SUPPORTING INFORMATION

Total Synthesis of Scytonemide A Employing Weinreb AM Solid-Phase Resin

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Determination of Loading Efficiency[S1]

The Fmoc-Leu loaded Weinreb resin (100 mg, substitution = 0.44 mmol/g for synthesis of **6a**, 0.73 mmol/g for synthesis of **12a/b**) was shaken in a solution of piperidine/DMF (3 mL, 1:9 v/v) for 5 min and then repeated for 10 min. The deprotection solutions were combined and an aliquot (150 µL) was diluted 20-fold to 3 mL. 300 µL of this solution was then diluted 10-fold to 3 mL and placed in a quartz cuvette to measure UV absorbance of the piperidine-fulvene adduct (λ = 289.8 nm, ε_c = 6089 M^{-1} cm^{-1} as recommended by Eissler et al[S2]) for quantification of Leu loaded onto the resin.

Equation for Loading Efficiency:

$$Loading\ \left(\frac{mmol}{g}\right) = \frac{(Abs_{289.8} * v_{cuvette} * D)}{(e_c * l * m^{resin})}$$

where $V_{cuvette}$ = 3 mL

D (dilution factor) = 200

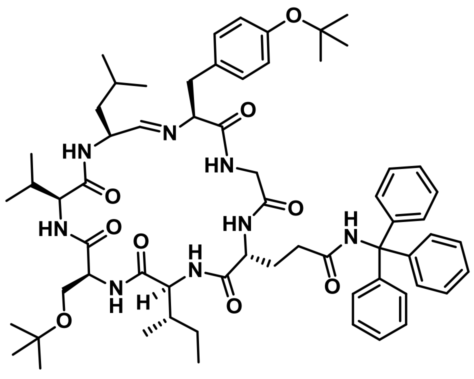
ε_c[S2] = 6089 $mL*mmol^{-1}*cm^{-1}$

l (path length) = 1 cm

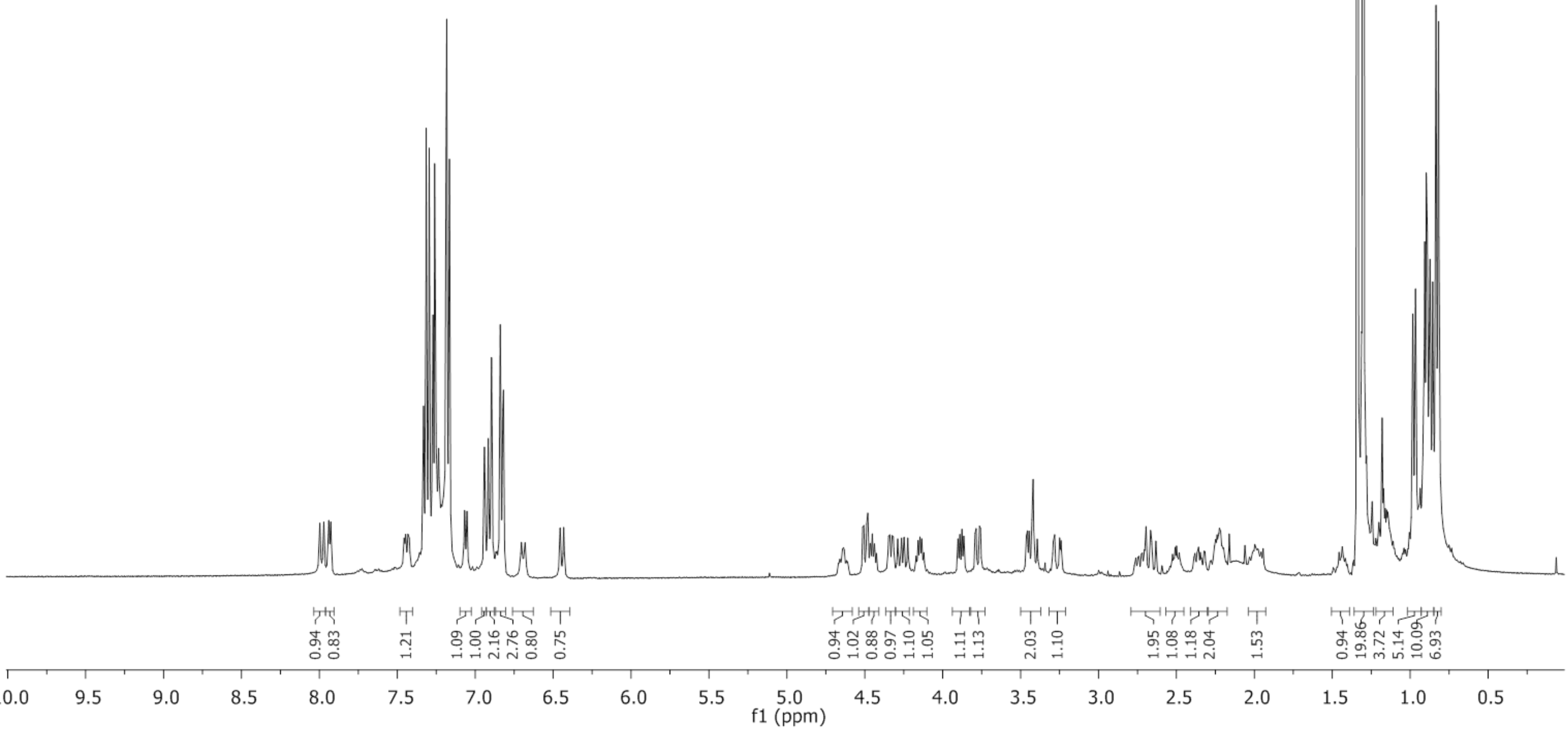
m^{resin} = 100 mg

Weinreb Resin, substitution = 0.44 mmol/g: $Abs_{298.8}$ = 0.336, loading = 0.331 mmol/g

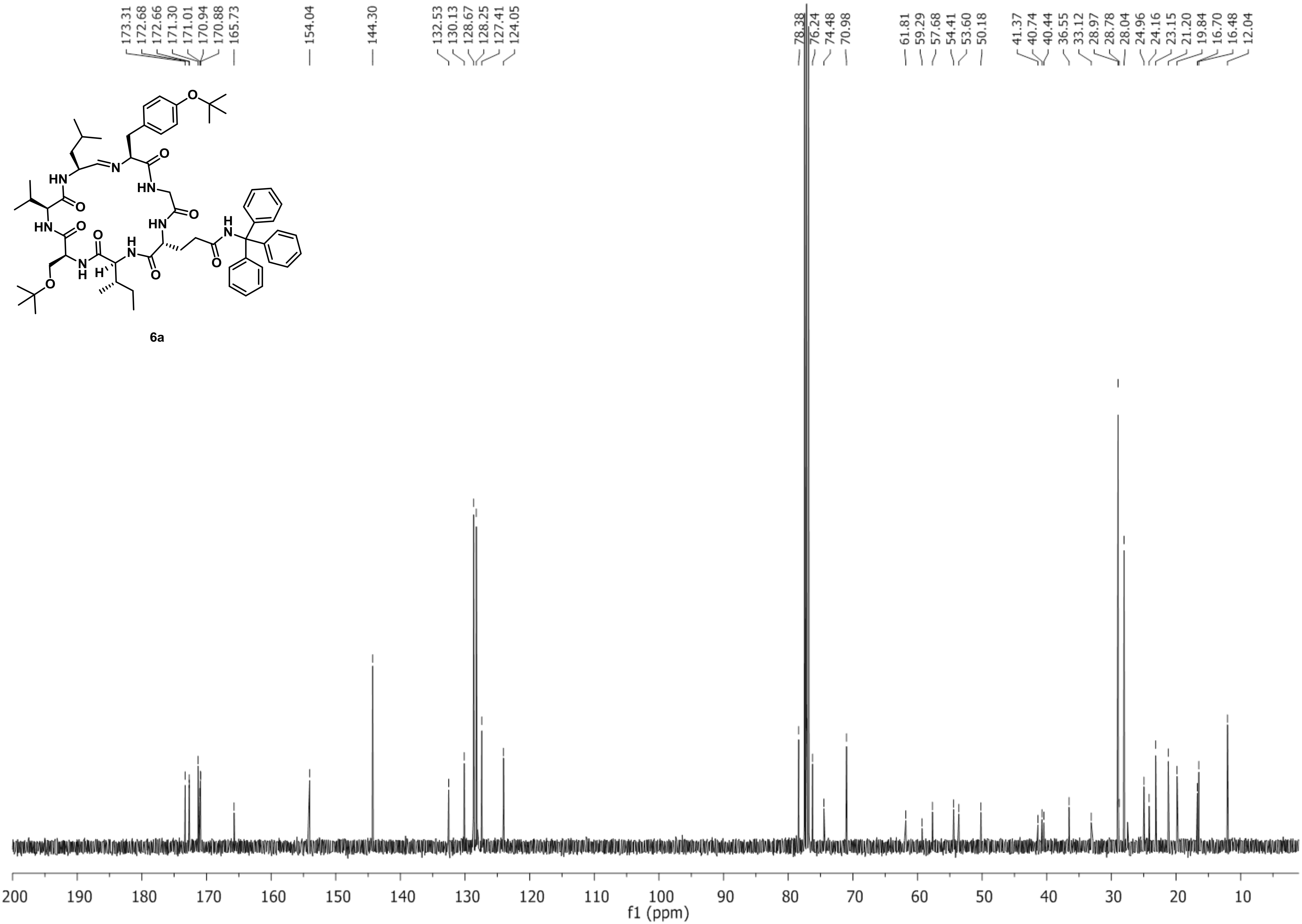
Weinreb Resin, substitution = 0.73 mmol/g: $Abs_{298.8}$ = 0.299, loading = 0.295 mmol/g



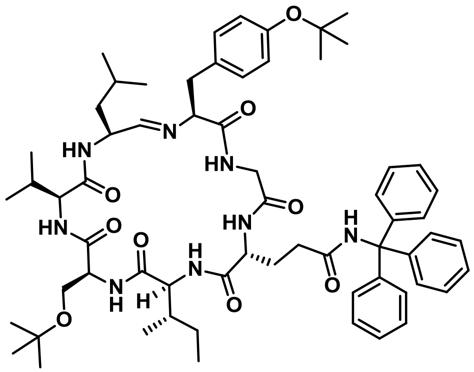
6a



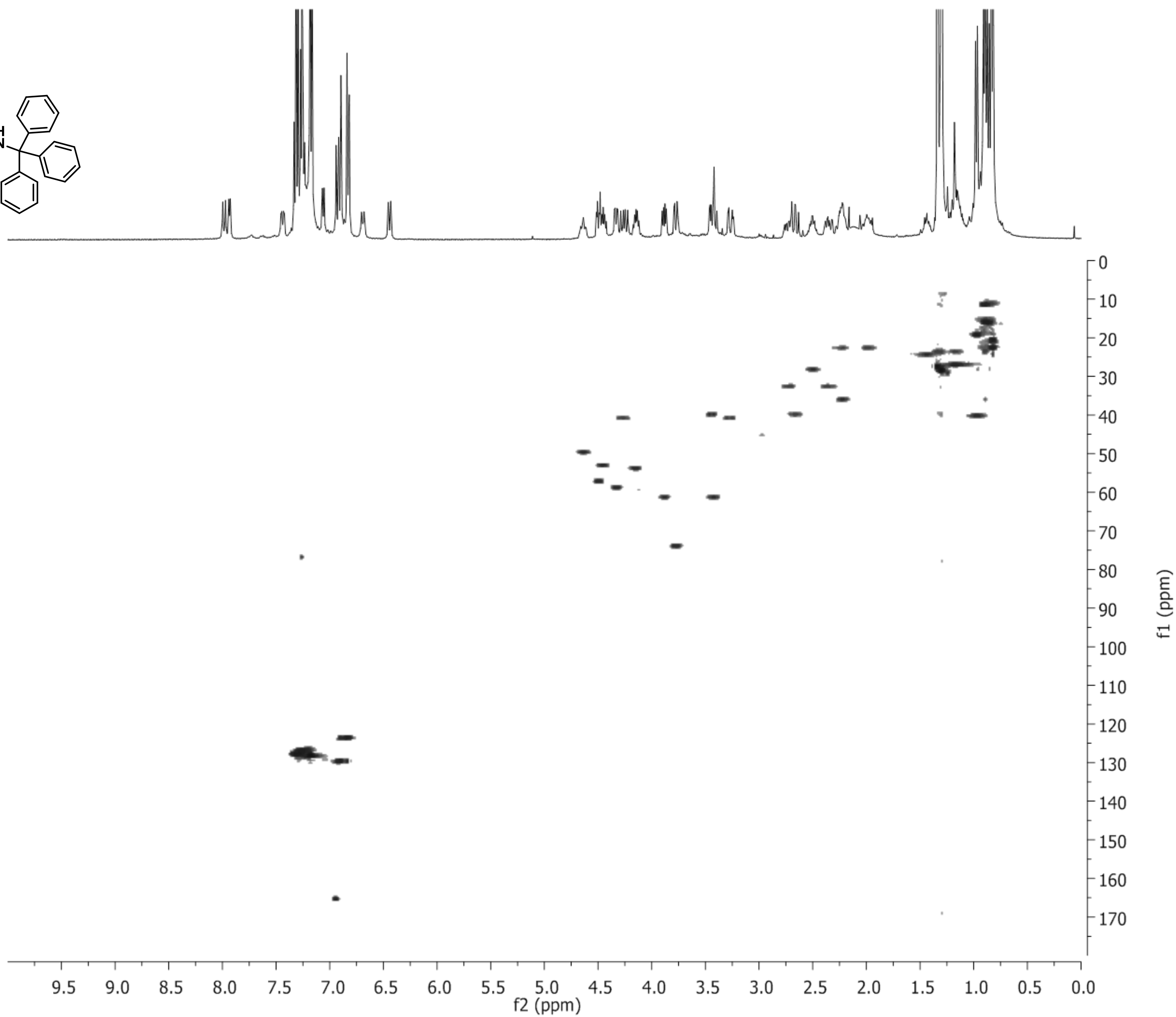
^{1}H NMR ($CDCl_3$, 400 MHz) of compound **6a.**



