

Supplementary Material

Design, synthesis and characterization of novel gamma-aminobutyric acid type A receptor ligands

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1. Figure S1. Showing halogen bond interactions

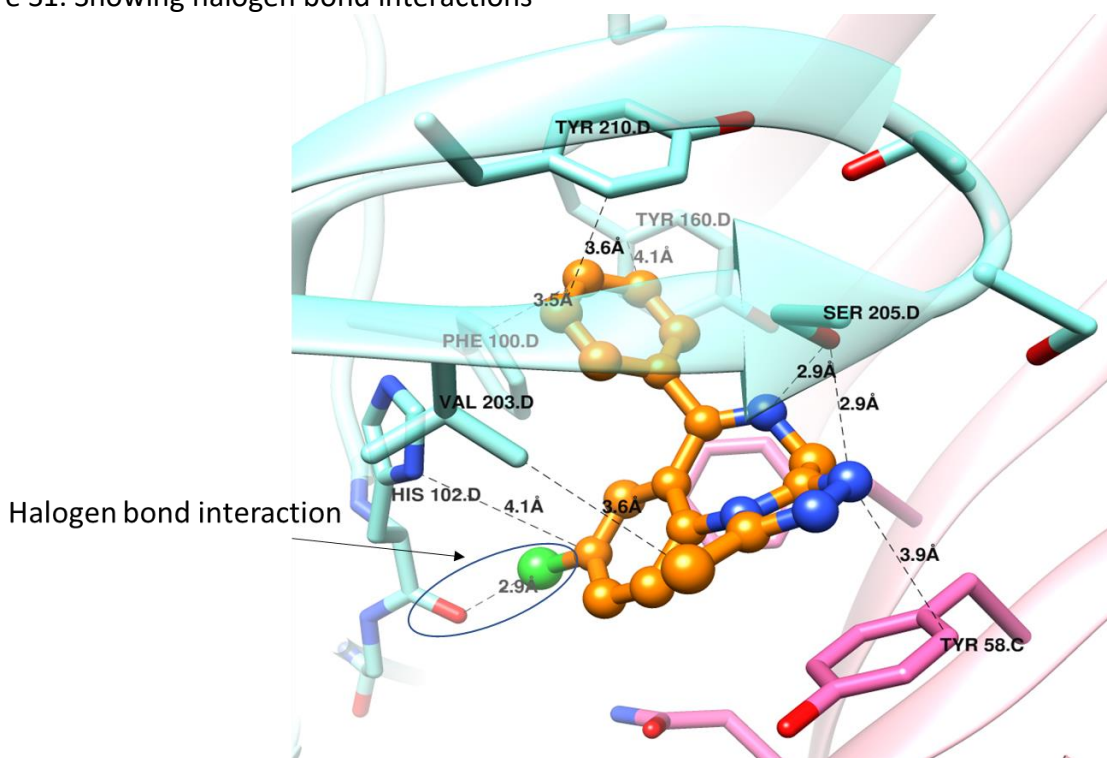


Figure S1. Showing halogen bond interaction in complex of alprazolam (orange) with $\alpha 1\beta 3\gamma 2L$ GABA_A receptor (PDB: 6HUO) at $\alpha 1\gamma 2$ interface benzodiazepine binding site [$\alpha 1$ (represented as chain D, color: aquamarine) and $\gamma 2$ (represented as chain C, color: orchid)], dashed lines indicate halogen and hydrogen bonds.

2. Method of molecular docking: The Ligand-protein interactions were analyzed by molecular docking using AutoDock Vina 1.5.6. The PDB file of the CryoEM structure of the human full-length $\alpha 1\beta 3\gamma 2L$ GABA_A receptor in the complex with alprazolam (6HUO) was downloaded from the Protein Data Bank and was prepared for docking by fixing missing bonds or atoms, adding polar hydrogens and assigning charges by AM1-BCC, and removing water molecules. The proteins were validated by first removing the bound ligand (alprazolam) and this was followed by docking it in the same binding site. The compounds were drawn, and energy minimized in Chimera.¹ A grid size of 17 Å x 17 Å x 17 Å and centered at coordinates 152.80 (x), 163.02 (y), and 161.14 (z) were used. Illustrations of the 3D models were generated using Chimera and Python.¹⁻² The dockings were performed with standard search parameters and poses with the best scores were selected for the analysis.

