*Supporting Information for*

# *Tandem Dearomatization/Enantioselective Allylic Alkylation of Pyridines*

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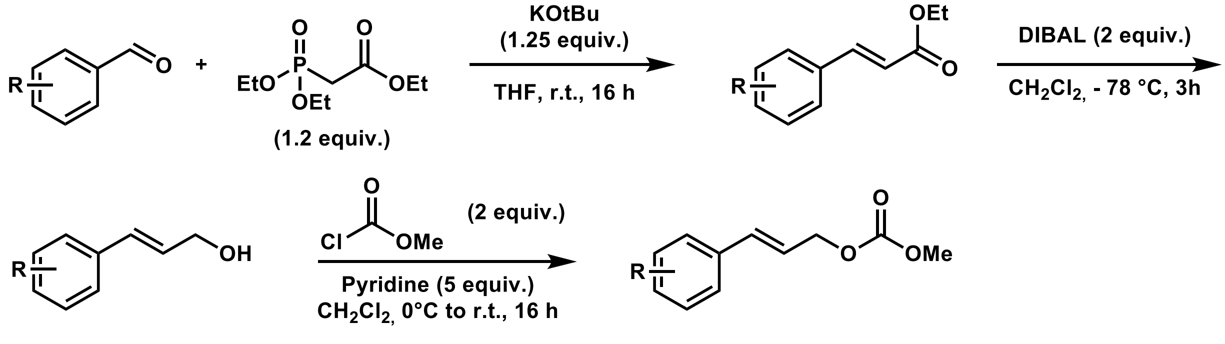
## Materials and Methods

Unless otherwise stated, reactions were performed in oven-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Solvents were dried by passage through an activated alumina column under argon. Reaction temperatures stated in the manuscript or this document are reported as temperature of the surrounding metal heating blocks. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching or $KMnO_4$ staining. Silicycle Silia*Flash*® P60 Academic Silica gel (particle size 40–63 μm) was used for flash chromatography. $^1$H NMR spectra were recorded on Varian Inova 500 MHz and Bruker 400 MHz spectrometers and are reported relative to residual $CHCl_3$ (δ 7.26 ppm) or MeOH (δ 4.87 ppm). $^{13}$C NMR spectra were recorded on a Varian Inova 500 MHz spectrometer (125 MHz) and Bruker 400 MHz spectrometers (101 MHz) and are reported relative to $CHCl_3$ (δ 77.16 ppm) or MeOH (δ 49.00 ppm). $^{19}$F NMR and $^{31}$P NMR Spectra are reported without reference. Data for $^1$H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet. Data for $^{13}$C NMR are reported in terms of chemical shifts (δ ppm) plus (multiplicity, coupling constant (Hz)) in appropriate cases. IR spectra were obtained by use of a Perkin Elmer Spectrum BXII spectrometer or Nicolet 6700 FTIR spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm$^{-1}$). Optical rotations were measured with a Jasco P-2000 polarimeter operating on the sodium D-line (589 nm), using a 100 mm path-length cell. Analytical SFC was performed with a Mettler SFC supercritical $CO_2$ analytical chromatography system utilizing Chiralpak (AD-H, AS-H or IC) or Chiralcel (OD-H, OJ-H, or OB-H) columns (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. High resolution mass spectra (HRMS) were obtained from Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI+), or mixed ionization mode (MM: ESI-APCI+). Absolute configuration of **7a** was determined by X-ray diffraction, and all other products are assigned by analogy. Reagents were purchased from commercial sources and used as received unless otherwise stated. 3-Fluoropyridine, 3-chloropyridine, 4-chloropyridine and 4-(trifluoromethyl)-pyridine were distilled over $CaH_2$ under nitrogen atmosphere prior to use. Diethylsilane was used as received. No significant differences in reactivity and yield were observed from different commercial sources (SigmaAldrich, Gelest or Alfa Aesar). The used Iridium ($[Ir(coe)_2Cl]_2$) catalyst was purchased from Strem Chemicals, Inc, transferred to the glovebox and used as received. The used Palladium catalyst ($Pd(OAc)_2$) was purchased from SigmaAldrich, transferred to the glovebox and used as received.

## Supplementary Schemes: Substrate/reagent and ligand preparation

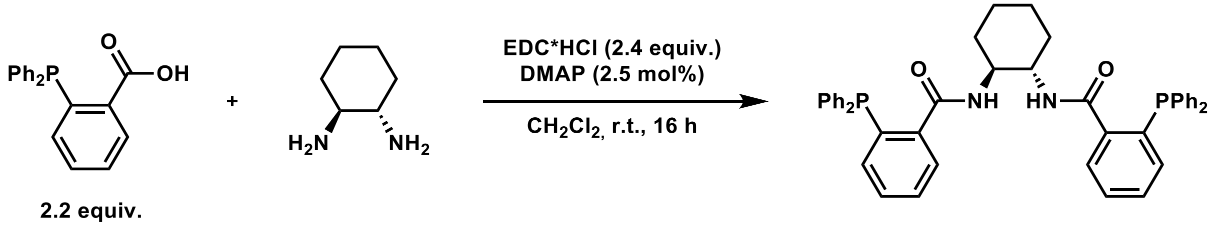
Scheme S1: General synthetic route to carbonate reagents (**2**)

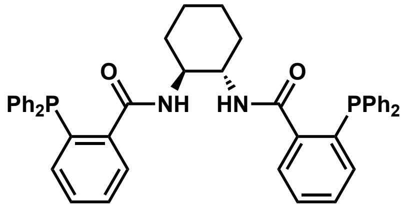
All carbonate reagents used in this study have previously been described in the literature and were prepared accordingly. The general synthetic route can be seen in Scheme 1. The analytical data agrees with the literature.



Scheme S2: General synthetic route to ligand **L3**

Ligands **L1-L10** were prepared either according to literature procedure, are commercially available or as described below. The detailed procedure for the optimized ligand **L3** that is used in this study can be seen below in Scheme 2.





***L3***
**Chemical Formula:** $C_{44}H_{40}N_2O_2P_2$
**Exact Mass: 690.2565**
**Molecular Weight: 690.7635**

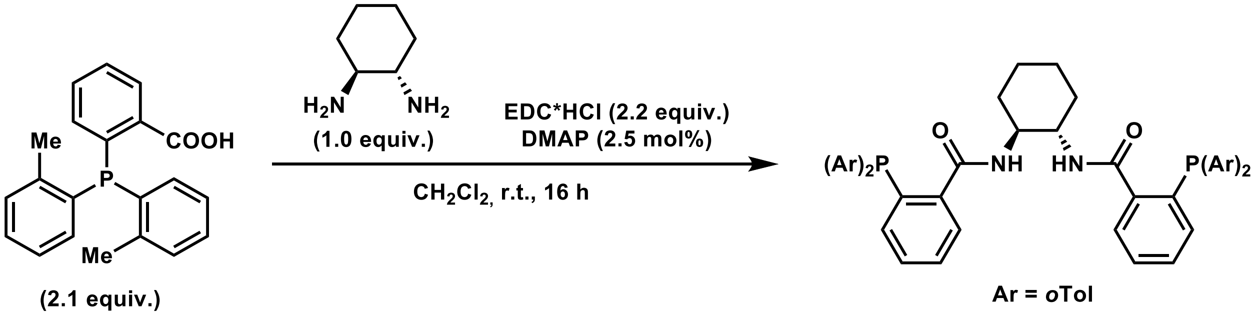
Ligand **L3** (DACH-Trost-Ligand) was prepared following the reaction in Scheme 2 according to a literature procedure (*European Journal of Organic Chemistry* **2007**, *7*, 1145). Therefore, commercial 2-(diphenylphosphaneyl)benzoic acid (15.48 g, 50.6 mmol, 2.2 equiv.) was dissolved in $CH_2Cl_2$ (120 mL). DMAP (70 mg, 0.575 mmol, 2.5 mol%) was added, followed by EDC*HCl (10.58 g, 55.2 mmol, 2.4 equiv.). The mixture was stirred at room temperature for 5 min. (1S,2S)-Cyclohexane-1,2-diamine (2.63 g, 23 mmol, 1.0 equiv.) in $CH_2Cl_2$ (30 mL) was added and the resulting mixture was stirred at room temperature for 16 hours. The reaction was quenched with saturated $NH_4Cl$ solution (~100 mL). The phases were separated, and the organic phase was dried over magnesium sulfate and filtered. The crude reaction mixture was submitted to flash column chromatography over silica gel using hexane/EtOAc = 7/3 as the eluent to yield a white solid (11.5 g). The white solids were redissolved in boiling MeCN (~350 mL) and slowly cooled to room temperature over night to yield white crystals (9.5 g, 13.75 mmol, 60% yield) (Figure S1).

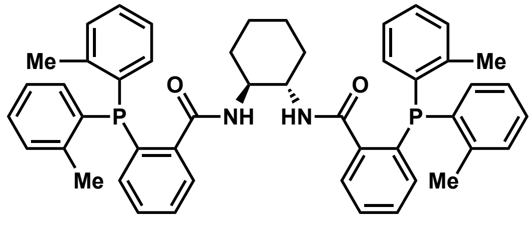
**$^1$H NMR (300 MHz, $CDCl_3$):** δ 7.60 – 7.55 (m, 2H), 7.34 – 7.16 (m, 24H), 6.94 – 6.87 (m, 2H), 6.32 (d, *J* = 7.2 Hz, 2H), 3.85 – 3.71 (m, 2H), 1.90 – 1.80 (m, 2H), 1.70 – 1.59 (m, 2H), 1.28 – 1.15 (m, 2H), 1.05 – 0.90 (m, 2H);

**$^{31}$P NMR (121 MHz, $CDCl_3$):** δ -9.75.

*Figure 1. Recrystallization of ligand **L3**.*

Scheme S3: General synthetic route to ligand **L9**





***L9***

**Chemical Formula:** $C_{48}H_{48}N_2O_2P_2$
**Exact Mass: 746.3191**
**Molecular Weight: 746.8715**

Ligand **L9** was prepared according to Scheme 3. Therefore 2-(di-o-tolylphosphaneyl)benzoic acid (0.97 g, 2.9 mmol, 2.1 equiv.) was dissolved in $CH_2Cl_2$ (10 mL). DMAP (4.3 mg, 0.035 mmol, 2.5 mol%) was added, followed by EDC*HCl (0.59 g, 3.08 mmol, 2.2 equiv.). The mixture was stirred at room temperature for 5 min. (1S,2S)-Cyclohexane-1,2-diamine (160 mg, 1.4 mmol, 1.0 equiv.) in $CH_2Cl_2$ (5 mL) was added and the resulting mixture was stirred at room temperature for 16 hours. The reaction was quenched with saturated $NH_4Cl$ solution (~20 mL). The phases were separated, and the organic phase was dried over magnesium sulfate and filtered. The crude reaction mixture was submitted to flash column chromatography over silica gel using hexane/EtOAc = 7/3 as the eluent to yield a white solid (0.81 g, 1.1 mmol, 79% yield).

**$^1$H NMR (400 MHz, CDCl$_3$):** δ 7.60 – 7.55 (m, 2H), 7.30 – 7.15 (m, 12H), 7.08 (t, *J* = 7.2 Hz, 2H), 7.02 – 6.96 (m, 2H), 6.87 (ddd, *J* = 7.5, 3.8, 1.5 Hz, 2H), 6.77 – 6.69 (m, 4H), 6.44 – 6.32 (bs, 2H), 3.77 – 3.66 (m, 2H), 2.33 (dd, *J* = 6.8, 1.6 Hz, 12H), 1.84 – 1.76 (m, 2H), 1.63 – 1.55 (m, 2H), 1.20 – 1.11 (m, 2H), 0.90 – 0.78 (m, 2H);

**$^{13}$C NMR (101 MHz, CDCl$_3$):** (several signals overlap, see spectra) δ 169.22, 169.21, 142.40, 142.14, 141.96, 141.68, 135.72, 135.60, 135.38, 135.26, 134.54, 134. 42, 134.35, 132.95, 132.90, 130.20, 130.18, 130.14, 130.10, 128.90, 128.75, 128.63, 127.80, 127.75, 126.42, 126.06, 53.71, 31.53, 24.56, 21.33, 21.25, 21.12, 21.04;

**$^{31}$P NMR (121 MHz, CDCl$_3$):** δ -24.79;

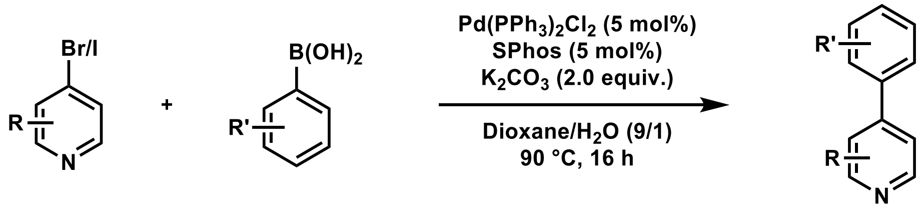
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 747.3269, found: 747.3271;

**R$_f$** (Hexane/EtOAc = 7/3): 0.21;

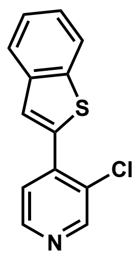
**ATR-IR** ν (cm$^{-1}$): 3750, 3055, 3005, 2936, 2856, 2242, 1922, 1732, 1696, 1636, 1586, 1522, 1464, 1453, 1434, 1378, 1328, 1306, 1269, 1202, 1161, 1130, 1033, 910, 872, 829, 799, 751, 733.

## General procedure 1: Suzuki-Miyaura cross coupling for the synthesis of substituted pyridines

Scheme S4: General procedure for the preparation of pyridine substrates



The pyridines (**1**) that were used in this study were either prepared according to literature procedure, were commercially available or were prepared as described above in Scheme 4. Pd(PPh$_3$)$_2$Cl$_2$ (5 mol%), SPhos (5 mol%) and K$_2$CO$_3$ (2.0 equiv.) were added to a 25 mL screw vial under air. The solid aryl boronic acid (1.2 equiv.) was added, followed by the pyridine (1.0 equiv.), if solid. The vial was sealed with a septum screw cap and evacuated using standard Schlenk line technology. The atmosphere was refilled with nitrogen. Dioxane and water (9/1) were added subsequentially (~0.2 M) and the mixture was stirred at room temperature. Pyridine (1.0 equiv.) was added, if liquid. The reaction mixture was then heated to 90 °C for 16 hours. The mixture was cooled to room temperature and diluted with EtOAc (~100 mL) and brine (~100 mL). The phases were separated and the organic phase was dried over magnesium sulfate and filtered. The pure aryl pyridines were separated by flash column chromatography over silica gel using hexane/EtOAc (typically 9/1 to 8/2) as eluent.



***1l***

**Chemical Formula:** $C_{13}H_8ClNS$
**Exact Mass: 245.0066**
**Molecular Weight: 245.7240**

4-(benzo[b]thiophen-2-yl)-3-chloropyridine **1l** was synthesized following the general procedure using 4-iodo-3-chloropyridine (1.0 g, 4.2 mmol, 1.0 equiv.) and benzo[b]thiophen-2-ylboronic acid (0.90 g, 5.04 mmol, 1.2 equiv.). The desired product **1l** was obtained as white solids (0.72 g, 2.93 mmol, 70% yield).

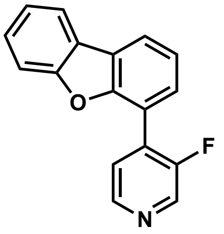
**$^1$H NMR (400 MHz, CDCl$_3$):** δ 8.71 (s, 1H), 8.51 (d, *J* = 5.1 Hz, 1H), 7.90 – 7.84 (m, 3H), 7.52 (dd, *J* = 5.1, 0.6 Hz, 1H), 7.43 – 7.38 (m, 2H);

**$^{13}$C NMR (101 MHz, CDCl$_3$):** δ 151.05, 148.00, 140.45, 140.13, 139.67, 137.18, 129.50, 126.42, 125.71, 124.97, 124.79, 124.58, 122.25;

**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 246.0144, found: 246.0140;

**R$_f$** (Hexane/EtOAc = 8.5/1.5): 0.18;

**ATR-IR** ν (cm$^{-1}$): 3054, 1578, 1473, 1435, 1396, 1239, 1103, 1040, 955, 864, 830, 761, 744, 722.



***1m***

**Chemical Formula:** $C_{17}H_{10}FNO$
**Exact Mass: 263.0746**
**Molecular Weight: 263.2714**

4-(dibenzo[b,d]furan-4-yl)-3-fluoropyridine **1m** was synthesized following the general procedure using 4-iodo-3-fluoropyridine (1.0 g, 4.5 mmol, 1.0 equiv.) and dibenzo[b,d]furan-4-ylboronic acid (1.14 g, 5.4 mmol, 1.2 equiv.). The desired product **1m** was obtained as white solids (0.5 g, 1.9 mmol, 42% yield).

**$^1$H NMR (400 MHz, CDCl$_3$):** δ 8.65 (d, *J* = 2.1 Hz, 1H), 8.58 (dd, *J* = 4.9, 1.0 Hz, 1H), 8.06 (dd, *J* = 7.7, 1.3 Hz, 1H), 8.01 (ddd, *J* = 7.7, 1.3, 0.7 Hz, 1H), 7.73 (dd, *J* = 6.3, 4.9 Hz, 1H), 7.63 – 7.57 (m, 2H), 7.52 – 7.44 (m, 2H), 7.39 (td, *J* = 7.5, 1.0 Hz, 1H);

**$^{13}$C NMR (101 MHz, CDCl$_3$):** δ 156.85 (d, *J* = 258.9 Hz), 156.30, 153.41, 145.93 (d, *J* = 5.2 Hz), 139.22 (d, *J* = 25.3 Hz), 131.78 (d, *J* = 12.0 Hz), 128.22 (d, *J* = 3.7 Hz), 127.81, 125.62, 125.26, 123.95, 123.27, 123.13, 121.92, 120.95, 117.58, 112.02;

**$^{19}$F NMR (282 MHz, CDCl$_3$):** δ -128.92 (d, *J* = 6.4 Hz);

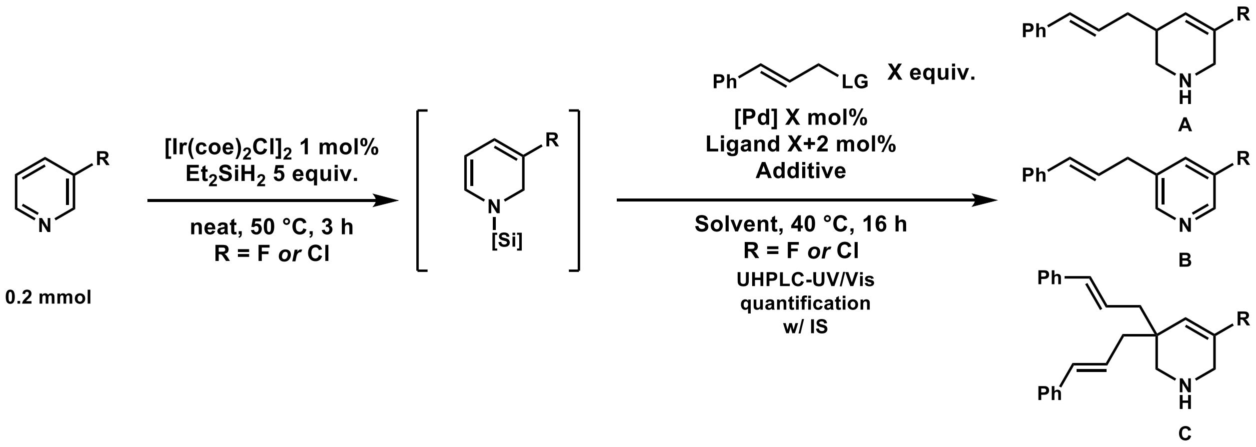
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 264.0825, found: 264.0818;

**R$_f$** (Hexane/EtOAc = 9/1): 0.38;

**ATR-IR** ν (cm$^{-1}$): 3055, 1601, 1470, 1450, 1421, 1406, 1264, 1206, 1188, 1153, 1050, 842, 831, 793, 743, 620.

## Optimization for the Dearomative Asymmetric Allylic Alkylation

Scheme S5: General reaction scheme for optimization of the asymmetric allylic alkylation



**Optimization Procedure:**

In a 2 mL screw vial, equipped with a magnetic stir bar was transferred to an argon filled glovebox. Chlor-bis-(cycloocten)-iridium(I) dimer ($[Ir(coe)_2Cl]_2$, 1.8 mg, 0.002 mmol, 1 mol%) was added to the vial. The vial was closed with a septum screw cap. The vial was transferred out of the glovebox. Diethyl silane ($Et_2SiH_2$, 130 µL, 1.0 mmol, 5.0 equiv.) was added and the resulting mixture was stirred at room temperature for 4 minutes. 3-Fluoroyridine (17 µL, 0.2 mmol, 1.0 equiv.) or 3-chloropyridine (19 µL, 0.2 mmol, 1.0 equiv.) was added and the resulting reaction mixture was stirred at 50 °C for 3 hours (R = F) or 1 hours (R = Cl). A separate 2 mL screw vial equipped with a magnetic stir bar was transferred to the glovebox. Ligand L$$ (X+2 mol%), palladium(II) acetate ($Pd(OAc)_2$, X mol%) and the additive, if solid were added. The vial was closed with a septum screw cap and transferred out of the glovebox. Dichloromethane ($CH_2Cl_2$, 1 mL) was added at room temperature under nitrogen. The mixture was stirred for 5 minutes and the additive was added, if liquid. The alkylation reagent was added, followed by the reaction mixture from the first 2 mL vial. The resulting mixture was then stirred at 40 °C for 16 h. The mixture was then cooled to room temperature and diluted with additional EtOAc (2 mL). 4-*tert*Butylpyridine (14.6 µL, 0.1 mmol) was added as internal standard. The mixture was homogenized and a small sample was prepared (~5 µL) that was diluted with additional EtOAc. The ratio between the product **A**, side products **B** and **C** and the internal standard was determined via UV/Vis absorption after separation via UHPLC.

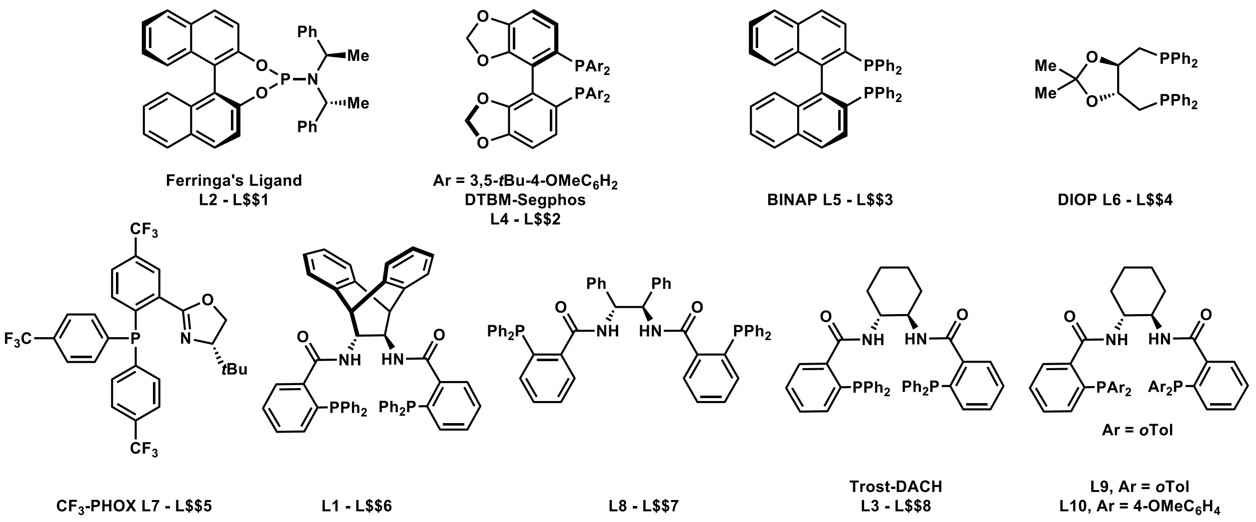


*Figure 2. Molecular structure of ligands used in this study.*

Table S1: Using 3-fluoroyridine (**1a**) as substrate (LG = $OCO_2Me$)

| # | R= | Solvent | [Pd] (mol%) | Ligand (7 mol%) | Additive (mol%) and/or Other variation | A /% | ee A /% | B /% | C /% |
|---|---|---|---|---|---|---|---|---|---|
| 1 | F | $CH_2Cl_2$ | $Pd_2dba_3$ (2.5) | $PPh_3$ (15) | - | 2 | - | 11 | <5 |
| 2 | F | $CH_2Cl_2$ | $Pd_2dba_3$ (2.5) | Ferringa L2 | - | <5 | 48 | n.d. | <5 |
| 3 | F | $CH_2Cl_2$ | $Pd_2dba_3$ (2.5) | DTBM Segphos L4 | - | <5 | 42 | n.d. | <5 |
| 4 | F | $CH_2Cl_2$ | $Pd_2dba_3$ (2.5) | BINAP L5 | - | <5 | 28 | 17 | <5 |
| 5 | F | $CH_2Cl_2$ | $Pd_2dba_3$ (2.5) | DIOP L6 | - | <5 | rac | n.d. | <5 |
| 6 | F | $CH_2Cl_2$ | $Pd_2dba_3$ (2.5) | $CF_3$Phox L7 | - | n.r. | - | - | - |
| 7 | F | $CH_2Cl_2$ | $Pd_2dba_3$ (2.5) | **L3** | - | **34** | **96** | **12** | **7** |
| 8 | F | $CH_2Cl_2$ | $Pd_2dba_3$ (2.5) | oTol L9 |  | n.r. | - | - | - |
| 9 | F | $CH_2Cl_2$ | $Pd_2dba_3$ (2.5) | L8 | - | n.r. | - | - | - |
| 10 | F | $CH_2Cl_2$ | $Pd_2dba_3$ (2.5) | Anden L1 | - | <5 | 30 | <5 | <5 |
| 11 | F | PhH | $Pd_2dba_3$ (2.5) | L3 | - | 18 | 98 | 11 | <5 |
| 12 | F | THF | $Pd_2dba_3$ (2.5) | L3 | - | 15 | 98 | 24 | <5 |
| 13 | F | Diox. | $Pd_2dba_3$ (2.5) | L3 | - | 20 | 98 | 15 | 3 |
| 14 | F | MeCN | $Pd_2dba_3$ (2.5) | L3 | - | n.r. | - | - | - |
| 15 | F | Hexane | $Pd_2dba_3$ (2.5) | L3 | - | n.r. | - | - | - |
| 16 | F | DMF | $Pd_2dba_3$ (2.5) | L3 | - | n.r. | - | - | - |
| 17 | F | HFIP | $Pd_2dba_3$ (2.5) | L3 | - | n.r. | - | - | - |
| 18 | F | DCE | $Pd_2dba_3$ (2.5) | L3 | - | 22 | n.d. | 15 | <5 |
| 19 | F | $CH_2Cl_2$ | $Pd_2dba_3$*$CHCl_3$ (2.5) | L3 | - | 38 | 96 | 9 | 10 |
| 20 | F | $CH_2Cl_2$ | $Pd_2dmba_3$ (2.5) | L3 | - | 23 | n.d. | 5 | <5 |
| 21 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | - | **38** | **96** | **8** | **5** |
| 22 | F | $CH_2Cl_2$ | $[Pd(cinnamyl)Cl]_2$ (2.5) | L3 | - | 28 | n.d. | 12 | <5 |
| 23 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | @ room temp. | 38 | n.d. | 20 | <5 |
| 24 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | LiO*t*Bu 1 eq. | n.r. | - | - | - |
| 25 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | LiOAc 1 eq. | 32 | n.d. | 17 | <5 |
| 26 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | $Na_2CO_3$ 1 eq. | 30 | n.d. | 16 | <5 |
| 27 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | DBU 1 eq. | 5 | n.d. | 12 | <5 |
| 28 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | $Et_3N$ 1 eq. | 38 | n.d. | 12 | <5 |
| 29 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | CsF 1 eq. | **44** | **96** | **14** | **<5** |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 30 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | AcOH 0.5 eq. | 35 | n.d. | 8 | n.d. |
| 31 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | $MesCO_2H$ 0.5 eq. | 26 | n.d. | 7 | n.d. |
| 32 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | $ZnOTf_2$ 0.2 eq. | n.r. | - | - | - |
| 33 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | $Ph_3B$ 0.2 eq. | n.r. | - | - | - |
| 34 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | Hantzsch 0.5 eq. | 44 | n.d. | 13 | <5 |
| 35 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | $NaBH(OAc)_3$ | 11 | n.d. | 20 | <5 |
| 36 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | CsF 0.2 eq. | **48** | **n.d.** | **10** | **<5** |
| 37 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | CsF 2.0 eq. | 35 | n.d. | 34 | <5 |
| 38 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | CsF 0.4 eq. | 45 | n.d. | 14 | <5 |
| 39 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | $ZnF_2$ 0.2 eq. | 20 | n.d. | 9 | <5 |
| 40 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | AgF 0.2 eq. | n.r. | - | - | - |
| 41 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | KF 0.2 eq. | 41 | n.d. | 13 | 4 |
| 42 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.2 eq. | 49 | 96 | 9 | 8 |
| 43 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq. | **49** | **96** | **8** | **6** |
| 44 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (10) | L3 | NaF 0.1 eq. | 46 | n.d. | 8 | 4 |
| 45 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | LiCl 0.2 eq. | 36 | n.d. | <5 | 17 |
| 46 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | LiBr 0.2 eq. | 24 | n.d. | <5 | 10 |
| 47 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | LiI 0.2 eq. | n.r. | - | - | - |
| 48 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | 4OMe L10 | NaF 0.2 eq. | 20 | n.d. | 12 | 7 |
| 49 | F | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | oTol L9 | NaF 0.2 eq. | n.r. | - | - | - |

Table S2: Using 3-chloropyridine (**1b**) as substrate (model substrate for compounds with increased substrate-specific selectivity for product C (dialkylated compounds)) (LG = $OCO_2Me$, if not mentioned otherwise):

| # | R= | Solvent | [Pd] (mol%) | Ligand (mol%) | Additive (mol%) and/or Other variation | A /% | ee A /% | B /% | C /% |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq. | 27 | n.d. | 24 | 43 |
| 2 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq. @ 60 °C | 11 | n.d. | <5 | <5 |
| 3 | Cl | PhH | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq. | 24 | n.d. | 22 | 21 |
| 4 | Cl | THF | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq. | 18 | n.d. | 18 | 28 |
| 5 | Cl | EtOAc | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq. | n.r. | - | - | - |
| 6 | Cl | Acetone | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq. | n.r. | - | - | - |
| 7 | Cl | MeOH | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq. | 21 | n.d. | 30 | 11 |
| 8 | Cl | $CCl_4$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq. | n.r. | - | - | - |

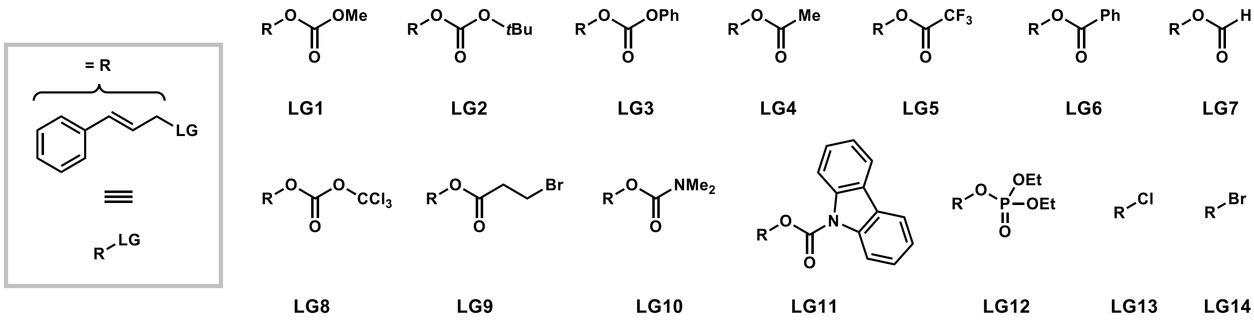
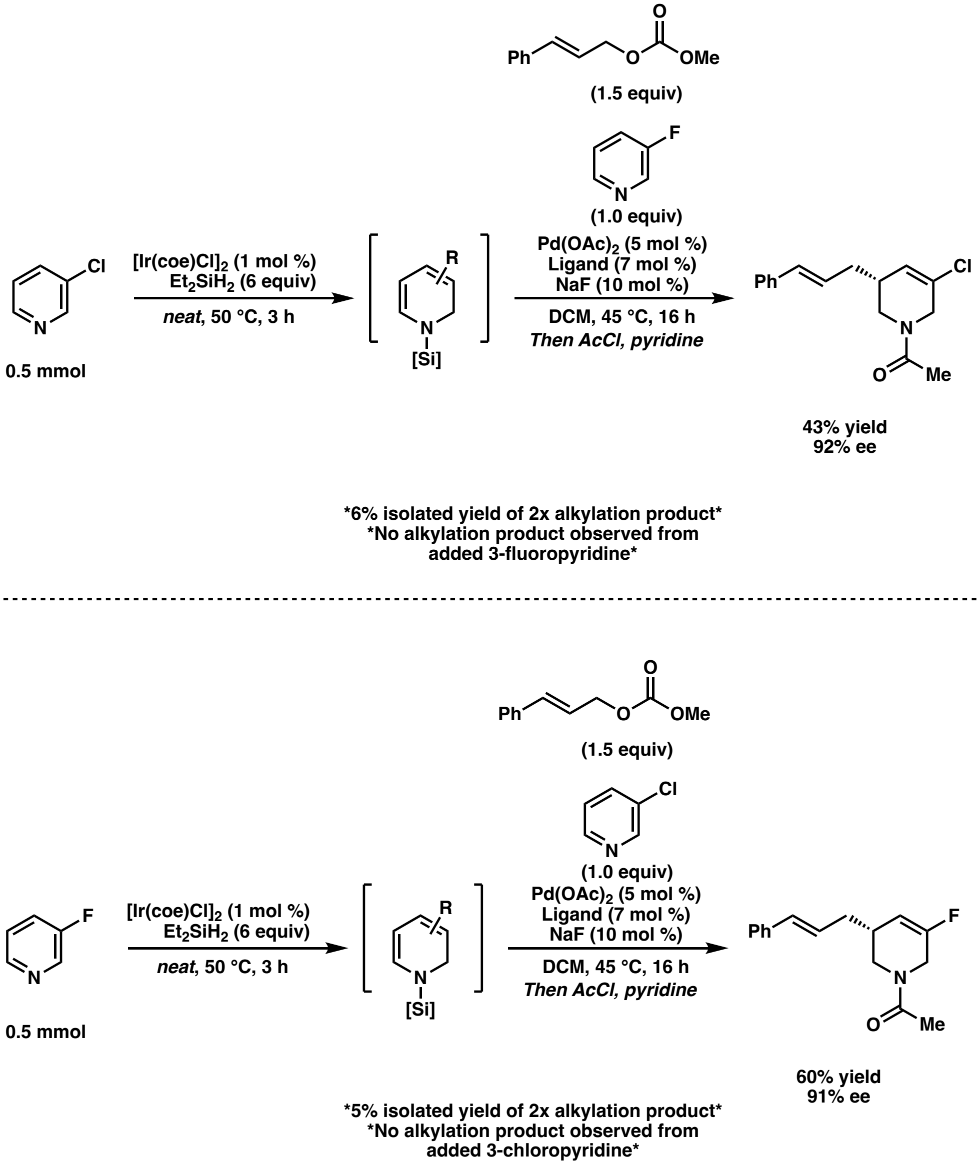


*Figure 3. Optimization of leaving groups.*

| # | R= | Solvent | [Pd] (mol%) | Ligand (mol%) | Additive (mol%) and/or Other variation | A /% | ee A /% | B /% | C /% |
|---|---|---|---|---|---|---|---|---|---|
| 9 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ **LG1** | 27 | n.d. | 24 | 43 |
| 10 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ **LG2** | 20 | n.d. | 18 | 38 |
| 11 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ **LG3** | 31 | n.d. | 10 | 32 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 12 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ **LG4** | 22 | n.d. | 21 | 24 |
| 13 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ **LG5** | 4 | n.d. | 17 | <5 |
| 14 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ **LG6** | 14 | n.d. | 18 | 38 |
| 15 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ **LG7** | 20 | n.d. | 21 | 13 |
| 16 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ **LG8** | 28 | n.d. | 7 | 38 |
| 17 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ **LG9** | n.r. | - | - | - |
| 18 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ **LG10** | n.r. | - | - | - |
| 19 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ **LG11** | n.r. | - | - | - |
| 20 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ **LG12** | 13 | n.d. | 31 | 20 |
| 21 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ **LG13** | n.r. | - | - | - |
| 22 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ **LG14** | n.r. | - | - | - |
| 23 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ under air | n.r. | - | - | - |
| 24 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ 2.5 eq. $Et_2SiH_2$ in step 1 | 29 | n.d. | 38 | 29 |
| 25 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ 7.5 eq. $Et_2SiH_2$ in step 1 | 37 | n.d. | 16 | 24 |
| 26 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ 0.5 mol% $[Ir]_2$ in step 1 | 14 | n.d. | 34 | 45 |
| 27 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ 2.5 mol% $[Ir]_2$ in step 1 | 5 | n.d. | <5 | <5 |
| 28 | Cl | $CH_2Cl_2$ | $Pd(OAc)_2$ (5) | L3 | NaF 0.1 eq./ $PhCO_2H$ 0.2 eq. | **17** | **n.d.** | **7** | **61** |

**Scheme S6: Mixed pyridine control experiments**



*6% isolated yield of 2x alkylation product*
*No alkylation product observed from added 3-fluoropyridine*

*5% isolated yield of 2x alkylation product*
*No alkylation product observed from added 3-chloropyridine*

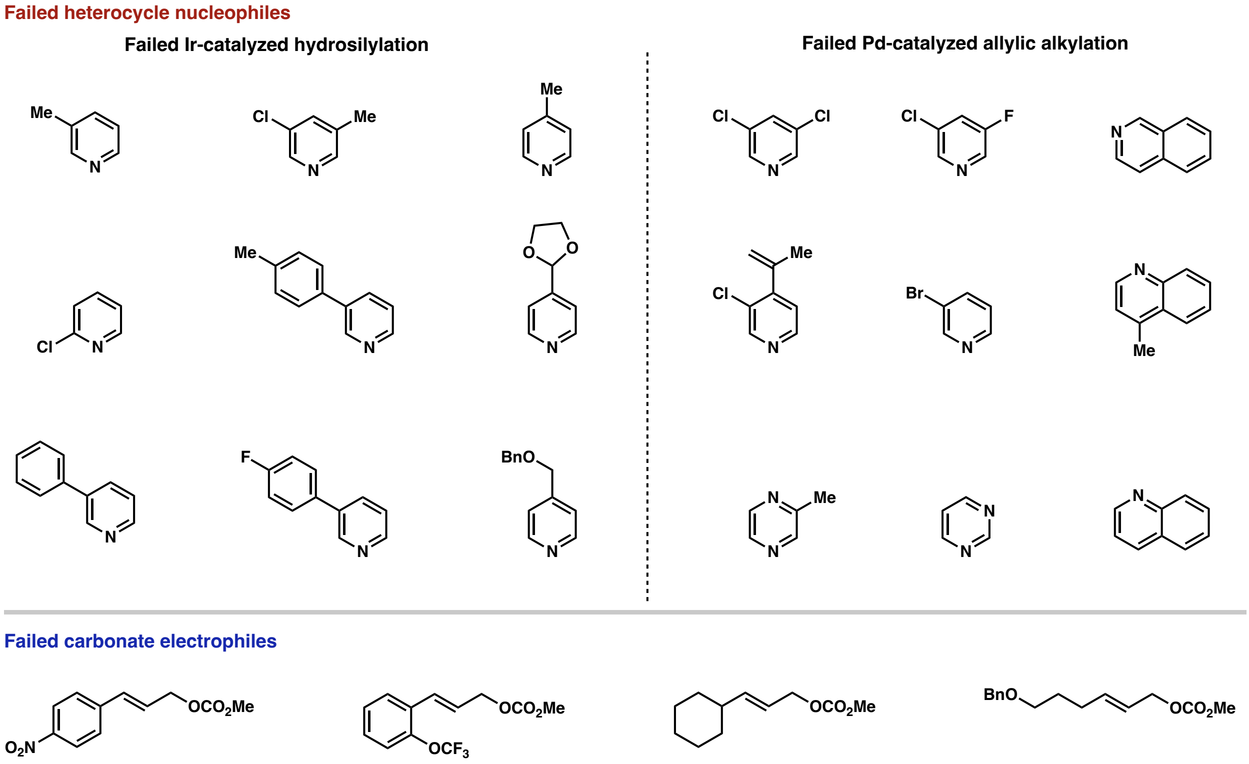
Mixed pyridine control experiments were performed as followed. Chlor-bis-(cycloocten)-iridium(I) dimer ([Ir(coe)$_2$Cl]$_2$, 4.5 mg, 0.005 mmol, 1 mol%) was added to a 1 dram vial equipped with a magnetic stir bar. Diethyl silane (Et$_2$SiH$_2$, 389 µL, 3.0 mmol, 6.0 equiv.) was added and the resulting mixture was stirred at room temperature for 15 minutes. 3-fluoropyridine or 3-chloropyridine (0.5 mmol, 1.0 equiv.) was added and the resulting reaction mixture was stirred at 50 °C for 3 hours. A separate 1 dram screw vial equipped with a magnetic stir bar was transferred to the glovebox. Ligand **L3** (24.2 mg, 0.035 mmol, 7 mol%), NaF (2.1 mg, 0.05 mmol, 10 mol%) and palladium(II) acetate (Pd(OAc)$_2$, 5.6 mg, 0.025 mmol, 5 mol%) were added. The vial was closed with a septum screw cap and transferred out of the glovebox. Dichloromethane (CH$_2$Cl$_2$, 2.5 mL) was added at room temperature under nitrogen. The mixture was stirred for 5 minutes. Cinnamyl methyl carbonate (144.2 mg, 0.75 mmol, 1.5 equiv.) was added, followed by the reaction mixture from the 1 dram vial. An additional equivalent of the alternative 3-halopyridine was added (0.5 mmol, 1.0 equiv). The resulting mixture was then stirred at 40 °C for 24 h. The mixture was then cooled to room temperature and diluted with additional dichloromethane (2.5 mL). Pyridine (121 µL, 1.5 mmol, 3.0 equiv.) was added as a base, followed by acetyl chloride (107 µL, 1.5 mmol, 3.0 equiv.). The mixture was stirred at room temperature for 16 h. Afterwards, acetic acid (0.5 mL) was added and the mixture was stirred at room temperature for 2 hours. The mixture was diluted with dichloromethane and an aqueous work up with 4 M NaOH solution was performed to neutralize the acetic acid. The aqueous phase was extracted with dichloromethane once and ethyl acetate once. The combined organic fractions were dried over magnesium sulfate. The solvent was evaporated and the residue was submitted to flash column chromatography over silica gel using a solvent mixture of hexane/ethyl acetate (typically 7/3 to 1/1) as the eluent.

Note 1: The ratios of monoalkylation and bisalkylation were obtained via isolation from column chromatography.

Note 2: No allylic alkylation product of any kind was obtained from the pyridine added at the Pd-catalyzed allylic alkylation step, suggesting that the iridium catalyzed dearomative hydrosilylation is not active during the Pd-catalyzed step.

Note 3: The hydrosilylation of the starting pyridines was incomplete, suggesting the yield could be increased through further optimization of this step.

## Scheme S7: List of Unsuccessful Substrates

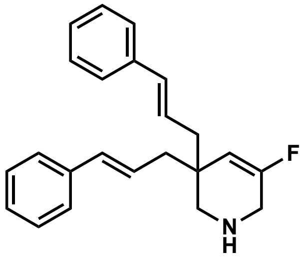


## Product Characterization: Bisalkylated products

### General procedure A for the synthesis of bisalkylated products (5)

Unless otherwise mentioned, compounds (**5**) were synthesized as followed: In a 2 mL screw vial, equipped with a magnetic stir bar, the corresponding pyridine (0.5 mmol, 1.0 equiv.) if solid was added to the vial. The vial was then transferred to an argon filled glovebox. Chlor-bis-(cyclooctenyl)-iridium(I) dimer ([Ir(coe)$_2$Cl]$_2$, 4.5 mg, 0.005 mmol, 1 mol%) was added to the vial. The vial was closed with a septum screw cap. The vial was transferred out of the glovebox. Diethyl silane (Et$_2$SiH$_2$, 389 µL, 3.0 mmol, 6.0 equiv.) was added and the resulting mixture was stirred at room temperature for 4 minutes. Pyridine (0.5 mmol, 1.0 equiv.) if liquid was added and the resulting reaction mixture was stirred at 50 °C for the appropriate time (1 – 3 hours). A separate 10 mL screw vial equipped with a magnetic stir bar was transferred to the glovebox. Ligand **L3** (24.2 mg, 0.035 mmol, 7 mol%), NaF (2.1 mg, 0.05 mmol, 10 mol%), PhCOOH (12.2 mg, 0.1 mmol, 20 mol%) and palladium(II) acetate (Pd(OAc)$_2$, 5.6 mg, 0.025 mmol, 5 mol%) were added. The vial was closed with a septum screw cap and transferred out of the glovebox. Dichloromethane (CH$_2$Cl$_2$, 2.5 mL) was added at room temperature under nitrogen. The mixture was stirred for 5 minutes. Cinnamyl methyl carbonate (192.2 mg, 1.0 mmol, 2.0 equiv.) was added, followed by the reaction mixture from the 2 mL vial. The resulting mixture was then stirred at 40 °C for 24 h. Afterwards, the reaction mixture was cooled to room temperature and acetic acid (1 mL) was added and the mixture was stirred at room temperature for 2 hours. The mixture was diluted with dichloromethane and an aqueous work up with 4 M NaOH solution was performed to neutralize the acetic acid. The aqueous phase was extracted with dichloromethane once and ethyl acetate once. The combined organic fractions were dried over magnesium sulfate. The solvent was evaporated and the residue was submitted to flash column chromatography over silica gel using a solvent mixture of hexane/acetone = 7/3 as the eluent.

**Product characterization**



***5a***

**Chemical Formula:** C$_{23}$H$_{24}$FN
**Exact Mass: 333.1893**
**Molecular Weight: 333.4504**

**3,3-dicinnamyl-5-fluoro-1,2,3,6-tetrahydropyridine 5a** was synthesized following the general procedure A using 3-fluoropyridine (43 µL, 0.5 mmol, 1.0 equiv.) as substrate. The desired compound was obtained as colorless oil (43.7 mg, 0.131 mmol, 26% yield over two steps).

**$^1$H NMR (400 MHz, CDCl$_3$):** δ 7.29 – 7.20 (m, 8H), 7.16 – 7.11 (m, 2H), 6.36 (d, *J* = 15.7 Hz, 2H), 6.13 (dt, *J* = 15.5, 7.5 Hz, 2H), 5.15 (d, *J* = 18.3 Hz, 1H), 3.48 (bs, 1H), 3.25 (d, *J* = 1.5 Hz, 2H), 2. 68 (s, 2H), 2.28 – 2.17 (m, 4H);

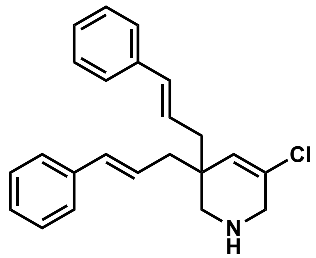
**$^{13}$C NMR (101 MHz, CDCl$_3$):** δ 158.98 (d, *J* = 264.0 Hz), 137.39, 133.55, 128.72, 127.44, 126.25, 125.71, 108.17 (d, *J* = 10.2 Hz), 51.98 (d, *J* = 2.0 Hz), 43.70 (d, *J* = 30.2 Hz), 42.32 (d, *J* = 2.3 Hz), 39.76 (d, *J* = 4.7 Hz);

**$^{19}$F NMR (282 MHz, CDCl$_3$):** δ –110.42 (d, *J* = 18.3 Hz);

**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 334.1971, found: 334.1958;

**R$_f$** (Hexane/acetone = 7/3): 0.23;

**ATR-IR** ν (cm$^{-1}$): 3058, 3025, 2919, 2850, 1698, 1652, 1598, 1576, 1558, 1495, 1448, 1372, 1270, 1159, 1092, 1027, 967, 922, 853, 745, 694.



***5b***
**Chemical Formula:** $C_{23}H_{24}ClN$
**Exact Mass: 349.1597**
**Molecular Weight: 349.9020**

**5-chloro-3,3-dicinnamyl-1,2,3,6-tetrahydropyridine 5b** was synthesized following the general procedure A using 3-chloropyridine (47 µL, 0.5 mmol, 1.0 equiv.) as substrate. The desired compound was obtained as colorless oil (82.2 mg, 0.235 mmol, 47% yield over two steps).

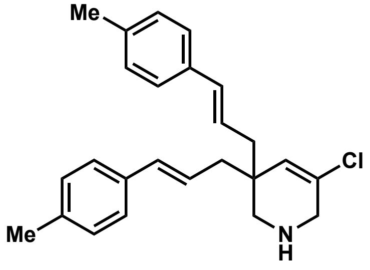
**$^1$H NMR (400 MHz, CDCl$_3$):** δ 7.28 – 7.20 (m, 8H), 7.16 – 7.11 (m, 2H), 6.36 (d, *J* = 15.8 Hz, 2H), 6.11 (dt, *J* = 15.5, 7.5 Hz, 2H), 5.76 – 5.72 (m, 1H), 3.28 (d, *J* = 1.7 Hz, 2H), 2.71 (s, 2H), 2.42 (bs, 1H), 2.28 – 2.16 (m, 4H);

**$^{13}$C NMR (101 MHz, CDCl$_3$):** δ 137.32, 133.68, 132.23, 130.07, 128.71, 127.47, 126.25, 125.41, 51.48, 50.00, 41.90, 41.58;

**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 350.1676, found: 350.1671;

**R$_f$** (Hexane/acetone = 7/3): 0.23;

**ATR-IR** ν (cm$^{-1}$): 3054, 3025, 2916, 1651, 1599, 1494, 1448, 1072, 1004, 966, 856, 744, 692.



***5c***
**Chemical Formula:** $C_{25}H_{28}ClN$
**Exact Mass: 377.1910**
**Molecular Weight: 377.9560**

**5-chloro-3,3-bis((*E*)-3-(*p*-tolyl)allyl)-1,2,3,6-tetrahydropyridine 5c** was synthesized following the general procedure A using 3-chloropyridine (47.5 µL, 0.5 mmol, 1.0 equiv.) as substrate and (*E*)-methyl (3-(*p*-tolyl)allyl) carbonate (206 mg, 1.0 mmol, 2.0 equiv.). The desired compound was obtained as colorless oil (40 mg, 0.106 mmol, 21% yield over two steps).

**$^1$H NMR (400 MHz, CDCl$_3$):** δ 7.26 (d, *J* = 8.1 Hz, 4H), 7.13 (d, *J* = 7.8 Hz, 4H), 6.42 (d, *J* = 15.8 Hz, 2H), 6.14 (dt, *J* = 15.5, 7.5 Hz, 2H), 5.82 (s, 1H), 3.36 (d, *J* = 1.7 Hz, 2H), 2.79 (s, 2H), 2.34 (s, 6H), 2.29 (ddd, *J* = 8.0, 4.9, 1.3 Hz, 4H), 2.03 (s, 1H);

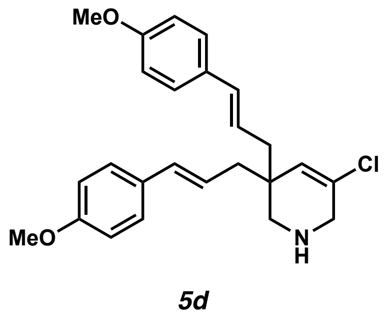
**$^{13}$C NMR (101 MHz, CDCl$_3$):** δ 137.3, 134.6, 133.5, 132.2, 130.2, 129.4, 126.2, 124.4, 51.5, 49.2, 41.9, 41.6, 21.3;

**$^{19}$F NMR (282 MHz, CDCl$_3$):** δ –110.42 (d, *J* = 18.3 Hz);

**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 378.1989, found: 378.2011;

**R$_f$** (*n*-hexane/ethyl acetate = 7/2): 0.27;

**ATR-IR** ν (cm$^{-1}$): 3023, 2920, 1747, 1699, 1651, 1512, 1435, 1264, 1108, 968, 795.



***5d***
**Chemical Formula:** $C_{25}H_{28}ClNO_2$
**Exact Mass: 409.1809**
**Molecular Weight: 409.9540**

**5-chloro-3,3-bis((E)-3-(4-methoxyphenyl)allyl)-1,2,3,6-tetrahydropyridine 5d** was synthesized following the general procedure A using 3-chloropyridine (47.5 μL, 0.5 mmol, 1.0 equiv.) as substrate and (*E*)-3-(4-methoxyphenyl)allyl methyl carbonate (222 mg, 1.0 mmol, 2.0 equiv.). The desired compound was obtained as colorless oil (57 mg, 0.139 mmol, 28% yield over two steps).

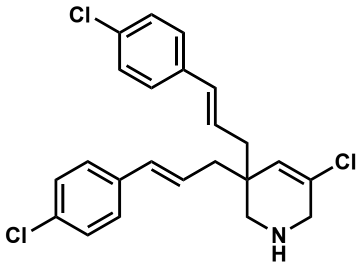
**$^1$H NMR (400 MHz, CDCl$_3$):** δ 7.21 (d, *J* = 8 Hz, 4H), 6.78 (d, *J* = 8 Hz, 4H), 6.31 (d, *J* = 15.8 Hz, 2H), 5.98 (ddd, *J* = 15.4, 8.0, 7.1 Hz, 2H), 5.75 (s, 1H), 3.73 (s, 6H), 3.29 (s, 2H), 2.87 (br s, 1H), 2.72 (s, 2H), 2.26 – 2.14 (m, 4H);

**$^{13}$C NMR (101 MHz, CDCl$_3$):** δ 159.1, 133.0, 130.3, 130.2, 128.3, 127.4, 123.2, 114.1, 55.4, 51.5, 50.0, 41.9, 41.6;

**HRMS**: m/z (ESI) calculated for (M + H)$^+$: 410.1887, found: 410.1861;

**R$_f$** (*n*-hexane/ethyl acetate/acetone = 7/2/1): 0.12;

**ATR-IR** ν (cm$^{-1}$): 3029, 3002, 2931, 2834, 1653, 1606, 1576, 1510, 1461, 1441, 1298, 1248, 1174, 1107, 1034, 1034, 967, 905, 839, 753, 644.



***5e***
**Chemical Formula:** $C_{23}H_{22}Cl_3N$
**Exact Mass: 417.0818**
**Molecular Weight: 418.7860**

**5-chloro-3,3-bis((*E*)-3-(4-chlorophenyl)allyl)-1,2,3,6-tetrahydropyridine 5e** was synthesized following the general procedure A using 3-chloropyridine (47.5 μL, 0.5 mmol, 1.0 equiv.) as substrate and (*E*)-3-(4-chlorophenyl)allyl methyl carbonate (226 mg, 1.0 mmol, 2.0 equiv.). The desired compound was obtained as yellowish oil (63 mg, 0.150 mmol, 30% yield over two steps).

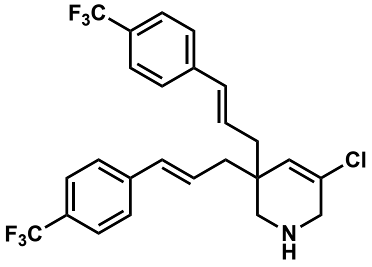
**$^1$H NMR (400 MHz, CDCl$_3$):** δ 7.27 (s, 8H), 6.40 (d, *J* = 15.8 Hz, 2H), 6.25 – 6.03 (m, 2H), 5.81 (s, 1H), 3.37 (d, *J* = 1.7 Hz, 2H), 2.79 (s, 2H), 2.35 – 2.27 (m, 4H), 2.21 (br s, 1H);

**$^{13}$C NMR (101 MHz, CDCl$_3$):** δ 135.7, 133.1, 132.5, 132.5, 129.8, 128.9, 127.5, 126.1, 51.5, 49.6, 41.9, 41.6;

**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 418.0896, found: 418.0882;

**R$_f$** (*n*-hexane/ethyl acetate/acetone = 7/2/1): 0.19;

**ATR-IR** ν (cm$^{-1}$): 3027, 2917, 2839, 1651, 1489, 1434, 1404, 1264, 1093, 1012, 969, 896, 846, 736.



***5f***
**Chemical Formula:** $C_{25}H_{22}ClF_6N$
**Exact Mass: 485.1345**
**Molecular Weight: 485.8984**

**5-chloro-3,3-bis((*E*)-3-(4-(trifluoromethyl)phenyl)allyl)-1,2,3,6-tetrahydropyridine 5f** was synthesized following the general procedure A using 3-chloropyridine (47.5 µL, 0.5 mmol, 1.0 equiv.) as substrate and (*E*)-methyl (3-(4-(trifluoromethyl)phenyl)allyl) carbonate (260 mg, 1.0 mmol, 2.0 equiv.). The desired compound was obtained as colorless oil (52 mg, 0.107 mmol, 21% yield over two steps).

**$^1$H NMR (400 MHz, CDCl$_3$):** δ 7.57 (d, *J* = 8.2 Hz, 4H), 7.44 (d, *J* = 8.3 Hz, 4H), 6.50 (d, *J* = 15.8 Hz, 2H), 6.30 (dt, *J* = 15.6, 7.5 Hz, 2H), 5.83 (s, 1H), 3.40 (s, 2H) 2.82 (s, 2H), 2.53–2.28 (m, 5H);

**$^{13}$C NMR (101 MHz, CDCl$_3$):** δ 140.1, 132.7, 132.4, 129.6, 129.4 (q, *J* = 32.3 Hz), 128.1, 126.4, 125.7 (q, *J* = 3.9 Hz), 124.3 (q, *J* = 272 Hz), 51.3, 49.9, 42.0, 41.6;

**$^{19}$F NMR (282 MHz, CDCl$_3$):** δ –62.5;

**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 486.1423, found: 486.1413;

**R$_f$** (*n*-hexane/ethyl acetate/acetone = 7/2/1): 0.19;

**ATR-IR** ν (cm$^{-1}$): 2921, 1652, 1615, 1415, 1326, 1170, 1160, 1123, 1068, 1016, 971, 953, 861.

**Product Characterization: Monoalkylated products**

**General procedure B for the synthesis of 6 (electron poor pyridine substrates)**

Some compounds **6** were synthesized as followed (as mentioned in the product characterization): In a 2 mL screw vial, equipped with a magnetic stir bar, the corresponding pyridine (0.5 mmol, 1.0 equiv.) if solid was added to the vial. The vial was then transferred to an argon filled glovebox. Chlor-bis-(cyclooctene)-iridium(I) dimer ($[Ir(coe)_2Cl]_2$, 4.5 mg, 0.005 mmol, 1 mol%) was added to the vial. The vial was closed with a septum screw cap. The vial was transferred out of the glovebox. Diethyl silane ($Et_2SiH_2$, 389 µL, 3.0 mmol, 6.0 equiv.) was added and the resulting mixture was stirred at room temperature for 4 minutes. Pyridine (0.5 mmol, 1.0 equiv.) if liquid was added and the resulting reaction mixture was stirred at 50 °C for the appropriate time (0.5 – 3 hours). A separate 10 mL screw vial equipped with a magnetic stir bar was transferred to the glovebox. Ligand **L3** (24.2 mg, 0.035 mmol, 7 mol%), NaF (2.1 mg, 0.05 mmol, 10 mol%) and palladium(II) acetate ($Pd(OAc)_2$, 5.6 mg, 0.025 mmol, 5 mol%) were added. The vial was closed with a septum screw cap and transferred out of the glovebox. Dichloromethane ($CH_2Cl_2$, 2.5 mL) was added at room temperature under nitrogen. The mixture was stirred for 5 minutes. Cinnamyl methyl carbonate (144.2 mg, 0.75 mmol, 1.5 equiv.) was added, followed by the reaction mixture from the 2 mL vial. The resulting mixture was then stirred at 40 °C for 24 h. The mixture was then cooled to room temperature and diluted with additional dichloromethane (2.5 mL). Pyridine (121 µL, 1.5 mmol, 3.0 equiv.) was added as a base, followed by acetyl chloride (107 µL, 1.5 mmol, 3.0 equiv.). The mixture was stirred at room temperature for 16 h. Afterwards, acetic acid (0.5 mL) was added and the mixture was stirred at room temperature for 2 hours. The mixture was diluted with dichloromethane and an aqueous work up with 4 M NaOH solution was performed to neutralize the acetic acid. The aqueous phase was extracted with dichloromethane once and ethyl acetate once. The combined organic fractions were dried over magnesium sulfate. The solvent was evaporated and the residue was submitted to flash column chromatography over silica gel using a solvent mixture of hexane/ethyl acetate (typically 7/3 to 1/1) as the eluent.

**General procedure C for the synthesis of 6 (neutral or electron rich pyridines)**

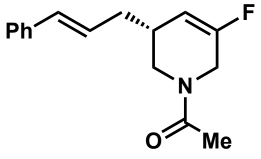
Some compounds **6** were synthesized as followed (as mentioned in the product characterization): In a 2 mL screw vial, equipped with a magnetic stir bar, the corresponding pyridine (0.5 mmol, 1.0 equiv.) if solid was added to the vial. The vial was then transferred to an argon filled glovebox. Chlor-bis-(cyclooctene)-iridium(I) dimer ($[Ir(coe)_2Cl]_2$, 2.3 mg, 0.0025 mmol, 0.5 mol%) was added to the vial. Diethyl silane ($Et_2SiH_2$, 389 µL, 3.0 mmol, 6.0 equiv.) was added and the resulting mixture was stirred at room temperature for 4 minutes. Pyridine (0.5 mmol, 1.0 equiv.) if liquid was added and the vial was closed with a screw cap and the resulting reaction mixture was stirred at 45 °C for 6 h. The mixture was cooled to room temperature and additional $[Ir(coe)_2Cl]_2$ catalyst (2.3 mg, 0.0025 mmol, 0.5 mol%) and $Et_2SiH_2$ (195 µL, 1.5 mmol, 3 equiv.) were added and the mixture was again stirred at 45 °C for 12 hours. The mixture was again cooled to room temperature and additional $[Ir(coe)_2Cl]_2$ catalyst (2.3 mg, 0.0025 mmol, 0.5 mol%) and $Et_2SiH_2$ (195 µL, 1.5 mmol, 3 equiv.) were added for the third time and the mixture again stirred at 45 °C for 2 hours. Afterwards, the mixture was transferred out of the glovebox. A separate 10 mL screw vial equipped with a magnetic stir bar was transferred to the glovebox.

Ligand **L3** (24.2 mg, 0.035 mmol, 7 mol%), NaF (2.1 mg, 0.05 mmol, 10 mol%) and palladium(II) acetate ($Pd(OAc)_2$, 5.6 mg, 0.025 mmol, 5 mol%) were added. The vial was closed with a septum screw cap and transferred out of the glovebox. Dichloromethane ($CH_2Cl_2$, 2.5 mL) was added at room temperature under nitrogen. The mixture was stirred for 5 minutes. Cinnamyl methyl carbonate (144.2 mg, 0.75 mmol, 1.5 equiv.) was added, followed by the reaction mixture from the 2 mL vial. The resulting mixture was then stirred at 40 °C for 24 h. The mixture was then cooled to room temperature and diluted with additional dichloromethane (2.5 mL). Pyridine (121 µL, 1.5 mmol, 3.0 equiv.) was added as a base, followed by acetyl chloride (107 µL, 1.5 mmol, 3.0 equiv.). The mixture was stirred at room temperature for 16 h. Afterwards, acetic acid (0.5 mL) was added and the mixture stirred at room temperature for 2 hours. The mixture was diluted with dichloromethane and an aqueous work up with 4 M NaOH solution was performed to neutralize the acetic acid. The aqueous phase was extracted with dichloromethane once and ethyl acetate once. The combined organic fractions were dried over magnesium sulfate. The solvent was evaporated and the residue was submitted to flash column chromatography over silica gel using a solvent mixture of hexane/ethyl acetate (typically 7/3 to 1/1) as the eluent.

### General procedure D for the synthesis of 6 (alternative for neutral or electron rich pyridines)

Some compounds **6** were synthesized as followed (as mentioned in the product characterization): In a 4 mL screw vial, equipped with a magnetic stir bar, the corresponding pyridine (0.5 mmol, 1.0 equiv.) if solid was added to the vial. The vial was then transferred to an argon filled glovebox. Chlor-bis-(cycloocten)-iridium(I) dimer ($[Ir(coe)_2Cl]_2$, 6.9 mg, 0.0075 mmol, 1.5 mol%) was added to the vial. Diethyl silane ($Et_2SiH_2$, 518 µL, 4.0 mmol, 8.0 equiv.) was added followed by dichloromethane ($CH_2Cl_2$, 1.0 mL), and the resulting mixture was stirred at room temperature for 20 minutes. Pyridine (0.5 mmol, 1.0 equiv.) if liquid was added neat to the reaction mixture and the vial was closed with a screw cap. The resulting reaction mixture was stirred at 45 °C for 6–16 h (depending on the pyridine). Afterwards, the mixture was transferred out of the glovebox. A separate 10 mL screw vial equipped with a magnetic stir bar was transferred to the glovebox. Ligand **L3** (24.2 mg, 0.035 mmol, 7 mol%), NaF (2.1 mg, 0.05 mmol, 10 mol%) and palladium(II) acetate ($Pd(OAc)_2$, 5.6 mg, 0.025 mmol, 5 mol%) were added. The vial was closed with a septum screw cap and transferred out of the glovebox. Dichloromethane ($CH_2Cl_2$, 2.5 mL) was added at room temperature under nitrogen. The mixture was stirred for 5 minutes. Cinnamyl methyl carbonate (144.2 mg, 0.75 mmol, 1.5 equiv.) was added, followed by the reaction mixture from the 2 mL vial. The resulting mixture was then stirred at 40 °C for 24 h. The mixture was then cooled to room temperature and diluted with additional dichloromethane (2.5 mL). Pyridine (121 µL, 1.5 mmol, 3.0 equiv.) was added as a base, followed by acetyl chloride (107 µL, 1.5 mmol, 3.0 equiv.). The mixture was stirred at room temperature for 16 h. Afterwards, acetic acid (0.5 mL) was added and the mixture stirred at room temperature for 2 hours. The mixture was diluted with dichloromethane and an aqueous work up with 4 M NaOH solution was performed to neutralize the acetic acid. The aqueous phase was extracted with dichloromethane once and ethyl acetate once. The combined organic fractions were dried over magnesium sulfate. The solvent was evaporated and the residue was submitted to flash column chromatography over silica gel using a solvent mixture of hexane/ethyl acetate (typically 7/3 to 2/8) as the eluent.

**Product characterization for mono alkylated products (6)**



***6a***

**Chemical Formula:** $C_{16}H_{18}FNO$
**Exact Mass: 259.1372**
**Molecular Weight: 259.3244**

**(R)-1-(3-cinnamyl-5-fluoro-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6a** was synthesized following the general procedure B. Therefore, 3-fluoropyridine (43 µL, 0.5 mmol, 1.0 equiv.) was used. The desired product was isolated as colorless oil (55.3 mg, 0.213 mmol, 43% yield over three steps).

**$^1$H NMR (400 MHz, $CDCl_3$)** (as mixture of E/Z amide bond isomers): δ 7.37 – 7.27 (m, 4H), 7.25 – 7.18 (m, 1H), 6.48 – 6.40 (m, 1H), 6.20 – 6.10 (m, 1H), 5.47 – 5.40 (m, 0.4H), 5.36 (ddt, *J* = 16.1, 3.5, 1.5 Hz, 0.6H), 4.18 – 4.05 (m, 1.4H), 3.97 (dt, *J* = 4.0, 2.0 Hz, 0.6H), 3.90 (dd, *J* = 13.1, 4.6 Hz, 0.4H), 3.53 (dd, *J* = 13.4, 4.5 Hz, 0.6H), 3.26 (dt, *J* = 13.4, 6.8 Hz, 1H), 2.56 – 2.44 (m, 1H), 2.34 – 2.17 (m, 2H), 2.13 – 2.11 (m, 3H);

**$^{13}$C NMR (101 MHz, $CDCl_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ 169.81, 169.64*, 156.33 (d, *J* = 255.5 Hz), 154.84 (d *J* = 255.2 Hz)*, 137.34*, 137.04, 133.01, 132.75*, 128.75, 128.63*, 127.62, 127.35*, 126.68, 126.24*, 126.19, 106.12 (d, *J* = 11.0 Hz)*, 104.49 (d, *J* = 12.3 Hz), 47.65, 44.84 (d, *J* = 39.2 Hz)*, 42.99*, 41.16 (d, *J* = 39.9 Hz), 36.86 (d *J* = 2.0 Hz)*, 36.77 (d, *J* = 2.3 Hz), 34.29 (d, *J* = 6.3 Hz), 33.37 (d, *J* = 5.9 Hz)*, 22.02*, 21.55;

**$^{19}$F NMR (282 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ –114.85 (dd, *J* = 16.4, 5.0 Hz), –116.04 (dd, *J* = 16.4, 5.1 Hz)*;

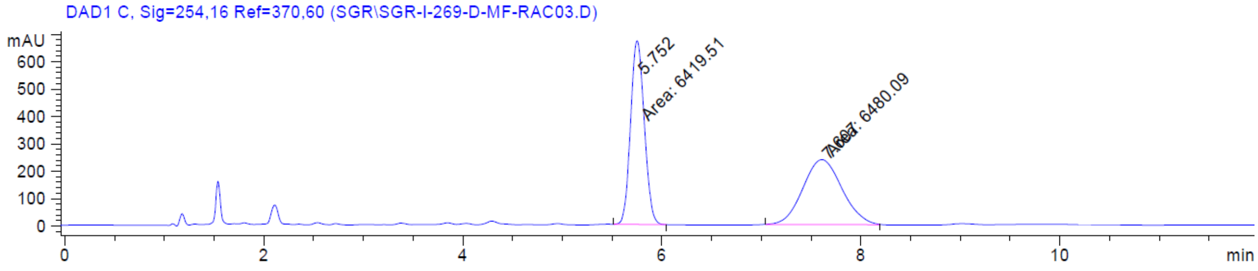
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 260.1451, found: 260.1438;

**$R_f$** (Hexane/EtOAc = 6/4): 0.15;

**ATR-IR** ν ($cm^{-1}$): 3853, 3745, 3675, 3648, 3026, 2914, 1707, 1652, 1491, 1436, 1380, 1361, 1274, 1230, 1162, 1106, 1070, 1032, 969, 831, 745, 695, 682, 618;

**$[\alpha]_D^{25}$:** – 42.82 (c 1.0, $CHCl_3$);

**Chiral SFC Separation:** 20% MeOH, 2.5 mL/min, AD-H column, λ = 254 nm, $t_R$ (min): minor = 5.75 (area: 2.74%), major = 7.61 (area: 97.26%), 94.5% enantiomeric excess.



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Signal 2: DAD1 C, Sig=254,16 Ref=370,60

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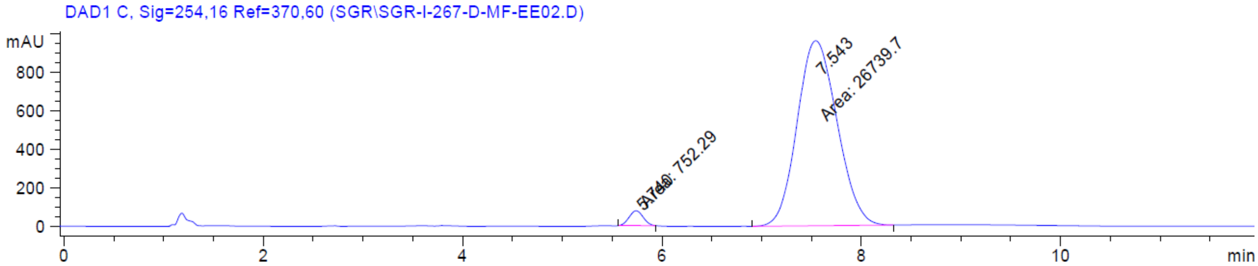

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Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
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   2   7.543 MM    0.4648 2.67397e4  958.75690  97.2636
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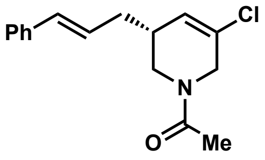


***6b***

**Chemical Formula:** $C_{16}H_{18}ClNO$
**Exact Mass: 275.1077**
**Molecular Weight: 275.7760**

**(R)-1-(5-chloro-3-cinnamyl-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6b** was synthesized following the general procedure B. Therefore, 3-chloropyridine (48 µL, 0.5 mmol, 1.0 equiv.) was used. The desired product was isolated as colorless oil (52.0 mg, 0.138 mmol, 38% yield over three steps).

**$^1$H NMR (400 MHz, CD$_3$OD)** (as mixture of E/Z amide bond isomers): δ 7.40 – 7.35 (m, 2H), 7.32 – 7.25 (m, 2H), 7.23 – 7.16 (m, 1H), 6.53 – 6.43 (m, 1H), 6.29 – 6.19 (m, 1H), 6.03 (dt, *J* = 3.8, 1.9 Hz, 0.4H), 5.99 (dt, *J* = 3.7, 1.8 Hz, 0.6H), 4.23 – 4.02 (m, 2H), 3.75 (dd, *J* = 13.1, 4.7 Hz, 0.4H), 3.69 (dd, *J* = 13.7, 4.7 Hz, 0.6 H), 3.45 (dd, *J* = 13.1, 6.3 Hz, 0.4H), 3.37 – 3.32 (m, 0.6H), 2.65 – 2.57 (m, 0.6H), 2.52 – 2.45 (m,0.4H), 2.34 – 2.18 (m, 2H), 2.13 – 2.11 (m, 3H);

**$^{13}$C NMR (101 MHz, CD$_3$OD)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ 172.01, 172.00*, 138.77*, 138.58, 134.01, 133.86*, 129.59, 129.52*, 129.22*, 129.07, 128.44*, 128.36, 128.21*, 128.11, 127.72, 127.15, 51.06*, 48.16, 47.26, 43.15*, 38.22, 37.74*, 37.30*, 37.11, 21.69*, 21.23;

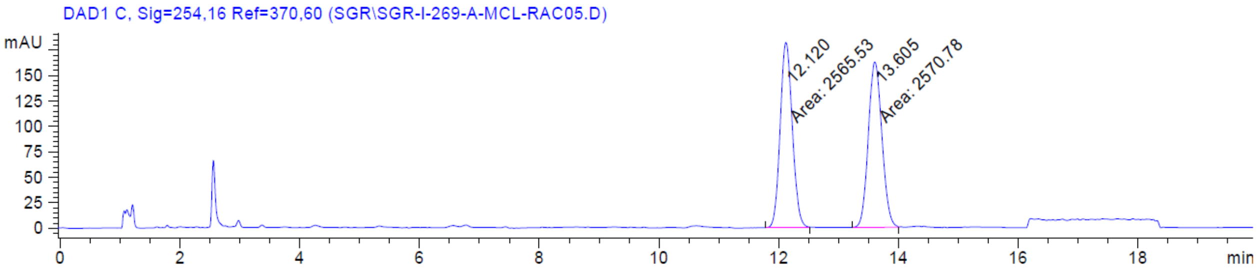
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 276.1155, found: 276.1174;

**R$_f$** (Hexane/EtOAc = 6/4): 0.15;

**ATR-IR** ν (cm$^{-1}$): 3852, 3734, 3673, 3648, 3025, 2920, 1716, 1647, 1490, 1424, 1369, 1272, 1231, 968, 847, 780, 768, 746, 695, 678;

**$[\alpha]_D^{25}$:** – 22.17 (c 1.0, CHCl$_3$);

**Chiral SFC Separation:** 10% *i*PrOH, 2.5 mL/min, AD-H column, λ = 254 nm, $t_R$ (min): major = 11.94 (area: 96.32%), minor = 13.46 (area: 3.68%), 92.6% enantiomeric excess.



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Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height      Area
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----|-------|----|-------|----------|----------|--------|
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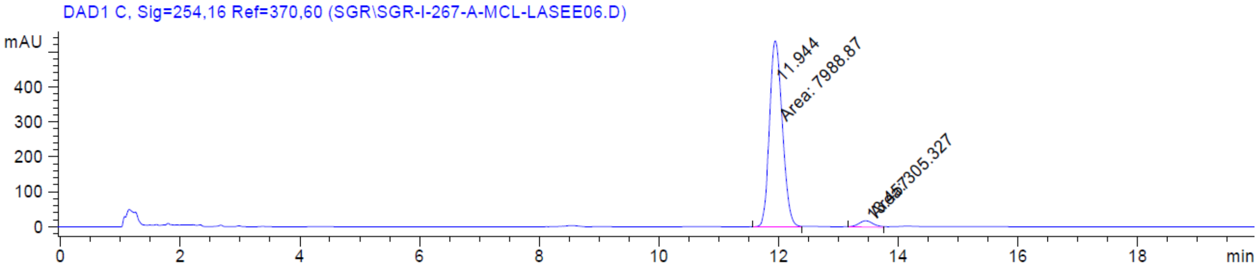

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Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height      Area
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----|-------|----|-------|----------|----------|--------|
   1  11.944 MM    0.2497 7988.87451  533.30609  96.3188
   2  13.457 MM    0.2841  305.32715   17.91254   3.6812
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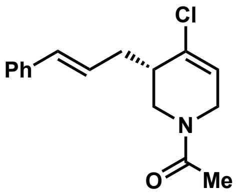


**6c**
**Chemical Formula:** $C_{16}H_{18}ClNO$
**Exact Mass: 275.1077**
**Molecular Weight: 275.7760**

**(S)-1-(4-chloro-3-cinnamyl-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6c** was synthesized following the general procedure B. Therefore, 4-chloropyridine (57 mg, 0.5 mmol, 1.0 equiv.) was used. The desired product was isolated as colorless oil (37.5 mg, 0.136 mmol, 27% yield over three steps).

**$^1$H NMR (400 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers): δ 7.39 – 7.34 (m, 2H), 7.31 – 7.24 (m, 2H), 7.22 – 7.15 (m, 1H), 6.57 – 6.45 (m, 1H), 6.29 – 6.19 (m, 1H), 5.94 – 5.89 (m, 1H), 4.41 – 4.34 (m, 1H), 4.16 (dd, *J* = 17.7, 3.9 Hz, 0.5H), 3.96 (dt, *J* = 17.7, 2.6 Hz, 0.5H), 3.81 (dd, *J* = 13.7, 3.3 Hz, 0.5H), 3.73 (dt, *J* = 18.8, 2.6 Hz, 0.5H), 3.54 (dd, *J* = 13.7, 4.2 Hz, 0.5H), 3.19 (dd, *J* = 13.2, 4.3 Hz, 0.5H), 2.74 – 2.47 (m, 2H), 2.42 – 2.21 (m, 1H), 2.11 (s, 1.5H), 2.06 (s, 1.5H);

**$^{13}$C NMR (101 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers, approx. 1/1 mixture): δ 172.49, 172.33, 138.88, 138.56, 135.14, 134.17, 134.10, 134.05, 129.60, 129.50, 128.40, 128.18, 127.81, 127.39, 127.17, 127.16, 123.17, 122.71, 48.03, 47.05, 43.74, 43.72, 43.48, 43.14, 35.18, 35.13, 21.61, 21.26;

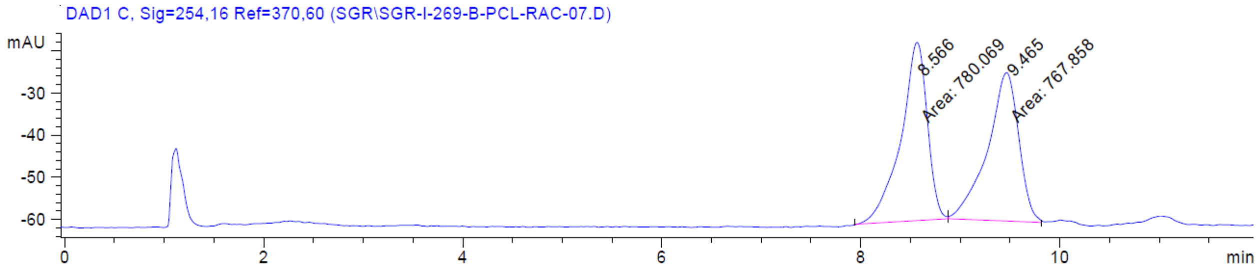
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 276.1155, found: 276.1131;

**$R_f$** (Hexane/EtOAc = 6/4): 0.11;

**ATR-IR** ν ($cm^{-1}$): 3866, 3733, 3648, 2922, 1646, 1425, 1360, 1237, 1032, 1010, 969, 822, 770, 746, 718, 699;

**$[\alpha]_D^{25}$:** – 31.97 (c 0.33, $CHCl_3$);

**Chiral SFC Separation:** 7% MeOH, 2.5 mL/min, AS-H column, λ = 254 nm, $t_R$ (min): major = 8.49 (area: 91.60%), minor = 9.43 (area: 8.40%), 83.2% enantiomeric excess.



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Signal 2: DAD1 C, Sig=254,16 Ref=370,60

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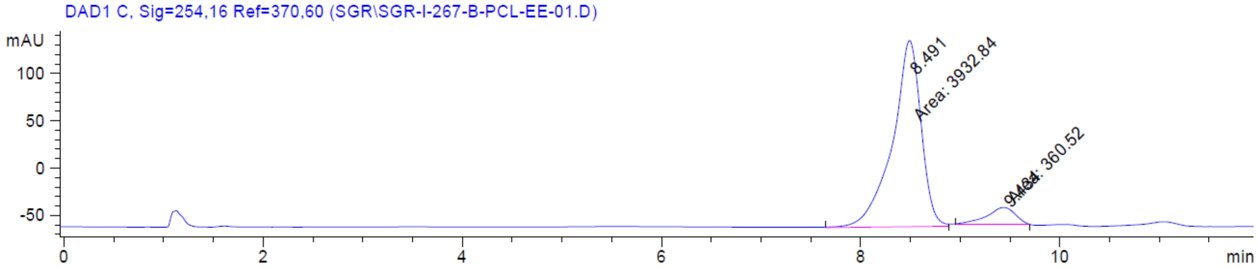

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Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area       Height      Area
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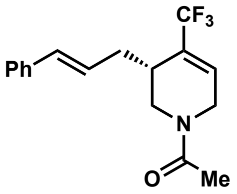


***6d***

**Chemical Formula:** $C_{17}H_{18}F_3NO$
**Exact Mass: 309.1340**
**Molecular Weight: 309.3322**

**(R)-1-(3-cinnamyl-4-(trifluoromethyl)-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6d** was synthesized following the general procedure B. Therefore, 4-(trifluoromethyl)pyridine (58 µL, 0.5 mmol, 1.0 equiv.) was used. The desired product was isolated as colorless oil (47.3 mg, 0.153 mmol, 31% yield over three steps).

**$^1$H NMR (400 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers): δ 7.39 – 7.35 (m, 2H), 7.32 – 7.25 (m, 2H), 7.23 – 7.16 (m, 1H), 6.55 – 6.42 (m, 2H), 6.28 – 6.19 (m, 1H), 4.67 (dd, *J* = 13.2, 1.8 Hz, 0.5H),4.59 (dt, *J* = 20.7, 3.2 Hz, 0.5H), 4.34 (dt, *J* = 19.4, 3.3 Hz, 0.5H), 4.08 – 4.00 (m, 0.5H), 3.95 (dd, *J* = 13.5, 2.2 Hz, 0.5H), 3.75 – 3.66 (m, 0.5H), 3.30 – 3.18 (m, 0.5H), 2.83 – 2.73 (m, 1H), 2.66 – 2.58 (m, 1H), 2.49 (ddd, *J* = 13.8, 7.2, 2.5 Hz, 0.5H), 2.33 – 2.15 (m, 1H), 2.10 (s, 1.5H), 2.08 (s, 1.5H);

**$^{13}$C NMR (101 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers, approx. 1/1 mixture, $^§$ = E/Z signal overlapping): δ 172.95, 172.71, 138.84, 138.45, 134.25, 134.16, 131.50 (q, *J* = 30.1 Hz), 130.76 (q, *J* = 30.1 Hz), 130.33 (q, *J* = 6.1 Hz), 129.99 (q, *J* = 6.2 Hz), 129.63, 129.51, 128.48, 128.21, 127.96, 127.41, 127.20, 127.17, 125.03 (q, *J* = 271.8 Hz), 124.97 (q, *J* = 271.6 Hz), 46.89, 45.92, 42.67, 41.88, 36.04$^§$, 35.27$^§$, 21.73, 21.34;

**$^{19}$F NMR (282 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers, roughly 1/1 mixture): δ –67.86 (q, *J* = 2.7 Hz), – 67.98 (q, *J* = 3.0 Hz);

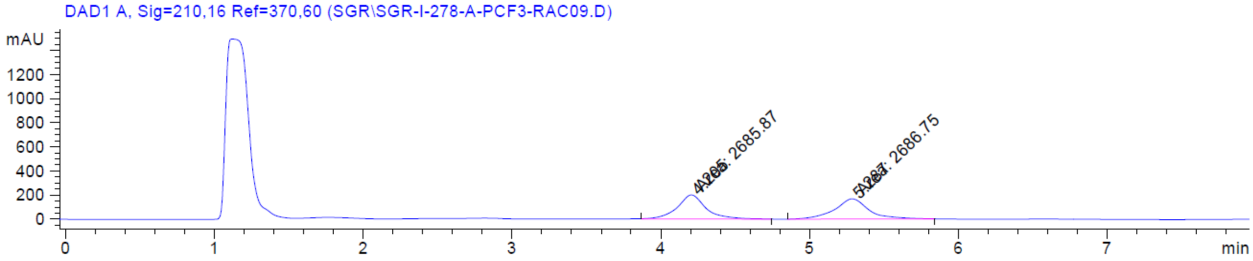
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 310.1419, found: 310.1417;

**$R_f$** (Hexane/EtOAc = 6/4): 0.20;

**ATR-IR** ν ($cm^{-1}$): 3674, 3026, 2922, 1734, 1652, 1490, 1423, 1373, 1337, 1296, 1261, 1241, 1206, 1162, 1115, 1072, 1019, 986, 836, 825, 742, 695, 676, 658;

**$[\alpha]_D^{25}$:** – 47.62 (c 1.0, $CHCl_3$);

**Chiral SFC Separation:** 5% MeOH, 2.5 mL/min, AS-H column, λ = 210 nm, $t_R$ (min): major = 4.14 (area: 96.60%), minor = 5.22 (area: 3.40%), 93.2% enantiomeric excess.



