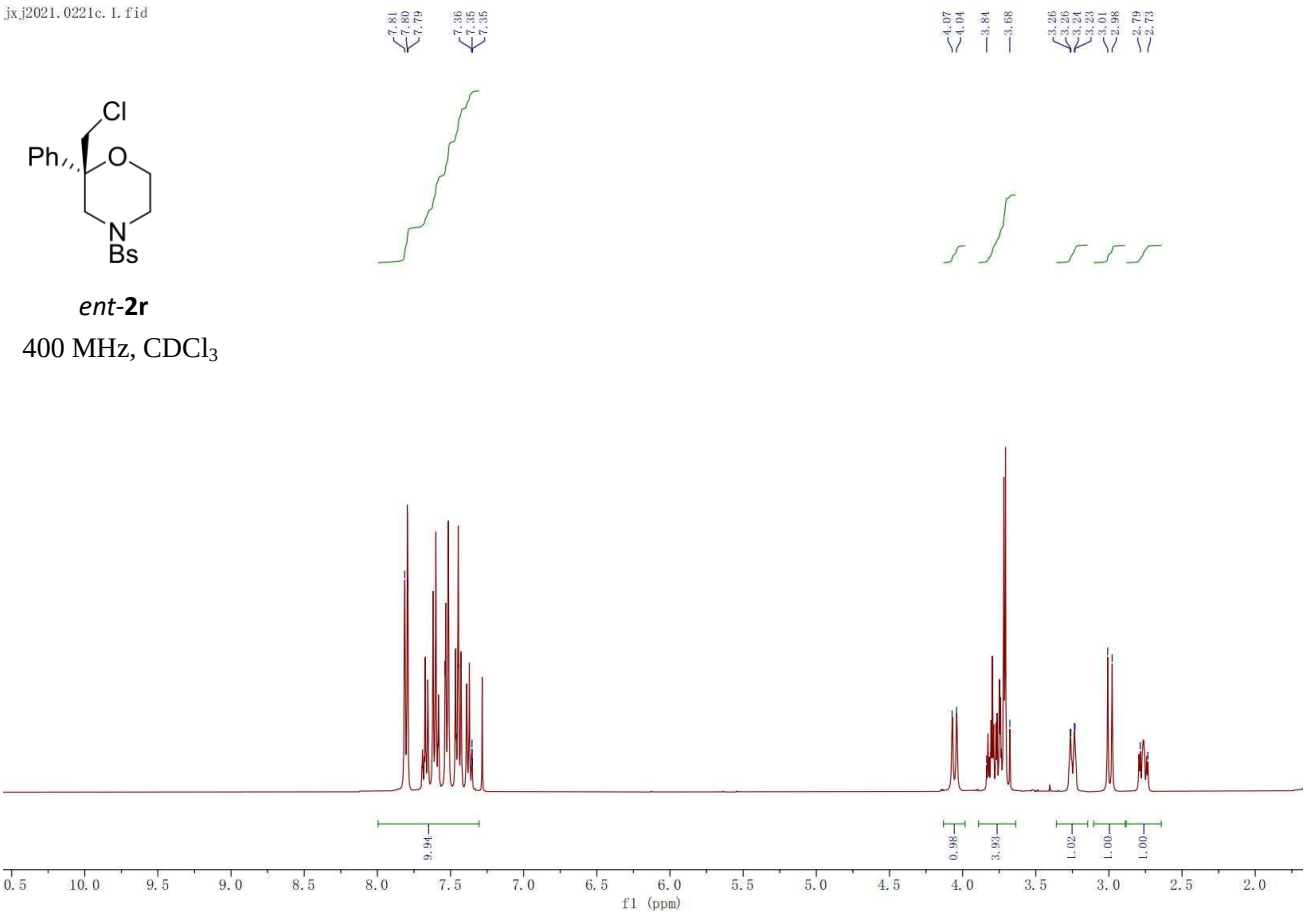
2d-I

400 MHz, $CDCl_3$



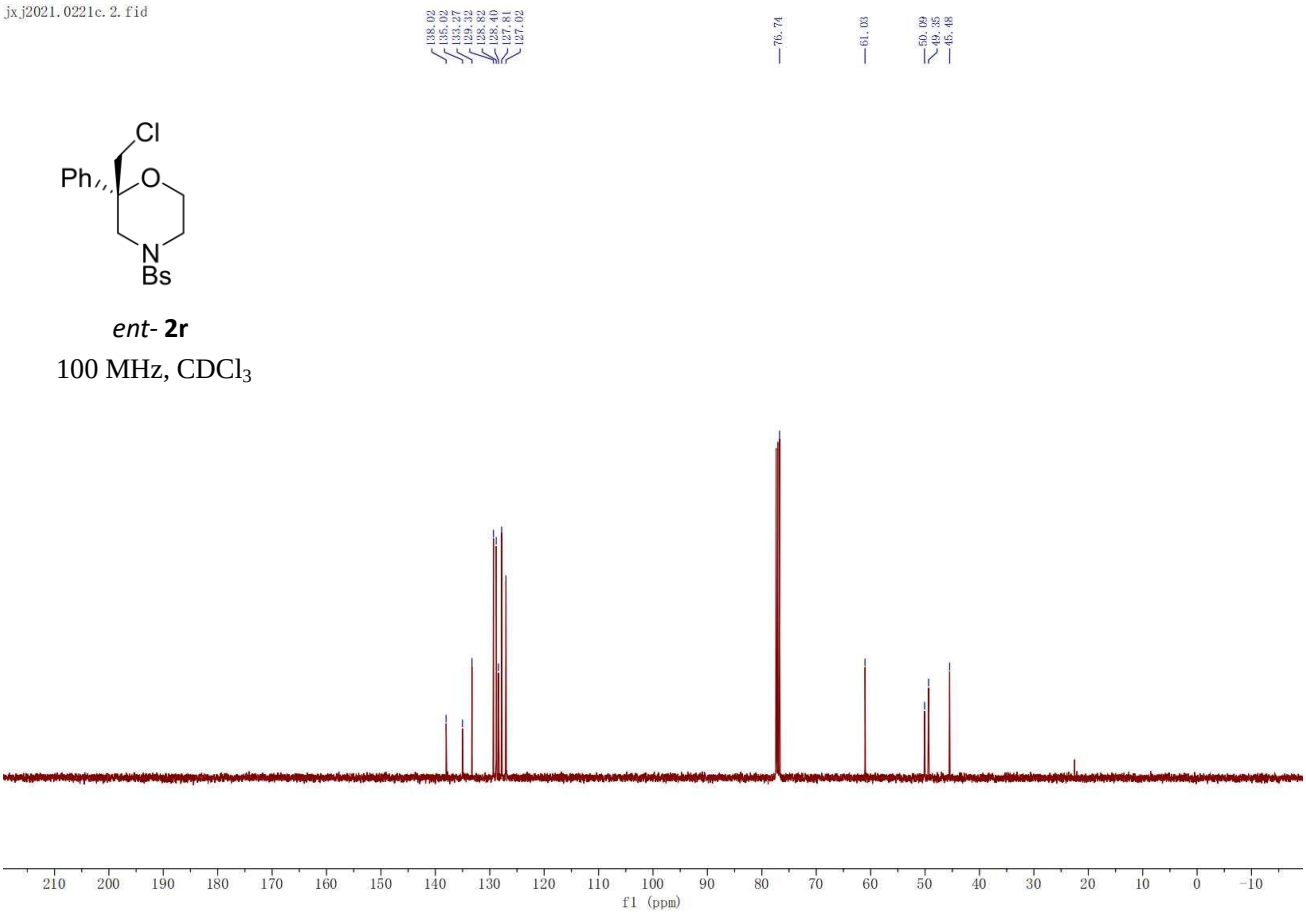
