Supplementary material

New cyclic glycolipids from *Silene succulenta* promote *in vitro* MCF-7 breast carcinoma cells apoptosis by cell cycle arrest and *in silico* mitotic Mps1/TTK inhibition

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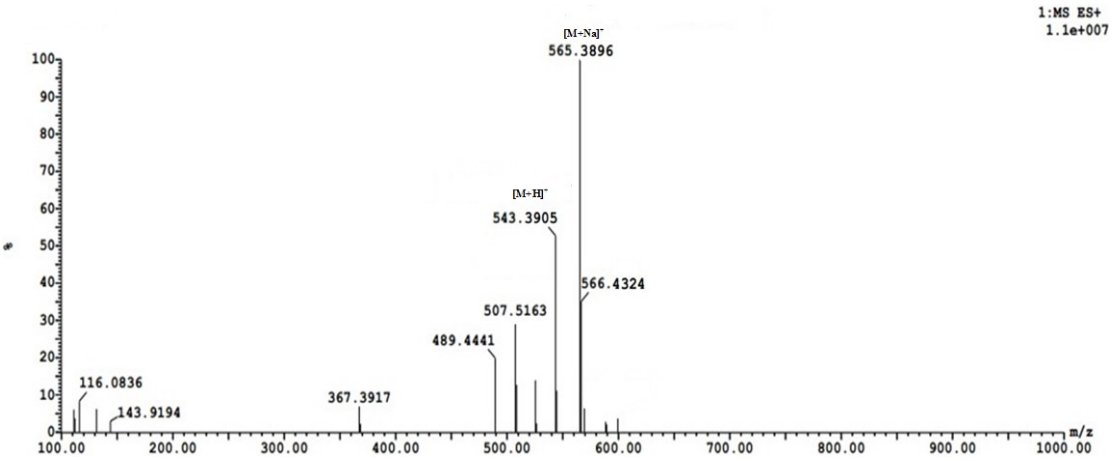
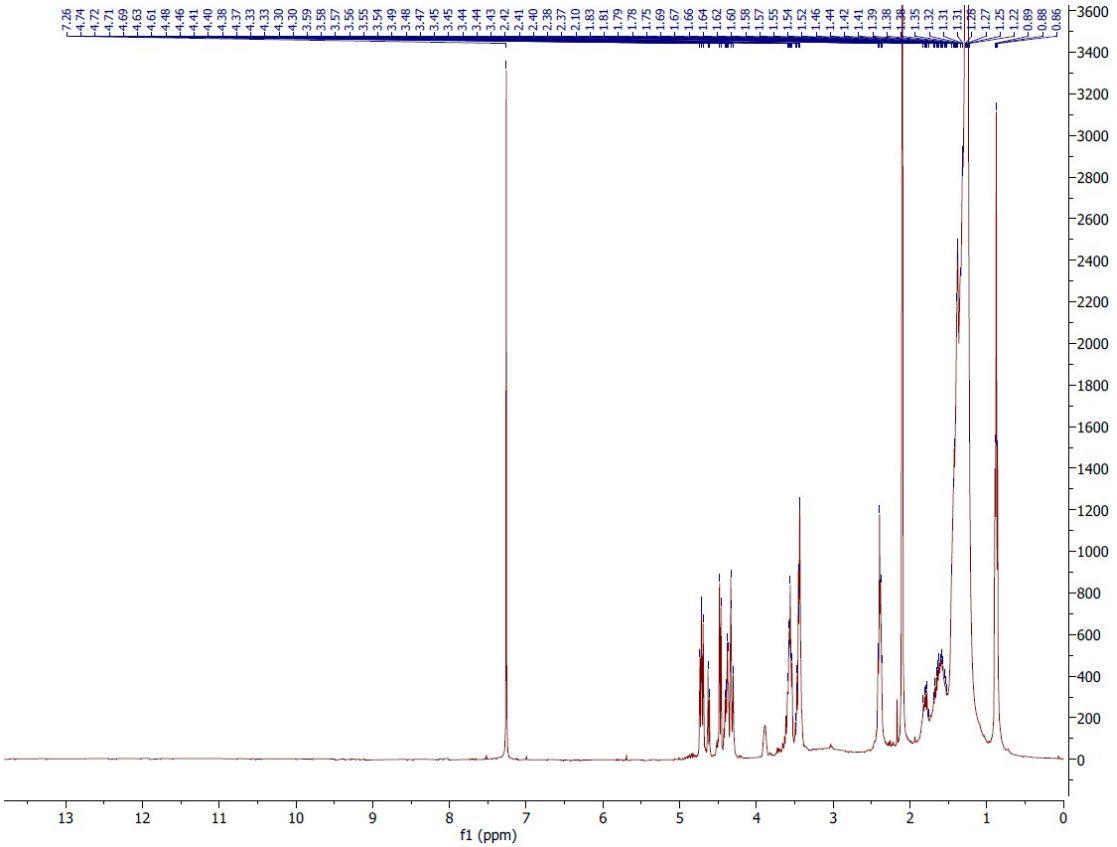
Abstract

