Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Carbohydrate Receptors Combining both a Macrocyclic Building Block and Flexible Side Arms as Recognition Units: Binding Properties of Compounds with CH_2OH Groups as Side Arms

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1 Description of the binding studies

1.1 ^{1}H NMR titrations

^{1}H NMR titrations were carried out in $CDCl_3$ at 25°C (chloroform was stored over activated molecular sieves and deacidified). Dilution experiments show that the receptors do not self-aggregate in the used concentration range.

Stock solutions in $CDCl_3$ were prepared for the receptor and sugar. These solutions and the corresponding solvent were combined in a manner so that the concentration of the receptor was kept constant and that of the sugar varied. For each titration 15-20 samples were prepared and the ^{1}H NMR spectra were recorded. For each receptor-sugar system at least two ^{1}H NMR titrations were carried out.

1.2 Microcalorimetric titrations.

Isothermal titration calorimetry (ITC) measurements were performed in $CDCl_3$ and water-containing $CDCl_3$ at 298 K using a power compensation calorimeter VP-ITC (Malvern). A solution of octyl-β-D-glucopyranoside was injected stepwise (8 µL × 30 times) into a dilute solution of receptor (appr. 0.3 mM) in $CDCl_3$ or water-containing $CDCl_3$ (0.035 mol/L and 0.07 mol/L H_2O in $CDCl_3$). The measured heat rate was recorded as a function of time and converted into enthalpies by integration of the appropriate reaction peaks using NanoAnalyze software provided by TA Instruments. Dilution effects were corrected by subtracting the results of a blank experiment. For each receptor-sugar system at least three titrations were carried out.

It should be noted that initial microcalorimetric studies were performed using microcalorimeter TAM (Thermal Activity Monitor, Thermometrics); however, the required long measurement time (up to 20 h compared with 2 h in the case of VP-ITC) was less favorable for the investigation of the binding processes in chloroform.

1.3 Binding studies in two-phase systems: Liquid-liquid extraction ($CDCl_3$/H_2O)

To study the extraction of monosaccharides from water into organic phase, aqueous sugar solutions (1 M) were equilibrated with the corresponding receptor in chloroform (1 mM solution) at 25 °C. Solutions of receptor in chloroform were then shaken vigorously with aqueous carbohydrate, the phases were separated, and the organic phase was passed through hydrophobic filter paper to remove residual aqueous solution (similar to the procedure used by Davis et al., see references below). The chloroform was evaporated and the residue analysed by ^{1}H NMR, first in $CDCl_3$ and afterwards in DMSO-d_6 (after the evaporation of $CDCl_3$).

T. Velasco, G. Lecollinet, T. Ryan, A. P. Davis, *Org. Biomol. Chem.* **2004**, *2*, 645-647

T. J. Ryan, G. Lecollinet, T. Velasco, A. P. Davis, *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4863-4866

2 Microcalorimetric titrations in water-containing $CDCl_3$.

2.1 Titration of **13** with **24** in water-containing $CDCl_3$ (0.035 mol/L H_2O)

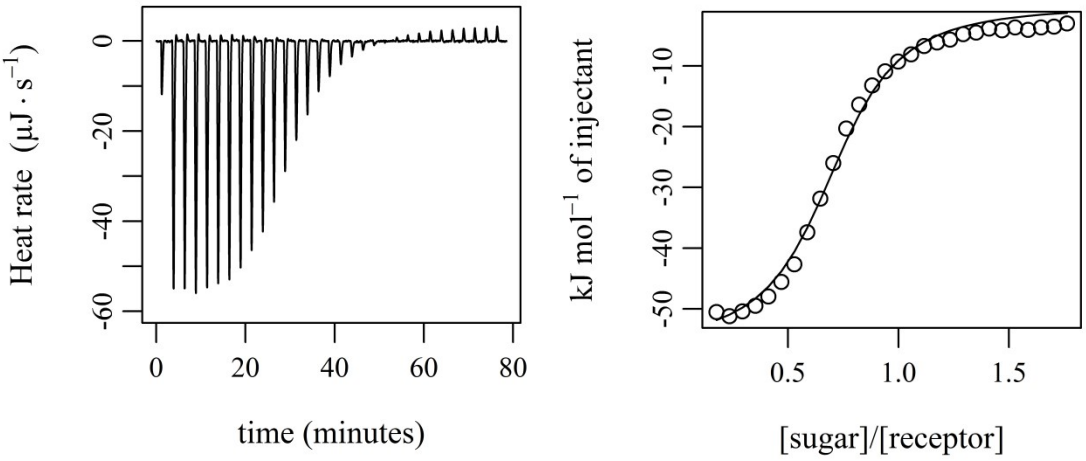


Figure S1. ITC thermogram (left) and titration curve-fitting (right) of **13** with **24** in water-containing $CDCl_3$ (0.035 mol/L H_2O). Titration mode: addition of **24** ($c_{syringe}$ = 3.09mM) into **13** (c_{cell} = 0.30 mM) at 298 K in 30 steps.

2.2 Titration of **13** with **24** in water-containing $CDCl_3$ (0.07 mol/L H_2O)

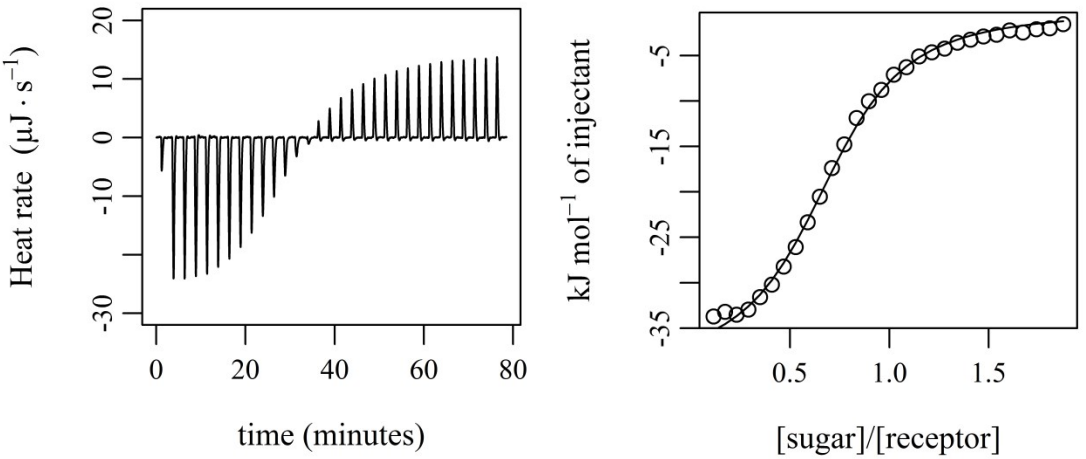


Figure S2. ITC thermogram (left) and titration curve-fitting (right) of 13 with 24 in water-containing $CDCl_3$ (0.07 mol/L H_2O). Titration mode: addition of **24** ($c_{syringe}$ = 3.02 mM) into **13** (c_{cell} = 0.30 mM) at 298 K in 30 steps.

