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1. Synthesis of f3

Intermediate linear scaffold was prepared on solid phase using Sieber amide resin, standard Fmoc chemistry and HBTU/DIEA as coupling agent / tertiary base in the coupling steps by Tetras multiple automatic peptide synthesizer.

The permanent protection groups chosen for the amino acid side chains were Boc (Lys) and *t*Bu (Asp and Glu). The Lys and Asp residues used for the cyclization were prepared with very acid labile protections O-2-phenylisopropyl ester (O-2-PhiPr) for Asp and N-methyltrityl (N-Mtt) for Lys. Treating the protected peptidyl resin with a mixture of 3.5% of trifluoroacetic acid (TFA) and 5% of triisopropyl silane (TIS) selectively unprotects these Lys and Asp sidechains and cleaves the otherwise fully protected peptide from the resins in a single reaction. Subsequently the partially deprotected peptide was cyclized by coupling of the free γ-carboxylic acid of Asp with the ε-amino group of Lys. This amide bridge formation was accomplished using benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate (PyBOP, 2.5-fold excess) in the presence of *N*,*N*-diisopropylethylamine (DIPEA, 6-fold excess) in DMF solution for 6 hours at room temperature.

After proofing cyclization by LC-MS, the other protecting groups were removed to obtain the final crude target molecule, by treating the protected cyclized intermediate with a mixture of TFA, TA, phenol, water, EDT and TIS (87.5:2.5:2.5:2.5:2.5:2.5) for 2 hours at room temperature. The final product was purified by MS assisted HPLC and characterized by LC-MS.

2. NMR Spectra of f3

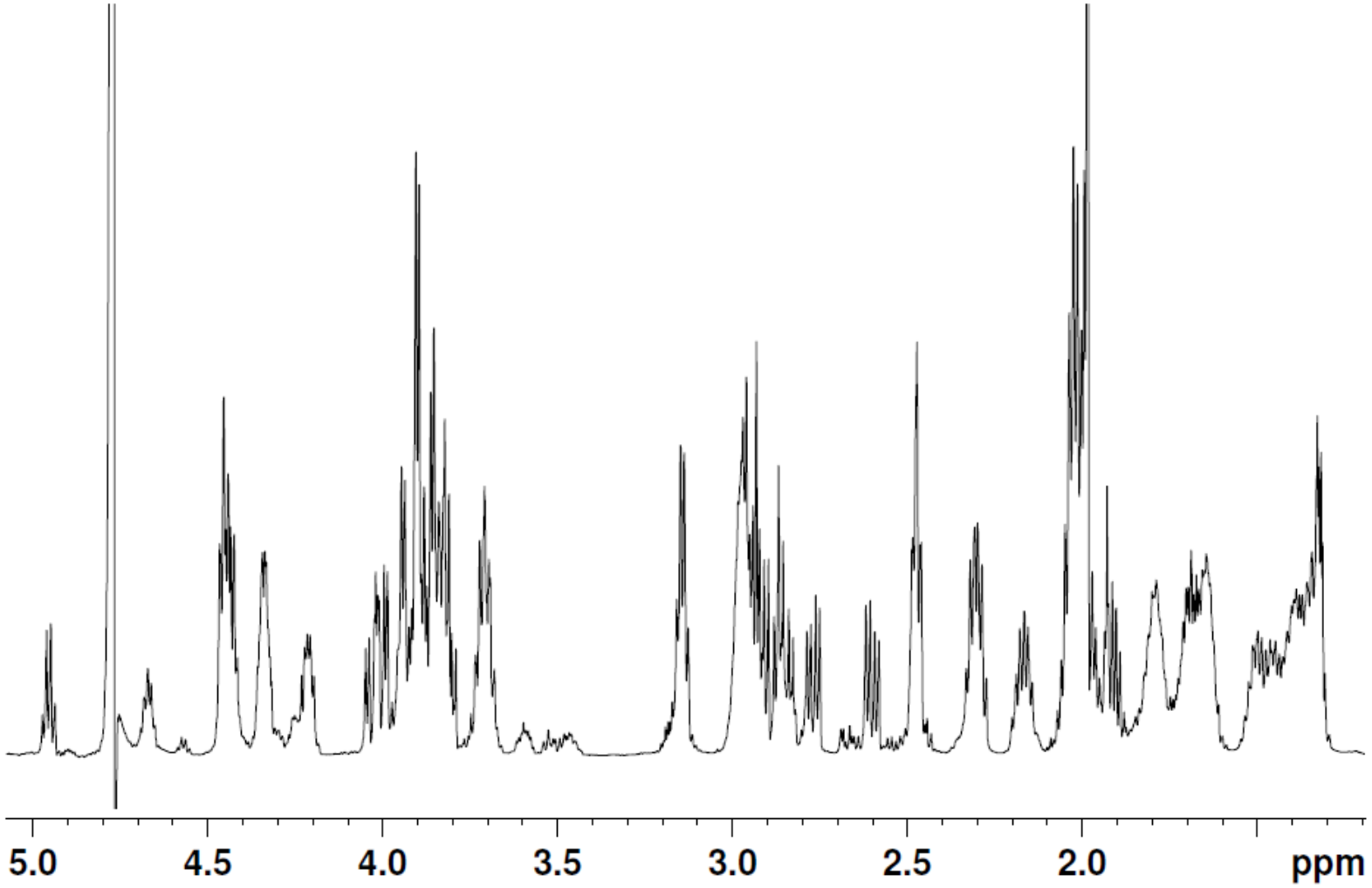

Figure S1. ^{1}H NMR of f3 from 1.2 to 5 ppm in 90% H_2O : 10% D_2O.

