

## Design and Synthesis of a Bivalent Ligand to Explore the Putative Heterodimerization of the Mu Opioid Receptor and the Chemokine Receptor CCR5

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## 1. HPLC methods and results

HPLC System: Varian Prostar 210;

Column: Microsorb-MV 100-5 C18 (250 × 4.6 mm);

Injection Volume: 10 µL;

Sample Concentrations: 0.2 – 0.4 mg/0.5 mL in mobile phase;

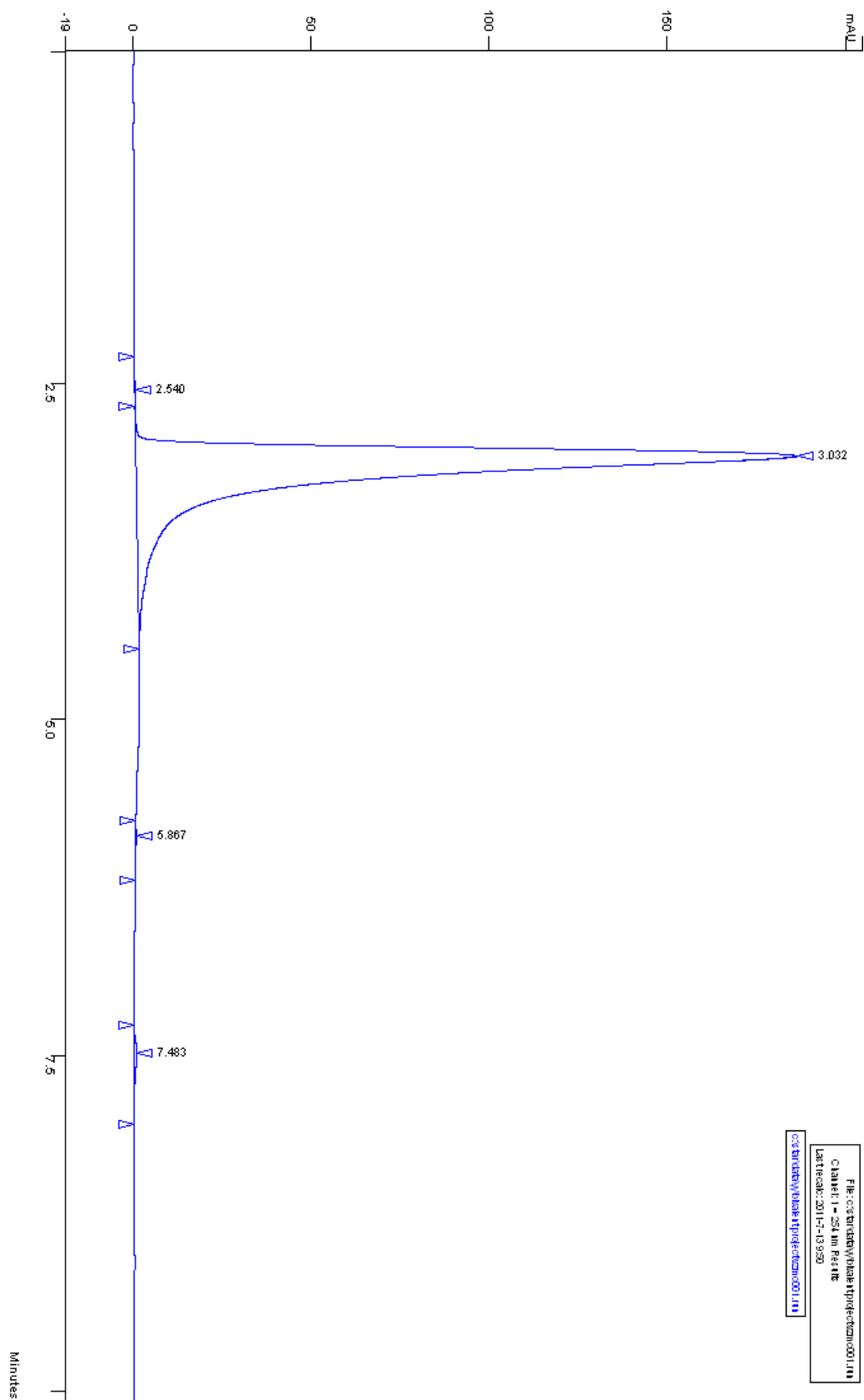
Single Wavelength: 254 (**1**, **3**) or 210 (**2**) nm;

Eluent: acetonitrile (0.1% TFA)/water (50/50) at 1 mL/min over 10 min.

Table 1. HPLC analysis of target compounds

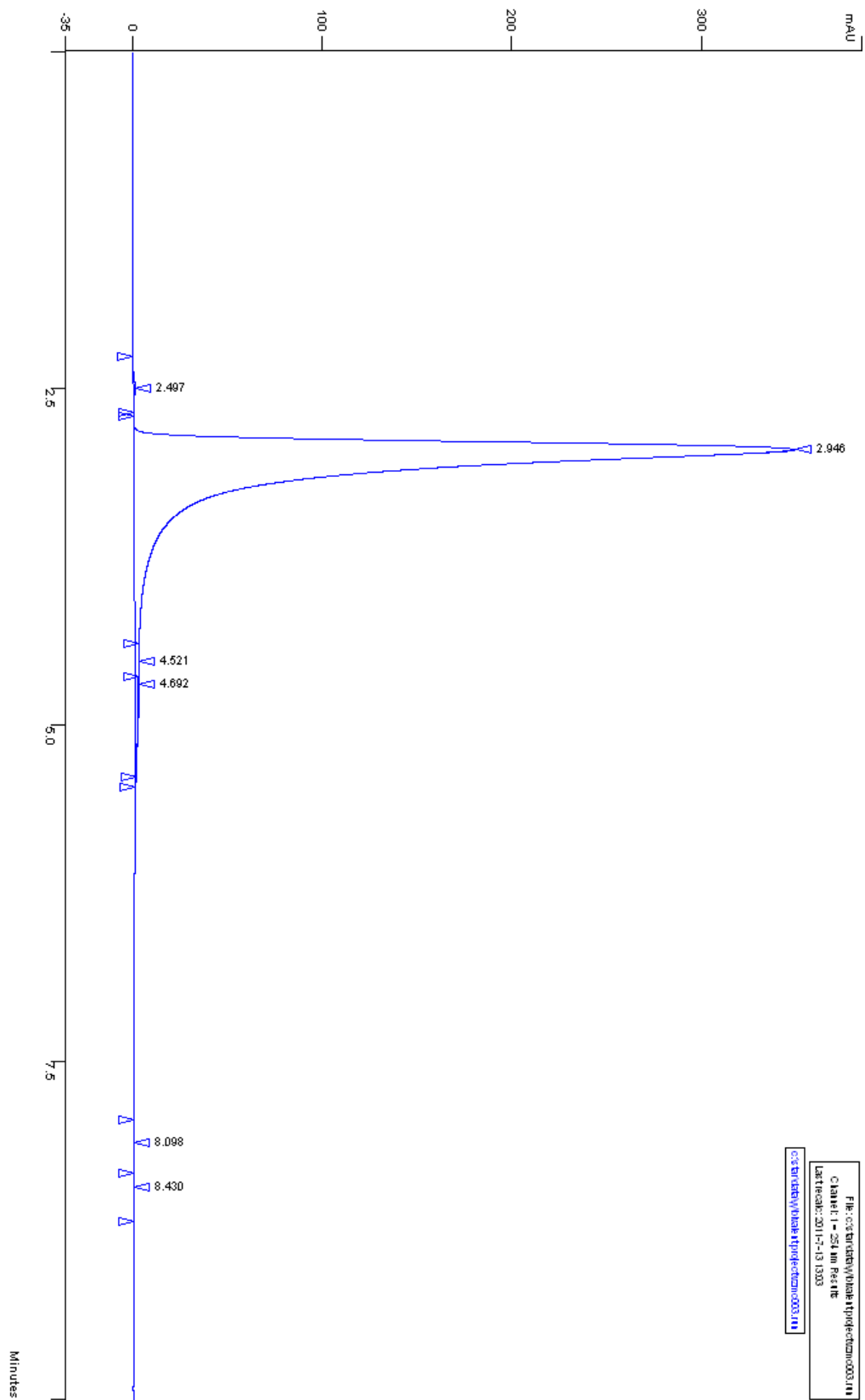
Compound	Code in spectrum	Retention time (min)	Purity (%)
<b>1</b>	VZMC001	3.032	99.45
<b>2</b>	VZMC002	2.798	98.70
<b>3</b>	VZMC003	2.946	99.39

