

Supporting Information

Total Synthesis of (\pm)-Rocaglamide *via* Oxidation-Initiated Nazarov Cyclization

John A. Malona, Kevin Cariou, William T. Spencer III, and Alison J. Frontier*

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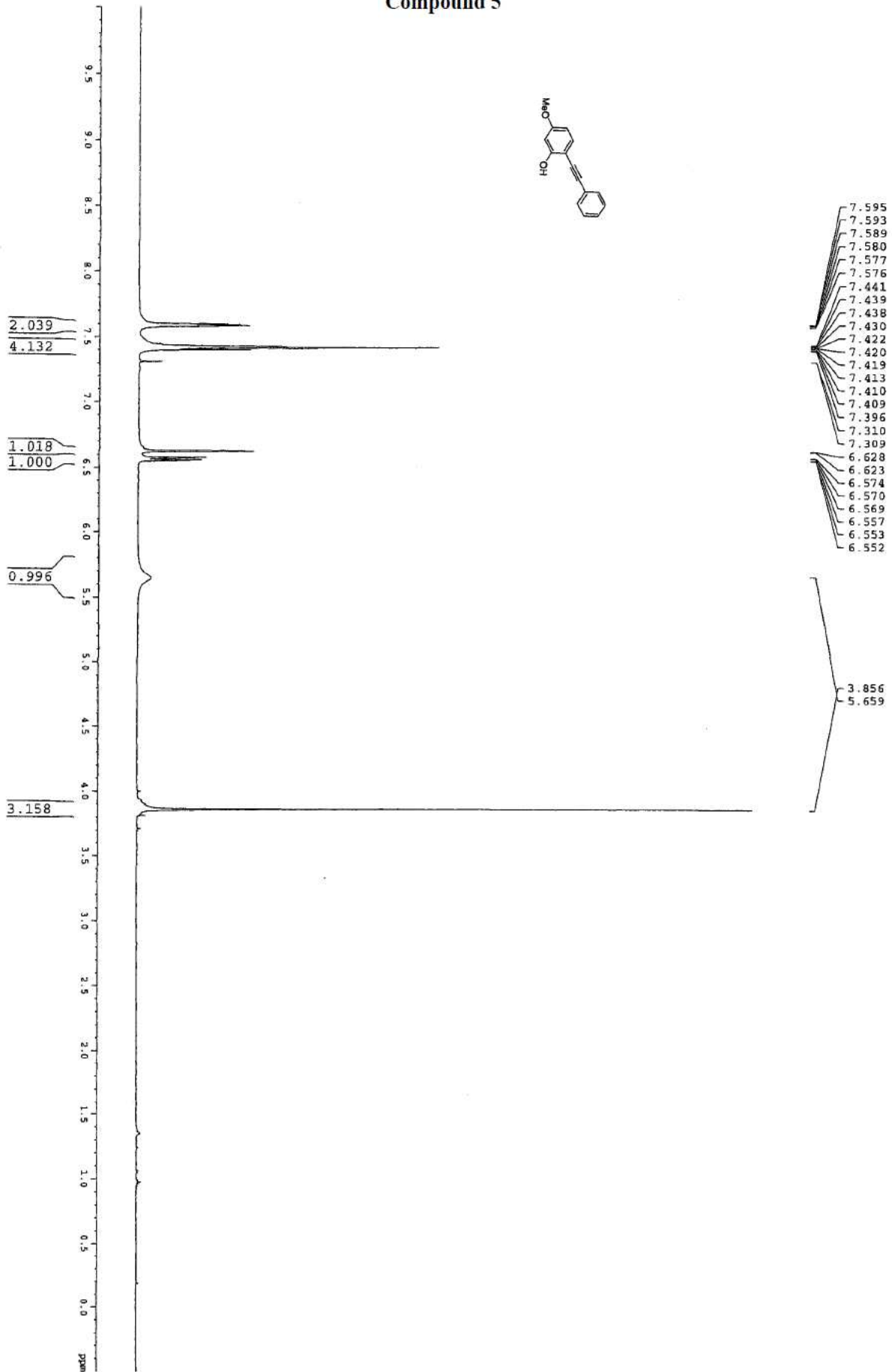
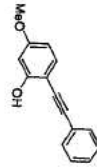
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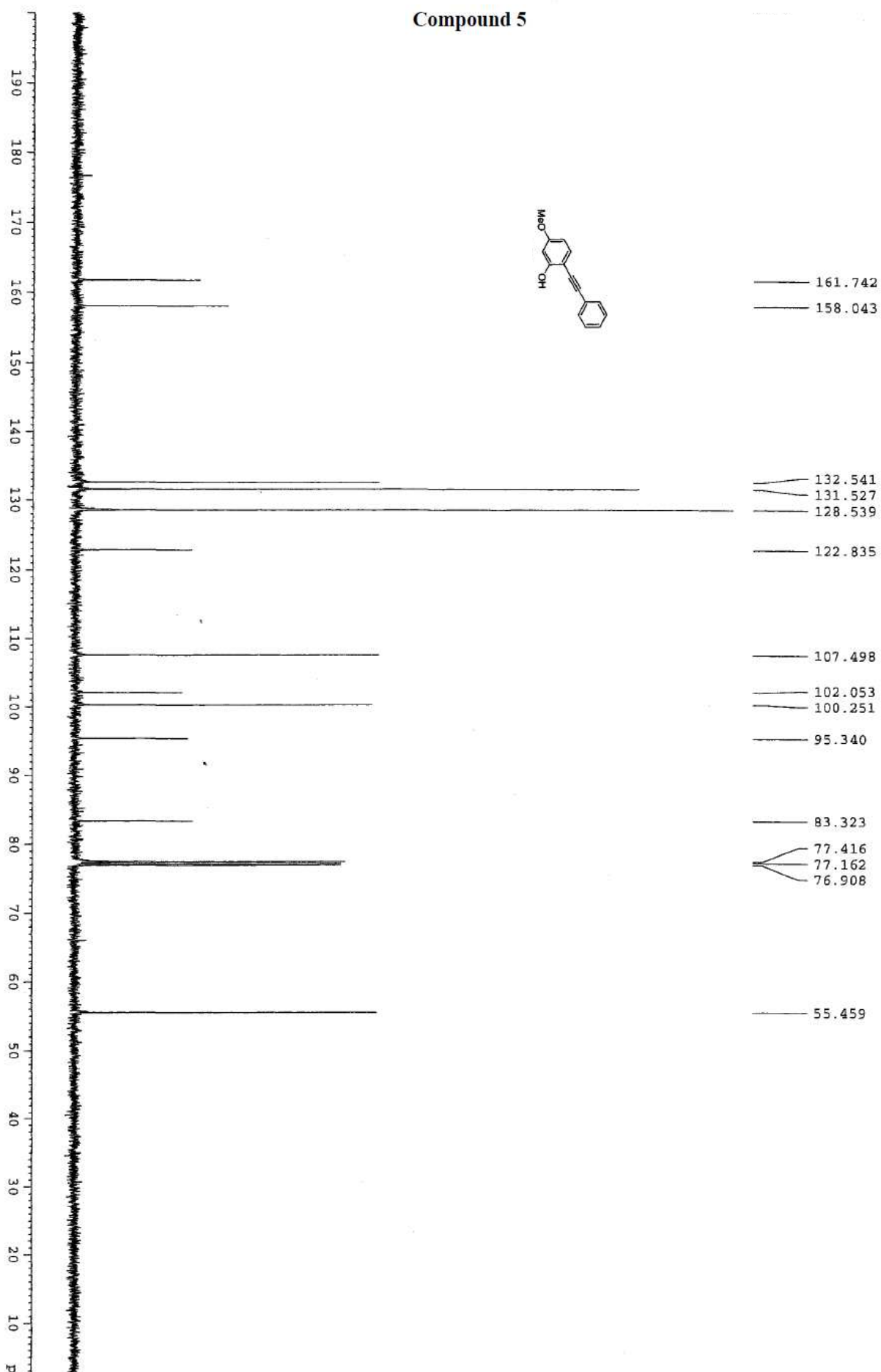
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1.0. Spectral Data.

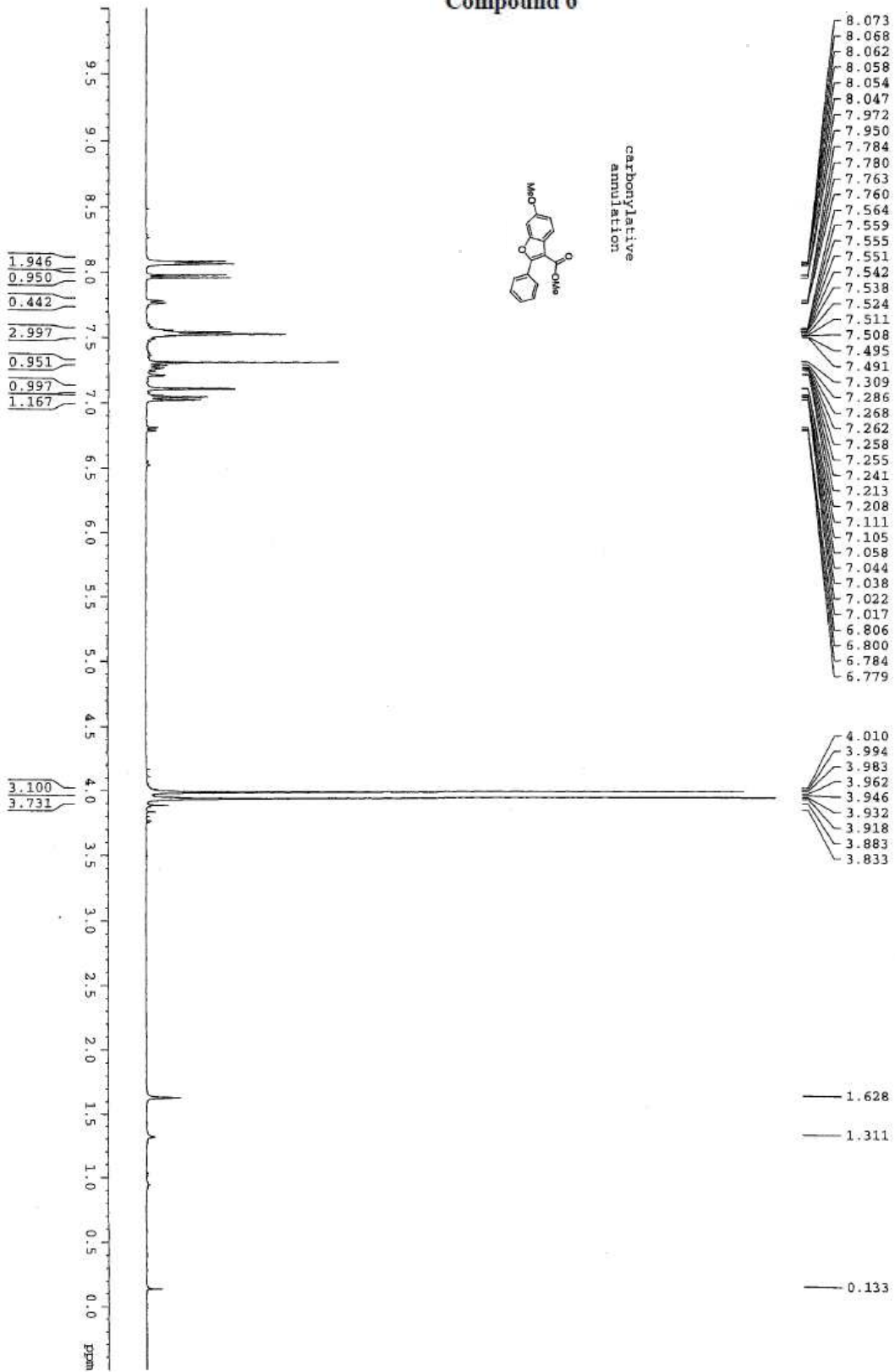
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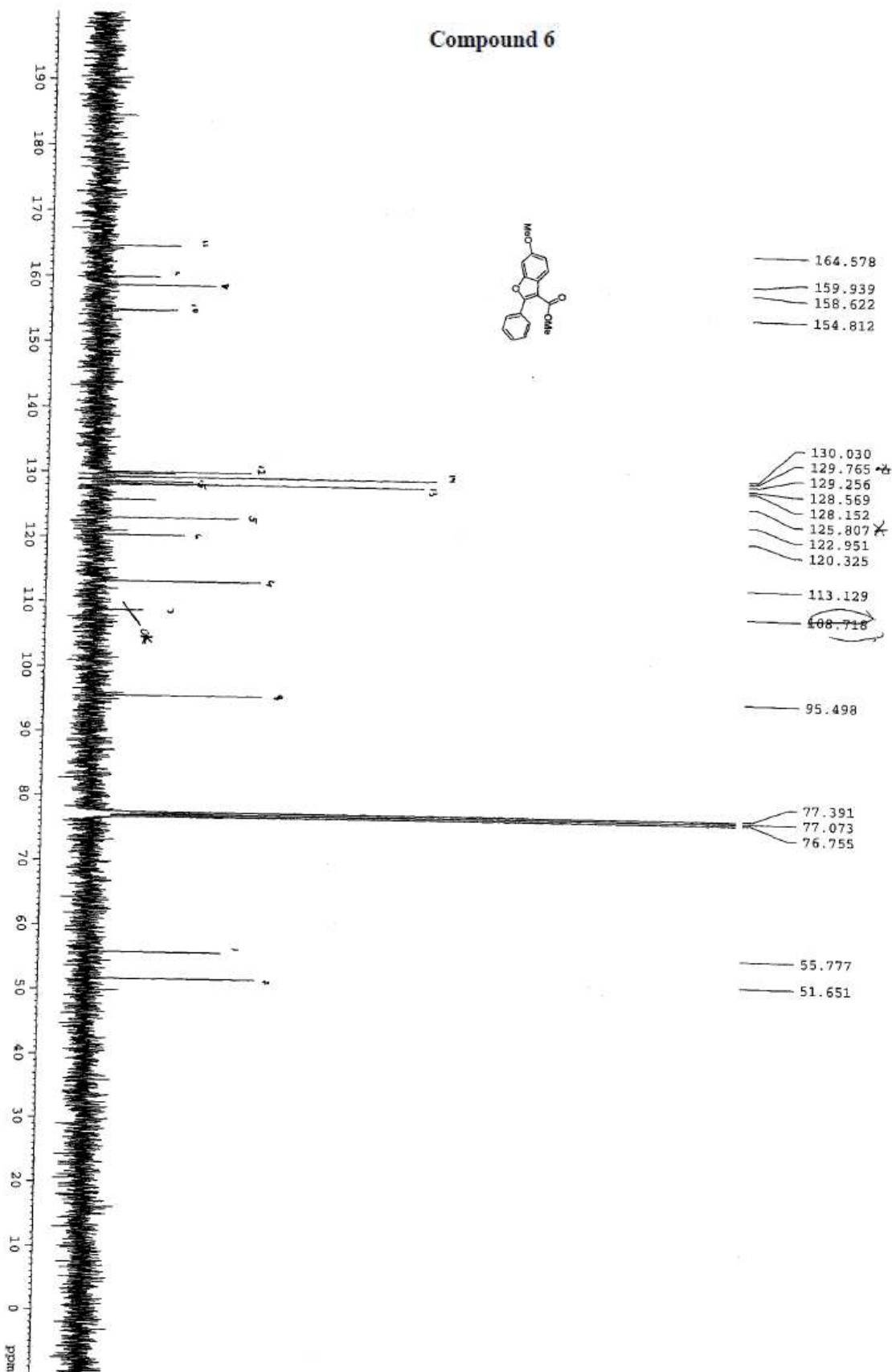
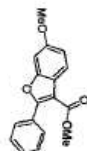
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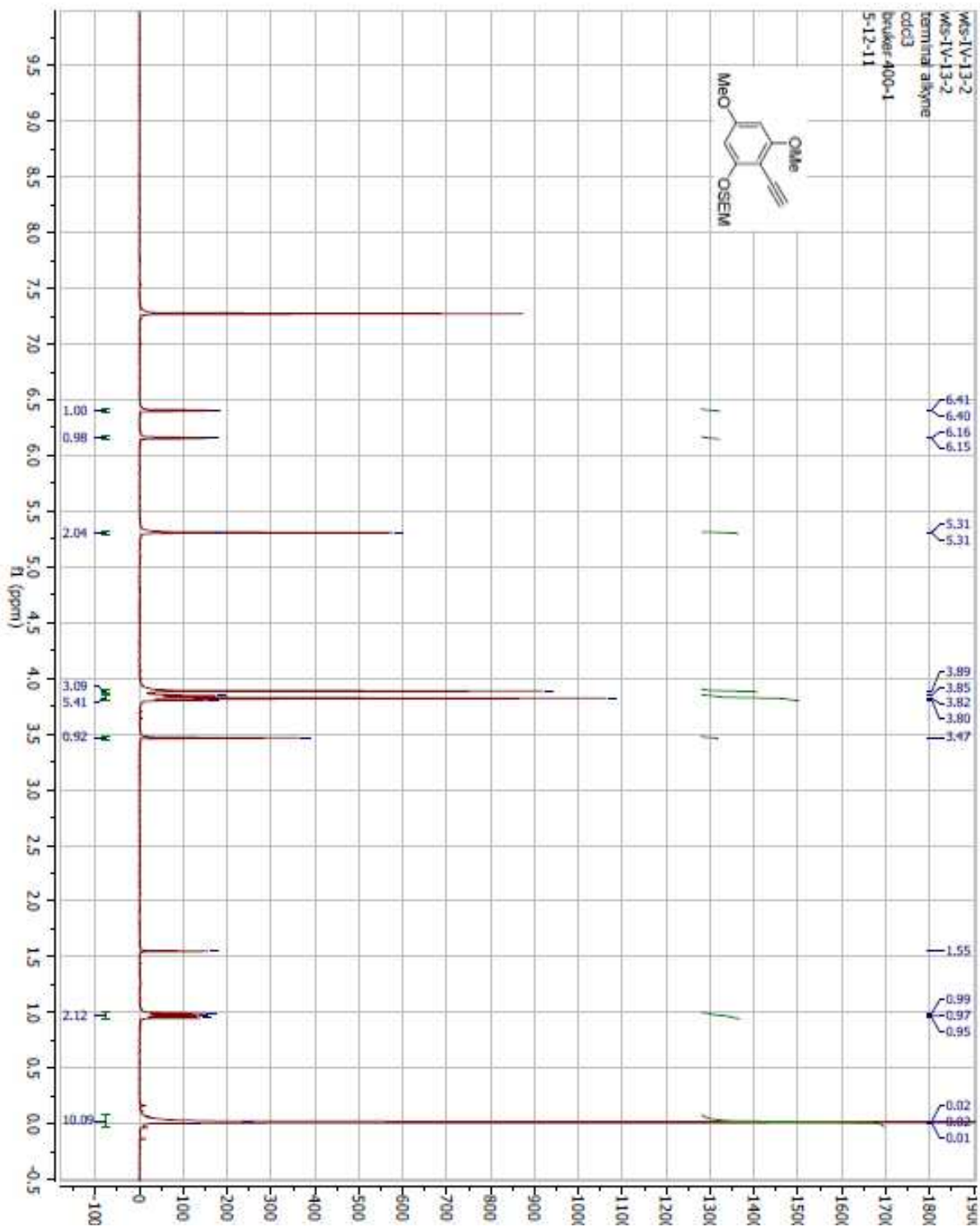
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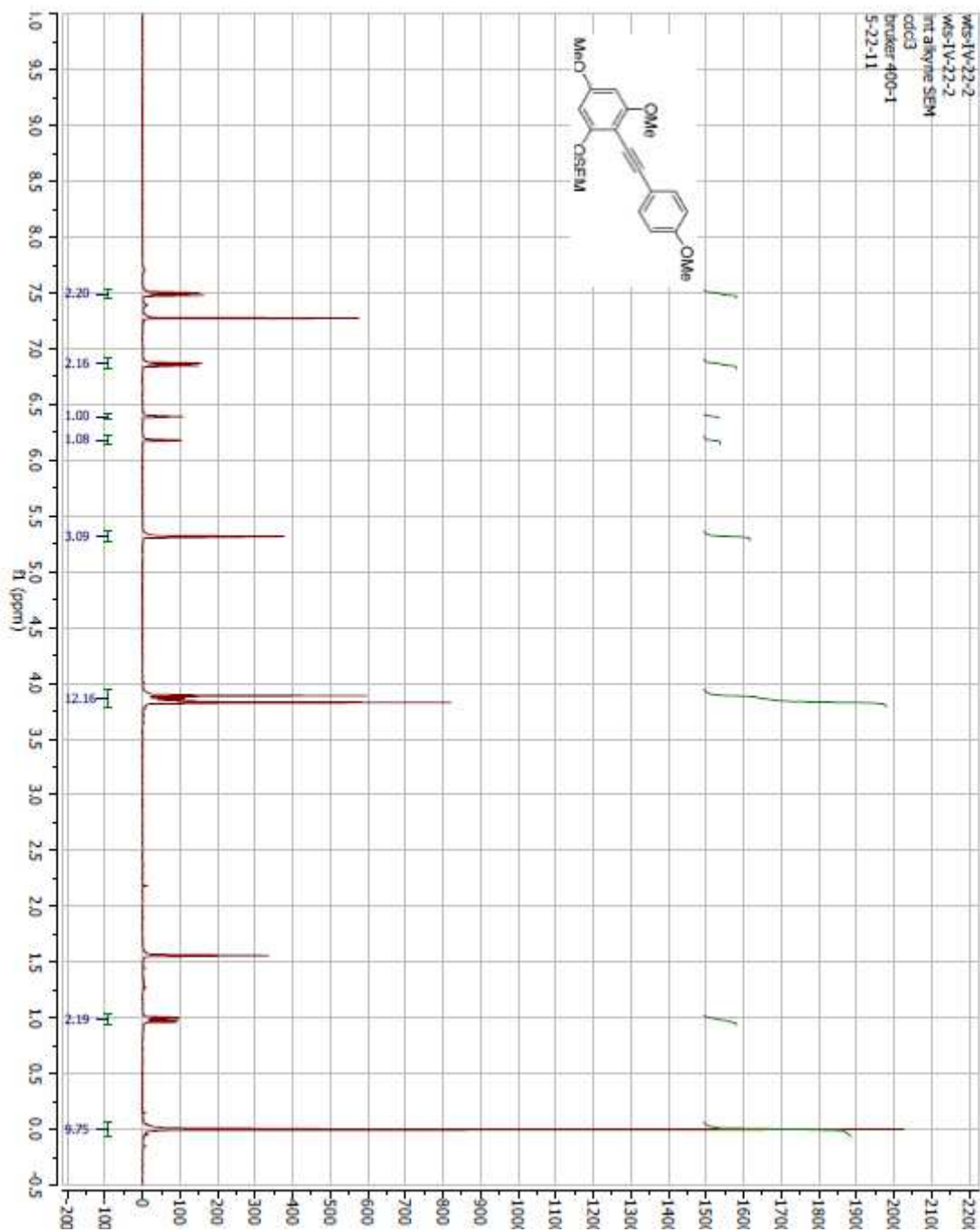
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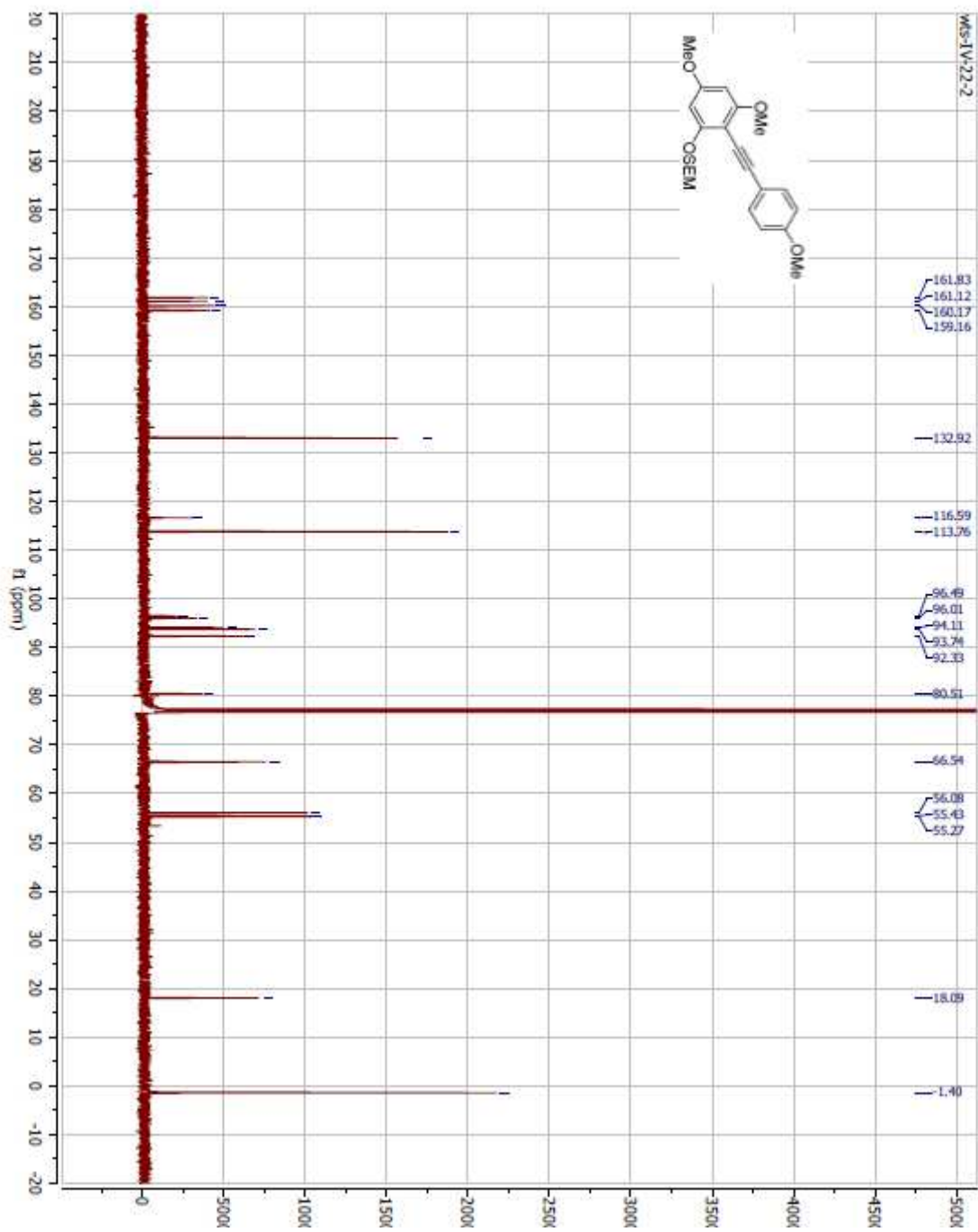
Compound 7a



