

Supplementary information

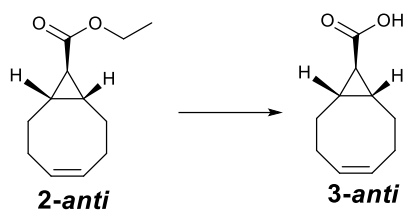
**A concise synthesis of *anti*-bicyclo[6.1.0]nonyne carboxylic acid.**

Mackenzie Weir,<sup>a</sup> Beatrice Vaccari,<sup>a,b</sup> Aidan Matthews,<sup>a</sup> Graeme Turnbull<sup>a</sup> and Valery Kozhevnikov\*<sup>a</sup>

<sup>a</sup> Department of Applied Sciences, Northumbria University, Ellison Building, Newcastle upon Tyne, NE1 8ST, U.K.

<sup>b</sup> Dipartimento di Chimica dell'Università degli Studi di Milano, Via C. Golgi 19, I-20133, Milan, Italy

### Synthesis of acid **3-anti** by ester hydrolysis of ester **2-anti**



The ester **2-anti** (4.91 g, 25.3 mmol, 1 eq.) was dissolved in ethanol (60 ml). A warm (50°C) solution of lithium hydroxide monohydrate (1.6 g, 38.0 mmol, 1.5 eq.) in water (30 ml) was added. The reaction mixture was stirred and heated under reflux for **30 minutes**. The mixture was allowed to cool to RT and evaporated. The residue was diluted with water to a volume of 150 mL. 2M aqueous HCl (20 mL, 40 mmol) was added, causing formation of the solid. The solid was filtered off, washed with water to give acid **3-anti** as a colourless solid. Yield 3.5 g (84%). NMR data is identical to previously published (Figure S4).<sup>1</sup>

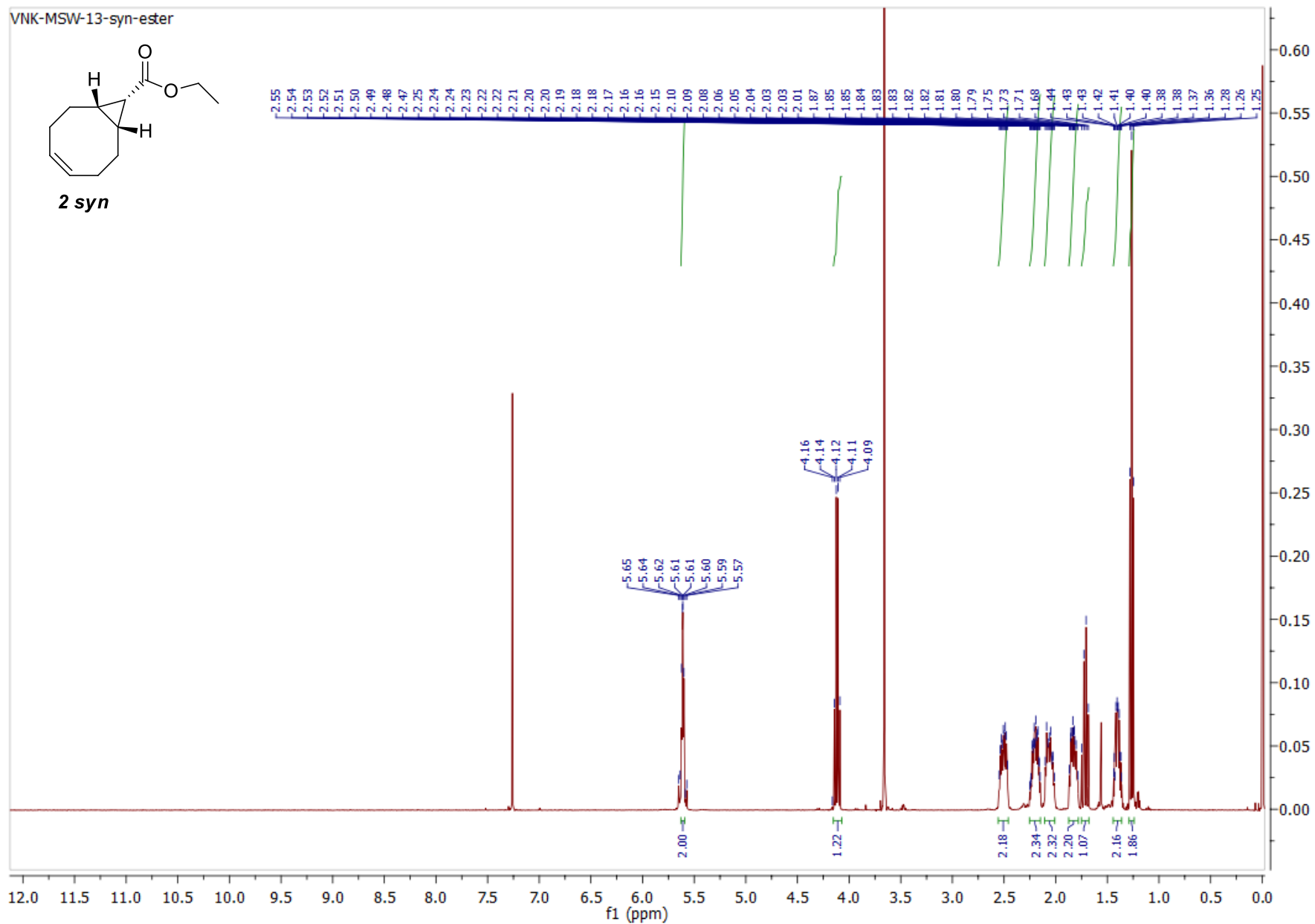


Figure S1.  $^1\text{H}$  NMR spectrum of **2-syn** in CDCl<sub>3</sub>. (1) O'Brien, J. G. K.; Chintala, S. R.; Fox, J. M. Stereoselective Synthesis of Bicyclo[6.1.0]nonene Precursors of the Bioorthogonal Reagents s-TCO and BCN. *The Journal of Organic Chemistry* **2018**, *83* (14), 7500-7503. DOI: 10.1021/acs.joc.7b02329.