### Bivalent ligand 1



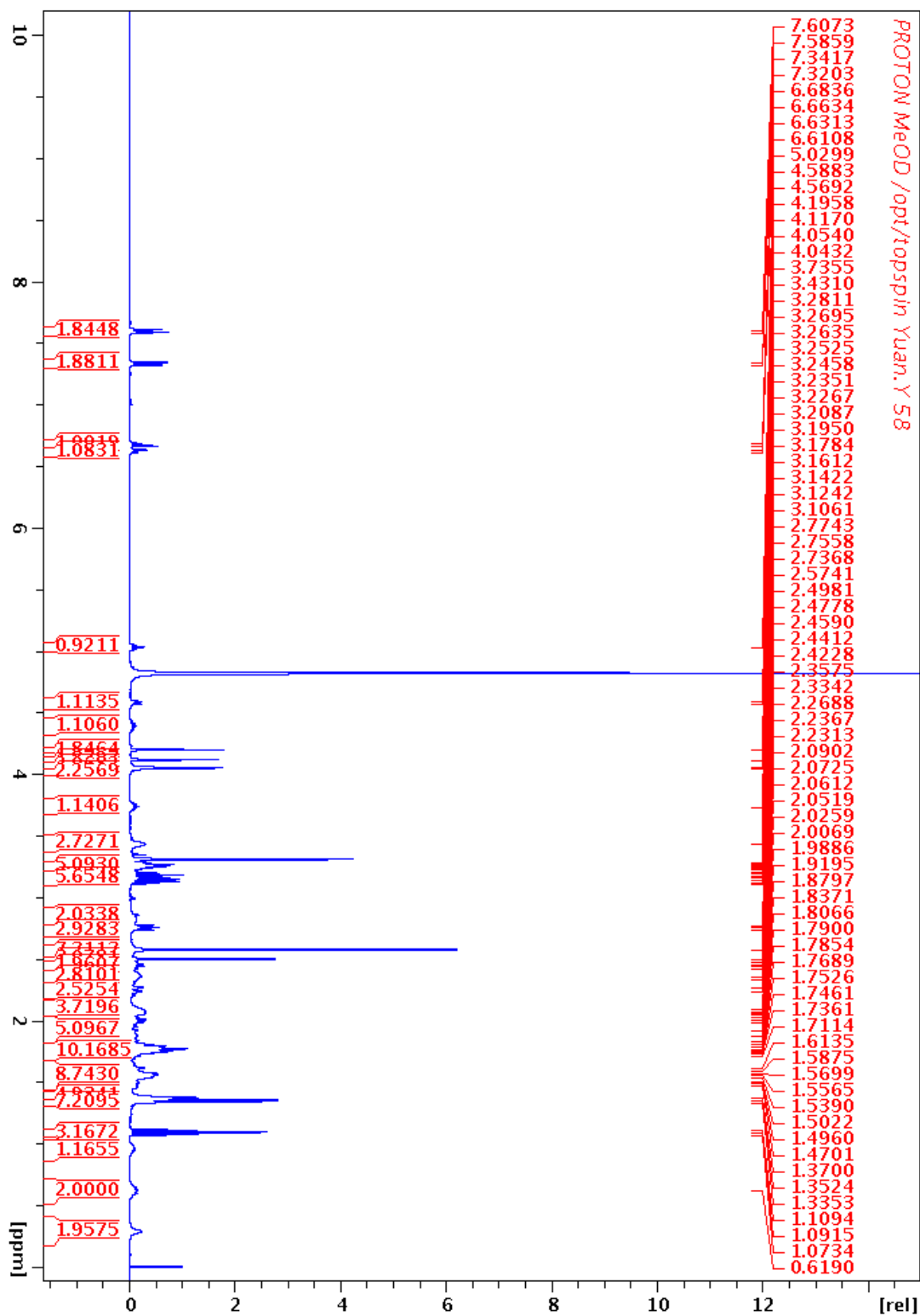


**Monovalent ligand 3**

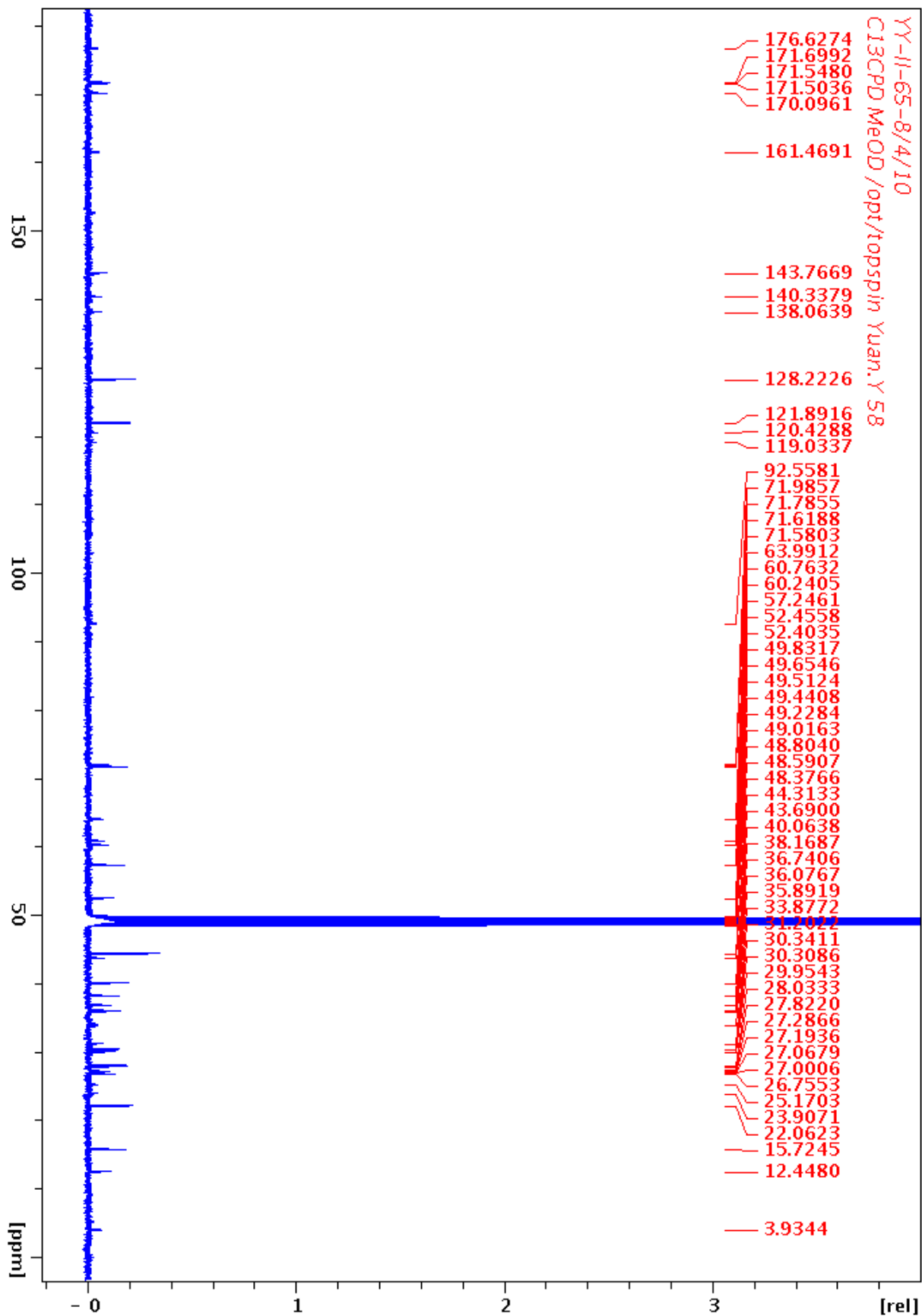


## 2. NMR Spectrum

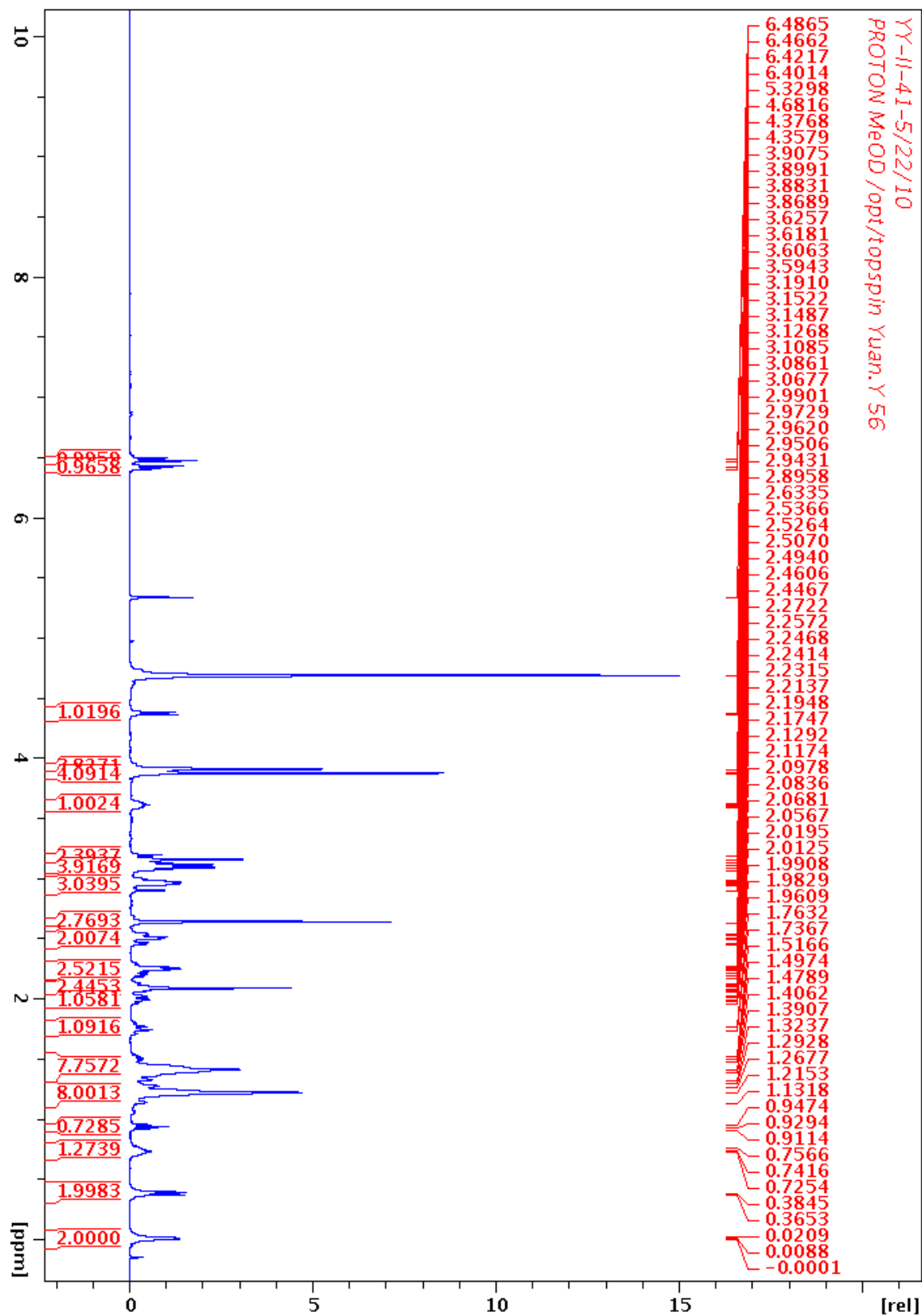
### Bivalent ligand 1

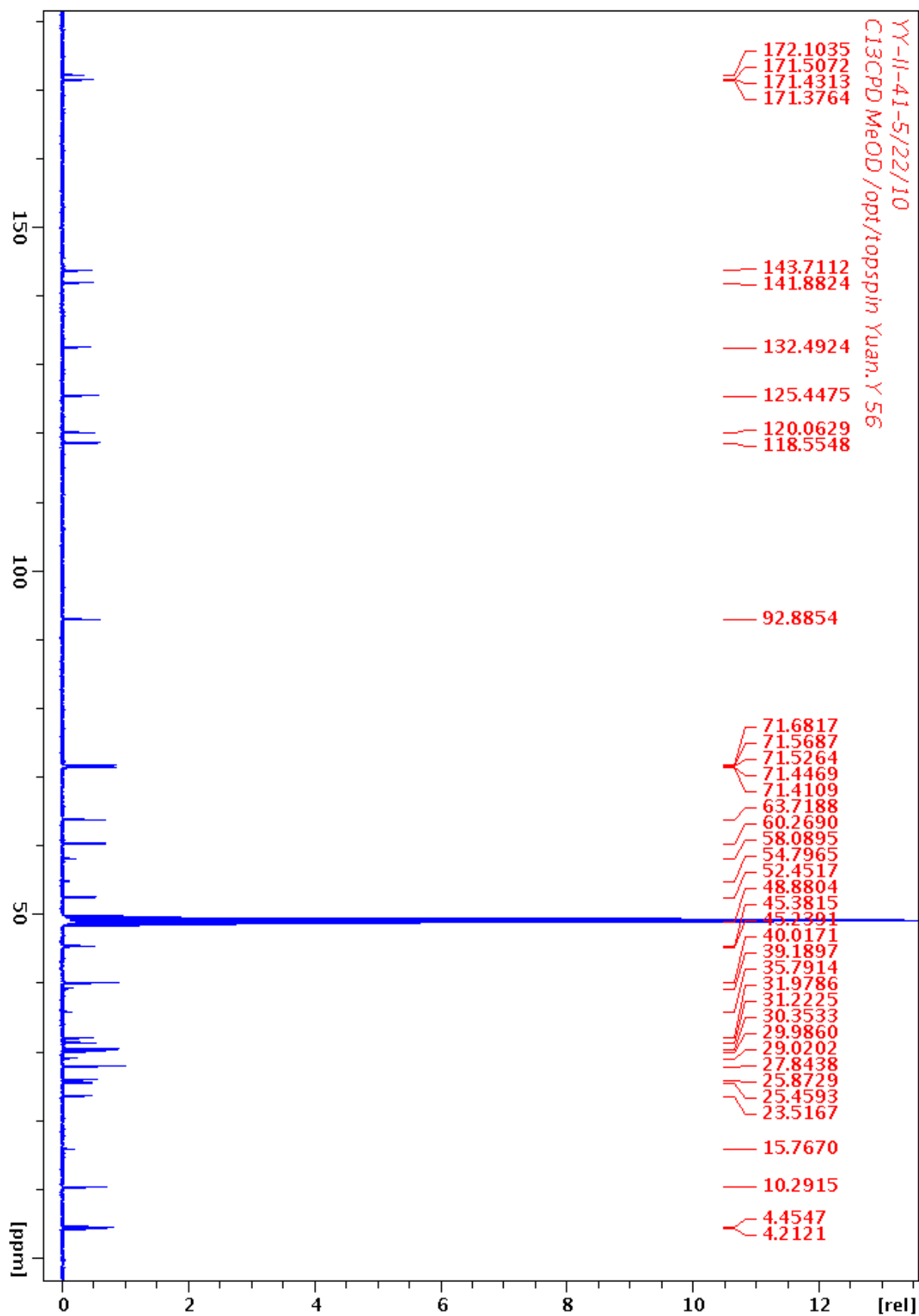




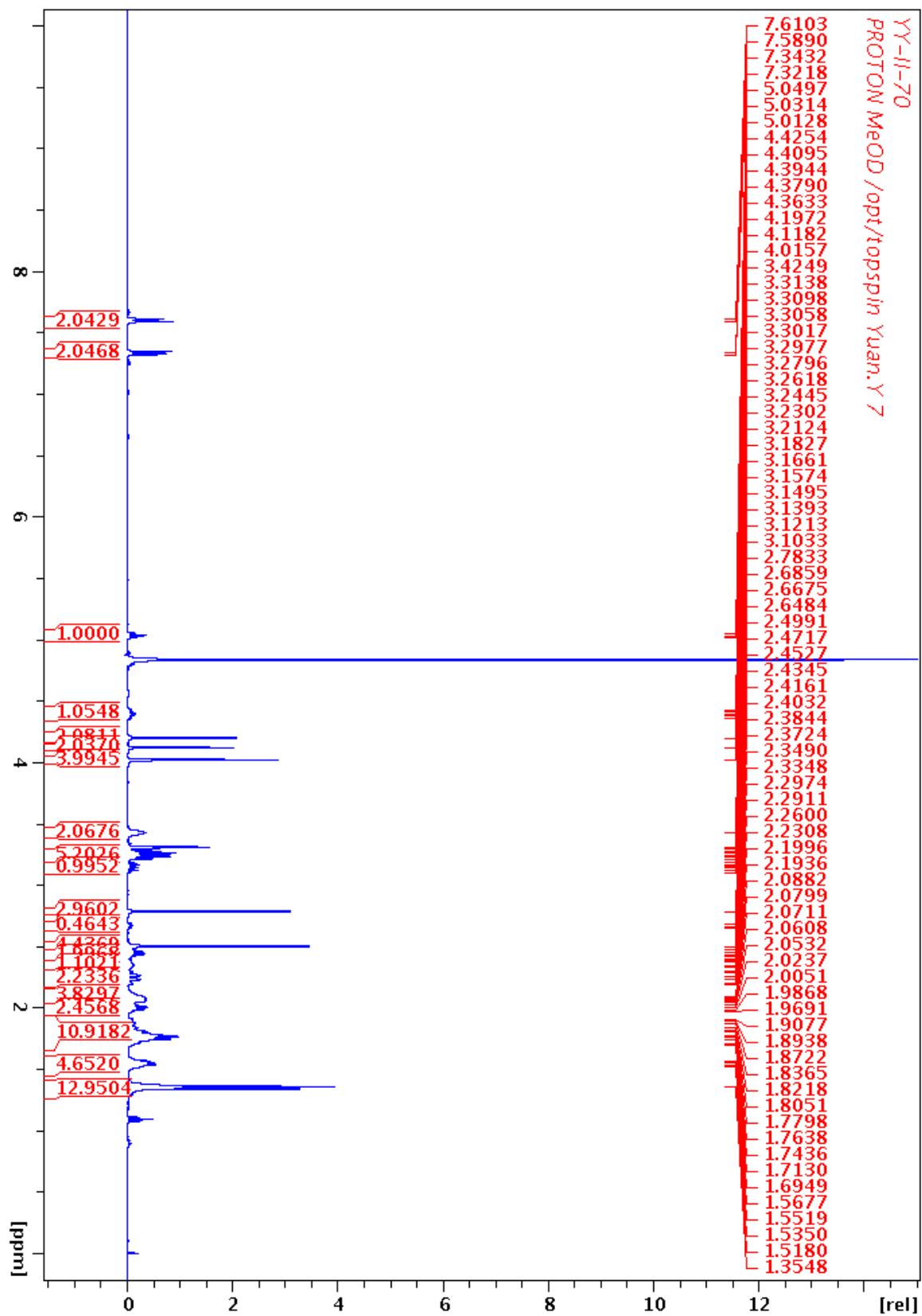


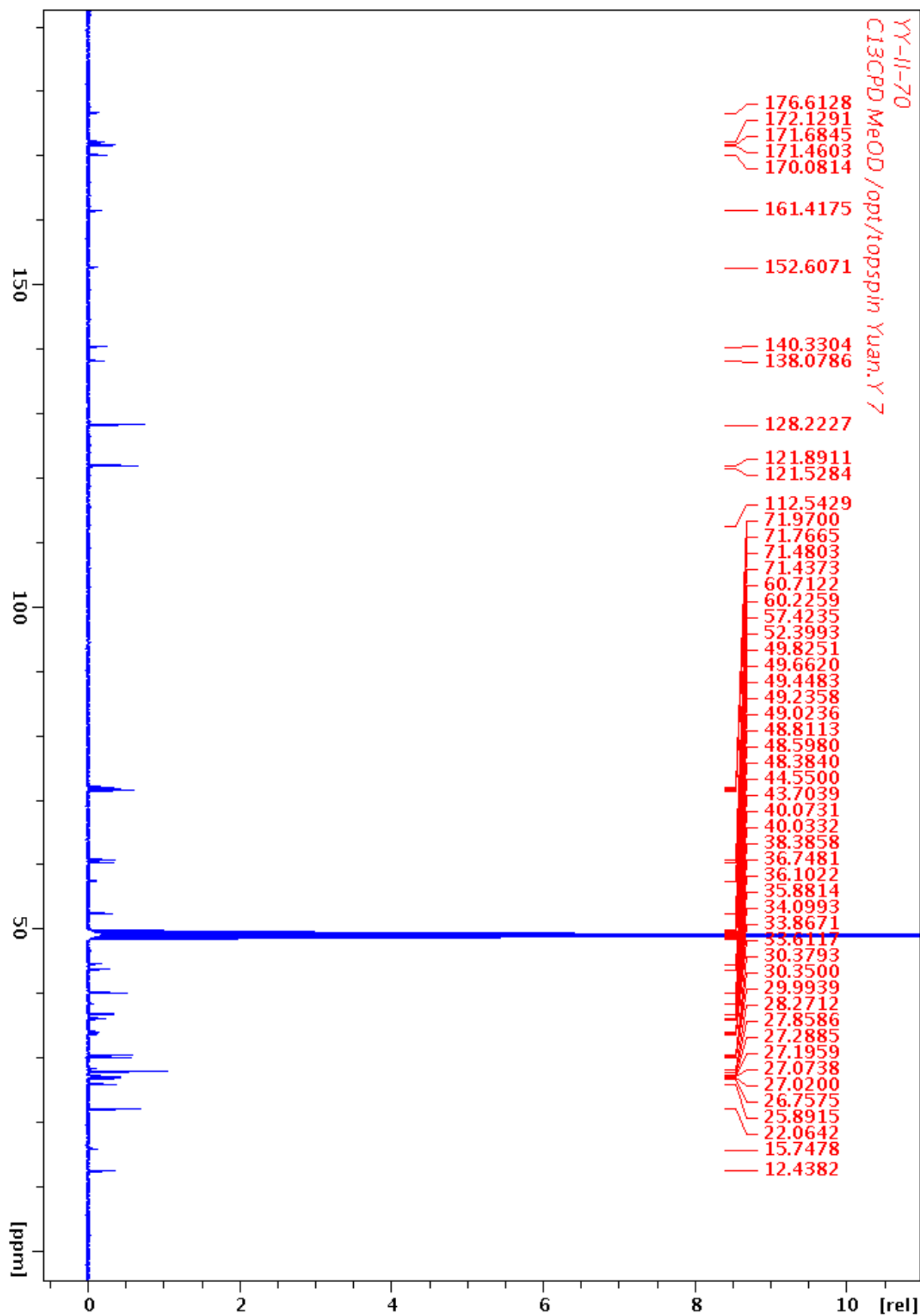
### Monovalent ligand 2



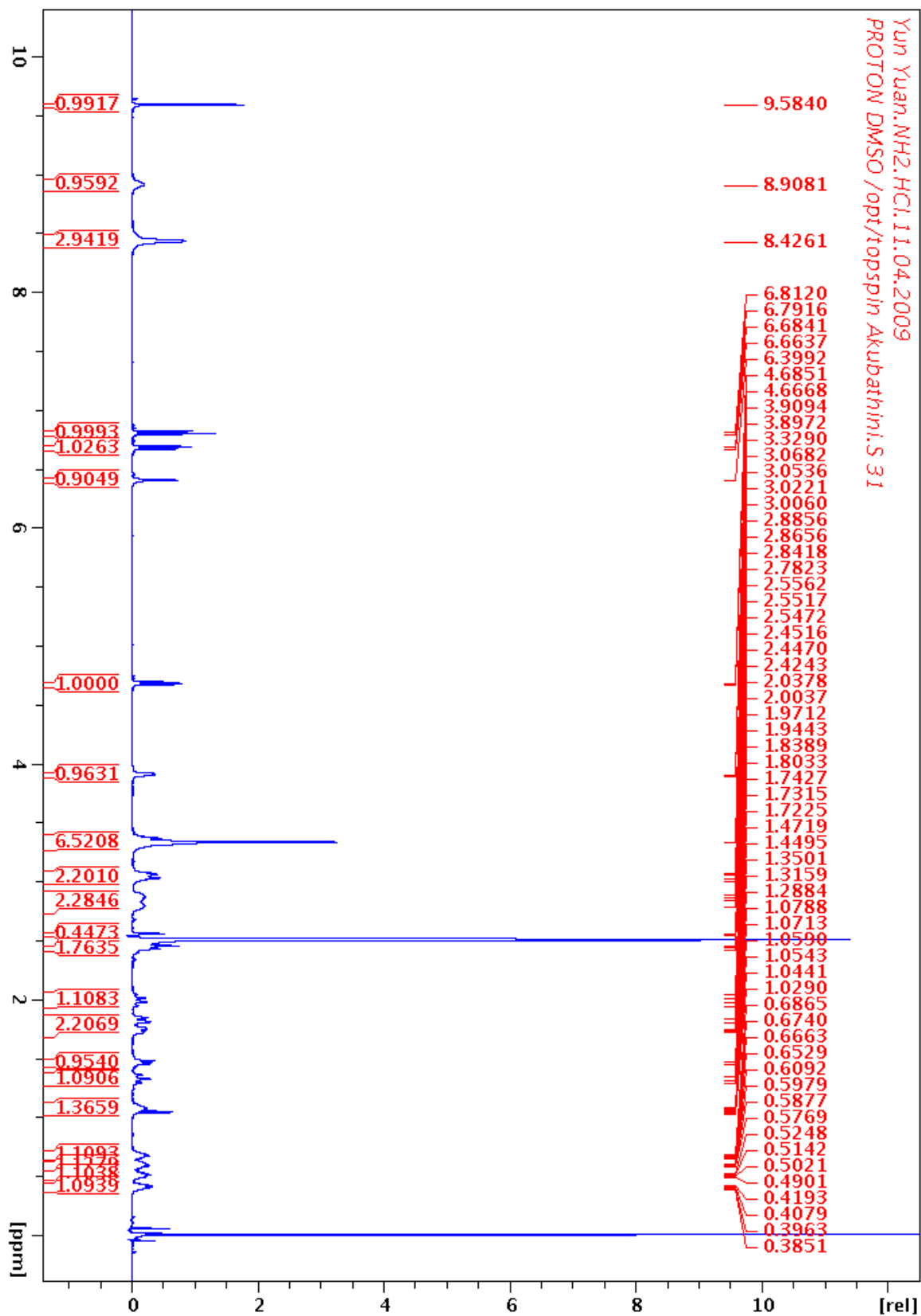


### Monovalent ligand 3

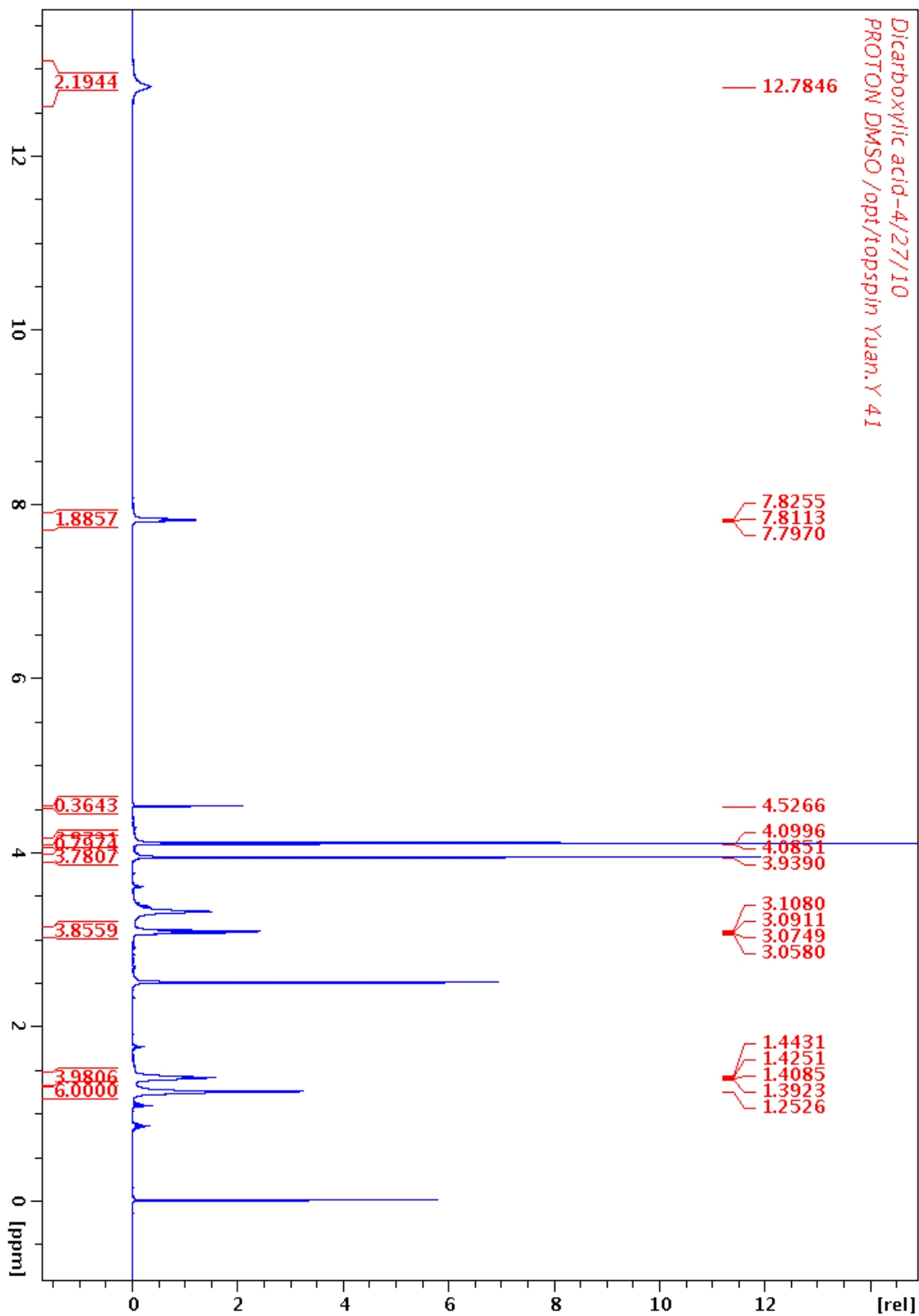


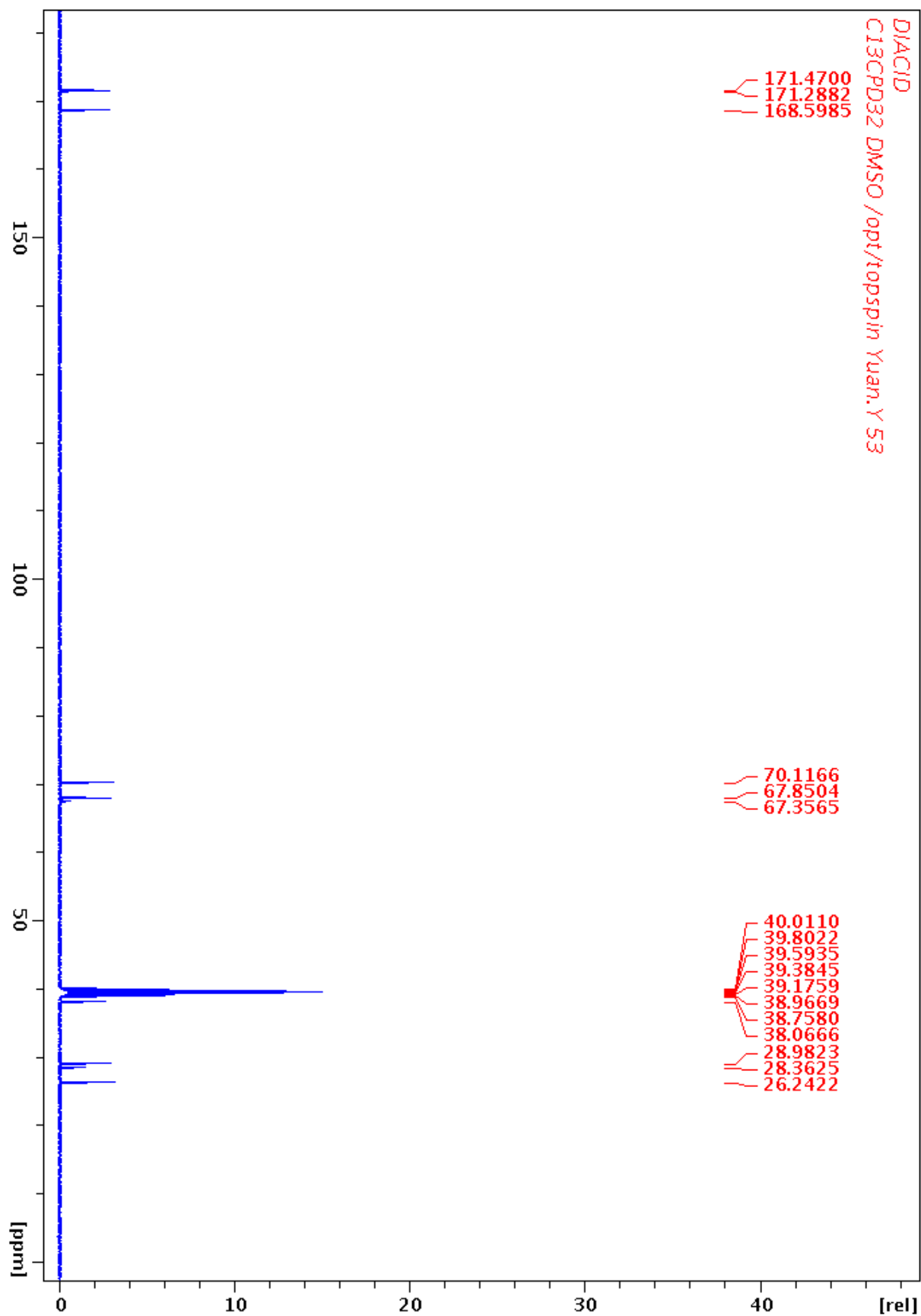


6 $\beta$ -Naltrexamine hydrochloride salt (4·2HCl)



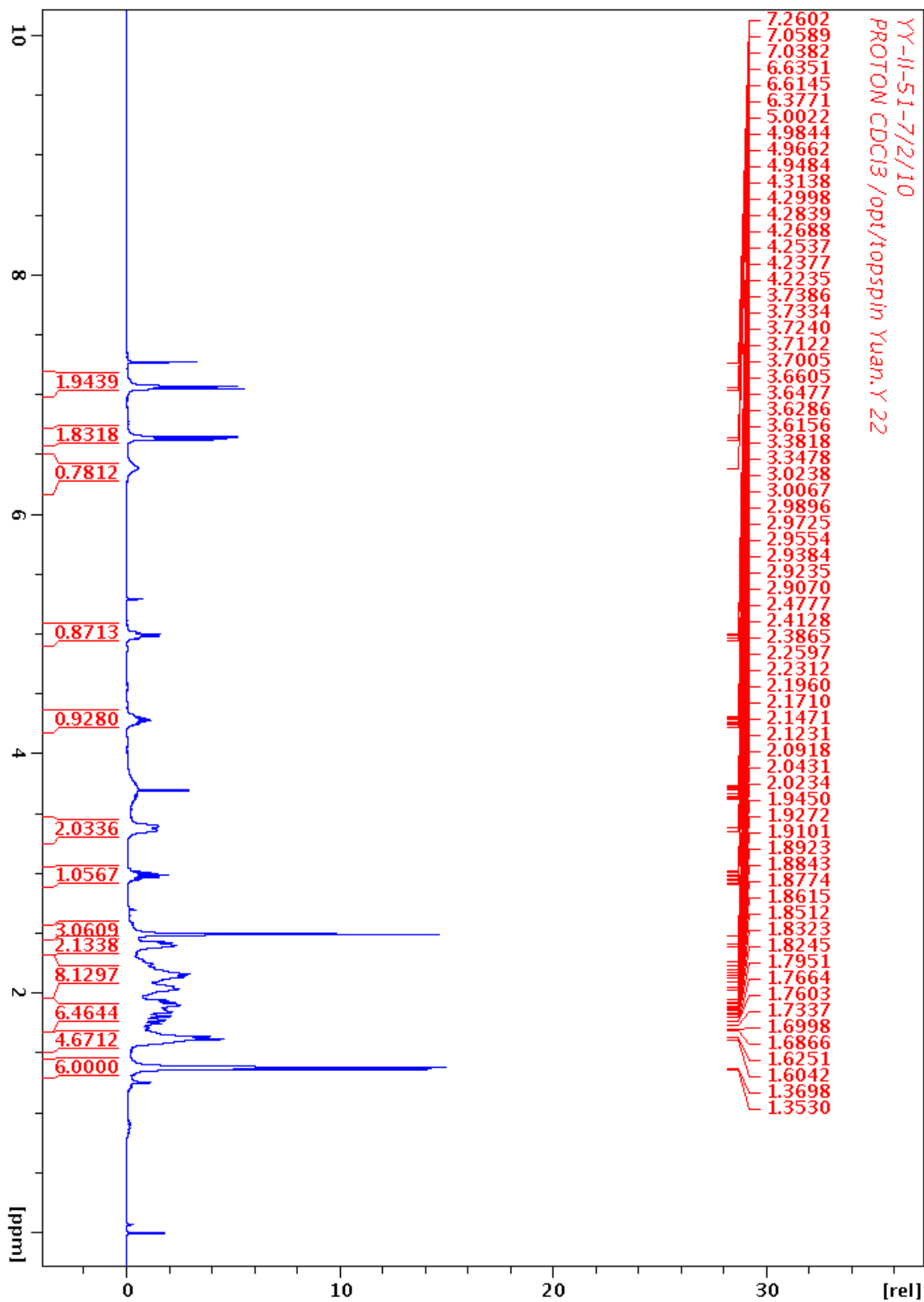
5,15-Dioxo-3,17-dioxa-diazanonadecane-1,19-dioic acid (**5**)