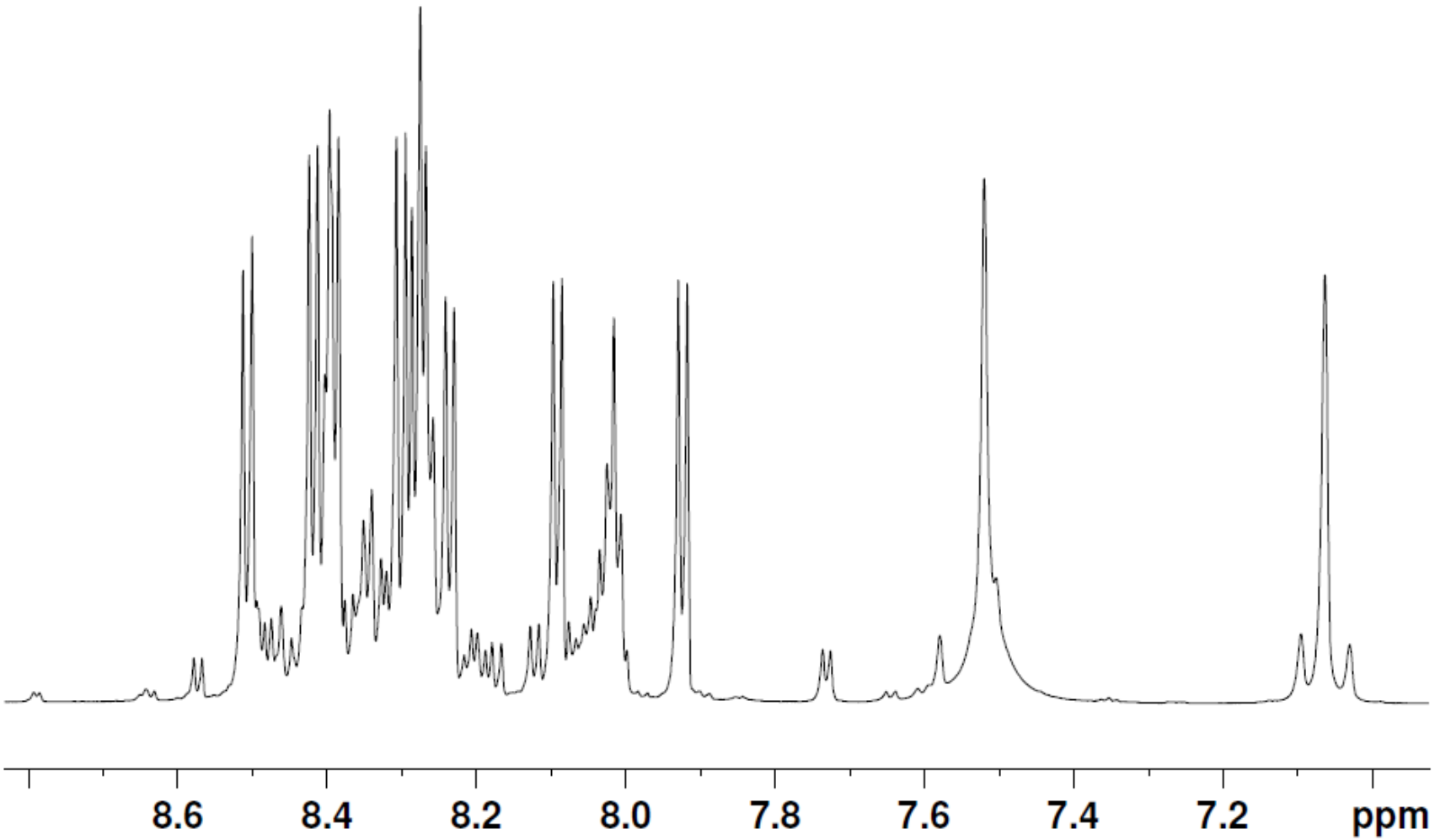

Figure S2. ^{1}H NMR of f3 from 7 to 8.8 ppm in 90% H_2O : 10% D_2O.

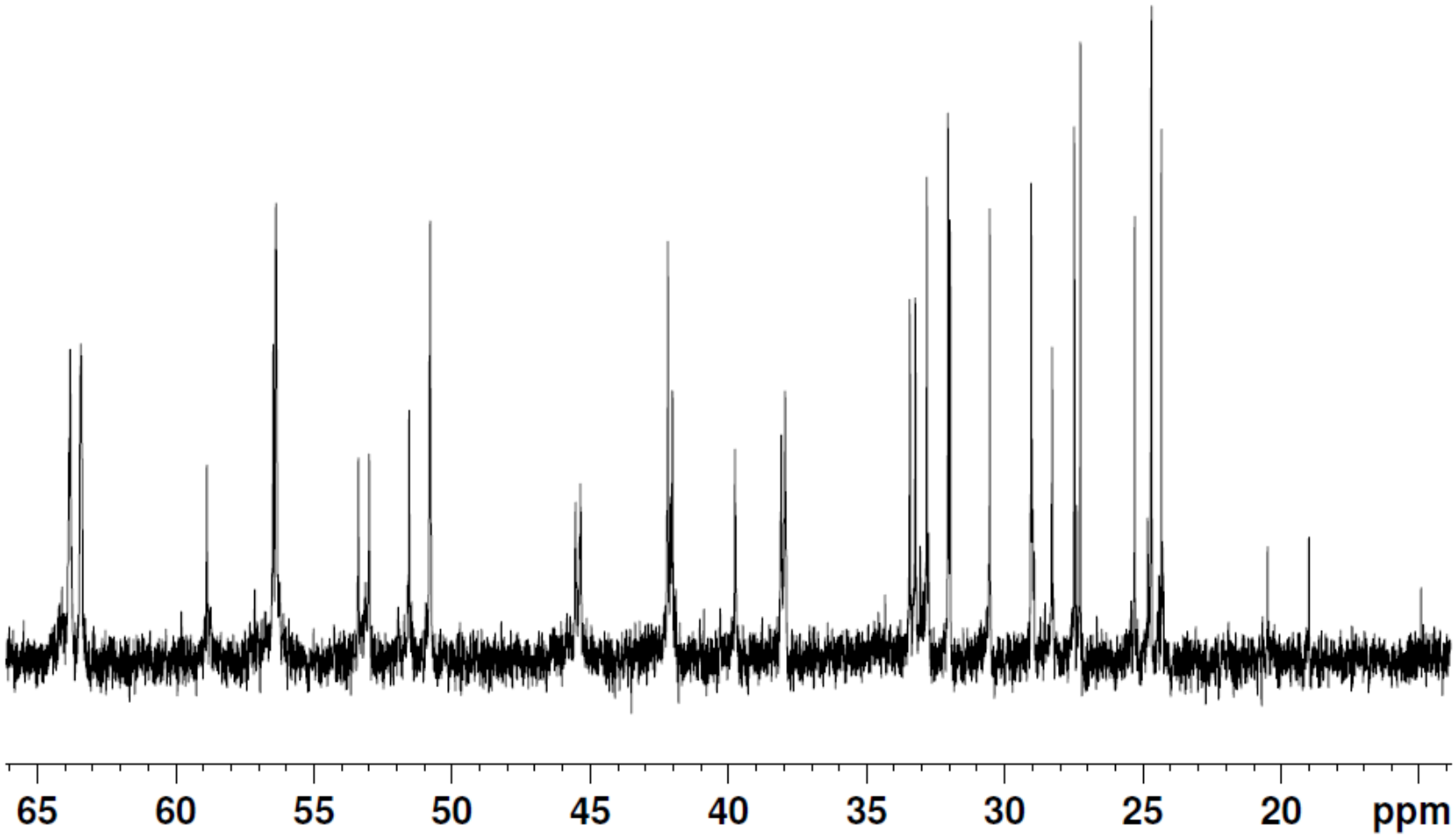

Figure S3. ^{13}C NMR of f3 from 14 to 66 ppm in 90% H_2O : 10% D_2O.

