Supporting information for

Pentacyclic Triterpenoids from *Ziziphus jujuba* Lamk. Fruits as Dual Inhibitors of PTP1B and *α*-Glucosidase: *In Vitro* and *In Silico* Evaluation

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Abstract

Ziziphus jujuba Lamk. (Táo Ta) are widely used in order of in traditional Asian medicine as superfruits. An ethanol extract of *Z. jujuba* fruit exhibited remarkable inhibition against PTP1B and was isolated via bioassay-guided fractionation, resulting in the identification of fifteen active triterpenoids (**1**–**15**), including betulinic acid (**1**), corosolic acid (**2**), oleanolic acid (**3**), alphitolic acid (**4**), maslinic acid (**5**), 3-*O*-*cis*-*p*-coumaroyl alphitolic acid (**6**), 3-*O*-*trans*-*p*-coumaroyl alphitolic acid (**7**), 2-*O*-*trans*-*p*-coumaroyl alphitolic acid (**8**), 2-*O*-*cis*-*p*-coumaroyl alphitolic acid (**9**), ceanothic acid (**10**), zizyberanalic acid (**11**), *trans*-*p*-coumaroyl betulinic acid (**12**), betulonic acid (**13**), ursolic acid (**14**), and oleanonic acid (**15**). These chemical structures were identified using nuclear magnetic resonance spectrocopy (NMR) and compared to those reported in other papers. Among the compounds tested for their effect against PTP1B and *α*-glucosidase, compounds **1**–**3** displayed the most potent inhibitory activity, with ranging from IC_{50} values from 6.75 to 17.02 μM. Besides, Compounds **4**, **10**, and **13** exhibited weak PTP1B inhibitory activity (IC_{50} = 53.42 to 90.90 μM), whereas **5**–**15** showed no inhibitory effect in all tested concentrations. Additionally, molecular docking and molecular dynamics simulations were performed to evaluate the binding affinity of compounds **1**–**3** toward PTP1B and *α*-glucosidase, two key enzymes involved in glucose homeostasis. These interactions may contribute to the modulation of insulin signaling pathways and postprandial glucose levels, thereby improving glycemic control in diabetes. Moreover, *in silico* ADME and toxicity prediction further suggested that **1**–**3** possess favorable pharmacokinetic properties and lower predicted toxicity. These findings provide a rational basis for using *Ziziphus* sourced from Vietnam to develop potential PTP1B and *α*-glucosidase dual inhibitors, warranting further investigations, and are considered the first report on the chemical and bioactive investigation of this species.

Keywords: *Ziziphus jujuba* Lamk., pentacyclic triterpenoids, PTP1B inhibition, *α*-glucosidase, molecular docking, molecular dynamics, ADME/toxicity prediction

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Figure S28. ^{1}H NMR spectrum of compound **15** (400 MHz, chloroform-*d*)

Figure S29. ^{13}C NMR spectrum of compound **15** (100 MHz, chloroform-*d*)

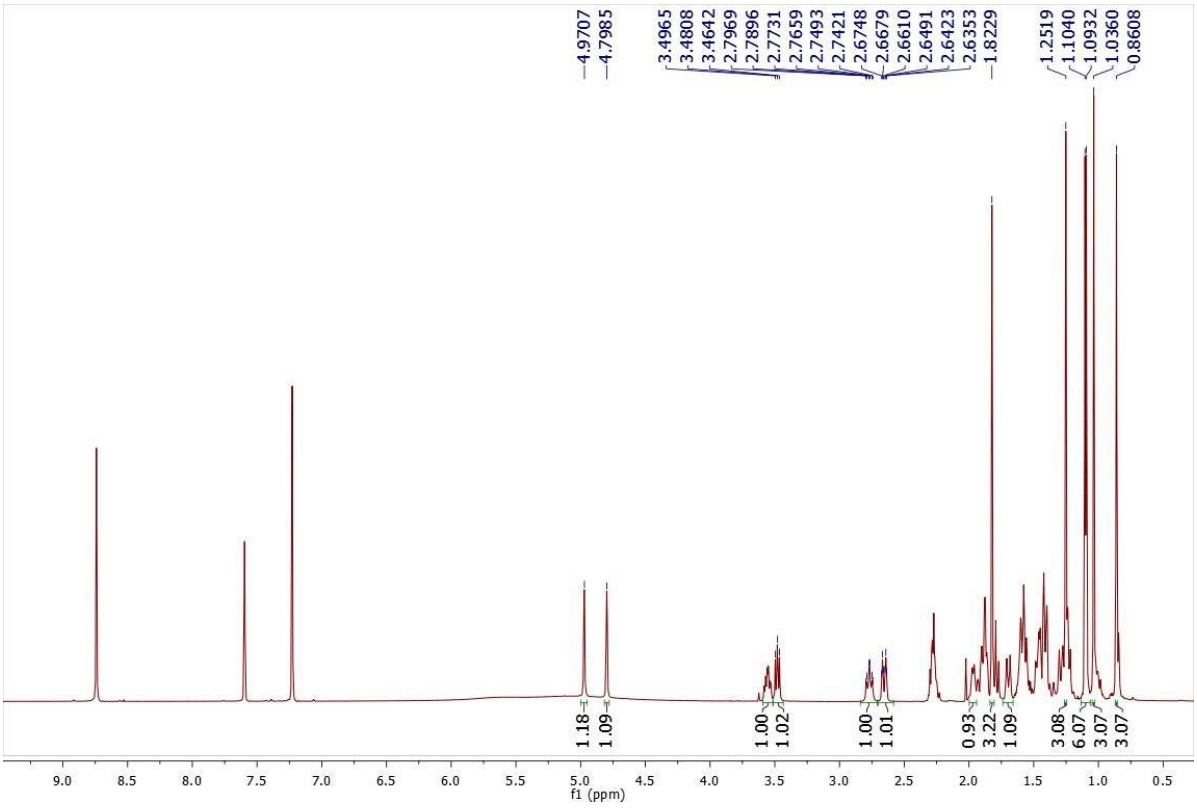

Figure S1: ^{1}H NMR spectrum of compound **1** (500 MHz, pyridine-d_5)

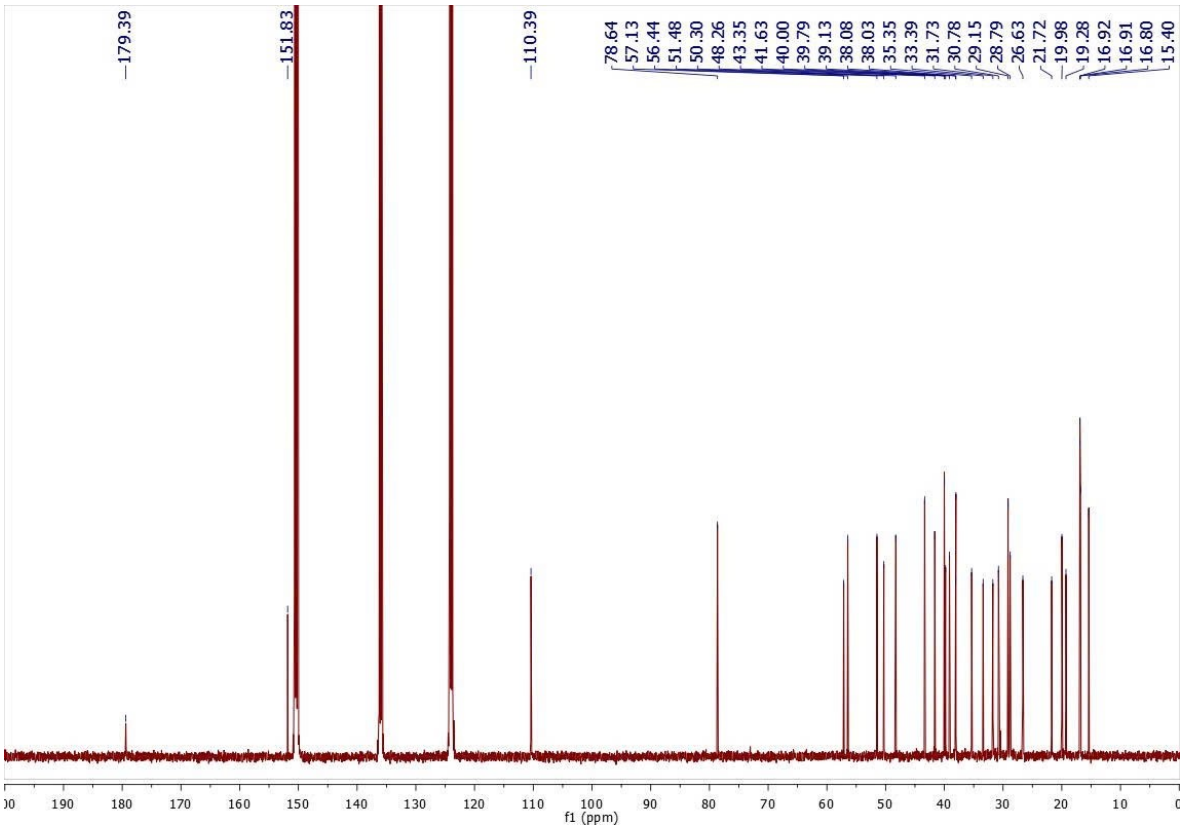

Figure S2. ^{13}C NMR spectrum of compound **1** (500 MHz, pyridine-d_5)

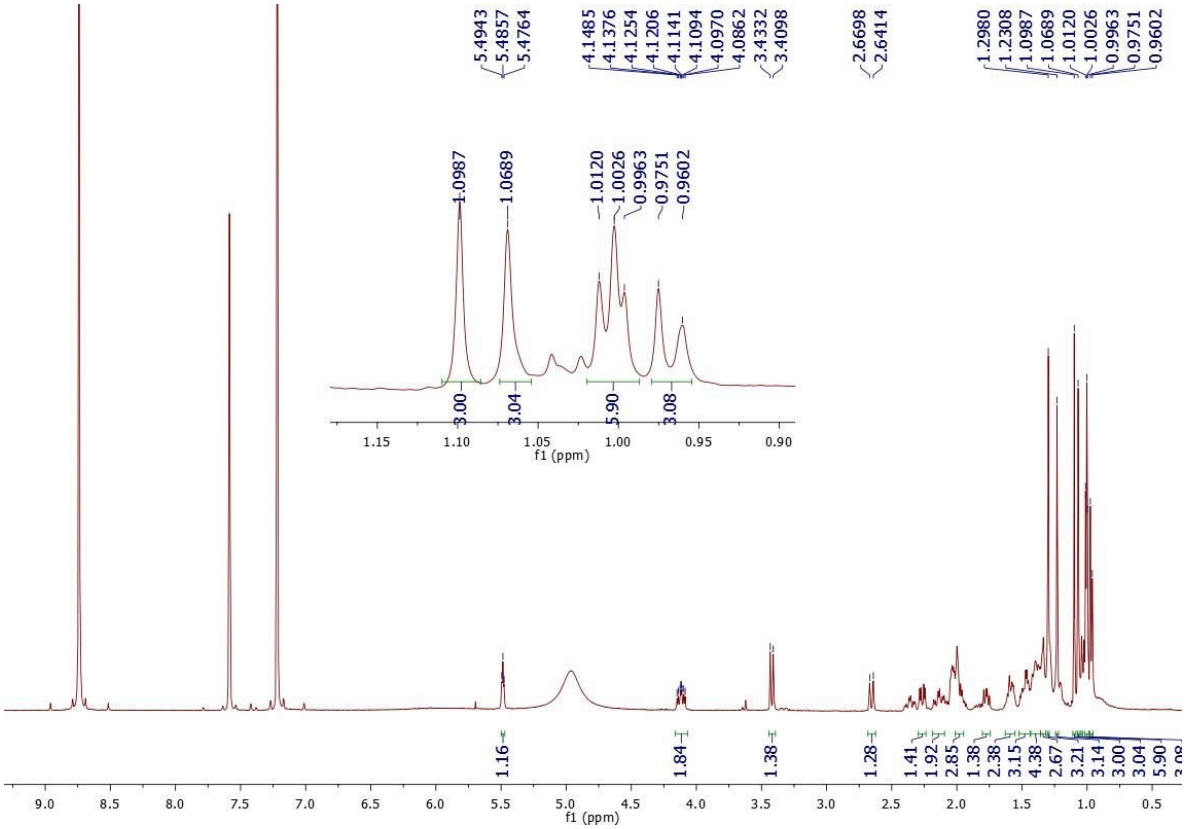

Figure S3: ^{1}H NMR spectrum of compound **2** (500 MHz, pyridine-d_5)