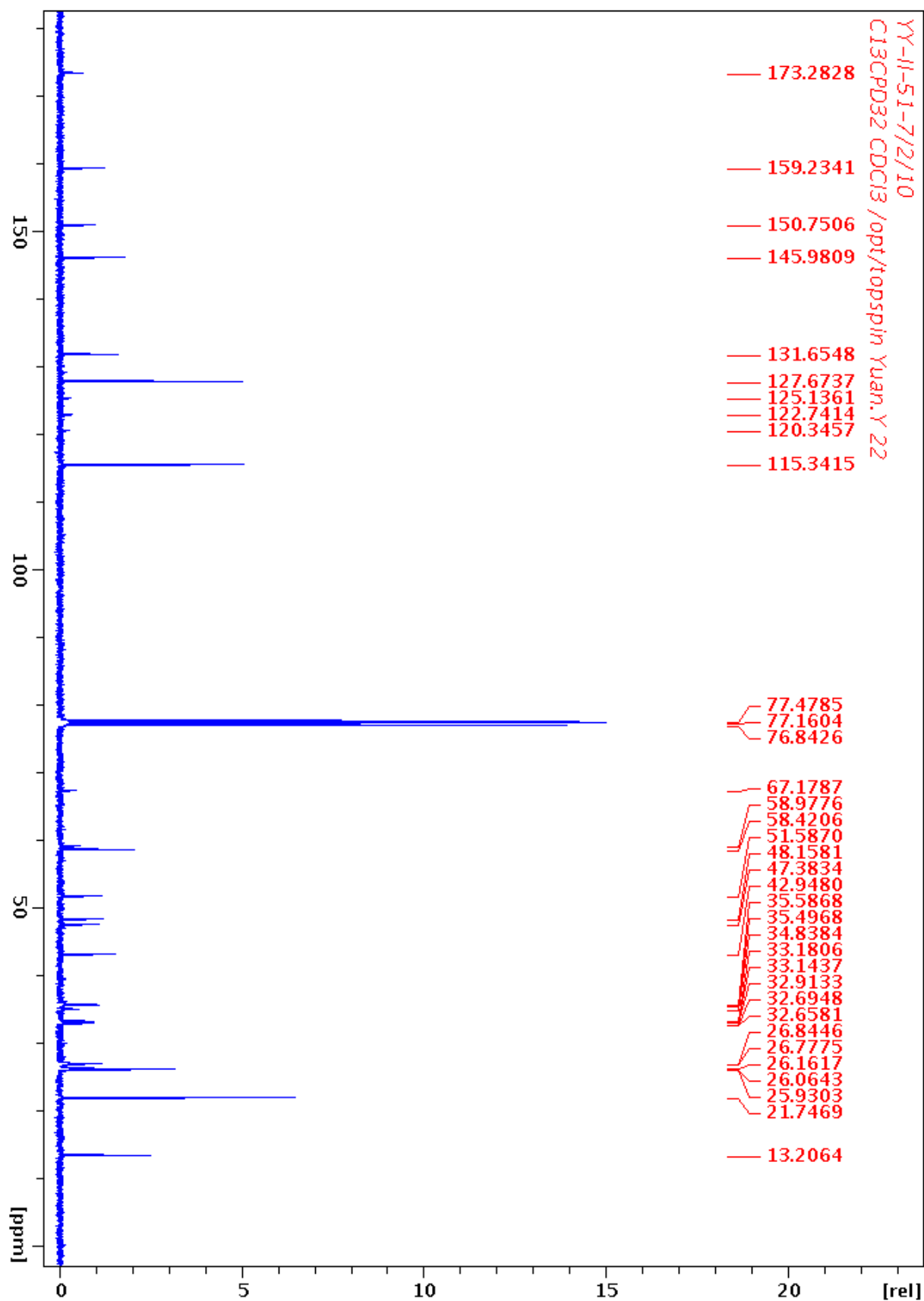




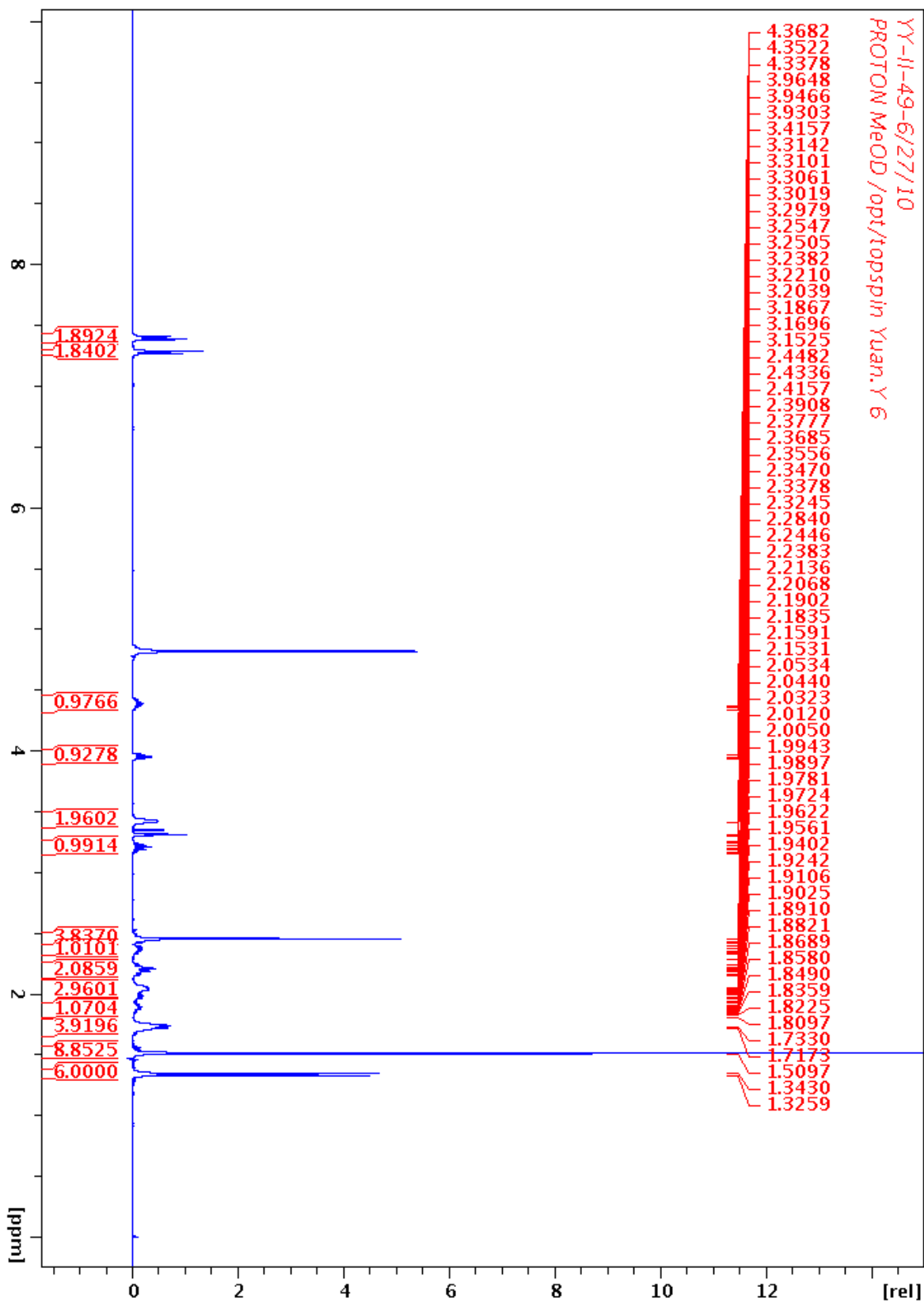


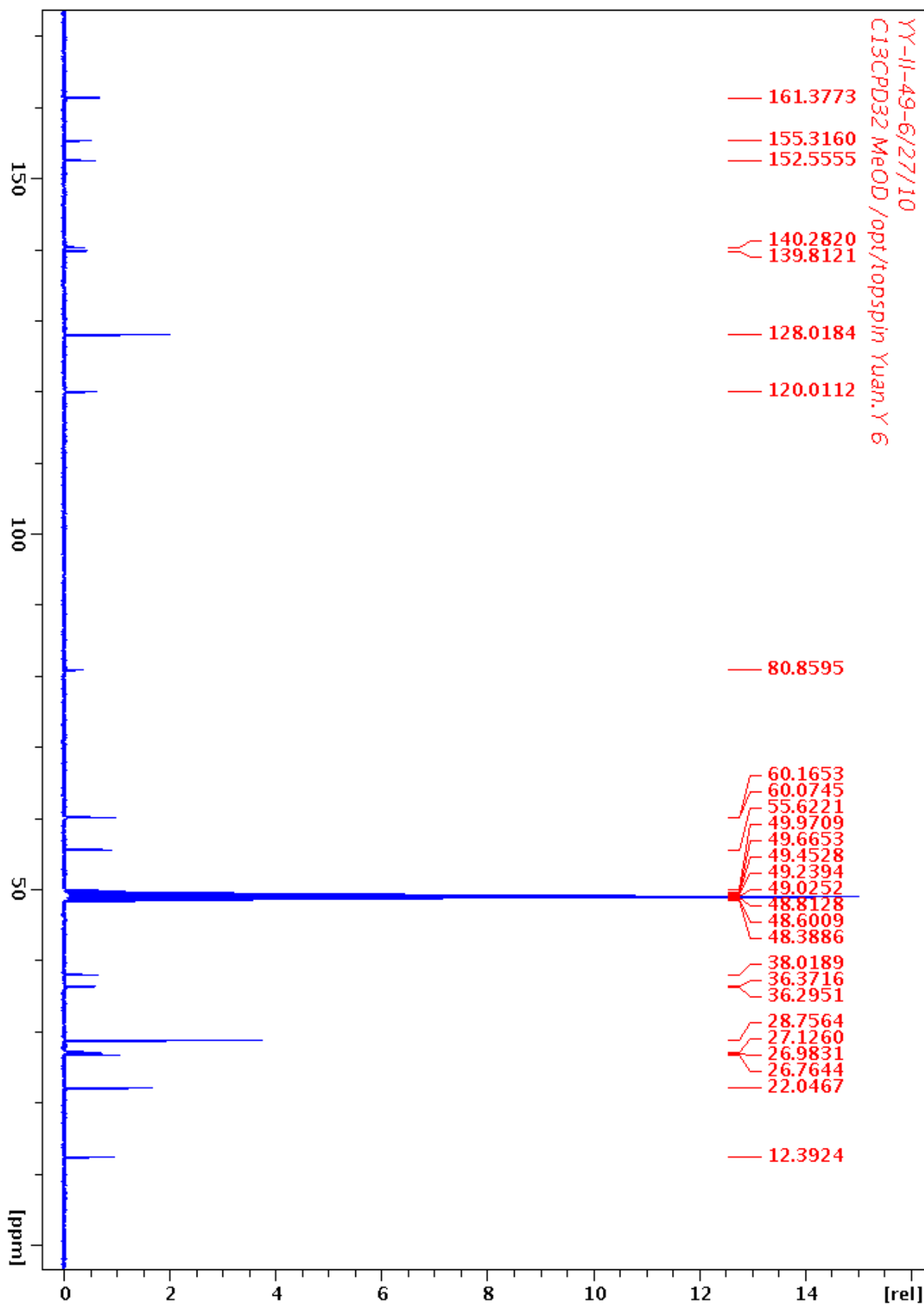
4-NH<sub>2</sub>-Maraviroc (6)