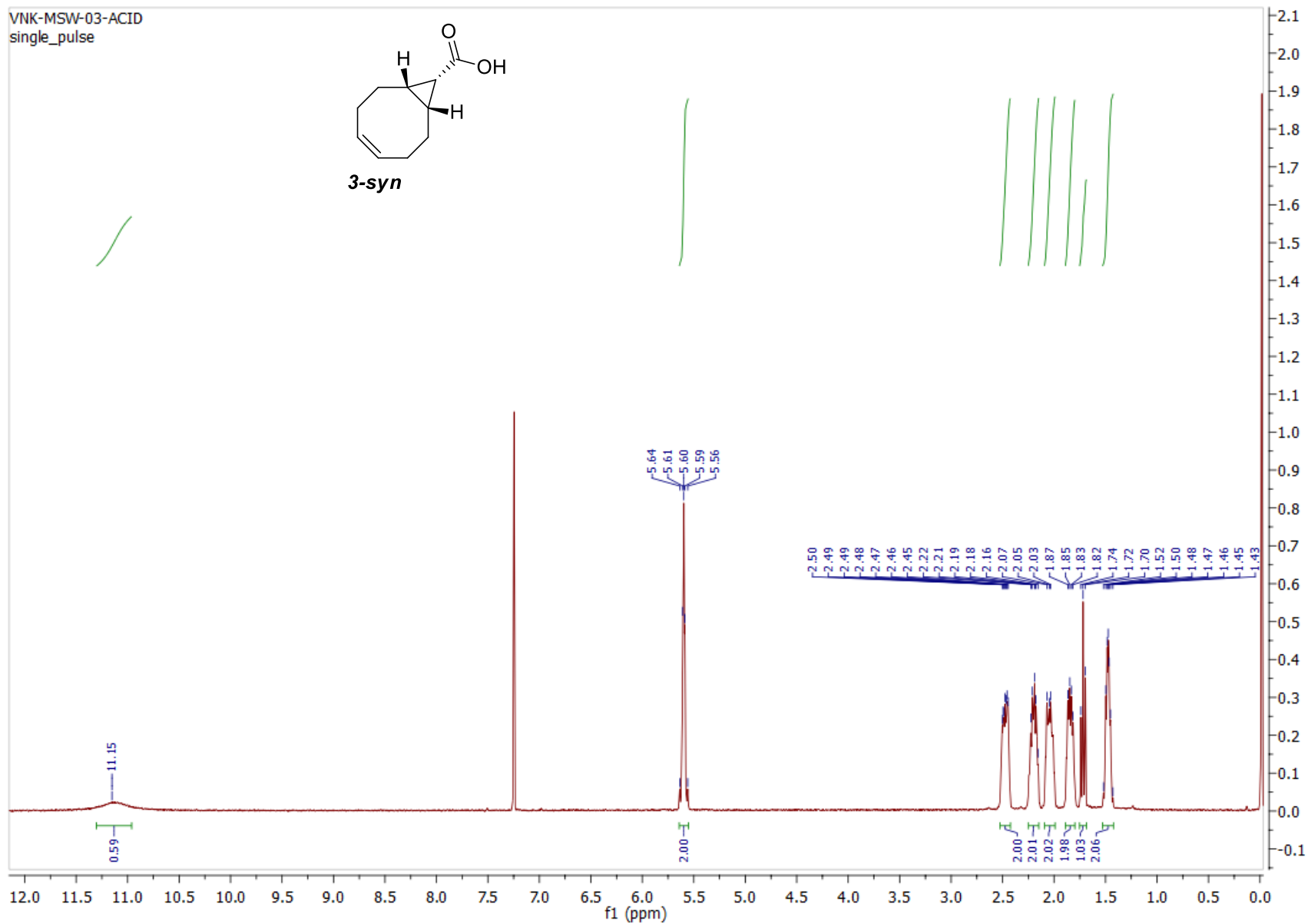


Figure S2:  $^1\text{H}$  NMR spectrum of **3-syn** in  $\text{CDCl}_3$ .