3. Chiral HPLC analysis report of the racemic mixture of oxazolines **5c** and **5d** (10 % EtOH in Hexane)

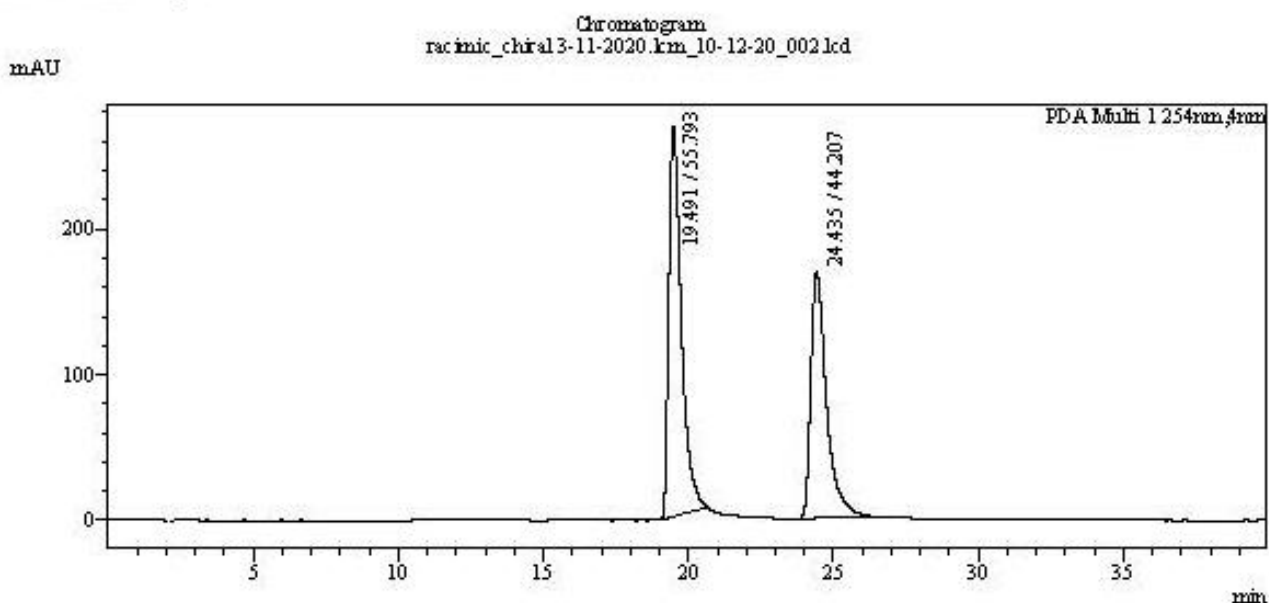
Analysis Report

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 Sample ID :
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 Batch Filename : 10-12-20.lcb
 Vial # : Vial 2
 Injection Volume : 5 uL
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Sample Type : Unknown
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 Acquired by : Kamal Pandey
 Processed by : Kamal Pandey

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<Peak Table>

racimic_chiral 3-11-2020.lcm_10-12-20_002.lcd

(3D)DAD Ch1 254nm

| Peak# | Ret. Time | Area% |
|-------|-----------|---------|
| 1 | 19.491 | 55.793 |
| 2 | 24.435 | 44.207 |
| Total | | 100.000 |