2d-I

100 MHz, $CDCl_3$



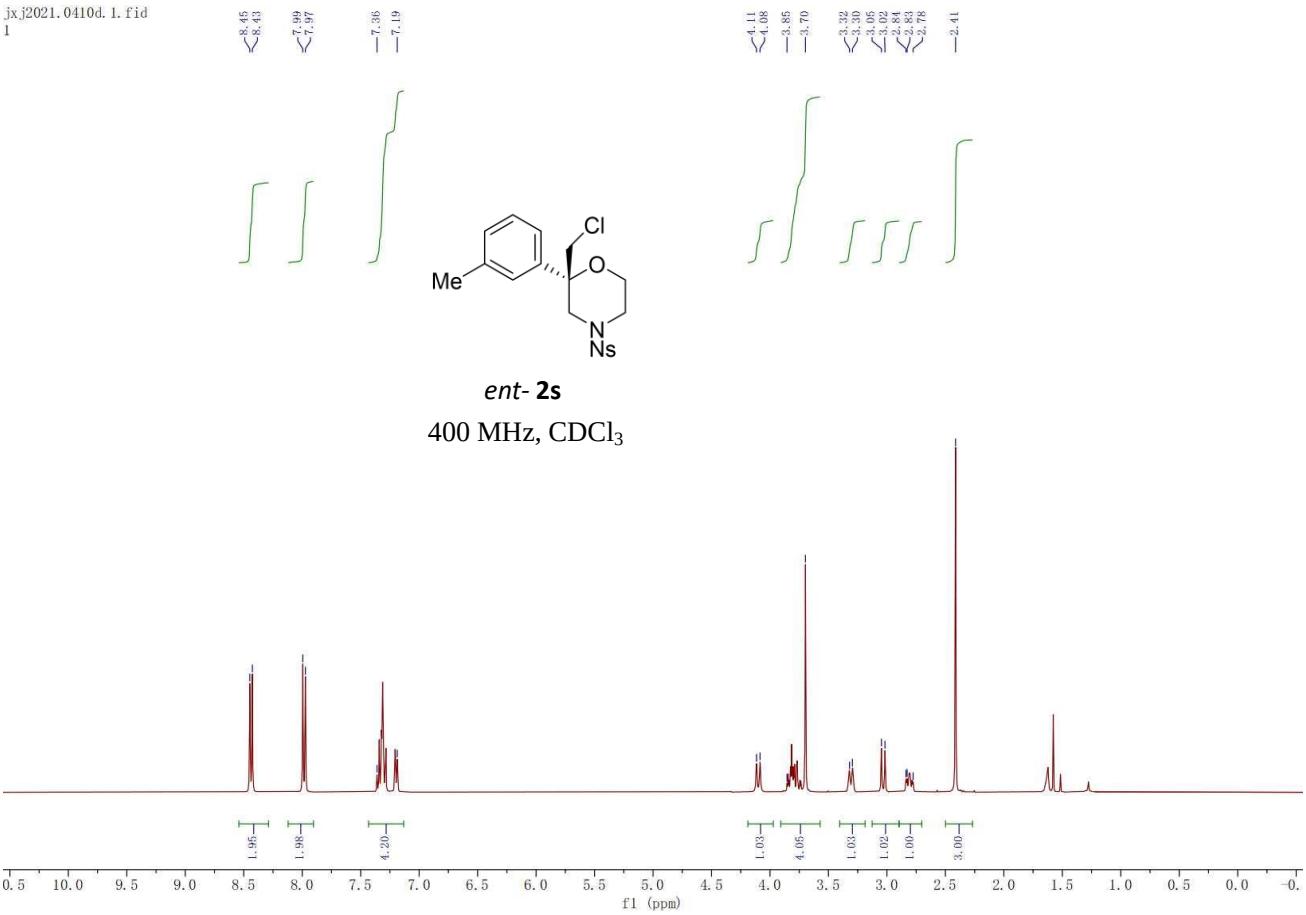
ent-**2r**

