Supporting Information

Intramolecular *N*-Me and *N*-H Aminoetherification for the Synthesis of *N*-Unprotected 3-Amino-*O*-Heterocycles

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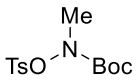
Contents

1 General Procedures

All reactions were carried out under a nitrogen atmosphere in oven-dried glassware unless otherwise noted. When needed, nonaqueous reagents were transferred under argon *via* syringe or cannula and dried prior to use. Dry solvents were obtained by passing deoxygenated solvents through activated alumina columns (MBraun SPS-800 series Solvent Purification System). The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or CD_3OD on a Bruker AV II-400 MHz spectrometer (^{1}H NMR at 400 MHz, ^{13}C NMR at 100 MHz) or Bruker Avance DRX-600 spectrometer (^{1}H NMR at 600 MHz, ^{13}C NMR at 151 MHz). The chemical shifts are reported in ppm relative to residual $CHCl_3$ (δ 7.26) or CH_3OH (3.31 ppm) for ^{1}H NMR and $CDCl_3$ (δ 77.00) CD_3OD (49.00) for ^{13}C NMR. MS experiments were performed on an Agilent 5973N instrument for EI-MS and a Waters Micromass GCT Premier instrument for High-resolution mass. Unless otherwise noted, all reagent-grade chemicals and other solvents were obtained from commercial suppliers and were used as received. Diastereomeric ratios (dr) were determined by ^{1}H NMR analysis of crude reaction mixtures. Melting points (MP) were determined in open capillaries using an Optimelt (Stanford Research Systems) melting point system and are uncorrected. Reaction mixtures were heated using aluminum heating blocks maintained at specified temperatures on magnetic stirrer hotplates. Starting materials **1a–q** are known compounds and were identified by comparison of their spectral data with those reported in the literature.

2 Synthesis of Starting Materials

2.1 *N*-Boc-*N*-methyl-*O*-tosyl hydroxylamine (S1)



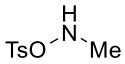
Potassium carbonate (14.5 g, 0.1 mol) was added to an ice cold solution of *N*-methyl hydroxylamine hydrochloride (16.7 g, 0.2 mol) in THF/H_2O (1:1, 80 ml). A solution of di-*tert*-butyl dicarbonate (48.0 g, 0.2 mol) in THF (60 ml) was added dropwise and stirring was continued for 2 hours at 0 °C and then 3 hours at room temperature. The solution was reduced *in vacuo* and the residue dissolved in dichloromethane (100 ml), washed with water (3 × 40 ml), brine (50 ml) and dried with anhydrous magnesium sulfate. The solvent was removed to yield a pale orange oil. The oil was dissolved in dichloromethane (250 ml) were added triethylamine (30.6 ml, 0.22 mol) and *p*-toluenesulfonyl chloride (41.94 g, 0.22 mol). The reaction mixture was allowed to warm to ambient temperature and stirring was continued for 18 hours after which time the organic phase was washed with 2.0 M aq. hydrochloric acid (2 × 50 ml). The dichloromethane was further washed with brine (50 ml) and dried with anhydrous sodium sulphate. The solvent was removed under reduced pressure to yield the crude product which was recrystallized from petroleum ether to give the title compound as a colourless solid (47.5 g, 78.8%).

Spectral data matched those reported previously, as well as the commercial material.[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.86 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 3.24 (s, 3H), 2.45 (s, 3H), 1.21 (s, 9H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.0, 145.7, 131.1, 129.7, 129.5, 83.3, 40.1, 27.5, 21.7.

2.2 *N*-Methyl-*O*-tosyl hydroxylamine (2)



To an ice-cold solution of *N*-Boc-*N*-methyl-*O*-tosyl hydroxylamine (**S1**) (3.0 g, 10 mmol) in dichloromethane (15 ml), was added excess trifluoroacetic acid (14.8 ml, 200 mmol). The reaction was allowed to stir for 3 hours at 0 °C before pouring onto ice water (50 ml) and extracting with dichloromethane (3 × 30 ml). The combined organic layers were dried over anhydrous sodium sulfate and concentrated to yield a clear oil which solidified upon cooling (1.9 g, 95%).

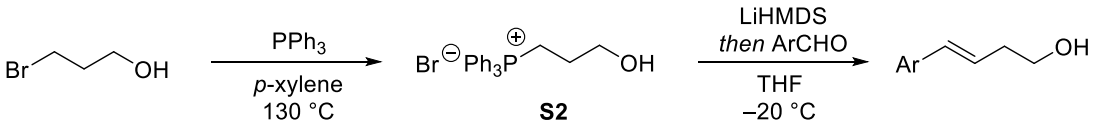
Spectral data matched those reported previously.[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 6.17 (br s, 1H), 2.74 (s, 3H), 2.45 (s, 3H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.9, 132.2, 129.5, 128.9, 40.1, 21.6.

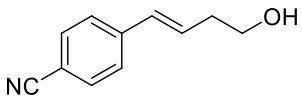
[1]John, O. R. S.; Killeen, N. M.; Knowles, D. A.; Yau, S. C.; Bagley, M. C.; Tomkinson, N. C. O. Direct α-Oxytosylation of Carbonyl Compounds: One-Pot Synthesis of Heterocycles. *Org. Lett.* **2007**, *9*, 4009−4012.

2.3 General Procedure for Synthesis of Styryl Alcohols



Under argon atmosphere, triphenylphosphine (9.5 g, 36.2 mmol), 3-bromopropan-1-ol (5.0 g, 36 mmol) and *p*-xylene (30 mL) were added in a round bottom flask equipped with a mechanical stirrer. The mixture was heated to 130 °C and stirred for 6 h. After that, the reaction was then cooled to room temperature and diethyl ether (50 mL) was added. The solids were collected by filtration and dried under vacuum to afford 3-(triphenylphosphonium) propan-1-ol bromide (**S2**) as a white solid which was used in the next step without further purification. Lithium *bis*(trimethylsilyl)amide (LiHMDS, 10.5 mmol, 1.0 M in THF) was added dropwise at –20 °C to a suspension of (3-propan-1-ol)triphenylphosphonium bromide (4.5 mmol) in 10 mL of tetrahydrofuran. The solution was stirred at –20 °C for 1 hour and aldehyde (3.75 mmol) was added dropwise. After that, the mixture was stirred at the same temperature for 2 hours. The mixture was warmed to room temperature and stirred for another 12 hours, then saturated aqueous NH_4Cl solution (20 mL) was added. The organic layer was dried over $MgSO_4$ and then concentrated under reduced pressure. The residue was purified by flash column chromatography (EtOAc/Petroleum ether = 1/5; v/v).

2.3.1 (*E*)-4-(4-hydroxybut-1-en-1-yl)benzonitrile (1i)



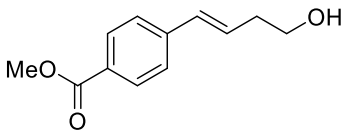
White solid; (3.0 g, 48%)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (d, 2H, *J* = 8.0 Hz), 7.42 (d, 2H, *J* = 8.4 Hz), 6.50 (d, 1H, *J* = 16.0 Hz), 6.41–6.34 (m, 1H), 3.79 (t, 2H, *J* = 6.4 Hz), 2.54–2.49 (m, 2H), 1.75 (br s, 1H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.8, 132.3, 131.0, 131.0, 126.5, 119.0, 110.3, 61.7, 36.3.

HRMS (ESI) m/z: $[M]^+$ Calcd for $C_{11}H_{11}NO$ 173.0841; Found 173.0840.

2.3.2 Methyl (*E*)-4-(4-hydroxybut-1-en-1-yl)benzoate (1j)



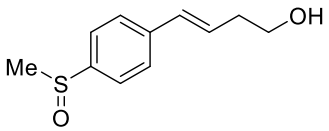
White solid; (3.8 g, 52% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, 2H, *J* = 8.4 Hz), 7.40 (d, 2H, *J* = 8.4 Hz), 6.52 (d, 1H, *J* = 16.0 Hz), 6.39–6.31 (m, 1H), 3.90 (s, 3H), 3.78 (t, 2H, *J* = 5.8 Hz), 2.54–2.48 (m, 2H), 1.67 (br s, 1H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.9, 141.7, 131.7, 129.9, 129.5, 128.6, 125.9, 61.8, 52.0, 36.4.

HRMS (ESI) m/z: $[M]^+$ Calcd for $C_{12}H_{14}O_3$ 206.0943; Found 206.0945.

2.3.3 (*E*)-4-(4-(methylsulfinyl)phenyl)but-3-en-1-ol (1l)



White solid; (4.3 g, 57% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59–7.51 (m, 2H), 7.48–7.43 (m, 2H), 6.50 (d, 1H, *J* = 16.0 Hz), 6.37–6.29 (m, 1H), 3.76 (t, 2H, *J* = 6.2 Hz), 2.52–2.47 (m, 2H), 2.14 (br s, 1H).

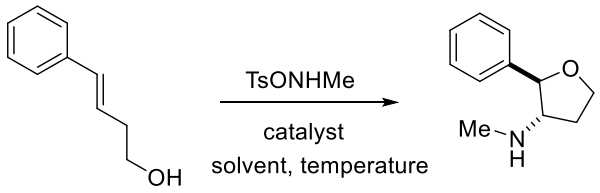
{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.7, 140.4, 131.1, 129.5, 126.8, 123.8, 61.7, 43.8, 36.4.

HRMS (ESI) m/z: $[M]^+$ Calcd for $C_{11}H_{14}O_2S$ 210.0715; Found 210.0716.

3 Aminoetherification

3.1 Optimization

Table S1. Optimization studies for intermolecular *N*-Me aminoetherification.[a]



1a **3a**

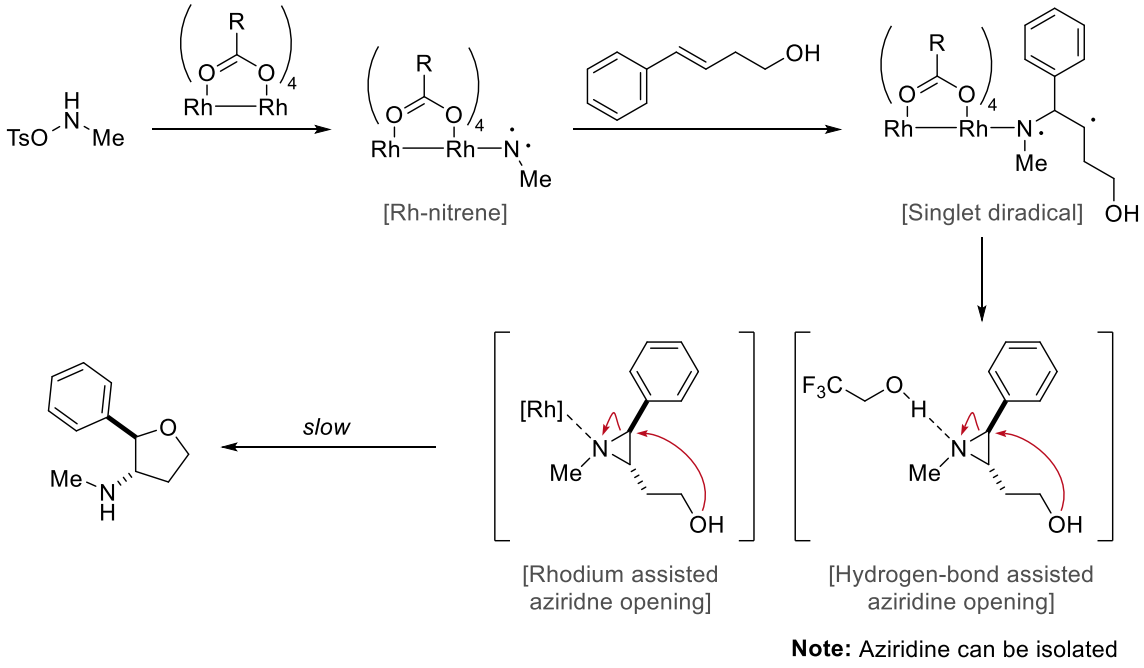
#	Catalyst (mol-%)	Solvent	Temperature/Time	Yield (%)
1	1% $Rh_2(esp)_2$	THF (0.2 M)	65 °C, 5 h	<10[b]
2	1% $Rh_2(esp)_2$	MeCN (0.2 M)	65 °C, 5 h	<10[b]
3	1% $Rh_2(esp)_2$	TFE (0.2 M)	65 °C, 5 h	73
4	1% $Rh_2(esp)_2$	TFE (0.2 M)	rt, 2 h, then 80 °C, 1 h	66
5	1% $Rh_2(esp)_2$	TFE (0.2 M)	rt, 2 h, then 50 °C, overnight	37
6	1% $Rh_2(esp)_2$	TFE (0.2 M)	rt, 2 h, then 50 °C, 5 h	70
7	1% $Rh_2(esp)_2$	TFE (0.1 M)	rt, 2 h, then 65 °C, 5 h	78
8	1% $Rh_2(esp)_2$	TFE (0.2 M)	rt, 2 h, then 65 °C, 5 h	84
9	1% $Rh_2(esp)_2$	TFE (0.5 M)	rt, 2 h, then 65 °C, 5 h	75
10	0.5% $Rh_2(esp)_2$	TFE (0.2 M)	rt, 2 h, then 65 °C, 5 h	81

[a] Yields of isolated product. [b] Yields determined by LC-MS

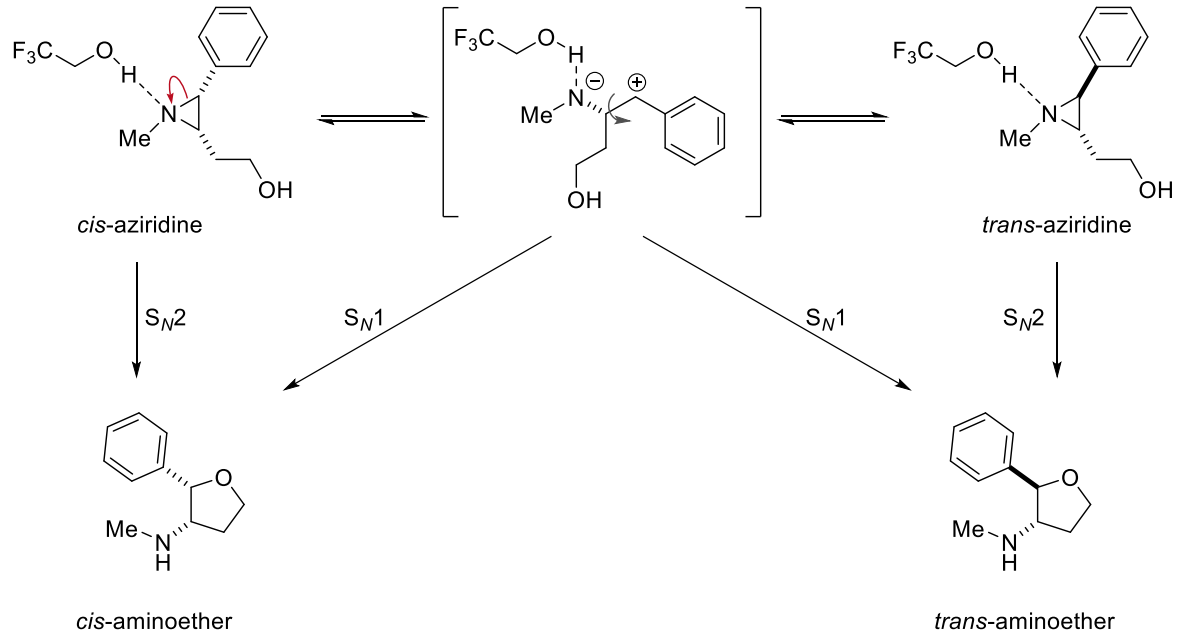
3.2 Proposed mechanisms

The aziridination mechanism has previously been established computationally.[2]

A Proposed aziridination-aziridine opening mechanism



B Proposed pathways for the *cis*-aziridine scrambling *via* a benzylic carbocation intermediate



Scheme S1: Mechanistic proposals for the cascade process and the stereochemical scrambling.

[2] Jat, J. L.; Paudyal, M. P.; Gao, H.; Xu, Q.-L.; Yousufuddin, M.; Devarajan, D.; Ess, D. H.; Kürti, L.; Falck, J. R. Direct Stereospecific Synthesis of Unprotected *N*-H and *N*-Me Aziridines from Olefins. *Science*, **2014**, *343*, 61–65.

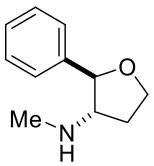
3.3 General Procedure

$Rh_2(esp)_2$ (Du Bois' catalyst, 1 mol%) was added to a vigorously stirring (1400 rpm), rt solution of alkene (1.0 equiv) and TsONHMe (1.5 equiv) in dry CF_3CH_2OH (0.1 M) in an 8 ml screw-cap vial under argon at rt, unless otherwise specified. The reaction was stirred at the specified temperature and monitored by TLC (DCM:MeOH = 10:100; UV; Ninhydrin stain). More catalyst and aminating agent were added, if required. After the alkene was consumed (about 2 h), the reaction was heated at 50 or 65 °C until LCMS show the reaction was completed, then the reaction mixture was diluted with EtOAc and washed with saturated aqueous Na_2CO_3 solution. The aqueous layer was extracted twice with EtOAc and the combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified on pre-packed SiO_2 columns using a CombiFlash automated flash chromatography unit (DCM:MeOH = 100:1 to 100:15).

Notes:

- Vigorous stirring is needed for a successful initiation of the reaction.
- If no product is seen after first 30 min, a second portion of $Rh_2(esp)_2$ has to be added to the vigorously stirred reaction mixture.
- A successful reaction turns opaque and dark brown.

3.4 (2*R**,3*S**)-*N*-methyl-2-phenyltetrahydrofuran-3-amine (3a)



Following the general procedure, (*E*)-4-phenylbut-3-en-1-ol (**1a**) (148.2 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 4 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (150.6 mg, 85%).

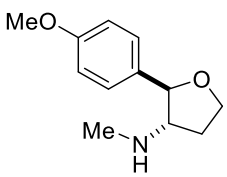
Note: For determination of relative stereochemistry see section 4.1.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37–7.33 (m, 4H), 7.30–7.26 (m, 1H), 4.65 (d, 1H, *J* = 5.0 Hz), 4.18 (td, 1H, *J* = 8.3, 5.3 Hz), 4.09 (app. q., 1H, *J* = 7.7 Hz), 3.15 (dt, 1H, *J* = 7.0, 5.2 Hz), 2.46 (s, 3H), 2.23 (dq, 1H, *J* = 12.6, 7.4 Hz), 1.88 (ddt, 1H, *J* = 12.6, 7.7, 5.2 Hz), 1.29 (br s, 1H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.6, 128.5, 127.6, 125.9, 85.6, 68.1, 67.5, 34.9, 32.1.

HRMS (ESI^+) Calcd. for $[C_{11}H_{15}NO+H]^+$ 178.1226, Found 178.1227.

3.5 (2*R**,3*S**)-2-(4-methoxyphenyl)-*N*-methyltetrahydrofuran-3-amine (3b)



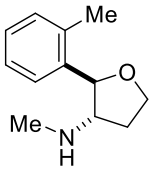
Following the general procedure, (*E*)-4-(4-methoxyphenyl)but-3-en-1-ol **1b** (178.2 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 4 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (176.2 mg, 85%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.29–7.27 (m, 2H), 6.89–6.86 (m, 2H), 4.53 (d, 1H, *J* = 5.6 Hz), 4.16–4.12 (m, 1H), 4.07–4.03 (m, 1H), 3.12 (s, 3H), 3.10–3.07 (m, 1H), 2.42 (s, 3H), 2.25–2.20 (m, 1H), 1.88–1.80 (m, 1H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.1, 133.4, 127.3, 113.8, 85.5, 67.9, 67.2, 55.2, 35.0, 32.3.

HRMS (ESI$^+$) Calcd. for $[C_{12}H_{17}NO_2+H]^+$ 208.1332, Found 208.1336.

3.6 (2*R**,3*S**)-*N*-methyl-2-(*o*-tolyl)tetrahydrofuran-3-amine (3c)



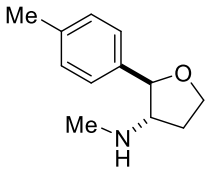
Following the general procedure, (*E*)-4-(*o*-tolyl)but-3-en-1-ol **1c** (162.2 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 4 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (162.6 mg, 85%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.36–7.34 (m, 1H), 7.22–7.12 (m, 3H), 4.89 (d, 1H, *J* = 4.0 Hz), 4.27–4.21 (m, 1H), 4.11–4.05 (m, 1H), 3.18–3.15 (m, 1H), 2.46 (s, 3H), 2.39 (s, 3H), 2.19–2.14 (m, 1H), 1.90–1.85 (m, 1H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 139.7, 135.0, 130.4, 127.3, 126.0, 125.7, 83.3, 67.5, 66.9, 34.9, 31.4, 19.5.

HRMS (ESI$^+$) Calcd. for $[C_{12}H_{17}NO+H]^+$ 192.1383, Found 192.1386.

3.7 (2*R**,3*S**)-*N*-methyl-2-(*p*-tolyl)tetrahydrofuran-3-amine (3d)



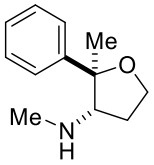
Following the general procedure, (*E*)-4-(*p*-tolyl)but-3-en-1-ol **1d** (162.2 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 4 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (145.3 mg, 76%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.24 (d, 2H, *J* = 8.0 Hz), 7.15 (d, 2H, *J* = 7.6 Hz), 4.57 (d, 1H, *J* = 5.2 Hz), 4.19-4.13 (m, 1H), 4.08-4.04 (m, 1H), 3.12-3.08 (m, 1H), 2.43 (s, 3H), 2.34 (s, 3H), 2.24-2.19 (m, 1H), 1.88-1.80 (m, 1H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$): δ 138.5, 137.2, 129.1, 125.9, 85.6, 68.1, 67.3, 34.9, 32.2, 21.1.

HRMS (ESI$^+$) Calcd. for $[C_{12}H_{17}NO+H]^+$ 192.1383, Found 192.1382.

3.8 (2*R**,3*S**)-*N*,2-dimethyl-2-phenyltetrahydrofuran-3-amine (3e)



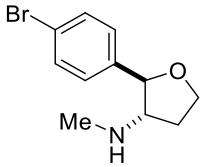
Following the general procedure, (*E*)-4-phenylpent-3-en-1-ol **1e** (162.2 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 4 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (156.8 mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.46–7.43 (m, 2H), 7.34–7.31 (m, 2H), 7.25–7.20 (m, 1H), 4.09–4.03 (m, 1H), 3.97–3.91 (m, 1H), 3.23–3.20 (m, 1H), 2.80 (s, 3H), 2.48 (s, 3H), 2.08–2.05 (m, 1H), 1.86–1.83 (m, 1H), 1.46 (s, 3H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.6, 128.1, 126.5, 124.5, 85.2, 68.6, 65.0, 35.3, 31.2, 23.1.