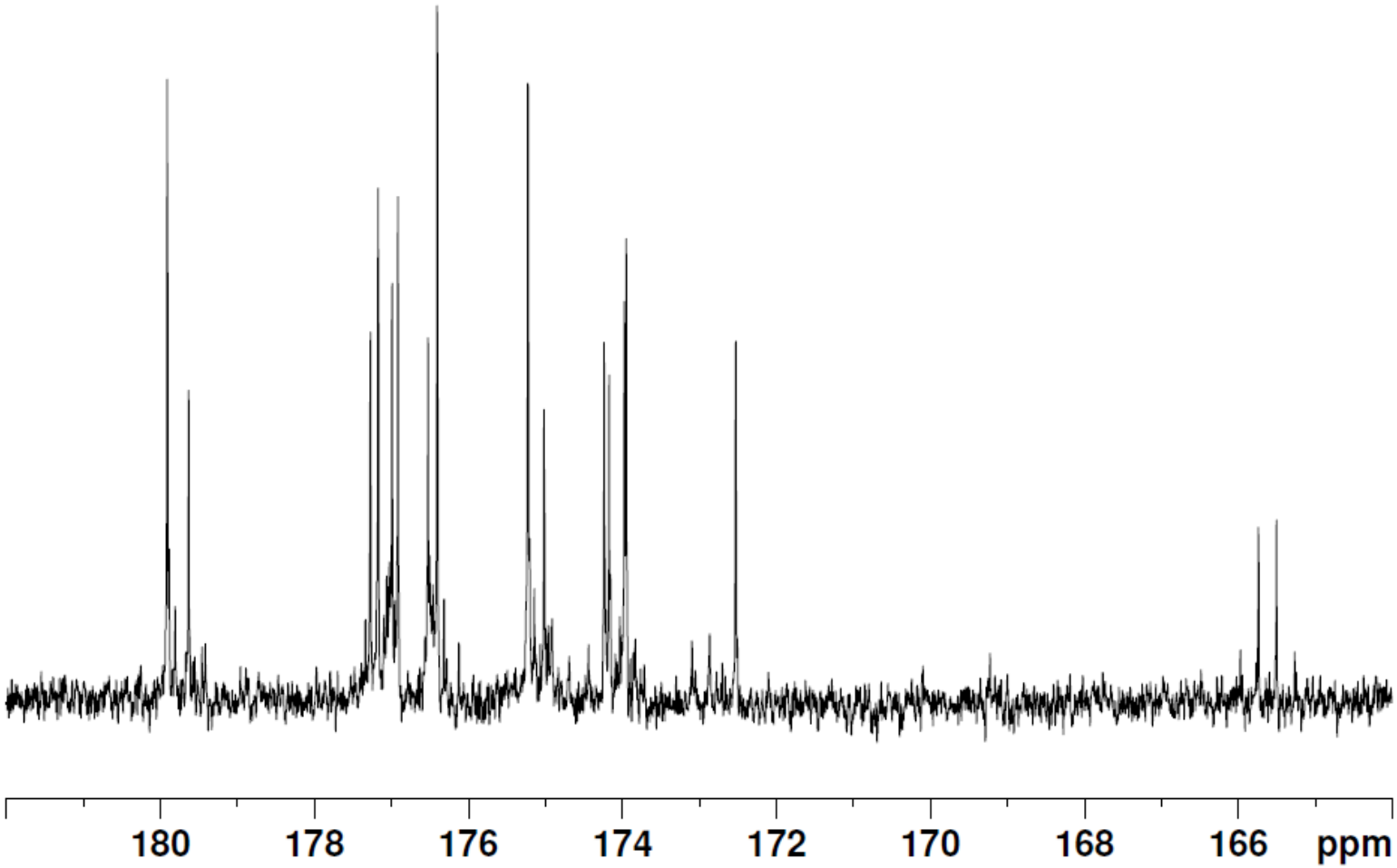

Figure S4. ^{13}C NMR of f3 from 164 to 182 ppm in 90% H_2O : 10% D_2O.