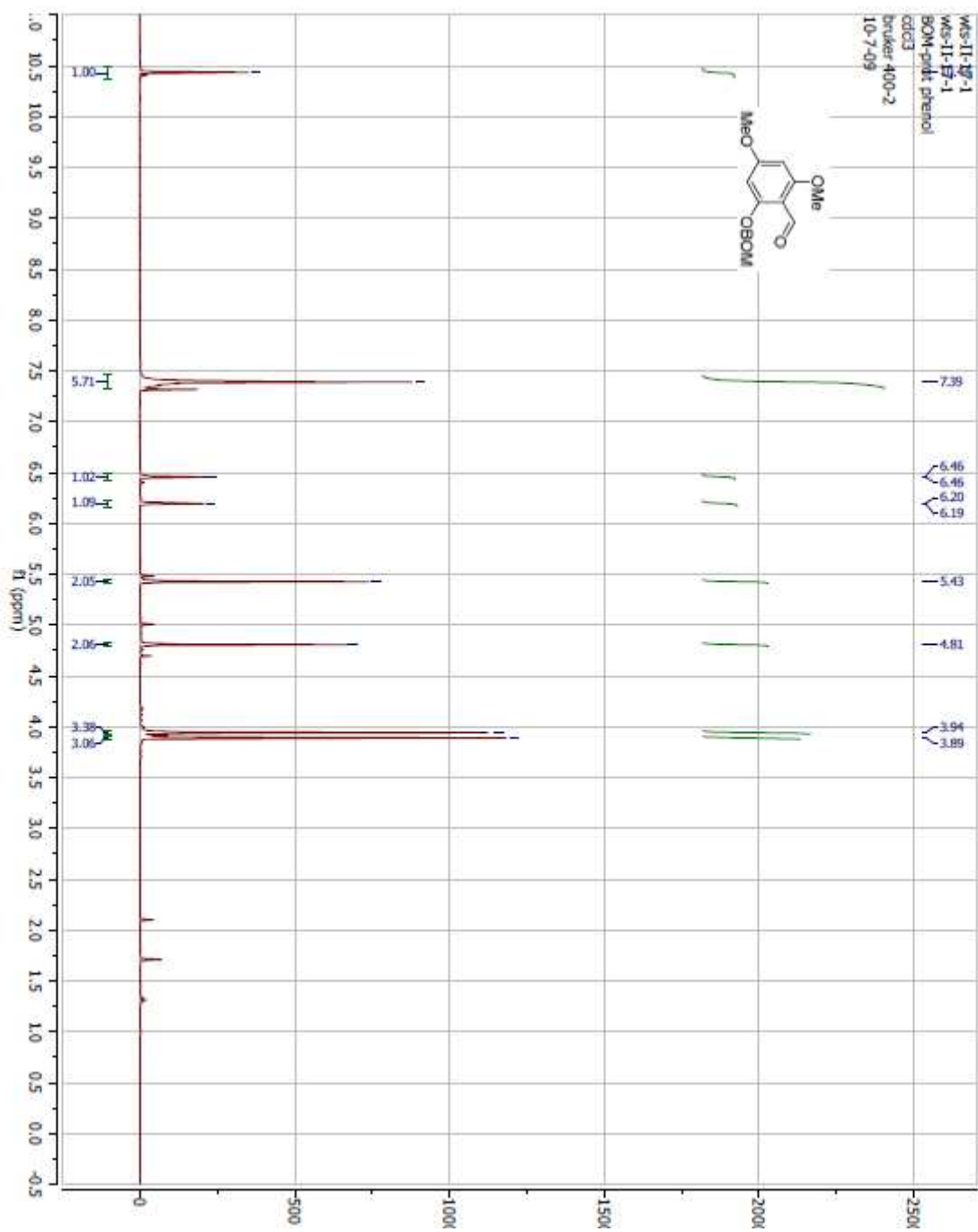
Compound 8a



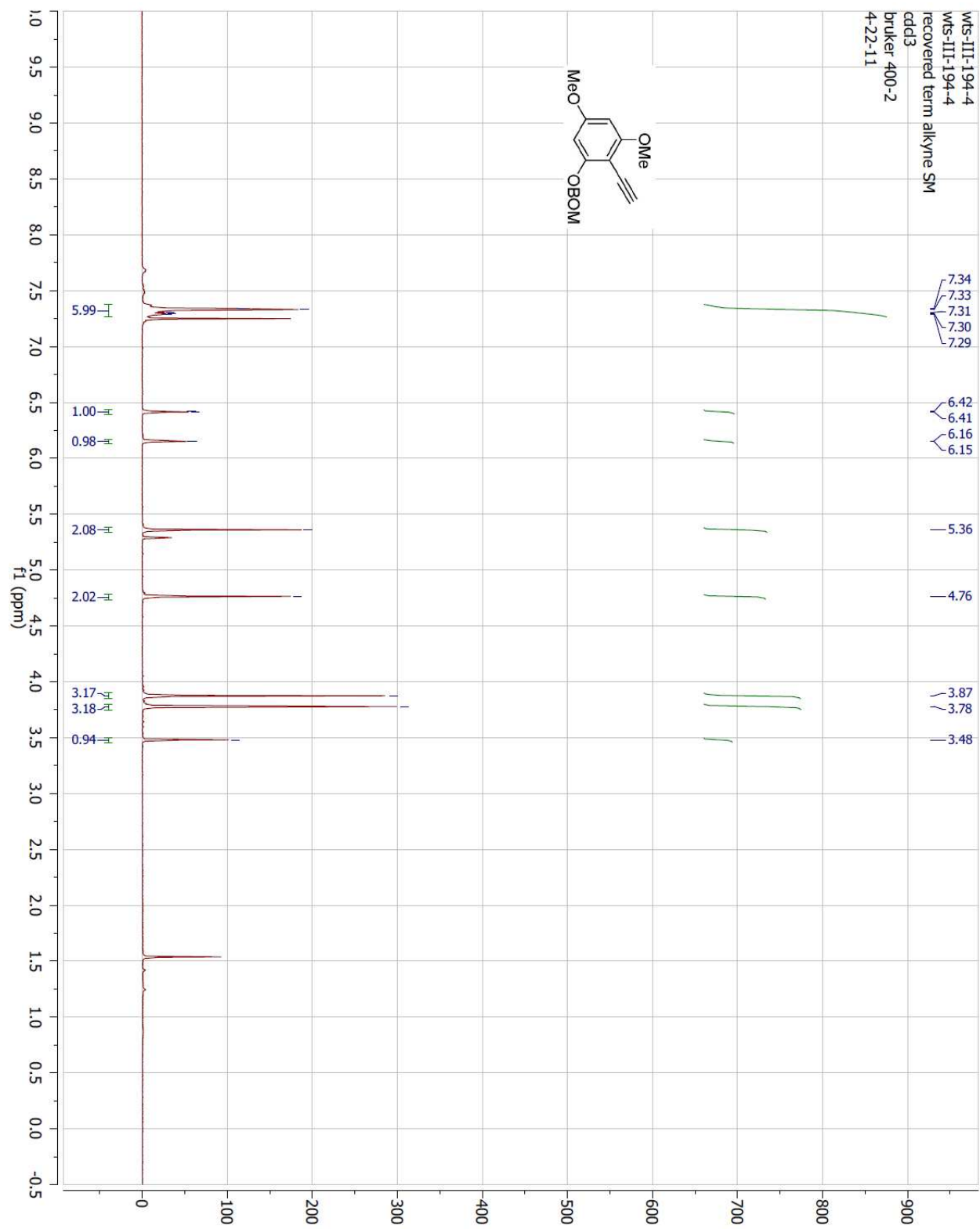
Compound 8a



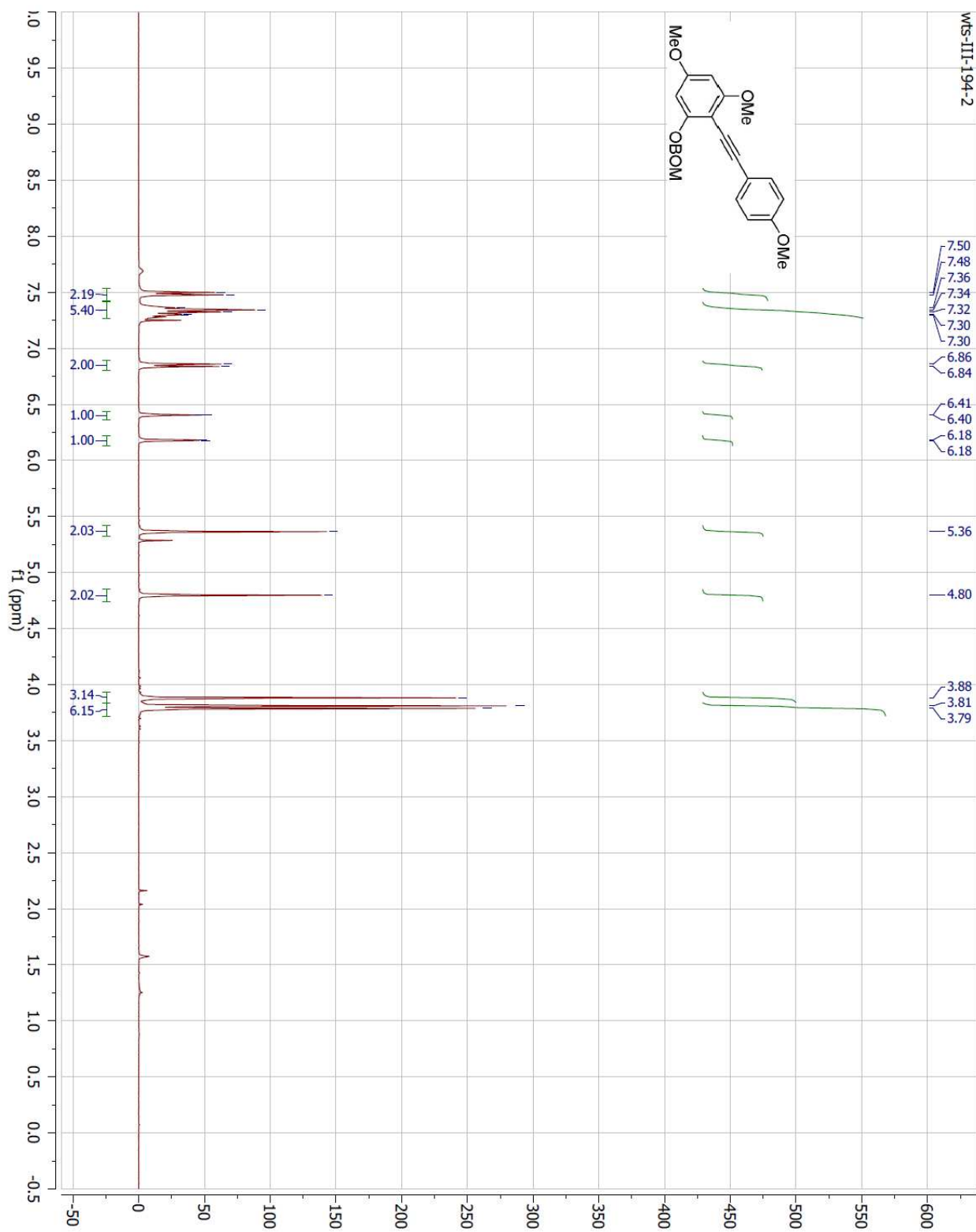
2,4-dimethoxy-6-((2-(trimethylsilyl)ethoxy)methoxy)benzaldehyde (precursor to 7)



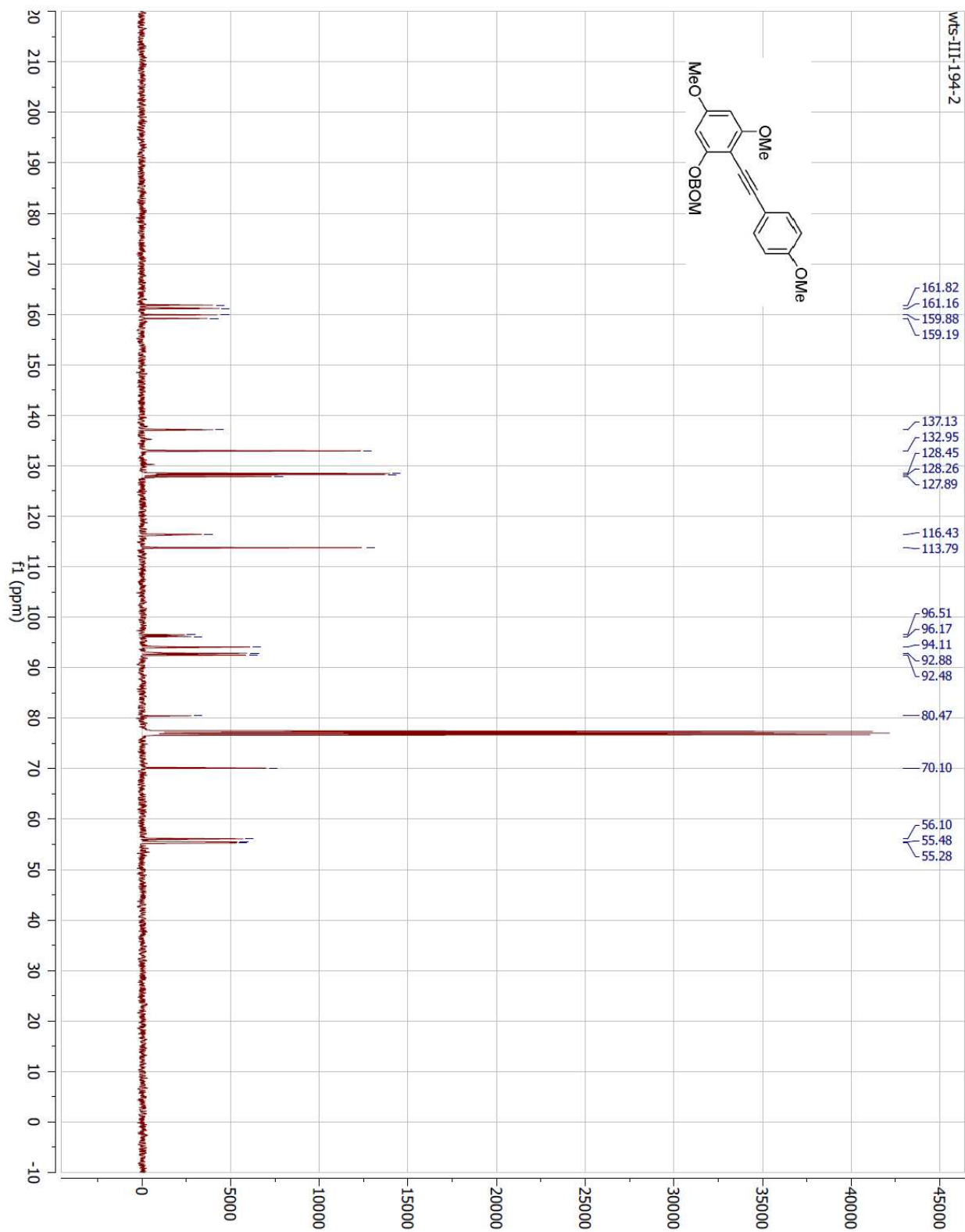
Compound 7b



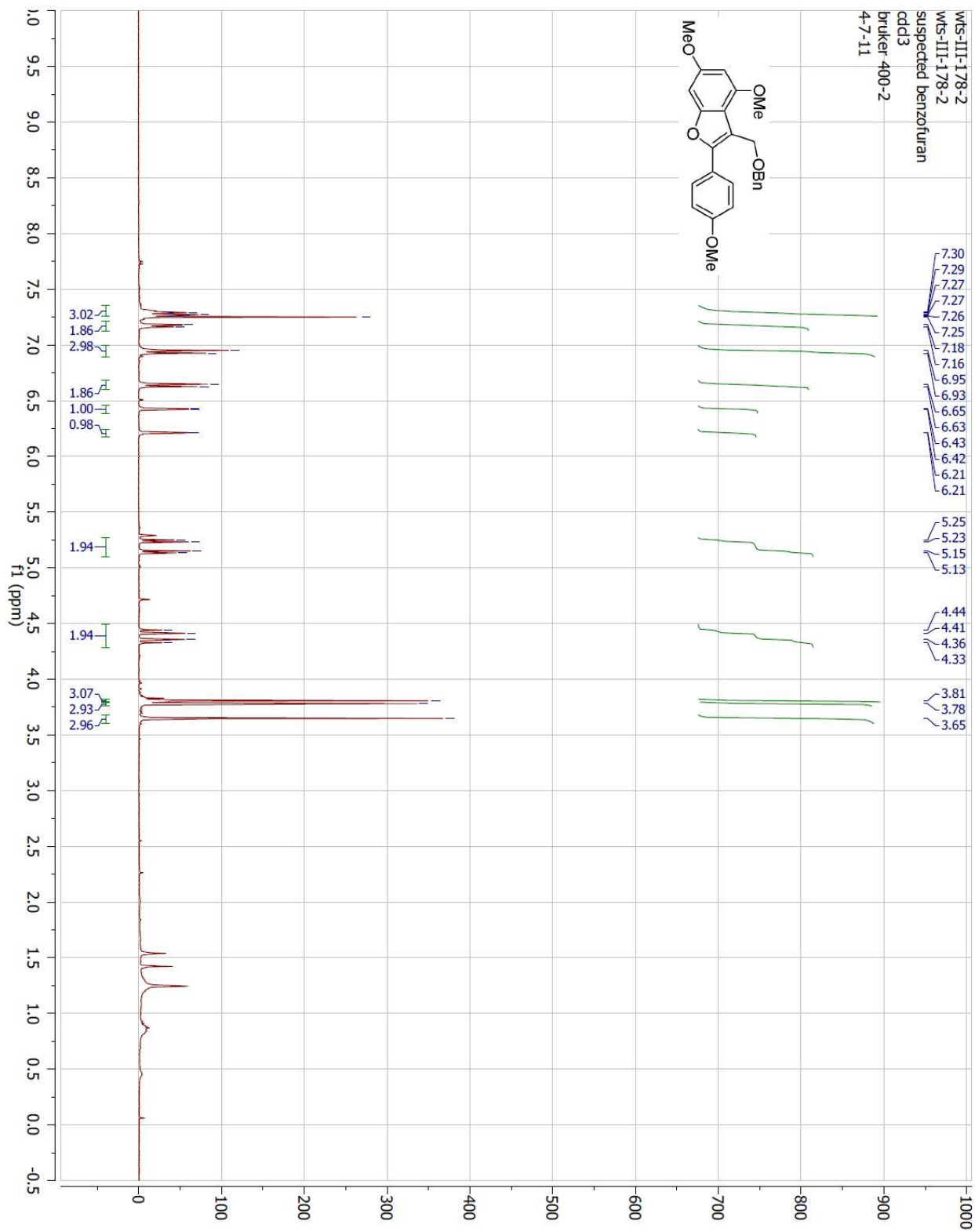
Compound 8b



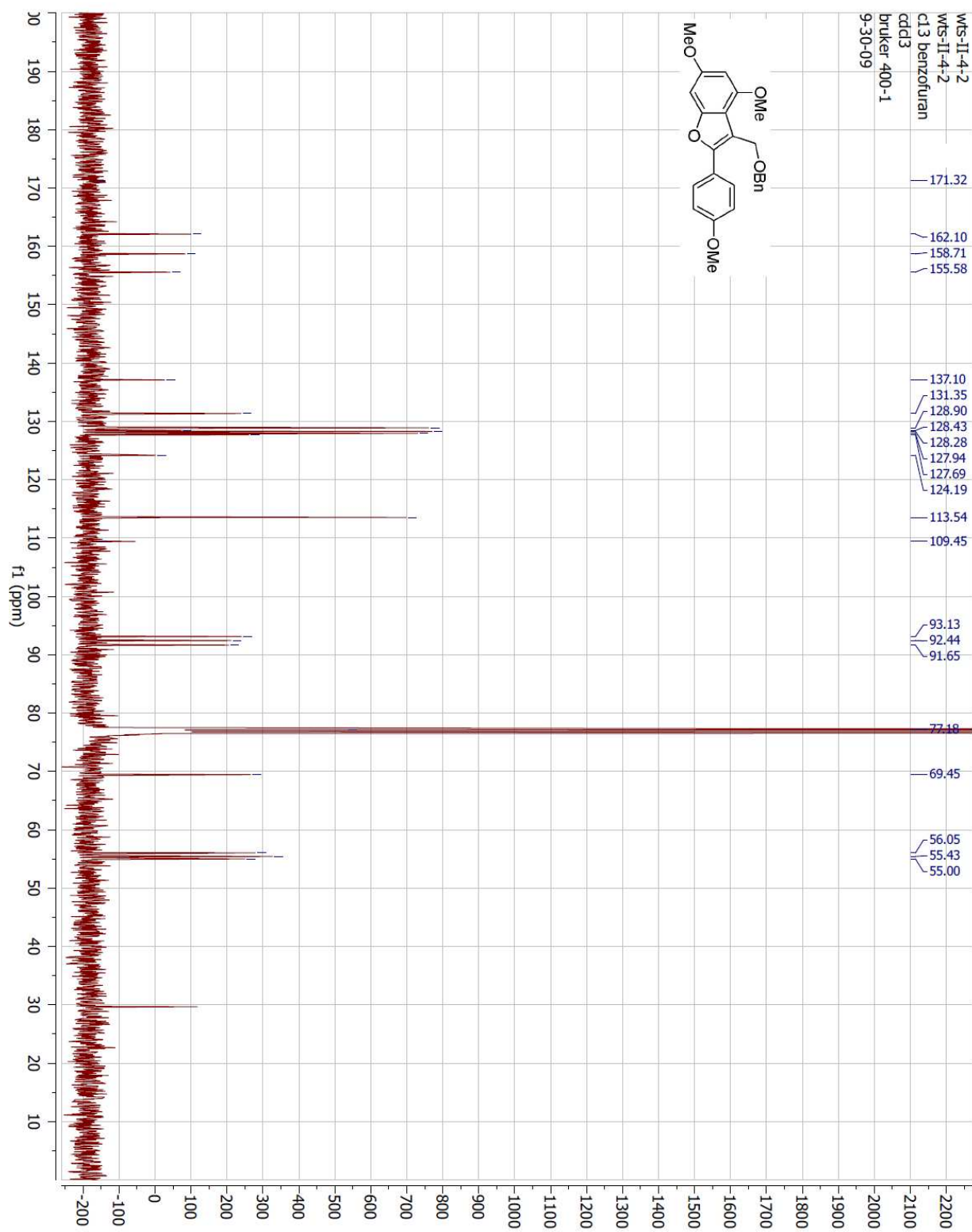
Compound 8b



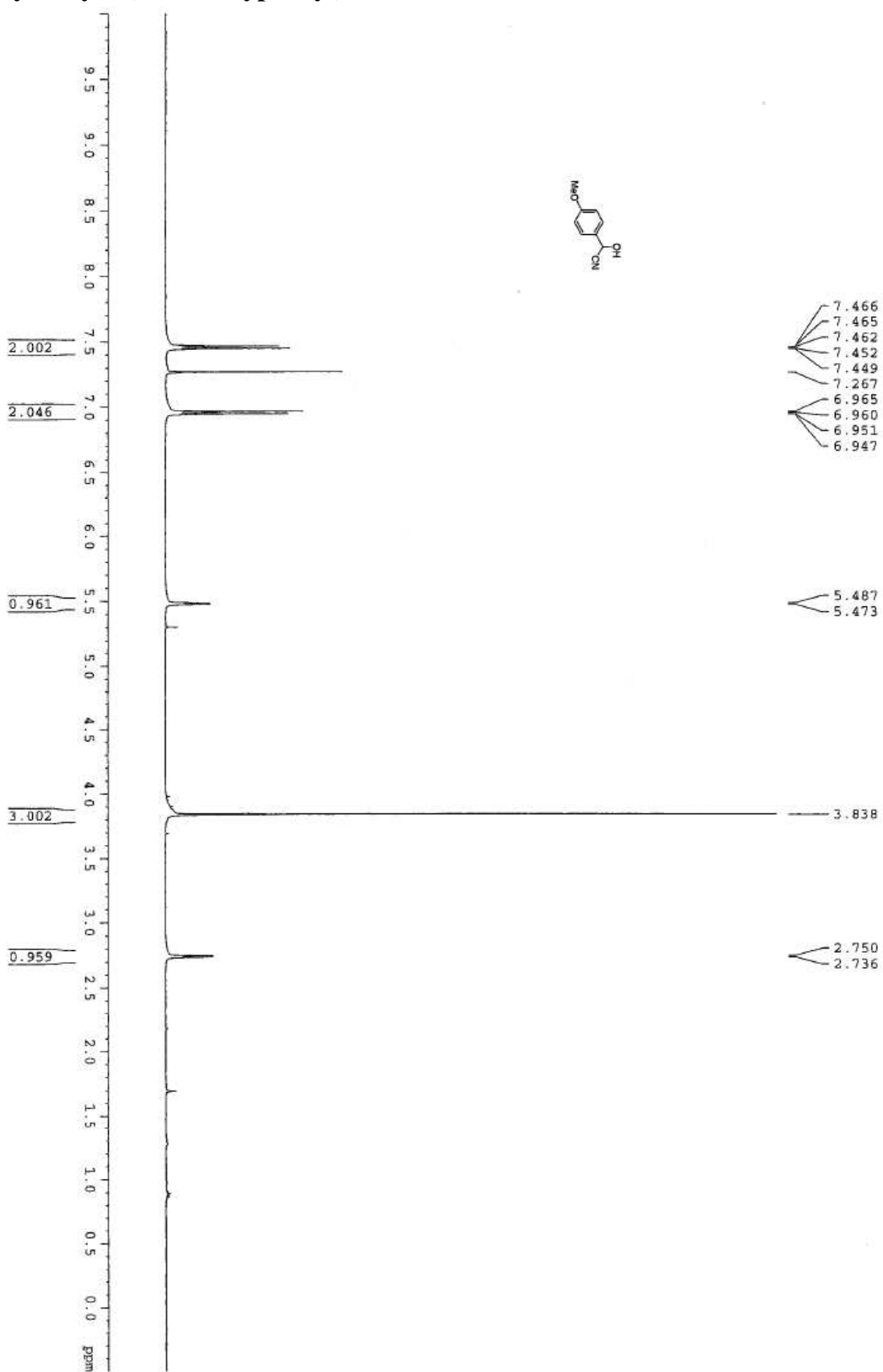
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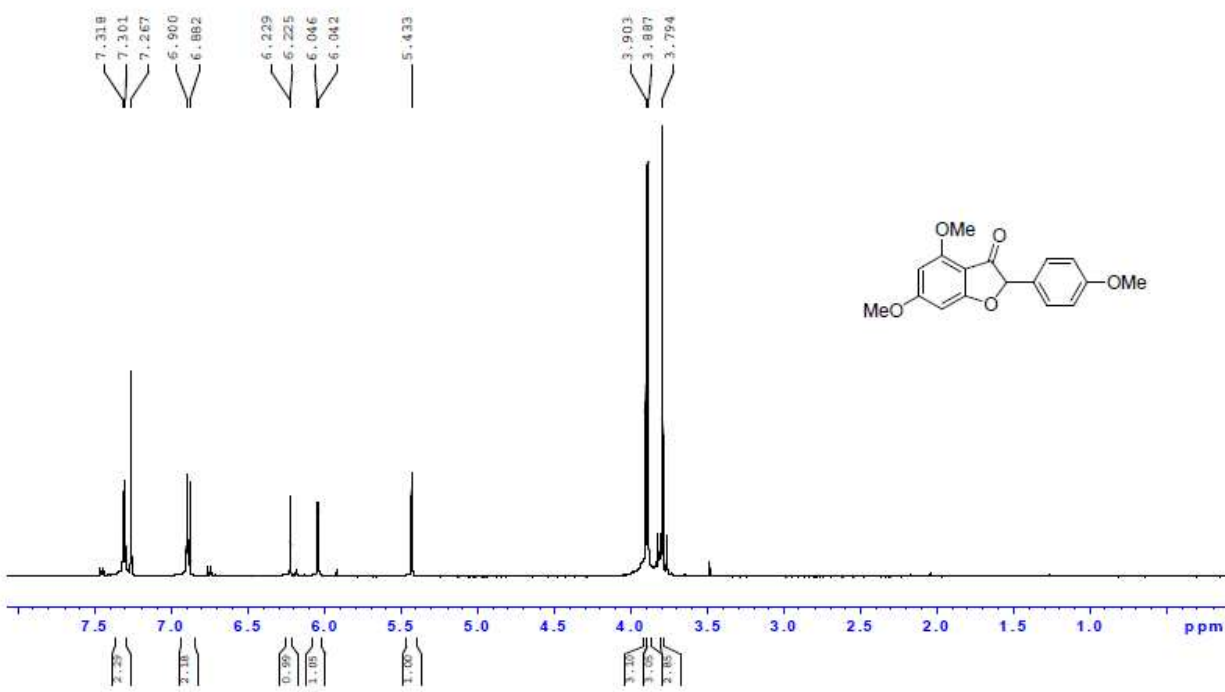
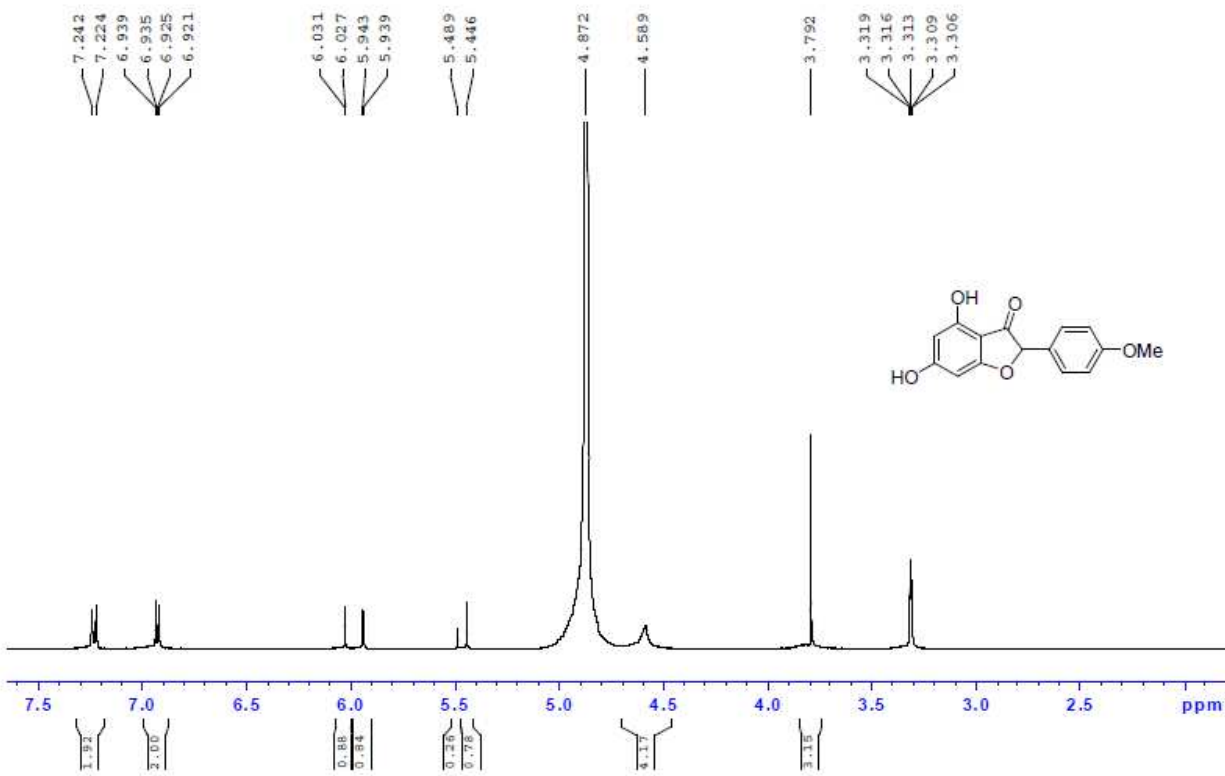
Compound 9



