

# Sterols and Triterpenes from *Dobera glabra* Growing in Saudi Arabia and their Cytotoxic Activity

Wael M. Abdel-Mageed <sup>1,2</sup>, Ali A. El-Gamal <sup>1,3,\*</sup>, Shaza M. Al-Massarani <sup>1</sup>, Omer. A. Basudan <sup>1</sup>, Farid A. Badria <sup>3</sup>, Maged S. Abdel-Kader <sup>4,5</sup>, Adnan J. Al-Rehaily <sup>1</sup> and Hanan Y. Al-Ati <sup>1</sup>

<sup>1</sup> Department of Pharmacognosy, College of Pharmacy, King Saud University, P.O. Box 2457, Riyadh 11451, Saudi Arabia; wabdelmageed@ksu.edu.sa (W.M.A.-M.); salmassarani@ksu.edu.sa (S.M.A.-M.); basudan@ksu.edu.sa (O.A.B.); ajhmkl@hotmail.com (A.J.A.-R.); hati@ksu.edu.sa (H.Y.A.-A.)

<sup>2</sup> Pharmacognosy Department, Faculty of Pharmacy, Assiut University, Assiut 71526, Egypt

<sup>3</sup> Department of Pharmacognosy, Faculty of Pharmacy, Mansoura University, El-Mansoura 35516, Egypt; faridbadria@gmail.com

<sup>4</sup> Pharmacognosy Department, College of Pharmacy, Sattam Bin Abdulaziz University, Al-kharj 11942, Saudi Arabia; mpharm101@hotmail.com

<sup>5</sup> Department of Pharmacognosy, College of Pharmacy, Alexandria University, Alexandria 21215, Egypt

\* Correspondence: aelgamel@ksu.edu.sa; Tel: +00-9665-6978-0176

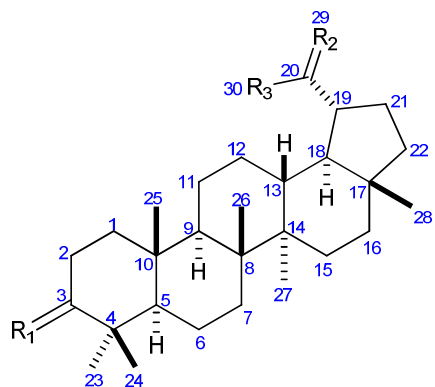
E-mail address: [aelgamel@ksu.edu.sa](mailto:aelgamel@ksu.edu.sa) (A. A. El-Gamal).

**Abstract:** A new lupane caffeoyl ester, lup-20(29)-ene 3 $\beta$ -caffeate-30-al (**7**), and a new oleanane-type triterpene, 3 $\beta$ -hydroxyolean-13(18)-en-12-one (**17**), were isolated from the aerial parts of *Dobera glabra* (Forssk), along with ten known triterpenes, including seven lupane-type lupeol (**1**), 30-nor-lup-3 $\beta$ -ol-20-one (**2**),  $\Delta^1$ -lupenone (**3**), lup-20(29)-en-3 $\beta$ ,30-diol (**4**), lupeol caffeate (**5**), 30-hydroxy lup-20(29)-ene 3 $\beta$ -caffeate (**6**), and betunaldehyde (**8**); three oleanane-type compounds were also identified, comprising  $\delta$ -amyrone (**15**),  $\delta$ -amyrin (**16**), and 11-oxo- $\beta$ -amyrin (**18**); together with six sterols, comprising  $\beta$ -sitosterol (**9**), stigmasterol (**10**), 7 $\alpha$ -hydroxy- $\beta$ -sitosterol (**11**), 7 $\alpha$ -hydroxy-stigmasterol (**12**), 7-keto- $\beta$ -sitosterol (**13**), and 7-keto-stigmasterol (**14**). Their structures were elucidated using a variety of spectroscopic techniques, including 1D ( $^1\text{H}$ ,  $^{13}\text{C}$ , and DEPT-135  $^{13}\text{C}$ ) and 2D ( $^1\text{H}$ - $^1\text{H}$  COSY,  $^1\text{H}$ - $^{13}\text{C}$  HSQC, and  $^1\text{H}$ - $^{13}\text{C}$  HMBC) nuclear magnetic resonance (NMR) and accurate mass spectroscopy. Subsequently, the different plant extracts and some of the isolated compounds (**1–9**, **11** and **13**) were investigated for their possible cytotoxic activity in comparison to cisplatin against a wide array of aggressive cancer cell lines, such as colorectal cancer (HCT-116), hepatocellular carcinoma (HepG-2), and prostate cancer (PC-3) cell lines. Compound **11** displayed broad cytotoxicity against all of the tested cell lines ( $\text{IC}_{50} \cong 8 \mu\text{g/mL}$  in all cases), and a high safety margin against normal *Vero* cells ( $\text{IC}_{50} = 70 \mu\text{g/mL}$ ), suggesting that **11** may be a highly selective and effective anticancer agent candidate. Notably, the evidence indicated that the mode of action of compound **11** could possibly consist of the inhibition of phosphodiesterase I (80.2% enzyme inhibition observed at 2  $\mu\text{M}$  compound concentration).

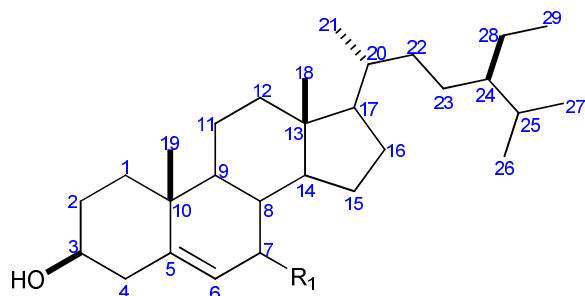
**Keywords:** *Dobera glabra*; Salvadoraceae; Triterpenes; Steroids, Cytotoxic activity, Phosphodiesterase inhibition.

## Content

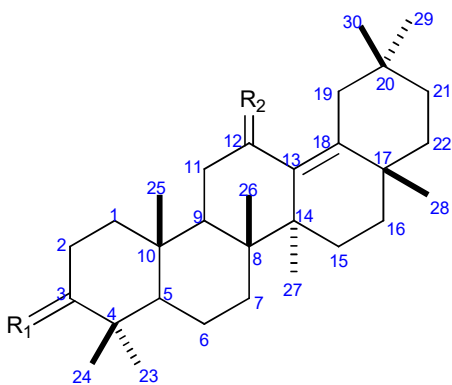
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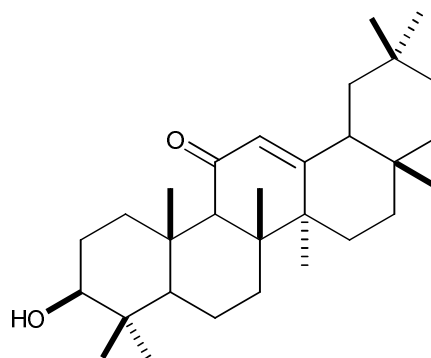
- 1** R<sub>1</sub> = α-H, β-OH, R<sub>2</sub> = CH<sub>2</sub>, R<sub>3</sub> = CH<sub>3</sub>  
**2** R<sub>1</sub> = α-H, β-OH, R<sub>2</sub> = O, R<sub>3</sub> = CH<sub>3</sub>  
**3** R<sub>1</sub> = O, <sup>1,2</sup>Δ, R<sub>2</sub> = CH<sub>2</sub>, R<sub>3</sub> = CH<sub>3</sub>  
**4** R<sub>1</sub> = α-H, β-OH, R<sub>2</sub> = CH<sub>2</sub>, R<sub>3</sub> = CH<sub>2</sub>OH  
**5** R<sub>1</sub> = caffeoyl, R<sub>2</sub> = CH<sub>2</sub>, R<sub>3</sub> = CH<sub>3</sub>  
**6** R<sub>1</sub> = caffeoyl, R<sub>2</sub> = CH<sub>2</sub>, R<sub>3</sub> = CH<sub>2</sub>OH  
**7** R<sub>1</sub> = caffeoyl, R<sub>2</sub> = CH<sub>2</sub>, R<sub>3</sub> = CHO  
**8** R<sub>1</sub> = α-H, β-OH, R<sub>2</sub> = O, R<sub>3</sub> = OH



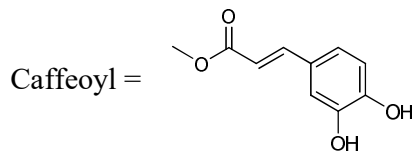
- 9** R<sub>1</sub> = H  
**10** R<sub>1</sub> = H, <sup>22,23</sup>Δ  
**11** R<sub>1</sub> = OH  
**12** R<sub>1</sub> = OH, <sup>22,23</sup>Δ  
**13** R<sub>1</sub> = O  
**14** R<sub>1</sub> = O, <sup>22,23</sup>Δ



- 15** R<sub>1</sub> = O, R<sub>2</sub> = H<sub>2</sub>  
**16** R<sub>1</sub> = α-H, β-OH, R<sub>2</sub> = H<sub>2</sub>  
**17** R<sub>1</sub> = α-H, β-OH, R<sub>2</sub> = O



**18**



**Fig. 1S.** Structures of compounds (1–18) isolated from *D. glabra*.

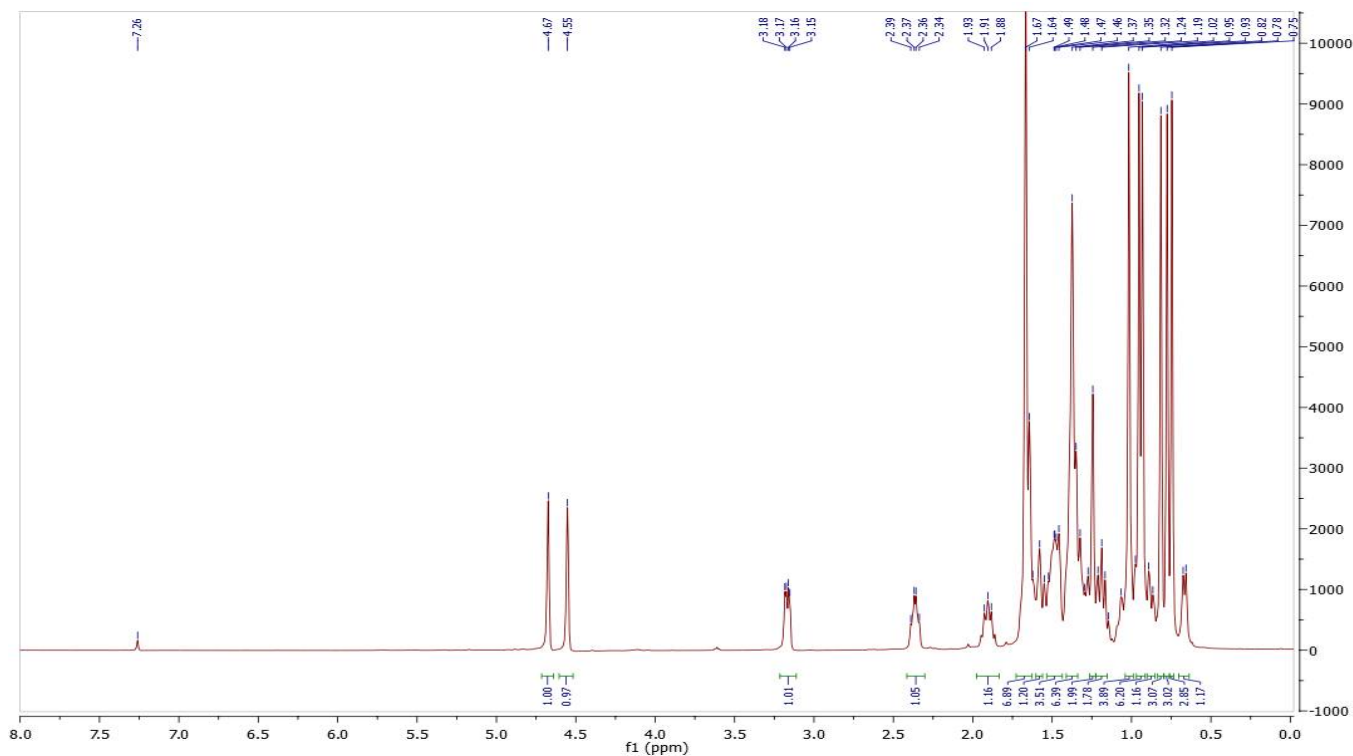


Figure 2S. <sup>1</sup>H NMR spectrum of compound (1) (500 MHz, CDCl<sub>3</sub>)

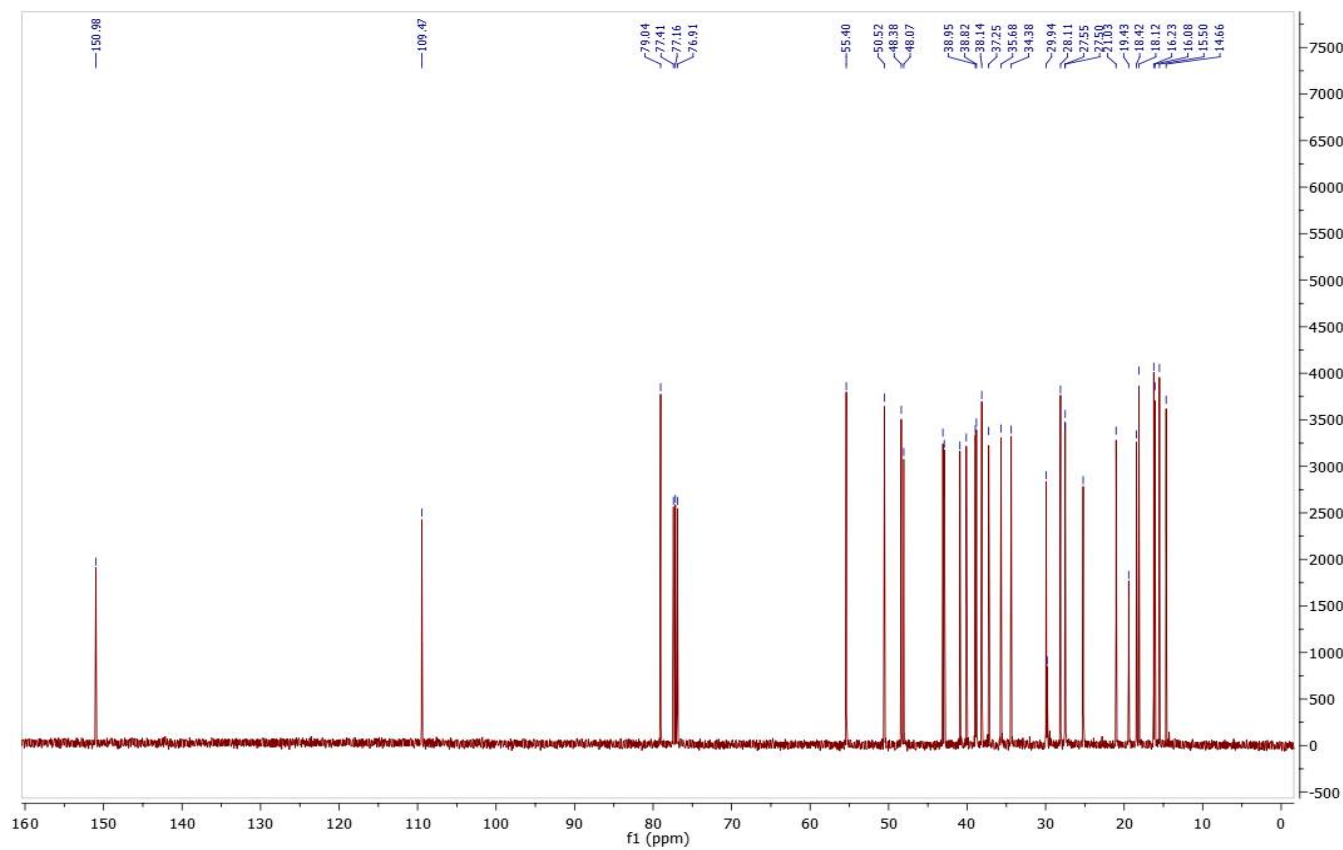
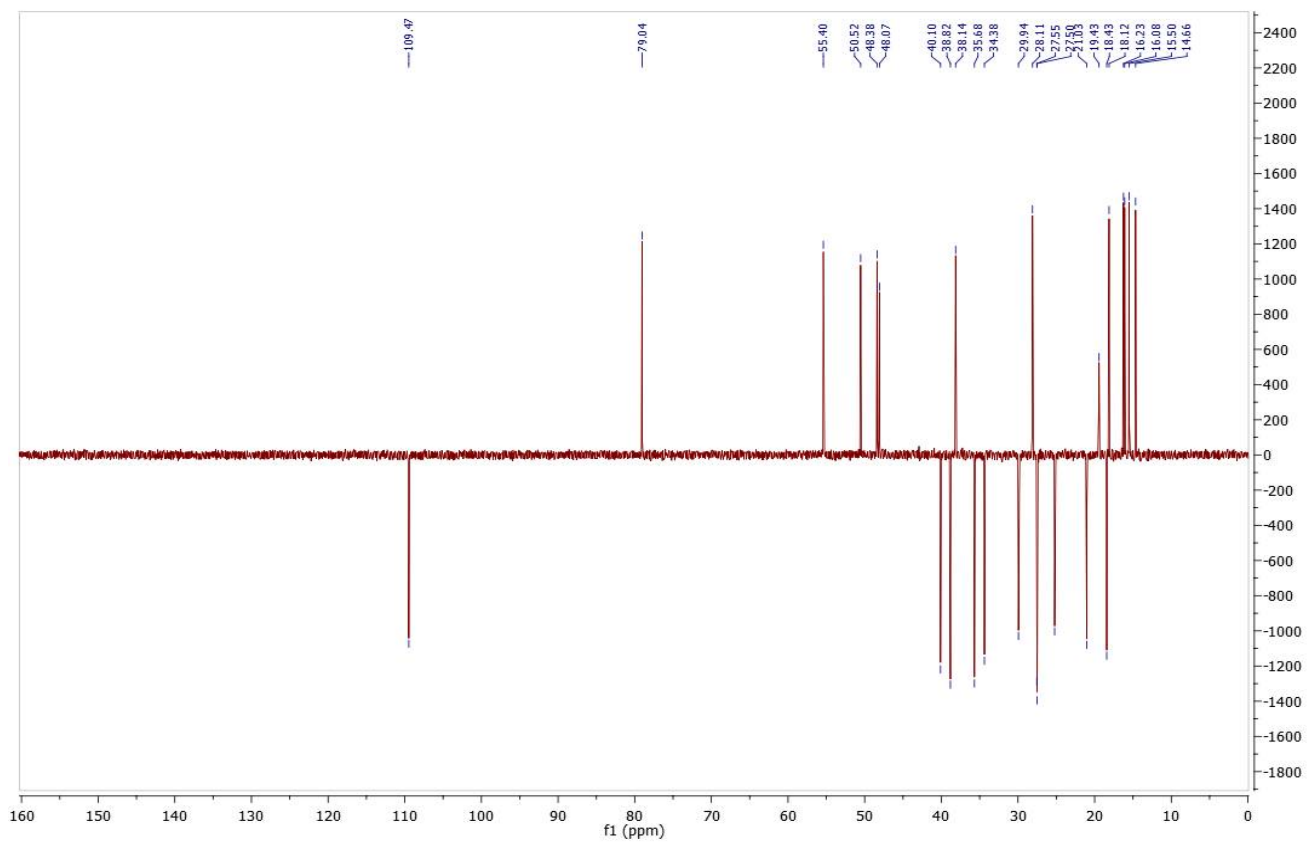


Figure 3S. <sup>13</sup>C NMR spectrum of compound (1) (125 MHz, CDCl<sub>3</sub>)



**Figure 4S.** DEPT  $^{13}\text{C}$  NMR spectrum of compound (1) (125 MHz,  $\text{CDCl}_3$ )

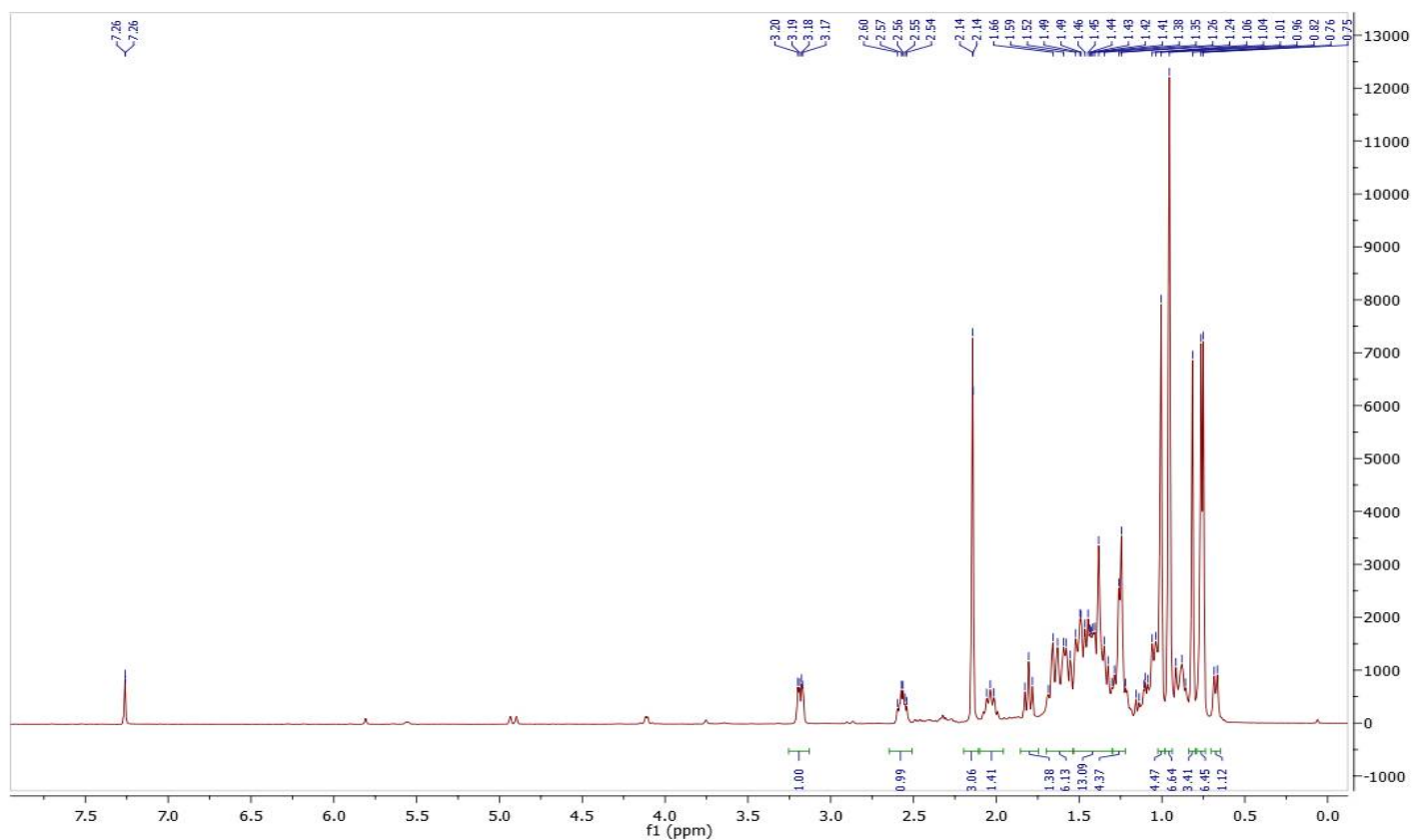


Figure 5S. <sup>1</sup>H NMR spectrum of compound (2) (500 MHz, CDCl<sub>3</sub>)

