

Supporting Information

Stereoselective total synthesis of (+)-oploxyne A, (-)-oploxyne B and their C-10 epimers and structure revision of natural oploxyne B

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Biological experiments:

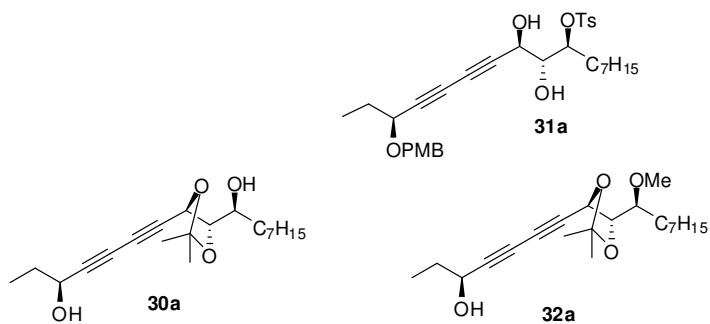
Screening for cytotoxicity

The synthesized compounds have been evaluated for their cytotoxicity in four different human cancer cell lines (A549, DU-145, MCF-7 and SK-N-SH). A protocol of 48 h continuous drug exposure has been used and MTT assay has been employed to estimate cell viability as described earlier¹³. The cell lines were grown in Dulbecco's Modified Eagles Medium (DMEM) containing 10% fetal bovine serum and 2mM L-glutamine for A549 cells and for all other cell lines Minimum Essential Medium (MEM) was used in place of DMEM. Cells were seeded into 96-well plates in 100 microliters at plating densities depending on the doubling time of individual cell lines. The plates were incubated at 37 °C, 5% CO₂, 95% air, and 100% relative humidity for 16 h prior to addition of experimental drugs. Aliquots of 1 µL of the drug dilutions were added to cells resulting in the required final drug concentrations. For each compound four different concentrations (1, 10, 50 and 100 µM) were evaluated for 48 h, and each were done in triplicate wells. After the termination of incubation, 10 µl of MTT (5 mg/ mL) was added to cells and further incubated for 1 h. Later, cells were washed thrice with Dulbecco's phosphate buffered saline and the formazon dye was dissolved by the addition of 100 µl of DMSO.¹³ Absorbance was read at 560 nm using Tecan Multimode reader. IC₅₀ values were derived from the obtained data (see table below).

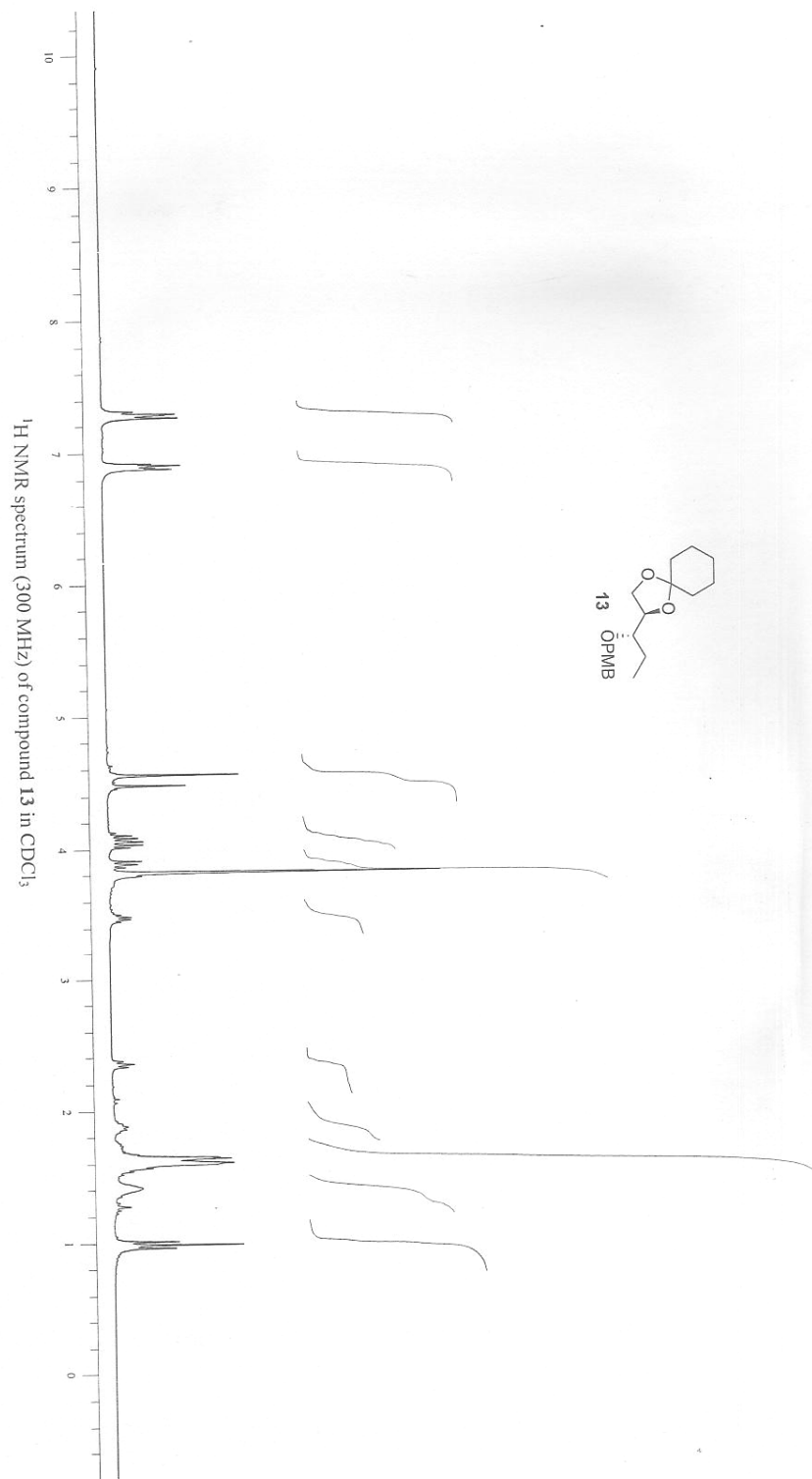
	IC ₅₀ values (μM)			
COMPOUND	A549	DU-145	MCF-7	SK-N-SH
3	NT	86 ± 2	27 ± 1	7 ± 1
4	25 ± 7	24 ± 2	28 ± 2	12 ± 4
5	45 ± 5	17 ± 1	92 ± 3	30 ± 7
6	NT	93 ± 3	27 ± 1	28 ± 2
7	195 ± 5	161 ± 14	81 ± 7	58 ± 2
8	65 ± 1	88 ± 4	115 ± 3	47 ± 2
8a	148±31	135±5	82±5	53±2
9	78 ± 1.5	74 ± 11	103 ± 9	45 ± 1
11	>200	>200	>200	186 ± 11
26	195 ± 5	160 ± 30	78 ± 9	57 ± 3
29	177 ± 22	121 ± 14	97 ± 3	80 ± 11
30	111 ± 11	91 ± 13	171 ± 29	51 ± 1
30a	115±5	110±23	93±1	55±3
31a	196±4	106±9	83±5	62±1
32	>200	>200	>200	173 ± 4
32a	198±2	>200	78±2	59±1
33	183 ± 17	140 ± 5	101 ± 3	61 ± 4
Doxorubicin (reference)	11.5 ± 1	11 ± 1.5	12 ± 1	9 ± 1

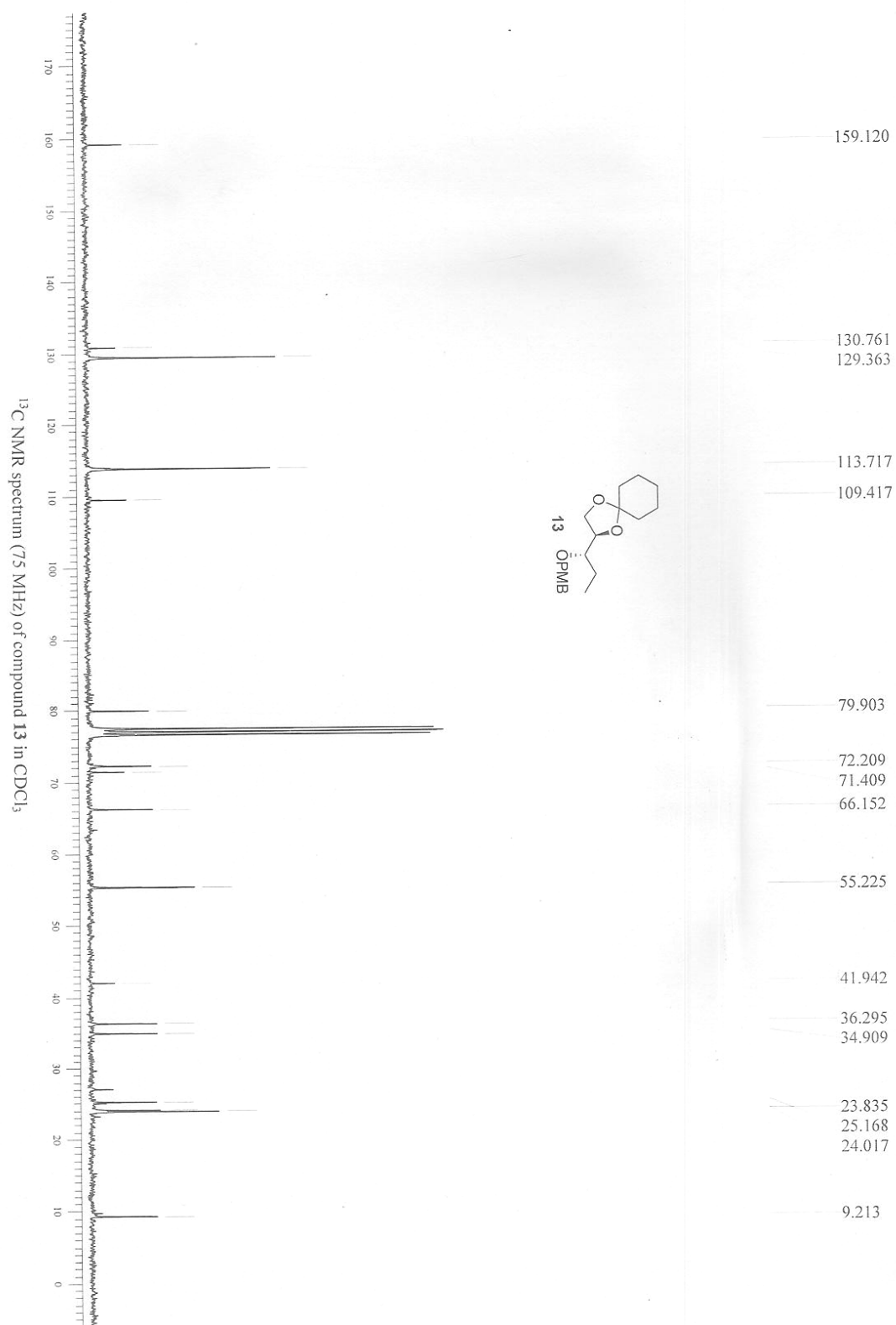
*NT: No significant toxicity

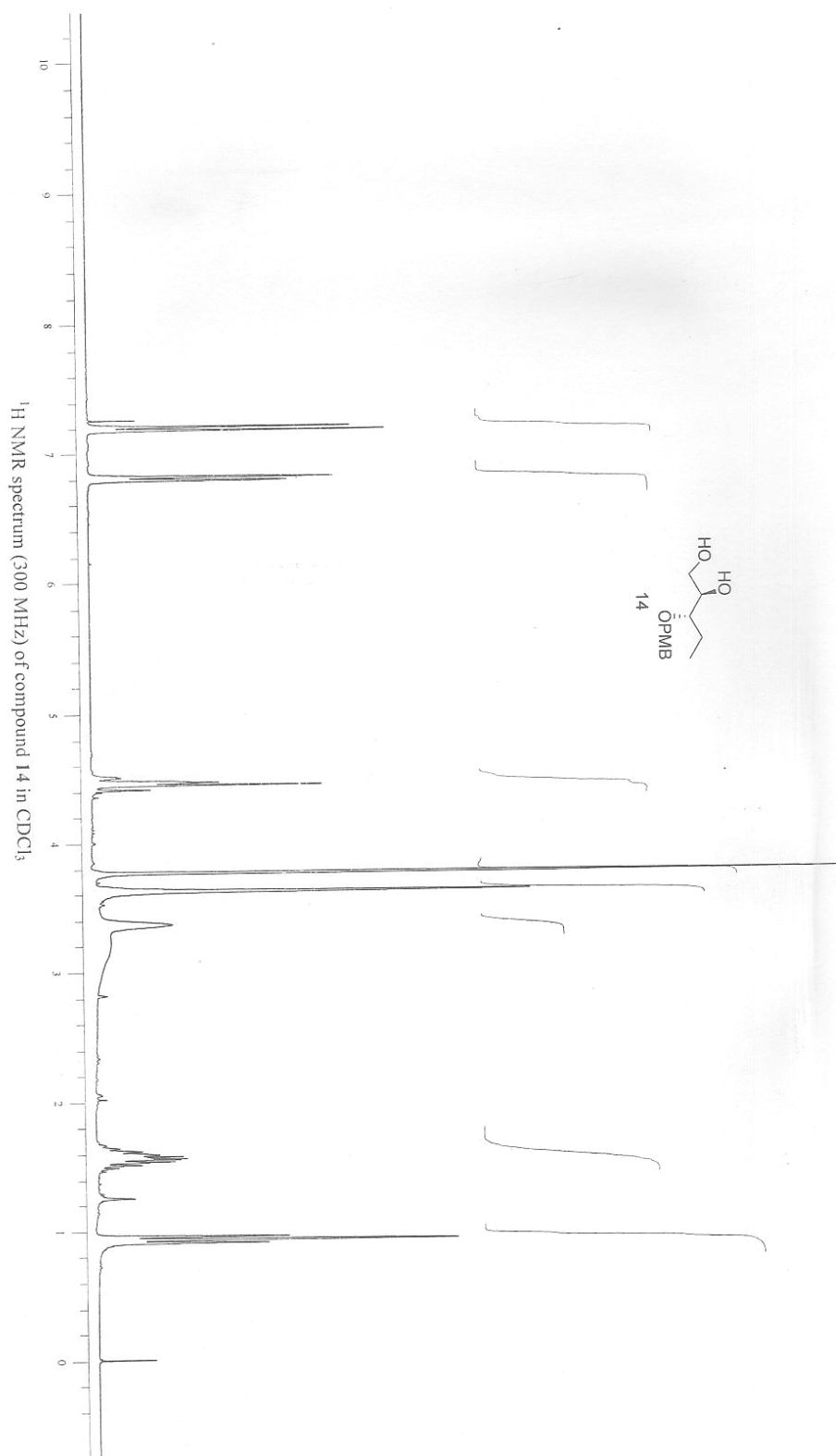
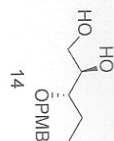
Structures of other compounds screened for biological activity.