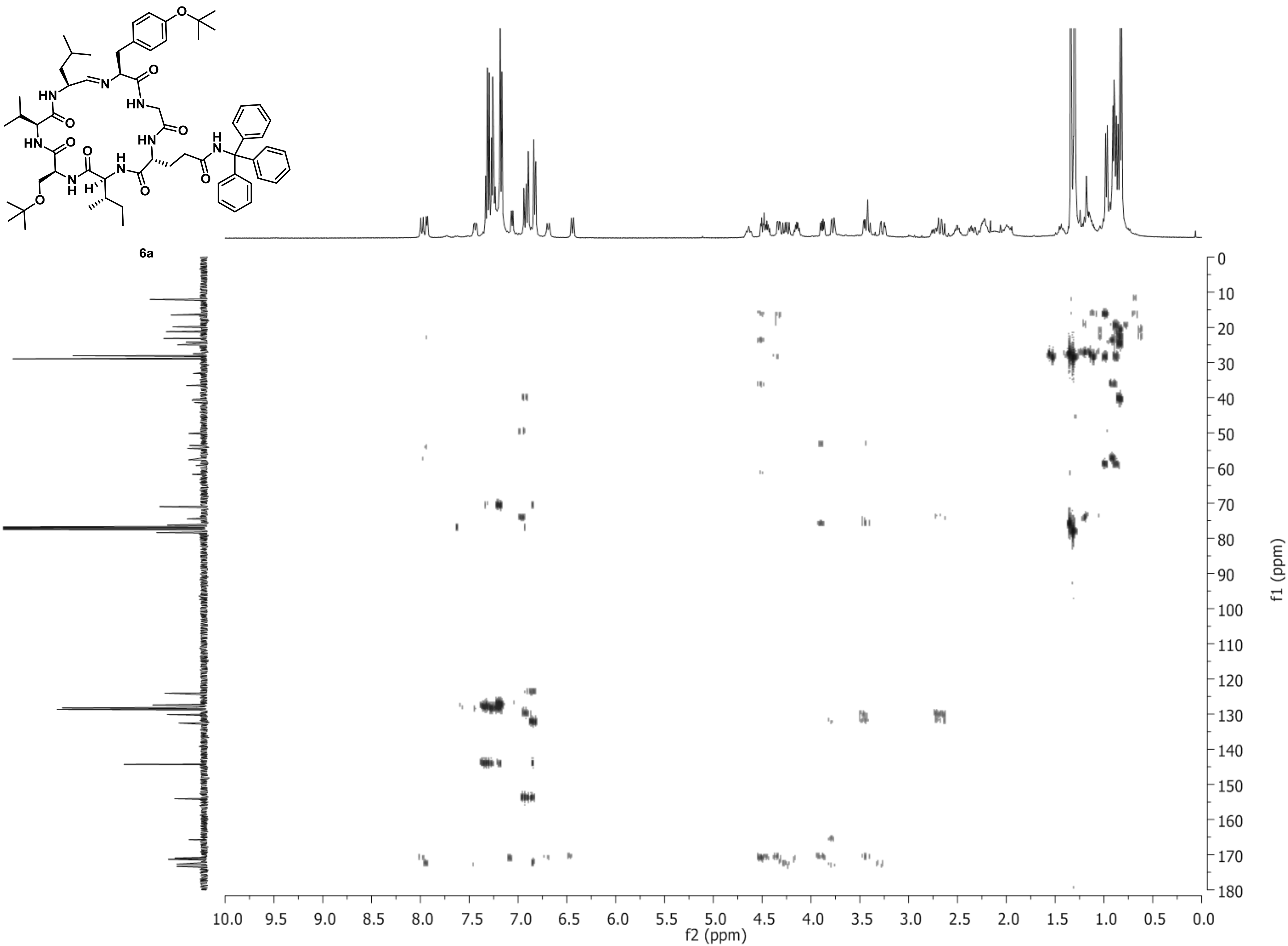
^{13}C NMR ($CDCl_3$, 101 MHz) of compound **6a.**



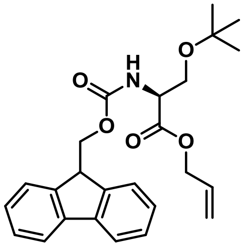
6a



HSQC NMR ($CDCl_3$, 400 MHz) of compound **6a.**



HMBC NMR ($CDCl_3$, 400 MHz) of compound **6a.**



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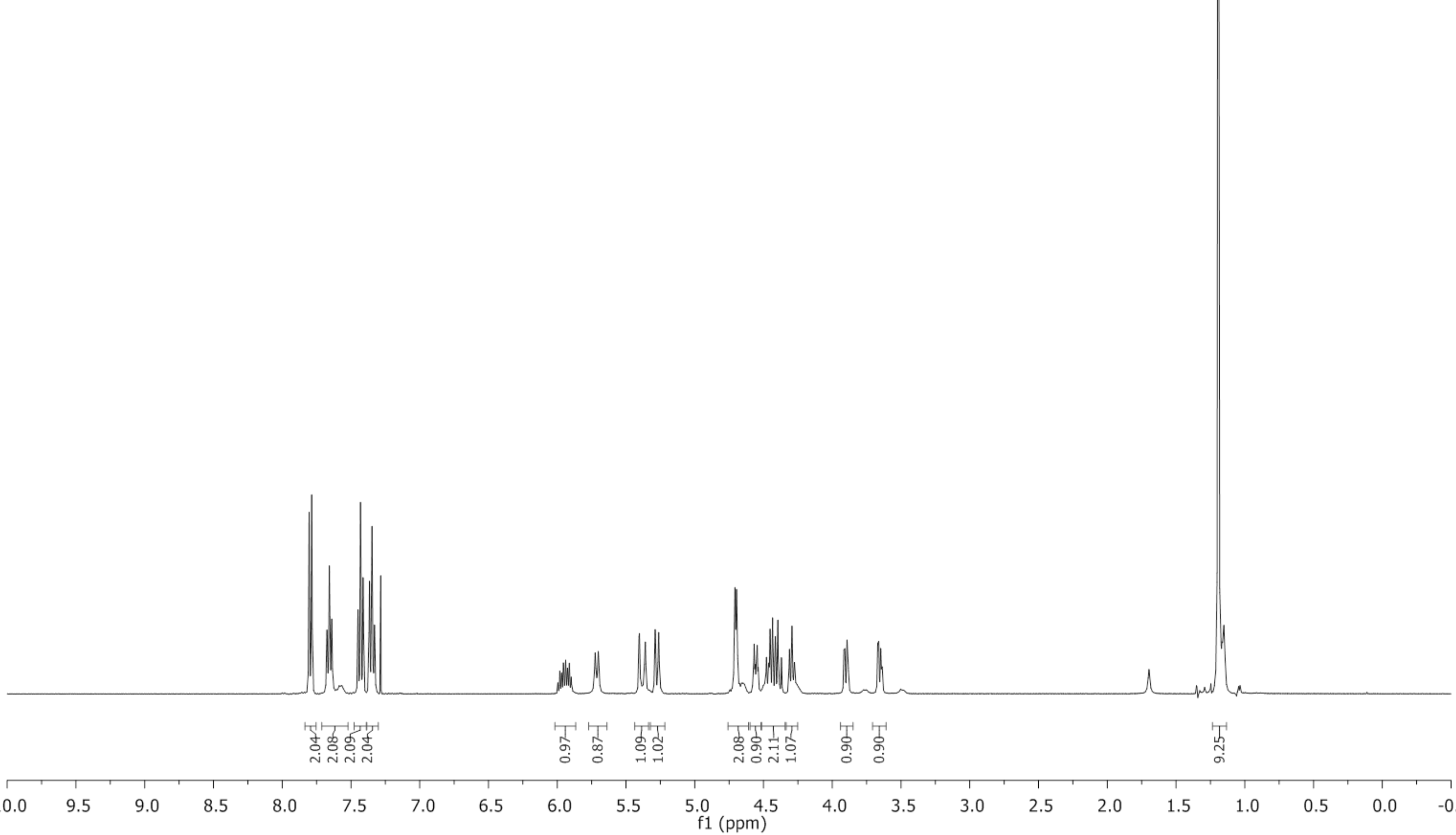
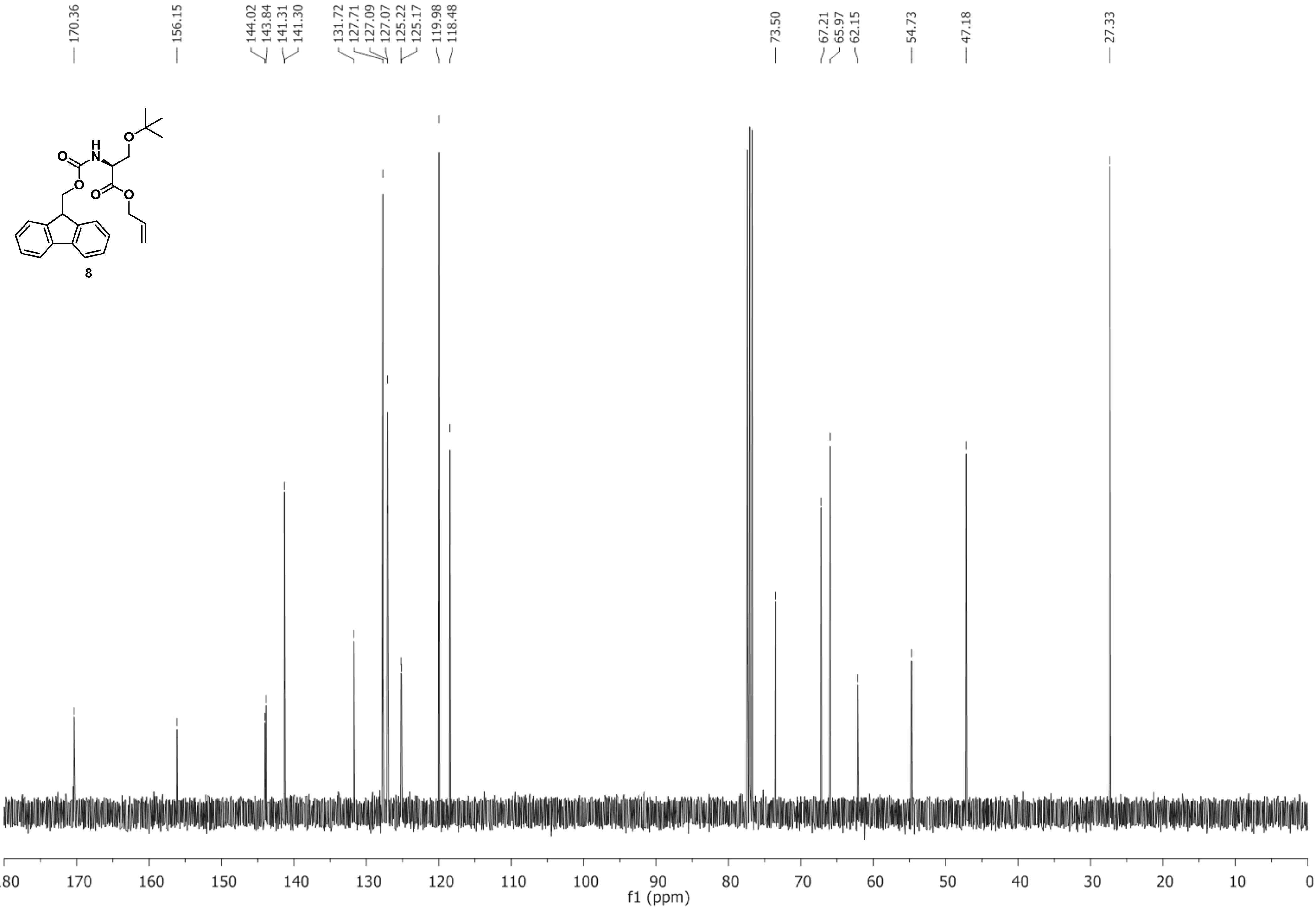
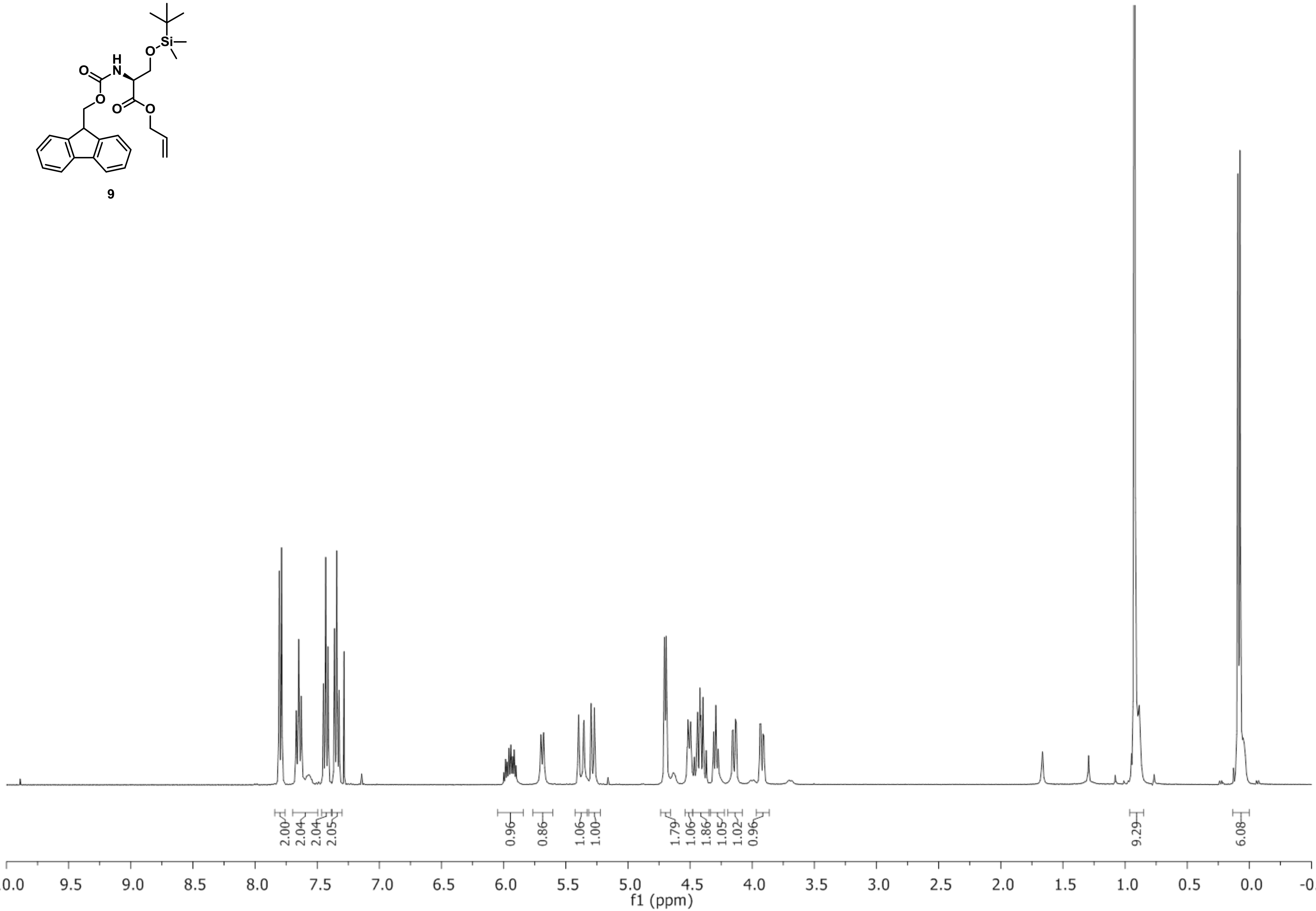


