

# Supplementary material

## Discovery of guanidine derivatives from *Buthus martensii* Karsch with metal-binding and cholinesterase inhibition properties

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**Figure S1.** HR-ESI-MS spectrum of martensine A (**1**)

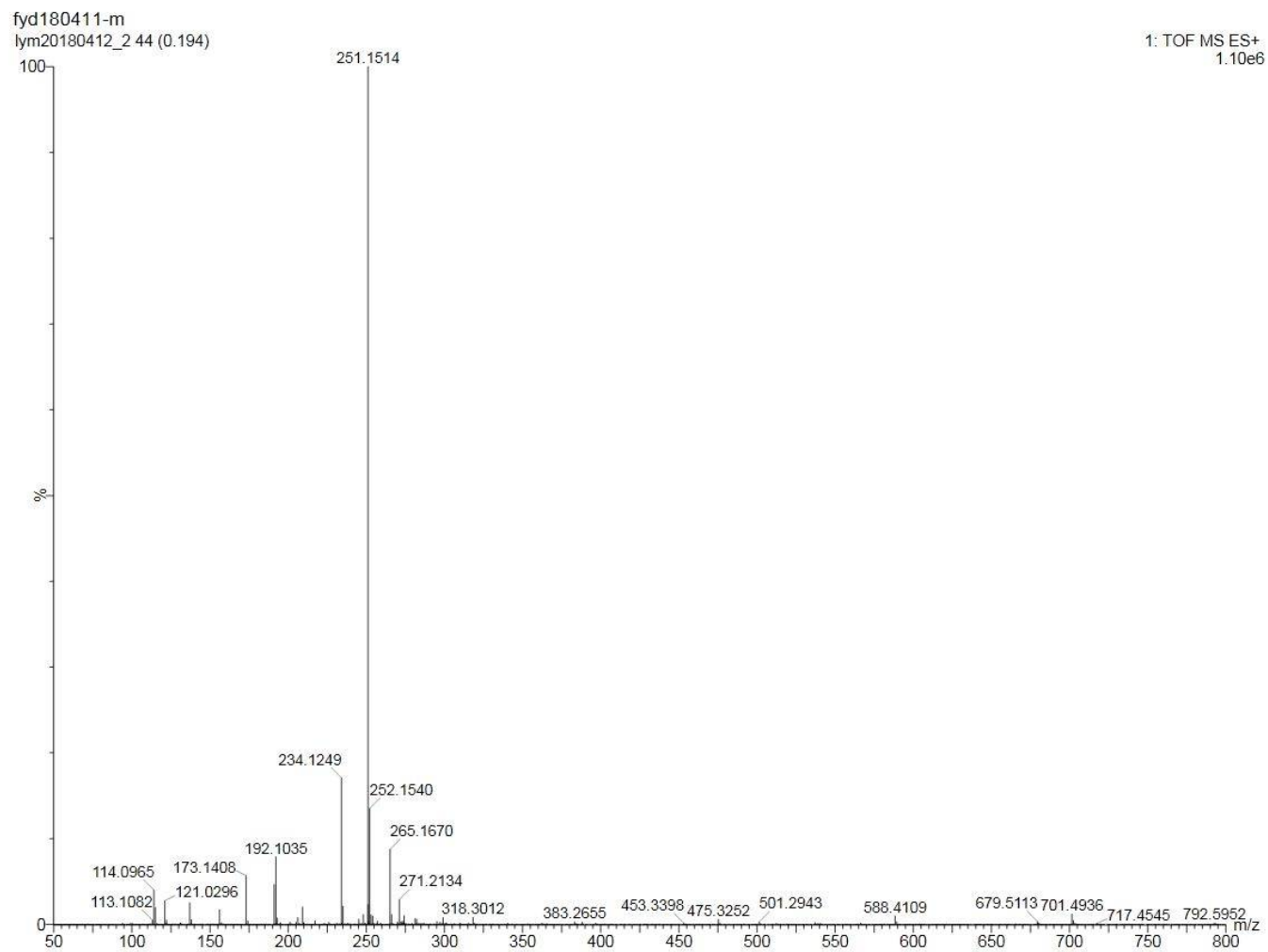
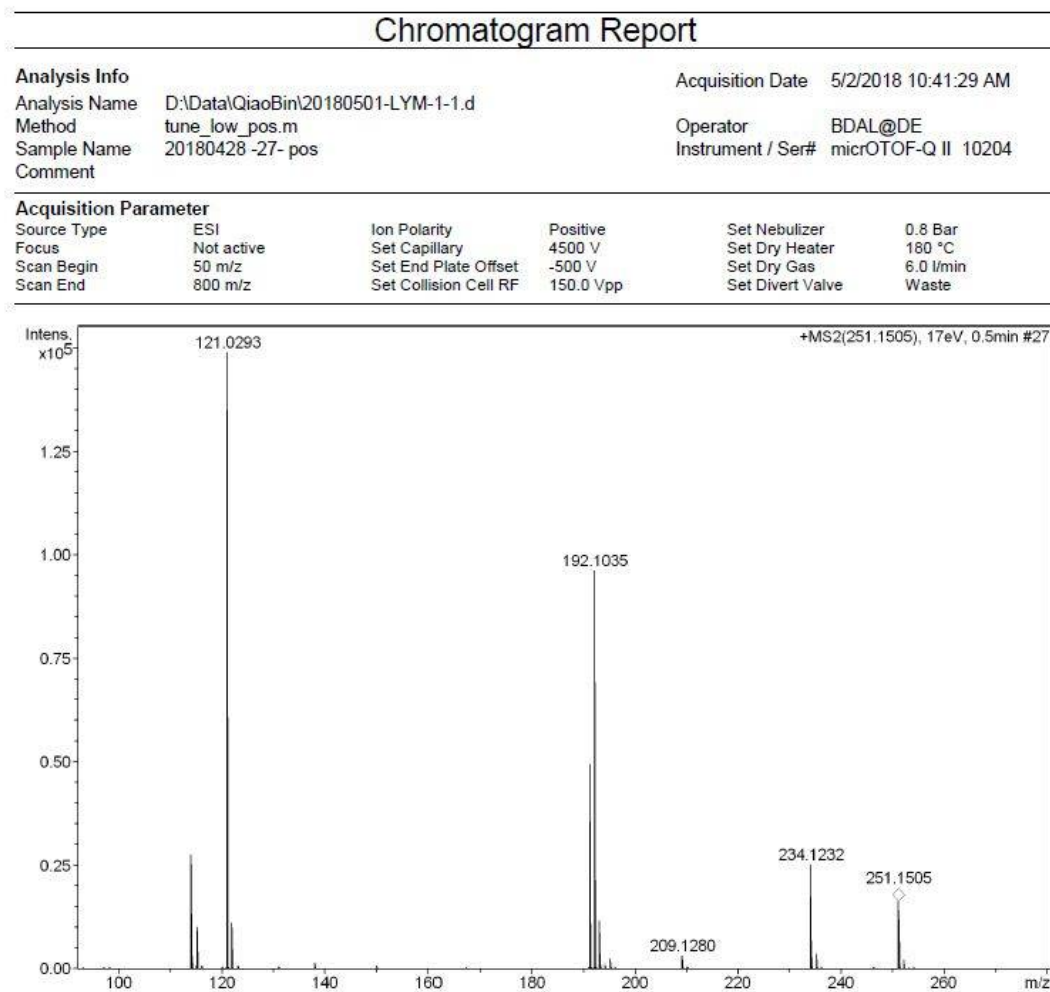
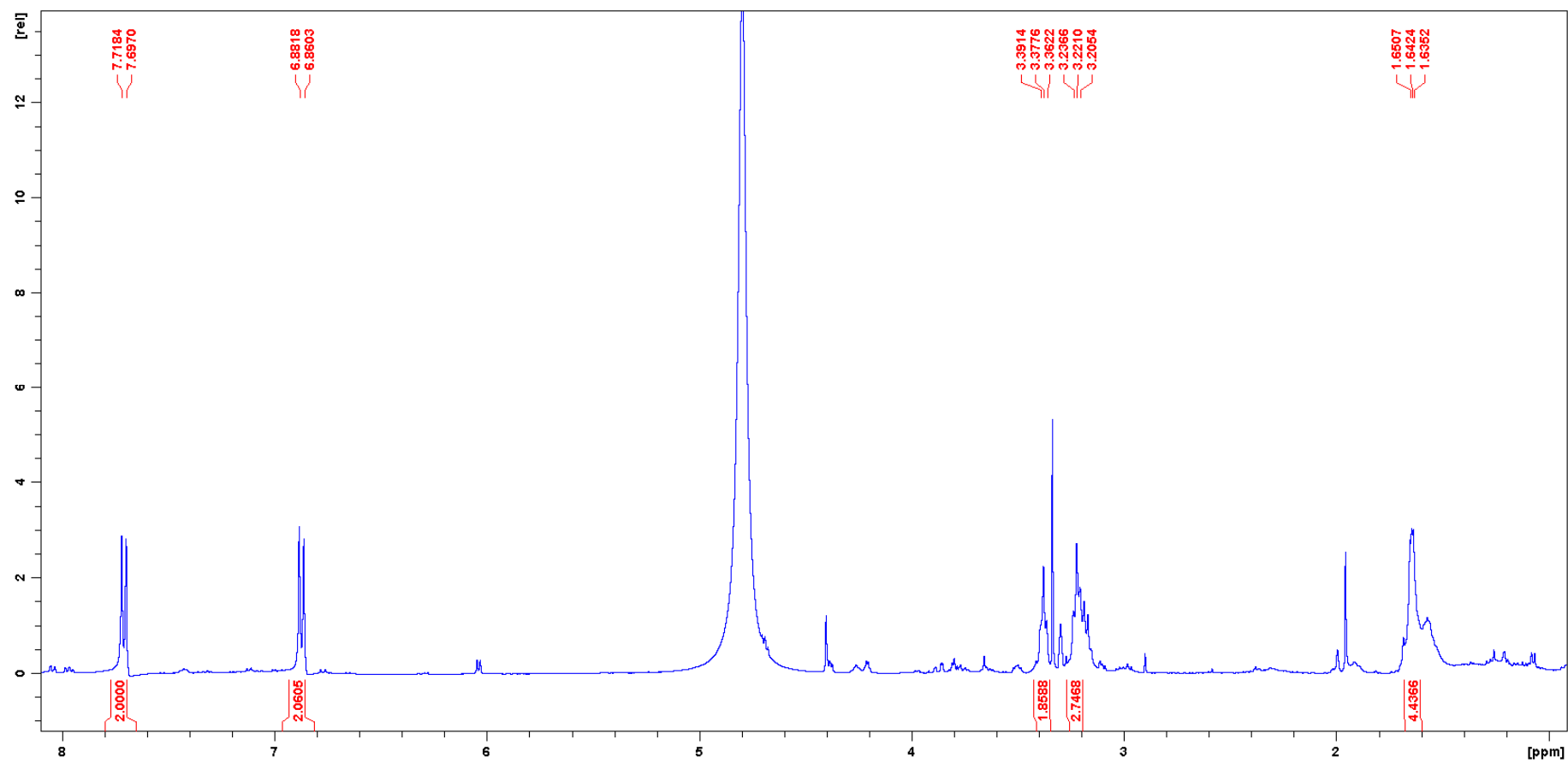