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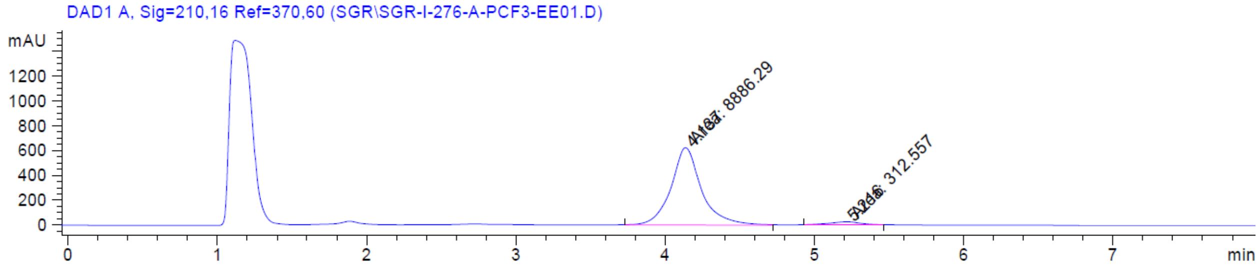

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Signal 1: DAD1 A, Sig=210,16 Ref=370,60

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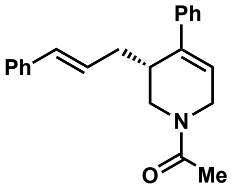
----|-------|----|-------|----------|----------|--------|
   1   4.137 MM    0.2372 8886.29492  624.26160  96.6022
   2   5.216 MM    0.2225  312.55685   23.41279   3.3978
```



***6e***

**Chemical Formula:** $C_{22}H_{23}NO$
**Exact Mass: 317.1780**
**Molecular Weight: 317.4320**

**(R)-1-(3-cinnamyl-4-phenyl-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6e** was synthesized following the general procedure C or D. Therefore, 4-phenylpyridine (78.1 mg, 0.5 mmol, 1.0 equiv.) was used. The desired product was isolated as pale-yellow oil (38.3 mg, 0.120 mmol, 24% yield over three steps).

**$^1$H NMR (400 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers): δ 7.45 – 7.40 (m, 2H), 7.38 – 7.32 (m, 2H), 7.30 – 7.20 (m, 5H), 7.18 – 7.11 (m, 1H), 6.37 (d, *J* = 15.8 Hz, 0.5H), 6.32 (d, *J* = 15.8 Hz, 0.5H), 6.21 – 6.12 (m, 1H), 6.02 (t, *J* = 3.4 Hz, 0.5H), 5.98 (t, *J* = 3.3 Hz, 0.5H), 4.62 (d, *J* = 12.6 Hz, 0.5H), 4.56 (dd, *J* = 19.7, 3.6 Hz, 0.5H), 4.27 (dd, *J* = 18.4, 3.9 Hz, 0.5H), 4.13 – 4.02 (m, 0.5H), 3.99 – 3.93 (m, 0.5H), 3.80 – 3.72 (m, 0.5H), 3.46 (dd, *J* = 13.3, 3.4 Hz, 0.5H), 3.14 – 3.08 (m, 0.5H), 3.06 – 2.95 (m, 1H), 2.40 – 2.14 (m, 2H), 2.12 (s, 1.5H), 2.10 (s, 1.5H);

**$^{13}$C NMR (101 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers, roughly 1/1 mixture, $^§$ = E/Z signal overlapping): δ 172.64, 172.48, 141.71, 141.14, 141.04, 140.93, 139.03, 138.66, 133.43, 133.24, 129.67$^§$, 129.53, 129.41, 129.12, 128.67, 128.61, 128.57, 128.23, 127.97, 127.09$^§$, 127.07, 127.01, 121.92, 121.64, 47.82, 47.13, 43.69, 42.94, 38.72, 38.59, 36.34, 36.28, 21.74, 21.34;

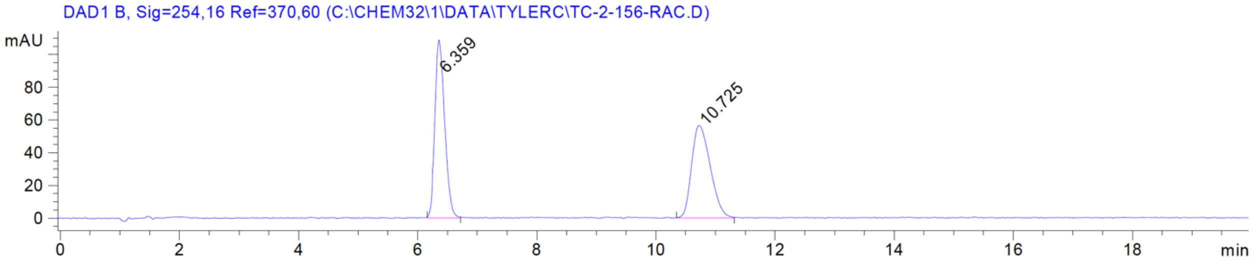
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 318.1858, found: 318.1854;

**$R_f$** (Hexane/EtOAc = 4/6): 0.30;

**ATR-IR** ν ($cm^{-1}$): 3216, 3056, 3027, 2929, 1633, 1494, 1435, 1370, 1331, 1265, 1075, 1035, 971, 882, 766, 740, 698;

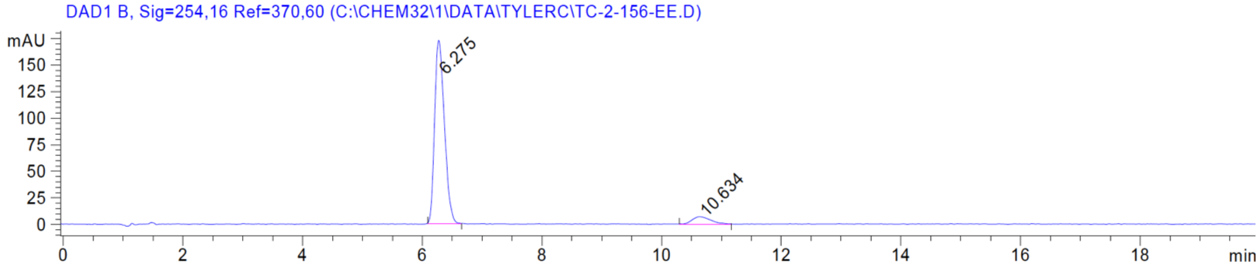
**[α]$_D$$^{25}$:** – 4.93 (c 0.85, $CHCl_3$);

**Chiral SFC Separation:** 20% iPrOH, 2.5 mL/min, AD-H column, λ = 254 nm, $t_R$ (min): major = 6.680 (area: 93.0%), minor = 11.213 (area: 7.0%), 86.0% enantiomeric excess.



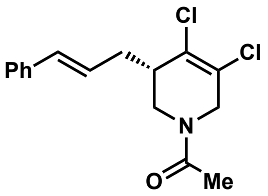
```
Signal 2: DAD1 B, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area       Height      Area
  #    [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.359 BB    0.1777 1244.61230  108.63536  50.4051
   2  10.725 BB    0.3412 1224.60437   56.42291  49.5949
```



```
Signal 2: DAD1 B, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area       Height      Area
  #    [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.275 BB    0.1763 1960.29517  172.92909  93.0373
   2  10.634 BB    0.3147  146.70486    6.93692   6.9627
```



***6f***

**Chemical Formula:** $C_{16}H_{17}Cl_2NO$
**Exact Mass: 309.0687**
**Molecular Weight: 310.2180**

**(S)-1-(4,5-dichloro-3-cinnamyl-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6f** was synthesized following the general procedure B. Therefore, 3,4-dichloropyridine (74.0 mg, 0.5 mmol, 1.0 equiv.) was used. The desired product was isolated as colorless oil (55.0 mg, 0.177 mmol, 35% yield over three steps).

**$^1$H NMR (400 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers): δ 7.39 – 7.35 (m, 2H), 7.32 – 7.26 (m, 2H), 7.24 – 7.17 (m, 1H), 6.57 – 6.46 (m, 1H), 6.26 – 6.17 (m, 1H), 4.57 – 4.51 (m, 0.5H), 4.42 (dd, *J* = 13.3, 2.0 Hz, 0.5H), 4.32 (dt, *J* = 17.0, 1.2 Hz, 0.5H), 4.16 (dd, *J* = 17.0, 1.9 Hz, 0.5H), 3.92 (dd, *J* = 17.9, 1.5 Hz, 0.5H), 3.82 (dd, *J* = 13.9, 3.2 Hz, 0.5H), 3.58 (dd, *J* = 13.9, 4.1 Hz, 0.5H), 3.18 (dd, *J* = 13.3, 4.2 Hz, 0.5H), 2.81 – 2.68

(m, 1H), 2.66 – 2.56 (m, 1H), 2.39 (dddd, $J$ = 14.6, 9.3, 8.0, 1.1 Hz, 0.5H), 2.31 – 2.21 (m, 0.5H), 2.11 (s, 1.5H), 2.10 (s, 1.5H);

**$^{13}$C NMR (101 MHz, CD$_3$OD)** (as mixture of E/Z amide bond isomers, roughly 1/1 mixture, $^{\S}$ = E/Z signal overlapping): δ 172.09, 171.97, 138.73, 138.40, 134.47, 134.46, 132.13, 131.04, 129.62, 129.52, 128.50, 128.27, 127.32, 127.19$^{\S}$, 127.01, 126.21, 125.45, 51.77, 48.17, 47.77, 44.88, 44.82, 42.82, 35.22$^{\S}$, 21.61, 21.16;

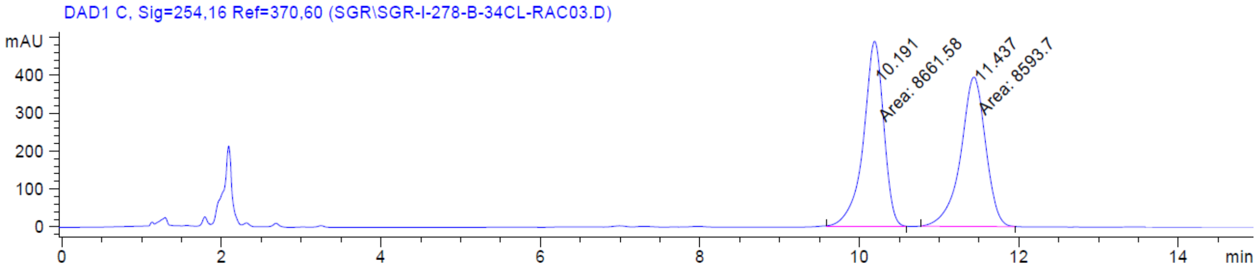
**HRMS**: m/z (ESI) calculated for (M + H)$^+$: 310.0765, found: 310.0756;

**R$_f$** (Hexane/EtOAc = 6/4): 0.37;

**$[\alpha]_D^{25}$:** – 18.23 (c 1.0, CHCl$_3$);

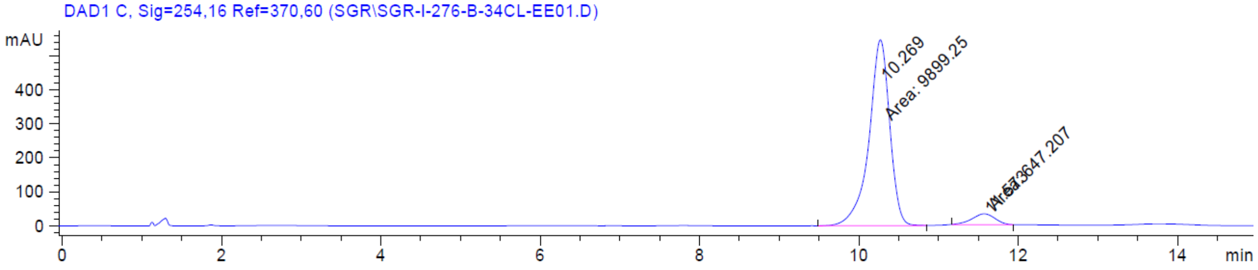
**ATR-IR** ν (cm$^{-1}$): 3853, 3734, 3648, 3025, 2919 1716, 1654, 1492, 1420, 1363, 1330, 1276, 1234, 1143, 1032, 985, 884, 825, 749, 695, 682;

**Chiral SFC Separation:** 10% MeOH, 2.5 mL/min, OD-H column, λ = 254 nm, t$_R$ (min): major = 10.27 (area: 93.86%), minor = 11.57 (area: 6.14%), 87.7% enantiomeric excess.



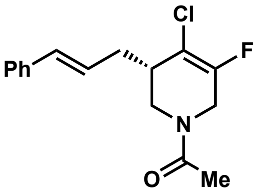
```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]         %
----|-------|----|-------|----------|----------|--------|
   1  10.191 MM    0.2949 8661.58203  489.44498  50.1967
   2  11.437 MM    0.3629 8593.69727  394.65631  49.8033
```



```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.269 MM    0.3012 9899.25098  547.71069  93.8633
   2  11.573 MM    0.3375  647.20721   31.95667   6.1367
```



***6g***

**Chemical Formula:** $C_{16}H_{17}ClFNO$
**Exact Mass: 293.0983**
**Molecular Weight: 293.7664**

**(S)-1-(4-chloro-3-cinnamyl-5-fluoro-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6g** was synthesized following the general procedure B. Therefore, 4-chloro-3-fluoropyridine (65.8 mg, 0.5 mmol, 1.0 equiv.) was used. The desired product was isolated as colorless oil (72.2 mg, 0.246 mmol, 49% yield over three steps).

**$^1$H NMR (400 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers): δ 7.39 – 7.33 (m, 2H), 7.32 – 7.24 (m, 2H), 7.23 – 7.15 (m, 1H), 6.57 – 6.44 (m, 1H), 6.27 – 6.16 (m, 1H), 4.49 – 4.41 (m, 0.6H), 4.34 – 4.24 (m, 0.8H), 4.15 – 4.07 (m, 0.4H), 3.93 – 3.85 (m, 0.6H), 3.74 (dd, *J* = 13.9, 3.3 Hz, 0.6H), 3.54 (dd, *J* = 13.8, 4.1 Hz, 0.6H), 3.19 (dd, *J* = 13.4, 4.1, 0.4H), 2.74 – 2.49 (m, 2H), 2.40 – 2.29 (m, 0.6H), 2.27 – 2.17 (m, 0.4H), 2.13 – 2.06 (m, 3H);

**$^{13}$C NMR (101 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ 172.39, 172.35*, 152.61 (d, *J* = 257.2 Hz), 152.00 (d, *J* = 258.0 Hz)*, 138.73*, 138.42, 134.40*, 134.38, 129.62, 129.52*, 128.47, 128.25*, 127.40, 127.18$^§$, 127.08*, 113.29 (d, *J* = 11.2 Hz)*, 112.32 (d, *J* = 11.8 Hz), 48.03 46.24 (d, *J* = 37.0 Hz)*, 43.11*, 42.67 (d, *J* = 37.5 Hz), 42.04, 41.91*, 34.91, 34.89*, 21.62*, 21.16;

**$^{19}$F NMR (282 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ –116.04 (d, *J* = 5.9 Hz), –116.99 (d, *J* = 5.8 Hz)*;

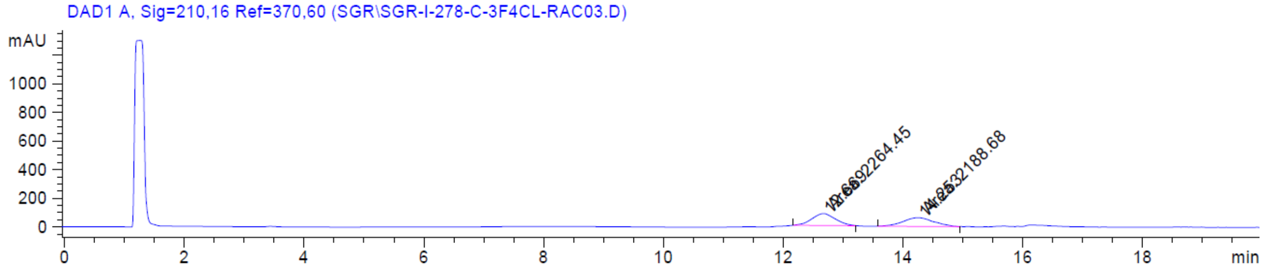
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 294.1061, found: 294.1045;

**$R_f$** (Hexane/EtOAc = 6/4): 0.21;

**ATR-IR** ν (cm$^{-1}$): 3363, 2931, 1716, 1652, 1435, 1372, 1236, 1036, 992, 734, 699;

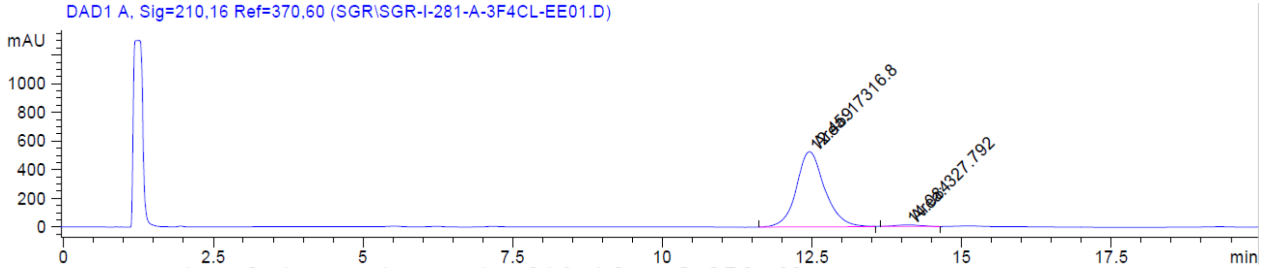
**$[\alpha]_D^{25}$:** – 25.73 (c 1.0, $CHCl_3$);

**Chiral SFC Separation:** 10% iPrOH, 2.5 mL/min, OD-H column, λ = 210 nm, $t_R$ (min): major = 12.46 (area: 98.14%), minor = 14.08 (area: 1.86%), 96.3% enantiomeric excess.



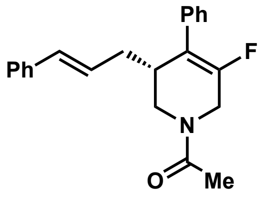
```
Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  12.669 MM    0.4542 2264.45215   83.09532  50.8508
   2  14.253 MM    0.5970 2188.67920   61.09854  49.1492
```



```
Signal 1: DAD1 A, Sig=210,16 Ref=370,60

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  12.459 MM    0.5493 1.73168e4  525.40576  98.1423
   2  14.084 MM    0.4721  327.79208   11.57163   1.8577
```



***6h***

**Chemical Formula:** $C_{22}H_{22}FNO$
**Exact Mass: 335.1685**
**Molecular Weight: 335.4224**

**(R)-1-(3-cinnamyl-5-fluoro-4-phenyl-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6h** was synthesized following the general procedure C or D. Therefore, 3-fluoro-4-phenylpyridine (86.6 mg, 0.5 mmol, 1.0 equiv.) was used. The desired product was isolated as colorless oil (34.7 mg, 0.103 mmol, 21% yield over three steps).

**$^{1}$H NMR (400 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers): δ 7.43 – 7.35 (m, 4H), 7.32 – 7.21 (m, 5H), 7.19 – 7.12 (m, 1H), 6.42 – 6.29 (m, 1H), 6.16 – 6.07 (m, 1H), 4.62 (d, *J* = 18.1 Hz, 0.6H), 4.51 (dd, *J* = 13.2, 2.4 Hz, 0.4H), 4.39 (d, *J* = 17.0 Hz, 0.4H), 4.10 (dt, *J* = 16.9, 1.6 Hz, 0.4H), 3.90 (dd, *J* = 13.7, 2.8 Hz, 0.6H), 3.80 (d, *J* = 18.0 Hz, 0.6H), 3.55 (dd, *J* = 13.6, 3.8 Hz, 0.6H), 3.14 (dd, *J* = 13.2, 3.9 Hz, 0.4H), 3.10 – 3.02 (m, 0.6H), 2.97 – 2.89 (m, 0.4H), 2.37 – 2.29 (m, 0.6H), 2.25 – 2.18 (m, 1H), 2.17 – 2.13 (m, 3H), 2.11 – 2.05 (m, 0.4H);

**$^{13}$C NMR (101 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *, $^{\S}$ = E/Z signal overlapping): δ 171.23, 171.16*, 150.92 (d, *J* = 254.8 Hz), 150.40 (d, *J* = 255.3 Hz)*, 137.52*, 137.18, 134.41*, 134.30, 132.32, 132.21*, 128.20*, 128.17, 128.13, 128.10$^{\S}$, 128.03*, 127.25*, 127.23, 126.89, 126.82*, 126.66$^{\S}$, 125.71*, 125.69, 117.69 (d, *J* = 5.4 Hz)*, 117.05 (d, *J* = 6.0 Hz), 46.55, 44.44 (d, *J* = 41.8 Hz)*, 41.62*, 41.00 (d, *J* = 42.1 Hz), 38.11 (d, *J* = 3.7 Hz), 37.78 (d, *J* = 3.4 Hz)*, 34.80 (d, *J* = 3.0 Hz)$^{\S}$, 20.36*, 19.92;

**$^{19}$F NMR (282 MHz, CD$_3$OD)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ –119.33 (d, *J* = 5.6 Hz), –120.31 (d, *J* = 5.7 Hz)*;

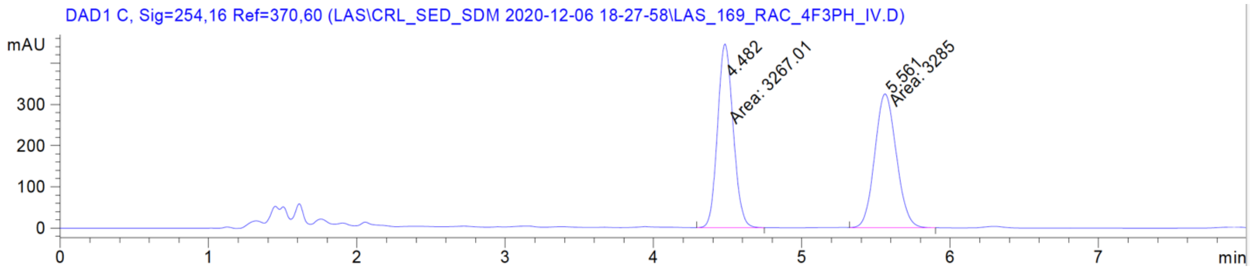
**HRMS**: m/z (ESI) calculated for (M + H)$^+$: 336.1764, found: 336.1774;

**R$_f$** (Hexane/EtOAc = 6/4): 0.19;

**ATR-IR** ν (cm$^{-1}$): 3024, 2930, 1734, 1652, 1496, 1426, 1373, 1242, 1205, 1180, 1051, 1009, 970, 820, 749, 698;

**[α]$_D$$^{25}$:** – 67.87 (c 1.0, CHCl$_3$);

**Chiral SFC Separation:** 30% MeOH, 2.5 mL/min, OJ-H column, λ = 254 nm, t$_R$ (min): major = 4.596 (area: 96.3%), minor = 5.677 (area: 3.7%), 92.6% enantiomeric excess.



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Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1   4.482 MM    0.1217 3267.01074  447.36011  49.8627
  2   5.561 MM    0.1682 3285.00098  325.46252  50.1373
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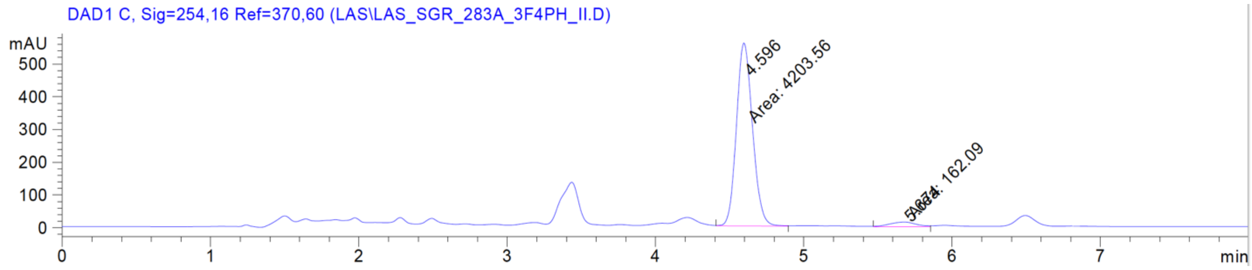

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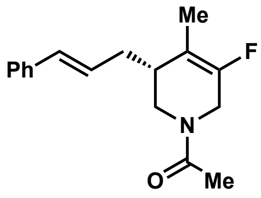
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1   4.596 MM    0.1251 4203.55566  559.99762  96.2872
  2   5.674 MM    0.1996  162.08955   13.53266   3.7128
```



***6i***

**Chemical Formula:** $C_{17}H_{20}FNO$
**Exact Mass: 273.1529**
**Molecular Weight: 273.3514**

**(R)-1-(3-cinnamyl-5-fluoro-4-methyl-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6i** was synthesized following the general procedure D. Therefore, 3-fluoro-4-methylpyridine (52 µL, 0.5 mmol, 1.0 equiv.) was used. The desired product was isolated as pale-yellow oil (60.2 mg, 0.22 mmol, 44% yield over three steps).
Note: Using 2 mol% [Ir(coe)Cl]$_2$ and 10 mol% Pd(OAc)$_2$ delivers product in a higher yield, but lower enantioselectivity (76.6 mg, 0.28 mmol, 56% yield, 77% ee).

**$^1$H NMR (400 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers): δ 7.39 – 7.29 (m, 4H), 7.26 – 7.17 (m, 1H), 6.46 (ddd, *J* = 15.8, 3.8, 2.3 Hz, 1H), 6.28 – 6.07 (m, 1H), 4.54 – 4.38 (m, 0.65H), 4.20 (dd, *J* = 13.2, 3.3 Hz, 0.35H), 4.00 (dt, *J* = 15.9, 2.0 Hz, 0.35H), 3.90 (dtd, *J* = 16.1, 2.0, 1.1 Hz, 0.35H), 3.77 – 3.66 (m, 0.65H), 3.62 (dd, *J* = 13.4, 3.0 Hz, 0.65H), 3.30 (ddd, *J* = 13.3, 3.9, 1.0 Hz, 0.65H), 3.11 (dd, *J* = 13.2, 4.0 Hz, 0.35H), 2.45 – 2.29 (m, 0.7H), 2.23 – 2.14 (overlap, 2.3H), 2.10 (s, 2H), 2.08 (s, 1H), 1.75 (dd, *J* = 4.5, 2.3 Hz, 3H);

**$^{13}$C NMR (101 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *) δ 170.2, 169.8*, 150.5 (d, *J* = 248.7 Hz ), 149.3 (d, *J* = 248.7 Hz )*, 137.6*, 137.0, 132.9, 132.6*, 128.8, 128.6*, 127.8, 127.6, 127.7*, 127.2*, 126.3*, 126.2, 112.7 (d, *J* = 8.4 Hz)*, 111.1 (d, *J* = 9.5 Hz), 46.4, 44.8 (d, *J* = 41.0 Hz)*, 41.9*, 41.8 (d, *J* = 41.8 Hz), 39.5 (d, *J* = 4.8 Hz), 38.8 (d, *J* = 4.4 Hz)*, 34.5 (d, *J* = 2.7 Hz)*, 34.4 (d, *J* = 3.1 Hz), 22.0*, 21.5, 12.4 (dd, *J* = 6.2, 1.8 Hz);

**$^{19}$F NMR (282 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ -120.71 – -120.73 (m), -122.01 – -122.04 (m)*;

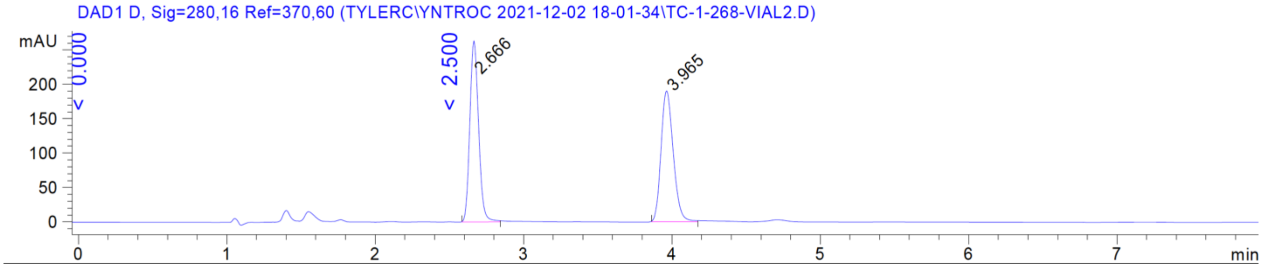
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 274.1602, found 274.1605;

**R$_f$** (Hexane/EtOAc) = 4/6): 0.65;

**$[\alpha]_D^{25}$:** – 8.75 (c 1.0, CHCl$_3$);

**ATR-IR** ν (cm$^{-1}$): 3022, 2918, 1728, 1648, 1438, 1387, 1369, 1234, 1158, 1070, 969, 918, 750, 724, 693;

**Chiral SFC Separation:** 25% iPrOH, 2.5 mL/min, AD-H column, λ = 254 nm or 280 nm, t$_R$ (min): major = 2.596 (area: 96.8%), minor = 3.846 (area: 3.2%), 93.6% enantiomeric excess.



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Signal 3: DAD1 D, Sig=280,16 Ref=370,60

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   2.666 BB    0.0644 1081.70117  260.62692  49.7744
   2   3.965 BB    0.0910 1091.50793  190.15250  50.2256
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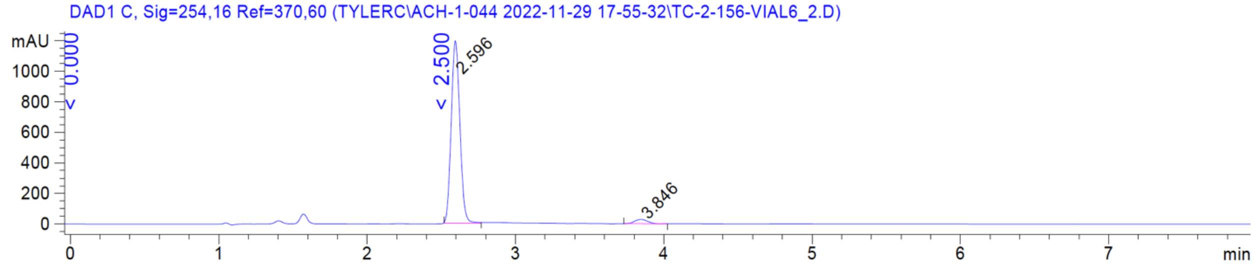
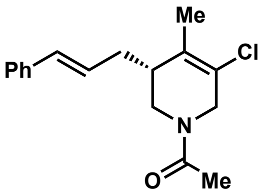


```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   2.596 BB    0.0678 4862.83008 1186.93994  96.7838
   2   3.846 BB    0.0895  161.59549   28.79920   3.2162
```



***6j***

**Chemical Formula:** $C_{17}H_{20}ClNO$
**Exact Mass: 289.1233**
**Molecular Weight: 289.8030**

**(R)-1-(5-chloro-3-cinnamyl-4-methyl-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6j** was synthesized following the general procedure D. Therefore, 3-chloro-4-methylpyridine (55 µL, 0.5 mmol, 1.0 equiv.) was used. The desired product was isolated as pale-yellow oil (68.2 mg, 0.235 mmol, 47% yield over three steps).
Note: Using 2 mol% $[Ir(coe)Cl]_2$ and 10 mol% $Pd(OAc)_2$ delivers product in a higher yield, but lower enantioselectivity (108.8 mg, 0.375 mmol, 75% yield, 72% ee).

**$^1$H NMR (400 MHz, $CDCl_3$)** (as mixture of E/Z amide bond isomers): δ 7.41 – 7.27 (m, 4H), 7.27 – 7.13 (m, 1H), 6.46 (dt, *J* = 15.7, 1.5 Hz, 1H), 6.28 – 6.08 (m, 1H), 4.57 (dt, *J* = 18.0, 1.9 Hz, 0.65H), 4.35 (dd, *J* = 13.2, 2.9 Hz, 0.35H), 4.07 (dt, *J* = 16.6, 1.9 Hz, 0.35H), 3.96 (dt, *J* = 16.6, 2.0 Hz, 0.35H), 3.81 – 3.64 (m, 1.3H), 3.40 – 3.26 (m, 0.65H), 3.04 (dd, *J* = 13.2, 4.0 Hz, 0.35H), 2.56 – 2.47 (m, 0.75H), 2.41 – 2.24 (m, 1.35H), 2.23 – 2.15 (m, 1H), 2.10 (s, 3H), 1.97 – 1.87 (m, 3H);

**$^{13}$C NMR (101 MHz, $CDCl_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *) δ 169.89, 169.43*, 137.51*, 136.96, 133.05, 132.80*, 132.69*, 130.79, 128.79, 128.59*, 127.67, 127.61, 127.24*, 127.16*, 126.26*, 126.13, 123.49, 121.87*, 50.54*, 46.89, 46.01, 42.22, 41.94*, 41.52*, 34.60*, 34.33, 21.94*, 21.43, 18.38*, 18.33;

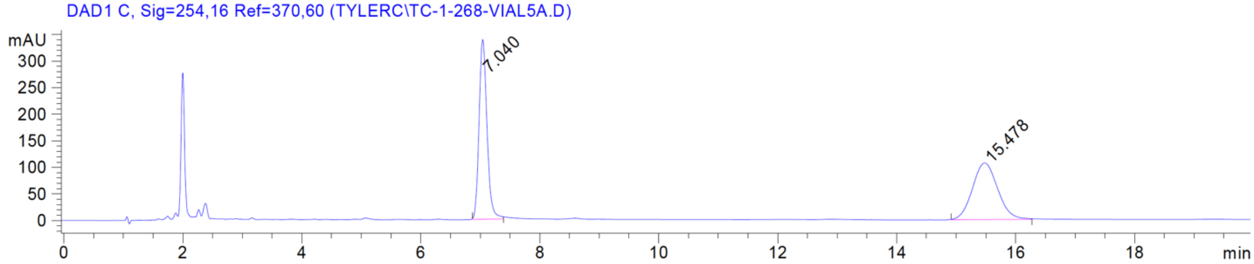
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 290.1306, found 290.1317;

**$R_f$** (Hexane/EtOAc = 4/6) : 0.60;

**ATR-IR** ν (cm$^{-1}$): 3236, 3027, 2924, 1644, 1434, 1369, 1241, 1014, 972, 894, 749, 694, 655;

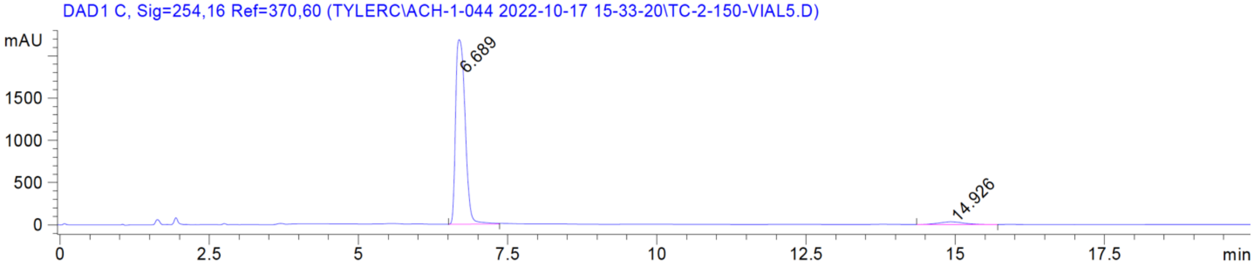
**[α]$_D$$^{25}$:** – 9.97 (c 1.0, $CHCl_3$);

**Chiral SFC Separation:** 15% iPrOH, 2.5 mL/min, AD-H column, λ = 254 nm, t$_R$ (min): major = 6.689 (area: 96.5%), minor = 14.926 (area: 3.5%), 93.0% enantiomeric excess.



```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width      Area       Height      Area
  #    [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1    7.040 BB    0.1443 3134.57324  337.63516  49.9836
  2   15.478 BB    0.4555 3136.62598  106.54130  50.0164
```



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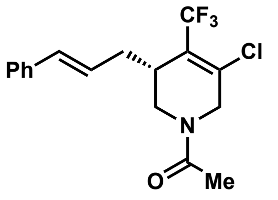
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width      Area       Height      Area
  #    [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
  1    6.689 BB    0.1781 2.43808e4  2186.42725  96.5063
  2   14.926 BB    0.4392  882.61859   31.47048   3.4937
```



***6k***

**Chemical Formula:** $C_{17}H_{17}ClF_3NO$
**Exact Mass: 343.0951**
**Molecular Weight: 343.7742**

**(R)-1-(5-chloro-3-cinnamyl-4-(trifluoromethyl)-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6k** was synthesized following the general procedure B. Therefore, 3-chloro-4-(trifluoromethyl)pyridine (90.8 mg, 0.5 mmol, 1.0 equiv.) was used. The desired product was isolated as colorless oil (33.9 mg, 0.099 mmol, 20% yield over three steps).

**$^1$H NMR (400 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers): δ 7.40 – 7.35 (m, 2H), 7.32 – 7.26 (m, 2H), 7.24 – 7.16 (m, 1H), 6.55 – 6.43 (m, 1H), 6.27 – 6.18 (m, 1H), 4.80 – 4.69 (m, 1H), 4.51 – 4.43 (m, 0.5H), 4.25 – 4.16 (m, 0.5H), 4.01 – 3.95 (m, 0.5H), 3.84 – 3.75 (m, 0.5H), 3.37 – 3.32 (m, 0.5H), 2.95 – 2.89 (m, 0.5H), 2.83 – 2.72 (m, 1H), 2.57 – 2.49 (m, 0.5H), 2.44 – 2.36 (m, 0.5H), 2.35 – 2.25 (m, 0.5H), 2.21 – 2.15 (m, 0.5H), 2.13 (s, 1.5H), 2.11 (s, 1.5H);

**$^{13}$C NMR (101 MHz, CD$_3$OD)** (as mixture of E/Z amide bond isomers, roughly 1/1 mixture): δ 172.45, 172.23, 138.71, 138.32, 135.74, (q, *J* = 3.9 Hz), 135.13 (q, *J* = 4.0 Hz), 134.64$^{§}$, 129.65, 129.53, 129.39, 129.09, 128.58, 128.33, 127.29, 127.22, 127.21, 126.91, 124.04 (q, *J* = 274.1 Hz), 123.97 (q, *J* = 274.0 Hz), 51.72, 48.51, 46.36, 41.26, 38.18, 38.16, 36.19, 36.14, 21.68, 21.24;

**$^{19}$F NMR (282 MHz, CD$_3$OD)** (as mixture of E/Z amide bond isomers, roughly 1/1 mixture): δ -62.48, -62.63;

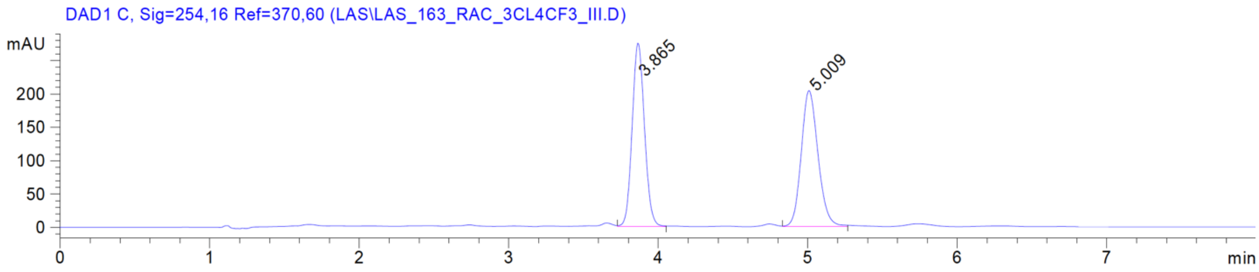
**HRMS**: m/z (ESI) calculated for (M + H)$^+$: 344.1029, found: 344.1021;

**R$_f$** (Hexane/EtOAc = 6/4): 0.18;

**ATR-IR** ν (cm$^{-1}$): 3026, 2927, 1735, 1653, 1493, 1423, 1364, 1287, 1262, 1242, 1210, 1185, 1132, 1052, 985, 887, 772, 744, 694, 649, 610;

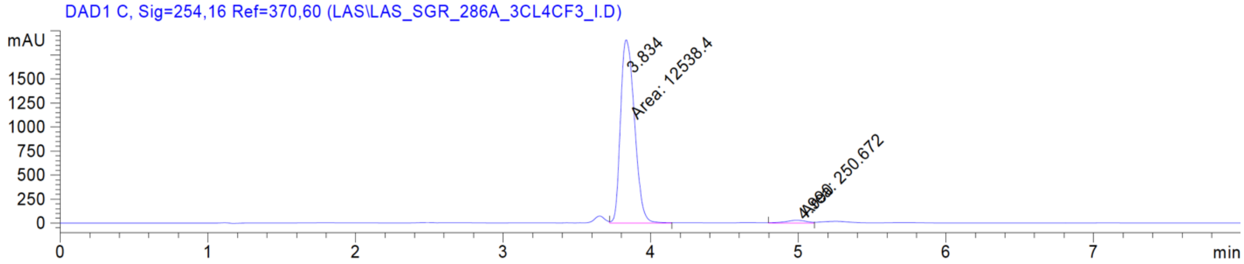
**[α]$_D$$^{25}$:** – 7.31 (c 1.0, CHCl$_3$);

**Chiral SFC Separation:** 10% MeOH, 2.5 mL/min, OJ-H column, λ = 254 nm, t$_R$ (min): major = 3.834 (area: 98.0%), minor = 4.990 (area: 2.0%), 96.0% enantiomeric excess.



```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   3.865 VB    0.0869 1570.85596  273.97107  49.6514
   2   5.009 VB    0.1194 1592.91370  203.42432  50.3486
```



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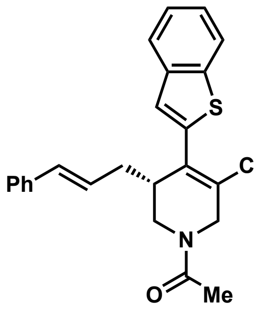
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   3.834 MM    0.1089 1.25384e4  1919.23767  98.0400
   2   4.990 MM    0.1466  250.67191   28.49819   1.9600
```



**6l**

**Chemical Formula:** $C_{24}H_{22}ClNOS$
**Exact Mass: 407.1111**
**Molecular Weight: 407.9560**

**(R)-1-(4-(benzo[b]thiophen-2-yl)-5-chloro-3-cinnamyl-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6l** was synthesized following the general procedure C or D. Therefore, 4-(benzo[b]thiophen-2-yl)-3-chloropyridine (122.9 mg, 0.5 mmol, 1.0 equiv.) was used. The desired product was isolated as yellow oil (103.8 mg, 0.255 mmol, 51% yield over three steps).
Note: Using 2 mol% $[Ir(coe)Cl]_2$ and 10 mol% $Pd(OAc)_2$ delivers product in a higher yield, but lower enantioselectivity (113.8 mg, 0.28 mmol, 56% yield, 80% ee).

**$^1$H NMR (400 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers signals of minor isomer are indicated with *, $^{\S}$ = two signals overlapping): δ 7.81 – 7.73 (m, 2H), 7.51 (s, 0.4H)*, 7.50 (s, 0.6H), 7.35 – 7.27 (m, 2H), 7.24 – 7.09 (m, 5H), 6.33 (d, $J$ = 7.6 Hz, 0.4H)*, 6.29 (d, $J$ = 7.6 Hz, 0.6H), 6.16 – 6.04 (m, 1H), 4.74 (d, $J$ = 19.0 Hz, 0.6H), 4.59 (d, $J$ = 11.8 Hz, 0.4H)*, 4.40 (d, $J$ = 17.9 Hz, 0.4H)*, 4.11 (dd, $J$ = 17.9, 1.2 Hz, 0.4H)*, 3.86 – 3.75 (m, 1.2H)$^{\S}$, 3.38 (dd, $J$ = 13.5, 3.4, 0.6H), 3.05 – 2.98 (m, 0.6H), 2.96 – 2.86 (m, 0.8H)*$^{\S}$, 2.40 – 2.12 (m, 2H), 2.08 (s, 1.2H)*, 2.05 (s, 1.8H);

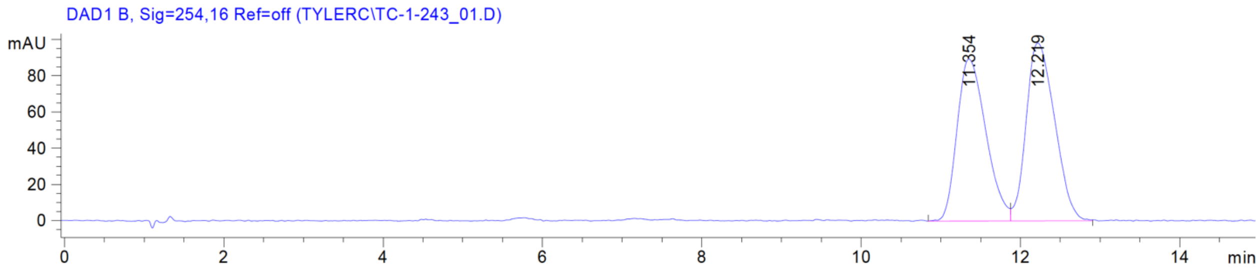
**$^{13}$C NMR (101 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *, $^{\S}$ = E/Z signal overlapping): δ 172.13, 171.95*, 141.10$^{\S}$, 140.57$^{\S}$, 140.53, 140.49$^{\S}$, 140.34*, 138.76*, 138.37, 133.93, 133.91*, 132.12*, 131.29, 129.54, 129.43*, 128.36, 128.21, 128.11*, 127.84*, 127.15*, 127.12, 126.50$^{\S}$, 126.05$^{\S}$, 125.72*, 125.63, 124.94*, 124.92, 122.95$^{\S}$, 52.00*, 48.71, 46.94, 43.48*, 43.45, 42.06*, 36.32*, 36.27, 21.68*, 21.26;
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 408.1189, found: 408.1208;

**$R_f$** (Hexane/EtOAc = 1/1): 0.26;

**ATR-IR** ν ($cm^{-1}$): 3055, 3025, 2926, 1652, 1495, 1435, 1359, 1305, 1238, 1157, 1129, 1068, 1030, 968, 922, 860, 832, 745, 728, 695, 613;

**$[\alpha]_D^{25}$:** – 81.02 (c 1.0, $CHCl_3$);

**Chiral SFC Separation:** 30% MeOH, 2.5 mL/min, IC column, λ = 254 nm, $t_R$ (min): major = 12.233 (area: 97.3%), minor = 11.410 (area: 2.7%), 94.6% enantiomeric excess.



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Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.354 VV    0.3963 2260.10962   89.58550  48.0283
   2  12.219 VB    0.3680 2445.68018   98.39331  51.9717
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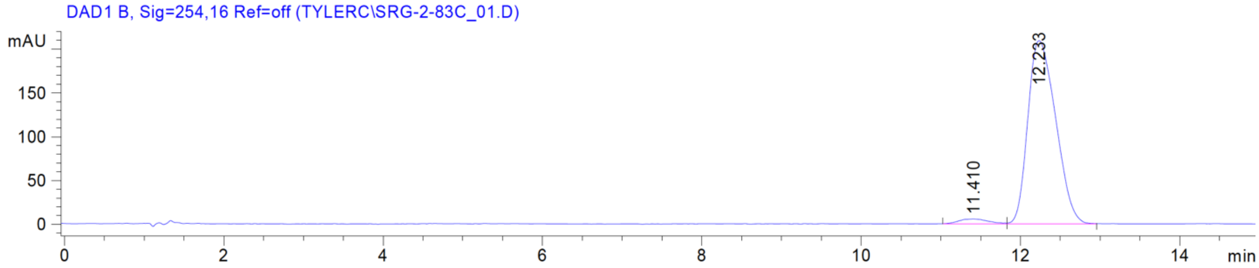
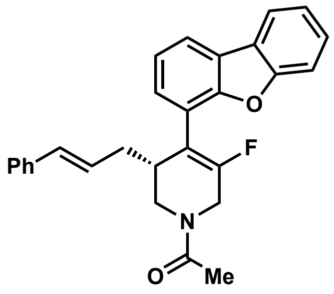


```
Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.410 BV    0.3061  138.32794    5.48661   2.6563
   2  12.233 VB    0.3909 5069.24756  209.07002  97.3437
```



***6m***

**Chemical Formula: $C_{28}H_{24}FNO_2$**
**Exact Mass: 425.1791**
**Molecular Weight: 425.5034**

**(*R*)-1-(3-cinnamyl-4-(dibenzo[*b*,*d*]furan-4-yl)-5-fluoro-3,6-dihydropyridin-1(2*H*)-yl)ethan-1-one 6m** was synthesized following the general procedure C or D. Therefore, 4-(dibenzo[b,d]furan-4-yl)-3-fluoropyridine (131.6 mg, 0.5 mmol, 1.0 equiv.) was used. The desired product was isolated as yellow amorphous solid (89.2 mg, 0.21 mmol, 42% yield over three steps). Note: Using 2 mol% $[Ir(coe)Cl]_2$ and 10 mol% $Pd(OAc)_2$ delivers product in a higher yield, but lower enantioselectivity (114.7 mg, 0.27 mmol, 54% yield, 78% ee, 68% yield BRSM).

**$^1$H NMR (400 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers): δ 8.01 – 7.96 (m, 1H), 7.93 (td, *J* = 5.2, 3.7 Hz, 1H), 7.61 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.49 (ddd, *J* = 8.4, 7.3, 1.4 Hz, 1H), 7.43 – 7.32 (m, 3H), 7.28 – 7.12 (m, 5H), 6.33 (d, *J* = 15.9 Hz, 0.65H), 6.27 (d, *J* = 15.8 Hz, 0.35H), 6.10 (t, *J* = 7.6 Hz, 0.35H), 6.01 (ddd, *J* = 15.8, 8.5, 5.8 Hz, 0.65H), 4.80 (dd, *J* = 18.3, 1.6 Hz, 0.65H), 4.37 – 4.26 (m, 0.70H), 4.14 (dd, *J* = 16.8, 2.0 Hz, 0.35H), 3.99 (dd, *J* = 18.3, 1.8 Hz, 0.65H), 3.84 (dd, *J* = 13.4, 3.4 Hz, 0.65H), 3.69 (dd, *J* = 13.4, 4.0 Hz, 0.65H), 3.58 (dd, *J* = 13.3, 4.3 Hz, 0.35H), 3.32 – 3.20 (m, 1H), 2.42 – 2.32 (m, 0.70H), 2.32 – 2.23 (m, 1.3H), 2.21 (d, *J* = 4.9 Hz, 3H);

**$^{13}$C NMR (101 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *) δ 170.18, 169.74 (d, *J* = 1.7 Hz)*, 156.14*, 156.11, 153.62 (overlap)*, 152.52 (d, *J* = 258.3 Hz), 151.19 (d, *J* = 258.2 Hz)*, 137.41*, 136.91, 132.77, 132.51*, 128.59, 128.41*, 128.03, 128.00, 127.72*, 127.69*, 127.52*, 127.43, 127.03*, 126.87*, 126.10*, 126.01, 124.76, 124.19, 122.97 (overlap)*, 122.88 (overlap)*, 120.82, 120.38*, 120.35*, 118.85 (d, *J* = 1.9 Hz), 114.34 (d, *J* = 6.7 Hz)*, 113.02 (d, *J* = 7.7 Hz), 111.85 (overlap)*, 46.76, 45.24 (d, *J* = 39.7 Hz)*, 42.33*, 41.70 (d, *J* = 40.5 Hz), 38.35 (d, *J* = 3.0 Hz), 37.54 (d, *J* = 2.8 Hz)*, 35.26 (d, *J* = 2.8 Hz)*, 35.16 (d, *J* = 3.0 Hz), 22.08*, 21.53;

**$^{19}$F NMR (282 MHz, $CD_3OD$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ -112.15 – -112.26 (m), -113.31 (d, *J* = 4.7 Hz)*;

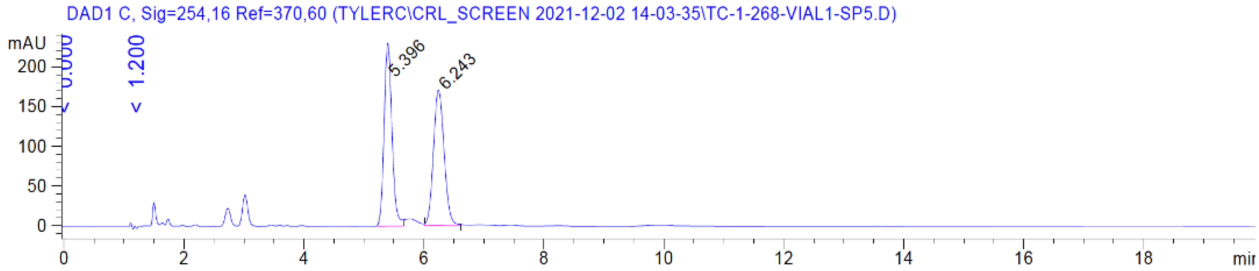
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 426.1864, found 426.1872;

**$R_f$** (Hexane/acetone = 3/7): 0.40;

**ATR-IR** ν ($cm^{-1}$): 3439, 3027, 2930, 1648, 1450, 1414, 1378, 1352, 1257, 1233, 1180, 1046, 1012, 983, 922, 843, 798, 752, 737;

**$[\alpha]_D^{25}$:** – 17.72 (c 0.304, $CHCl_3$);

**Chiral SFC Separation:** 30% MeOH, 2.5 mL/min, AD-H column, λ = 254 nm, $t_R$ (min): major = 6.303 (area: 98.5%), minor = 5.431 (area: 1.5%), 97.0% enantiomeric excess.



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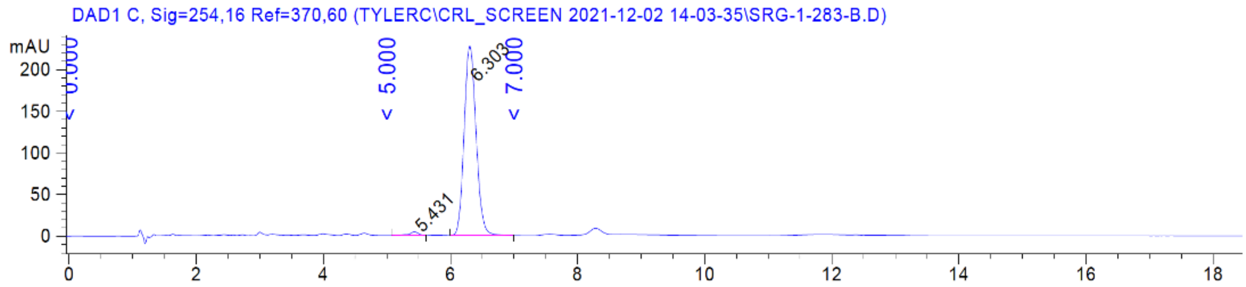
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.396 BB    0.1392 2114.76562  230.07974  50.1048
   2   6.243 BB    0.1920 2105.91846  170.63986  49.8952
```



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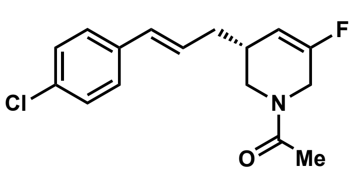
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.431 BV    0.1582   44.71070    4.19887   1.4915
   2   6.303 VB    0.2013 2953.04980  227.77563  98.5085
```



*6n*

**Chemical Formula:** $C_{16}H_{17}ClFNO$
**Exact Mass: 293.0983**
**Molecular Weight: 293.7664**

**(*R*,*E*)-1-(3-(3-(4-chlorophenyl)allyl)-5-fluoro-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6n** was synthesized following the general procedure B using 3-fluoropyridine (43 µL, 0.5 mmol, 1.0 equiv.) as substrate and (*E*)-3-(4-chlorophenyl)allyl methyl carbonate (170 mg, 0.75 mmol, 1.5 equiv.). The desired compound was obtained as yellowish oil (42 mg, 0.143 mmol, 29% yield over three steps).

**$^1$H NMR (400 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers): δ 7.30–7.23 (m, 4H), 6.44–6.34 (m, 1H), 6.18–6.06 (m, 1H), 5.46–5.30 (m, 1H), 4.18–4.04 (m, 1H), 4.02–3.91 (m, 1H), 3.84 (dd, *J* = 13.1, 4.7 Hz, 0.4H), 3.53 (dd, *J* = 13.4, 4.5 Hz, 0.6H), 3.36–3.21 (m, 1H), 2.57–2.42 (m, 1H), 2.32–2.15 (m, 2H), 2.11 (s, 3H);

**$^{13}$C NMR (101 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ 169.8, 169.7*, 156.4 (d, *J* = 257 Hz), 154.9 (d, *J* = 256 Hz)*, 135.8*, 135.5, 133.2, 132.9*, 131.8, 131.6*, 128.9, 128.7*, 127.4*, 127.4, 127.4, 106.0 (d, *J* = 11.0 Hz)*, 104.3 (d, *J* = 12.5 Hz), 47.7, 44.8 (d, *J* = 39 Hz)*, 42.9*, 41.1 (d, *J* = 40 Hz), 36.8 (d, *J* = 2.2 Hz)*, 36.7 (d, *J* = 2.6 Hz), 34.2 (d, *J* = 6.2 Hz), 33.3 (d, *J* = 5.9 Hz)*, 22.0*, 21.5;

**$^{19}$F NMR (282 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ –112.2 (dd, *J* = 15.9, 5.0 Hz), –114.2 (dd, *J* = 16.1, 5.2 Hz)*;

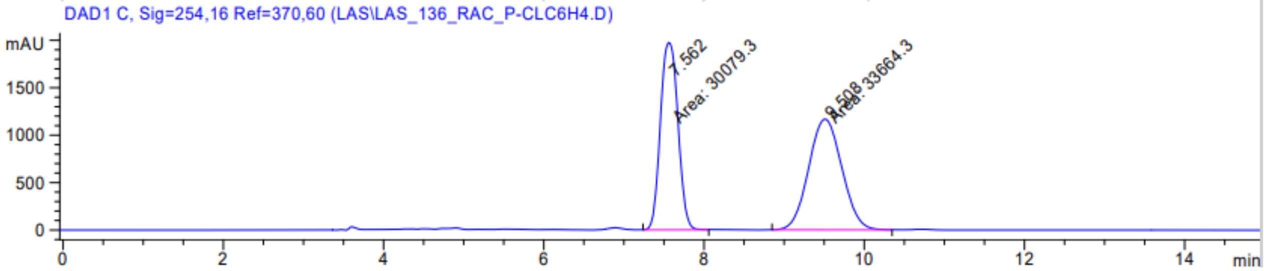
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 294.1061, found: 294.1080;

**R$_f$** (*n*-hexane/EtOAc = 6/4): 0.26;

**ATR-IR** ν (cm$^{-1}$): 2913, 1705, 1645, 1490, 1428, 1231, 1091, 1012, 973, 828, 729;

**$[\alpha]_D^{25}$:** – 33.26 (c 1.0, CHCl$_3$);

**Chiral SFC Separation:** 30% MeOH, 2.5 mL/min, AD-H column, λ = 254 nm, $t_R$ (min): minor = 7.65 (area: 2.17%), major = 9.41 (area: 97.83%), 95.7% enantiomeric excess.



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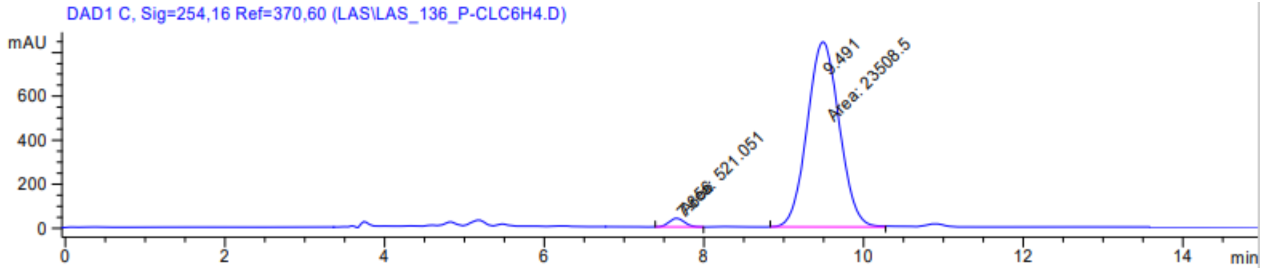
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   7.562 MM    0.2539 3.00793e4 1974.43616  47.1880
   2   9.508 MM    0.4801 3.36643e4 1168.63647  52.8120

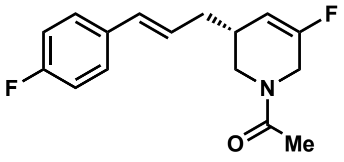
Totals :                  6.37436e4 3143.07263
```



```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   7.656 MM    0.2214  521.05127   39.22103   2.1684
   2   9.491 MM    0.4650 2.35085e4  842.62915  97.8316

Totals :                  2.40295e4  881.85018
```



***6o***

**Chemical Formula:** $C_{16}H_{17}F_2NO$
**Exact Mass: 277.1278**
**Molecular Weight: 277.3148**

**(*R*,*E*)-1-(5-fluoro-3-(3-(4-fluorophenyl)allyl)-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6o** was synthesized following the general procedure B using 3-fluoropyridine (43 µL, 0.5 mmol, 1.0 equiv.) as substrate and (*E*)-3-(4-fluorophenyl)allyl methyl carbonate (158 mg, 0.75 mmol, 1.5 equiv.). The desired compound was obtained as yellowish oil (47 mg, 0.169 mmol, 34% yield over three steps).

**$^1$H NMR (400 MHz, $CDCl_3$)** (as mixture of E/Z amide bond isomers): δ 7.33–7.27 (m, 2H), 7.03–6.94 (m, 2H), 6.40 (dd, *J* = 15.8, 7.2 Hz, 1H), 6.12–6.00 (m, 1H), 5.46–5.30 (m, 1H), 4.18–4.05 (m, 1H), 4.03–3.91 (m, 1H), 3.86 (dd, *J* = 13.1, 4.7 Hz, 0.4H), 3.53 (dd, *J* = 13.6, 4.5 Hz, 0.6H), 3.33–3.22 (m, 1H), 2.50 (br s, 1H), 2.30–2.15 (m, 2H), 2.12 (s, 3H);

**$^{13}$C NMR (101 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ 169.8, 169.7*, 162.3 (d, *J* = 248 Hz), 162.2 (d, *J* = 246 Hz)*, 156.4 (d, *J* = 257 Hz), 154.9 (d, *J* = 257 Hz)*, 133.52 (d, *J* = 3.3 Hz)*, 133.20 (d, *J* = 3.3 Hz), 131.8, 131.6*, 127,7 (d, *J* = 8.1 Hz)*, 127.7 (d, *J* = 8.1 Hz), 126.4 (d, *J* = 2.6 Hz)*, 126.4 (d, *J* = 2.2 Hz), 115.6 (d, *J* = 22.2 Hz), 115.5 (d, *J* = 21.2 Hz)*, 106.1 (d, *J* = 11 Hz)*, 104.4 (d, *J* = 12.5 Hz), 47.7, 44.8 (d, *J* = 39.2 Hz)*, 42.9*, 41.2 (d, *J* = 40 Hz), 36.8 (d, *J* = 2.2 Hz)*, 36.7 (d, *J* = 2.6 Hz), 34.3 (d, *J* = 6.2 Hz), 33.4 (d, *J* = 5.9 Hz)*, 22.0*, 21.5;

**$^{19}$F NMR (282 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ –112.35 (dd, *J* = 16.3, 5.0 Hz), –114.30 (dd, *J* = 16.1, 5.7 Hz)*, –114.55 – (–114.70)(m), –115.05 – (–115.20)(m)*;

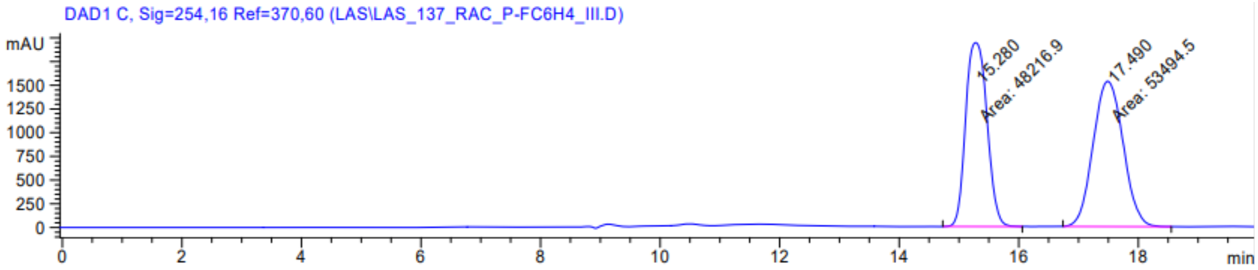
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 278.1356, found: 278.1364;

**R$_f$** (*n*-hexane/EtOAc = 6/4): 0.14;

**ATR-IR** ν (cm$^{-1}$): 2922, 1646, 1508, 1428, 1228, 837, 728;

**$[\alpha]_D^{25}$:** – 43.08 (c 1.0, CHCl$_3$);

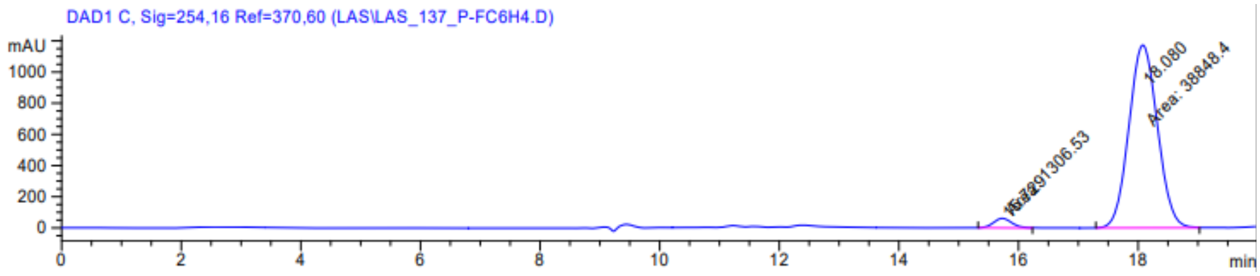
**Chiral SFC Separation:** 10% MeOH, 2.5 mL/min, AD-H column, λ = 254 nm, $t_R$ (min): minor = 15.73 (area: 3.25%), major = 18.08 (area: 96.75%), 93.5% enantiomeric excess;

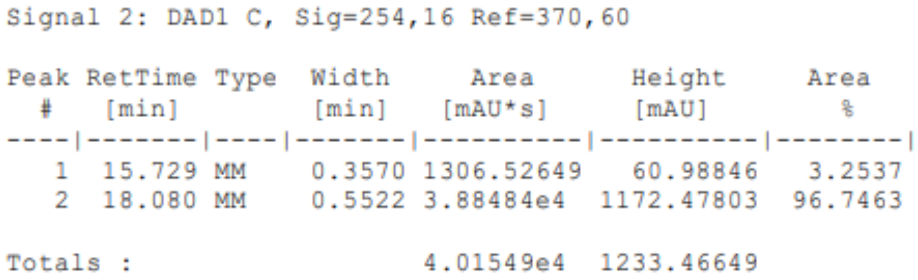


```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]         [min]  [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.280 MM    0.4145 4.82169e4  1938.92371  47.4056
   2  17.490 MM    0.5819 5.34945e4  1532.15027  52.5944

Totals :                  1.01711e5  3471.07397
```

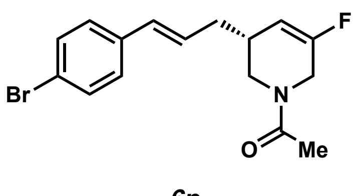




```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  15.729 MM    0.3570 1306.52649   60.98846   3.2537
   2  18.080 MM    0.5522 3.88484e4  1172.47803  96.7463

Totals :                  4.01549e4  1233.46649
```



***6p***

**Chemical Formula:** $C_{16}H_{17}BrFNO$
**Exact Mass: 337.0478**
**Molecular Weight: 338.2204**

**(*R*,*E*)-1-(3-(3-(4-bromophenyl)allyl)-5-fluoro-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6p** was synthesized following the general procedure B using 3-fluoropyridine (43 µL, 0.5 mmol, 1.0 equiv.) as substrate and (*E*)-3-(4-bromophenyl)allyl methyl carbonate (203 mg, 0.75 mmol, 1.5 equiv.). The desired compound was obtained as yellowish oil (45 mg, 0.133 mmol, 27% yield over three steps).

**$^1$H NMR (400 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers): δ 7.45–7.38 (m, 2H), 7.20 (d, *J* = 7.6 Hz, 2H), 6.37 (dd, *J* = 15.9, 6.7 Hz, 1H), 6.20–6.08 (m, 1H), 5.45–5.30 (m, 1H), 4.18–4.04 (m, 1H), 4.03–3.90 (m, 1H), 3.83 (dd, *J* = 13.1, 4.7 Hz, 0.4H), 3.53 (dd, *J* = 13.4, 4.5 Hz, 0.6H), 3.34–3.20 (m, 1H), 2.48 (br s, 1H), 2.32–2.16 (m, 2H), 2.11 (s, 3H);

**$^{13}$C NMR (101 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ 169.8*, 169.7, 156.4 (d, *J* = 257 Hz), 154.9 (d, *J* = 257 Hz)*, 136.3*, 135.9, 131.9*, 131.8, 131.7, 131.6*, 127.8*, 127.7, 127.6*, 127.5, 121.3, 121.0*, 106.1 (d, *J* = 11.4 Hz)*, 104.3 (d, *J* = 12.5 Hz), 47.7, 44.8 (d, *J* = 39.2 Hz)*, 42.9*, 41.1 (d, *J* = 39.6 Hz), 36.8 (d, *J* = 2.2 Hz)*, 36.8 (d, *J* = 2.6 Hz), 34.2 (d, *J* = 6.6 Hz), 33.3 (d, *J* = 5.9 Hz)*, 22.0*, 21.5;

**$^{19}$F NMR (282 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ –112.22 (dd, *J* = 16.1, 4.7 Hz), –114.16 (dd, *J* = 16.3, 5.4 Hz);

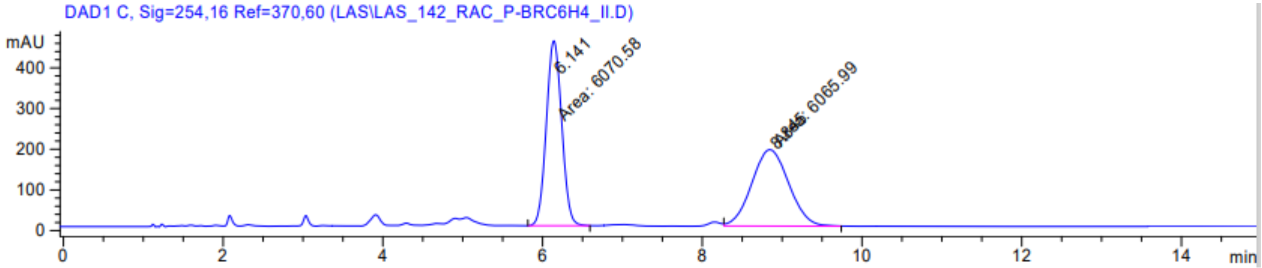
**HRMS**: m/z (ESI) calculated for $(M+H)^+$: 338.0556, found: 338.0554;

**R$_f$** (*n*-hexane/EtOAc = 1/1): 0.23;

**ATR-IR** ν (cm$^{-1}$): 2917, 1706, 1648, 1486, 1426, 1379, 1229, 1164, 1071, 1007, 969, 838;

**$[\alpha]_D^{25}$:** – 36.48 (c 1.0, CHCl$_3$);

**Chiral SFC Separation:** 30% MeOH, 2.5 mL/min, AD-H column, λ = 254 nm, $t_R$ (min): minor = 6.15 (area: 3.17%), major = 8.83 (area: 96.83%), 93.6% enantiomeric excess.



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Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]    [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.141 MM     0.2225 6070.58252  454.82550  50.0189
   2   8.845 MM     0.5376 6065.99072  188.07510  49.9811

Totals :                   1.21366e4   642.90060
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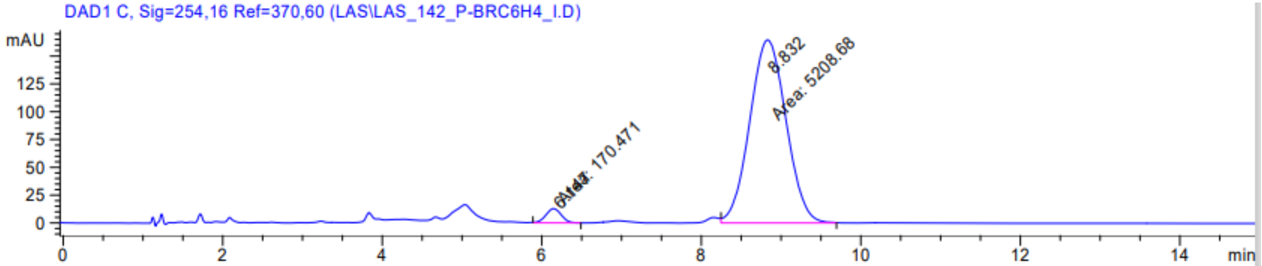

```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]    [mAU*s]    [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.147 MM     0.2215  170.47104   12.82446   3.1691
   2   8.832 FM     0.5278 5208.68311  164.49005  96.8309

Totals :                   5379.15414  177.31451
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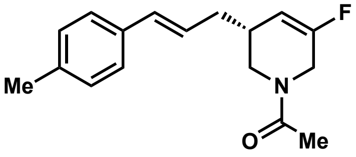


***6q***

**Chemical Formula:** $C_{17}H_{20}FNO$

**Exact Mass: 273.1529**

**Molecular Weight: 273.3514**

**(*R*,*E*)-1-(5-fluoro-3-(3-(p-tolyl)allyl)-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6q** was synthesized following the general procedure B using 3-fluoropyridine (43 µL, 0.5 mmol, 1.0 equiv.) as substrate and (*E*)-methyl (3-(*p*-tolyl)allyl) carbonate (174 mg, 0.75 mmol, 1.5 equiv.). The desired compound was obtained as colourless oil (61 mg, 0.223 mmol, 45% yield over three steps).

**$^1$H NMR (400 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers): δ 7.27–7.21 (m, 2H), 7.16–7.08 (m, 2H), 6.40 (dd, *J* = 15.8, 7.6 Hz, 1H), 6.15–6.03 (m, 1H), 5.48–5.30 (m, 1H), 4.19–4.03 (m, 1H), 4.01–3.94 (m, 1H), 3.91 (dd, *J* = 13.1, 4.7 Hz, 0.4H), 3.52 (dd, *J* = 13.5, 4.5 Hz, 0.6H), 3.24 (td, *J* = 13.4, 6.5 Hz, 1H), 2.49 (br s, 1H), 2.35–2.30 (m, 3H), 2.30–2.16 (m, 2H), 2.11 (s, 3H);

**$^{13}$C NMR (101 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ 169.8, 169.6*, 156.24 (d, *J* = 255 Hz), 154.7 (d, *J* = 256 Hz)*, 137.4, 137.1*, 134.5*, 134.2, 132.8, 132.5*, 129.4, 129.3*, 126.1*, 126.0, 125.6, 125.6*, 106.1 (d, *J* = 11.0 Hz)*, 104.5 (d, *J* = 12.1 Hz), 47.0, 44.8 (d, *J* = 39 Hz)*, 43.0*, 41.1 (d, *J* = 39 Hz), 36.8 (d, *J* = 2.2 Hz)*, 36.7 (d, *J* = 2.6 Hz), 34.3 (d, *J* = 6.2 Hz), 33.4 (d, *J* = 5.9 Hz)*, 22.0*, 21.5, 21.5*, 21.2;

**$^{19}$F NMR (282 MHz, CDCl$_3$):** δ–112.55 (dd, *J* = 15.9, 5.0 Hz), –114.44 (dd, *J* = 16.3, 5.4 Hz);

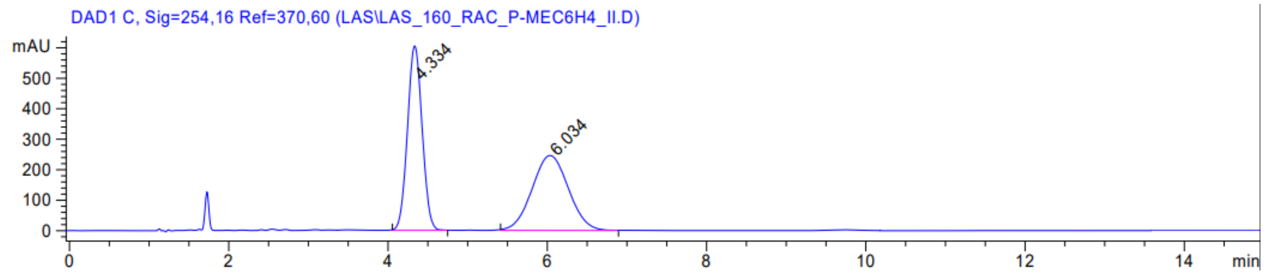
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 274.1607, found: 274.1610;

**R$_f$** (*n*-hexane/EtOAc = 6/4): 0.21;

**ATR-IR** ν (cm$^{-1}$): 3022, 2919, 1708, 1652, 1512, 1427, 1380, 1274, 1230, 1161, 1109, 1035, 970, 825, 788;

**[α]$_D^{25}$:** – 41.25 (c 1.0, CHCl$_3$);

**Chiral SFC Separation:** 30% MeOH, 2.5 mL/min, AD-H column, λ = 254 nm, t$_R$ (min): minor = 4.34 (area: 3.57%), major = 6.00 (area: 96.43%), 92.86% enantiomeric excess.



```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width      Area      Height     Area
  #   [min]        [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.334 BB    0.2012 7725.56982  604.15234  49.8360
   2   6.034 BB    0.4972 7776.40967  245.71536  50.1640

Totals :                  1.55020e4   849.86771
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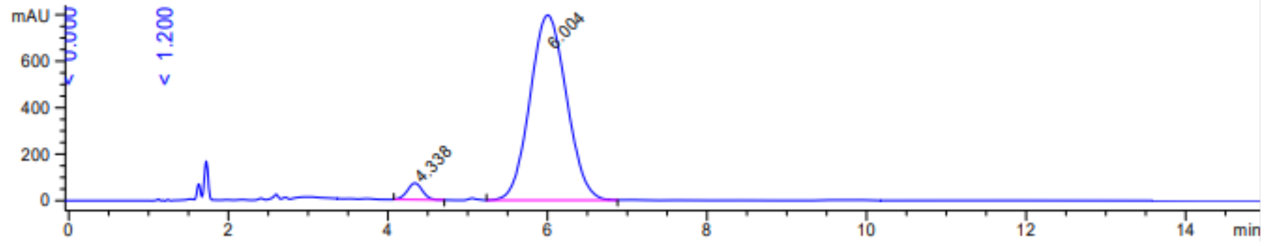

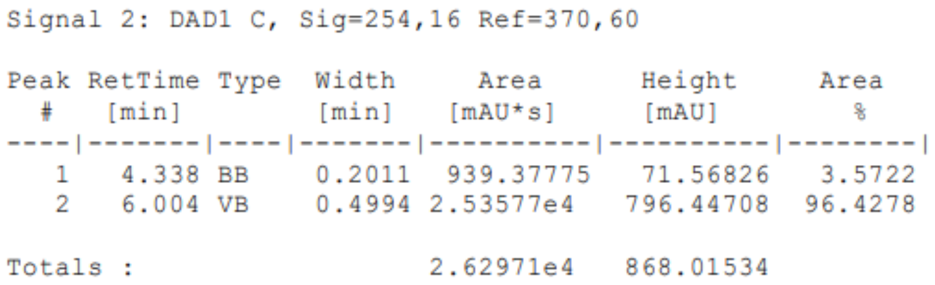

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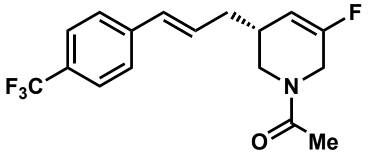
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.338 BB    0.2011  939.37775   71.56826   3.5722
   2   6.004 VB    0.4994 2.53577e4   796.44708  96.4278

Totals :                  2.62971e4   868.01534
```



***6r***

**Chemical Formula:** $C_{17}H_{17}F_4NO$
**Exact Mass: 327.1246**
**Molecular Weight: 327.3226**

**(*R*,*E*)-1-(5-fluoro-3-(3-(4-(trifluoromethyl)phenyl)allyl)-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6r** was synthesized following the general procedure B using 3-fluoropyridine (43 µL, 0.5 mmol, 1.0 equiv.) as substrate and (*E*)-methyl (3-(4-(trifluoromethyl)phenyl)allyl) carbonate (195 mg, 0.75 mmol, 1.5 equiv.). The desired compound was obtained as colourless oil (50 mg, 0.153 mmol, 31% yield over three steps).

**$^1$H NMR (400 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers): δ 7.59–7.51 (m, 2H), 7.47–7.40 (m, 2H), 6.56–6.43 (m, 1H), 6.33–6.20 (m, 1H), 5.48–5.30 (m, 1H), 4.19–4.06 (m, 1H), 4.04–3.93 (m, 1H), 3.85–3.78 (m, 0.4H), 3.59–3.50 (m, 0.6H), 3.40–3.22 (m, 1H), 2.60–2.45 (br s, 1H), 2.38–2.19 (m, 2H), 2.12 (s, 3H);

**$^{13}$C NMR (101 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ 169.8, 169.7*, 156.5 (d, *J* = 256 Hz), 155.0 (d, *J* = 256 Hz)*, 140.8*, 140.5, 131.8, 131.6*, 129.6*, 129.5, 129.3, 129.0*, 126.4*, 126.4, 125.8 (q, *J* = 3.7 Hz), 125.6 (q, *J* = 4.0 Hz)*, 106.0 (d, *J* = 11.4 Hz)*, 104.3 (d, *J* = 12.5 Hz), 47.8, 44.9 (d, *J* = 39 Hz), 42.8*, 41.2 (d, *J* = 40 Hz), 36.9, 36.8*, 34.2 (d, *J* = 6.2 Hz), 33.3 (d, *J* = 6.2 Hz)*, 22.0*, 21.6; The carbon atom for the CF$_3$-group was not detected.

**$^{19}$F NMR (282 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ –62.44* (s), –62.50 (s), –112.06 (dd, *J* = 15.9, 5.0 Hz), –114.02 (dd, *J* = 16.3, 5.0 Hz)*;

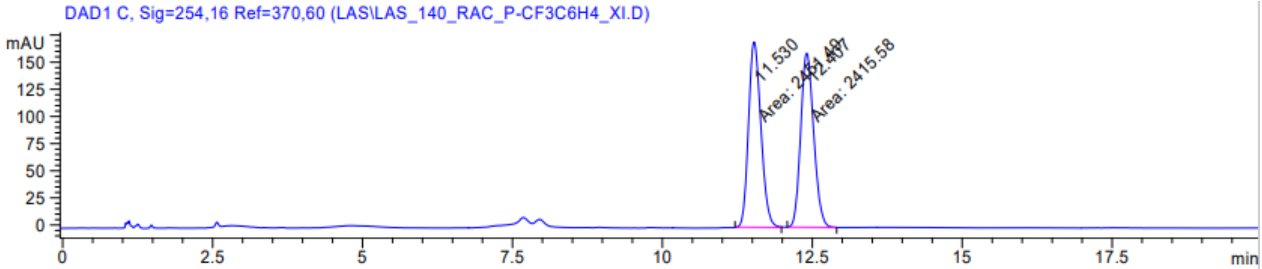
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 328.1325, found: 328.1338;

**R$_f$** (*n*-hexane/EtOAc = 6/4): 0.18;

**ATR-IR** ν (cm$^{-1}$): 2921, 1651, 1434, 1326, 1233, 1163, 1121, 1067, 1016, 839;

**$[\alpha]_D^{25}$:** – 26.31 (c 1.0, CHCl$_3$);

**Chiral SFC Separation:** 7% *i*PrOH, 2.5 mL/min, AD-H column, λ = 254 nm, t$_R$ (min): major = 11.26 (area: 97.72%), minor = 12.22 (area: 2.28%), 95.4% enantiomeric excess.



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Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.530 MM    0.2391 2451.48804  170.85316  50.3689
   2  12.407 MM    0.2509 2415.58301  160.48860  49.6311

Totals :                  4867.07104  331.34177
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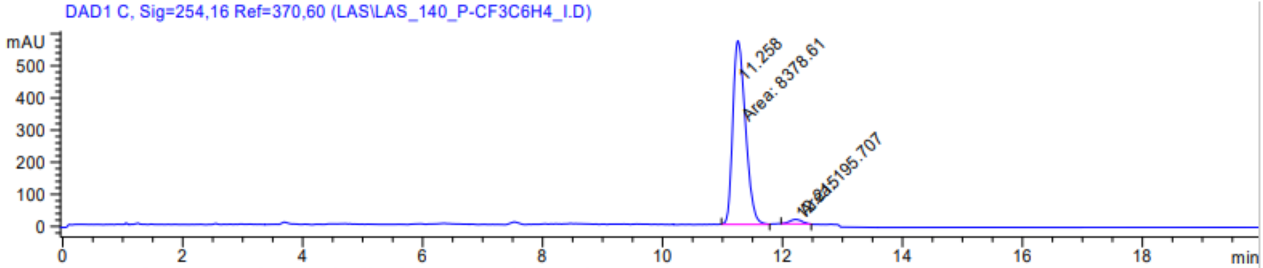

```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.258 MM    0.2440 8378.60938  572.39178  97.7175
   2  12.215 MM    0.2372  195.70685   13.75326   2.2825

Totals :                  8574.31622  586.14504
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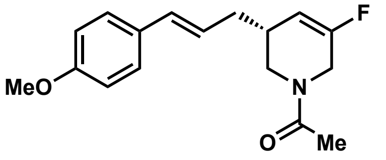


***6s***

**Chemical Formula:** $C_{17}H_{20}FNO_2$
**Exact Mass: 289.1478**
**Molecular Weight: 289.3504**

**(*R*,*E*)-1-(5-fluoro-3-(3-(4-methoxyphenyl)allyl)-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6s** was synthesized following the general procedure B using 3-fluoropyridine (43 µL, 0.5 mmol, 1.0 equiv.) as substrate and (*E*)-3-(4-methoxyphenyl)allyl methyl carbonate (168 mg, 0.75 mmol, 1.5 equiv.). The desired compound was obtained as colourless oil (49 mg, 0.169 mmol, 34% yield over three steps).

**$^1$H NMR (400 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers): δ 7.31–7.23 (m, 2H), 6.88–6.80 (m, 2H), 6.44–6.32 (m, 1H), 6.07–5.93 (m, 1H), 5.48–5.30 (m, 1H), 4.18–4.05 (m, 1H), 4.02–3.93 (s, 1H), 3.93–3.87 (m, 0.4H), 3.81–3.79 (m, 3H), 3.52 (dd, *J* = 13.6, 4.6 Hz, 0.6H), 3.33–3.17 (m, 1H), 2.49 (br s, 1H), 2.39–2.13 (m, 2H), 2.11 (s, 3H);

**$^{13}$C NMR (101 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ 169.8, 169.6*, 159.2, 159.0*, 156.3 (d, *J* = 256 Hz), 154.8 (d, *J* = 256

Hz)*, 132.4, 132.1*, 130.2*, 129.9, 127.4*, 127.3, 124.4*, 124.4, 114.1, 114.0*, 106.2 (d, *J* = 11.0 Hz)*, 104.6 (d, *J* = 12.5 Hz), 55.4, 55.4*, 47.6, 44.8 (d, *J* = 39 Hz)*, 43.0*, 41.2 (d, *J* = 40 Hz), 36.8 (d, *J* = 2.2 Hz)*, 36.8 (d, *J* = 2.6 Hz), 34.4 (d, *J* = 6.2 Hz), 33.5 (d, *J* = 5.9 Hz)*, 22.0*, 21.5;

**$^{19}$F NMR (282 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ–112.61 (dd, *J* = 15.9, 5.0 Hz), –114.52 (dd, *J* = 16.8, 5.4 Hz)*;

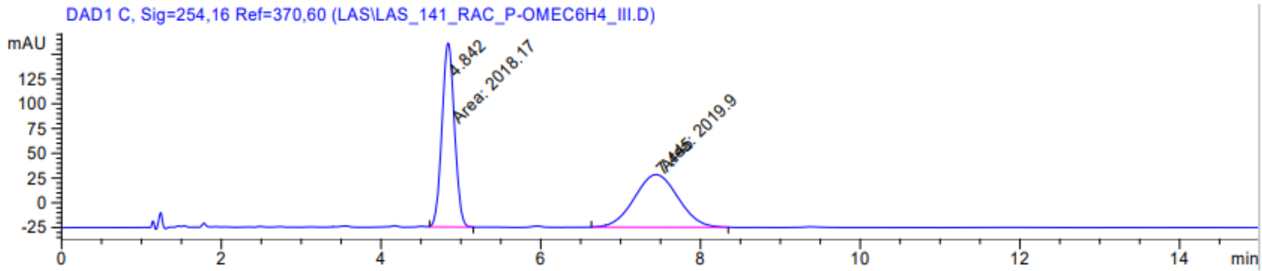
**HRMS**: m/z (ESI) calculated for (M + H)$^+$: 290.1556, found: 290.1563;

**R$_f$** (*n*-hexane/EtOAc = 6/4): 0.24;

**ATR-IR** ν (cm$^{-1}$): 2915, 1647, 1511, 1456, 1248, 1173, 1159, 1032;

**[α]$_D^{25}$:** – 35.38 (c 1.0, CHCl$_3$);

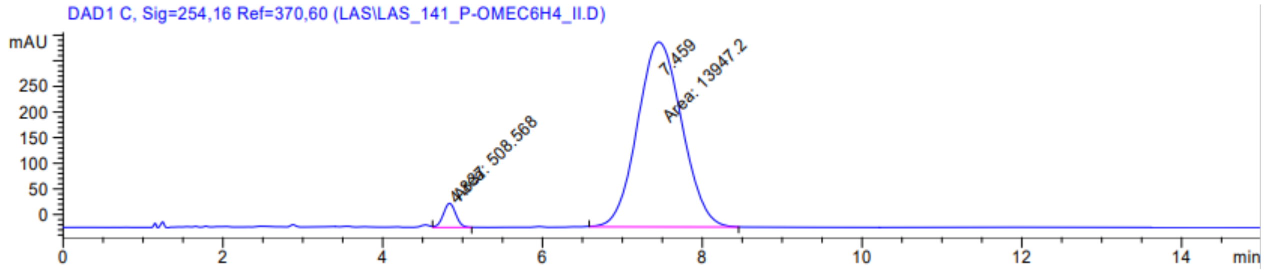
**Chiral SFC Separation:** 35% MeOH, 2.5 mL/min, AD-H column, λ = 254 nm, t$_R$ (min): minor = 4.84 (area: 3.52%), major = 7.46 (area: 96.48%), 93.0% enantiomeric excess.

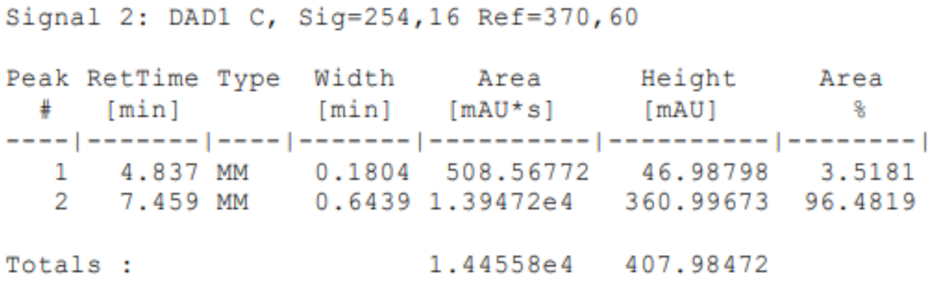


```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.842 MM    0.1808 2018.17383  186.01950  49.9786
   2   7.445 MM    0.6333 2019.90381   53.15785  50.0214

Totals :                  4038.07764  239.17735
```

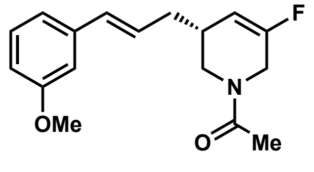




```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.837 MM    0.1804  508.56772   46.98798   3.5181
   2   7.459 MM    0.6439 1.39472e4   360.99673  96.4819

Totals :                  1.44558e4   407.98472
```



***6t***
**Chemical Formula:** $C_{17}H_{20}FNO_2$
**Exact Mass: 289.1478**
**Molecular Weight: 289.3504**

**(*R*,*E*)-1-(5-fluoro-3-(3-(3-methoxyphenyl)allyl)-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6t** was synthesized following the general procedure B using 3-fluoropyridine (43 µL, 0.5 mmol, 1.0 equiv.) as substrate and (*E*)-3-(3-methoxyphenyl)allyl methyl carbonate (167 mg, 0.75 mmol, 1.5 equiv.). The desired compound was obtained as colourless oil (52 mg, 0.180 mmol, 36% yield over three steps).

**$^1$H NMR (400 MHz, $CD_2Cl_2$)** (as mixture of E/Z amide bond isomers): δ 7.26–7.18 (m, 1H), 6.98–6.93 (m, 1H), 6.91–6.87 (m, 1H), 6.81–6.74 (m, 1H), 6.42 (dd, *J* = 15.8, 9.7 Hz, 1H), 6.25–6.14 (m, 1H), 5.48–5.34 (m, 1H), 4.15–3.92 (m, 2H), 3.86–3.77 (m, 3.4H), 3.54 (dd, *J* = 13.2, 4.9 Hz, 0.6H), 3.30–3.20 (m, 1H), 2.58–2.42 (m, 1H), 2.32–2.15 (m, 2H), 2.10–2.06 (m, 3H);

**$^{13}$C NMR (101 MHz, $CD_2Cl_2$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ 169.7, 169.6*, 160.3, 160.3*, 156.8 (d, J = 256 Hz), 155.5 (d, *J* = 256 Hz)*, 139.2*, 139.0, 132.8, 132.6*, 129.9, 129.8*, 127.7*, 127.7, 119.0, 119.0*, 113.2, 113.1*, 111.8, 111.7*, 106.2 (d, *J* = 11.0 Hz)*, 104.9 (d, *J* = 12.1 Hz), 55.5, 55.5*, 47.9, 45.0 (d, *J* = 39 Hz)*, 43.0*, 41.2 (d, *J* = 40 Hz), 37.1*, 36.9, 34.6 (d, *J* = 6.2 Hz), 33.7 (d, *J* = 5.9 Hz)*, 22.1*, 21.6;

**$^{19}$F NMR (282 MHz, $CD_2Cl_2$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ–113.52 (dd, *J* = 16.6, 4.7 Hz), –115.27 (dd, *J* = 16.8, 4.5 Hz);

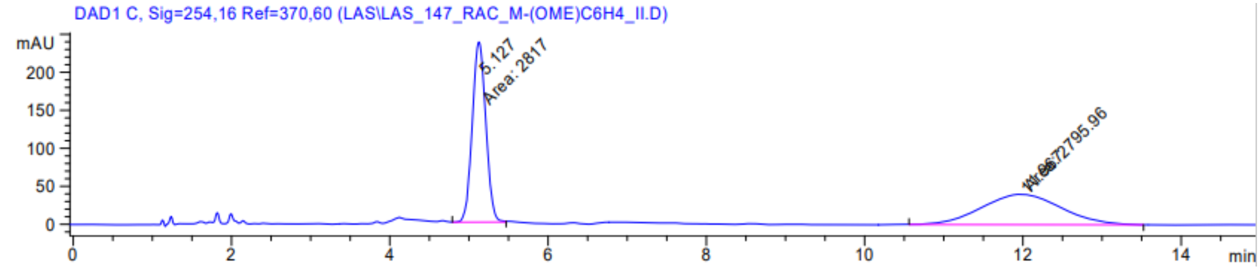
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 290.1556, found: 290.1560;

**$R_f$** (*n*-hexane/EtOAc = 6/4): 0.17;

**ATR-IR** ν ($cm^{-1}$): 2922, 1706, 1651, 1598, 1578, 1431, 1380, 1264, 1233, 1158, 1041, 972, 834, 776, 689;

**$[\alpha]_D^{25}$:** – 40.94 (c 1.0, $CHCl_3$);

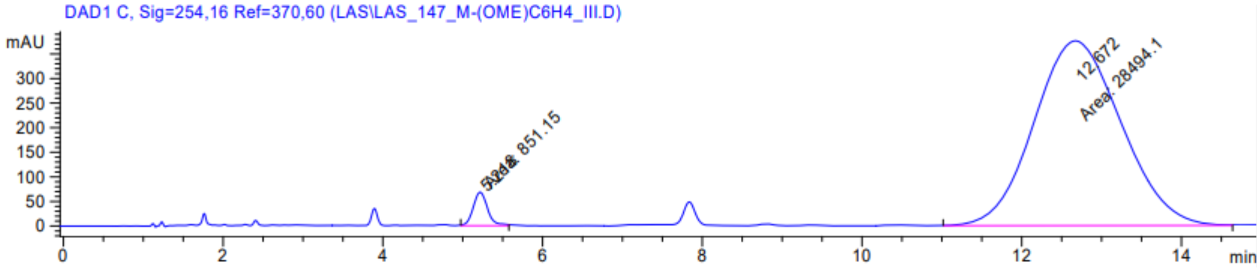
**Chiral SFC Separation:** 30% MeOH, 2.5 mL/min, AD-H column, λ = 254 nm, $t_R$ (min): minor = 5.22 (area: 2.90%), major = 12.67 (area: 97.10%), 94.2% enantiomeric excess.



```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area       Height      Area
  #   [min]         [min]    [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   5.127 MM    0.1978 2816.99536  237.34180  50.1874
   2  11.967 MM    1.1664 2795.95776   39.95090  49.8126

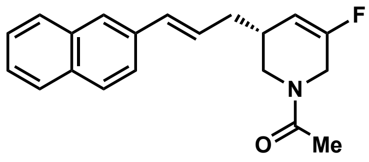
Totals :                  5612.95313  277.29269
```



```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area       Height      Area
  #   [min]         [min]    [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   5.218 MM    0.2081  851.15015   68.15288   2.9005
   2  12.672 MM    1.2638 2.84941e4  375.75864  97.0995

Totals :                  2.93453e4  443.91151
```



***6u***

**Chemical Formula:** $C_{20}H_{20}FNO$
**Exact Mass: 309.1529**
**Molecular Weight: 309.3844**

**(*R*,*E*)-1-(5-fluoro-3-(3-(naphthalen-2-yl)allyl)-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6u** was synthesized following the general procedure B using 3-fluoropyridine (43 µL, 0.5 mmol, 1.0 equiv.) as substrate and (*E*)-methyl (3-(naphthalen-2-yl)allyl) carbonate (181 mg, 0.75 mmol, 1.5 equiv.). The desired compound was obtained as colourless oil (39 mg, 0.126 mmol, 25% yield over three steps).

**$^{1}$H NMR (400 MHz, $CD_2Cl_2$)** (as mixture of E/Z amide bond isomers): δ 7.85–7.77 (m, 3H), 7.72 (s, 1H), 7.64–7.58 (m, 1H), 7.52–7.40 (m, 2H), 6.67–6.58 (m, 1H), 6.39–6.28 (m, 1H), 5.53–5.37 (m, 1H), 4.18–3.95 (m, 2H), 3.84 (dd, *J* = 13.0, 4.7 Hz, 0.4H), 3.56 (dd, *J* = 13.6, 4.5 Hz, 0.6H), 3.37–3.23 (m, 1H), 2.60–2.46 (m, 1H), 2.40–2.22 (m, 2H), 2.11–2.07 (m, 3H);

**$^{13}$C NMR (101 MHz, $CD_2Cl_2$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *, one signal is overlapping): δ169.7, 169.6*, 156.8 (d, *J* = 256 Hz), 155.5 (d, *J* = 256 Hz)*, 135.3*, 135.0, 134.1*, 134.0, 133.3, 133.2*, 133.0, 132.8*, 128.5, 128.4*, 128.2, 128.0, 128.0*, 127.9*, 126.7, 126.6*, 126.2, 126.1, 126.0*, 126.0*, 123.9*, 123.8, 106.3 (d, *J* = 11.0 Hz)*, 104.9 (d, *J* = 12.1 Hz), 47.9, 45.0 (d, *J* = 39 Hz)*, 43.6*, 41.2 (d, *J* = 39 Hz), 37.2 (d, *J* = 2.2 Hz)*, 37.1 (d, *J* = 2.6 Hz), 34.6 (d, *J* = 6.2 Hz), 33.8 (d, *J* = 5.9 Hz)*, 22.1*, 21.6;

**$^{19}$F NMR (282 MHz, $CD_2Cl_2$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ–113.47 (dd, *J* = 16.8, 5.0 Hz), –115.23 (dd, *J* = 16.6, 5.2 Hz);

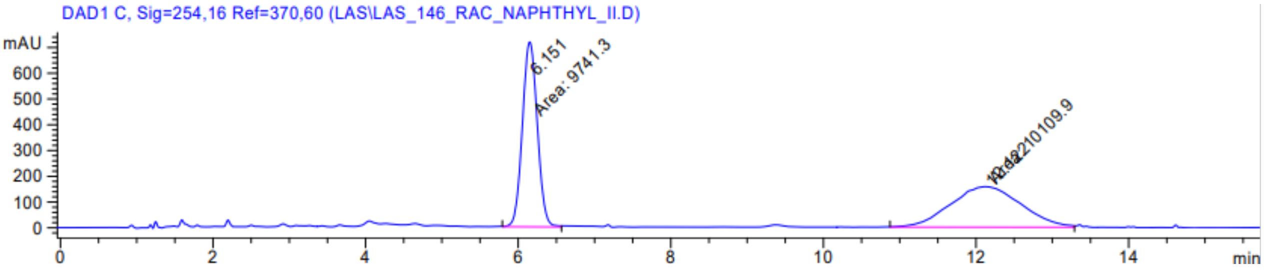
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 310.1602, found: 310.1289;

**$R_f$** (*n*-hexane/EtOAc = 6/4): 0.21;

**ATR-IR** ν (cm$^{-1}$): 2918, 1737, 1712, 1651, 1506, 1428, 1383, 1271, 1229, 1165, 967, 897, 860, 825, 748, 617;

**$[\alpha]_D^{25}$:** – 47.73 (c 1.0, $CHCl_3$);

**Chiral SFC Separation:** 45% MeOH, 2.5 mL/min, AD-H column, λ = 254 nm, $t_R$ (min): minor = 6.13 (area: 2.20%), major = 12.21 (area: 97.80%), 95.6% enantiomeric excess.



```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.151 MM    0.2260 9741.30273  718.51941  49.0717
   2  12.122 MM    1.0702 1.01099e4   157.44484  50.9283

Totals :                  1.98512e4   875.96425
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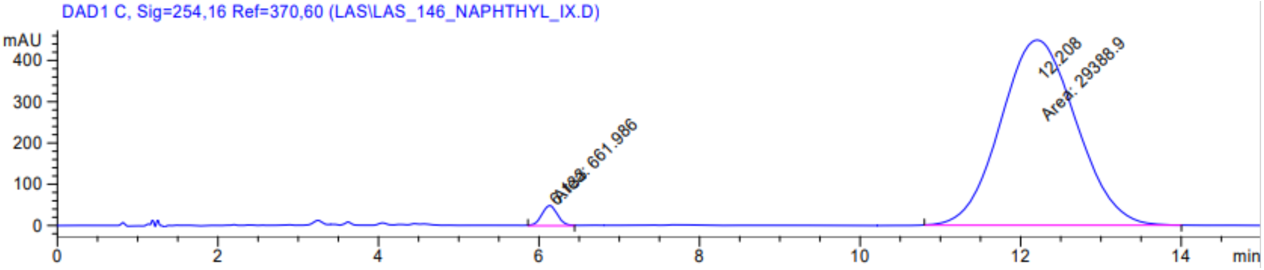

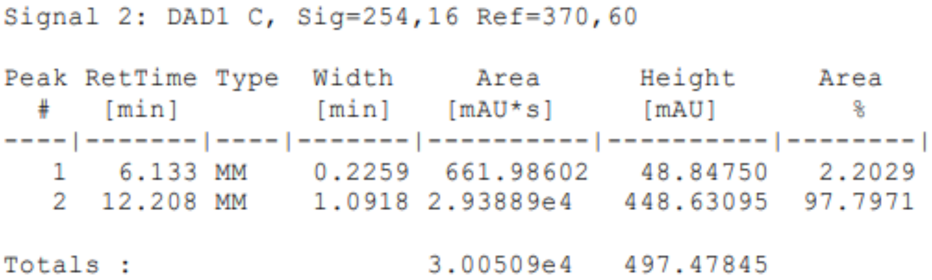

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Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.133 MM    0.2259  661.98602   48.84750   2.2029
   2  12.208 MM    1.0918 2.93889e4   448.63095  97.7971

Totals :                  3.00509e4   497.47845
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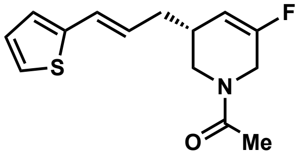


*6v*

**Chemical Formula:** $C_{14}H_{16}FNOS$
**Exact Mass: 265.0937**
**Molecular Weight: 265.3464**

**(*R*,*E*)-1-(5-fluoro-3-(3-(thiophen-2-yl)allyl)-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6v** was synthesized following the general procedure B using 3-fluoropyridine (43 µL, 0.5 mmol, 1.0 equiv.) as substrate and (*E*)-methyl (3-(thiophen-2-yl)allyl) carbonate (149 mg, 0.75 mmol, 1.5 equiv.). The desired compound was obtained as colorless oil (34 mg, 0.128 mmol, 26% yield over three steps).

