# Supplementary material

# Introduction of nonacidic side chains on 6-ethylcholane scaffolds in the identification of potent bile acid receptor agonists with improved pharmacokinetic properties

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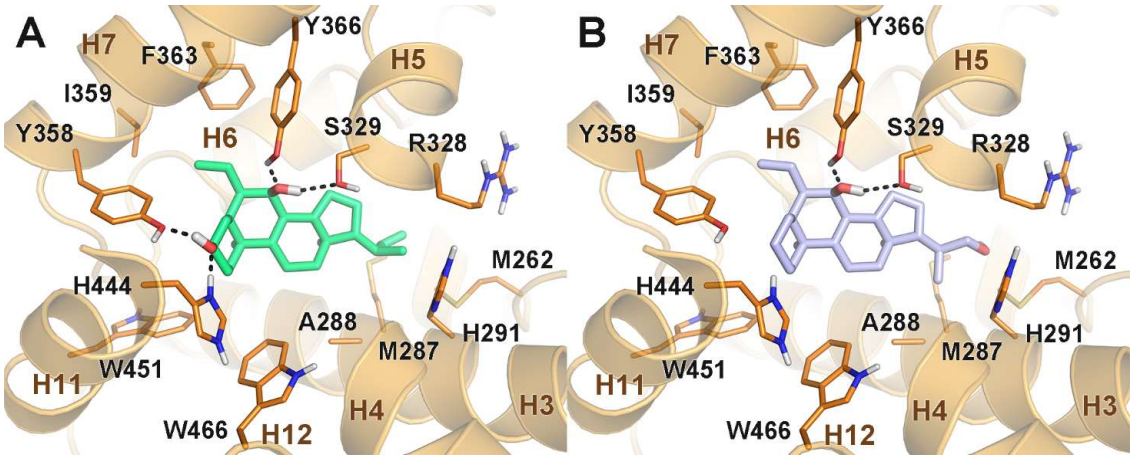


**Figure S1.** Docking pose of **1** (A) and **6** (B) at the FXR ligand binding domain. Compounds **1** and **6** are depicted as green and light blue sticks, respectively. FXR is shown as orange cartoons. Amino acids important for ligand binding are shown as sticks. Non-polar hydrogens are omitted for clarity. Hydrogen bonds are shown as dashed black lines.

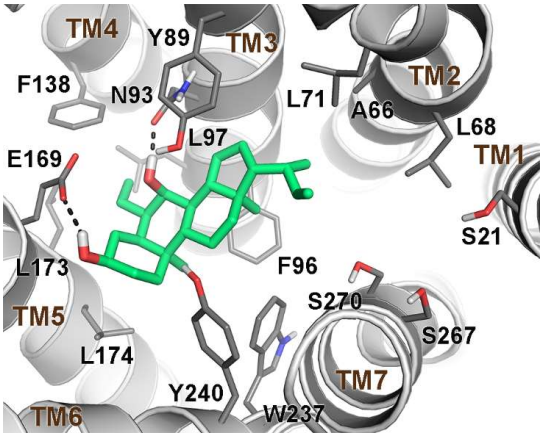


**Figure S2.** Docking pose of **1** in the GPBAR1 homology model.[3] Compound **1** is depicted as green sticks, while GPBAR1 is shown as grey cartoons. Amino acids important for ligand binding are shown as sticks. Non-polar hydrogens are omitted for clarity. Hydrogen bonds are shown as dashed black lines.