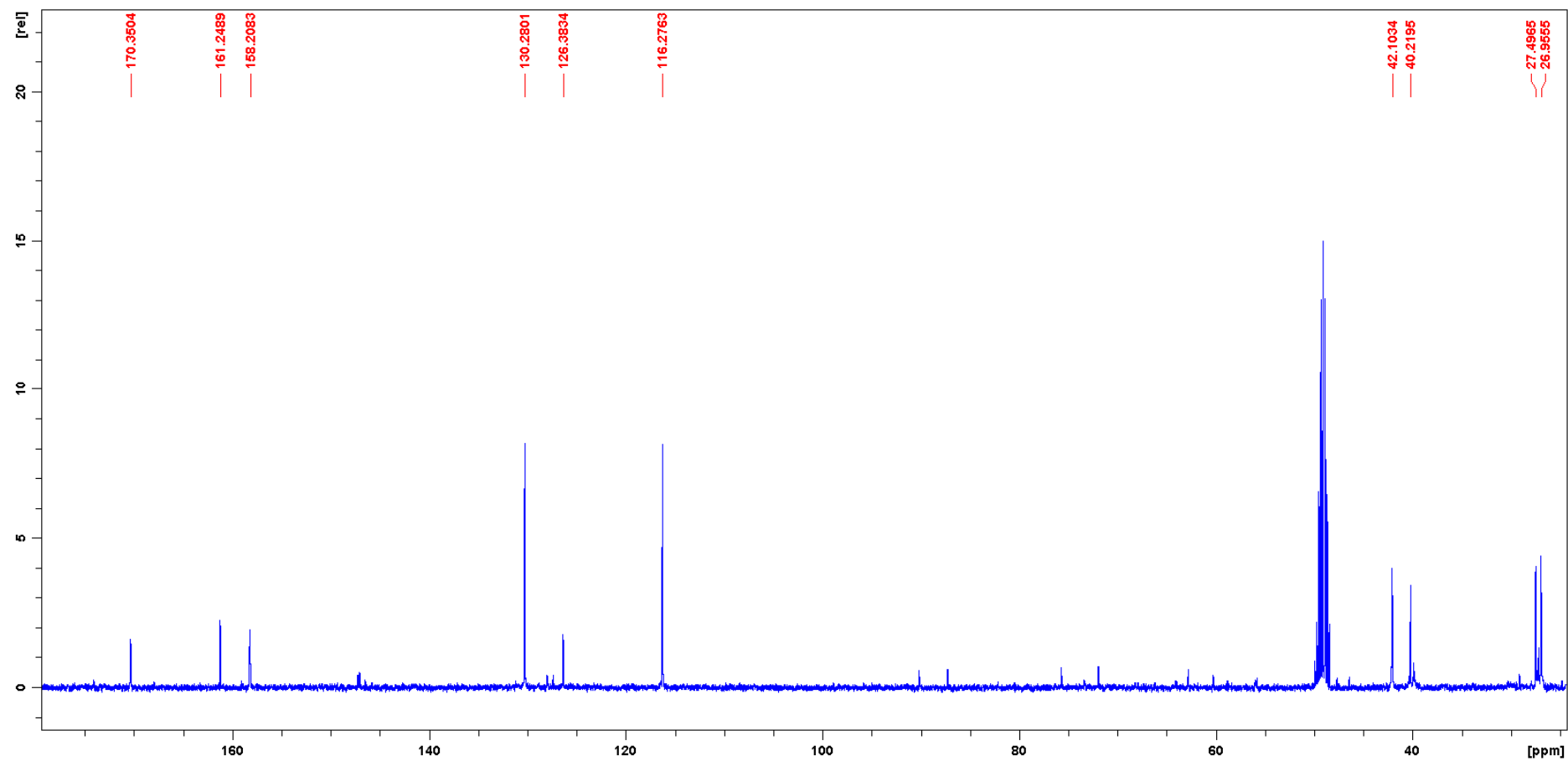
Figure S2. HR-ESI-MS<sup>2</sup> spectrum ( $M' = 251.1514$  [ $M+H$ ]<sup>+</sup>) of martensine A (1)



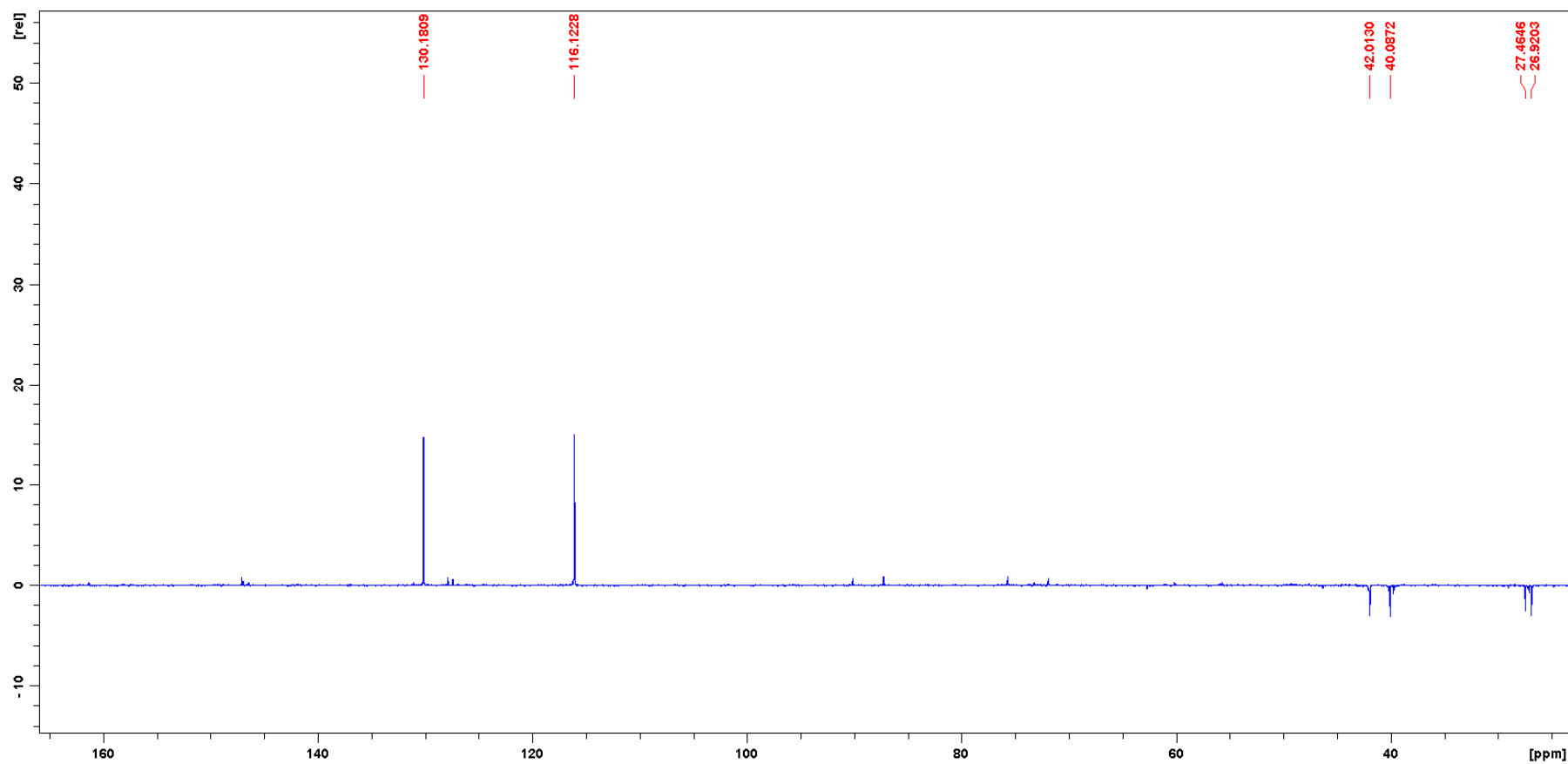
**Figure S3.**  $^1\text{H}$  NMR spectrum ( $\text{CD}_3\text{OD}$ ) of martensine A (**1**)



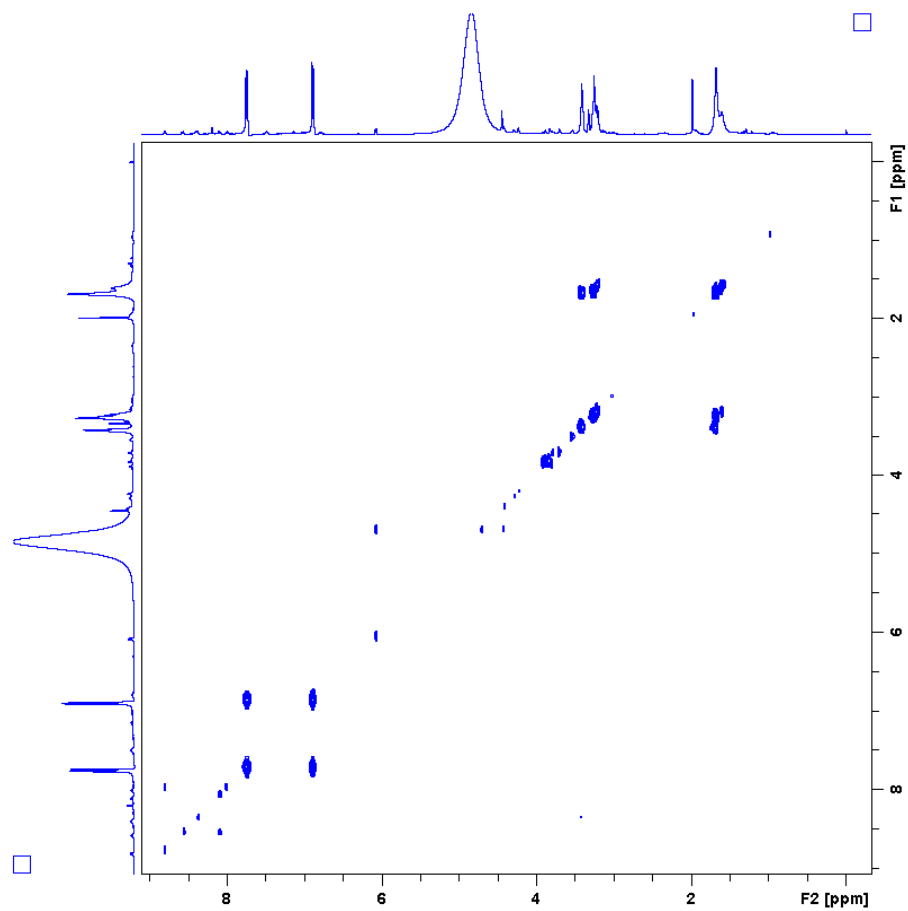
**Figure S4.**  $^{13}\text{C}$  NMR spectrum ( $\text{CD}_3\text{OD}$ ) of martensine A (**1**)