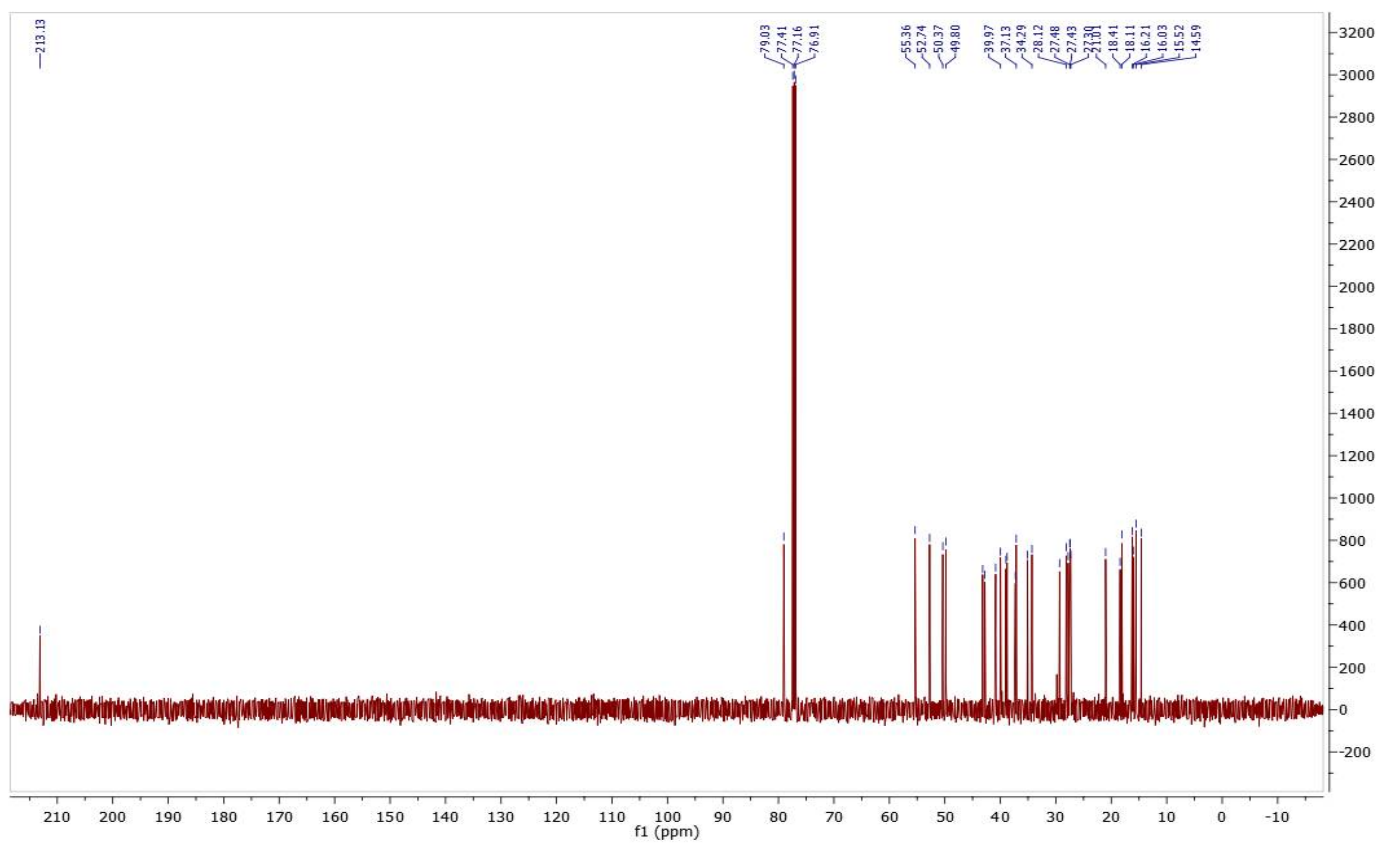
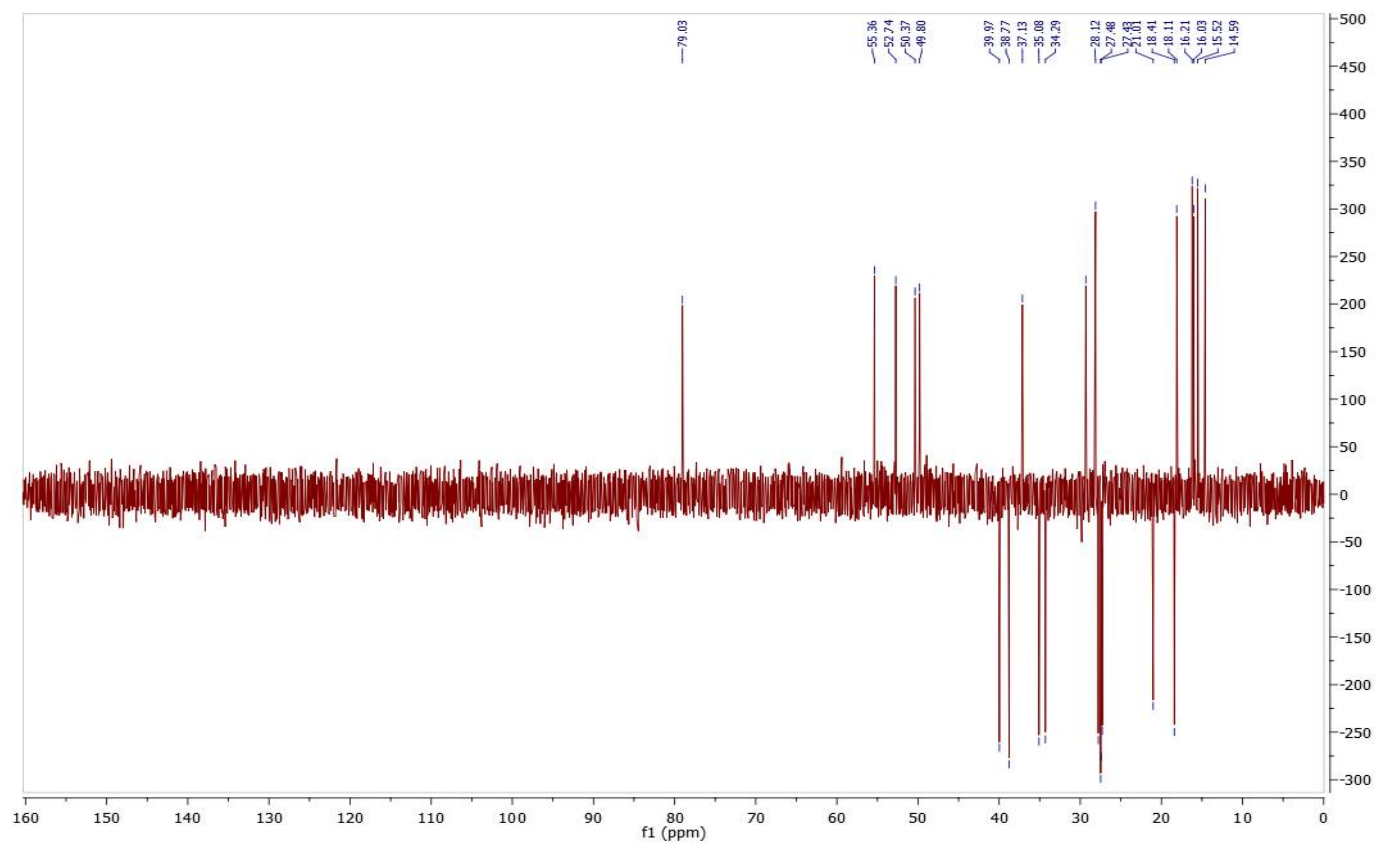


Figure 6S. <sup>13</sup>C NMR spectrum of compound (2) (125 MHz, CDCl<sub>3</sub>)



**Figure 7S.** DEPT  $^{13}\text{C}$  NMR spectrum of compound (2) (125 MHz,  $\text{CDCl}_3$ )



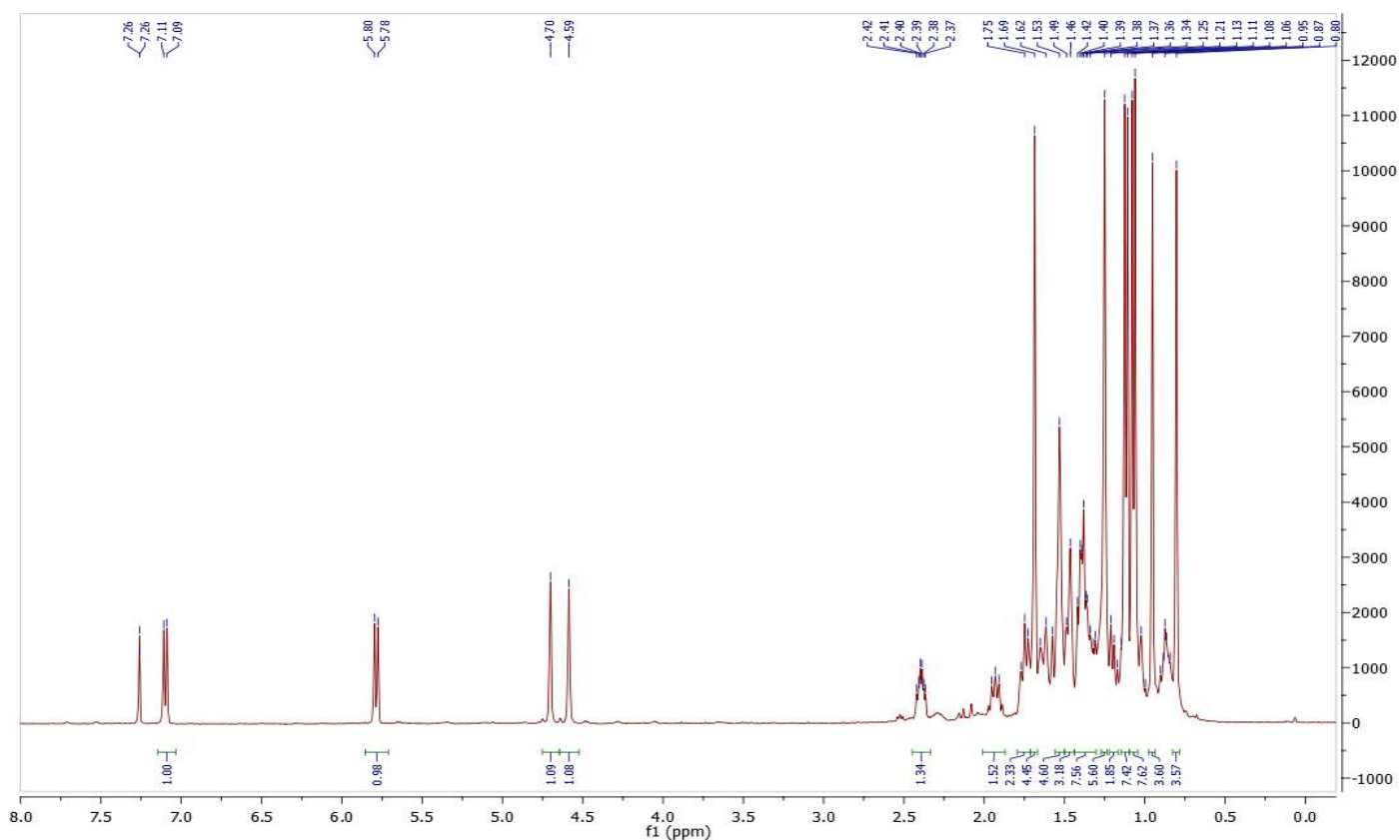
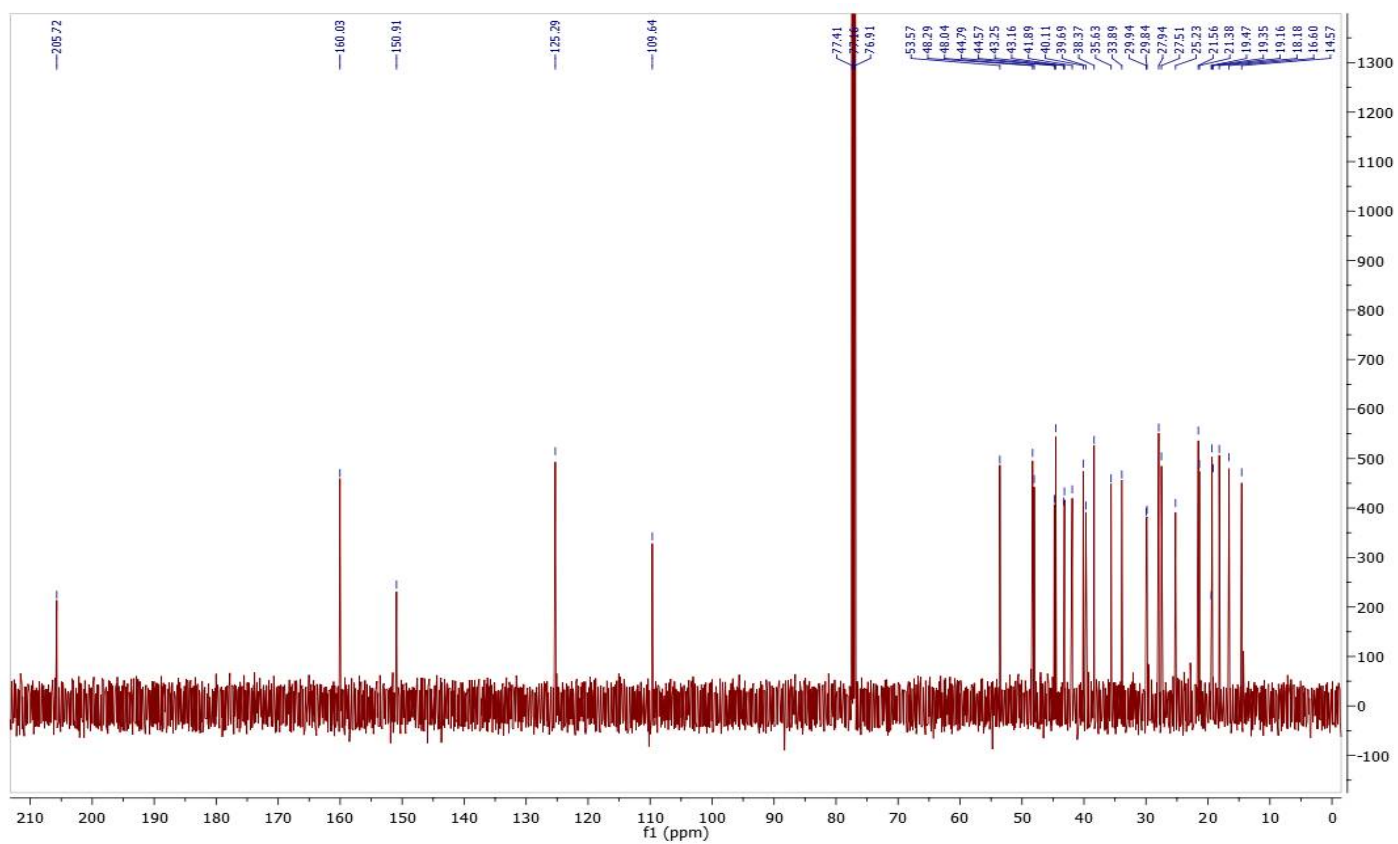
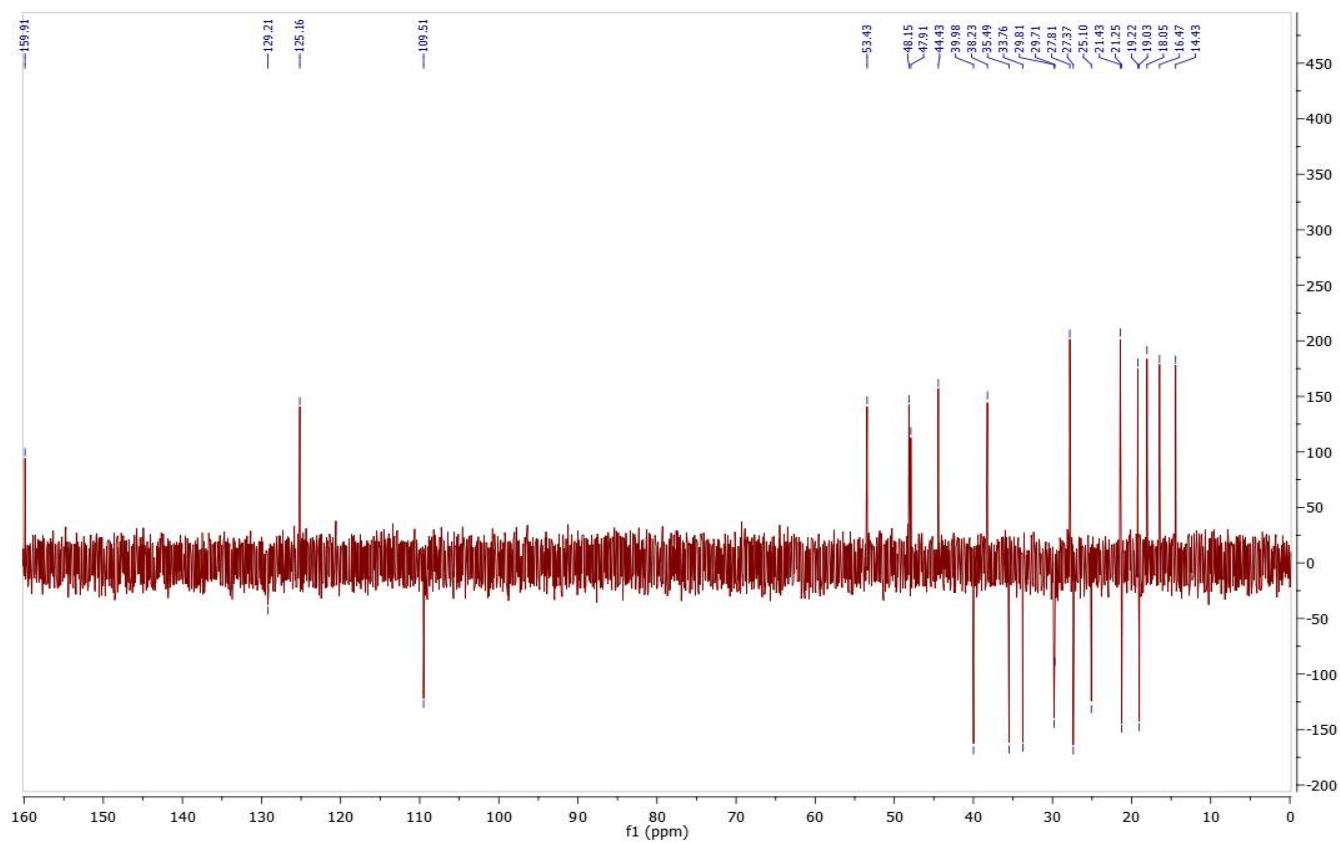


Figure 8S. <sup>1</sup>H NMR spectrum of compound (3) (500 MHz, CDCl<sub>3</sub>)



9

Figure 9S. <sup>13</sup>C NMR spectrum of compound (3) (125 MHz, CDCl<sub>3</sub>)



**Figure 10S.** DEPT  $^{13}\text{C}$  NMR spectrum of compound (**3**) (125 MHz,  $\text{CDCl}_3$ )

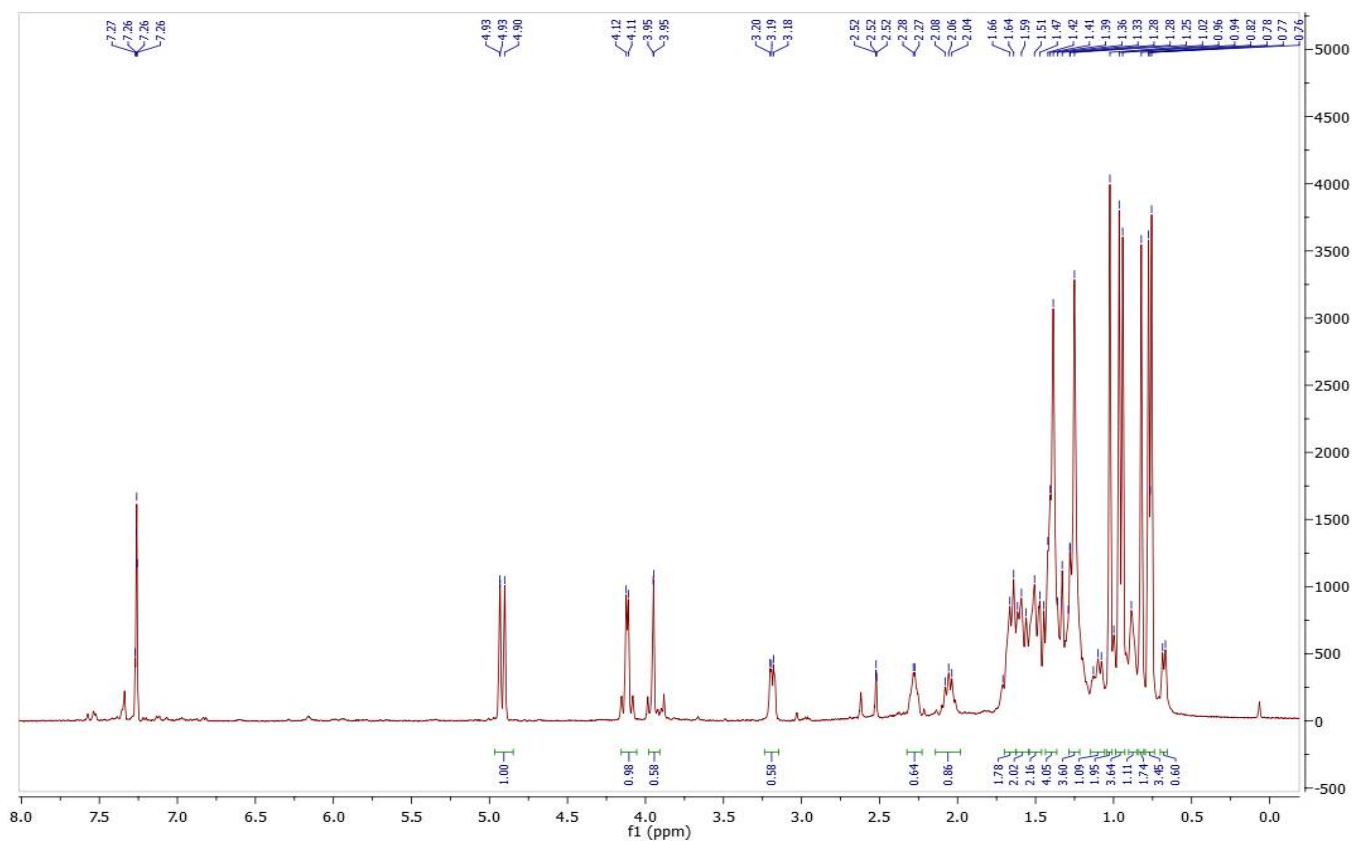


Figure 11S. <sup>1</sup>H NMR spectrum of compound (4) (500 MHz, CDCl<sub>3</sub>)

