

# Reliably Regioselective Dialkyl Ether Cleavage with Mixed Boron Trihalides

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## 1. Experimental

### 1.1 General Information

Reactions were carried out in oven-dried (> 130 °C) or flame-dried glassware under a positive nitrogen atmosphere, unless otherwise stated. Transfer of anhydrous reagents was accomplished with oven-dried syringes or cannulae. Dichloromethane (DCM), toluene (PhMe), and tetrahydrofuran (THF) were passed through a column of activated molecular sieves (4Å, LC technologies). Benzene (C<sub>6</sub>H<sub>6</sub>) was vacuum-distilled (twice) and stored under nitrogen over oven-dried (> 200 °C) molecular sieves (3Å or 4Å). Deuterated dichloromethane (*d*<sup>2</sup>-DCM) and deuterated chloroform (CDCl<sub>3</sub>) were stored in a container with oven-dried (> 200 °C) molecular sieves (3Å or 4Å). Thin layer chromatography was performed on glass plates pre-coated with 0.25 mm silica gel with a fluorescent indicator UV<sub>254</sub> (EMD Millipore). Flash chromatography columns were packed with 230-400 mesh silica gel (Silacyle). All reagents were purchased from commercial suppliers: Sigma Aldrich, AK Scientific, and Acros, at purity greater than (95%), unless otherwise specified. Proton nuclear magnetic resonance spectra (<sup>1</sup>H NMR) were recorded at 400 or 500 MHz, and coupling constants (*J*) are reported in Hertz (Hz). Carbon nuclear magnetic resonance spectra (<sup>13</sup>C NMR) were recorded at 100 or 125 MHz. Proton decoupled boron nuclear magnetic resonance spectra (<sup>11</sup>B{<sup>1</sup>H} NMR) were recorded at 160 MHz, usually using a quartz NMR tube to avoid background signals (*vide infra*). The chemical shifts were reported on the δ scale (ppm) and referenced to the residual protonated solvent (<sup>1</sup>H) or to the deuterated solvent (<sup>13</sup>C) peaks: CDCl<sub>3</sub> (7.26 ppm, <sup>1</sup>H; 77.06 ppm, <sup>13</sup>C), and CD<sub>2</sub>Cl<sub>2</sub> (5.32 ppm, <sup>1</sup>H; 53.5 ppm, <sup>13</sup>C). *s* = singlet, *d* = doublet, *t* = triplet, *dt* = double of triplets, *m* = multiplet. Unless otherwise stated, Boron (<sup>11</sup>B NMR) nuclear magnetic resonance

spectra were recorded without any chemical shift adjustment. In cases where the NMR tube used in the measurement of  $^{11}\text{B}$  NMR nuclear magnetic resonance spectra was not made of quartz, spectral adjustment (backward linear prediction) was done to subtract the contribution of borosilicates from the measurements. For chromatography conditions, EA refers to ethyl acetate and Hex refers to hexanes.

## **2. Synthesis of starting materials and products**

### **2.1 General procedures for the synthesis of ethers**

#### **Allyl ether syntheses:**

Under an atmosphere of nitrogen at room temperature, the starting alcohol (1.0 g, 1.0 equiv.) was dissolved in 20 mL dry THF in a 1-necked, flame-dried, round bottomed flask. To this solution sodium hydride (2.0 equiv.) was added and allowed to stir for 30 minutes at room temperature. Allyl bromide (2.0 equiv.) was added and the reaction mixture was stirred at room temperature for 10 minutes before heating to reflux overnight. After cooling to room temperature, 30 mL of water was added to quench the reaction. After the addition of diethyl ether (30 mL), the organic layer was separated and washed with water (3x30 mL), dried over  $\text{MgSO}_4$ , filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (1-5% EA in Hex) on silica gel to afford the desired product.

#### **Benzyl ether syntheses:**

Under an atmosphere of nitrogen at room temperature, the starting alcohol (1.0 g, 1.0 equiv.) was dissolved in 20 mL dry THF in a 1-necked, flame-dried, round bottomed flask. To this solution sodium hydride (2.0 equiv.) was added and allowed to stir for 30 minutes

at room temperature. Benzyl bromide (1.2 equiv.) was added and the reaction mixture was stirred at room temperature for 10 minutes before heating to reflux overnight. After cooling to room temperature, 30 mL water was added to quench the reaction. After the addition of diethyl ether (30 mL), the organic layer was separated and washed with water (3x30 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (1-5% EA in Hex) on silica gel to afford the desired product.

**Propargyl ether syntheses:**

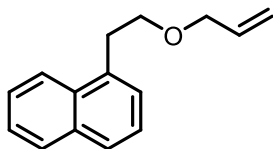
Under an atmosphere of nitrogen at room temperature, the starting alcohol (1.0 g, 1.0 equiv.) was dissolved in 20 mL dry THF in a 1-necked, flame-dried, round bottomed flask. To this solution sodium hydride (1.5 equiv.) was added and allowed to stir for 30 minutes at room temperature. Benzyl bromide (1.2 equiv.) was added and the reaction mixture was stirred at room temperature for 10 minutes before heating to reflux overnight. After cooling to room temperature, 30 mL water was added to quench the reaction. After the addition of diethyl ether (30 mL), the organic layer was separated and washed with water (3x30 mL), dried over MgSO<sub>4</sub>, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (1-5% EA in Hex) on silica gel to afford the desired product.

**t-Butyl ether syntheses:**

t-Butyl ether was synthesized following the McClure procedure.<sup>[1]</sup>

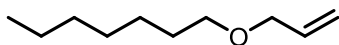
## Characterization of Ethers

### 1-(2-(allyloxy)ethyl)naphthalene (1)



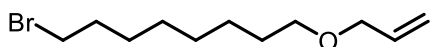
1.12 g (86%) of product was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[2]</sup>

### 1-(allyloxy)heptane (9)



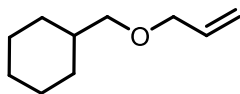
0.67 g (49%) of product was isolated following the general procedure. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.97-5.87 (m, 1H), 5.29-5.24 (m, 1H), 5.18-5.14 (m, 1H), 3.96 (dt, *J* = 5.6, 1.4 Hz, 2H), 3.42 (t, *J* = 6.7 Hz, 2H), 1.62-1.55 (m, 2H), 1.36-1.28 (m, 8H), 0.88 (t, *J* = 7.0 Hz, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 135.2, 116.7, 71.8, 70.6, 31.9, 29.8, 29.2, 26.2, 22.6, 14.1. HRMS (EI) *m/z*: [M-H] Calcd for C<sub>10</sub>H<sub>19</sub>O 155.1436; Found 155.1435.

### 1-(allyloxy)-8-bromooctane (10)



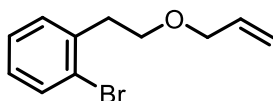
0.26 g (43%) of product was isolated following the general procedure. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.95-5.88 (m, 1H), 5.28-5.24 (m, 1H), 5.18-5.15 (m, 1H), 3.97-3.95 (m, 2H), 3.43-3.38 (m, 4H), 1.88-1.82 (m, 2H), 1.61-1.55 (m, 2H), 1.45-1.40 (m, 2H), 1.37-1.30 (m, 6H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 135.1, 116.7, 71.8, 70.4, 34.0, 32.8, 29.7, 29.3, 28.7, 28.1, 26.1; HRMS (EI) *m/z*: [M-C<sub>2</sub>H<sub>5</sub>] Calcd for C<sub>9</sub>H<sub>16</sub>OBr 219.0384; Found 219.0384.

**((allyloxy)methyl)cyclohexane (11)**



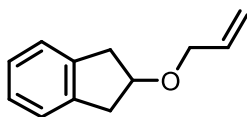
0.78 g (58%) of product was isolated following the general procedure.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.96–5.86 (m, 1H), 5.29–5.23 (m, 1H), 5.17–5.14 (m, 1H), 3.95 (dt,  $J = 5.6, 1.4$  Hz, 2H) 3.23 (d,  $J = 6.4$  Hz, 2H), 1.78–1.53 (m, 6H), 1.30–1.10 (m, 3H), 0.98–0.88 (m, 2H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  135.3, 116.5, 76.4, 72.0, 38.2, 30.2, 26.7, 25.9; HRMS (EI)  $m/z$ :  $[\text{M}-\text{H}]$  Calcd for  $\text{C}_{10}\text{H}_{17}\text{O}$  153.1279; Found 153.1280.

**1-(2-(allyloxy)ethyl)-2-bromobenzene (12)**



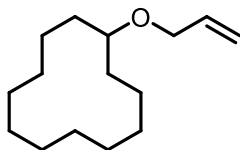
0.61 g (51%) of product was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[3]</sup>

**2-(allyloxy)-2,3-dihydro-1H-indene (13)**



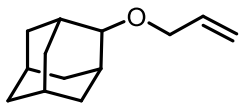
1.19 g (91%) of product was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[4]</sup>

**(allyloxy)cyclododecane (14)**



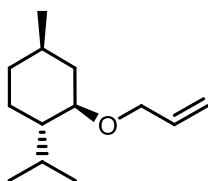
1.12 g (91%) of product was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[5]</sup>

**2-(allyloxy)adamantane (15)**



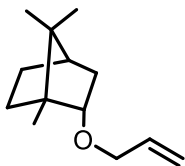
1.12 g (88%) of product was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[6]</sup>

**(1S,2R,4R)-2-(allyloxy)-1-isopropyl-4-methylcyclohexane (16)**



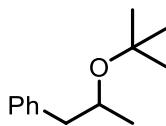
1.17 g (92%) of product was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[7]</sup>

**(1S,2S,4R)-2-(allyloxy)-1,7,7-trimethylbicyclo[2.2.1]heptane (17)**



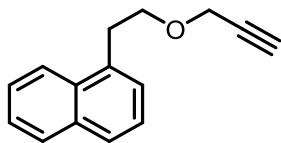
0.67 g (53%) was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[7]</sup>

**(2-(allyloxy)propyl)benzene (6)**



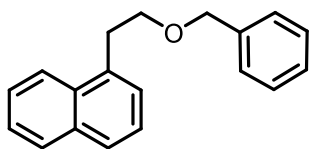
1.25 g (65%) of product was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[8]</sup>

### 1-(2-(prop-2-yn-1-yloxy)ethyl)naphthalene (7)



0.92 g (75%) of product was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[9]</sup>

### 1-(2-(benzyloxy)ethyl)naphthalene (8)



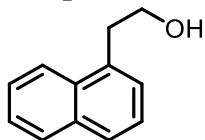
1.41 g (93%) of product was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[10]</sup>

## 2.2 General Procedure for the synthesis of alcohols:

A solution of  $\text{BCl}_3$  (100  $\mu\text{L}$ , 1.0 M in  $\text{CH}_2\text{Cl}_2$ , 0.10 mmol) was mixed with  $\text{BBr}_3$  (100  $\mu\text{L}$ , 1.0 M in  $\text{CH}_2\text{Cl}_2$ , 0.10 mmol) in an NMR tube containing 0.2 mL of  $\text{CD}_2\text{Cl}_2$  or  $\text{CDCl}_3$ . After 5 minutes, with occasional stirring using a vortex mixer (1 min, 2-3x), the solution was placed in a  $-78^\circ\text{C}$  cooling bath, and the desired ether (0.4 mmol, 2 equiv. relative to the total boron halides, dissolved in 0.2 mL of  $\text{CH}_2\text{Cl}_2$ ) was added dropwise over 5 min. The solution was maintained at  $-78^\circ\text{C}$  and allowed to reach  $10-20^\circ\text{C}$  overnight (*vide infra*). After completion, the reaction was quenched and washed with water (3x10 mL), dried over  $\text{MgSO}_4$ , filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (5-20% EA in Hex) on silica gel to afford the desired product.

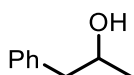
## *Characterization of Alcohols*

### **1-naphthaleneethanol [SI 1]**



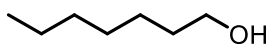
62 mg (90%) of alcohol was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[11]</sup>

### **3-phenyl-2-propanol [SI 2]**



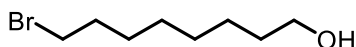
33 mg (61%) of alcohol was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[12]</sup>

### **1-heptanol [SI 3]**



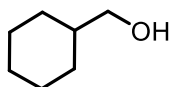
41 mg (88%) of alcohol was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[13]</sup>

### **8-bromo-1-octanol [SI 4]**



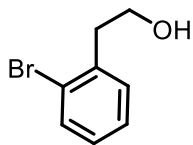
63 mg (87%) of alcohol was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[14]</sup>

### **cyclohexanemethanol [SI 5]**



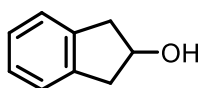
40 mg (87%) of alcohol was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[15]</sup>

### 2-(2-bromophenyl)ethanol [SI 6]



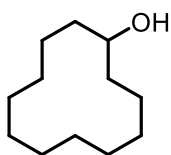
69 mg (86%) of alcohol was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[16]</sup>

### 2-indanol [SI 7]



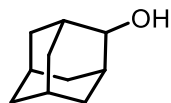
39 mg (73%) of alcohol was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[17]</sup>

### cyclododecanol [SI 8]



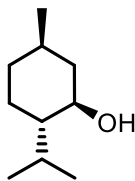
38 mg (61%) of alcohol was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[18]</sup>

### 2-adamantanol [SI 9]



36 mg (59%) of alcohol was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[19]</sup>

### menthol [SI 10]



36 mg (57%) of alcohol was isolated following the general procedure. Spectral data were in agreement with those previously reported.<sup>[20]</sup>

### borneol [SI 11]



44 mg (72%) of alcohol was isolated following the general procedure. Borneol is commercially available, and the spectral data match the authentic sample from the commercial supplier.

## 2.3 Titration of diethyl ether with BCl<sub>3</sub>:

### *Preparation of control solutions for in-situ intermediate comparison*

BCl<sub>3</sub> in CD<sub>2</sub>Cl<sub>2</sub>:

A solution of BCl<sub>3</sub> (100 μL, 1.0 M CH<sub>2</sub>Cl<sub>2</sub>, 0.10 mmol) was added to 0.4 mL CD<sub>2</sub>Cl<sub>2</sub>. The solution was vortexed for 1 min at room temperature, and the <sup>11</sup>B NMR spectrum was acquired for BCl<sub>3</sub>: <sup>11</sup>B-NMR (128 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 47.7. The spectral data was in agreement with that previously reported.<sup>[21]</sup>

### *Titration of BCl<sub>3</sub> with Et<sub>2</sub>O, formation (Et<sub>2</sub>O)BCl<sub>3</sub> coordination complex:*

A solution of BCl<sub>3</sub> (100 μL, 1.0 M CH<sub>2</sub>Cl<sub>2</sub>, 0.10 mmol) was added to 0.4 mL CD<sub>2</sub>Cl<sub>2</sub>. The solution was vortexed for 1 min at room temperature, and Et<sub>2</sub>O (0.1 mmol) was added to the reaction mixture and again vortexed for 1 min at room temperature.

(Et<sub>2</sub>O)BCl<sub>3</sub>: <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 3.70 (brs, 4H), 1.25 (brs, 6H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 54.2, 15.1; <sup>11</sup>B NMR (160 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 10.8.<sup>[21]</sup> This complex is stable at -78 to 70 °C. No substantial decomposition of the complex was observed at 70 °C, unless the reaction was heated to reflux in PhMe (110 °C).

## 2.4 Titration of diethyl ether with BBr<sub>3</sub>:

### *Preparation of control solutions for in-situ intermediate comparison*

BBr<sub>3</sub> in CD<sub>2</sub>Cl<sub>2</sub>:

A solution of BBr<sub>3</sub> (100 μL, 1.0 M CH<sub>2</sub>Cl<sub>2</sub>, 0.10 mmol) was added to 0.4 mL CD<sub>2</sub>Cl<sub>2</sub>. The solution was vortexed for 1 min at room temperature, and the <sup>11</sup>B-NMR spectrum was acquired for BBr<sub>3</sub>: <sup>11</sup>B NMR (128 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 40.0. The spectral data was in agreement with that previously reported.<sup>[21]</sup>

### *Titration of BBr<sub>3</sub> with Et<sub>2</sub>O, formation (Et<sub>2</sub>O)BBr<sub>3</sub> coordination complex:*

A solution of BBr<sub>3</sub> (100 μL, 1.0 M CH<sub>2</sub>Cl<sub>2</sub>, 0.10 mmol) was added to 0.4 mL CD<sub>2</sub>Cl<sub>2</sub>. The solution was vortexed for 1 min at room temperature, the solution temperature was cooled to -78°C and Et<sub>2</sub>O (0.1 mmol) was added dropwise, the ether was allowed to diffuse in the solution for ca. 10 min. The spectra of the complex was obtained within 5 mins at room temperature. (Et<sub>2</sub>O)BBr<sub>3</sub>: <sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 3.70 (brs, 4H), 1.25 (brs, 6H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 54.2, 15.1; <sup>11</sup>B NMR (160 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ -6.1.

The Et<sub>2</sub>OBBBr<sub>3</sub> complex decomposed rapidly at room temperature within 2 hours to furnish EtOBBBr<sub>2</sub>: <sup>11</sup>B NMR (160 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 25.9. Addition of second molar equivalent of Et<sub>2</sub>O to EtOBBBr<sub>2</sub> furnished a new complex, assigned as (Et<sub>2</sub>O)B(OEt)Br<sub>2</sub>: <sup>11</sup>B NMR (160 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ -6.0. The (Et<sub>2</sub>O)B(OEt)Br<sub>2</sub> complex decomposed rapidly at room temperature within 1 hour to furnish two new boron peaks assigned as (EtO)<sub>2</sub>BBBr: <sup>11</sup>B NMR (160 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 22.3.

*Discussion:*

Based on these results, it is clear that the  $\text{BCl}_3$  is reticent to react productively with dialkyl ethers and that  $\text{BBr}_3$  is prone to decomposition, presumably to generate  $\text{B}_2\text{O}_3$ , in addition to the expected  $(\text{EtO})_2\text{BBr}$  adduct, indicating the instability of this type of intermediate. These observations account for a reduced yield of recovered alcohol when the cleavage of dialkyl ethers (*vide supra*) was done in the presence of  $\text{BBr}_3$  alone. Despite low recovery of alcohol products, a substantial amount of alkyl bromide could be isolated.

**2.5 Titration of diethyl ether with  $\text{BCl}_3/\text{BBr}_3$ :**

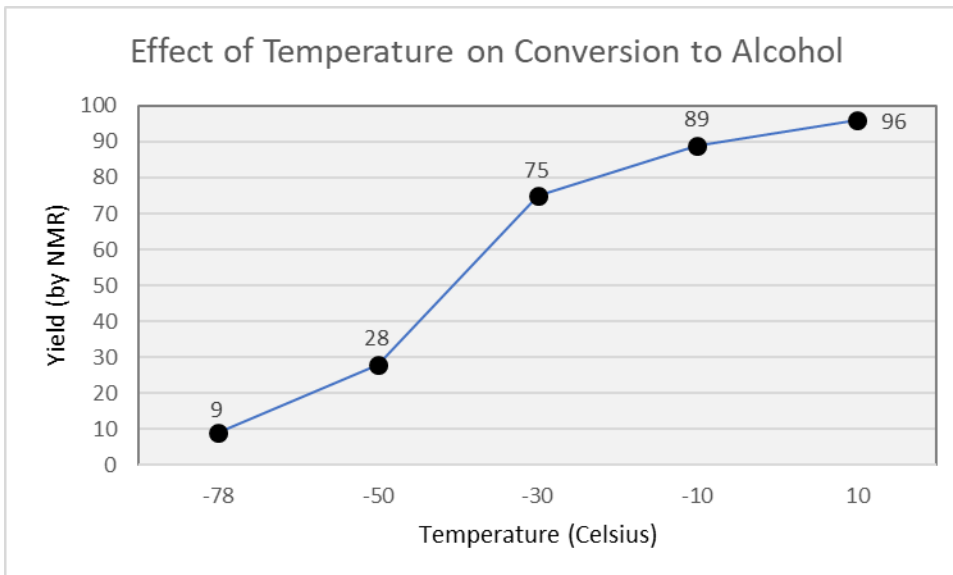
$\text{BCl}_3/\text{BBr}_3$  in  $\text{CD}_2\text{Cl}_2$ :

A solution of  $\text{BCl}_3$  (100  $\mu\text{L}$ , 1.0 M  $\text{CH}_2\text{Cl}_2$ , 0.1 mmol, 0.25 equiv.), and  $\text{BBr}_3$  (100  $\mu\text{L}$ , 1.0 M  $\text{CH}_2\text{Cl}_2$ , 0.10 mmol, 0.25 equiv.) was added to 0.4 mL  $\text{CD}_2\text{Cl}_2$ . The solution was vortexed for 1 min at room temperature, and analyzed by  $^{11}\text{B}$  NMR:  $^{11}\text{B}$  NMR (128 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  46.6.<sup>[21]</sup> ( $\text{BCl}_3$ , integration: 0.6), 45.0 (integration: 1.9), 42.4 (integration: 2.2), 39.0 ( $\text{BBr}_3$  integration: 1.0).<sup>[21]</sup> We have assigned the peak at 45.0 as  $\text{BCl}_2\text{Br}$ , and the peak at 42.4 as  $\text{BClBr}_2$  based on literature trends.<sup>[21]</sup>

The resulting solution was then cooled to  $-78^\circ\text{C}$ , followed by addition of  $\text{Et}_2\text{O}$  (21  $\mu\text{L}$ , 0.2 mmol, 0.5 equiv.) to afford four ether complexes:  $^{11}\text{B}$  NMR (128 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  10.0 [ $(\text{Et}_2\text{O})\text{BCl}_3$ ],<sup>[21]</sup> 5.5 [ $(\text{Et}_2\text{O})\text{BCl}_2\text{Br}$ ], -0.1 [[ $(\text{Et}_2\text{O})\text{BClBr}_2$ ], -6.4 [ $(\text{Et}_2\text{O})\text{BBr}_3$ ]. The relative ratio of these ether complexes was in good agreement with the ratio of the starting Lewis acids. These complexes decomposed within 8 hours upon warming to room temperature, affording three new boron peaks. These peaks were assigned as follows:  $^{11}\text{B}$  NMR (128 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  30.8 [ $\text{B}(\text{OEt})\text{Cl}_2$ ],<sup>[21]</sup> 28.9 [ $\text{B}(\text{OEt})\text{BrCl}$ ], and 25.9 [ $\text{B}(\text{OEt})\text{Br}_2$ ].

The solution containing these three boron intermediates was then cooled to  $-78\text{ }^{\circ}\text{C}$ , and a second addition of  $\text{Et}_2\text{O}$  ( $21\text{ }\mu\text{L}$ ,  $0.2\text{ mmol}$ ,  $0.5\text{ equiv.}$ ) was added to afford three ether complexes. These decomposed upon warming at room temperature to 4 boron peaks assigned as:  $^{11}\text{B}$  NMR ( $128\text{ MHz}$ ,  $\text{CD}_2\text{Cl}_2$ )  $\delta$   $30.6$  [ $\text{B}(\text{OEt})\text{Cl}_2$ ],  $23.0$  [ $\text{B}(\text{OEt})_2\text{Cl}$ ],<sup>[21]</sup>  $19.0$  [ $\text{B}(\text{OEt})_3$ ], and  $10.8$  [ $(\text{OEt}_2)\text{B}(\text{OEt})\text{Cl}_2$ ]. There was also some indication of very minor amounts of [ $\text{B}(\text{OEt})_2\text{Br}$ ] which were nearly undetectable. Therefore, we assign the final ratio of [ $\text{B}(\text{OEt})_2\text{Cl}$ ] and [ $\text{B}(\text{OEt})_2\text{Br}$ ] to be  $> 10:1$ .

## 2.6 Evaluation of Temperature Effects on Reaction Rate



### Procedure:

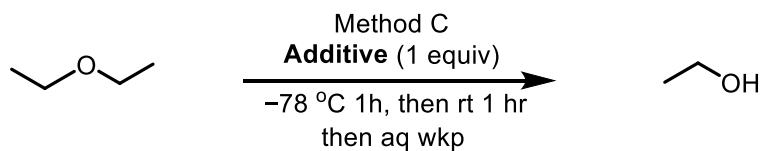
A solution of  $\text{BCl}_3$  ( $100\text{ }\mu\text{L}$ ,  $1.0\text{ M}$  in  $\text{CH}_2\text{Cl}_2$ ,  $0.10\text{ mmol}$ ,  $0.33\text{ equiv}$ ) was mixed with  $\text{BBr}_3$  ( $100\text{ }\mu\text{L}$ ,  $1.0\text{ M}$  in  $\text{CH}_2\text{Cl}_2$ ,  $0.10\text{ mmol}$ ,  $0.33\text{ equiv}$ ) in an NMR tube containing  $0.2\text{ mL}$  of  $\text{CD}_2\text{Cl}_2$  or  $\text{CDCl}_3$ . After 5 minutes, with occasional stirring using a vortex mixer (1 min, 2-3x), the solution was placed in a  $-78\text{ }^{\circ}\text{C}$  cooling bath. Mesitylene ( $42\text{ }\mu\text{L}$ ,  $0.30\text{ mmol}$ ,  $1.0\text{ equiv}$ ) was added dropwise followed by **SI1** ( $64\text{ mg}$ ,  $0.30\text{ mmol}$ ,  $1.0\text{ equiv}$ , dissolved in  $0.2\text{ mL}$   $\text{CH}_2\text{Cl}_2$ ). The solution was maintained at  $-78\text{ }^{\circ}\text{C}$  for one hour, then

removed from the bath and placed in a cooling bath of designated temperature (see table). After one hour, the reaction was analyzed by  $^{11}\text{B}$  NMR,  $^1\text{H}$  NMR, and  $^{13}\text{C}$  NMR to determine the extent of additive degradation by integrating relative to mesitylene.

*Discussion:*

It is likely that different substrates react at different rates. When using diethyl ether, for example, the reaction must be at room temperature for a full two hours longer than the normal 16 hour warming in order to allow the reaction to complete. For no other substrate examined did we see this sluggishness. Additionally, we would like to note that during our analysis of temperature vs. conversion to alcohol, we observed no obvious point of exotherm in these reactions.

## 2.7 Degredation of Additives under Reaction Conditions



entry	additive	% additive remaining	degredation product
1		94	ND
2		84	ND
3		quant	ND
4	$\text{N}\equiv\text{C}-\text{CH}_3$	quant	ND
5		<5	allylamine

Reactions were performed at 0.6 M in a mixture of  $\text{CH}_2\text{Cl}_2/\text{CDCl}_3$ . <sup>a</sup>Yields were determined by NMR with mesitylene internal standard. quant = quantitative conversion. ND = not determined

### Procedure:

Under an atmosphere of nitrogen at room temperature, a solution of  $\text{BCl}_3$  (100  $\mu\text{L}$ , 1.0 M in  $\text{CH}_2\text{Cl}_2$ , 0.10 mmol, 0.33 equiv) was mixed with  $\text{BBr}_3$  (100  $\mu\text{L}$ , 1.0 M in  $\text{CH}_2\text{Cl}_2$ , 0.10 mmol, 0.33 equiv) in an NMR tube containing 0.2 mL of  $\text{CD}_2\text{Cl}_2$  or  $\text{CDCl}_3$ . After 5 minutes, with occasional stirring using a vortex mixer (1 min, 2-3x), the solution was placed in a  $-78\text{ }^{\circ}\text{C}$  cooling bath. Mesitylene (42  $\mu\text{L}$ , 0.30 mmol, 1.0 equiv) and the additive (0.30 mmol, 1.0 equiv) was added dropwise followed by the diethyl ether (31  $\mu\text{L}$ , 0.30 mmol, 1.0 equiv). The solution was maintained at  $-78\text{ }^{\circ}\text{C}$  for one hour, then removed from the bath allowed to reach room temperature. After one hour, the reaction was analyzed by  $^{11}\text{B}$  NMR,  $^1\text{H}$

NMR, and  $^{13}\text{C}$  NMR to determine the extent of additive degradation by integrating relative to mesitylene.

## 2.8 Example of Scaled Up Ether Cleavage Reaction

A solution of  $\text{BCl}_3$  (400  $\mu\text{L}$ , 1.0 M in  $\text{CH}_2\text{Cl}_2$ , 0.40 mmol, 0.33 equiv) was mixed with  $\text{BBr}_3$  (400  $\mu\text{L}$ , 1.0 M in  $\text{CH}_2\text{Cl}_2$ , 0.40 mmol, 0.33 equiv) in a 25 mL, 1-necked, flame-dried, round bottomed flask containing 0.8 mL of  $\text{CH}_2\text{Cl}_2$ . After 5 minutes stirring using a stir bar, the flask was placed in a  $-78\text{ }^\circ\text{C}$  cooling bath, and ether **SI1** (1.2 mmol, 1.0 equiv), dissolved in an additional 0.8 mL of  $\text{CH}_2\text{Cl}_2$ , was added dropwise over 5 min to the boron reagents. The solution was maintained at  $-78\text{ }^\circ\text{C}$  and allowed to reach  $10\text{--}20\text{ }^\circ\text{C}$  overnight (*vide infra*, ~16 h). After completion, the reaction was quenched and washed with water (3x15 mL), dried over  $\text{MgSO}_4$ , filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (5-20% EA in Hex) on silica gel to afford the desired product as a white solid (0.186 g, 89%).