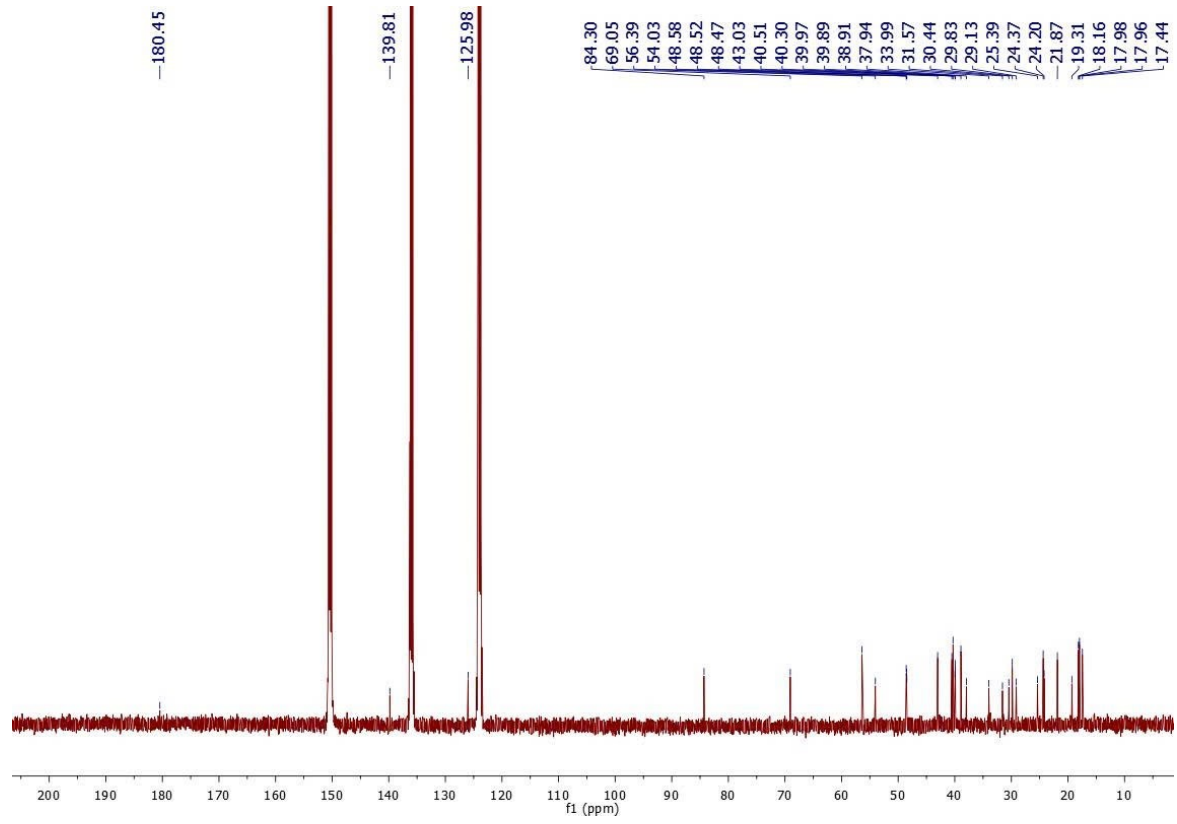

Figure S4. ^{13}C NMR spectrum of compound **2** (500 MHz, pyridine-d_5)

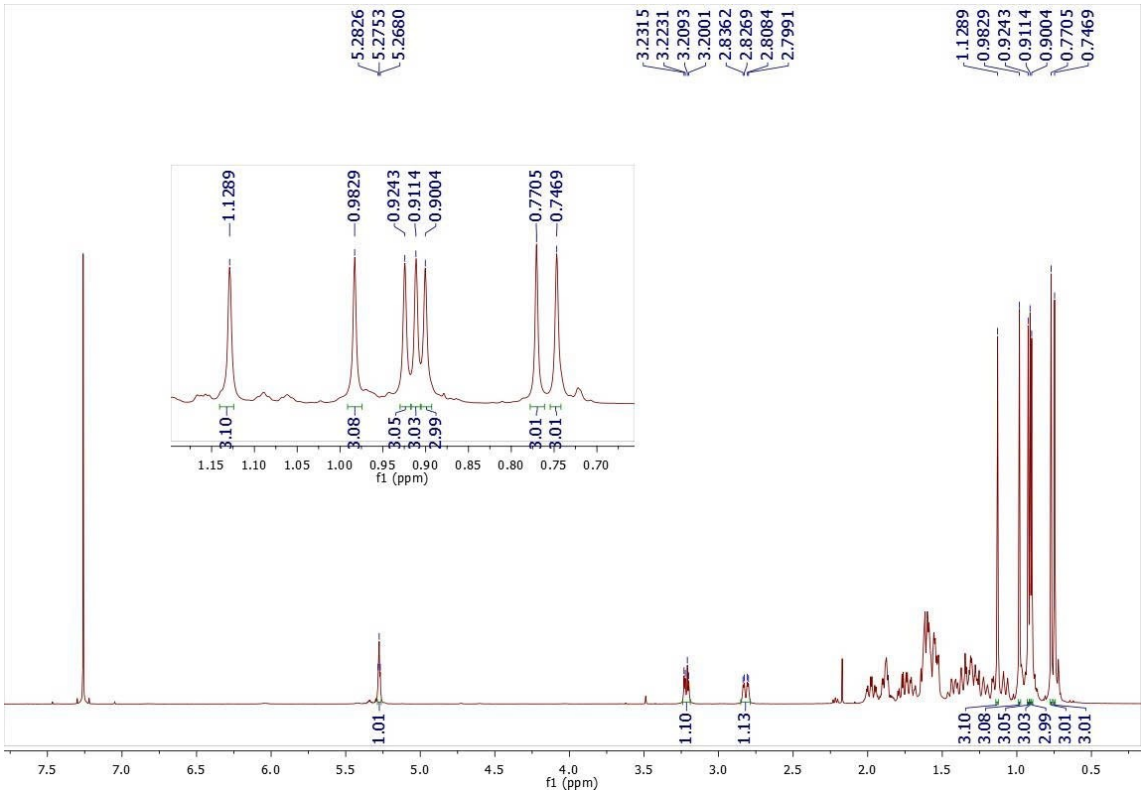

Figure S5: ^{1}H NMR spectrum of compound **3** (500 MHz, chloroform-*d*)

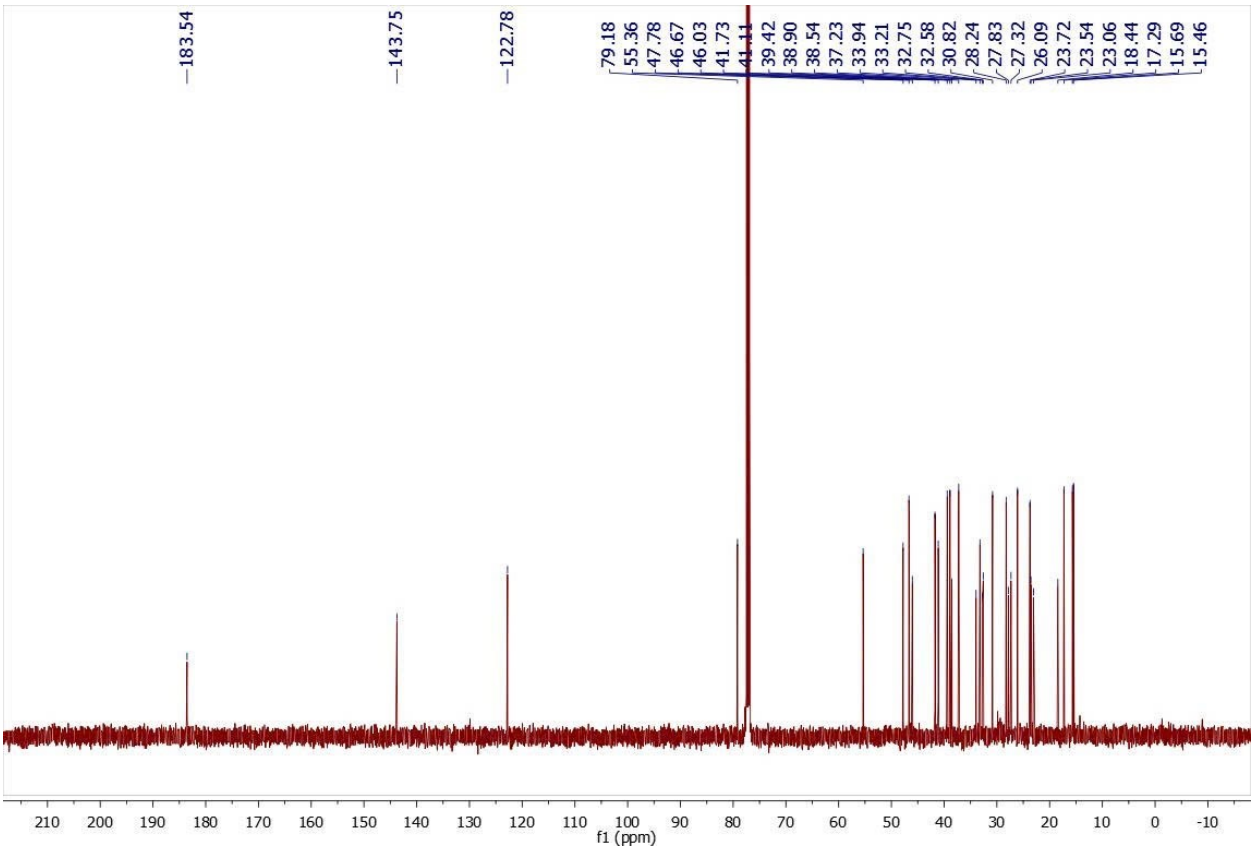

Figure S6. ^{13}C NMR spectrum of compound **3** (500 MHz, chloroform-*d*)

