

## Supporting Information

### **Synthesis and Antitumor Evaluation of Biotin-SN38-valproic acid Conjugates**

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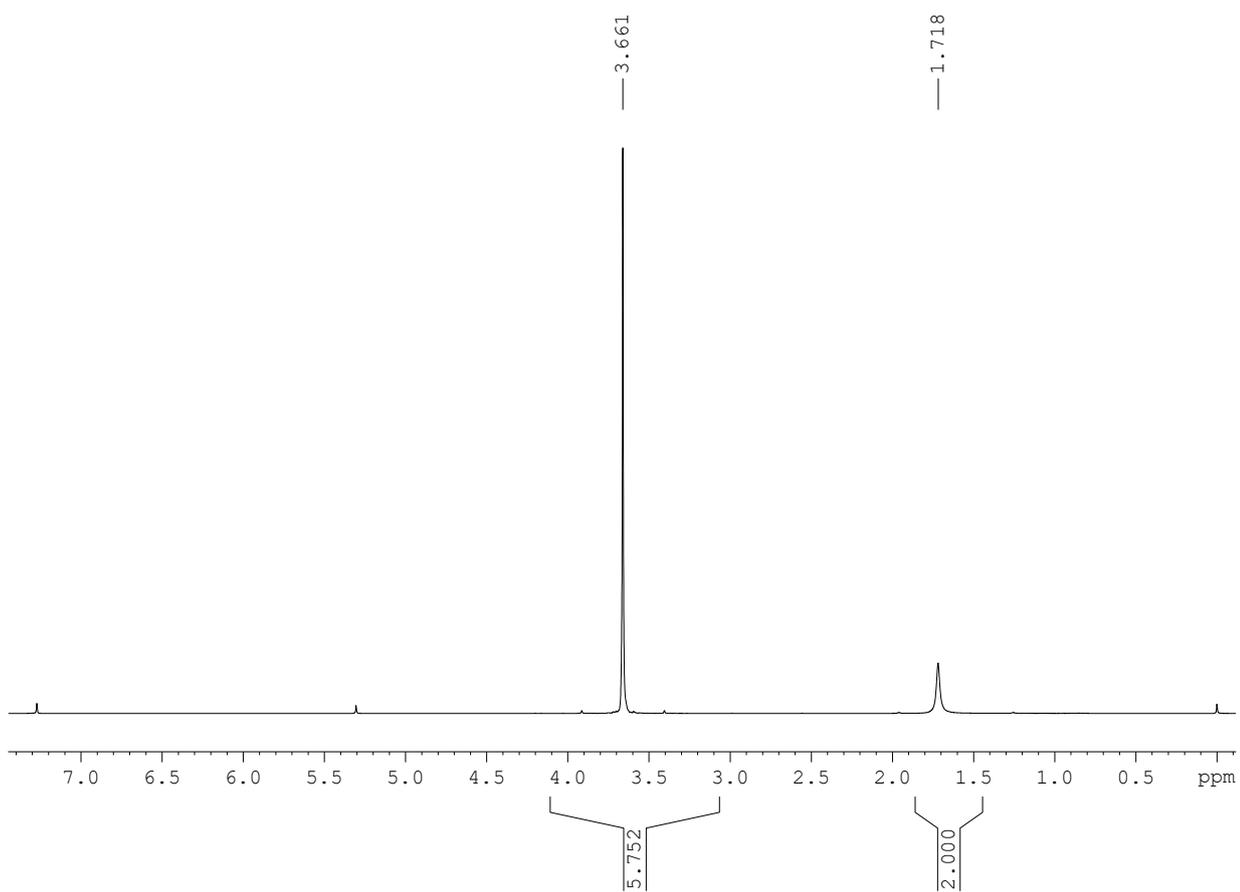
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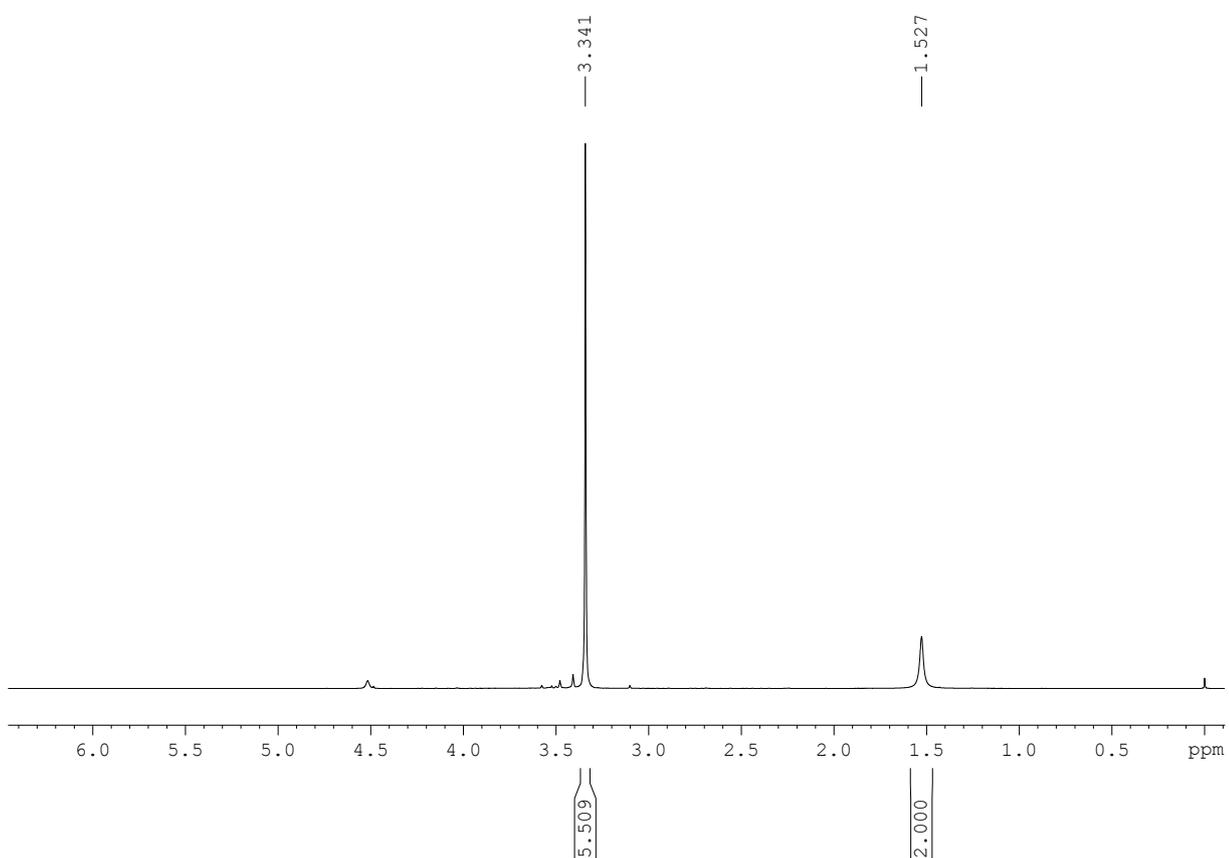
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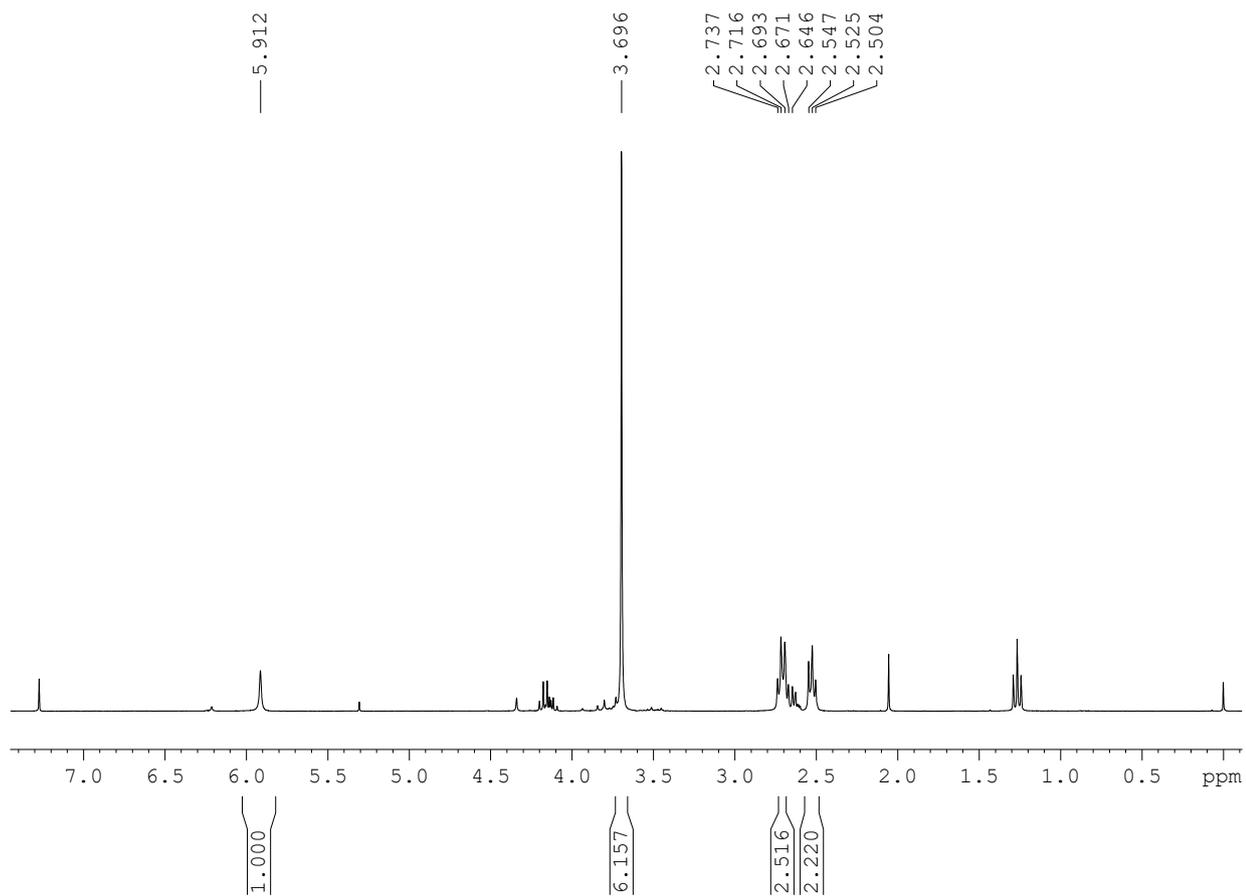
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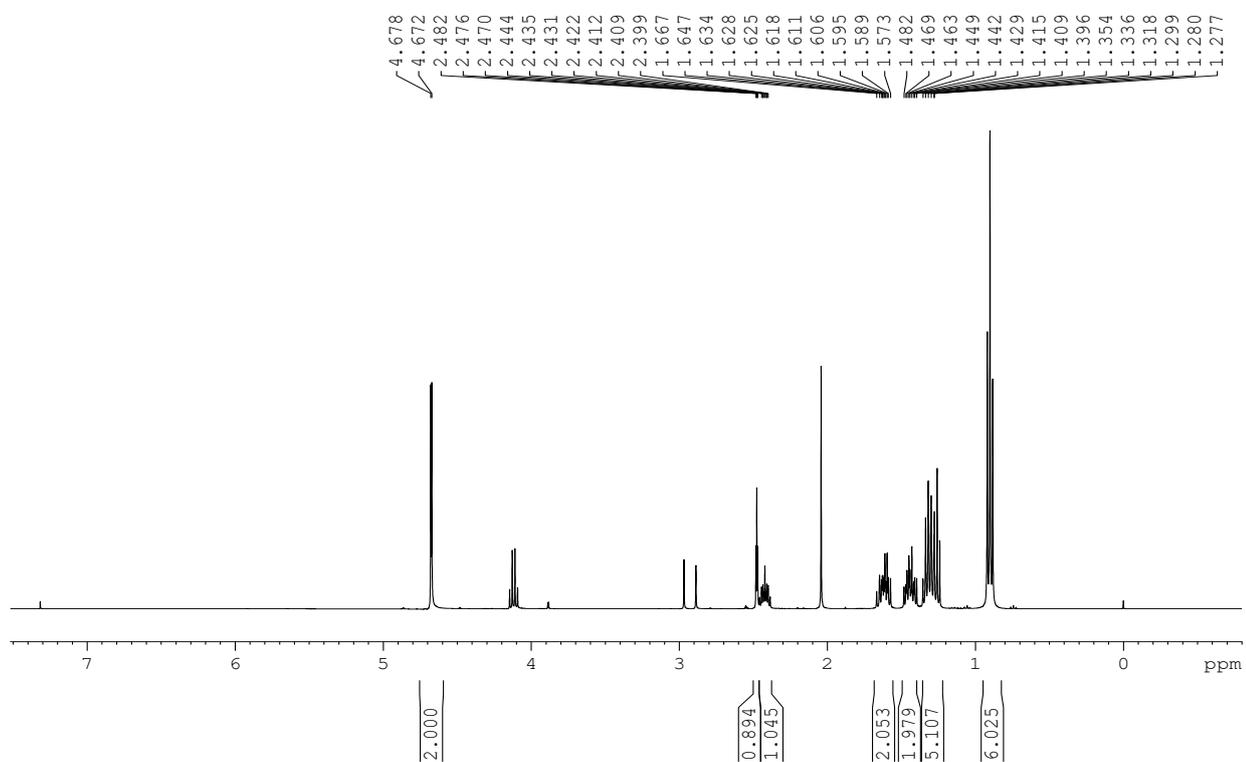
**Figure S1.** <sup>1</sup>H NMR spectrum of compound **1** (300 MHz, Chloroform-*d*)