In vitro anticancer screening of *Silene succulenta* Forssk. aerial parts (Caryophyllaceae) showed that the *n*-hexane fraction was the highly effective fraction against breast carcinoma cell lines (MCF-7) with IC_{50} = 15.5 µg/mL. The bioactive-guided approach led to the isolation of two new cyclic glucolipids from the *n*-hexane fraction identified as; 1,2`-cyclic ester of 11-oxy-(6`-*O*-acetyl-*β*-D-glucopyranosyl) behenic acid (**1**) as a C-11 epimeric mixture and 11(*R*)-oxy-(*β*-D-glucopyranosyl)-1,2`-cyclic ester of behenic acid (**2**). *In vitro* cytotoxicity study showed potential suppression of MCF-7 cells with IC_{50} values of 11.7 ± 0.04 and 6.6 ± 0.01 µg/mL for compounds **1** and **2**, respectively compared to doxorubicin (IC_{50} = 3.83 ± 0.01 µg/mL). Accordingly, the cell cycle tracking for the most active compound (**2**) was only assessed. The cell cycle investigation showed that compound **2** altered the cell cycle at G0/G1, S, and G2/M phases in MCF-7 treated cells. In addition, its powerful apoptotic ability resulted in a significant increase in the early and late stages of apoptosis. Moreover, molecular docking analysis which was done against the anticancer mitotic (or spindle assembly) checkpoint target Mps1 kinase showed that the two new cyclic glycolipids (**1** & **2**) possess high binding affinity equal to − 7.7 and − 7.6 kcal/mol, respectively, compared to its ATP ligand. Overall, this report emphasizes that natural cyclic glycolipids can be used as potential antitumour breast cancer agents.

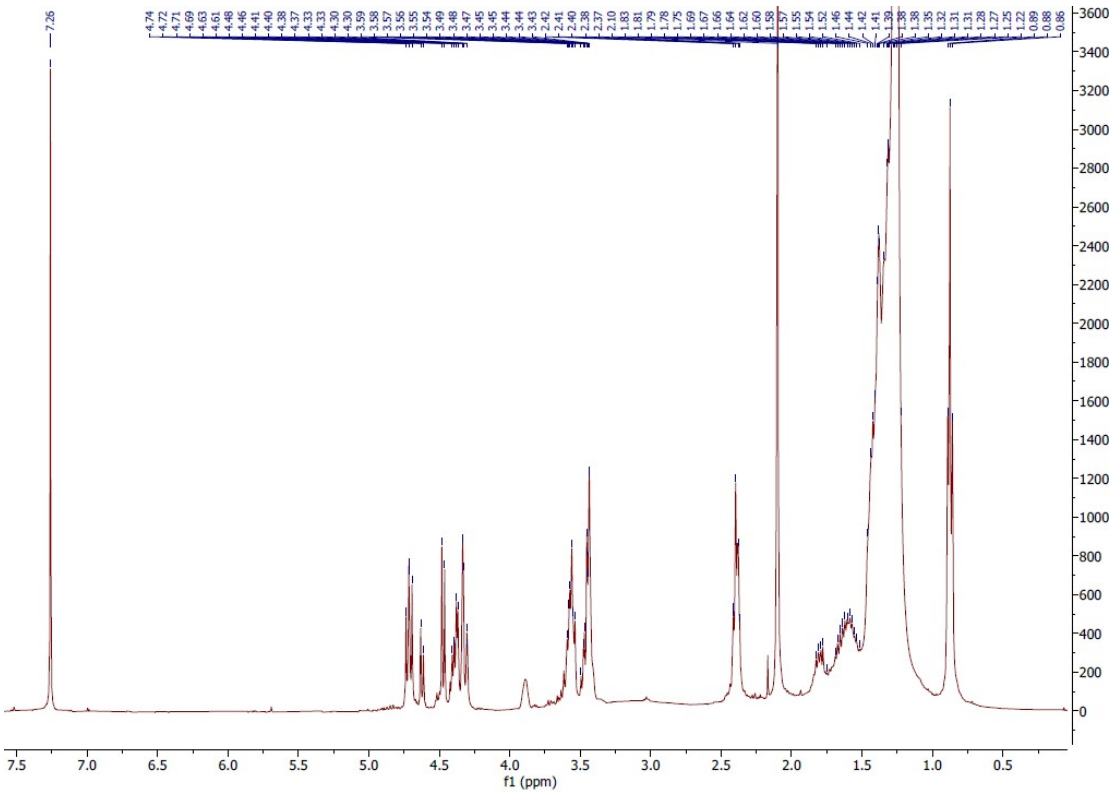
Keywords: *Silene succulenta*; Caryophyllaceae; Cyclic glycolipids; Cytotoxicity; Molecular Docking; Mps1/TTK protein kinase