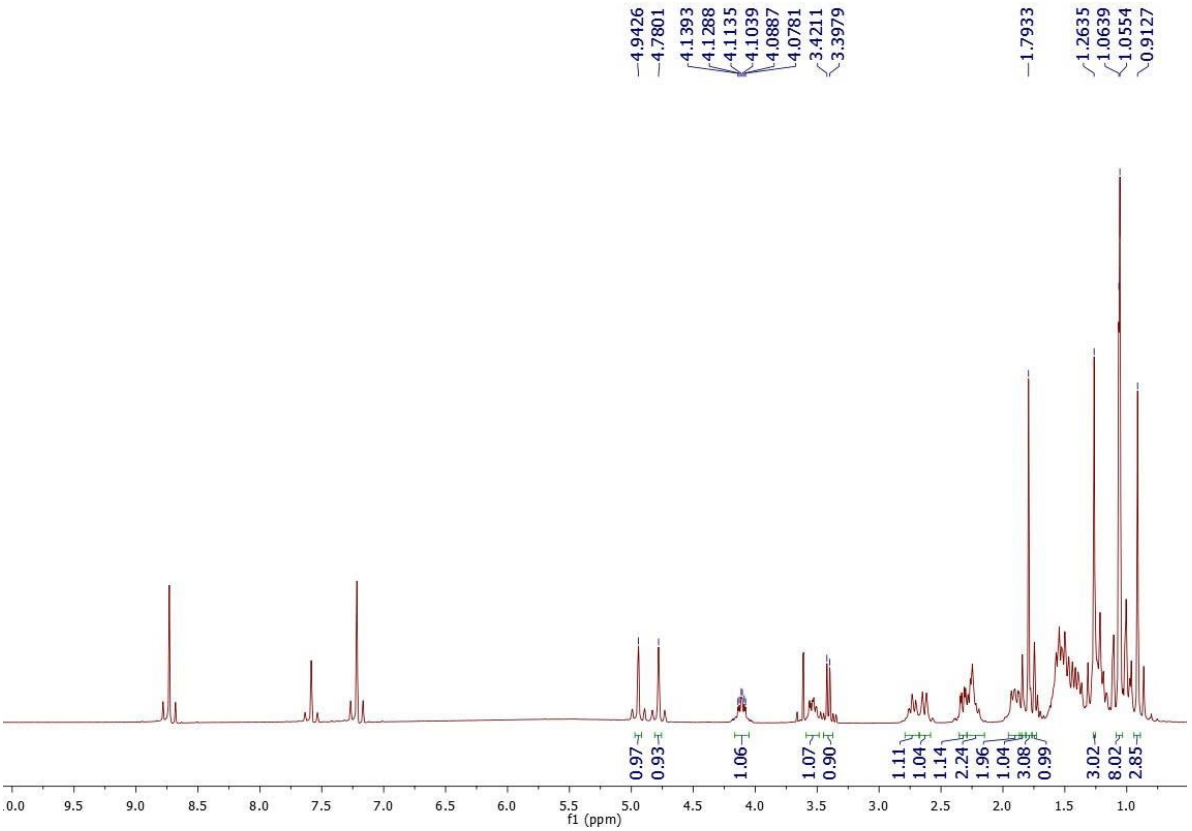

Figure S7: ^{1}H NMR spectrum of compound **4** (500 MHz, pyridine-d_5)

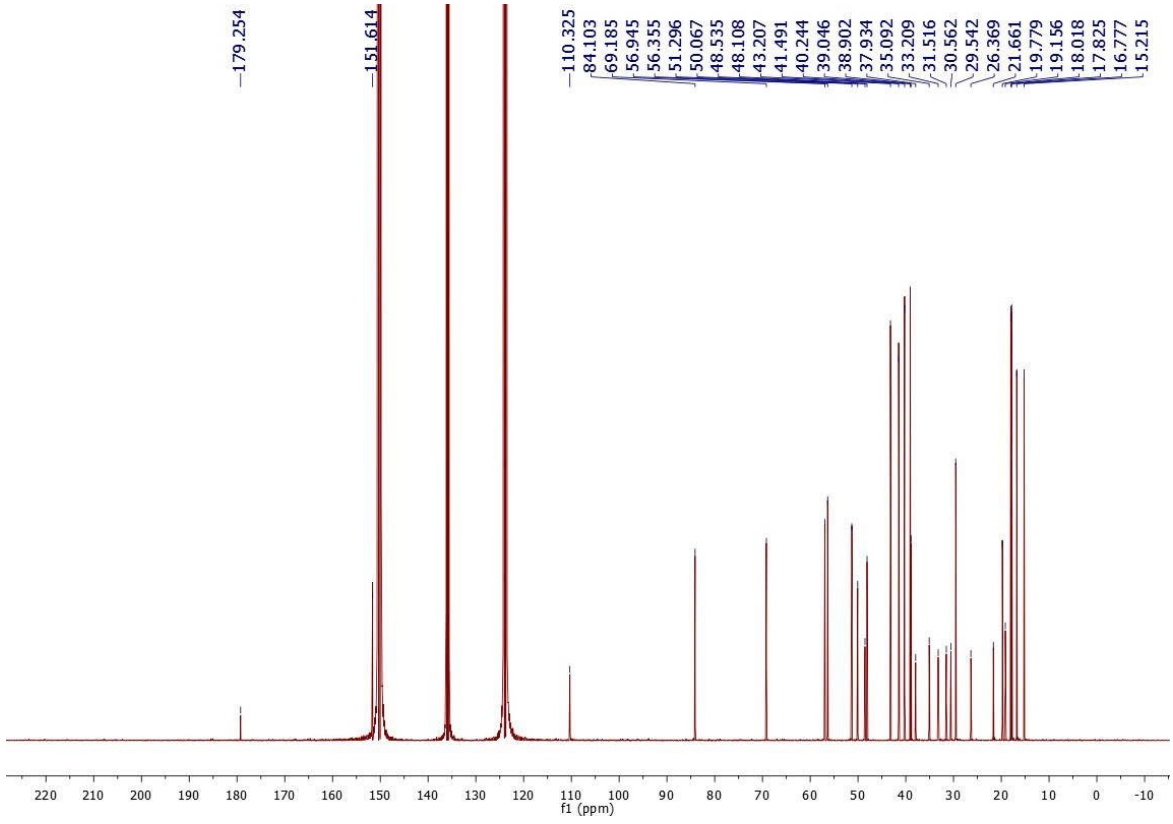

Figure S8. ^{13}C NMR spectrum of compound **4** (500 MHz, pyridine-d_5)

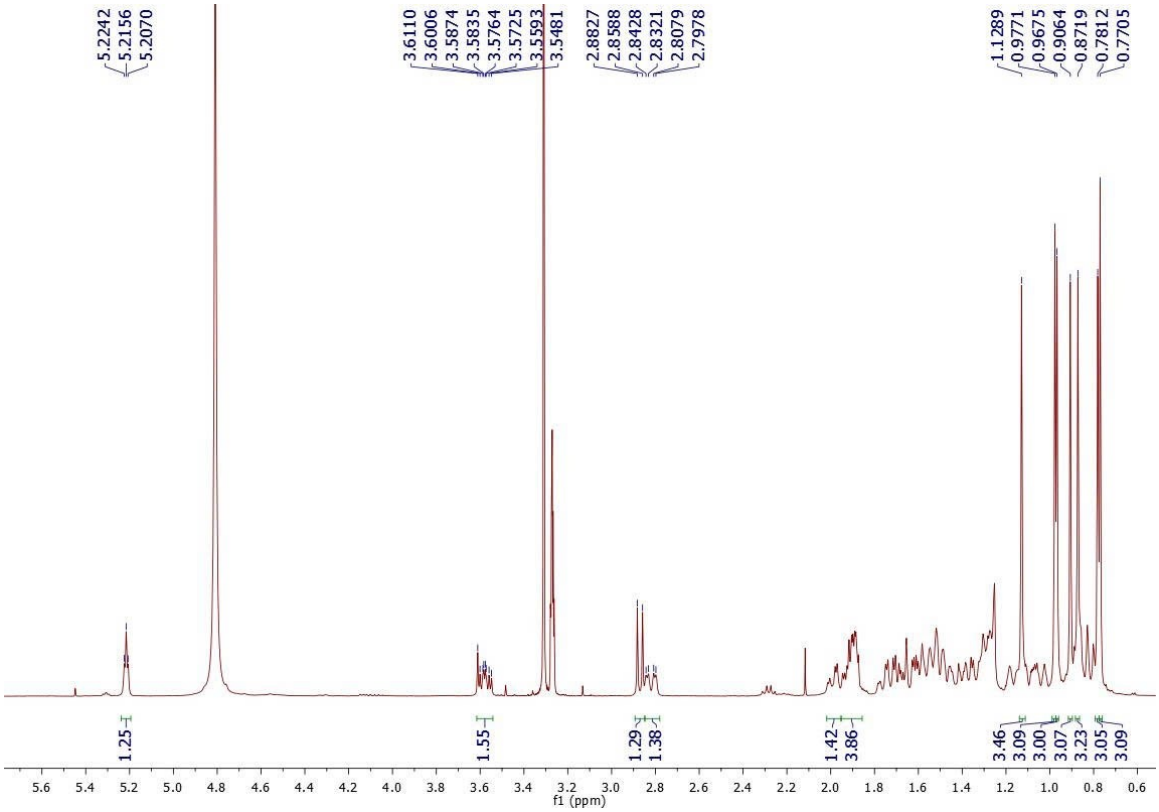

Figure S9: ^{1}H NMR spectrum of compound **5** (400 MHz, methanol-d_4)

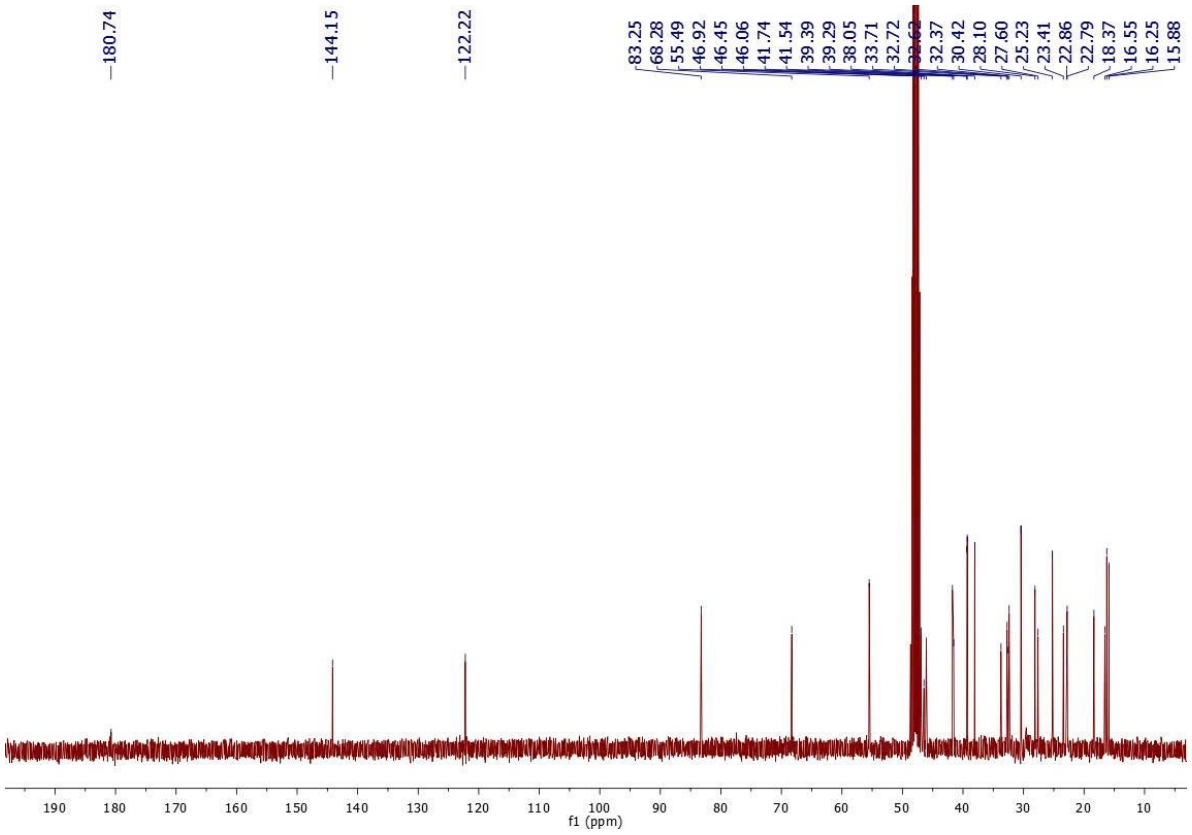

Figure S10. ^{13}C NMR spectrum of compound **5** (400 MHz, methanol-d_4)