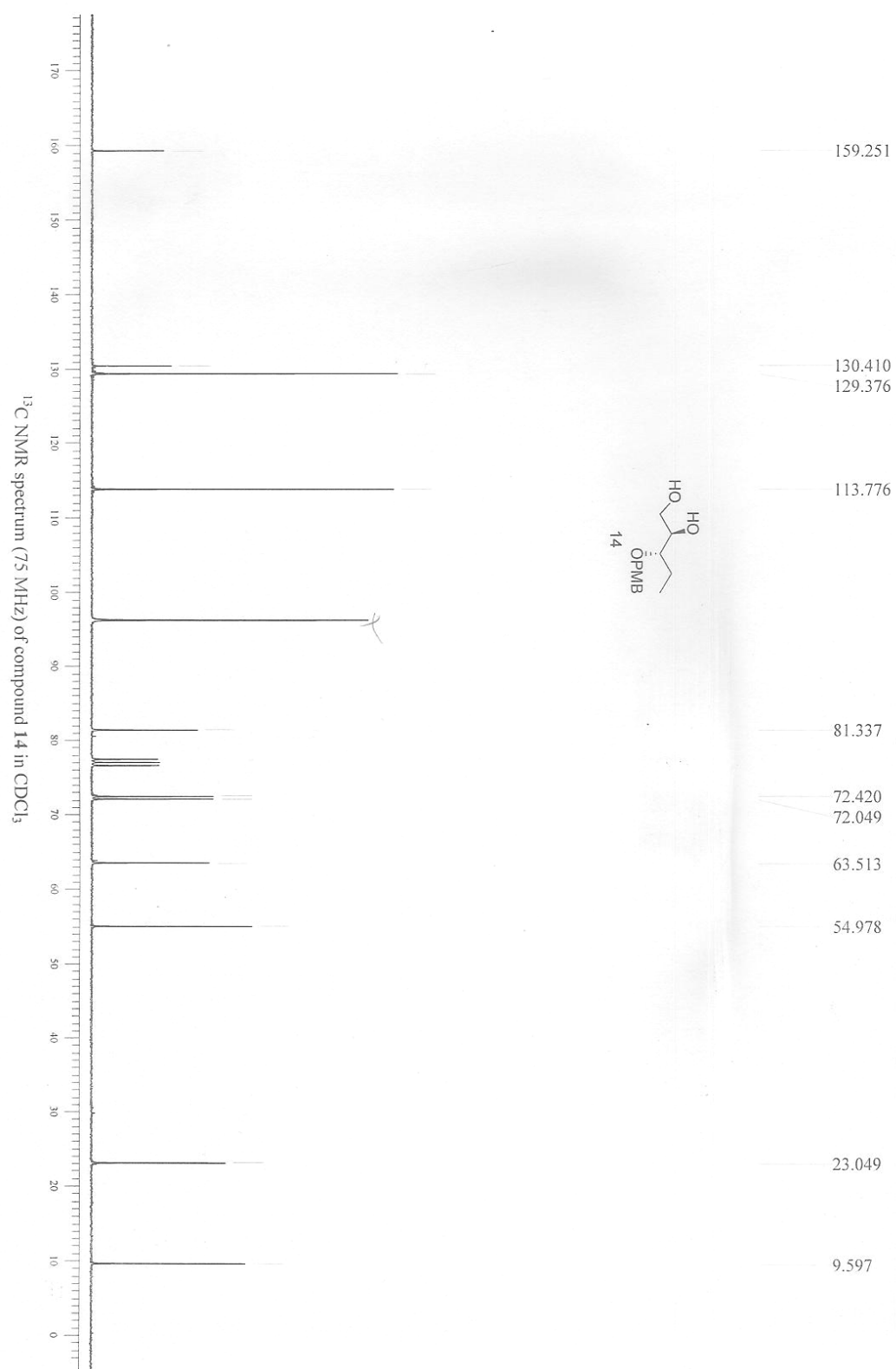


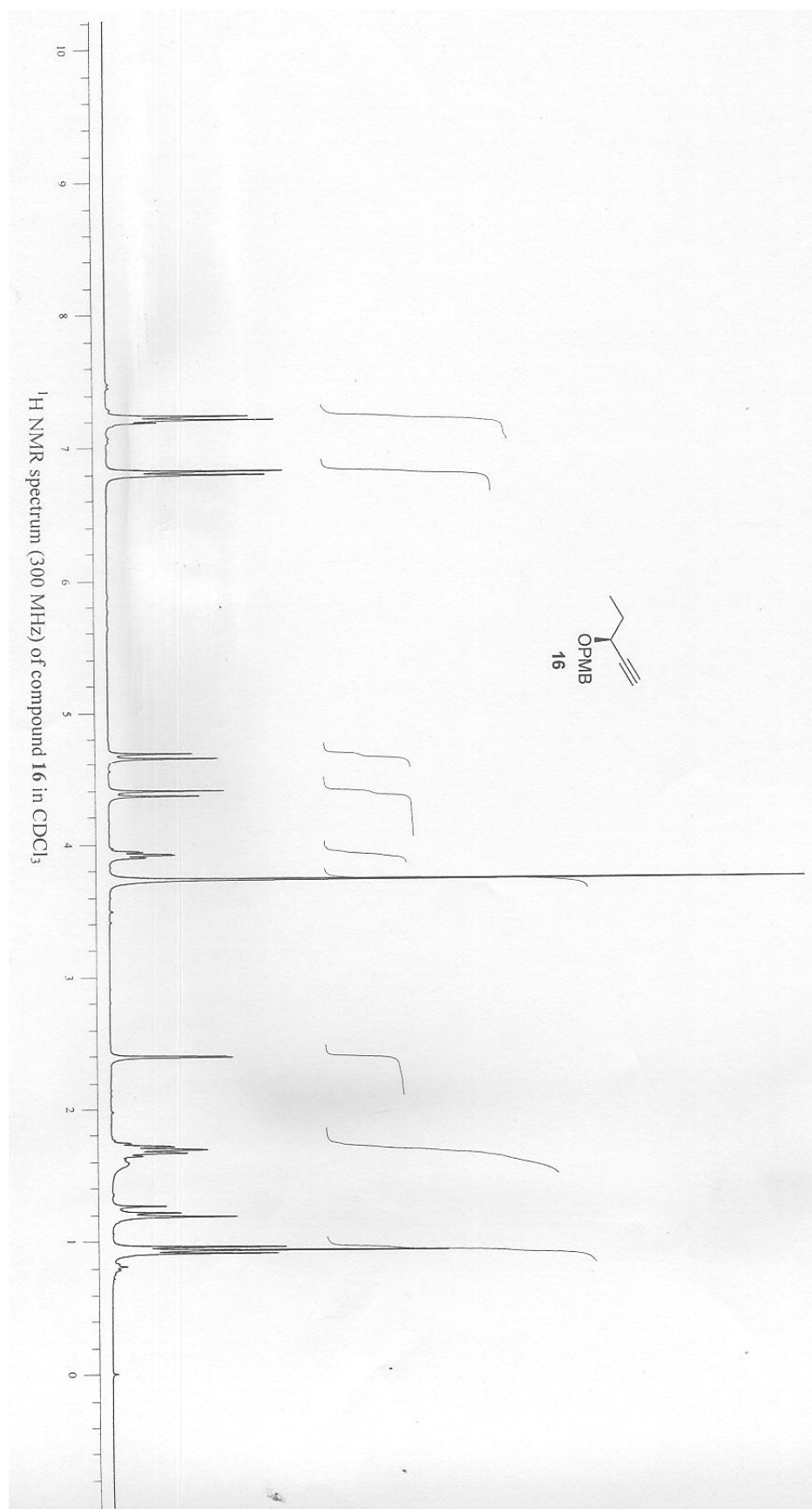
Spectra



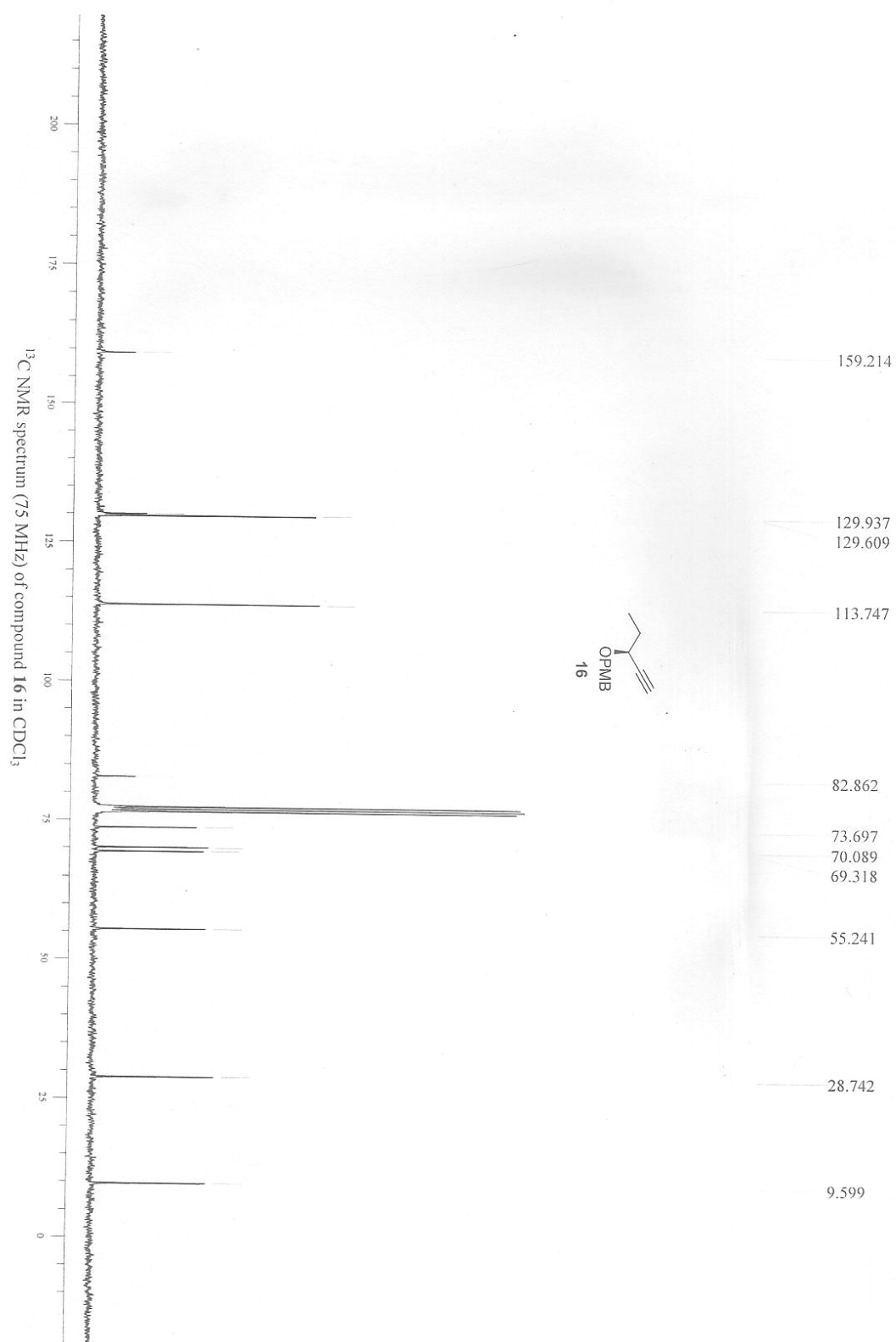


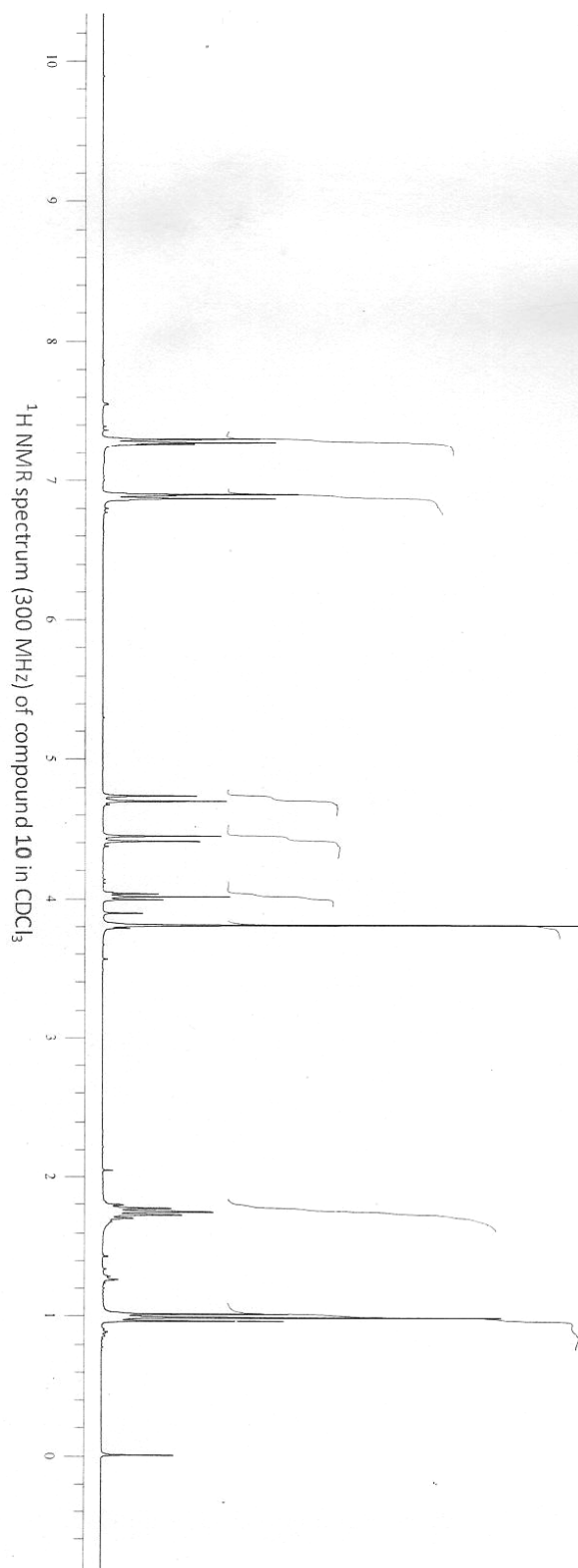
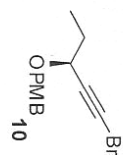


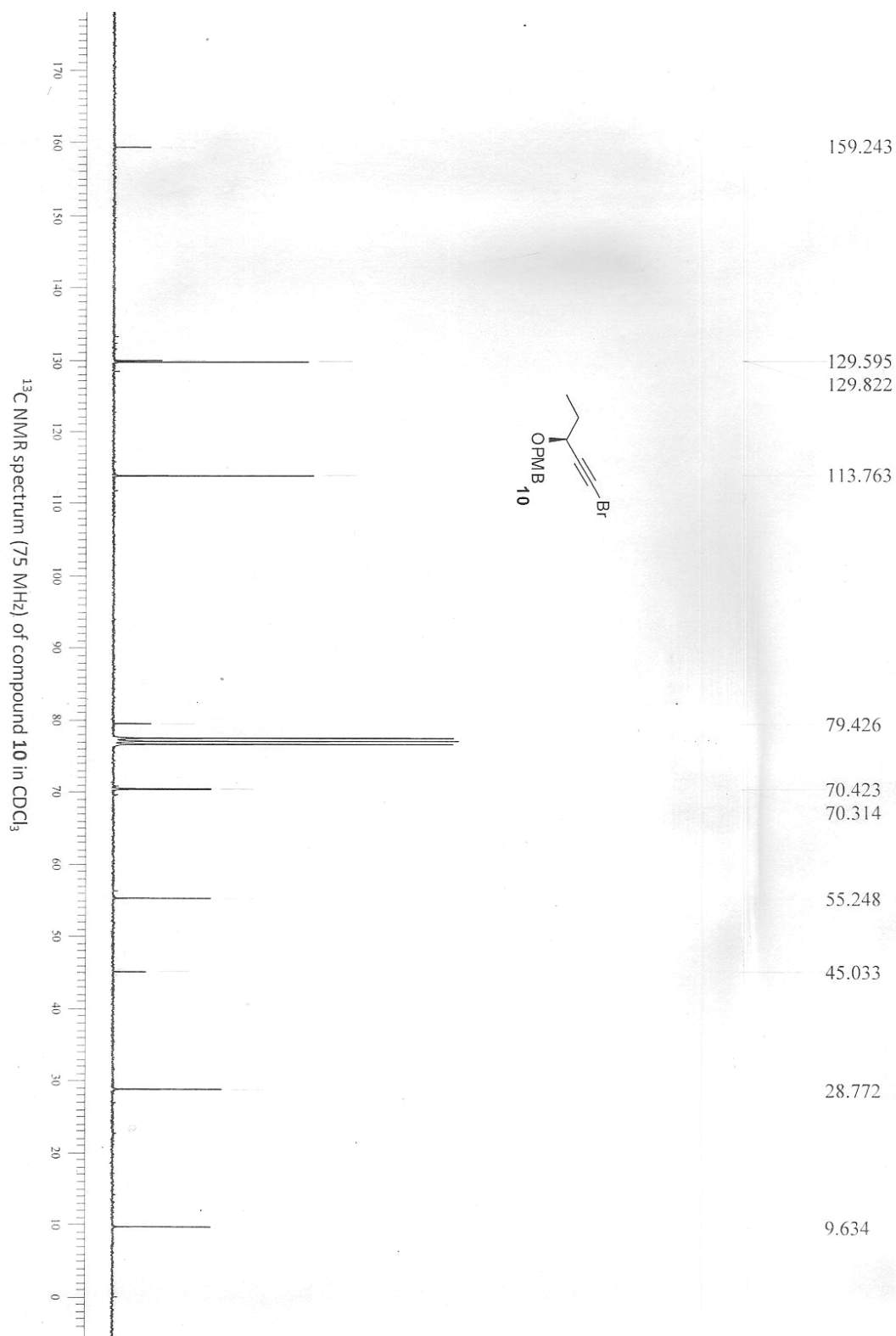


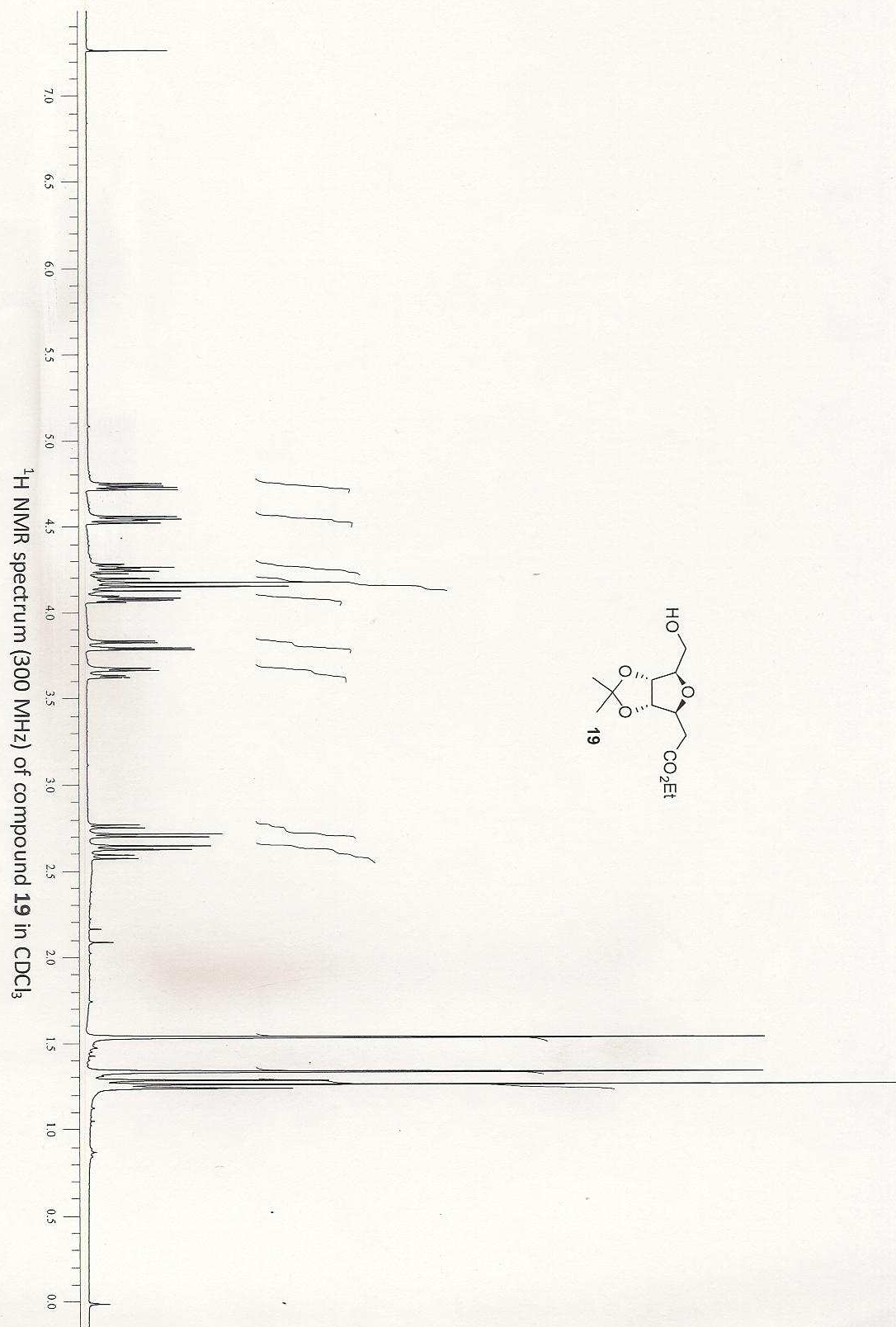


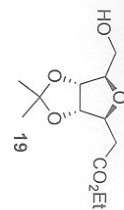
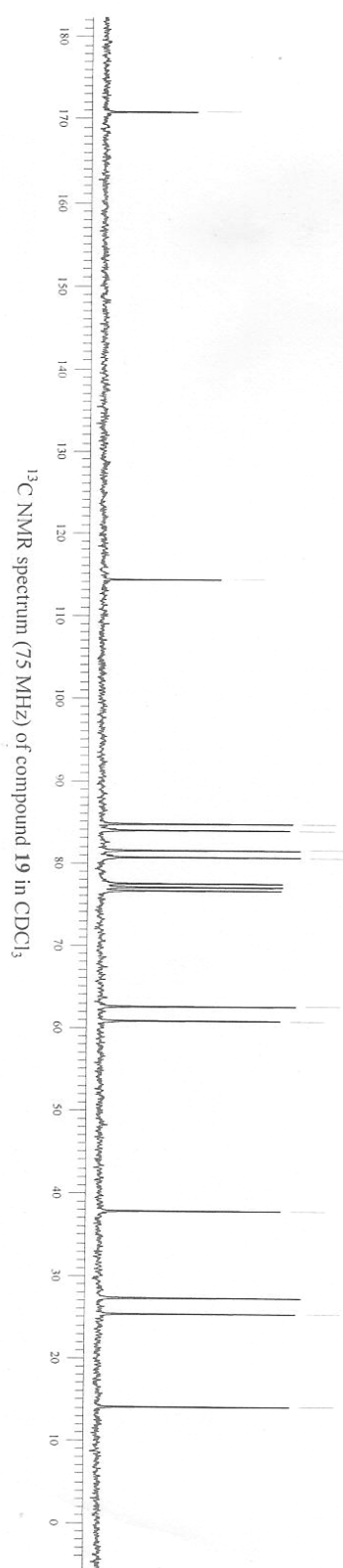
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114.213

