Electronic Supporting Information

Conformationally-Locked *C*-Glycosides: Tuning Aglycone Interactions for Optimal Chaperone Behaviour in Gaucher Fibroblasts

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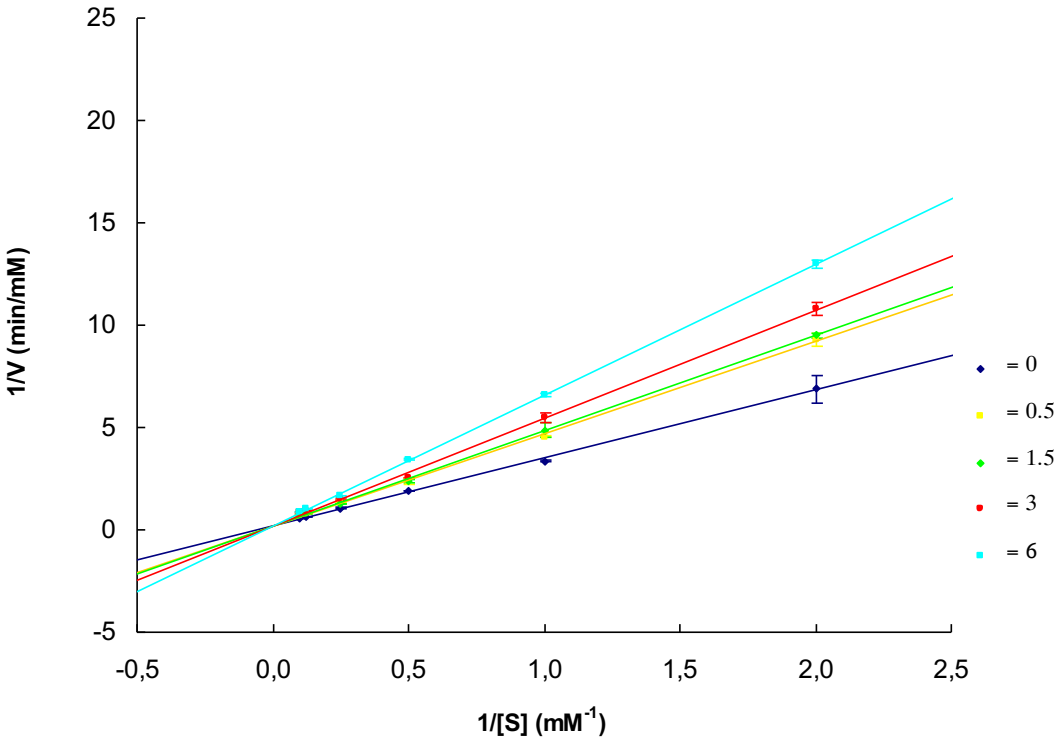
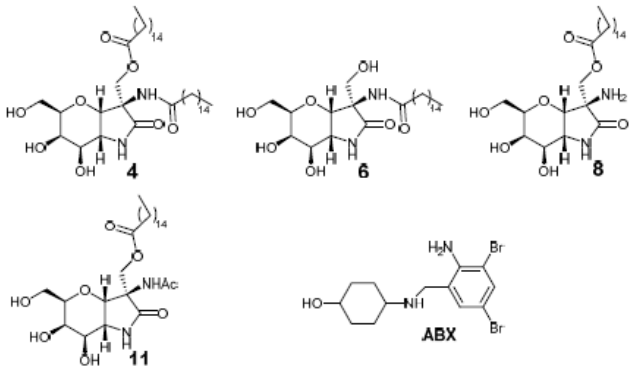


Lineweaver-Burk Plot for K_i determination (9.2 μM) of **APP11** against β-galactosidase (bovine liver) (pH 7.3). We have performed two replicas of each experiment.

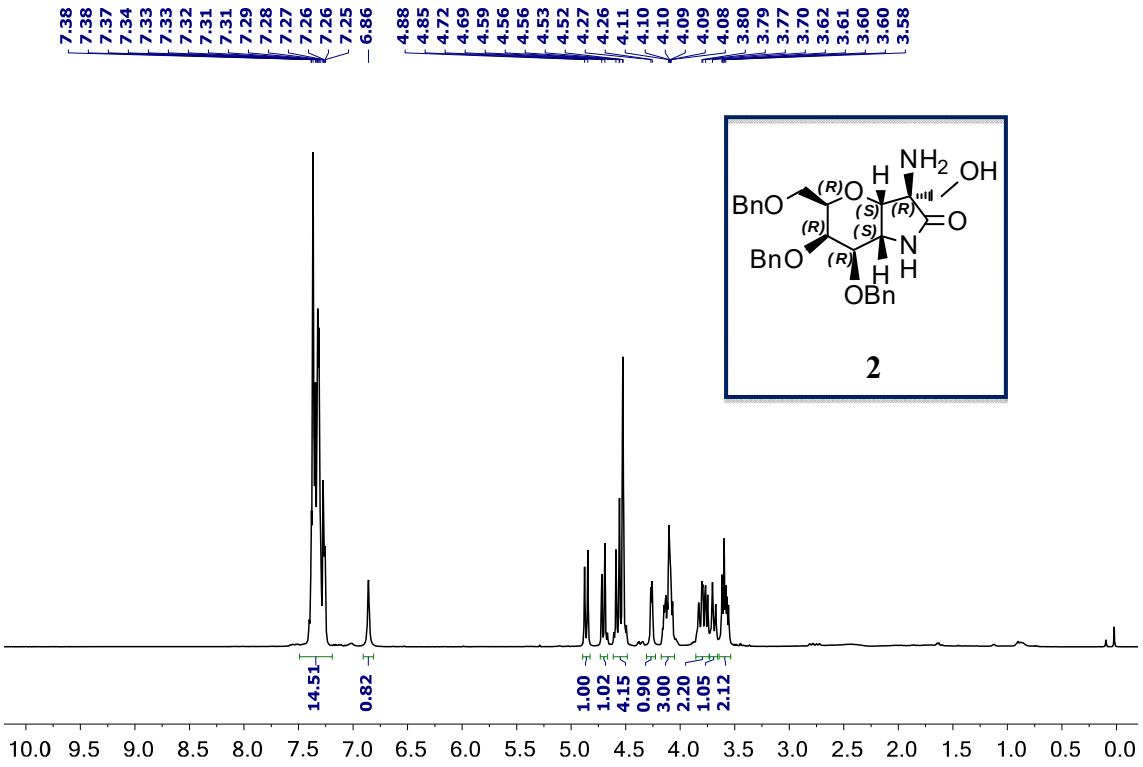
Table S1. IC_{50} values (μM) against human GCase for APP derivatives **4**, **6**, **8** and **11**.



Compound	GCase pH 7	GCase pH 5
4	41±1	470±20
6	23±1	272±10
8	49±2	606±10
11	67±5	707±20
ABX	7.6±0.5	90±5