HRMS (ESI$^+$) Calcd. for $[C_{12}H_{17}NO+H]^+$ 192.1383, Found 192.1386.

3.9 (2*R**,3*S**)-2-(4-bromophenyl)-*N*-methyltetrahydrofuran-3-amine (3f)



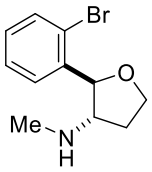
Following the general procedure, (*E*)-4-(4-bromophenyl)but-3-en-1-ol **1f** (227.1 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 4 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (207.5 mg, 81%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.48–7.44 (m, 2H), 7.24–7.22 (m, 2H), 4.56 (d, 1H, *J* = 5.2 Hz), 4.18–4.12 (m, 1H), 4.09–4.05 (m, 1H), 3.09–3.04 (m, 1H), 2.43 (s, 3H), 2.22–2.16 (m, 1H), 1.88–1.80 (m, 1H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.8, 131.5, 127.6, 121.3, 85.0, 68.2, 67.5, 35.0, 32.2.

HRMS (ESI$^+$) Calcd. for $[C_{11}H_{14}BrNO+H]^+$ 256.0332, Found 256.0334.

3.10 (2*R**,3*S**)-2-(4-bromophenyl)-*N*-methyltetrahydrofuran-3-amine (3g)



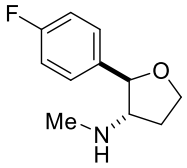
Following the general procedure, (*E*)-4-(2-bromophenyl)but-3-en-1-ol **1g** (227.1 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 4 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (147.6 mg, 78%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.54–7.29 (m, 1H), 7.45–7.43 (m, 1H), 7.34–7.30 (m, 1H), 7.15–7.11 (m, 1H), 5.04 (d, 1H, *J* = 2.8 Hz), 4.32–4.27 (m, 1H), 4.18–4.12 (m, 1H), 3.24–3.21 (m, 1H), 2.50 (s, 3H), 2.05–1.98 (m, 1H), 1.92–1.86 (m, 1H), 1.68 (br s, 1H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.4, 132.5, 128.7, 127.4, 127.4, 121.6, 85.3, 68.2, 67.4, 34.9, 30.6.

HRMS (ESI^+) Calcd. for $[C_{11}H_{14}BrNO+H]^+$ 256.0332, Found 256.0331.

3.11 (2*R**,3*S**)-2-(4-fluorophenyl)-*N*-methyltetrahydrofuran-3-amine (3h)



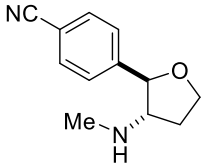
Following the general procedure, (*E*)-4-(4-fluorophenyl)but-3-en-1-ol **1h** (166.2 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 4 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (152.3 mg, 78%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35-7.29 (m, 2H), 7.05-7.00 (m, 2H), 4.57 (d, 1H, *J* = 5.6 Hz), 4.18-4.13 (m, 1H), 4.08-4.04 (m, 1H), 3.10-3.06 (m, 1H), 2.43 (s, 3H), 2.24-2.19 (m, 1H), 1.89-1.81 (m, 1H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.2 (d, *J* = 243.9 Hz), 137.3 (d, *J* = 3.0 Hz), 127.6 (d, *J* = 8.0 Hz), 115.2 (d, *J* = 21.3 Hz), 85.1, 68.1, 67.4, 34.9, 32.2.

HRMS (ESI^+) Calcd. for $[C_{11}H_{14}FNO+H]^+$ 196.1132, Found 196.1133.

3.12 4-((2*R**,3*S**)-3-(methylamino)tetrahydrofuran-2-yl)benzonitrile (3i)



Following the general procedure, (*E*)-4-(4-hydroxybut-1-en-1-yl)benzonitrile **1i** (173.2 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5

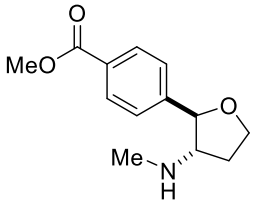
mL) at rt for 2 h, then at 65 °C for 4 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (153.5 mg, 76%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63–7.61 (m, 2H), 7.46 (d, 2H, *J* = 8.0 Hz), 4.64 (d, 1H, *J* = 4.8 Hz), 4.19–4.14 (m, 1H), 4.09–4.05 (m, 1H), 3.10–3.05 (m, 1H), 2.45 (s, 3H), 2.18–2.15 (m, 1H), 1.89–1.82 (m, 1H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.6, 132.2, 126.4, 118.8, 111.1, 84.7, 68.5, 67.8, 34.9, 32.2.

HRMS (ESI$^+$) Calcd. for $[C_{12}H_{14}N_2O+H]^+$ 203.1179, Found 203.1177.

3.13 Methyl 4-((2*R**,3*S**)-3-(methylamino)tetrahydrofuran-2-yl)benzoate (3j)



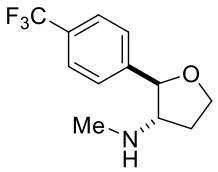
Following the general procedure, methyl (*E*)-4-(4-hydroxybut-1-en-1-yl)benzoate **1j** (206.2 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 4 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (193.3 mg, 81%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03–7.99 (m, 2H), 7.42 (d, 2H, *J* = 8.0 Hz), 4.67 (d, 1H, *J* = 5.2 Hz), 4.21–4.15 (m, 1H), 4.11–4.07 (m, 1H), 3.90 (s, 2H), 3.12–3.08 (m, 1H), 2.45 (s, 3H), 2.21–2.16 (m, 1H), 1.87–1.82 (m, 1H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.9, 147.2, 129.7, 129.3, 125.7, 85.2, 68.5, 67.7, 52.0, 35.0, 32.2.

HRMS (ESI$^+$) Calcd. for $[C_{13}H_{17}NO_3+H]^+$ 236.1281, Found 236.1285.

3.14 (2*R**,3*S**)-N-methyl-2-(4-(trifluoromethyl)phenyl)tetrahydrofuran-3-amine (3k)



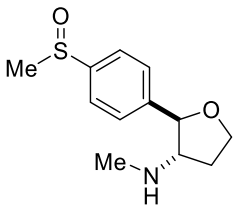
Following the general procedure, (*E*)-4-(4-(trifluoromethyl)phenyl)but-3-en-1-ol **1k** (216.2 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 4 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (183.6 mg, 75%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (d, 2H, *J* = 8.4 Hz), 7.47 (d, 2H, *J* = 8.4 Hz), 4.67 (d, 1H, *J* = 4.8 Hz), 4.21–4.15 (m, 1H), 4.12–4.06 (m, 1H), 3.12–3.08 (m, 1H), 2.46 (s, 3H), 2.20–2.17 (m, 1H), 1.89–1.82 (m, 1H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$): δ 146.1 (d, *J* = 1.1 Hz), 129.6 (q, *J* = 32.2 Hz), 126.3 (q, *J* = 248.9 Hz), 126.0, 125.3 (q, *J* = 2.8 Hz), 84.9, 68.4, 67.7, 34.9, 32.2.

HRMS (ESI$^+$) Calcd. for $[C_{12}H_{14}F_3NO+H]^+$ 246.1100, Found 246.1102.

3.15 (2*R**,3*S**)-*N*-methyl-2-(4-(methylsulfinyl)phenyl)tetrahydrofuran-3-amine (3l)



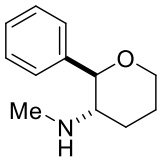
Following the general procedure, (*E*)-4-(4-(methylsulfinyl)phenyl)but-3-en-1-ol **1l** (210.3 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 4 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (138.6 mg, 58%).

^{1}H NMR (400 MHz, CD_3OD) δ: 7.71 (d, 2H, *J* = 8.0 Hz), 7.60 (d, 2H, *J* = 8.4 Hz), 4.71 (d, 1H, *J* = 4.8 Hz), 4.20–4.16 (m, 1H), 4.10–4.06 (m, 1H), 3.18–3.14 (m, 1H), 2.80 (s, 3H), 2.38 (s, 3H), 2.26–2.17 (m, 1H), 1.95–1.88 (m, 1H).

{^{1}H}^{13}C NMR (100 MHz, CD_3OD) δ: 147.4, 145.1, 128.4, 125.1, 86.2, 69.5, 68.7, 43.5, 34.7, 32.6.

HRMS (ESI$^+$) Calcd. for $[C_{12}H_{17}NO_2S+H]^+$ 240.1053, Found 240.1052.

3.16 (2*R**,3*S**)-*N*-methyl-2-phenyltetrahydro-2*H*-pyran-3-amine (3m)



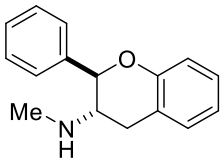
Following the general procedure, (*E*)-5-phenylpent-4-en-1-ol **3m** (206.2 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 4 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (145.1 mg, 76%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40–7.29 (m, 5H), 4.09–4.05 (m, 1H), 3.99 (d, 1H, *J* = 9.2 Hz), 3.57–3.51 (m, 1H), 2.59–2.52 (m, 1H), 2.28–2.22 (m, 1H), 2.20 (s, 3H), 1.91–1.71 (m, 2H), 1.42–1.35 (m, 1H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.0, 128.6, 128.3, 127.6, 85.2, 68.6, 60.9, 33.3, 29.4, 25.5.

HRMS (ESI$^+$) Calcd. for $[C_{12}H_{17}NO+H]^+$ 192.1383, Found 192.1386.

3.17 (2*S**,3*R**)-*N*-methyl-2-phenylchroman-3-amine (3n)



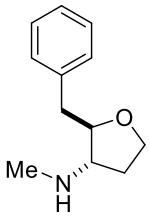
Following the general procedure, 2-cinnamylphenol **1n** (210.3 mg, 1mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 4 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (140.2 mg, 73%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.45–7.35 (m, 5H), 7.17–7.11 (m, 2H), 6.94–6.90 (m, 2H), 4.87 (d, 1H, *J* = 7.2 Hz), 3.13–3.02 (m, 2H), 2.79–2.73 (m, 1H), 2.39 (s, 3H), 1.17 (br s, 1H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.3, 139.0, 129.9, 128.7, 128.4, 127.5, 127.0, 120.7, 120.4, 116.4, 81.2, 57.1, 33.5, 30.5.

HRMS (ESI$^+$) Calcd. for $[C_{16}H_{17}NO+H]^+$ 240.1383, Found 240.1386.

3.18 (2*R**,3*S**)-2-benzyl-*N*-methyltetrahydrofuran-3-amine (3o)



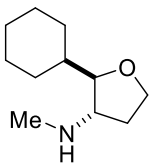
Following the general procedure, (*E*)-5-phenylpent-3-en-1-ol **4** (162.2 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 64 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (116.5 mg, 61%).

^{1}H NMR (400 MHz, CD_3OD) δ: 7.29–7.21 (m, 3H), 7.20–7.17 (m, 1H), 3.91–3.80 (m, 3H), 2.98–2.94 (m, 1H), 2.88–2.77 (m, 2 H), 2.24 (s, 3H), 2.14–2.06 (m, 1H), 1.78–1.71 (m, 1H).

{^{1}H}^{13}C NMR (100 MHz, CD_3OD) δ: 139.7, 130.5, 129.3, 127.4, 85.9, 67.5, 65.4, 41.3, 34.4, 32.8.

HRMS (ESI$^+$) Calcd. for $[C_{12}H_{17}NO+H]^+$ 192.1383, Found 192.1385.

3.19 (2*R**,3*S**)-2-cyclohexyl-*N*-methyltetrahydrofuran-3-amine (3p)



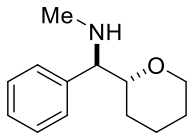
Following the general procedure, (*E*)-4-cyclohexylbut-3-en-1-ol **5** (154.3 mg, 1 mmol), TsONHMe (**2**) (301.8 mg, 1.5 mmol), and $Rh_2(esp)_2$ (7.6 mg, 0.01 mmol) were stirred in dry CF_3CH_2OH (5 mL) at rt for 2 h, then at 65 °C for 72 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a yellow oil (95.2 mg, 52%).

^{1}H NMR (400 MHz, CD_3OD) δ: 3.86–3.79 (m, 2H), 3.43–3.40 (m, 1H), 3.10–3.06 (m, 1H), 2.38 (s, 3H), 2.09–1.99 (m, 1H), 1.82–1.76 (m, 4H), 1.68–1.67(m, 2H), 1.42–1.01 (m, 6H).

{^{1}H}^{13}C NMR (100 MHz, CD_3OD) δ: 89.8, 67.5, 63.6, 42.4, 34.3, 33.0, 30.9, 29.5, 27.6, 27.3, 27.1.

HRMS (ESI^+) Calcd. for $[C_{11}H_{21}NO+H]^+$ 184.1696, Found 184.1695.

3.20 (*R**)-*N*-methyl-1-phenyl-1-((*R**)-tetrahydro-2*H*-pyran-2-yl)methanamine (3q)



Following the general procedure, (*Z*)-6-phenylhex-5-en-1-ol **1q** (53 mg, 0.3 mmol), TsONHMe (**2**) (90 mg, 0.45 mmol), and $Rh_2(esp)_2$ (4.5 mg, 6 µmol) were stirred in dry CF_3CH_2OH (3 mL) at rt for 2 h, then at 50 °C for 21 h. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:5) afforded the title product as a faint yellow oil (29 mg, 48%).

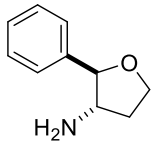
***R*$_f$**: 0.4 (10% MeOH/DCM).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.20–7.44 (m, 5H), 4.01–4.10 (m, 1H), 3.47 (td, *J* = 11.8, 2.7 Hz, 1H), 3.29–3.38 (m, 2H), 2.22 (br s, 1H), 2.20 (s, 3H), 1.67–1.75 (m, 1H), 1.45–1.62 (m, 2H), 1.26–1.37 (m, 1H), 1.09–1.23 (m, 2H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.3, 128.5, 128.2, 127.4, 81.6, 71.0, 68.6, 34.3, 28.6, 26.0, 23.2.

HRMS (ESI^+) Calcd. for $[C_{13}H_{19}NO+H]^+$ 206.1539, Found 206.1532.

3.21 (2*R**,3*S**)-2-phenyltetrahydrofuran-3-amine (5)



Following the general procedure, (*E*)-4-(phenyl)but-3-en-1-ol **1a** (50 mg, 0.34 mmol, 1.0 equiv.) and $NbzONH_2$ (**4**) (½ of 122.9 mg, 0.67 mmol, 2.0 equiv.) were stirred in dry CF_3CH_2OH (3.4 mL) for 15 min to achieve a homogenous suspension. To the vigorously stirred solution $Rh_2(esp)_2$ (½ of 5.1 mg, 6.8 µmol, 0.02 equiv.) was added in one portion and stirring continued for 30 min. After 30 min the rest of aminating agent and $Rh_2(esp)_2$ were added and the reaction mixture stirred at rt for 2 h (consumption of olefin by TLC 95:5 DCM/MeOH), and then at 65 °C for 74 h. The reaction mixture was quenched with 5 mL aq. sat. Na_2CO_3, extracted with EtOAc (3 × 10 mL) and the combined organic layers dried with Na_2SO_4 and

concentrated *in vacuo*. Chromatographic purification of the crude product by using CombiFlash (DCM:MeOH=100:1 to 100:15) afforded the title product as a brown oil (30.2 mg, 55%).

***R*$_f$**: 0.47 (15% MeOH/DCM, Ninhydrin stain: red).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.36–7.34 (m, 4H), 7.31–7.27 (m, 1H), 4.42 (d, *J* = 6.1 Hz, 1H), 4.17 (dt, *J* = 8.2, 6.5 Hz, 1H), 4.12 (td, *J* = 8.4, 6.0 Hz), 3.41–3.24 (m, 1H), 2.3 (dtd, *J* = 13.1, 7.5, 6.1 Hz), 1.83 (ddt, *J* = 12.4, 8.2, 6.7 Hz), 1.72 (br. s, 2H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.2, 128.6, 127.8, 125.9, 88.6, 67.2, 60.2, 35.3.

HRMS (ESI$^+$) Calcd. for $[C_{10}H_{14}NO+H]^+$ 164.1075, Found 164.1075.

4 Determination of relative configurations of 3a and 3q

4.1 NOESY study on 3a

The protons and carbons signals were assigned based on ^{1}H coupling data, ^{1}H-^{1}H-COSY, ^{1}H-^{13}C-HSQC and DEPT-135. ^{1}H-^{1}H NOESY data was used to establish the solution-state major conformer as well as the relative 2,3-*trans* stereochemistry of the system.

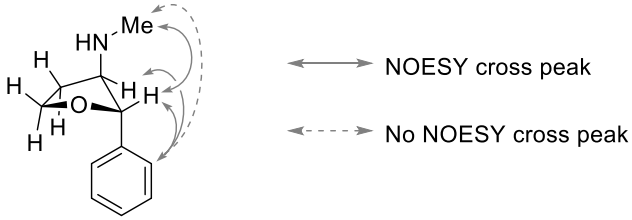
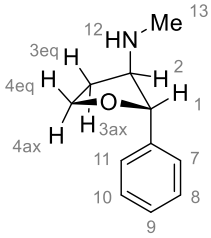


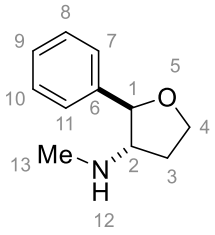
Figure S1. NOESY cross peaks observed for **3a**.

Table S2. ^{1}H signal assignment of **3a**.



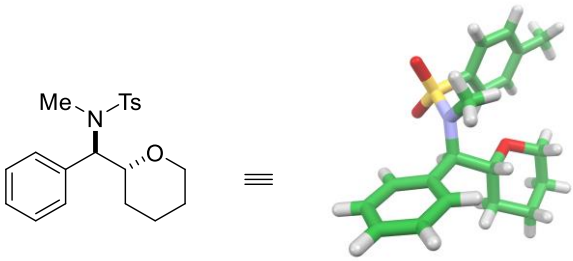
Shift (ppm)	**Integral**	**Multiplicity**	**H**
7.37 – 7.33	4H	m	7, 8, 10, 11
7.30 – 7.26	1H	m	9
4.65	1H	d, *J* = 5.0 Hz	1
4.18	1H	td, *J* = 8.3, 5.3 Hz	4*ax*
4.09	1H	app. q, *J* = 7.7 Hz	4*eq*
3.15	1H	dt, *J* = 7.0, 5.2 Hz	2
2.46	3H	s	13
2.23	1H	dq, *J* = 12.6, 7.4 Hz	3*ax*
1.88	1H	ddt, *J* = 12.6, 7.7, 5.2 Hz	3*eq*
1.84	1H	br. s	12

Table S3. ^{13}C signal assignment of **3a**.



Shift (ppm)	**C**	**DEPT-135**
141.6	6	C
128.5	8, 10	CH
127.6	9	CH
125.9	7, 11	CH
85.6	1	CH
68.1	2	CH
67.5	4	CH_2
34.9	13	CH_3
32.1	3	CH_2

4.2 *N*,4-dimethyl-*N*-((*R**)-phenyl((*R**)-tetrahydro-2*H*-pyran-2-yl)methyl) benzenesulfonamide (S2)



[ScXRD]

To a stirred solution of amine **3q** (30 mg, 0.15 mmol) in dry CH_2Cl_2 (2 mL) at rt was added pyridine (15 µL) and *p*-toluenesulfonyl chloride (34 mg, 0.18 mmol). After 24 h, the volatiles were evaporated and the crude product was purified by preparative TLC using 20% EtOAc/hexanes as eluent to isolate the title compound as white solid (28 mg, 52%).

Note: For details on scXRD, see section 6.

MP: 123.6 °C.

***R*$_f$**: 0.4 (20% EtOAc/Hexane).

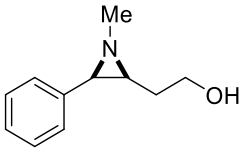
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.61–7.65 (m, 2H), 7.22–7.27 (m, 5H), 7.15–7.19 (m, 2H), 5.02 (d, *J* = 8.0 Hz, 1H), 3.68–3.86 (m, 2H), 3.27 (td, *J* = 11.4, 2.6 Hz, 1H), 2.73 (s, 3H), 2.36 (s, 3H), 1.75–1.83 (m, 1H), 1.18–1.55 (m, 5H).

{^{1}H}^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.4, 137.3, 137.2, 128.9, 128.5, 128.4, 127.7, 127.7, 75.9, 68.2, 64.2, 30.0, 29.4, 25.7, 23.2, 21.4.

HRMS (ESI^+) Calcd. for $[C_{20}H_{25}NO_3S+H]^+$ 382.1447, Found 382.1455.

5 *Cis*-Aminoetherification

5.1 (2-((2*S**,3*R**)-1-methyl-3-phenylaziridin-2-yl)ethan-1-ol (6)



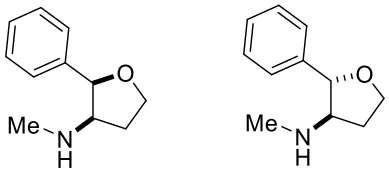
$Rh_2(esp)_2$ (15.2 mg, 0.02 mmol) and TsONHMe (**2**) (0.301 g, 1.5 mmol) were added to a stirred solution of olefin *cis*-**1b** (0.148 g, 1.0 mmol) in TFE (10.0 mL) at rt. After 2 h (when TLC analysis showed the completion of reaction), the reaction mixture was diluted with CH_2Cl_2 (10 mL) and aqueous sodium bicarbonate solution (2 mL) was added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (10 mL × 2). The combined organic layers were washed with brine (5 mL), dried (Na_2SO_4) and concentrated in *vacuo*. The crude product was purified by preparative TLC using EtOAc as eluent to furnish the title compound as colorless oil (0.125 g, 71%).

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.32 – 7.28 (m, 3H), 7.21 – 7.24 (m, 1H), 3.77 (ddd, *J* = 10.5, 8.8, 4.2 Hz, 1H), 3.65 (dt, *J* = 10.4, 5.2 Hz, 1H), 2.54 (s, 3H), 2.53 (d, overlapping with 2.54 methyl signal, 1H), 1.84 (dd, *J* = 13.6, 6.4 Hz, 1H), 1.50 (ddd, *J* = 14.9, 9.7, 5.4 Hz, 1H), 1.40 – 1.32 (m, 1H).

