

## *Supplementary Information*

### **Structure–Activity Relationship Studies on an Antitumor Marine Macrolide Using Aplyronine A–Swinholide A Hybrid**

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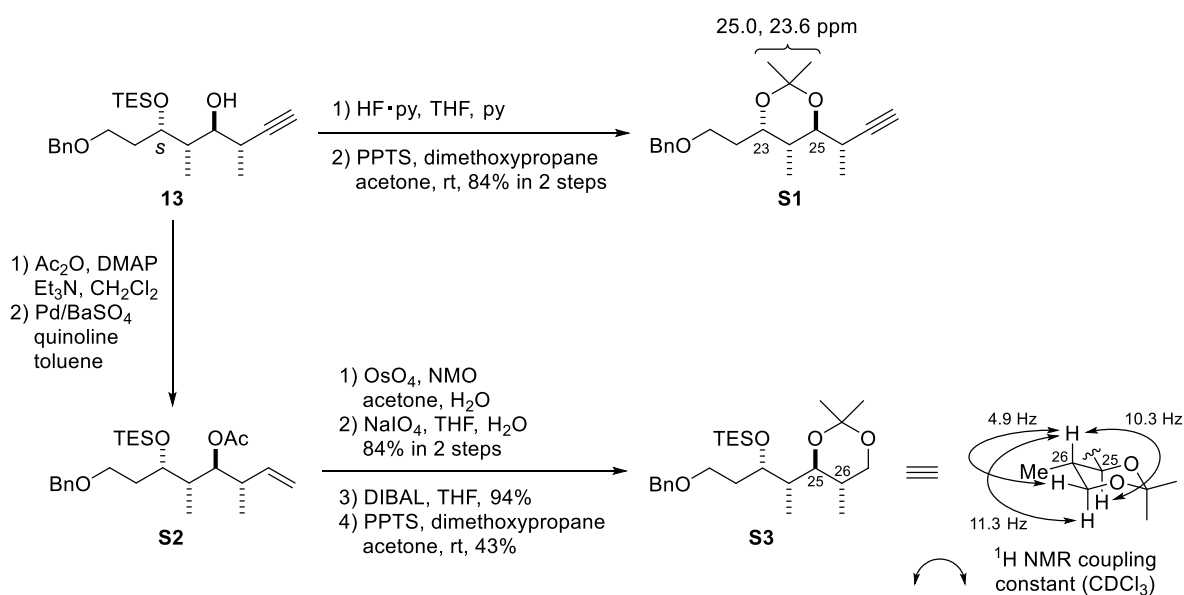
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## Determination of the absolute configurations at C25 and C26 in **13**

The stereochemistry of **13** was determined as follows (Scheme S1). Acetylene **13** was converted into 1,3-acetonide **S1**. The relative stereochemistry of C23 and C25 in **S1** was determined to be anti by the  $^{13}\text{C}$  chemical shifts of two acetonide methyl groups ( $\delta_{\text{C}}$  23.6, 25.0).<sup>1</sup> In addition, acetylene **13** was converted into 1,3-acetonide **S3**, and the relative stereochemistry of C25 and C26 was determined to be anti by  $^1\text{H}$ - $^1\text{H}$  coupling constants.



**Scheme S1.** Determination of the absolute configurations at C25 and C26 in **13**

## Reference

- 1) Rychnovsky, S. D.; Rogers, B.; Yang, G. *J. Org. Chem.* **1993**, *58*, 3511.

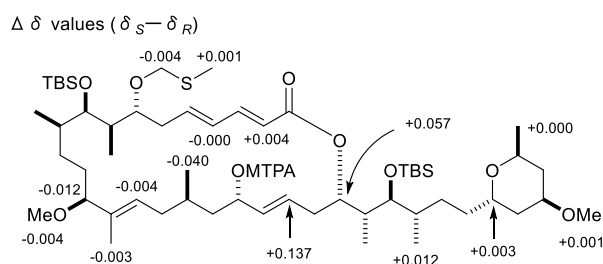
## Determination of the absolute configuration at C19 of **S26**

### (*S*)-MTPA ester of **26**

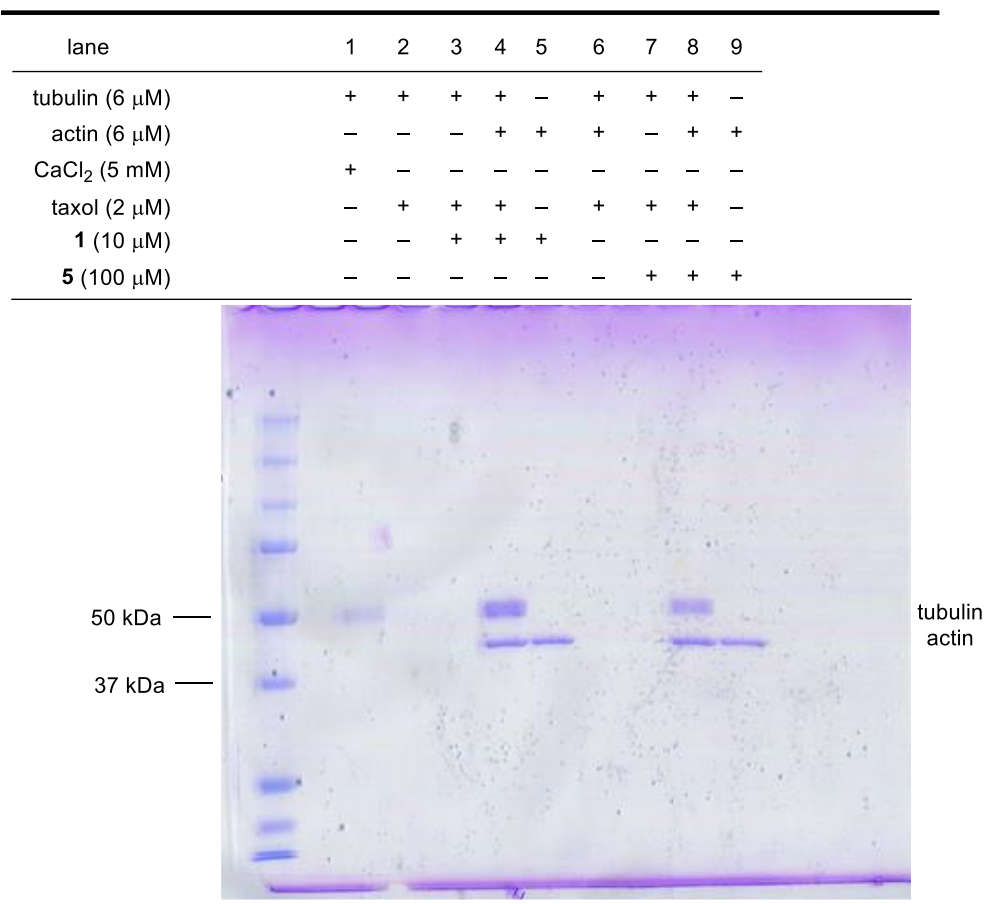
To a stirred solution of alcohol **26** (2.5 mg, 2.5  $\mu\text{mol}$ ) in  $\text{CH}_2\text{Cl}_2$  (1.0 mL) were added (*R*)-(+)-MTPACl (9.4  $\mu\text{L}$ , 50  $\mu\text{mol}$ ) and DMAP (9.1 mg, 75  $\mu\text{mol}$ ). The reaction mixture was stirred at room temperature for 2 h, poured into saturated aqueous  $\text{NaHCO}_3$  (2.0 mL), and extracted with  $\text{CH}_2\text{Cl}_2$  (3.0 mL  $\times$  3). The combined extracts were washed with brine (5 mL), dried over  $\text{Na}_2\text{SO}_4$ , and concentrated. The crude product was purified by preparative TLC (hexane–EtOAc 9 : 1) to afford (*S*)-MTPA ester of **26** (2.6 mg, 87%) as a colorless oil.

### (*R*)-MTPA ester of **26**

A solution of alcohol **26** (2.9 mg, 2.9  $\mu\text{mol}$ ) in  $\text{CH}_2\text{Cl}_2$  (1.0 mL) was similarly treated with (*S*)-(–)-MTPACl and DMAP to afford (*R*)-MTPA ester of **26** (2.8 mg, 80%) as a colorless oil.

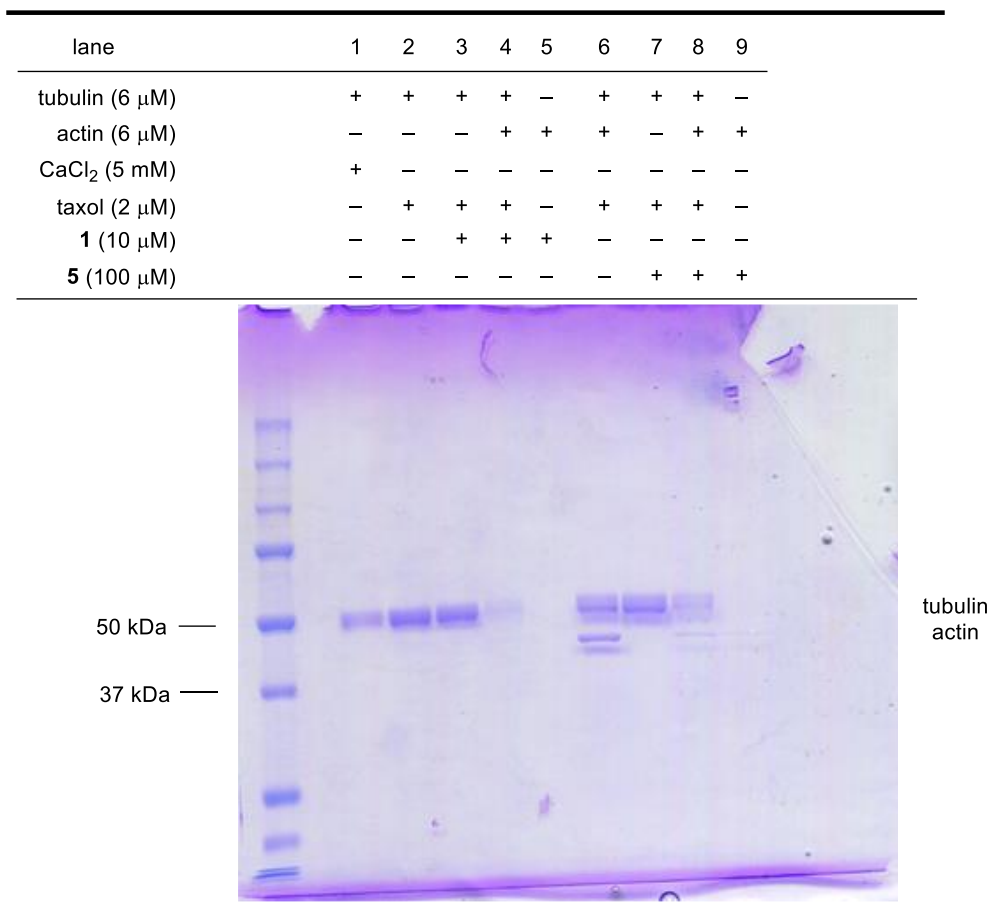


**Figure S1.** The  $\Delta \delta$  values ( $\delta_S - \delta_R$ ) for MTPA esters of **26**



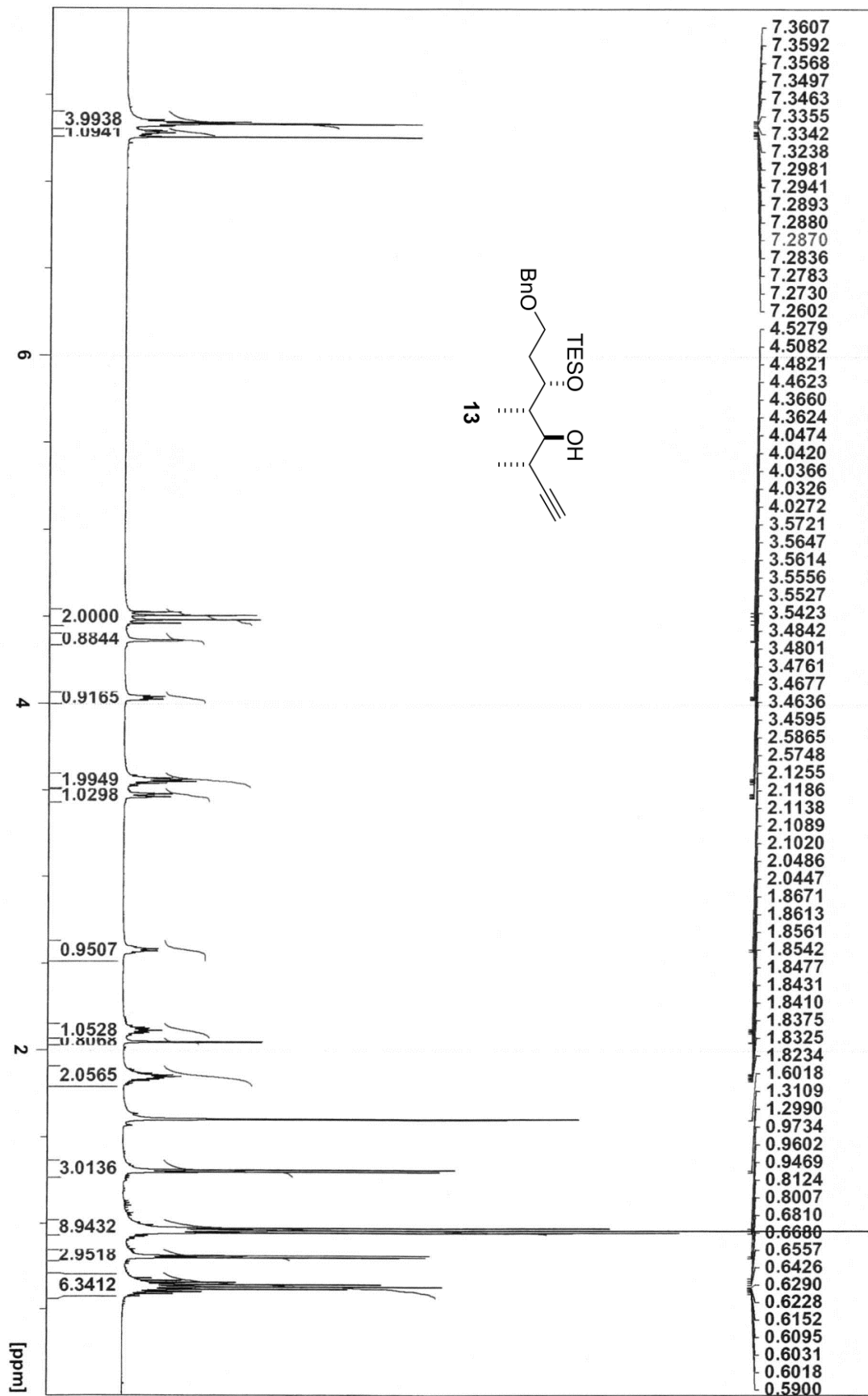
**Figure S2.** SDS-PAGE of the supernatants

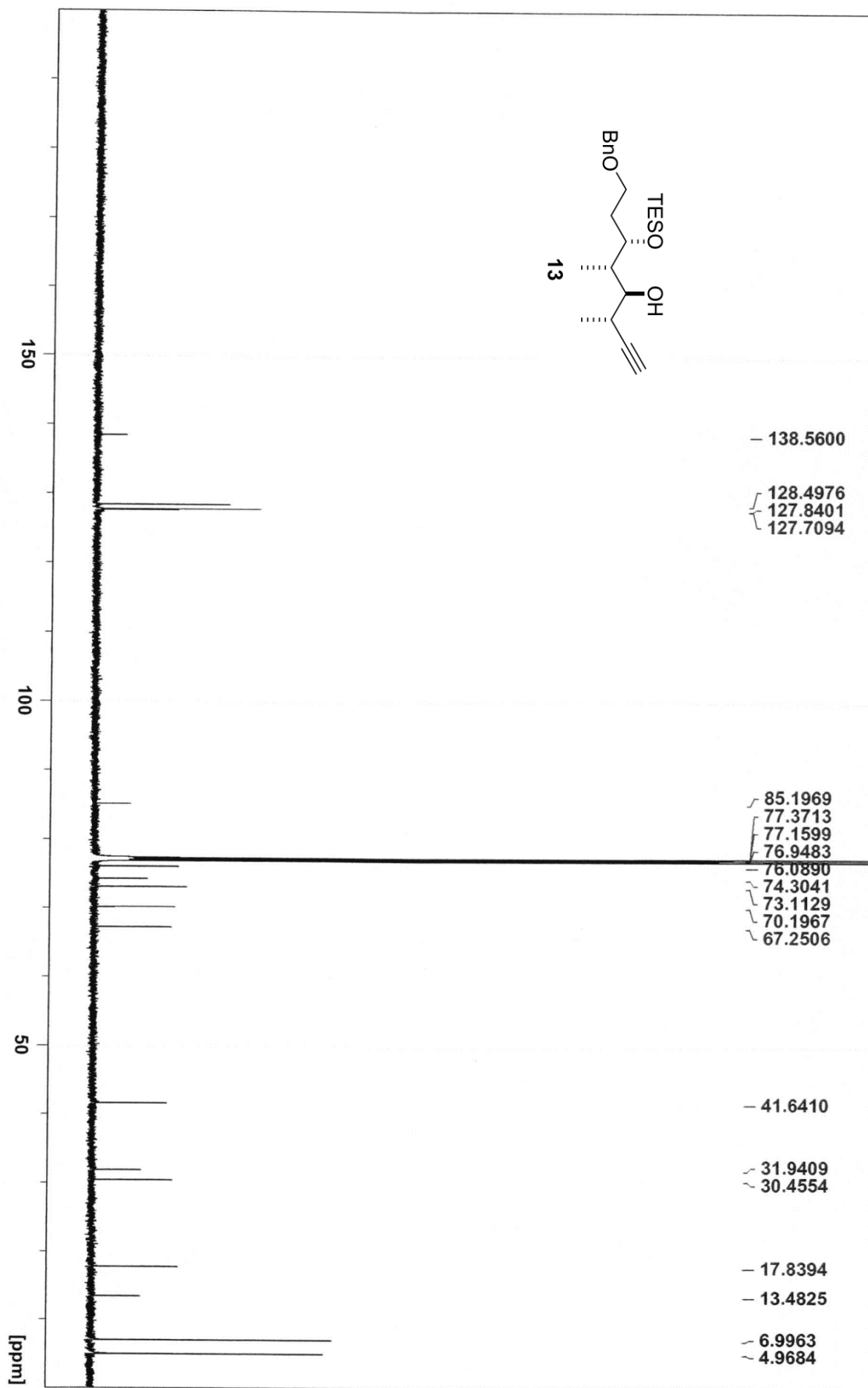
Tubulin was polymerized with taxol in the presence of actin and/or **1** or **5**, and then precipitated by ultracentrifugation. Depolymerized proteins in the supernatant were analyzed by SDS-PAGE, and detected with CBB stain.



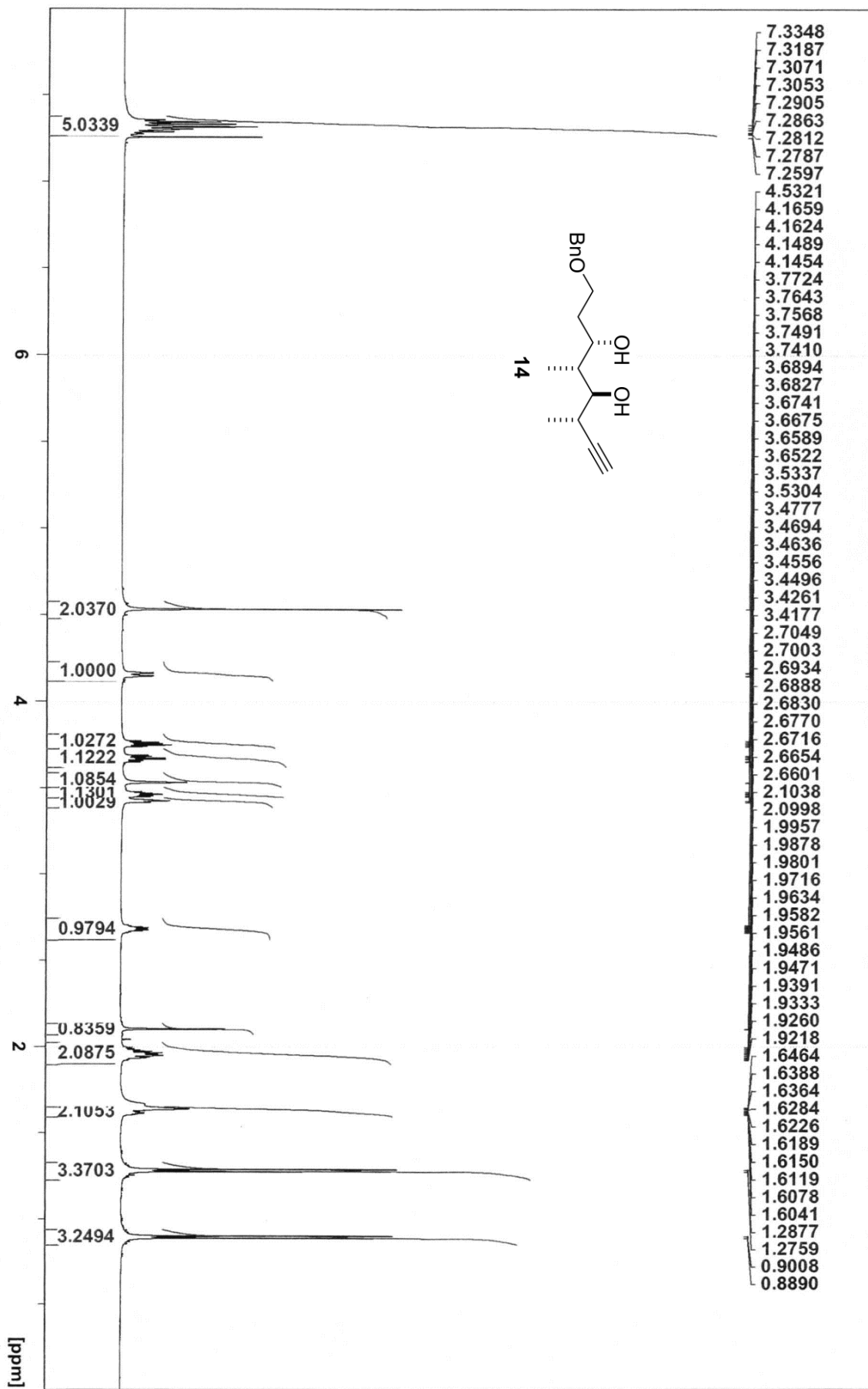
**Figure S3.** SDS-PAGE of the precipitates

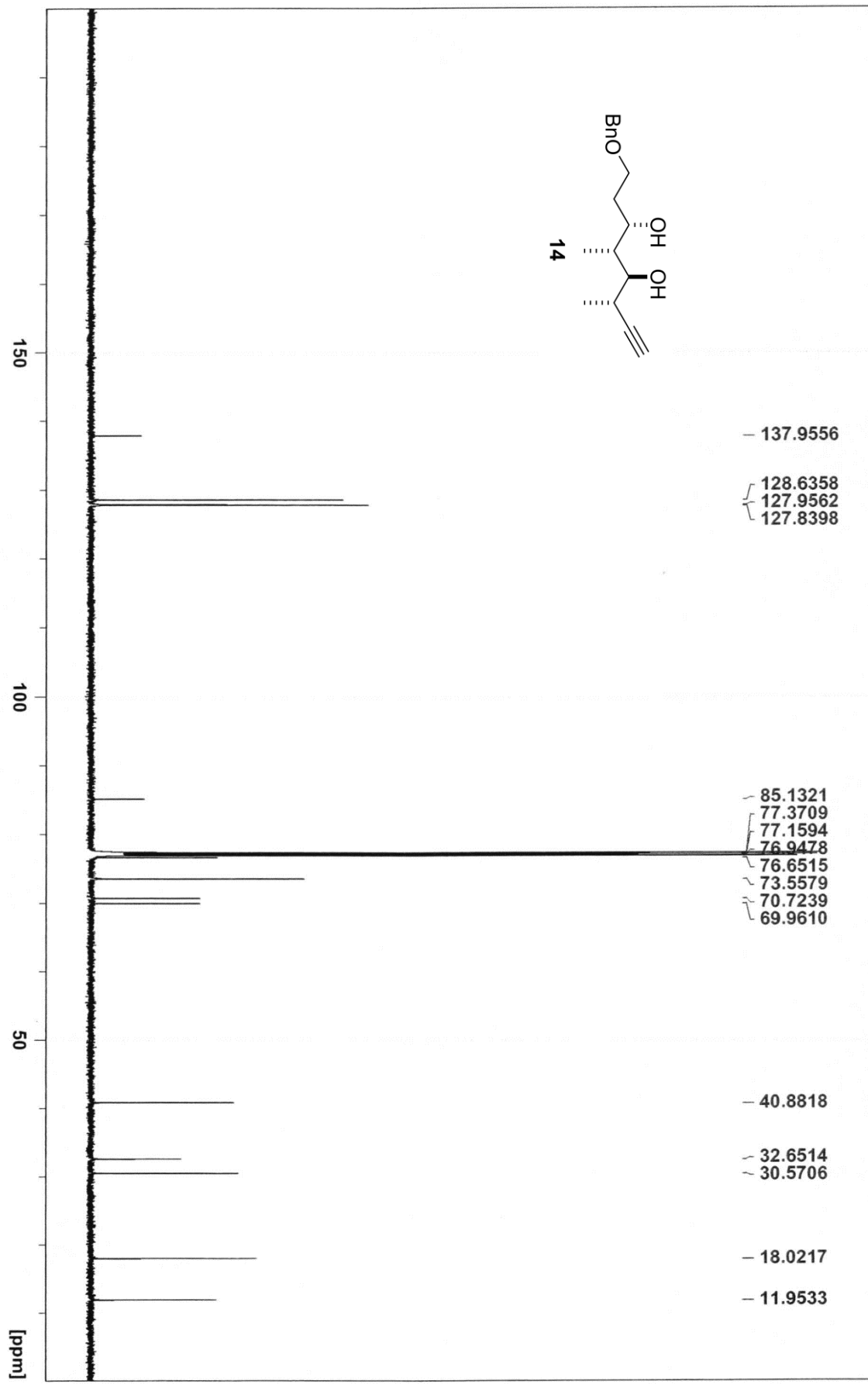
Tubulin was polymerized with taxol in the presence of actin and/or **1** or **5**, and then precipitated by ultracentrifugation. Polymerized proteins in the precipitate were analyzed by SDS-PAGE, and detected with CBB stain.