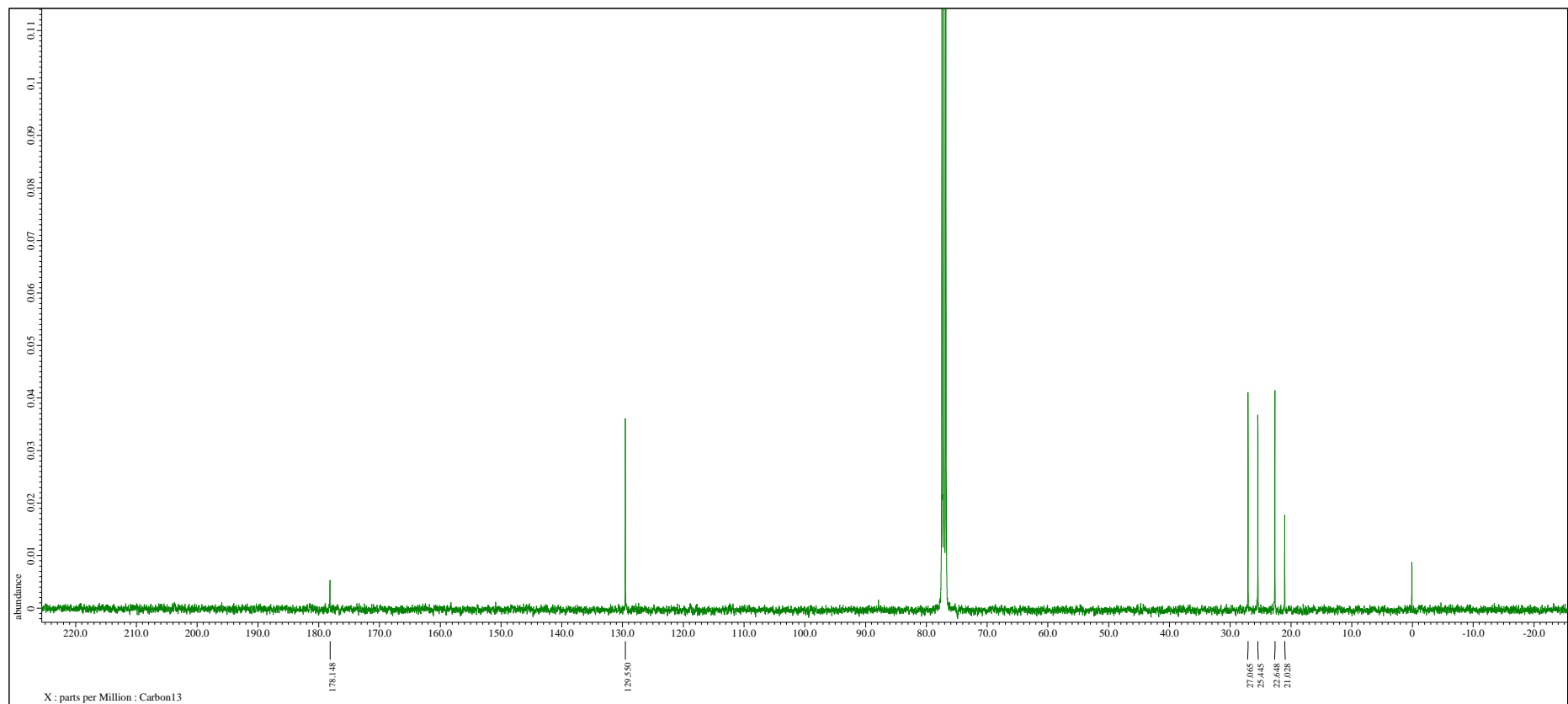


Figure S3:  $^{13}\text{C}$  NMR spectrum of **3-syn** in  $\text{CDCl}_3$ .

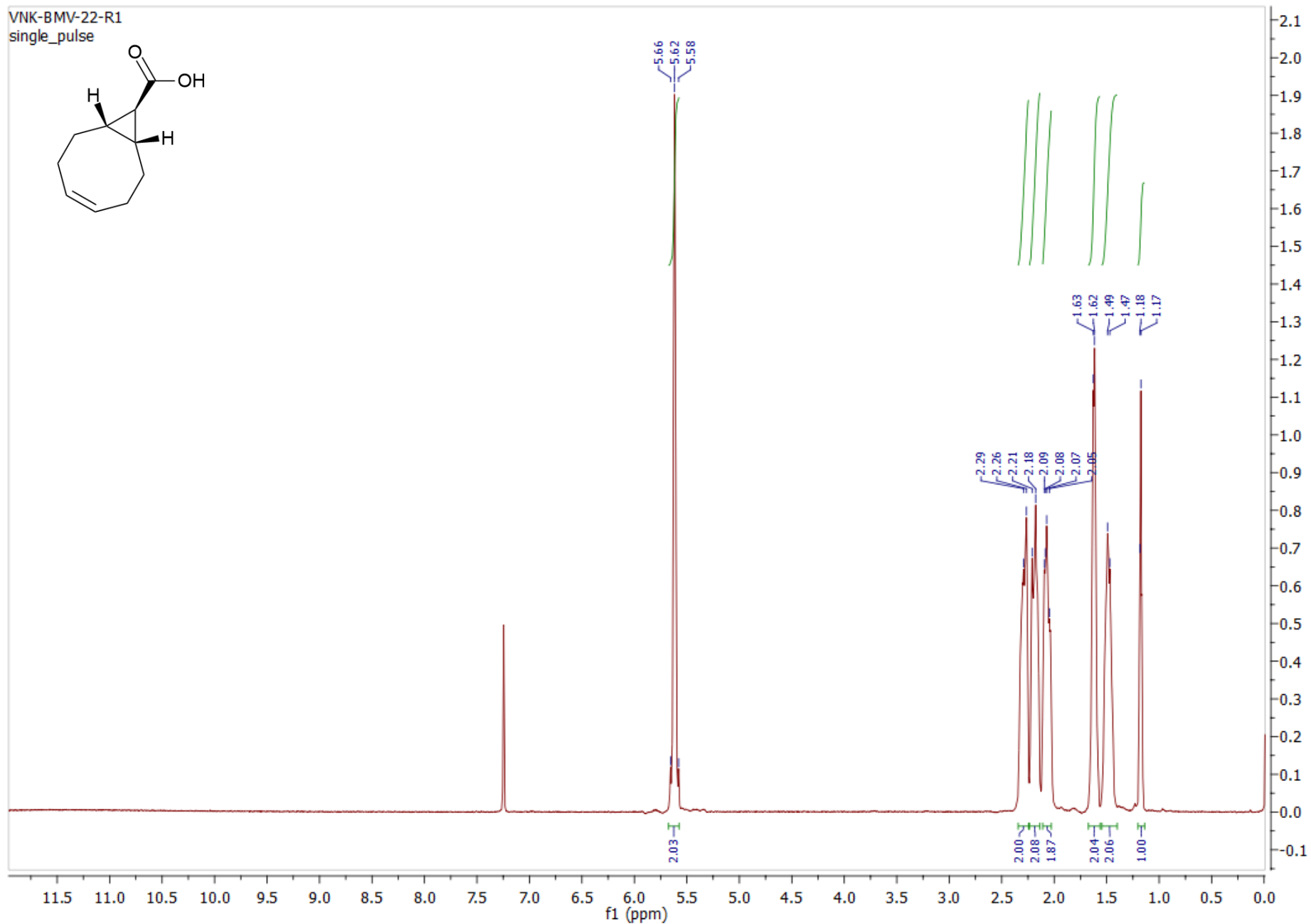


Figure S4:  $^1\text{H}$  NMR spectrum of **3-anti** in  $\text{CDCl}_3$ .