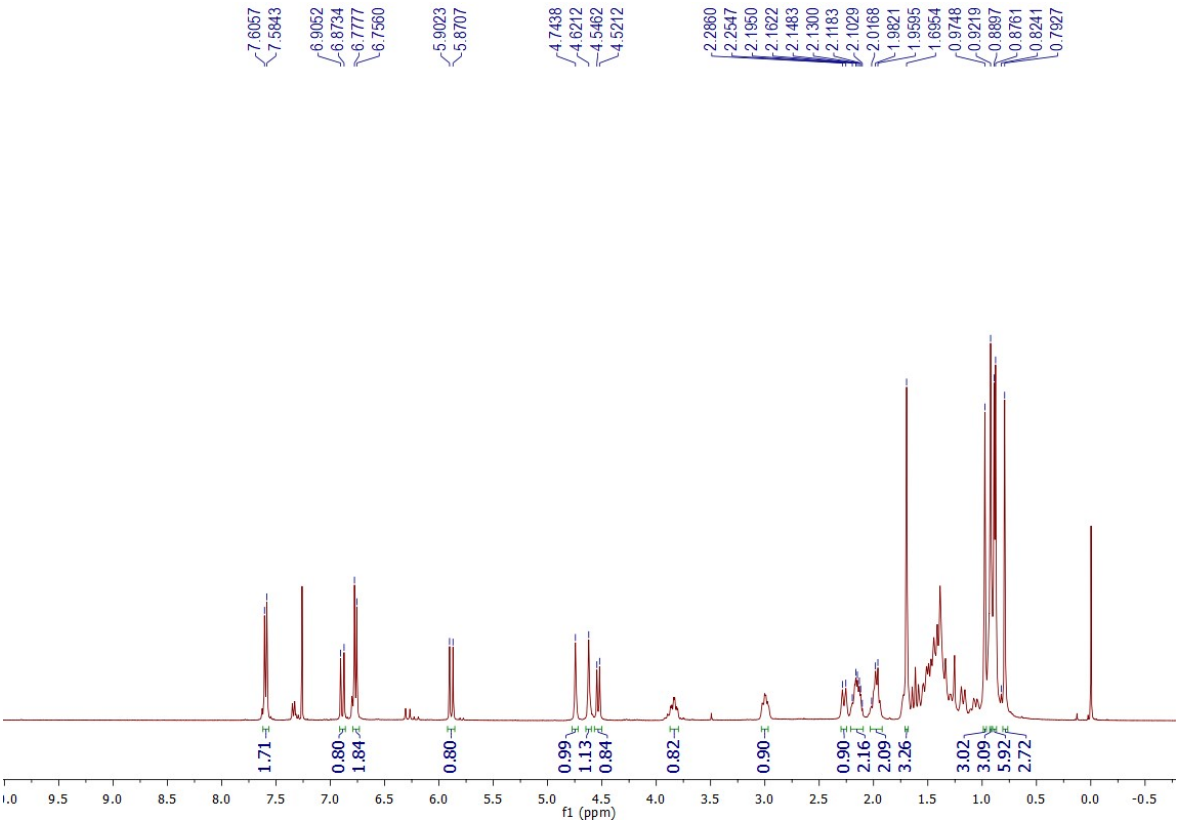

Figure S11: ^{1}H NMR spectrum of compound **6 (**400 MHz, chloroform-*d*)

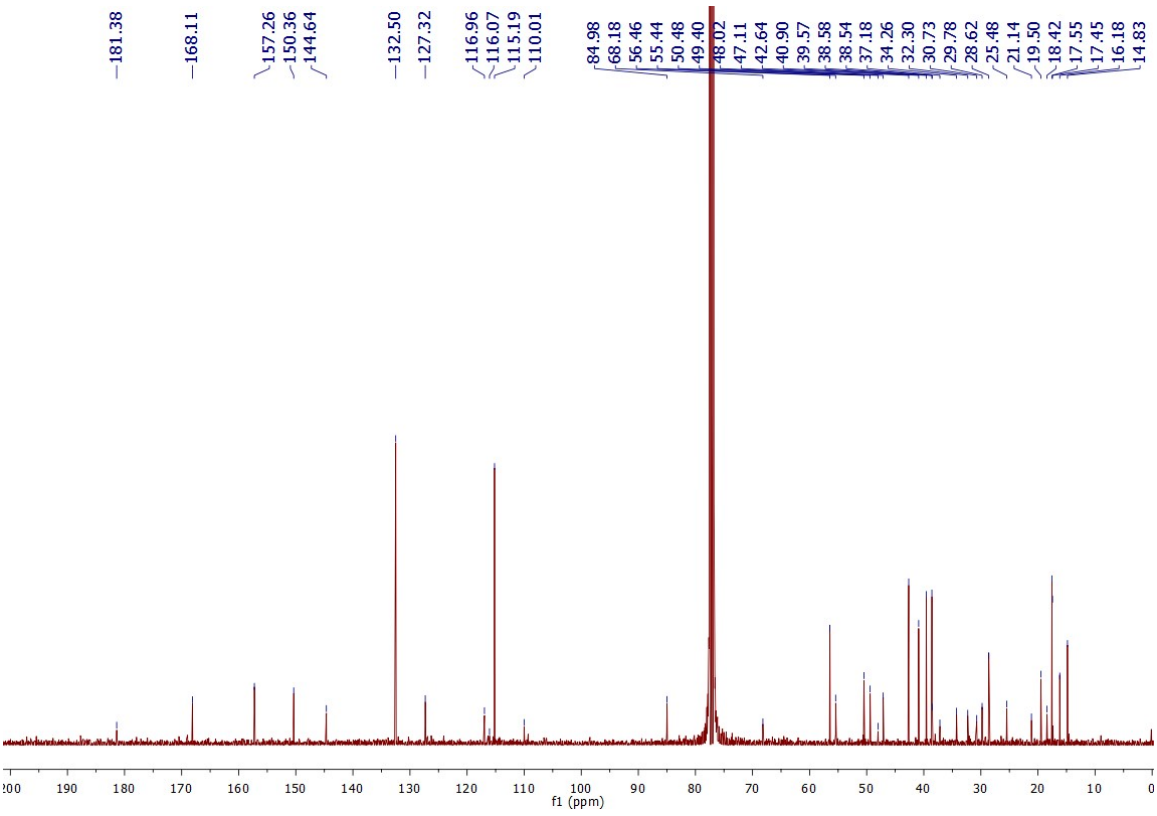

Figure S12. ^{13}C NMR spectrum of compound **6** (100 MHz, chloroform-*d*)

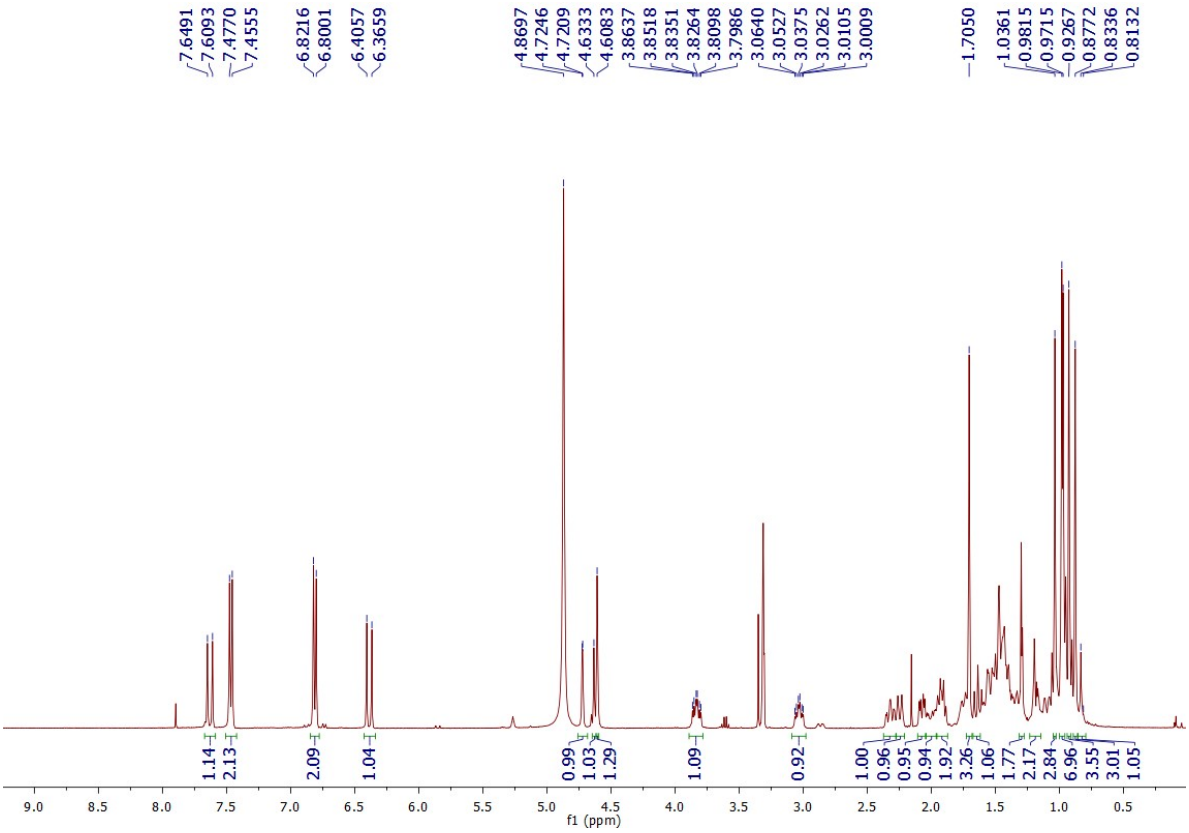

Figure S13: ^{1}H NMR spectrum of compound **7** (400 MHz, methanol-d_4)

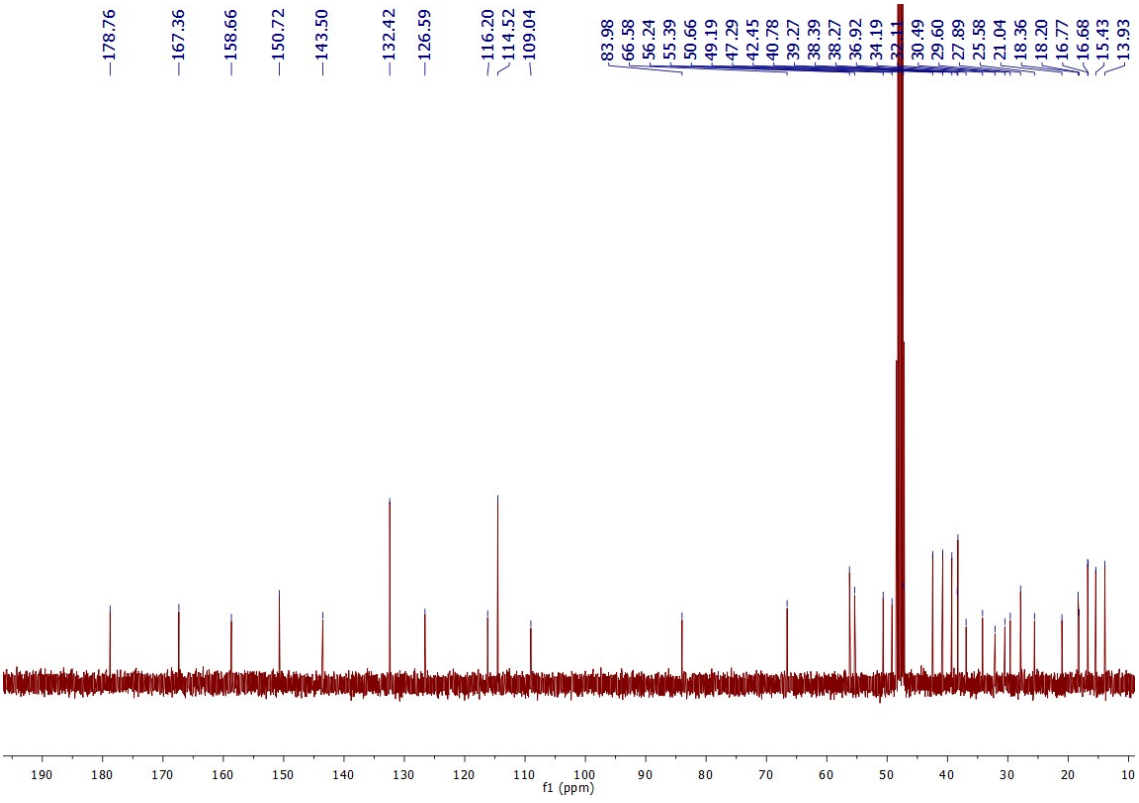

Figure S14. ^{13}C NMR spectrum of compound **7** (100 MHz, methanol-d_4)