400 MHz, $CDCl_3$



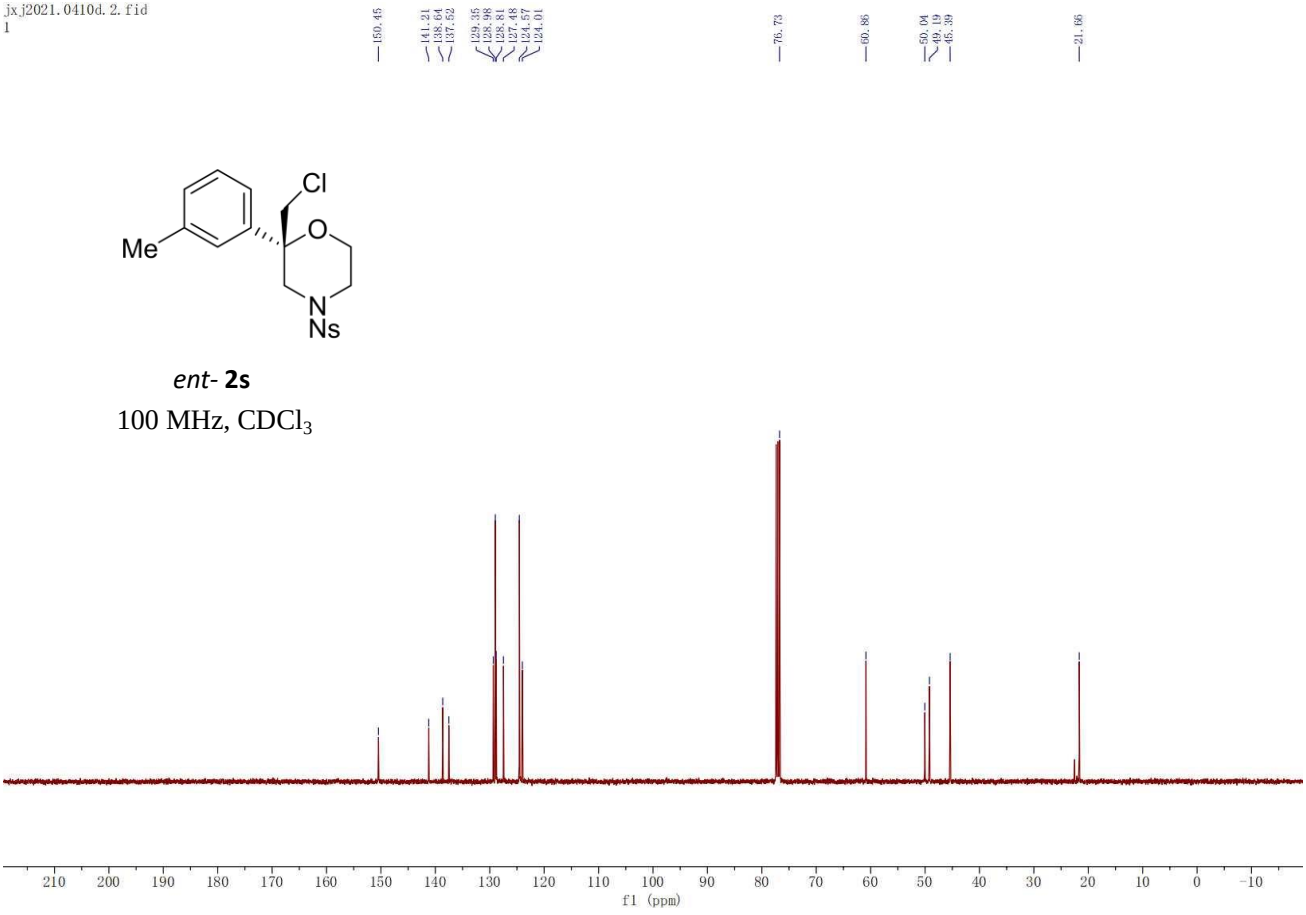
ent- **2r**

100 MHz, $CDCl_3$