4. Chiral HPLC analysis report of oxazoline **5c** (KPP-III-96B in 10 % EtOH in Hexane)

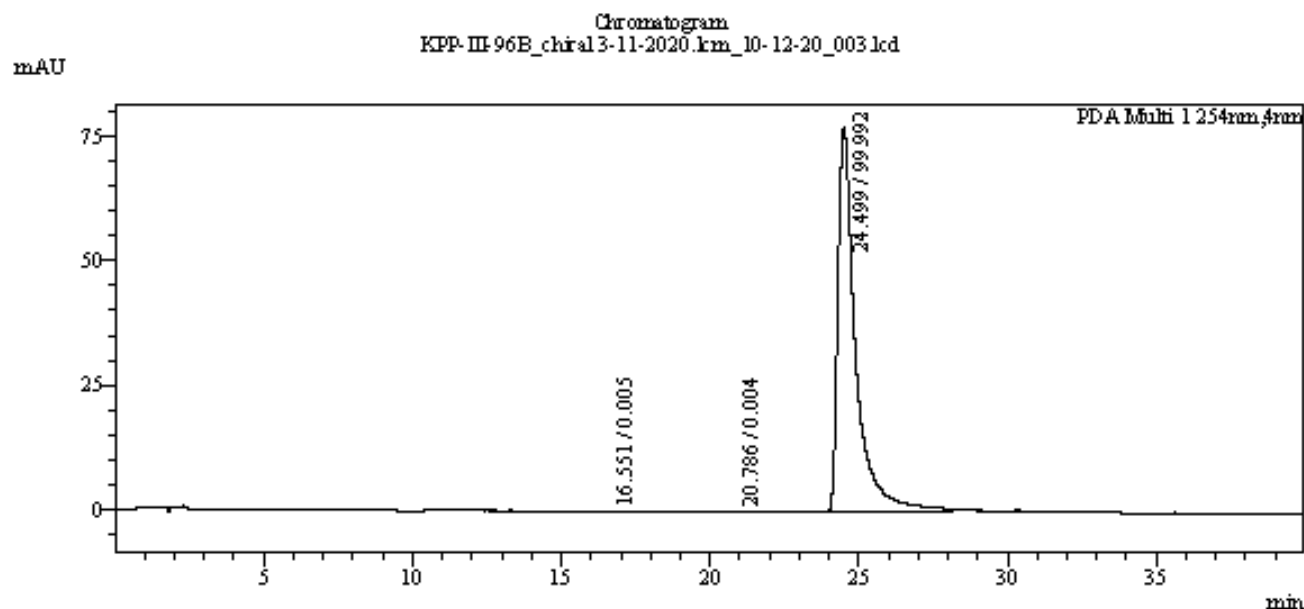
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(3D)DAD Ch1 254nm

| Peak# | Ret. Time | Area% |
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| 2 | 20.786 | 0.004 |
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| Total | | 100.000 |

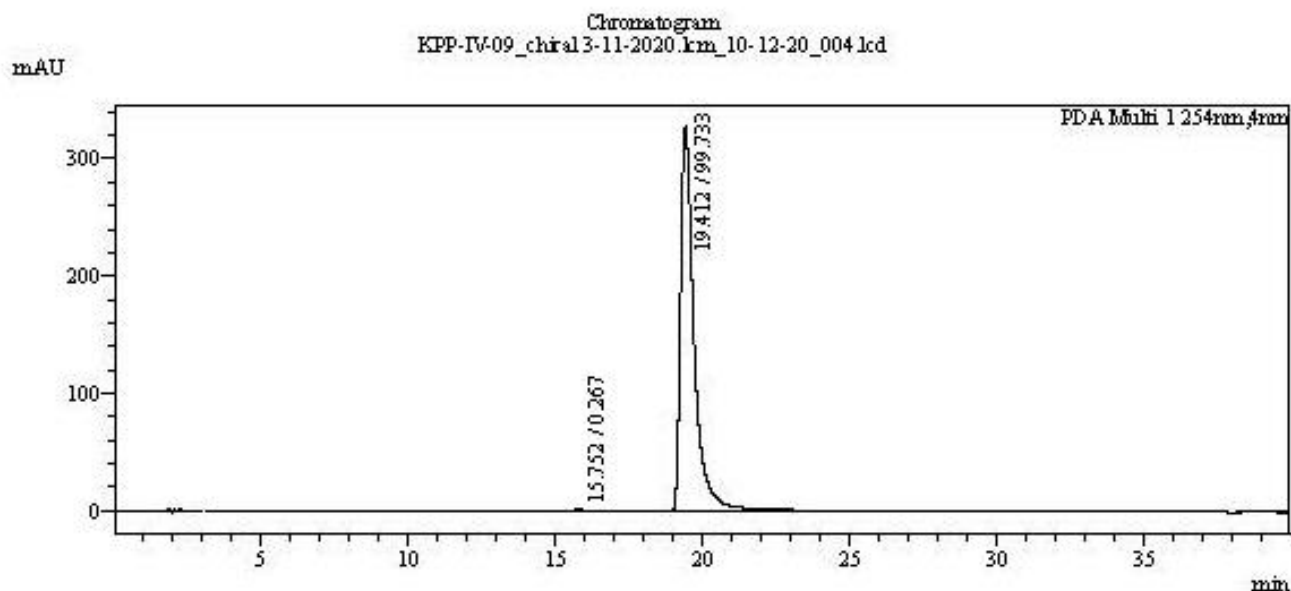
5. Chiral HPLC analysis report of oxazoline **5d** (KPP-IV-09 in 10 % EtOH in Hexane)