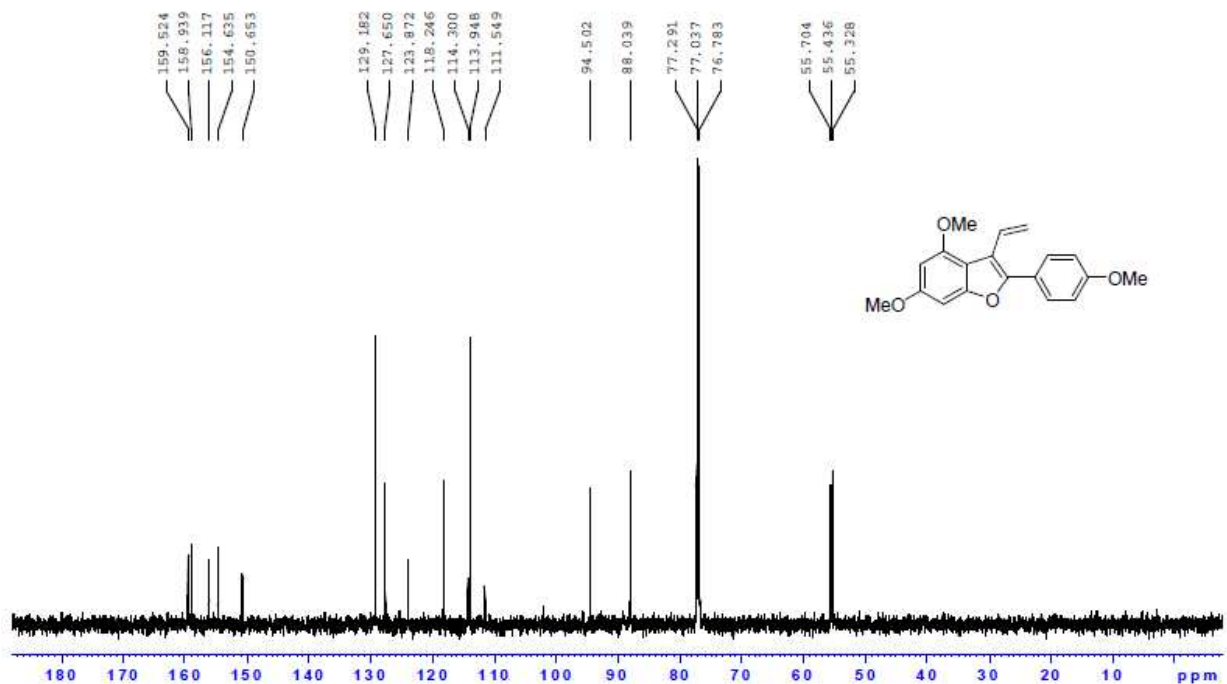
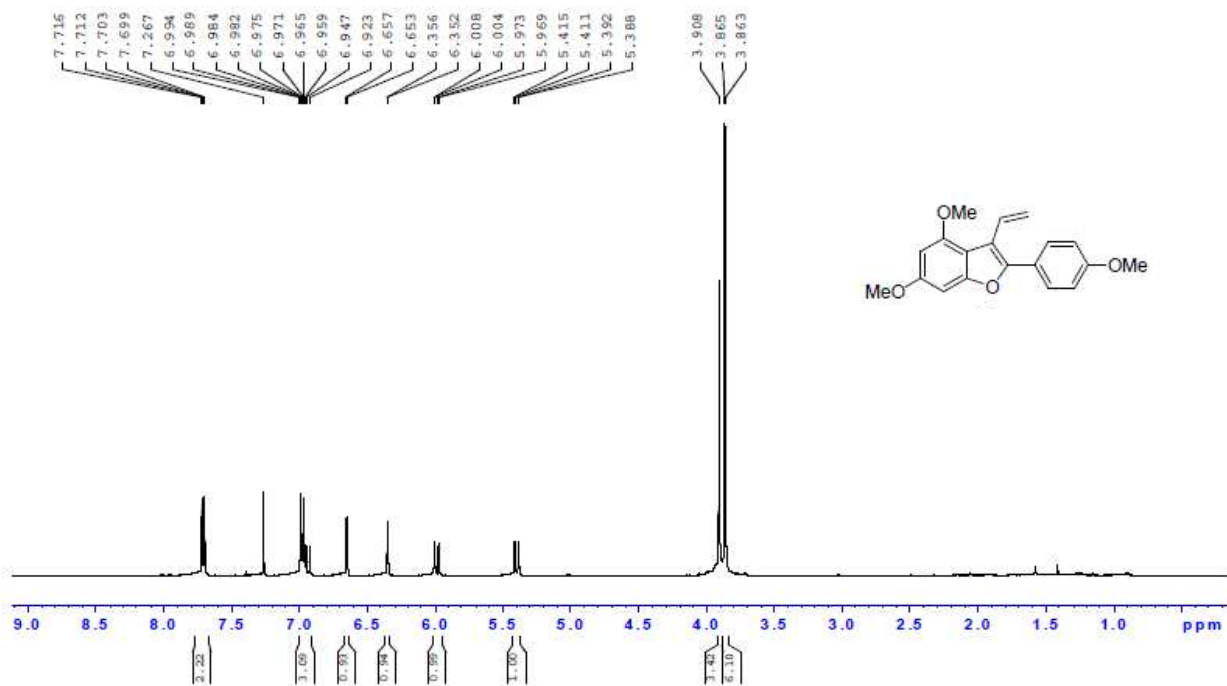
2-hydroxy-2-(4-methoxyphenyl)acetonitrile



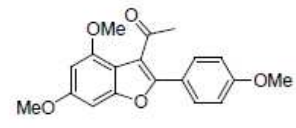
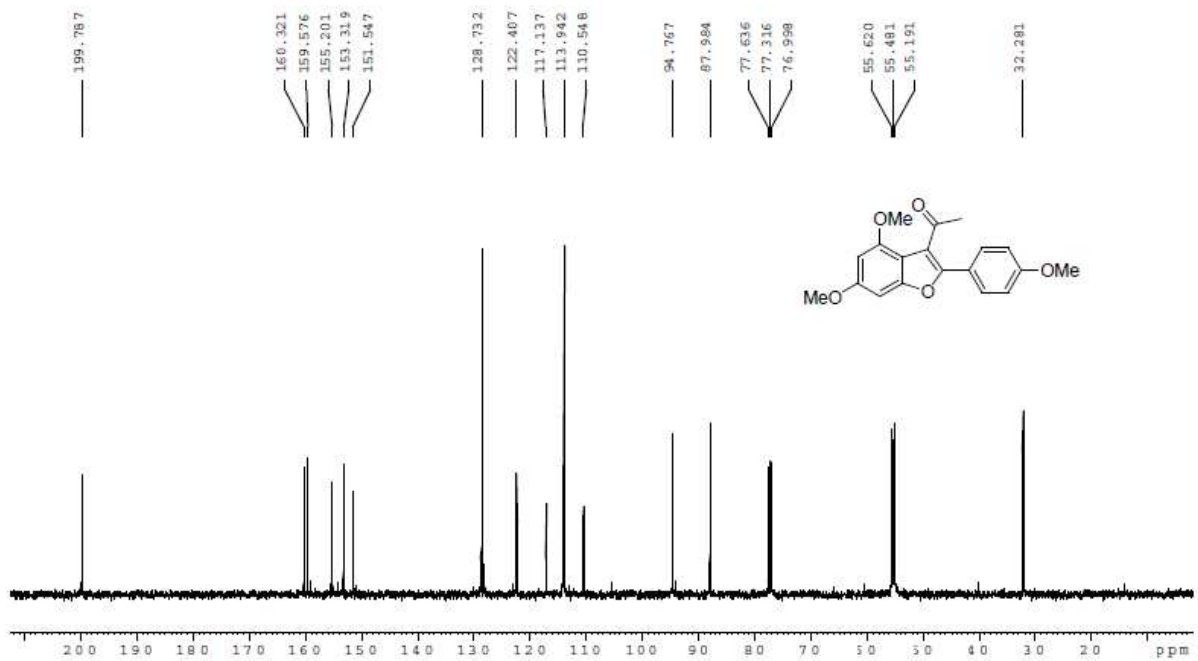
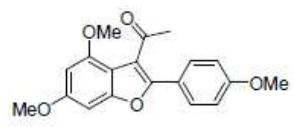
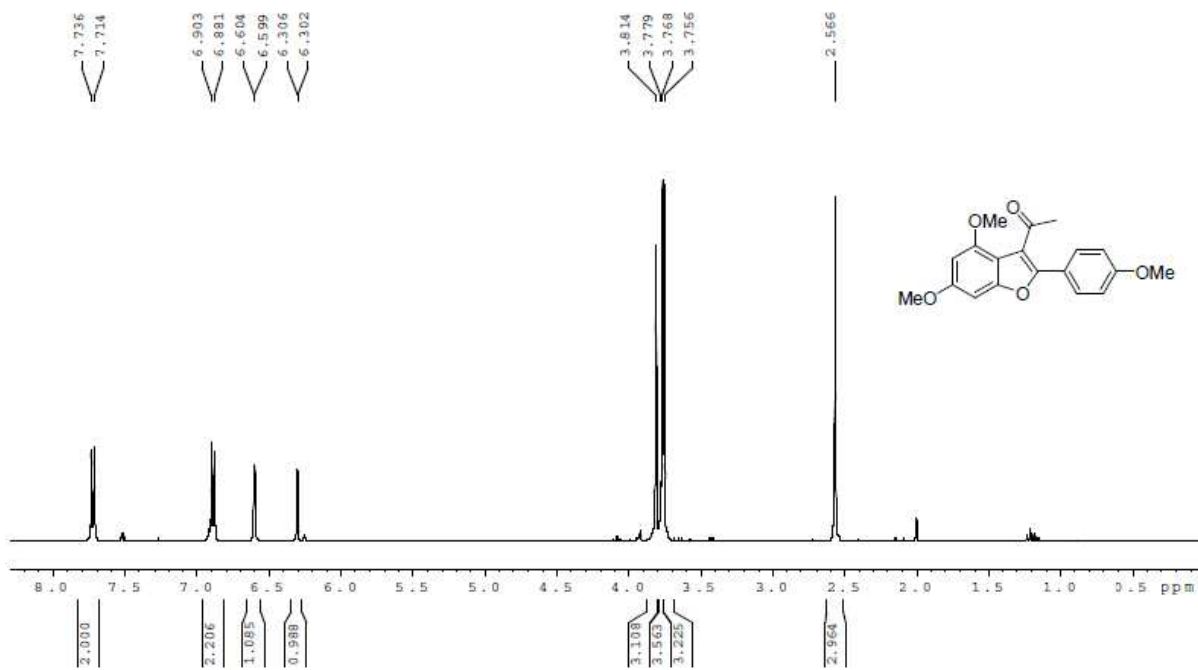
Compound 10 Precursor then Compound 10



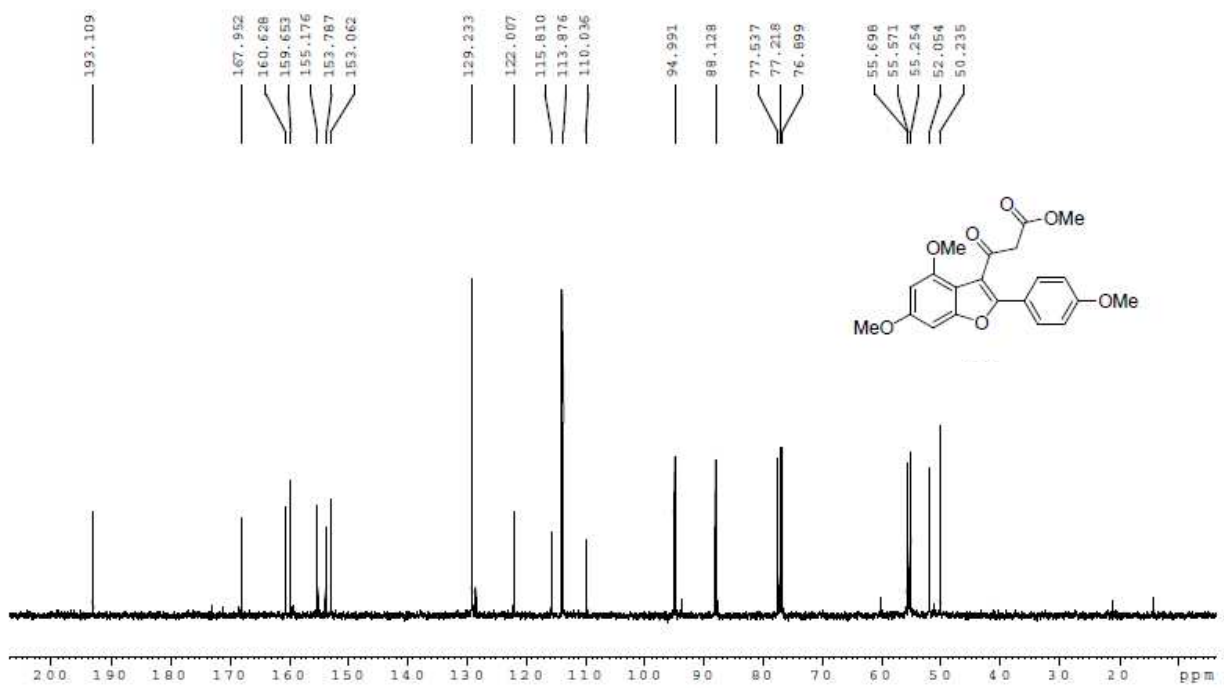
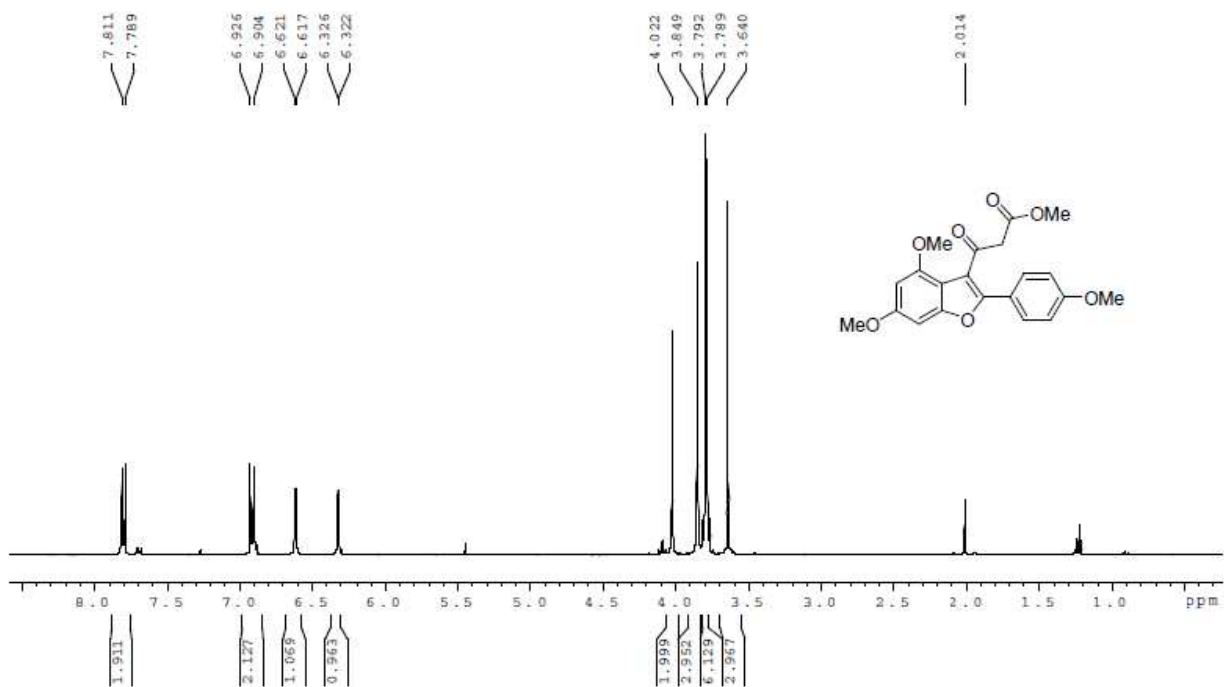
Compound 11



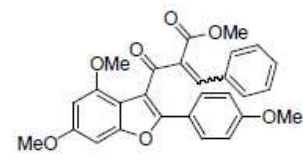
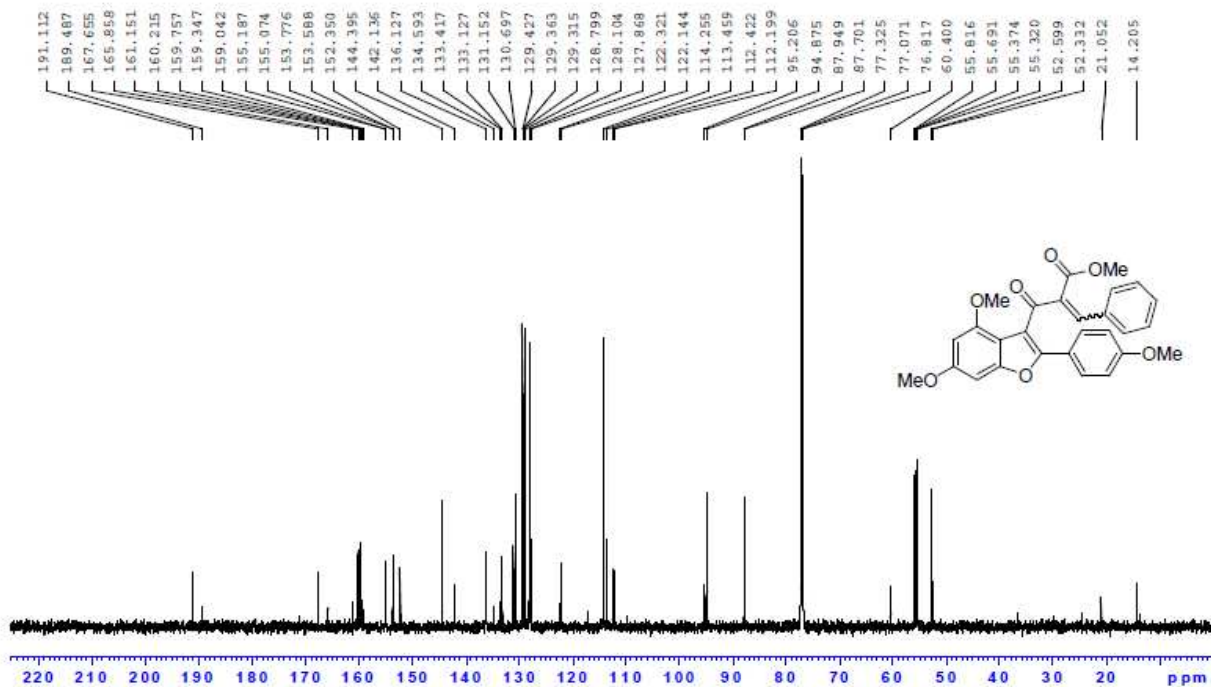
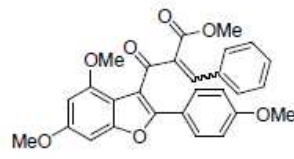
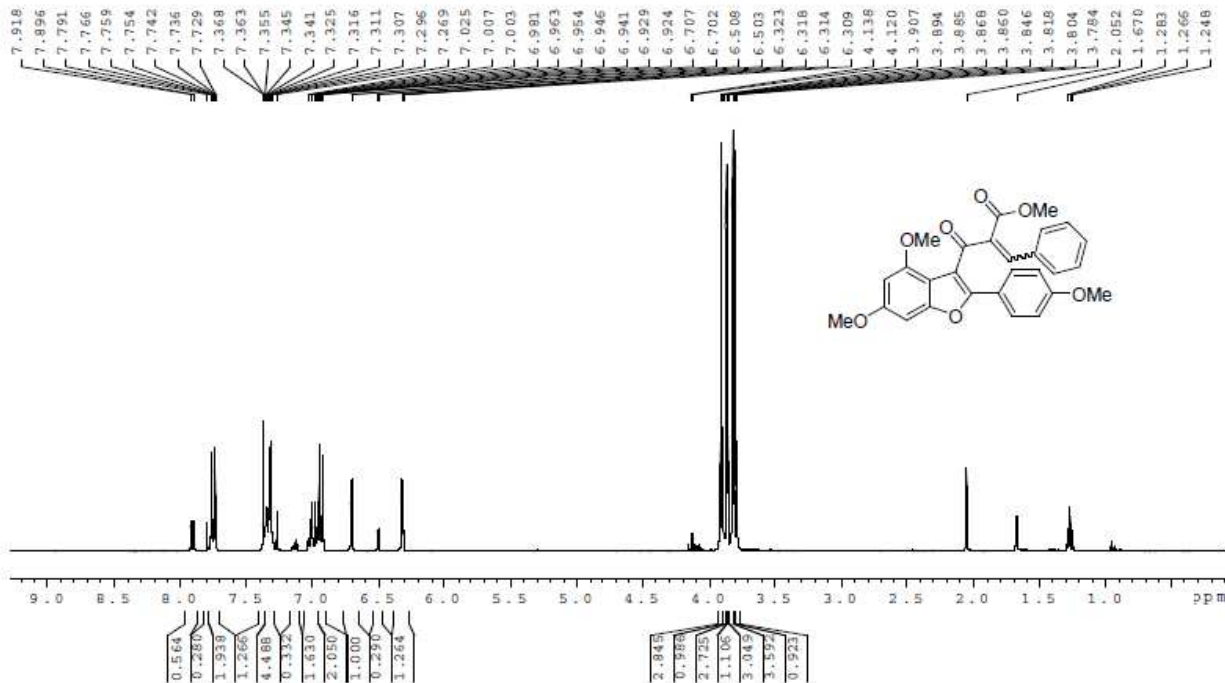
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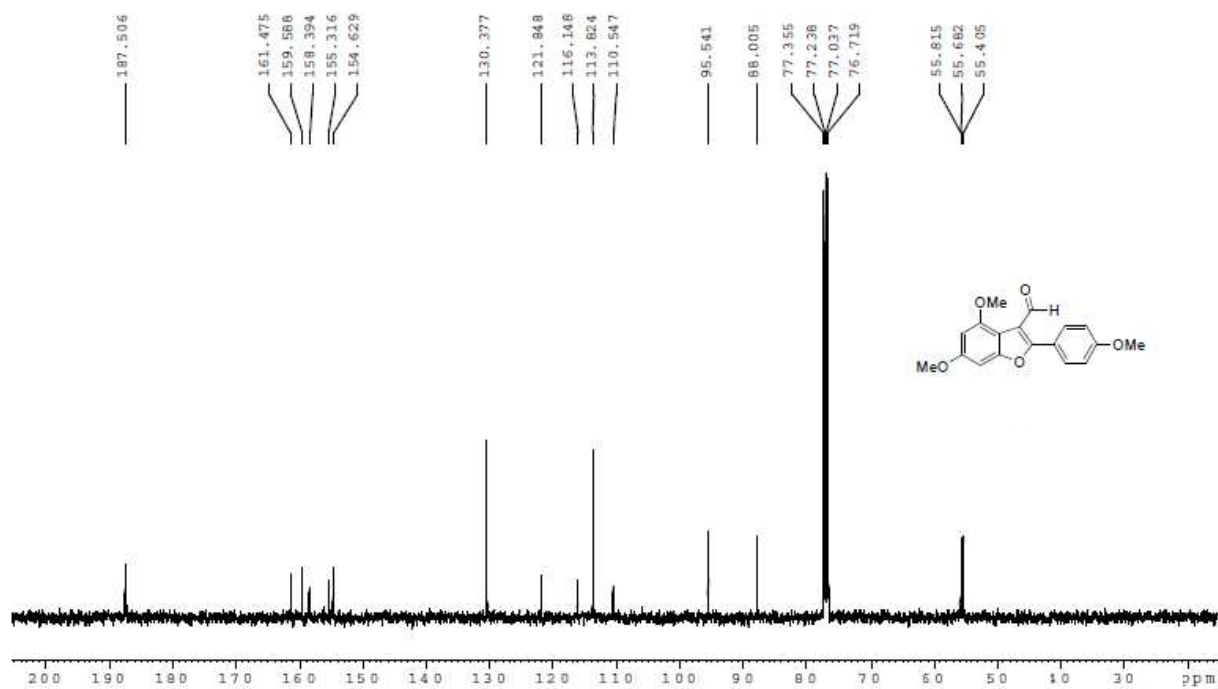
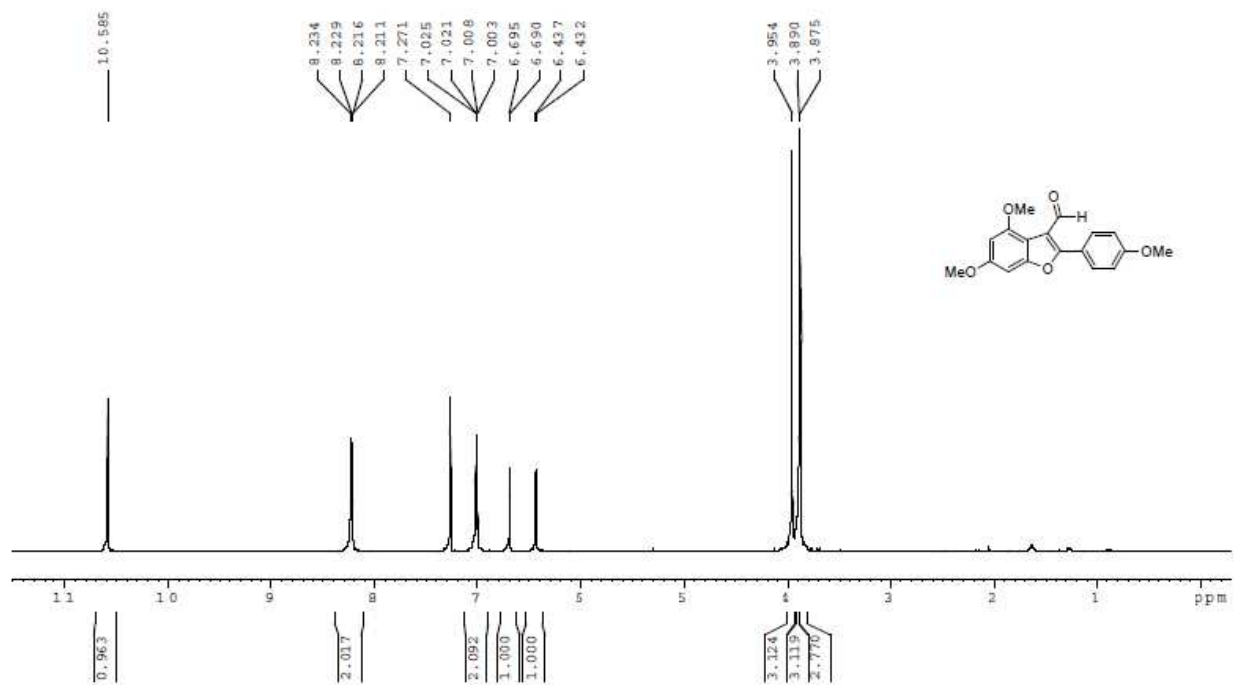
Compound 13