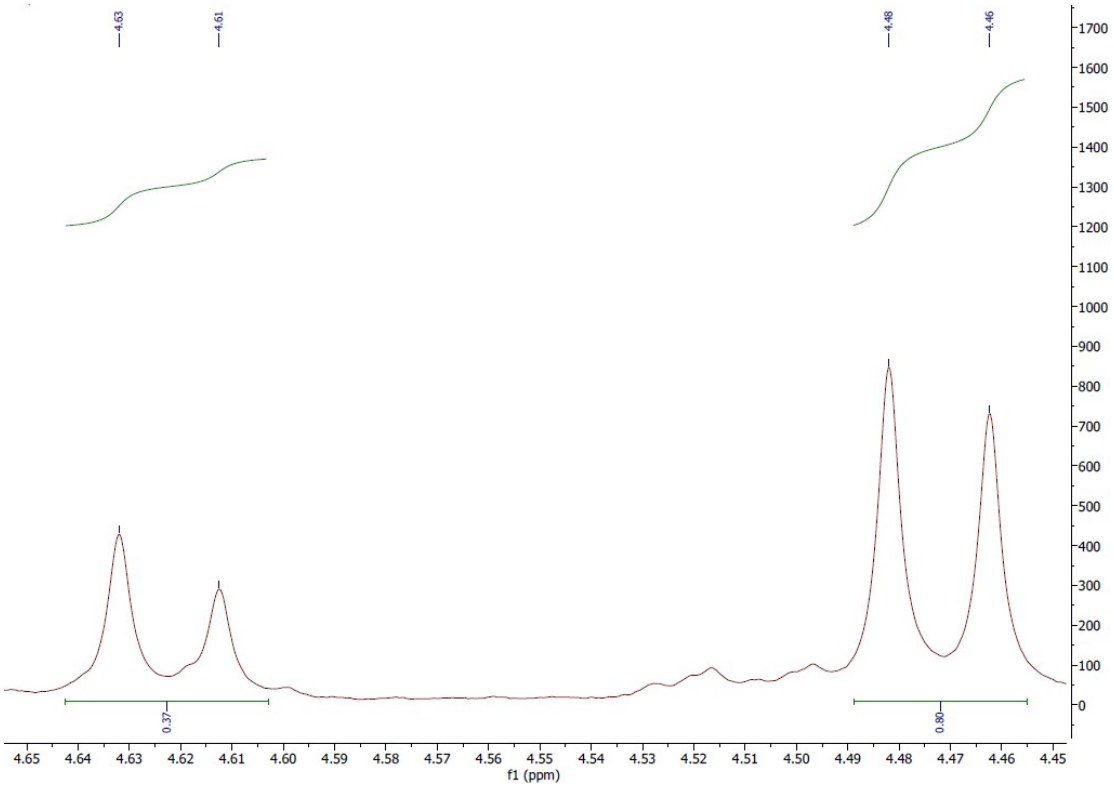
Suppl. Fig. S1. Positive HRESI-MS of compound **1**



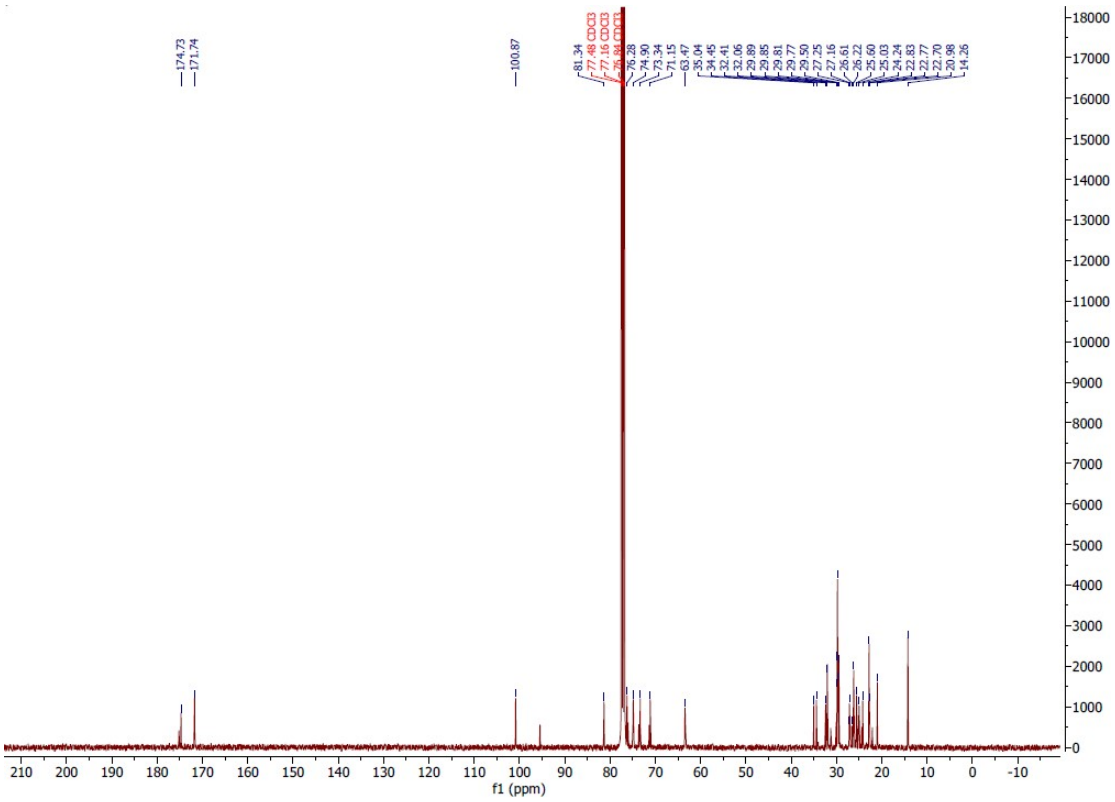
Suppl. Fig. S2. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **1**