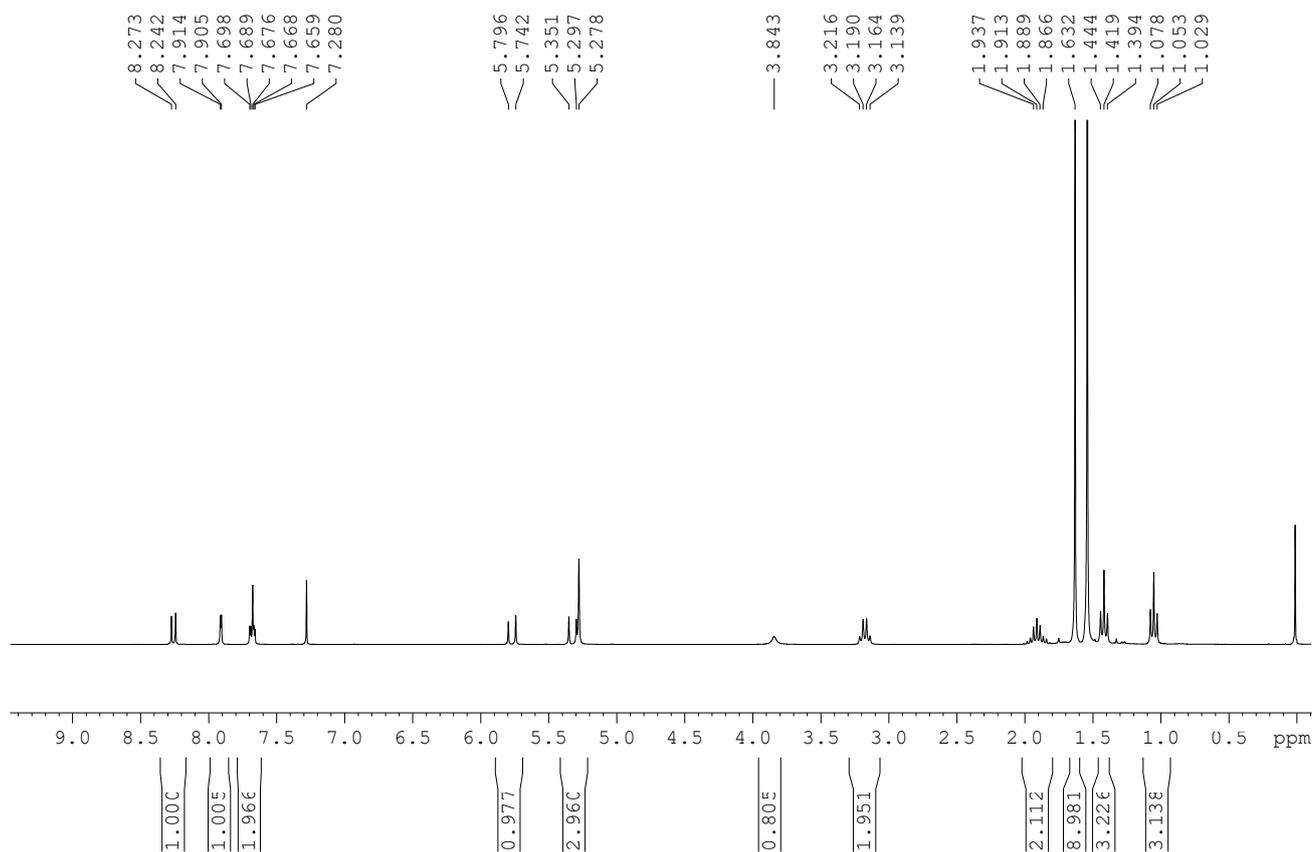
**Figure S2.** <sup>1</sup>H NMR spectrum of compound **2** (300 MHz, Chloroform-*d*)