**$^1$H NMR (400 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers): δ 7.12 (dd, *J* = 11.0, 5.1 Hz, 1H), 6.98–6.92 (m, 1H), 6.92–6.88 (m, 1H), 6.61–6.52 (m, 1H), 6.04–5.92 (m, 1H), 5.47–5.30 (m, 1H), 4.18–3.92 (m, 2H), 3.84 (dd, *J* = 13.1, 4.6 Hz, 0.4H), 3.53 (dd, *J* = 13.4, 4.5 Hz, 0.6H), 3.33–3.22 (m, 1H), 2.55–2.40 (s, 1H), 2.30–2.14 (m, 2H), 2.12 (s, 3H);

**$^{13}$C NMR (101 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ 169.8, 169.7*, 156.4 (d, *J* = 256 Hz), 154.9 (d, *J* = 256 Hz)*, 142.5*, 142.1, 127.5, 127.4*, 126.5*, 126.4, 126.2, 125.9*, 125.3, 125.1*, 124.0, 123.7*, 106.0 (d, *J* = 11.0 Hz)*, 104.4 (d, *J* = 12.5 Hz), 47.7, 44.9 (d, *J* = 39 Hz)*, 42.9*, 41.2 (d, *J* = 40 Hz), 36.7 (d, *J* = 2.2 Hz)*, 36.63 (d, *J* = 2.6 Hz), 34.3 (d, *J* = 6.2 Hz), 33.3 (d, *J* = 5.9 Hz)*, 22.0*, 21.6;

**$^{19}$F NMR (282 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ –112.35 (dd, *J* = 16.3, 5.0 Hz), –114.23 (dd, *J* = 16.3, 5.0 Hz)*;

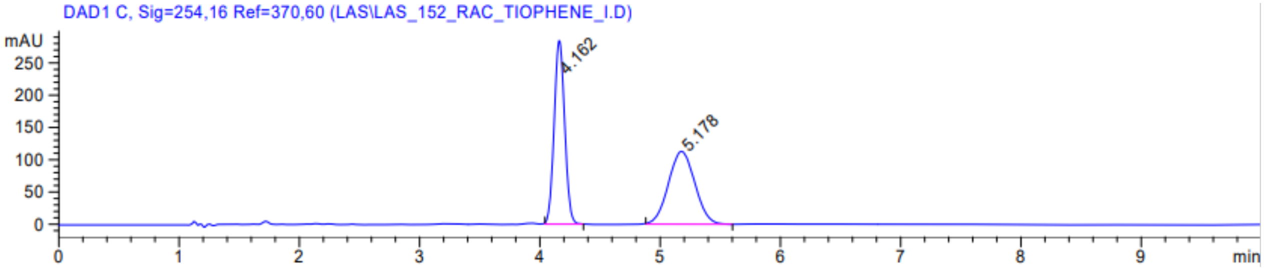
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 266.1009, found: 266.1006;

**R$_f$** (*n*-hexane/EtOAc = 6/4): 0.18;

**ATR-IR** ν (cm$^{-1}$): 2921, 1732, 1651, 1427, 1378, 1236, 1159, 1039, 697;

**$[\alpha]_D^{25}$:** – 35.56 (c 1.0, CHCl$_3$);

**Chiral SFC Separation:** 30% MeOH, 2.5 mL/min, AD-H column, λ = 254 nm, $t_R$ (min): minor = 4.22 (area: 2.98%), major = 5.28 (area: 97.02%), 94.0% enantiomeric excess.



```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.162 BB    0.0991 1731.62109  283.99393  50.0738
   2   5.178 BB    0.2385 1726.51636  112.82227  49.9262

Totals :                  3458.13745  396.81620
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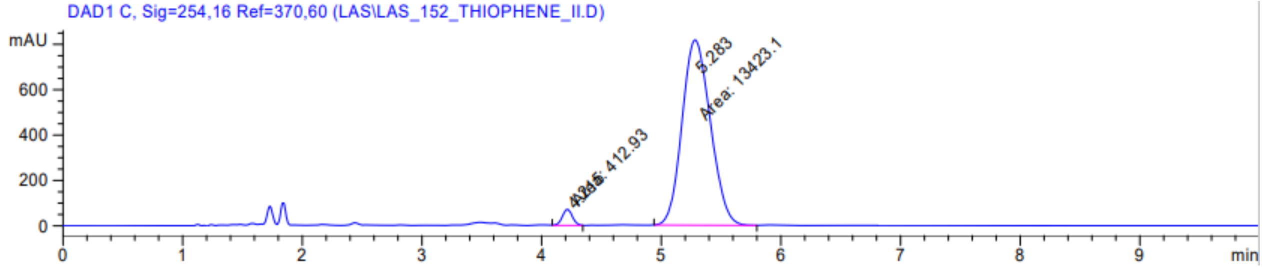

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Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.215 MM    0.0971  412.92996   70.84860   2.9845
   2   5.283 MM    0.2736 1.34231e4  817.65662  97.0155

Totals :                  1.38360e4  888.50522
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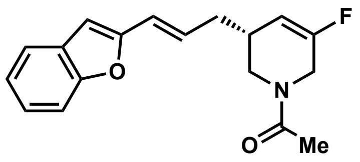


***6w***

**Chemical Formula:** $C_{18}H_{18}FNO_2$
**Exact Mass: 299.1322**
**Molecular Weight: 299.3454**

**(*R*,*E*)-1-(3-(3-(benzofuran-2-yl)allyl)-5-fluoro-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6w** was synthesized following the general procedure B using 3-fluoropyridine (43 µL, 0.5 mmol, 1.0 equiv.) as substrate and (*E*)-3-(benzofuran-2-yl)allyl methyl carbonate (174 mg, 0.75 mmol, 1.5 equiv.). The desired compound was obtained as colourless oil (58 mg, 0.194 mmol, 39% yield over three steps).

**$^1$H NMR (400 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers): δ 7.47–7.38 (m, 1H), 7.38–7.32 (m, 1H), 7.22–7.06 (m, 2H), 6.46–6.40 (m, 1H), 6.35–6.27 (m, 2H), 5.42–5.24 (m, 1H), 4.12–3.84 (m, 2H), 3.75 (dd, *J* = 12.7, 4.6 Hz, 0.4H), 3.47 (dd, *J* = 12.5, 4.5 Hz, 0.6H), 3.28 (dd, *J* = 13.1, 6.5 Hz, 0.4H), 3.19 (dd, *J* = 13.6, 6.1 Hz, 0.6H), 2.52–2.37 (s, 1H), 2.30–2.11 (m, 2H), 2.07–2.00 (m, 3H);

**$^{13}$C NMR (101 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ 169.8, 169.7*, 156.4 (d, *J* = 257 Hz), 155.0 (d, *J* = 257 Hz)*, 154.8, 154.7*, 154.5*, 154.2, 129.2, 129.1*, 129.0, 128.9*, 124.6, 124.4*, 123.0, 122.8*, 121.5, 121.3*, 121.0, 120.9*, 110.9, 110.9*, 105.9 (d, *J* = 11.0 Hz)*, 104.4 (d, *J* = 12.5 Hz), 104.1, 103.8*, 47.6, 44.8 (d, *J* = 39 Hz)*, 42.8*, 41.1 (d, *J* = 40 Hz), 36.8 (d, *J* = 2.6 Hz)*, 36.7 (d, *J* = 2.6 Hz), 34.2 (d, *J* = 6.2 Hz), 33.2 (d, *J* = 5.9 Hz)*, 22.0*, 21.5;

**$^{19}$F NMR (282 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ–112.16 (dd, *J* = 16.1, 4.7 Hz), –114.03 (dd, *J* = 16.1, 5.2 Hz)*;

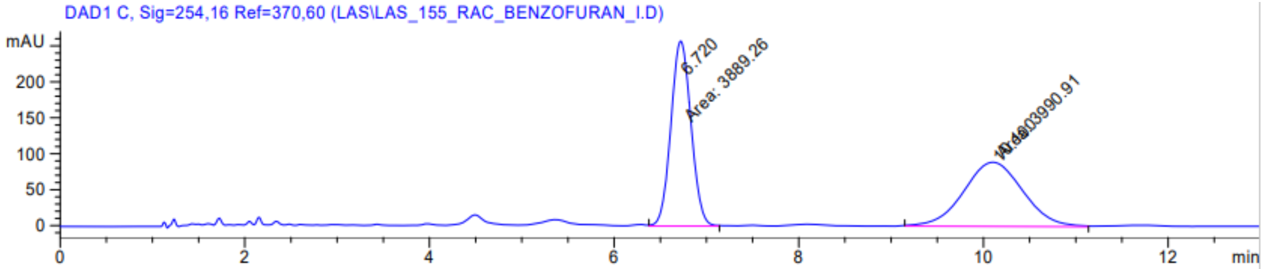
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 300.1400, found: 300.1385;

**R$_f$** (*n*-hexane/EtOAc = 6/4): 0.14;

**ATR-IR** ν (cm$^{-1}$): 2917, 1711, 1650, 1452, 1380, 1254, 1230, 1163, 1105, 965, 882, 826, 751;

**$[\alpha]_D^{25}$:** – 34.73 (c 1.0, CHCl$_3$);

**Chiral SFC Separation:** 30% MeOH, 2.5 mL/min, AD-H column, λ = 254 nm, $t_R$ (min): minor = 6.83 (area: 2.62%), major = 10.22 (area: 97.38%), 94.8% enantiomeric excess.



```
Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.720 MM    0.2516 3889.25513  257.60300  49.3550
   2  10.100 MM    0.7447 3990.90601   89.32148  50.6450

Totals :                  7880.16113  346.92448
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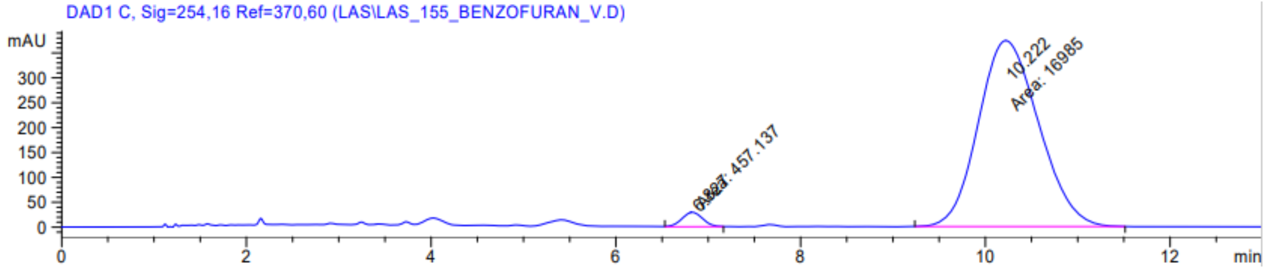

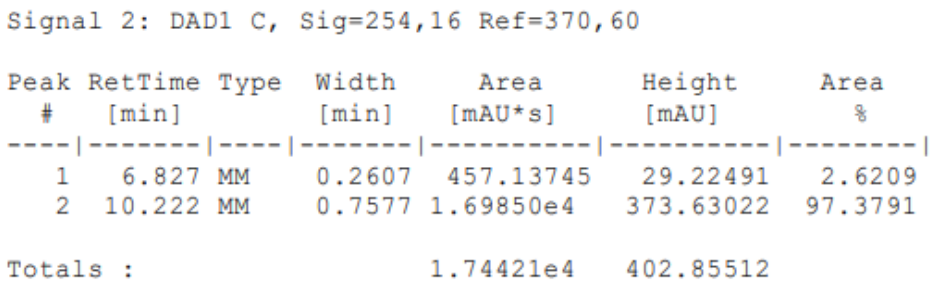

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Signal 2: DAD1 C, Sig=254,16 Ref=370,60

Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.827 MM    0.2607  457.13745   29.22491   2.6209
   2  10.222 MM    0.7577 1.69850e4   373.63022  97.3791

Totals :                  1.74421e4   402.85512
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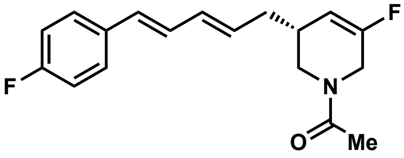


***6x***

**Chemical Formula:** $C_{18}H_{19}F_2NO$
**Exact Mass: 303.1435**
**Molecular Weight: 303.3528**

**1-((*R*)-5-fluoro-3-((2*E*,4*E*)-5-(4-fluorophenyl)penta-2,4-dien-1-yl)-3,6-dihydropyridin-1(2H)-yl)ethan-1-one 6x** was synthesized following the general procedure B using 3-fluoropyridine (43 µL, 0.5 mmol, 1.0 equiv.) as substrate and (2*E*,4*E*)-5-(4-fluorophenyl)penta-2,4-dien-1-yl methyl carbonate (236 mg, 0.75 mmol, 1.5 equiv.). The desired compound was obtained as colourless oil (31 mg, 0.102 mmol, 20% yield over three steps).

**$^{1}$H NMR (400 MHz, $CD_2Cl_2$)** (as mixture of E/Z amide bond isomers): δ 7.34–7.21 (m, 2H), 6.99–6.85 (m, 2H), 6.69–6.56 (m, 1H), 6.44–6.30 (m, 1H), 6.24–6.09 (m, 1H), 5.71 (ddd, *J* = 14.9, 7.5, 7.5 Hz, 1H), 5.37–5.24 (m, 1H), 4.08–3.83 (m, 2H), 3.72 (dd, *J* = 13.1, 4.7 Hz, 0.4H), 3.44 (dd, *J* = 13.5, 4.6 Hz, 0.6H), 3.20–3.07 (m, 1H), 2.47–2.29 (m, 1H), 2.19–2.05 (m, 2H), 2.04–1.96 (s, 3H);

**$^{13}$C NMR (101 MHz, $CD_2Cl_2$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ 169.8, 169.7*, 162.6 (d, *J* = 247 Hz), 162.5 (d, *J* = 246 Hz)*, 156.8 (d, *J* = 255 Hz), 155 (d, *J* = 256 Hz)*, 134.2 (d, *J* = 2.9 Hz)*, 134.0 (d, *J* = 3.3 Hz), 133.4, 133.2*, 132.1*, 131.8, 130.3, 130.0*, 129.1 (d, *J* = 2.6 Hz)*, 128.9 (d, *J* = 2.2 Hz), 128.1 (d, *J* = 7.7 Hz), 128.1 (d, *J* = 8.1 Hz)*, 115.9 (d, *J* = 21.6 Hz), 115.8 (d, *J* = 22.0 Hz)*, 106.3 (d, *J* = 11 Hz)*, 104.9 (d, *J* = 12.1 Hz), 47.9, 45.0 (d, *J* = 39 Hz)*, 42.9*, 41.2 (d, *J* = 40 Hz), 36.9 (d, *J* = 2.2 Hz)*, 36.8 (d, *J* = 2.2 Hz), 34.6 (d, *J* = 6.2 Hz), 33.7 (d, *J* = 5.9 Hz)*, 22.1*, 21.7;

**$^{19}$F NMR (282 MHz, $CD_2Cl_2$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *): δ –113.6 (dd, *J* = 16.1, 4.7 Hz, $C_{Alkyl}F$), –115.24 – (–115.43 (m, $C_{Alkyl}F$*, $C_{Aryl}F$), –115.48 – (–115.60 (m, $C_{Aryl}F$*));

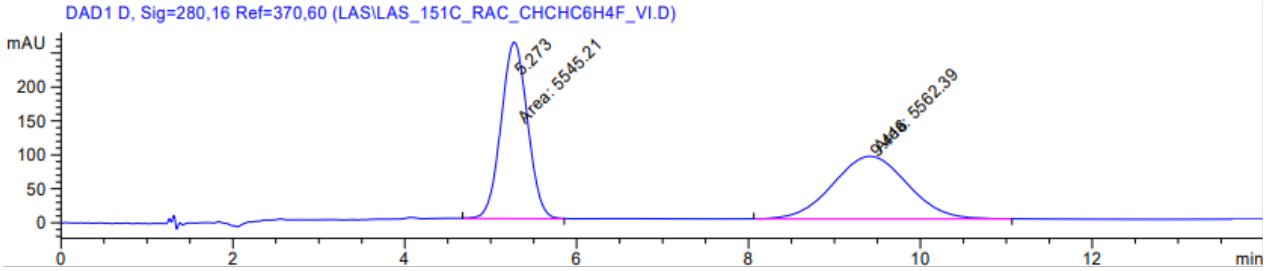
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 304.1513, found: 304.1500;

**R$_f$** (*n*-hexane/EtOAc = 6/4): 0.21;

**ATR-IR** ν (cm$^{-1}$): 2916, 1707, 1650, 1599, 1507, 1428, 1379, 1275, 1228, 1159, 1095, 1060, 1034, 989, 833;

**$[\alpha]_D^{25}$:** – 33.48 (c 1.0, $CHCl_3$);

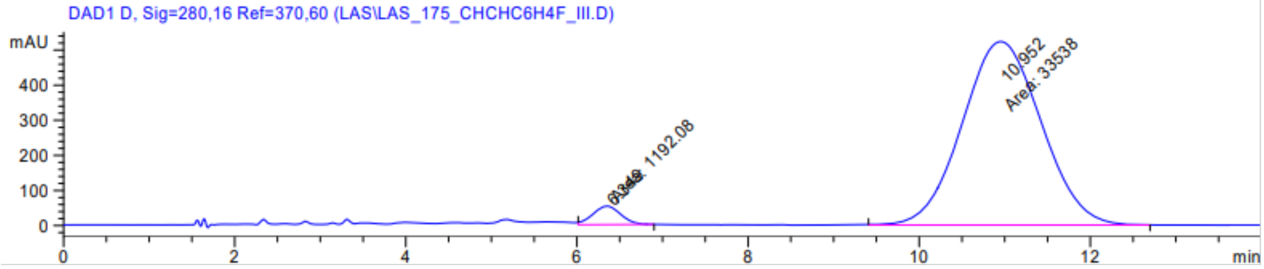
**Chiral SFC Separation:** 40% MeOH, 2.5 mL/min, AD-H column, λ = 280 nm, $t_R$ (min): minor = 6.35 (area: 3.43%), major = 10.95 (area: 96.57%), 93.1% enantiomeric excess.



```
Signal 3: DAD1 D, Sig=280,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   5.273 MM    0.3555 5545.20654  259.98407  49.9226
   2   9.416 MM    1.0051 5562.39063   92.23834  50.0774

Totals :                  1.11076e4   352.22241
```



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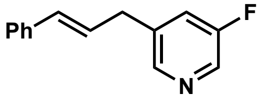
Signal 3: DAD1 D, Sig=280,16 Ref=370,60

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   6.349 MM    0.3749 1192.08069   52.99109   3.4324
   2  10.952 MM    1.0693 3.35380e4   522.74005  96.5676