2.3 Titration of **12** with **24** in water-containing $CDCl_3$ (0.035 mol/L H_2O)

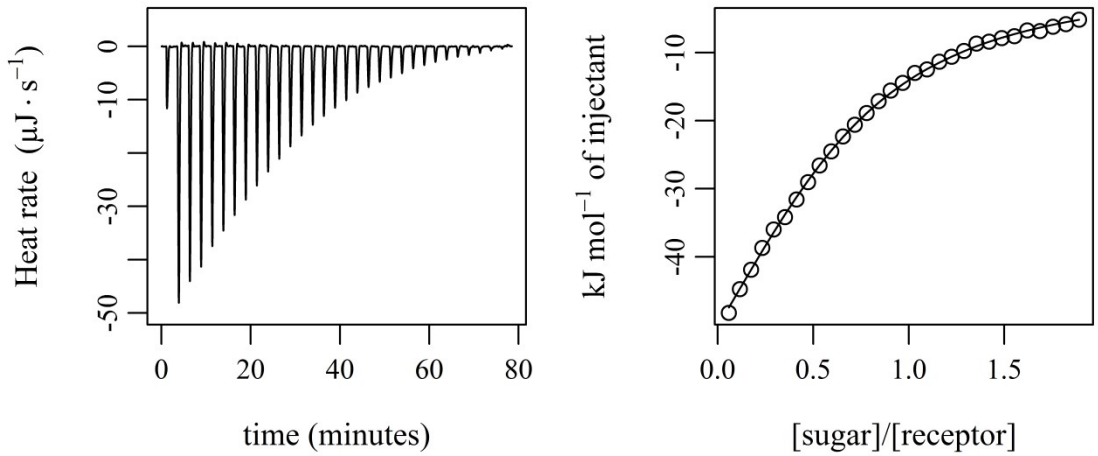


Figure S3. ITC thermogram (left) and titration curve-fitting (right) of **12** with **24** in in water-containing $CDCl_3$ (0.035 mol/L H_2O). Titration mode: addition of **24** ($c_{syringe}$ = 3.01 mM) into **12** (c_{cell} = 0.30 mM) at 298 K in 30 steps.

2.4 Titration of **13** with **24** in water-containing $CDCl_3$ (0.035 mol/L H_2O)

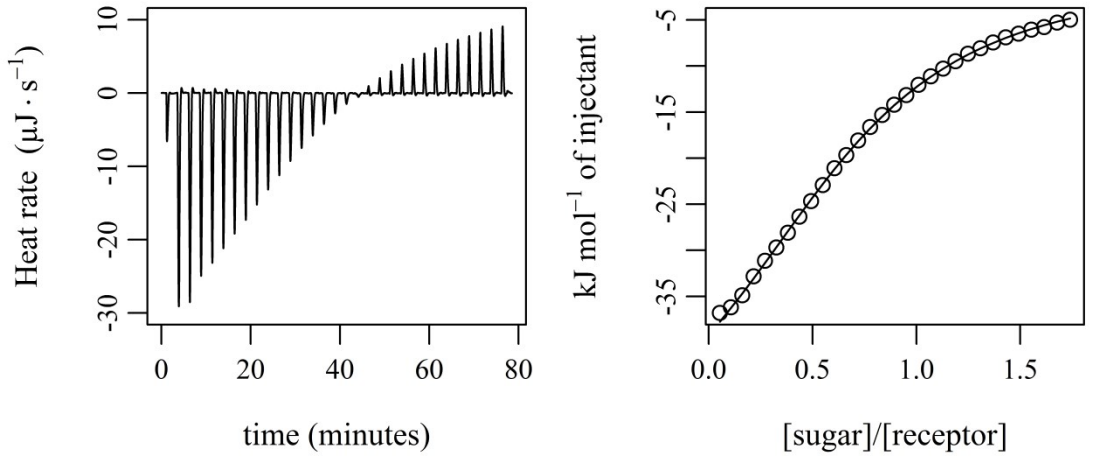


Figure S4. ITC thermogram (left) and titration curve-fitting (right) of of **12** with **24** in in water-containing $CDCl_3$ (0.07 mol/L H_2O). Titration mode: addition of **24** ($c_{syringe}$ = 3.01 mM) into **12** (c_{cell} = 0.30 mM) at 298 K in 30 steps.

3 Molecular modelling calculations (examples)

Program MacroModel V.8.5, OPLS 2001 force field, MCMM, 50000 steps.

a) b)

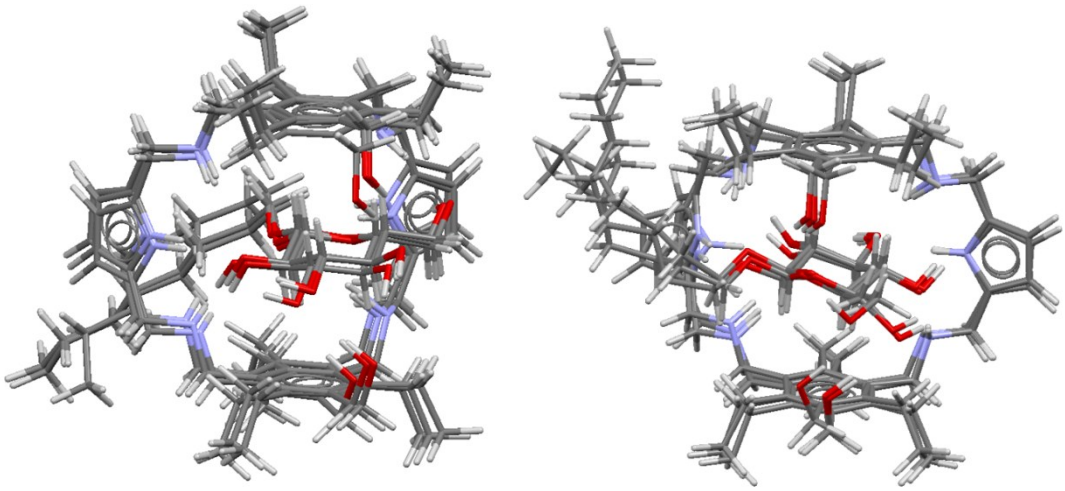


Figure S5. Energy-minimized structure of the 1:1 complex formed between **13** and octyl-β-glucoside **24**. Shown are three structures with lowest energy: (a) octyl chain of **24** between the bridges, (b) octyl chain next to the bridges.

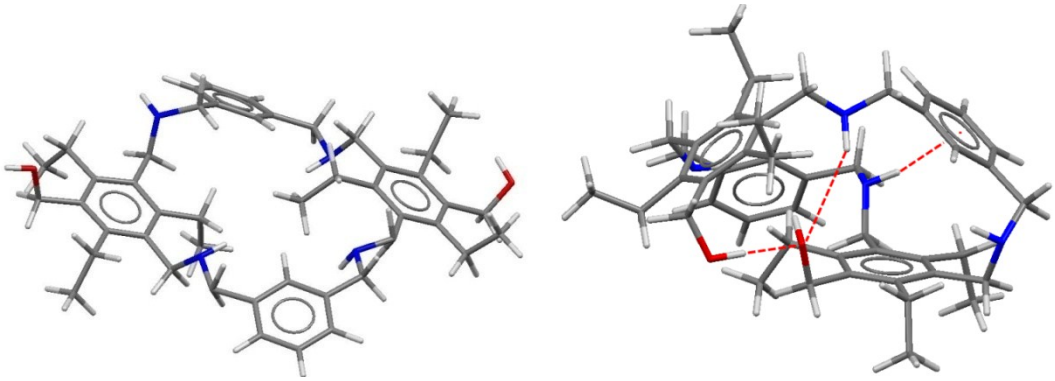


Figure S6. Examples of energy-minimized structures of compound **12** (Color code: N, blue; O, red; C, gray). The possible intramolecular OH···O, NH···O and NH···π interactions are shown as broken lines.

