

## **Supplementary material related to the article:**

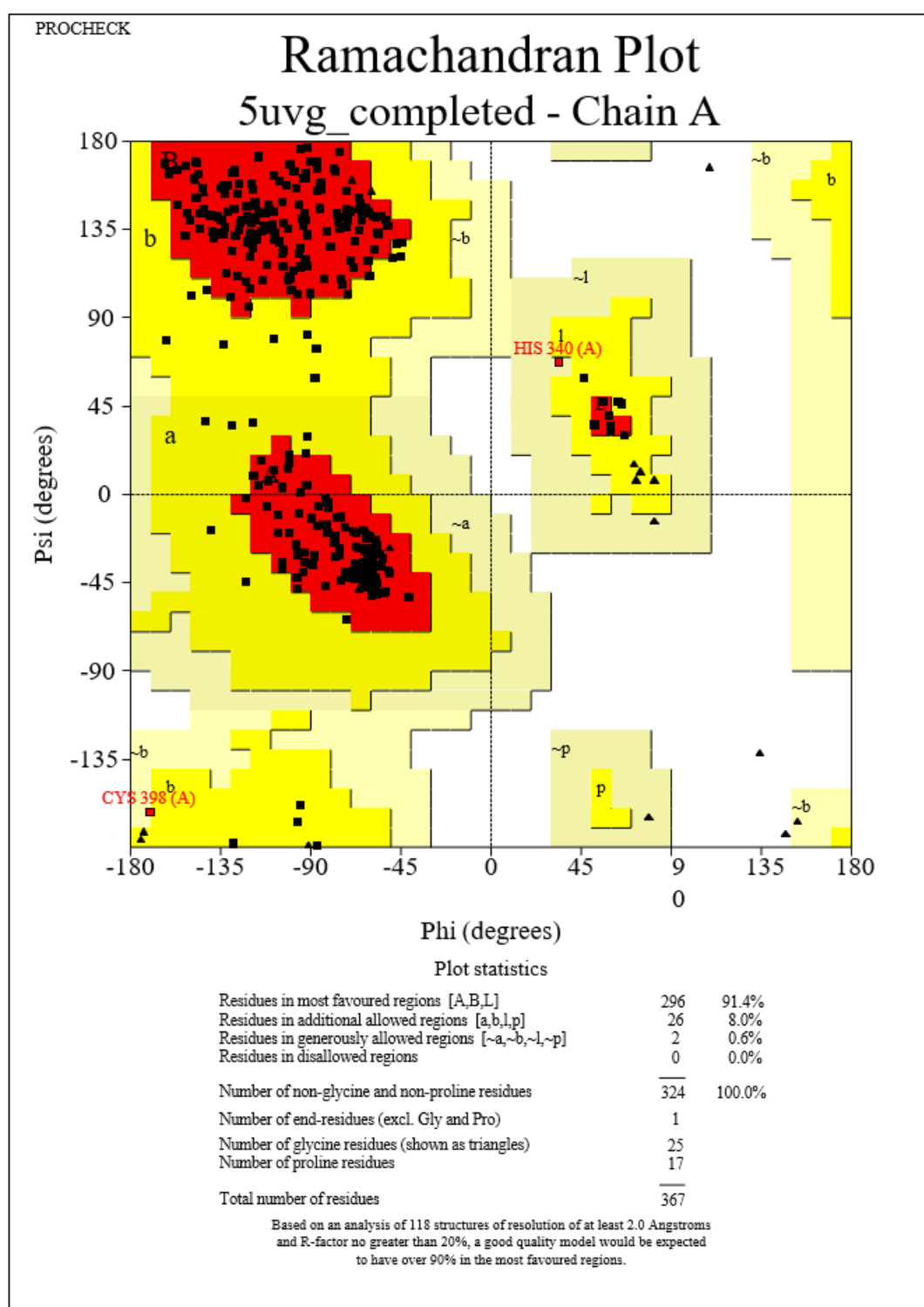
**Allosteric inhibition of neutral sphingomyelinase 2 (nSMase2) by DPTIP:  
from antitubercular activity to deciphering its binding site through in silico  
studies and experimental validation**