**Figure S5.** DEPT 135 spectrum of martensine A (**1**)

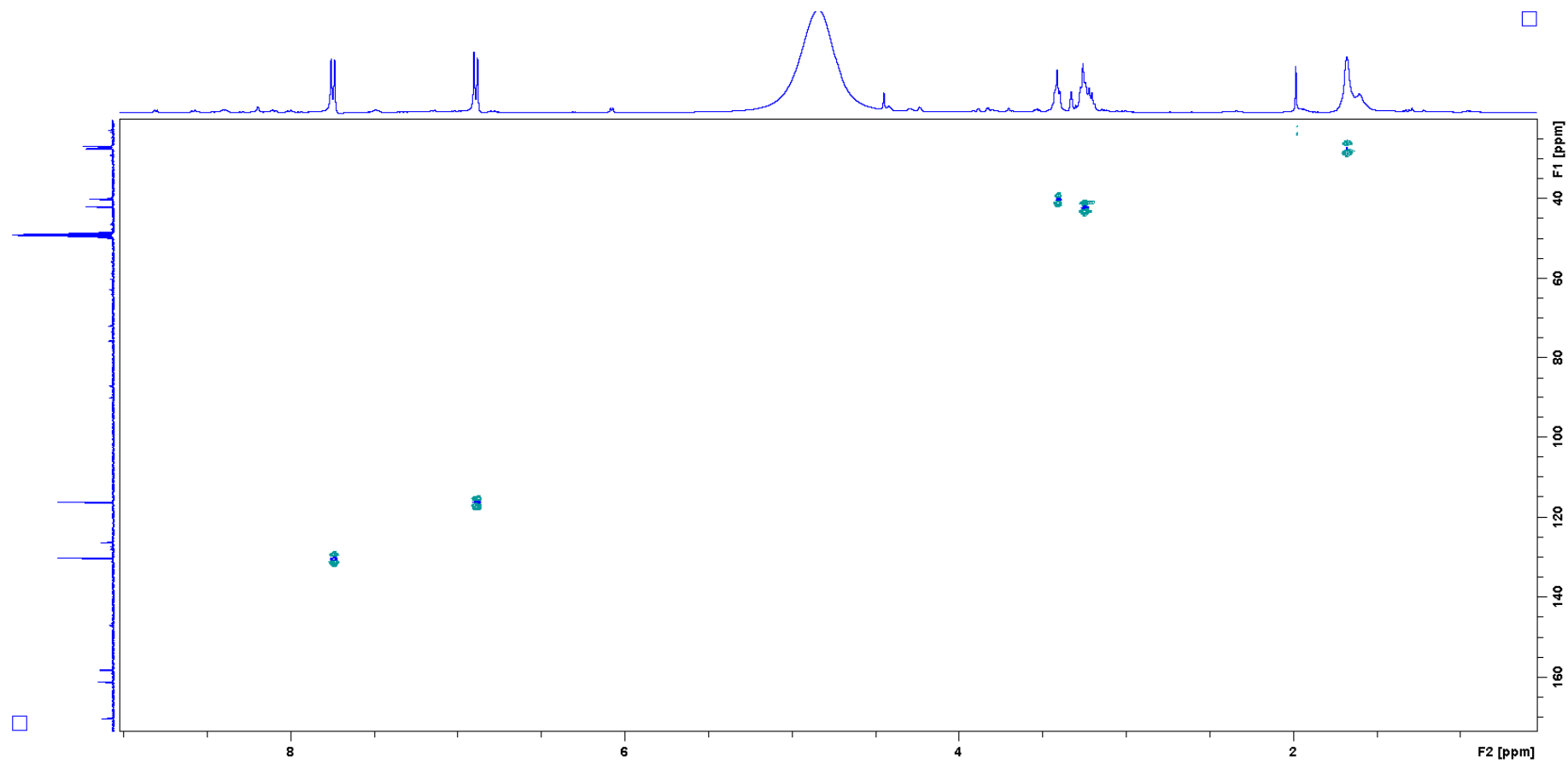


**Figure S6.**  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of martensine A (**1**)



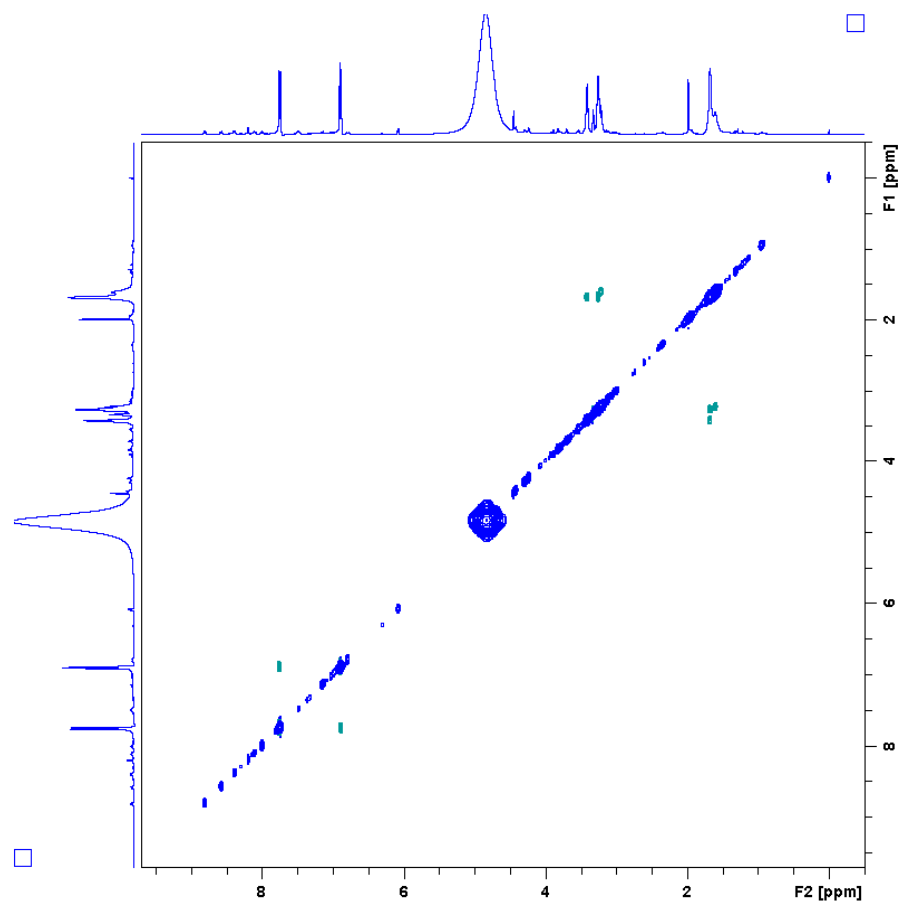


**Figure S7.** HSQC spectrum of martensine A (**1**)

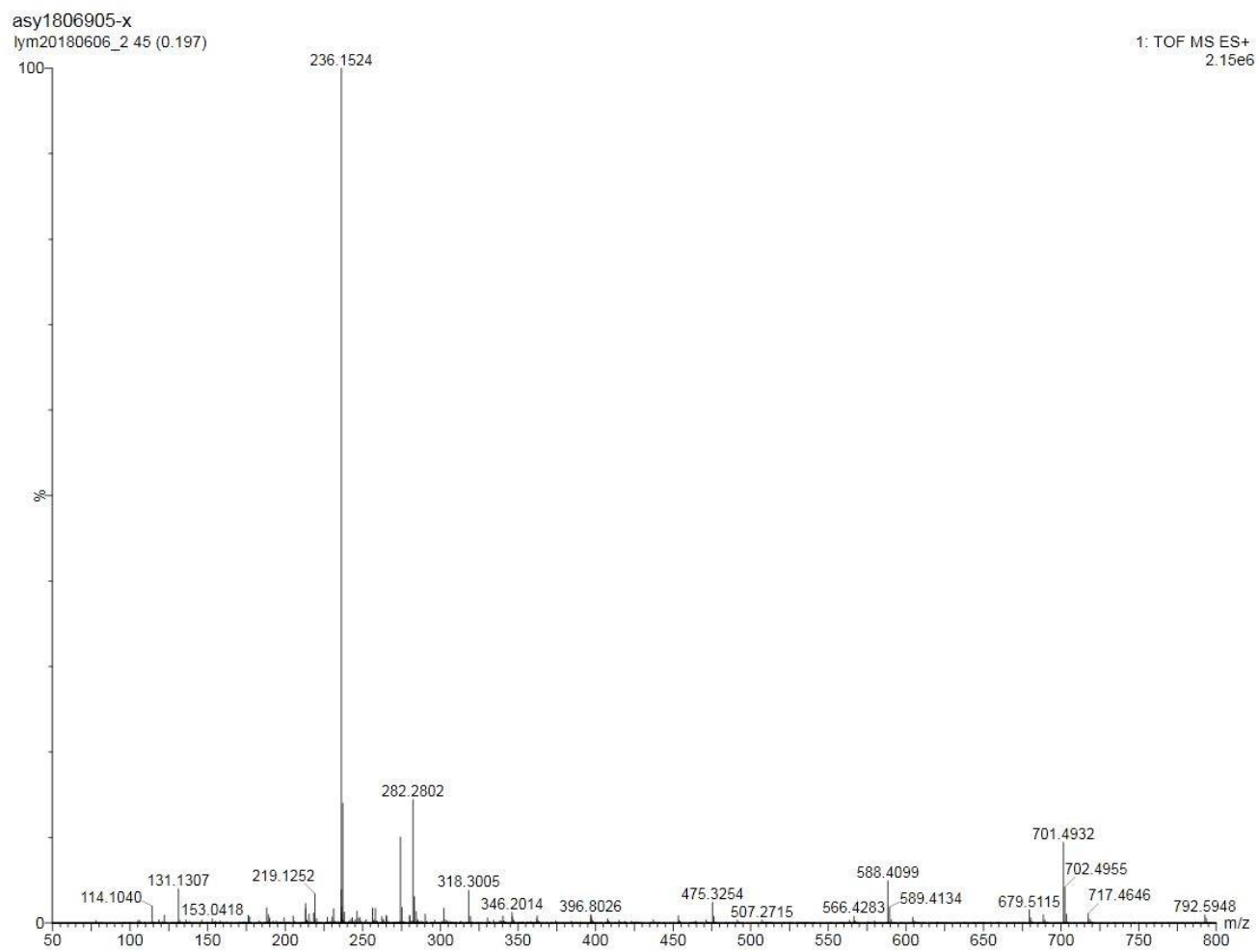




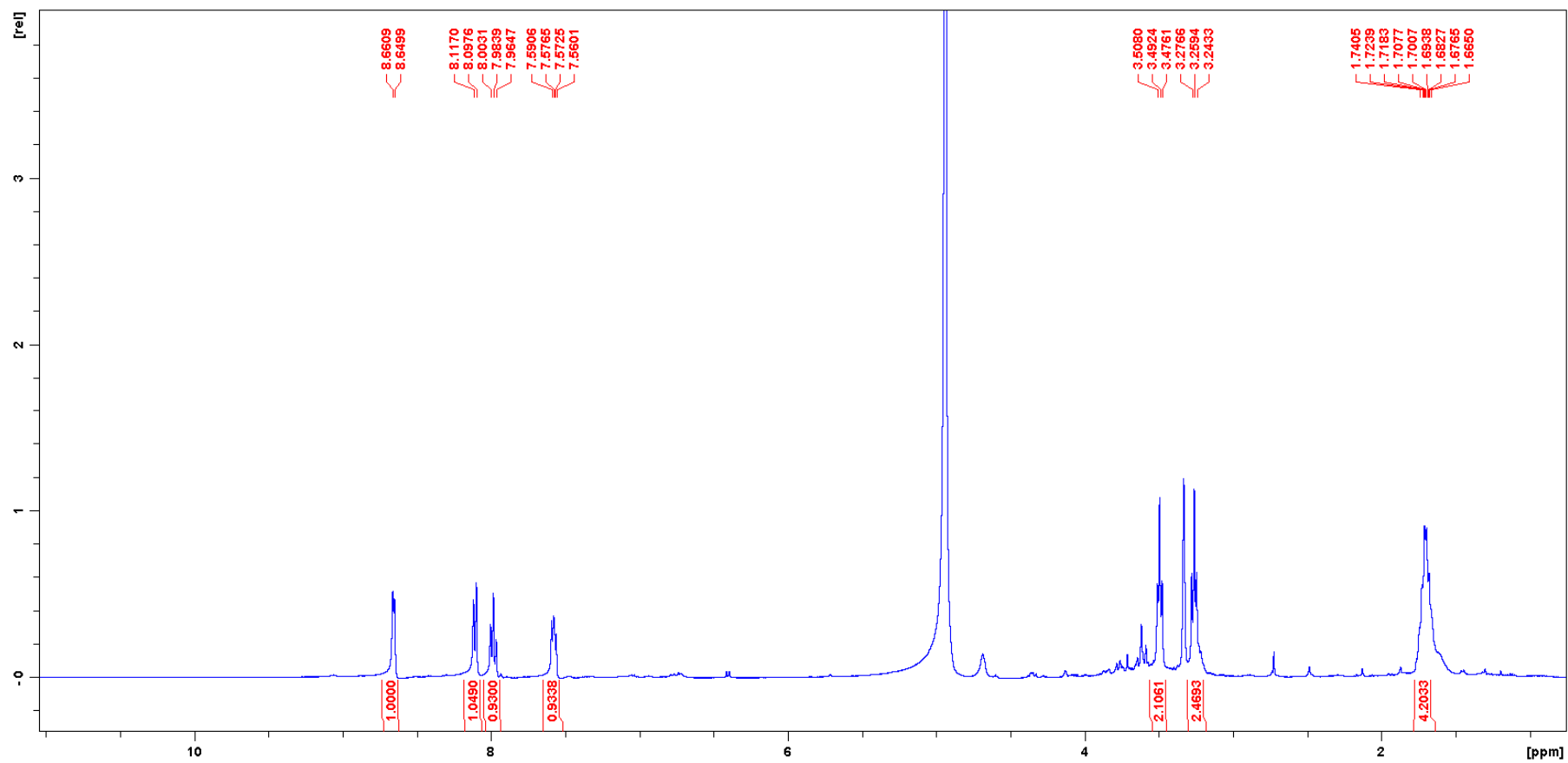
**Figure S9.** NOESY spectrum of martensine A (**1**)