Analysis Report

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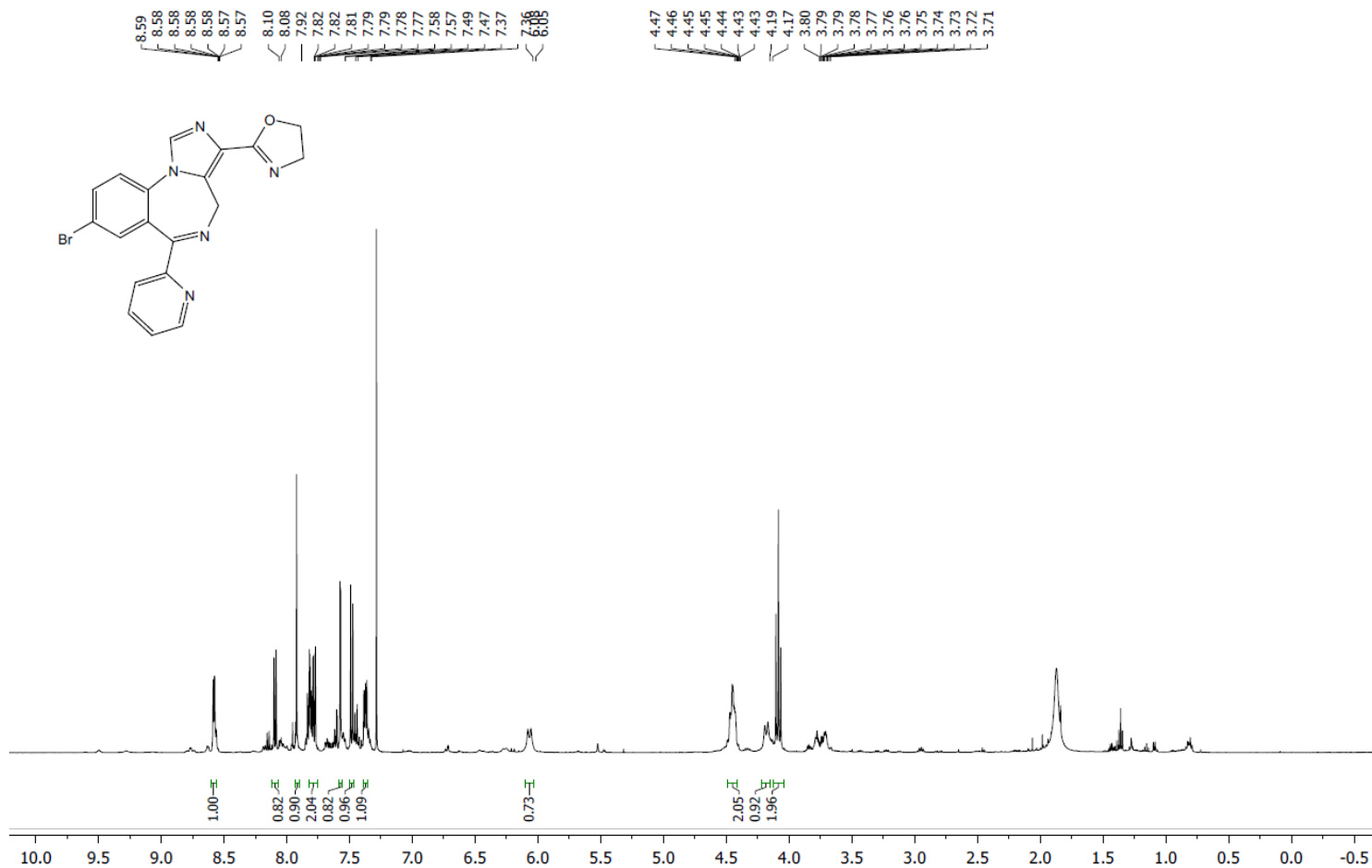