{^{1}H}^{13}C NMR (126 MHz, $CDCl_3$) δ: 136.8, 128.1, 127.6, 126.8, 61.7, 47.5, 46.6, 45.9, 28.9.

HRMS (ESI^+) Calcd. for $[C_{11}H_{15}NO+H]^+$ 178.1226, Found 178.1229.

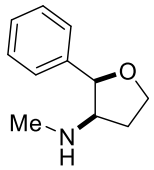
5.2 (2*R**,3*R**)-*N*-methyl-2-phenyltetrahydrofuran-3-amine and (2*R**,3*S**)-*N*-methyl-2-phenyltetrahydrofuran-3-amine (*cis*-3a)



$Rh_2(esp)_2$ (3.8 mg, 0.5 mmol, 1 mol%) and TsONHMe (**2**) (0.151 g, 0.75 mmol were added to a stirred solution of (*Z*)-4-phenylbut-3-en-1-ol (*Z*-**1a**) (74 mg, 0.5 mmol) in TFE (5 mL) at rt. After 30 min (when TLC analysis showed the completion of reaction), the reaction mixture was warmed to 60 °C and stirred for 18 h. The reaction mixture was diluted with EtOAc (10 mL) and aqueous sodium bicarbonate solution (2 mL) was added. The layers were separated and the aqueous layer was extracted with EtOAc (10 mL × 2). The combined organic layers were washed with brine (5 mL), dried (Na_2SO_4) and concentrated in *vacuo*. The crude product was purified by Combi Flash column chromatography using 2-5% MeOH:CH_2Cl_2 followed by preparative TLC using 5% MeOH:CH_2Cl_2 as eluent to furnish the two inseparable diastereomers as faint yellow oil (48 mg, 67%, combined yield).

***cis*-(±)-*N*-methyl-2-phenyltetrahydrofuran-3-amine:**

Characterized after further purification with a second prep-TLC (5% MeOH:CH_2Cl_2 to furnish an enriched ~1:1 mixture of diastereomers).



^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.34–7.39 (m, 4H), 7.27–7.32 (m, 1H), 4.98 (d, *J* = 5.3 Hz, 1H), 4.25 (dd, *J* = 14.7, 7.8 Hz, 1H), 3.98 (td, *J* = 8.3, 5.7 Hz, 1H), 3.36–3.40 (m, 1H), 2.25 (s, 3H), 2.16–2.23 (m, 1H), 1.99–2.05 (m, 1H), 1.18 (broad s, 1H).

{^{1}H}^{13}C NMR (126 MHz, $CDCl_3$) δ: 138.5, 128.6, 127.7, 126.8, 83.6, 67.1, 63.5, 34.9, 31.9.

HRMS (ESI^+) Calcd. for $[C_{11}H_{15}NO+H]^+$ 178.1226, Found 178.1227.

6 Crystallographic data for S2

Diffraction data were collected on a Bruker APEX II with graphite-monochromated Mo Kαradiation (λ = 0.71073 Å). The cell parameters were obtained from the least-squares refinement of the spots (from 60 collected frames) using the Apex 2 program. Data collection, data processing, and structure solution were performed using the Apex 2 program. Initial atomic positions were located using intrinsic phasing and the structures were refined by least-squares methods using SHELXL-2017. Calculated hydrogen positions were input and refined in a riding manner along with the attached carbons.

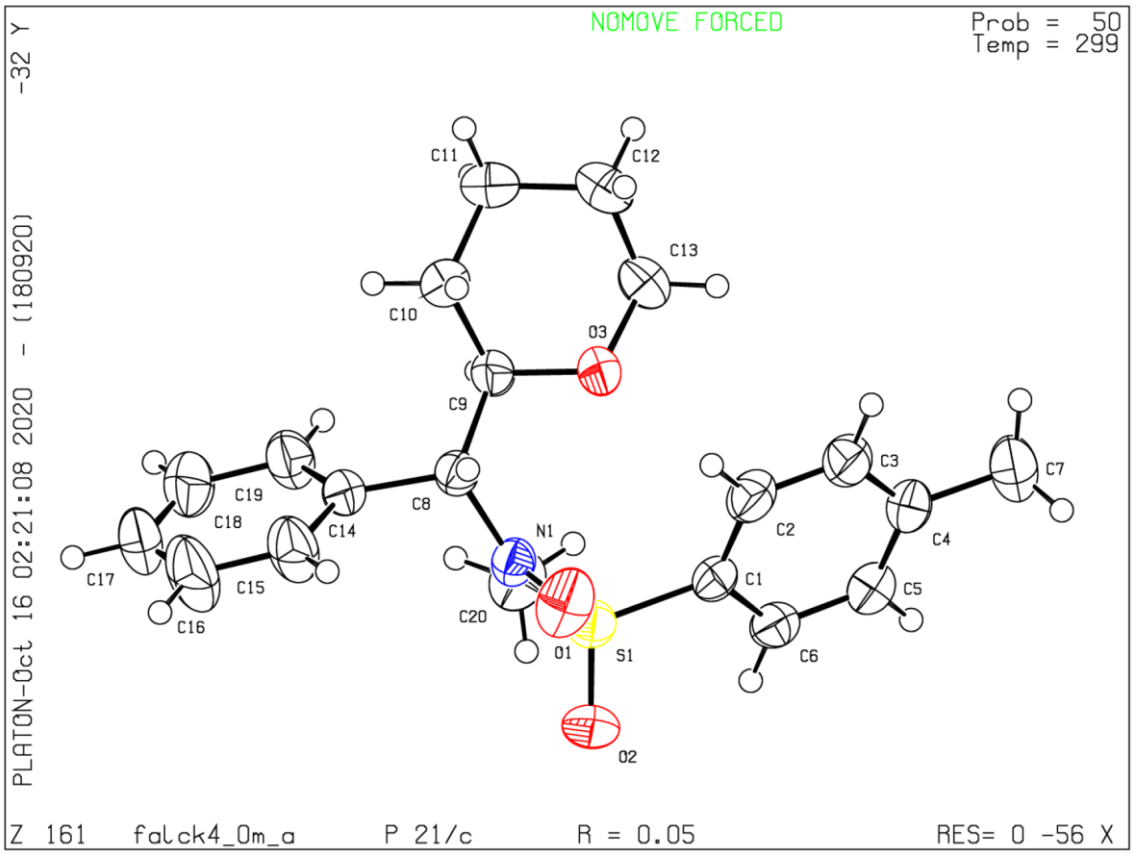
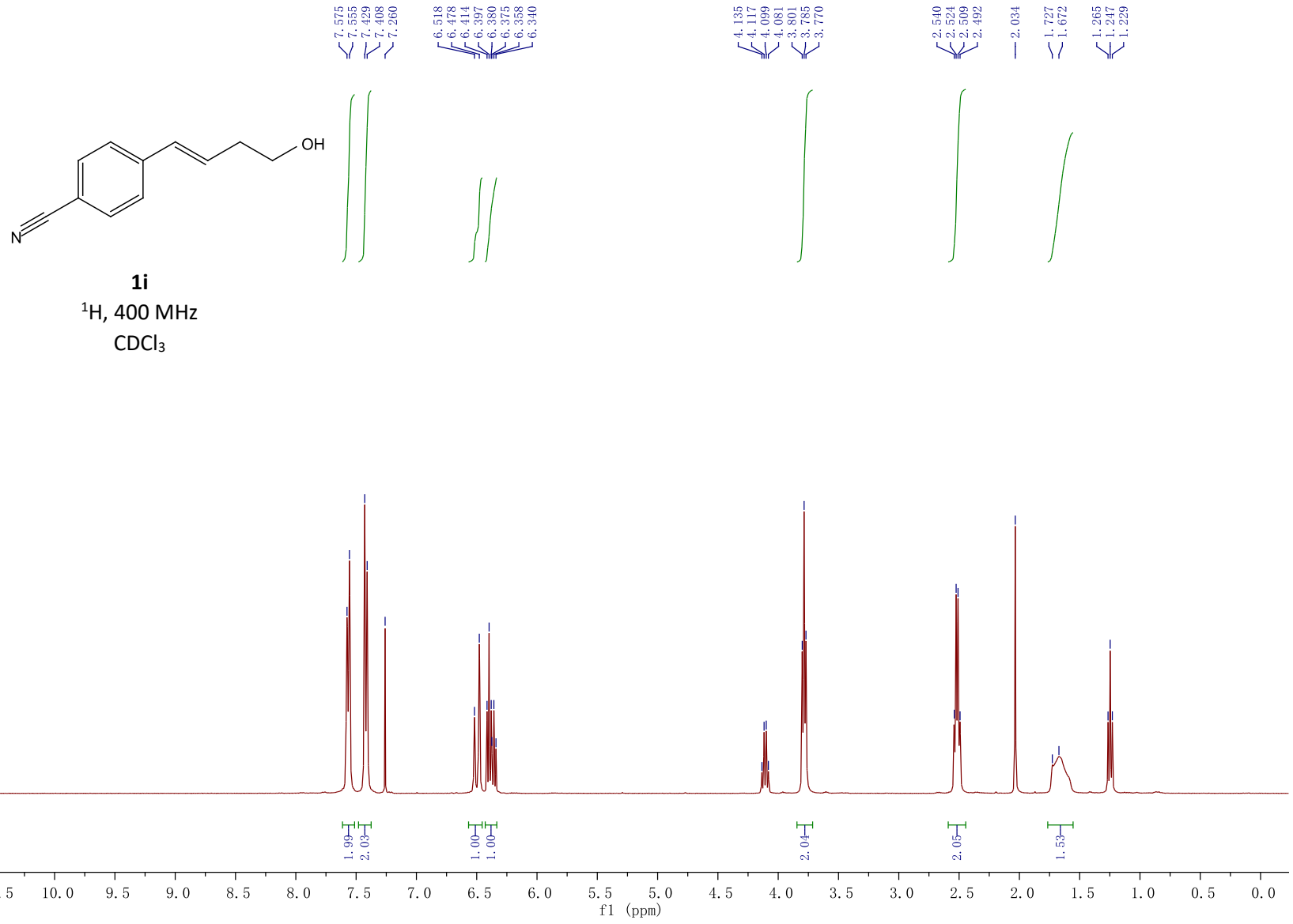


Table S4: Crystal data and structure refinement for $C_{20}H_{25}NO_3S$ (**S2**)

Identification code	falck4_0m_a	
Empirical formula	C20 H25 N O3 S	
Formula weight	359.47	
Temperature	299(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 9.3481(14) Å	α= 90°.
	b = 11.8624(17) Å	β= 100.756(4)°.
	c = 17.695(3) Å	γ = 90°.
Volume	1927.7(5) Å^3	
Z	4	

Density (calculated)	1.239 Mg/m^3
Absorption coefficient	0.186 mm^{-1}
F(000)	768
Crystal size	0.662 x 0.367 x 0.186 mm^3
Theta range for data collection	3.196 to 30.507°.
Index ranges	-13<=h<=13, -16<=k<=16, -25<=l<=25
Reflections collected	28839
Independent reflections	5885 [R(int) = 0.0305]
Completeness to theta = 25.000°	99.7 %
Absorption correction	Numerical
Max. and min. transmission	1.000 and 0.941
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5885 / 0 / 228
Goodness-of-fit on F^2	1.248
Final R indices [I>2sigma(I)]	R1 = 0.0491, wR2 = 0.1623
R indices (all data)	R1 = 0.0716, wR2 = 0.1804
Extinction coefficient	n/a
Largest diff. peak and hole	0.251 and -0.244 $e.Å^{-3}$

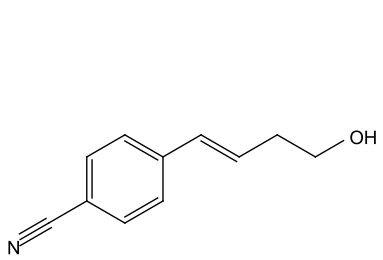
8 Spectral data



1i

^{1}H, 400 MHz

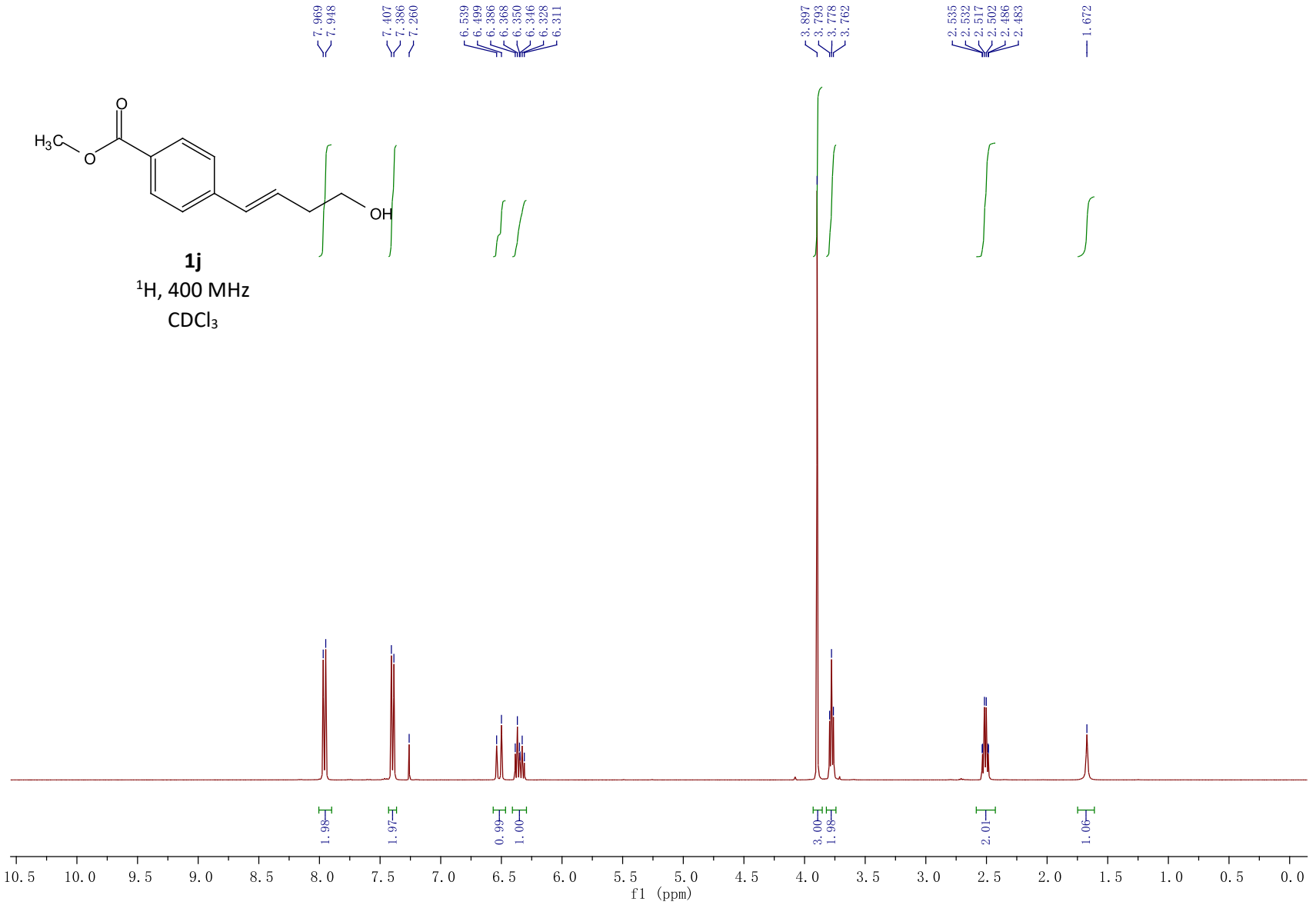
$CDCl_3$

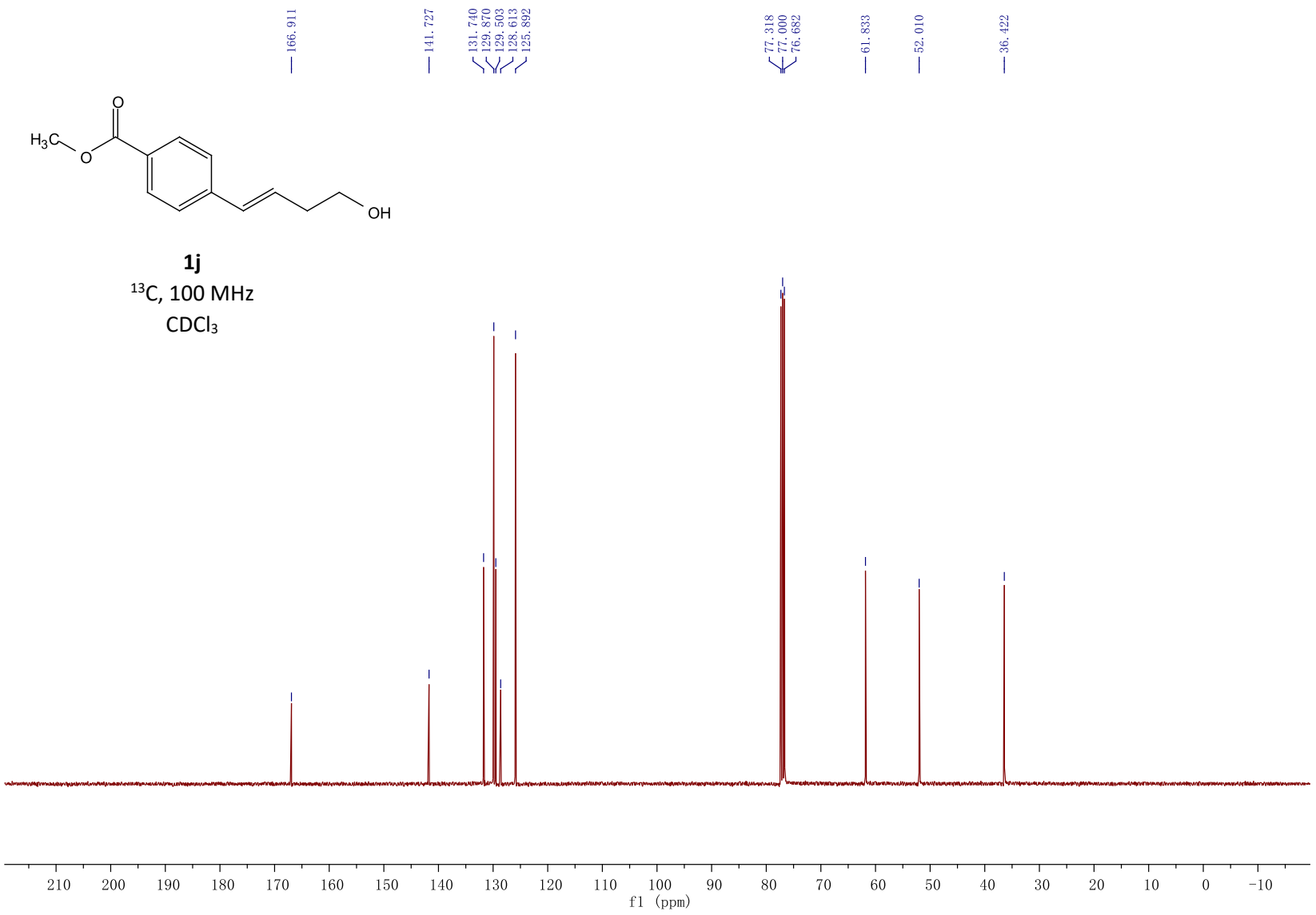


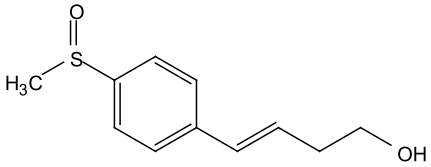
1i

^{13}C, 100 MHz

$CDCl_3$


7.969
7.948
7.407
7.386
7.260
6.539
6.499
6.386
6.368
6.350
6.346
6.328
6.311
3.897
3.793
3.778
3.762
2.535
2.532
2.517
2.502
2.486
2.483
1.672
O
H3C
O
OH
1j
1H, 400 MHz
CDCl3
1.98
1.97
0.99
1.00
3.00
1.98
2.01
1.06
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

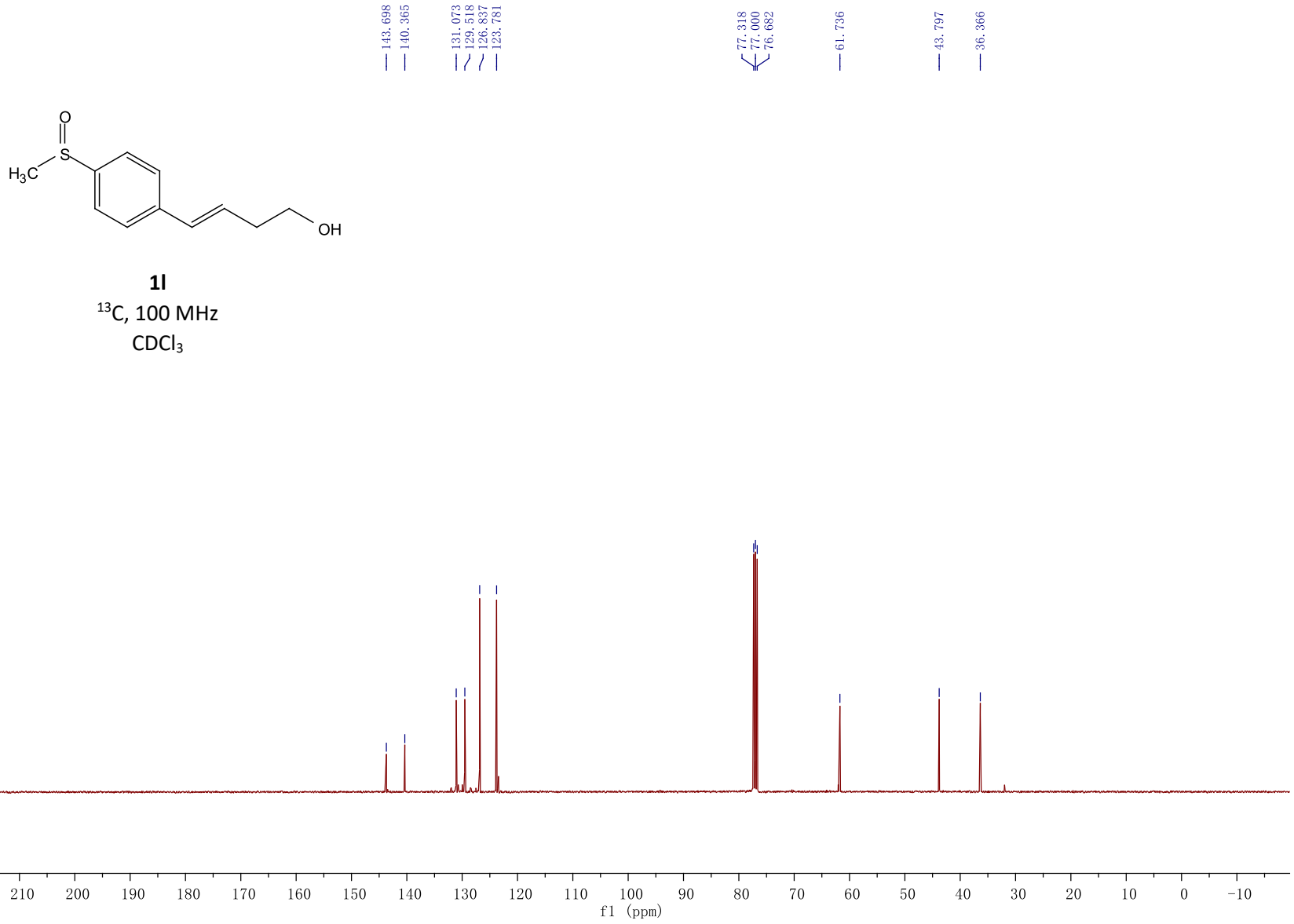

166.911
141.727
131.740
129.870
129.503
128.613
125.892
77.318
77.000
76.682
61.833
52.010
36.422
O
H3C
O
OH
1j
13C, 100 MHz
CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