## 3. References

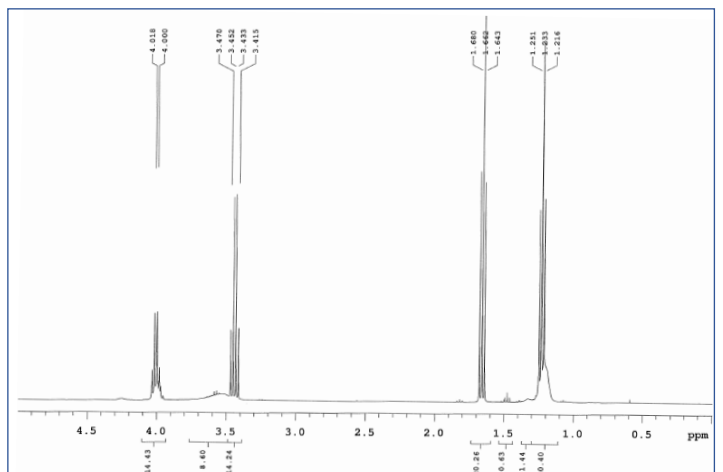
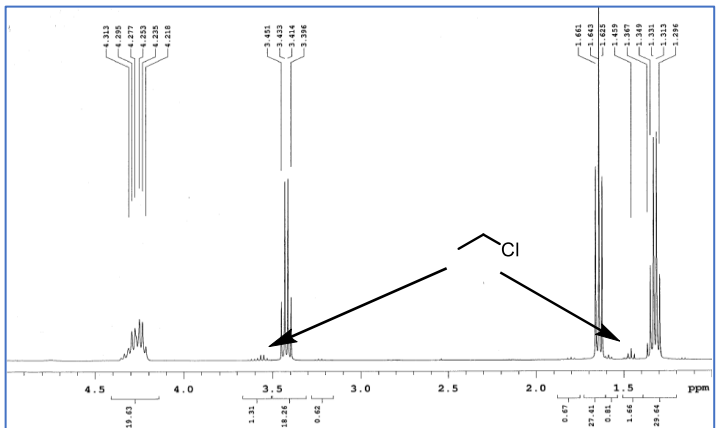
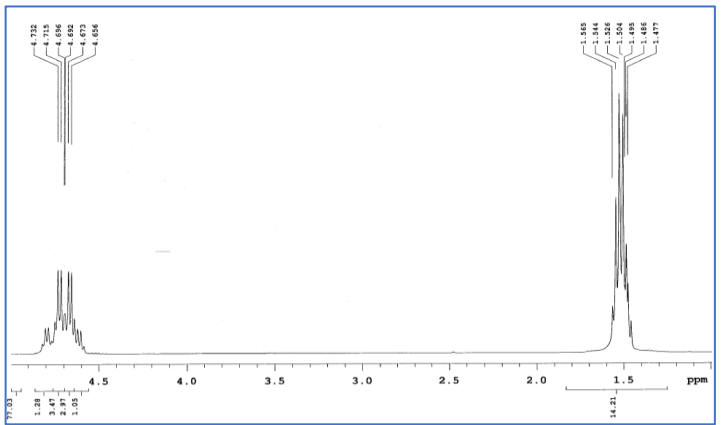
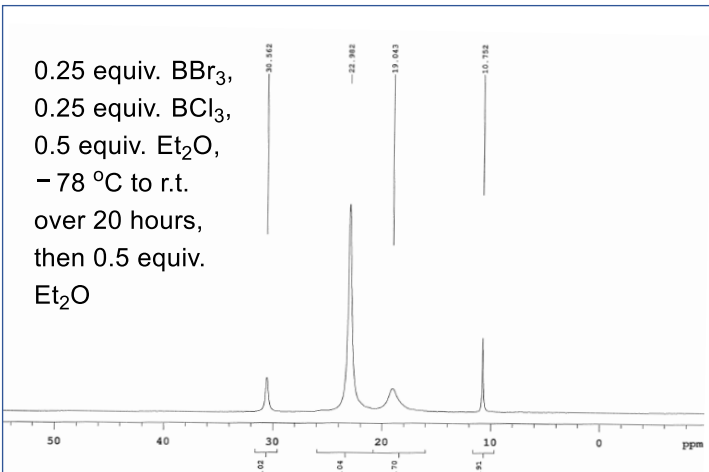
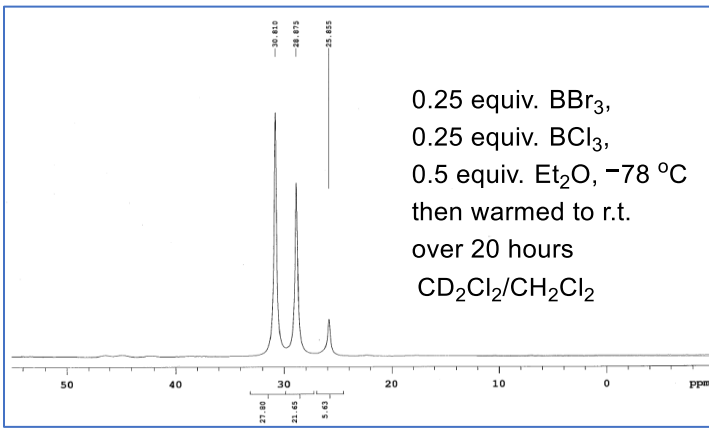
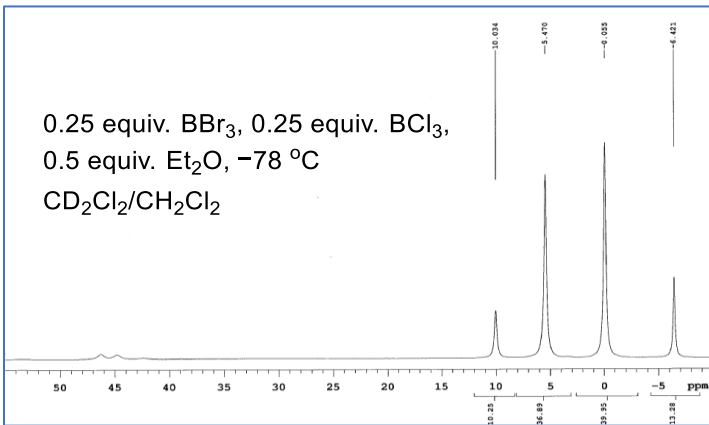
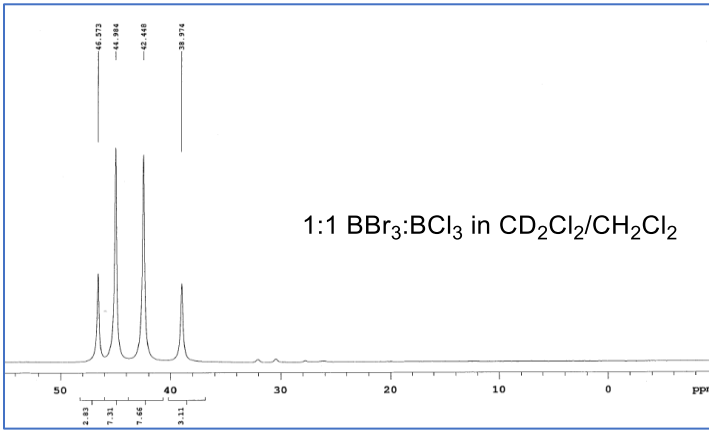
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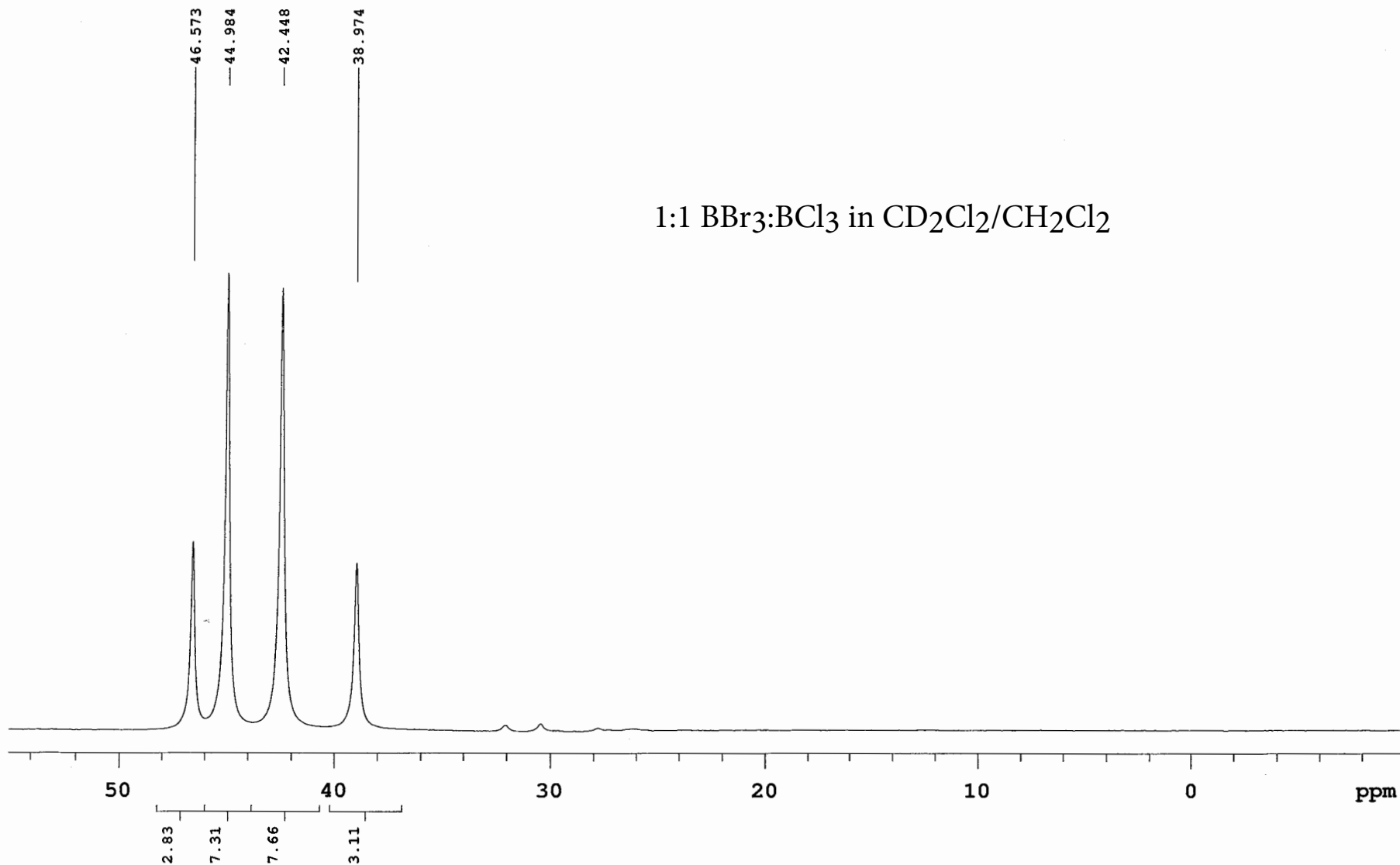
# Titration Experiment NMRs

<sup>11</sup>B NMR

<sup>1</sup>H NMR

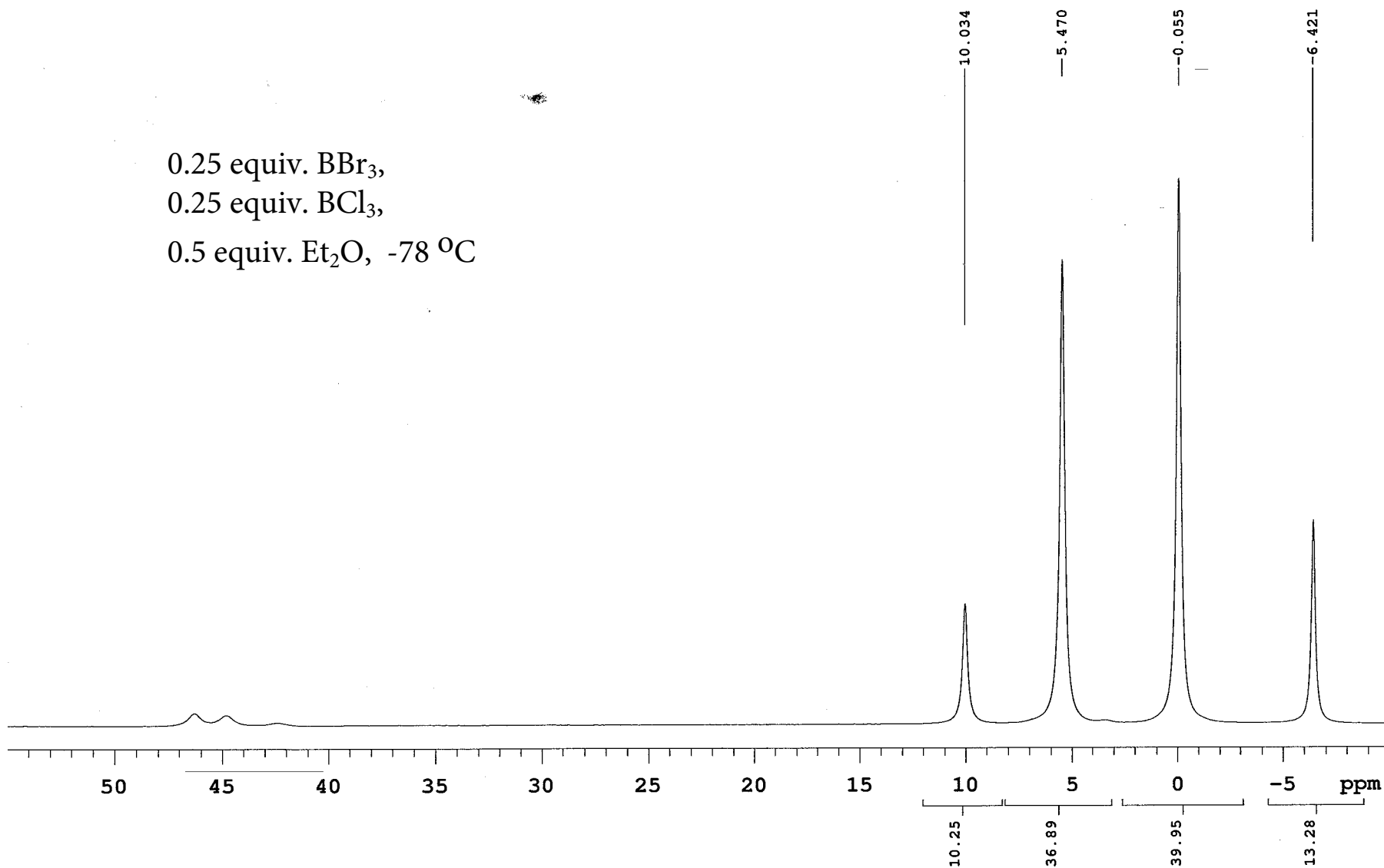


128.329 MHz B11{H1} 1D in d2o  
temp 25.9 C -> actual temp = 27.0 C, onenmr probe



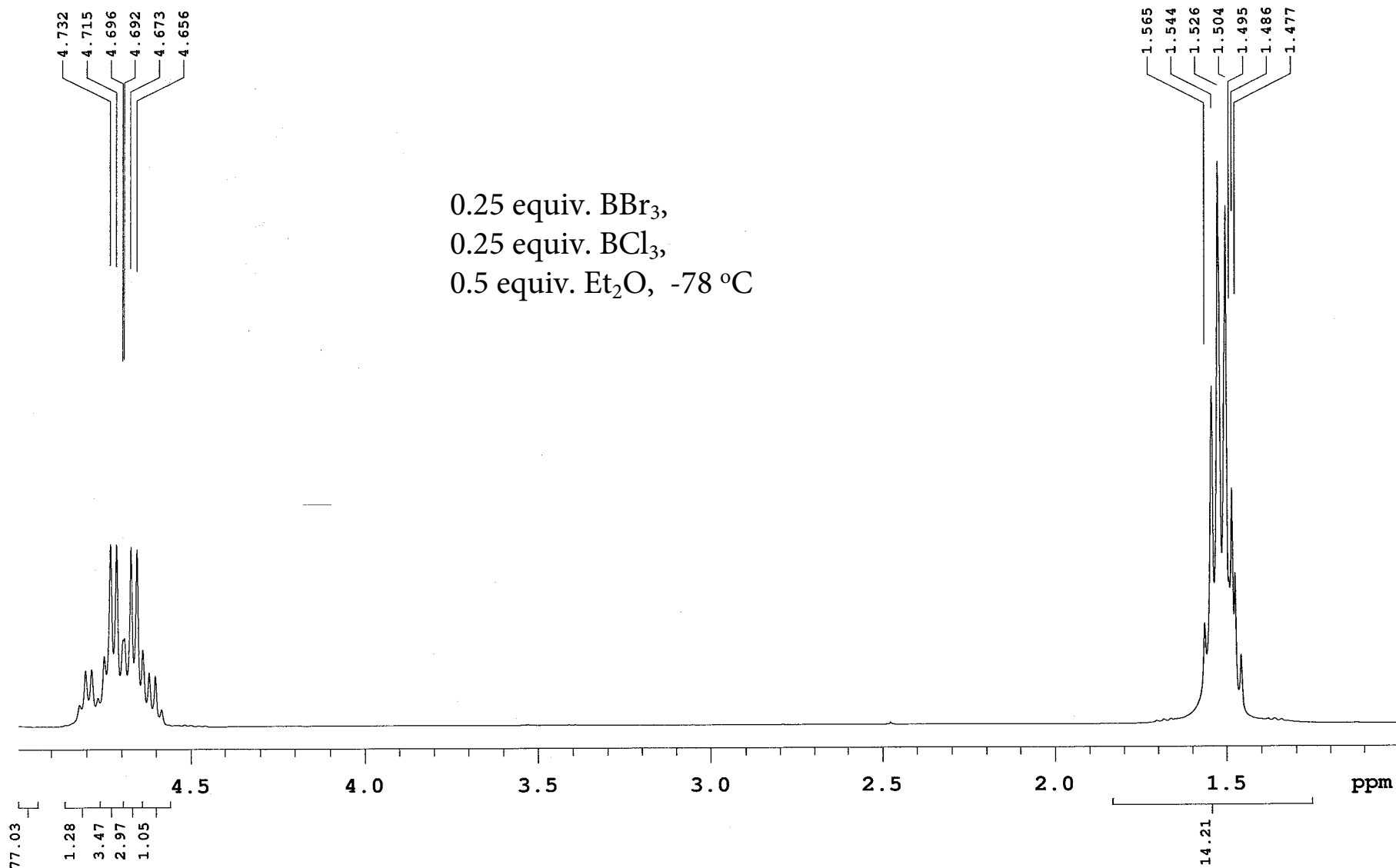
Florence Williams, BCl<sub>3</sub>BBr<sub>3</sub>w/Et<sub>2</sub>O-1, -78C  
 128.318 MHz B11{H1} 1D in cd<sub>2</sub>cl<sub>2</sub>  
 temp -71.1 C -> actual temp = -78.0 C, sw400 probe

0.25 equiv. BBr<sub>3</sub>,  
 0.25 equiv. BCl<sub>3</sub>,  
 0.5 equiv. Et<sub>2</sub>O, -78 °C



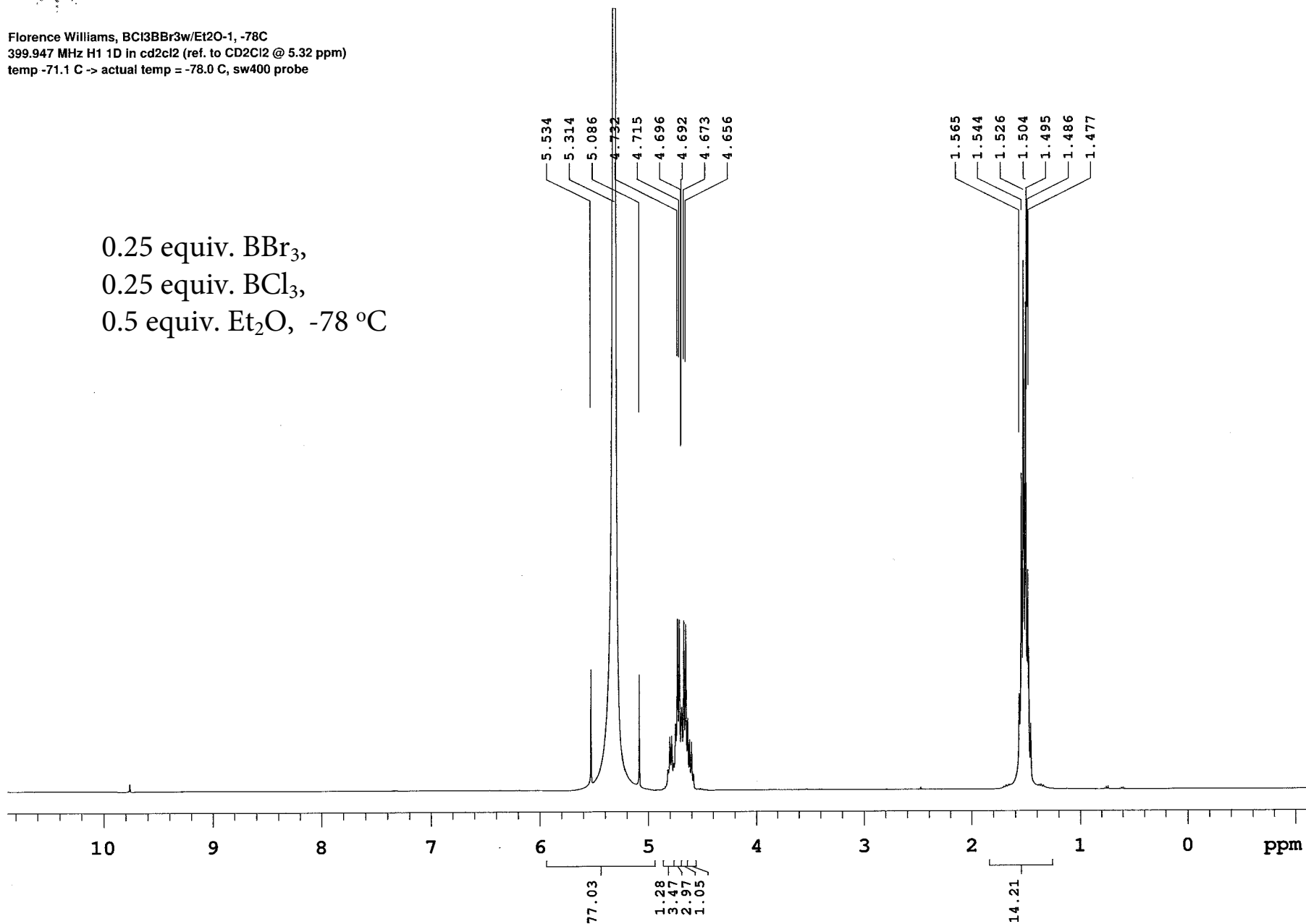
Florence Williams, BCl3BBr3w/Et2O-1, -78C  
 399.947 MHz H1 1D in cd2cl2 (ref. to CD2Cl2 @ 5.32 ppm)  
 temp -71.1 C -> actual temp = -78.0 C, sw400 probe

0.25 equiv. BBr<sub>3</sub>,  
 0.25 equiv. BCl<sub>3</sub>,  
 0.5 equiv. Et<sub>2</sub>O, -78 °C

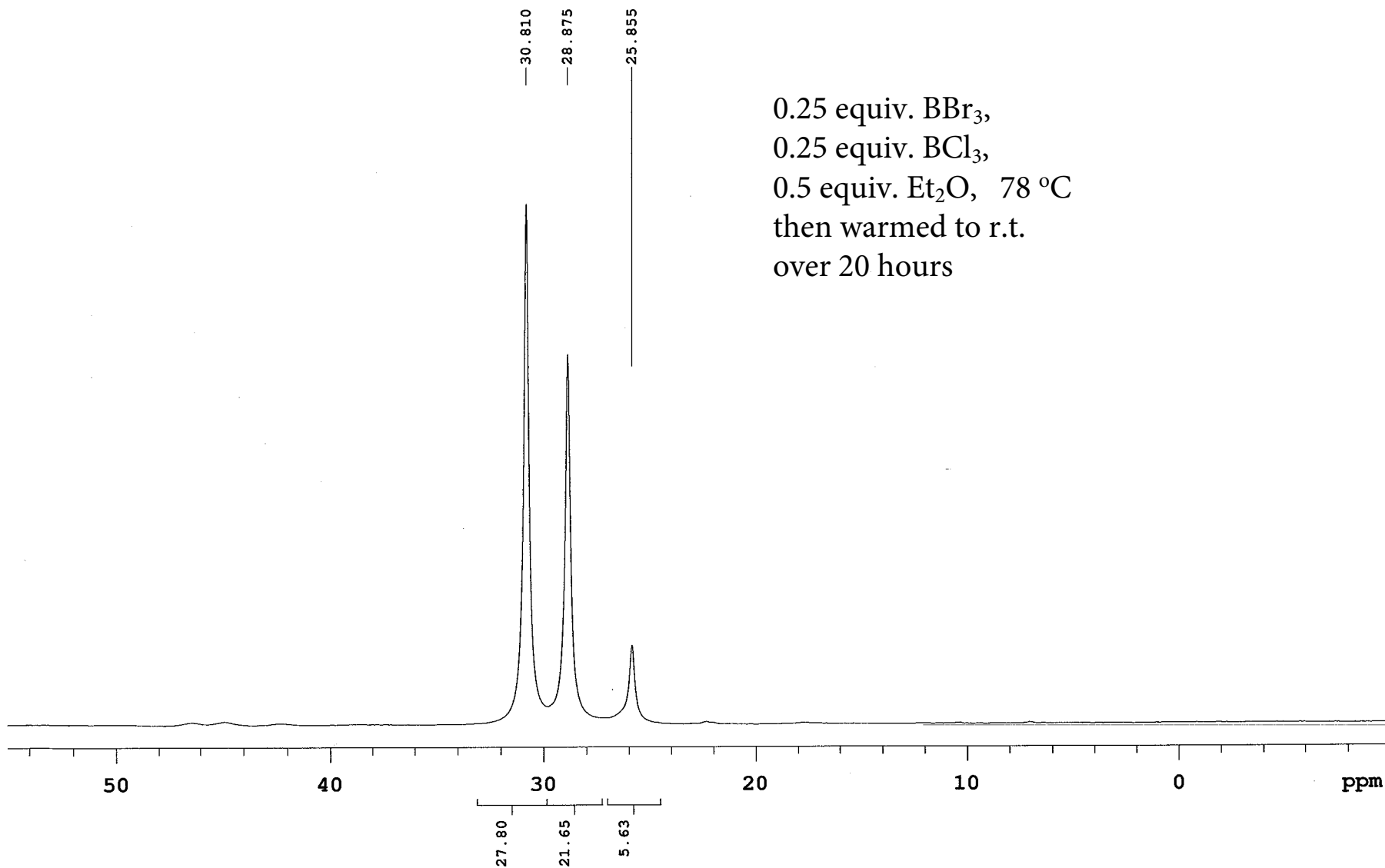


Florence Williams, BC13BBR3w/Et2O-1, -78C  
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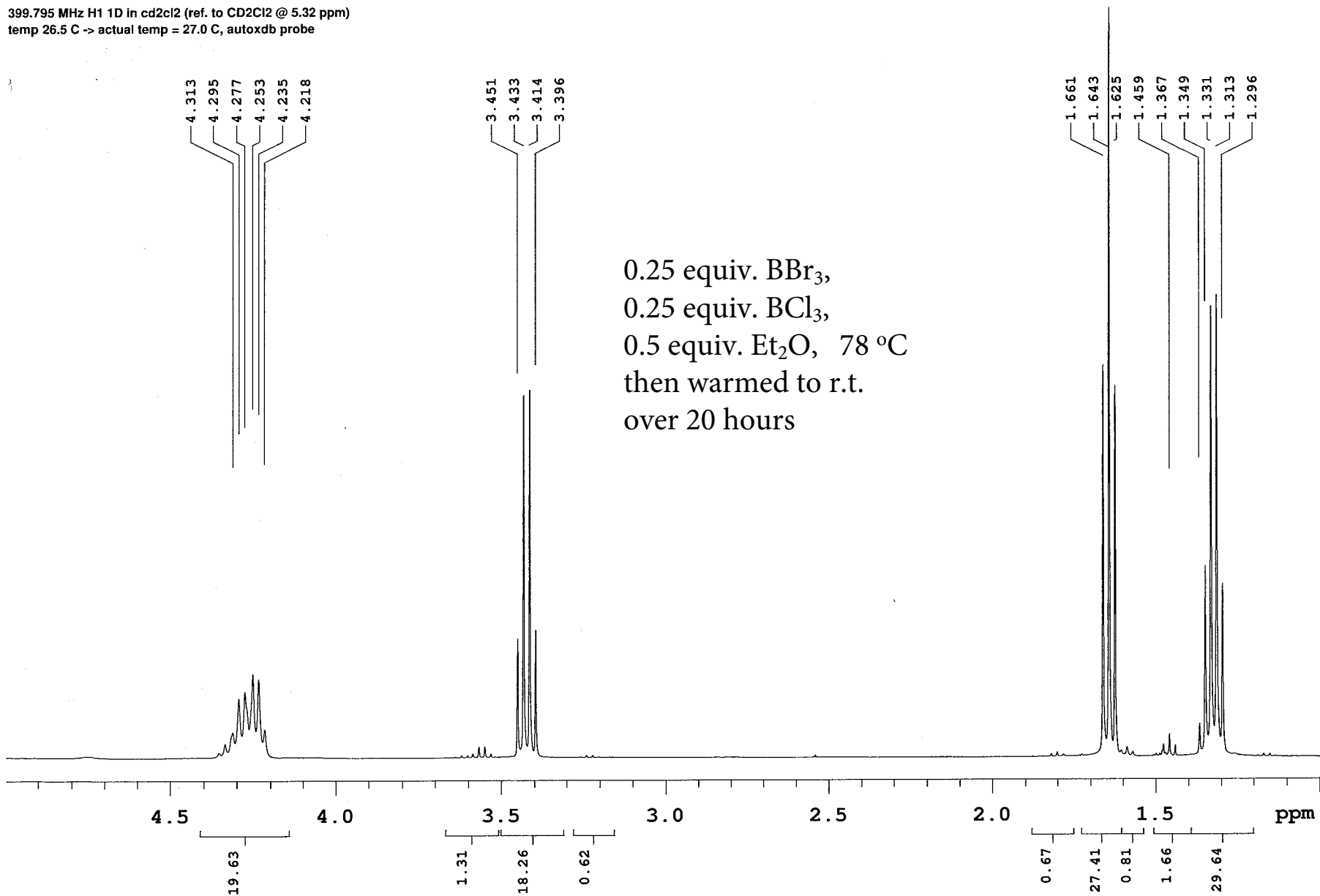
0.25 equiv. BBr<sub>3</sub>,  
 0.25 equiv. BCl<sub>3</sub>,  
 0.5 equiv. Et<sub>2</sub>O, -78 °C



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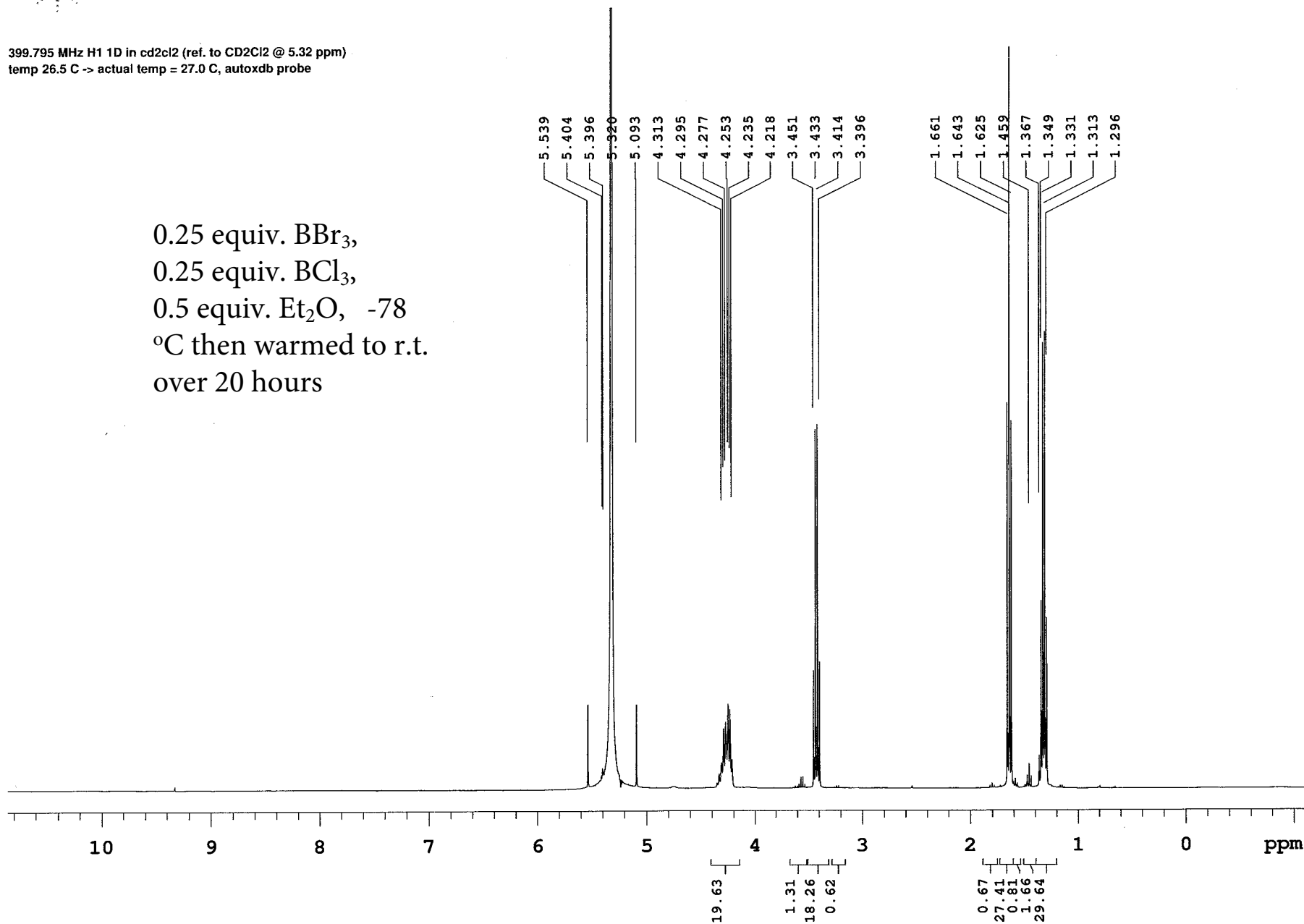


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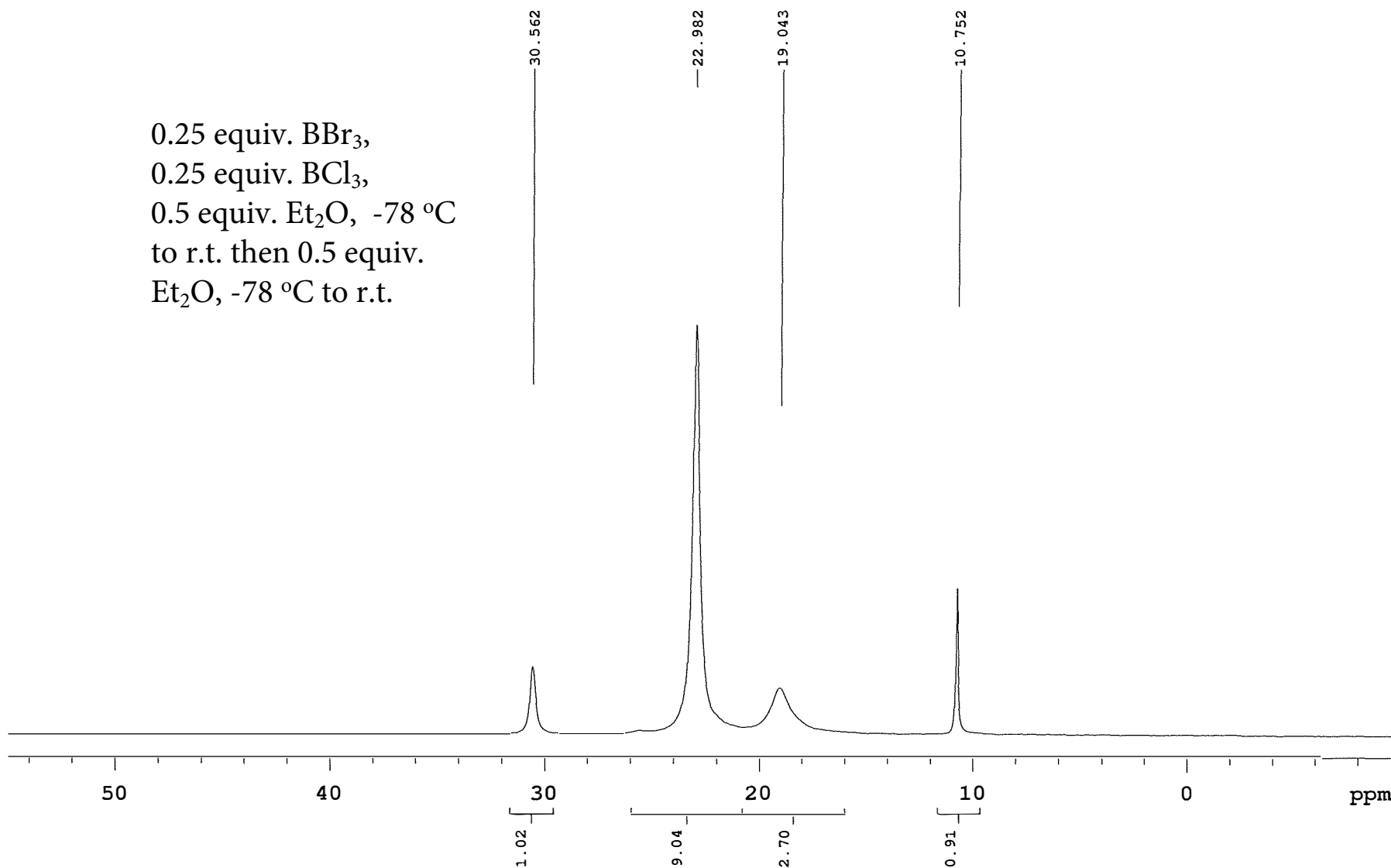
399.795 MHz H1 1D in cd2cl2 (ref. to CD2Cl2 @ 5.32 ppm)  
 temp 26.5 C -> actual temp = 27.0 C, autotdb probe

0.25 equiv. BBr<sub>3</sub>,  
 0.25 equiv. BCl<sub>3</sub>,  
 0.5 equiv. Et<sub>2</sub>O, -78  
 °C then warmed to r.t.  
 over 20 hours

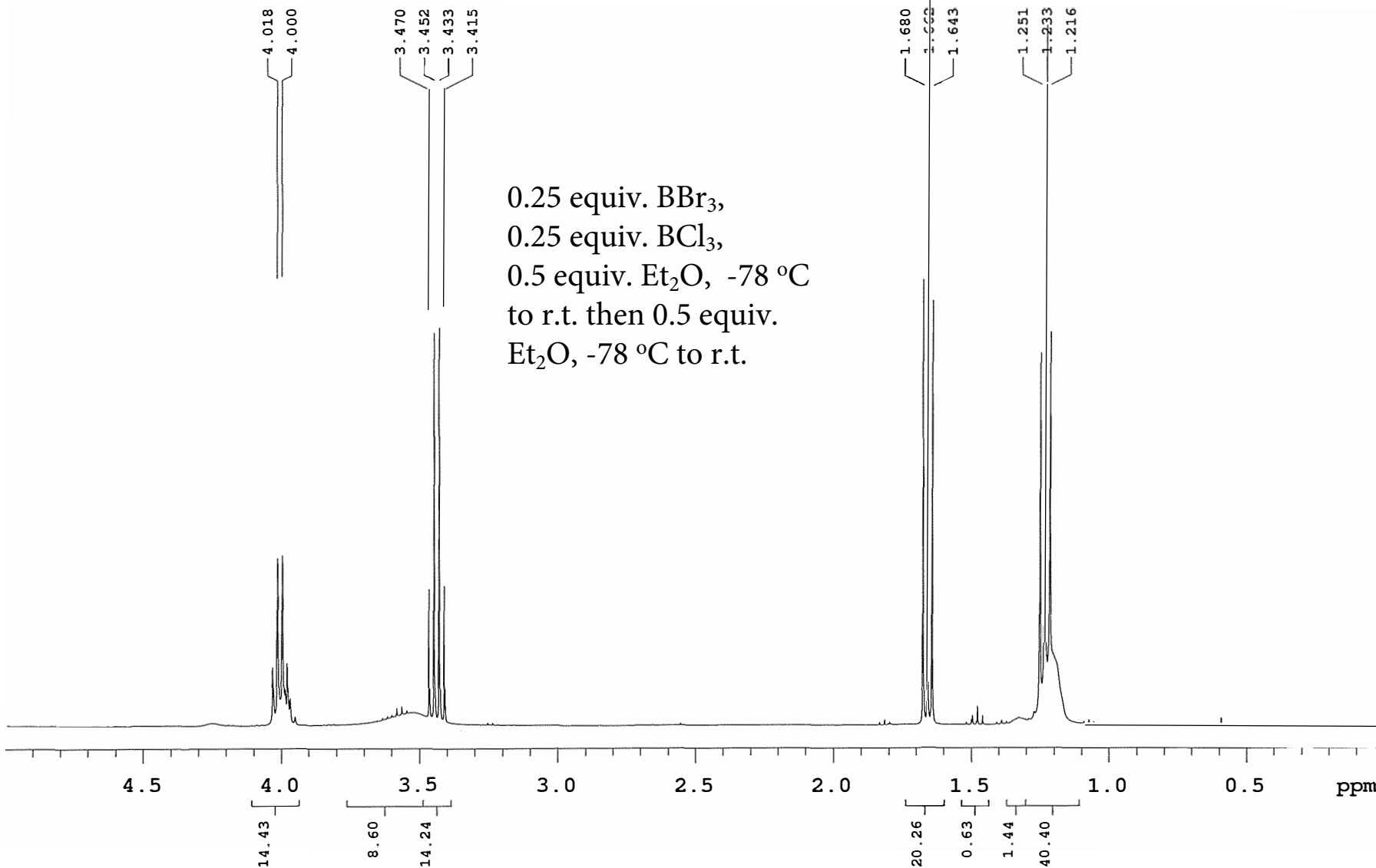


128.328 MHz B11{H1} 1D in cd2cl2  
 temp 25.9 C -> actual temp = 27.0 C, onenmr probe

0.25 equiv. BBr<sub>3</sub>,  
 0.25 equiv. BCl<sub>3</sub>,  
 0.5 equiv. Et<sub>2</sub>O, -78 °C  
 to r.t. then 0.5 equiv.  
 Et<sub>2</sub>O, -78 °C to r.t.