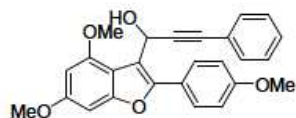
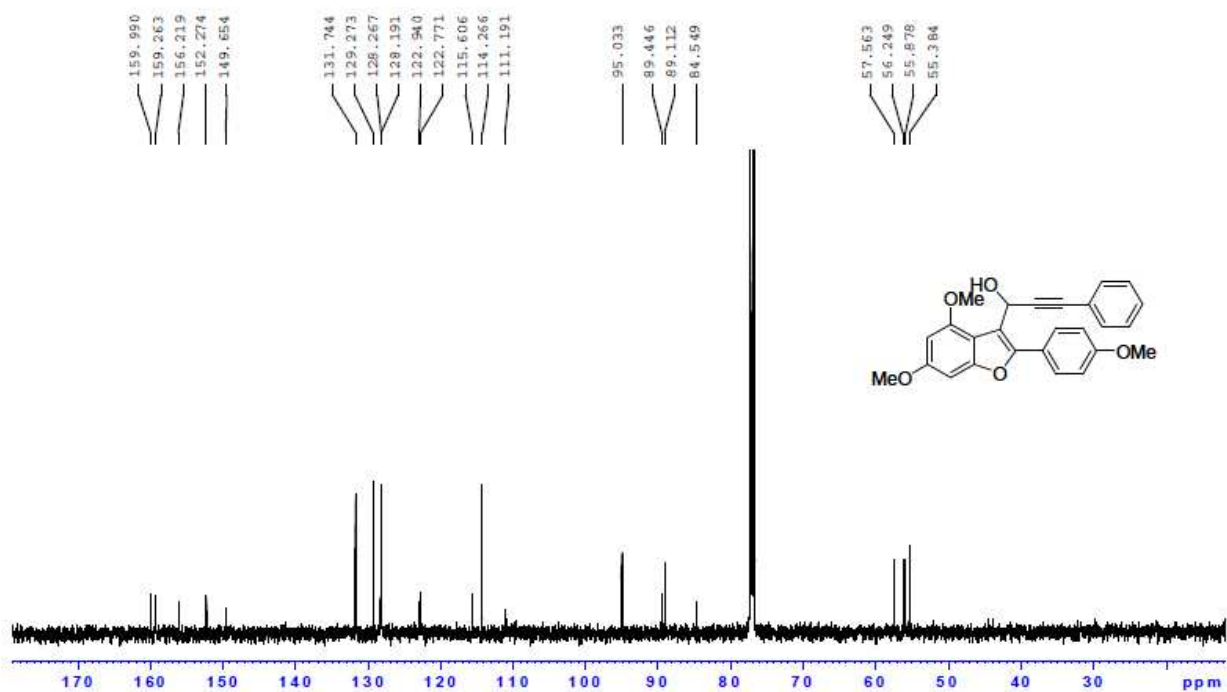
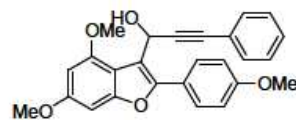
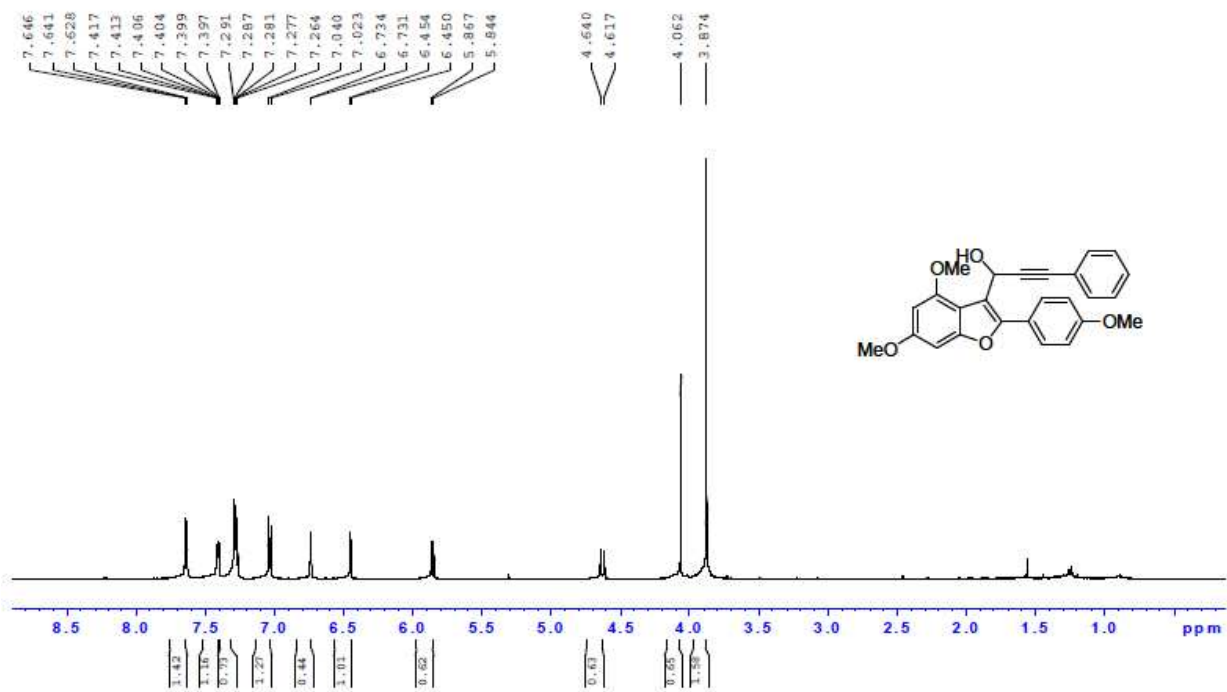
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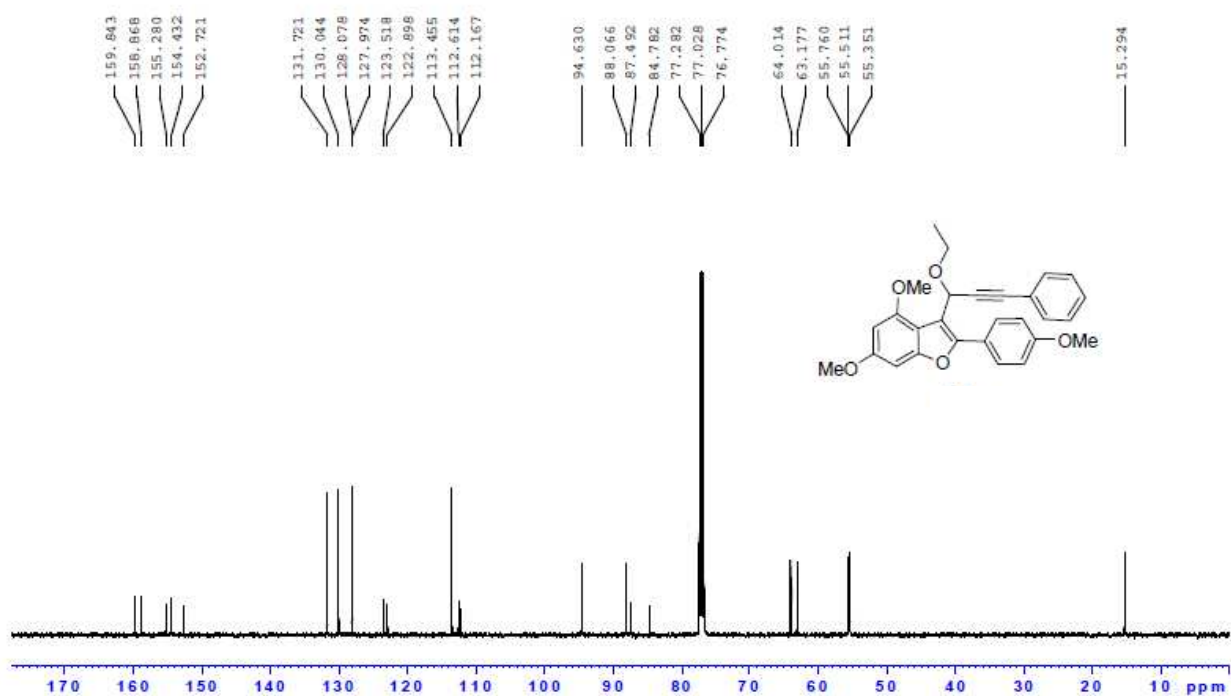
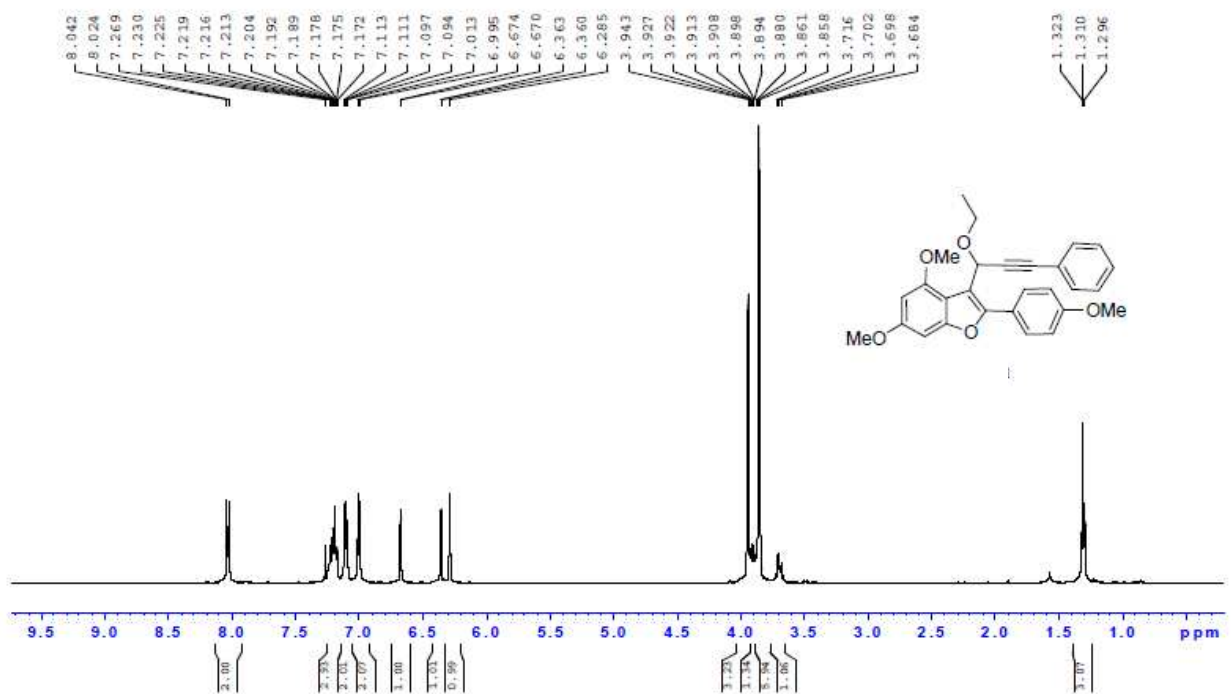
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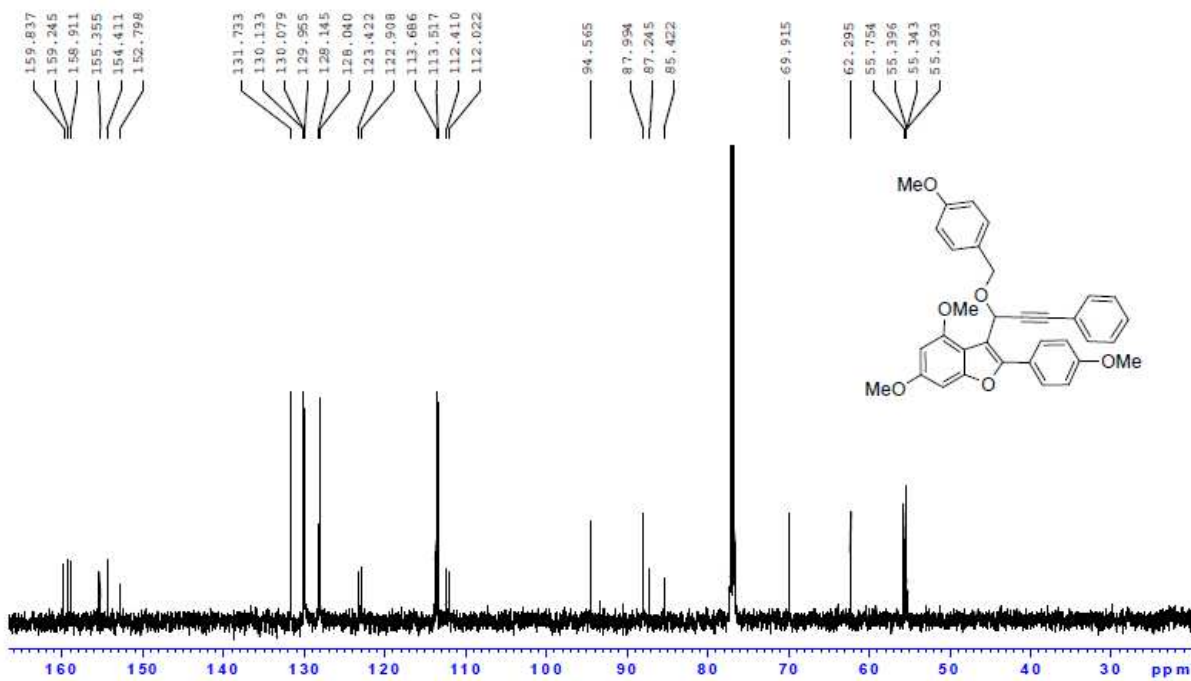
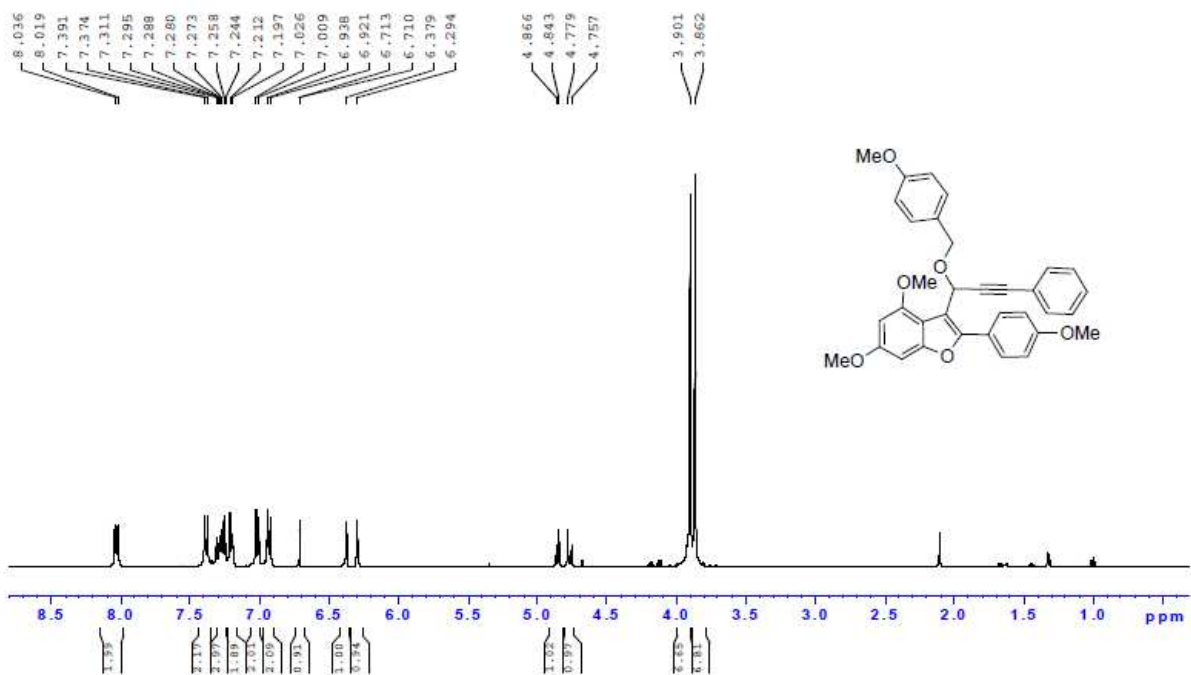
Compound 17a



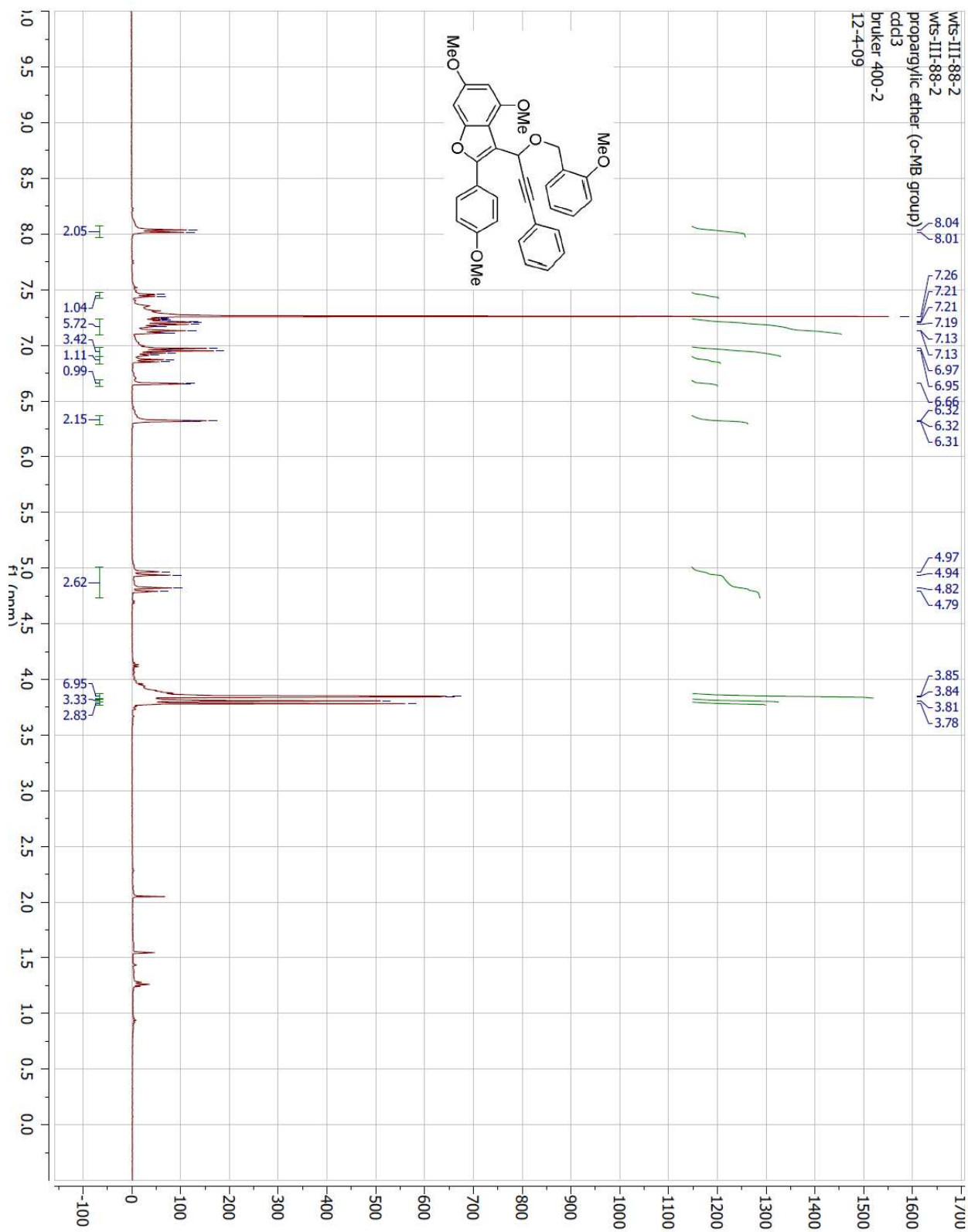
Compound 18a



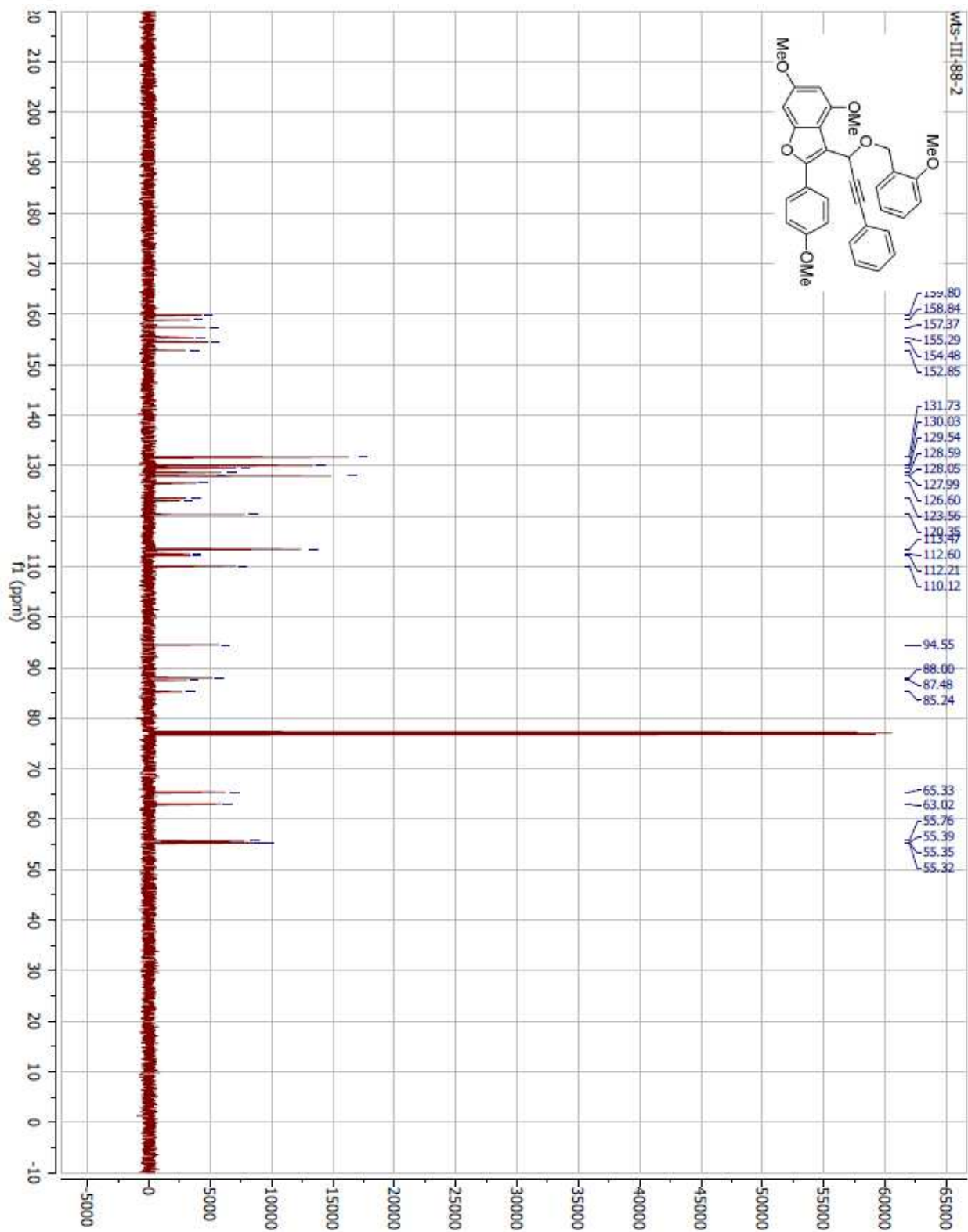
Compound 18b



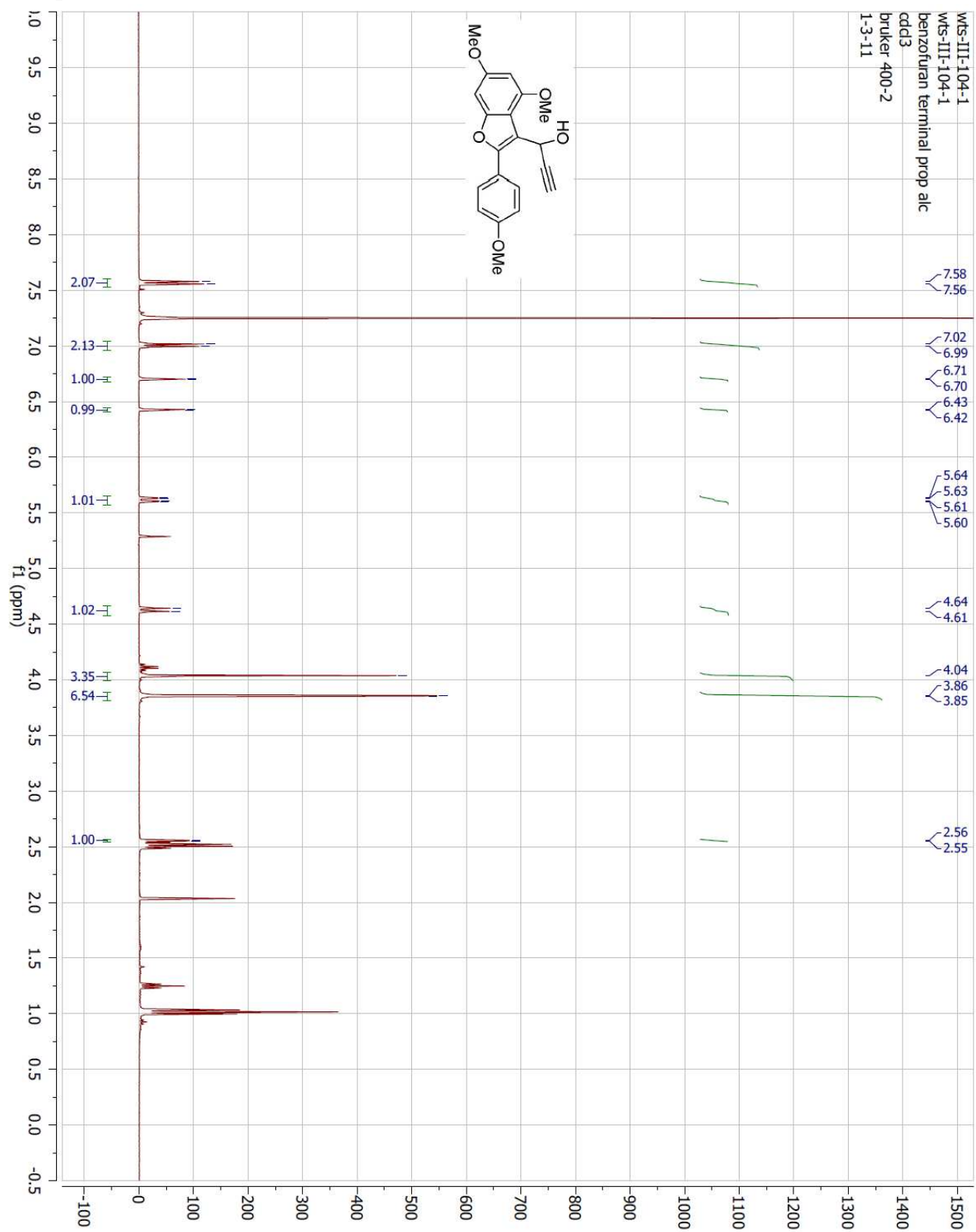
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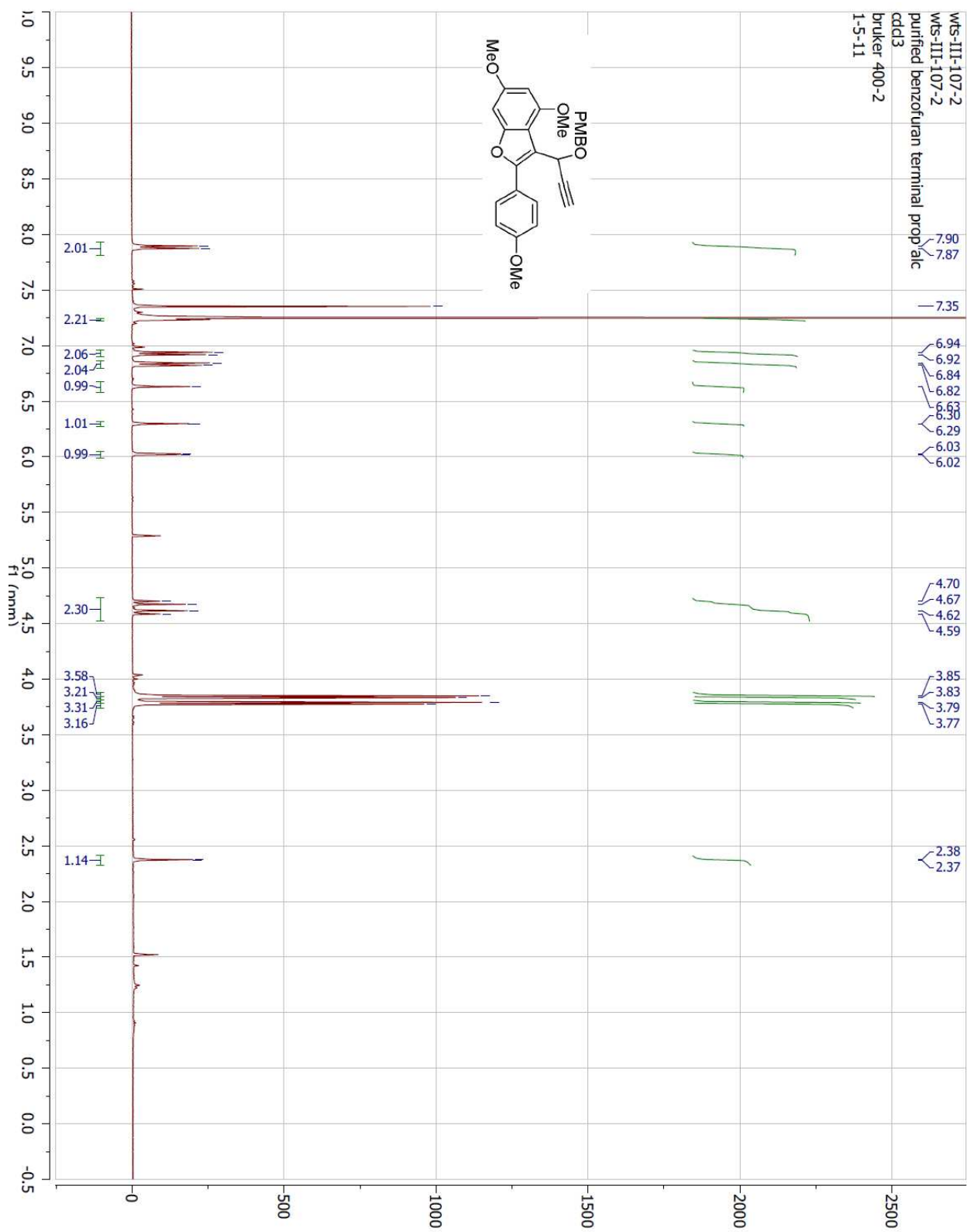
Compound 18c