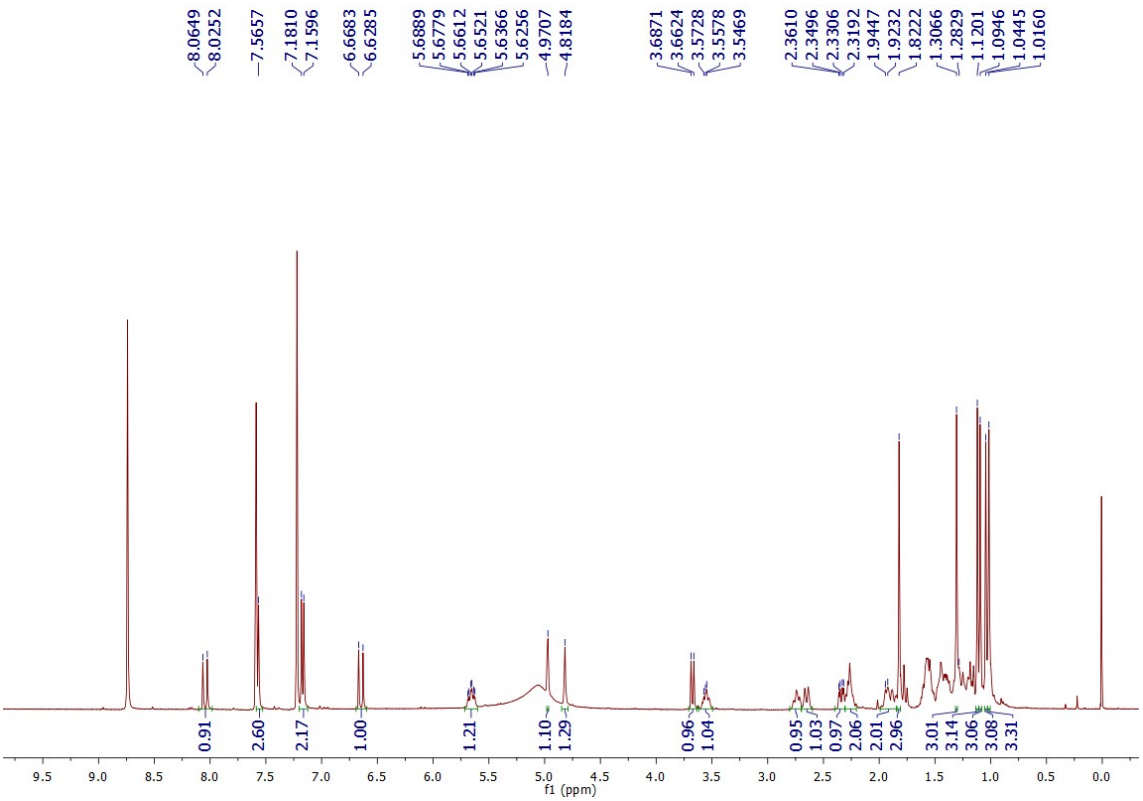

Figure S15: ^{1}H NMR spectrum of compound **8** (400 MHz, pyridine-d_5)

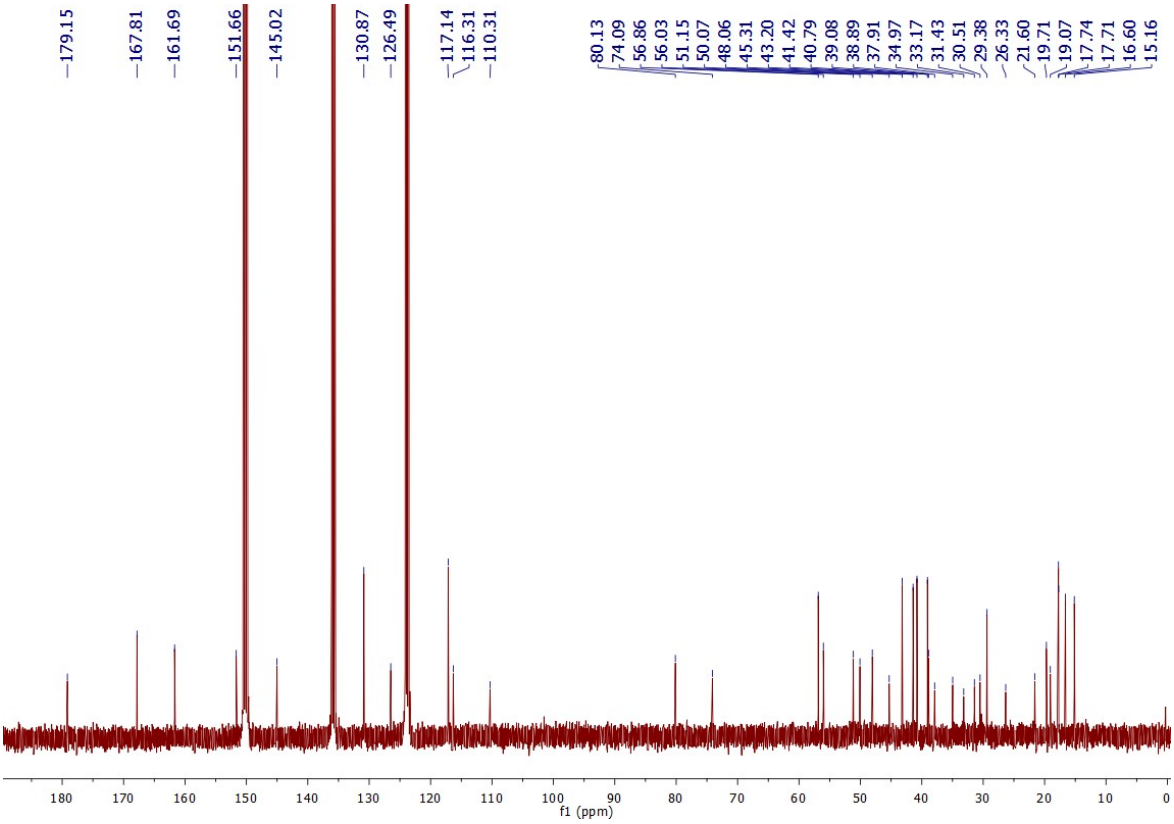

Figure S16. ^{13}C NMR spectrum of compound **8** (100 MHz, pyridine-d_5)

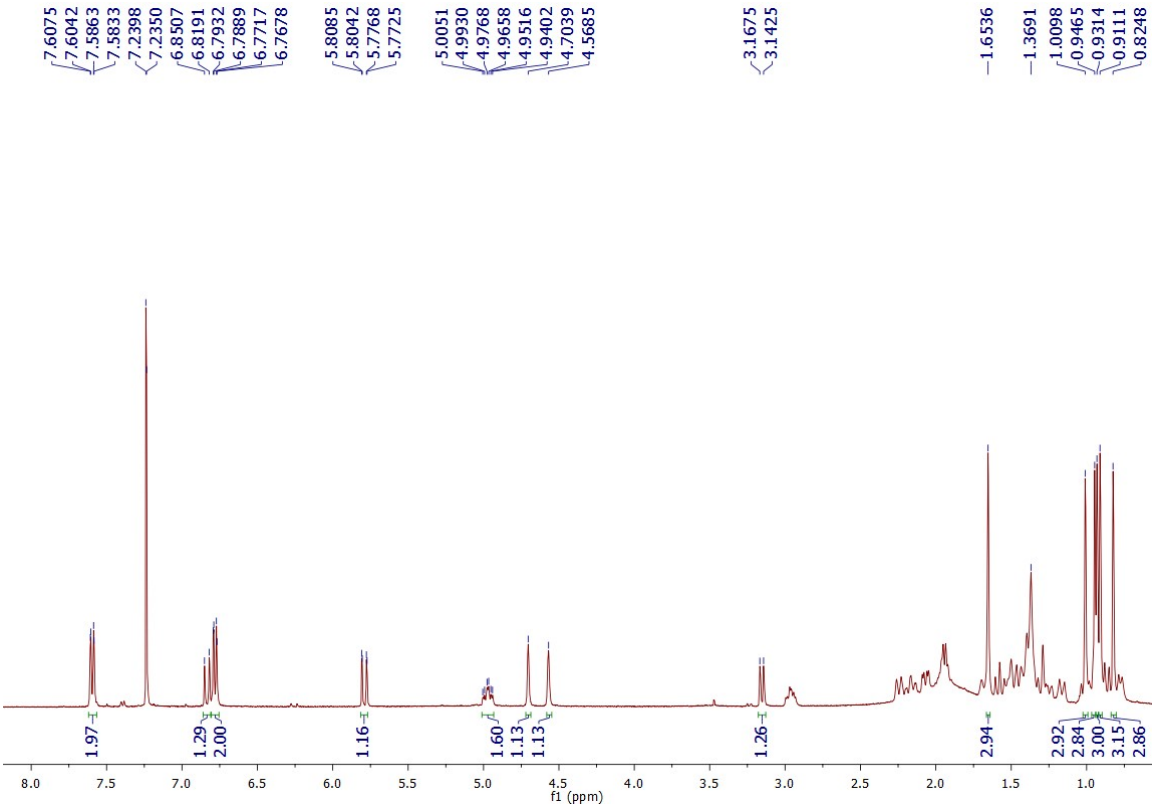

Figure S17: ^{1}H NMR spectrum of compound **9** (400 MHz, chloroform-*d*)

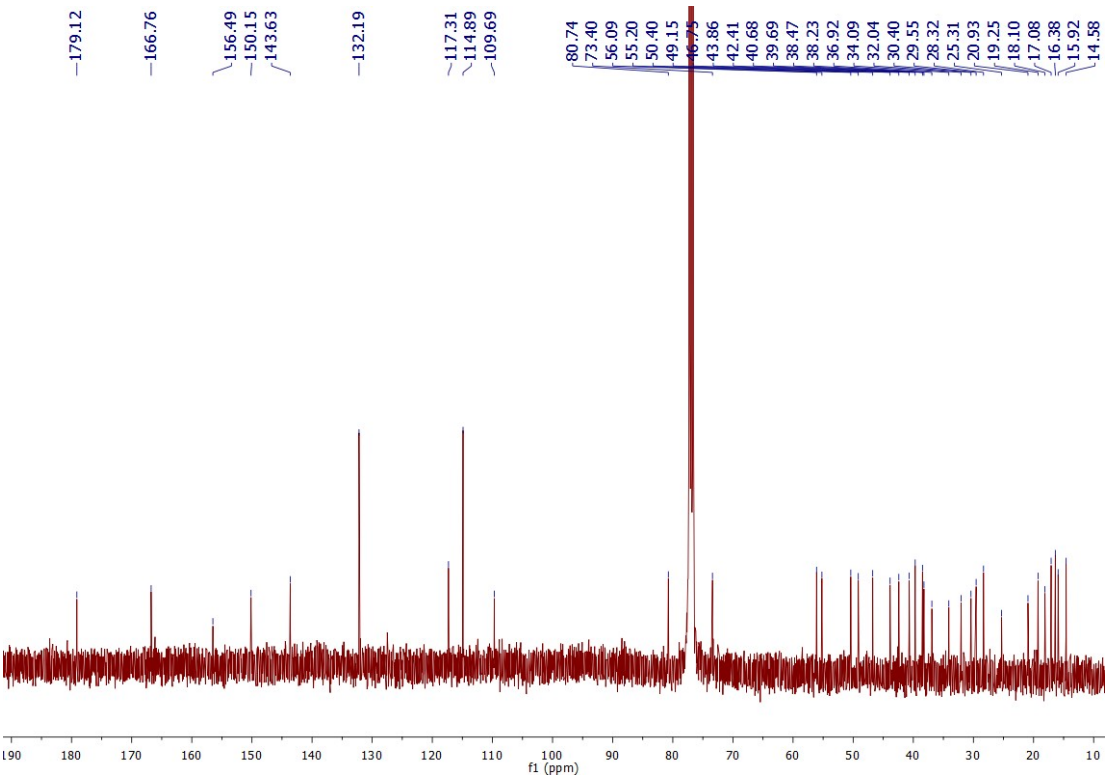

Figure S18. ^{13}C NMR spectrum of compound **9** (100 MHz, chloroform-*d*)