a) b)

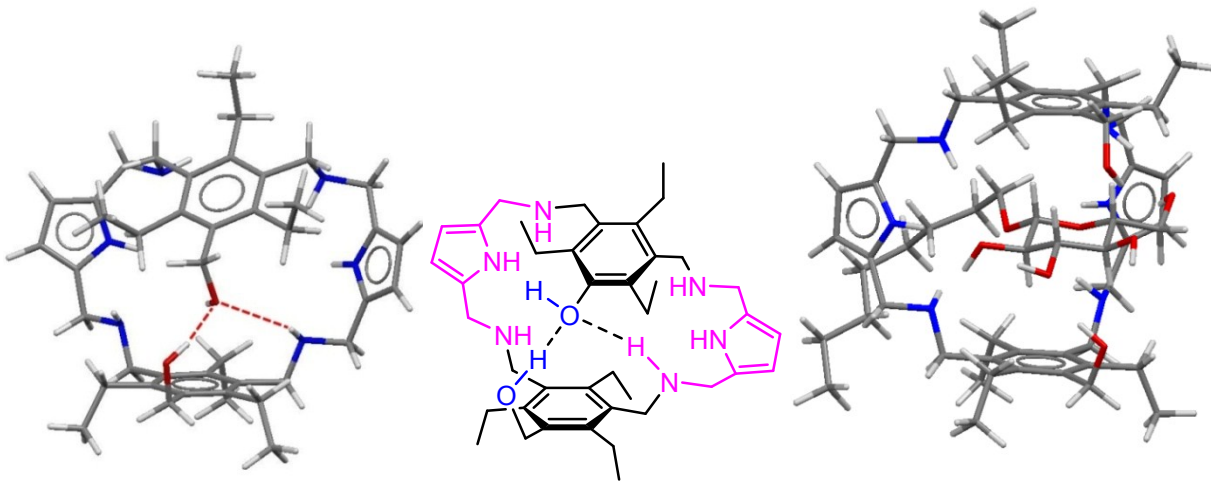
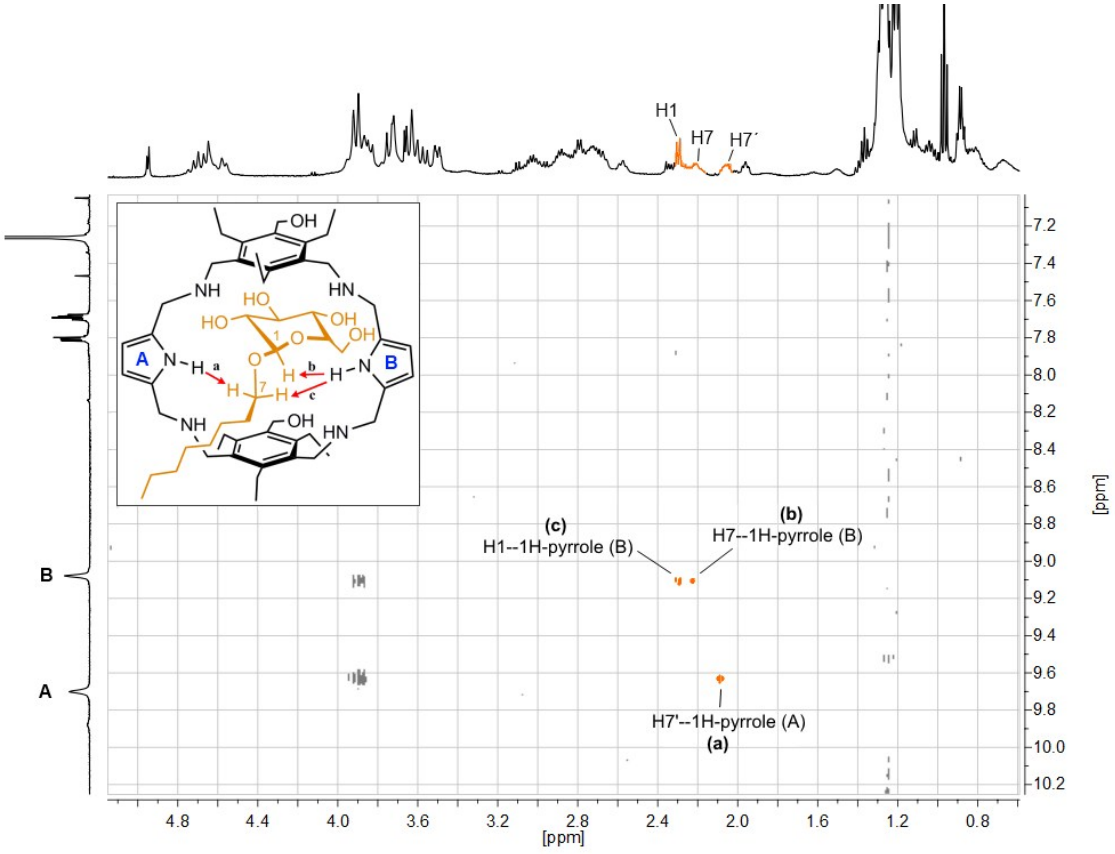


Figure S7. (a) Energy-minimized structure of **13** with marked intramolecular OH···O and NH···O hydrogen bonds indicated by the calculations. (b) Energy-minimized structure of the1:1 complex formed between **13** and octyl β-glucoside **24**.

4 ROESY experiments for **13•24** and **14•24**

a)



b)

