Supplementary Material

Binding pose analysis of hydroxyethylamine based β-secretase inhibitors and application thereof to the design and synthesis of novel indeno[1,2-*b*]indole based inhibitors

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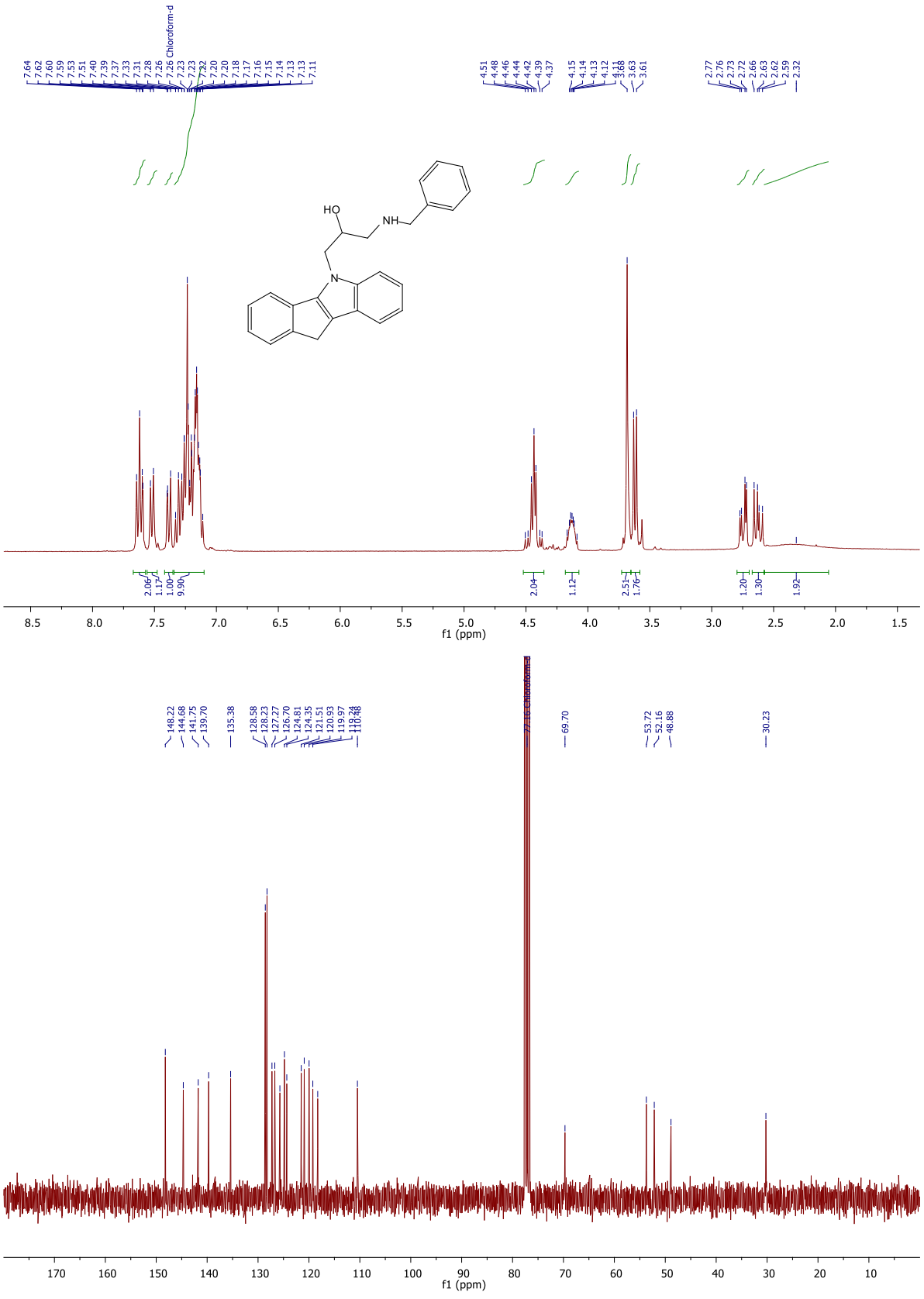
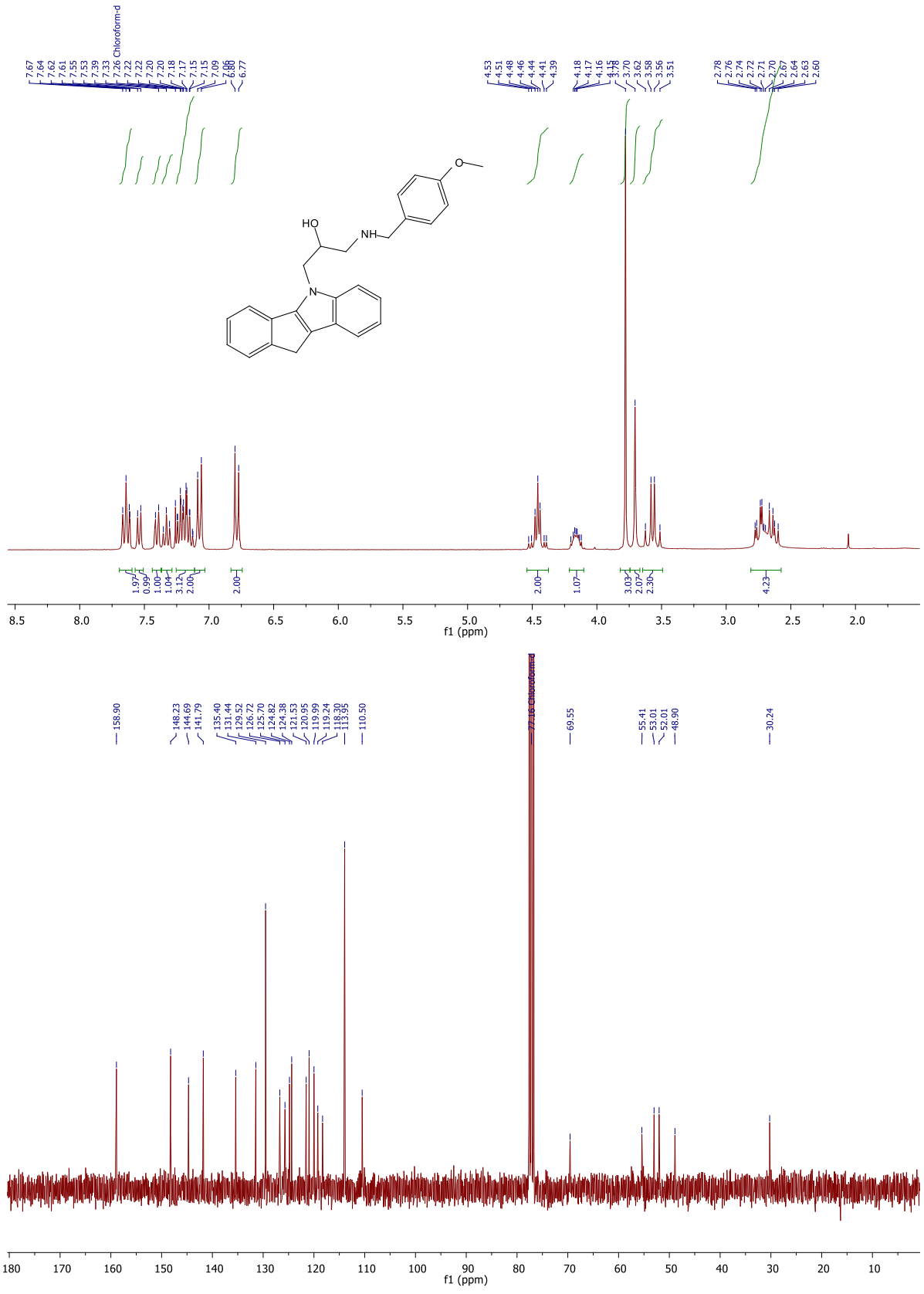
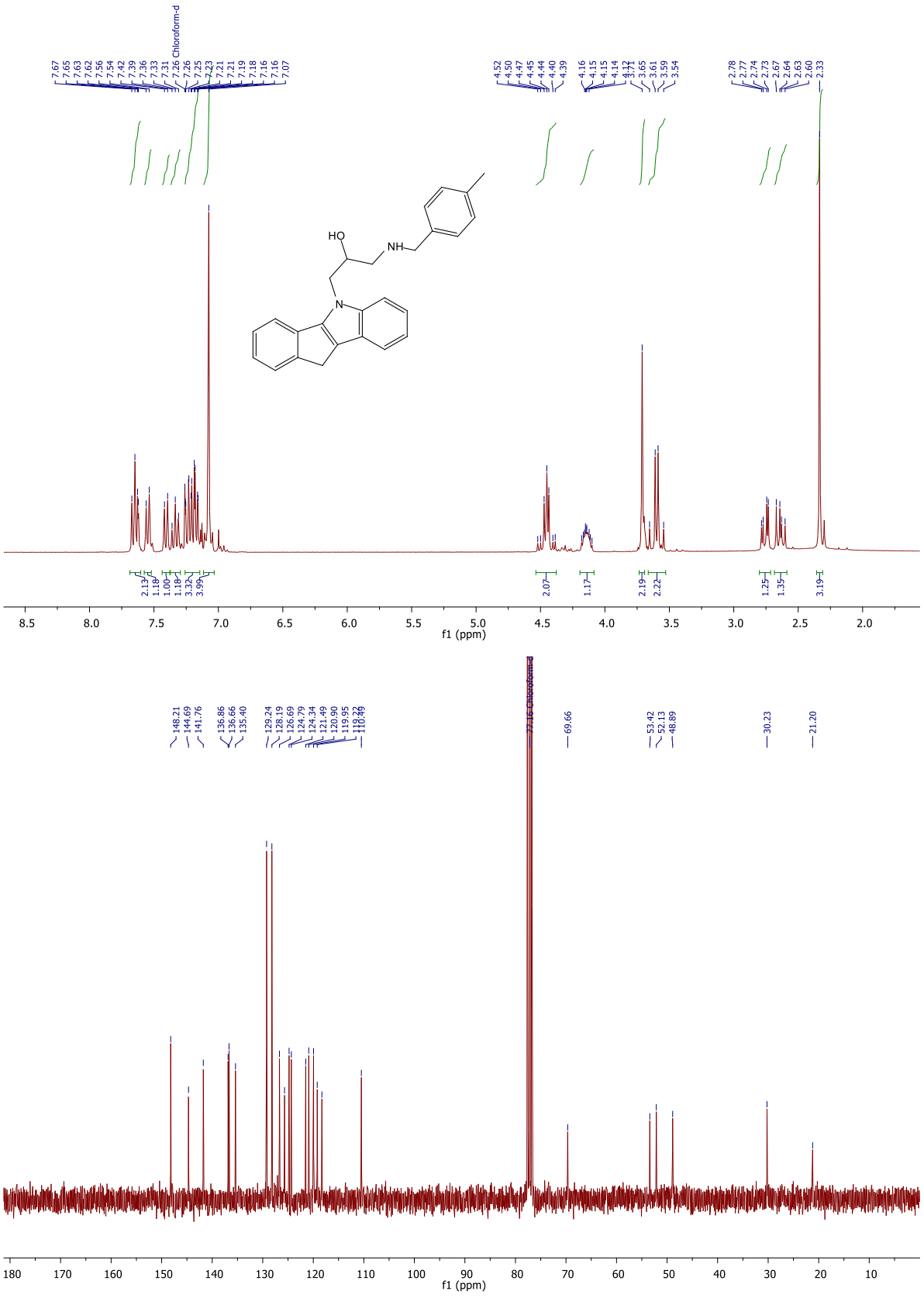
1. ^{1}H and ^{13}C NMR spectra of **4**