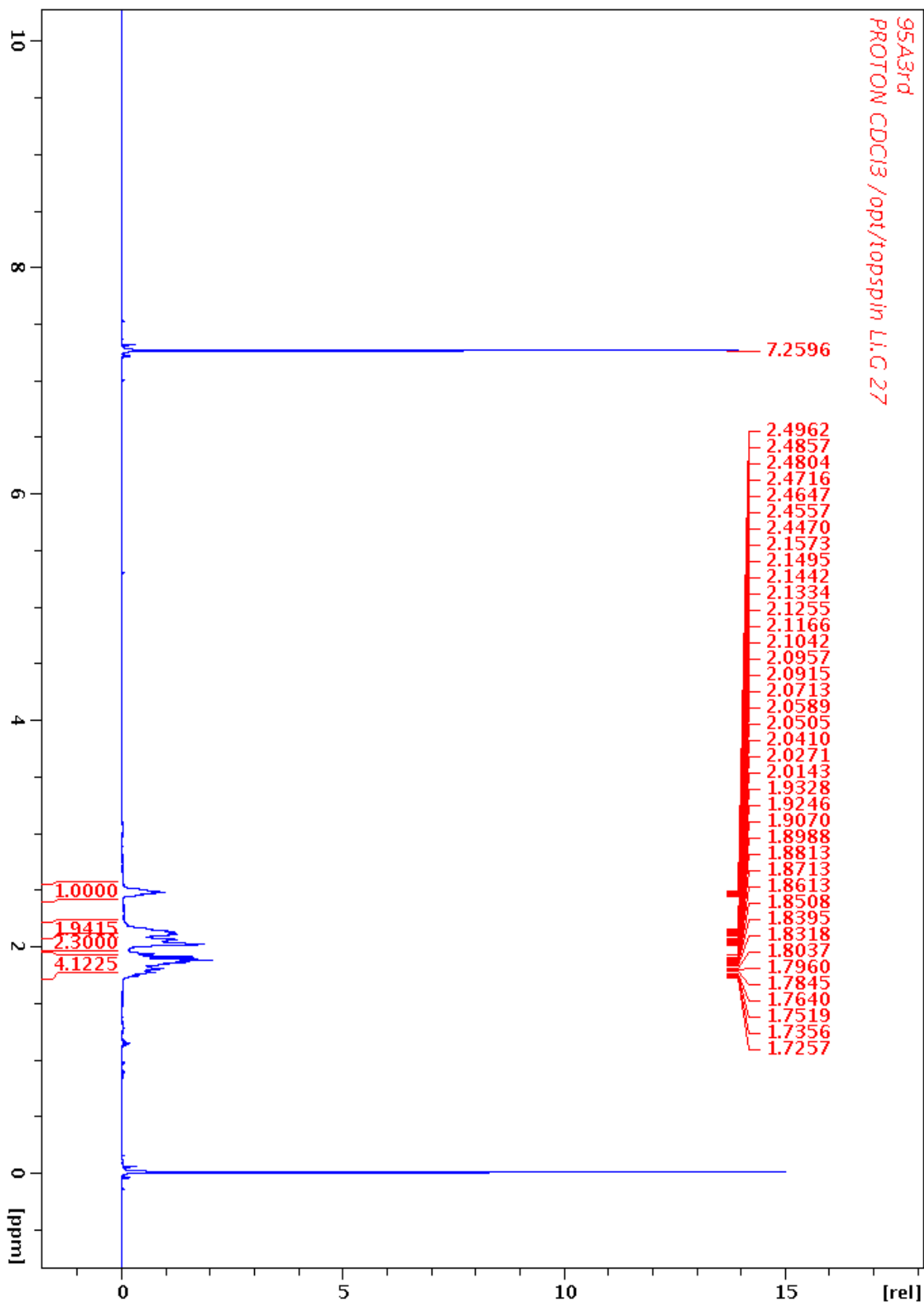


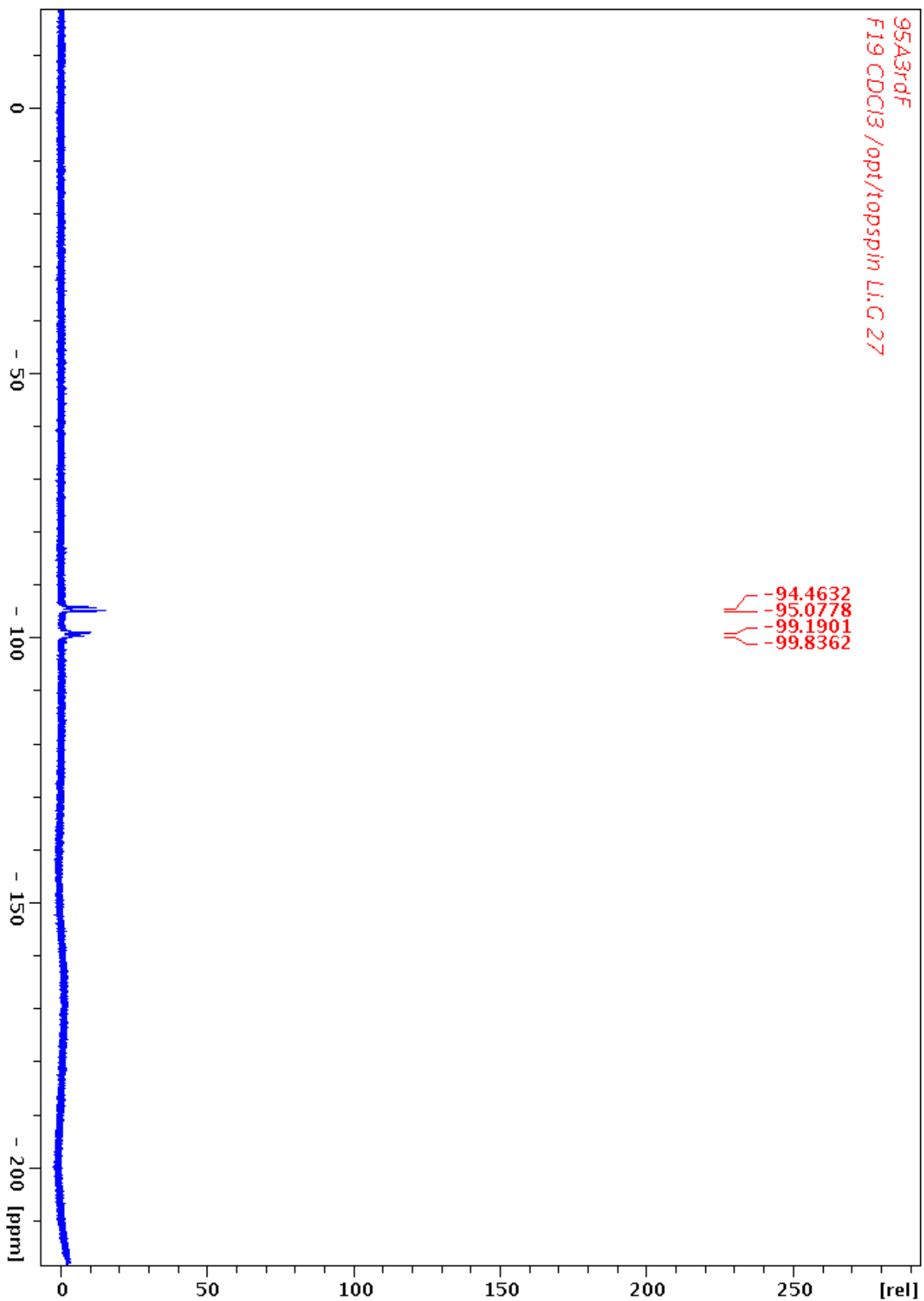
### Compound 7



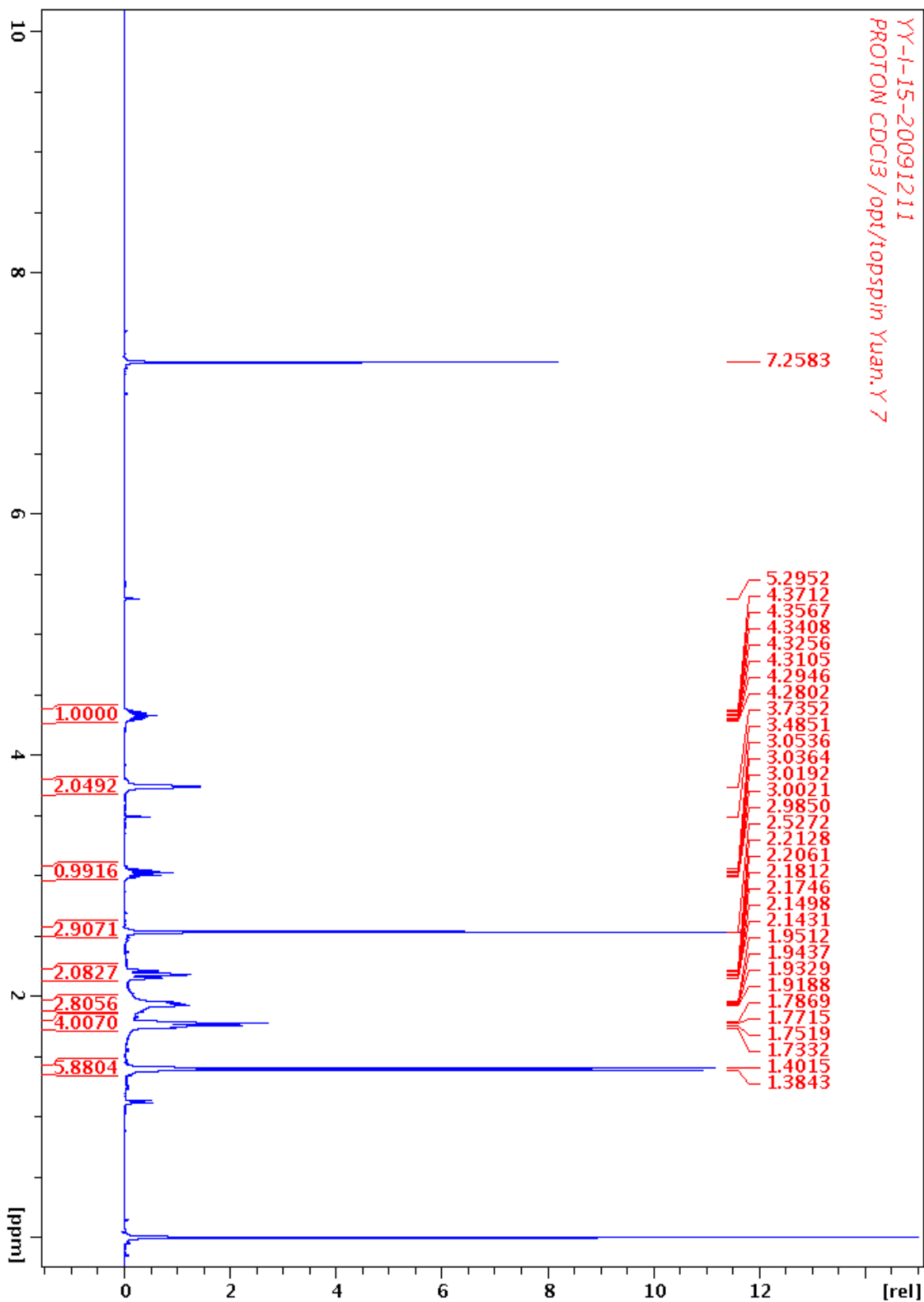


### Compound 8

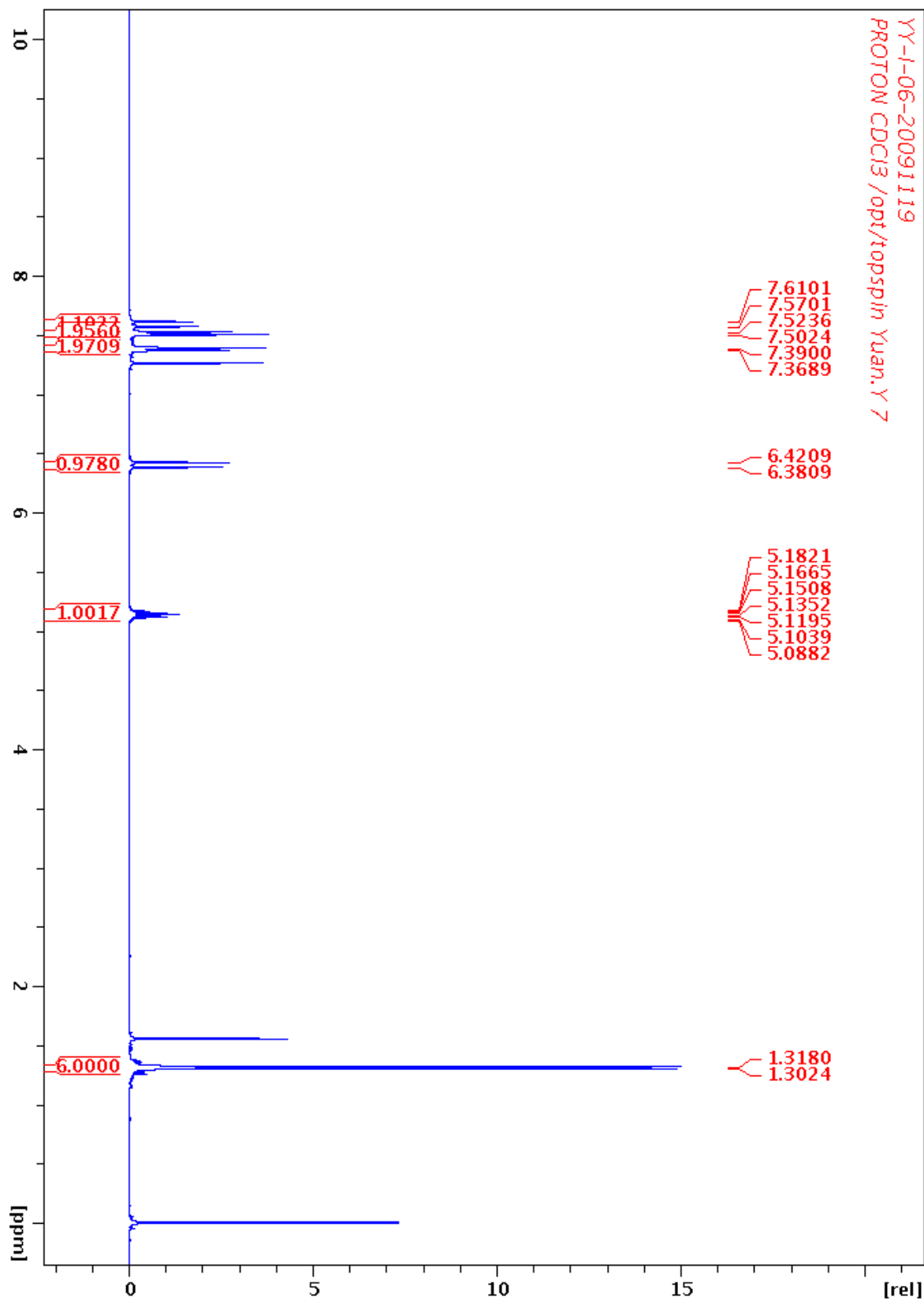




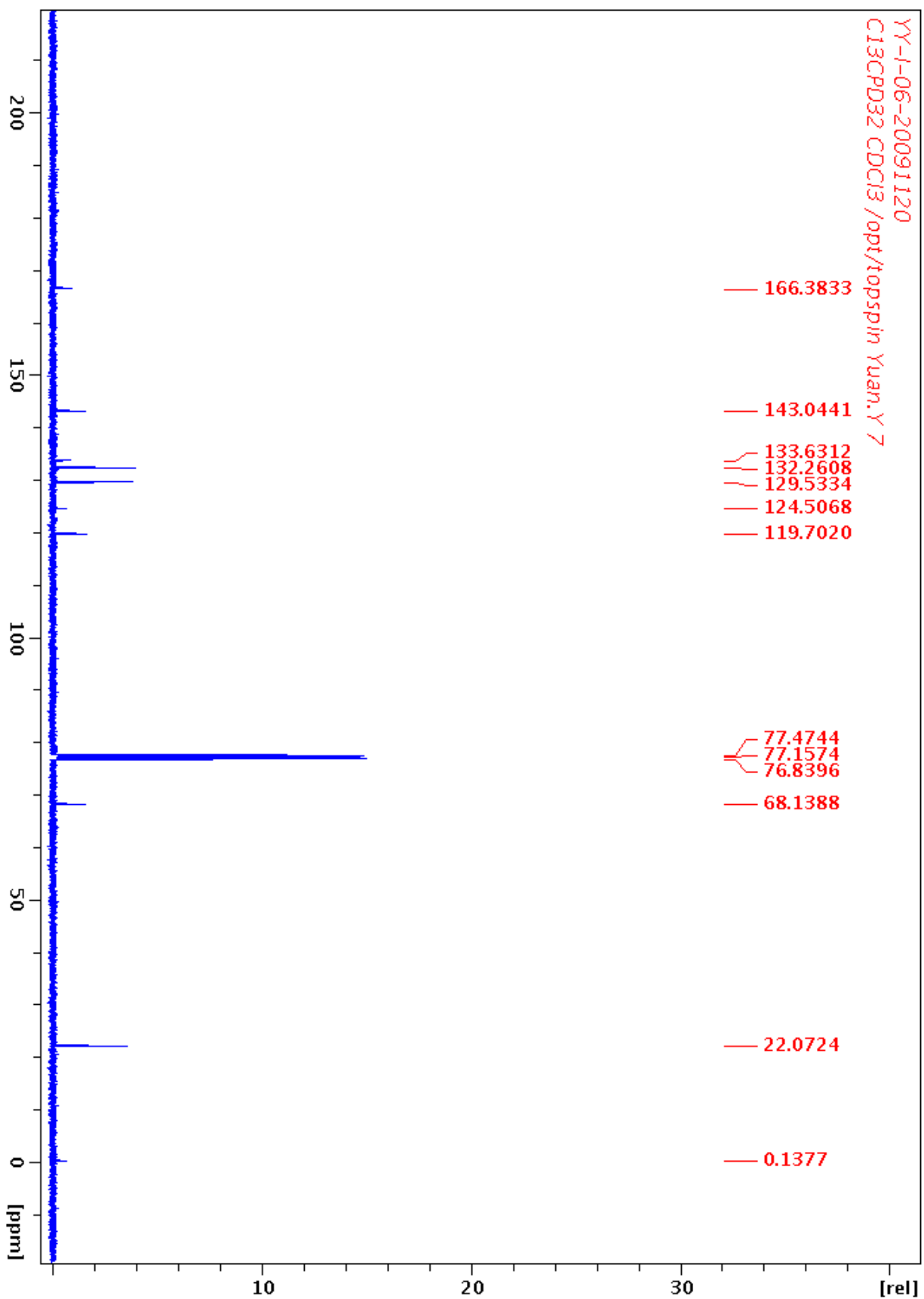
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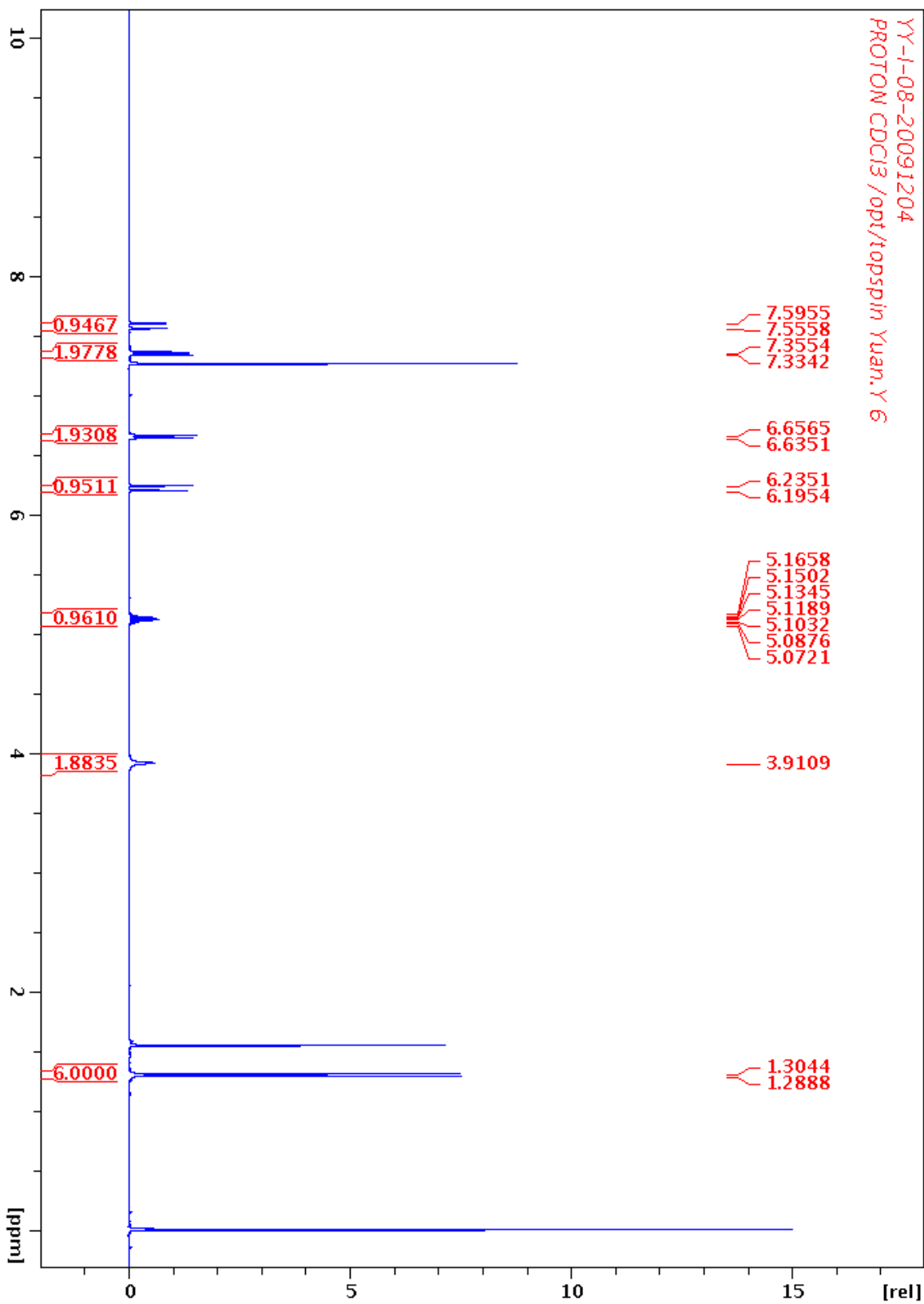
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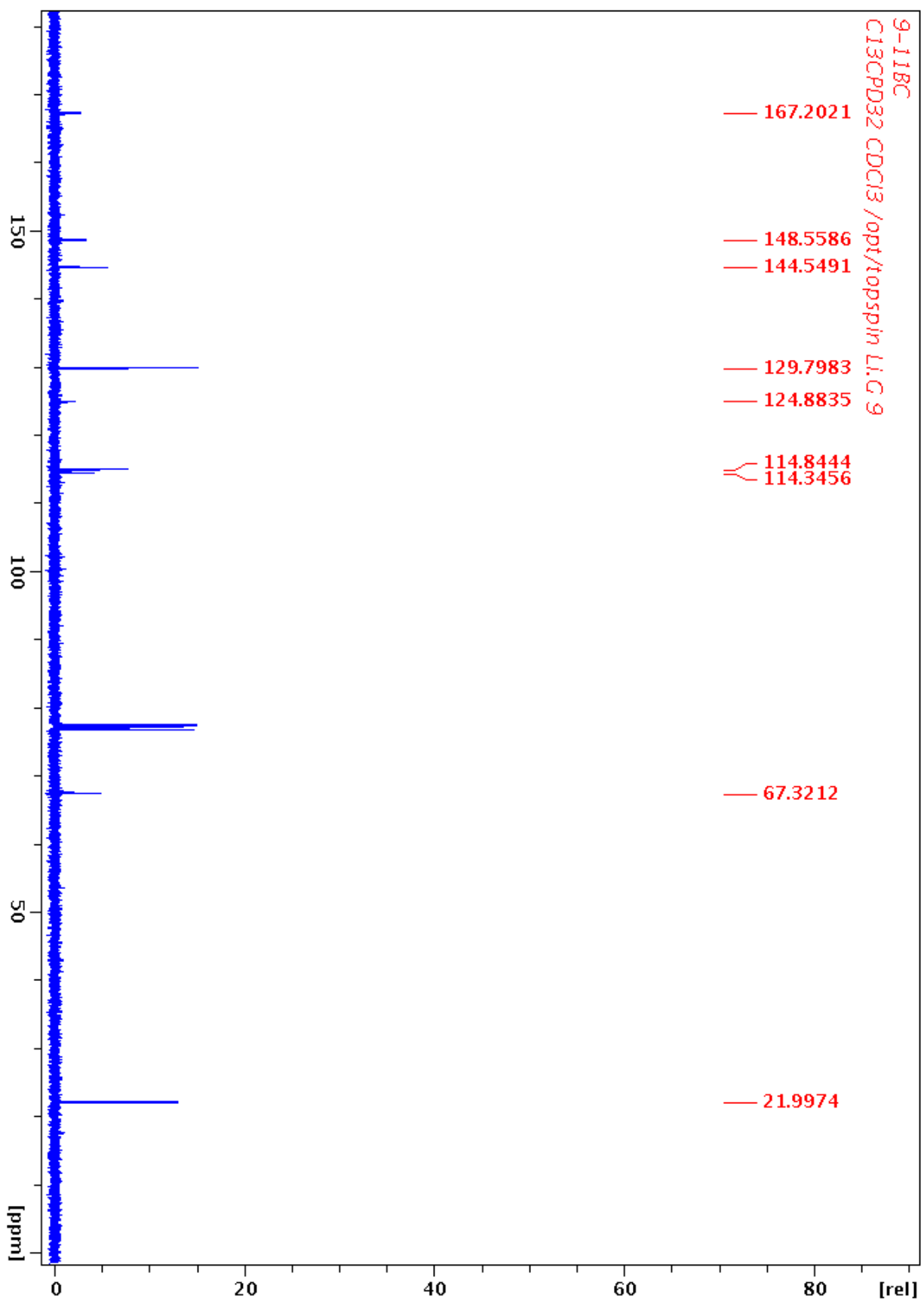




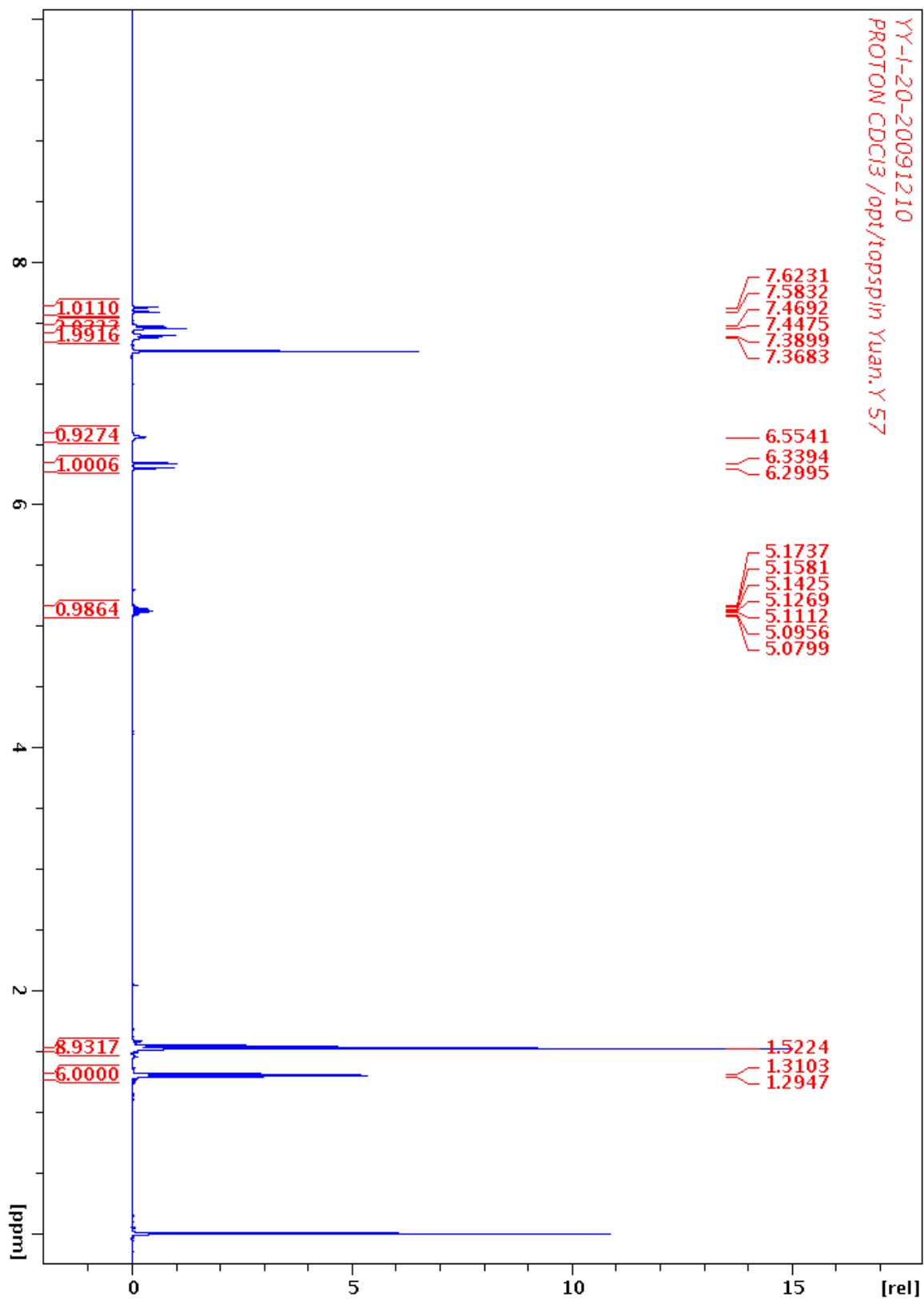


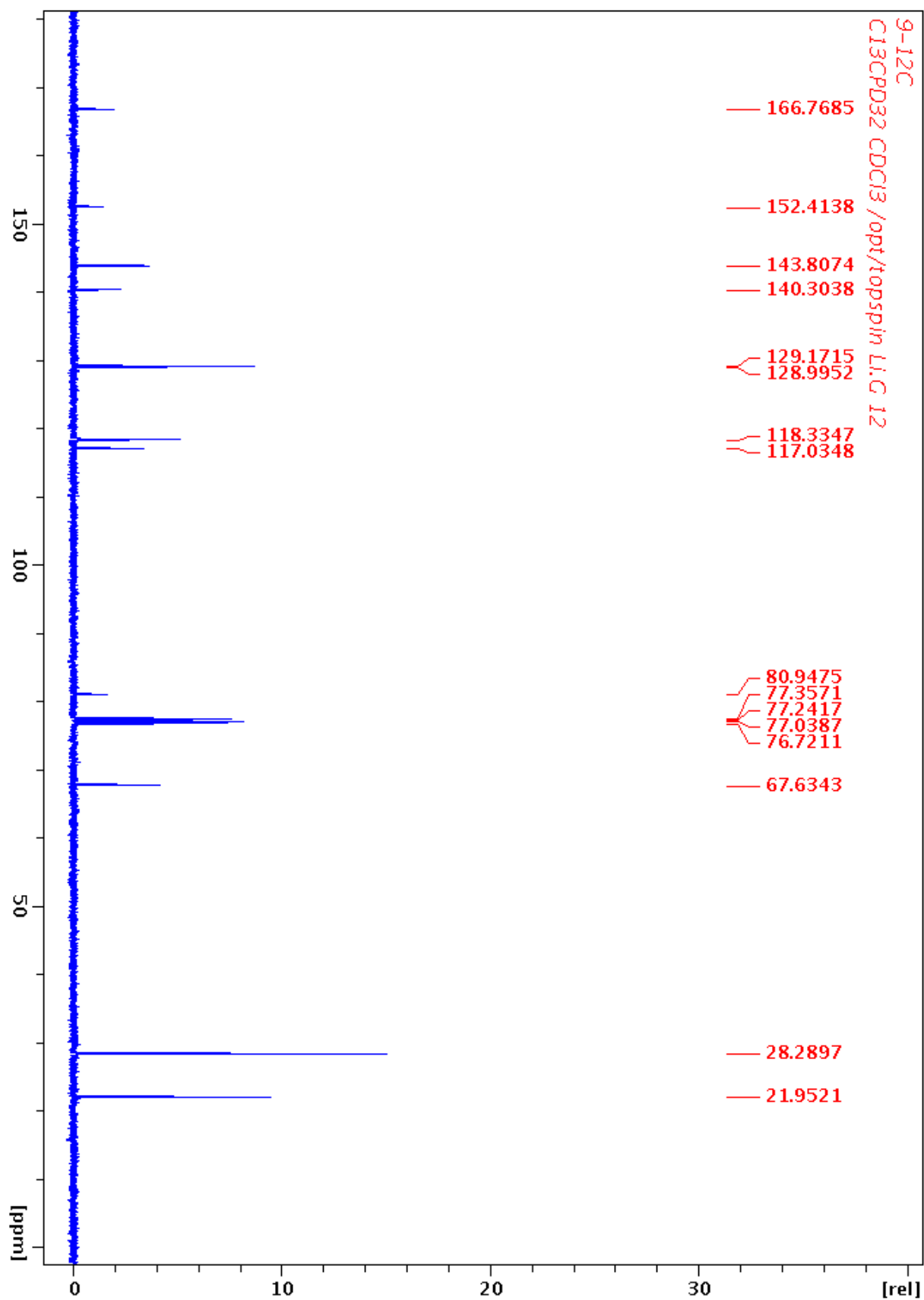
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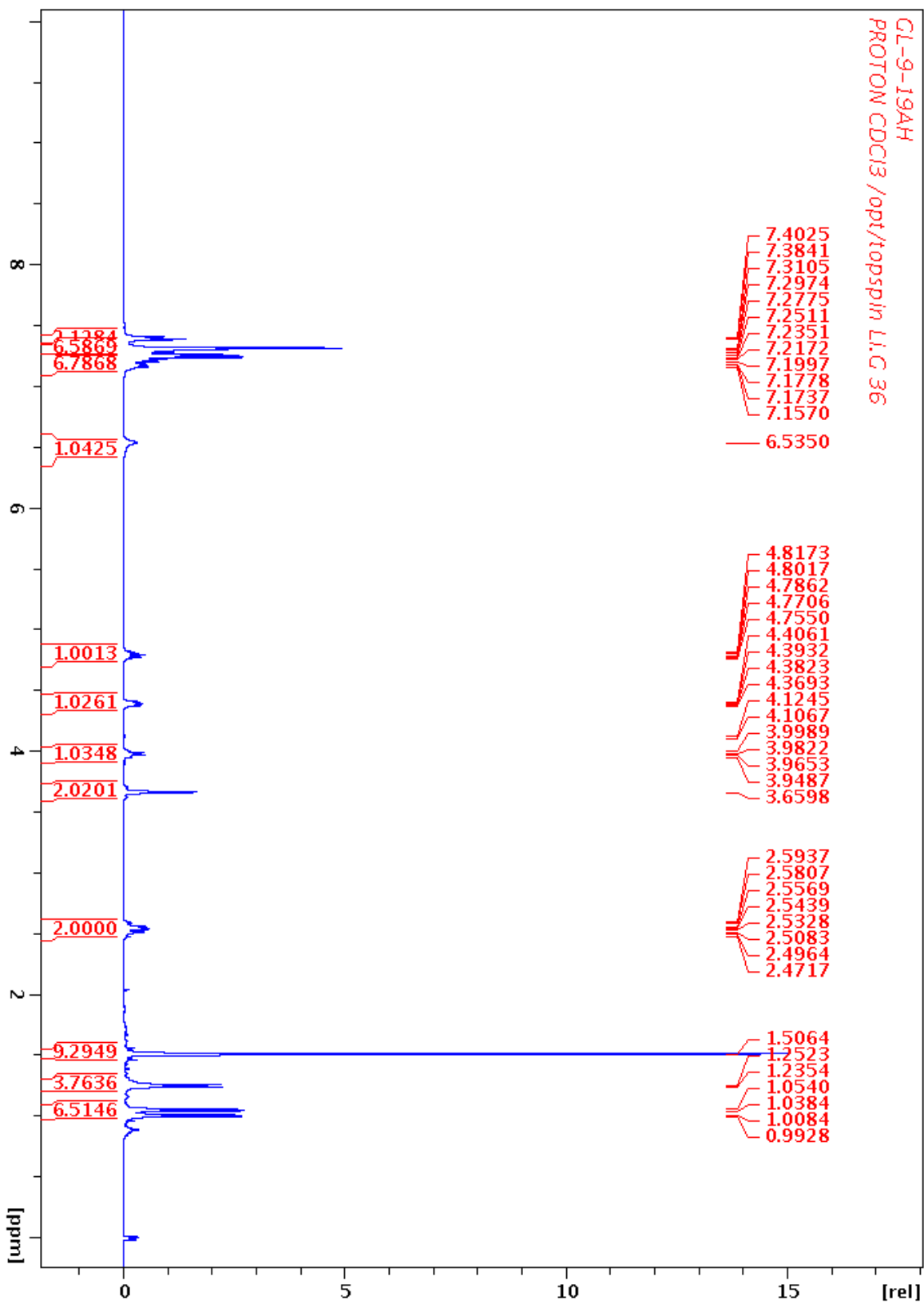