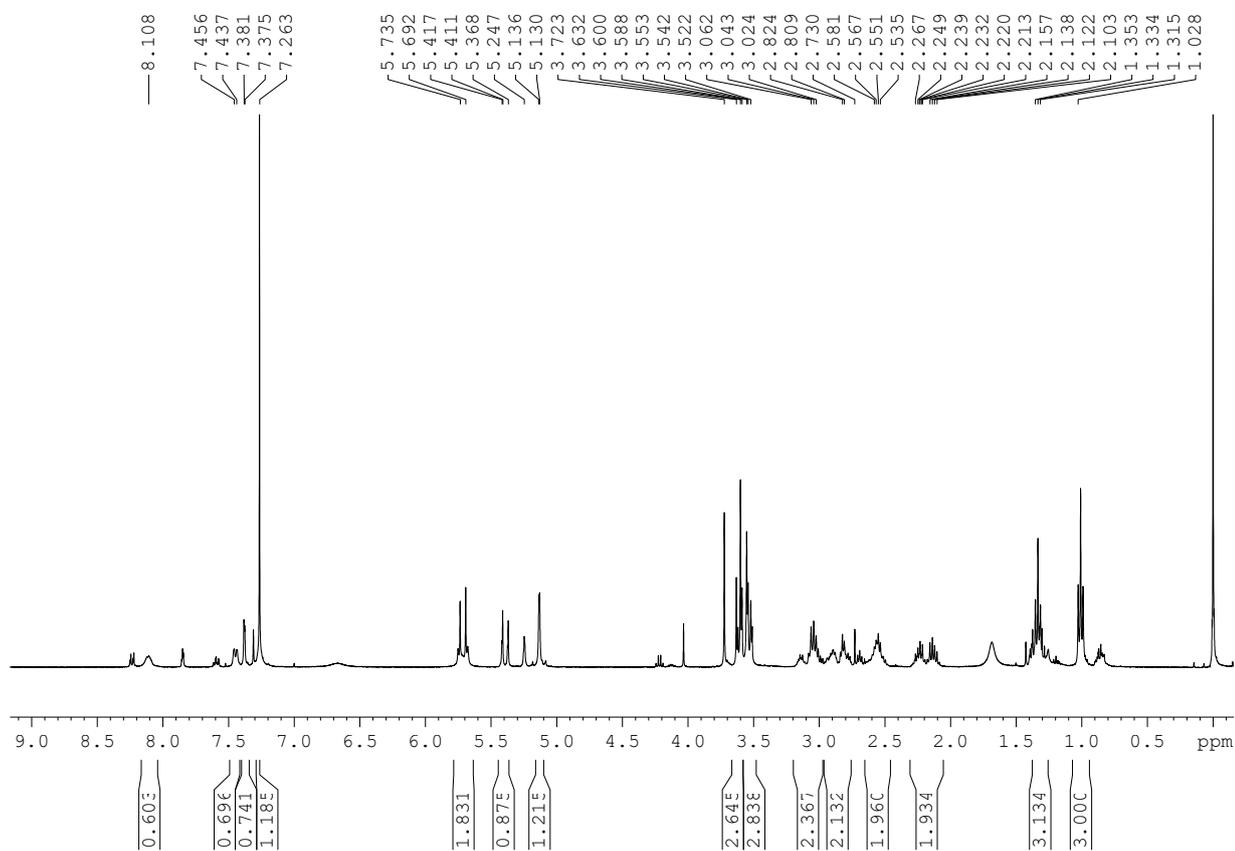
**Figure S3.**  $^1\text{H}$  NMR spectrum of compound **3** (300 MHz, Chloroform-*d*)