**Figure S3.** $^{1}H$ NMR (400 MHz, $CDCl_3$) of compound **1**

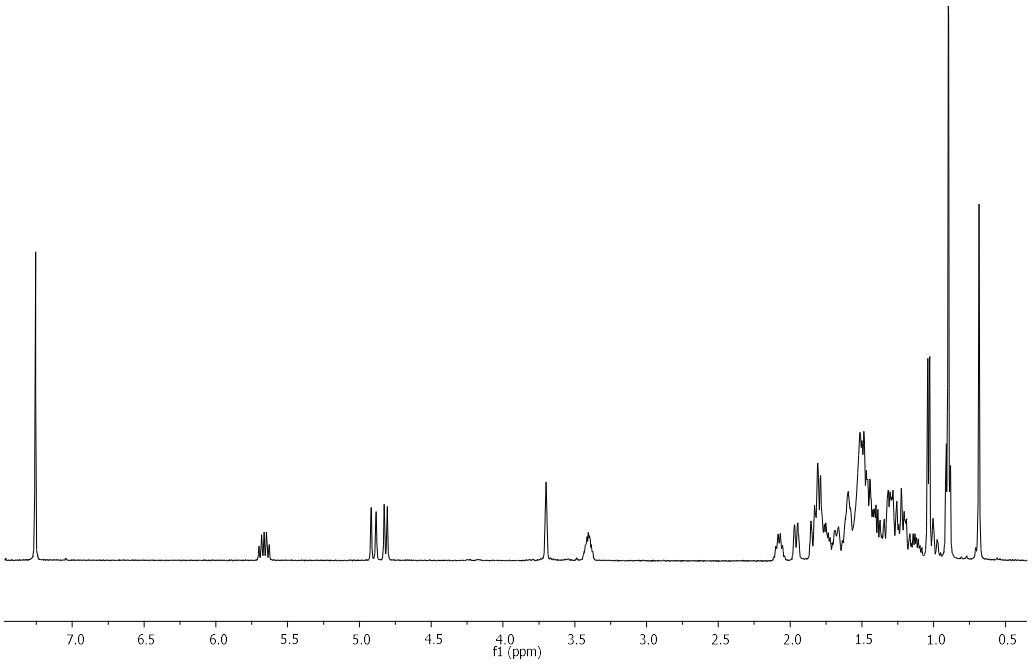


**Figure S4.** $^{13}C$ NMR (100 MHz, $CDCl_3$) of compound **1**

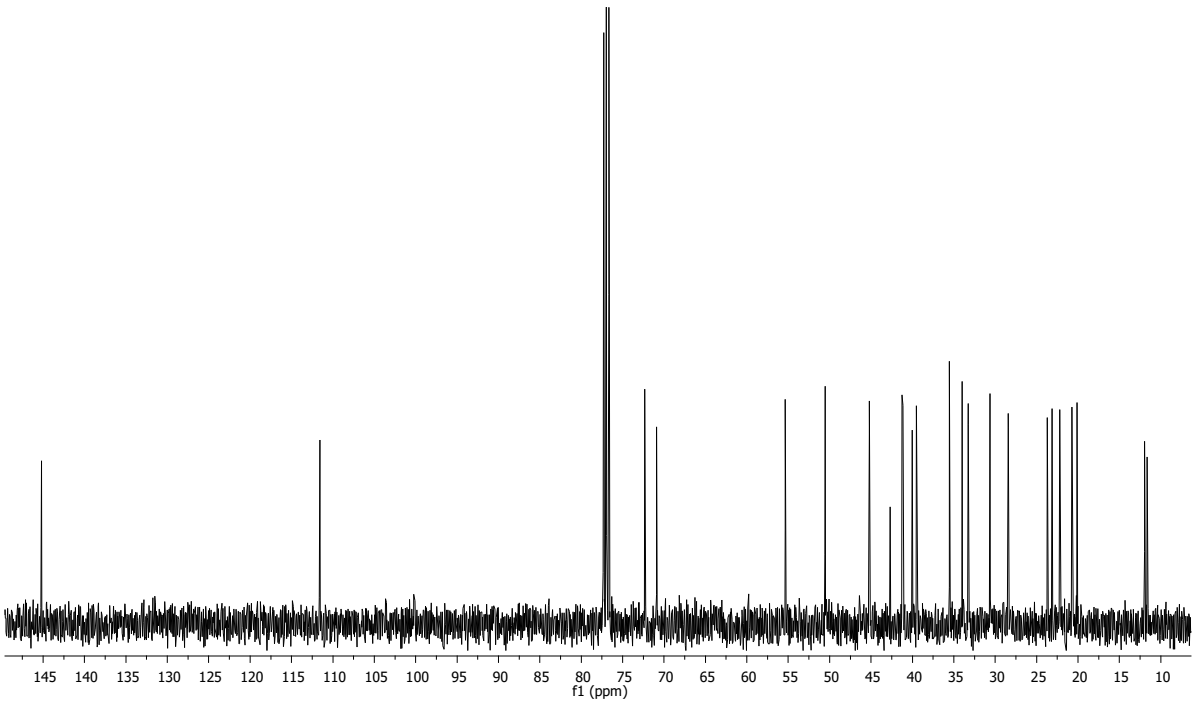