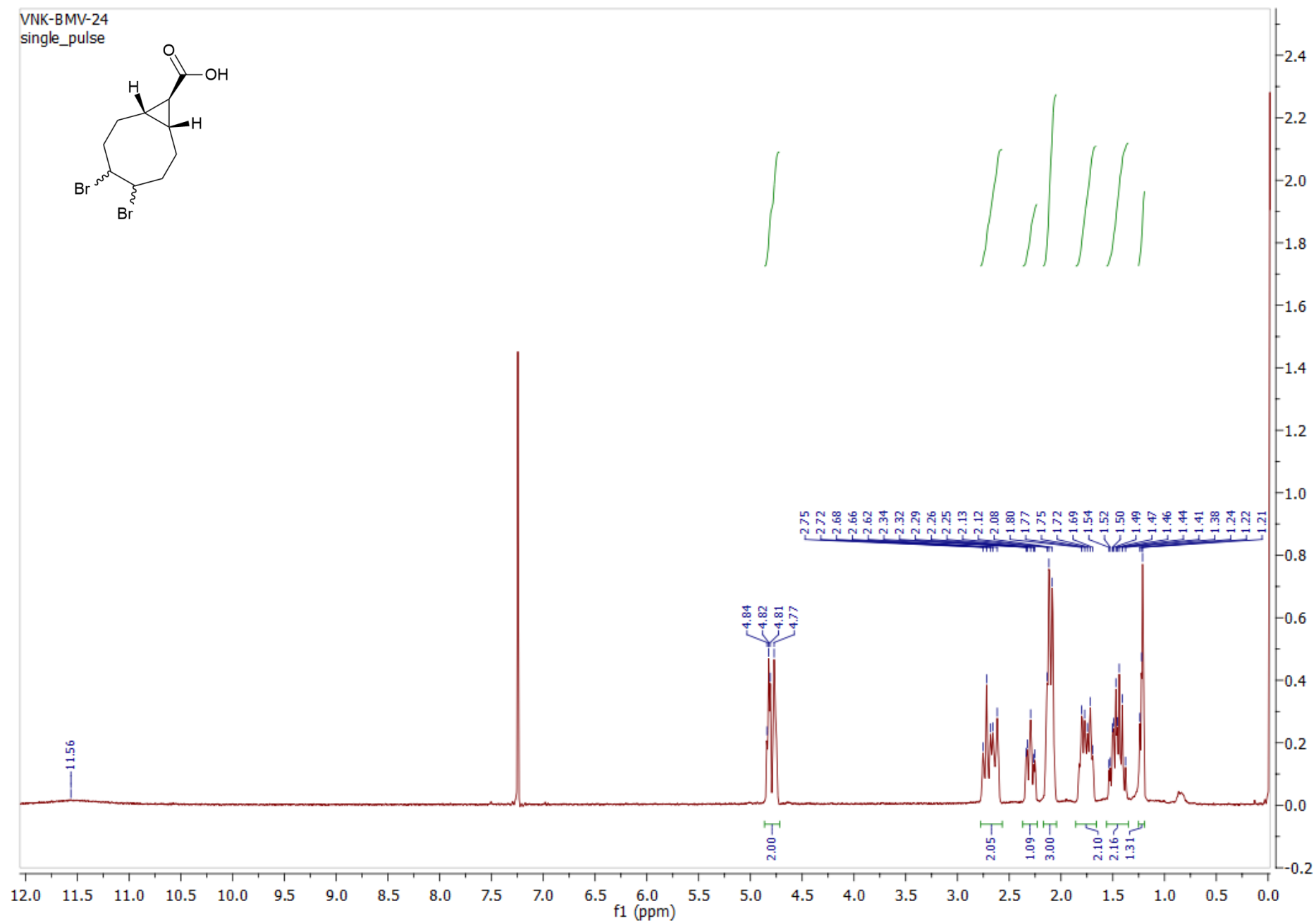


Figure S5:  $^1\text{H}$  NMR spectrum of **4-anti** in  $\text{CDCl}_3$ .