1l

^{1}H, 400 MHz

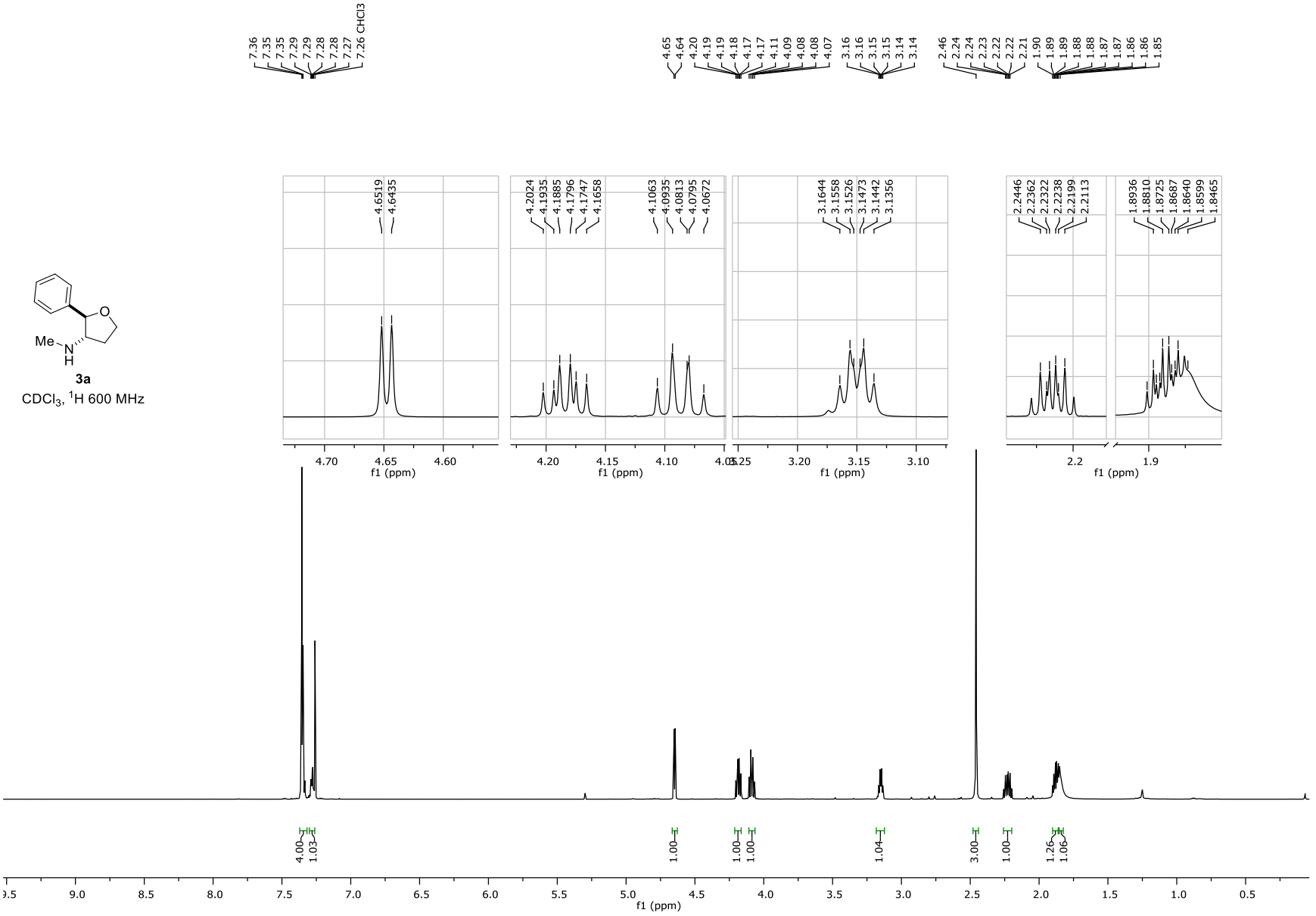
$CDCl_3$

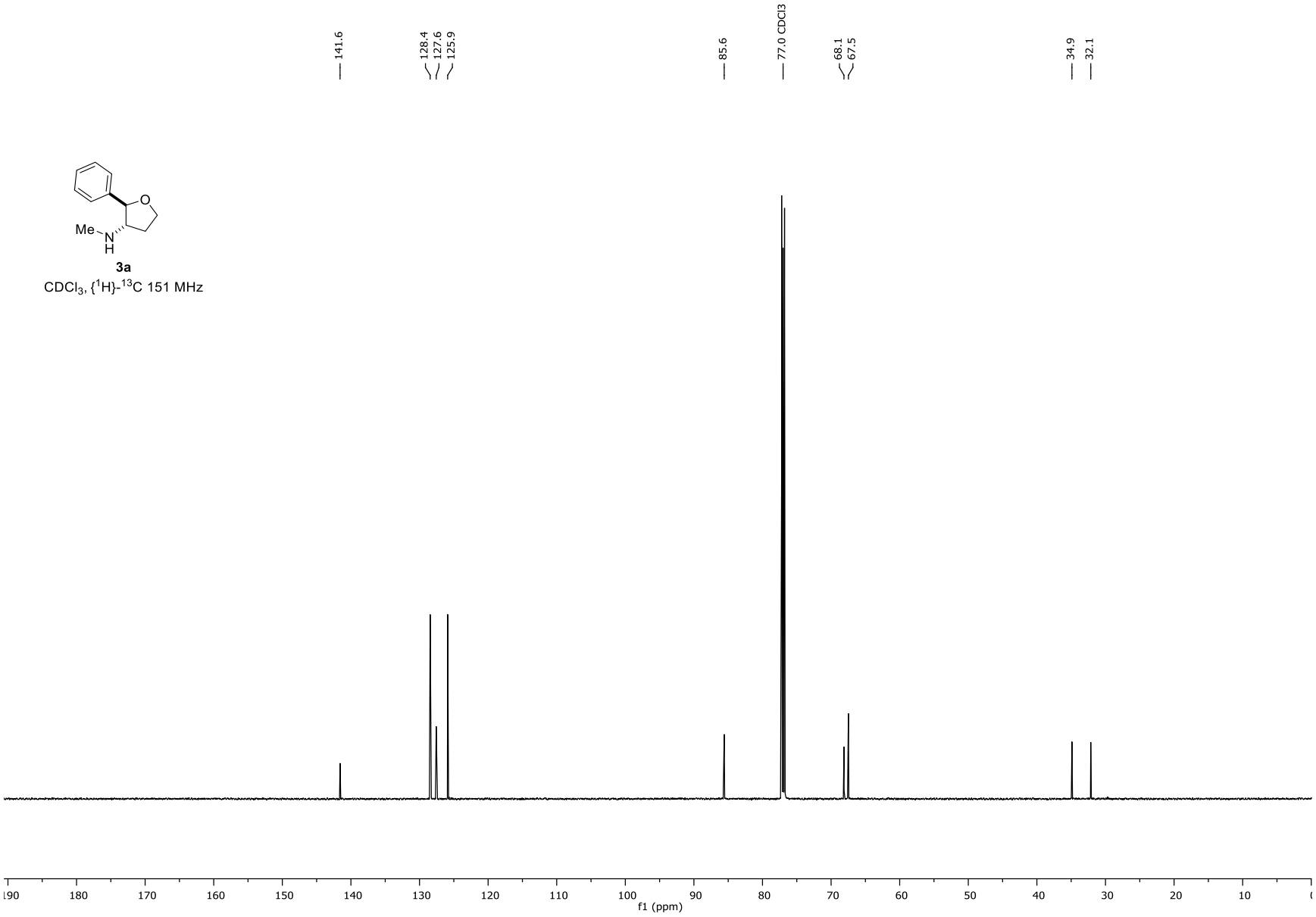


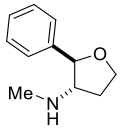
1l

^{13}C, 100 MHz

$CDCl_3$

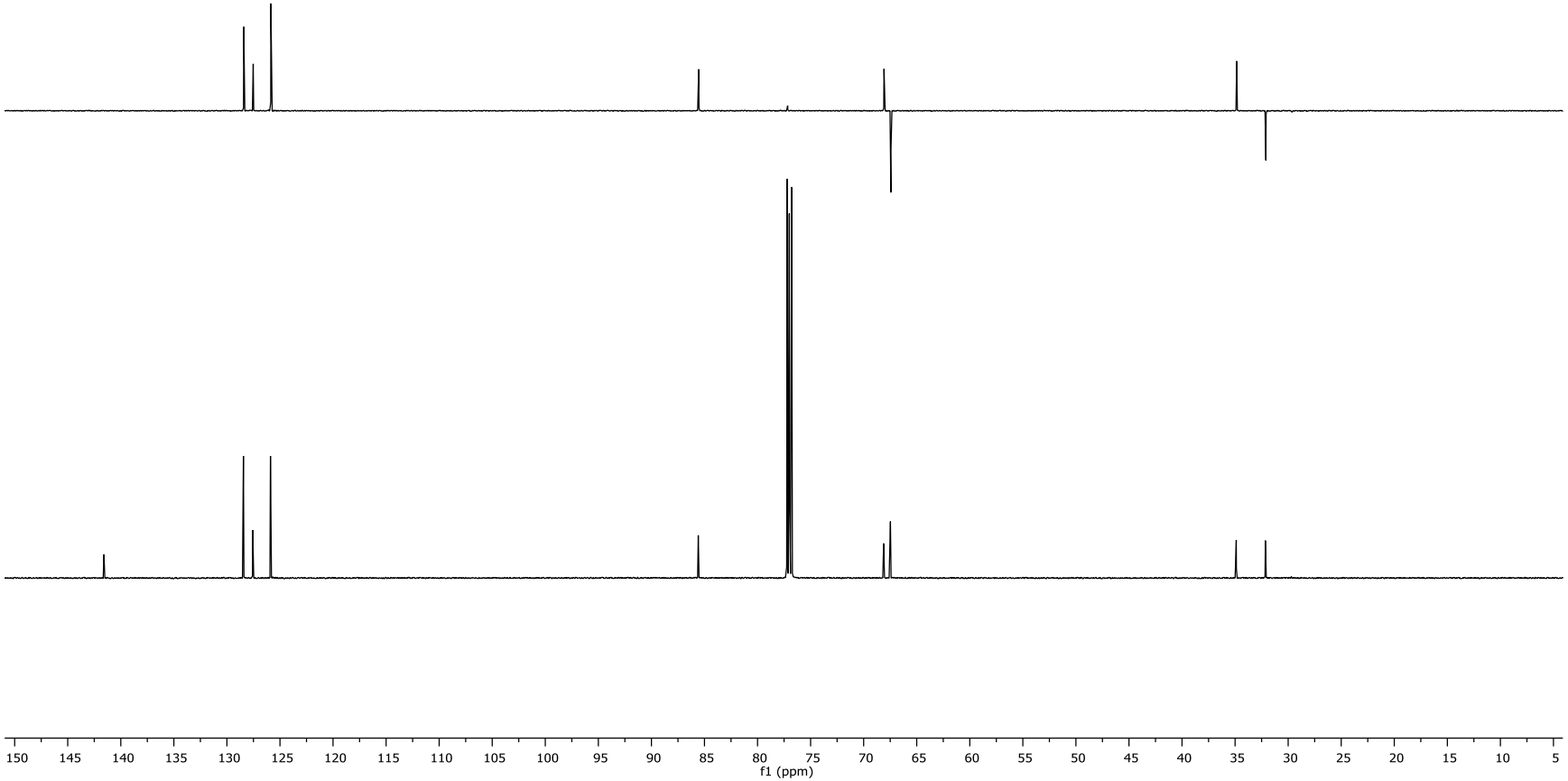

7.36
7.35
7.35
7.29
7.29
7.28
7.28
7.27
7.26 CHCl3
4.65
4.64
4.20
4.19
4.19
4.18
4.17
4.17
4.11
4.09
4.08
4.08
4.07
3.16
3.16
3.15
3.15
3.14
3.14
2.46
2.24
2.24
2.23
2.22
2.22
2.21
1.90
1.89
1.89
1.88
1.88
1.87
1.87
1.86
1.86
1.85
4.6519
4.6435
4.2024
4.1935
4.1885
4.1796
4.1747
4.1658
4.1063
4.0935
4.0813
4.0795
4.0672
3.1644
3.1558
3.1526
3.1473
3.1442
3.1356
2.2446
2.2362
2.2322
2.2238
2.2199
2.2113
1.8936
1.8810
1.8725
1.8687
1.8640
1.8599
1.8465
Me
N
H
O
3a
CDCl3, 1H 600 MHz
f1 (ppm)
4.00
1.03
1.00
1.00
1.00
1.04
3.00
1.00
1.26
1.06

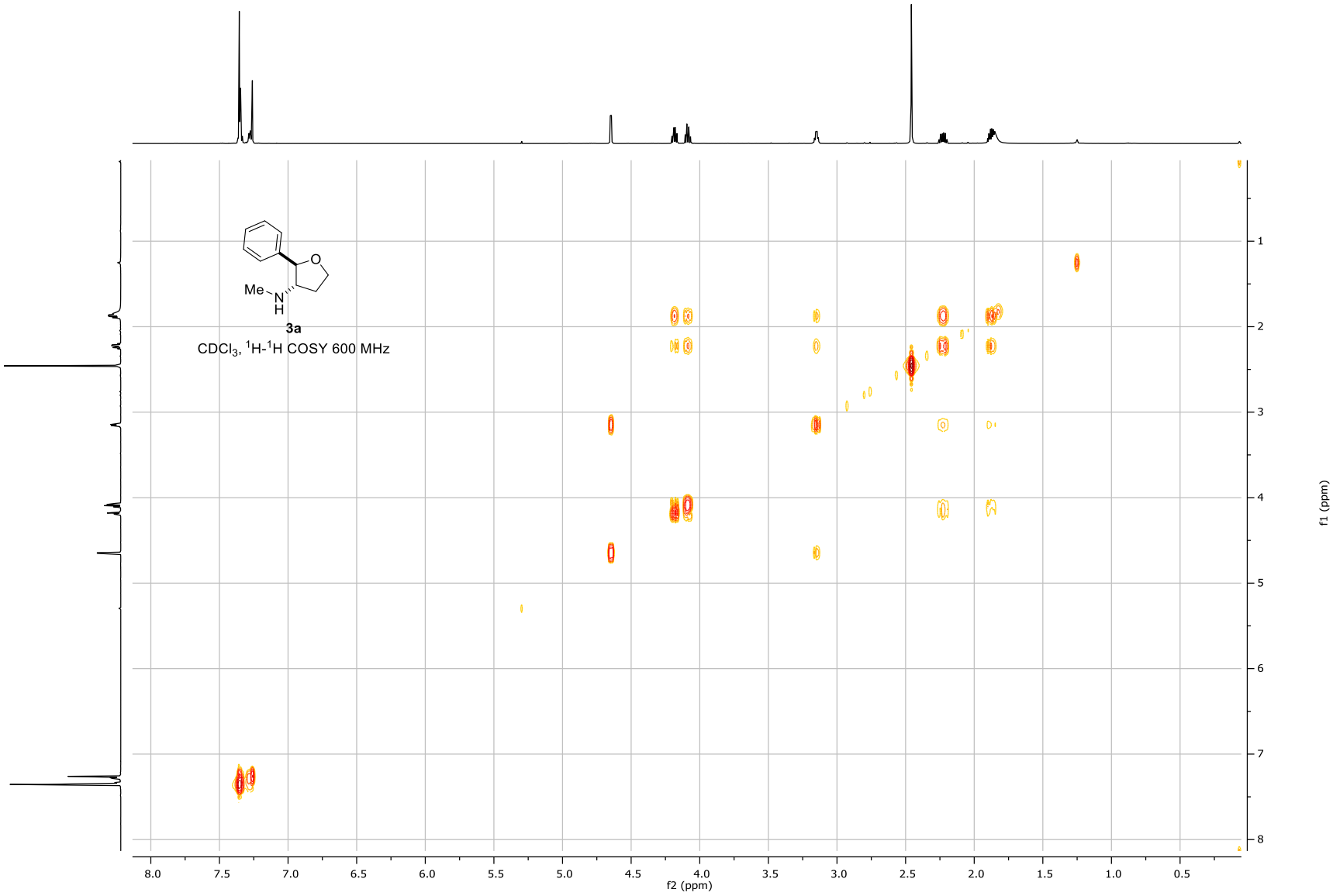

141.6
128.4
127.6
125.9
85.6
77.0 CDCl3
68.1
67.5
34.9
32.1
Me
N
H
O
3a
CDCl3, {1H}-13C 151 MHz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

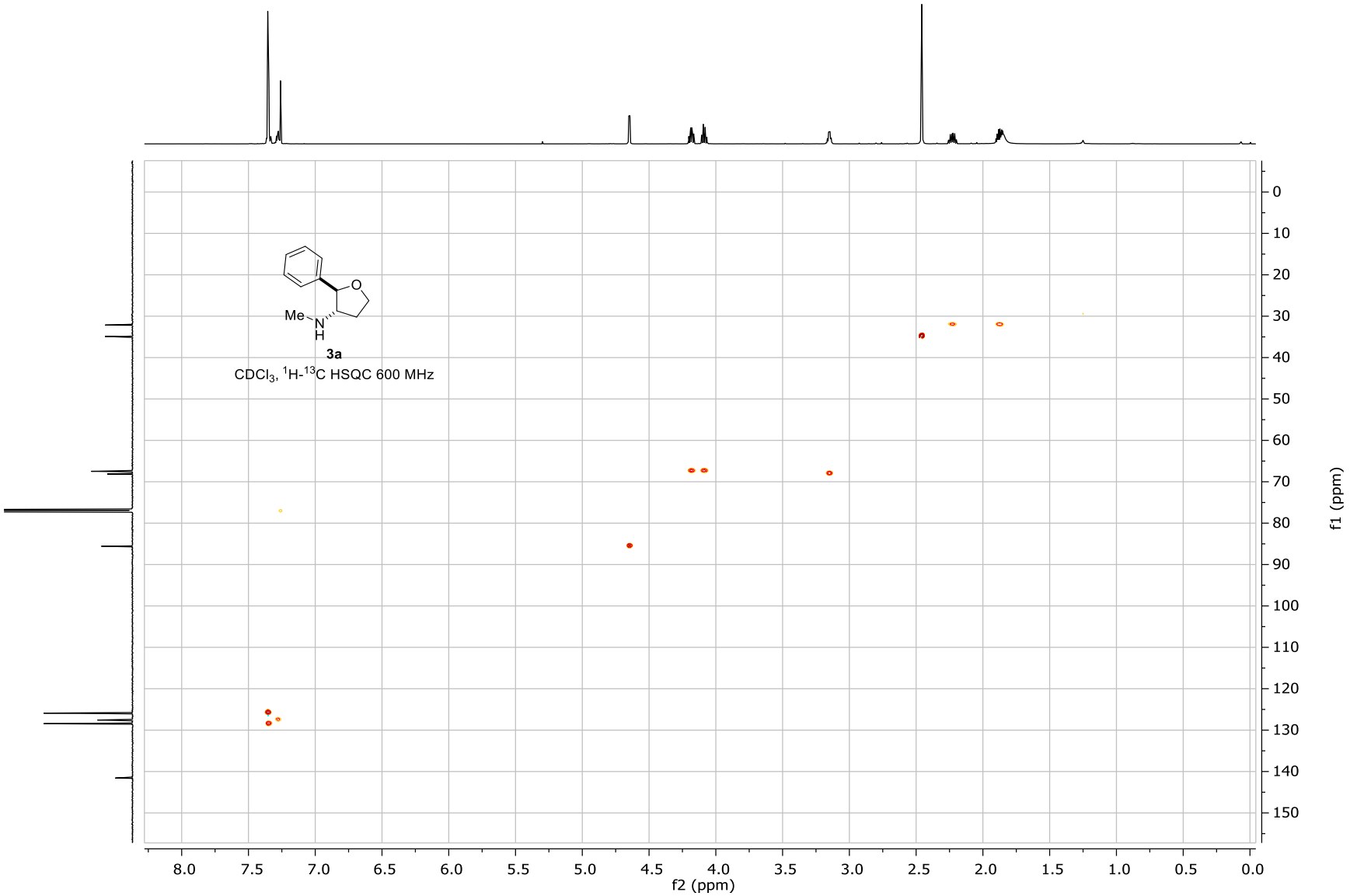


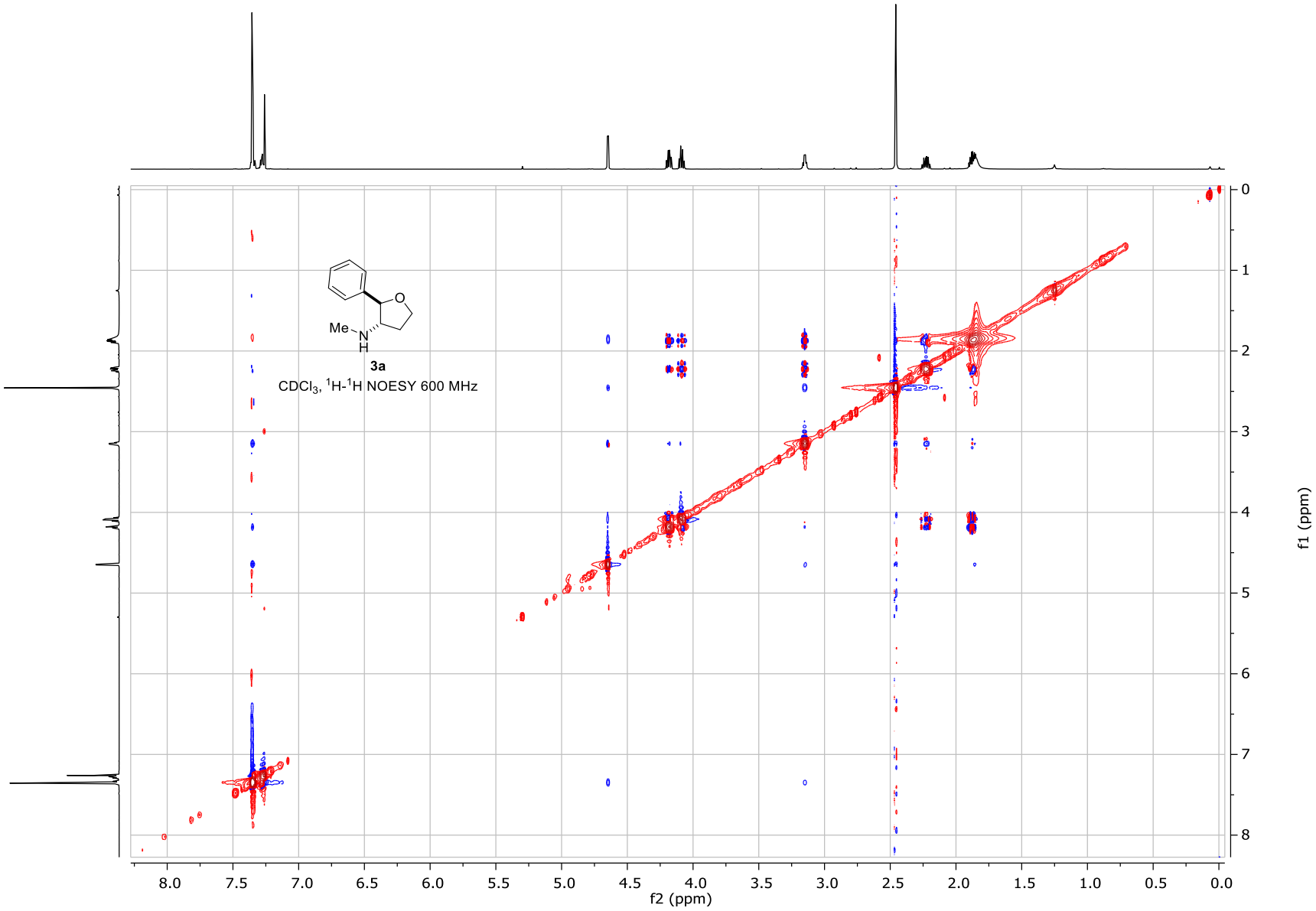
3a

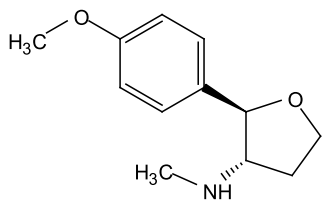
$CDCl_3$, DEPT-135, 151 MHz




Me
N
H
O
3a
CDCl3, 1H-1H COSY 600 MHz
f2 (ppm)
f1 (ppm)


