

## Electronic Supplementary Information (ESI)

### **Enantioselective Synthesis of $\delta$ -/ $\gamma$ -Alkoxy- $\beta$ -hydroxy- $\alpha$ -alkylsubstituted Weinreb amides via DKR-ATH: Application to the Synthesis of Advanced Intermediate of (-)-Brevisamide**

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Vemulapalli and Jagadeesh Bharatam

**S2**      **General Information**

**S3-S4**    **General procedure for the synthesis of racemic compounds**

**S5– S39**    **$^1\text{H}$  NMR and  $^{13}\text{C}$ NMR Spectra's**

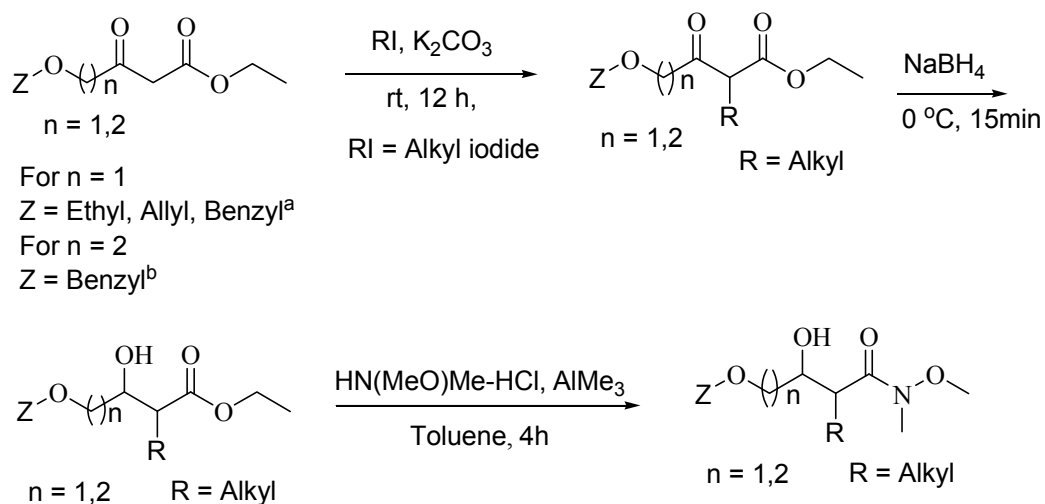
**S40-S65**   **HPLC data**

**S66– S70**   **NMR (NOE) - study**

### General information:

All reactions were conducted under an atmosphere of nitrogen (IOLAR Grade I). Apparatus used for reactions were oven dried. THF was distilled over sodium benzophenone ketyl before use and 2-propanol distilled over calcium hydride. All other chemicals used were commercially available. Progress of the reactions was monitored by TLC on pre-coated silica gel 60 F-254. Evaporation of solvents was performed at reduced pressure on a rotary evaporator. Column chromatography was carried out with silica gel grade 60-120 and 100-200 mesh.  $^1\text{H}$  NMR spectra were recorded at 300 & 500 MHz and  $^{13}\text{C}$  NMR 75 MHz in  $\text{CDCl}_3$ . 1D ( $^1\text{H}$ ,  $^1\text{H}$ - $^1\text{H}$  homo-nuclear decoupling and  $^{13}\text{C}$ ) and 2D (gDQCOSY, NOESY, TOCSY and HSQC) NMR spectra of Compounds **9**, **11**, and **13** were recorded on a Avance 500 MHz ( $^{13}\text{C}$  at 125 MHz) spectrometer in  $\text{CDCl}_3$  at 298 K. Chemical shifts ( $\delta$ ) are reported in ppm. Tetramethylsilane ( $\delta = 0.00$  ppm for  $^1\text{H}$ ) and  $\text{CDCl}_3$  ( $\delta = 77.00$  ppm for  $^{13}\text{C}$ ) were used as the internal standard. Scalar coupling constants ( $J$ ) are reported in hertz (Hz). The following abbreviations are used to designate the multiplicities: s = singlet, d = doublet, t = triplet, dd = doublet of doublet, ddd = doublet of doublet of doublet, td = triplet of doublet, m = multiplet, br.s = broad singlet. Mass spectral data were compiled using MS (ESI), and High resolution mass spectra (HRMS) were recorded by ESI probe in positive mode using ORBITRAP analyser. Optical rotations were recorded on high sensitive polarimeter with 1mL cell. The enantiomeric purity was determined by chiral HPLC using Chiral OD-H, AS-H and IA columns.

### General procedure for the synthesis of racemic Weinreb amides 3a-m:



#### Ethyl 4-(aloxo)-2-alkyl-3-oxobutanoate:

To a stirred solution of aloxy keto ester (1 mmol) and K<sub>2</sub>CO<sub>3</sub> (2.5 mmol) in acetone, Alkyl iodide (2 mmol) was added allowed to stir for 12 h at room temperature. The reaction mixture was quenched and filtered through cellite pad and concentrated to give crude residue. The crude residue was purified by column chromatography using hexane / ethyl acetate (95/5) as an eluent, Yield: 60 - 88%.

#### Ethyl 4-(aloxo)-3-hydroxy-2-alkylbutanoate:

To a stirred solution of Ethyl 4-(aloxo)-2-alkyl-3-oxobutanoate (1 mmol) in methanol, NaBH<sub>4</sub> (0.3 mmol) was added allowed to stir for 15min at 0 °C. The reaction mixture was quenched with aq.NH<sub>4</sub>Cl, extracted with EtOAc, dried, and concentrated to give crude residue. The crude residue was purified by column chromatography using hexane / ethyl acetate (90/10) as an eluent, Yield: 80- 95%.

#### 4-(aloxo)-N-methoxy-N-methyl 2-alkyl -3-oxobutanamide :

To a suspension of *N,O*-dimethylhydroxylamine hydrochloride (2.50 mmol) in benzene, was added trimethyl aluminium (2.50 mmol, 2M in toluene) was added dropwise at 0 °C and the resulting solution was stirred at rt for 1 h. To this Ethyl 4-(aloxo)-3-hydroxy-2-alkylbutanoate

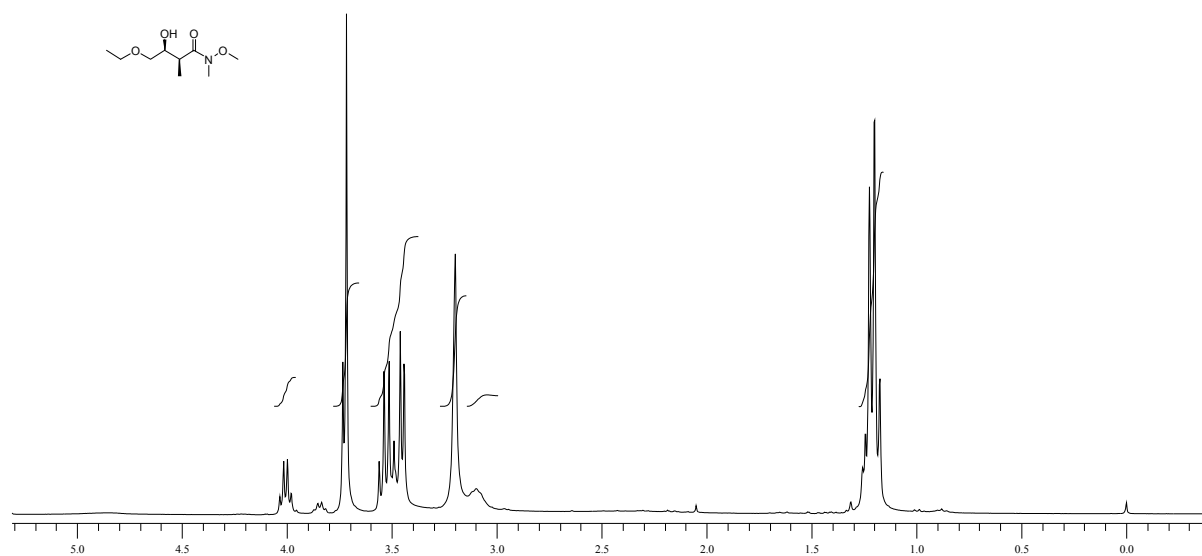
(1 mmol) was added, and the resulting reaction mixture was heated to reflux for 3 h. The reaction mixture was cooled to 0 °C, and was quenched with 1N HCl, extracted with DCM, dried over NaSO<sub>4</sub>, and concentrated to give crude residue. The crude residue was purified by column chromatography using hexane / ethyl acetate (70/30) as an eluent, Yield: 60 - 80%.

**References:**

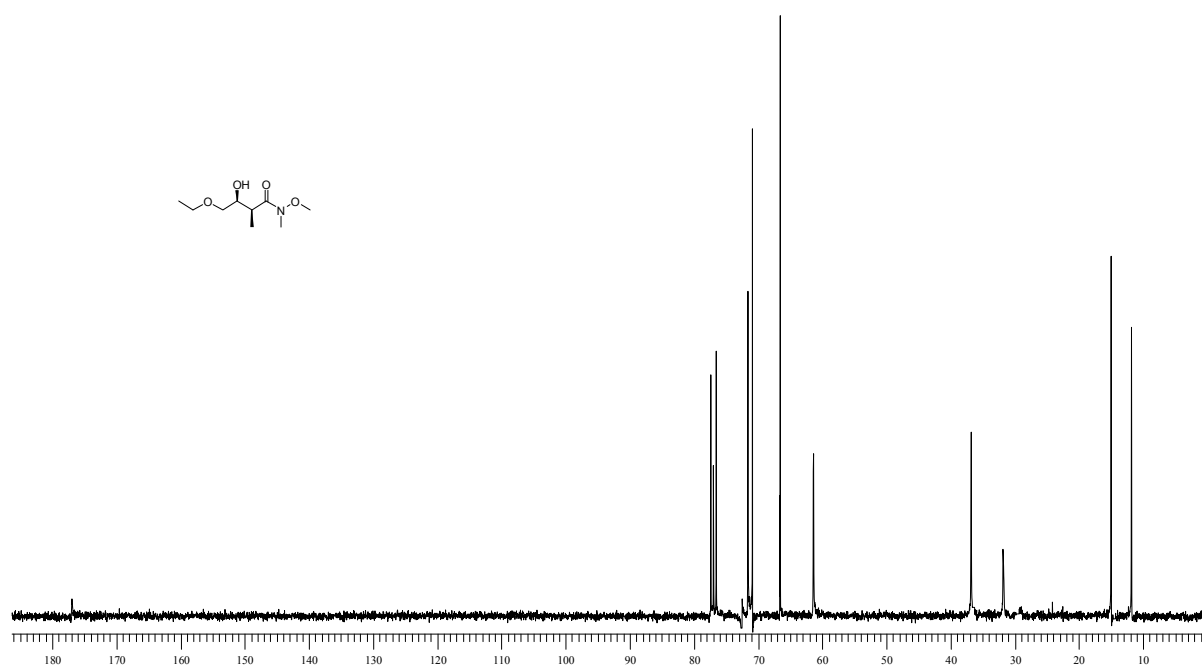
- a) W. Fan, W. Li, X. Ma, X. Tao, X. Li, Y. Yao, X. Xie, Z. Zhang, *J. Org. Chem.* 2011, **76**, 9444-9451;
- b) T. Allen A, J.D. Meese, Y.L. Huerou, B. Steven A, R. Todd T, G. Steven S, G. Indrani, K. Tomas, S. Francis, C. Kevin, L. Joseph P, *Bioorg. Med. Chem. Lett.* 2008, **18**, 509-512.

## $^1\text{H}$ NMR and $^{13}\text{C}$ NMR Spectr's:

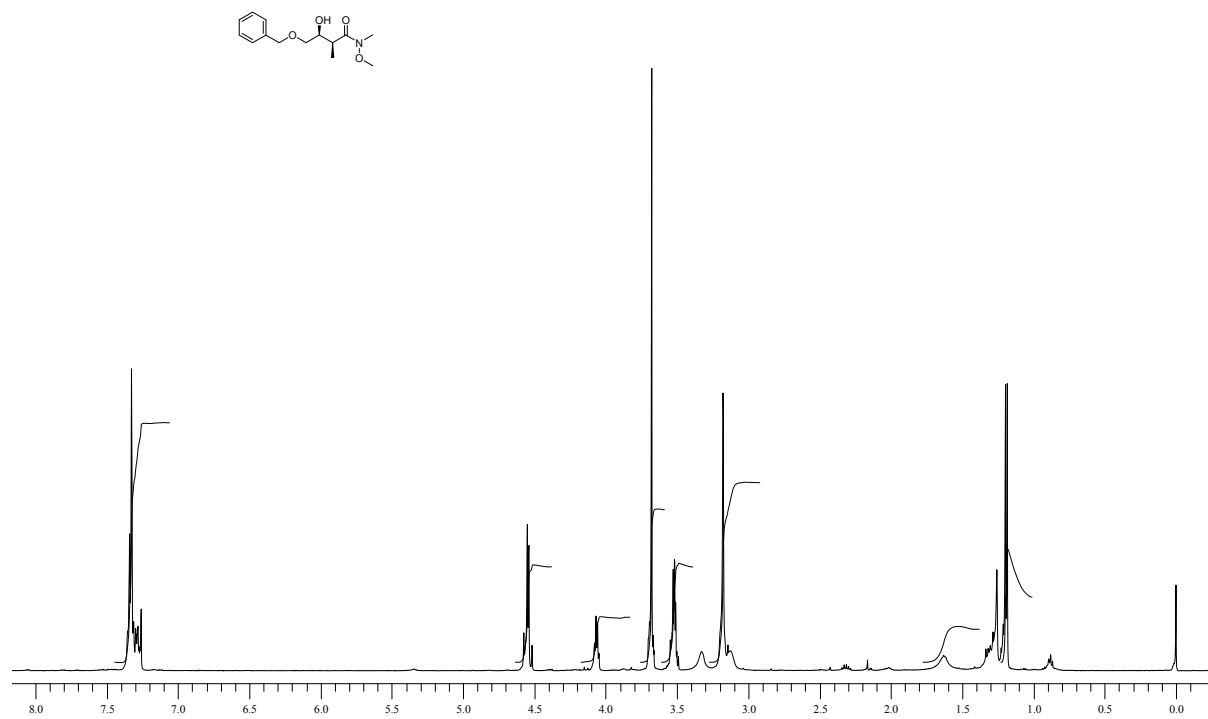
### $^1\text{H}$ NMR spectra of, **3b** (300 MHz):



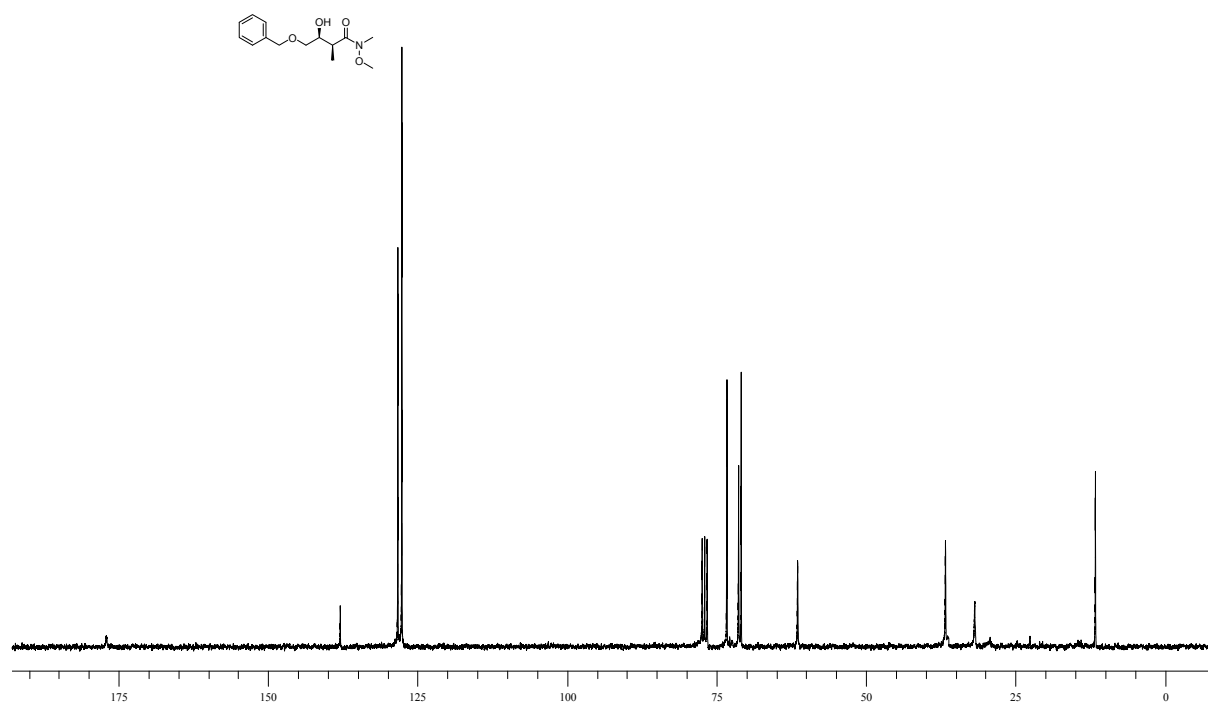
### $^{13}\text{C}$ NMR of compound **3b** (75 MHz):



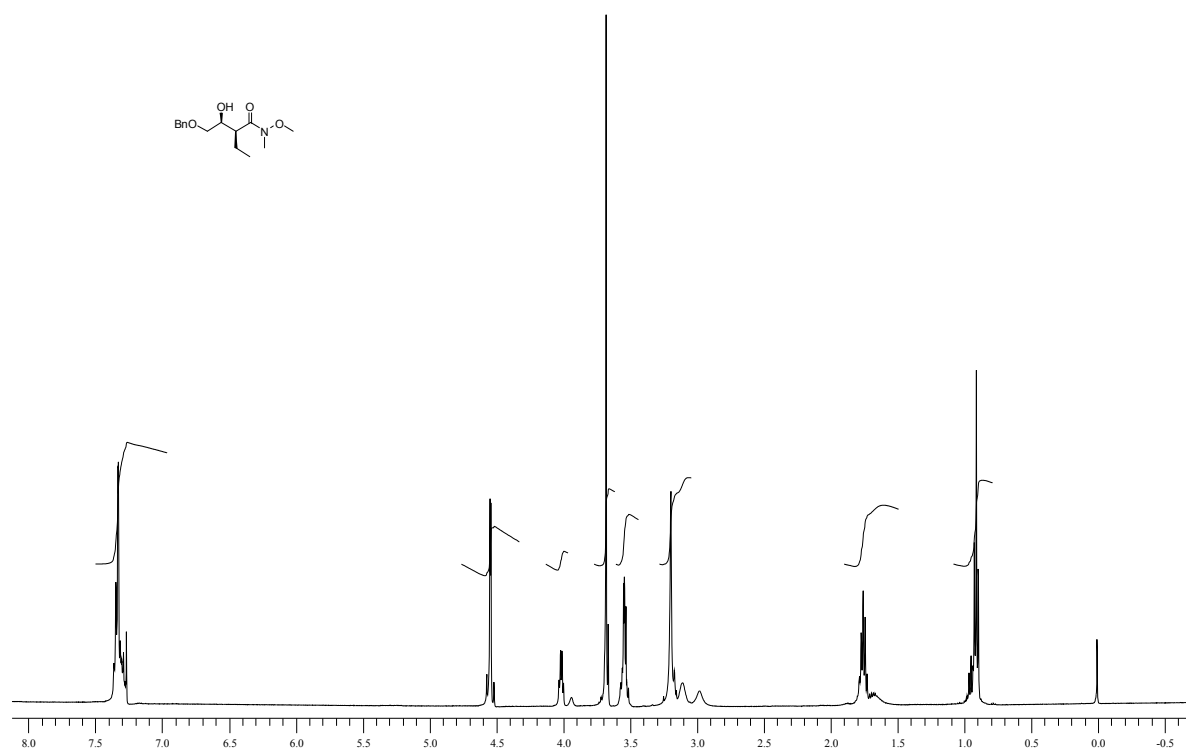
### $^1\text{H}$ NMR spectra of, 3c (300 MHz)



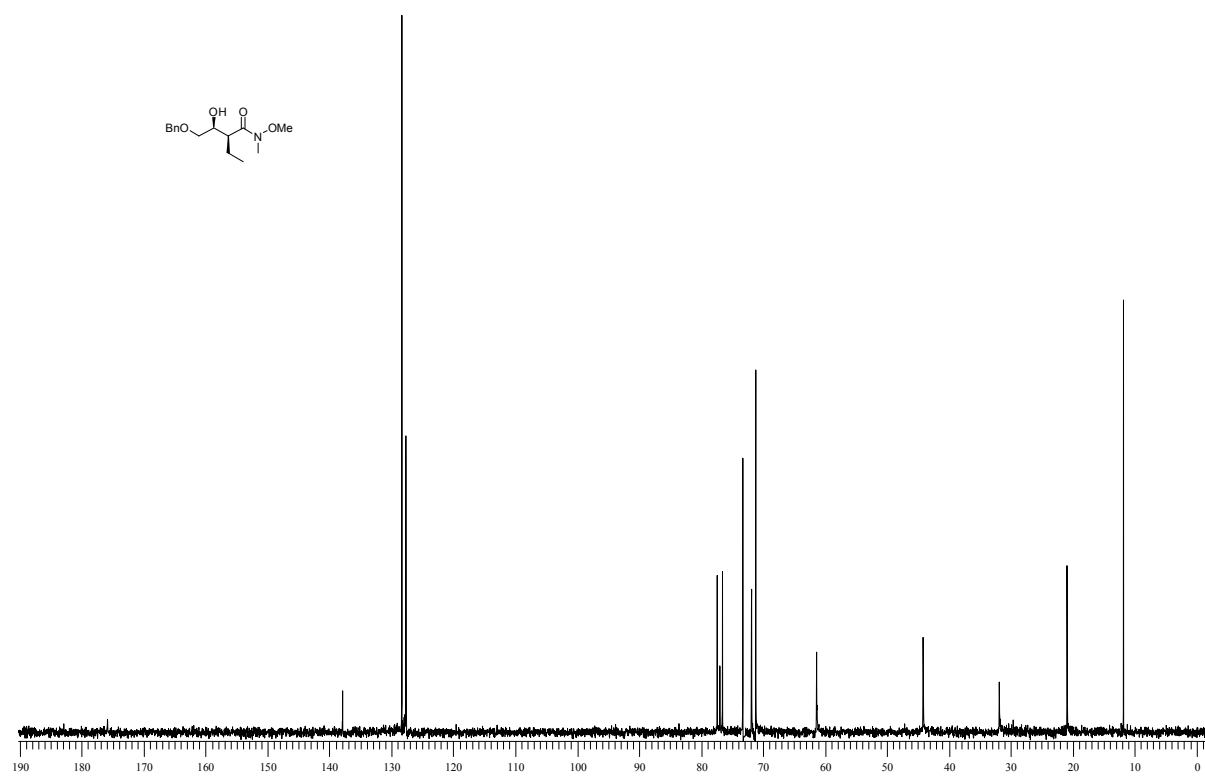
### $^{13}\text{C}$ NMR of compound, 3c (75 MHz)



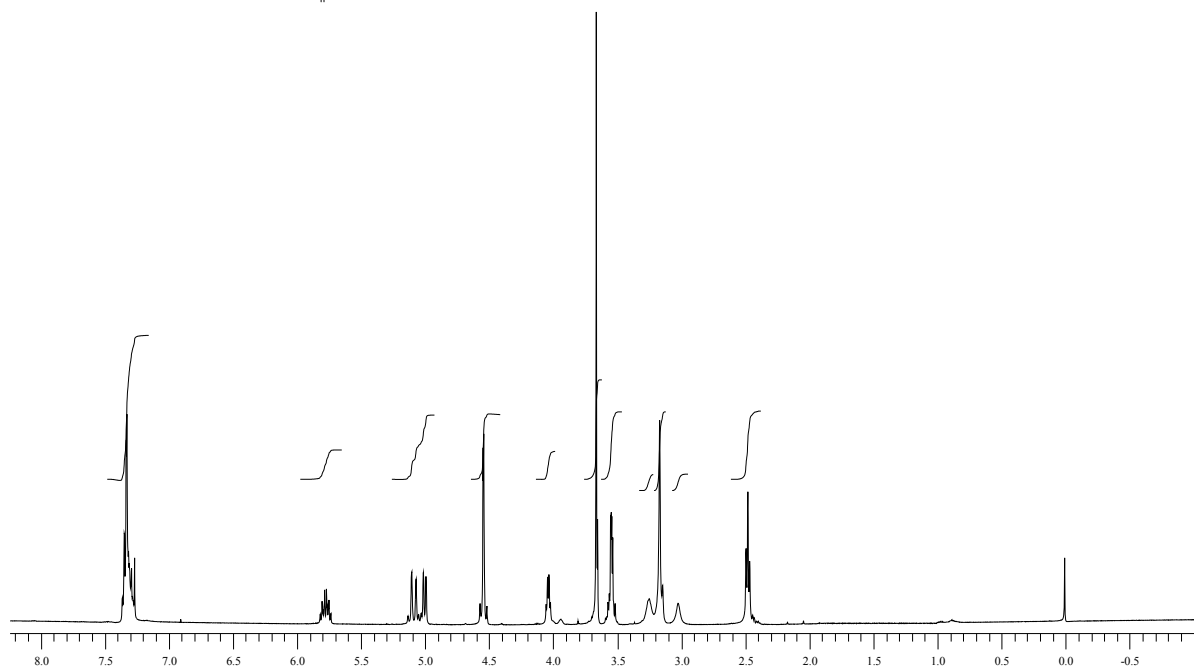
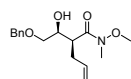
**<sup>1</sup>H NMR spectra of, 3d (500 MHz):**



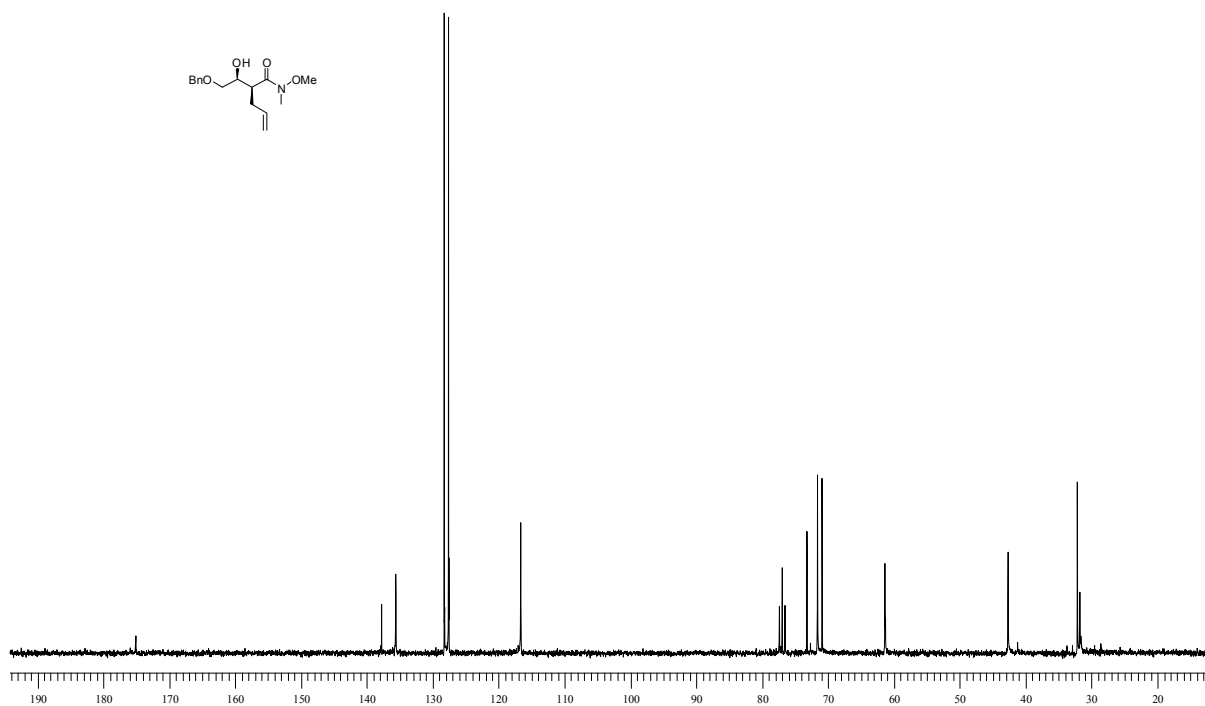
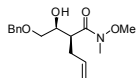
**<sup>13</sup>C NMR of compound 3d (75 MHz):**



**<sup>1</sup>H NMR spectra of, 3e (500 MHz):**

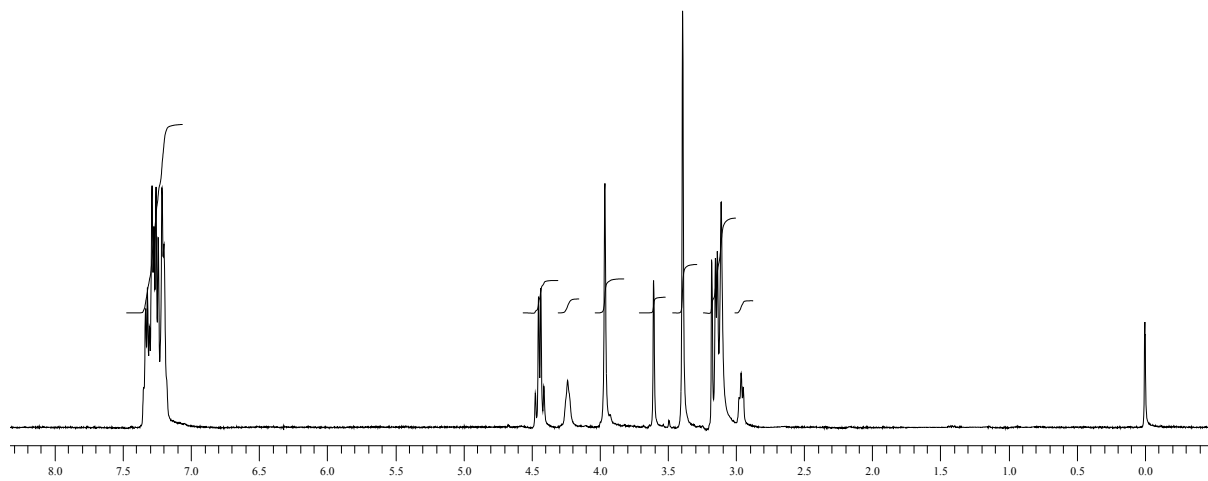
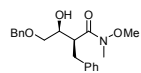


**<sup>13</sup>C NMR of compound 3e (75 MHz):**

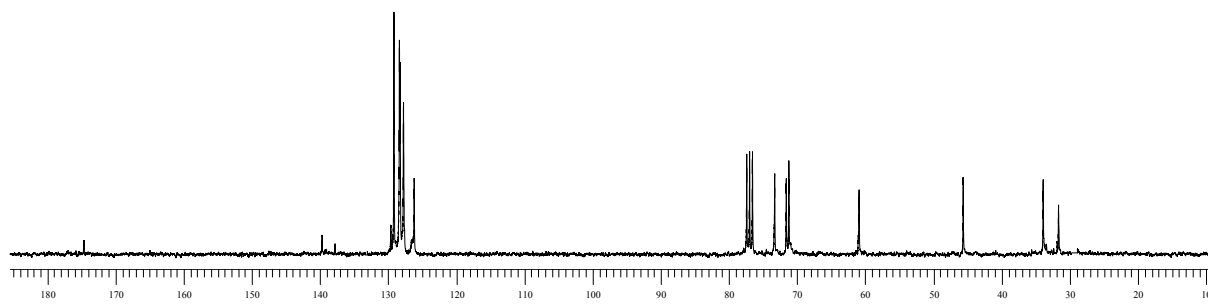
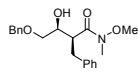




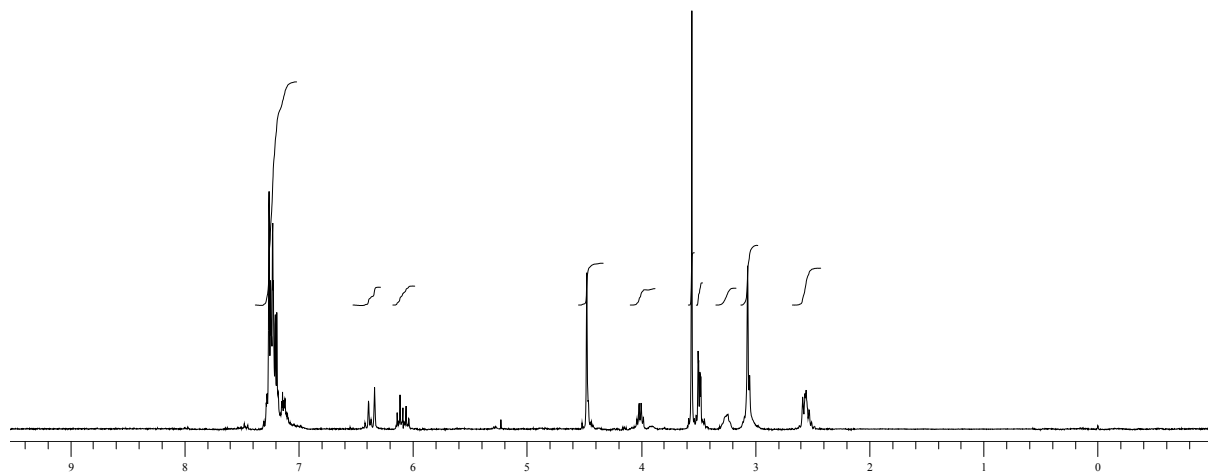
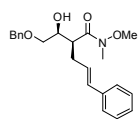
**<sup>1</sup>H NMR spectra of, 3f (500 MHz):**



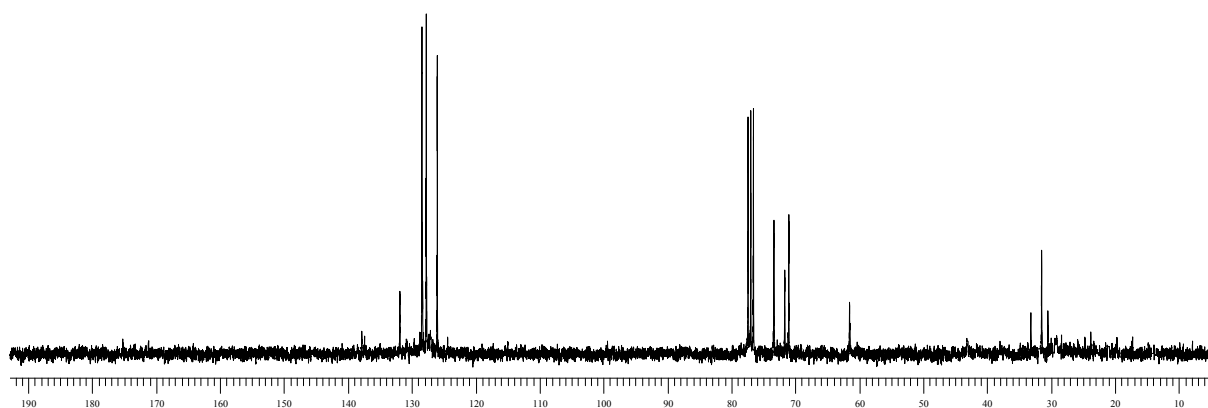
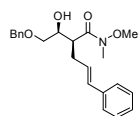
**<sup>13</sup>C NMR of compound 3f (75 MHz):**