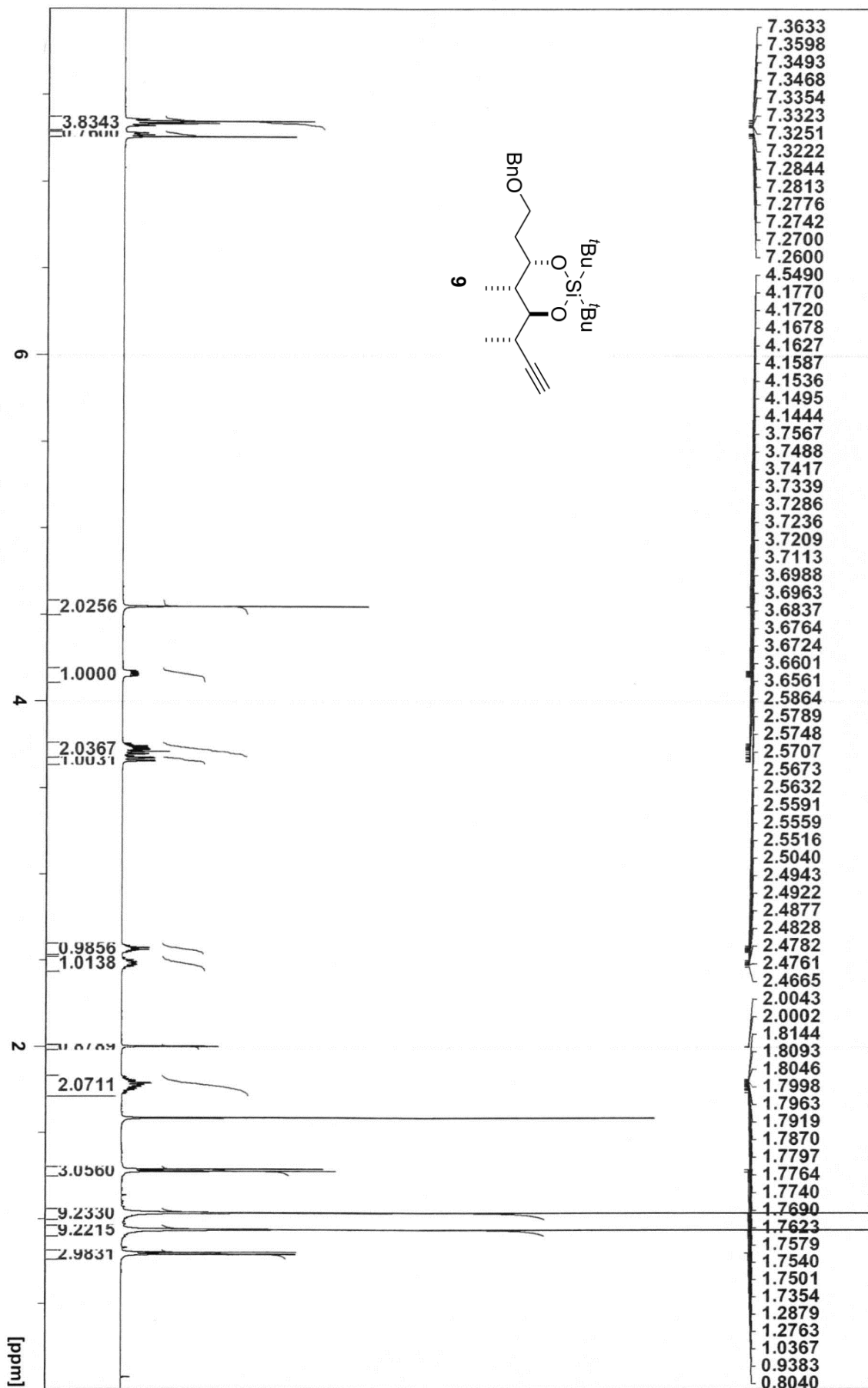


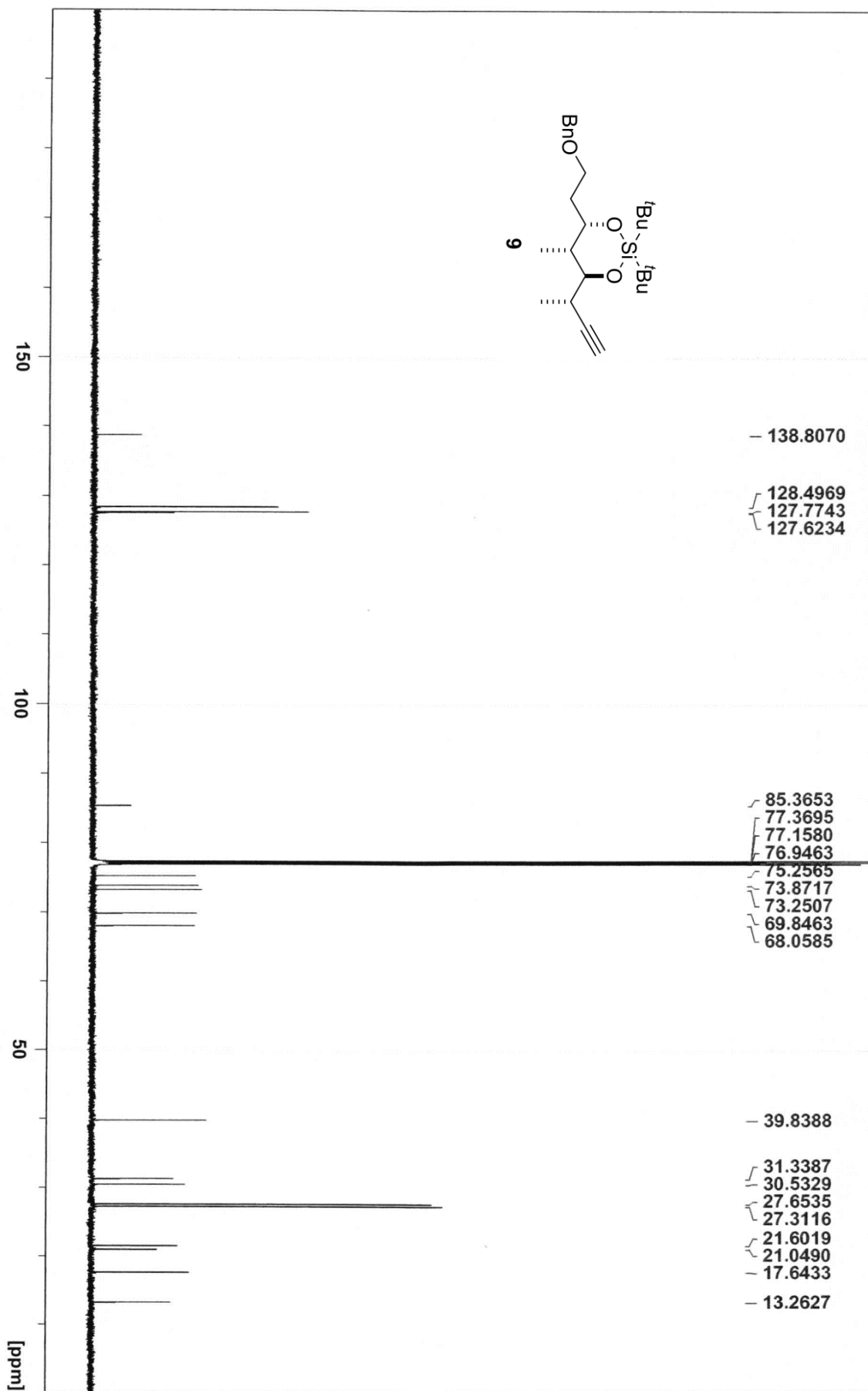


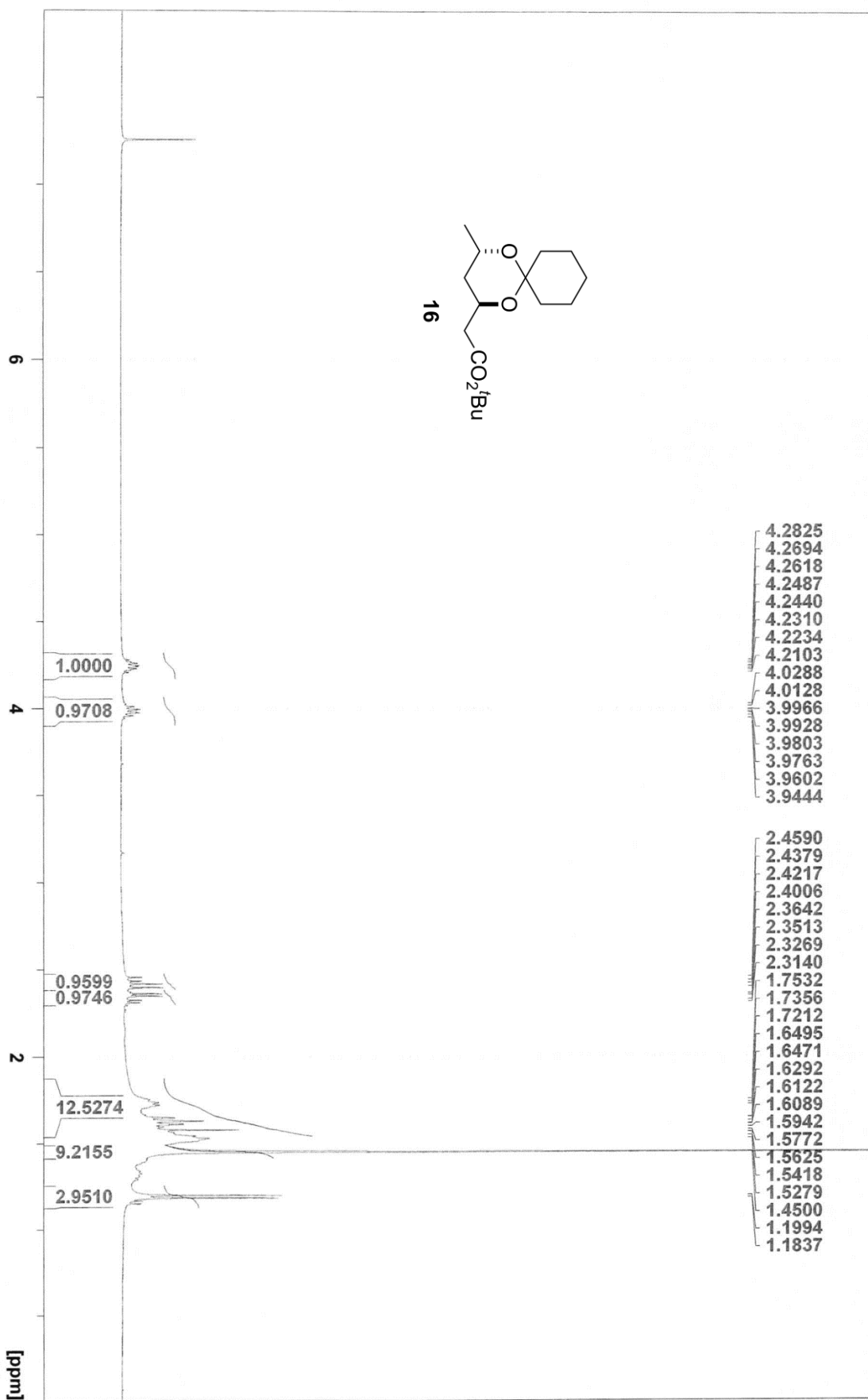


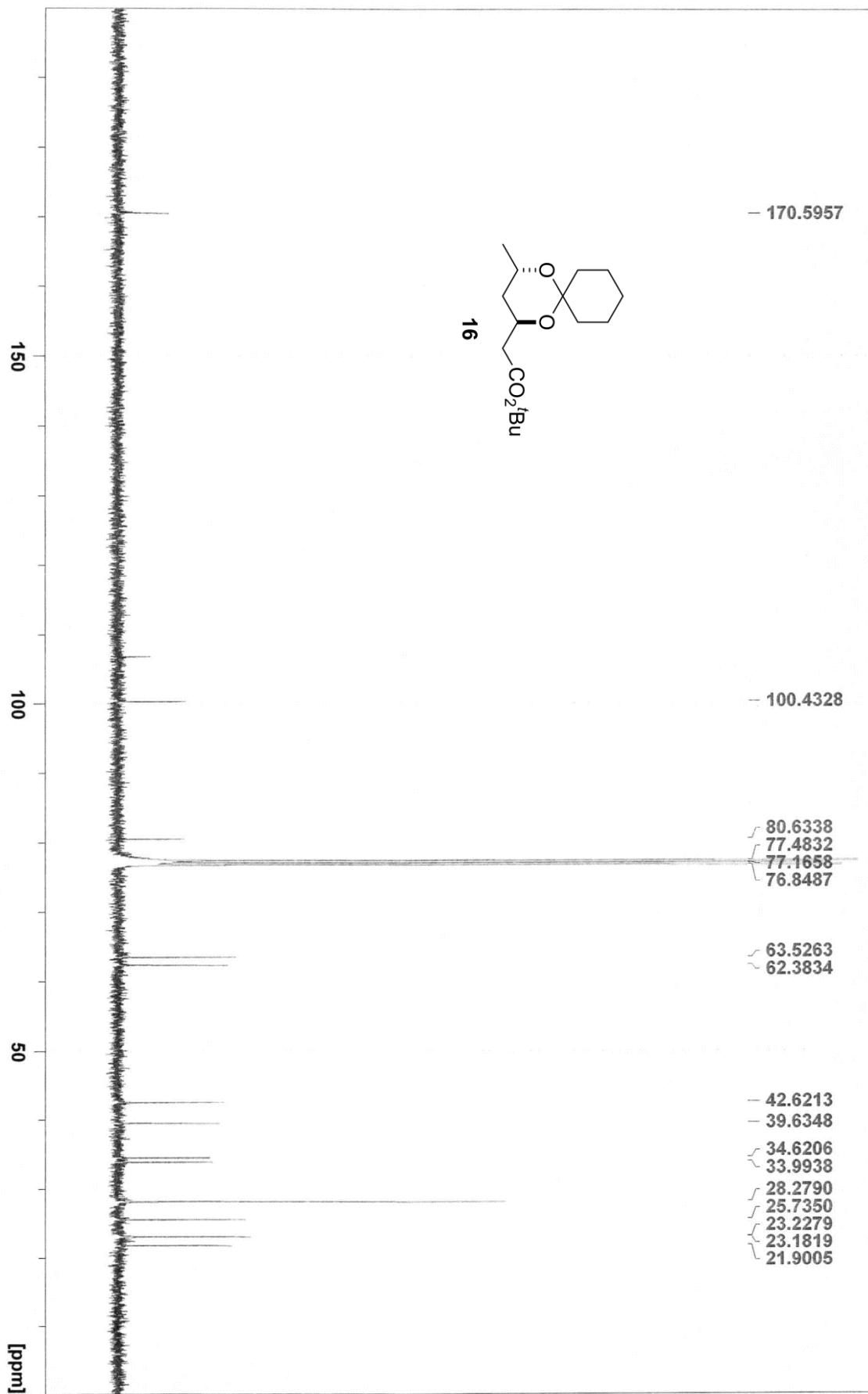


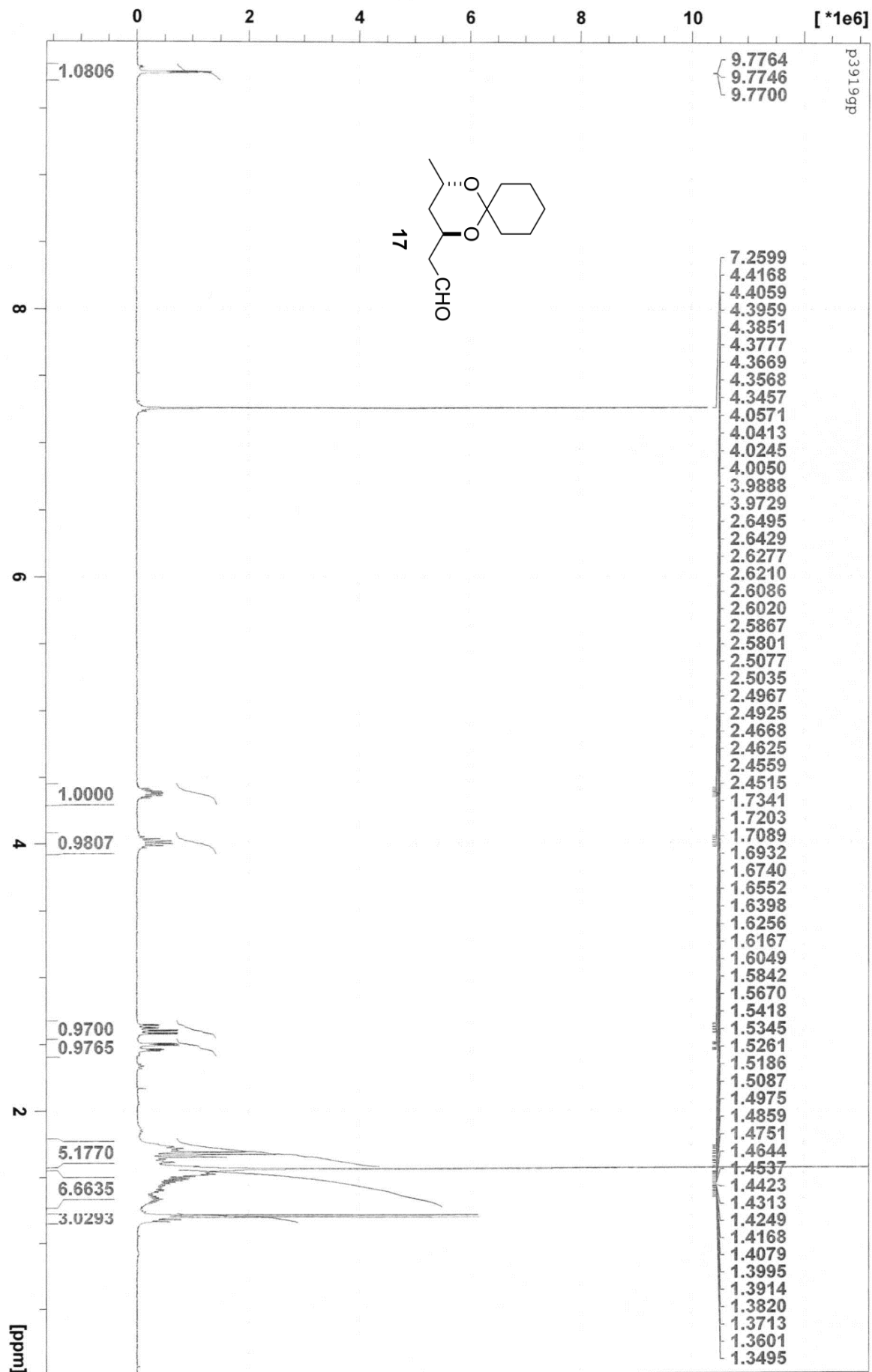


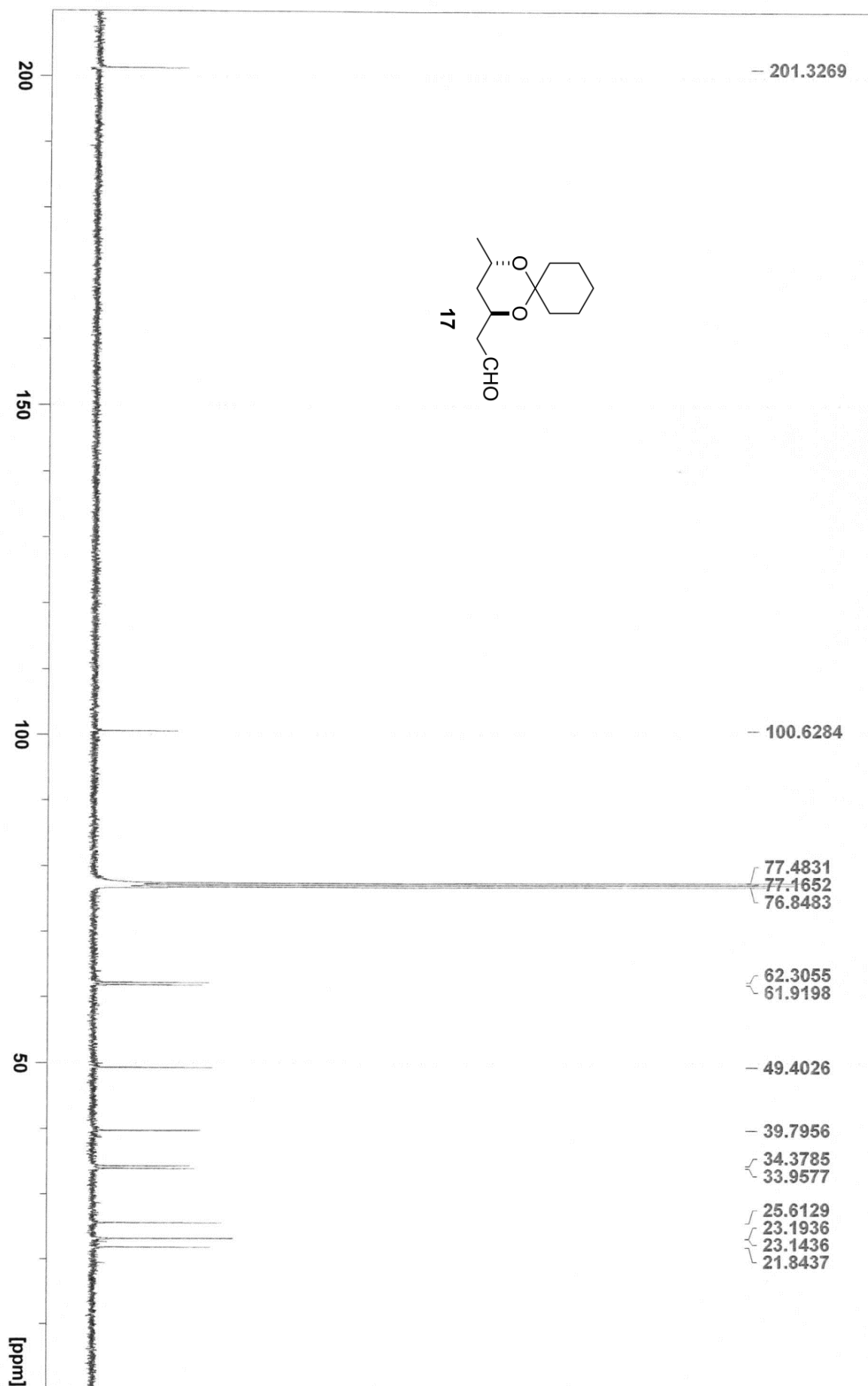




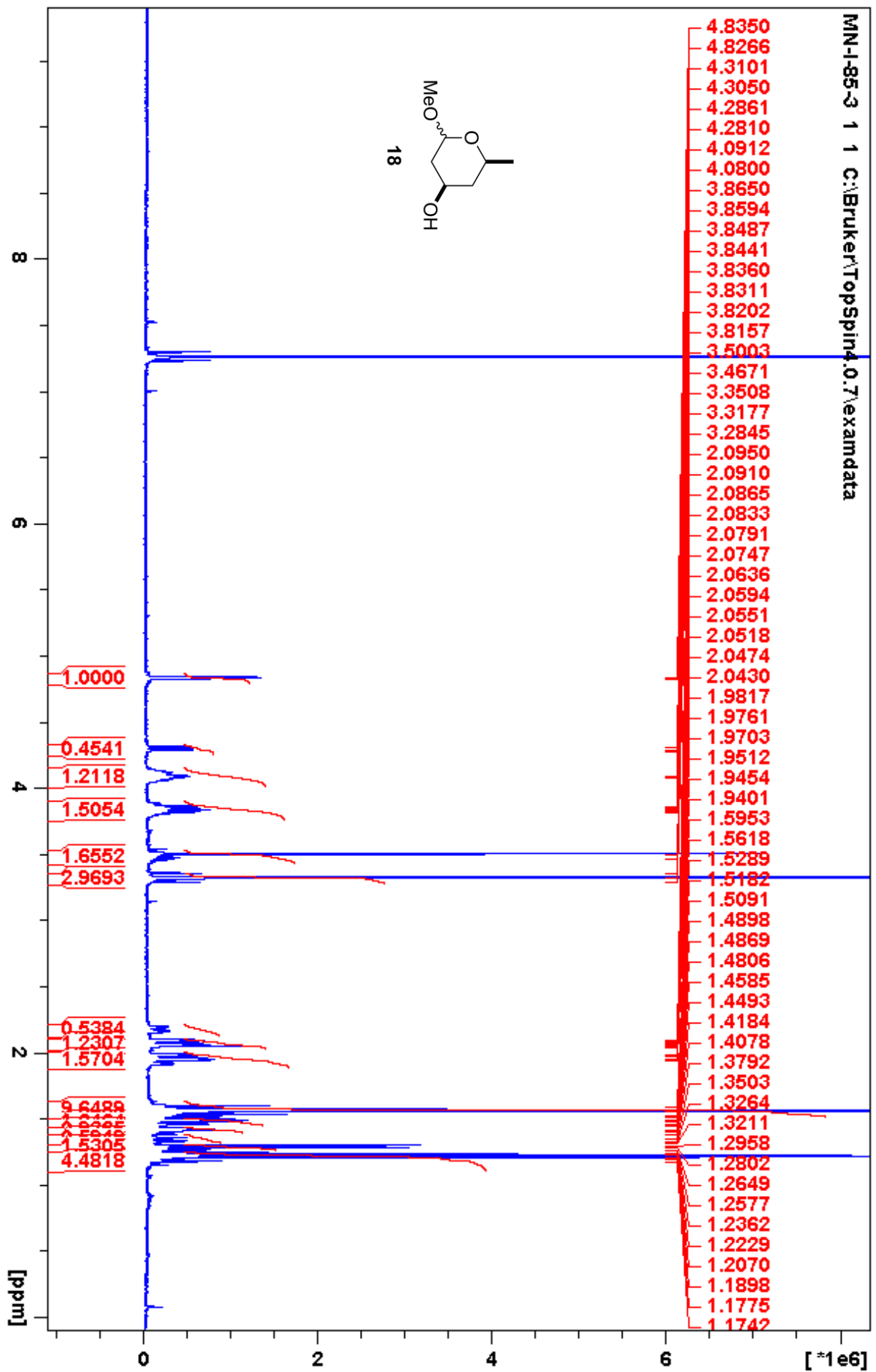


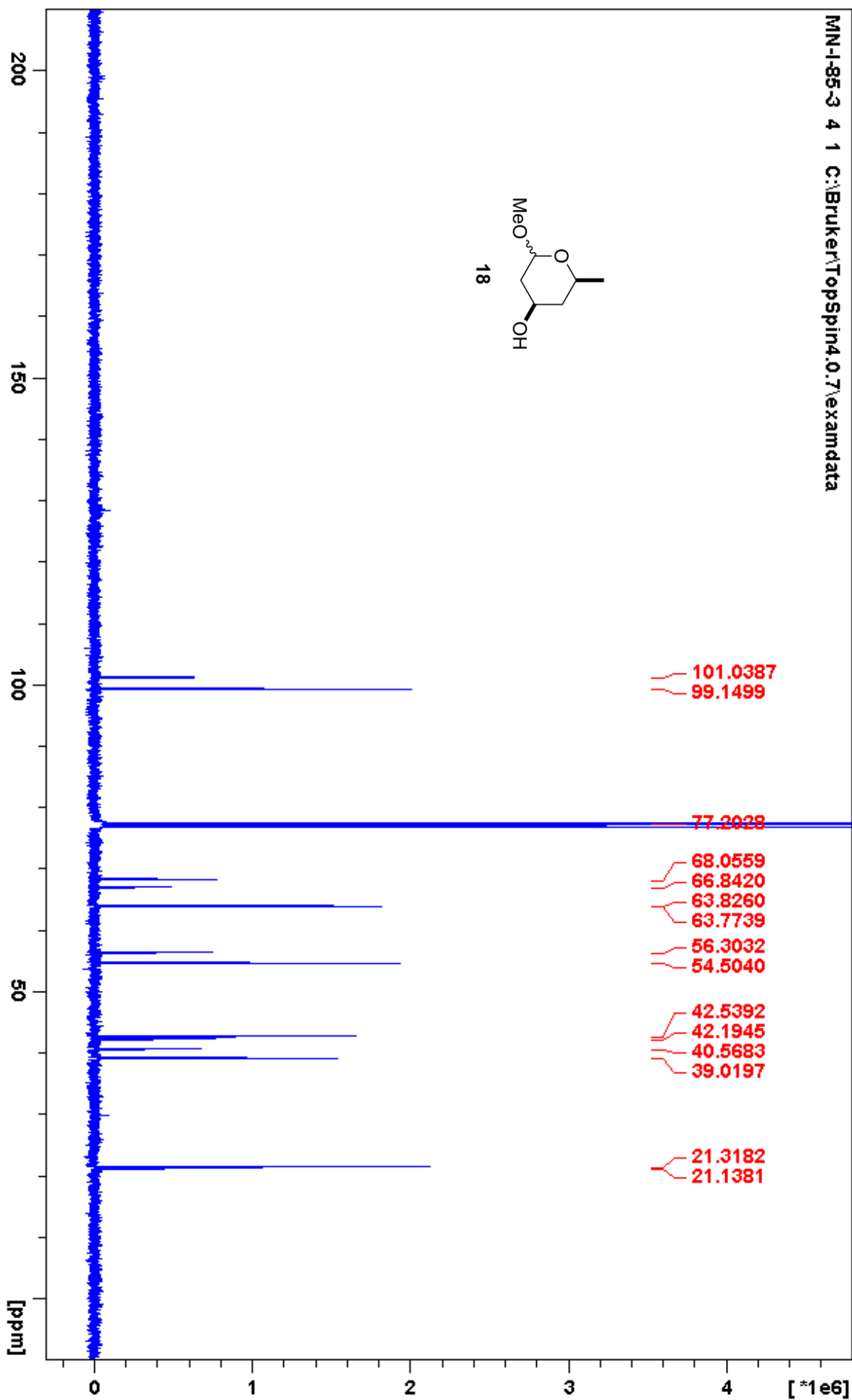
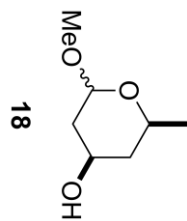