**Figure S4.**  $^1\text{H}$  NMR spectrum of compound **4** (400 MHz, Chloroform-*d*)



**Figure S5.**  $^1\text{H}$  NMR spectrum of compound 5 (300 MHz, Chloroform-*d*)



**Figure S6.**  $^1\text{H}$  NMR spectrum of compound 7 (400 MHz, Chloroform-*d*)

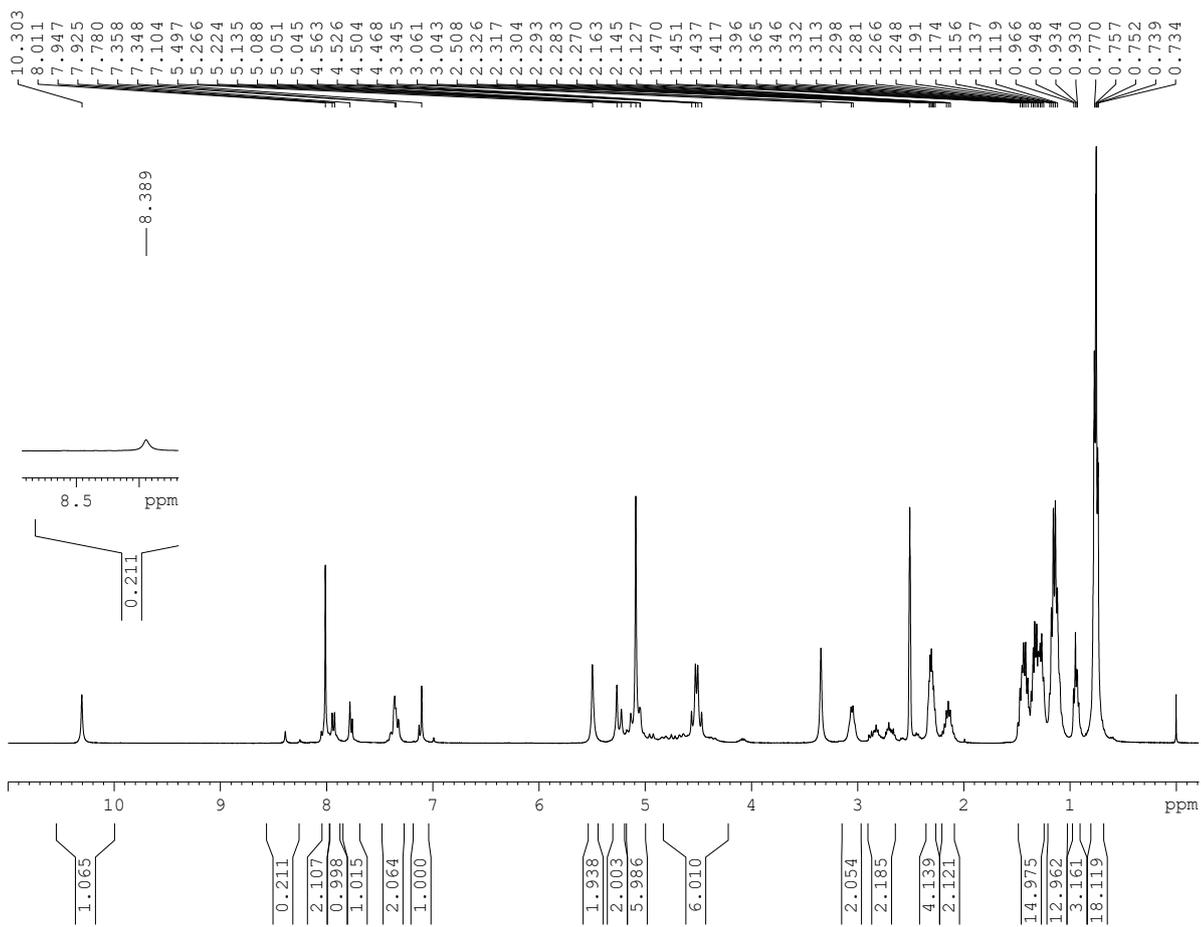
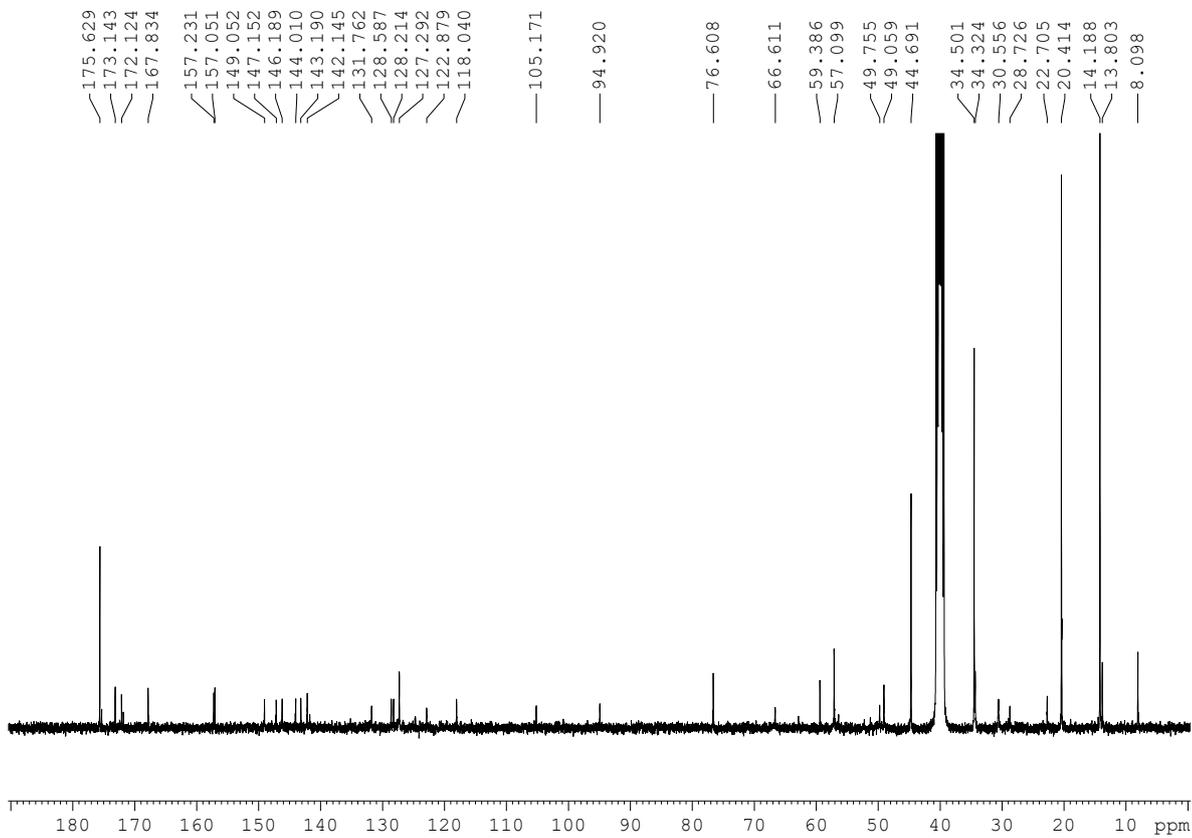
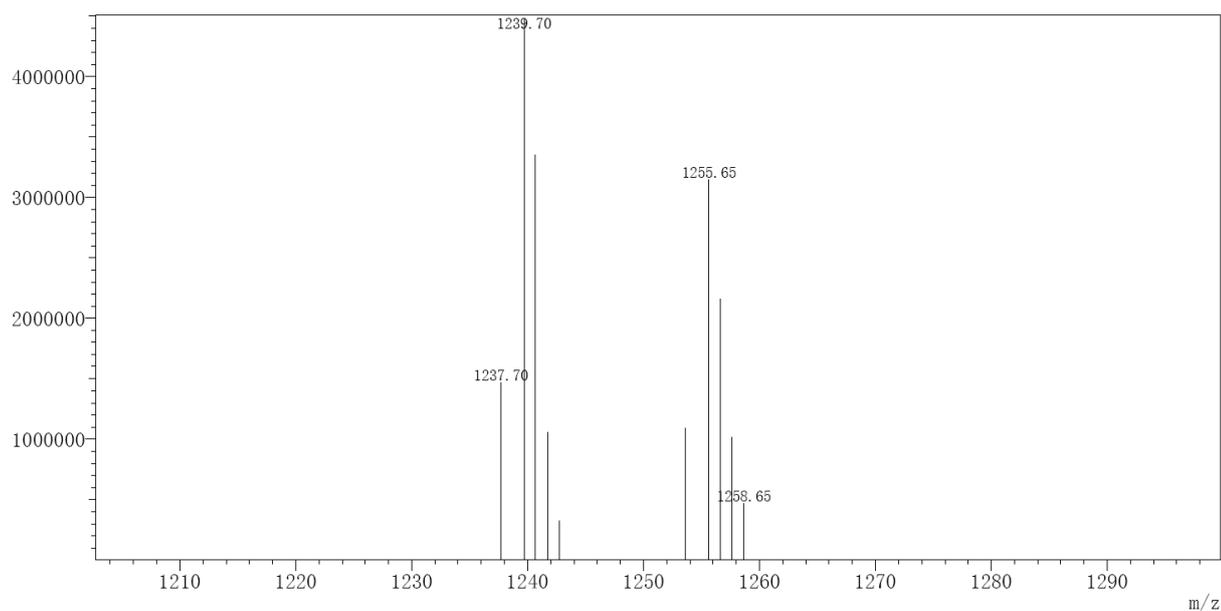