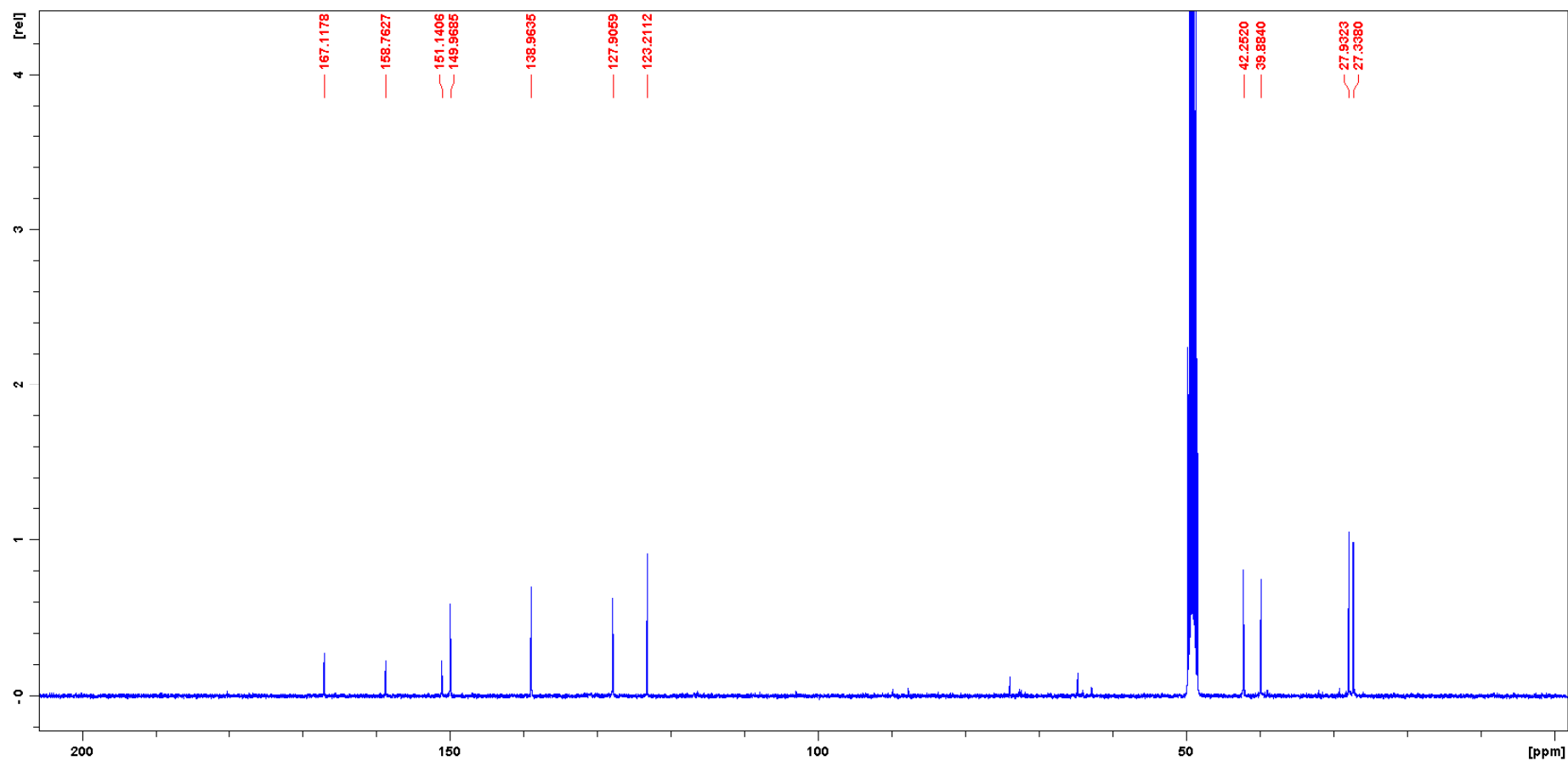
**Figure S10.** HR-ESI-MS spectrum of martensine B (**2**)



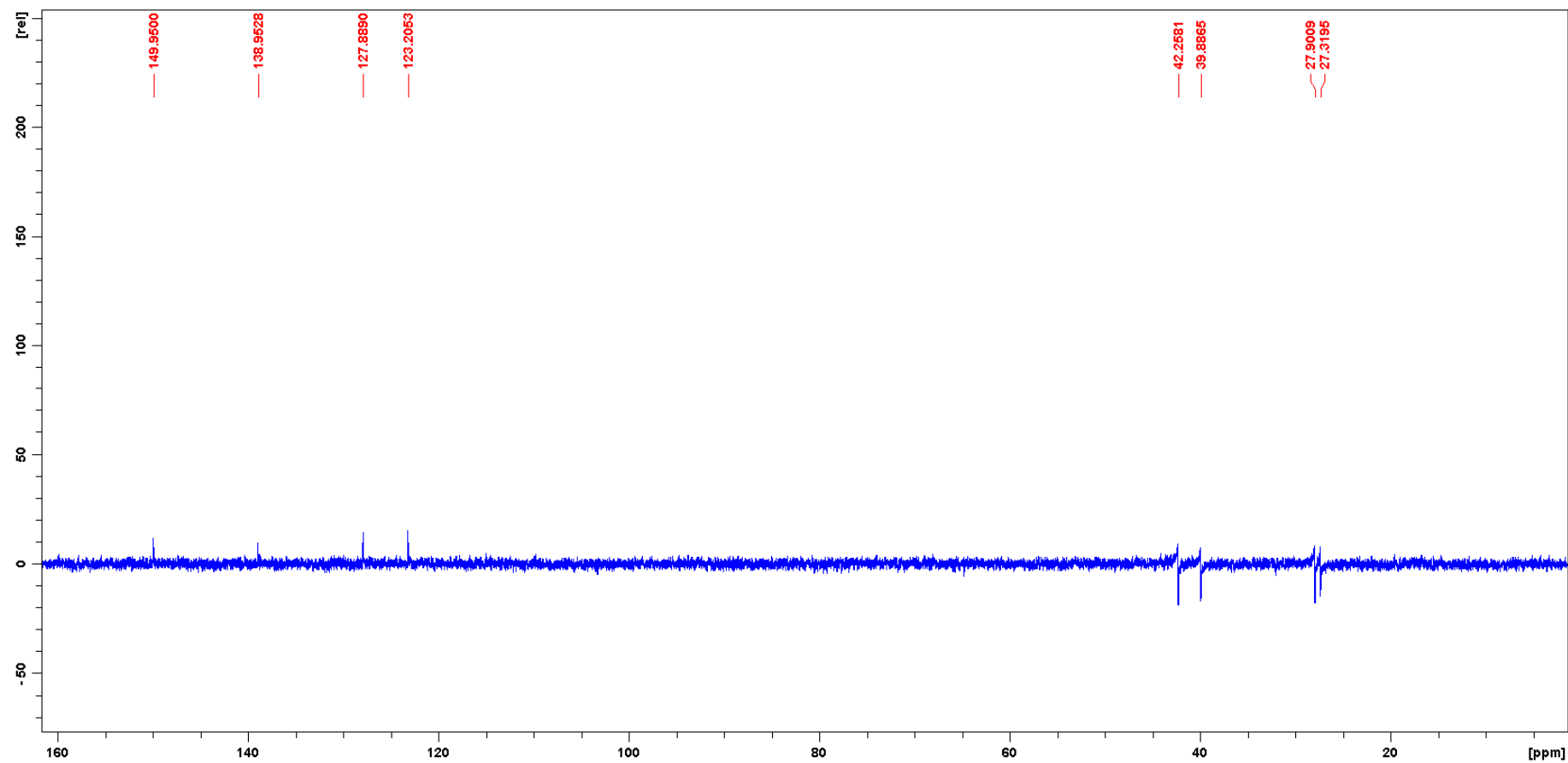
**Figure S11.**  $^1\text{H}$  NMR spectrum ( $\text{CD}_3\text{OD}$ ) of martensine B (**2**)



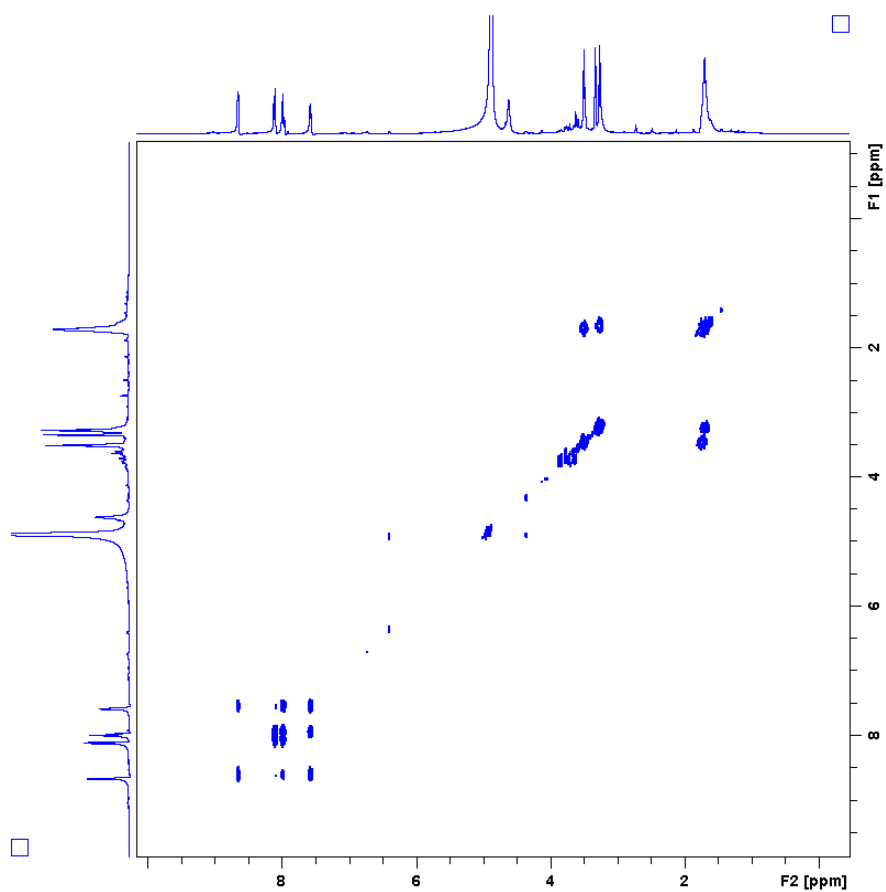
**Figure S12.**  $^{13}\text{C}$  NMR spectrum ( $\text{CD}_3\text{OD}$ ) of martensine B (**2**)