**Figure S5.** $^{1}H$ NMR (400 MHz, $CD_3OD$) of compound **2**

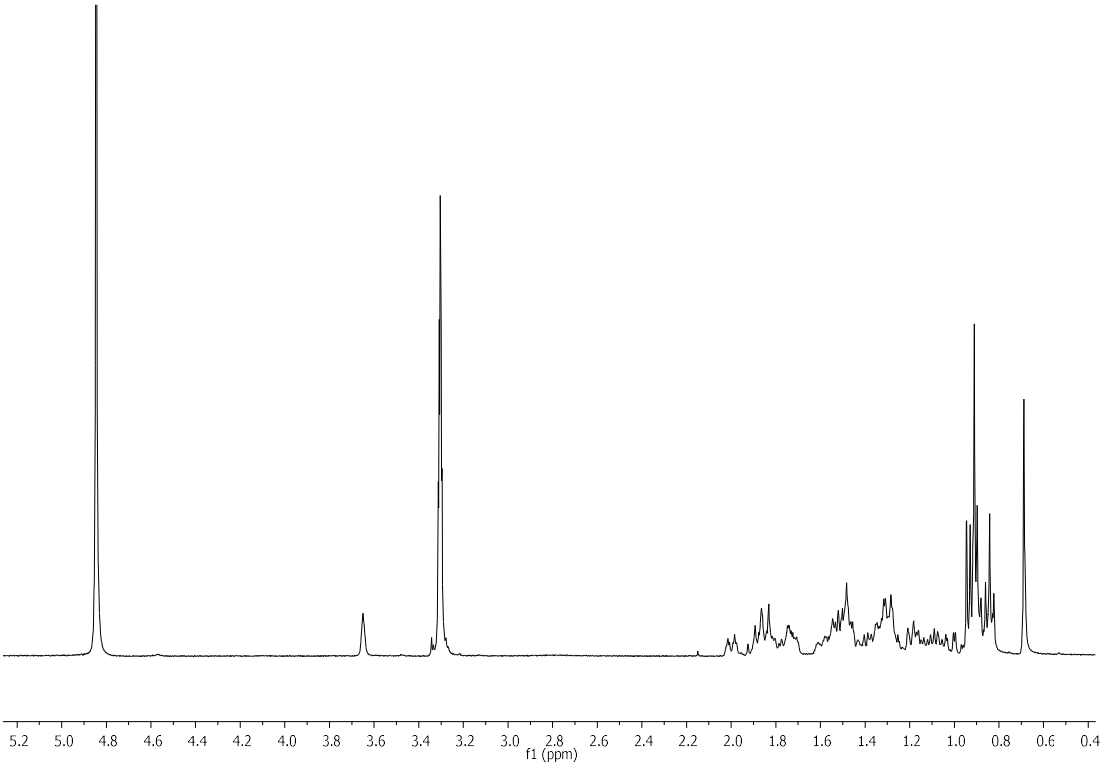


**Figure S6.** $^{13}C$ NMR (100 MHz, $CD_3OD$) of compound **2**

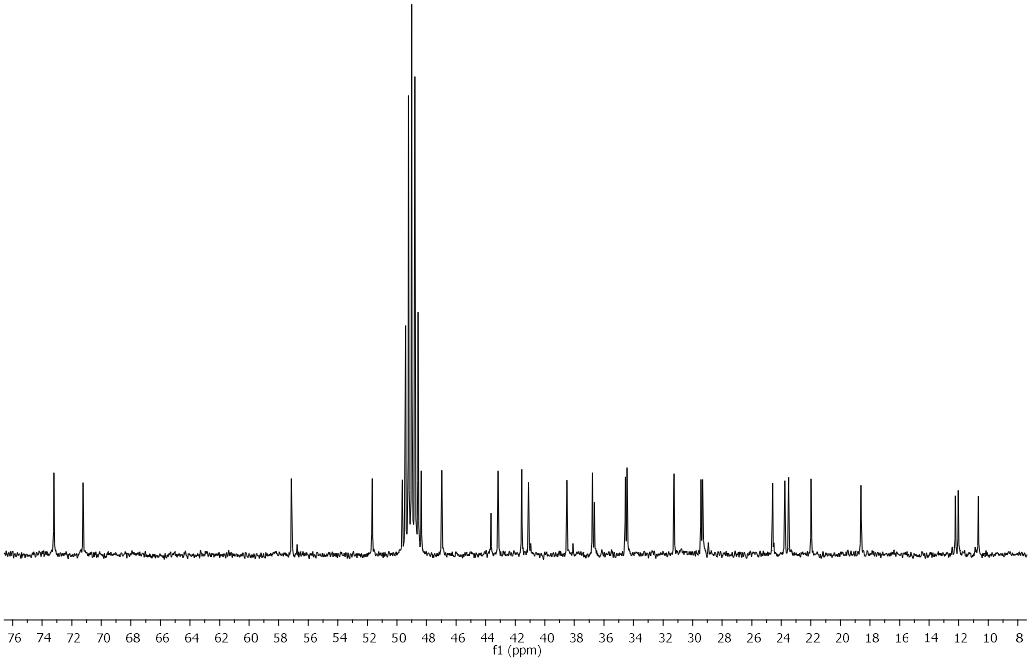

**Figure S7.** $^{1}H$ NMR (400 MHz, $CDCl_3$) of