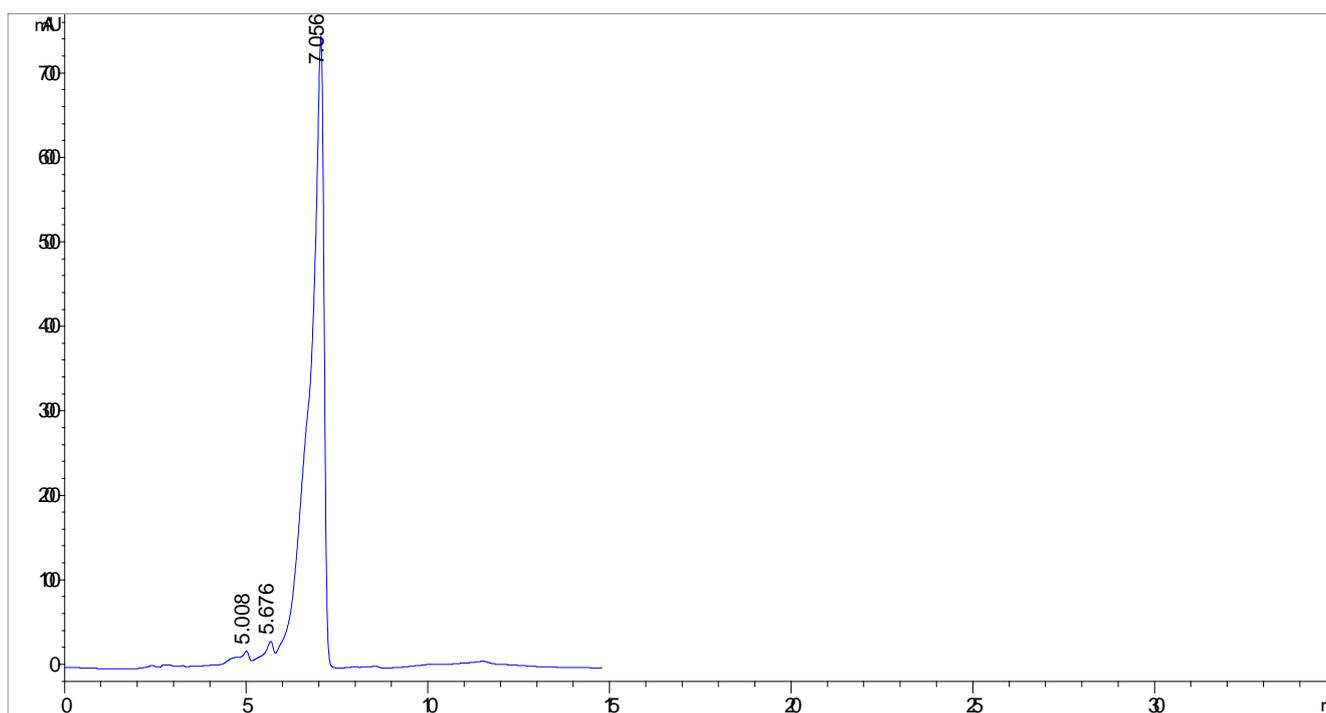
Figure S7.  $^1\text{H}$  NMR spectrum of compound **8** (400 MHz,  $\text{DMSO-}d_6$ )