Totals :                  3.47301e4   575.73114
```

**Product Characterization: Rearomatized product**



***4a***

**Chemical Formula:** $C_{14}H_{12}FN$
**Exact Mass: 213.0954**
**Molecular Weight: 213.2554**

**3-cinnamyl-5-fluoropyridine 4a** was synthesized as followed. In a 2 mL screw vial equipped with a magnetic stir bar was then transferred to an argon filled glovebox. Chlor-bis-(cycloocten)-iridium(I) dimer ($[Ir(coe)_2Cl]_2$, 2.3 mg, 0.0025 mmol, 0.5 mol%) was added to the vial, closed with a septum screw cap and transferred out of the glovebox. Diethyl silane ($Et_2SiH_2$, 97 µL, 0.75 mmol, 1.5 equiv.) was added and the resulting mixture was stirred at room temperature for 4 minutes. 3-Fluoro pyridine (43 µL, 0.5 mmol, 1.0 equiv.) was added and the resulting reaction mixture was stirred at 50 °C for 5 h. A separate 10 mL screw vial equipped with a magnetic stir bar was transferred to the glovebox. Ligand **L3** (24.2 mg, 0.035 mmol, 7 mol%) and palladium(II) acetate ($Pd(OAc)_2$, 5.6 mg, 0.025 mmol, 5 mol%) were added. The vial was closed with a septum screw cap and transferred out of the glovebox. Dichloromethane ($CH_2Cl_2$, 2.5 mL) was added at room temperature under nitrogen. The mixture was stirred for 5 minutes Cinnamyl methyl carbonate (192.2 mg, 1.0 mmol, 2.0 equiv.) was added, followed by the reaction mixture from the 2 mL vial. The resulting mixture was then stirred at 40 °C for 16 h. Afterwards, the reaction mixture was cooled to room temperature and the solvent was evaporated. The residue was submitted to flash column chromatography over silica gel using a solvent mixture of hexane/ethyl acetate = 8/2 as the eluent. The desired product **4a** was obtained as colorless oil (30.1 mg, 0.14 mmol, 28% yield).

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.36 – 8.33 (m, 2H), 7.38 – 7.34 (m, 2H), 7.34 – 7.27 (m, 3H), 7.26 – 7. 21 (m, 1H), 6.49 (d, *J* = 15.8 Hz, 1H), 6.29 (dt, *J* = 15.8, 6.9 Hz, 1H), 3.58 (d, 6.7 Hz, 2H);

**$^{13}$C NMR (101 MHz, $CDCl_3$):** δ 159.72 (d, *J* = 256.8 Hz), 146.00 (d, *J* = 3.7 Hz), 137.54 (d, *J* = 3.2 Hz), 136.91, 136.22 (d, *J* = 23.1 Hz), 132.78, 128.76, 127.74, 126.86, 126.34, 123.01 (d, *J* = 17.8 Hz), 36.00 (d, *J* = 1.4 Hz);

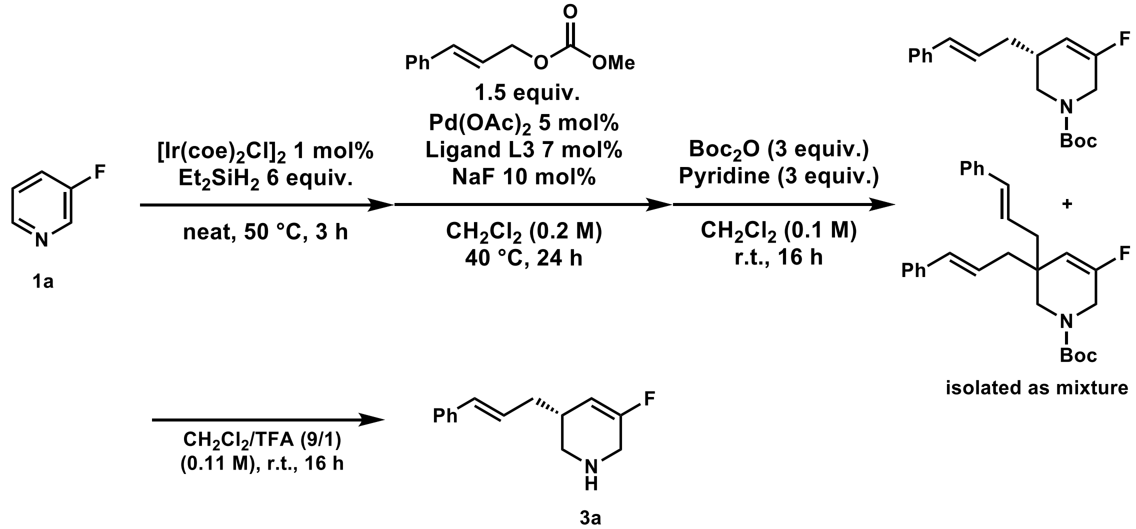
**$^{19}$F NMR (282 MHz, $CDCl_3$):** δ -127.24 (dd, *J* = 9.3, 1.7 Hz);

**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 214.1032, found: 214.1005;

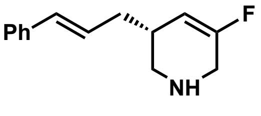
**$R_f$** (Hexane/EtOAc = 8/2): 0.47;

**ATR-IR** ν (cm$^{-1}$): 3734, 3029, 2922, 1599, 1576, 1496, 1448, 1431, 1259, 1144, 1026, 965, 879, 808, 780, 754, 697, 676.

### Synthesis of Free NH Product 3



*Scheme 1. Synthetic route to free N-H product* ***3a****.*



***3a***

**Chemical Formula:** $C_{14}H_{16}FN$
**Exact Mass: 217.1267**
**Molecular Weight: 217.2874**

**(R)-3-cinnamyl-5-fluoro-1,2,3,6-tetrahydropyridine 3a** was synthesized in a following the synthetic sequence in Scheme S6. A 10 mL screw vial was transferred to an argon filled glovebox. Chlor-bis-(cycloocten)-iridium(I) dimer ([Ir(coe)$_2$Cl]$_2$, 22.4 mg, 0.025 mmol, 1 mol%) was added to the vial. The vial was closed with a septum screw cap. The vial was transferred out of the glovebox. Diethyl silane (Et$_2$SiH$_2$, 1.94 mL, 15.0 mmol, 6.0 equiv.) was added and the resulting mixture was stirred at room temperature for 4 minutes. 3-Fluoropyridine (215 µL, 2.5 mmol, 1.0 equiv.) was added and the resulting reaction mixture was stirred at 50 °C for 3 hours. A separate 25 mL screw vial equipped with a magnetic stir bar was transferred to the glovebox. Ligand **L3** (120.8 mg, 0.175 mmol, 7 mol%), NaF (10.5 mg, 0.25 mmol, 10 mol%) and palladium(II) acetate (Pd(OAc)$_2$, 28.1 mg, 0.125 mmol, 5 mol%) were added. The vial was closed with a septum screw cap and transferred out of the glovebox. Dichloromethane (CH$_2$Cl$_2$, 12.5 mL) was added at room temperature under nitrogen. The mixture was stirred for 5 minutes. Cinnamyl methyl carbonate (720.8 mg, 3.75 mmol, 1.5 equiv.) was added, followed by the reaction mixture from the 10 mL vial. The resulting mixture was then stirred at 40 °C for 24 h. The mixture was then cooled to room temperature and diluted with additional dichloromethane (10 mL). Pyridine (604 µL, 7.5 mmol, 3.0 equiv.) was added as a base, followed by di-tert-butyl dicarbonate (1.72 mL, 7.5 mmol, 3.0 equiv.). The mixture was stirred at room temperature for 16 h and then transferred to a 50 mL flask and diluted with MeOH (20 mL). Imidazole (510 mg, 7.5 mmol, 3.0 equiv.) were added and the mixture was stirred for 2 hours to decompose residual Boc$_2$O. The solvent was evaporated and the crude subjected to flash column chromatography over silica gel using a solvent mixture of hexane/ethyl acetate (20/1) as the eluent. An inseparable mixture of the mono-alkylated and bisalkylated N-Boc compounds were isolated as colorless oil and directly used for the deprotection step. The mixture was redissolved in CH$_2$Cl$_2$ (20 mL) at room temperature. TFA (2mL) was added dropwise and the resulting solution was stirred at room temperature for 16 hours. An aqueous workup with 4M NaOH was performed to neutralize the

TFA. The aqueous phase was extracted with EtOAc three times and the combined organic phases were dried over magnesium sulfate and filtered. The mono-alkylated NH tetrahydropyridine **3a** was purified by flash column chromatography over silica gel using a solvent mixture of hexane/acetone (7/3 to 1/1) as the eluent. The desired compound was isolated as colorless oil (122 mg, 0.56 mmol, 22% yield over 4 steps). The absolute configuration was adopted from product **6a**. The enantioselectivity was not again measured for the free N-H product **3a**.

**$^1$H NMR (400 MHz, CDCl$_3$):** δ 7.37 – 7.28 (m, 4H), 7.24 – 7.19 (m, 1H), 6.46 – 6.40 (m, 1H), 6.17 (dt, *J* = 15.8, 7.3 Hz, 1H), 5.29 (ddt, *J* = 17.7, 3.1, 1.5 Hz, 1H), 3.42 – 3.30 (m, 2H), 3.03 (ddd, *J* = 12.9, 4.9, 2.1 Hz, 1H), 2.56 (ddd, *J* = 12.9, 7.1, 1.0 Hz, 1H), 2.43 (tqt, *J* = 7.4, 5.1, 2.5 Hz, 1H), 2.32 – 2.19 (m, 2H), 2.11 (bs, 1H);

**$^{13}$C NMR (101 MHz, CDCl$_3$):** δ 159.12 (d, *J* = 261.9 Hz), 137.45, 132.20, 128.67, 127.63, 127.30, 126.16, 104.91 (d, *J* = 11.0 Hz), 48.13 (d, *J* = 1.7 Hz), 44.20 (d, *J* = 30.1 Hz), 37.54 (d, *J* = 2.2 Hz), 35.10 (d, *J* = 4.8 Hz);

**$^{19}$F NMR (282 MHz, CDCl$_3$):** δ -110.91 (dd, *J* = 17.5, 5.3 Hz);

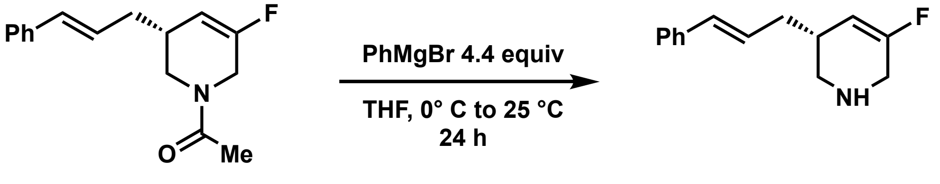
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 218.1345, found: 218.1343;

**R$_f$** (Hexane/acetone = 7/3): 0.23;

**ATR-IR** ν (cm$^{-1}$): 3056, 3025, 2914, 2844, 1700, 1598, 1494, 1448, 1367, 1279, 1156, 1108, 1070, 1047, 1029, 966, 910, 841, 744, 694;

**$[\alpha]_D^{25}$:** – 8.24 (c 0.9, CHCl$_3$).

## General Procedure: Alternative route to free NH product 3a

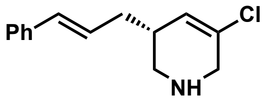


*6a* *3a*

*Scheme 2. Alternative route to **3a**.*

**(R)-3-cinnamyl-5-fluoro-1,2,3,6-tetrahydropyridine 3a** was synthesized following the synthetic sequence in Scheme S7. (R)-1-(3-cinnamyl-5-fluoro-3,6-dihydropyridin-1(2H)-yl)ethan-1-one (26 mg, 0.1 mmol, 1.0 equiv.) was dissolved in tetrahydrofuran (THF, 180 µL) in a 4 mL screw cap vial equipped with a septum screw cap. The reaction mixture was cooled to 0 °C and a solution of phenyl magnesium bromide (PhMgBr 1 M in THF, 440 µL, 0.44 mmol, 4.4 equiv.) was added slowly at 0 °C. The reaction was allowed to warm to ambient temperature and stirred for 24 hours. The reaction mixture was then cooled to 0 °C and an aqueous workup with 2 M HCl (2.0 mL) was added dropwise. The acidic aqueous layer was extracted with EtOAc (3 x 5 mL) to remove any organic impurities. The acidic aqueous phase was then basified with

$NaHCO_3$ and the resulting aqueous phase was then extracted with EtOAc (3 x 5 mL). The resulting organic layer was dried with $Na_2SO_4$ and filtered and the solvent was evaporated and the mono-alkylated NH tetrahydropyridine **3a** was purified by flash column chromatography over silica gel using a solvent mixture of hexane/acetone (7/3 to 1/1) as the eluent. The desired compound was isolated as colorless oil (17.4 mg, 0.08 mmol, 80% yield). The enantioselectivity was not again measured for the free N-H product **3a**. The spectra match the spectra of free amine **3a** using the method described in scheme 6. *Note: some product was observed in the organic layer prior to basification, product can be obtained by flash column chromatography over silica gel using a solvent mixture of hexane/acetone (7/3 to 1/1) as the eluent.*



***3b***

**Chemical Formula:** $C_{14}H_{16}ClN$
**Exact Mass: 233.0971**
**Molecular Weight: 233.7390**

**(R)-5-chloro-3-cinnamyl-1,2,3,6-tetrahydropyridine 3b** was synthesized following the procedure reported in Scheme S7 (R)-1-(3-cinnamyl-5-chloro-3,6-dihydropyridin-1(2H)-yl)ethan-1-one (27.5 mg, 0.1 mmol, 1.0 equiv.). The desired compound was obtained as colourless oil (20.5 mg, 0.088 mmol, 88% yield). The absolute configuration was adopted from product **6b**. The enantioselectivity was not again measured for the free N-H product **3b**.

**$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.38 – 7.28 (m, 4H), 7.25 – 7.20 (m, 1H), 6.44 (d, $J$ = 16.0 Hz, 1H), 6.22 – 6.10 (m, 1H), 5.90 (dt, $J$ = 3.5, 1.7 Hz, 1H), 3.50 – 3.34 (m, 2H), 3.09 (dd, $J$ = 13.1, 5.1 Hz, 1H), 2.61 (dd, $J$ = 13.1, 7.4 Hz, 1H), 2.43 (ddq, $J$ = 10.1, 5.0, 2.7 Hz, 1H), 2.26 (tdd, $J$ = 7.4, 4.0, 1.3 Hz, 1H);

**$^{13}$C NMR (101 MHz, $CDCl_3$)** 137.36, 132.48, 131.88, 128.71, 127.41, 127.22, 127.05, 126.21, 50.14, 47.43, 37.54, 37.08;

**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 234.1044, found 234.1048;

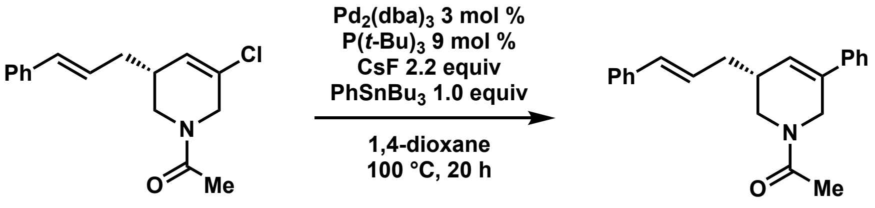
**$R_f$** ($n$-hexane/acetone = 1/1): 0.35;

**ATR-IR** ν ($cm^{-1}$): 3026, 2919, 2851, 1654, 1449, 969, 749, 697;

**$[\alpha]_D^{25}$:** – 13.39 (c 0.93, $CHCl_3$);

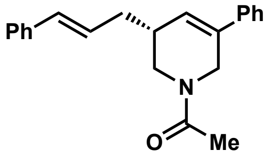
## Follow up chemistry and product derivatization

### Cross coupling reactions of 6b



***6b*** ***8, 82% yield***

*Scheme S8. Stille Cross Coupling of vinyl chloride **6b**.*



***8***

**Chemical Formula:** $C_{22}H_{23}NO$
**Exact Mass: 317.1780**
**Molecular Weight: 317.4320**

**(*R*)-1-(3-cinnamyl-5-phenyl-3,6-dihydropyridin-1(2*H*)-yl)ethan-1-one 8** was synthesized following the synthetic sequence in Scheme S8. A 4 mL screw cap vial was transferred to an argon filled glovebox. Bis(dibenzylideneacetone)palladium(0) (Pd$_2$dba$_3$, 3 mg, 0.003 mmol, 3 mol%) was added to a vial with tri-*tert*-butylphosphine (P(*t*-Bu)$_3$, 2 mg, 0.009 mmol, 9 mol%) and cesium fluoride (CsF, 33 mg, 0.22 mmol, 2.2 equiv.). Dioxane (200 μL) was added to mixture and stirred at ambient temperature for 5 minutes. (R)-1-(3-cinnamyl-5-chloro-3,6-dihydropyridin-1(2H)-yl)ethan-1-one (27.5 mg, 0.1 mmol, 1.0 equiv.) was dissolved in dioxane (200 μL) and added to the reaction mixture followed by tributylphenylstannane (PhSnBu$_3$, 34 μL, 0.1 mmol, 1.0 equiv.). The reaction mixture was sealed with a septum screw cap and heated to 100 °C for 20 hours. The reaction mixture was cooled to room temperature, filtered through a plug of silica and washed with copious amounts of ethyl acetate. The solvent was evaporated and the crude reaction mixture was purified by flash chromatography over silica gel using a solvent mixture of hexane/EtOAc (7/3 to 2/8) as the eluent. The desired compound was isolated as a pale-yellow oil (26.1 mg, 0.082 mmol, 82% yield). The absolute configuration was adopted from product **6b**. The enantioselectivity was not again measured for the cross-coupled product **8**.

**$^1$H NMR (400 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers): δ 7.48 – 7.28 (m, 9H), 7.26 – 7.19 (m, 1H), 6.55 – 6.44 (m, 1H), 6.32 – 6.23 (m, 1H), 6.23 – 6.14 (m, 1H), 4.54 (dt, *J* = 18.0, 2.2 Hz, 0.65H), 4.39 (dt, *J* = 18.1, 2.3 Hz, 0.65H), 4.30 (dt, *J* = 4.8, 2.4 Hz, 0.7H), 4.14 (dd, *J* = 12.8, 5.0 Hz, 0.35H), 3.67 (dd, *J* = 13.2, 4.7 Hz, 0.65H), 3.40 – 3.30 (m, 0.65H), 3.22 (dd, *J* = 12.8, 7.5 Hz, 0.35H), 2.68 – 2.55 (m, 1H), 2.46 – 2.29 (m, 2H), 2.18 (s, 1H), 2.18 (s, 1.1H), 2.17 (s, 1.9H);

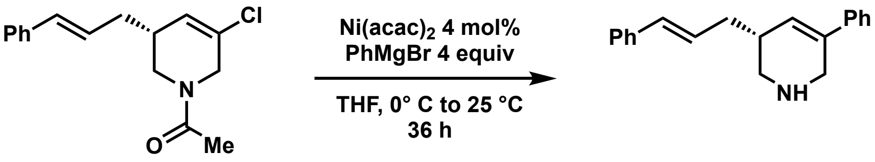