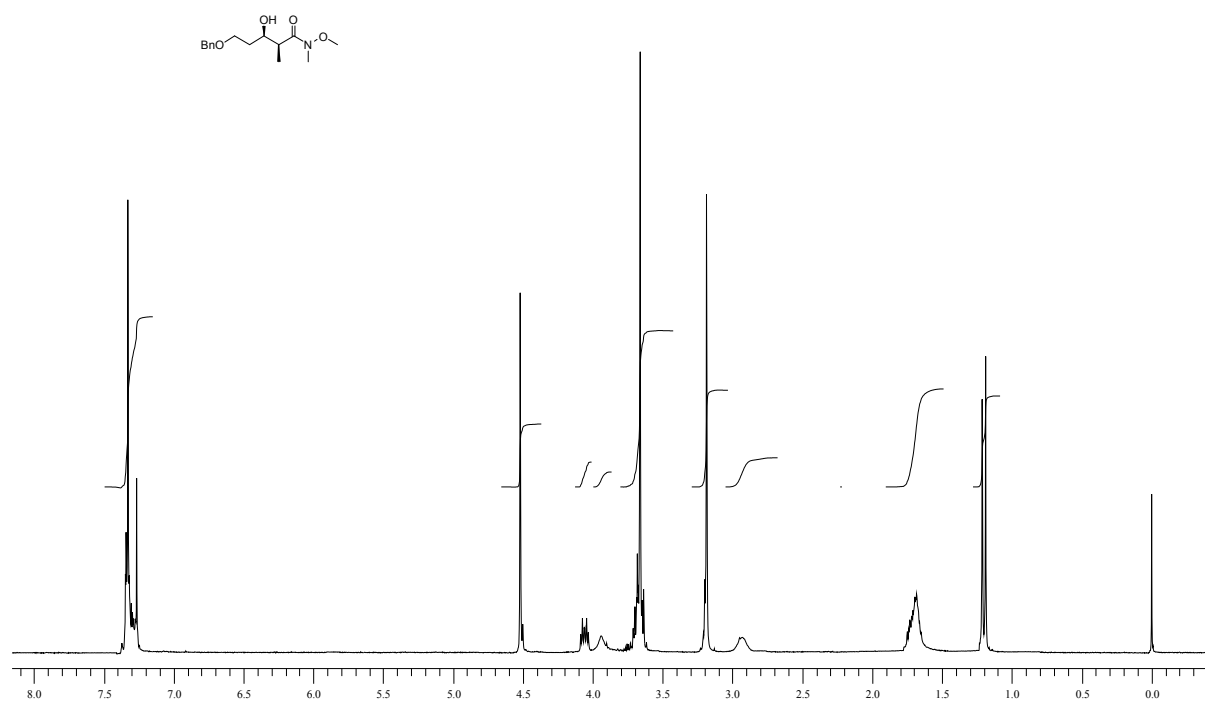
**<sup>1</sup>H NMR spectra of, 3g (300 MHz):**



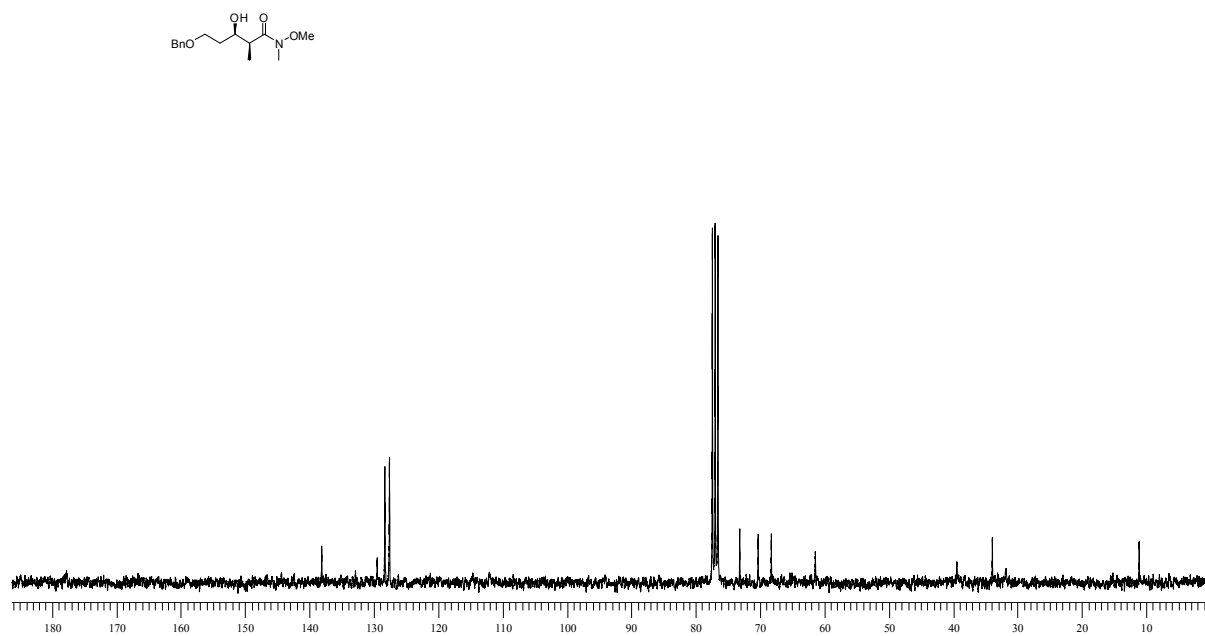
**<sup>13</sup>C NMR of compound 3g (75 MHz):**



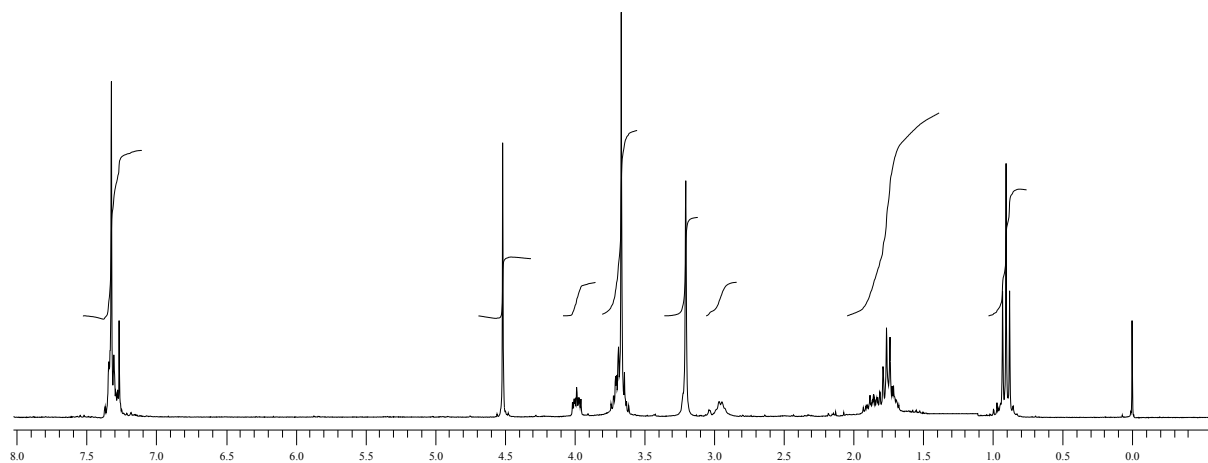
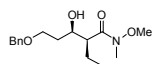
**<sup>1</sup>H NMR spectra of, 3h (300 MHz):**



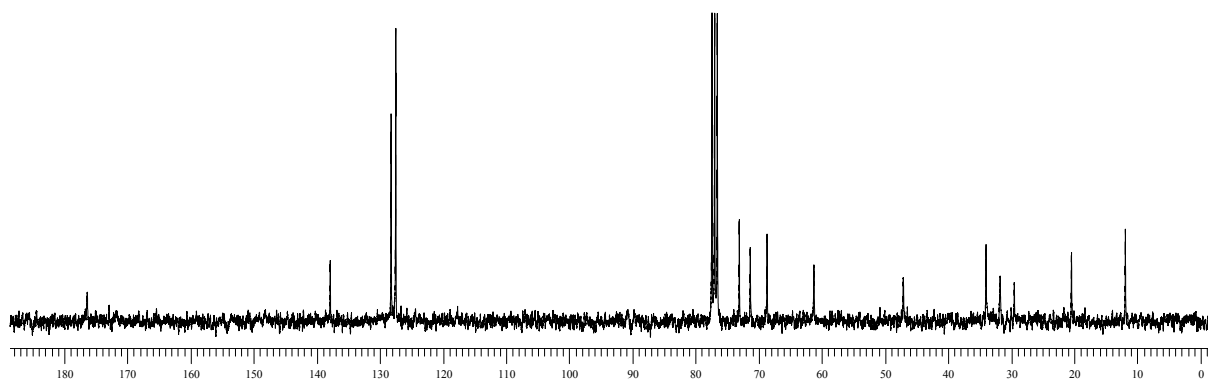
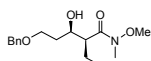
**<sup>13</sup>C NMR of compound 3h (75 MHz):**



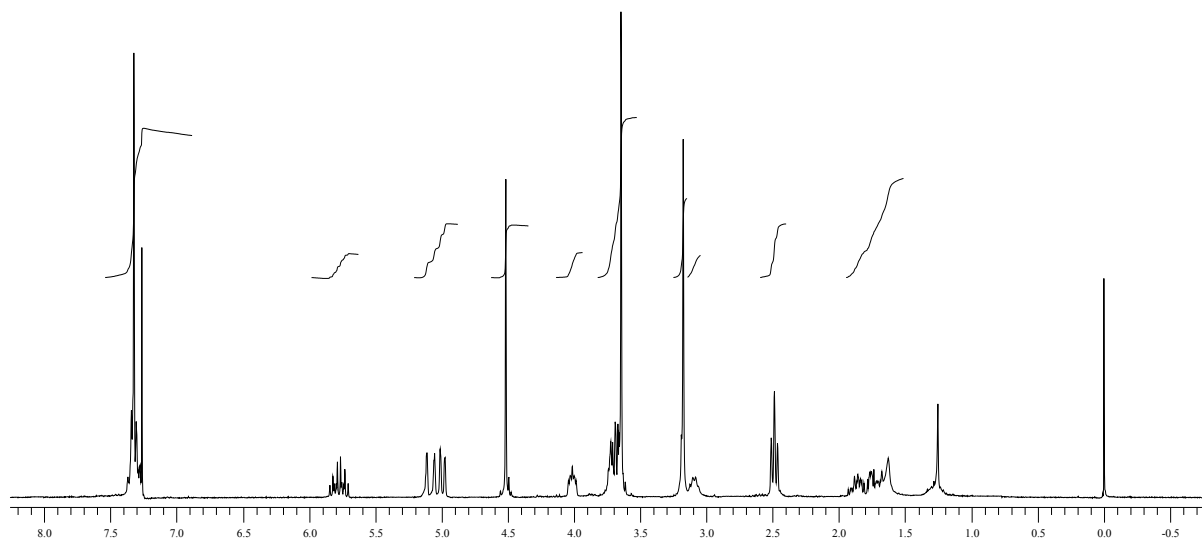
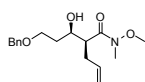
**<sup>1</sup>H NMR spectra of, 3i (300 MHz):**



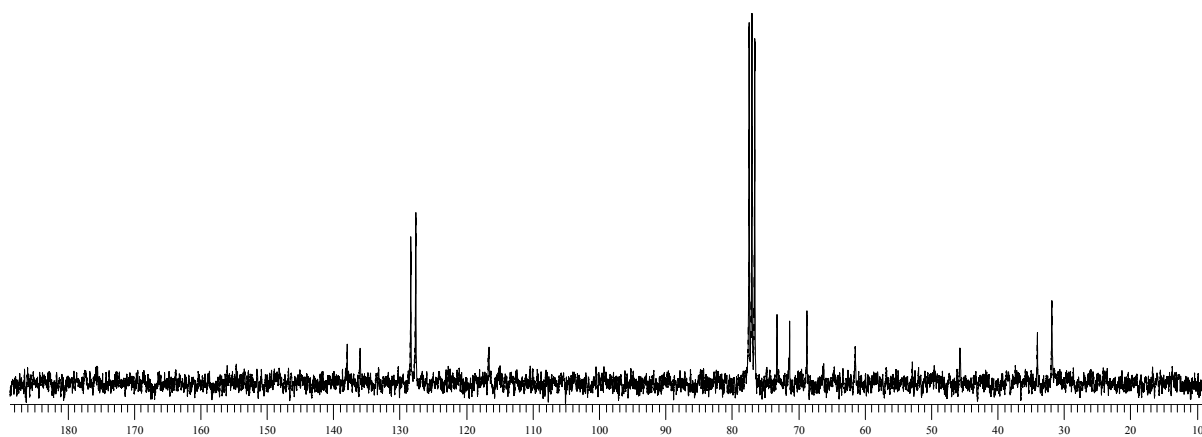
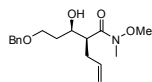
**<sup>13</sup>C NMR of compound 3i (75 MHz):**



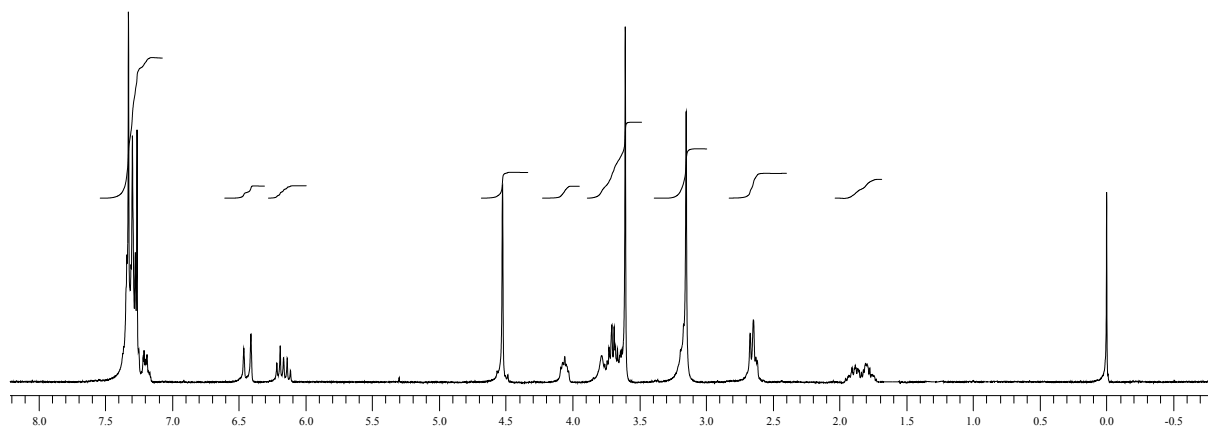
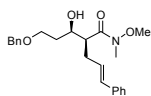
**<sup>1</sup>H NMR spectra of, 3j (500 MHz):**



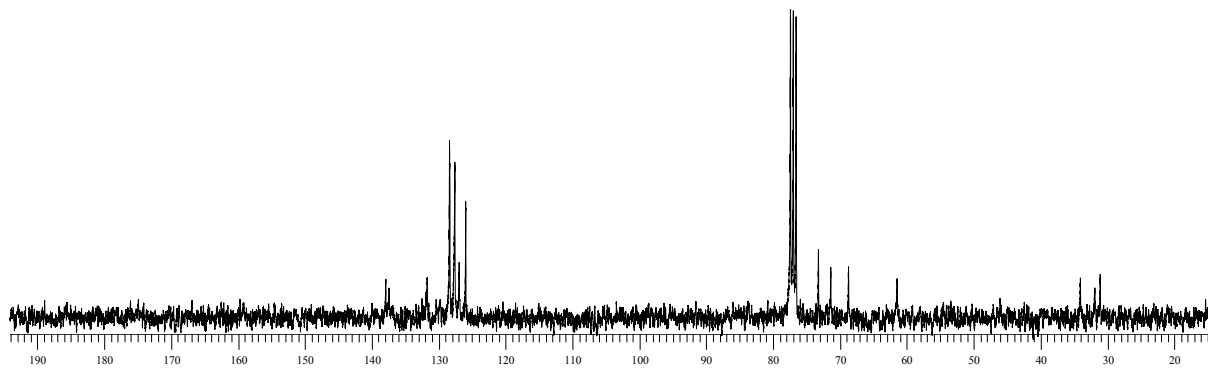
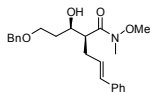
**<sup>13</sup>C NMR of compound 3j (75 MHz)::**



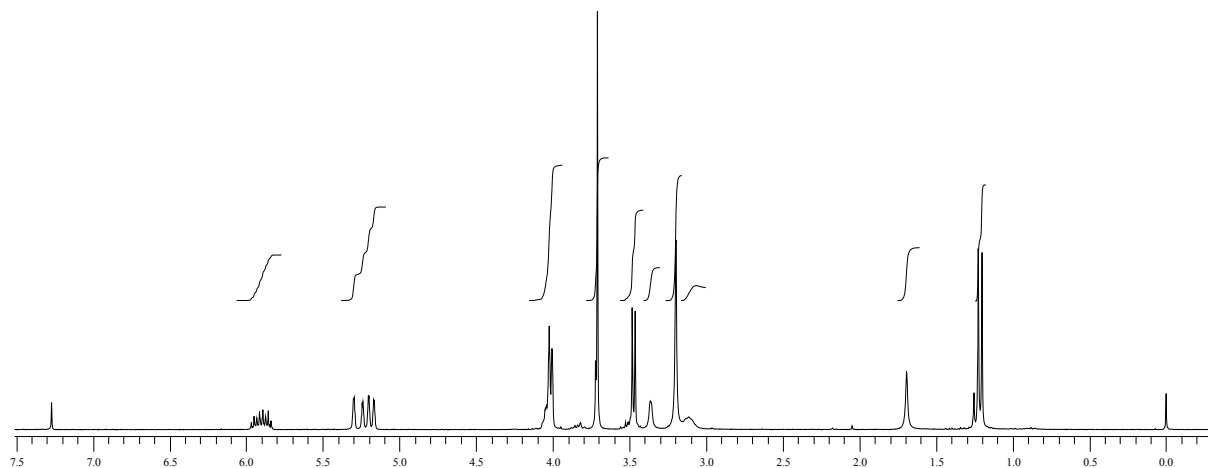
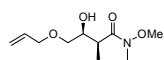
**<sup>1</sup>H NMR spectra of, 3k (500 MHz):**



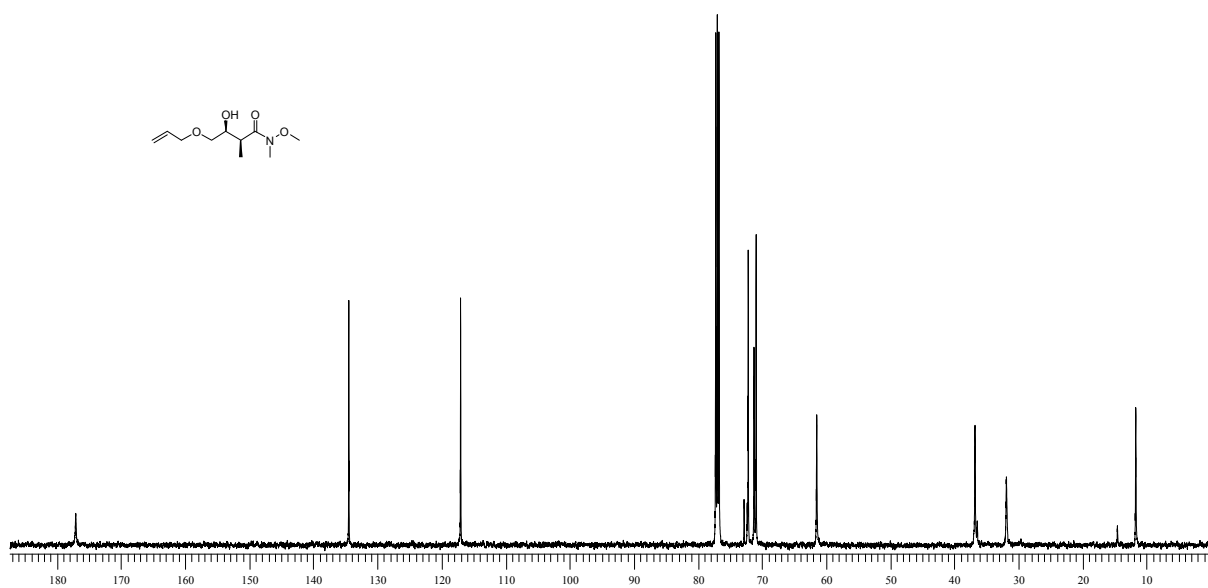
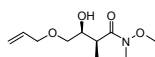
**<sup>13</sup>C NMR of compound 3k (75 MHz):**



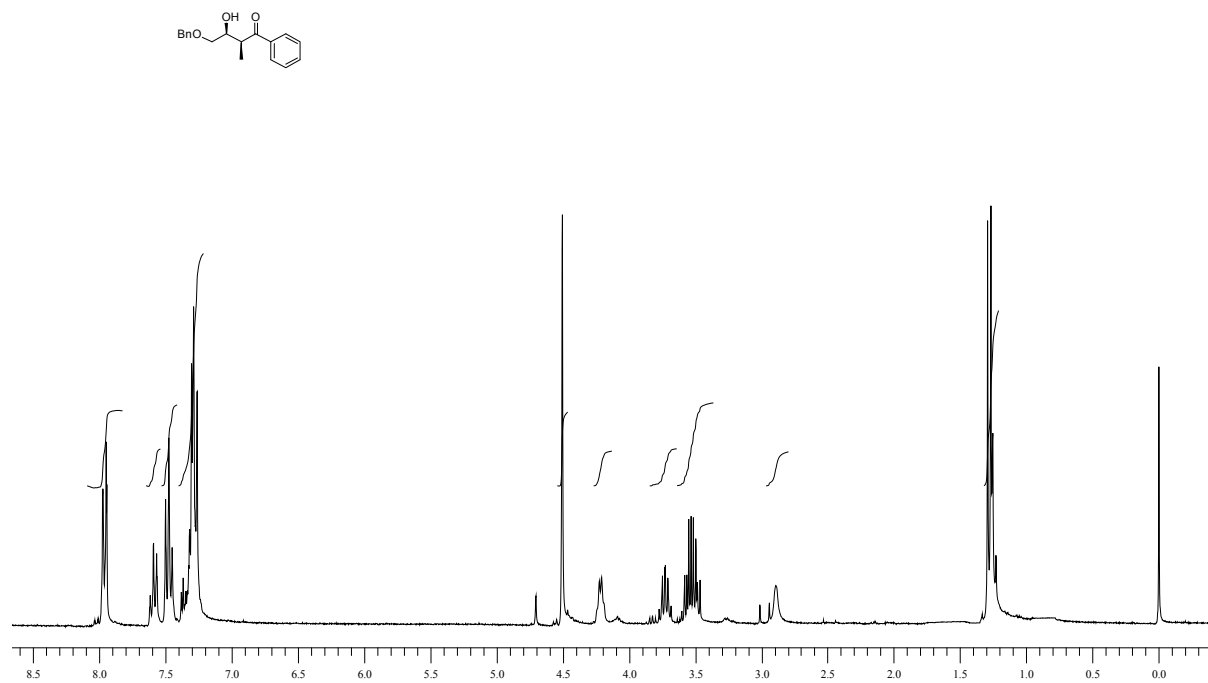
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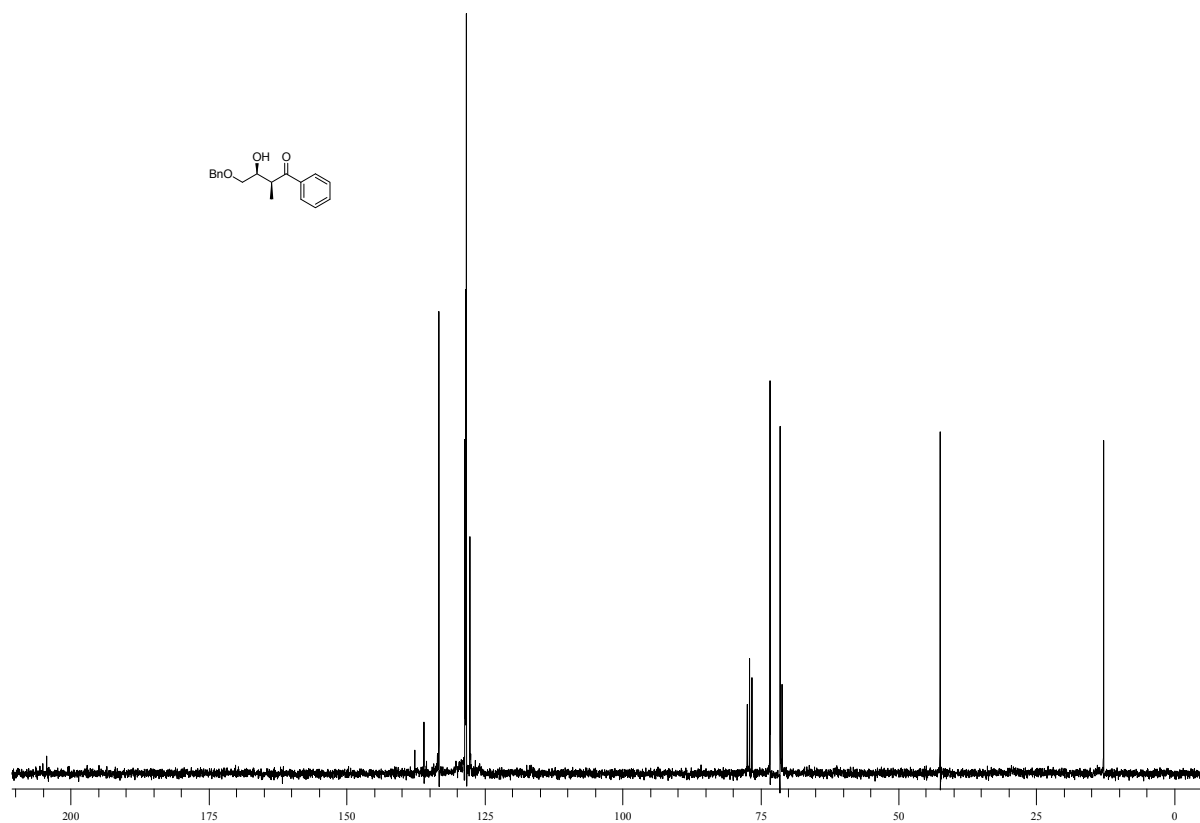
**<sup>13</sup>C NMR of compound 31 (75 MHz):**



**<sup>1</sup>H NMR spectra of, 3m (500 MHz):**

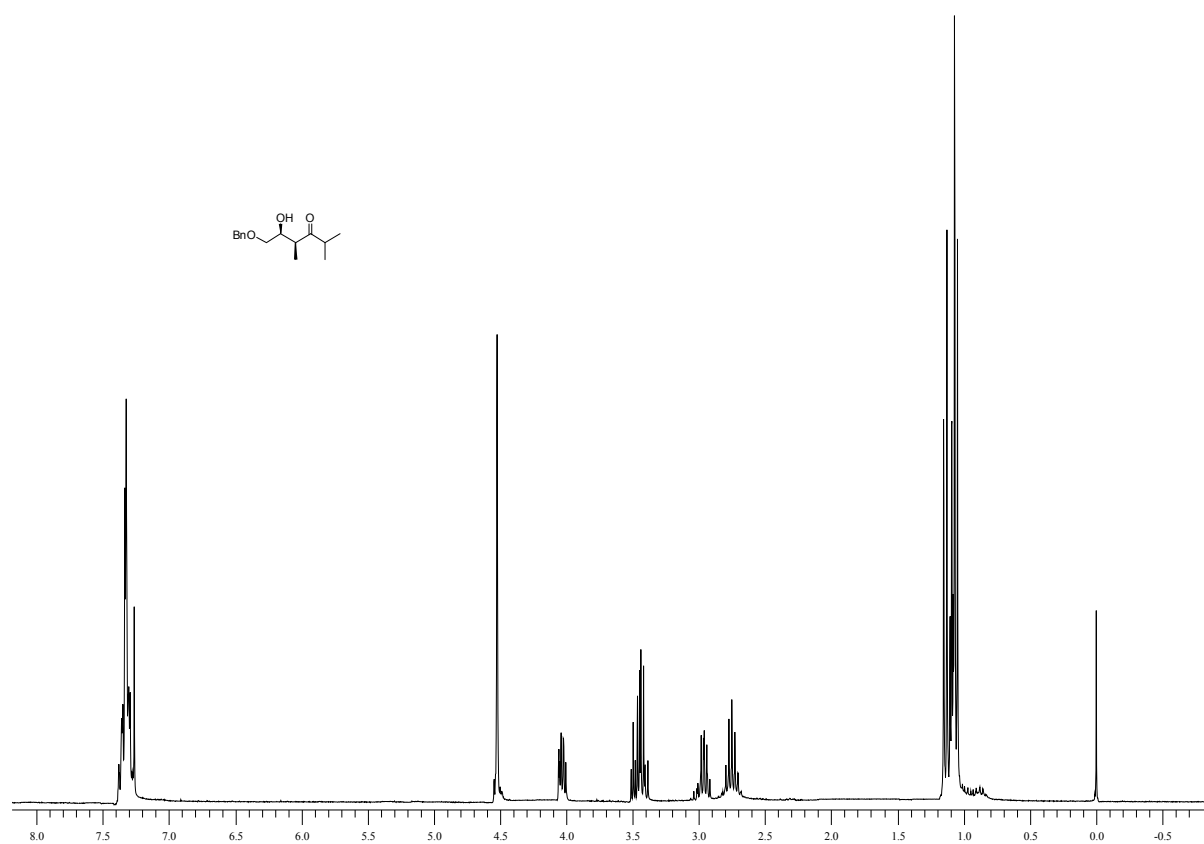


**<sup>13</sup>C NMR of compound 3m (75 MHz):**

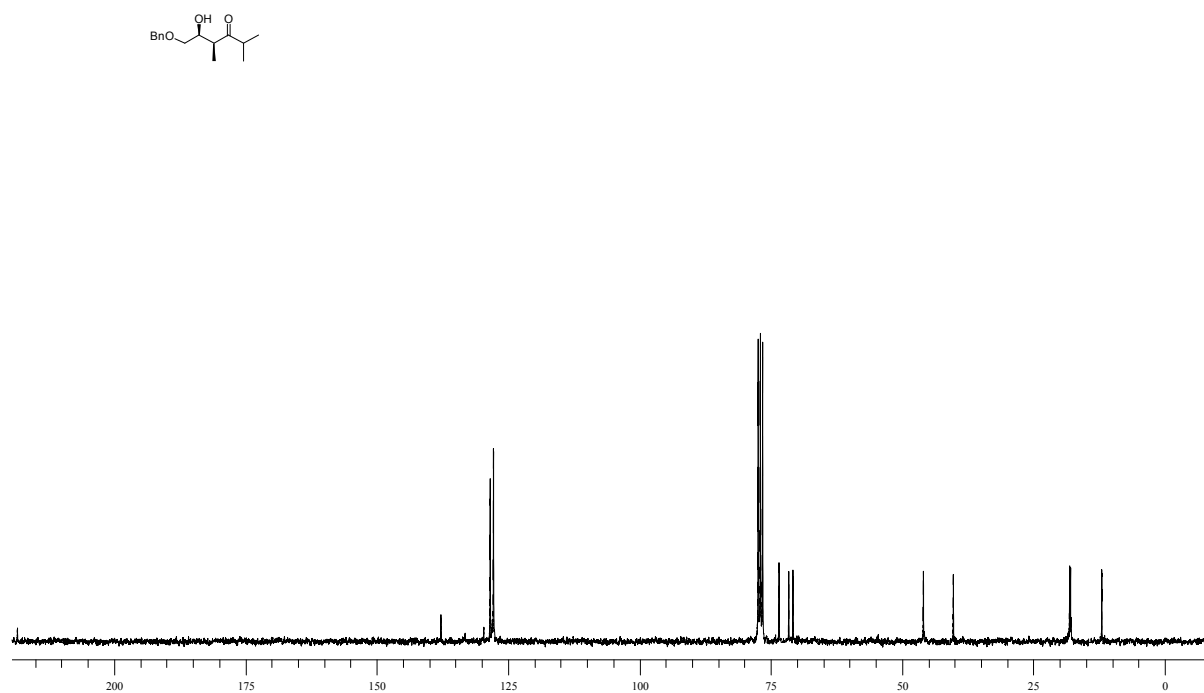




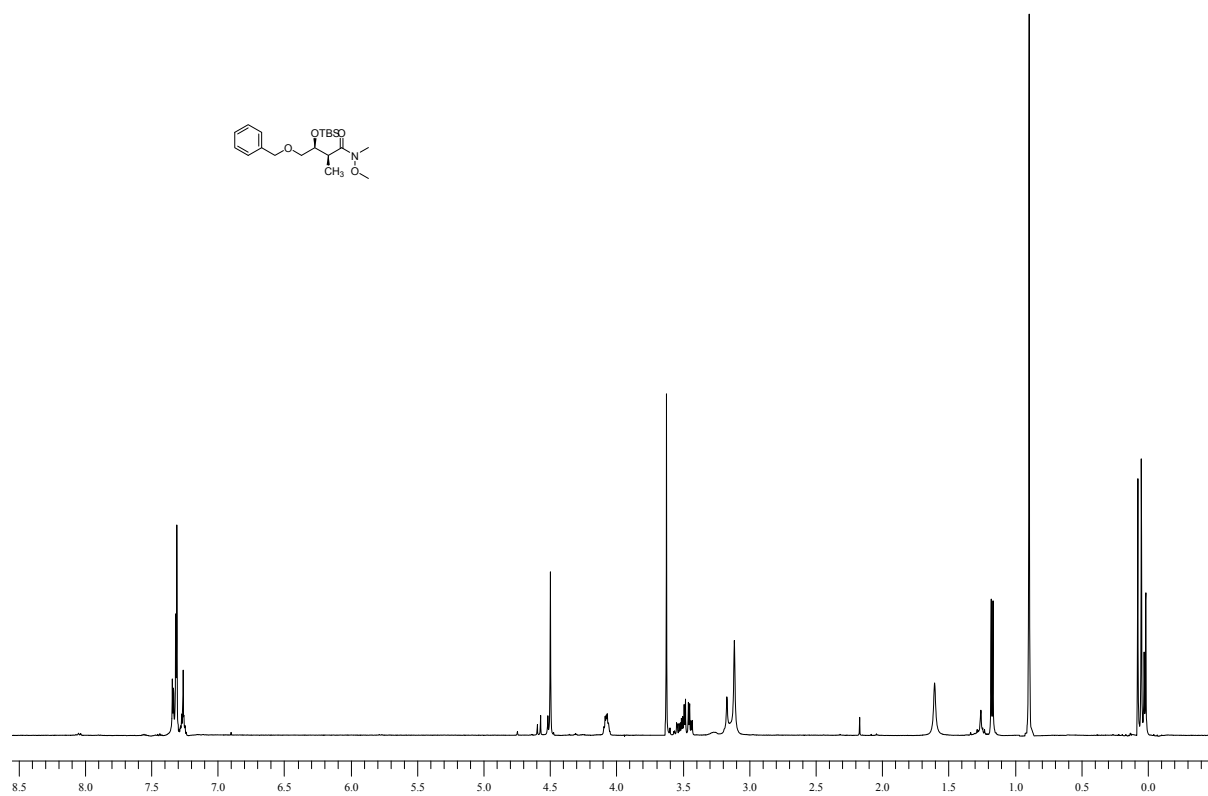
**<sup>1</sup>H NMR spectra of 3n (300 MHz):**