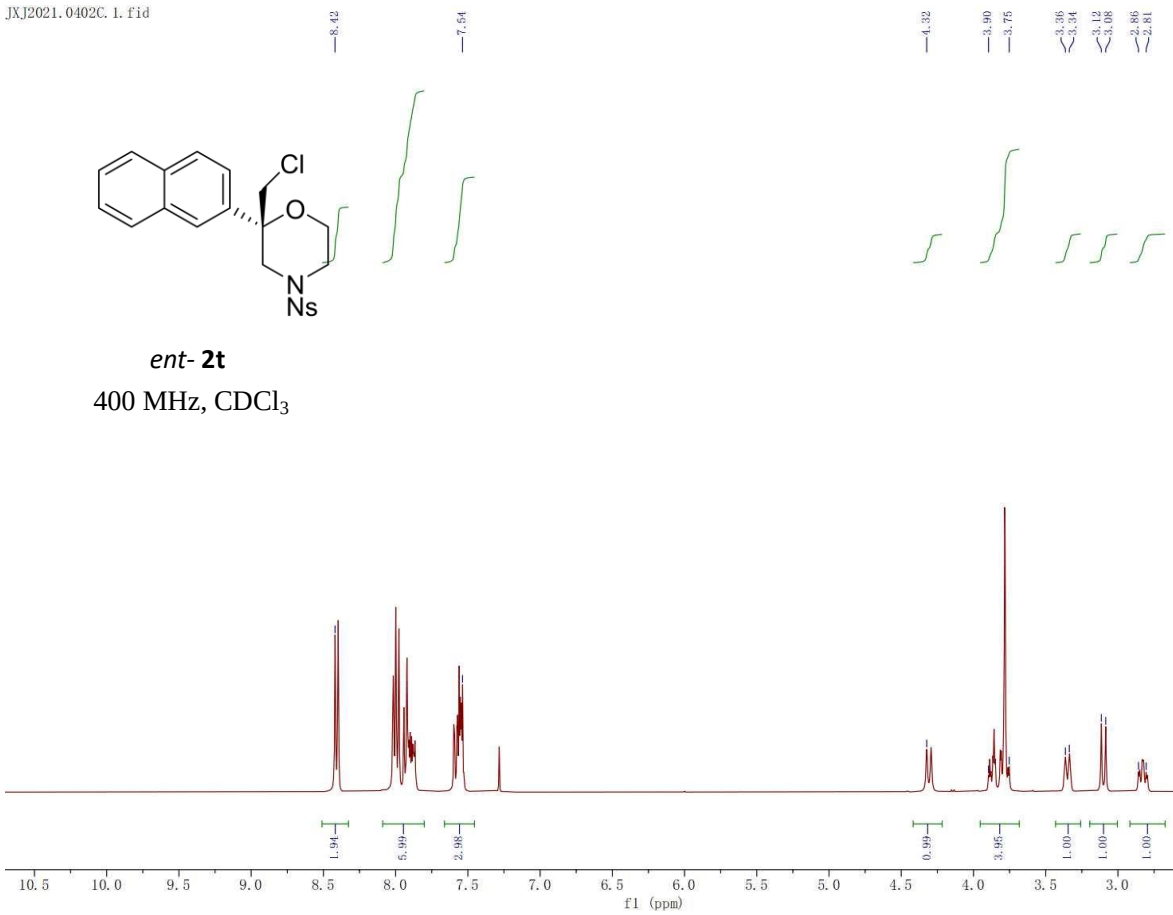
ent- **2s**

400 MHz, $CDCl_3$



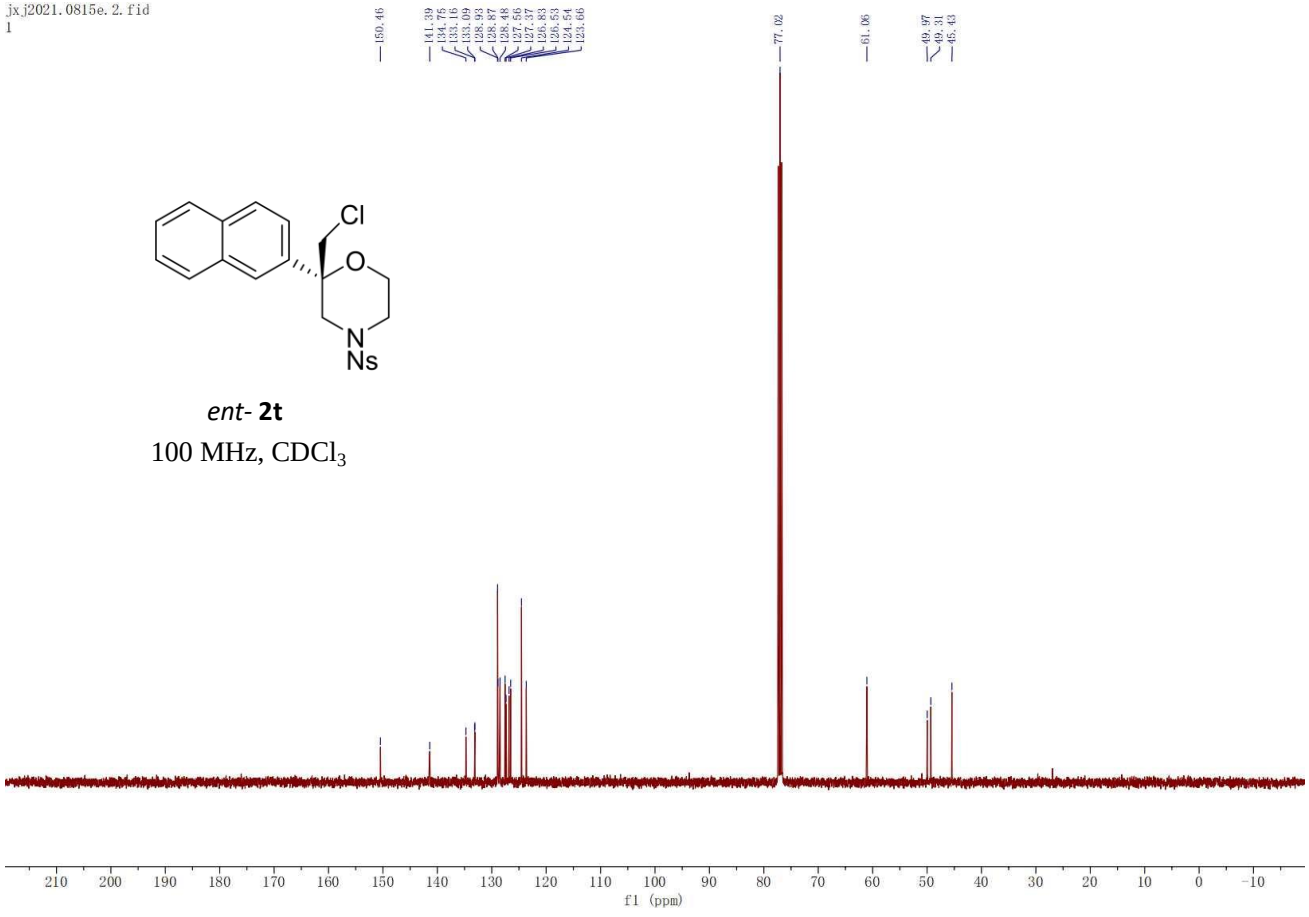