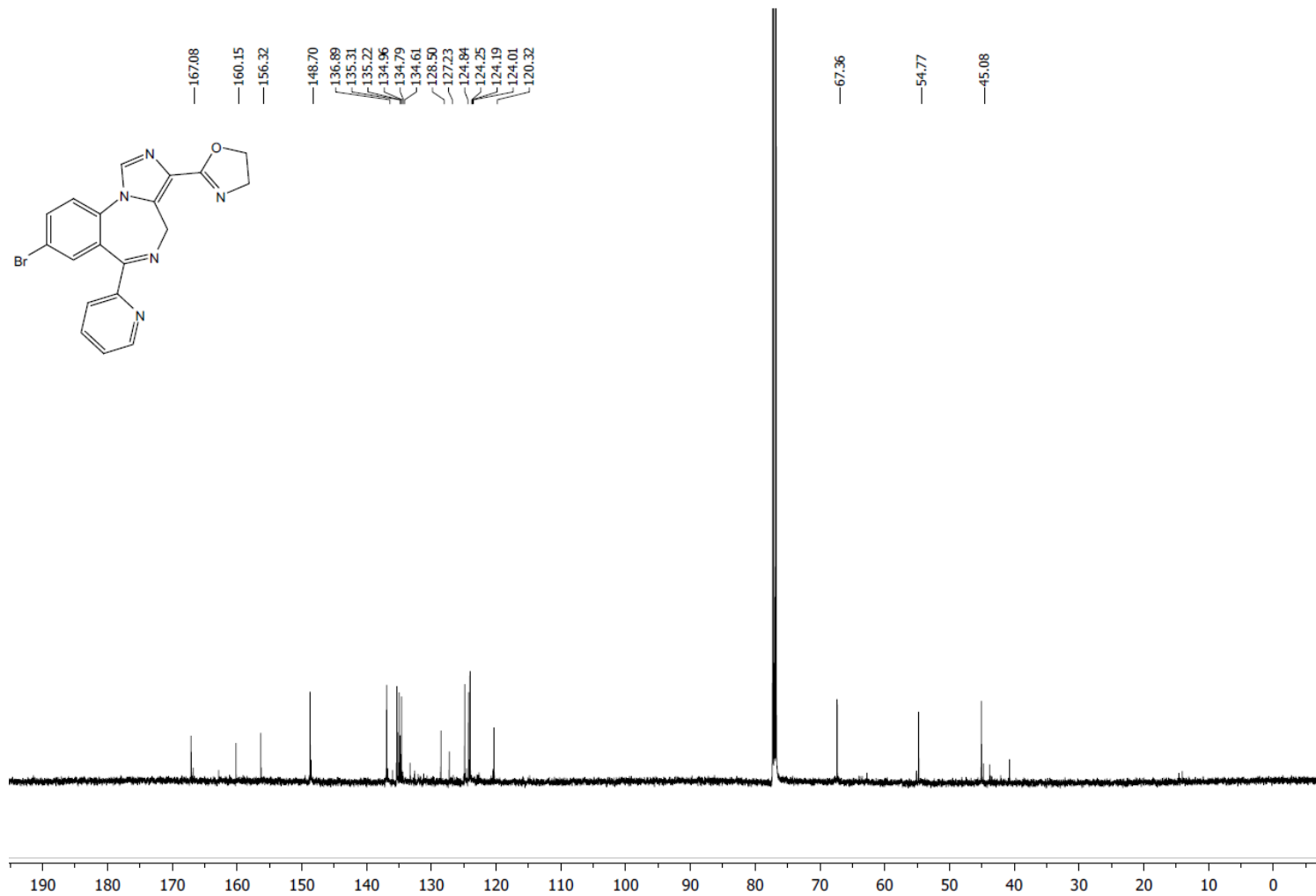
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