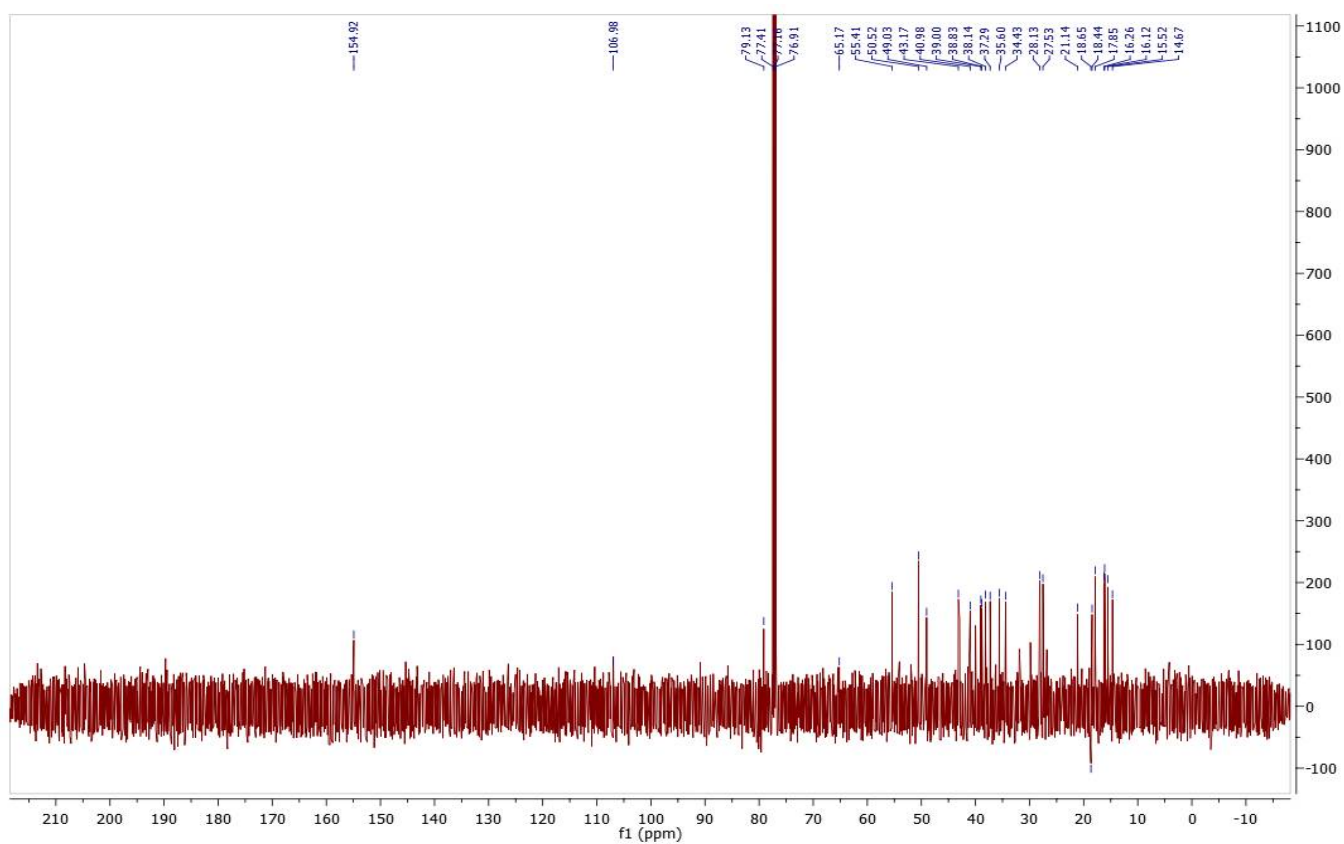


Figure 12S. <sup>13</sup>C NMR spectrum of compound (4) (125 MHz, CDCl<sub>3</sub>)

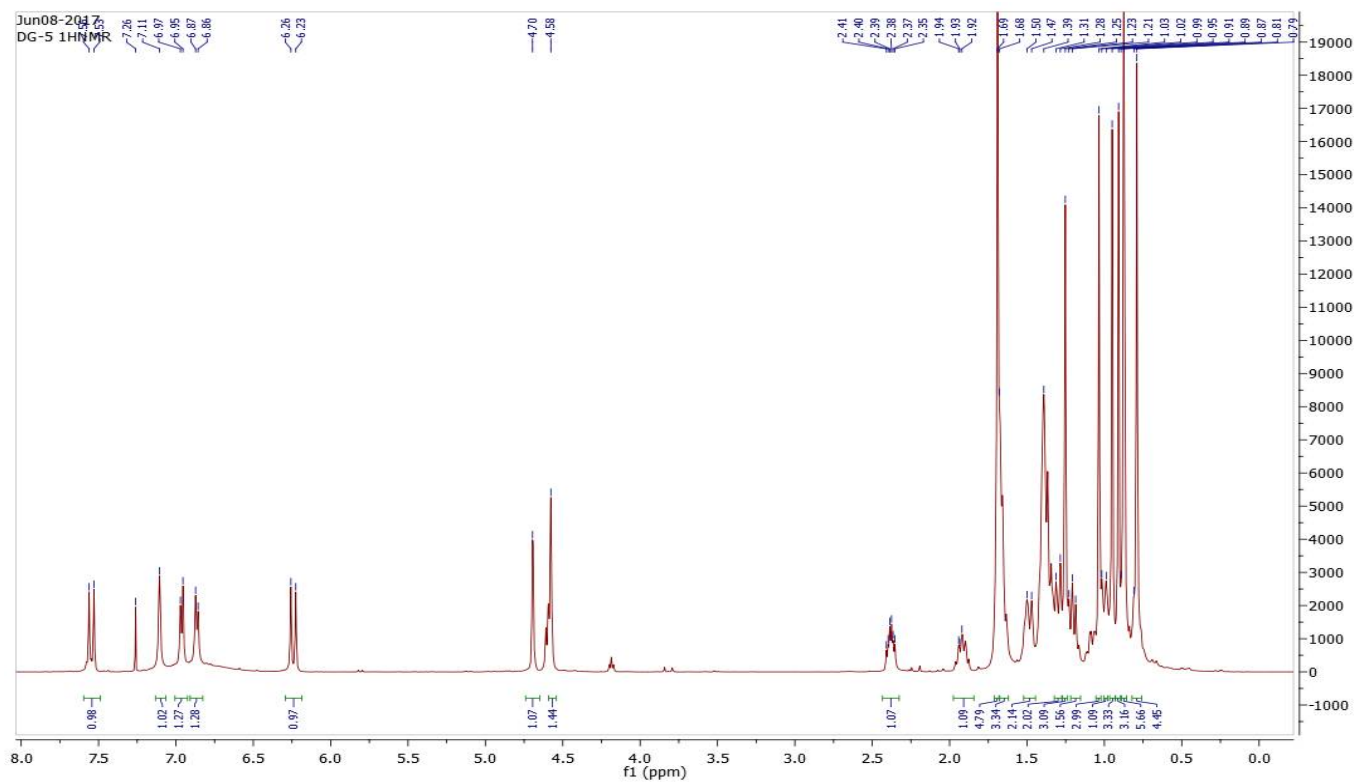
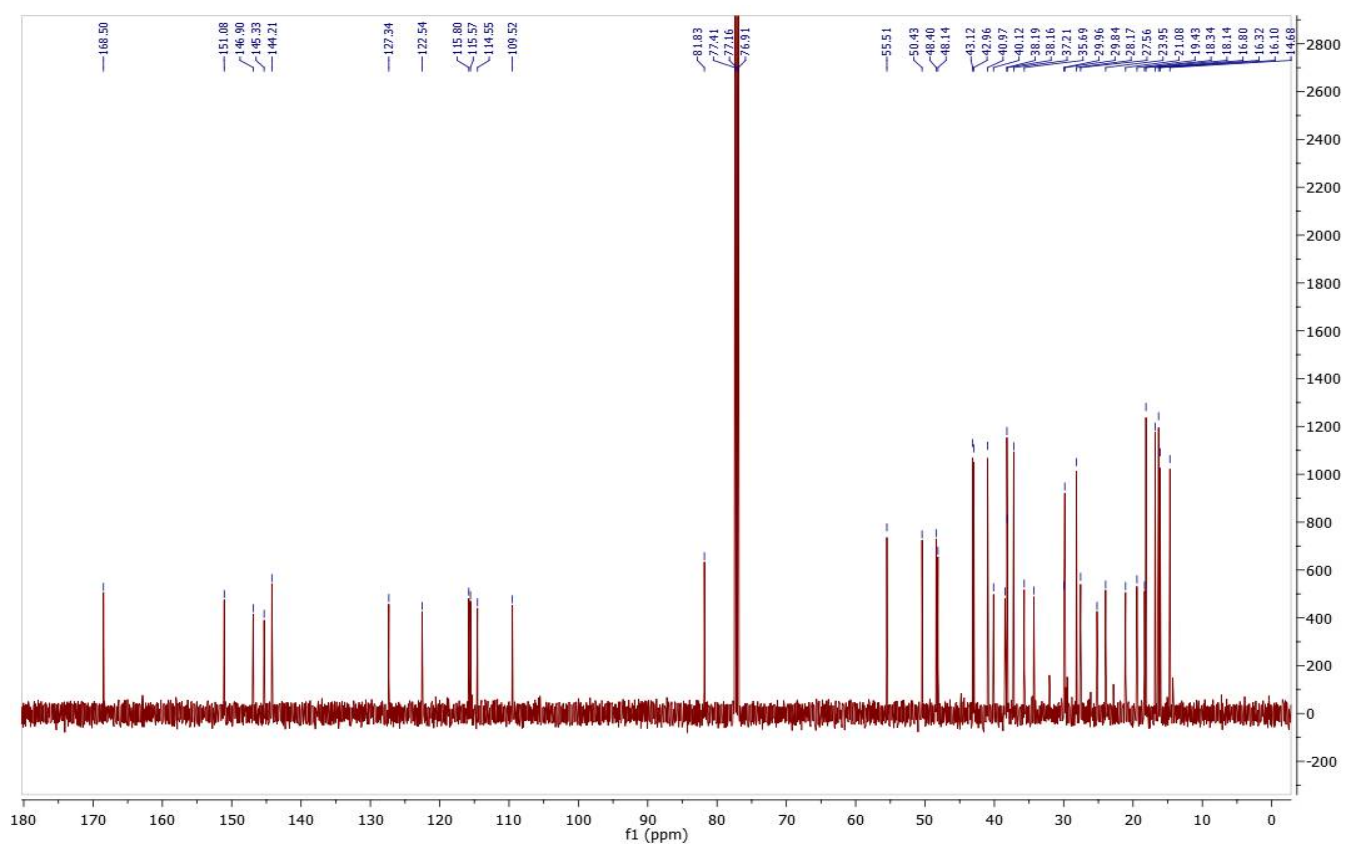


Figure 13S.  $^1\text{H}$  NMR spectrum of compound (5) (500 MHz,  $\text{CDCl}_3$ )



12  
Figure 14S.  $^{13}\text{C}$  NMR spectrum of compound (5) (125 MHz,  $\text{CDCl}_3$ )

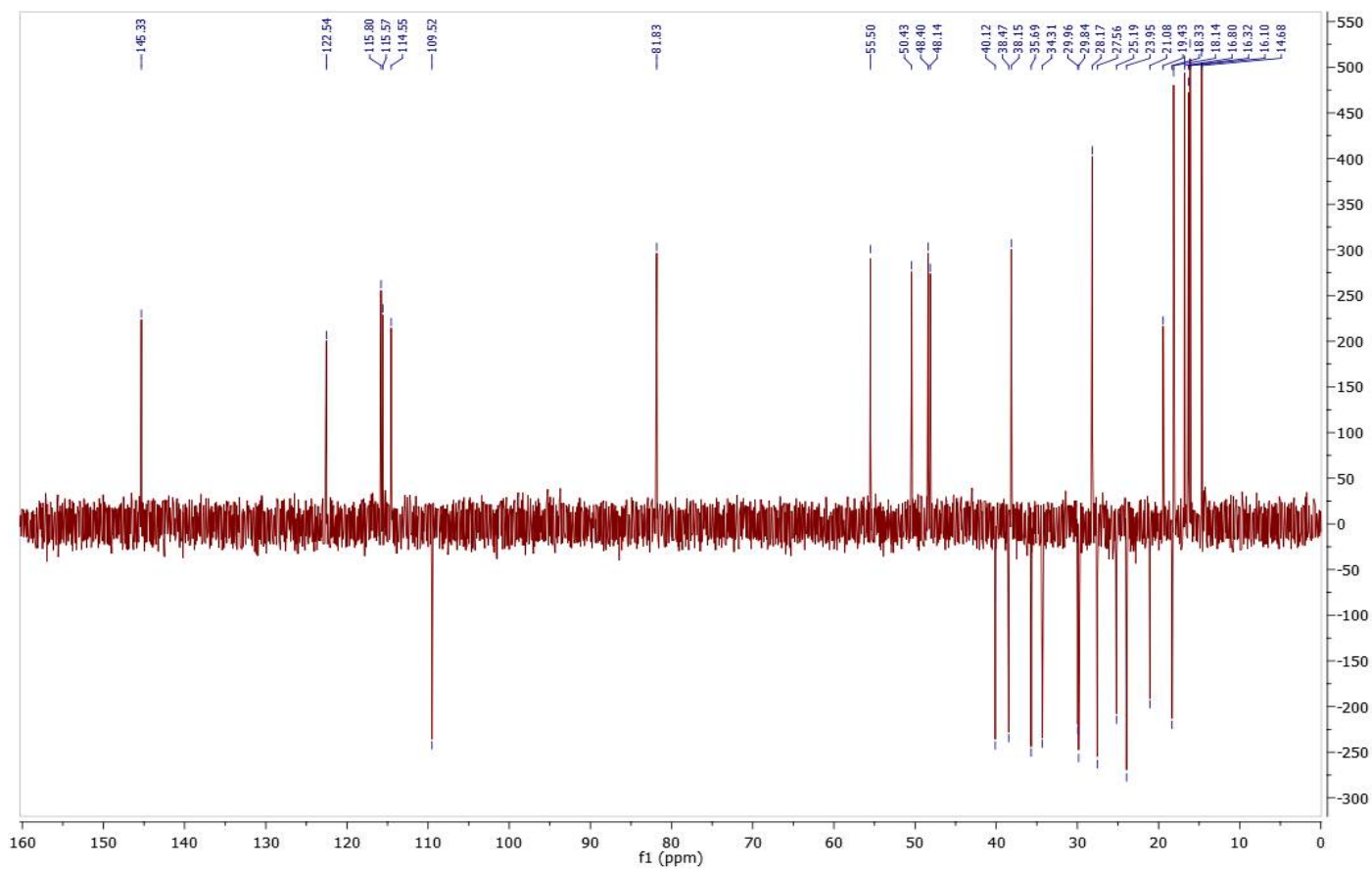


Figure 15S. DEPT  $^{13}\text{C}$  NMR spectrum of compound (5) (125 MHz,  $\text{CDCl}_3$ )

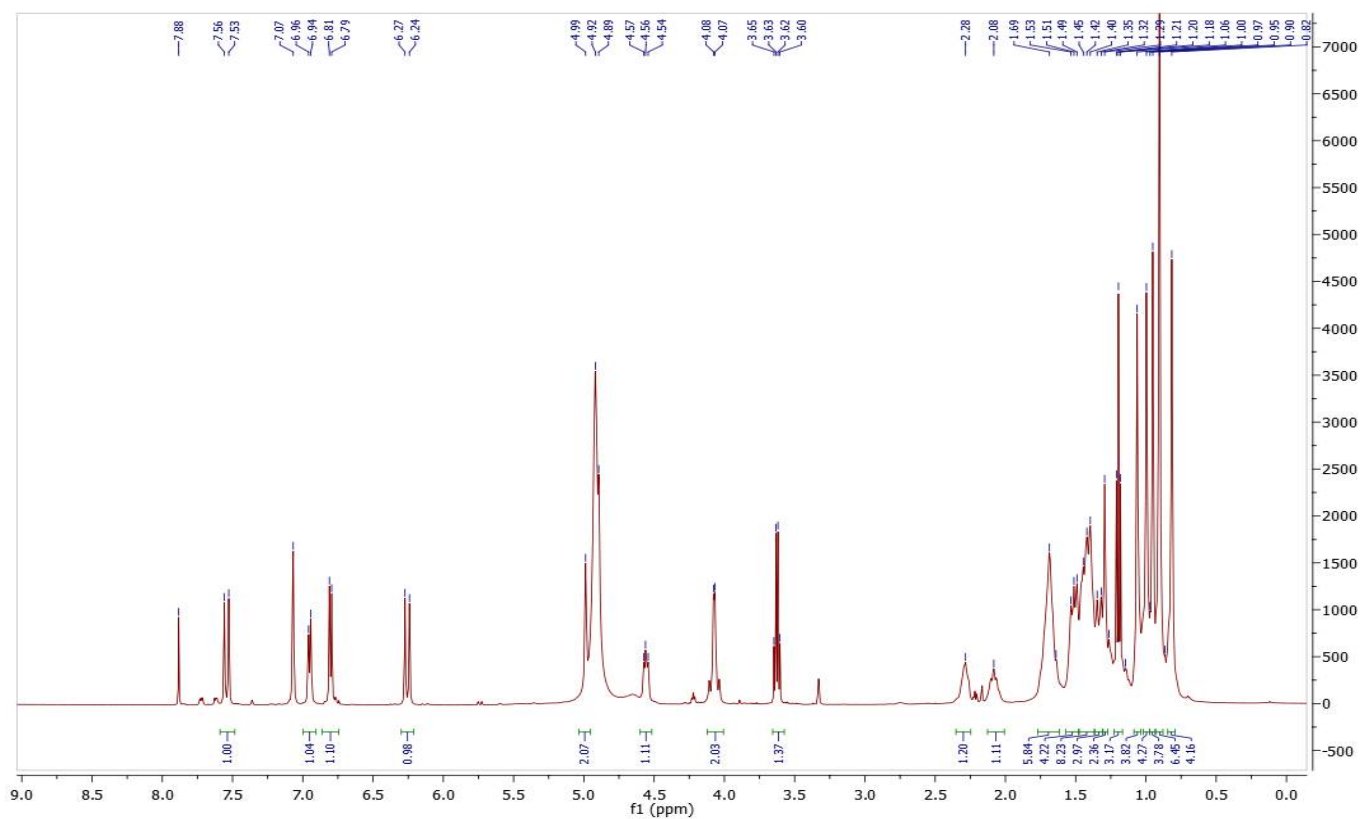


Figure 16S. <sup>1</sup>H NMR spectrum of compound (6) (500 MHz, CDCl<sub>3</sub>)

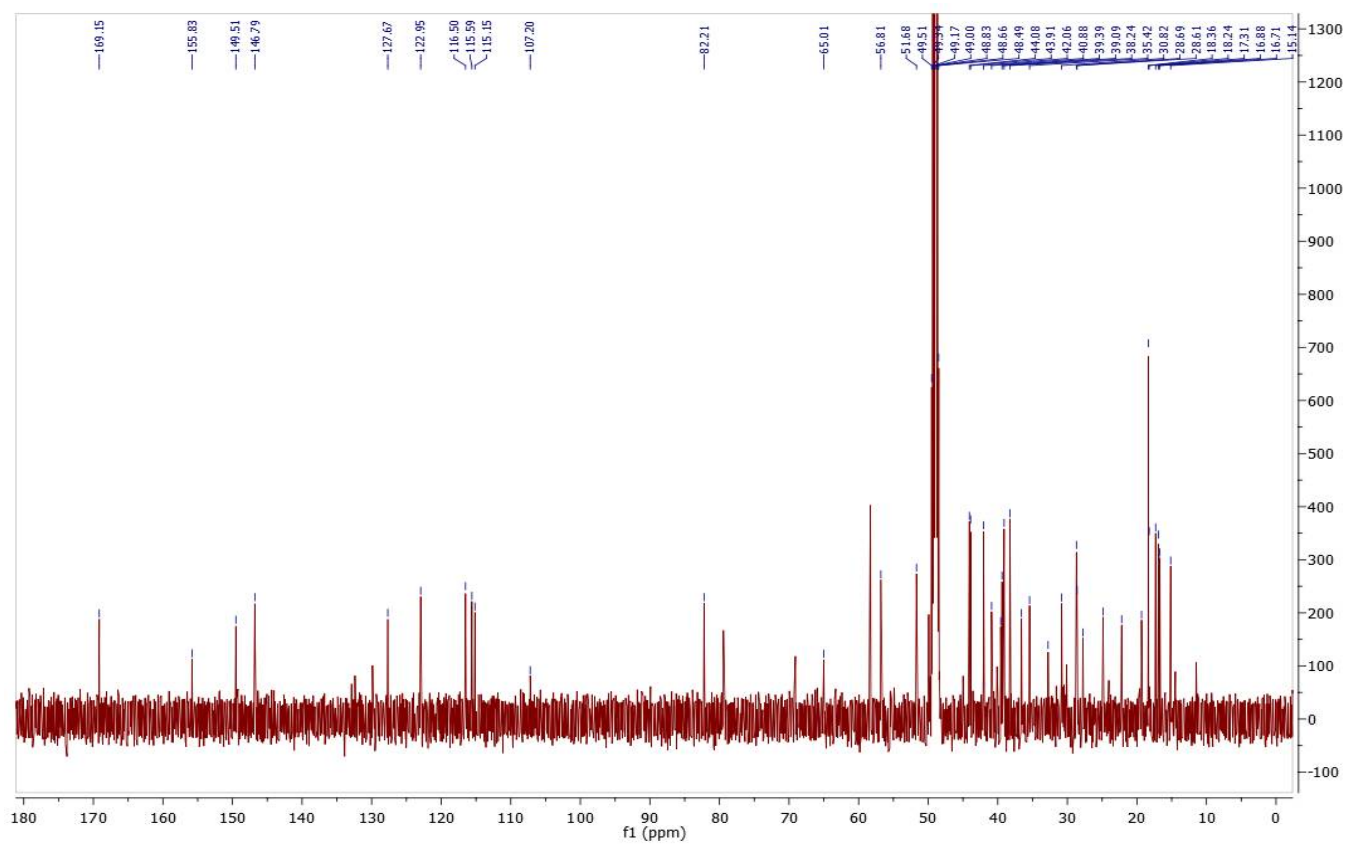
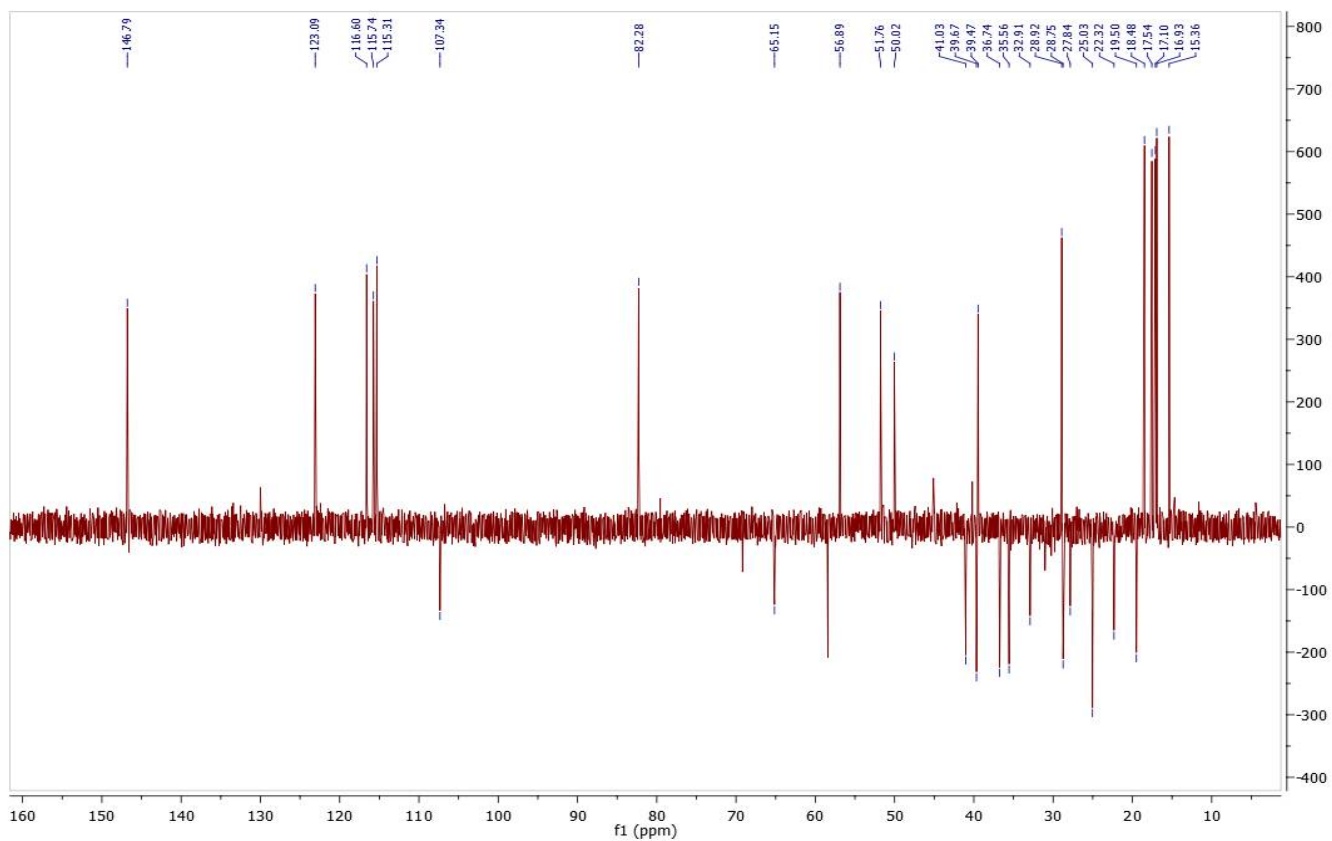