ent- **2s**

100 MHz, $CDCl_3$



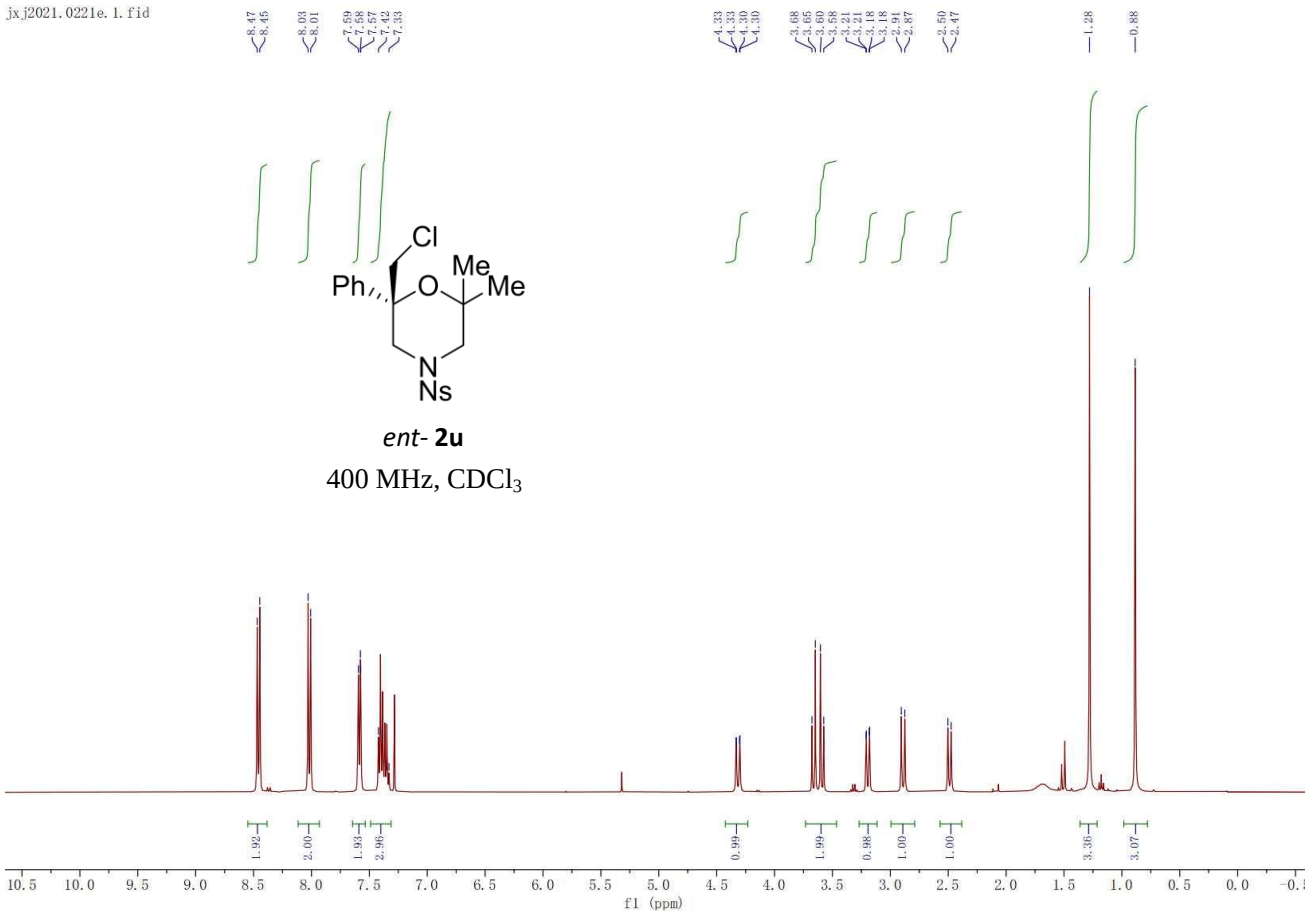
ent- **2t**

