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Supporting Information

Mechanism-Based Design of the First GlnA4-Specific Inhibitors

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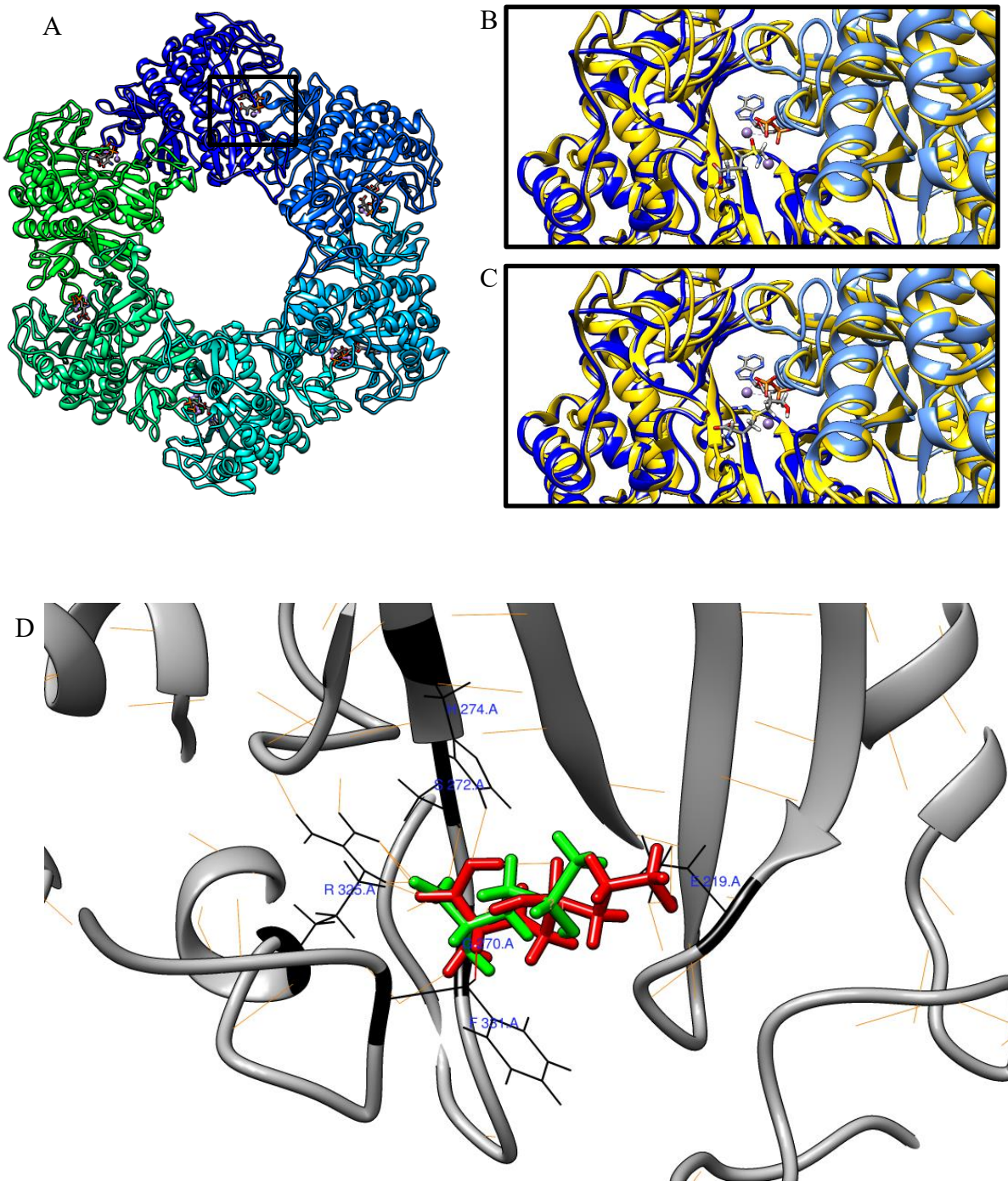
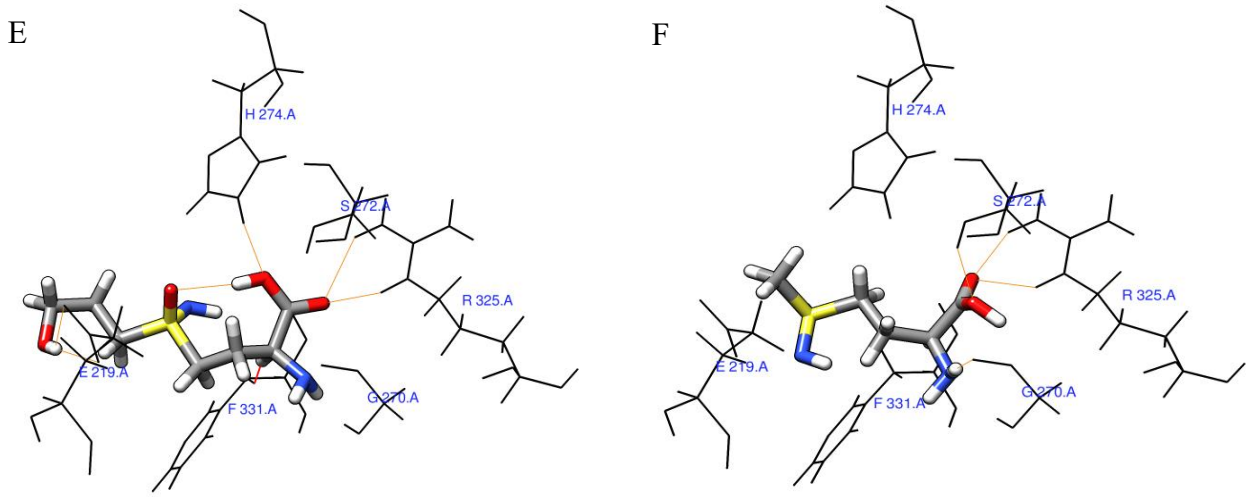
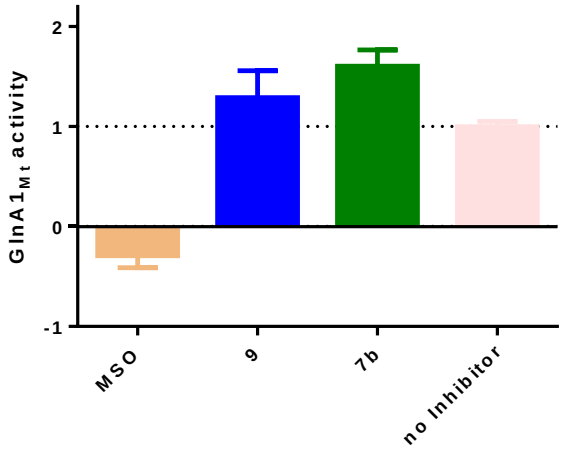
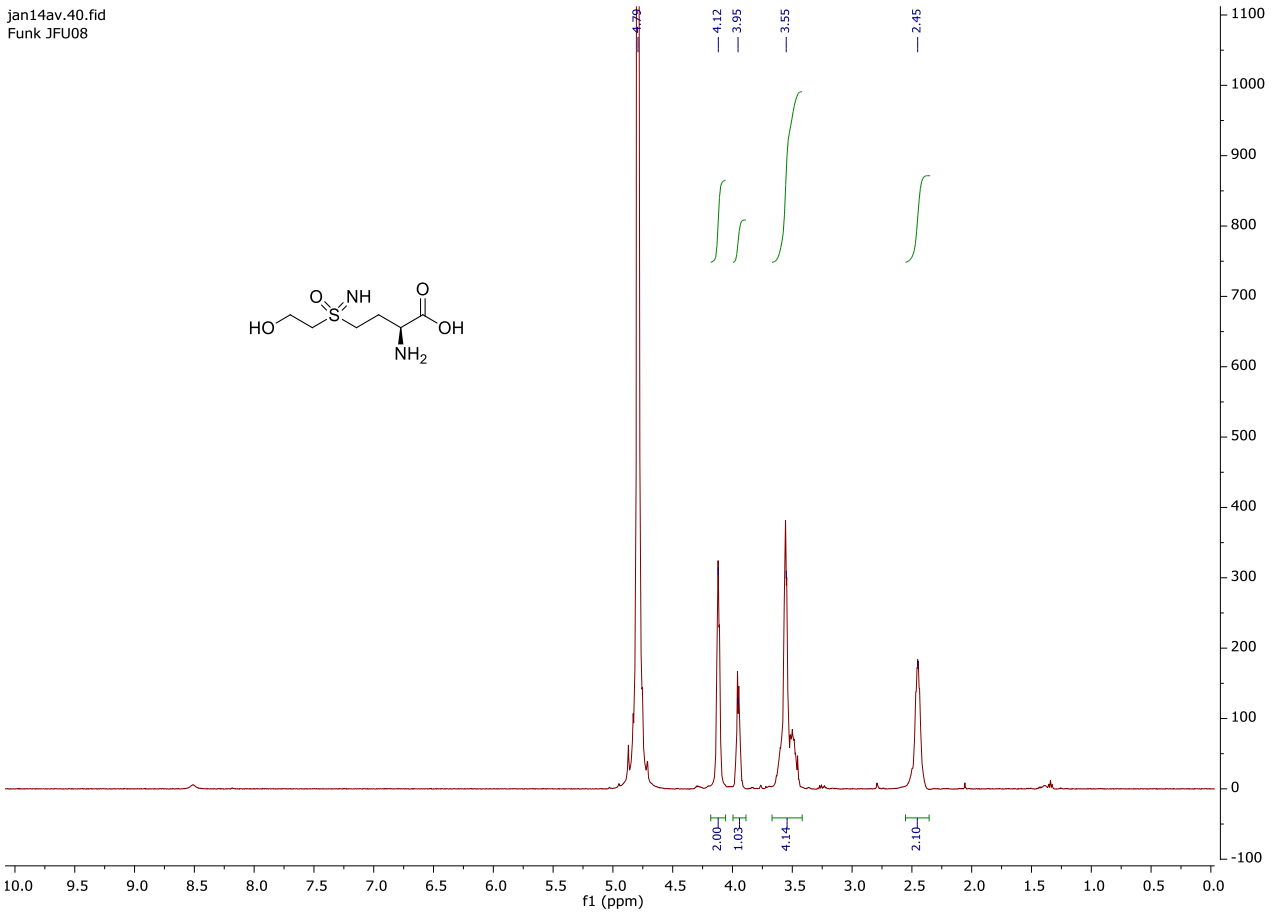