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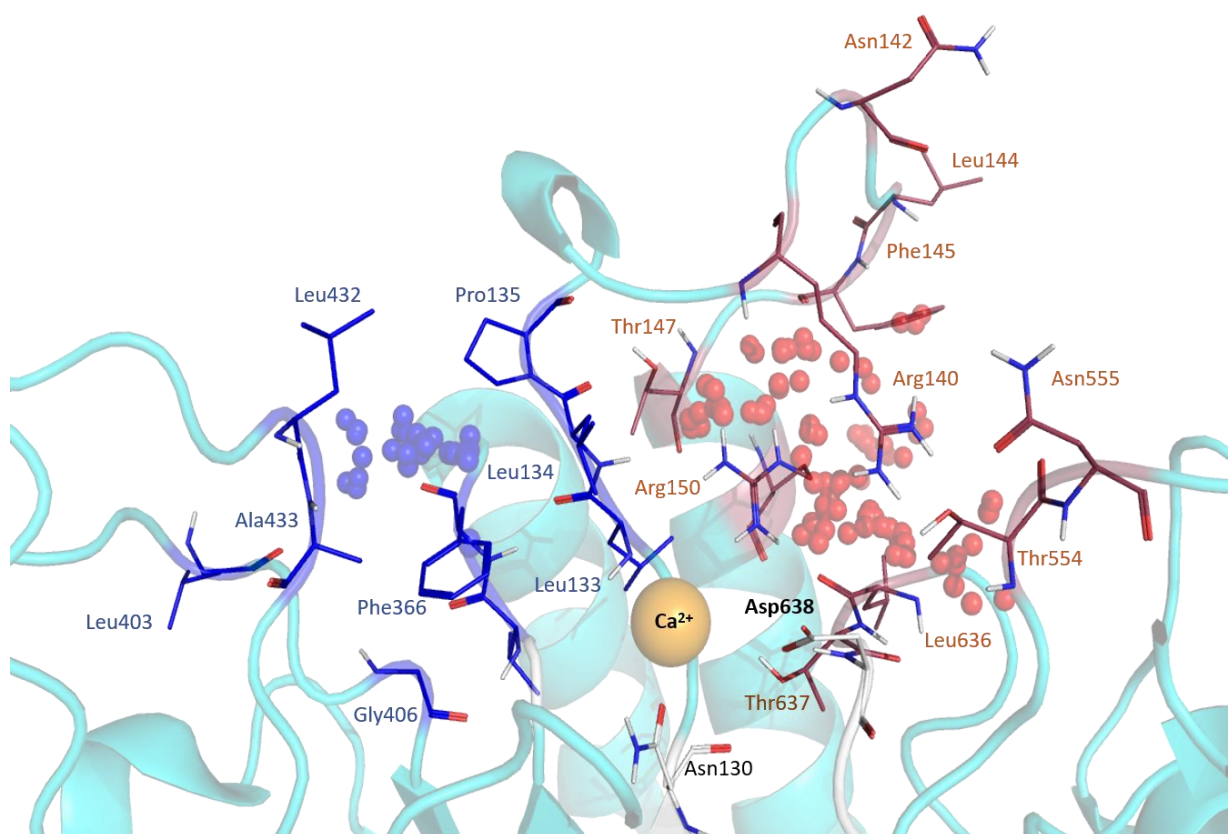
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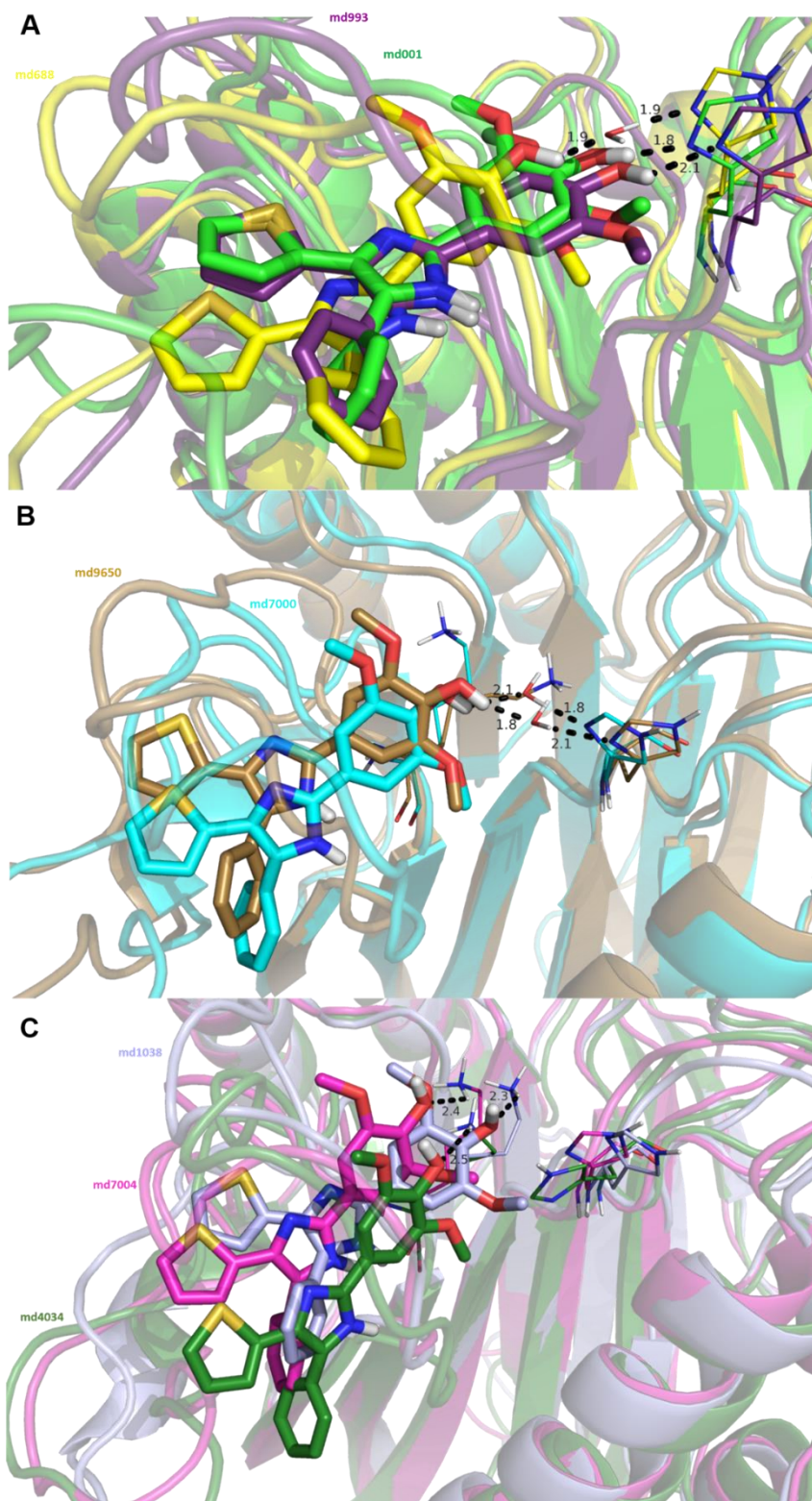
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**Figure S1.** Ramachandran plot of nSMase2 model after loop modeling and structure refinement.