400 MHz, $CDCl_3$



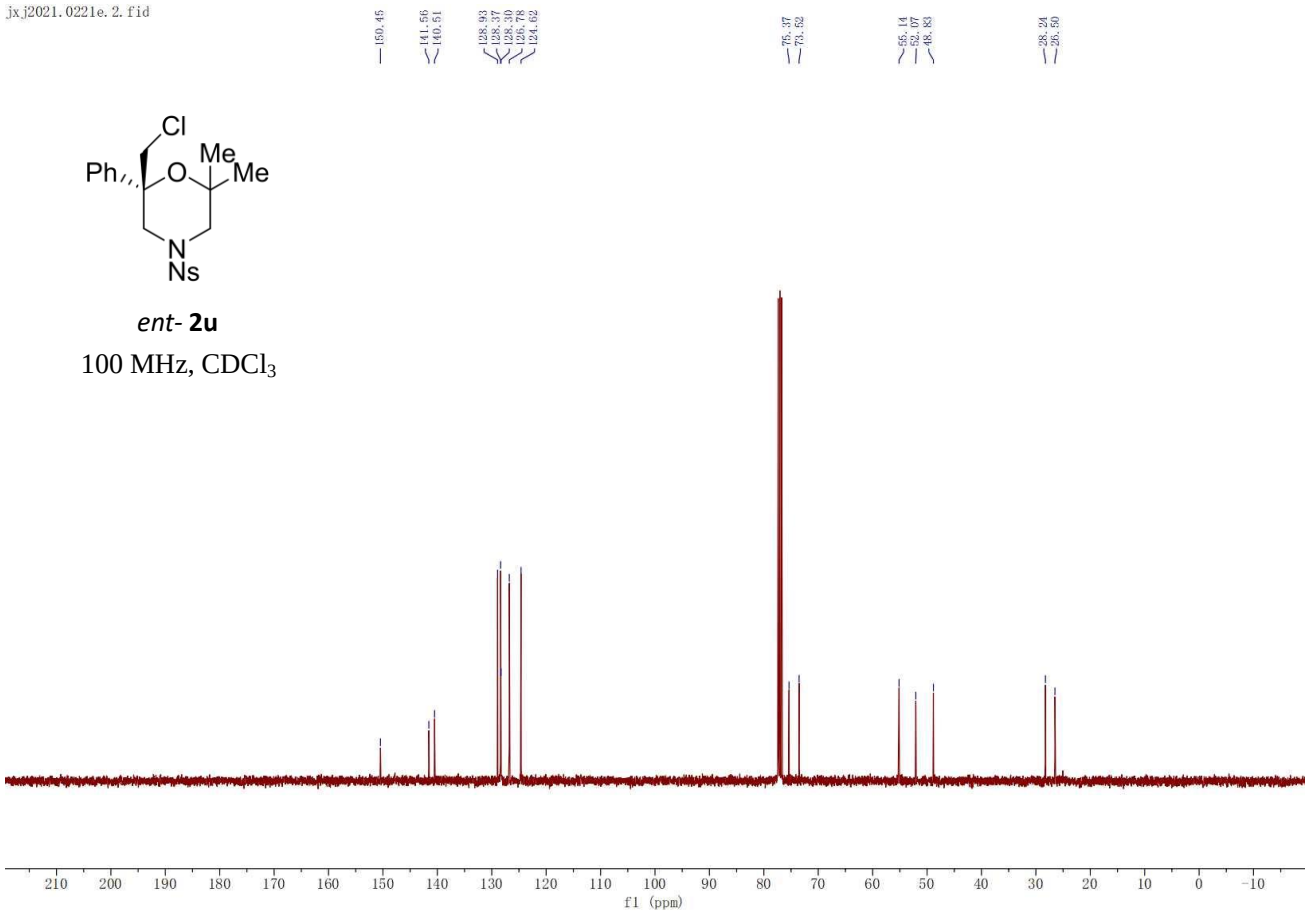
ent- **2t**

100 MHz, $CDCl_3$