A
B
C
D
H 274.A
R 325.A
E 219.A
F 351.A

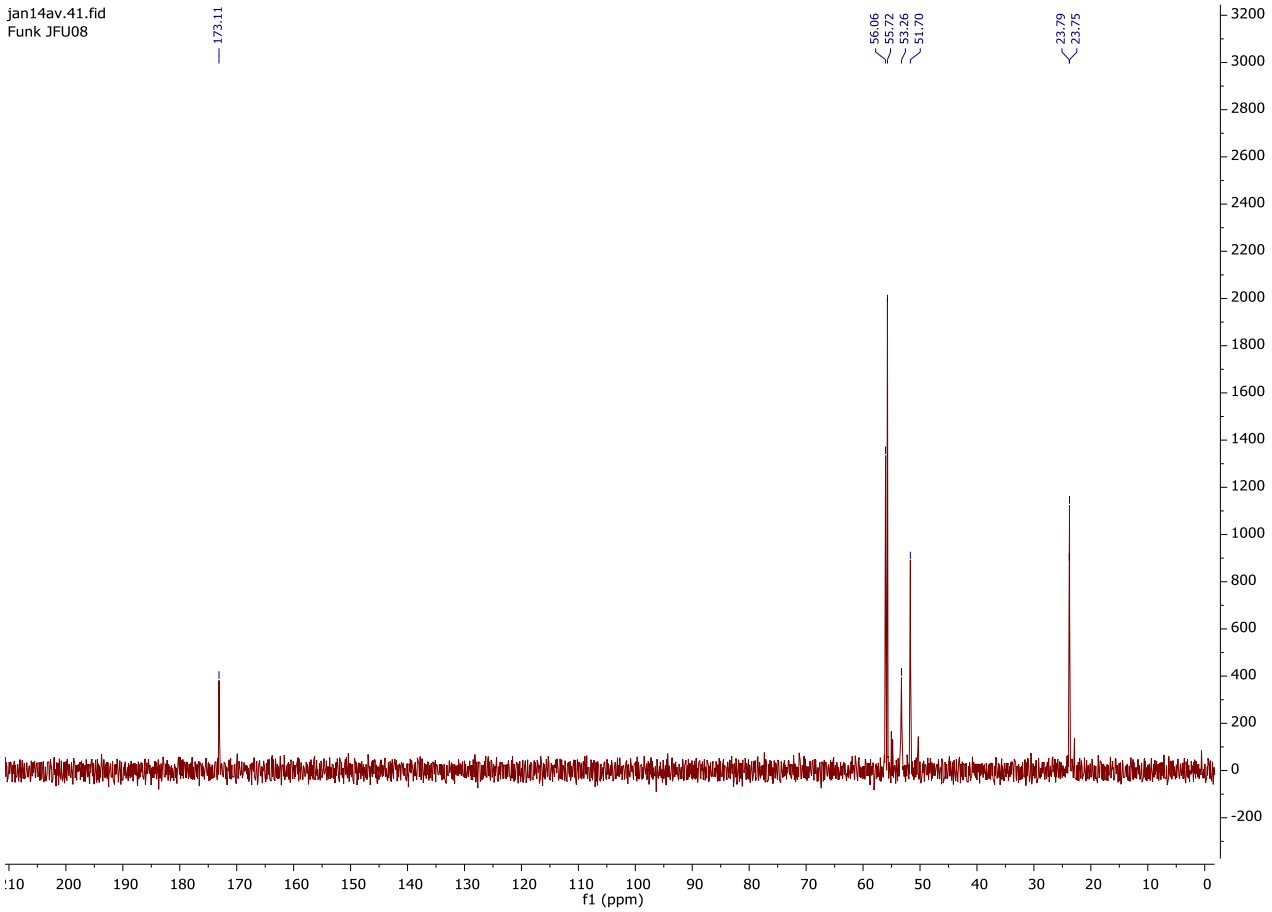


SI Figure 1. A) Model structure of GlnA4$_{Sc}$ superposed with GSI$_{St}$ (PDB: 1FPY) as described by KRYSENKO *et al.*,[1] with the ligand-protein docking model with inhibitors and ADP. B) Magnification of the active site of GlnA4$_{Sc}$ (blue) with MSO **4**, GSI$_{St}$ in yellow. C) Magnification of the active site of GlnA4$_{Sc}$ (blue) with compound **7b**, GSI$_{St}$ in yellow. Spheres show metal ions. D) Overlay of modeled MSO (red) and **7b** (green) in the structure of GnA4$_{Sc}$ (grey and black). E) Compound **7b** and F) MSO (colored by heteroatom) with the interacting residues of GlnA4$_{Sc}$ (black) and possible interactions (orange lines). Interactions in the glutamate binding site (Ser272, Arg325, Gly270, Phe331) are conserved. **7b** shows an additional interaction with E219, which is not detected for MSO.