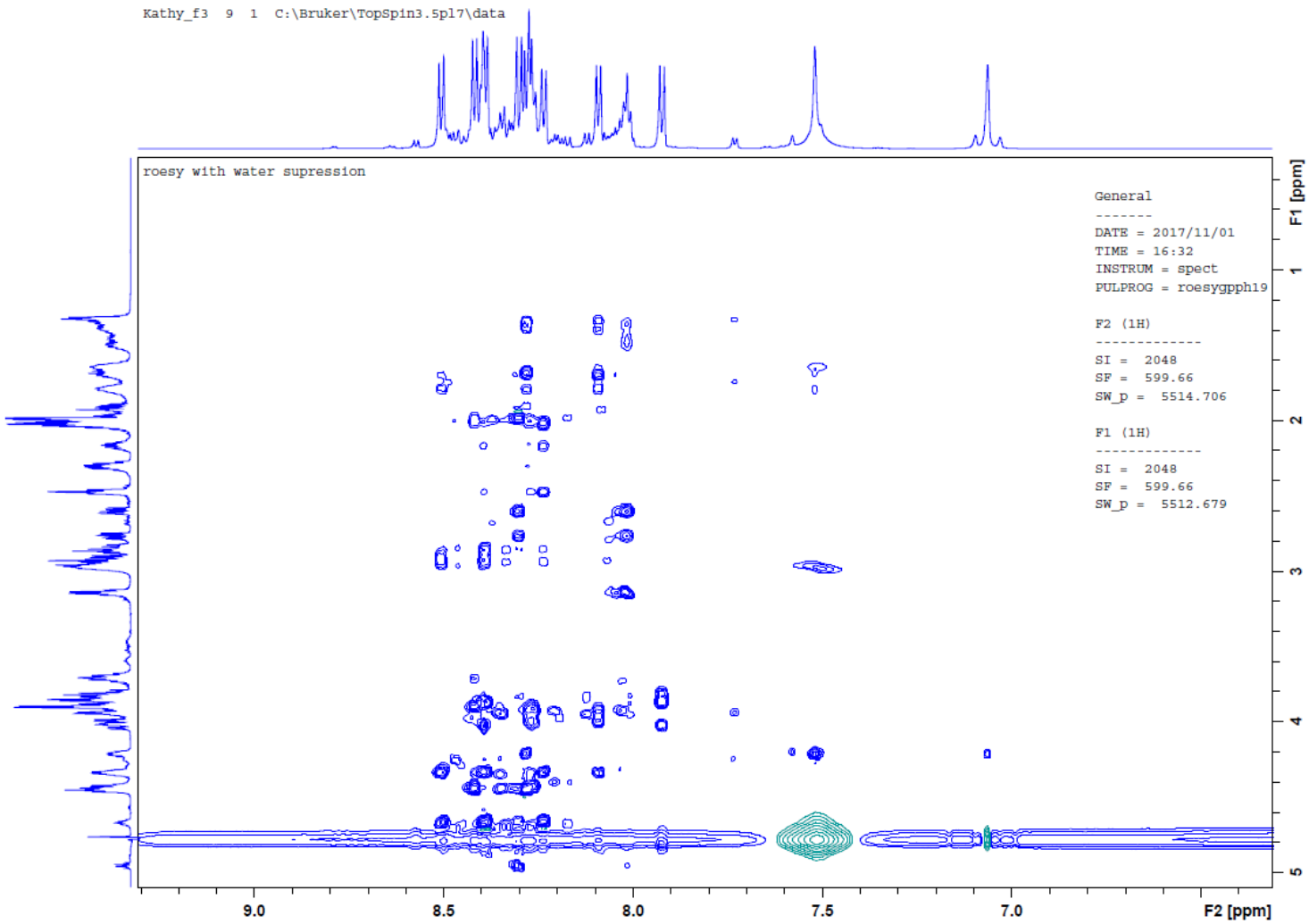

Figure S5. ROESY of f3 in 90% H_2O : 10% D_2O from 6.5 to 9 ppm on x axes and from 1 to 5 on y axes.

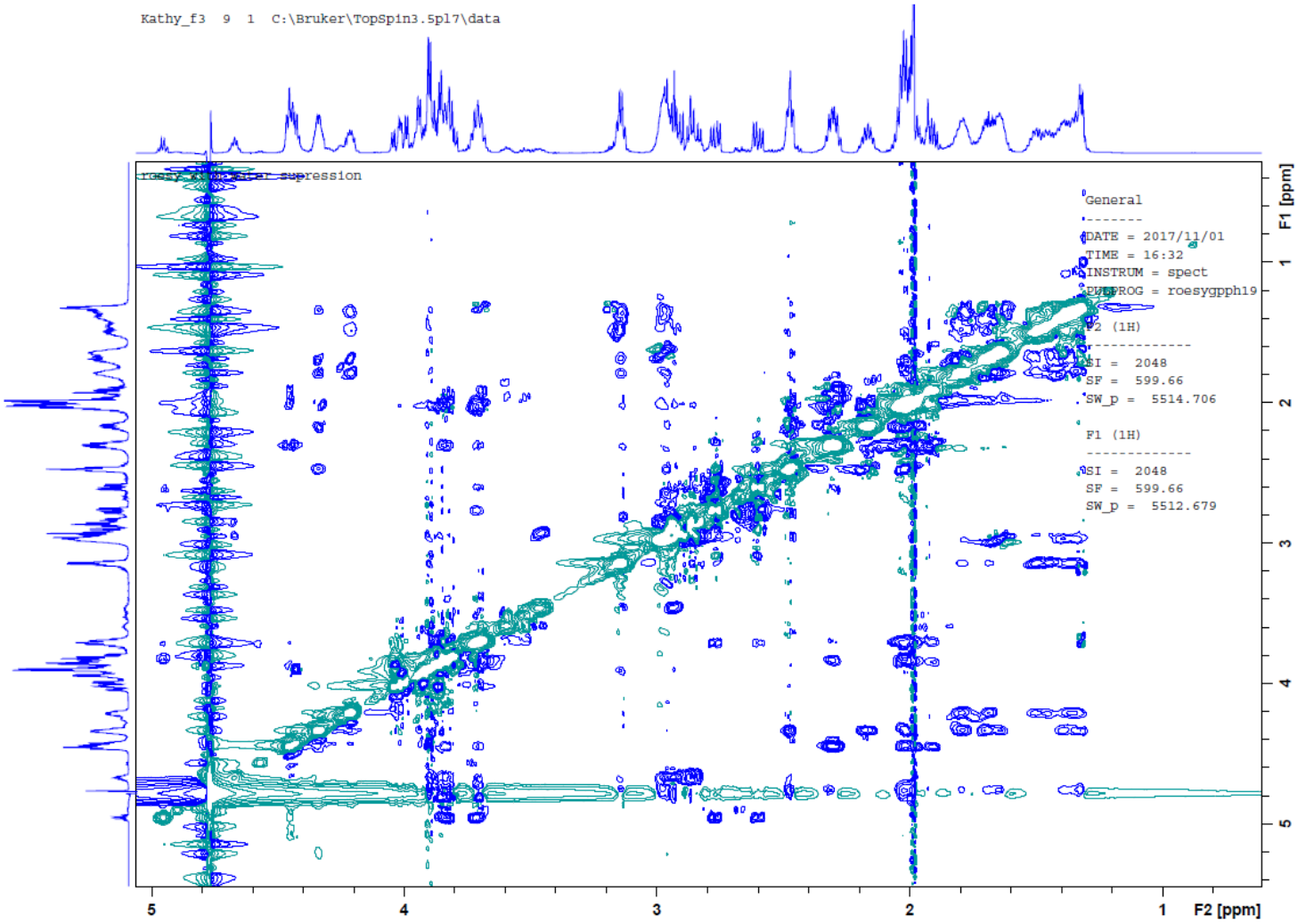

Figure S6. ROESY of f3 in 90% H_2O : 10% D_2O from 1 to 5 ppm on x axes and from 1 to 5 on y axes.