compound **3**

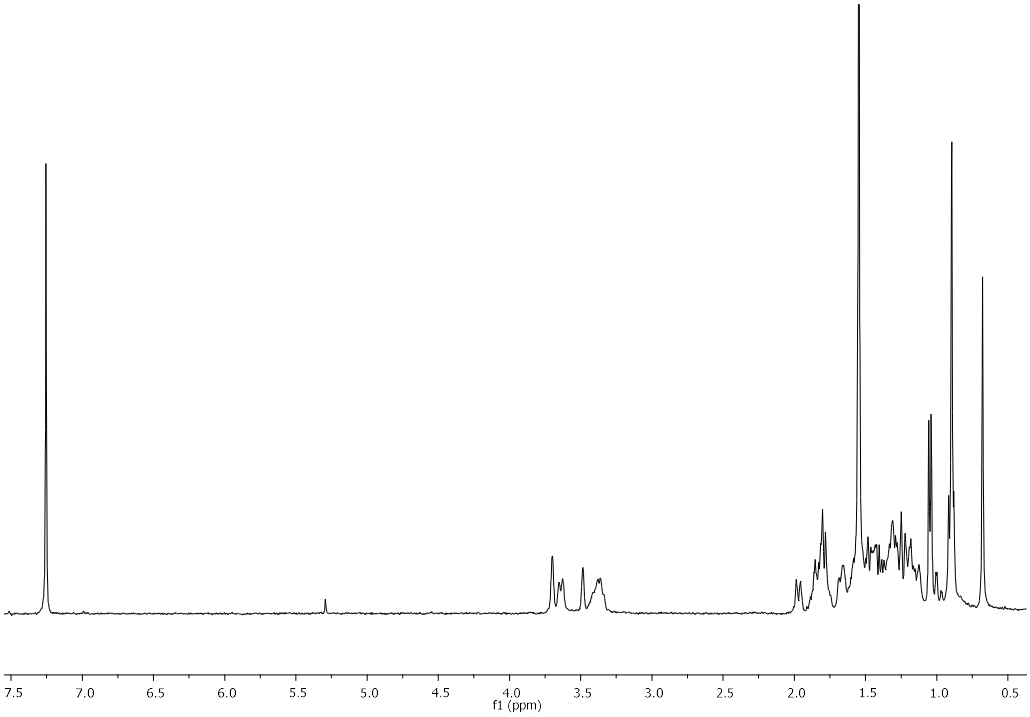


**Figure S8.** $^{13}C$ NMR (100 MHz, $CDCl_3$) of compound **3**

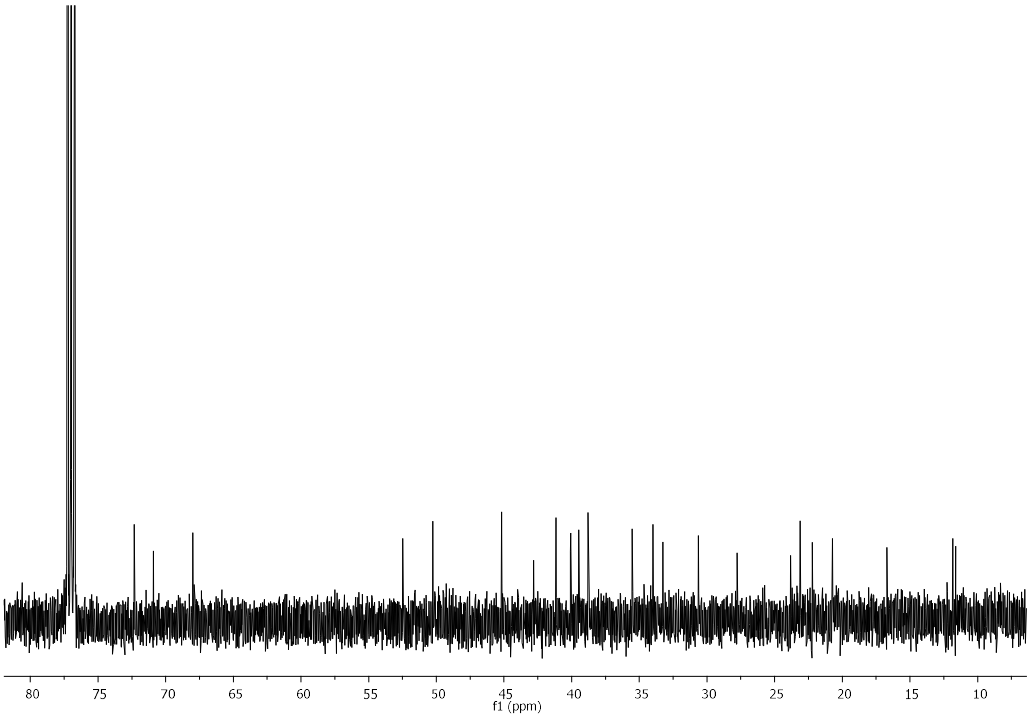

**Figure S9.** $^{1}H$ NMR (400 MHz, $CDCl_3$) of compound **4**

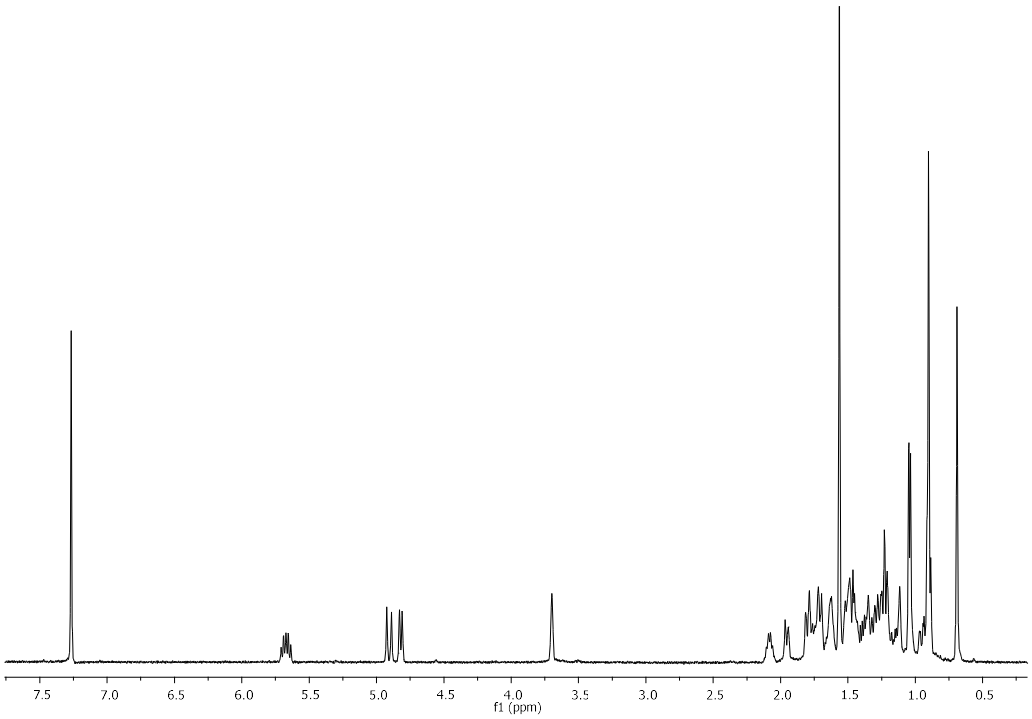