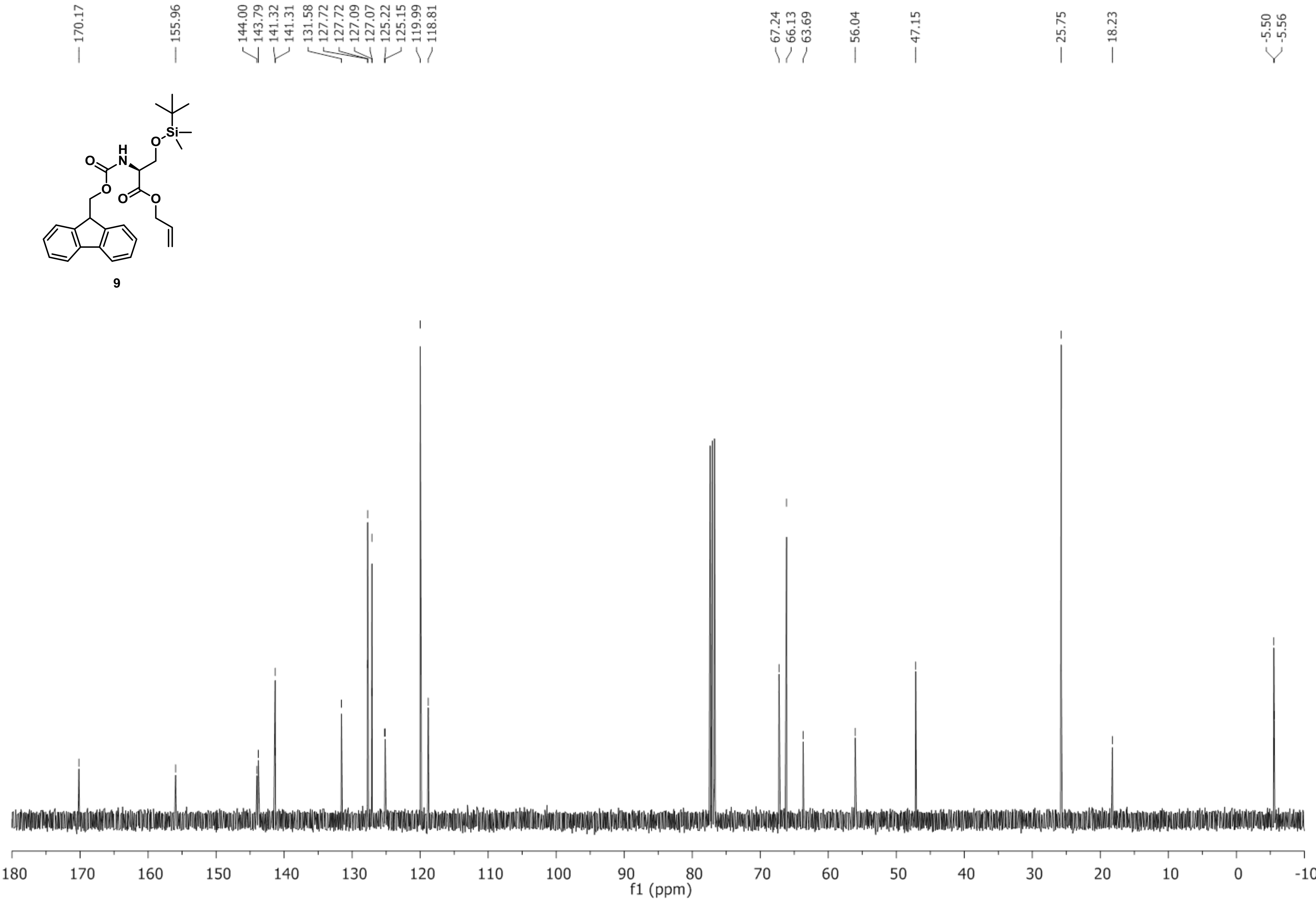
^1H NMR ($CDCl_3$, 400 MHz) of compound **8.**



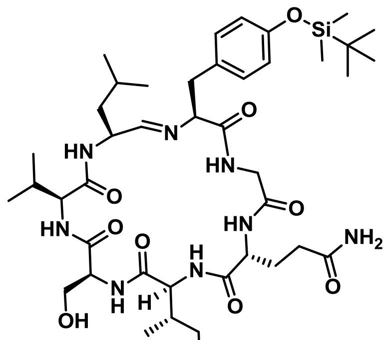
^{13}C NMR ($CDCl_3$, 101 MHz) of compound **8.**



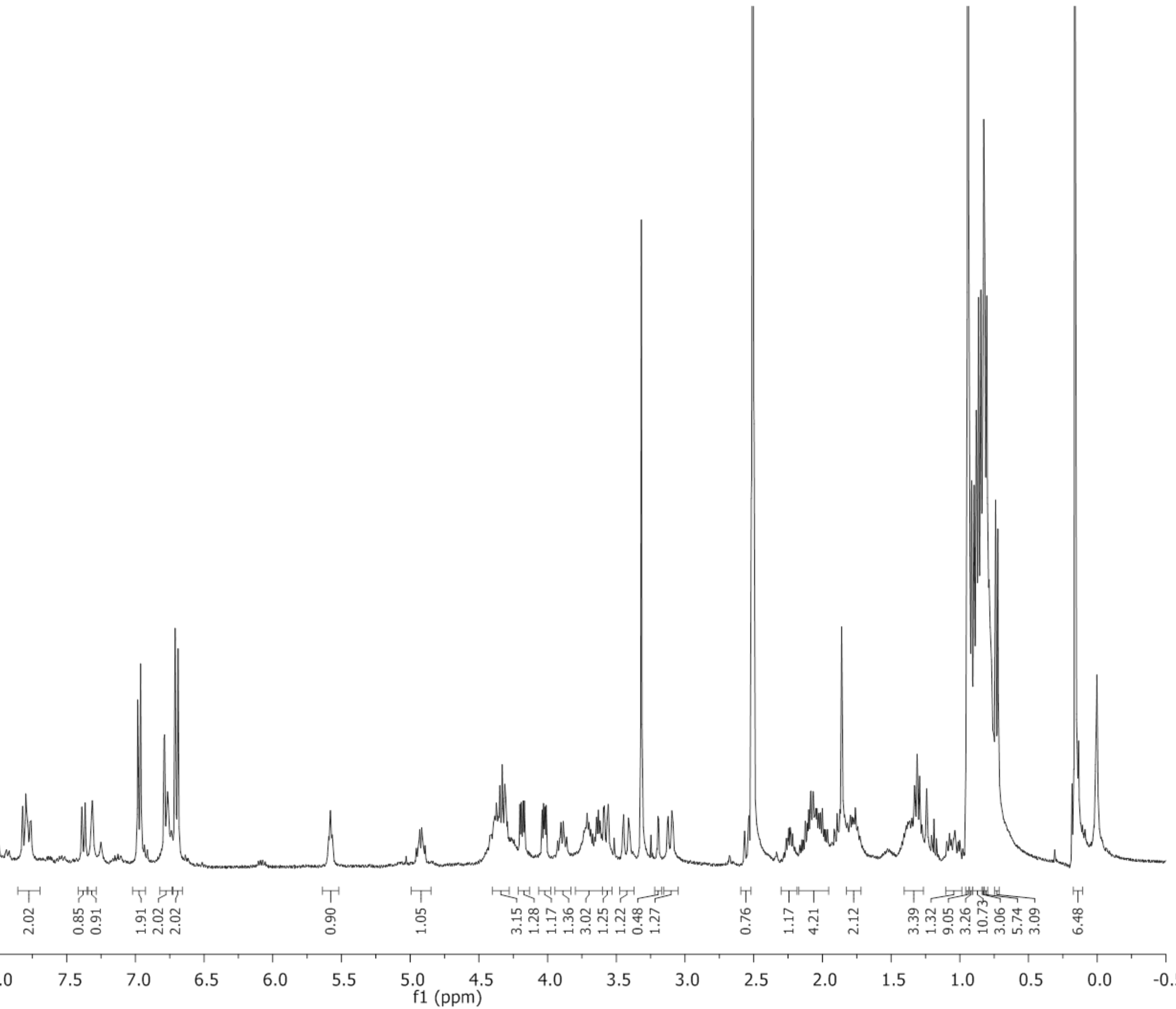
^{1}H NMR ($CDCl_3$, 400 MHz) of compound **9**.



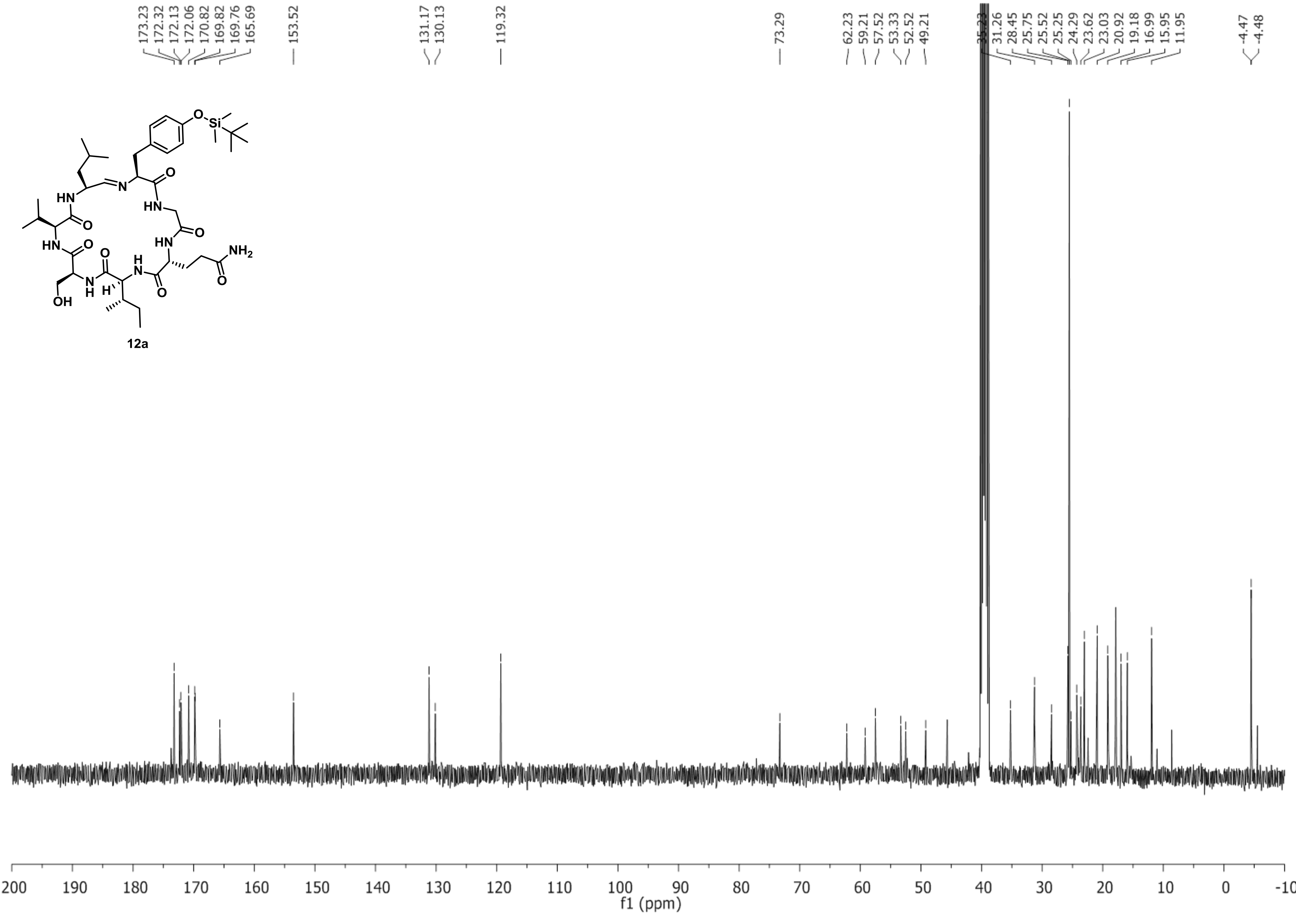
^{13}C NMR ($CDCl_3$, 101 MHz) of compound **9**.



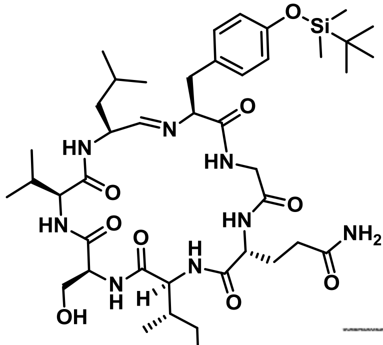
12a



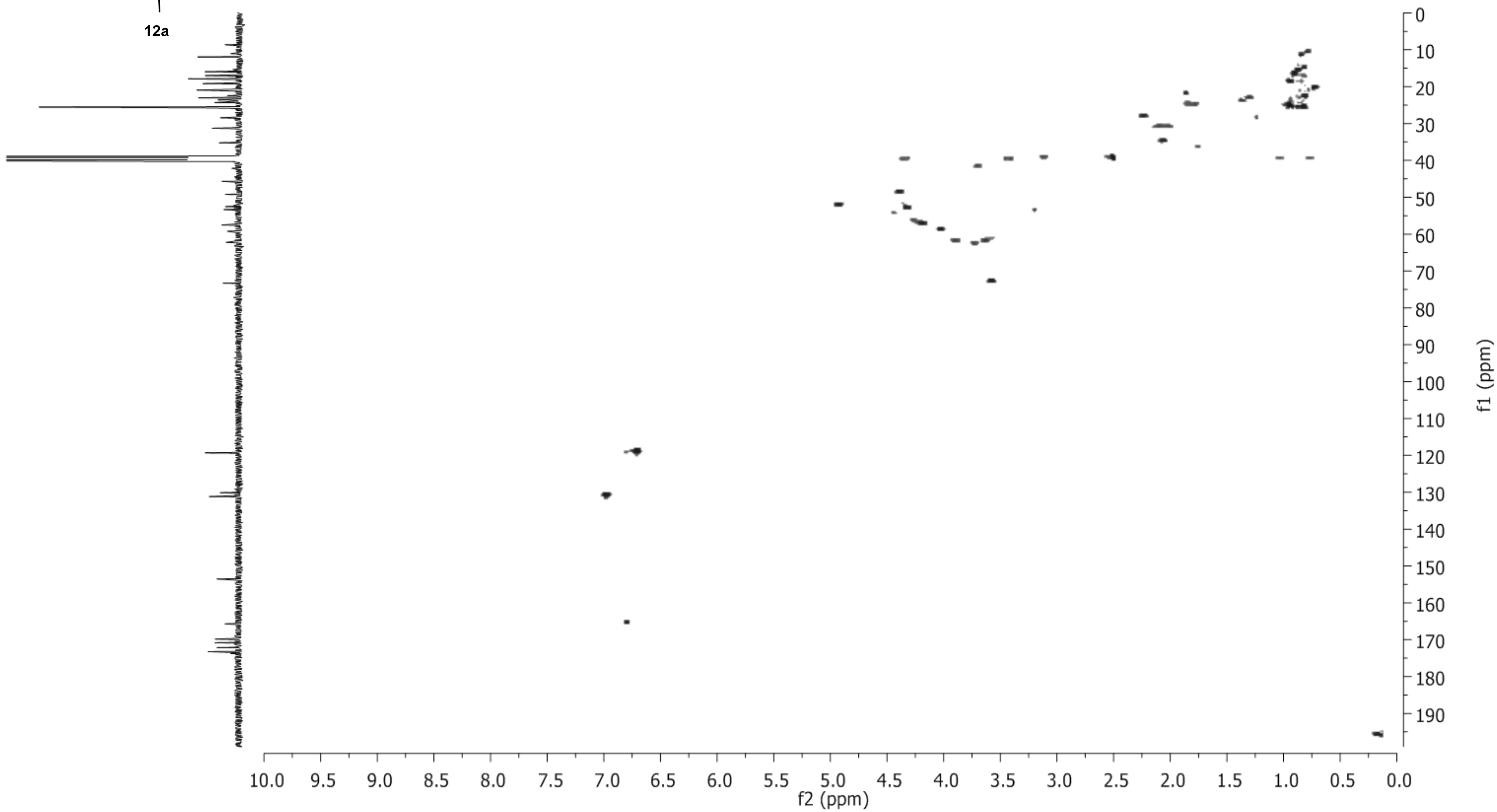
[1]H NMR (d_6-DMSO, 400 MHz) of compound **12a**.