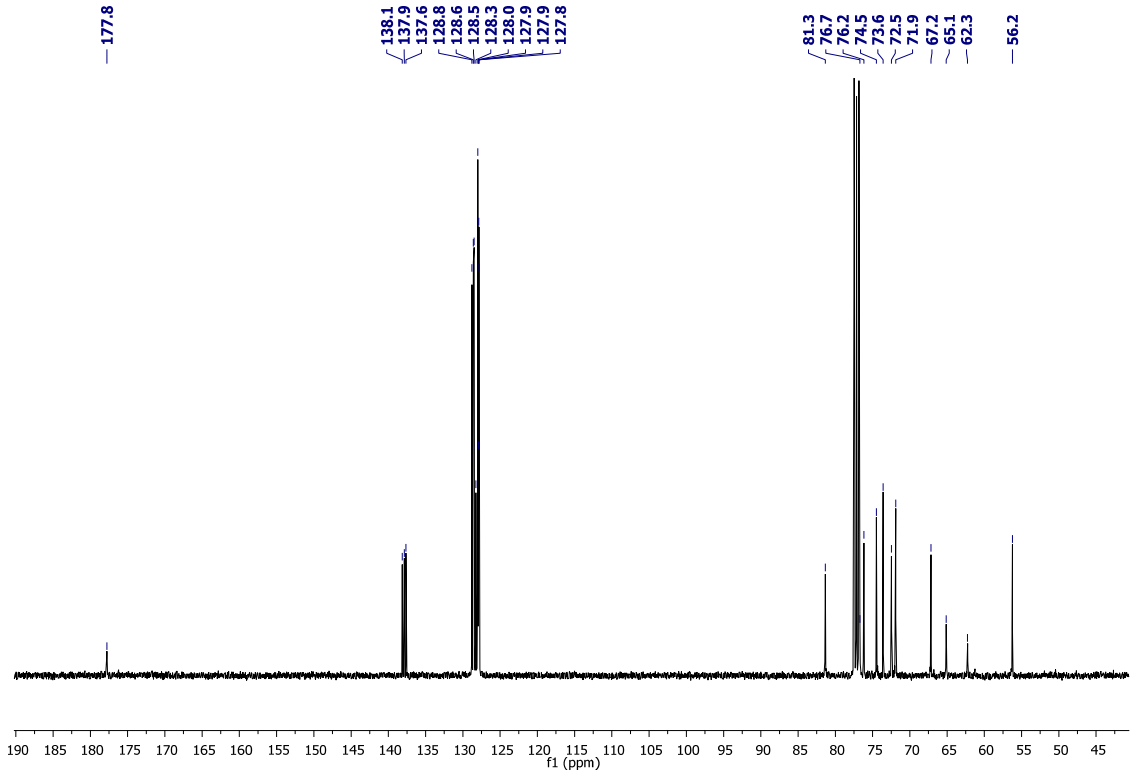
Compound 2

^{1}H NMR 400 MHz in $CDCl_3$

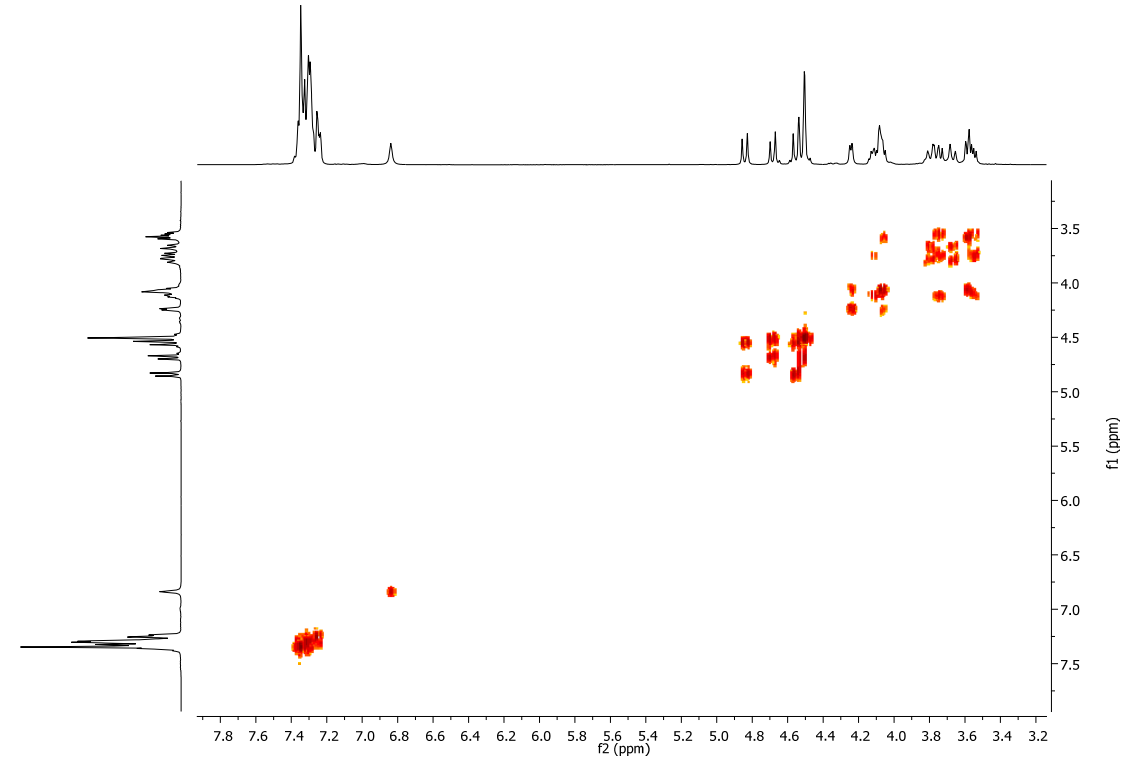


2

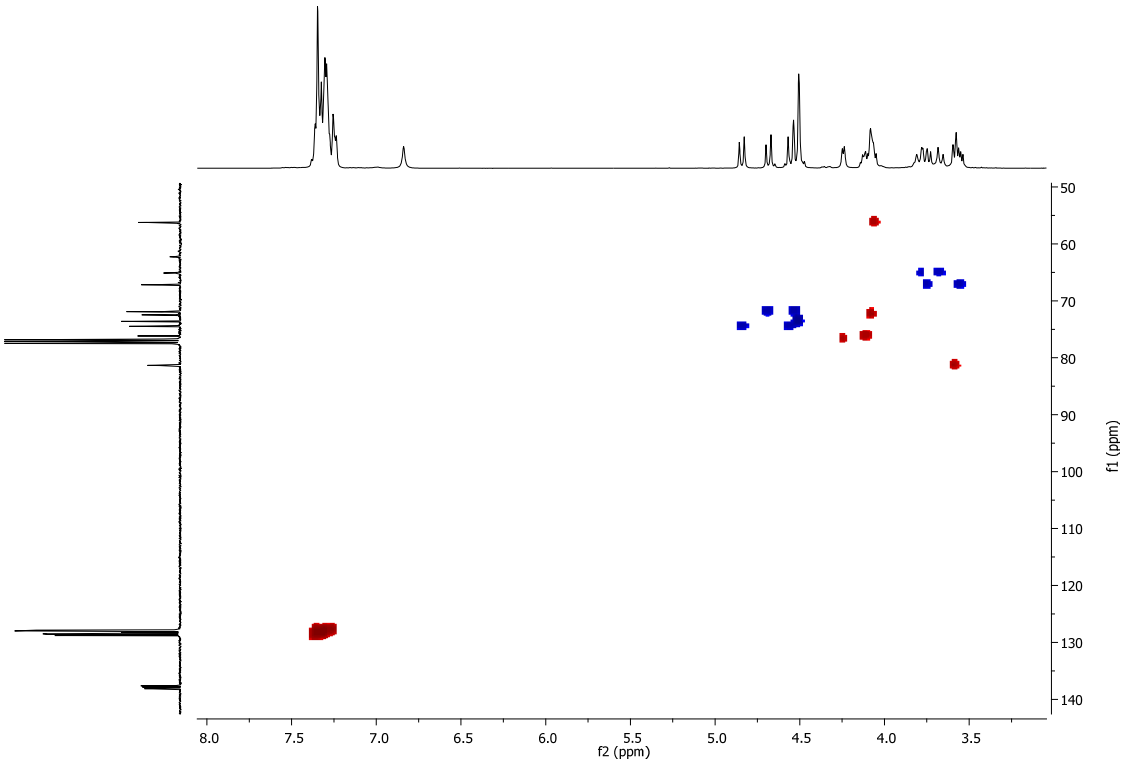
^{13}C NMR 100MHz in $CDCl_3$



COSY in $CDCl_3$

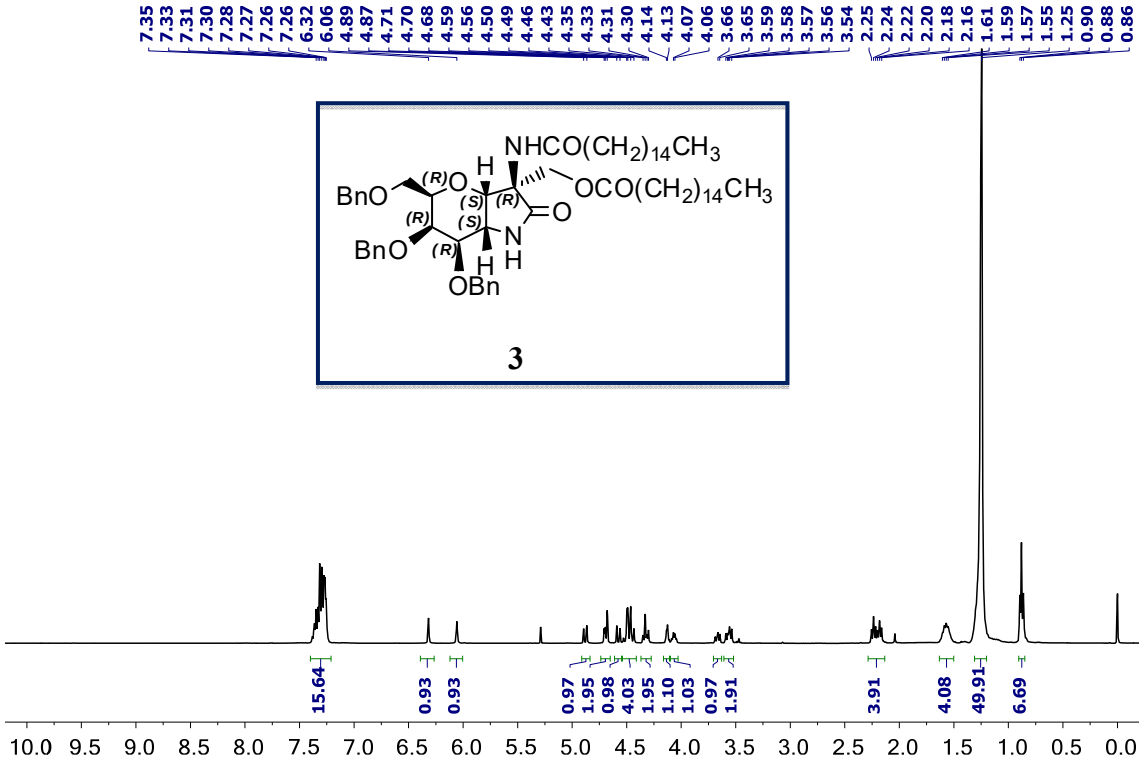


HSQC in $CDCl_3$

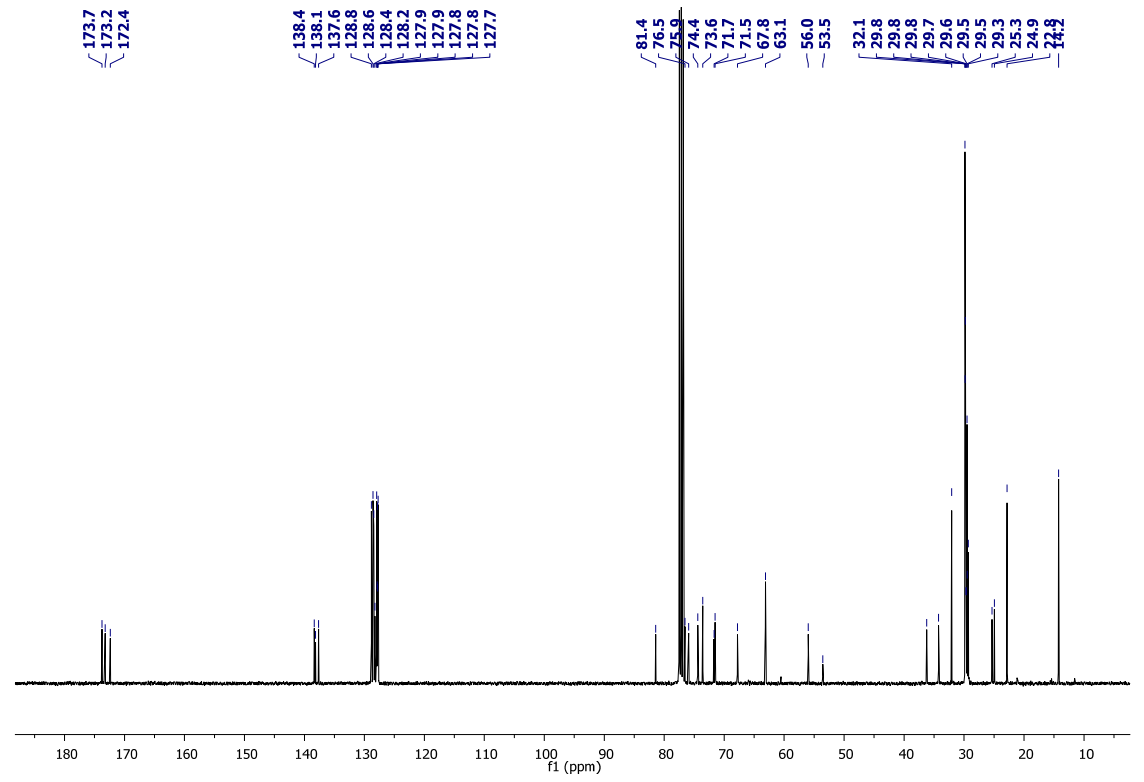


Compound 3

^{1}H NMR 400 MHz in $CDCl_3$



^{13}C NMR 100MHz in $CDCl_3$



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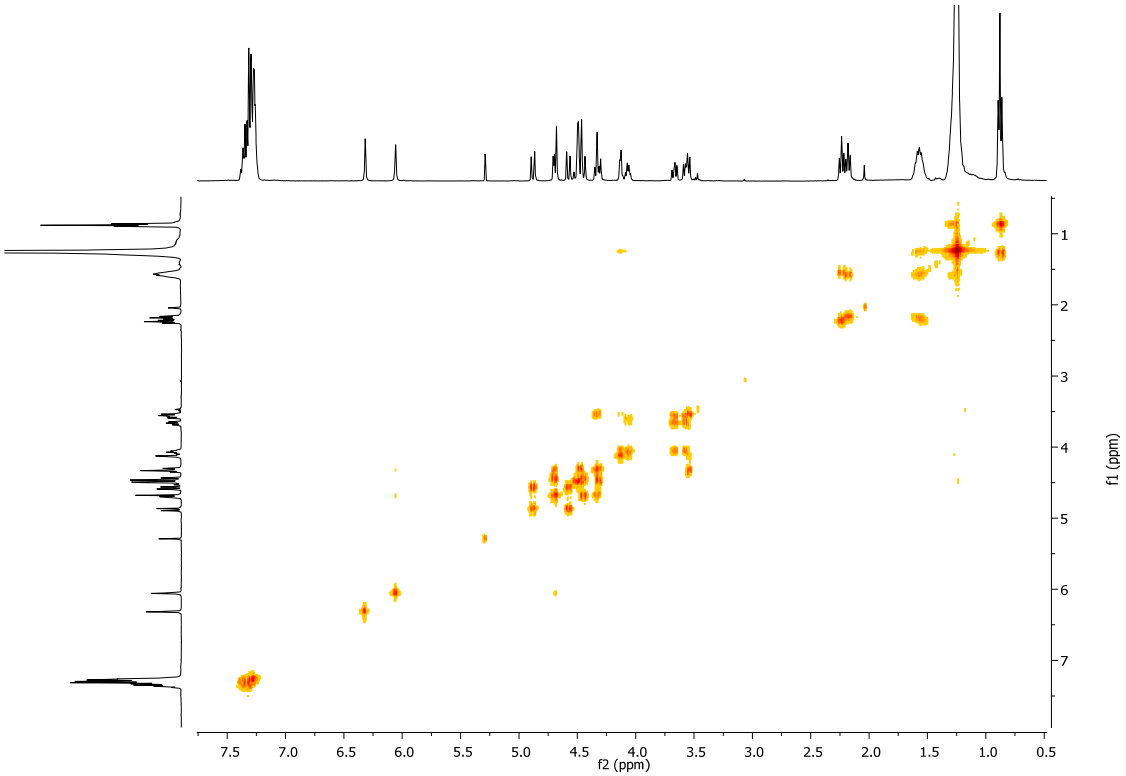

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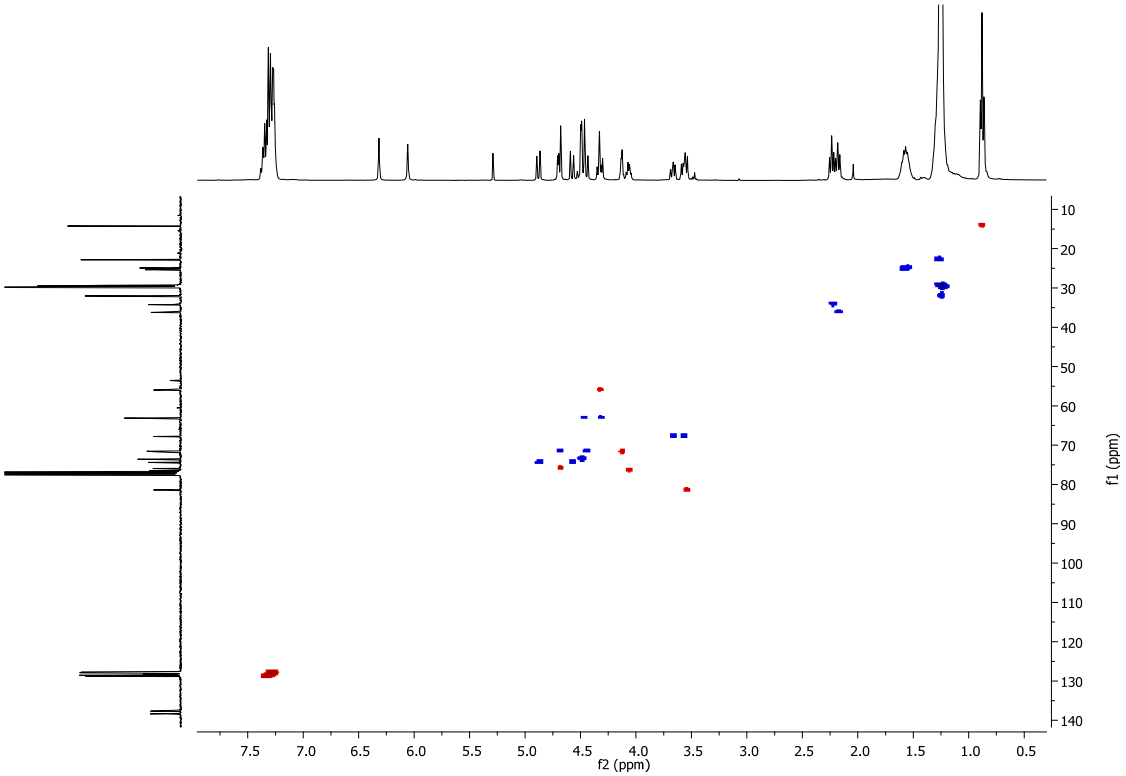
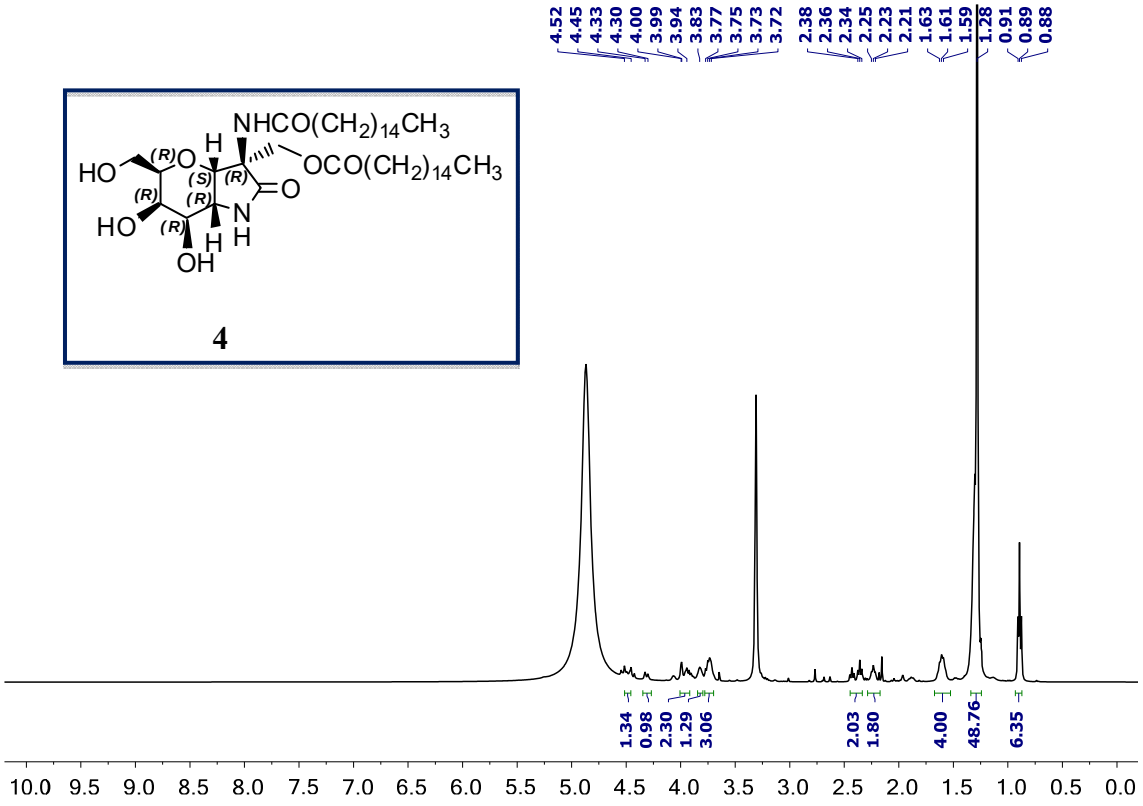
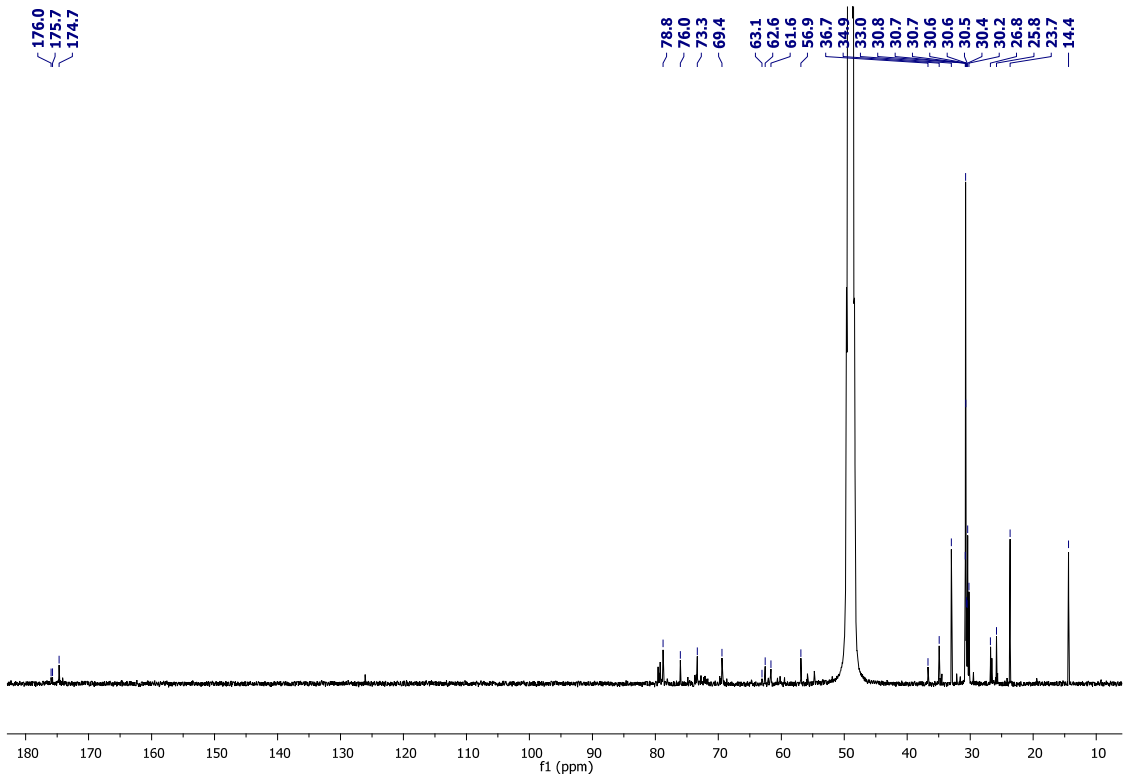