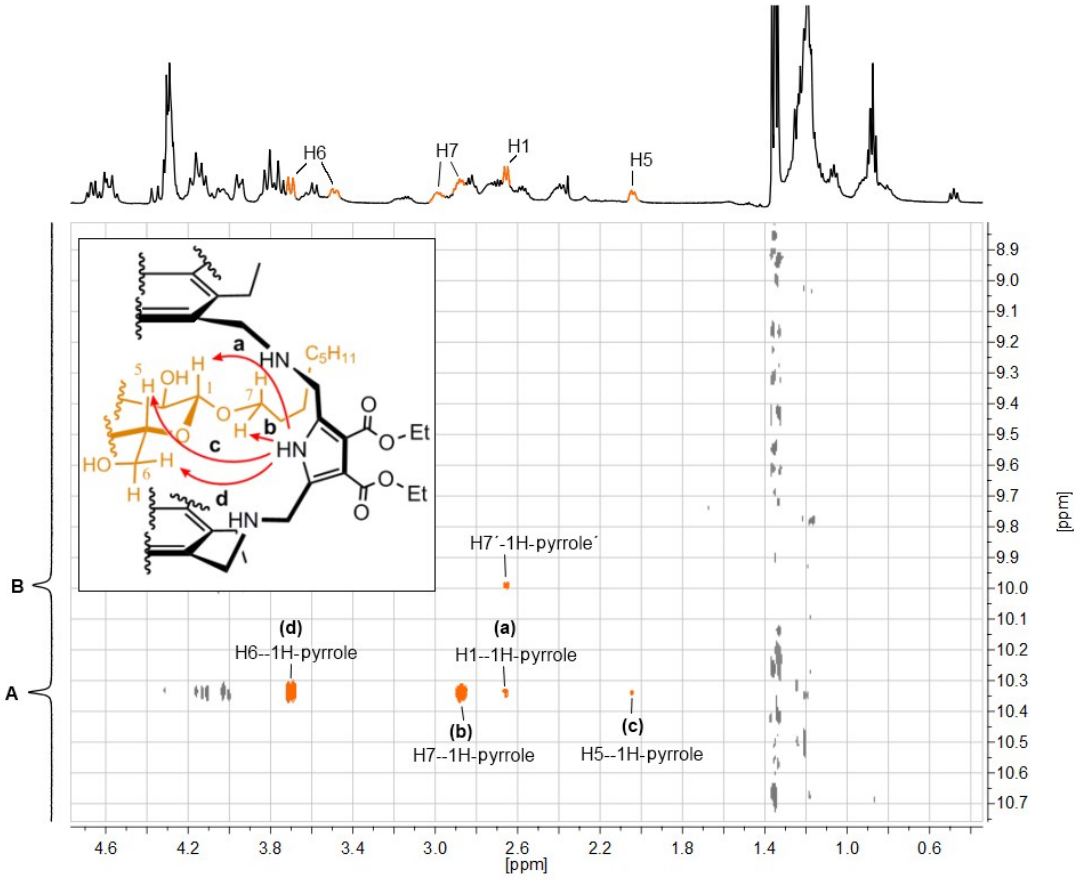


Figure S8. Partial ROESY spectrum of receptor **13** (a) and **14** (b) (1 mM) with β-glucoside **24** (1 mM) showing intermolecular connections between carbohydrate and receptor (mixing time = 165 ms)

5. ^{1}H and ^{13}C NMR spectra of compounds **12-14**, **17** and **18**.

5.1. ^{1}H and ^{13}C NMR spectra of compound **12**.

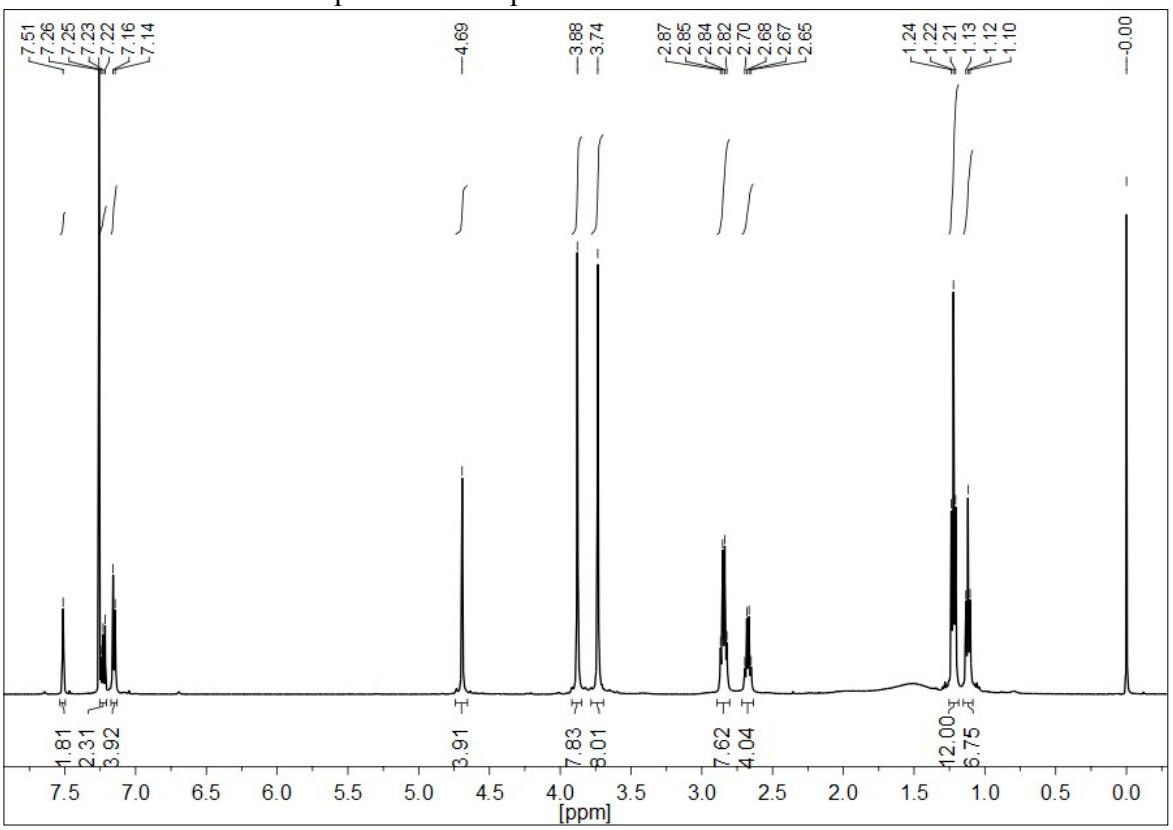


Figure S9. ^{1}H NMR spectrum of compound **12** in $CDCl_3$.

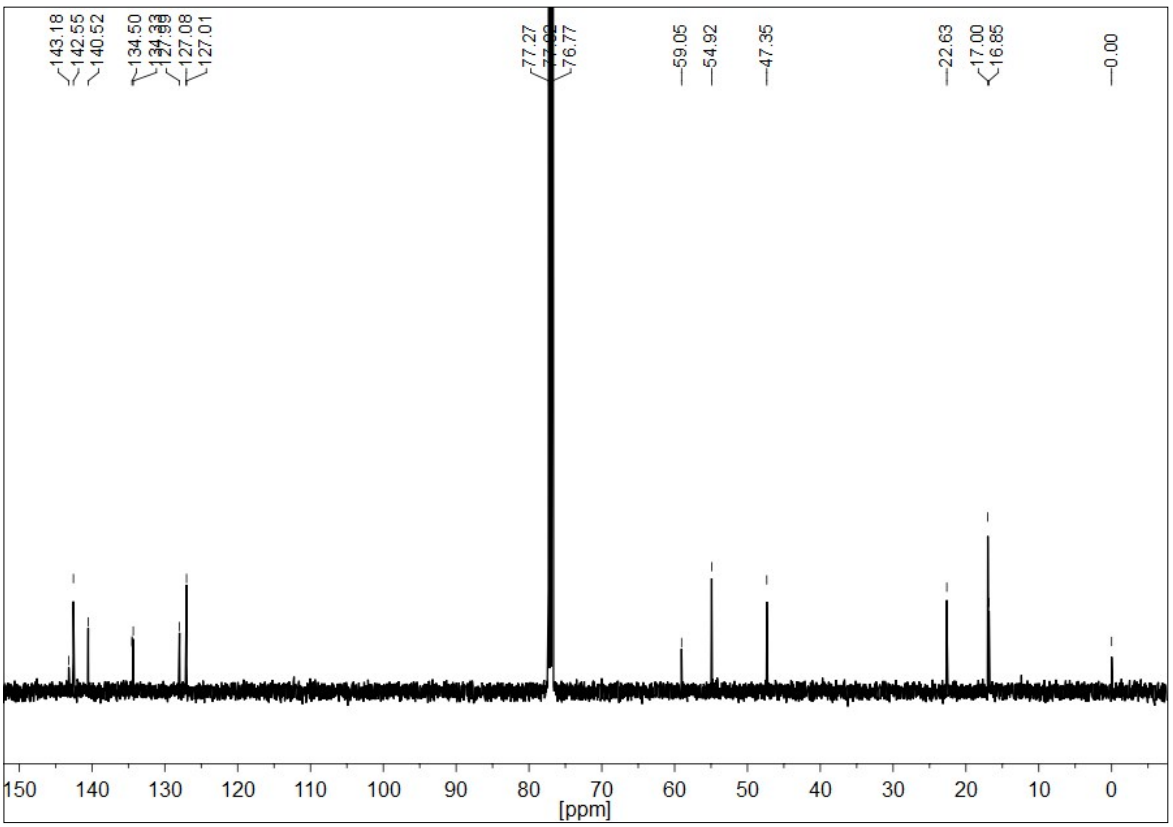


Figure S10. ^{13}C NMR spectrum of compound **12** in $CDCl_3$.