Figure 17S. <sup>13</sup>C NMR spectrum of compound (6) (125 MHz, CDCl<sub>3</sub>)



**Figure 18S.** DEPT  $^{13}\text{C}$  NMR spectrum of compound (6) (125 MHz,  $\text{CDCl}_3$ )

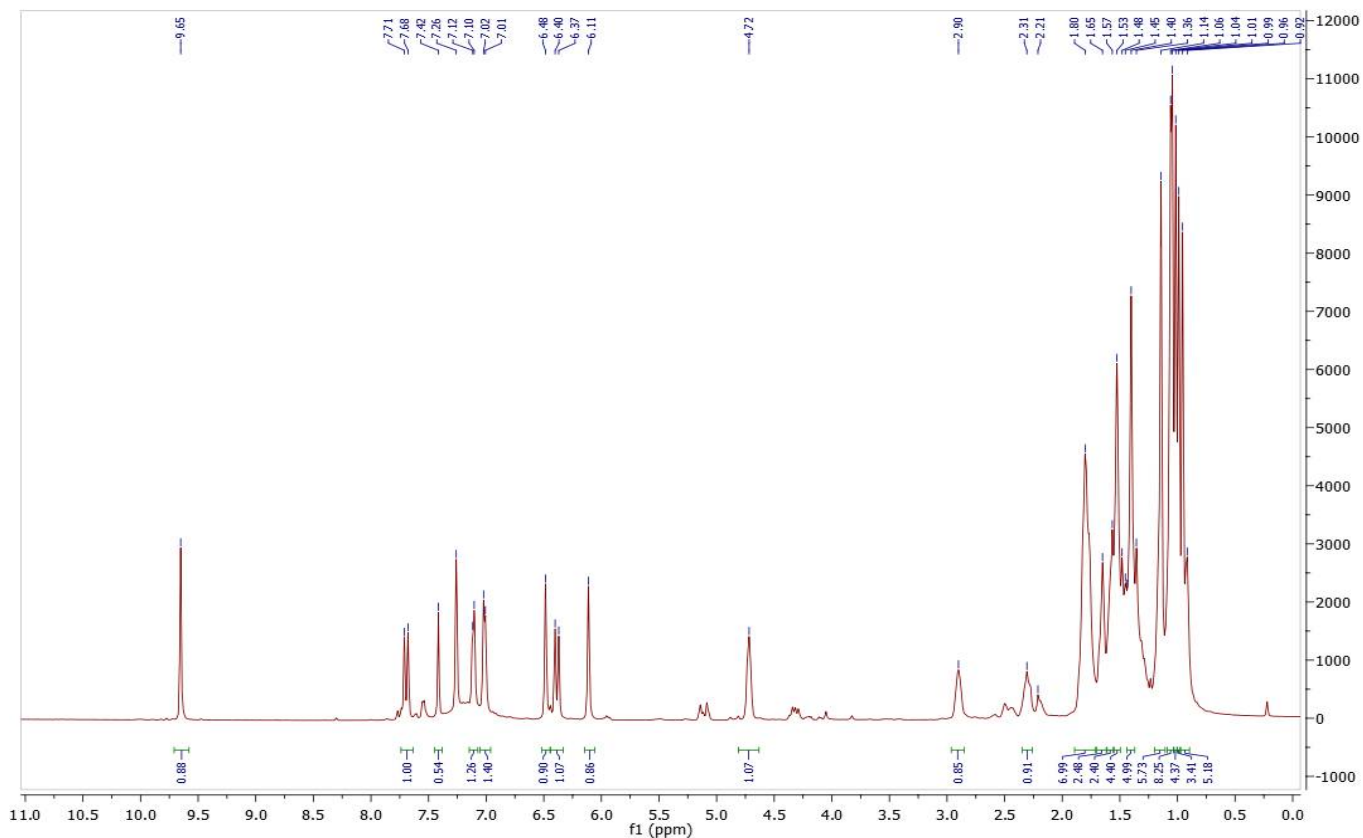


Figure 19S. <sup>1</sup>H NMR spectrum of compound (7) (500 MHz, CDCl<sub>3</sub>)

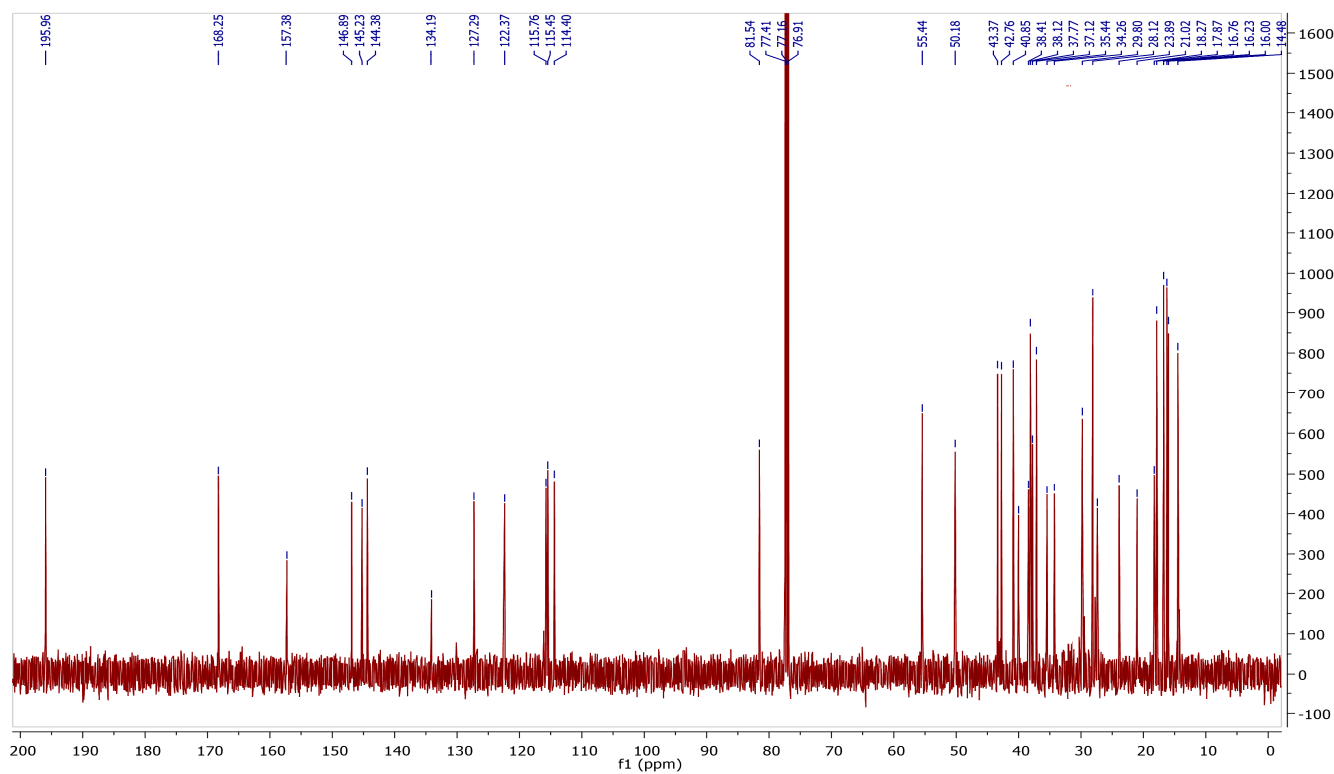


Figure 20S. <sup>13</sup>C NMR spectrum of compound (7) (125 MHz, CDCl<sub>3</sub>)



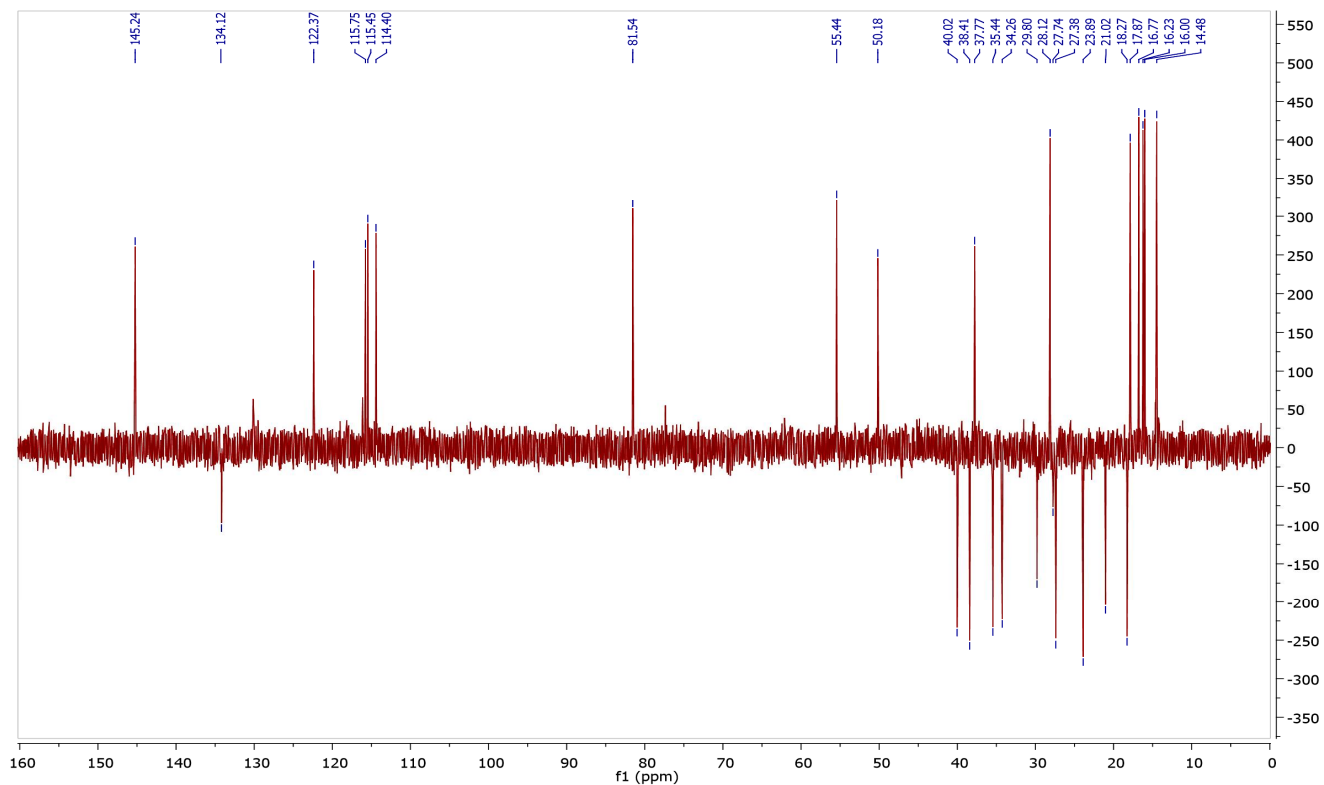


Figure 21S. DEPT  $^{13}\text{C}$  NMR spectrum of compound (7) (125 MHz,  $\text{CDCl}_3$ )

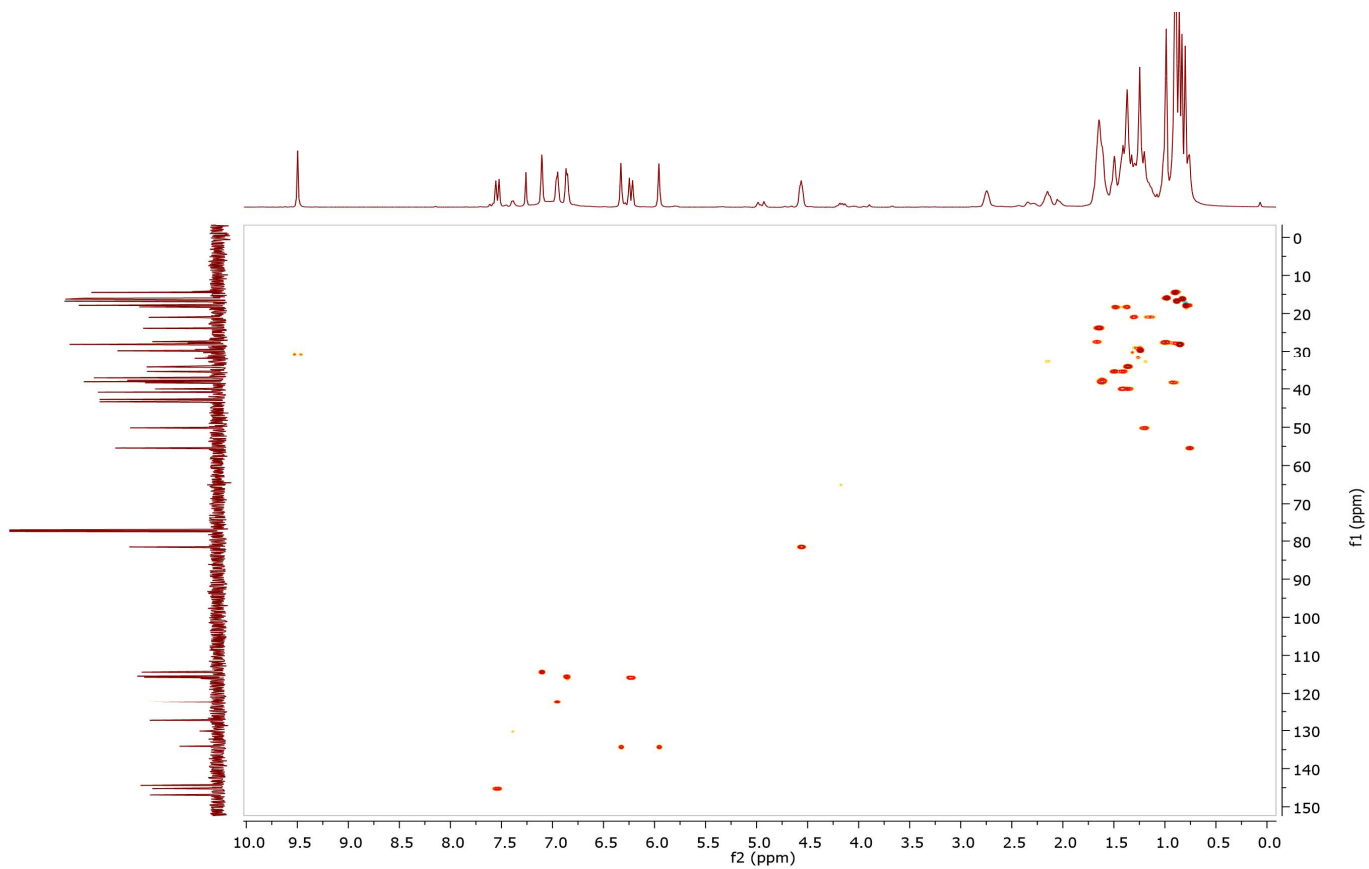
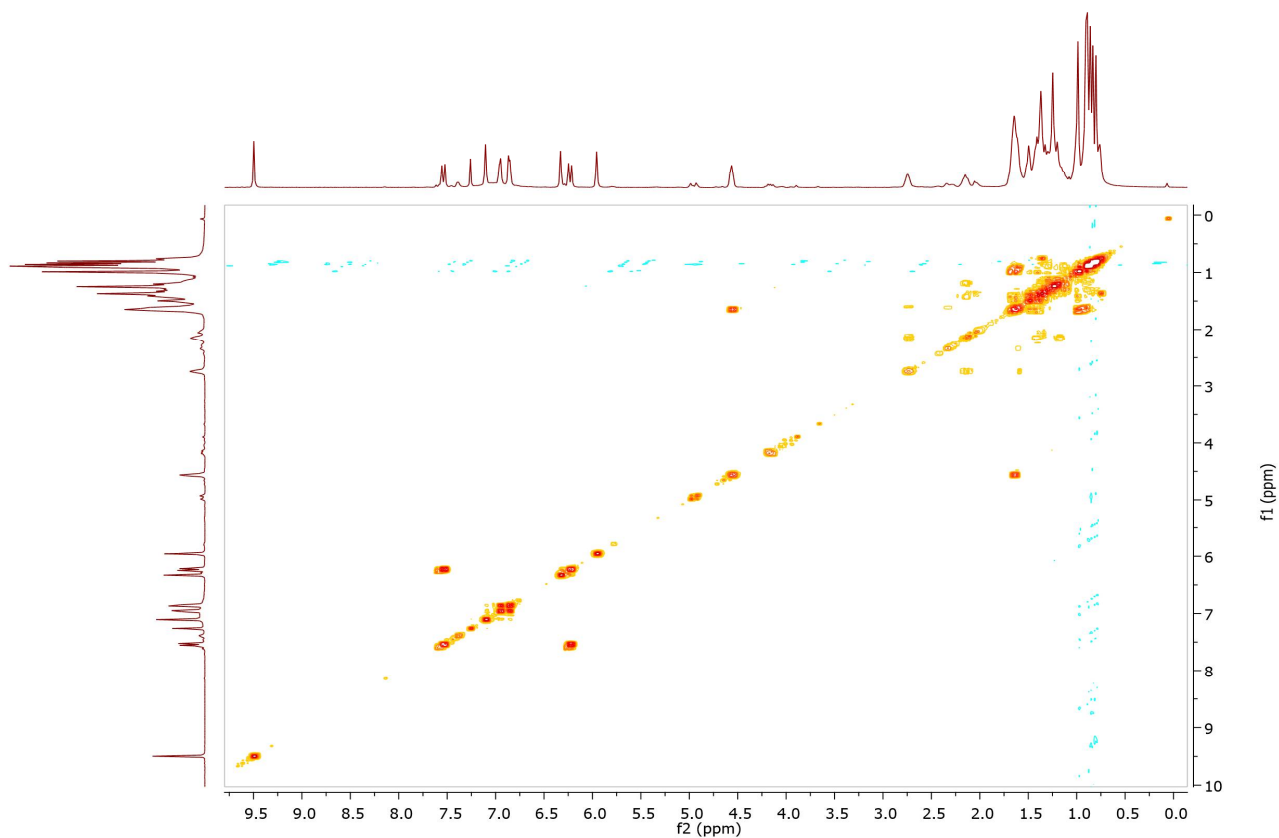
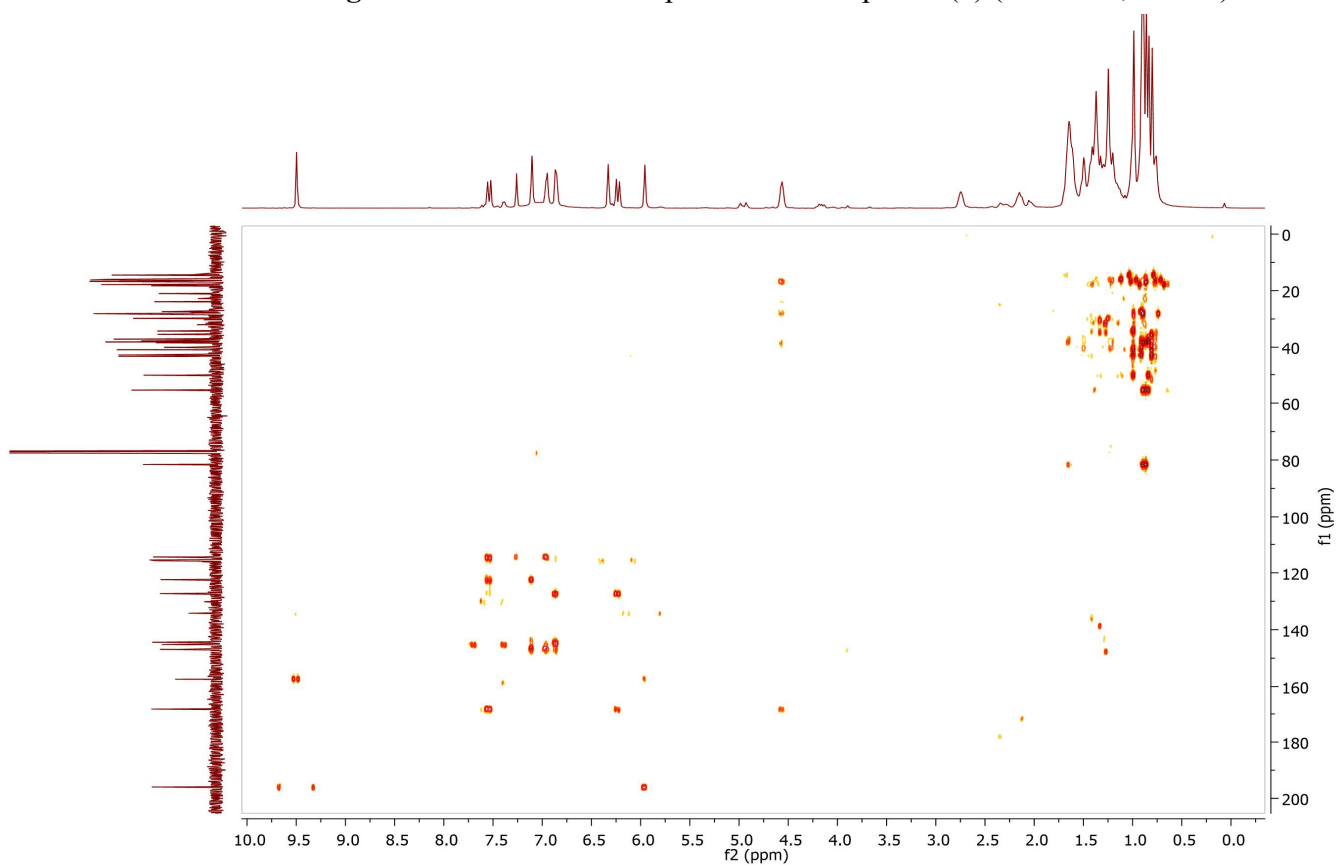