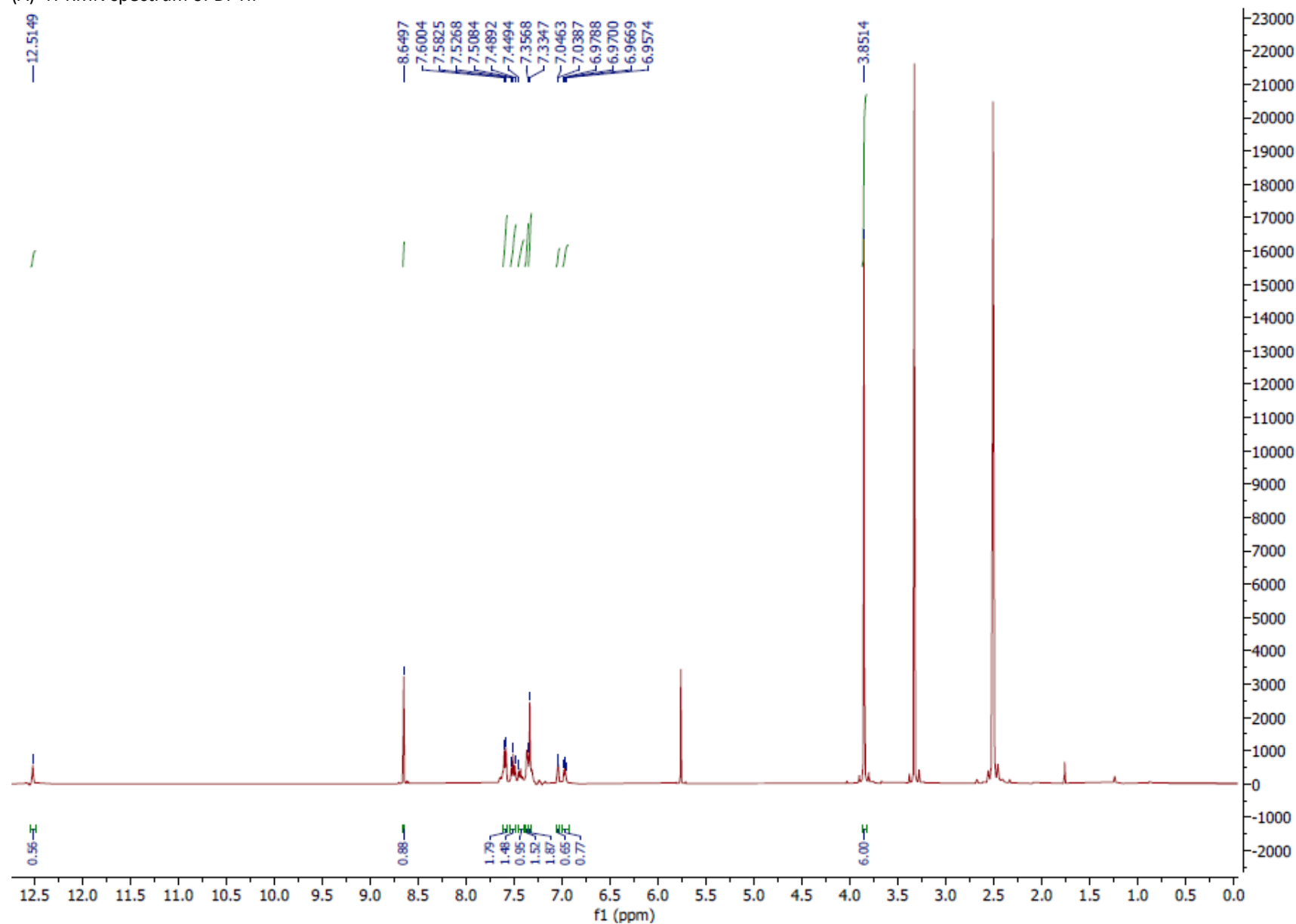
**Figure S2.** P1 (alpha spheres from Fpocket shown in blue and residues in blue lines) and P2 (alpha spheres shown in red spheres and residues in red lines) Active site residues are shown in grey lines and labeled