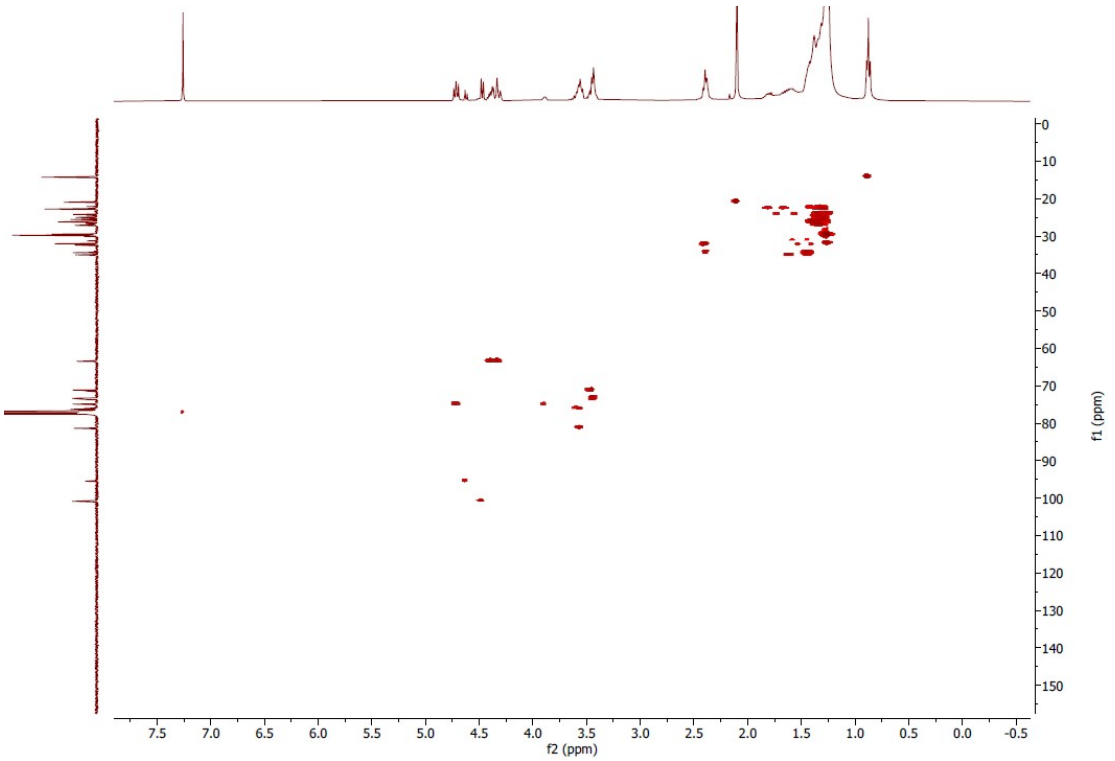
Suppl. Fig. S2-1. Expanded ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **1**