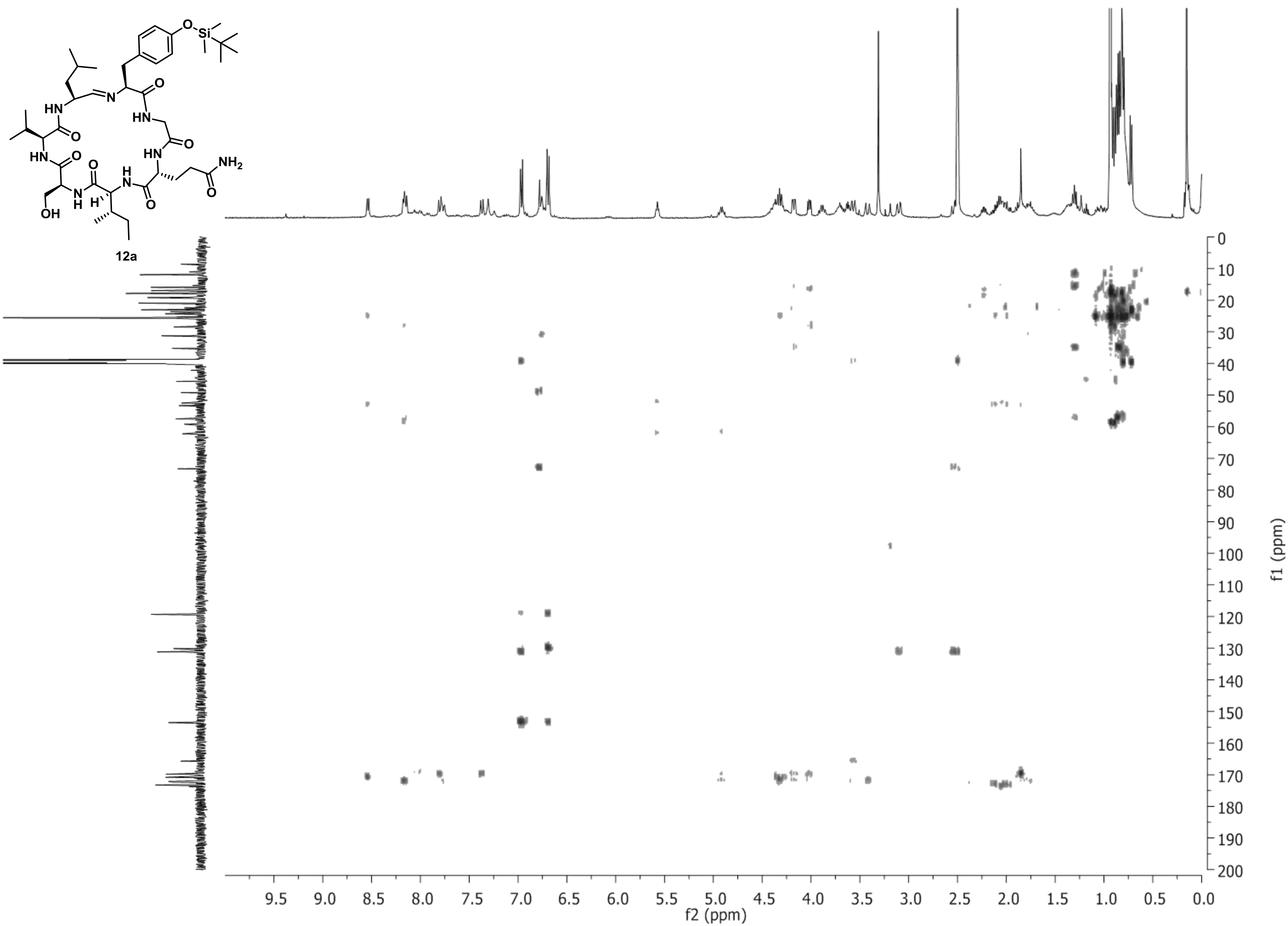
^{13}C NMR (d_6-DMSO, 101 MHz) of compound **12a**.



12a



HSQC NMR (d_6-DMSO, 400 MHz) of compound **12a**.



HMBC NMR (d_6-DMSO, 400 MHz) of compound **12a**.

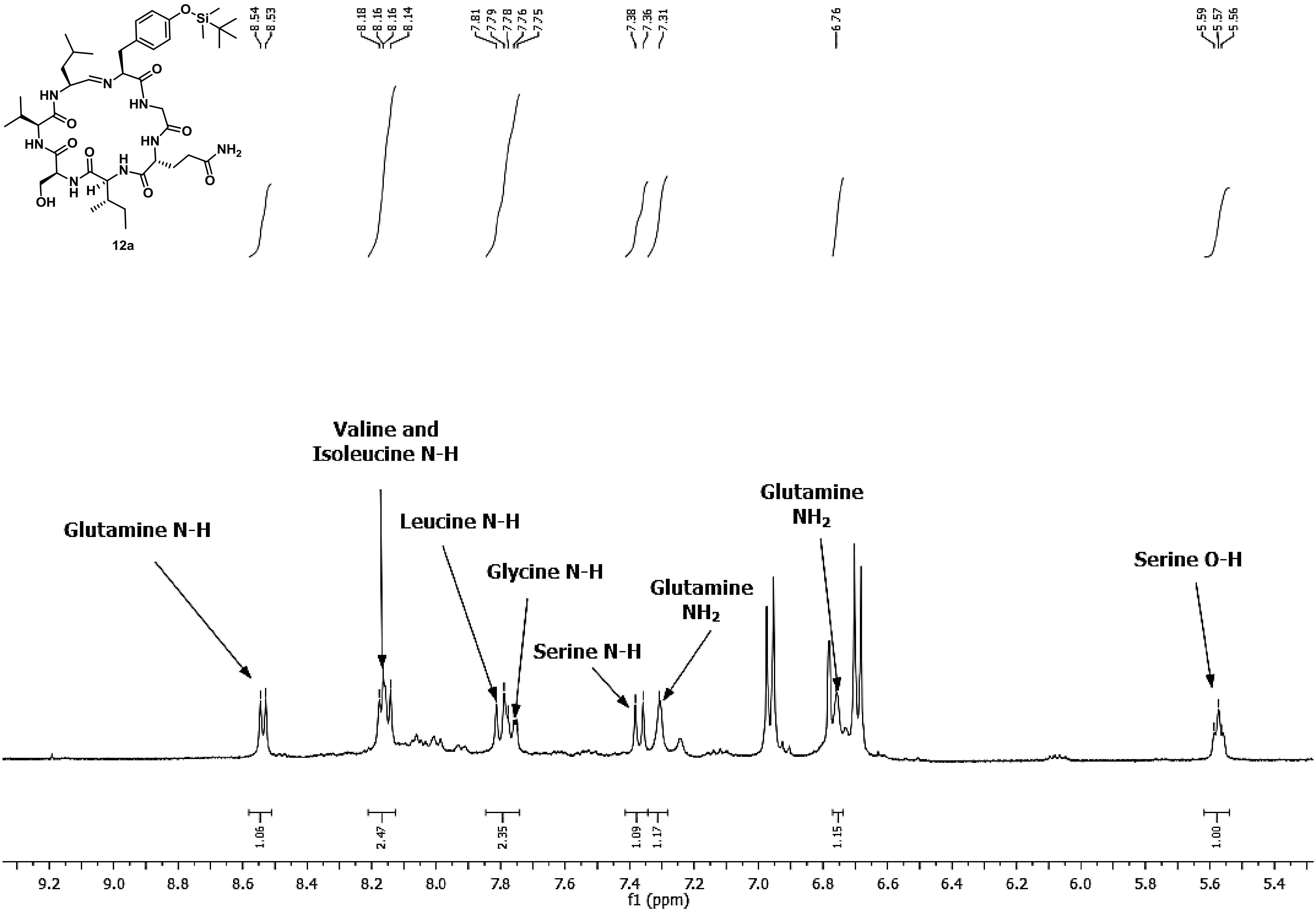


Figure S1. Assignment of –NH and –OH protons in ^{1}HNMR for **12a**.

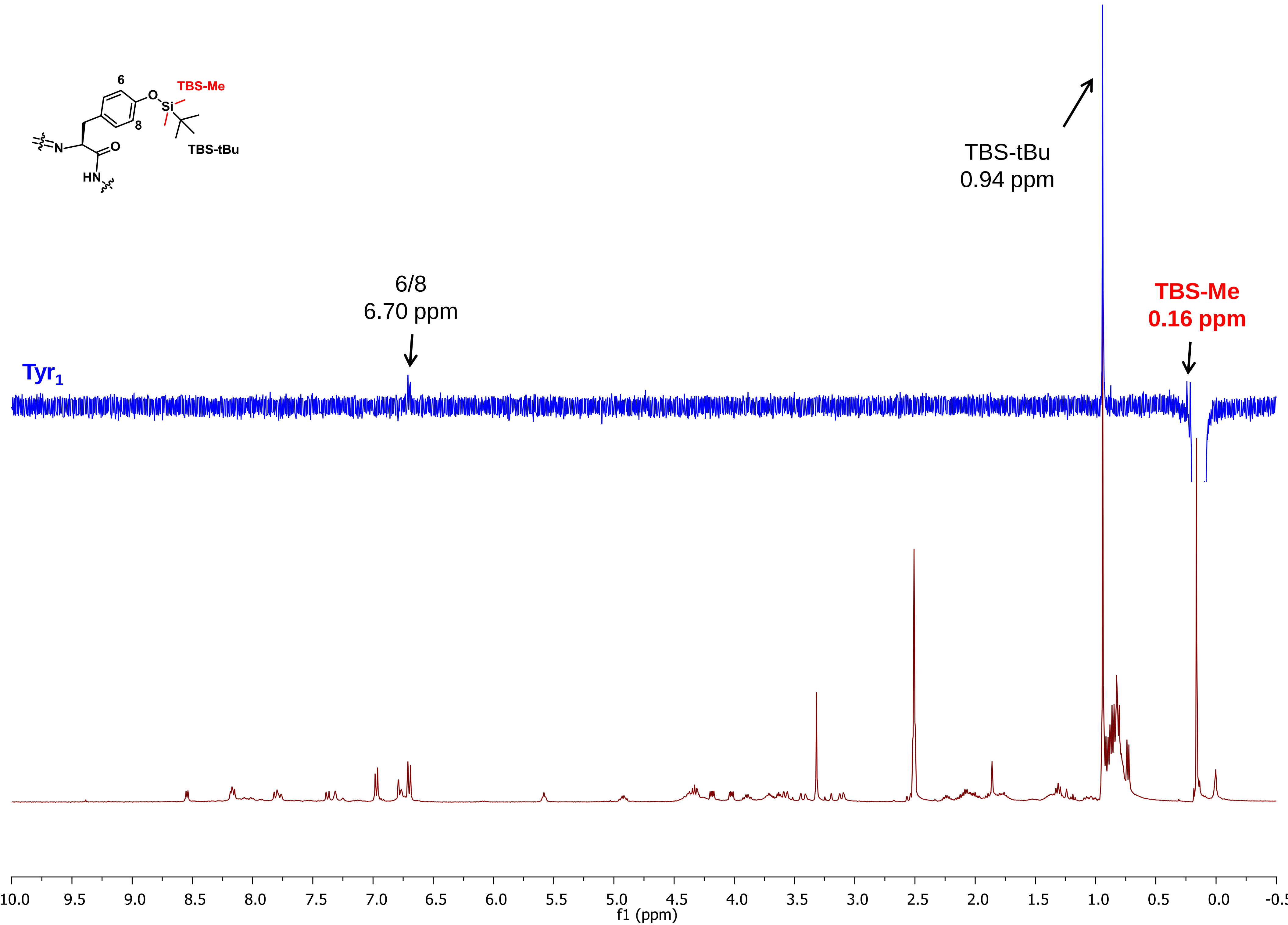


Figure S2. Selective NOESY for TBS-Me (0.16 ppm) for **12a**.