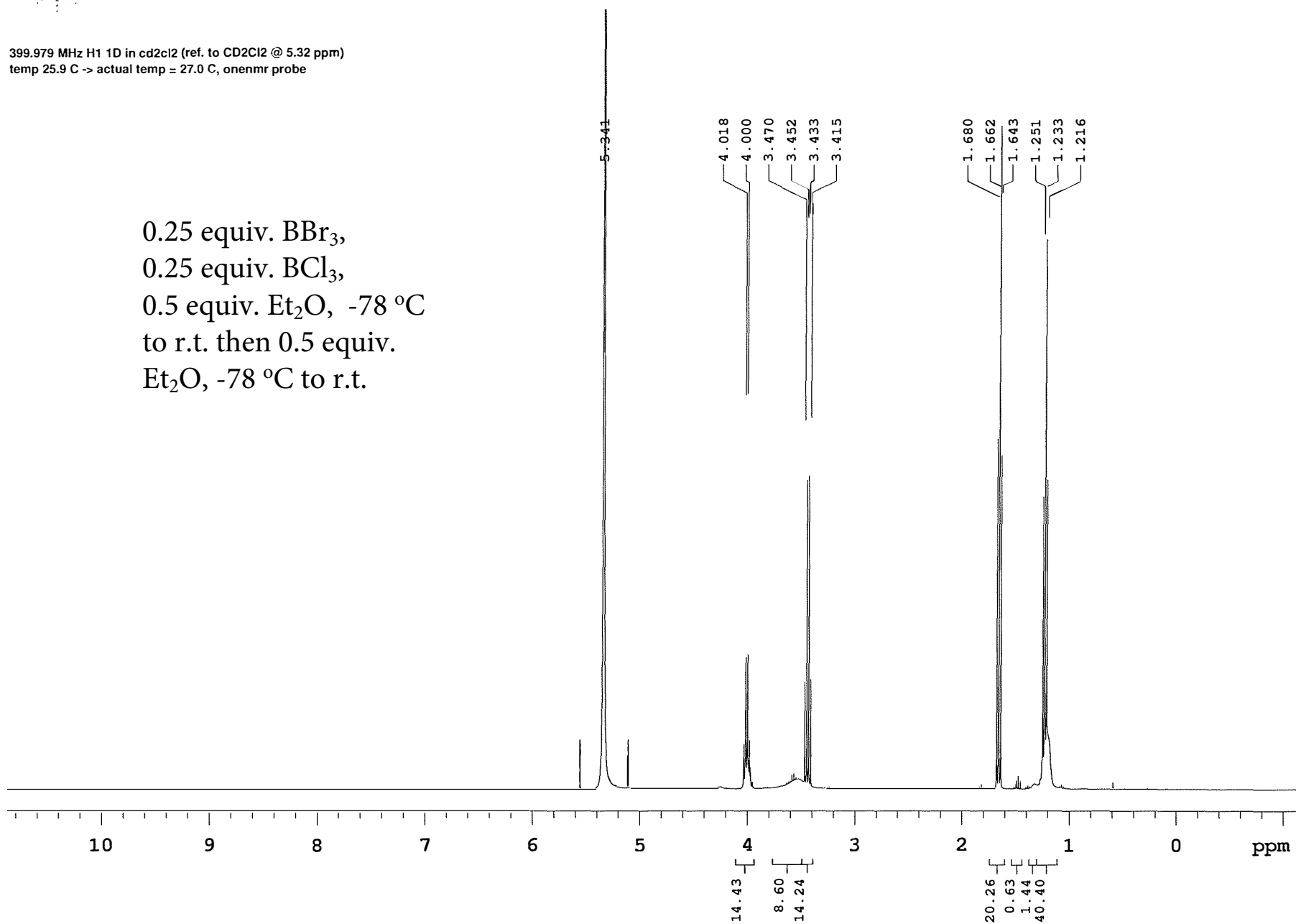


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 temp 25.9 C -> actual temp = 27.0 C, onenmr probe



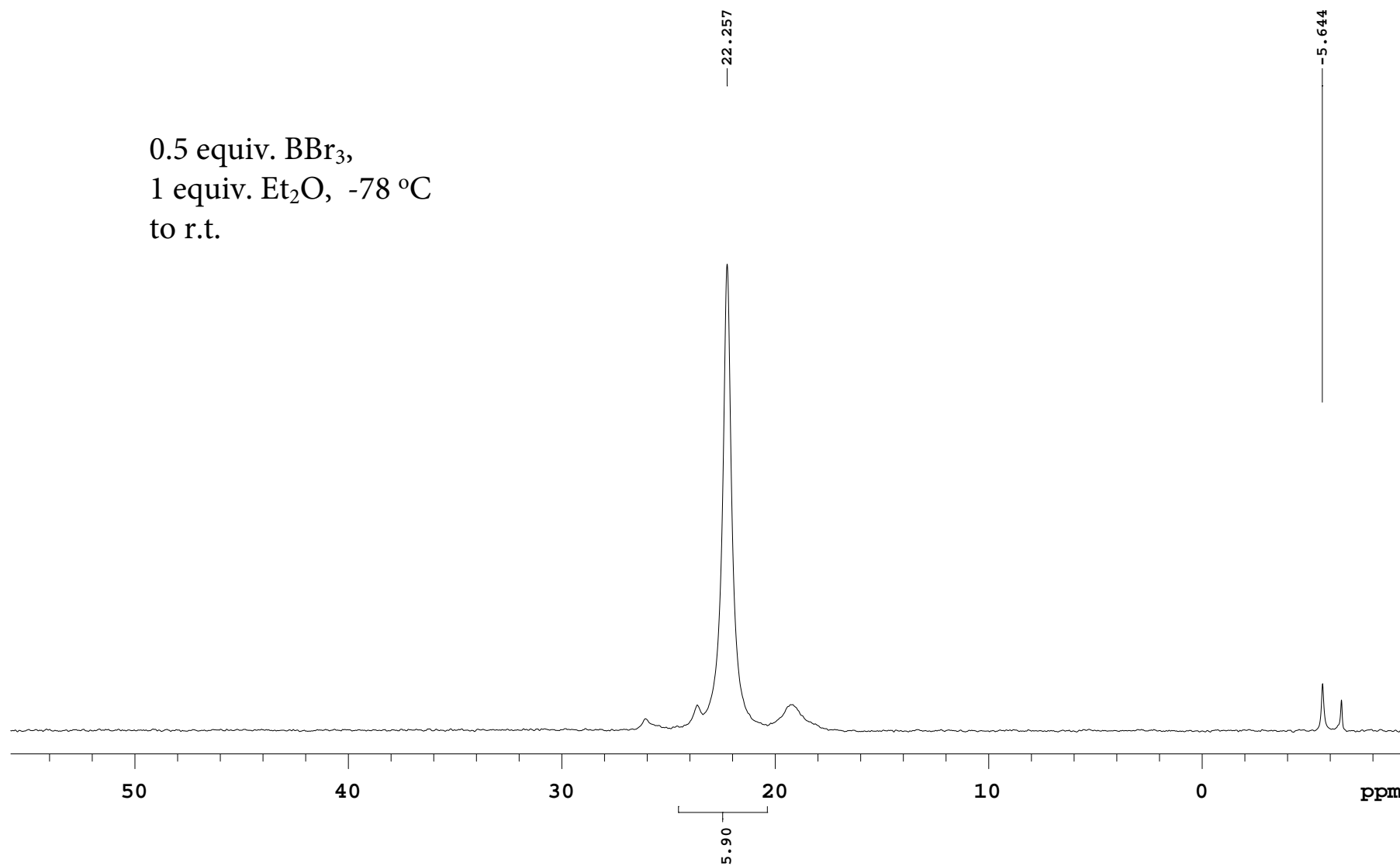
399.979 MHz H1 1D in cd2cl2 (ref. to CD2Cl2 @ 5.32 ppm)  
 temp 25.9 C -> actual temp = 27.0 C, onenmr probe

0.25 equiv. BBr<sub>3</sub>,  
 0.25 equiv. BCl<sub>3</sub>,  
 0.5 equiv. Et<sub>2</sub>O, -78 °C  
 to r.t. then 0.5 equiv.  
 Et<sub>2</sub>O, -78 °C to r.t.



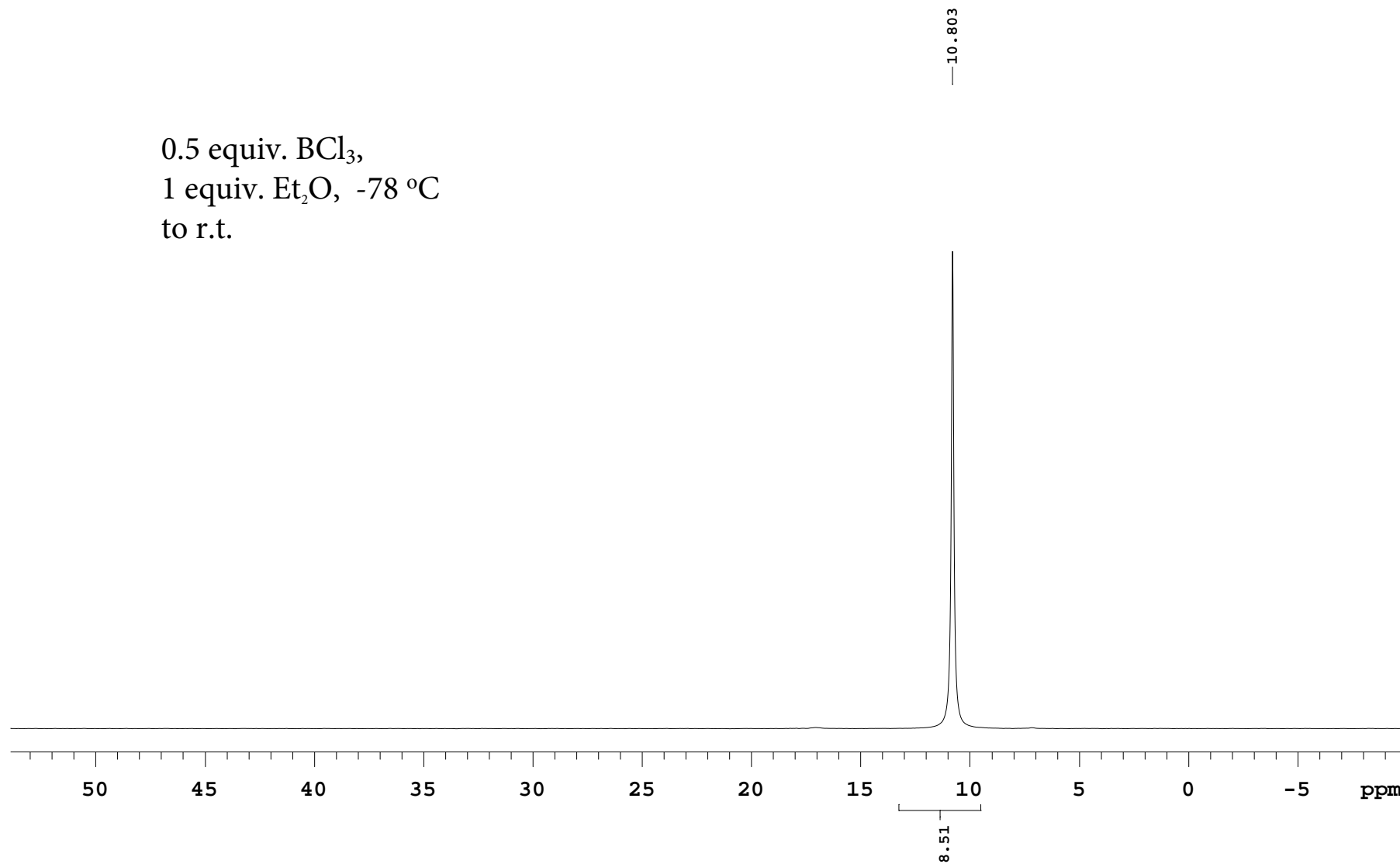
128.328 MHz B11{H1} 1D in cdcl3  
temp 25.9 C -> actual temp = 27.0 C, onenmr probe

0.5 equiv. BBr<sub>3</sub>,  
1 equiv. Et<sub>2</sub>O, -78 °C  
to r.t.

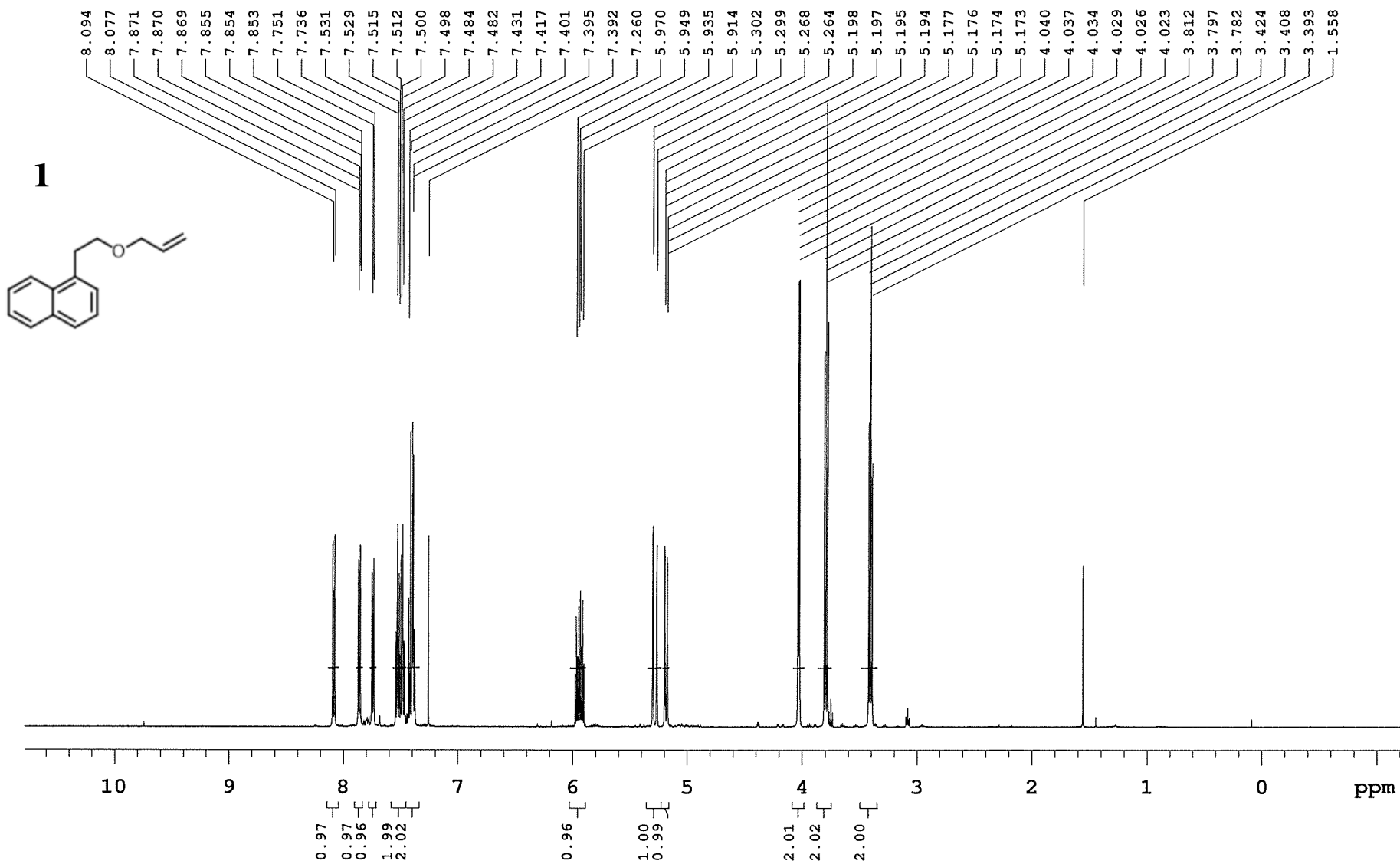


128.328 MHz B11{H1} 1D in cdcl3  
temp 25.9 C -> actual temp = 27.0 C, onenmr probe

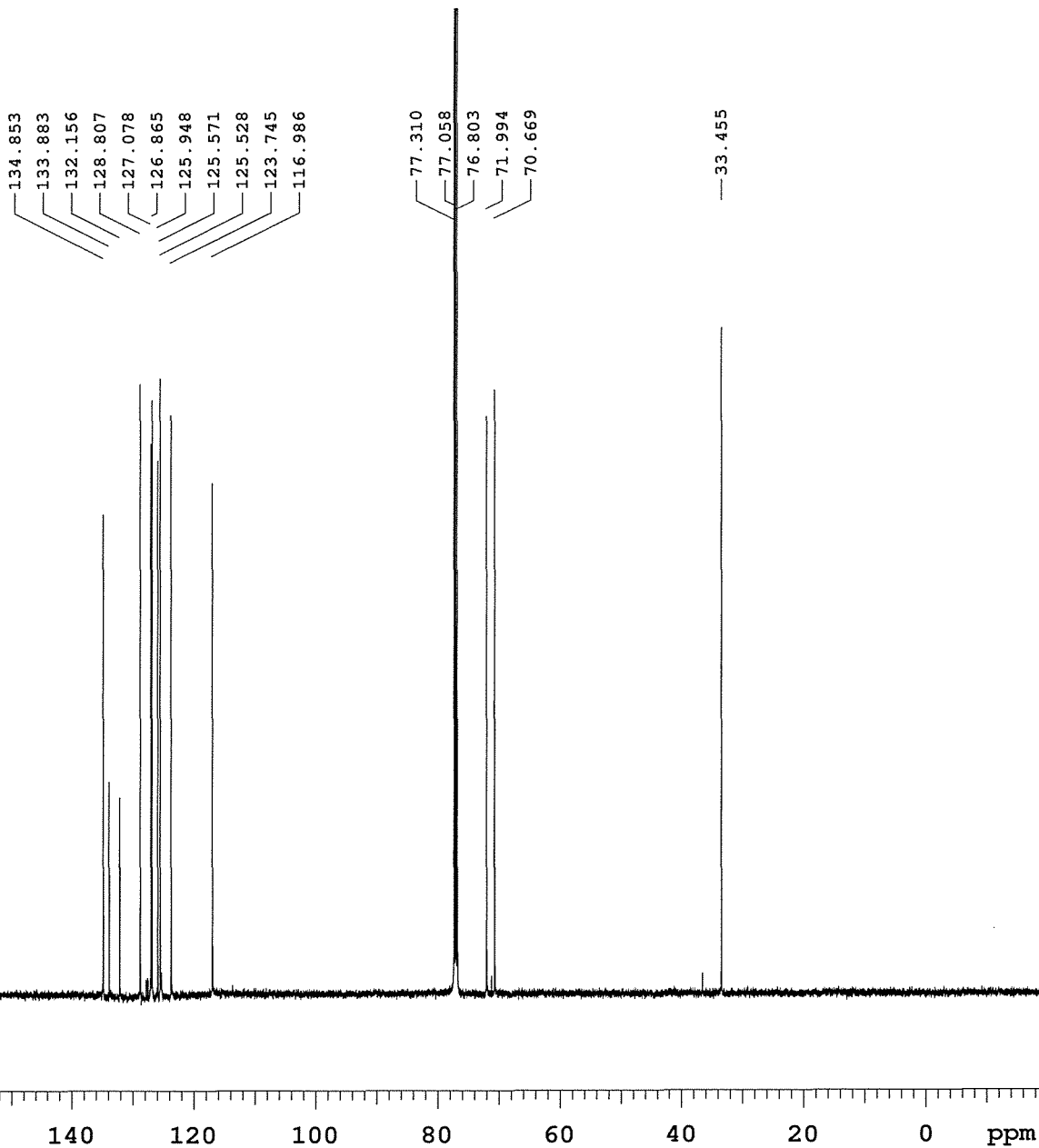
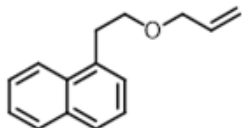
0.5 equiv. BCl<sub>3</sub>,  
1 equiv. Et<sub>2</sub>O, -78 °C  
to r.t.



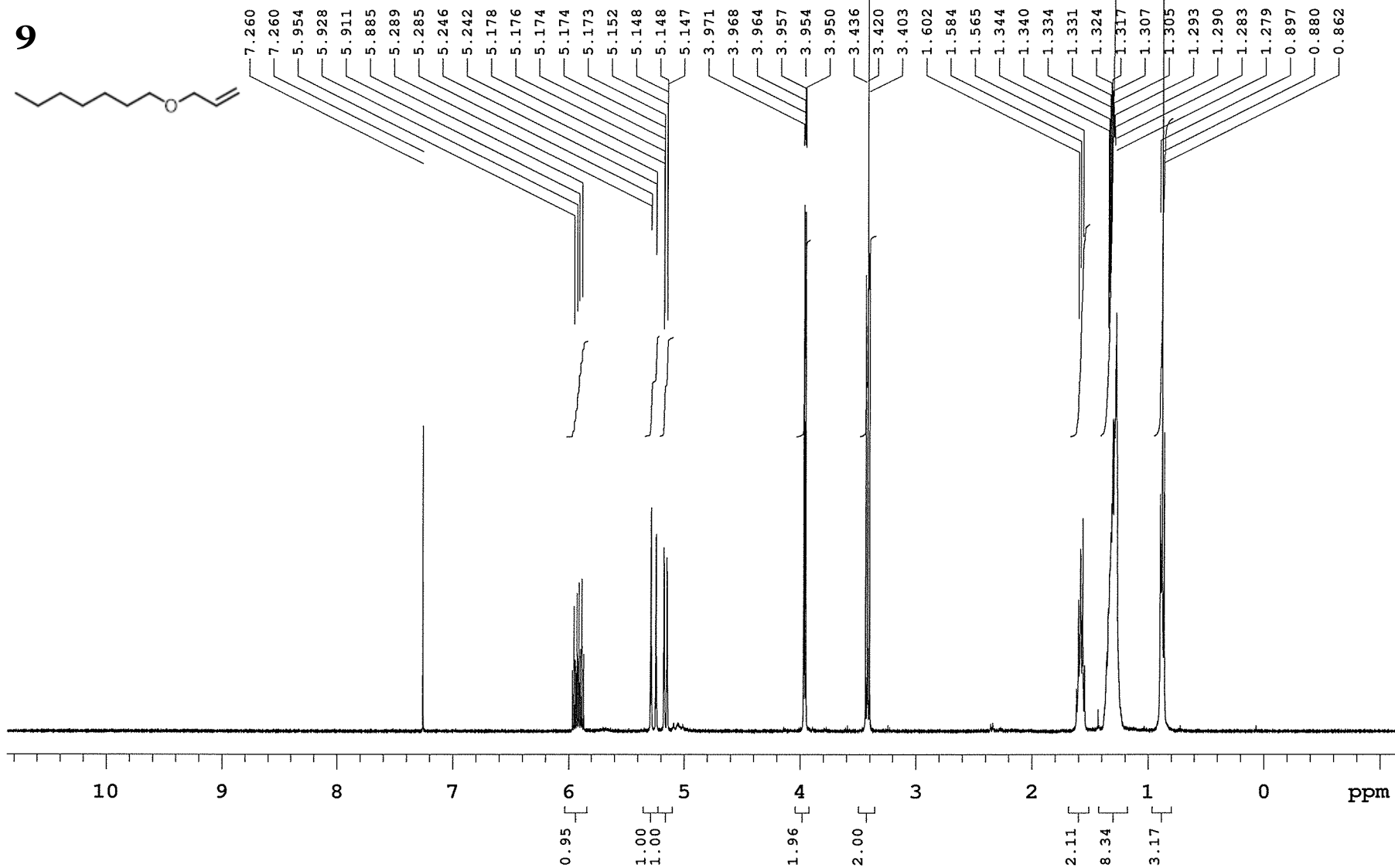
Nam, NT-1-naphthaleneethanol\_allyl\_ether\_after\_column  
 499.797 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, cold dual probe



**1**  
 Nam, NT-1-naphthaleneethanol\_allyl\_ether\_after\_column  
 125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, cold dual probe

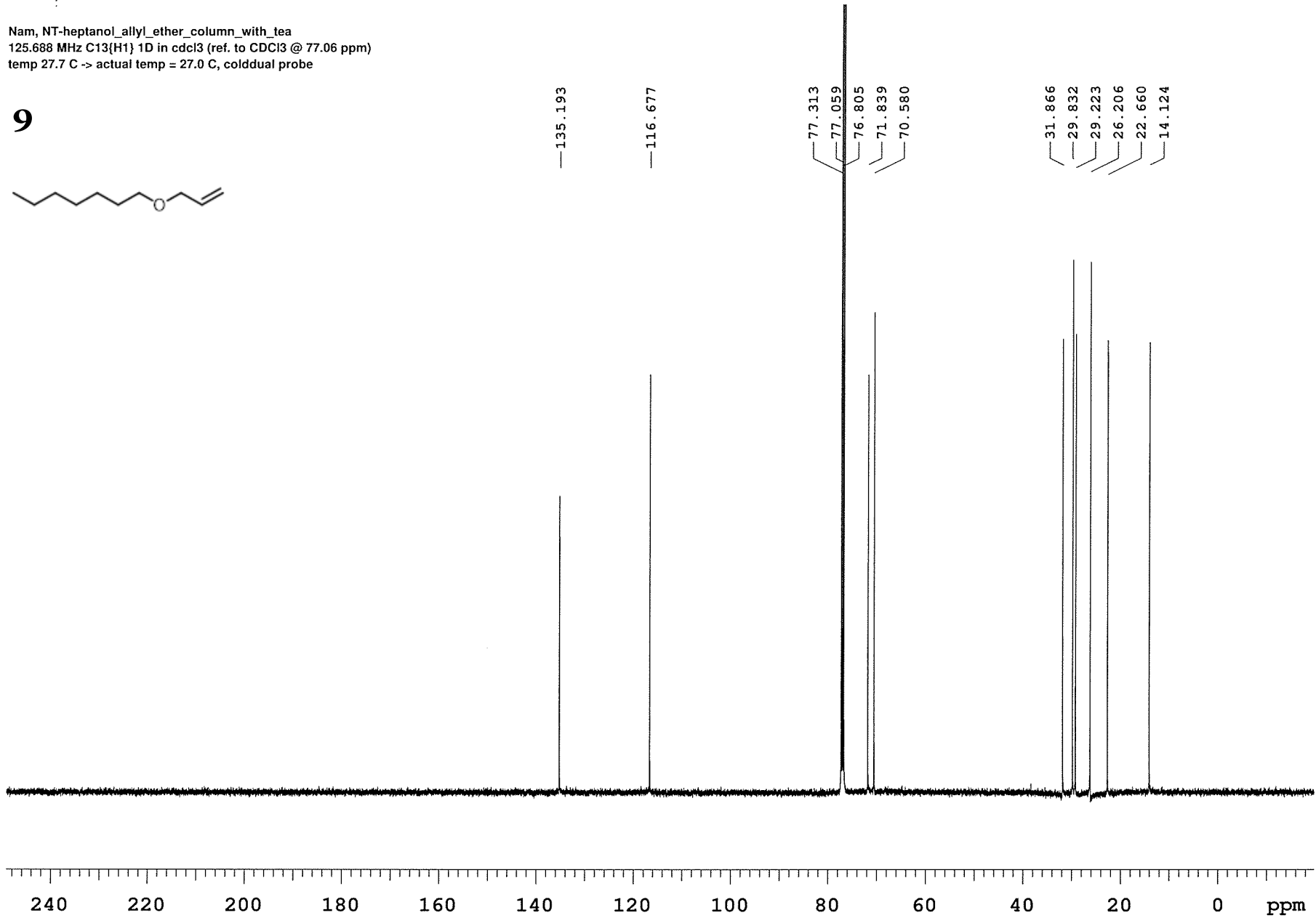


399.978 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
 temp 25.9 C -> actual temp = 27.0 C, onenmr probe