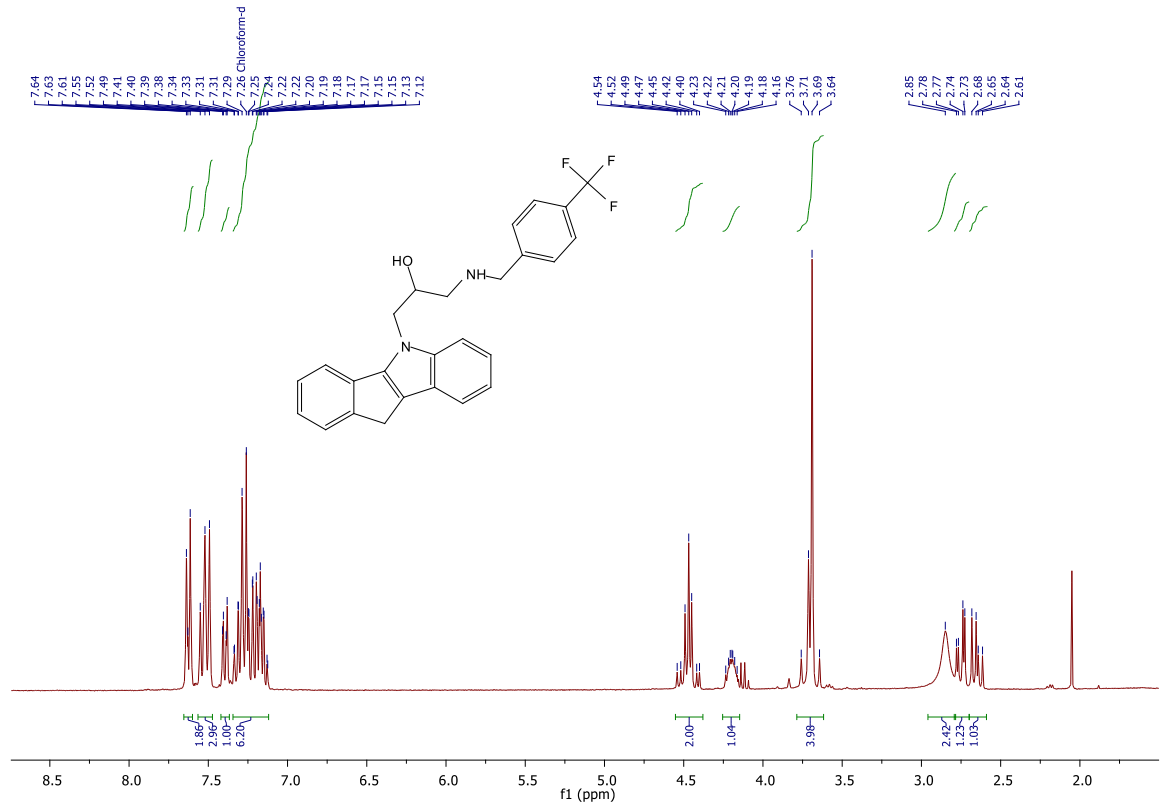
2. ^{1}H and ^{13}C NMR spectra of **5**