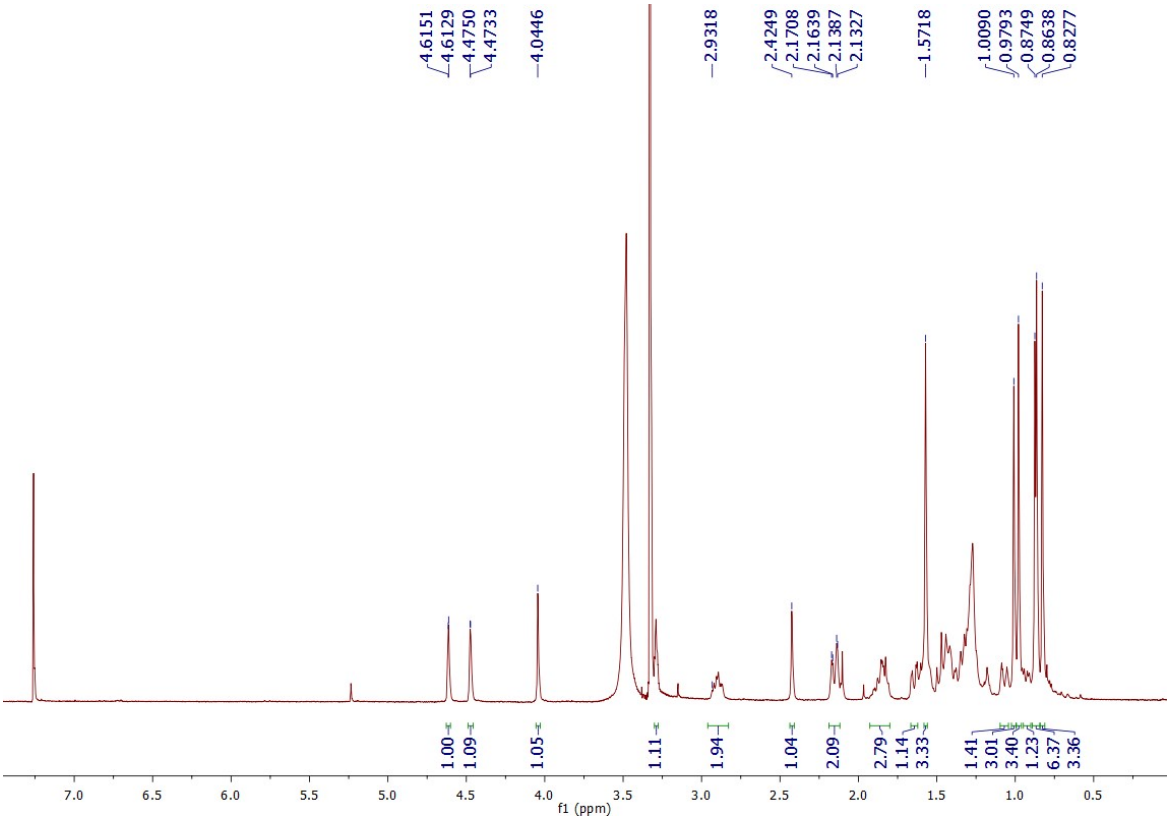

Figure S19: ^{1}H NMR spectrum of compound **10** (400 MHz, chloroform-*d*+ methanol-d_4 10:1)

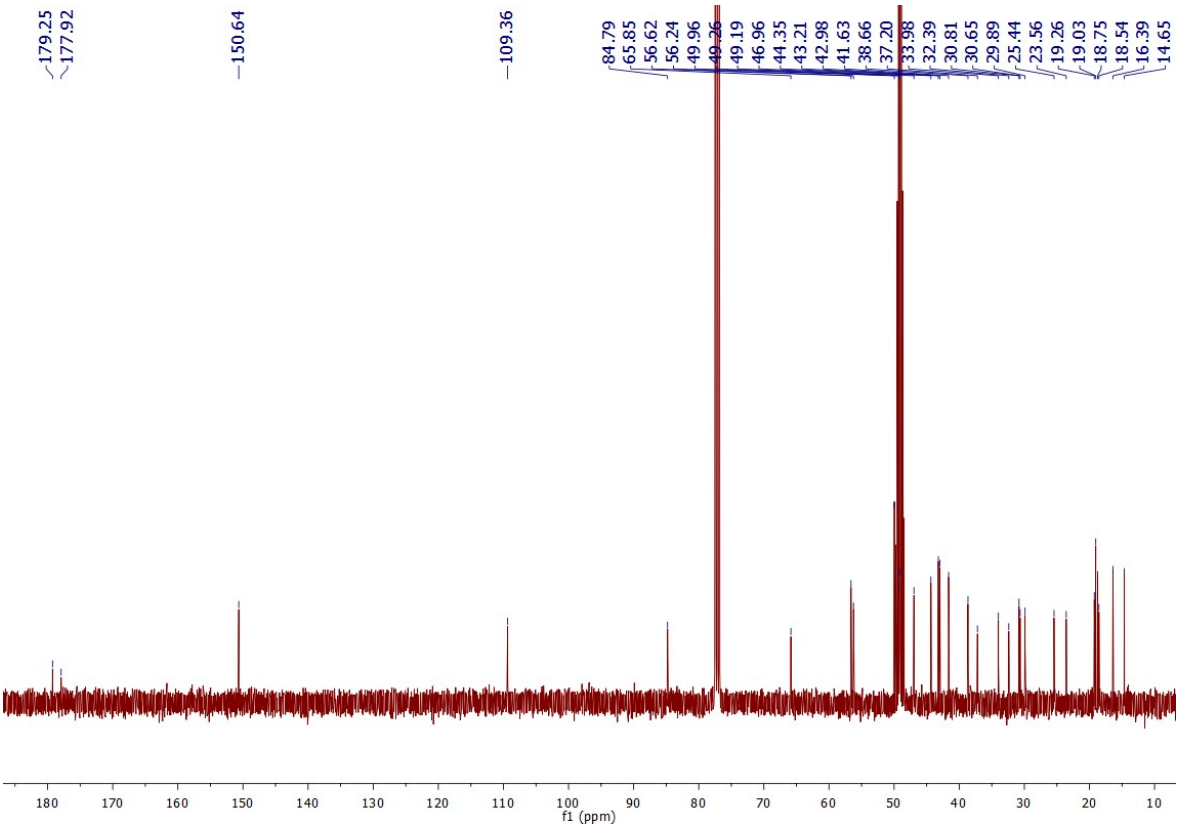

Figure S20. ^{13}C NMR spectrum of compound **10** (400 MHz, chloroform-*d*+ methanol-d_4 10:1)

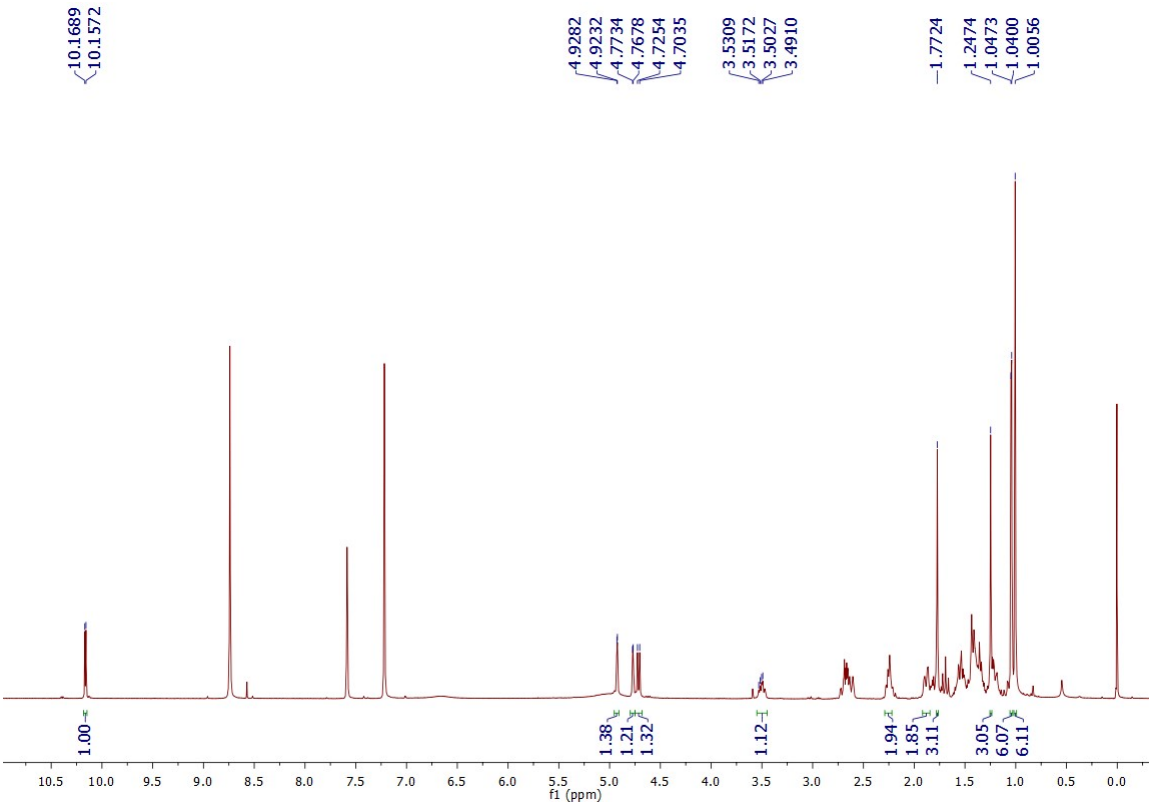

Figure S21: ^{1}H NMR spectrum of compound **11** (400 MHz, pyridine-d_5)