**$^{13}$C NMR (101 MHz, CDCl$_3$)** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *)**:** δ 169.9, 169.7*, 138.82*, 138.7, 137.5, 137.2*, 135.2, 133.8*, 132.8, 132.5*, 128.8*, 128.8, 128.7 (overlap)*, 128.1*, 128.0*, 127.9, 127.6, 127.3*, 127.3 (overlap)*, 127.3, 126.3*, 126.2, 125.8*, 125.5 (overlap)*, 125.2, 47.6, 47.6*, 43.5, 43.0*, 37.0*, 36.8, 36.4*, 35.5, **29.8**, 22.2*, 21.8; (bold is impurity)

**HRMS**: m/z (ESI) calculated for (M + H)$^+$: 318.1852, found 318.1867;

**R$_f$** (Hexane/acetone = 3/7): 0.4;

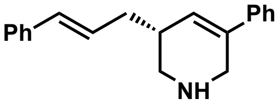
**ATR-IR** ν (cm$^{-1}$): 3027, 2924, 2853, 1625, 1447, 1317, 1269, 1033, 970, 751, 696, 689, 665;

**[α]$_D^{25}$:** – 5.14 (c 1.0, CHCl$_3$).



**6b** **9, 83% yield**

*Scheme 9. Kumada-type Cross Coupling of vinyl chloride **6b**.*



**9**

**Chemical Formula:** $C_{20}H_{21}N$
**Exact Mass: 275.1674**
**Molecular Weight: 275.3950**

**(*R*)-3-cinnamyl-5-phenyl-1,2,3,6-tetrahydropyridine 9** was synthesized following the synthetic sequence in Scheme S9. A 4 mL screw cap vial was charged with nickel(II) acetylacetonate (Ni(acac)$_2$, 1.0 mg, 0.004 mmol, 4 mol%) and dissolved in tetrahydrofuran (THF, 100 μL). The reaction mixture was cooled to 0 °C, and phenyl magnesium bromide (PhMgBr 1 M in THF, 400 μL, 0.4 mmol, 4.0 equiv.) was added to the reaction mixture dropwise. (R)-1-(3-cinnamyl-5-chloro-3,6-dihydropyridin-1(2H)-yl)ethan-1-one (27.5 mg, 0.1 mmol, 1.0 equiv.) was dissolved in tetrahydrofuran (THF, 200 μL) and added to the reaction mixture at 0 °C and allowed to warm to ambient temperature overnight. After 36 hours, the reaction was cooled to 0 °C and an aqueous workup was performed with saturated $NH_4Cl$ (1 mL). The aqueous phase was extracted with EtOAc (3 x 10 mL) and the organic layer was dried over $Na_2SO_4$ and filtered. The solvent was evaporated and the crude reaction mixture was purified by flash chromatography over silica gel using a solvent mixture of methanol/ethyl acetate (1/9) with 1% triethyl amine as the eluent. The desired compound was isolated as a pale-yellow amorphous solid (22.8 mg, 0.083 mmol, 83% yield). The absolute configuration was adopted from product **6b**. The enantioselectivity was not again measured for the cross-coupled product **9**.

**$^1$H NMR (400 MHz, $CDCl_3$)** $^1$H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 8H), 7.22 (d, *J* = 7.0 Hz, 2H), 6.51 (d, *J* = 15.7 Hz, 1H), 6.21 (s, 1H), 6.15 (dd, *J* = 15.5, 7.5 Hz, 1H), 4.07 (d, *J* = 16.4 Hz, 1H), 3.98 (d, *J* = 16.5 Hz, 1H), 3.56 (dd, *J* = 12.3, 5.4 Hz, 1H), 3.06 (s, 1H), 2.88 (t, *J* = 10.9 Hz, 1H), 2.44 (t, *J* = 6.9 Hz, 2H).
$Et_3N$•HCl present $^1$H NMR (400 MHz, $CDCl_3$) δ 3.13 (q, *J* = 7.3 Hz, 2H) 1.44 – 1.34 (m, 3H).
*Note: Titration of amine **9** with $Et_3N$ resulted in better resolution in peaks due to solubility issues of **9** in $CDCl_3$*

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 8H), 7.25 – 7.19 (m, 2H), 6.48 (d, *J* = 15.8 Hz, 1H), 6.22 (dt, *J* = 15.8, 7.2 Hz, 1H), 6.16 (s, 1H), 3.92 – 3.75 (m, 2H), 3.36 – 3.26 (m, 1H), 2.79 – 2.63 (m, 2H), 2.41 – 2.31 (m, 2H). without $Et_3N$ trituration.

**$^{13}$C NMR (101 MHz, $CDCl_3$)** $^{13}$C NMR (101 MHz, $CDCl_3$) δ 137.11, 136.92, 133.75, 130.70, 128.93, 128.75, 128.60, 127.69, 126.48, 126.36, 125.44, 125.30, 44.90, 43.25, 36.66, 32.63,
$Et_3N$•HCl present $^{13}$C NMR (101 MHz, $CDCl_3$) δ 46.07, 8.78
*Note: Titration of amine **9** with $Et_3N$ resulted in better resolution in peaks due to solubility issues of **9** in $CDCl_3$*
$^{13}$C NMR (101 MHz, $CDCl_3$) δ 138.93, 137.36, 134.68,p 132.64, 128.70, 128.69, 127.83, 127.41, 127.16, 126.84, 126.25, 125.17, 46.98, 45.58, 37.32, 34.65. without $Et_3N$ trituration.

**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 276.1747, found 276.1755;

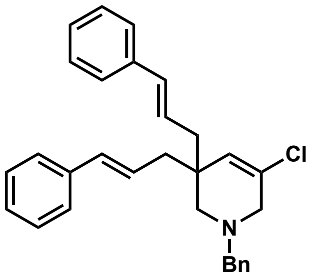
**R$_f$** (methanol/ethyl acetate = 1/9): 0.4;

**ATR-IR** ν (cm$^{-1}$): 2924, 1634, 1447, 969, 738, 751, 694;

**$[\alpha]_D^{25}$:** – 6.80 (c 0.833, CHCl$_3$);

### Ring-closing metathesis

### Synthesis of 10a



***10a***

**Chemical Formula:** $C_{30}H_{30}ClN$
**Exact Mass: 439.2067**
**Molecular Weight: 440.0270**

**1-Benzyl-5-chloro-3,3-dicinnamyl-1,2,3,6-tetrahydropyridine 10a** Benzyl bromide (247 µL, 2.07 mmol, 3.0 equiv.) and triethyl amine (96 µL, 0.69 mmol, 1.0 equiv.) were added to 5-chloro-3,3-bis((*E*)-3-(phenyl)allyl)-1,2,3,6-tetrahydropyridine (**5b**, 242 mg, 0.69 mmol, 1.0 equiv.) in dichloromethane (4 mL). The resulting reaction mixture was stirred at room temperature for 19 h. The reaction was quenched with a saturated aqueous ammonium chloride solution (2 mL). The phases were separated and the aqueous phase was extracted with dichloromethane (3 x 2 mL). The combined organic phases were washed with brine (1 x 2 mL), dried over sodium sulphate, and concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel using *n*-hexane/ethyl acetate gave the title compound **10a** (260 mg, 0.59 mmol, 86%) as colourless oil.

**$^1$H NMR (400 MHz, CDCl$_3$):** δ 7.38–7.27 (m, 13H), 7.25–7.19 (m, 2H), 6.36 (d, *J* = 15.8 Hz, 2H), 6.13 (dt, *J* = 15.4, 7.4 Hz, 2H), 5.79 (s, 1H), 3.57 (s, 2H), 3.10 (s, 2H), 2.43–2.25 (m, 6H);

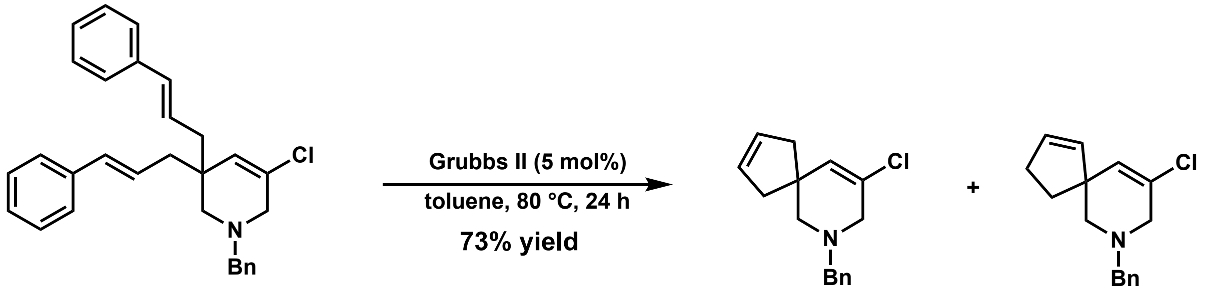
**$^{13}$C NMR (101 MHz, CDCl$_3$)** *(one carbon signal is overlapping)***:** δ 138.3, 137.6, 133.2, 130.2, 129.2, 129.1, 128.6, 128.5, 127.4, 127.3, 126.2, 126.0, 62.6, 58.8, 58.0, 42.8, 41.2;

**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 440.2145, found: 440.2150;

**R$_f$** (*n*-hexane/EtOAc = 10/1): 0.58;

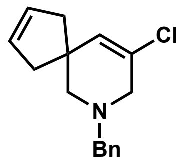
**ATR-IR** ν (cm$^{-1}$): 3028, 2922, 2853, 1681, 1495, 1452, 1265, 1073, 1028, 970, 826, 738, 699, 676;

**Ring-closing metathesis of 10a**



***10a*** ***11a*** **(6:4)** ***11a'***

*Scheme 10. Ring closing metathesis of 10a*



***11a***

**Chemical Formula:** $C_{16}H_{18}ClN$
**Exact Mass: 259.1128**
**Molecular Weight: 259.7770**

**1-Benzyl-5-chloro-3,3-dicinnamyl-1,2,3,6-tetrahydropyridine 11a.** A solution of 1-benzyl-5-chloro-3,3-dicinnamyl-1,2,3,6-tetrahydropyridine **10a** (50 mg, 0.11 mmol, 1.0 equiv.) in toluene (1 mL) was added to a 10-mL screw vial charged with dichloro[1,3-bis(2,4,6-trimethylphenyl)-2-imidazolidinylidene](benzylidene)-(tricyclohexylphosphine)ruthenium(II) (Grubbs II, 4.8 mg, 5.7 µmol, 5 mol%) under a nitrogen atmosphere. The resulting mixture was stirred at 80°C for 24 hours. The reaction mixture was cooled to room temperature and filtered through a small plug silica gel. The volatiles were remover under reduced pressure. Purification of the residue by flash chromatography on silica gel using *n*-hexane/ethyl acetate (100:0 to 20:1) gave the title compound **11a** in mixture with the isomer **11a'** (21 mg, 0.081 mmol, 73%, ratio 6:4 for **11a**:**11a'**) as colourless oil.

**$^{1}$H NMR (400 MHz, CDCl$_3$):** δ 7.31 (dd, J = 13.6, 6.6 Hz, 4H), 7.27 – 7.21 (m, 1H), 5.81 (s, 0.4H), 5.74 (d, J = 5.9 Hz, 0.4H), 5.65 (s, 0.4H), 5.59 – 5.54 (m, 1.2H), 5.31 – 5.30 (m, 1H), 3.57 (s, 2H), 3.04 (s, 2H), 2.34 (d, J = 45.6 Hz, 5H), 1.85 – 1.68 (m, 1H);

**$^{13}$C NMR (101 MHz, CDCl$_3$):** δ 138.7, 136.5, 132.6, 131.8, 130.6, 129.3, 129.2, 128.6, 128.1, 128.0, 127.5, 127.5, 62.3, 62.2, 61.3, 59.4, 58.2, 57.9, 53.1, 45.9, 45.0, 35.5, 31.3;

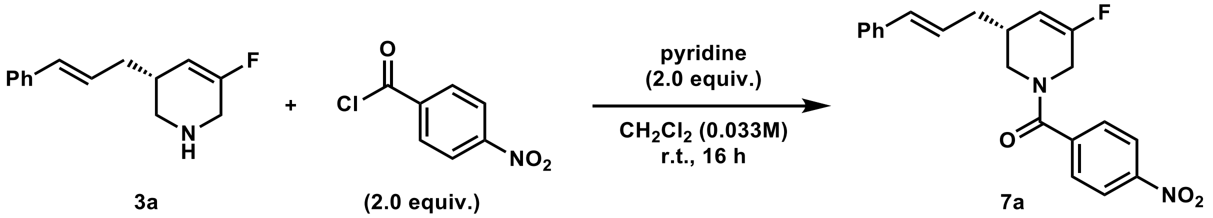
**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 260.1206, found: 260.1226;

**R$_f$** (*n*-hexane/EtOAc = 20/1): 0.07;

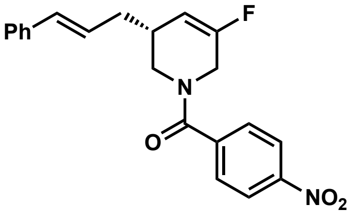
**ATR-IR** ν (cm$^{-1}$): 3028, 1917, 2840, 2798, 1654, 1494, 1457, 1312, 1148, 1064, 967, 848, 741, 698, 680.

## X ray crystallographic analysis

### Synthesis of 7a



*Scheme 11. Derivatization for crystallization.*



*7a*

**Chemical Formula:** $C_{21}H_{19}FN_2O_3$
**Exact Mass: 366.1380**
**Molecular Weight: 366.3924**

**(R)-(3-cinnamyl-5-fluoro-3,6-dihydropyridin-1(2H)-yl)(4-nitrophenyl)methanone 7a** was synthesized following the reaction in Scheme 9. Therefore, (R)-3-cinnamyl-5-fluoro-1,2,3,6-tetrahydropyridine (35.9 mg, 0.165 mmol, 1.0 equiv.) was dissolved in $CH_2Cl_2$ (5 mL) under air at room temperature. Pyridine (26.6 µL, 0.33 mmol, 2.0 equiv.) was added, followed by 4-nitrobenzoyl chloride (61.2 mg, 0.33 mmol, 2.0 equiv.). The resulting mixture was stirred at room temperature for 16 hours and then quenched with brine. The aqueous phase was extracted with EtOAc. The combined organic phases were dried over magnesium sulfate and filtered. The crude was subjected to flash column chromatography over silica gel using a solvent mixture of hexane/EtOAc (7/3) as the eluent. The desired compound was obtained as white solids (60.0 mg, 0.164 mmol, 99%).

**$^1$H NMR (400 MHz, $CD_3OD$):** (as mixture of E/Z amide bond isomers) δ 8.33 – 8.19 (m, 2H), 7.71 – 7.60 (m, 2H), 7.42 – 7.12 (m, 5H), 6.53 (d, *J* = 15.8 Hz, 0.3H), 6.36 – 6.25 (m, 0.3H), 6.20 (d, *J* = 15.9 Hz, 0.7H), 6.01 – 5.90 (dt, *J* = 15.2 Hz, 0.7H), 5.48 (d, *J* = 16.2 Hz, 1H), 4.38 – 4.24 (m, 1.4H), 4.00 – 3.92 (m, 0.6H), 3.90 – 3.68 (m, 0.7H), 3.52 (dd, *J* = 13.6, 4.6 Hz, 0.7H), 3.27 (dd, *J* = 13.7, 6.1 Hz, 0.6H), 2.68 – 2.48 (m, 1H), 2.39 –2.21 (m, 1.3H), 2.13 – 2.03 (m, 0.7H);

**$^{13}$C NMR (101 MHz, $CD_3OD$):** (as mixture of E/Z amide bond isomers, signals of minor isomer are indicated with *) δ 170.77, 170.49*, 156.51 (d, *J* = 253.8 Hz), 156.07 (d, *J* = 252.8 Hz)*, 150.05*, 149.83, 142.70, 142.61*, 138.80*, 138.29, 133.89*, 133.67, 129.55*, 129.47, 129.46, 129.31*, 128.32, 127.77*, 127.61, 127.21*, 126.91, 124.91, 106.76 (d, *J* = 10.1 Hz)*, 106.16 (d, *J* = 12.1 Hz), 47.15 (d, *J* = 40.3 Hz)*, 44.67, 42.16 (d, *J* = 40.8 Hz), 37.98*, 36.95, 35.34 (d, *J* = 6.3 Hz), 34.65*;

**$^{19}$F NMR (282 MHz, $CD_3OD$):** (as mixture of E/Z amide bond isomers, signal of minor isomer is indicated with *) δ -114.94 (dd, *J* = 16.2, 4.9 Hz), -115.88 – -116.01 (m)*;

**HRMS**: m/z (ESI) calculated for $(M + H)^+$: 367.1458, found: 367.1483;

**$R_f$** (Hexane/EtOAc = 7/3): 0.35;

**ATR-IR** ν (cm$^{-1}$): 3027, 2913, 2856, 1709, 1643, 1601, 1521, 1495, 1434, 1380, 1347, 1380, 1347, 1314, 1286, 1263, 1179, 1132, 1107, 1030, 1012, 969, 863, 853, 772, 742, 696.

**Crystallization procedure**

Crystals suitable for X-ray crystallographic analysis were obtained by dissolving the white solids (60.0 mg, 0.164 mmol) in hot Methanol (~4 mL). The solvent was allowed to slowly evaporate over 48 hours to obtain white crystals.
**CCDC#2234165.**

The crystal structure of **7a** was registered in the Cambridge crystallographic data center and can be found as CCDC#2234165.

**Experimental details**

Low-temperature diffraction data ($\phi$-and $\omega$-scans) were collected on a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON II CPAD detector with Cu $K_\alpha$ radiation ($\lambda$ = 1.54178 Å) from an I$\mu$S micro-source for the structure of compound V20222. The structure was solved by direct methods using SHELXS (Sheldrick, G. M. *Acta Cryst.* **1990**, A46, 467-473.) and refined against $F^2$ on all data by full-matrix least squares with SHELXL-2017 (Sheldrick, G. M. *Acta Cryst.* **2015**, C71, 3-8.) using established refinement techniques (Müller, P. *Crystallography Reviews* **2009**, *15*, 57-83). All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the *U* value of the atoms they are linked to (1.5 times for methyl groups).

Compound **7a** (internal compound number **V20222**) crystallizes in the triclinic space group *P*1 with two molecules in the asymmetric unit.

Table 1. Crystal data and structure refinement for V20222.

| | | |
|---|---|---|
| Identification code | V20222 | |
| Empirical formula | C42 H38 F2 N4 O6 | |
| Formula weight | 732.76 | |
| Temperature | 106(2) K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Triclinic | |
| Space group | P1 | |
| Unit cell dimensions | a = 7.5776(5) Å | α= 71.507(6)°. |
| | b = 9.8771(9) Å | β= 76.607(4)°. |
| | c = 13.5619(9) Å | γ = 70.196(8)°. |