**Figure S13.** DEPT 135 spectrum of martensine B (2)

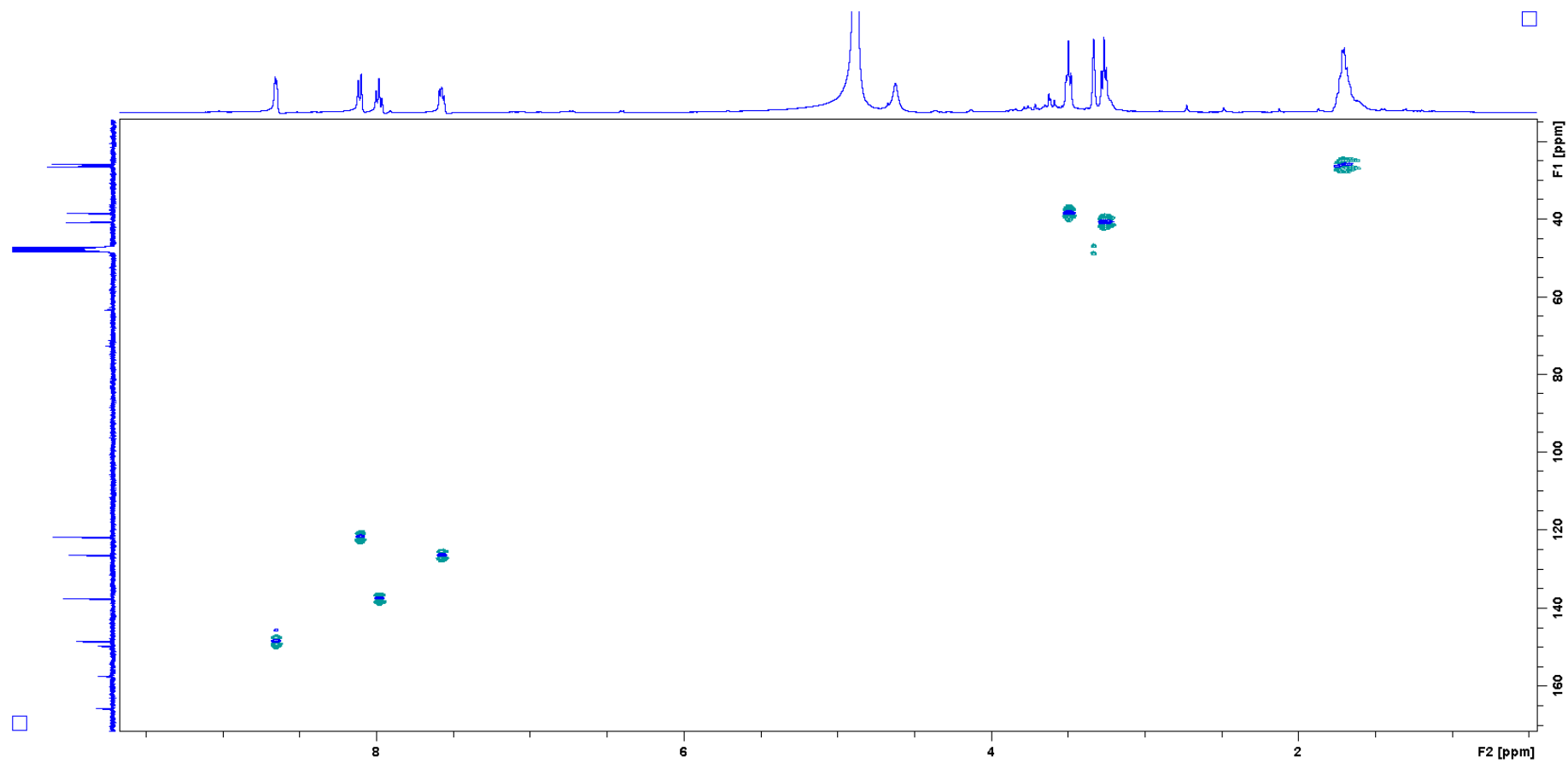


**Figure S14.**  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of martensine B (**2**)

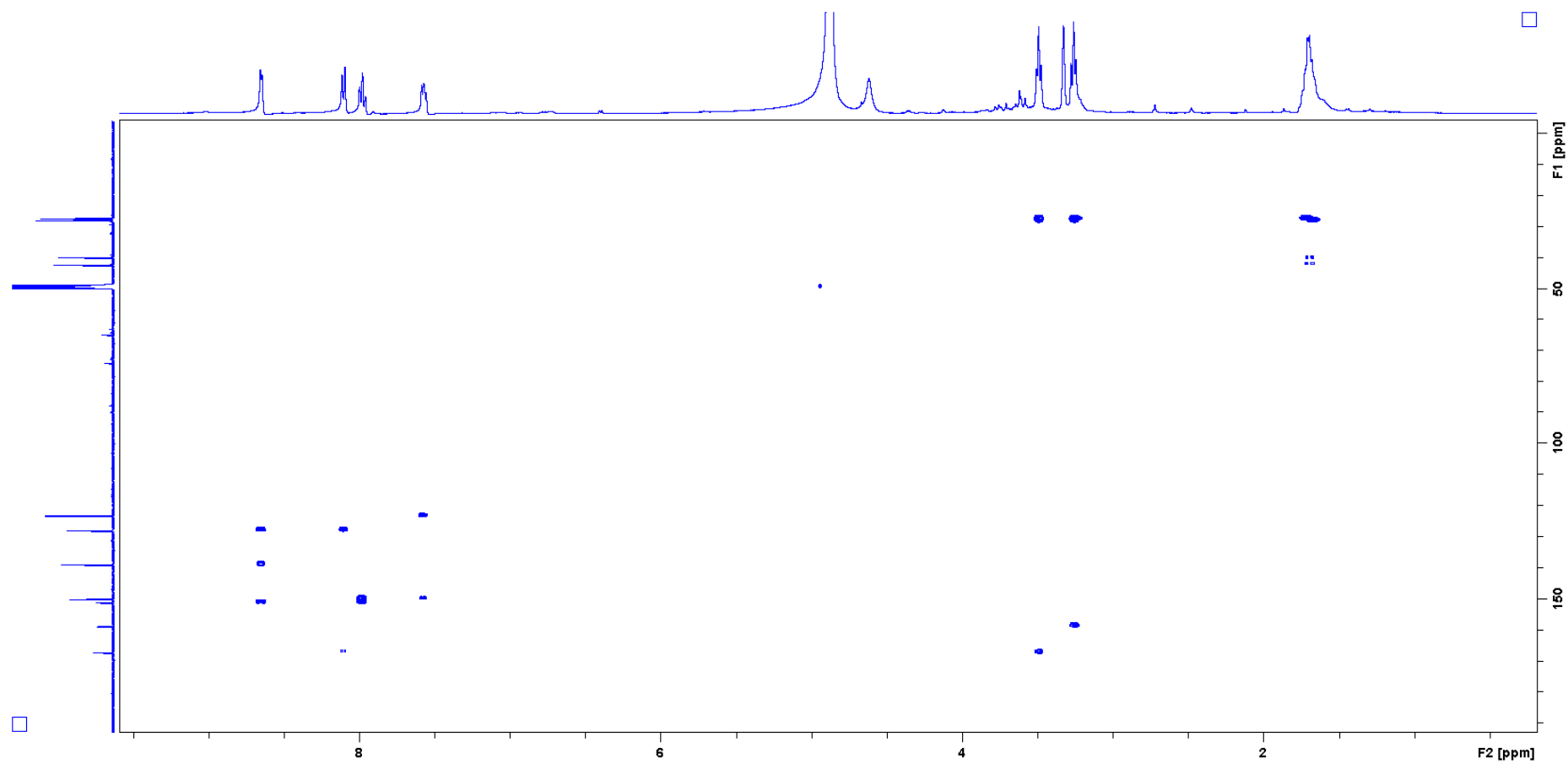




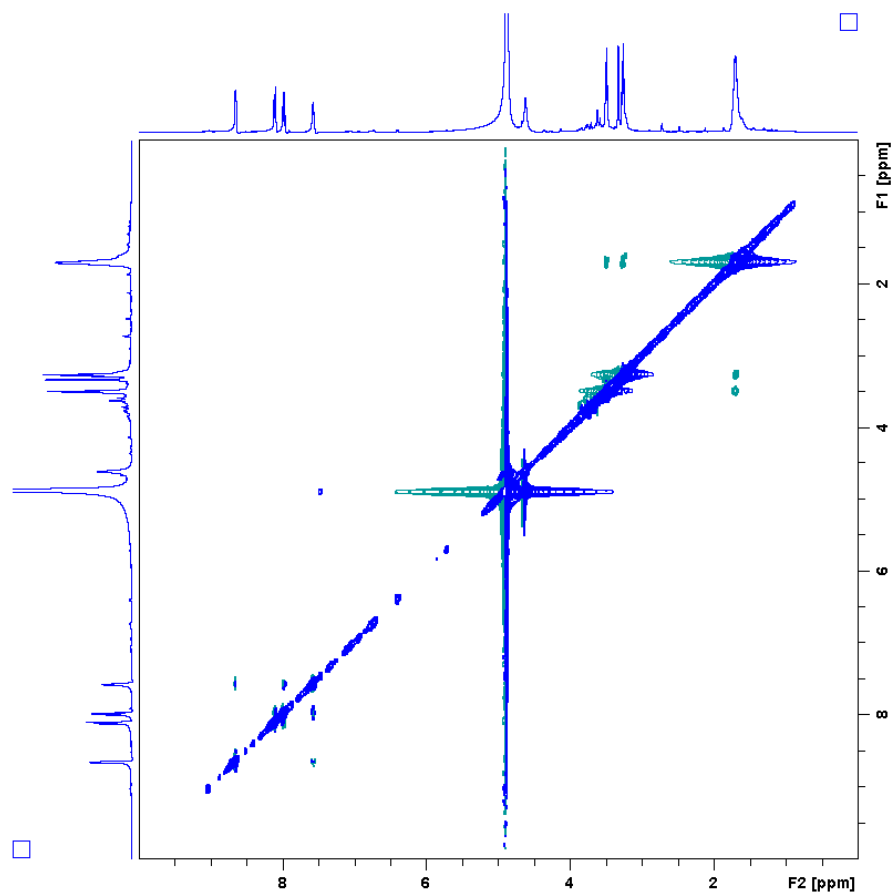
**Figure S15.** HSQC spectrum of martensine B (**2**)



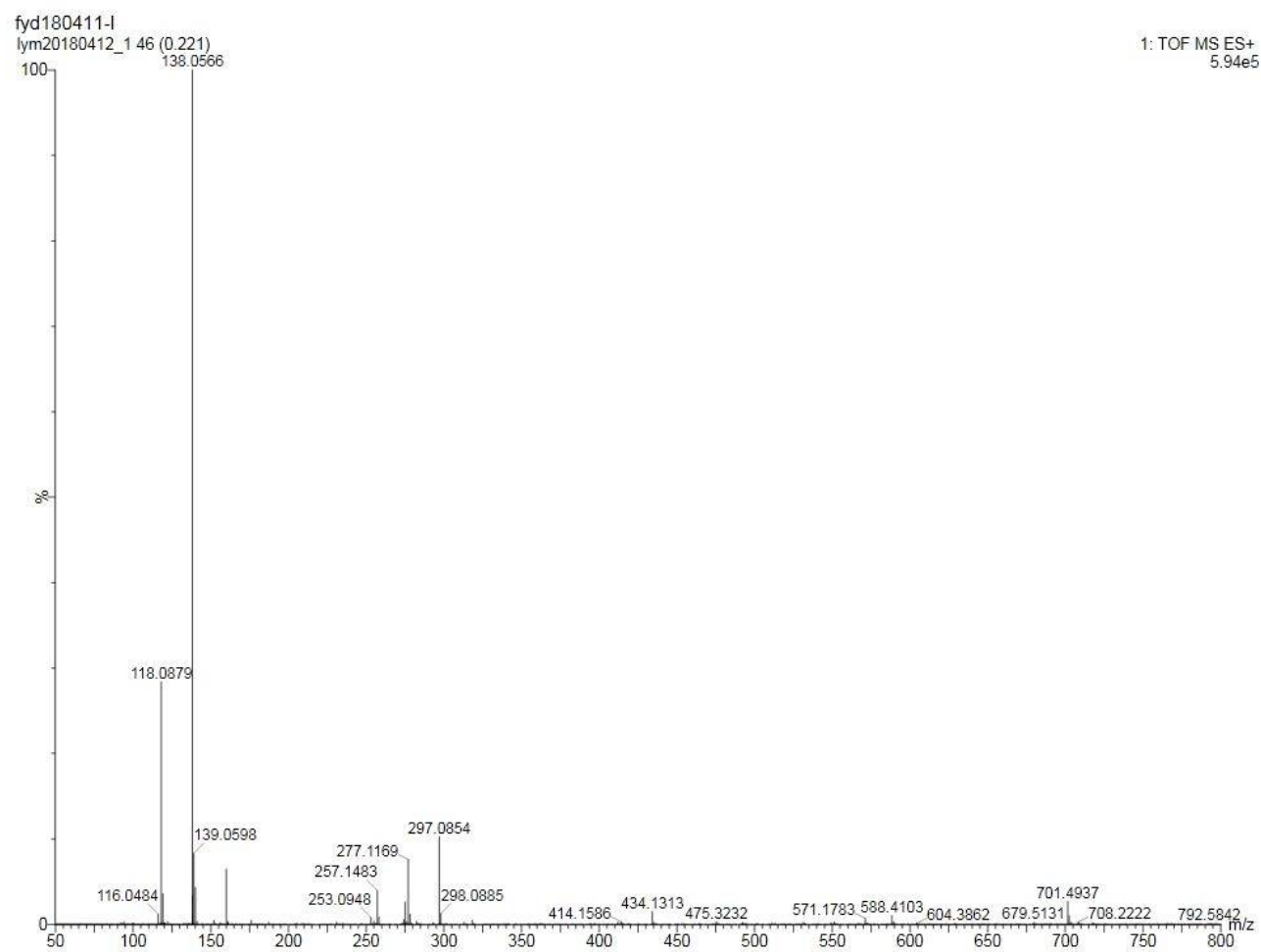
**Figure S16.** HMBC spectrum of martensine B (2)