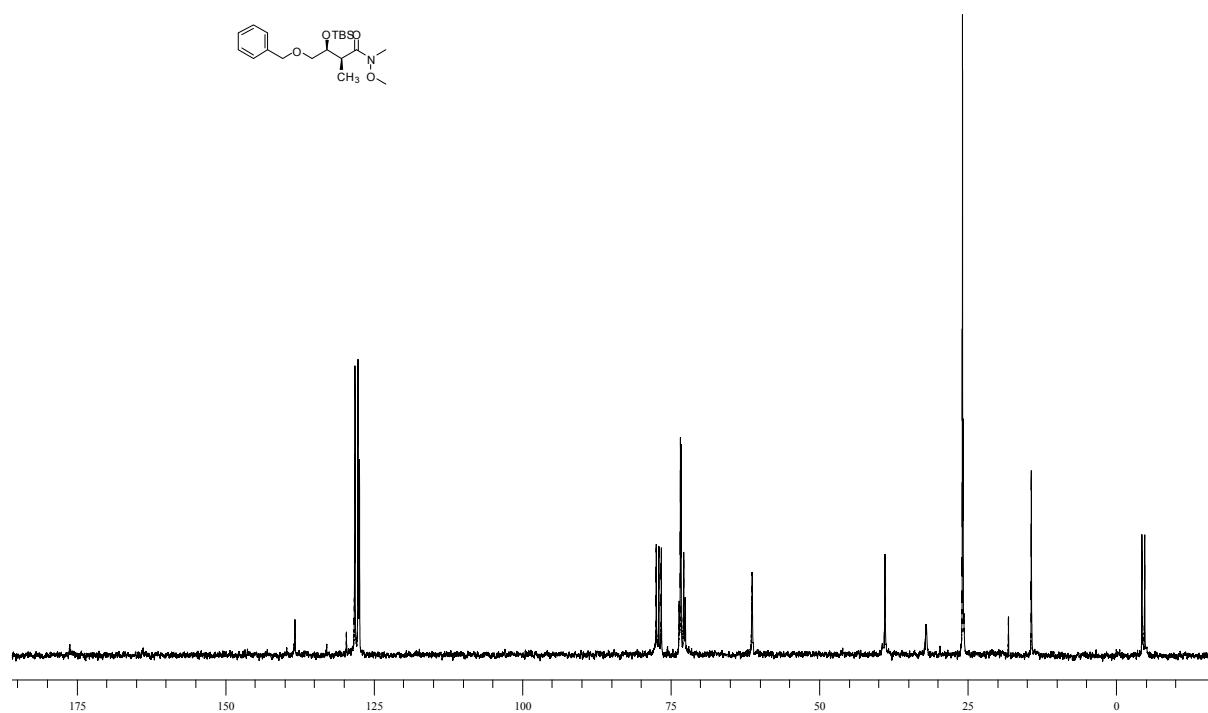
**<sup>13</sup>C NMR of compound 3n (75 MHz):**



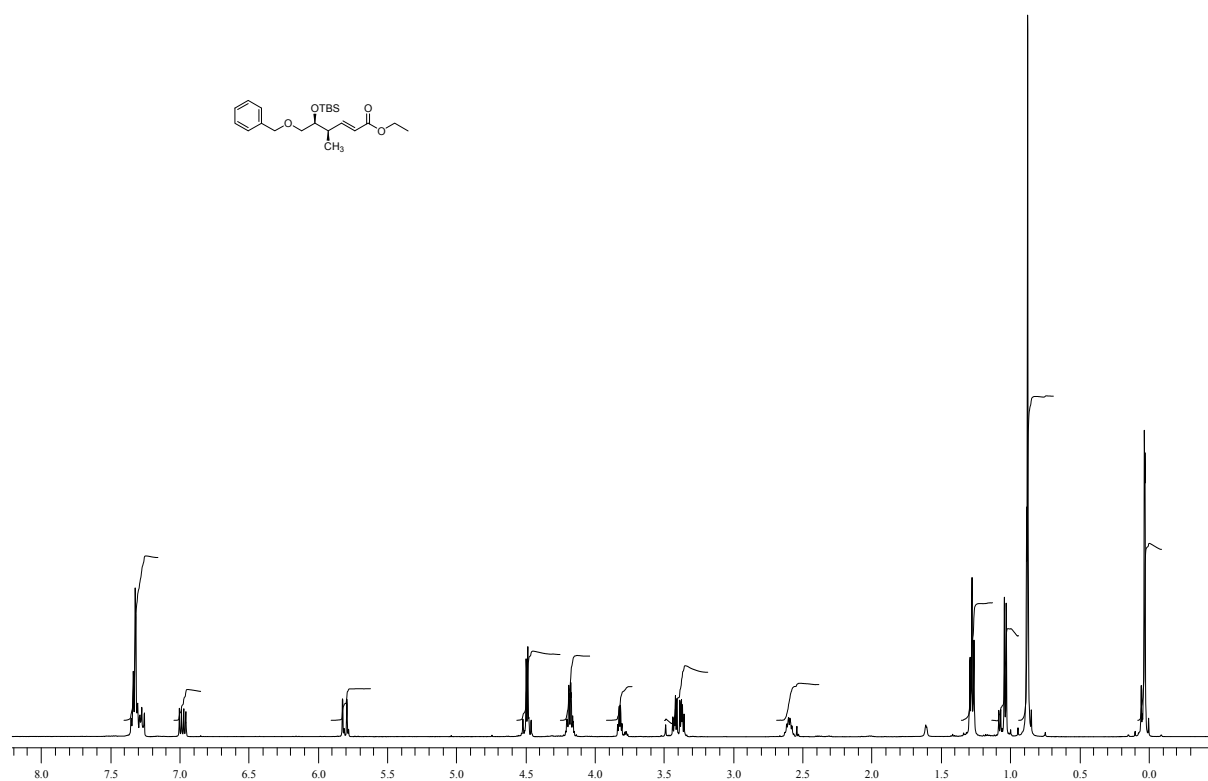
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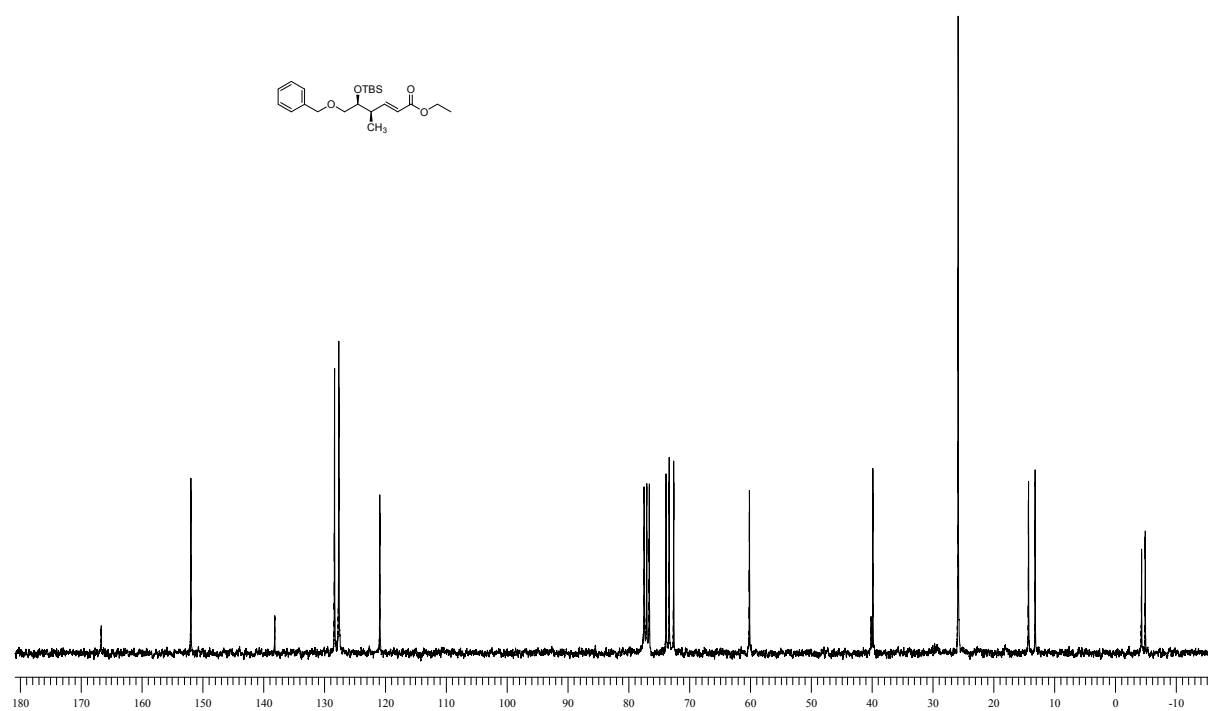
### <sup>13</sup>C NMR of compound (75 MHz)



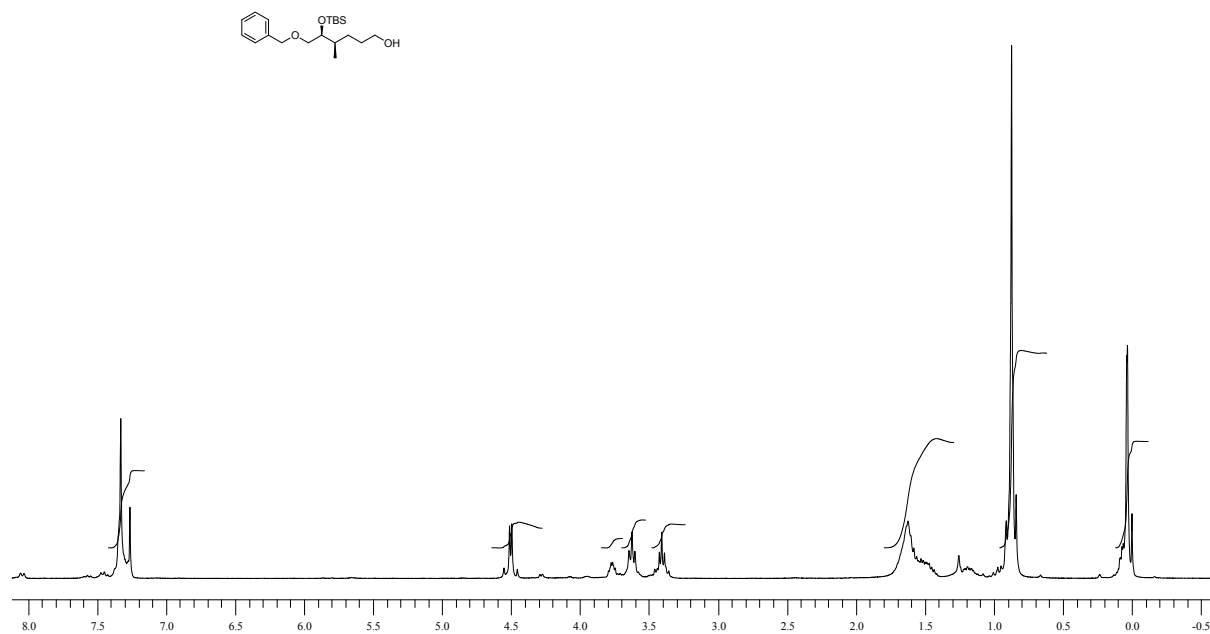
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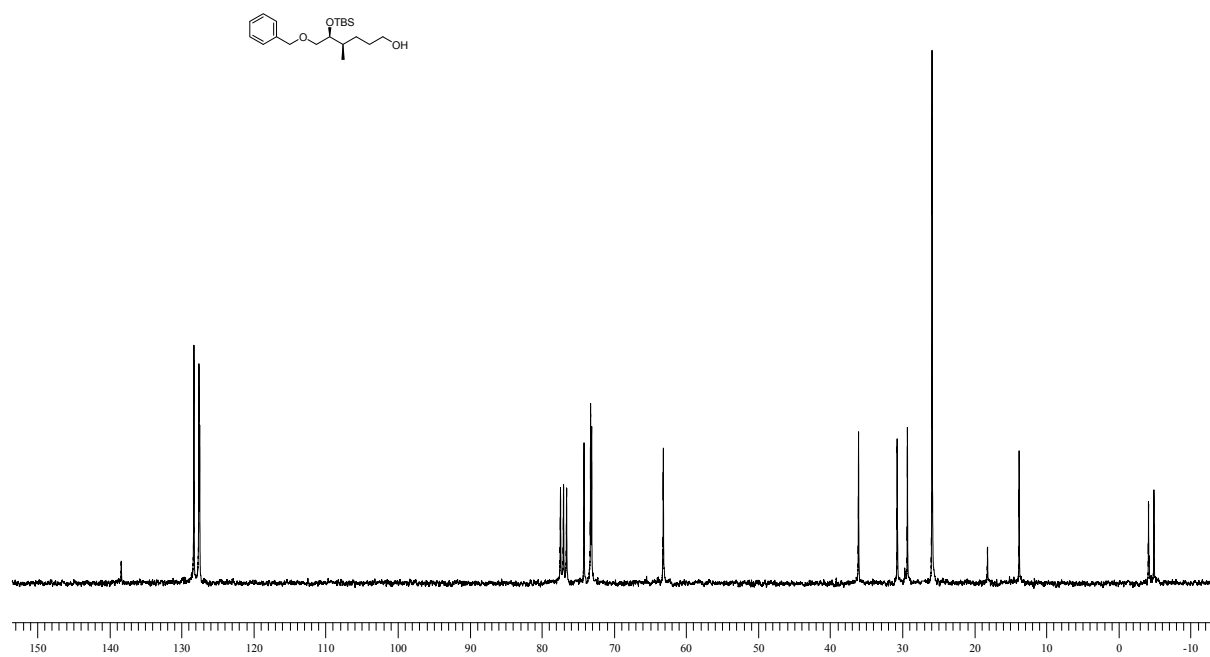
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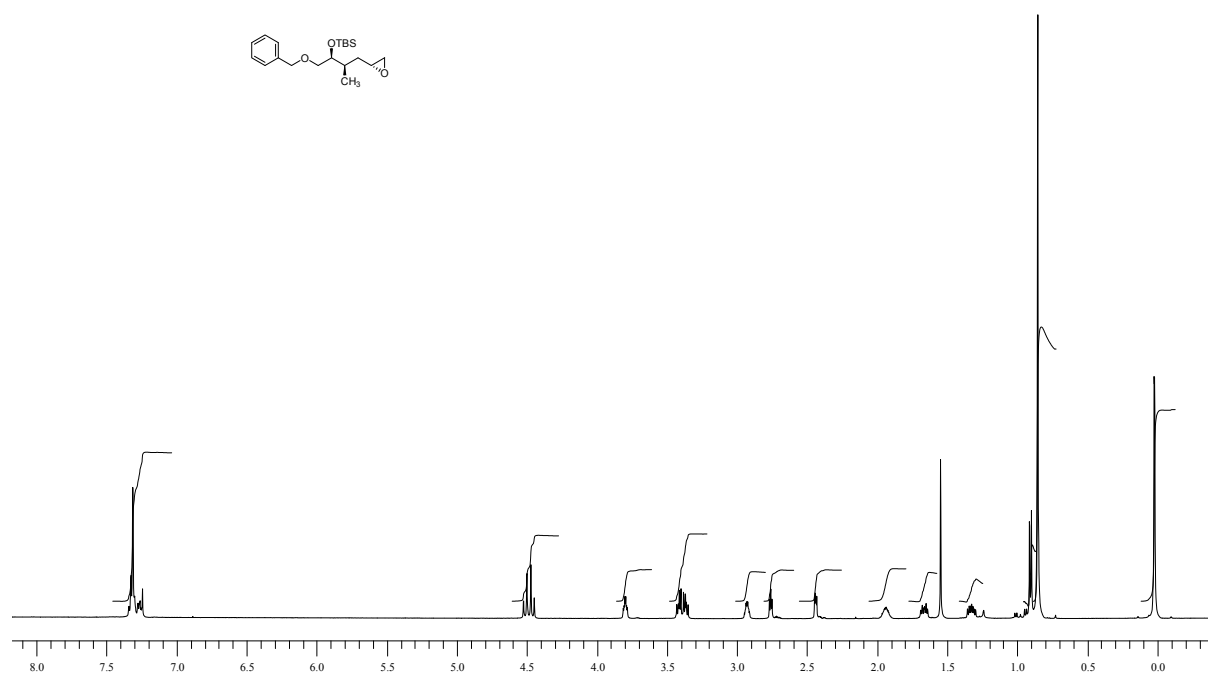
**<sup>1</sup>H NMR spectra of, 4 (300 MHz)**



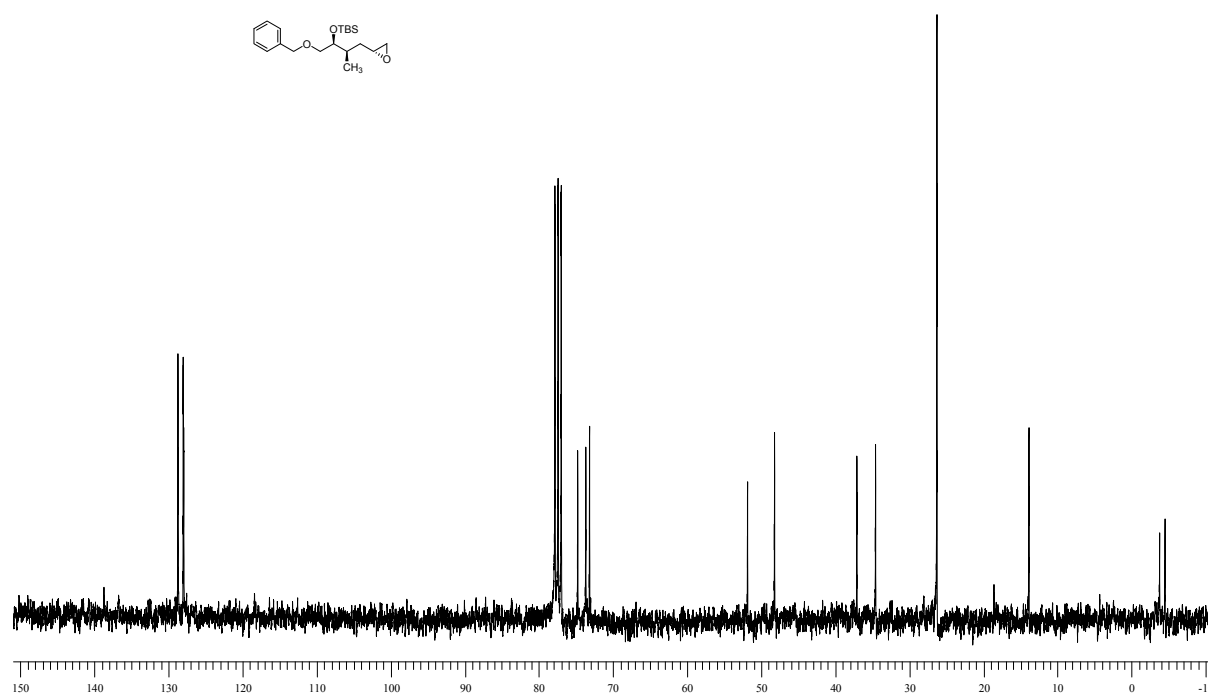
**<sup>13</sup>C NMR of compound, 4 (75 MHz)**



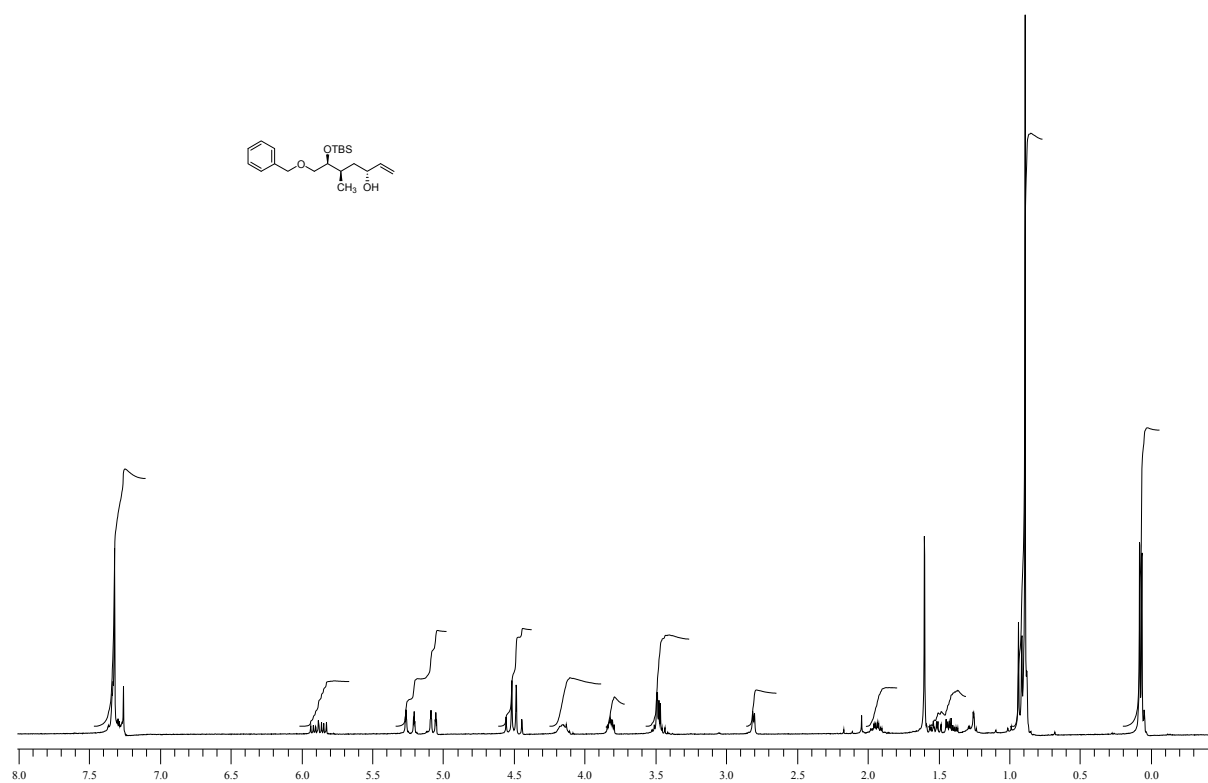
**<sup>1</sup>H NMR spectra of, 5 (300 MHz)**



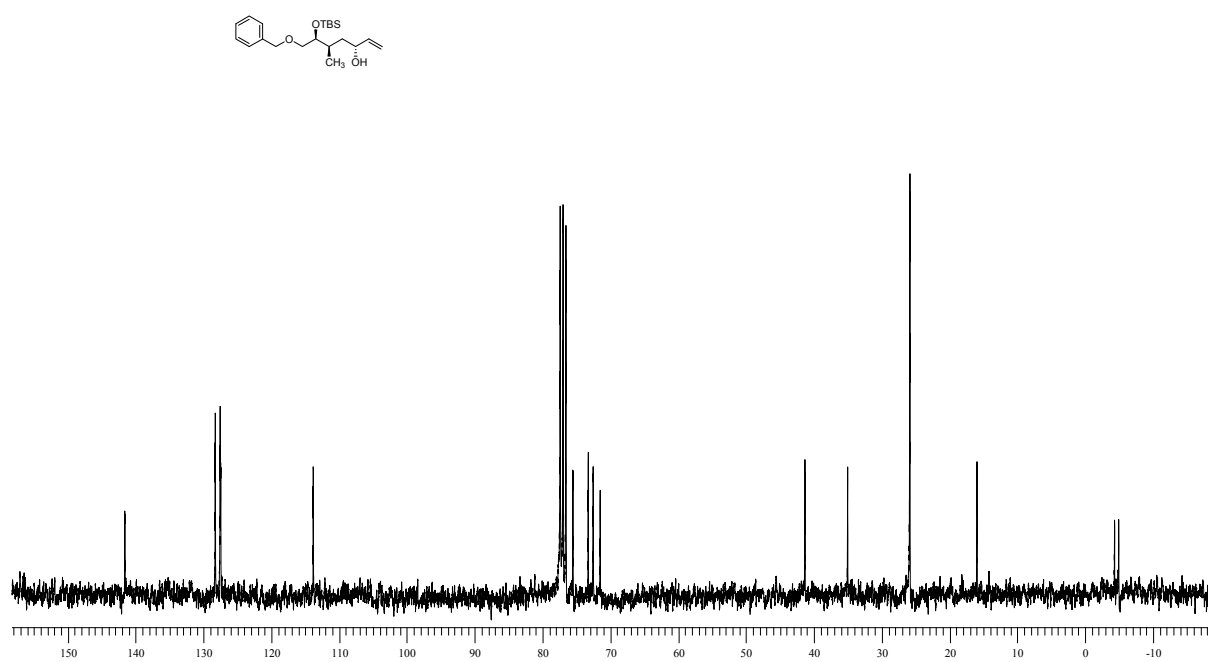
**<sup>13</sup>C NMR of compound, 5 (75 MHz)**



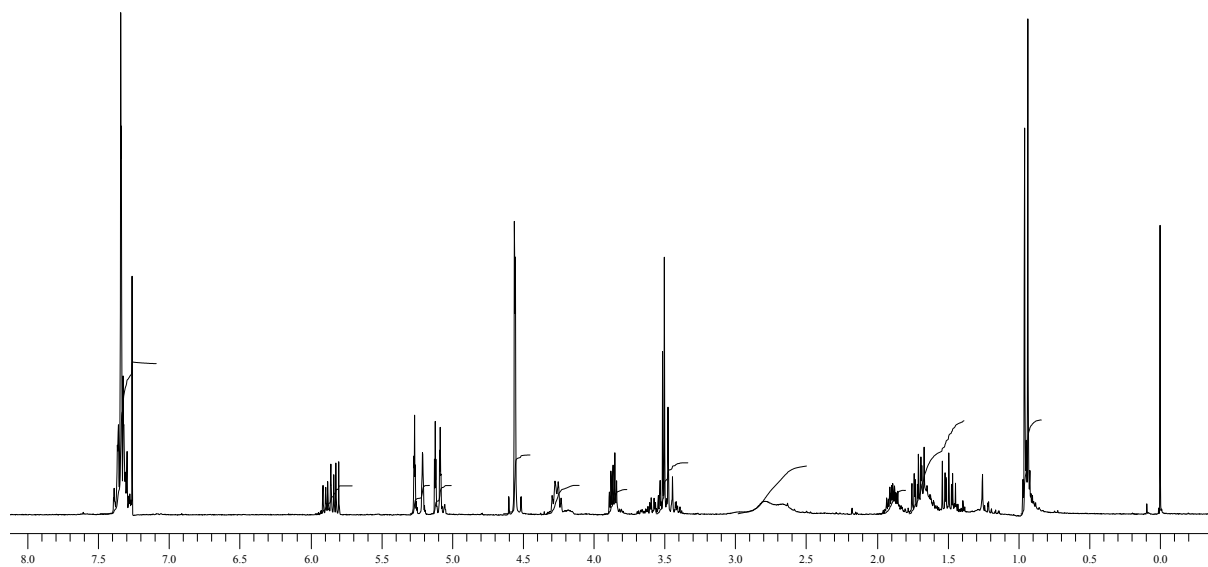
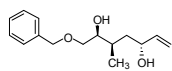
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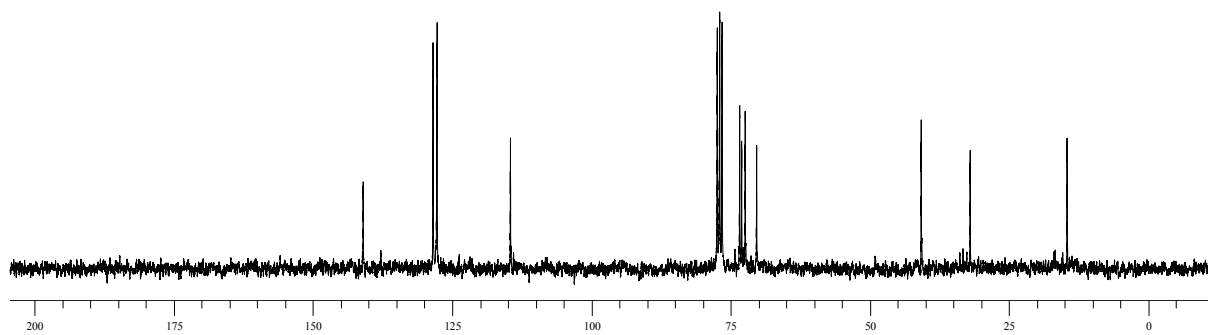
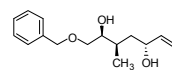
### $^{13}\text{C}$ NMR of compound (75 MHz)



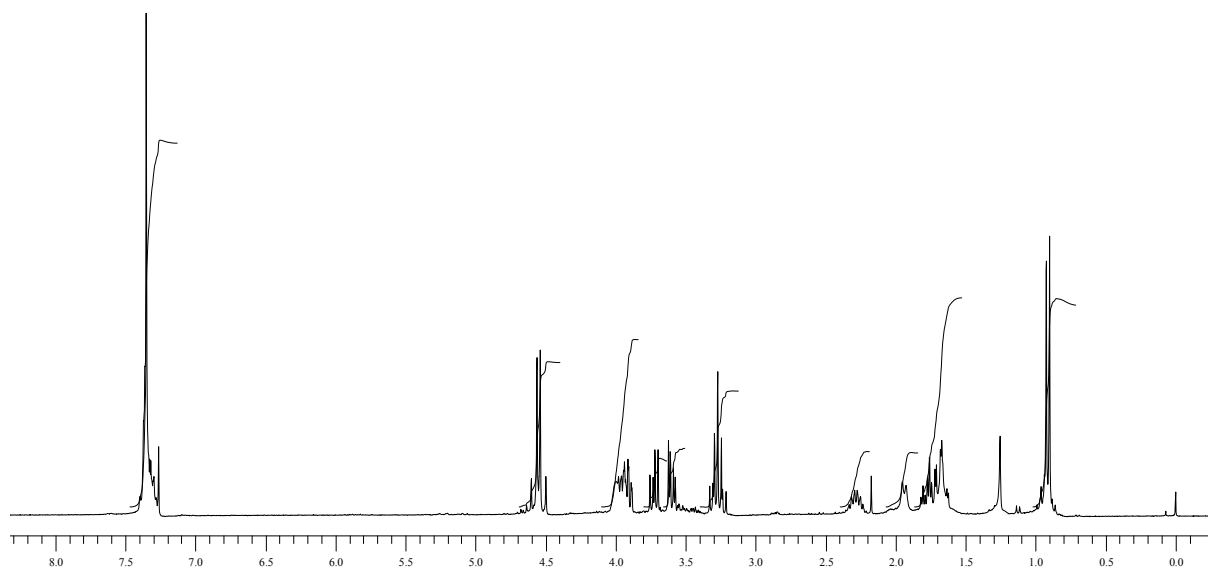
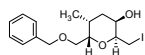
### <sup>1</sup>H NMR spectra of, 6 (300 MHz)



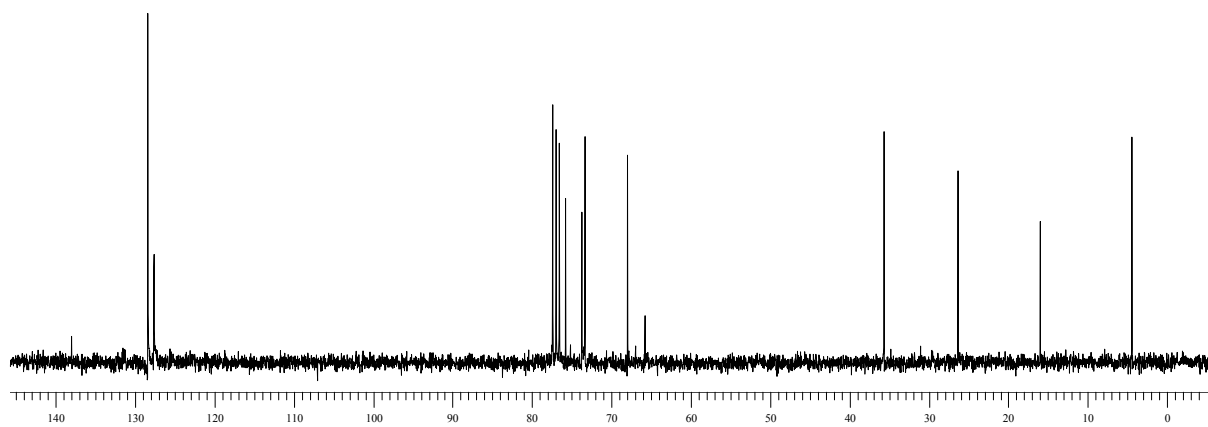
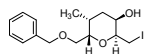
### <sup>13</sup>C NMR of compound, 6 (75 MHz)