| Volume | 896.88(13) Å$^3$ | |
| Z | 1 | |
| Density (calculated) | 1.357 Mg/m$^3$ | |

| | |
|---|---|
| Absorption coefficient | 0.815 mm$^{-1}$ |
| F(000) | 384 |
| Crystal size | 0.250 x 0.150 x 0.100 mm$^{3}$ |
| Theta range for data collection | 3.470 to 74.499°. |
| Index ranges | -9<=h<=9, -12<=k<=12, -16<=l<=16 |
| Reflections collected | 29009 |
| Independent reflections | 7038 [R(int) = 0.0265] |
| Completeness to theta = 67.679° | 99.7 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.7538 and 0.6794 |
| Refinement method | Full-matrix least-squares on F$^{2}$ |
| Data / restraints / parameters | 7038 / 3 / 487 |
| Goodness-of-fit on F$^{2}$ | 1.039 |
| Final R indices [I>2sigma(I)] | R1 = 0.0251, wR2 = 0.0666 |
| R indices (all data) | R1 = 0.0252, wR2 = 0.0666 |
| Absolute structure parameter | 0.05(2) |
| Extinction coefficient | n/a |
| Largest diff. peak and hole | 0.162 and -0.158 e.Å$^{-3}$ |

Table 2. Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for V20222. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| N(1) | 3744(2) | 7545(2) | 8229(1) | 20(1) |
| C(6) | 2563(2) | 6705(2) | 8395(1) | 21(1) |
| C(11) | 3068(2) | 5579(2) | 7770(1) | 20(1) |
| C(12) | 3195(2) | 4099(2) | 8322(1) | 23(1) |
| C(13) | 3628(3) | 3023(2) | 7785(1) | 25(1) |
| C(14) | 3923(2) | 3451(2) | 6699(1) | 23(1) |
| N(2) | 4425(2) | 2302(2) | 6126(1) | 28(1) |
| O(2) | 4342(3) | 1053(2) | 6619(1) | 44(1) |
| O(3) | 4889(2) | 2662(2) | 5171(1) | 39(1) |
| C(15) | 3771(2) | 4915(2) | 6128(1) | 23(1) |
| C(16) | 3314(2) | 5986(2) | 6673(1) | 23(1) |
| O(1) | 1111(2) | 6825(2) | 9034(1) | 29(1) |
| C(1) | 3228(2) | 8677(2) | 8808(1) | 22(1) |
| C(2) | 4929(3) | 8576(2) | 9236(1) | 23(1) |
| F(1) | 4465(2) | 9437(1) | 9925(1) | 31(1) |
| C(3) | 6683(3) | 7789(2) | 9022(1) | 25(1) |
| C(4) | 7208(2) | 6925(2) | 8205(1) | 22(1) |
| C(7) | 7881(3) | 5229(2) | 8673(1) | 25(1) |
| C(8) | 8587(2) | 4410(2) | 7829(1) | 24(1) |
| C(9) | 8227(3) | 3169(2) | 7871(1) | 25(1) |
| C(21) | 8824(2) | 2377(2) | 7039(1) | 25(1) |
| C(22) | 8998(3) | 857(2) | 7296(2) | 36(1) |
| C(23) | 9488(3) | 111(2) | 6514(2) | 44(1) |
| C(24) | 9787(3) | 851(3) | 5475(2) | 39(1) |
| C(25) | 9631(3) | 2360(3) | 5206(2) | 39(1) |
| C(26) | 9158(3) | 3116(2) | 5983(2) | 31(1) |
| C(5) | 5584(2) | 7403(2) | 7559(1) | 20(1) |
| N(101) | 6170(2) | 2464(2) | 1720(1) | 21(1) |
| C(106) | 4459(2) | 3365(2) | 1472(1) | 20(1) |
| C(111) | 3397(2) | 4513(2) | 2074(1) | 19(1) |
| C(112) | 2685(2) | 5983(2) | 1504(1) | 23(1) |

| | | | | |
|---|---|---|---|---|
| C(113) | 1732(2) | 7092(2) | 2015(1) | 25(1) |
| C(114) | 1482(2) | 6691(2) | 3104(1) | 22(1) |
| N(102) | 589(2) | 7862(2) | 3668(1) | 27(1) |
| O(102) | -41(2) | 9137(2) | 3153(1) | 37(1) |
| O(103) | 538(2) | 7498(2) | 4625(1) | 36(1) |
| C(115) | 2064(2) | 5231(2) | 3691(1) | 21(1) |
| C(116) | 3030(2) | 4138(2) | 3167(1) | 19(1) |
| O(101) | 3728(2) | 3288(2) | 776(1) | 31(1) |
| C(101) | 7173(3) | 1327(2) | 1147(2) | 26(1) |
| C(102) | 9157(2) | 1389(2) | 772(1) | 24(1) |
| F(101) | 10032(2) | 555(1) | 69(1) | 31(1) |
| C(103) | 10047(2) | 2107(2) | 1049(1) | 25(1) |
| C(104) | 9074(2) | 2969(2) | 1864(1) | 22(1) |
| C(107) | 8688(2) | 4663(2) | 1375(1) | 23(1) |
| C(108) | 8056(2) | 5529(2) | 2185(1) | 24(1) |
| C(109) | 6543(2) | 6705(2) | 2183(1) | 23(1) |
| C(121) | 5883(2) | 7606(2) | 2952(1) | 23(1) |
| C(122) | 4483(3) | 8971(2) | 2726(2) | 27(1) |
| C(123) | 3865(3) | 9880(2) | 3413(2) | 33(1) |
| C(124) | 4645(3) | 9453(2) | 4329(2) | 35(1) |
| C(125) | 6019(3) | 8099(3) | 4568(2) | 34(1) |
| C(126) | 6613(3) | 7175(2) | 3896(1) | 28(1) |
| C(105) | 7264(2) | 2550(2) | 2451(1) | 21(1) |

Table 3. Bond lengths [Å] and angles [°] for V20222.

| | |
|---|---|
| N(1)-C(6) | 1.353(2) |
| N(1)-C(1) | 1.4621(19) |
| N(1)-C(5) | 1.467(2) |
| C(6)-O(1) | 1.229(2) |
| C(6)-C(11) | 1.505(2) |
| C(11)-C(12) | 1.396(2) |
| C(11)-C(16) | 1.397(2) |
| C(12)-C(13) | 1.382(2) |
| C(12)-H(12) | 0.9500 |
| C(13)-C(14) | 1.383(2) |
| C(13)-H(13) | 0.9500 |
| C(14)-C(15) | 1.386(2) |
| C(14)-N(2) | 1.472(2) |
| N(2)-O(2) | 1.218(2) |
| N(2)-O(3) | 1.228(2) |
| C(15)-C(16) | 1.384(2) |
| C(15)-H(15) | 0.9500 |
| C(16)-H(16) | 0.9500 |
| C(1)-C(2) | 1.494(2) |
| C(1)-H(1A) | 0.9900 |
| C(1)-H(1B) | 0.9900 |
| C(2)-C(3) | 1.311(3) |
| C(2)-F(1) | 1.3670(19) |
| C(3)-C(4) | 1.510(2) |
| C(3)-H(3) | 0.9500 |
| C(4)-C(5) | 1.532(2) |
| C(4)-C(7) | 1.538(2) |
| C(4)-H(4) | 1.0000 |
| C(7)-C(8) | 1.503(2) |
| C(7)-H(7A) | 0.9900 |
| C(7)-H(7B) | 0.9900 |
| C(8)-C(9) | 1.325(3) |
| C(8)-H(8) | 0.9500 |
| C(9)-C(21) | 1.475(2) |

| | |
|---|---|
| C(9)-H(9) | 0.9500 |
| C(21)-C(26) | 1.394(3) |
| C(21)-C(22) | 1.395(3) |
| C(22)-C(23) | 1.391(3) |
| C(22)-H(22) | 0.9500 |
| C(23)-C(24) | 1.372(3) |
| C(23)-H(23) | 0.9500 |
| C(24)-C(25) | 1.387(3) |
| C(24)-H(24) | 0.9500 |
| C(25)-C(26) | 1.392(3) |
| C(25)-H(25) | 0.9500 |
| C(26)-H(26) | 0.9500 |
| C(5)-H(5A) | 0.9900 |
| C(5)-H(5B) | 0.9900 |
| N(101)-C(106) | 1.348(2) |
| N(101)-C(101) | 1.464(2) |
| N(101)-C(105) | 1.470(2) |
| C(106)-O(101) | 1.232(2) |
| C(106)-C(111) | 1.505(2) |
| C(111)-C(116) | 1.394(2) |
| C(111)-C(112) | 1.395(2) |
| C(112)-C(113) | 1.385(3) |
| C(112)-H(112) | 0.9500 |
| C(113)-C(114) | 1.387(3) |
| C(113)-H(113) | 0.9500 |
| C(114)-C(115) | 1.383(2) |
| C(114)-N(102) | 1.474(2) |
| N(102)-O(102) | 1.221(2) |
| N(102)-O(103) | 1.227(2) |
| C(115)-C(116) | 1.385(2) |
| C(115)-H(115) | 0.9500 |
| C(116)-H(116) | 0.9500 |
| C(101)-C(102) | 1.487(2) |
| C(101)-H(10A) | 0.9900 |
| C(101)-H(10B) | 0.9900 |
| C(102)-C(103) | 1.307(3) |

| | |
|---|---|
| C(102)-F(101) | 1.3653(18) |
| C(103)-C(104) | 1.512(2) |
| C(103)-H(103) | 0.9500 |
| C(104)-C(105) | 1.535(2) |
| C(104)-C(107) | 1.542(2) |
| C(104)-H(104) | 1.0000 |
| C(107)-C(108) | 1.497(2) |
| C(107)-H(10C) | 0.9900 |
| C(107)-H(10D) | 0.9900 |
| C(108)-C(109) | 1.327(3) |
| C(108)-H(108) | 0.9500 |
| C(109)-C(121) | 1.476(2) |
| C(109)-H(109) | 0.9500 |
| C(121)-C(126) | 1.395(3) |
| C(121)-C(122) | 1.399(3) |
| C(122)-C(123) | 1.392(2) |
| C(122)-H(122) | 0.9500 |
| C(123)-C(124) | 1.382(3) |
| C(123)-H(123) | 0.9500 |
| C(124)-C(125) | 1.384(3) |
| C(124)-H(124) | 0.9500 |
| C(125)-C(126) | 1.387(3) |
| C(125)-H(125) | 0.9500 |
| C(126)-H(126) | 0.9500 |
| C(105)-H(10E) | 0.9900 |
| C(105)-H(10F) | 0.9900 |

| | |
|---|---|
| C(6)-N(1)-C(1) | 118.35(13) |
| C(6)-N(1)-C(5) | 127.02(13) |
| C(1)-N(1)-C(5) | 114.55(13) |
| O(1)-C(6)-N(1) | 122.72(15) |
| O(1)-C(6)-C(11) | 119.18(15) |
| N(1)-C(6)-C(11) | 118.10(14) |
| C(12)-C(11)-C(16) | 120.15(15) |
| C(12)-C(11)-C(6) | 117.74(14) |
| C(16)-C(11)-C(6) | 122.03(14) |

| | |
|---|---|
| C(13)-C(12)-C(11) | 120.09(15) |
| C(13)-C(12)-H(12) | 120.0 |
| C(11)-C(12)-H(12) | 120.0 |
| C(12)-C(13)-C(14) | 118.47(16) |
| C(12)-C(13)-H(13) | 120.8 |
| C(14)-C(13)-H(13) | 120.8 |
| C(13)-C(14)-C(15) | 122.82(16) |
| C(13)-C(14)-N(2) | 118.58(15) |
| C(15)-C(14)-N(2) | 118.60(15) |
| O(2)-N(2)-O(3) | 123.48(16) |
| O(2)-N(2)-C(14) | 118.51(15) |
| O(3)-N(2)-C(14) | 118.01(15) |
| C(16)-C(15)-C(14) | 118.25(16) |
| C(16)-C(15)-H(15) | 120.9 |
| C(14)-C(15)-H(15) | 120.9 |
| C(15)-C(16)-C(11) | 120.16(15) |
| C(15)-C(16)-H(16) | 119.9 |
| C(11)-C(16)-H(16) | 119.9 |
| N(1)-C(1)-C(2) | 108.81(13) |
| N(1)-C(1)-H(1A) | 109.9 |
| C(2)-C(1)-H(1A) | 109.9 |
| N(1)-C(1)-H(1B) | 109.9 |
| C(2)-C(1)-H(1B) | 109.9 |
| H(1A)-C(1)-H(1B) | 108.3 |
| C(3)-C(2)-F(1) | 120.93(16) |
| C(3)-C(2)-C(1) | 127.66(16) |
| F(1)-C(2)-C(1) | 111.40(14) |
| C(2)-C(3)-C(4) | 120.60(16) |
| C(2)-C(3)-H(3) | 119.7 |
| C(4)-C(3)-H(3) | 119.7 |
| C(3)-C(4)-C(5) | 110.36(14) |
| C(3)-C(4)-C(7) | 112.79(14) |
| C(5)-C(4)-C(7) | 112.91(13) |
| C(3)-C(4)-H(4) | 106.8 |
| C(5)-C(4)-H(4) | 106.8 |
| C(7)-C(4)-H(4) | 106.8 |

| | |
|---|---|
| C(8)-C(7)-C(4) | 111.51(14) |
| C(8)-C(7)-H(7A) | 109.3 |
| C(4)-C(7)-H(7A) | 109.3 |
| C(8)-C(7)-H(7B) | 109.3 |
| C(4)-C(7)-H(7B) | 109.3 |
| H(7A)-C(7)-H(7B) | 108.0 |
| C(9)-C(8)-C(7) | 125.00(16) |
| C(9)-C(8)-H(8) | 117.5 |
| C(7)-C(8)-H(8) | 117.5 |
| C(8)-C(9)-C(21) | 126.33(16) |
| C(8)-C(9)-H(9) | 116.8 |
| C(21)-C(9)-H(9) | 116.8 |
| C(26)-C(21)-C(22) | 118.15(17) |
| C(26)-C(21)-C(9) | 121.81(16) |
| C(22)-C(21)-C(9) | 119.99(17) |
| C(23)-C(22)-C(21) | 120.51(19) |
| C(23)-C(22)-H(22) | 119.7 |
| C(21)-C(22)-H(22) | 119.7 |
| C(24)-C(23)-C(22) | 120.96(19) |
| C(24)-C(23)-H(23) | 119.5 |
| C(22)-C(23)-H(23) | 119.5 |
| C(23)-C(24)-C(25) | 119.29(19) |
| C(23)-C(24)-H(24) | 120.4 |
| C(25)-C(24)-H(24) | 120.4 |
| C(24)-C(25)-C(26) | 120.3(2) |
| C(24)-C(25)-H(25) | 119.9 |
| C(26)-C(25)-H(25) | 119.9 |
| C(25)-C(26)-C(21) | 120.82(18) |
| C(25)-C(26)-H(26) | 119.6 |
| C(21)-C(26)-H(26) | 119.6 |
| N(1)-C(5)-C(4) | 111.53(13) |
| N(1)-C(5)-H(5A) | 109.3 |
| C(4)-C(5)-H(5A) | 109.3 |
| N(1)-C(5)-H(5B) | 109.3 |
| C(4)-C(5)-H(5B) | 109.3 |
| H(5A)-C(5)-H(5B) | 108.0 |

| | |
|---|---|
| C(106)-N(101)-C(101) | 118.01(14) |
| C(106)-N(101)-C(105) | 127.73(13) |
| C(101)-N(101)-C(105) | 114.06(13) |
| O(101)-C(106)-N(101) | 122.89(15) |
| O(101)-C(106)-C(111) | 118.73(15) |
| N(101)-C(106)-C(111) | 118.38(14) |
| C(116)-C(111)-C(112) | 119.72(15) |
| C(116)-C(111)-C(106) | 122.18(14) |
| C(112)-C(111)-C(106) | 118.02(14) |
| C(113)-C(112)-C(111) | 120.59(15) |
| C(113)-C(112)-H(112) | 119.7 |
| C(111)-C(112)-H(112) | 119.7 |
| C(112)-C(113)-C(114) | 118.00(15) |
| C(112)-C(113)-H(113) | 121.0 |
| C(114)-C(113)-H(113) | 121.0 |
| C(115)-C(114)-C(113) | 122.74(15) |
| C(115)-C(114)-N(102) | 118.05(15) |
| C(113)-C(114)-N(102) | 119.20(15) |
| O(102)-N(102)-O(103) | 124.06(16) |
| O(102)-N(102)-C(114) | 117.96(15) |
| O(103)-N(102)-C(114) | 117.98(14) |
| C(114)-C(115)-C(116) | 118.36(15) |
| C(114)-C(115)-H(115) | 120.8 |
| C(116)-C(115)-H(115) | 120.8 |
| C(115)-C(116)-C(111) | 120.36(15) |
| C(115)-C(116)-H(116) | 119.8 |
| C(111)-C(116)-H(116) | 119.8 |
| N(101)-C(101)-C(102) | 109.27(14) |
| N(101)-C(101)-H(10A) | 109.8 |
| C(102)-C(101)-H(10A) | 109.8 |
| N(101)-C(101)-H(10B) | 109.8 |
| C(102)-C(101)-H(10B) | 109.8 |
| H(10A)-C(101)-H(10B) | 108.3 |
| C(103)-C(102)-F(101) | 121.33(15) |
| C(103)-C(102)-C(101) | 127.62(15) |
| F(101)-C(102)-C(101) | 111.05(14) |

| | |
|---|---|
| C(102)-C(103)-C(104) | 120.31(16) |
| C(102)-C(103)-H(103) | 119.8 |
| C(104)-C(103)-H(103) | 119.8 |
| C(103)-C(104)-C(105) | 110.90(14) |
| C(103)-C(104)-C(107) | 111.40(14) |
| C(105)-C(104)-C(107) | 112.08(13) |
| C(103)-C(104)-H(104) | 107.4 |
| C(105)-C(104)-H(104) | 107.4 |
| C(107)-C(104)-H(104) | 107.4 |
| C(108)-C(107)-C(104) | 112.63(14) |
| C(108)-C(107)-H(10C) | 109.1 |
| C(104)-C(107)-H(10C) | 109.1 |
| C(108)-C(107)-H(10D) | 109.1 |
| C(104)-C(107)-H(10D) | 109.1 |
| H(10C)-C(107)-H(10D) | 107.8 |
| C(109)-C(108)-C(107) | 124.73(16) |
| C(109)-C(108)-H(108) | 117.6 |
| C(107)-C(108)-H(108) | 117.6 |
| C(108)-C(109)-C(121) | 126.67(16) |
| C(108)-C(109)-H(109) | 116.7 |
| C(121)-C(109)-H(109) | 116.7 |
| C(126)-C(121)-C(122) | 117.92(16) |
| C(126)-C(121)-C(109) | 123.09(16) |
| C(122)-C(121)-C(109) | 118.98(16) |
| C(123)-C(122)-C(121) | 120.86(17) |
| C(123)-C(122)-H(122) | 119.6 |
| C(121)-C(122)-H(122) | 119.6 |
| C(124)-C(123)-C(122) | 120.34(19) |
| C(124)-C(123)-H(123) | 119.8 |
| C(122)-C(123)-H(123) | 119.8 |
| C(123)-C(124)-C(125) | 119.35(18) |
| C(123)-C(124)-H(124) | 120.3 |
| C(125)-C(124)-H(124) | 120.3 |
| C(124)-C(125)-C(126) | 120.56(18) |
| C(124)-C(125)-H(125) | 119.7 |
| C(126)-C(125)-H(125) | 119.7 |

| | |
|---|---|
| C(125)-C(126)-C(121) | 120.91(18) |
| C(125)-C(126)-H(126) | 119.5 |
| C(121)-C(126)-H(126) | 119.5 |
| N(101)-C(105)-C(104) | 111.07(13) |
| N(101)-C(105)-H(10E) | 109.4 |
| C(104)-C(105)-H(10E) | 109.4 |
| N(101)-C(105)-H(10F) | 109.4 |
| C(104)-C(105)-H(10F) | 109.4 |
| H(10E)-C(105)-H(10F) | 108.0 |

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2$x $10^3$) for V20222. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\, h^2 a^{*2}U^{11} + ... + 2\, h\, k\, a^*\, b^*\, U^{12}\, ]$

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| N(1) | 19(1) | 20(1) | 21(1) | -10(1) | -1(1) | -4(1) |