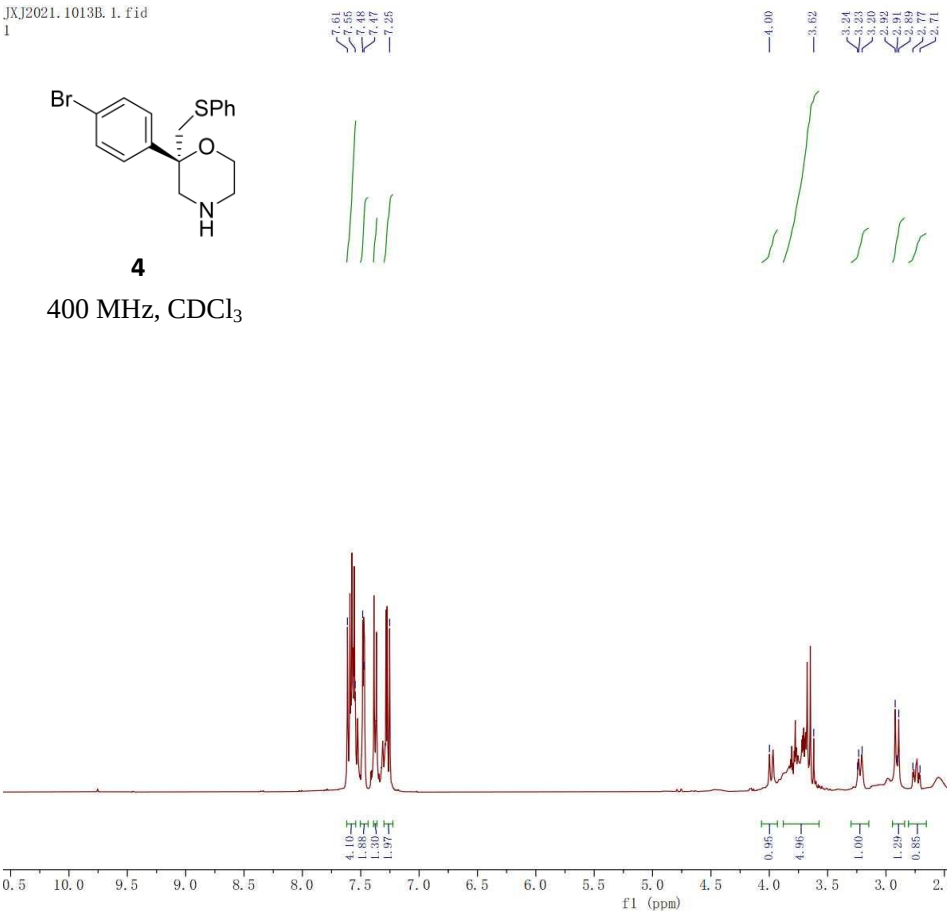
ent- **2u**

400 MHz, $CDCl_3$



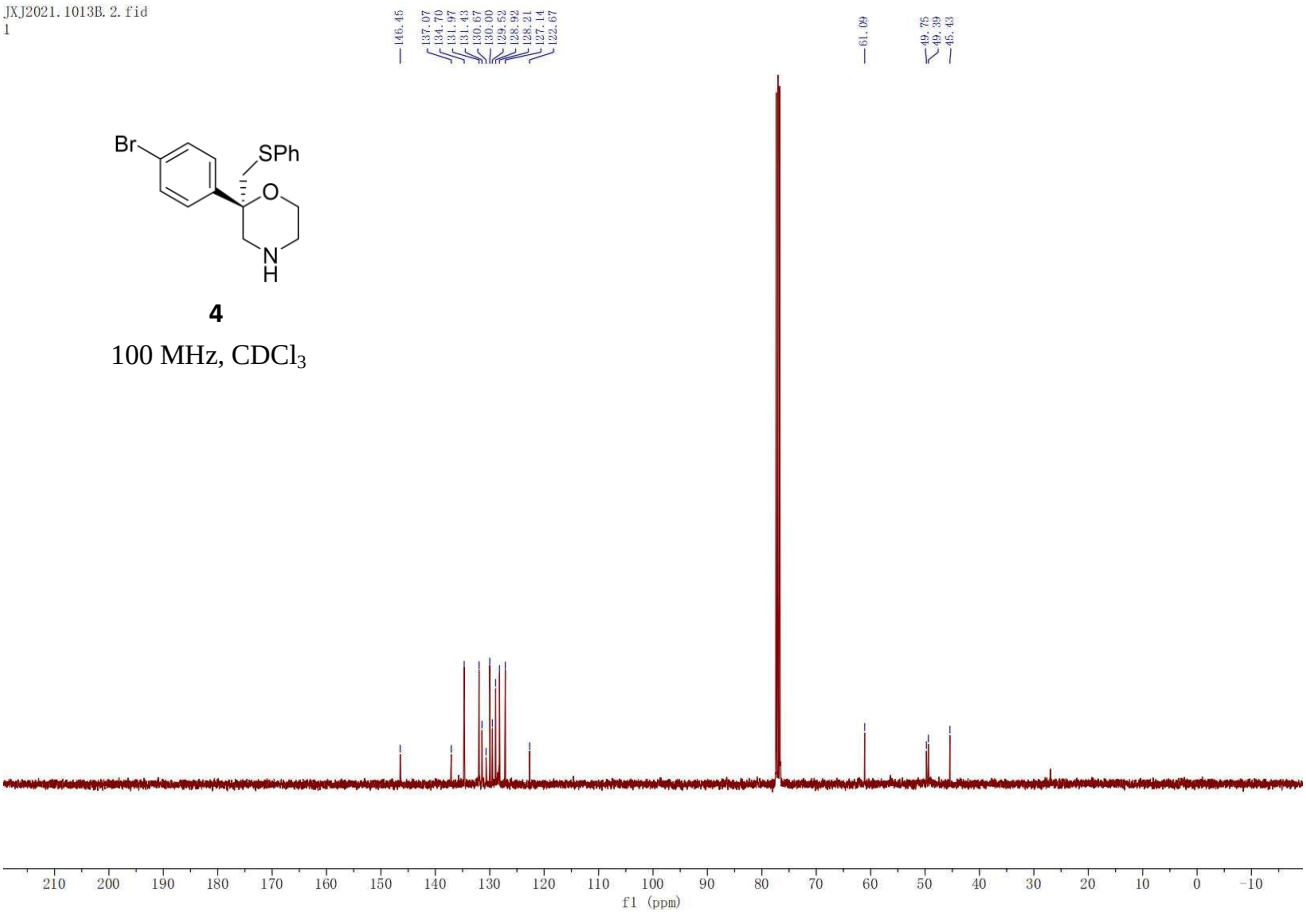
ent- **2u**

100 MHz, $CDCl_3$



4

400 MHz, $CDCl_3$



4

100 MHz, $CDCl_3$