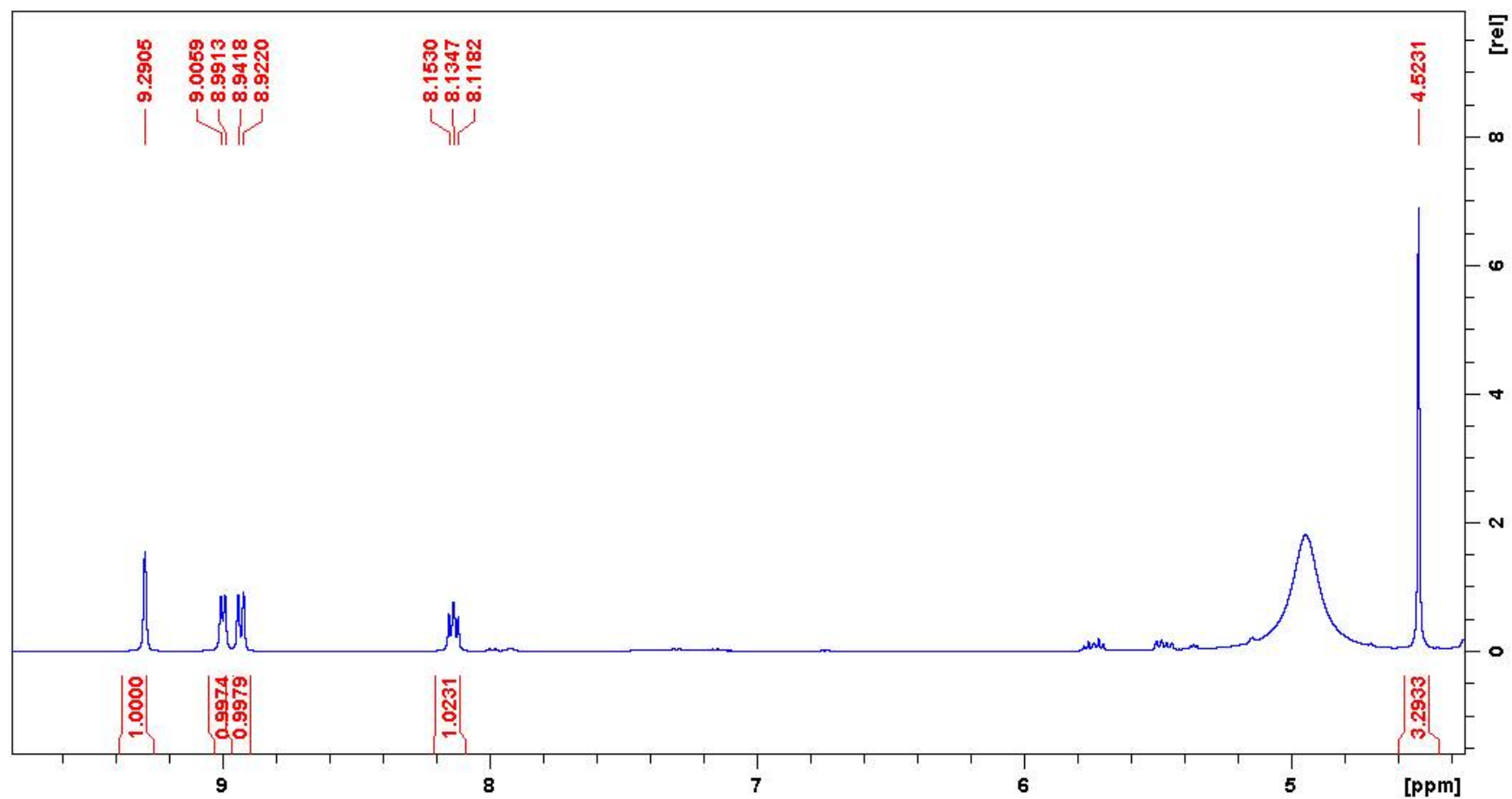
**Figure S17.** NOESY spectrum of martensine B (2)



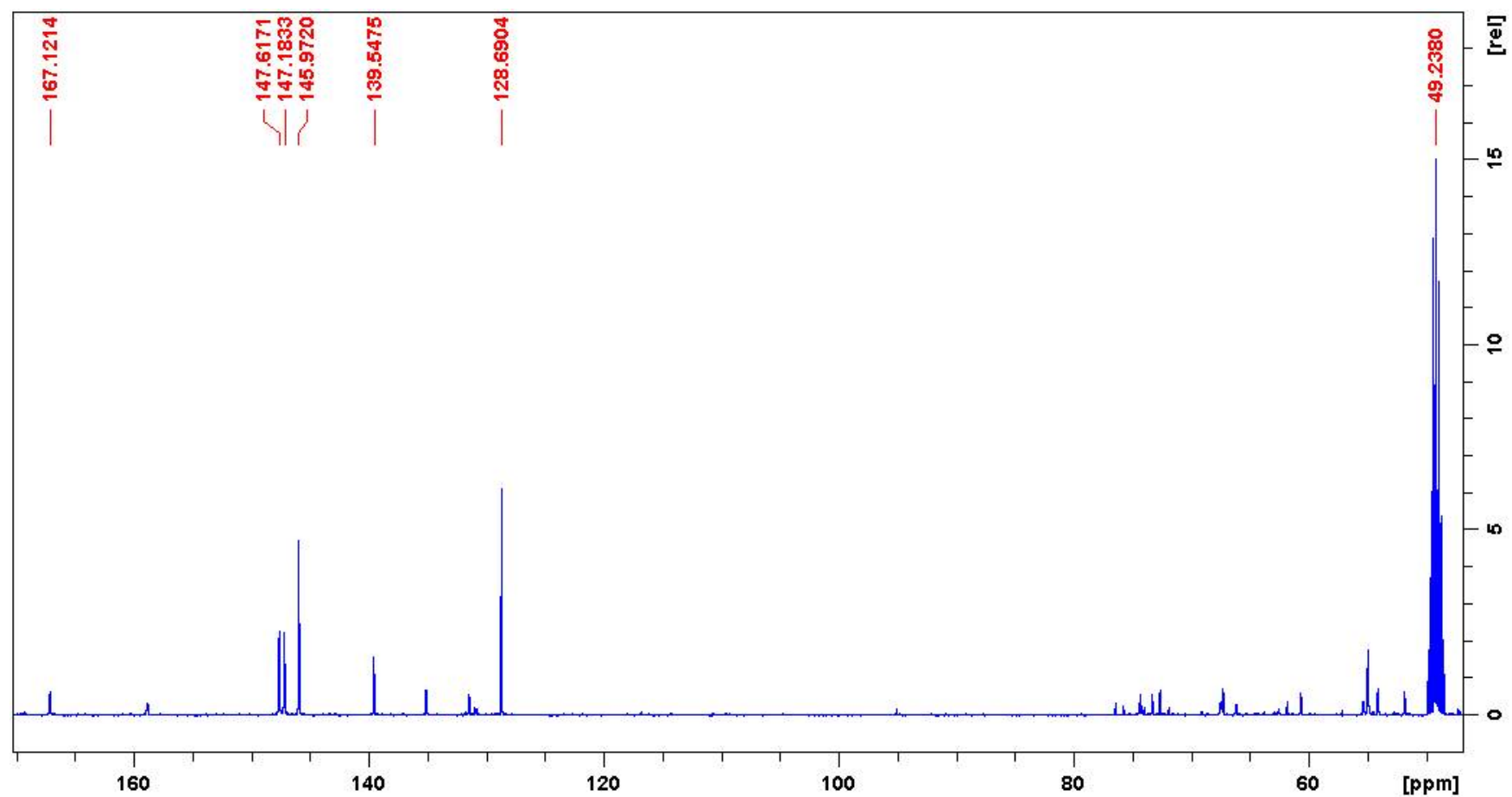
**Figure S18.** HR-ESI-MS spectrum of trigonelline (**3**)



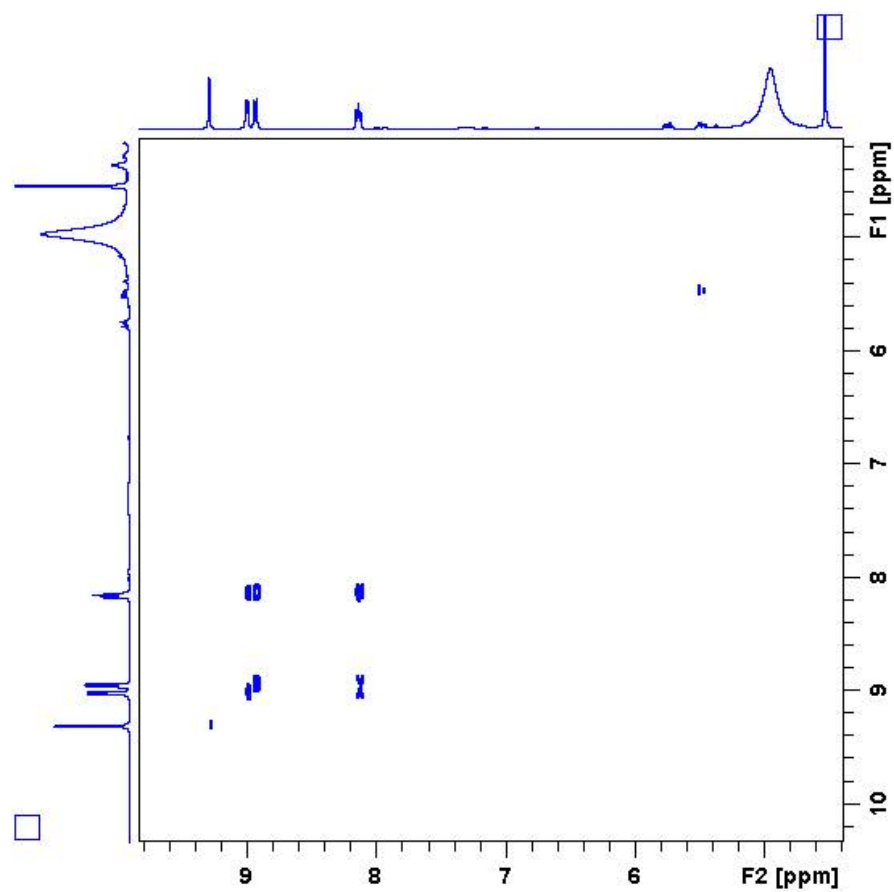
**Figure S19.**  $^1\text{H}$  NMR spectrum ( $\text{CD}_3\text{OD}$ ) of trigonelline (**3**)