Me
N
H
O
3a
CDCl3, 1H-13C HSQC 600 MHz
f2 (ppm)
f1 (ppm)

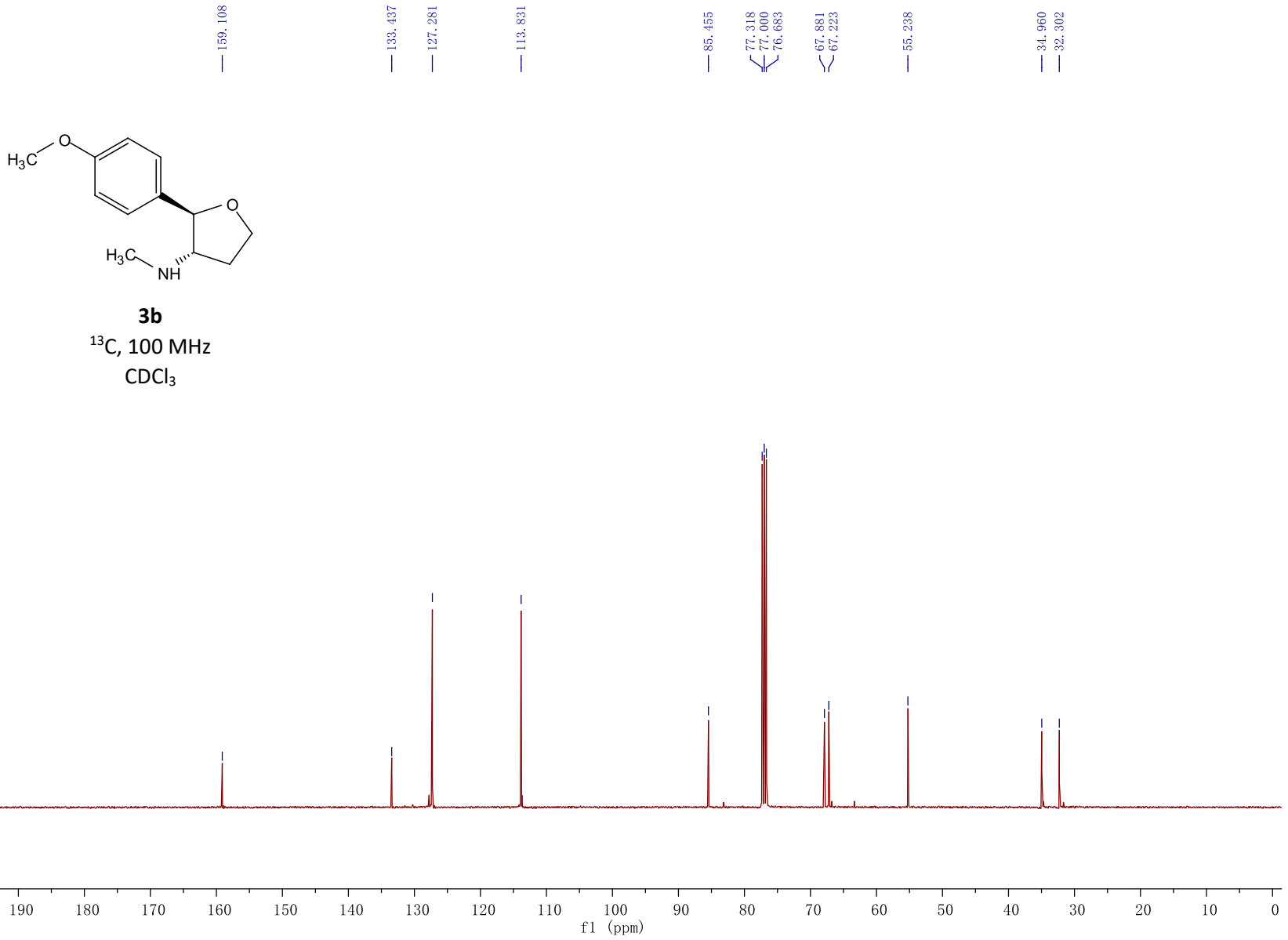

Me
N
H
O
3a
CDCl3, 1H-1H NOESY 600 MHz
f2 (ppm)
f1 (ppm)