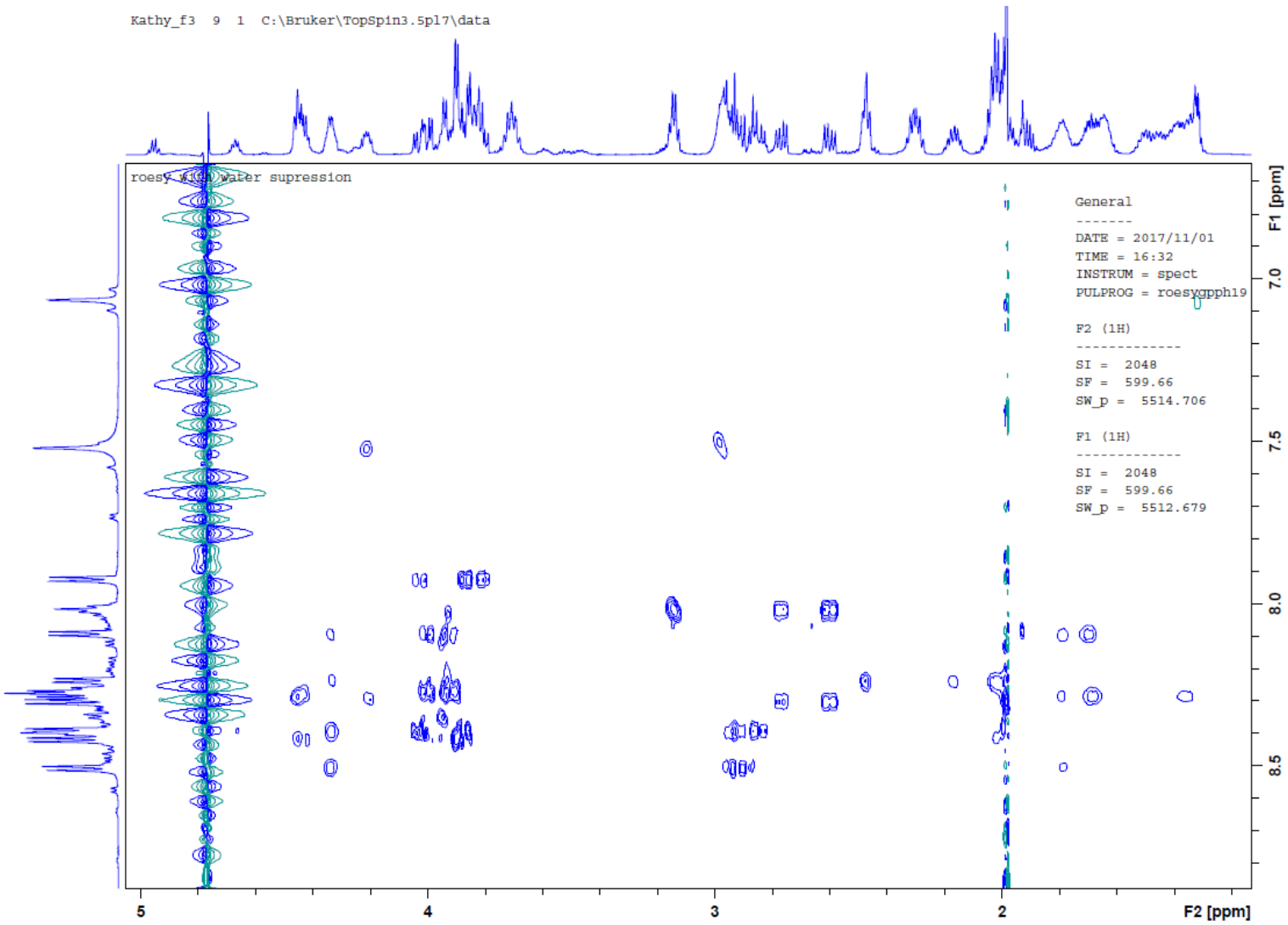

Figure S7. ROESY of f3 in 90% H_2O : 10% D_2O from 1 to 5 ppm on x axes and from 6.7 to 6.8ppm on y axes.

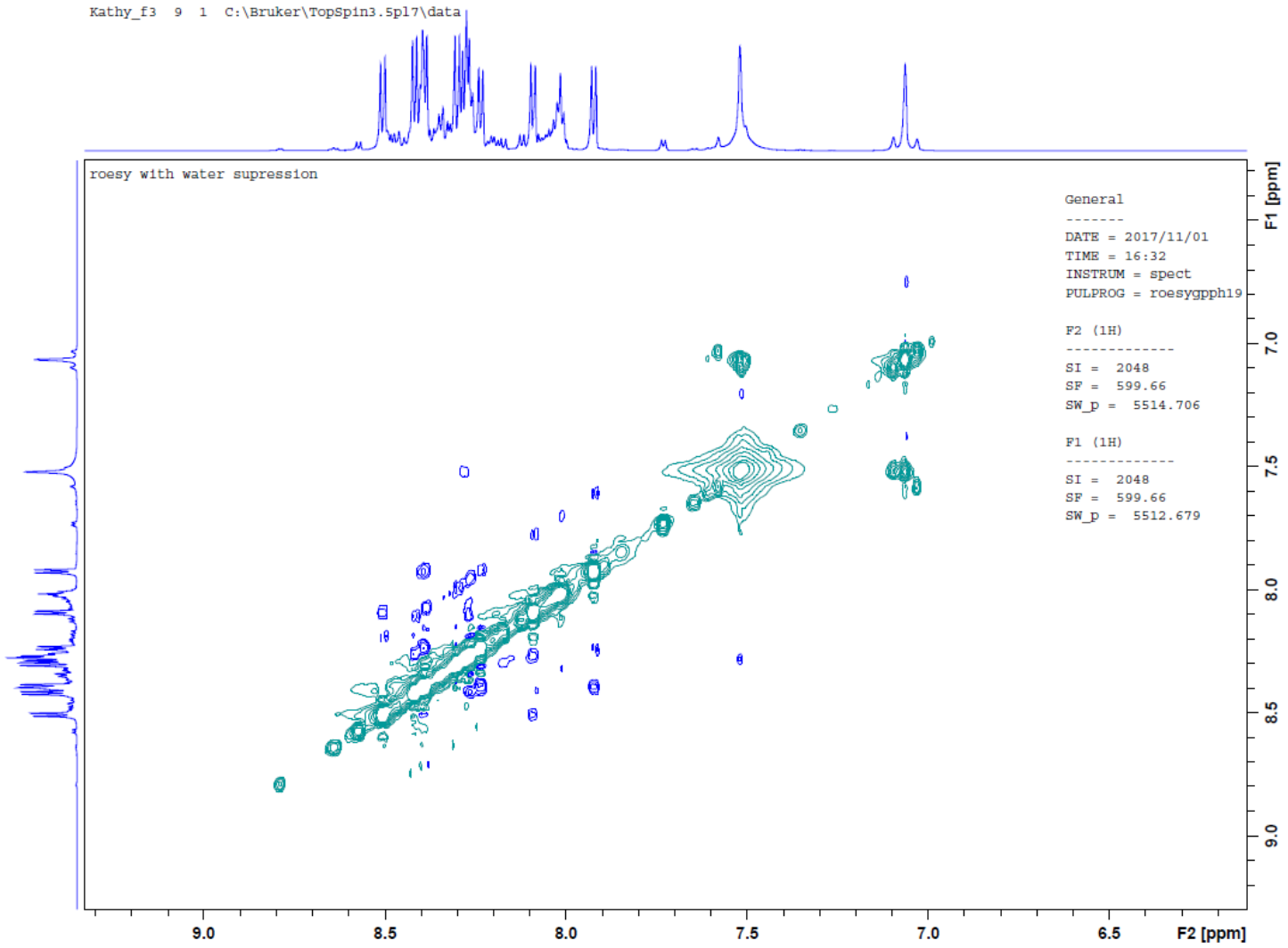

Figure S8. ROESY of f3 in 90% H_2O : 10% D_2O from 6.2 to 9.3 ppm on x axes and from 6.3 to 9.3 on y axes.