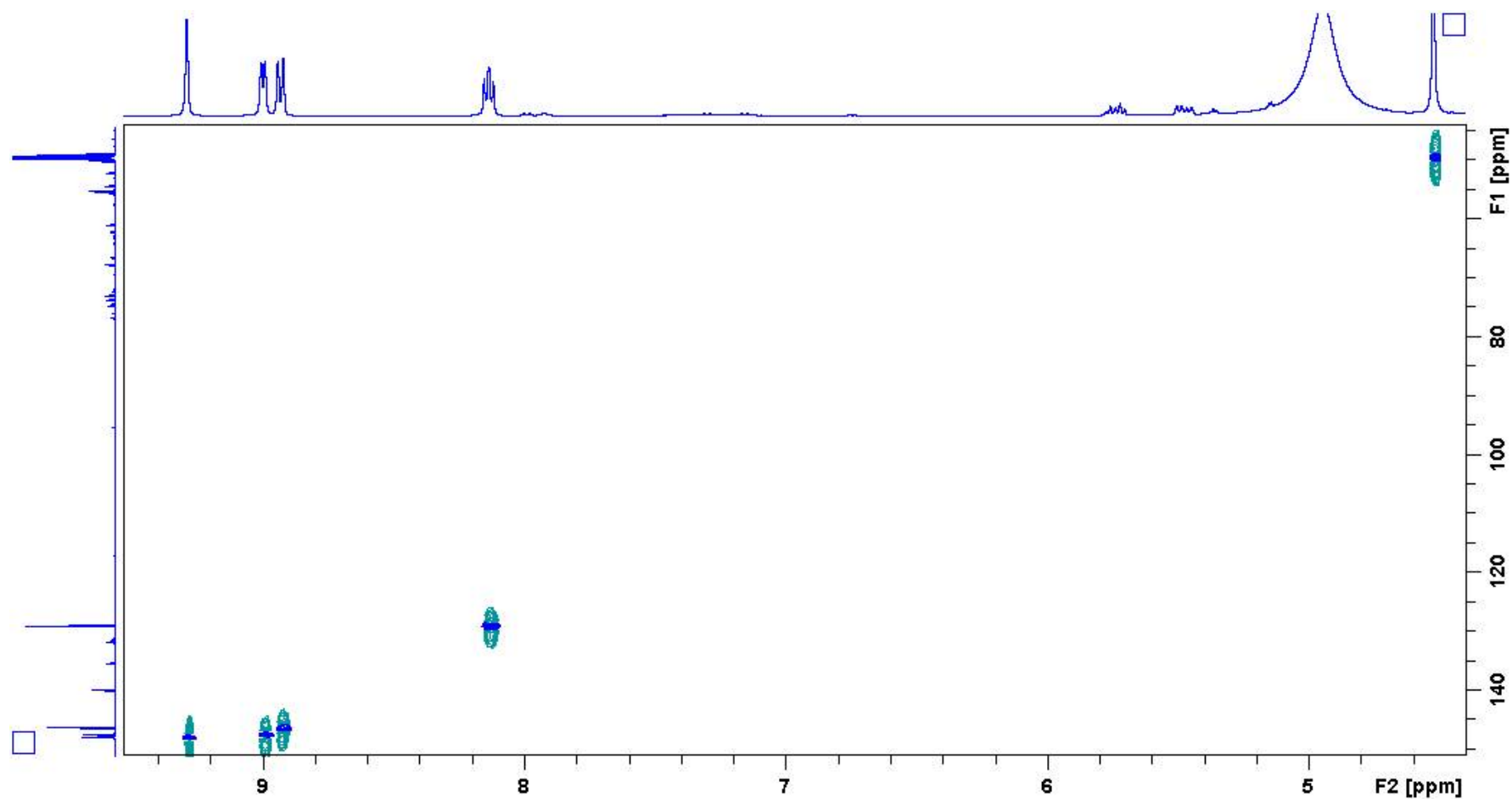
**Figure S20.**  $^{13}\text{C}$  NMR spectrum ( $\text{CD}_3\text{OD}$ ) of trigonelline (**3**)



**Figure S21.**  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of trigonelline (**3**)

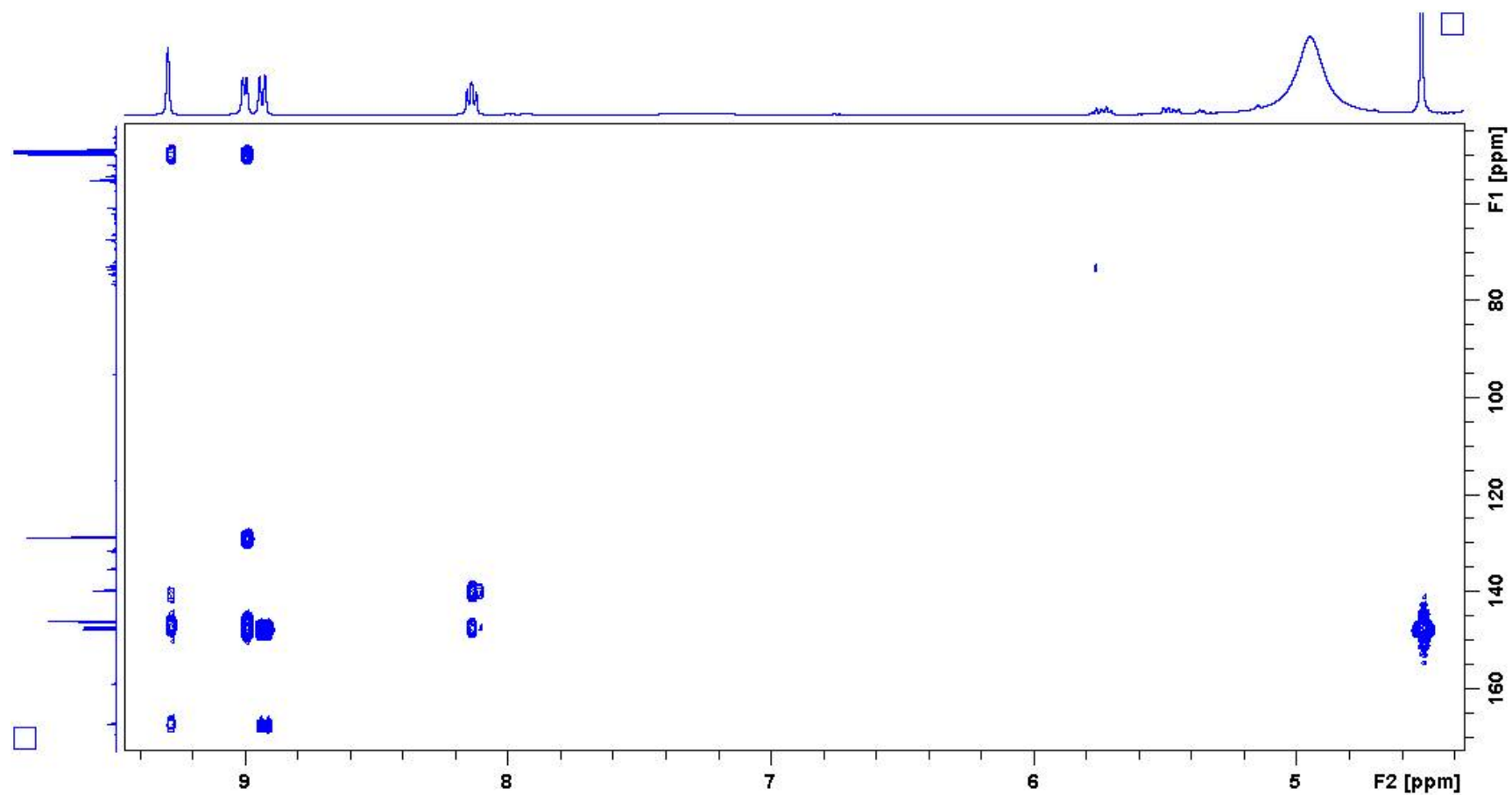


**Figure S22.** HSQC spectrum of trigonelline (**3**)

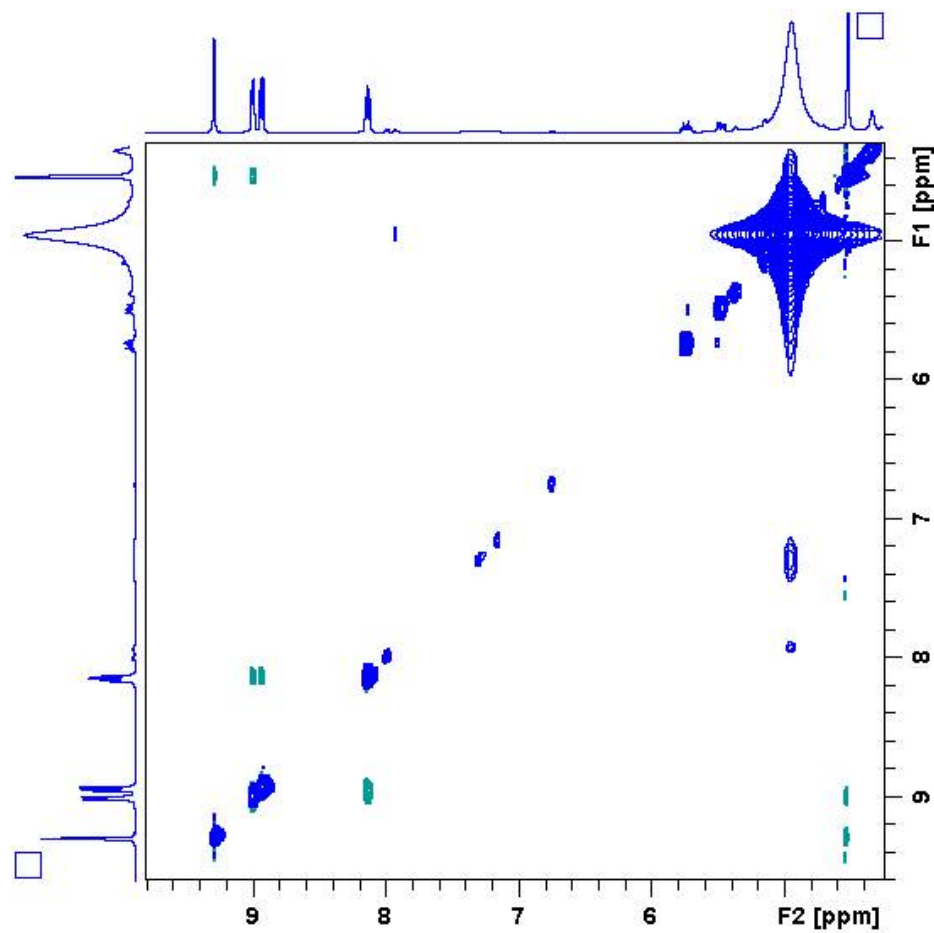




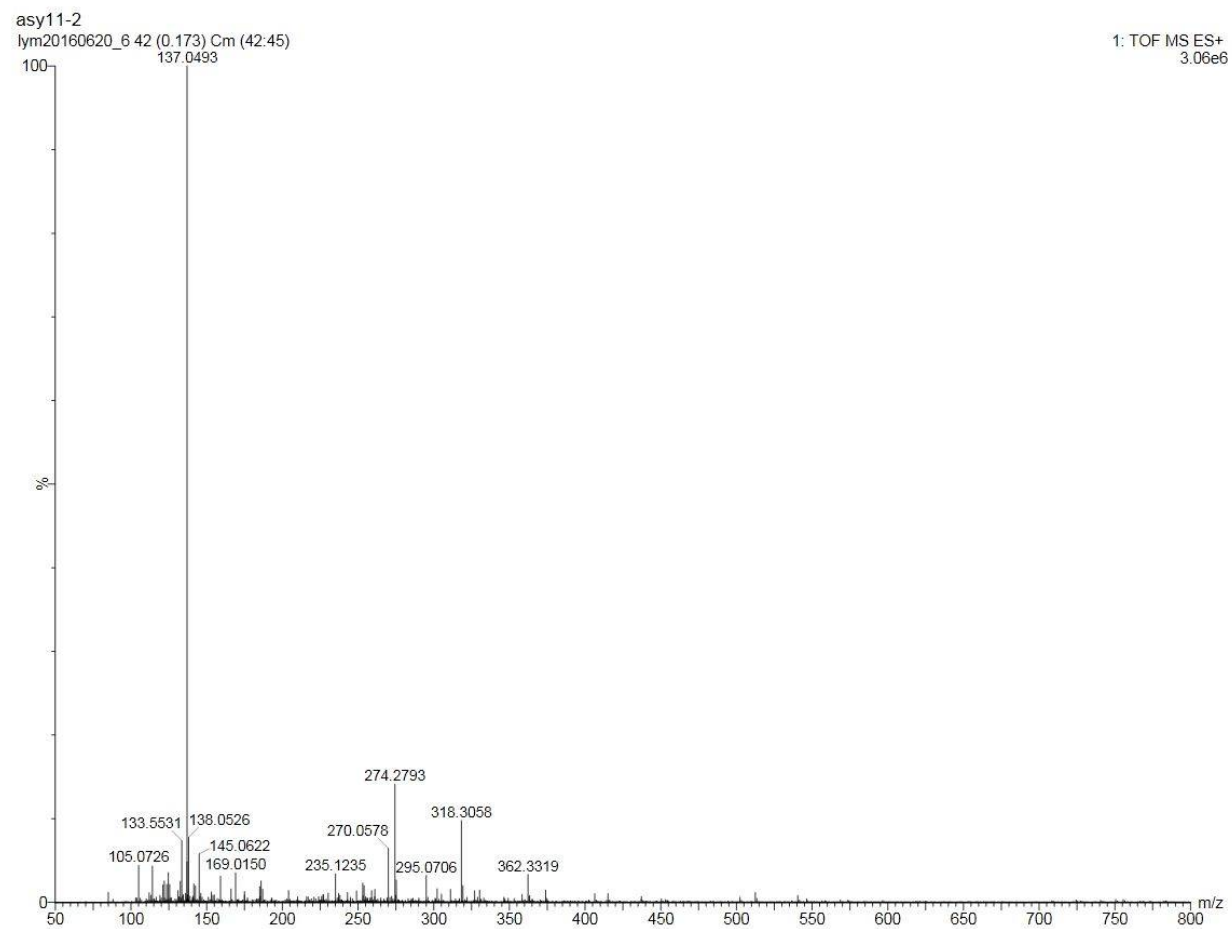
**Figure S23.** HMBC spectrum of trigonelline (**3**)