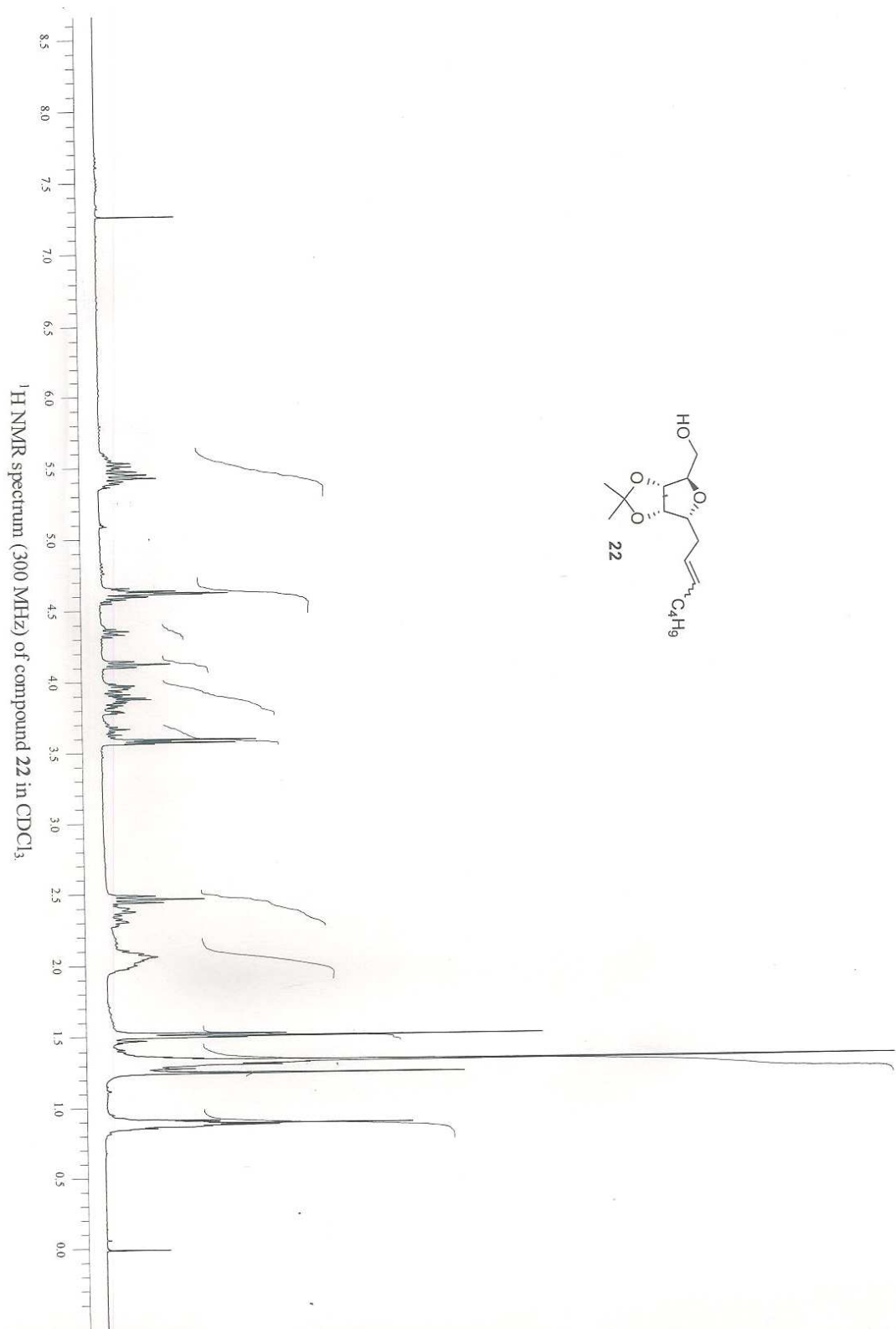
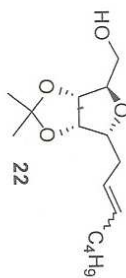
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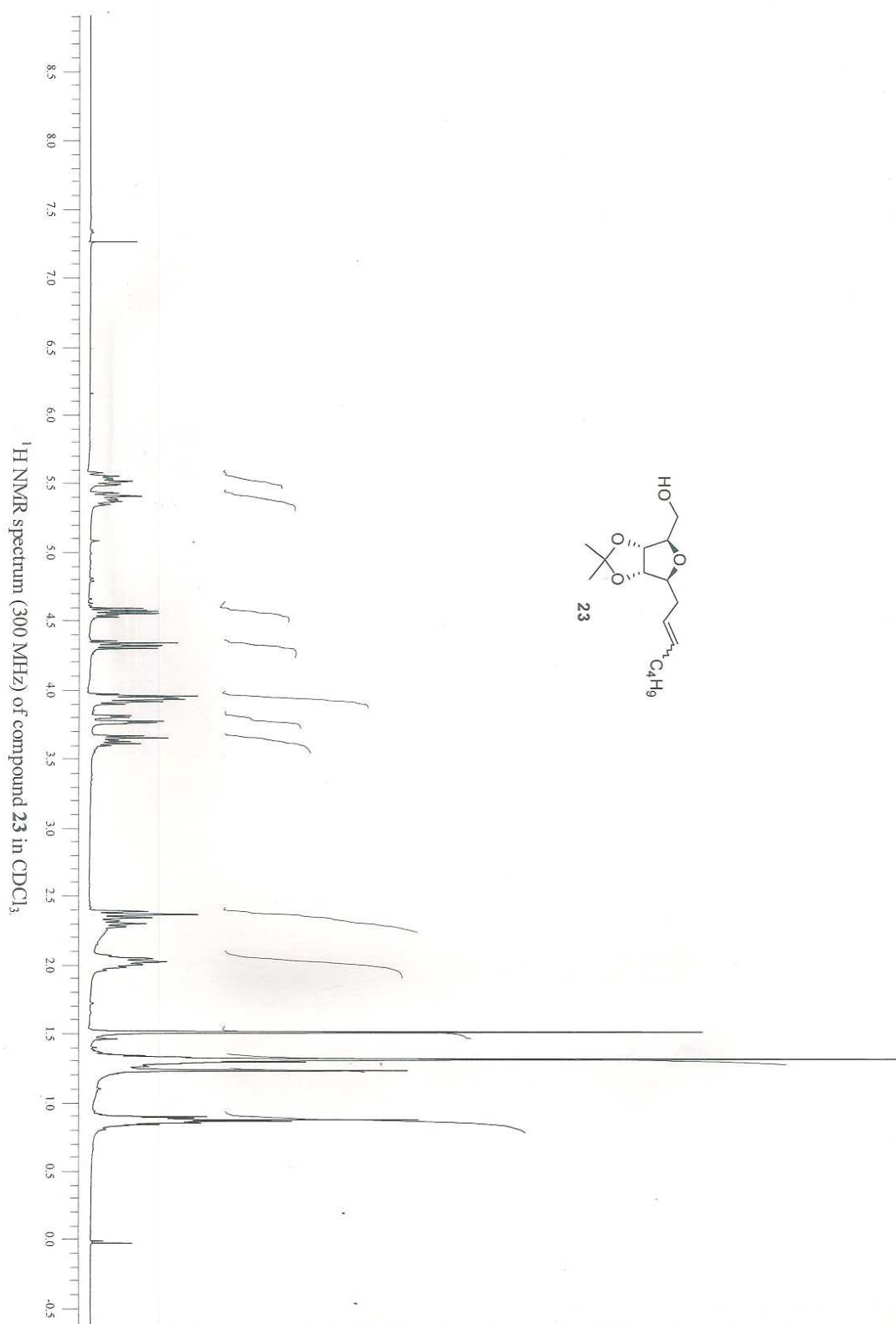
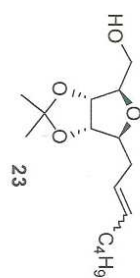
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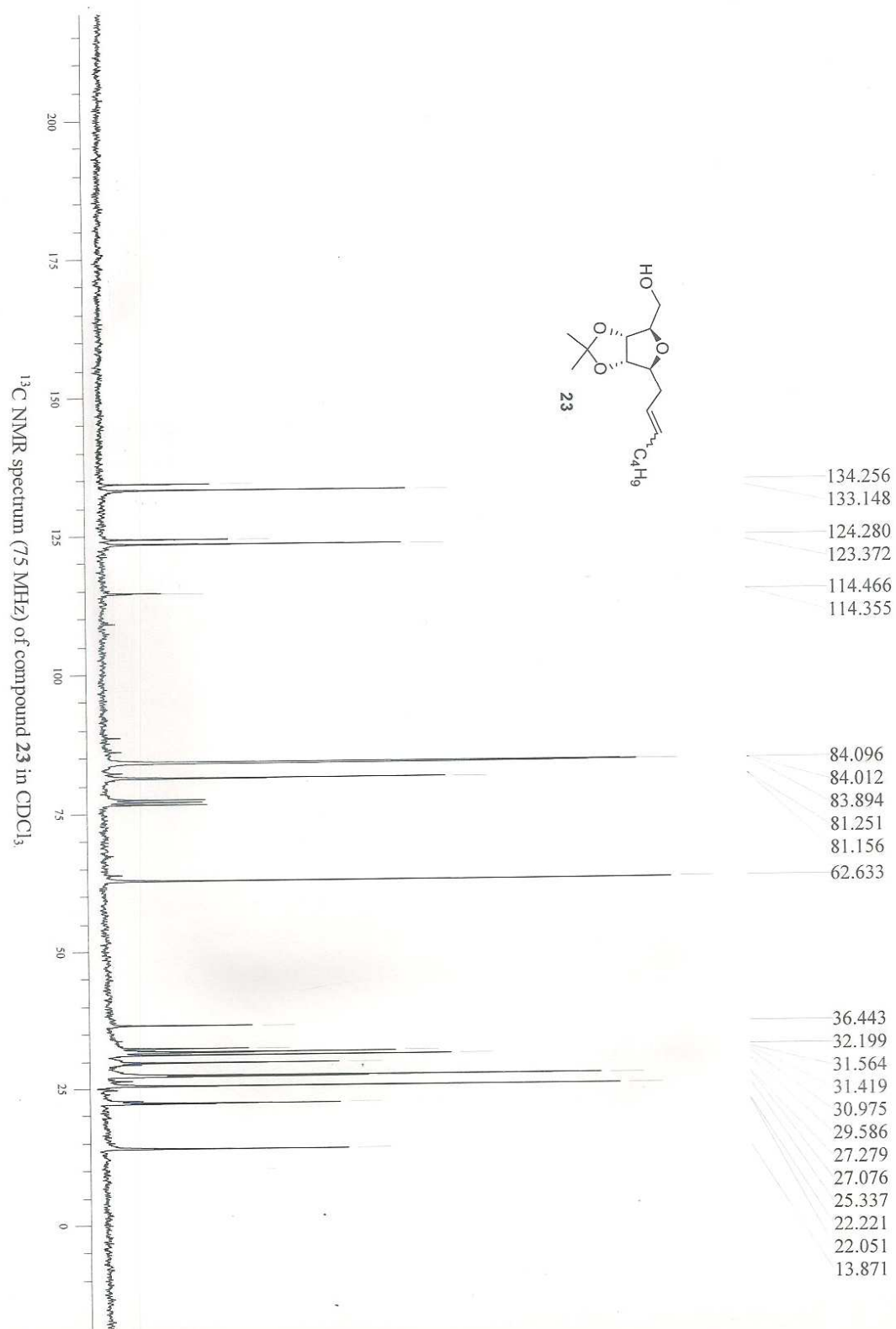
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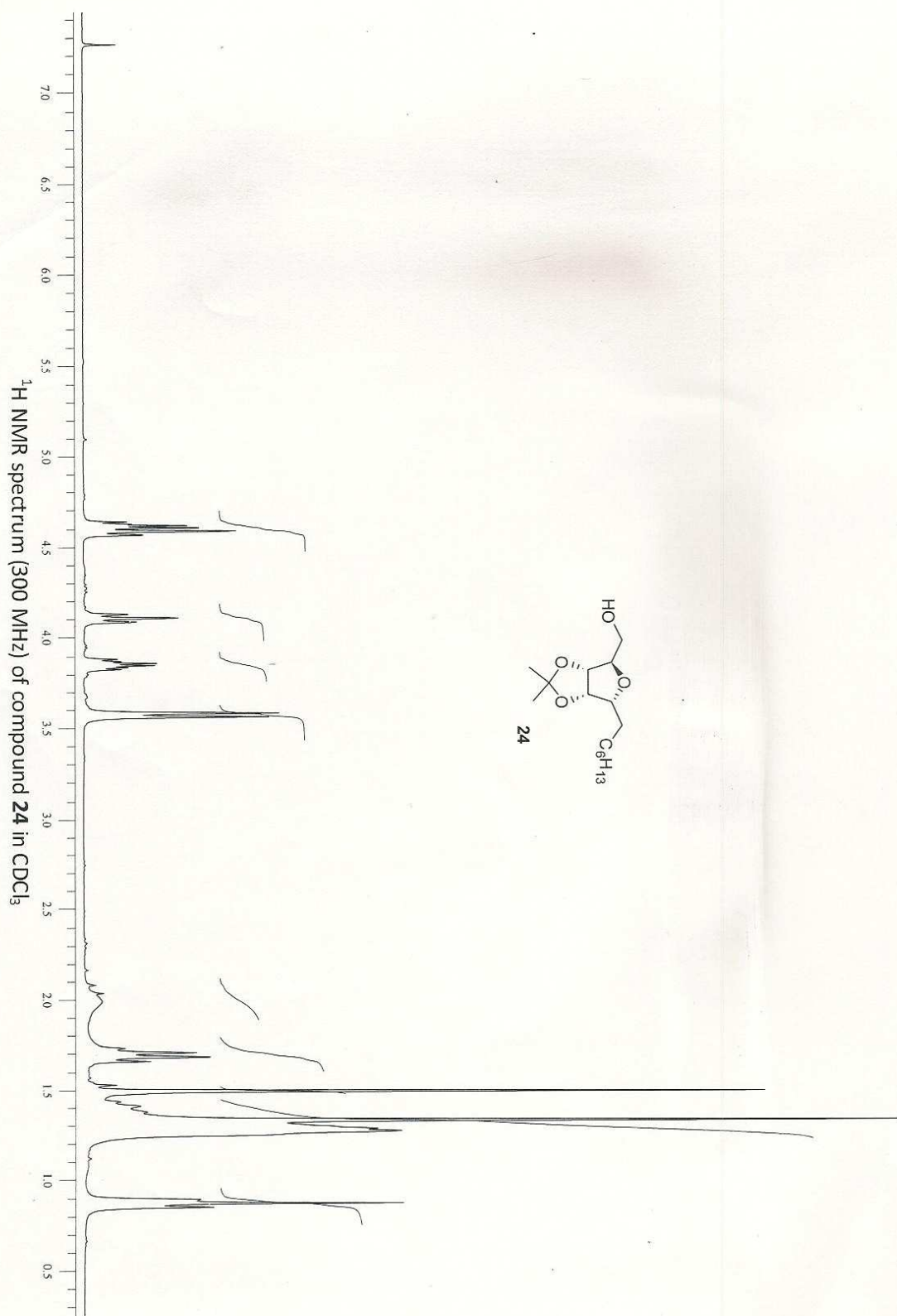
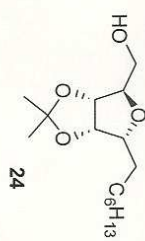
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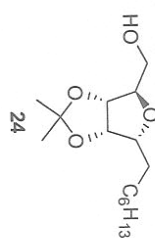
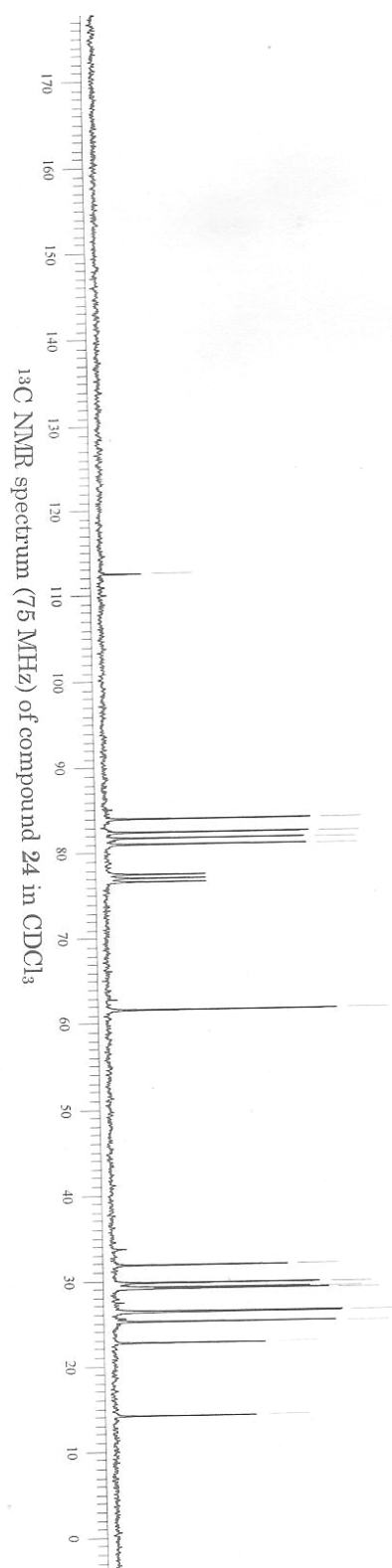
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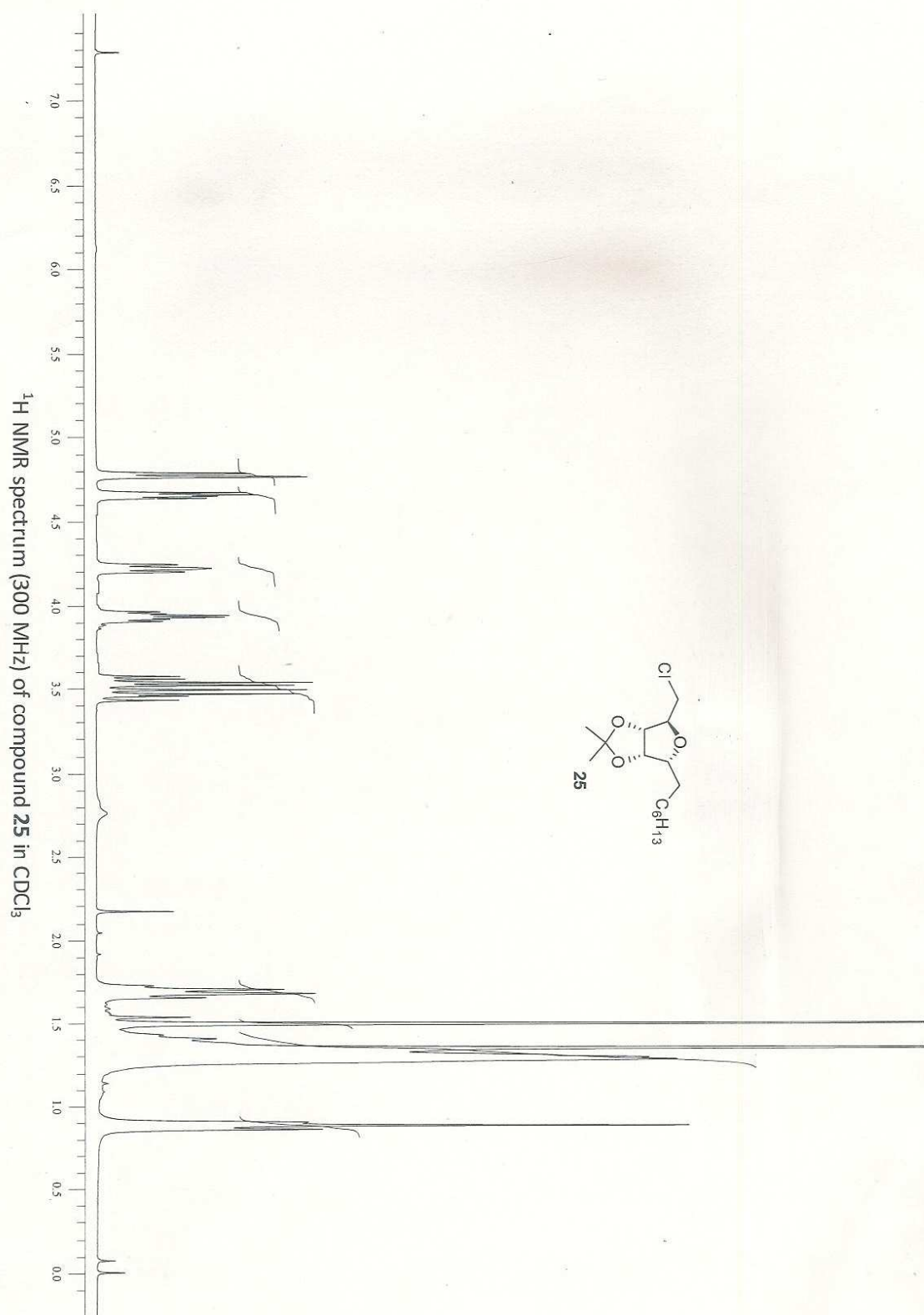
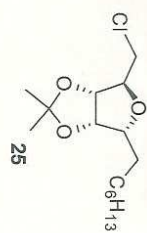


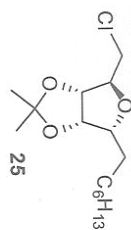
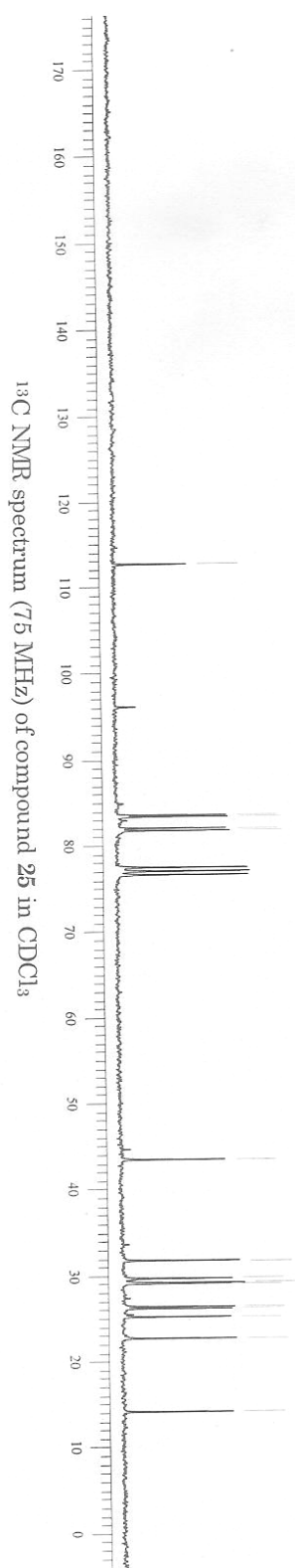
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80.925

61.537

31.763
29.690
29.151
29.008
26.309
26.209
25.096
22.630
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112.544