Compound 4

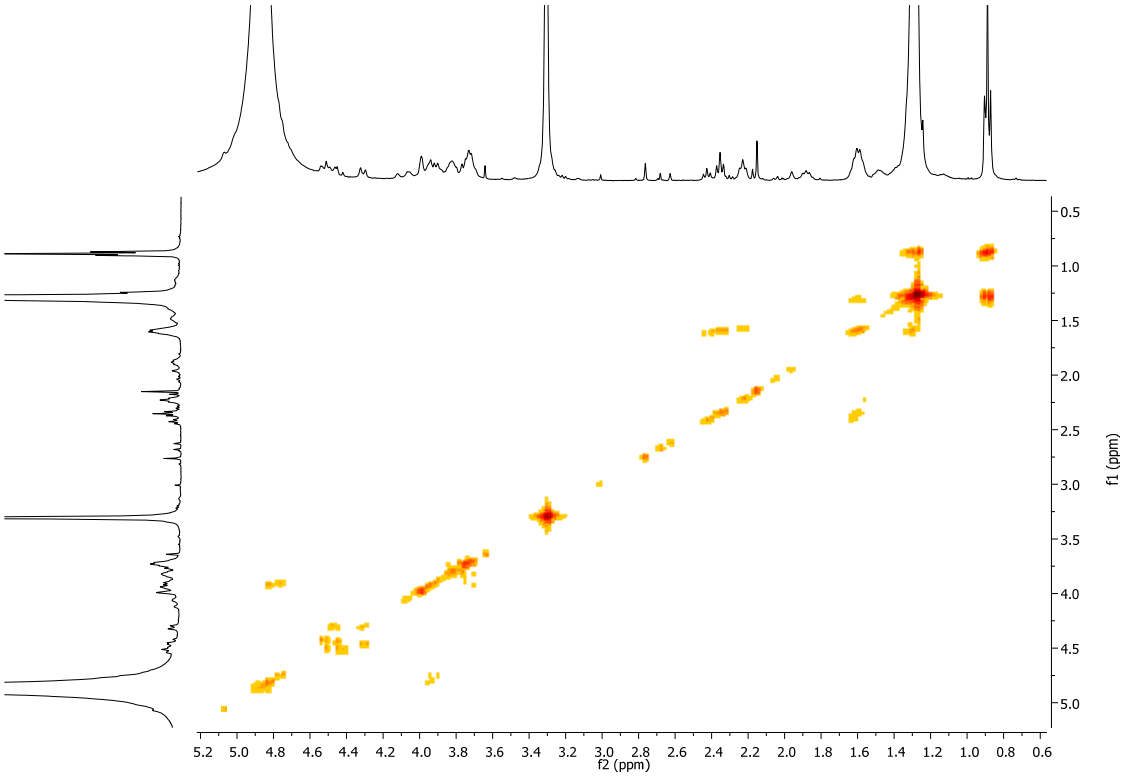
^{1}H NMR 400 MHz in CD_3OD



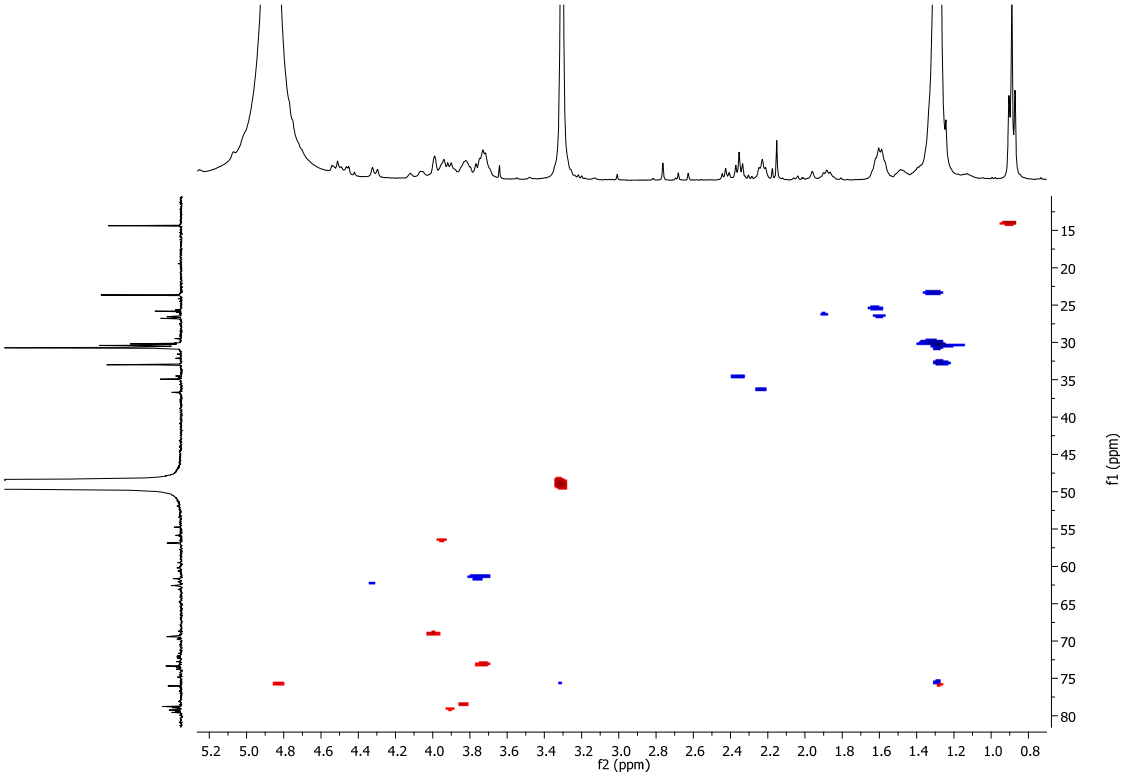
^{13}C NMR 100MHz in CD_3OD



COSY in CD_3OD

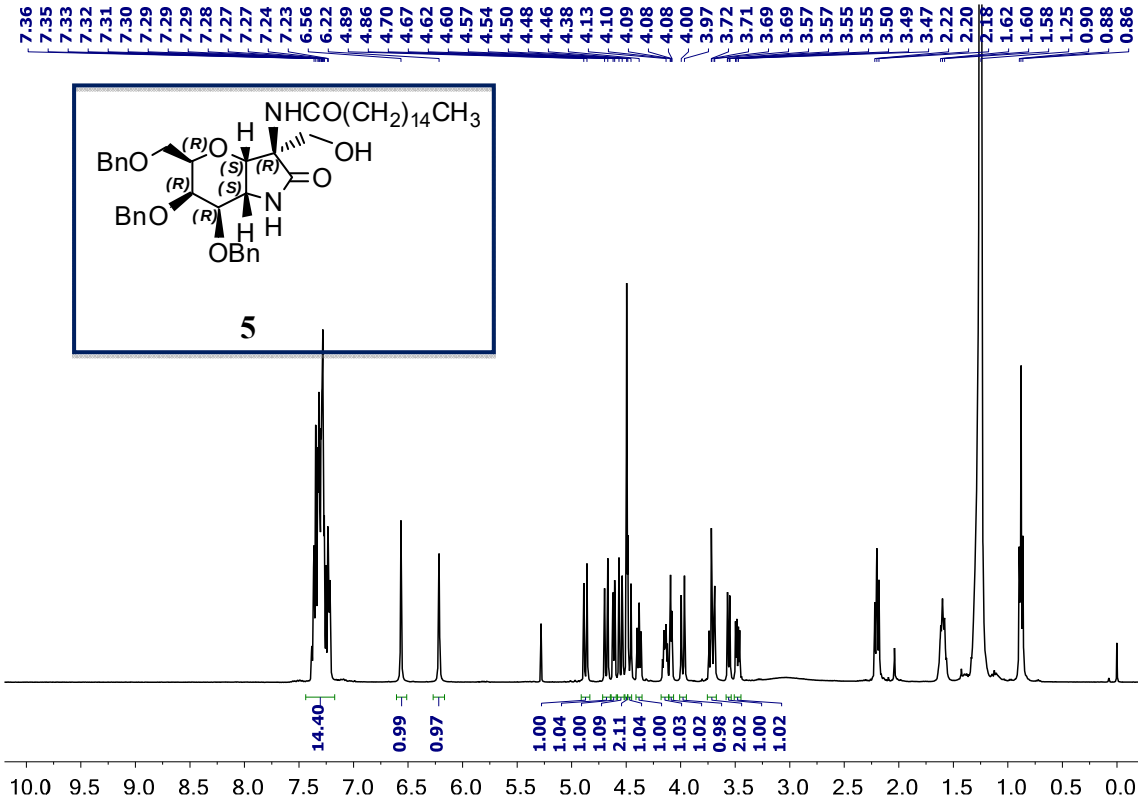


HSQC in CD_3OD

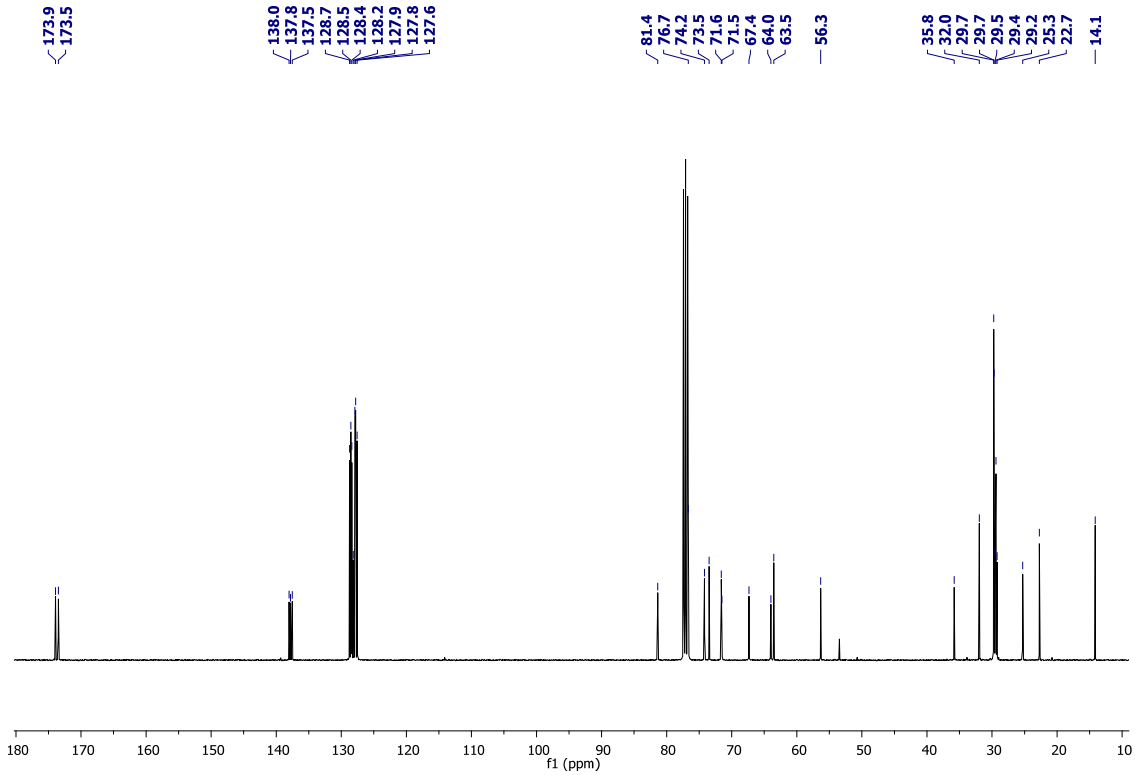


Compound 5

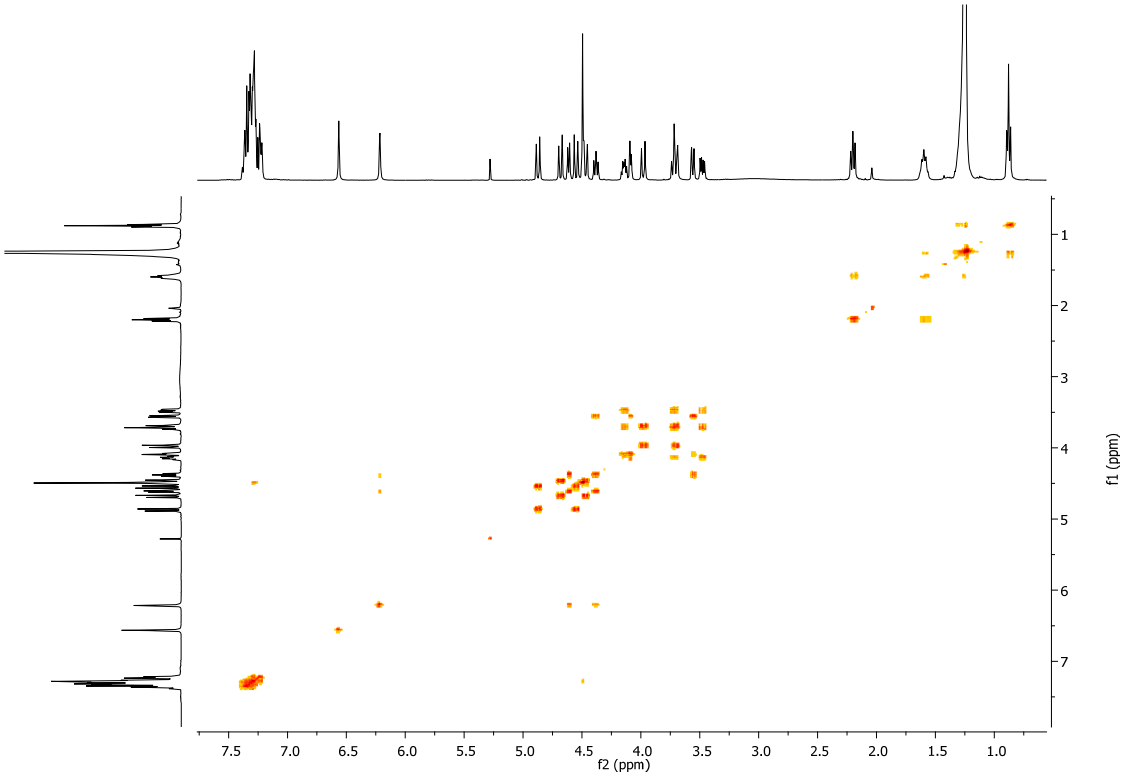
^{1}H NMR 400 MHz in $CDCl_3$



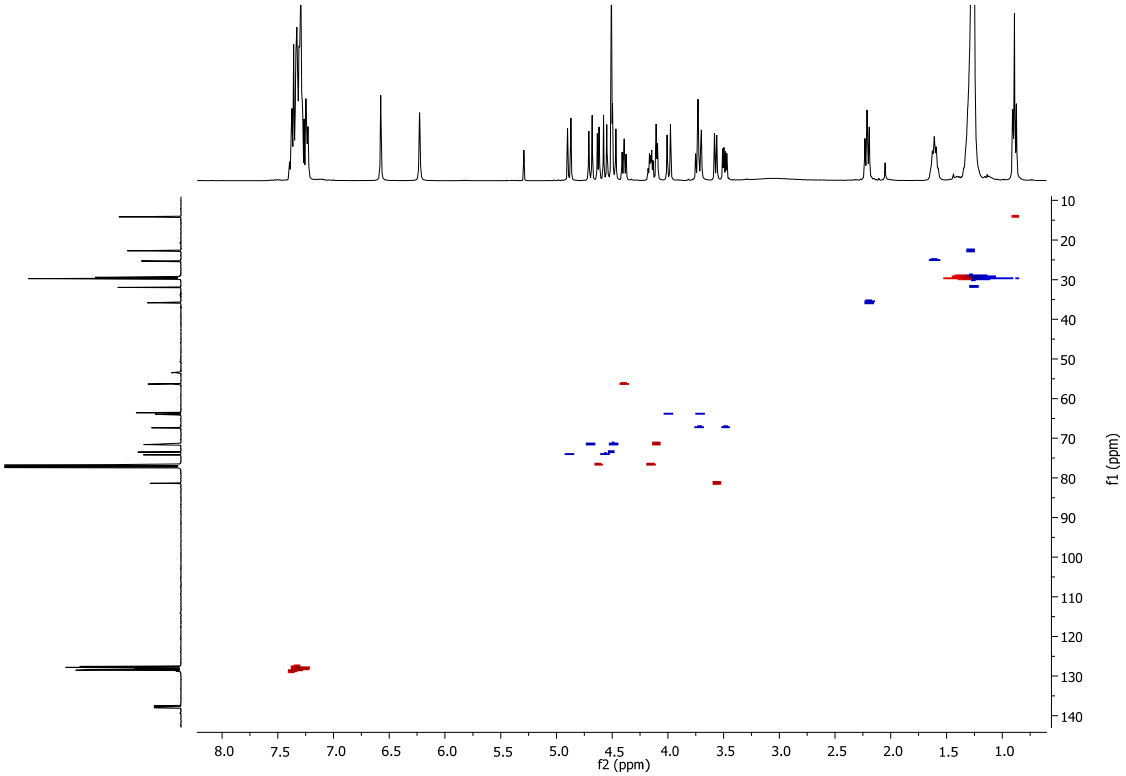
^{13}C NMR 100MHz in $CDCl_3$



COSY in $CDCl_3$

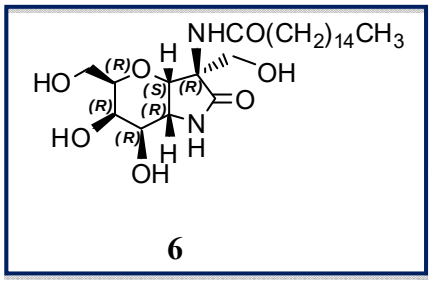


HSQC in $CDCl_3$



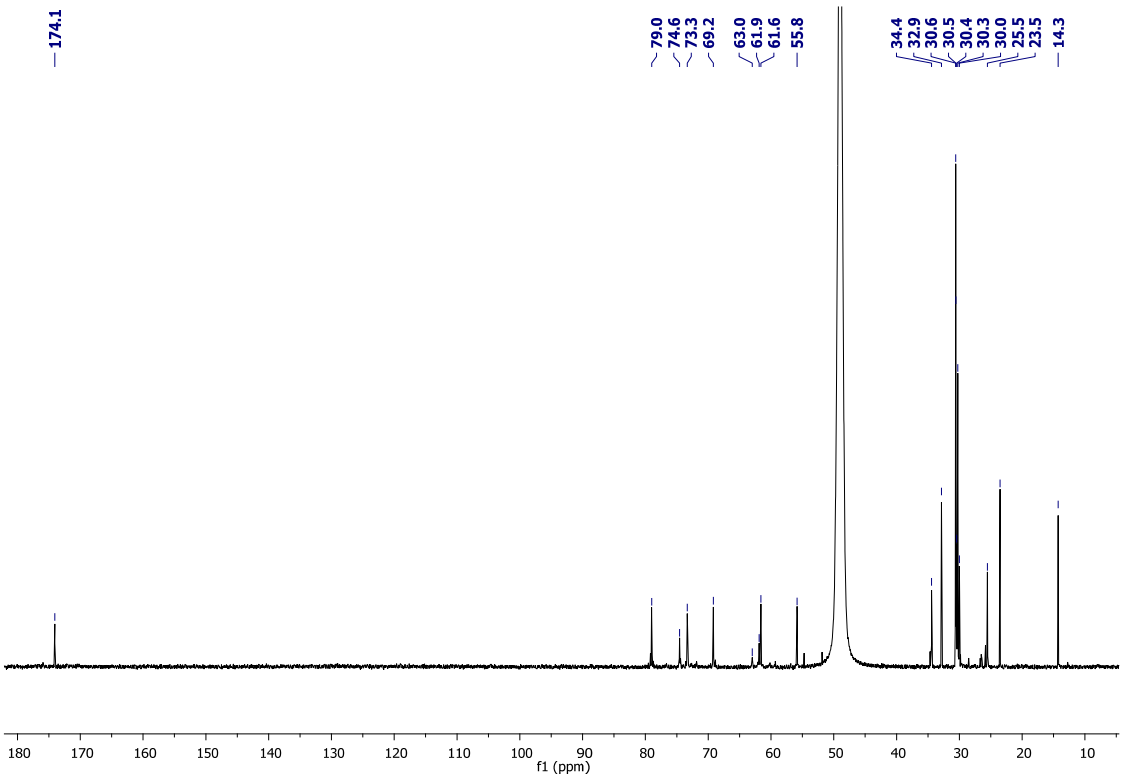
Compound 6