### <sup>1</sup>H NMR spectra of, 7 (300 MHz)

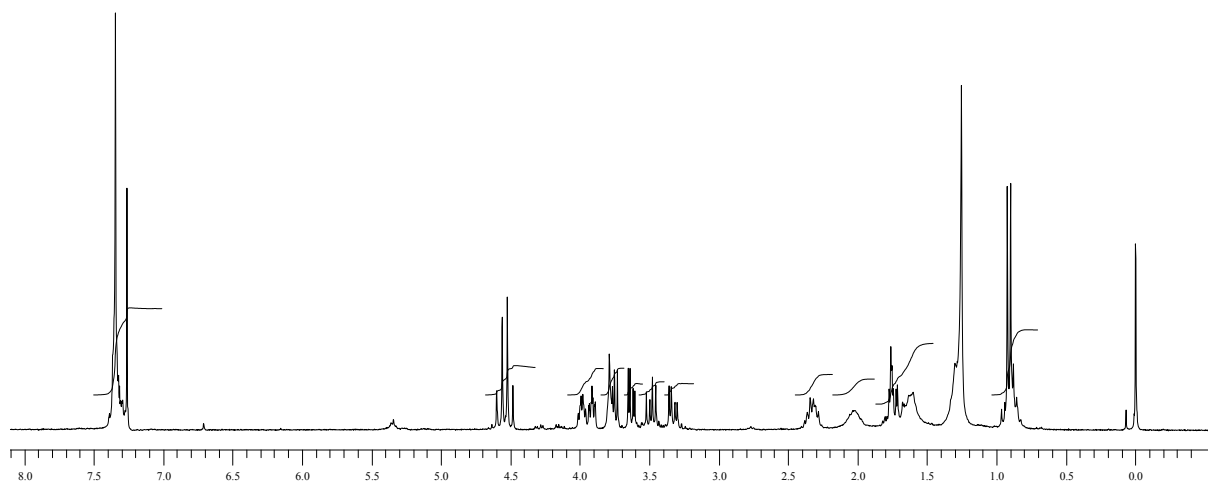
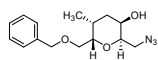


**<sup>13</sup>C NMR of compound, 7 (75 MHz)**

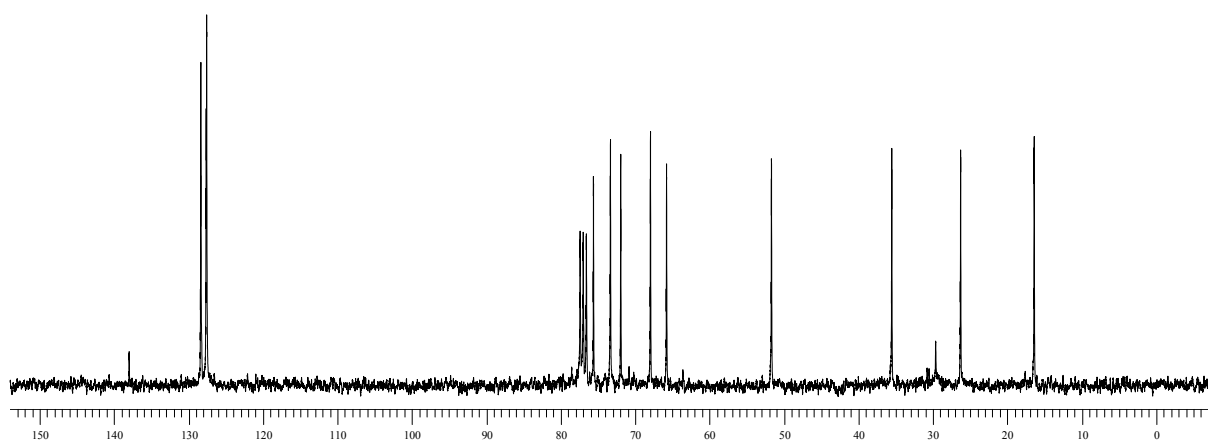
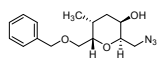




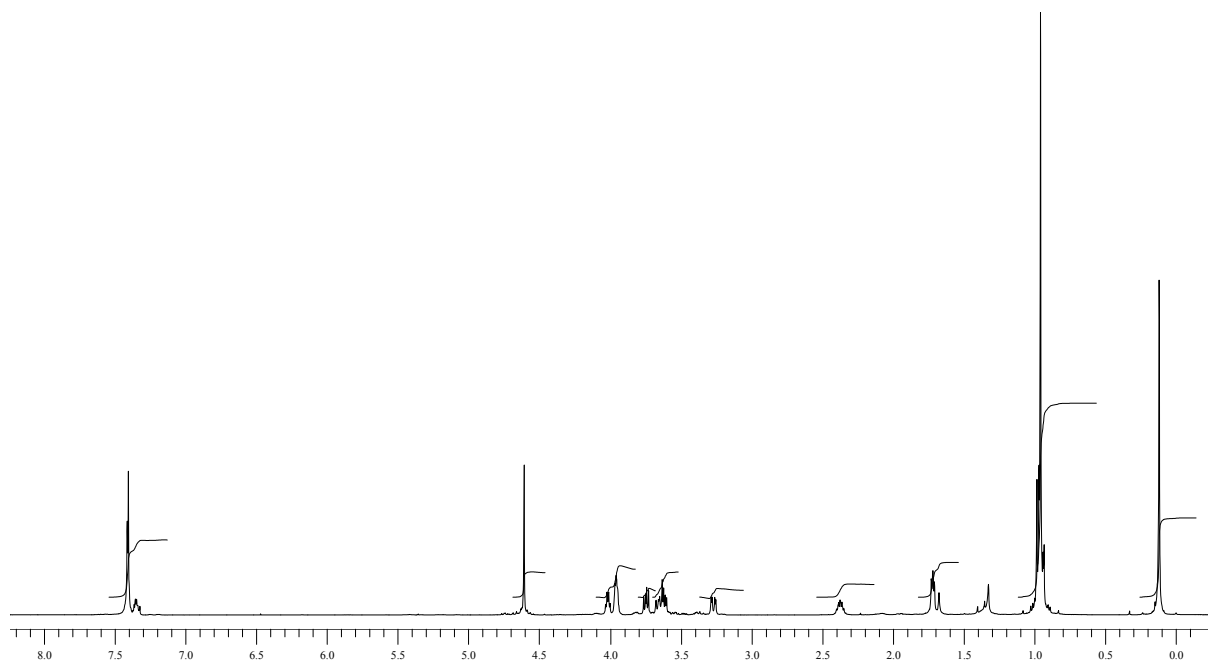
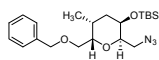
### <sup>1</sup>H NMR spectra (300 MHz)



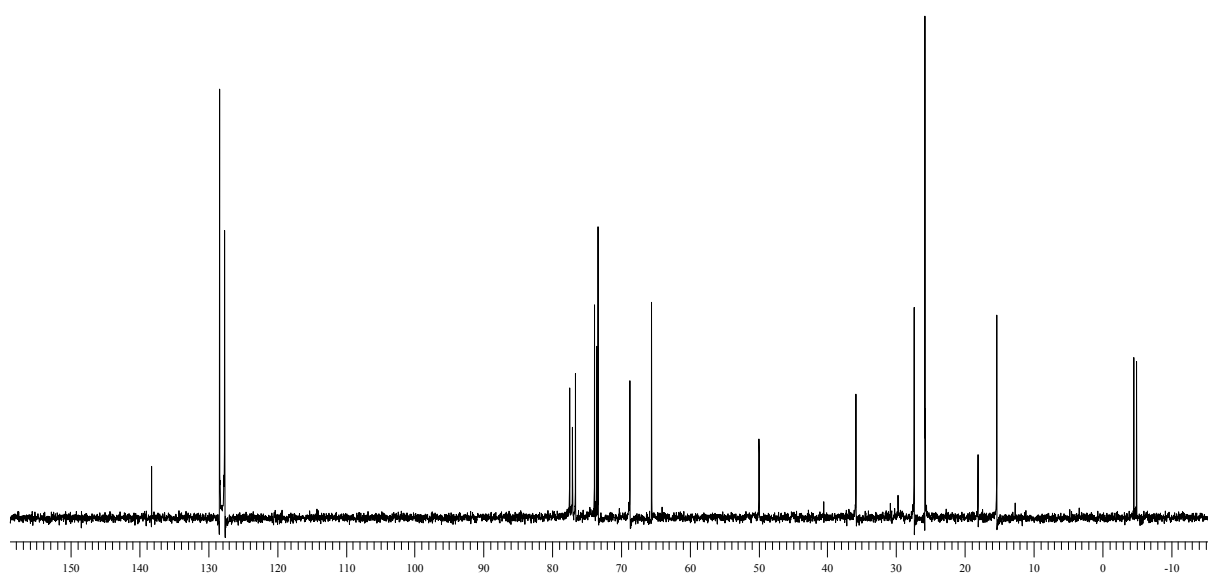
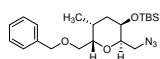
### <sup>13</sup>C NMR of compound (75 MHz)



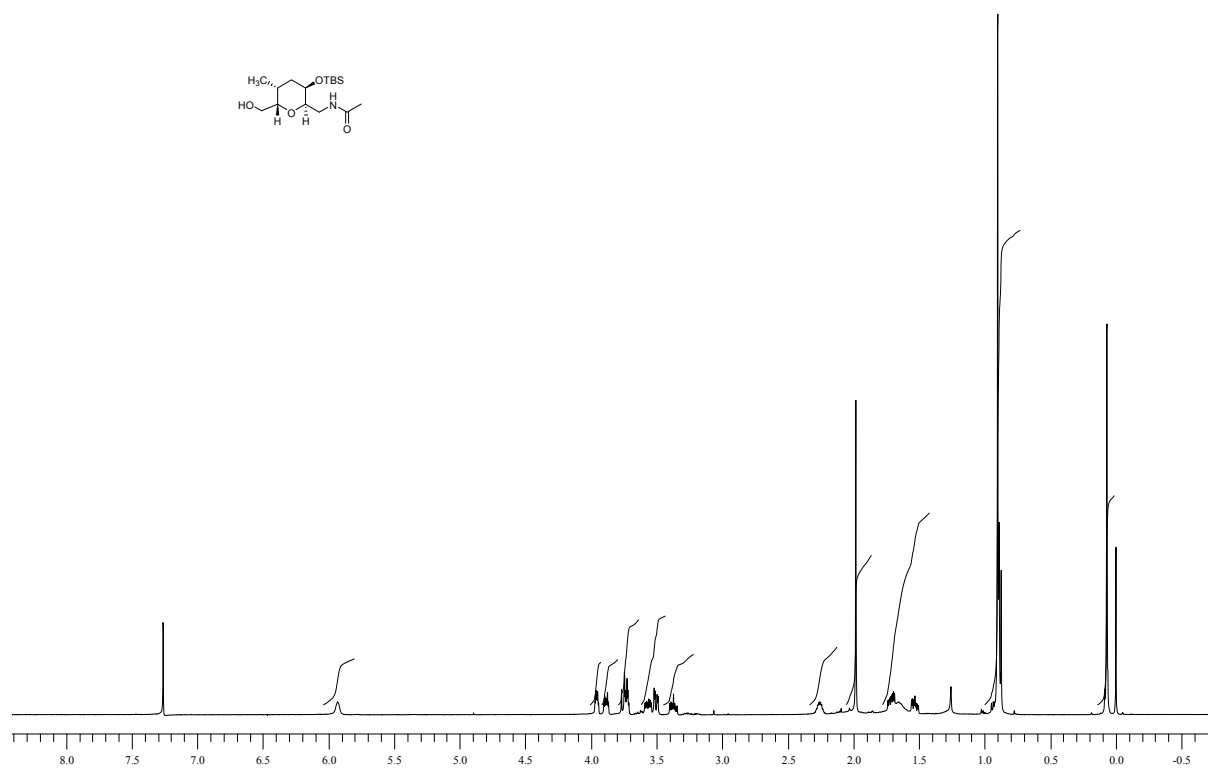
### $^1\text{H}$ NMR spectra of, 8 (300 MHz)



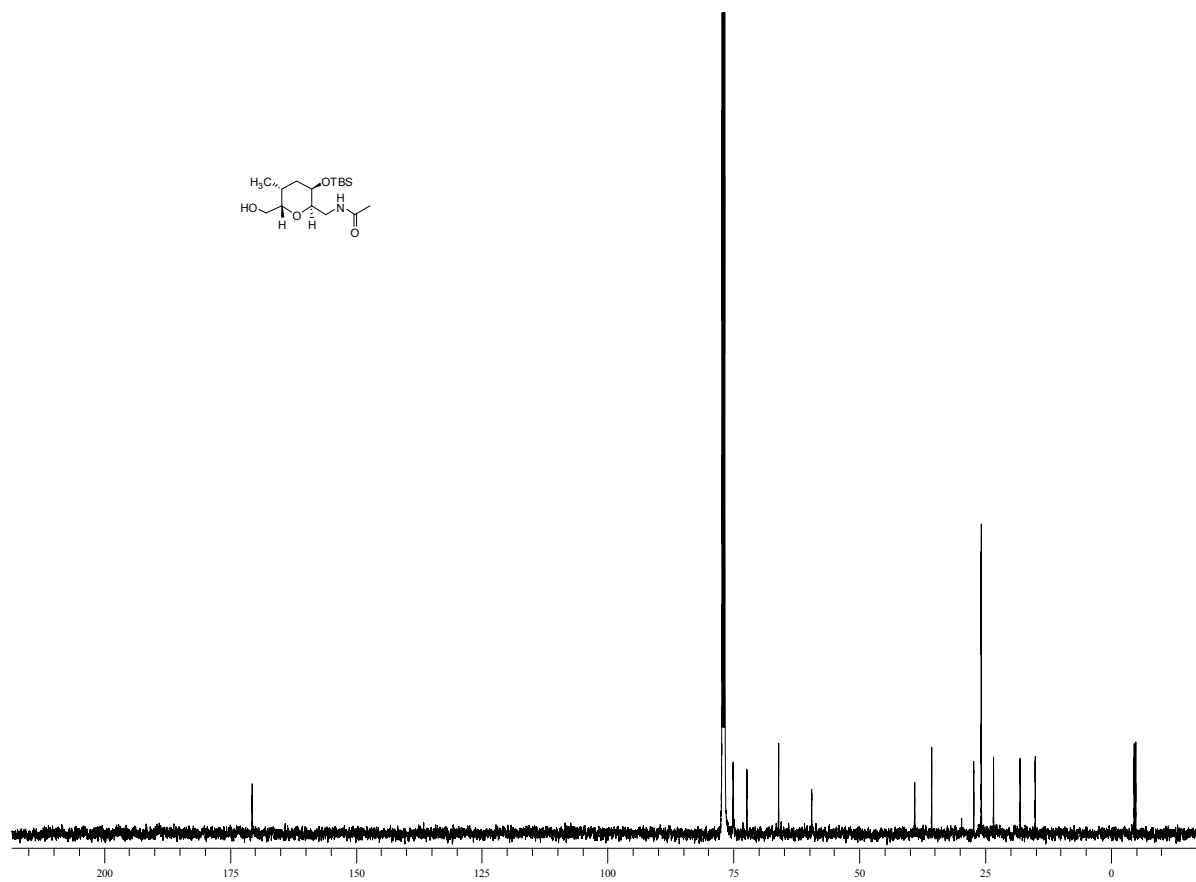
### $^{13}\text{C}$ NMR of compound, 8 (75 MHz)



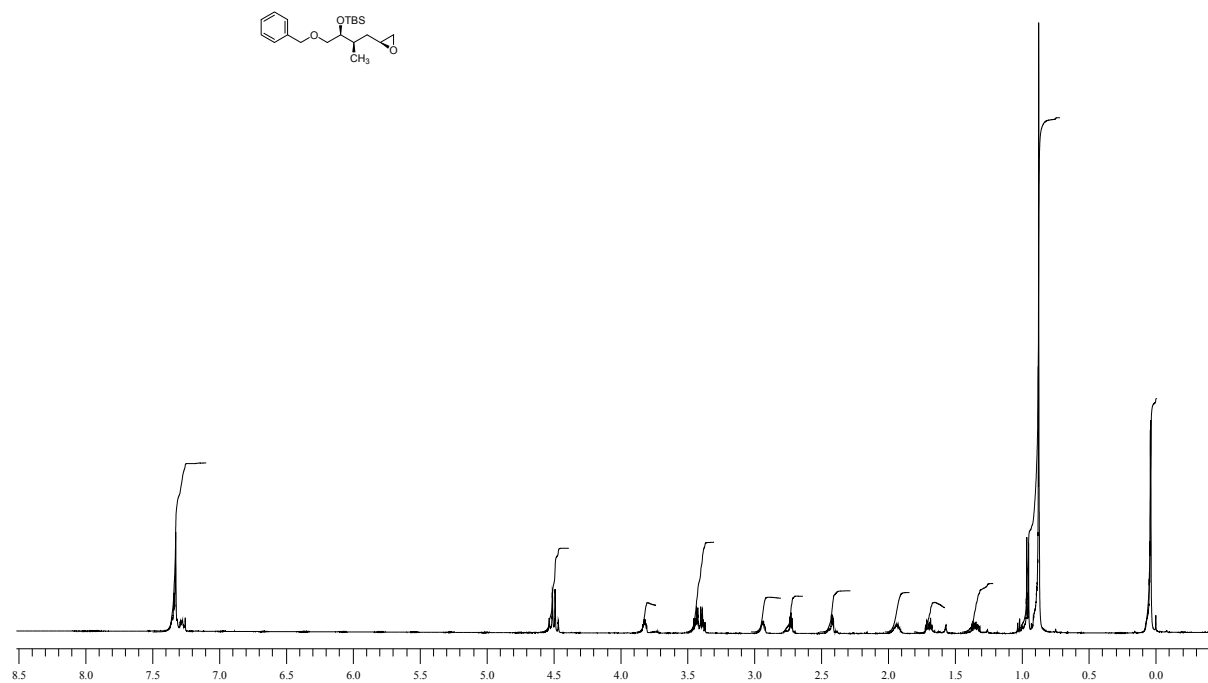
**<sup>1</sup>H NMR spectra of, 9 (300 MHz)**



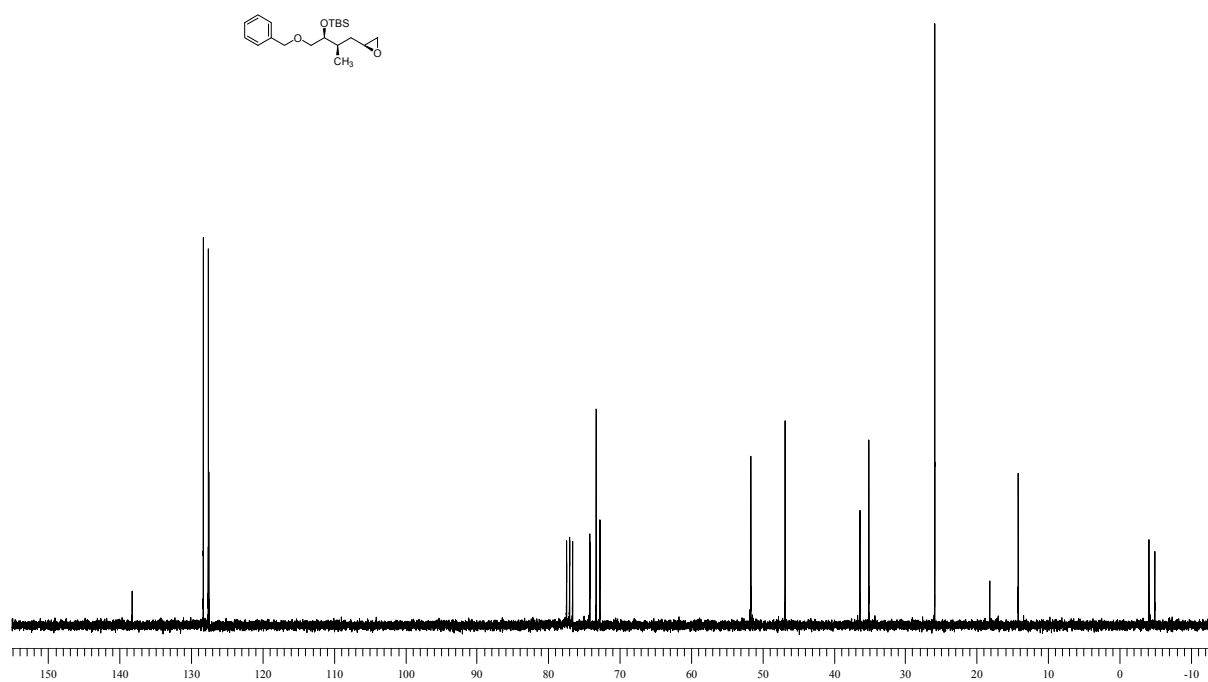
**<sup>13</sup>C NMR of compound, 9 (75 MHz)**



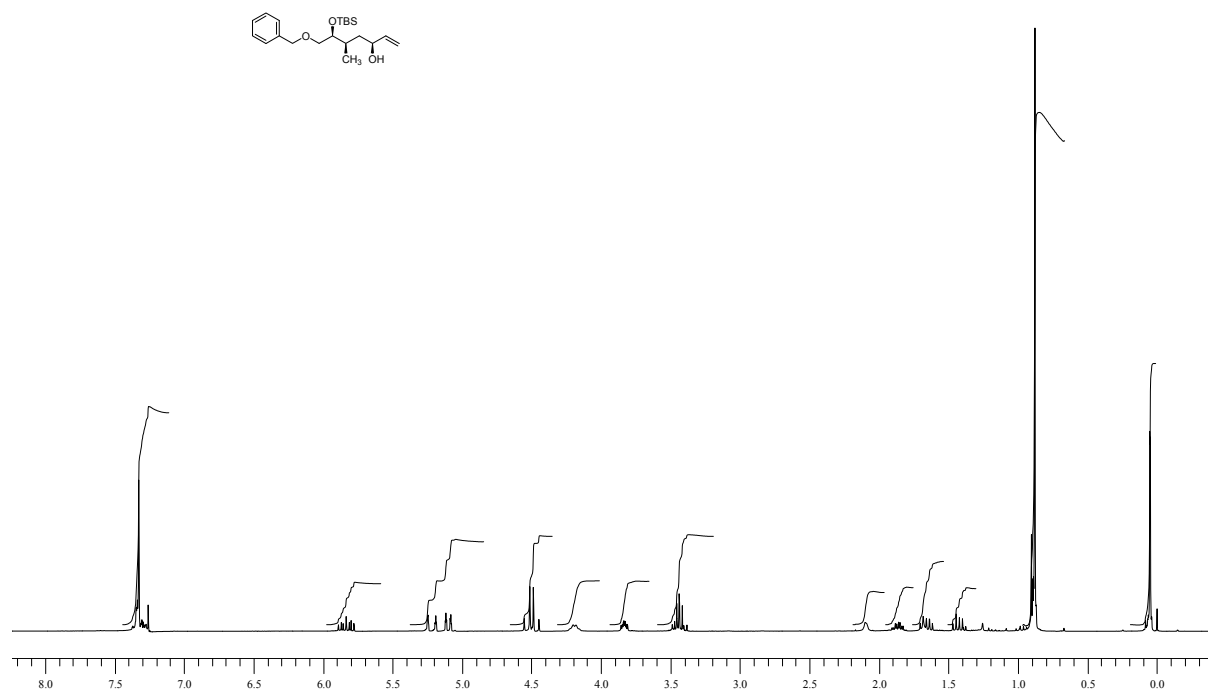
**<sup>1</sup>H NMR spectra of, 5a (300 MHz)**



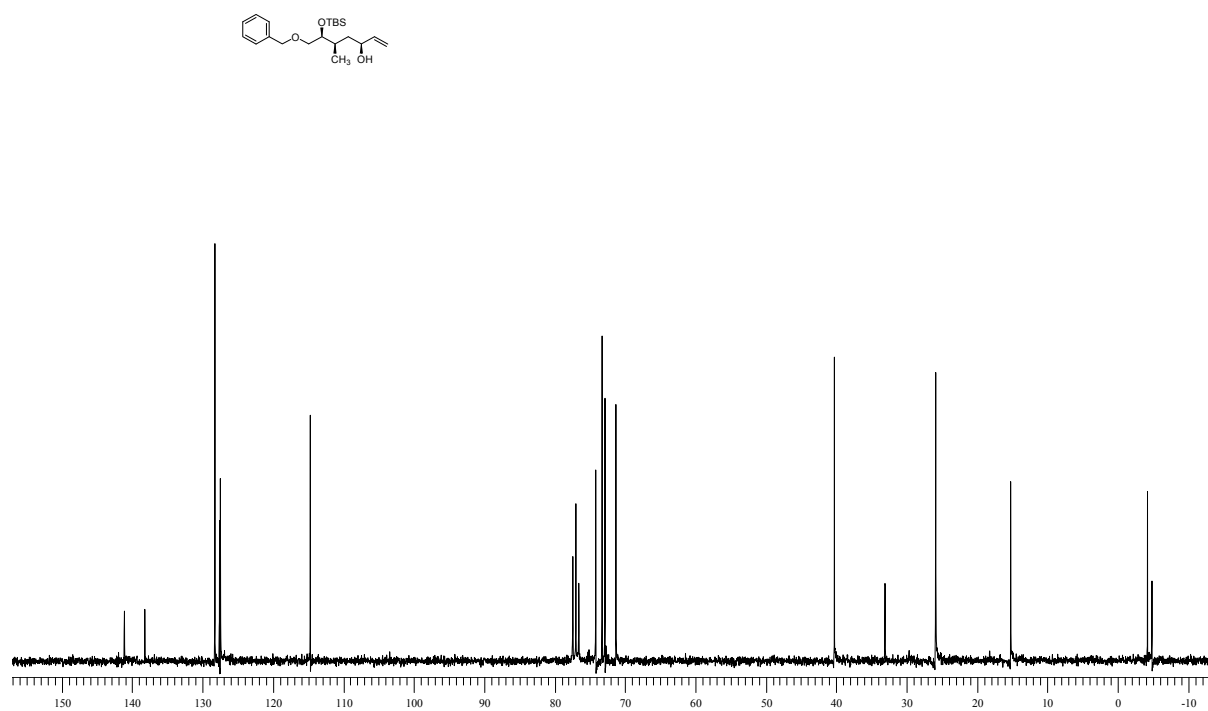
**<sup>13</sup>C NMR of compound, 5a (75 MHz)**



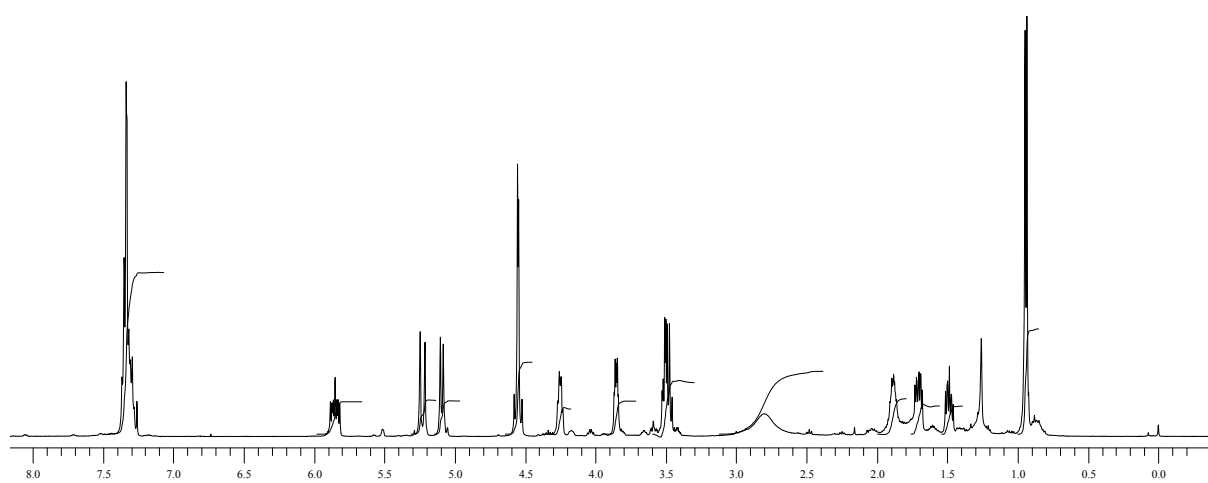
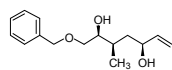
### $^1\text{H}$ NMR spectra (300 MHz)



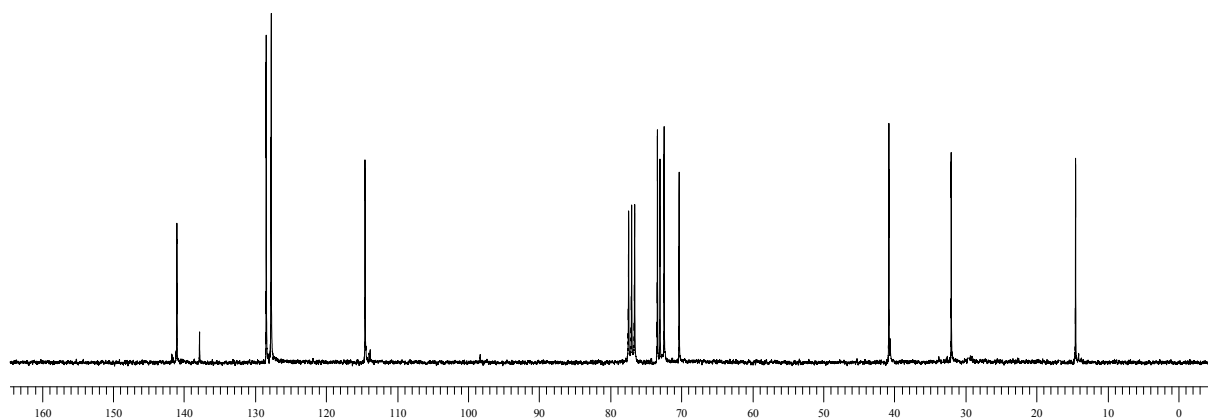
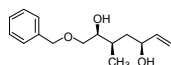
### $^{13}\text{C}$ NMR of compound (75 MHz)



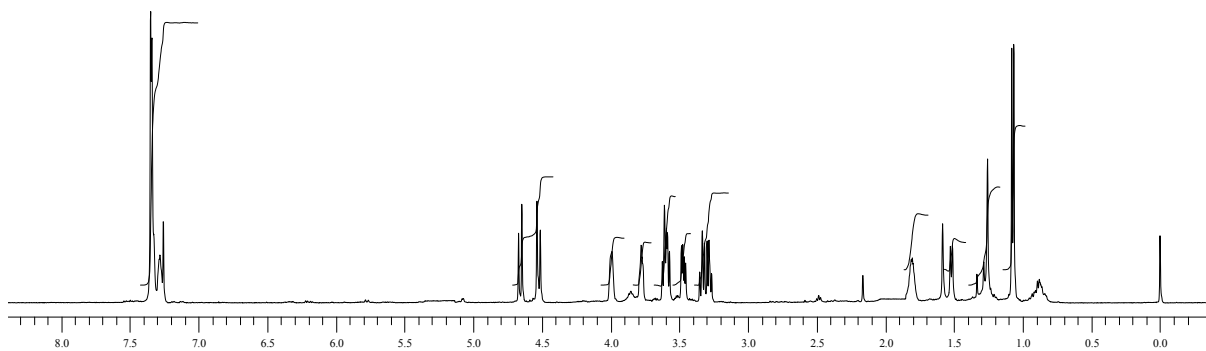
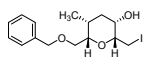
**<sup>1</sup>H NMR spectra of, 6a (300 MHz)**



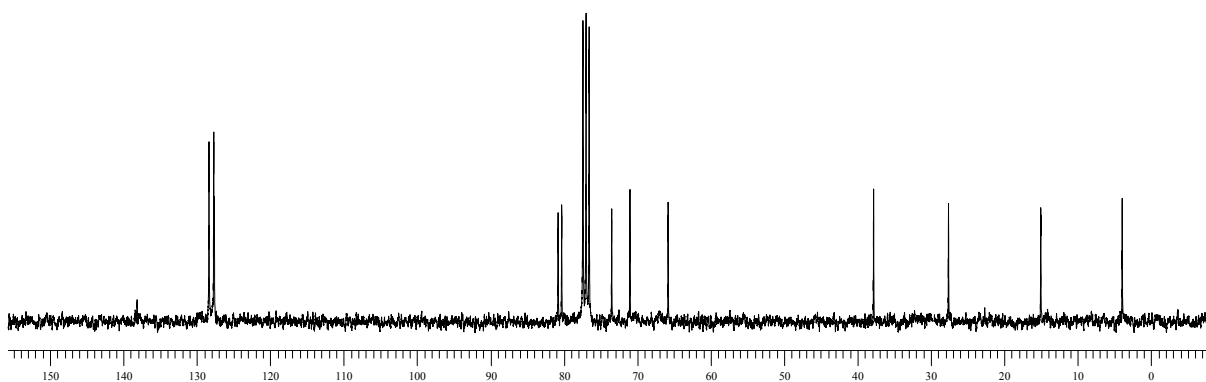
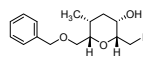
**<sup>13</sup>C NMR of compound, 6a (75 MHz)**



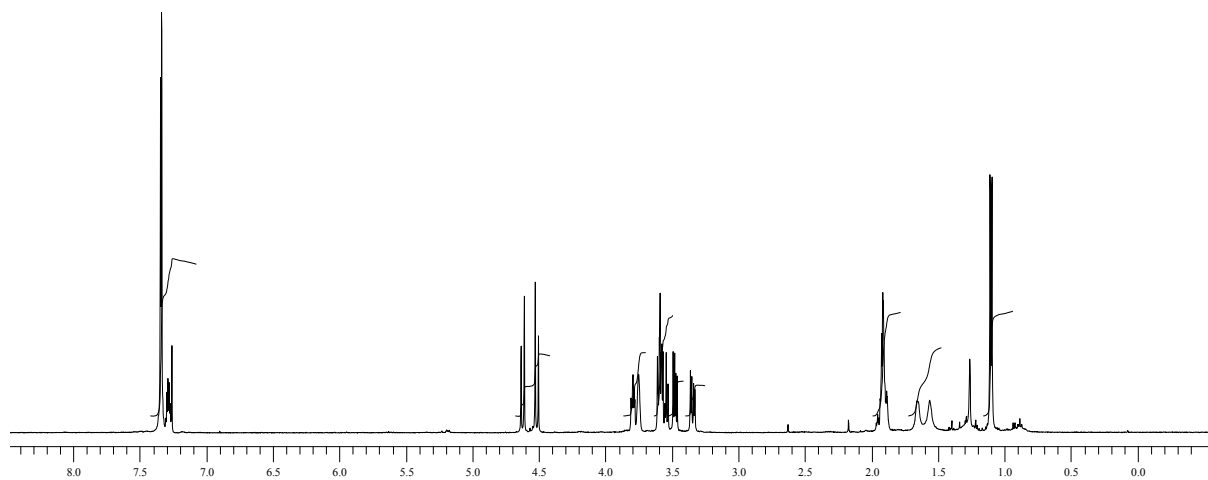
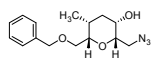
### $^1\text{H}$ NMR spectra of, 10 (300 MHz)