83.487

83.291

81.966

81.672

43.407

31.740

29.625

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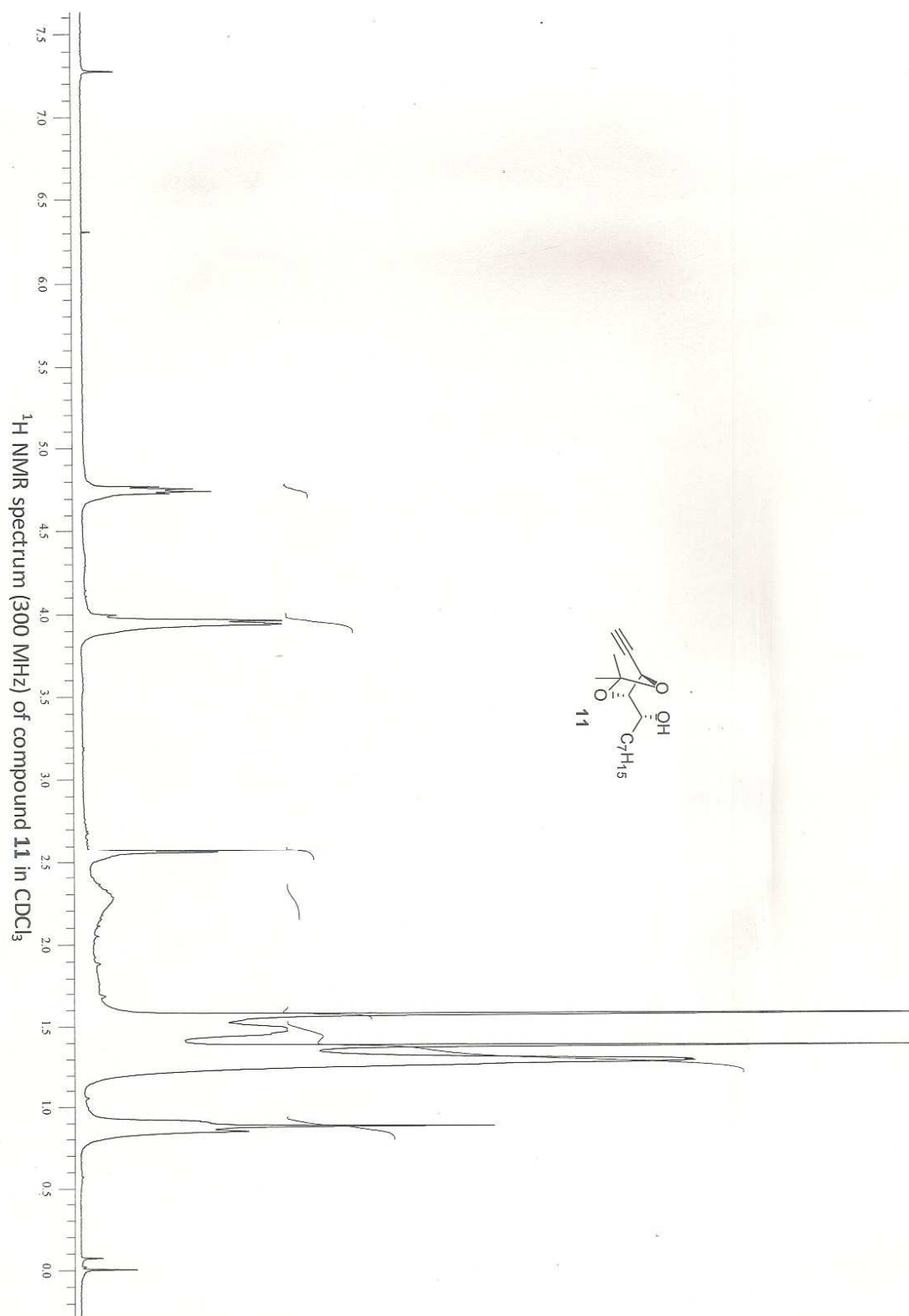
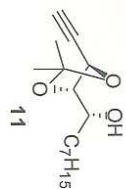
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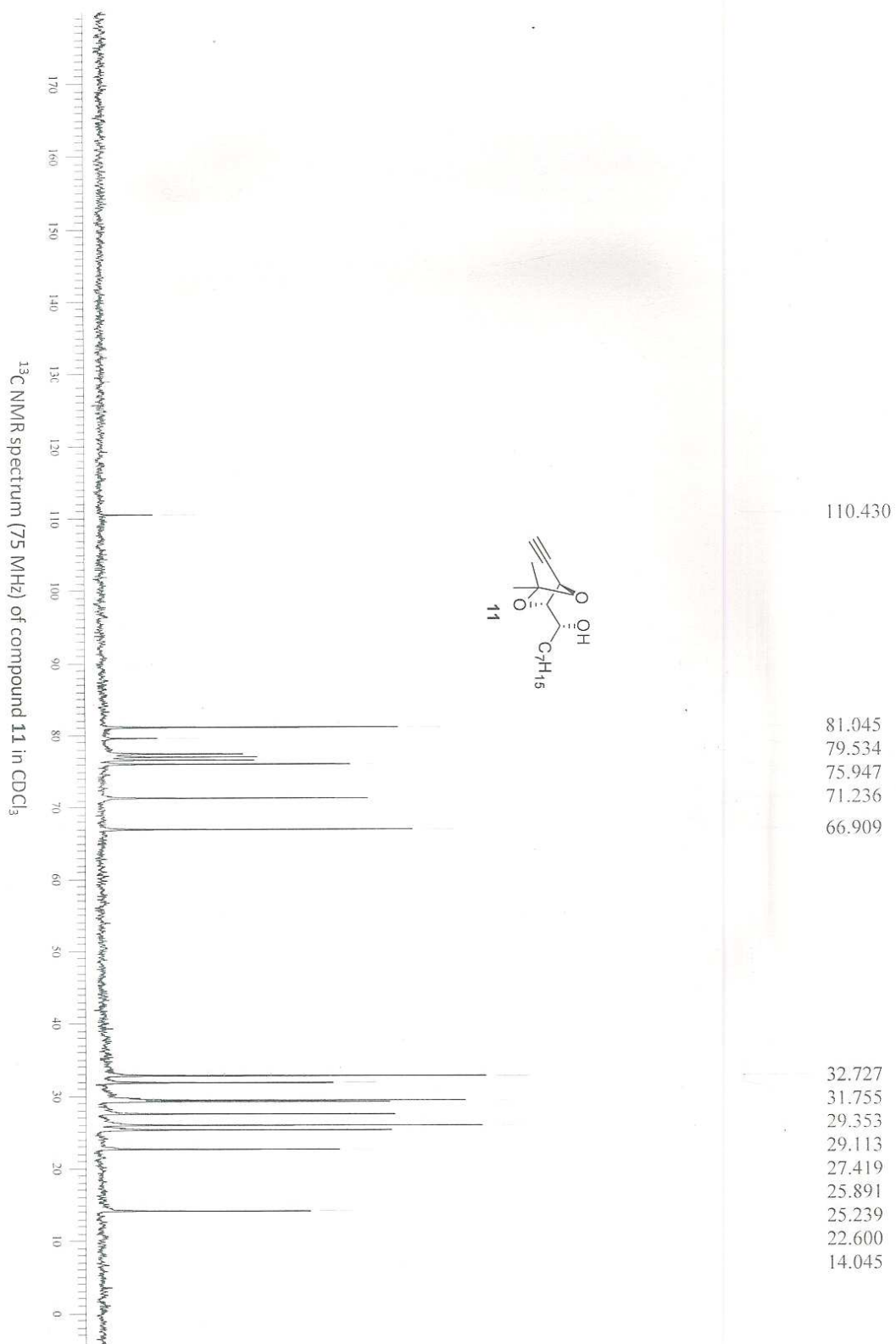
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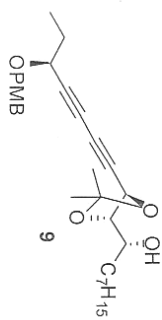
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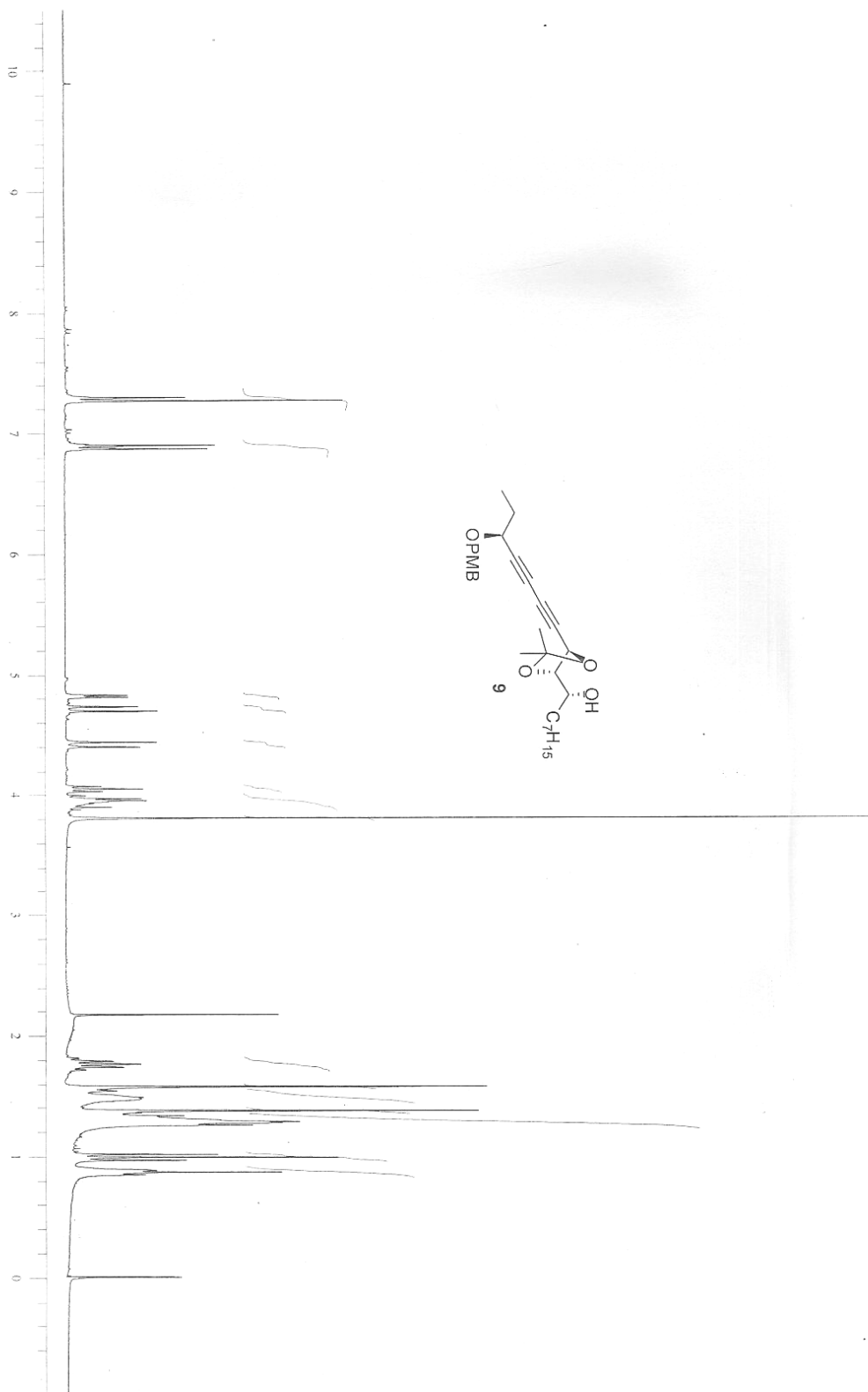
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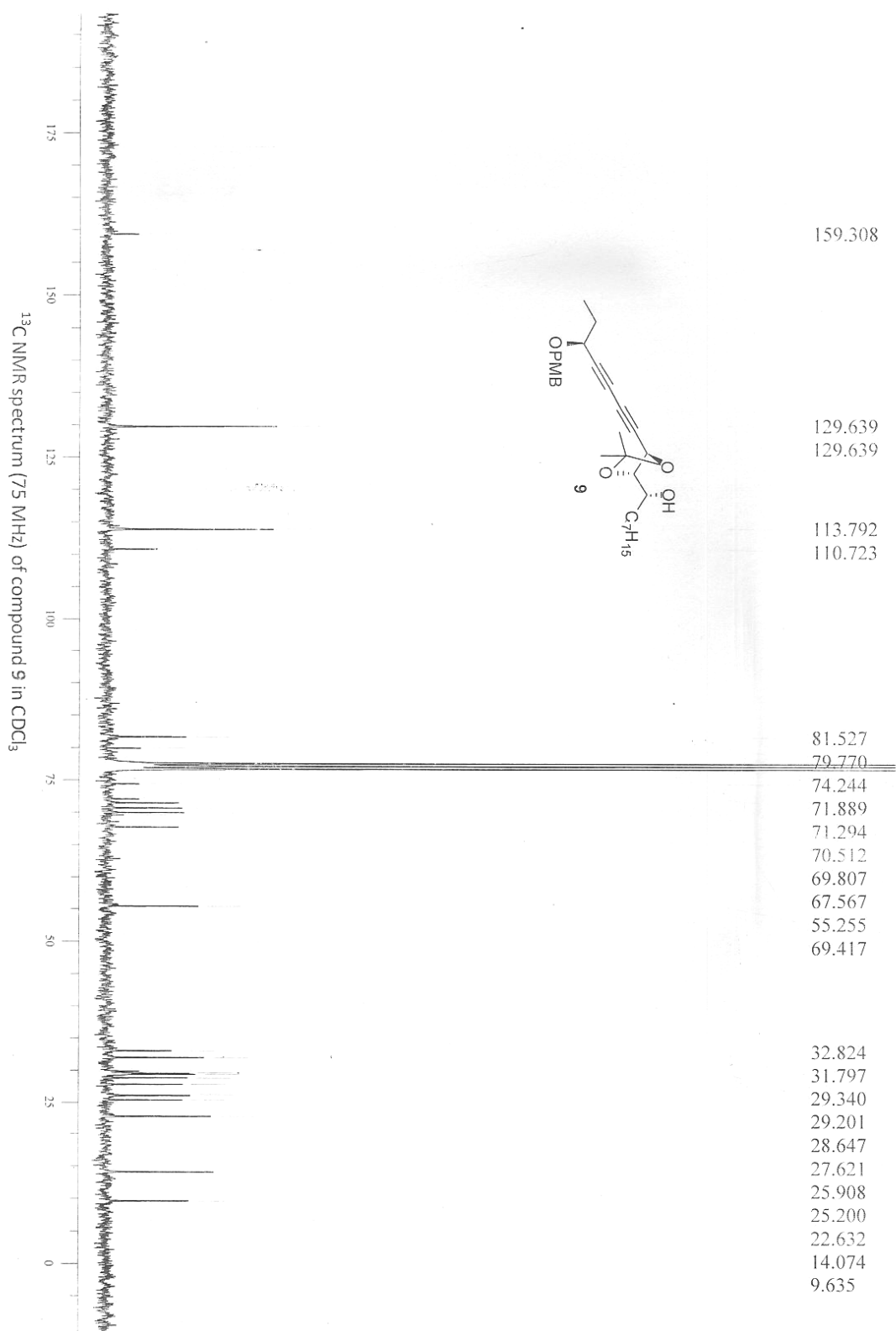


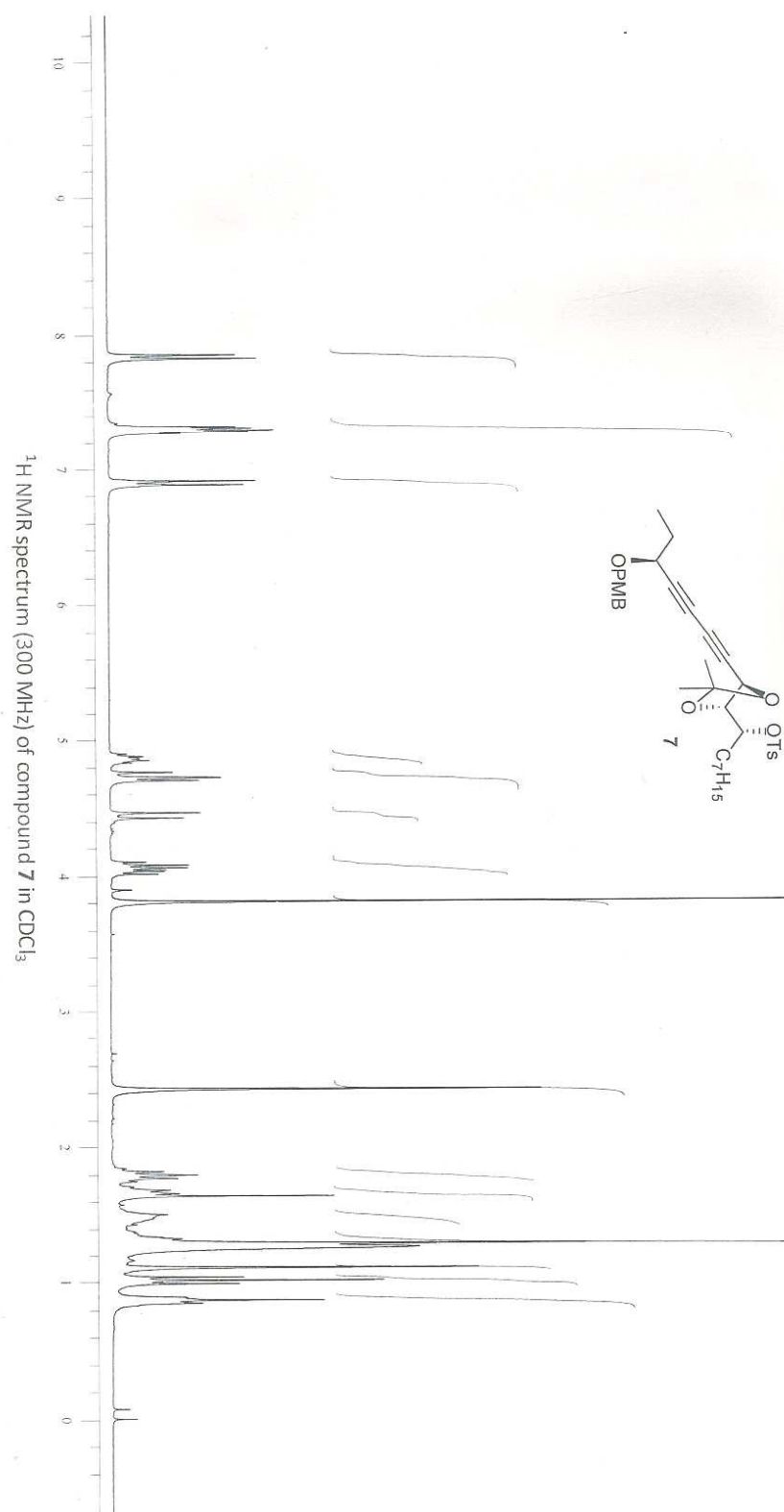


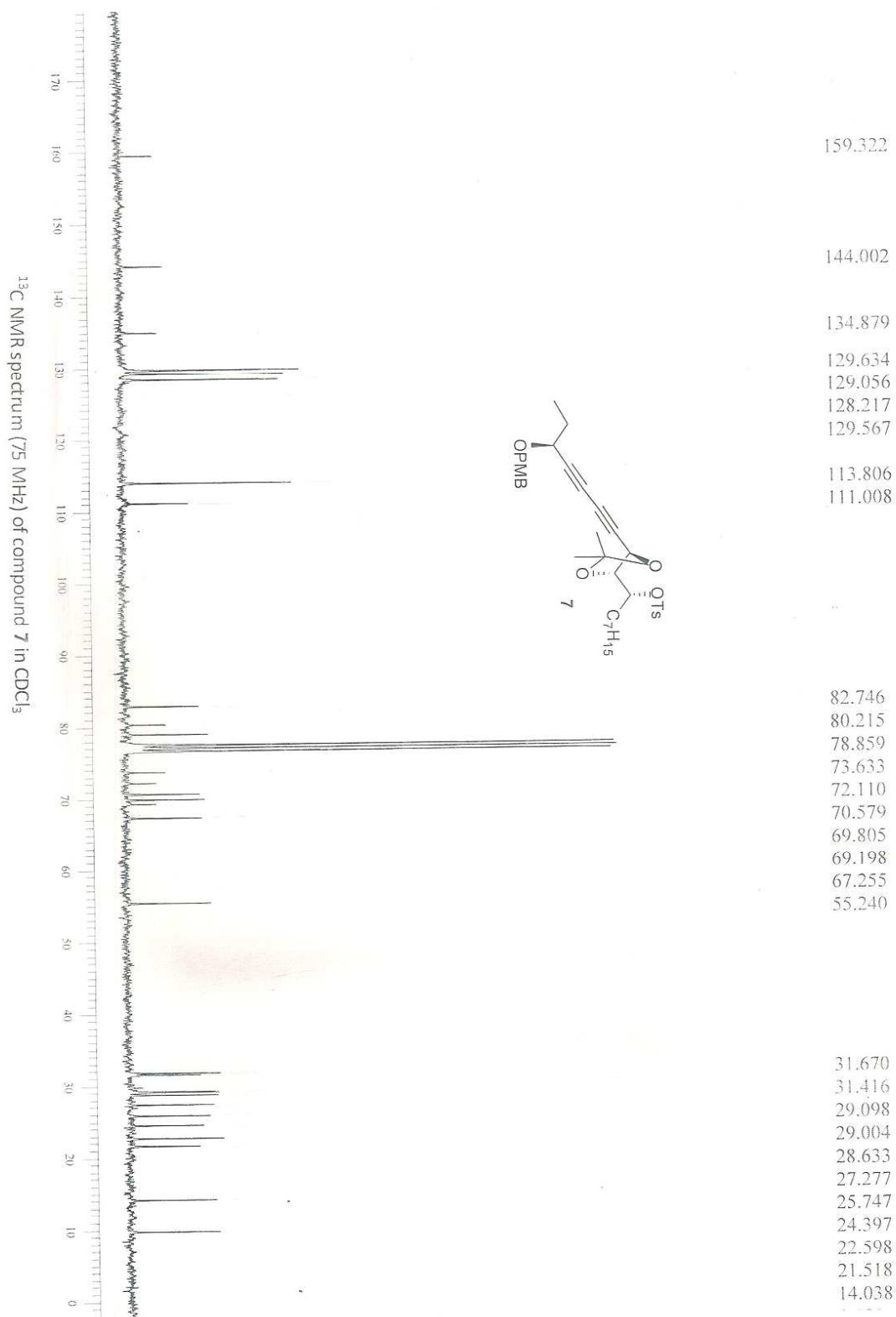


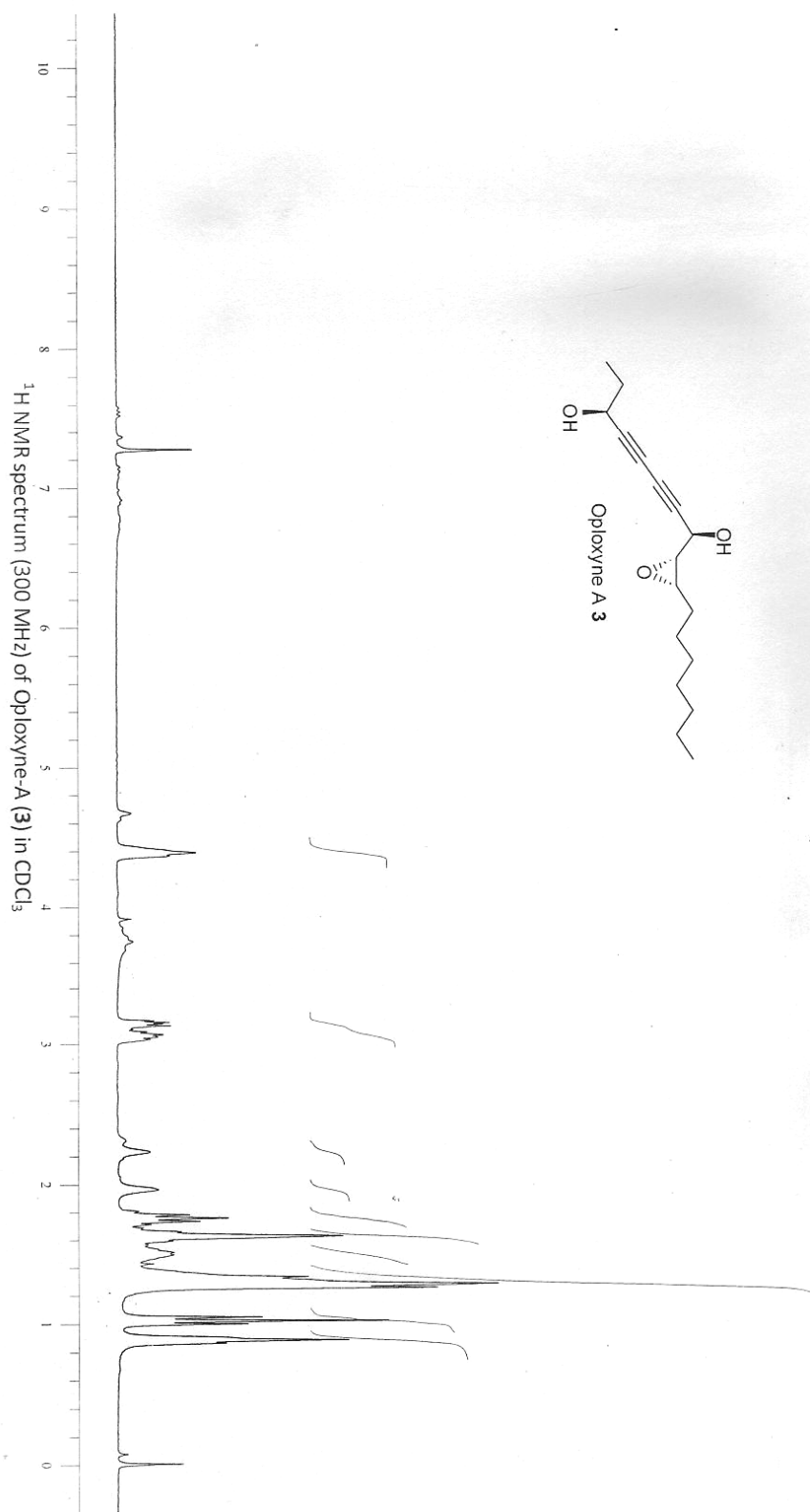
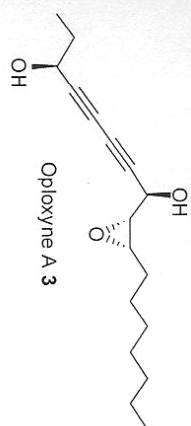
1H NMR spectrum (300 MHz) of compound **9** in $CDCl_3$