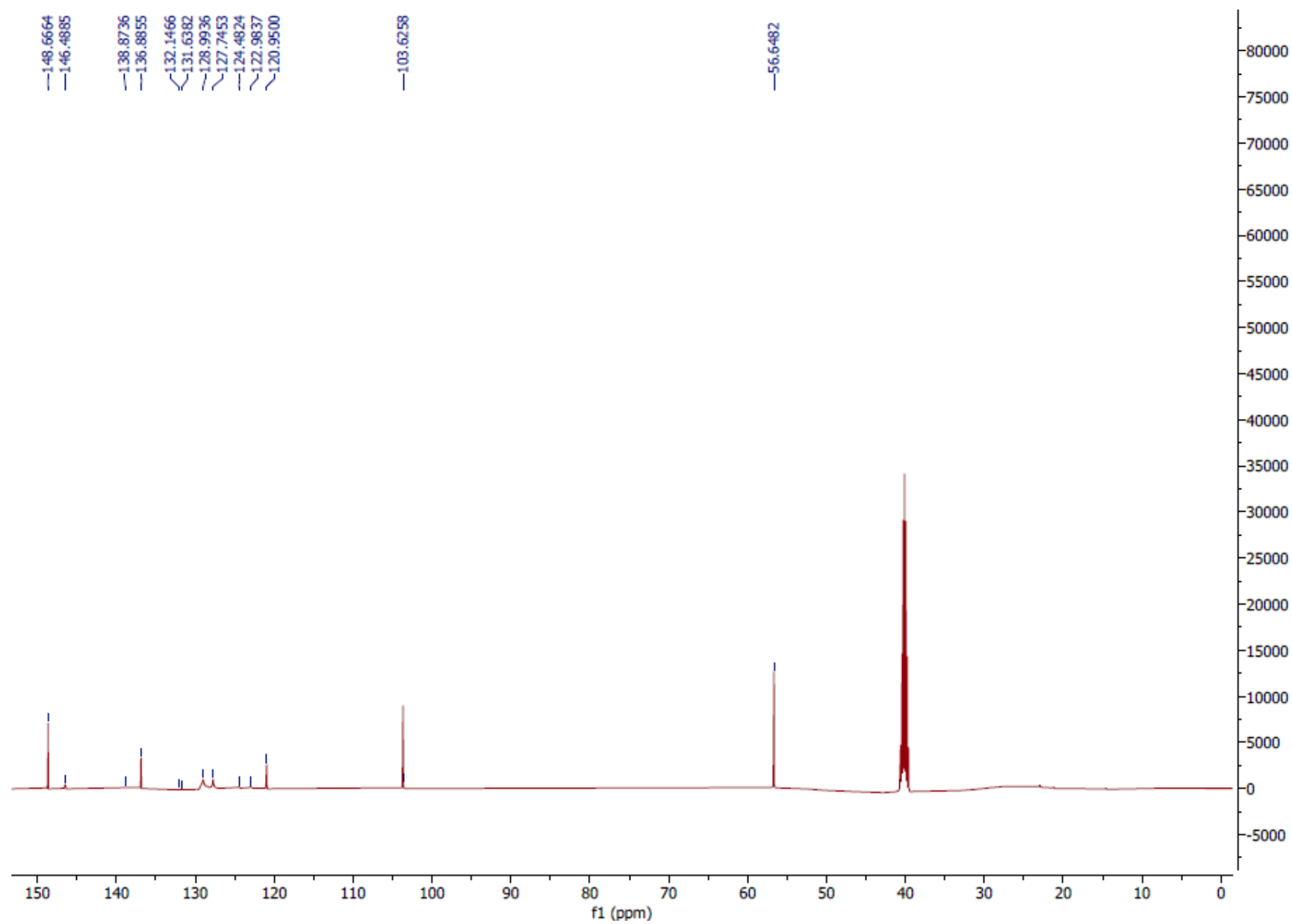
**Figure S3.** (A) and (B) Superimposition of selected MD simulation points showing the DPTIP phenolic OH – Nδ His463 interaction.(A) Md 001 (0 ns, green), md688 (13.76 ns, yellow) and md993 (19.86 ns, purple); (B) Md7000 (140 ns, cyan) and Md9650 (193 ns, sand). (C) Superimposition of selected MD simulation points showing the DPTIP phenolic OH – Nz Lys465 interaction. Md1038 (20,76 ns, lightblue), md4034 (80,68 ns, green) and md7004 (140,08 ns, magenta). Hydrogen bonds are shown as dashed lines and distances are indicated in Å. Water molecules are shown in lines.

**Figure S4.**  $^1\text{H}$ -RMN,  $^{13}\text{C}$ -RMN spectra and HPLC chromatogram of DPTIP

(A)  $^1\text{H}$ -RMN spectrum of DPTIP



(B)  $^{13}\text{C}$ -RMN spectrum of DPTIP



(C) HPLC Chromatogram of DPTIP (Rt = 6.7 min) at  $\lambda$  254 nm.