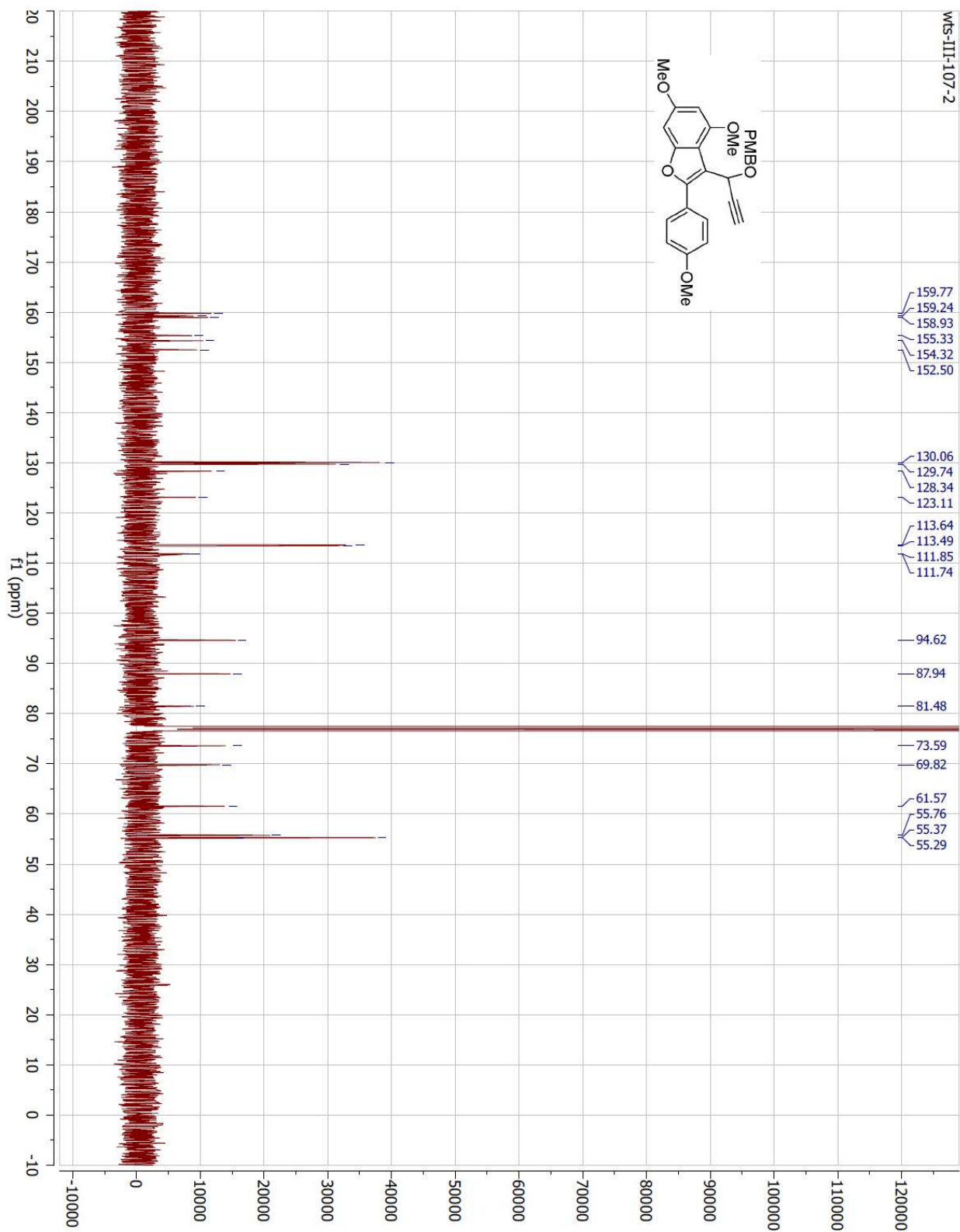
Compound 17b



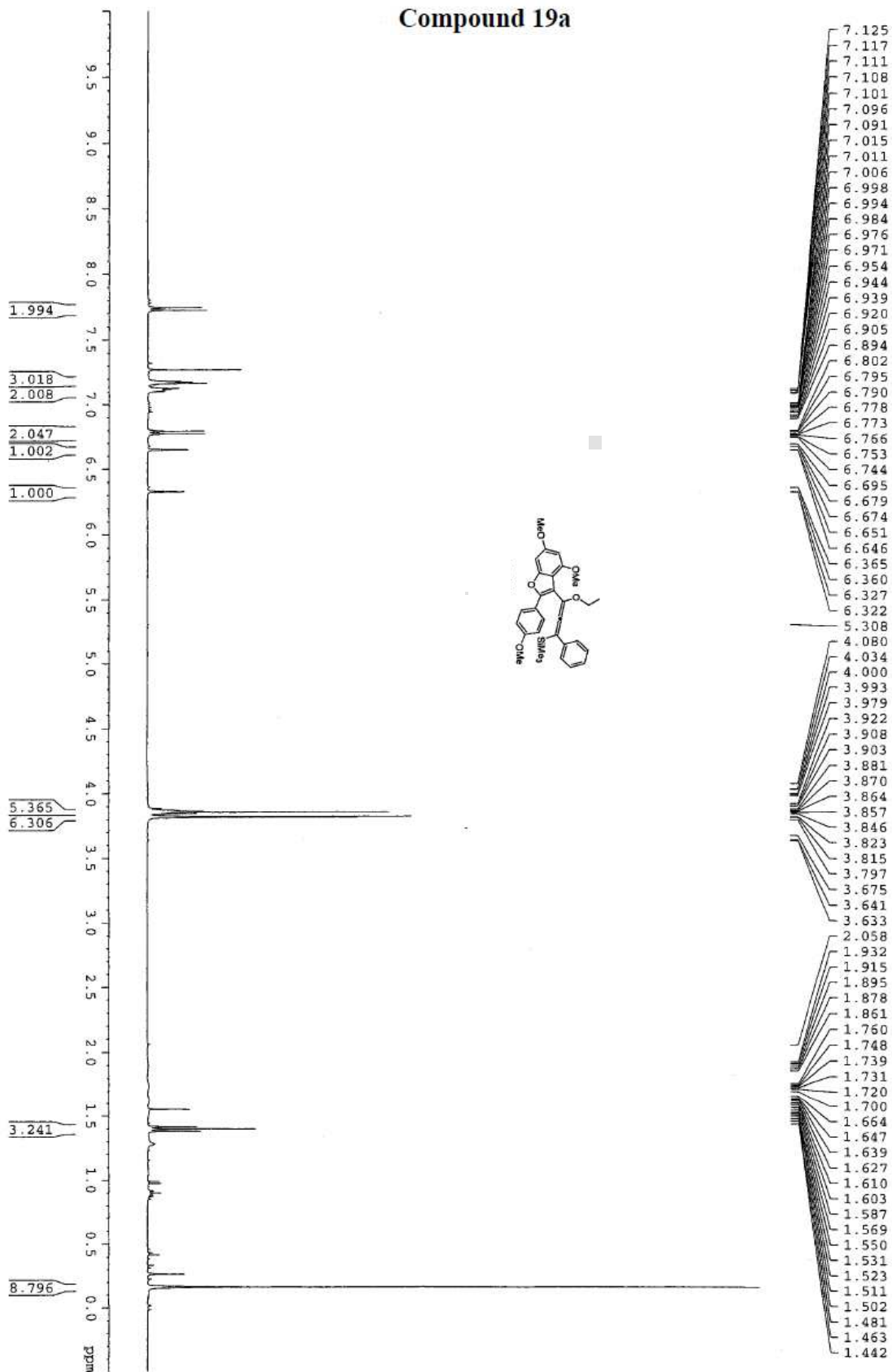
Compound 18d



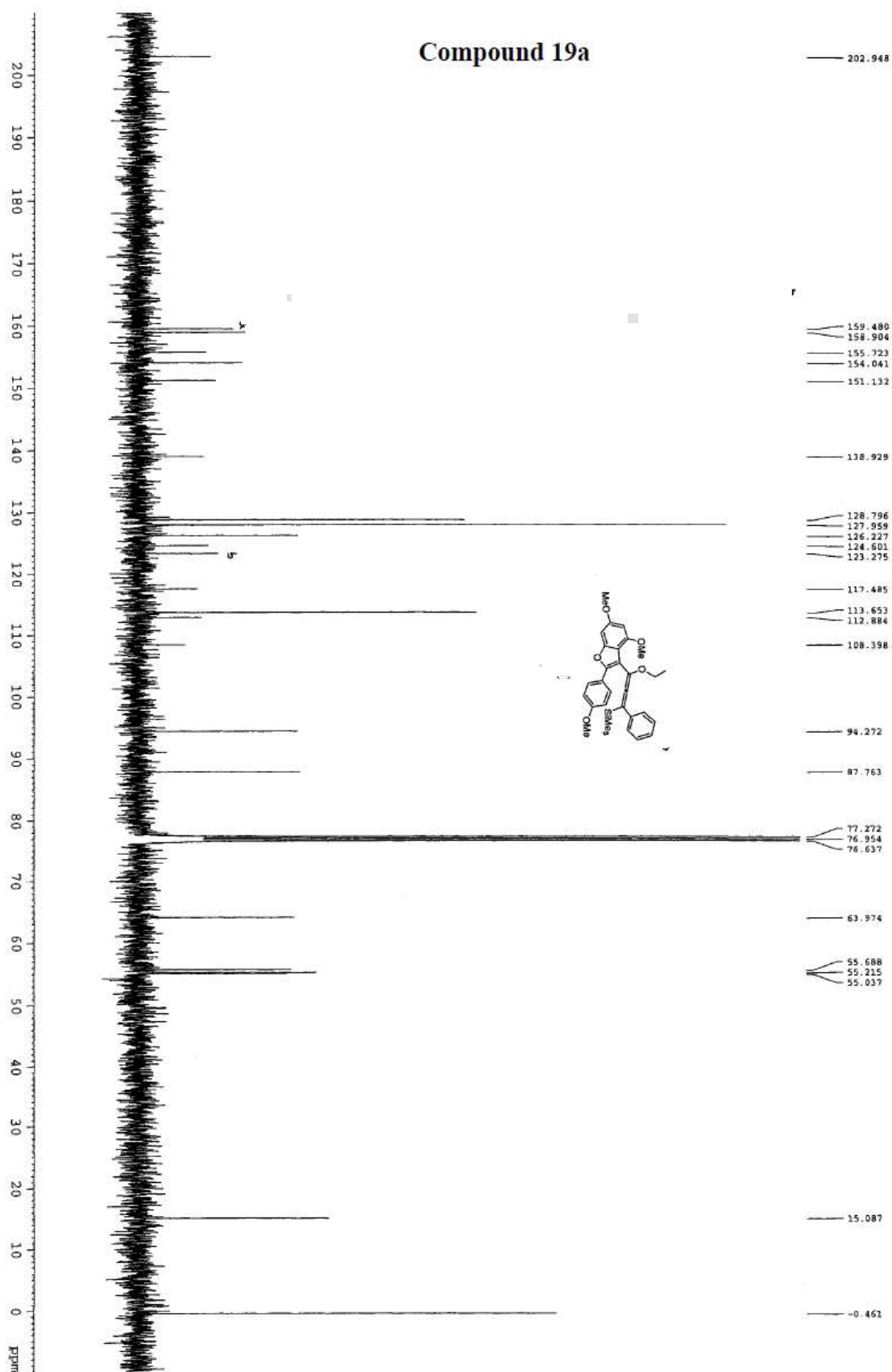
Compound 18d



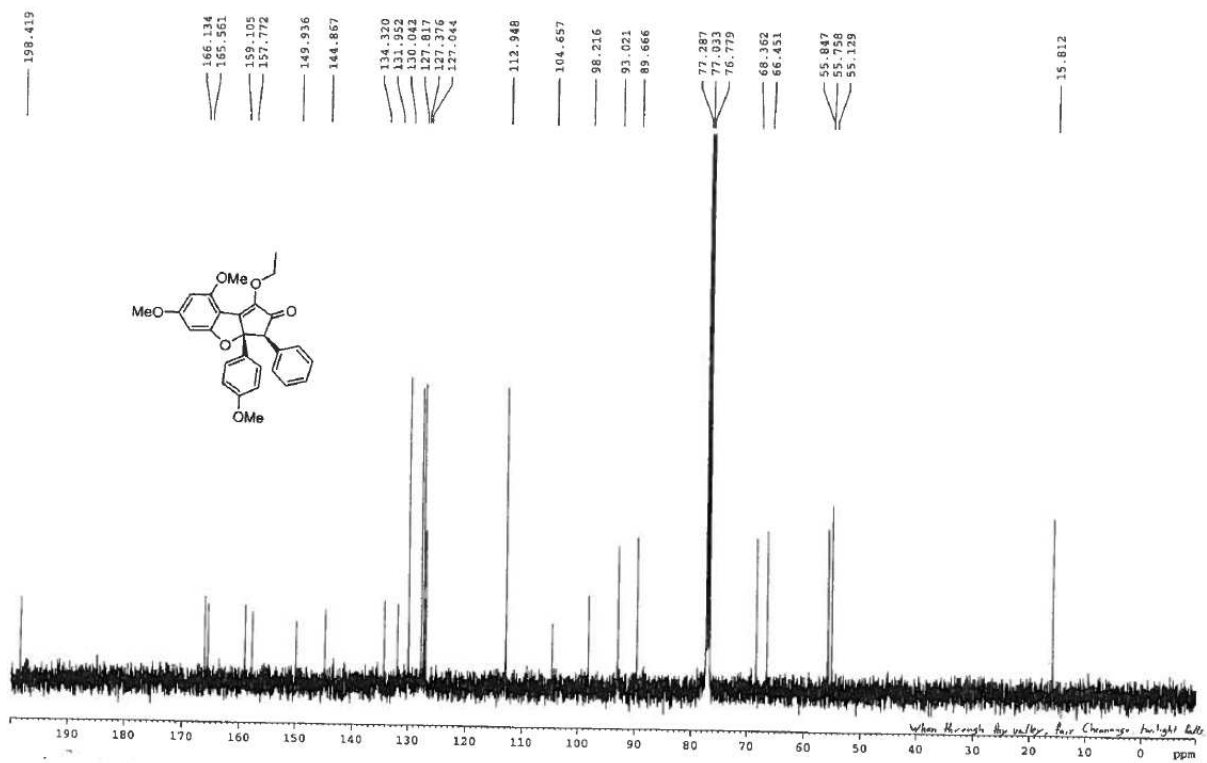
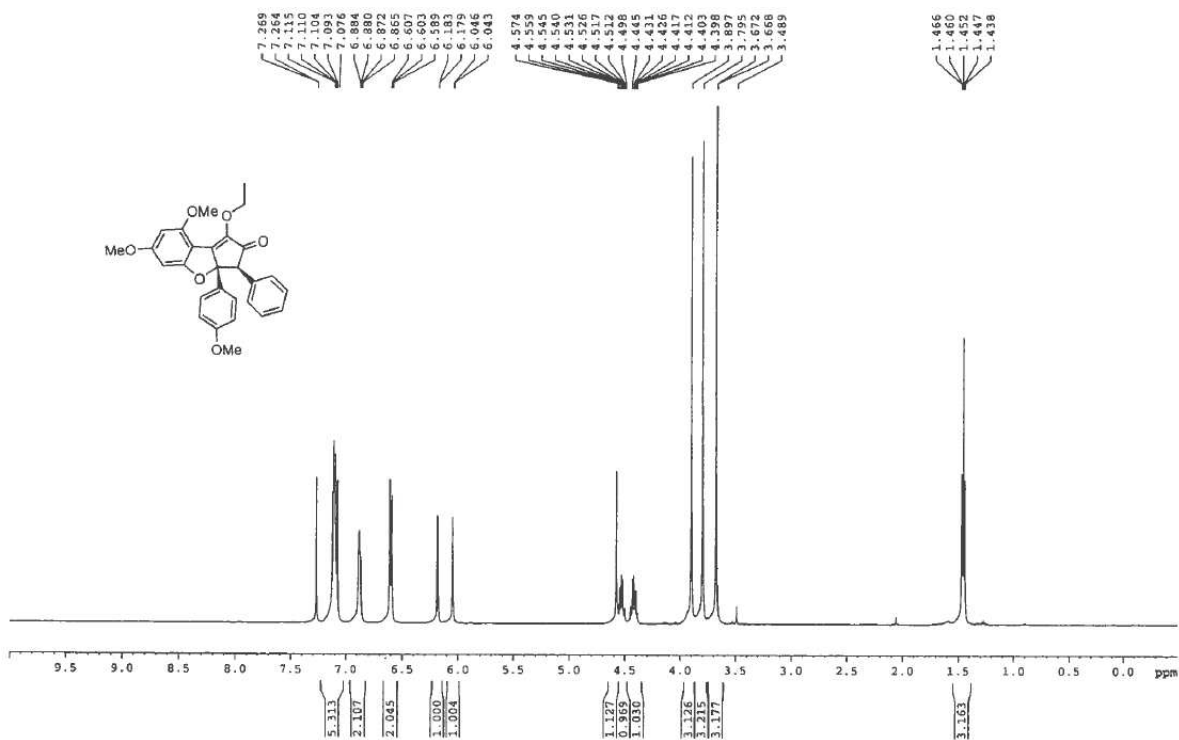
Compound 19a



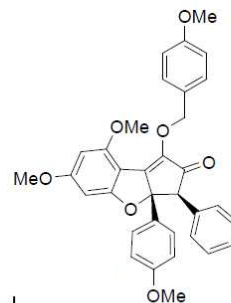
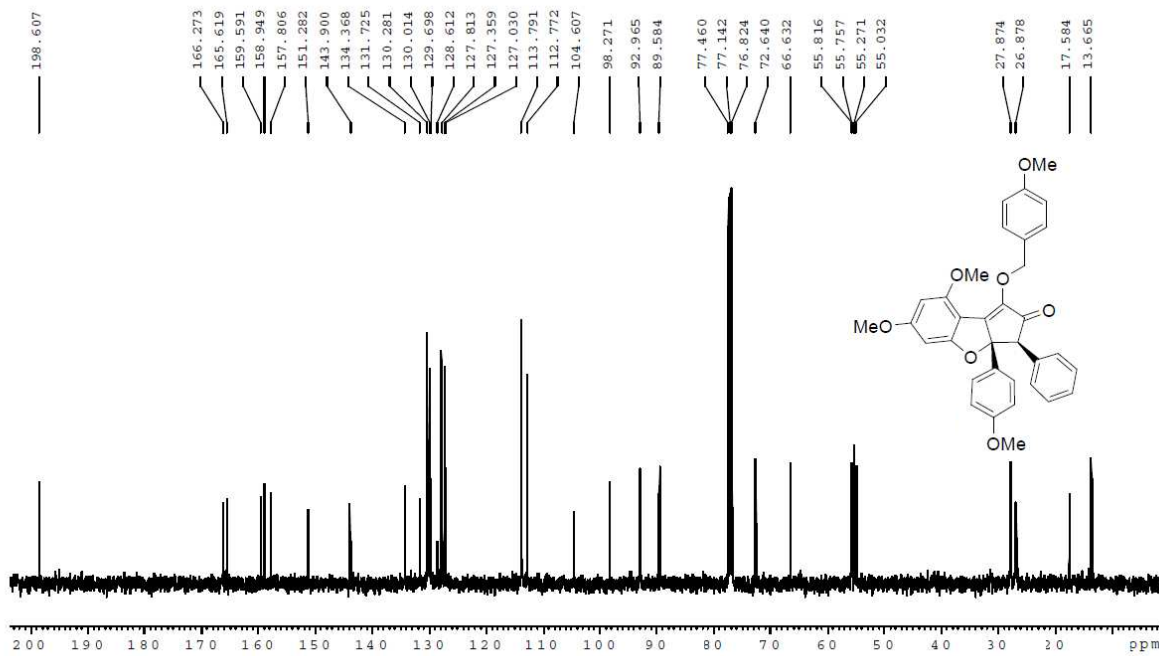
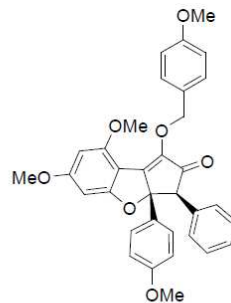
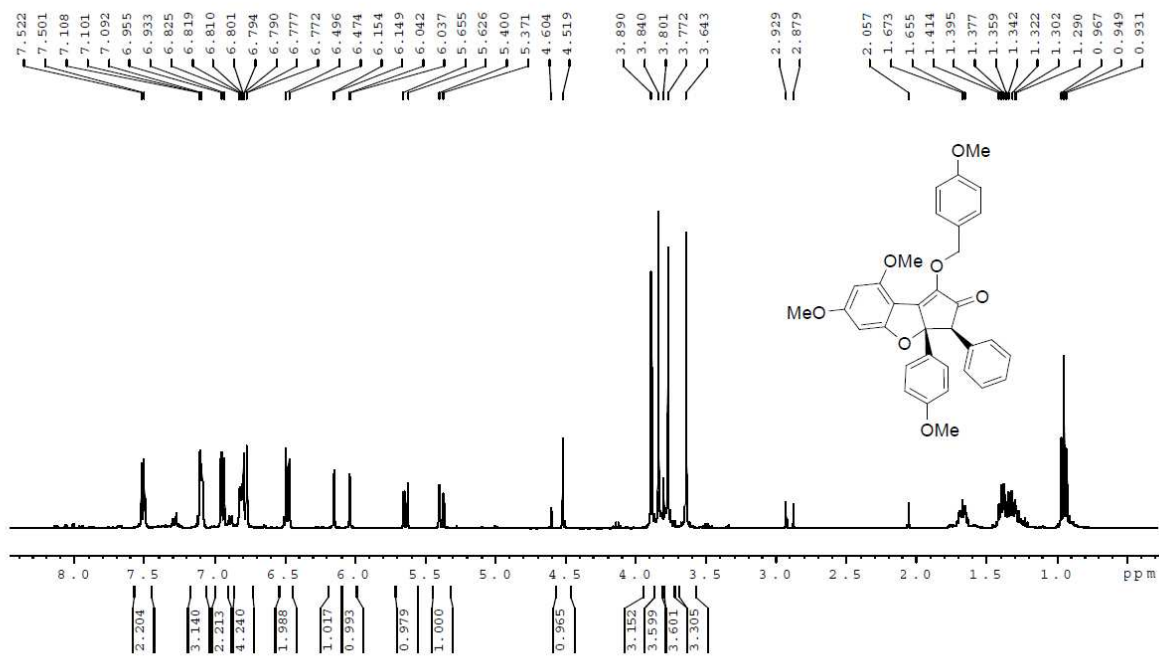
Compound 19a



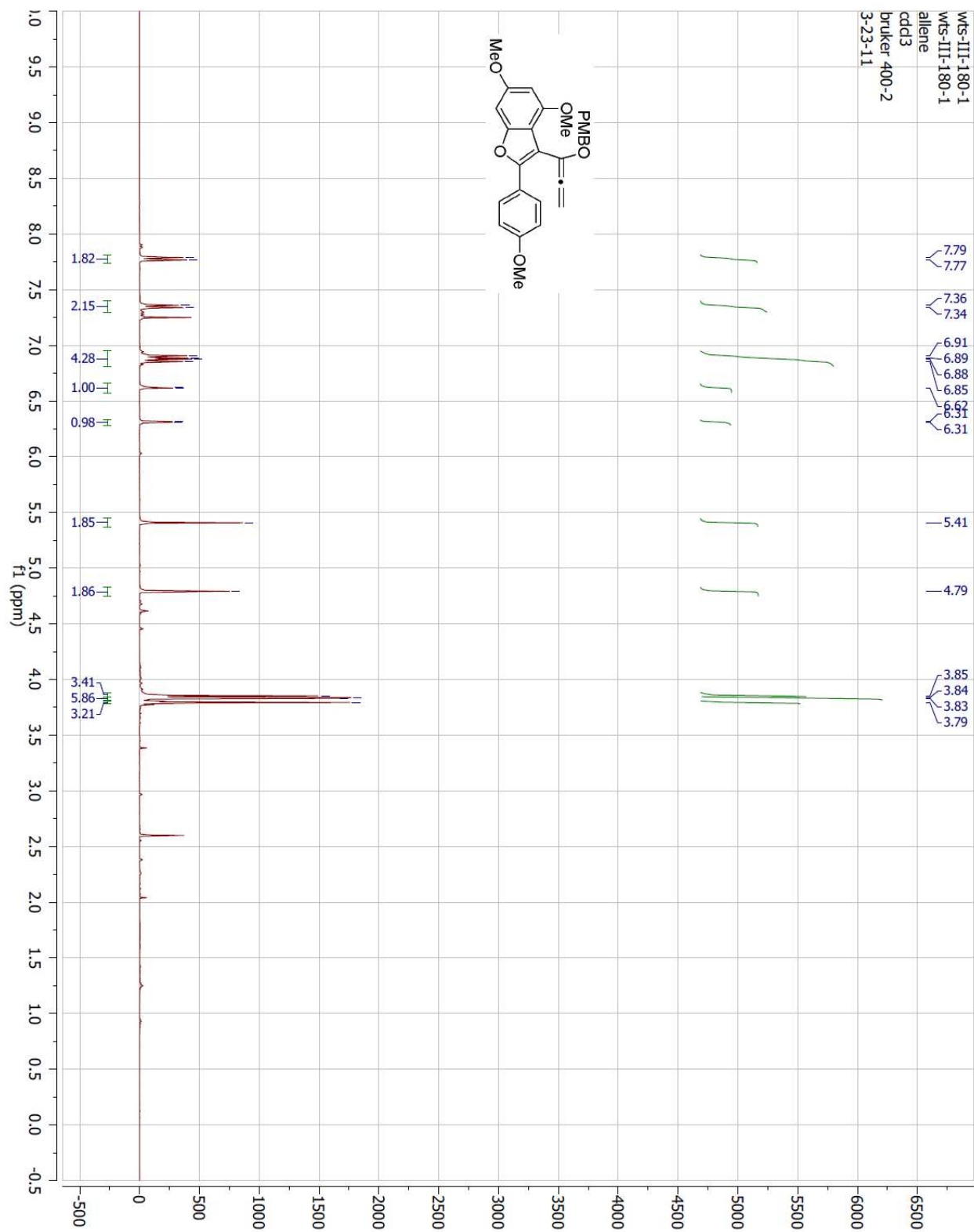
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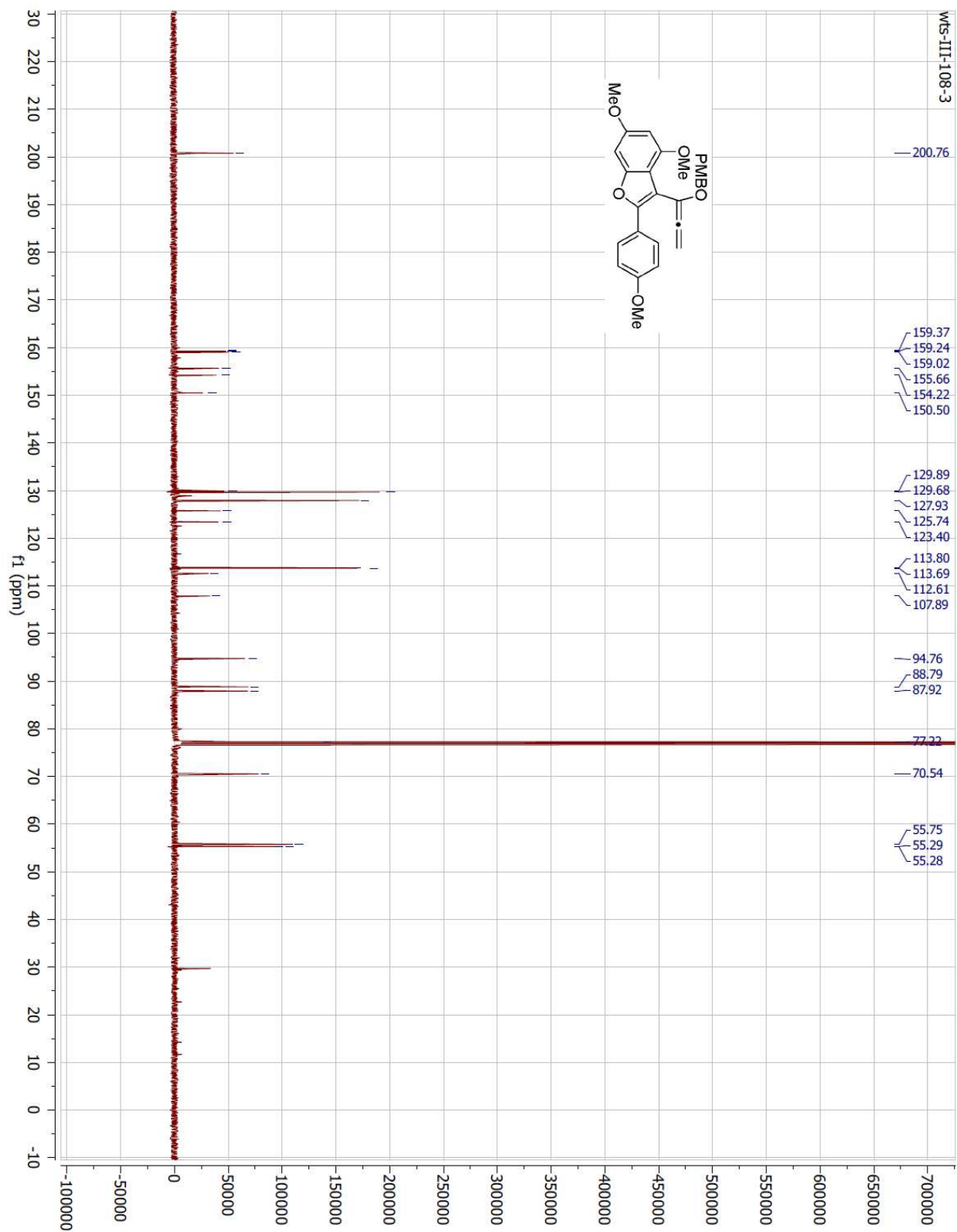
Compound 15b



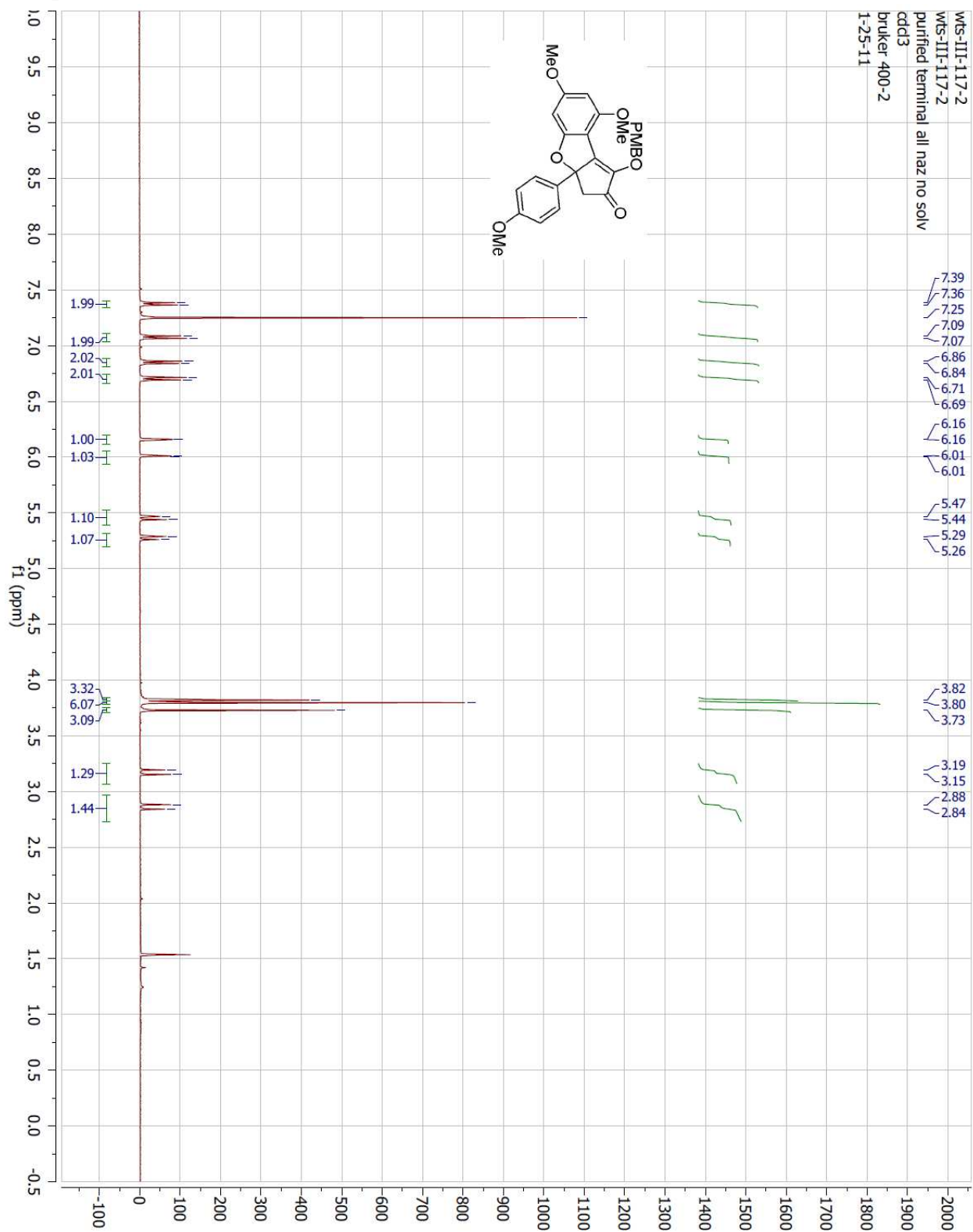
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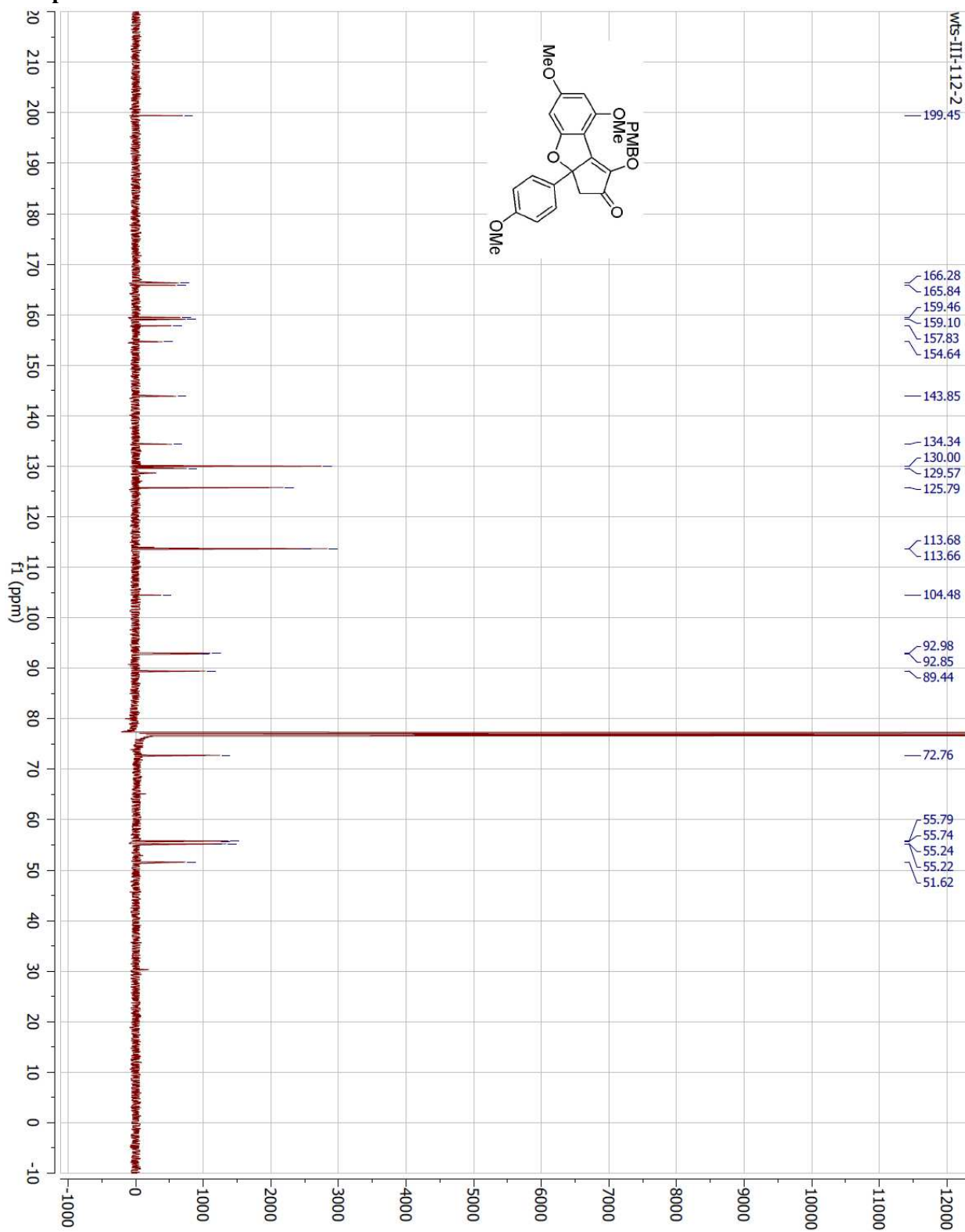
Compound 20