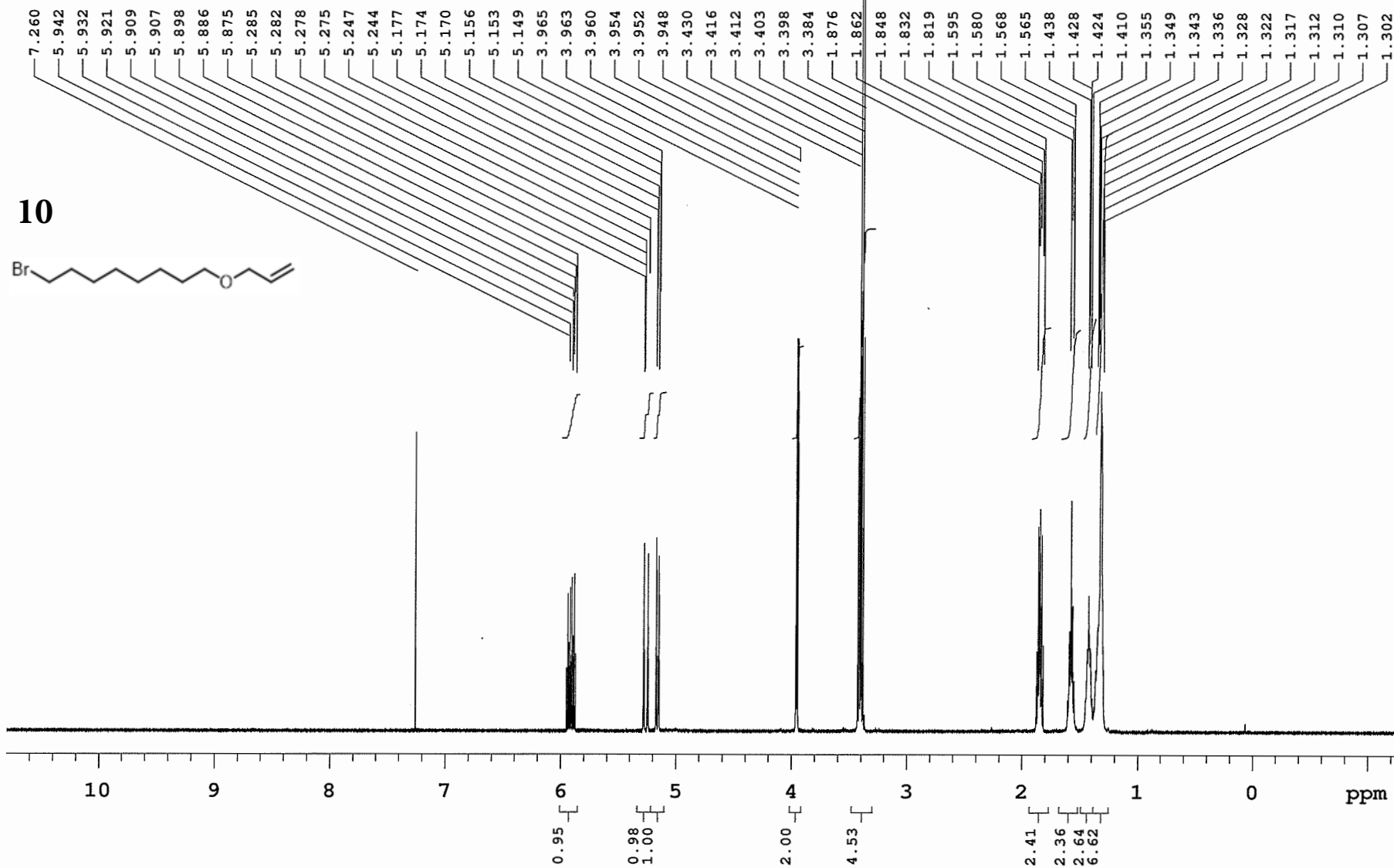


Nam, NT-heptanol\_allyl\_ether\_column\_with\_tea  
125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDCI3 @ 77.06 ppm)  
temp 27.7 C -> actual temp = 27.0 C, colddual probe

9

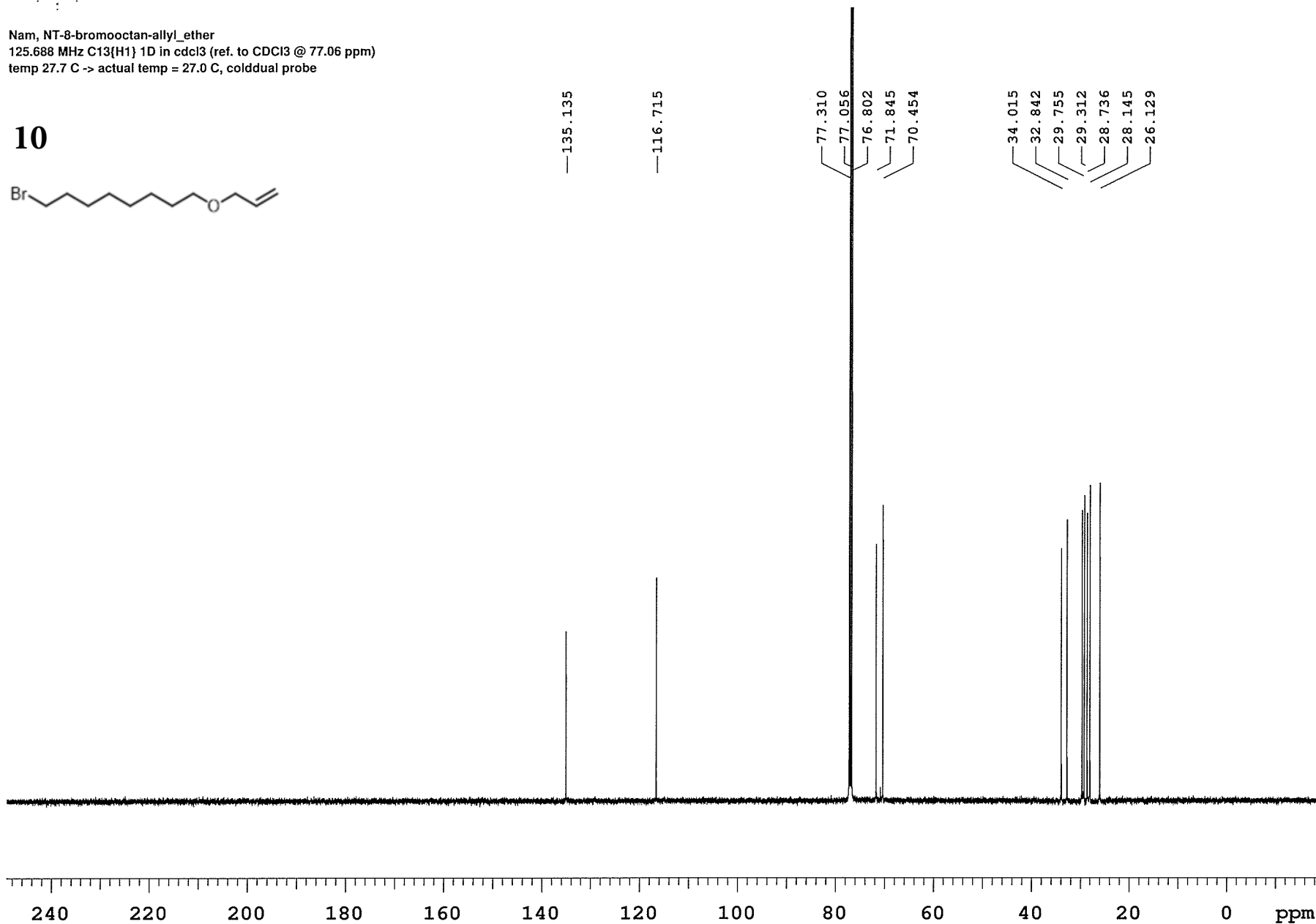
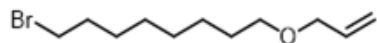


498.118 MHz H1 1D in cdc13 (ref. to CDCl3 @ 7.26 ppm)  
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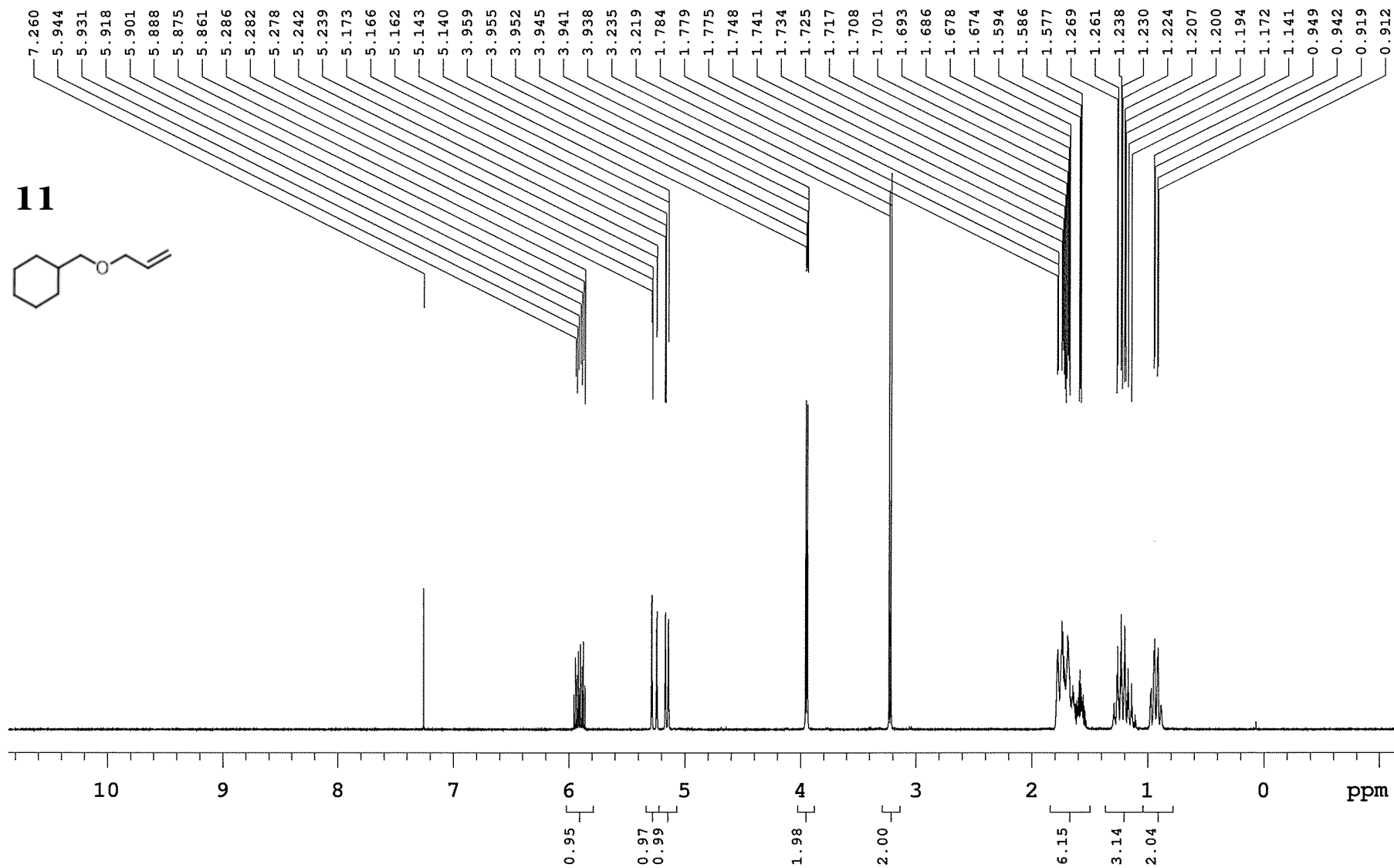


Nam, NT-8-bromooctan-allyl\_ether  
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temp 27.7 C -> actual temp = 27.0 C, cold dual probe

10

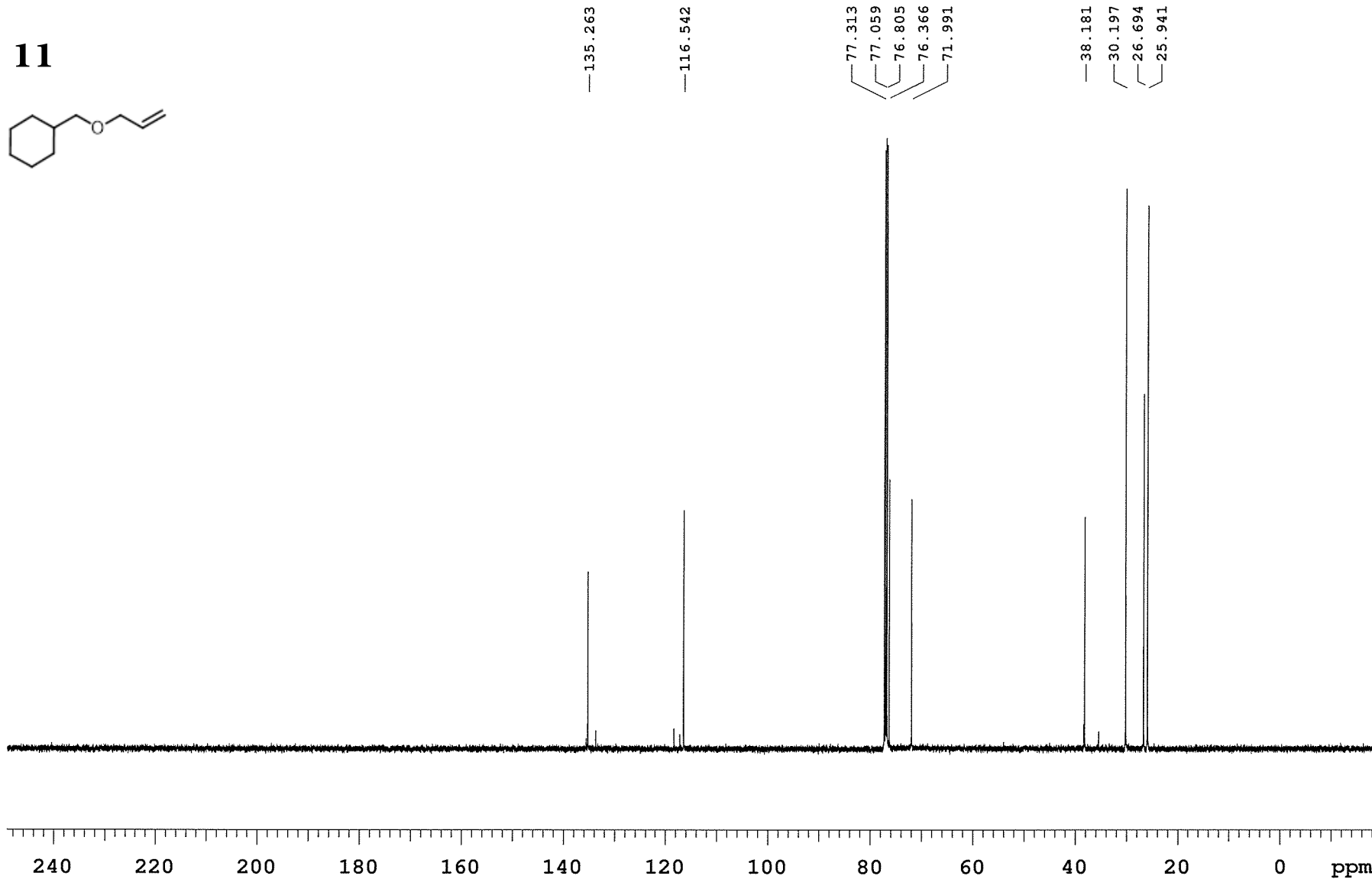
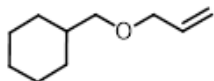


399.794 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
 temp 26.5 C -> actual temp = 27.0 C, autotdb probe

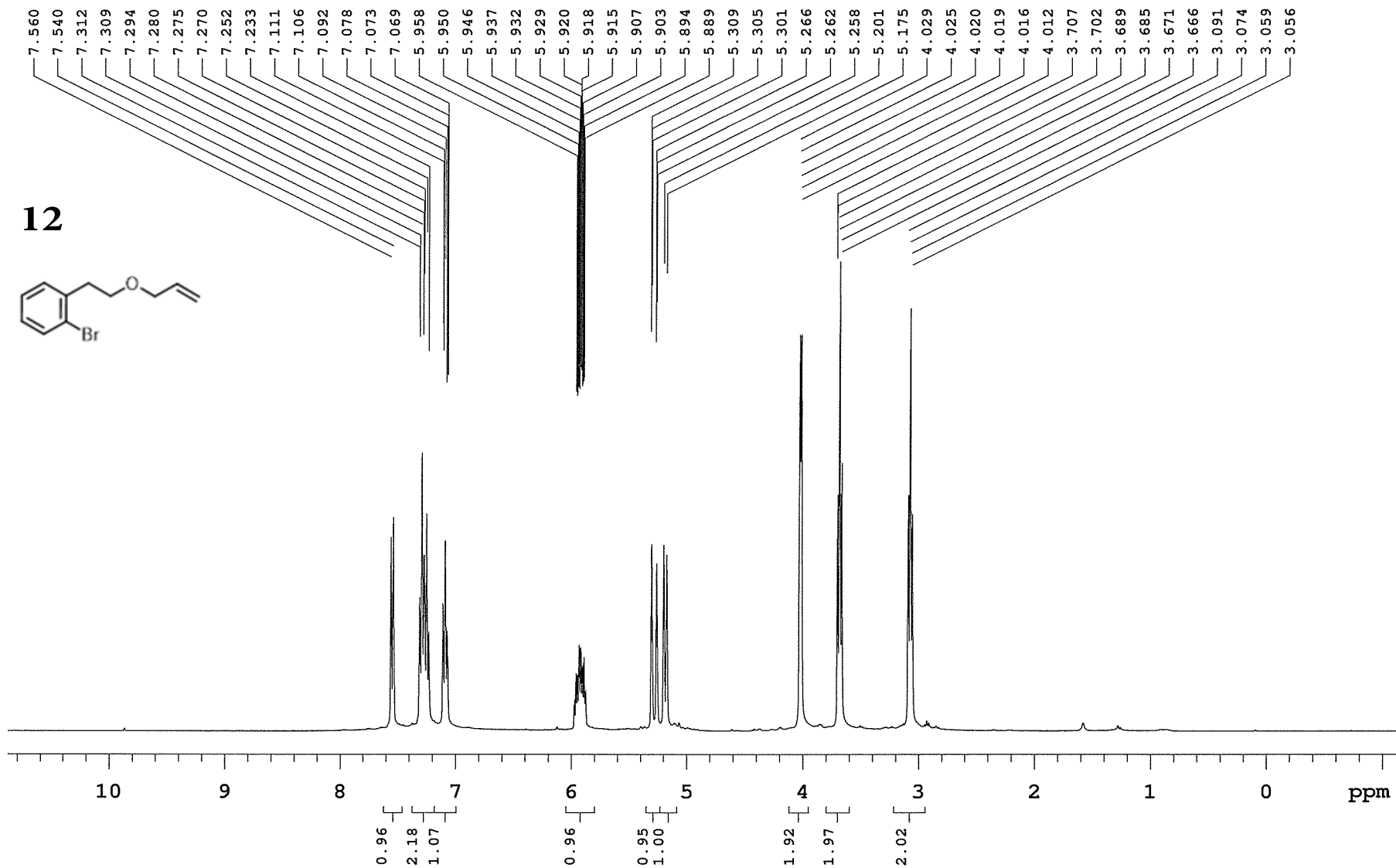


Nam, NT-cyclohexanemethanol\_allyl\_ether\_after\_column  
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 temp 27.7 C -> actual temp = 27.0 C, cold dual probe

**11**

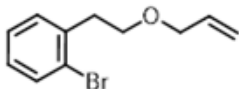


399.978 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
 temp 25.9 C -> actual temp = 27.0 C, onenmr probe



Nam, NT-2-bromo-phenyl\_ethanol\_allyl\_ether\_after\_column  
 125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDC13 @ 77.06 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, cold dual probe

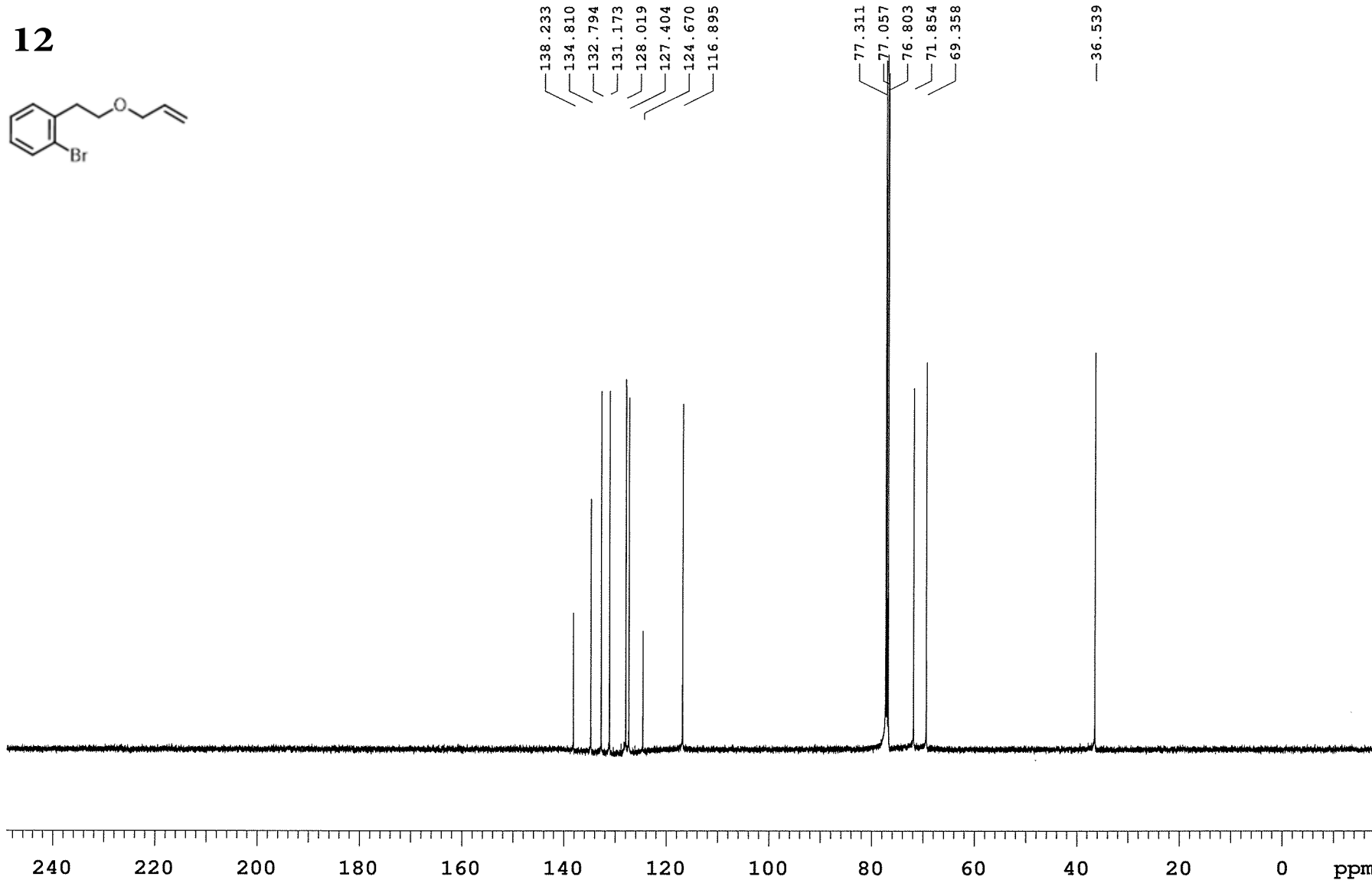
**12**



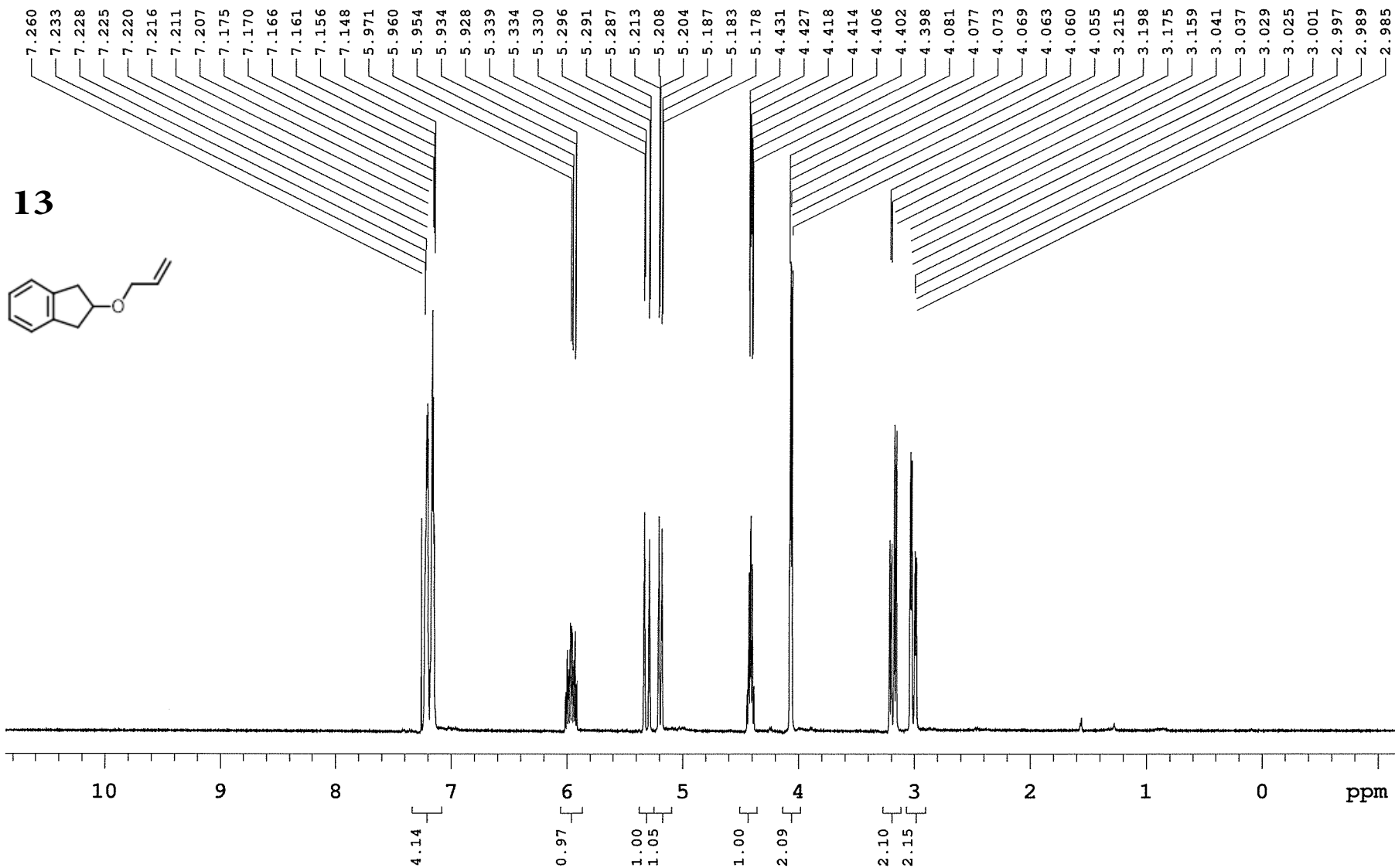
138.233  
 134.810  
 132.794  
 131.173  
 128.019  
 127.404  
 124.670  
 116.895

77.311  
 77.057  
 76.803  
 71.854  
 69.358

36.539

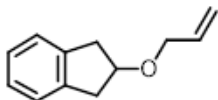


399.978 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
temp 25.9 C -> actual temp = 27.0 C, onenmr probe



Nam, nt-2-indanol\_allyl\_ether\_coulmn\_with\_tea  
 125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, coldddual probe

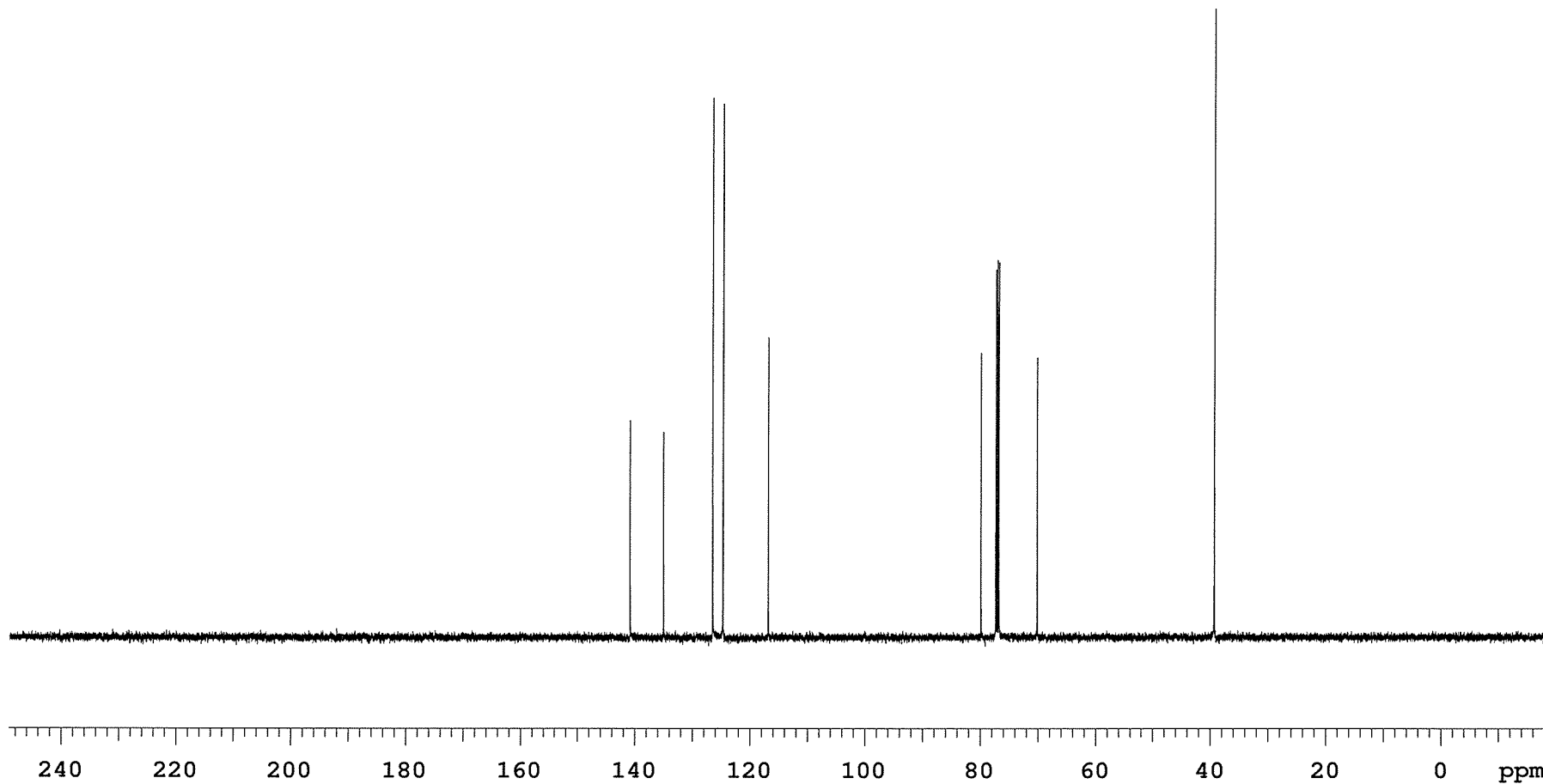
**13**



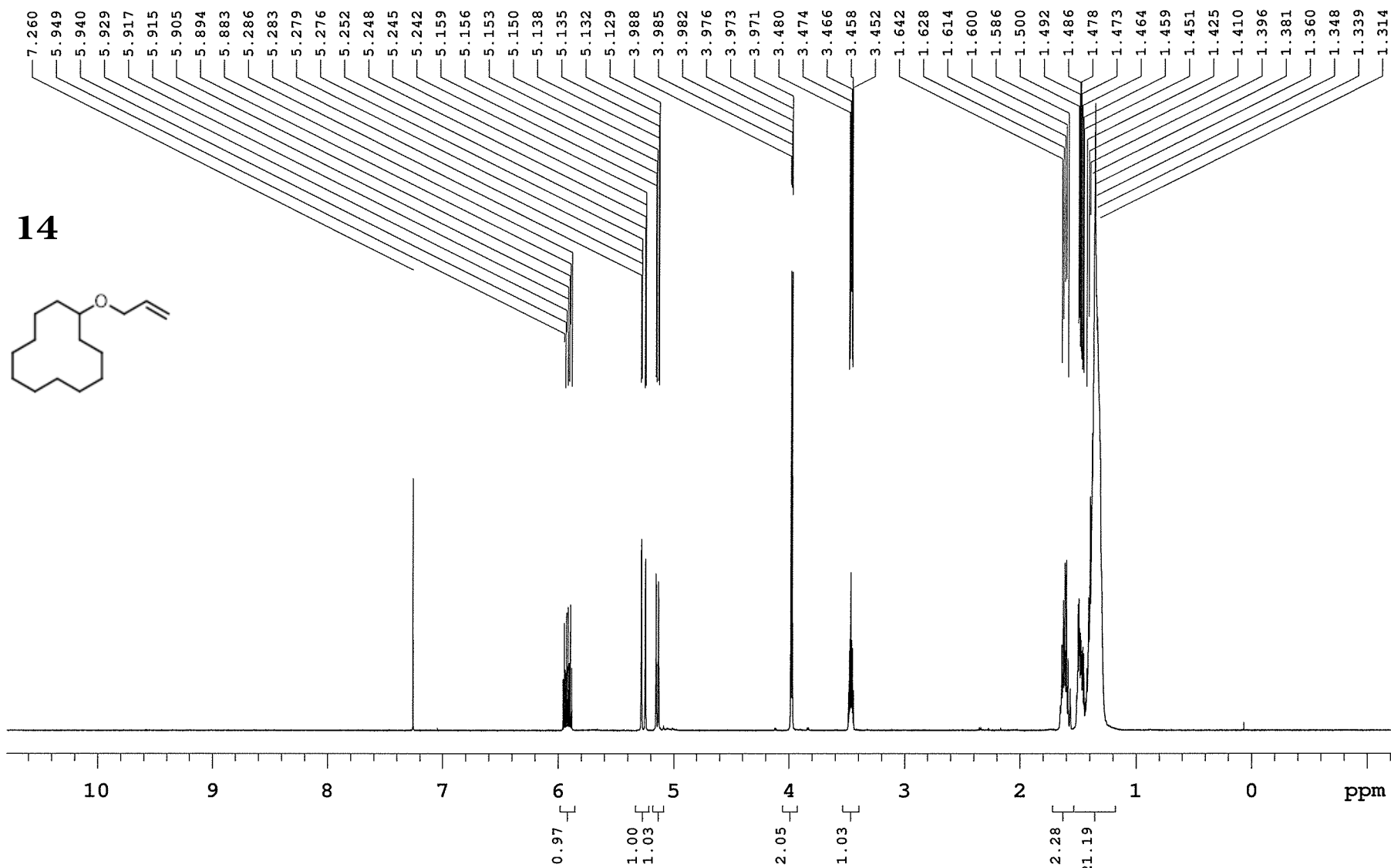
— 140.893  
 — 135.074  
 — 126.547  
 — 124.721  
 — 116.878