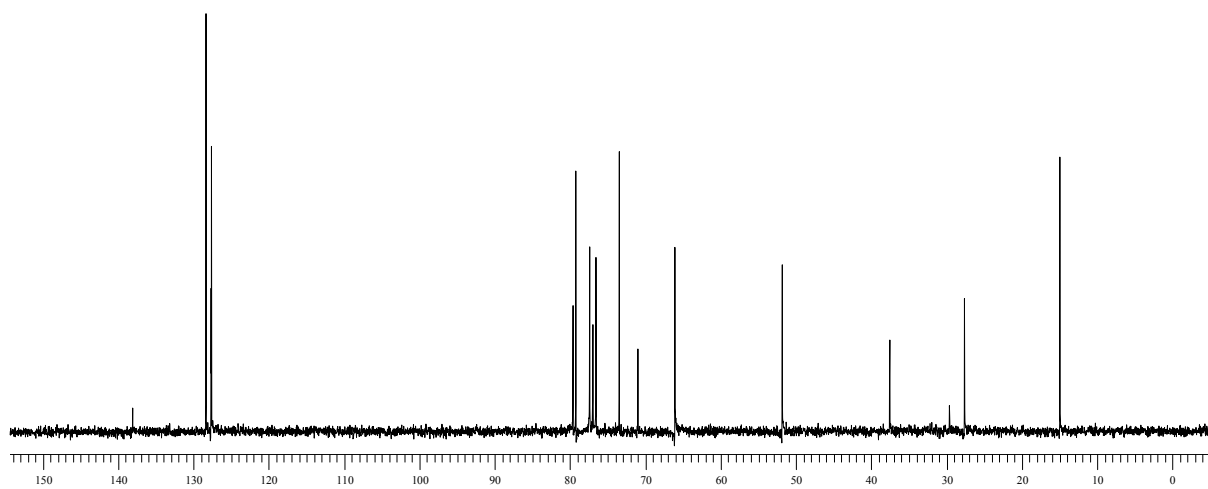
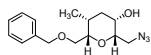
### $^{13}\text{C}$ NMR of compound, 10 (75 MHz)



### $^1\text{H}$ NMR spectra (300 MHz)

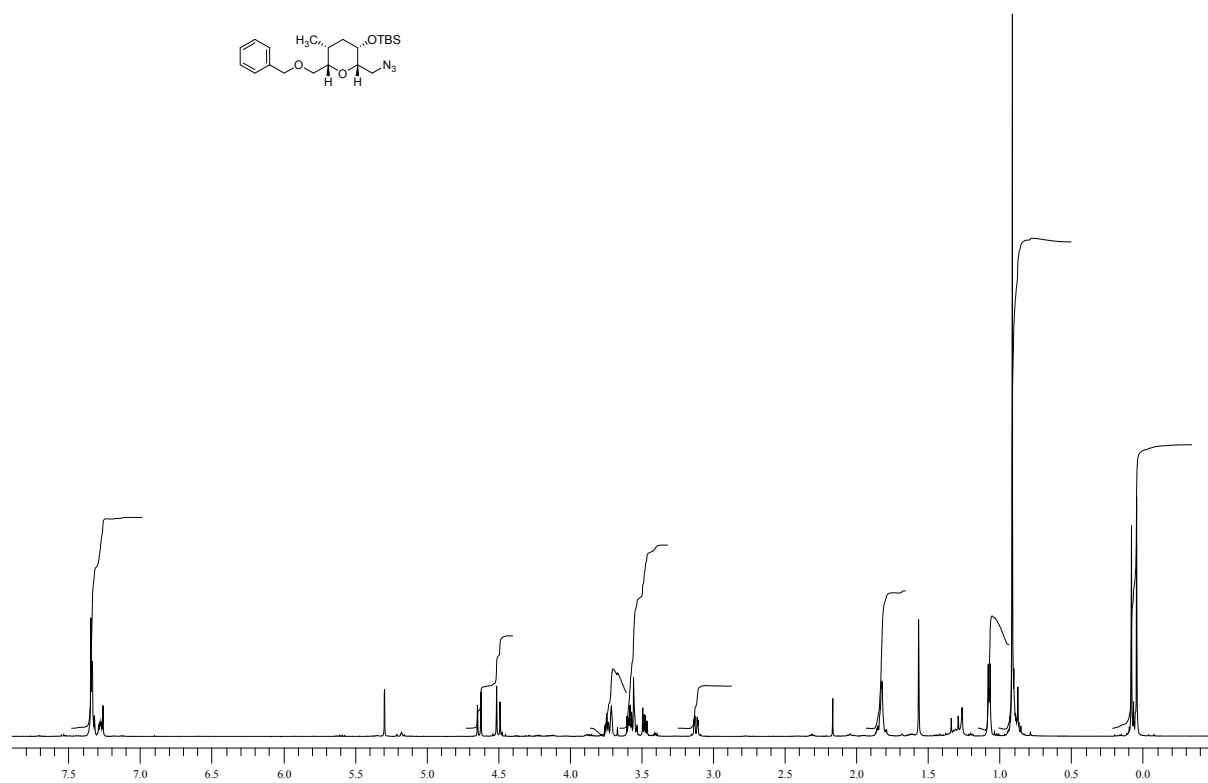


### $^{13}\text{C}$ NMR (75 MHz)

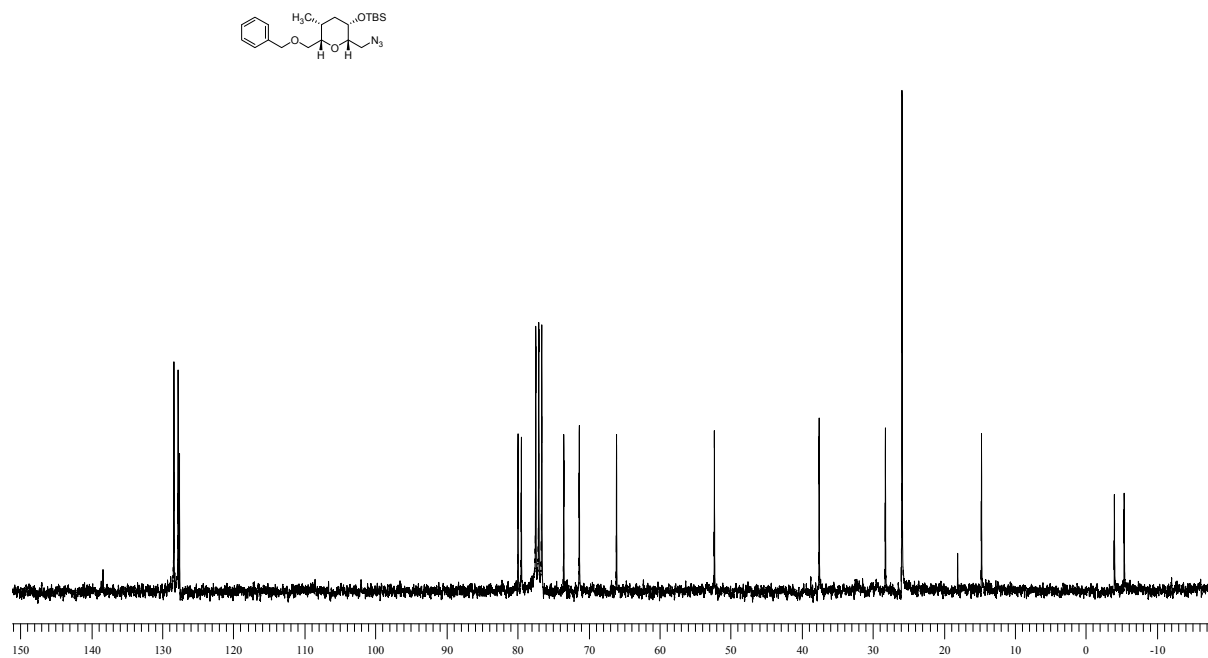




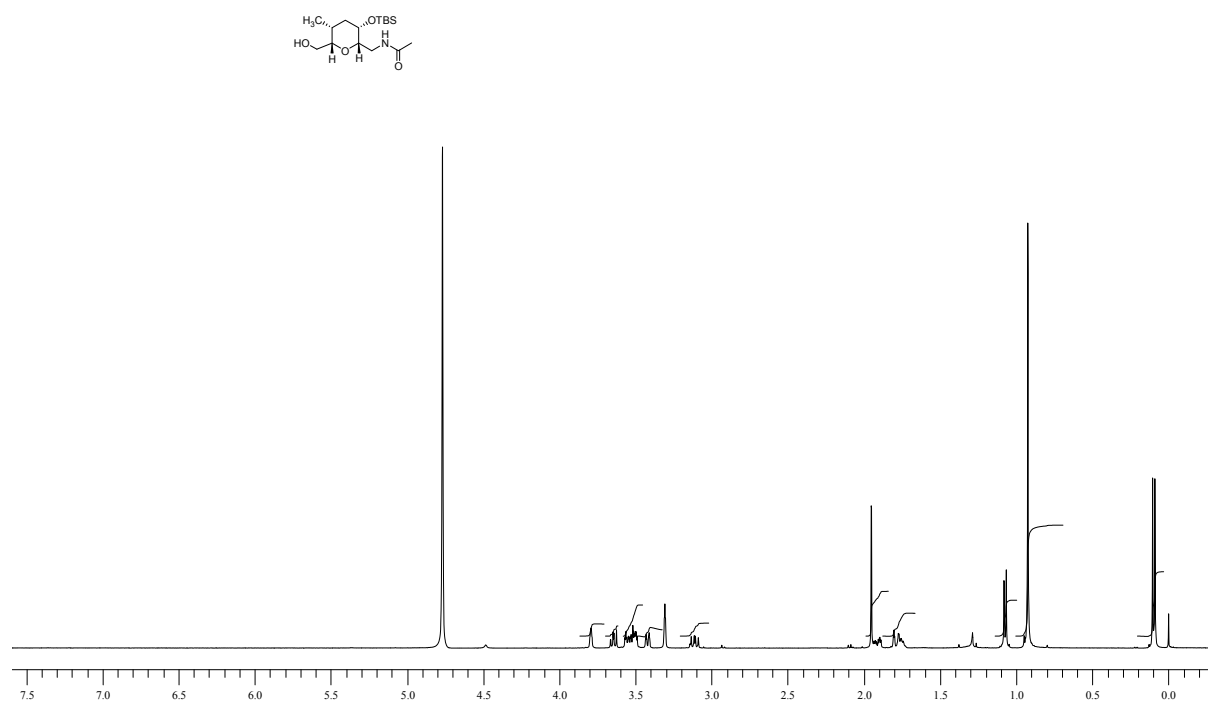
### $^1\text{H}$ NMR spectra (300 MHz)



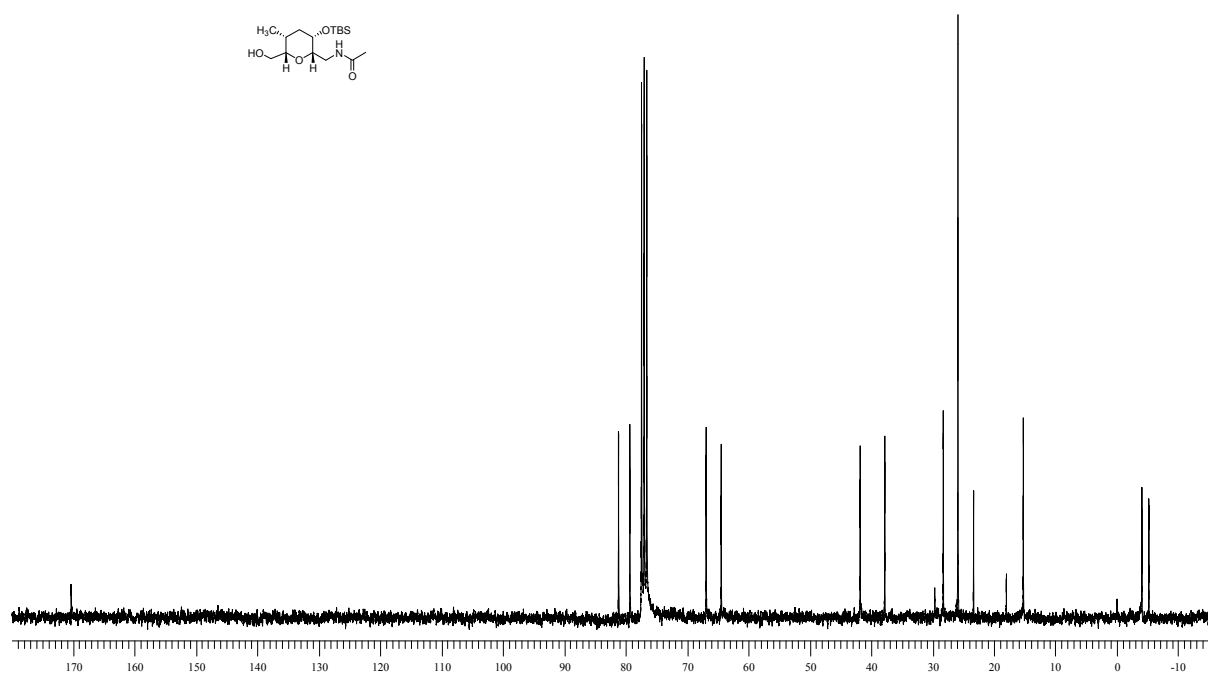
### $^{13}\text{C}$ NMR (75 MHz)



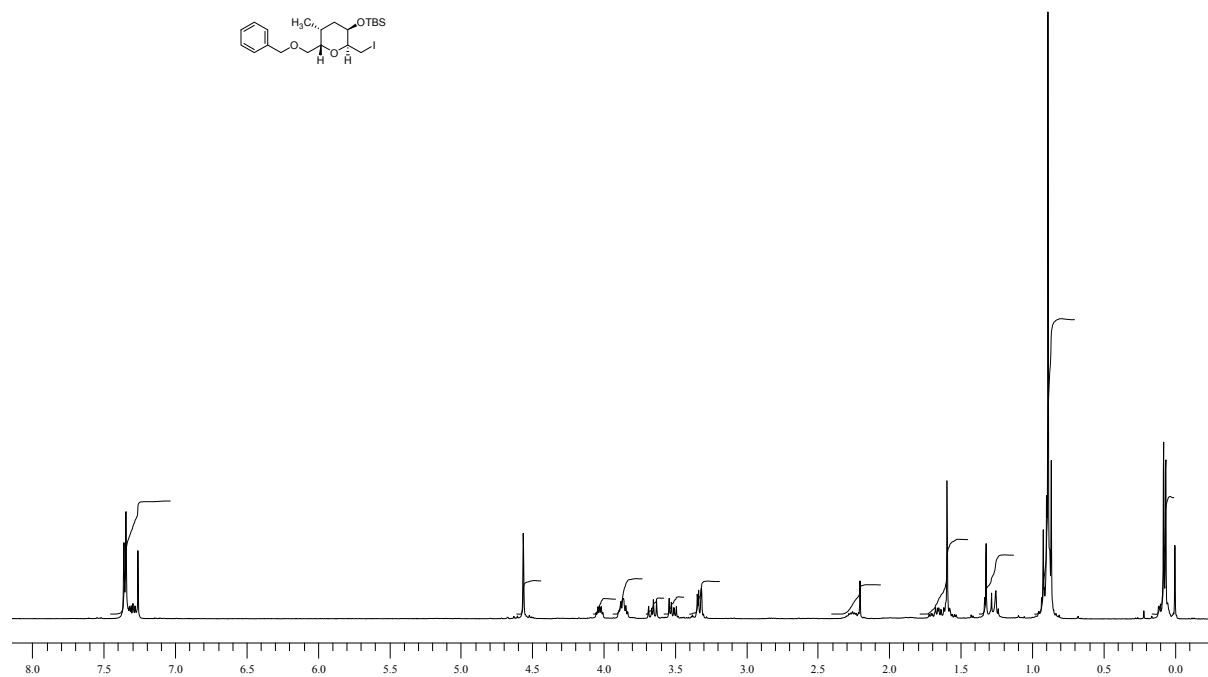
**$^1\text{H}$  NMR spectra of, 11 (300 MHz)**



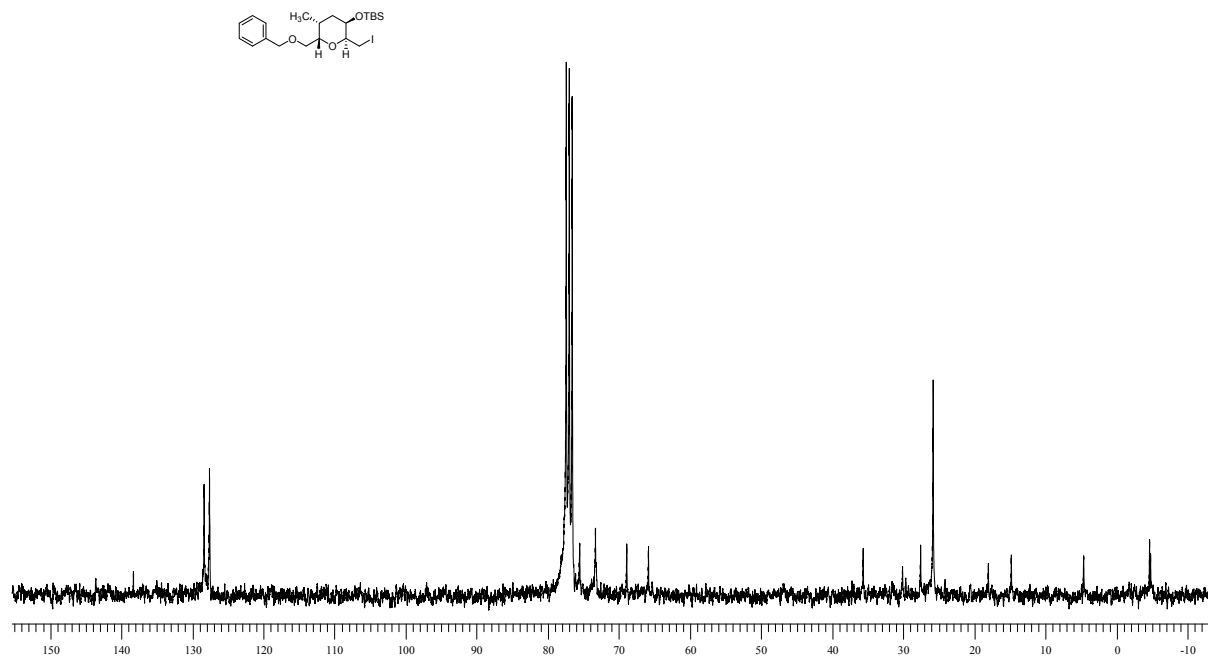
**$^{13}\text{C}$  NMR of compound, 11 (75 MHz)**



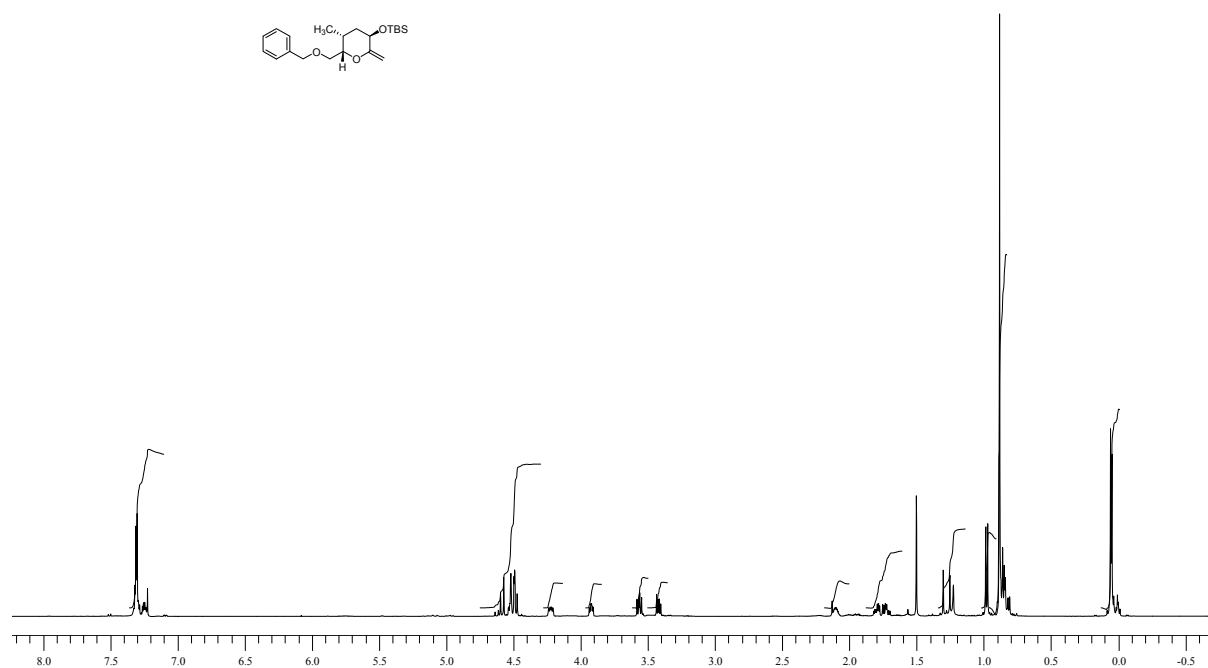
### <sup>1</sup>H NMR spectra (300 MHz)



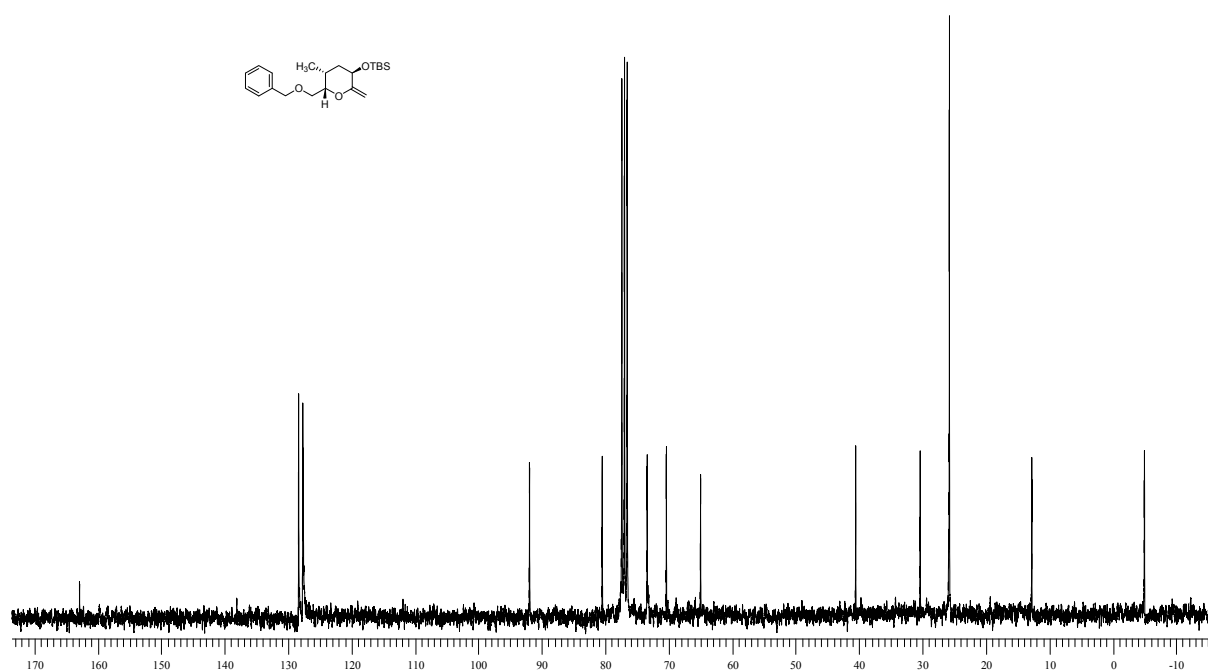
### <sup>13</sup>C NMR (75 MHz)



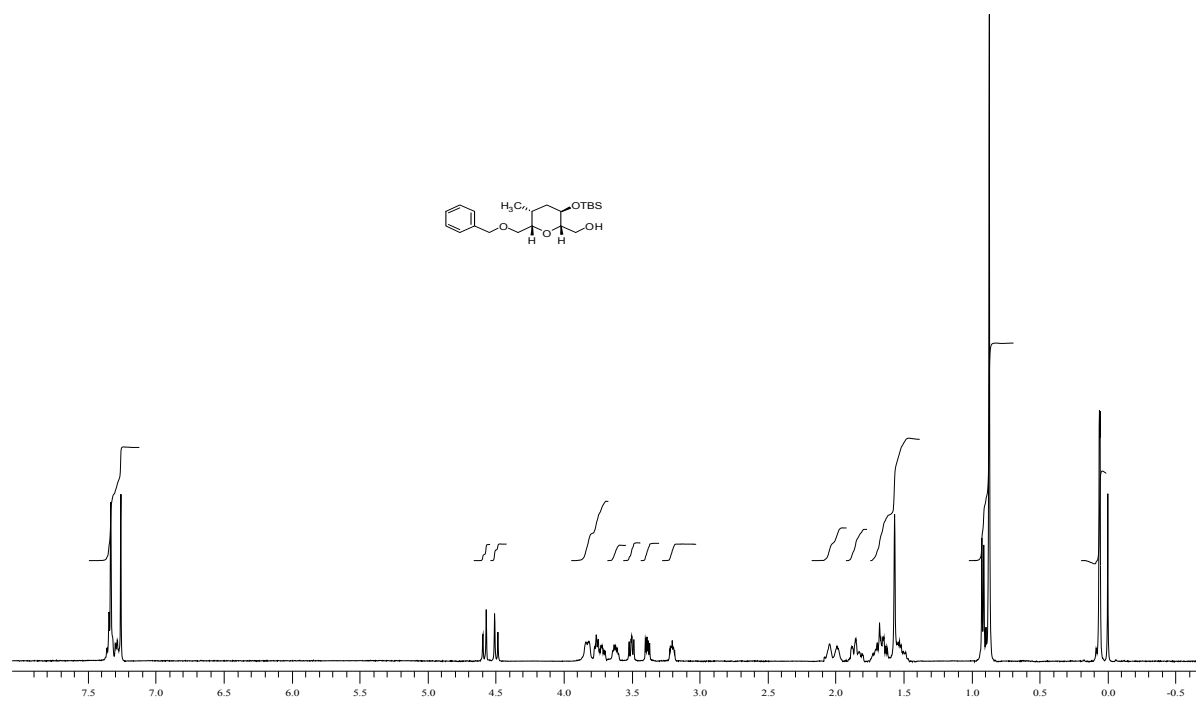
### $^1\text{H}$ NMR spectra of, 12 (300 MHz)



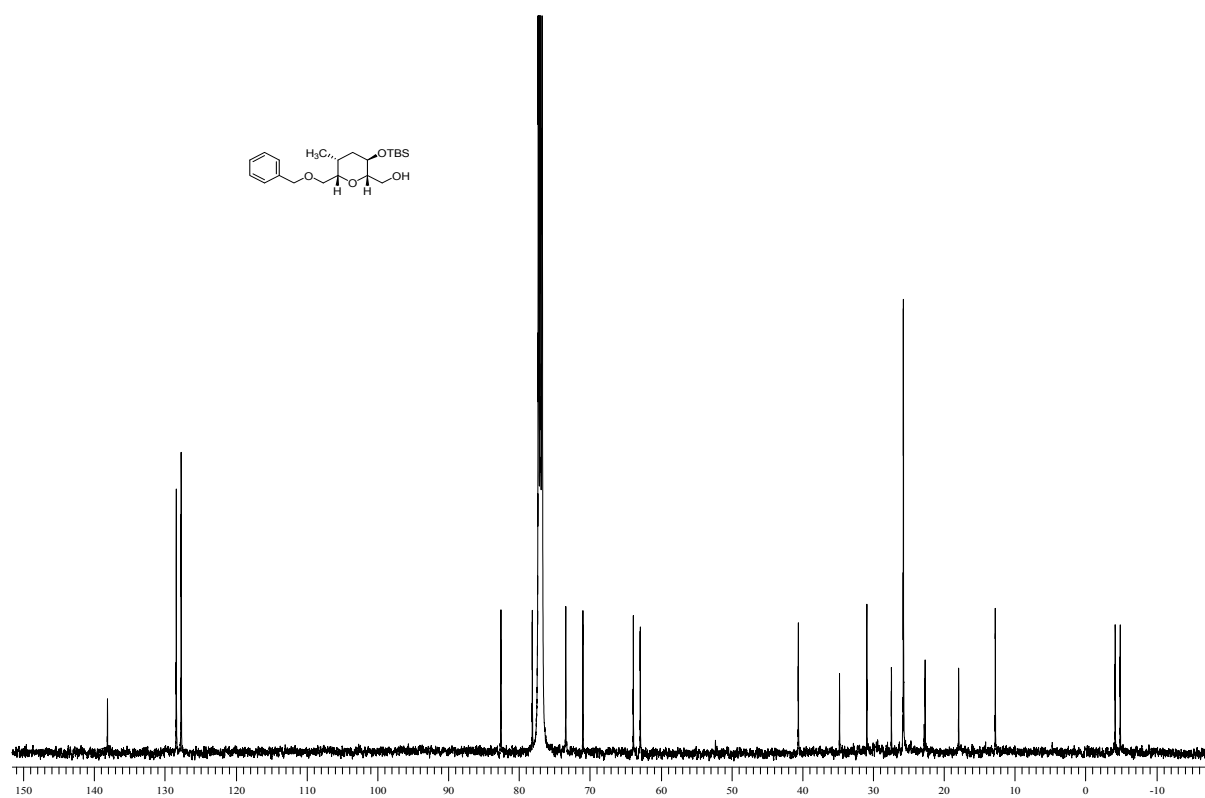
### $^{13}\text{C}$ NMR of compound, 12 (75 MHz)



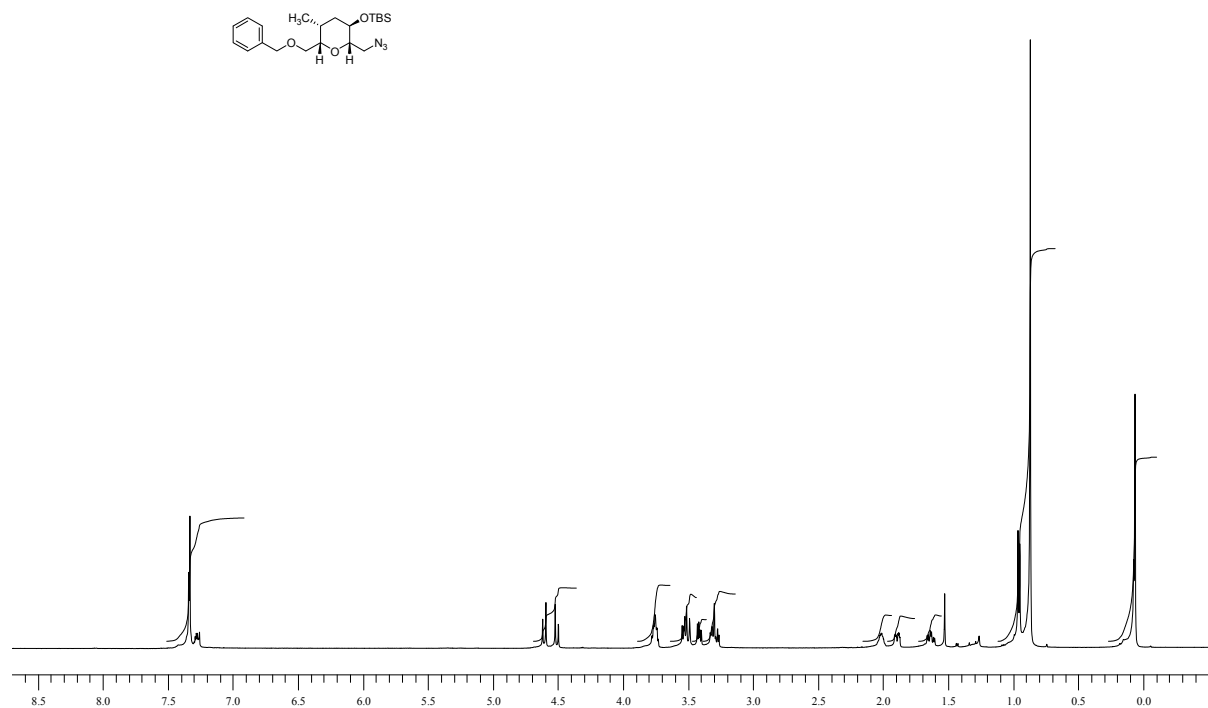
**<sup>1</sup>H NMR spectra of, 13 (300 MHz)**



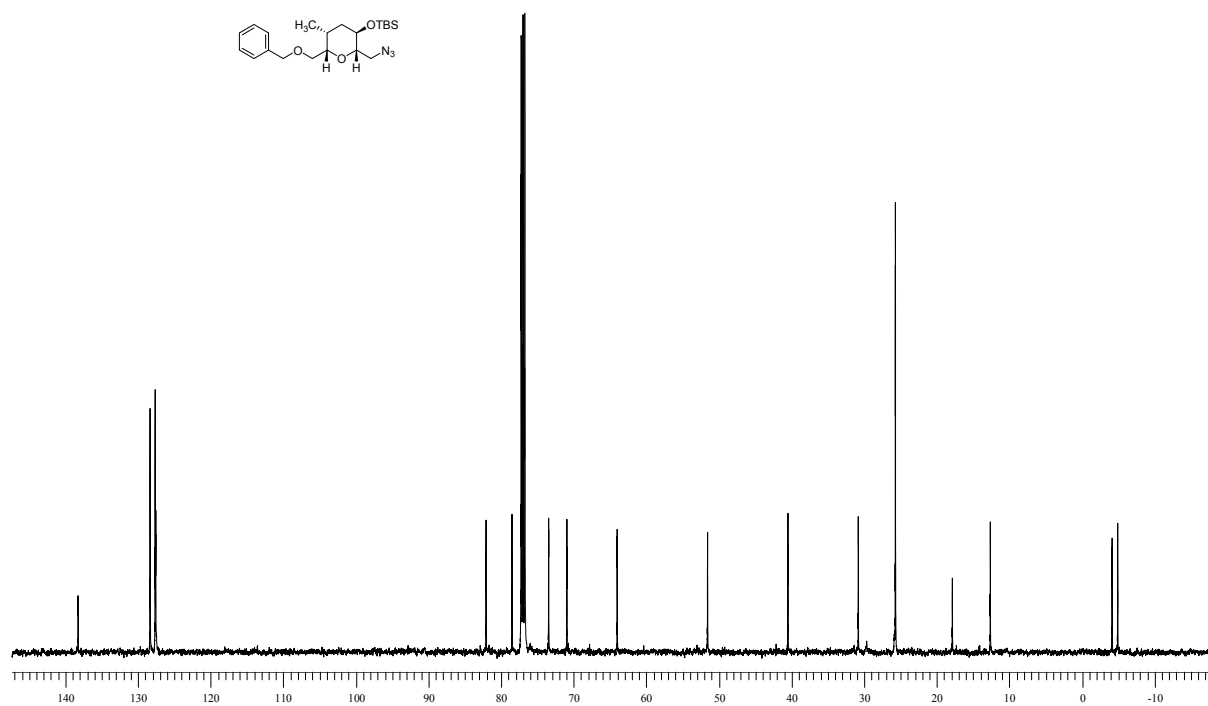
**<sup>13</sup>C NMR of compound, 13 (75 MHz)**