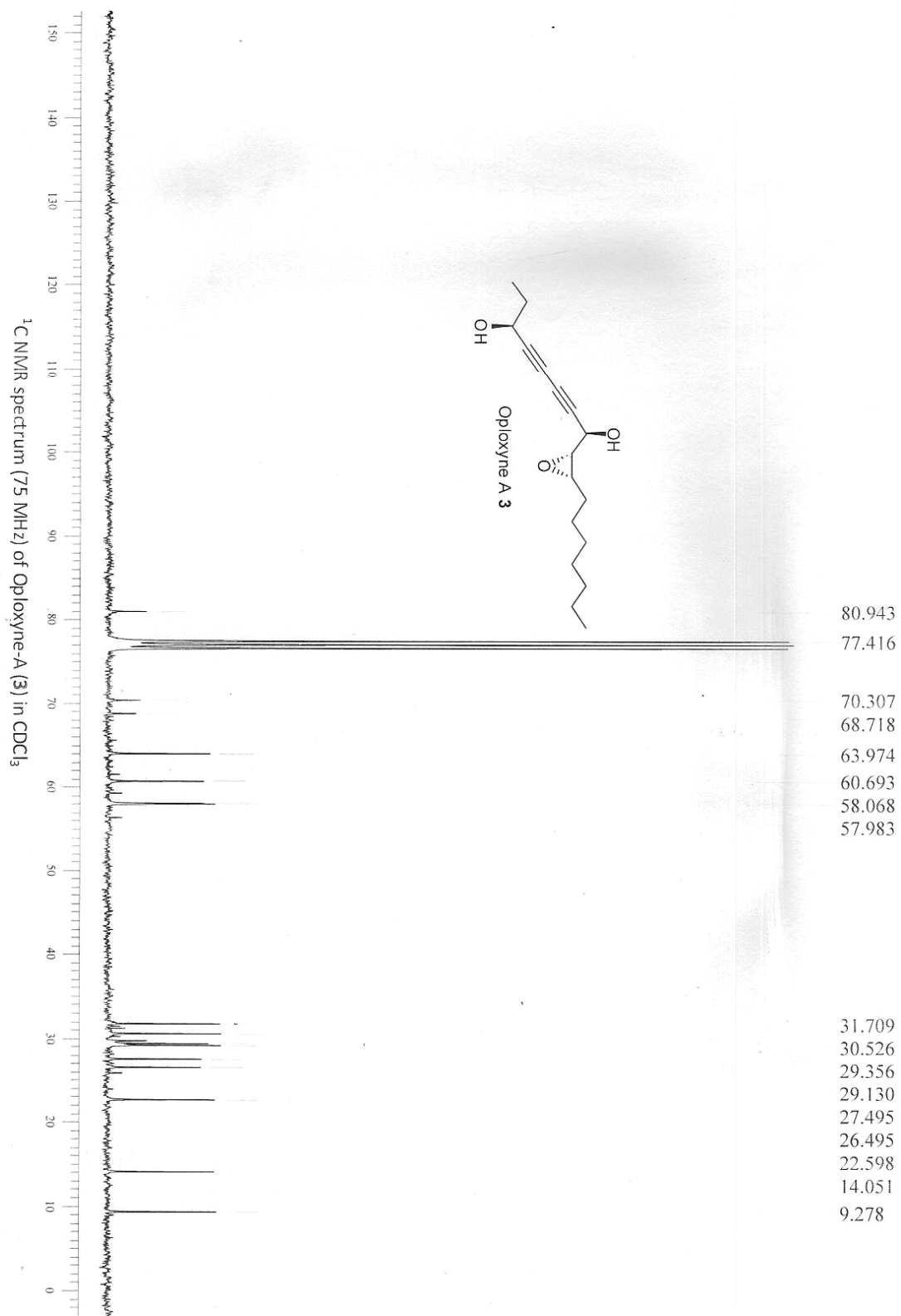


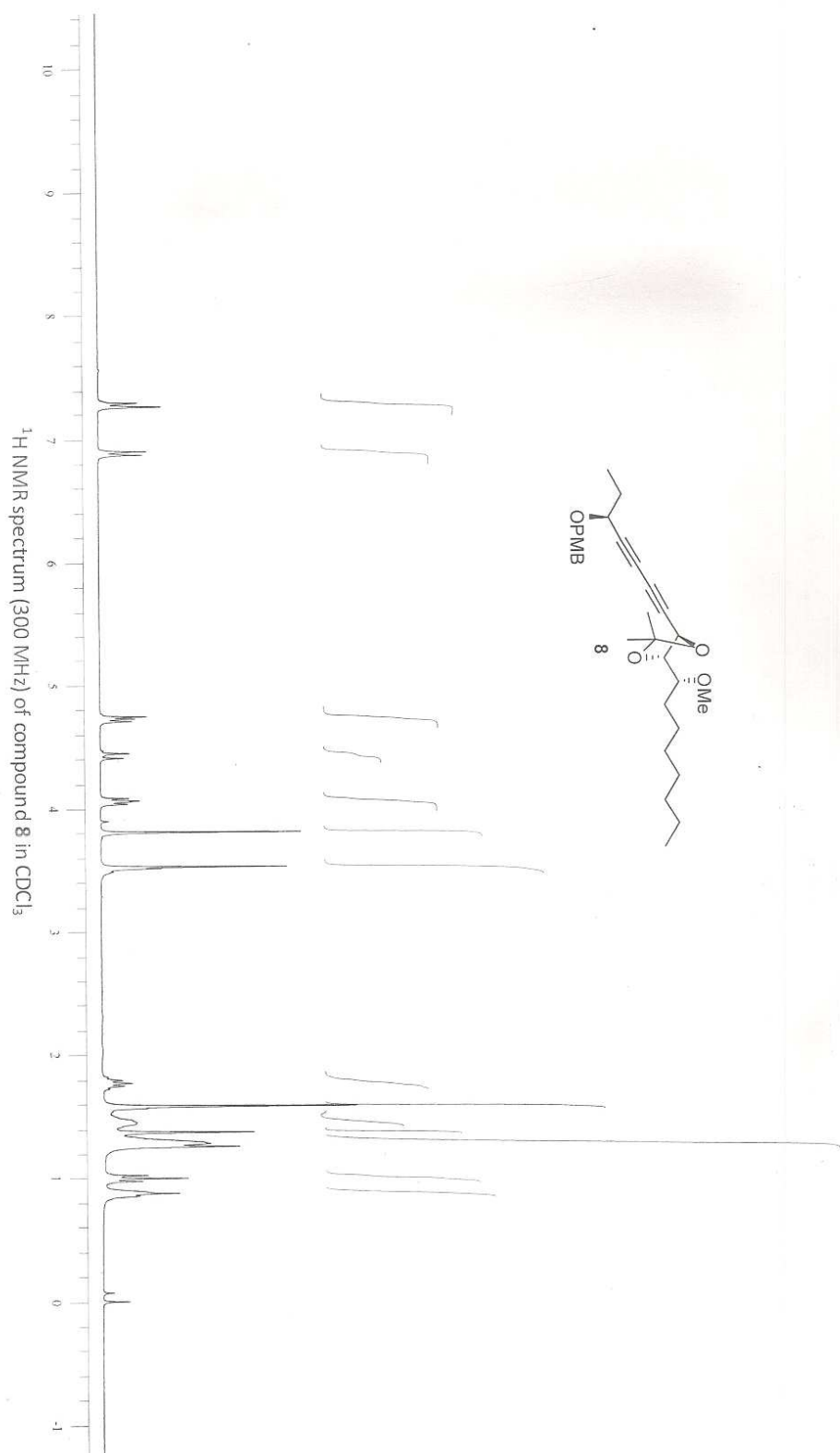
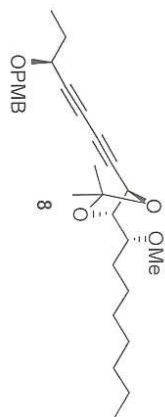


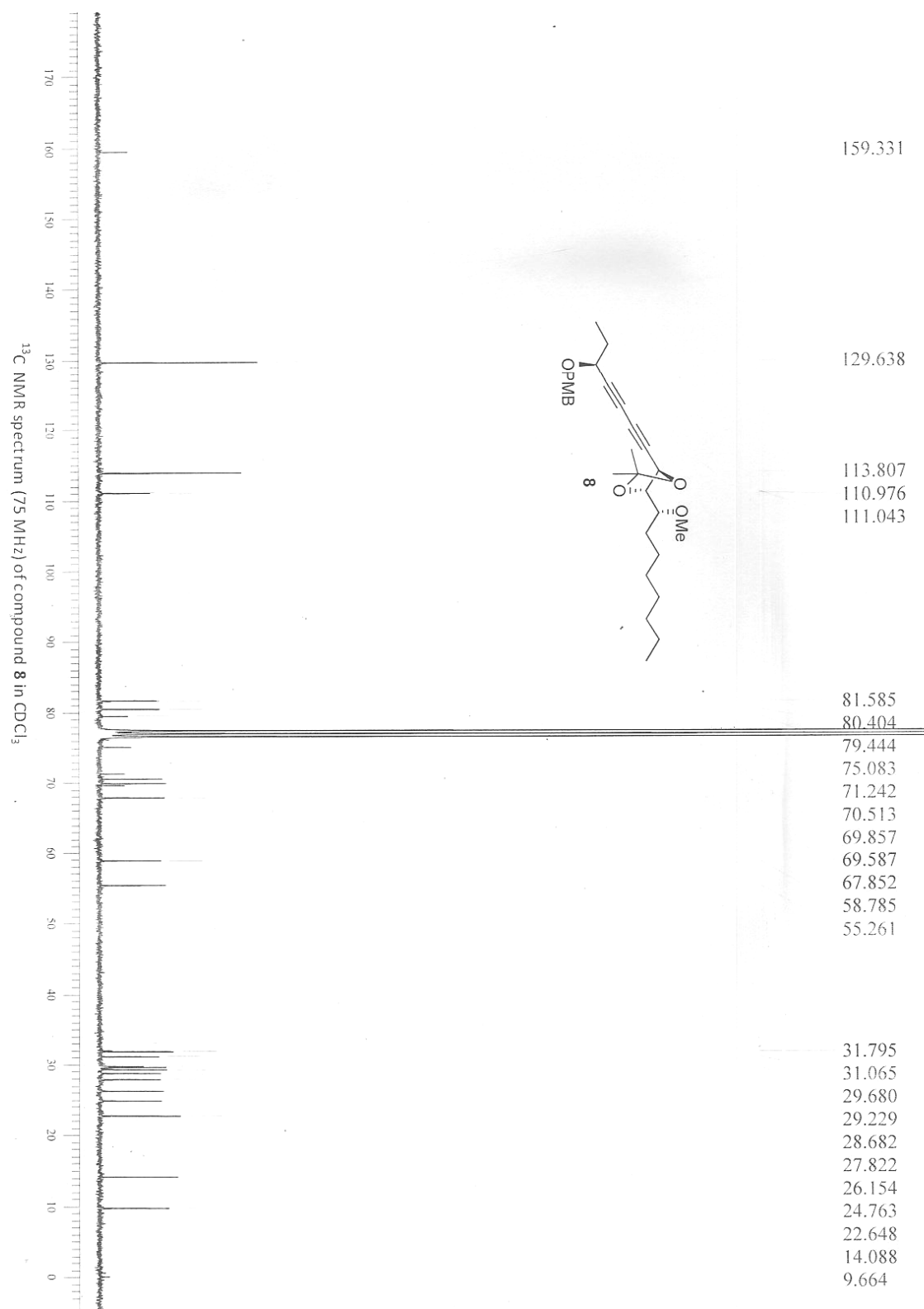


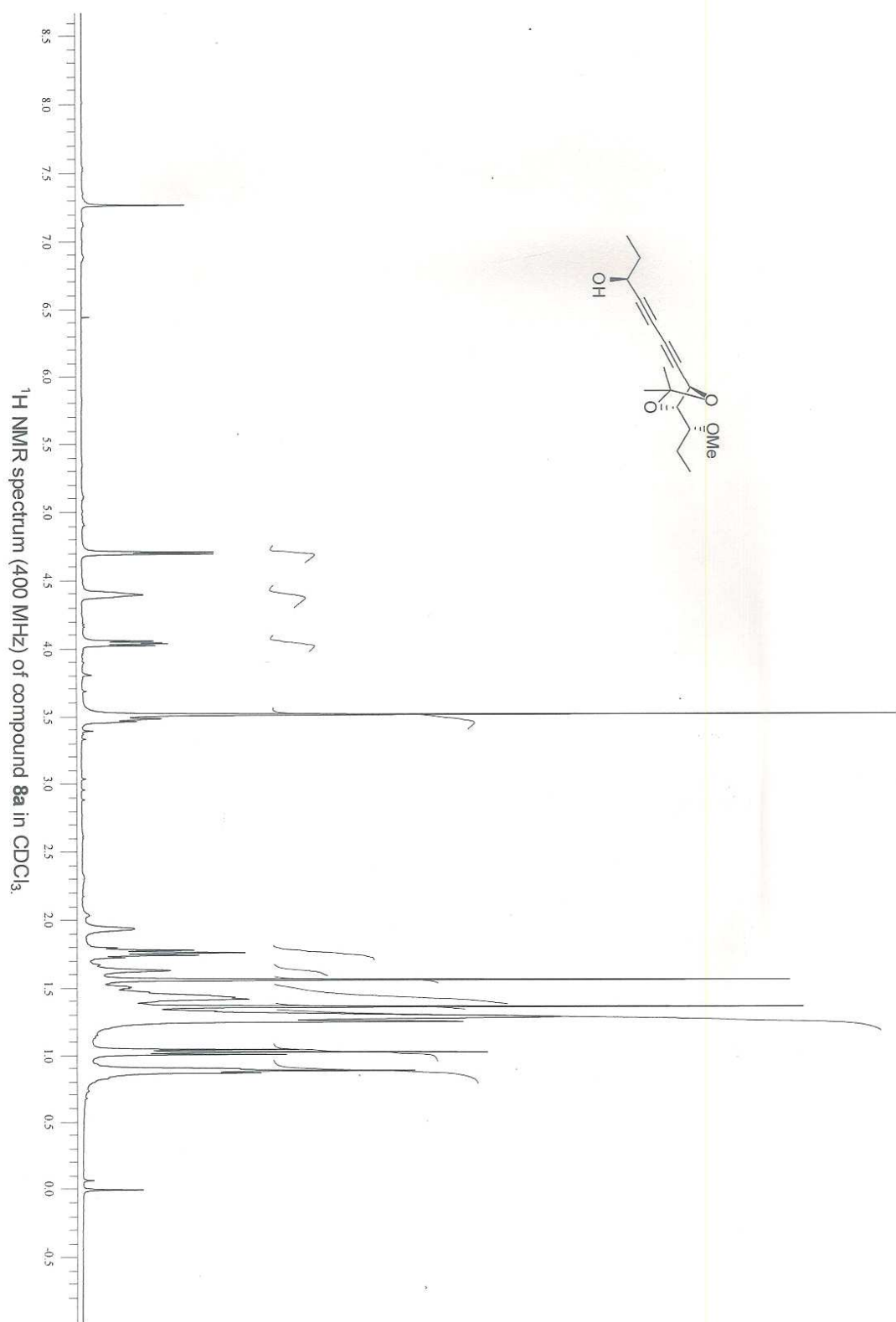
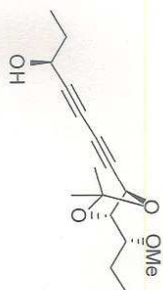


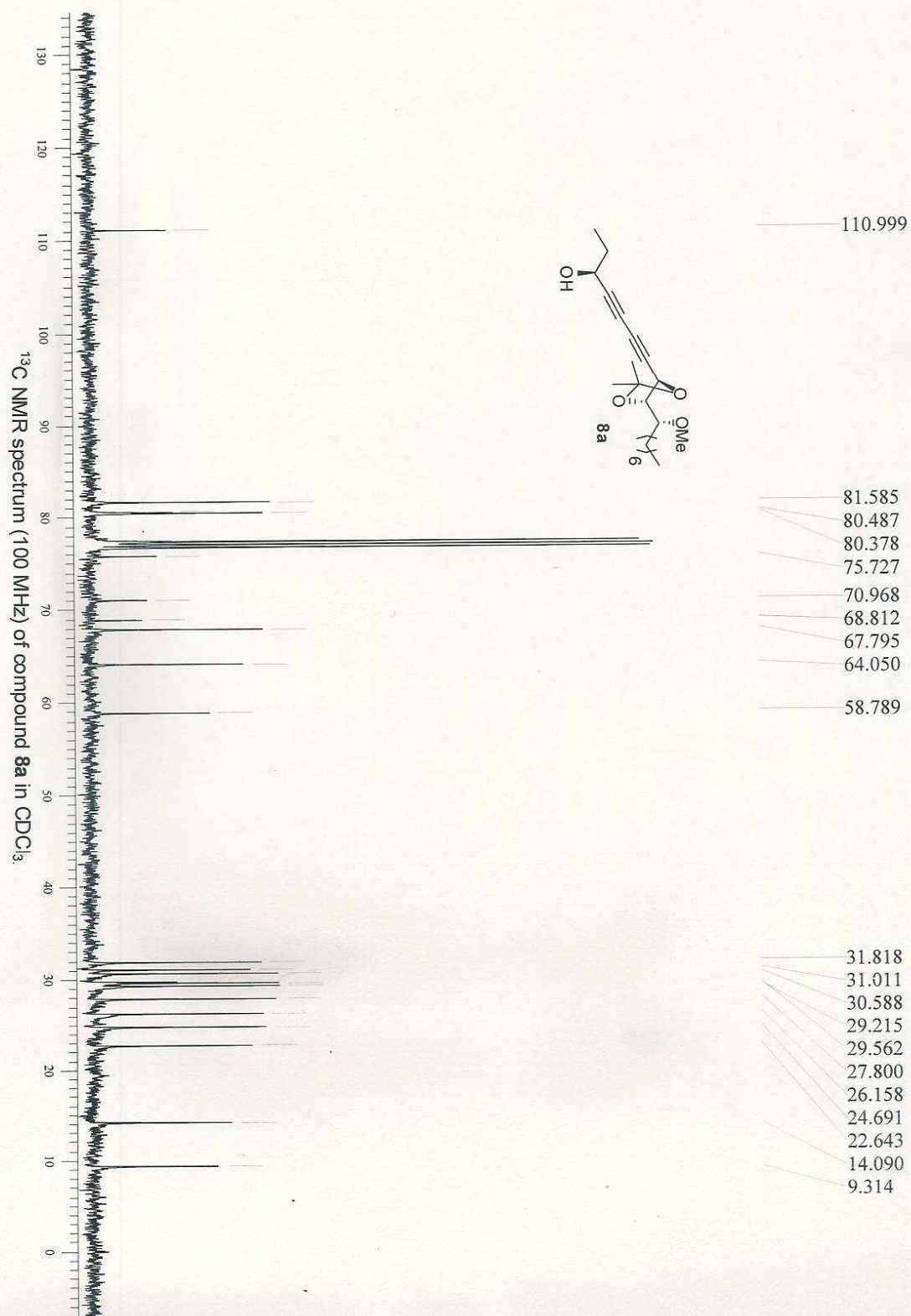




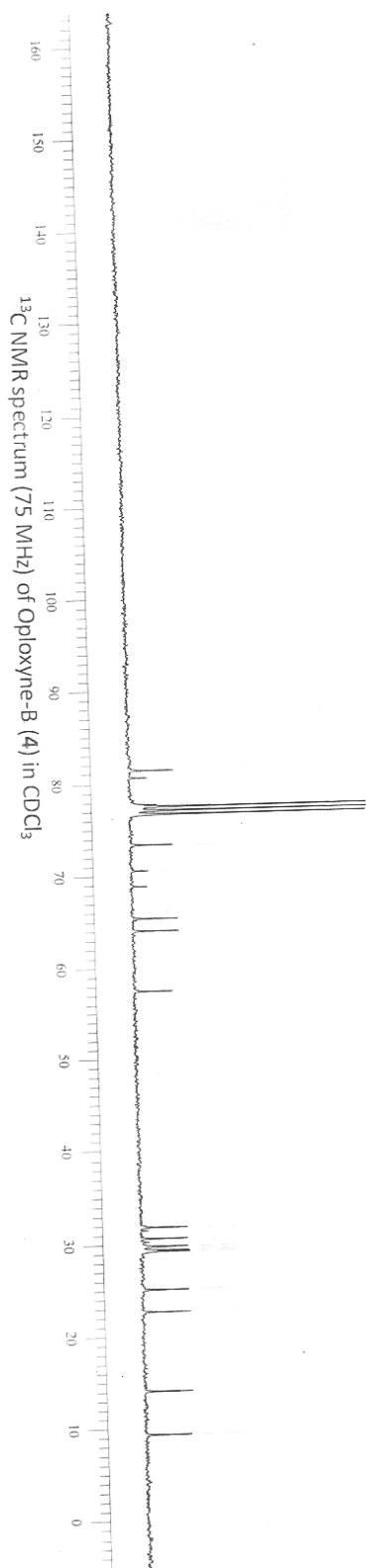
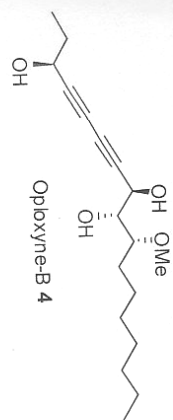






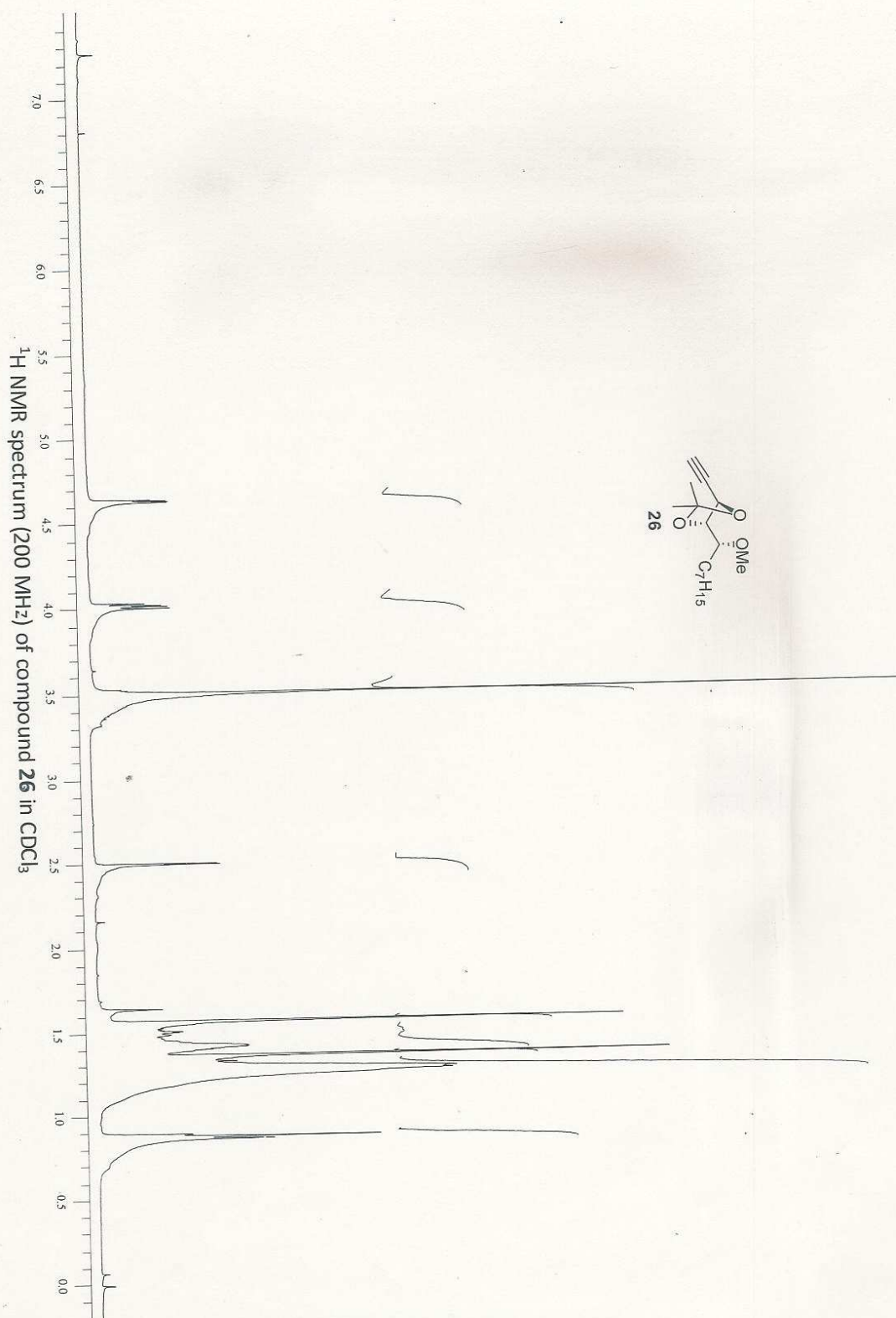


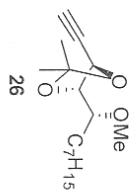
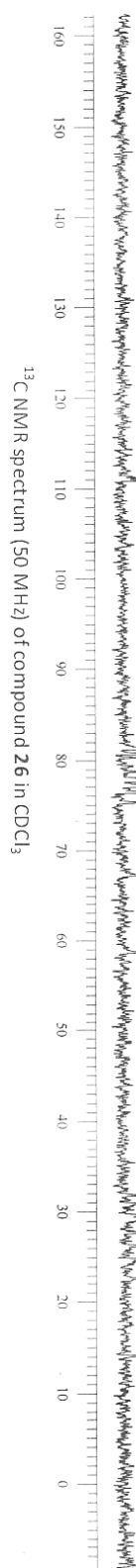