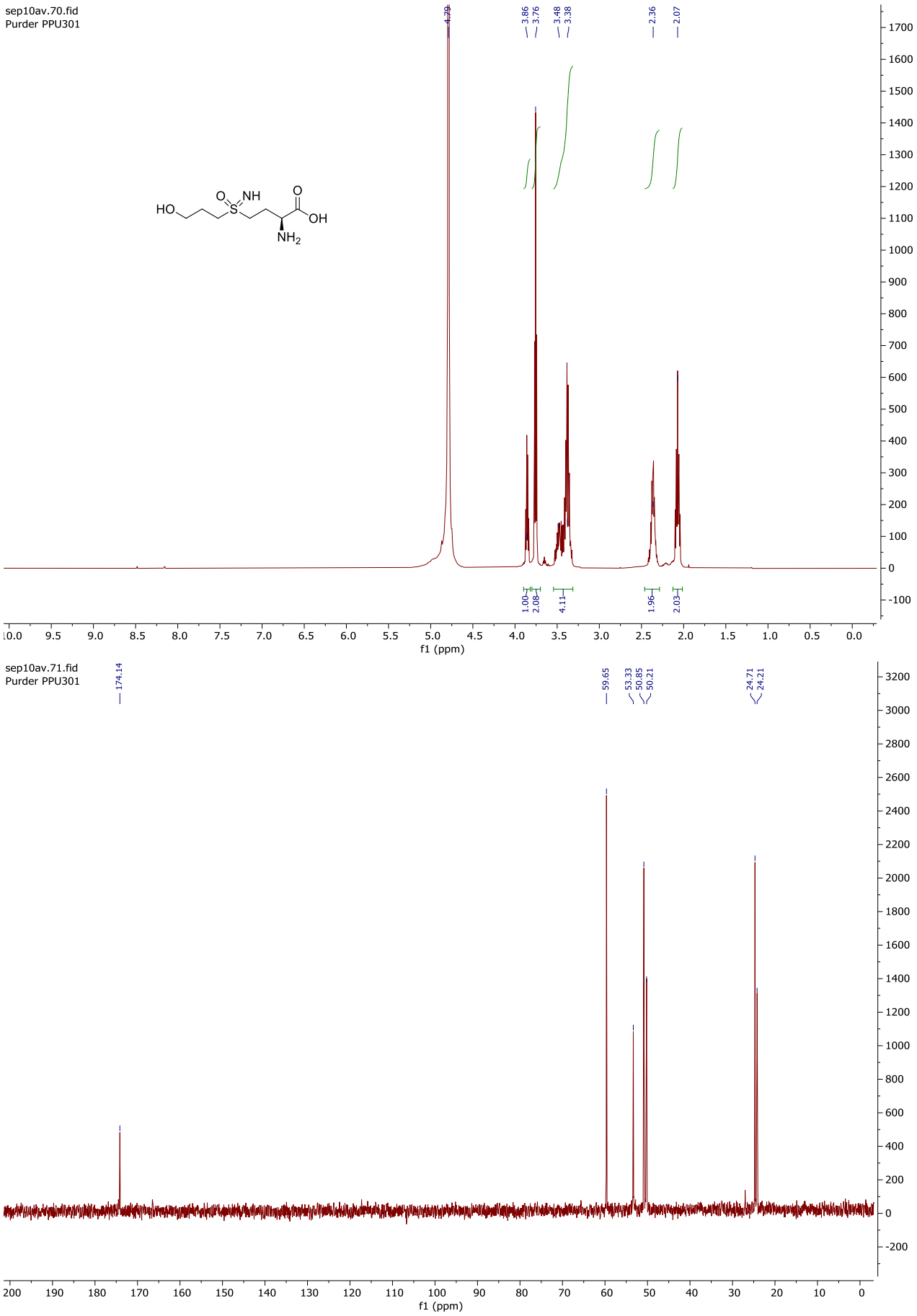


SI Figure 2. GlnA1$_{Mt}$ activity with MSO, **8** and **7b** at 5 mM.