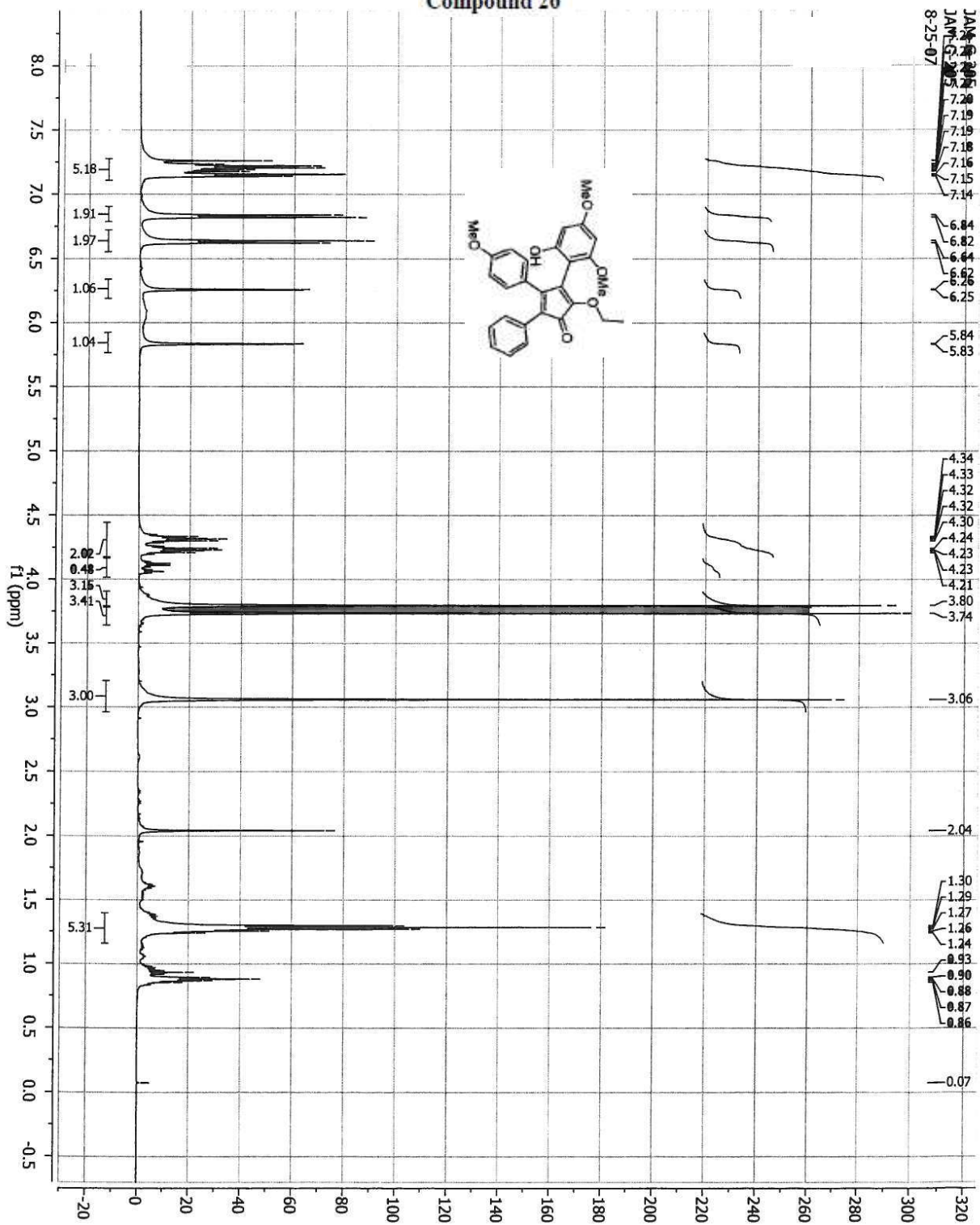
Compound 22

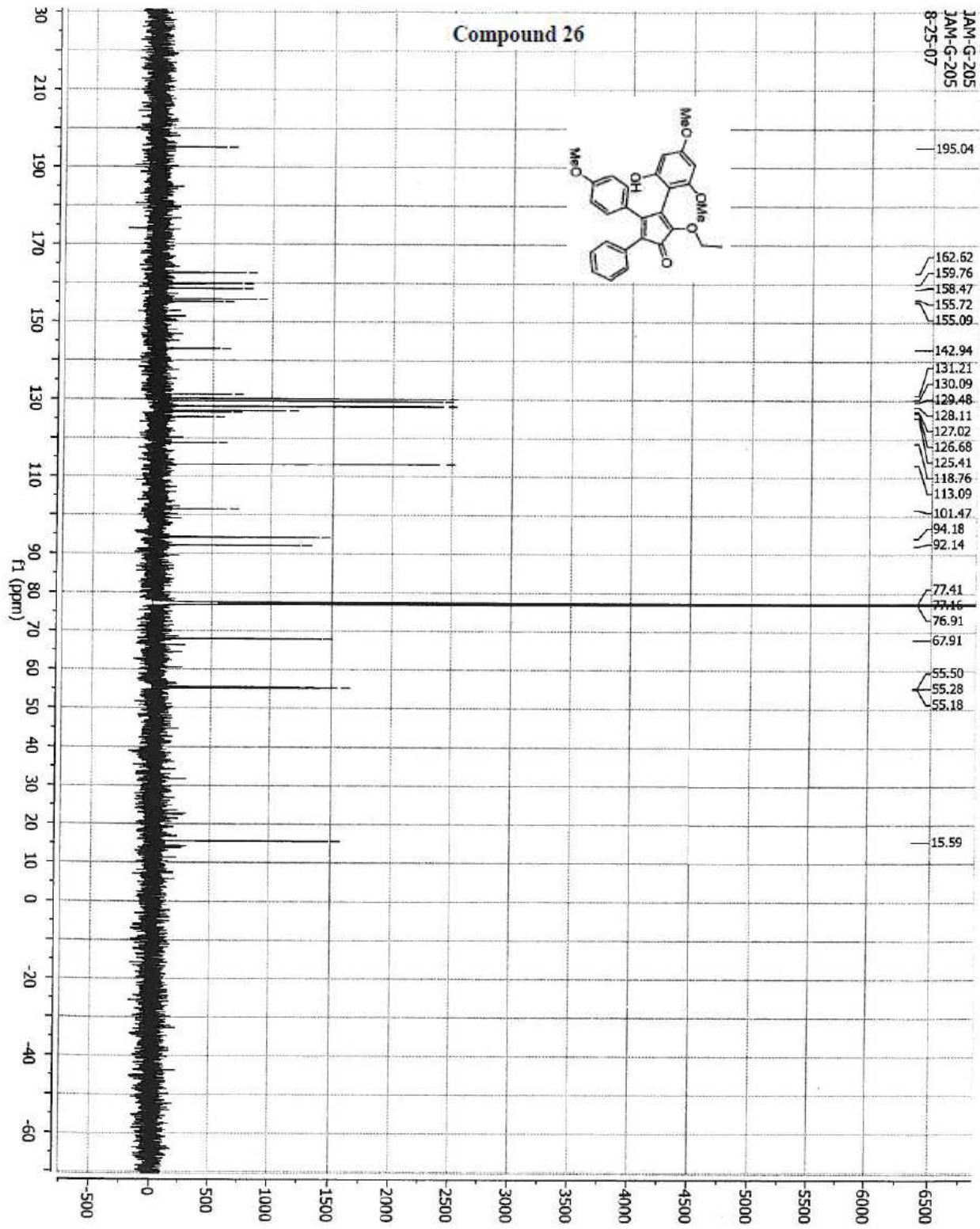


Compound 22



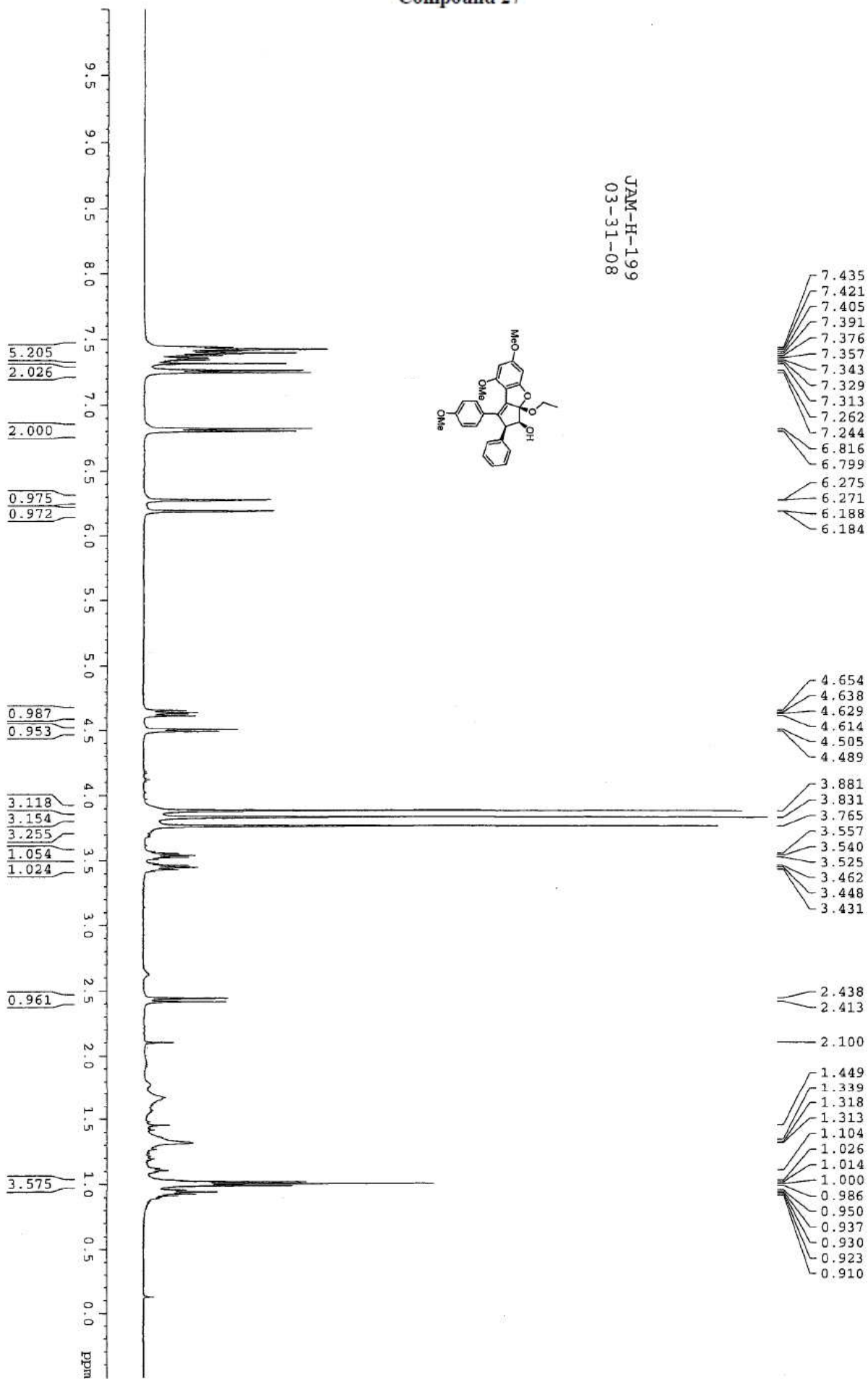
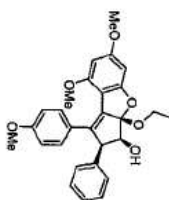
Compound 26





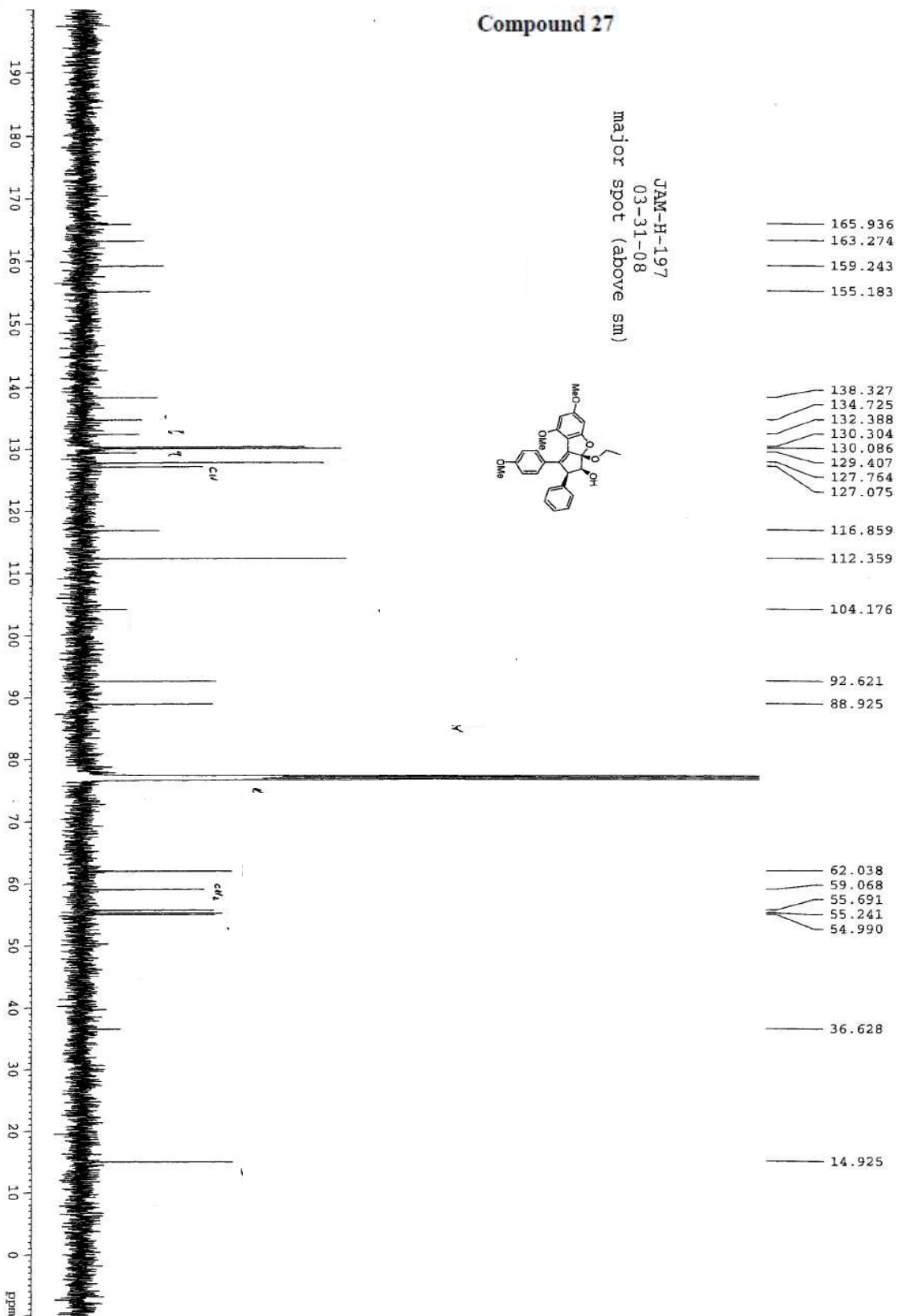
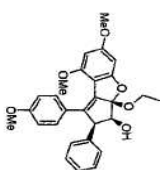
Compound 27

JAM-H-199
03-31-08



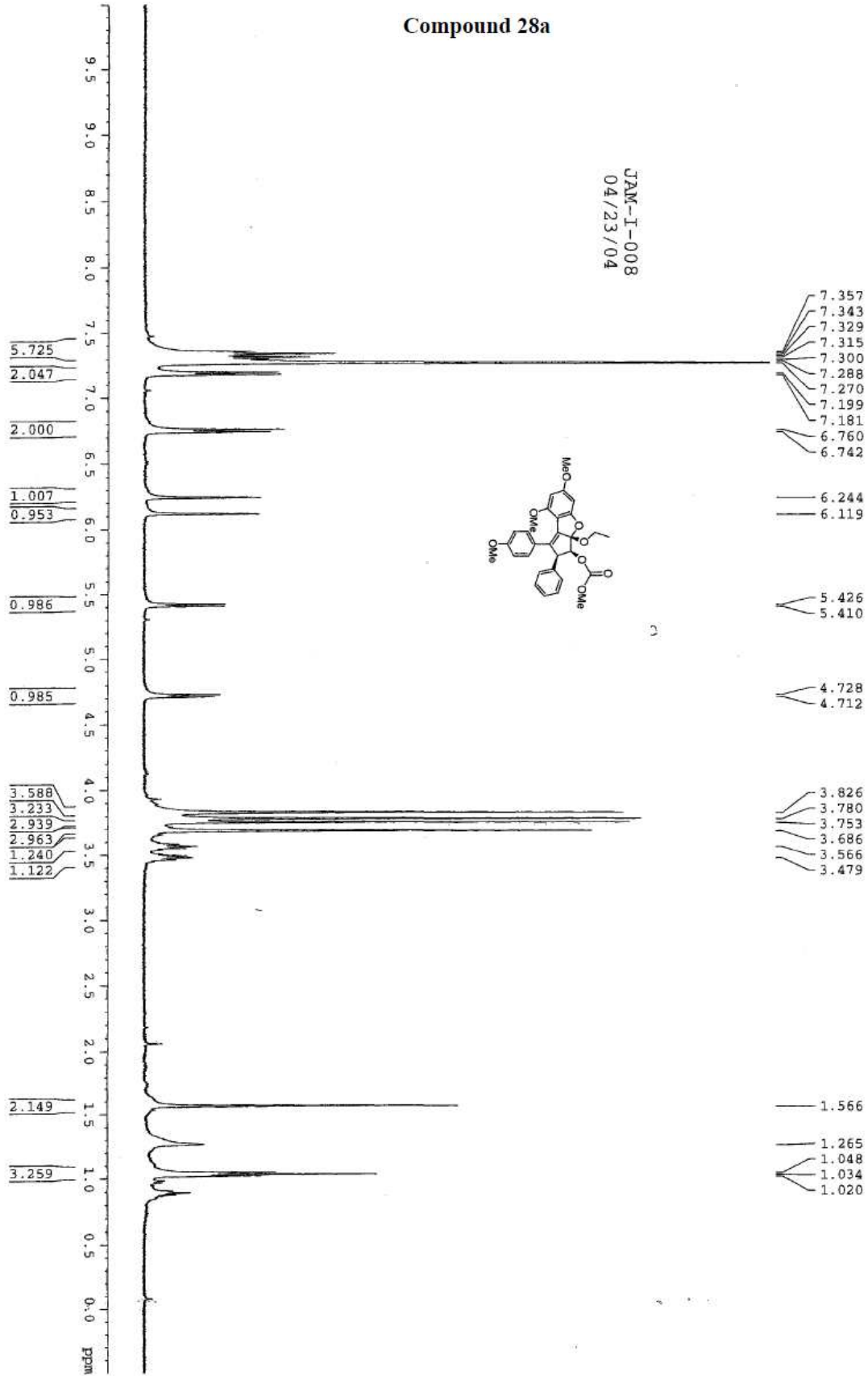
Compound 27

JAM-H-197
03-31-08
major spot (above sm)



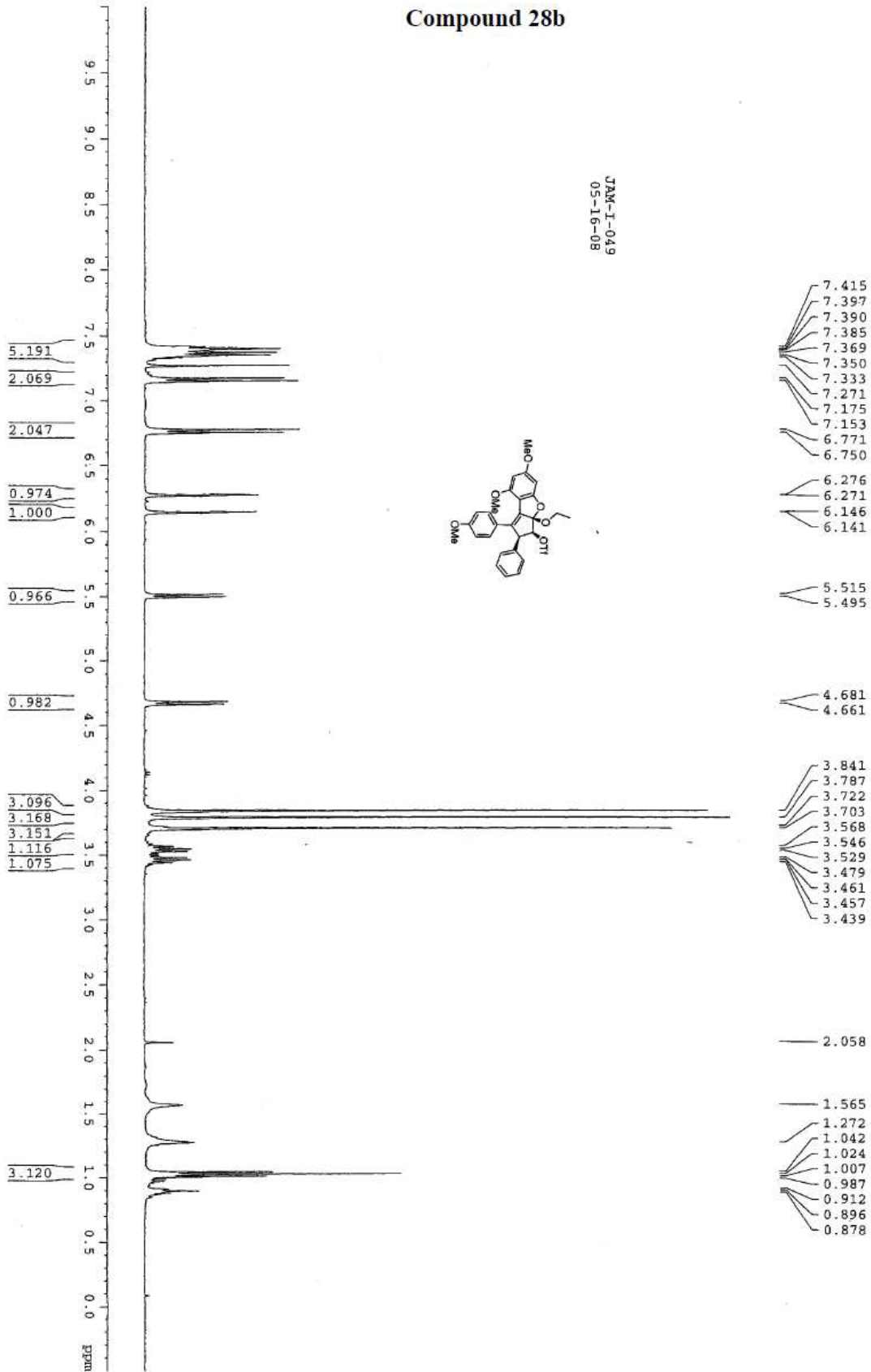
Compound 28a

JAM-I-008
04/23/04

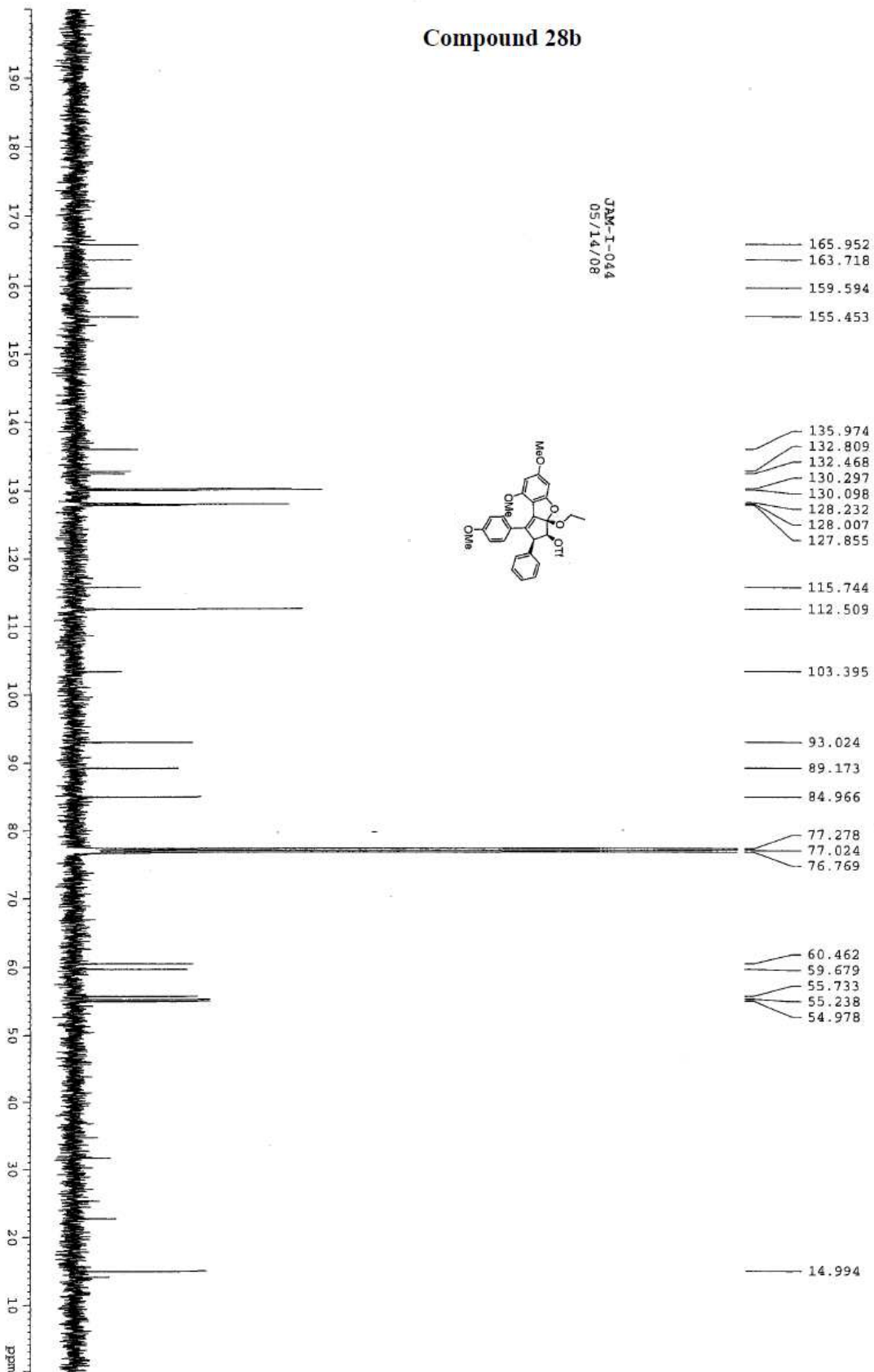


Compound 28b

JAM-I-049
05-16-08

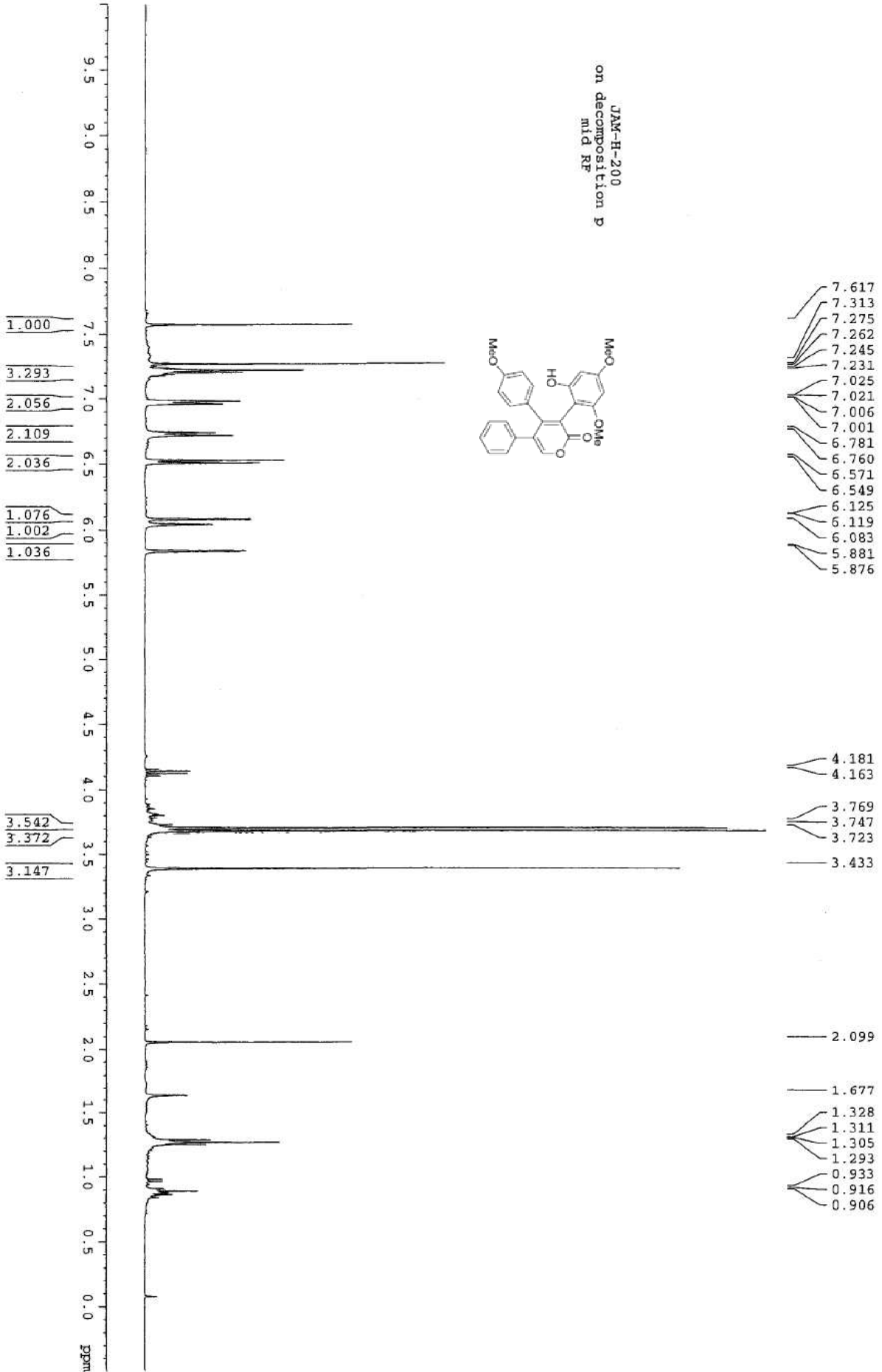
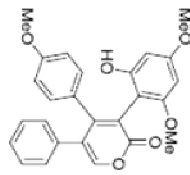