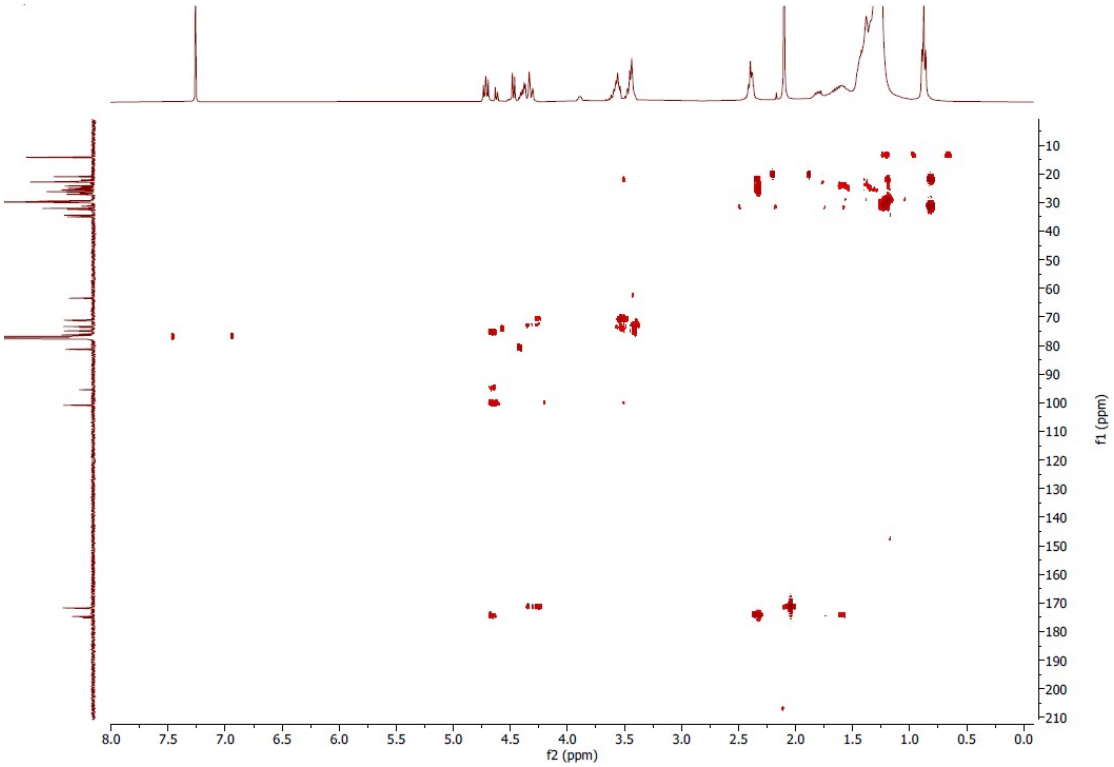
Suppl. Fig. S2-2. Expanded ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of the glucose anomeric protons (H-1`) for the two epimers of compound **1**



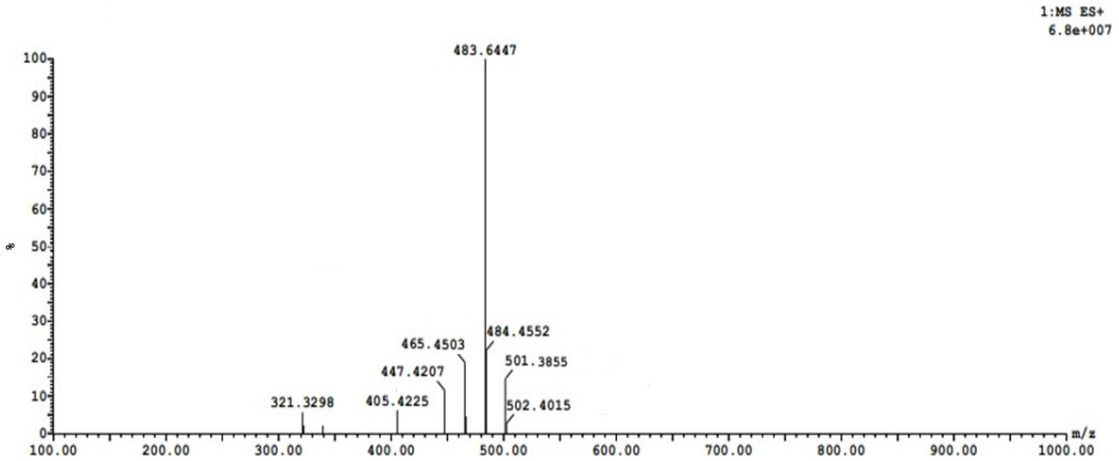
Suppl. Fig. S3. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **1**