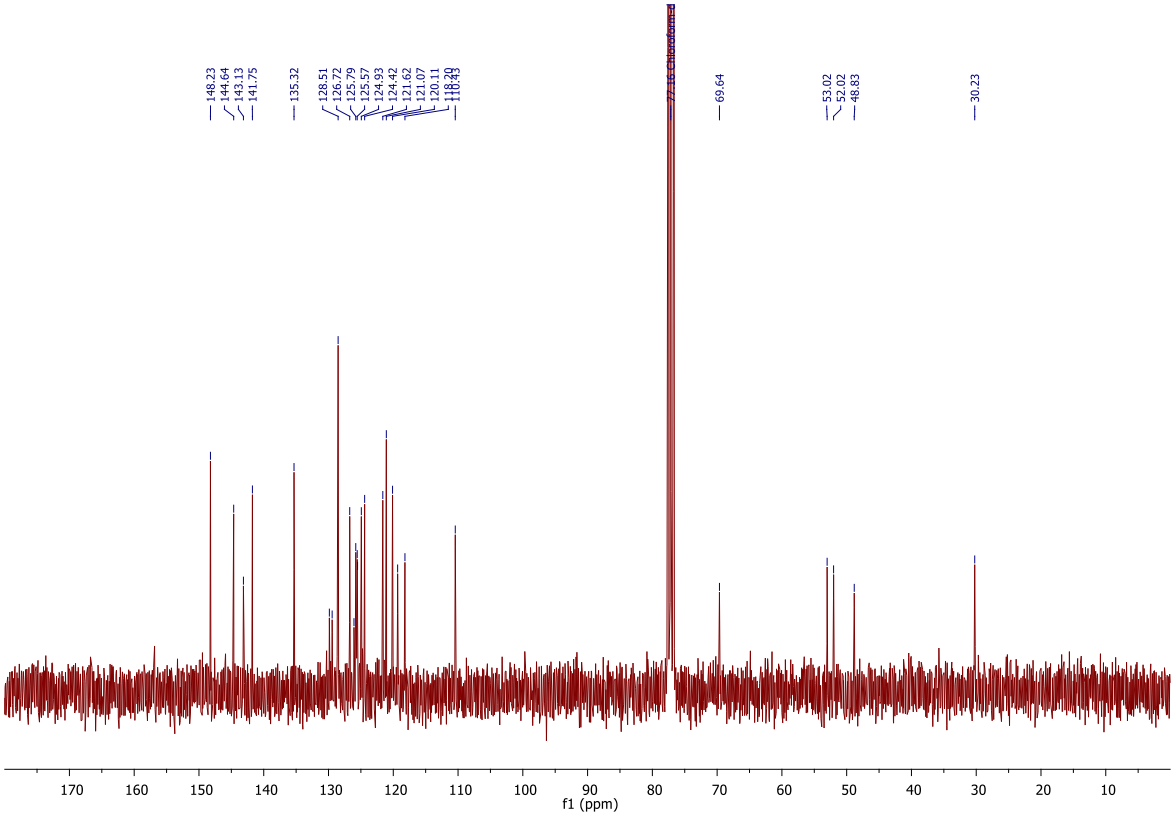


3. ^{1}H and ^{13}C NMR spectra of **6**

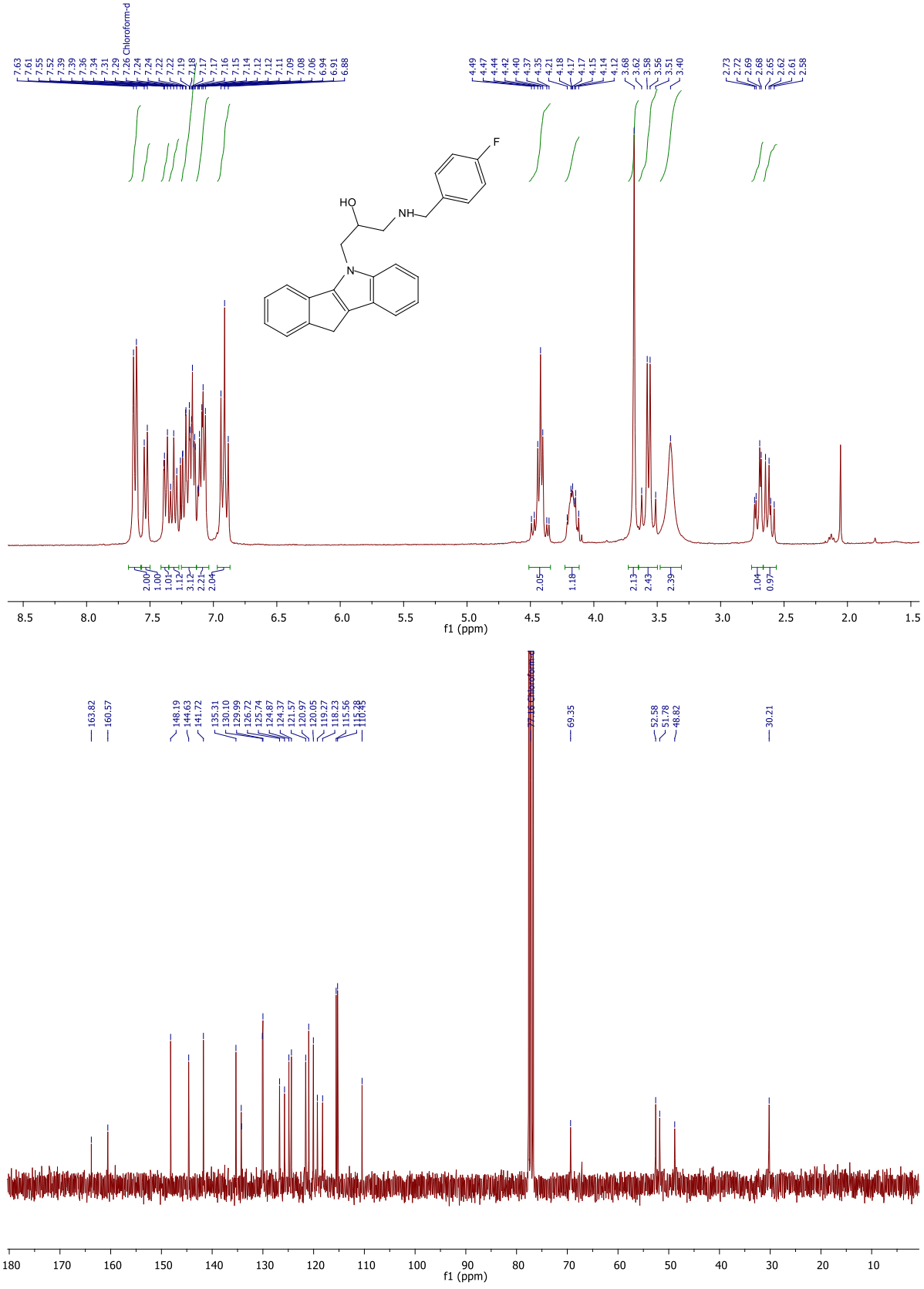


4. ^{1}H and ^{13}C NMR spectra of **7**

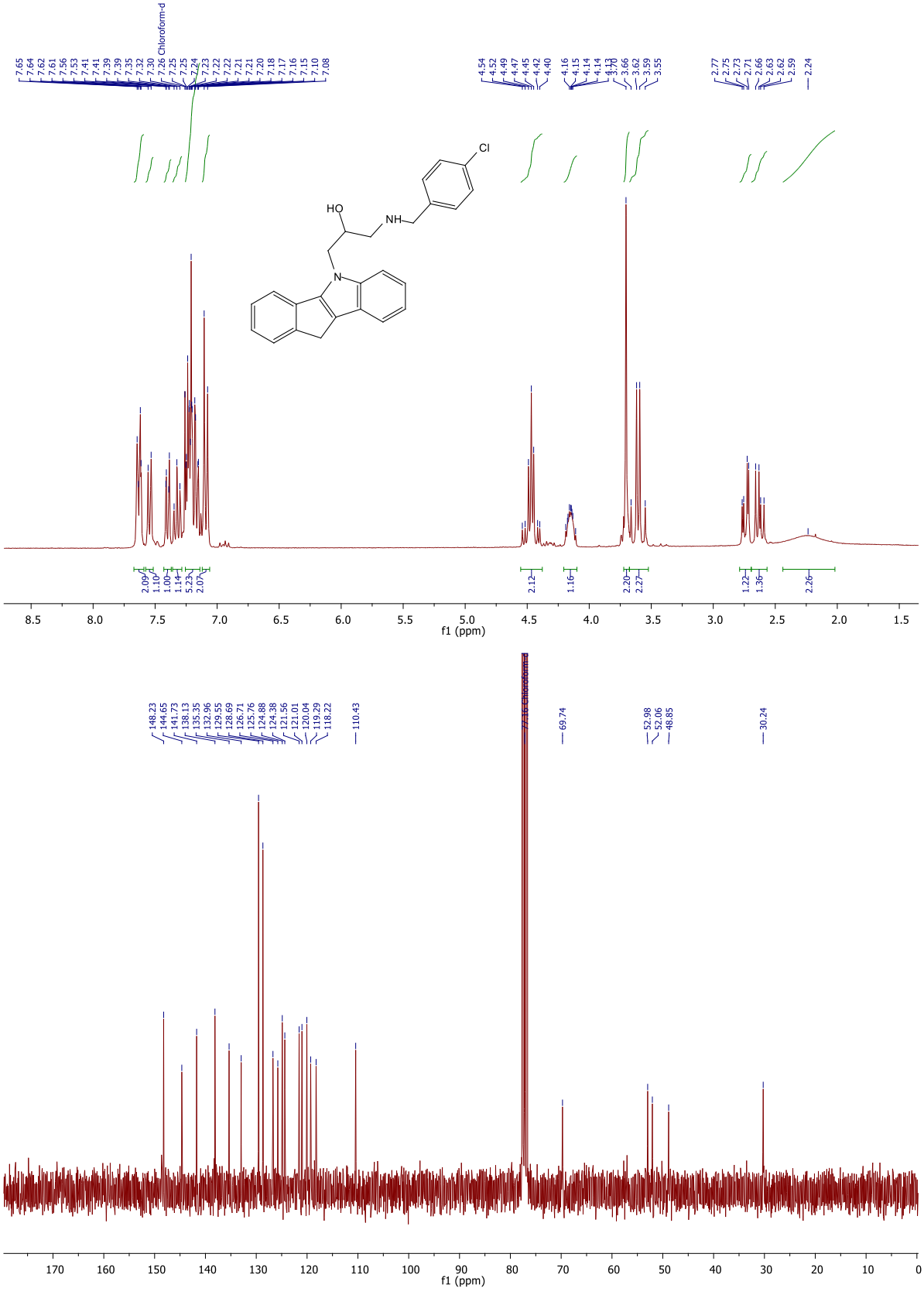




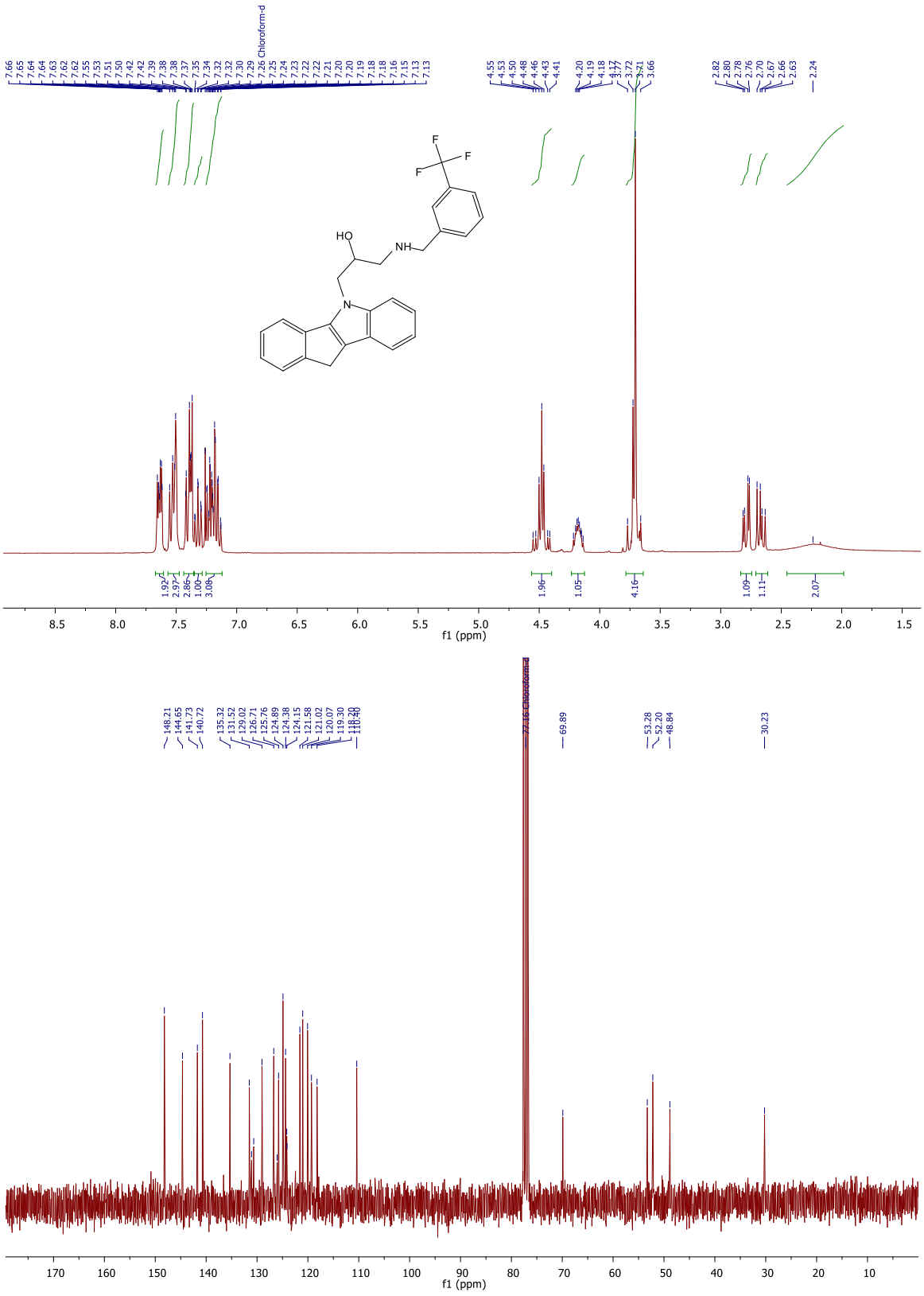
5. ^{1}H and ^{13}C NMR spectra of **8**