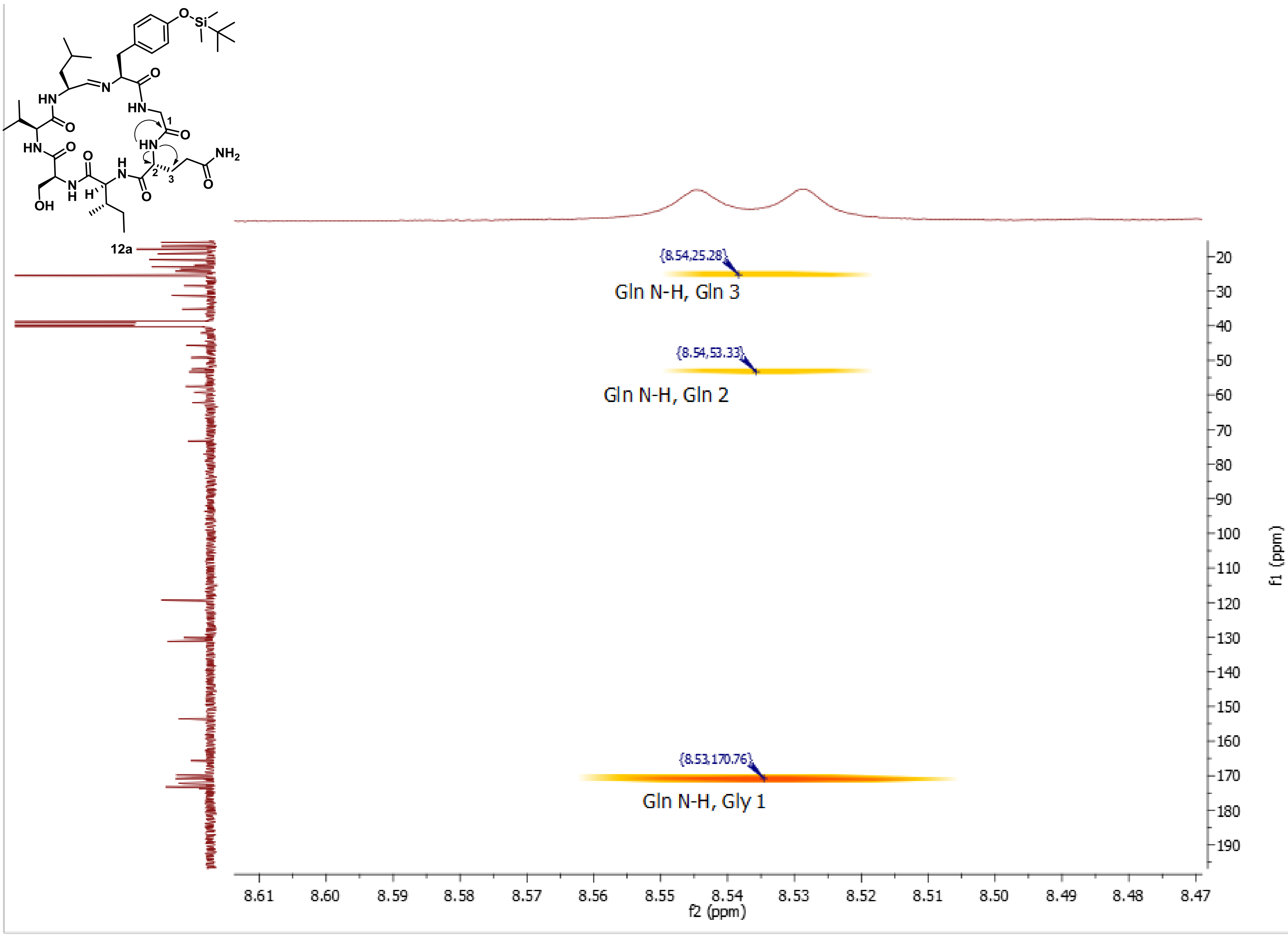


Figure S3. D-Gln_3 backbone –NH HMBC correlations for **12a**.

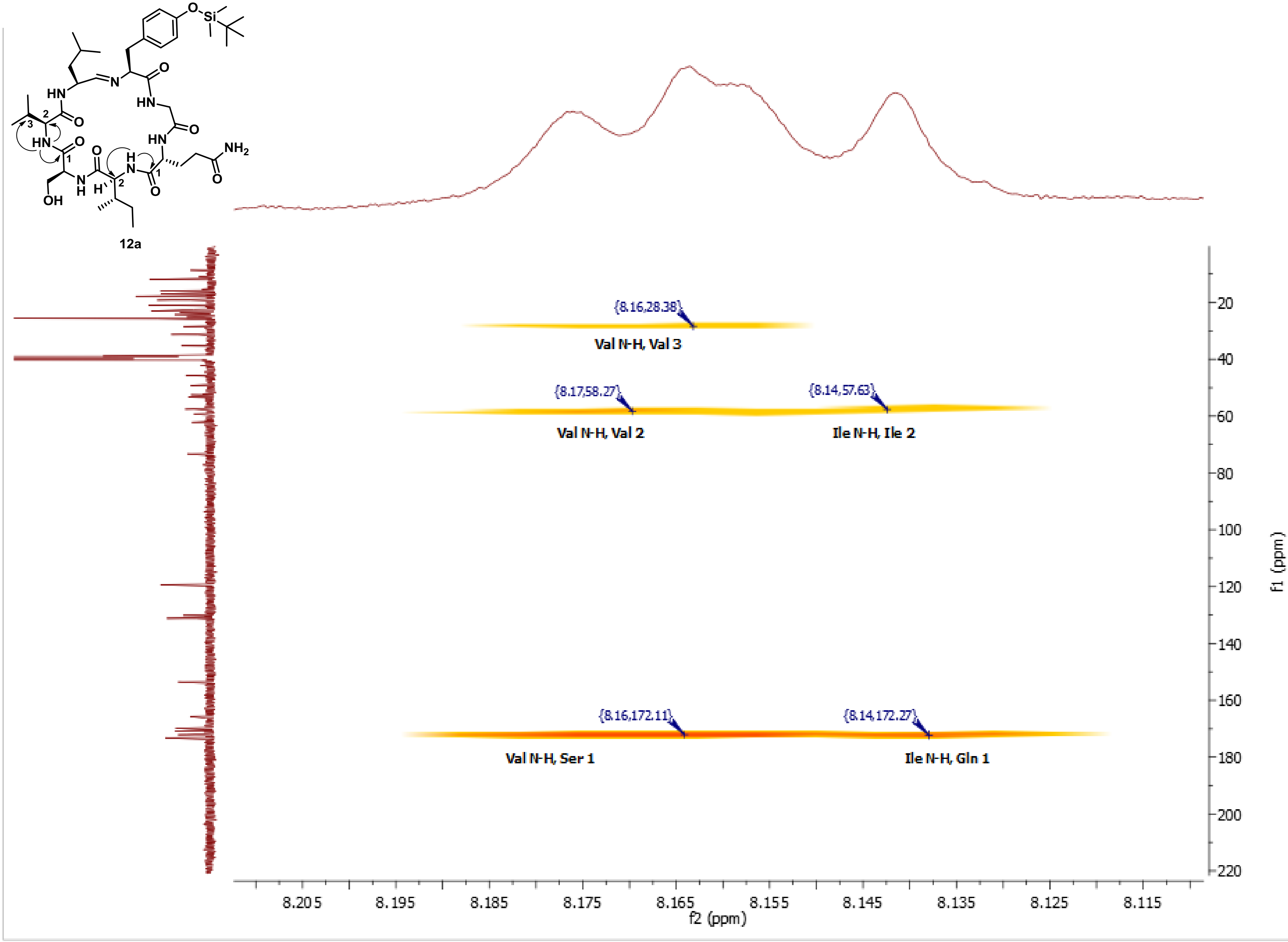


Figure S4. Val_6 and Ile_4 backbone –NH HMBC correlations for **12a**.

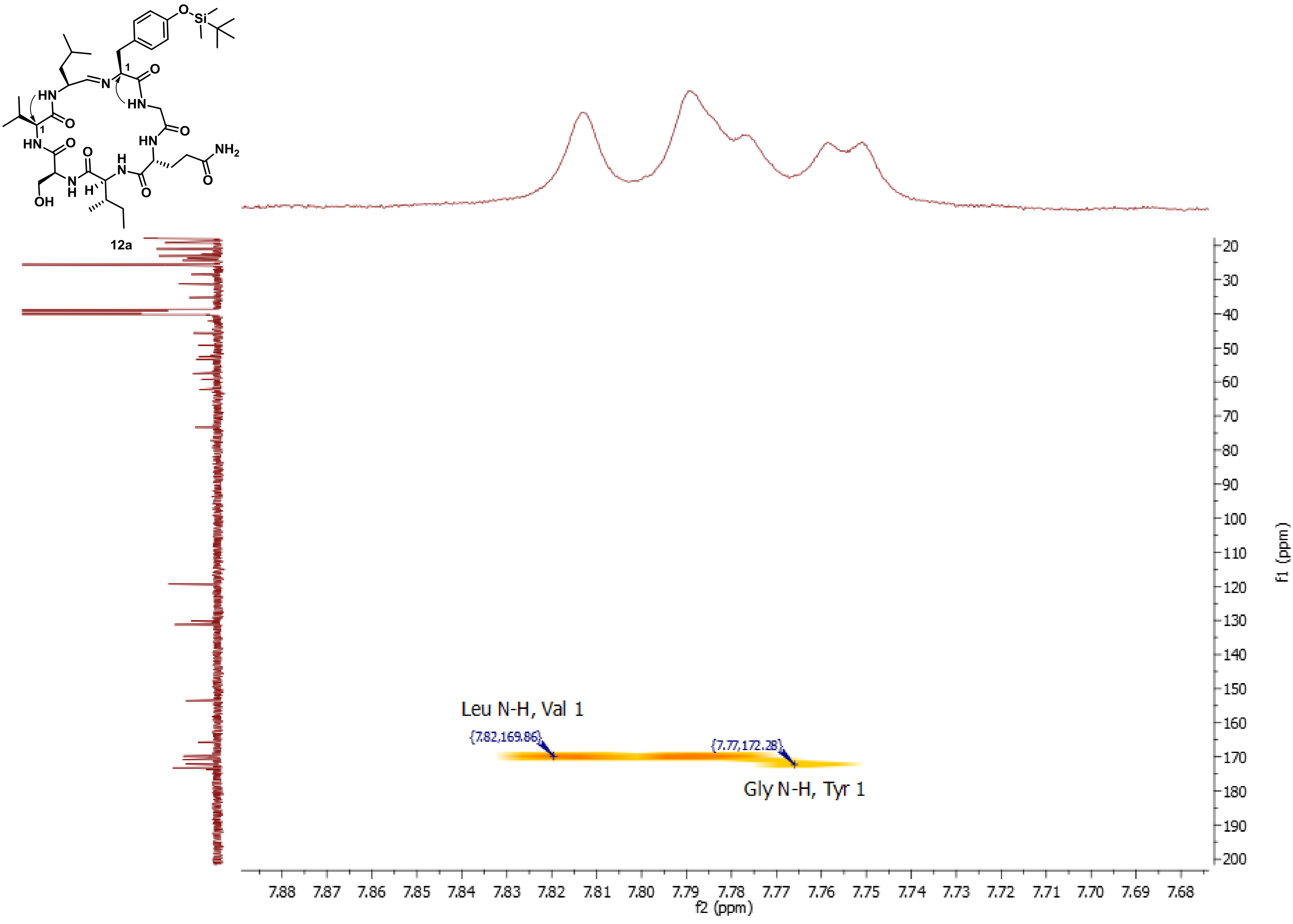


Figure S5. Leu_7 and Gly_2 backbone –NH HMBC correlations for **12a**.

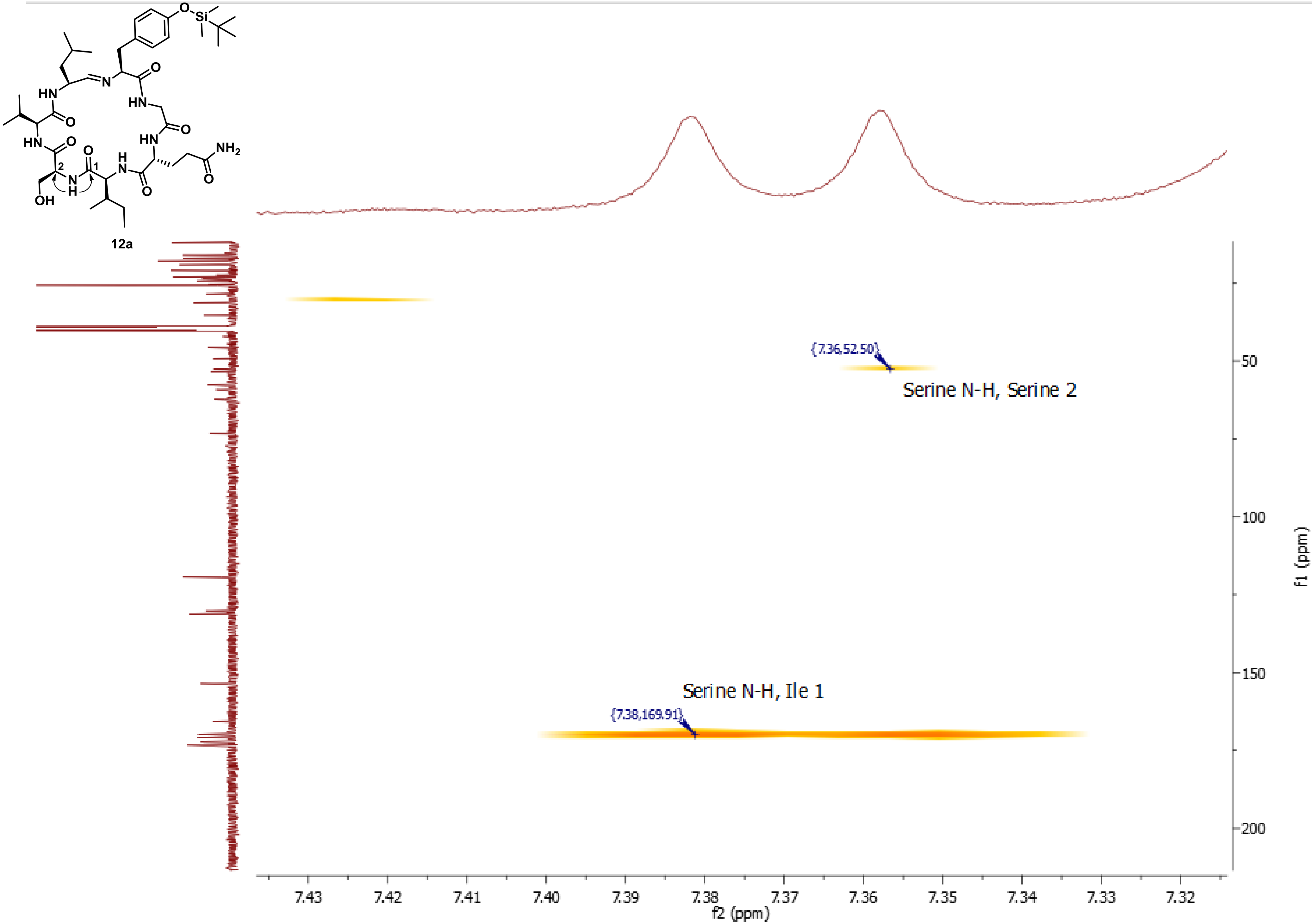
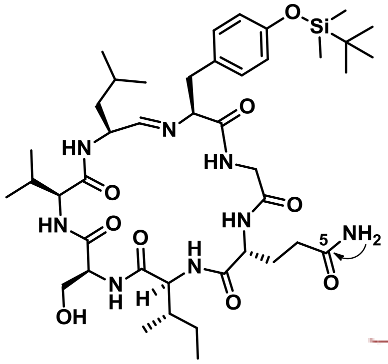


Figure S6. Ser$_5$ backbone –NH HMBC correlations for **12a**.