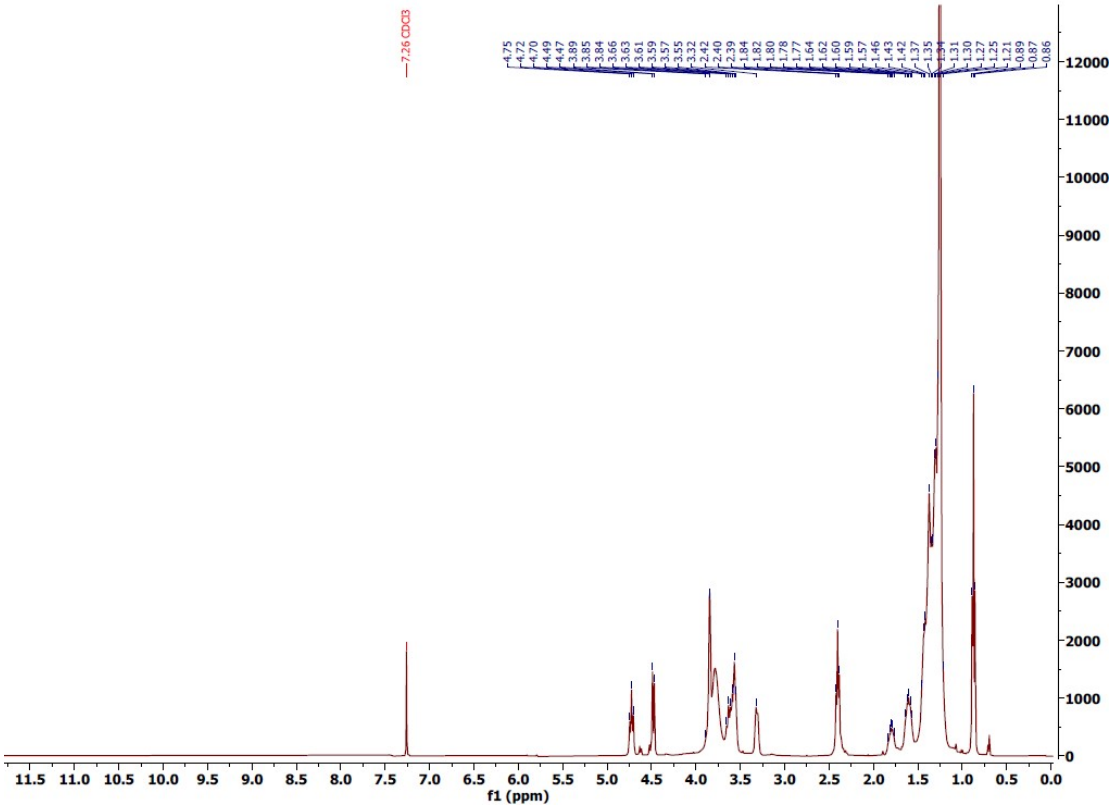
Suppl. Fig. S4. HSQC spectrum ($CDCl_3$) of compound **1**



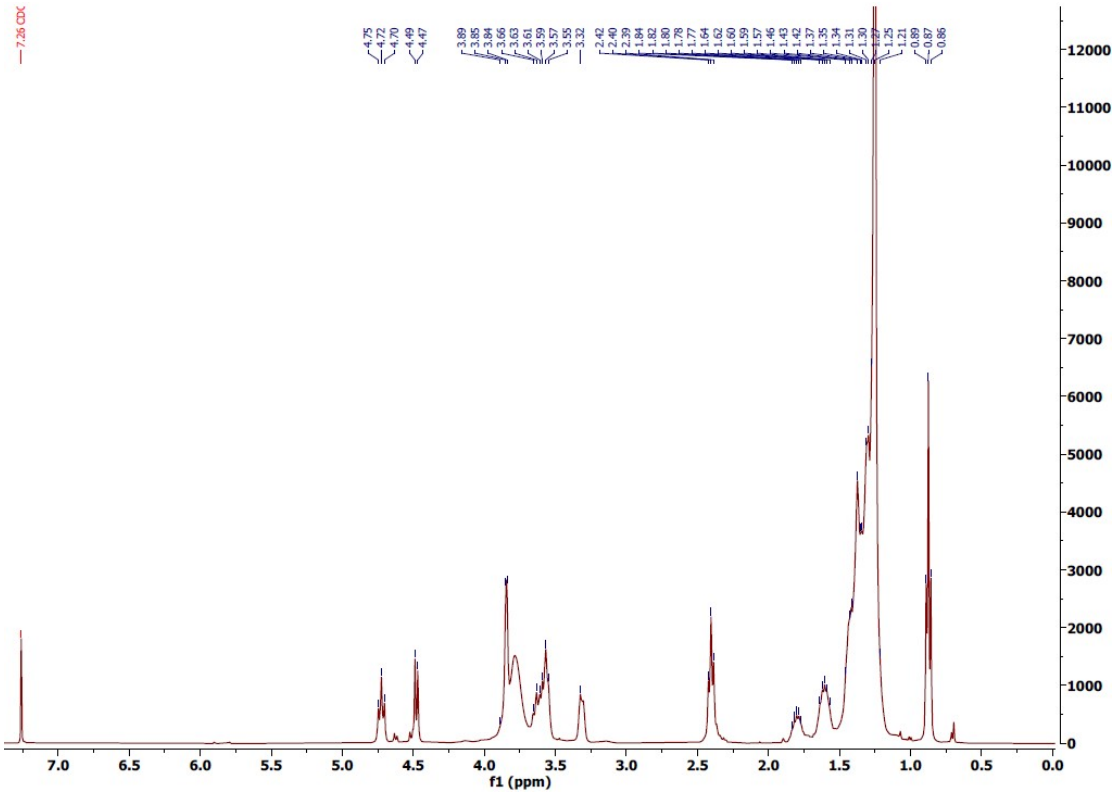
Suppl. Fig. S5. HMBC spectrum ($CDCl_3$) of compound **1**