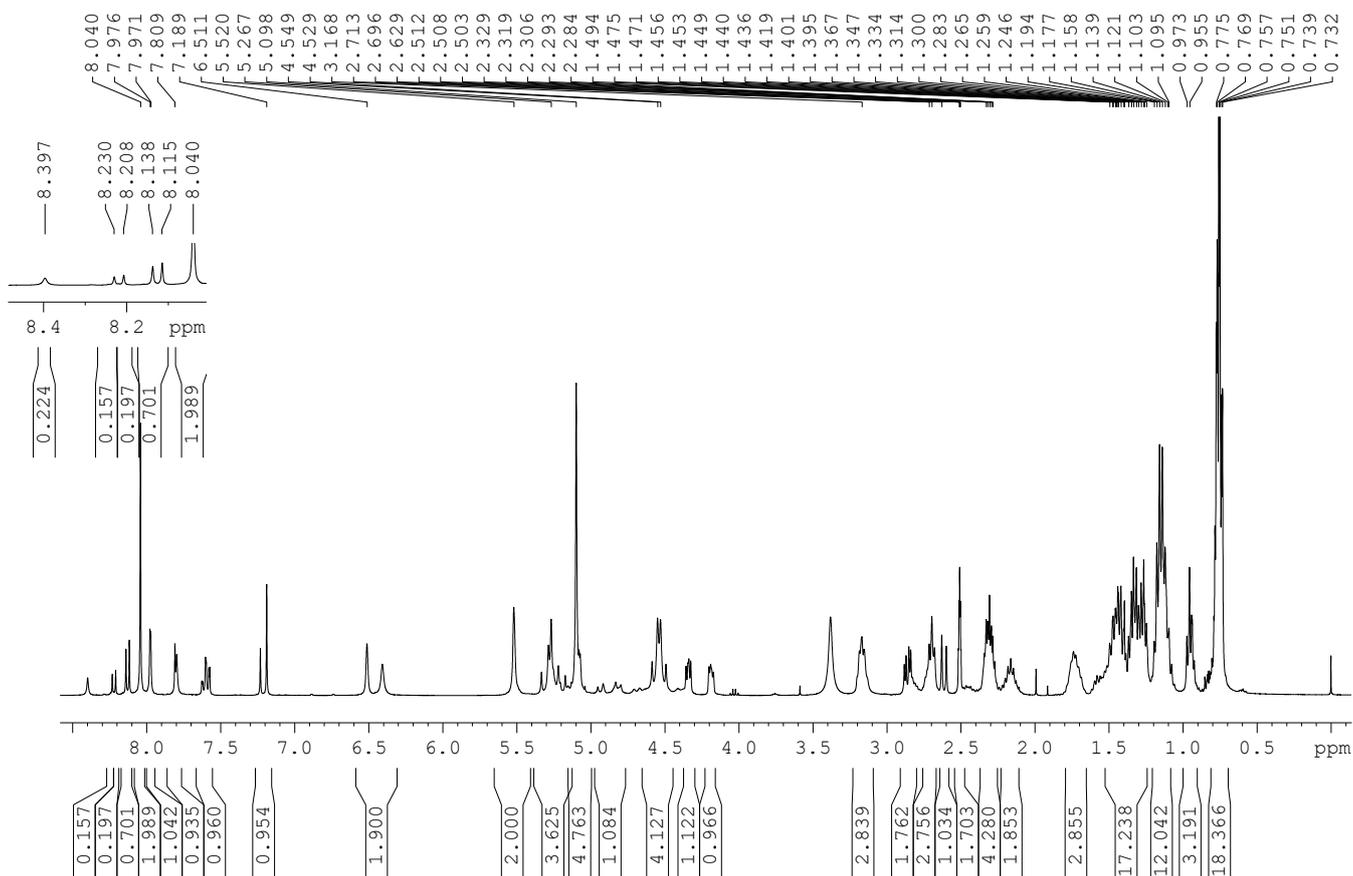
**Figure S8.**  $^{13}\text{C}$  NMR spectrum of compound **8** (101 MHz,  $\text{DMSO-}d_6$ )



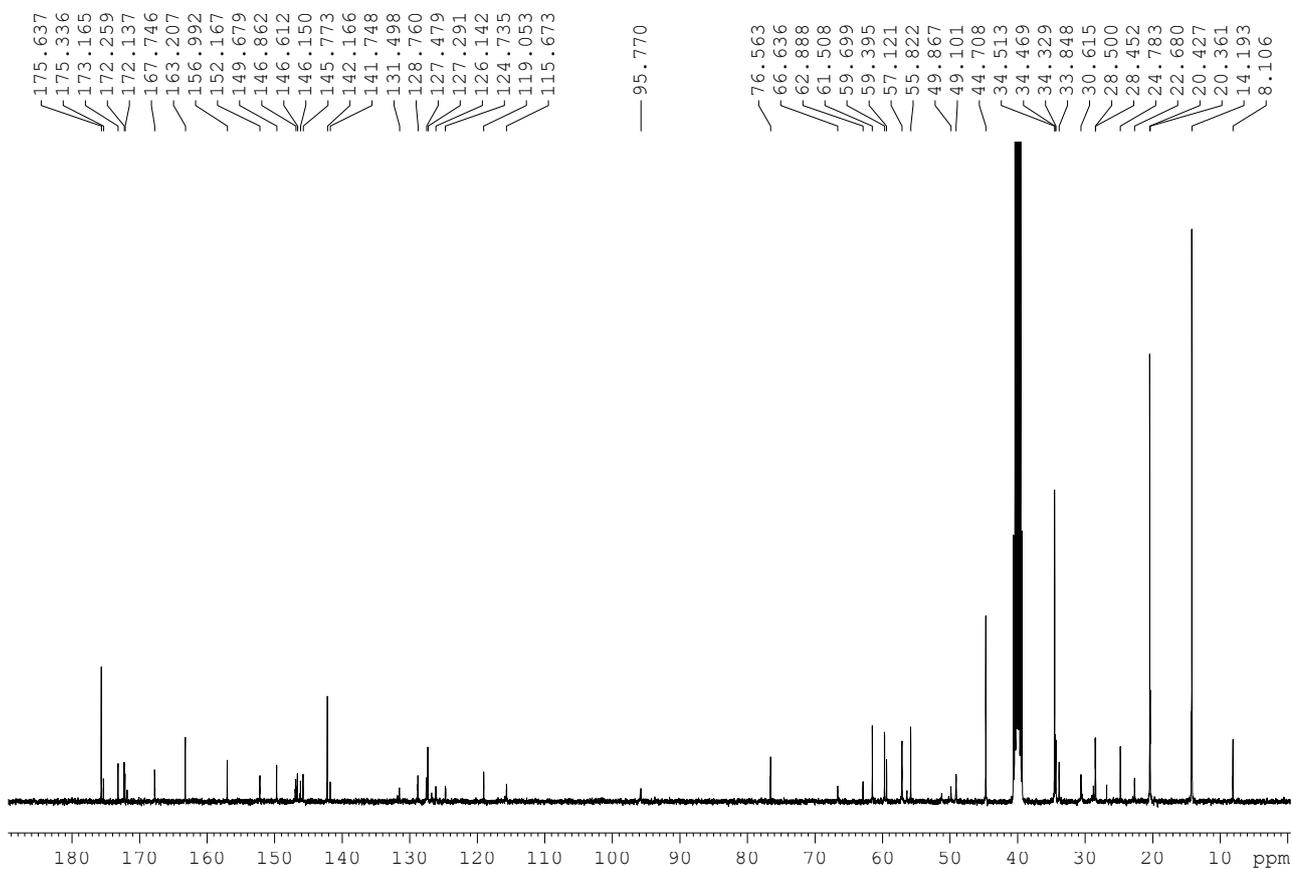
**Figure S9.** ESI-MS spectrum of compound **8**