**Figure S10.** $^{13}C$ NMR (100 MHz, $CDCl_3$) of compound **4**

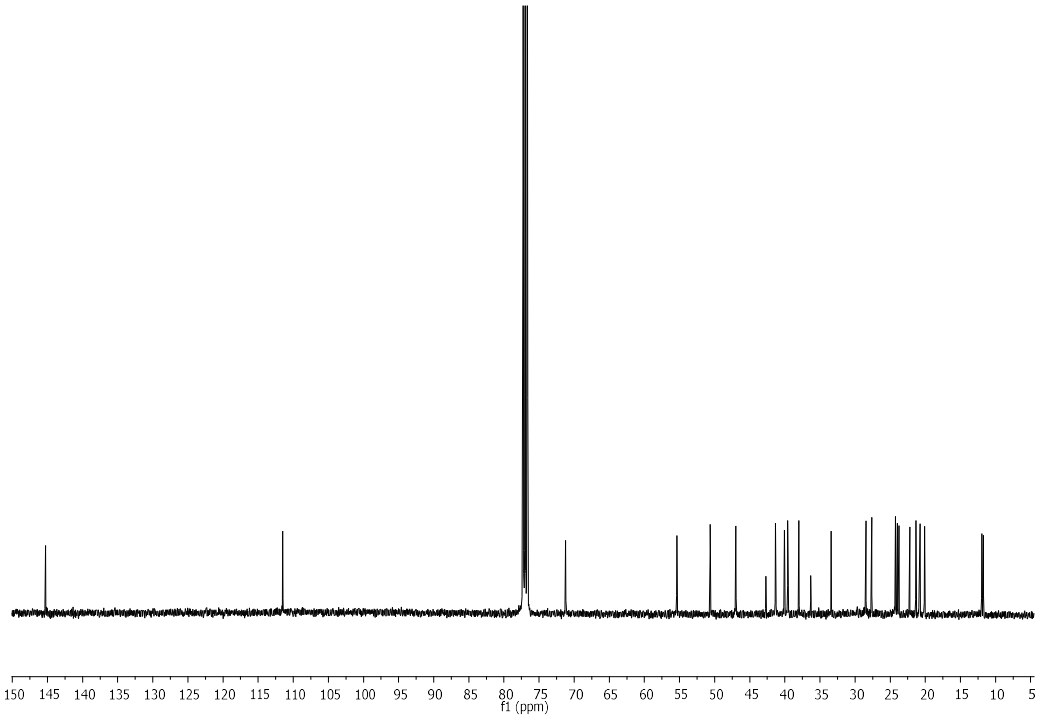

**Figure S11.** $^{1}H$ NMR (400 MHz, $CDCl_3$) of compound **5**

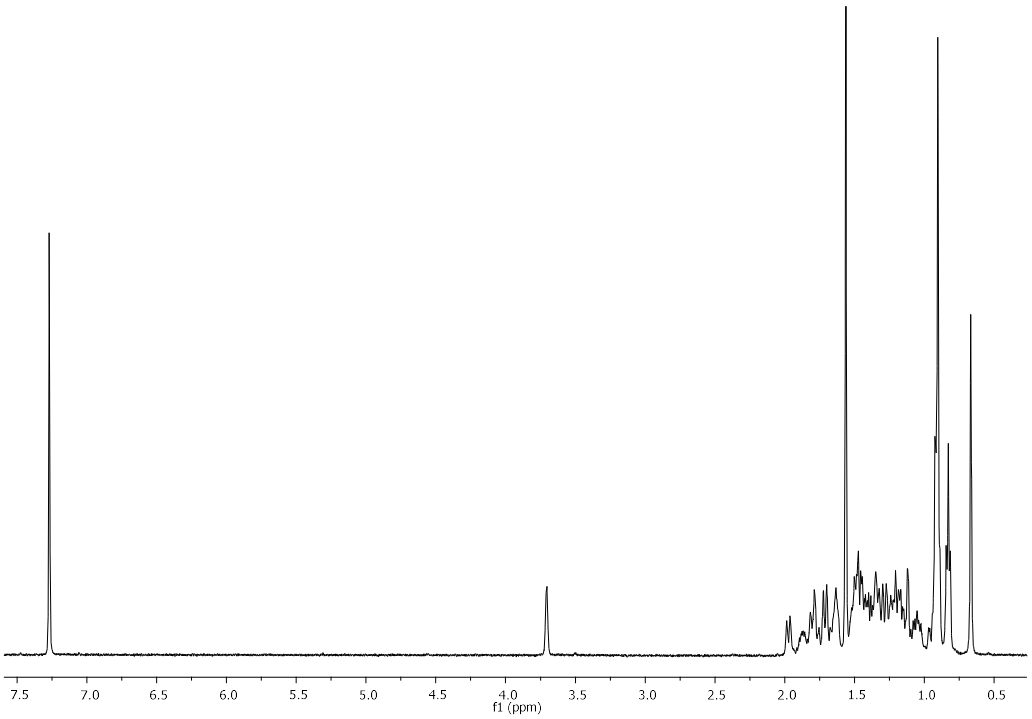