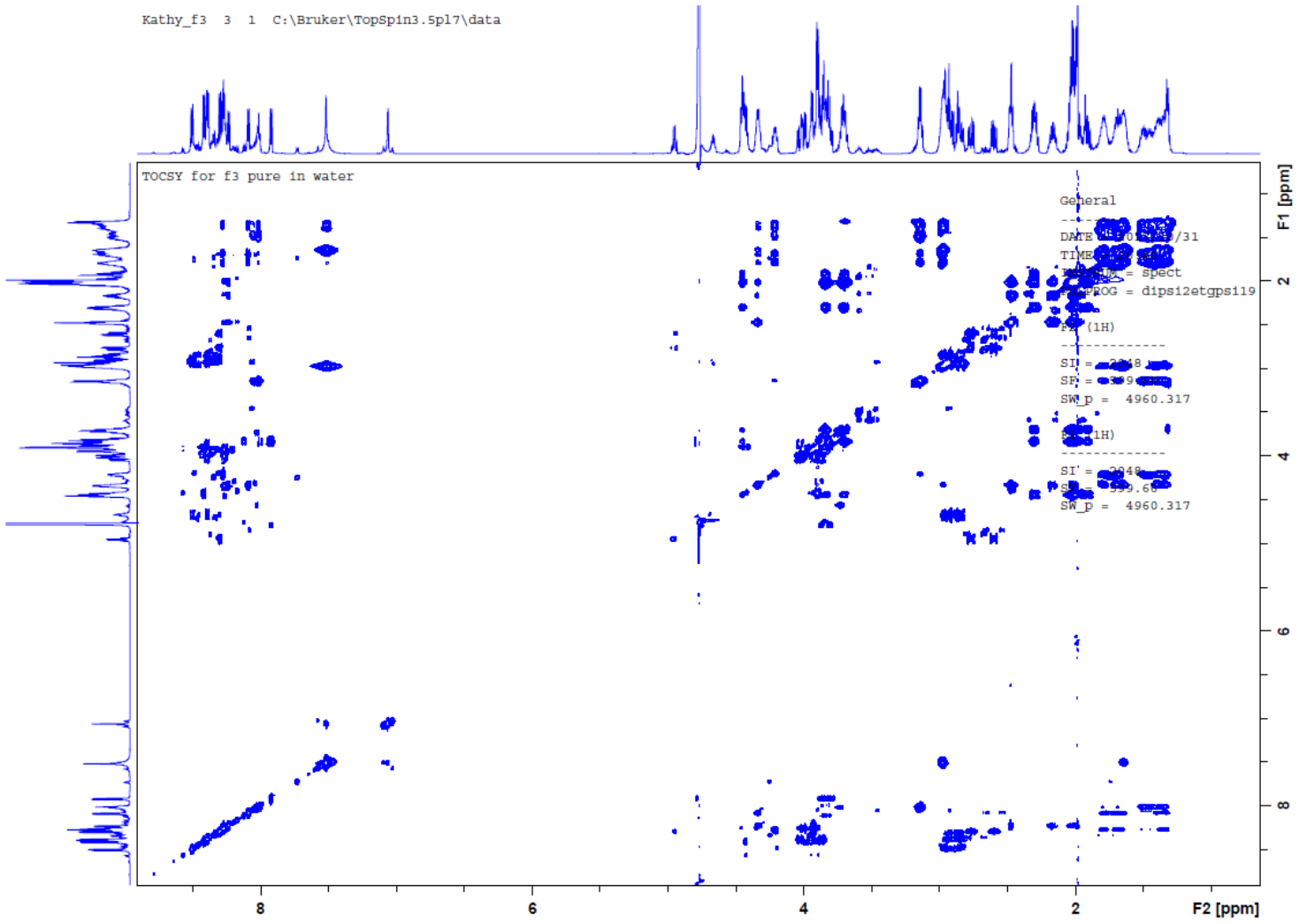

Figure S9. TOCSY of f3 in 90% H_2O : 10% D_2O.