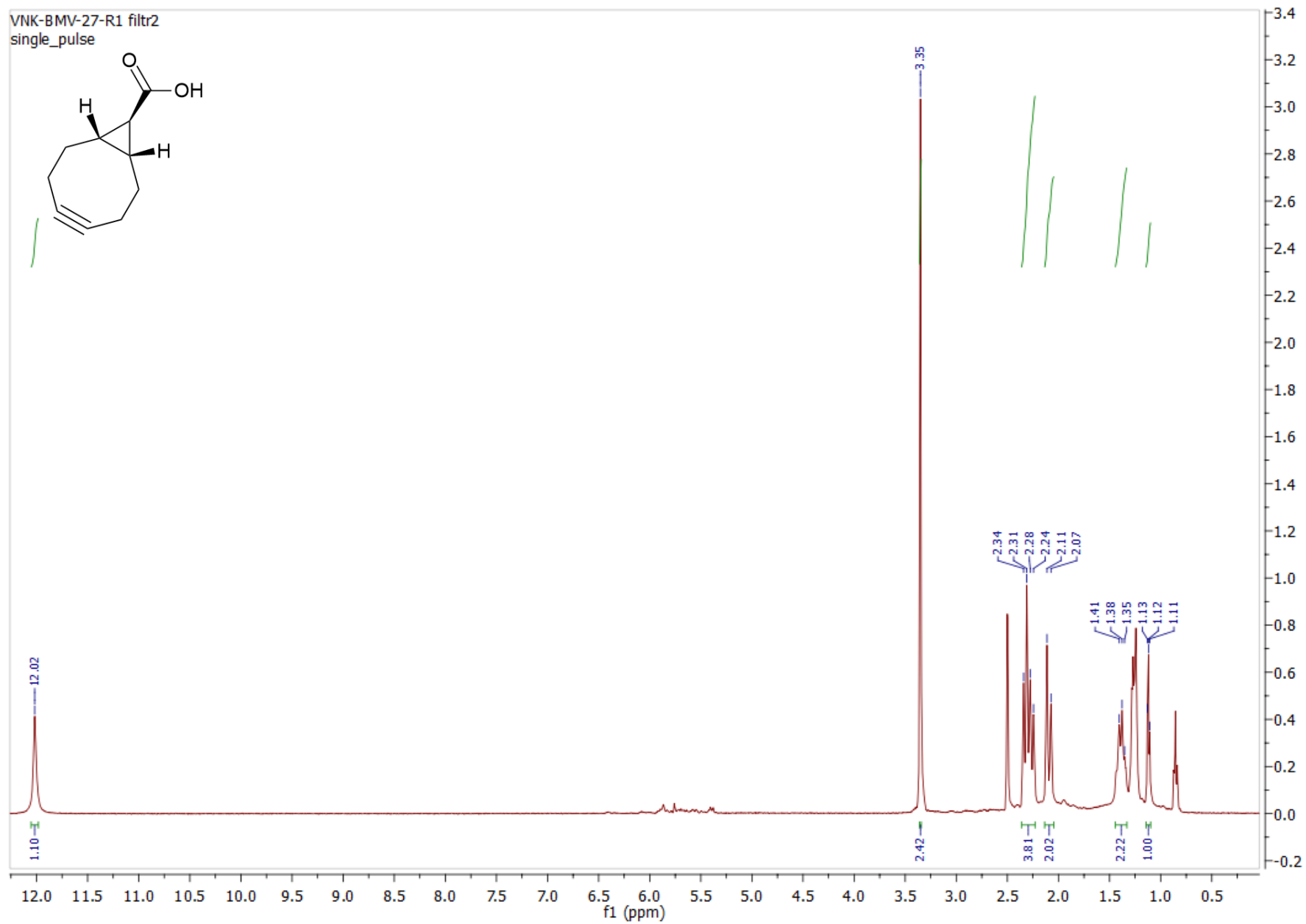


Figure S6:  $^1\text{H}$  NMR spectrum of **5-anti** in  $\text{DMSO-D}_6$ .