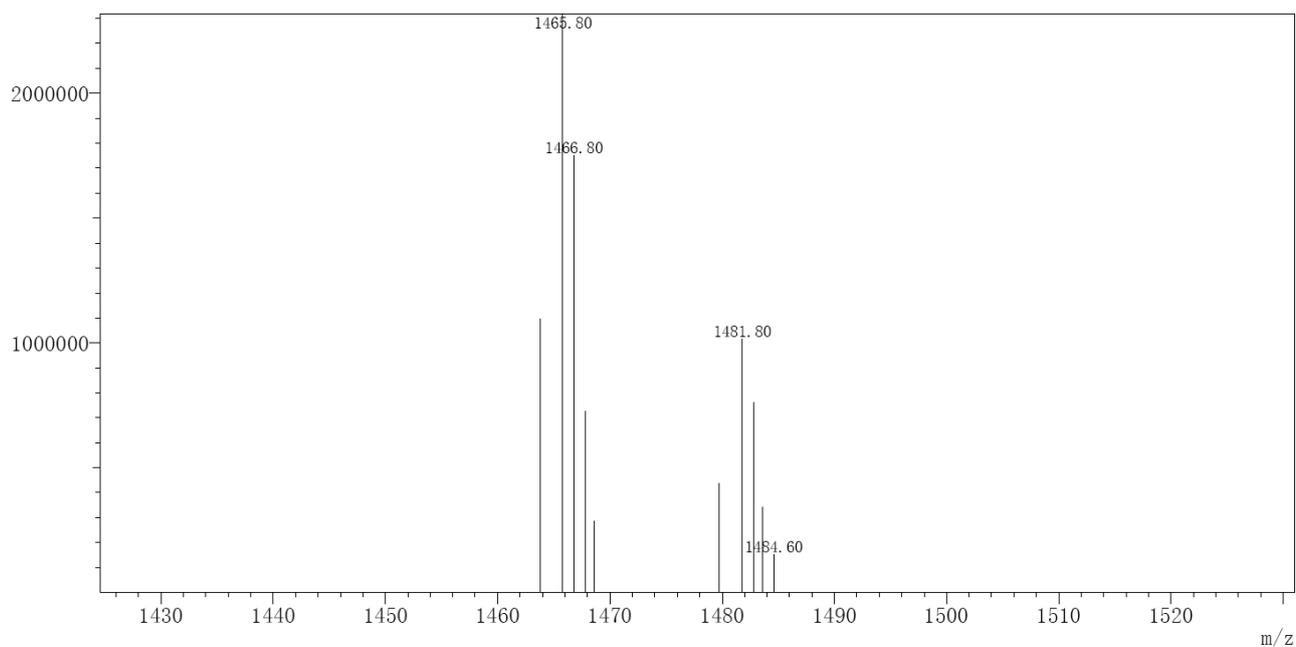
**Figure S10.** HPLC spectrum of compound **8** (acetonitrile- $\text{H}_2\text{O}$ =70:30, detection wavelength: 360 nm)



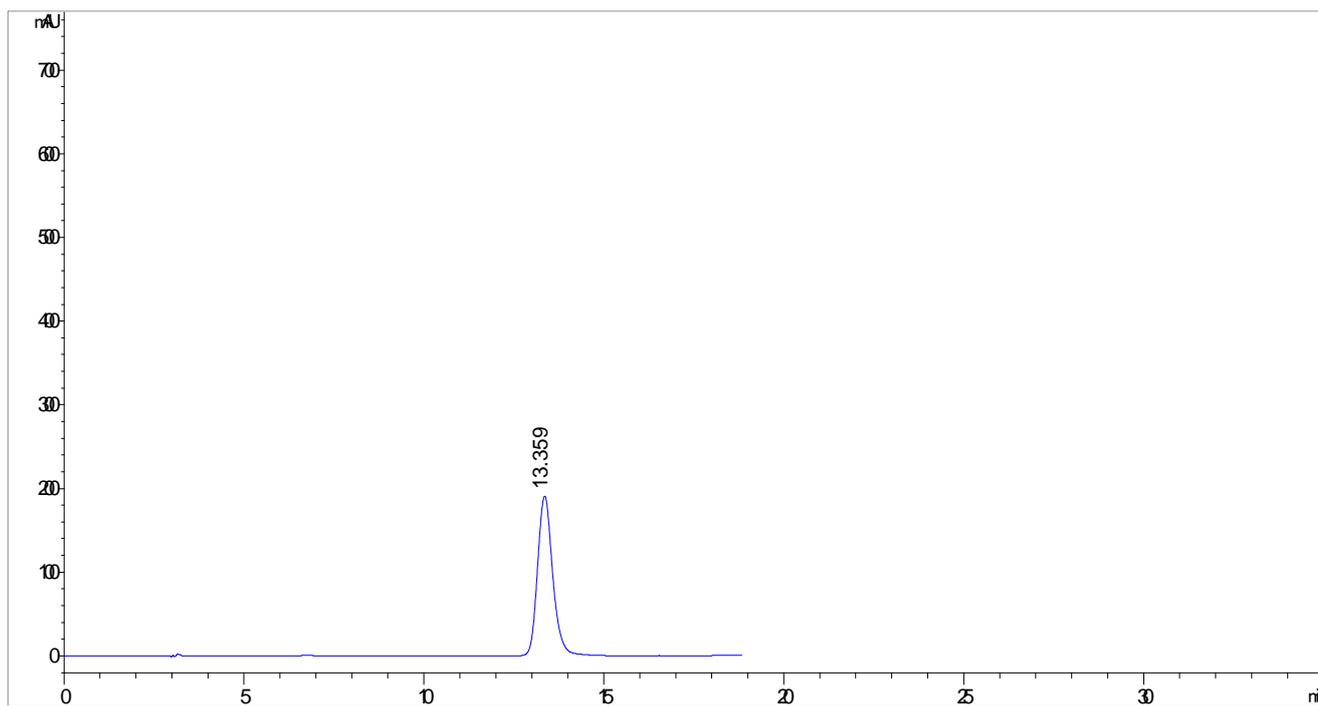
**Figure S11.**  $^1\text{H}$  NMR spectrum of compound **9** (400 MHz,  $\text{DMSO-}d_6$ )



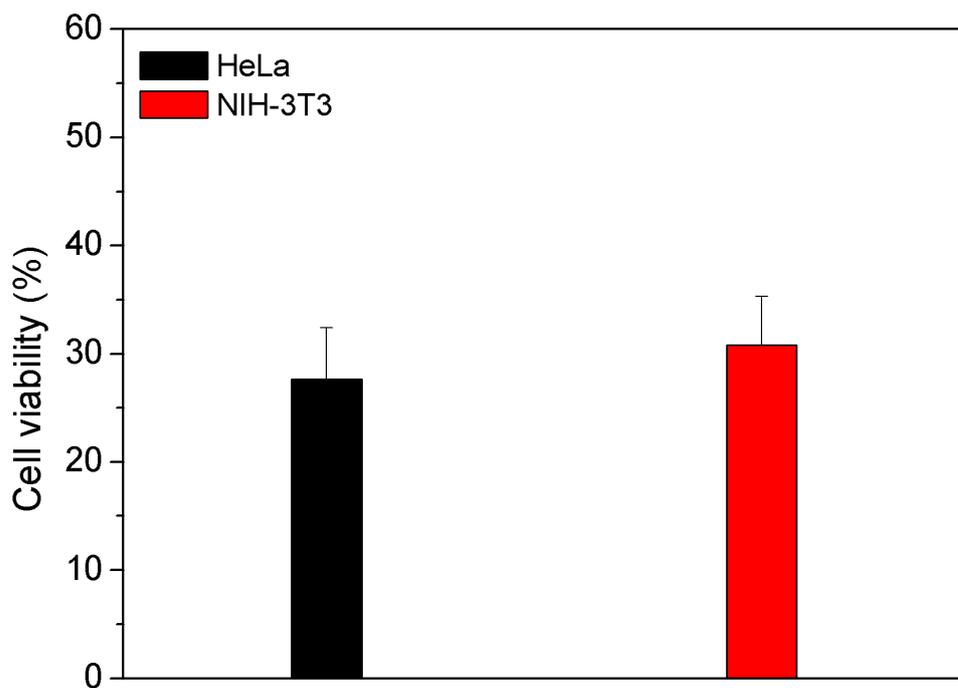
**Figure S12.**  $^{13}\text{C}$  NMR spectrum of compound **9** (101 MHz,  $\text{DMSO-}d_6$ )