3b

^{1}H, 400 MHz

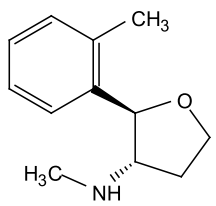
$CDCl_3$



3b

^{13}C, 100 MHz

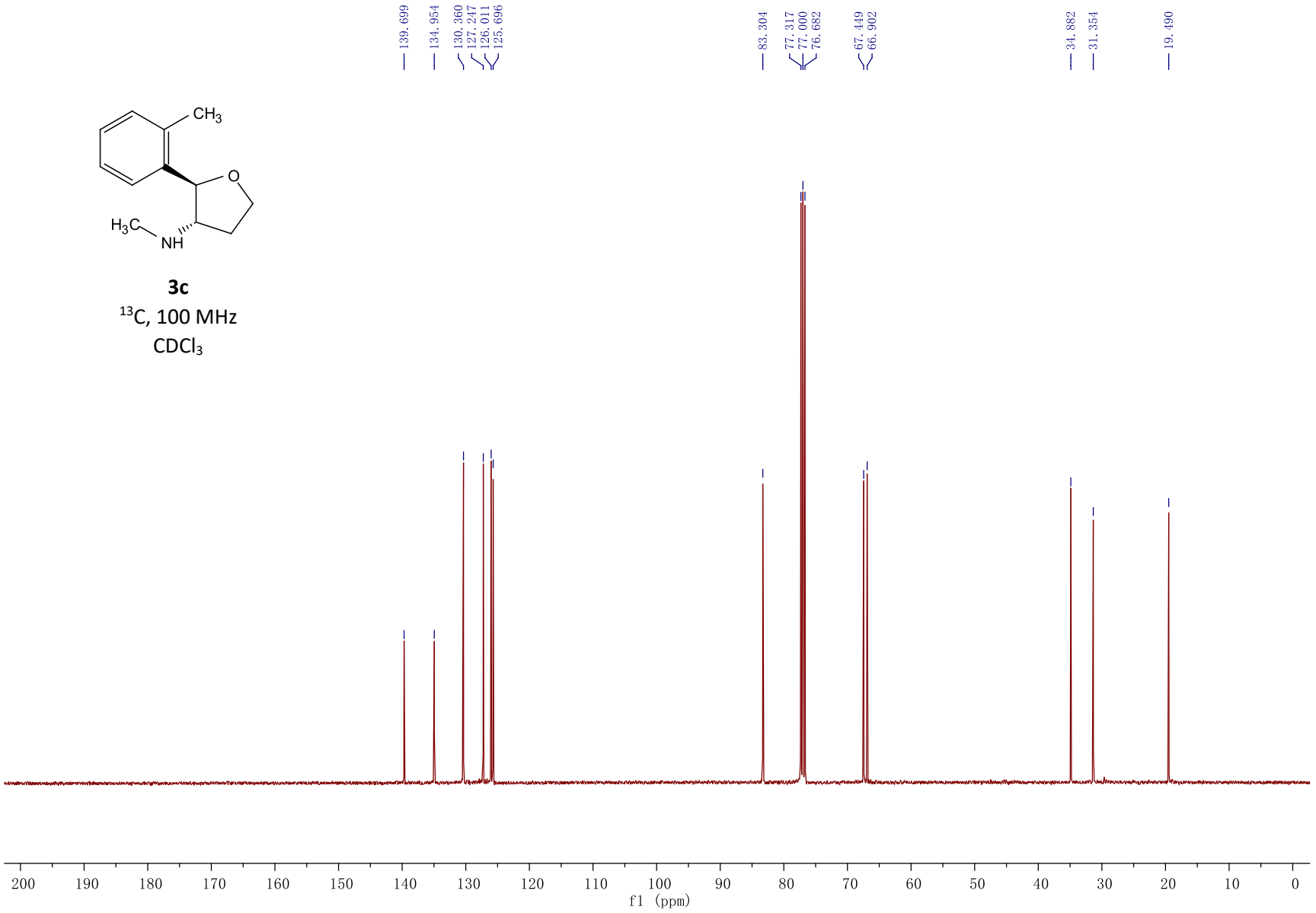
$CDCl_3$



3c

^{1}H, 400 MHz

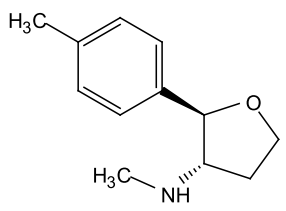
$CDCl_3$



3c

^{13}C, 100 MHz

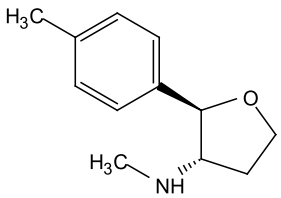
$CDCl_3$



3d

^{1}H, 400 MHz

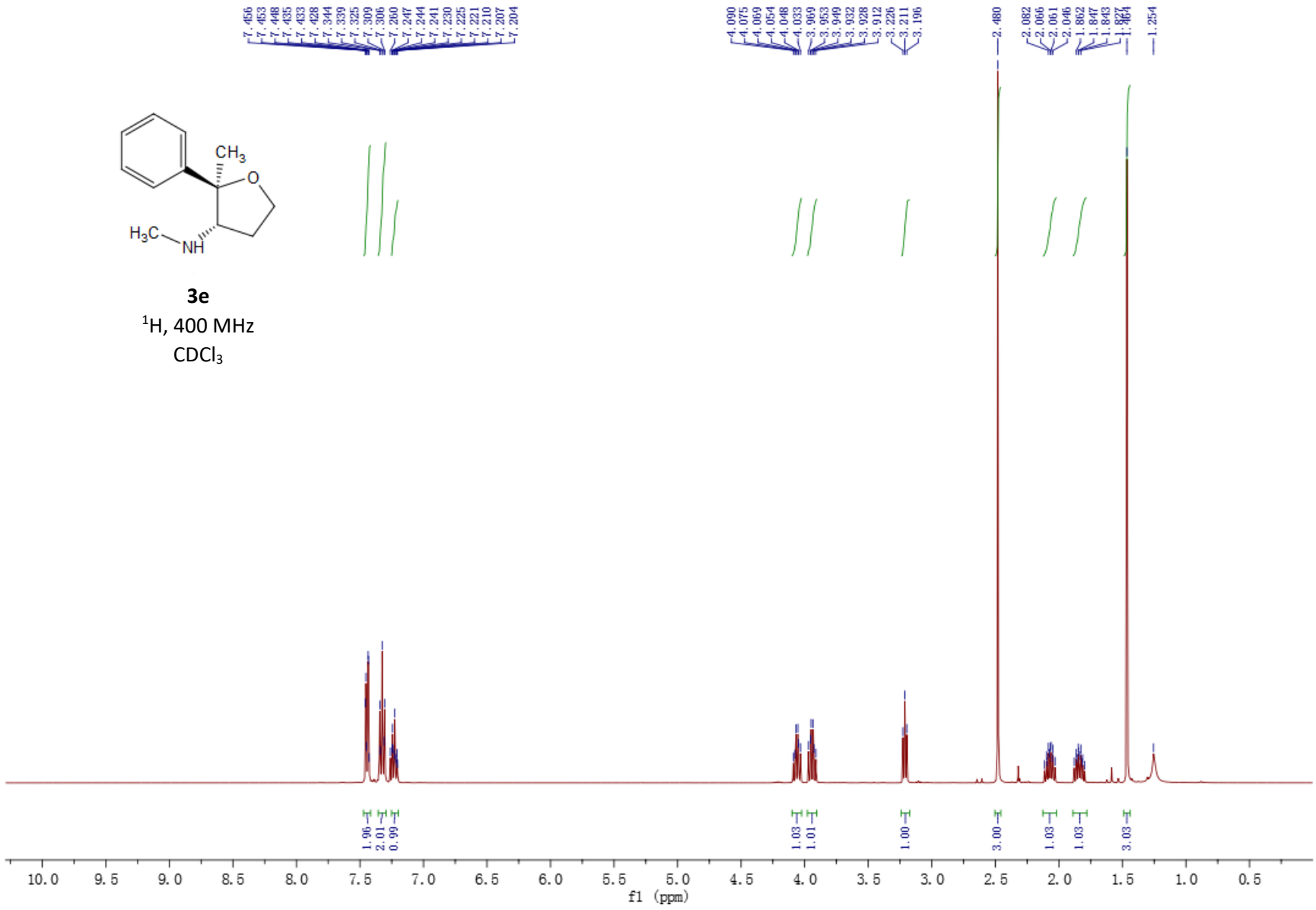
$CDCl_3$



3d

^{13}C, 100 MHz

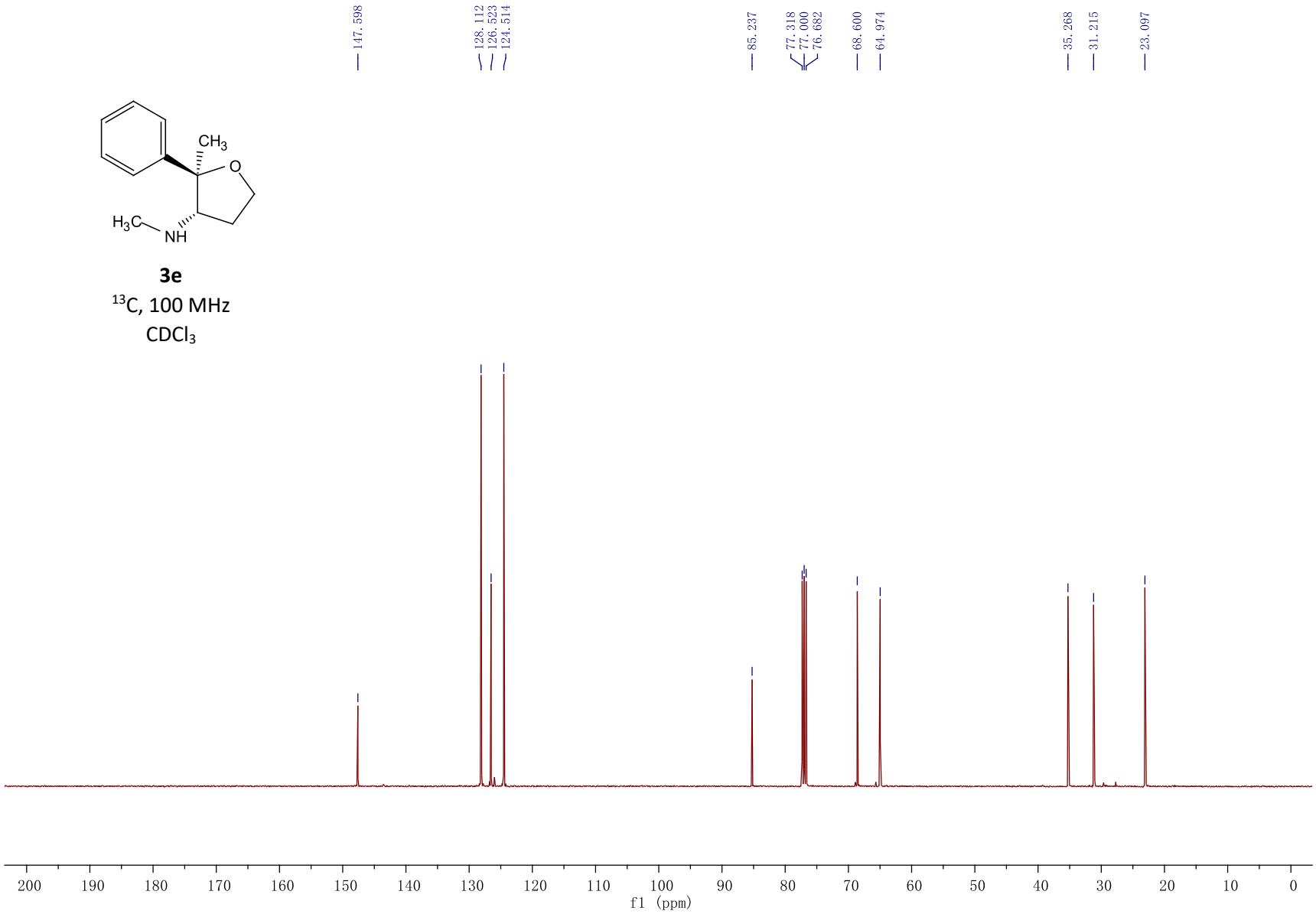
$CDCl_3$



3e

^{1}H, 400 MHz

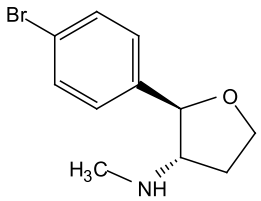
$CDCl_3$



3e

^{13}C, 100 MHz

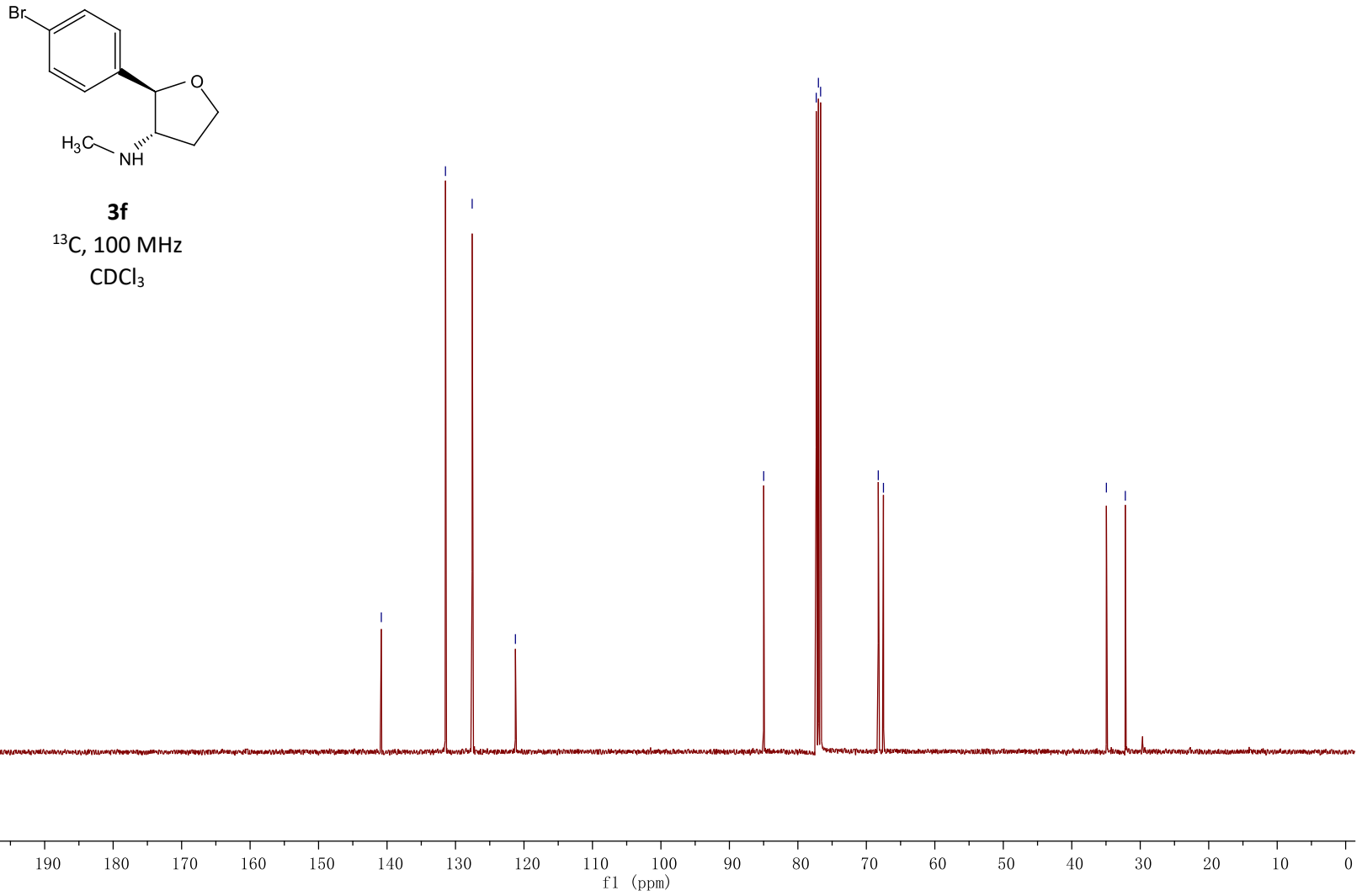
$CDCl_3$



3f

^{1}H, 400 MHz

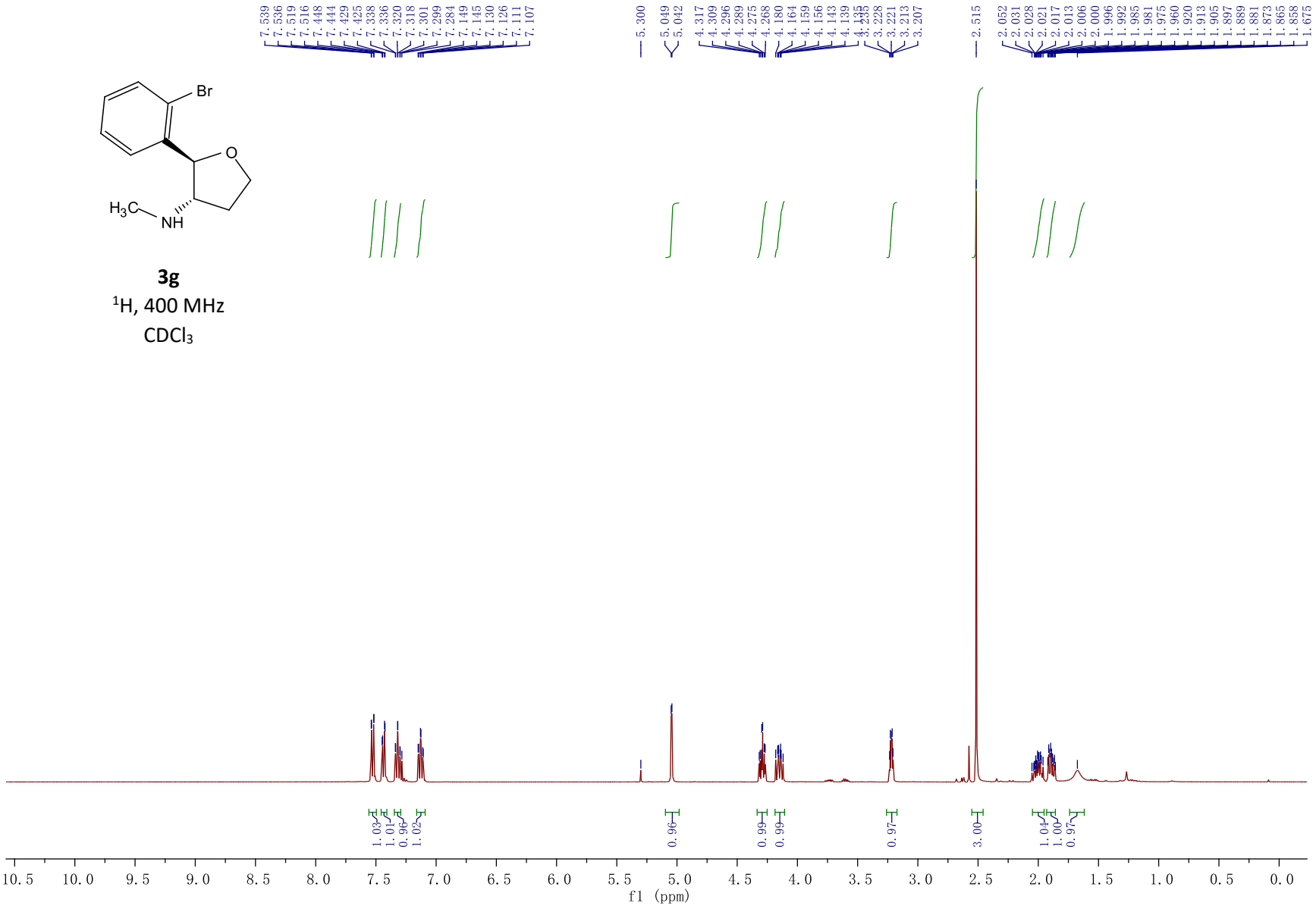
$CDCl_3$



3f

^{13}C, 100 MHz

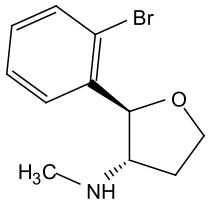
$CDCl_3$



3g

^{1}H, 400 MHz

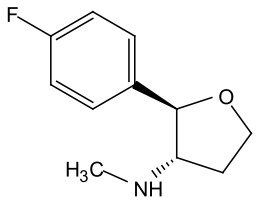
$CDCl_3$



3g

^{13}C, 100 MHz

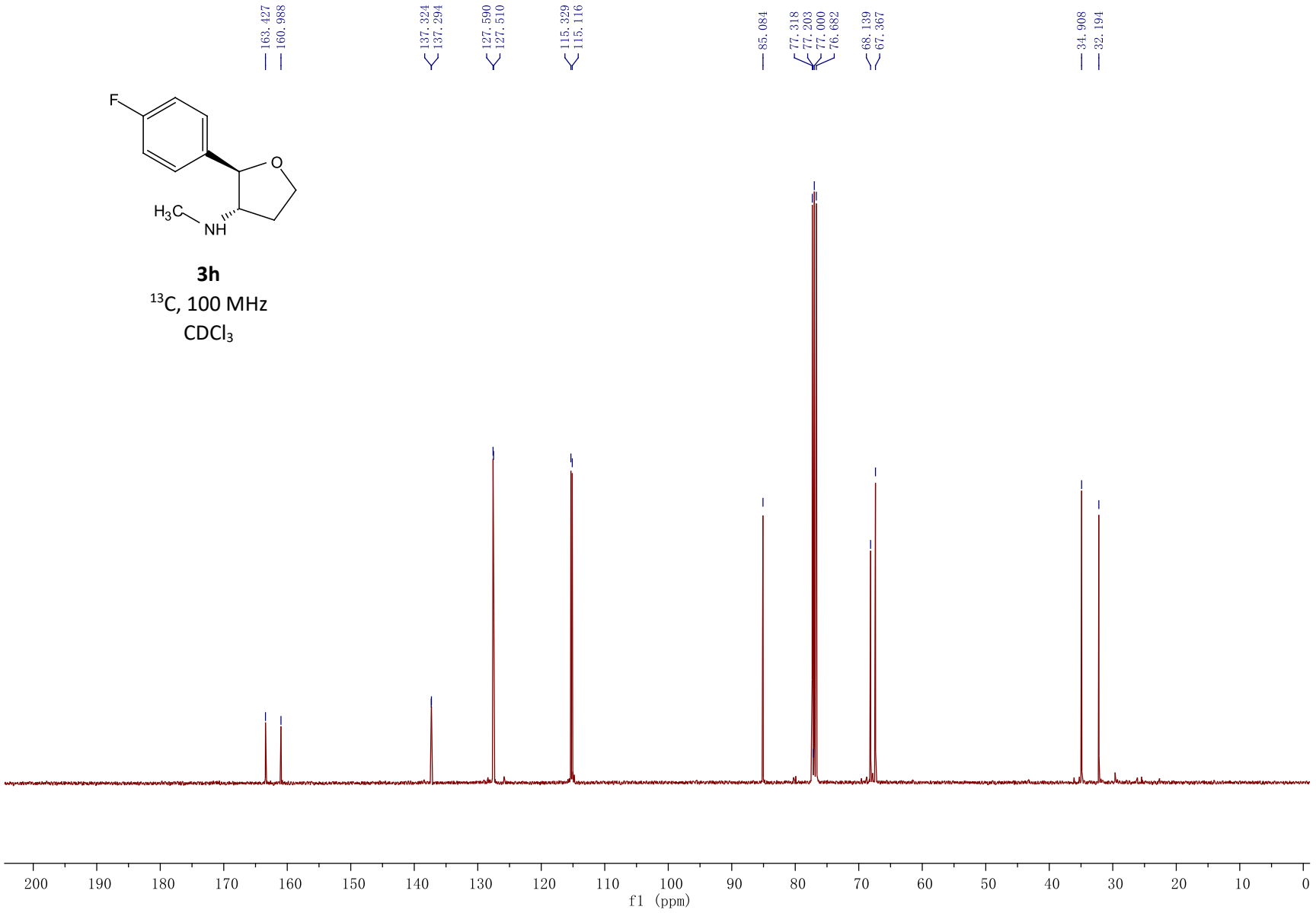
$CDCl_3$



3h

^{1}H, 400 MHz

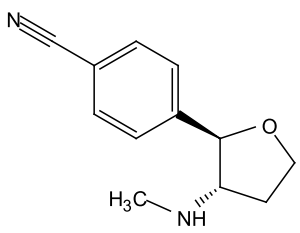
$CDCl_3$



3h

^{13}C, 100 MHz

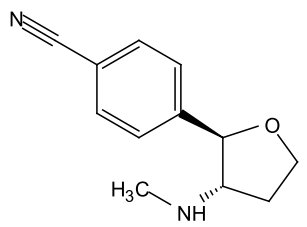
$CDCl_3$



3i

^{1}H, 400 MHz

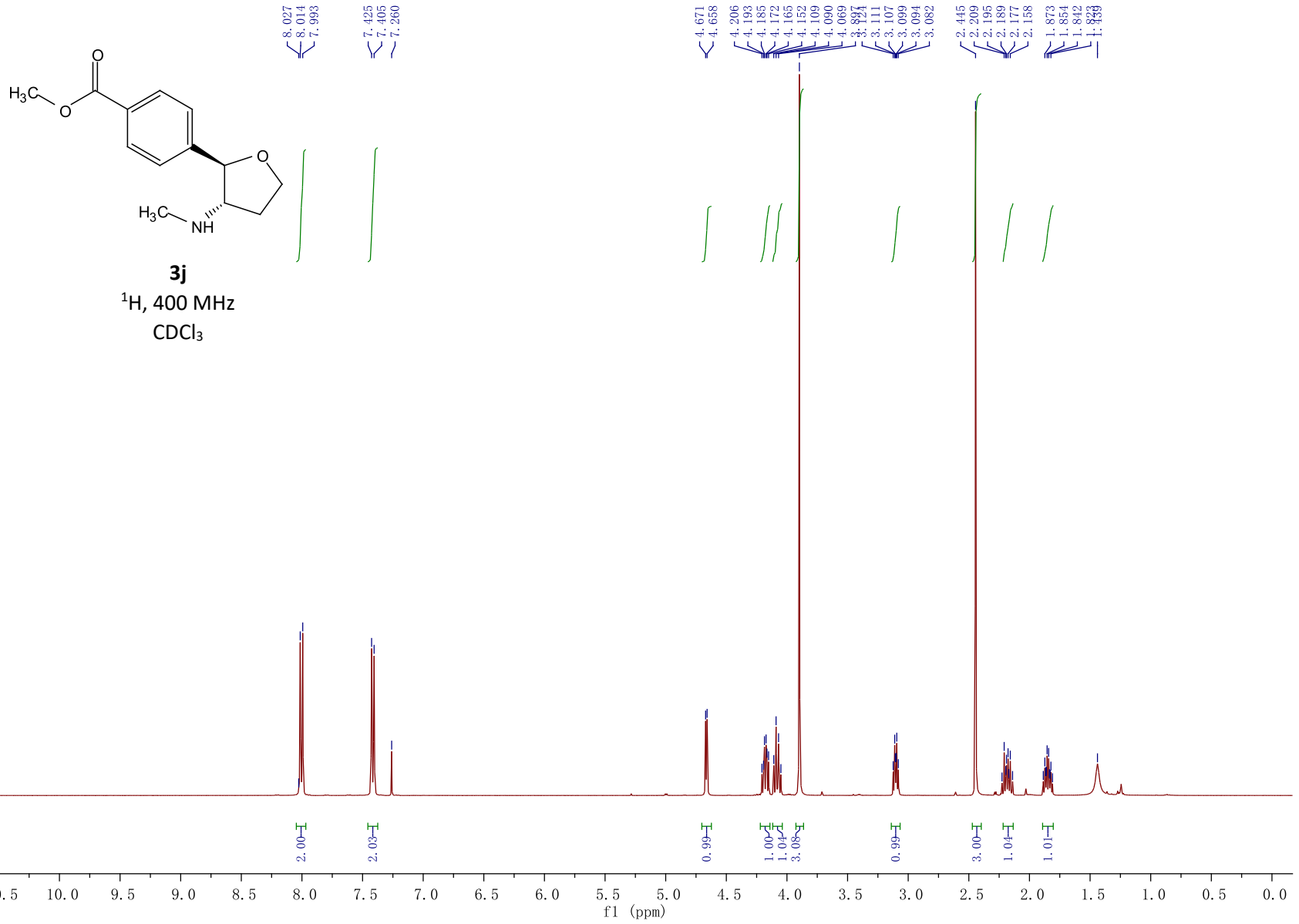
$CDCl_3$



3i

^{13}C, 100 MHz

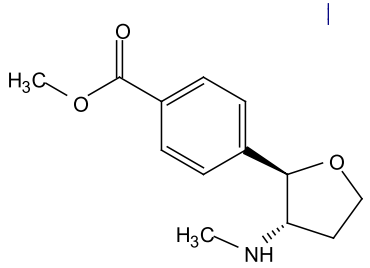
$CDCl_3$



3j

^{1}H, 400 MHz

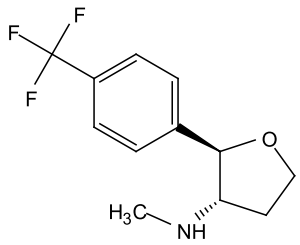
$CDCl_3$



3j

^{13}C, 100 MHz

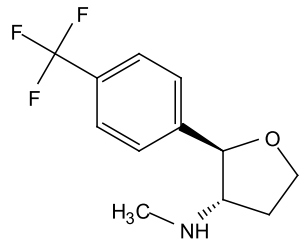
$CDCl_3$



3k

^{1}H, 400 MHz

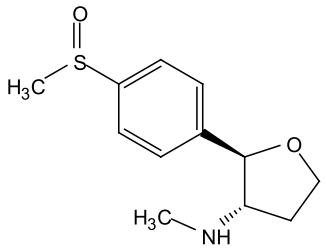
$CDCl_3$



3k

^{13}C, 100 MHz

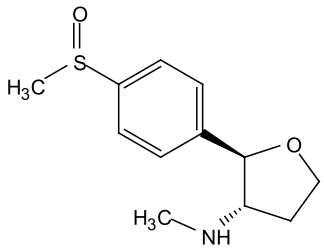
$CDCl_3$



3l

^{1}H, 400 MHz

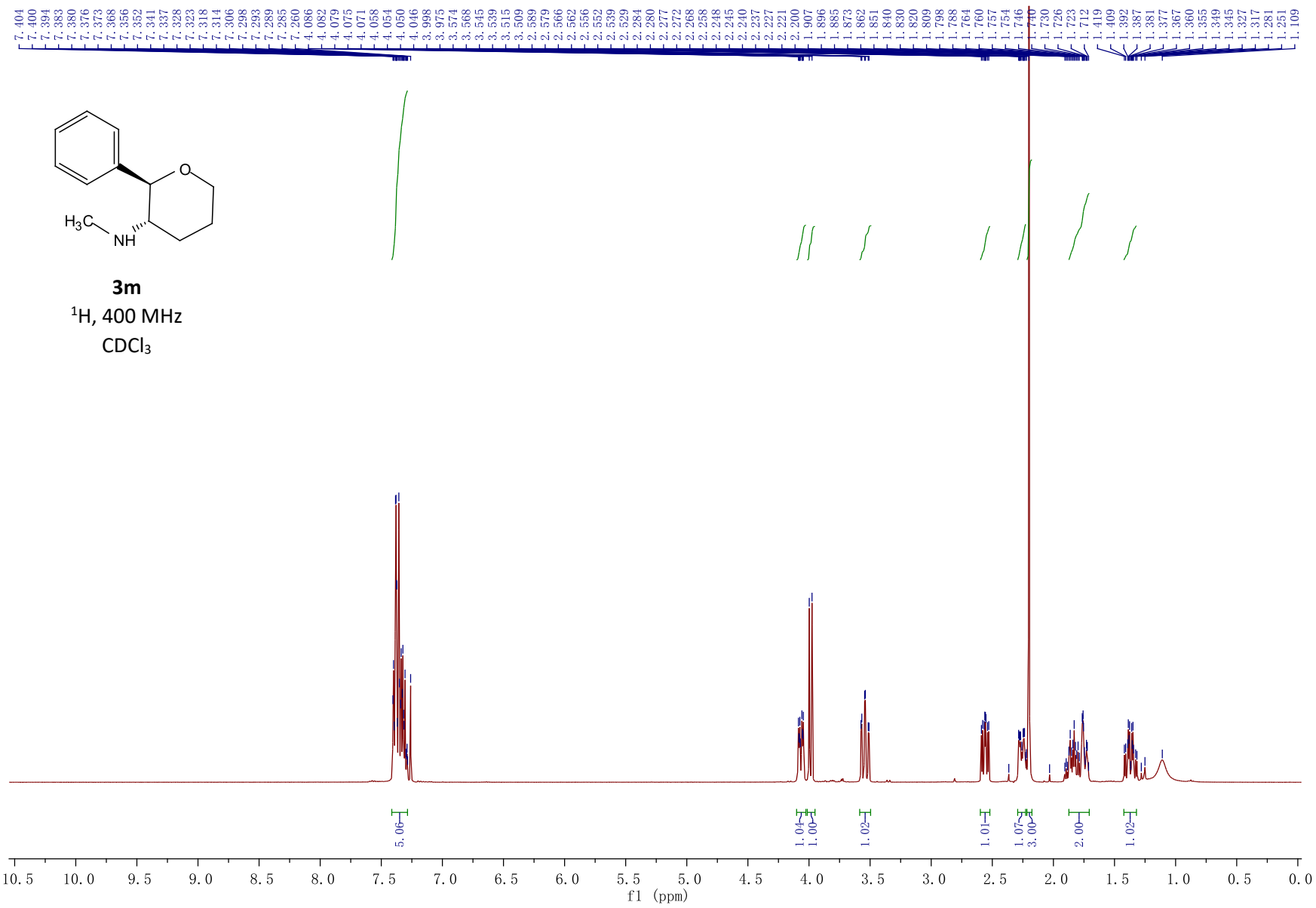
CD_3OD



3l

^{13}C, 100 MHz

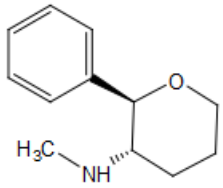
CD_3OD



3m