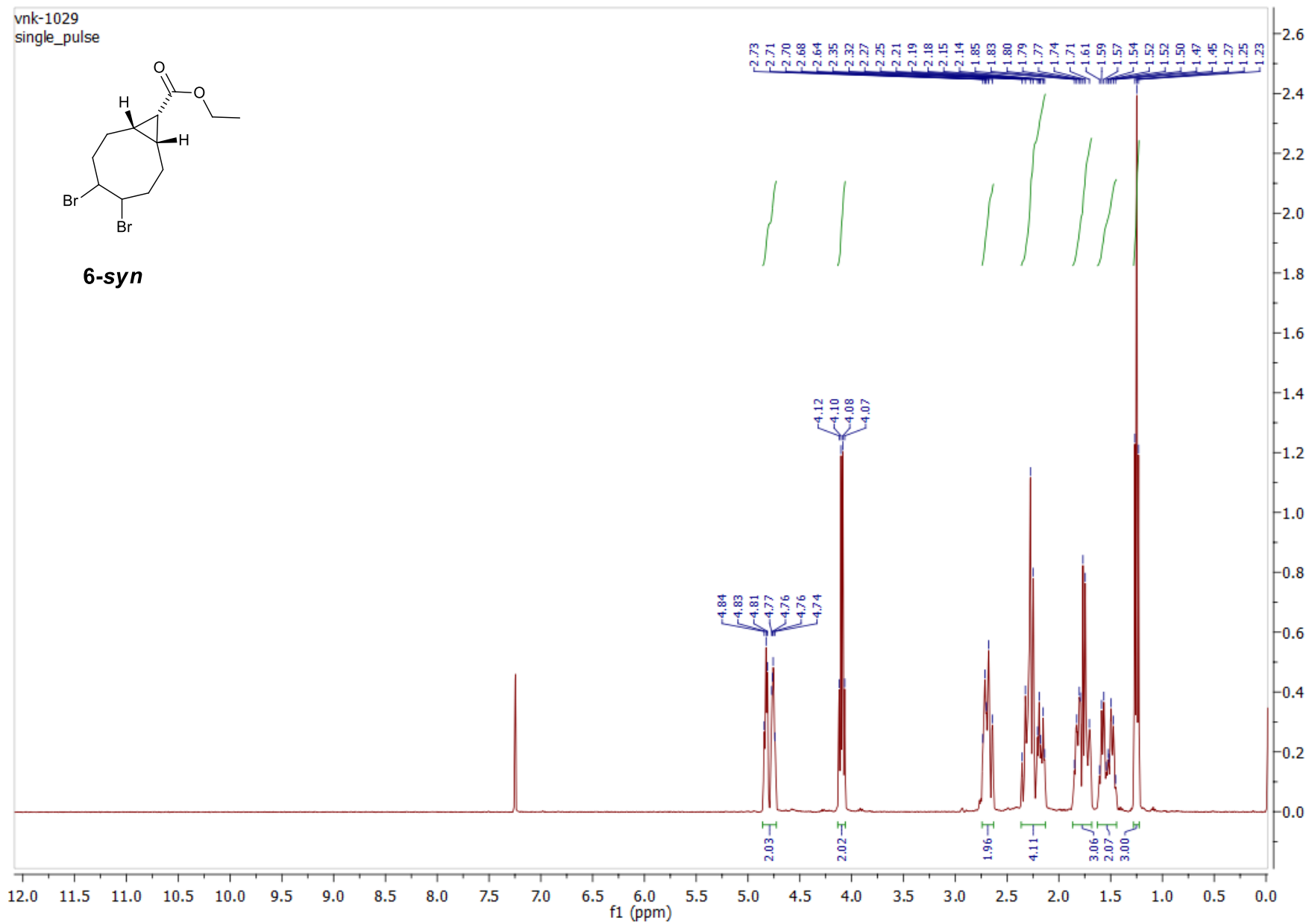


Figure S7:  $^1\text{H}$  NMR spectrum of **6-syn** in  $\text{CDCl}_3$ .

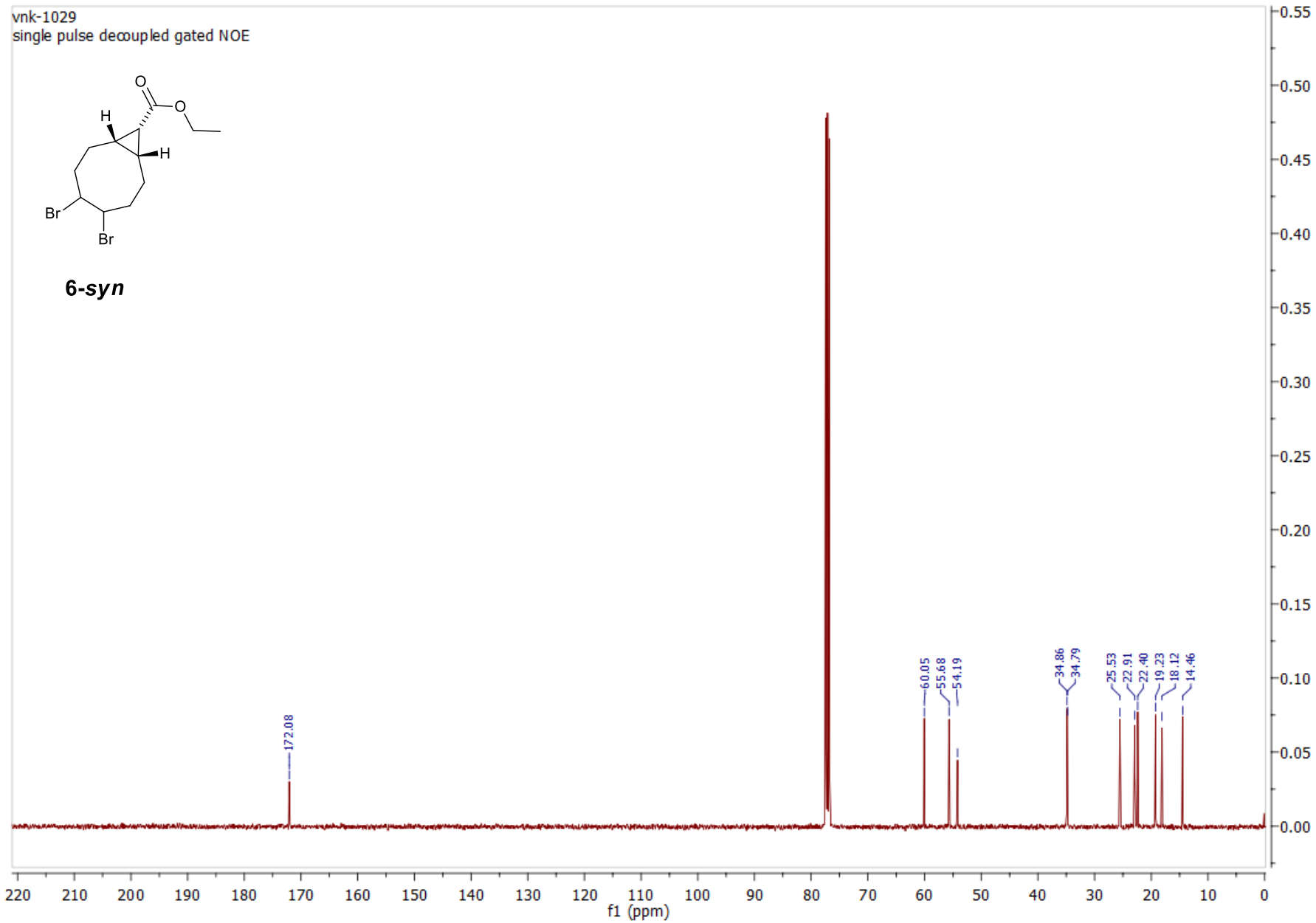


Figure S8:  $^{13}\text{C}$  NMR spectrum of **6-syn** in  $\text{CDCl}_3$ .