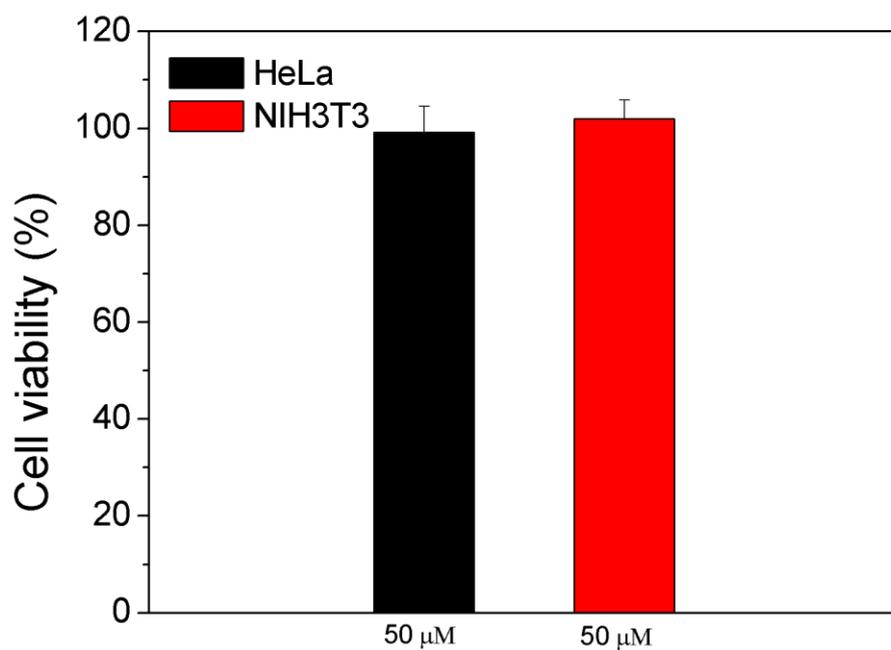
**Figure S13.** ESI-MS spectrum of compound **9**



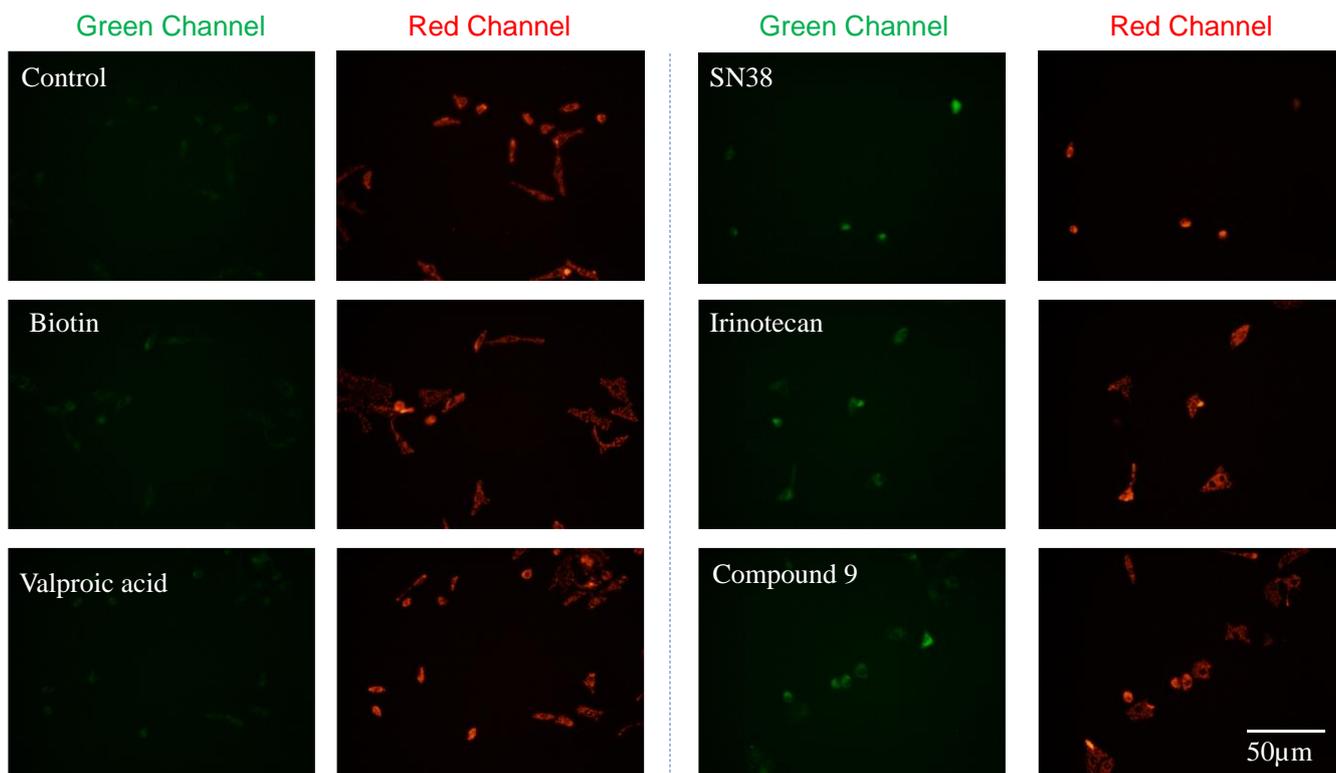
**Figure S14.** HPLC spectrum of compound **9** (acetonitrile-H<sub>2</sub>O=80:20,detection wavelength: 360 nm)



**Figure S15.** Effects of compound 8 on cell viability of HeLa cells and NIH3T3 cells. Cells were treated with 50  $\mu$ M of biotin for 48 h and assayed by MTT method.



**Figure S16.** Effects of biotin on cell viability. Cells were treated with 50  $\mu$ M of biotin for 48 h and assayed by MTT method.



**Figure S17.** Effects of the tested compounds on mitochondrial membrane potentials. HeLa cells were treated with 2  $\mu\text{M}$  of compounds (or 6  $\mu\text{M}$  of valproic acid) for 24 h and stained with JC-1 probe for determination of mitochondrial membrane potentials using fluorescence microscope.