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57.434

31.752
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29.303
29.171
25.023
22.597
14.037
9.294





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81.135

80.553

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80.190

67.174

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29.551

29.156

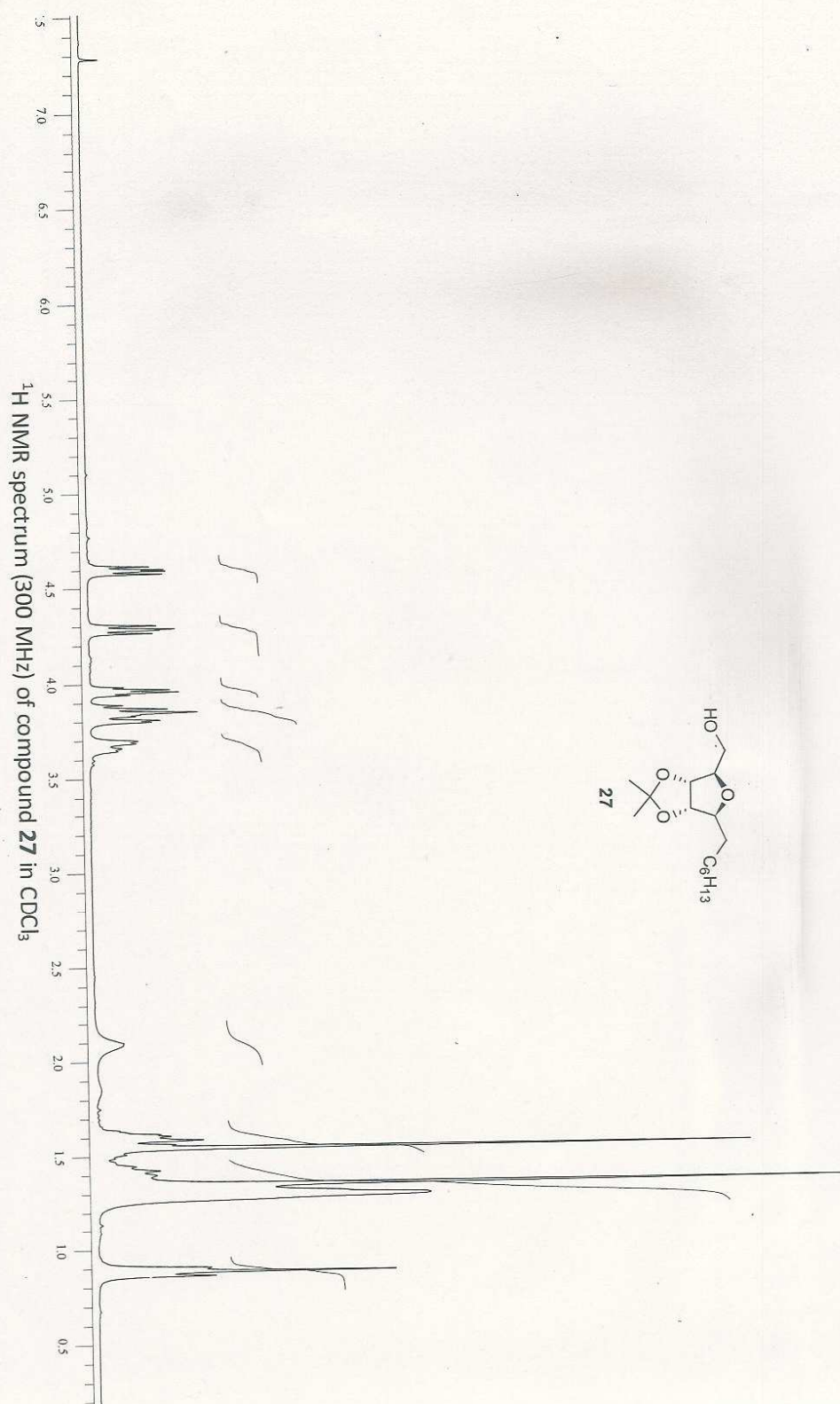
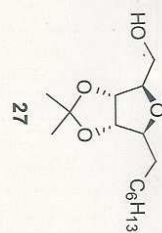
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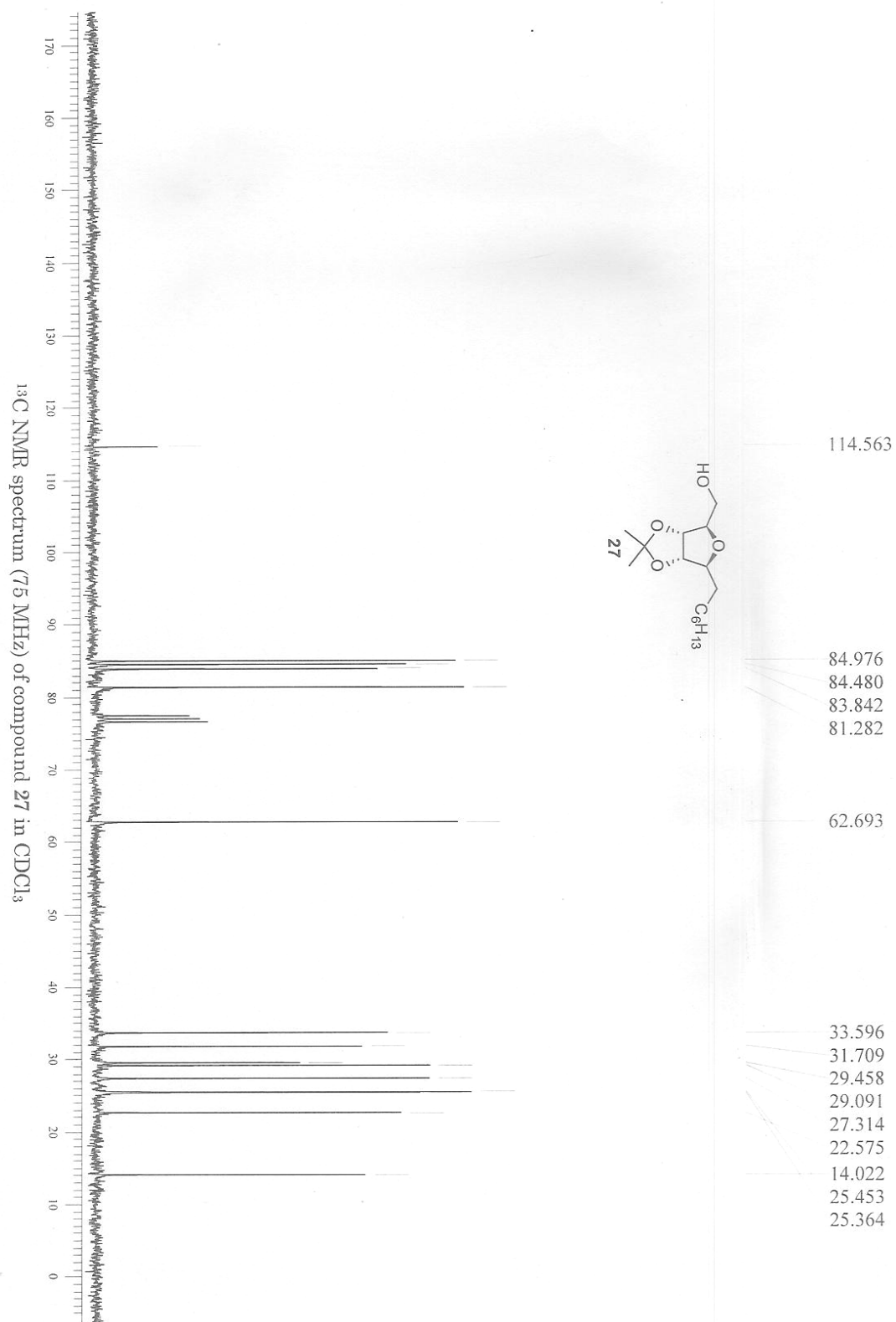
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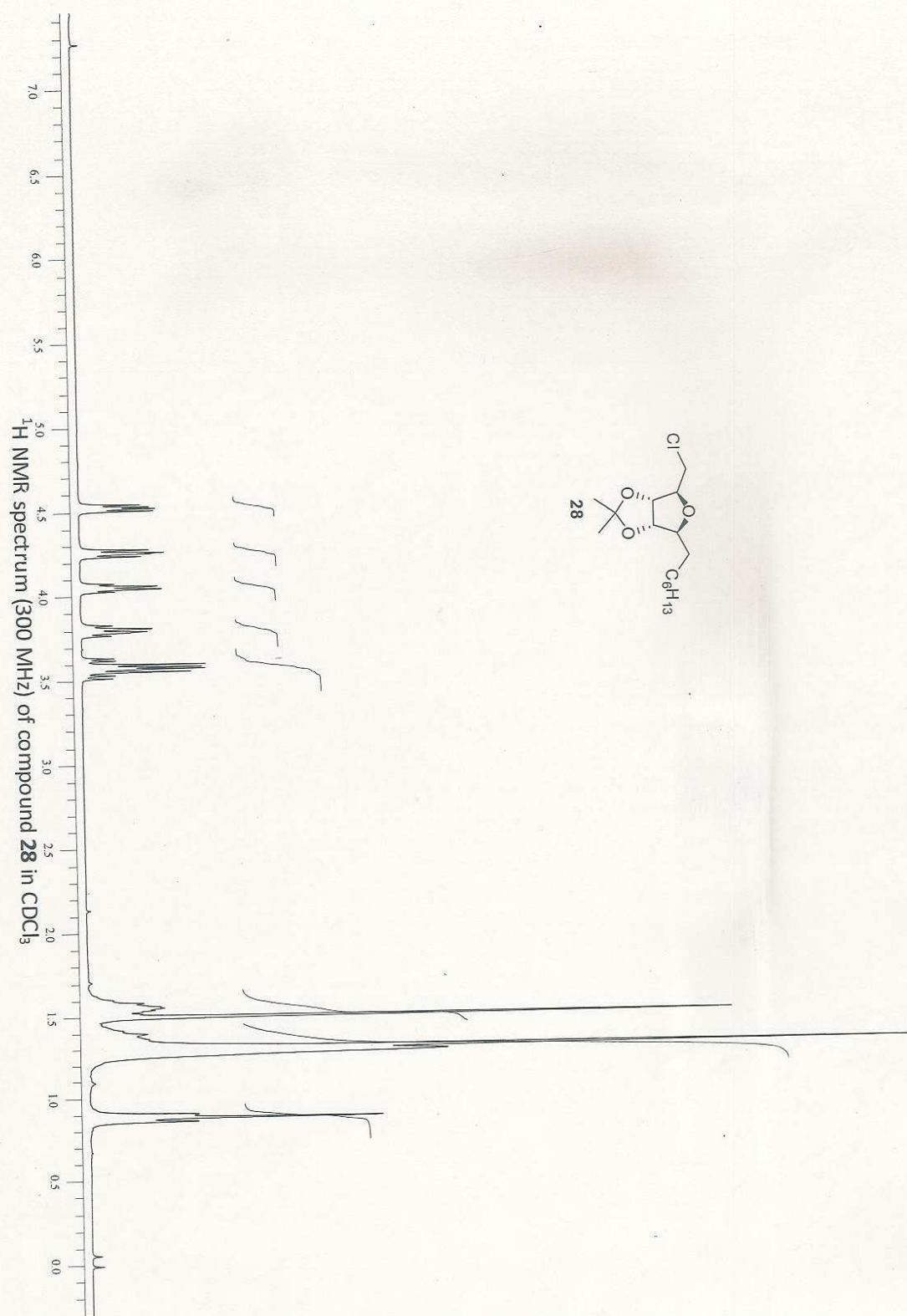
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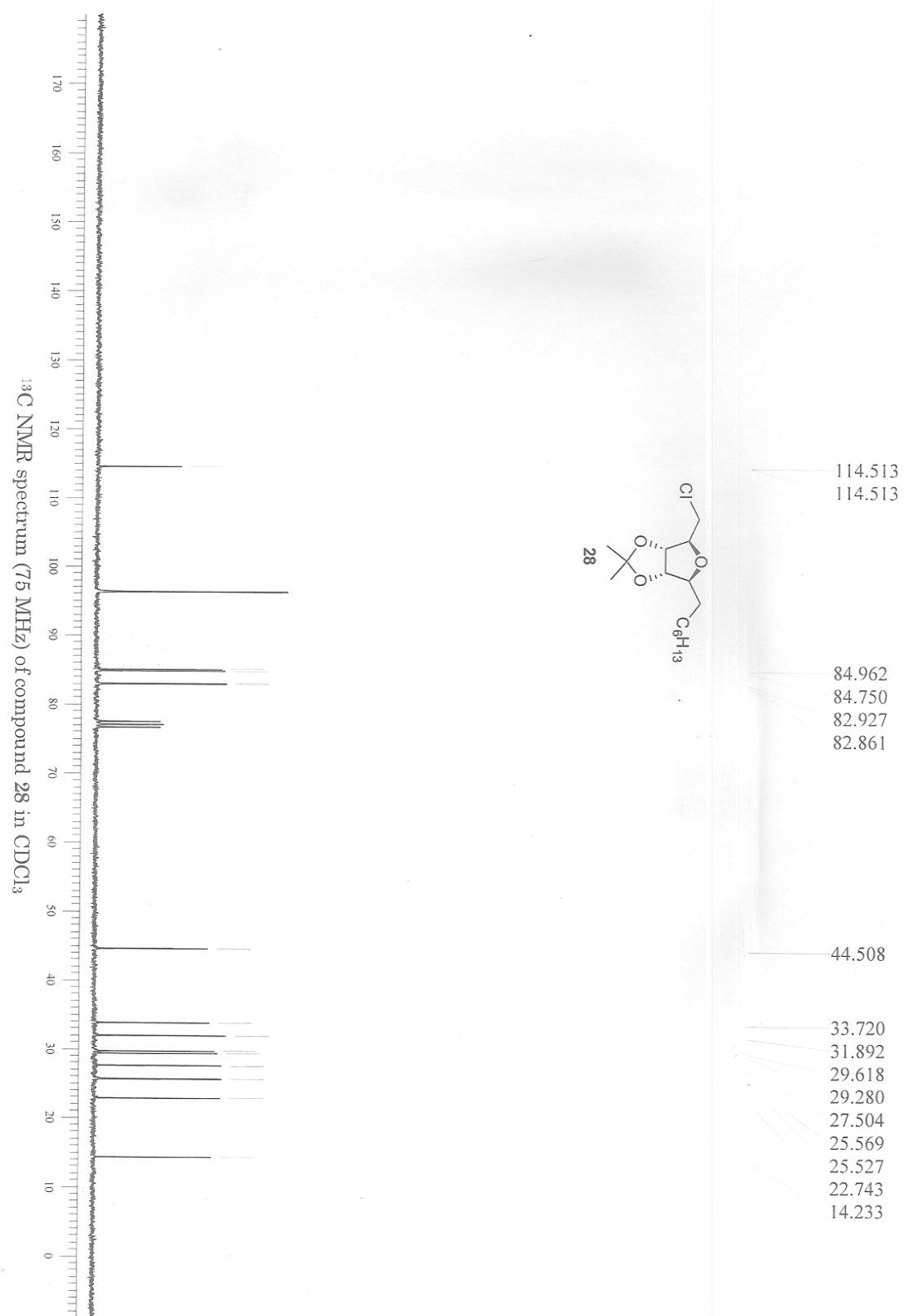
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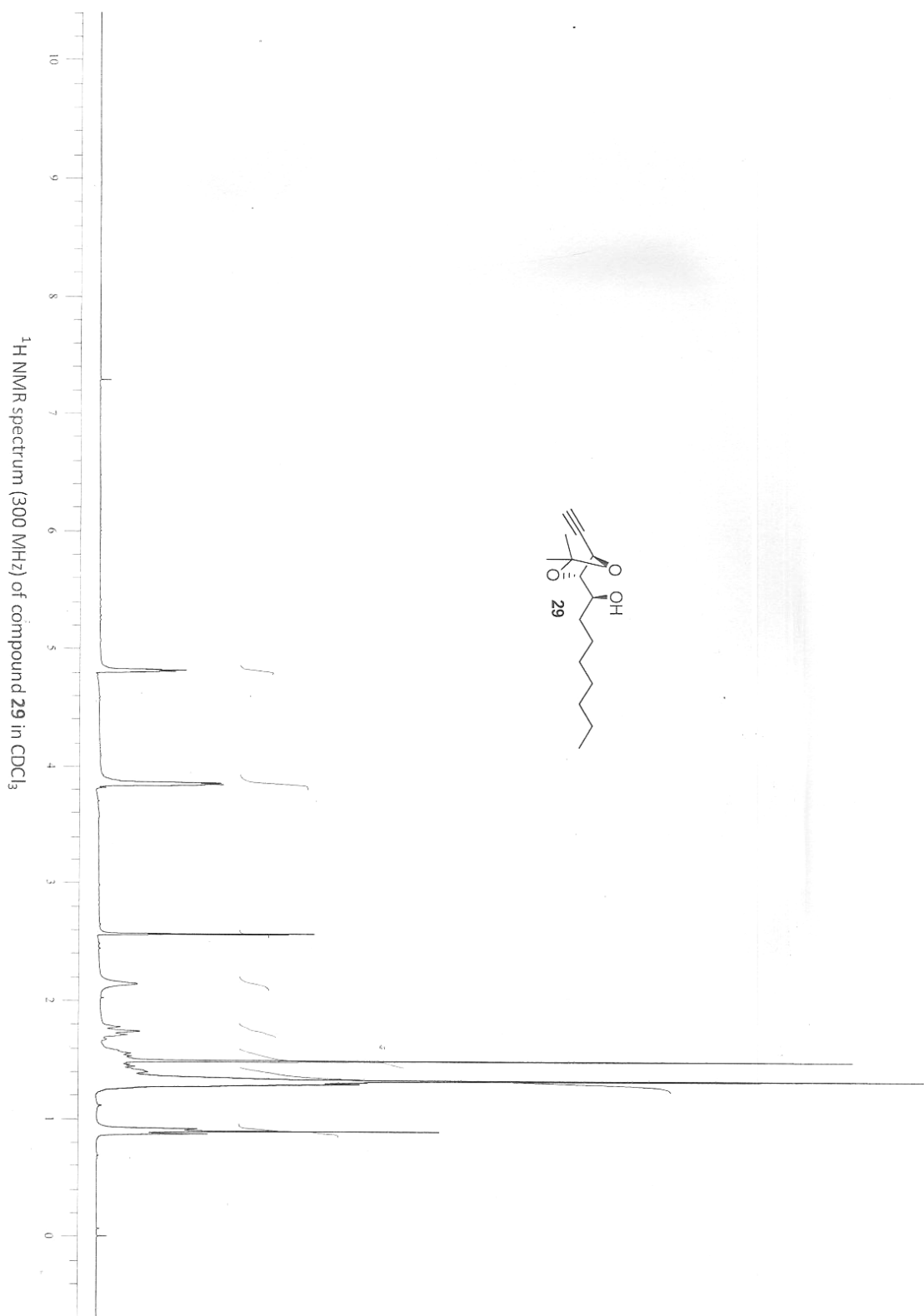
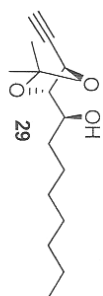
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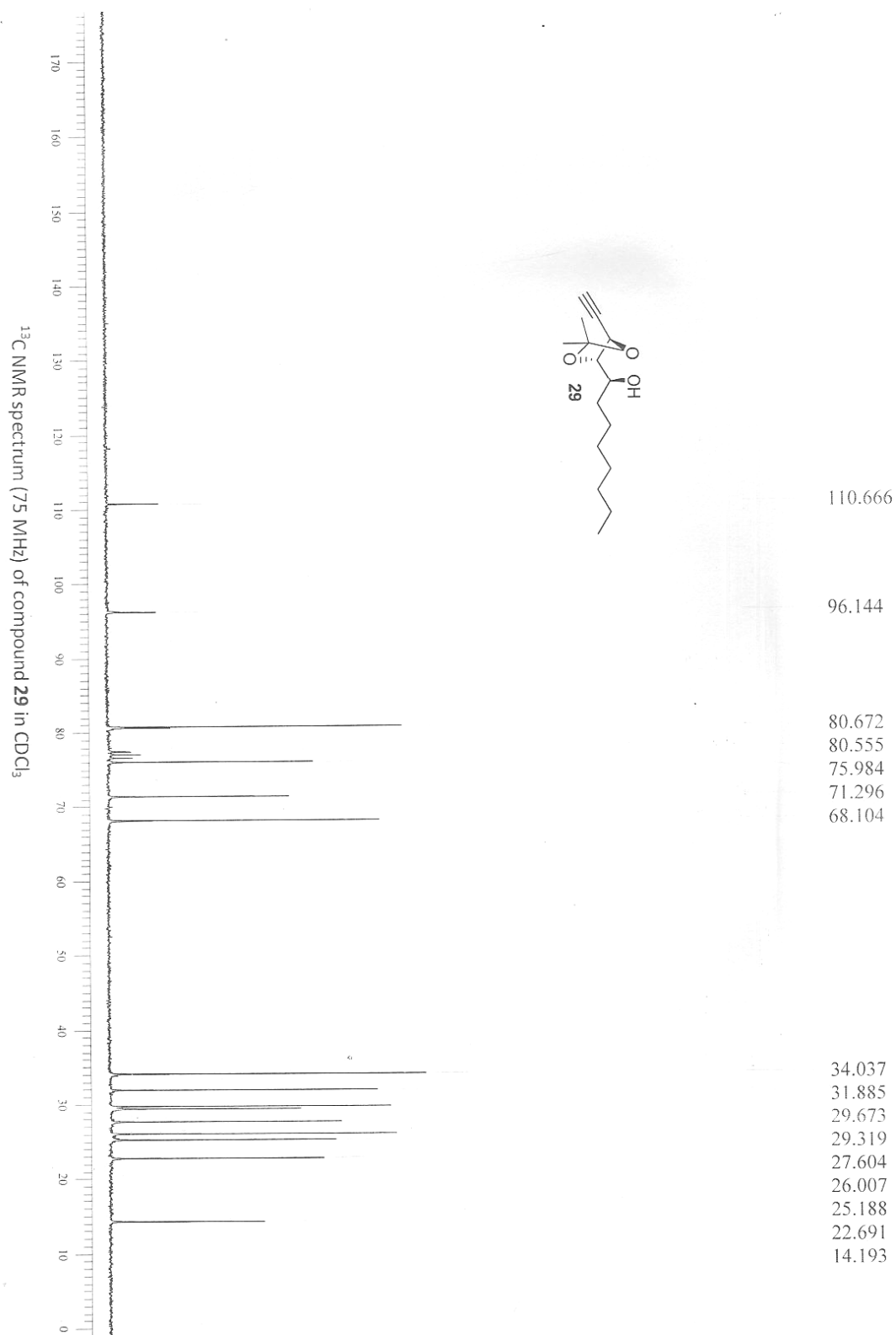