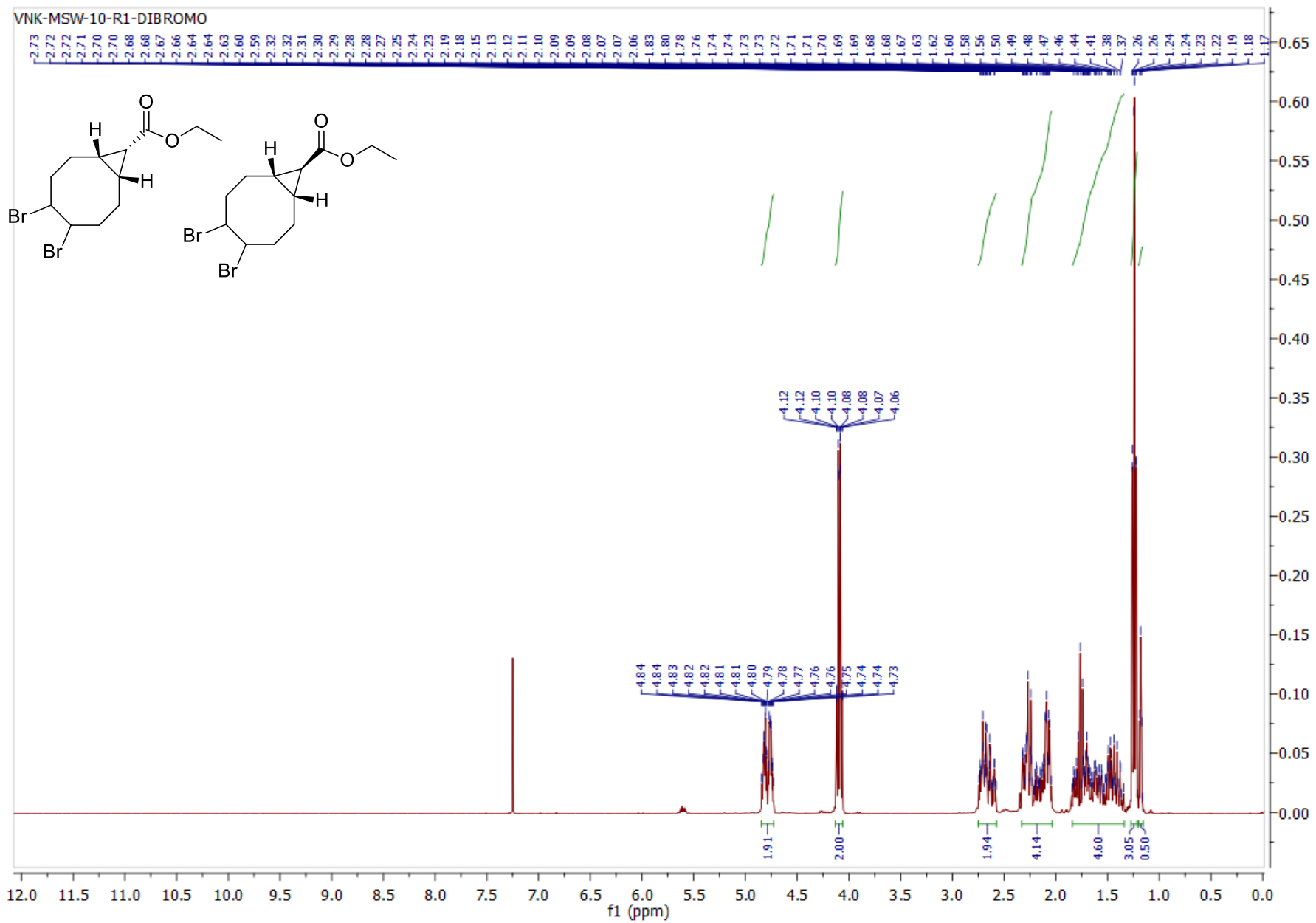


Figure S9:  $^1\text{H}$  NMR spectrum of **VNK-MSW-10-R1 (6-syn 6-anti)** in  $\text{CDCl}_3$ .