12a

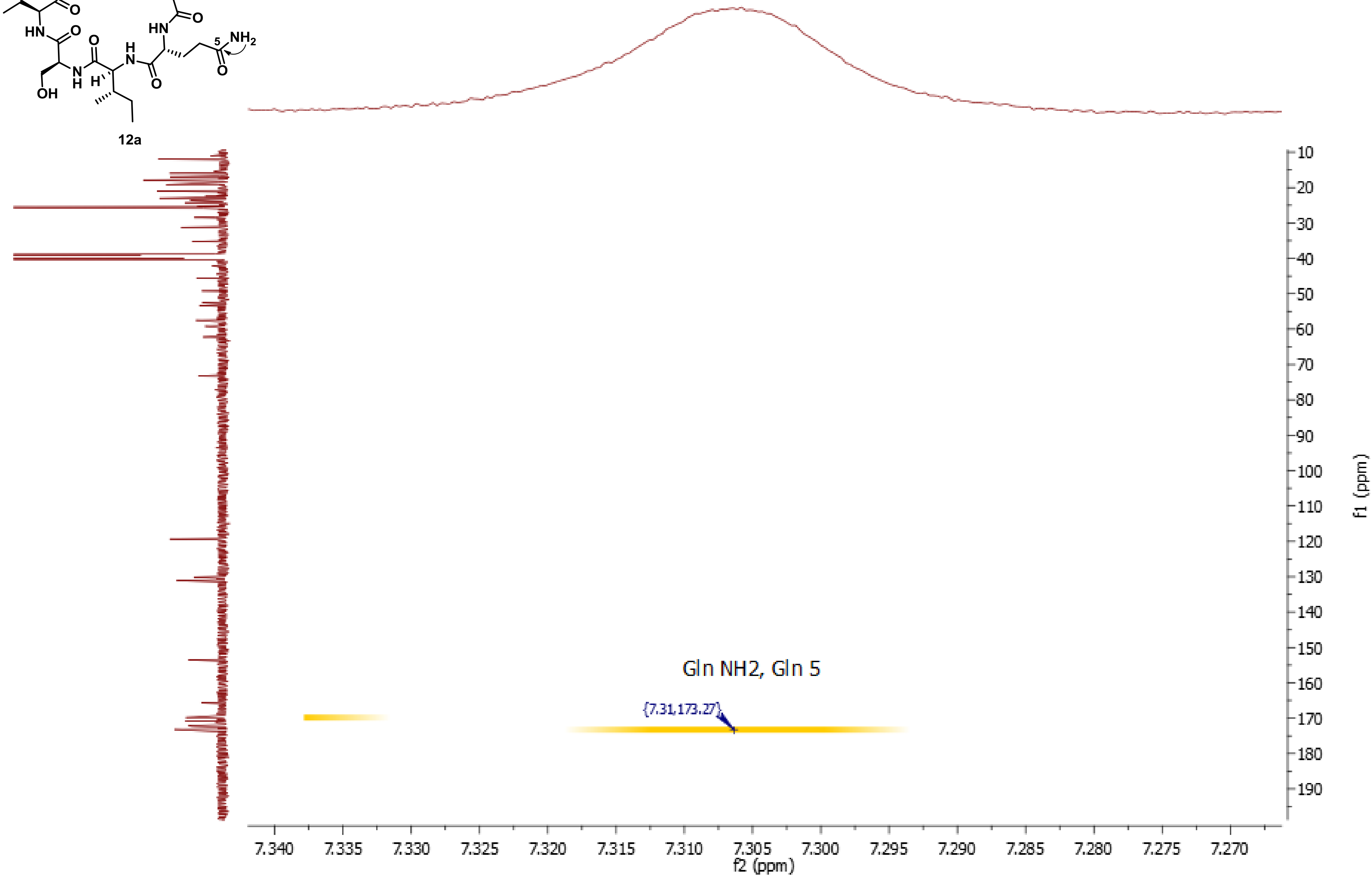


Figure S7A. D-Gln_3 side chain –NH HMBC correlations for **12a**.

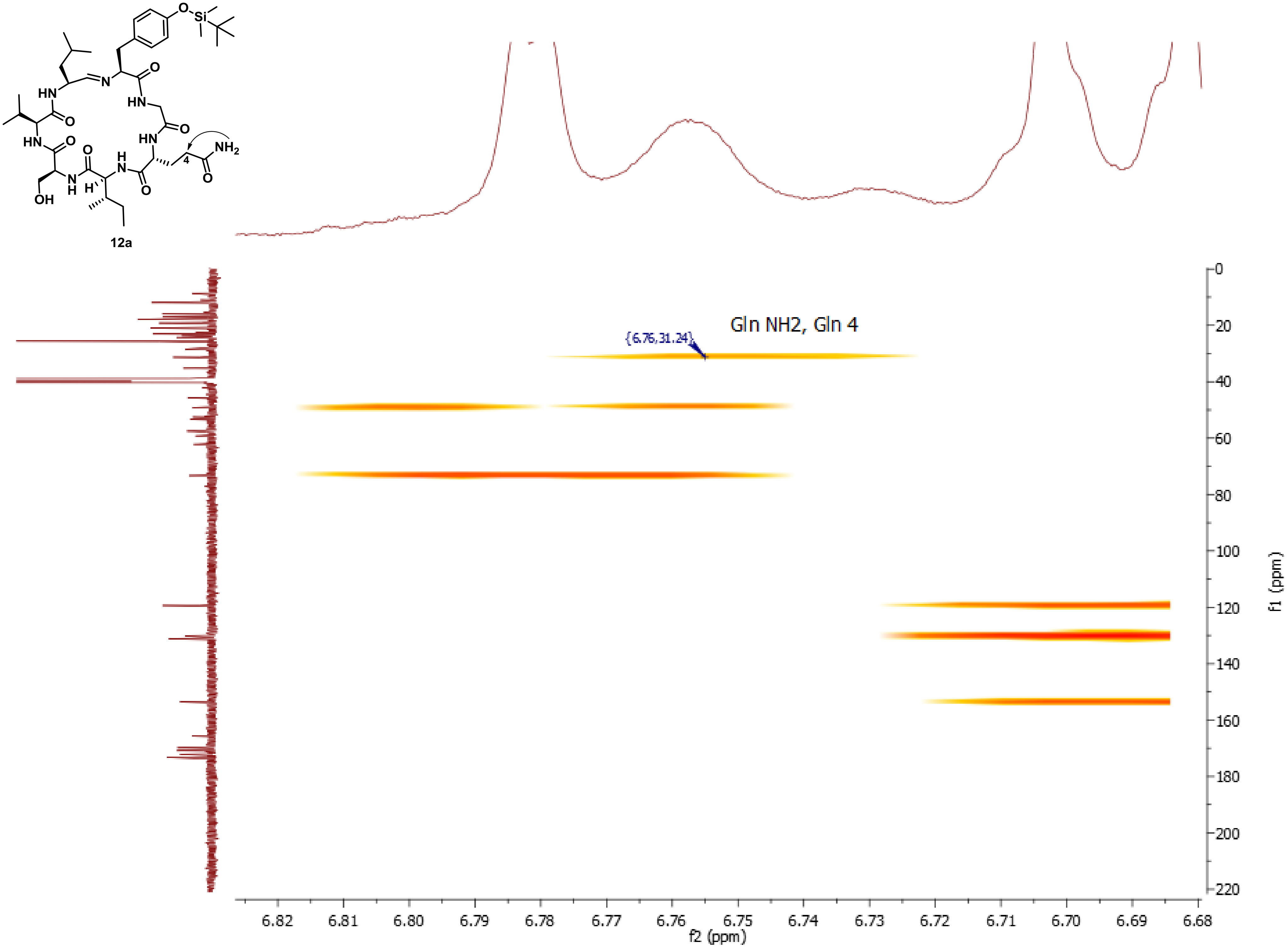


Figure S7B. D-Gln$_3$ side chain –NH HMBC correlations for **12a** (continued).

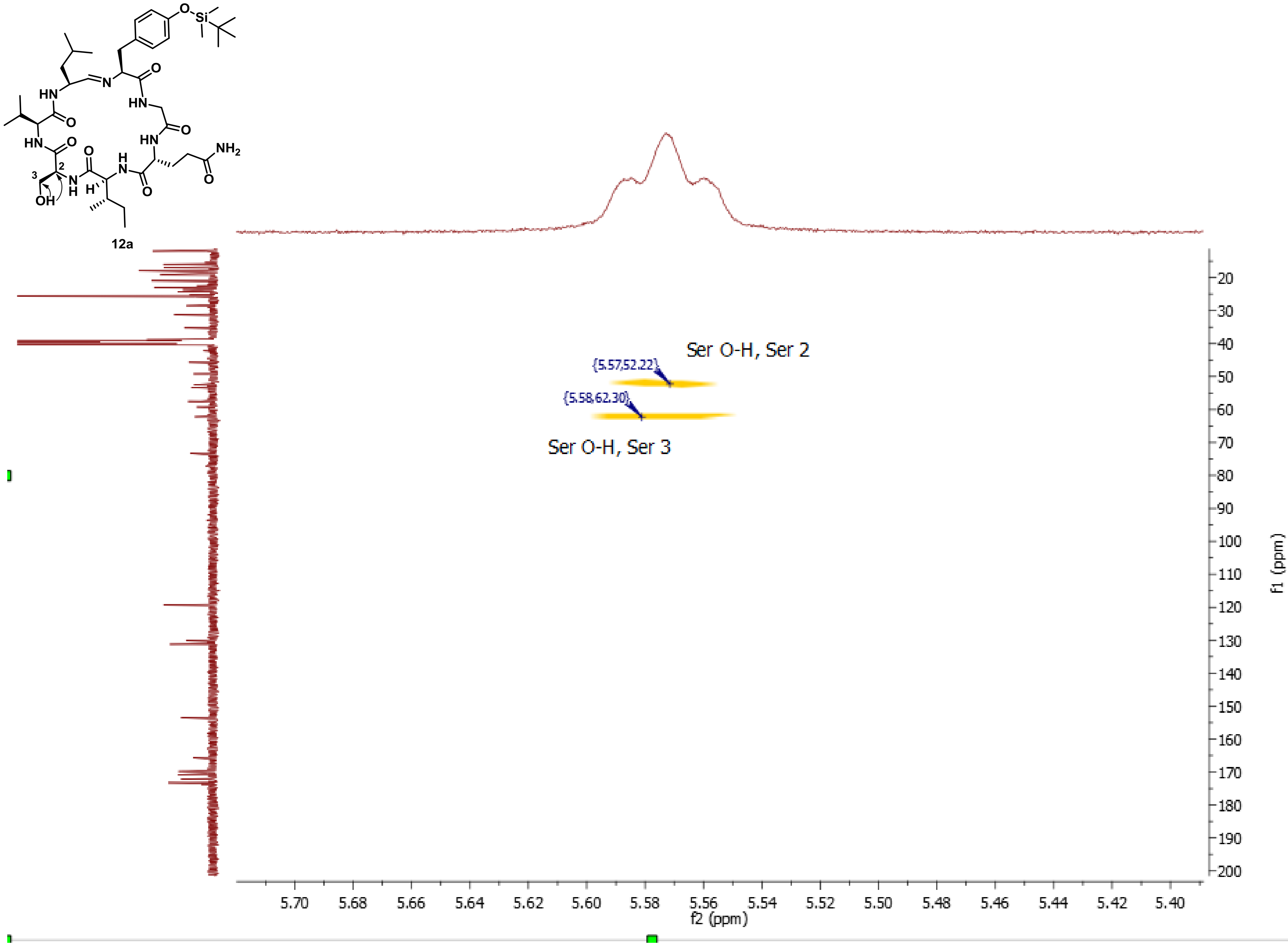
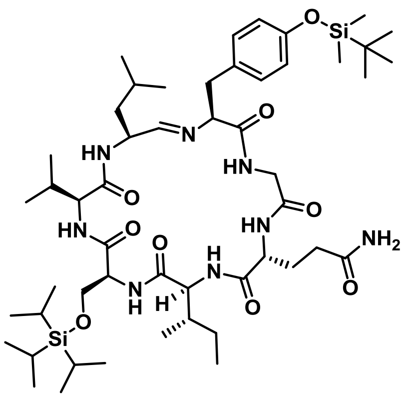
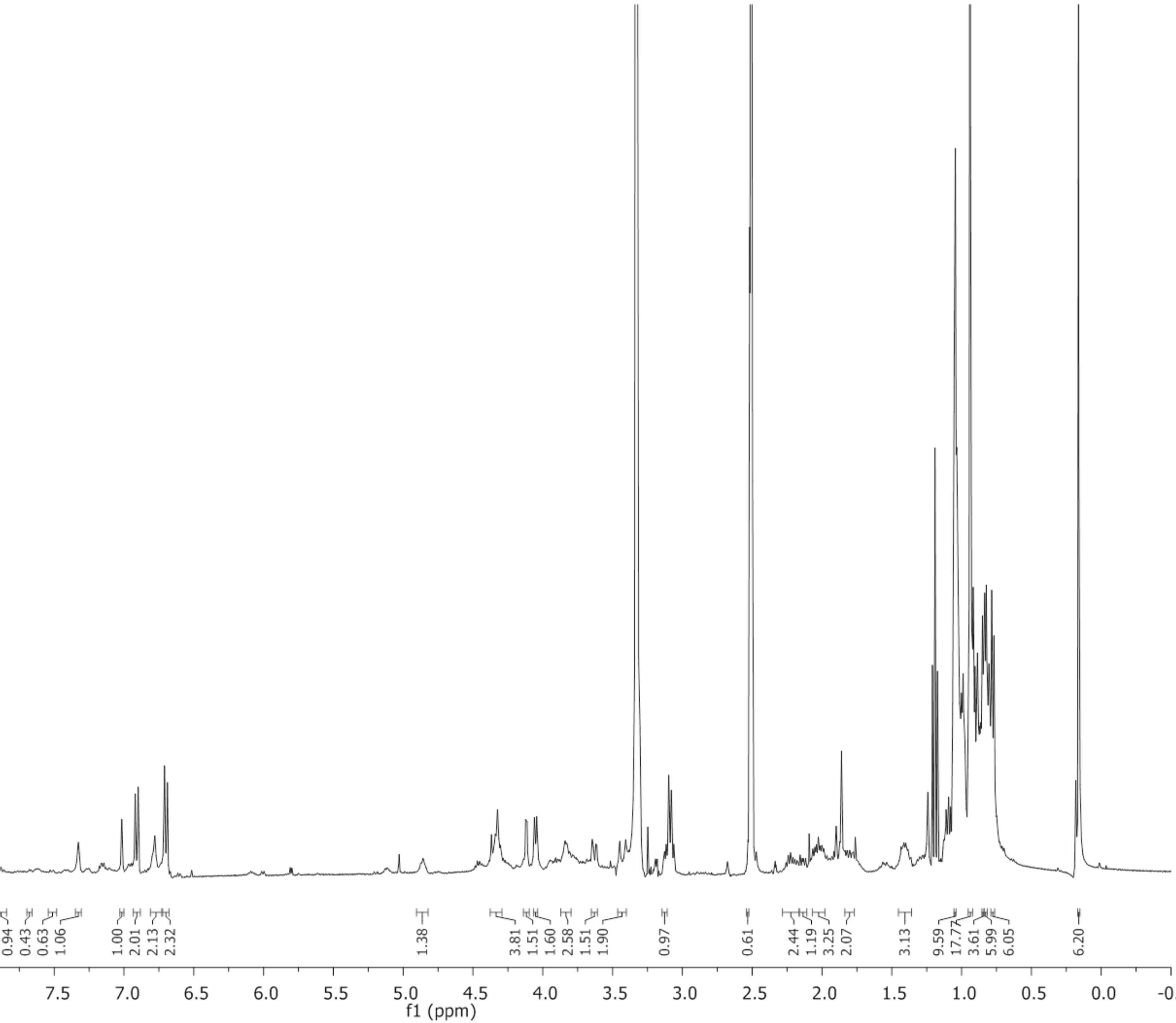