^{1}H NMR 400 MHz in CD_3OD

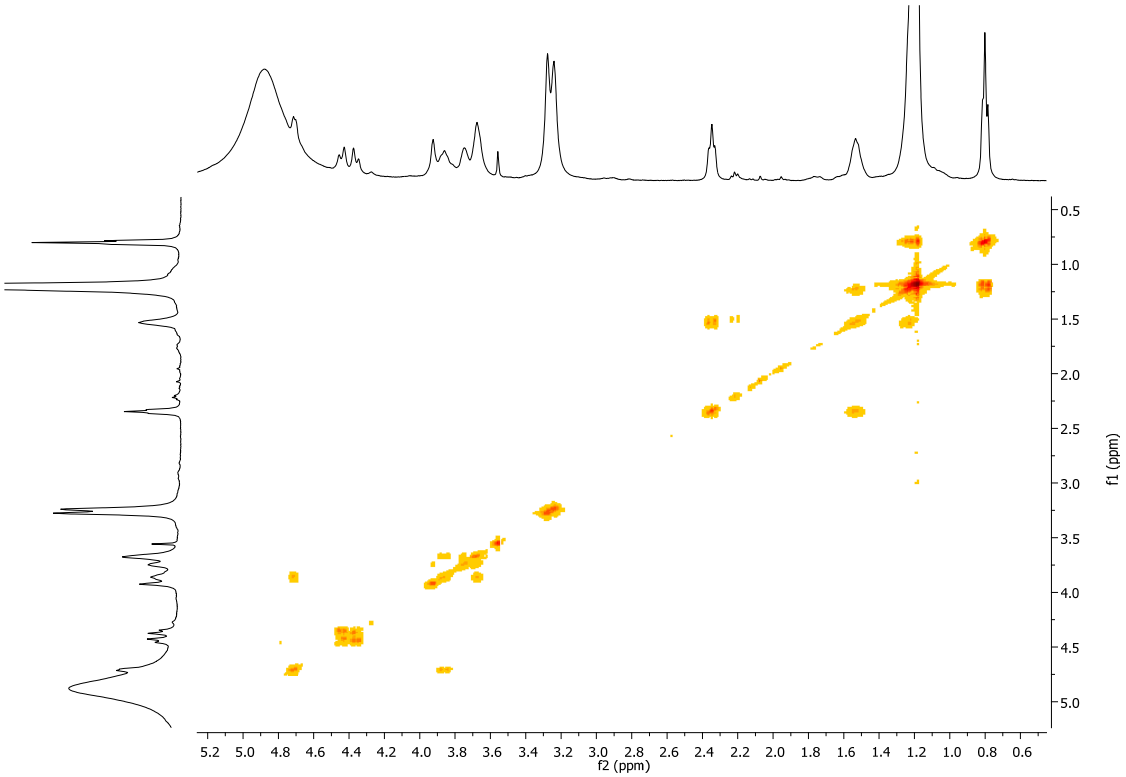


6

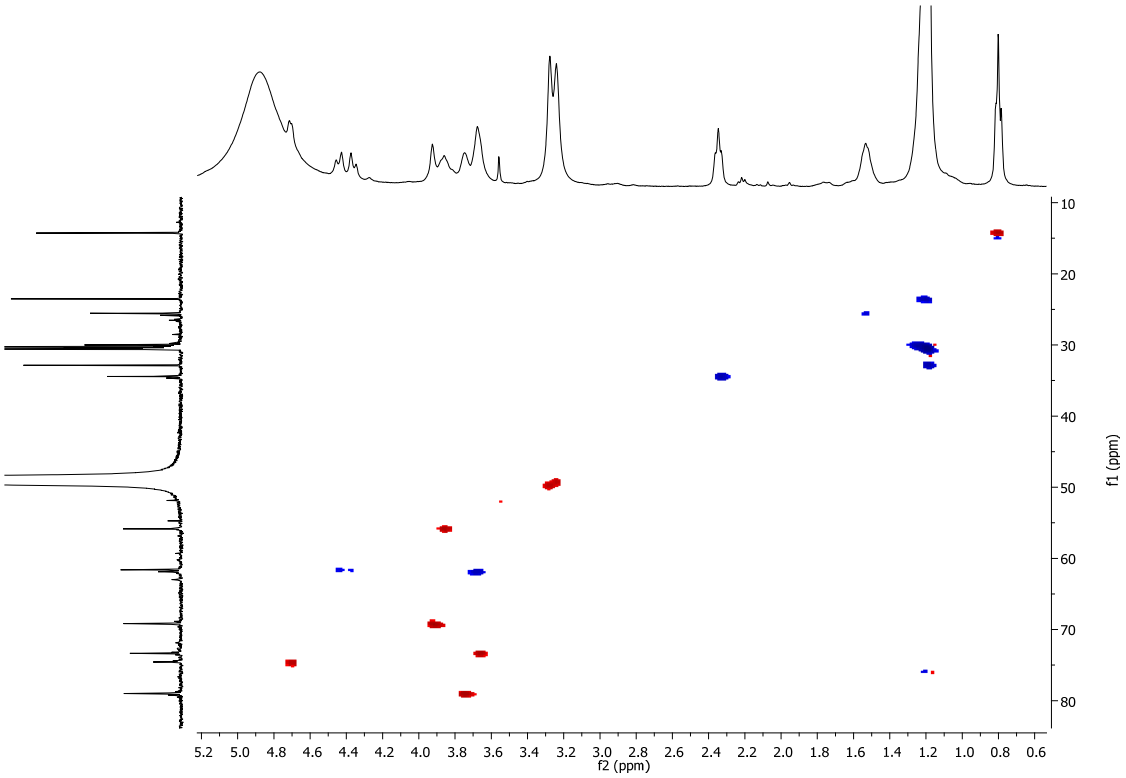
^{13}C NMR 100MHz in CD_3OD



COSY in CD_3OD

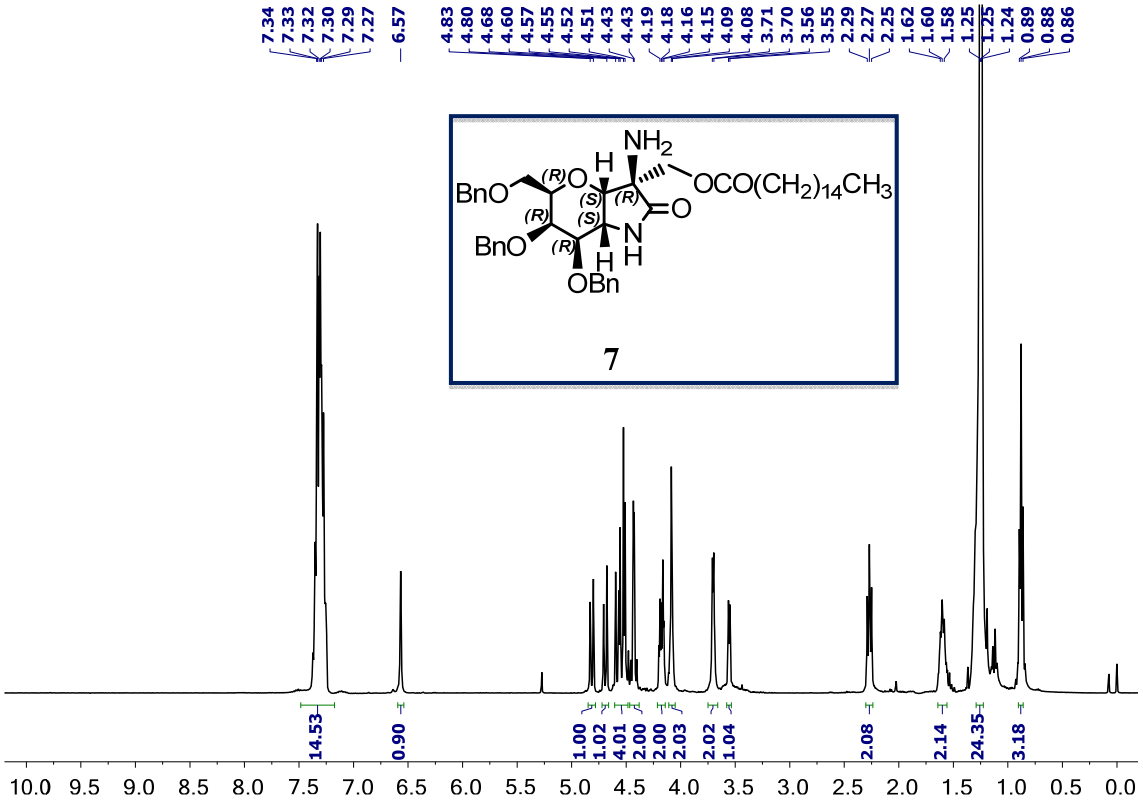


HSQC in CD_3OD



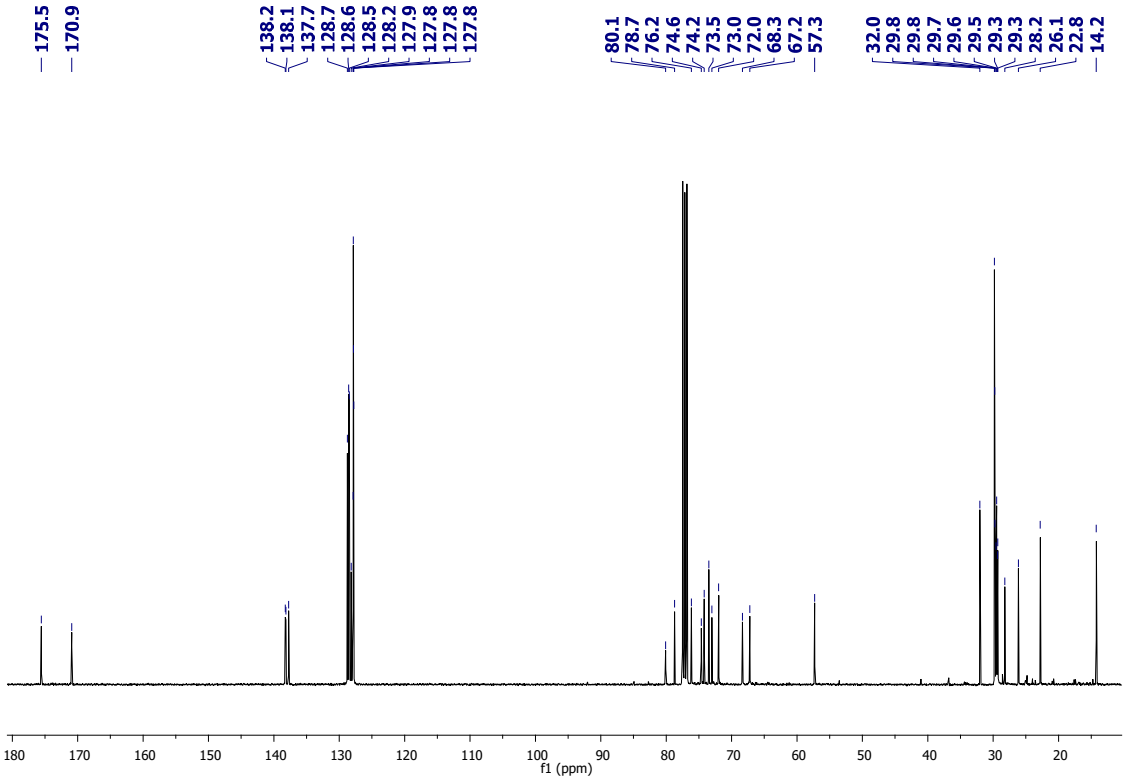
Compound 7

^{1}H NMR 400 MHz in $CDCl_3$



7

^{13}C NMR 100MHz in $CDCl_3$



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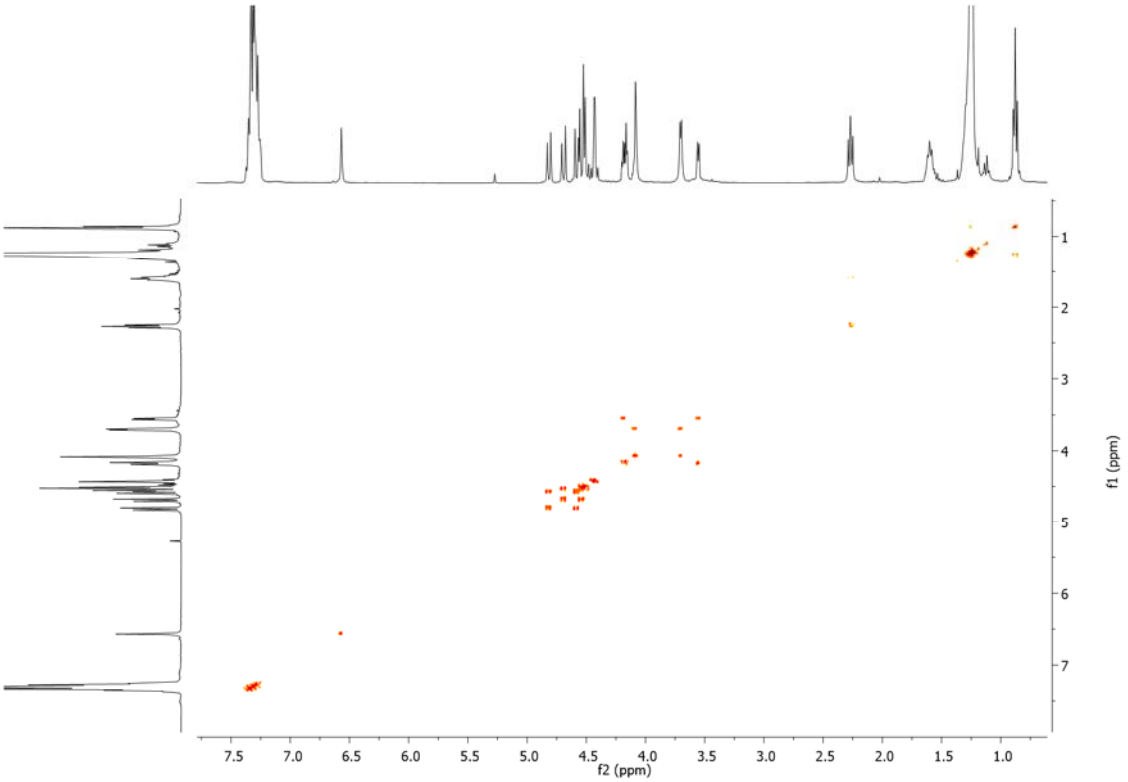

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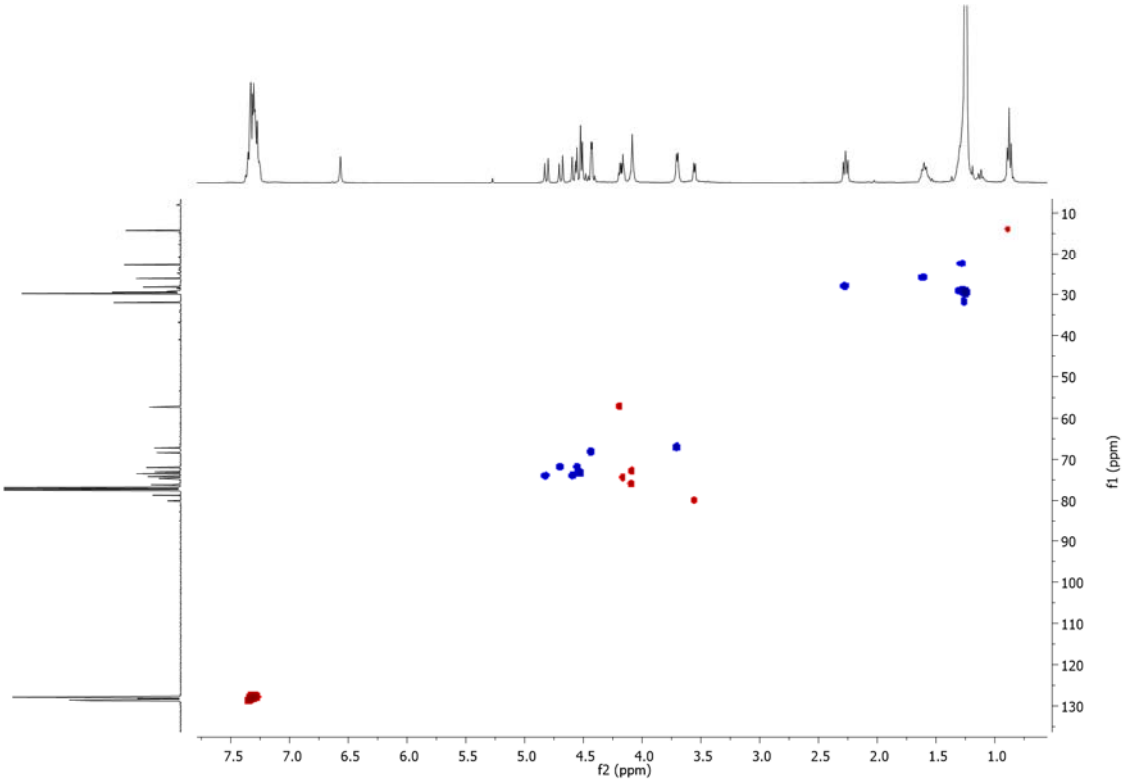
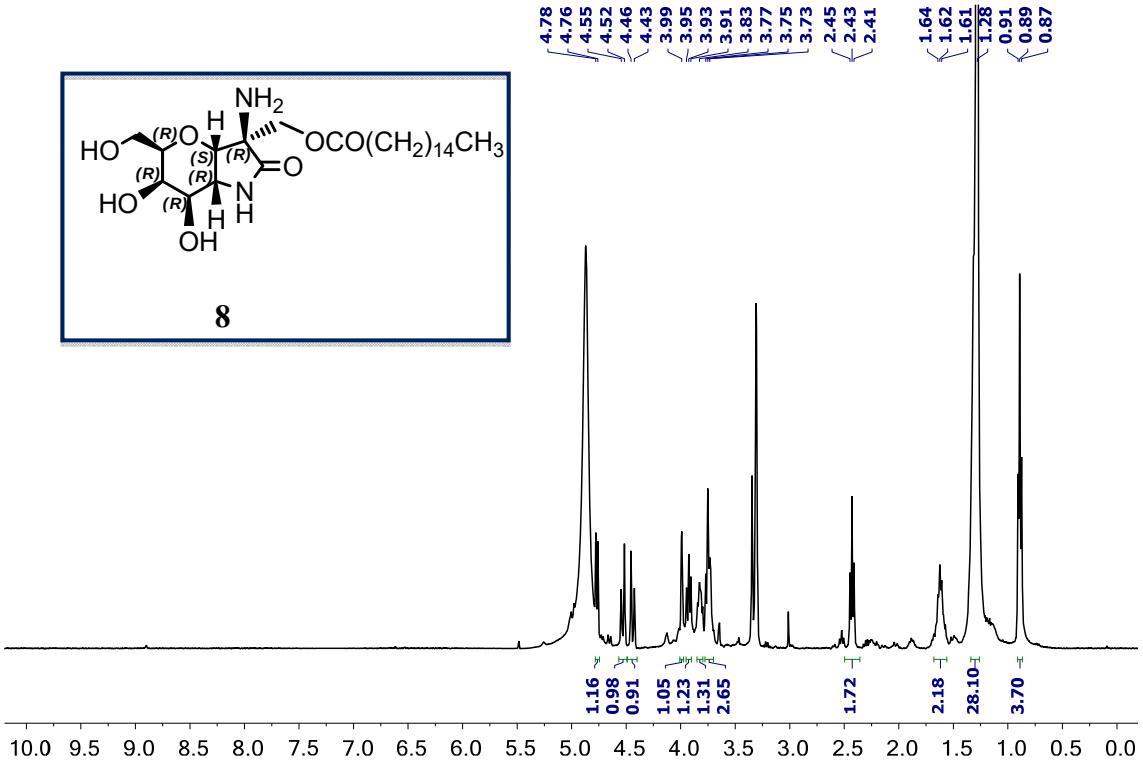