Compound 28b

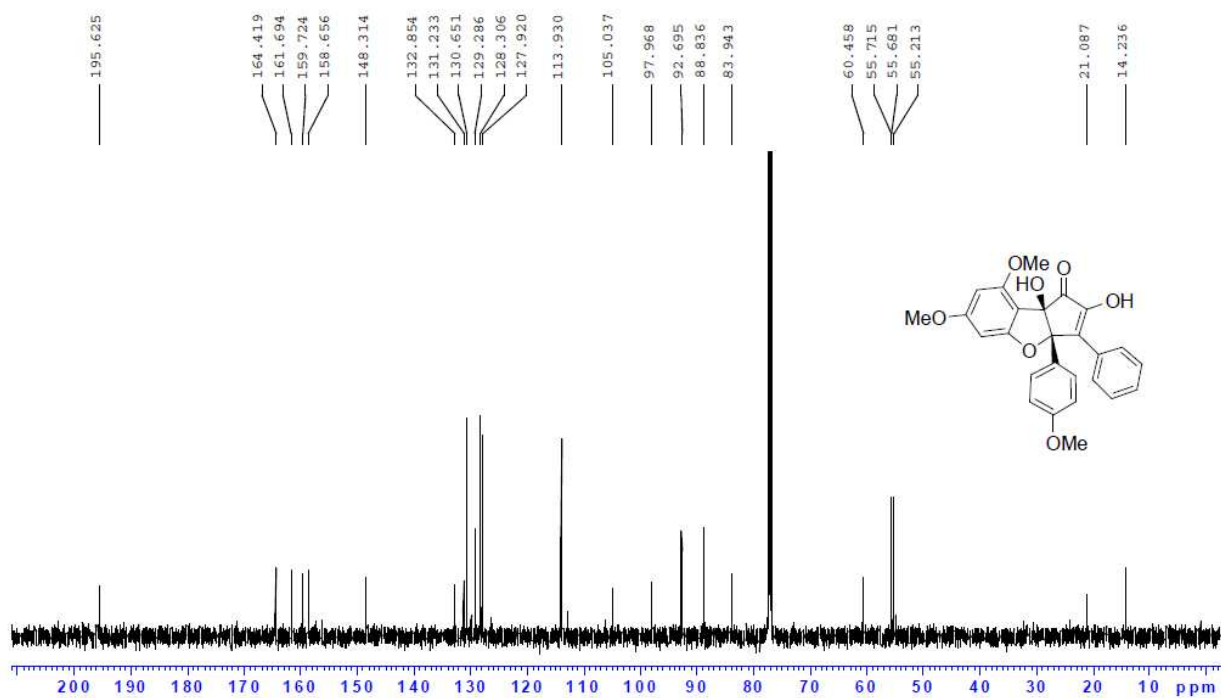
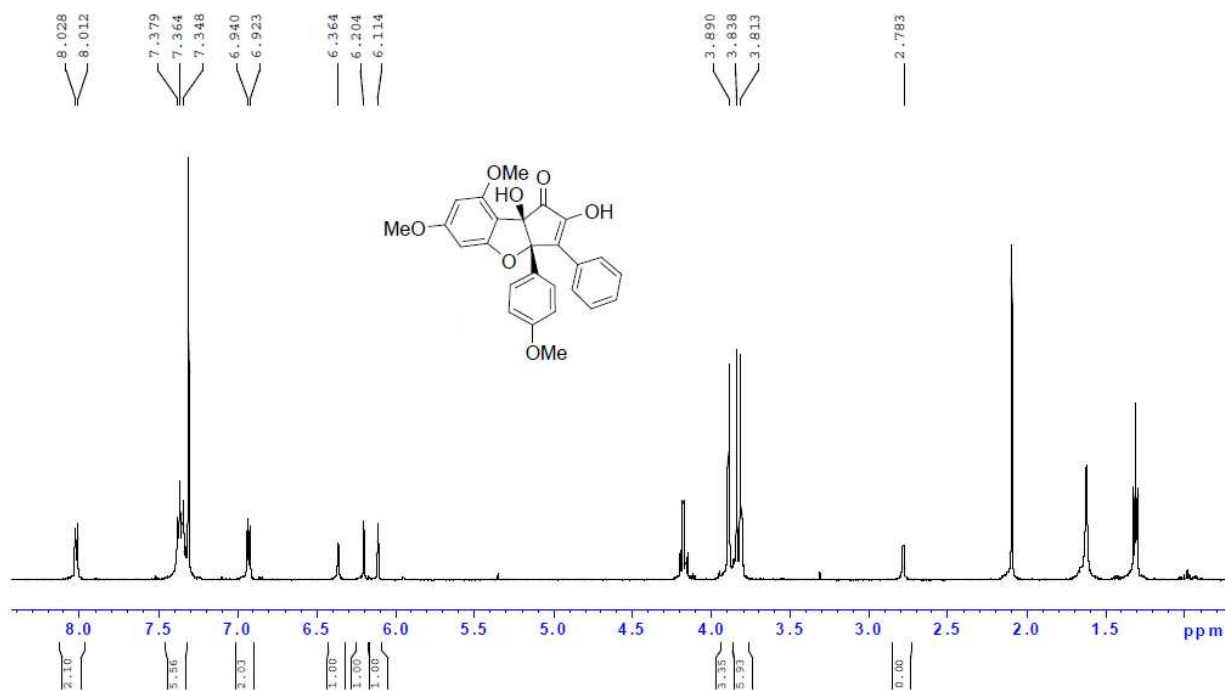


Compound 29

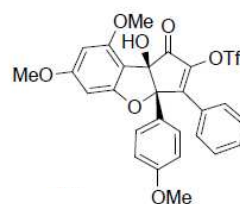
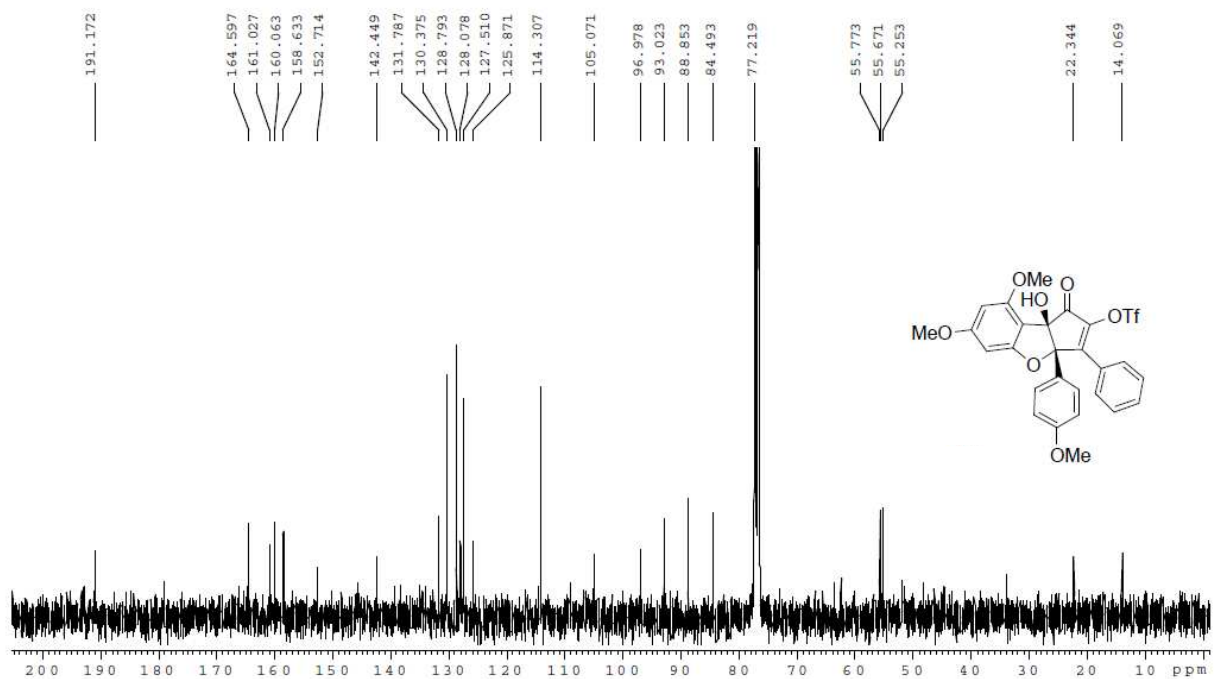
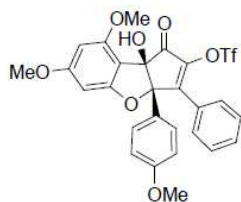
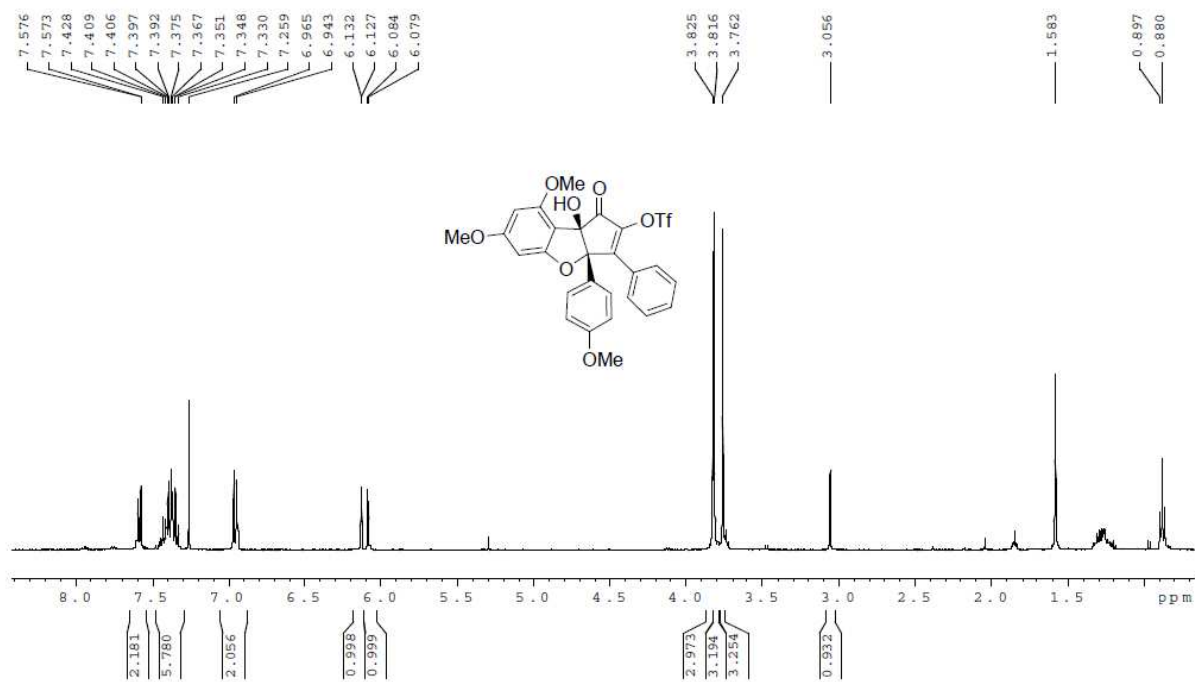
JAM-H-200
on decomposition p
mid RP



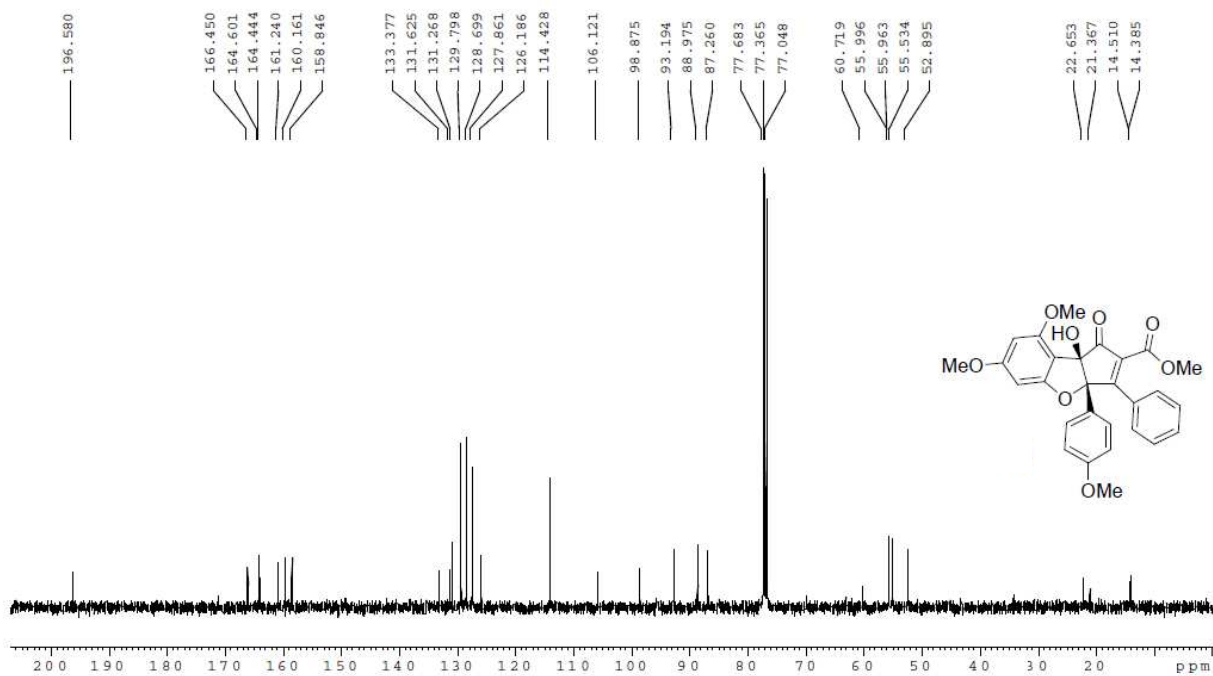
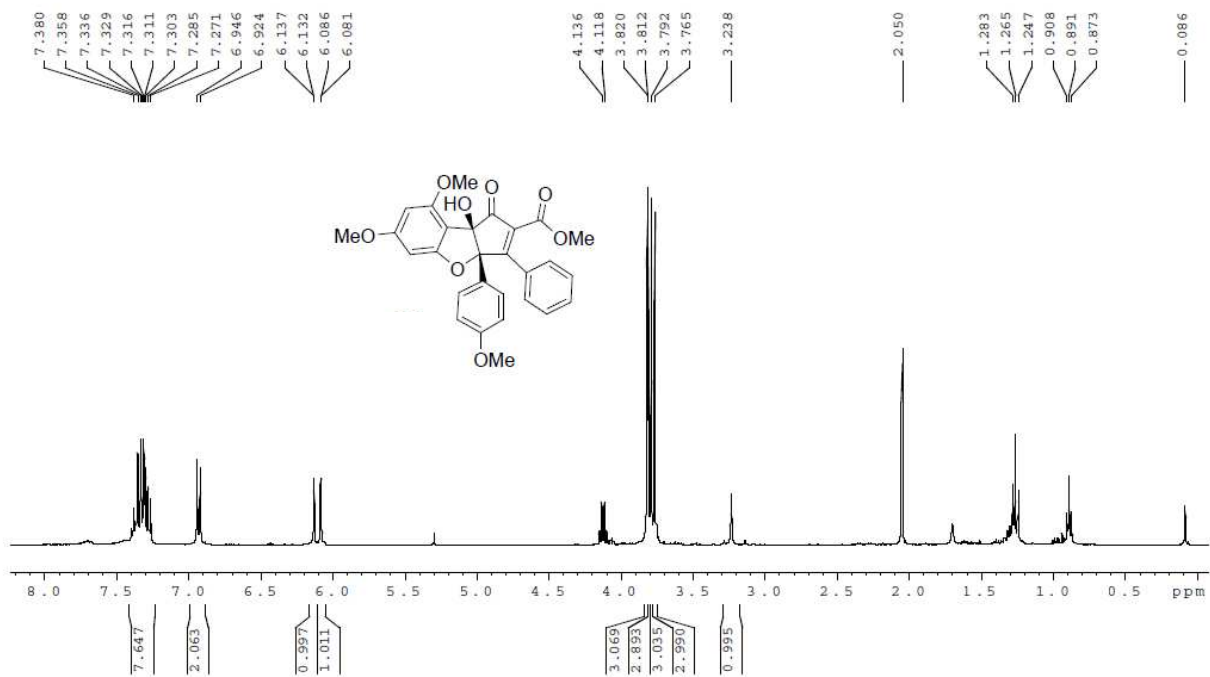
Compound 37



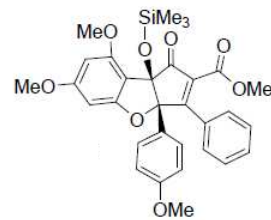
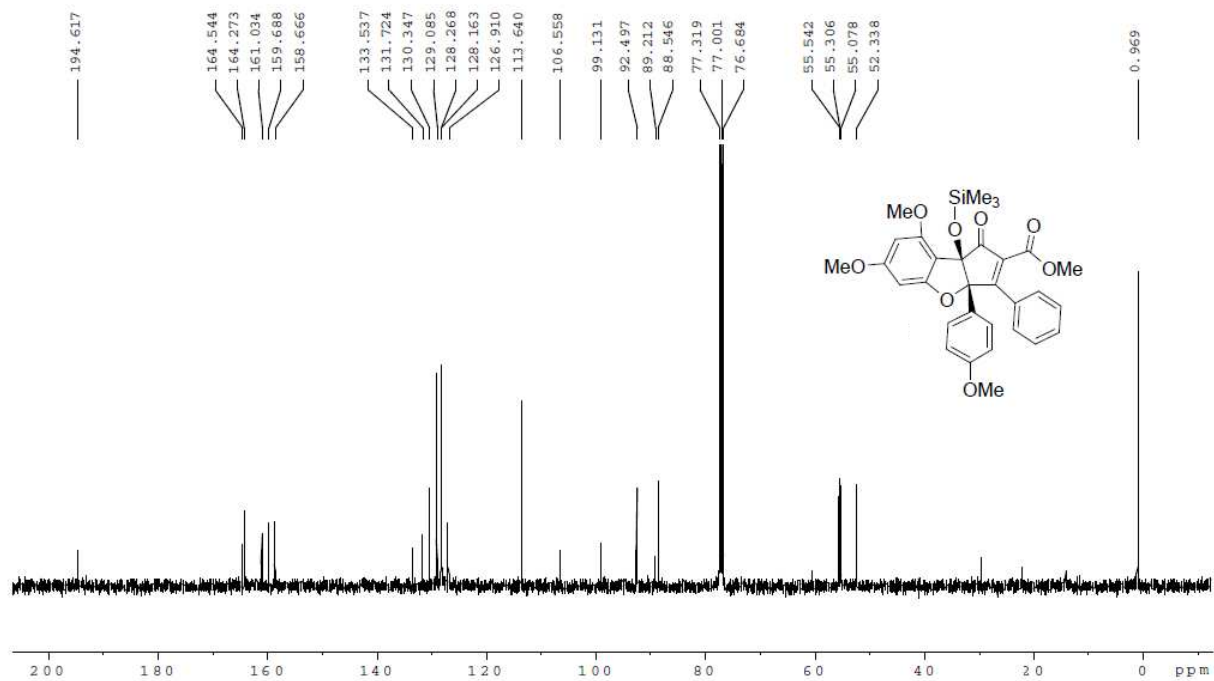
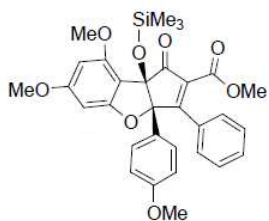
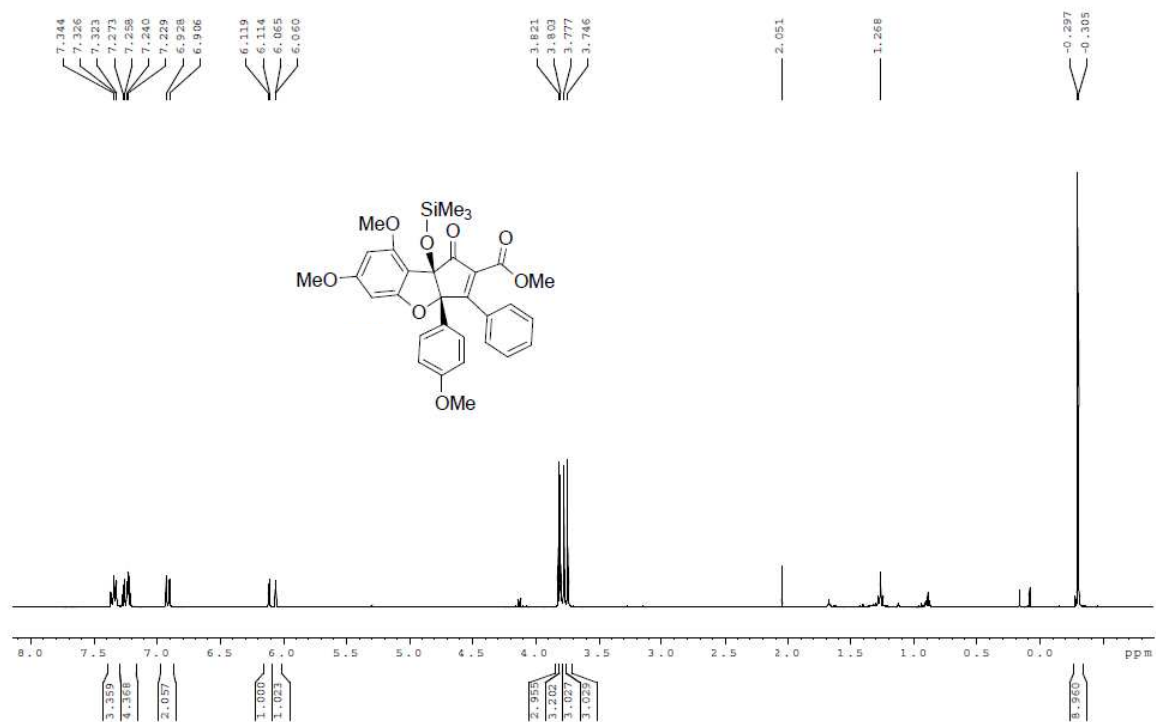
Compound 38



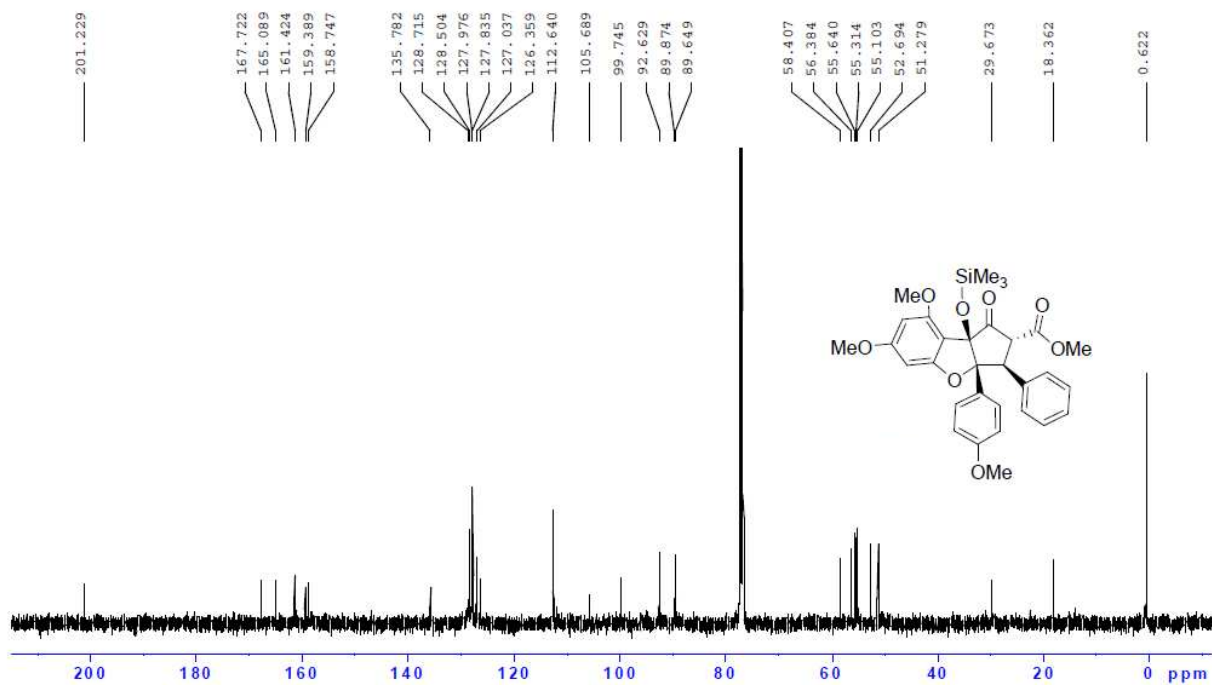
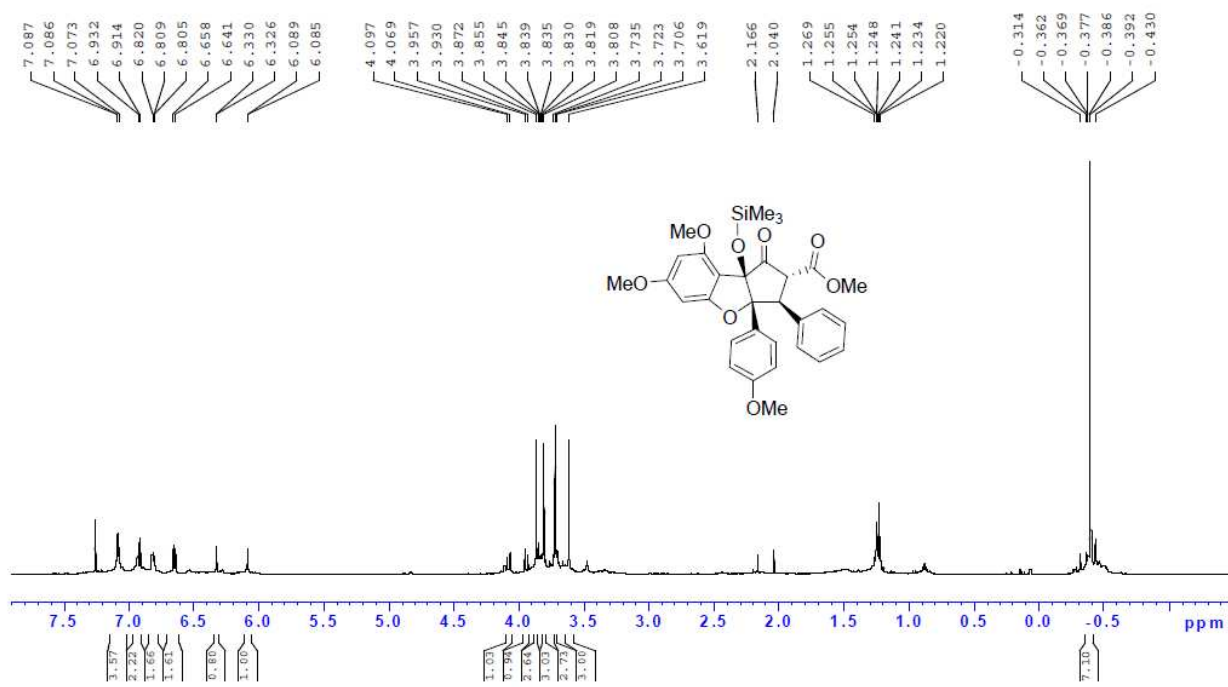
Compound 39