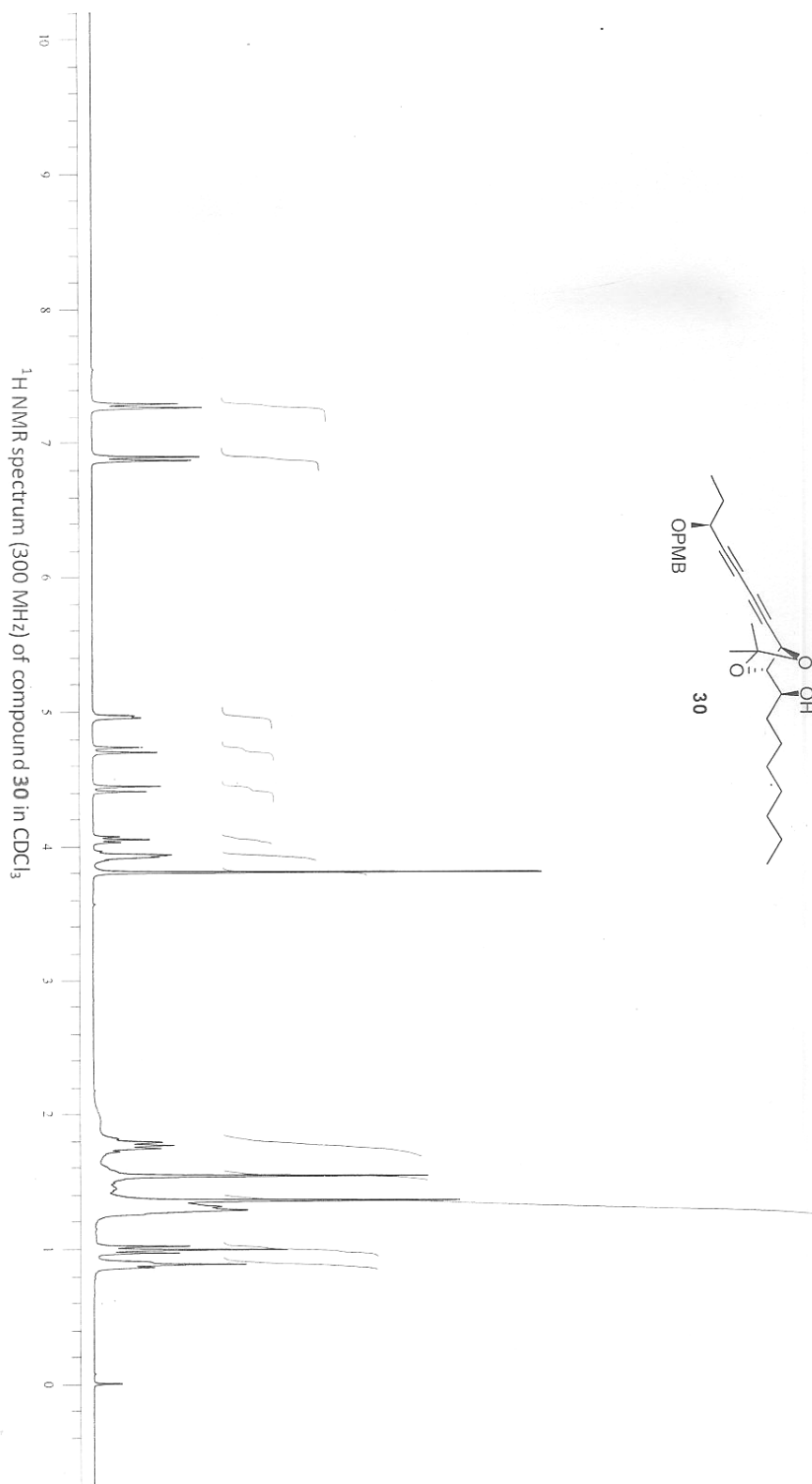
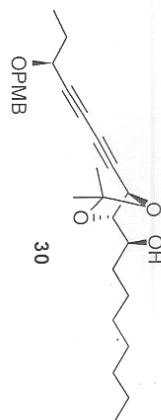


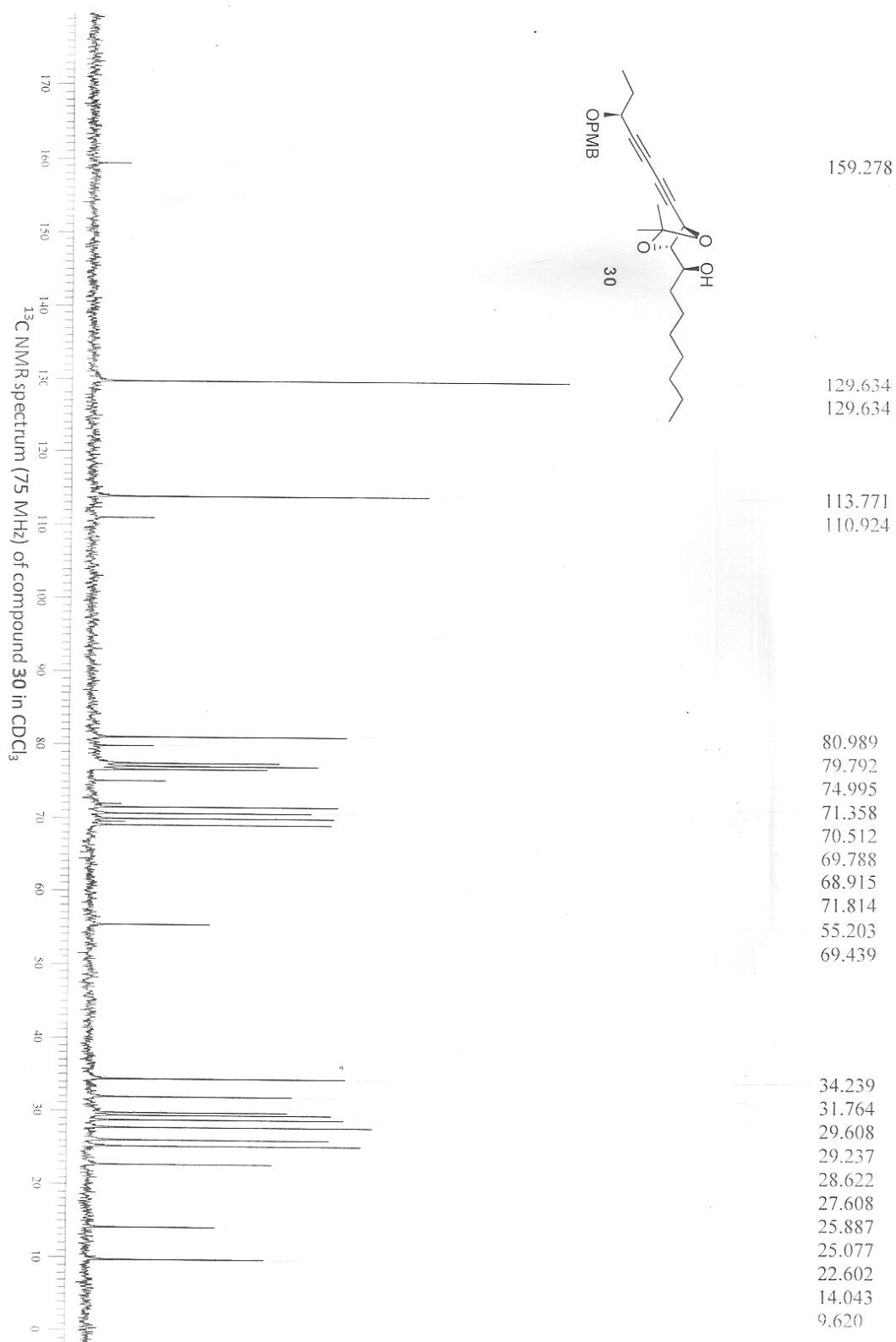


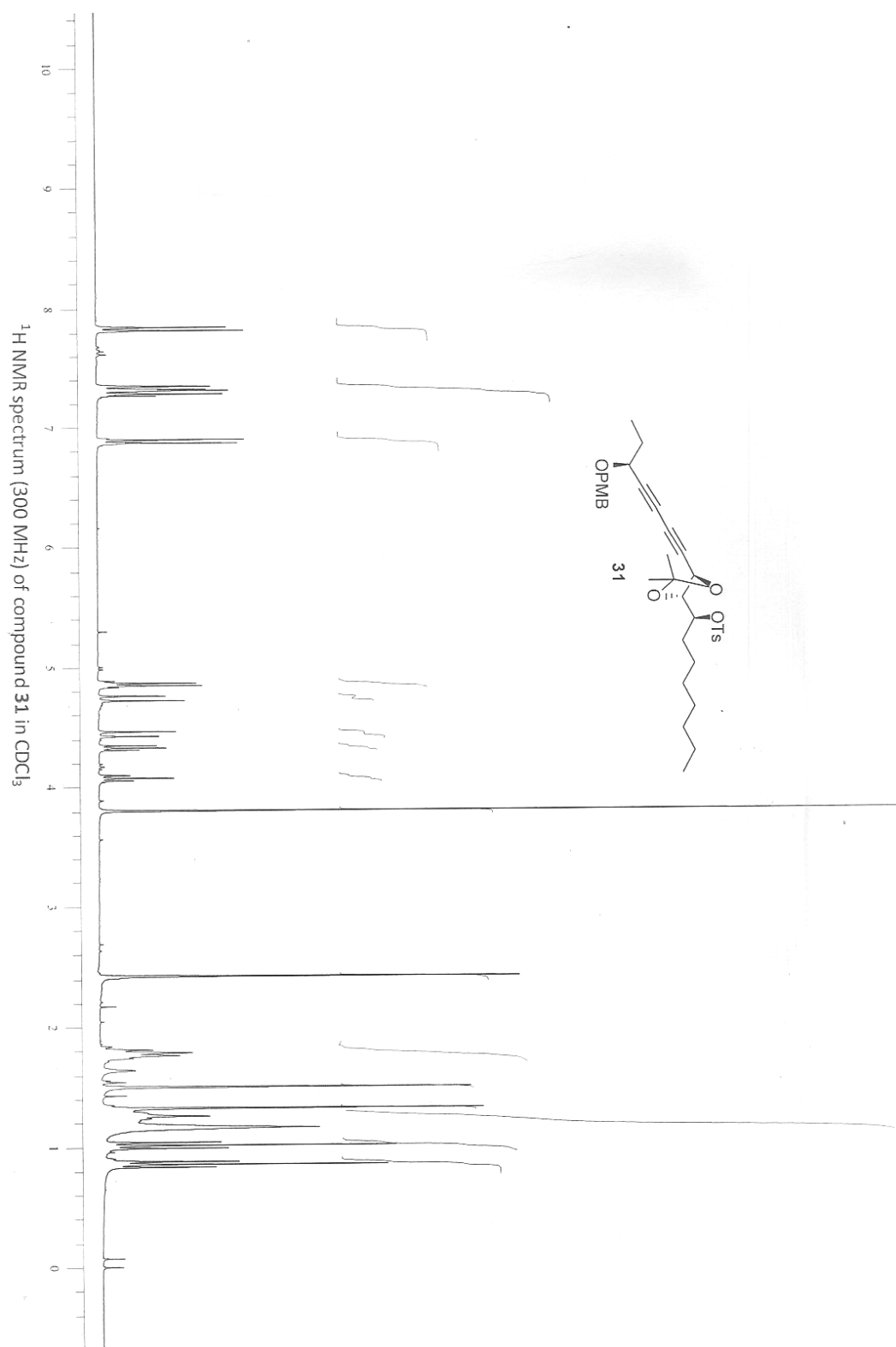


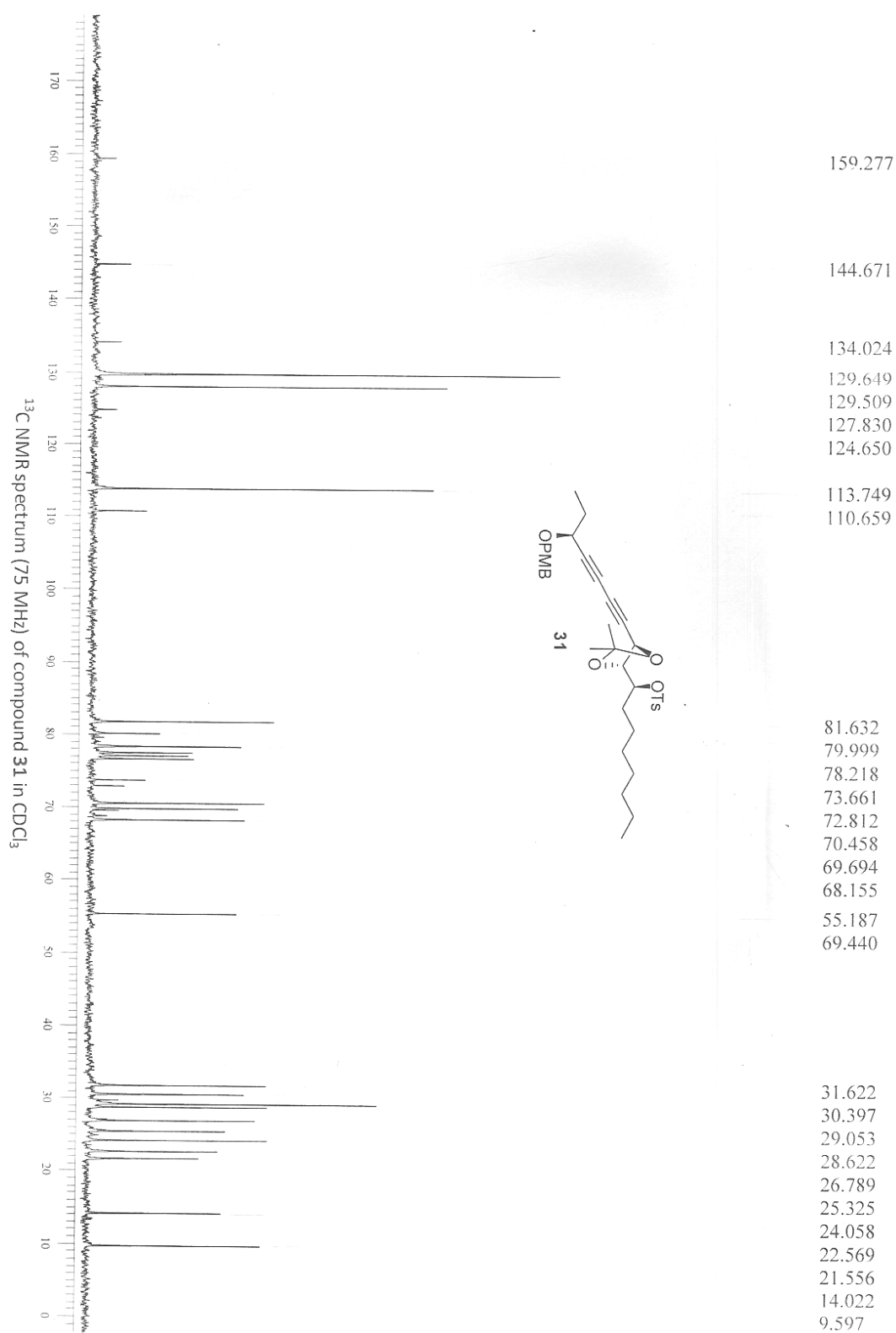


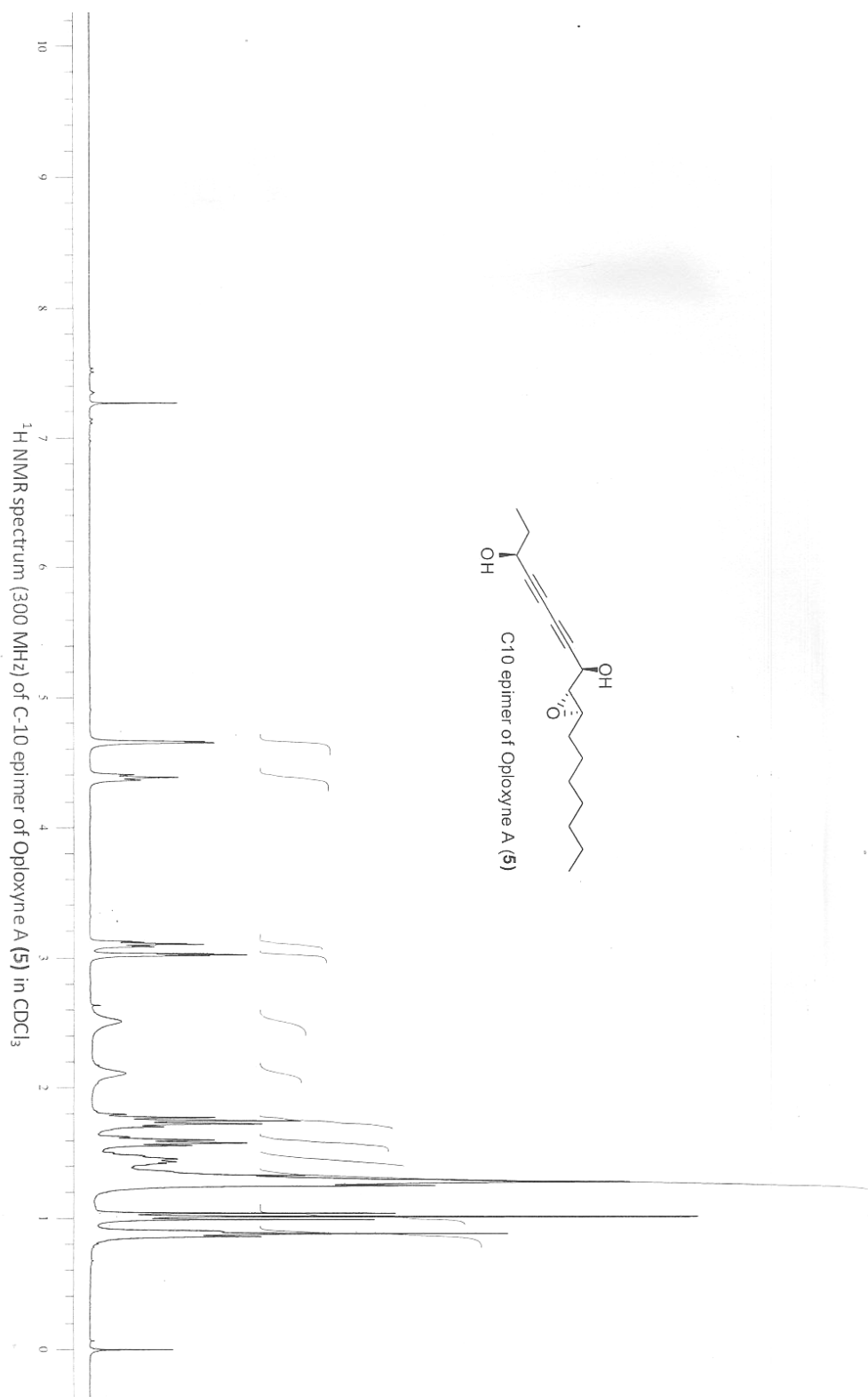
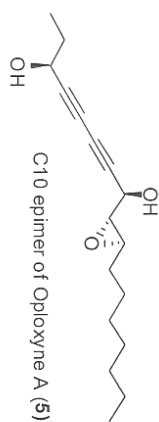