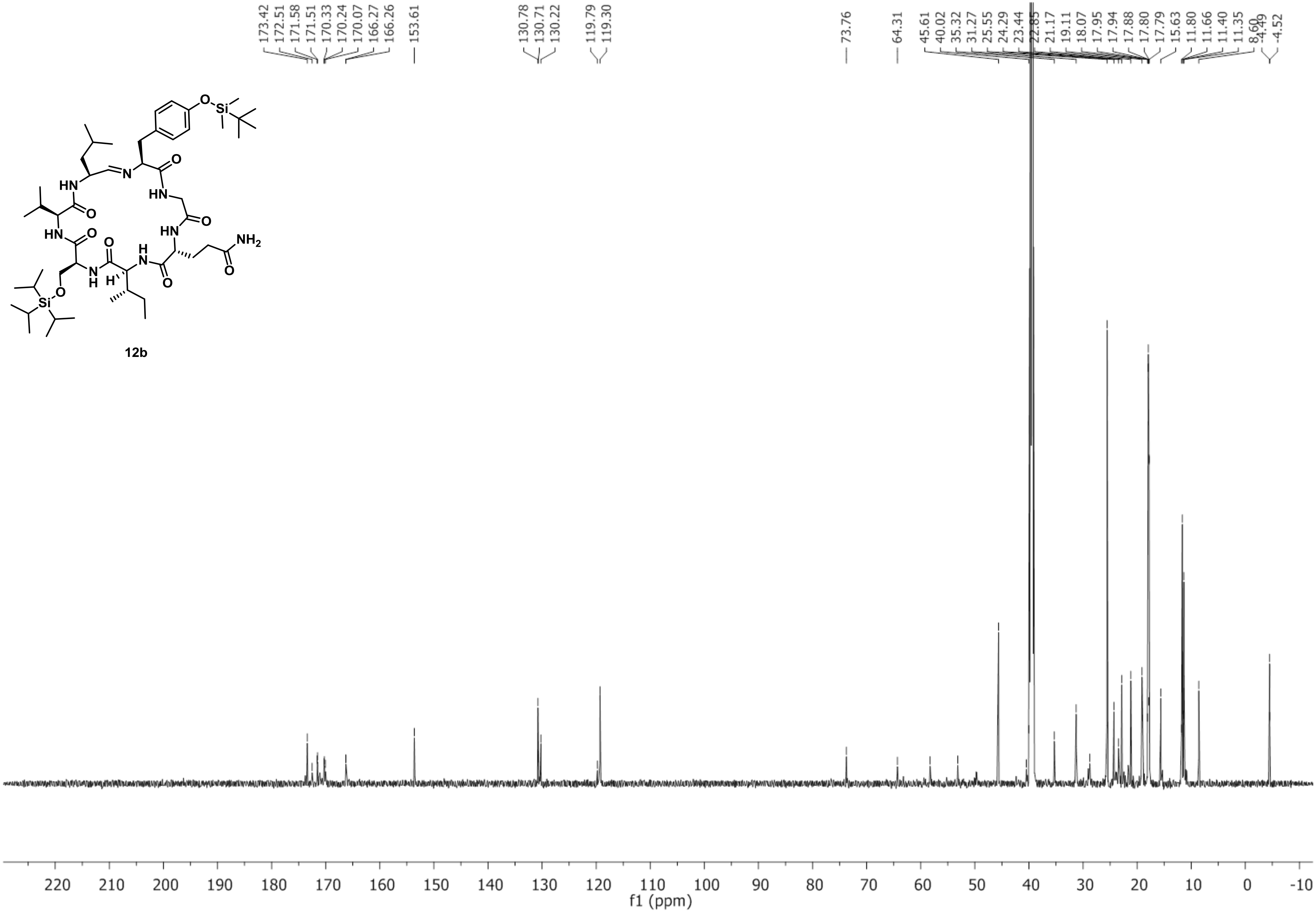
Figure S8. Ser_5 side chain -OH HMBC correlations for **12a**.



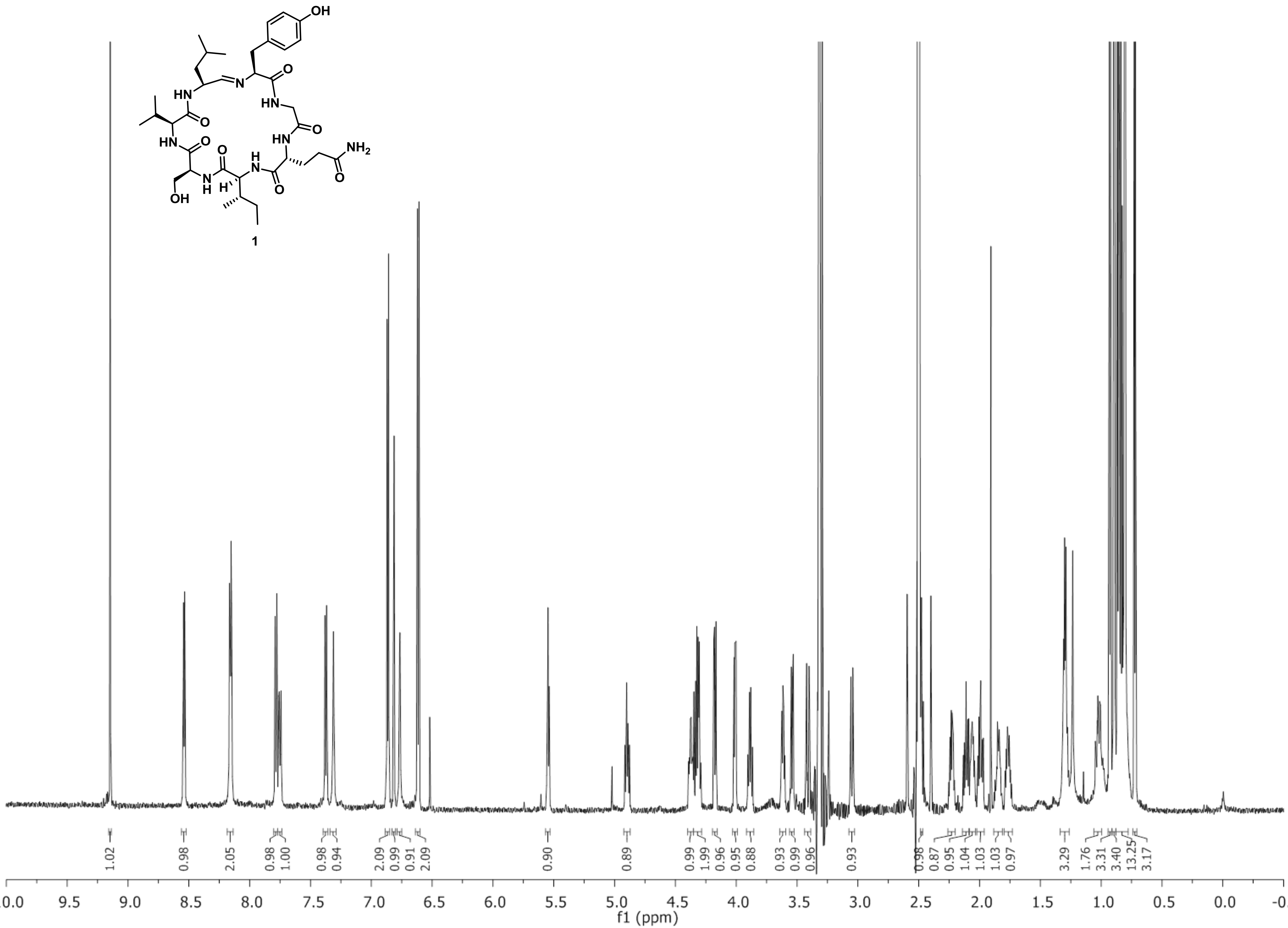
12b



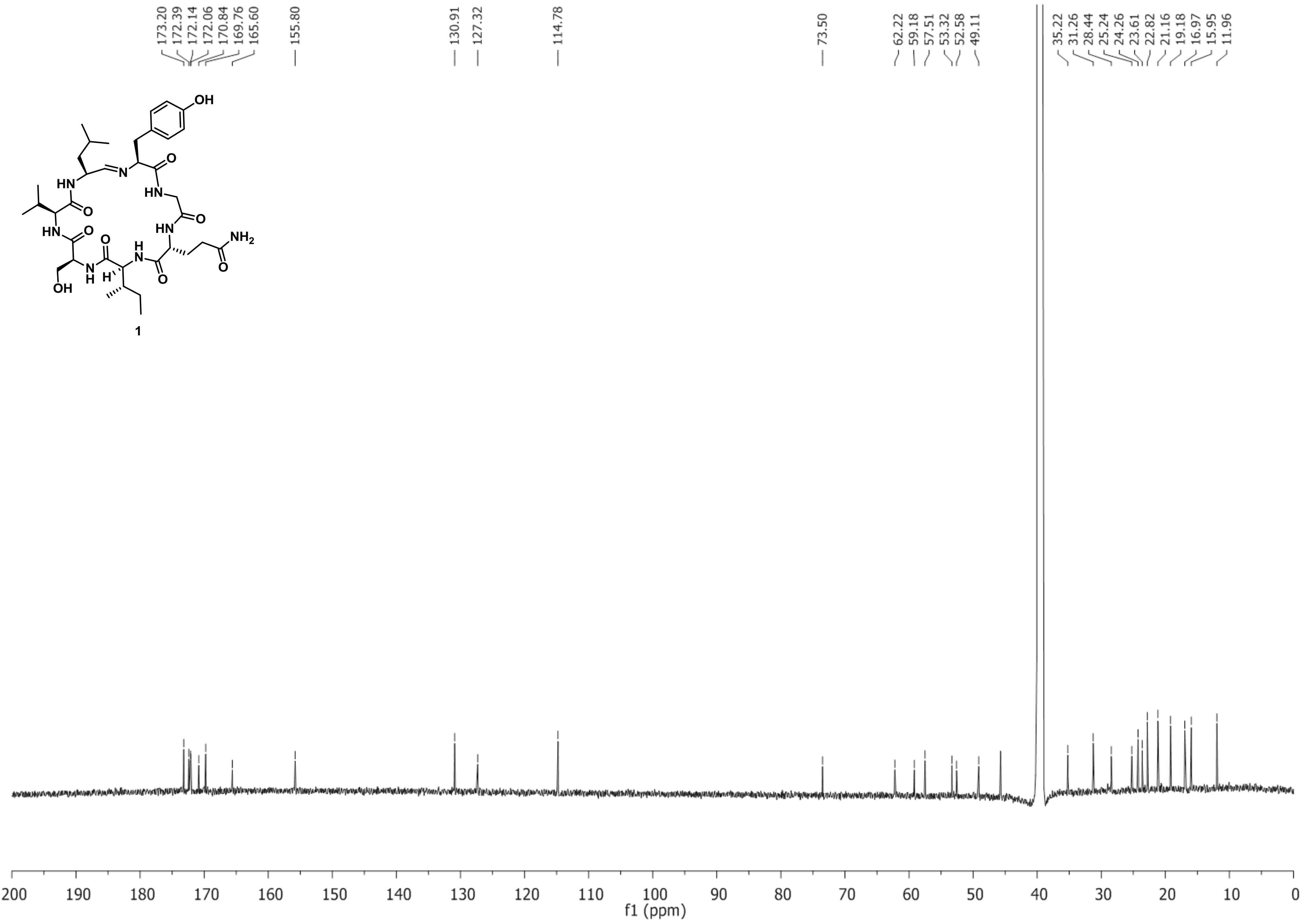
^{1}H NMR (d_6-DMSO, 400 MHz) of compound **12b**.



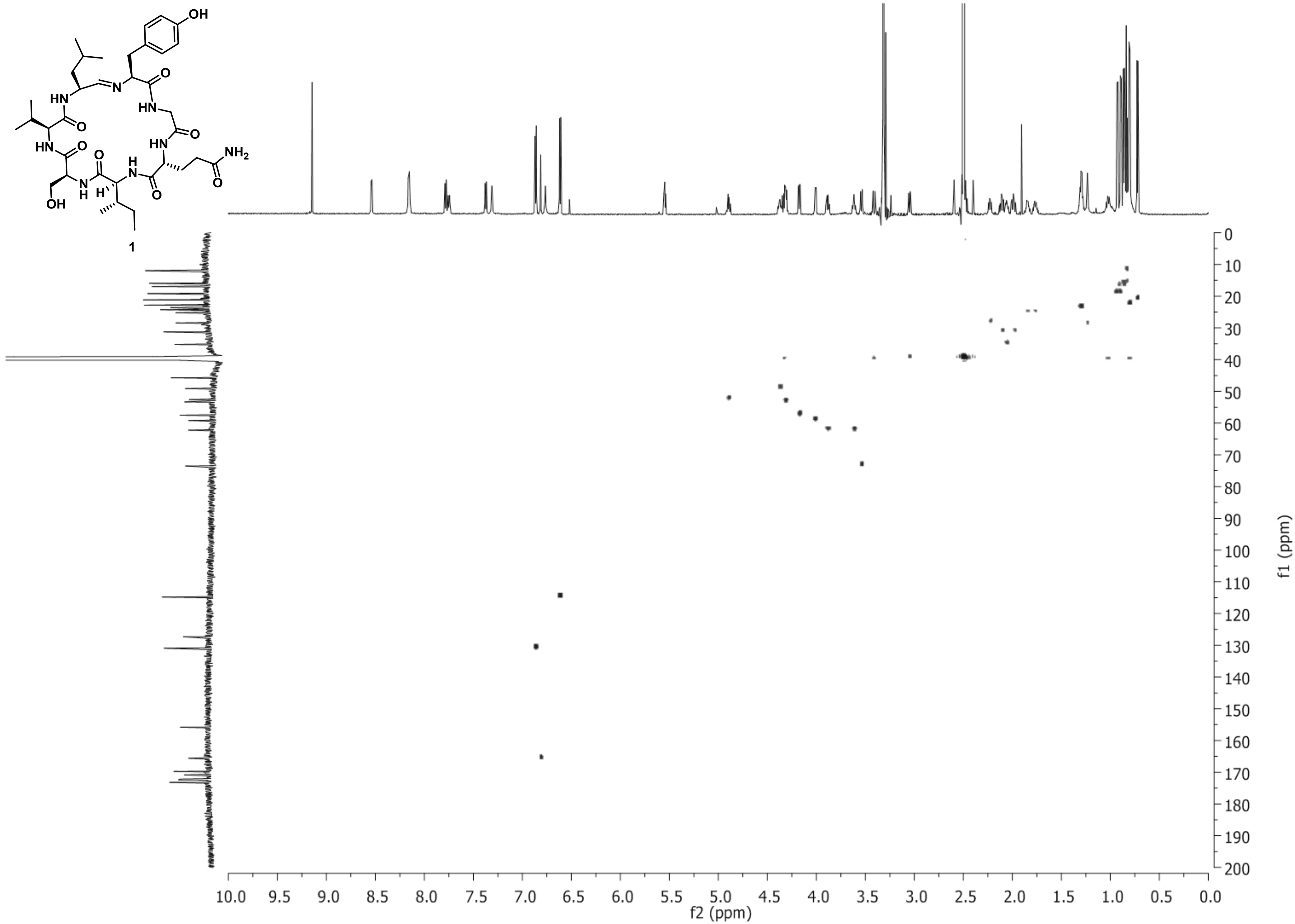
^{13}C NMR (d_6-DMSO, 176 MHz) of compound **12b**.