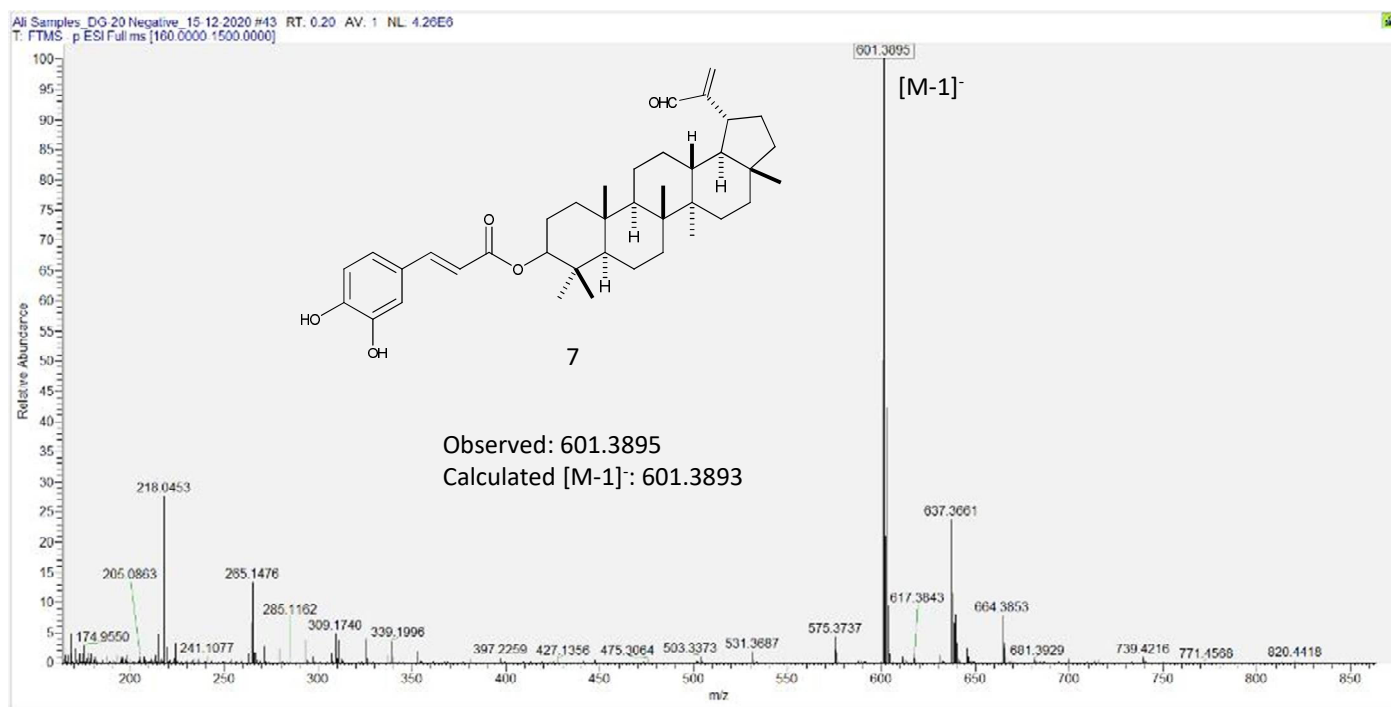
Figure 22S.  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum of compound (7) (500 MHz,  $\text{CDCl}_3$ )



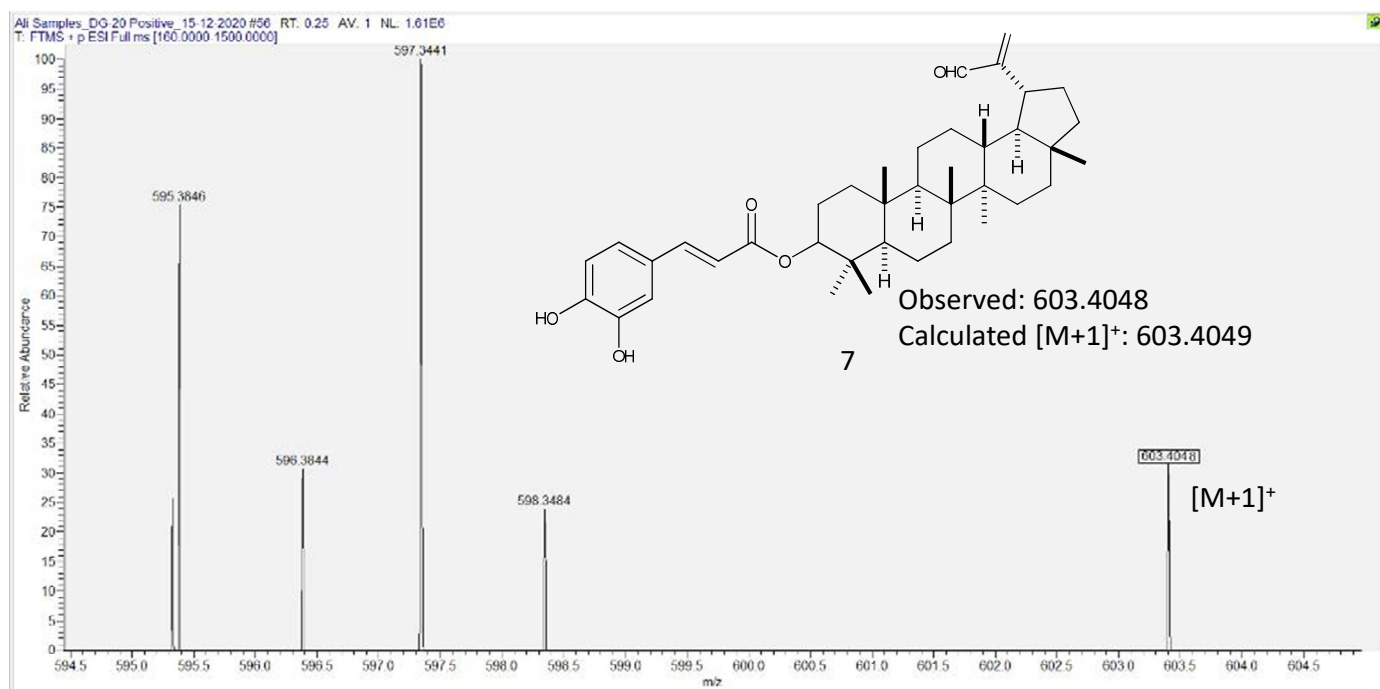
**Figure 23S.**  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of compound (7) (500 MHz,  $\text{CDCl}_3$ )



**Figure 24S.**  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum of compound (7) (500 MHz,  $\text{CDCl}_3$ )



**A**



**B**

**Figure 25S:** HRESIMS spectrum of compound (7) (A) negative mode, (B) positive mode.

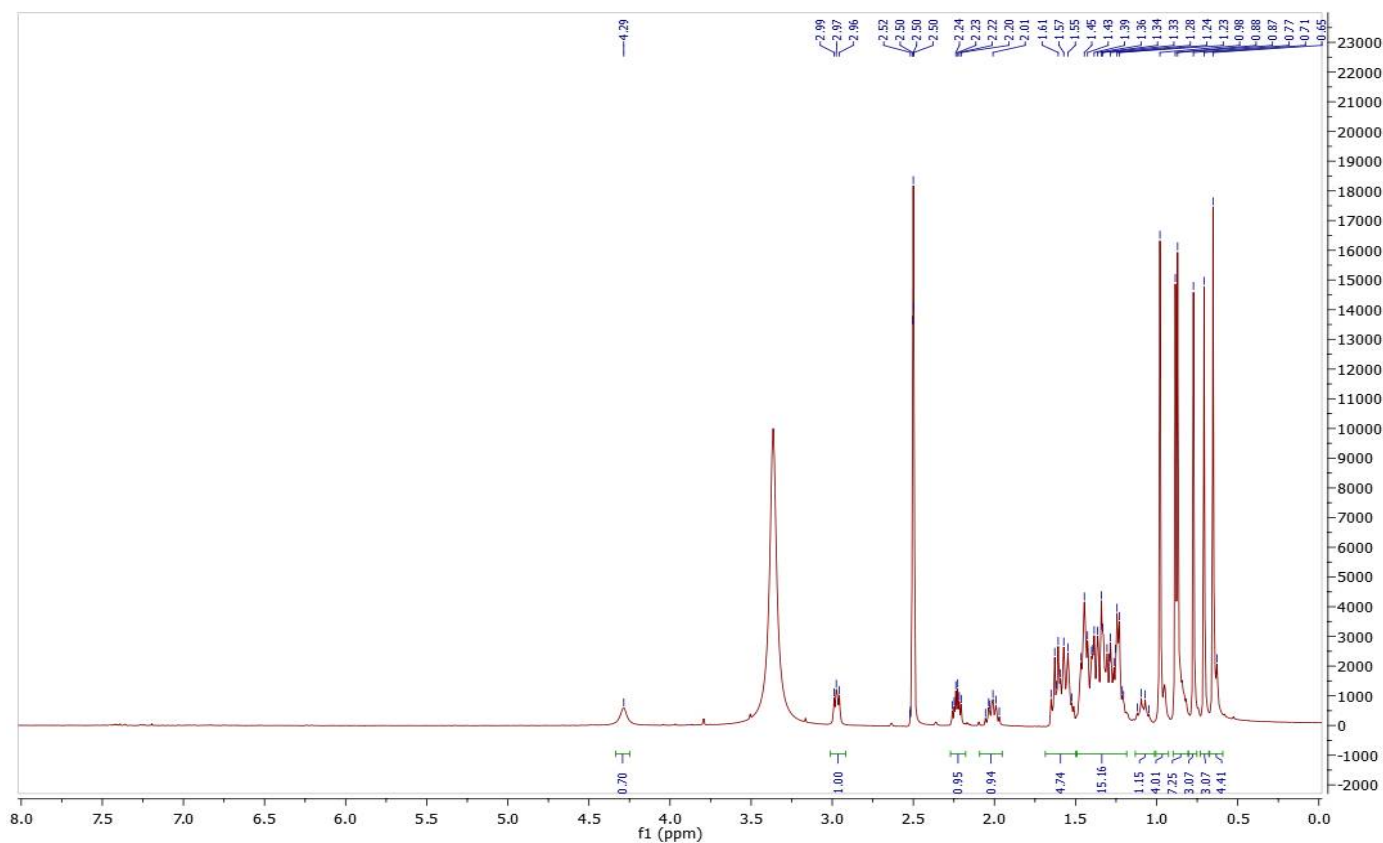


Figure 26S.  $^1\text{H}$  NMR spectrum of compound (8) (500 MHz,  $\text{DMSO}_6$ )

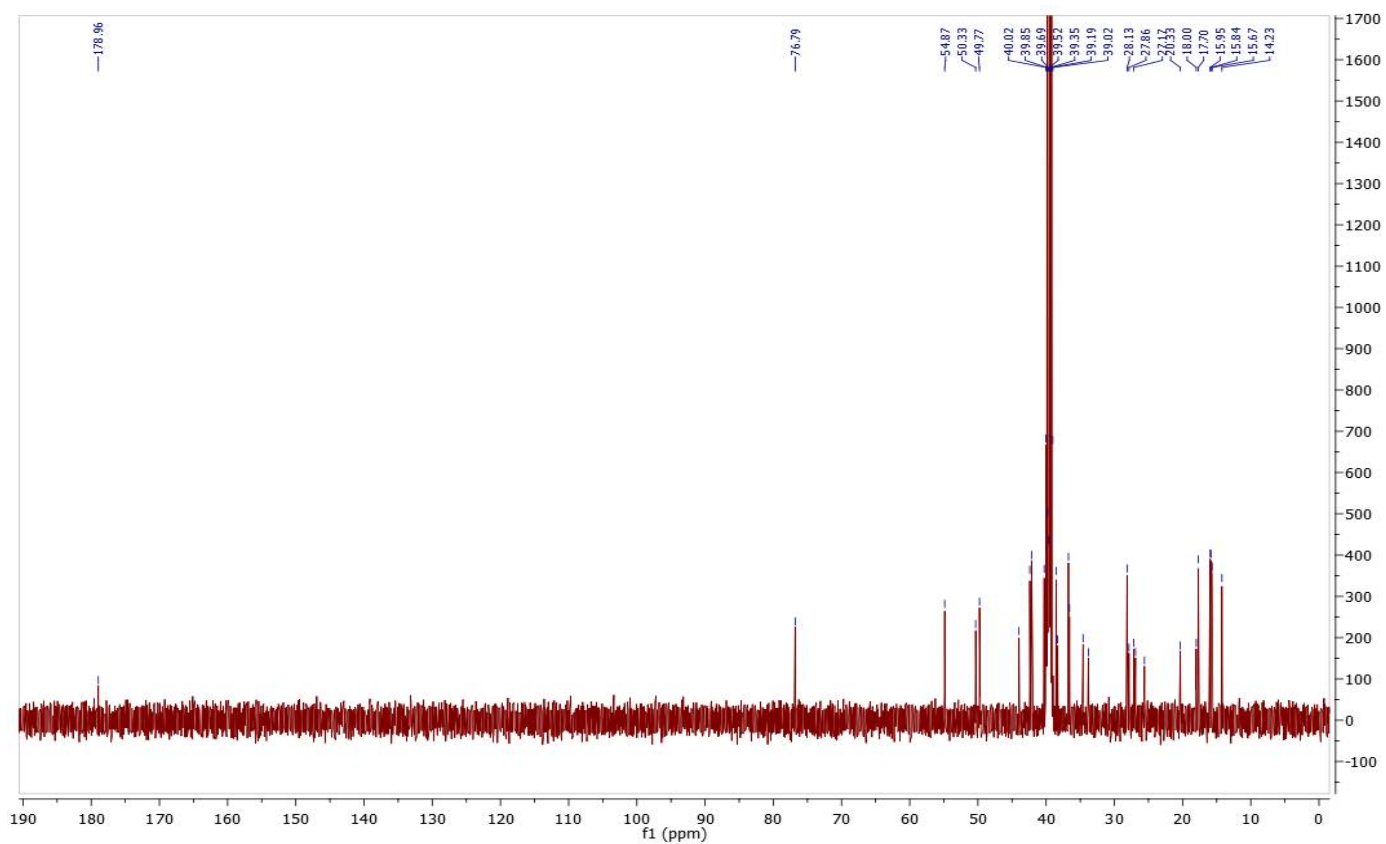
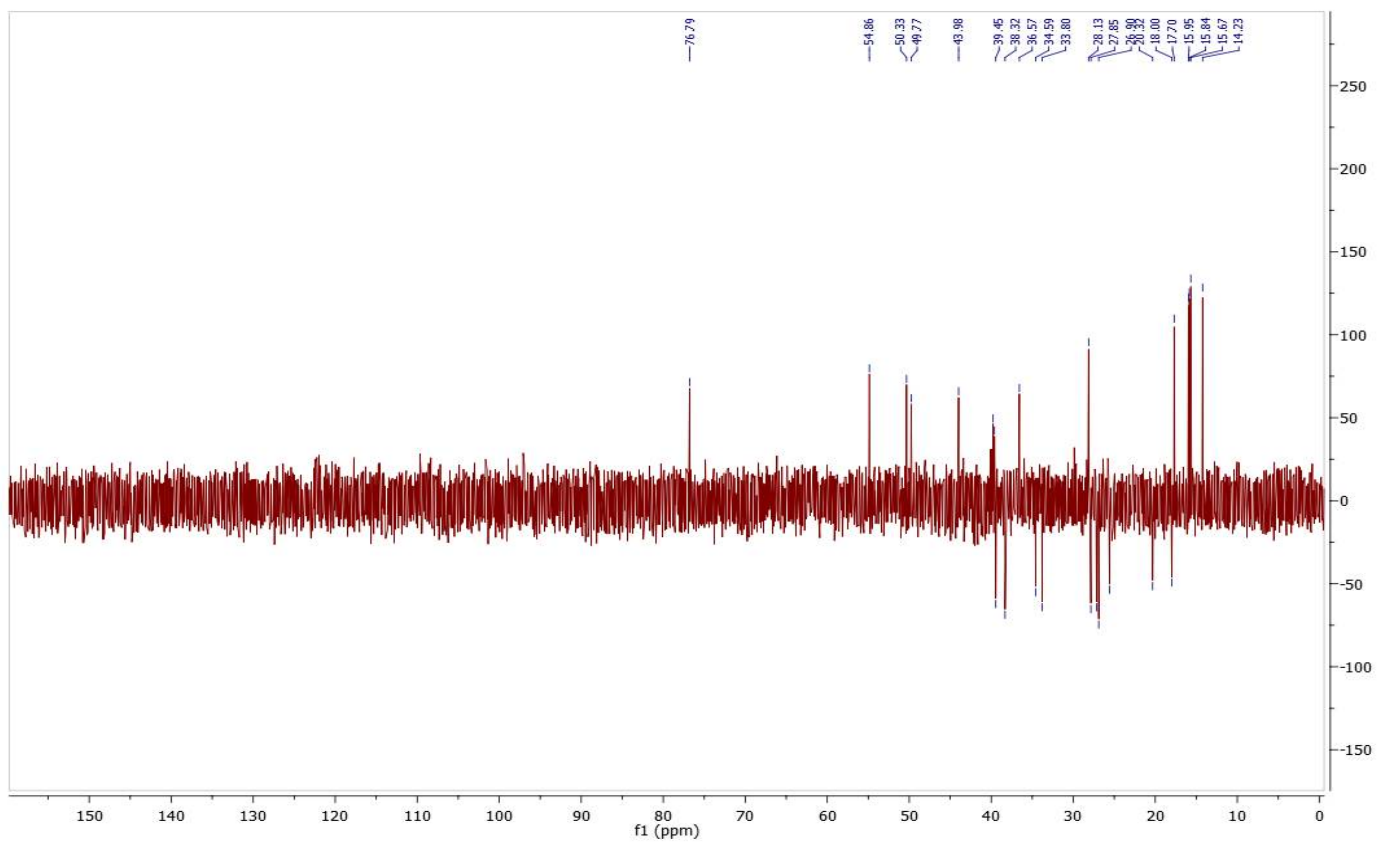


Figure 27S.  $^{13}\text{C}$  NMR spectrum of compound (8) (125 MHz,  $\text{DMSO}_6$ )



**Figure 28S.** DEPT  $^{13}\text{C}$  NMR spectrum of compound (8) (125 MHz,  $\text{DMSO}_6$ )

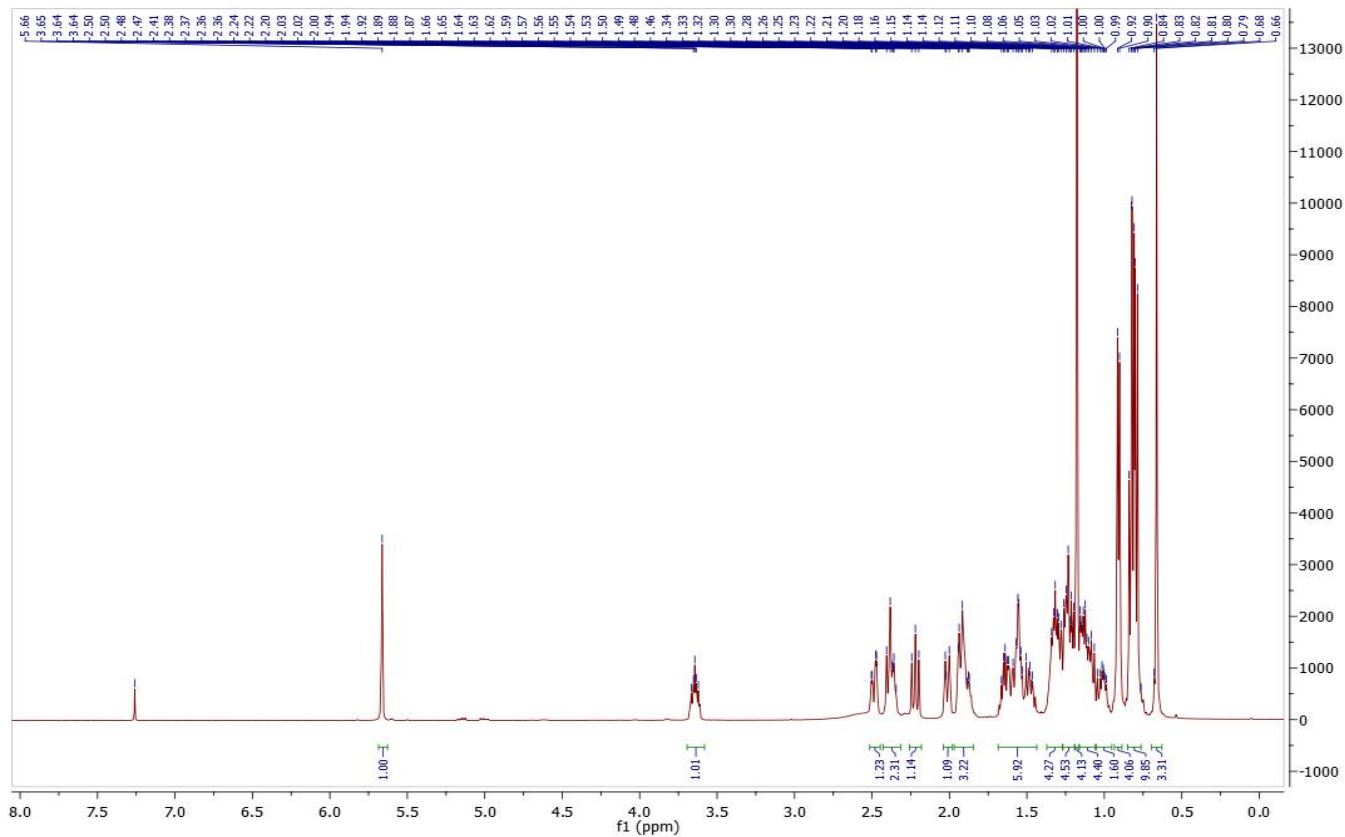


Figure 29S. <sup>1</sup>H NMR spectrum of compound (13) (500 MHz, CDCl<sub>3</sub>)