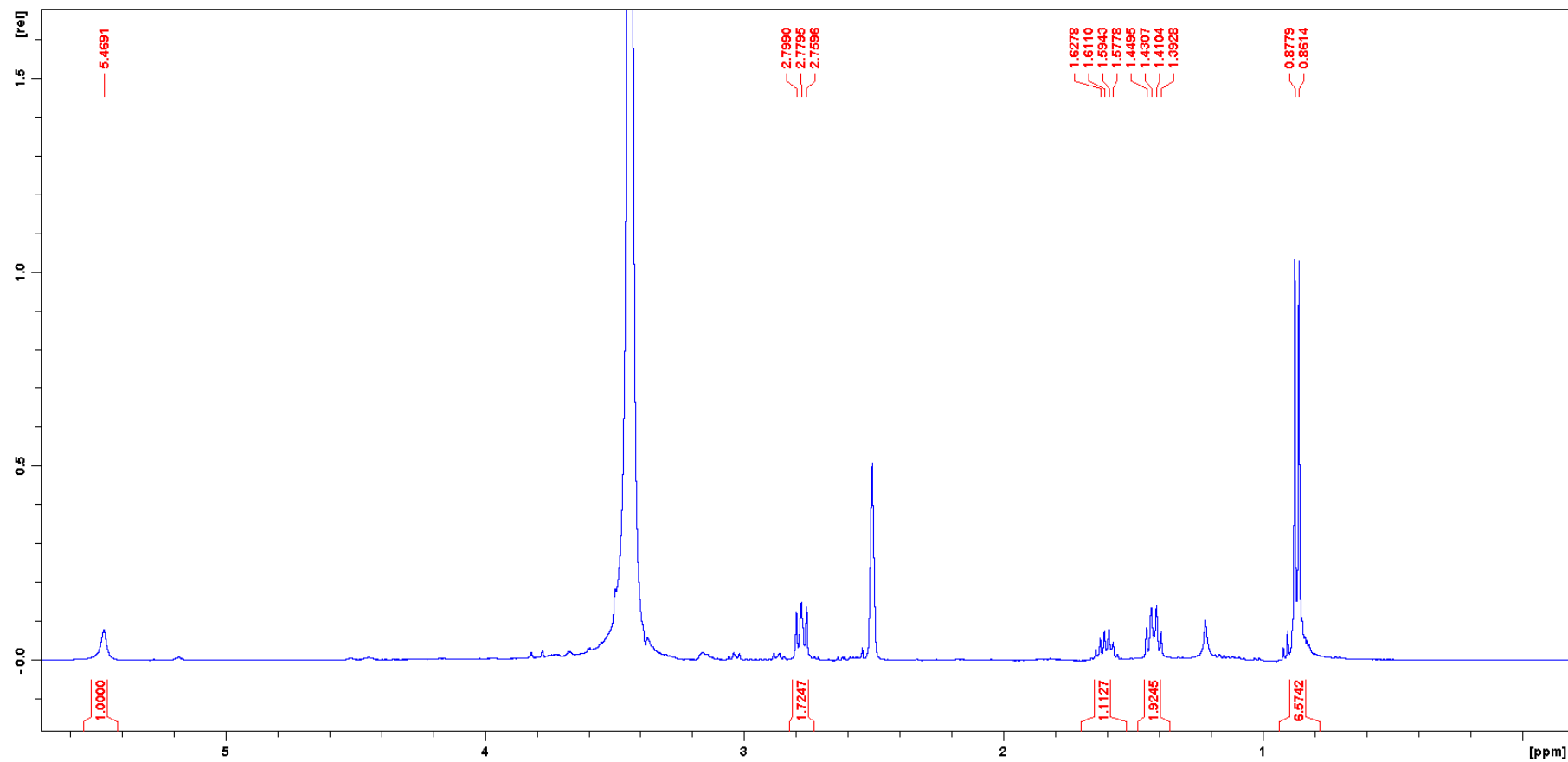
**Figure S24.** NOESY spectrum of trigonelline (**3**)



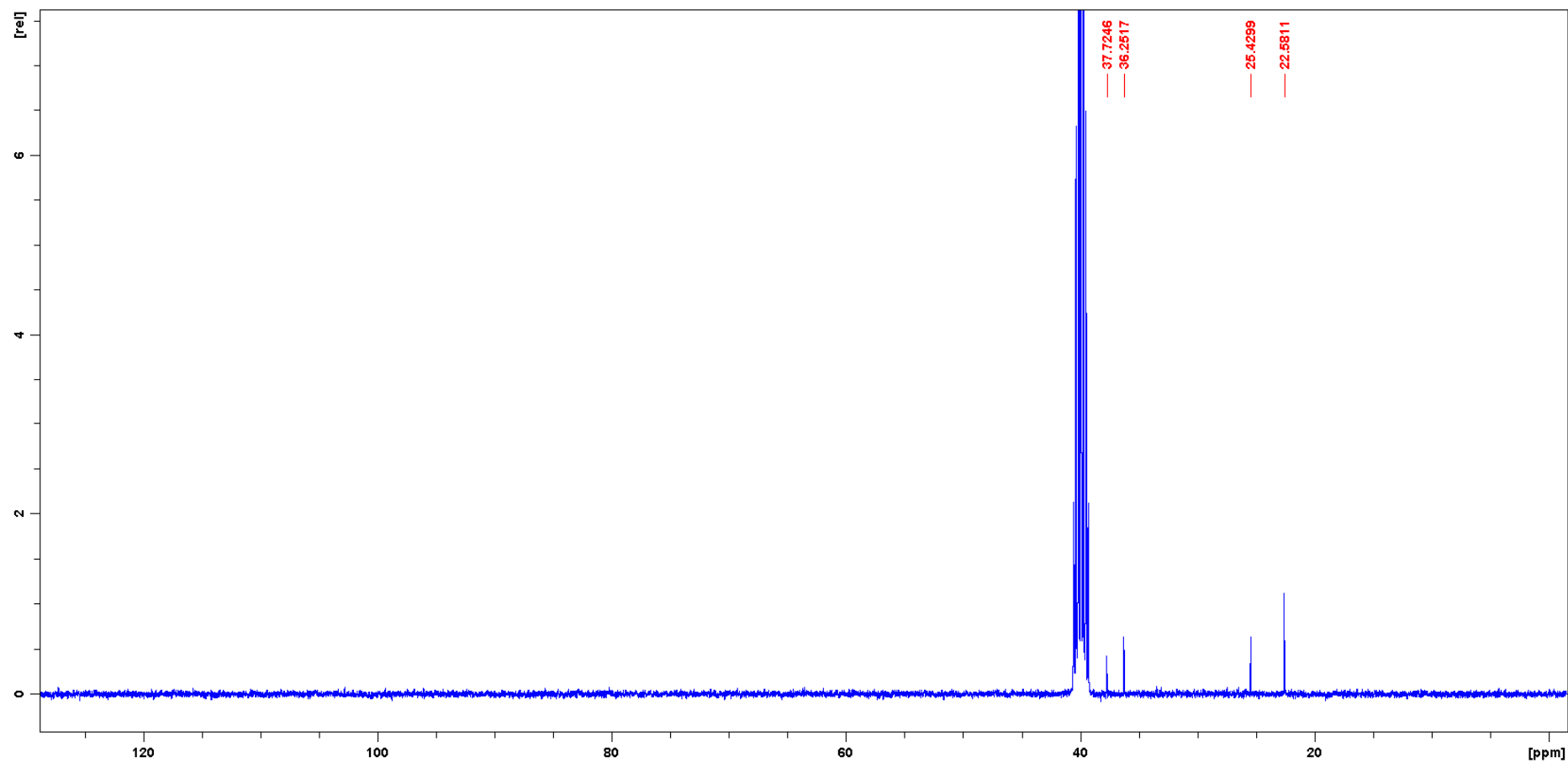
**Figure S25.** HR-ESI-MS spectrum of 3-methylbutyl hydrodisulfide (**4**)

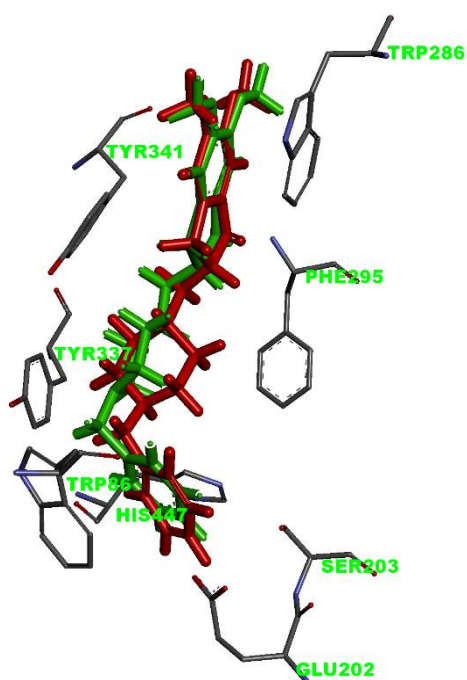


**Figure S26.**  $^1\text{H}$  NMR spectrum ( $\text{DMSO}-d_6$ ) of 3-methylbutyl hydrodisulfide (**4**)

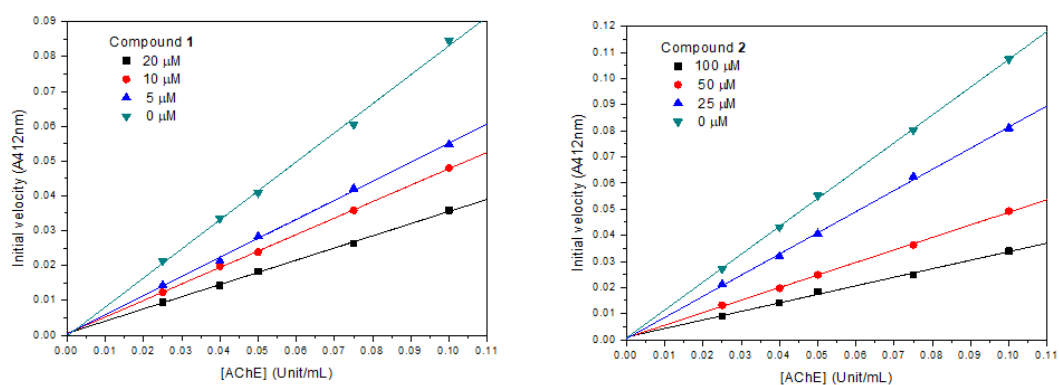


**Figure S27.**  $^{13}\text{C}$  NMR spectrum (DMSO- $d_6$ ) of 3-methylbutyl hydrodisulfide (**4**)





**Fig. S28.** Docking validation. Redocked donepezil (best-ranked docking solution) is reported in red sticks into the active site of AChE. Crystallographic donepezil is represented as green sticks.



**Fig. S29.** Plots of initial velocity versus enzyme concentration for the inhibition of compounds **1** and **2** on the hydrolysis activity of AChE.