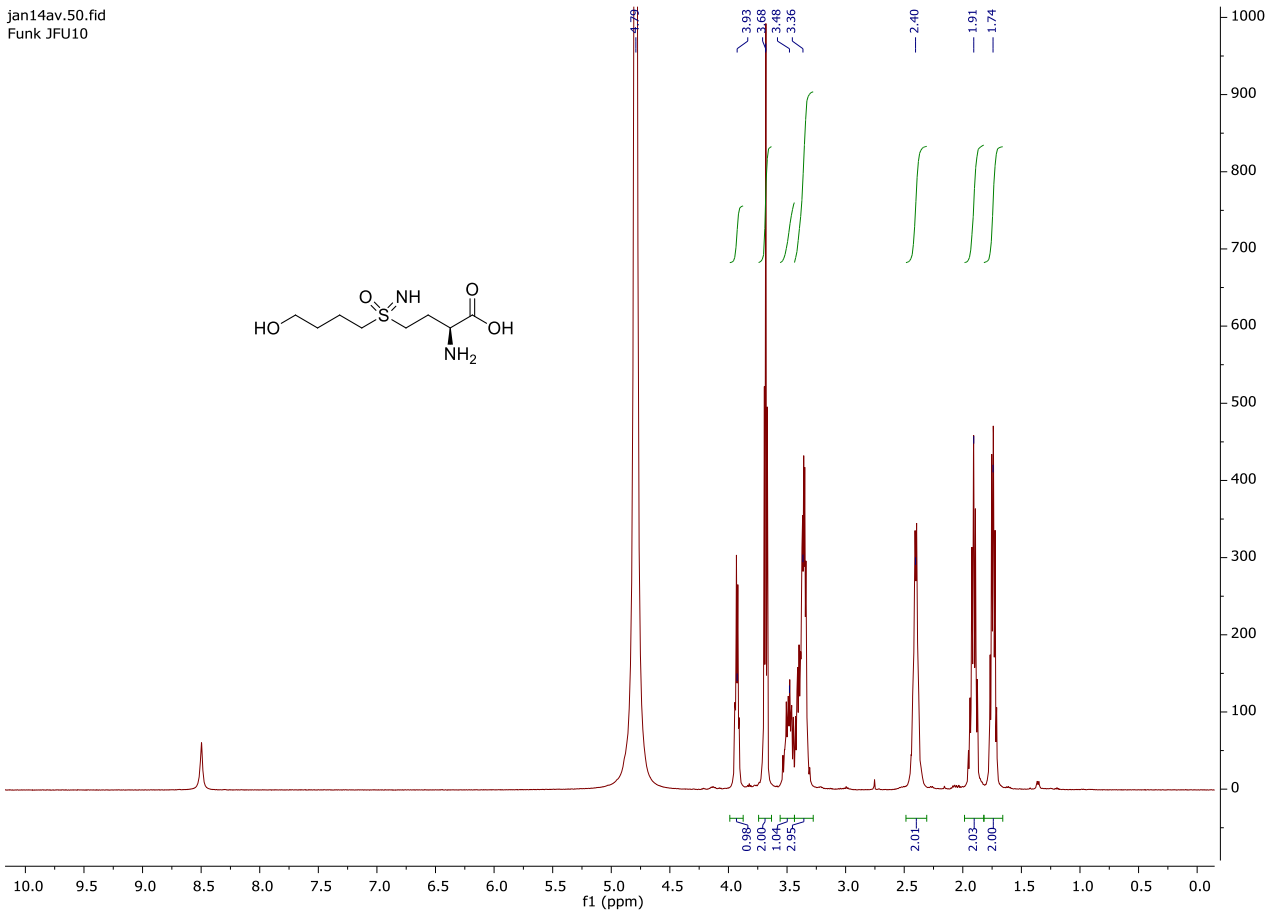


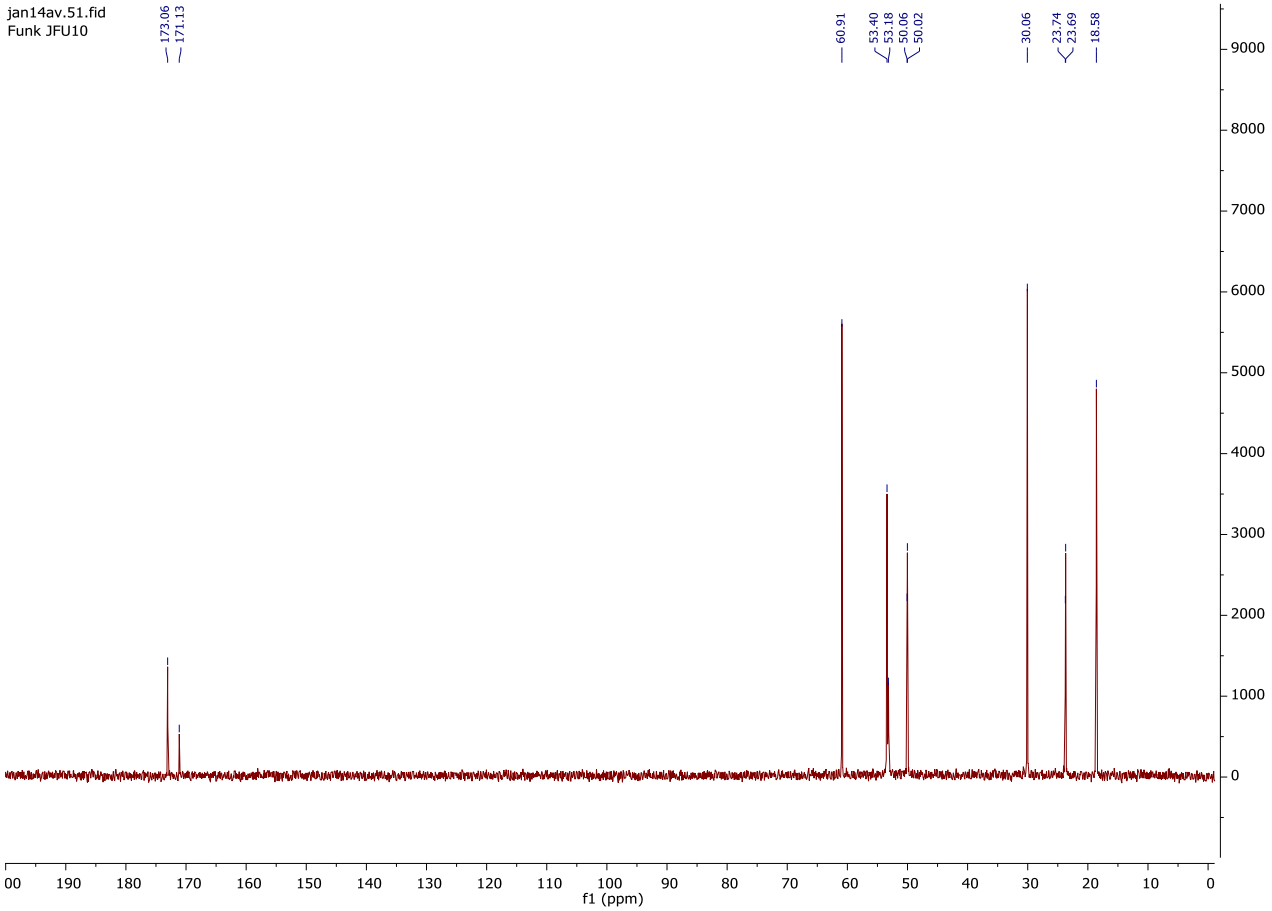


SI Figure 3. ^{1}H-NMR (500 MHz, D_2O) and ^{13}C-NMR (125 MHz, D_2O) spectra of compound **7a**.