79.896  
 77.318  
 77.063  
 76.809  
 70.152

— 39.369

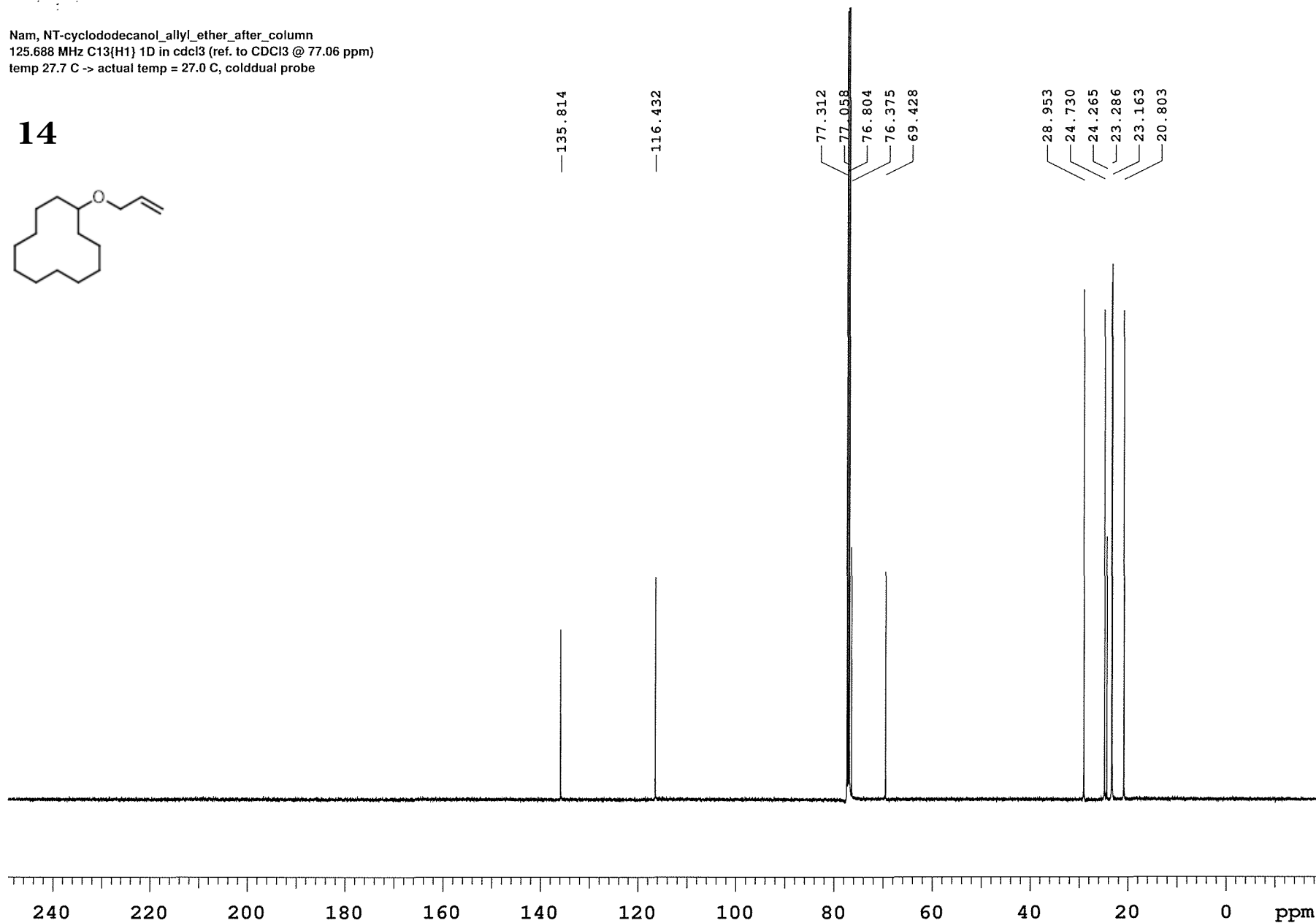
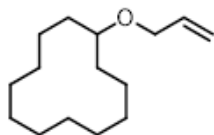


Nam, NT-cyclododecanol\_allyl\_ether\_after\_column  
 499.797 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, cold dual probe

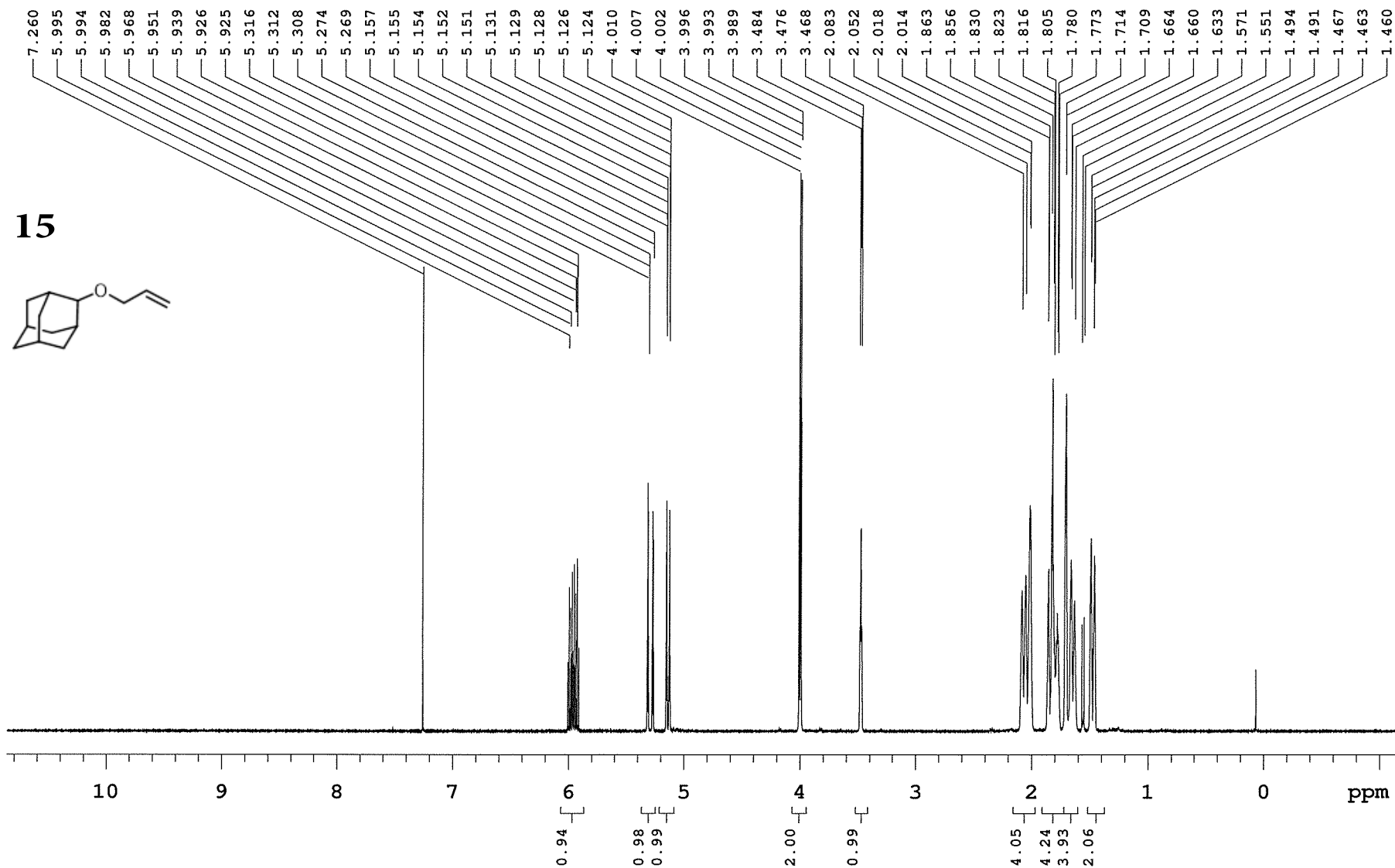


Nam, NT-cyclododecanol\_allyl\_ether\_after\_column  
125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm)  
temp 27.7 C -> actual temp = 27.0 C, cold dual probe

14

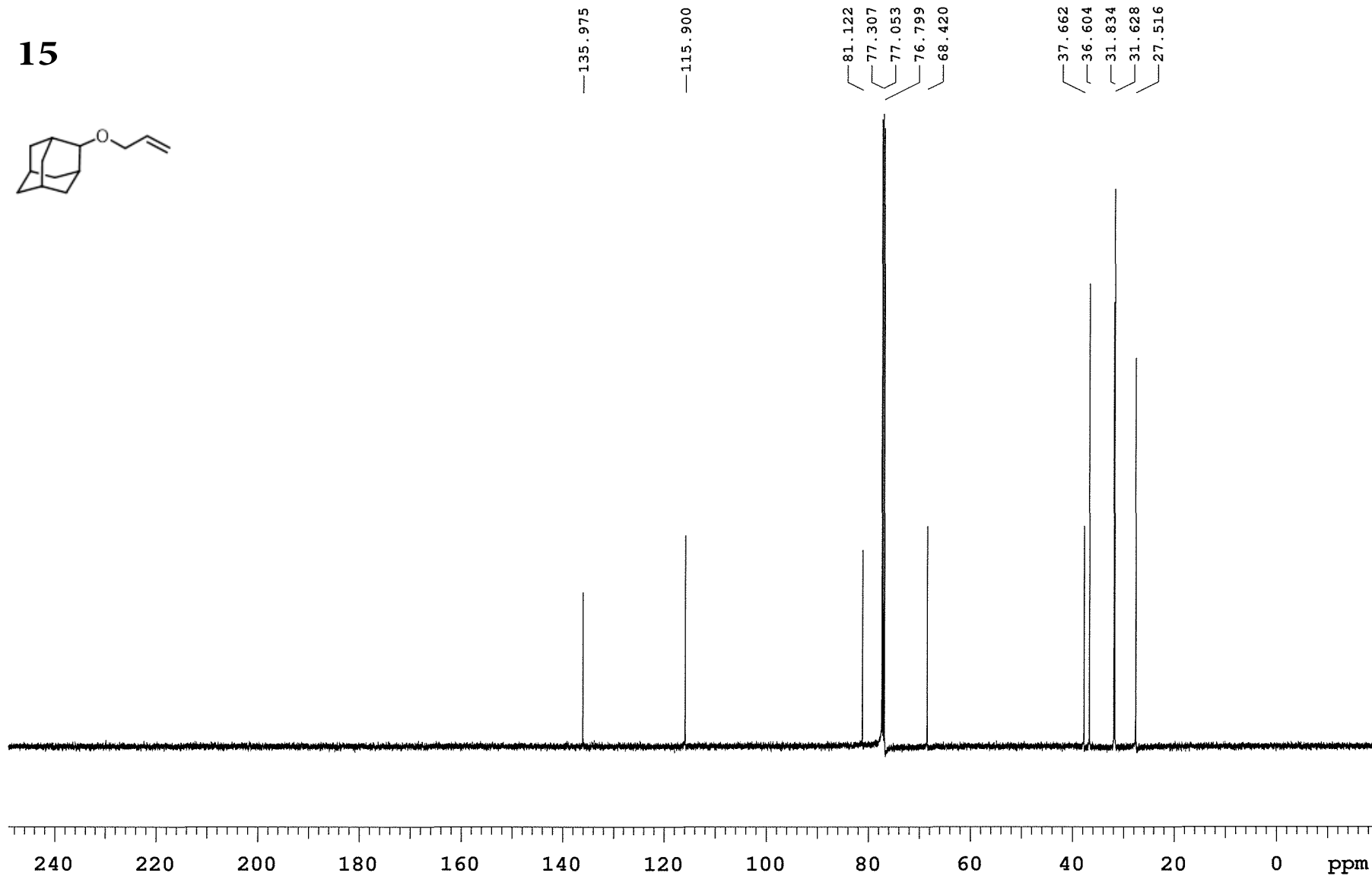
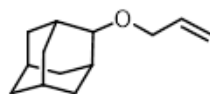


399.978 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
 temp 25.9 C -> actual temp = 27.0 C, onenmr probe

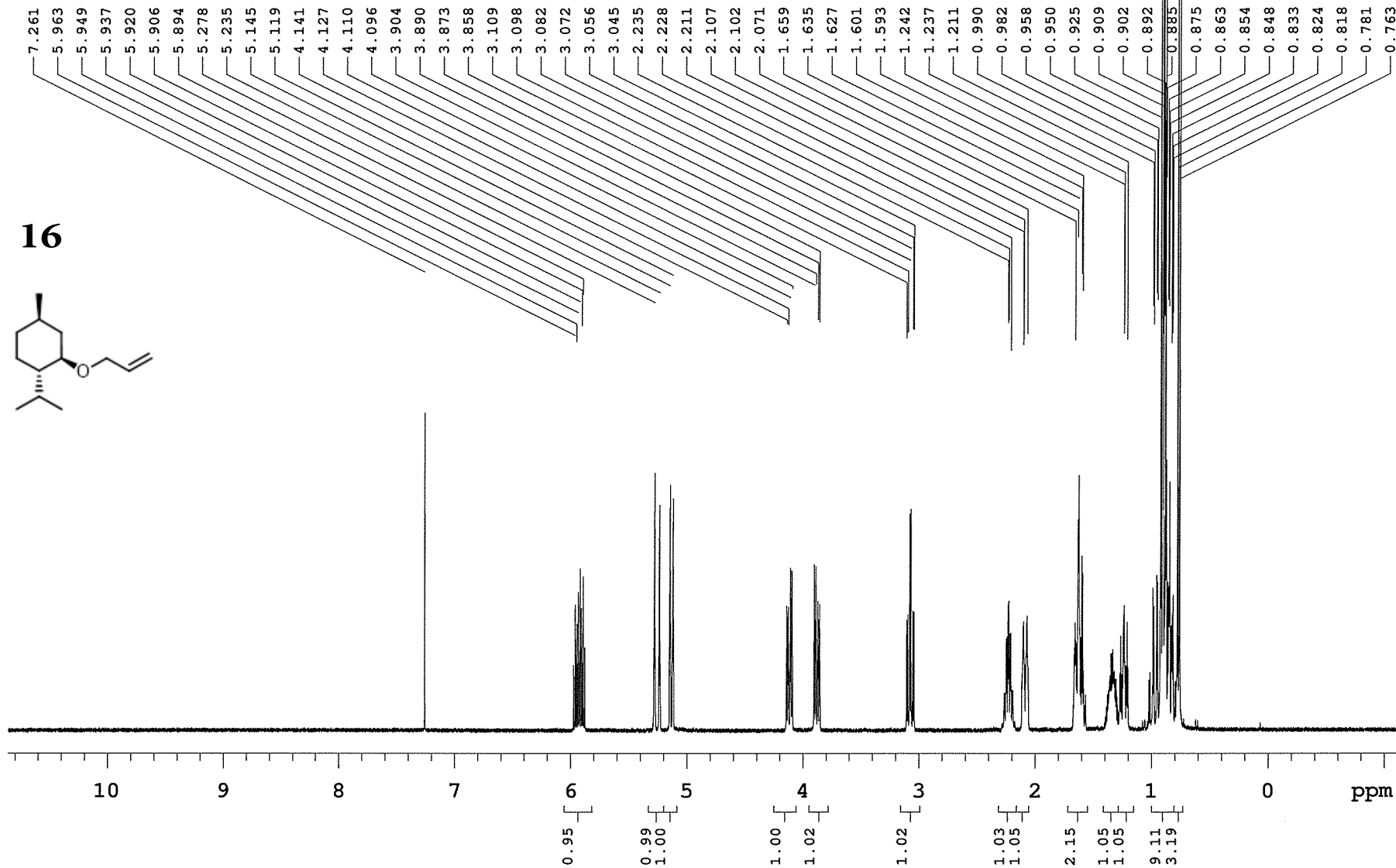


Nam, NT-2-adamantanol\_allyl\_ether\_after\_column  
 125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDC13 @ 77.06 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, coldddual probe

15

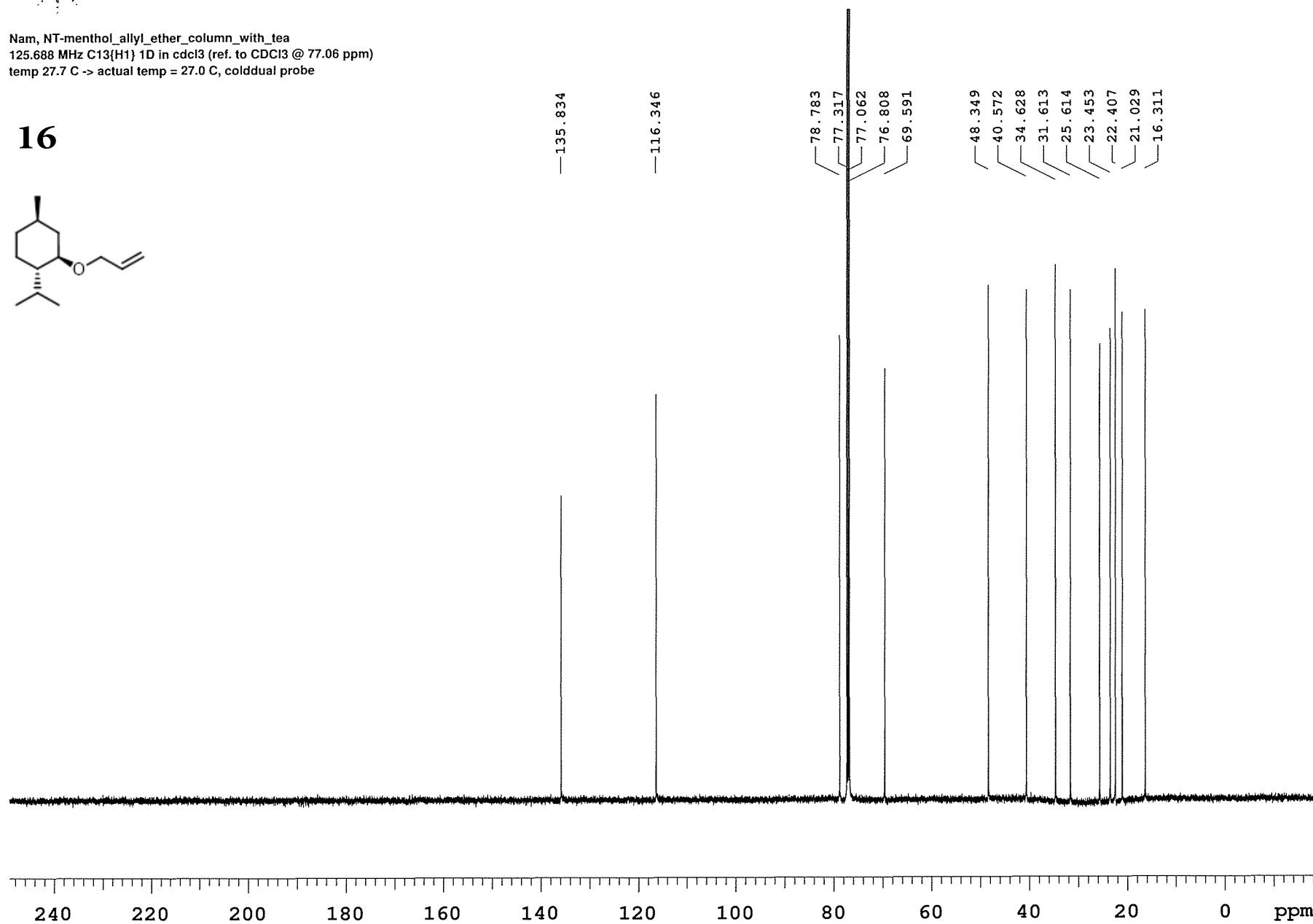
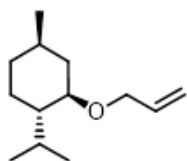


399.794 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
 temp 26.5 C -> actual temp = 27.0 C, autotdb probe



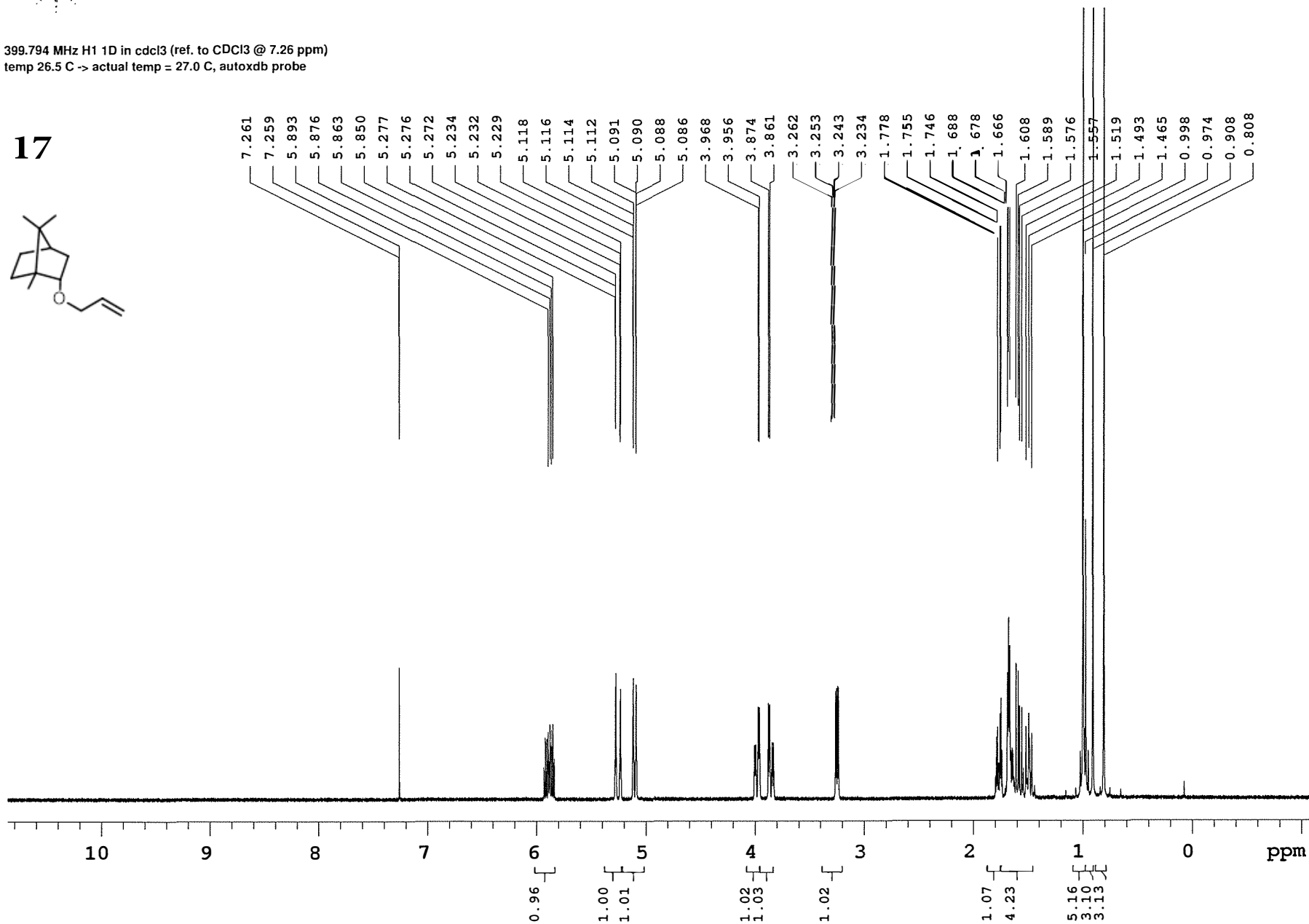
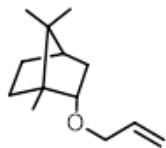
Nam, NT-menthol\_allyl\_ether\_column\_with\_tea  
 125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, cold dual probe

16



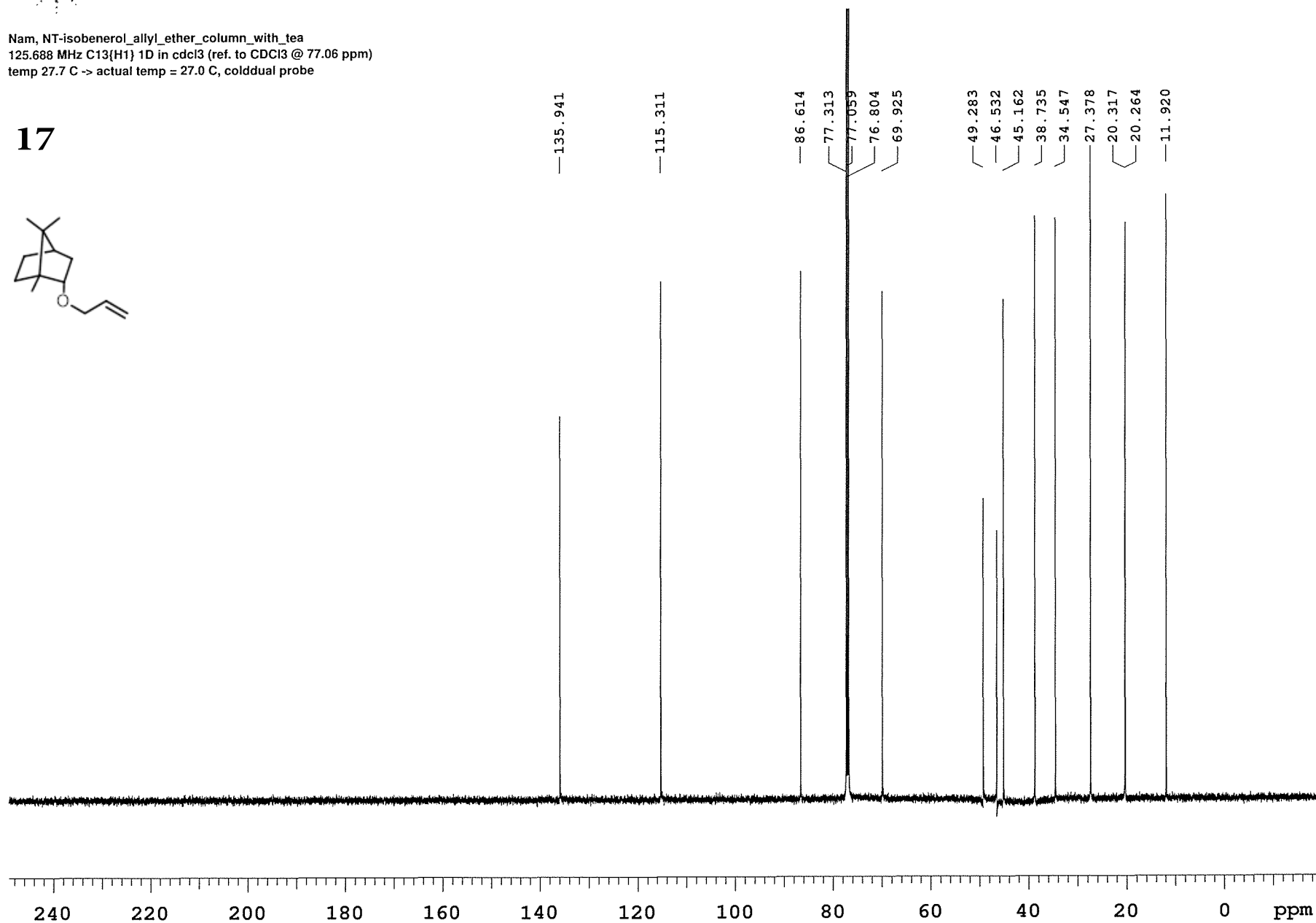
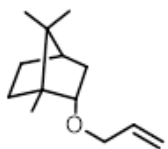
399.794 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
temp 26.5 C -> actual temp = 27.0 C, autotdb probe

17

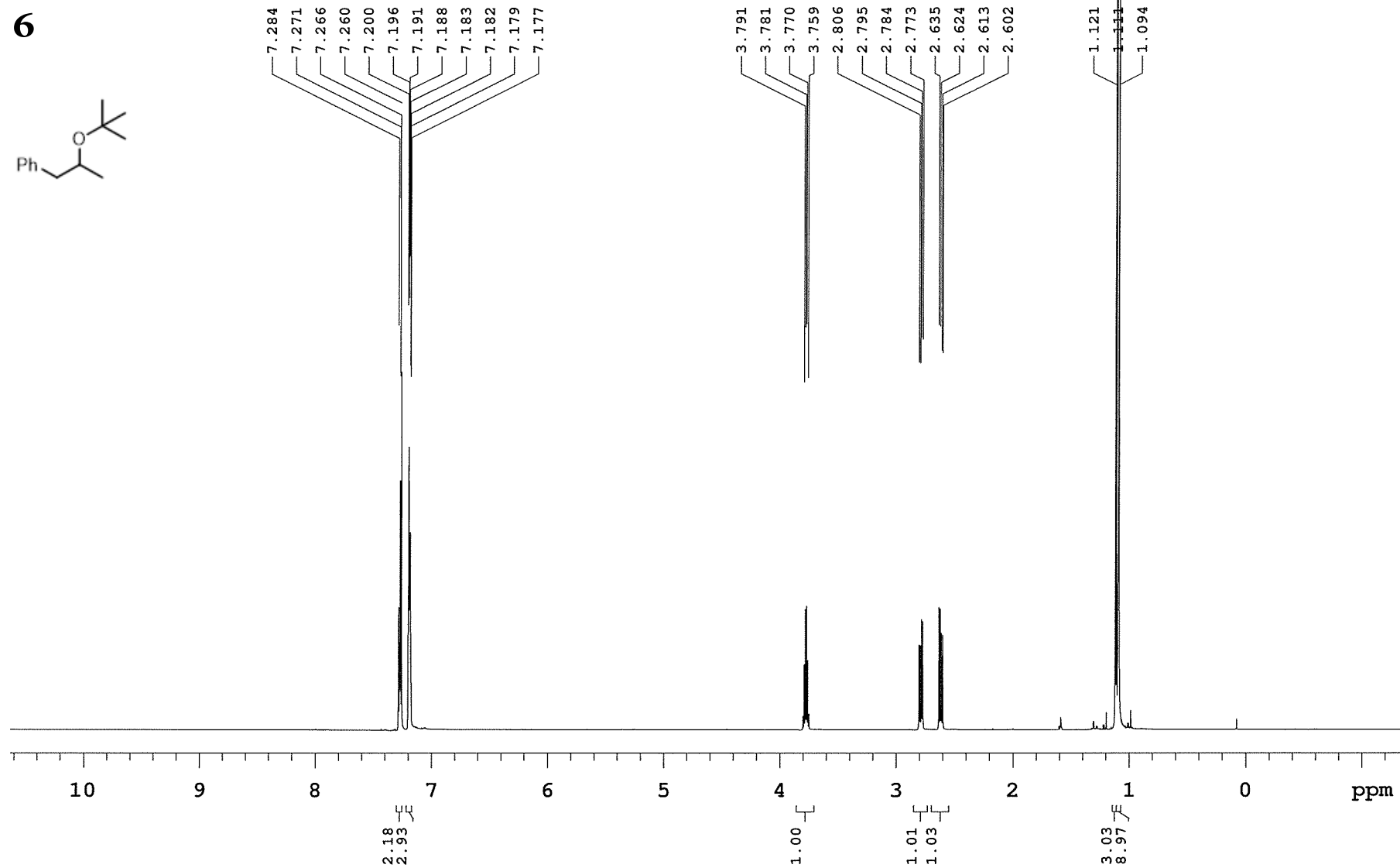
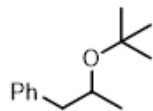


Nam, NT-isobenerol\_allyl\_ether\_column\_with\_tea  
125.688 MHz C13(H1) 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm)  
temp 27.7 C -> actual temp = 27.0 C, cold dual probe

17

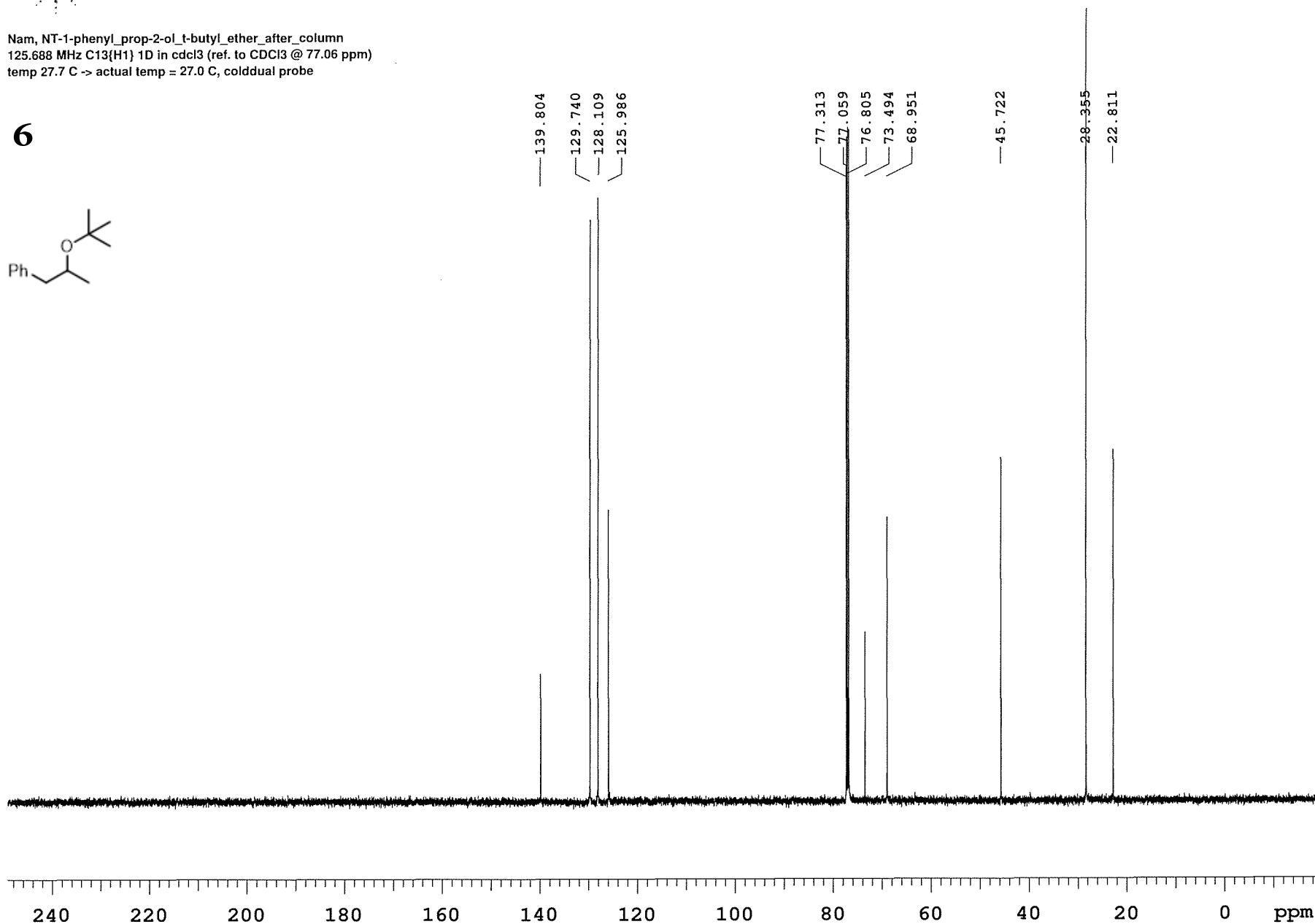
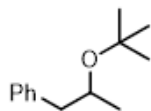