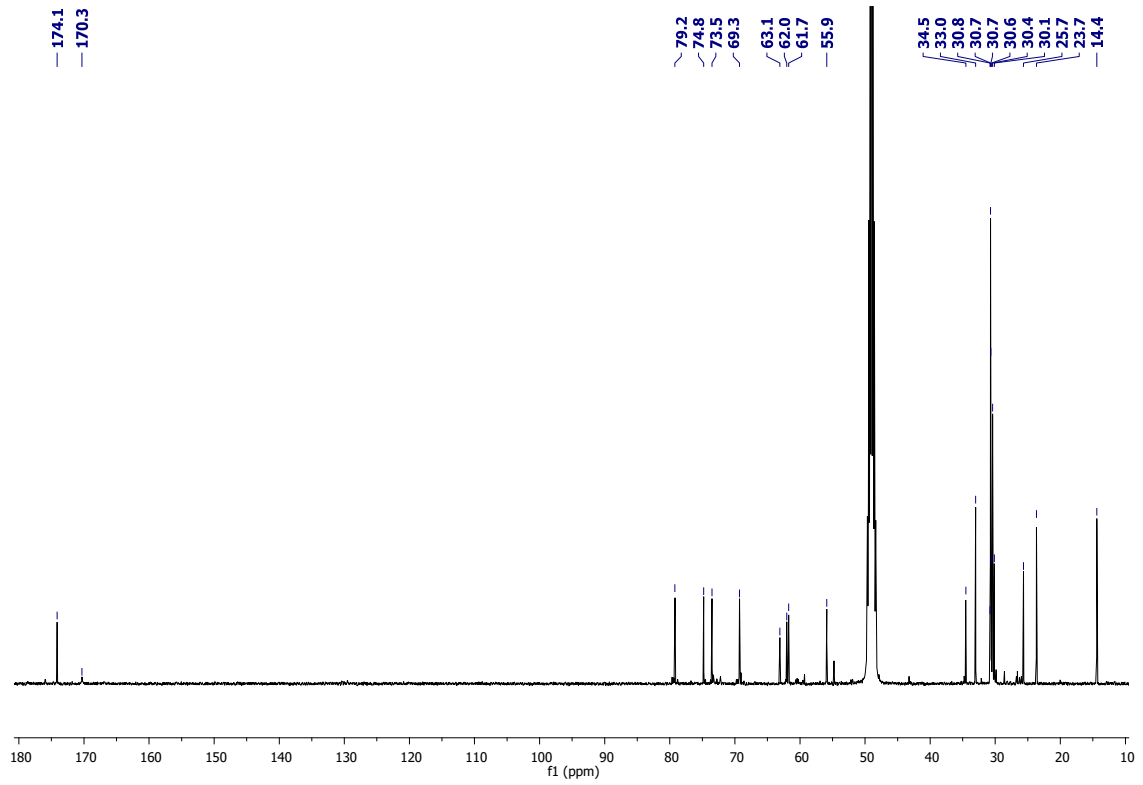
Compound 8

^{1}H NMR 400 MHz in CD_3OD

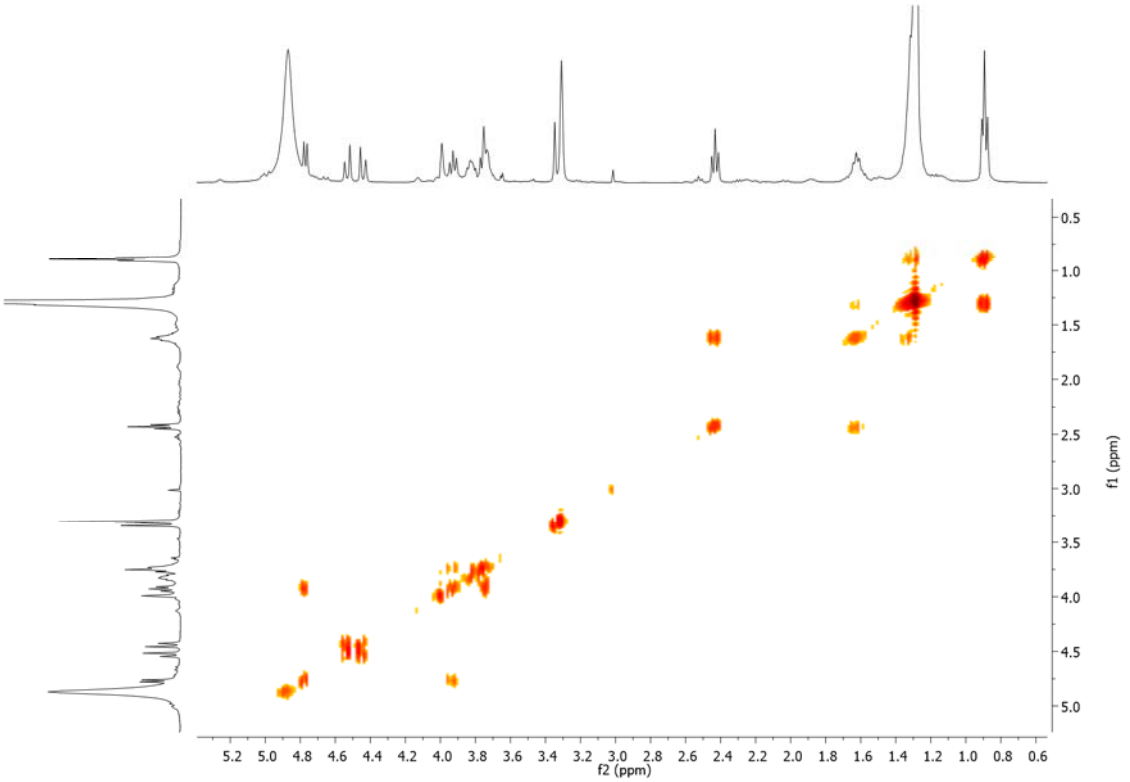


8

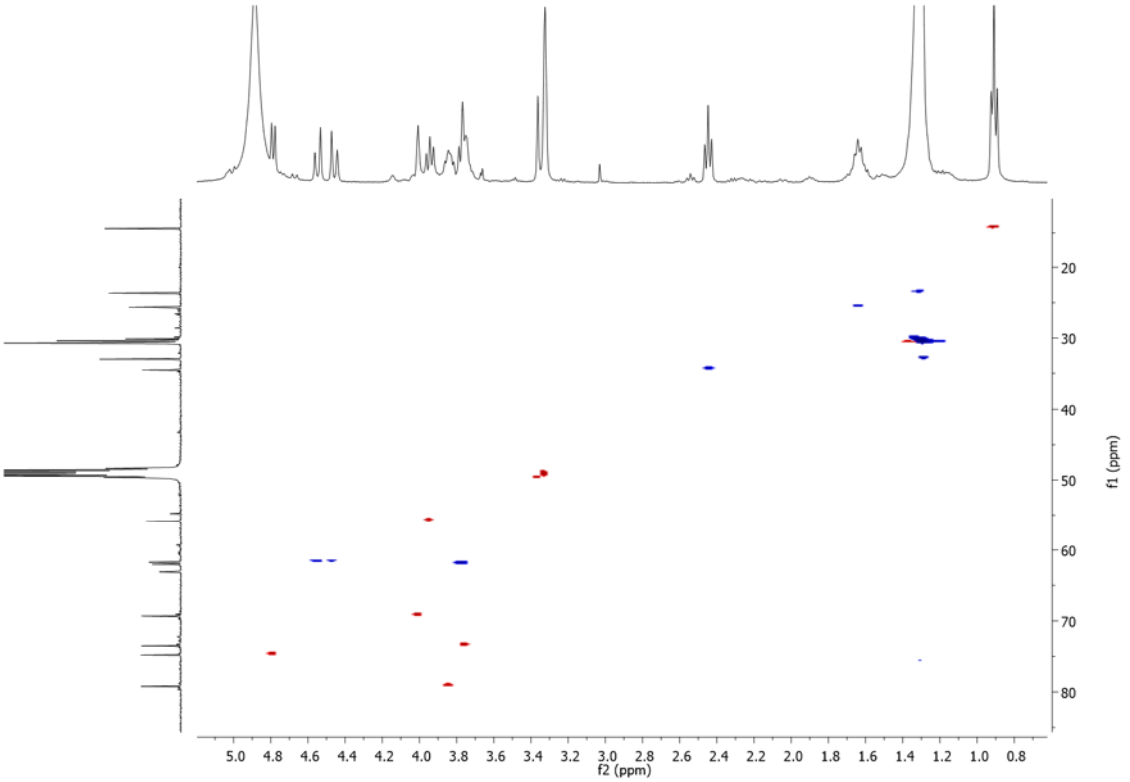
^{13}C NMR 100MHz in CD_3OD



COSY in CD_3OD

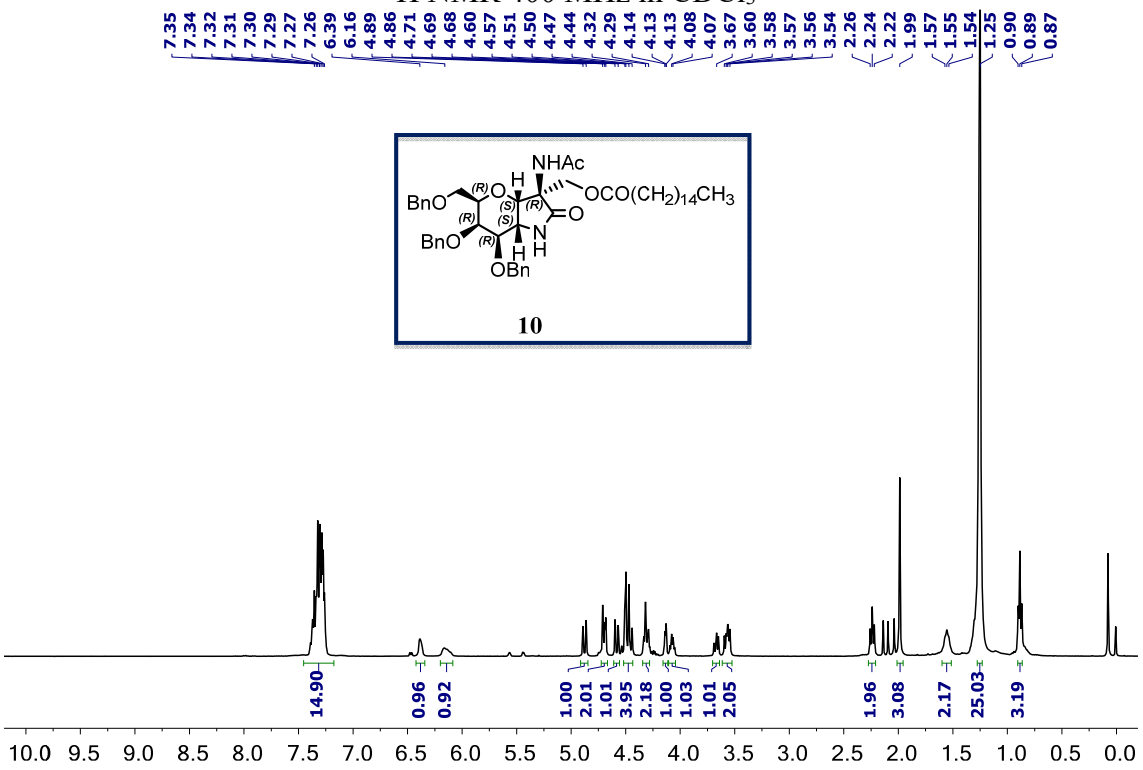


HSQC in CD_3OD

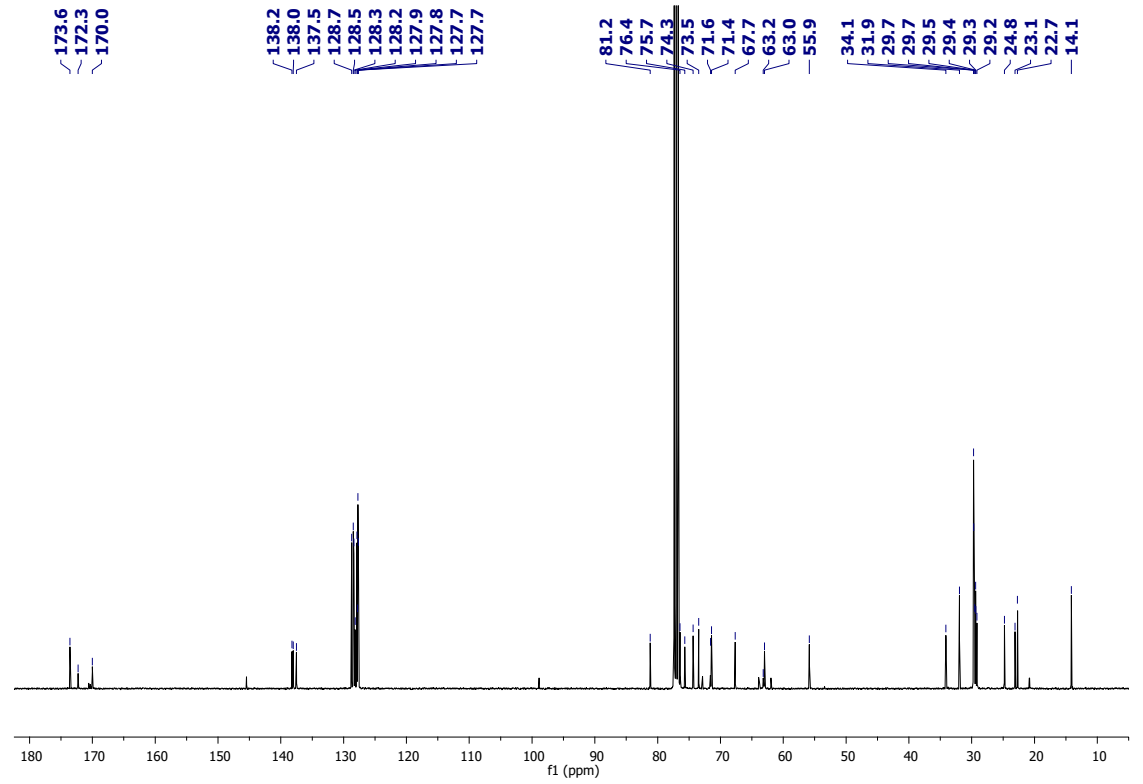


Compound 10

^{1}H NMR 400 MHz in $CDCl_3$



^{13}C NMR 100 MHz in $CDCl_3$



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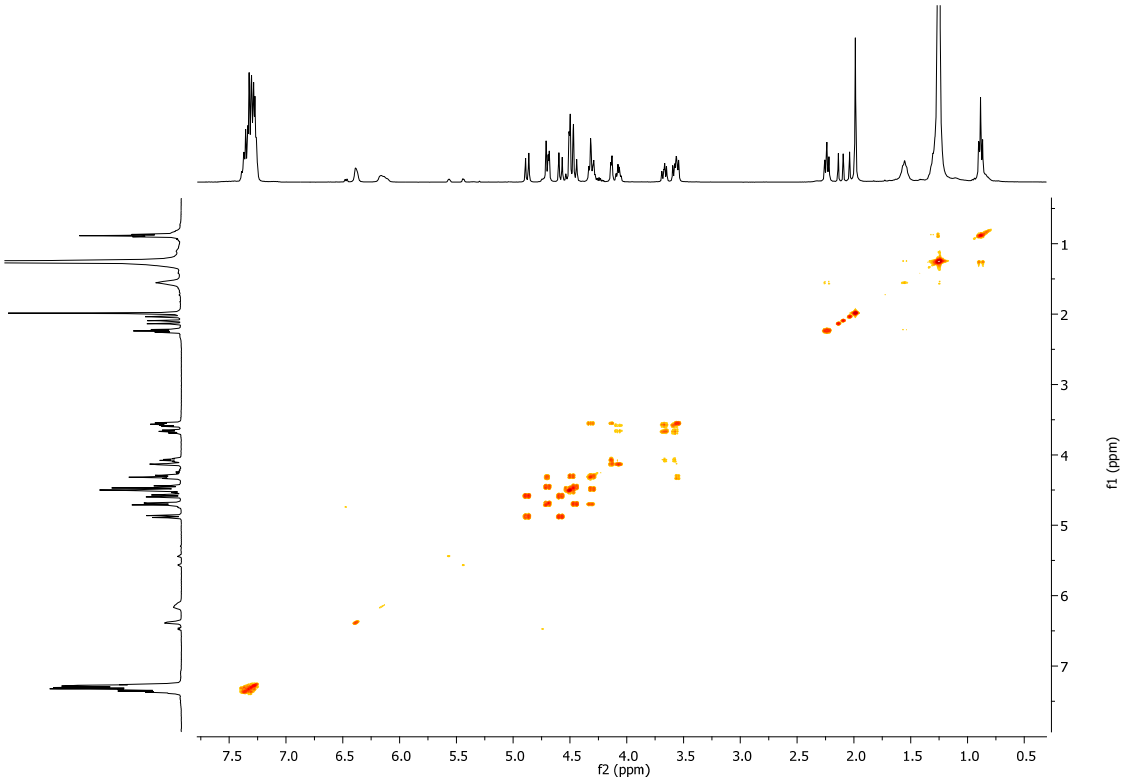

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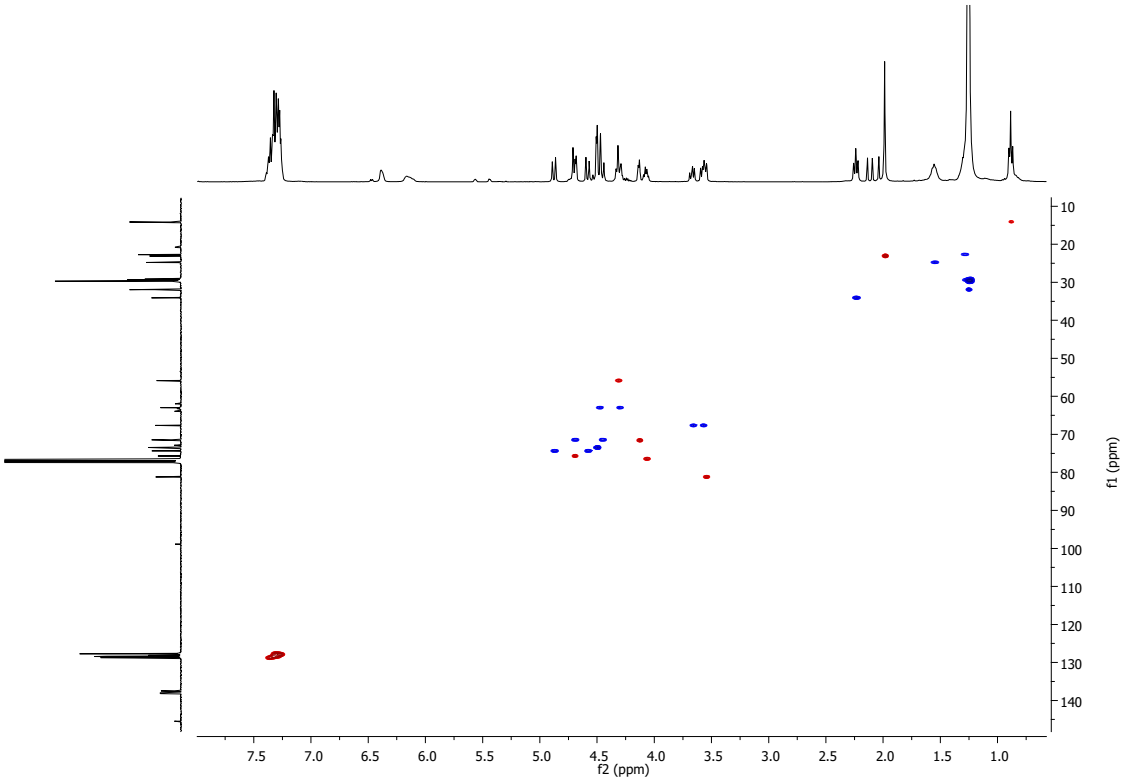
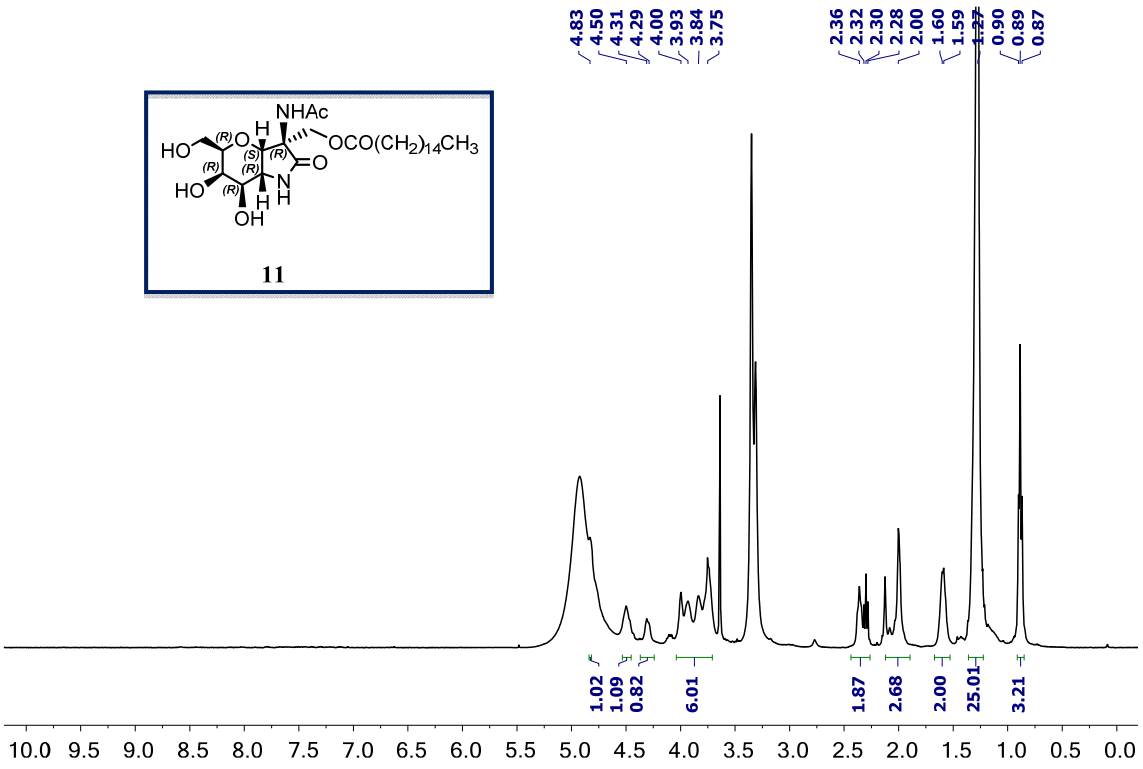
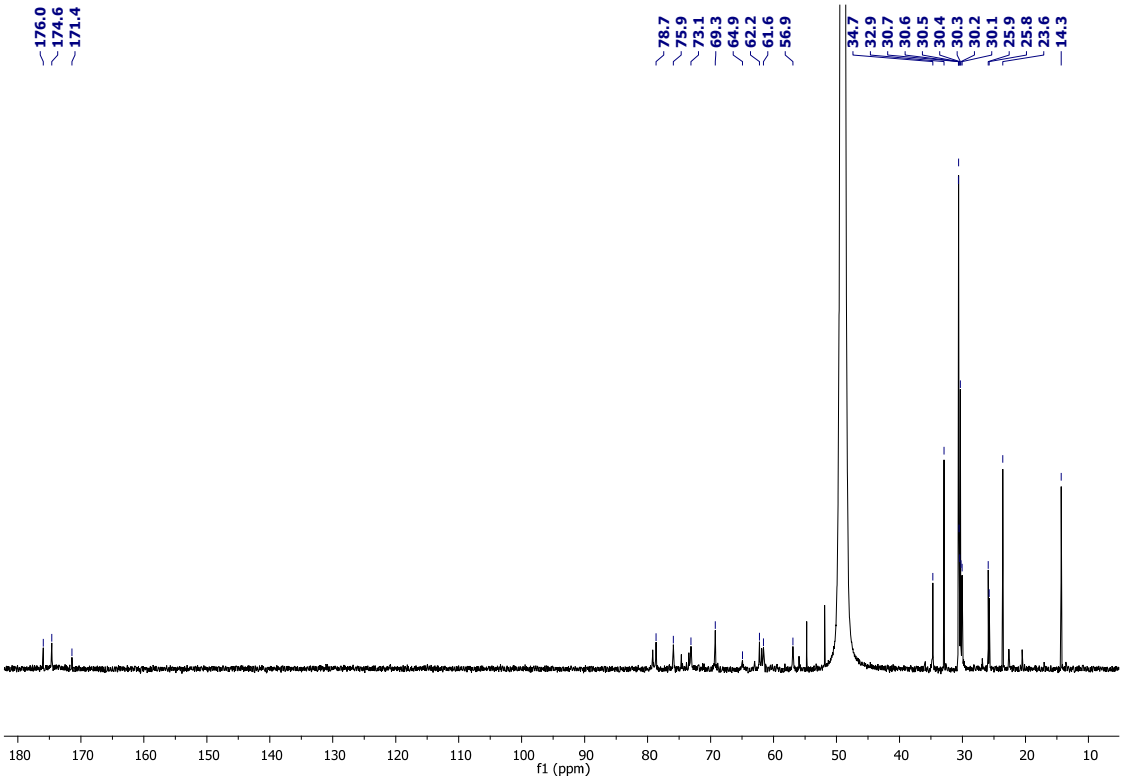