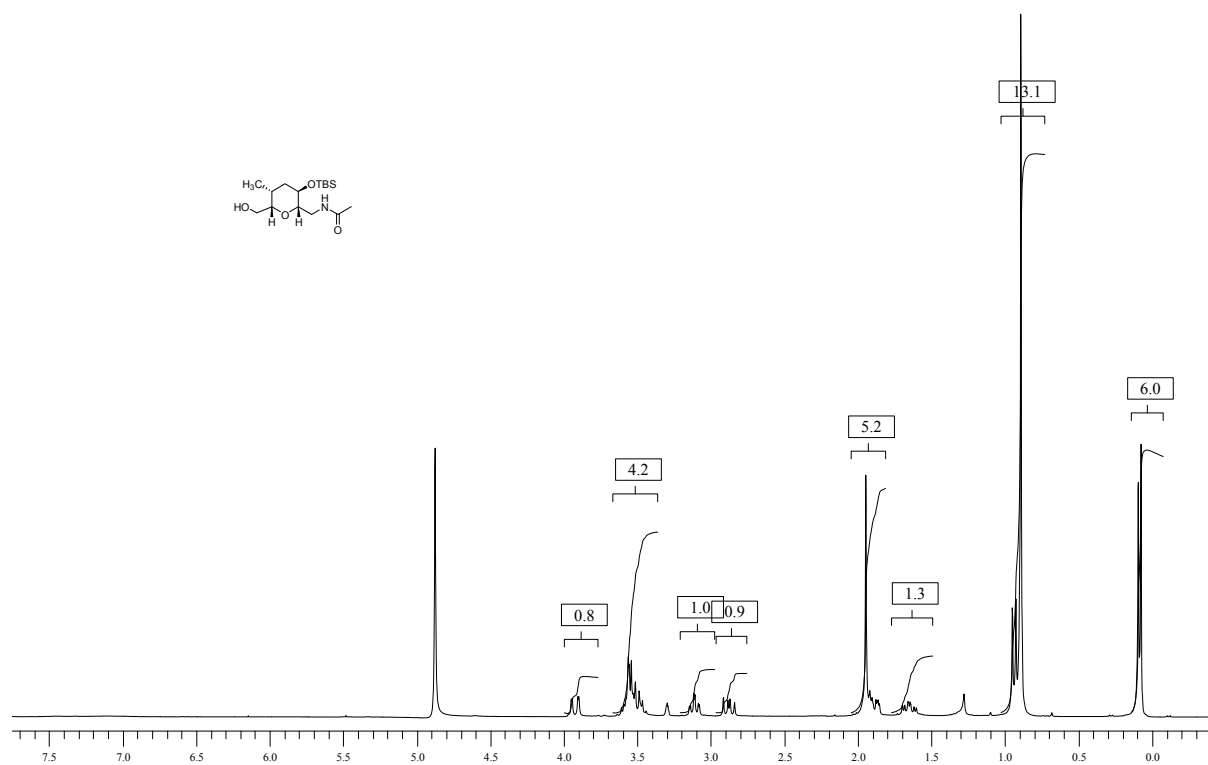
### $^1\text{H}$ NMR spectra of, 14 (300 MHz)



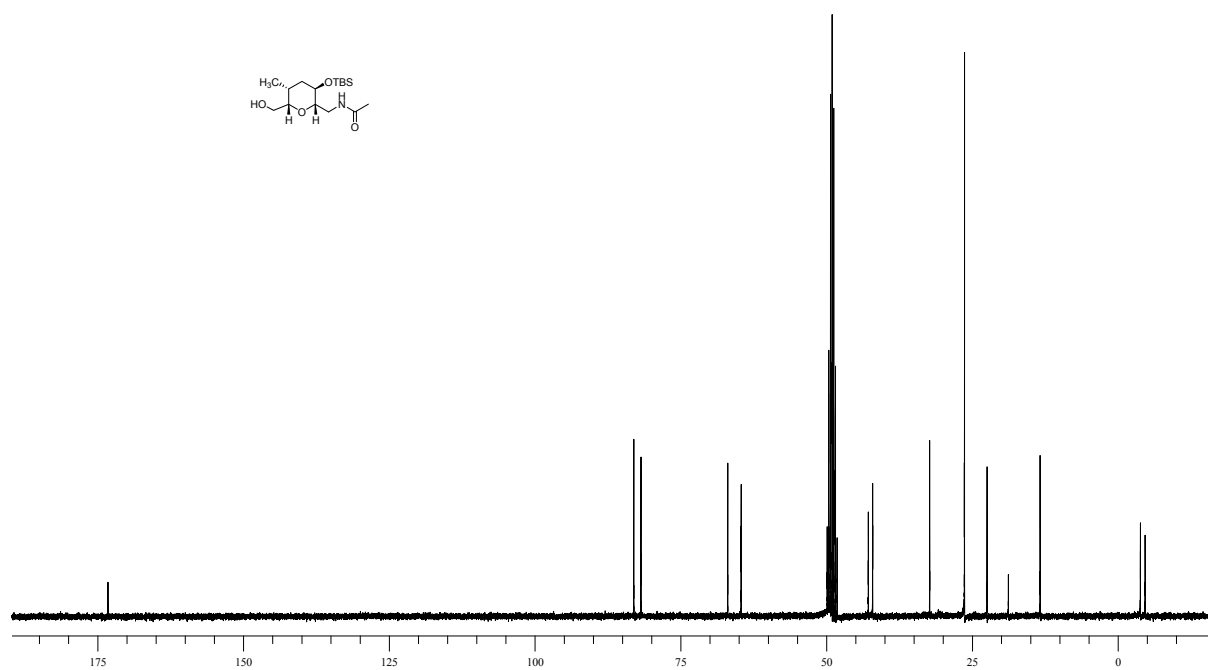
### $^{13}\text{C}$ NMR of compound, 14 (75 MHz)



**<sup>1</sup>H NMR spectra of, 15 (300 MHz)**

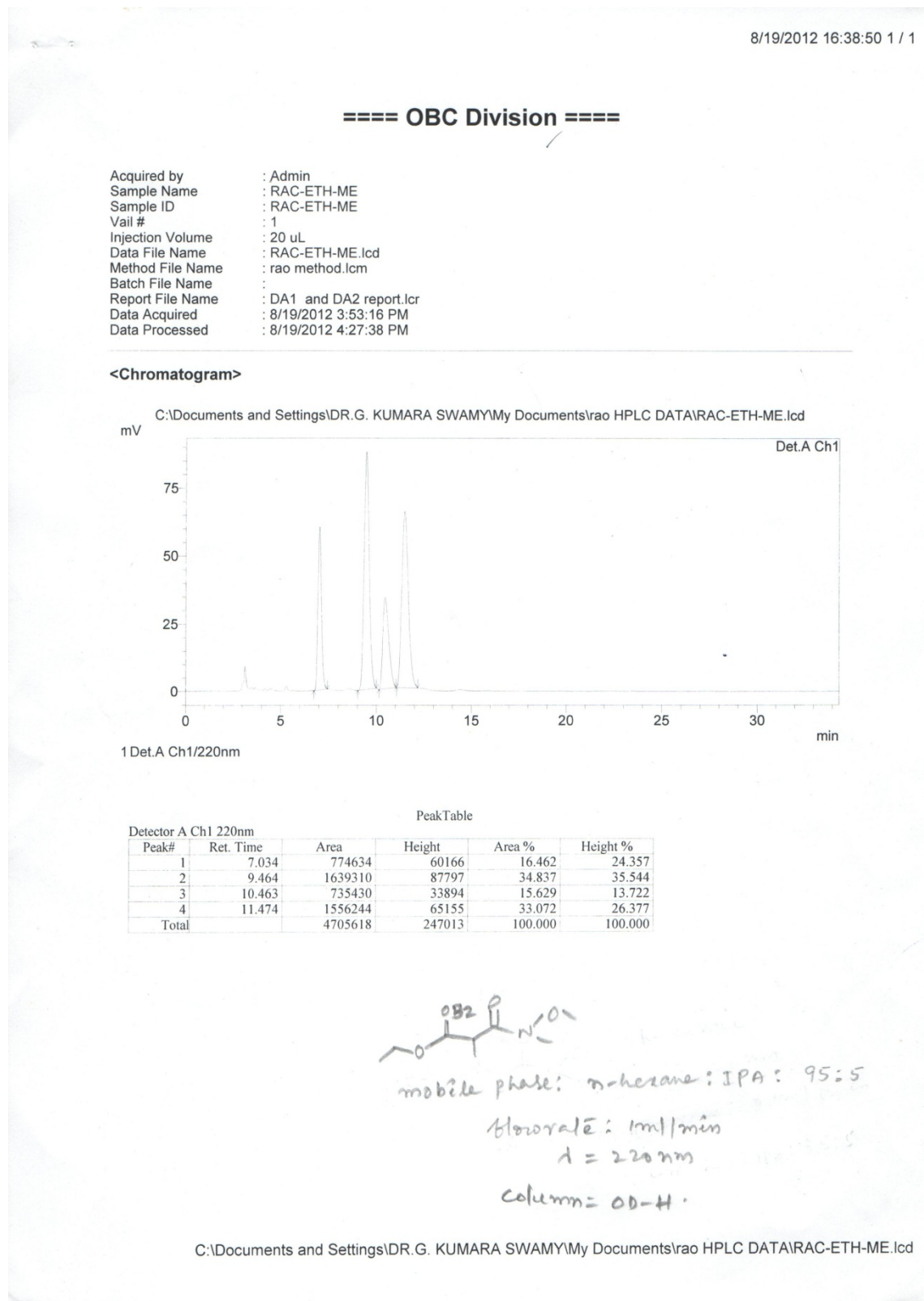


**<sup>13</sup>C NMR of compound, 15 (75 MHz)**



## HPLC data:

### HPLC of 3b, racemic:





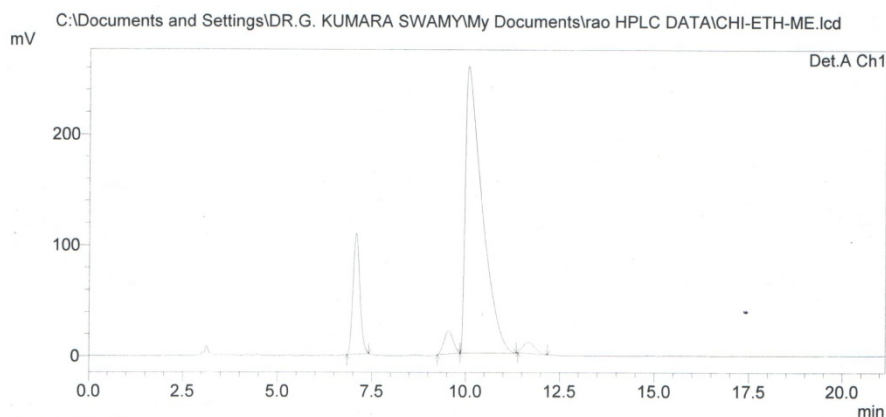
## HPLC of 3b, chiral:

8/19/2012 18:51:50 1 / 1

### ==== OBC Division ====

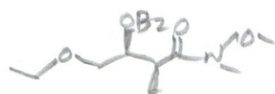
Acquired by : Admin  
Sample Name : CHI-ETH-ME  
Sample ID : CHI-ETH-ME  
Vial # : 1  
Injection Volume : 20 uL  
Data File Name : CHI-ETH-ME.lcd  
Method File Name : rao method.lcm  
Batch File Name :  
Report File Name : DA1 and DA2 report.lcr  
Data Acquired : 8/19/2012 6:25:51 PM  
Data Processed : 8/19/2012 6:47:02 PM

#### <Chromatogram>



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.075	1388340	108777	13.932	27.351
2	9.546	349919	20602	3.512	5.180
3	10.063	8012768	258605	80.410	65.024
4	11.668	213847	9721	2.146	2.444
Total		9964874	397705	100.000	100.000



mobile phase: n-hexane: IPA: 95:5

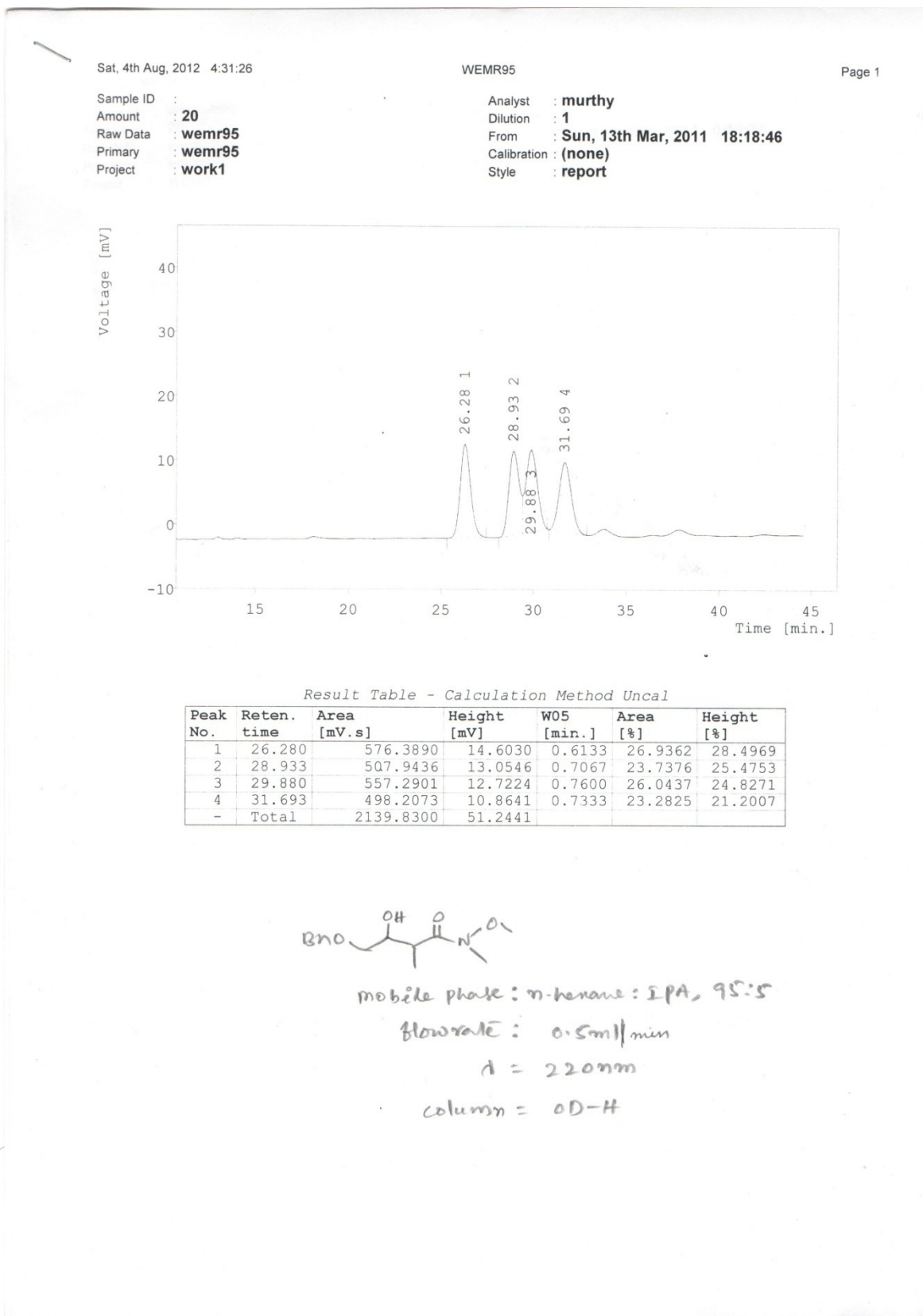
flow rate: 1ml/min

$\lambda = 220\text{nm}$

column = OD-H

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### HPLC of 3c, racemic:



### HPLC of 3c, chiral:

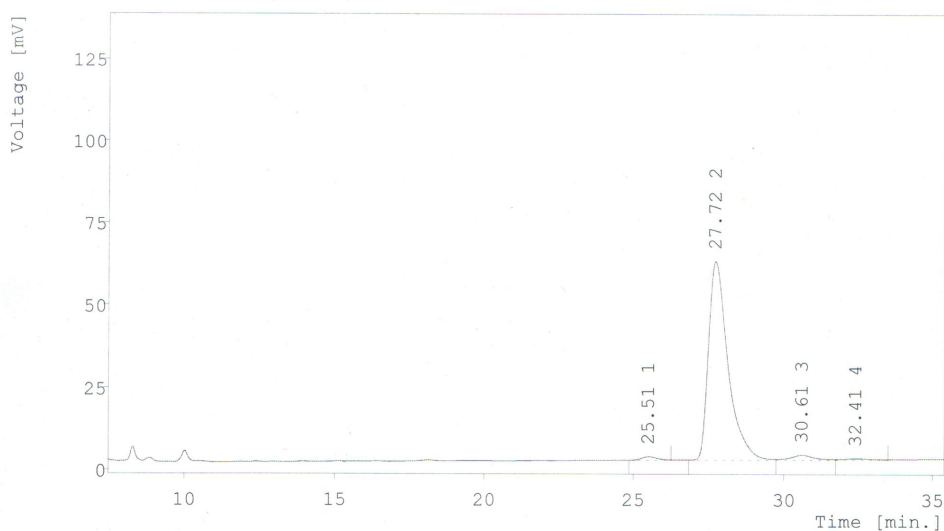
Sun, 14th Oct. 2012 12:44:48

WEMC95

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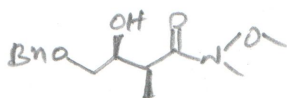
Sample ID : **wemch95**  
Amount : **20**  
Raw Data : **wemc95**  
Primary : **wemc95**  
Project : **work1**

Analyst : **murthy**  
Dilution : **1**  
From : **Mon, 14th Mar, 2011 0:10:24**  
Calibration : **(none)**  
Style : **report**



Result Table - Calculation Method Uncal

Peak No.	Reten. time	Area [mV.s]	Height [mV]	W05 [min.]	Area [%]	Height [%]
1	25.507	36.1390	1.0606	0.5600	1.2711	1.6769
2	27.720	2717.3407	60.4085	0.6667	95.5727	95.5093
3	30.613	73.2524	1.4512	0.7333	2.5764	2.2945
4	32.413	16.4875	0.3285	0.8000	0.5798	0.5193
-	Total	2843.2196	63.2488			



mobile phase : n-hexane : IPA, 95:5

flowrate : 0.5 ml/min

$\lambda$  = 220 nm

column = OD-H

### HPLC of 3d, racemic:

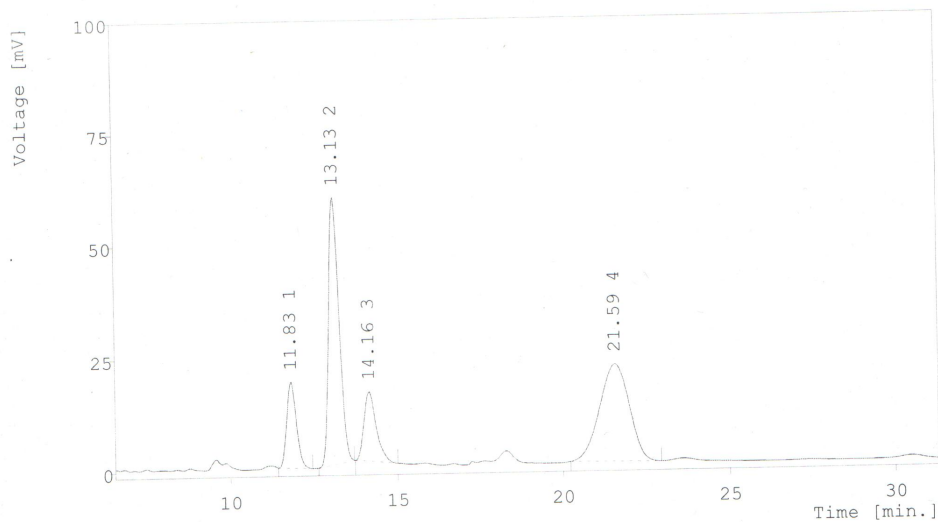
Sun, 14th Oct, 2012 12:14:14

RAETAS

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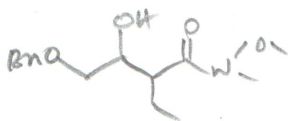
Sample ID : **worstet**  
Sample : **worstet**  
Amount : **20**  
Raw Data : **raetas**  
Primary : **raetas**  
Project : **work1**

Analyst : **murthy**  
Dilution : **1**  
From : **Fri, 3rd Aug, 2012 15:16:34**  
Calibration : **(none)**  
Style : **report**



Result Table - Calculation Method Uncal

Peak No.	Reten. time	Area [mV.s]	Height [mV]	W05 [min.]	Area [%]	Height [%]
1	11.827	389.1180	19.0589	0.3200	11.3823	16.5318
2	13.133	1287.7686	59.2194	0.3467	37.6692	51.3672
3	14.160	401.0742	15.3832	0.4000	11.7320	13.3434
4	21.587	1340.6615	21.6250	1.0000	39.2165	18.7576
-	Total	3418.6223	115.2866			



mobile phase: n-hexane : IPA, 95 : 5

flow rate: 1 ml/min

d = 220 mm

column = AS-H

### HPLC of 3d, chiral:

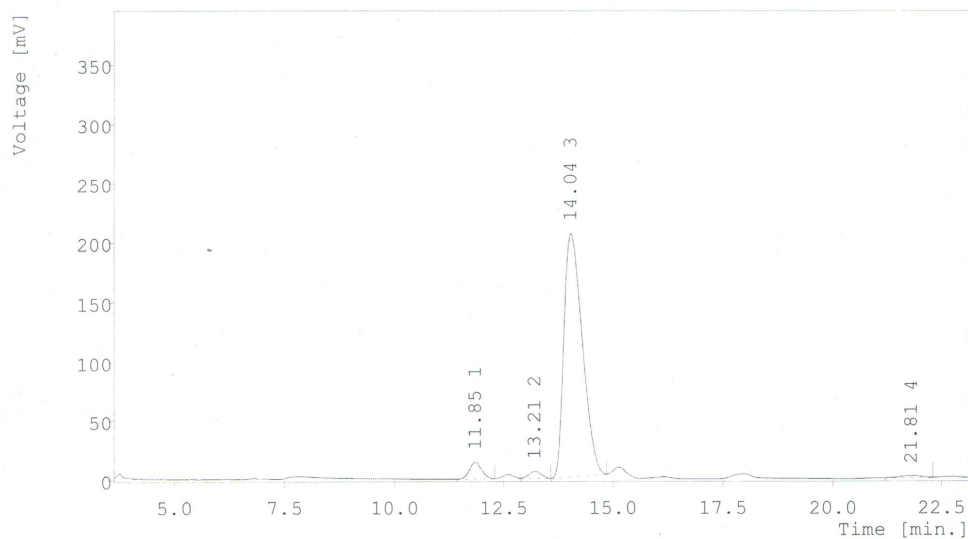
Sun, 14th Oct, 2012 12:21:19

CHETAS

Page 1

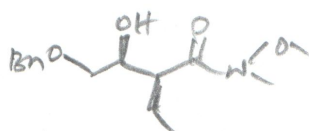
Sample ID : **raetas**  
Sample : **raetas**  
Amount : **20**  
Raw Data : **chetas**  
Primary : **chetas**  
Project : **work1**

Analyst : **murthy**  
Dilution : **1**  
From : **Fri, 3rd Aug, 2012 15:56:31**  
Calibration : **(none)**  
Style : **report**



Result Table - Calculation Method Uncal

Peak No.	Reten. time	Area [mV.s]	Height [mV]	W05 [min.]	Area [%]	Height [%]
1	11.853	279.5454	14.1352	0.3200	4.3385	6.2189
2	13.213	113.5960	5.9111	0.3333	1.7630	2.6006
3	14.040	5998.9375	205.5901	0.4800	93.1022	90.4502
4	21.813	51.3076	1.6601	0.5067	0.7963	0.7303
-	Total	6443.3864	227.2965			



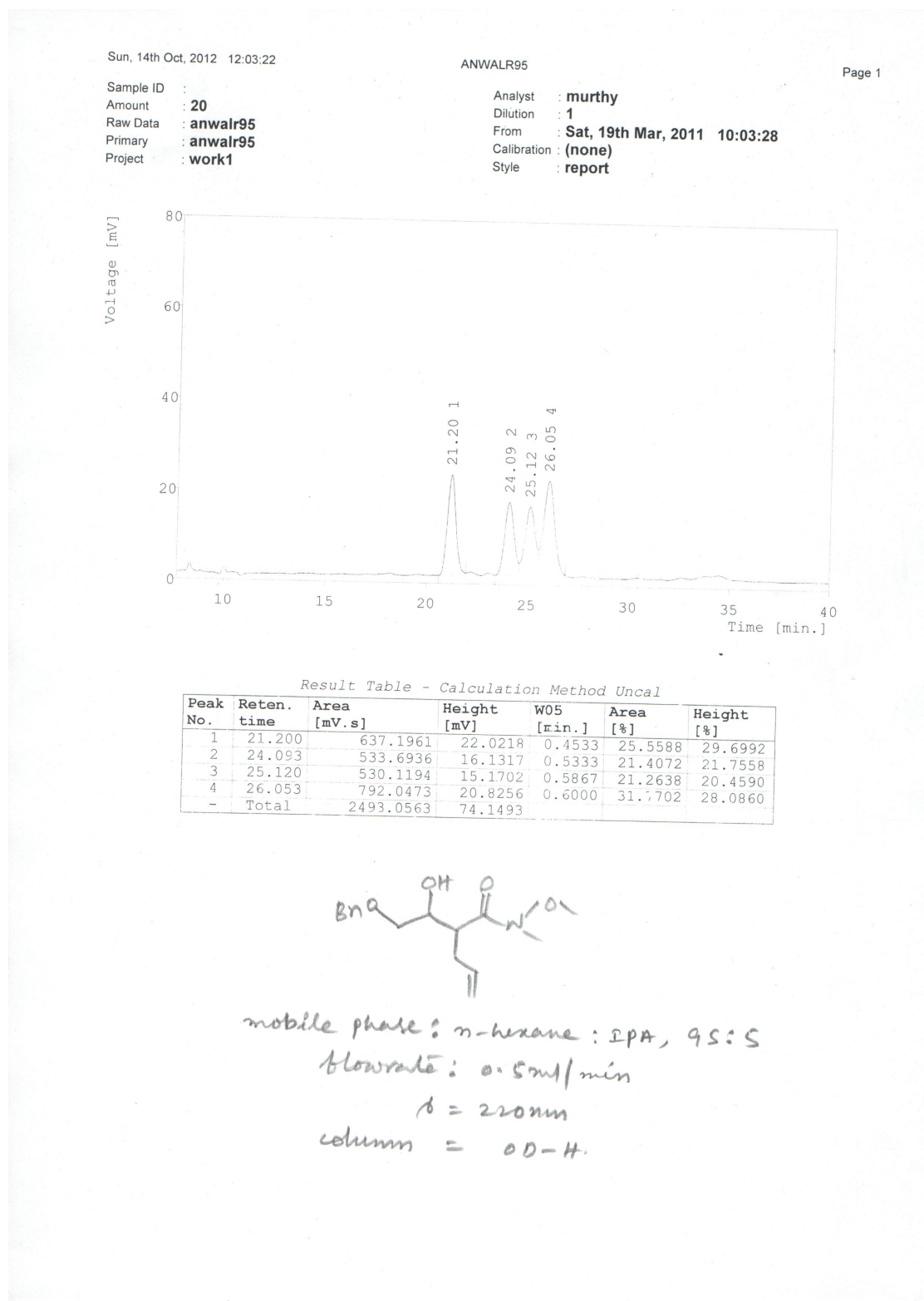
mobile phase: n-hexane: IPA, 95:5

flowrate: 1ml/min

d = 220nm

column = AS-H

### HPLC of 3e, racemic:



## HPLC of 3e, chiral:

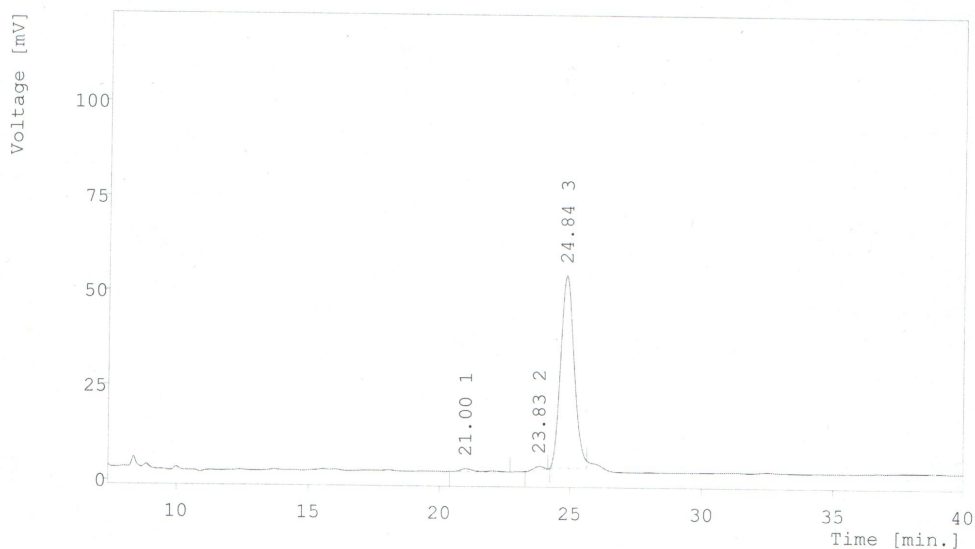
Sun, 14th Oct, 2012 12:06:56

ANWALC95

Page 1

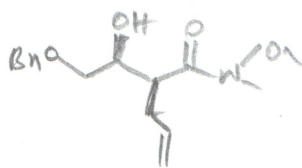
Sample ID : **anwalr95**  
Amount : **20**  
Raw Data : **anwalc95**  
Primary : **anwalc95**  
Project : **work1**

Analyst : **murthy**  
Dilution : **1**  
From : **Sat, 19th Mar, 2011 11:43:50**  
Calibration : **(none)**  
Style : **report**



Result Table - Calculation Method Uncal

Peak No.	Reten. time	Area [mV.s]	Height [mV]	W05 [min.]	Area [%]	Height [%]
1	21.000	30.8516	0.7671	0.4933	1.6431	1.4576
2	23.827	24.5156	0.9825	0.4267	1.3056	1.8670
3	24.840	1822.3102	50.8755	0.5733	97.0513	96.6754
-	Total	1877.6774	52.6251			



mobile phase : n-hexane : IPA, 95 : 5

flowrate : 0.5 ml/min,

d = 220 nm

column = OD-H.

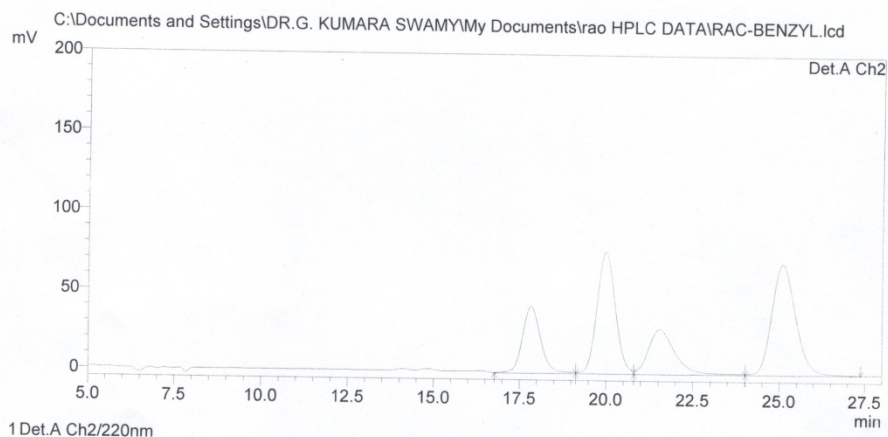
### HPLC of 3f, racemic:

9/19/2012 11:21:15 1 / 1

#### ==== OBC Division ====

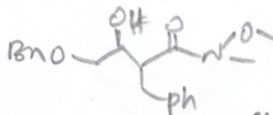
Acquired by : Admin  
Sample Name : RAC-BENZYL  
Sample ID : RAC-BENZYL  
Vial # : 1  
Injection Volume : 20 uL  
Data File Name : RAC-BENZYL.lcd  
Method File Name : purge.lcm  
Batch File Name :  
Report File Name : DA1 and DA2 report.lcr  
Data Acquired : 9/2/2012 4:09:54 PM  
Data Processed : 9/2/2012 4:47:01 PM

#### <Chromatogram>



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.824	1540337	41823	16.679	19.327
2	19.981	2817039	76673	30.504	35.431
3	21.537	1510370	28286	16.355	13.071
4	25.083	3367372	69618	36.463	32.171
Total		9235118	216400	100.000	100.000



mobile phase : hexane : PPA, 95 : 5  
flow rate : 0.8 ml/min  
d = 220nm  
column : AS-H.