**Figure S12.** $^{13}C$ NMR (100 MHz, $CDCl_3$) of compound **5**

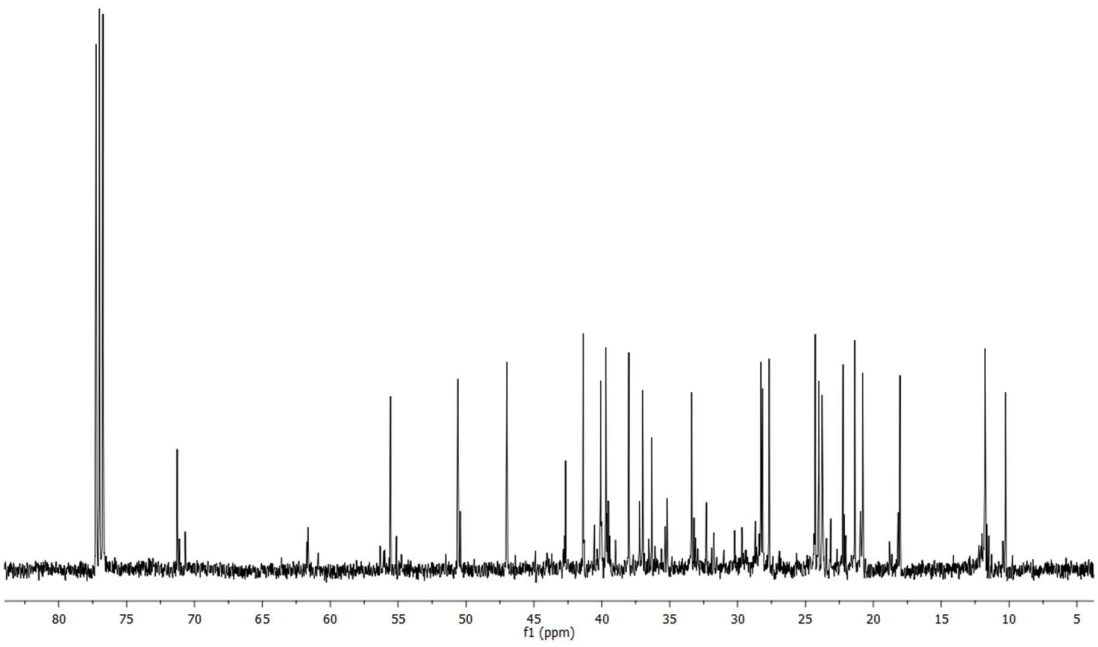

**Figure S13.** $^{1}H$ NMR (400 MHz, $CDCl_3$) of compound **6**

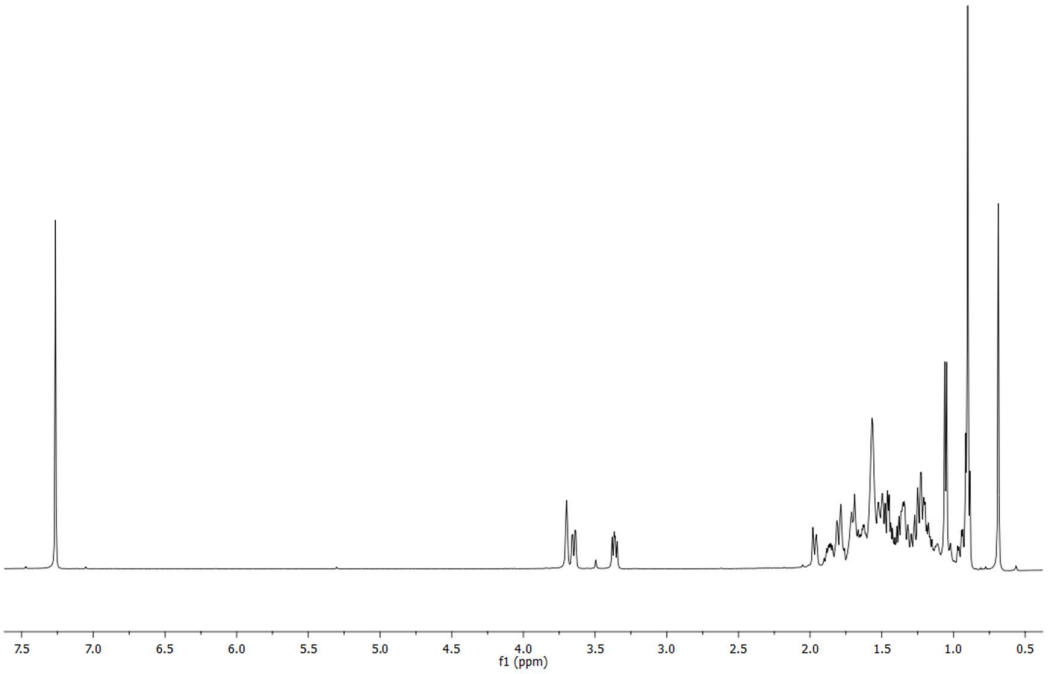