^{1}H, 400 MHz

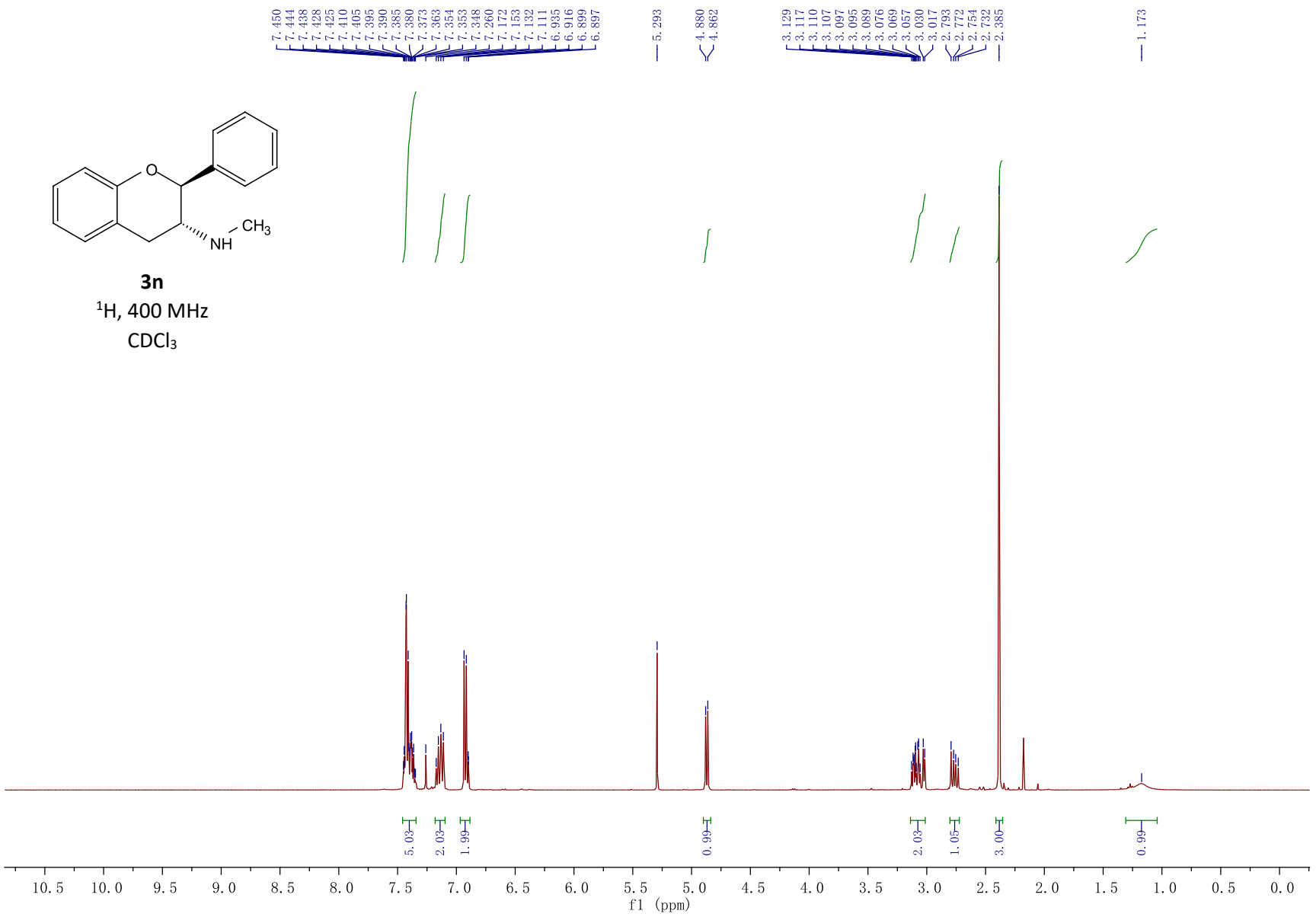
$CDCl_3$



3m

^{13}C, 100 MHz

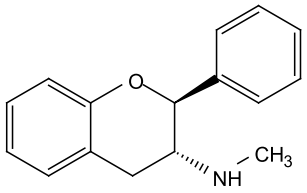
$CDCl_3$



3n

^{1}H, 400 MHz

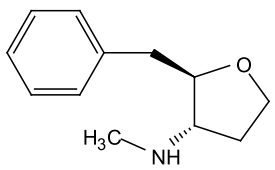
$CDCl_3$



3n

^{13}C, 100 MHz

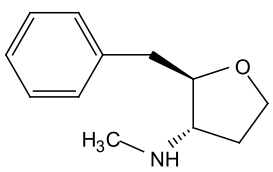
$CDCl_3$



3o

^{1}H, 400 MHz

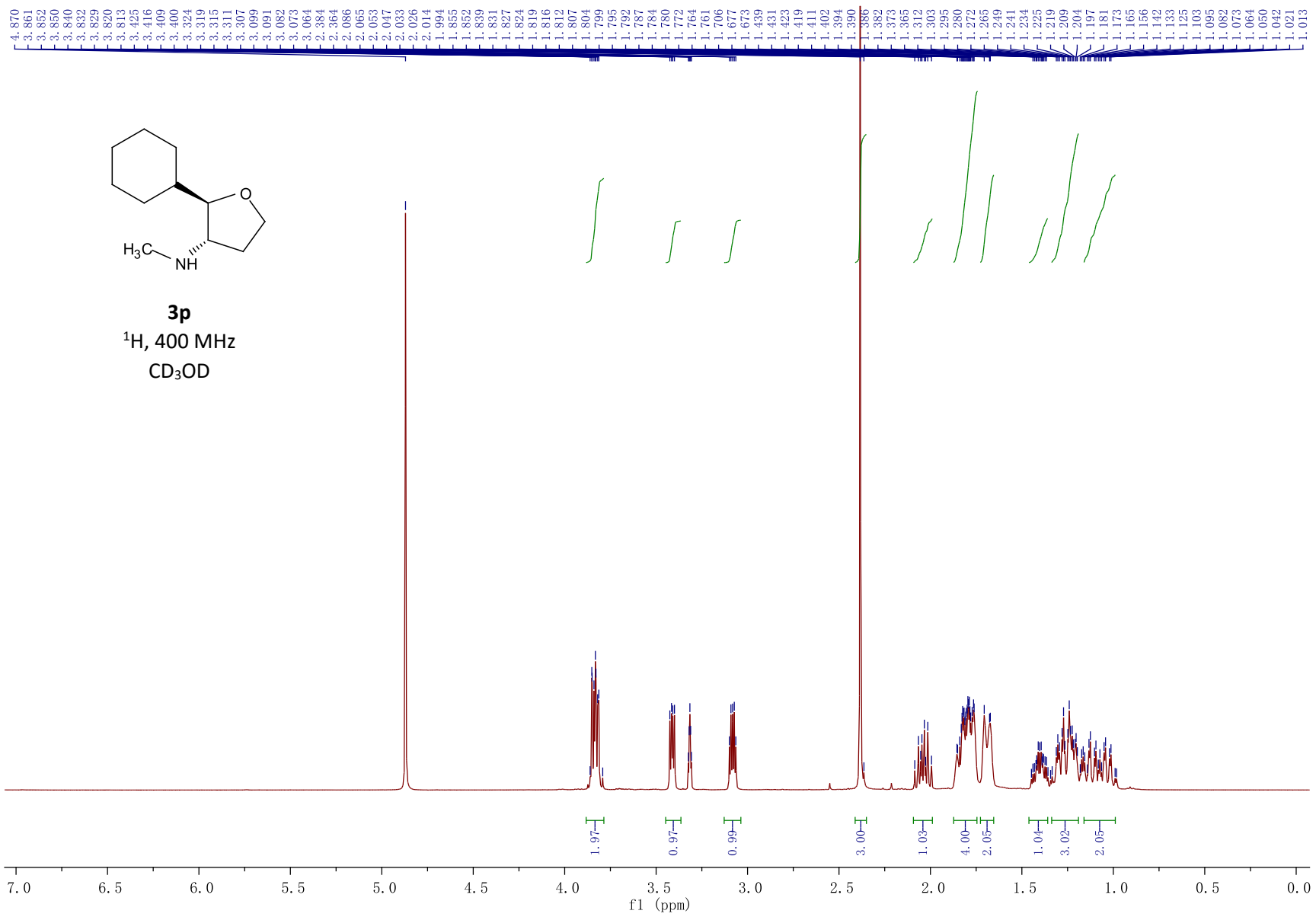
CD_3OD

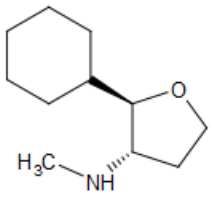


3o

^{13}C, 100 MHz

CD_3OD

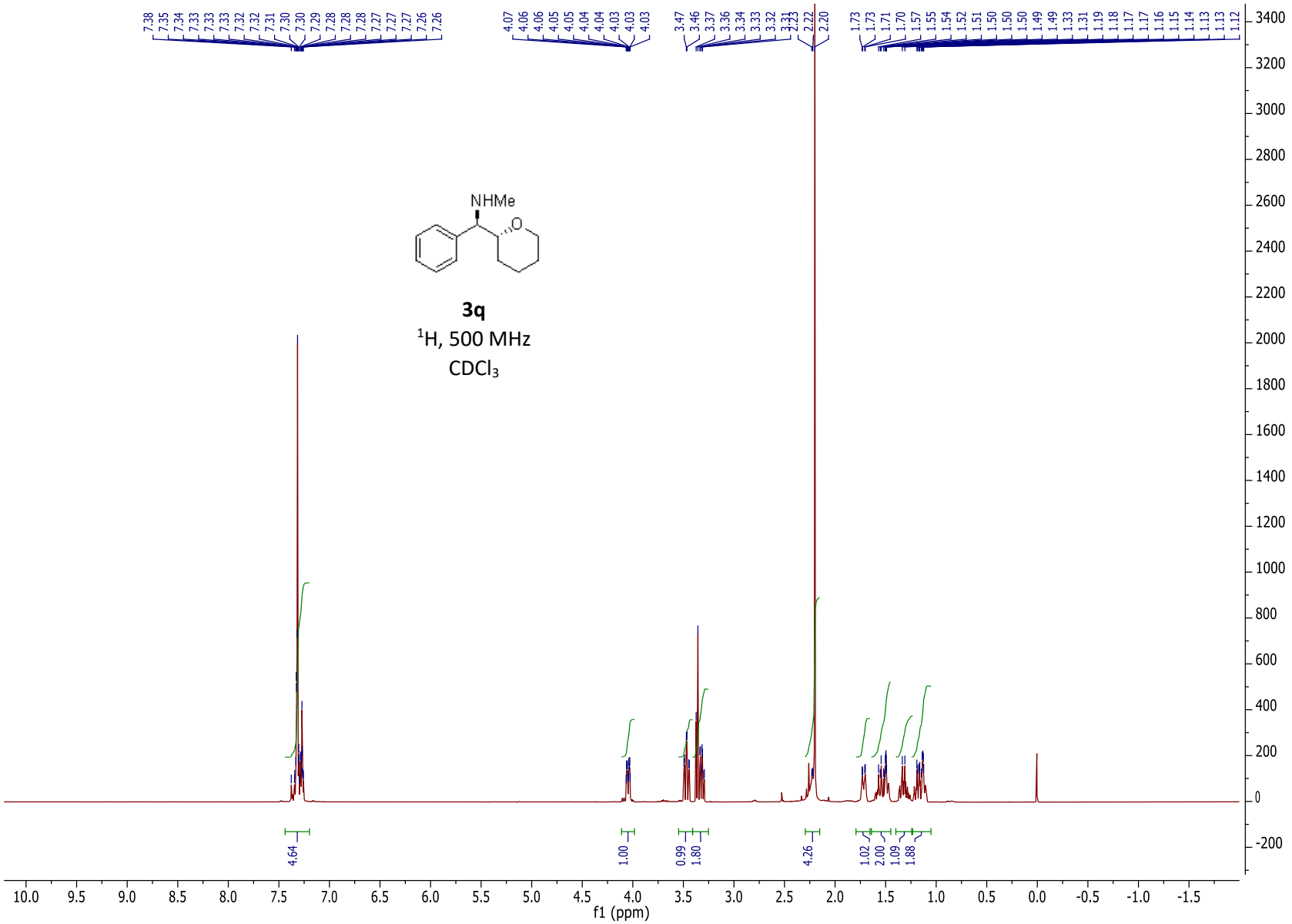

4.870
3.861
3.852
3.850
3.840
3.832
3.829
3.820
3.813
3.425
3.416
3.409
3.400
3.324
3.319
3.315
3.311
3.307
3.099
3.091
3.082
3.073
3.064
2.384
2.364
2.086
2.065
2.053
2.047
2.033
2.026
2.014
1.994
1.855
1.852
1.839
1.831
1.827
1.824
1.819
1.816
1.812
1.807
1.804
1.799
1.795
1.792
1.787
1.784
1.780
1.772
1.764
1.761
1.706
1.677
1.673
1.439
1.431
1.423
1.419
1.411
1.402
1.394
1.390
1.386
1.382
1.373
1.365
1.312
1.303
1.295
1.280
1.272
1.265
1.249
1.241
1.234
1.225
1.219
1.209
1.204
1.197
1.181
1.173
1.165
1.156
1.142
1.133
1.125
1.103
1.095
1.082
1.073
1.064
1.050
1.042
1.021
1.013
O
H3C
NH
3p
1H, 400 MHz
CD3OD
1.97
0.97
0.99
3.00
1.03
4.00
2.05
1.04
3.02
2.05
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

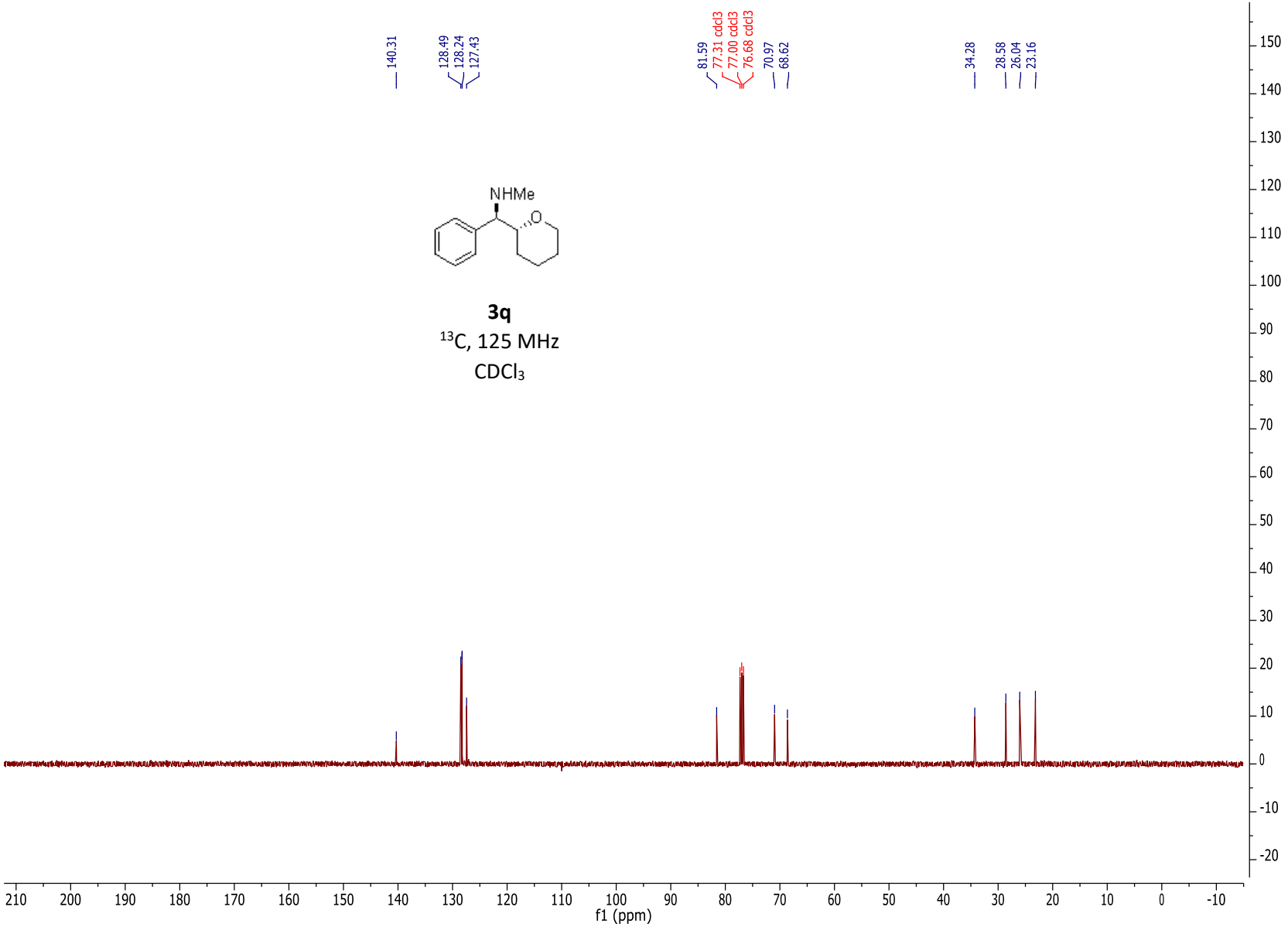


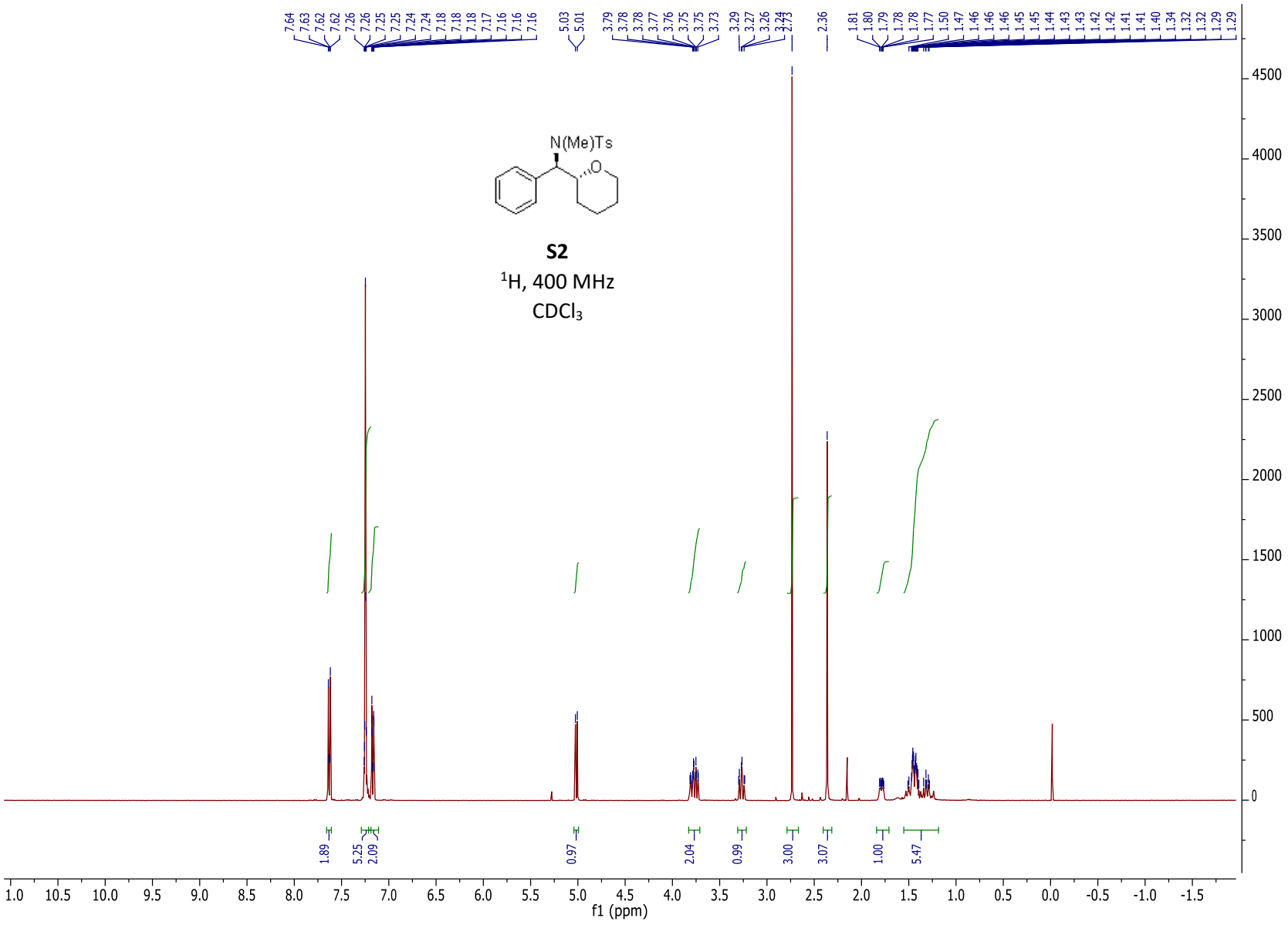
3p

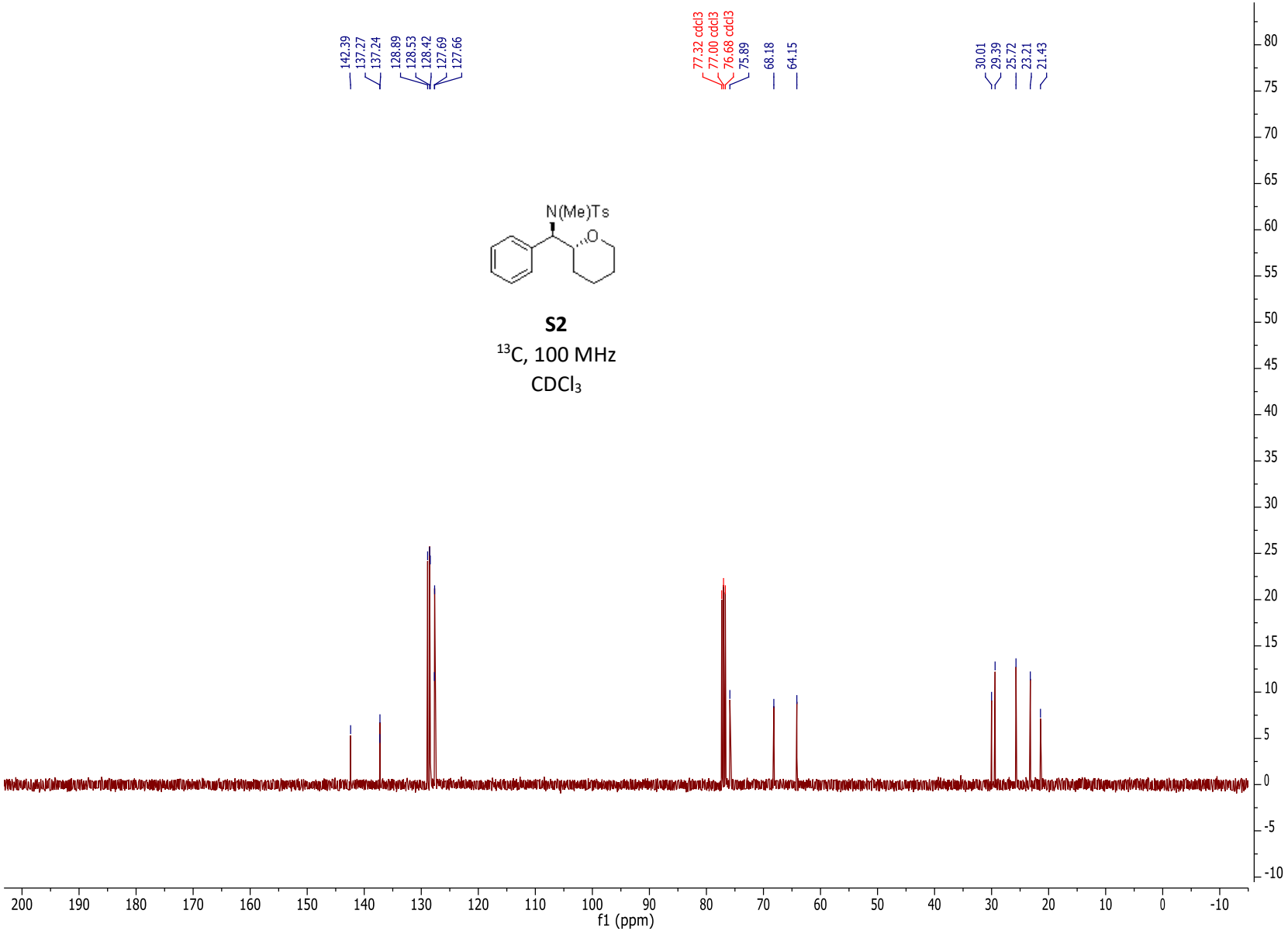
^{13}C, 100 MHz

CD_3OD


NHMe
O
3q
1H, 500 MHz
CDCl3
f1 (ppm)


140.31
128.49
128.24
127.43
81.59
77.31 cdcl3
77.00 cdcl3
76.68 cdcl3
70.97
68.62
34.28
28.58
26.04
23.16
NHMe
O
3q
13C, 125 MHz
CDCl3
f1 (ppm)

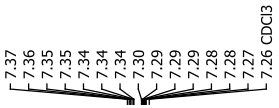

N(Me)Ts
O
S2
1H, 400 MHz
CDCl3
f1 (ppm)