5.2. ^{1}H and ^{13}C NMR spectra of compound **13**.

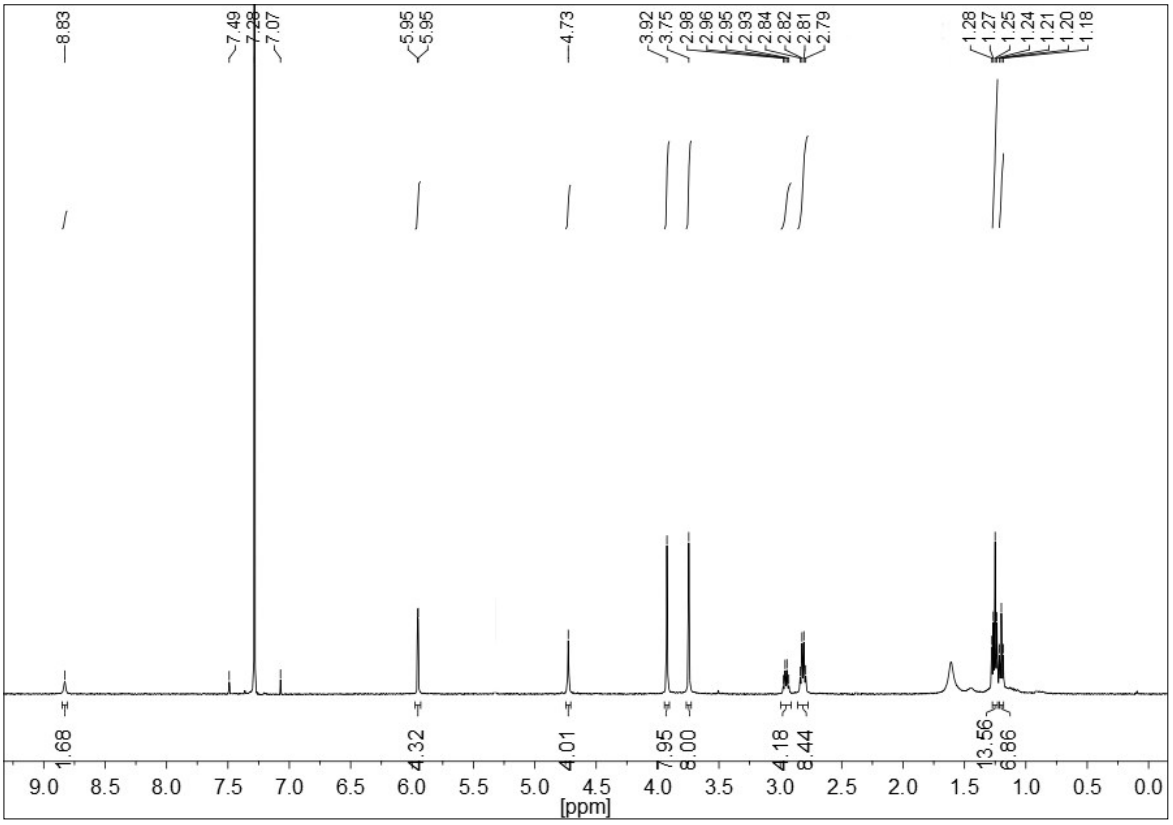


Figure S11a. ^{1}H NMR spectrum of compound **13** in $CDCl_3$ (0.3 mM).

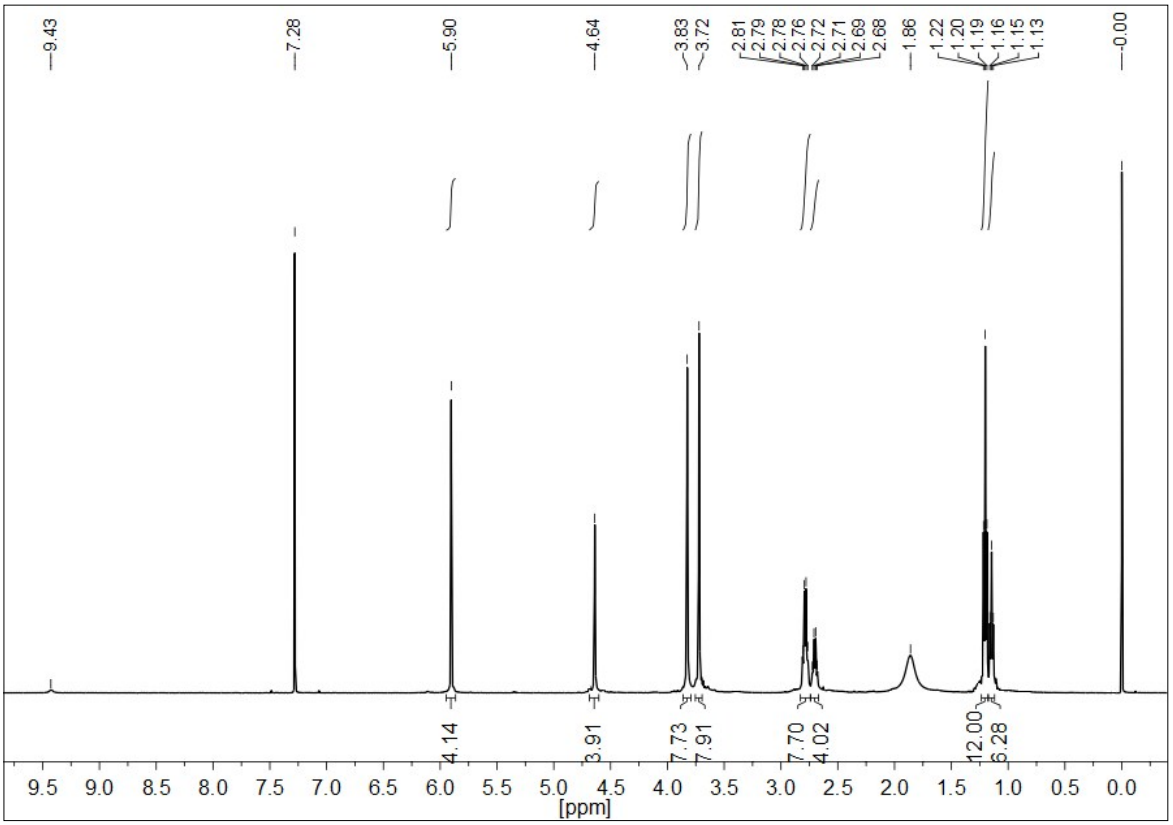


Figure S11b. ^{1}H NMR spectrum of compound **13** in $CDCl_3$ (≈ 1 mM).