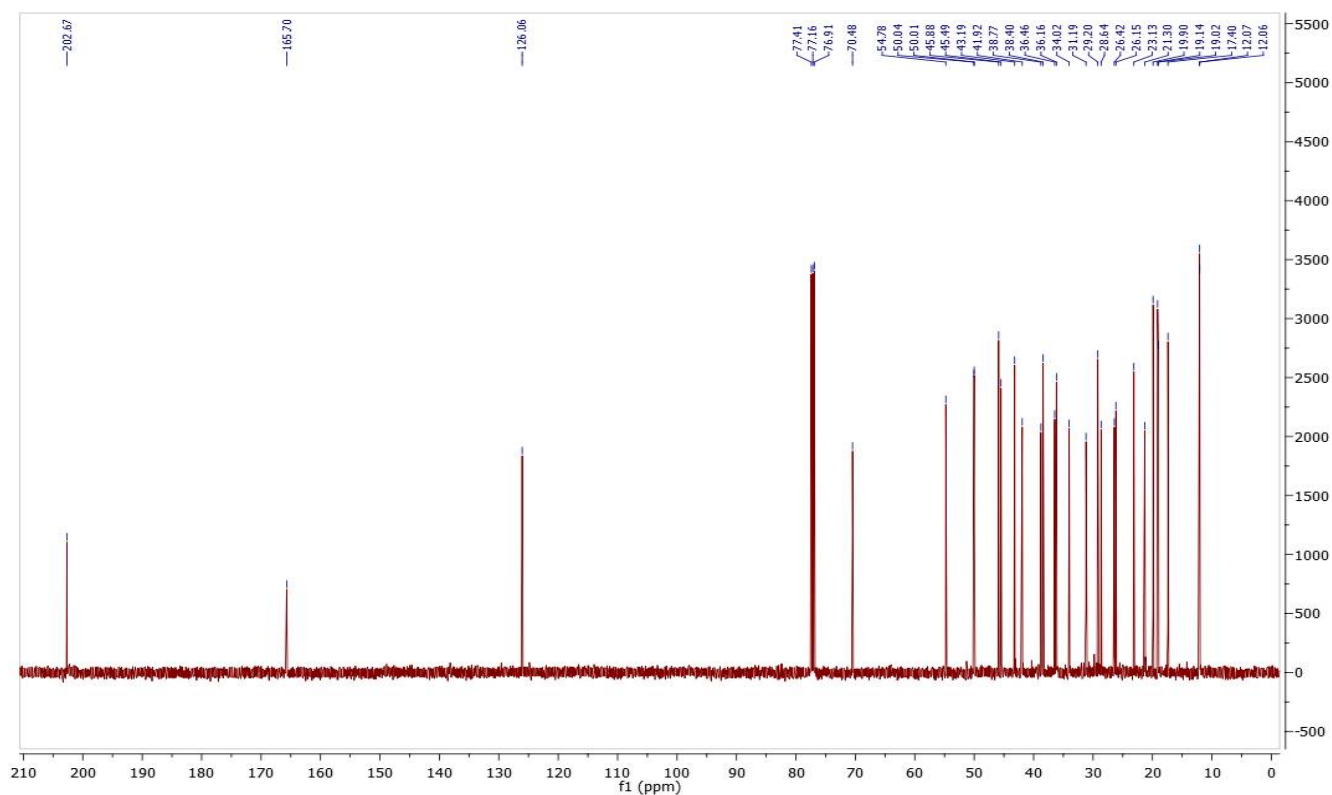


Figure 30S. <sup>13</sup>C NMR spectrum of compound (13) (125 MHz, CDCl<sub>3</sub>)

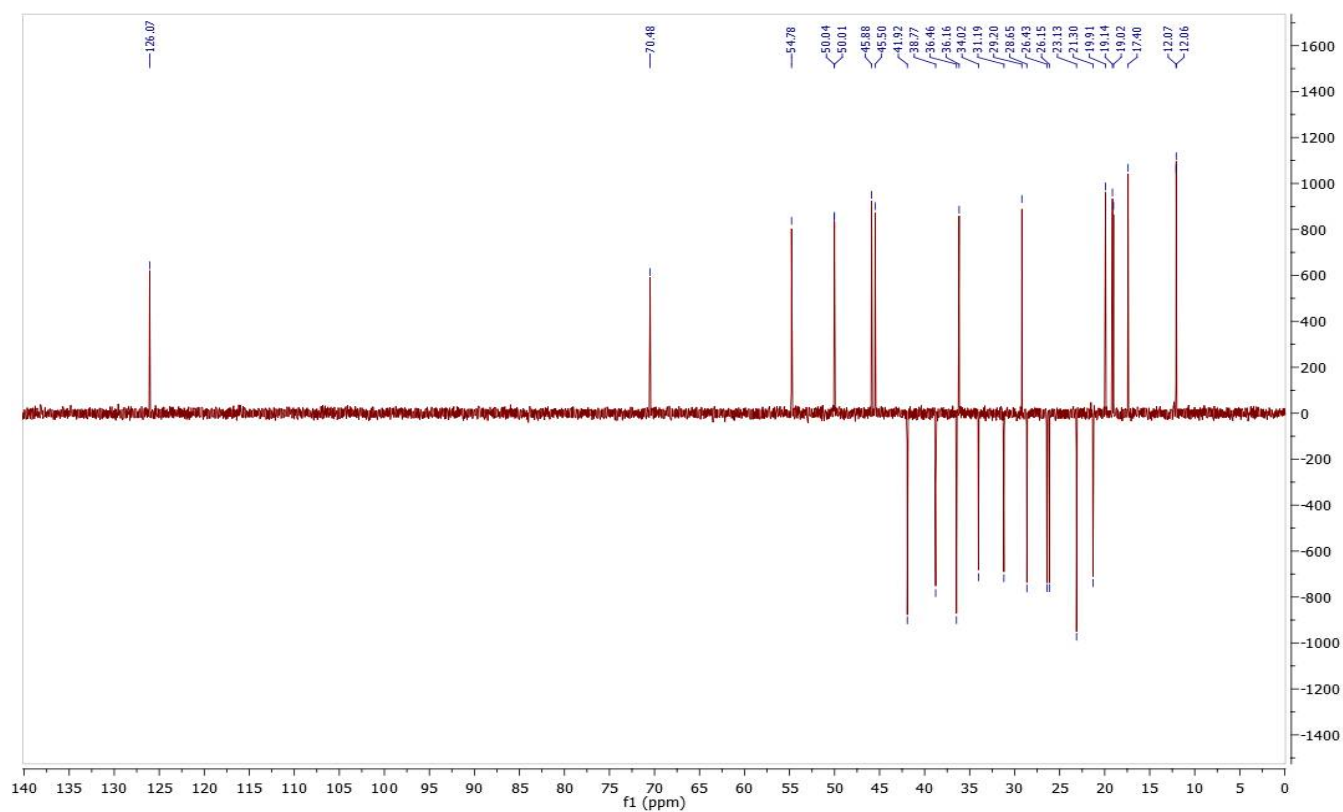


Figure 31S. DEPT  $^{13}\text{C}$  NMR spectrum of compound (13) (125 MHz,  $\text{CDCl}_3$ )

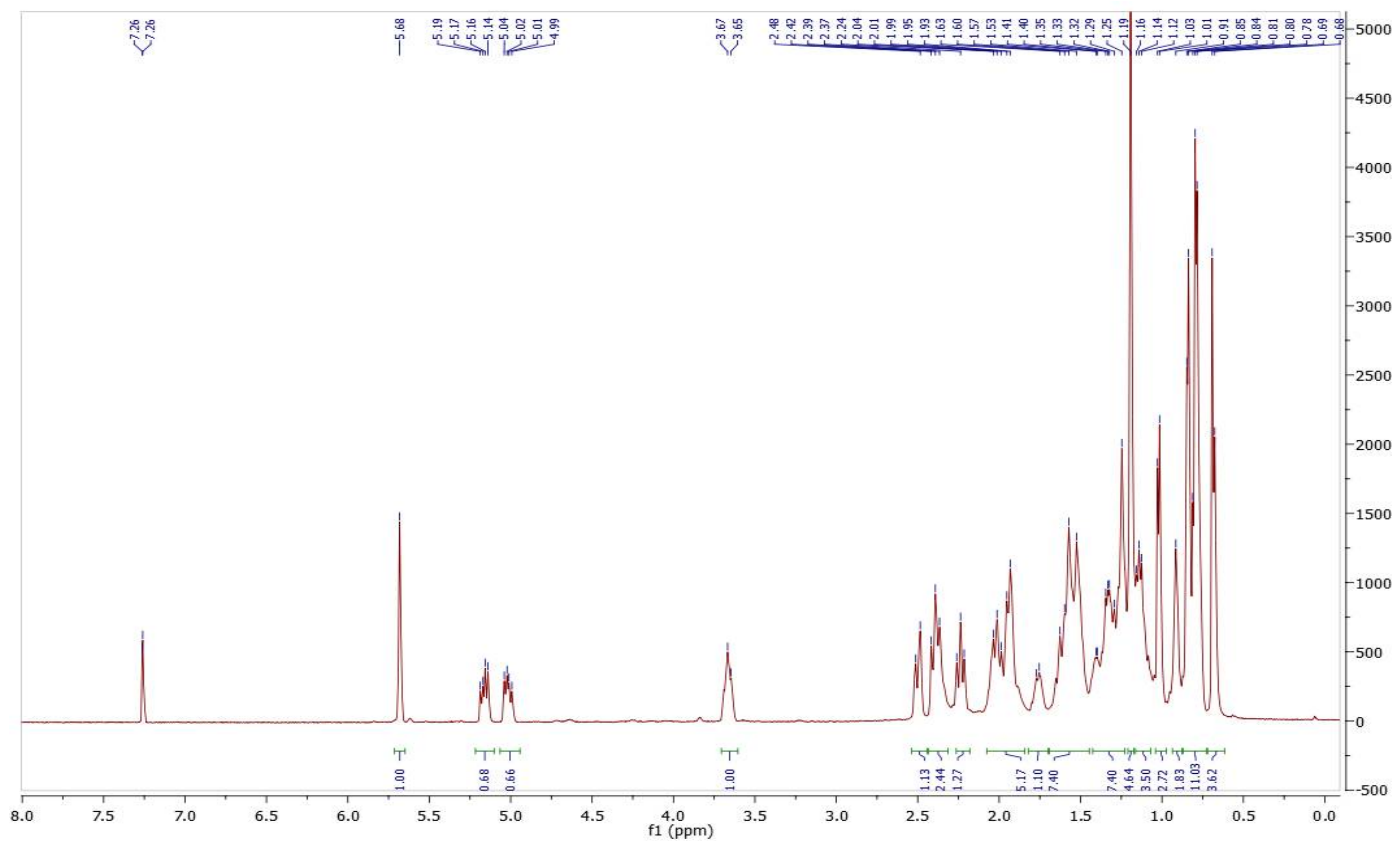


Figure 32S. <sup>1</sup>H NMR spectrum of compound (14) (500 MHz, CDCl<sub>3</sub>)

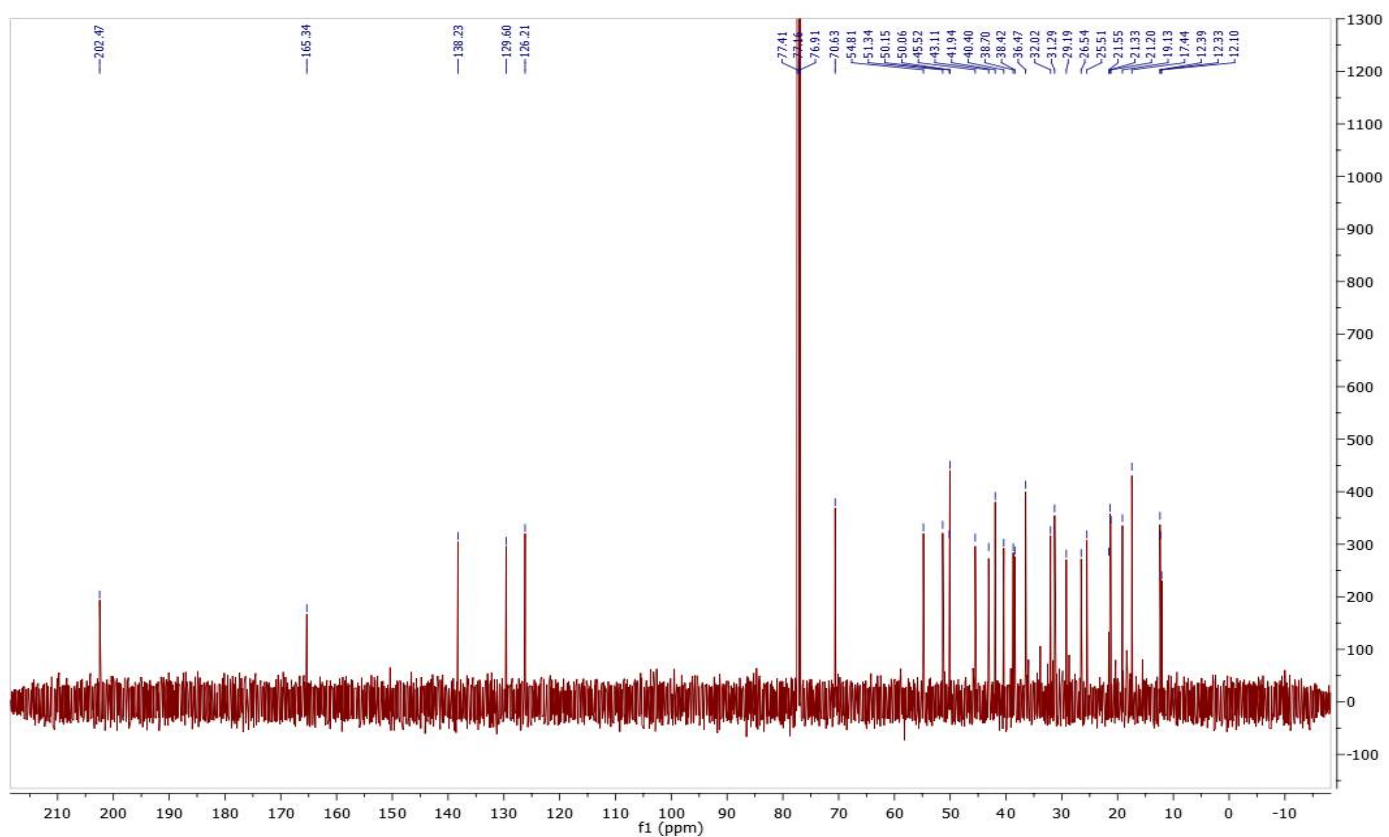
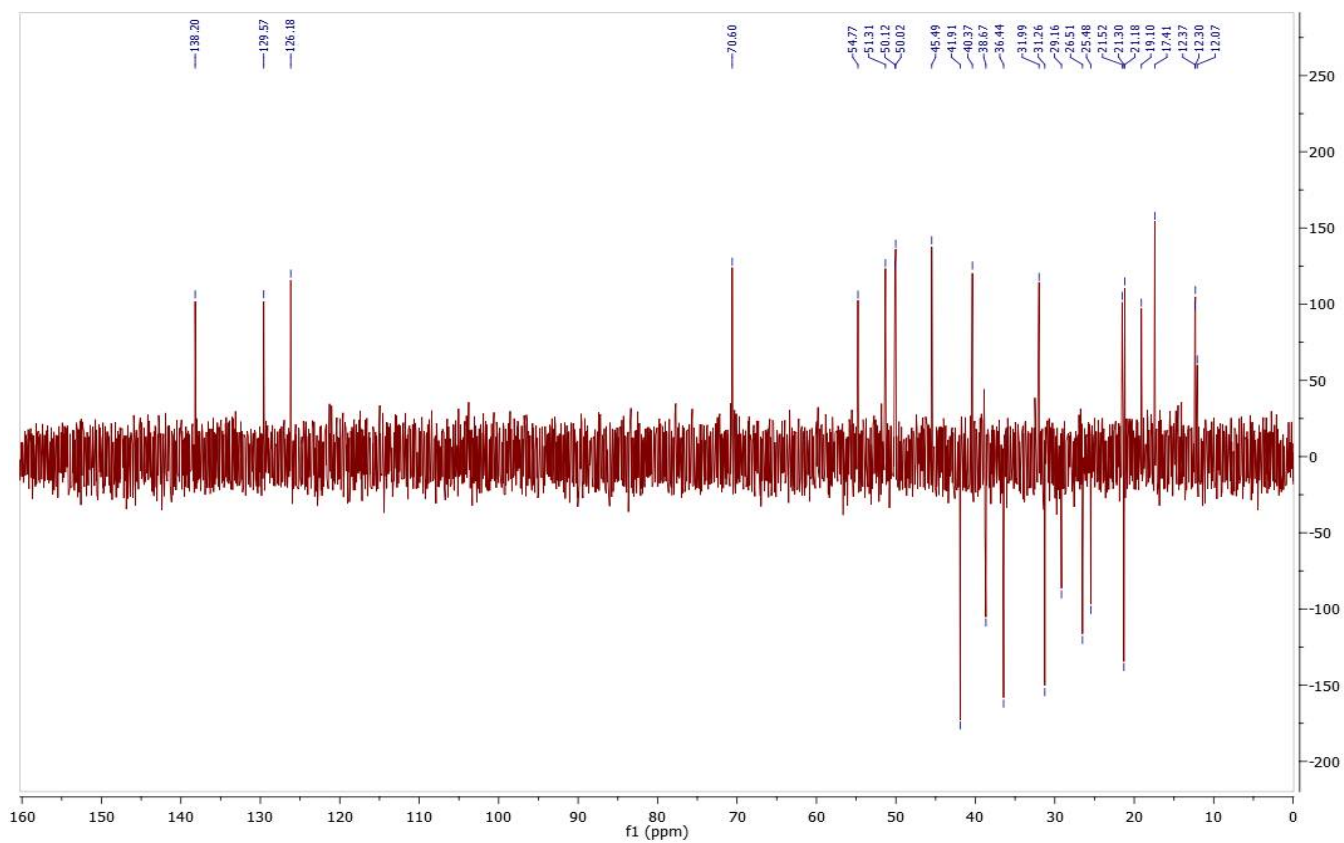


Figure 33S. <sup>13</sup>C NMR spectrum of compound (14) (125 MHz, CDCl<sub>3</sub>)





**Figure 34S.** DEPT  $^{13}\text{C}$  NMR spectrum of compound (14) (125 MHz,  $\text{CDCl}_3$ )

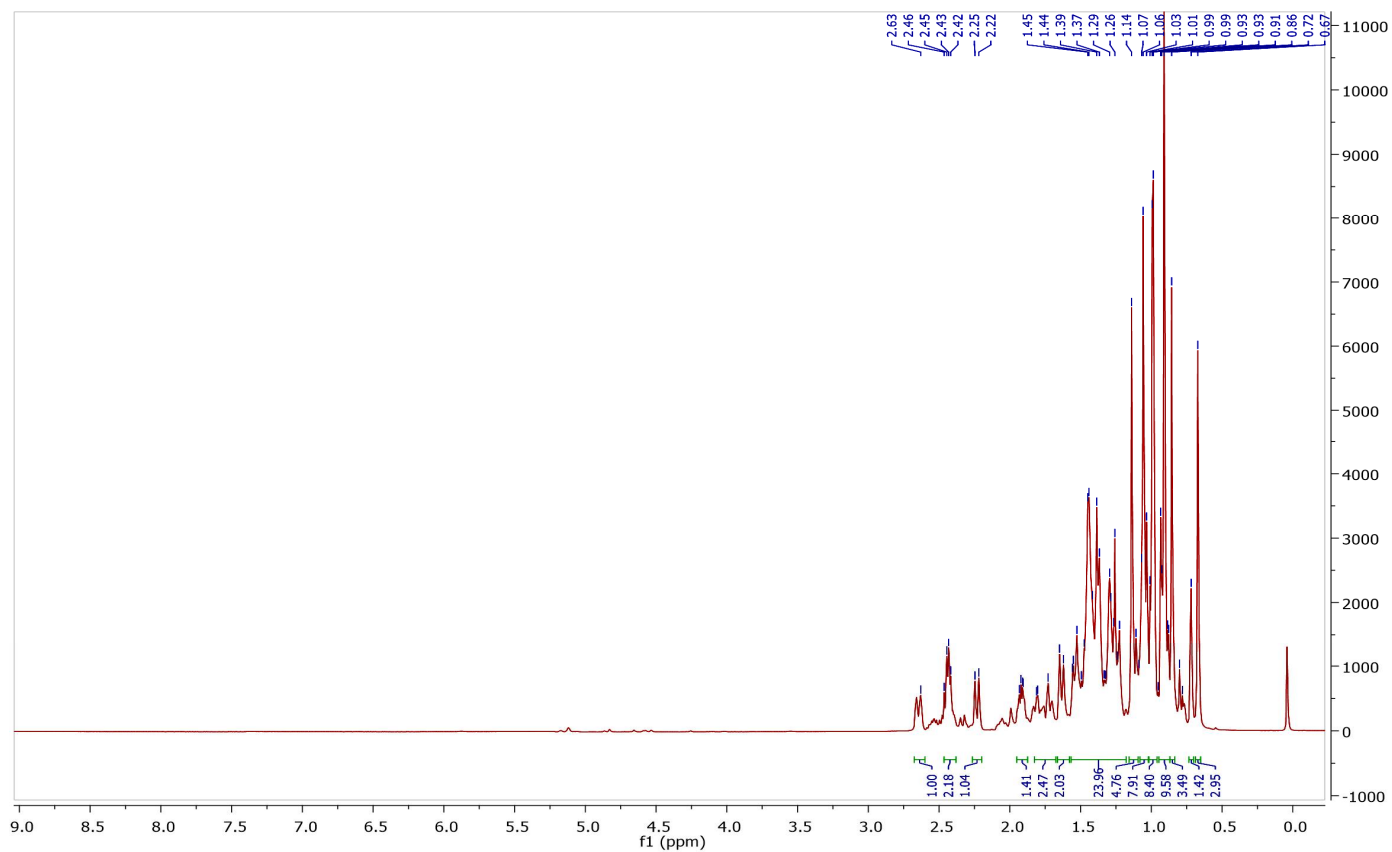


Figure 35S. <sup>1</sup>H NMR spectrum of compound (15) (500 MHz, CDCl<sub>3</sub>)