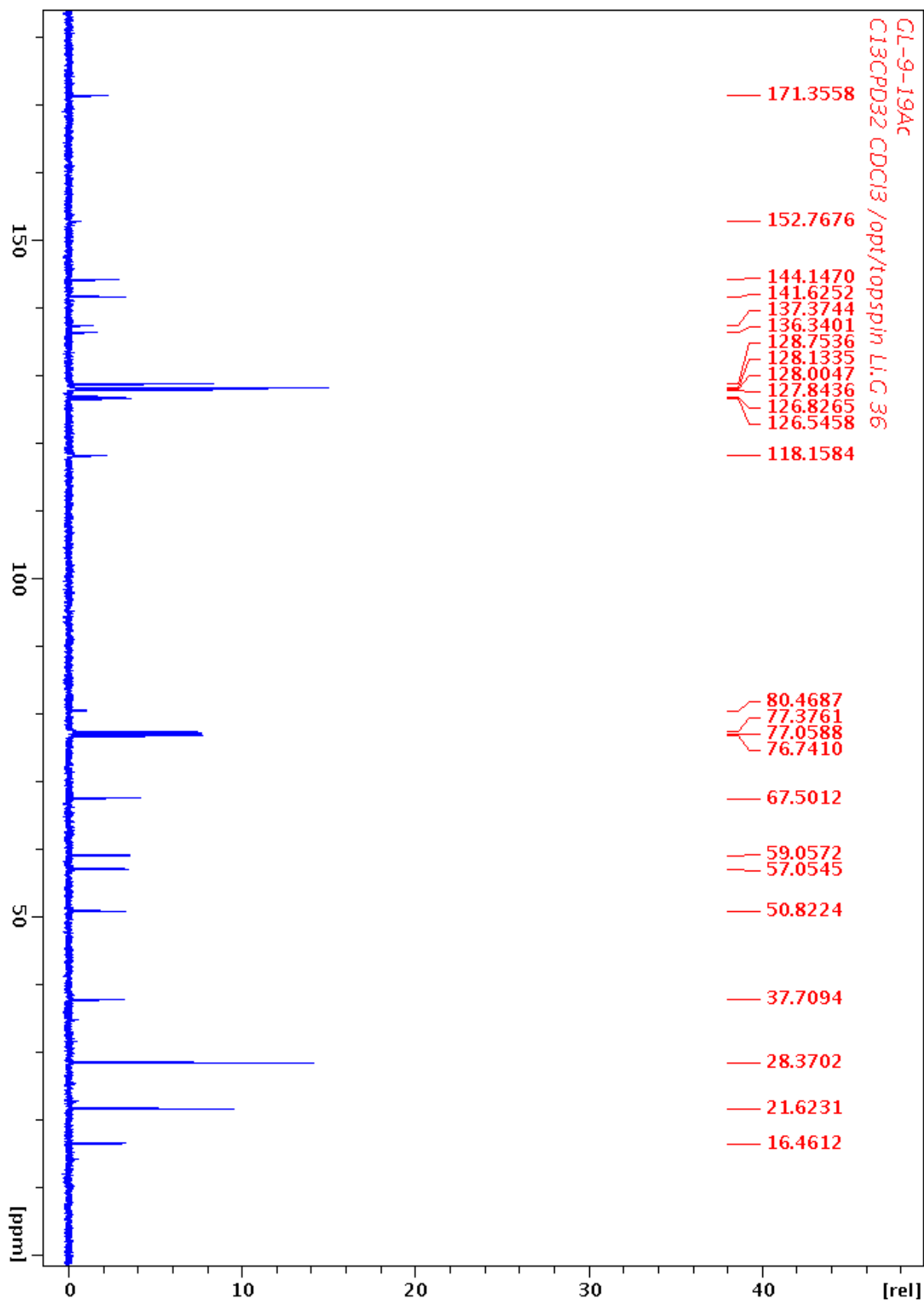
### Compound 14



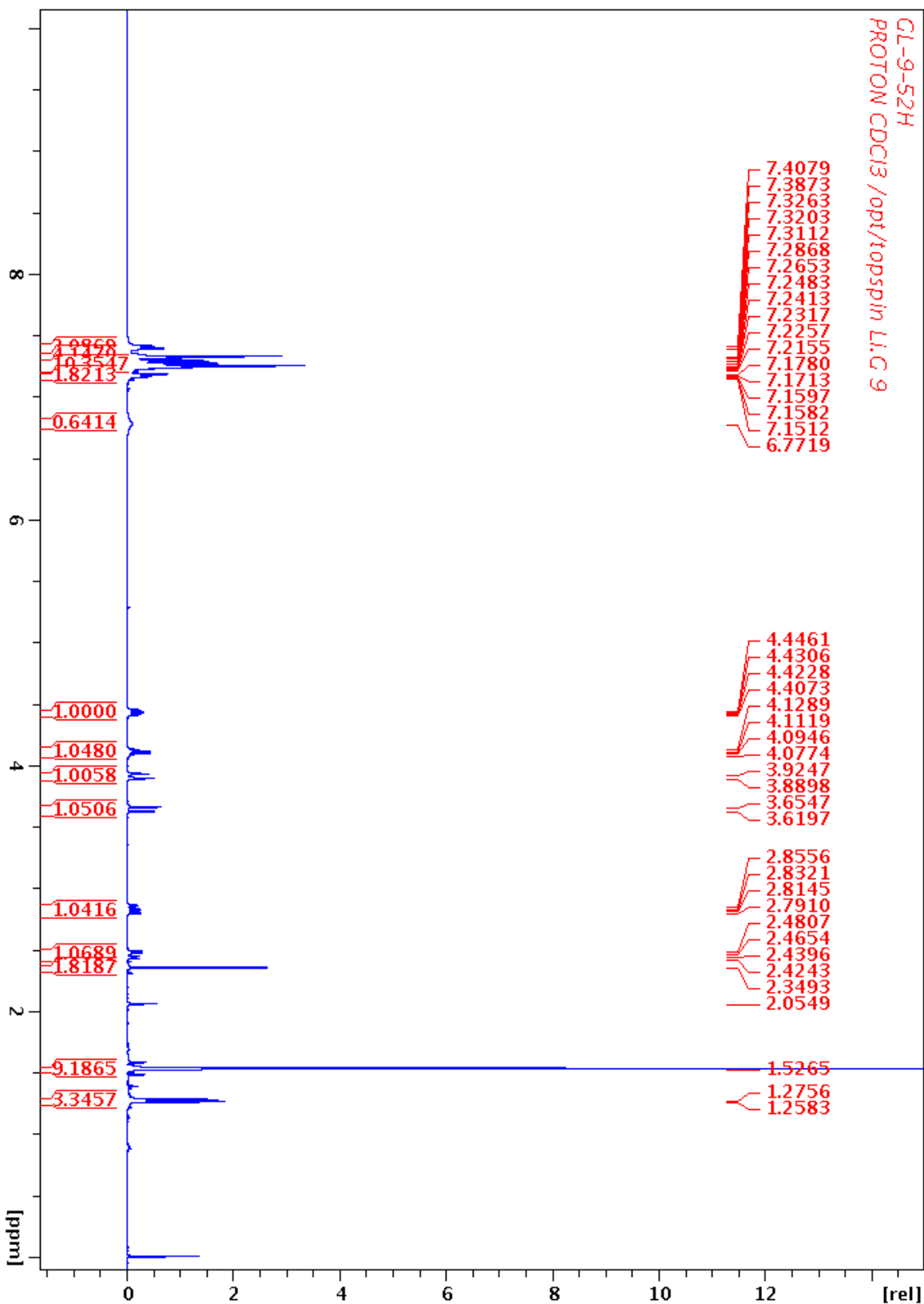


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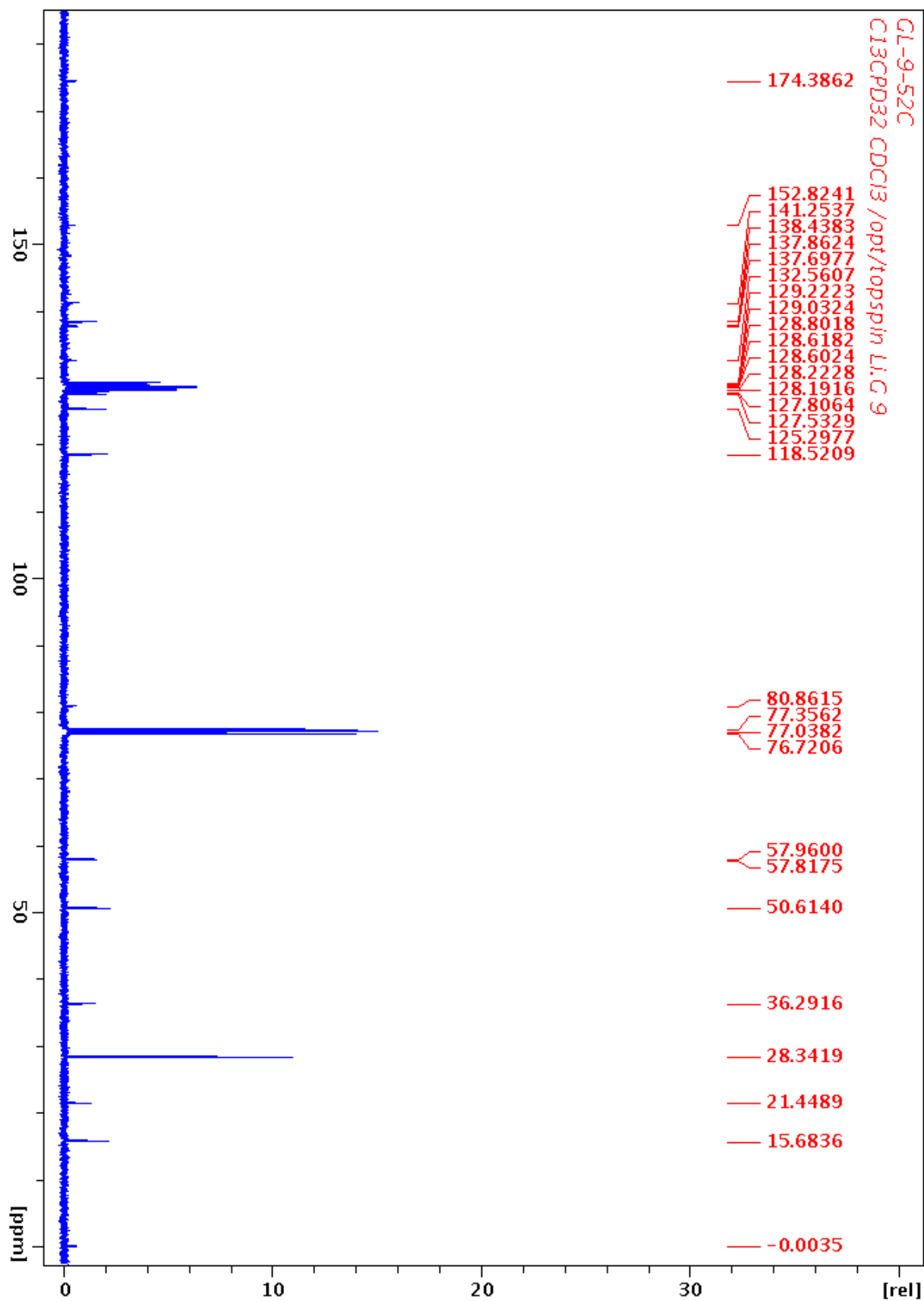




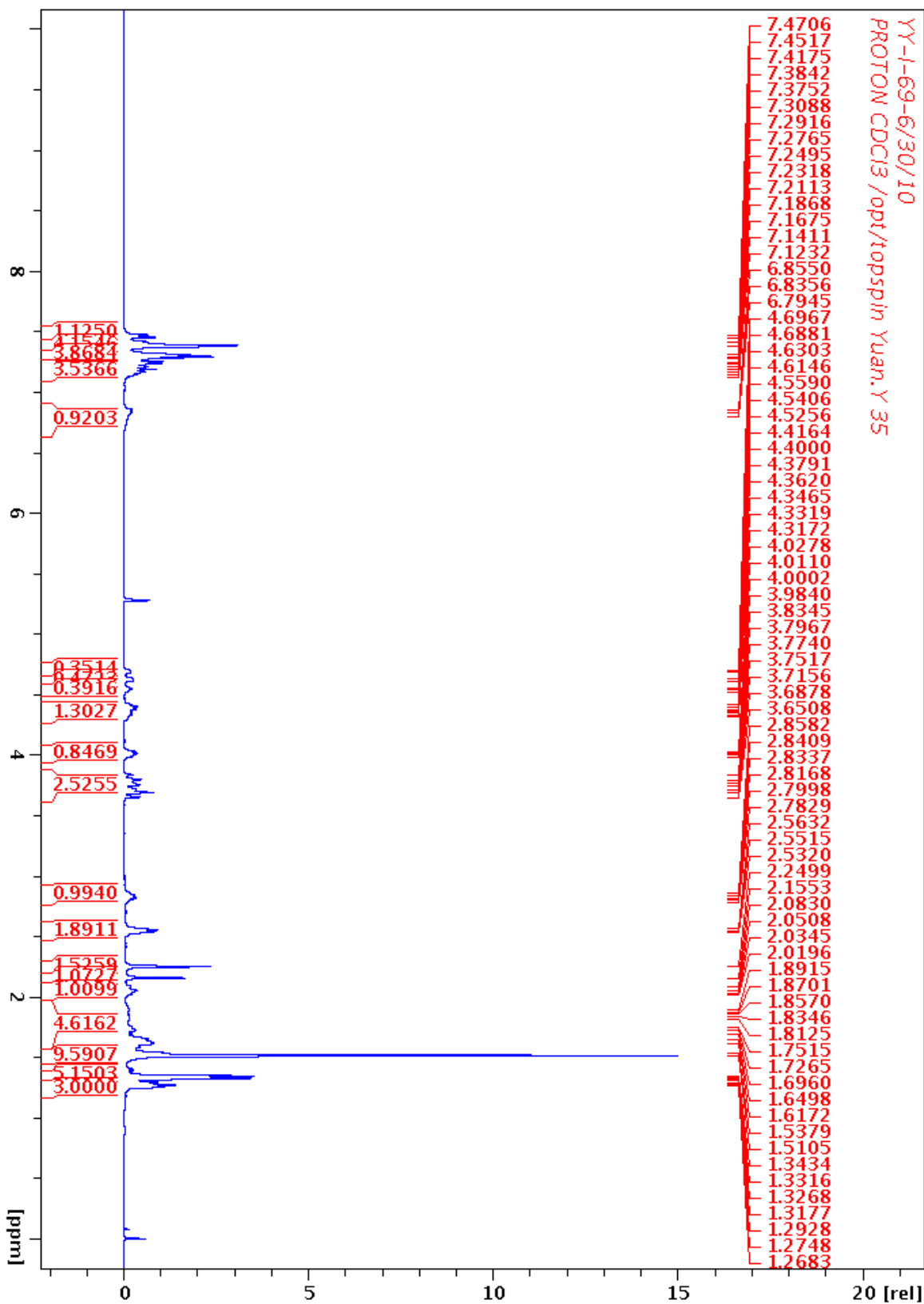
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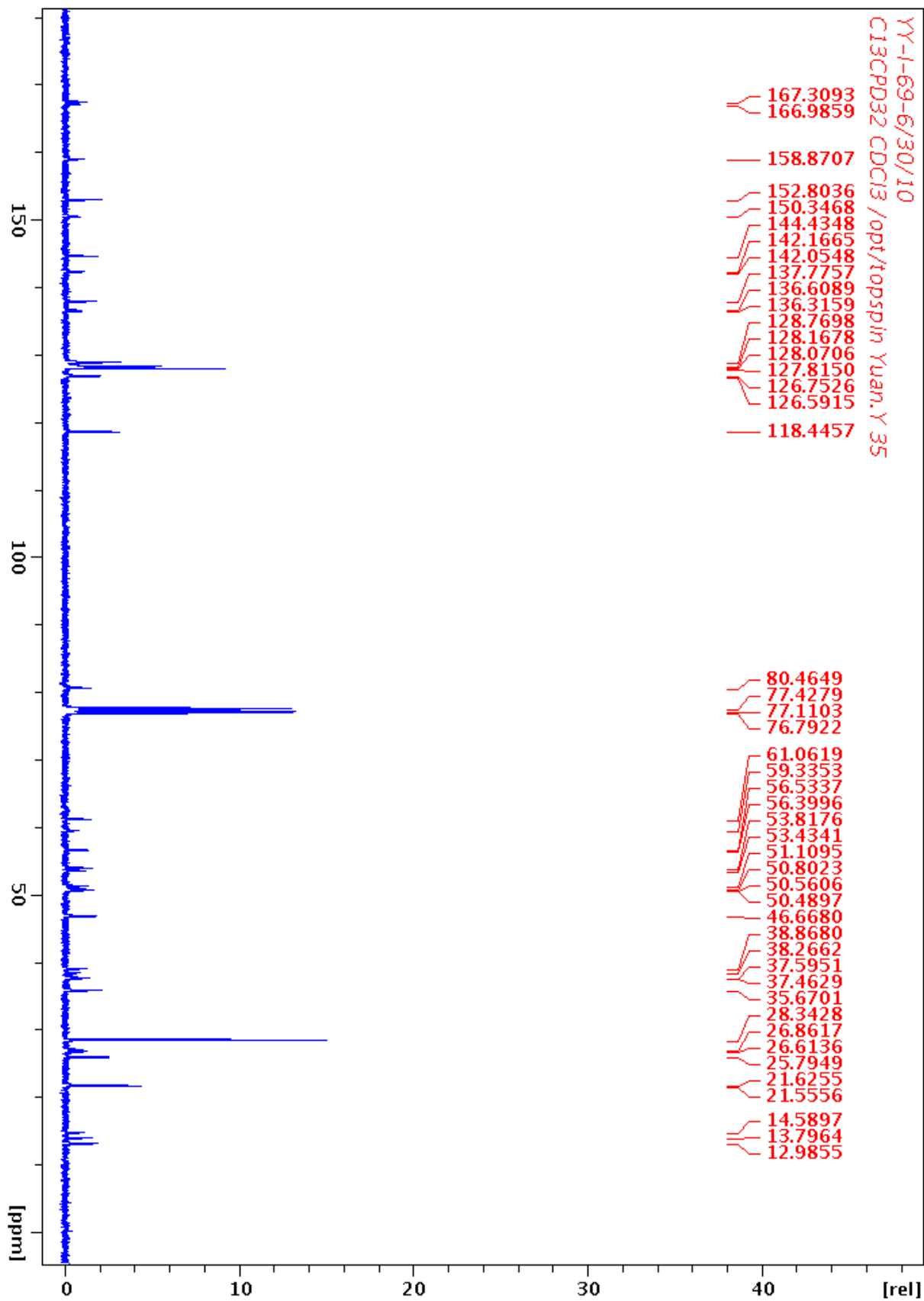