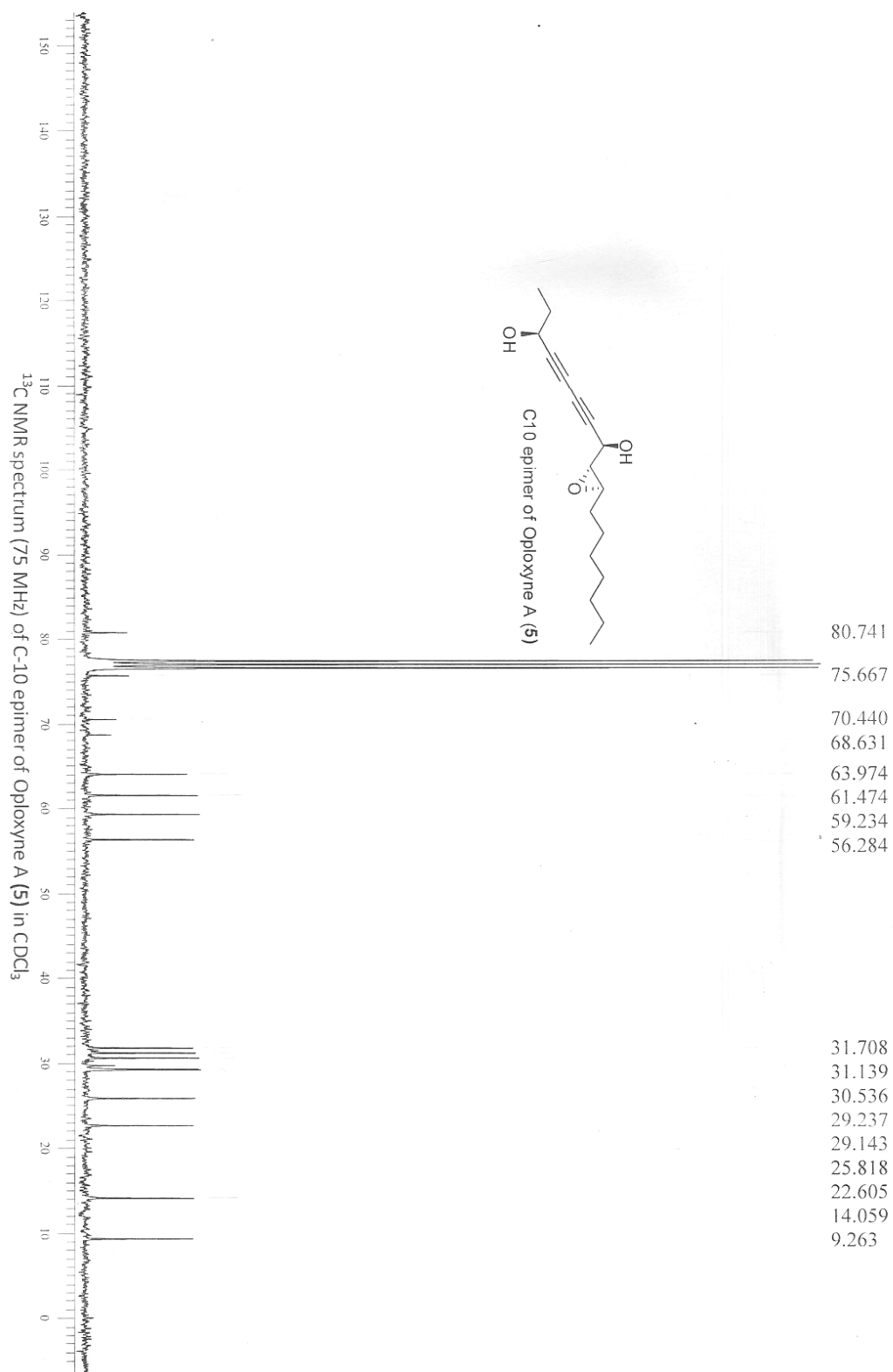


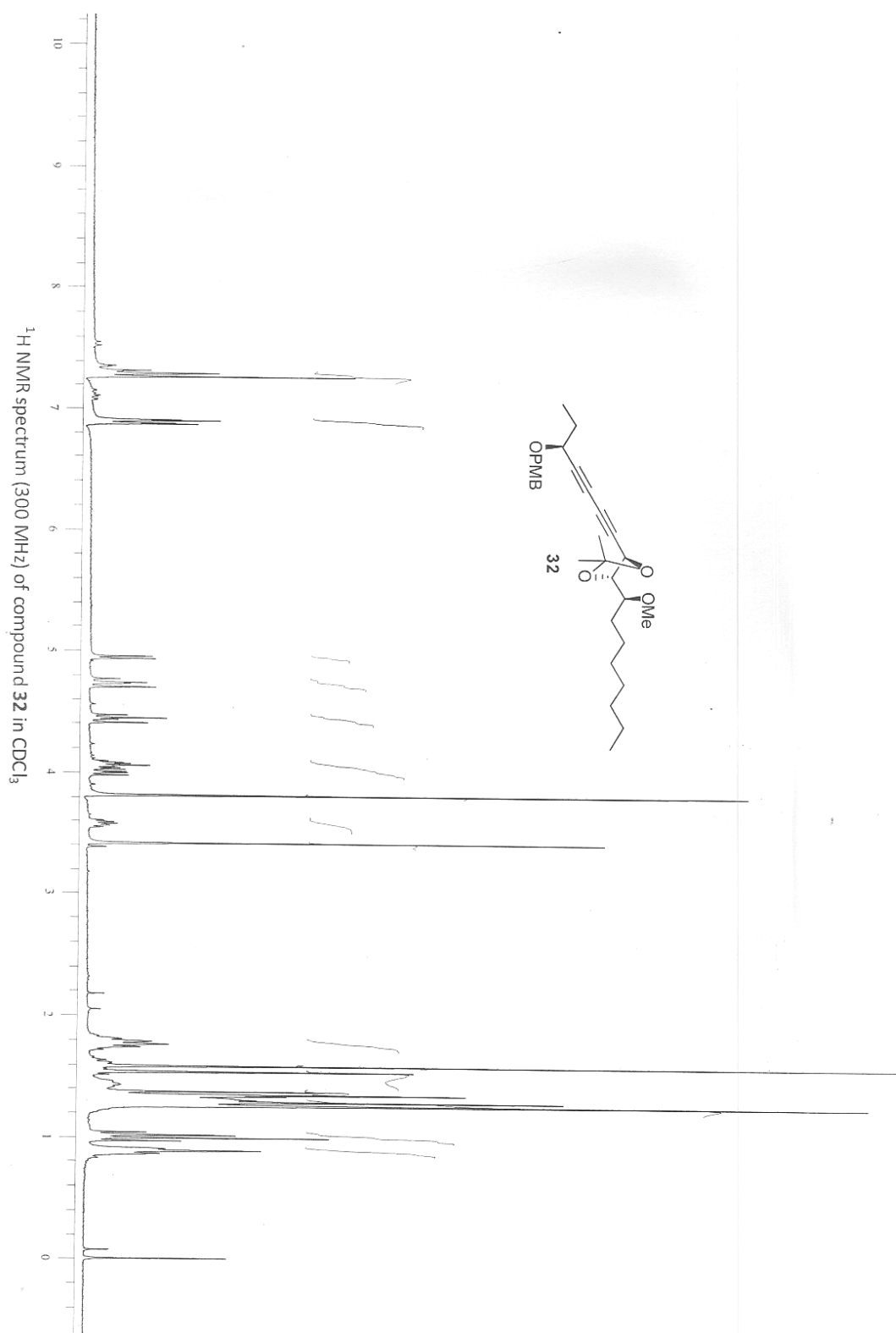
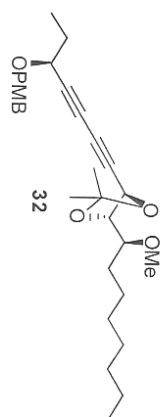


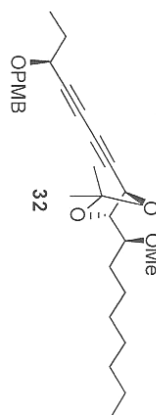
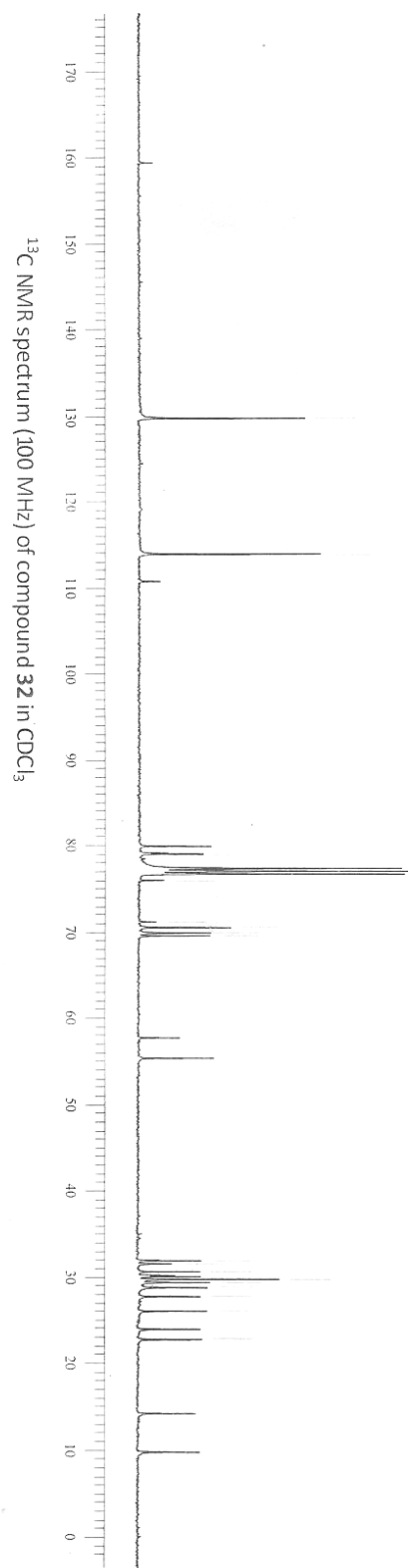












159.280

129.667

113.780

110.633

113.780

79.841

78.925

79.048

75.926

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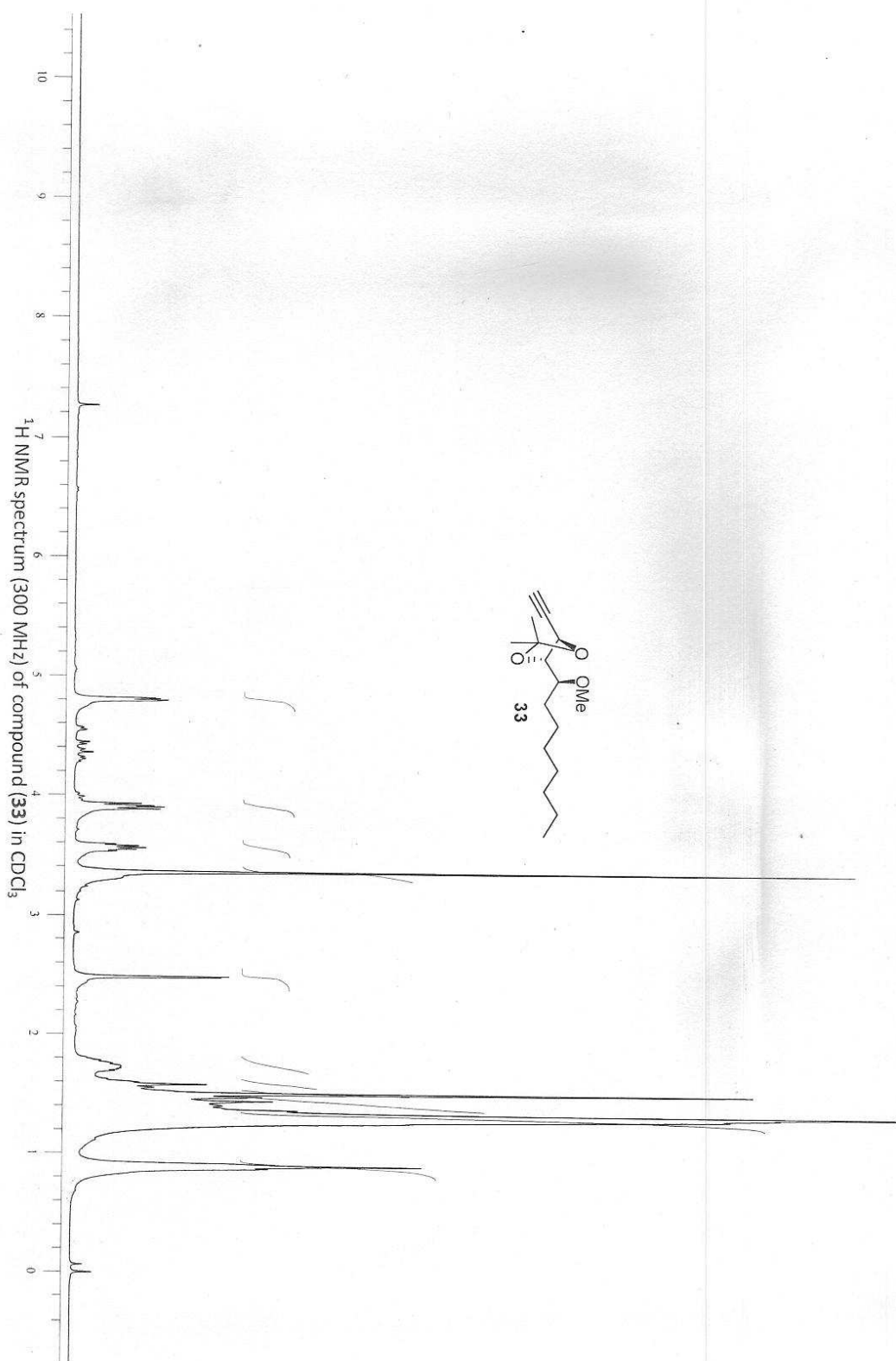
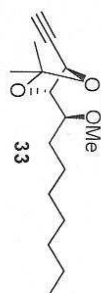
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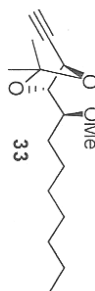
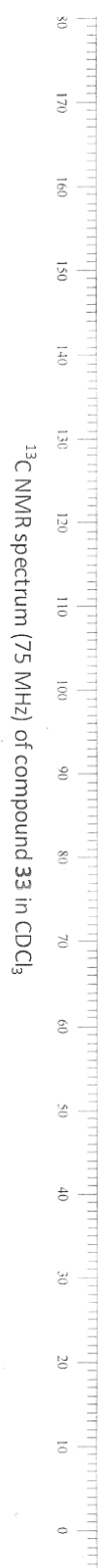
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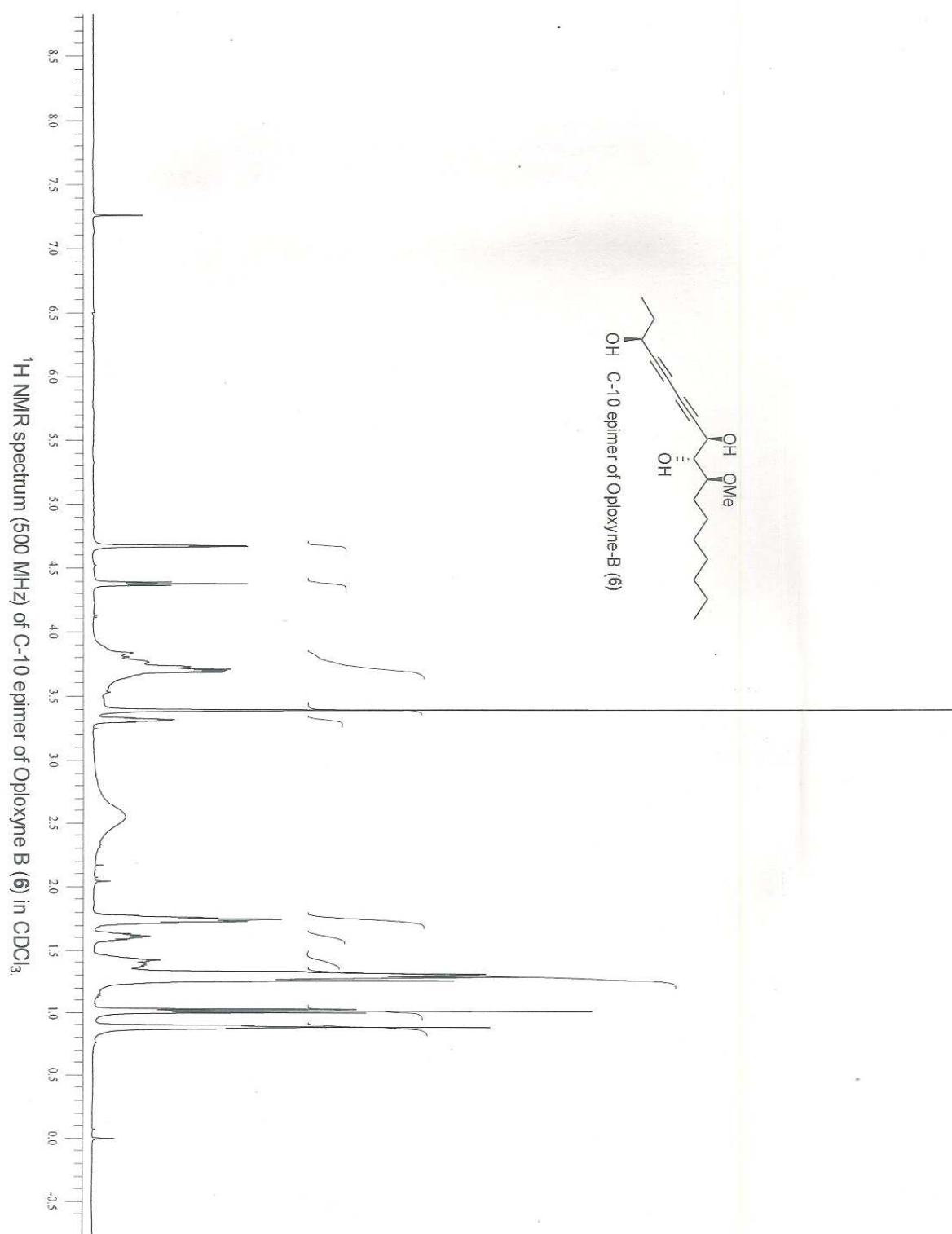
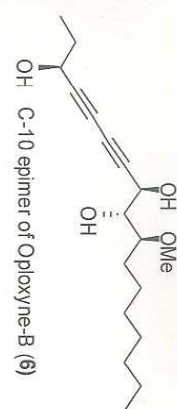
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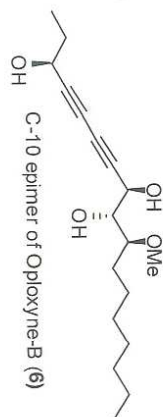
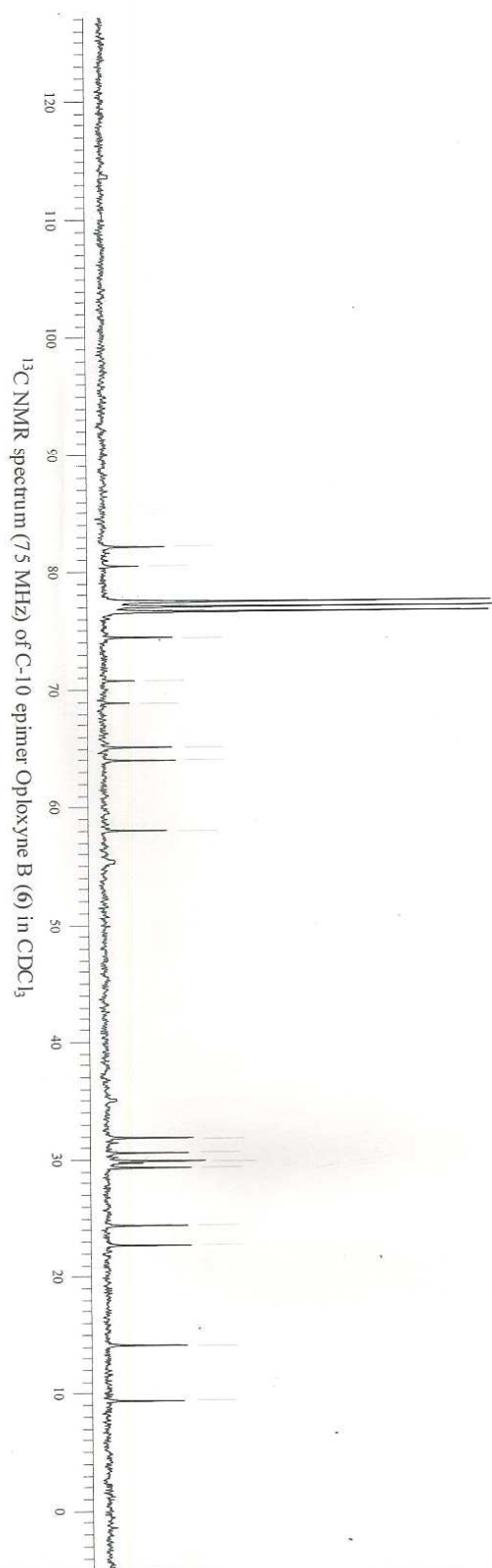
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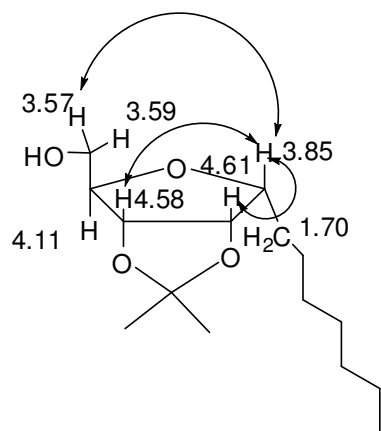




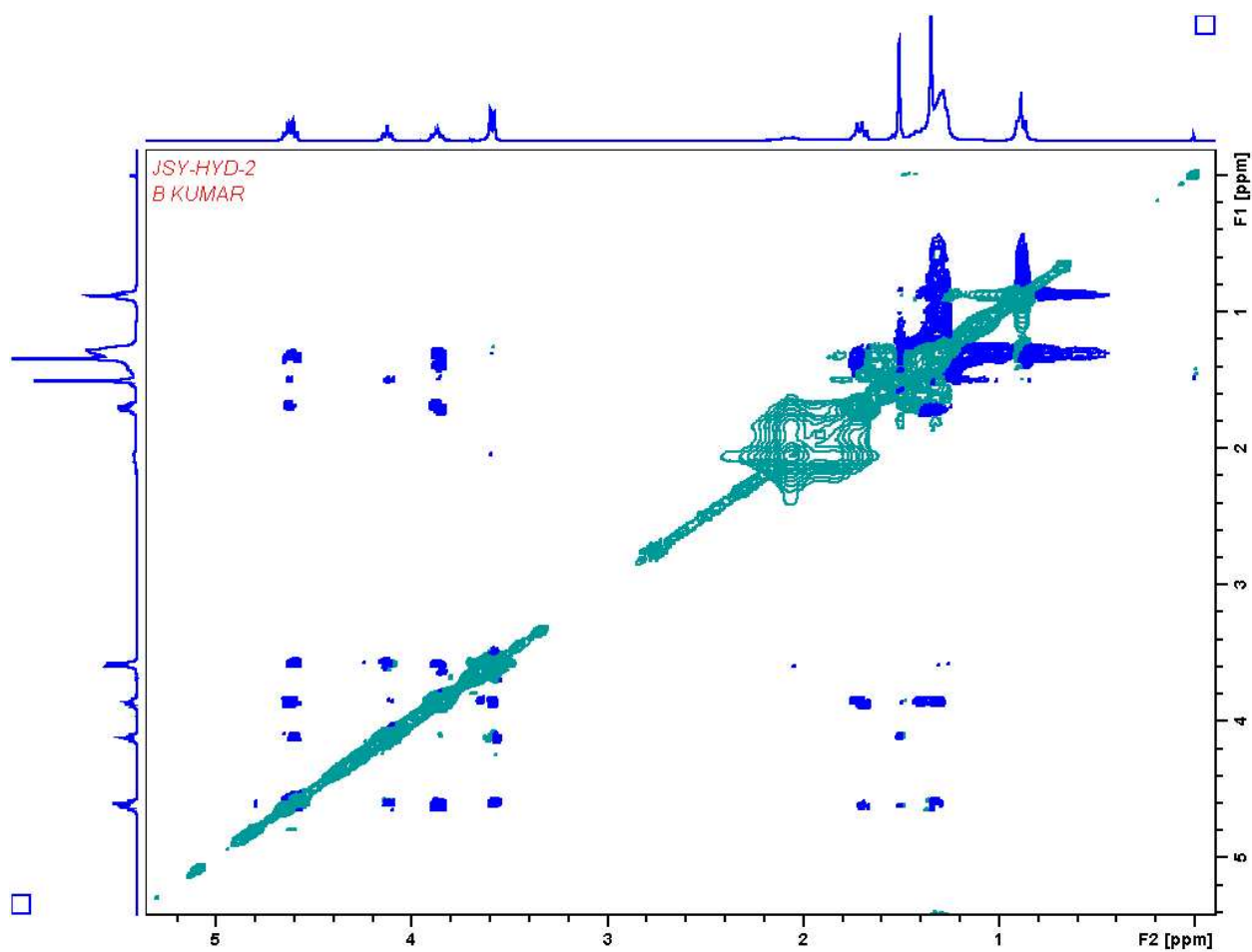
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68.835
65.061
63.943
57.951

31.812
30.535
29.260
24.317
22.633
29.870
29.836
14.061
9.315

Compound **24** showing strong NOE correlations



NOESY (300 MHz) spectrum of compound **24** in CDCl₃.



Key NOE correlations in the NOESY spectra of **8a** in CDCl₃ (300 MHz)