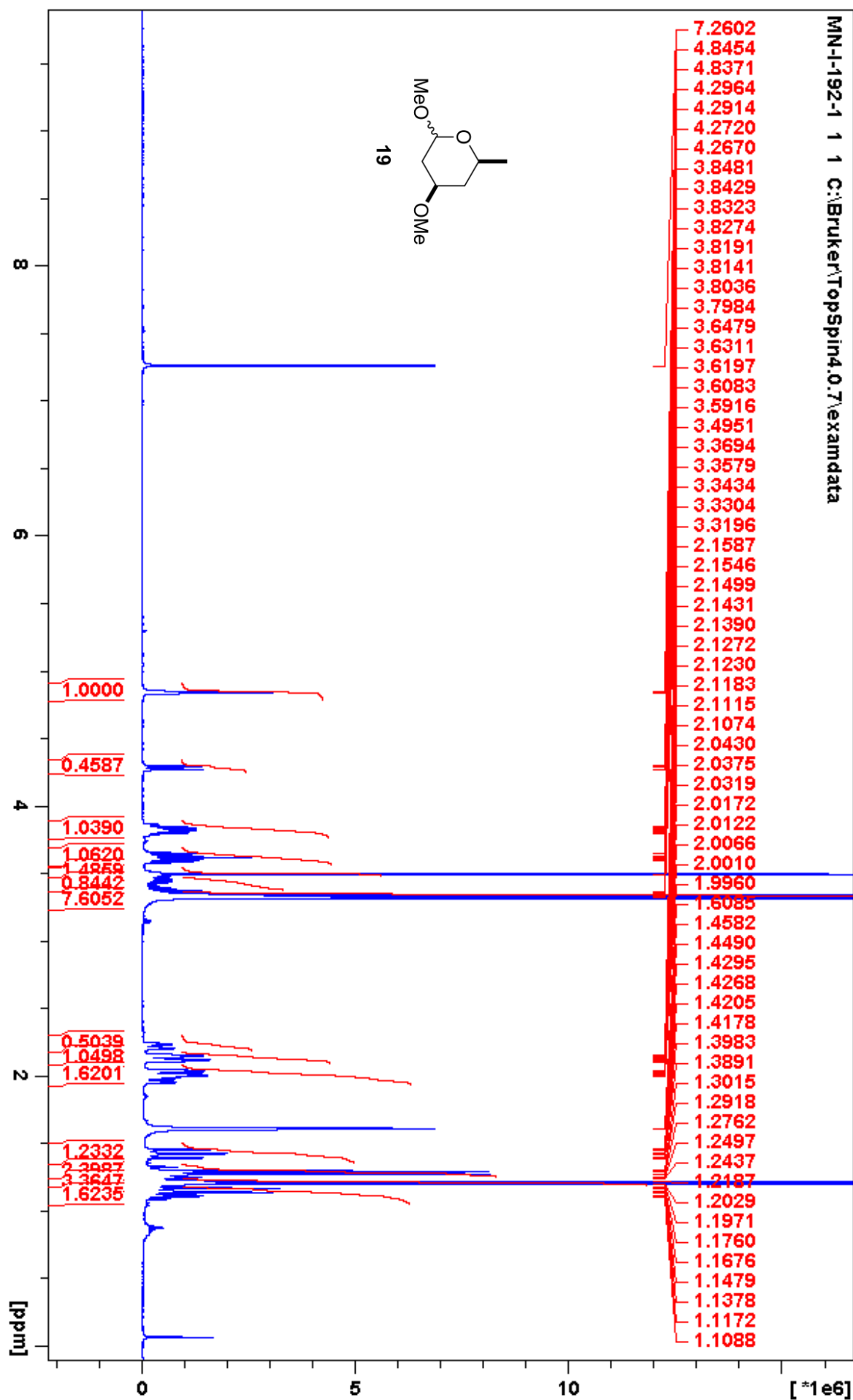
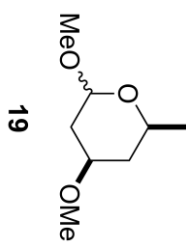


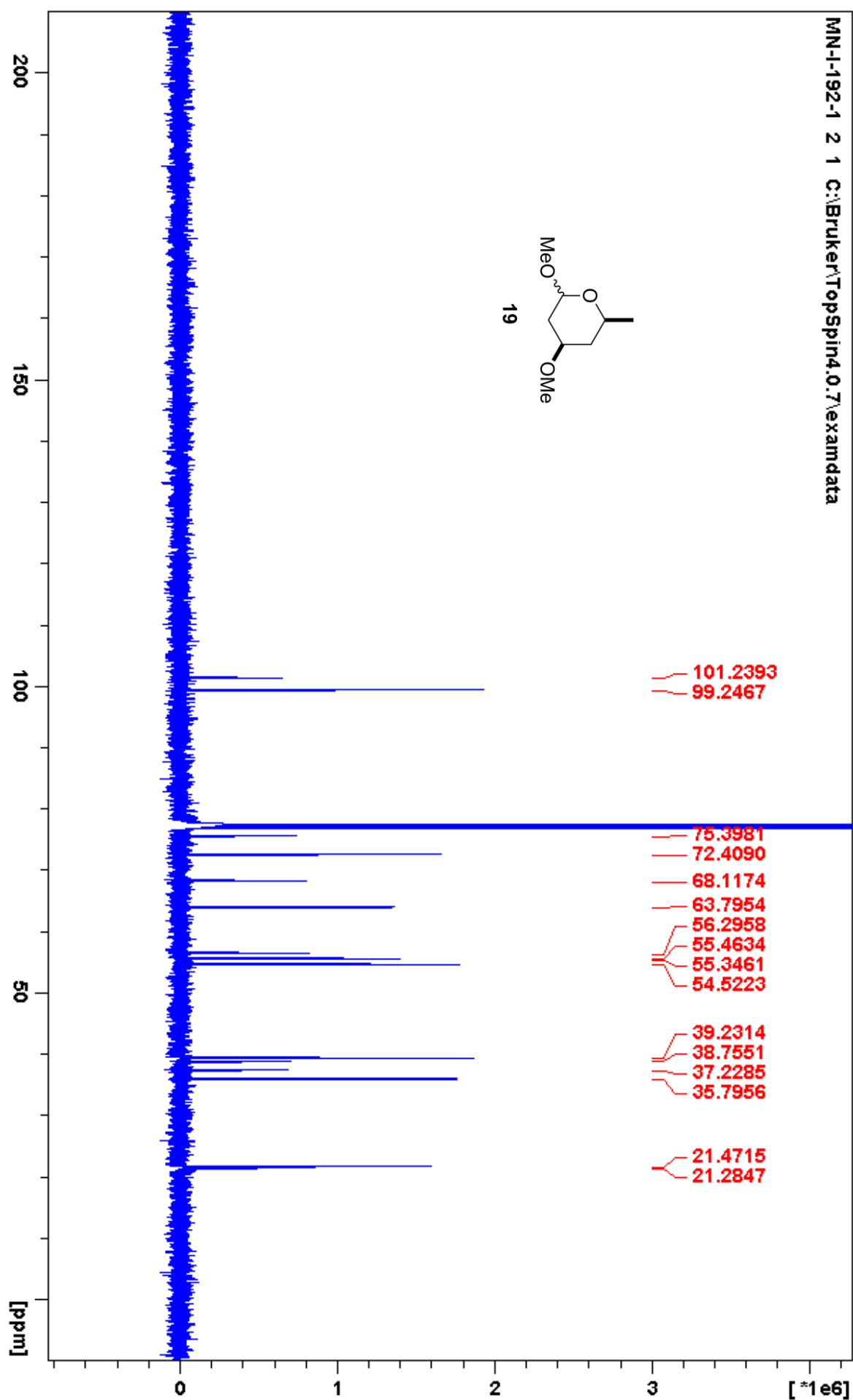
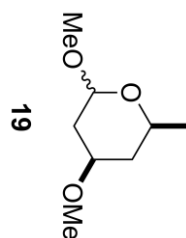




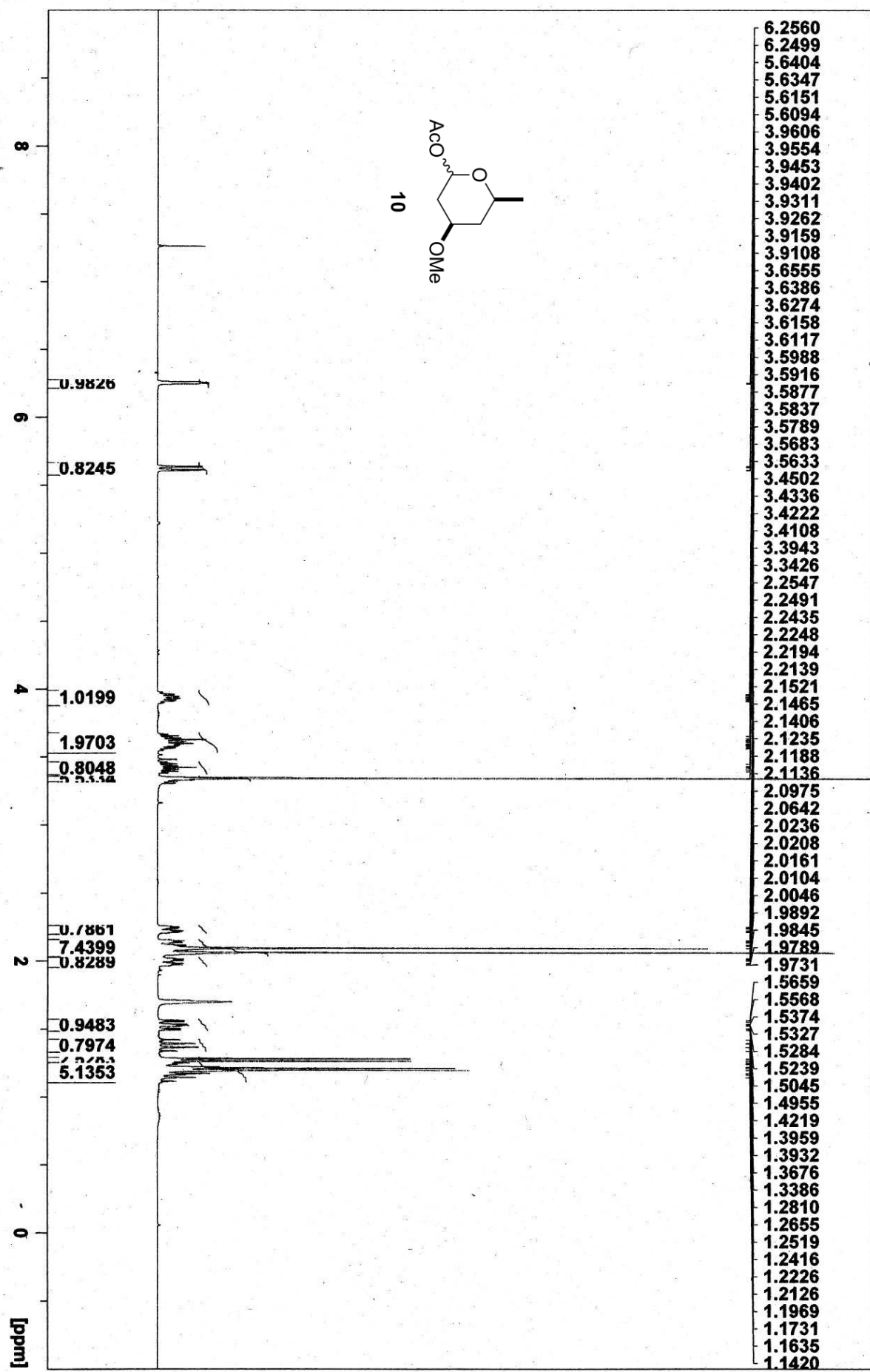


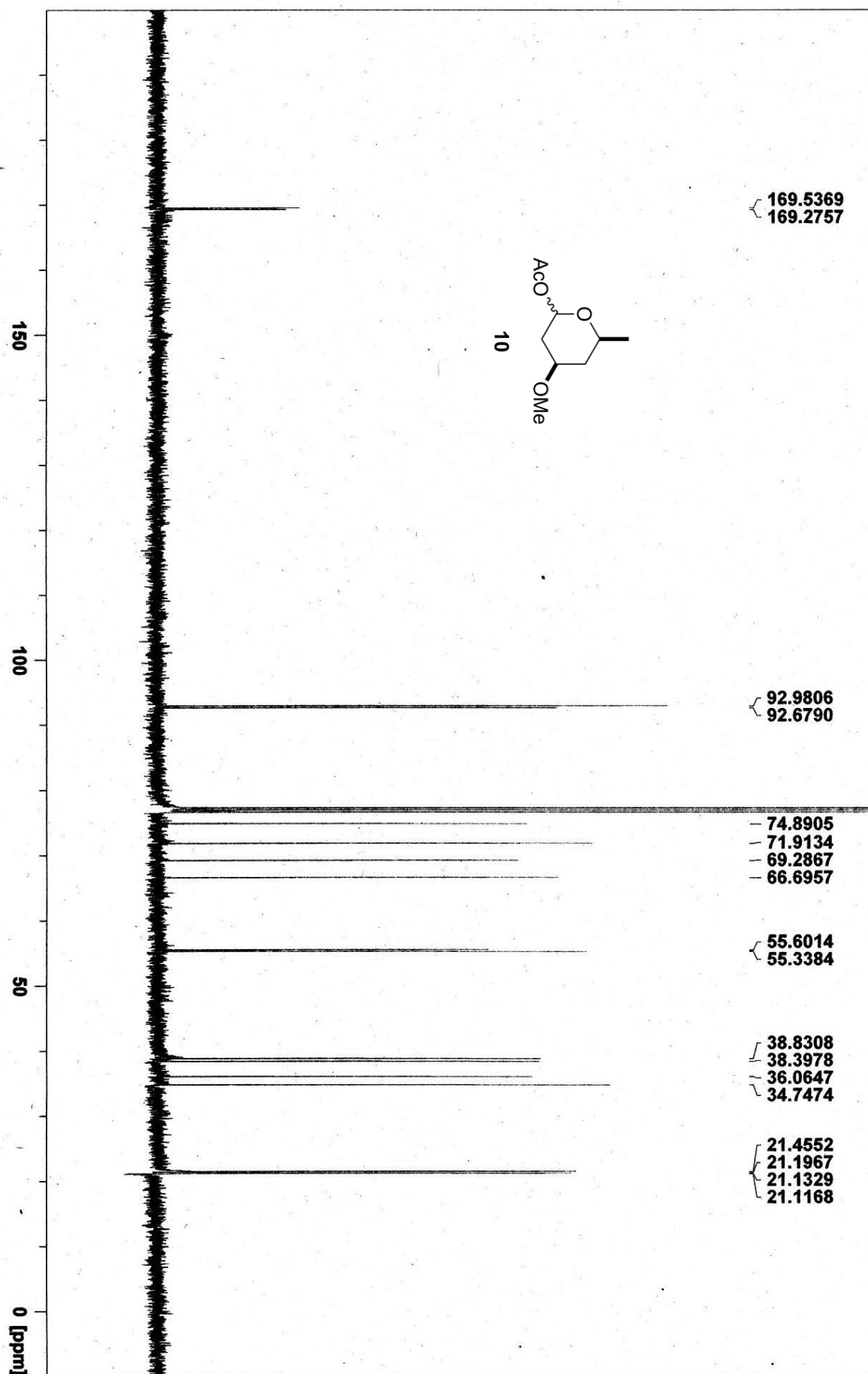


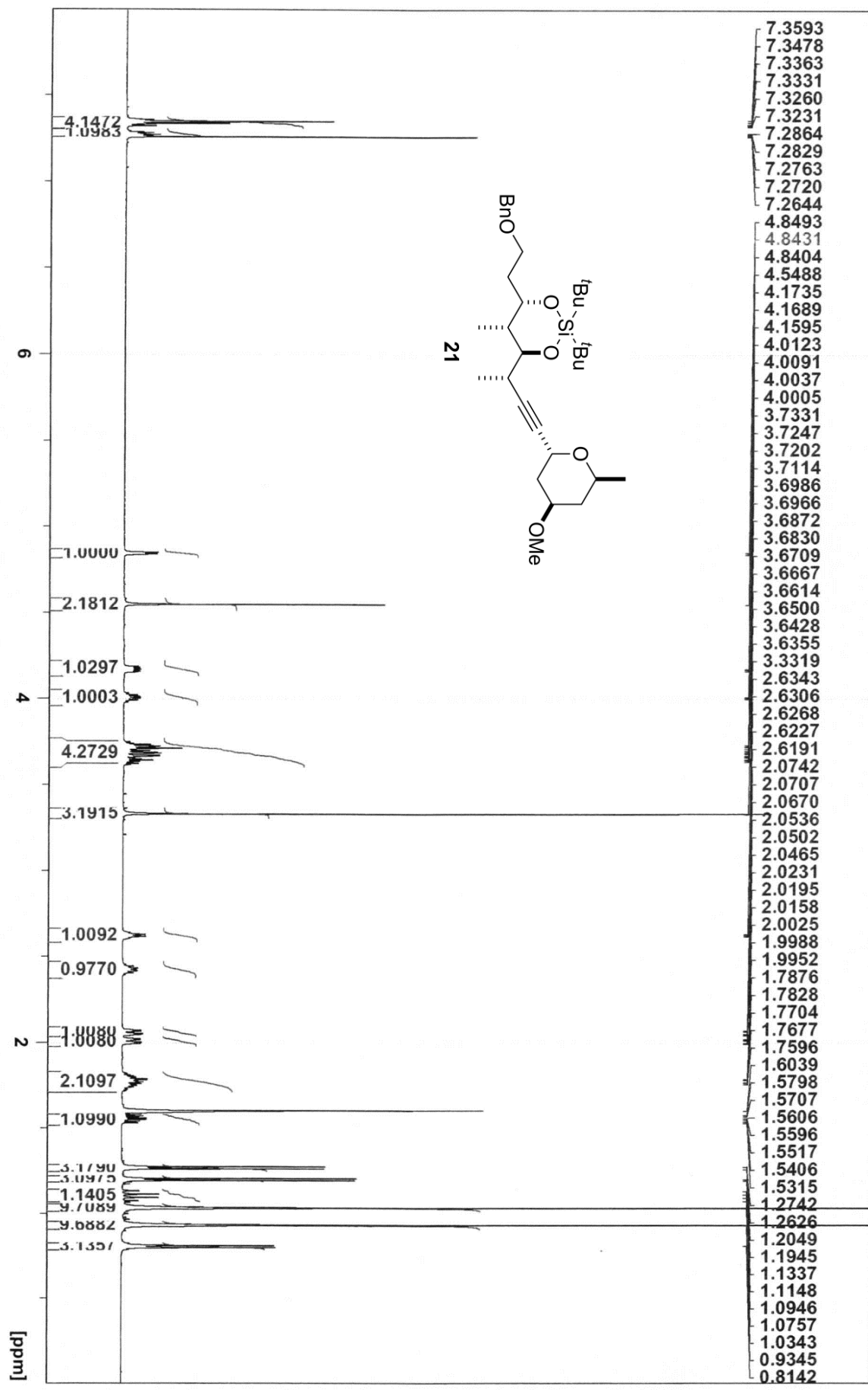


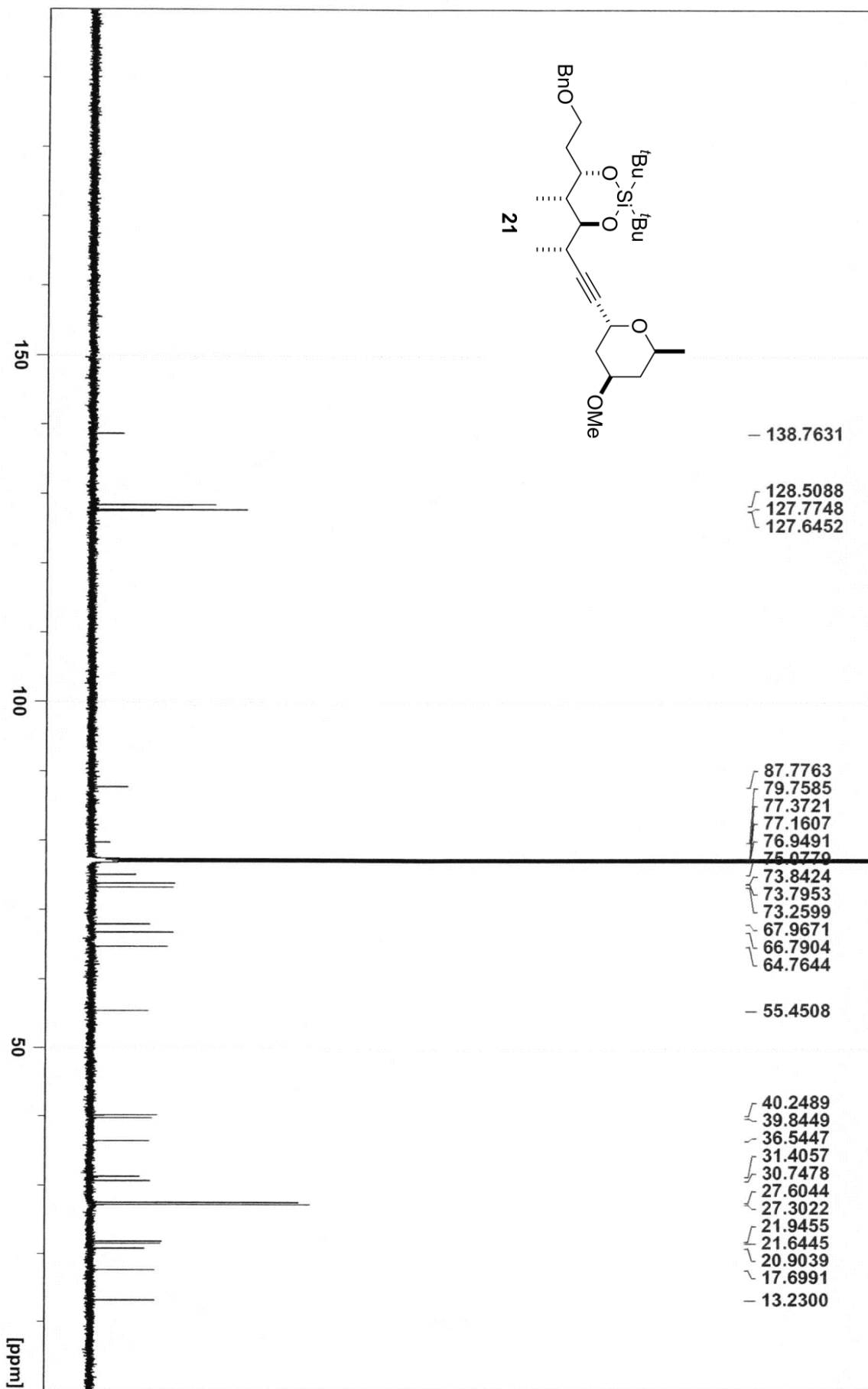


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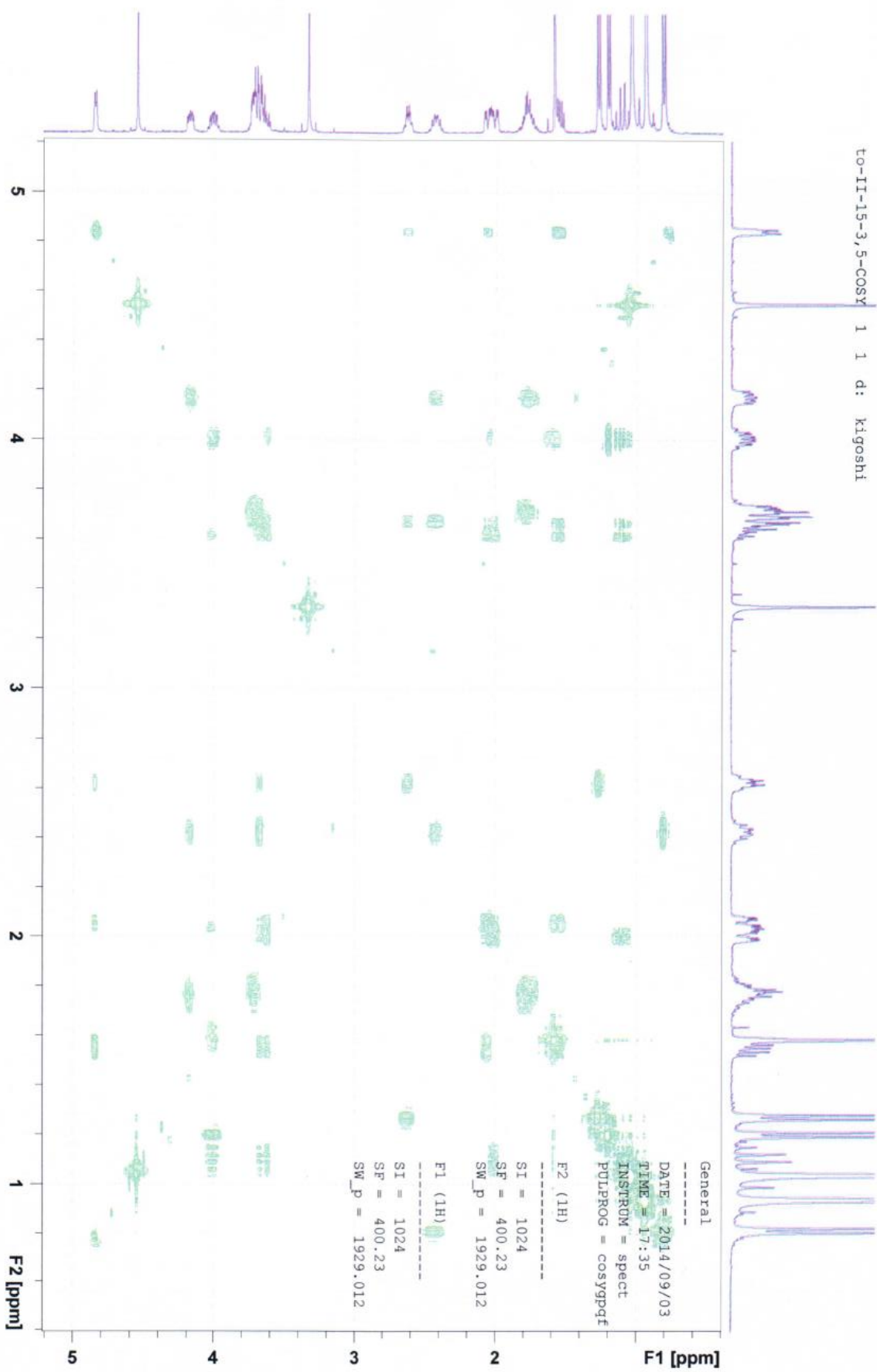