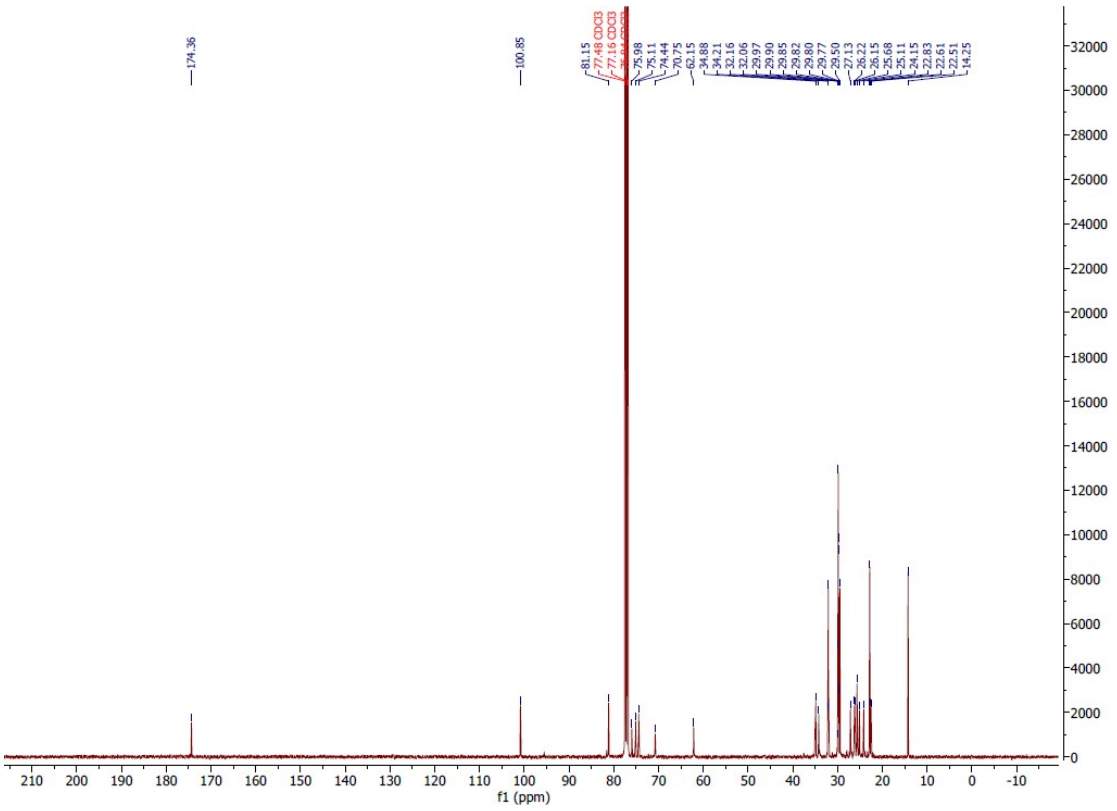
Suppl. Fig. S6. Positive HRESI-MS of compound **2**