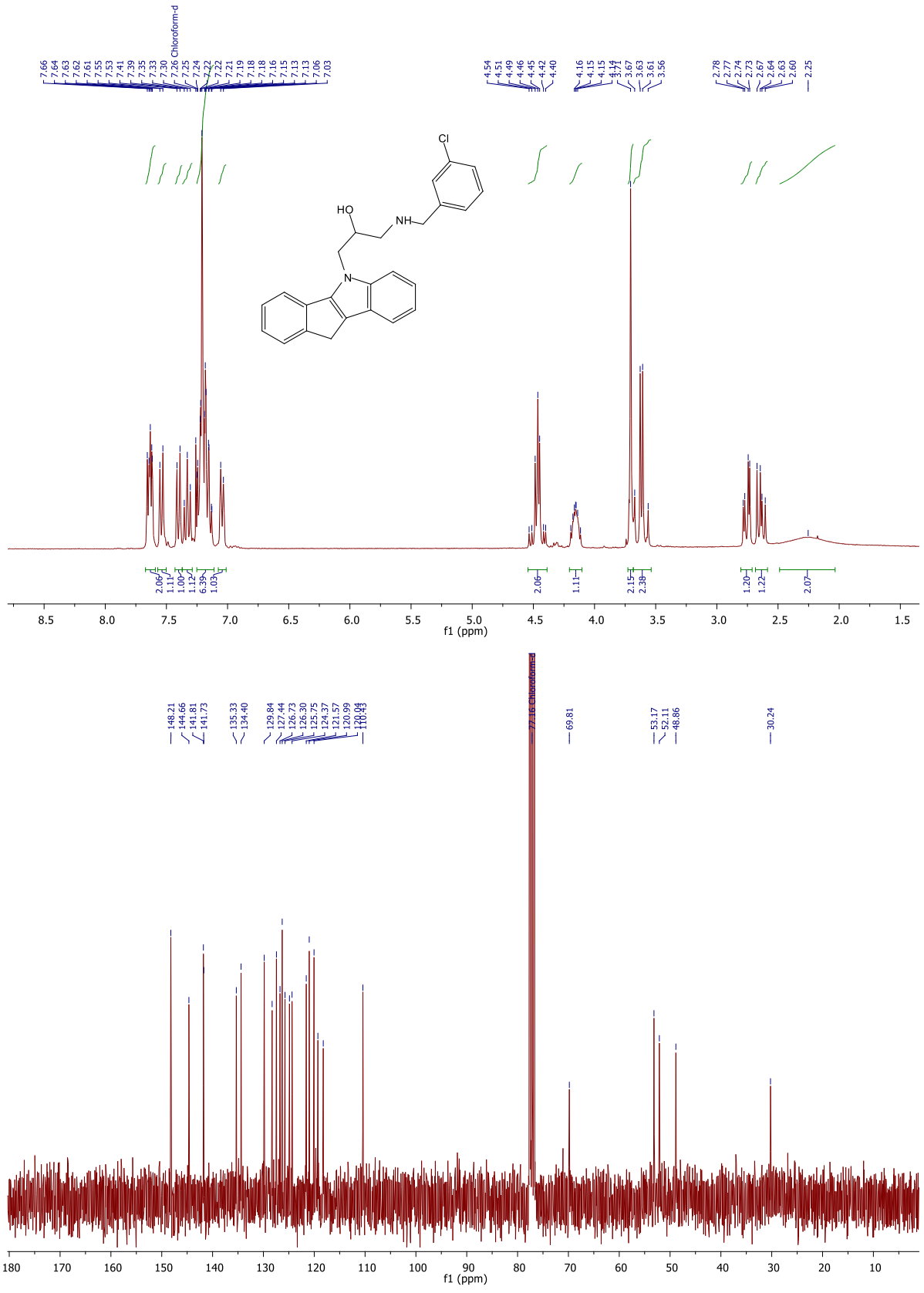
6. ^{1}H and ^{13}C NMR spectra of **9**



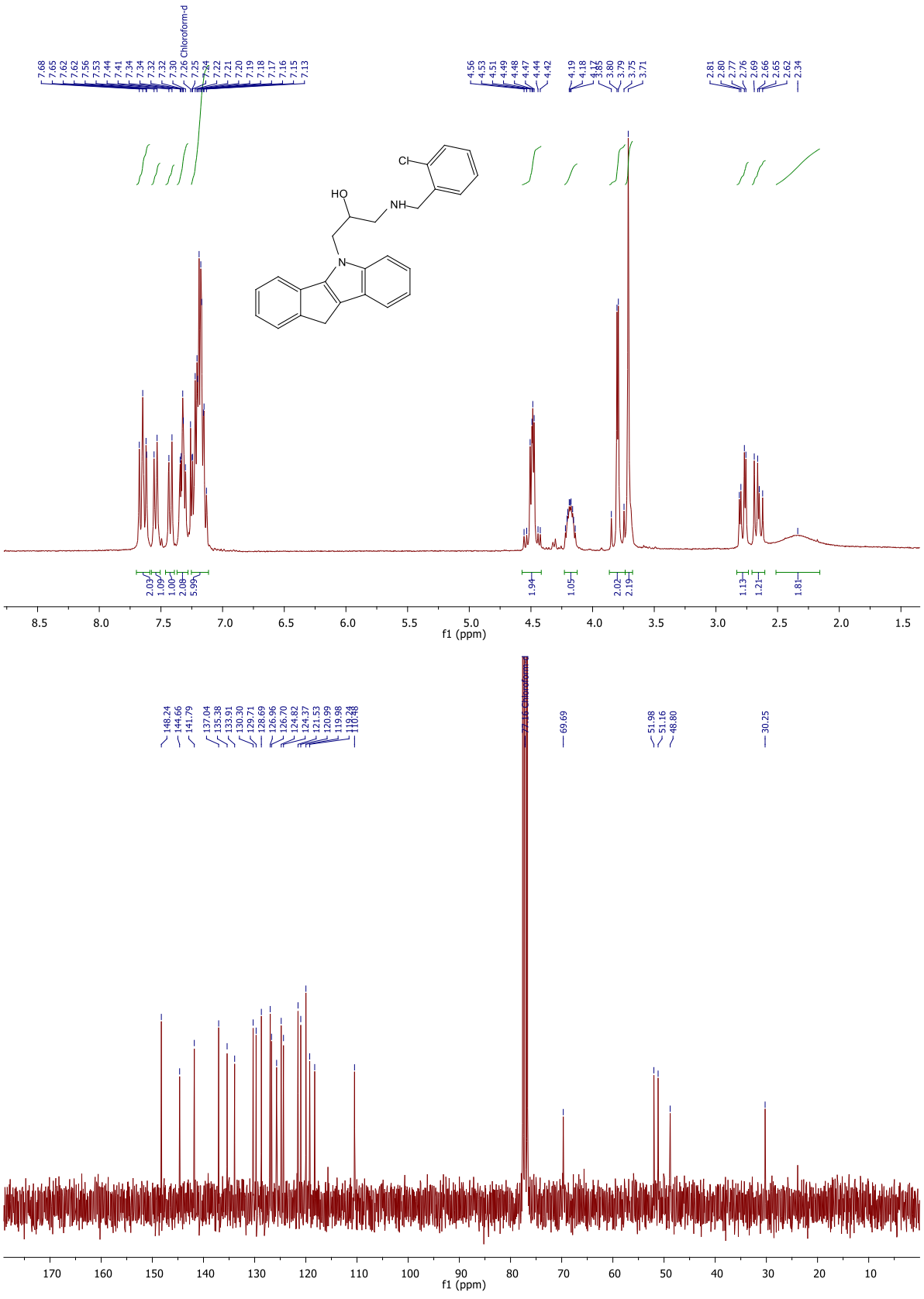
7. ^{1}H and ^{13}C NMR spectra of **10**



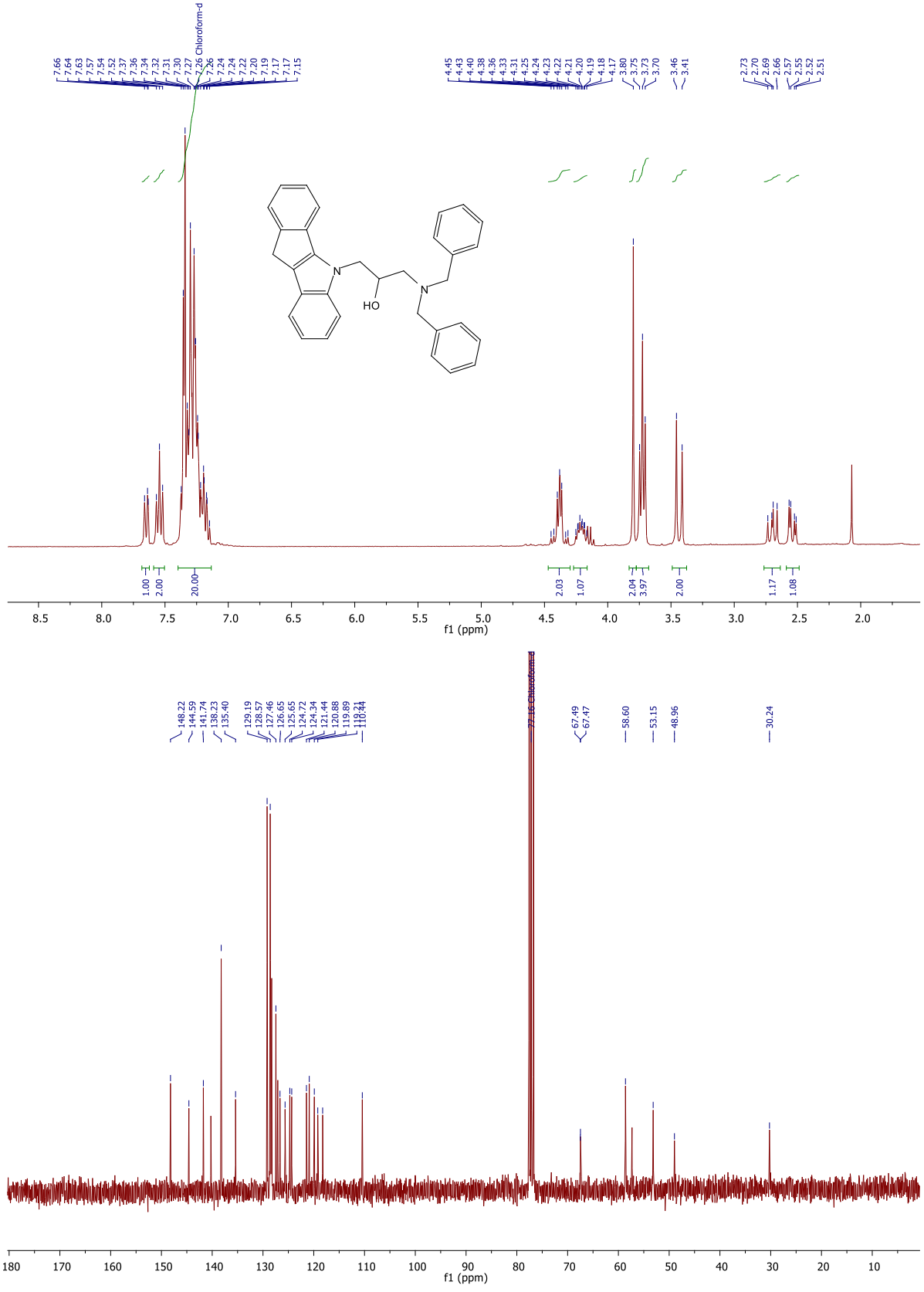
8. ^{1}H and ^{13}C NMR spectra of **11**