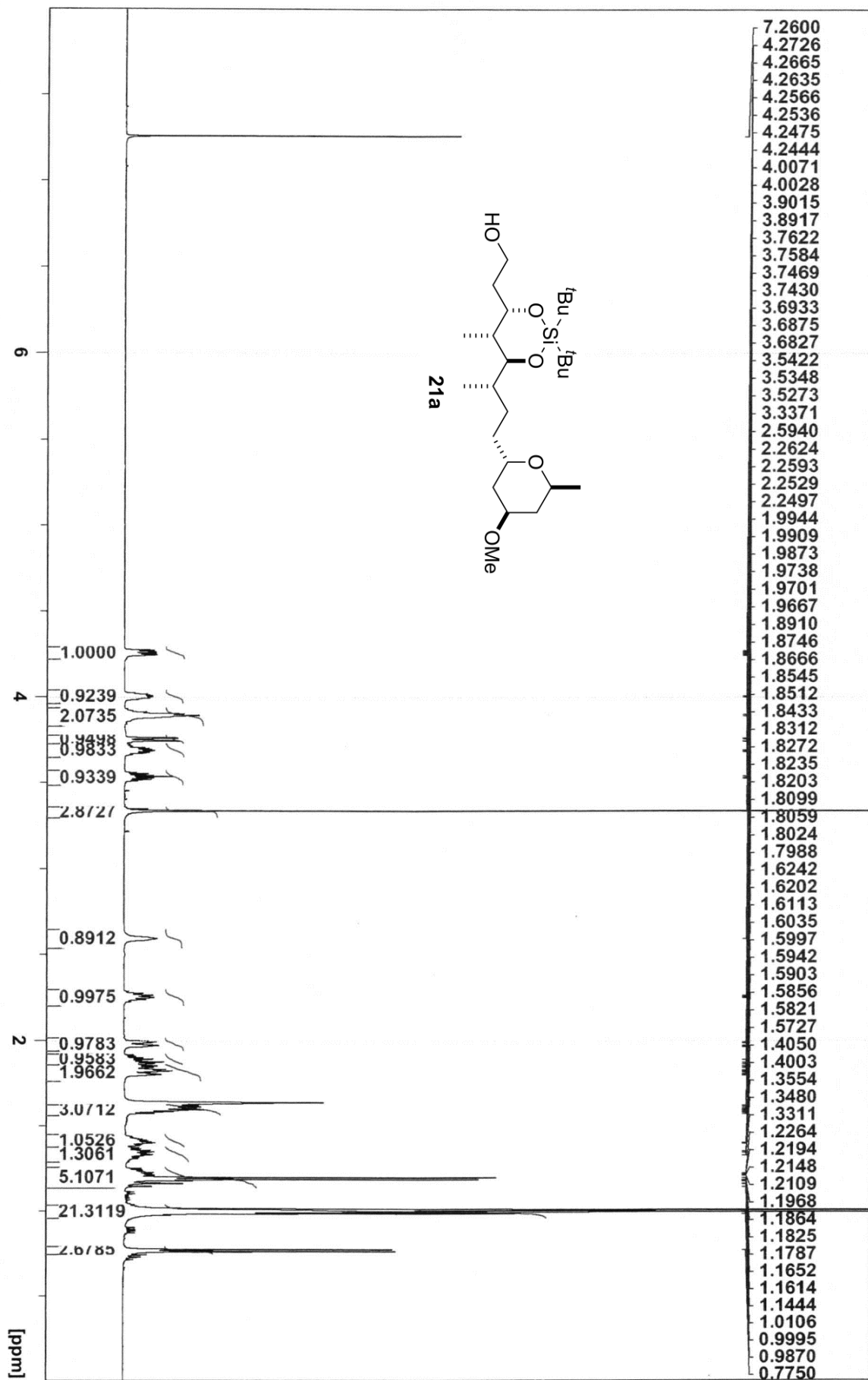


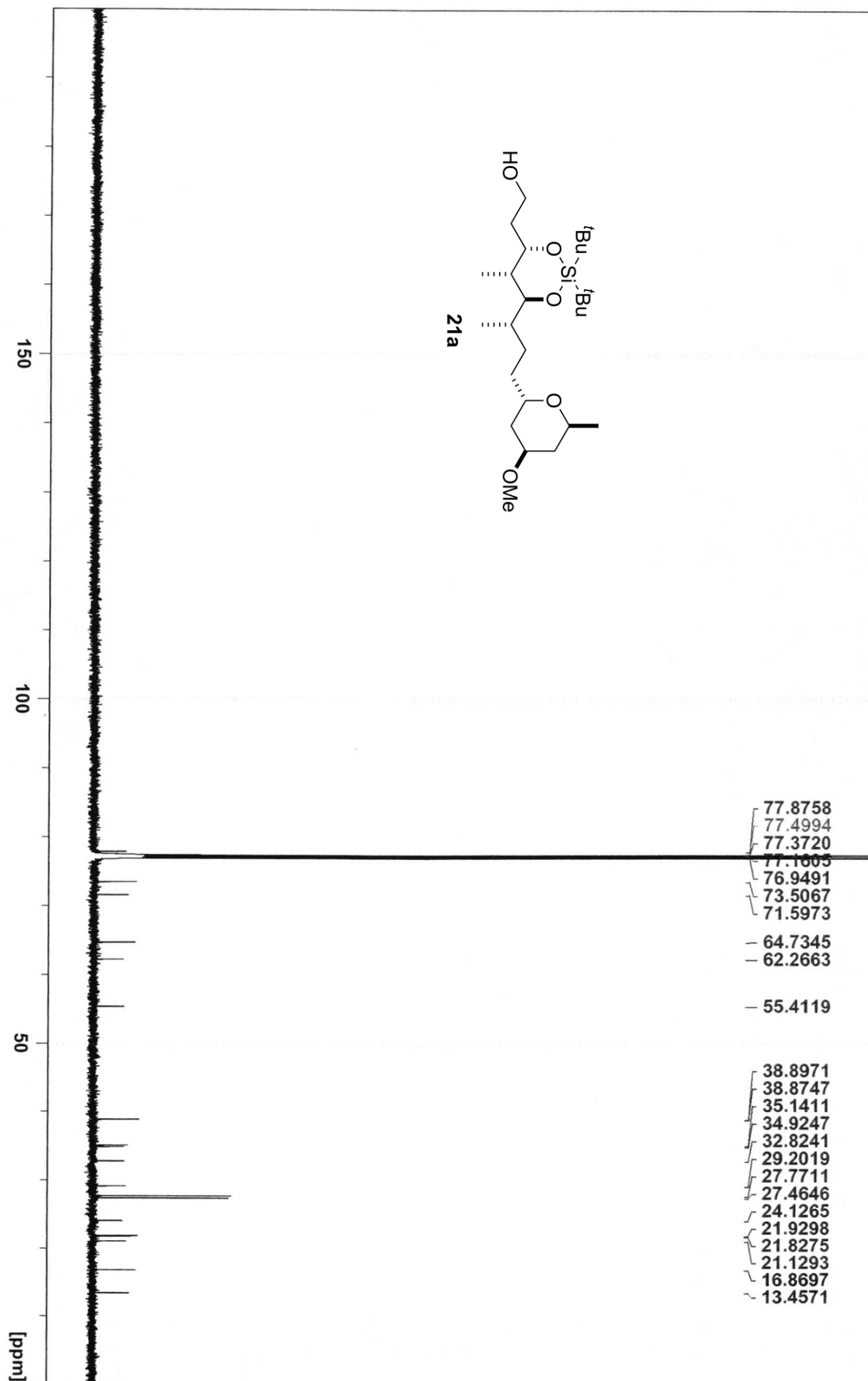


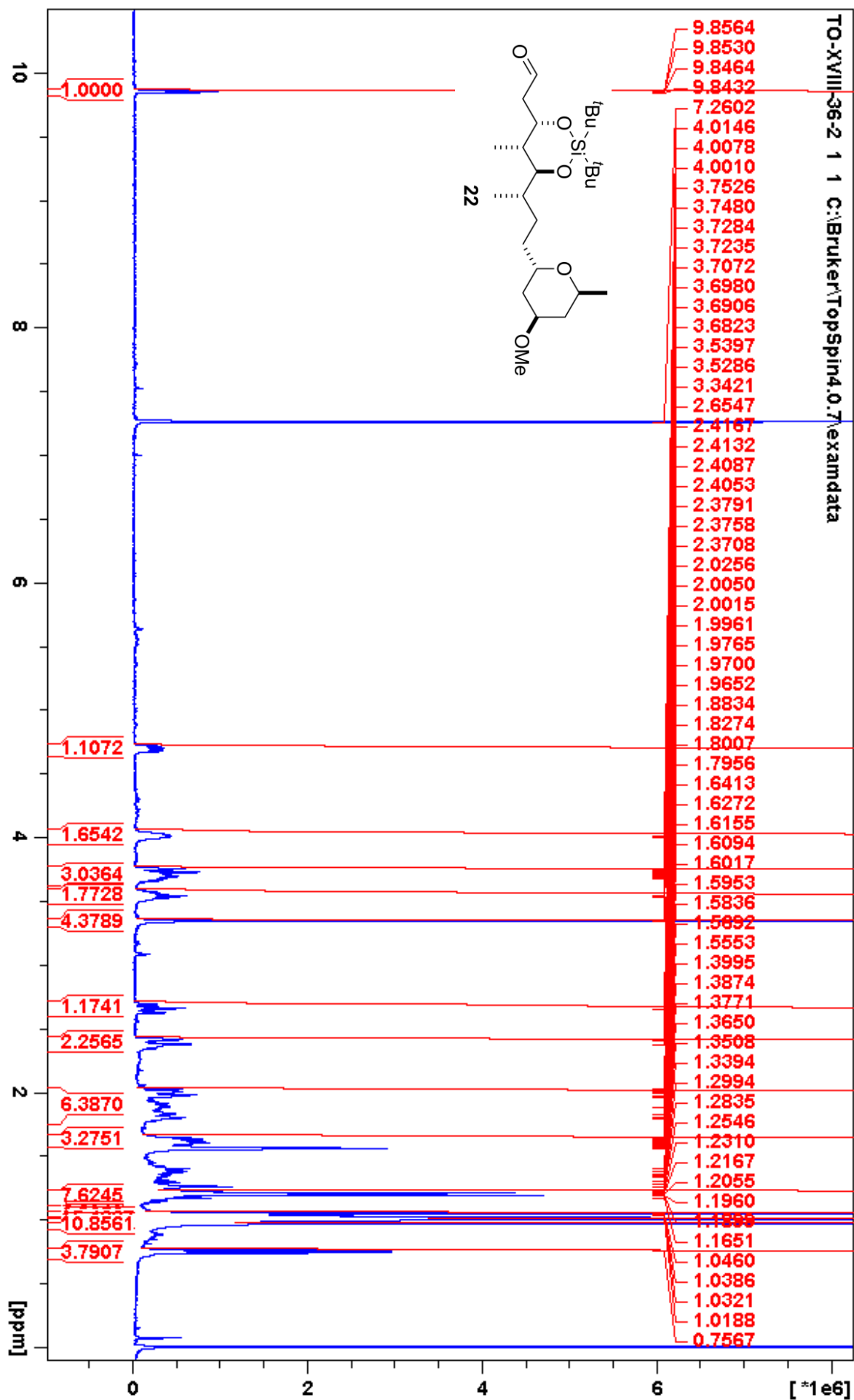
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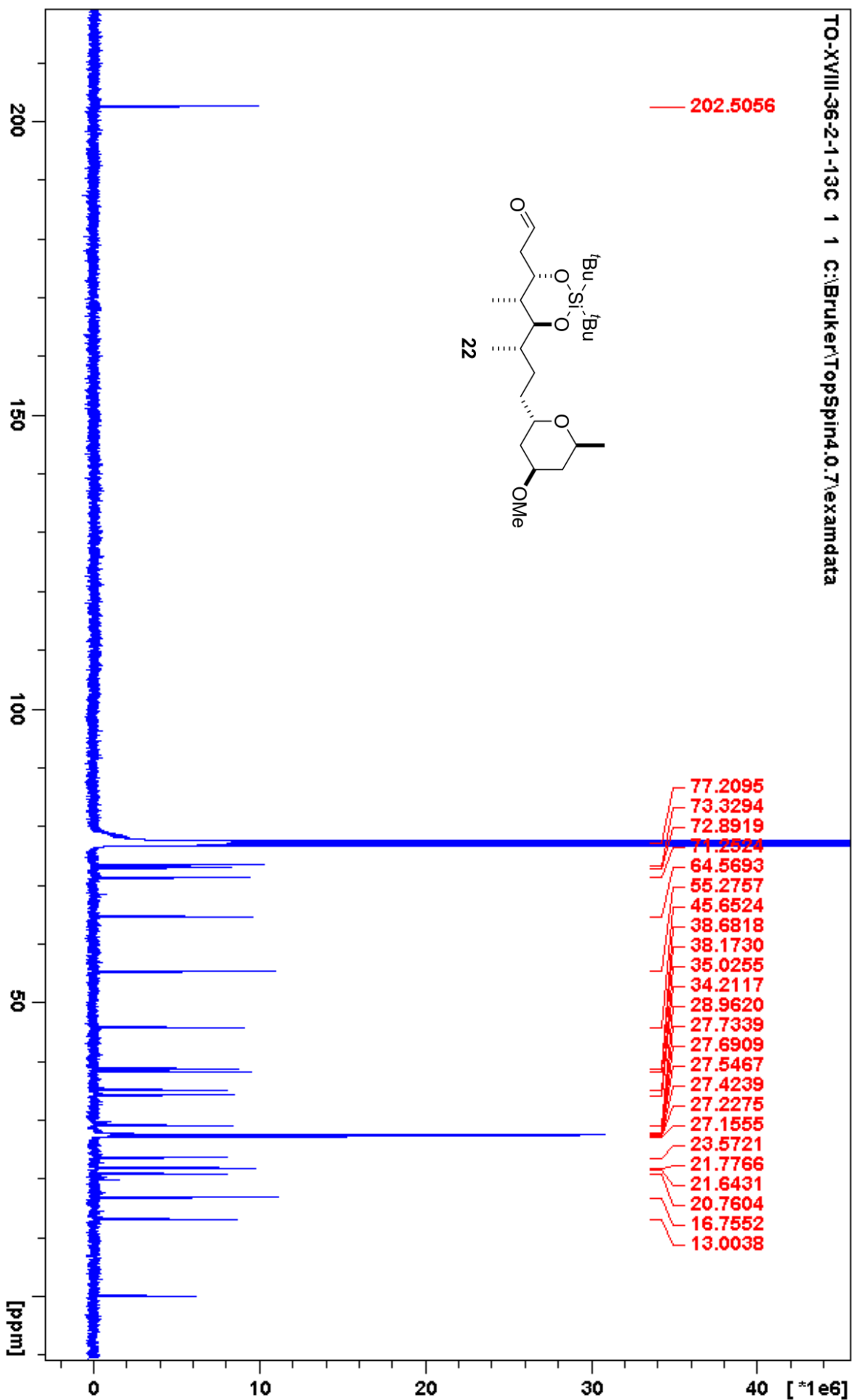