C:\Documents and Settings\DR.G. KUMARA SWAMY\My Documents\rao HPLC DATA\RAC-BENZYL.lcd



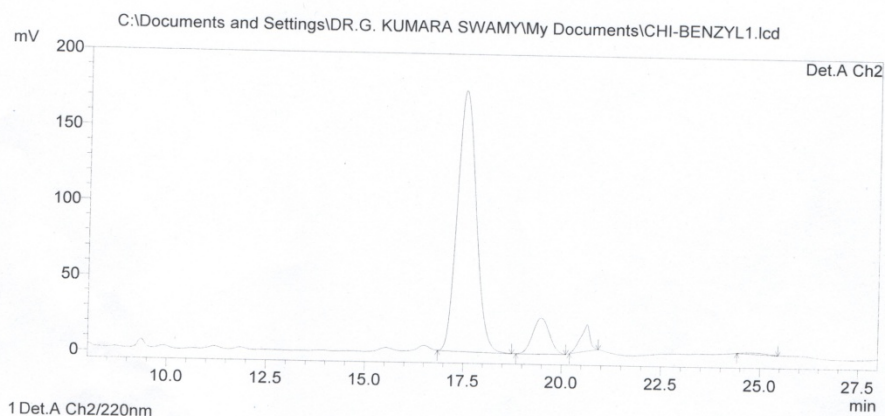
### HPLC of 3f, chiral:

9/19/2012 11:37:36 1 / 1

#### ==== OBC Division ====

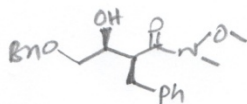
Acquired by : Admin  
Sample Name : CHI-BENZYL1  
Sample ID : CHI-BENZYL1  
Vial # : 1  
Injection Volume : 20 uL  
Data File Name : CHI-BENZYL1.lcd  
Method File Name : purge.lcm  
Batch File Name :  
Report File Name : DA1 and DA2 report.lcr  
Data Acquired : 9/2/2012 8:05:36 PM  
Data Processed : 9/2/2012 8:37:02 PM

#### <Chromatogram>



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.501	5772578	173124	84.965	80.422
2	19.477	700291	23952	10.307	11.126
3	20.643	285952	17302	4.209	8.037
4	24.726	35235	892	0.519	0.414
Total		6794056	215270	100.000	100.000



mobile phase: hexane: IPA, 95:5

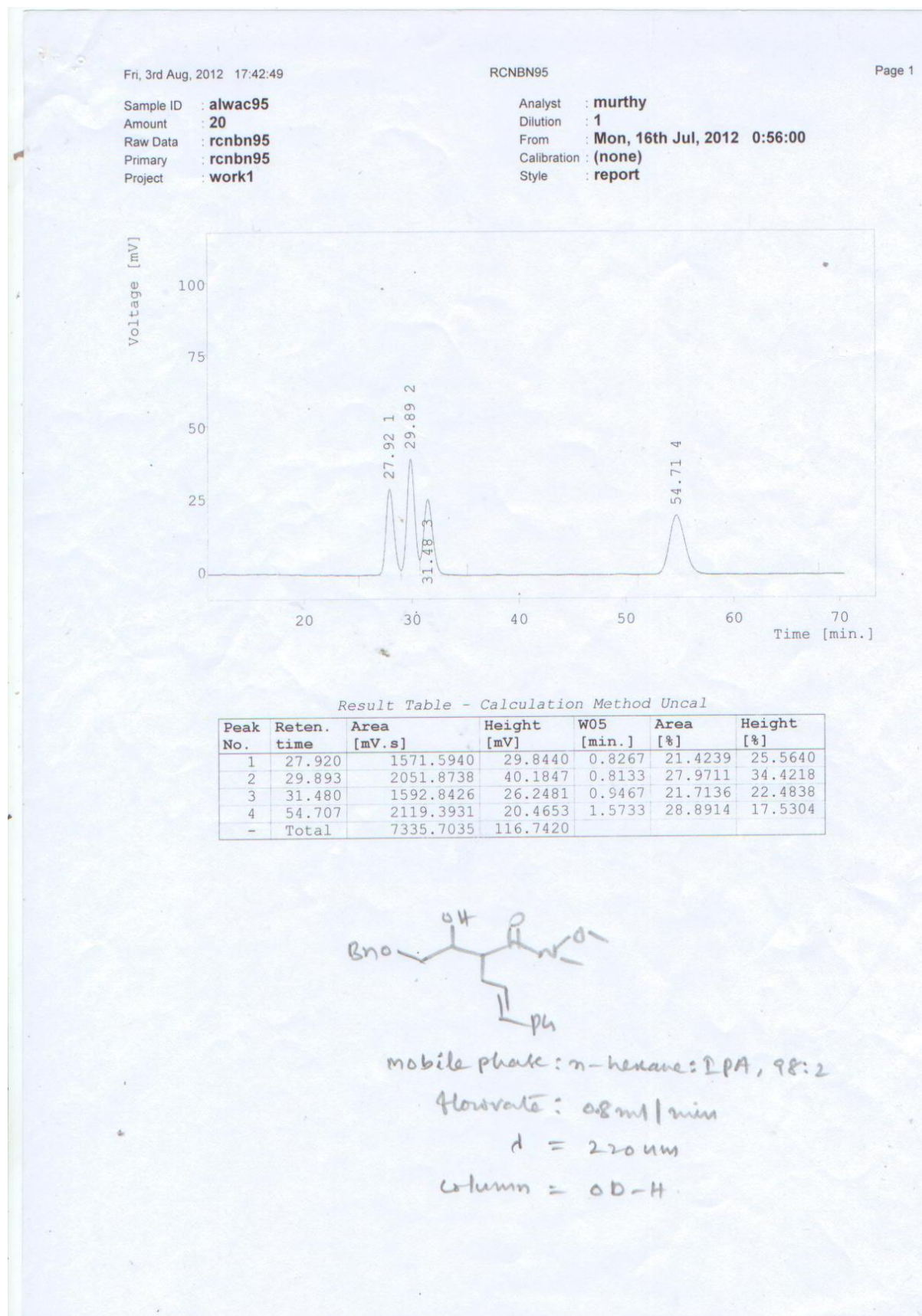
flowrate: 0.8 ml/min

$\lambda = 220\text{nm}$

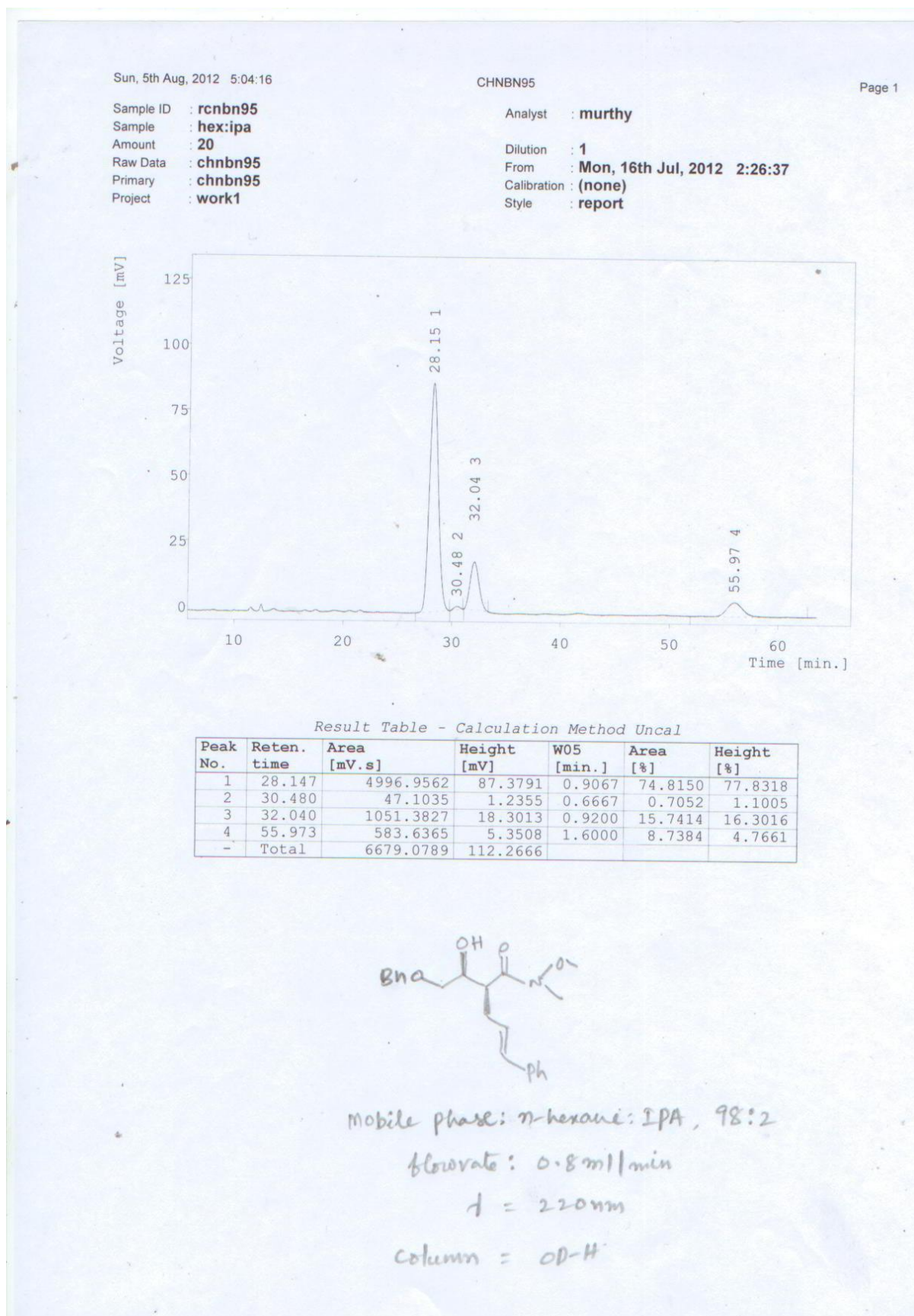
column: AS-H

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HPLC of 3g, racemic:



### HPLC of 3g, chiral:



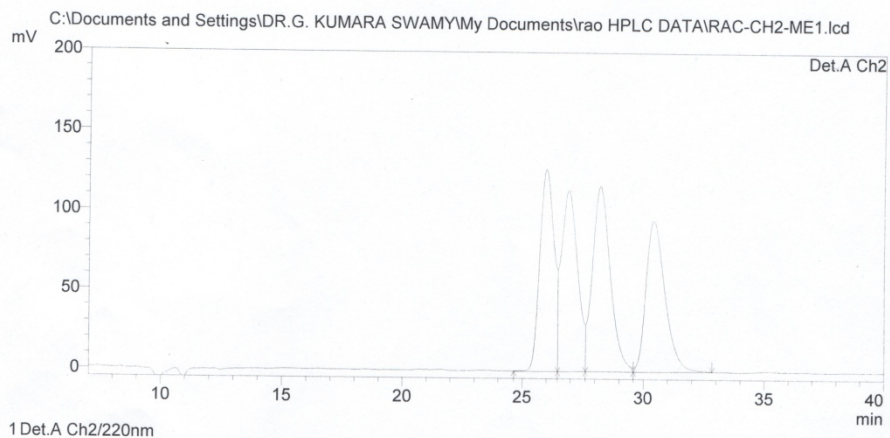
### HPLC of 3h, racemic:

9/19/2012 11:01:38 1 / 1

#### ==== OBC Division ====

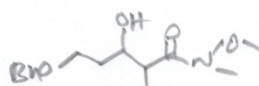
Acquired by : Admin  
Sample Name : RAC-CH2-ME1  
Sample ID : RAC-CH2-ME1  
Vial # : 1  
Injection Volume : 20 uL  
Data File Name : RAC-CH2-ME1.lcd  
Method File Name : purge.lcm  
Batch File Name :  
Report File Name : DA1 and DA2 report.lcr  
Data Acquired : 9/1/2012 12:41:52 PM  
Data Processed : 9/1/2012 1:22:24 PM

#### <Chromatogram>



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.964	5160317	126795	23.750	28.051
2	26.894	5368838	113755	24.710	25.166
3	28.199	6001736	116452	27.623	25.763
4	30.411	5196476	95017	23.917	21.021
Total		21727366	452019	100.000	100.000



mobile phase: hexane: 2PA, 95:5

flowrate: 0.5 ml/min,

$\lambda = 220\text{nm}$ ,

column: OD-H.

C:\Documents and Settings\DR.G. KUMARA SWAMY\My Documents\rao HPLC DATA\RAC-CH2-ME1.lcd

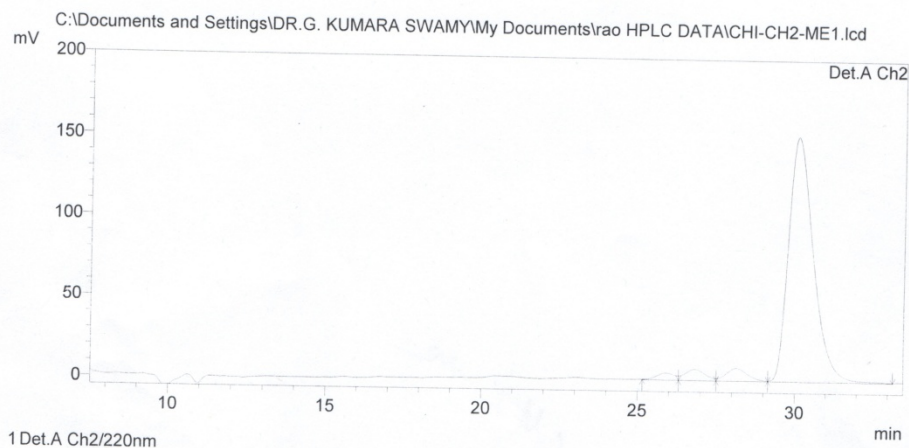
## HPLC of 3h, chiral:

9/19/2012 11:05:30 1 / 1

### ==== OBC Division ====

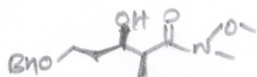
Acquired by : Admin  
Sample Name : CHI-CH2-ME1  
Sample ID : CHI-CH2-ME1  
Vial # : 1  
Injection Volume : 20 uL  
Data File Name : CHI-CH2-ME1.lcd  
Method File Name : purge.lcm  
Batch File Name :  
Report File Name : DA1 and DA2 report.lcr  
Data Acquired : 9/1/2012 3:30:21 PM  
Data Processed : 9/1/2012 4:09:43 PM

#### <Chromatogram>



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	25.892	156981	4061	1.713	2.396
2	26.811	291753	6664	3.184	3.932
3	28.136	360260	7705	3.932	4.547
4	30.051	8354057	151037	91.171	89.125
Total		9163051	169467	100.000	100.000



mobile phase: hexane: 2PA, 95:5

flowrate: 0.5 ml/min

d = 220 um

column: OD-H.

C:\Documents and Settings\DR.G. KUMARA SWAMY\My Documents\rao HPLC DATA\CHI-CH2-ME1.lcd

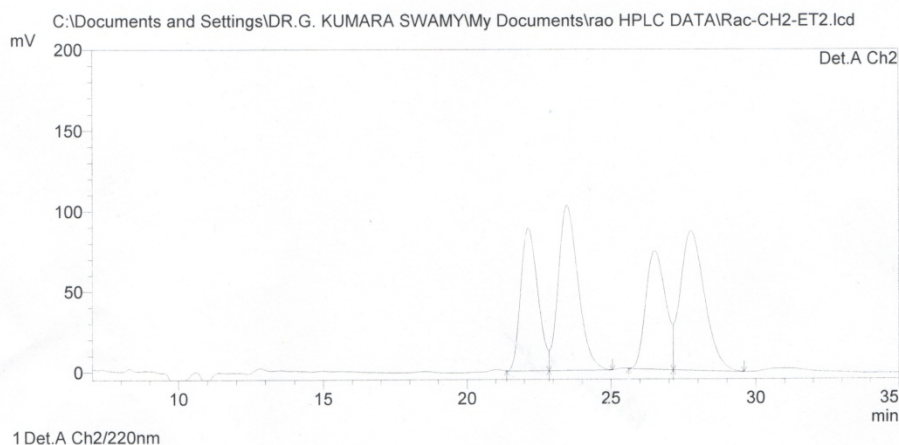
### HPLC of 3i, racemic:

9/19/2012 11:17:29 1 / 1

#### ==== OBC Division ====

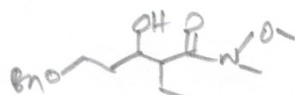
Acquired by : Admin  
Sample Name : Rac-CH2-ET2  
Sample ID : Rac-CH2-ET2  
Vial # : 1  
Injection Volume : 20 uL  
Data File Name : Rac-CH2-ET2.lcd  
Method File Name : purge.lcm  
Batch File Name :  
Report File Name : DA1 and DA2 report.lcr  
Data Acquired : 8/31/2012 12:24:09 PM  
Data Processed : 8/31/2012 1:00:42 PM

#### <Chromatogram>



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.142	3662374	88827	21.402	25.160
2	23.487	4898317	103027	28.625	29.182
3	26.518	3500909	73993	20.459	20.959
4	27.764	5050326	87197	29.513	24.699
Total		17111927	353045	100.000	100.000



mobile phase: hexane : IPA, 95 : 5

flow rate : 0.5 ml/min

$\lambda = 220\text{nm}$

column : OD-H.

C:\Documents and Settings\DR.G. KUMARA SWAMY\My Documents\rao HPLC DATA\Rac-CH2-ET2.lcd

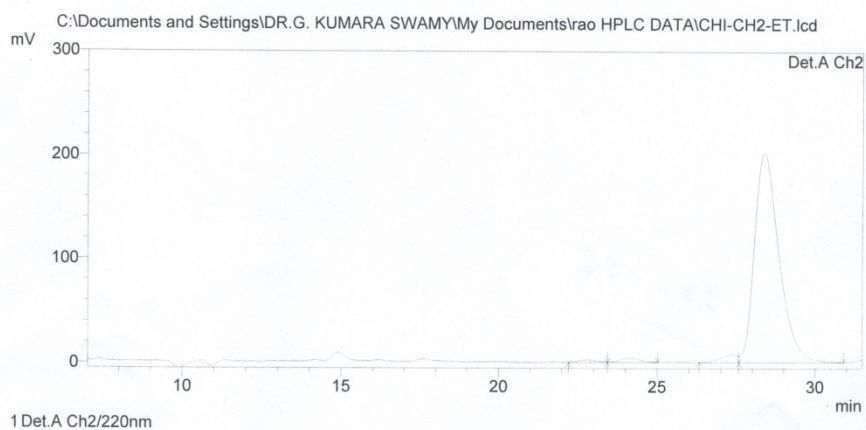
## HPLC of 3i, chiral:

9/19/2012 11:13:22 1 / 1

### ==== OBC Division ====

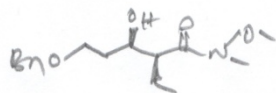
Acquired by : Admin  
Sample Name : CHI-CH2-ET  
Sample ID : CHI-CH2-ET  
Vial # : 1  
Injection Volume : 20 uL  
Data File Name : CHI-CH2-ET.lcd  
Method File Name : purge.lcm  
Batch File Name :  
Report File Name : DA1 and DA2 report.lcr  
Data Acquired : 9/1/2012 11:32:13 AM  
Data Processed : 9/1/2012 12:06:36 PM

#### <Chromatogram>



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.794	88386	2409	0.771	1.120
2	24.126	161577	3924	1.409	1.824
3	27.306	256452	7250	2.236	3.371
4	28.358	10962545	201525	95.584	93.686
Total		11468959	215108	100.000	100.000



mobile phase: hexane : IPA, 95:5

flow rate: 0.5 ml/min,

$\lambda = 220\text{nm}$

column: OD-H.

C:\Documents and Settings\DR.G. KUMARA SWAMY\My Documents\rao HPLC DATA\CHI-CH2-ET.lcd

### HPLC of 3j, racemic:

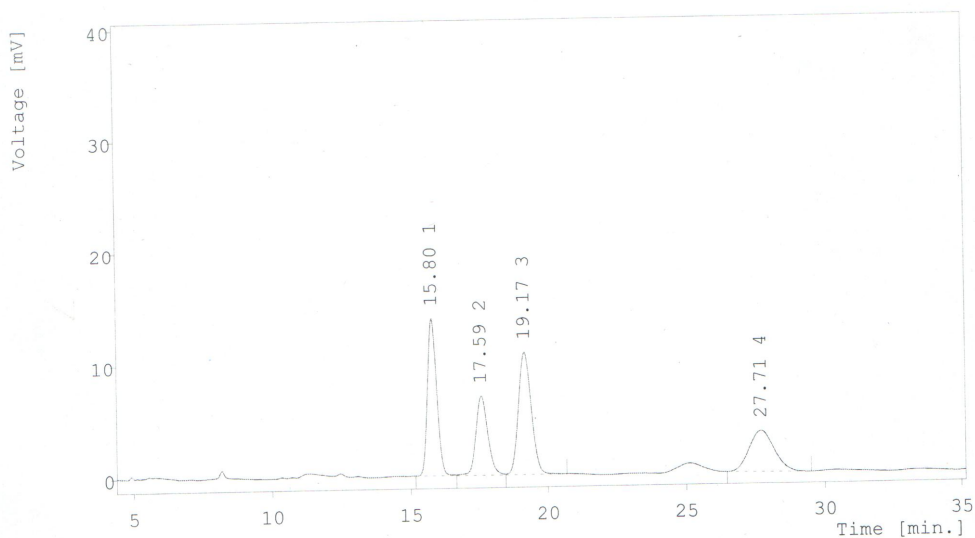
Sun, 14th Oct, 2012 12:25:32

BNCHR95

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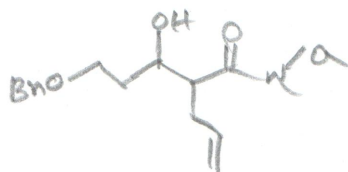
Sample ID : **ipahex**  
Amount : **20**  
Raw Data : **bnchr95**  
Primary : **bnchr95**  
Project : **work1**

Analyst : **murthy**  
Dilution : **1**  
From : **Sun, 15th Jul, 2012 19:27:36**  
Calibration : **(none)**  
Style : **report**



Result Table - Calculation Method Uncal

Peak No.	Reten. time	Area [mV.s]	Height [mV]	W05 [min.]	Area [%]	Height [%]
1	15.800	327.2803	13.9913	0.3733	29.0581	39.3186
2	17.587	212.2138	7.0448	0.4667	18.8417	19.7974
3	19.173	355.3189	10.8924	0.5200	31.5475	30.6101
4	27.707	231.4849	3.6559	1.0000	20.5527	10.2739
-	Total	1126.2978	35.5843			



mobile phase: n-hexane : IPA, 95:5

flowrate: 0.8 ml/min

d = 220 nm

column = AS-H.



### HPLC of 3j, chiral:

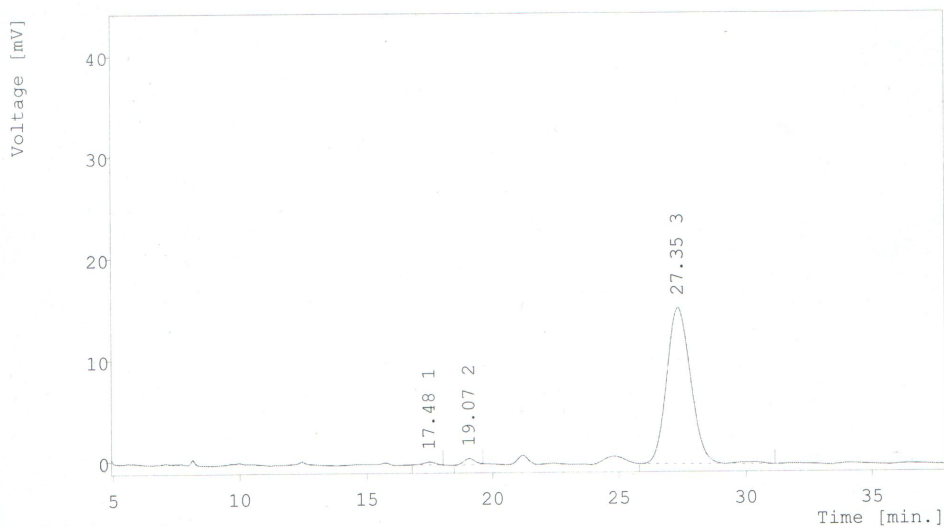
Sun, 14th Oct, 2012 12:29:48

BNCHC95

Page 1

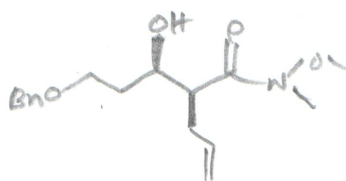
Sample ID : **bnchr95**  
Amount : **20**  
Raw Data : **bnchc95**  
Primary : **bnchc95**  
Project : **work1**

Analyst : **murthy**  
Dilution : **1**  
From : **Sun, 15th Jul, 2012 20:12:35**  
Calibration : **(none)**  
Style : **report**



Result Table - Calculation Method Uncal

Peak No.	Reten. time	Area [mV.s]	Height [mV]	W05 [min.]	Area [%]	Height [%]
1	17.480	8.6391	0.2817	0.4667	0.8240	1.7274
2	19.067	16.6156	0.5725	0.4800	1.5847	3.5102
3	27.347	1023.2314	15.4541	1.0267	97.5913	94.7624
-	Total	1048.4861	16.3083			



mobile phase : n-hexane : IPA, 95:5

flowrate : 0.8 ml/min

$\lambda = 220 \text{ nm}$

column = AS-H.

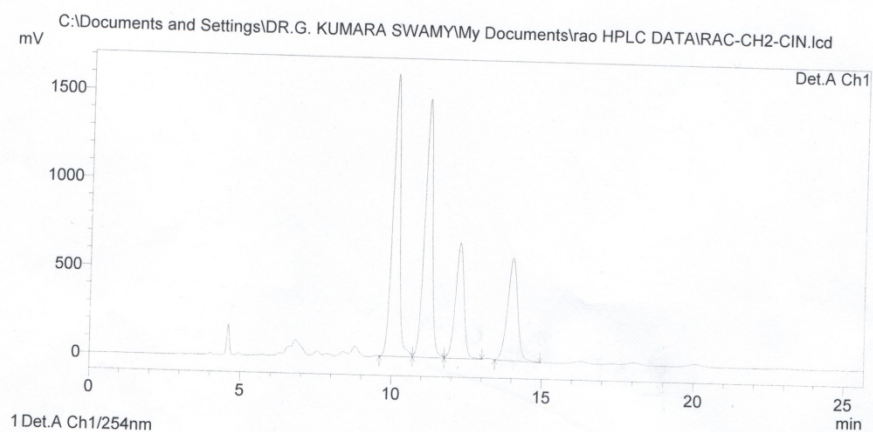
### HPLC of 3k, racemic:

9/19/2012 10:52:59 1 / 1

#### ==== OBC Division ====

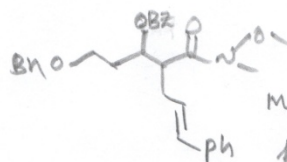
Acquired by : Admin  
Sample Name : RAC-CH2-CIN  
Sample ID : RAC-CH2-CIN  
Vial # : 1  
Injection Volume : 20 uL  
Data File Name : RAC-CH2-CIN.lcd  
Method File Name : purge.lcm  
Batch File Name :  
Report File Name : DA1 and DA2 report.lcr  
Data Acquired : 9/3/2012 1:17:37 PM  
Data Processed : 9/3/2012 1:43:18 PM

#### <Chromatogram>



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.067	26823820	1604302	33.575	37.220
2	11.151	26685601	1466957	33.402	34.034
3	12.242	12861167	655675	16.098	15.212
4	14.009	13521862	583340	16.925	13.534
Total		79892451	4310274	100.000	100.000



mobile phase: hexane:IPA, 90:10,

flow rate: 1ml/min

d = 2.5µm

column: IA

C:\Documents and Settings\DR.G. KUMARA SWAMY\My Documents\rao HPLC DATA\RAC-CH2-CIN.lcd

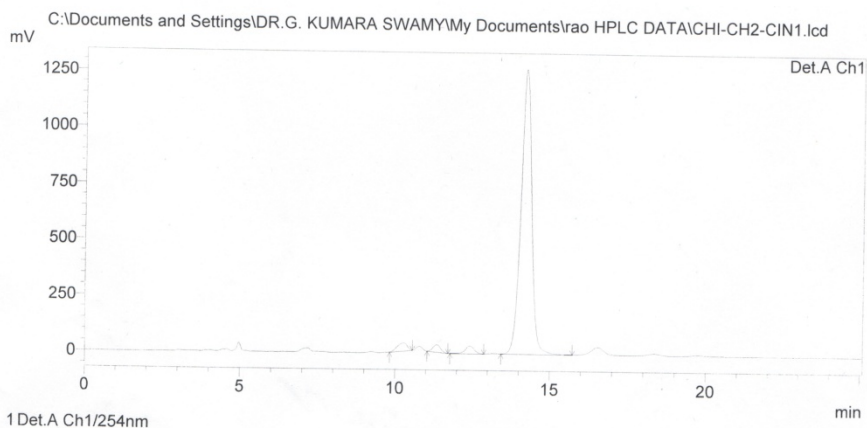
### HPLC of 3k, chiral:

9/19/2012 10:56:31 1 / 1

#### ==== OBC Division ====

Acquired by : Admin  
Sample Name : CHI-CH2-CIN1  
Sample ID : CHI-CH2-CIN1  
Vial # : 1  
Injection Volume : 20 uL  
Data File Name : CHI-CH2-CIN1.lcd  
Method File Name : purge.lcm  
Batch File Name :  
Report File Name : DA1 and DA2 report.lcr  
Data Acquired : 9/3/2012 3:40:18 PM  
Data Processed : 9/3/2012 4:05:26 PM

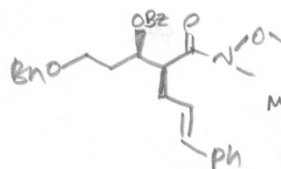
#### <Chromatogram>



Detector A Ch1 254nm

PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.277	797522	35575	2.458	2.594
2	11.354	558804	33046	1.722	2.409
3	12.435	675435	34066	2.082	2.484
4	14.201	30414559	1268856	93.738	92.513
Total		32446321	1371543	100.000	100.000



mobile phase: hexane: IPA, 90:10.

flow rate: 1ml/min,

$\lambda = 254 \text{ nm}$

column: IA.

C:\Documents and Settings\DR.G. KUMARA SWAMY\My Documents\rao HPLC DATA\CHI-CH2-CIN1.lcd

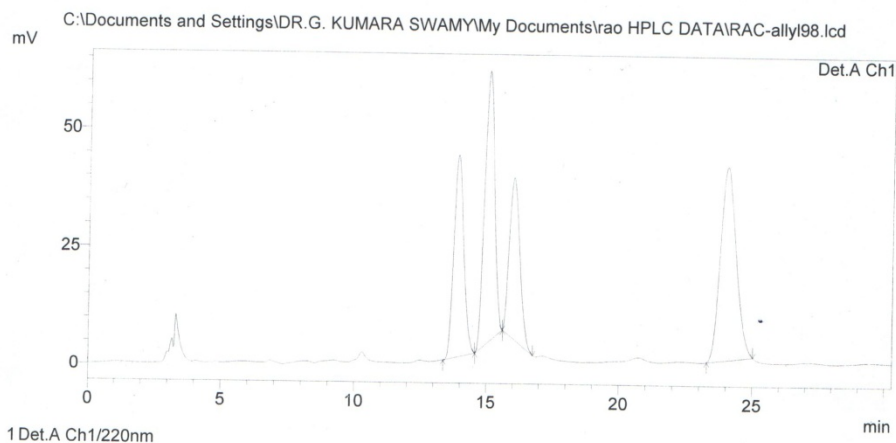
### HPLC of 3l, racemic:

8/24/2012 16:24:59 1 / 1

#### ==== OBC Division ====

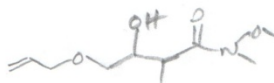
Acquired by : Admin  
Sample Name : RAC-allyl98  
Sample ID : RAC-allyl98  
Vial # : 1  
Injection Volume : 20 uL  
Data File Name : RAC-allyl98.lcd  
Method File Name : rao method.lcm  
Batch File Name :  
Report File Name : DA1 and DA2 report.lcr  
Data Acquired : 8/24/2012 3:05:38 PM  
Data Processed : 8/24/2012 3:35:57 PM

#### <Chromatogram>



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.889	1116765	42903	21.130	24.404
2	15.034	1508039	57685	28.533	32.812
3	15.999	951714	34104	18.007	19.399
4	24.018	1708648	41112	32.329	23.385
Total		5285166	175803	100.000	100.000



mobile phase : n-hexane : IPA = 98:2

flowrate : 1ml/min

d = 220nm

column = OD-H

C:\Documents and Settings\DR.G. KUMARA SWAMY\My Documents\rao HPLC DATA\RAC-allyl98.lcd

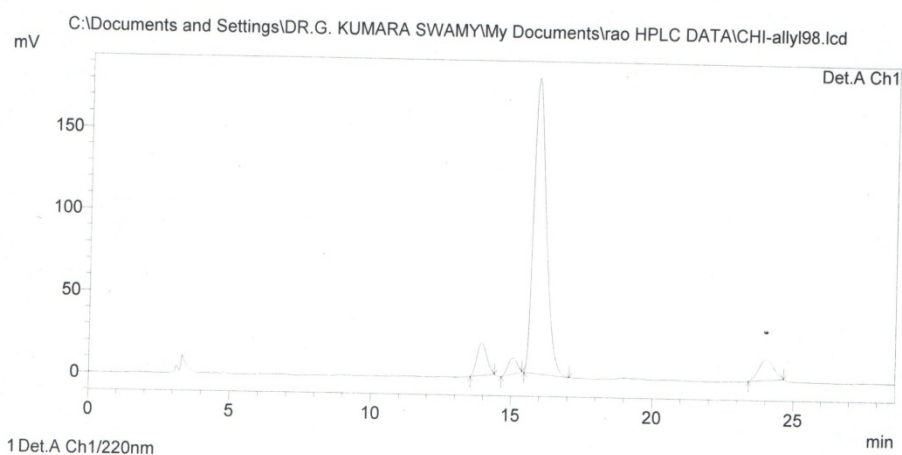
### HPLC of 3l, chiral:

8/24/2012 16:23:03 1 / 1

#### ==== OBC Division ====

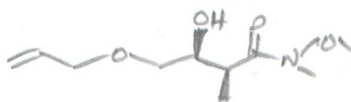
Acquired by : Admin  
Sample Name : CHI-allyl98  
Sample ID : CHI-allyl98  
Vial # : 1  
Injection Volume : 20 uL  
Data File Name : CHI-allyl98.lcd  
Method File Name : rao method.lcm  
Batch File Name :  
Report File Name : DA1 and DA2 report.lcr  
Data Acquired : 8/24/2012 3:45:00 PM  
Data Processed : 8/24/2012 4:13:40 PM