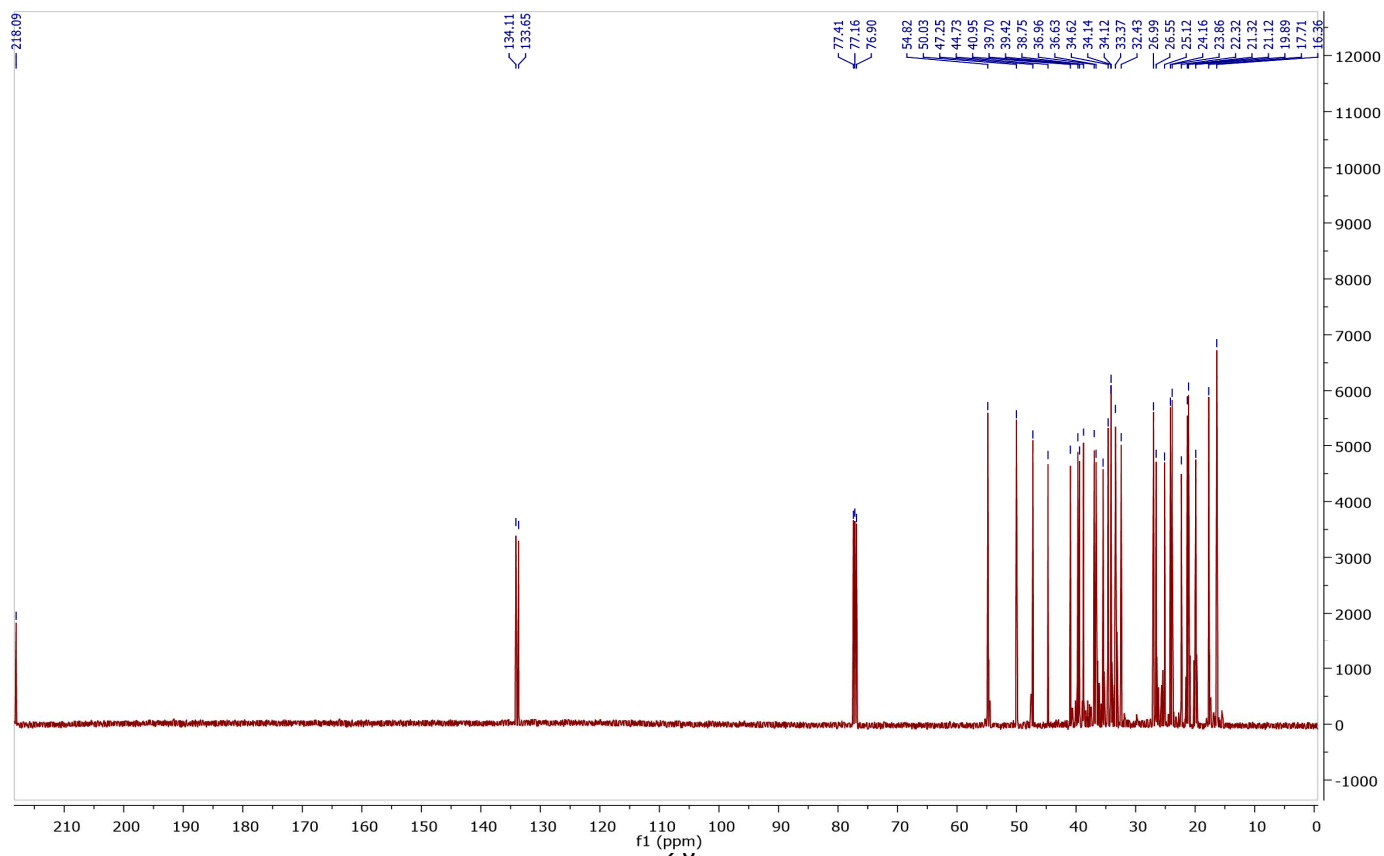


Figure 36S. <sup>13</sup>C NMR spectrum of compound (15) (125 MHz, CDCl<sub>3</sub>)

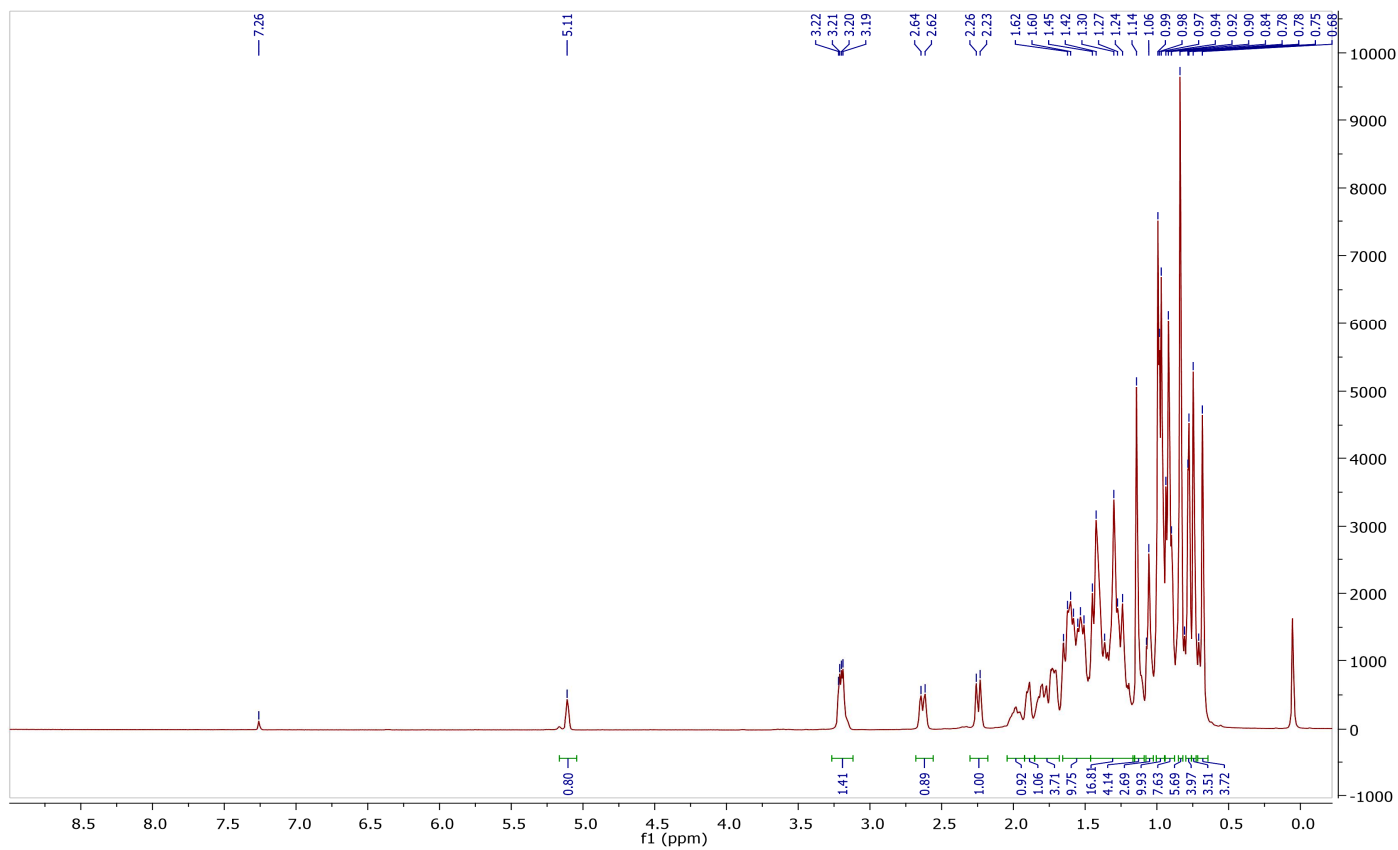


Figure 37S. <sup>1</sup>H NMR spectrum of compound (16) (500 MHz, CDCl<sub>3</sub>)

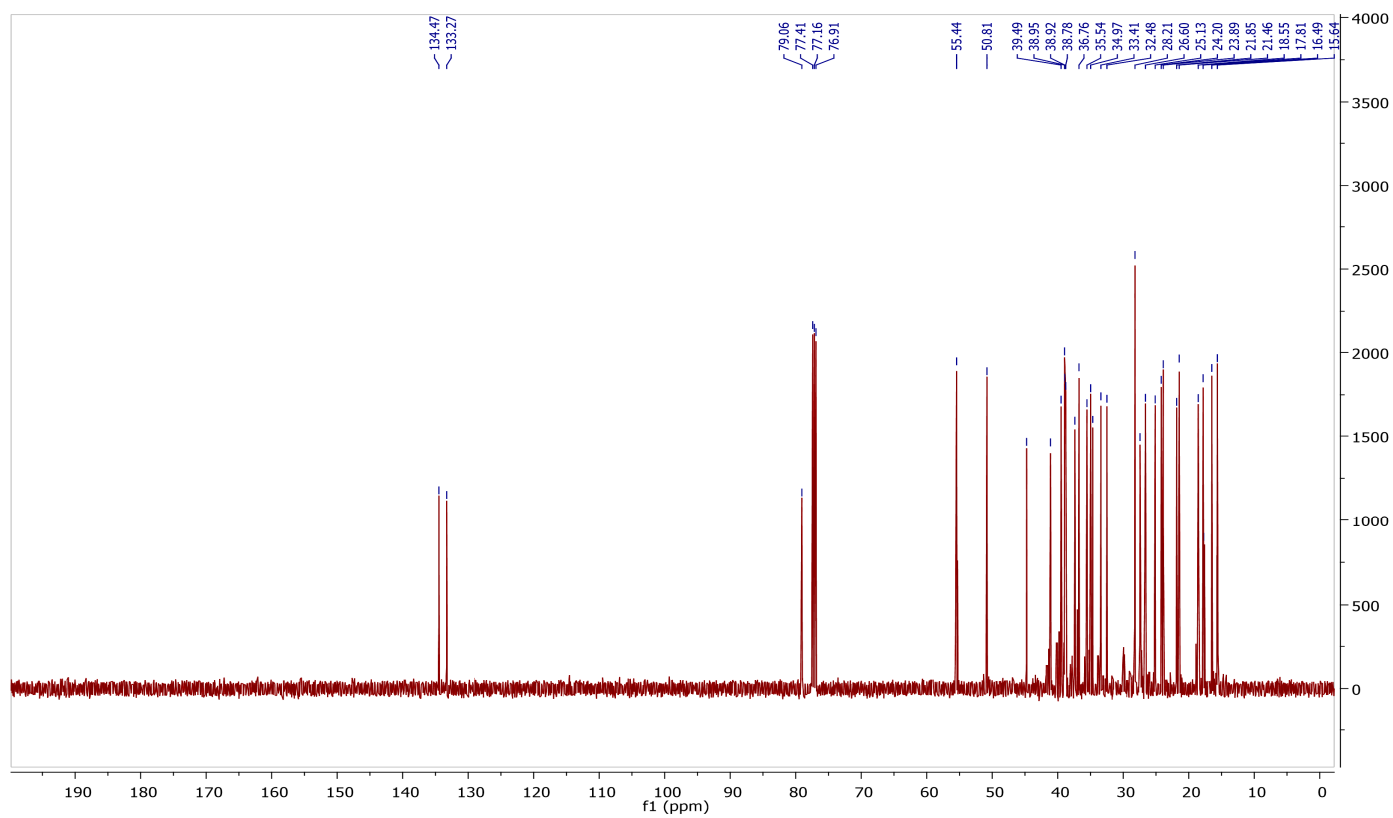


Figure 38S. <sup>13</sup>C NMR spectrum of compound (16) (125 MHz, CDCl<sub>3</sub>)

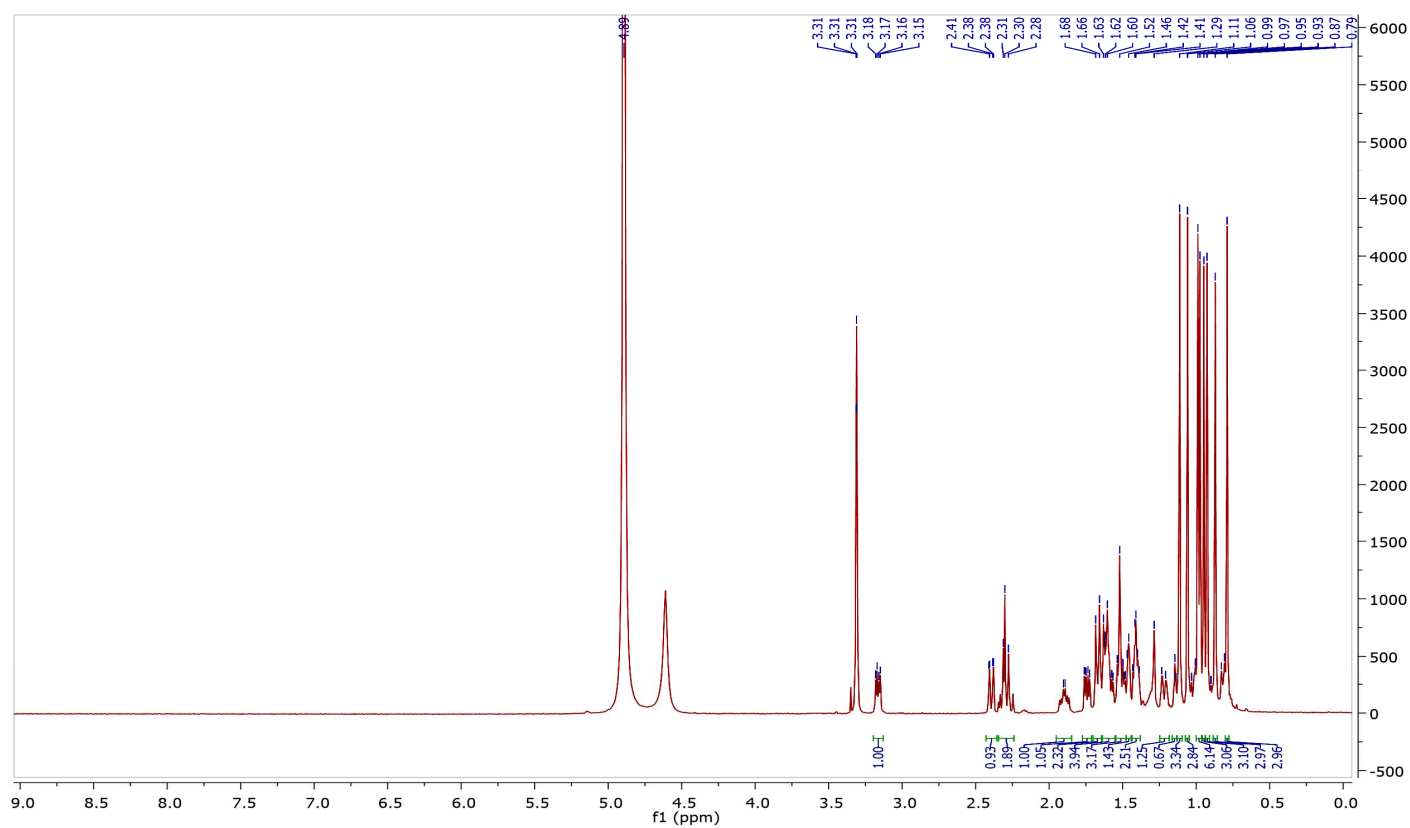


Figure 39S.  $^1\text{H}$  NMR spectrum of compound (17) (500 MHz,  $\text{CD}_3\text{OD}$ )

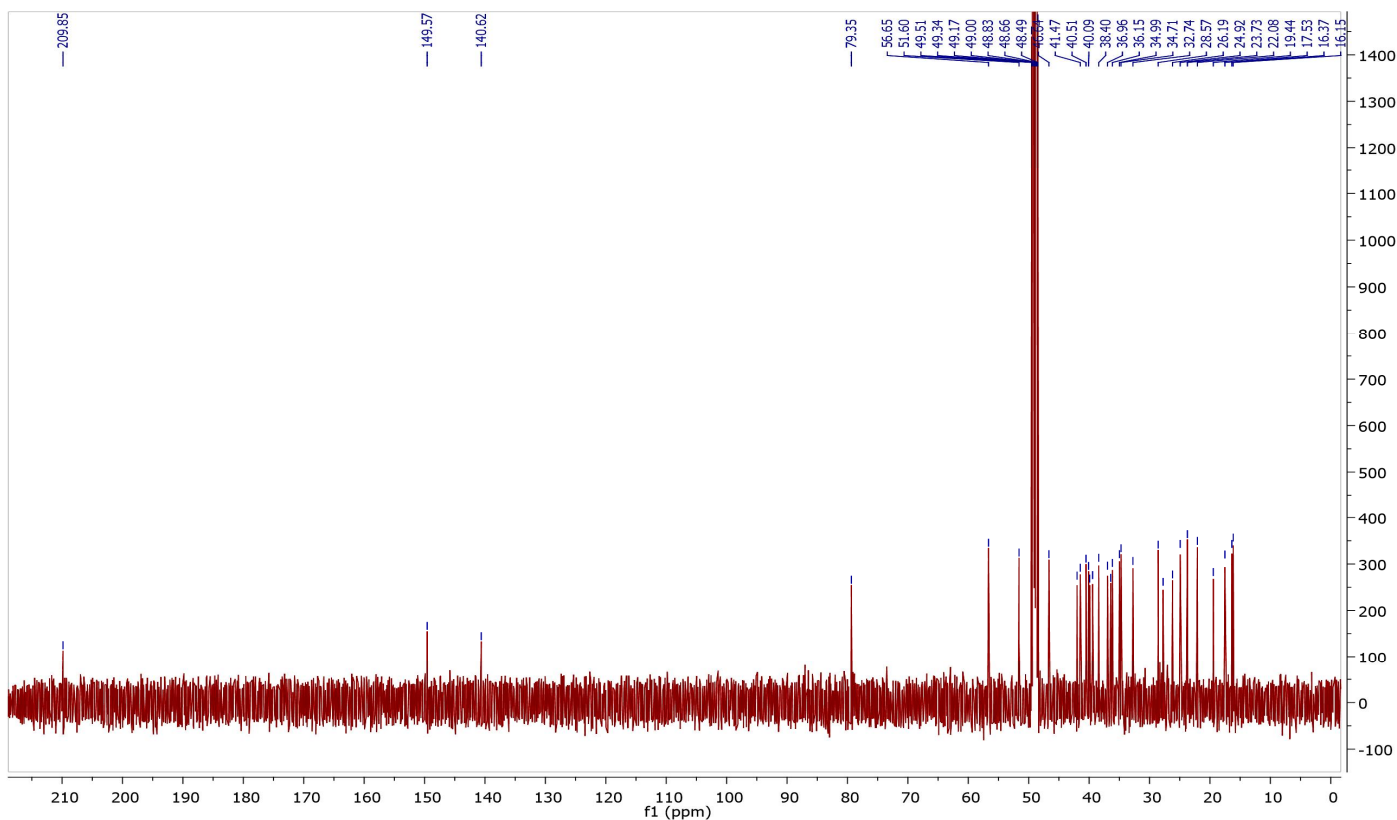


Figure 40S.  $^{13}\text{C}$  NMR spectrum of compound (17) (125 MHz,  $\text{CD}_3\text{O}$ )

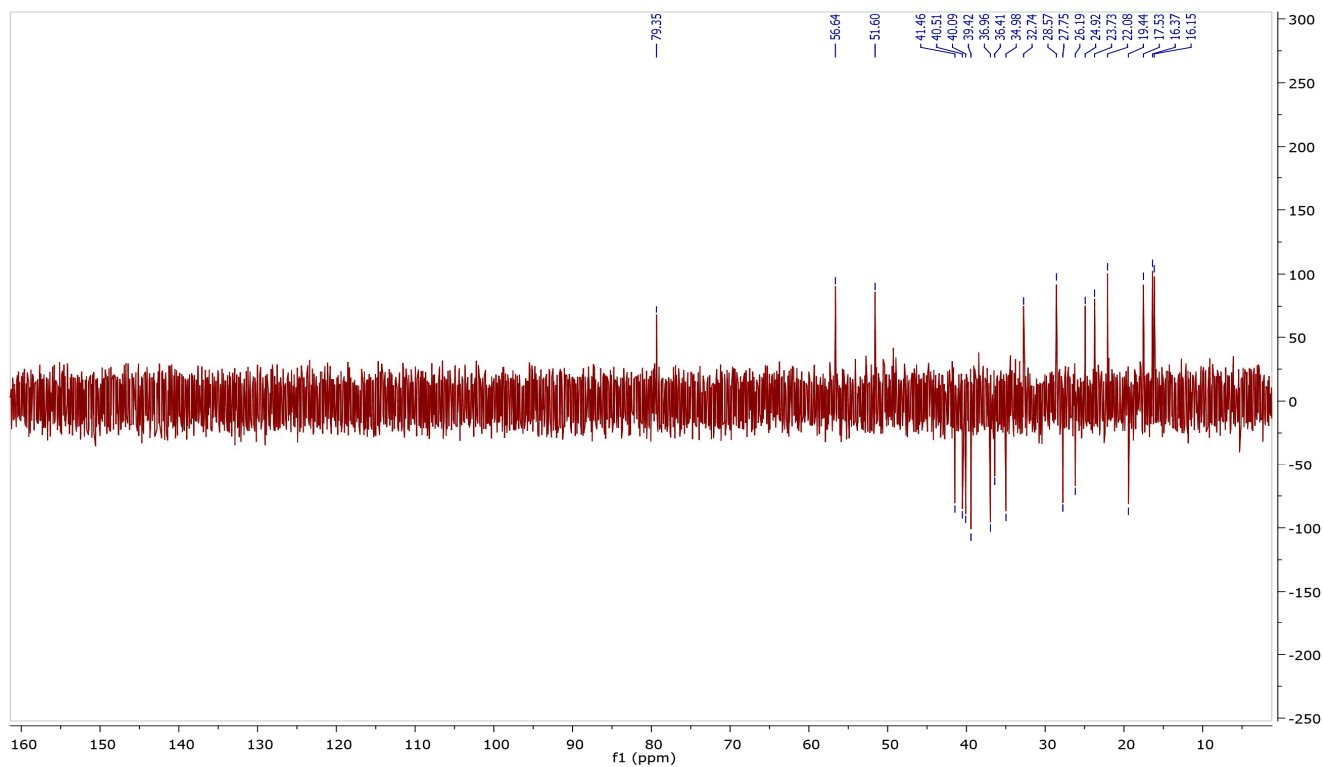


Figure 41S. DEPT  $^{13}\text{C}$  NMR spectrum of compound (17) (125 MHz,  $\text{CD}_3\text{OD}$ )