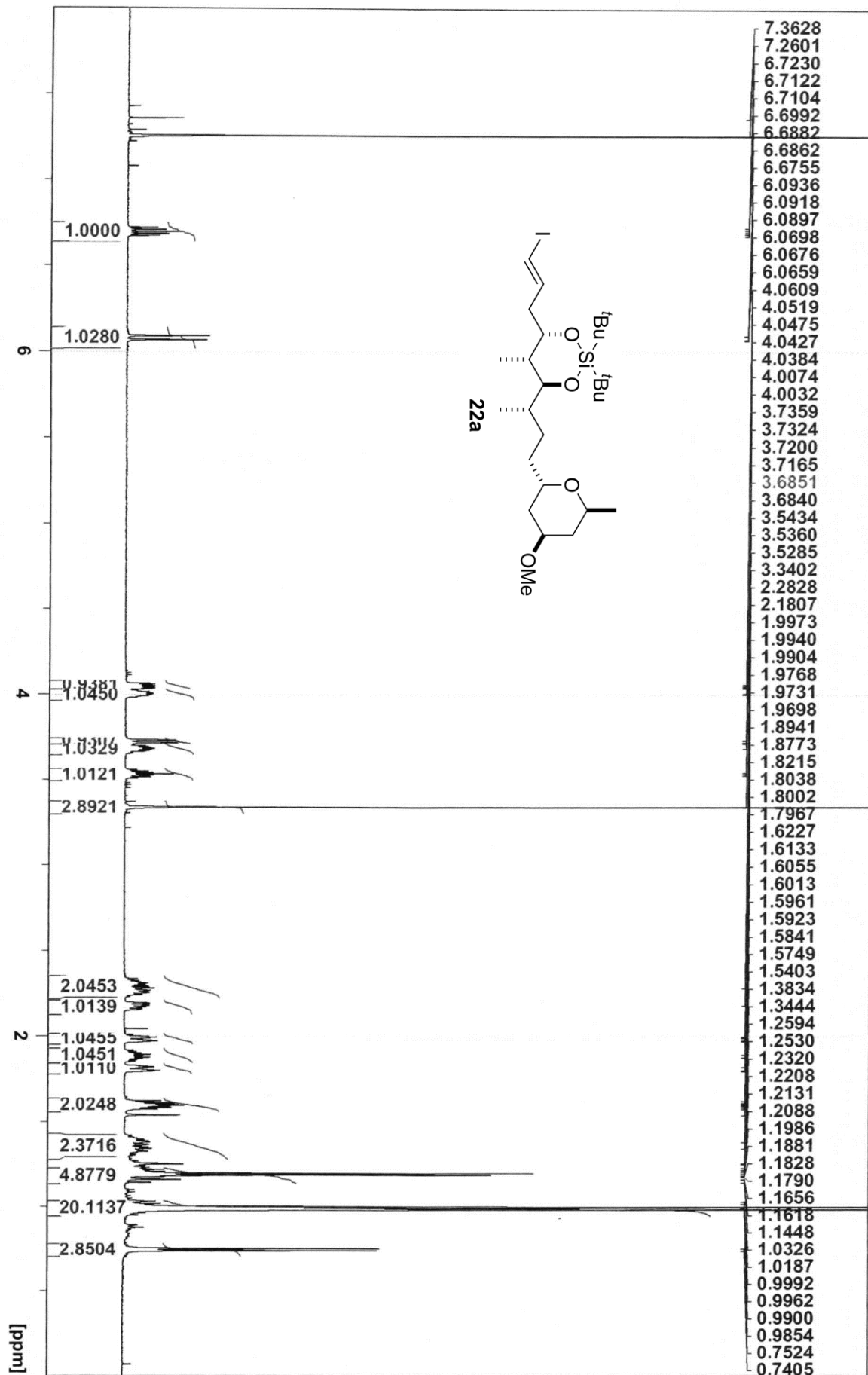
H-H COSY spectrum of compound 21

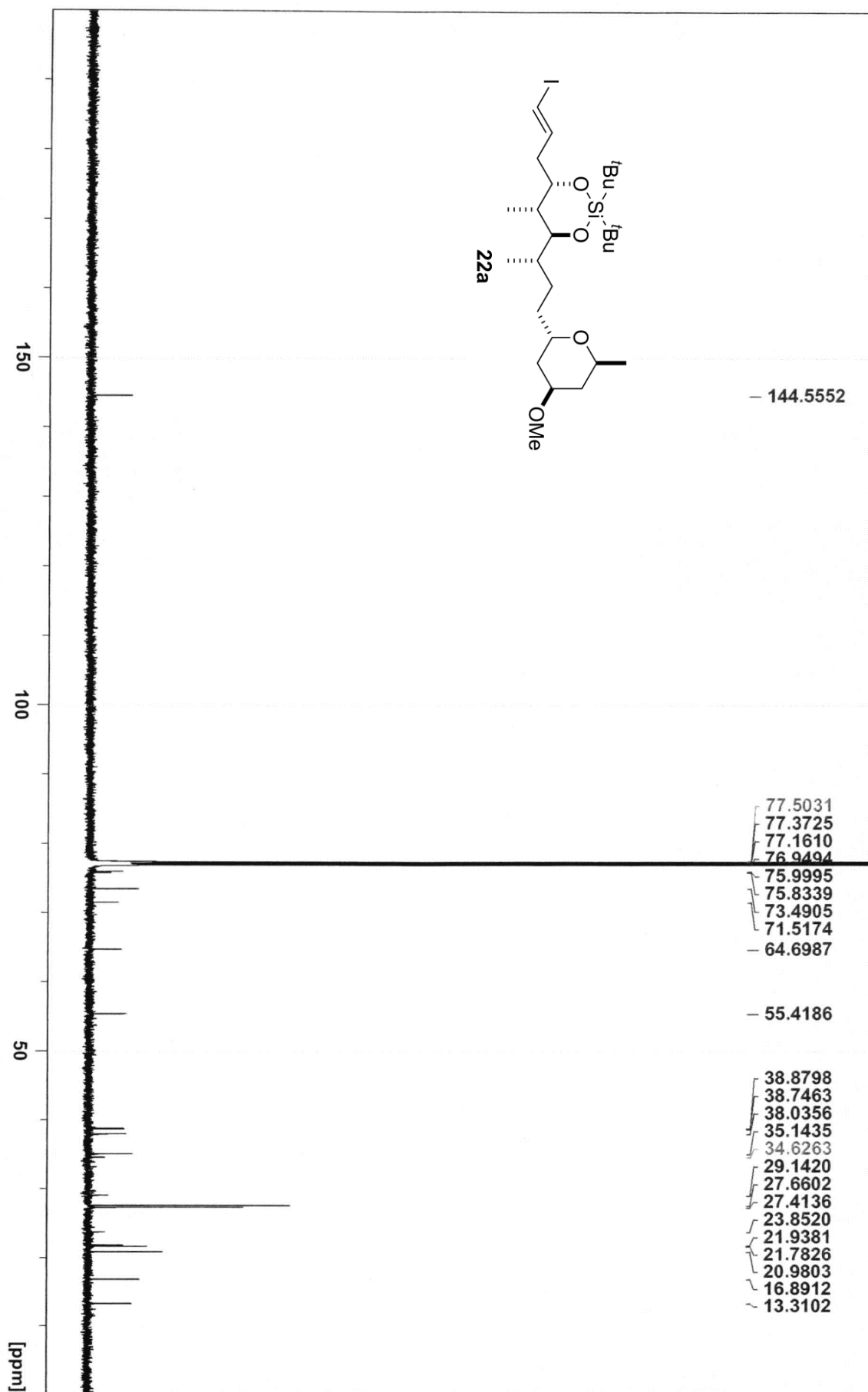


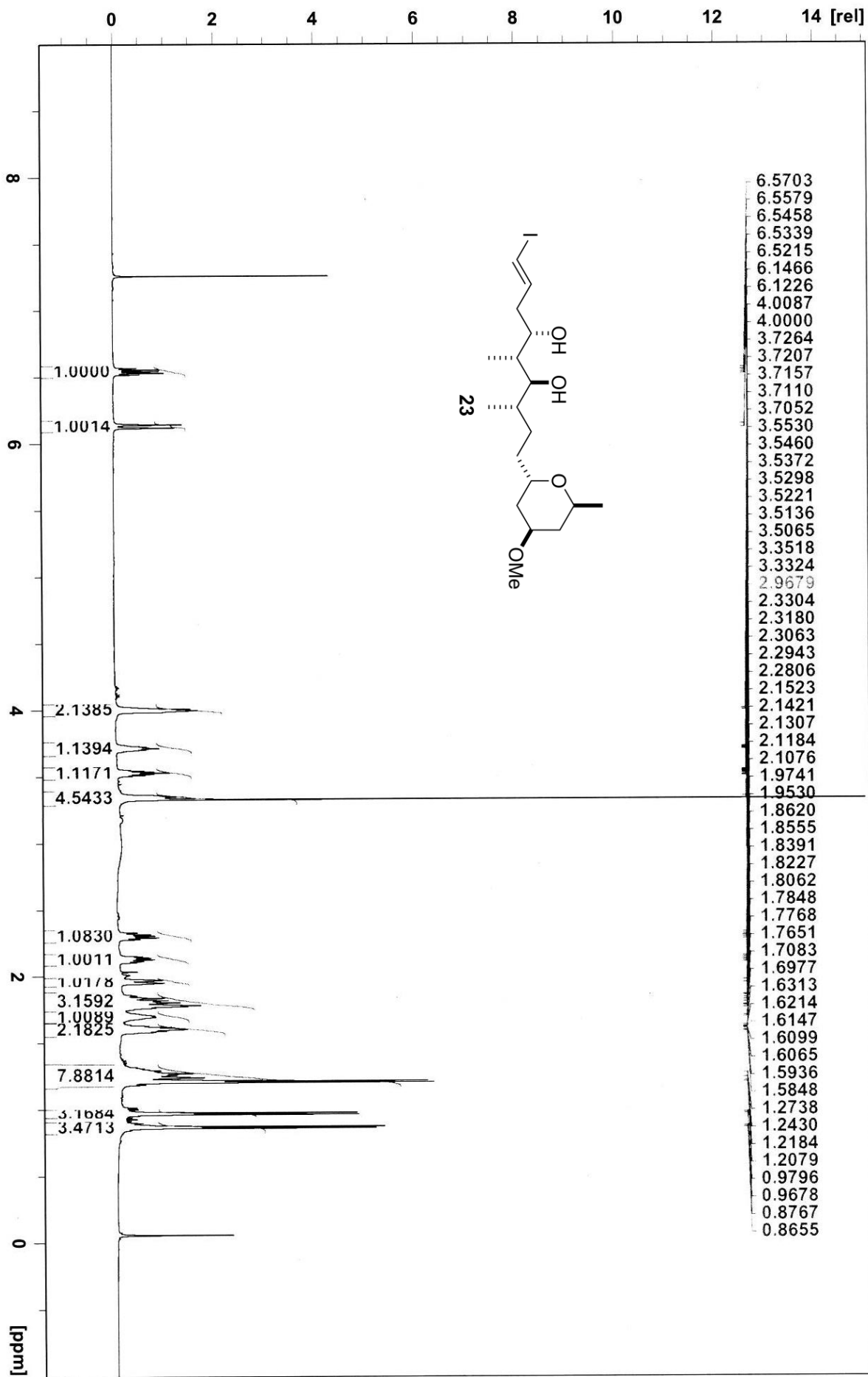




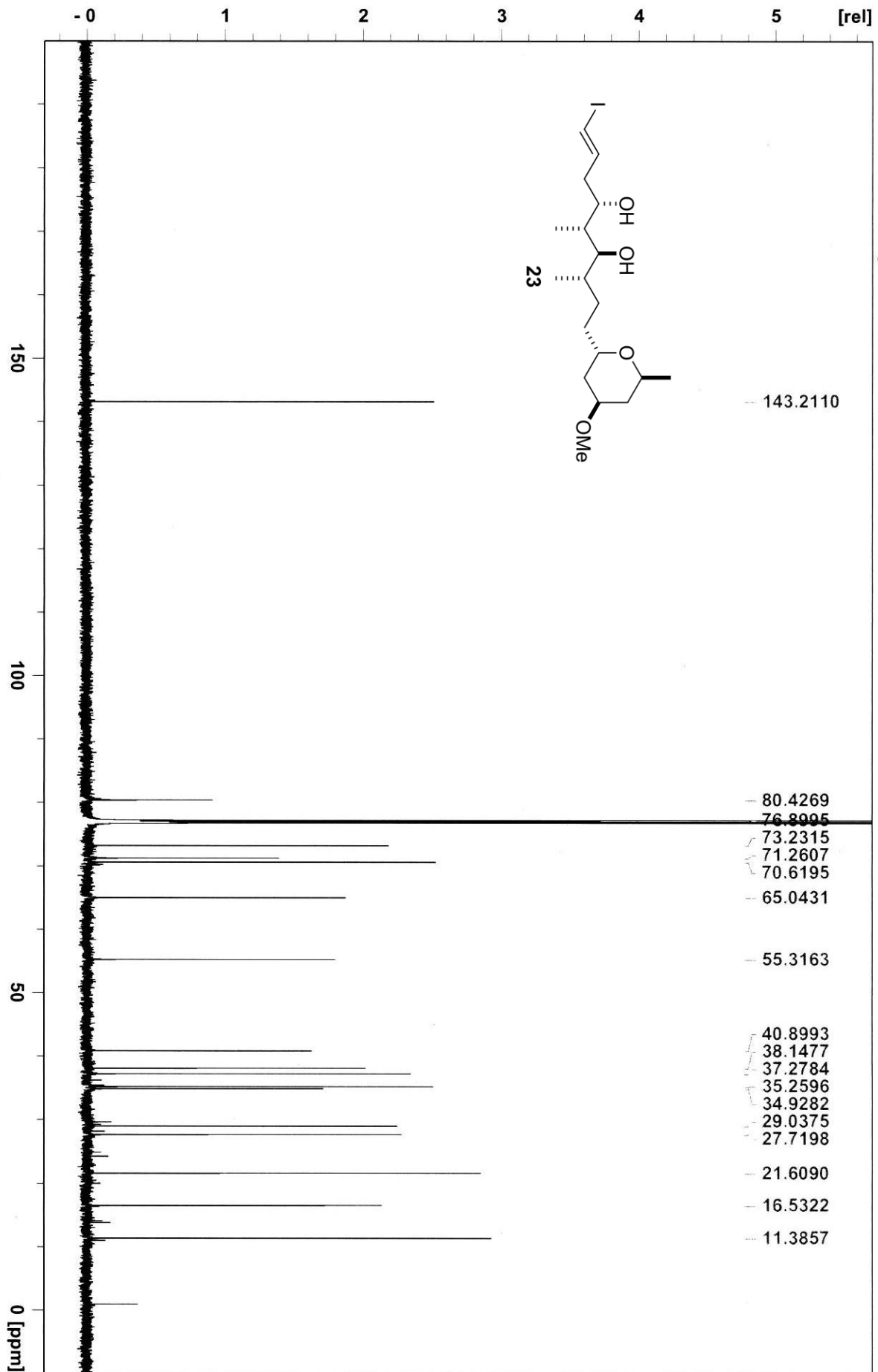


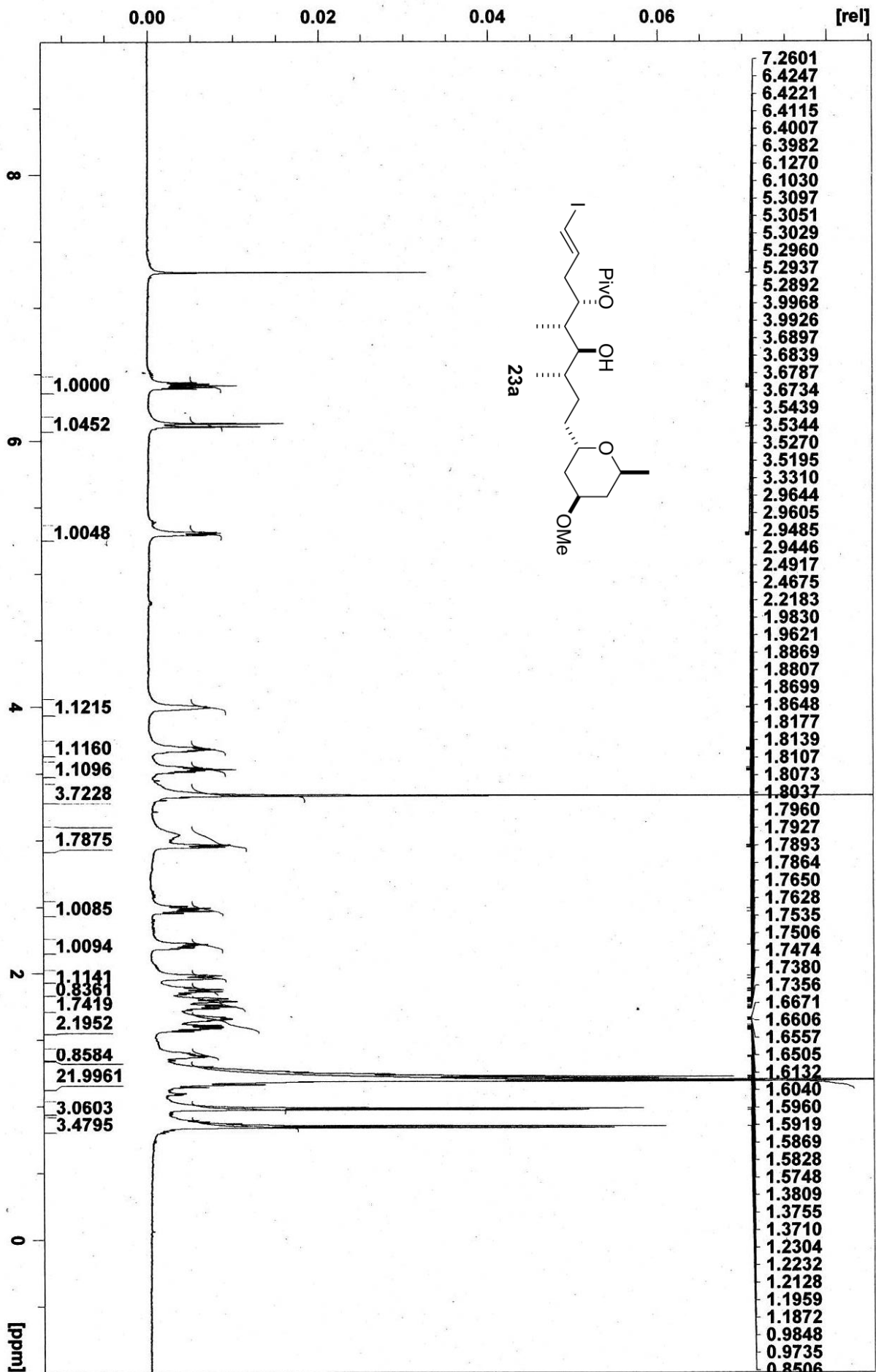


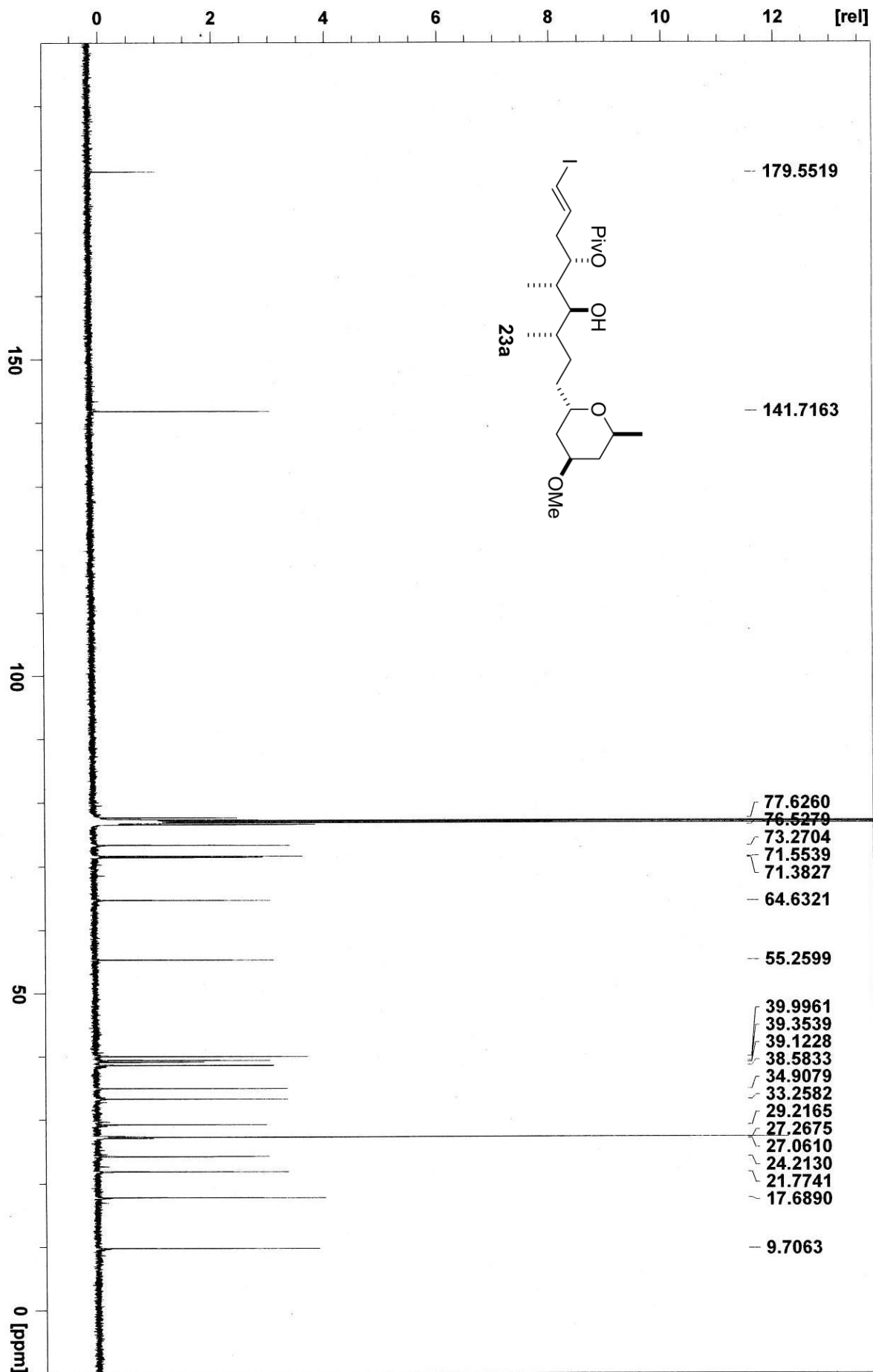


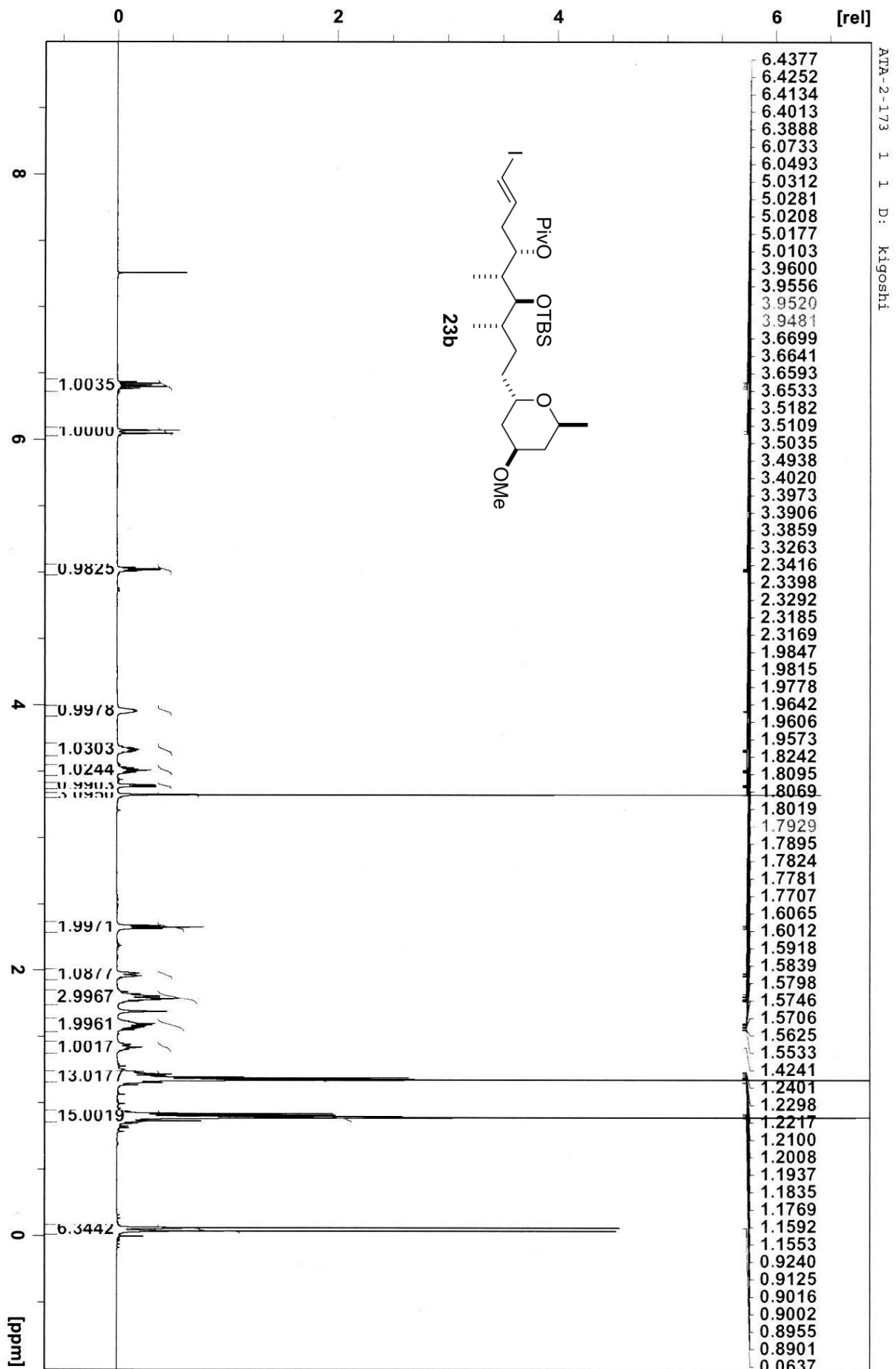


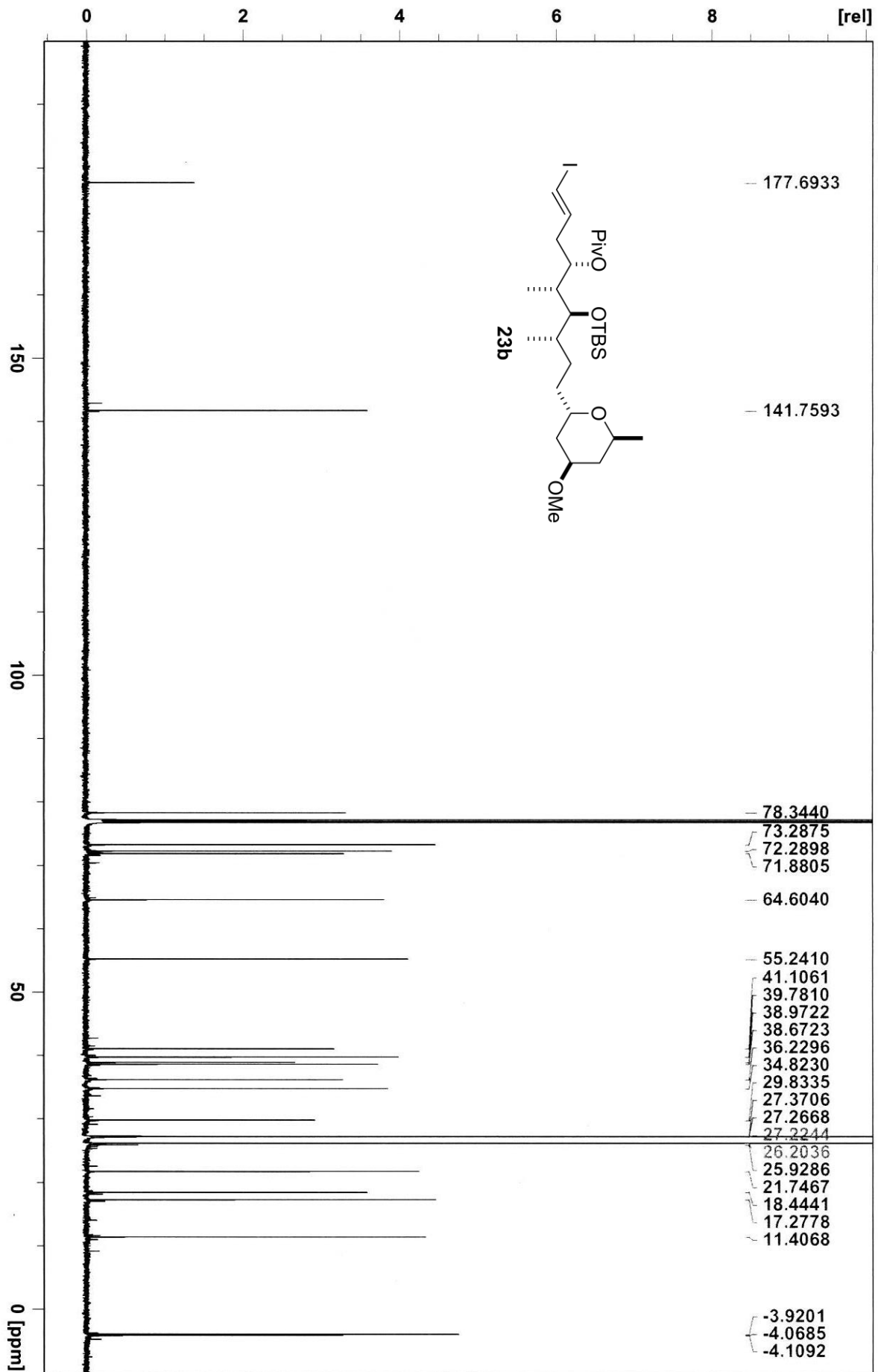


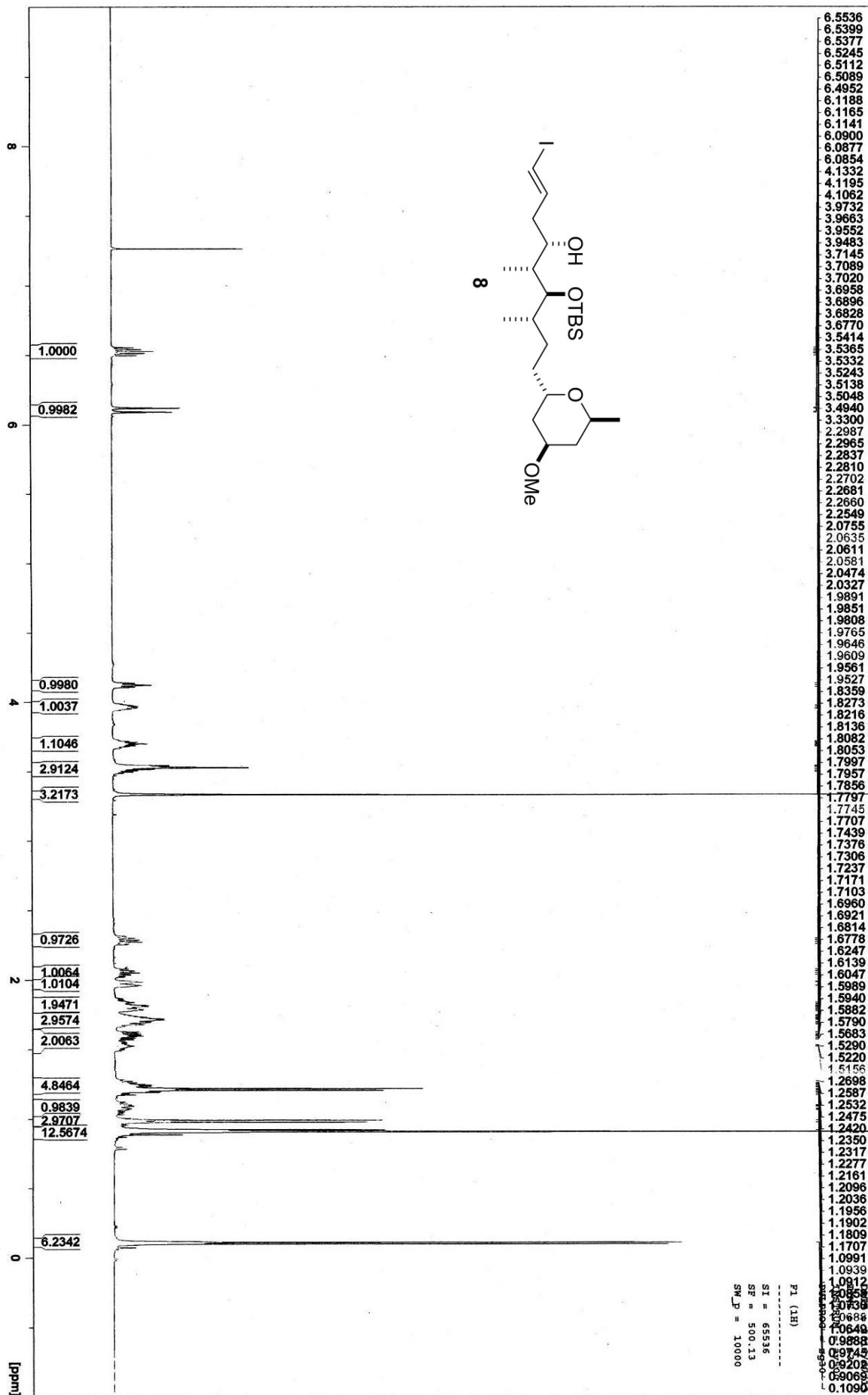








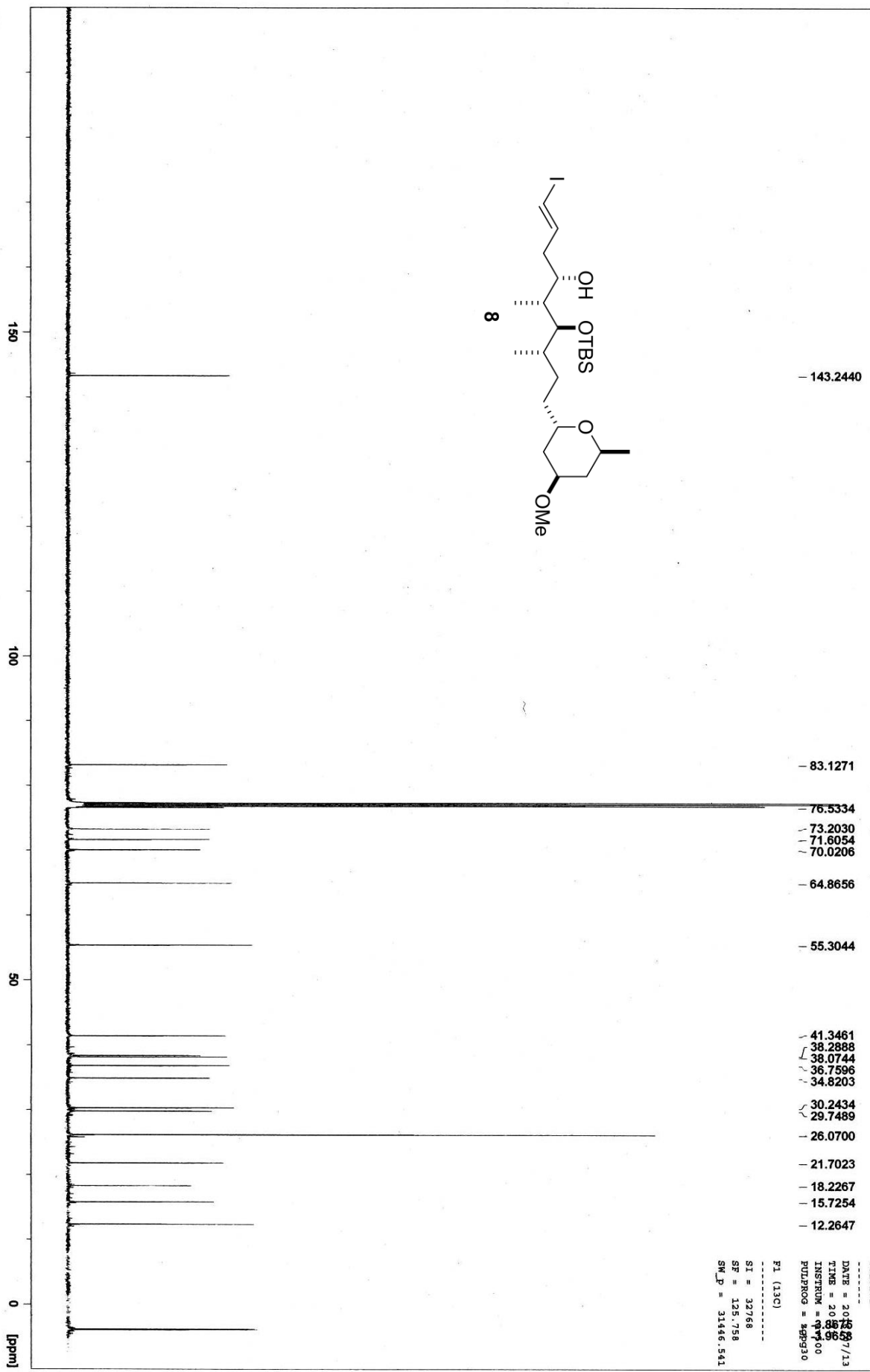
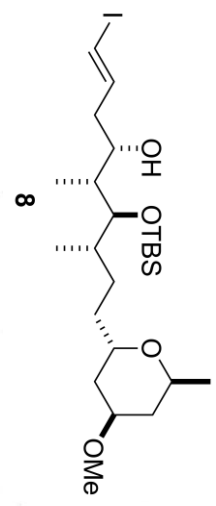