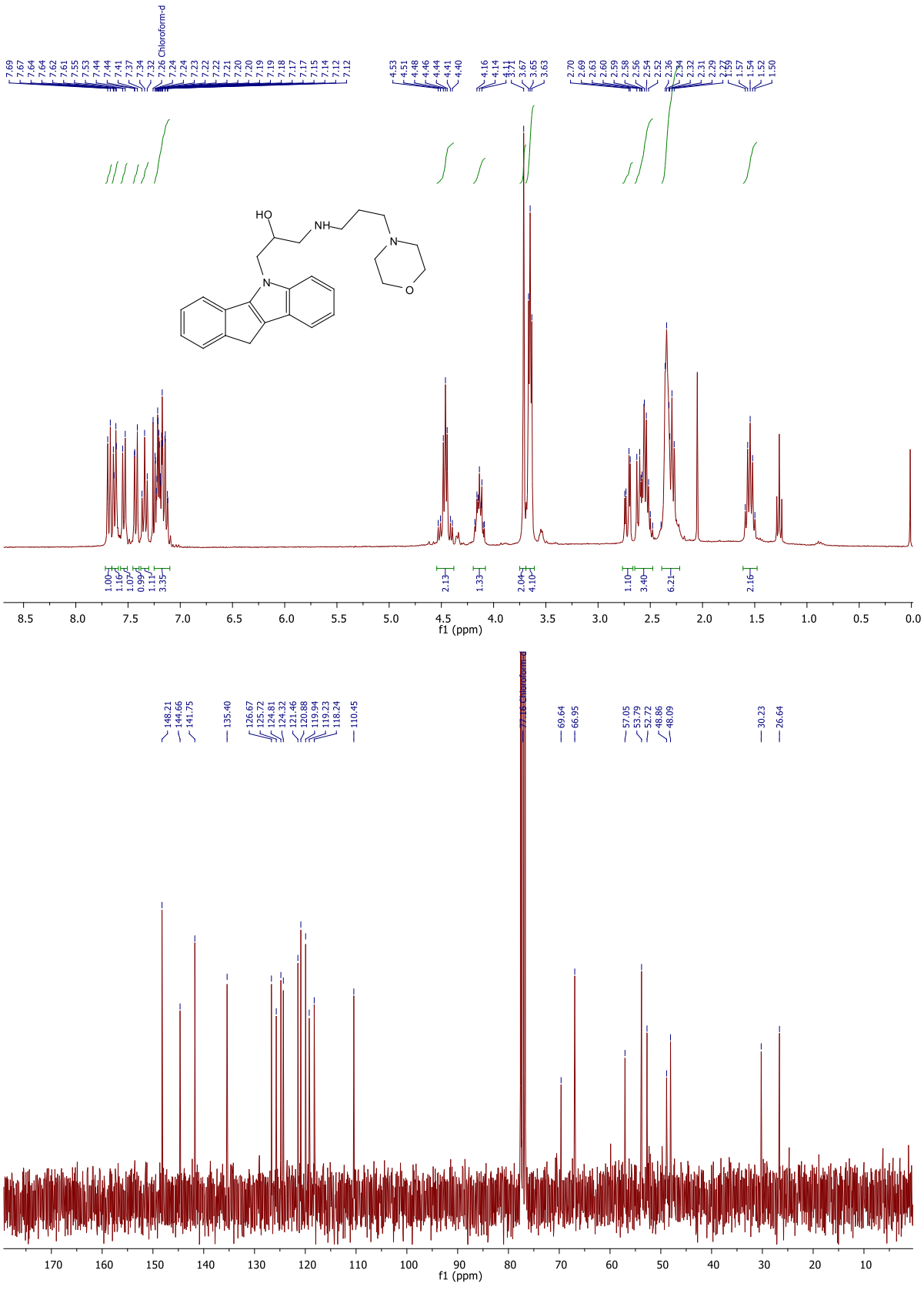
9. ^{1}H and ^{13}C NMR spectra of **12**



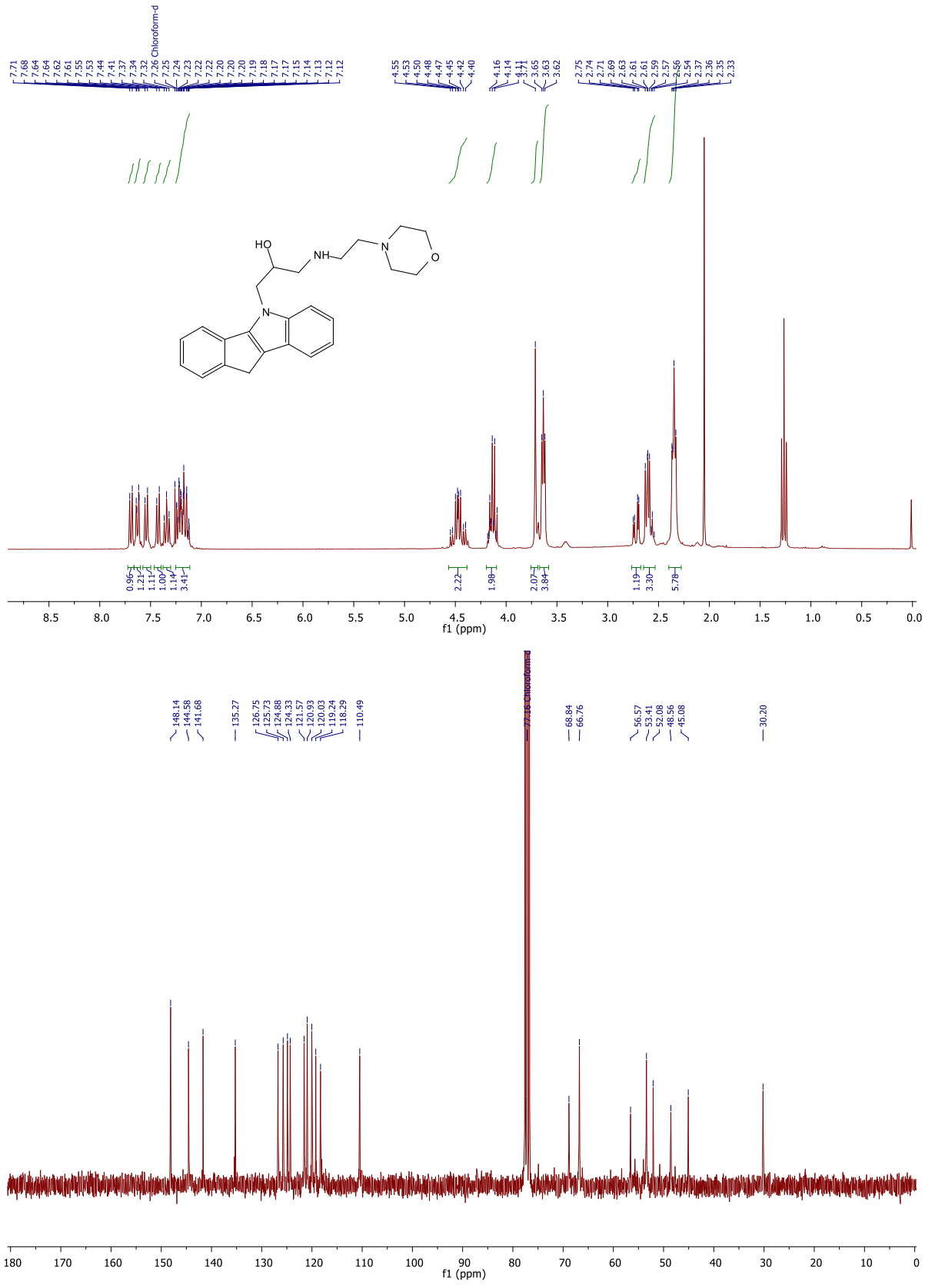
10. ^{1}H and ^{13}C NMR spectra of **13**