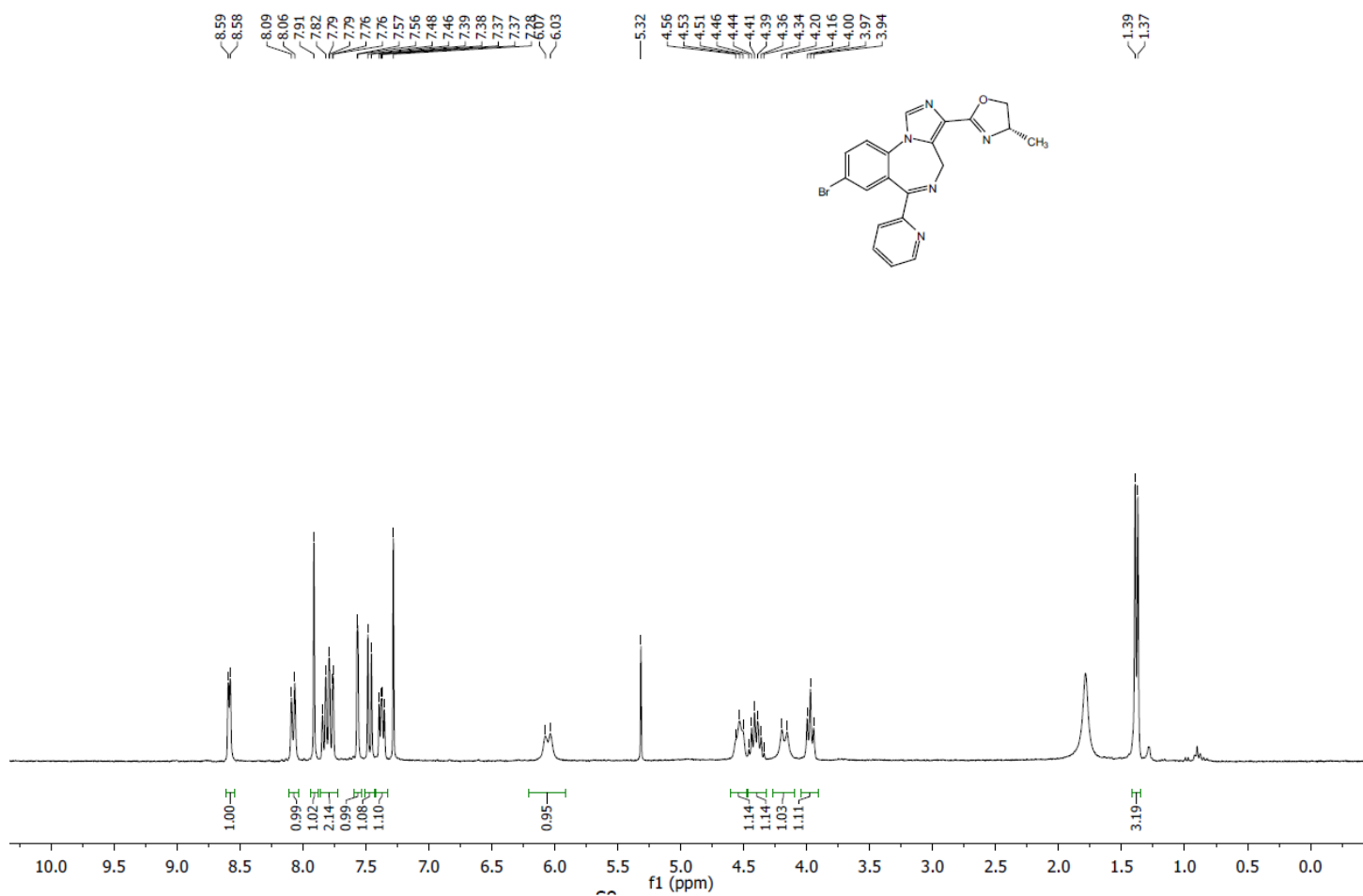
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