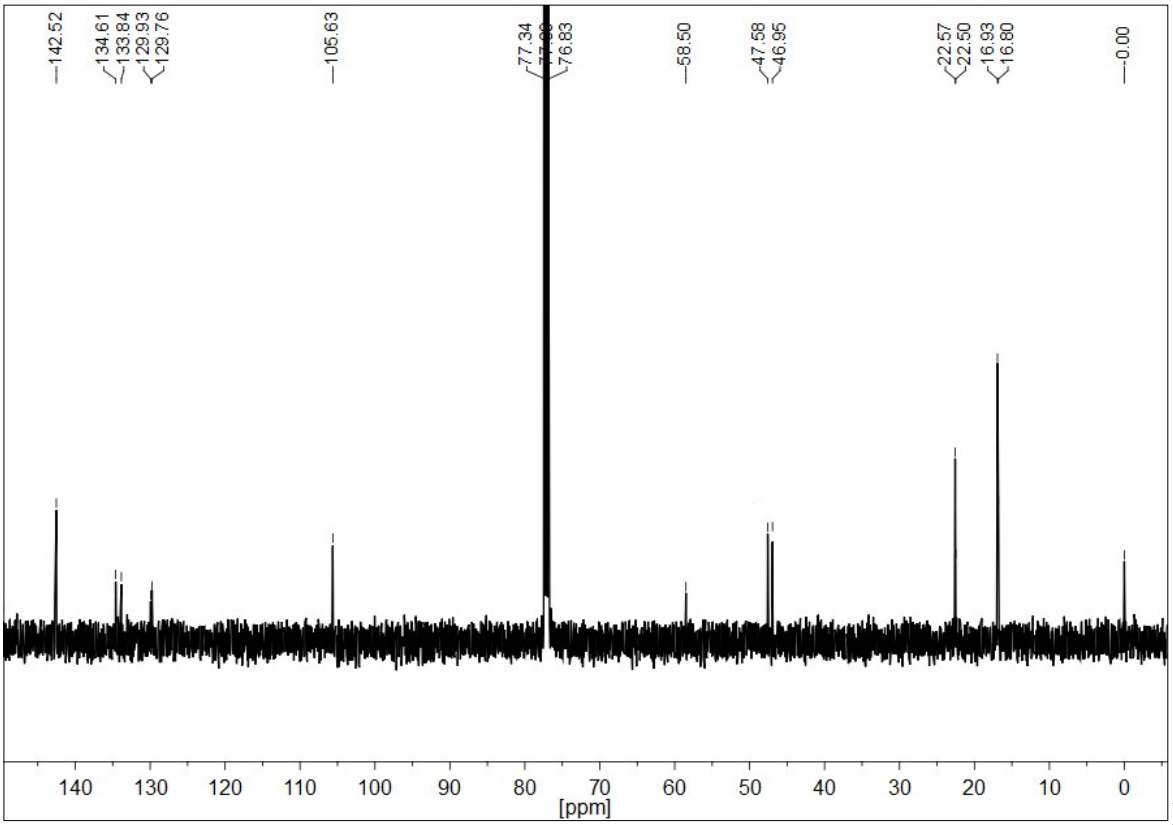


Figure S12. ^{13}C NMR spectrum of compound **13** in $CDCl_3$.

5.3 ^{1}H and ^{13}C NMR spectra of compound **14**.

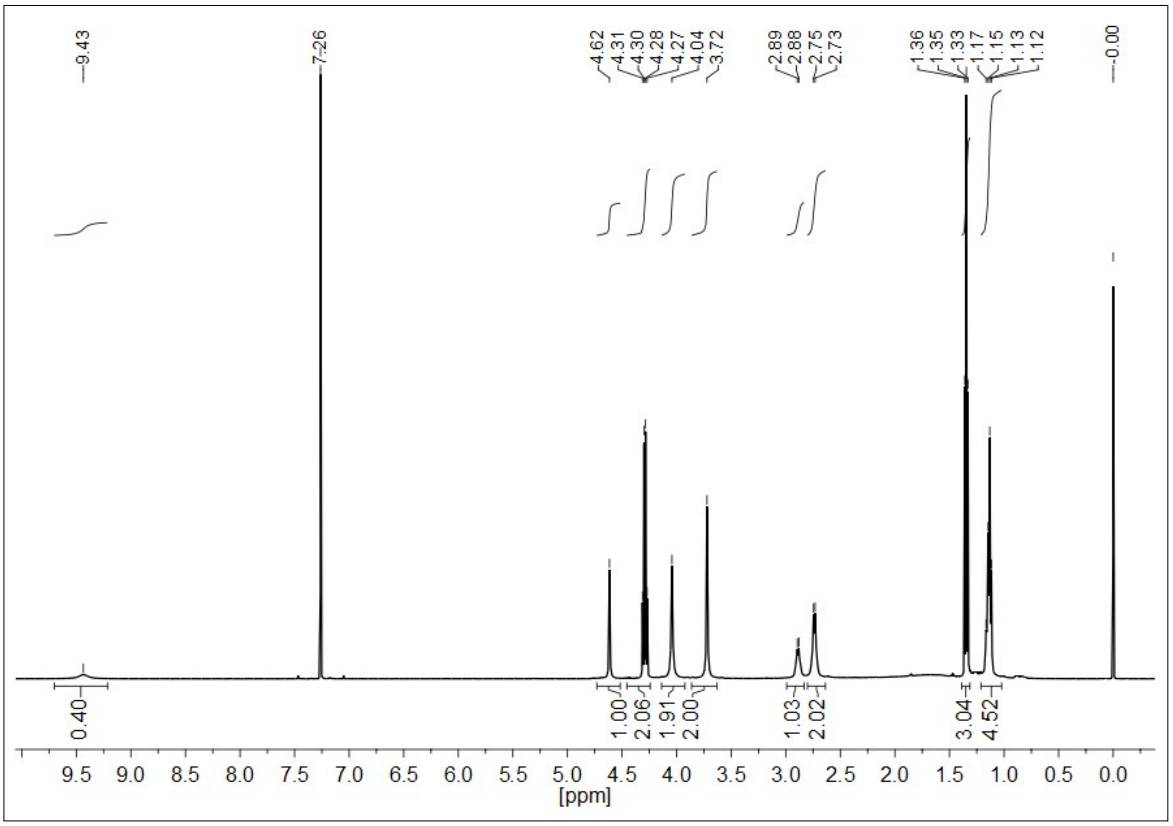


Figure S13. ^{1}H NMR spectrum of compound **14** in $CDCl_3$.