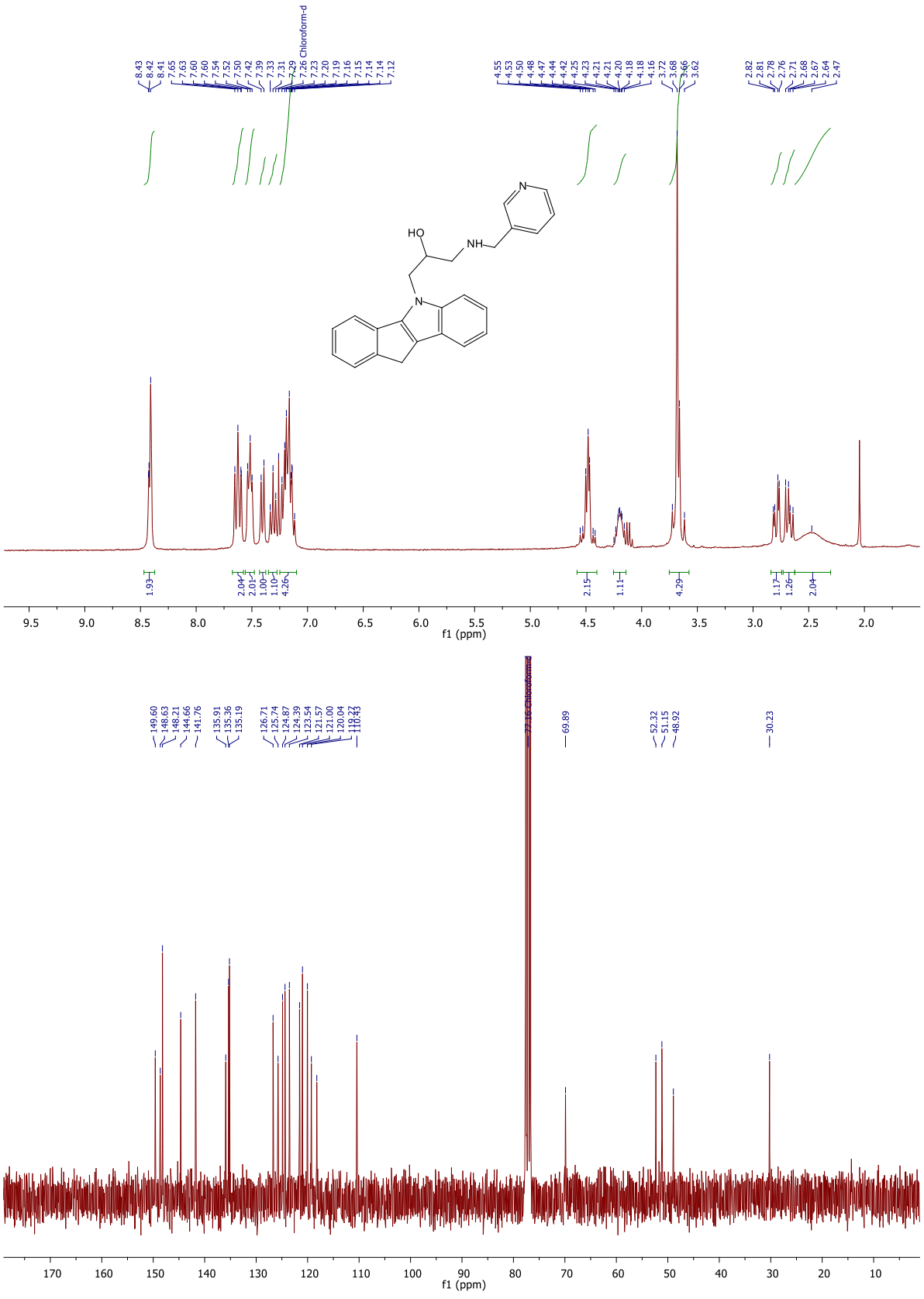
11. ^{1}H and ^{13}C NMR spectra of **14**



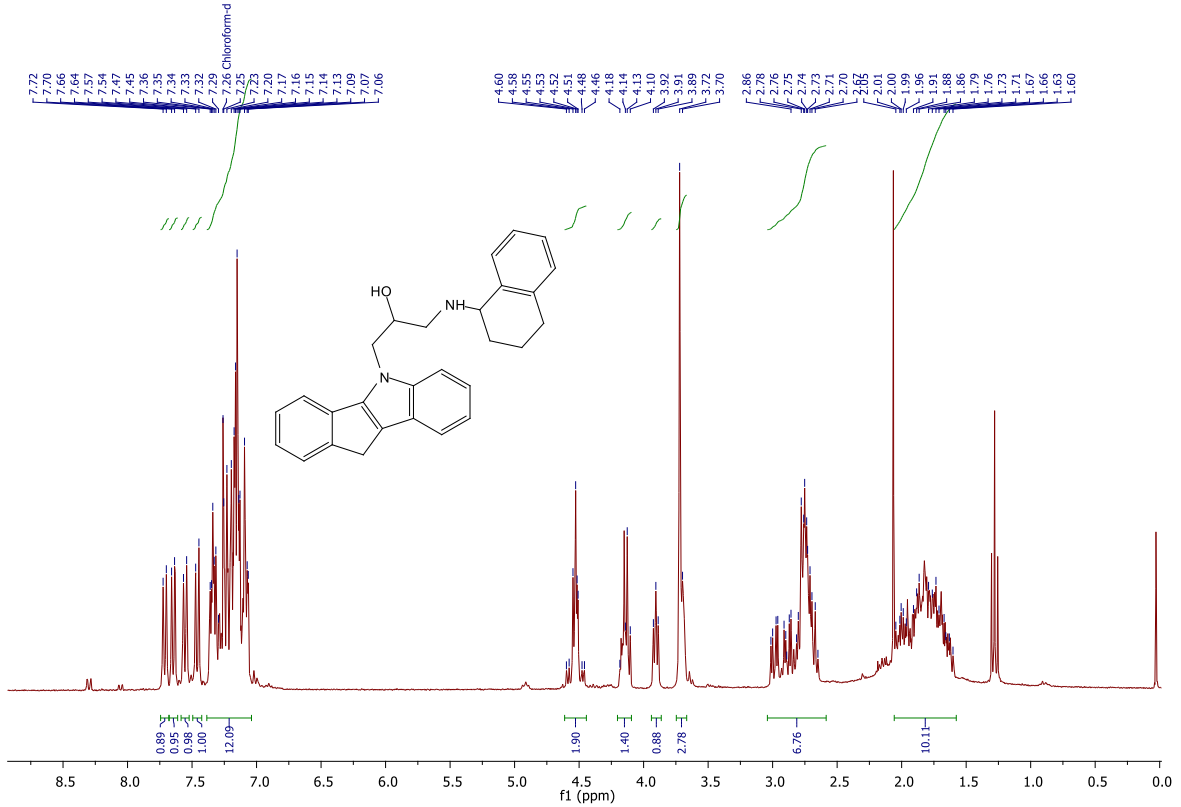
12. ^{1}H and ^{13}C NMR spectra of **15**