Compound 11

^{1}H NMR 400 MHz in CD_3OD



^{13}C NMR 100 MHz in CD_3OD



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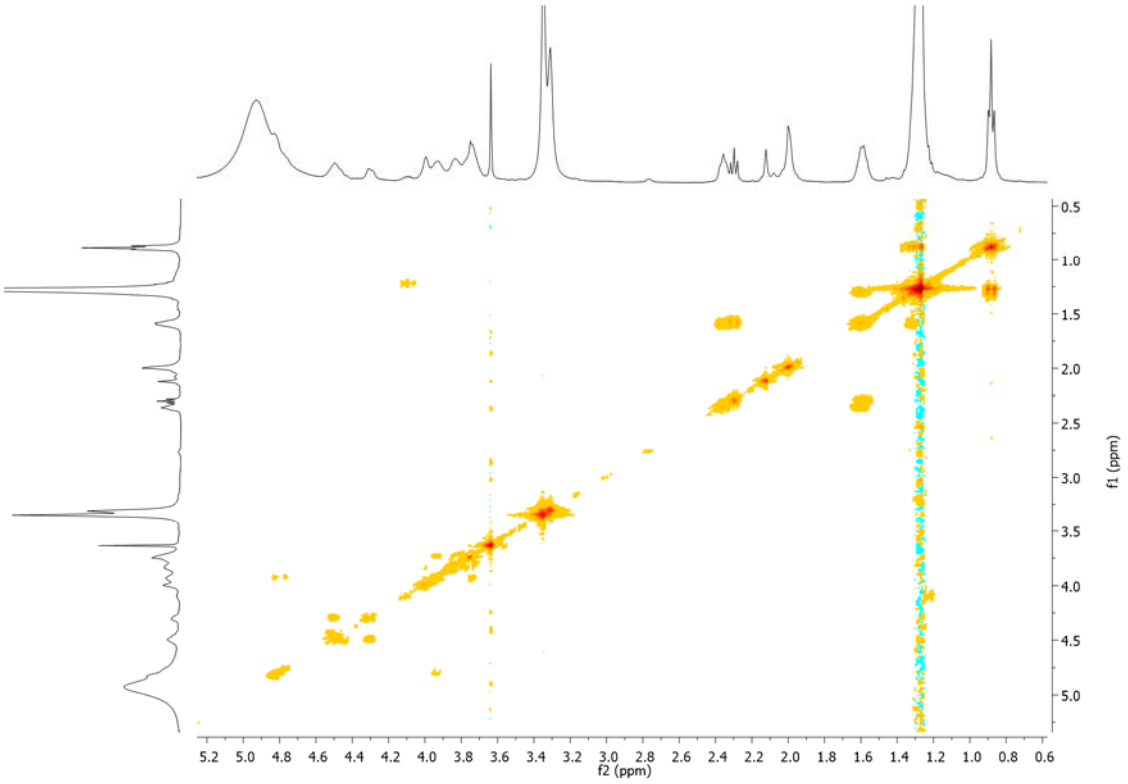

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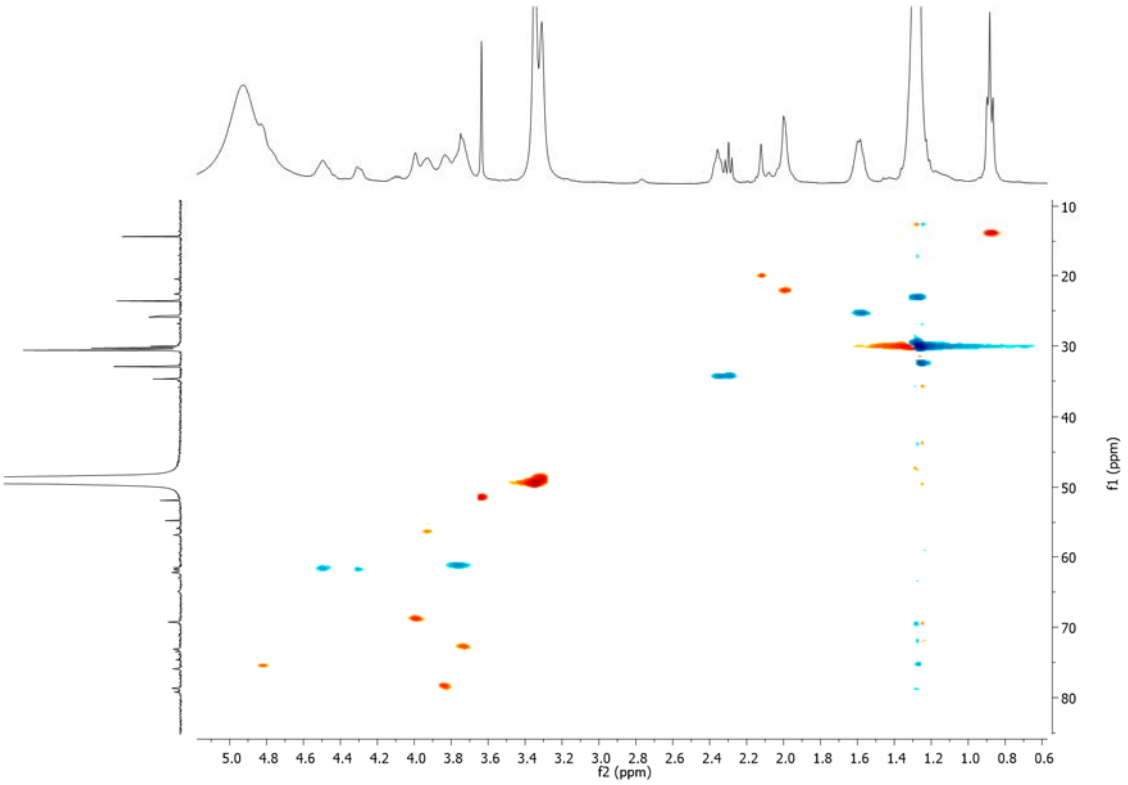
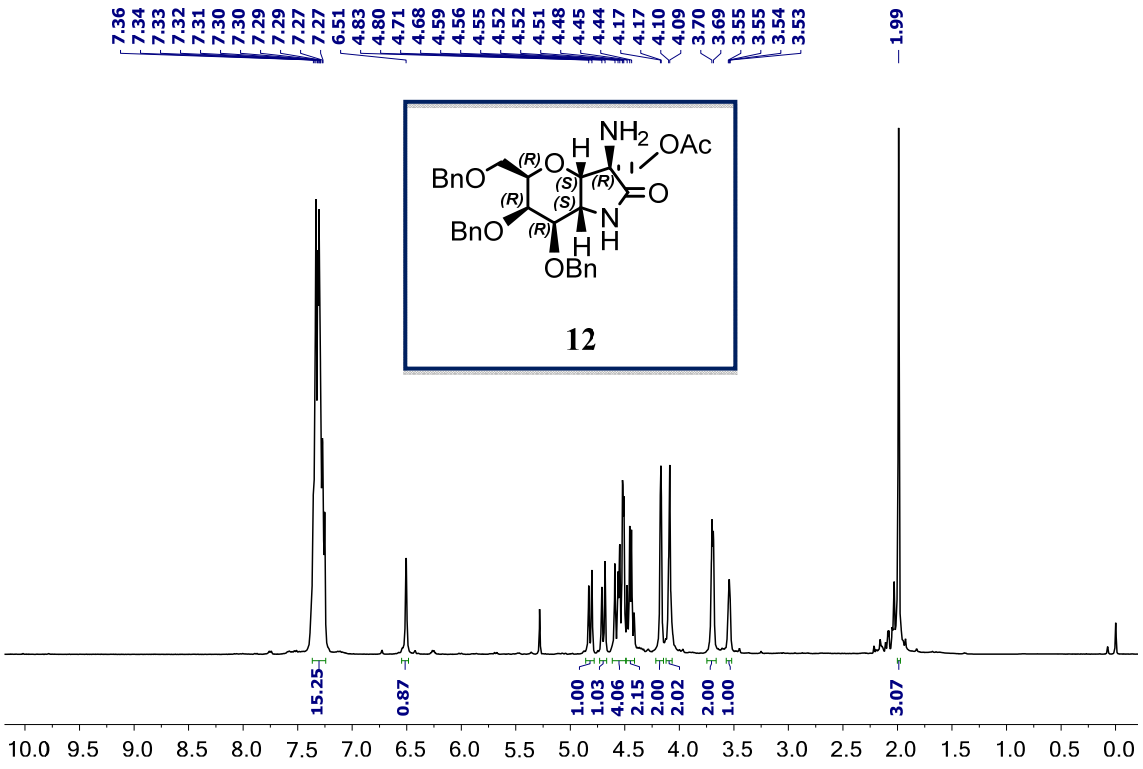