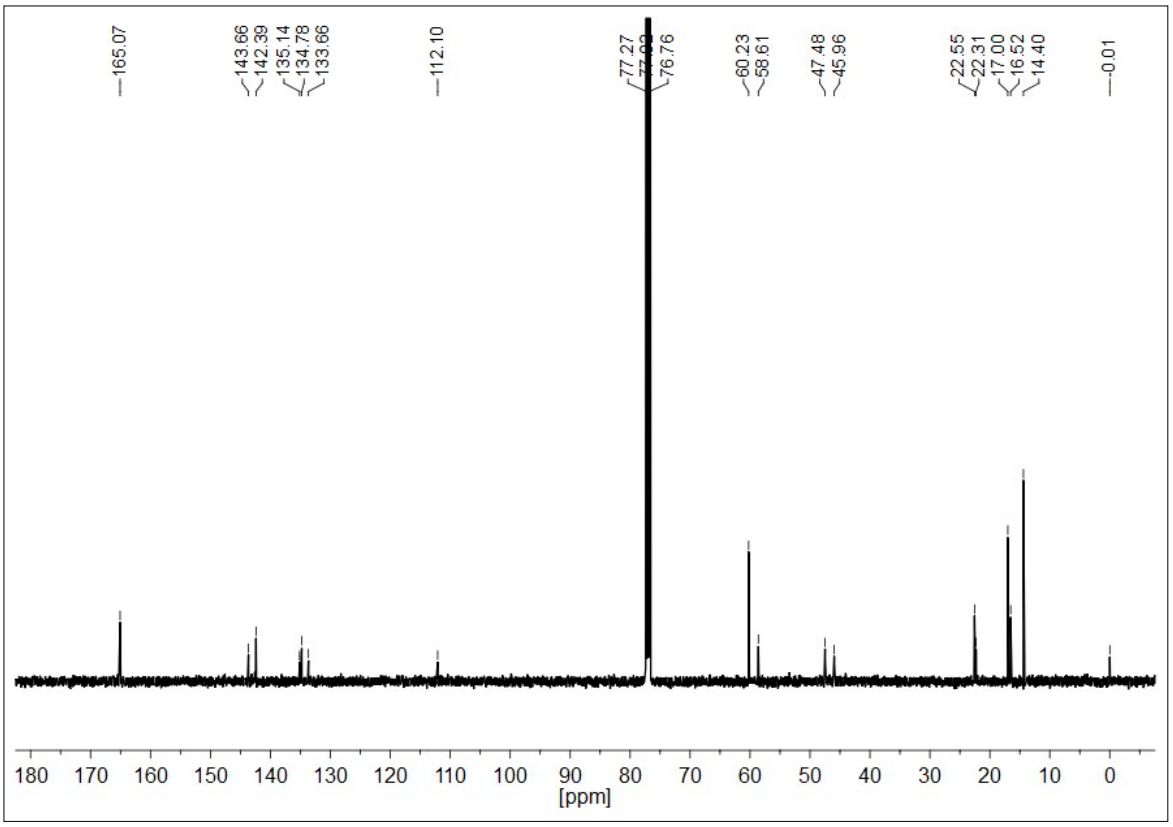


Figure S14. ^{13}C NMR spectrum of compound **14** in $CDCl_3$.

5.4 ^{1}H and ^{13}C NMR spectra of compound **17**.

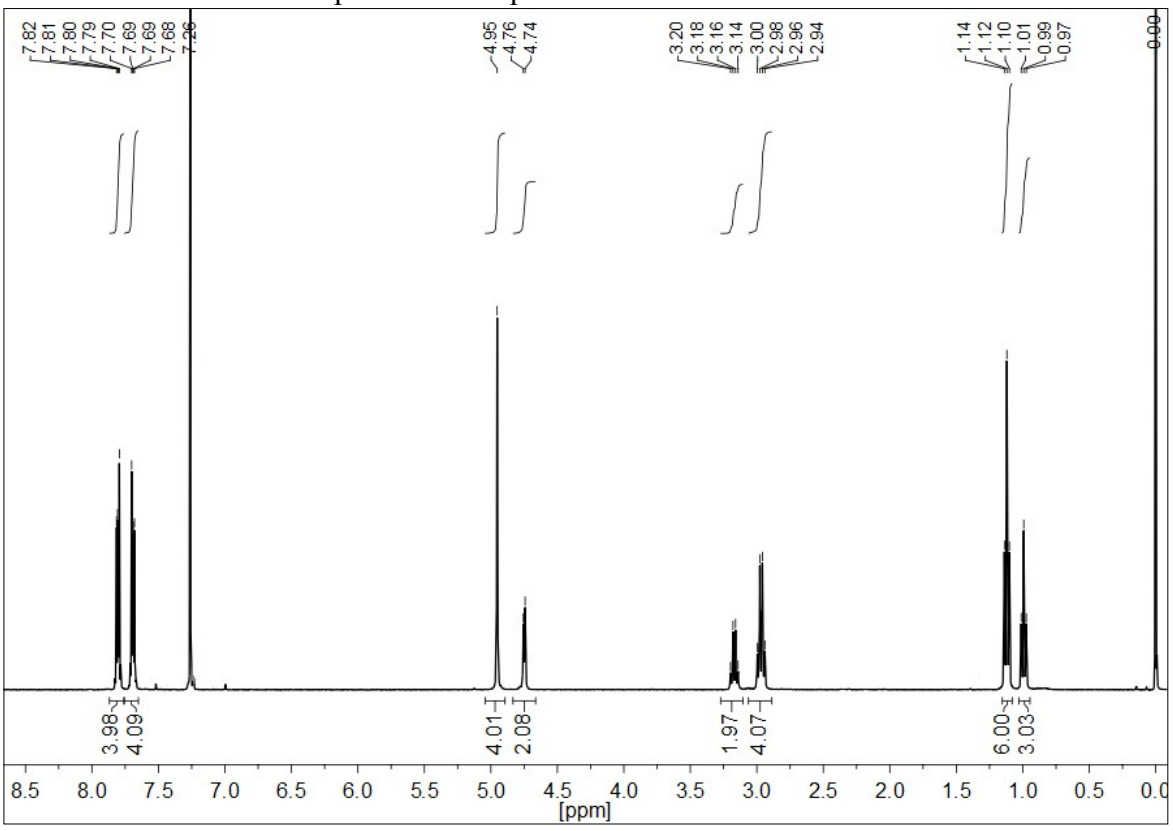


Figure S15. ^{1}H NMR spectrum of **17** in $CDCl_3$.

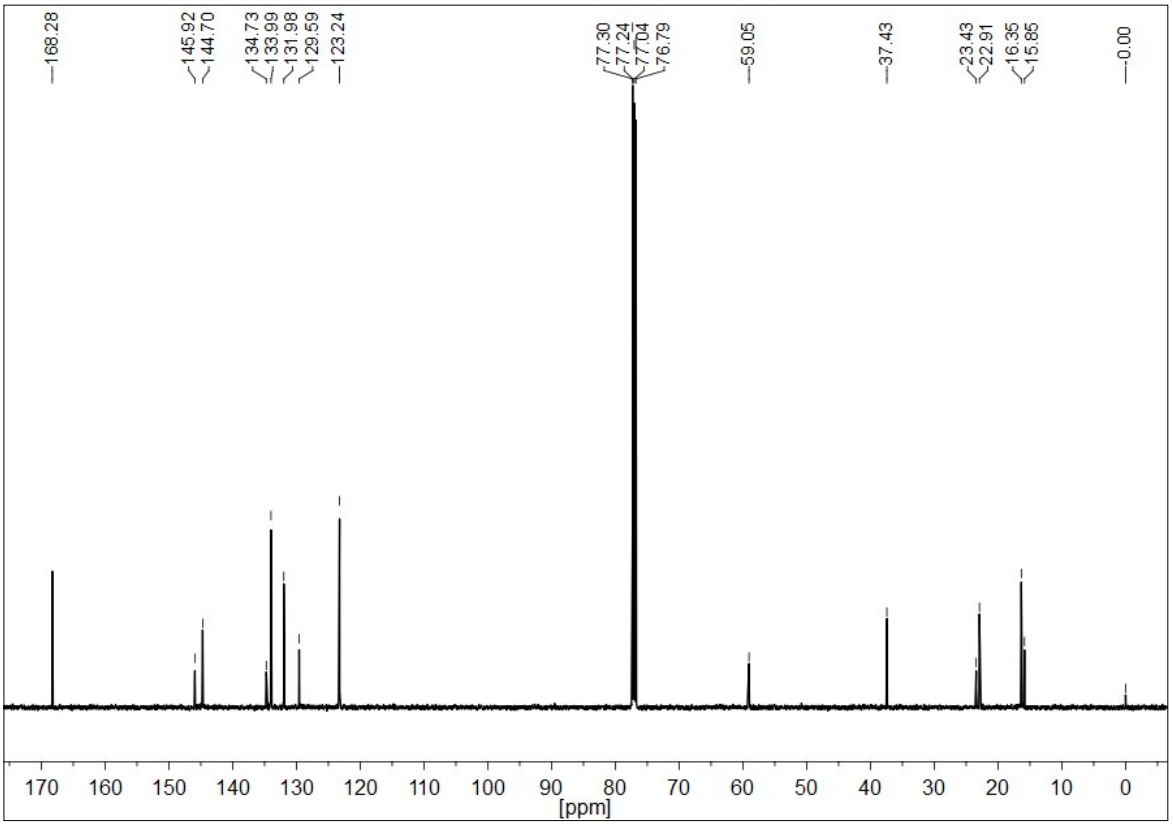


Figure S16. ^{13}C NMR spectrum of **17** in $CDCl_3$.