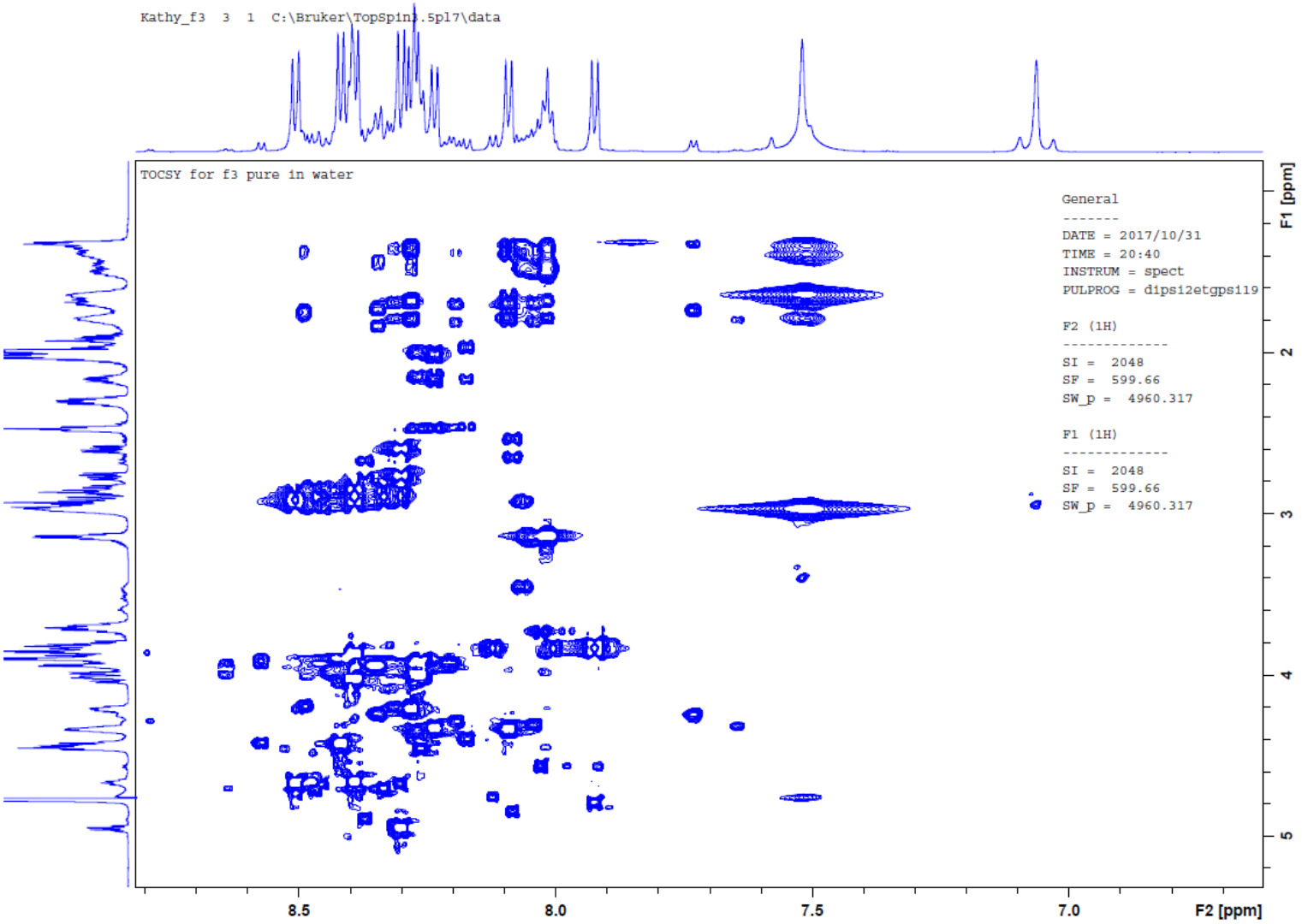

Figure S10. TOCSY of f3 in 90% H_2O : 10% D_2O from 6.7 to 8.8 ppm on x axes and from 1 to 5 on y axes.

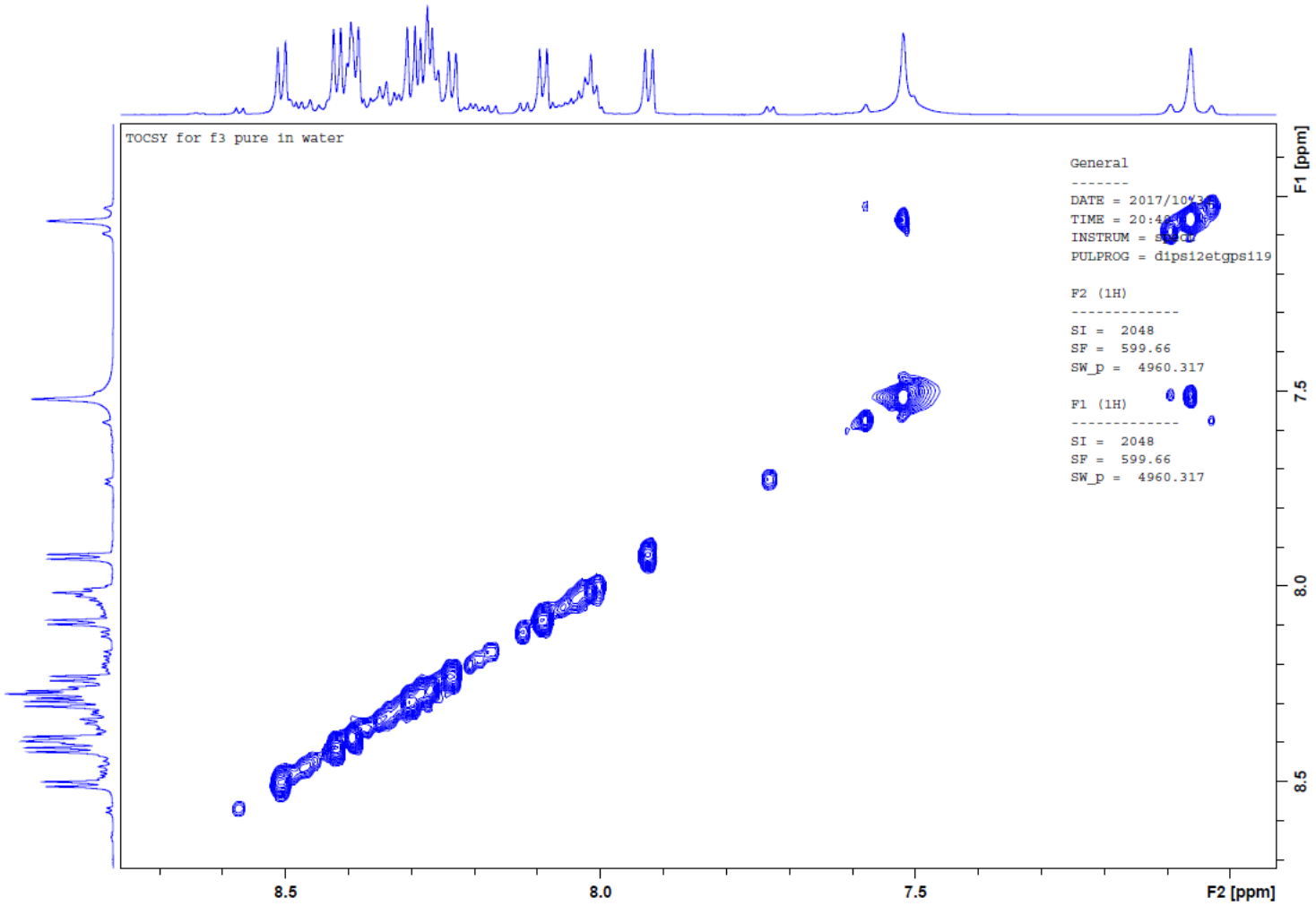

Figure S11. TOCSY of f3 in 90% H_2O : 10% D_2O from 6.9 to 8.7 ppm on x axes and from 6.9 to 8.7 on y axes.