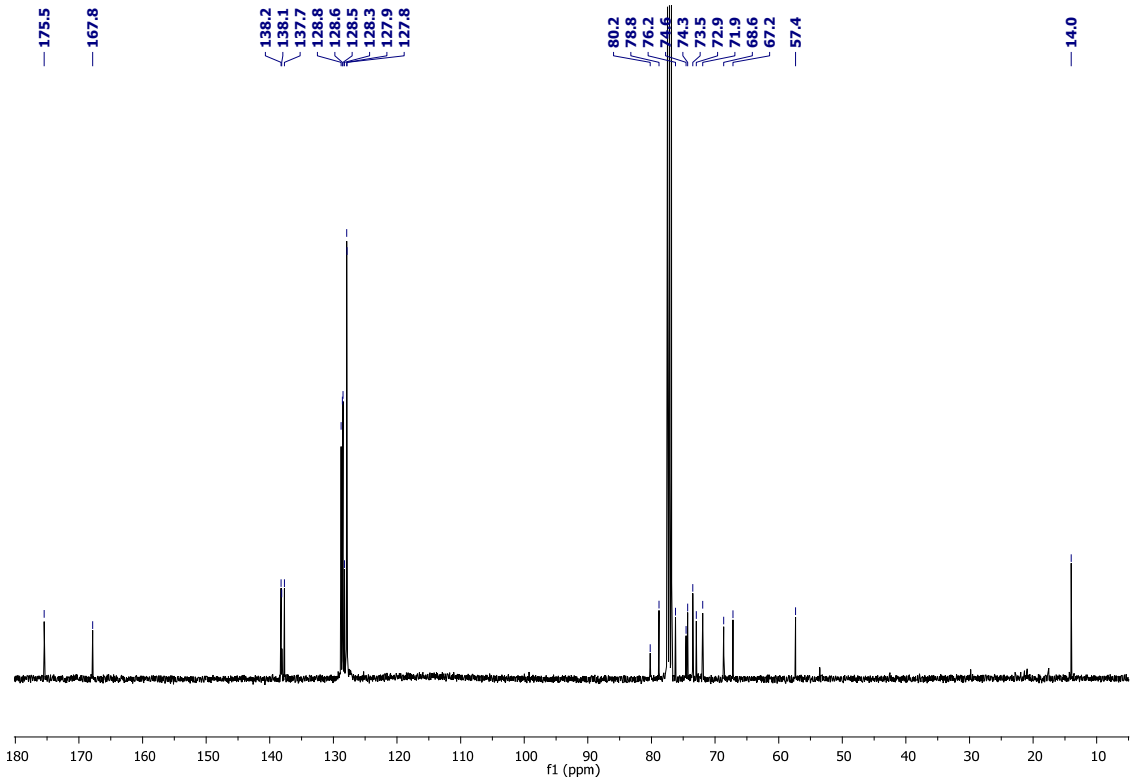
Compound 12

^{1}H NMR 400 MHz in $CDCl_3$

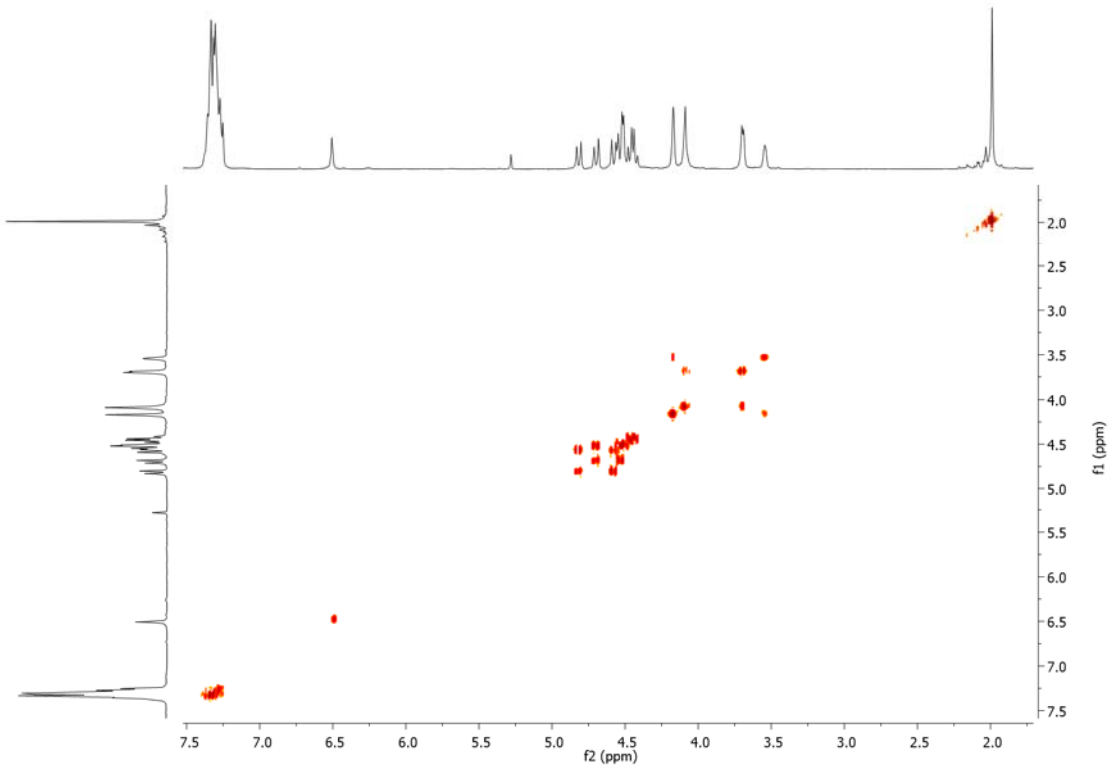


12

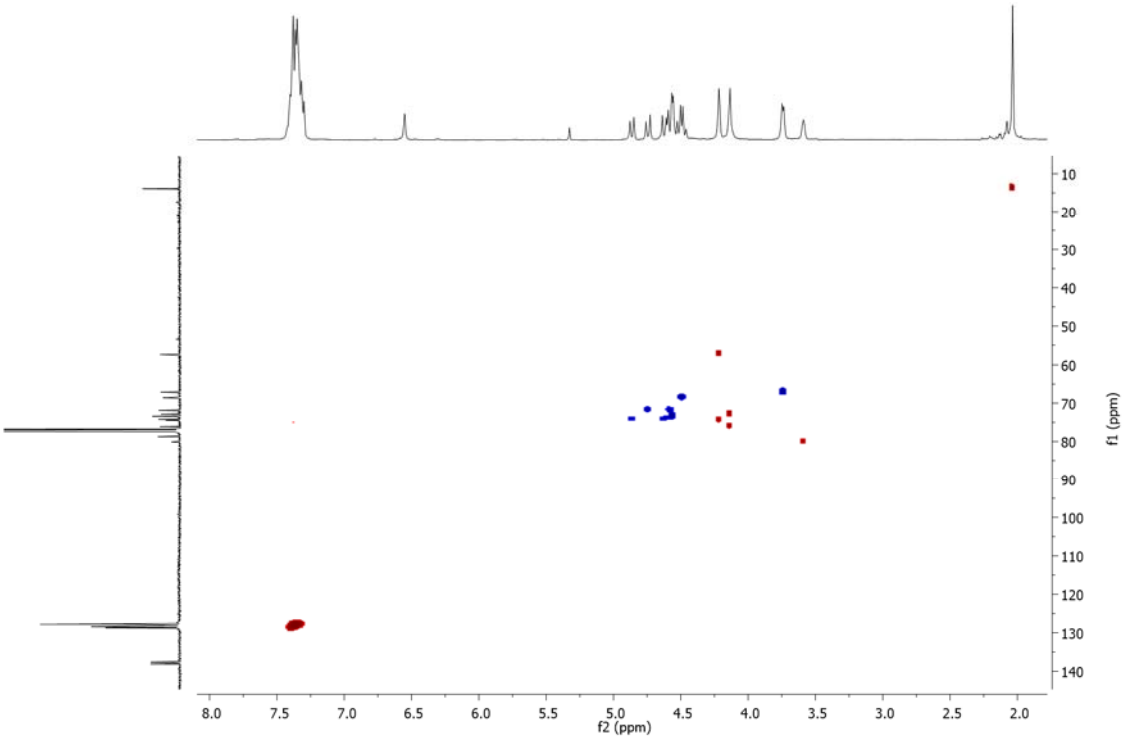
^{13}C NMR100 MHz in $CDCl_3$



COSY in $CDCl_3$

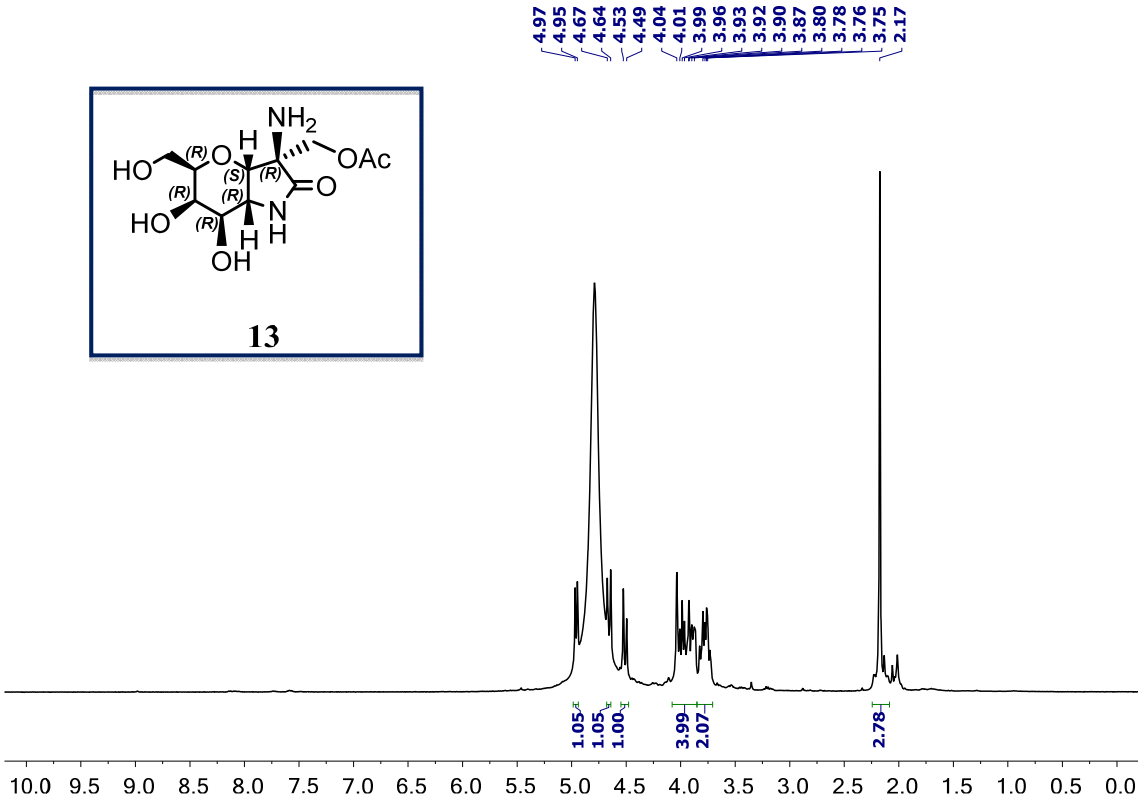


HSQC in $CDCl_3$

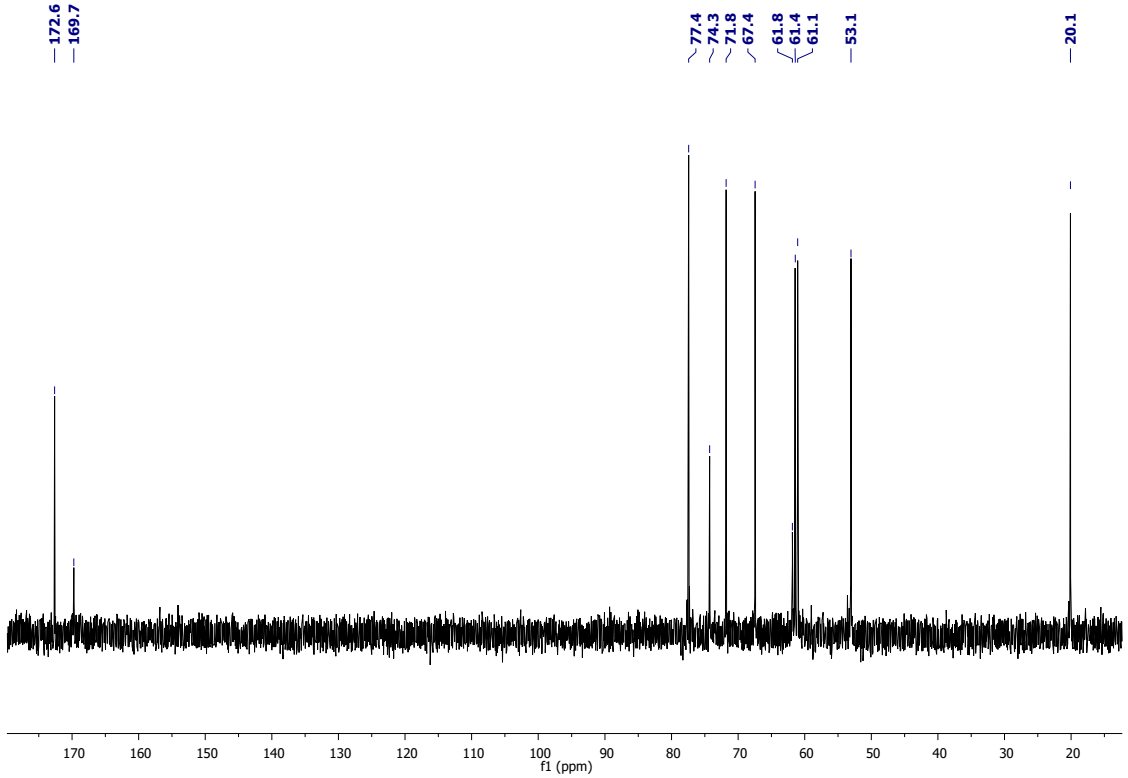


Compound 13

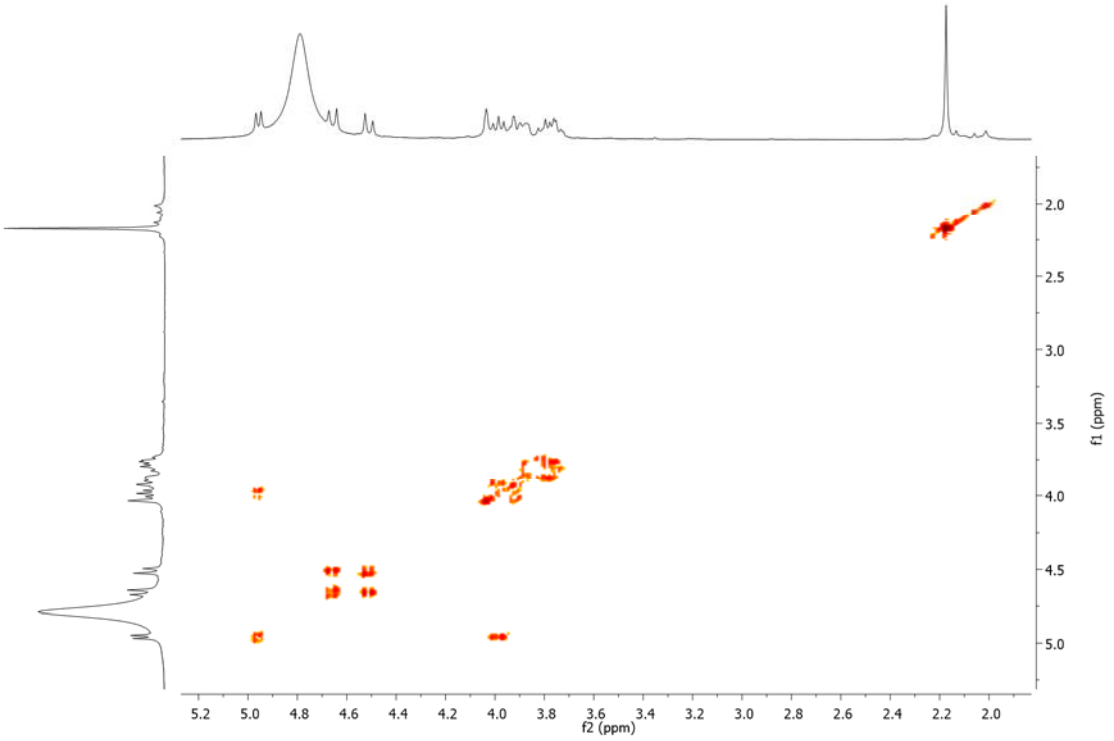
^{1}H NMR 400 MHz in D_2O



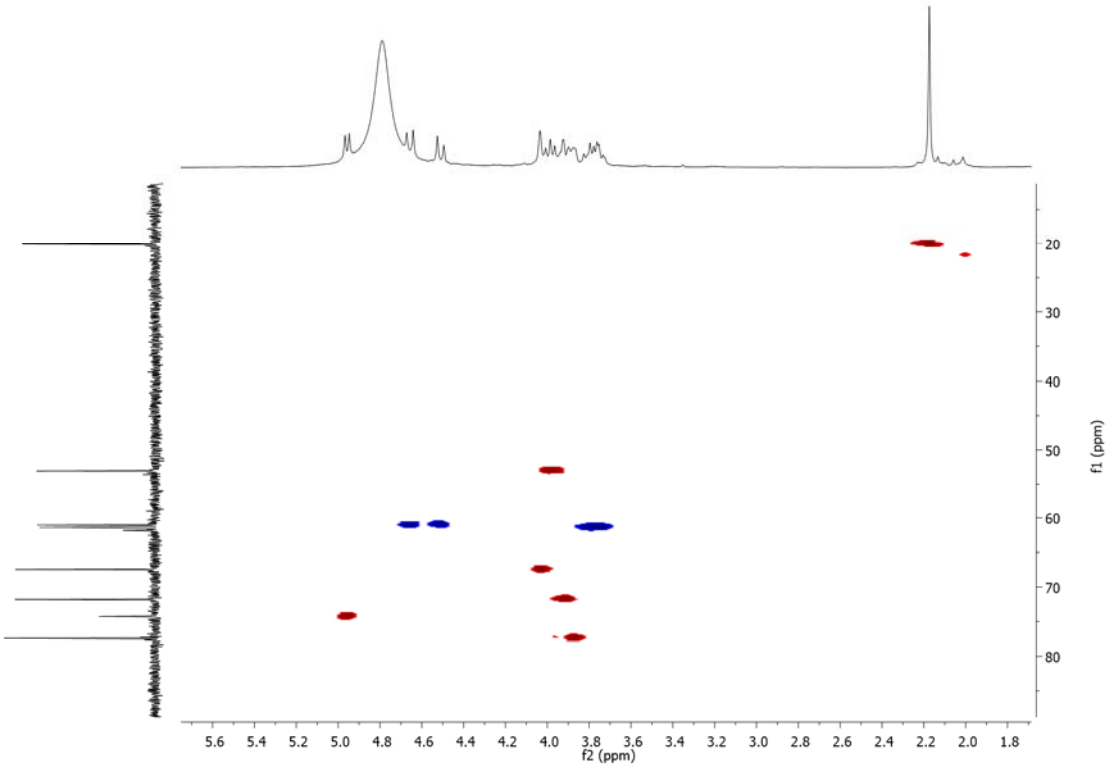
^{13}C NMR 100 MHz in D_2O



COSY in D_2O

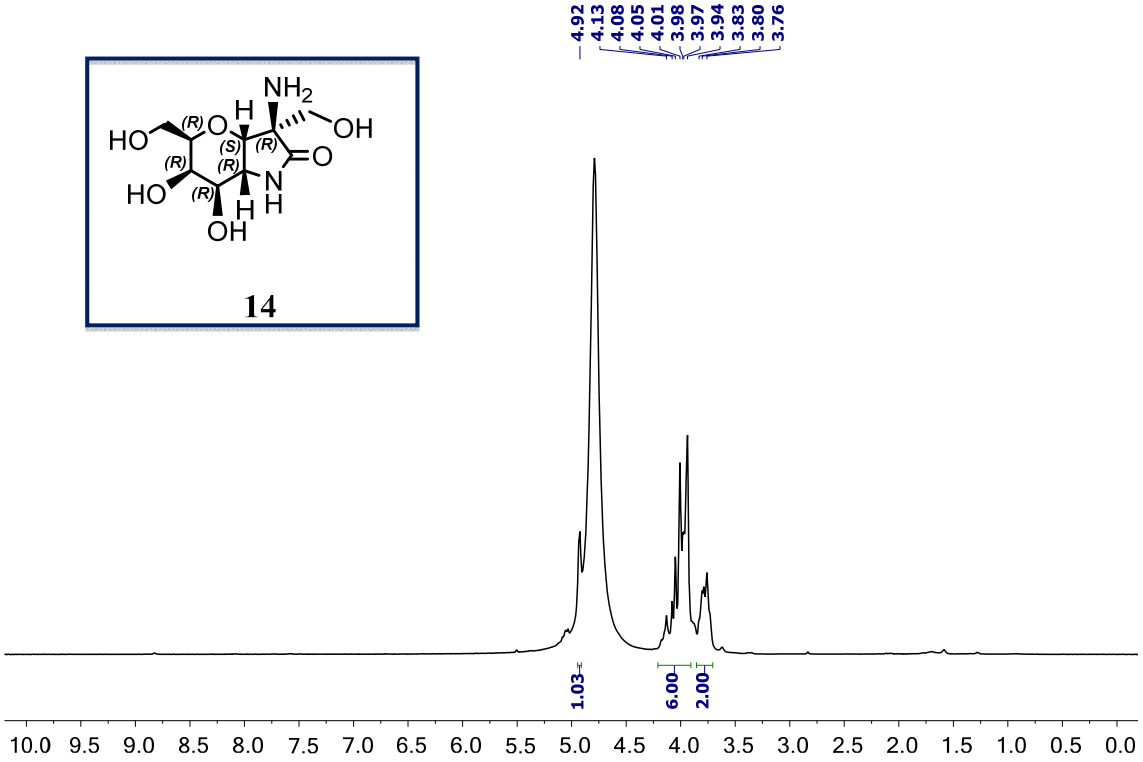


HSQC in D_2O

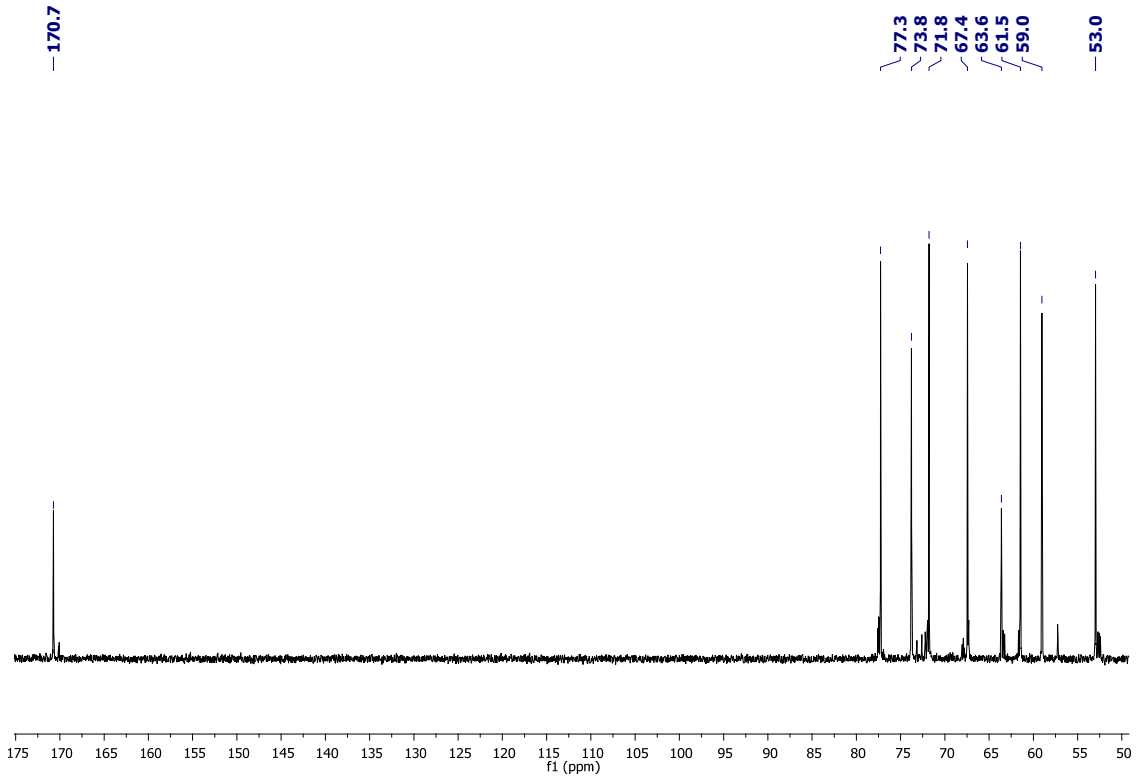


Compound 14

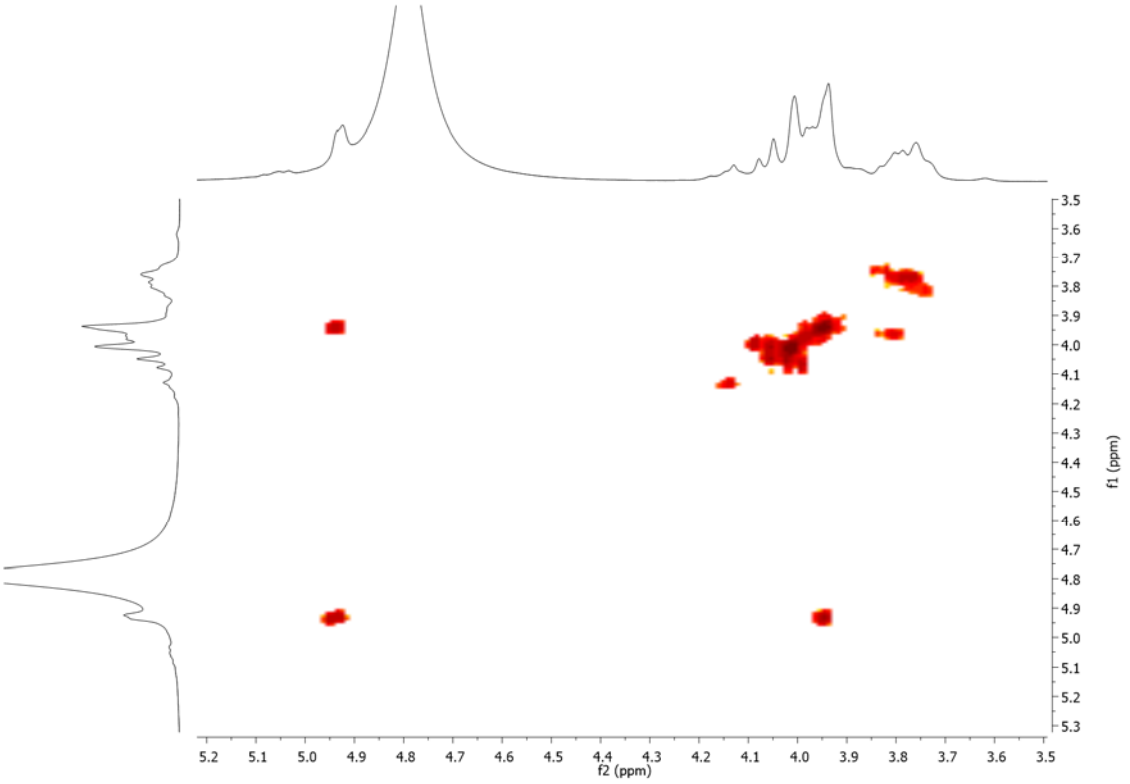
^{1}H NMR 400 MHz in D_2O



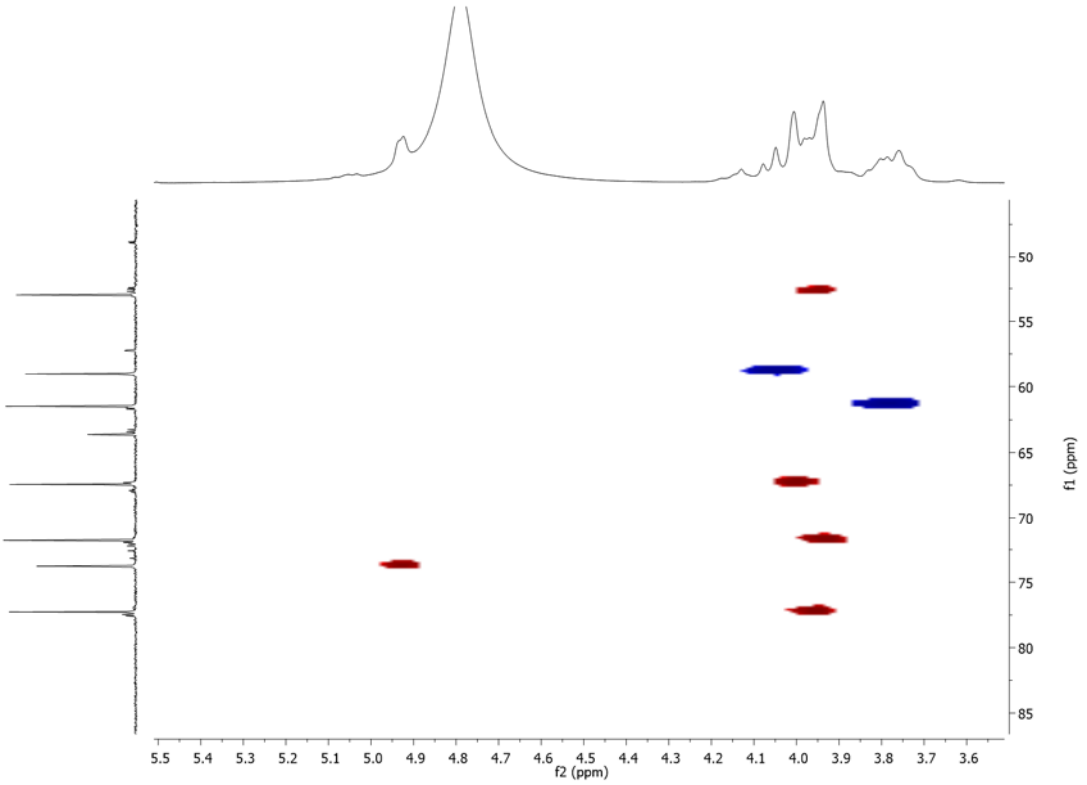
^{13}C NMR 100 MHz in D_2O



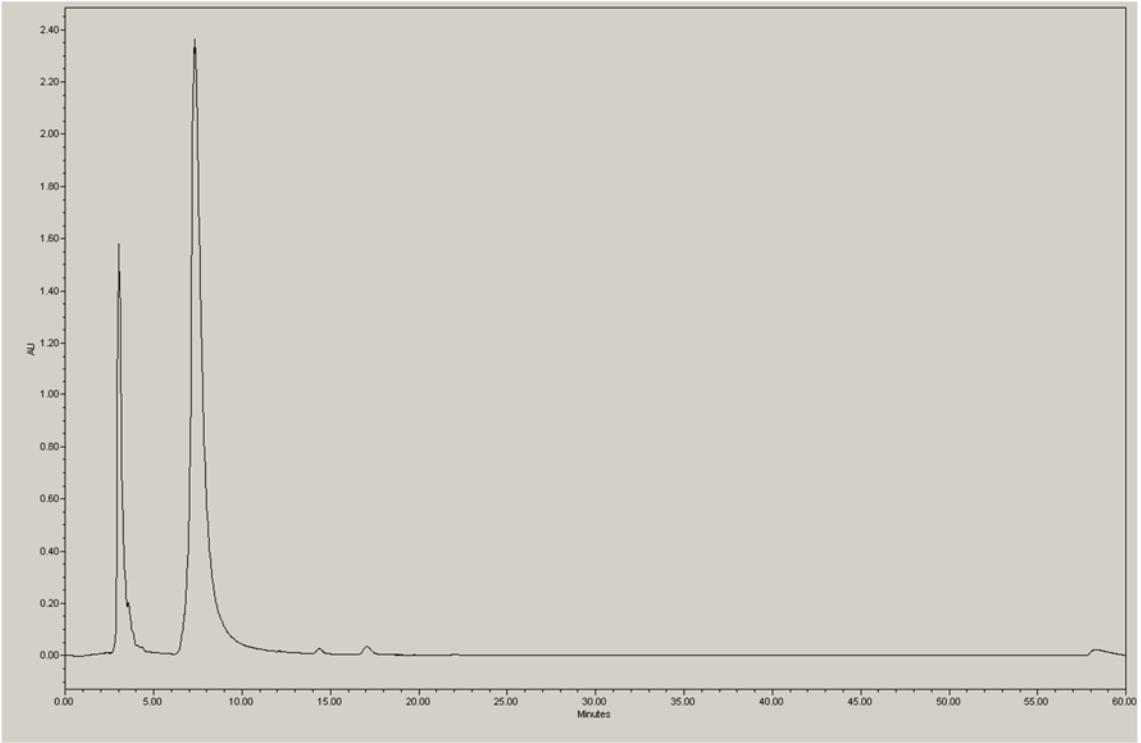
COSY in D_2O



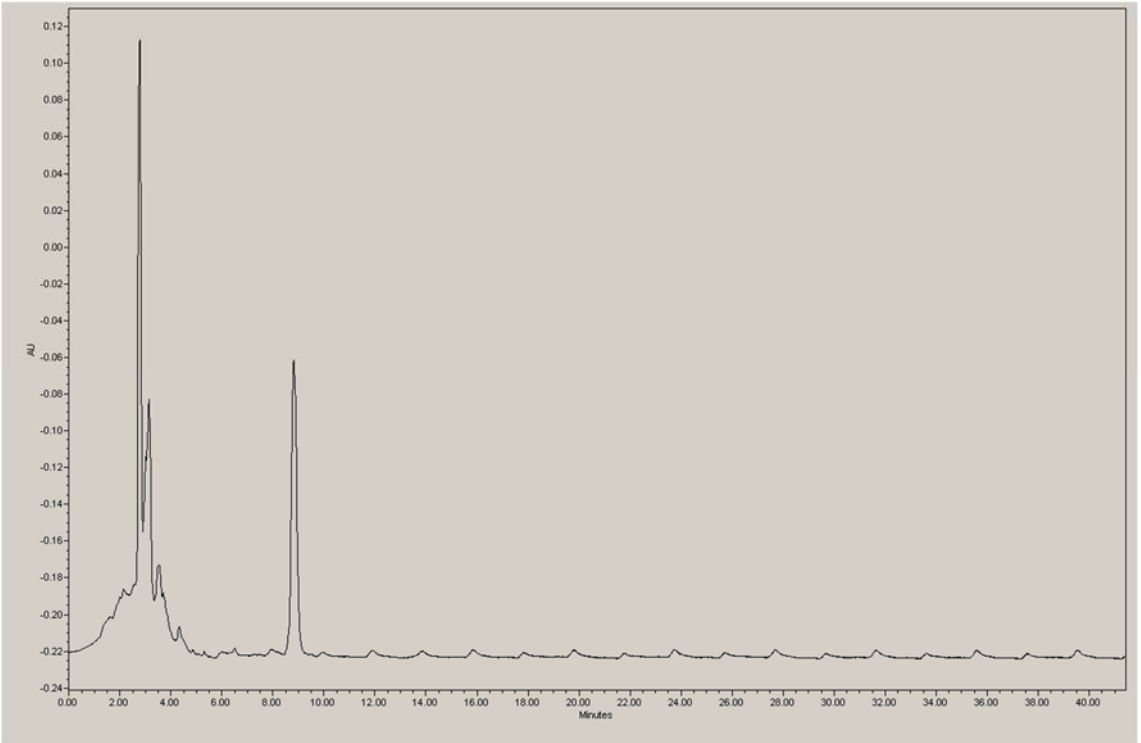
HSQC in D_2O



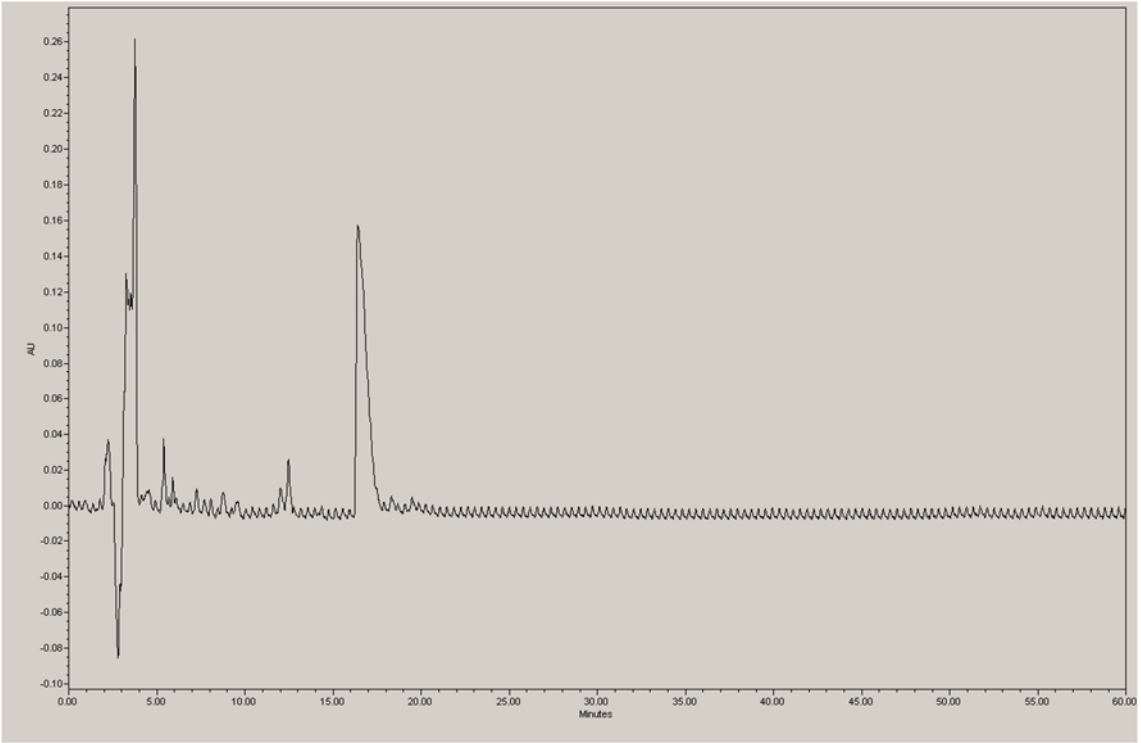
Compound 4. Analytical HPLC (H_2O + 0.1% TFA / MeCN, 2:98), 60 min, 1 ml/min, t_R 7.3 min. Column: Phenomenex Luna 5 µm C18 (2) 100 A, 250 x 4.60 mm. UV detection at 206 nm.



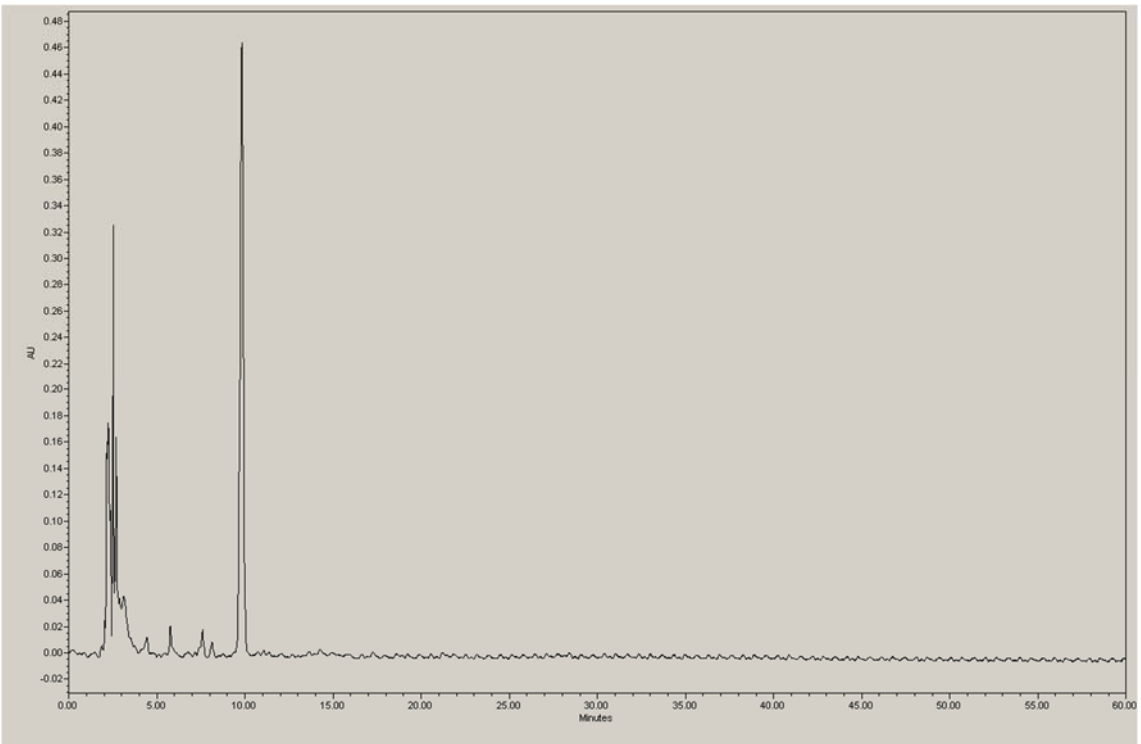