599.926 MHz H1 1D in cdcl3 (ref. to CDC13 @ 7.26 ppm)  
 temp 26.2 C -> actual temp = 27.0 C, autoxid probe

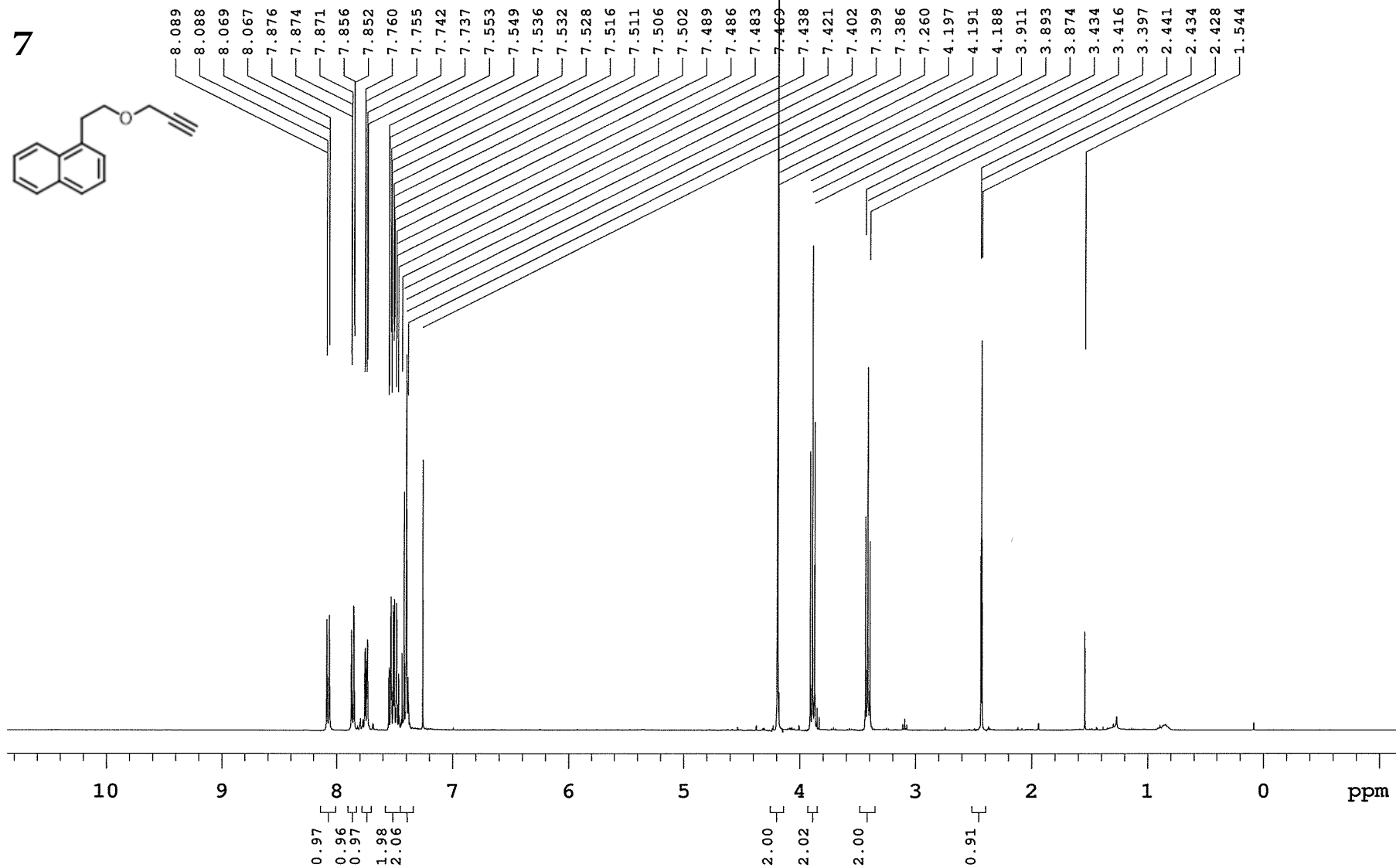
**6**


Nam, NT-1-phenyl\_prop-2-ol\_t-butyl\_ether\_after\_column  
 125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDC13 @ 77.06 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, cold dual probe

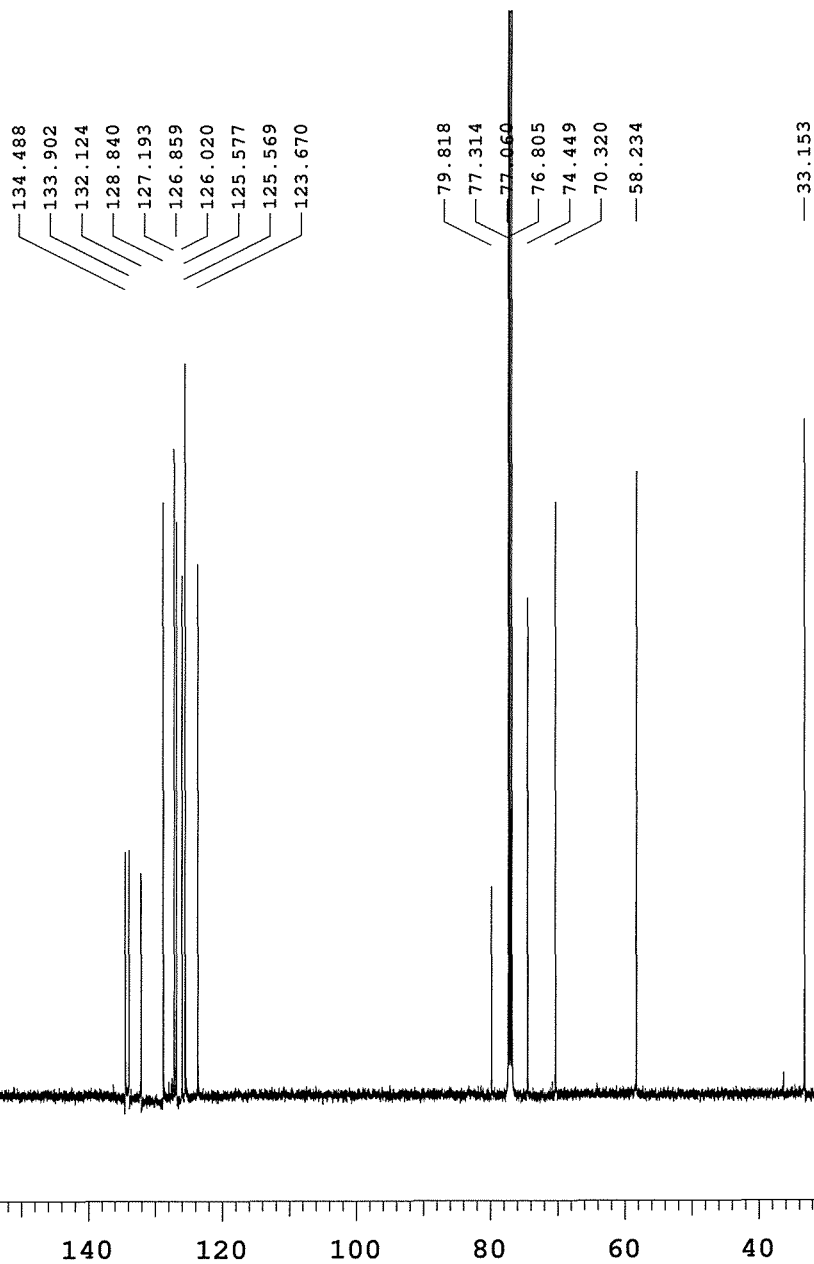
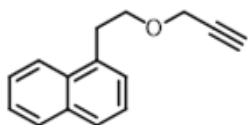
6



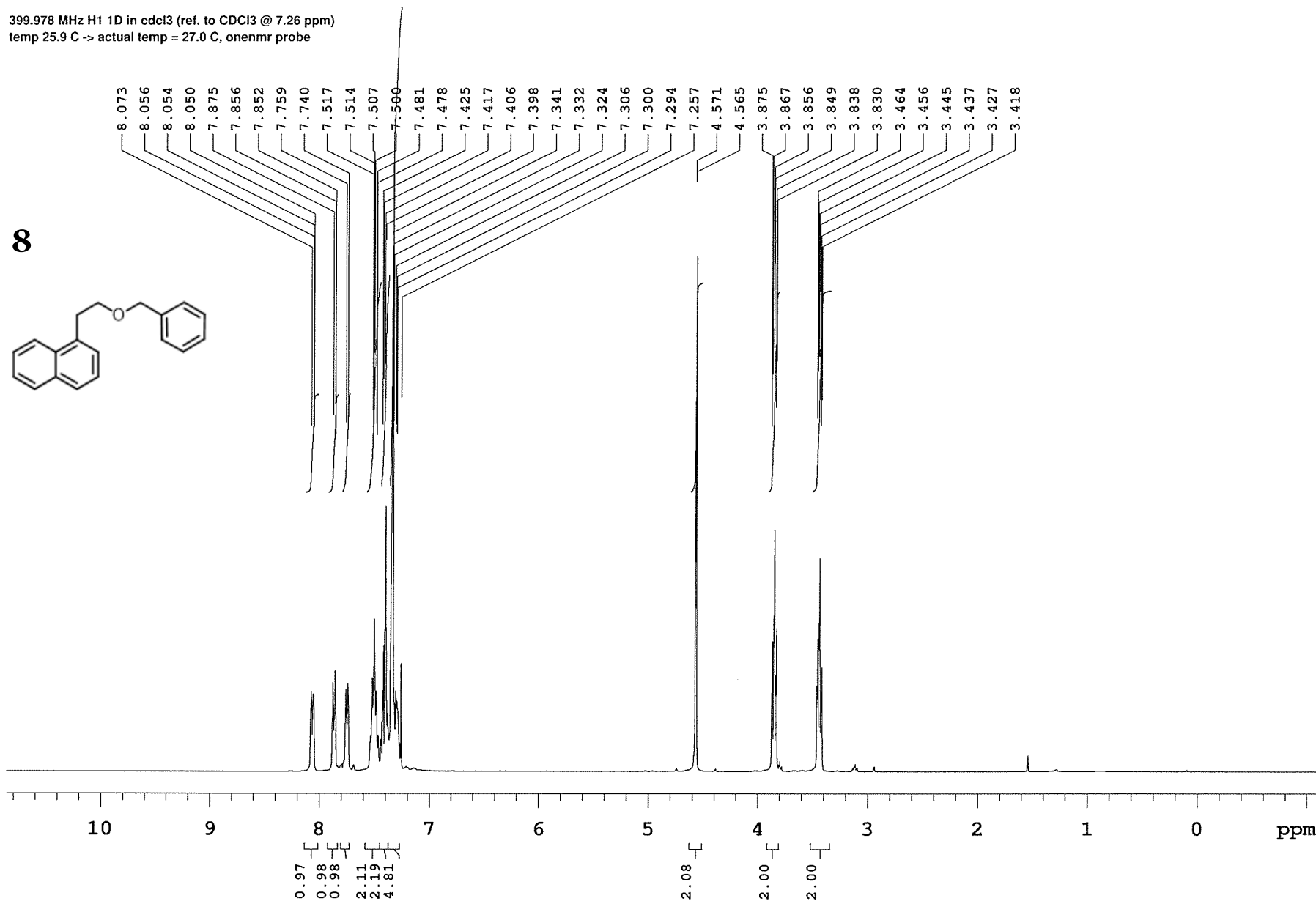
399.978 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
 temp 25.9 C -> actual temp = 27.0 C, onenmr probe



**7**  
 Nam, NT-1-naphthalene\_ethanol\_propargyl\_ether\_after\_column  
 125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, cold dual probe

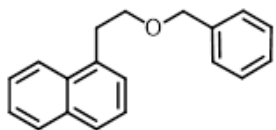


399.978 MHz H1 1D in cdcl3 (ref. to CDCI3 @ 7.26 ppm)  
 temp 25.9 C -> actual temp = 27.0 C, onenmr probe

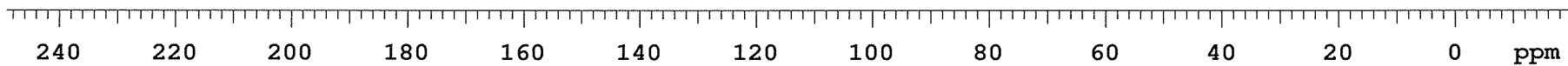
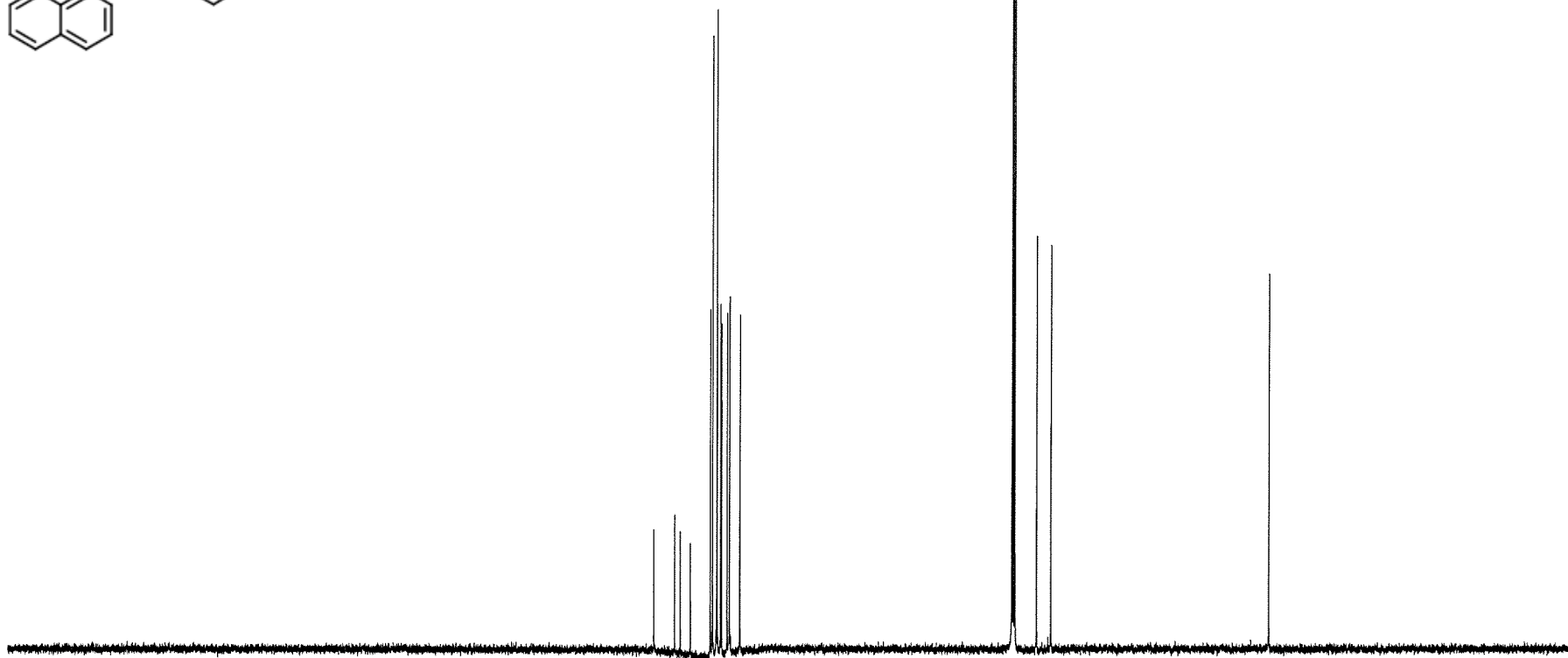


Nm, NT-1-naphthalene\_ethanol\_benzyl\_ether\_after\_column  
 125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDCI3 @ 77.06 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, colddual probe

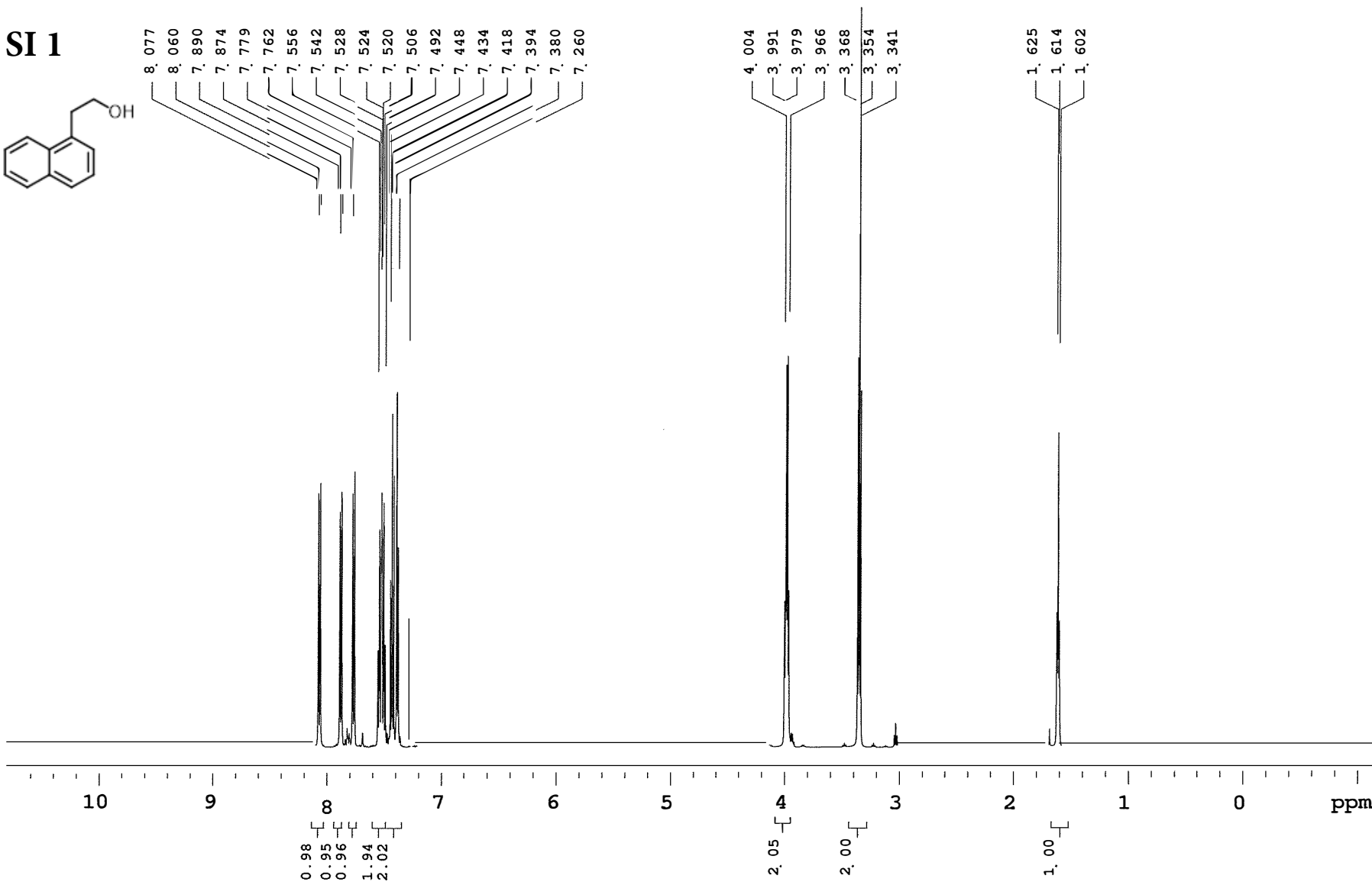
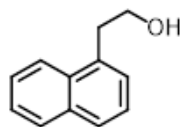
8



138.418  
 134.858  
 133.884  
 132.161  
 128.793  
 128.410  
 127.682  
 127.606  
 127.077  
 126.867  
 125.936  
 125.557  
 125.520  
 123.752  
 77.310  
 77.056  
 76.802  
 73.085  
 70.659  
 — 33.473

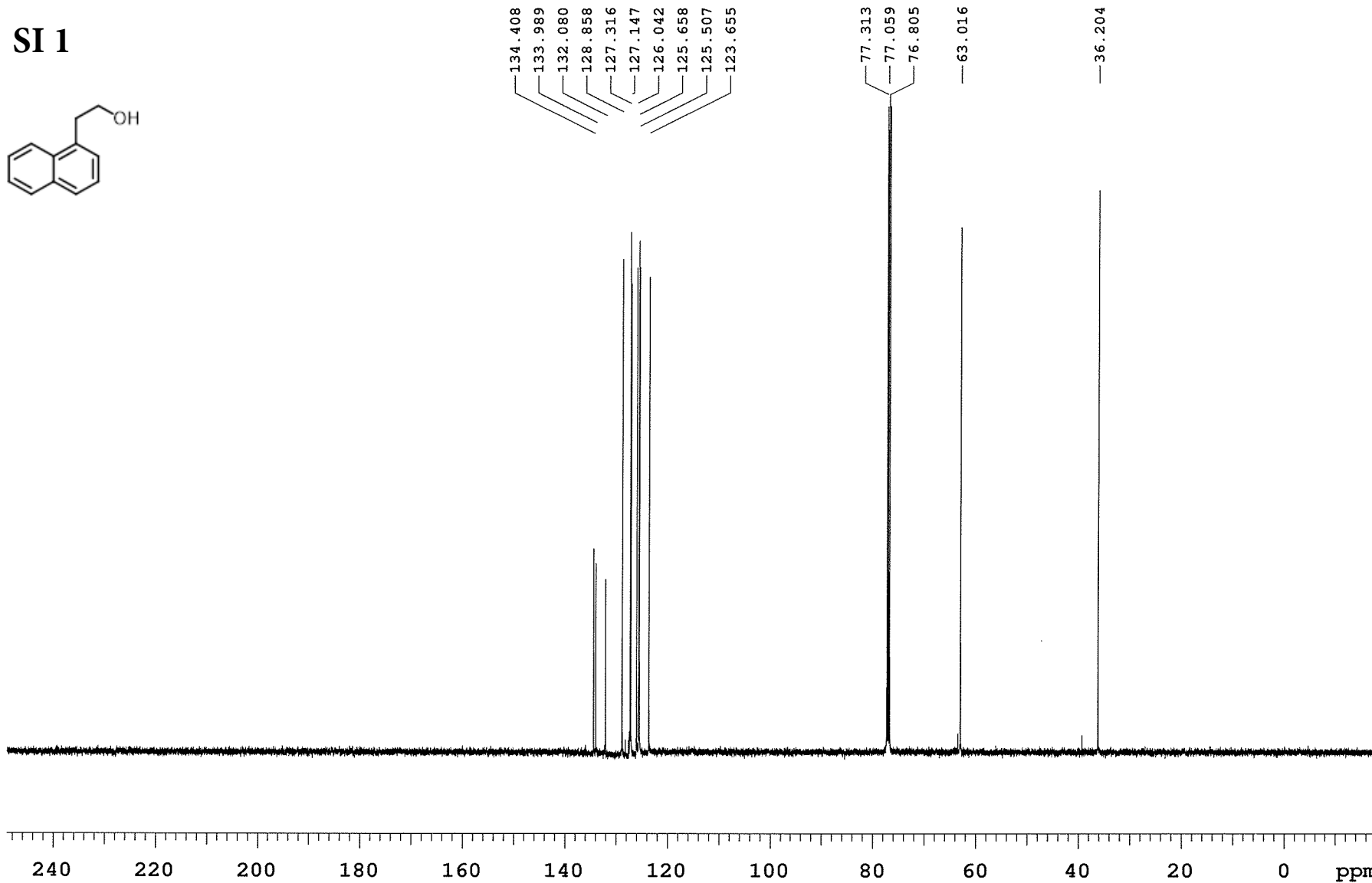
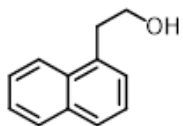


Nam, NT-naphthalene\_ethanol\_from\_BCI3\_alone  
 499.797 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, cold dual probe

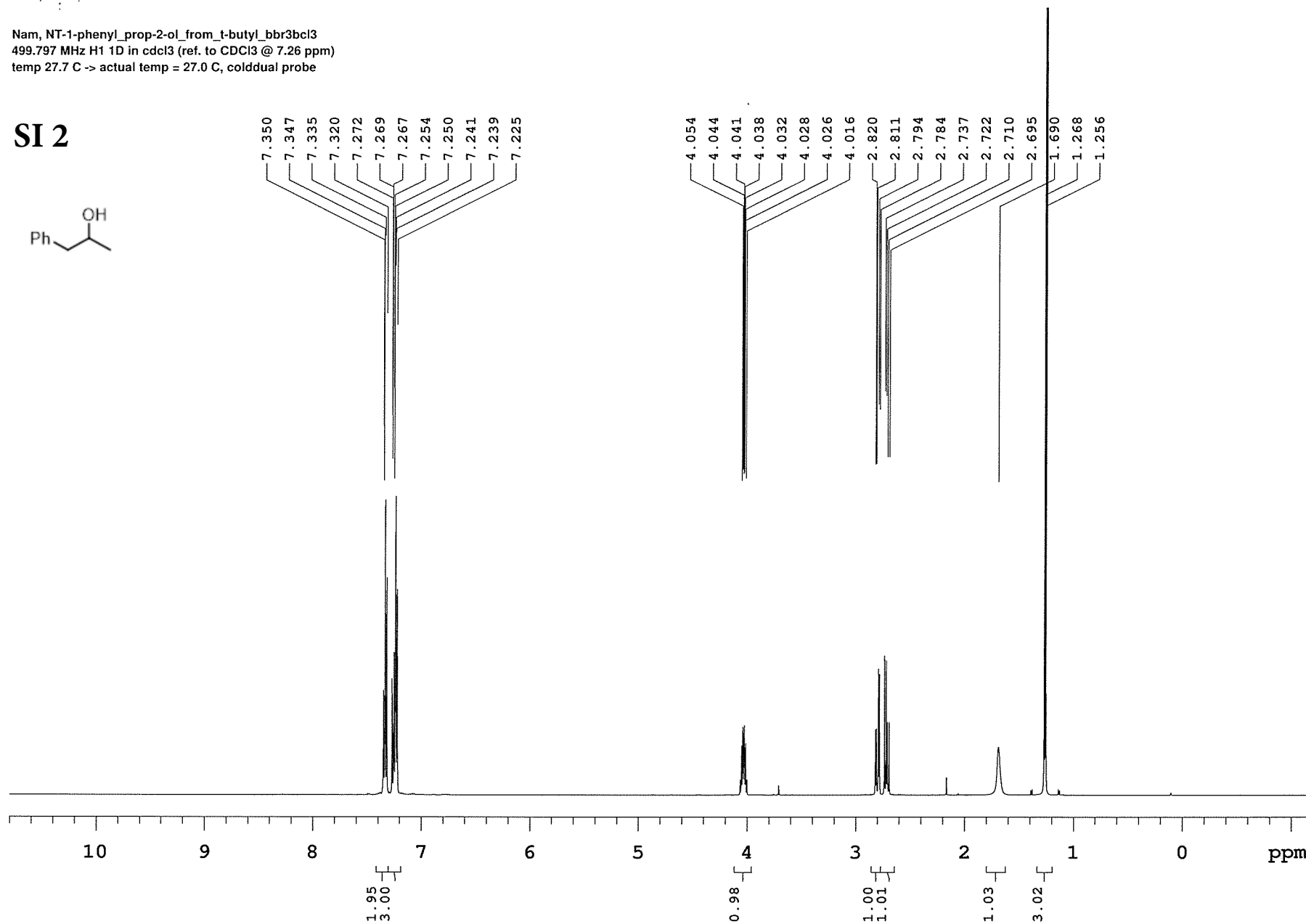
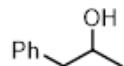
**SI 1**


Nam, NT-naphthalene\_ethanol\_from\_BCl3\_alone  
 125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, cold dual probe

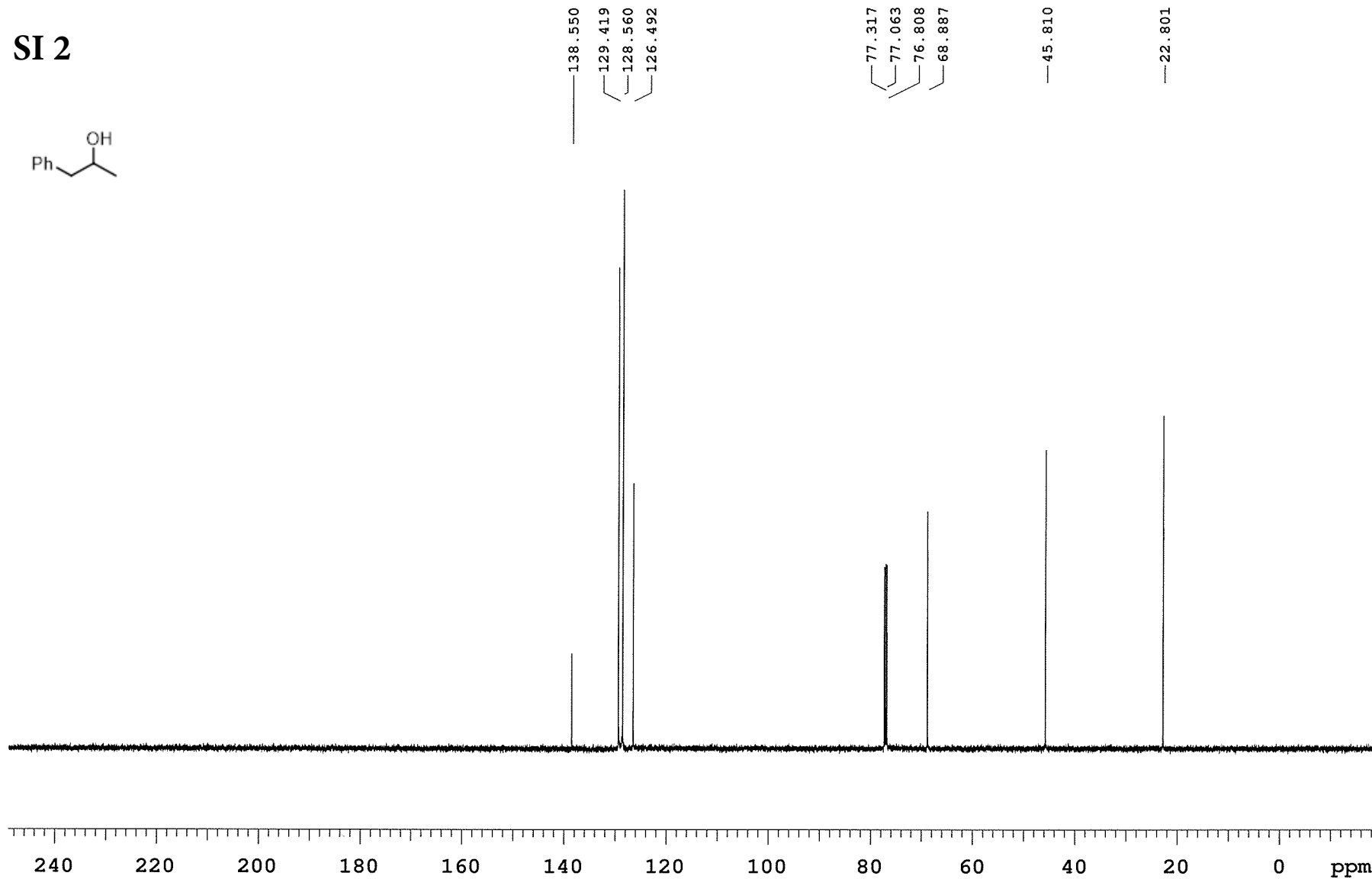
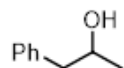
**SI 1**



Nam, NT-1-phenyl\_prop-2-ol\_from\_t-butyl\_bbr3bcl3  
 499.797 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, cold dual probe