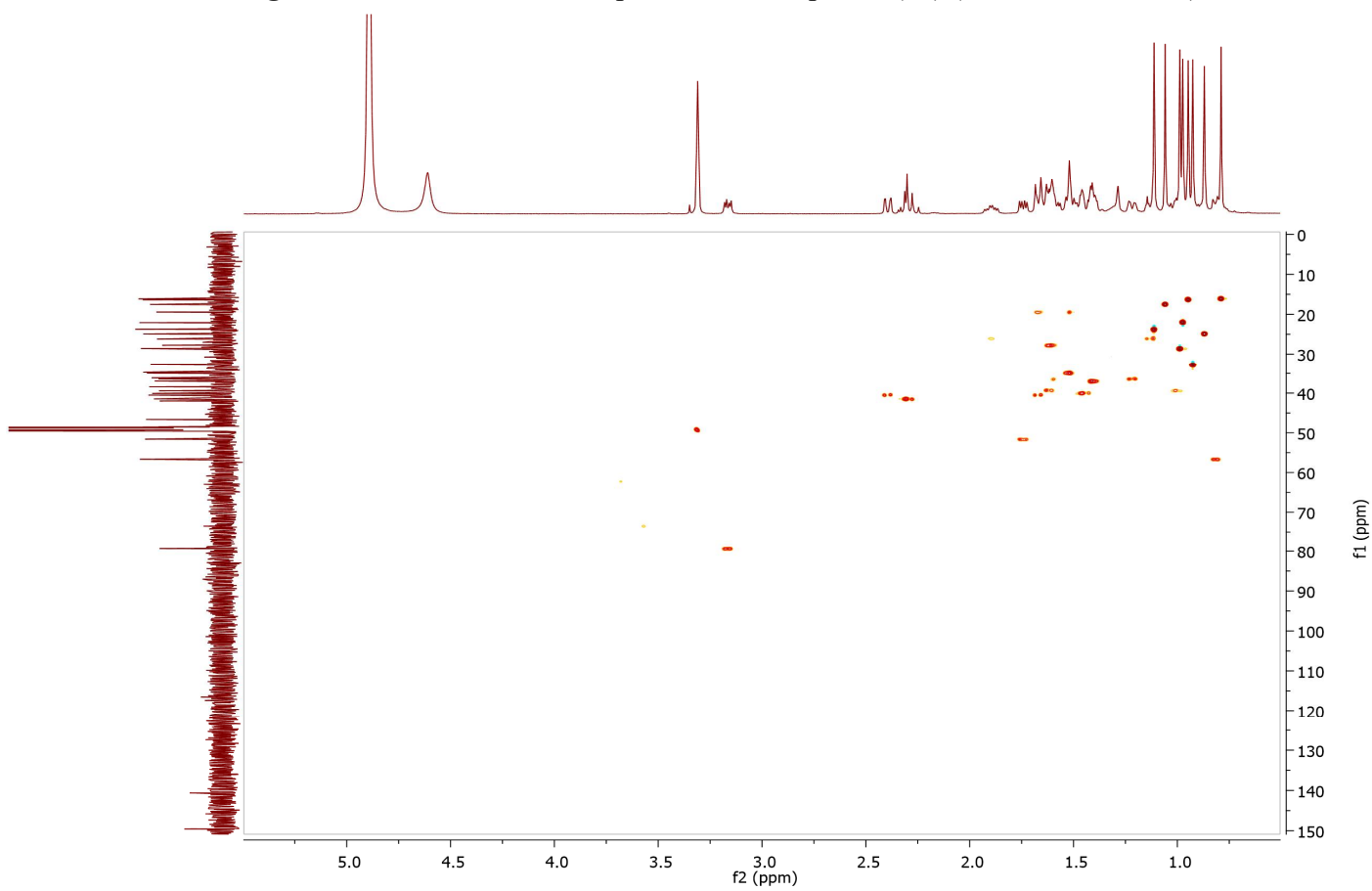
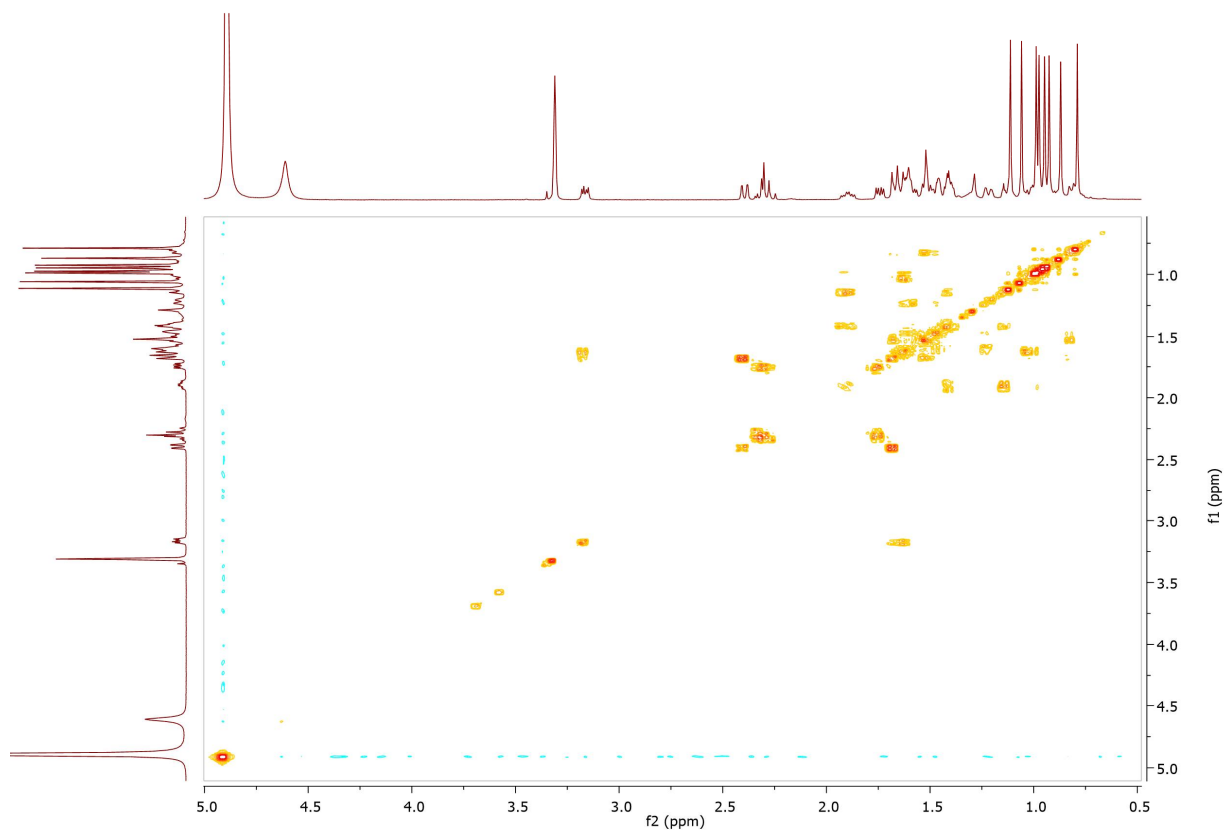
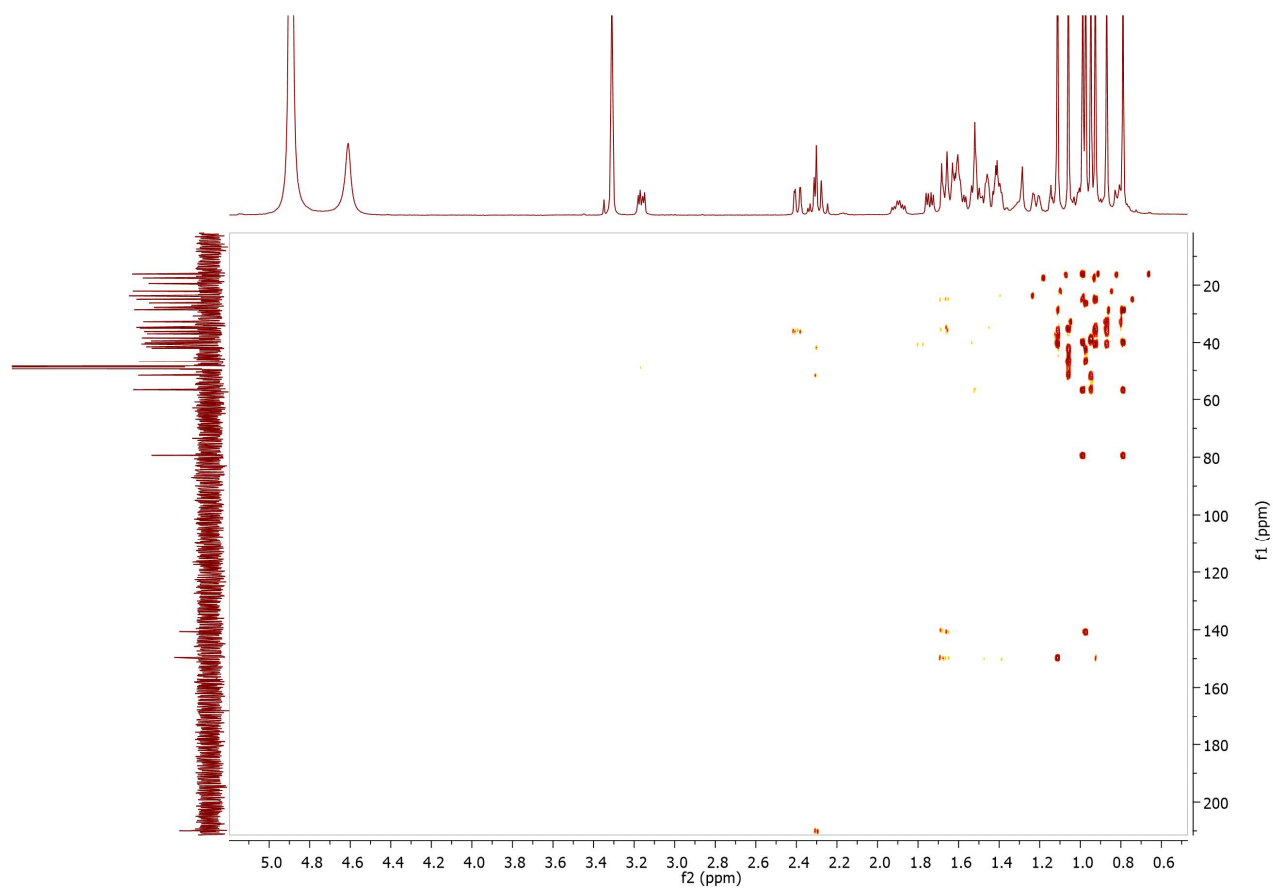


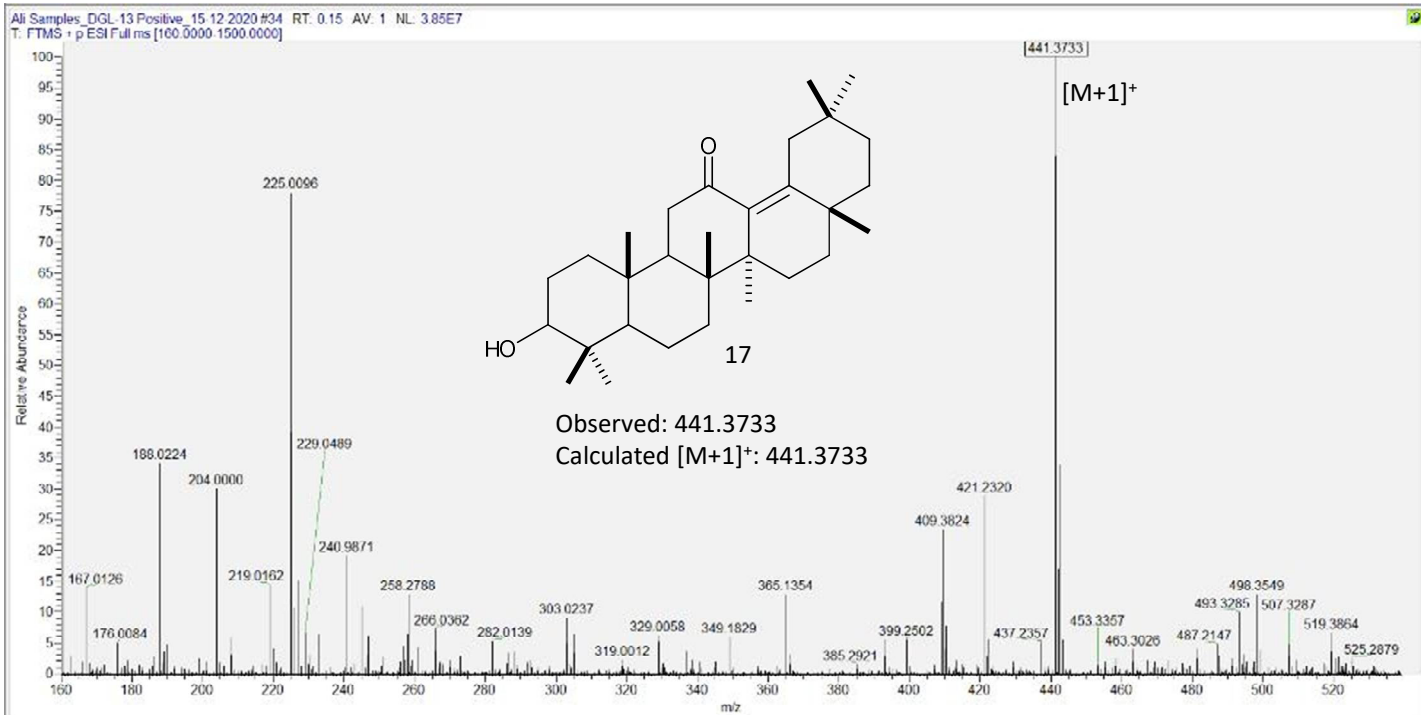
Figure 42S.  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum of compound (17) (500 MHz,  $\text{CD}_3\text{OD}$ )



**Figure 43S.**  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of compound (17) (500 MHz,  $\text{CD}_3\text{OD}$ )



**Figure 44S.**  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum of compound (17) (500 MHz,  $\text{CD}_3\text{OD}$ )



**Figure 45S:** HRESIMS spectrum of compound (17) positive mode.

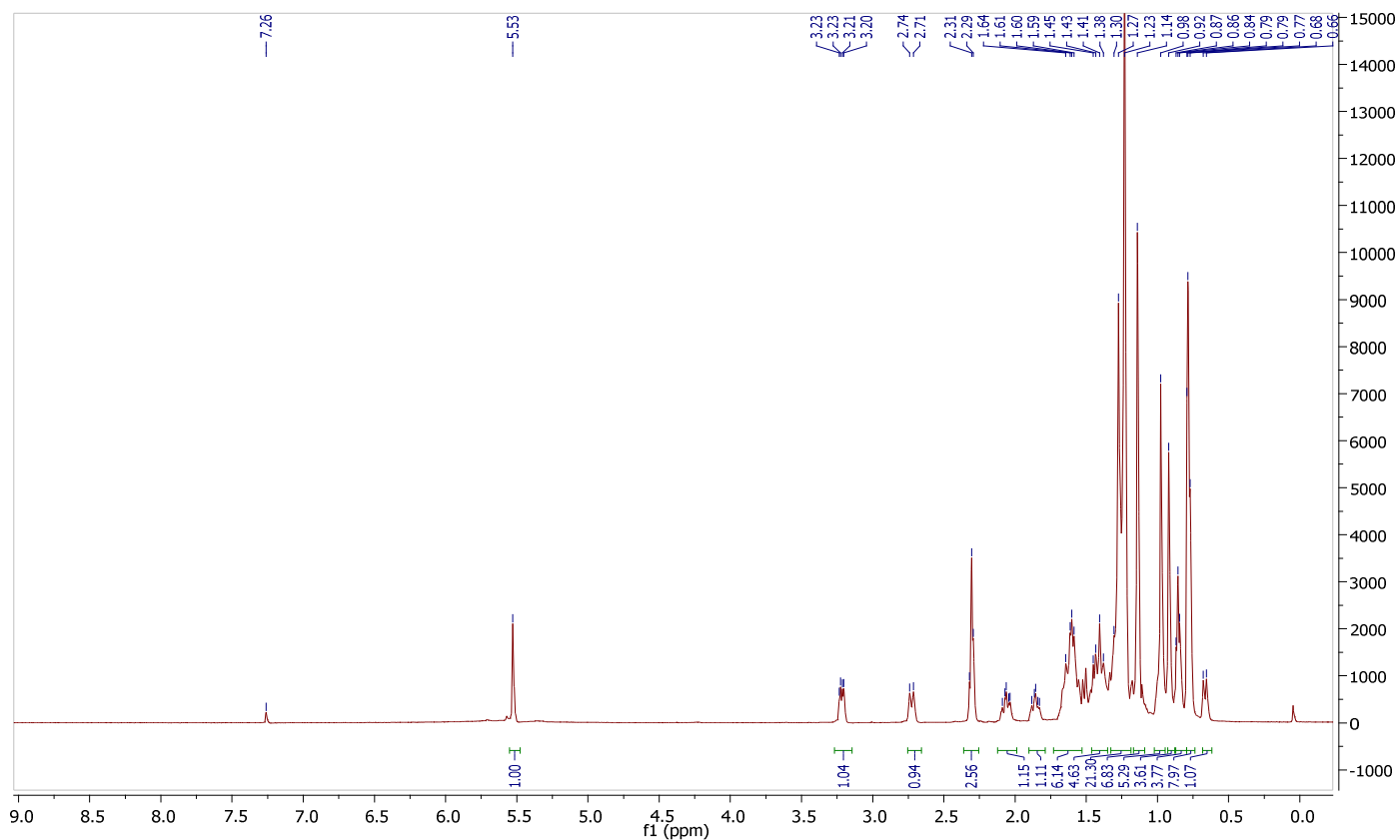


Figure 46S. <sup>1</sup>H NMR spectrum of compound (18) (500 MHz, CDCl<sub>3</sub>)

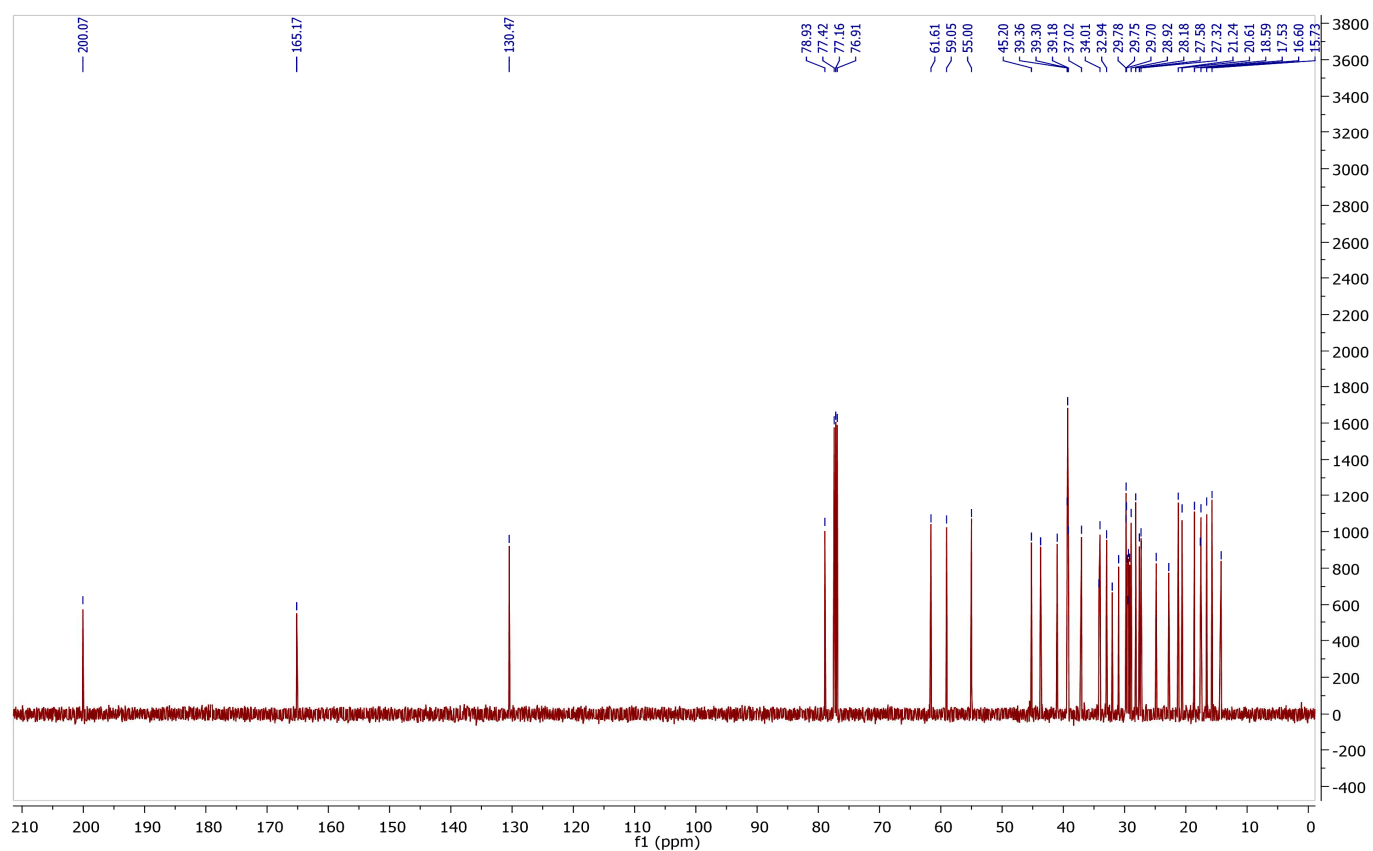


Figure 47S. <sup>13</sup>C NMR spectrum of compound (18) (125 MHz, CDCl<sub>3</sub>)



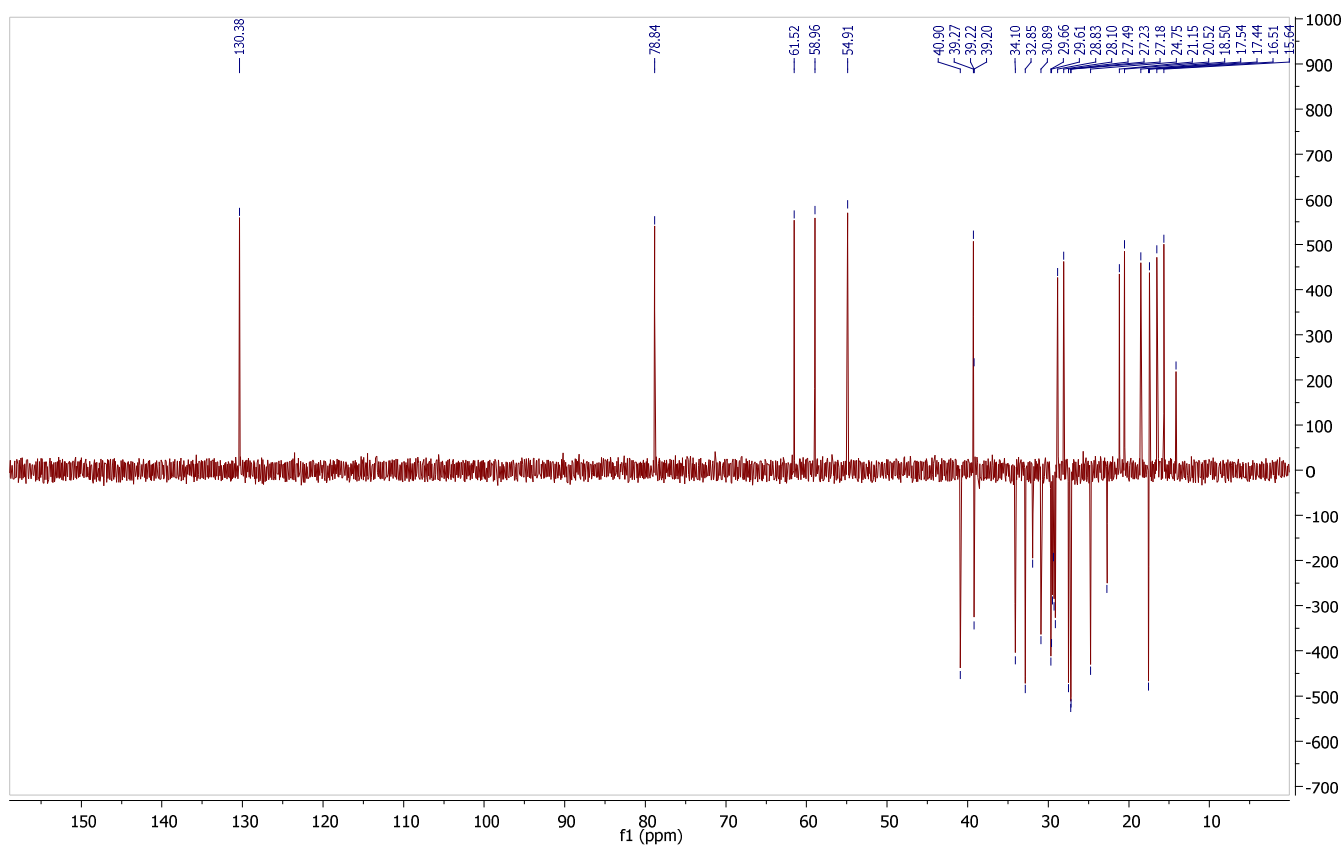


Figure 48S. DEPT <sup>13</sup>C NMR spectrum of compound (18) (125 MHz, CDCl<sub>3</sub>)