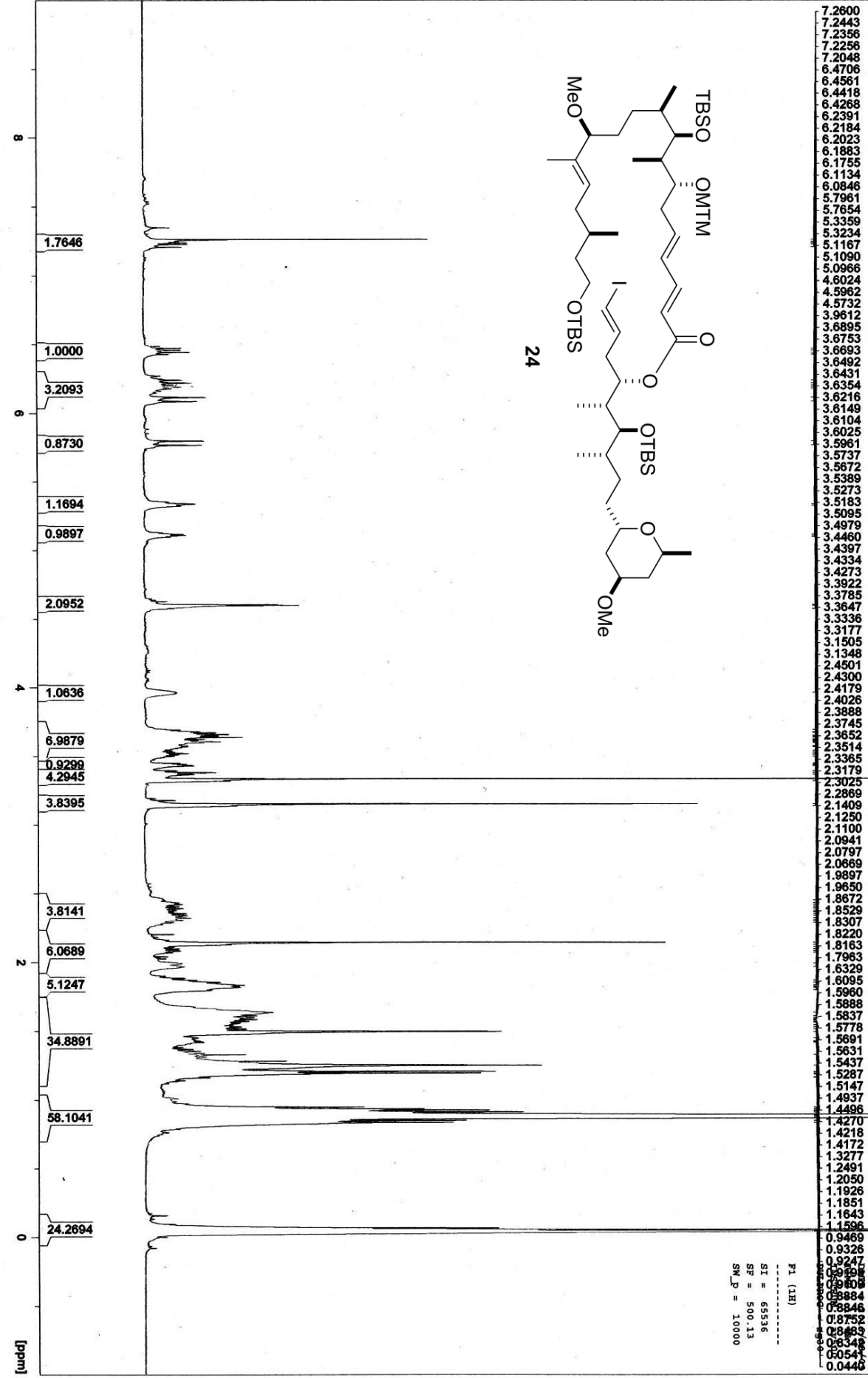
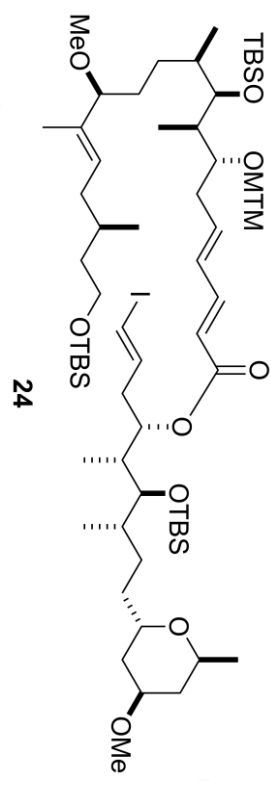
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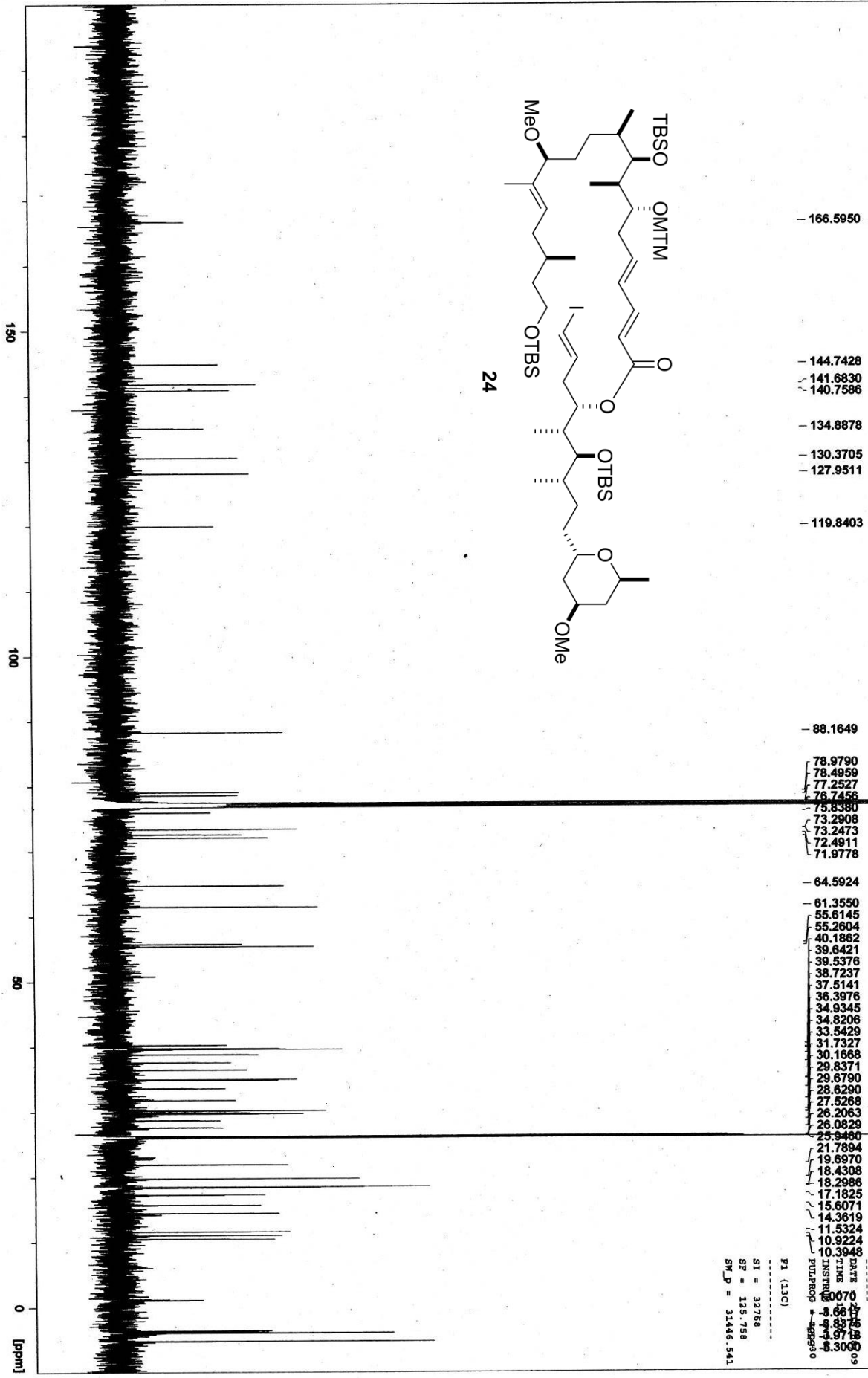
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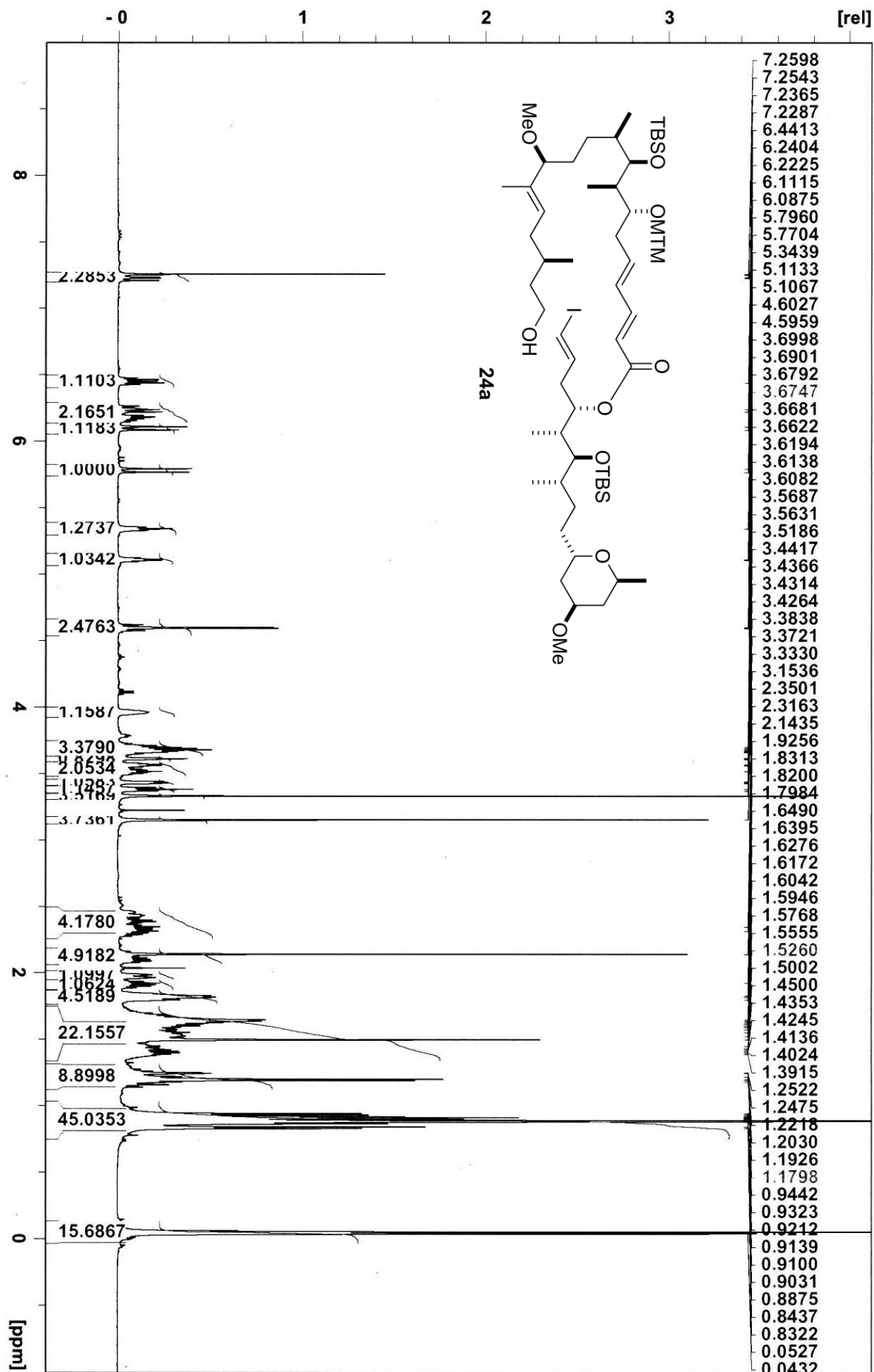
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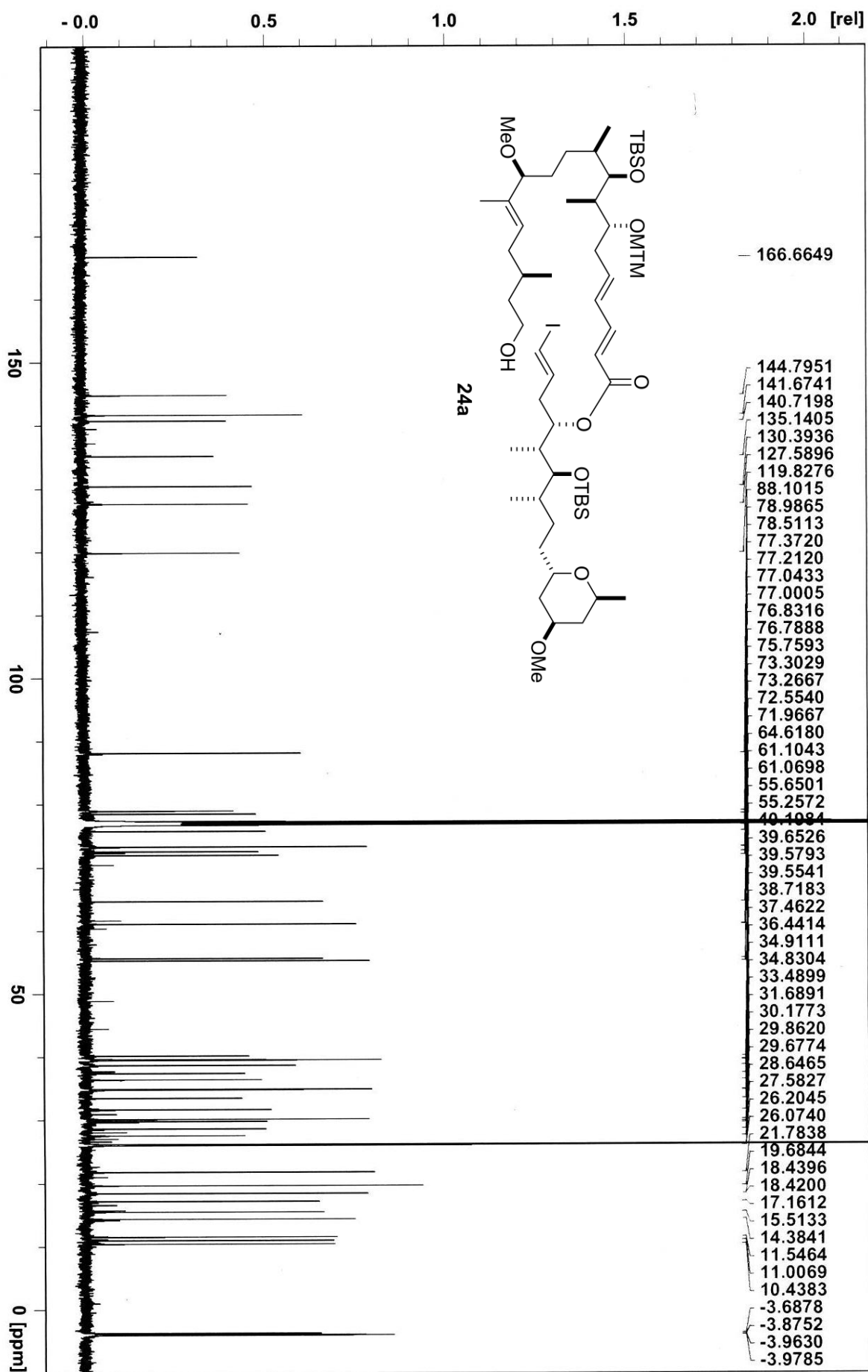


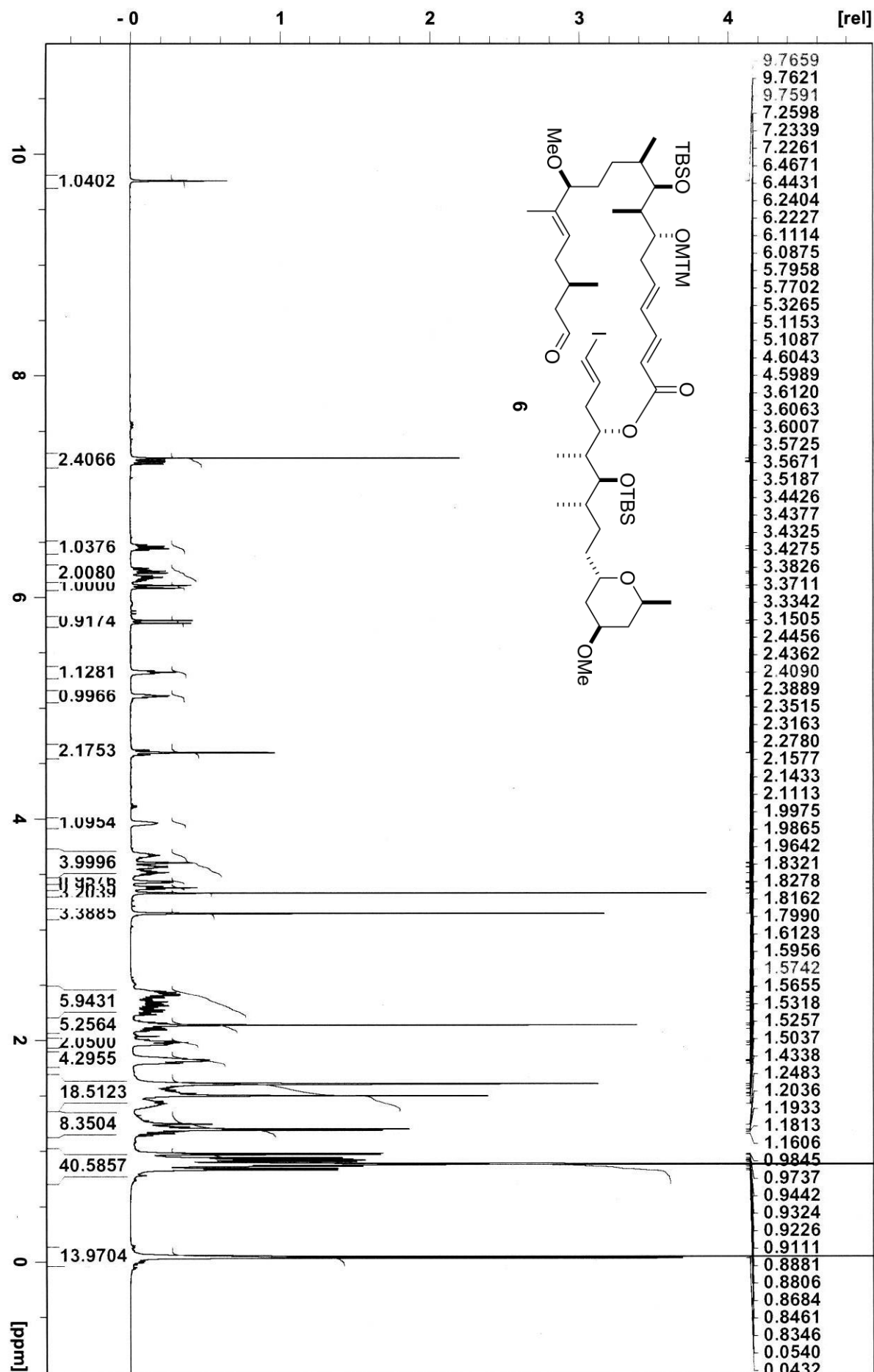


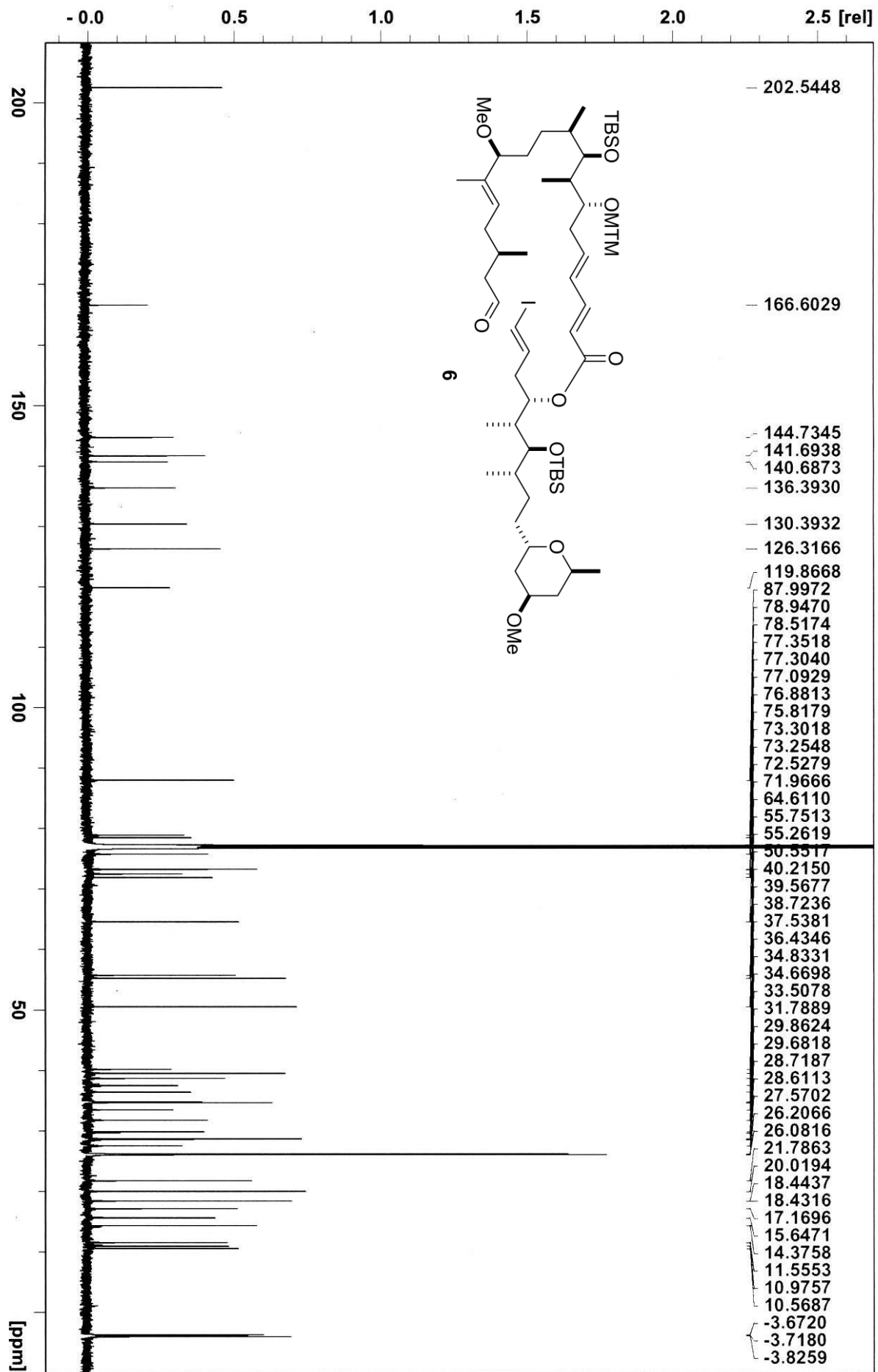
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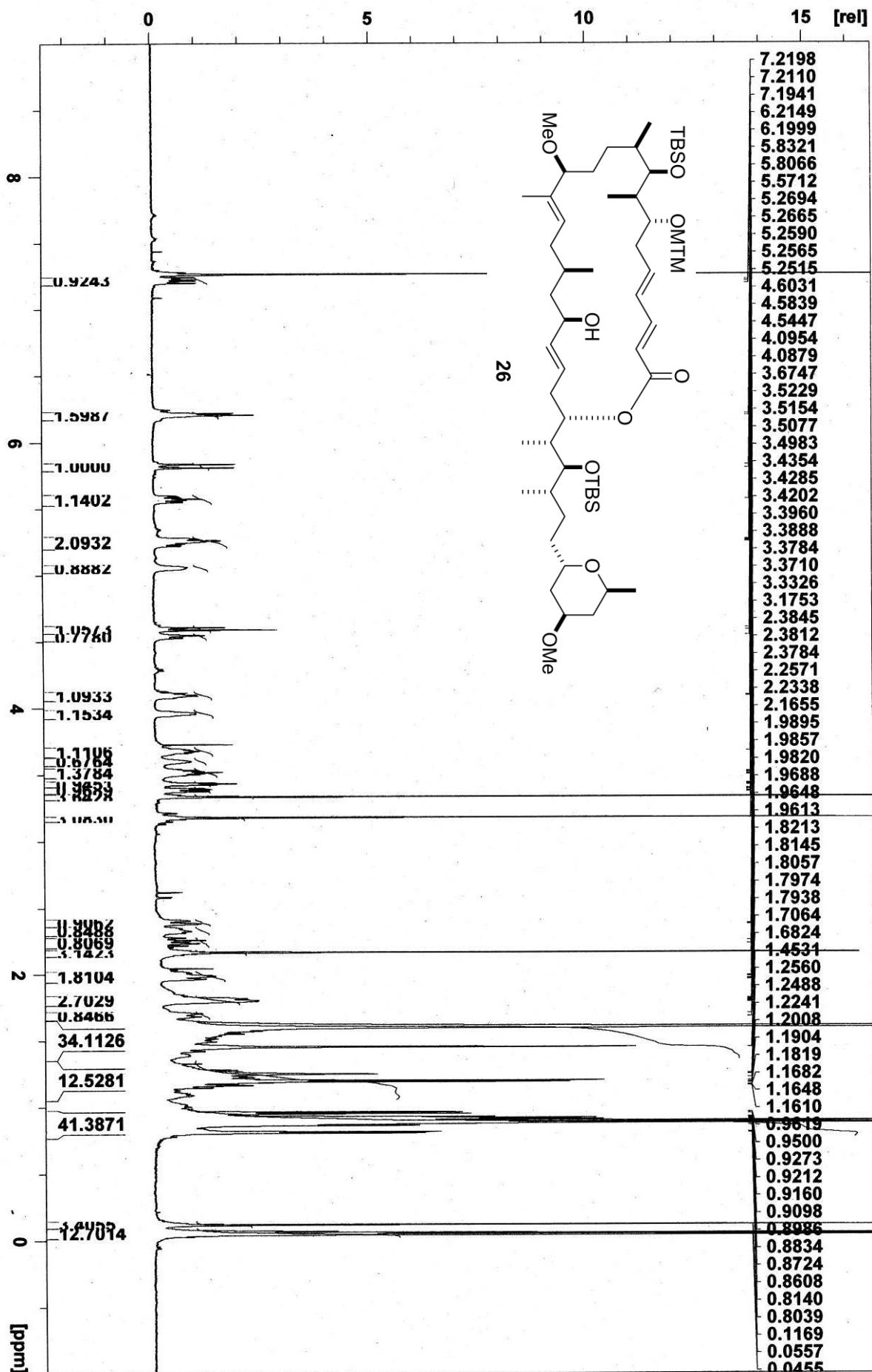
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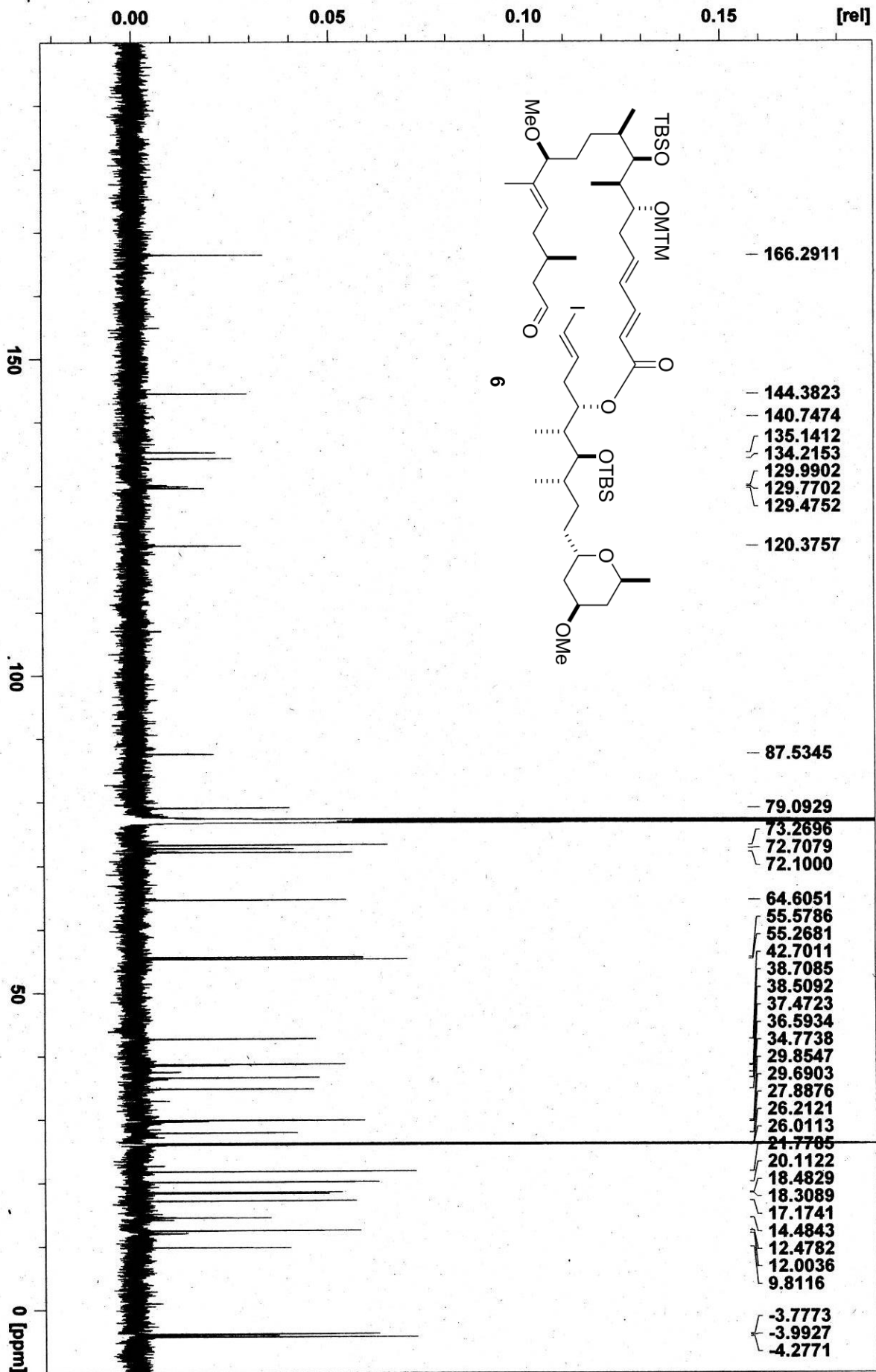