| C(6) | 20(1) | 22(1) | 21(1) | -7(1) | -5(1) | -3(1) |
| C(11) | 17(1) | 22(1) | 23(1) | -9(1) | -4(1) | -4(1) |
| C(12) | 26(1) | 26(1) | 19(1) | -5(1) | -4(1) | -9(1) |
| C(13) | 31(1) | 18(1) | 26(1) | -4(1) | -8(1) | -7(1) |
| C(14) | 24(1) | 21(1) | 25(1) | -9(1) | -8(1) | -2(1) |
| N(2) | 35(1) | 21(1) | 28(1) | -10(1) | -11(1) | -1(1) |
| O(2) | 72(1) | 20(1) | 40(1) | -11(1) | -5(1) | -11(1) |
| O(3) | 62(1) | 29(1) | 24(1) | -12(1) | -13(1) | -3(1) |
| C(15) | 28(1) | 24(1) | 20(1) | -6(1) | -7(1) | -6(1) |
| C(16) | 26(1) | 19(1) | 24(1) | -5(1) | -7(1) | -5(1) |
| O(1) | 22(1) | 35(1) | 34(1) | -19(1) | 4(1) | -10(1) |
| C(1) | 23(1) | 20(1) | 24(1) | -10(1) | -1(1) | -4(1) |
| C(2) | 29(1) | 21(1) | 22(1) | -10(1) | -2(1) | -9(1) |
| F(1) | 34(1) | 30(1) | 34(1) | -21(1) | -5(1) | -5(1) |
| C(3) | 25(1) | 26(1) | 28(1) | -11(1) | -4(1) | -10(1) |
| C(4) | 19(1) | 26(1) | 24(1) | -11(1) | 2(1) | -8(1) |
| C(7) | 23(1) | 25(1) | 24(1) | -10(1) | -3(1) | -3(1) |
| C(8) | 20(1) | 25(1) | 25(1) | -8(1) | -1(1) | -2(1) |
| C(9) | 24(1) | 24(1) | 24(1) | -5(1) | -3(1) | -4(1) |
| C(21) | 21(1) | 22(1) | 31(1) | -9(1) | 0(1) | -4(1) |
| C(22) | 41(1) | 24(1) | 40(1) | -6(1) | 3(1) | -11(1) |
| C(23) | 46(1) | 25(1) | 60(1) | -19(1) | 9(1) | -14(1) |
| C(24) | 37(1) | 40(1) | 48(1) | -29(1) | 13(1) | -16(1) |
| C(25) | 50(1) | 39(1) | 32(1) | -16(1) | 8(1) | -18(1) |
| C(26) | 38(1) | 23(1) | 31(1) | -10(1) | 3(1) | -10(1) |
| C(5) | 21(1) | 22(1) | 19(1) | -8(1) | 1(1) | -6(1) |
| N(101) | 20(1) | 20(1) | 23(1) | -11(1) | -2(1) | -2(1) |
| C(106) | 20(1) | 22(1) | 18(1) | -6(1) | -1(1) | -6(1) |
| C(111) | 16(1) | 21(1) | 23(1) | -8(1) | -4(1) | -4(1) |
| C(112) | 22(1) | 24(1) | 21(1) | -3(1) | -5(1) | -4(1) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C(113) | 23(1) | 18(1) | 30(1) | -2(1) | -7(1) | -3(1) |
| C(114) | 18(1) | 19(1) | 30(1) | -11(1) | -4(1) | -2(1) |
| N(102) | 22(1) | 21(1) | 38(1) | -14(1) | -4(1) | -1(1) |
| O(102) | 37(1) | 18(1) | 48(1) | -9(1) | -2(1) | 0(1) |
| O(103) | 43(1) | 30(1) | 36(1) | -20(1) | -12(1) | 3(1) |
| C(115) | 19(1) | 22(1) | 22(1) | -7(1) | -3(1) | -5(1) |
| C(116) | 19(1) | 16(1) | 22(1) | -4(1) | -5(1) | -3(1) |
| O(101) | 28(1) | 38(1) | 29(1) | -17(1) | -9(1) | -3(1) |
| C(101) | 27(1) | 25(1) | 31(1) | -17(1) | 0(1) | -5(1) |
| C(102) | 25(1) | 18(1) | 24(1) | -9(1) | -1(1) | 2(1) |
| F(101) | 30(1) | 28(1) | 34(1) | -20(1) | 4(1) | -1(1) |
| C(103) | 18(1) | 25(1) | 28(1) | -8(1) | -1(1) | 0(1) |
| C(104) | 18(1) | 23(1) | 25(1) | -11(1) | -6(1) | 0(1) |
| C(107) | 21(1) | 26(1) | 25(1) | -10(1) | -3(1) | -5(1) |
| C(108) | 22(1) | 26(1) | 26(1) | -11(1) | -5(1) | -7(1) |
| C(109) | 23(1) | 25(1) | 24(1) | -9(1) | -3(1) | -8(1) |
| C(121) | 21(1) | 24(1) | 26(1) | -9(1) | 2(1) | -11(1) |
| C(122) | 29(1) | 24(1) | 30(1) | -9(1) | -2(1) | -9(1) |
| C(123) | 33(1) | 24(1) | 42(1) | -15(1) | 4(1) | -10(1) |
| C(124) | 36(1) | 39(1) | 37(1) | -24(1) | 11(1) | -18(1) |
| C(125) | 35(1) | 50(1) | 23(1) | -16(1) | 4(1) | -18(1) |
| C(126) | 26(1) | 32(1) | 25(1) | -10(1) | 2(1) | -9(1) |
| C(105) | 19(1) | 22(1) | 21(1) | -8(1) | -5(1) | -1(1) |

Table 5. Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters ($Å^2$x $10^3$) for V20222.

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(12) | 2983 | 3831 | 9068 | 28 |
| H(13) | 3721 | 2013 | 8153 | 30 |
| H(15) | 3976 | 5175 | 5383 | 28 |
| H(16) | 3167 | 7002 | 6300 | 27 |
| H(1A) | 2196 | 8511 | 9390 | 26 |
| H(1B) | 2774 | 9681 | 8336 | 26 |
| H(3) | 7633 | 7761 | 9385 | 30 |
| H(4) | 8303 | 7213 | 7710 | 27 |
| H(7A) | 8909 | 4989 | 9091 | 29 |
| H(7B) | 6818 | 4893 | 9149 | 29 |
| H(8) | 9351 | 4812 | 7219 | 29 |
| H(9) | 7514 | 2749 | 8499 | 31 |
| H(22) | 8781 | 328 | 8011 | 43 |
| H(23) | 9617 | -927 | 6702 | 52 |
| H(24) | 10097 | 336 | 4946 | 47 |
| H(25) | 9849 | 2879 | 4489 | 47 |
| H(26) | 9062 | 4148 | 5790 | 37 |
| H(5A) | 5579 | 8371 | 7041 | 25 |
| H(5B) | 5790 | 6657 | 7167 | 25 |
| H(112) | 2856 | 6224 | 759 | 28 |
| H(113) | 1264 | 8098 | 1631 | 30 |
| H(115) | 1806 | 4984 | 4436 | 25 |
| H(116) | 3445 | 3128 | 3554 | 23 |
| H(10A) | 6528 | 1507 | 541 | 32 |
| H(10B) | 7167 | 328 | 1613 | 32 |
| H(103) | 11311 | 2087 | 736 | 30 |
| H(104) | 9959 | 2673 | 2390 | 27 |
| H(10C) | 9858 | 4866 | 936 | 28 |
| H(10D) | 7700 | 5008 | 912 | 28 |
| H(108) | 8792 | 5214 | 2740 | 28 |

| | | | | |
|---|---|---|---|---|
| H(109) | 5810 | 6996 | 1630 | 27 |
| H(122) | 3946 | 9282 | 2095 | 33 |
| H(123) | 2904 | 10799 | 3251 | 39 |
| H(124) | 4241 | 10083 | 4791 | 42 |
| H(125) | 6560 | 7800 | 5196 | 41 |
| H(126) | 7530 | 6236 | 4081 | 33 |
| H(10E) | 7606 | 1574 | 2973 | 25 |
| H(10F) | 6476 | 3304 | 2832 | 25 |

Table 6. Torsion angles [°] for V20222.

| | |
|---|---|
| C(1)-N(1)-C(6)-O(1) | -2.3(2) |
| C(5)-N(1)-C(6)-O(1) | 174.18(16) |
| C(1)-N(1)-C(6)-C(11) | 177.95(14) |
| C(5)-N(1)-C(6)-C(11) | -5.6(2) |
| O(1)-C(6)-C(11)-C(12) | -54.8(2) |
| N(1)-C(6)-C(11)-C(12) | 124.94(17) |
| O(1)-C(6)-C(11)-C(16) | 122.02(18) |
| N(1)-C(6)-C(11)-C(16) | -58.2(2) |
| C(16)-C(11)-C(12)-C(13) | 2.2(3) |
| C(6)-C(11)-C(12)-C(13) | 179.10(15) |
| C(11)-C(12)-C(13)-C(14) | -0.2(3) |
| C(12)-C(13)-C(14)-C(15) | -1.1(3) |
| C(12)-C(13)-C(14)-N(2) | 178.69(16) |
| C(13)-C(14)-N(2)-O(2) | 8.7(2) |
| C(15)-C(14)-N(2)-O(2) | -171.54(18) |
| C(13)-C(14)-N(2)-O(3) | -172.07(17) |
| C(15)-C(14)-N(2)-O(3) | 7.7(2) |
| C(13)-C(14)-C(15)-C(16) | 0.3(3) |
| N(2)-C(14)-C(15)-C(16) | -179.48(15) |
| C(14)-C(15)-C(16)-C(11) | 1.7(2) |
| C(12)-C(11)-C(16)-C(15) | -3.0(2) |
| C(6)-C(11)-C(16)-C(15) | -179.77(15) |
| C(6)-N(1)-C(1)-C(2) | 134.31(15) |
| C(5)-N(1)-C(1)-C(2) | -42.60(17) |
| N(1)-C(1)-C(2)-C(3) | 9.7(2) |
| N(1)-C(1)-C(2)-F(1) | -170.11(13) |
| F(1)-C(2)-C(3)-C(4) | -175.73(14) |
| C(1)-C(2)-C(3)-C(4) | 4.5(3) |
| C(2)-C(3)-C(4)-C(5) | 12.6(2) |
| C(2)-C(3)-C(4)-C(7) | -114.69(19) |
| C(3)-C(4)-C(7)-C(8) | -173.93(14) |
| C(5)-C(4)-C(7)-C(8) | 60.10(18) |
| C(4)-C(7)-C(8)-C(9) | -138.02(18) |
| C(7)-C(8)-C(9)-C(21) | 177.01(16) |

| | |
|---|---|
| C(8)-C(9)-C(21)-C(26) | -26.6(3) |
| C(8)-C(9)-C(21)-C(22) | 155.9(2) |
| C(26)-C(21)-C(22)-C(23) | -0.2(3) |
| C(9)-C(21)-C(22)-C(23) | 177.45(19) |
| C(21)-C(22)-C(23)-C(24) | -0.8(3) |
| C(22)-C(23)-C(24)-C(25) | 1.2(4) |
| C(23)-C(24)-C(25)-C(26) | -0.6(4) |
| C(24)-C(25)-C(26)-C(21) | -0.3(3) |
| C(22)-C(21)-C(26)-C(25) | 0.7(3) |
| C(9)-C(21)-C(26)-C(25) | -176.85(19) |
| C(6)-N(1)-C(5)-C(4) | -114.51(17) |
| C(1)-N(1)-C(5)-C(4) | 62.08(17) |
| C(3)-C(4)-C(5)-N(1) | -43.69(18) |
| C(7)-C(4)-C(5)-N(1) | 83.57(16) |
| C(101)-N(101)-C(106)-O(101) | -1.3(2) |
| C(105)-N(101)-C(106)-O(101) | 173.15(16) |
| C(101)-N(101)-C(106)-C(111) | 178.58(14) |
| C(105)-N(101)-C(106)-C(111) | -6.9(2) |
| O(101)-C(106)-C(111)-C(116) | 126.28(18) |
| N(101)-C(106)-C(111)-C(116) | -53.6(2) |
| O(101)-C(106)-C(111)-C(112) | -50.4(2) |
| N(101)-C(106)-C(111)-C(112) | 129.66(16) |
| C(116)-C(111)-C(112)-C(113) | 4.6(2) |
| C(106)-C(111)-C(112)-C(113) | -178.61(15) |
| C(111)-C(112)-C(113)-C(114) | -1.1(2) |
| C(112)-C(113)-C(114)-C(115) | -3.1(3) |
| C(112)-C(113)-C(114)-N(102) | 175.88(15) |
| C(115)-C(114)-N(102)-O(102) | -175.07(16) |
| C(113)-C(114)-N(102)-O(102) | 5.9(2) |
| C(115)-C(114)-N(102)-O(103) | 5.5(2) |
| C(113)-C(114)-N(102)-O(103) | -173.51(16) |
| C(113)-C(114)-C(115)-C(116) | 3.7(2) |
| N(102)-C(114)-C(115)-C(116) | -175.26(14) |
| C(114)-C(115)-C(116)-C(111) | -0.1(2) |
| C(112)-C(111)-C(116)-C(115) | -4.0(2) |
| C(106)-C(111)-C(116)-C(115) | 179.39(15) |

| | |
|---|---|
| C(106)-N(101)-C(101)-C(102) | 131.28(16) |
| C(105)-N(101)-C(101)-C(102) | -43.96(19) |
| N(101)-C(101)-C(102)-C(103) | 12.3(3) |
| N(101)-C(101)-C(102)-F(101) | -168.29(13) |
| F(101)-C(102)-C(103)-C(104) | -177.36(14) |
| C(101)-C(102)-C(103)-C(104) | 2.0(3) |
| C(102)-C(103)-C(104)-C(105) | 13.8(2) |
| C(102)-C(103)-C(104)-C(107) | -111.81(19) |
| C(103)-C(104)-C(107)-C(108) | -169.49(14) |
| C(105)-C(104)-C(107)-C(108) | 65.58(18) |
| C(104)-C(107)-C(108)-C(109) | -129.96(18) |
| C(107)-C(108)-C(109)-C(121) | -178.94(16) |
| C(108)-C(109)-C(121)-C(126) | -11.1(3) |
| C(108)-C(109)-C(121)-C(122) | 167.76(18) |
| C(126)-C(121)-C(122)-C(123) | 1.2(2) |
| C(109)-C(121)-C(122)-C(123) | -177.79(16) |
| C(121)-C(122)-C(123)-C(124) | 0.7(3) |
| C(122)-C(123)-C(124)-C(125) | -1.3(3) |
| C(123)-C(124)-C(125)-C(126) | 0.0(3) |
| C(124)-C(125)-C(126)-C(121) | 1.9(3) |
| C(122)-C(121)-C(126)-C(125) | -2.4(3) |
| C(109)-C(121)-C(126)-C(125) | 176.48(16) |
| C(106)-N(101)-C(105)-C(104) | -112.83(18) |
| C(101)-N(101)-C(105)-C(104) | 61.85(18) |
| C(103)-C(104)-C(105)-N(101) | -43.68(18) |
| C(107)-C(104)-C(105)-N(101) | 81.51(17) |

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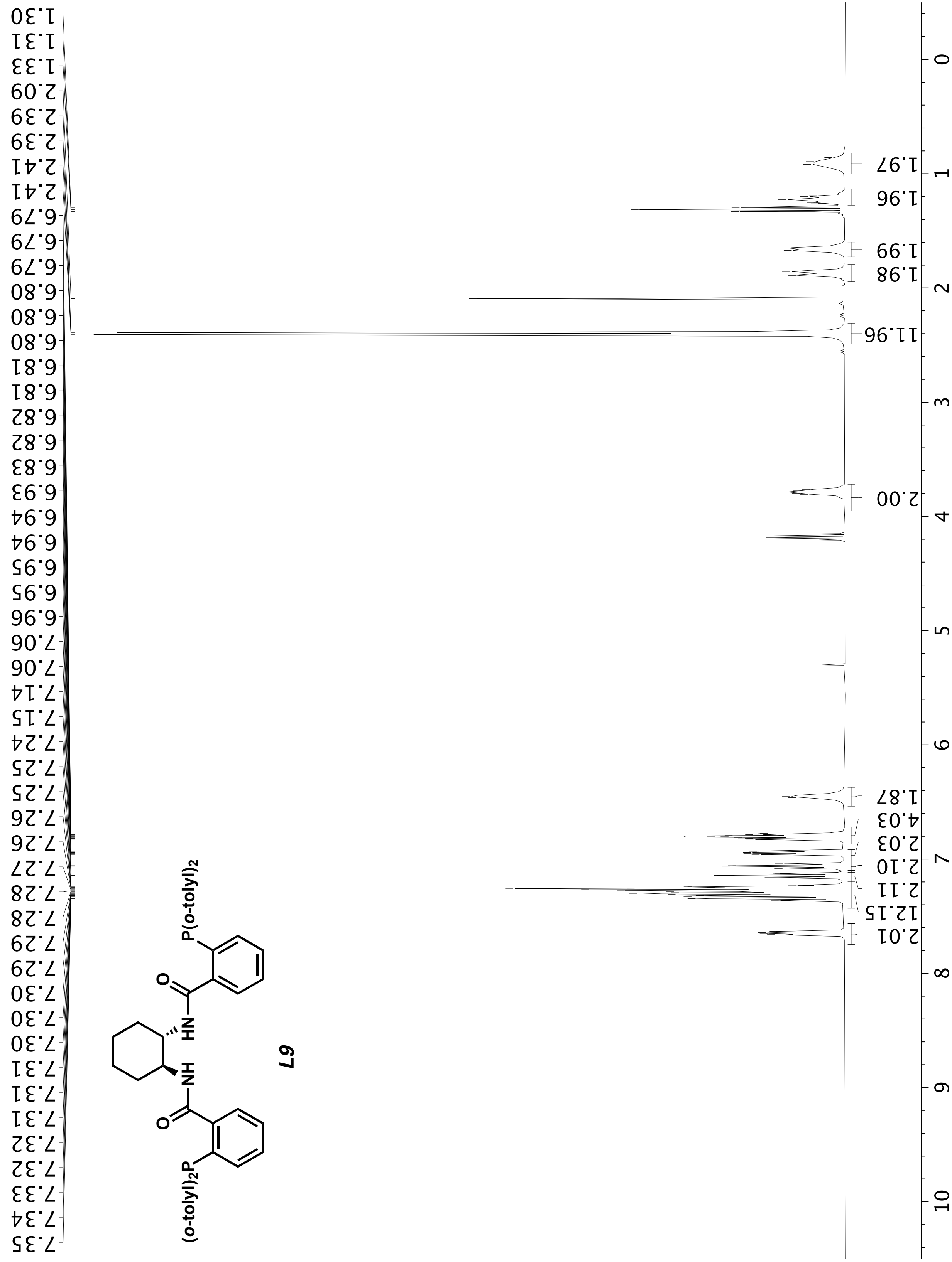
Symmetry transformations used to generate equivalent atoms:

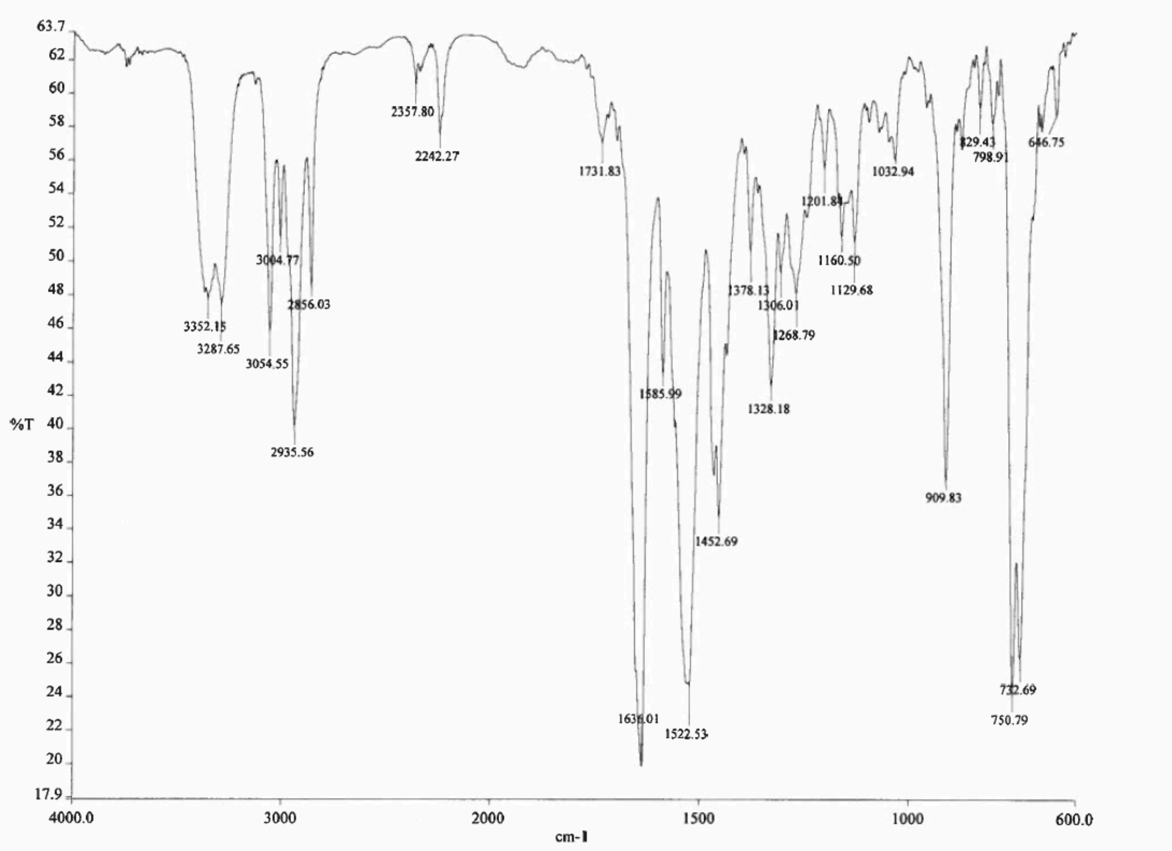
## Abbreviations

| | |
|---|---|
| DMAP | 4-Dimethylaminopyridine |
| EDC*HCl | 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride salt |
| EtOAc | Ethyl acetate |
| Tol | Toluene |
| KOtBu | Potassium *tert*-butoxide |
| SPhos | Dicyclohexyl(2′,6′-dimethoxy[1,1′-biphenyl]-2-yl)phosphane |
| DIBAL | Diisobutylaluminium hydride |
| coe | cyclooctene |

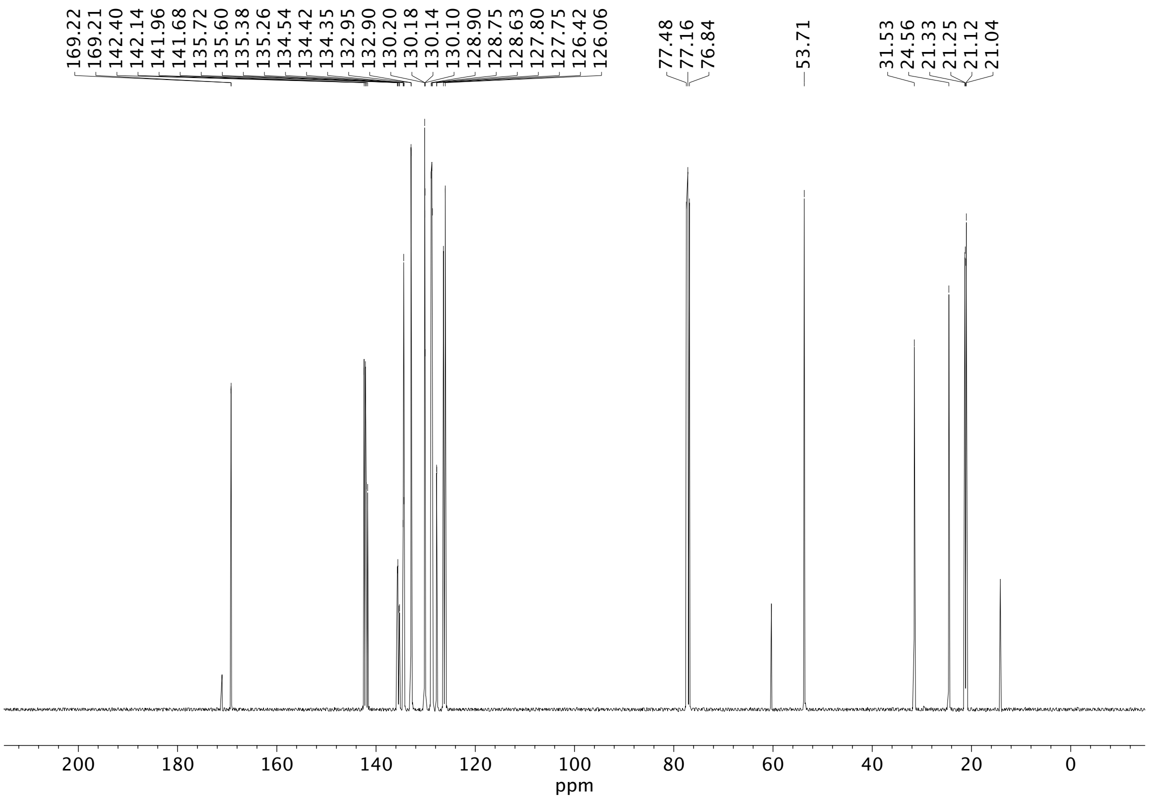
## NMR and IR Spectra of New Compounds



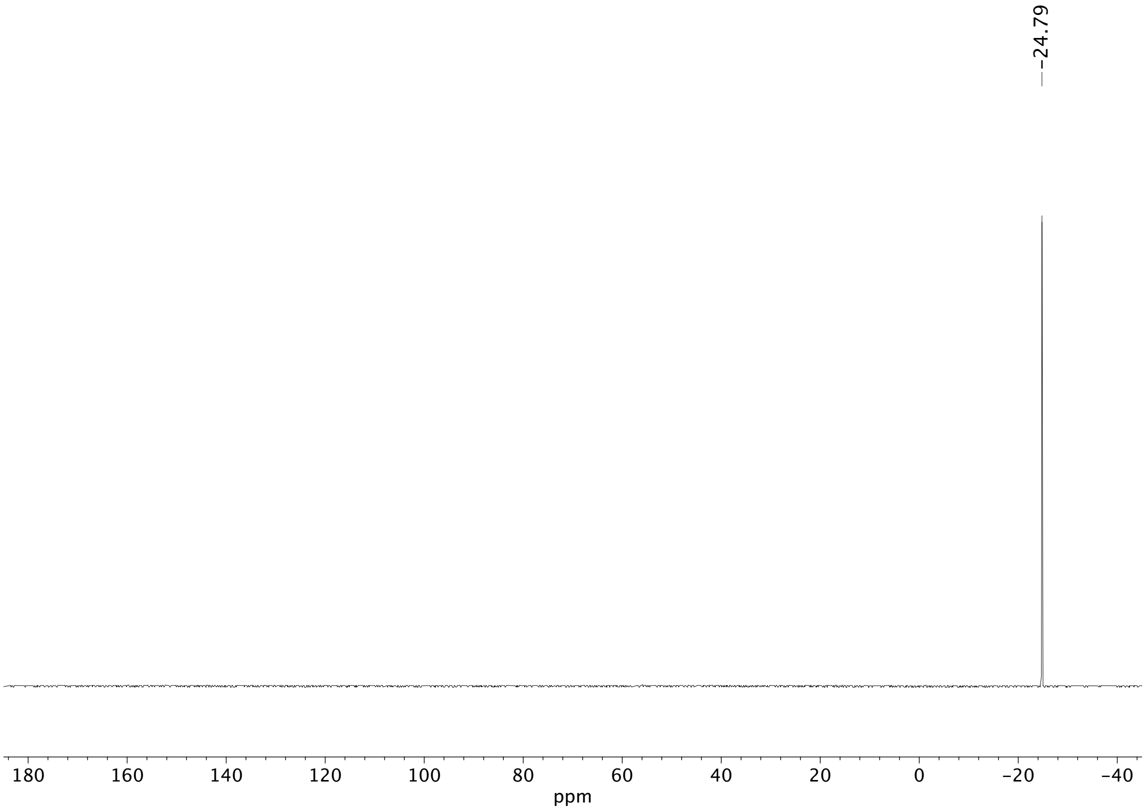
$^1$H NMR (400 MHz, CDCl$_3$) of compound **L9.**



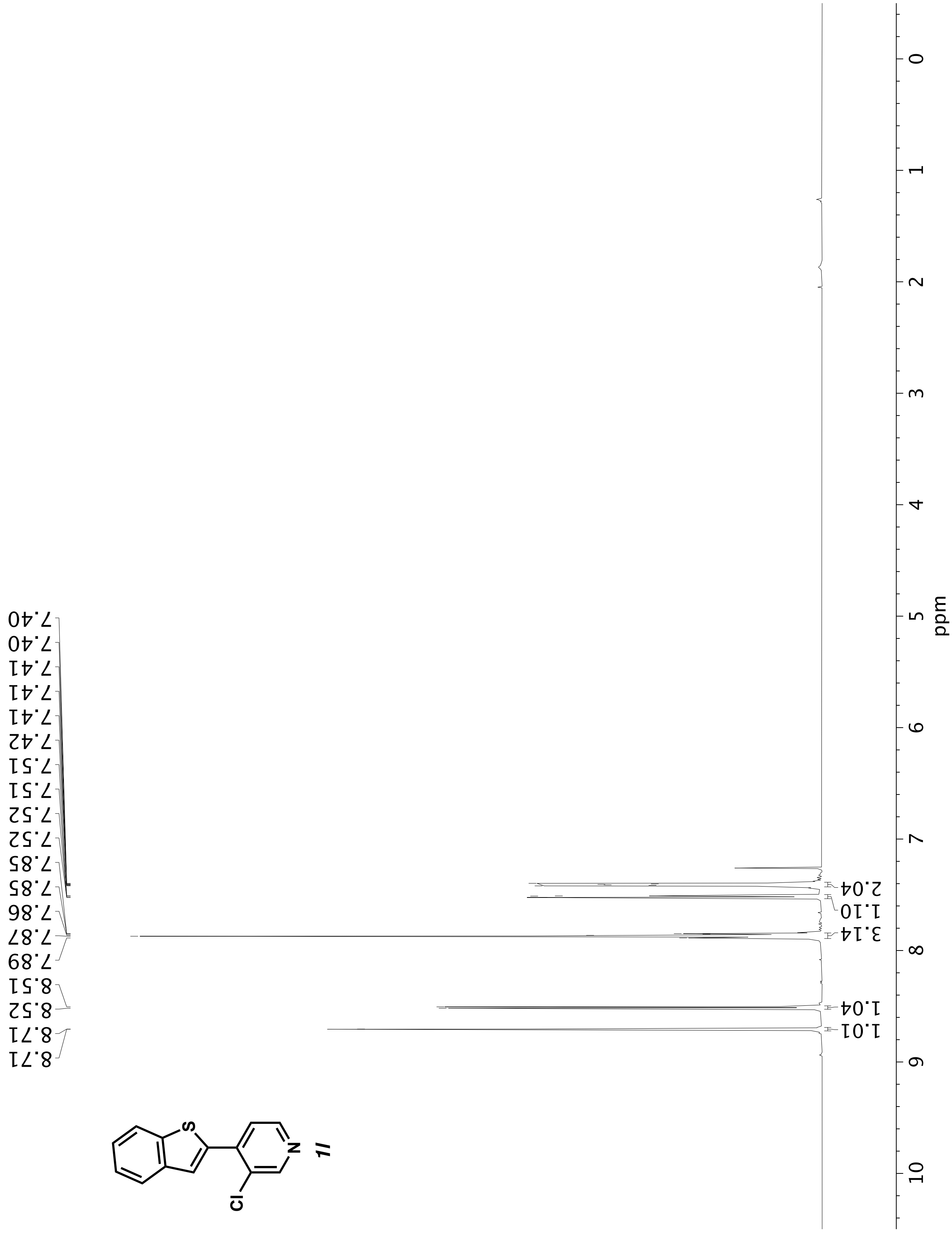
Infrared spectrum (Thin Film, NaCl) of compound **L9**.



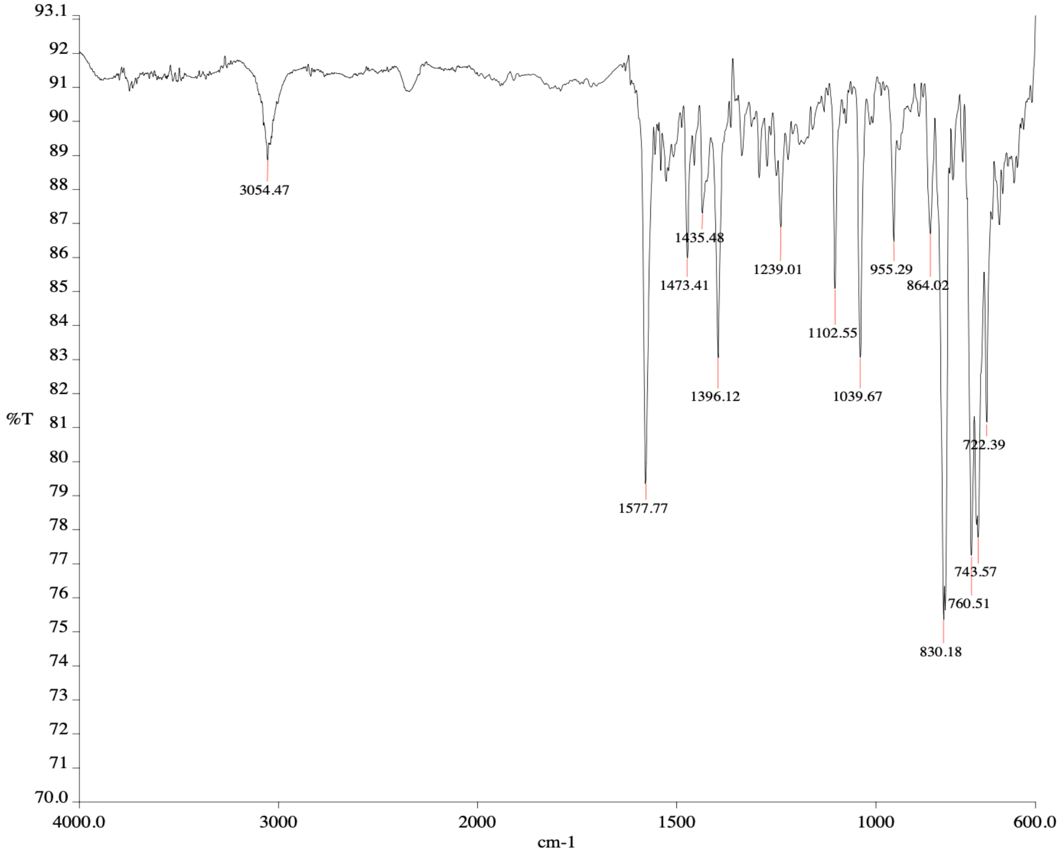
$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **L9**.



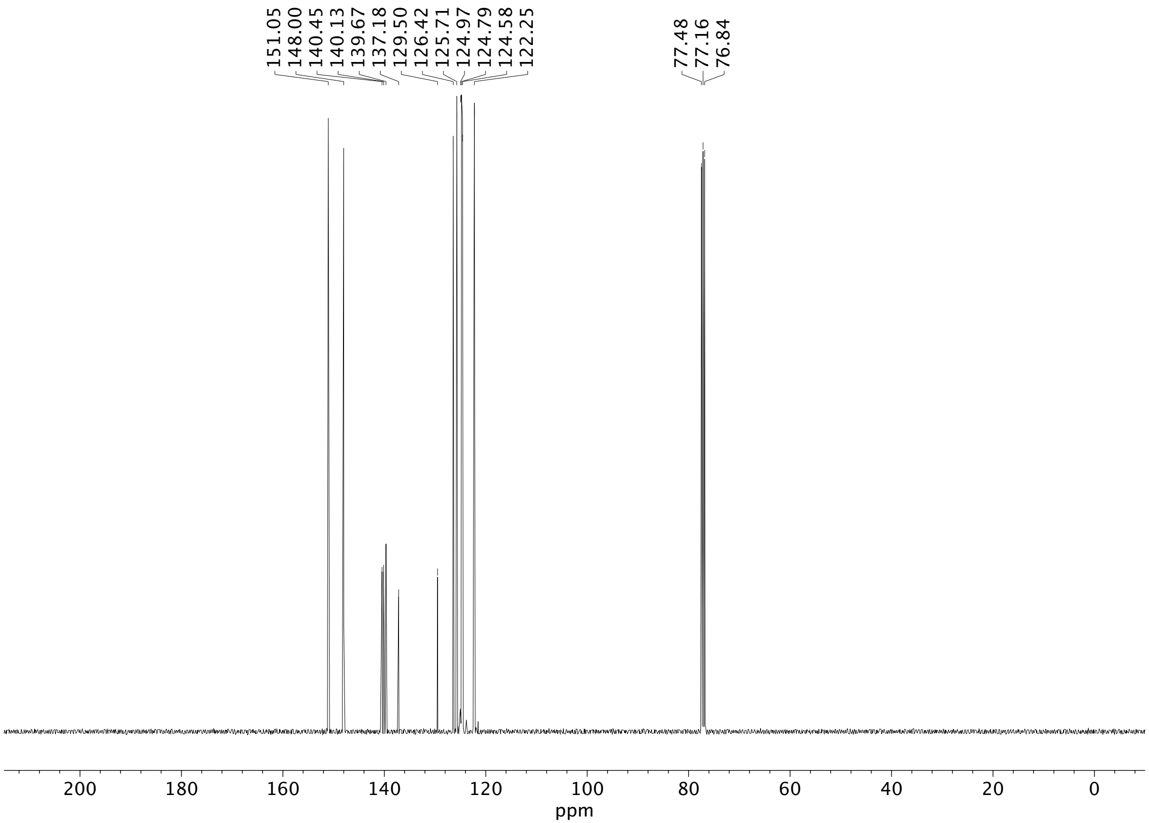
$^{31}$P NMR (121 MHz, CDCl$_3$) of compound **L9**.



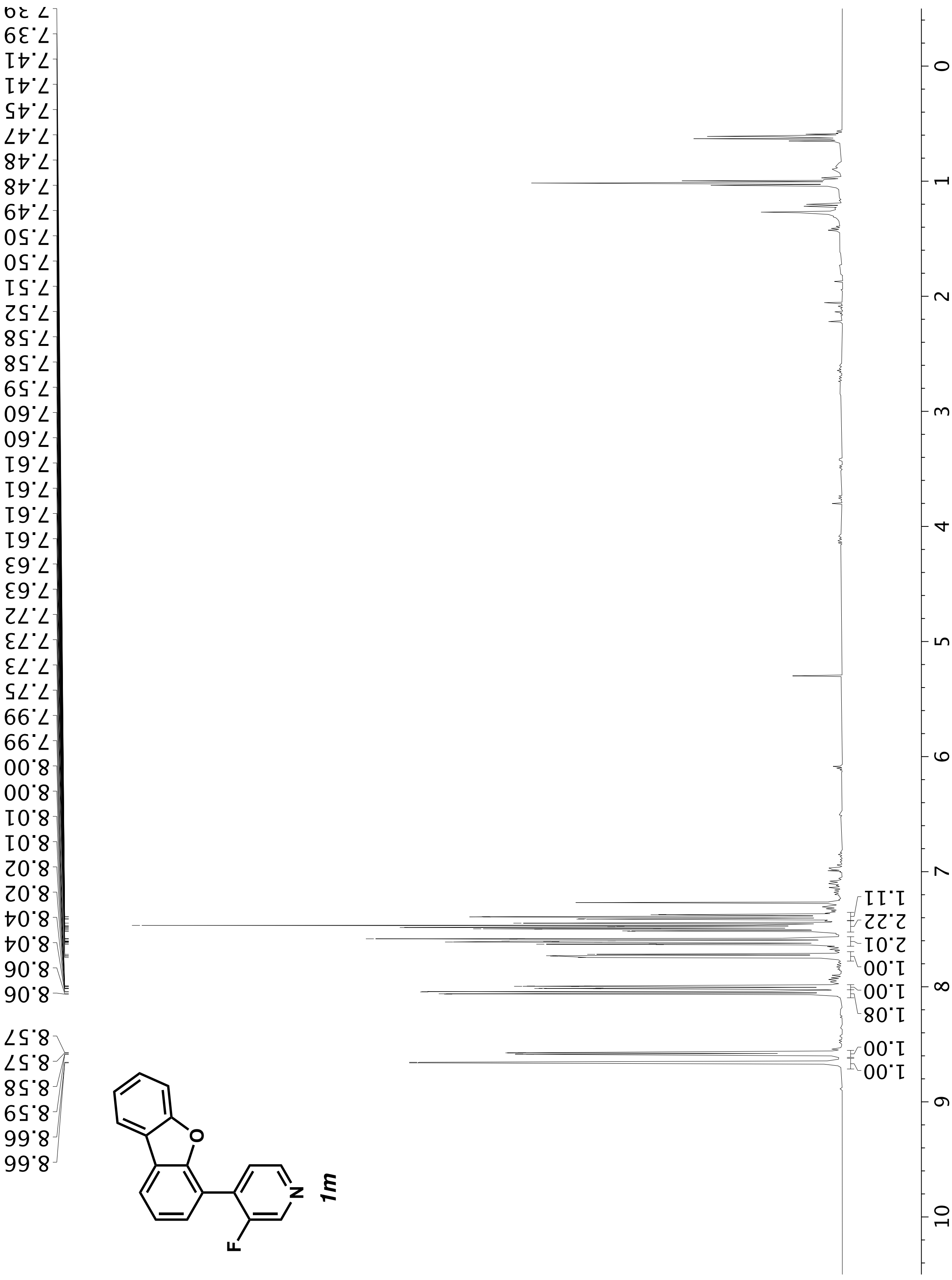
$^1$H NMR (400 MHz, $CDCl_3$) of compound **1l**.



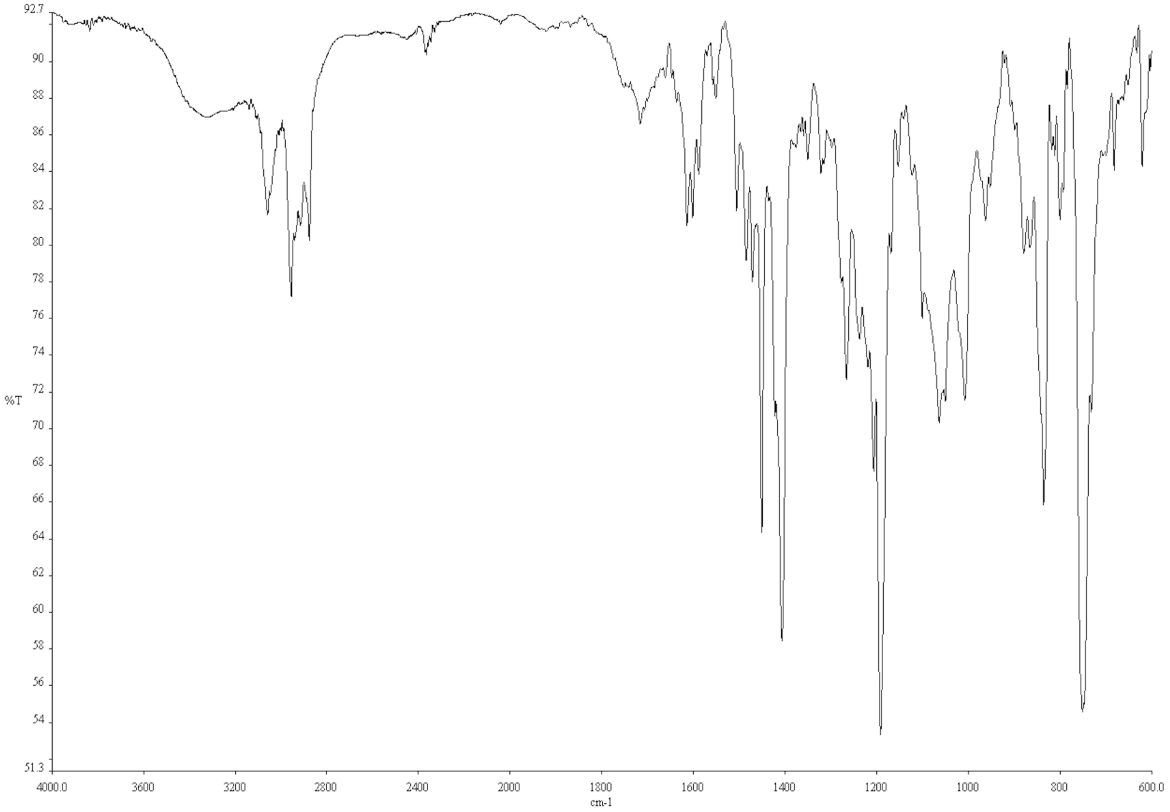
Infrared spectrum (Thin Film, NaCl) of compound **1l**.



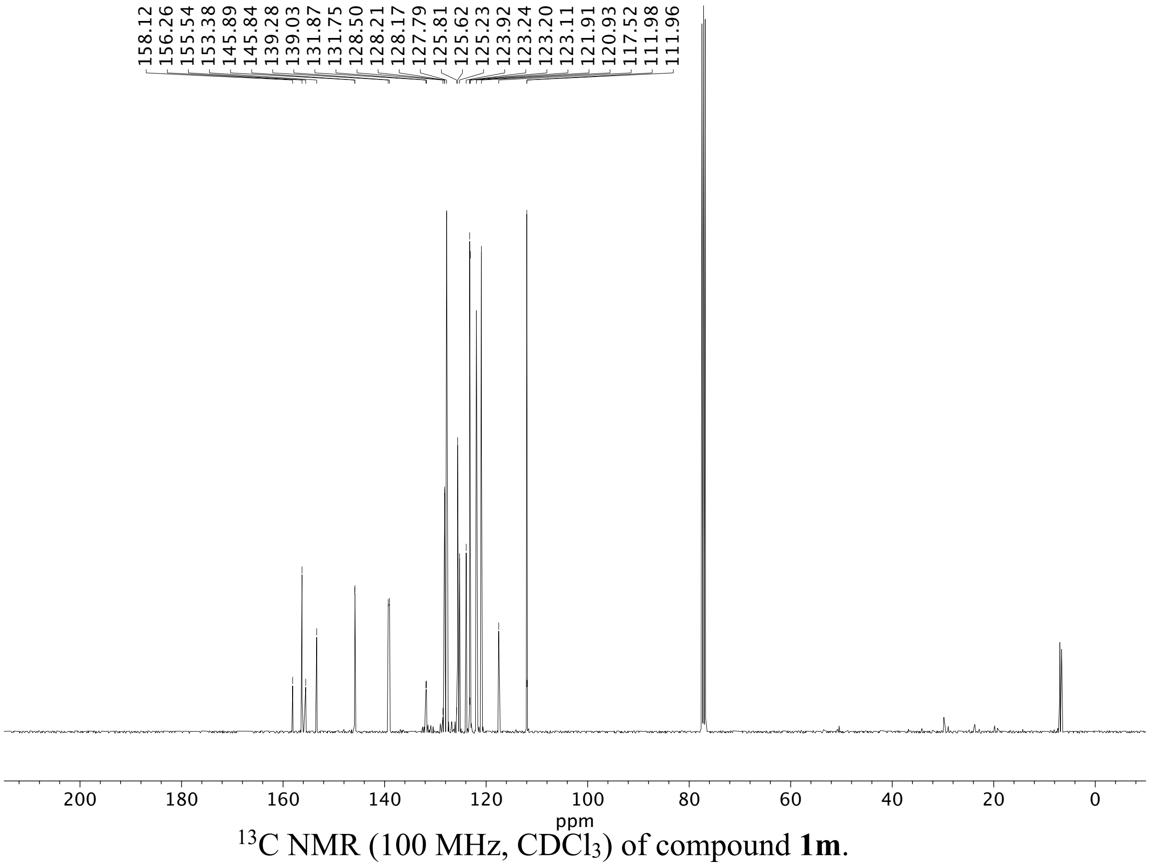
$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **1l**.



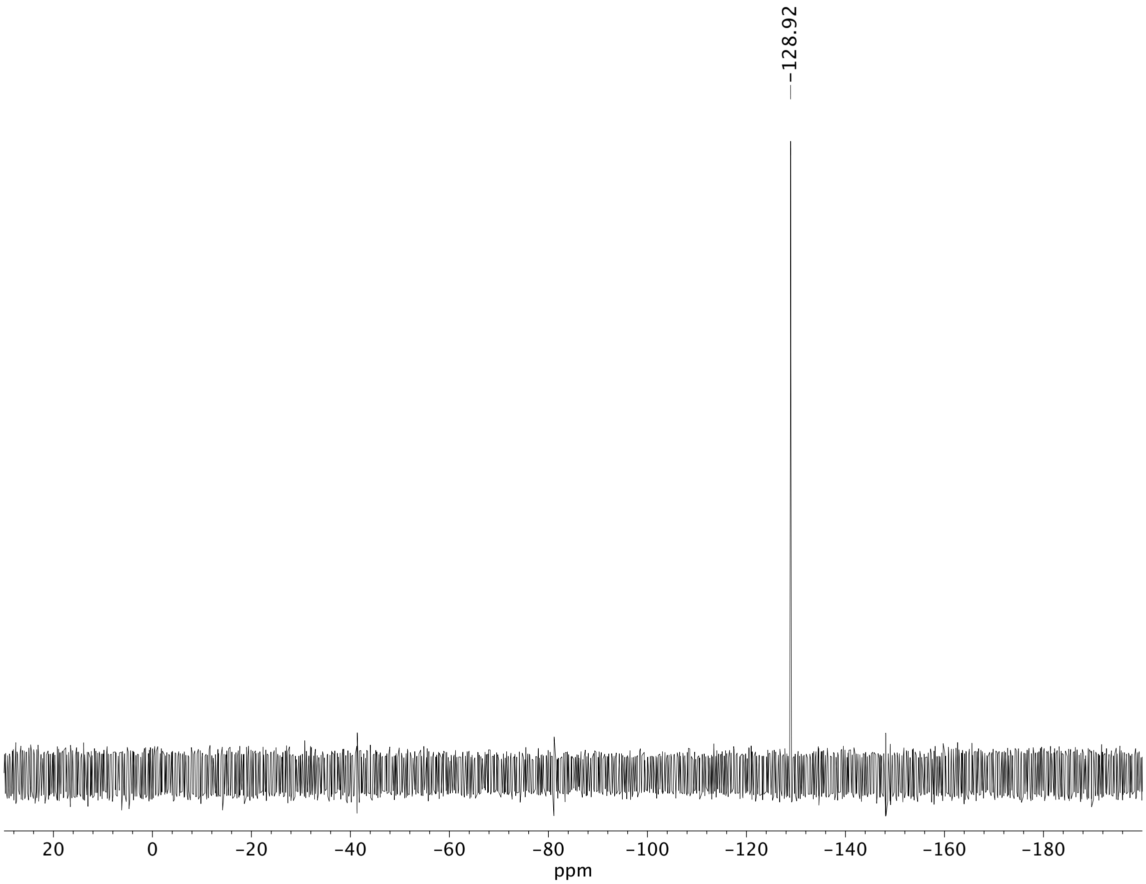
$^1$H NMR (400 MHz, CDCl$_3$) of compound **1m**.



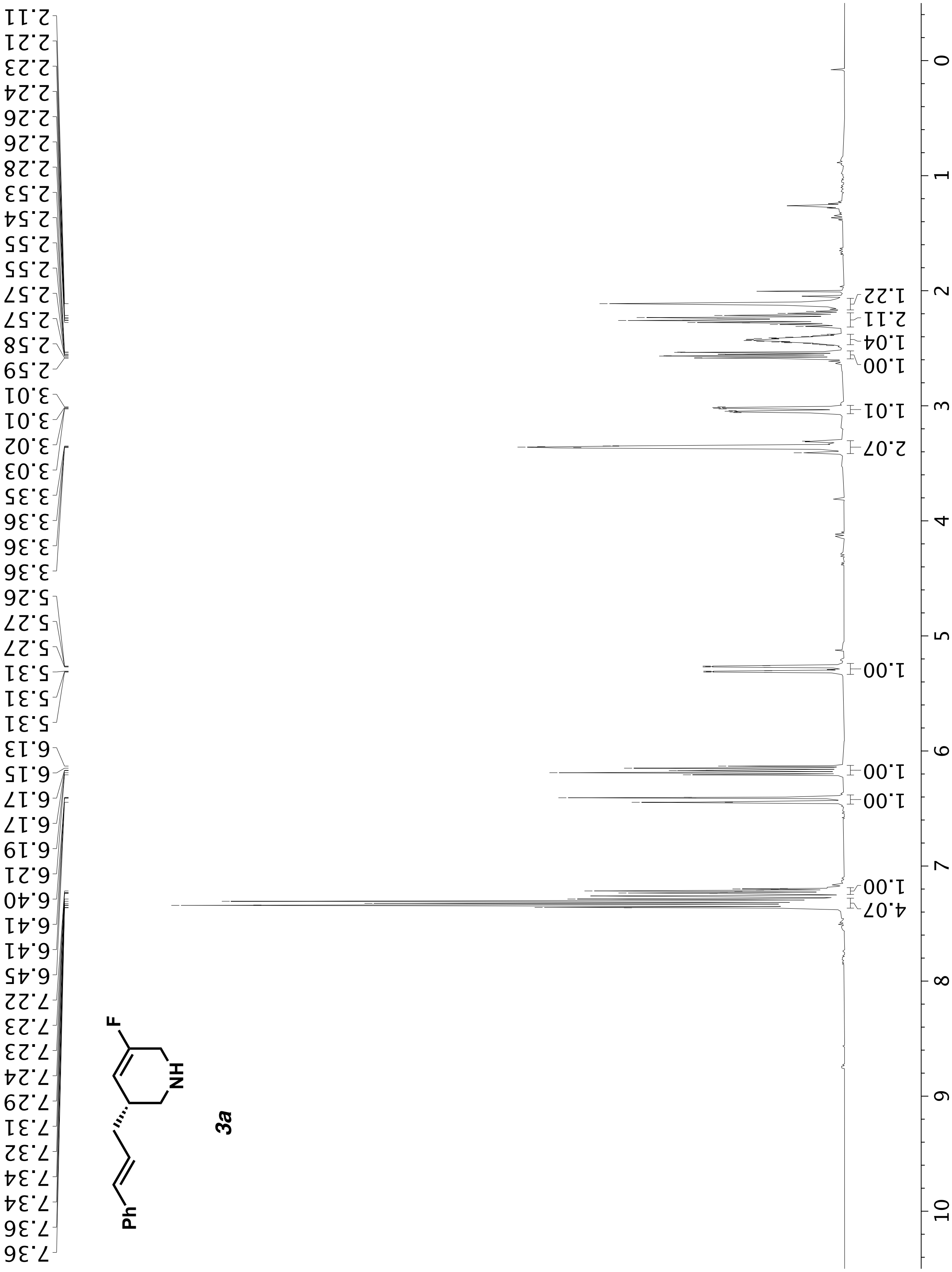
Infrared spectrum (Thin Film, NaCl) of compound **1m**.



$^{13}$C NMR (100 MHz, $CDCl_3$) of compound **1m**.

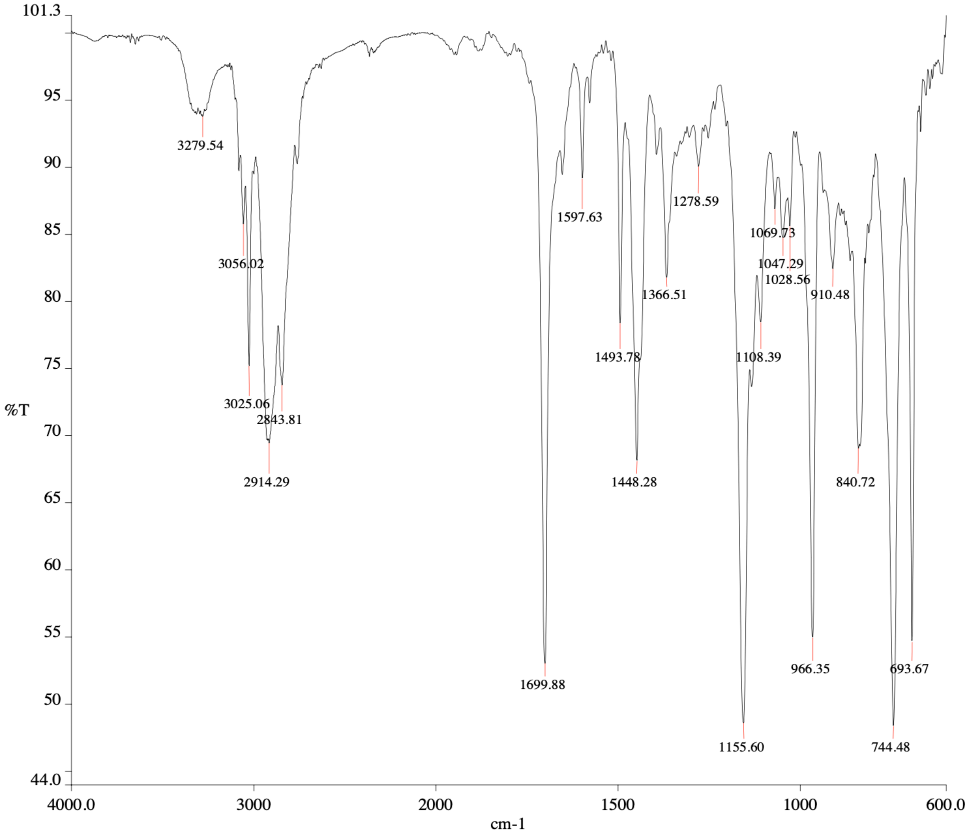


$^{19}$F NMR (282 MHz, $CDCl_3$) of compound **1m**.

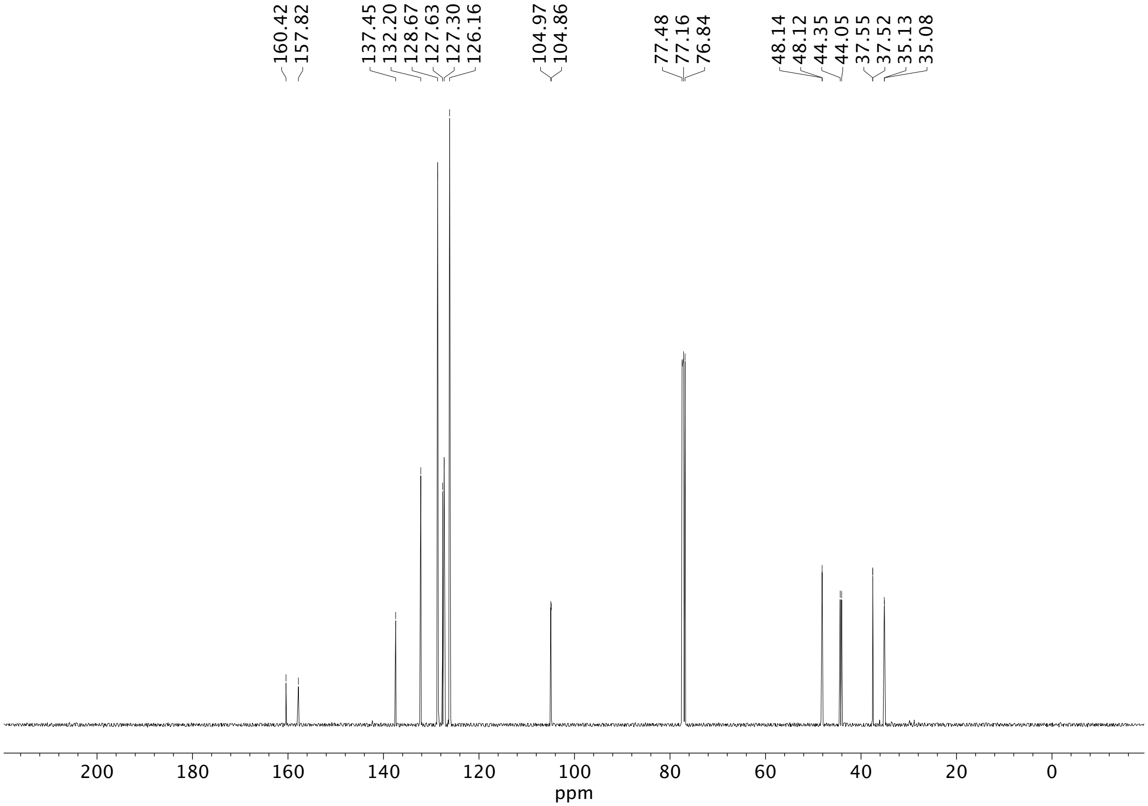


**3a**

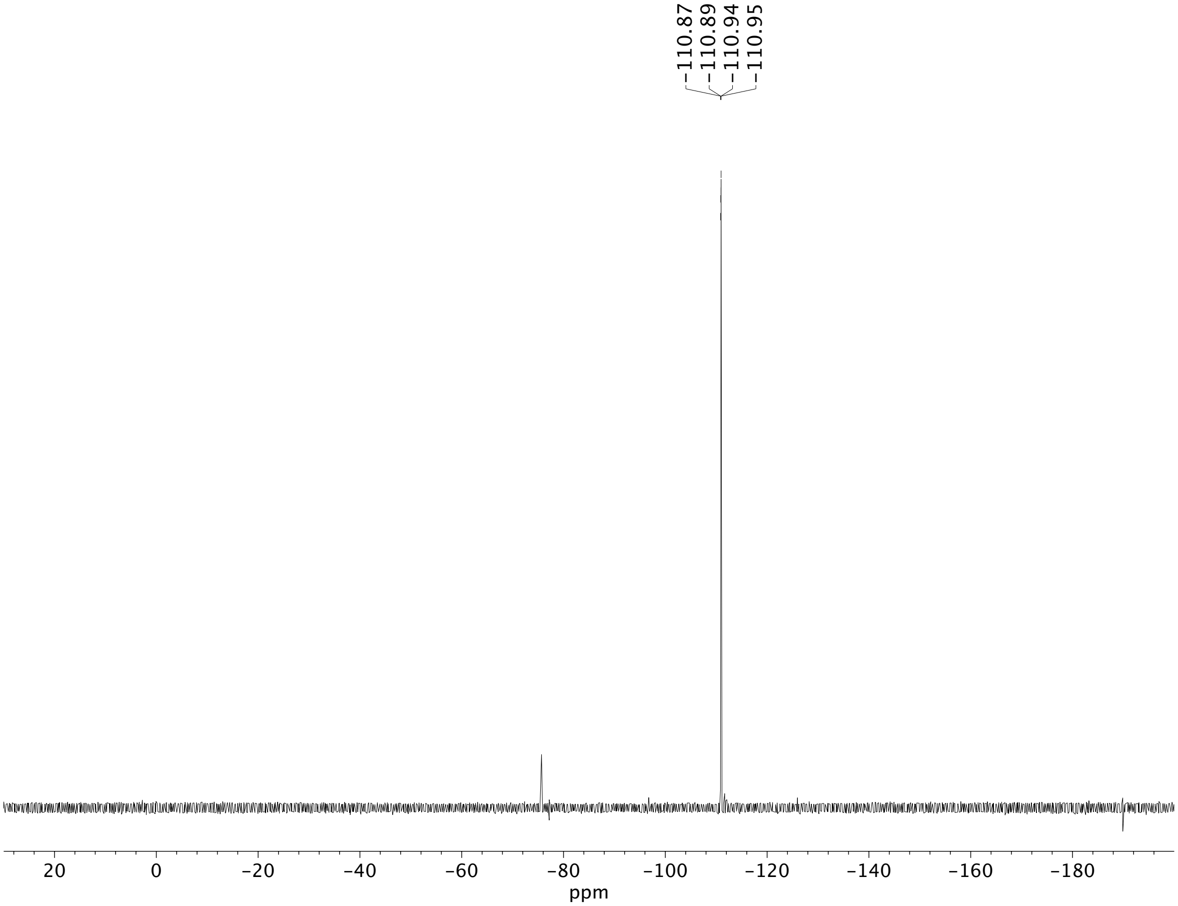
$^1$H NMR (400 MHz, CDCl$_3$) of compound **3a**.



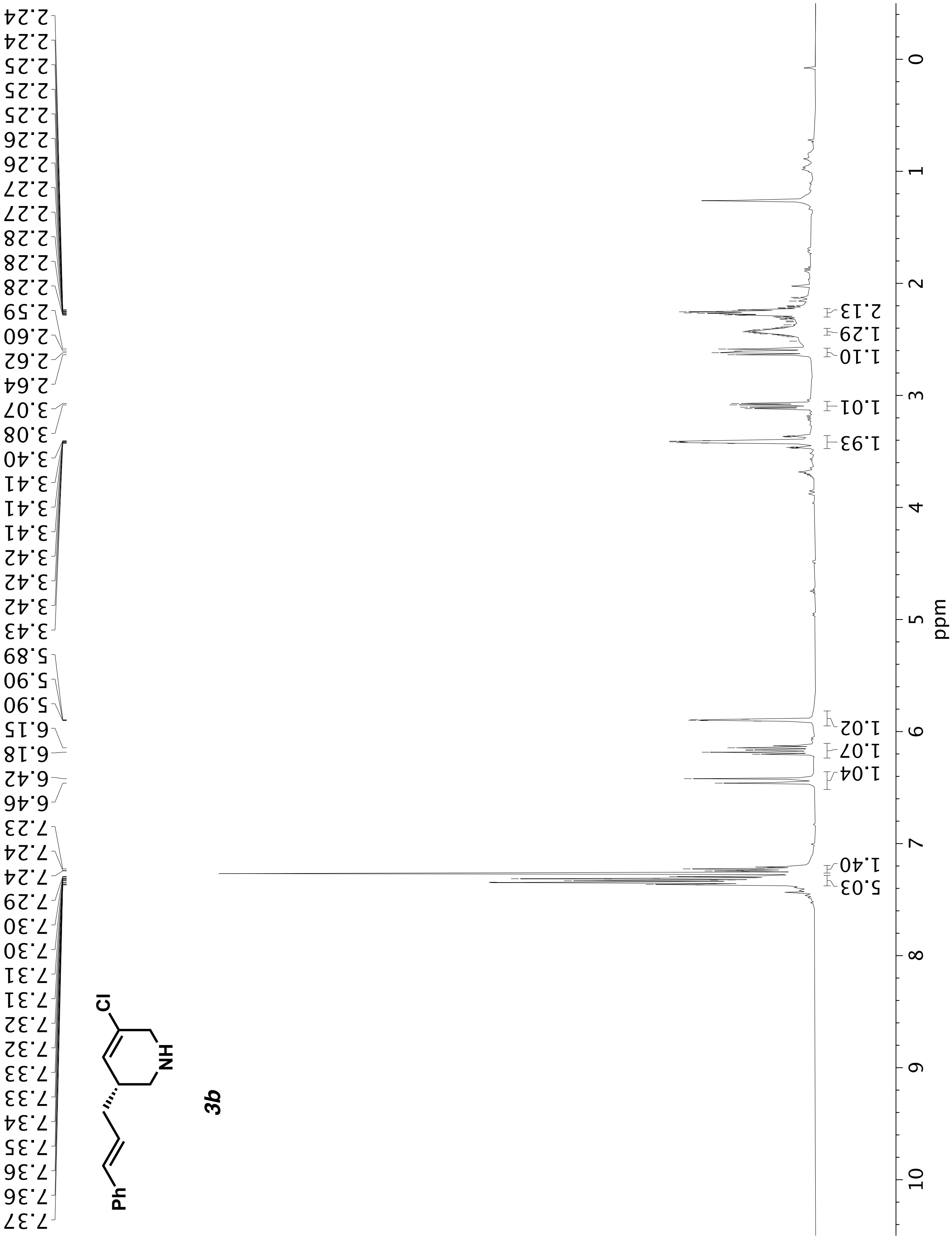
Infrared spectrum (Thin Film, NaCl) of compound **3a**.



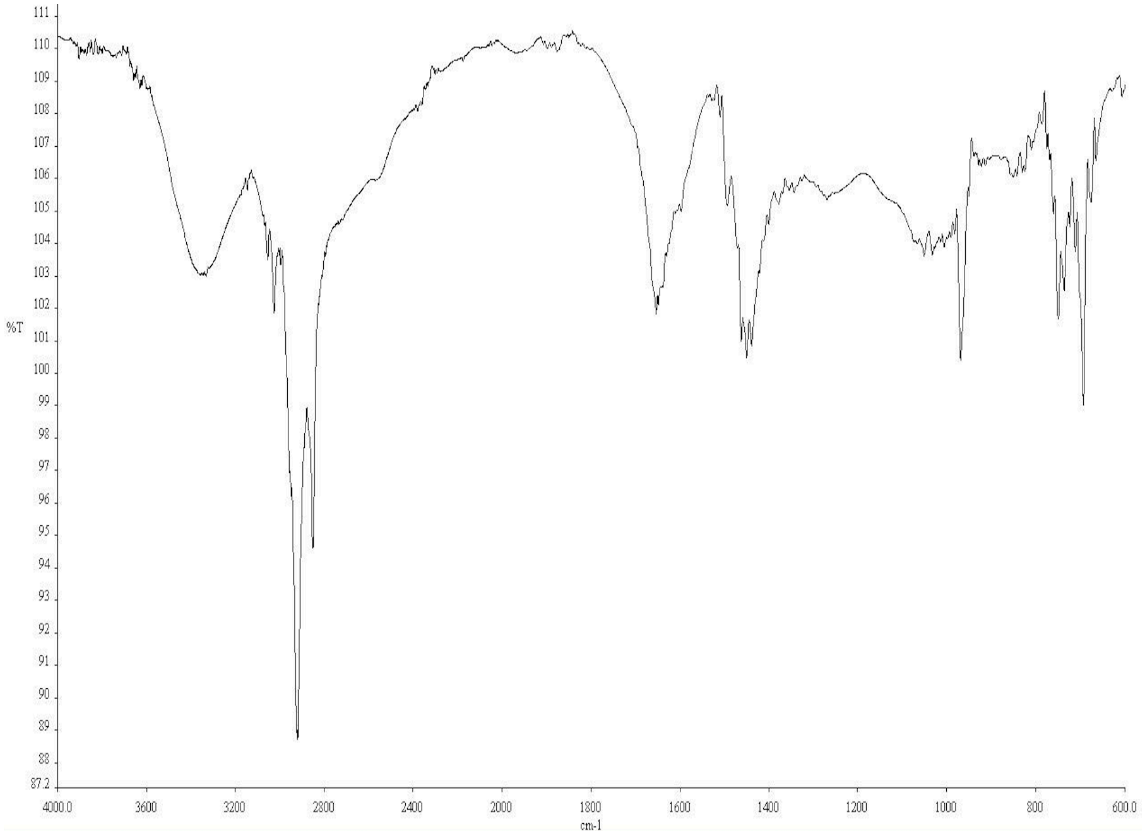
$^{13}C$ NMR (100 MHz, $CDCl_3$) of compound **3a**.



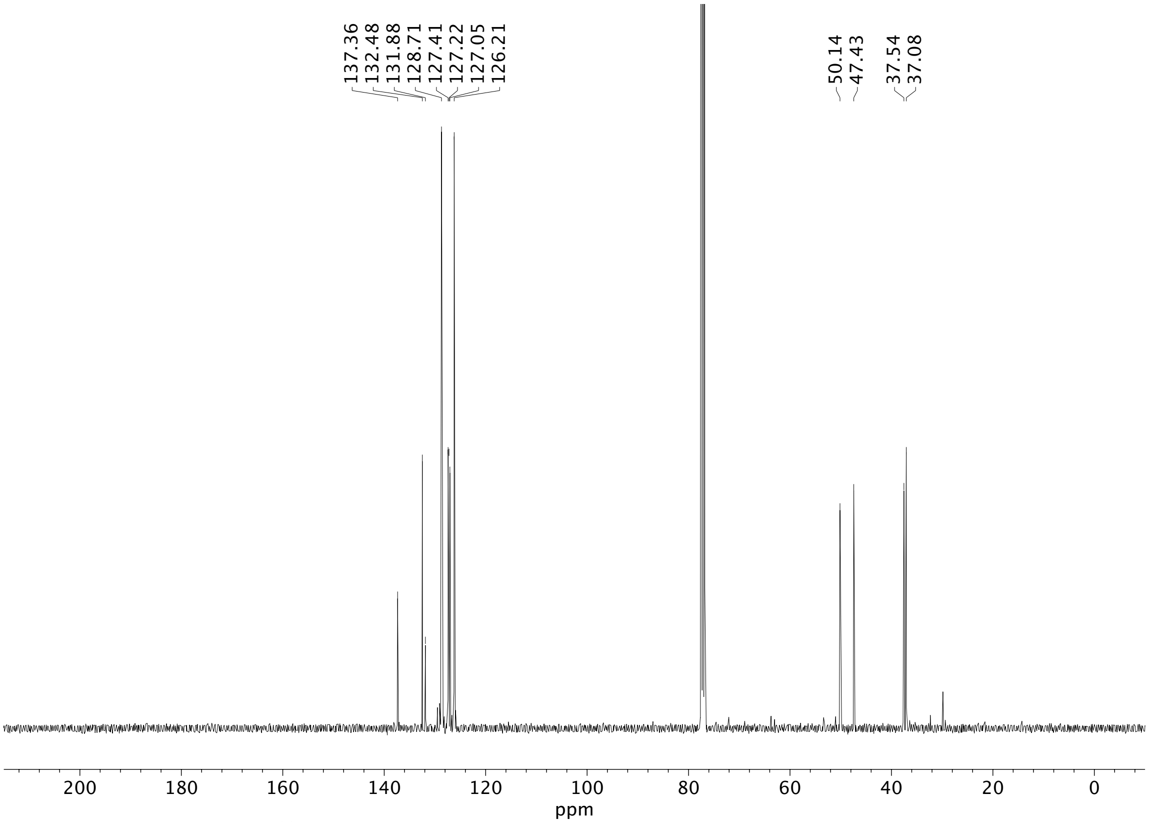
$^{19}$F NMR (282 MHz, CDCl$_3$) of compound **3a.**



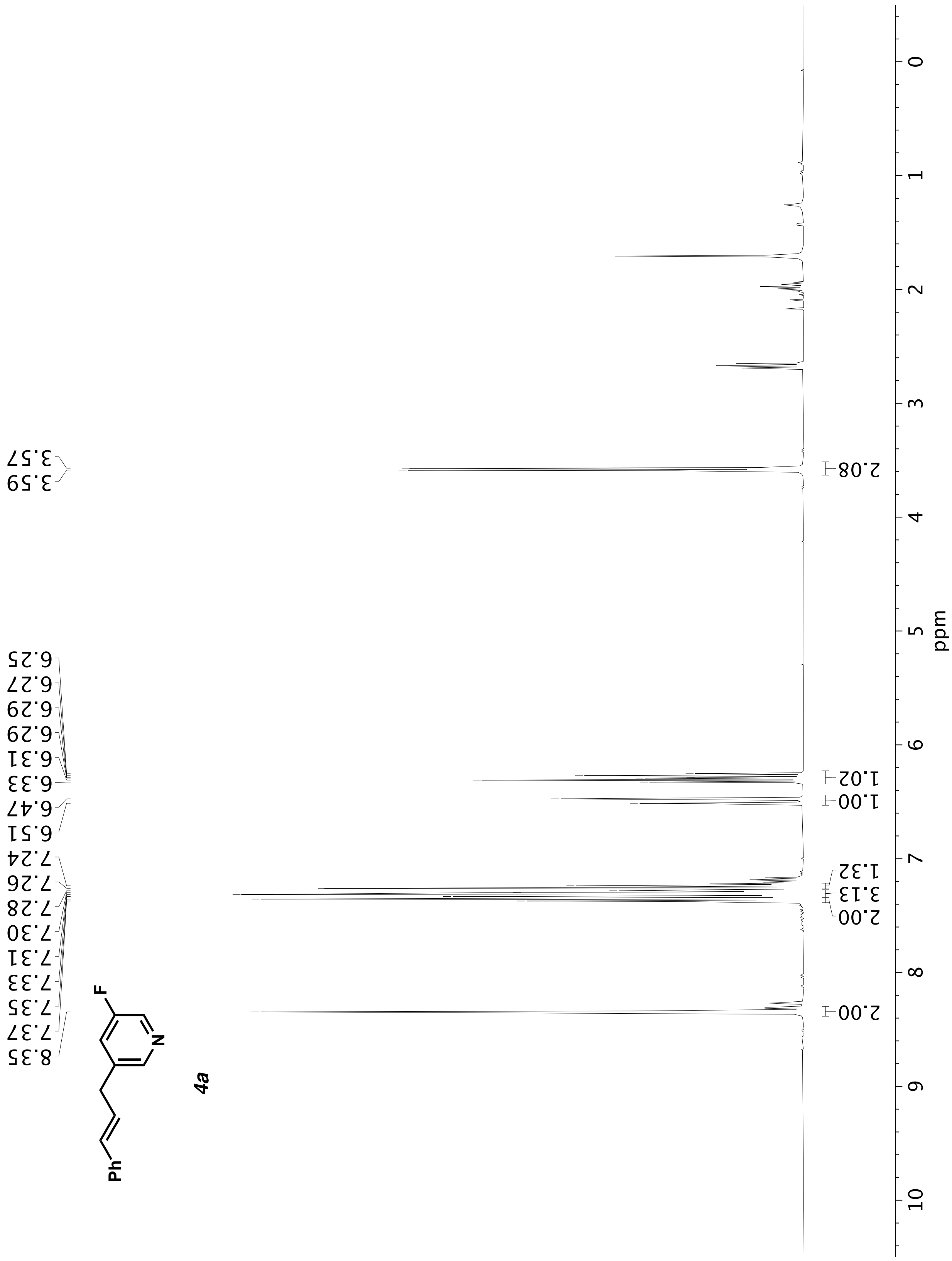
$^1$H NMR (400 MHz, CDCl$_3$) of compound **3b**.



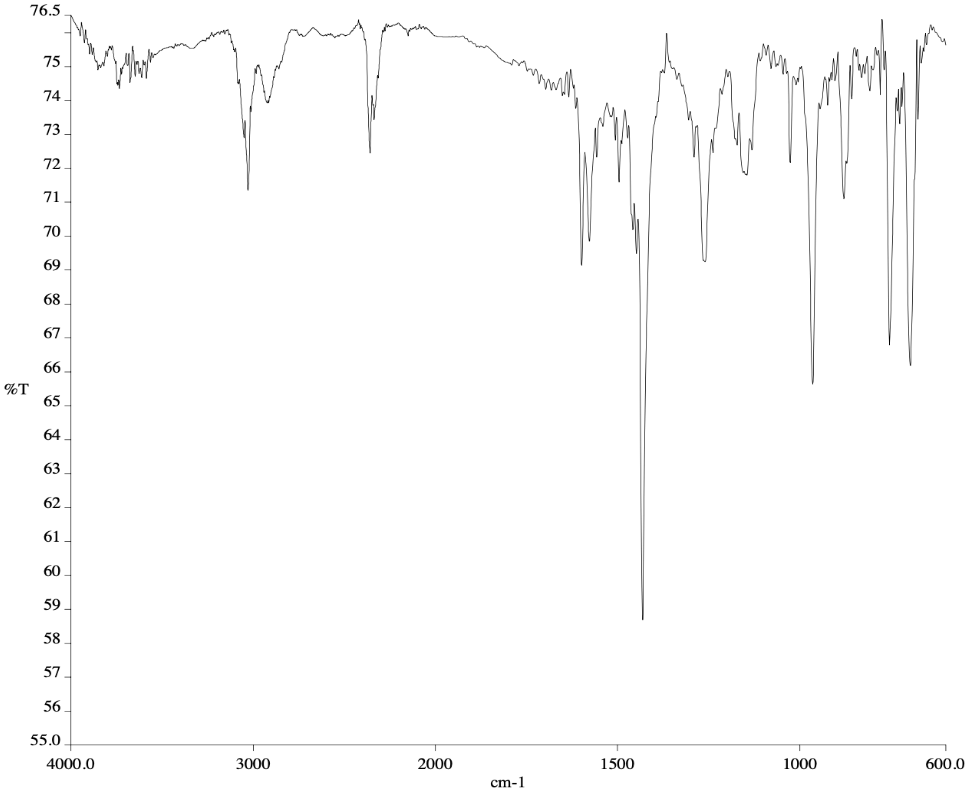
Infrared spectrum (Thin Film, NaCl) of compound **3b**.



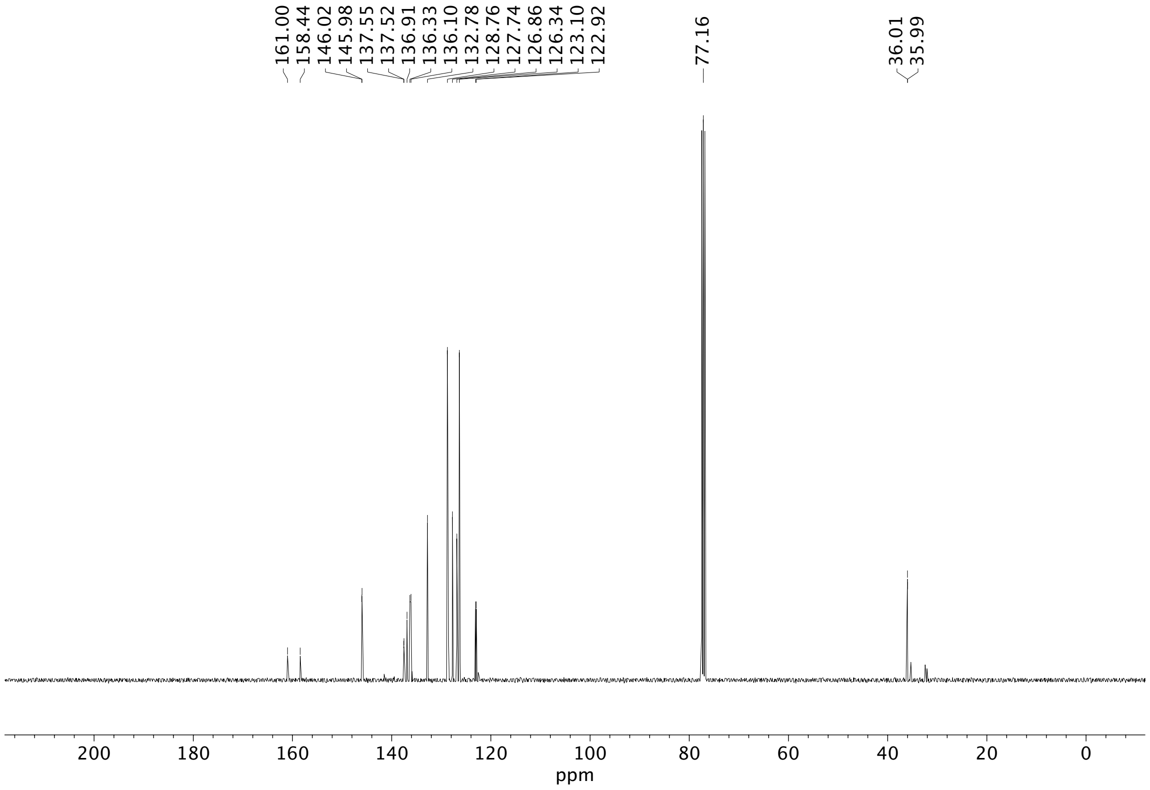
$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **3b**.



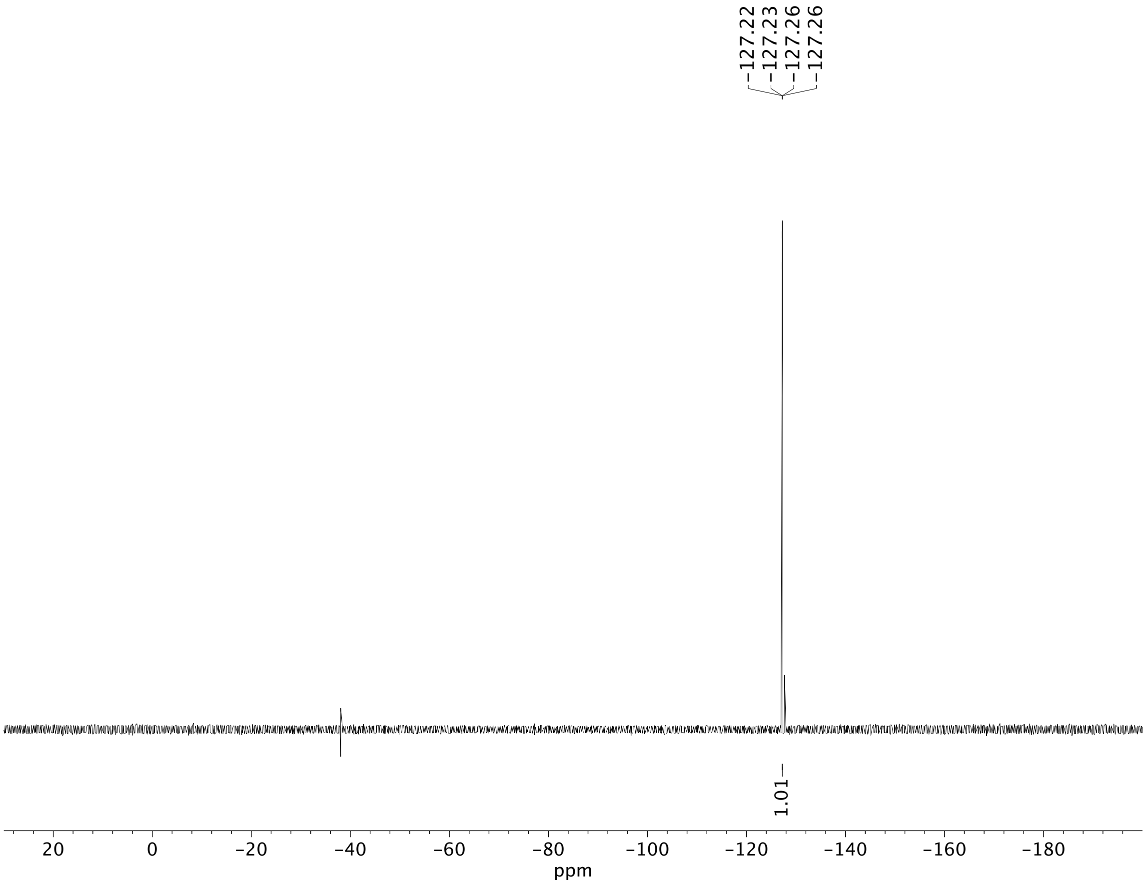
$^{1}$H NMR (400 MHz, CDCl$_3$) of compound **4a**



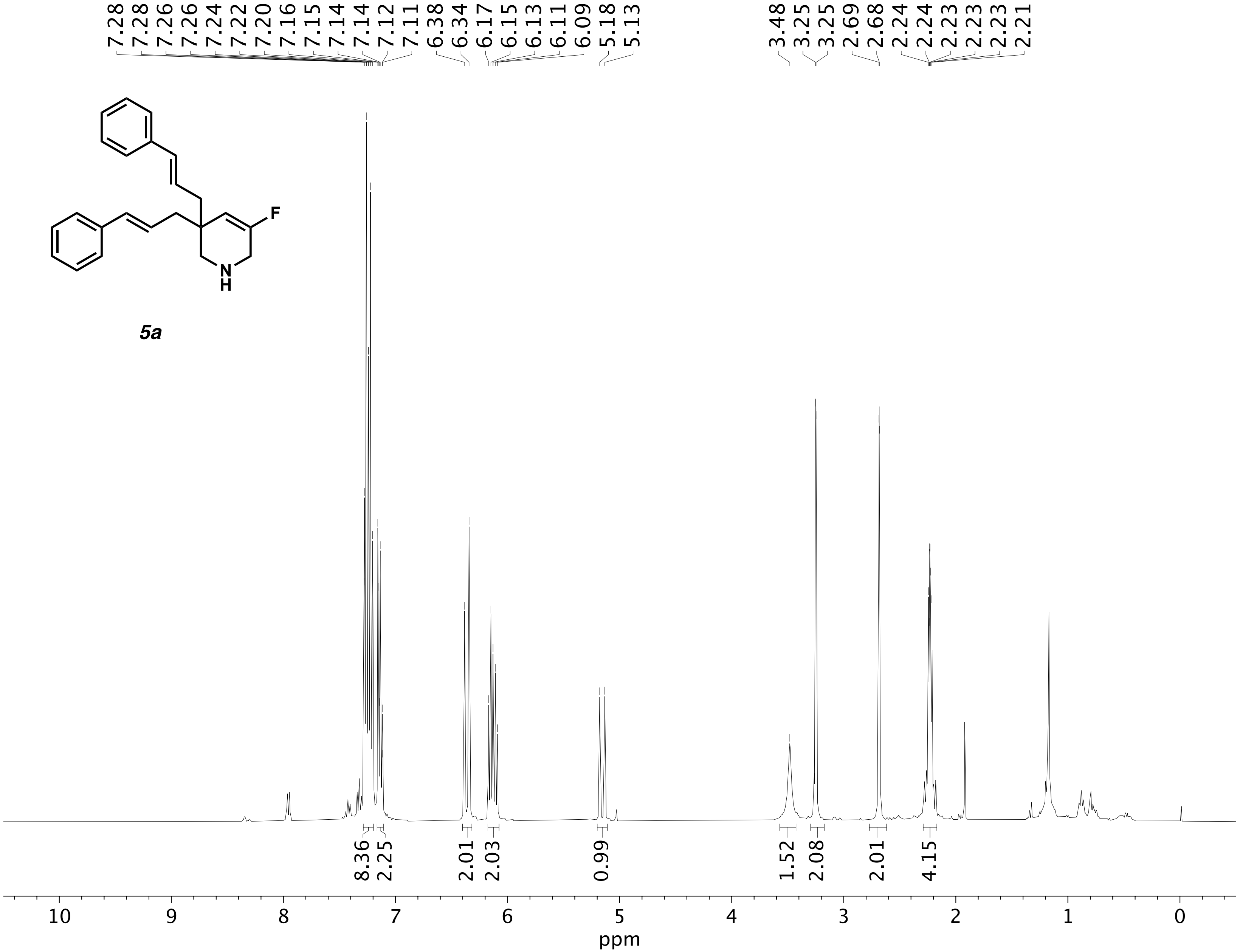
Infrared spectrum (Thin Film, NaCl) of compound **4a**.



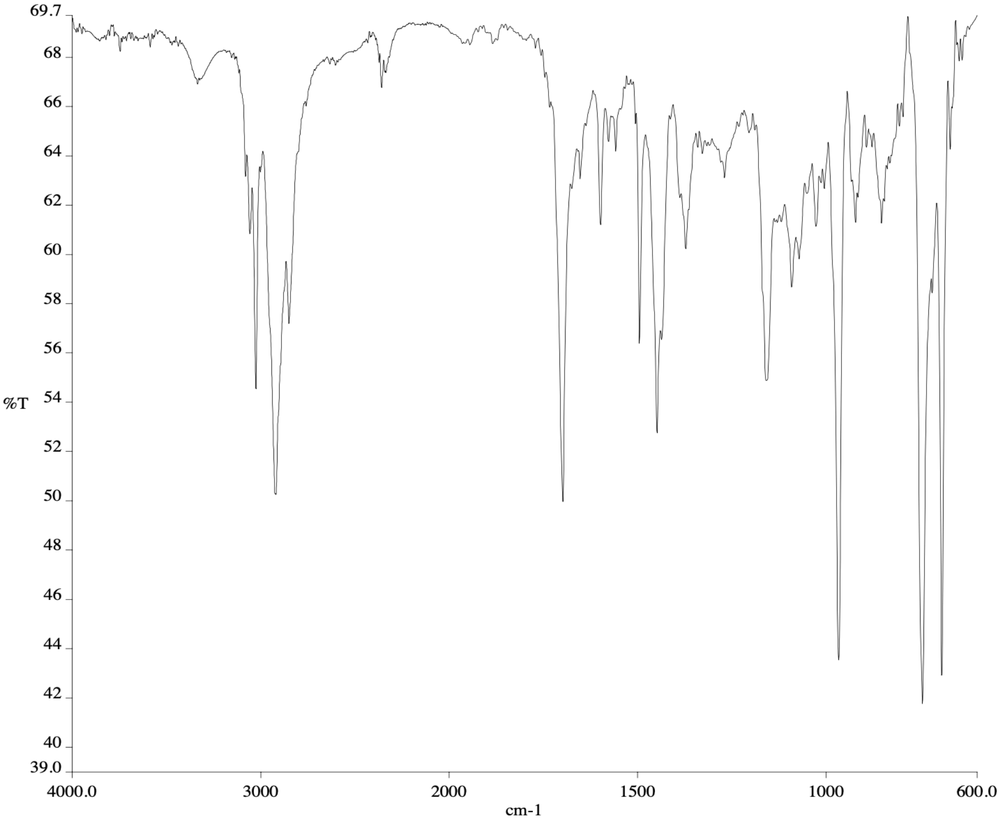
$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **4a**.



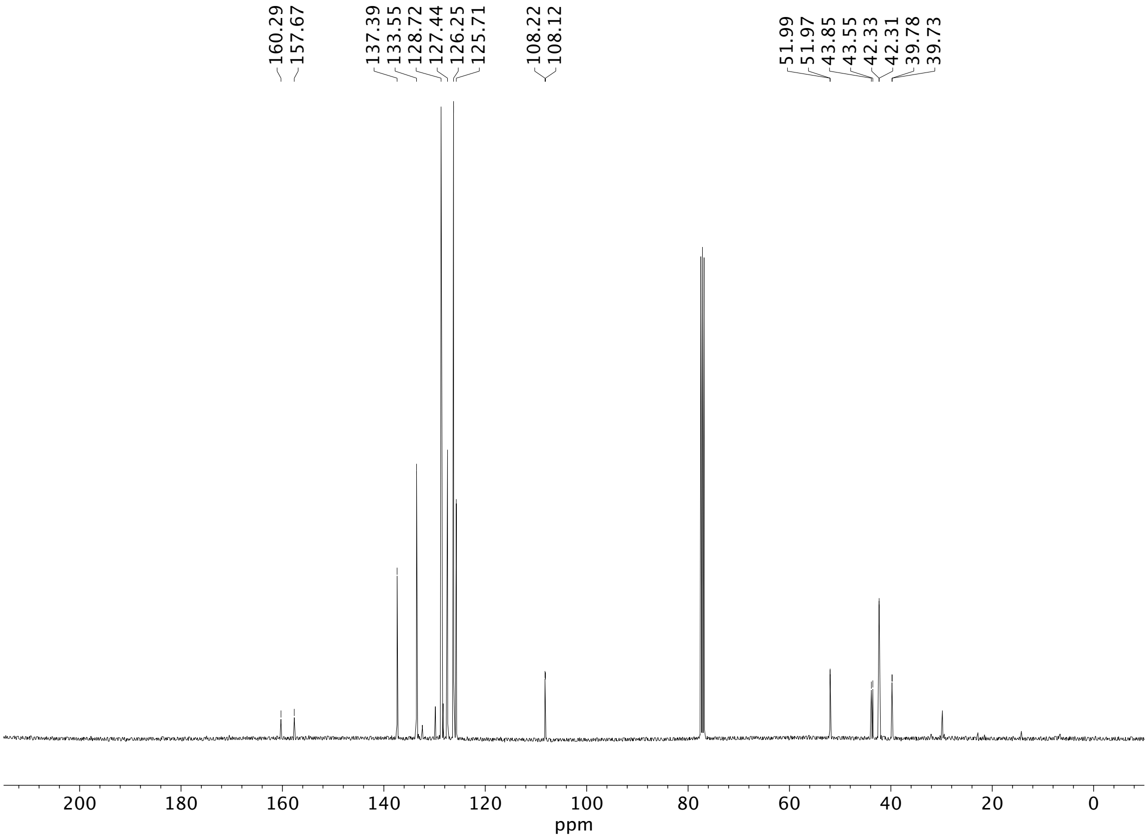
$^{19}$F NMR (282 MHz, CDCl$_3$) of compound **4a**.



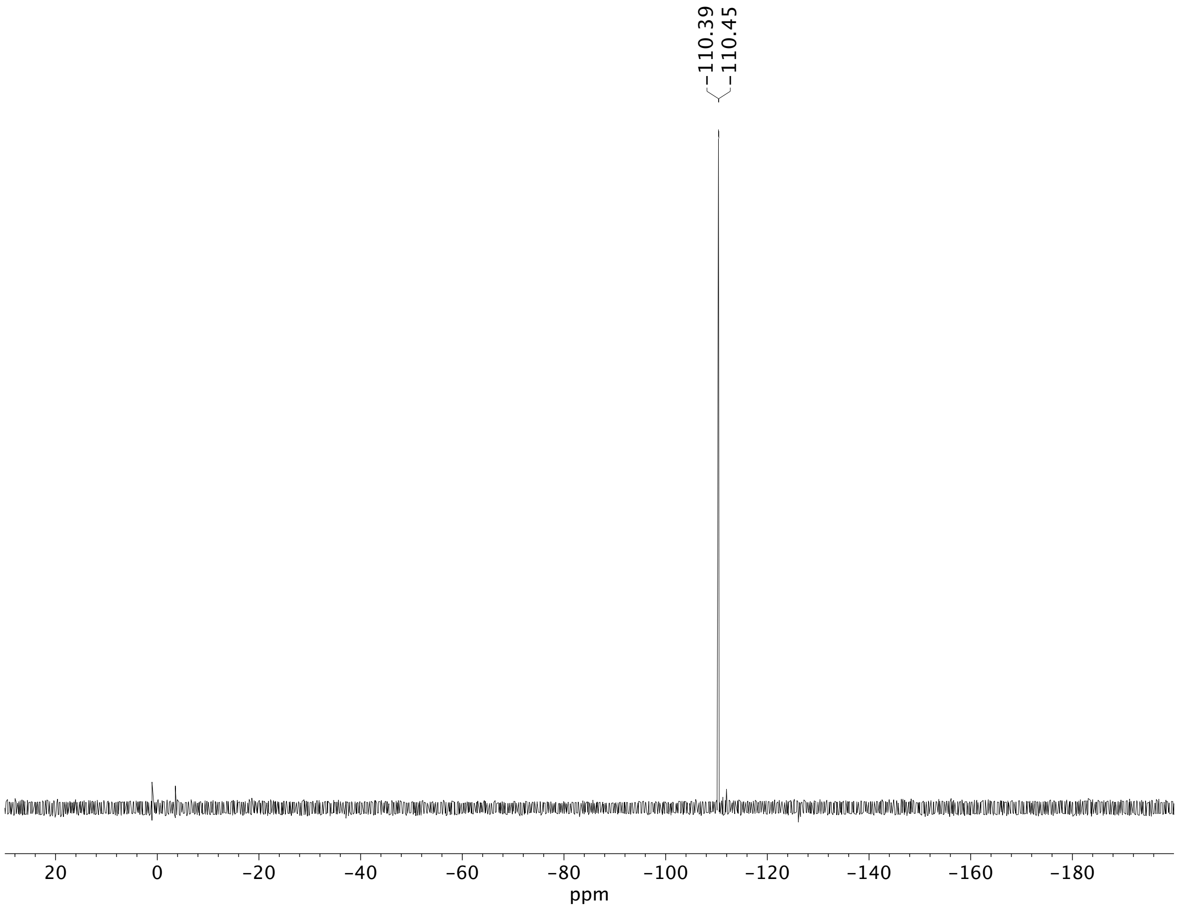
$^1$H NMR (400 MHz, CDCl$_3$) of compound **5a**.



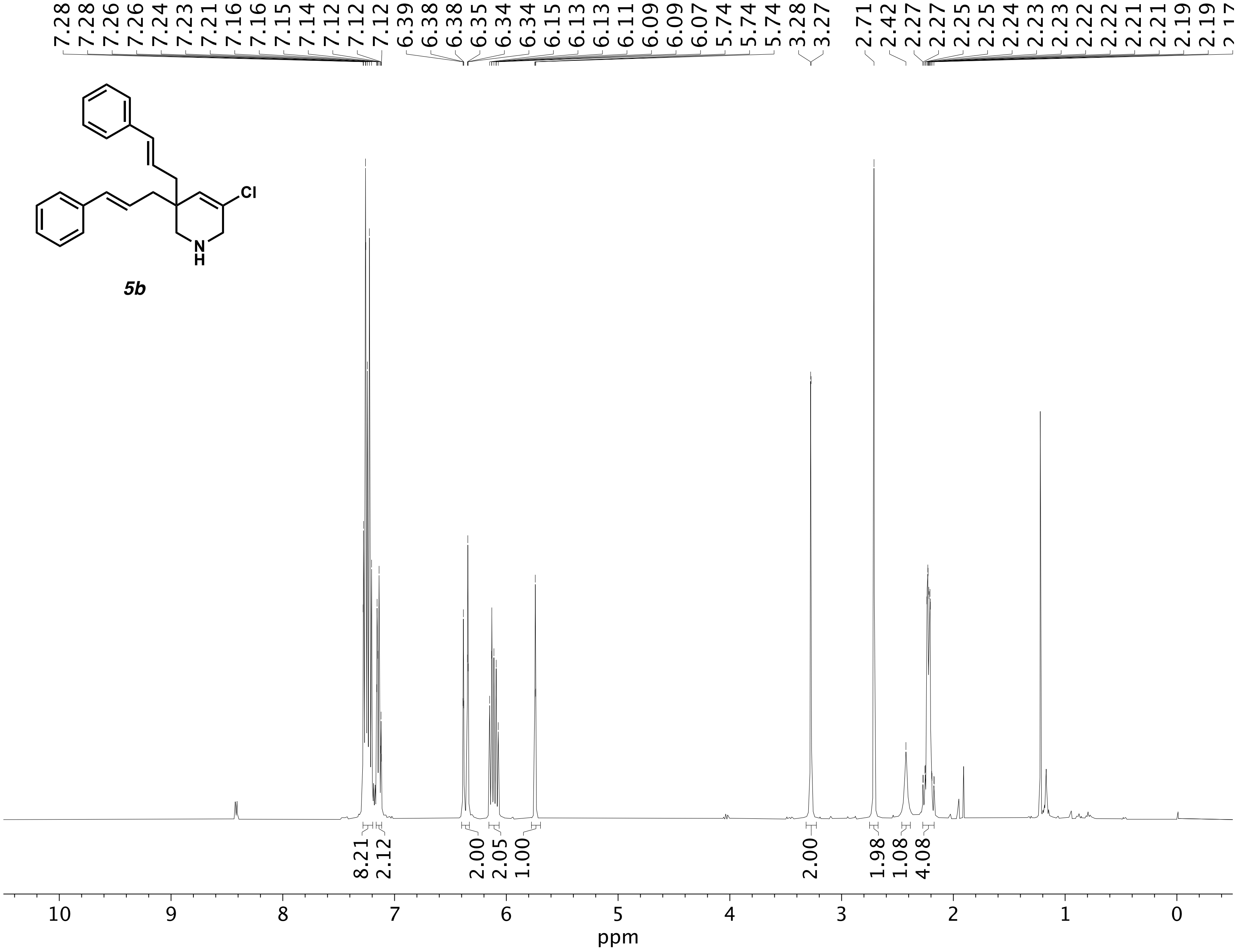
Infrared spectrum (Thin Film, NaCl) of compound **5a**.



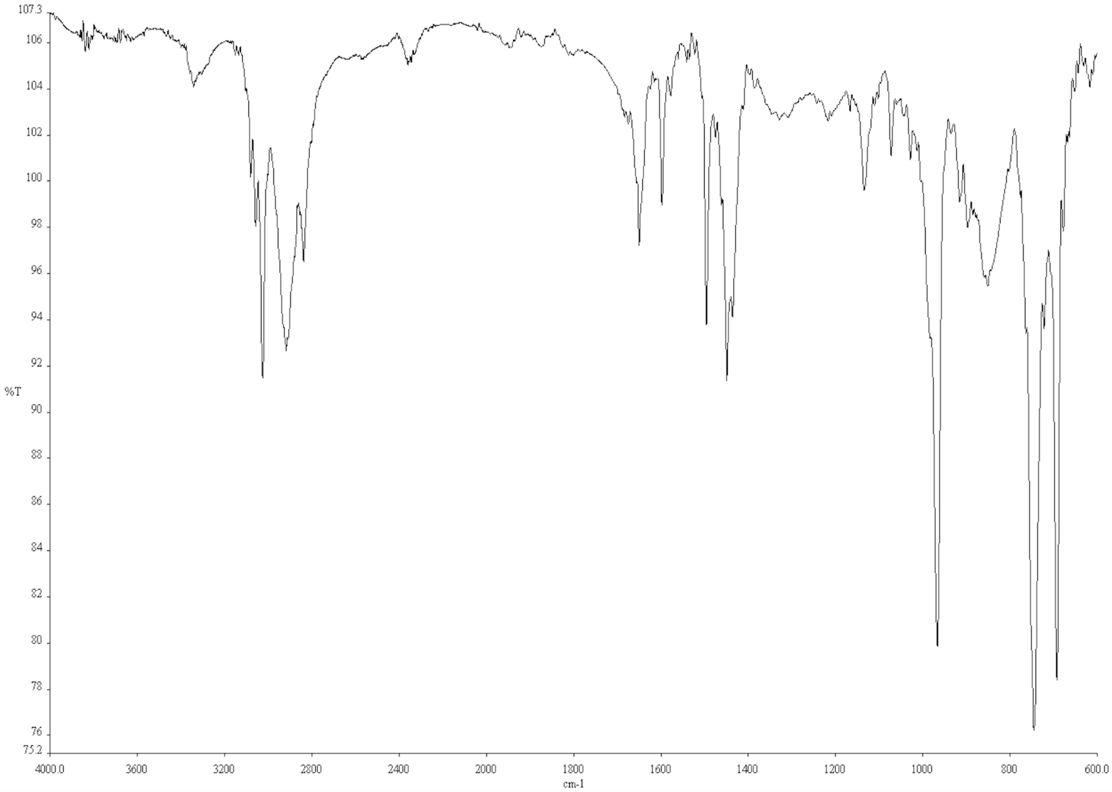
$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **5a**.



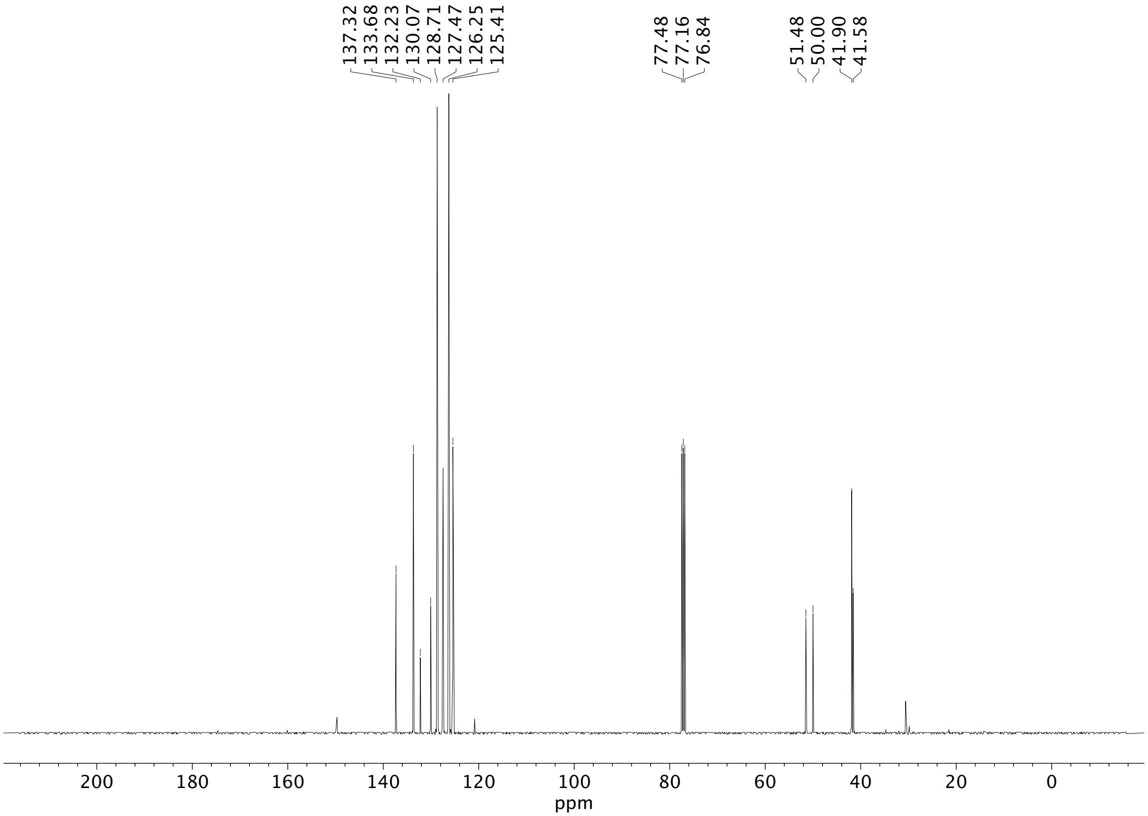
$^{19}$F NMR (282 MHz, CDCl$_3$) of compound **5a.**



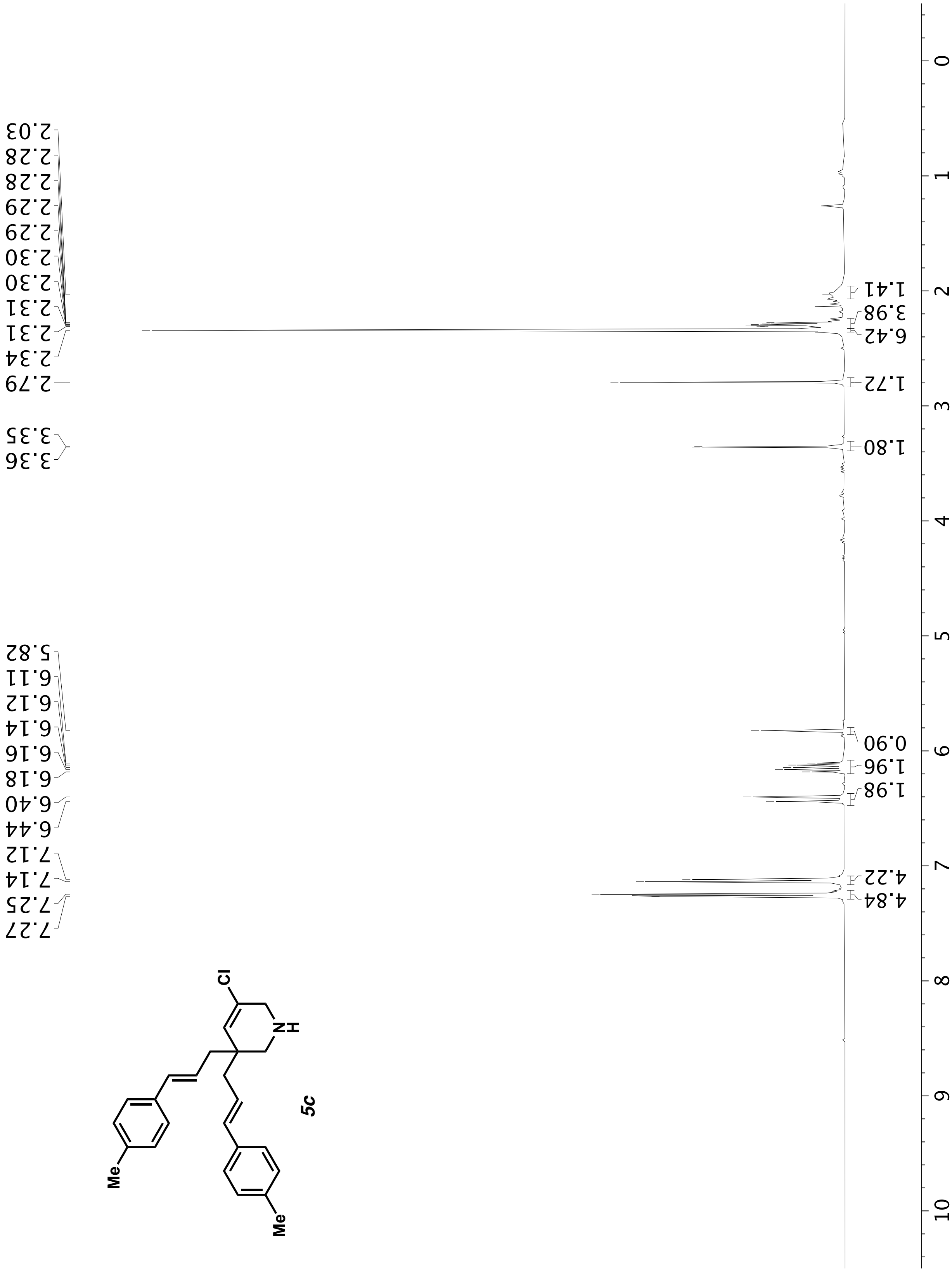
$^1$H NMR (400 MHz, CDCl$_3$) of compound **5b**.



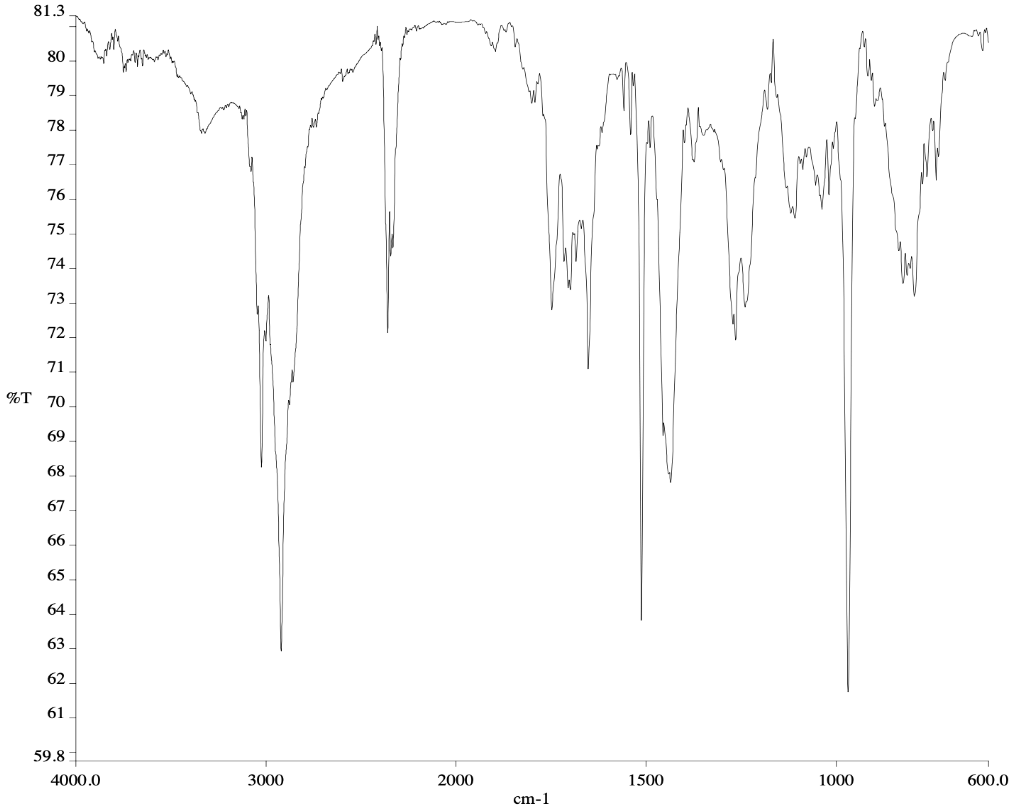
Infrared spectrum (Thin Film, NaCl) of compound **5b**.