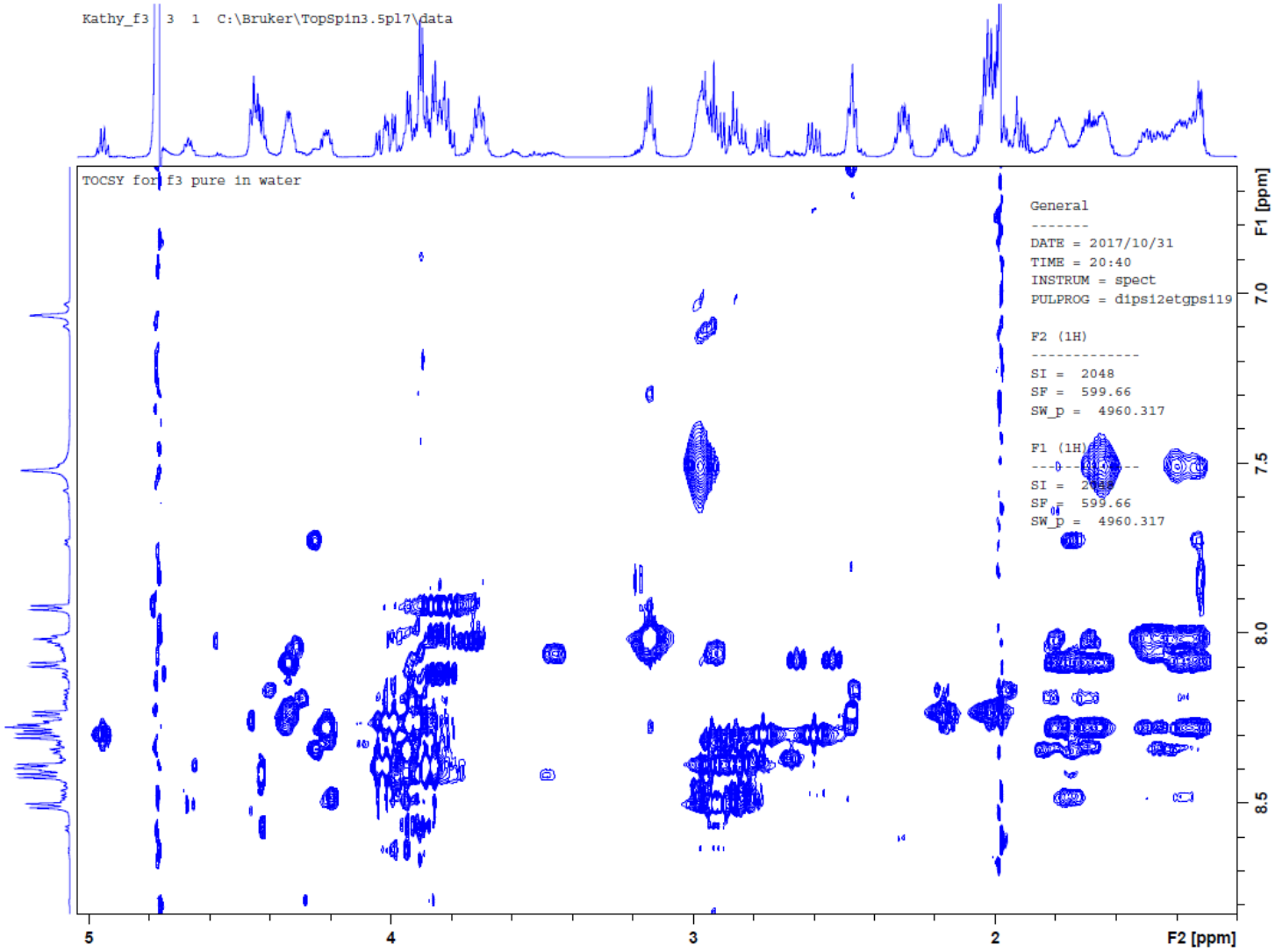

Figure S12. TOCSY of f3 in 90% H_2O : 10% D_2O from 1 to 5 ppm on x axes and from 6.7 to 8.8 on y axes.

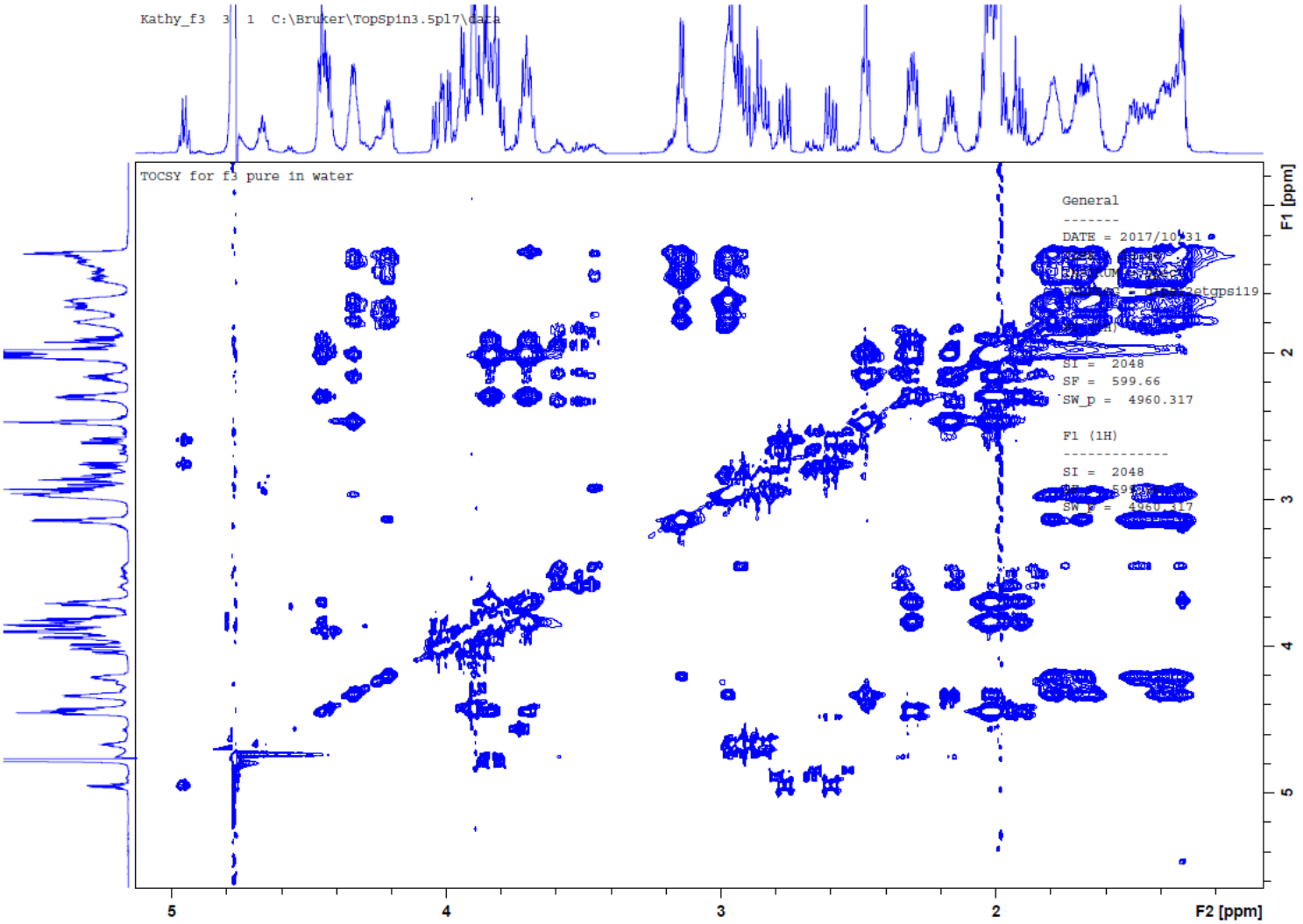

Figure S13. TOCSY of f3 in 90% H_2O : 10% D_2O from 1 to 5 ppm on x axes and from 1 to 5.5 on y axes.