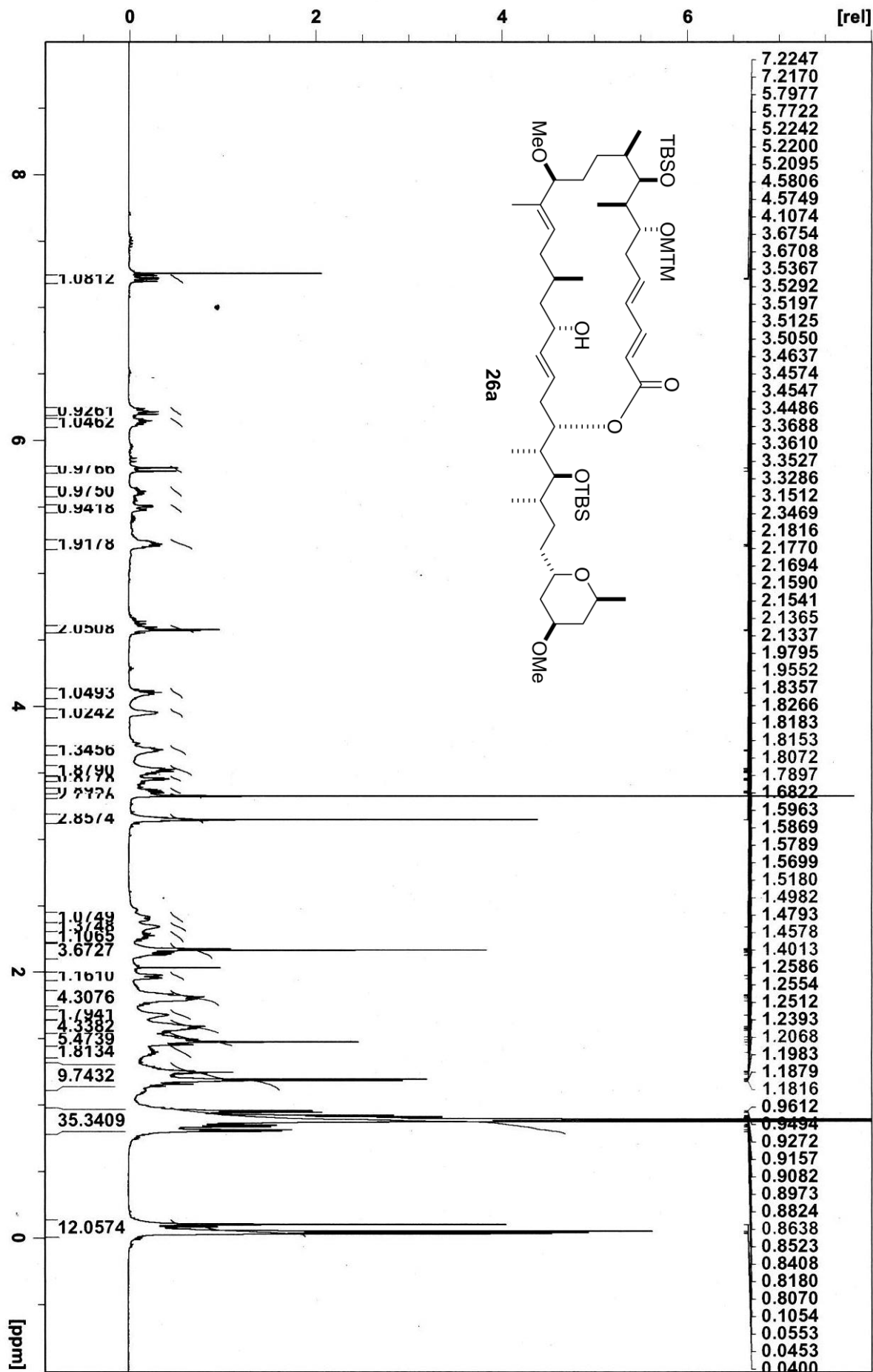




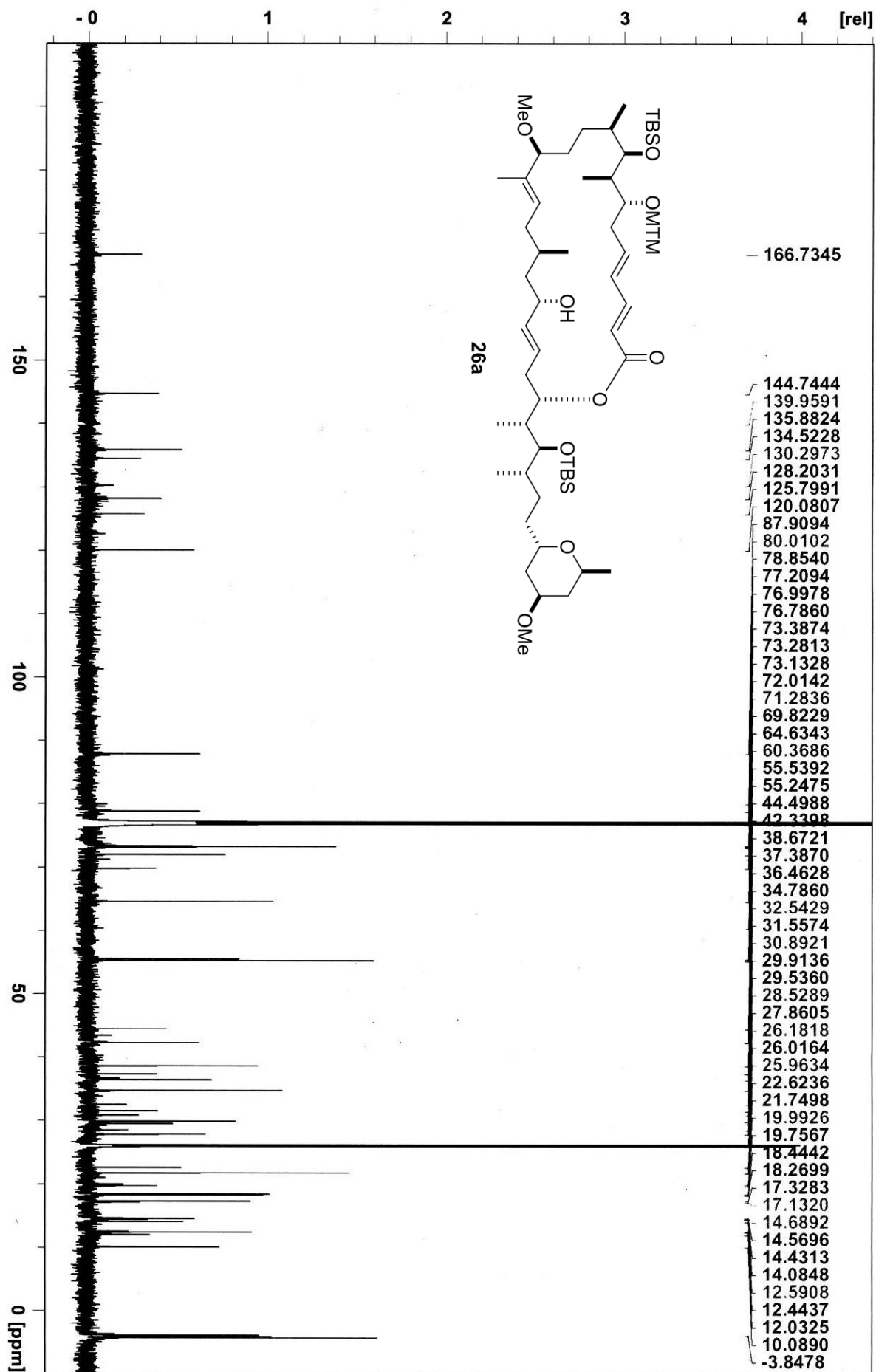


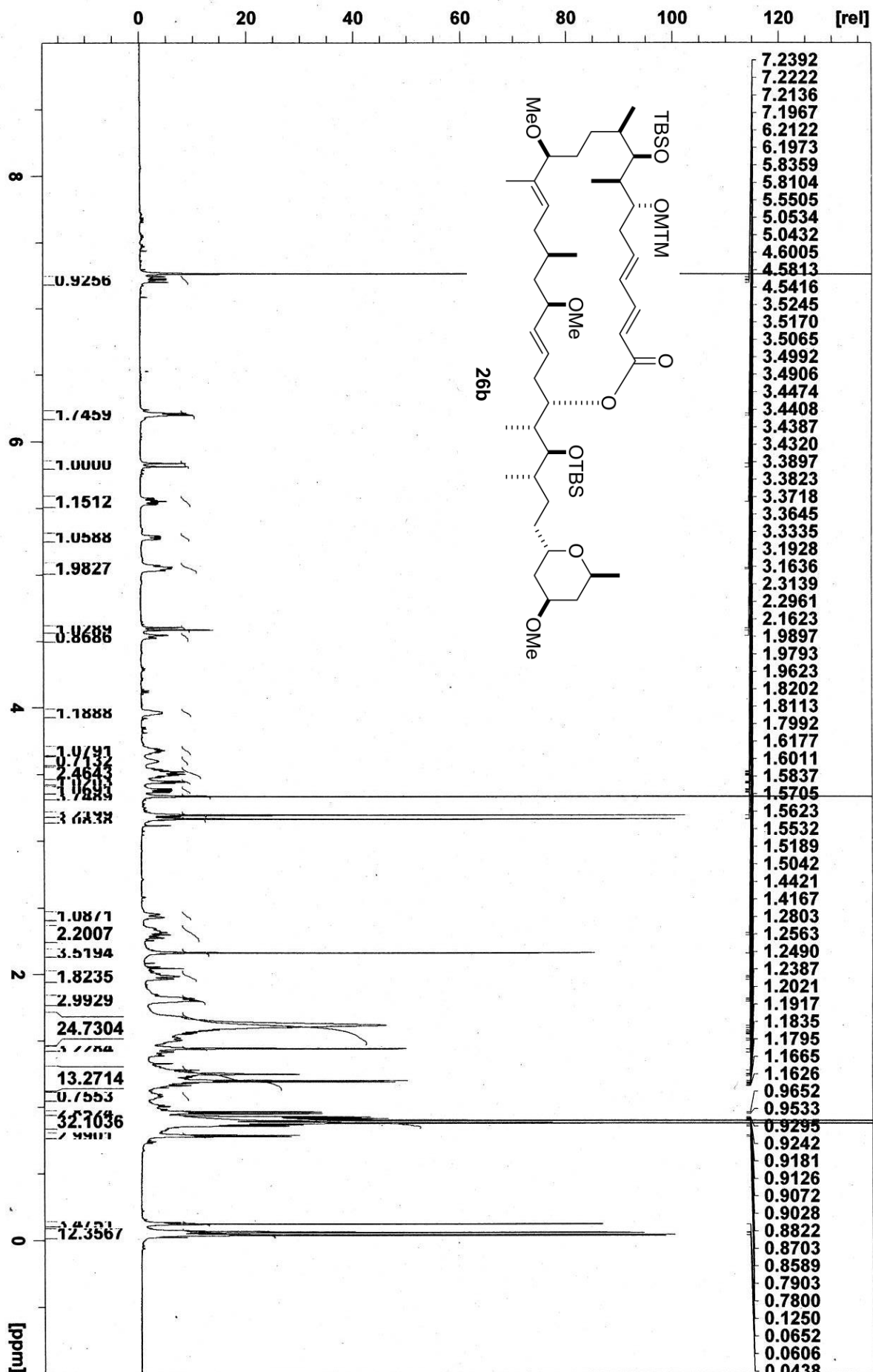


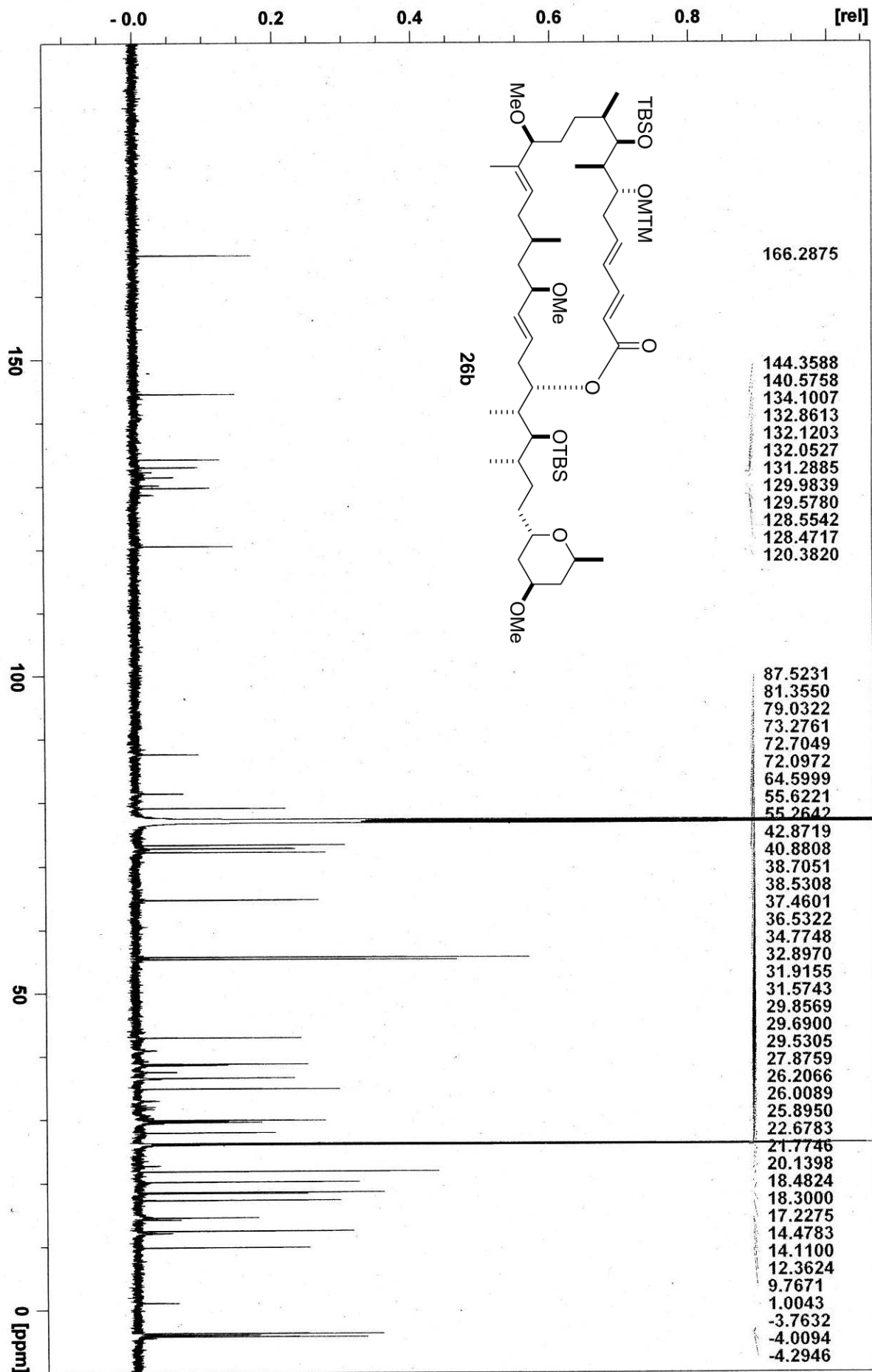


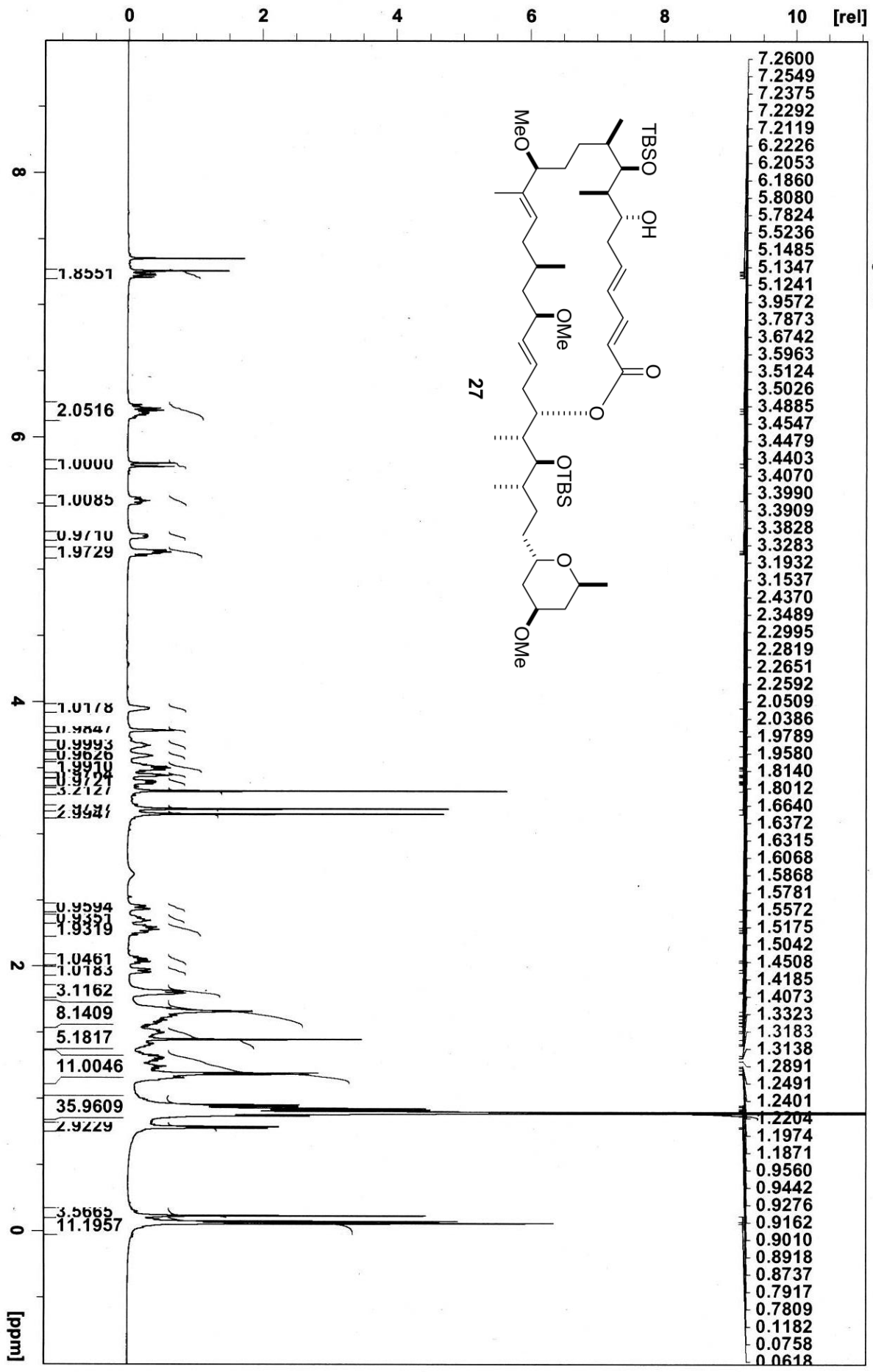


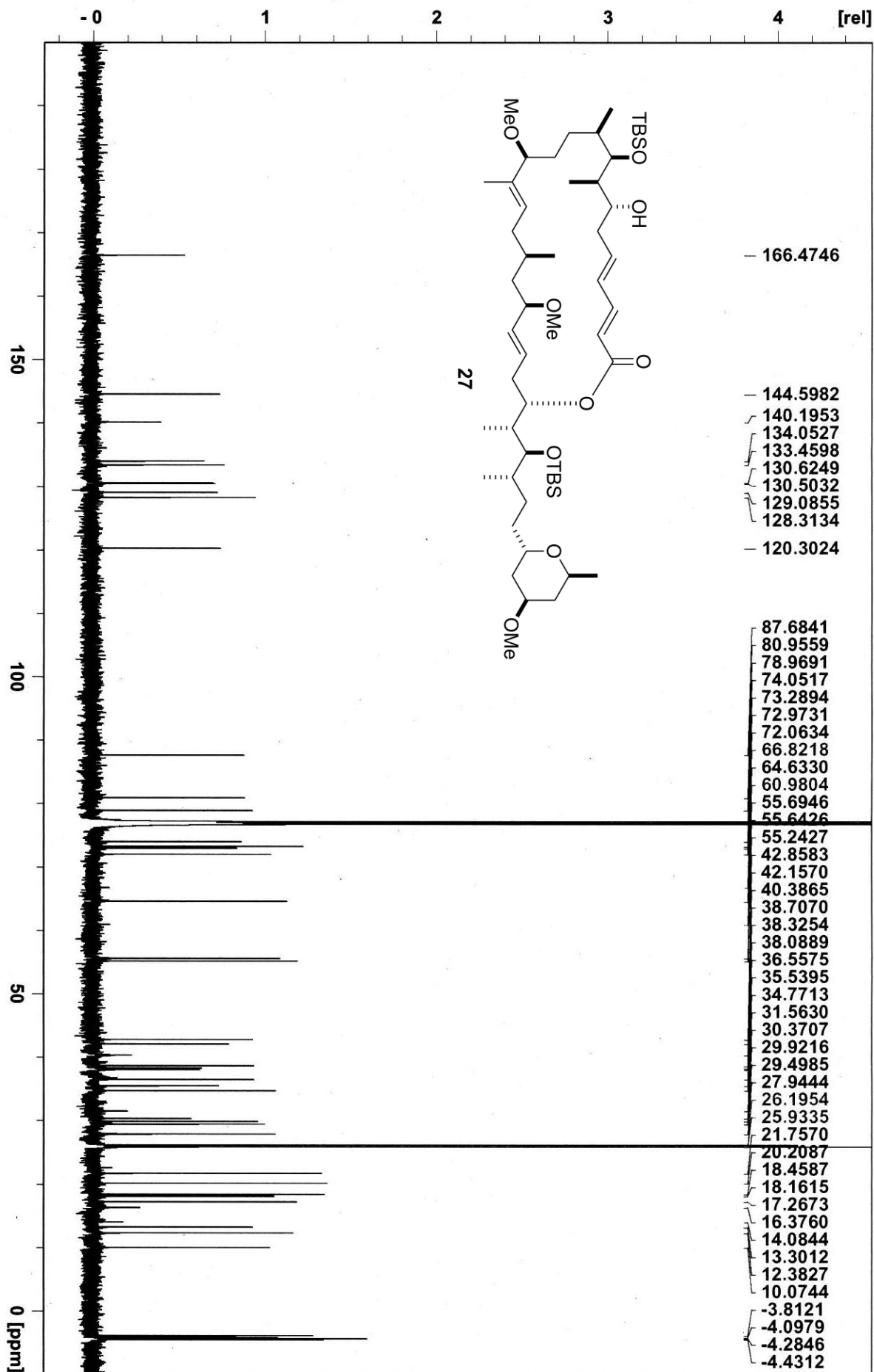




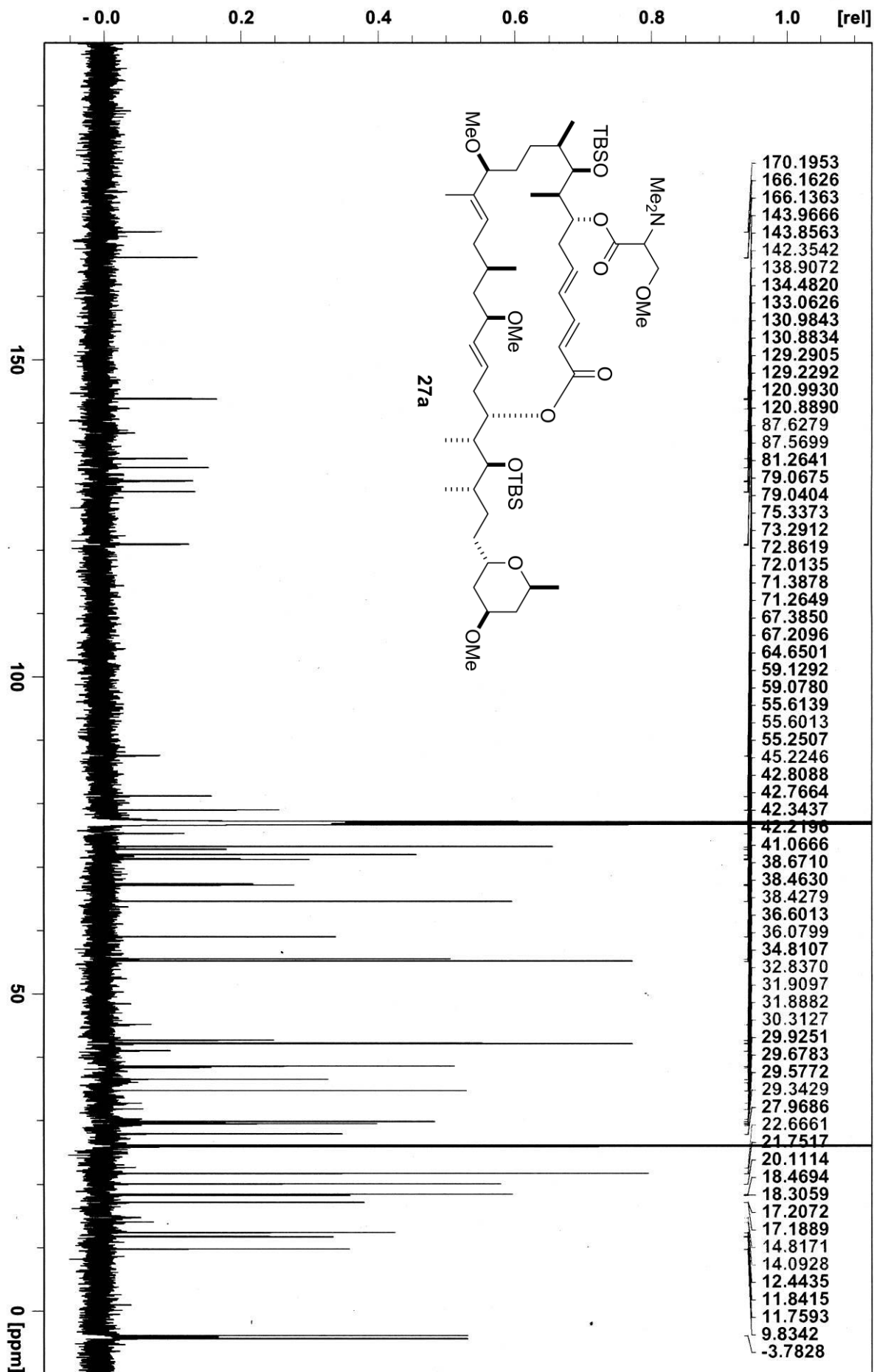


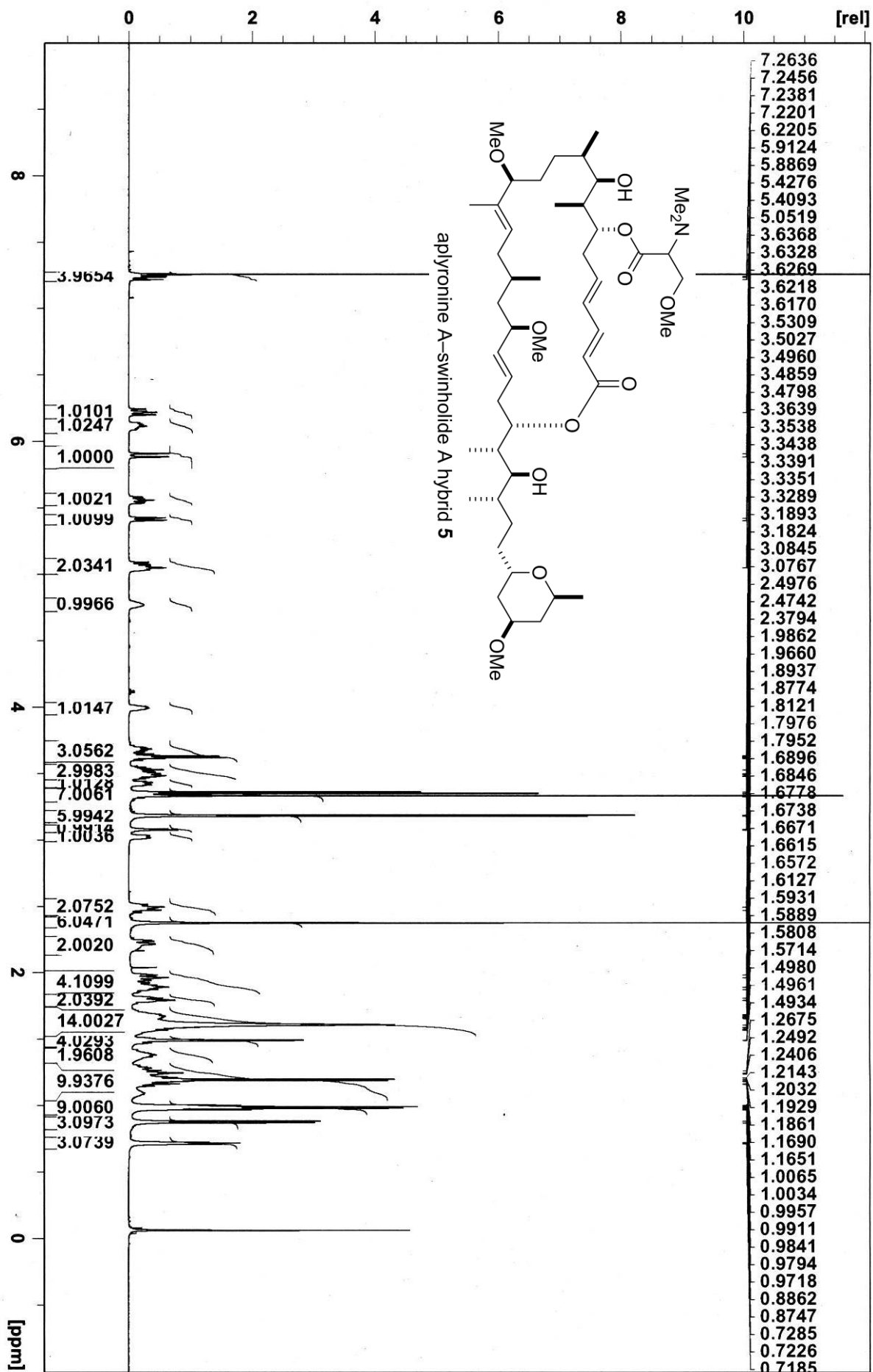




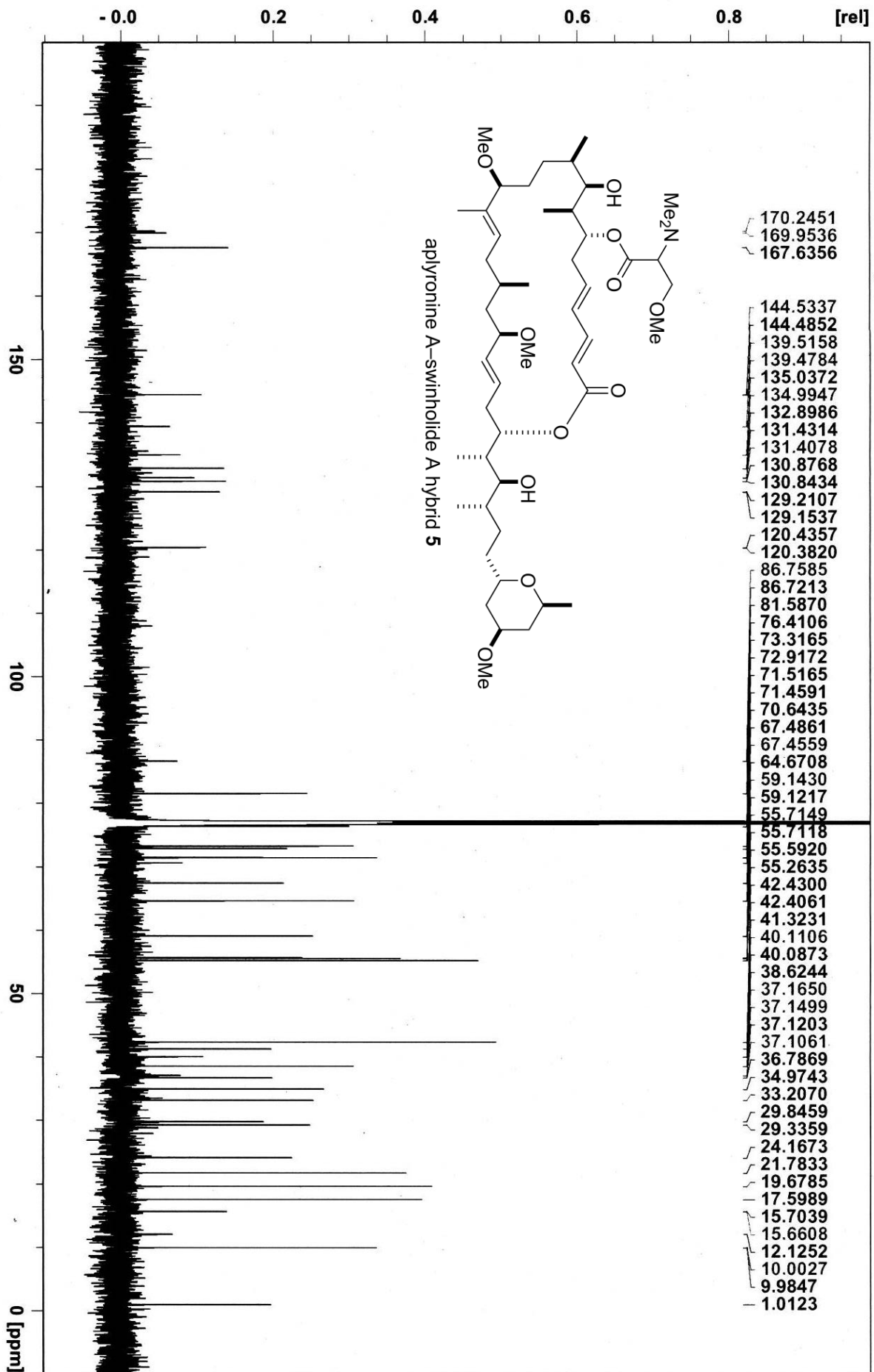


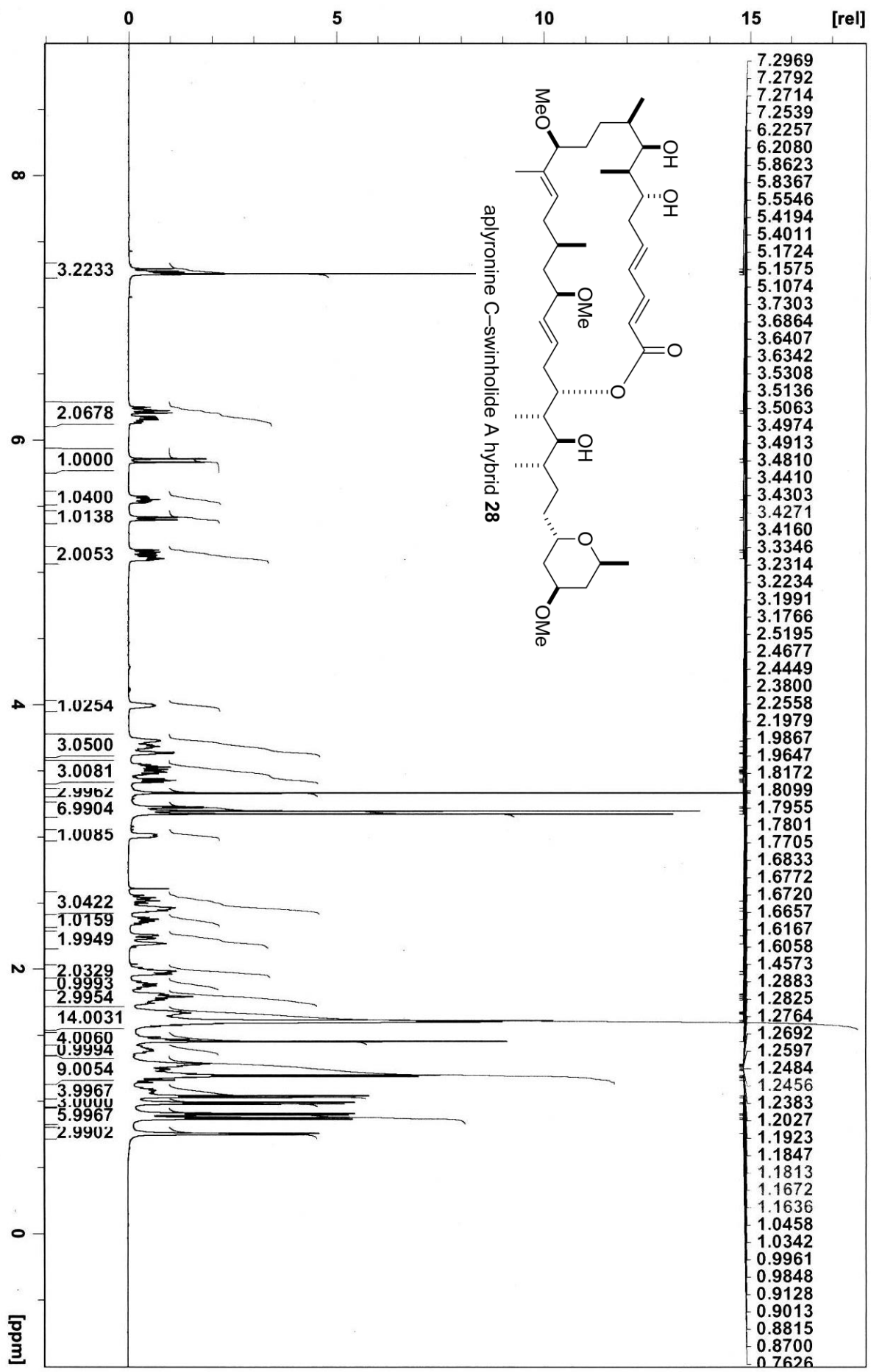