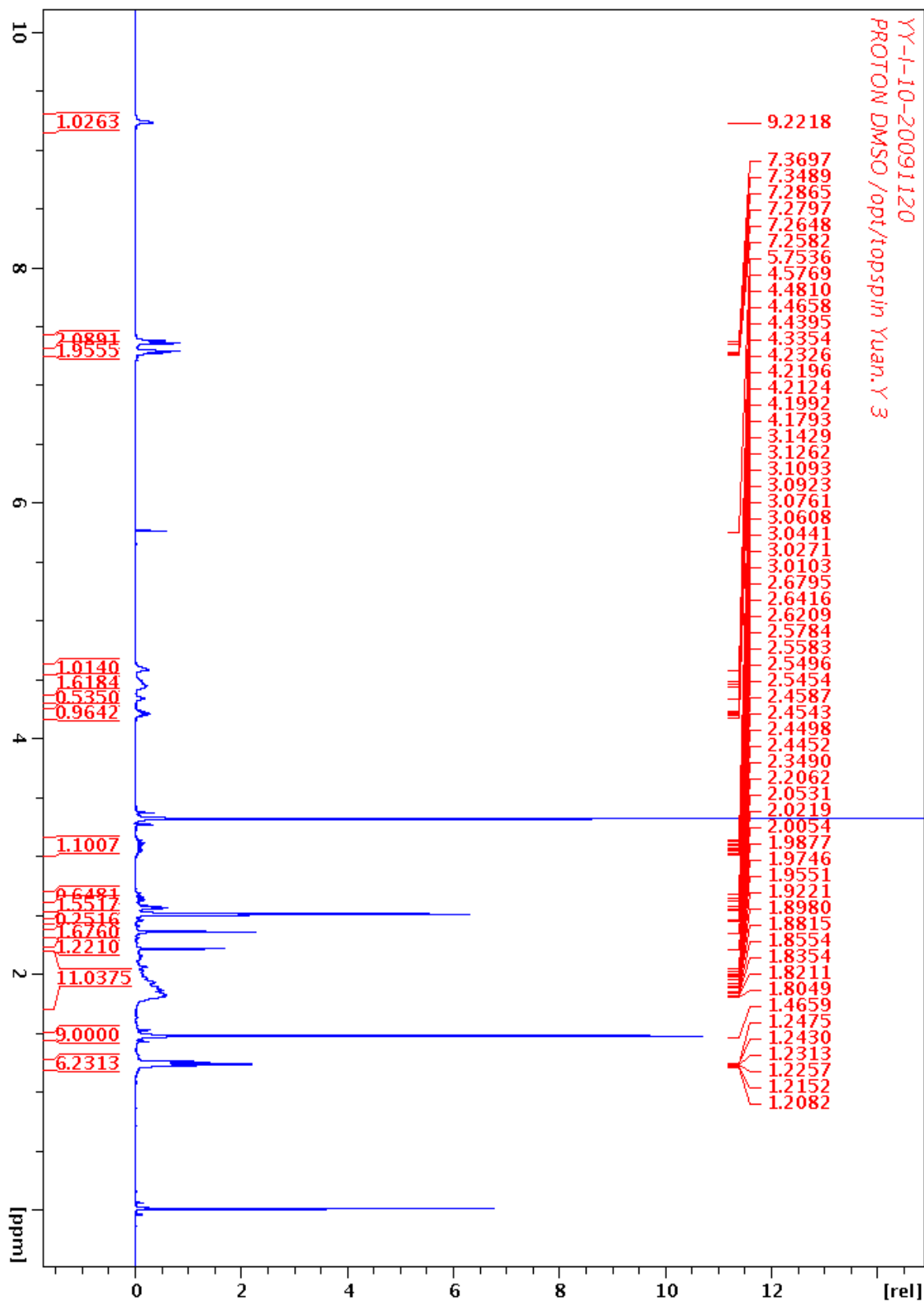


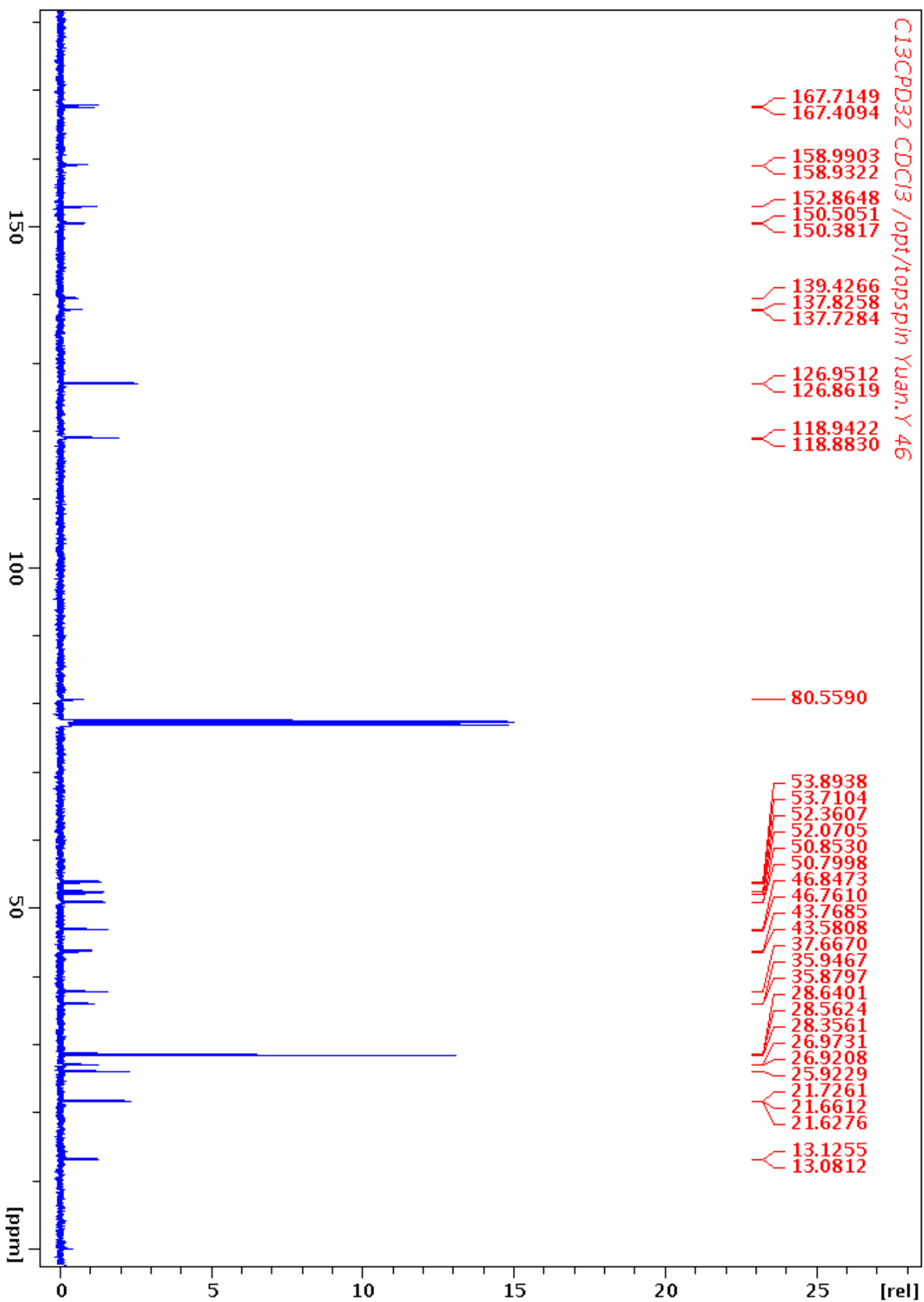
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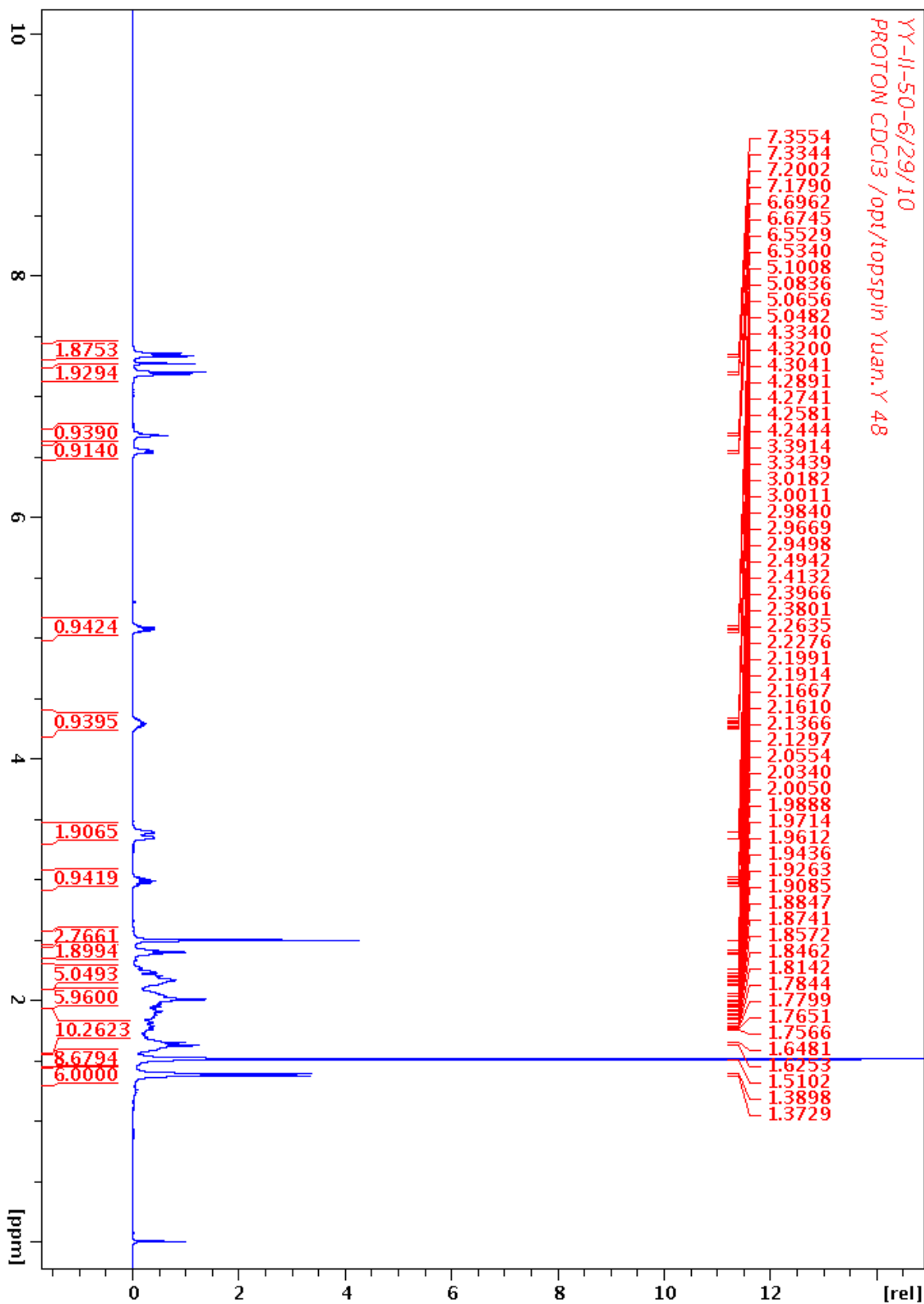


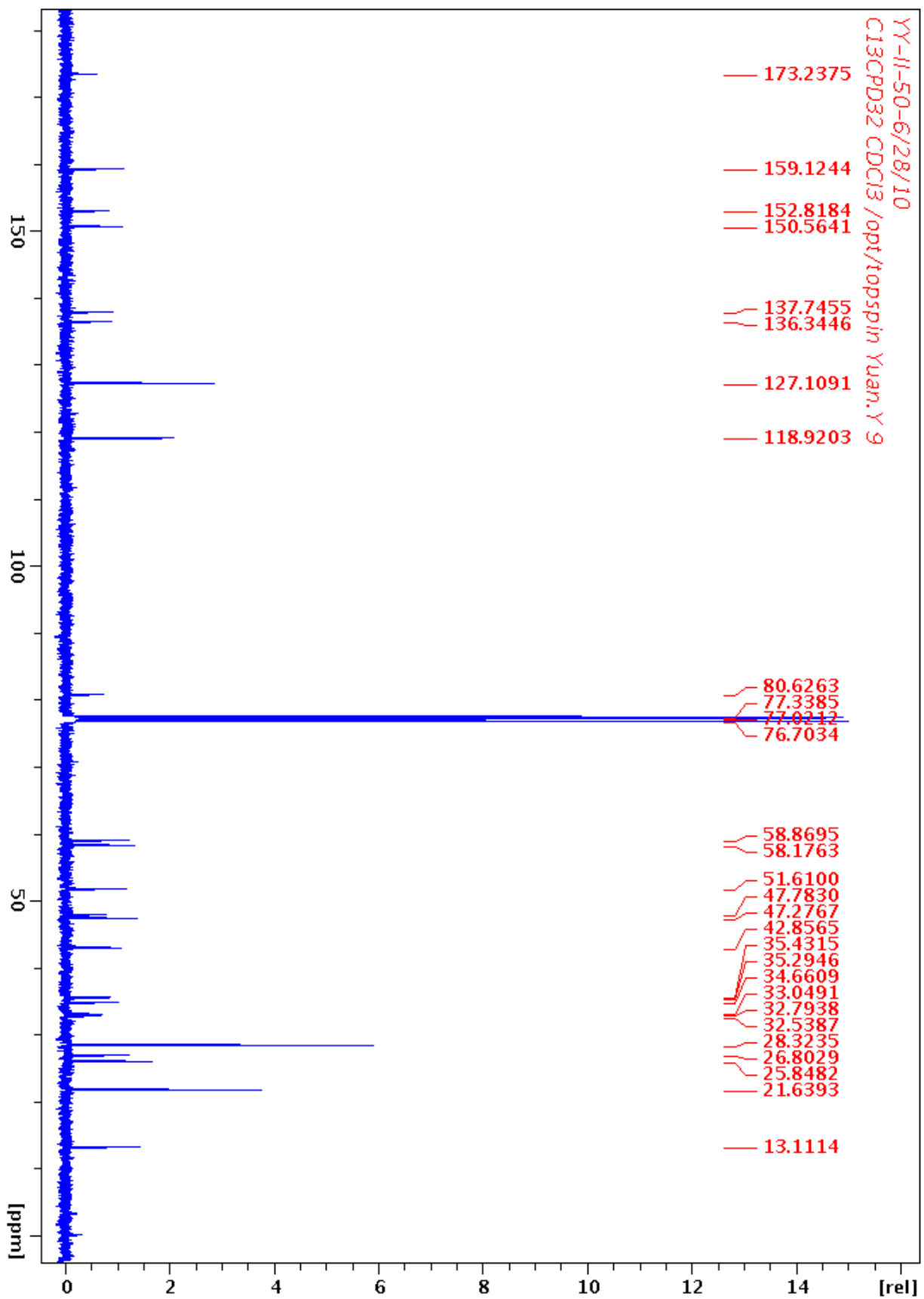
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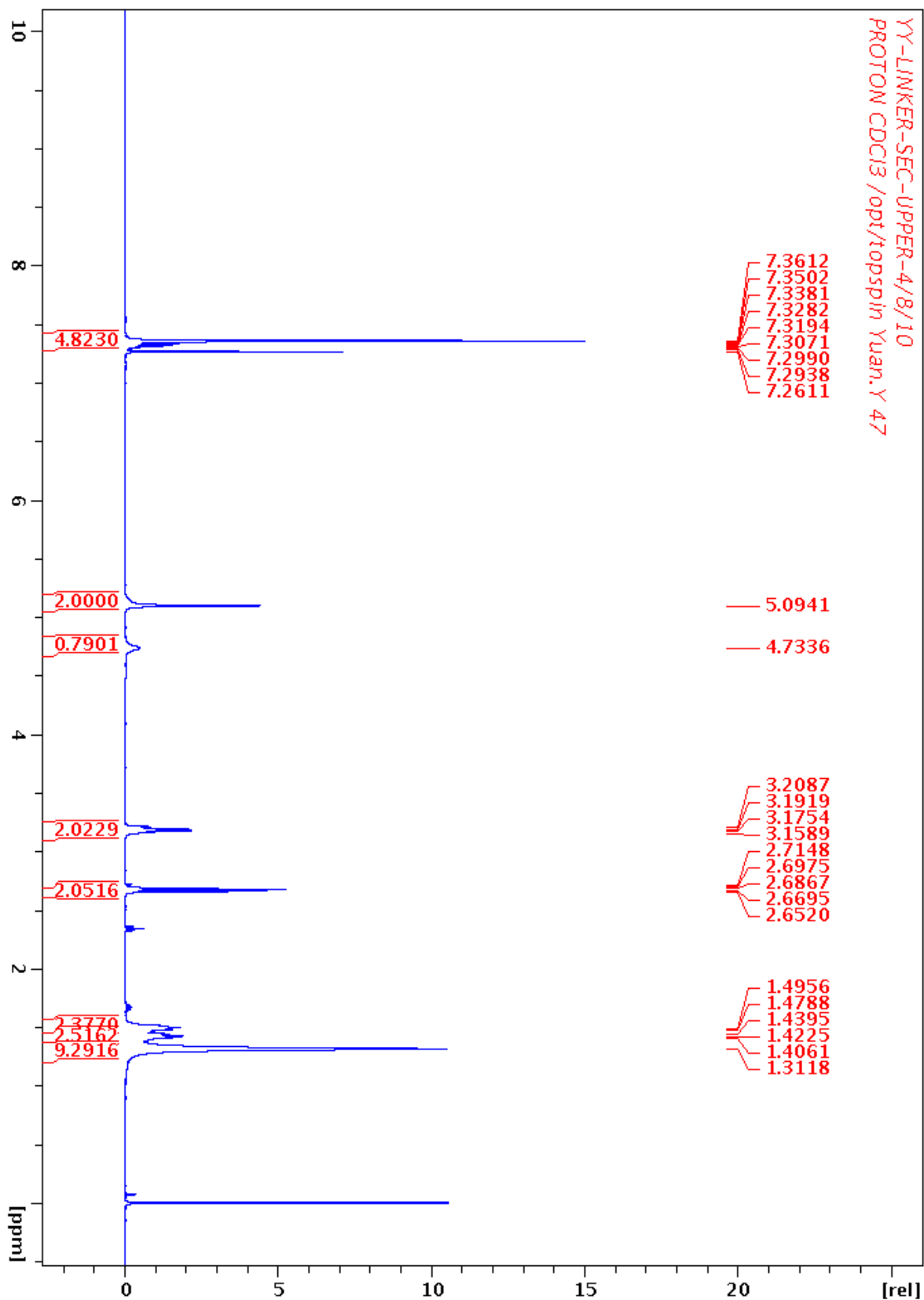