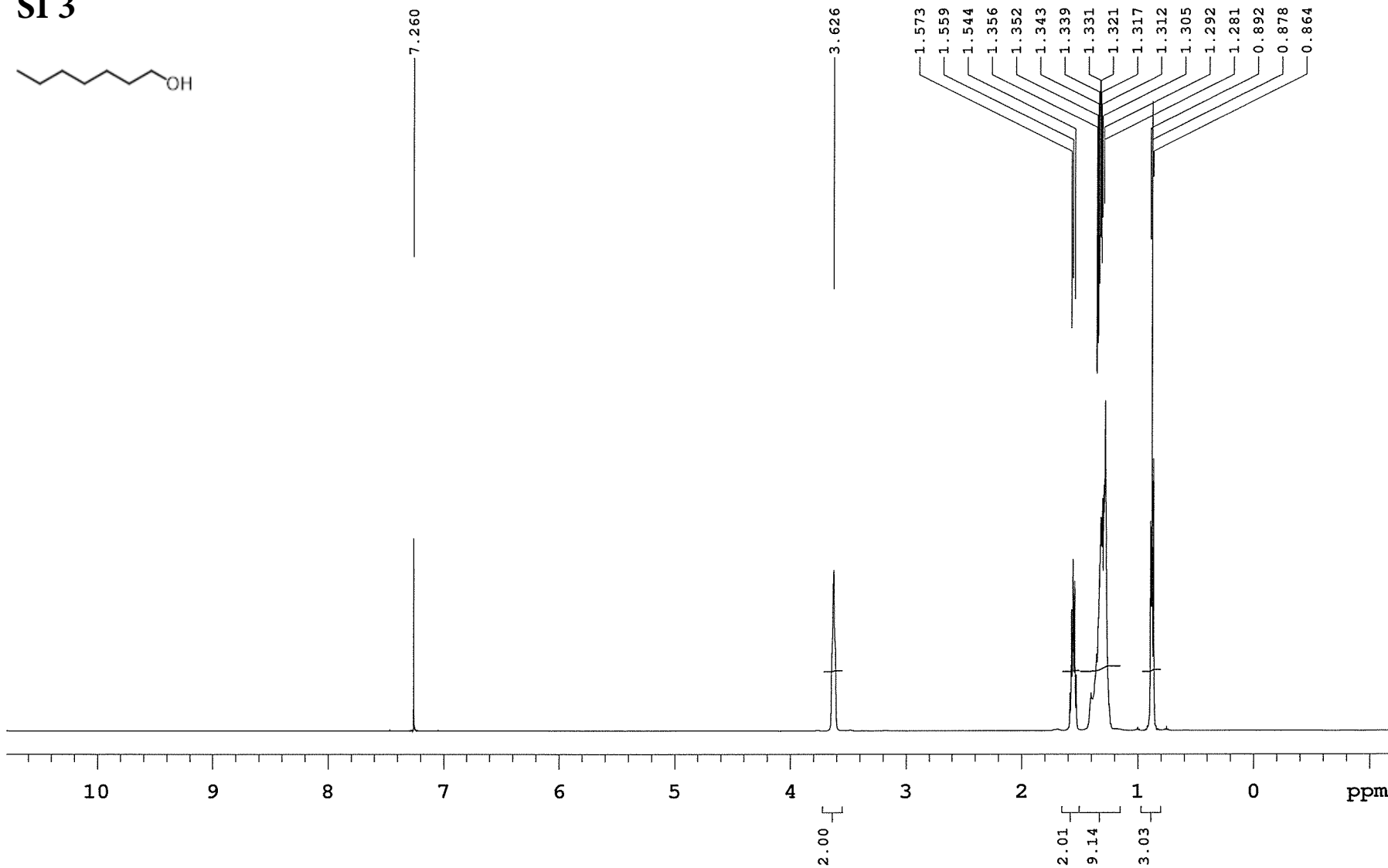
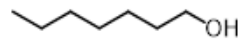
**SI 2**


Nam, NT-1-phenyl\_prop-2-ol\_from\_t-butyl\_bbr3bcl3  
 125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, cold dual probe

**SI 2**


Nam, NT-heptanol\_isolated  
499.797 MHz H1 1D in cdcl3 (ref. to CDCI3 @ 7.26 ppm)  
temp 27.7 C -> actual temp = 27.0 C, colddual probe

**SI 3**





Agilent Technologies

Department of Chemistry, University of Alberta

Recorded on: **u500, Jul 12 2018**  
Pulse Sequence: **s2pul**

Sweep Width(Hz): **33783.8**  
Digital Res.(Hz/pt): **0.26**

Acquisition Time(s): **1**  
Hz per mm(Hz/mm): **140.76**

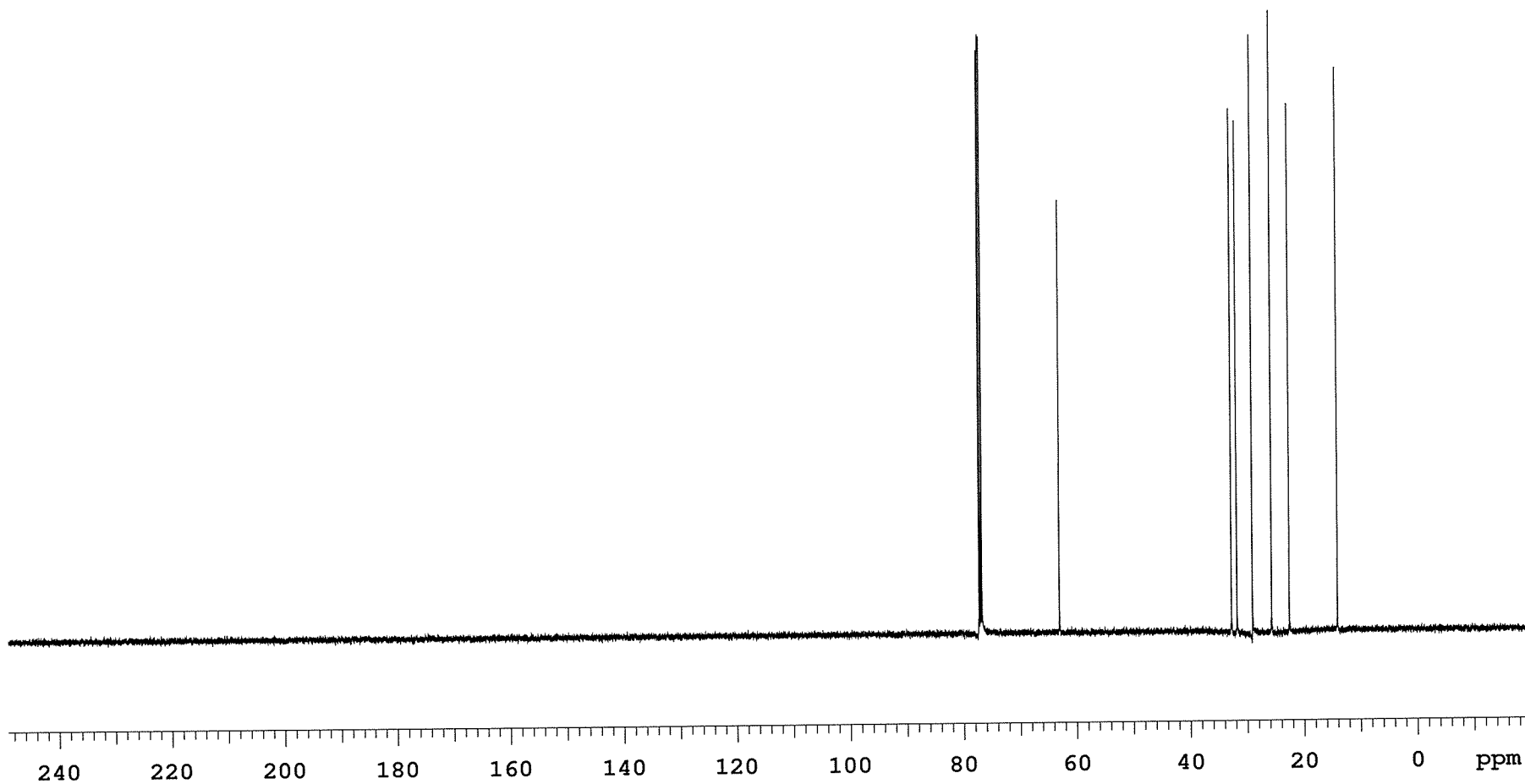
Relaxation Delay(s): **1**  
Completed Scans **68**

Nam, NT-heptanol\_isolated  
125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDC13 @ 77.06 ppm)  
temp 27.7 C -> actual temp = 27.0 C, colddual probe

SI 3

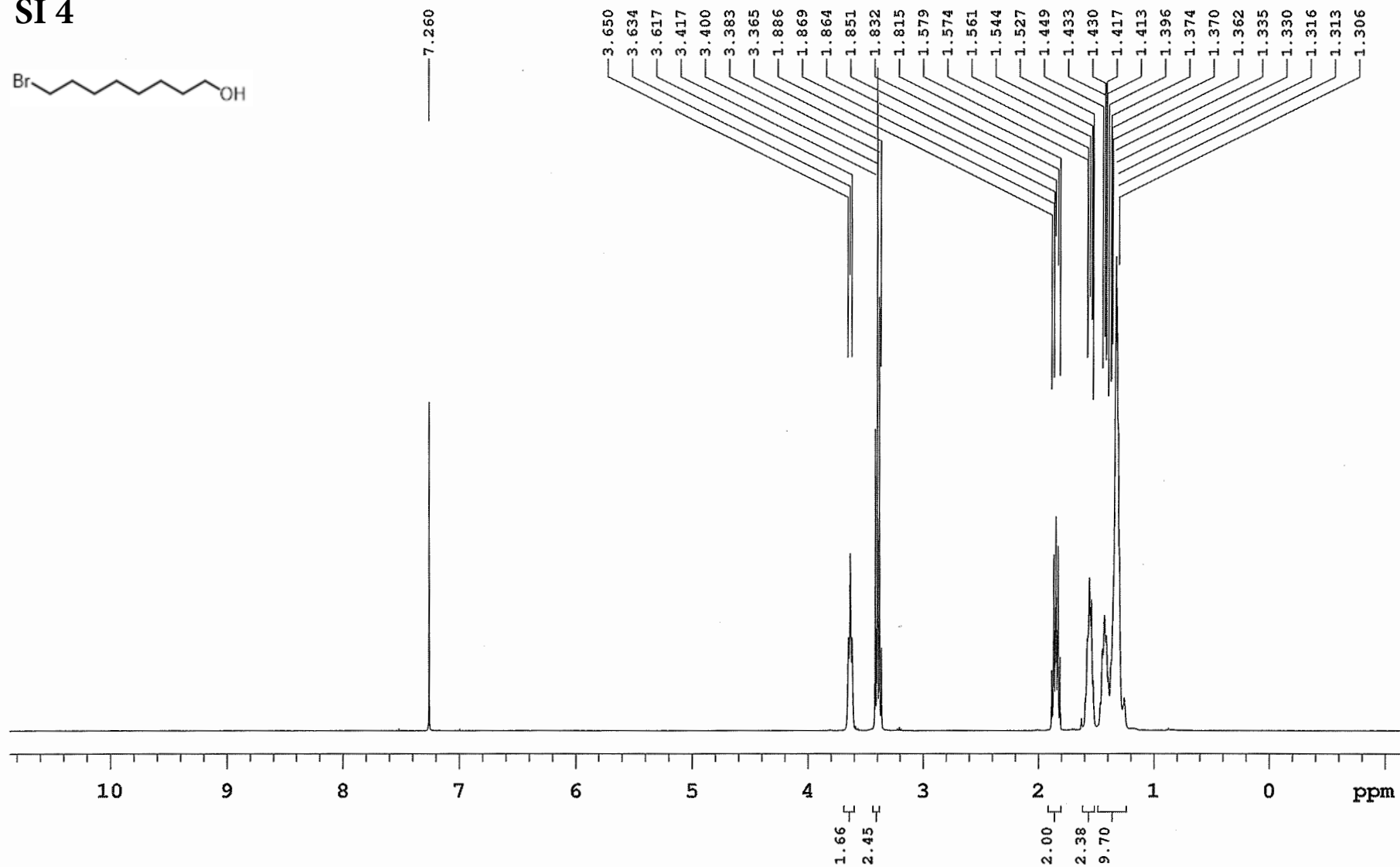
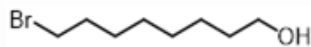


77.270  
77.018  
76.764  
63.065  
32.815  
31.822  
29.099  
25.709  
22.600  
14.063



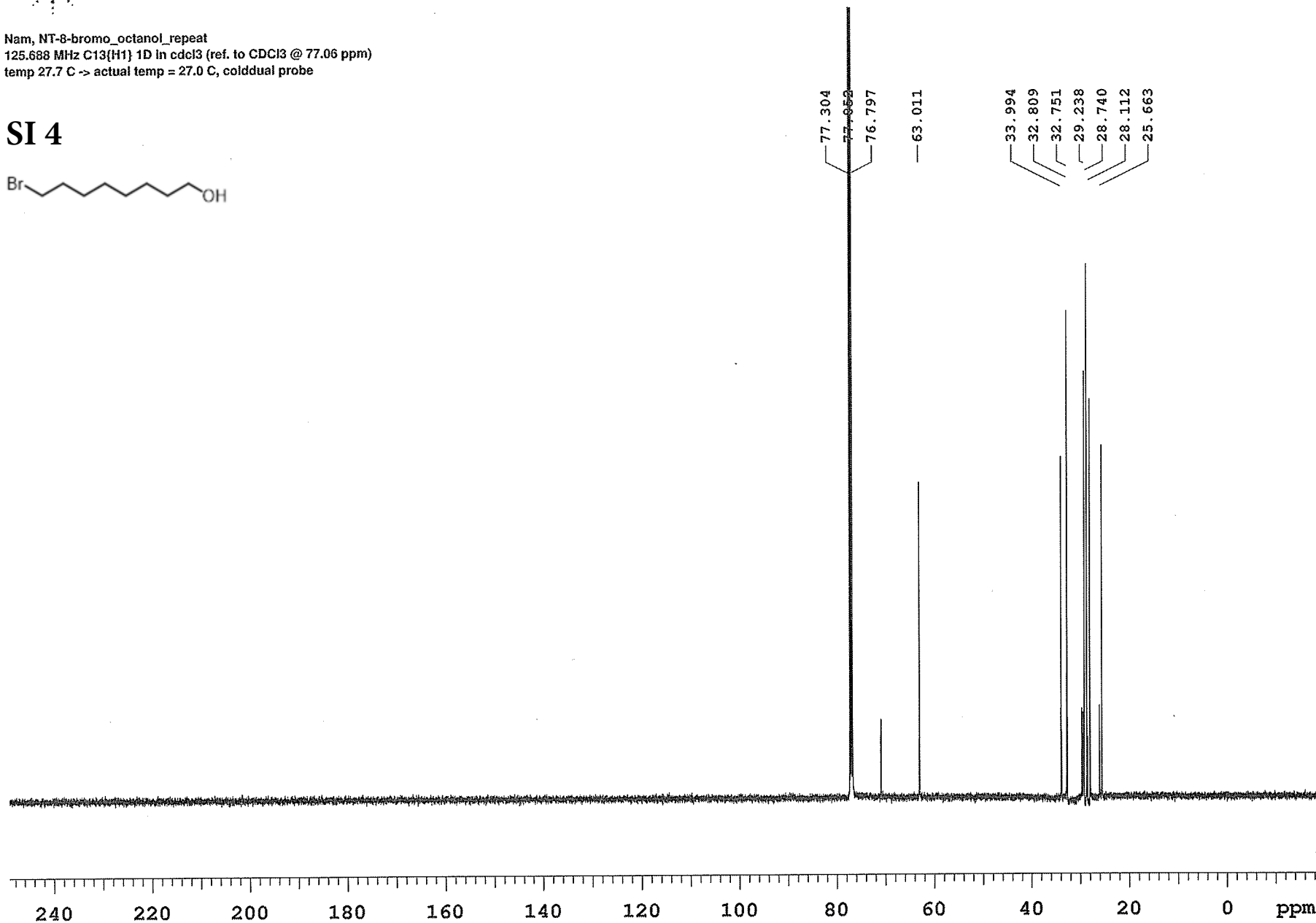
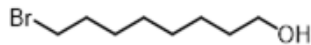
399.978 MHz H1 1D in cdcl3 (ref. to CDC13 @ 7.26 ppm)  
temp 25.9 C -> actual temp = 27.0 C, onenmr probe

SI 4

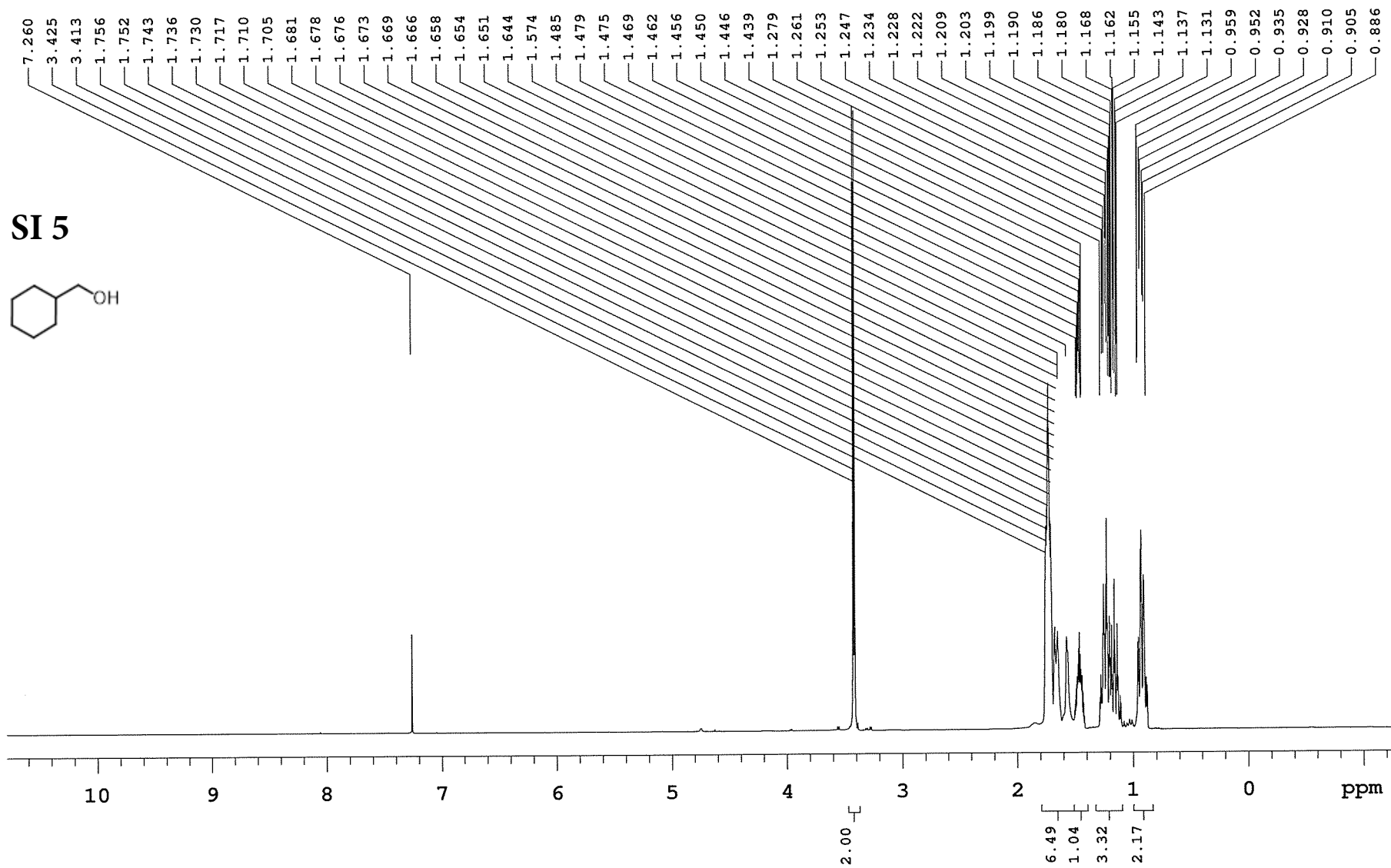


Nam, NT-8-bromo\_octanol\_repeat  
125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDC13 @ 77.06 ppm)  
temp 27.7 C -> actual temp = 27.0 C, cold dual probe

SI 4



Nam, NT-cyclohexanol\_from\_propargyl\_bbr3bcl3  
 499.797 MHz H1 1D in cdcl3 (ref. to CDCI3 @ 7.26 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, colddual probe





Agilent Technologies

Department of Chemistry, University of Alberta

Recorded on: **u500, Jun 17 2018**  
Pulse Sequence: **s2pul**

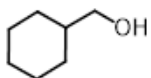
Sweep Width(Hz): **33783.8**  
Digital Res.(Hz/pt): **0.26**

Acquisition Time(s): **1**  
Hz per mm(Hz/mm): **140.76**

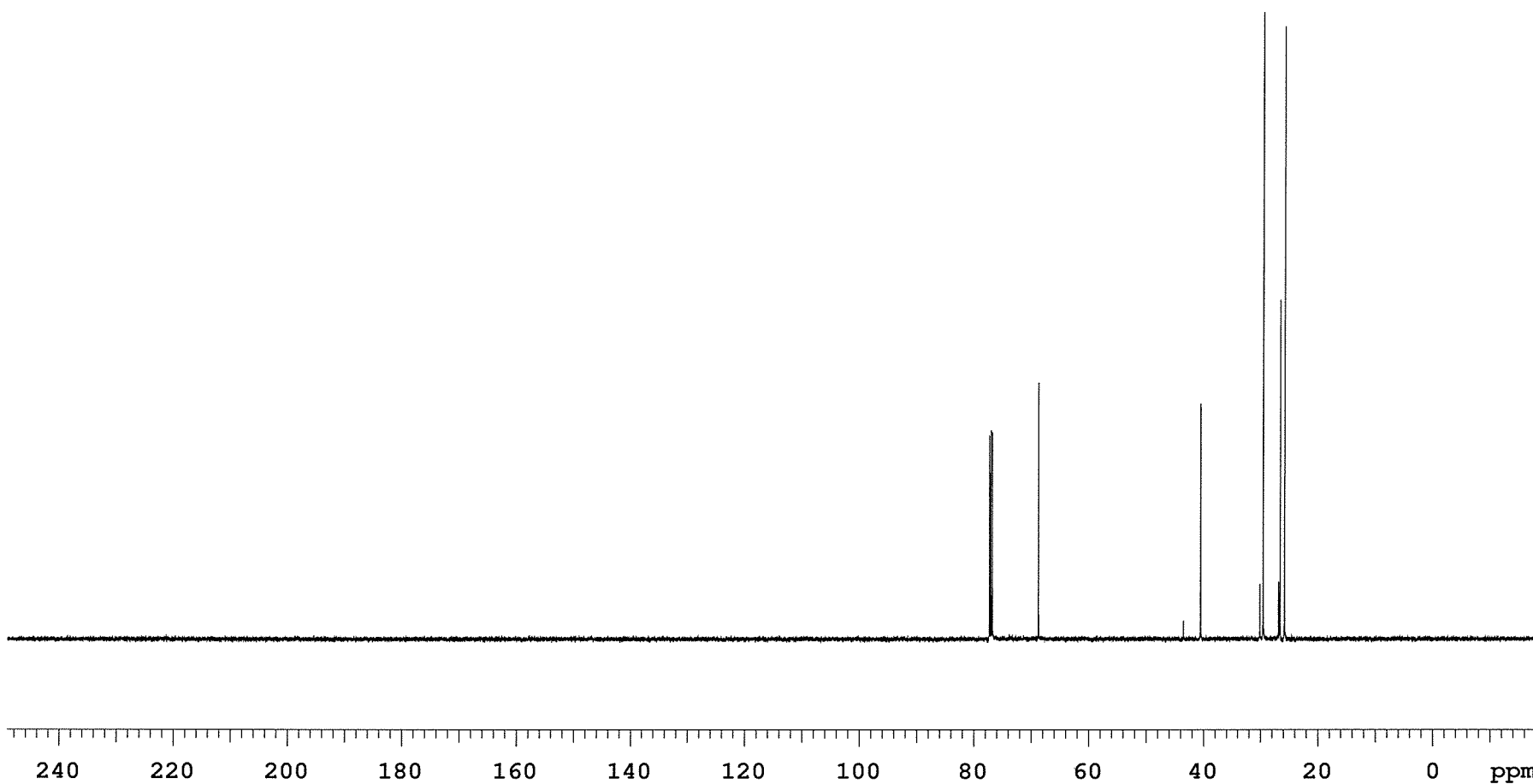
Relaxation Delay(s): **1**  
Completed Scans **28**

Nam, NT-cyclohexanol\_from\_propargyl\_bbr3bcl3  
125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm)  
temp 27.7 C -> actual temp = 27.0 C, colddual probe

SI 5

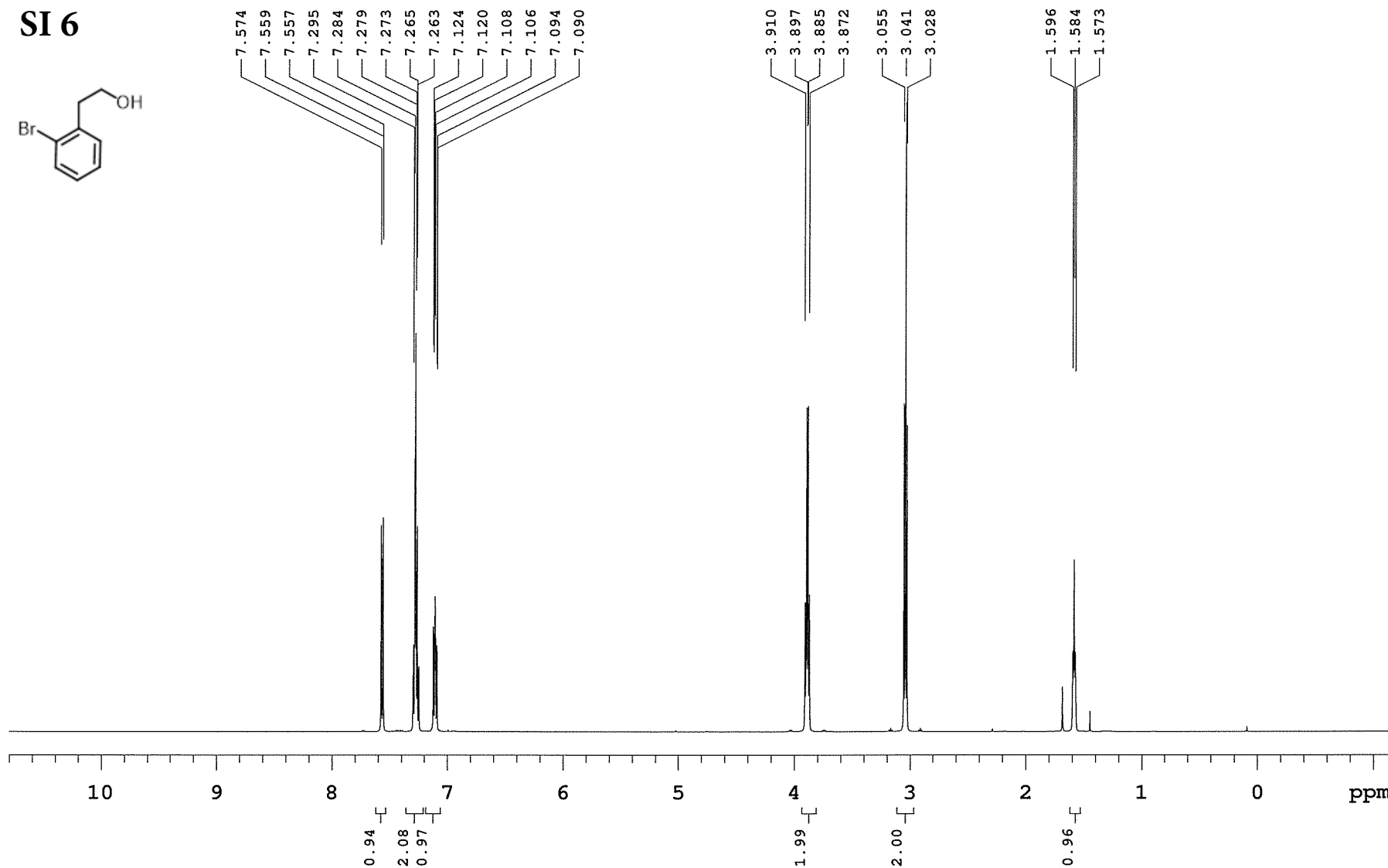
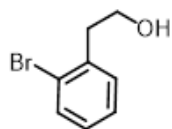


77.317  
77.062  
76.808  
68.754  
40.513  
29.597  
26.621  
25.867



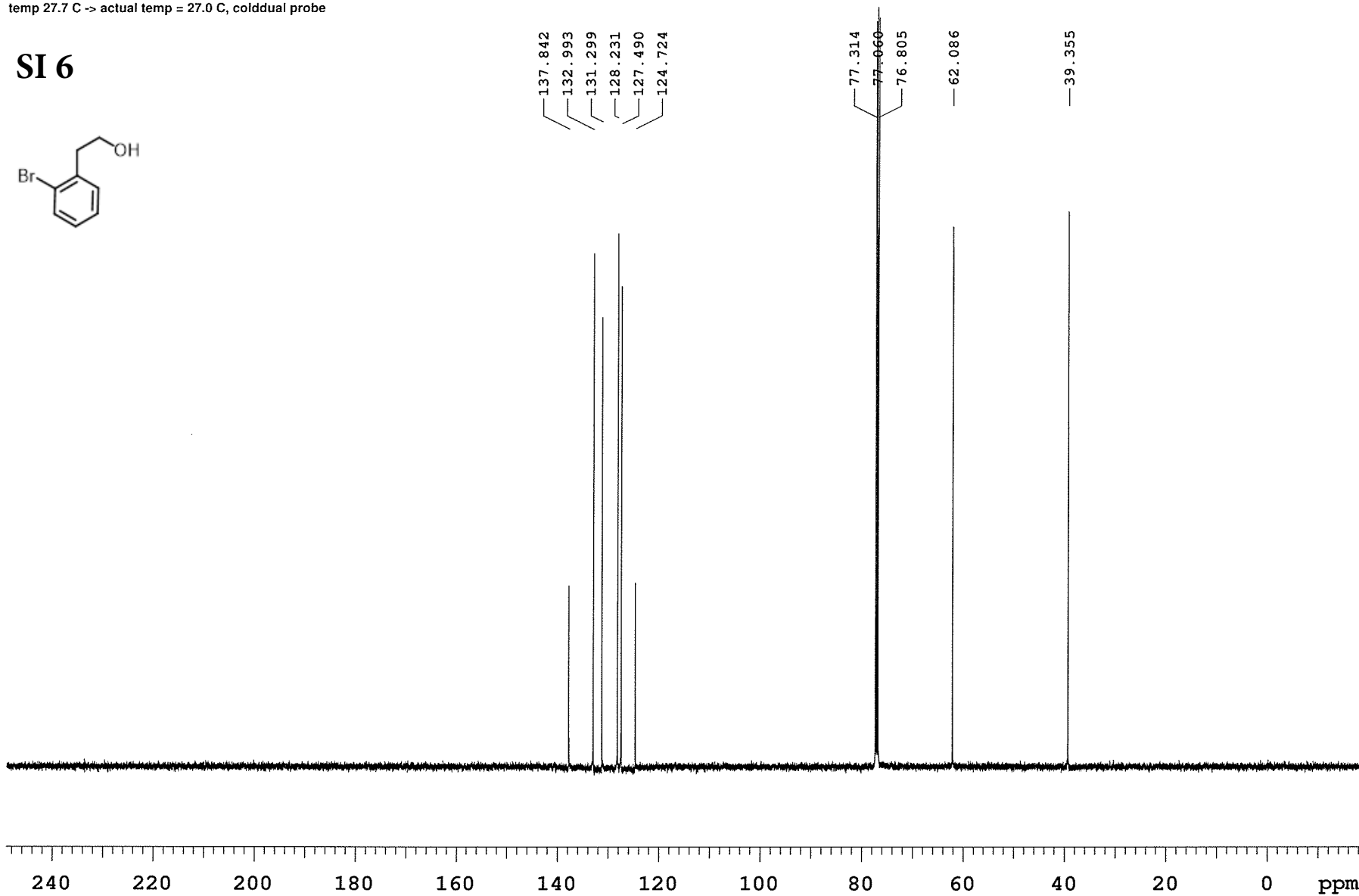
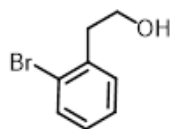
Nam, NT-2-bromobenzeneethanol\_isolated-1  
499.797 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
temp 27.7 C -> actual temp = 27.0 C, cold dual probe

**SI 6**



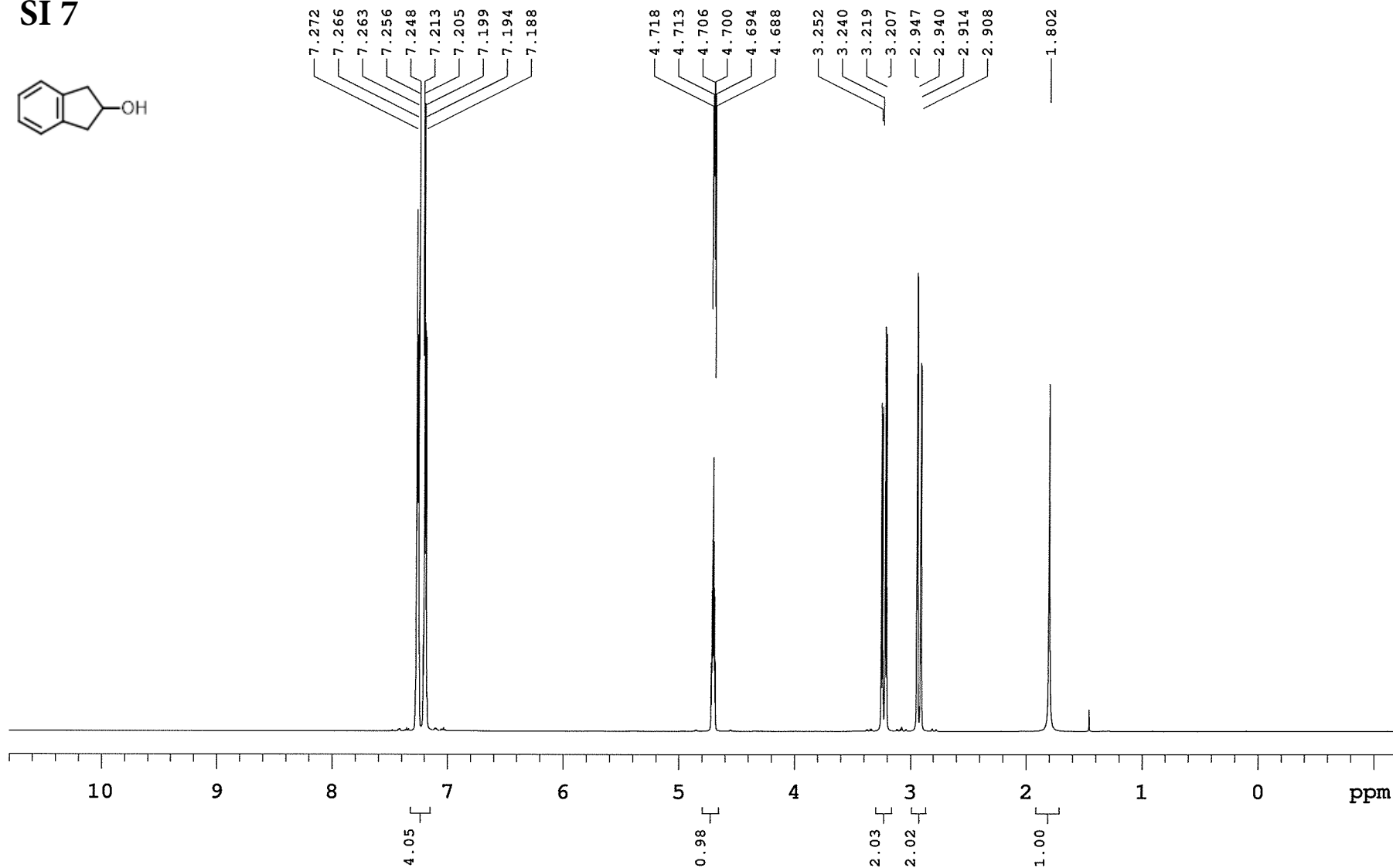
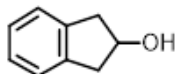
Nam, NT-2-bromobenzeneethanol\_isolated-1  
 125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, cold dual probe