5.5 ^{1}H and ^{13}C NMR spectra of compound **18**.

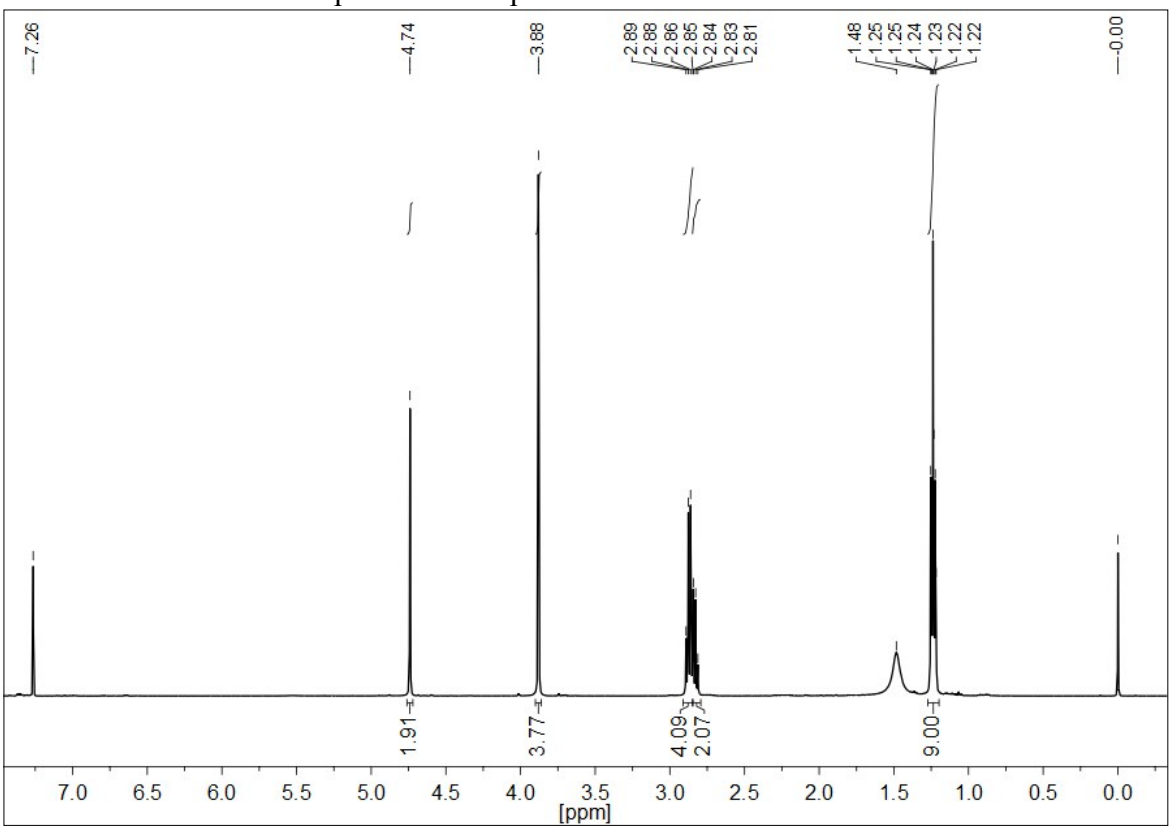


Figure S17. ^{1}H NMR spectrum of **18** in $CDCl_3$.

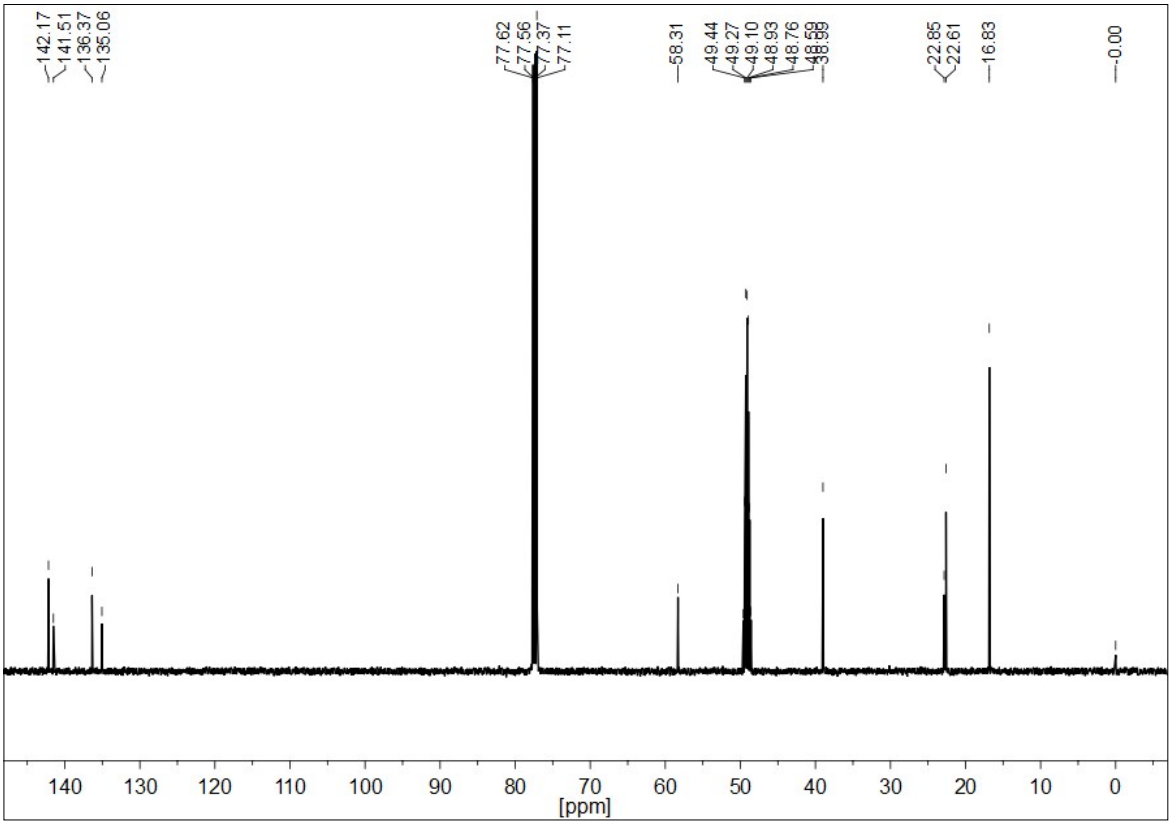


Figure S18. ^{13}C NMR spectrum of **18** in $CDCl_3/CD_3OD$ 50:1 (*v/v*).