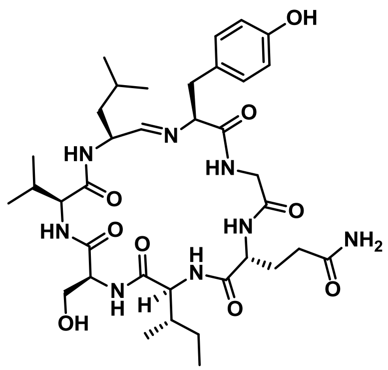
^{1}H NMR (d_6-DMSO, 700 MHz) of scytonemide A (**1**).



^{13}C NMR (d_6-DMSO, 176 MHz) of scytonemide A (**1**).



HSQC NMR (d_6-DMSO, 700 MHz) of scytonemide A (**1**).



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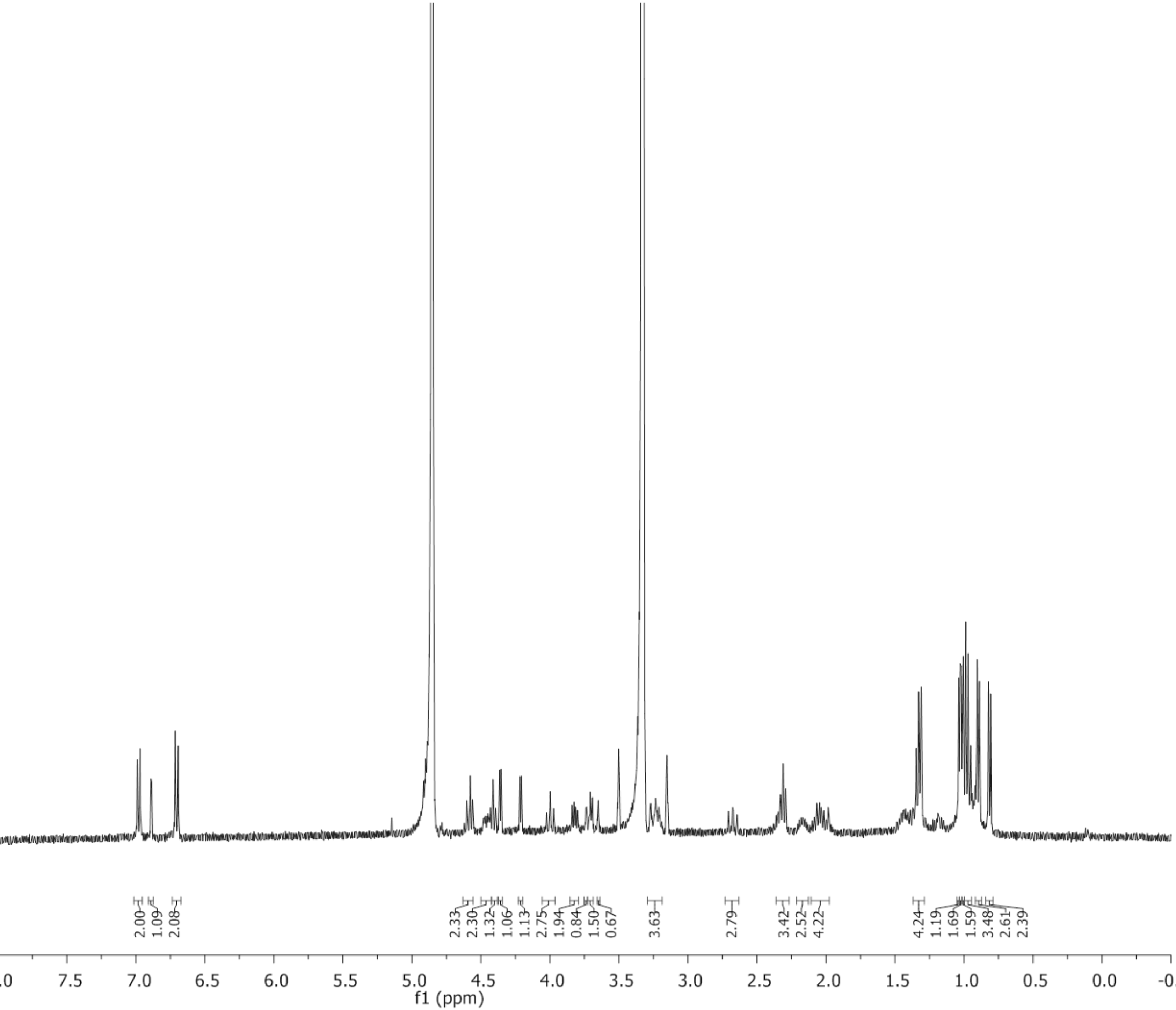
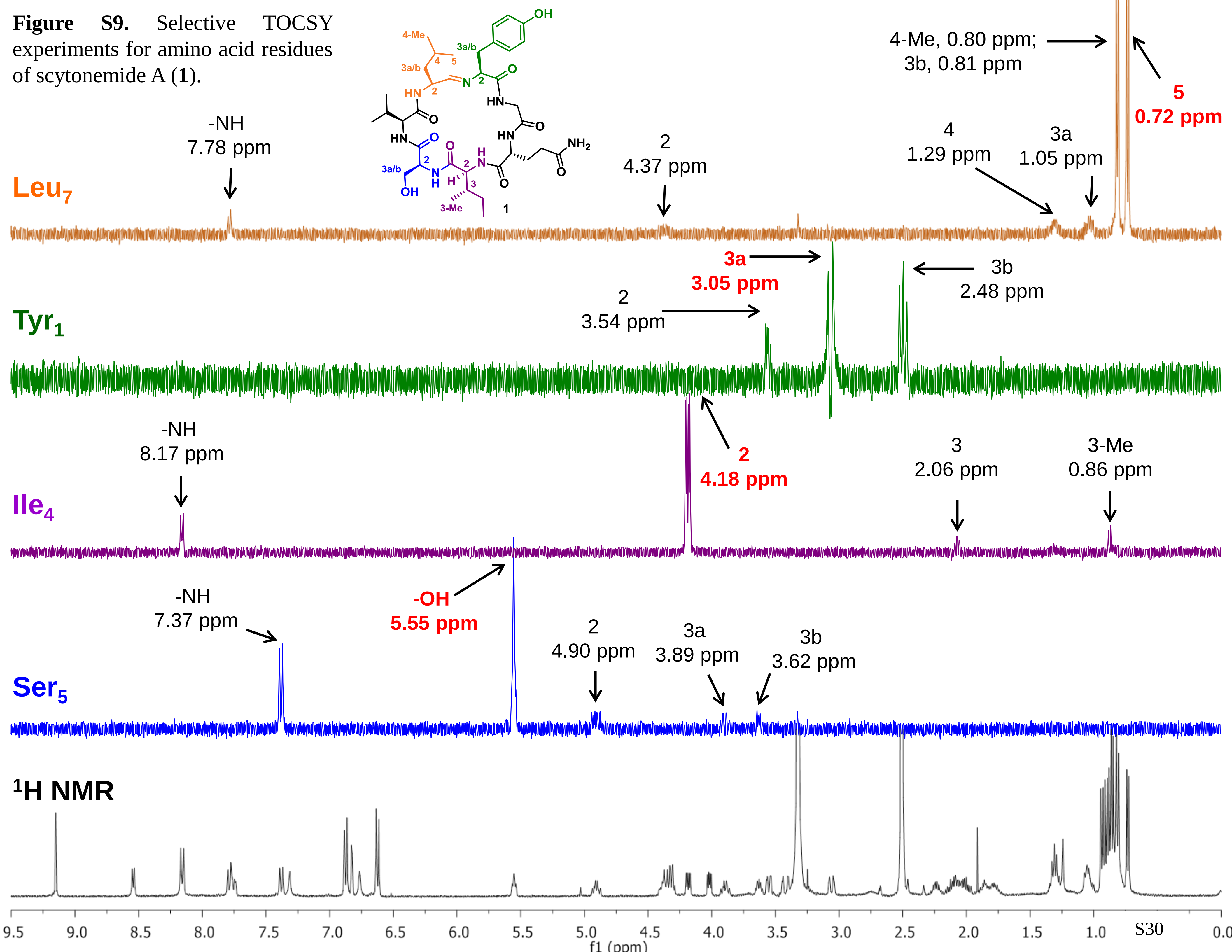


[1]H NMR (methanol-d_4, 400 MHz) of scytonemide A (**1**).

Figure S9. Selective TOCSY experiments for amino acid residues of scytonemide A (**1**).



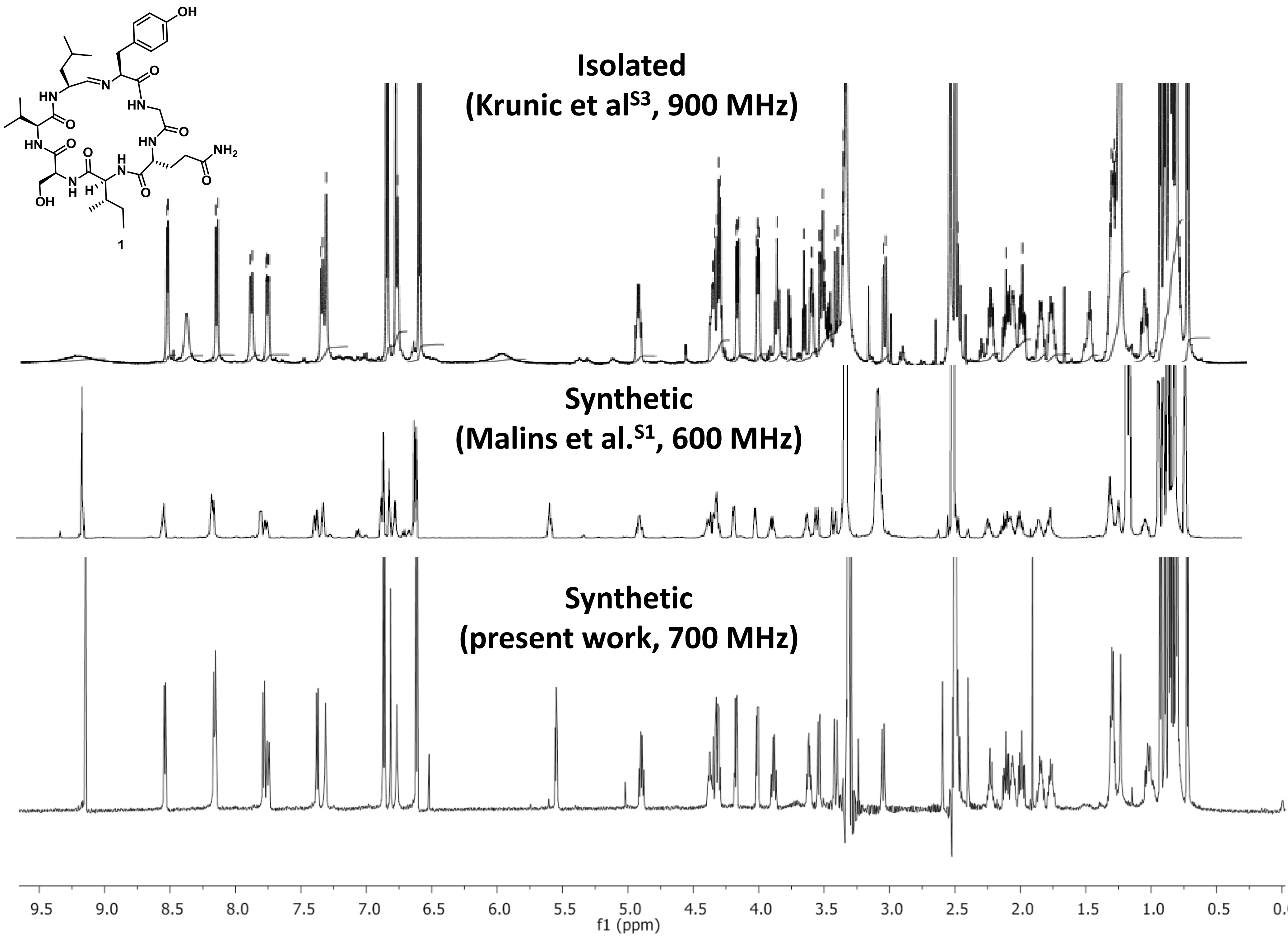


Figure S10. ^{1}H NMR spectra for isolated scytonemide A (**1**) (Krunic et al.[S1] top) and synthesized **1** (Malins et al.[S2] middle; present work, bottom).

References

(S1) Malins, L. R.; deGruyter, J. N.; Robbins, K. J.; Scola, P. M.; Eastgate, M. D.; Ghadiri, M. R.; Baran, P. S. *J. Am. Chem. Soc.* **2017**, *139*, 5233-5241.

(S2) Eissler, S.; Kley, M.; Bächle, D.; Loidl, G.; Meier, T.; Samson, D. *J. Pept. Sci.* **2017**, *23*, 757–762.

(S3) Krunic, A.; Vallat, A.; Mo, S.; Lantvit, D. D.; Swanson, S. M.; Orjala, J. *J. Nat. Prod.* **2010**, *73*, 1927–1932.