**Figure S14.** $^{13}C$ NMR (100 MHz, $CDCl_3$) of compound **6**

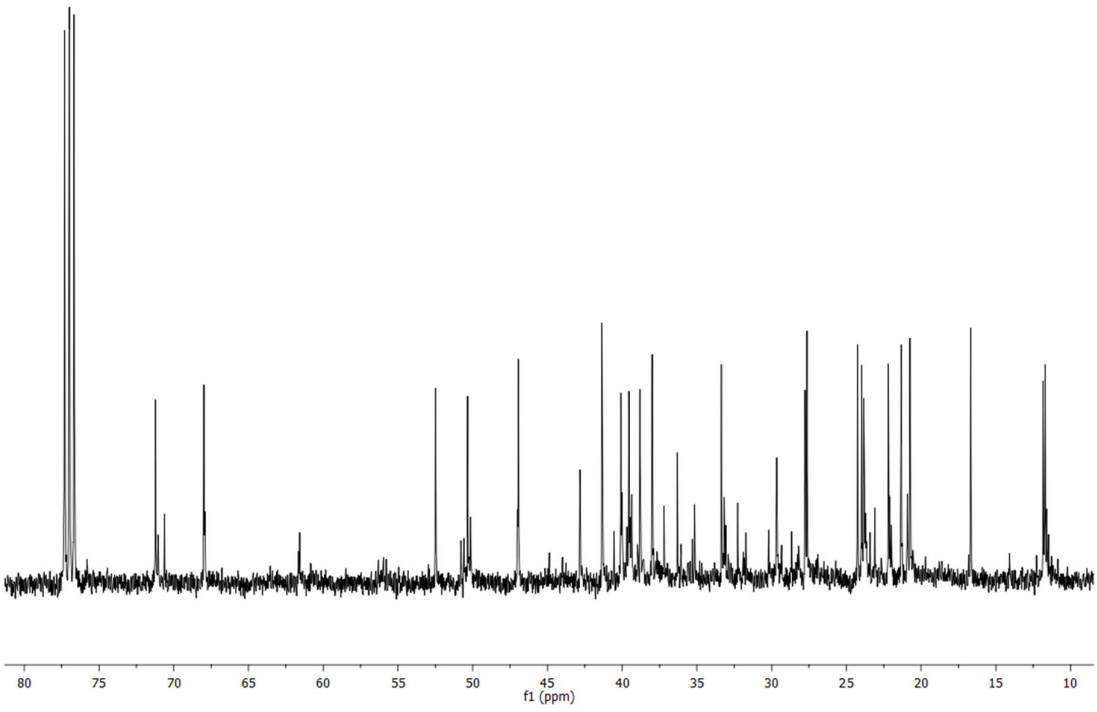

**Figure S15.** $^{1}H$ NMR (400 MHz, $CDCl_3$) of compound **8**

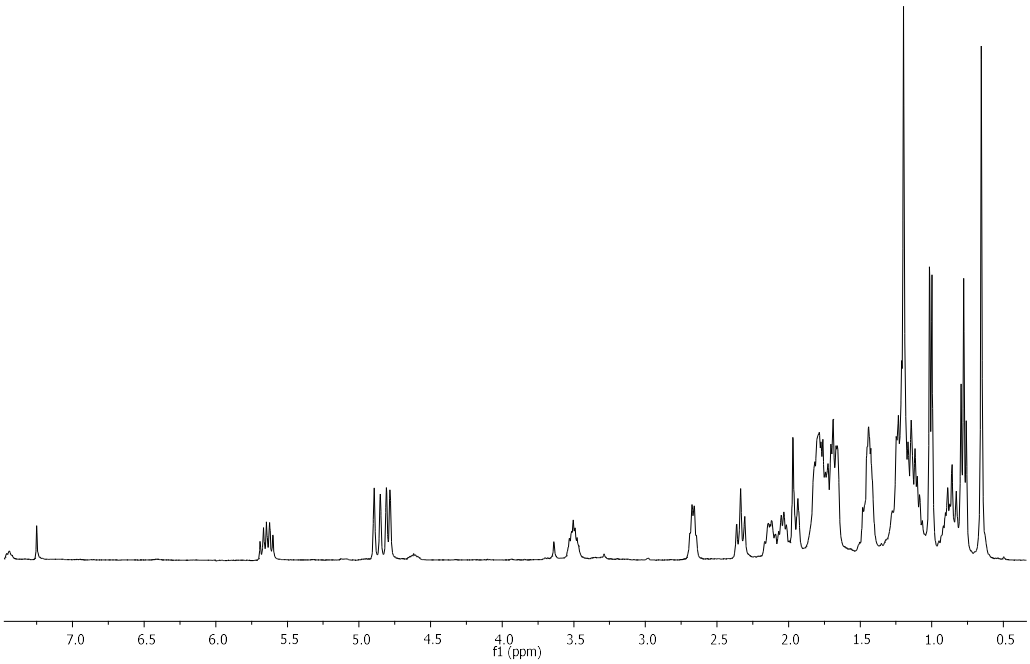


**Figure S16.