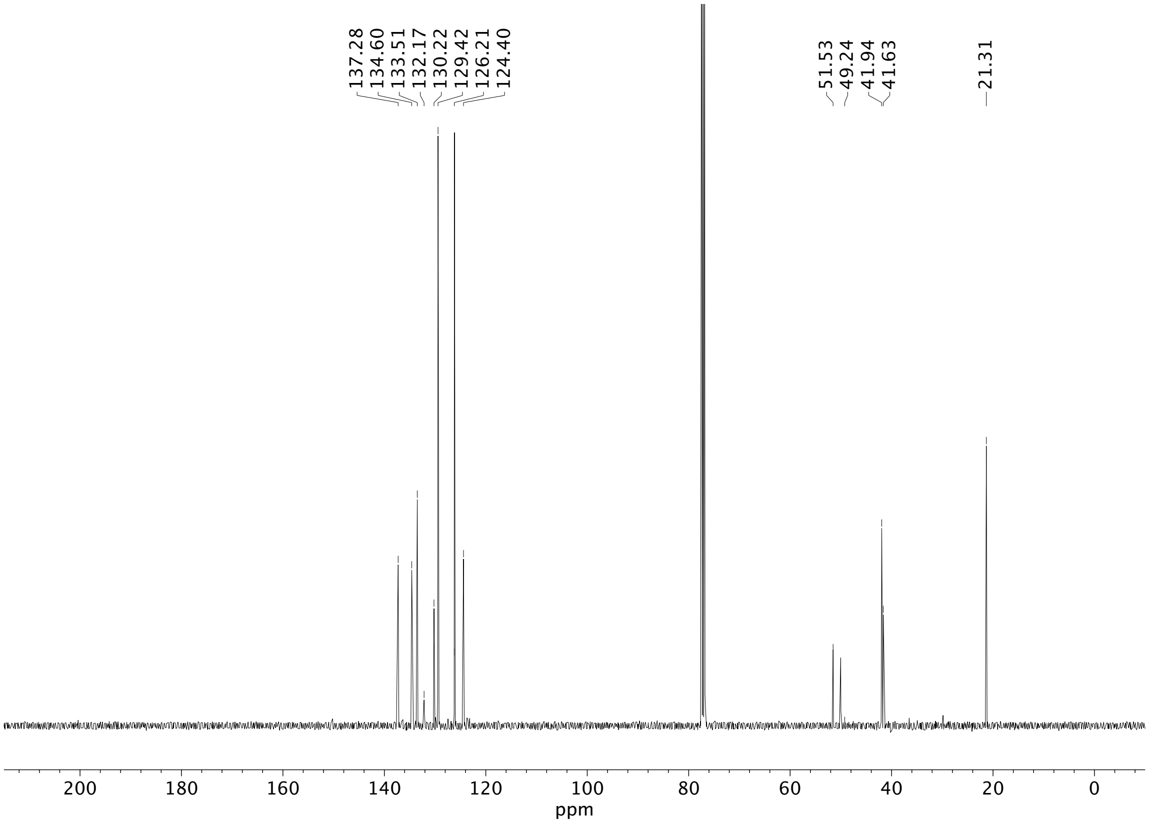
$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **5b**.



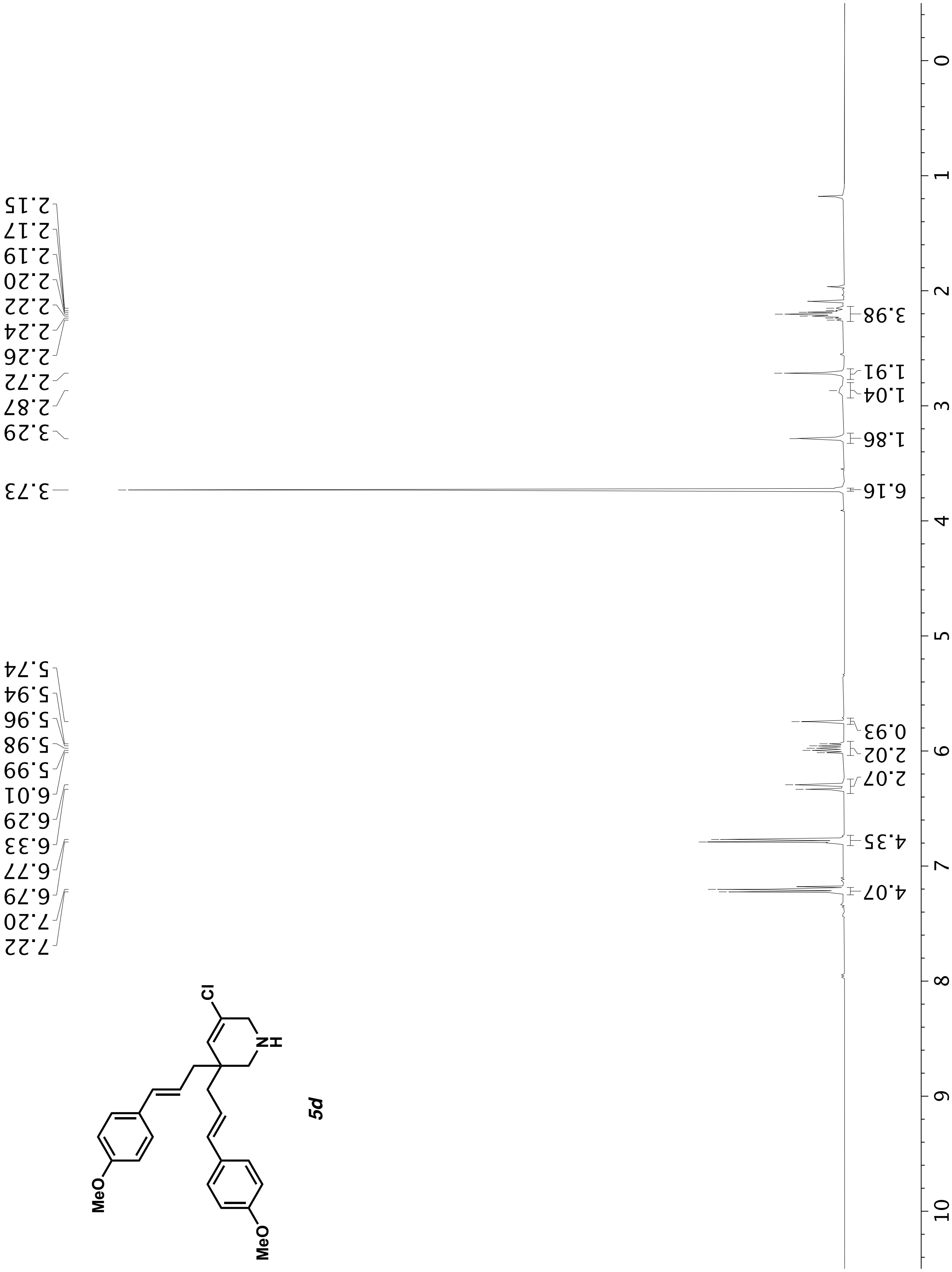
$^1$H NMR (400 MHz, $CDCl_3$) of compound **5c**.



Infrared spectrum (Thin Film, NaCl) of compound **5c**.

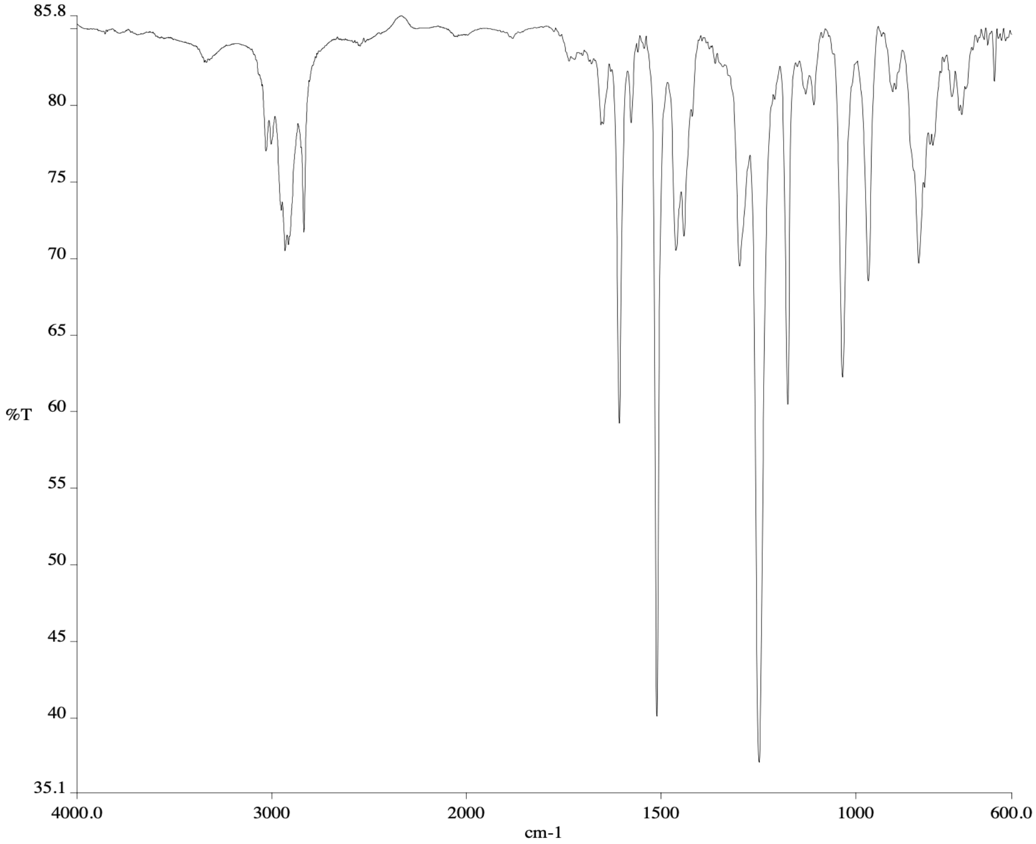


$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **5c**.

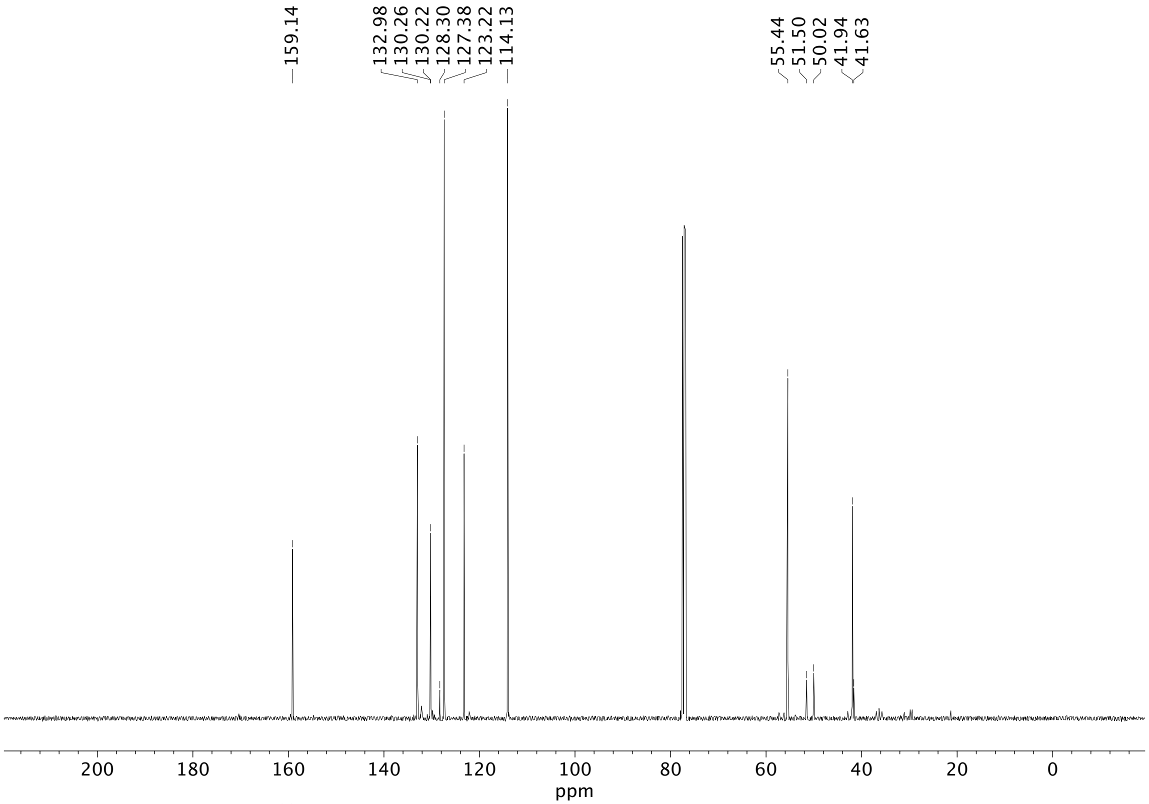


**5d**

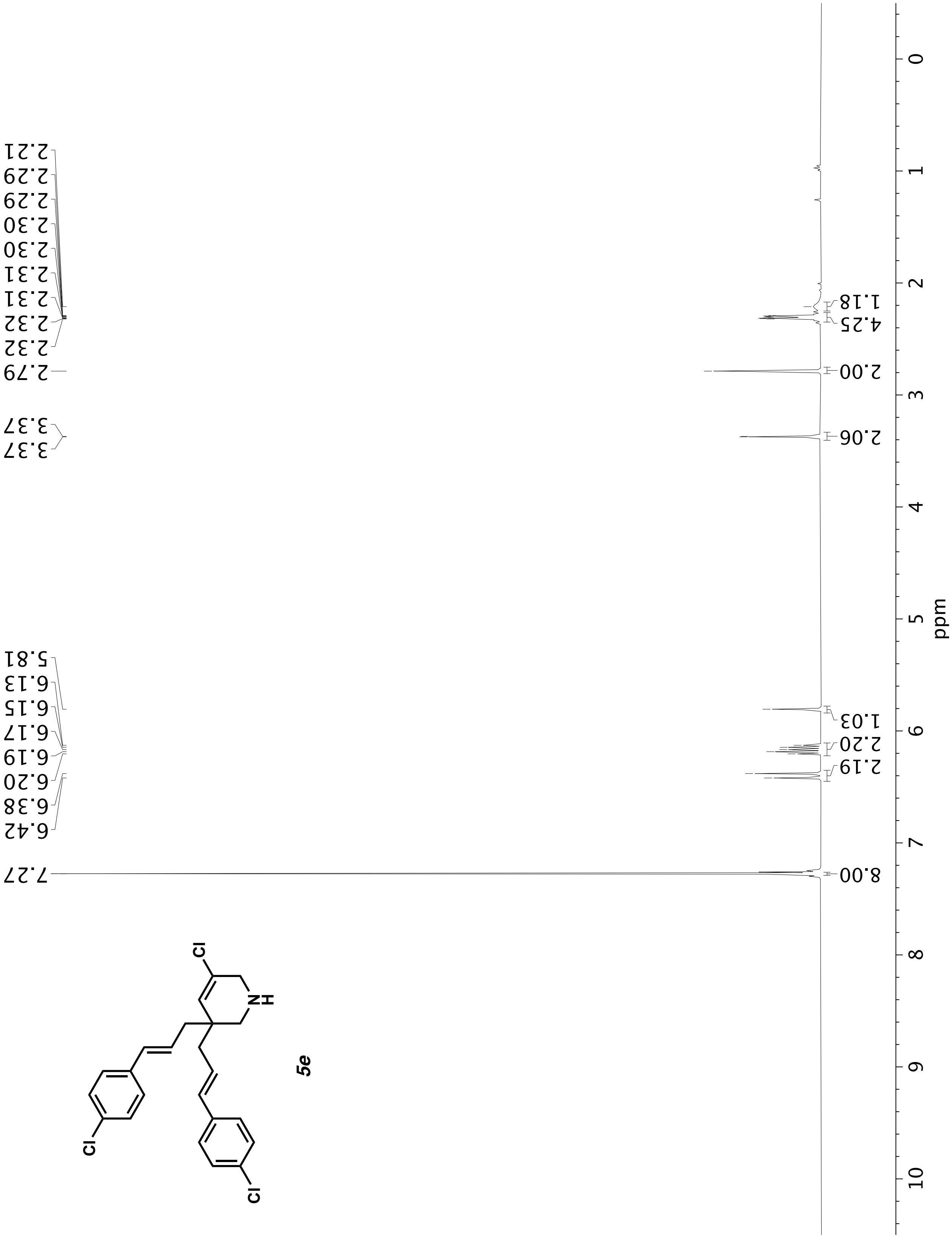
$^1$H NMR (400 MHz, CDCl$_3$) of compound **5d**.



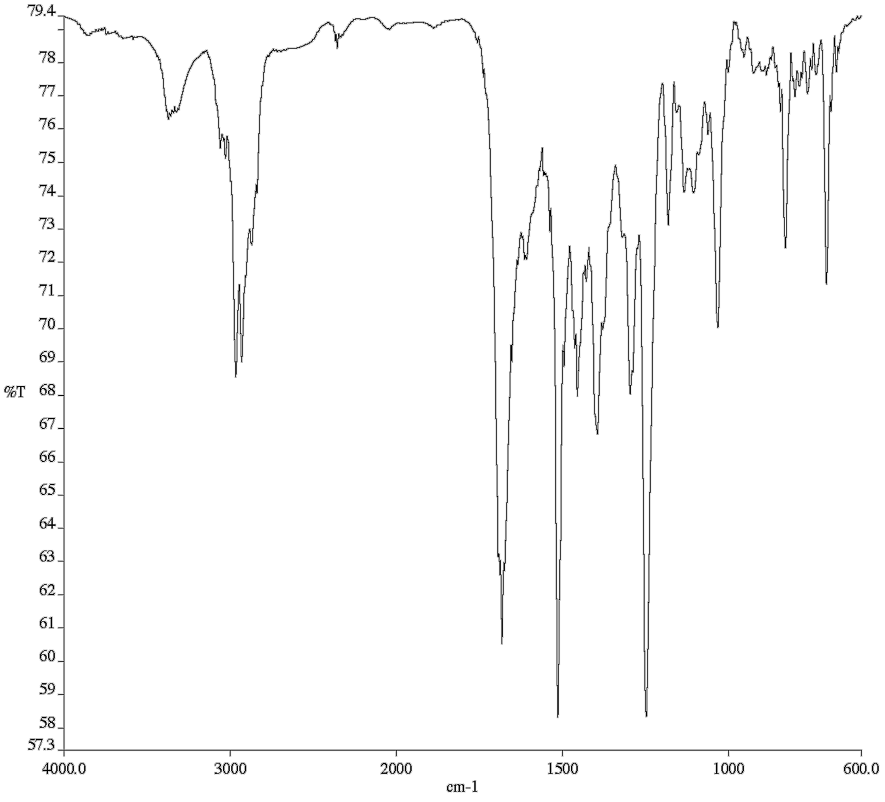
Infrared spectrum (Thin Film, NaCl) of compound **5d**.



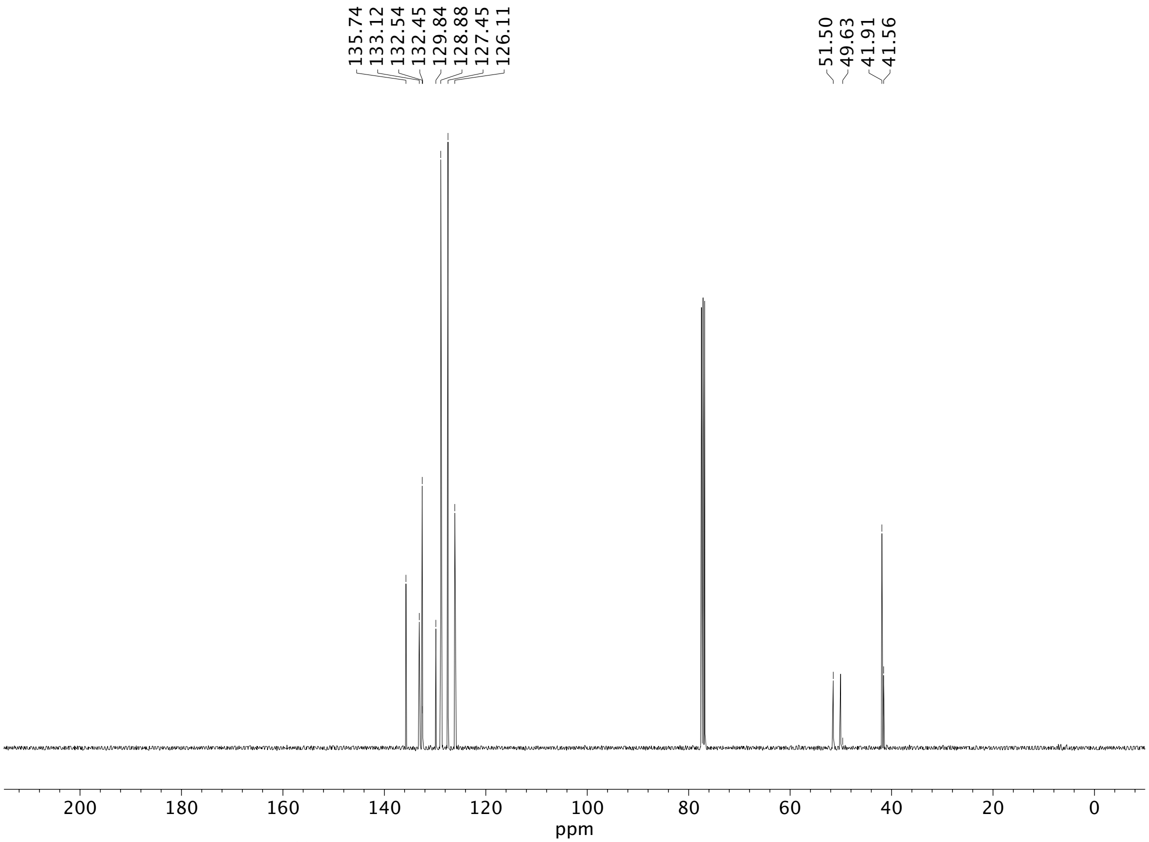
$^{13}C$ NMR (100 MHz, $CDCl_3$) of compound **5d**.



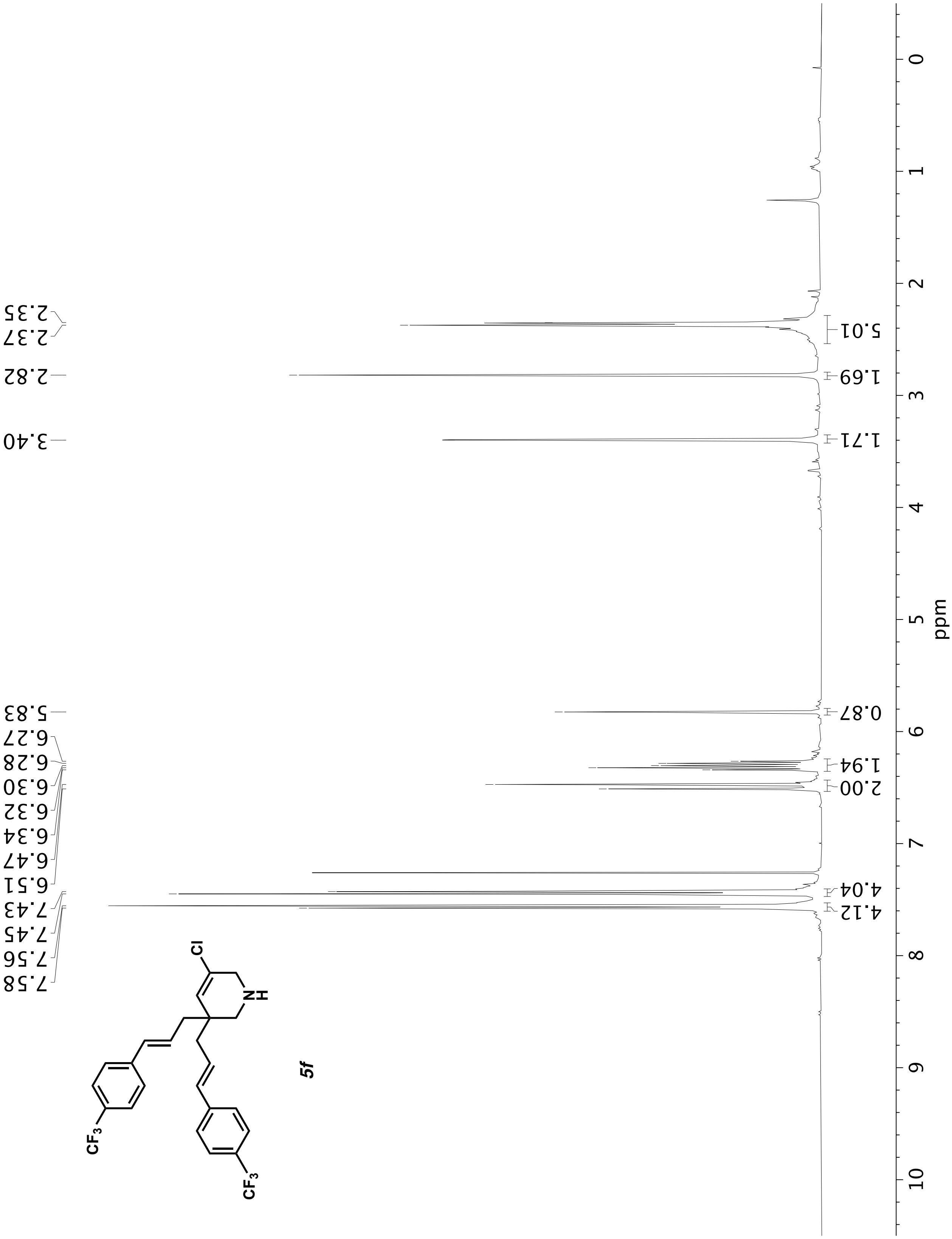
$^1$H NMR (400 MHz, CDCl$_3$) of compound **5e**.



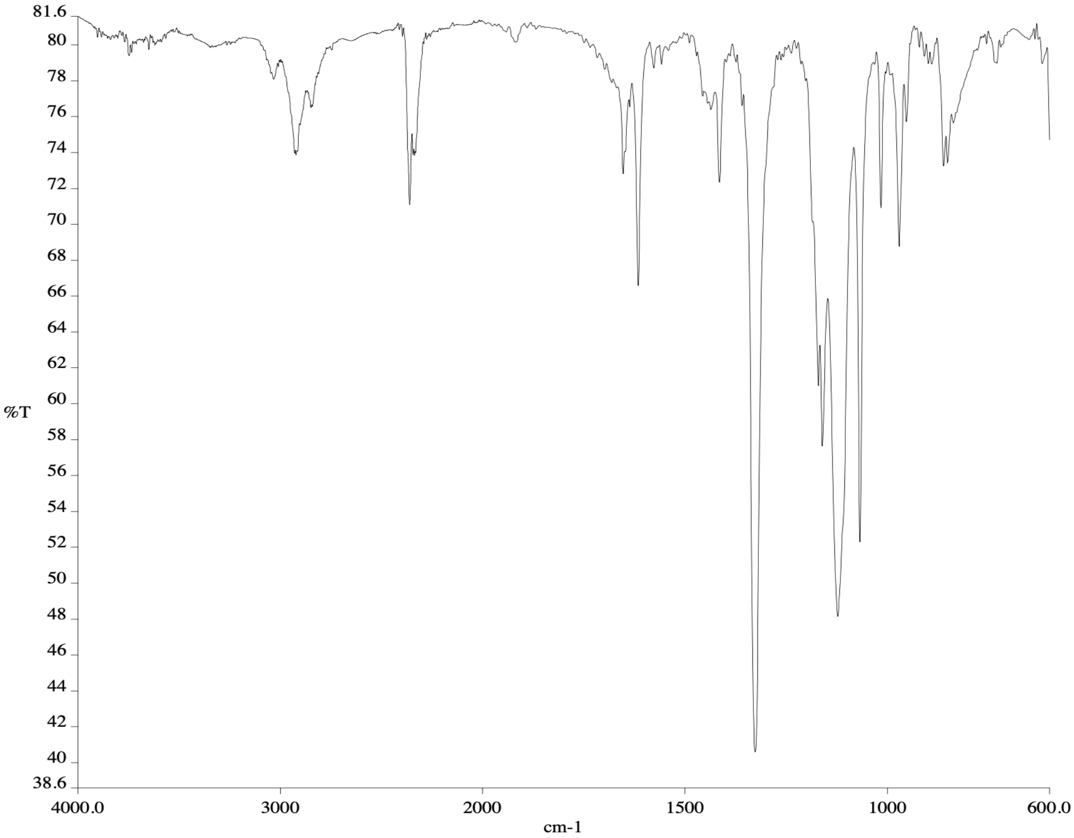
Infrared spectrum (Thin Film, NaCl) of compound **5e**.



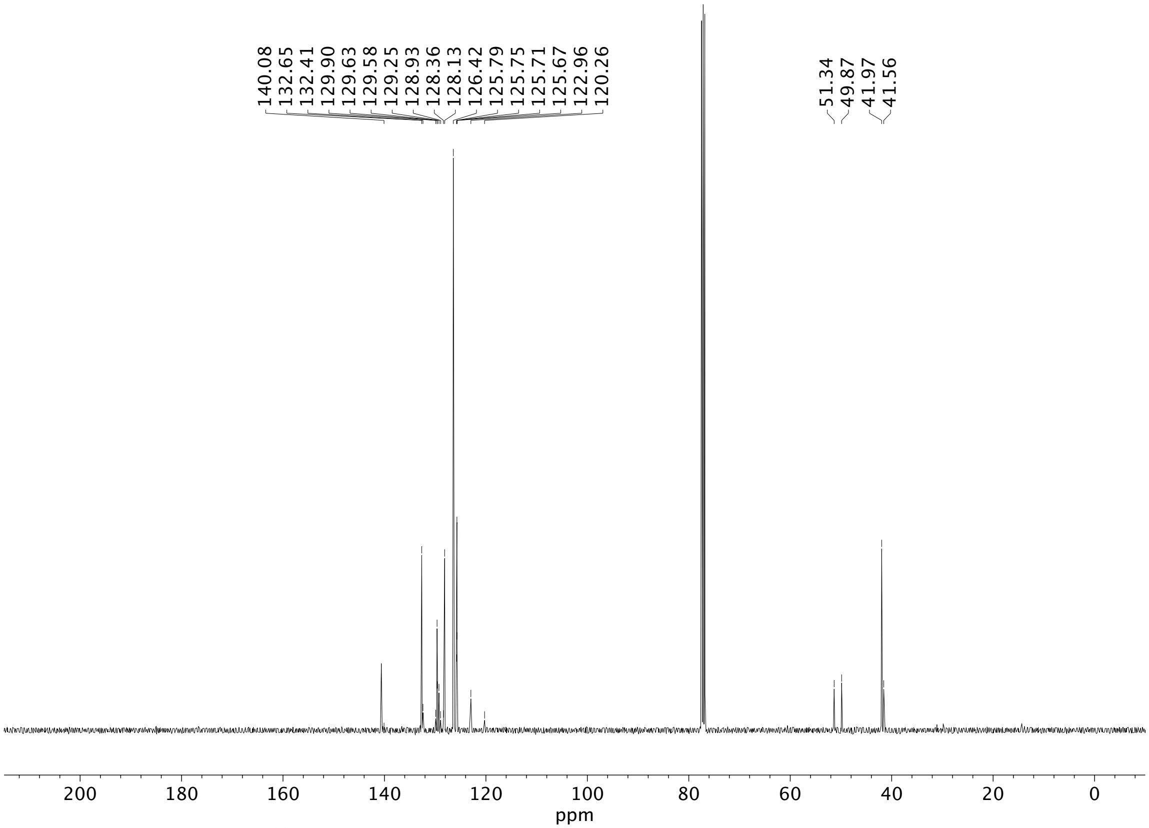
$^{13}C$ NMR (100 MHz, $CDCl_3$) of compound **5e**.



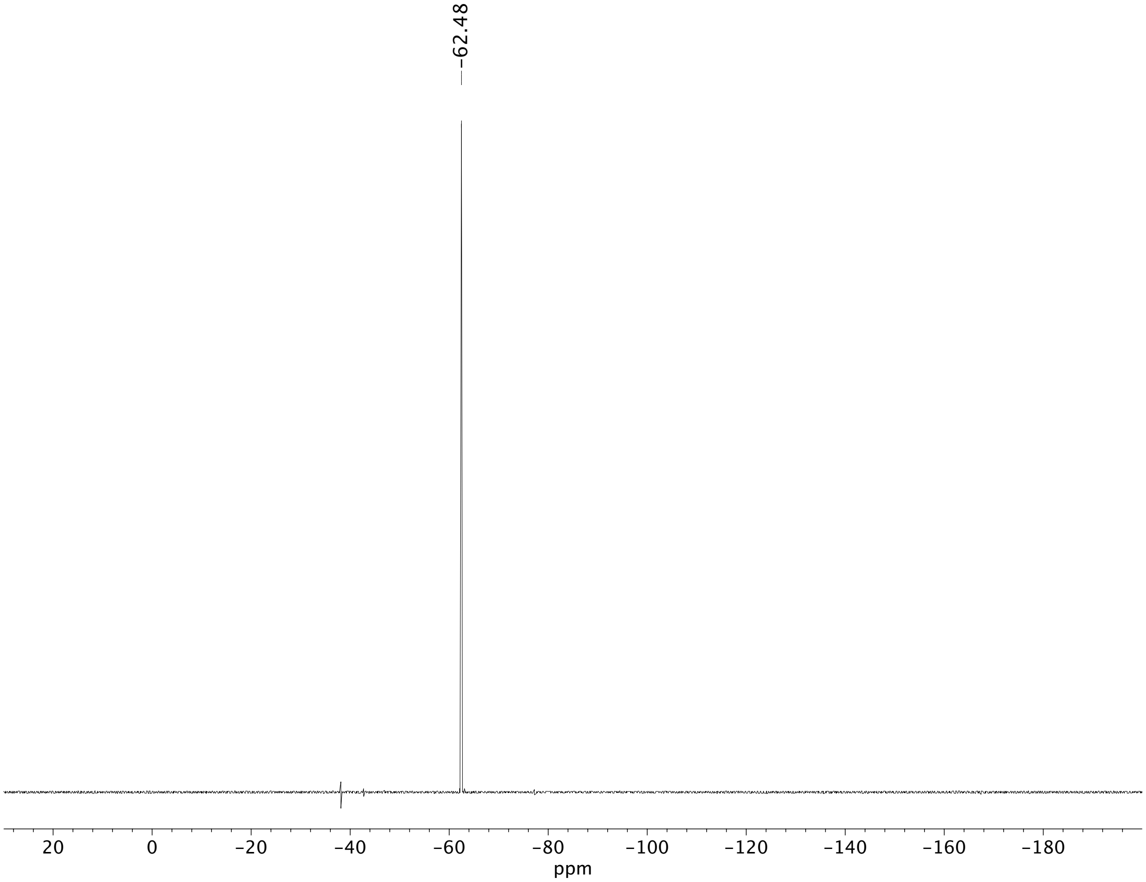
$^{1}$H NMR (400 MHz, CDCl$_3$) of compound **5f**.



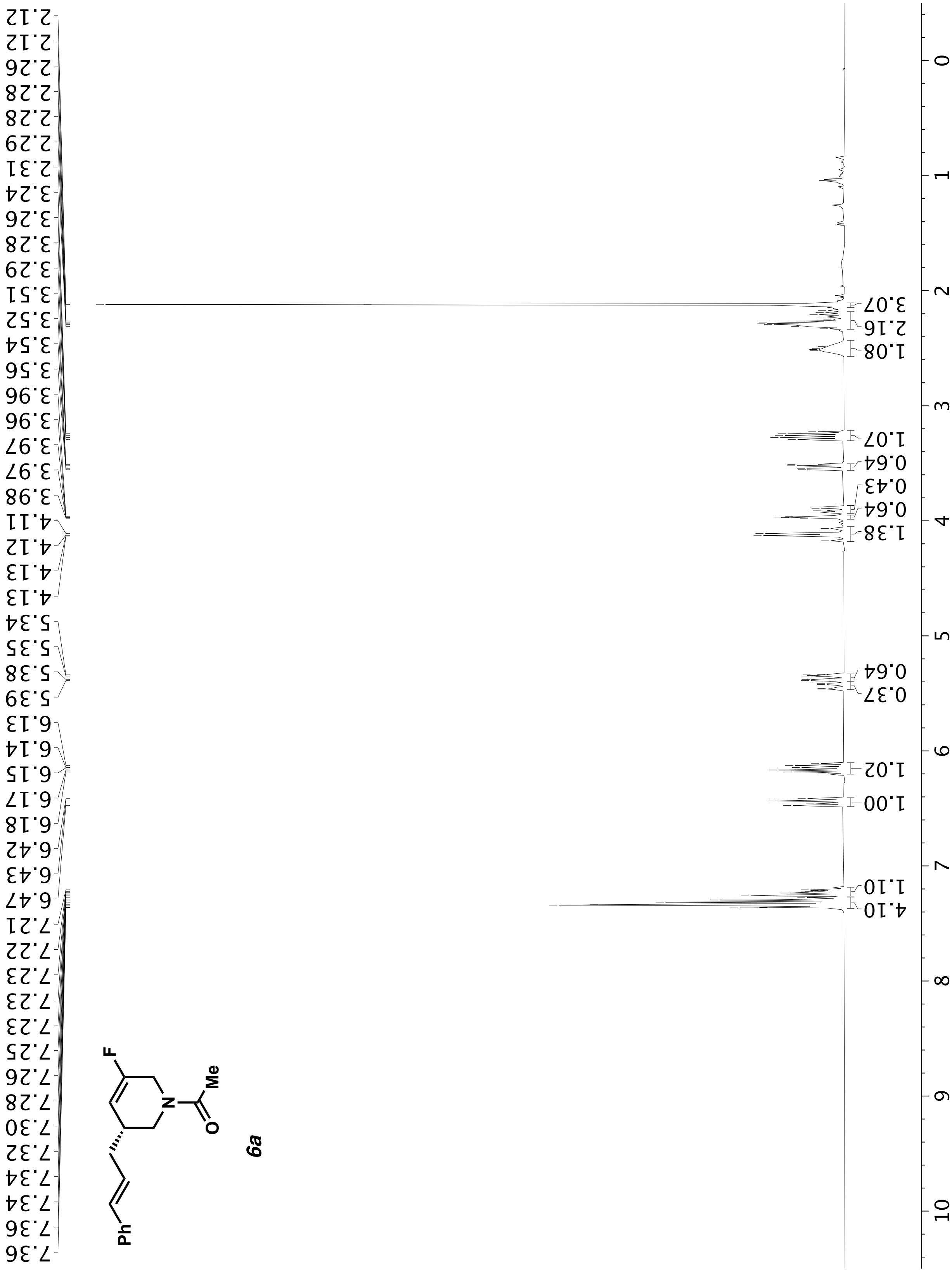
Infrared spectrum (Thin Film, NaCl) of compound **5f**.



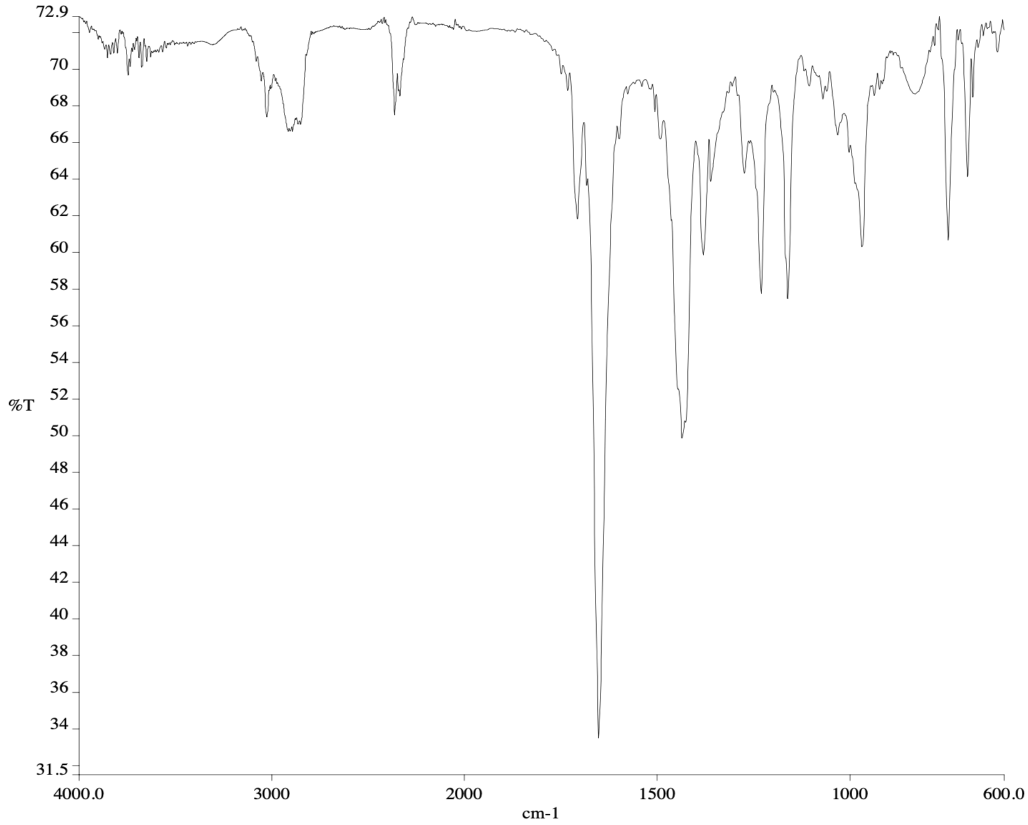
$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **5f**.



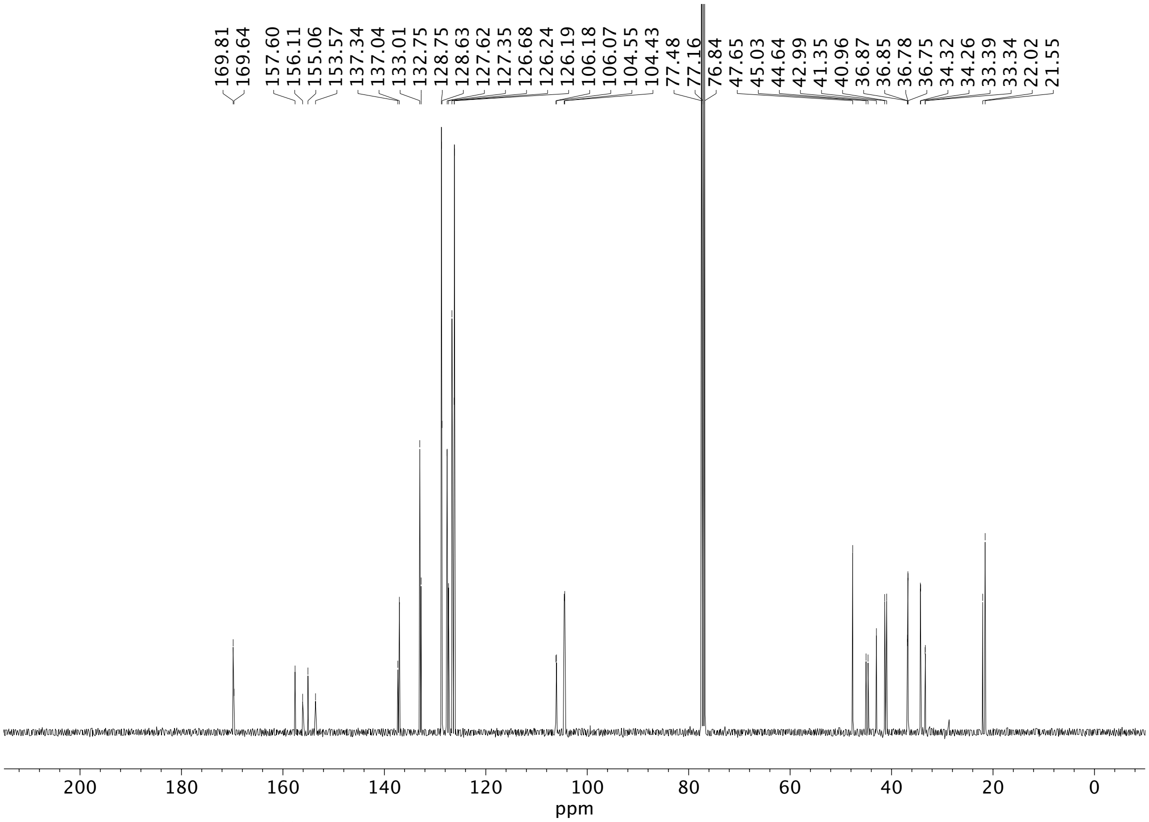
$^{19}$F NMR (282 MHz, CDCl$_3$) of compound **5f**.



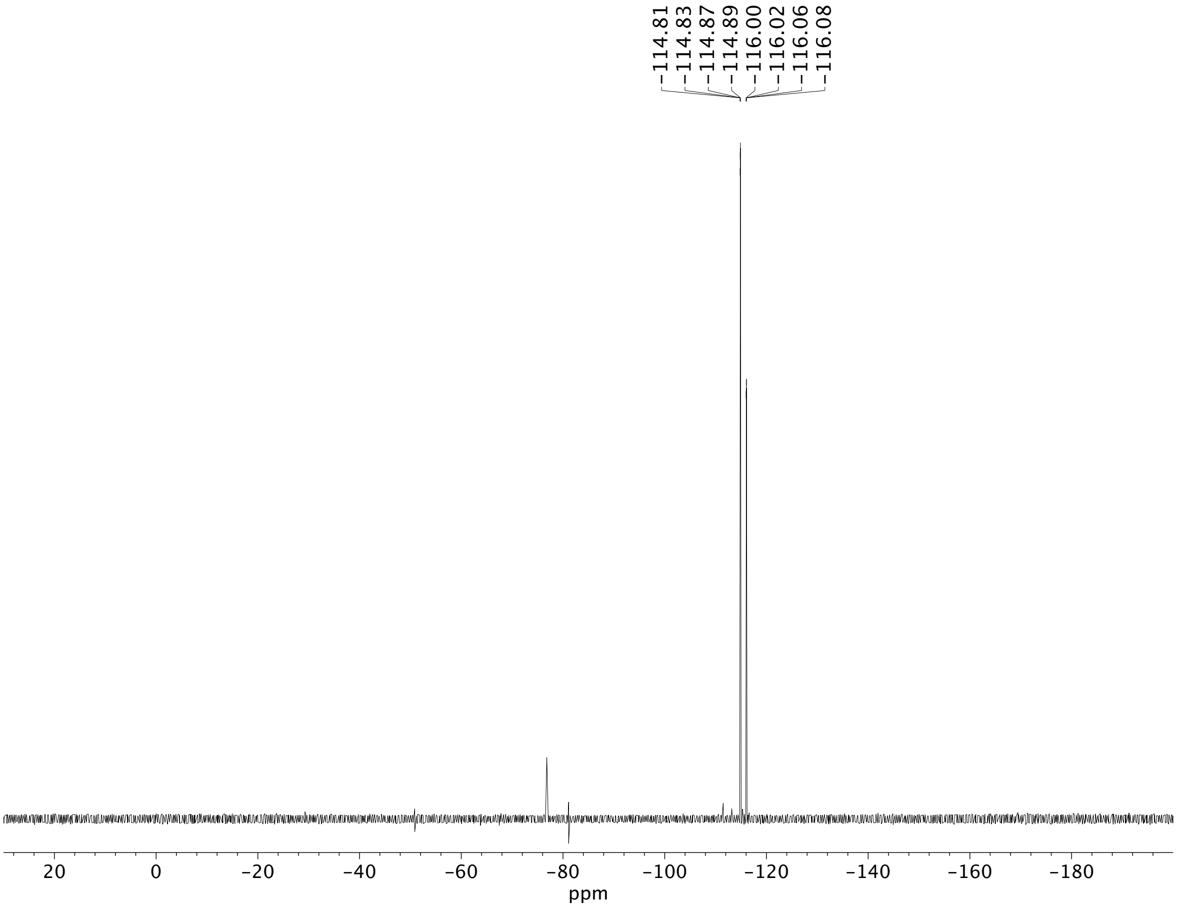
$^1$H NMR (400 MHz, CDCl$_3$) of compound **6a**.



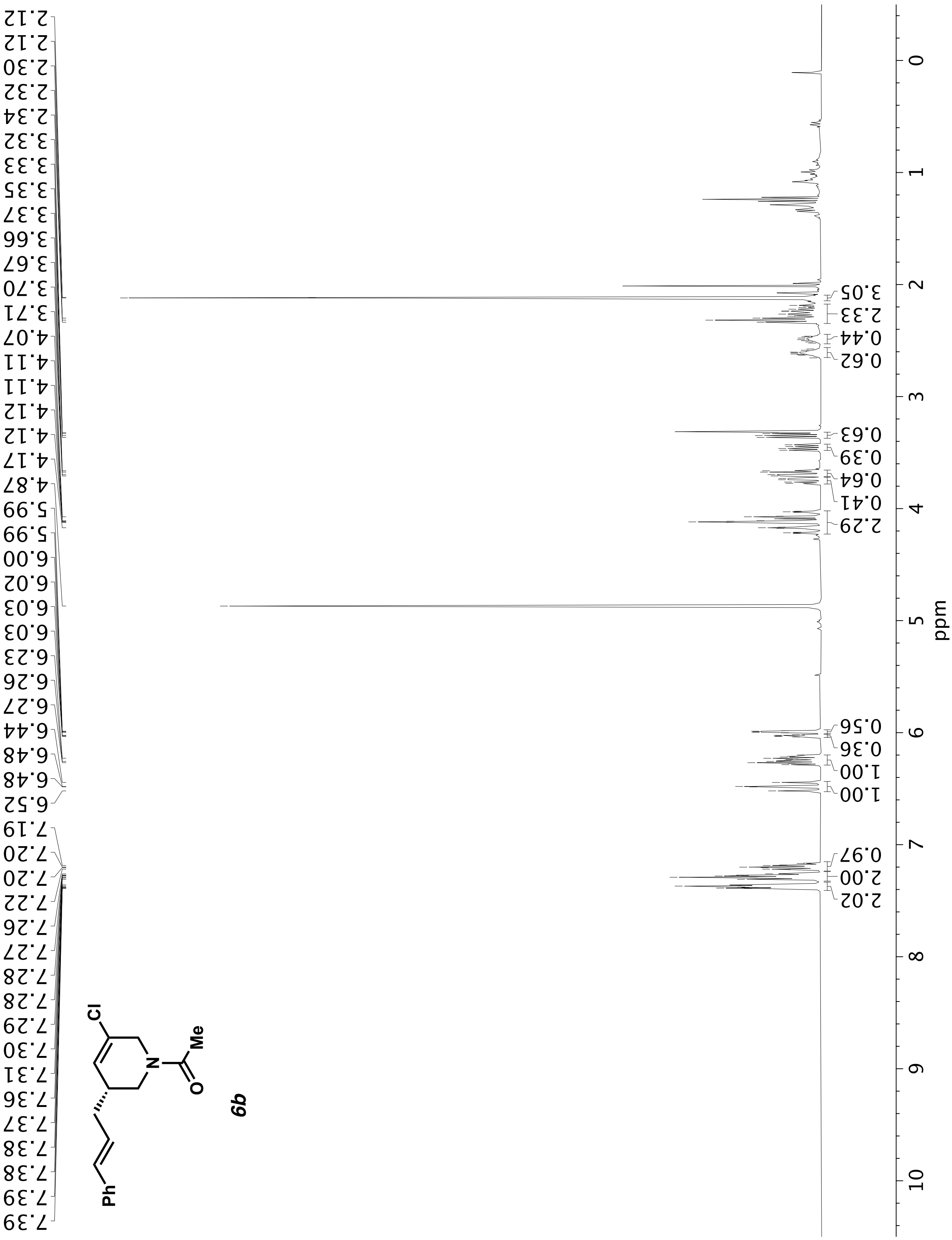
Infrared spectrum (Thin Film, NaCl) of compound **6a**.



$^{13}C$ NMR (100 MHz, $CDCl_3$) of compound **6a**.

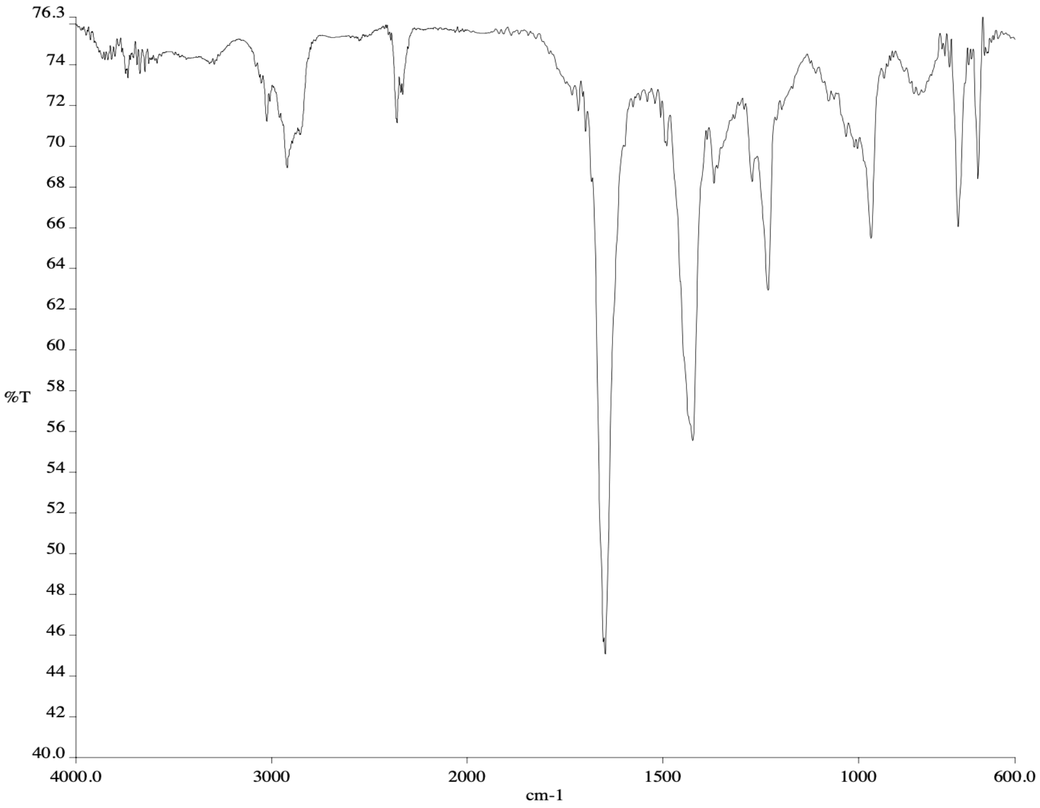


$^{19}$F NMR (282 MHz, $CD_3OD$) of compound **6a.**

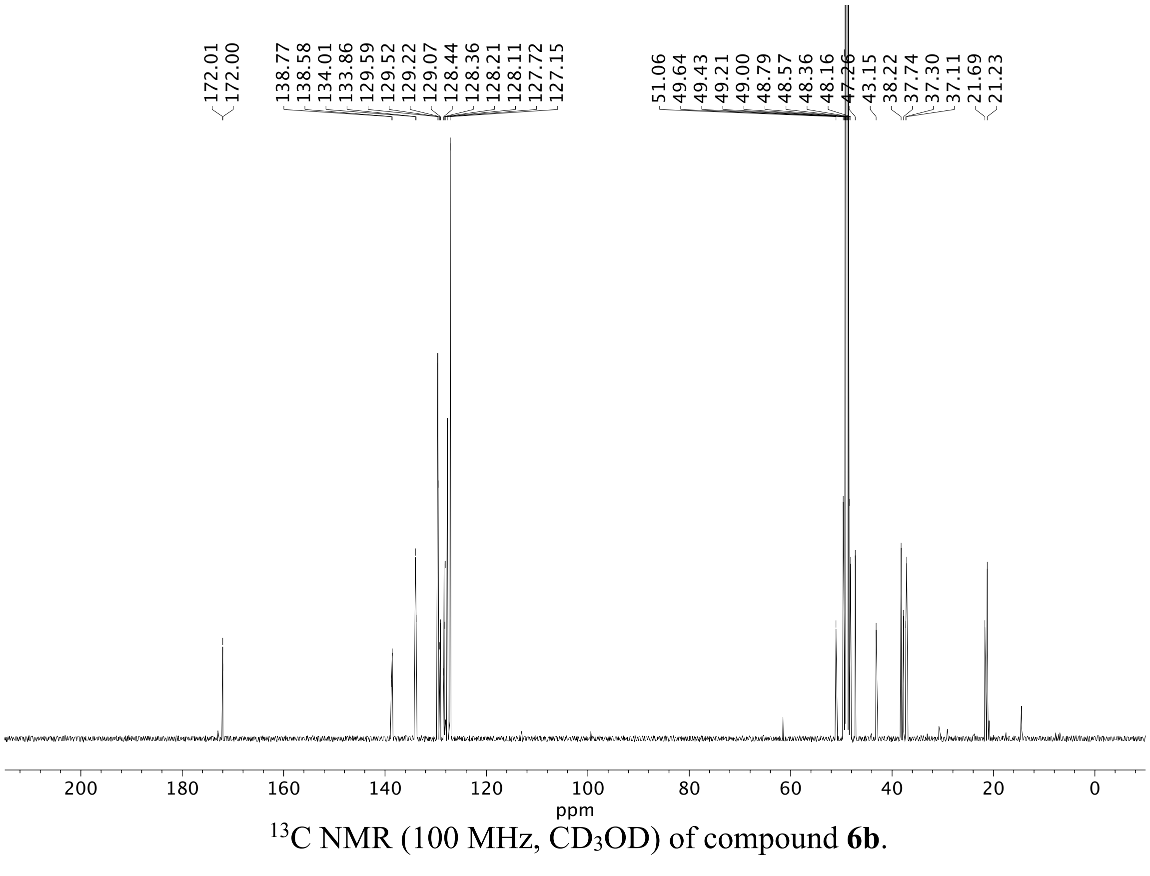


**6b**

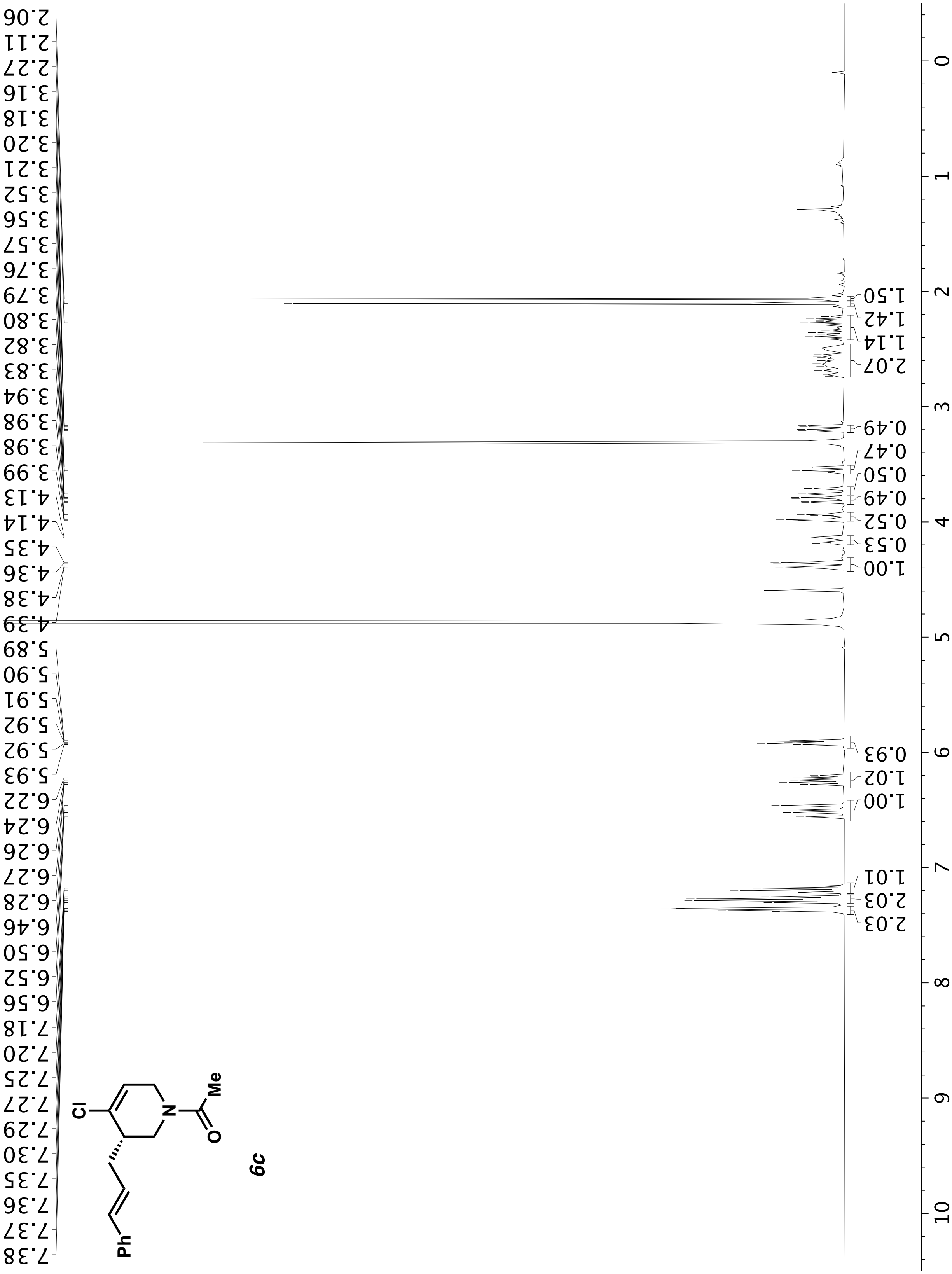
$^1$H NMR (400 MHz, CD$_3$OD) of compound **6b**



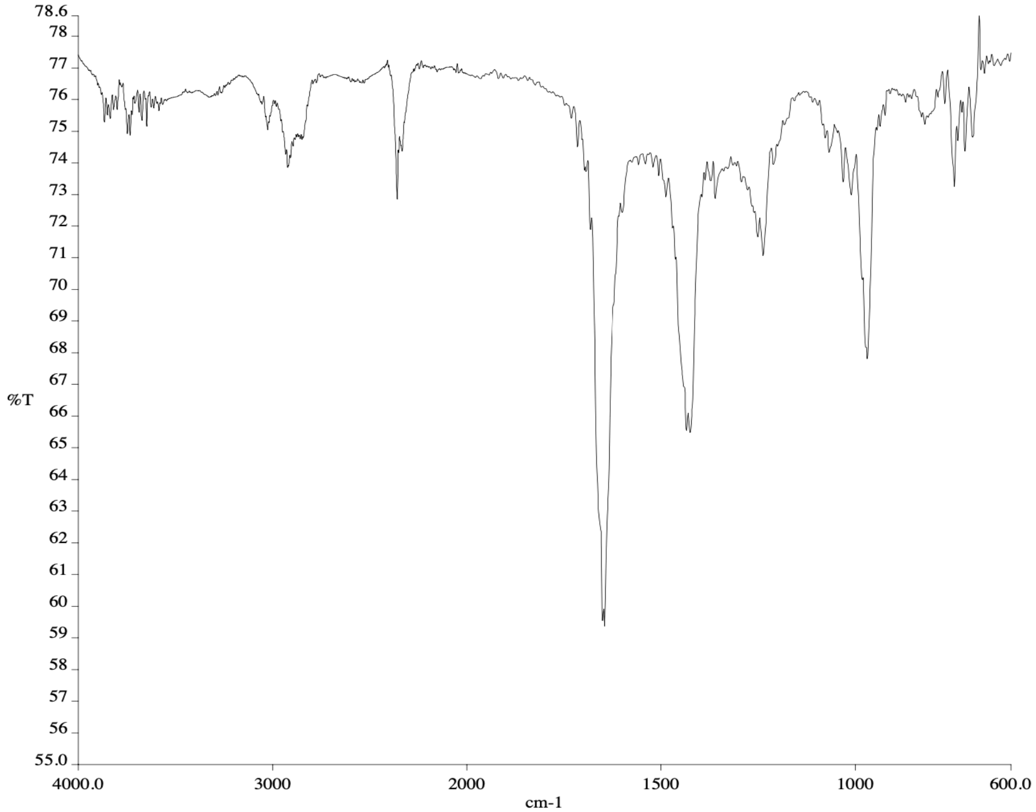
Infrared spectrum (Thin Film, NaCl) of compound **6b**.



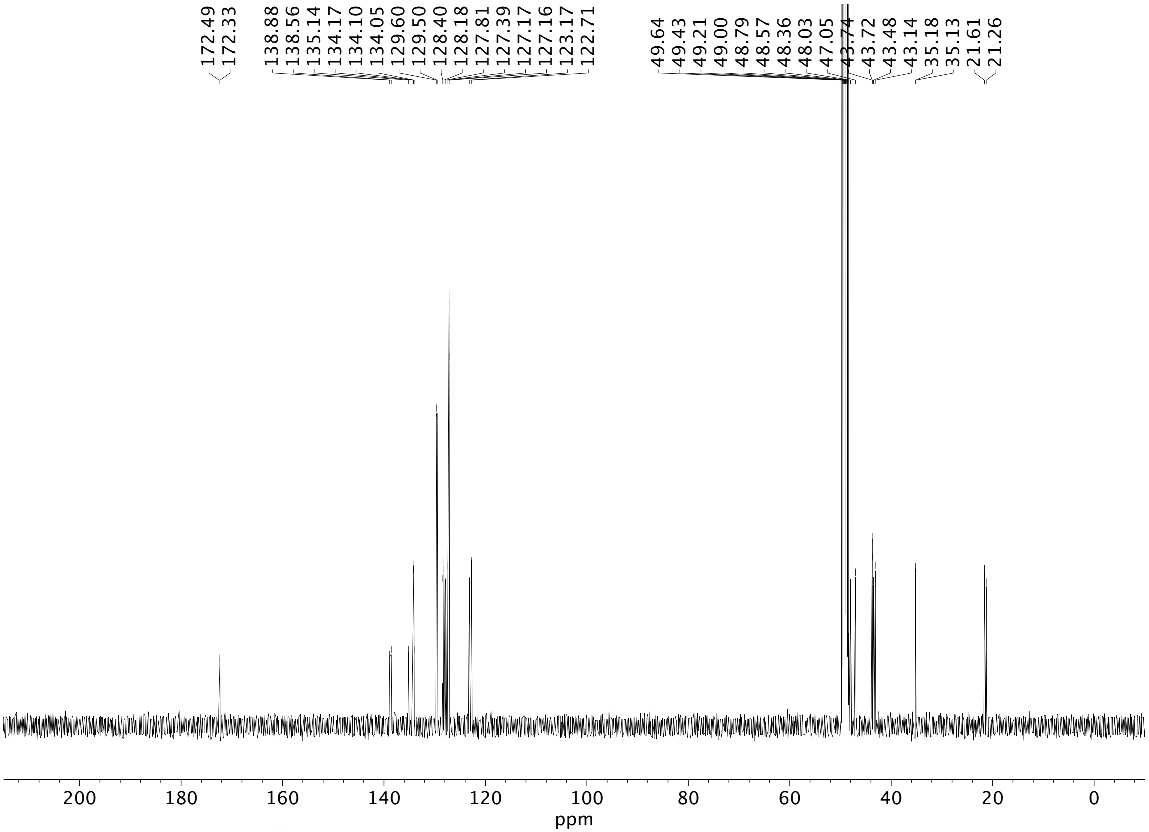
$^{13}$C NMR (100 MHz, $CD_3OD$) of compound **6b**.



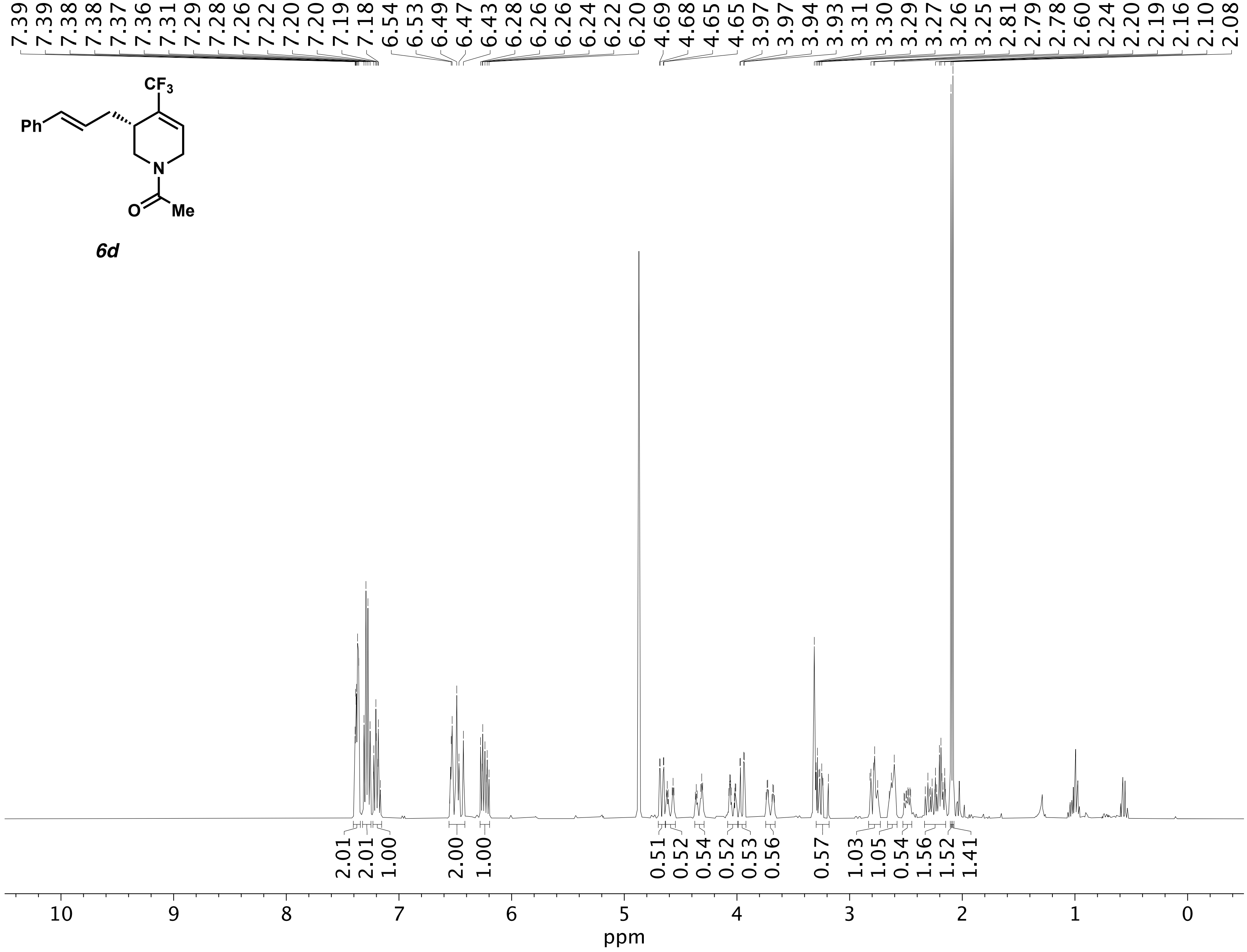
$^1$H NMR (500 MHz, CD$_3$OD) of compound **6c**.



Infrared spectrum (Thin Film, NaCl) of compound **6c**.

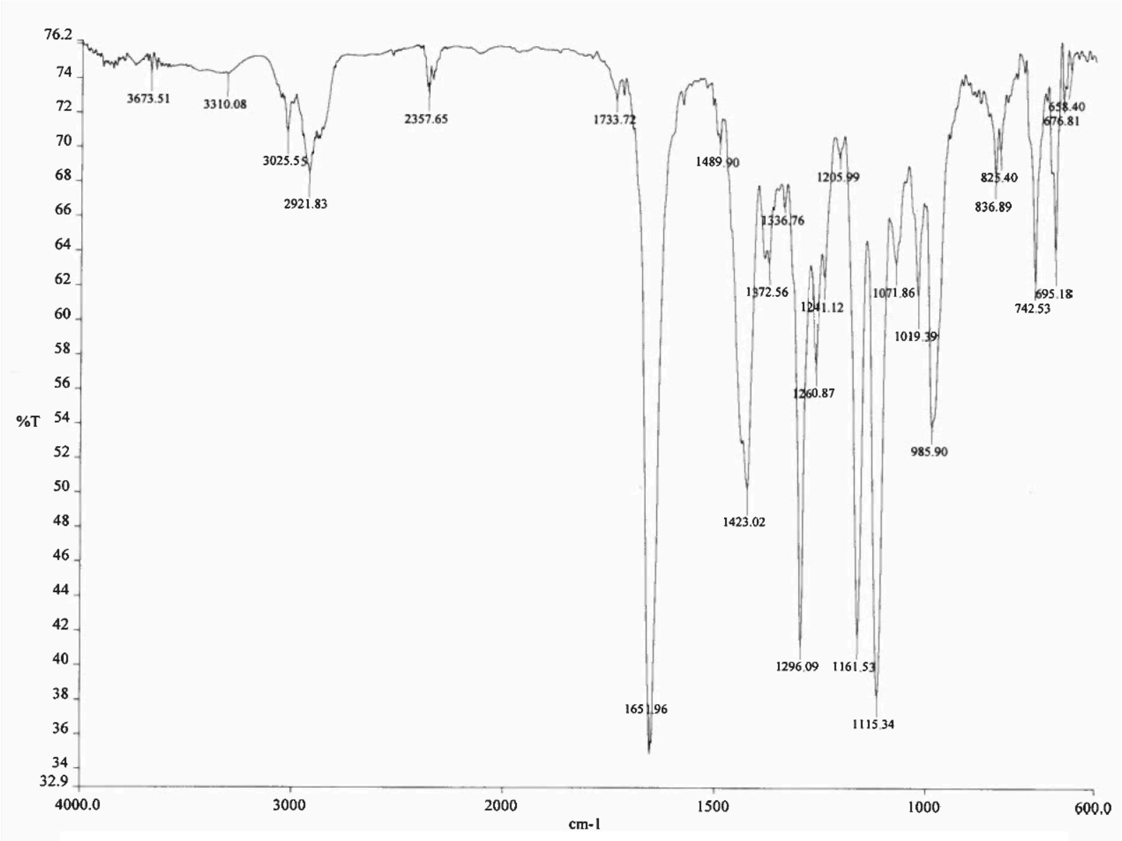


$^{13}$C NMR (100 MHz, $CD_3OD$) of compound **6c**.

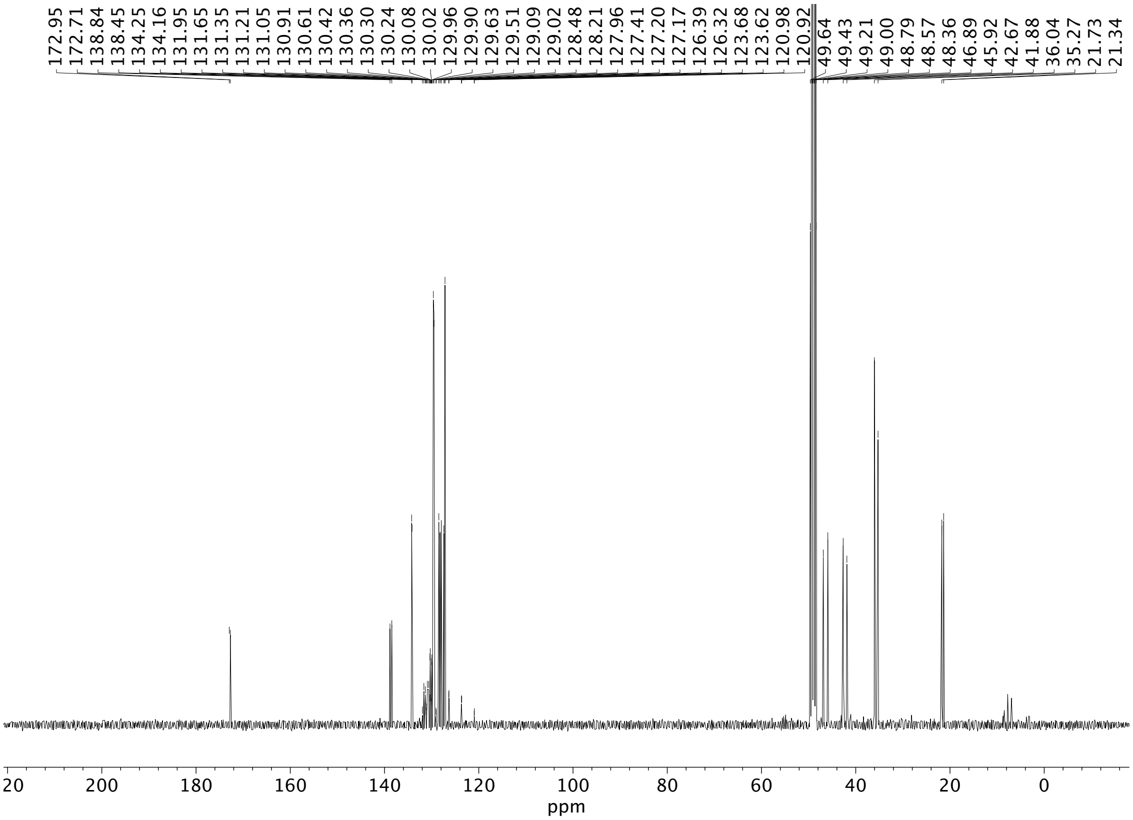


***6d***

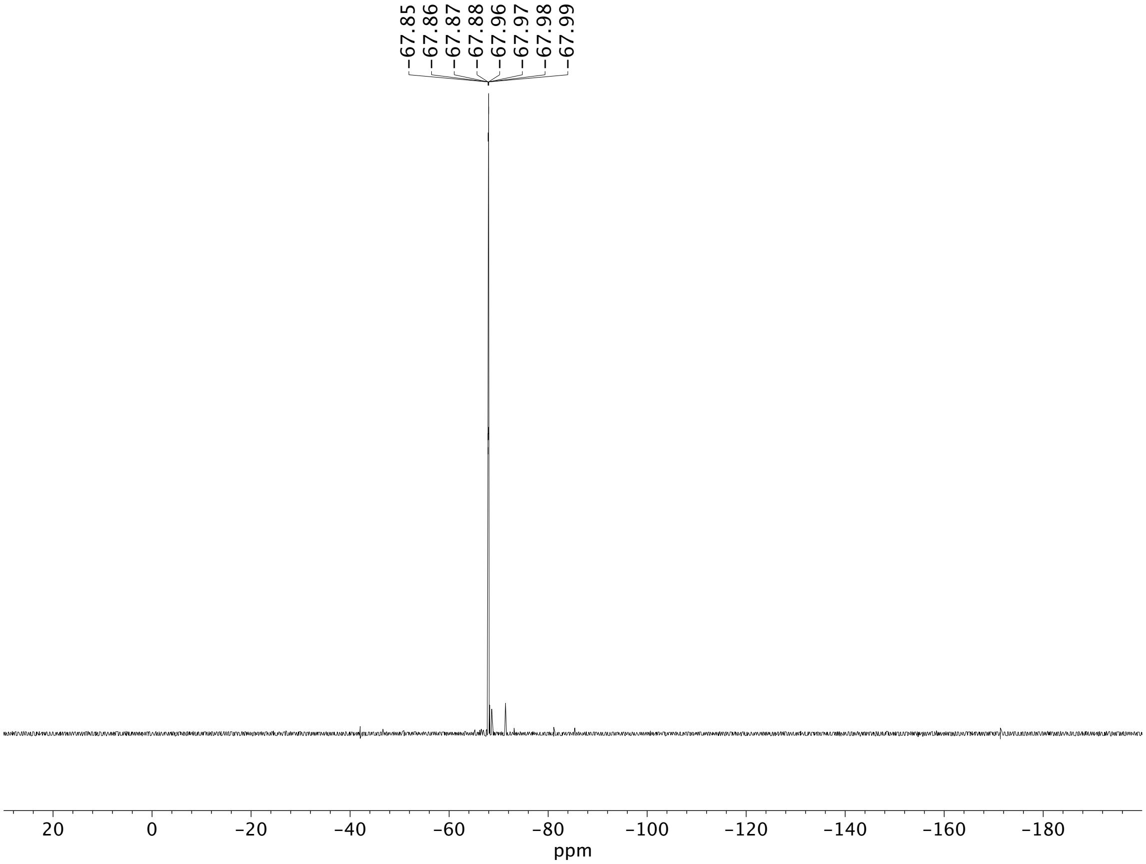
$^1$H NMR (400 MHz, CD$_3$OD) of compound **6d**.



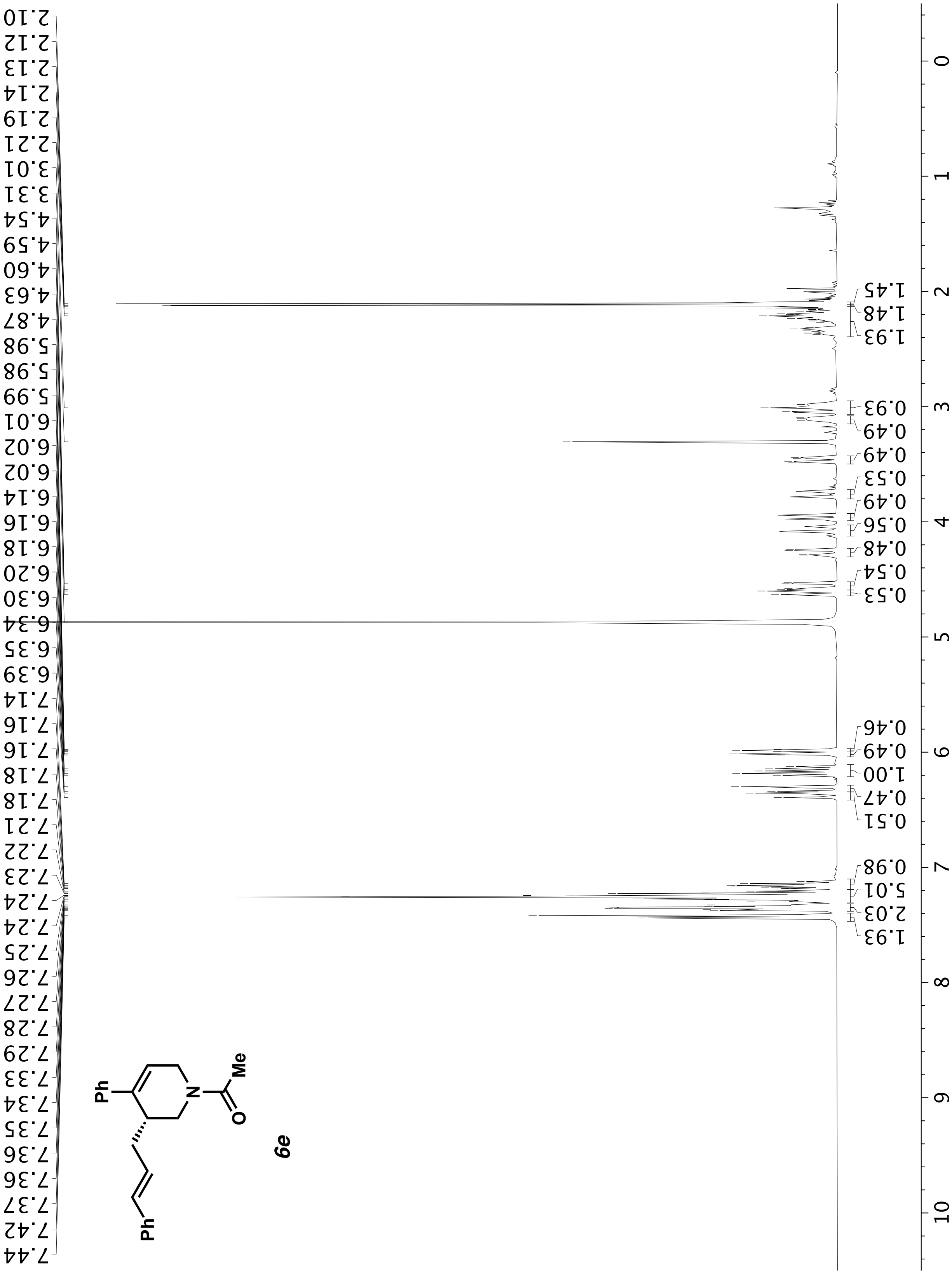
Infrared spectrum (Thin Film, NaCl) of compound **6d**.



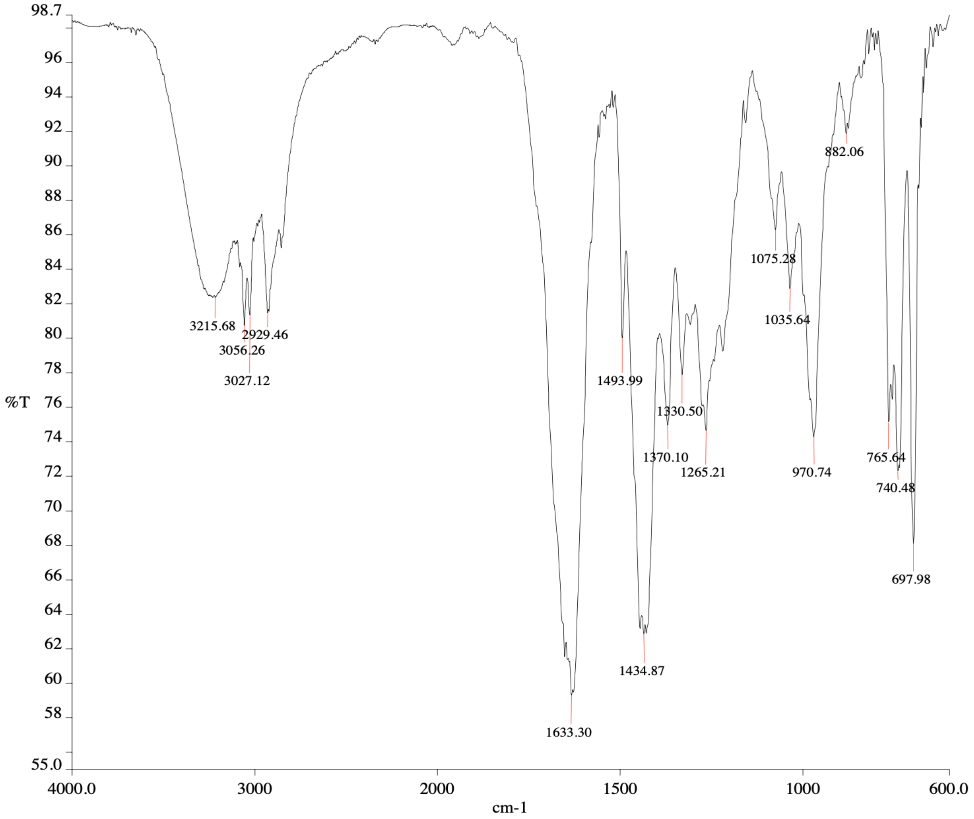
$^{13}$C NMR (100 MHz, CD$_3$OD) of compound **6d**.



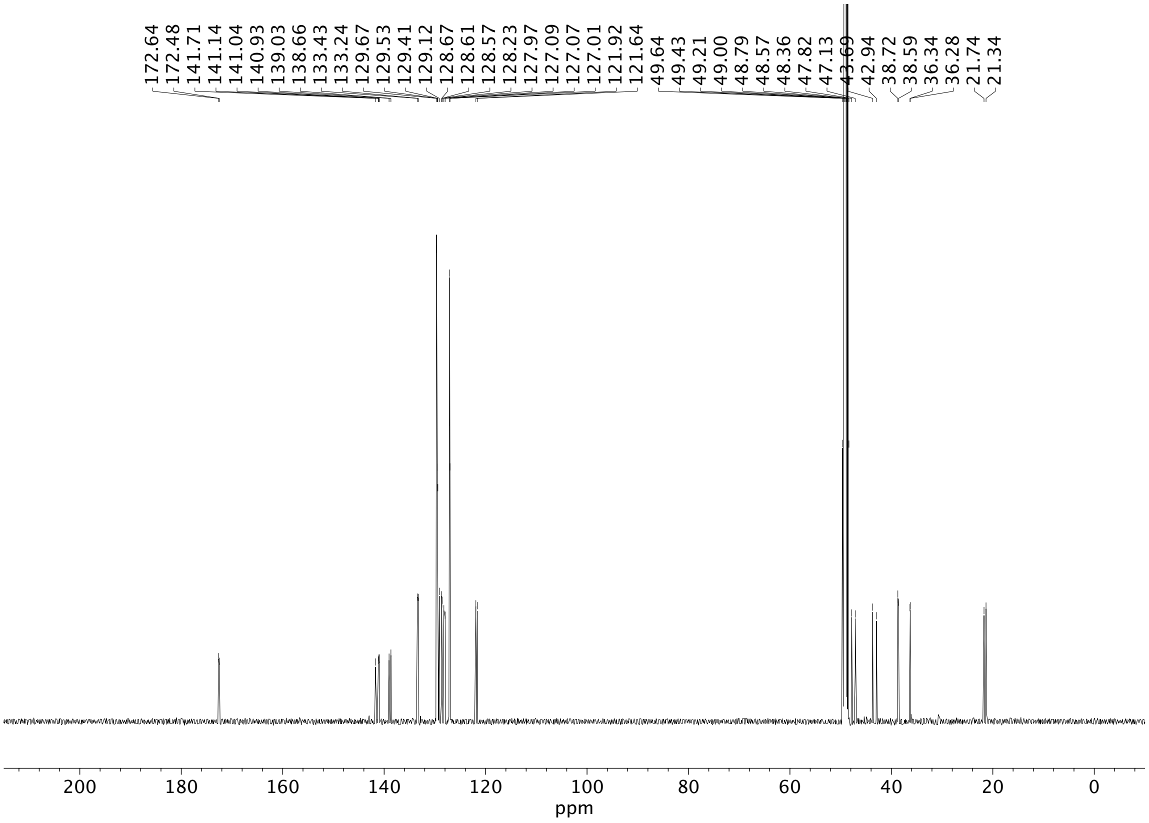
$^{19}$F NMR (282 MHz, CD$_3$OD) of compound **6d**.



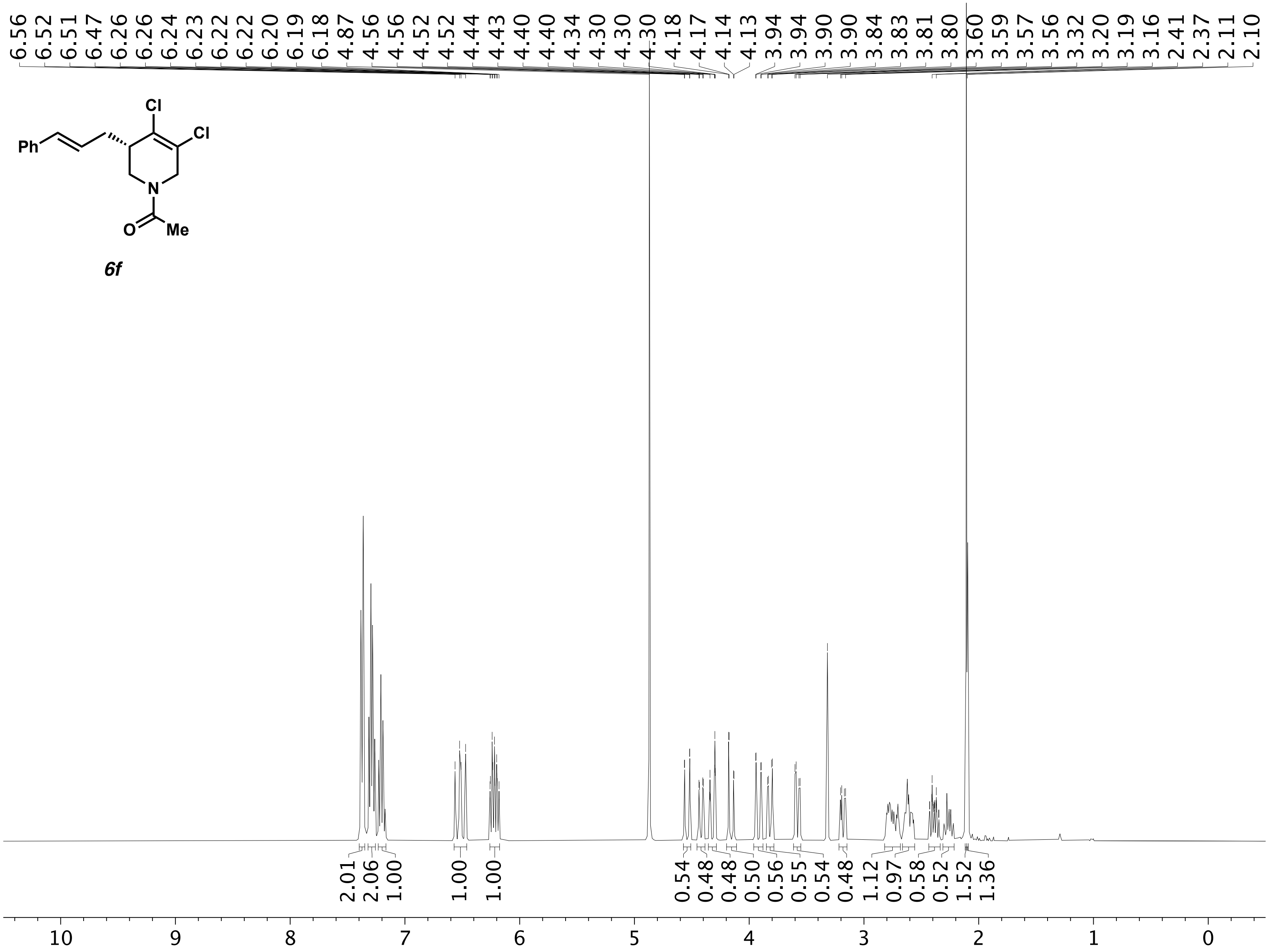
$^1$H NMR (400 MHz, $CD_3OD$) of compound **6e**.



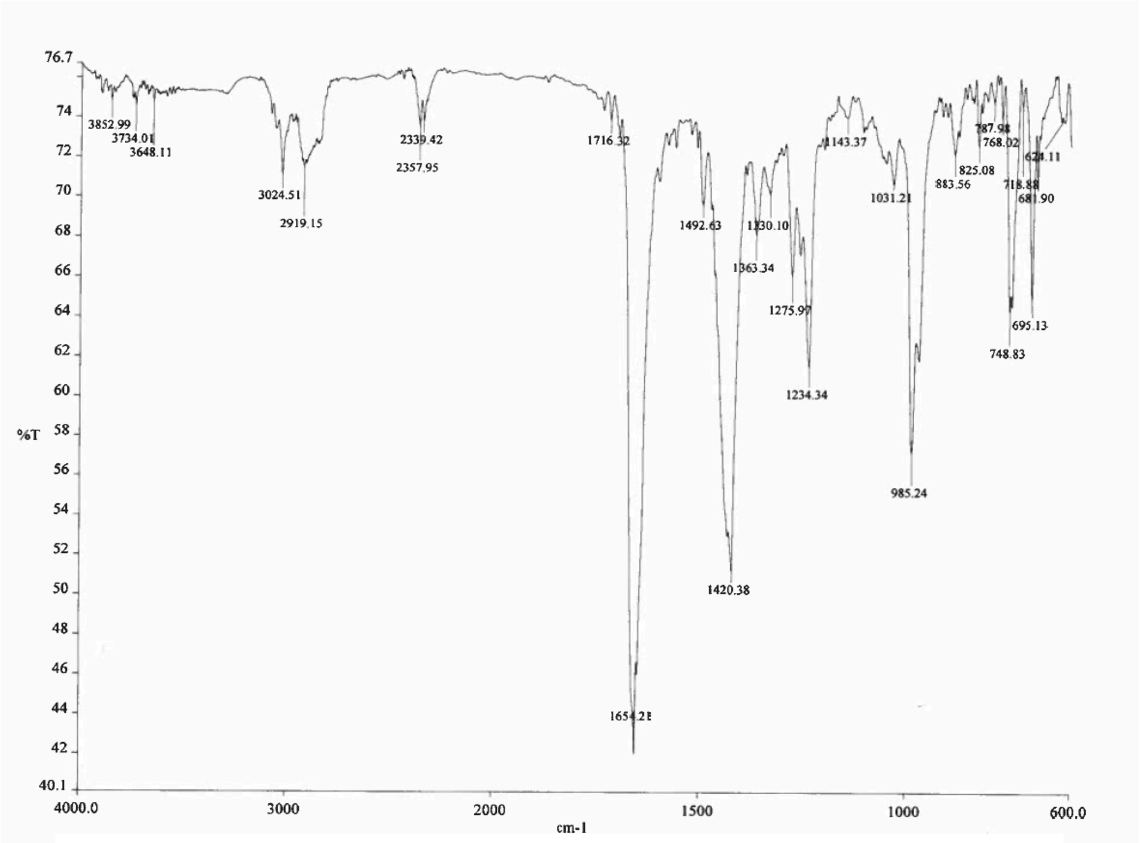
Infrared spectrum (Thin Film, NaCl) of compound **6e**.



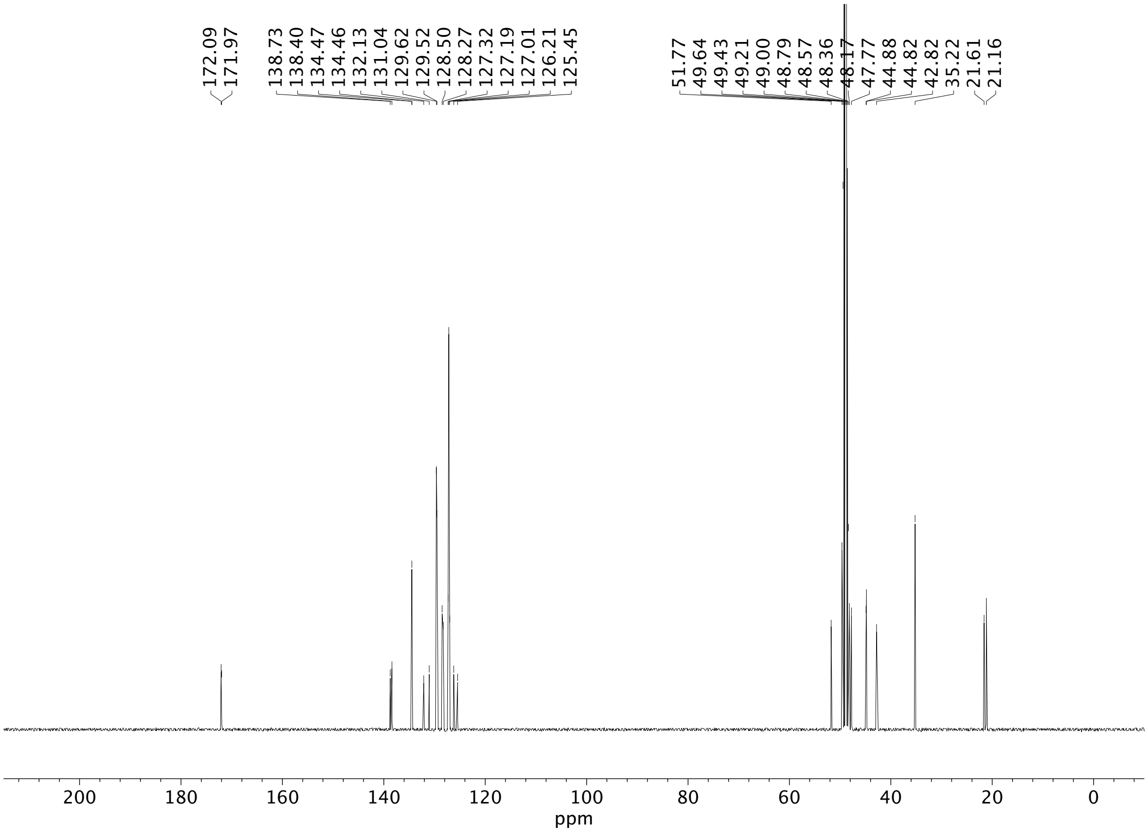
$^{13}$C NMR (100 MHz, CD$_3$OD) of compound **6e**.



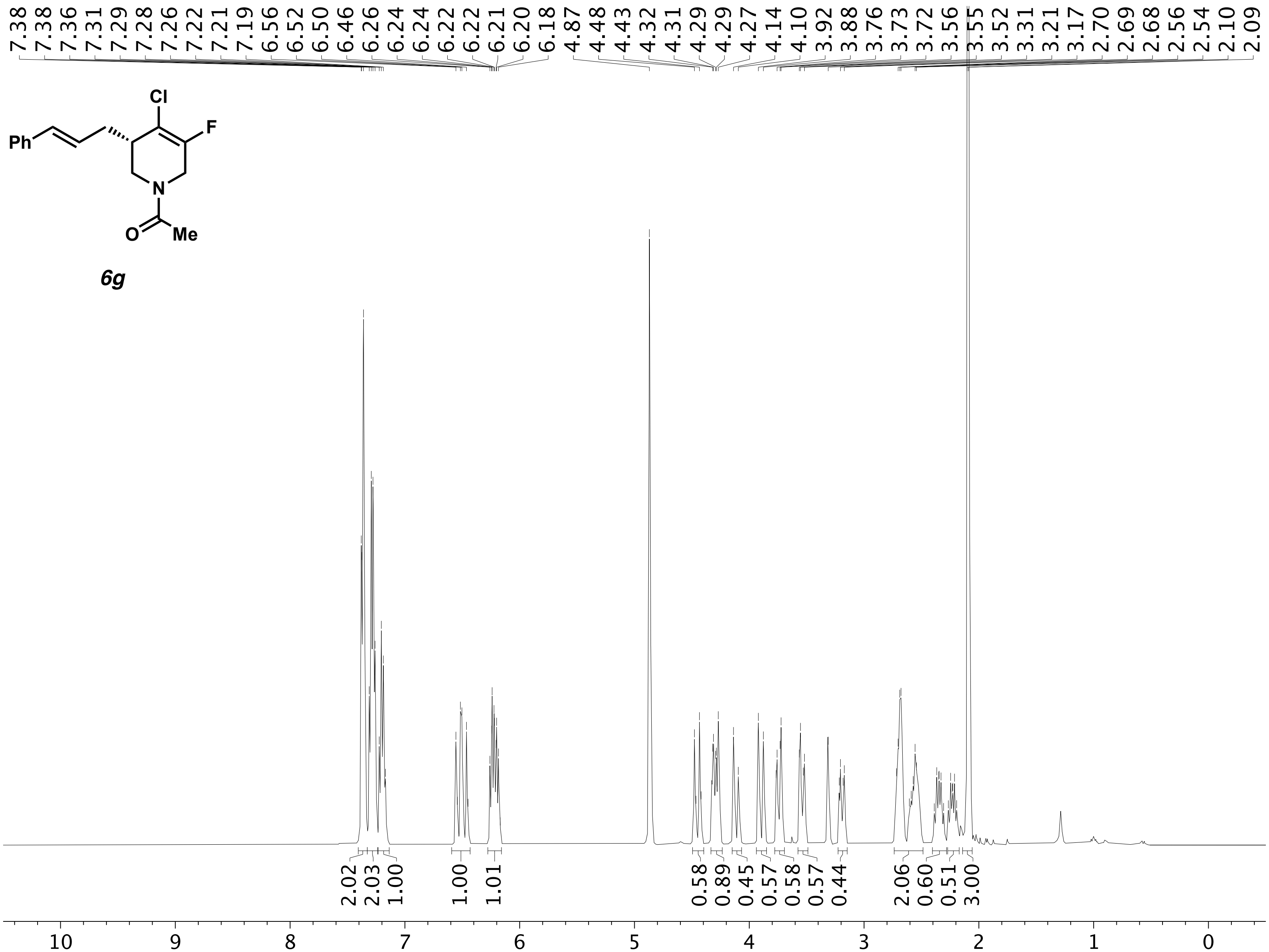
$^1$H NMR (400 MHz, CD$_3$OD) of compound **6f**.



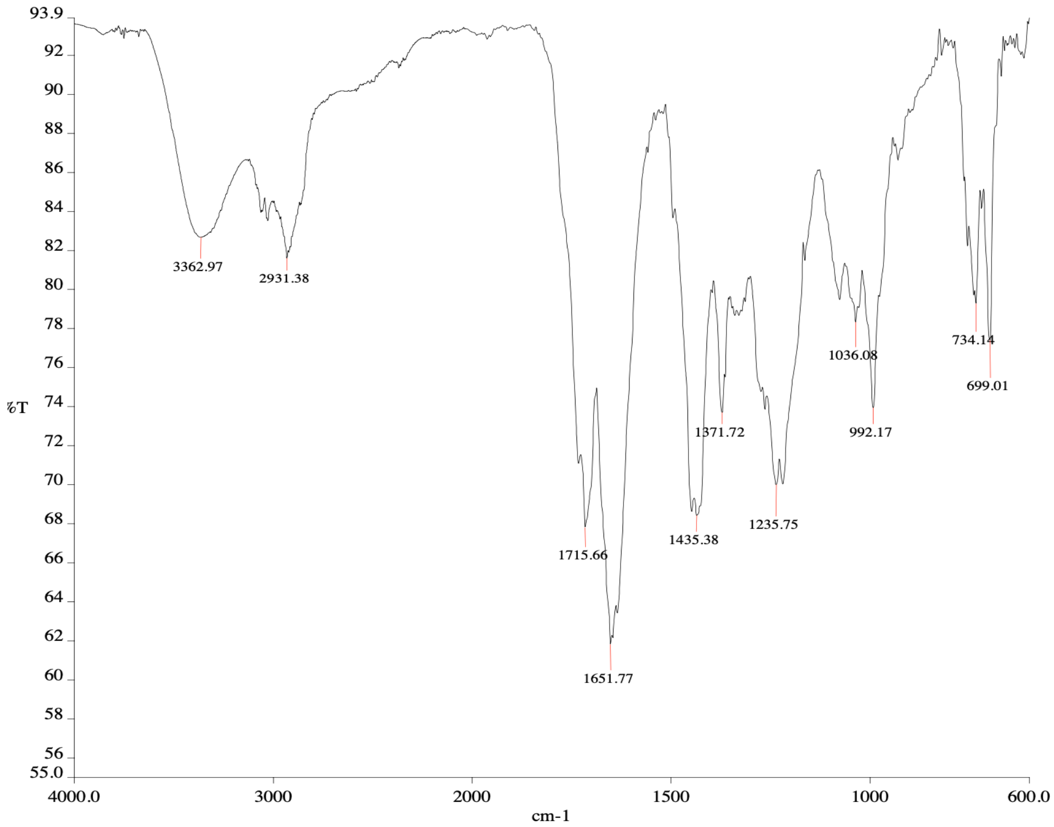
Infrared spectrum (Thin Film, NaCl) of compound **6f**.



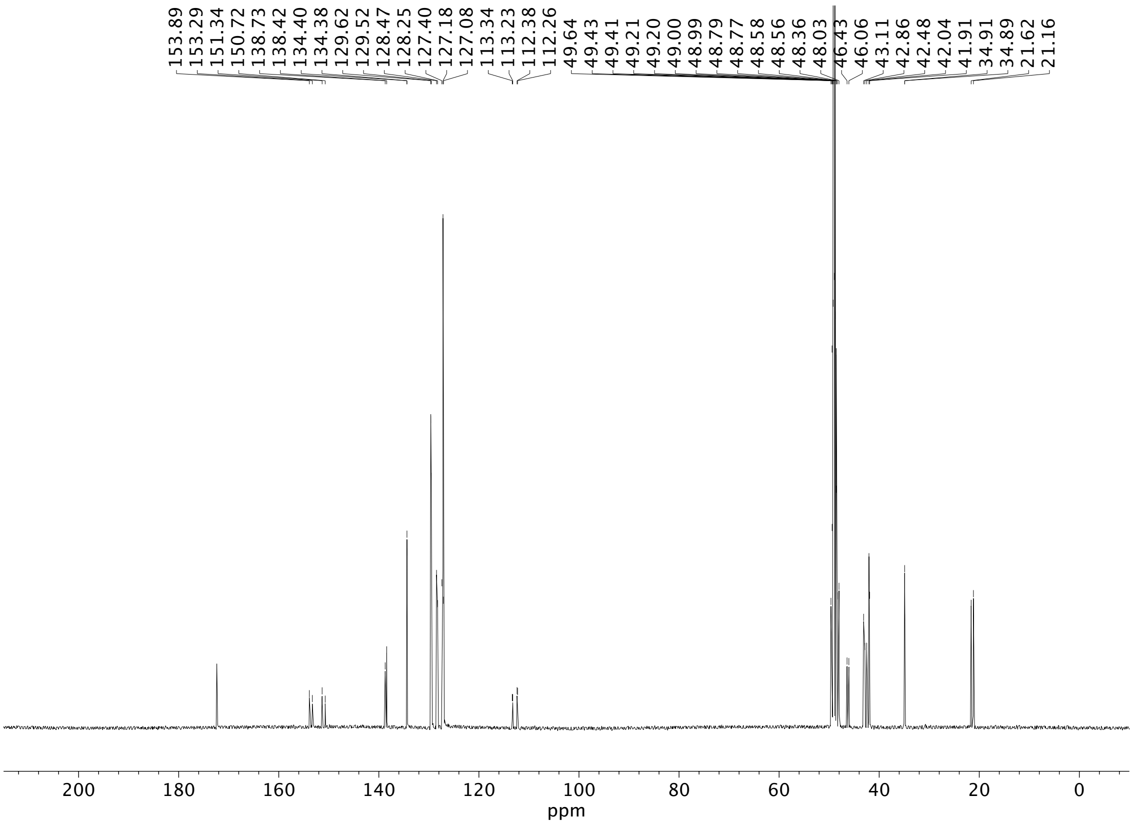
$^{13}$C NMR (100 MHz, CD$_3$OD) of compound **6f**.



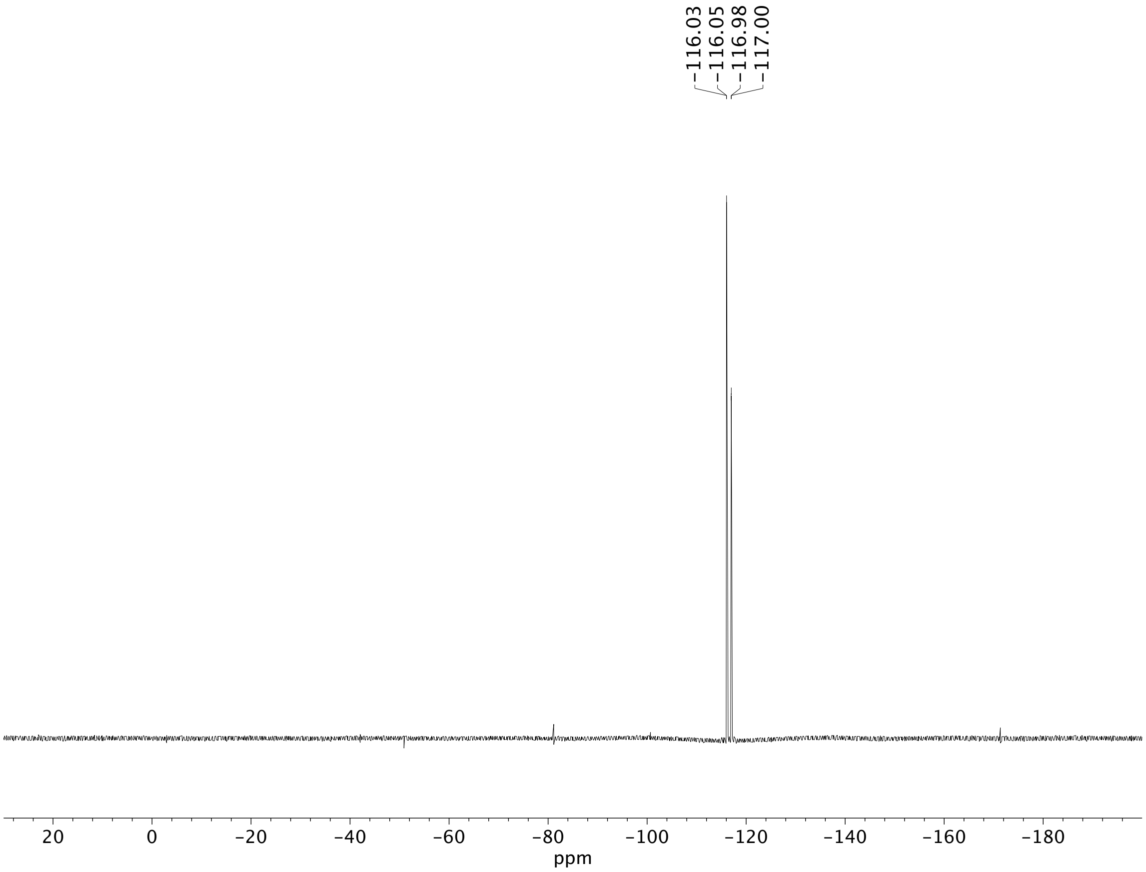
$^1$H NMR (400 MHz, CD$_3$OD) of compound **6g**.



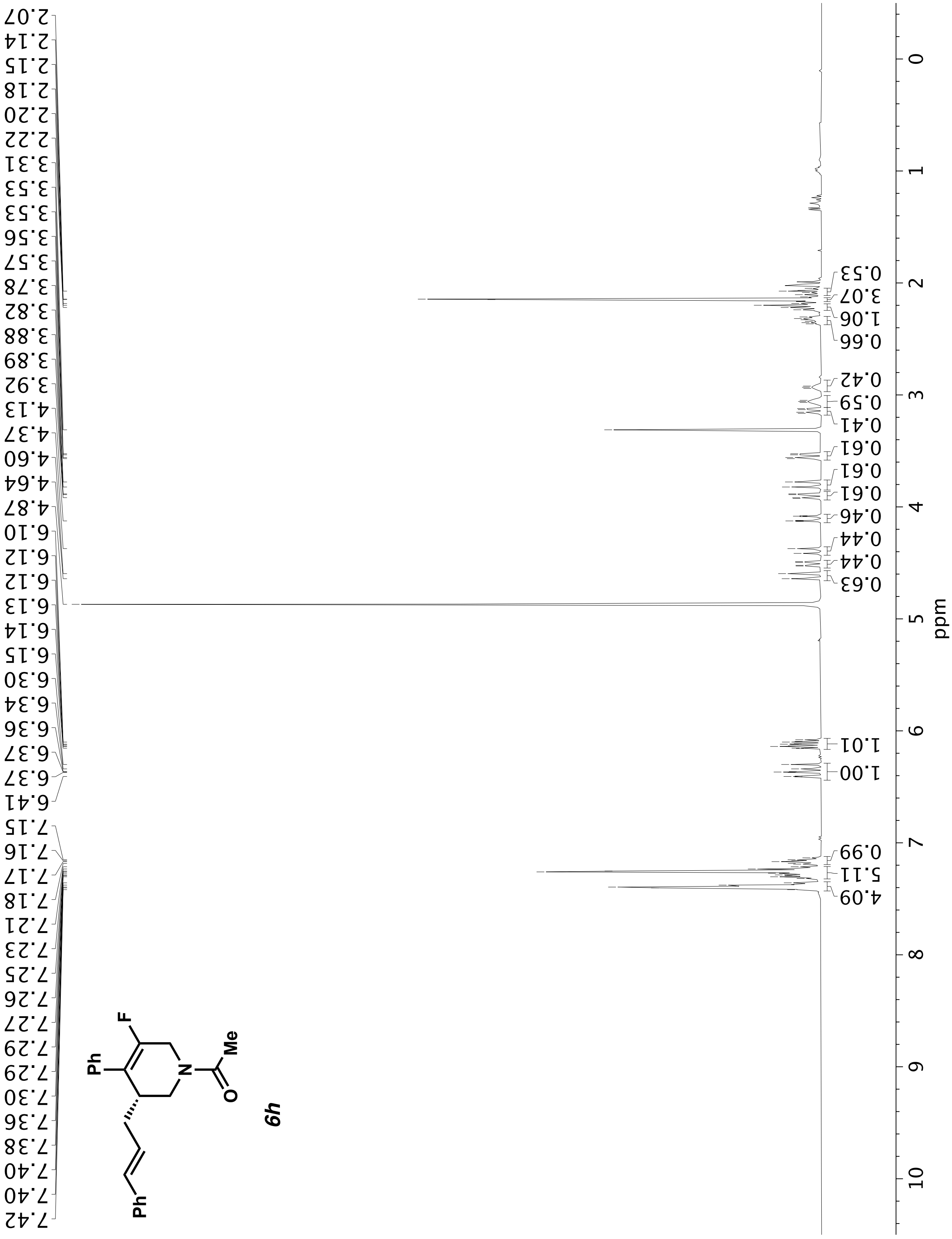
Infrared spectrum (Thin Film, NaCl) of compound **6g**.



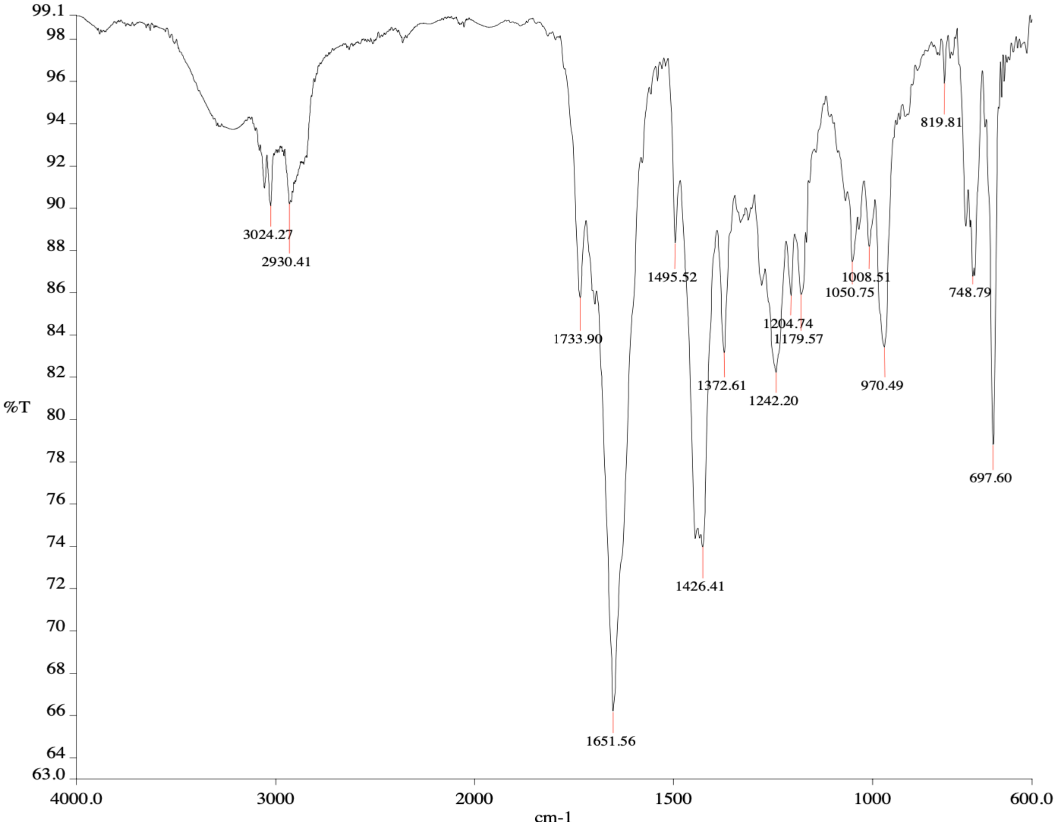
$^{13}$C NMR (100 MHz, $CD_3OD$) of compound **6g**.



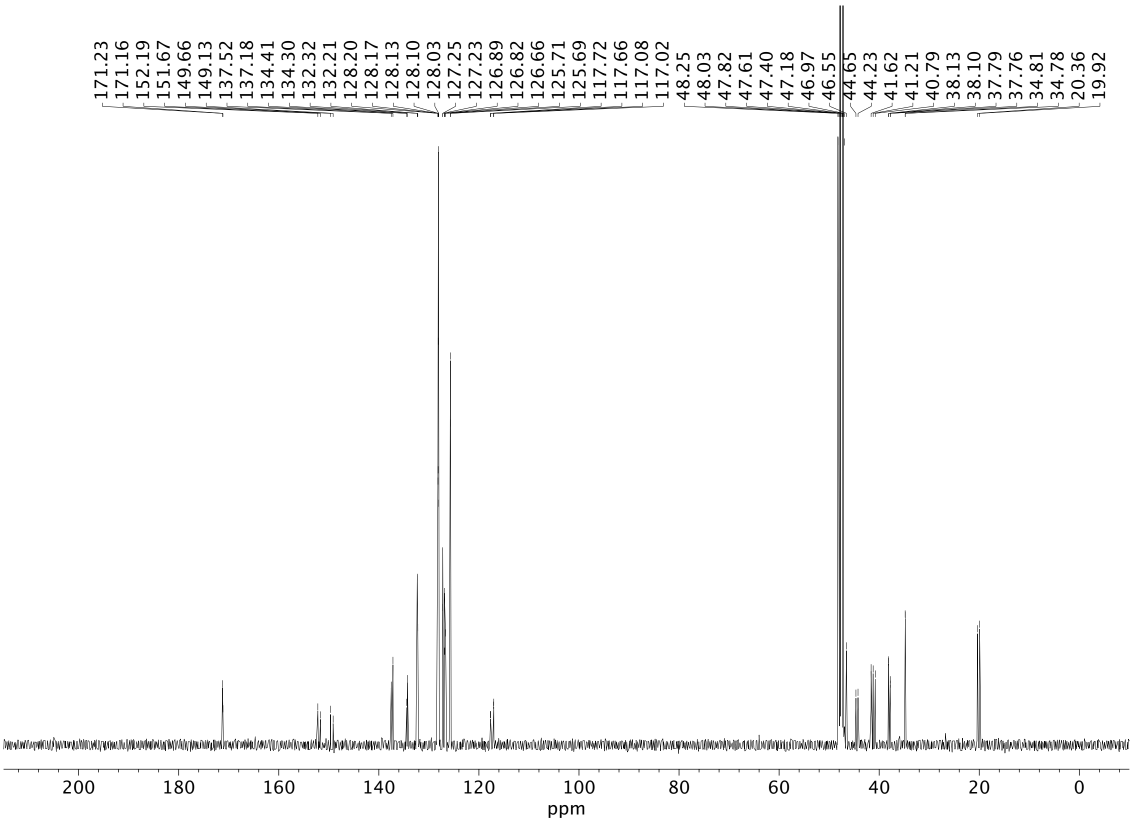
$^{19}$F NMR (282 MHz, $CD_3OD$) of compound **6g**.



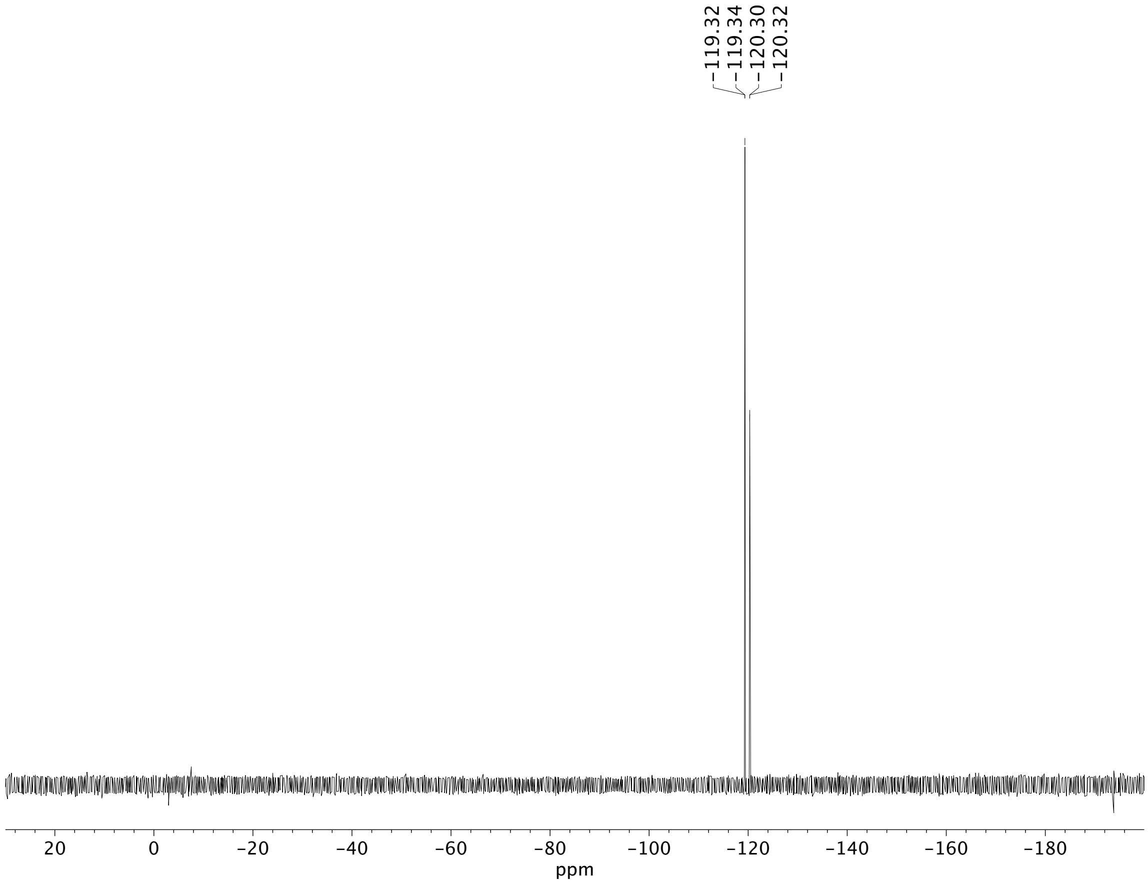
$^1$H NMR (400 MHz, $CD_3OD$) of compound **6h**.



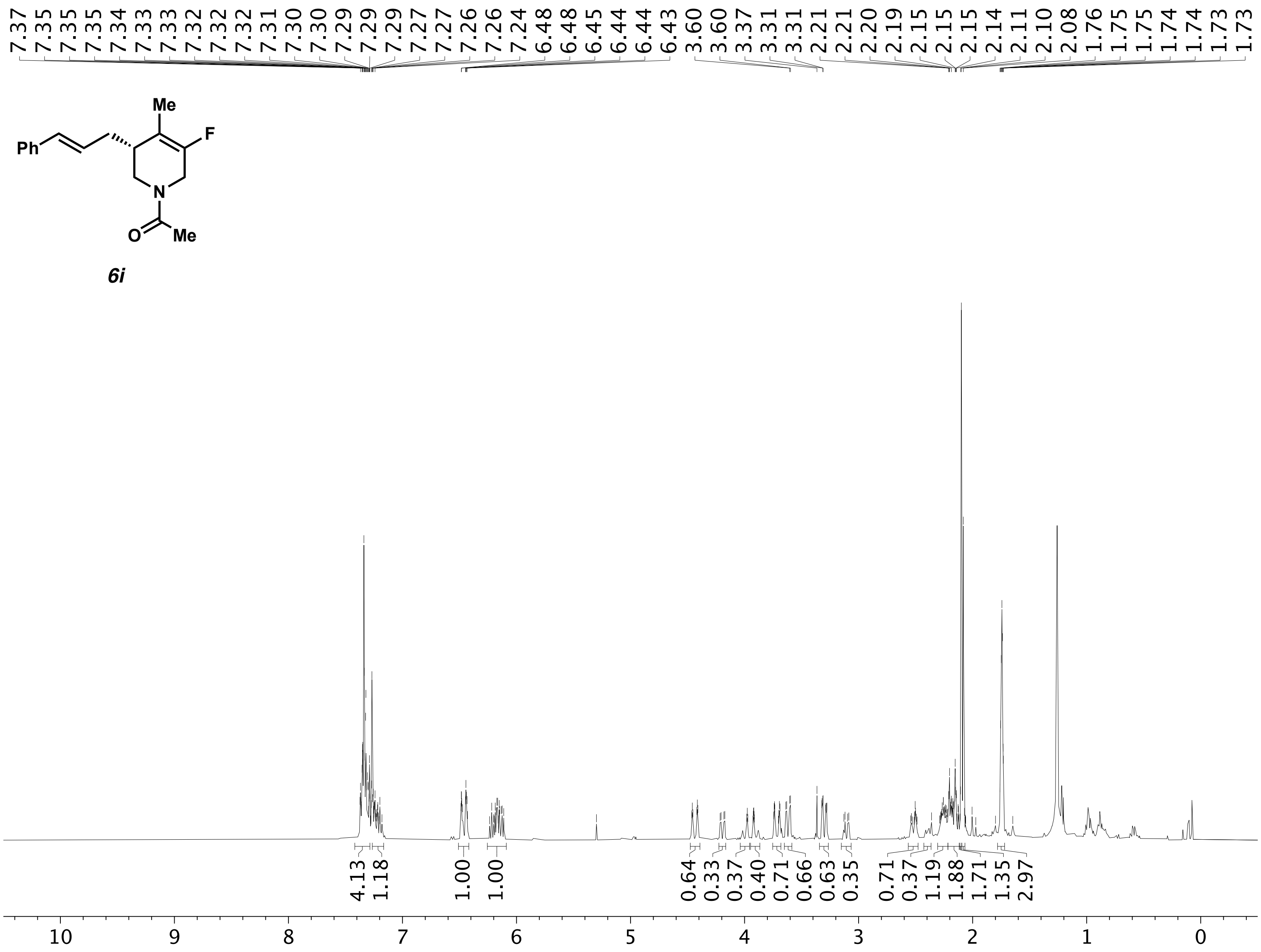
Infrared spectrum (Thin Film, NaCl) of compound **6h**.



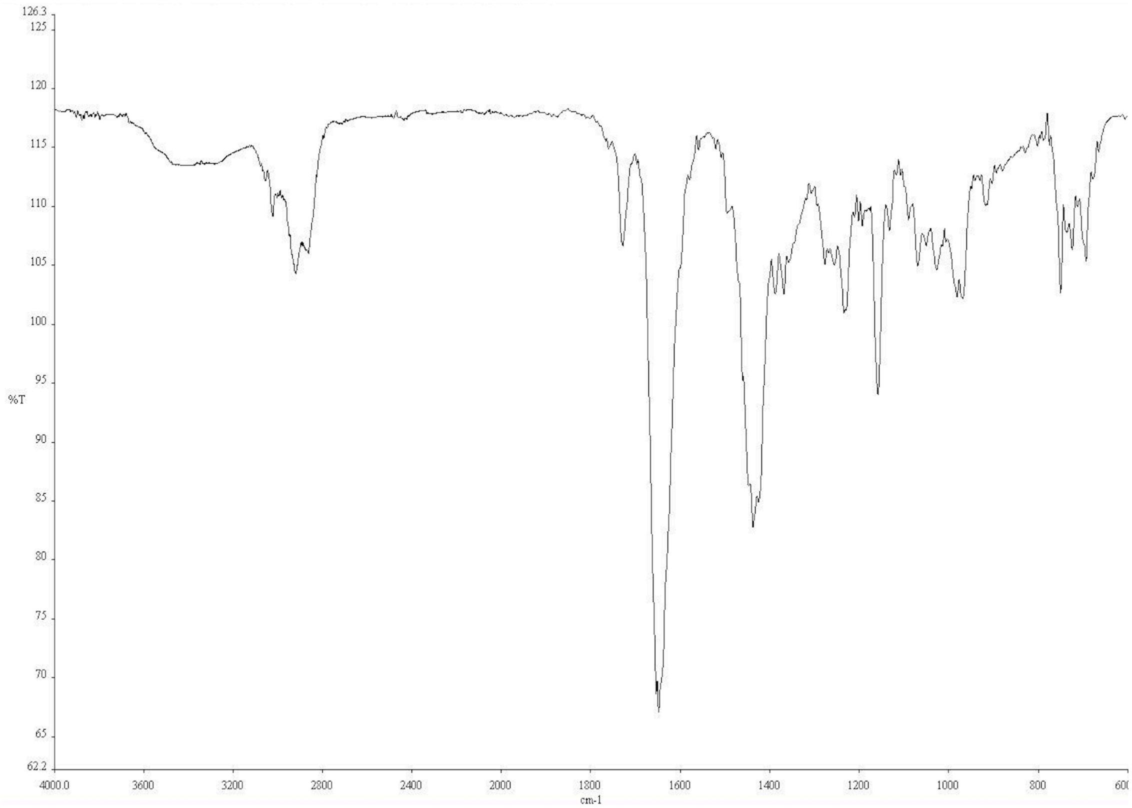
$^{13}$C NMR (100 MHz, $CD_3OD$) of compound **6h**.



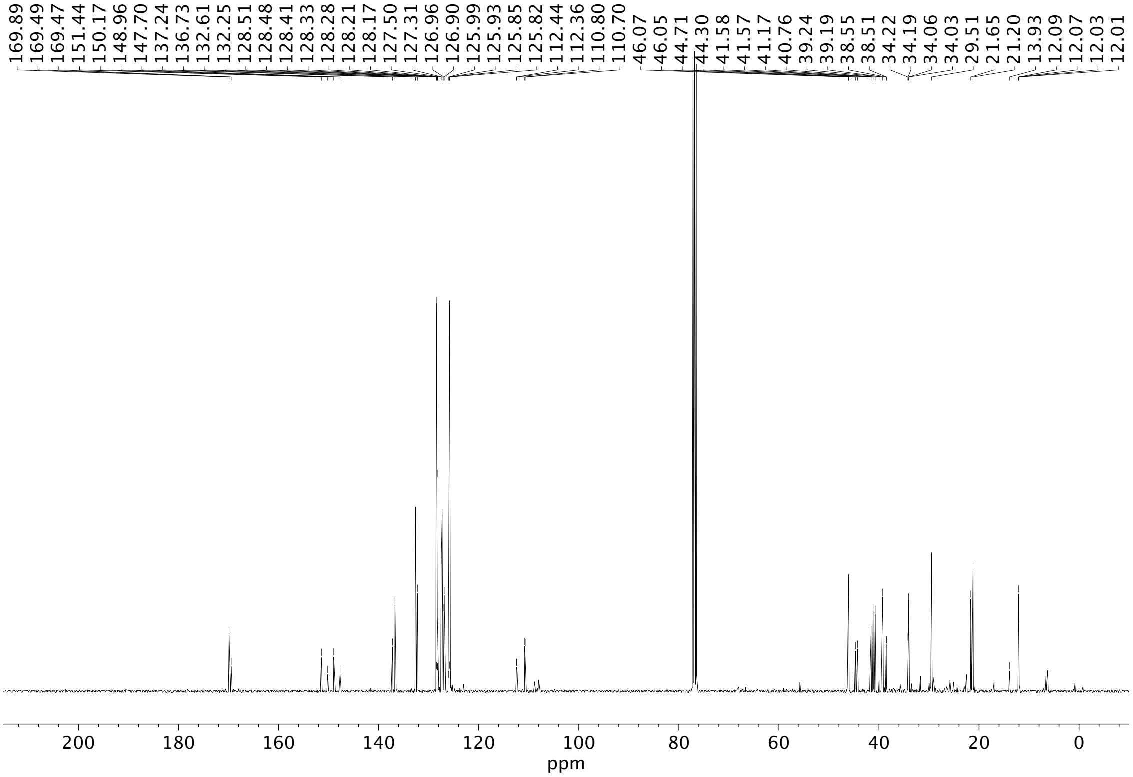
$^{19}$F NMR (282 MHz, $CD_3OD$) of compound **6h**.



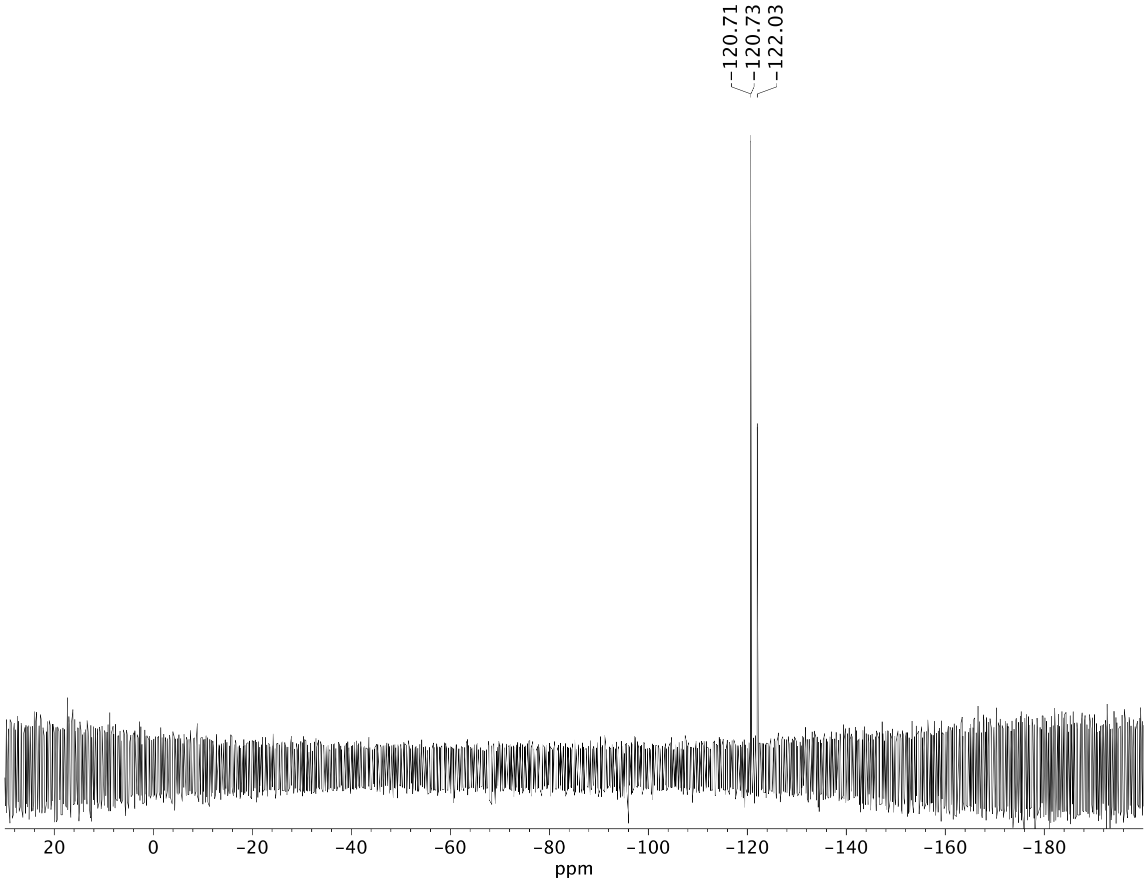
$^1$H NMR (400 MHz, CDCl$_3$) of compound **6i**.



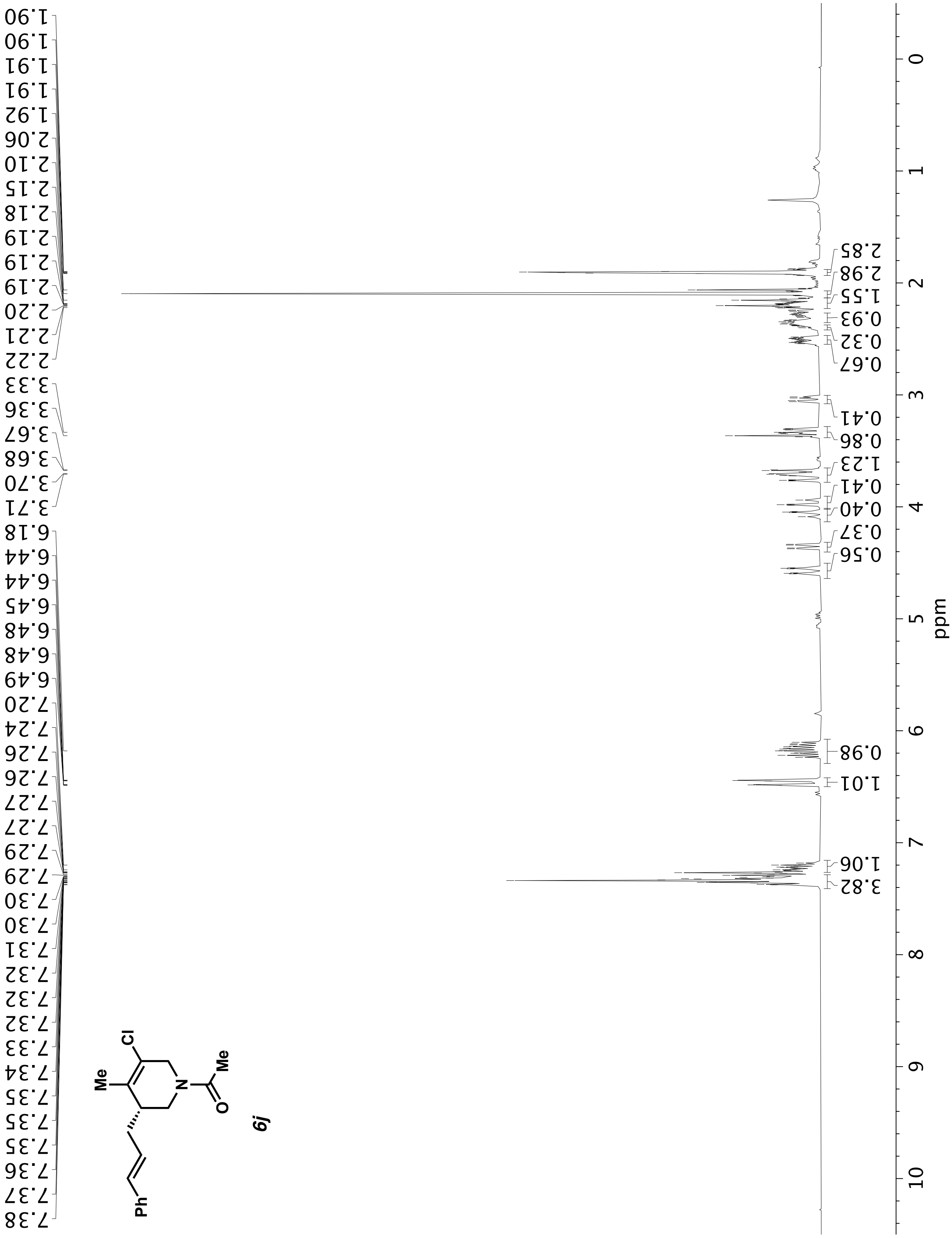
Infrared spectrum (Thin Film, NaCl) of compound **6i**.



$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **6i**.

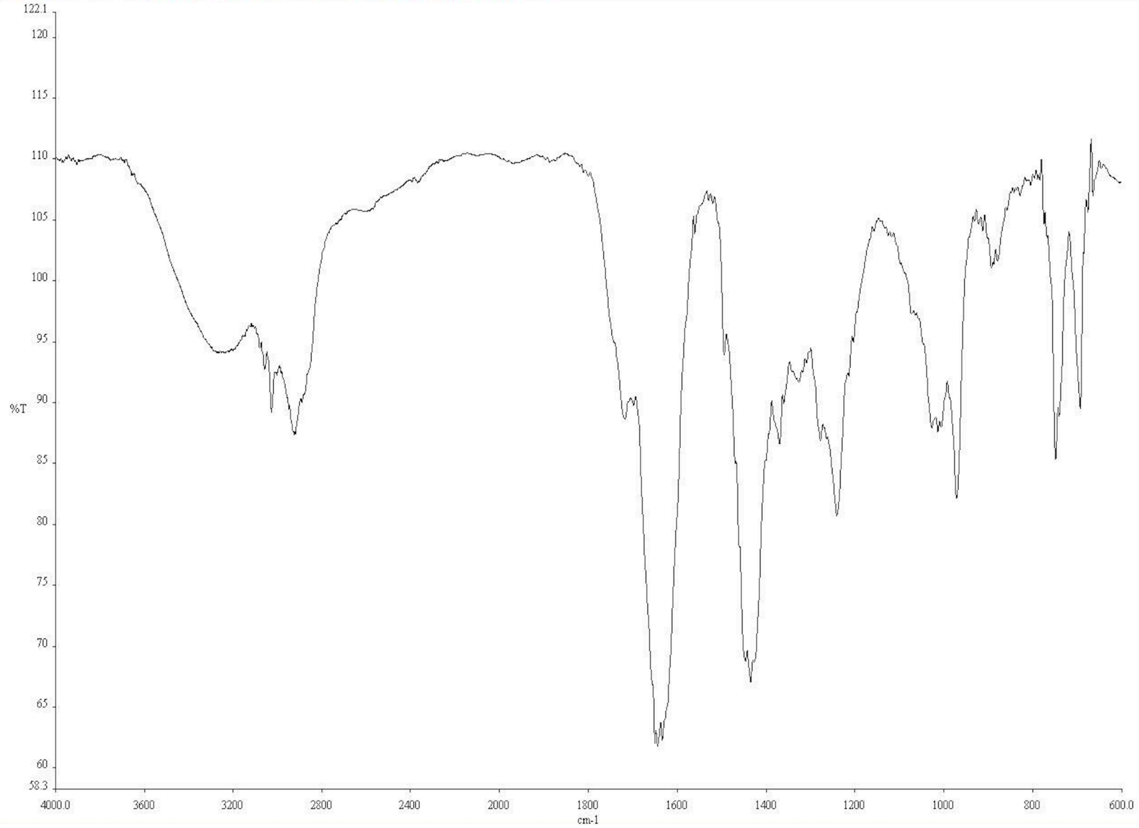


$^{19}F$ NMR (282 MHz, $CDCl_3$) of compound **6i**.

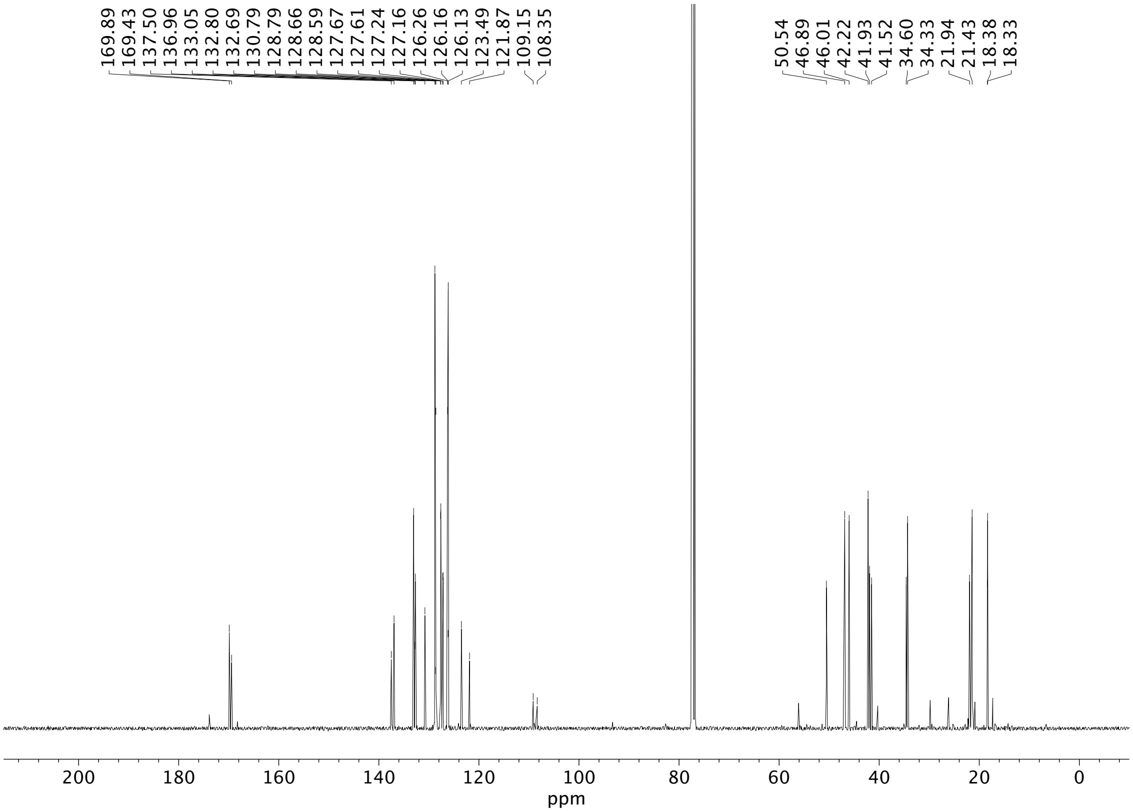


***6j***

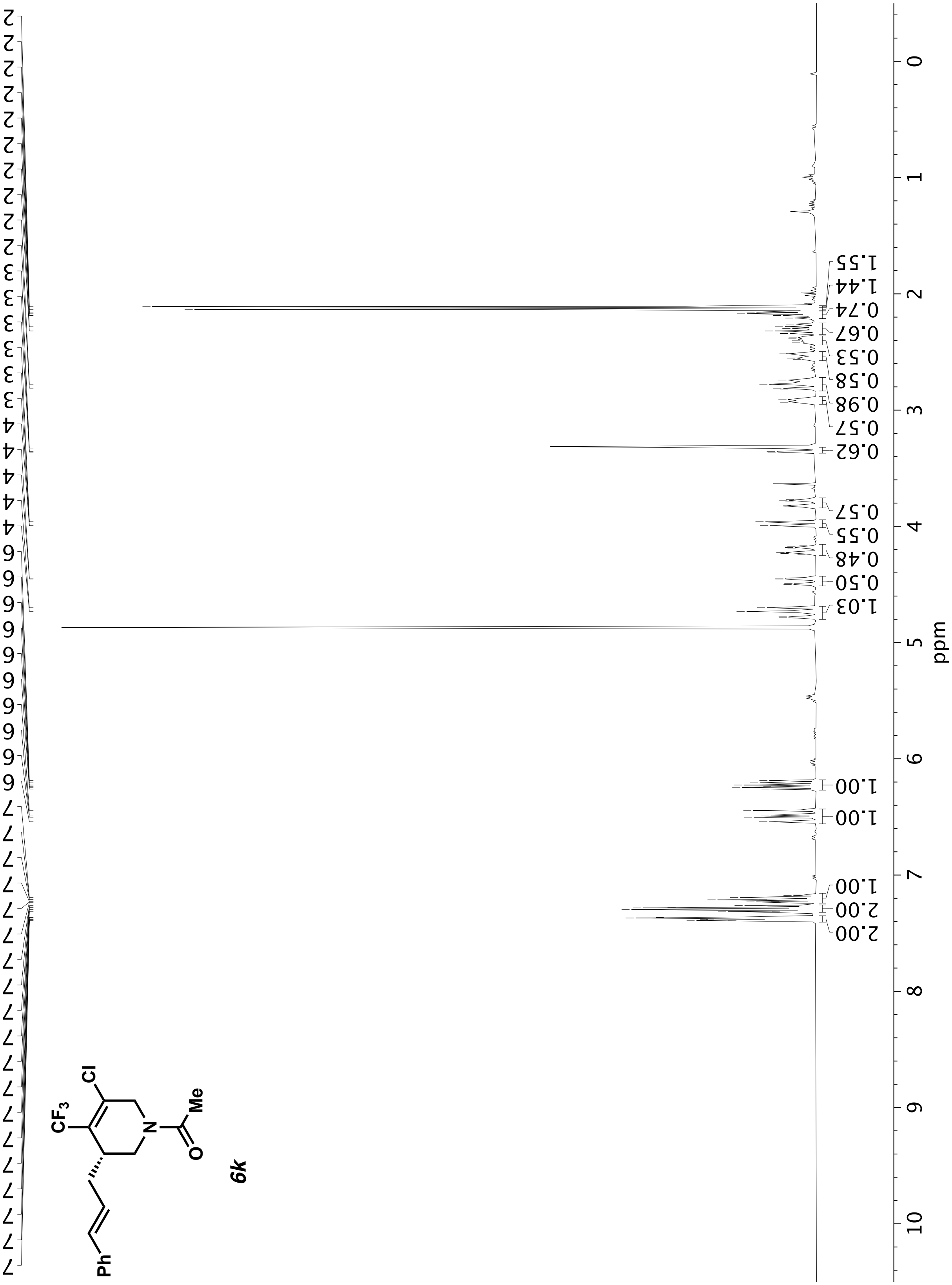
$^1$H NMR (400 MHz, CDCl$_3$) of compound **6j**



Infrared spectrum (Thin Film, NaCl) of compound **6j**.

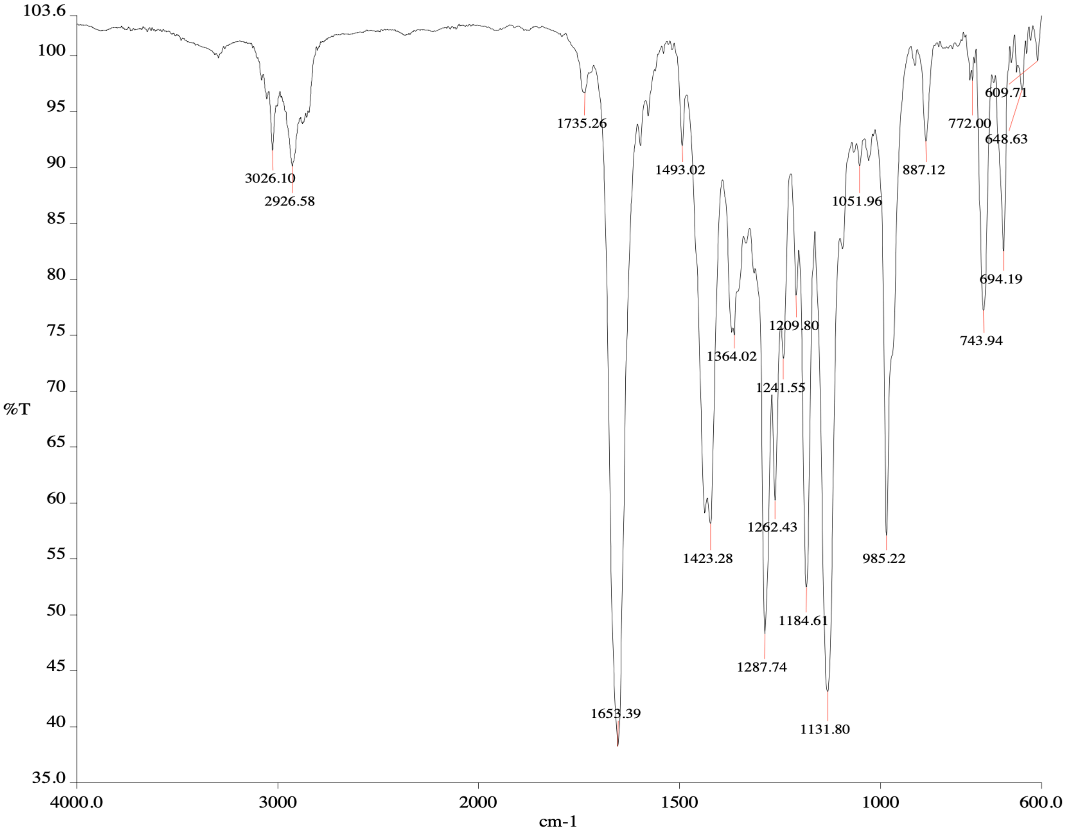


$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **6j**.

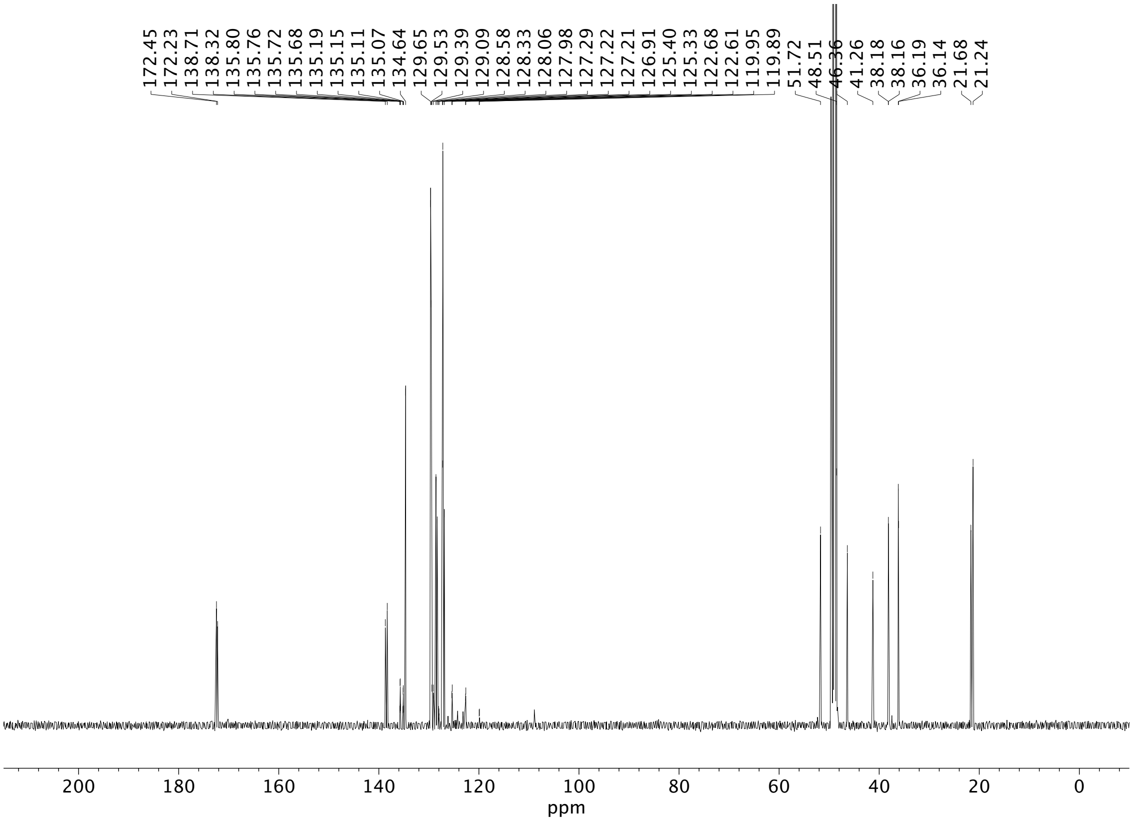


**6k**

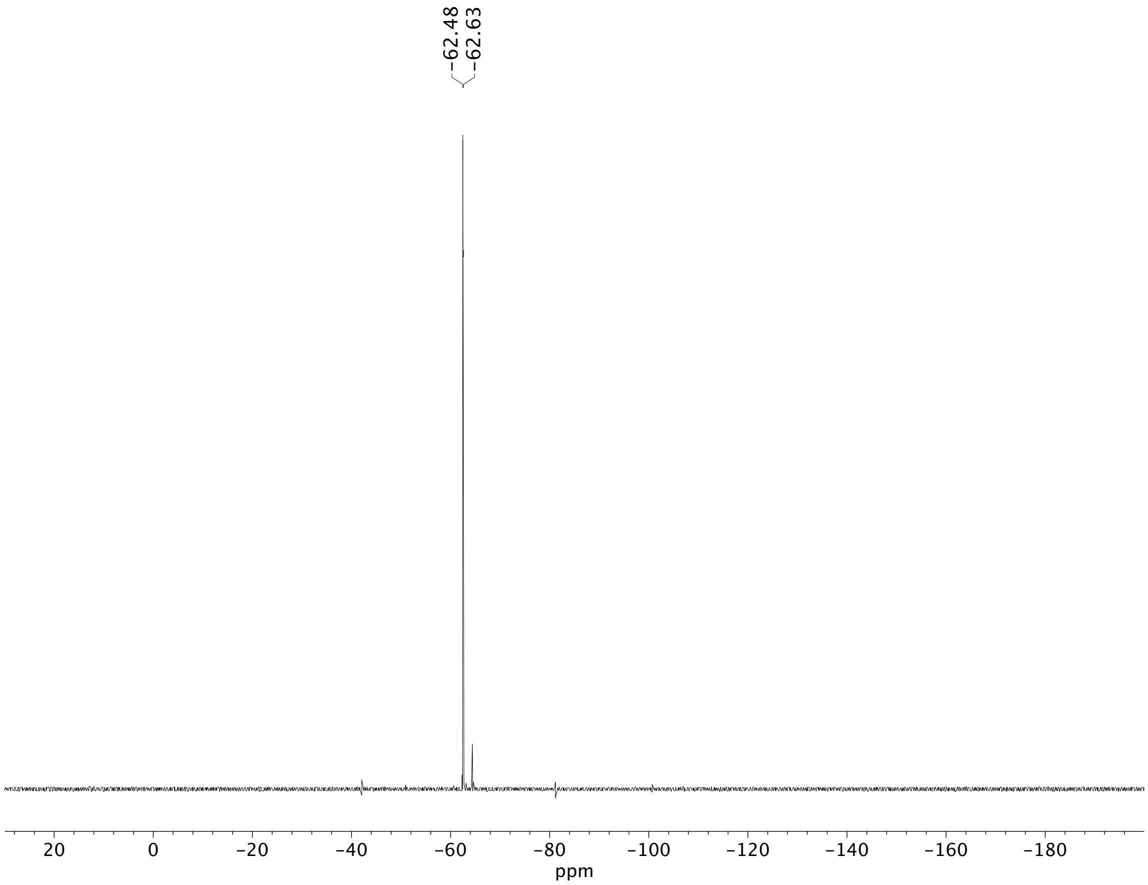
$^1$H NMR (400 MHz, CD$_3$OD) of compound **6k**.



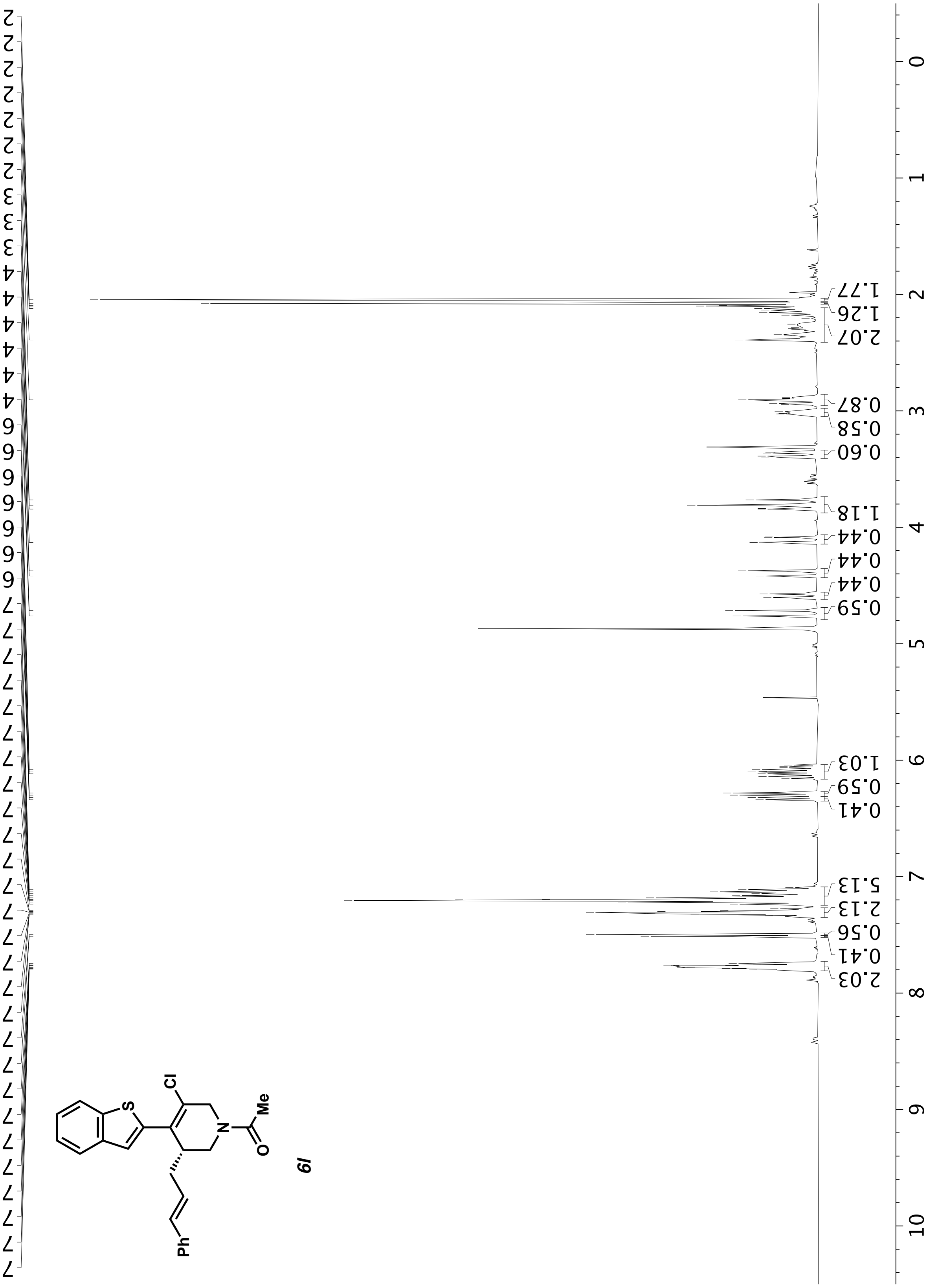
Infrared spectrum (Thin Film, NaCl) of compound **6k**.



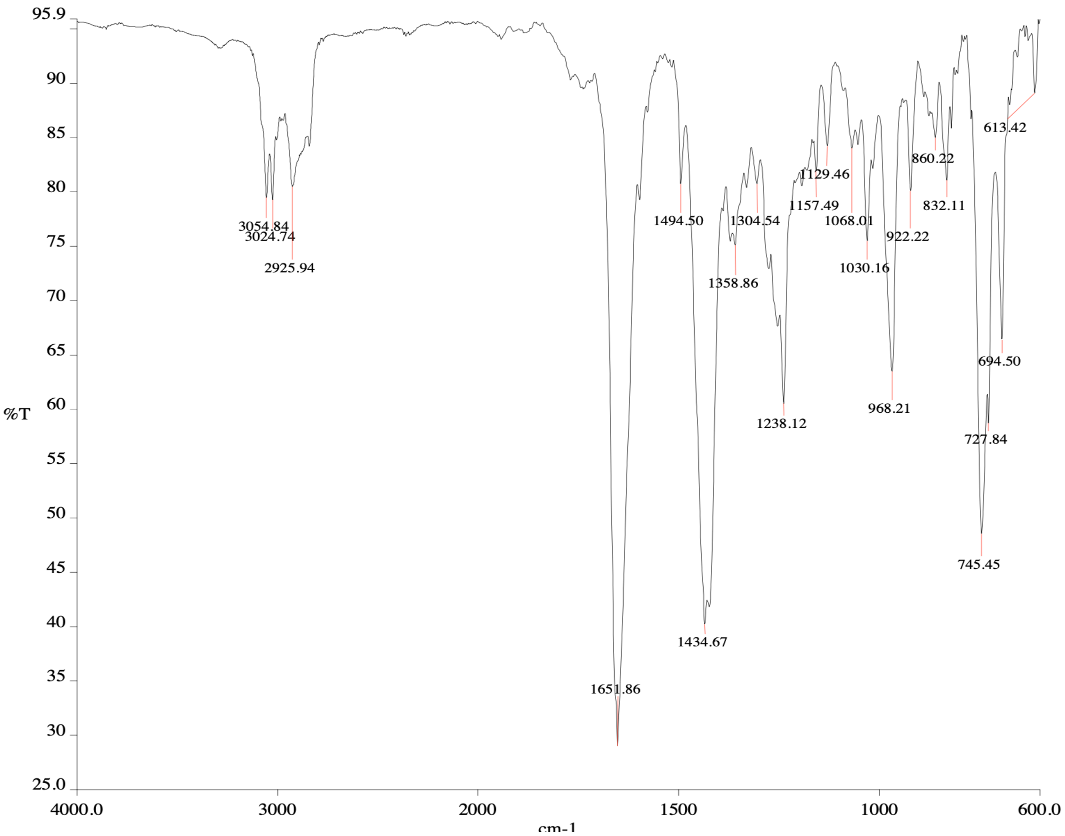
$^{13}$C NMR (100 MHz, CD$_3$OD) of compound **6k**.



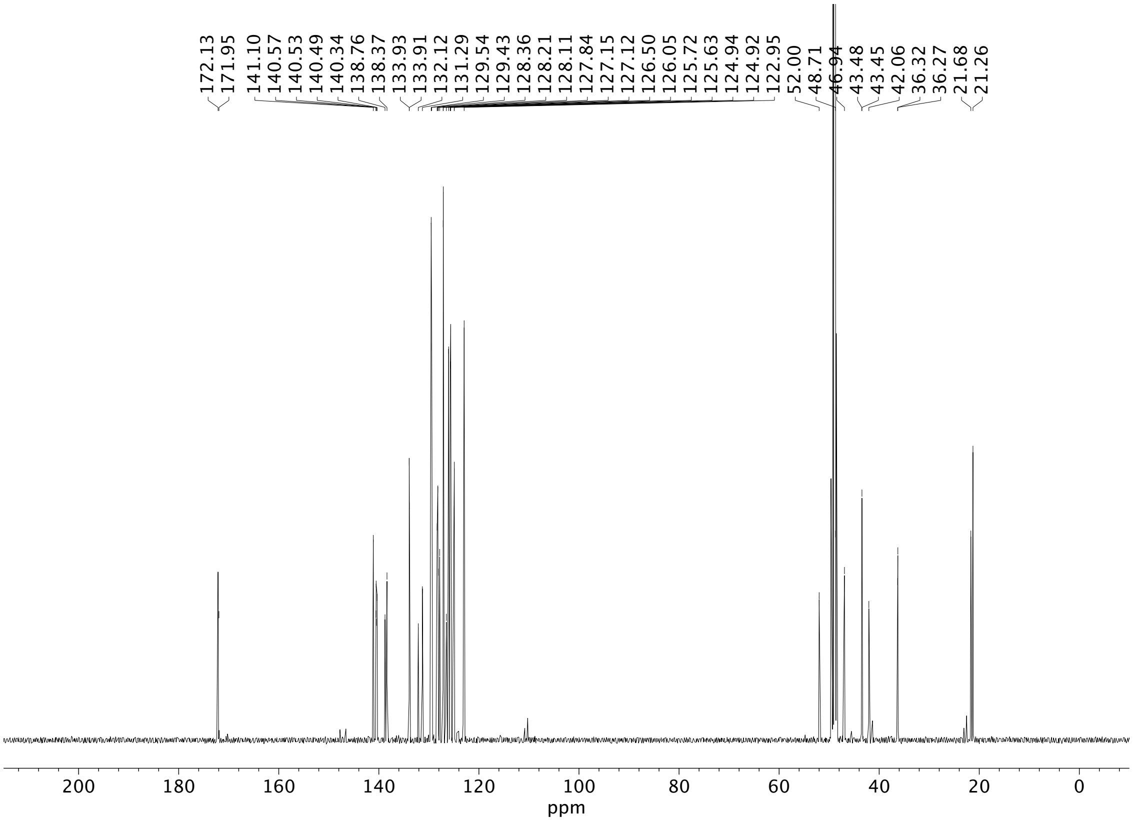
$^{19}$F NMR (282 MHz, CD$_3$OD) of compound **6k**.



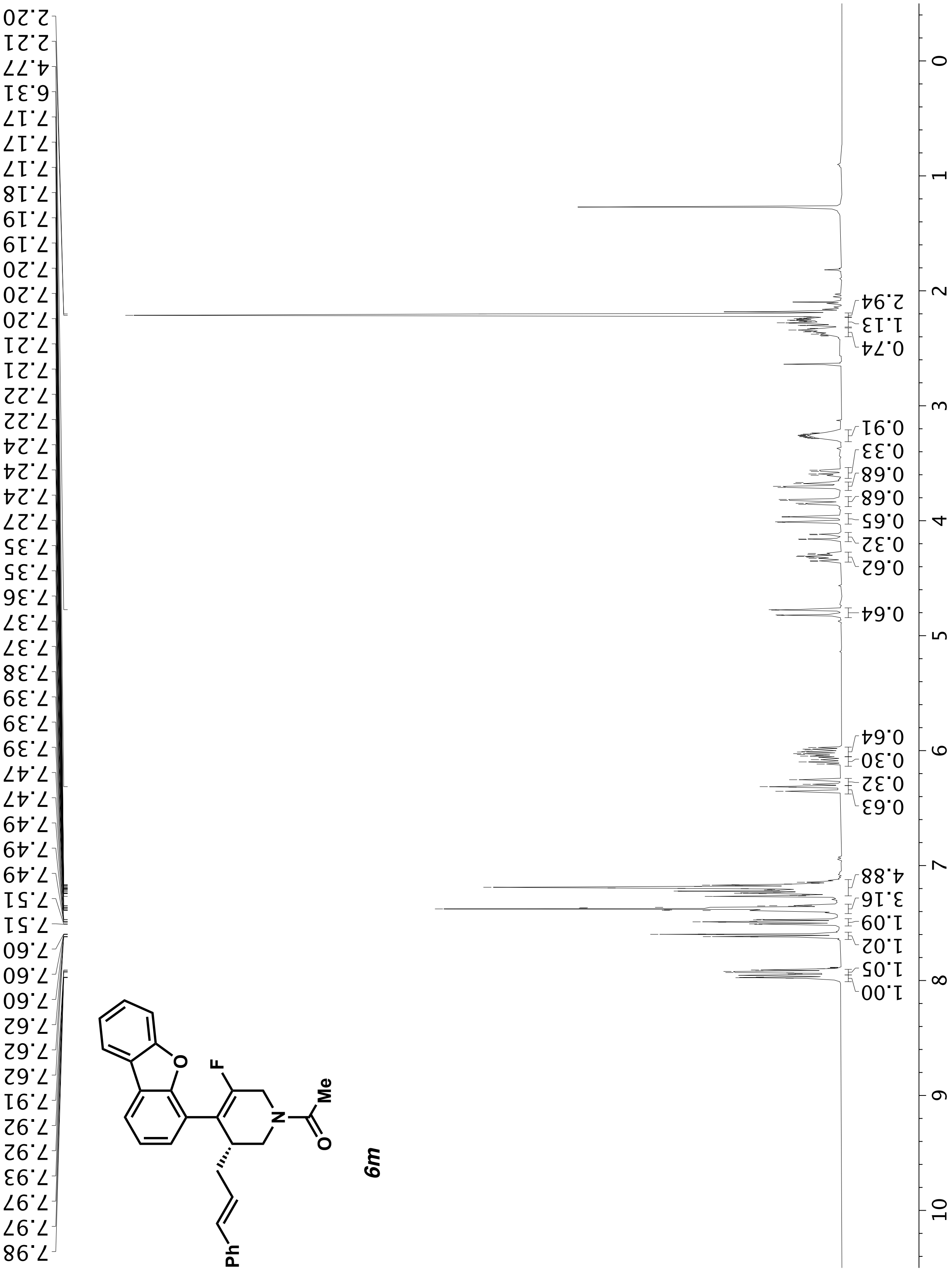
$^1$H NMR (400 MHz, CD$_3$OD) of compound **6l**.



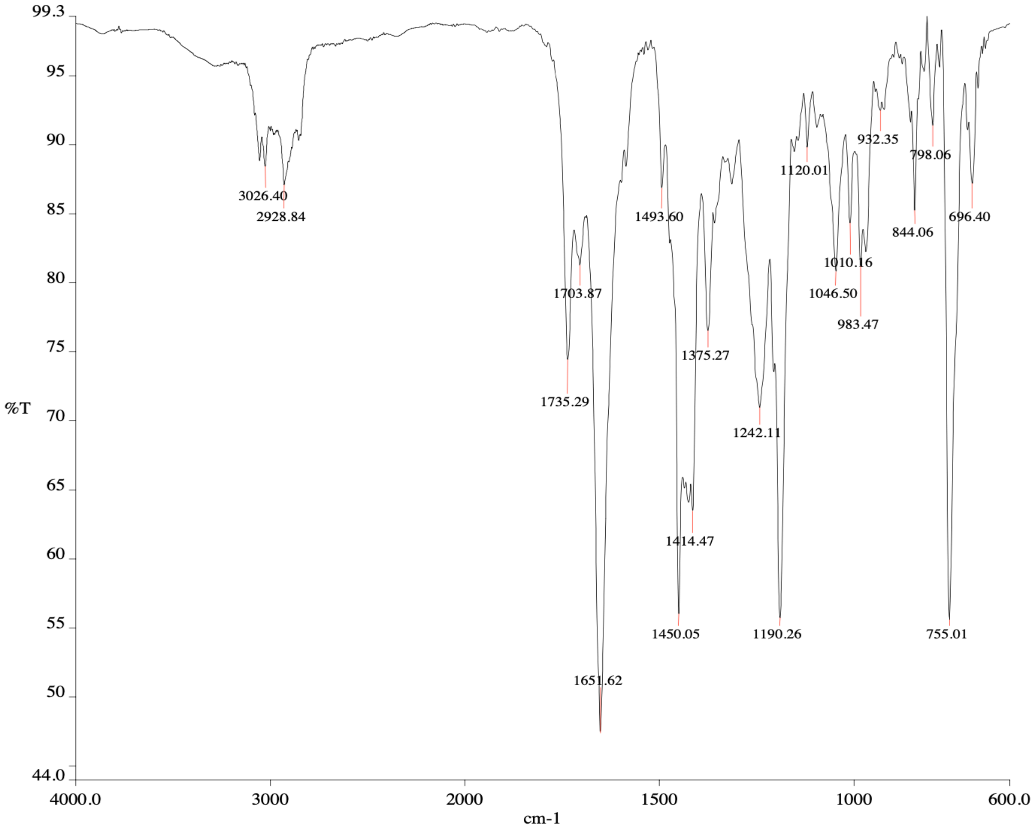
Infrared spectrum (Thin Film, NaCl) of compound **6l**.



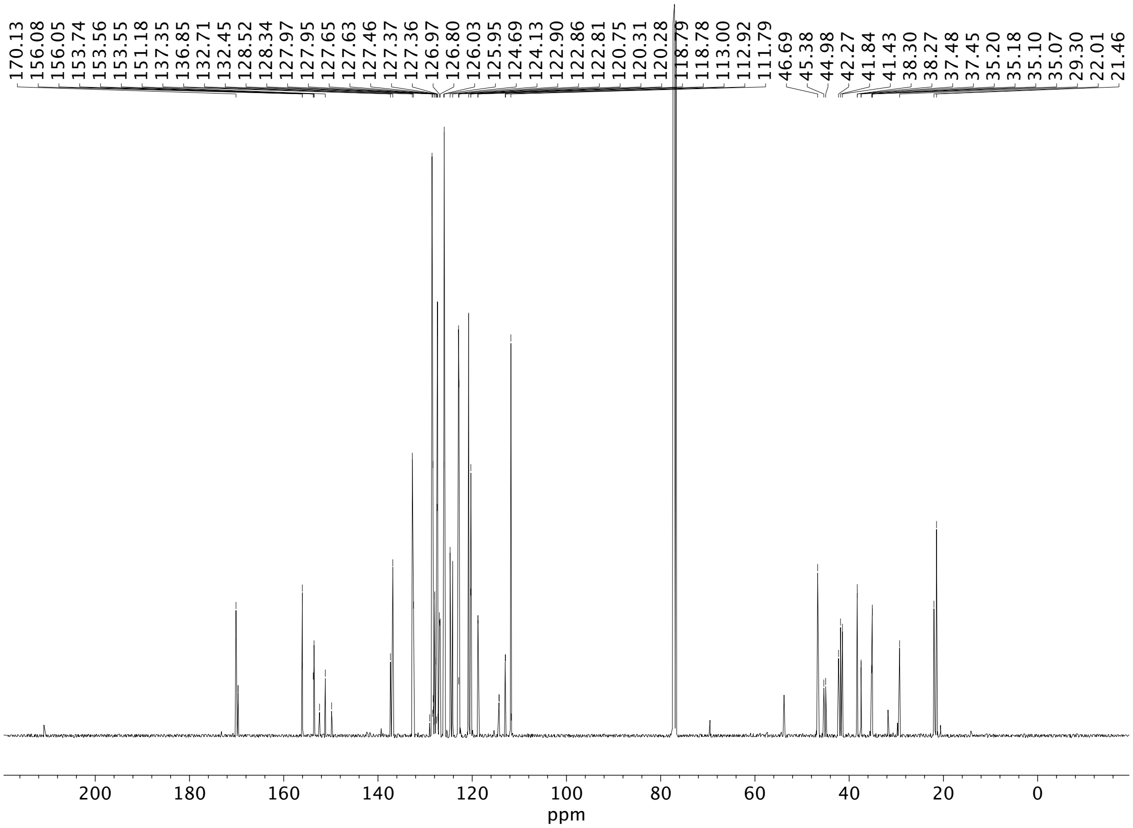
$^{13}$C NMR (100 MHz, $CD_3OD$) of compound **6l**.



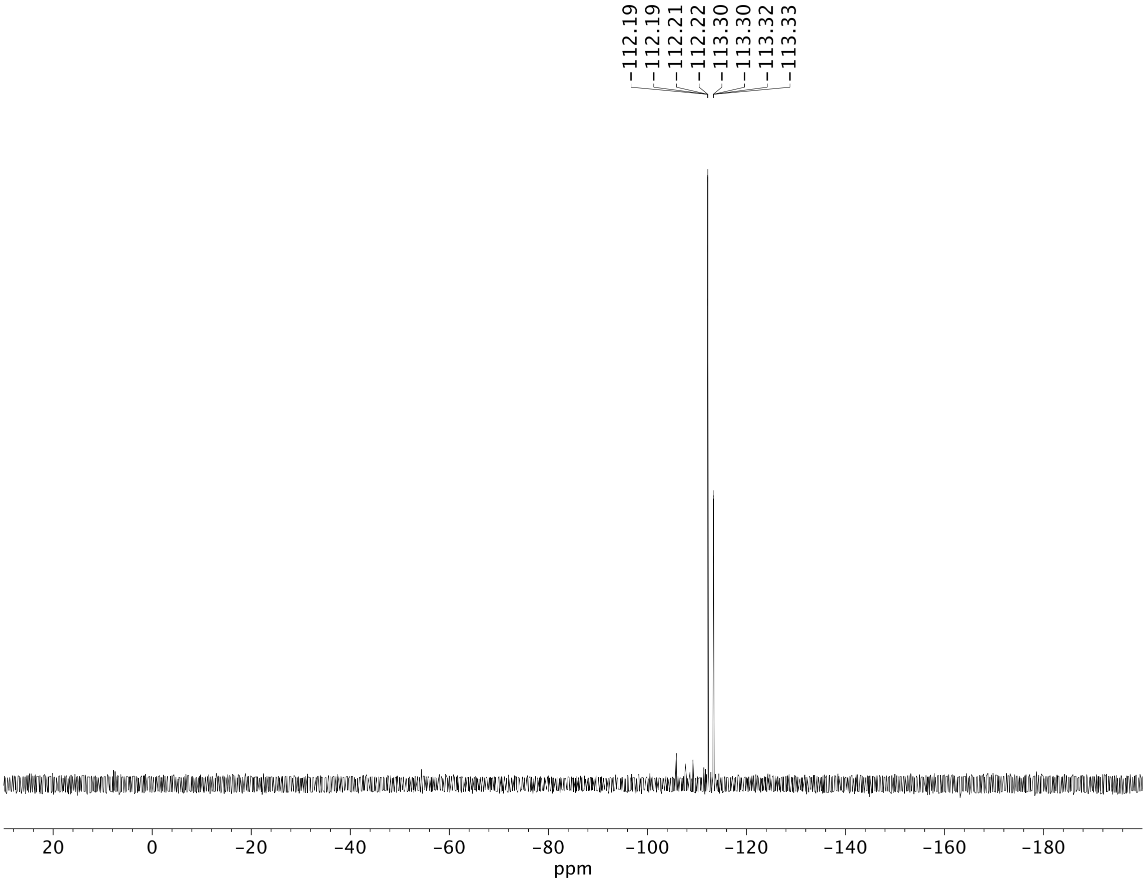
$^1$H NMR (400 MHz, CDCl$_3$) of compound **6m**.



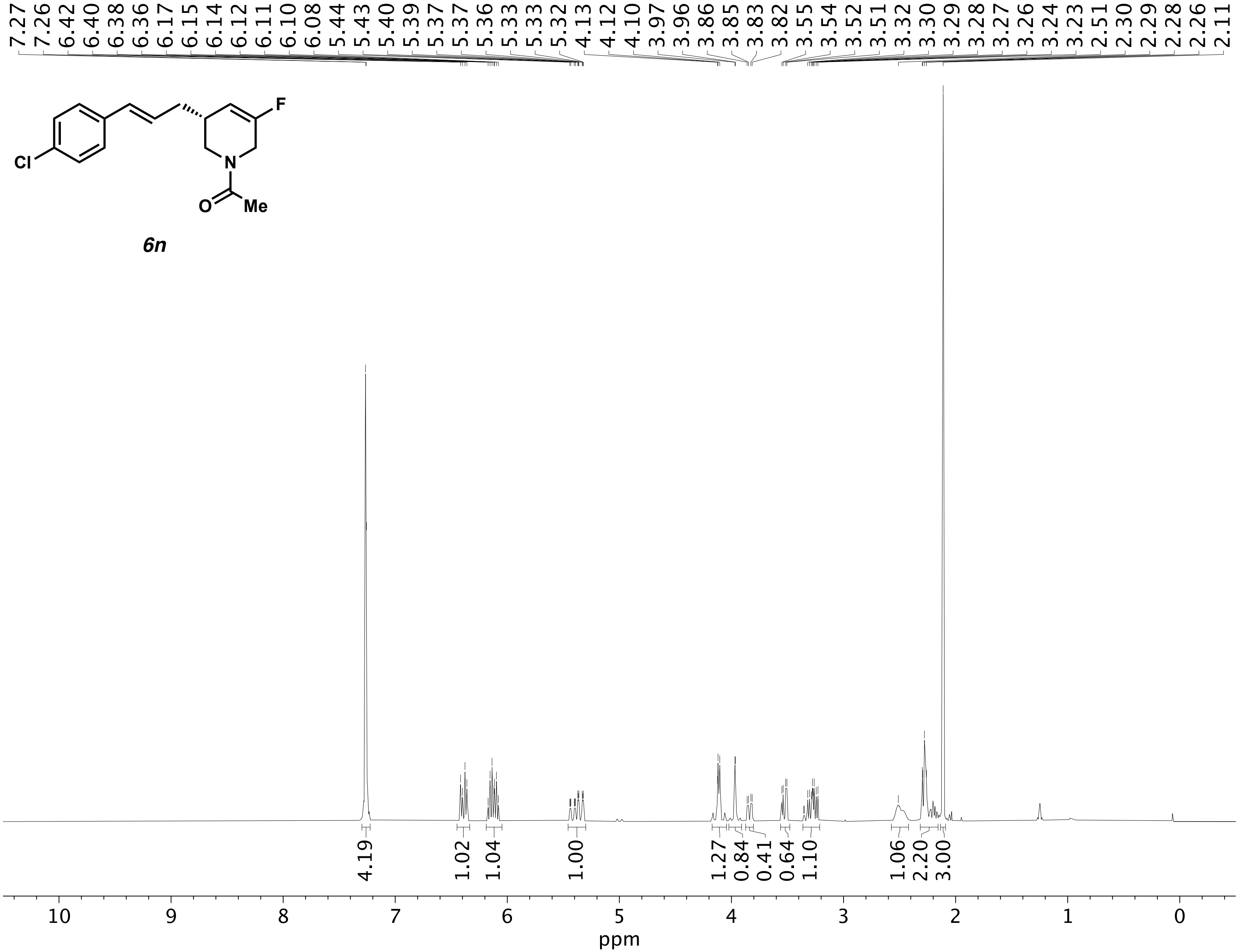
Infrared spectrum (Thin Film, NaCl) of compound **6m**.



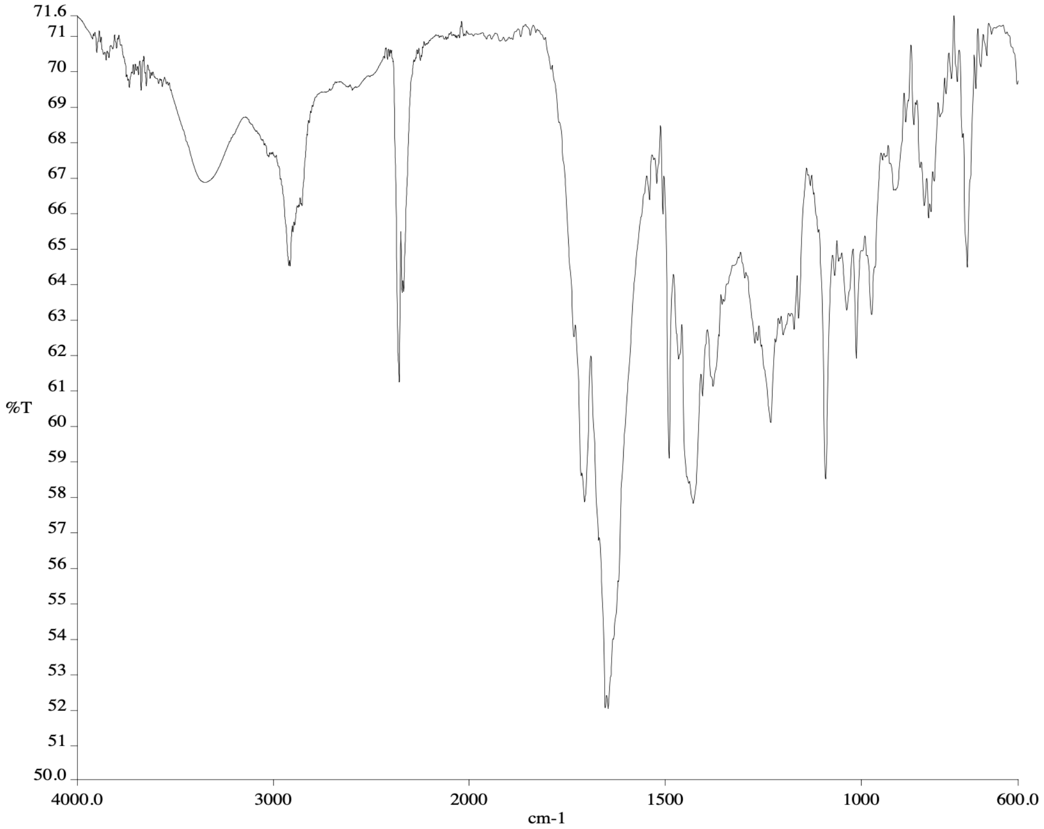
$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **6m**.



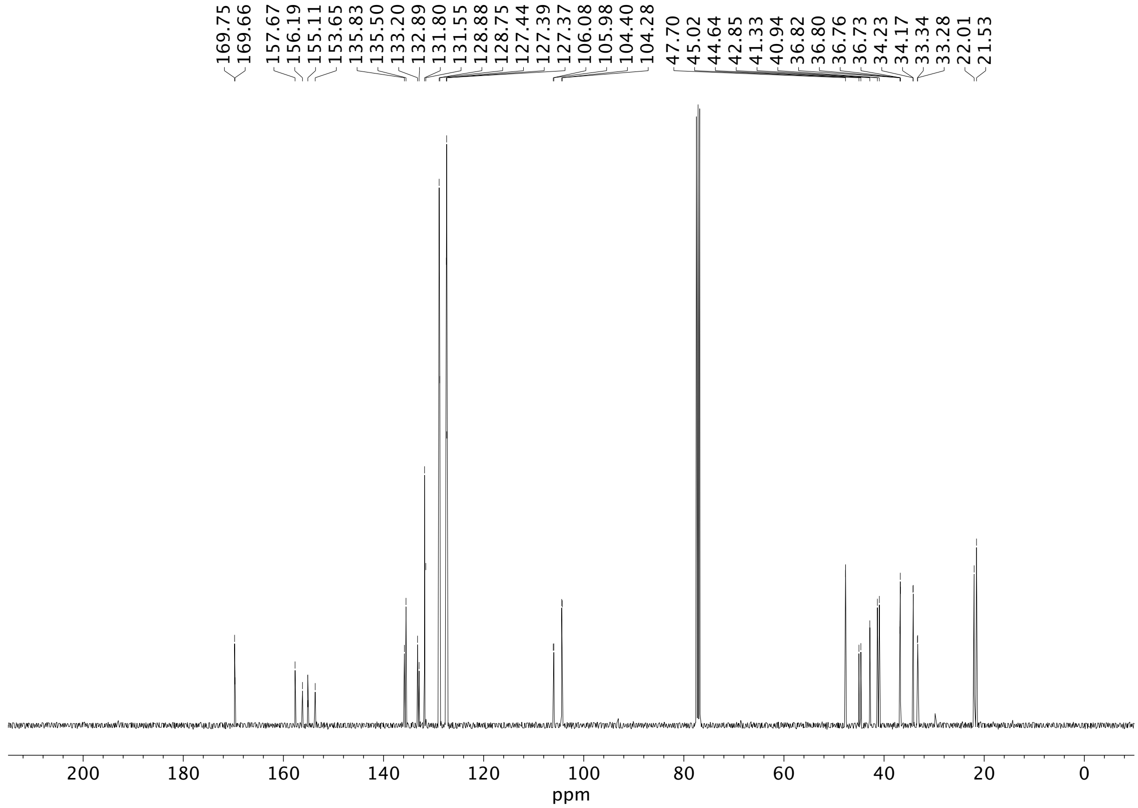
$^{19}$F NMR (282 MHz, CDCl$_3$) of compound **6m.**



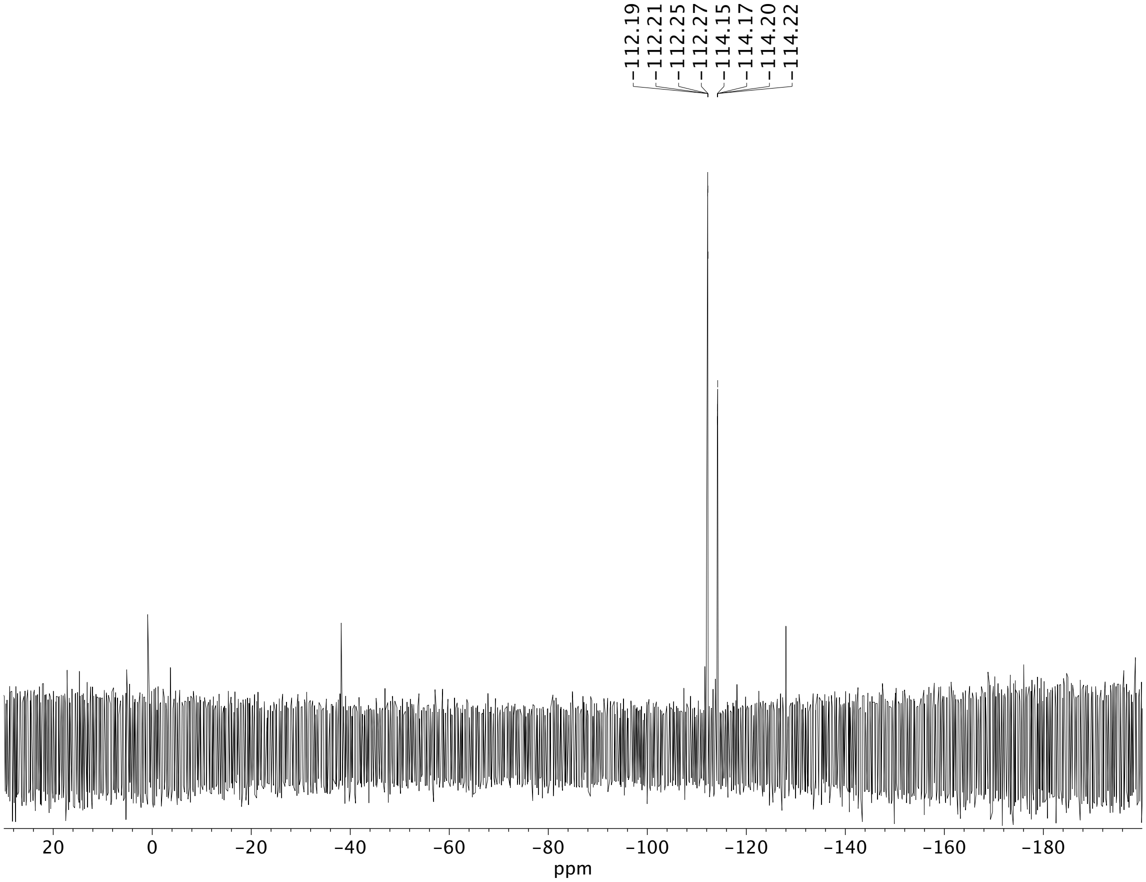
$^1$H NMR (400 MHz, CDCl$_3$) of compound **6n**.



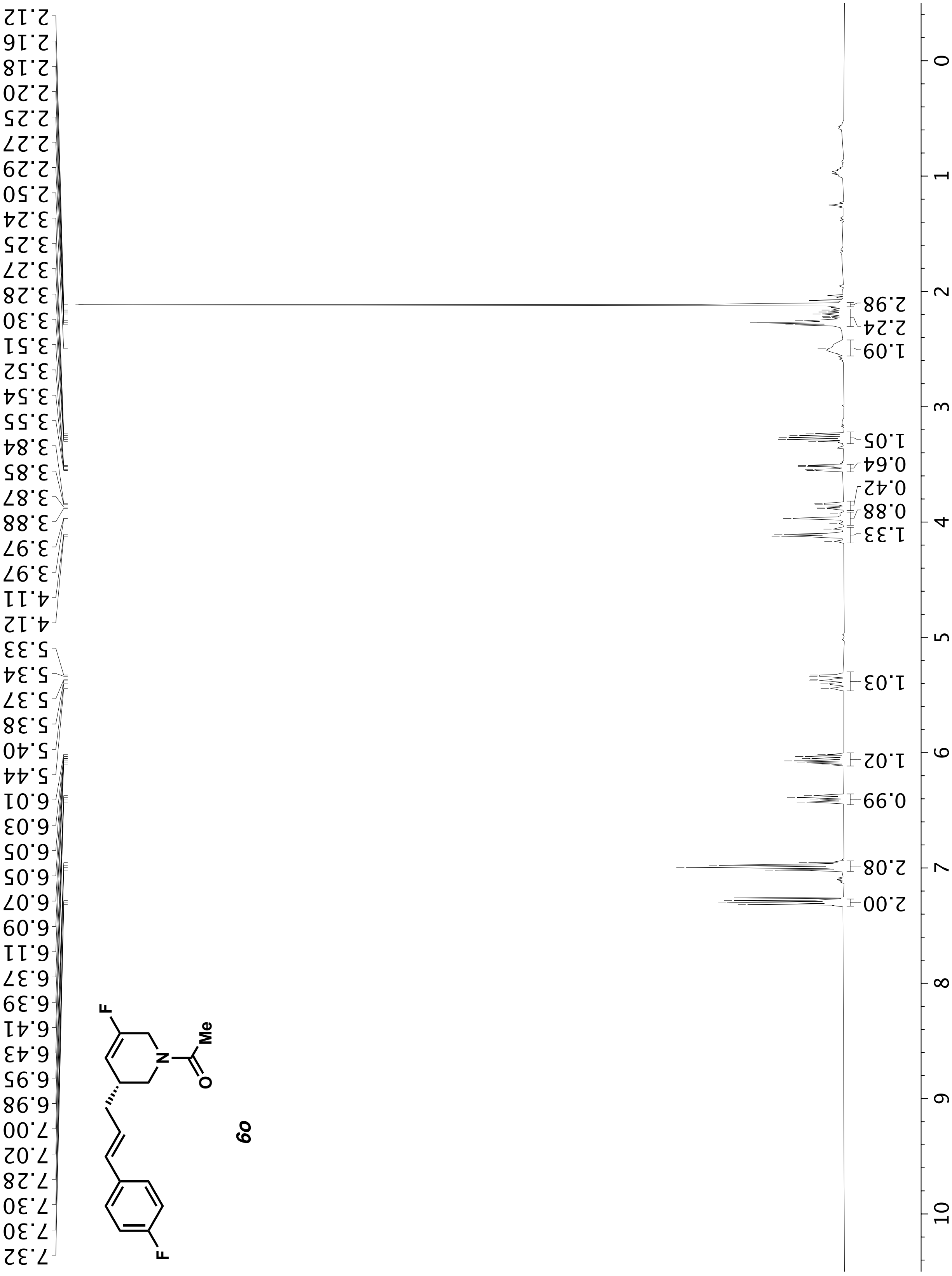
Infrared spectrum (Thin Film, NaCl) of compound **6n**.



$^{13}$C NMR (100 MHz, $CDCl_3$) of compound **6n**.

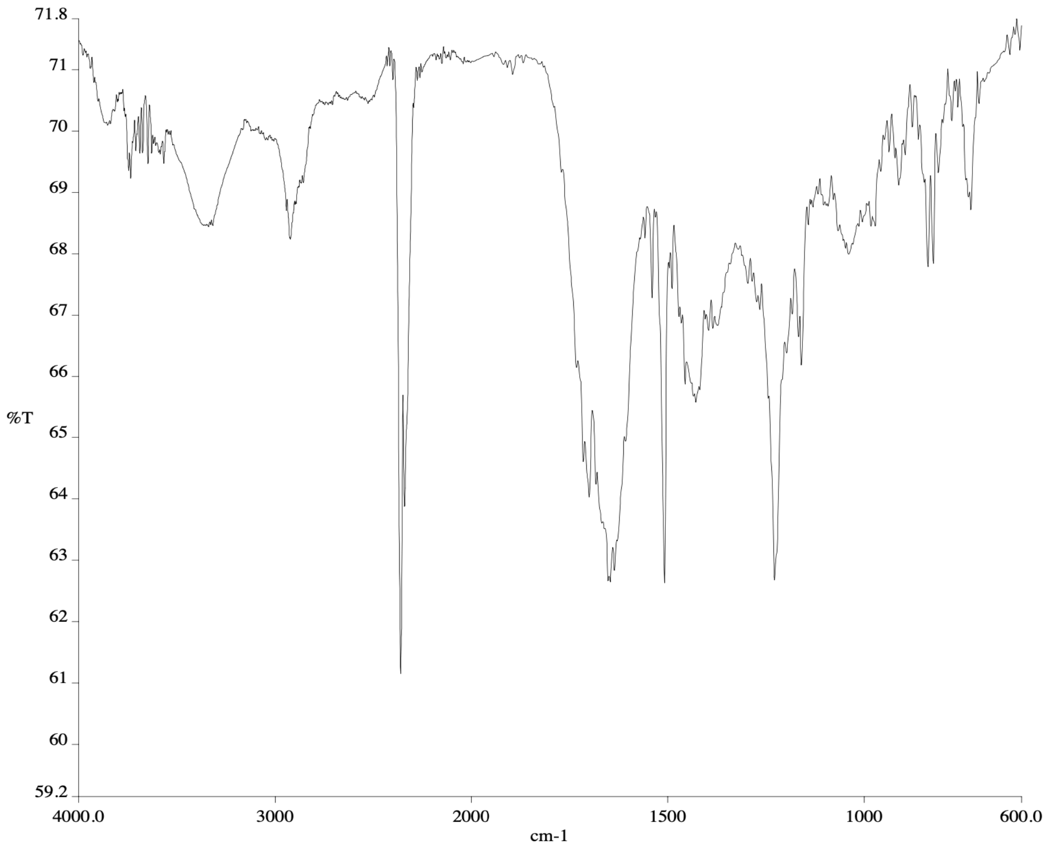


$^{19}$F NMR (282 MHz, CDCl$_3$) of compound **6n**.

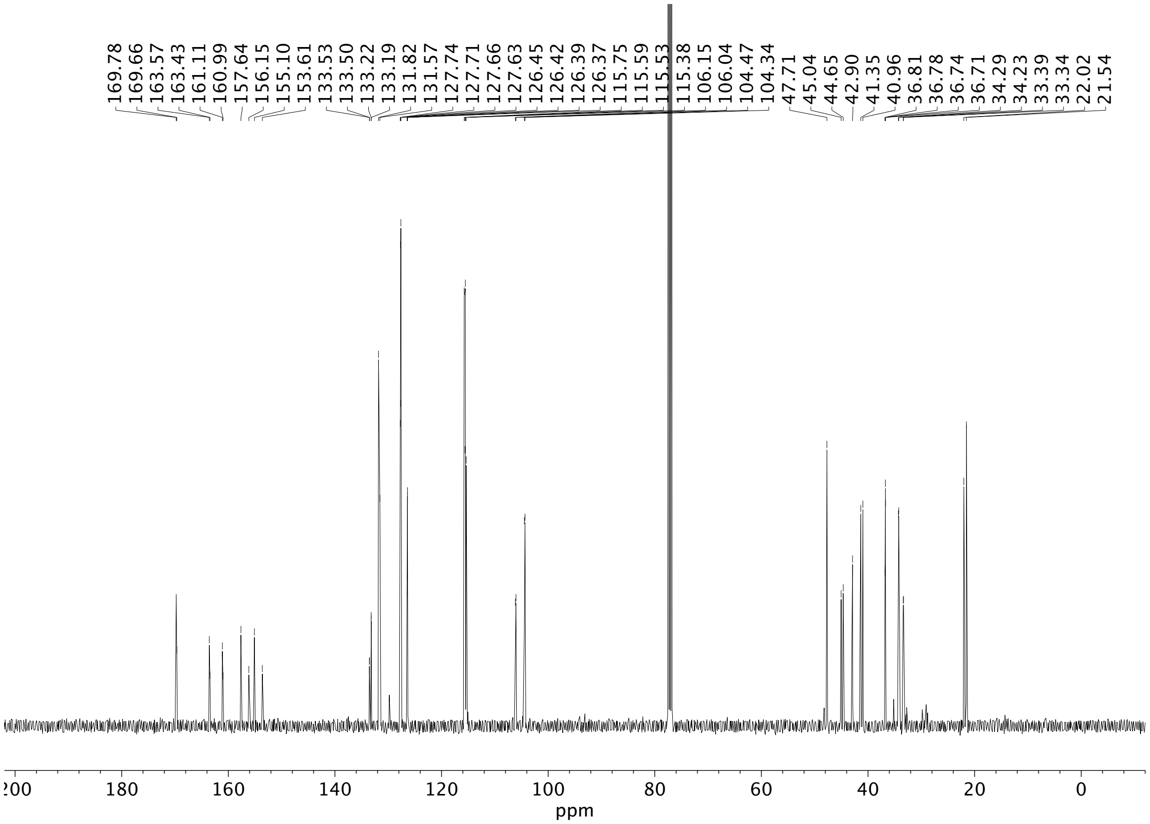


**6o**

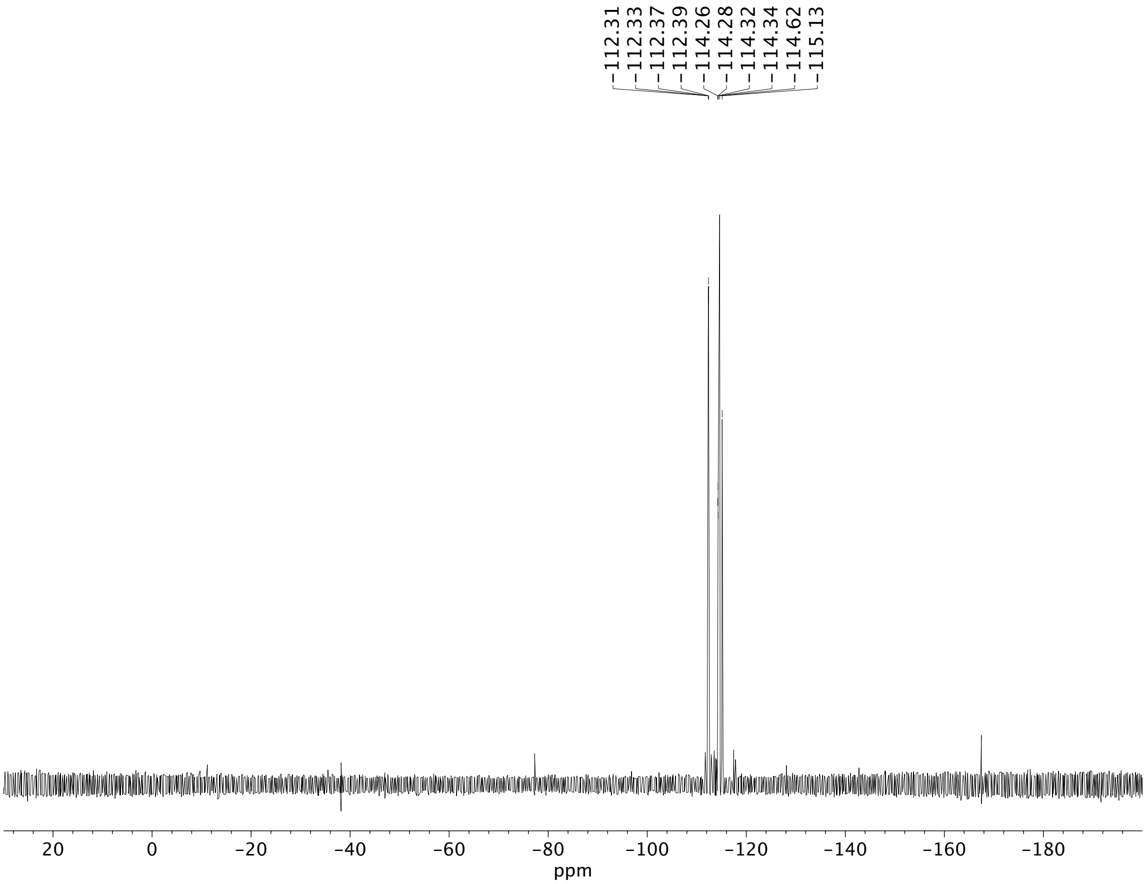
$^1$H NMR (400 MHz, CDCl$_3$) of compound **6o**.



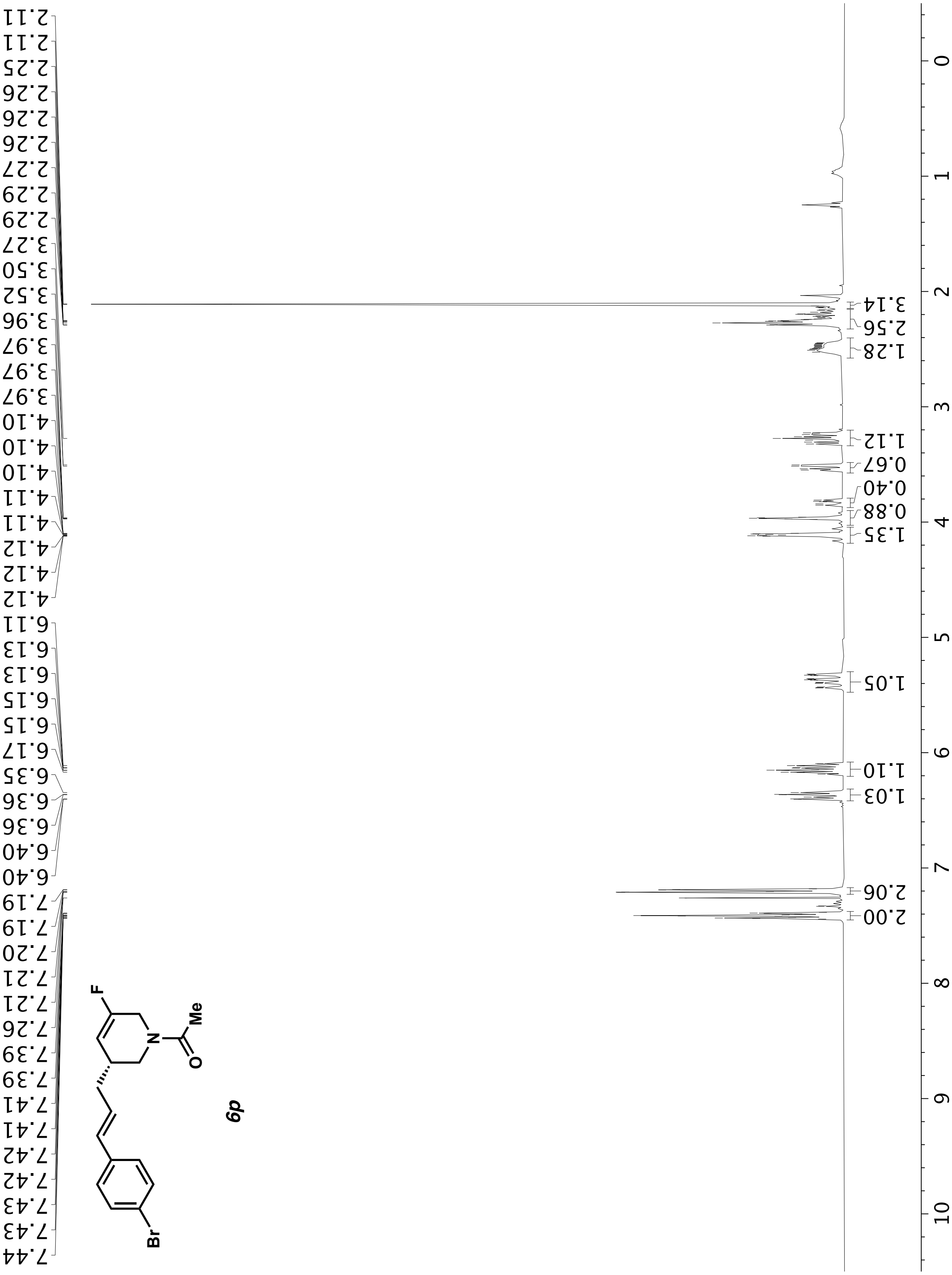
Infrared spectrum (Thin Film, NaCl) of compound **6o.**



$^{13}$C NMR (100 MHz, $CDCl_3$) of compound **6o**.

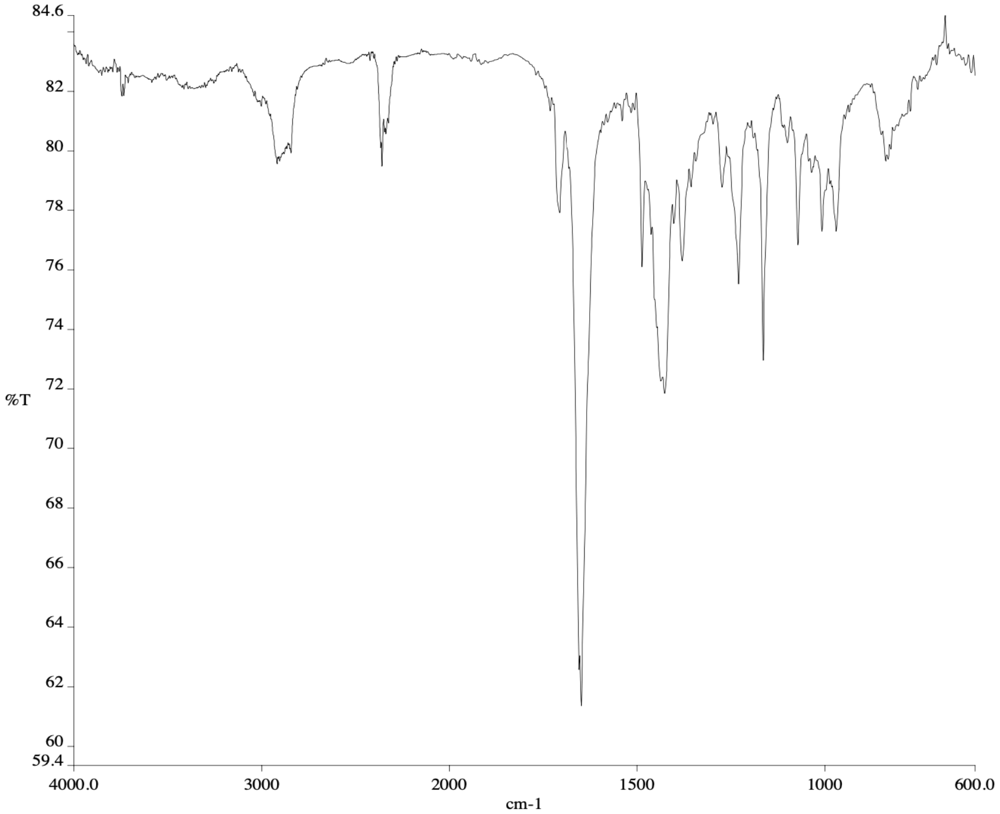


$^{19}$F NMR (282 MHz, $CDCl_3$) of compound **6o**.

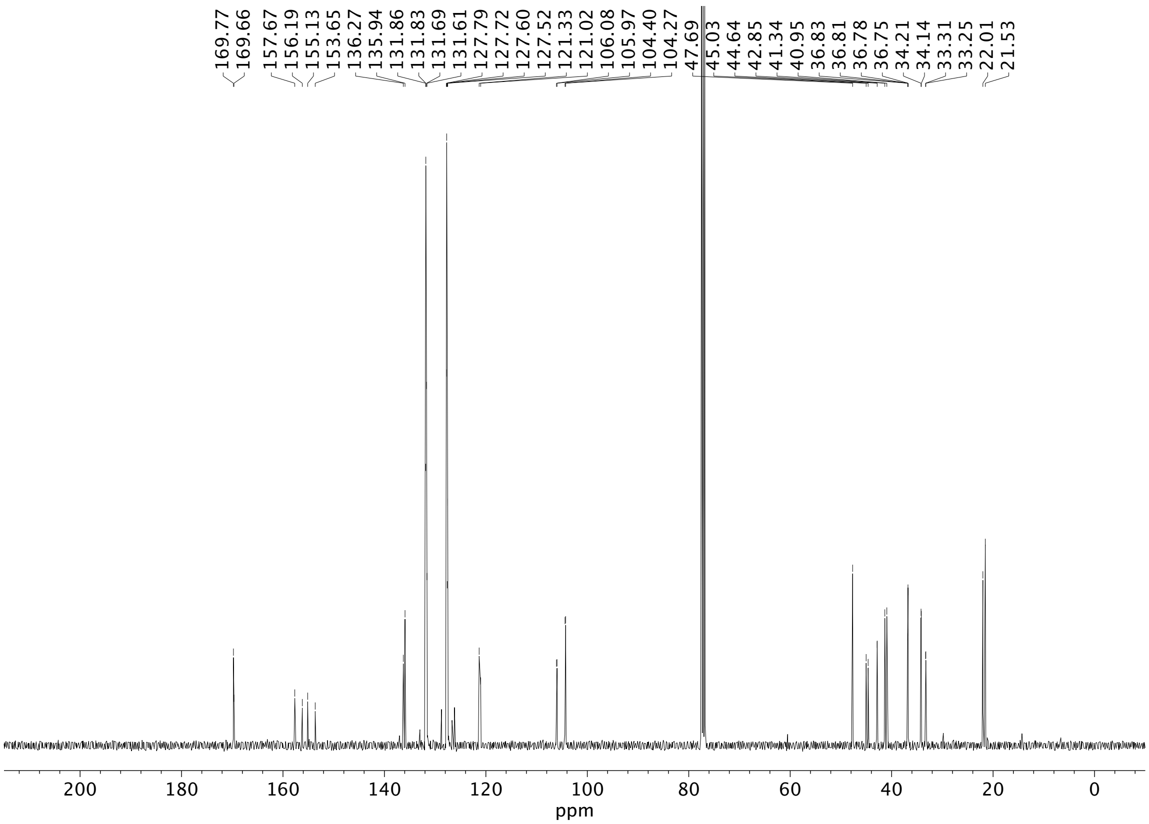


***6p***

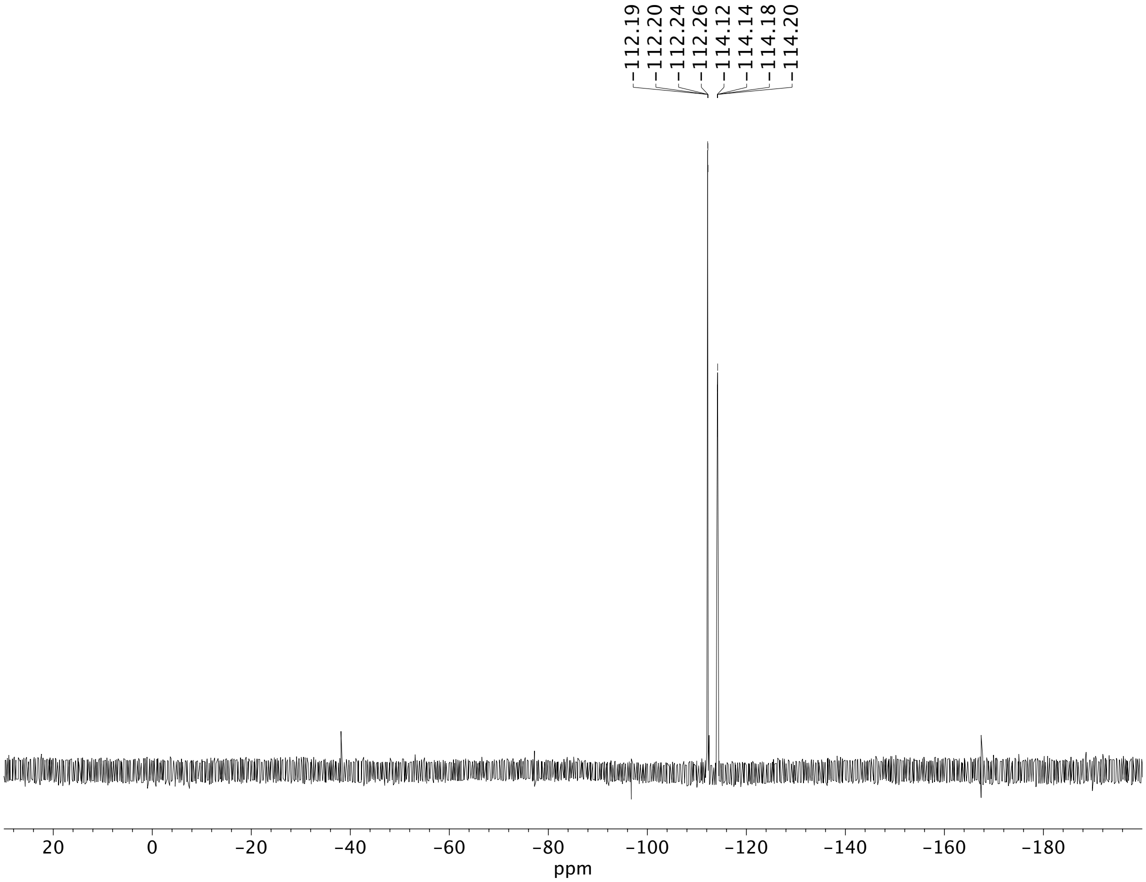
$^1$H NMR (400 MHz, CDCl$_3$) of compound **6p**.



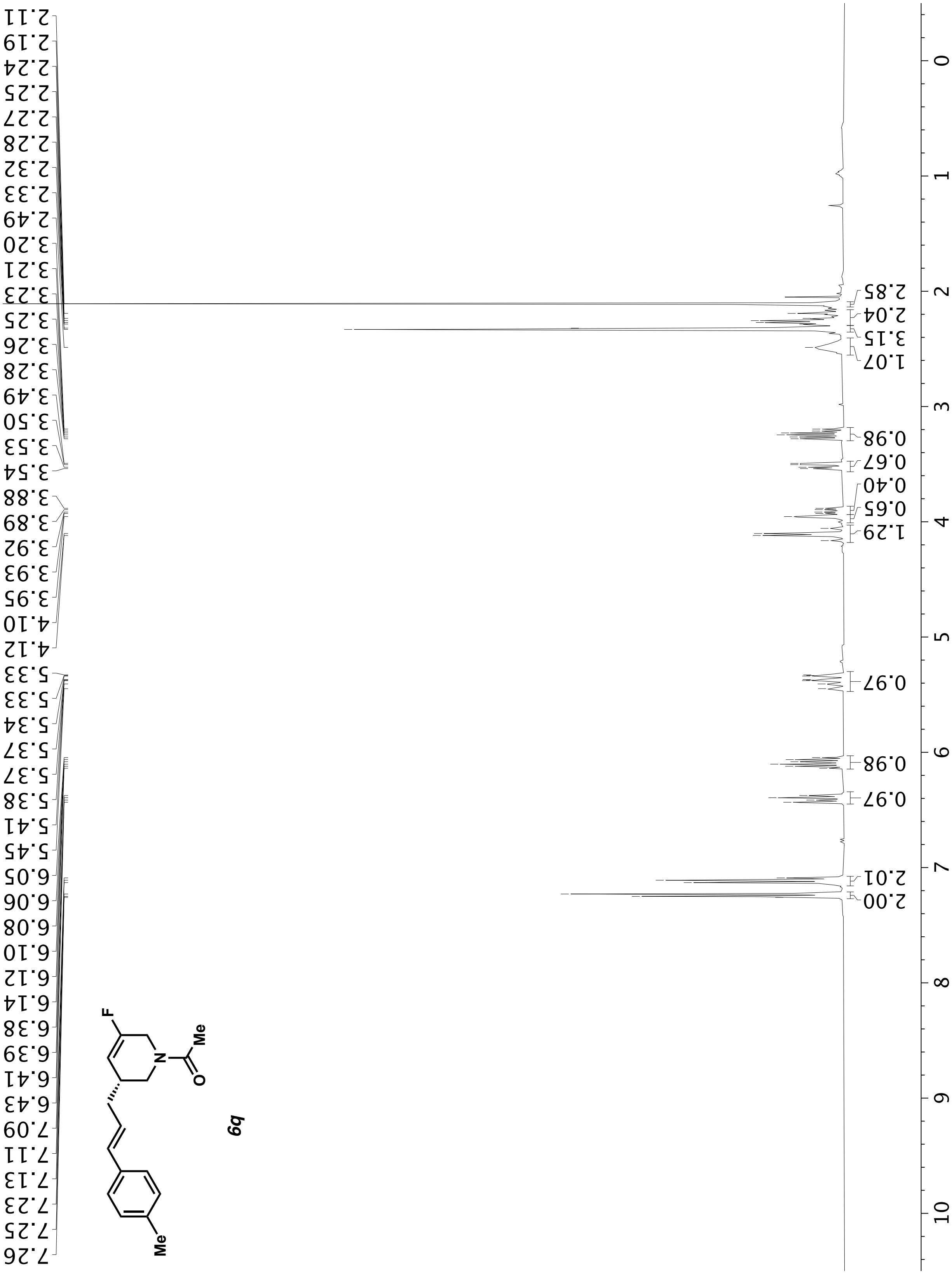
Infrared spectrum (Thin Film, NaCl) of compound **6p**.



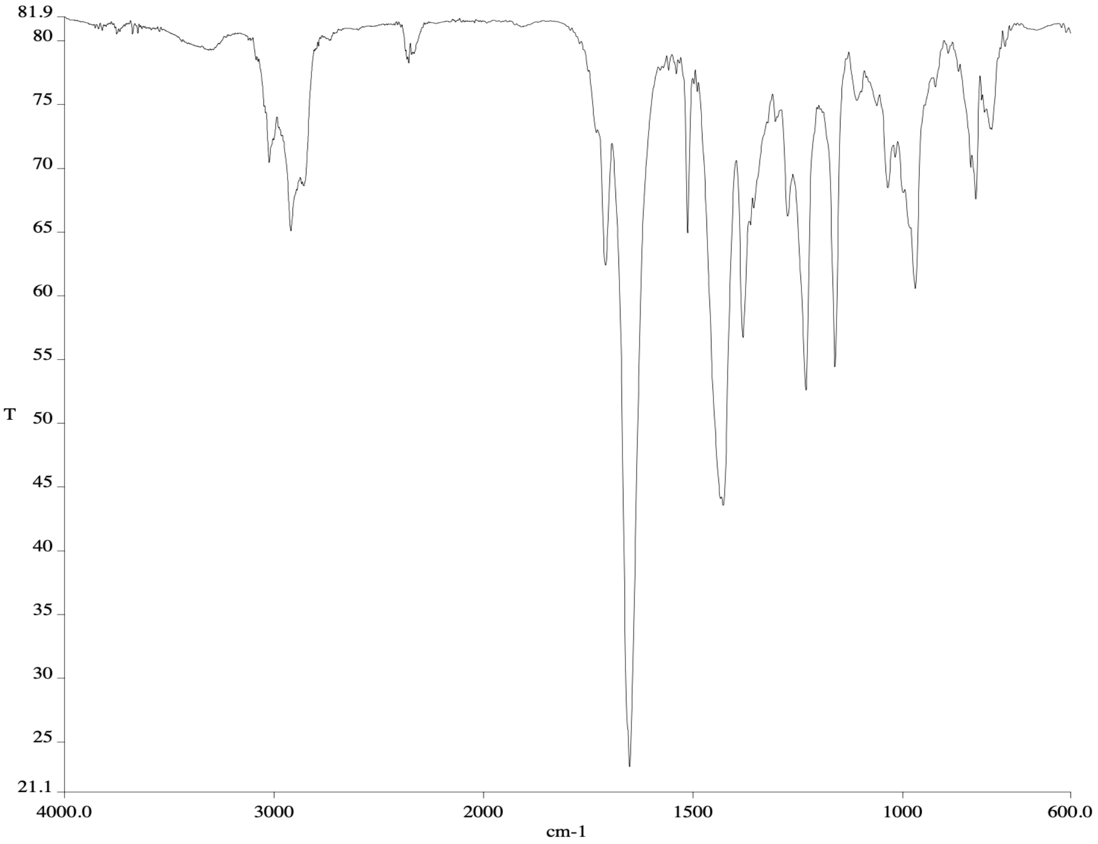
$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **6p**.



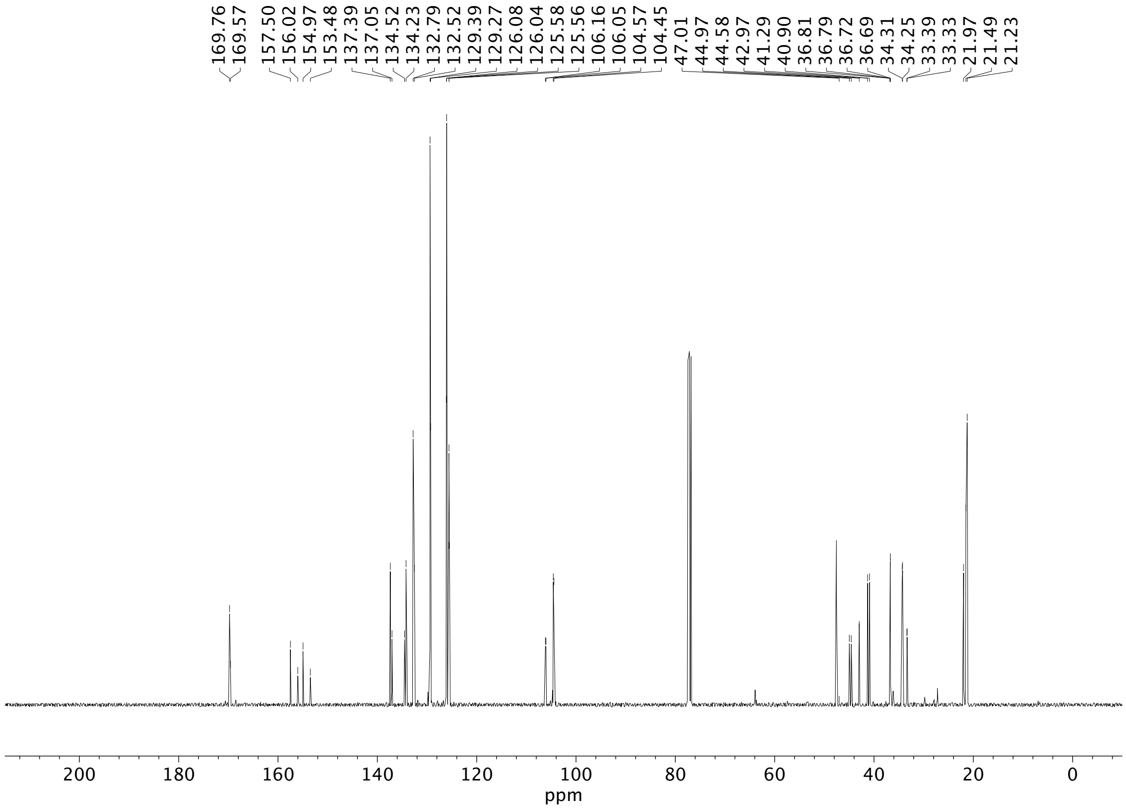
$^{19}$F NMR (282 MHz, CDCl$_3$) of compound **6p.**



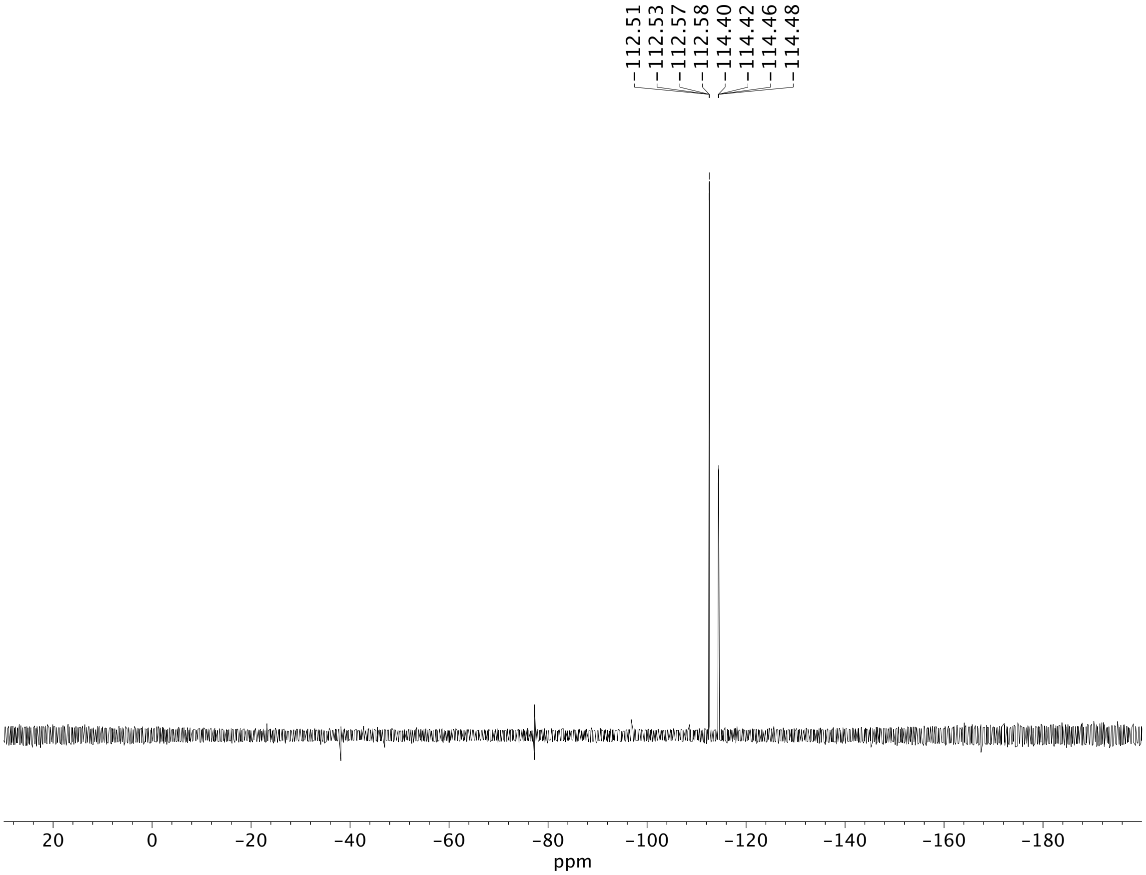
$^1$H NMR (400 MHz, CDCl$_3$) of compound **6q**.



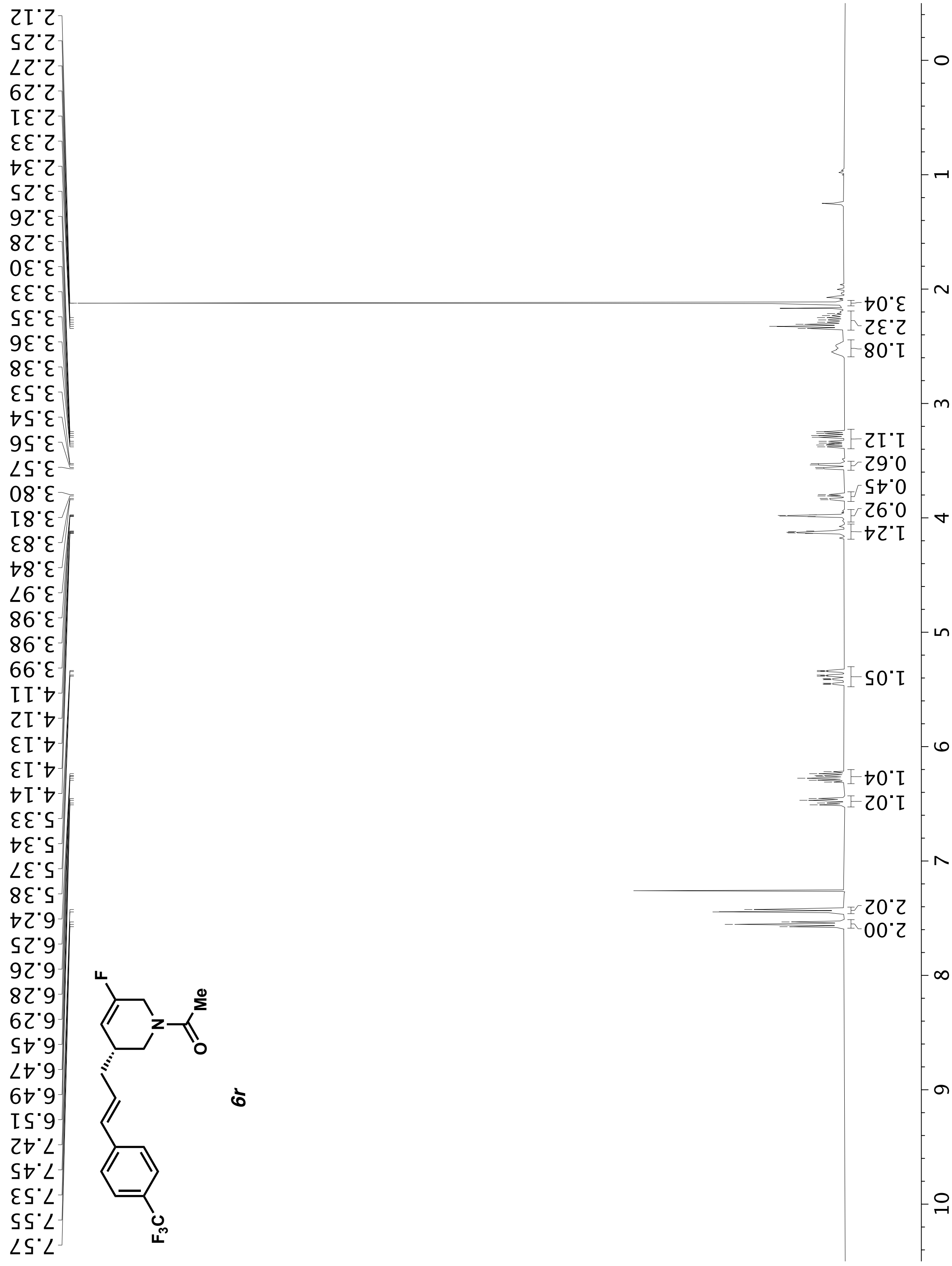
Infrared spectrum (Thin Film, NaCl) of compound **6q**.



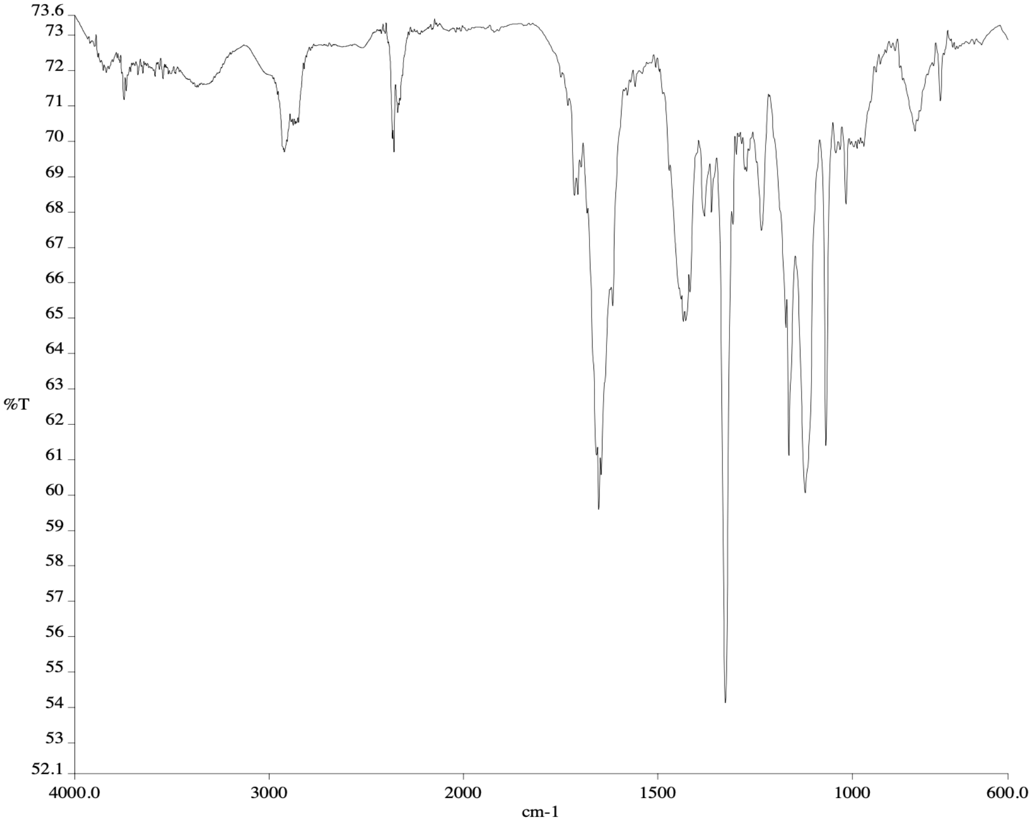
$^{13}C$ NMR (100 MHz, $CDCl_3$) of compound **6q**.



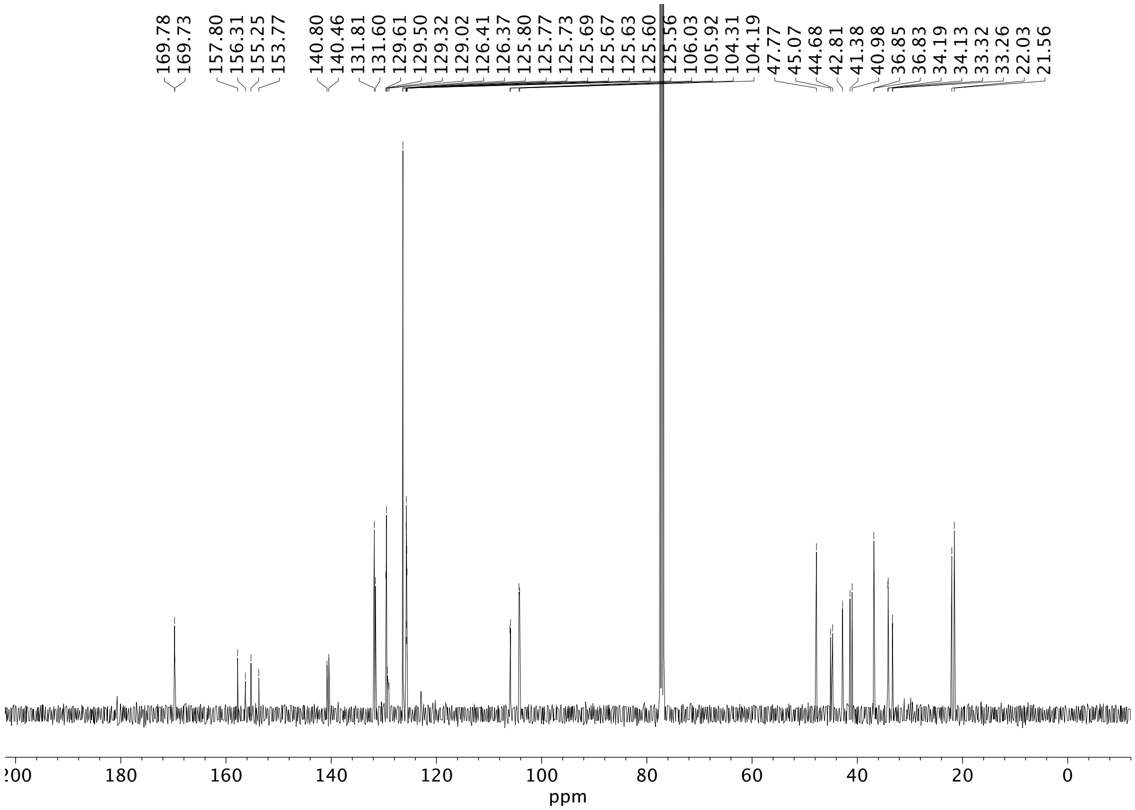
$^{19}$F NMR (282 MHz, CDCl$_3$) of compound **6q**.



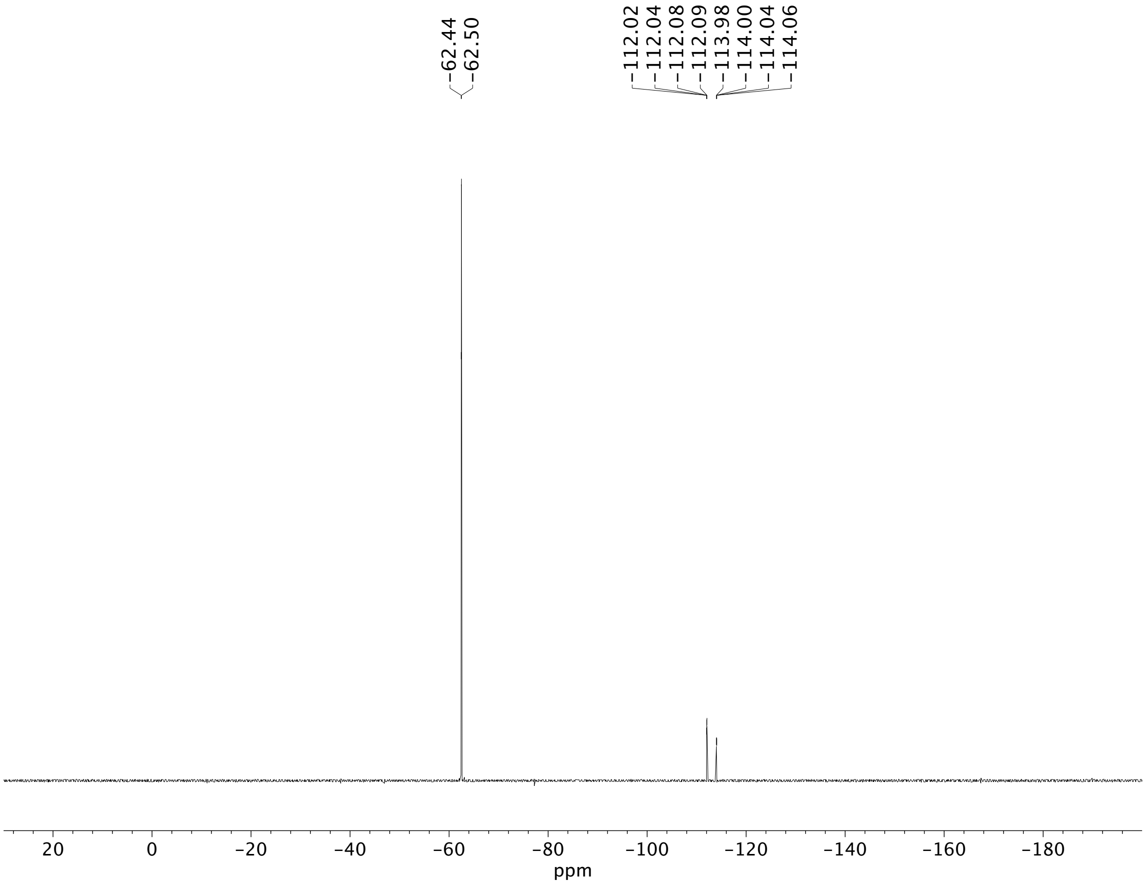
$^1$H NMR (400 MHz, CDCl$_3$) of compound **6r**.



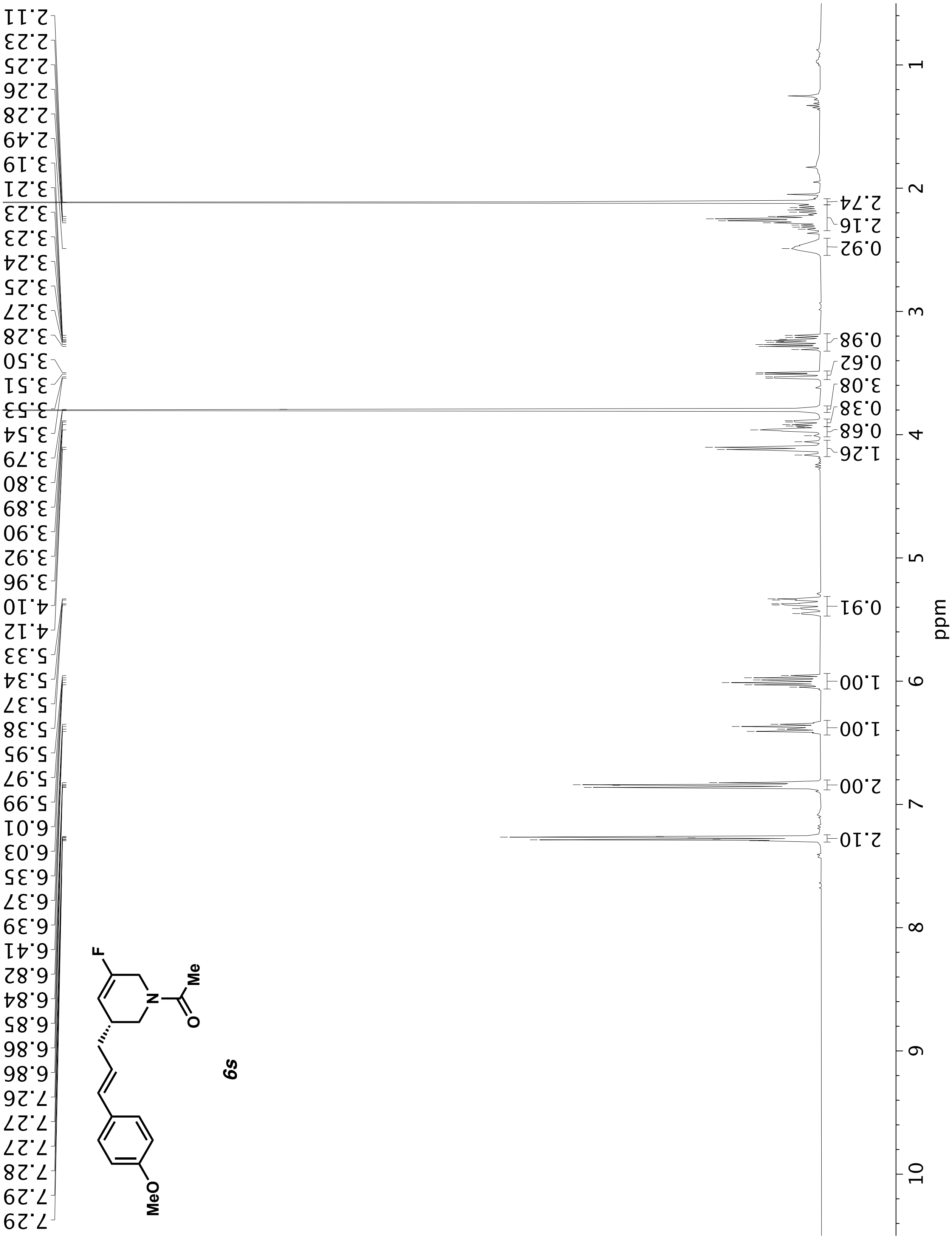
Infrared spectrum (Thin Film, NaCl) of compound **6r**.



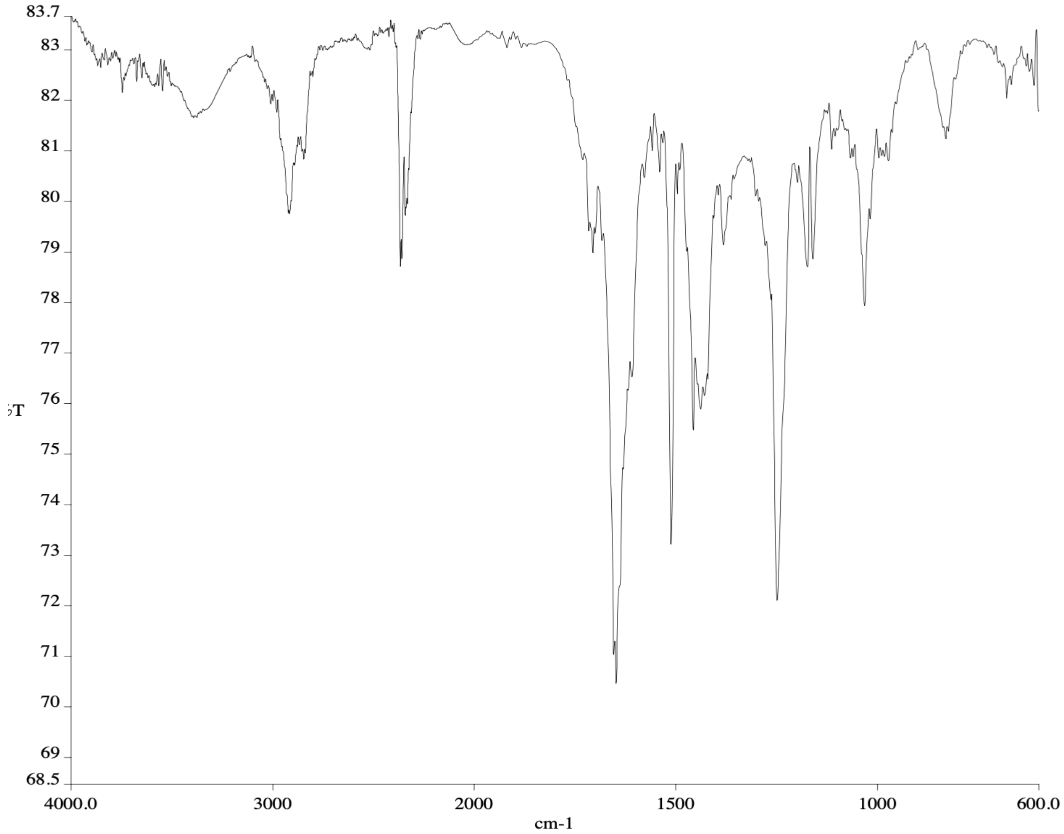
$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **6r**.



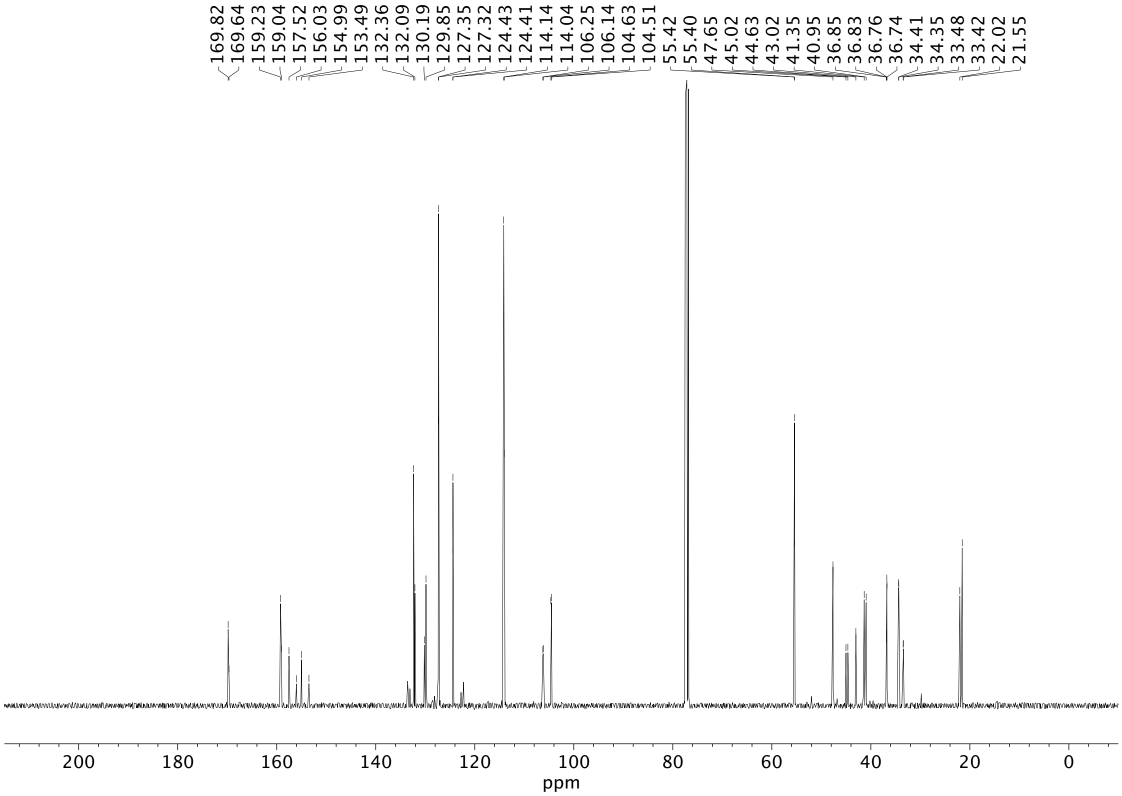
$^{19}$F NMR (282 MHz, CDCl$_3$) of compound **6r**.



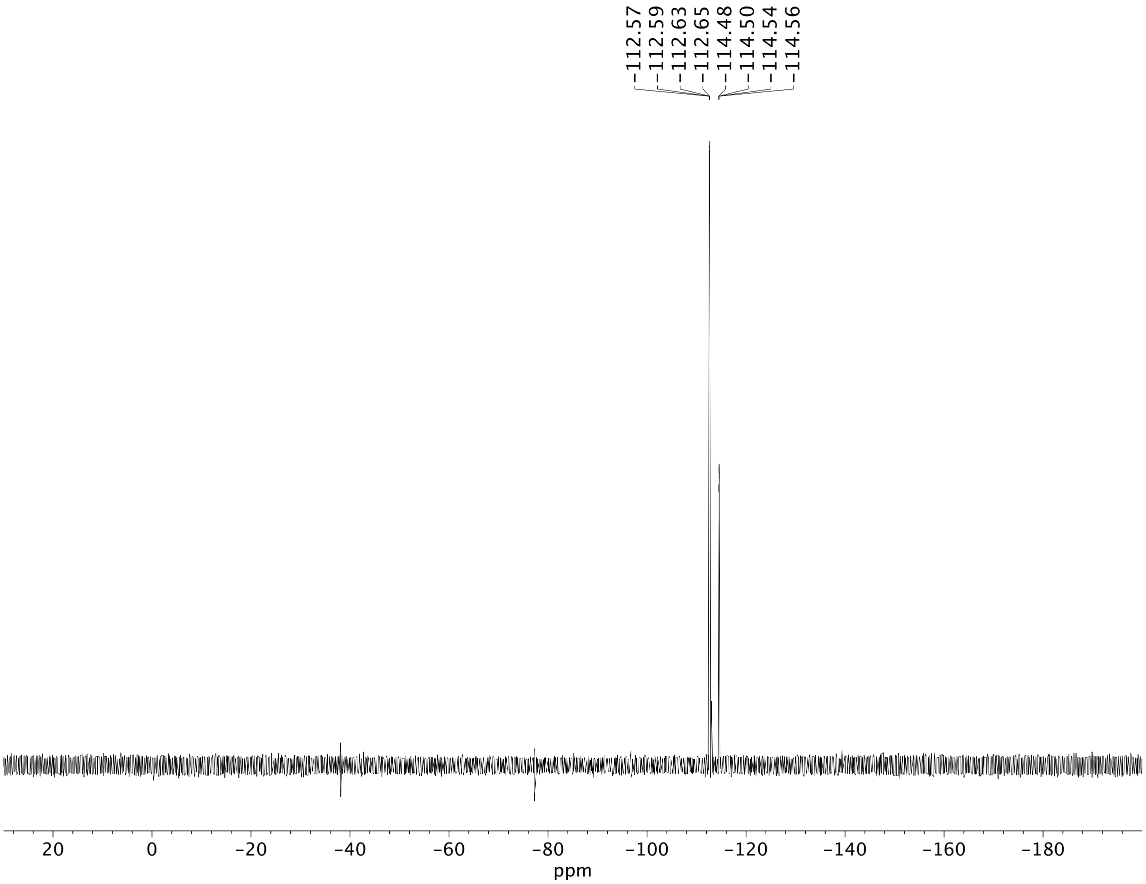
$^1$H NMR (400 MHz, CDCl$_3$) of compound **6s**.



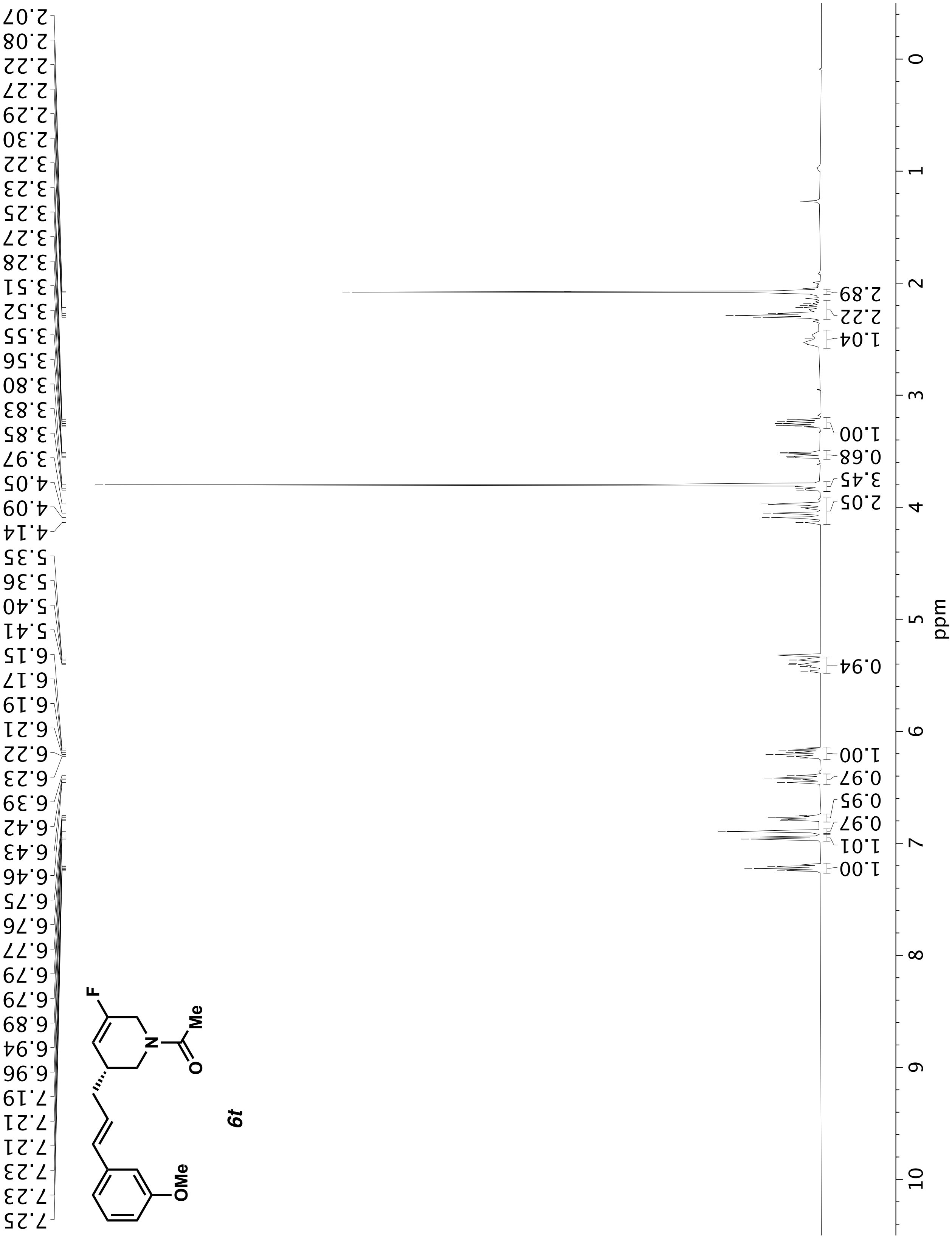
Infrared spectrum (Thin Film, NaCl) of compound **6s**.



$^{13}C$ NMR (100 MHz, $CDCl_3$) of compound **6s**.

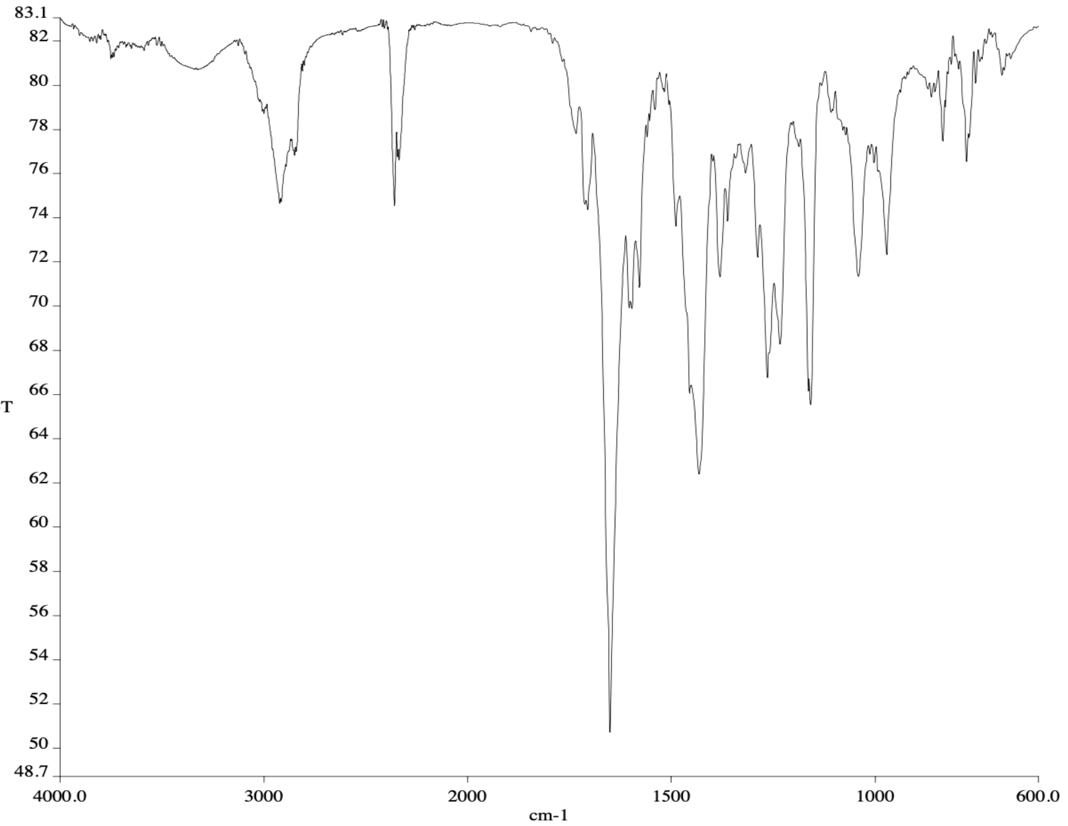


$^{19}$F NMR (282 MHz, $CDCl_3$) of compound **6s**.

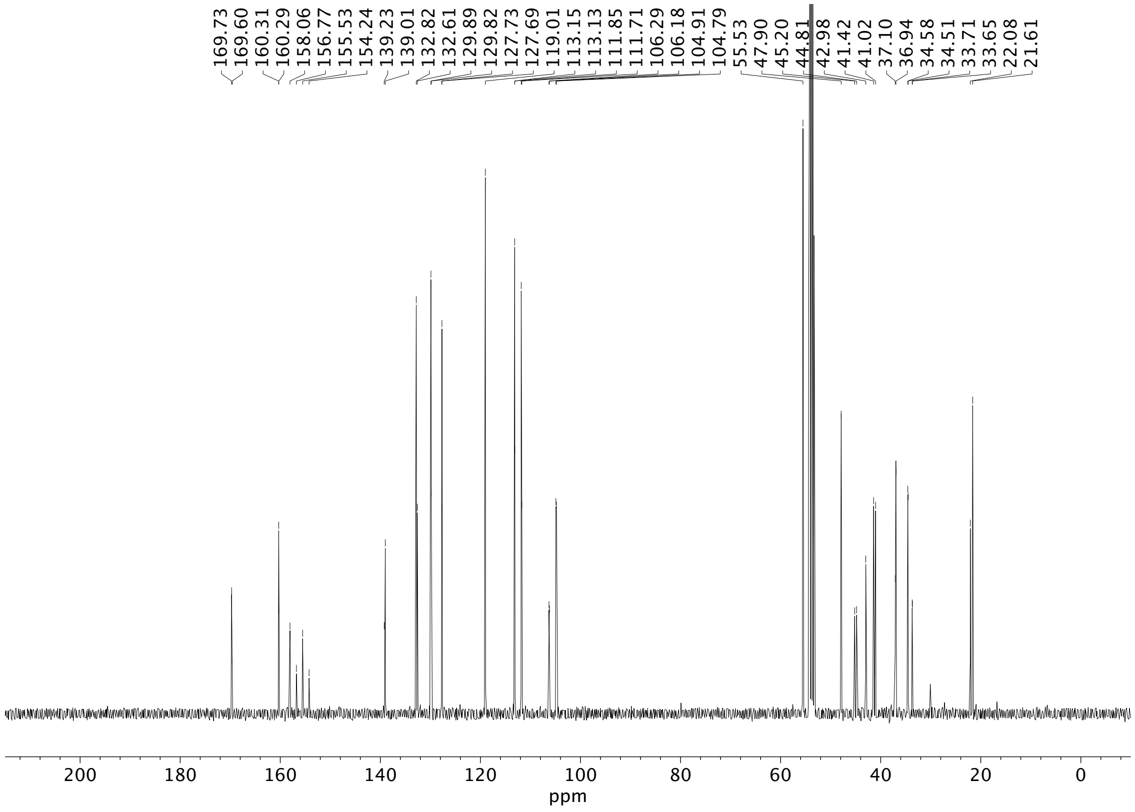


**6t**

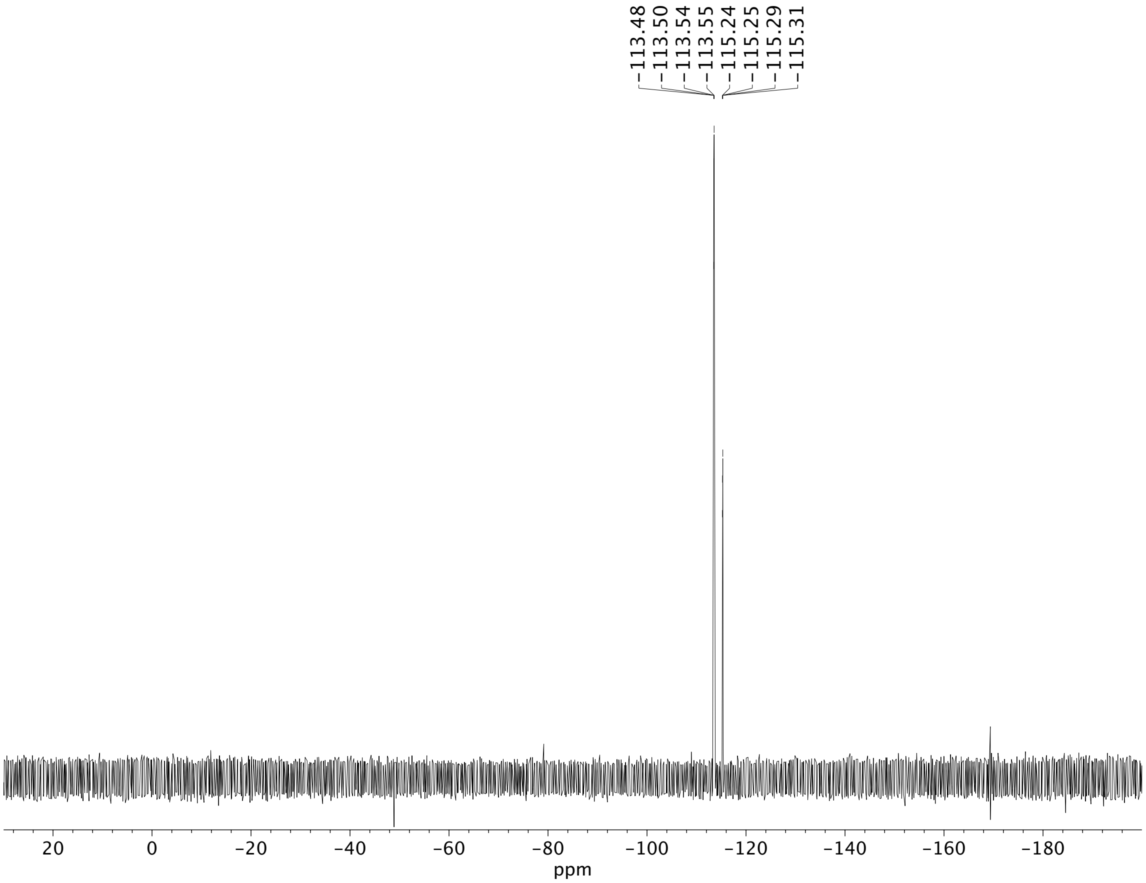
$^1$H NMR (400 MHz, $CD_2Cl_2$) of compound **6t.**



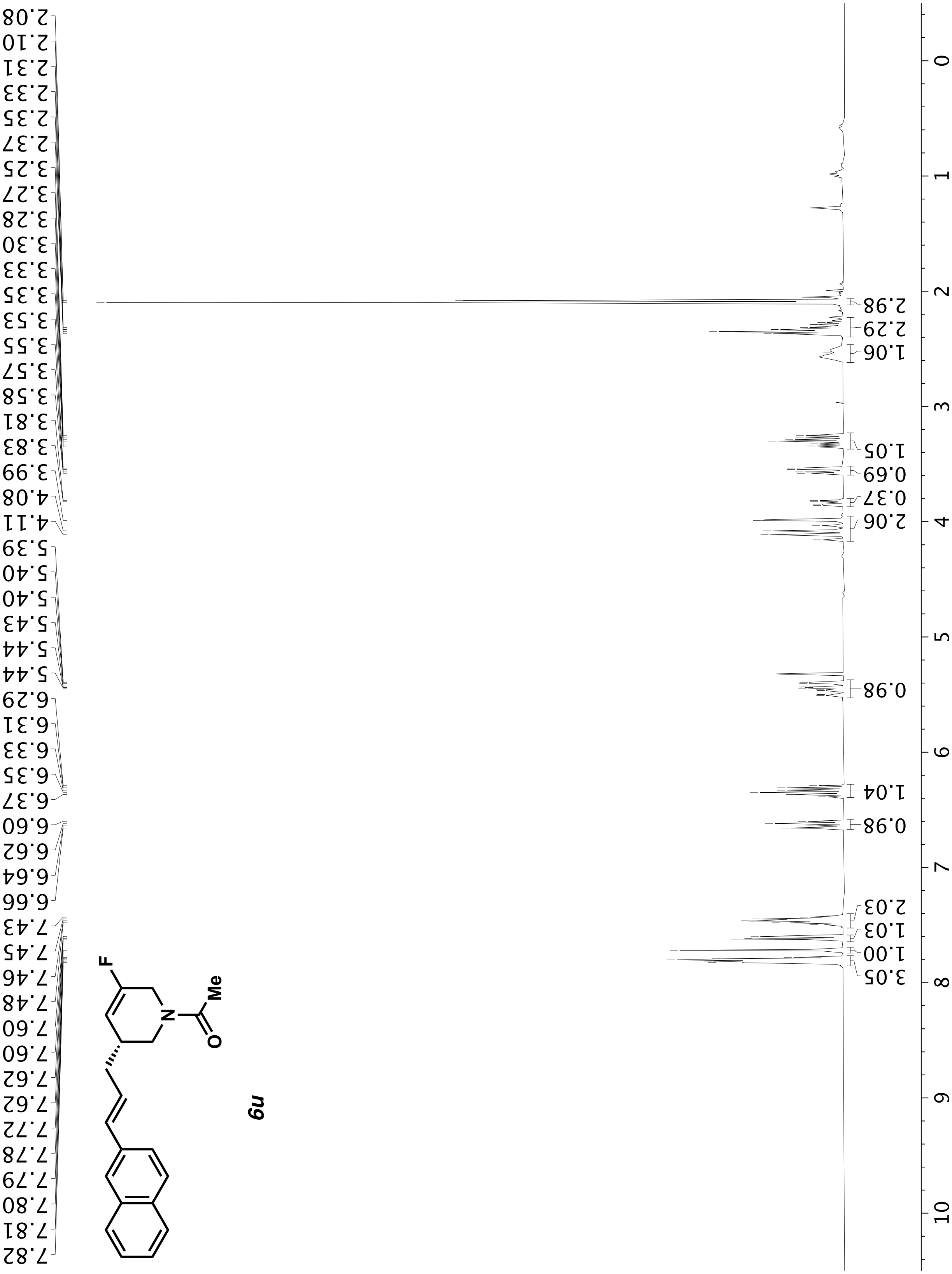
Infrared spectrum (Thin Film, NaCl) of compound **6t**.



$^{13}$C NMR (100 MHz, $CD_2Cl_2$) of compound **6t**.

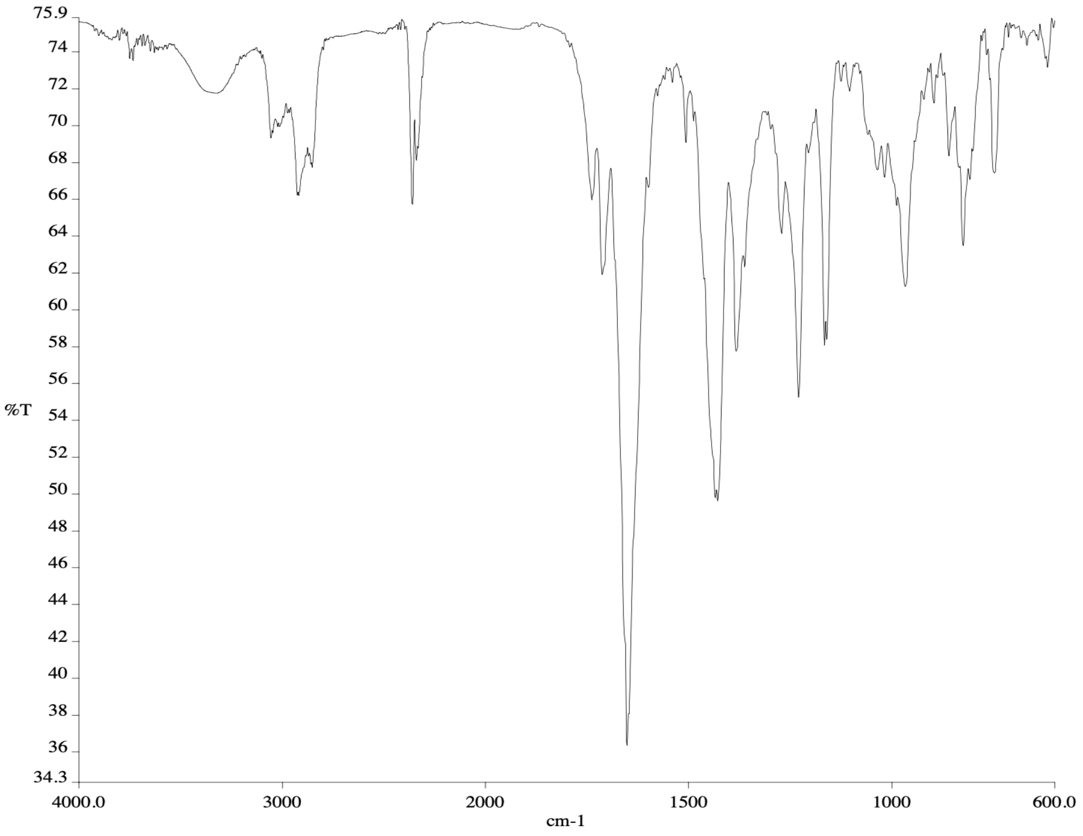


$^{19}$F NMR (282 MHz, $CD_2Cl_2$) of compound **6t.**

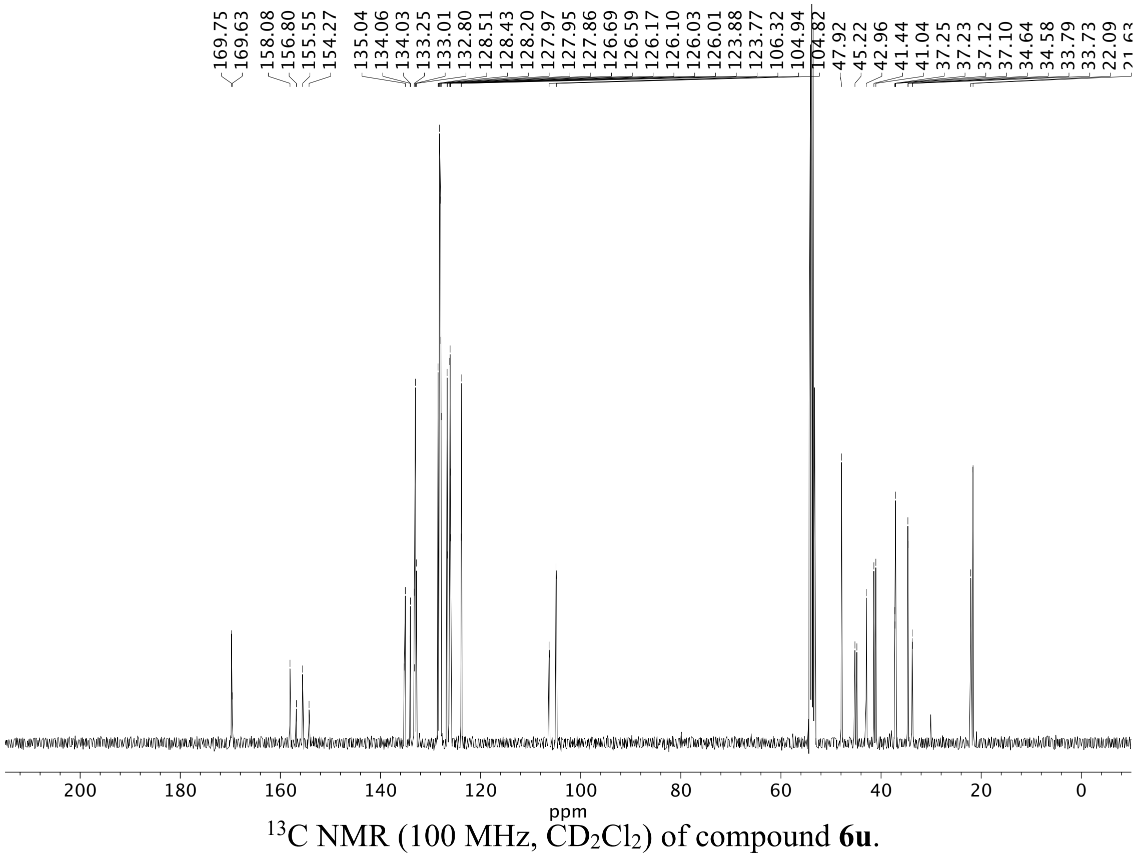


**6u**

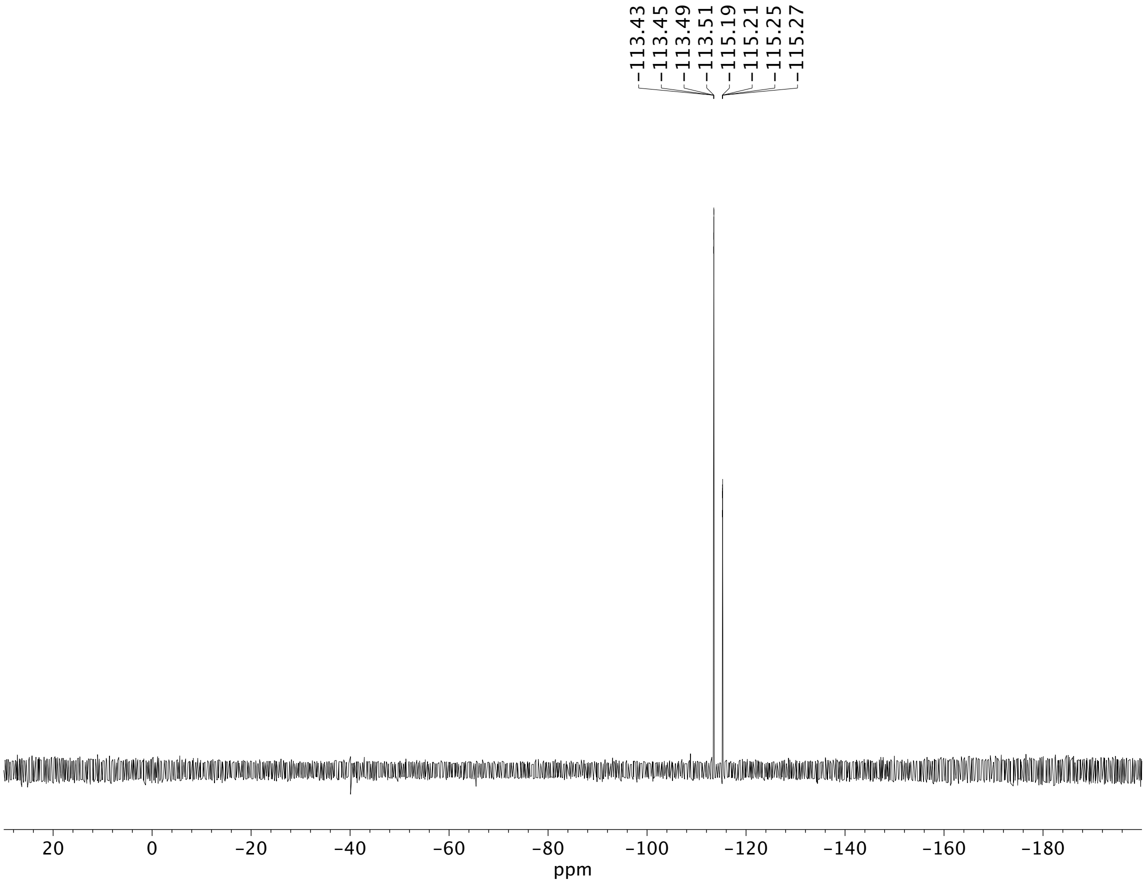
$^1$H NMR (400 MHz, $CD_2Cl_2$) of compound **6u.**



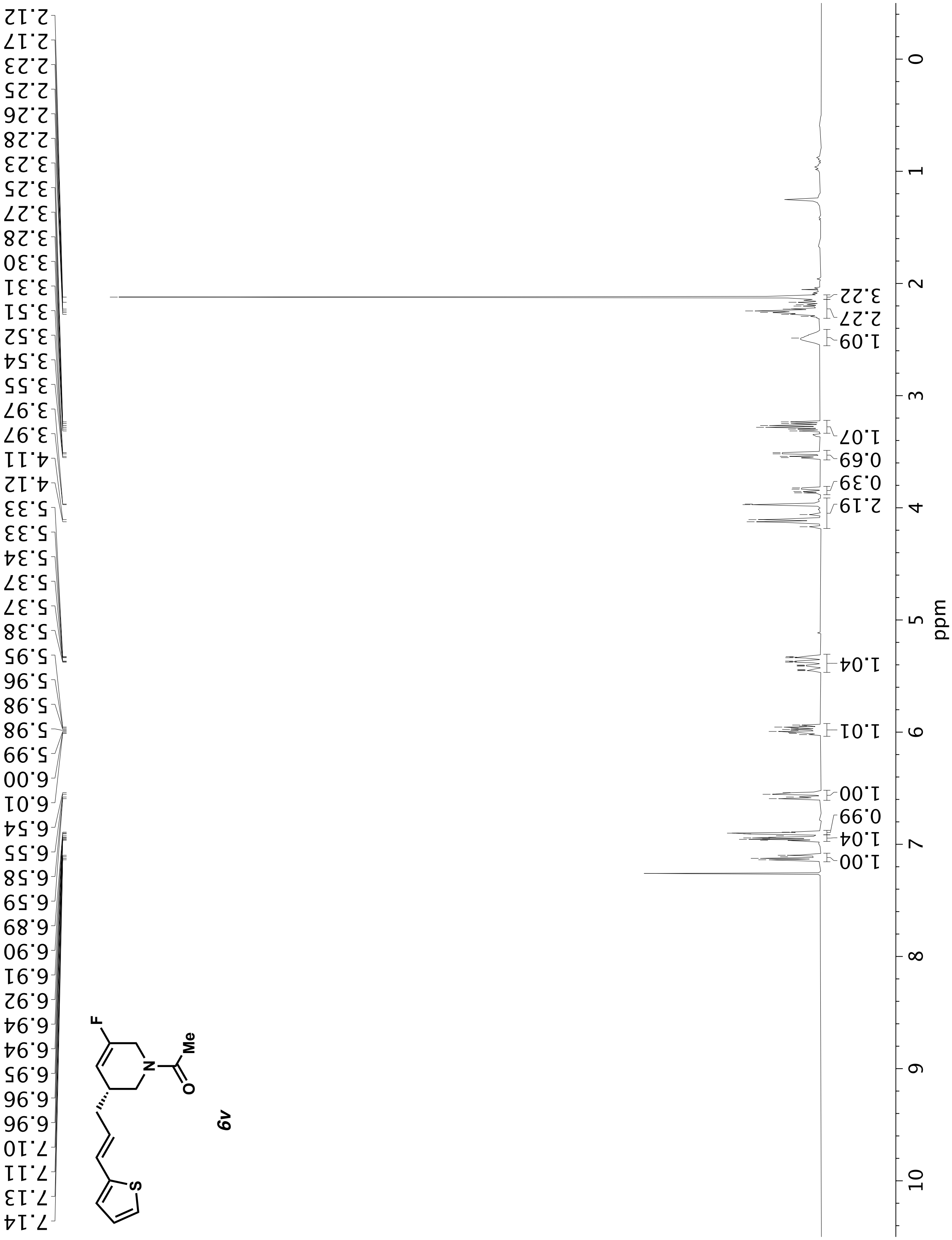
Infrared spectrum (Thin Film, NaCl) of compound **6u**.



$^{13}$C NMR (100 MHz, $CD_2Cl_2$) of compound **6u**.

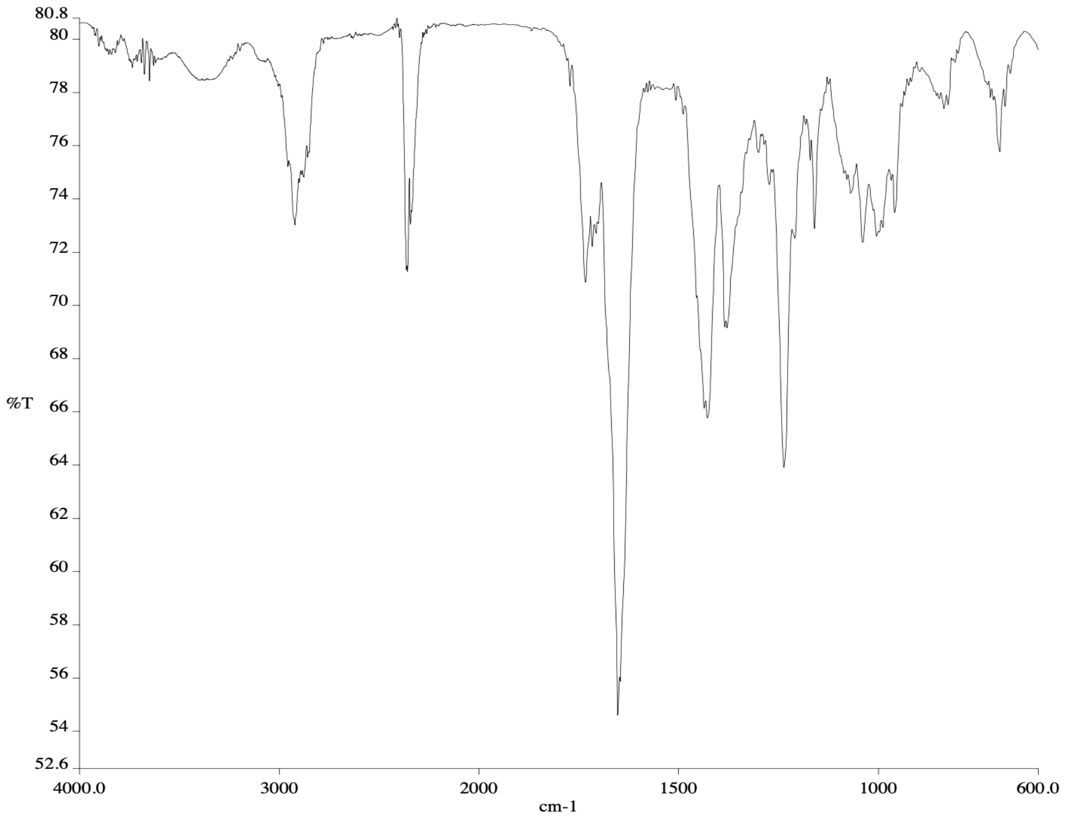


$^{19}$F NMR (282 MHz, $CD_2Cl_2$) of compound **6u.**

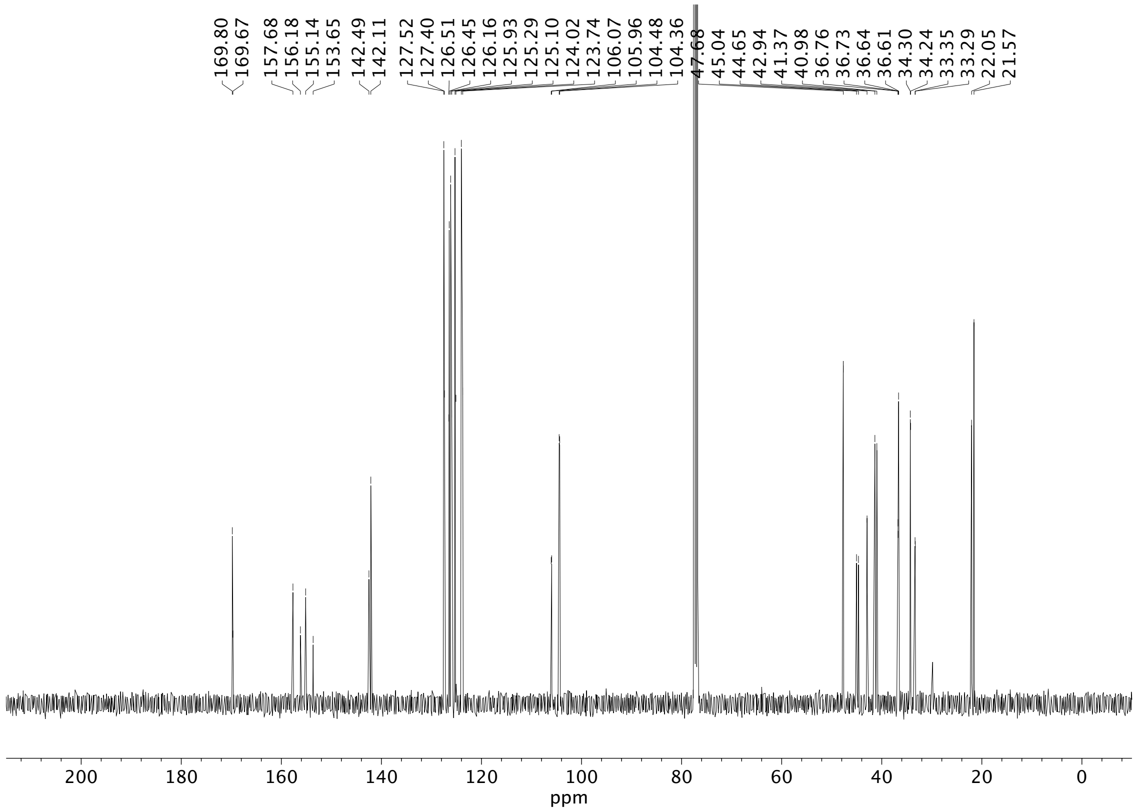


**6v**

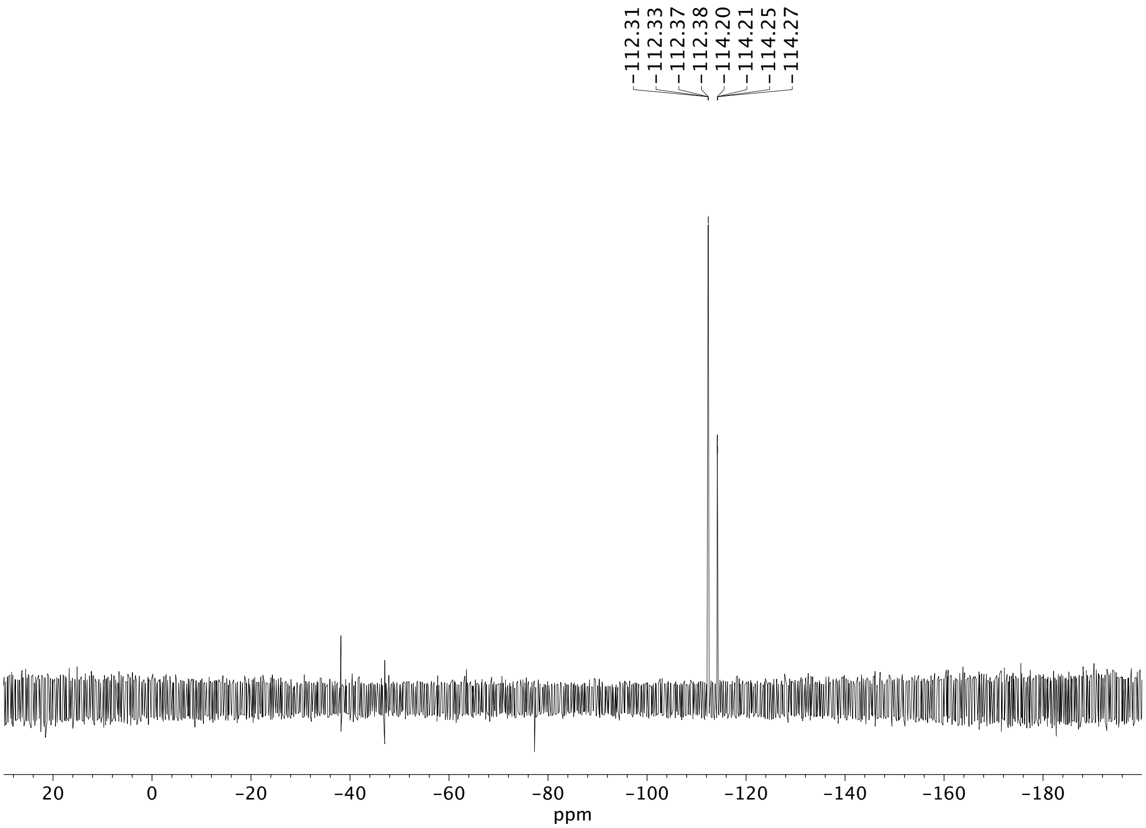
$^1$H NMR (400 MHz, CDCl$_3$) of compound **6v**.



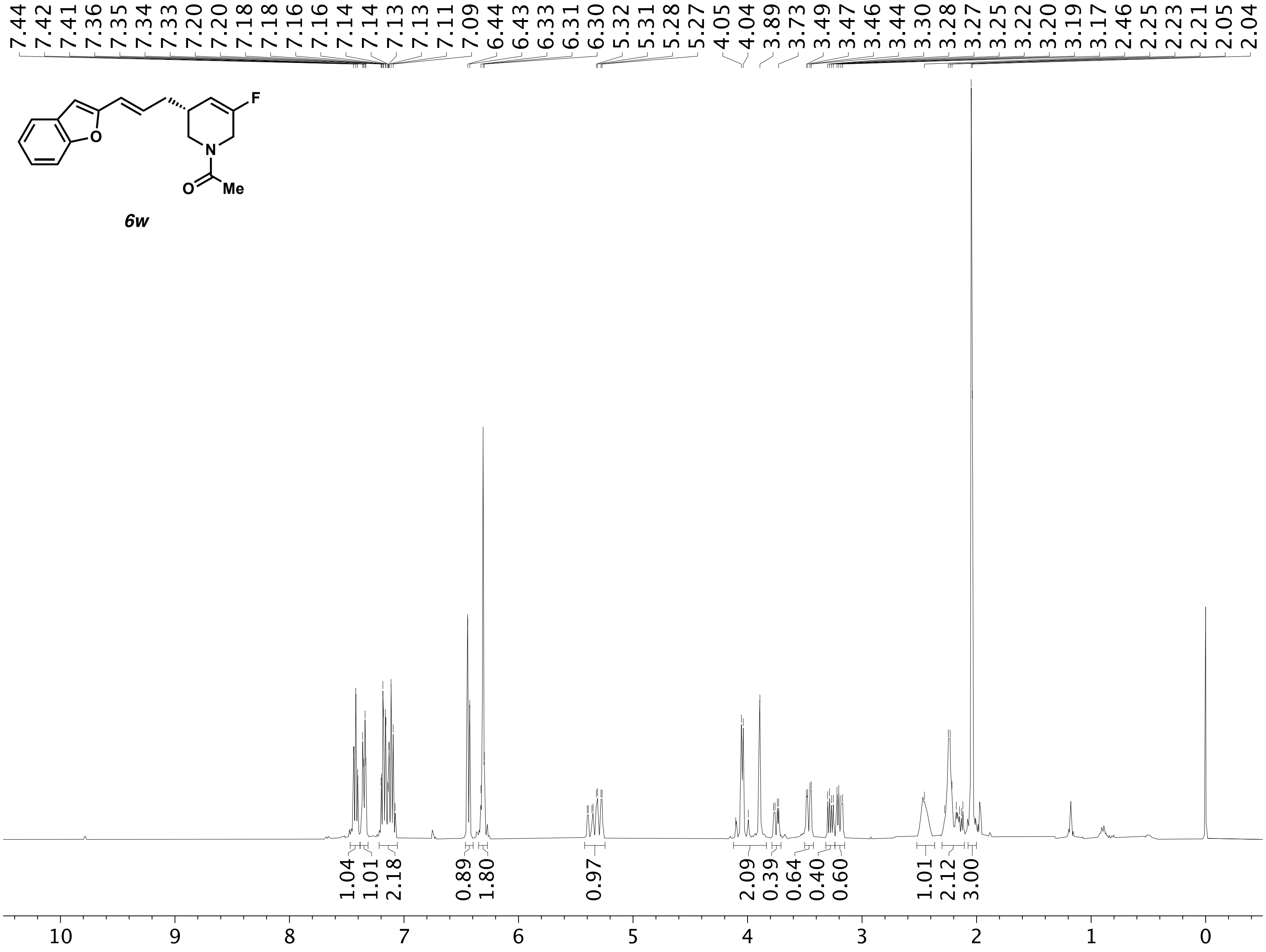
Infrared spectrum (Thin Film, NaCl) of compound **6v.**



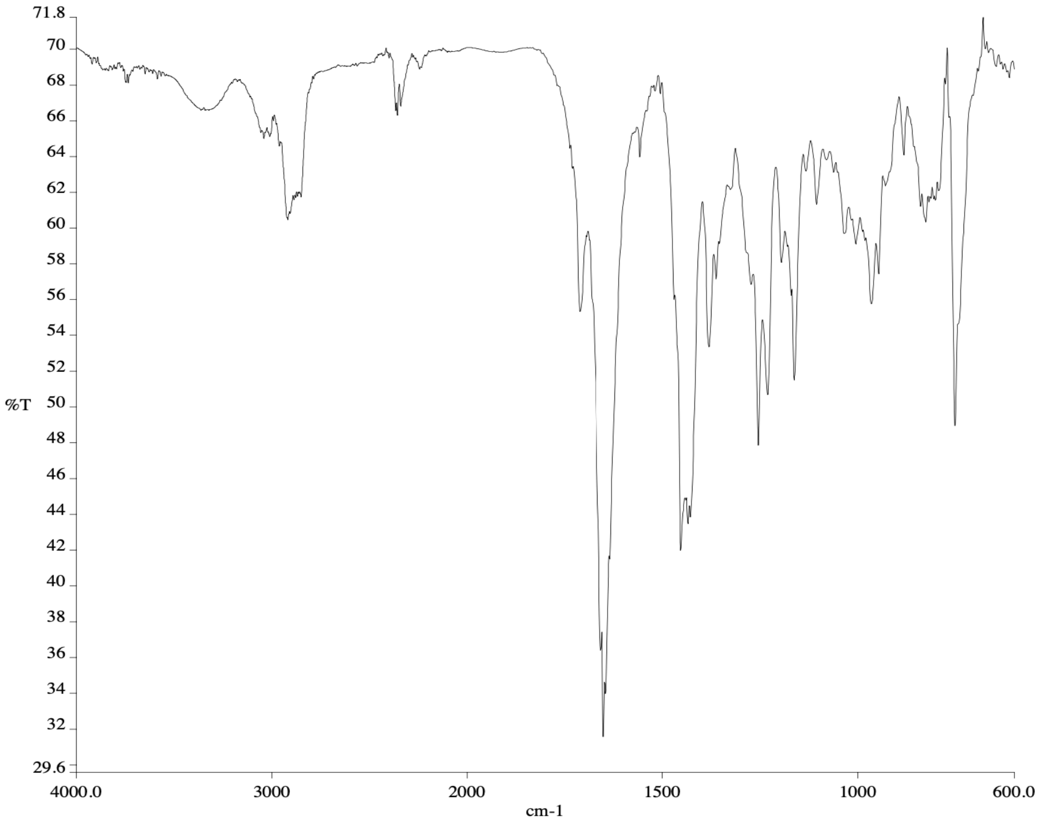
$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **6v**.



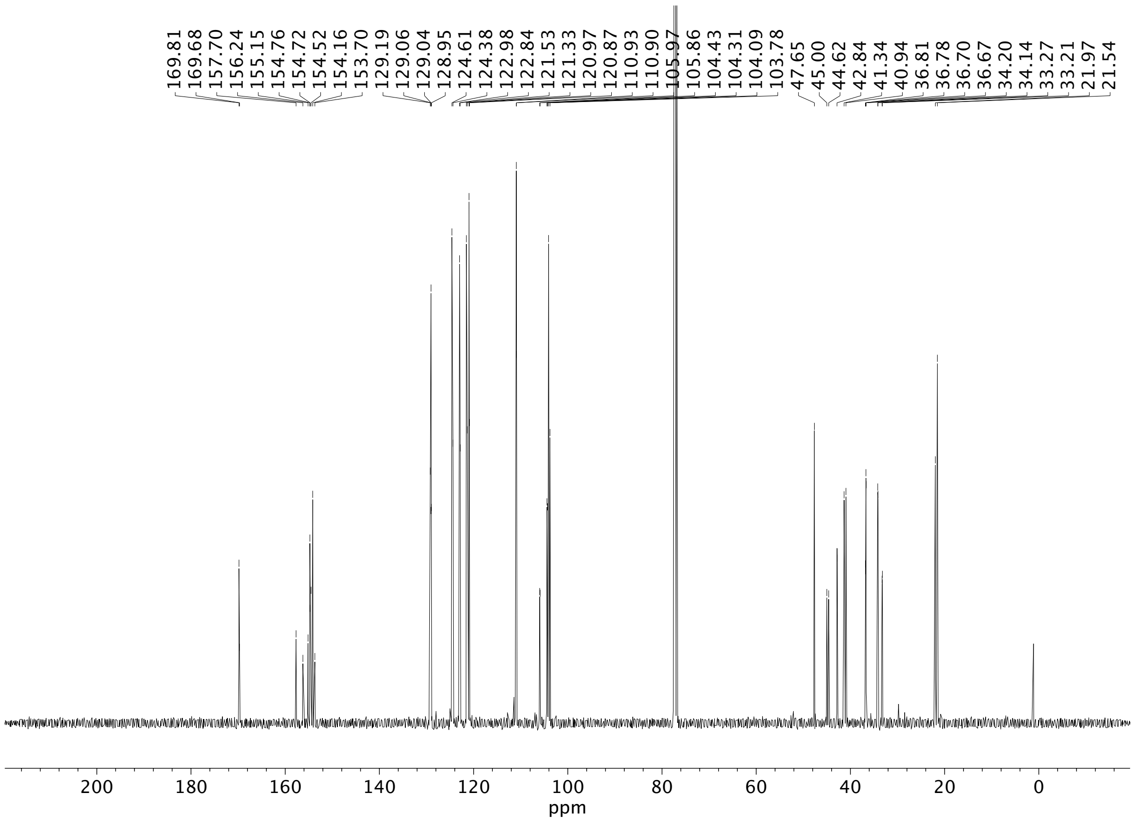
$^{19}$F NMR (282 MHz, $CDCl_3$) of compound **6v**.



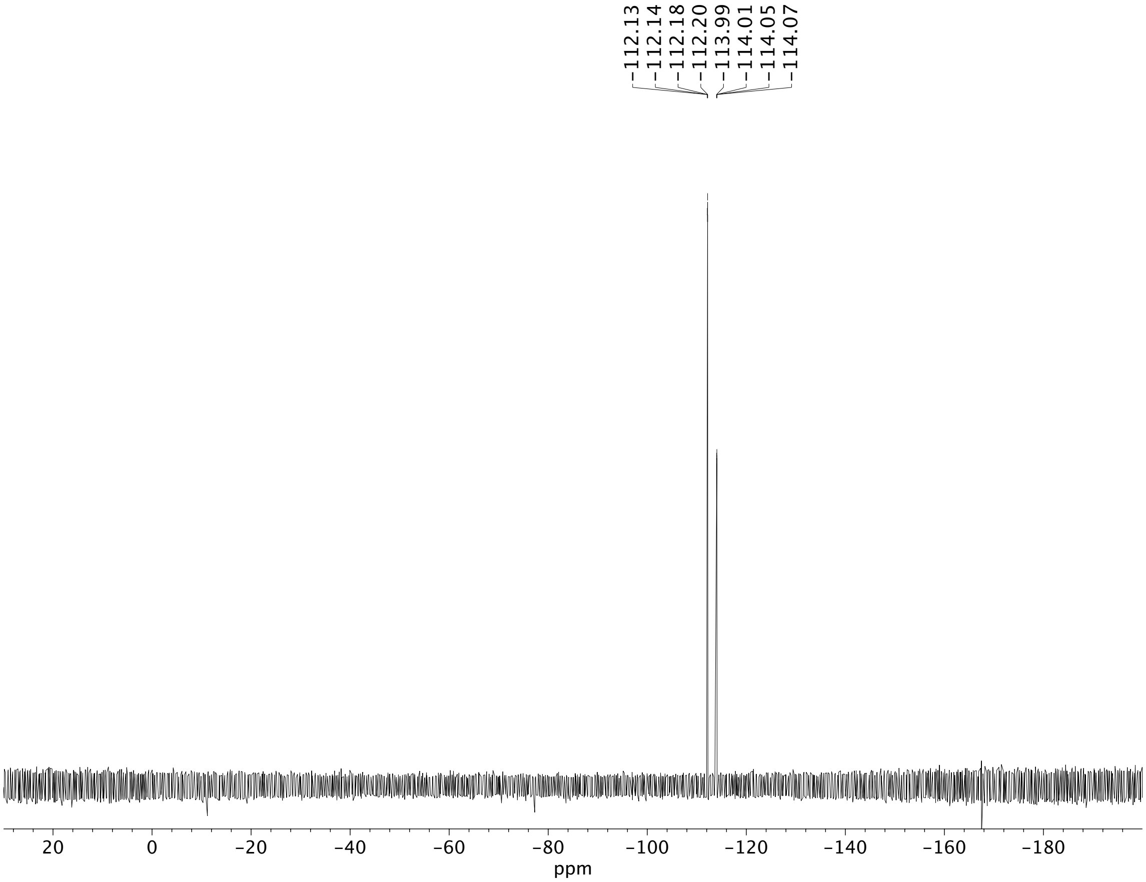
$^1$H NMR (400 MHz, CDCl$_3$) of compound **6w**.



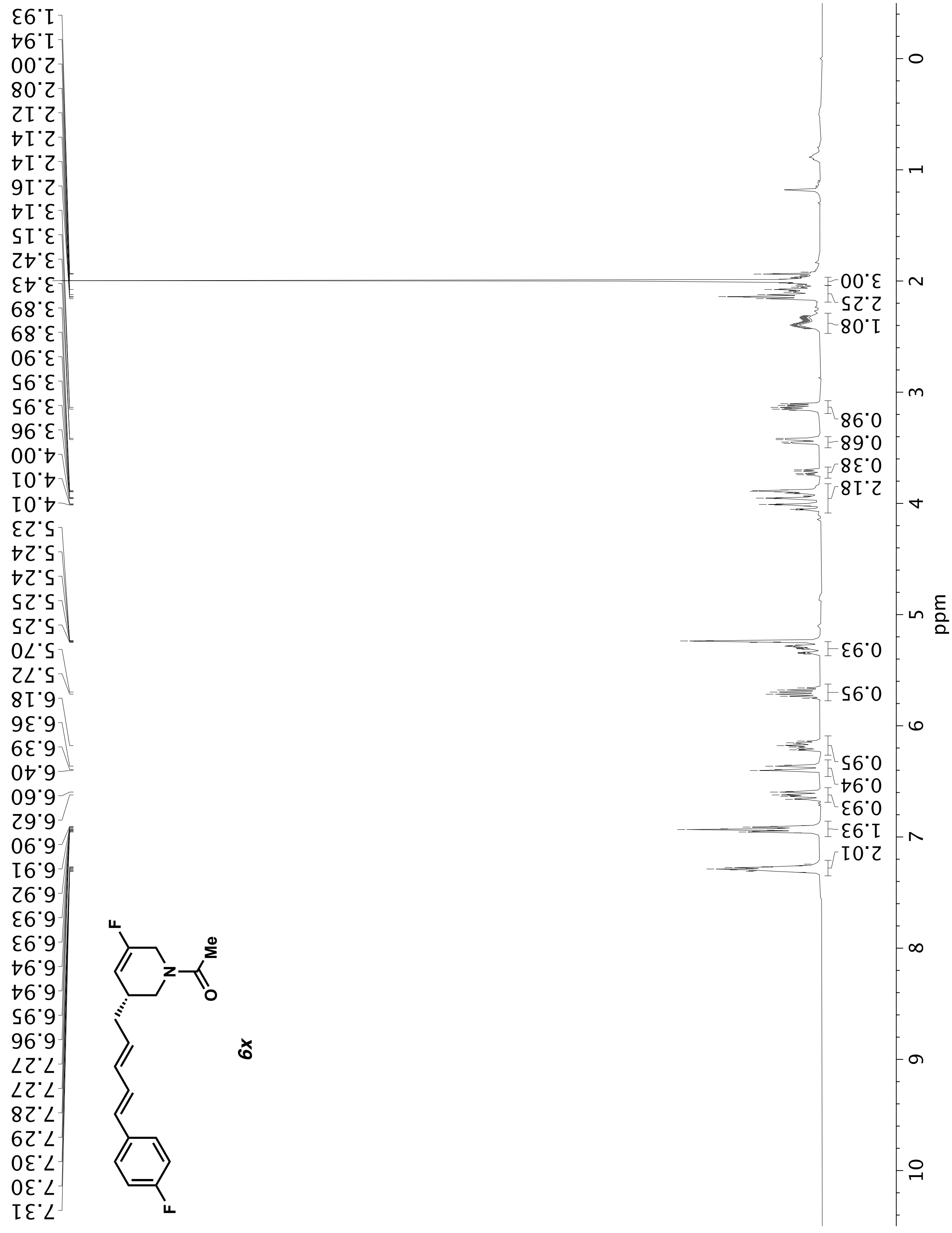
Infrared spectrum (Thin Film, NaCl) of compound **6w**.



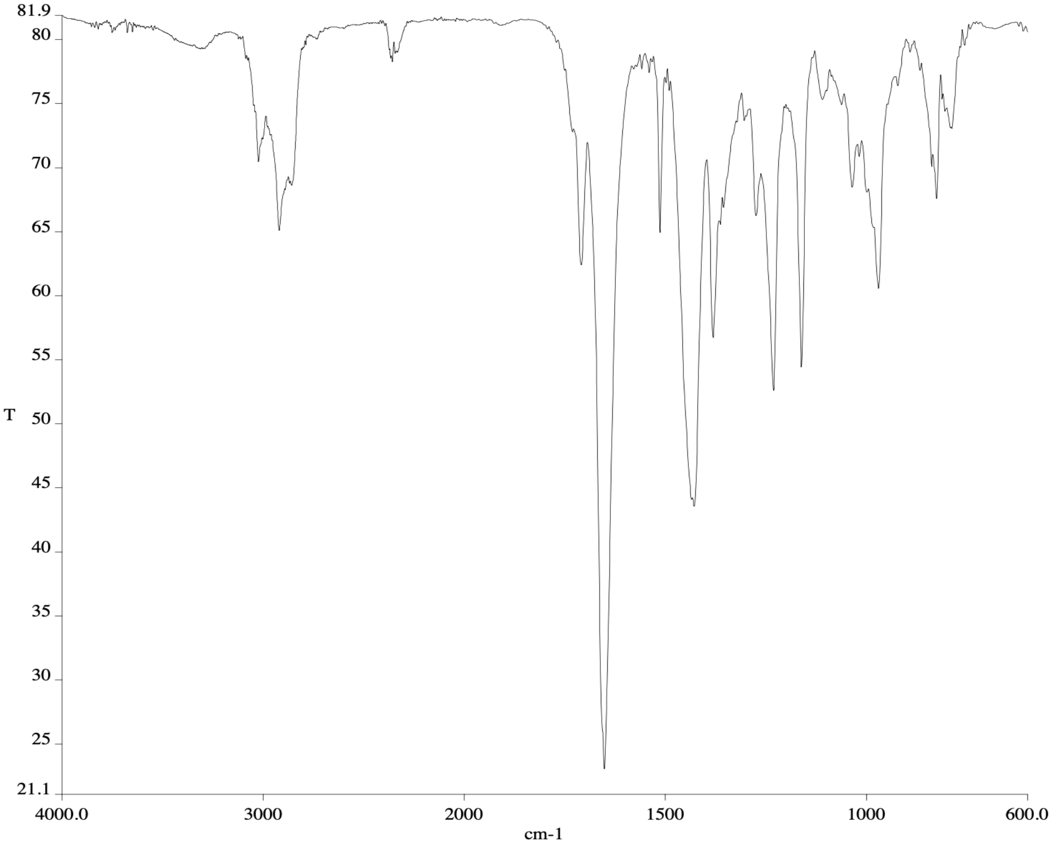
$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **6w**.



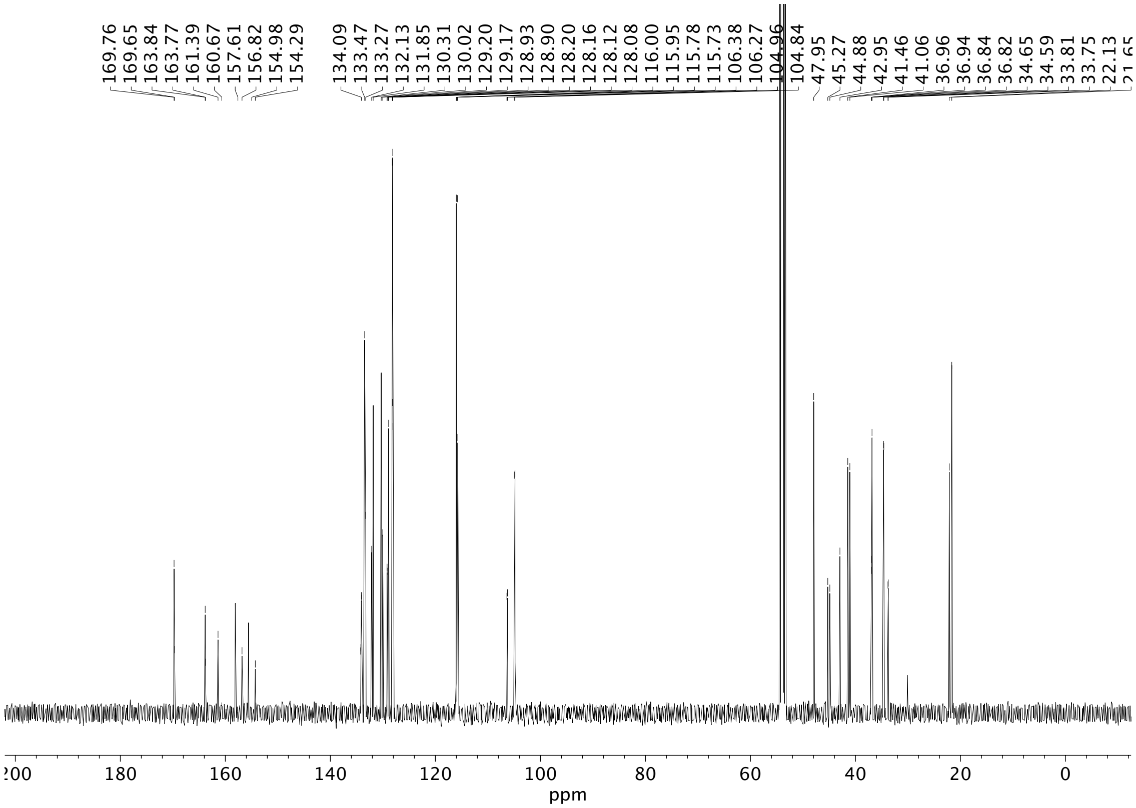
$^{19}$F NMR (282 MHz, CDCl$_3$) of compound **6w.**



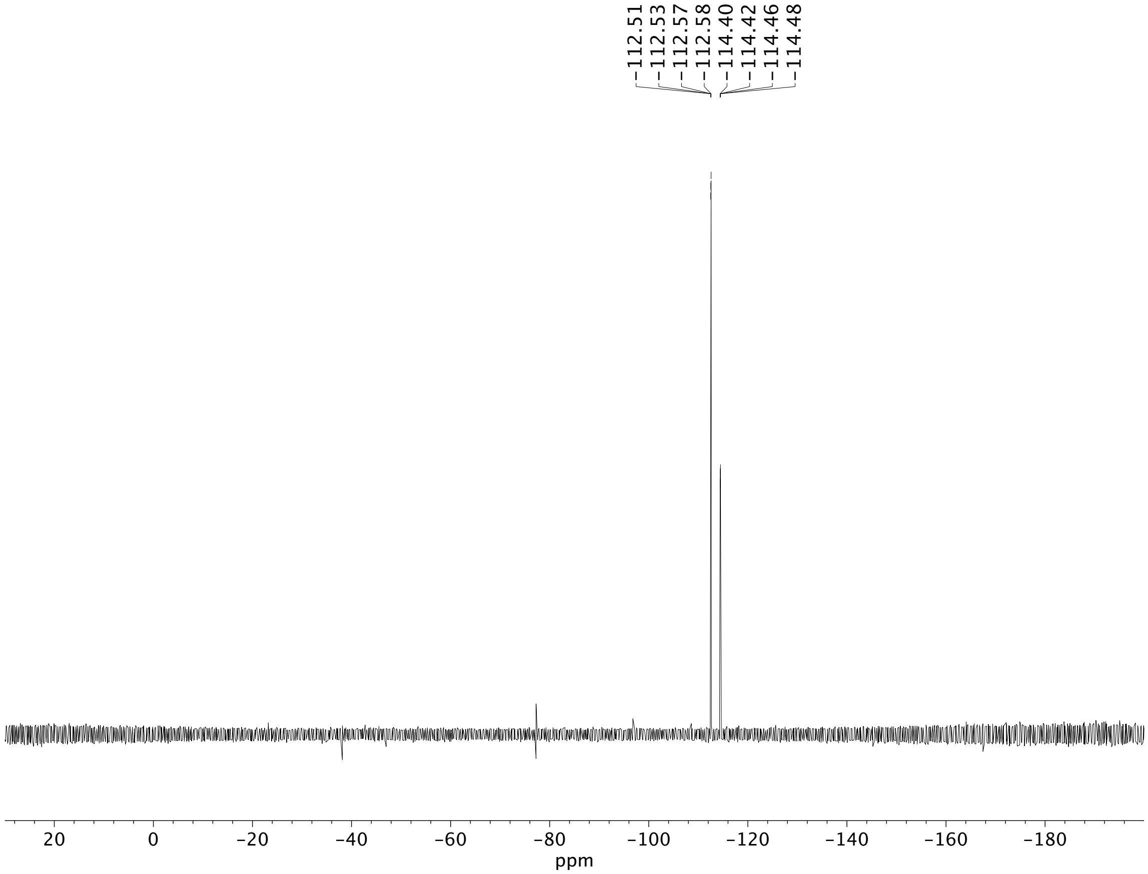
$^1$H NMR (400 MHz, $CD_2Cl_2$) of compound **6x**



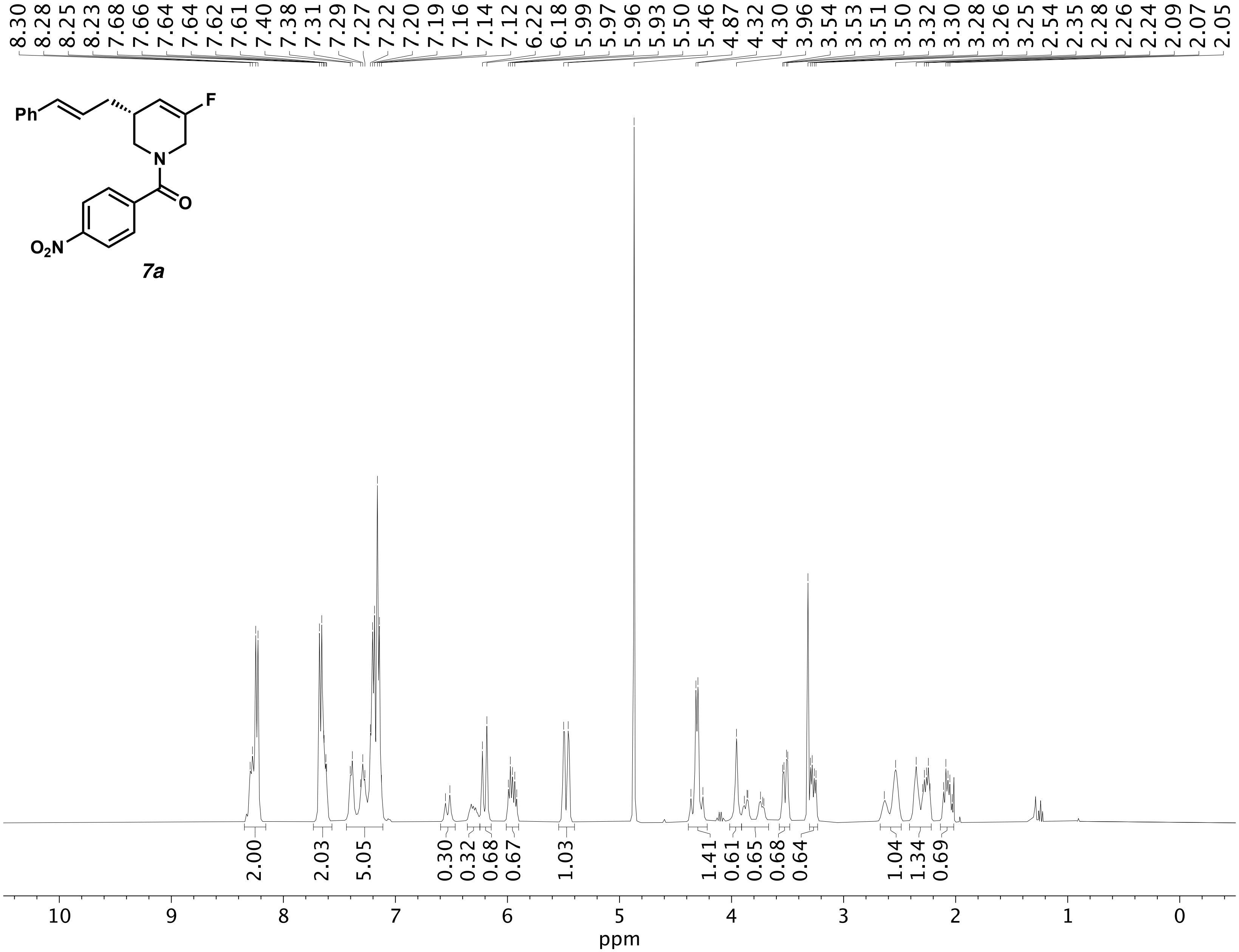
Infrared spectrum (Thin Film, NaCl) of compound **6x**.



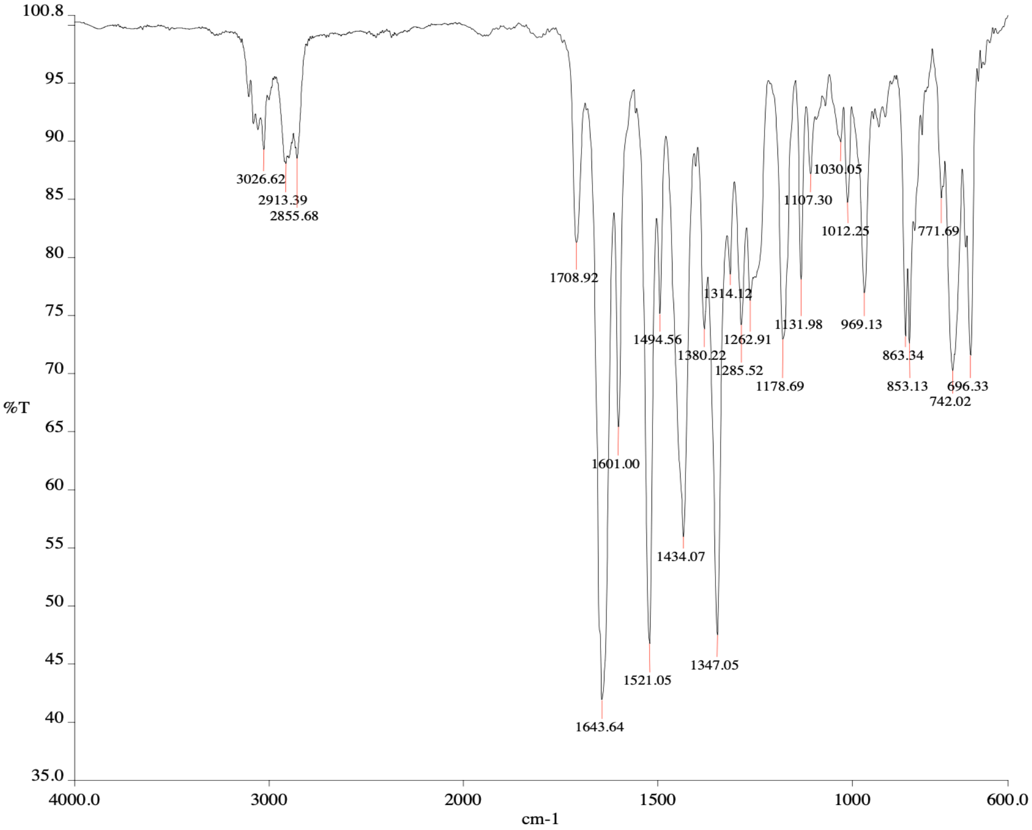
$^{13}$C NMR (100 MHz, $CD_2Cl_2$) of compound **6x**.



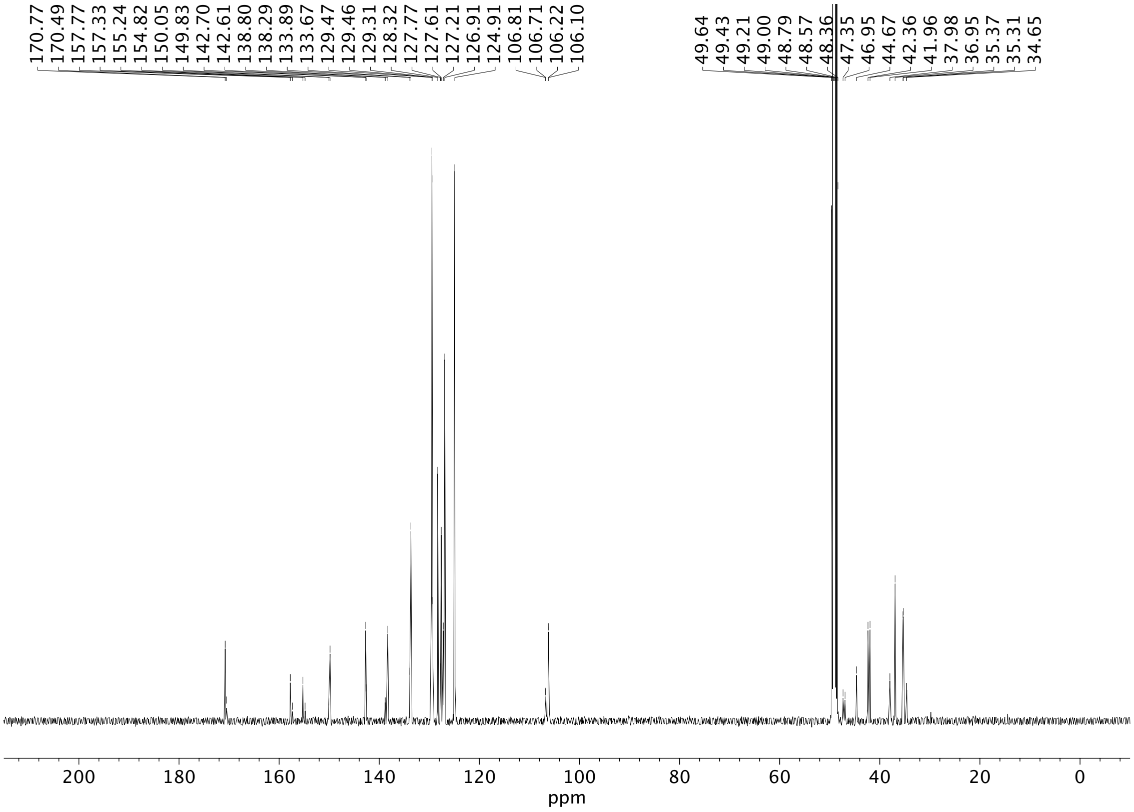
$^{19}$F NMR (282 MHz, $CD_2Cl_2$) of compound **6x**.



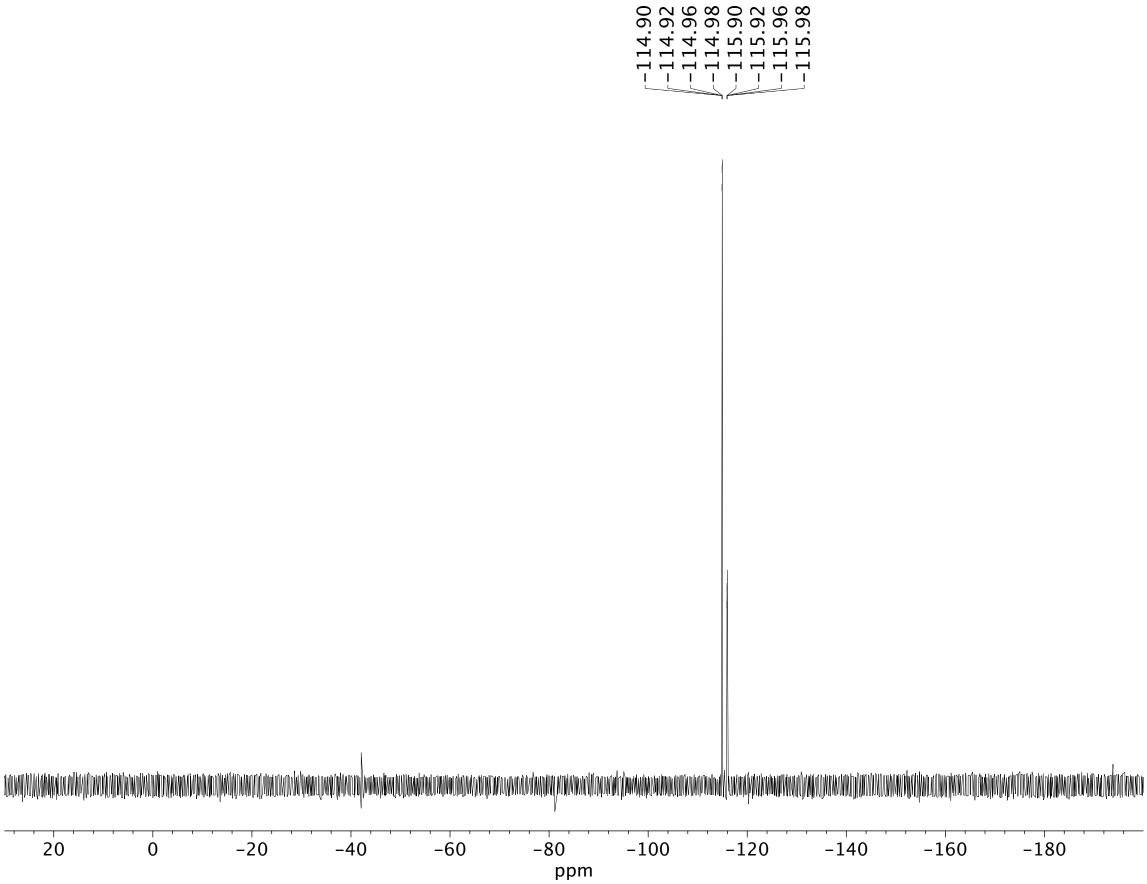
$^1$H NMR (500 MHz, CD$_3$OD) of compound **7a**.



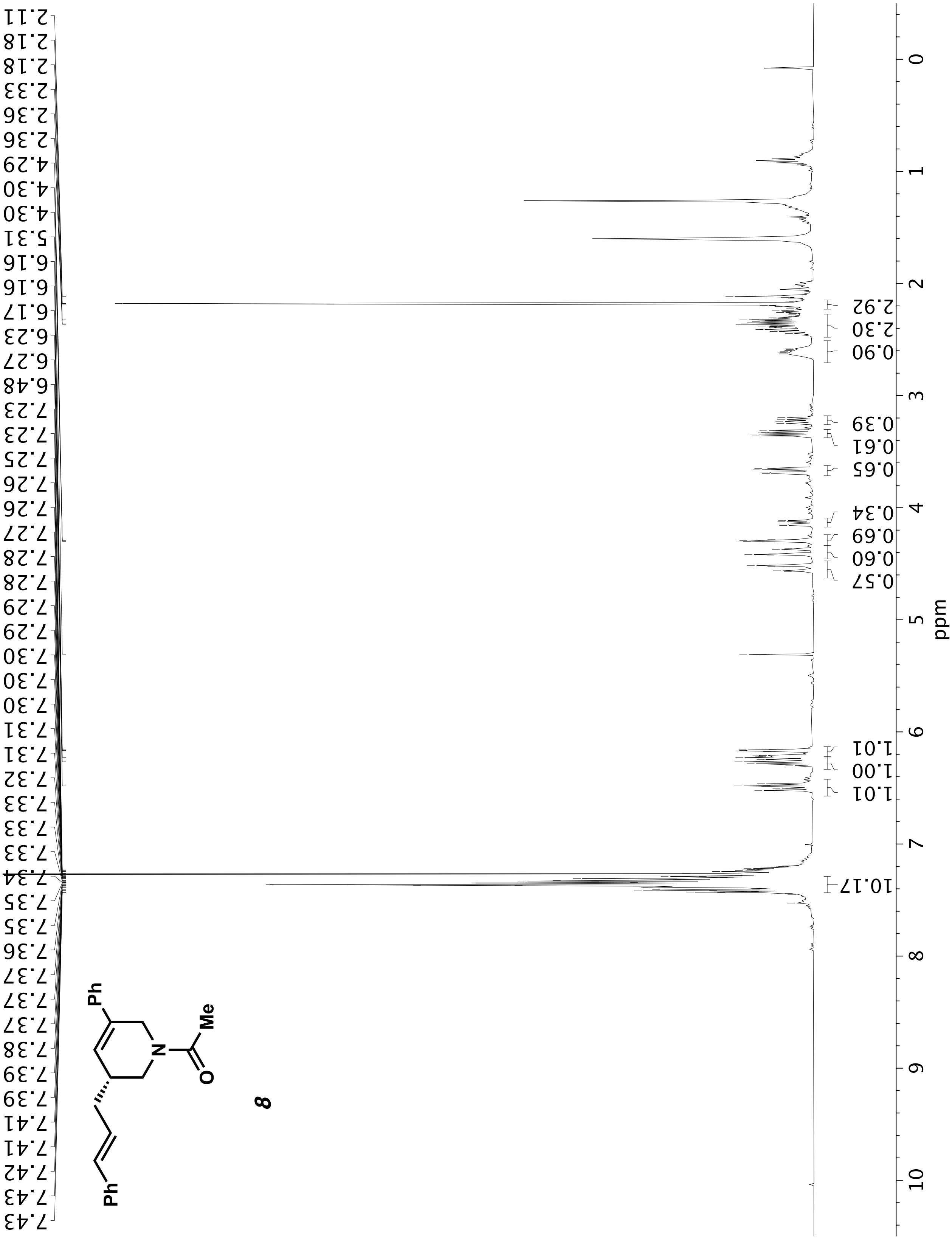
Infrared spectrum (Thin Film, NaCl) of compound **7a**.



$^{13}$C NMR (100 MHz, CD$_3$OD) of compound **7a**.

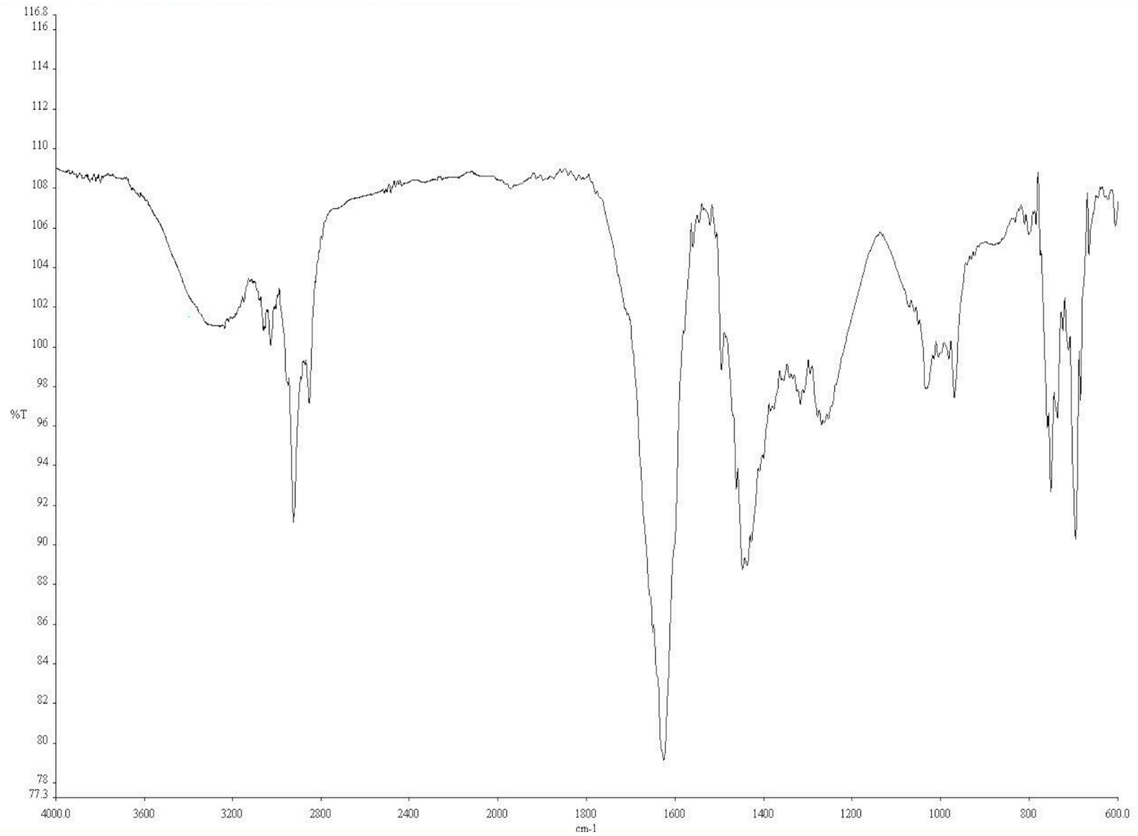


$^{19}$F NMR (282 MHz, $CD_3OD$) of compound **7a**.

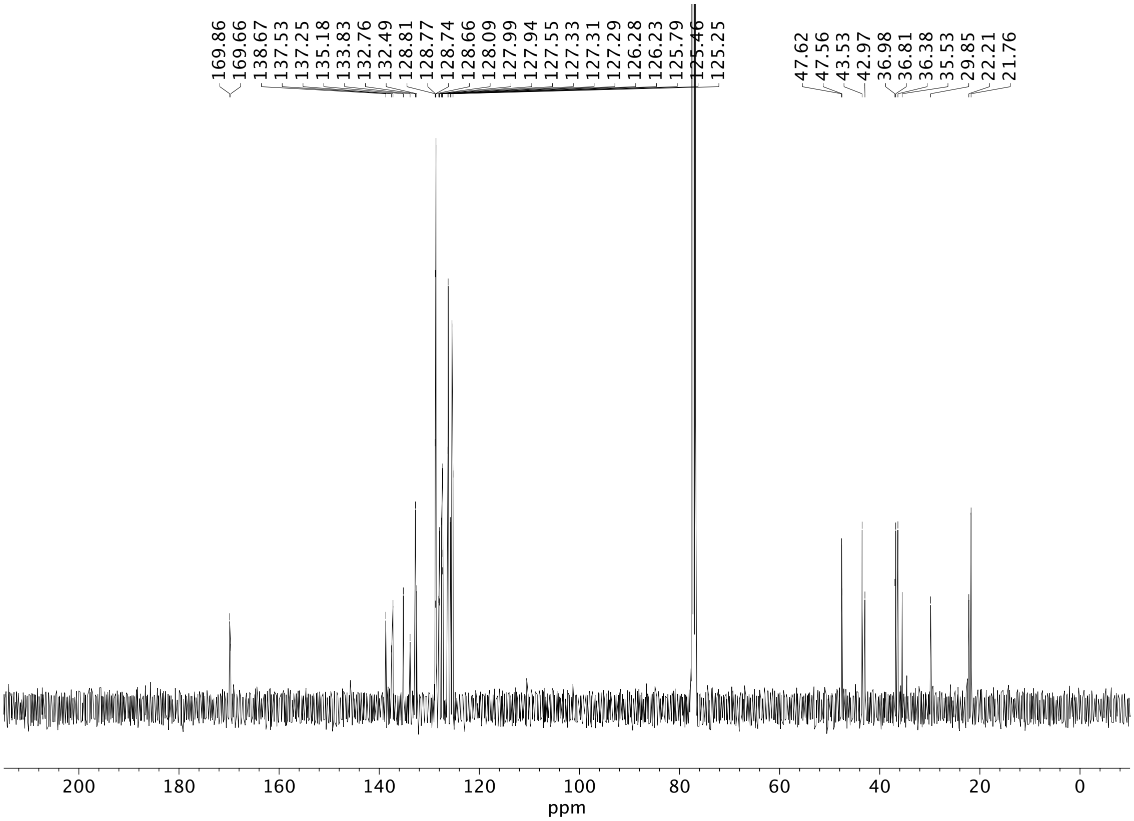


8

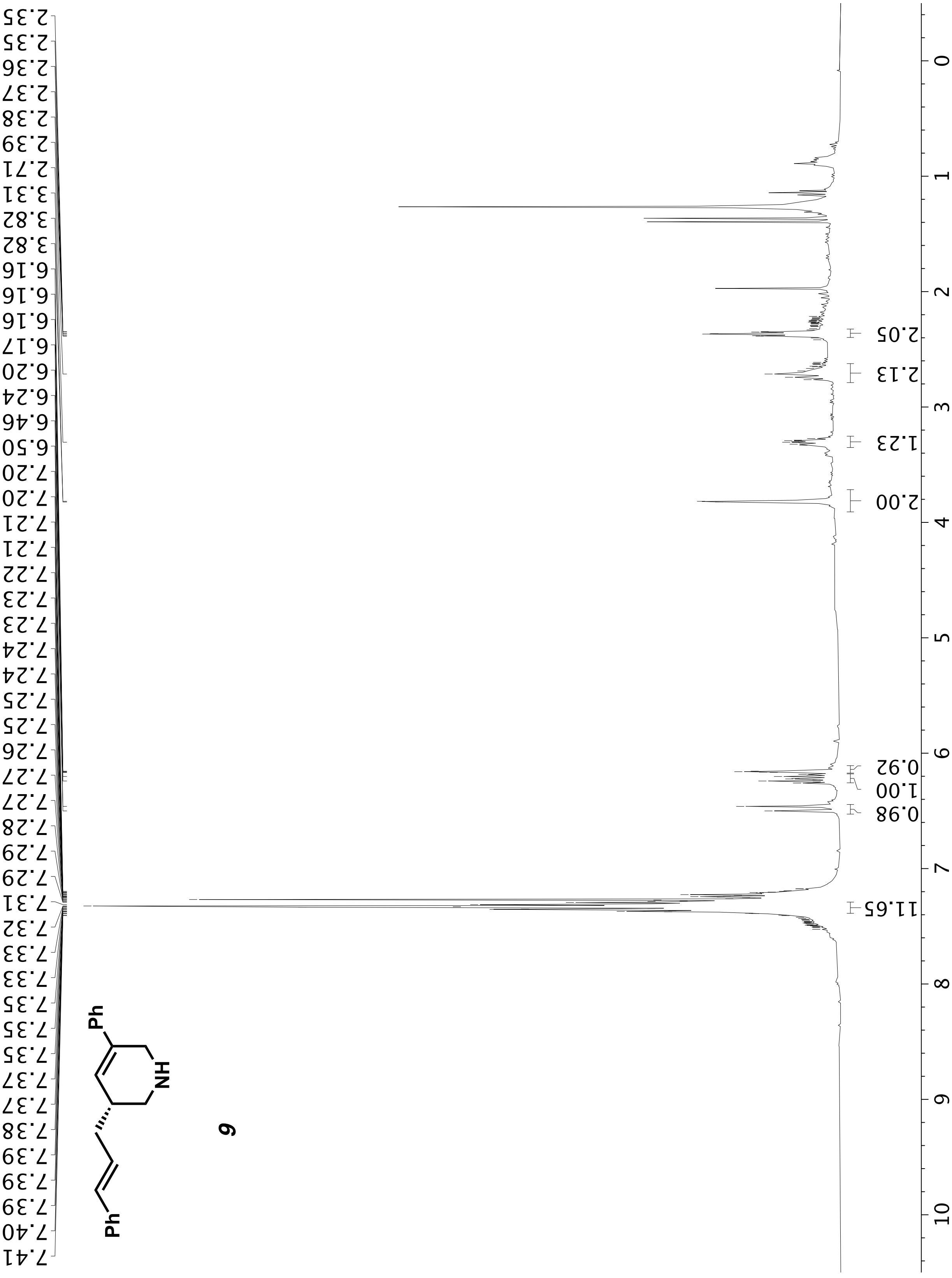
$^1$H NMR (400 MHz, CDCl$_3$) of compound **8**.



Infrared spectrum (Thin Film, NaCl) of compound **8**.

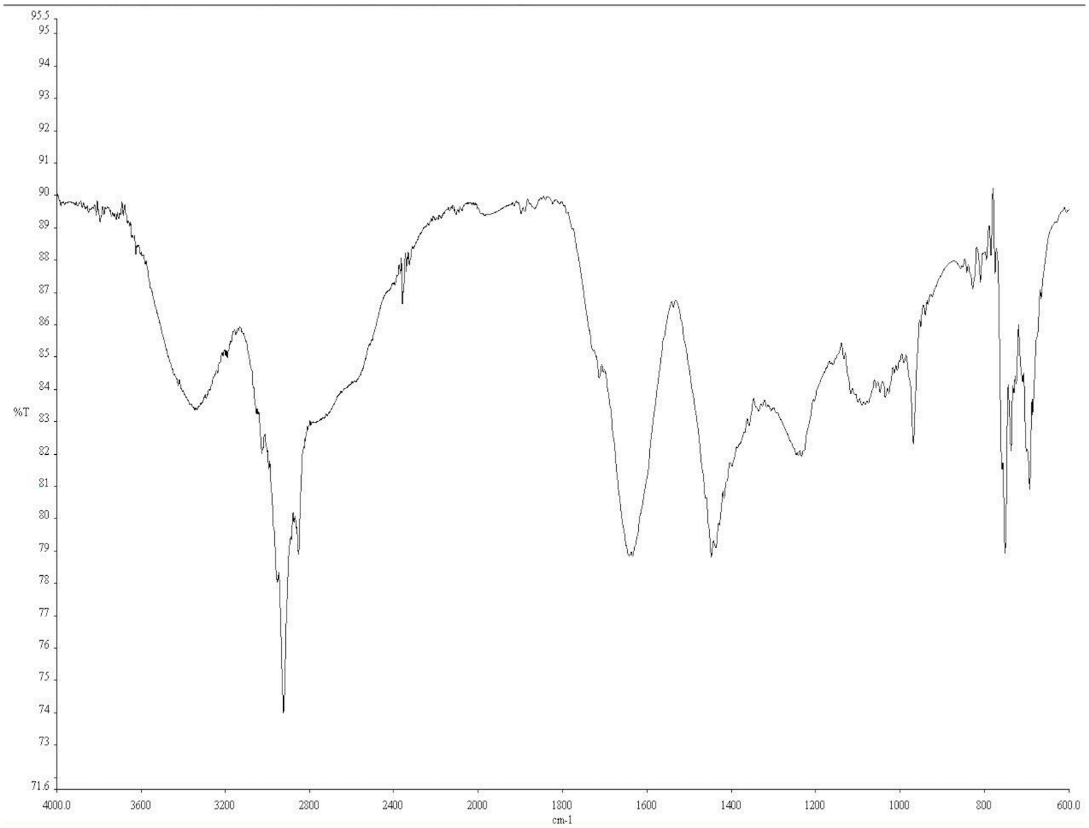


$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **8**.

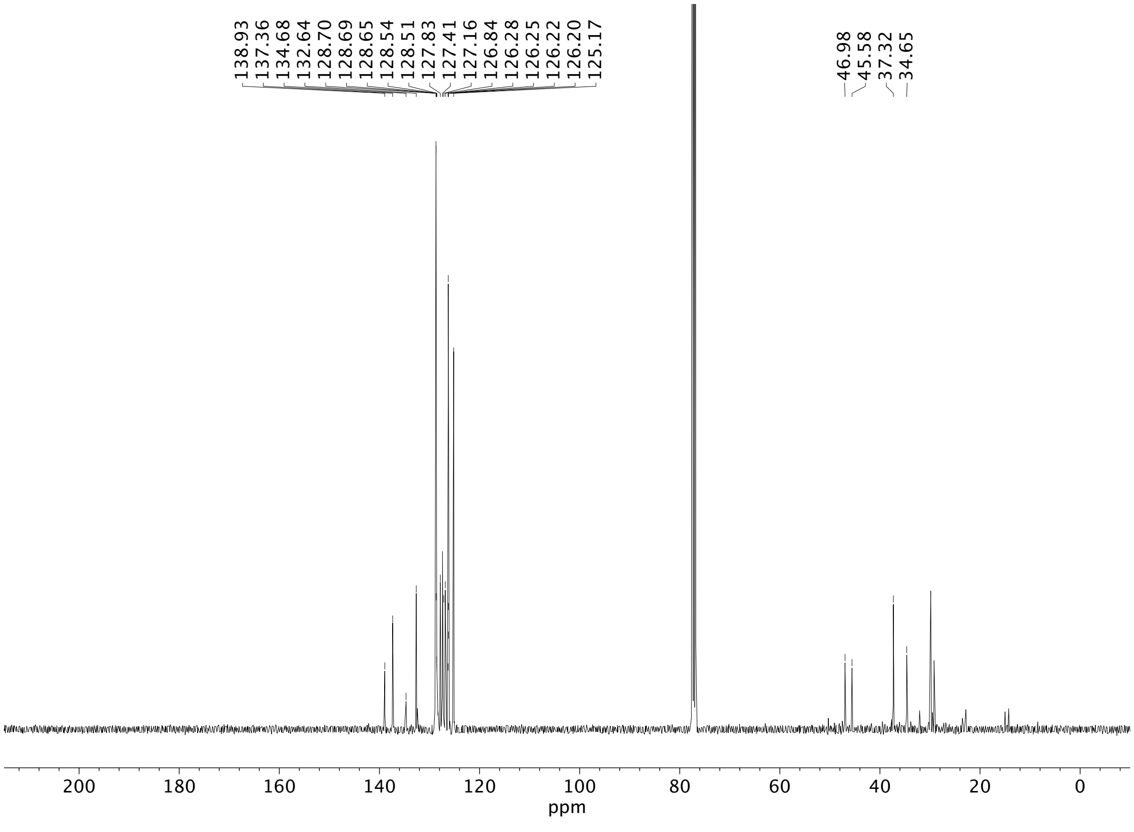


**9**

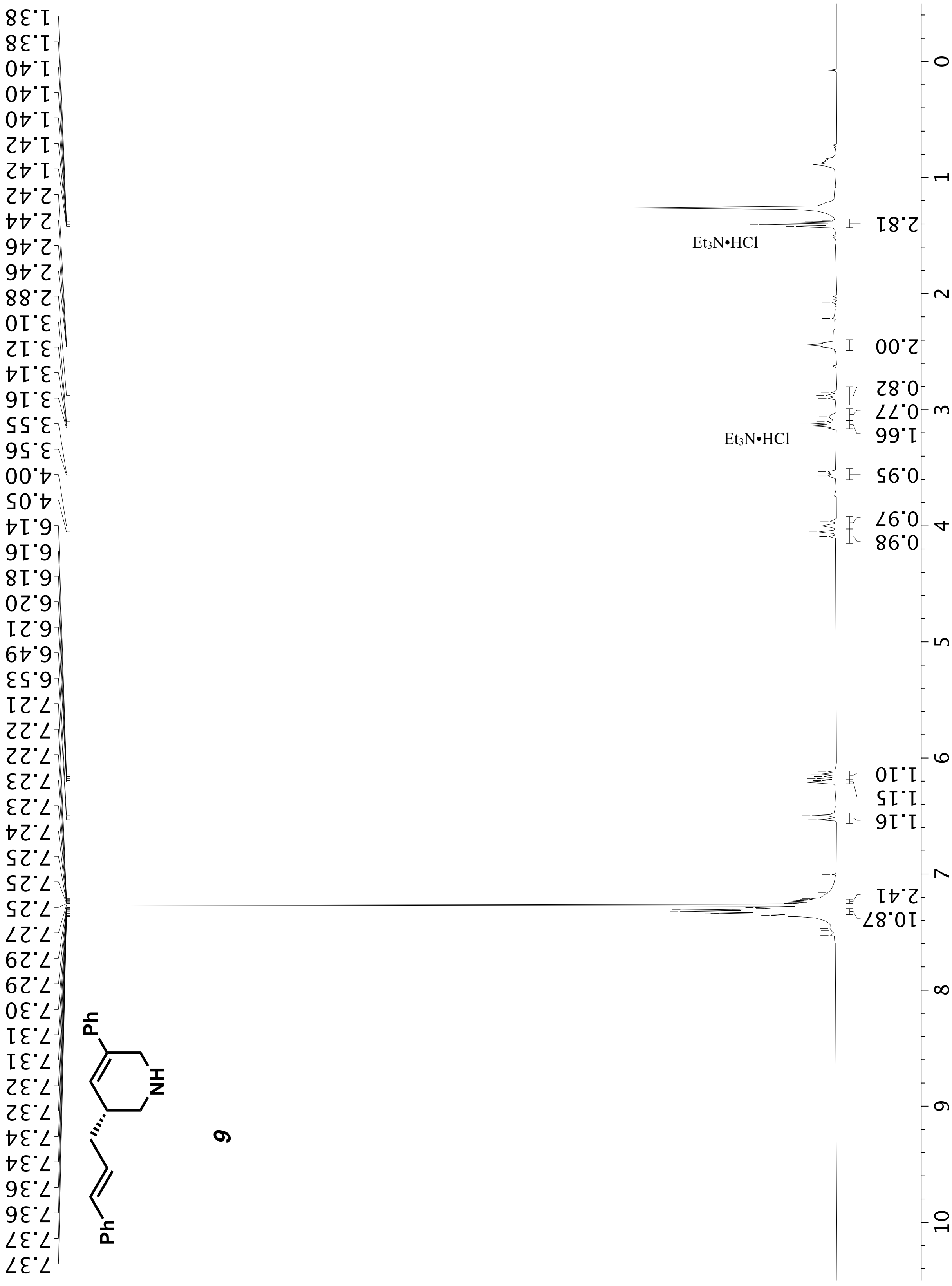
$^1$H NMR (400 MHz, CDCl$_3$) of compound **9**.



Infrared spectrum (Thin Film, NaCl) of compound **9**.

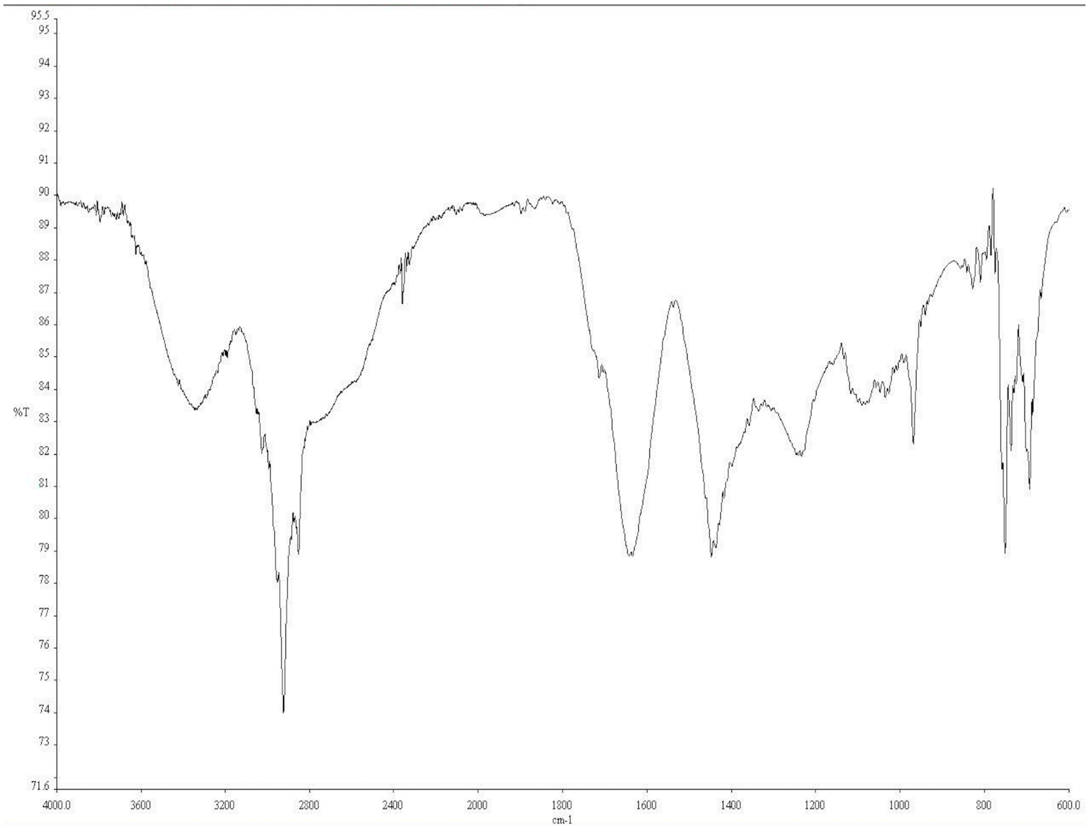


$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **9**.

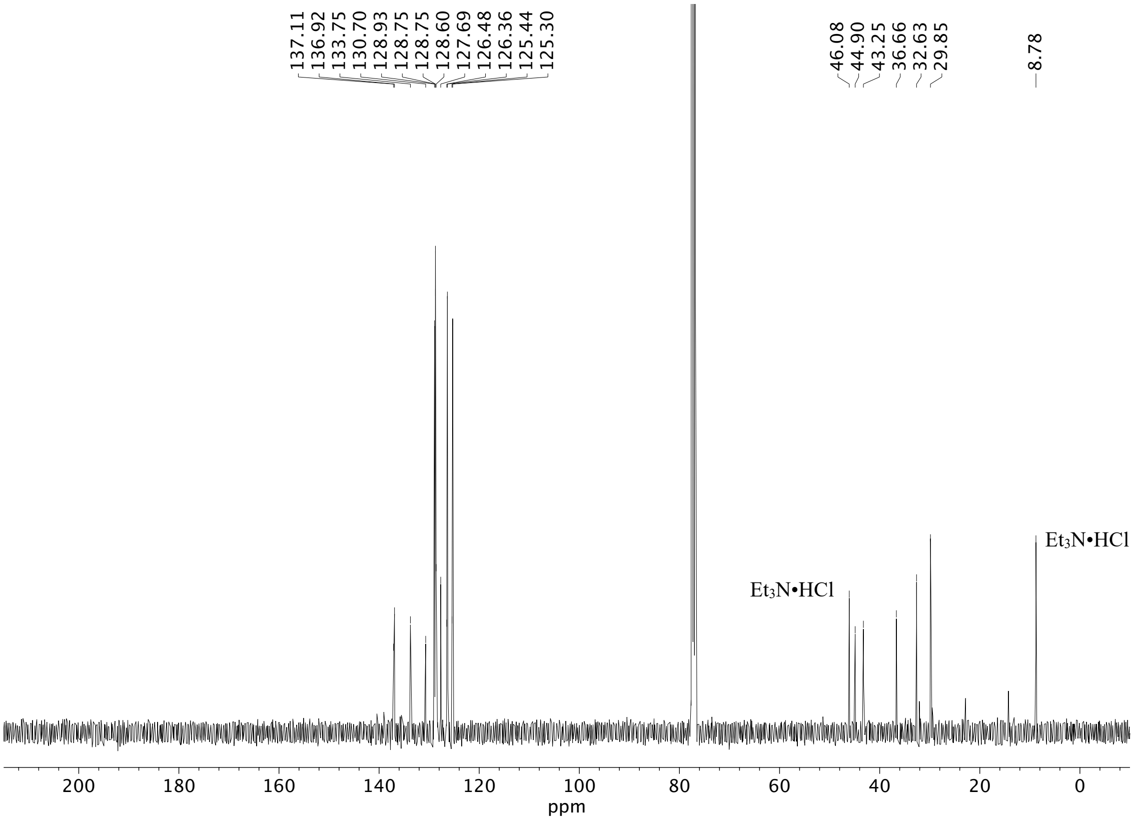


**9**

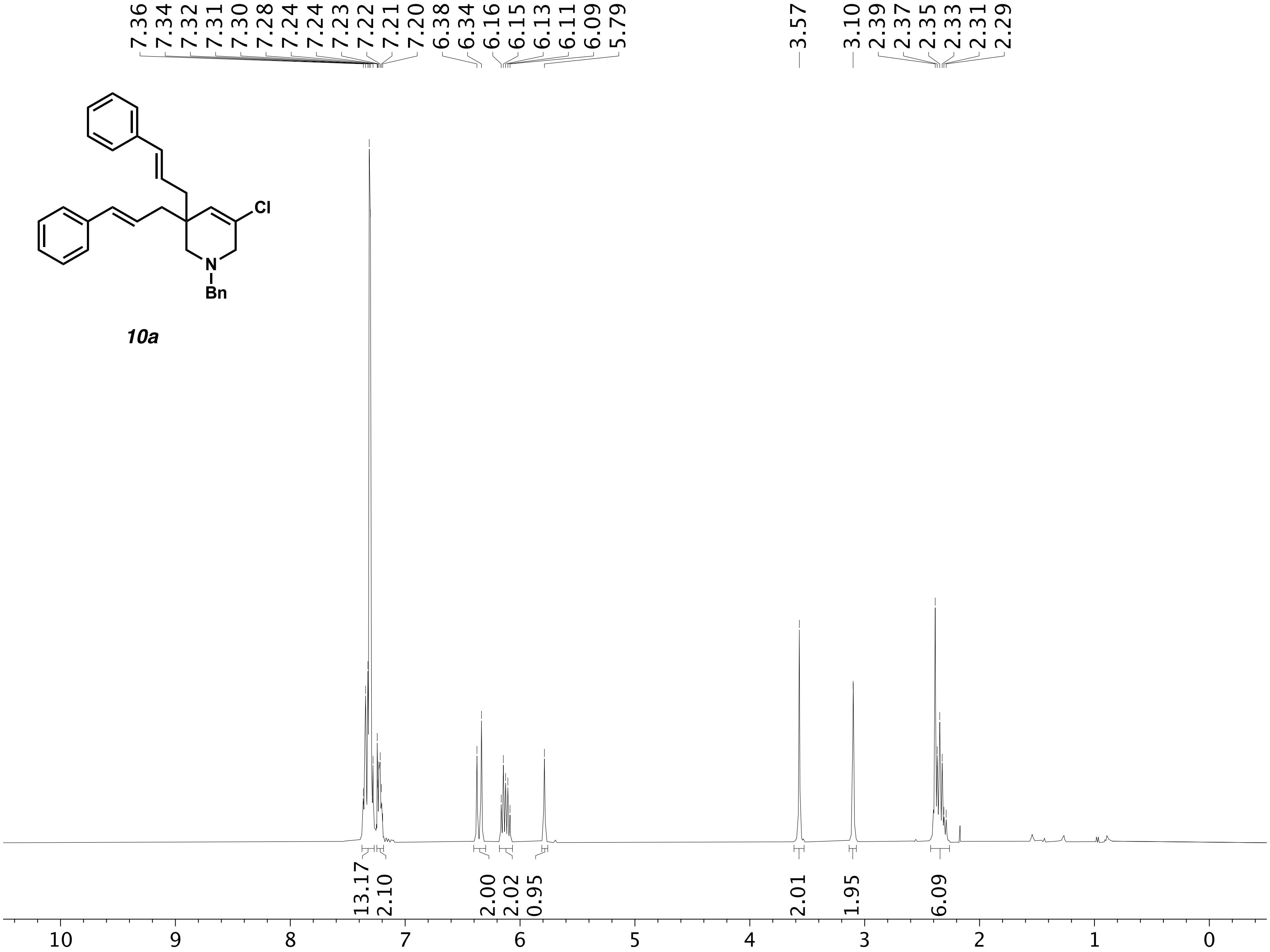
$^1$H NMR (400 MHz, CDCl$_3$) of compound **9**.



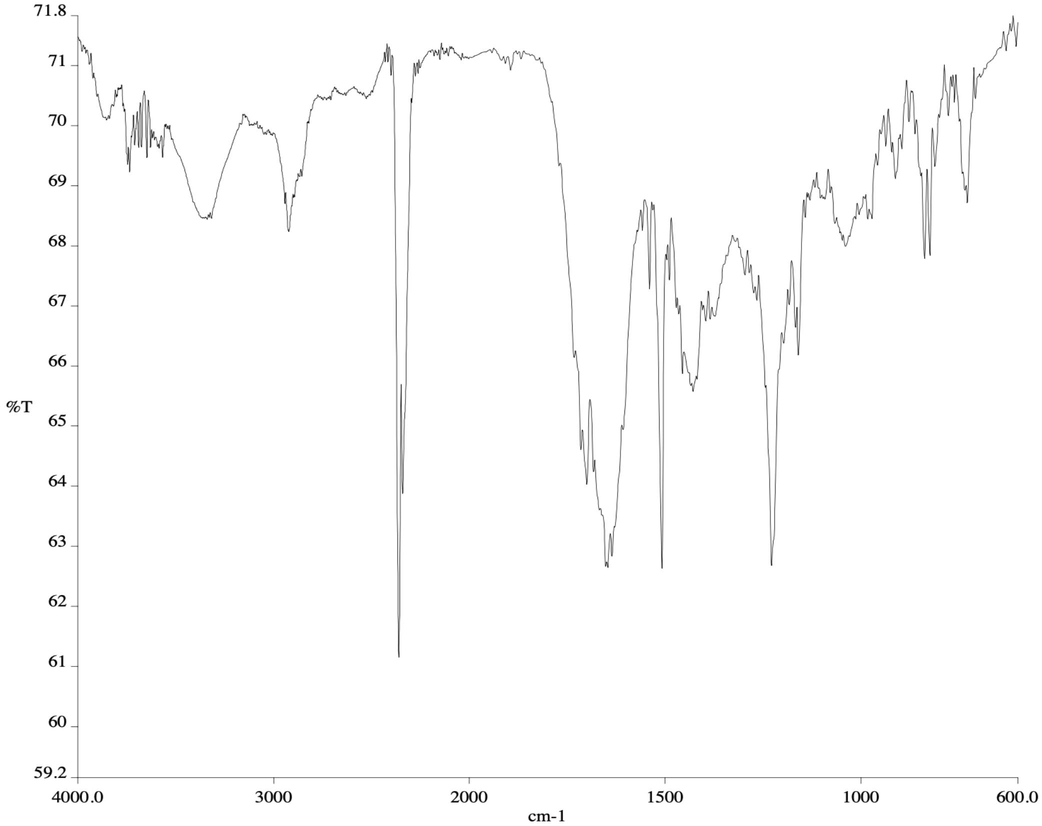
Infrared spectrum (Thin Film, NaCl) of compound **9**.



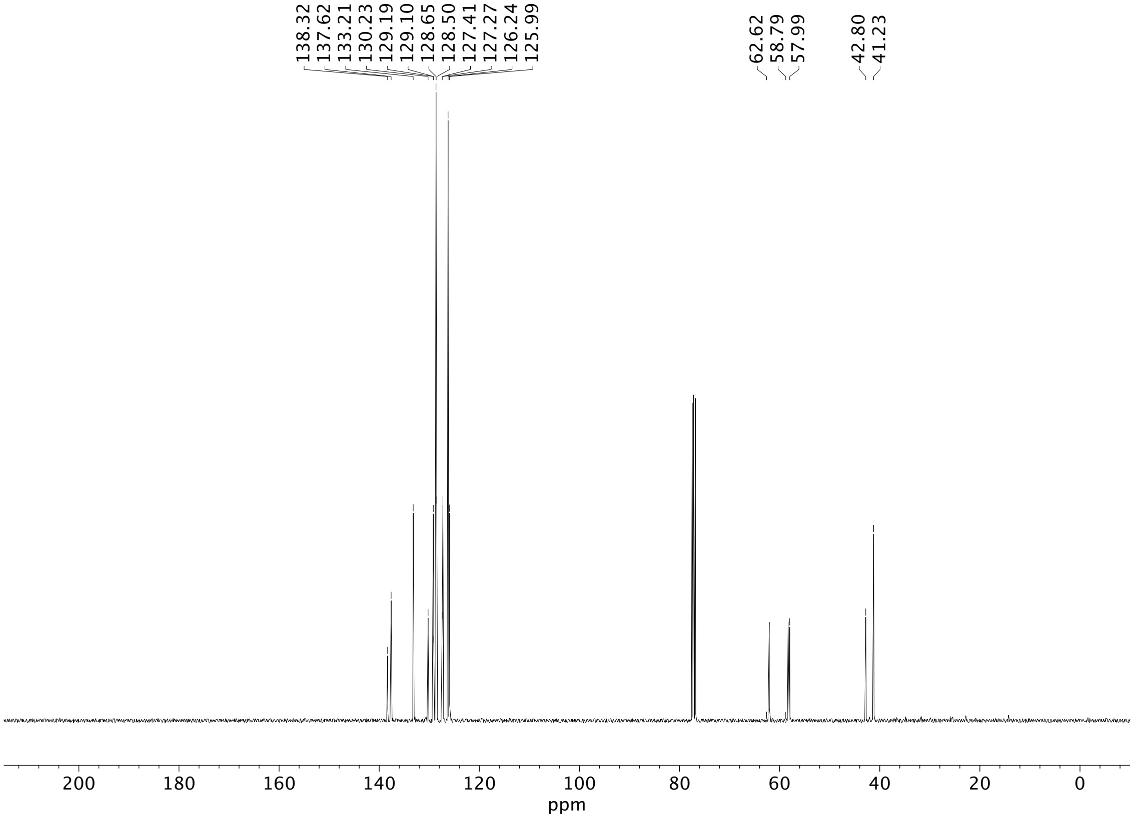
$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **9**.



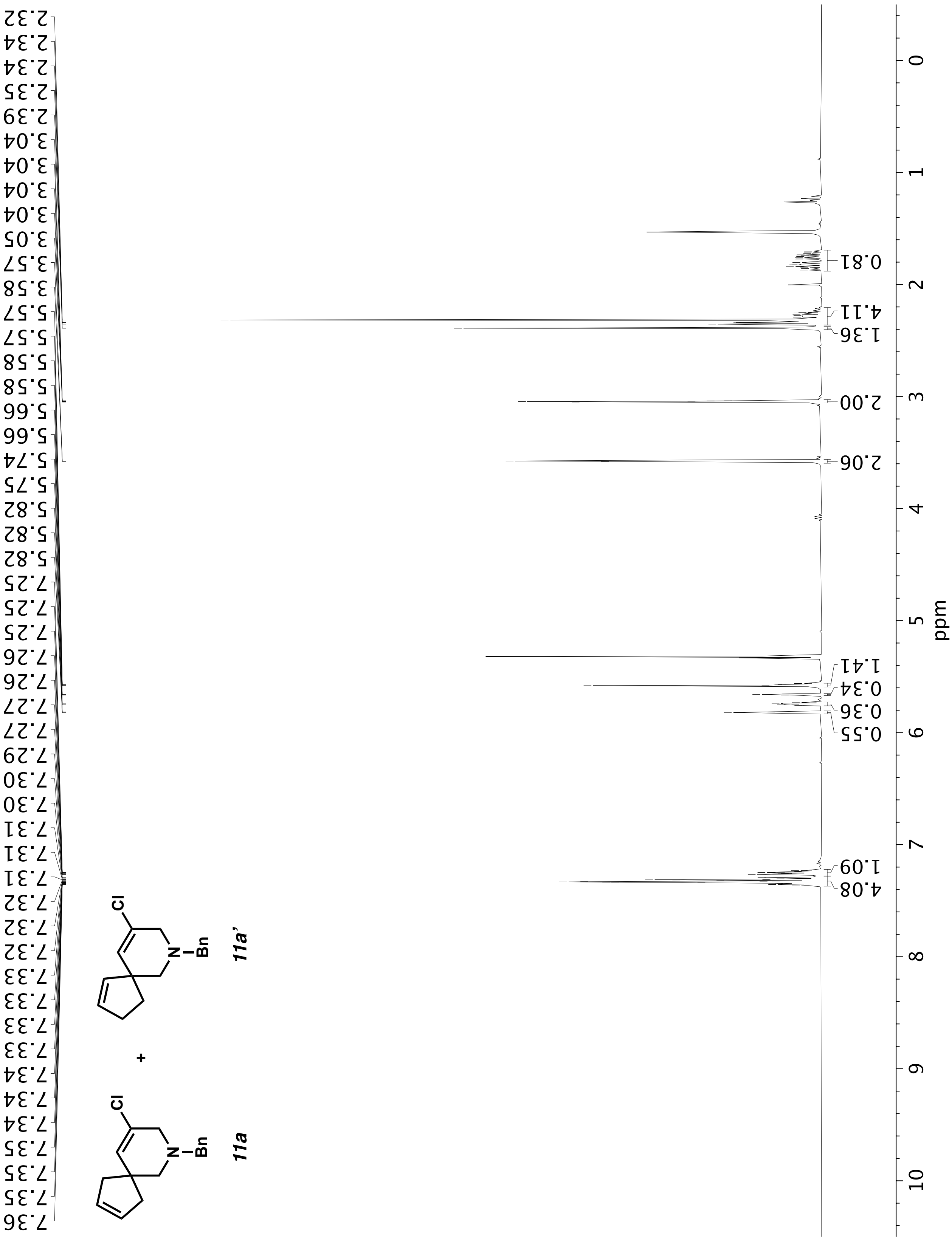
$^1$H NMR (400 MHz, CDCl$_3$) of compound **10a**.



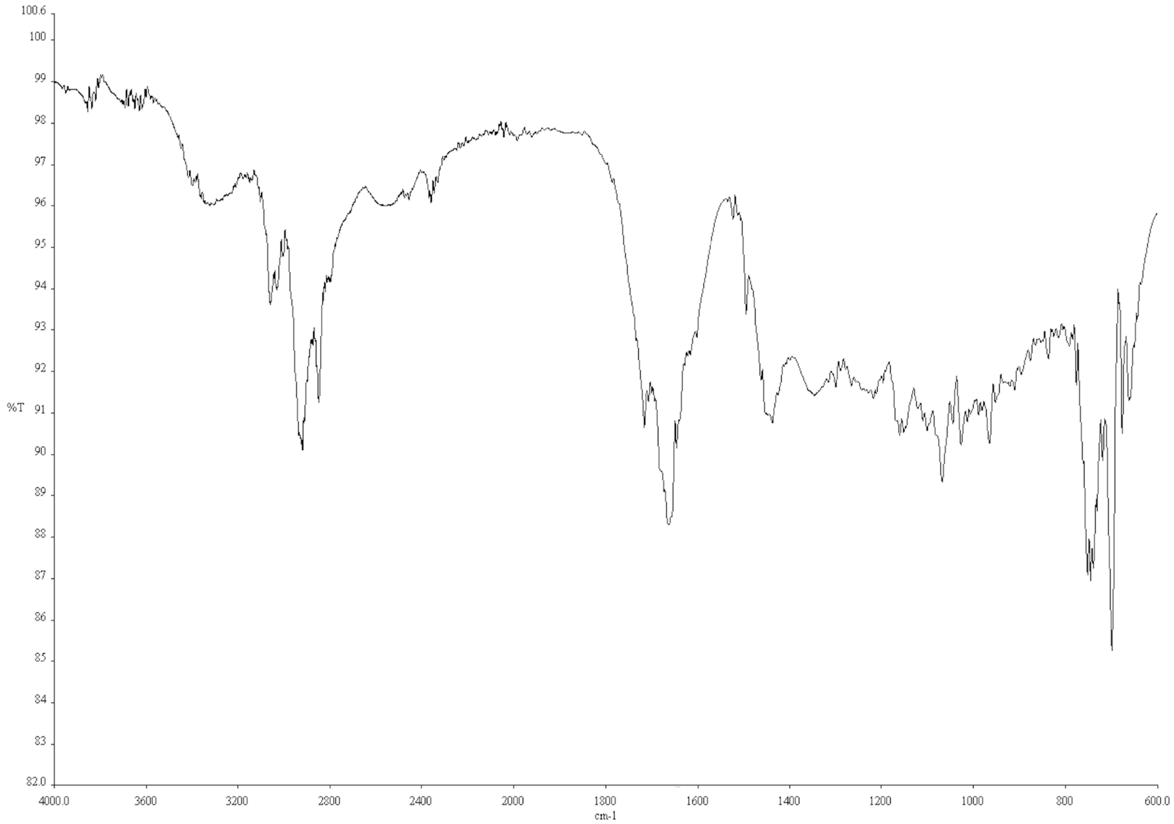
Infrared spectrum (Thin Film, NaCl) of compound **10a**.



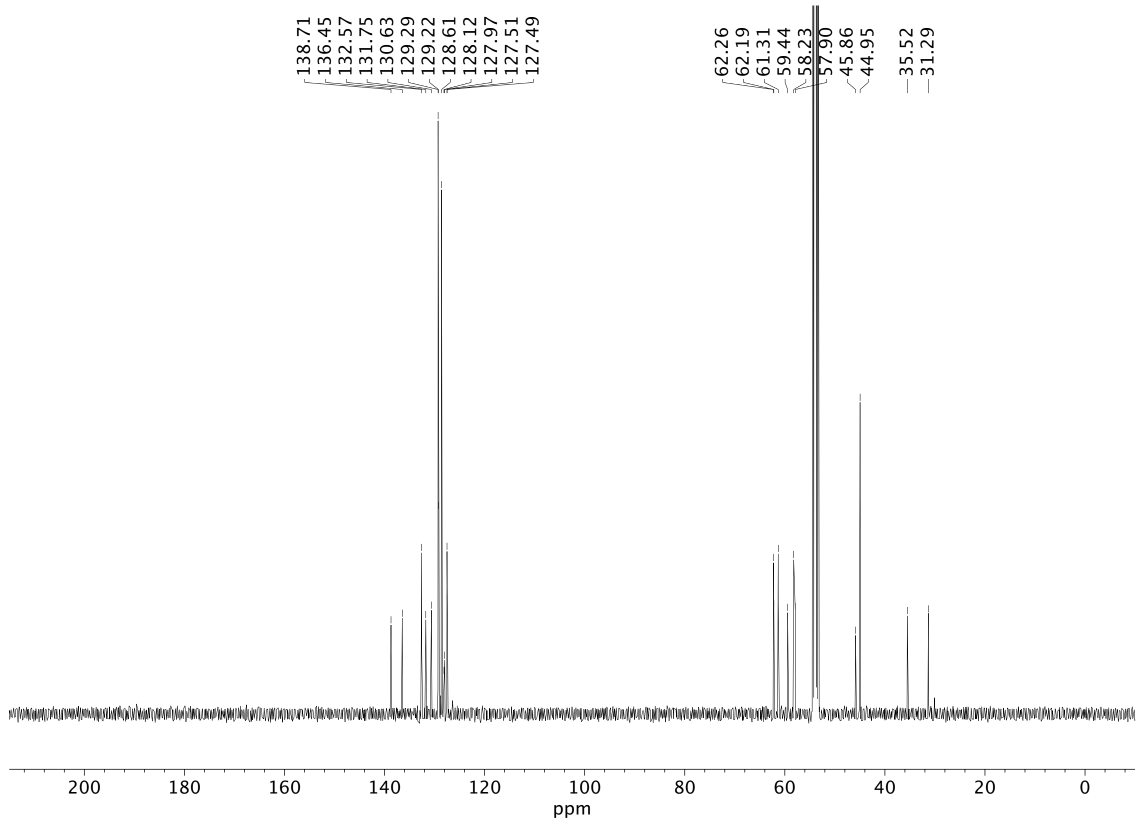
$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **10a**.



$^1$H NMR (400 MHz, CDCl$_3$) of compound **11a** and **11a'**



Infrared spectrum (Thin Film, NaCl) of compound **11a** and **11a'**.



$^{13}$C NMR (100 MHz, CDCl$_3$) of compound **11a** and **11a'**.