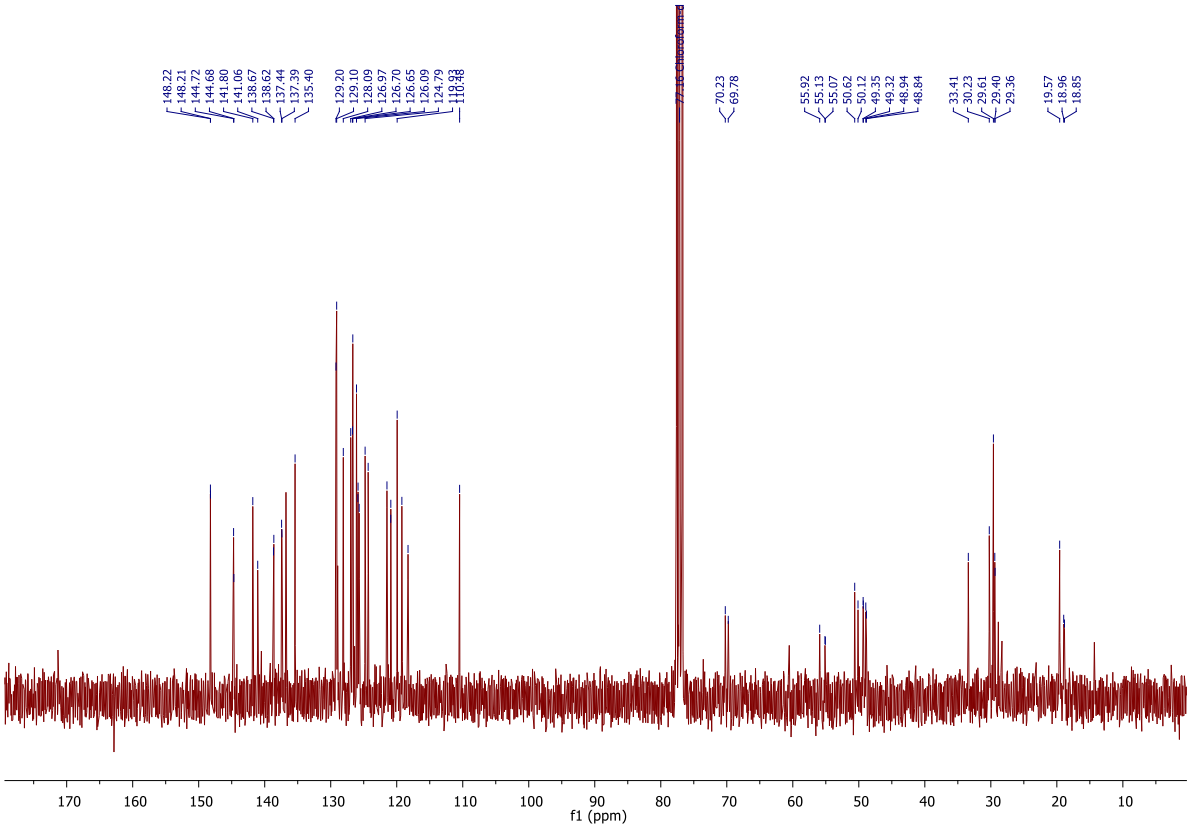


13. ^{1}H and ^{13}C NMR spectra of **16**

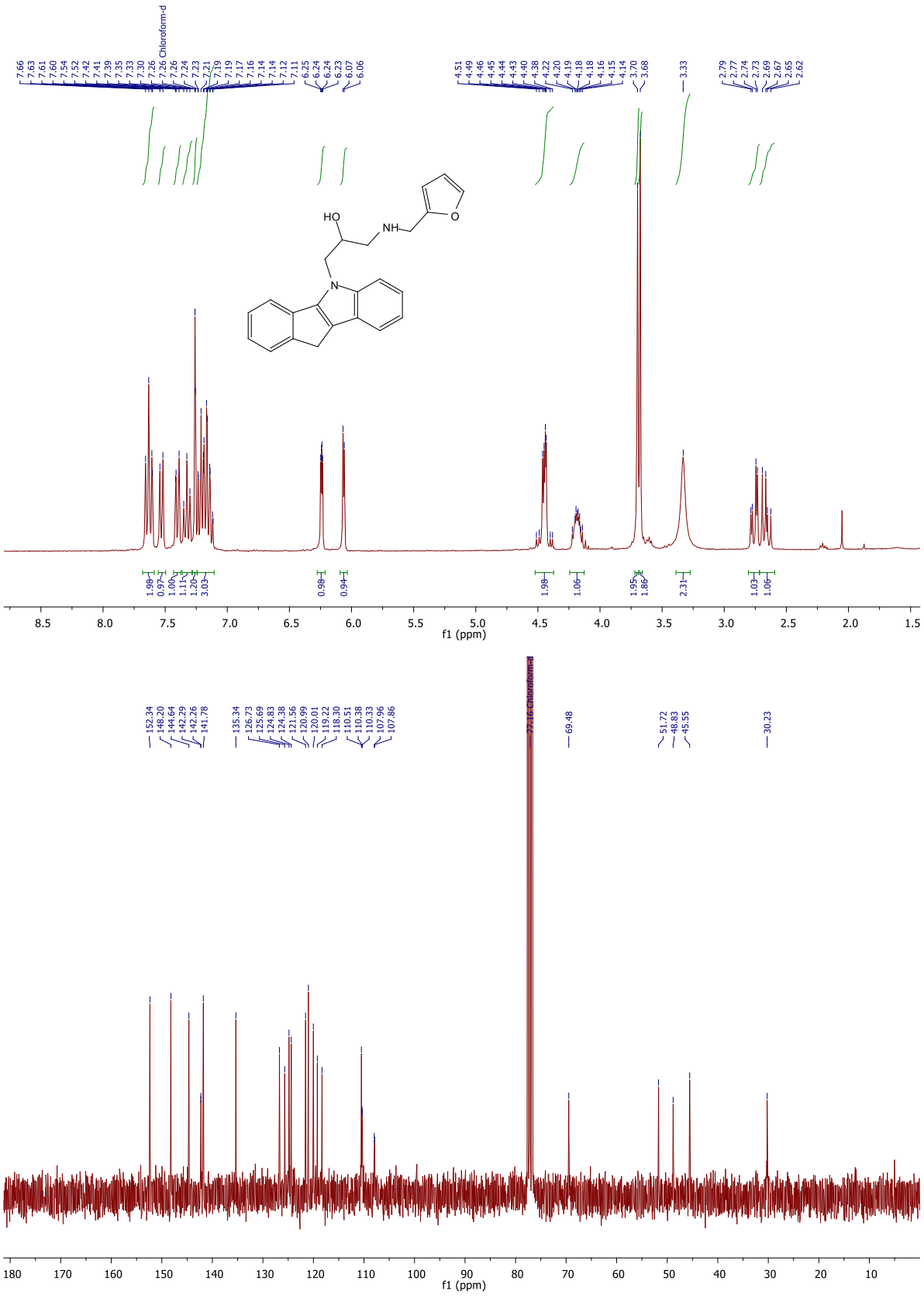


14. ^{1}H and ^{13}C NMR spectra of **17**

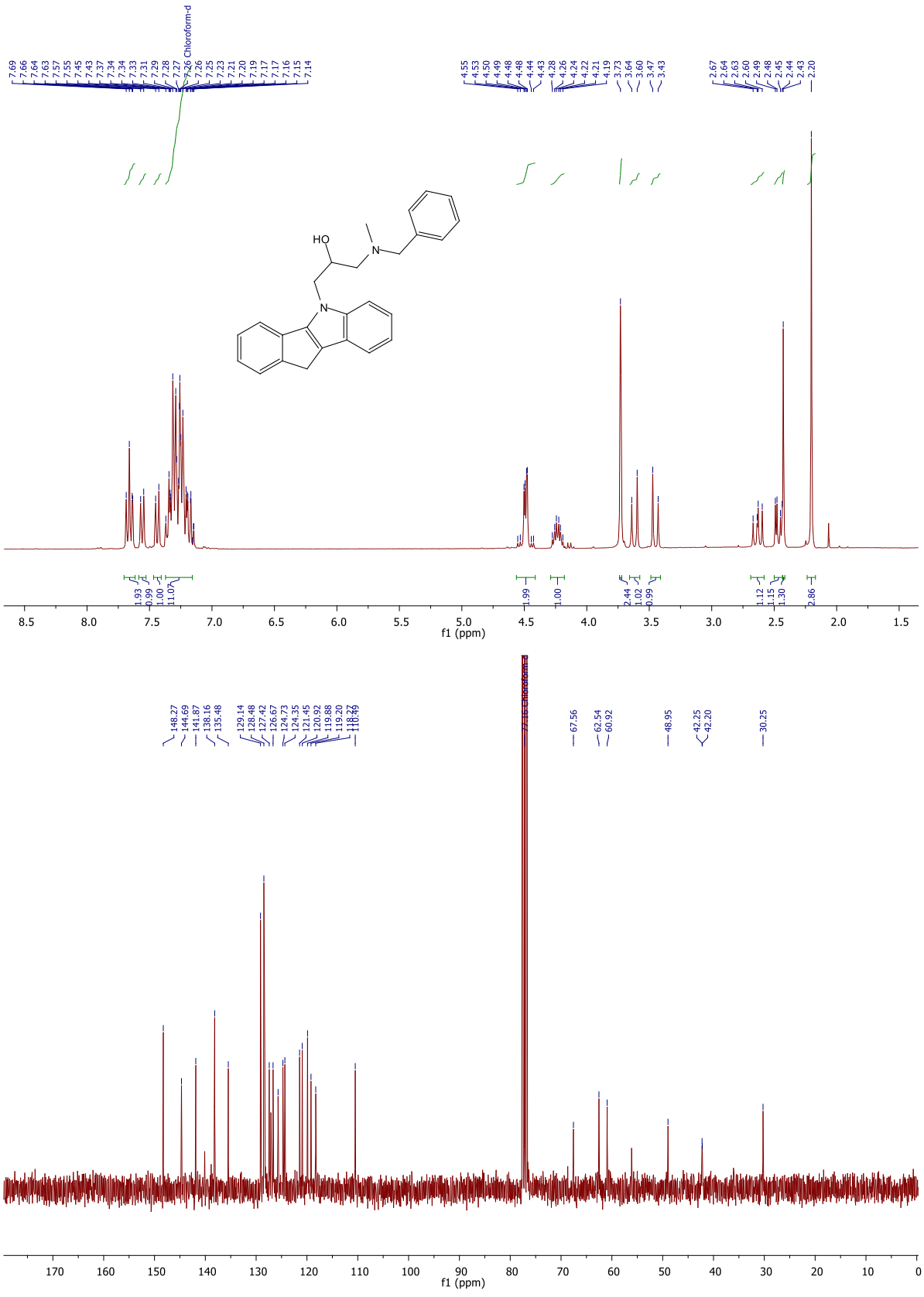




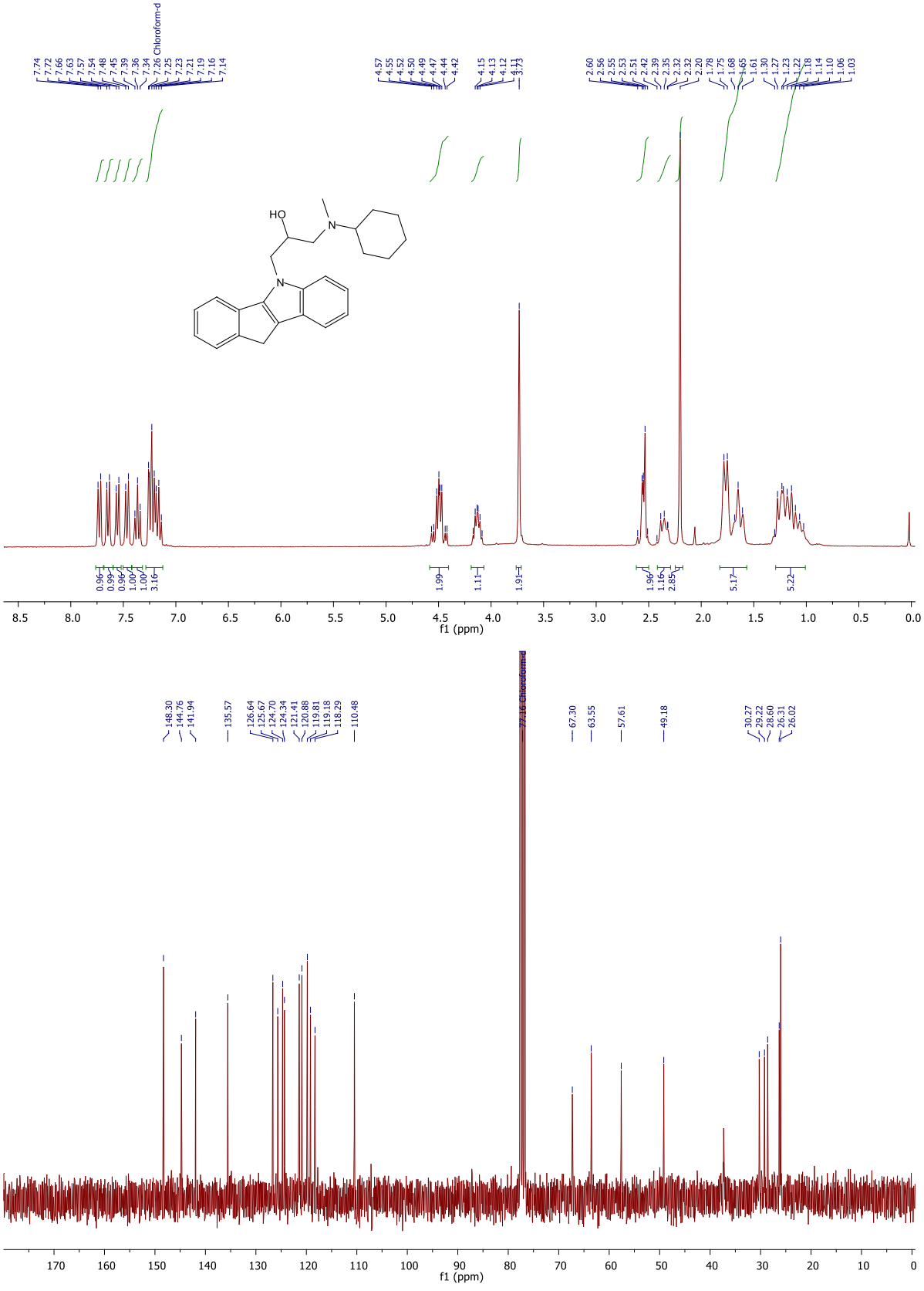
15. ^{1}H and ^{13}C NMR spectra of **18**



16. ^{1}H and ^{13}C NMR spectra of **19**



17. ^{1}H and ^{13}C NMR spectra of **20**



18. pKa prediction

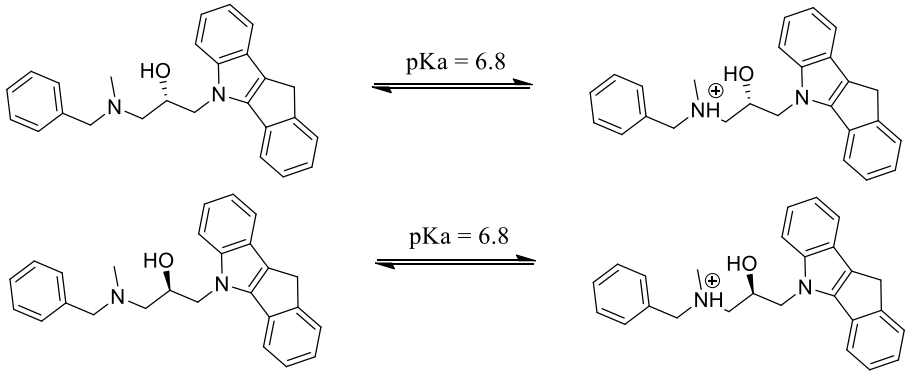


Figure S1. pK_a of selected atoms for enantiomers of compound **19**.