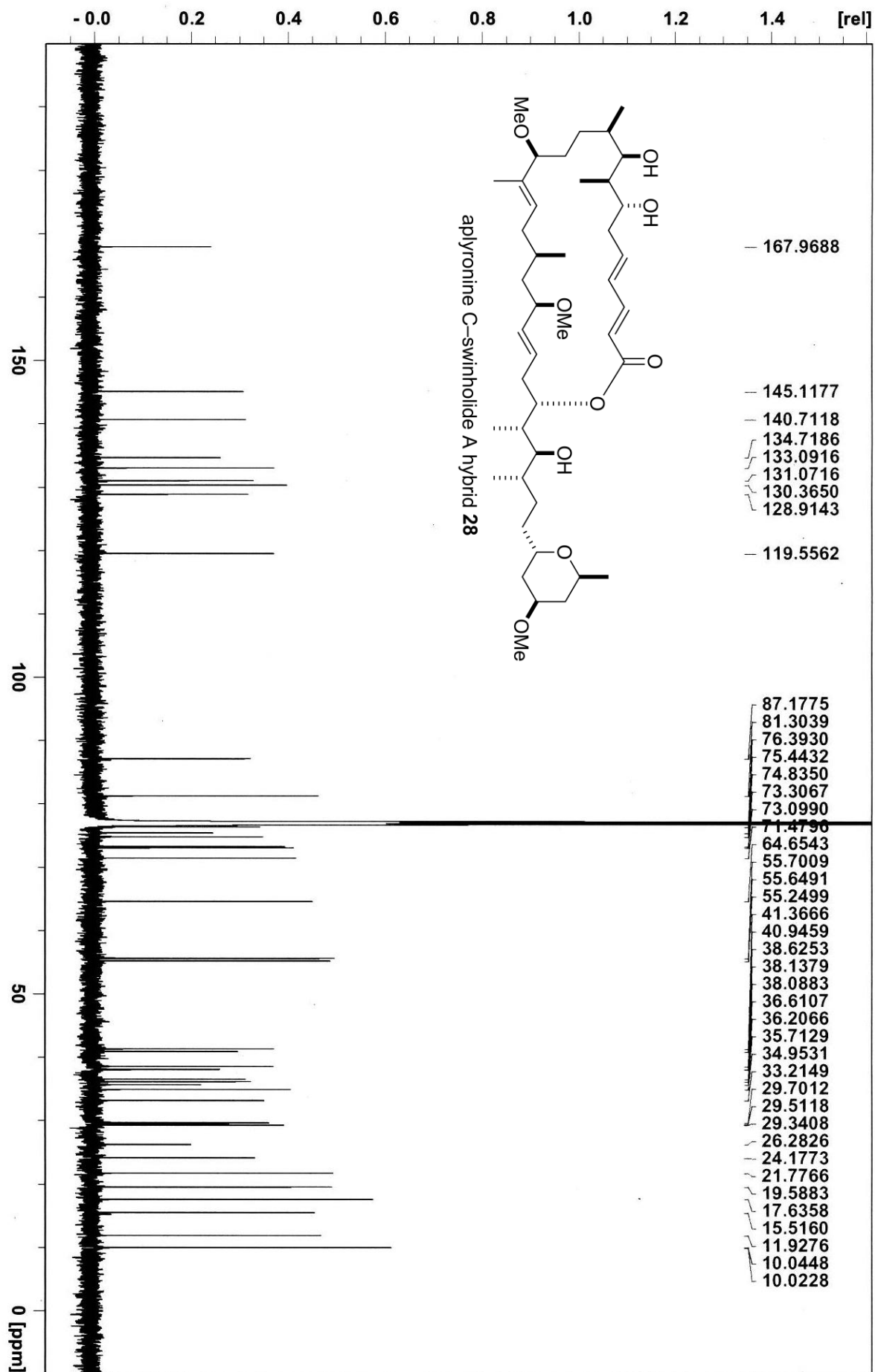


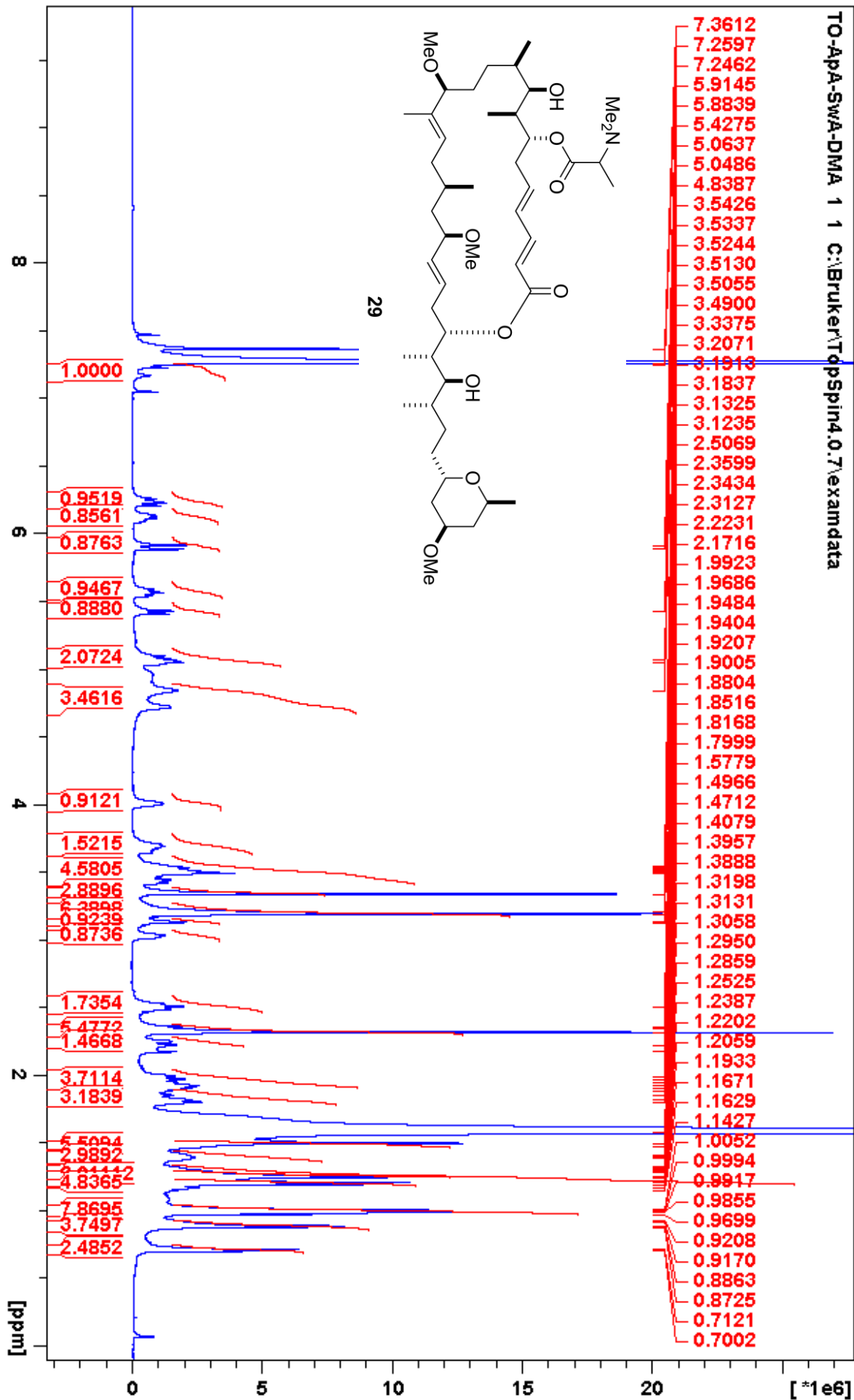


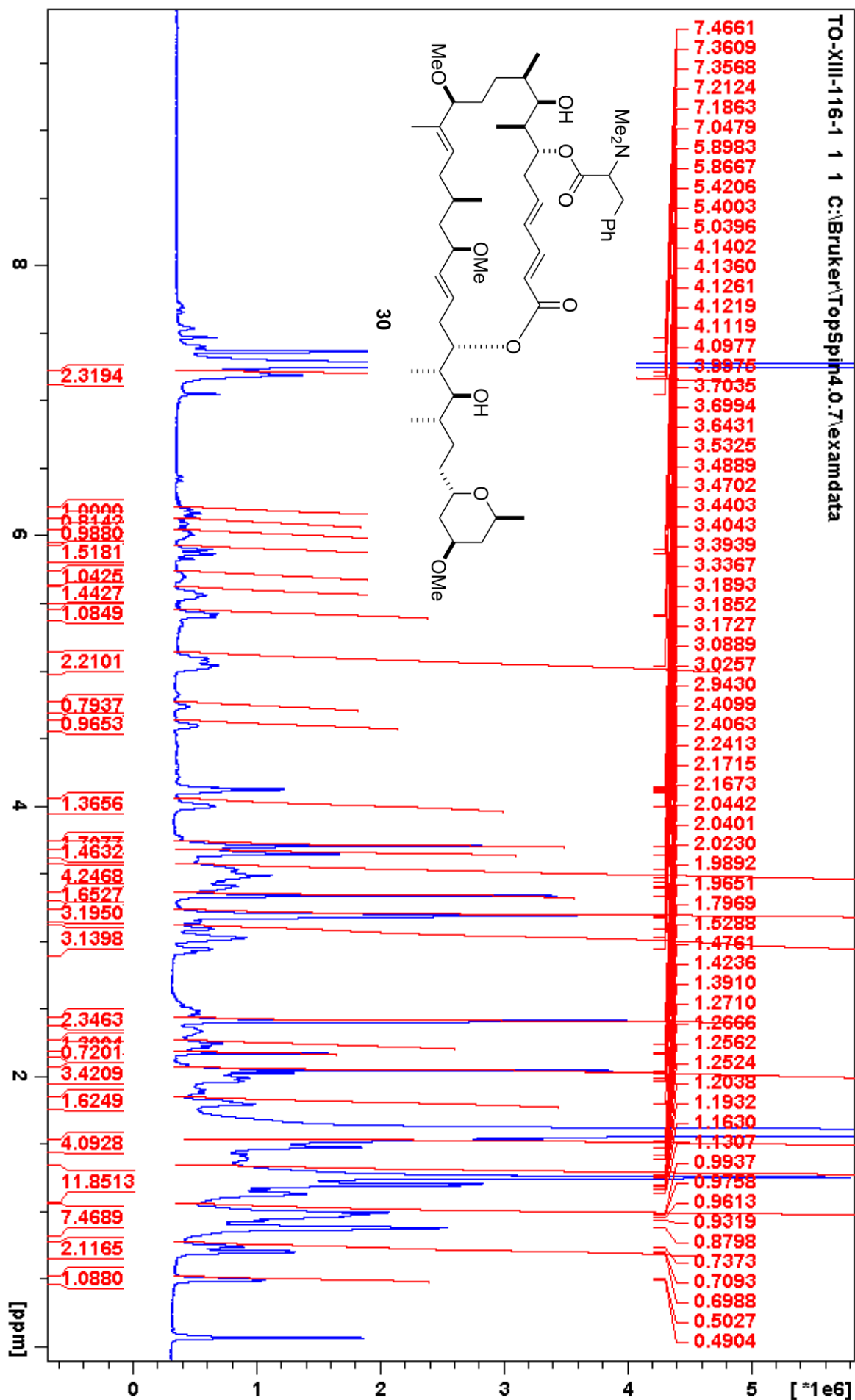


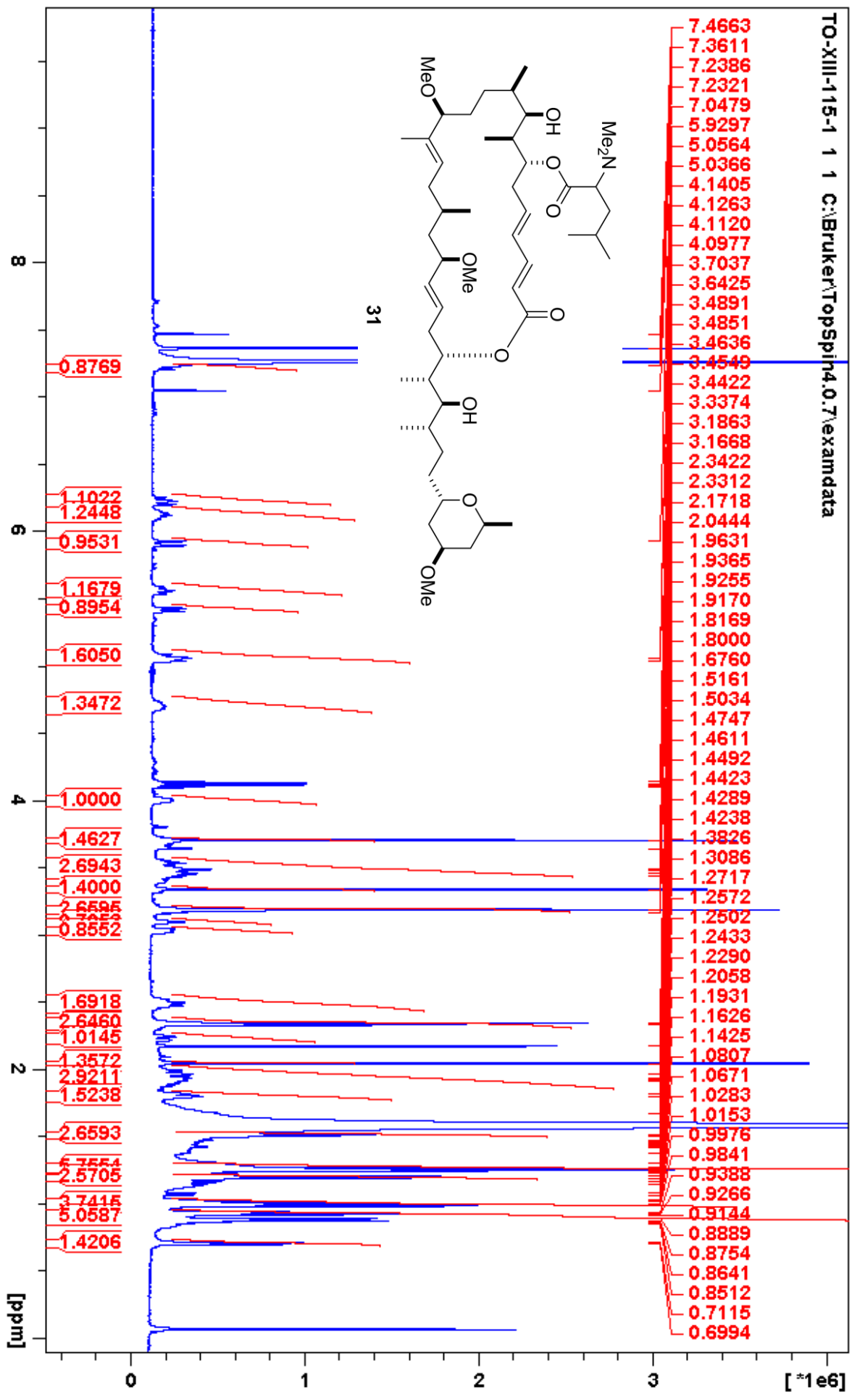


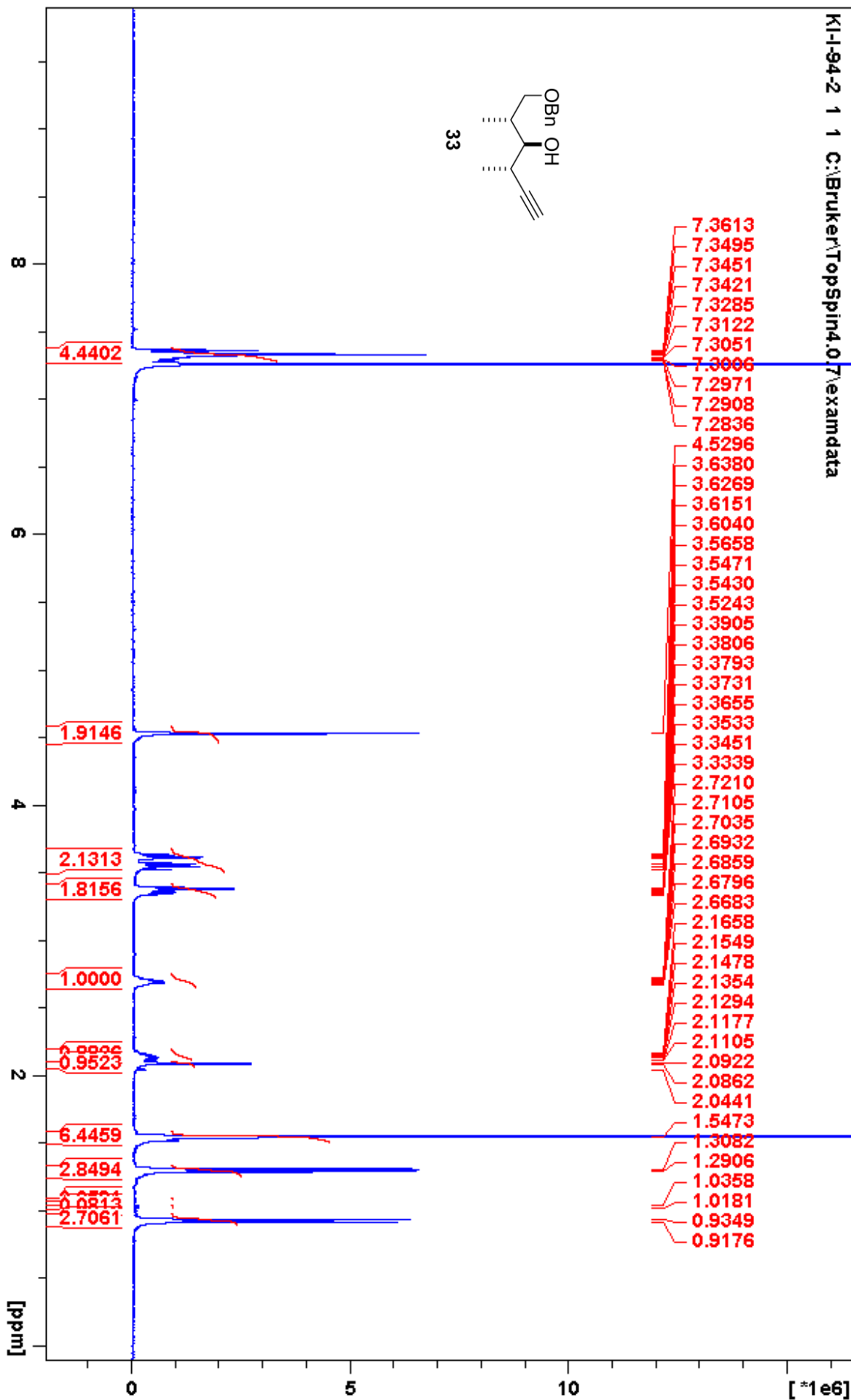
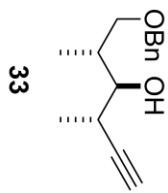


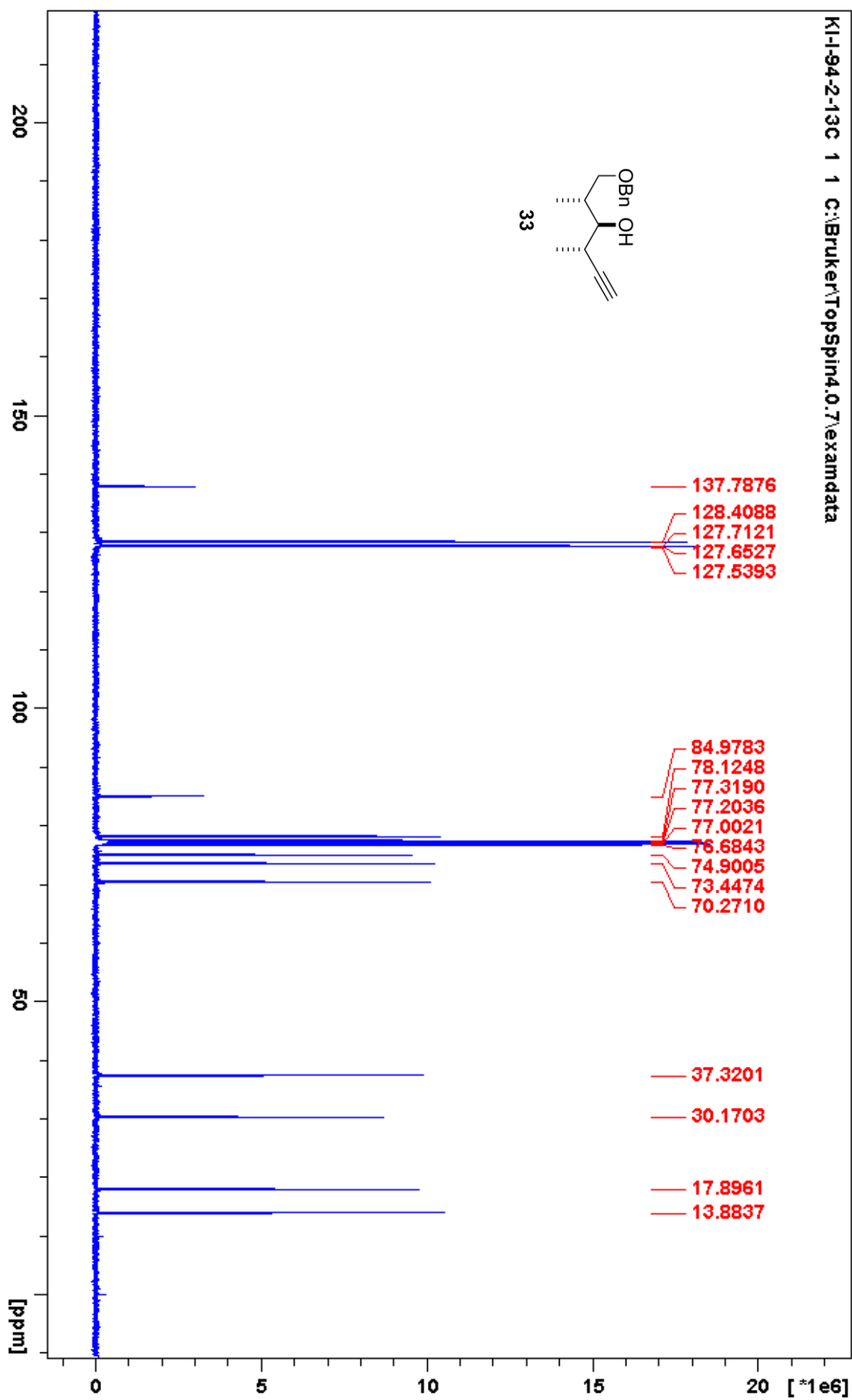
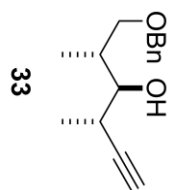














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