#### <Chromatogram>



PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.938	480251	19721	7.105	8.877
2	15.063	214221	9662	3.169	4.349
3	15.867	5596688	180163	82.804	81.097
4	24.023	467797	12611	6.921	5.677
Total		6758957	222156	100.000	100.000



mobile phase: n-hexane:IPA = 98:2

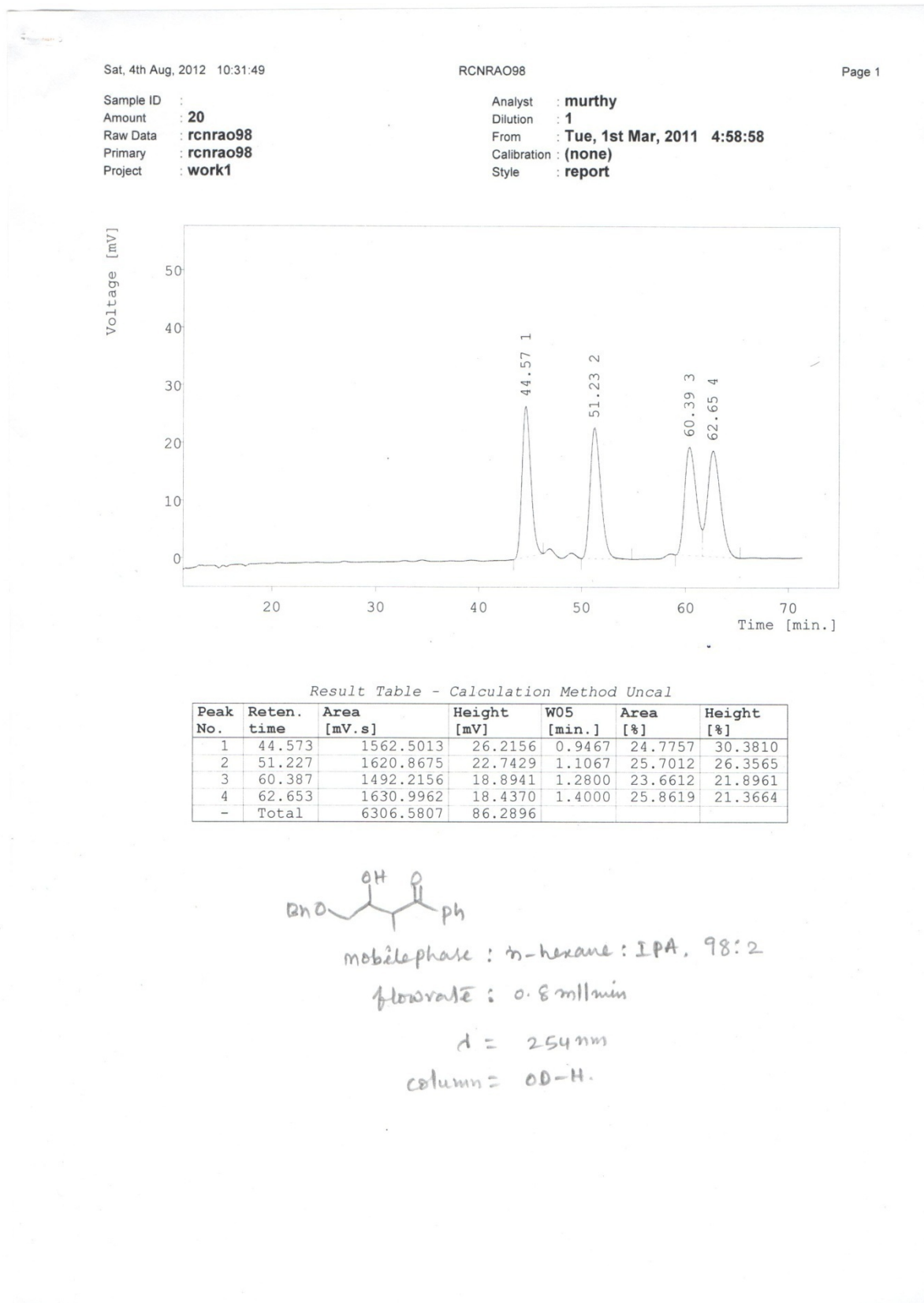
flow rate: 1ml/min

d = 220nm

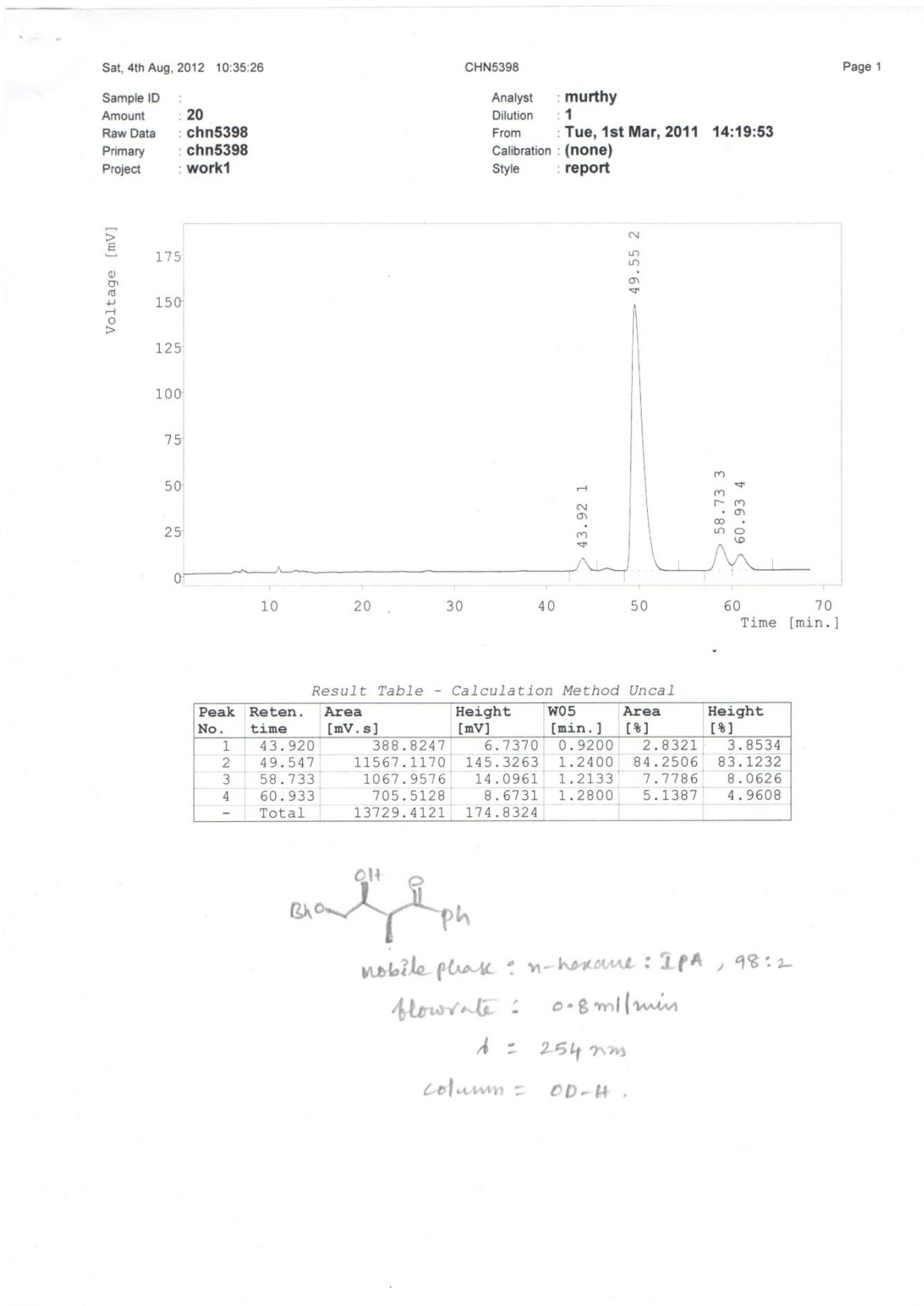
column = OD-H

C:\Documents and Settings\DR.G. KUMARA SWAMY\My Documents\rao HPLC DATA\CHI-allyl98.lcd

### HPLC of 3m, racemic:



### HPLC of 3m, chiral:



### HPLC of 3n, racemic:

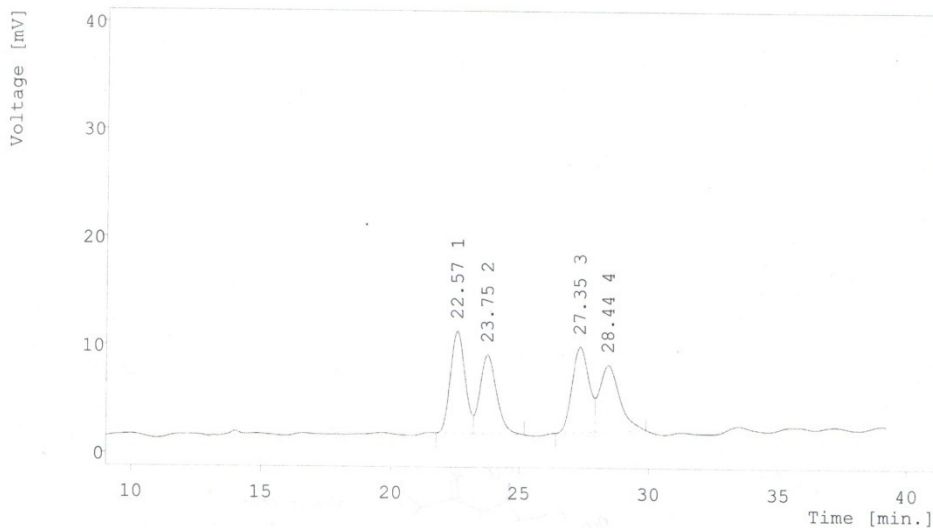
Fri, 3rd Aug, 2012 4:15:11

RAIS99

Page 1

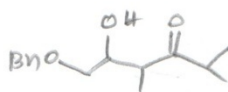
Sample ID :  
Amount : **20**  
Raw Data : **rais99**  
Primary : **rais99**  
Project : **work1**

Analyst : **murthy**  
Dilution : **1**  
From : **Fri, 3rd Aug, 2012 3:31:59**  
Calibration : **(none)**  
Style : **report**



Result Table - Calculation Method Uncal

Peak No.	Reten. time	Area [mV.s]	Height [mV]	W05 [min.]	Area [%]	Height [%]
1	22.573	377.9821	9.4758	0.6533	26.7370	30.6323
2	23.747	335.6388	7.3429	0.7067	23.7418	23.7374
3	27.347	361.8751	7.9275	0.7867	25.5977	25.6270
4	28.440	338.2074	6.1879	0.9733	23.9235	20.0033
-	Total	1413.7033	30.9341			



mobile phase : n-hexane : IPA, 99:1

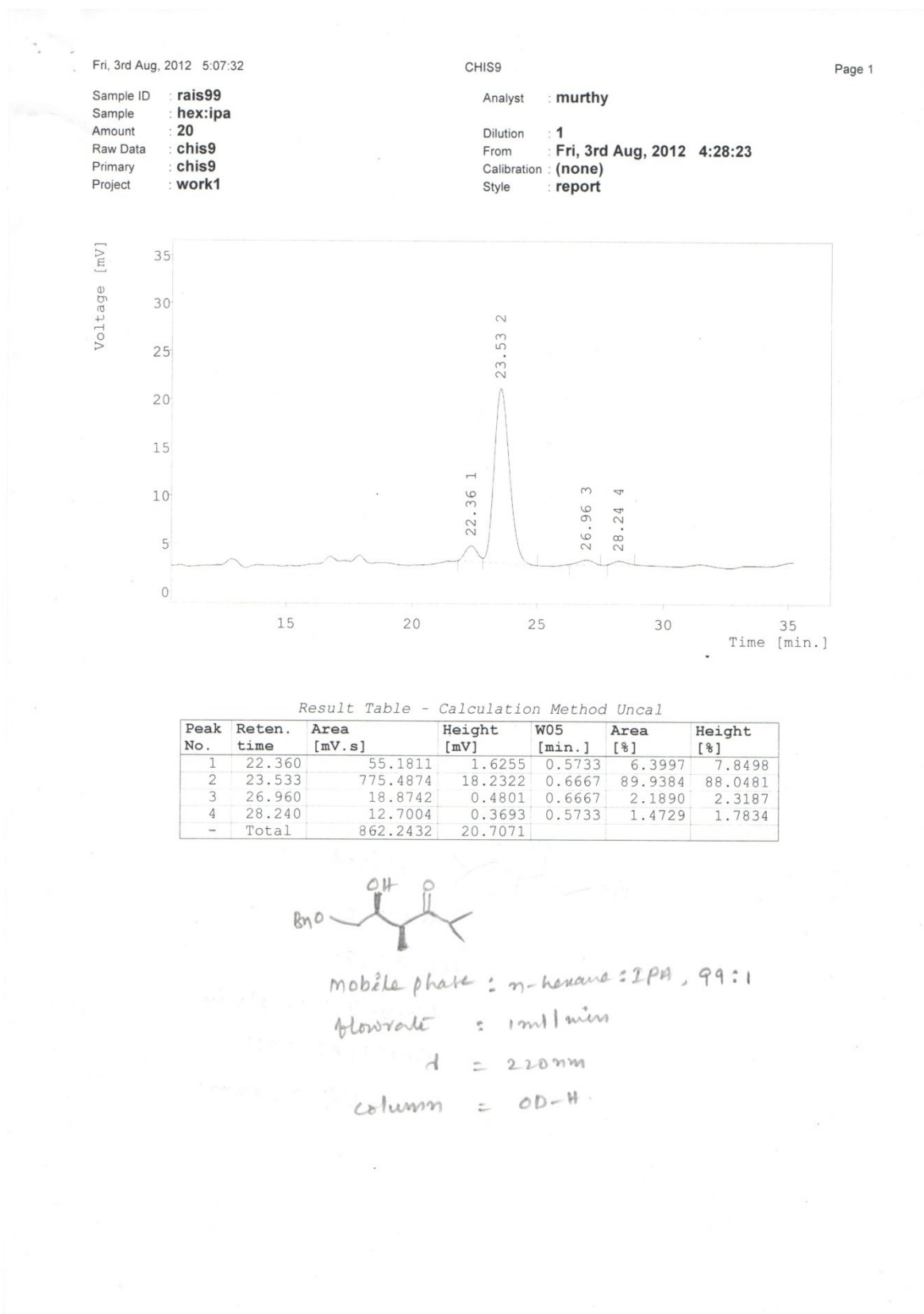
flow rate : 1ml/min

UV = 220 nm

column = OD-H.

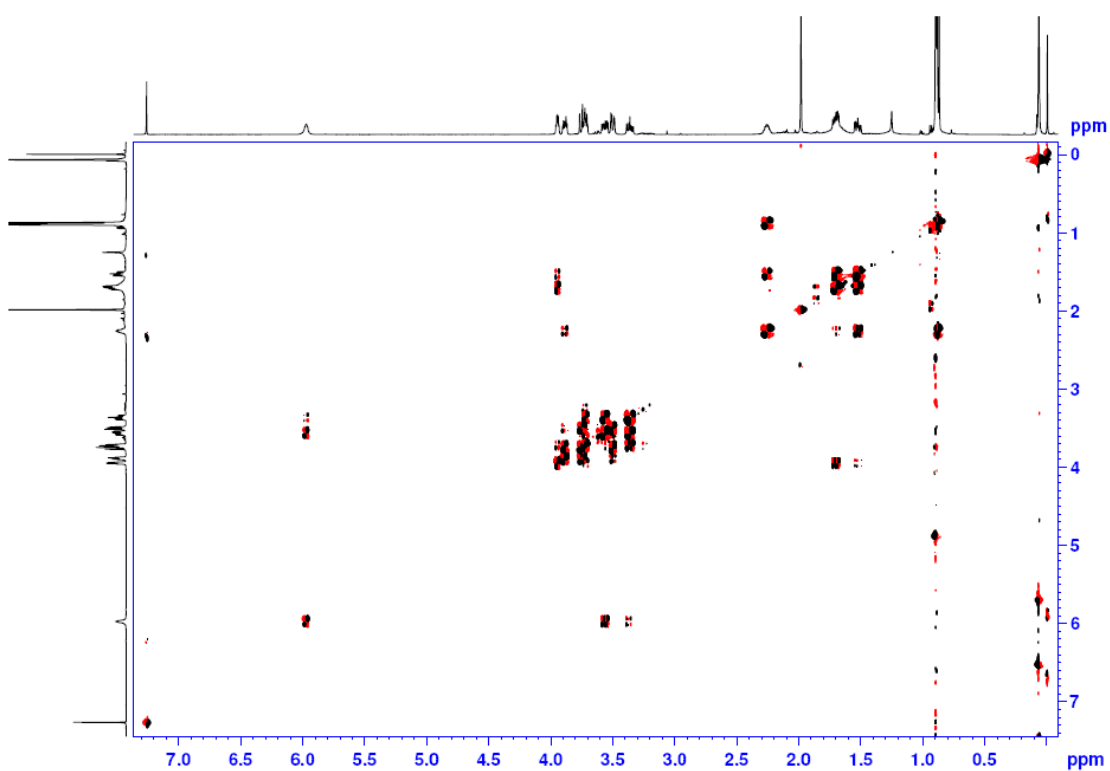
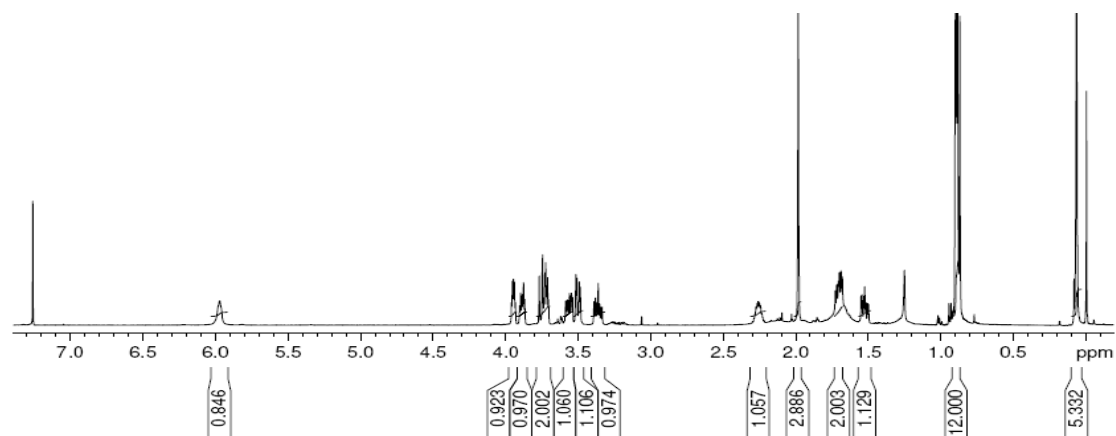


### HPLC of 3n, chiral:

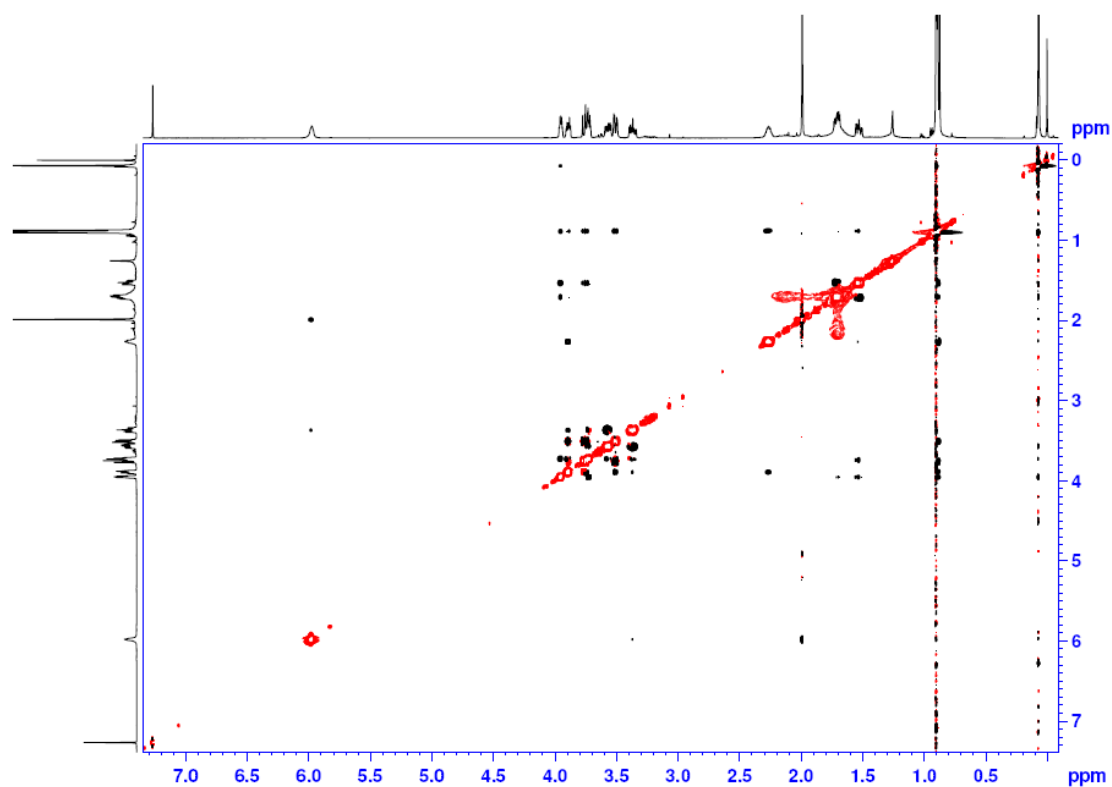


## NMR (NOE) - study

### Compound, 9:

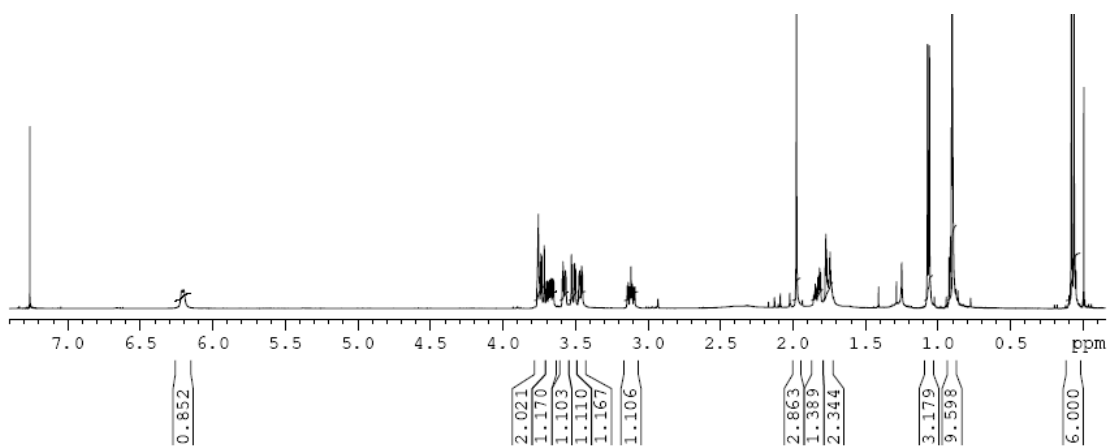


COSY Spectrum of Compound **9** ( $\text{CDCl}_3$ , 298 K, AVANCE 500 MHz)

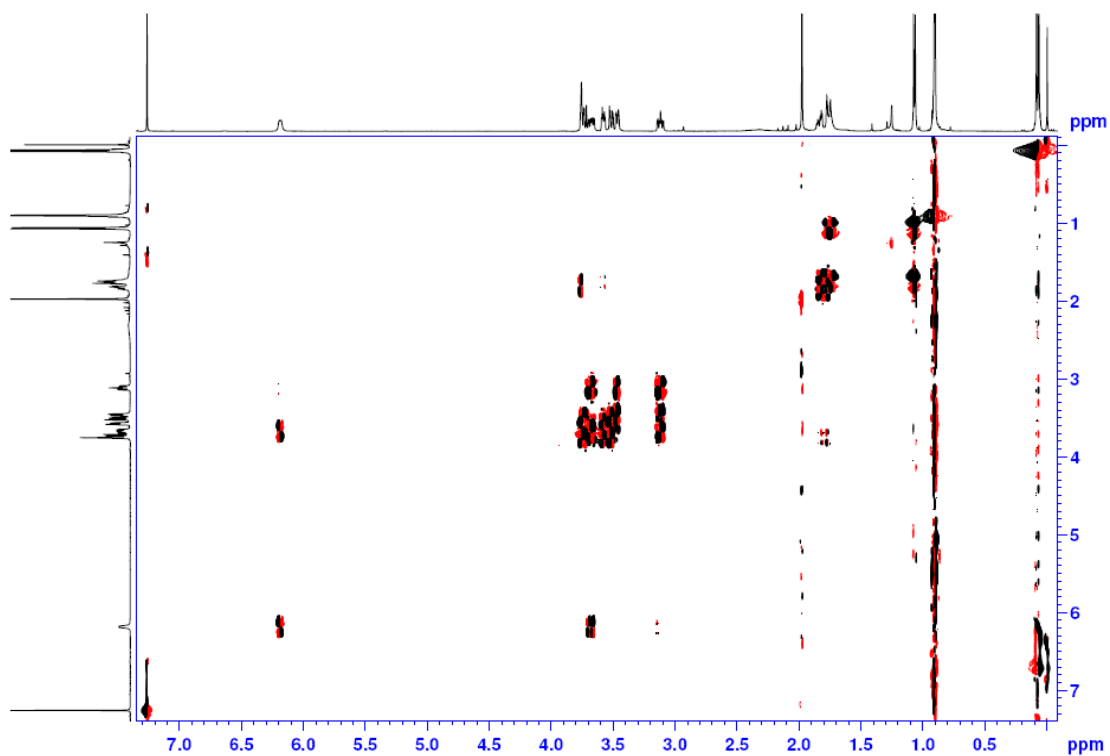


NOESY Spectrum of Compound **9** (CDCl<sub>3</sub>, 298 K, AVANCE 500 MHz)

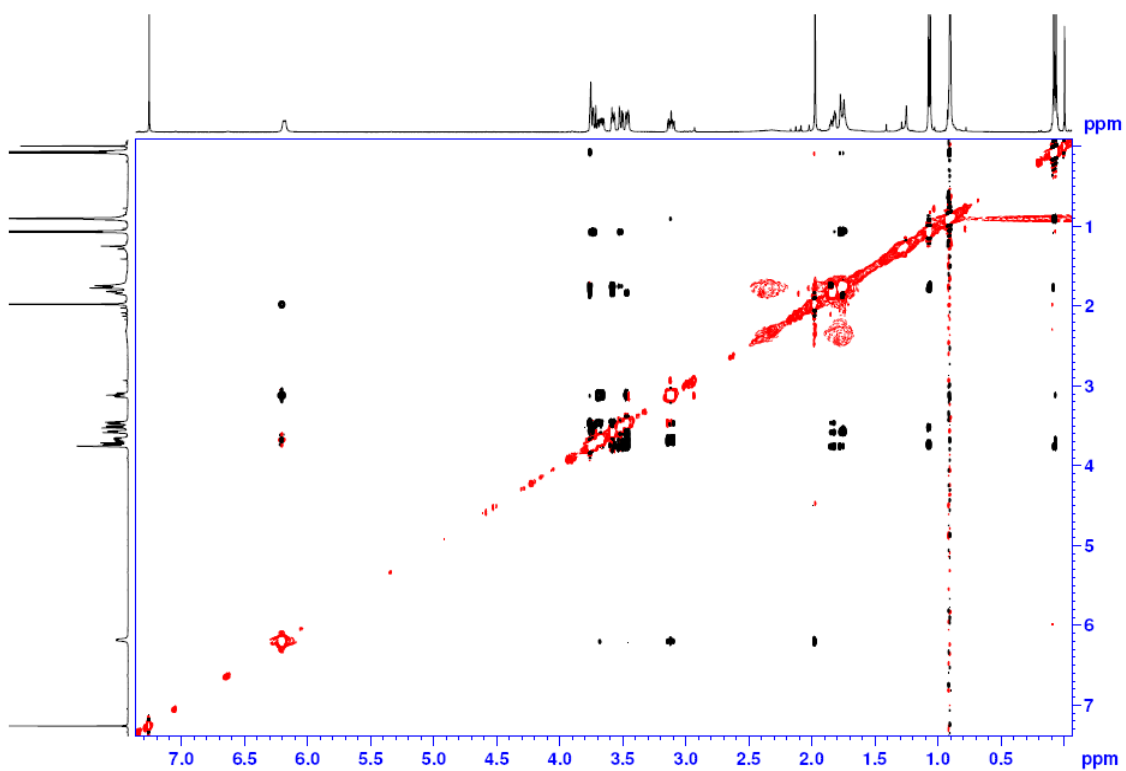
**Compound, 11:**



<sup>1</sup>H NMR Spectrum of compound **11** (CDCl<sub>3</sub>, 298 K, AVANCE 500 MHz)

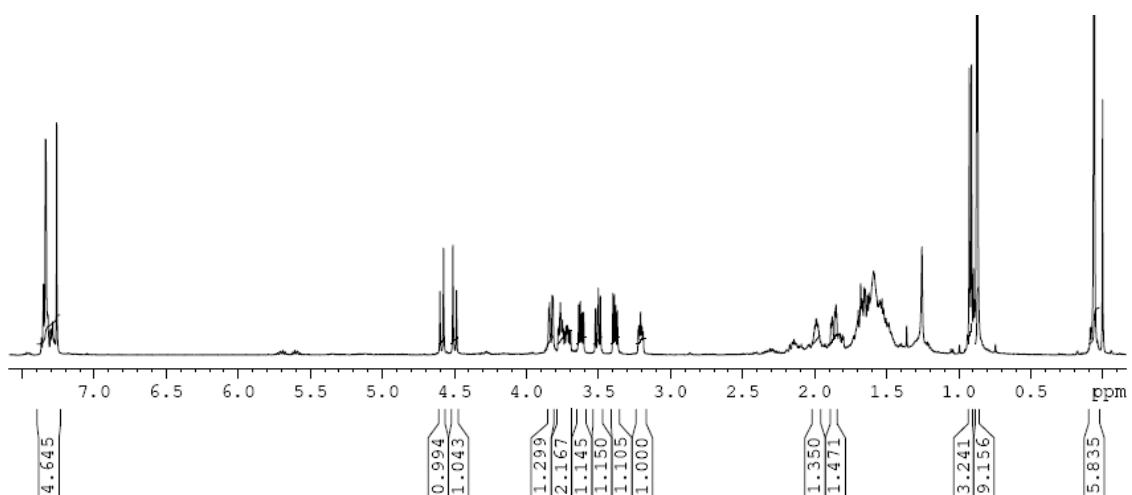


COSY Spectrum of Compound **11** (CDCl<sub>3</sub>, 298 K, AVANCE 500 MHz)

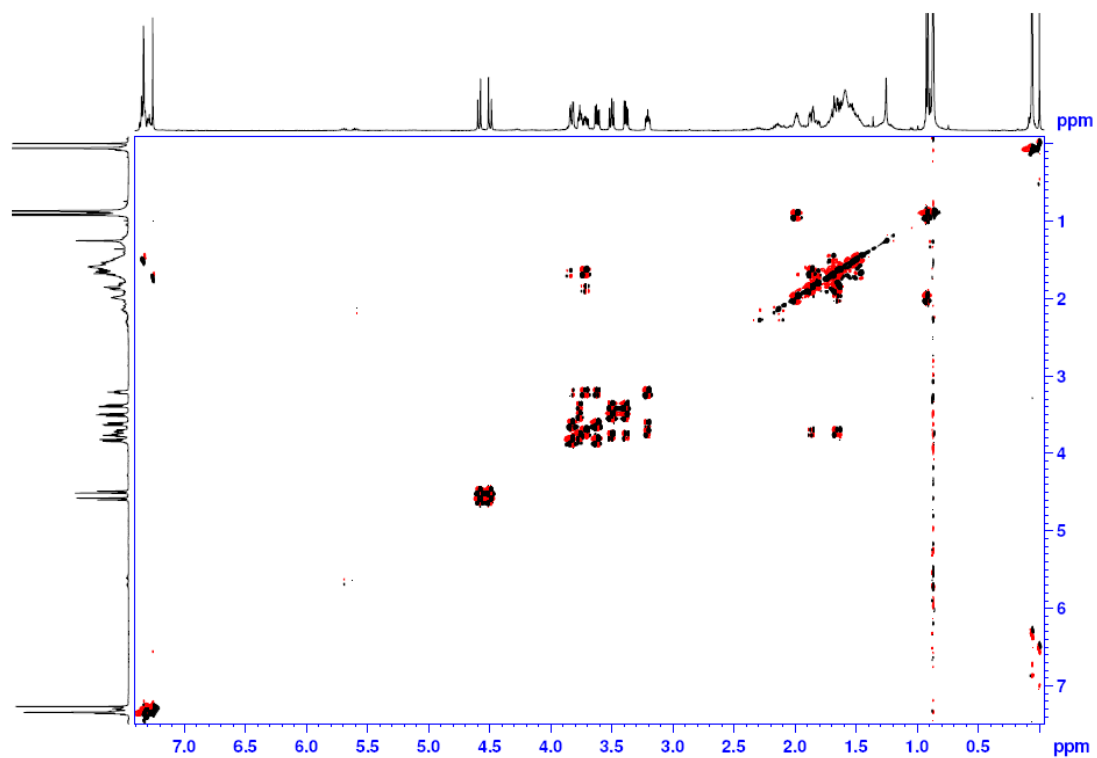


NOESY Spectrum of Compound **11** (CDCl<sub>3</sub>, 298 K, AVANCE 500 MHz)

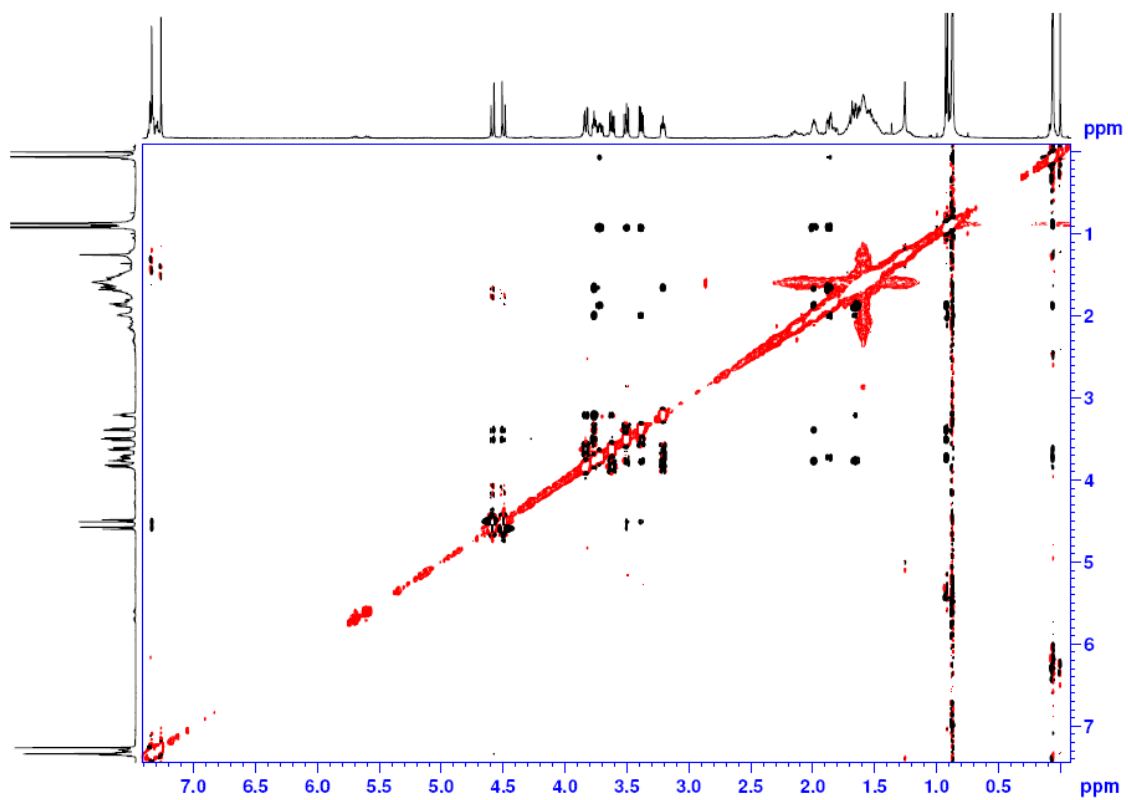
**Compound 15:**



$^1\text{H}$  NMR Spectrum of Compound **15** ( $\text{CDCl}_3$ , 298 K, AVANCE 500 MHz)



COSY Spectrum of Compound **15** ( $\text{CDCl}_3$ , 298 K, AVANCE 500 MHz)



NOESY Spectrum of Compound **15** ( $\text{CDCl}_3$ , 298 K, AVANCE 500 MHz)