**SI 6**



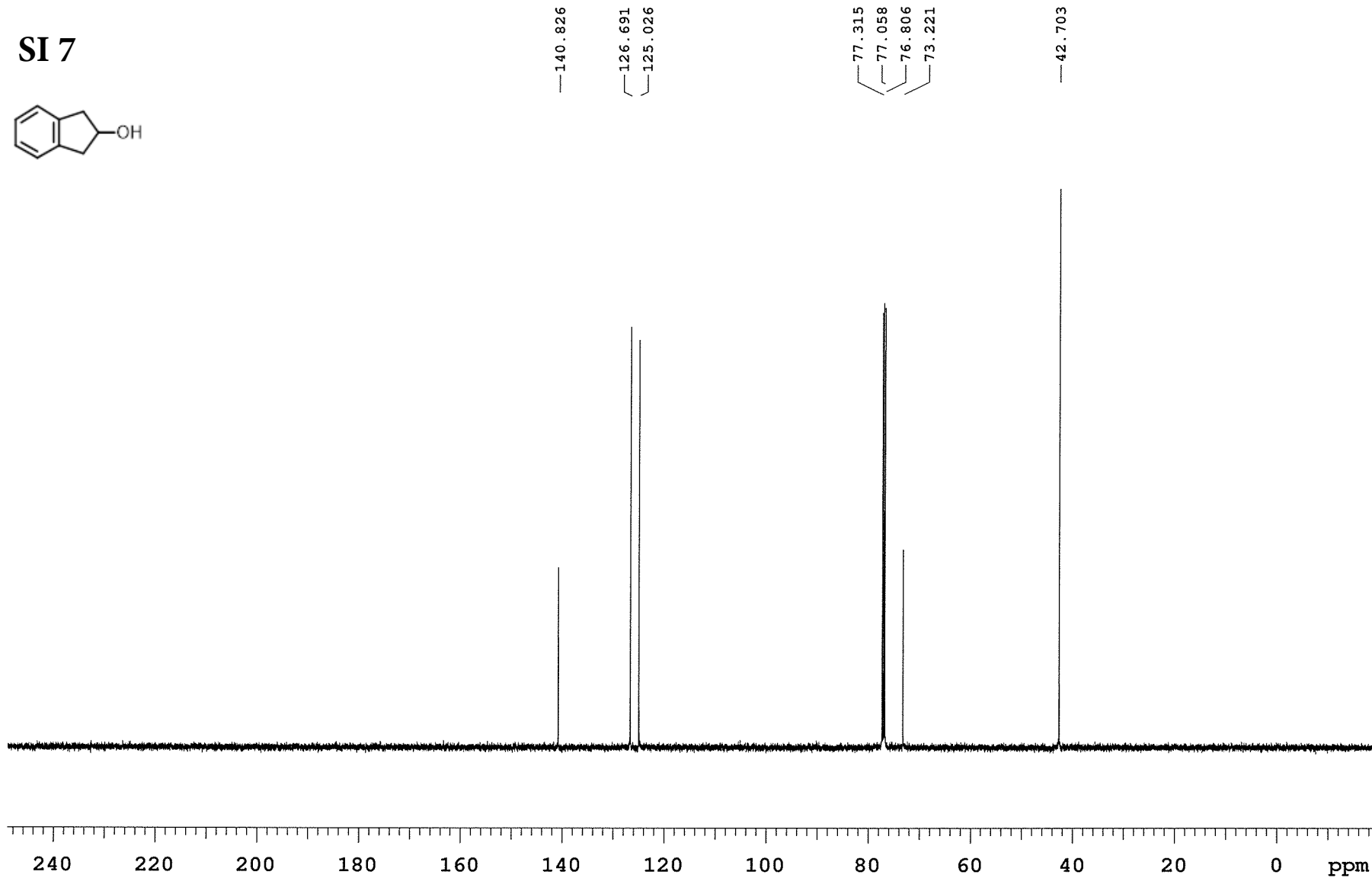
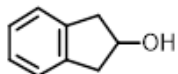
Nam, NT-indanol\_isolated\_from\_propargyl\_bbr3bc13  
499.797 MHz H1 1D in cdcl3 (ref. to CDC13 @ 7.26 ppm)  
temp 27.7 C -> actual temp = 27.0 C, colddual probe

**SI 7**



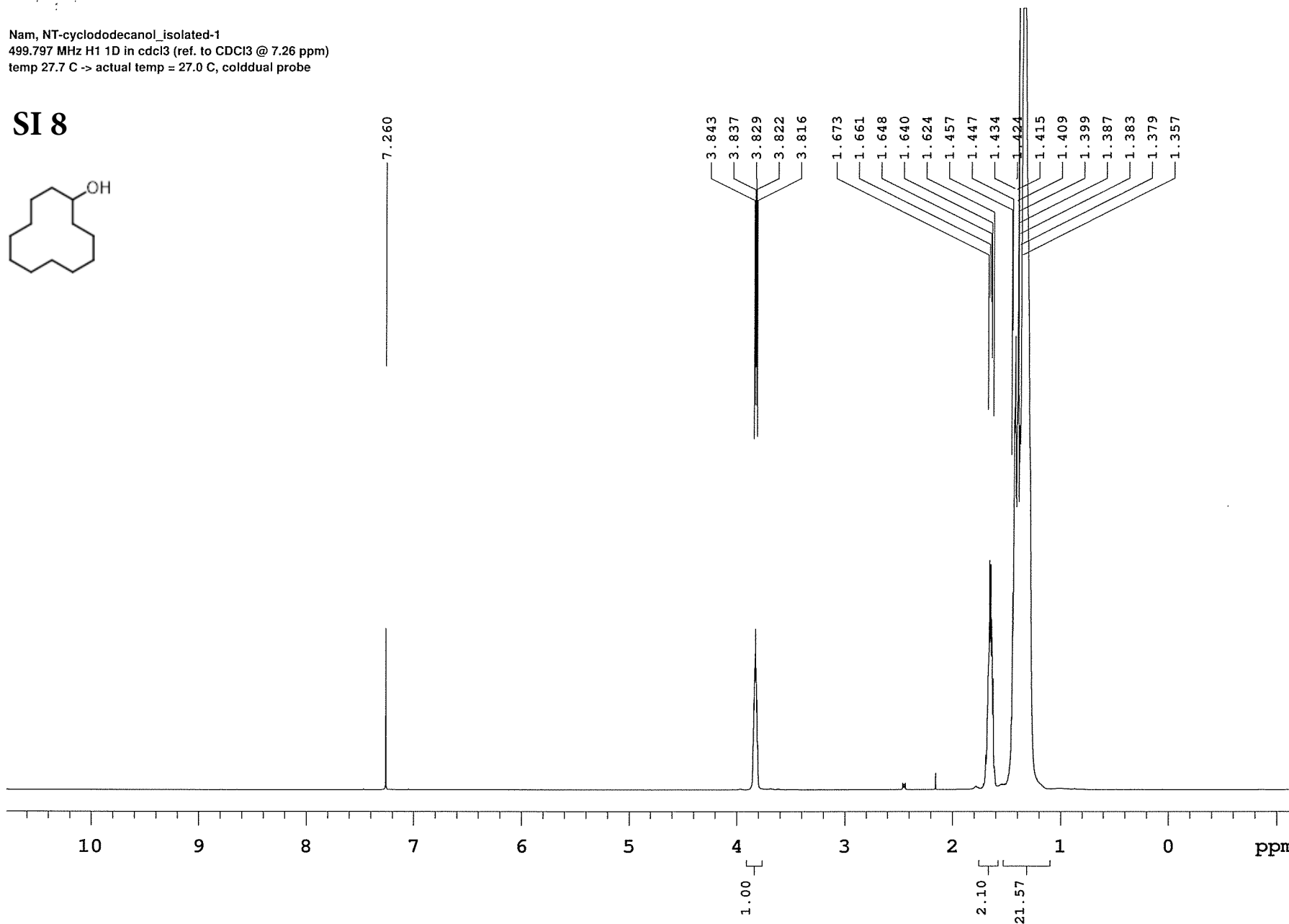
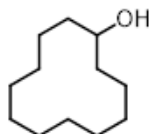
Nam, NT-indanol\_isolated\_from\_propargyl\_bbr3bc13  
 125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, coldddual probe

**SI 7**



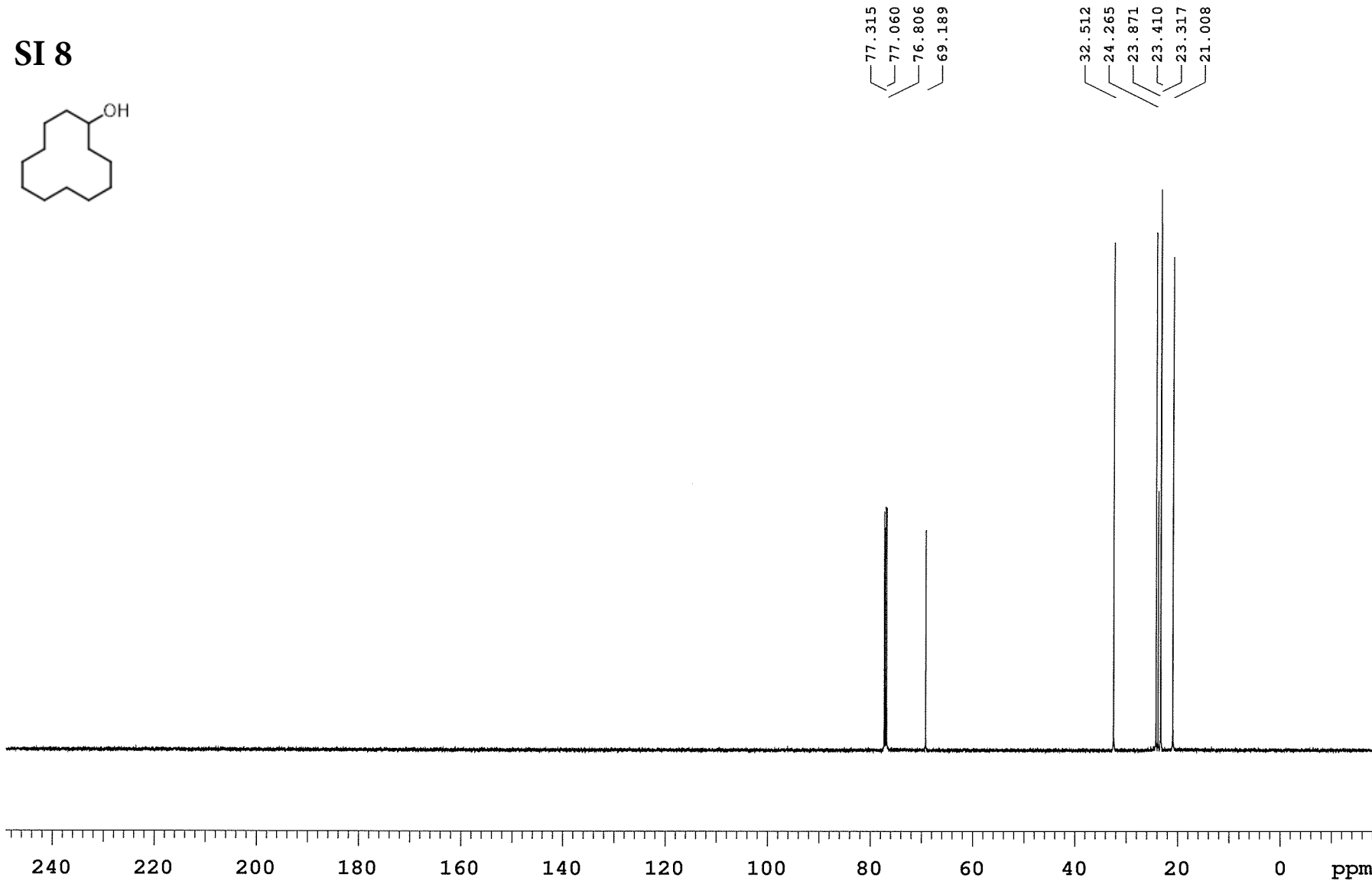
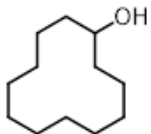
Nam, NT-cyclododecanol\_isolated-1  
499.797 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
temp 27.7 C -> actual temp = 27.0 C, cold dual probe

**SI 8**



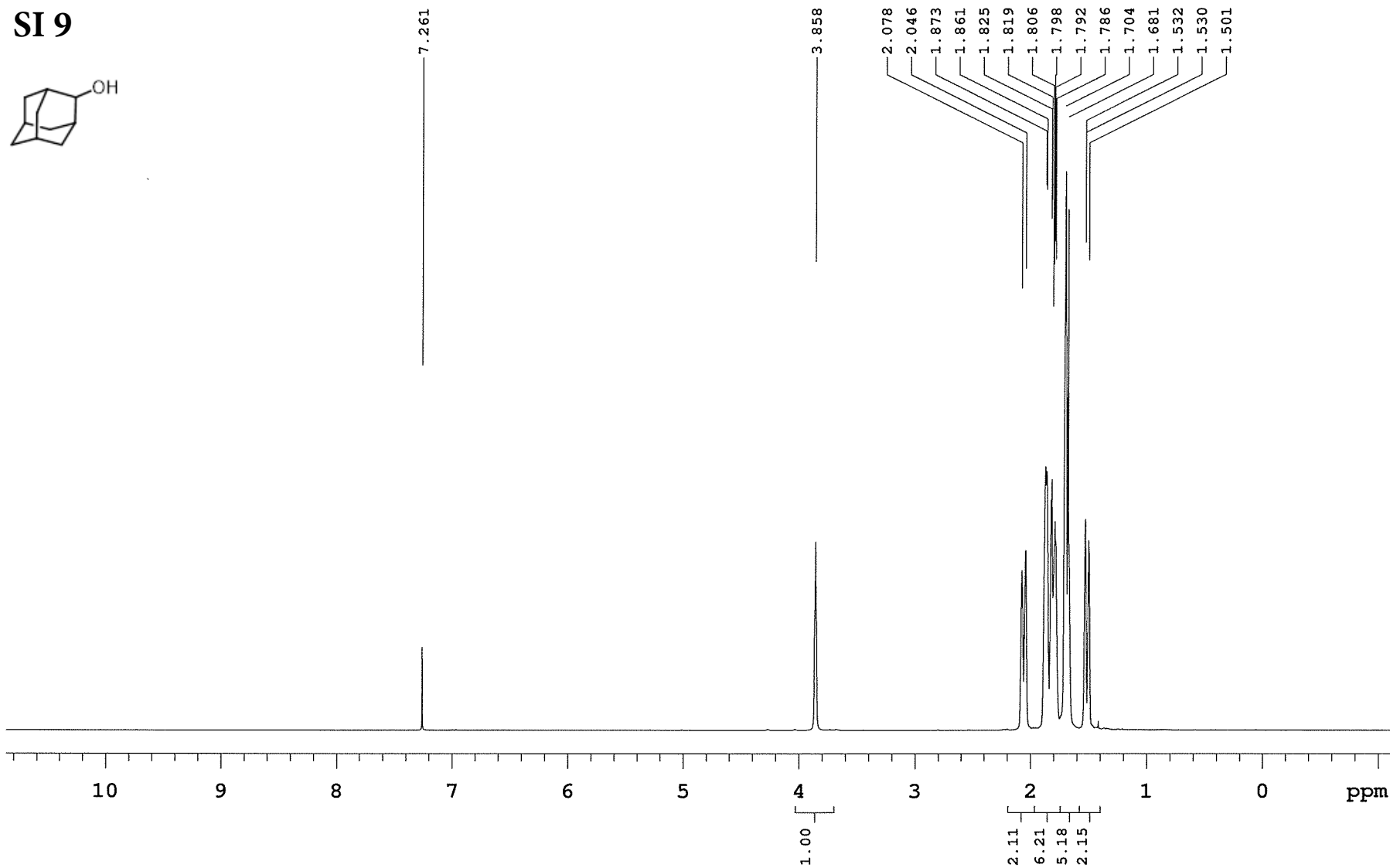
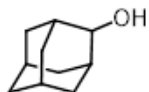
Nam, NT-isolated\_cyclododecanol\_-2  
 125.688 MHz C13{H1} 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm)  
 temp 27.7 C -> actual temp = 27.0 C, cold dual probe

**SI 8**



399.978 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
 temp 25.9 C -> actual temp = 27.0 C, onenmr probe

**SI 9**





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Recorded on: **mr400, Apr 9 2018**  
Pulse Sequence: **s2pul**

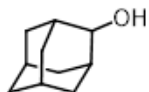
Sweep Width(Hz): **27173.9**  
Digital Res.(Hz/pt): **0.21**

Acquisition Time(s): **1**  
Hz per mm(Hz/mm): **113.22**

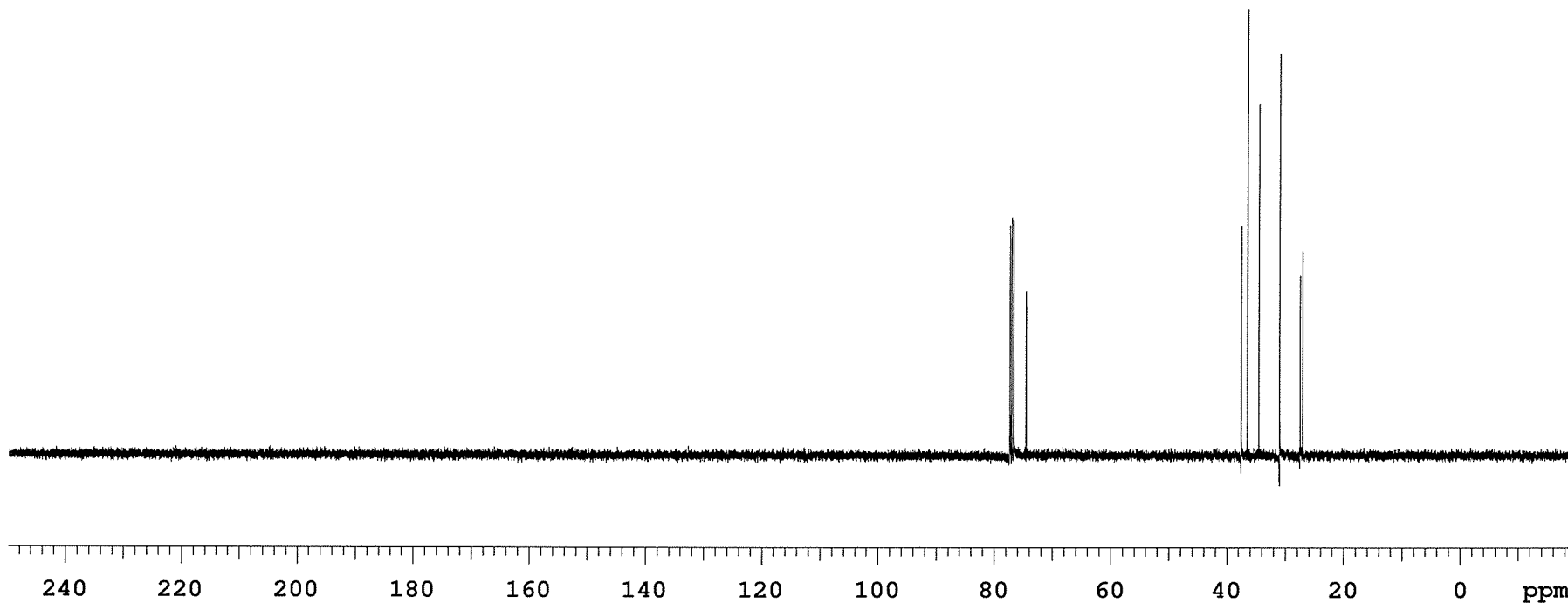
Relaxation Delay(s): **1**  
Completed Scans **60**

100.586 MHz C13{H1} 1D in cdcl3 (ref. to CDC13 @ 77.06 ppm)  
temp 25.9 C -> actual temp = 27.0 C, onenmr probe

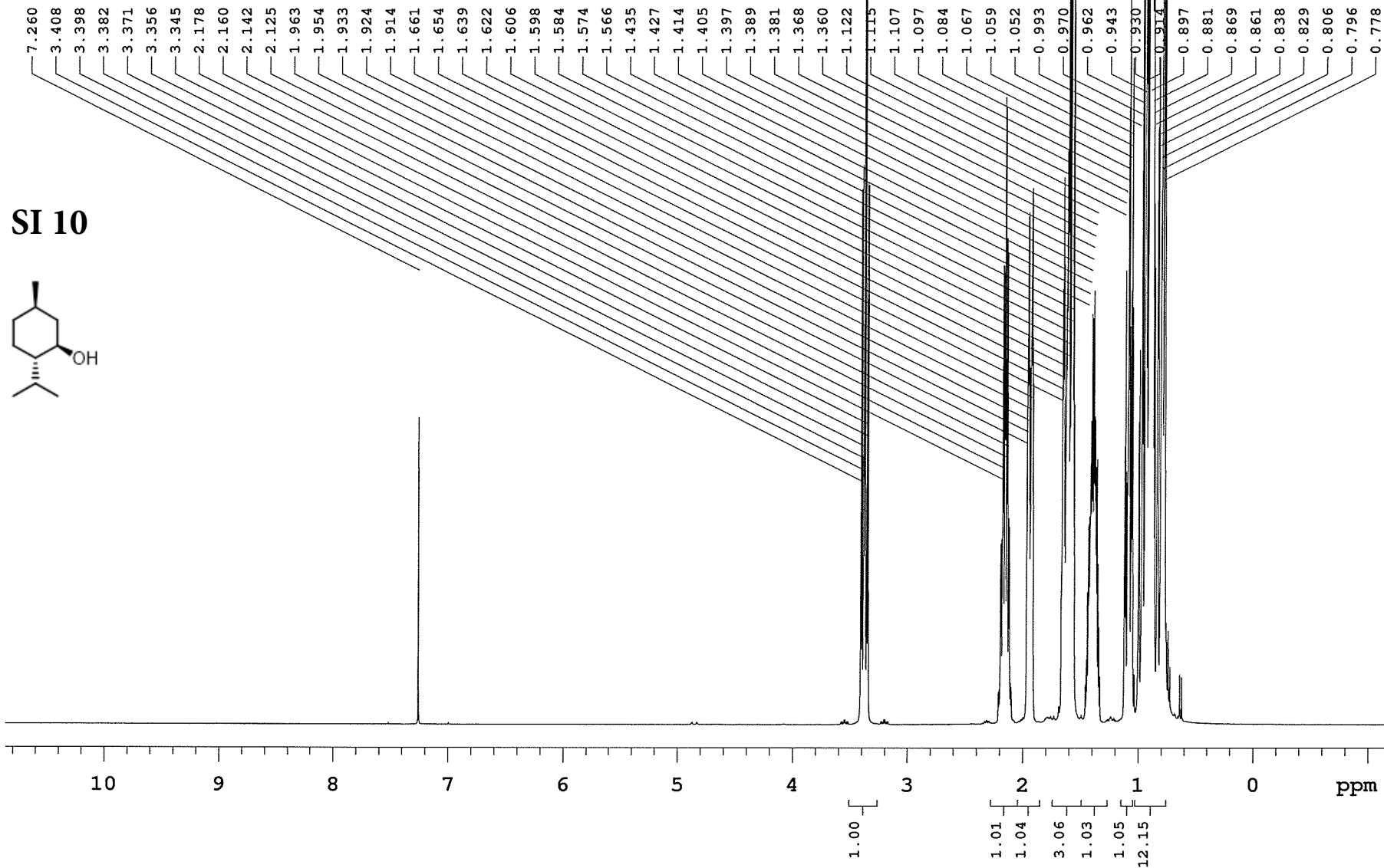
SI 9



77.379  
77.061  
76.744  
74.575  
37.629  
36.560  
34.599  
31.056  
27.568  
27.112

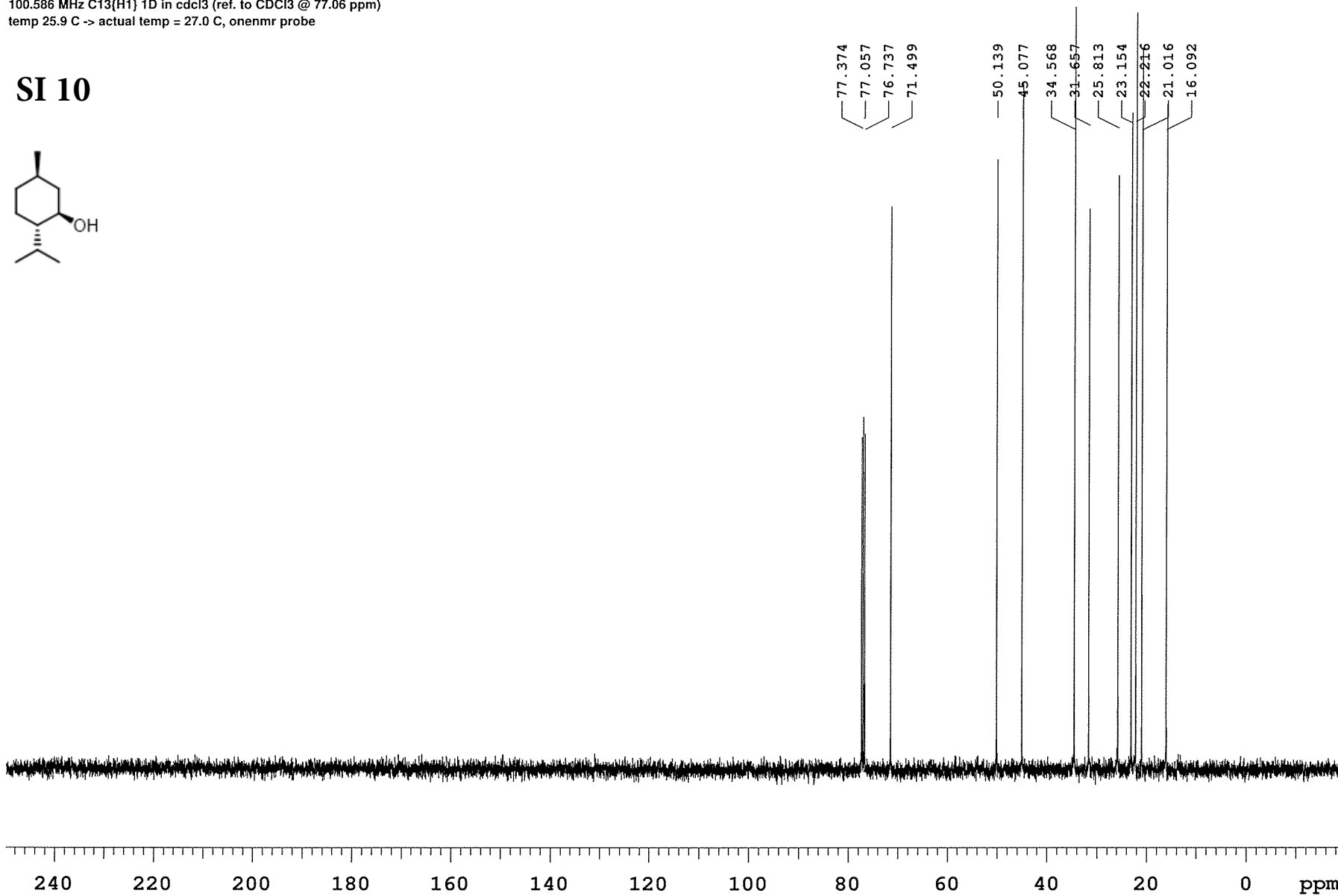
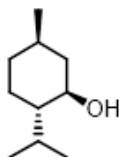


399.978 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
 temp 25.9 C -> actual temp = 27.0 C, onenmr probe



100.586 MHz C13{H1} 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm)  
 temp 25.9 C -> actual temp = 27.0 C, onenmr probe

**SI 10**





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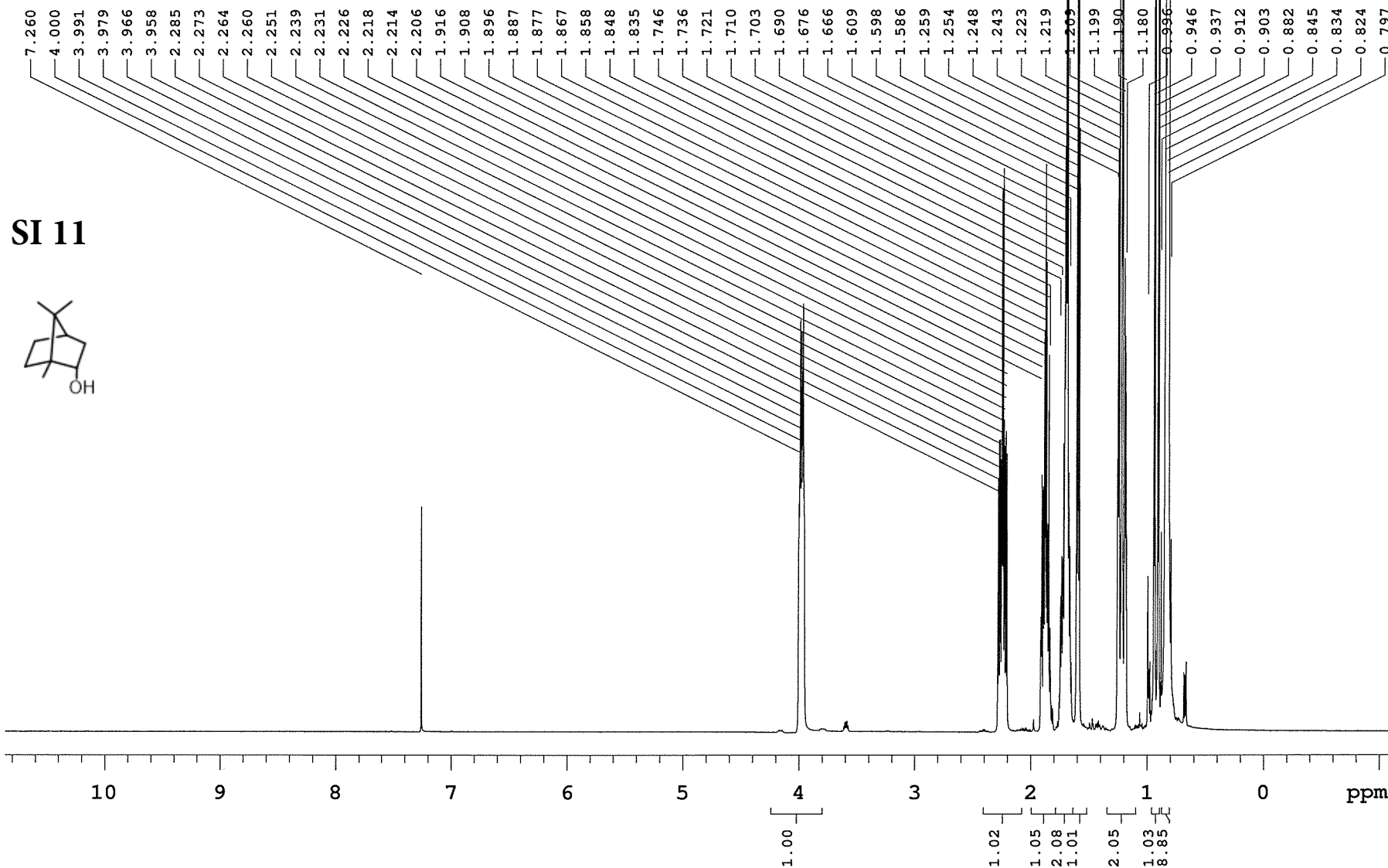
Recorded on: **i400, Apr 9 2018**  
Pulse Sequence: **s2pul**

Sweep Width(Hz): **4801.92**  
Digital Res.(Hz/pt): **0.07**

Acquisition Time(s): **4.998**  
Hz per mm(Hz/mm): **20.01**

Relaxation Delay(s): **0.1**  
Completed Scans **16**

399.794 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)  
temp 26.5 C -> actual temp = 27.0 C, autoxdb probe



100.539 MHz C13{H1} 1D in cdcl3 (ref. to CDCI3 @ 77.06 ppm)  
 temp 26.5 C -> actual temp = 27.0 C, autodb probe

**SI 11**