Compound 6. Analytical HPLC (H_2O + 0.1% TFA / MeCN, 5:95), 42 min, 1 ml/min, t_R 8.8 min. Column: Phenomenex Luna 5 mm C18 (2) 100 A, 250 x 4.60 mm. UV detection at 206 nm.

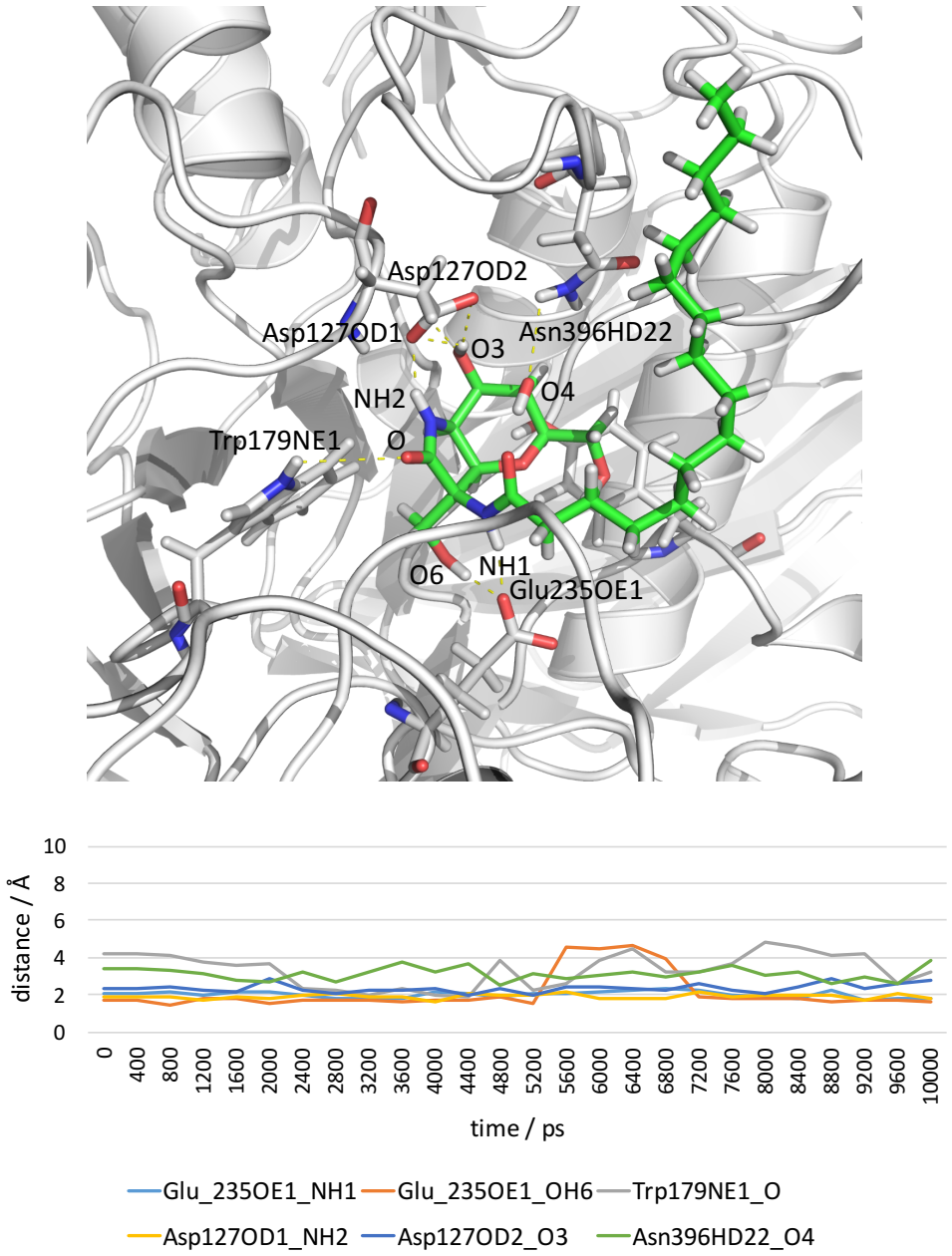


Compound 8. Analytical HPLC (H_2O + 0.1% TFA / MeCN, 50:50), 60 min, 1 ml/min, t_R 16.4 min. Column: Phenomenex Luna 5 mm C18 (2) 100 A, 250 x 4.60 mm. UV detection at 206 nm.

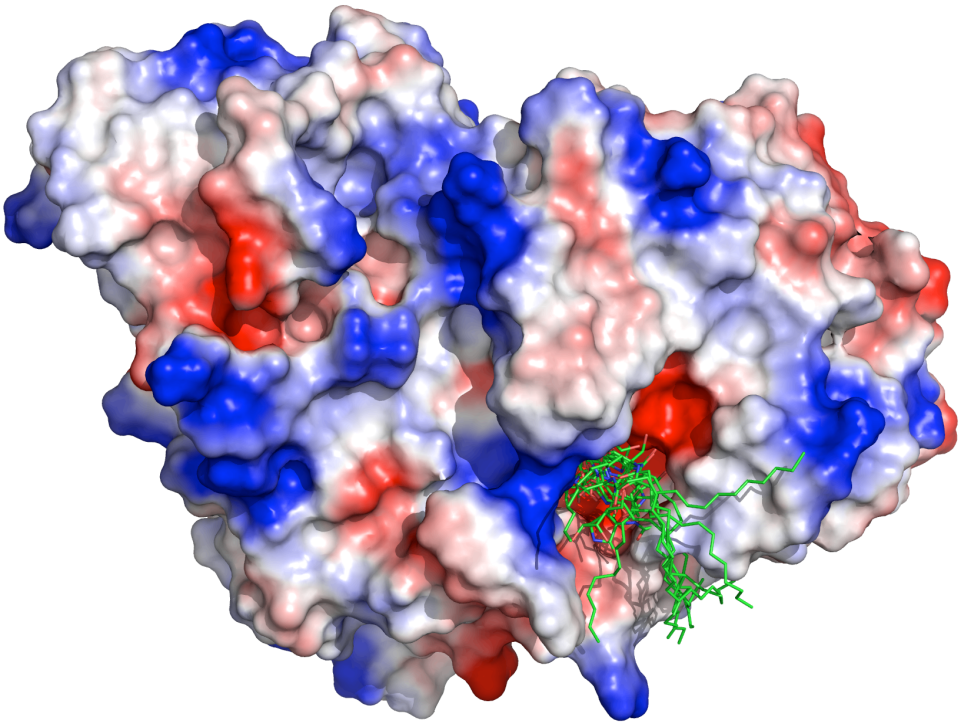


Compound 11. Analytical HPLC (H_2O + 0.1% TFA / MeCN, 70:30), 60 min, 1 ml/min, t_R 9.8 min. Column: Phenomenex Luna 5 mm C18 (2) 100 A, 250 x 4.60 mm. UV detection at 206 nm.





Distances between compound **6** in complex with the β-glucosidase (PDB code: 2WCG) and some residues of the enzyme obtained from the first 10 ns of the MD simulations in explicit water.



Ensembles obtained from the unrestrained 100 ns MD simulations performed on **6**:β-glucosidase complex. The electrostatic potential surface of the protein is also represented. Red represents a net negative surface potential, and blue denotes a net positive surface potential. Compound **6** is shown as a stick model colored according to atom type.