** $^{13}C$ NMR (100 MHz, $CDCl_3$) of compound **8**

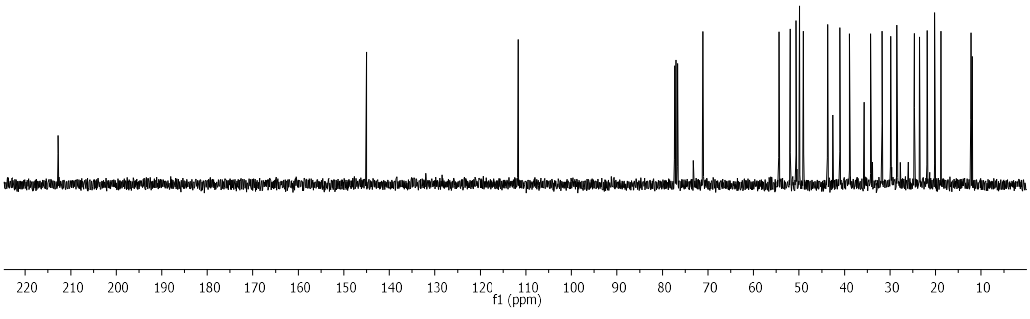

**Figure S17.** $^{1}H$ NMR (400 MHz, $CD_3OD$) of compound **10**

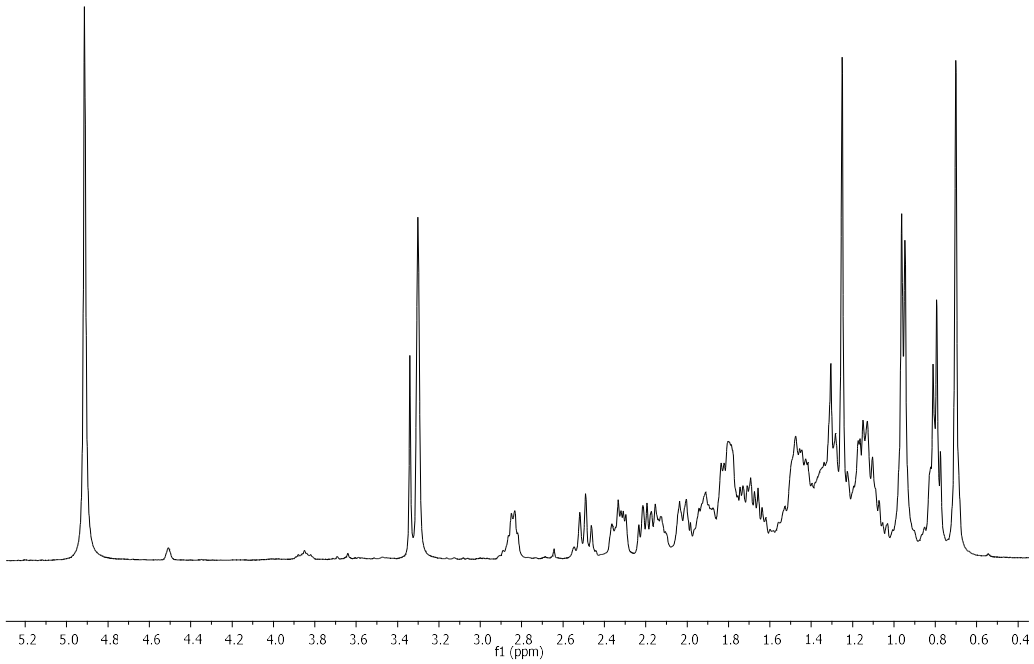


**Figure S18.** $^{13}C$ NMR (100 MHz, $CDCl_3$) of compound **10**