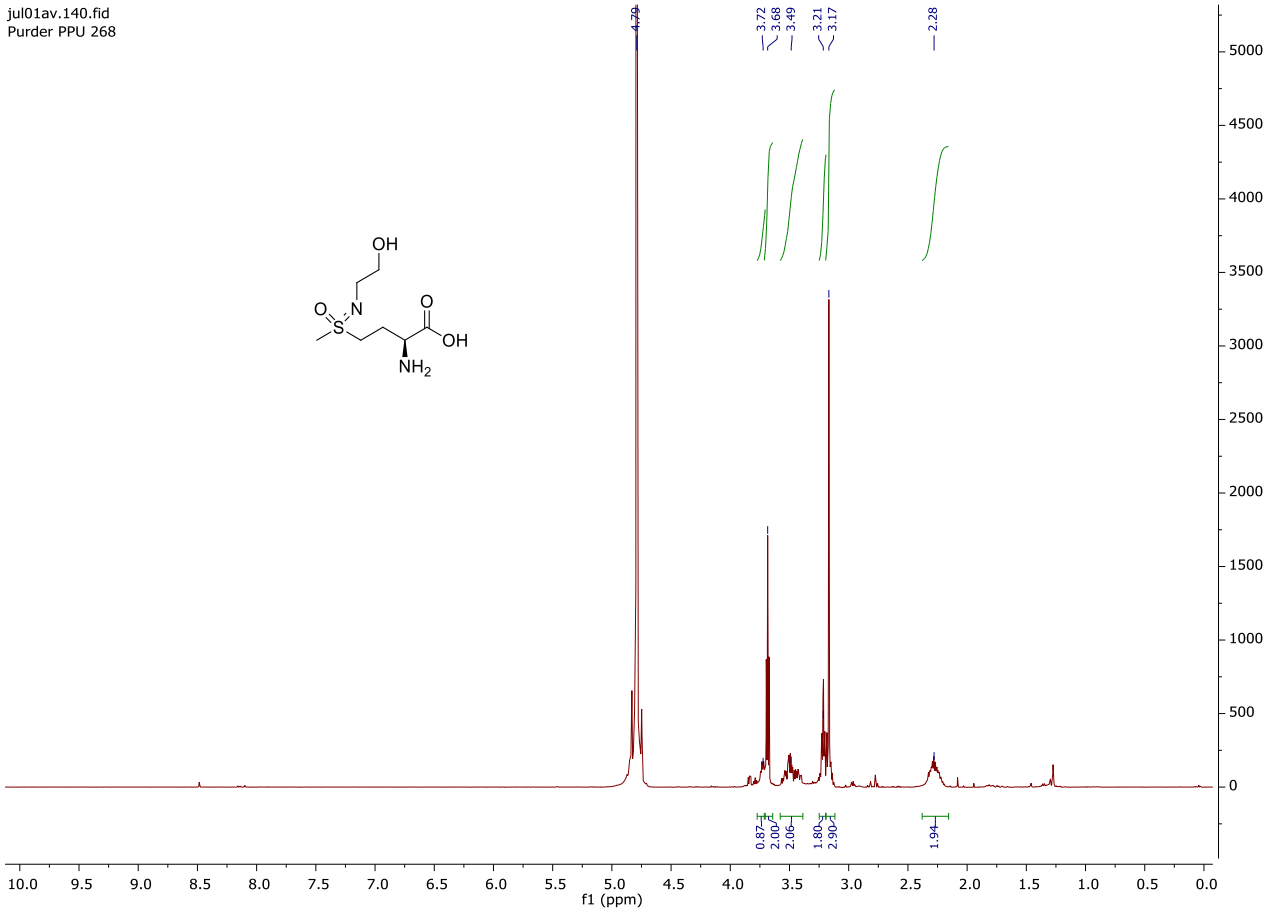


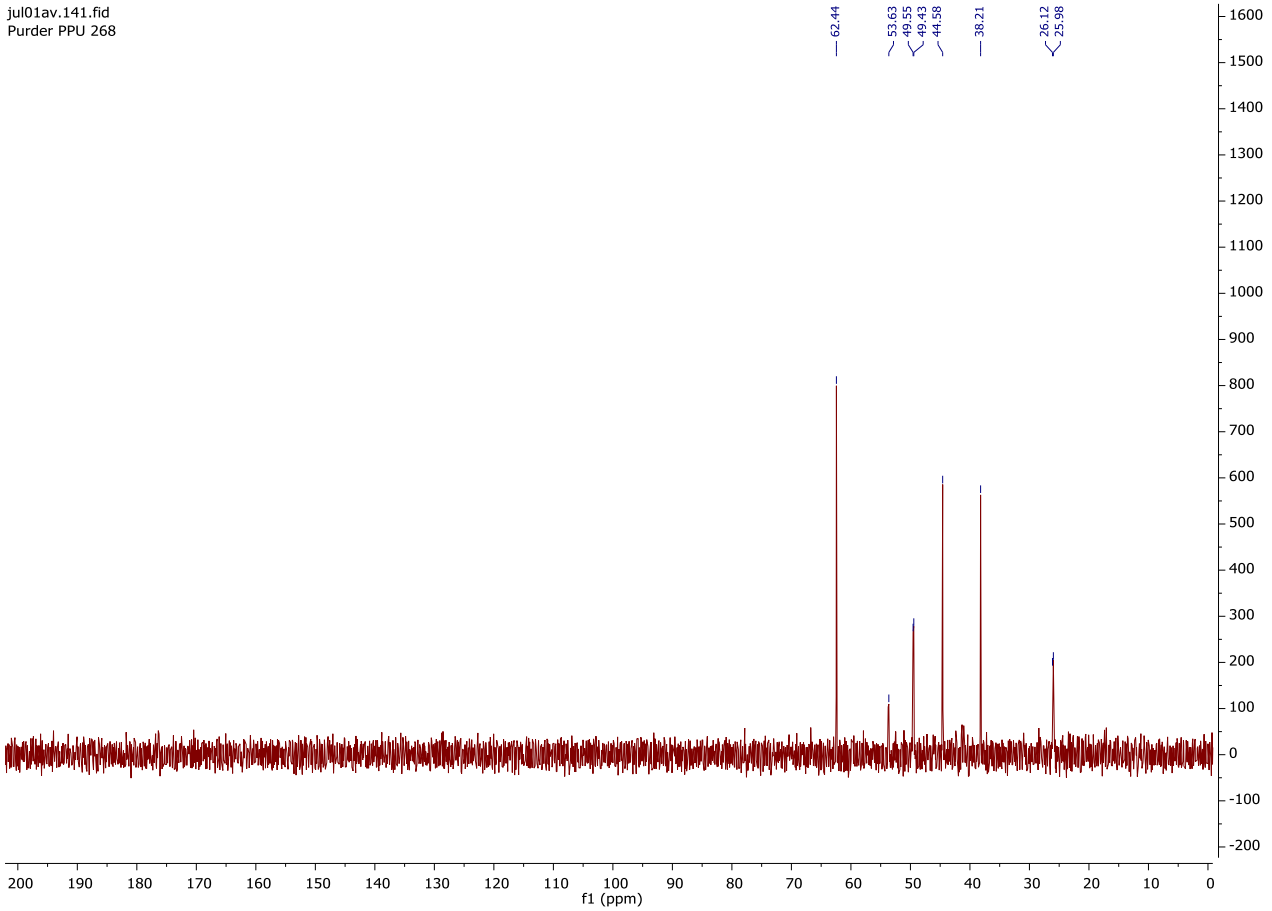
SI Figure 4. ^{1}H-NMR (500 MHz, D_2O) and ^{13}C-NMR (125 MHz, D_2O) spectra of compound **7b**.





SI Figure 5. ^{1}H-NMR (500 MHz, D_2O) and ^{13}C-NMR (125 MHz, D_2O) spectra of compound **7c**.





SI Figure 6. ^{1}H-NMR (500 MHz, D_2O) and ^{13}C-NMR (125 MHz, D_2O) spectra of compound **8**.

References

(1) S. Krysenko, A. Matthews, N. Okoniewski, A. Kulik, M. G. Girbas, O. Tsypik, C. S. Meyners, F. Hausch, W. Wohlleben, A. Bera, *mBio* **2019**, *10*.