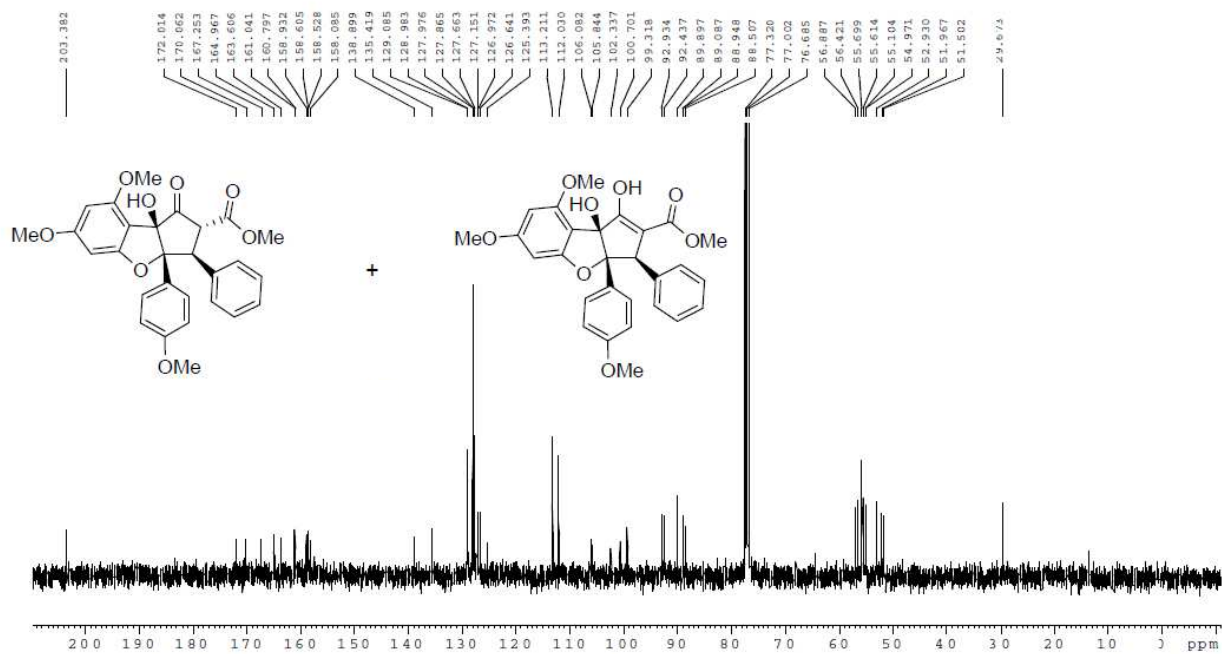
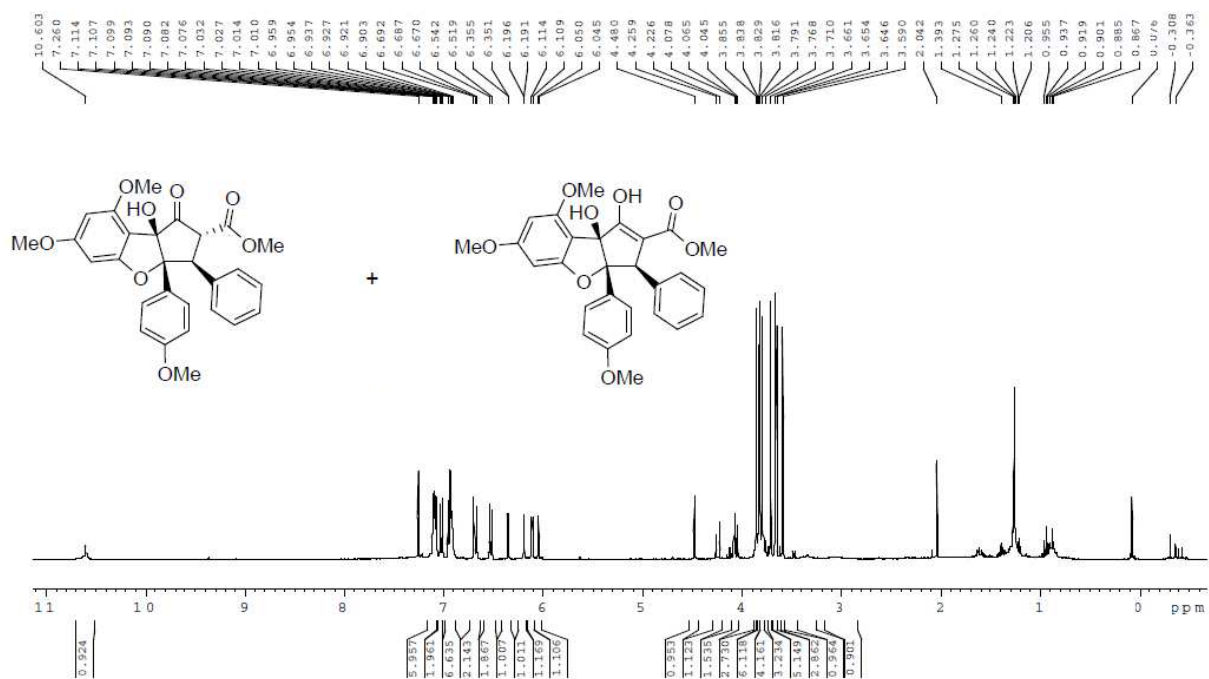
Compound 41



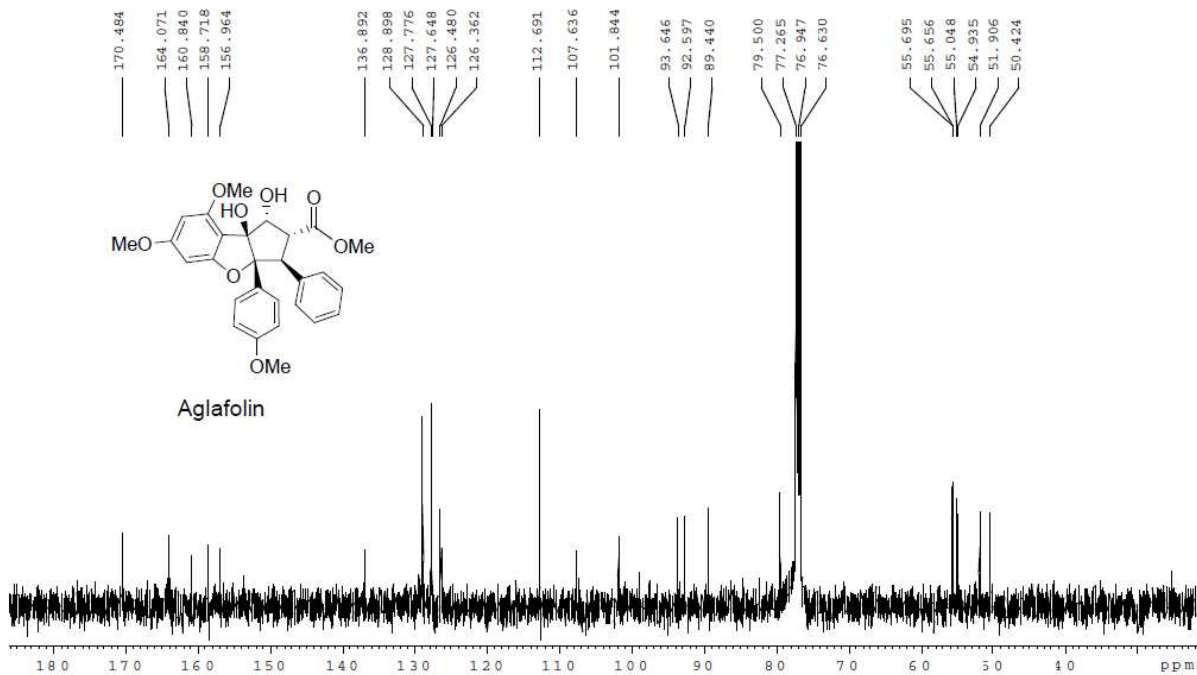
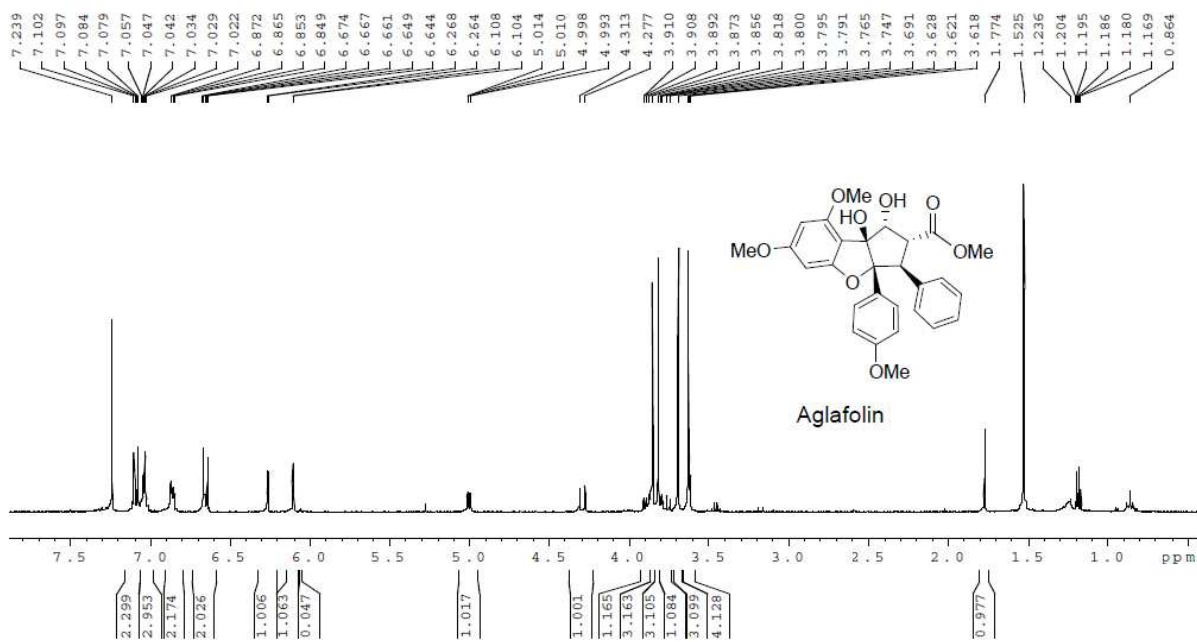
Compound 42



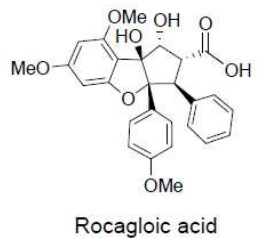
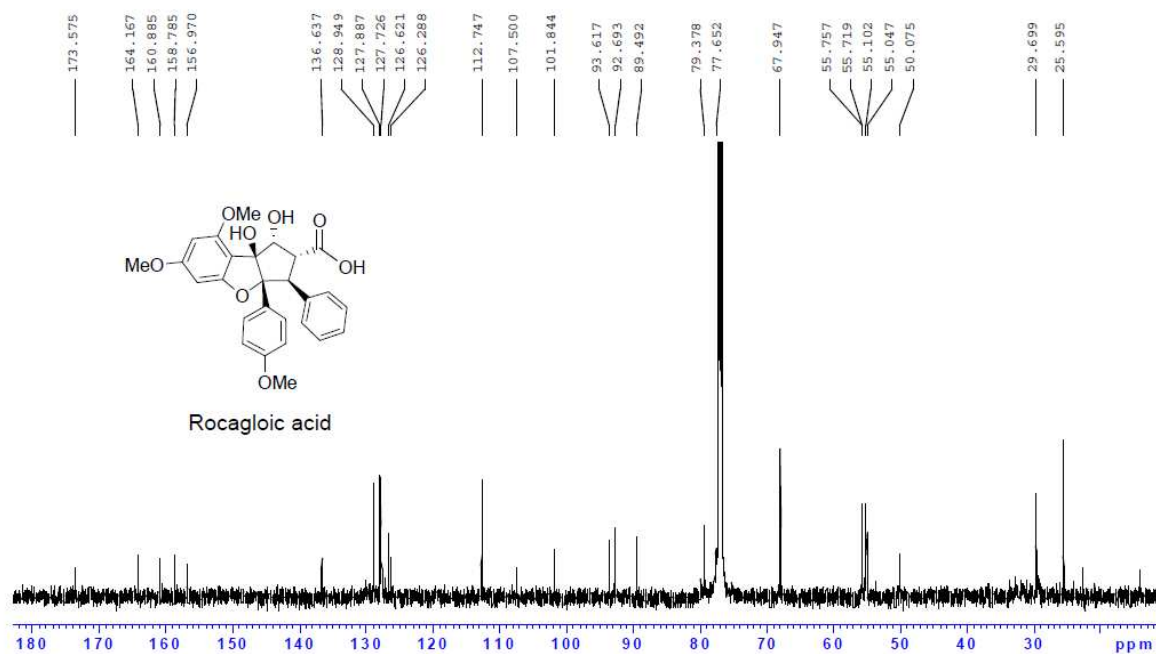
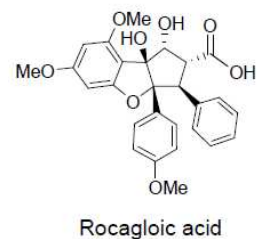
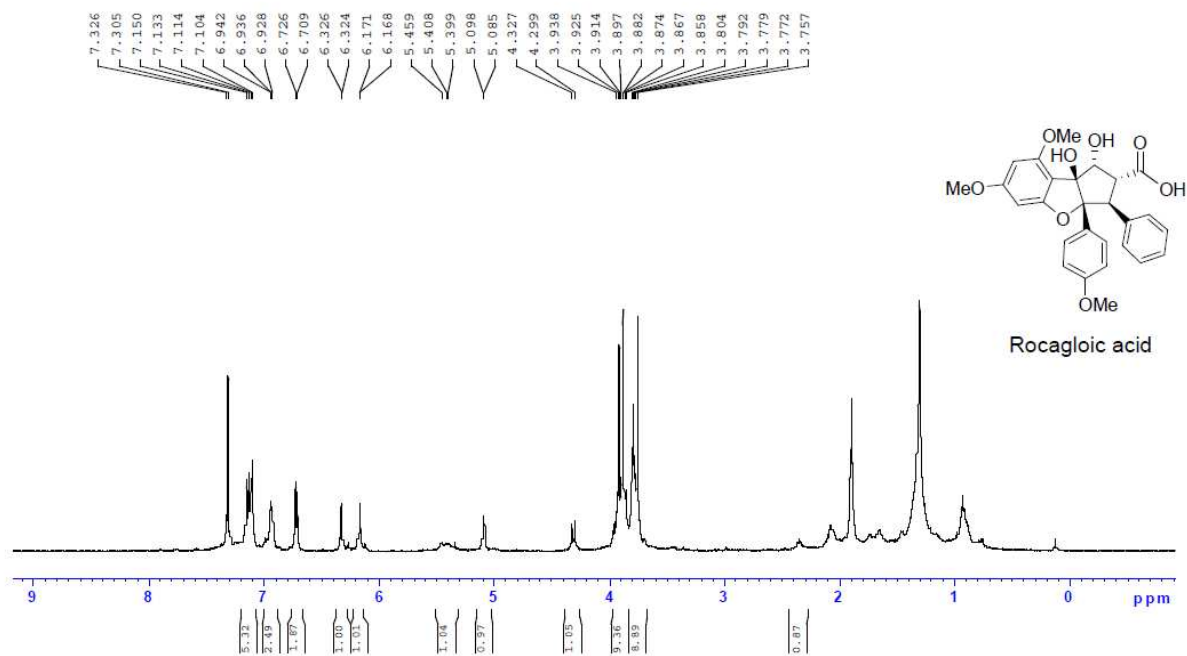
Compound 40



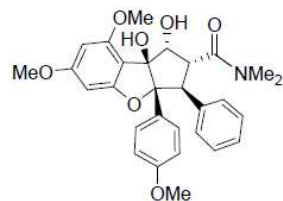
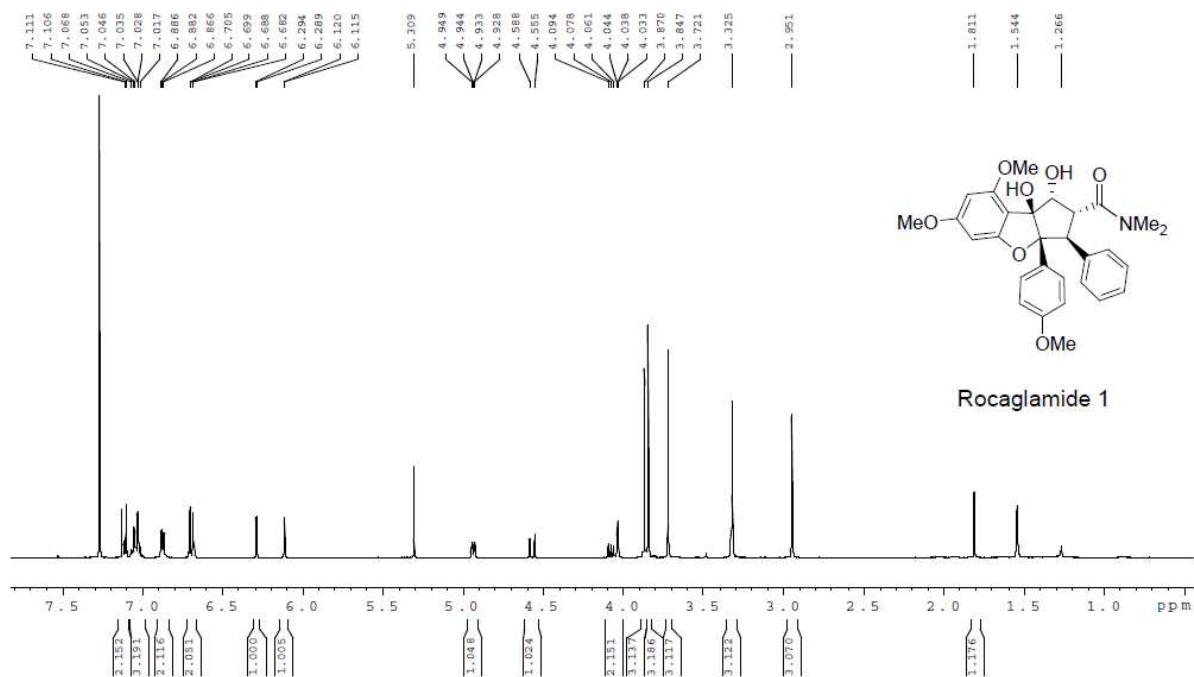
Compound 1e



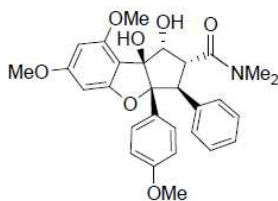
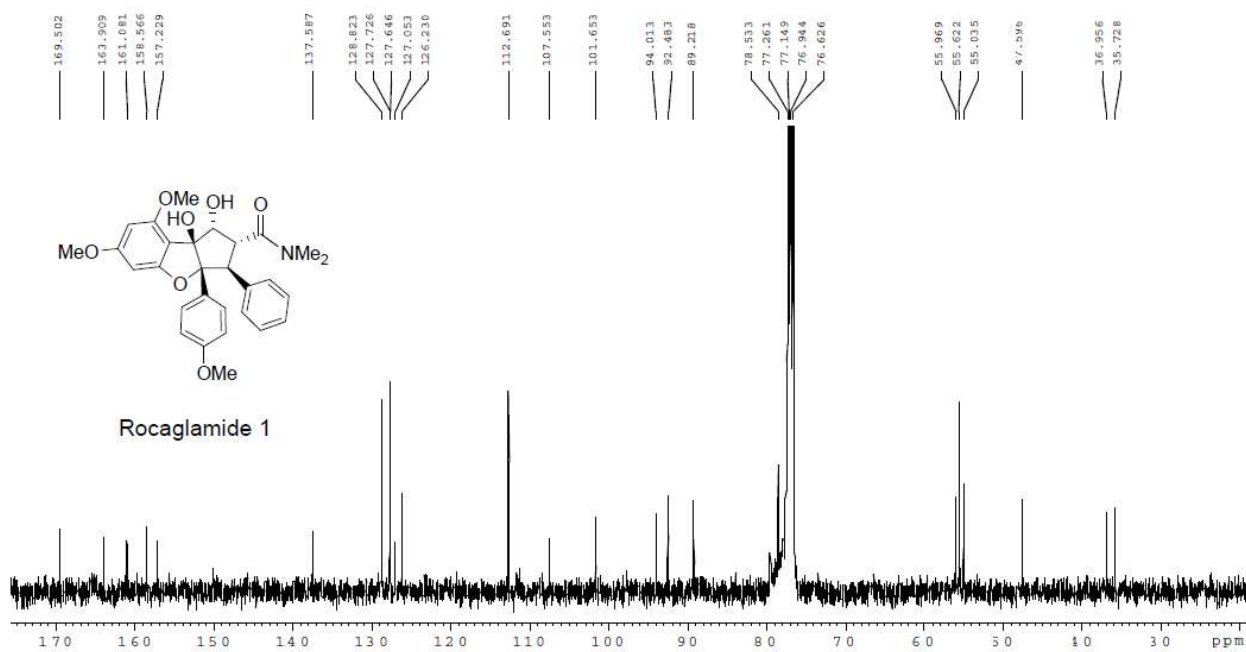
Compound 1d



Compound 1a



Rocaglamide 1

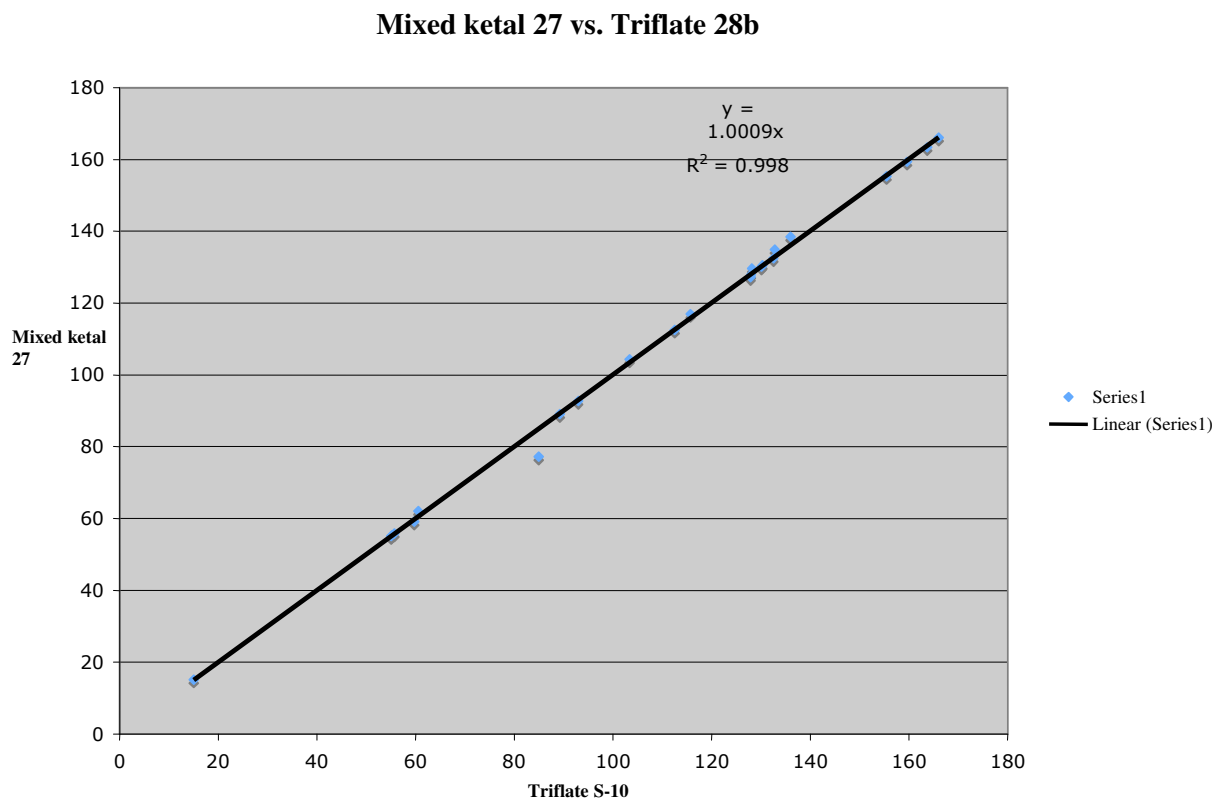


Rocaglamide 1

2.0. Justification for Structure Assignment of Mixed Ketal **27**.

The proposed structure of **27** is supported by characterization of two derivatives: carbonate **28a** (X-Ray crystal structure) and triflate **28b** (^1H and ^{13}C NMR data). Comparisons of ^1H and ^{13}C data for the mixed ketal and these derivatives reveal that the proton spectra for these compounds vary only in the loss of the doublet at 2.42 ppm (OH), a slight downfield shift of the benzylic proton (4.49 ppm in the free alcohol compared to 4.72 and 4.67 in the carbonate and triflate derivatives respectively) and a dramatic downfield shift of the proton *ipso* to the alcohol (4.63 ppm compared to 5.42 and 5.50 for the carbonate and triflate respectively) with concomitant deconvolution of its signal from a doublet of doublets to a simple doublet in both derivatives. All other signals remain largely unperturbed among all three compounds. The ^{13}C spectra also show excellent agreement between the three structures. When directly comparing the chemical shifts of the mixed ketal to those of the triflate (Graph 1, Table 1), the average difference in peak shift was 0.03 ppm with the single largest shift being at the alcohol bearing carbon moving downfield from 77.2 ppm in the mixed ketal to 85.0 ppm in the triflate; all other shift differences all being 2.5 ppm or less. Comparison of ketone **15a** to mixed ketal **27** shows a much weaker correlation (Graph 2, Table 1). We take this as indirect evidence that the reactant in these two reactions is the mixed ketal, which has been functionalized exclusively at the secondary alcohol.

Graph 1: Comparison of ^{13}C Chemical Shifts of Mixed Ketal **27** with Triflate **28b**.



Graph 2: Comparison of ^{13}C Chemical Shifts of Ketone **15a** with Mixed Ketal **27**.

Ketone 15a vs. Mixed Ketal 27

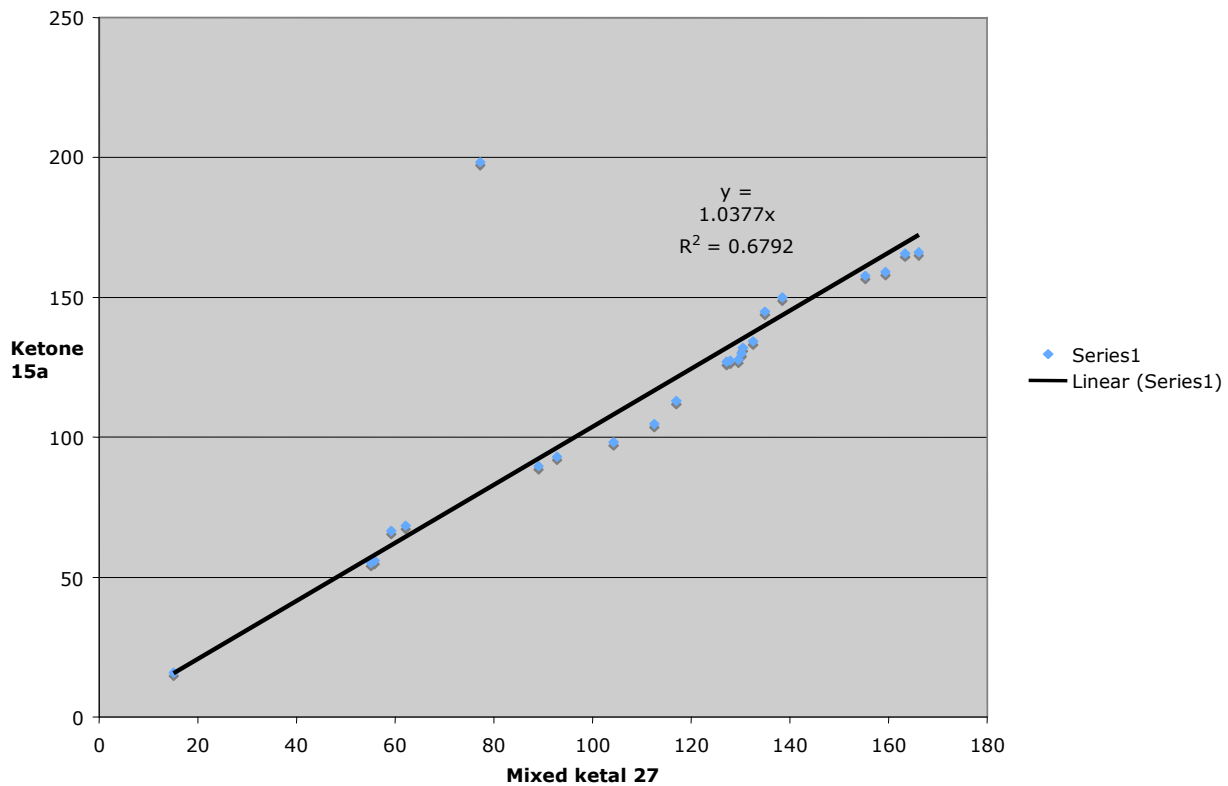


Table 1. Comparison of ^{13}C Chemical Shift Values of Triflate **S-10**, Mixed Ketal **27**, and Ketone **15a**.

Triflate S-10	Mixed Ketal 27	Ketone 15a
15	15.1	15.8
55	55.1	55.1
55.2	55.4	55.8
55.7	55.8	55.9
59.7	59.2	66.5
60.5	62.1	68.4
85	77.2	198.4
89.2	89.1	89.7
93	92.8	93
103.4	104.3	98.2
112.5	112.5	104.7
115.7	117	113
127.9	127.2	127
128	127.9	127.4
128.2	129.6	127.8
130.1	130.2	130
130.3	130.5	132
132.5	132.5	134.3
132.8	134.9	144.9
136	138.5	149.9
155.5	155.33	157.8
159.6	159.4	159.1
163.7	163.4	165.6
166	166.1	166.1