Compound 20

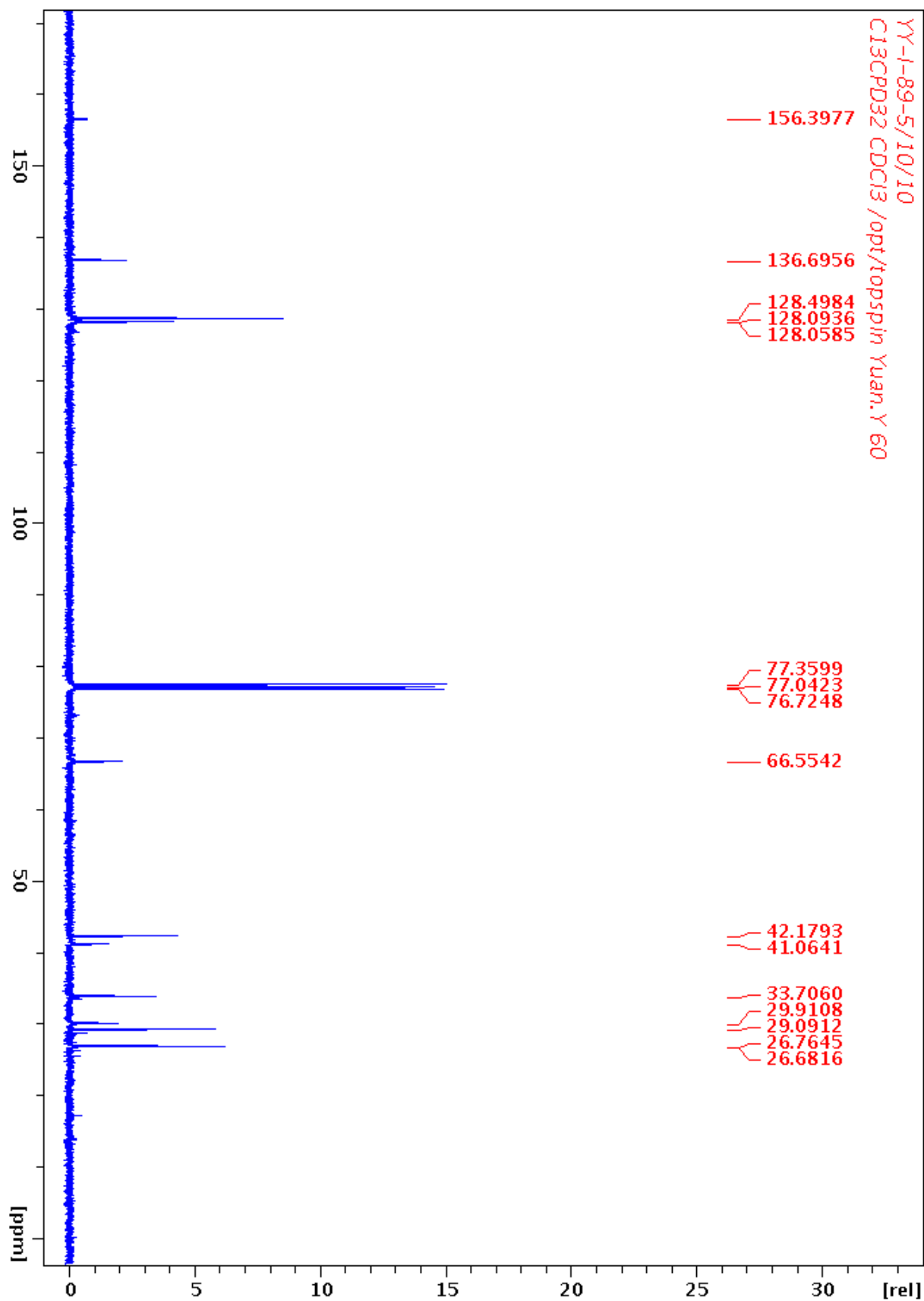




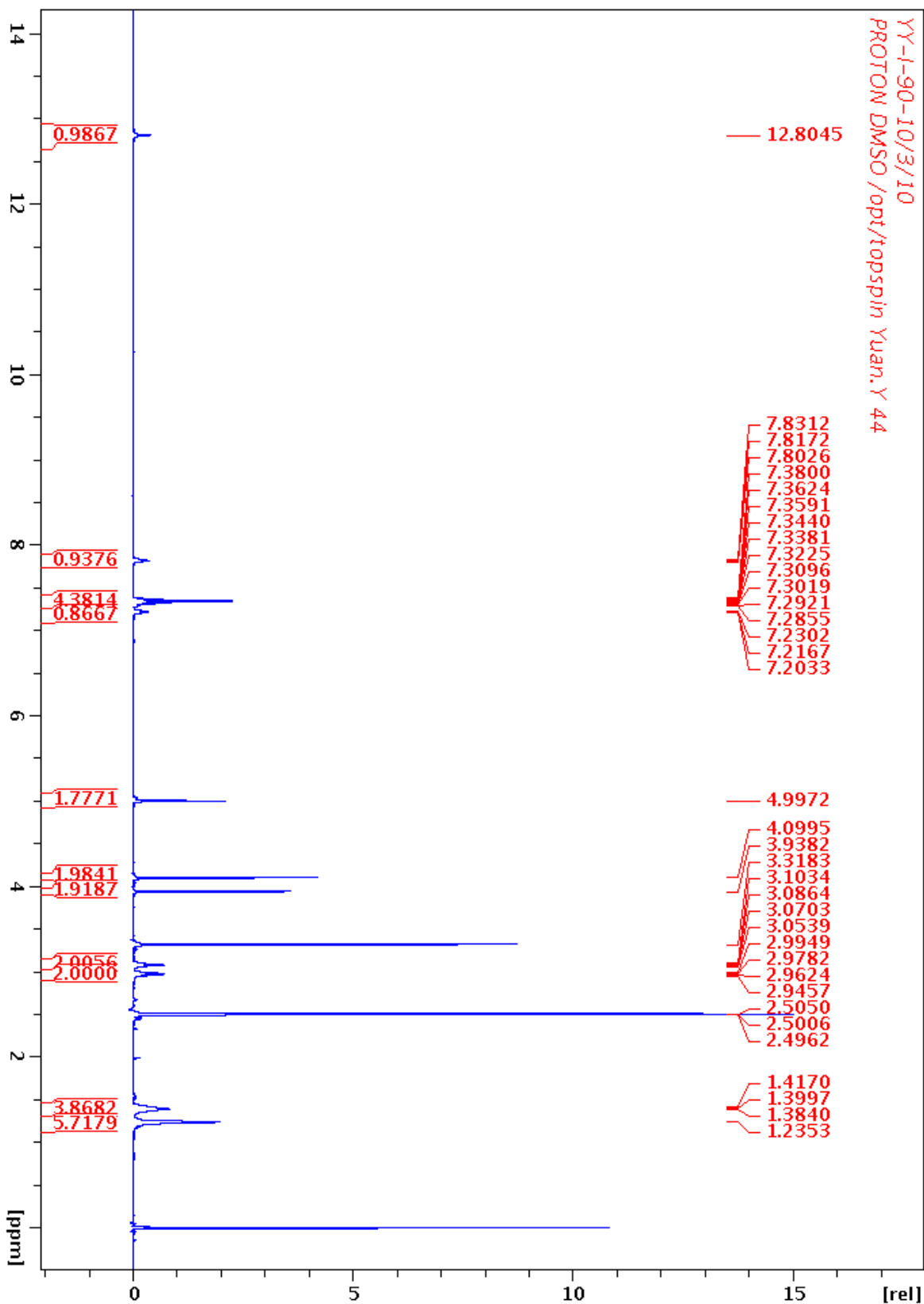
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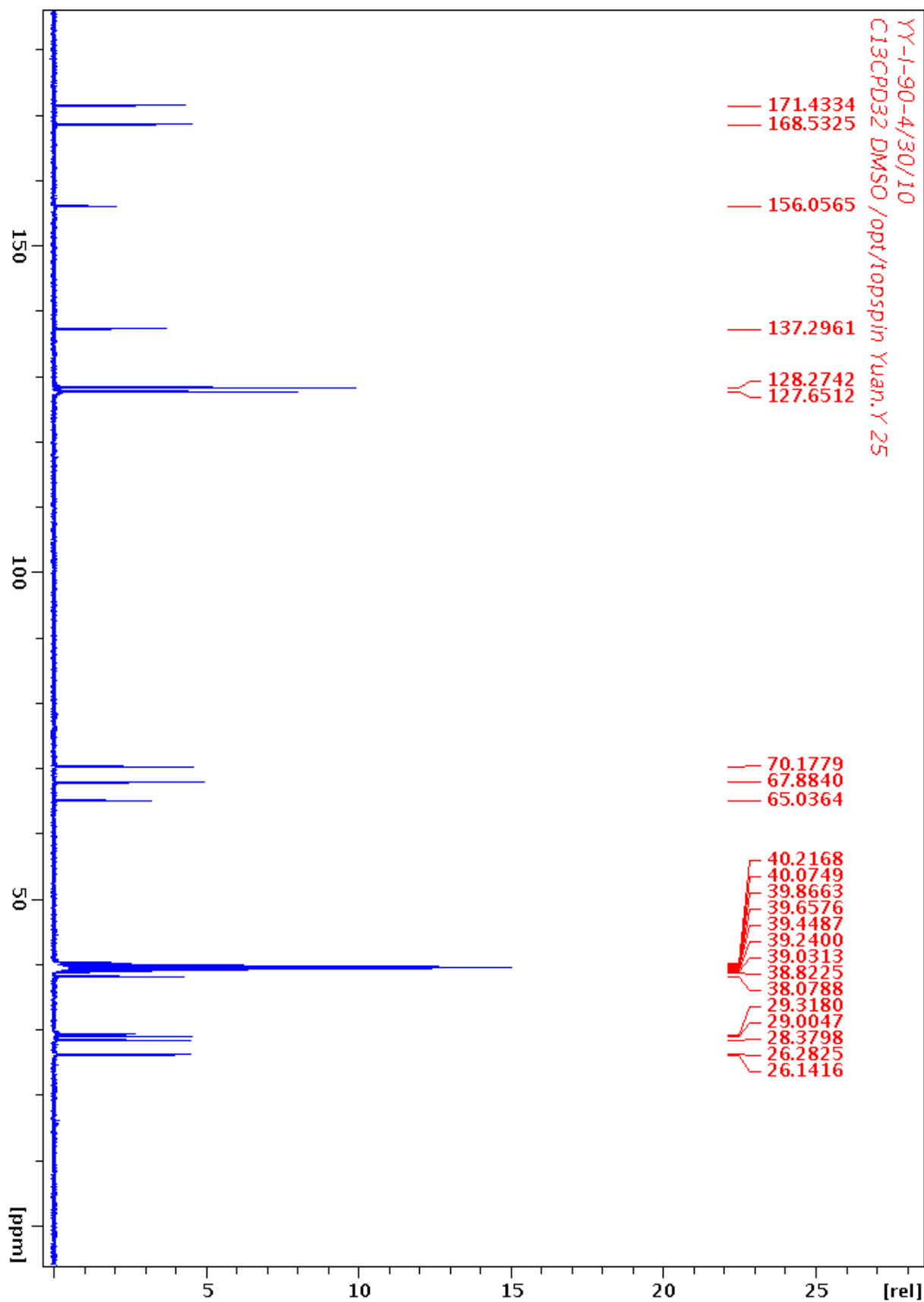