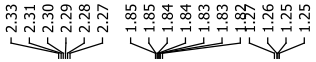


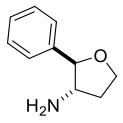
S2

^{13}C, 100 MHz

$CDCl_3$

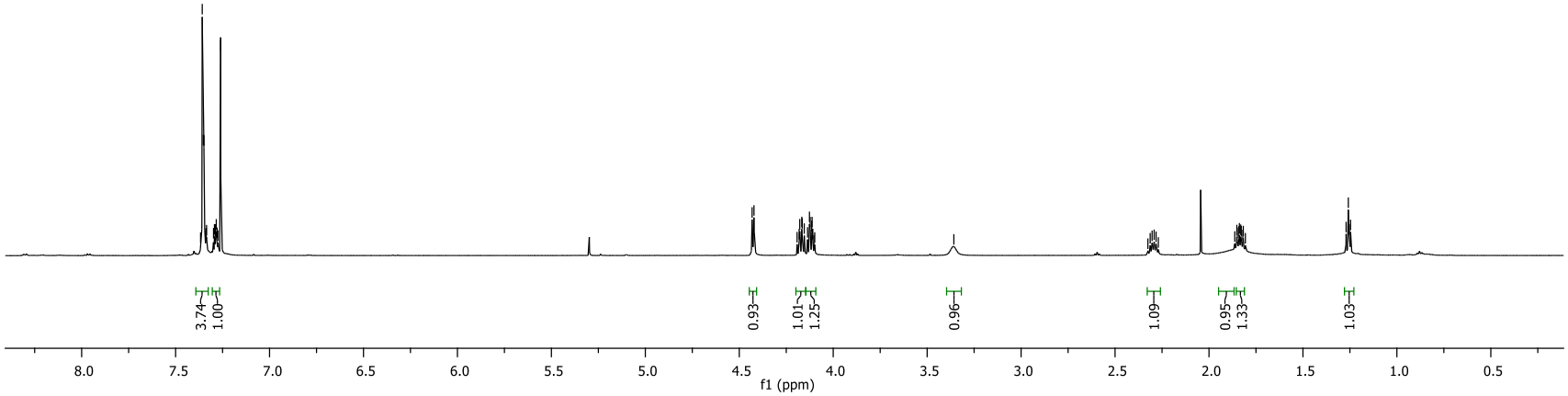


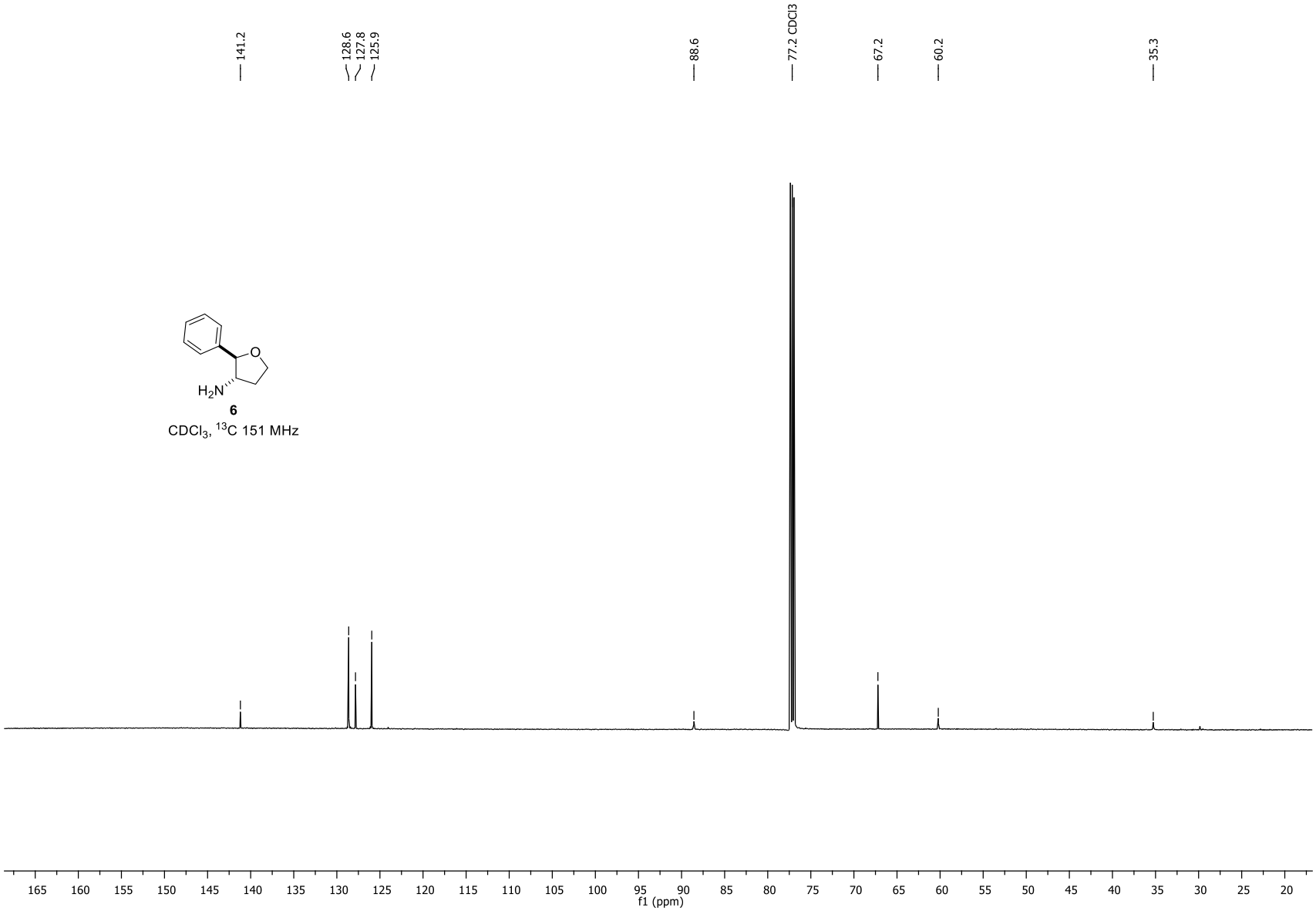


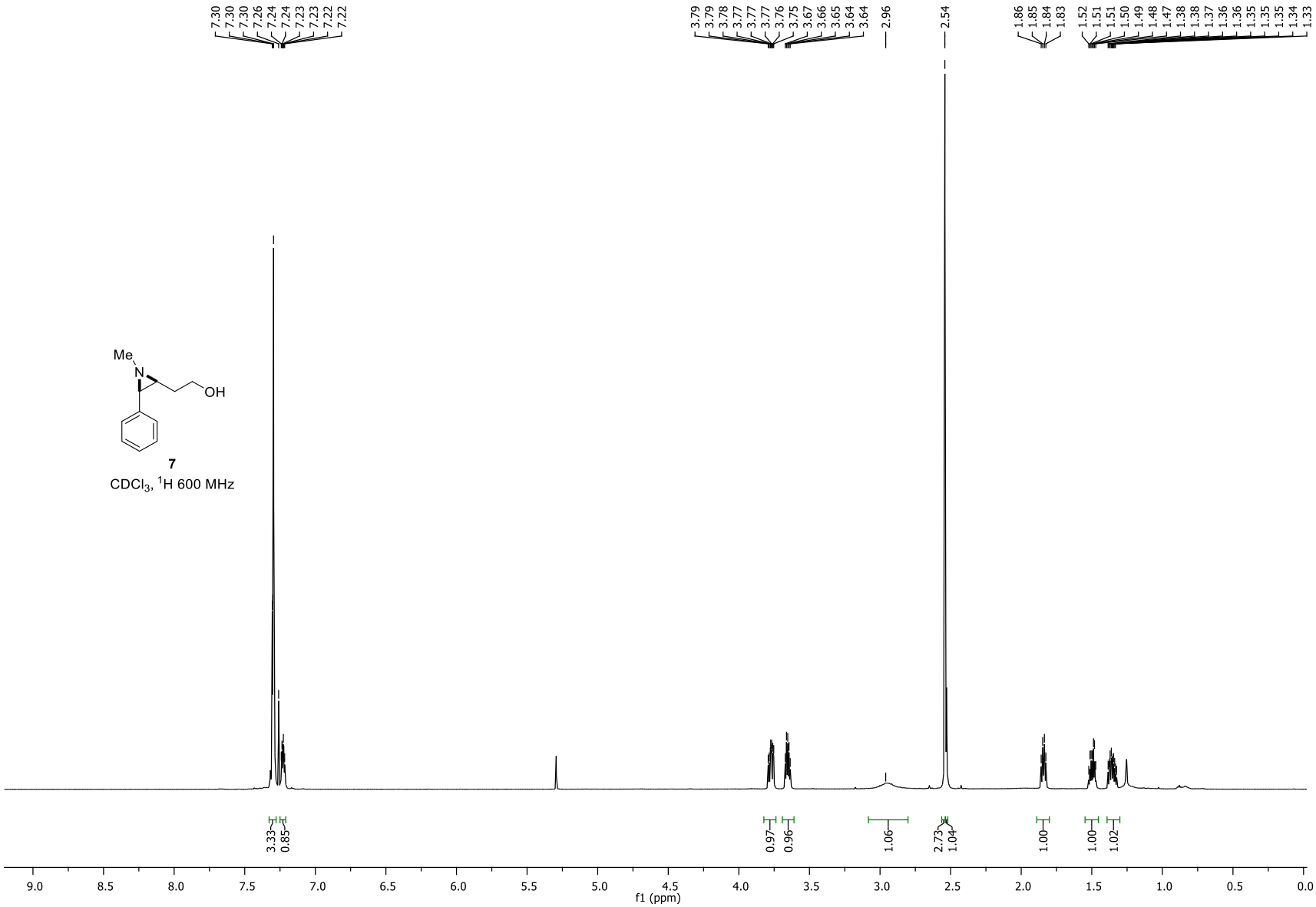


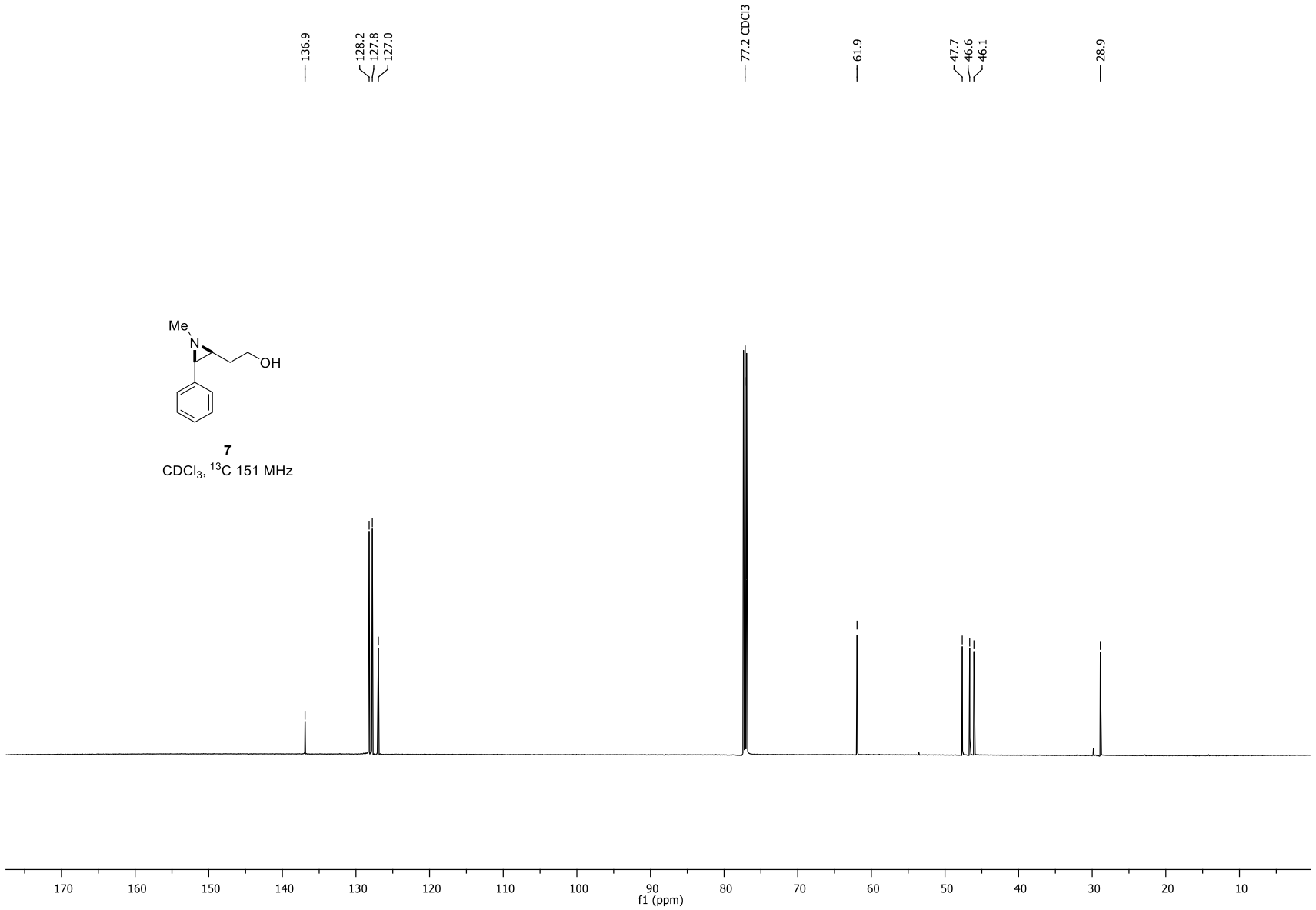
6

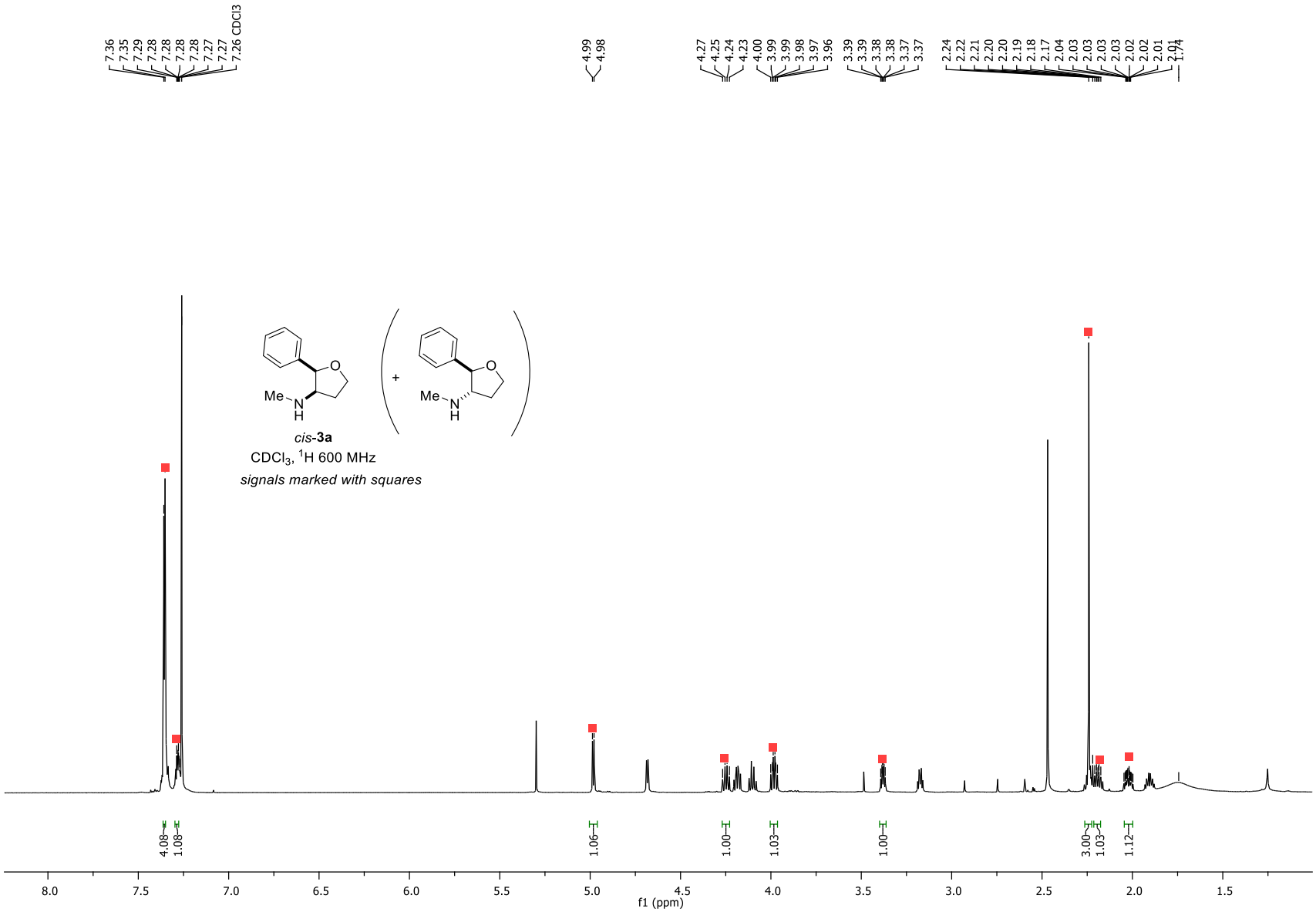
$CDCl_3$, ^1H 600 MHz

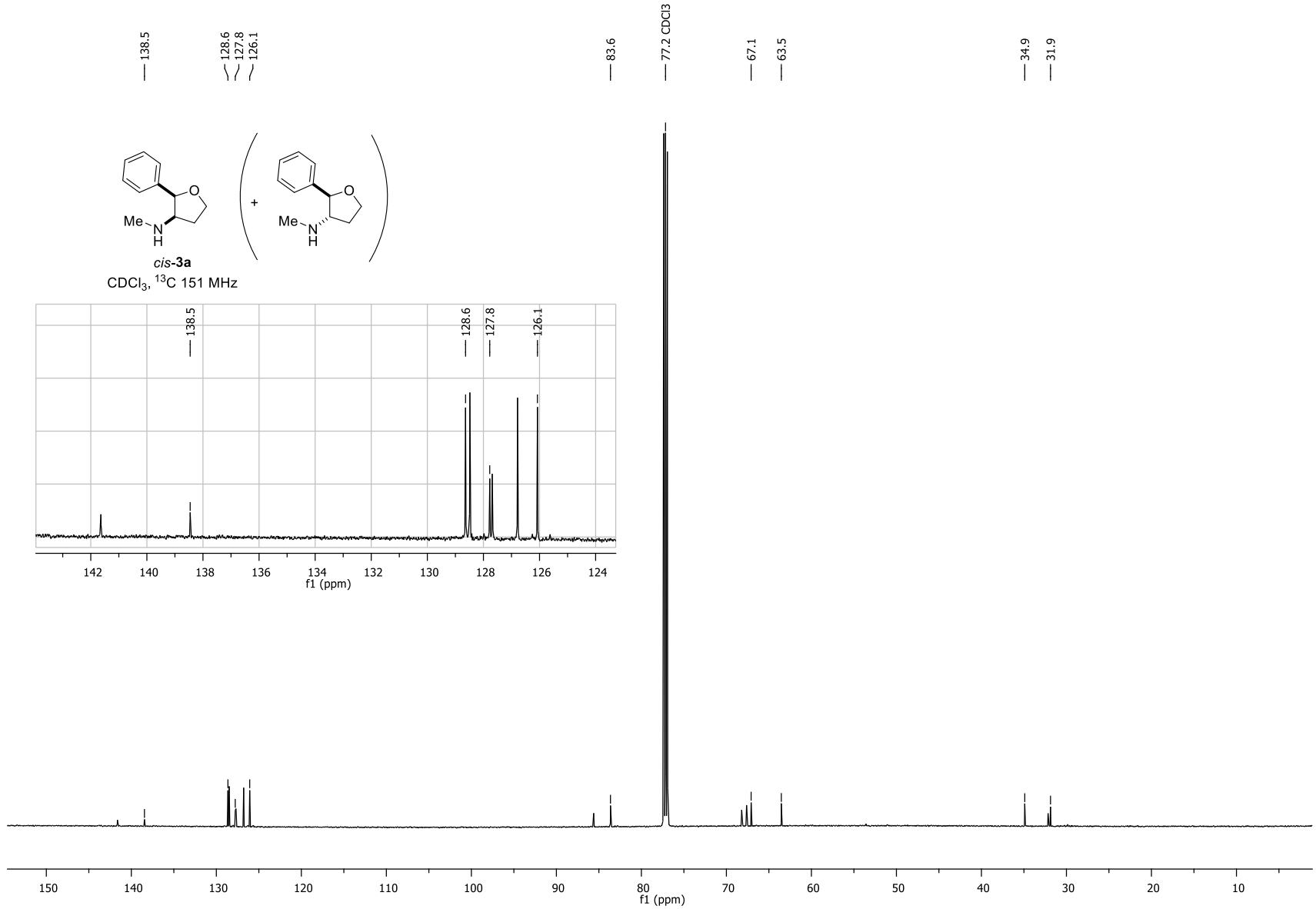



141.2
128.6
127.8
125.9
88.6
77.2 CDCl3
67.2
60.2
35.3
O
H2N
6
CDCl3, 13C 151 MHz
165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)


7.30
7.30
7.30
7.26
7.24
7.24
7.23
7.23
7.22
7.22
3.79
3.79
3.78
3.77
3.77
3.77
3.76
3.75
3.67
3.66
3.65
3.64
3.64
2.96
2.54
1.86
1.85
1.84
1.83
1.52
1.51
1.51
1.50
1.49
1.48
1.47
1.38
1.38
1.37
1.36
1.36
1.35
1.35
1.35
1.34
1.33
Me
N
OH
7
CDCl3, 1H 600 MHz
3.33
0.85
0.97
0.96
1.06
2.73
1.04
1.00
1.00
1.02
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


136.9
128.2
127.8
127.0
77.2 CDCl3
61.9
47.7
46.6
46.1
28.9
Me
N
OH
7
CDCl3, 13C 151 MHz
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.36
7.35
7.29
7.28
7.28
7.28
7.28
7.27
7.27
7.26 CDCl3
4.99
4.98
4.27
4.25
4.24
4.23
4.00
3.99
3.99
3.98
3.97
3.96
3.39
3.39
3.38
3.38
3.37
3.37
2.24
2.22
2.21
2.20
2.20
2.19
2.18
2.17
2.04
2.03
2.03
2.03
2.02
2.02
2.01
2.01
1.74
Me
N
H
O
+
cis-3a
CDCl3, 1H 600 MHz
signals marked with squares
4.08
1.08
1.06
1.00
1.03
1.00
3.00
1.03
1.12
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)


138.5
128.6
127.8
126.1
83.6
77.2 CDCl3
67.1
63.5
34.9
31.9
Me
N
H
O
+
cis-3a
CDCl3, 13C 151 MHz
f1 (ppm)