19. Following PDB protein crystal structures were utilised for ensemble docking:
1W51, 1XS7, 2F3E, 2F3F, 2QZK, 3CIC, 3DV1, 3DV5, 3K5C, 4K8S, 4KE0

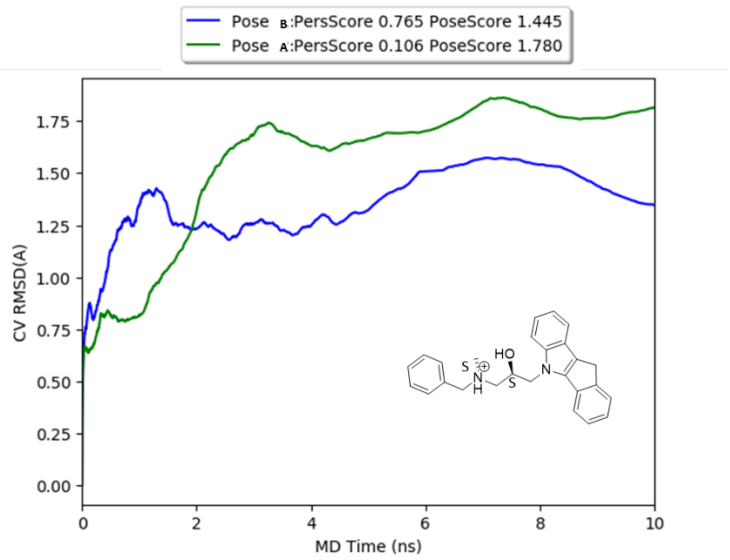


Figure S2. Binding pose metadynamics pose **19** (S,S). A plot of the ligands RMSD averaged over the course of the 7 metadynamic simulation, with each simulation being 10 ns.

20.

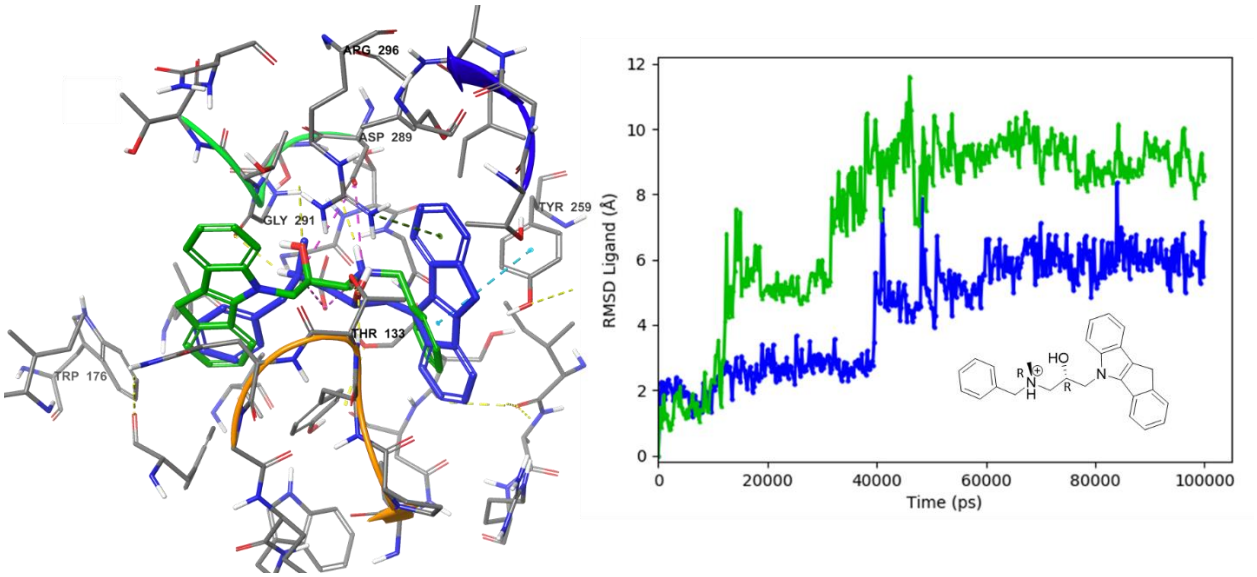


Figure S3. Overlaid docking poses of the two suggesting binding poses of an enantiomer of **19** (*R*,*R*), Pose A (blue) and pose B (green). A plot of the ligands RMSD during the course of the 100 ns MD simulation is shown for pose A and pose B in blue and green, respectively. The ligand RMSD indicates how stable the ligand is with respect to the protein's backbone.

21.

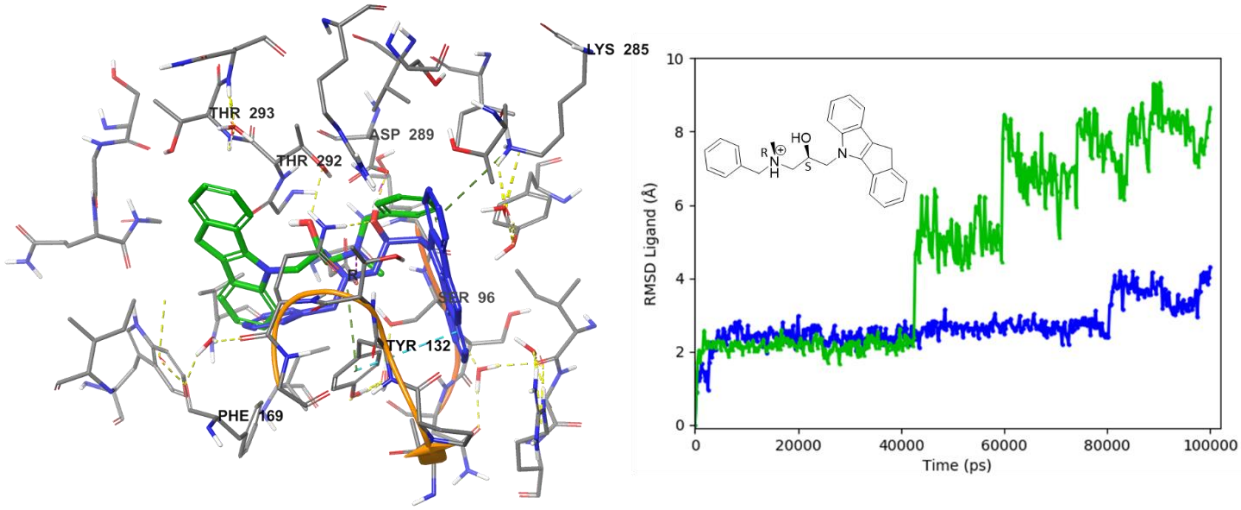
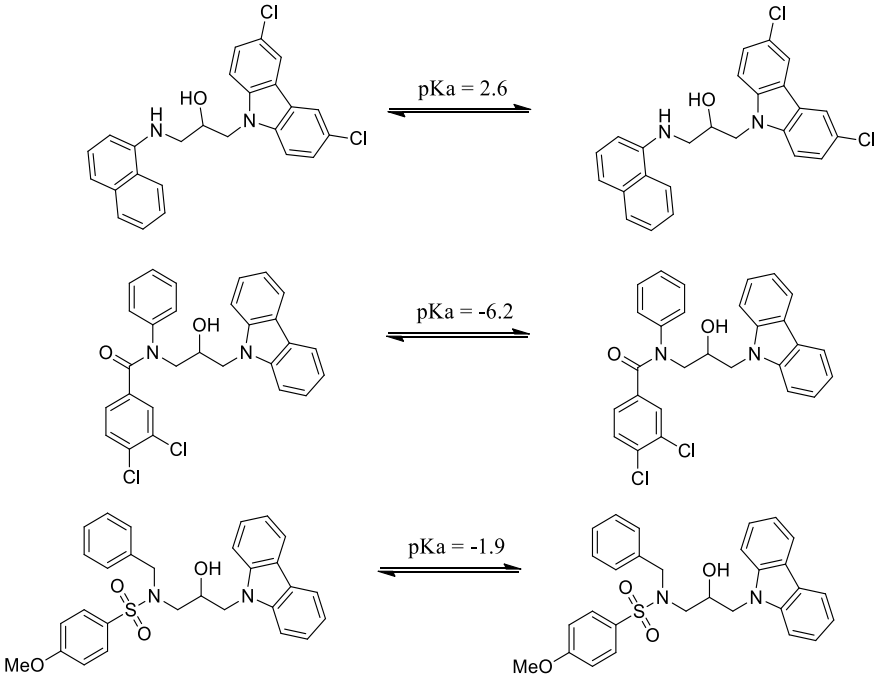


Figure S4. Overlaid docking poses of the two suggesting binding poses of an enantiomer of **19** (*R*,*S*), Pose A (blue) and pose B (green). A plot of the ligands RMSD during the course of the 100 ns MD simulation is shown for pose A and pose B in blue and green, respectively. The ligand RMSD indicates how stable the ligand is with respect to the protein's backbone.

22. pK_a of selected atoms for **1**, **2** and **3** from the Jaguar pKa protocol



24. ROC Curve of DUD-E trained RTF model for BACE1

25.