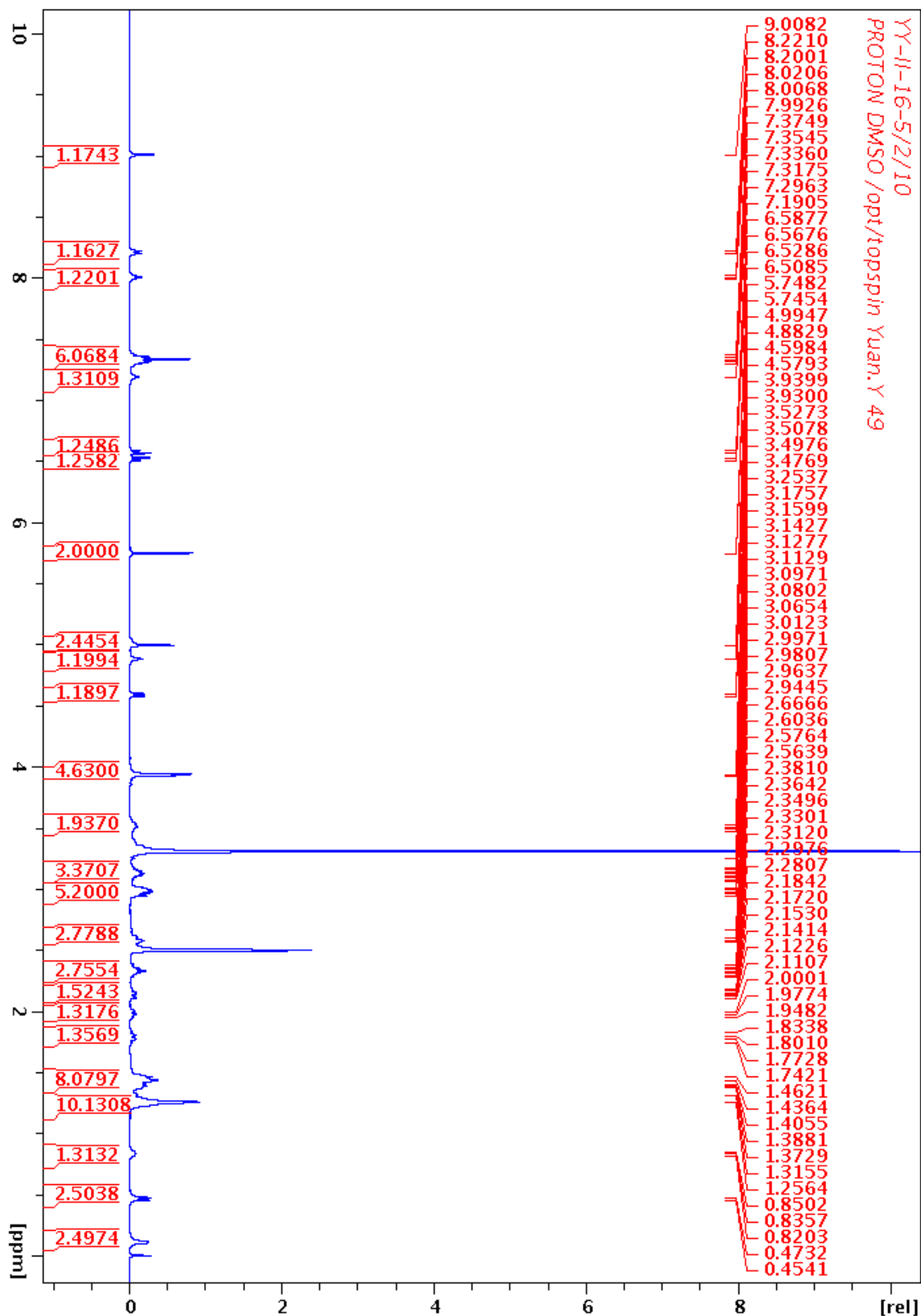


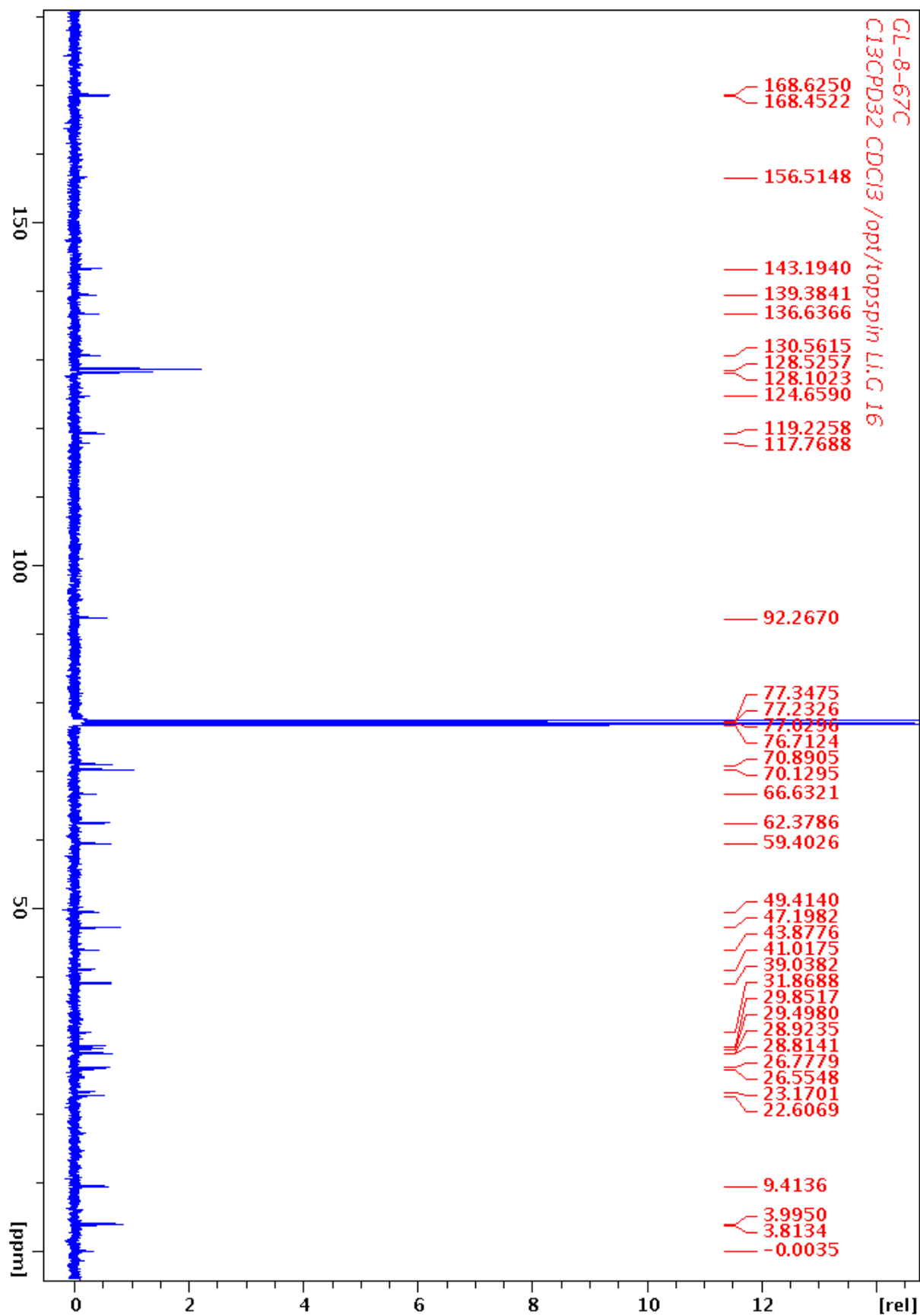
Compound 22



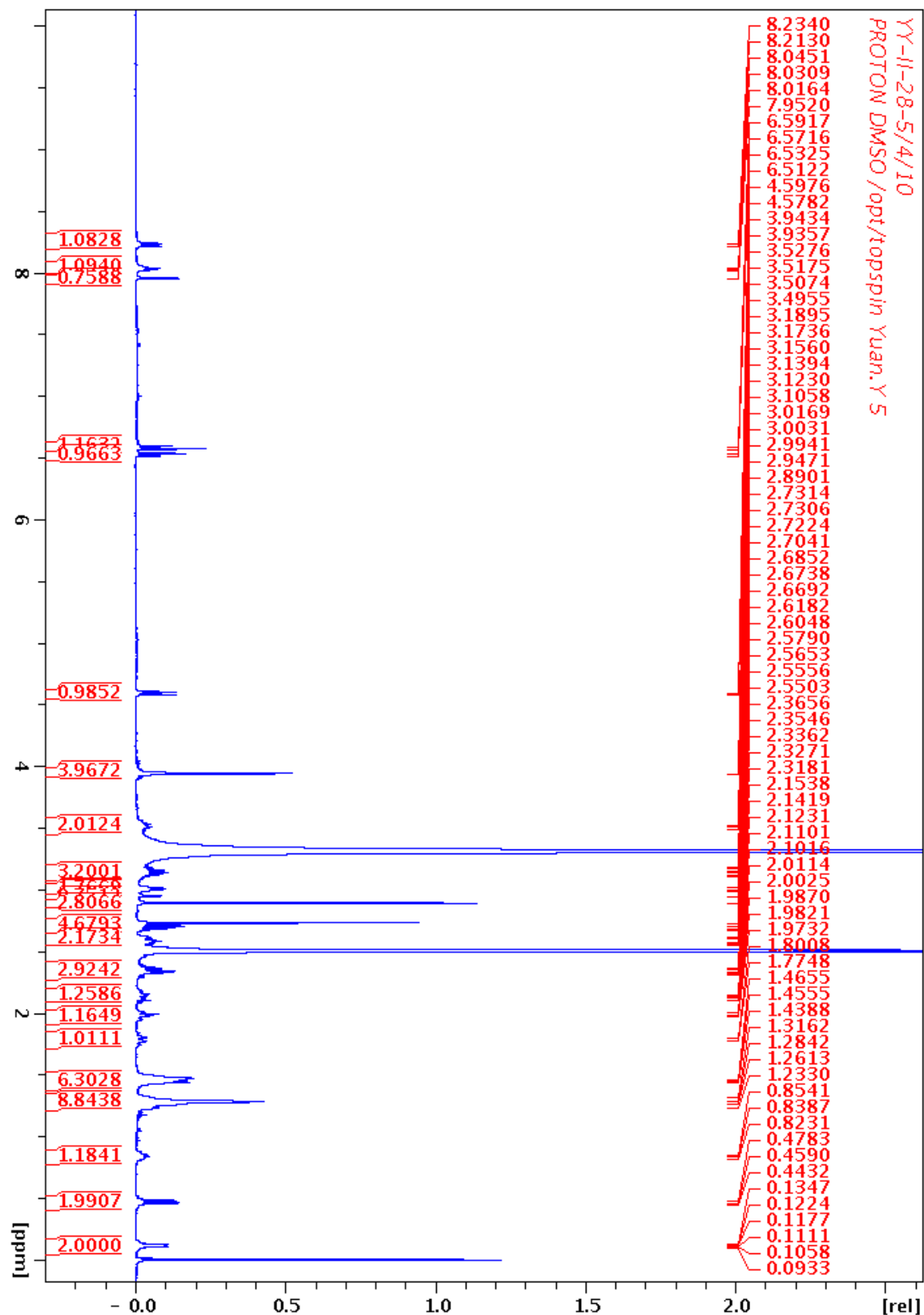


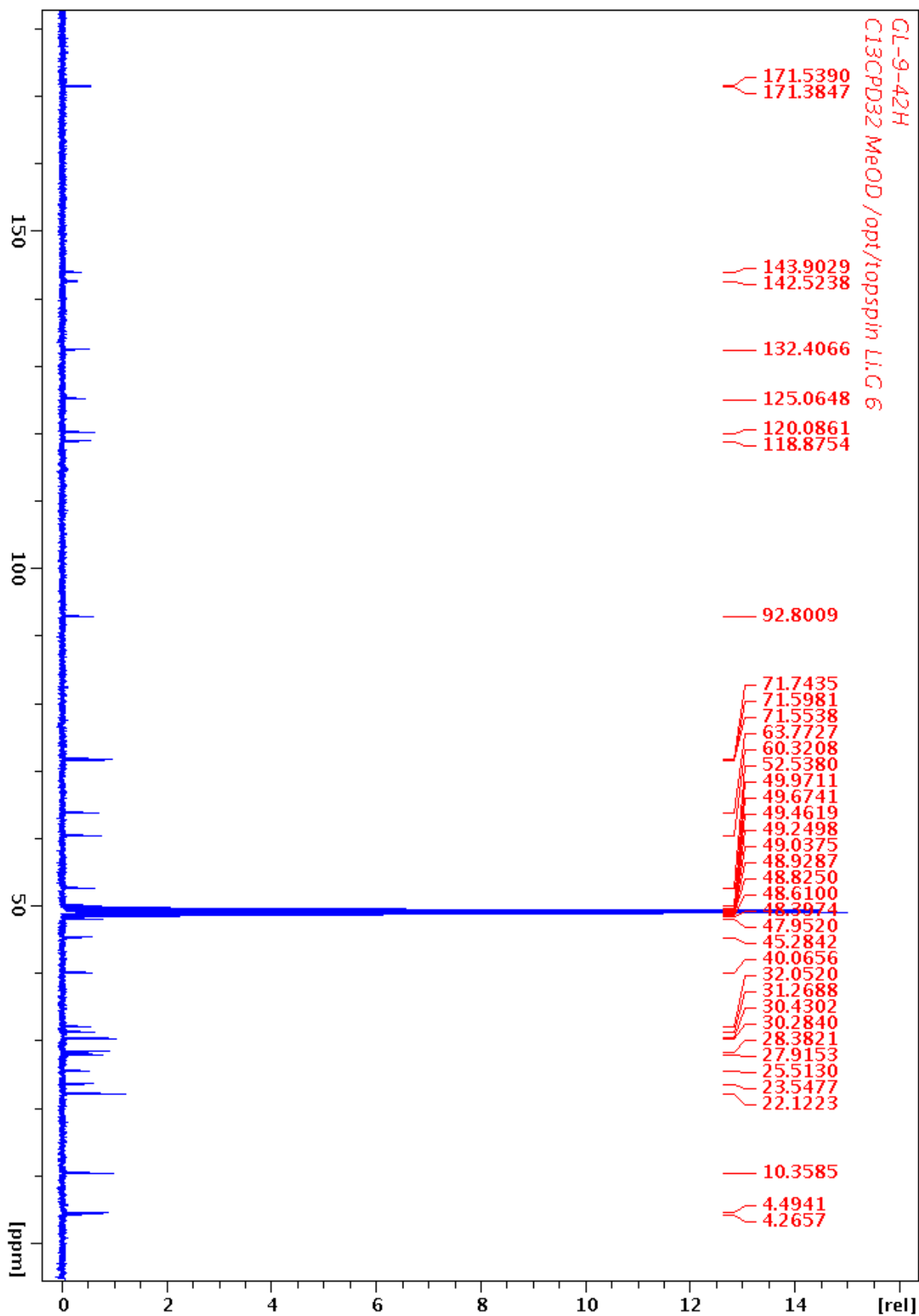
Compound 23



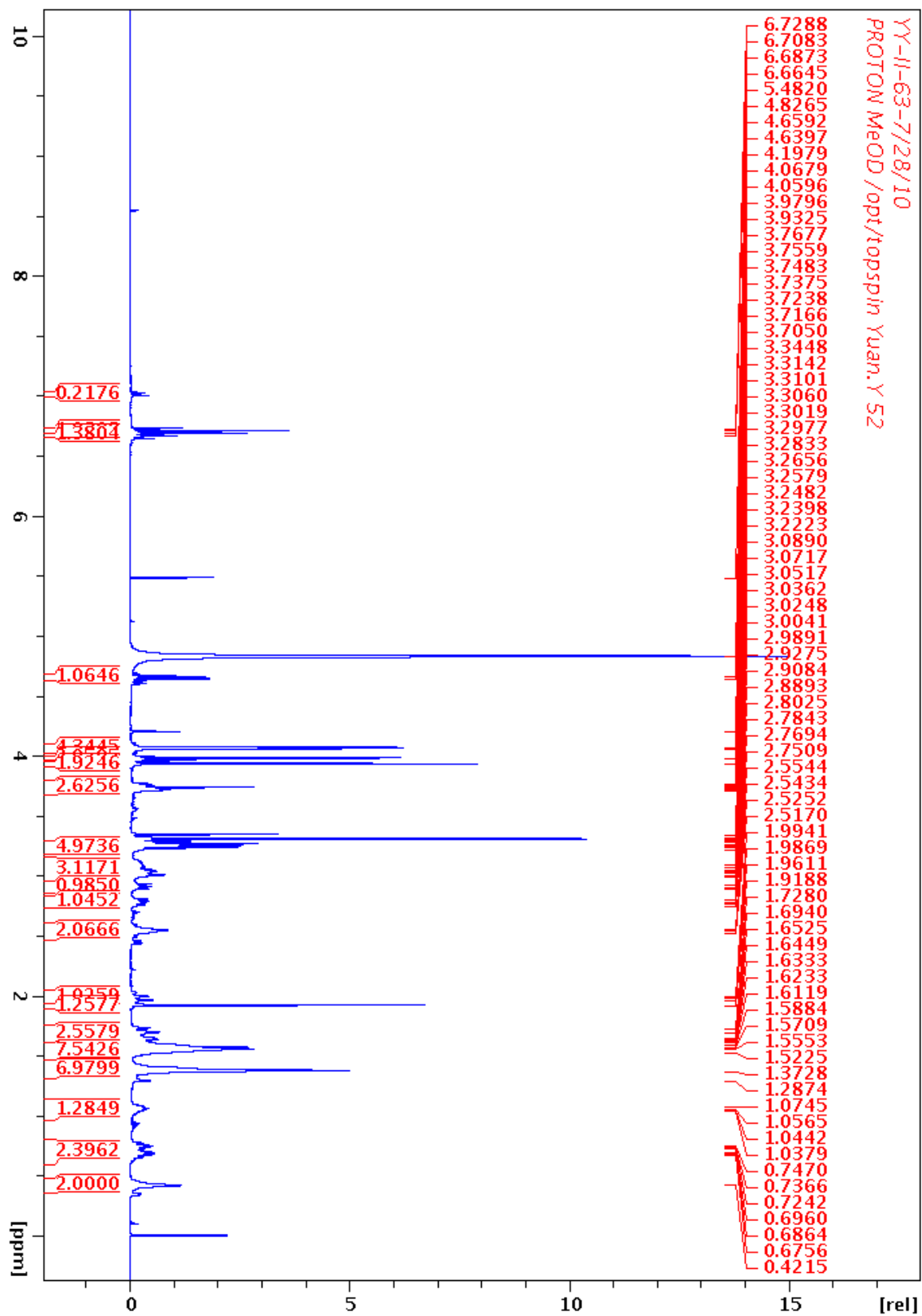


Compound 24

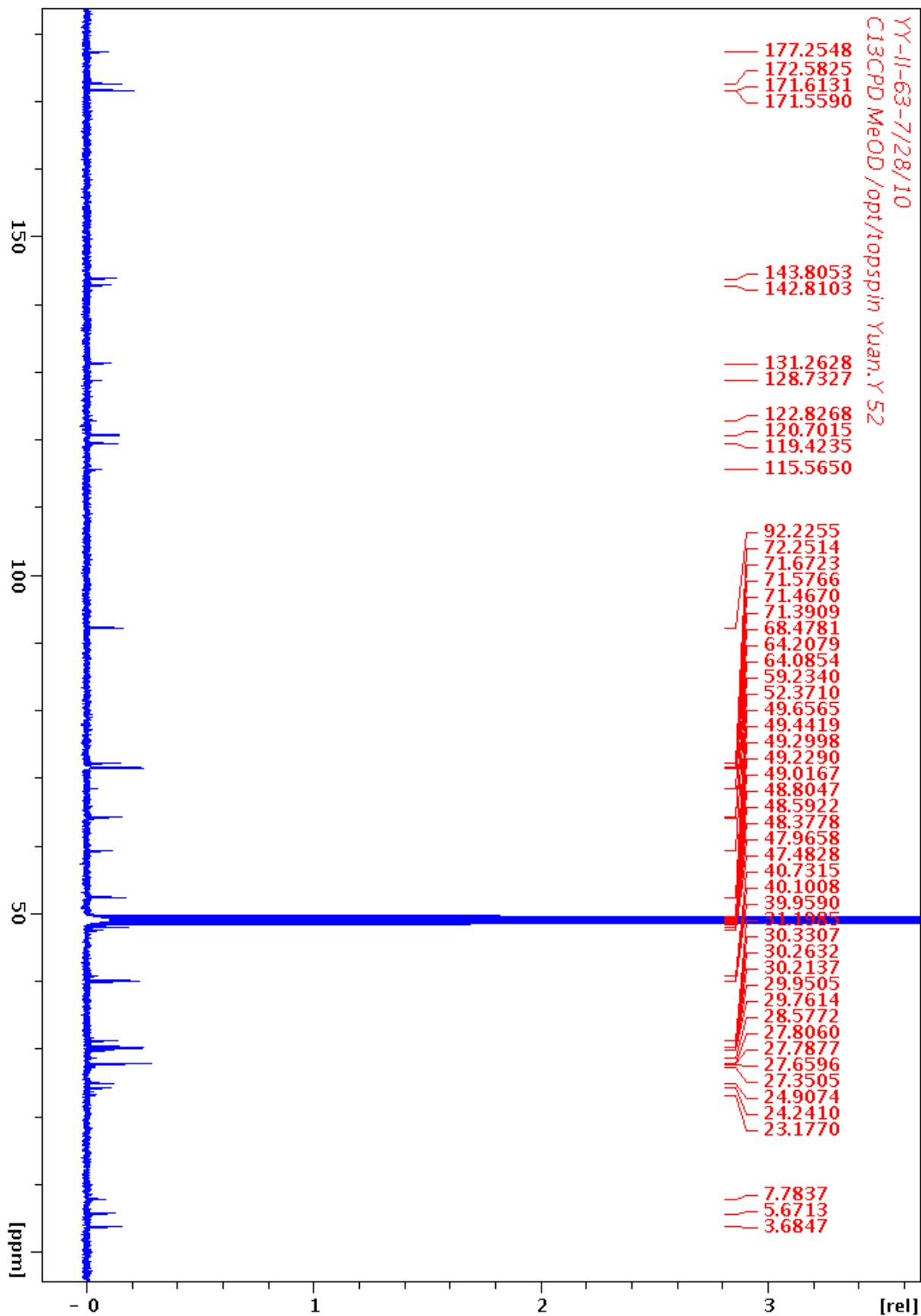




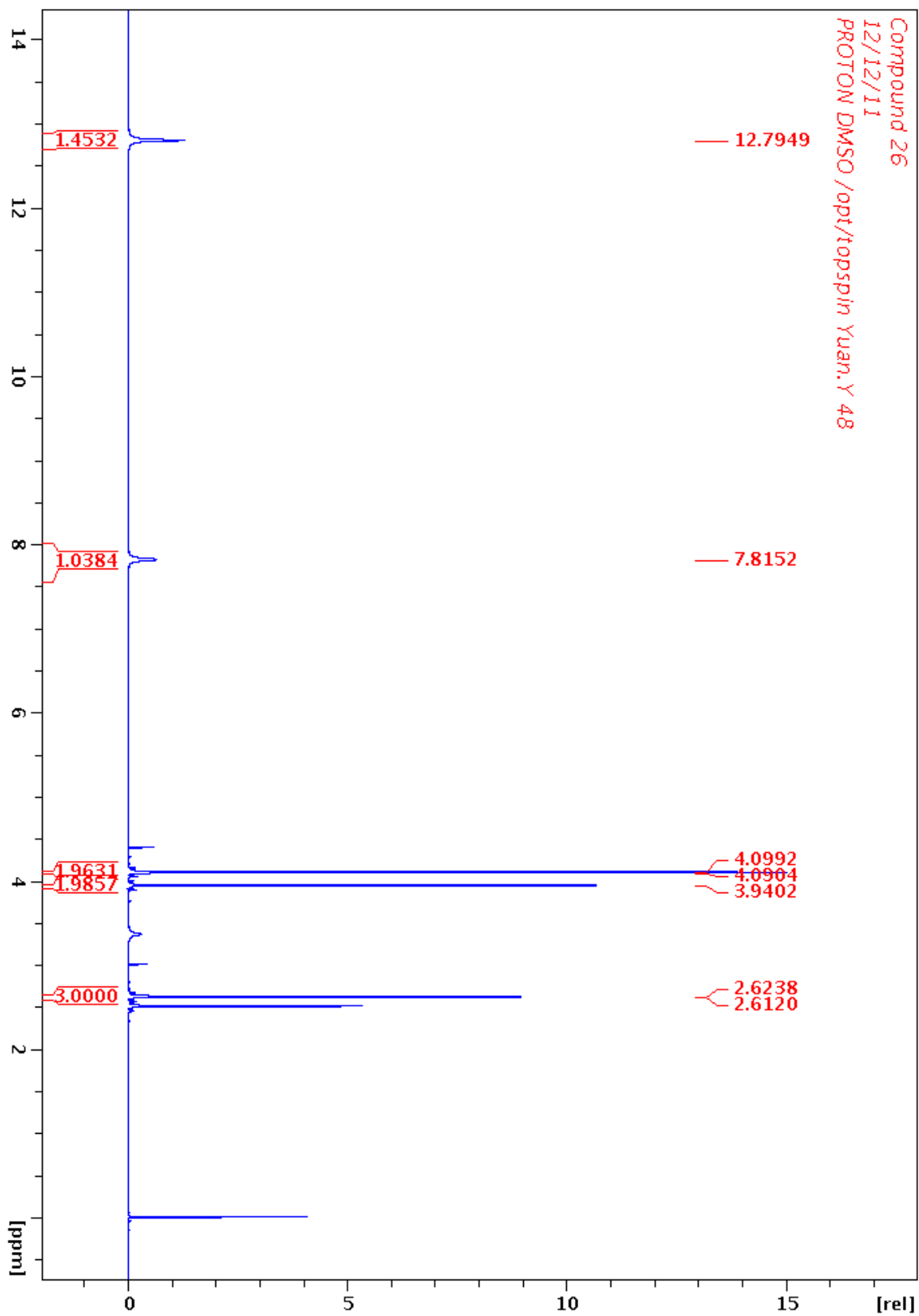
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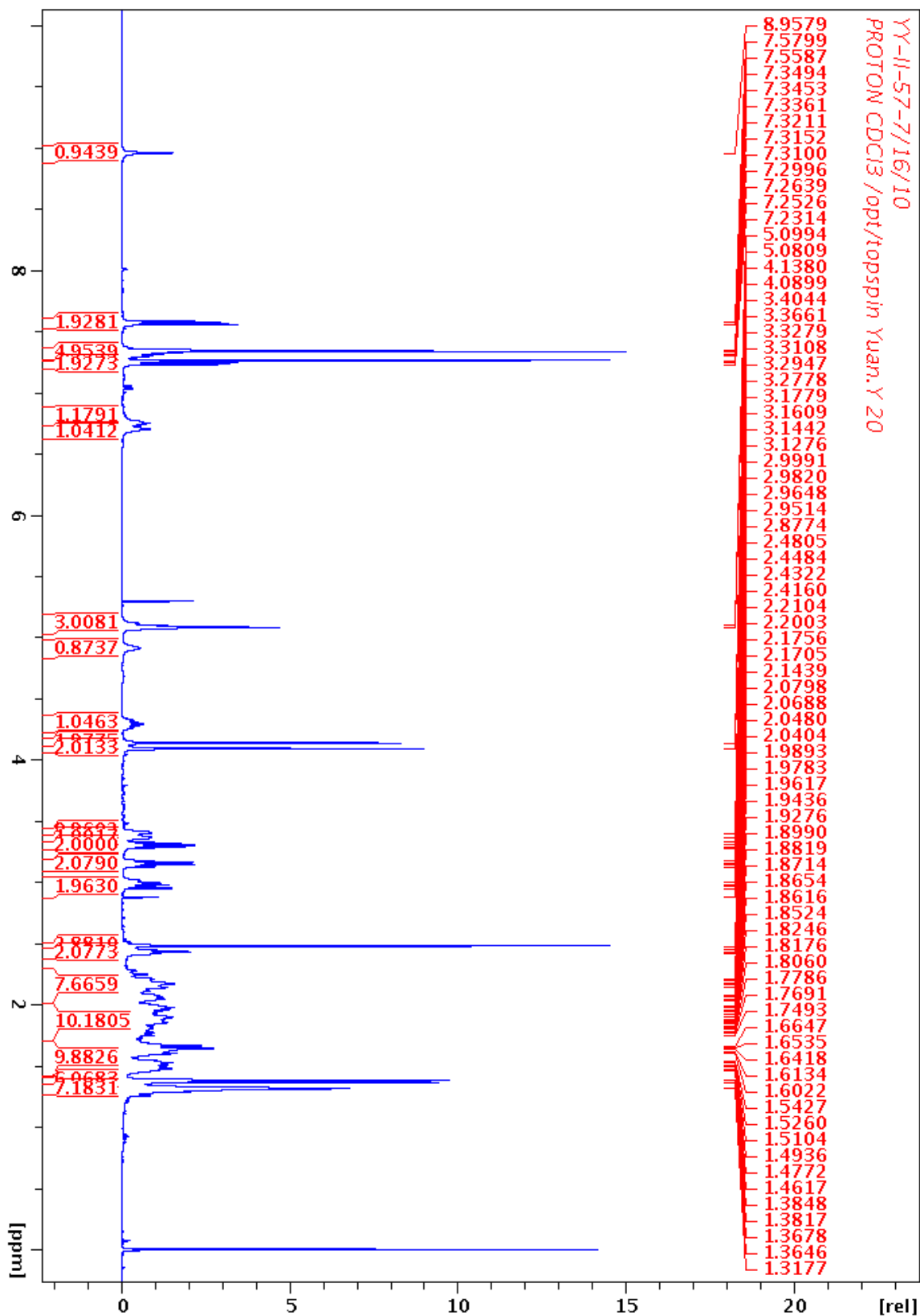


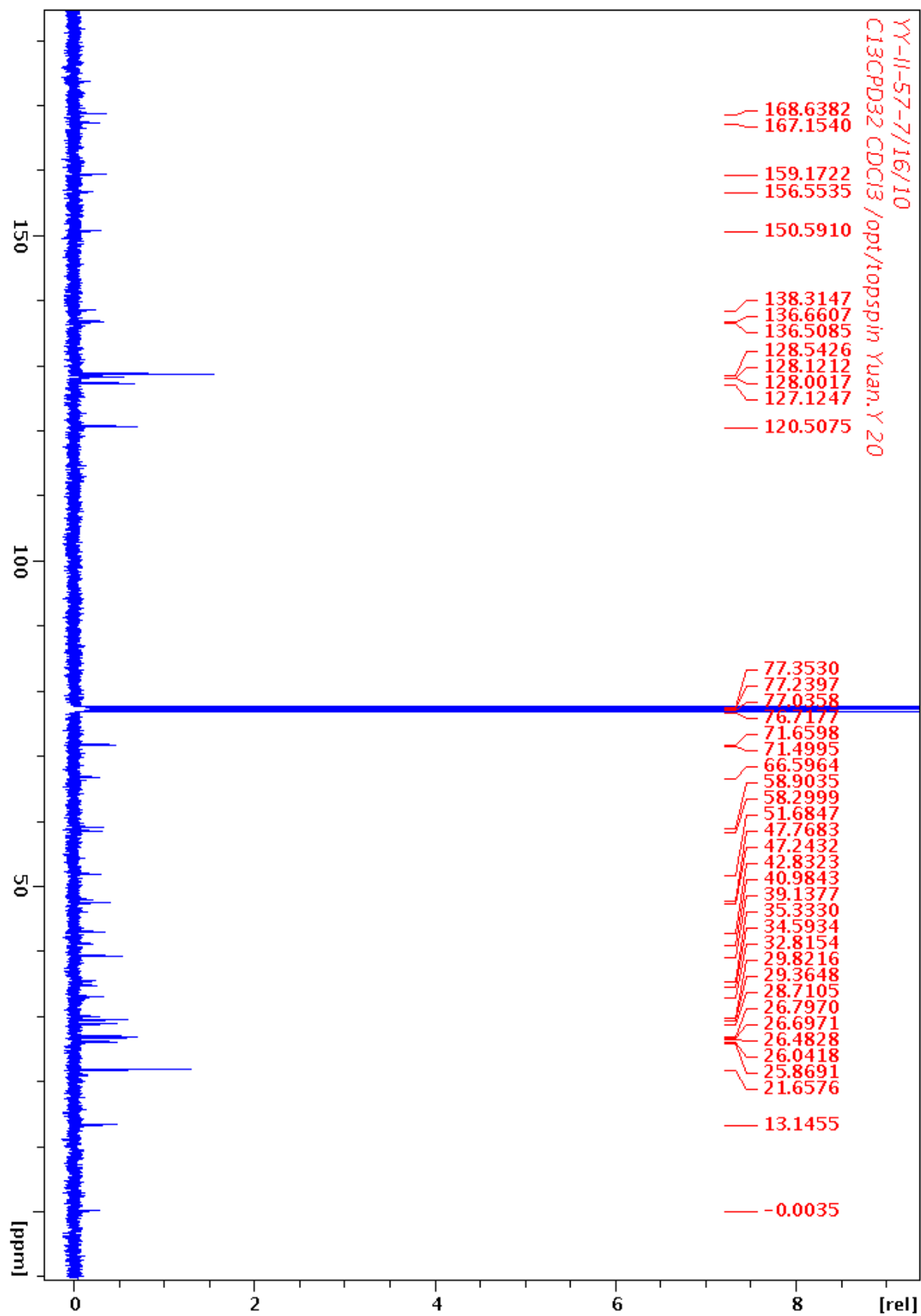


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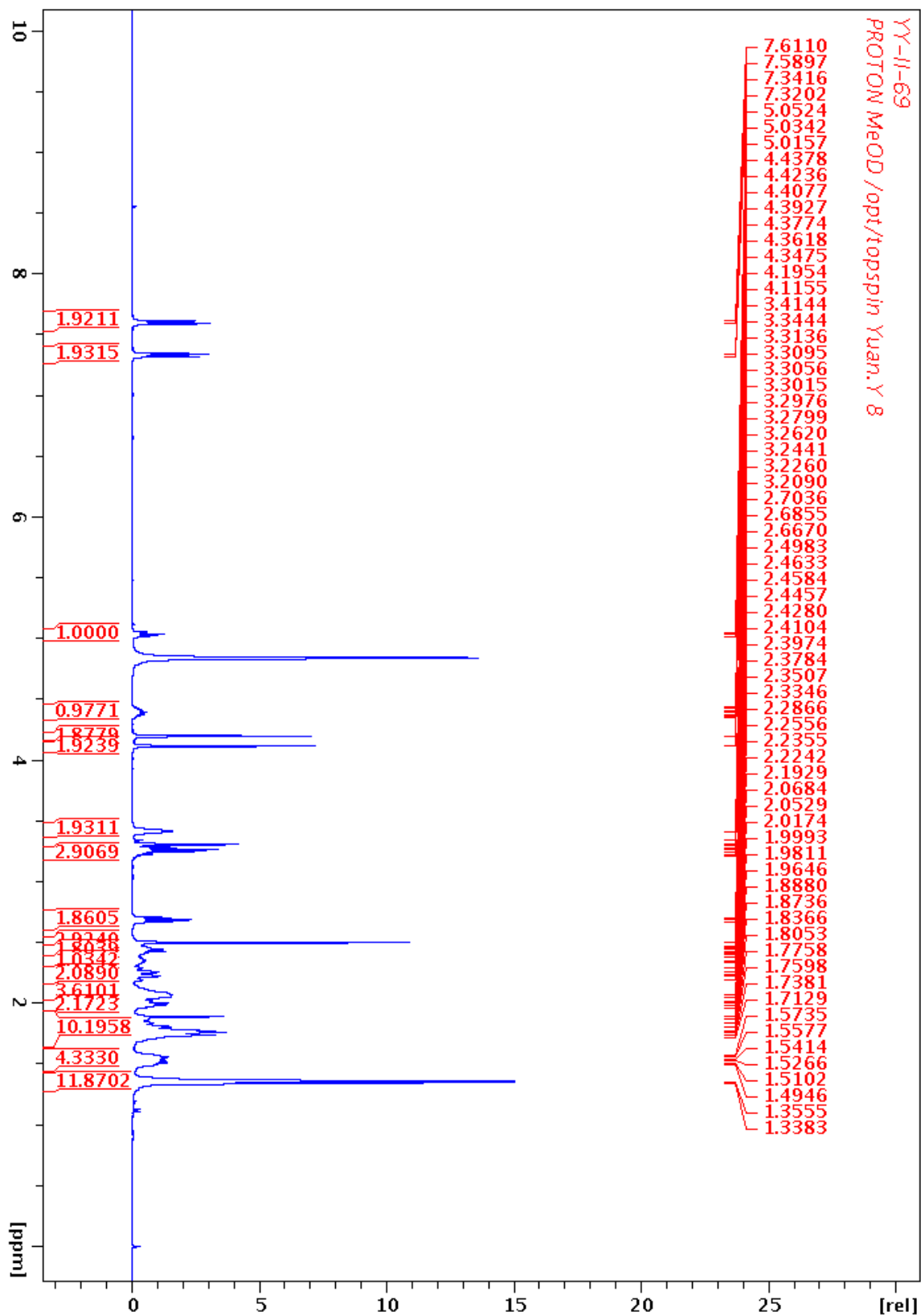


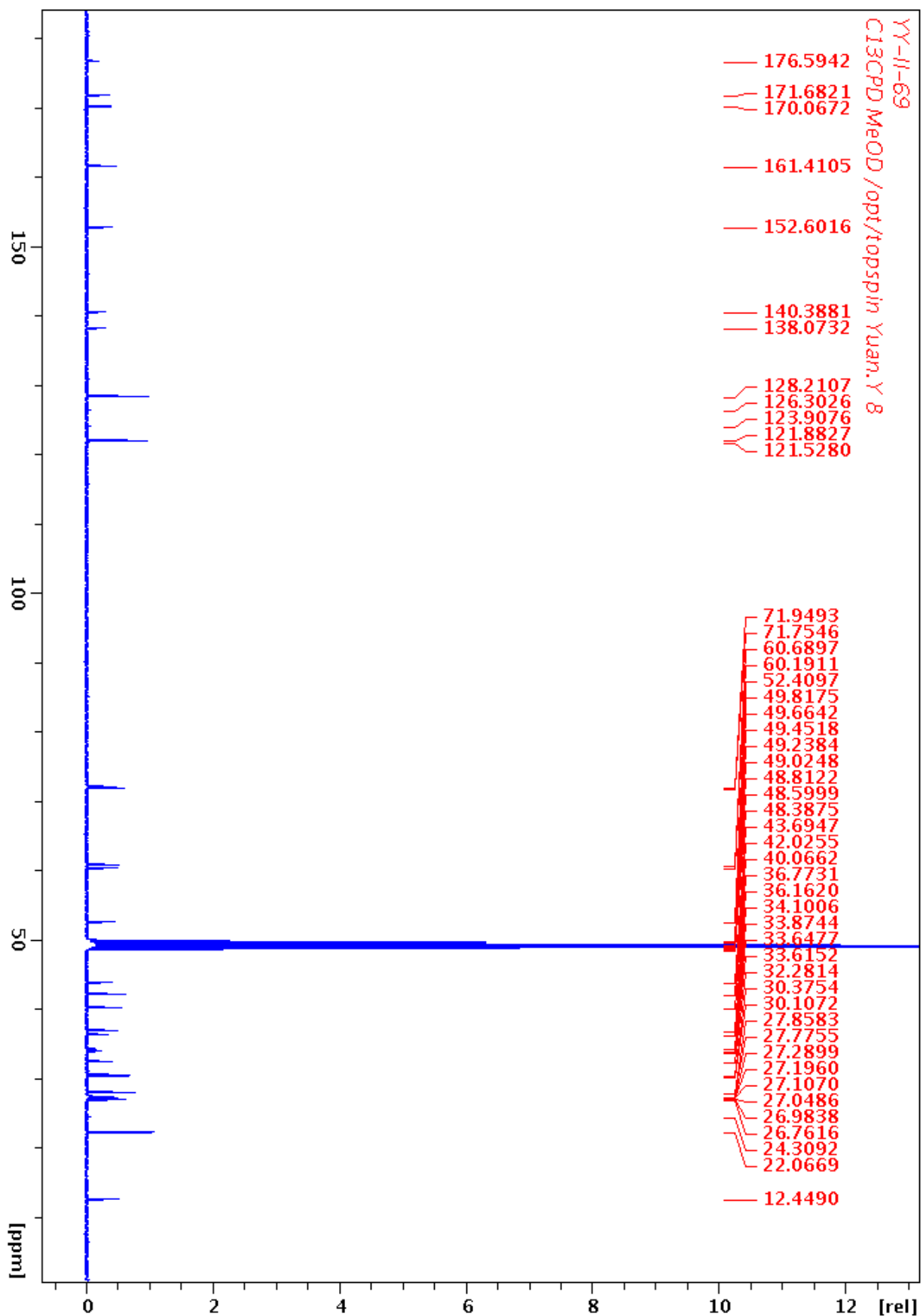
Compound 27





### Compound 28





# Maraviroc