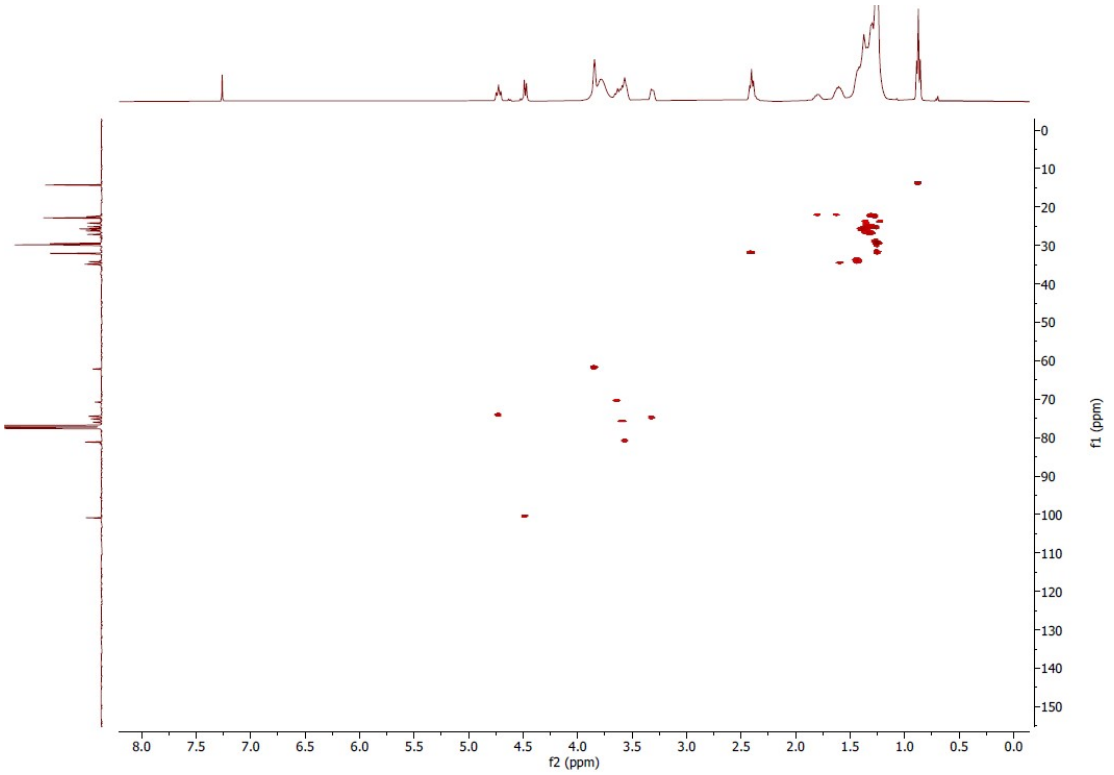
Suppl. Fig. S7. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **2**



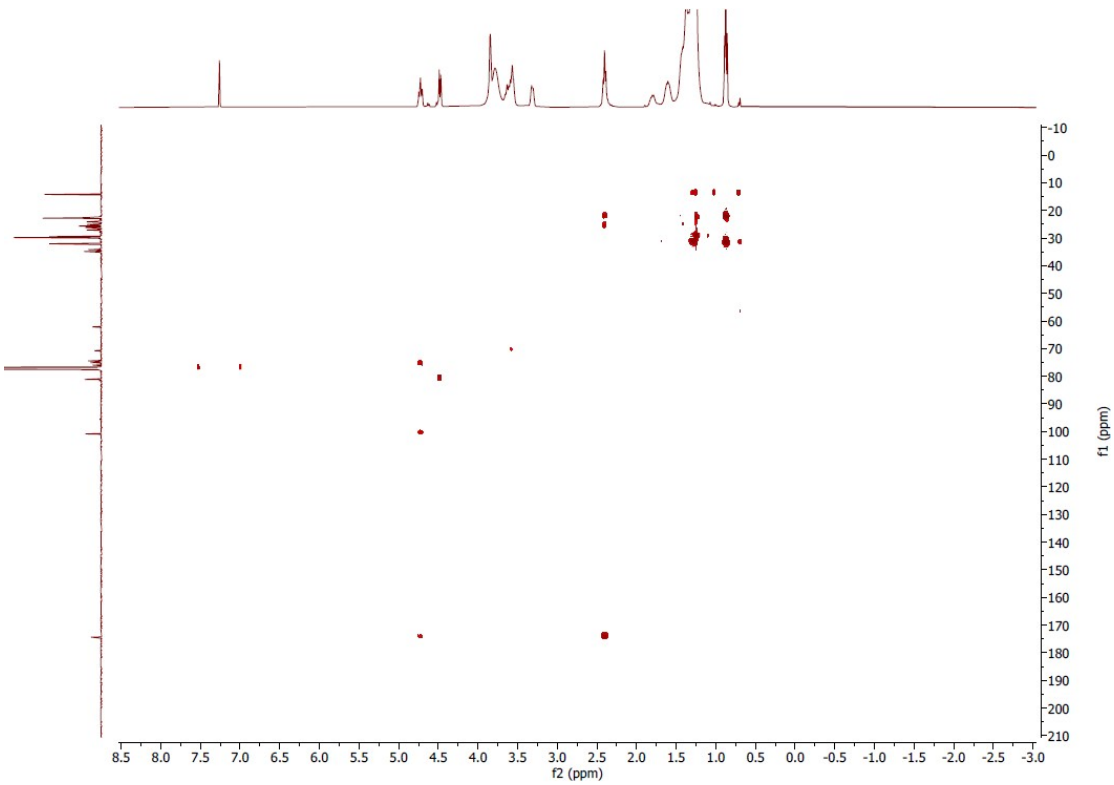
Suppl. Fig. S7-1. Expanded ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound **2**



Suppl. Fig. S8. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound **2**



Suppl. Fig. S9. HSQC spectrum ($CDCl_3$) of compound **2**



Suppl. Fig. S10. HMBC spectrum ($CDCl_3$) of compound **2**