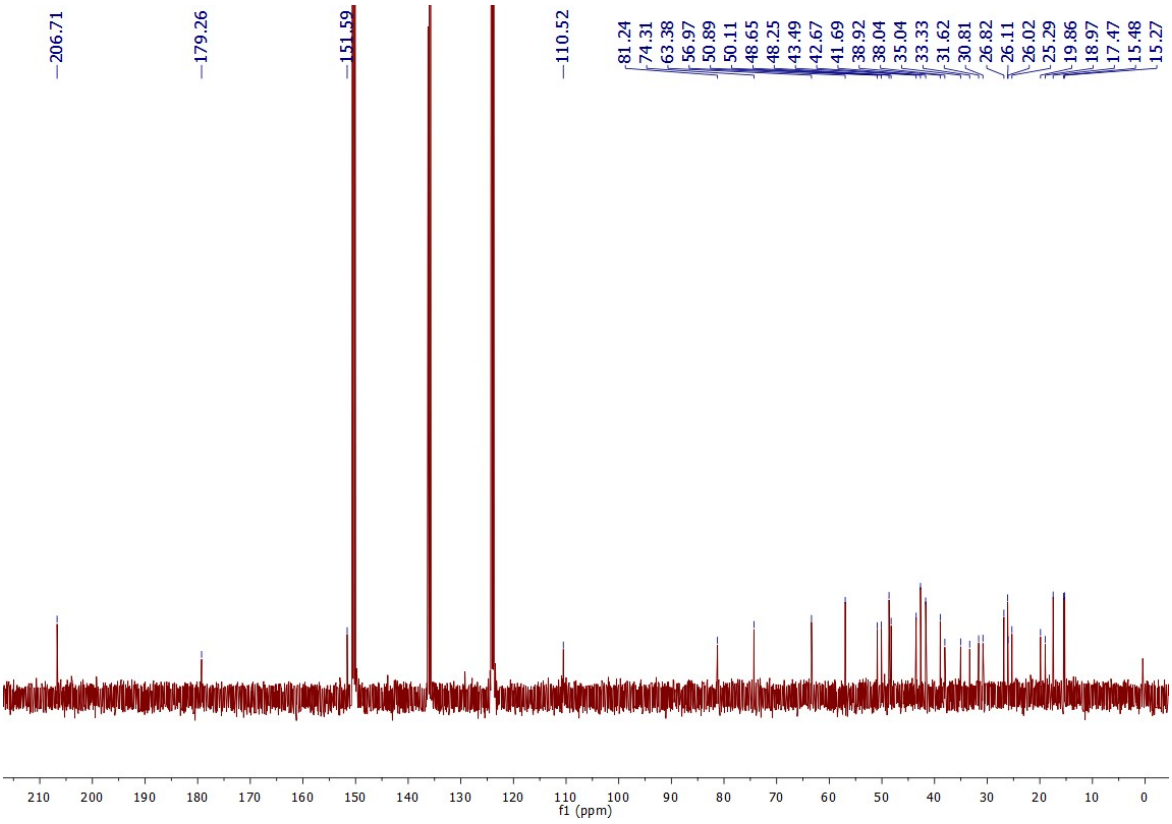

Figure S22. ^{13}C NMR spectrum of compound **11** (100 MHz, pyridine-d_5)

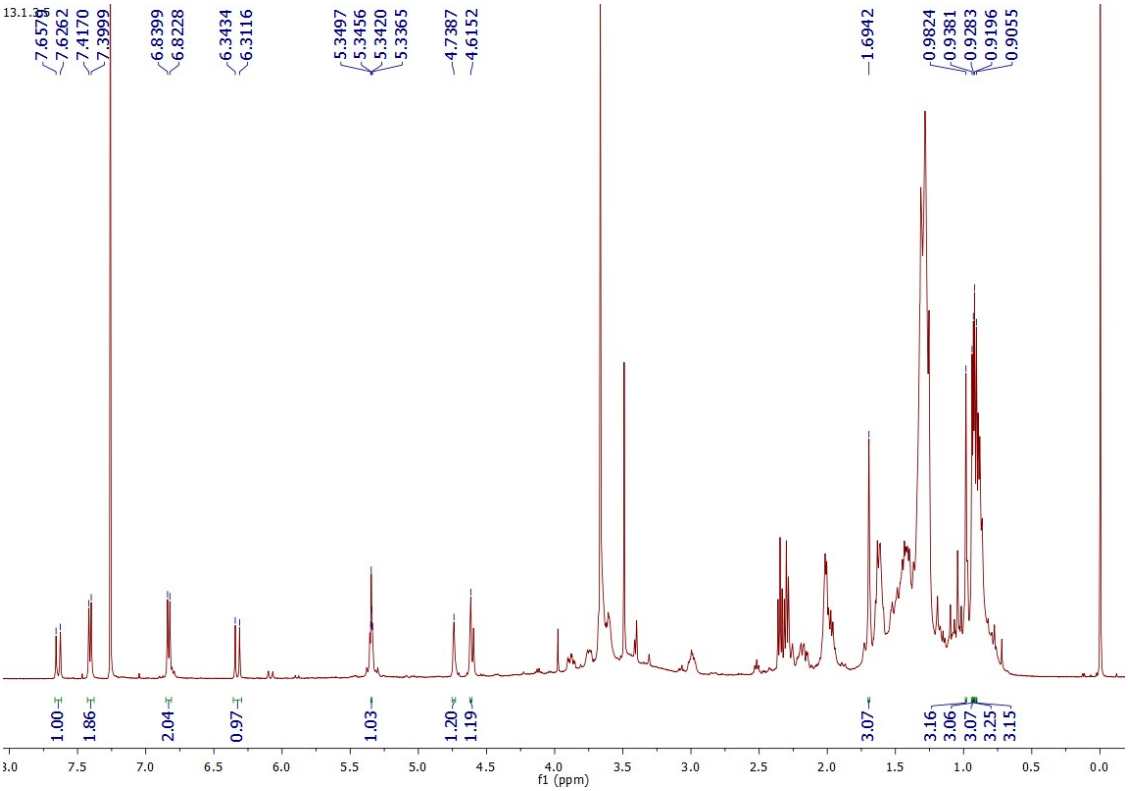

Figure S23: ^{1}H NMR spectrum of compound **12** (500 MHz, chloroform-*d*)

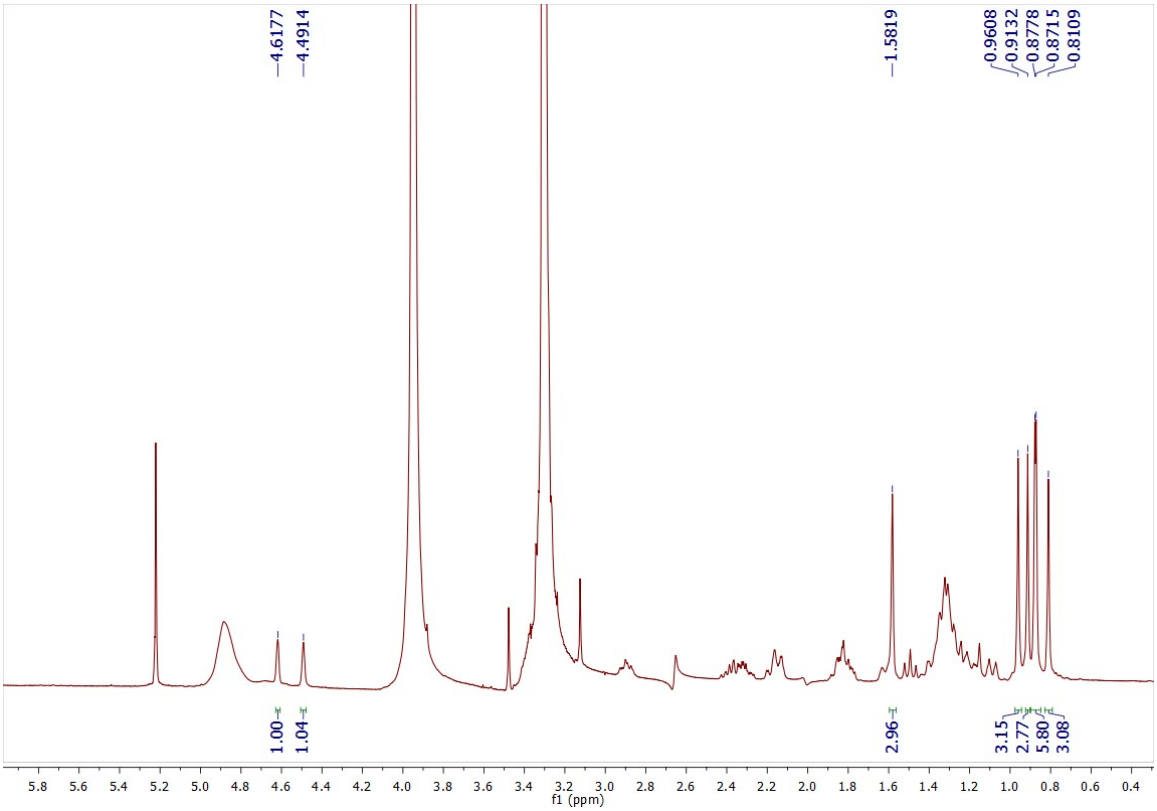

Figure S24: ^{1}H NMR spectrum of compound **13** (400 MHz, chloroform-*d*)

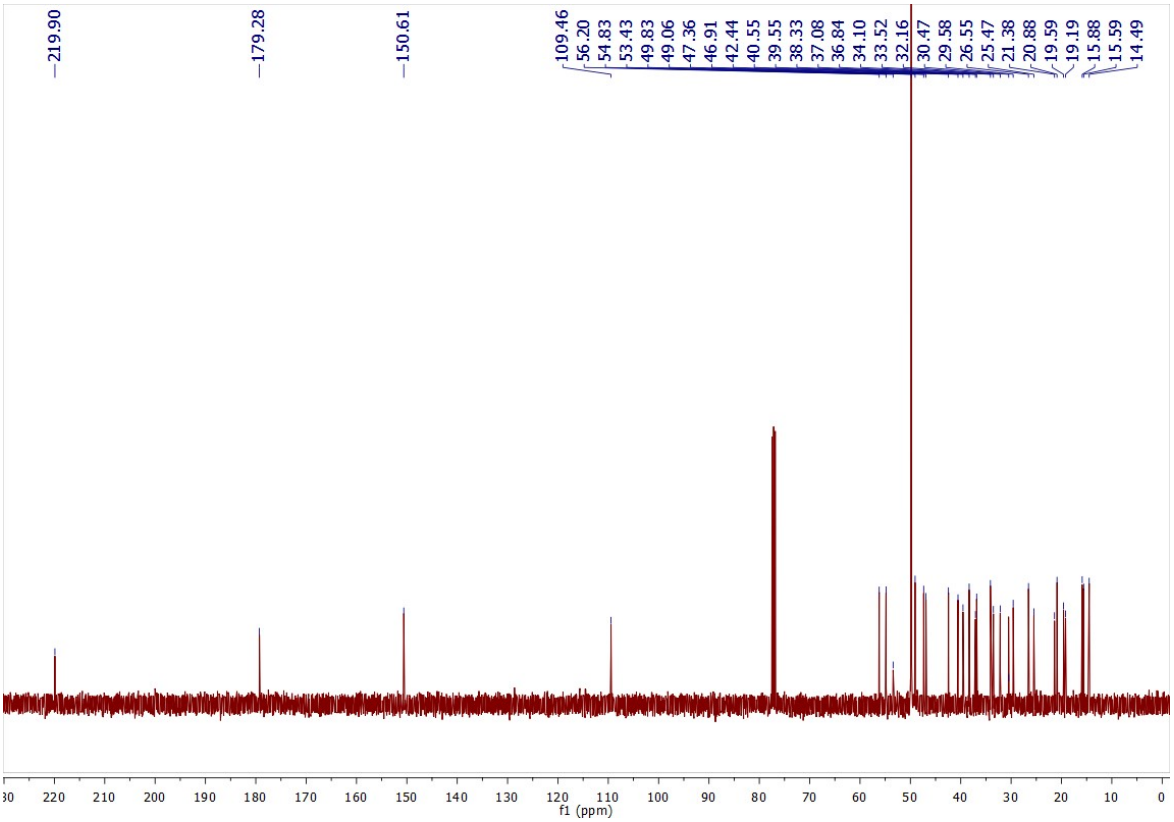

Figure S25. ^{13}C NMR spectrum of compound **13** (100 MHz, chloroform-*d*)