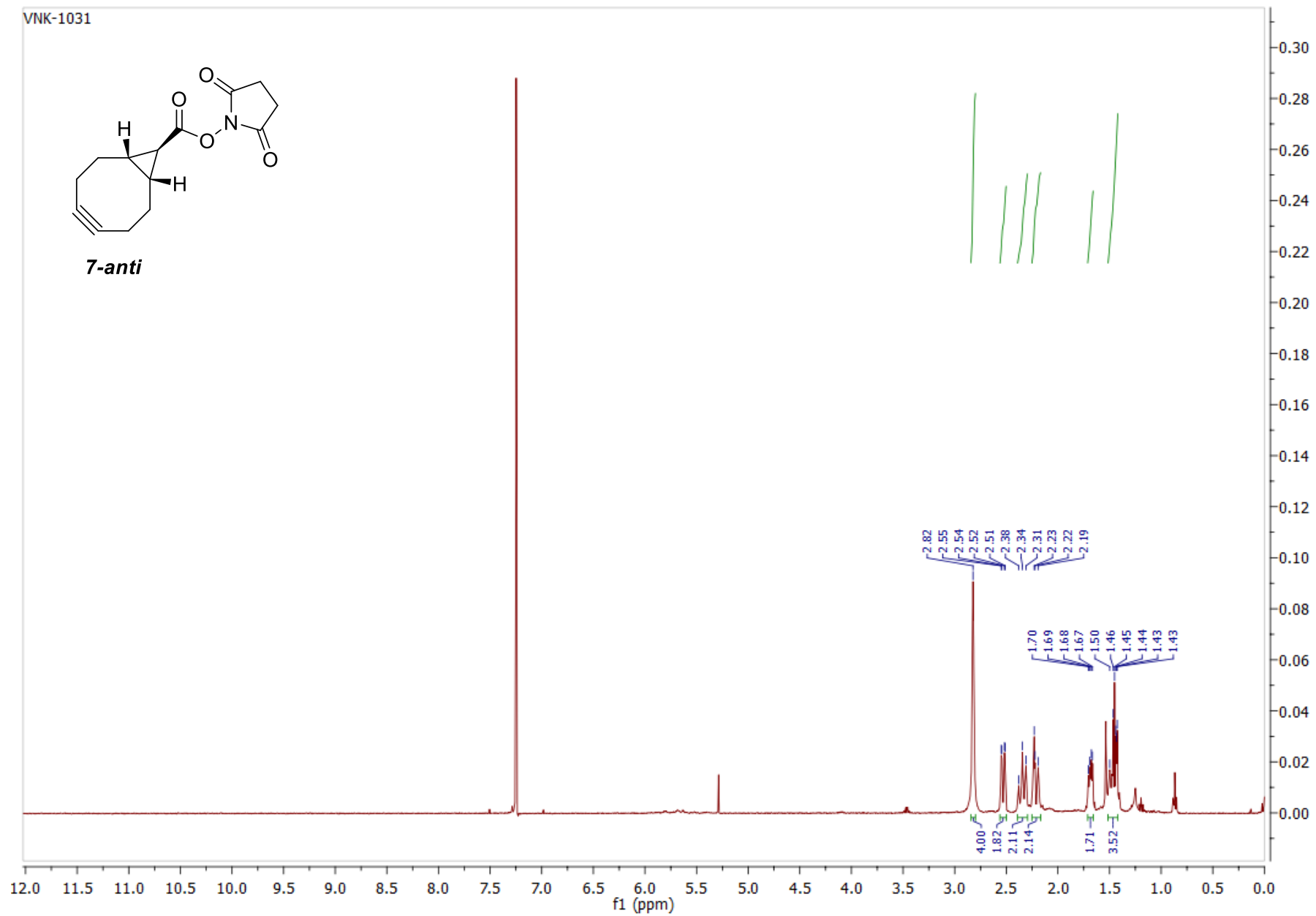


Figure S10:  $^1\text{H}$  NMR spectrum of **7-anti** in  $\text{CDCl}_3$ .

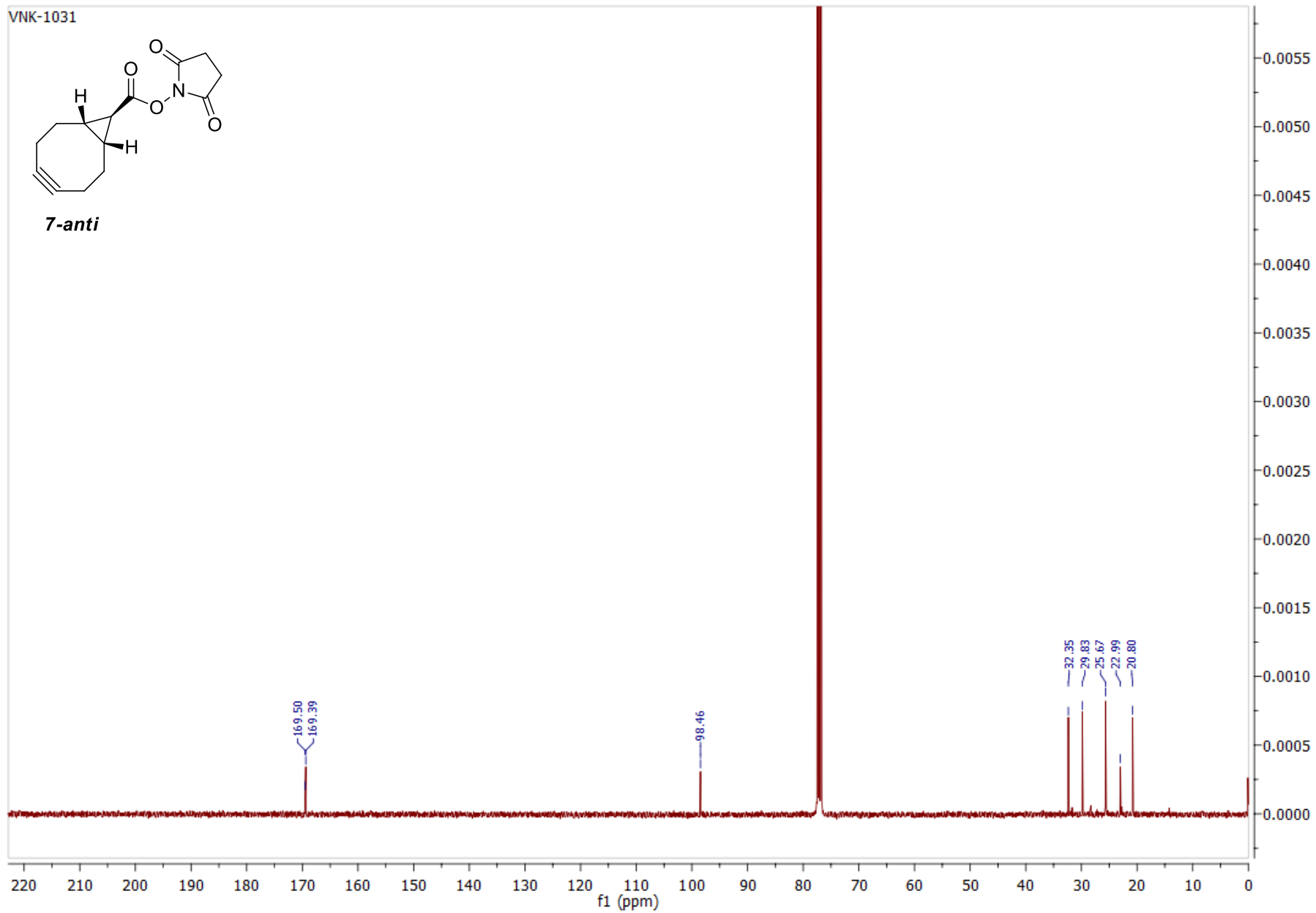


Figure S11: <sup>13</sup>C NMR spectrum of **7-anti** in CDCl<sub>3</sub>.