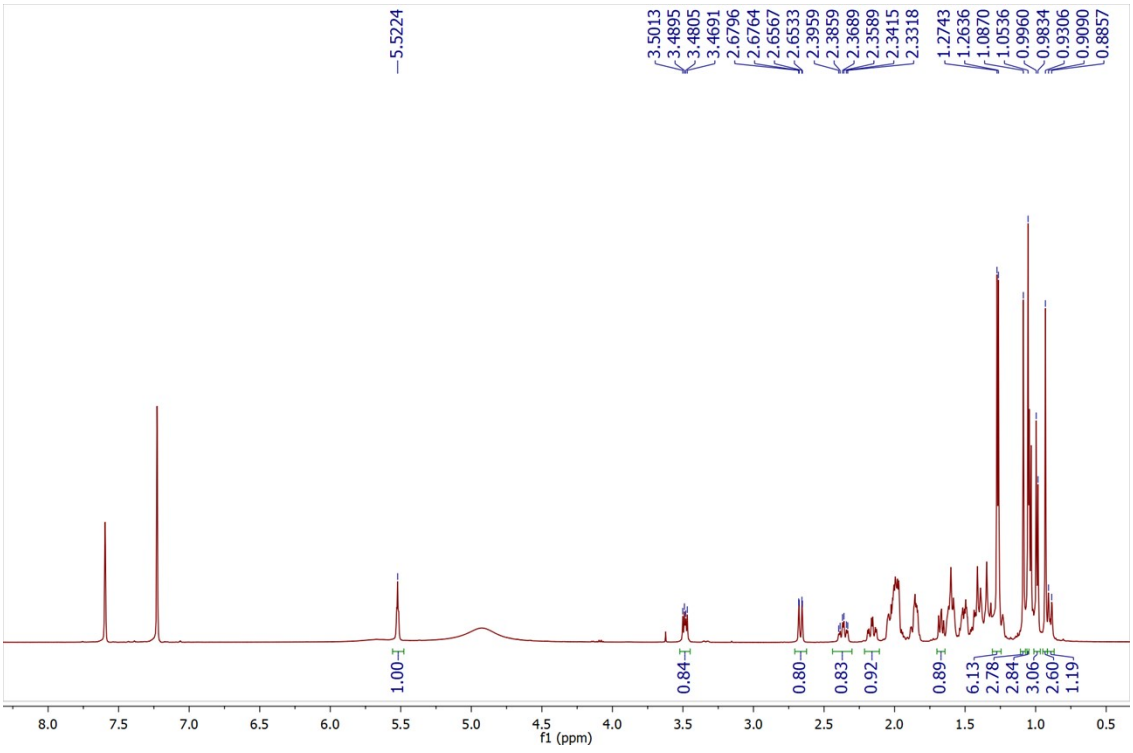

Figure S26: ^{1}H NMR spectrum of compound **14** (500 MHz, pyridine-d_5)

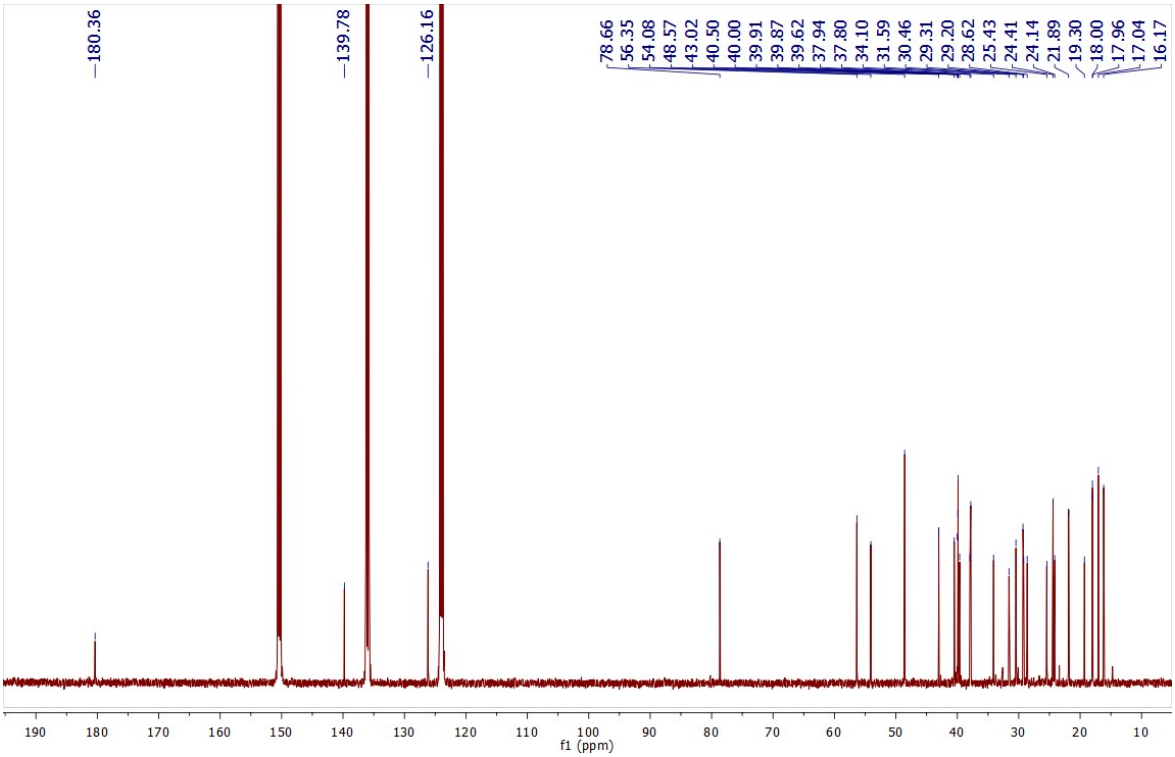

Figure S27. ^{13}C NMR spectrum of compound **14** (500 MHz, pyridine-d_5)

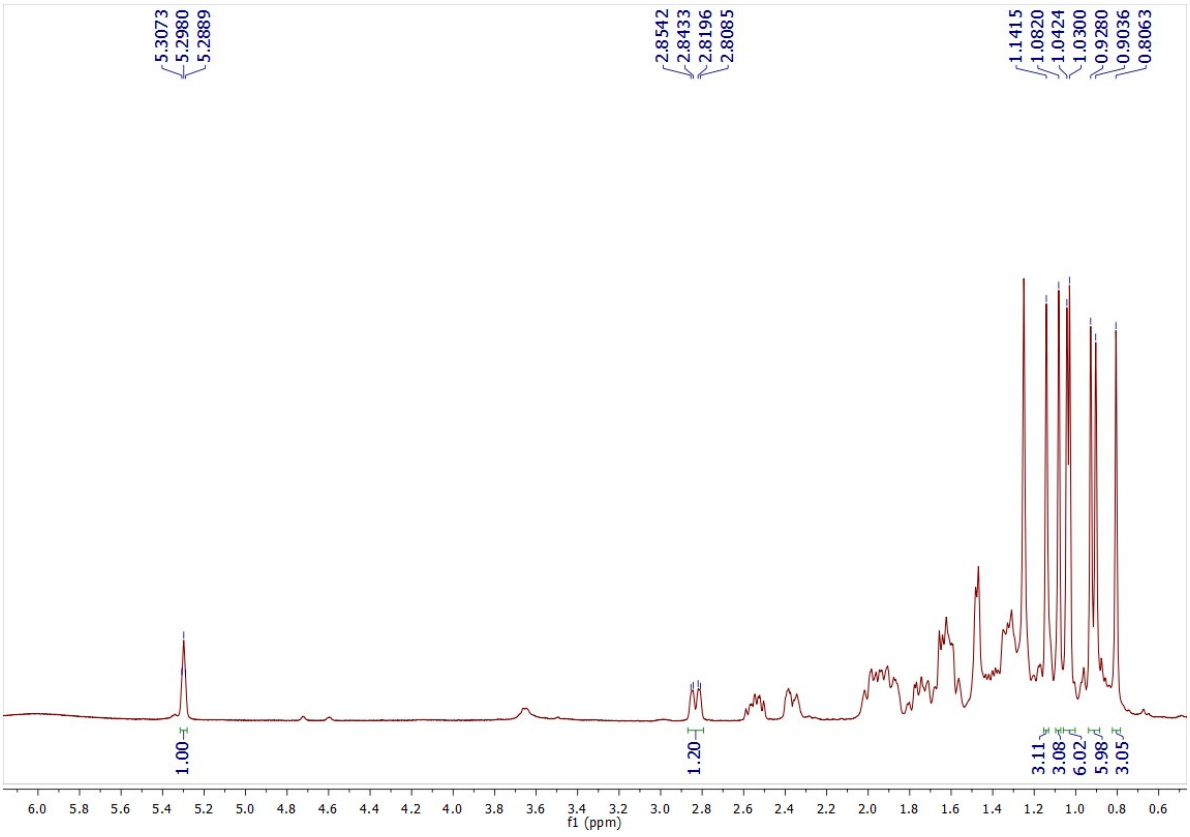

Figure S28: ^{1}H NMR spectrum of compound **15** (400 MHz, chloroform-*d*)

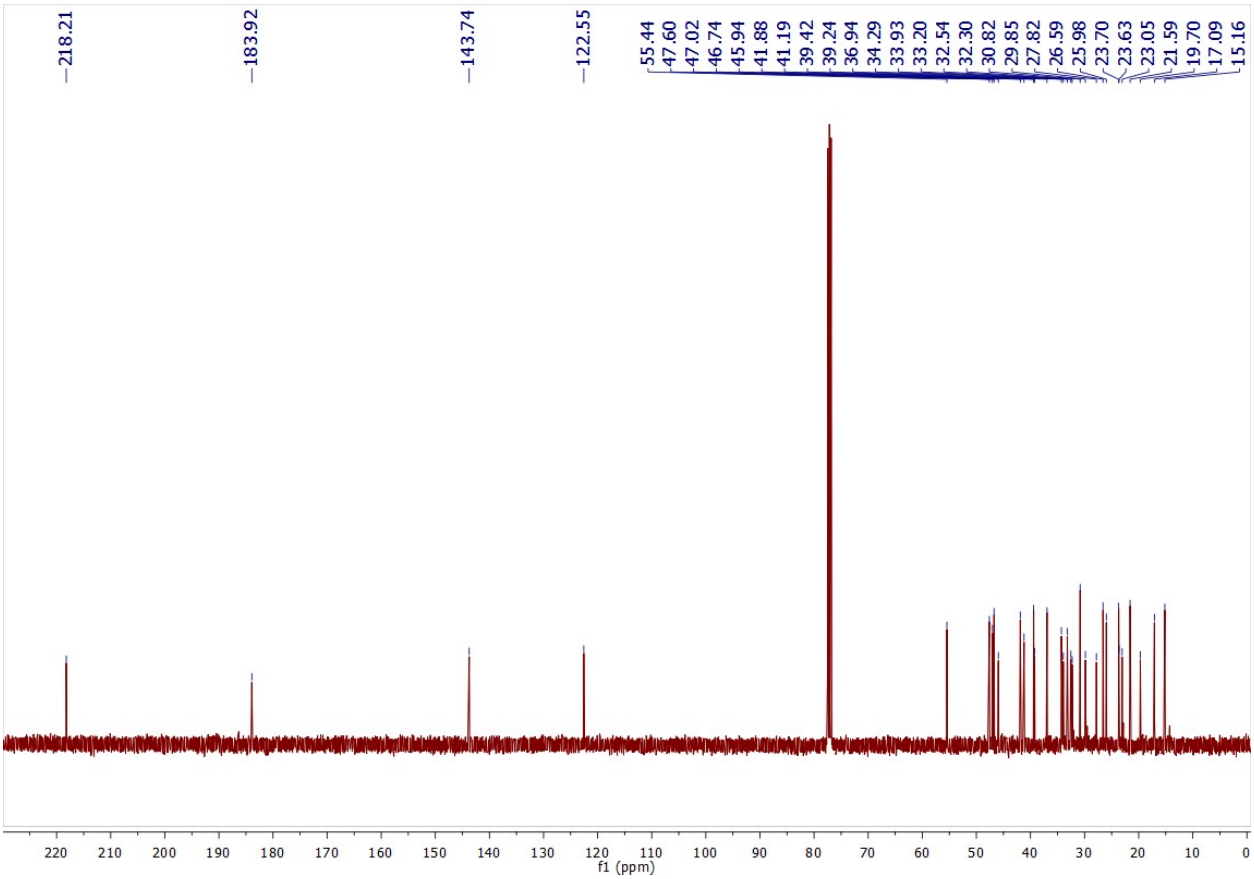

Figure S29. ^{13}C NMR spectrum of compound **15** (100 MHz, chloroform-*d*)