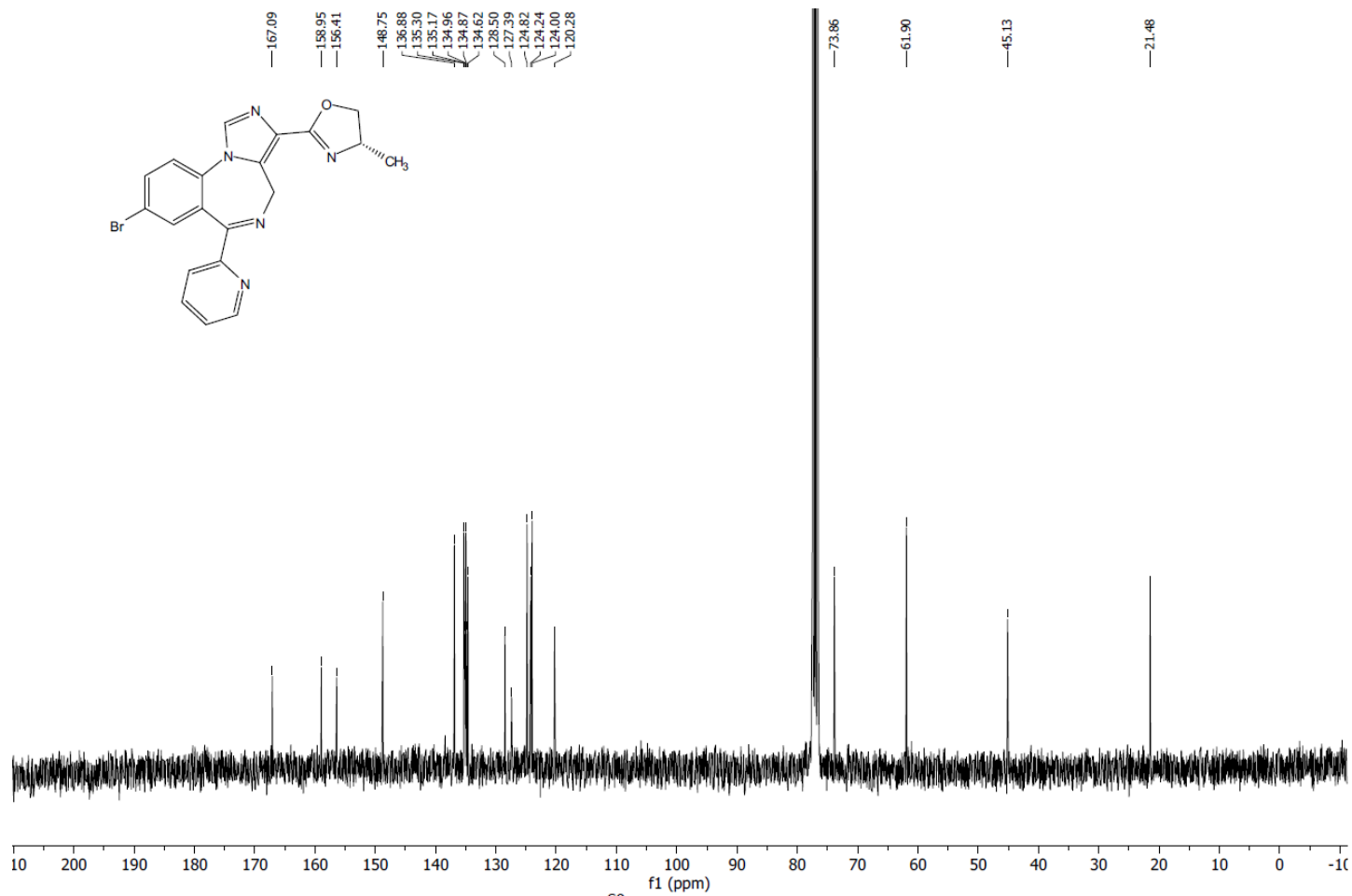
(3D)DAD Ch1 254nm

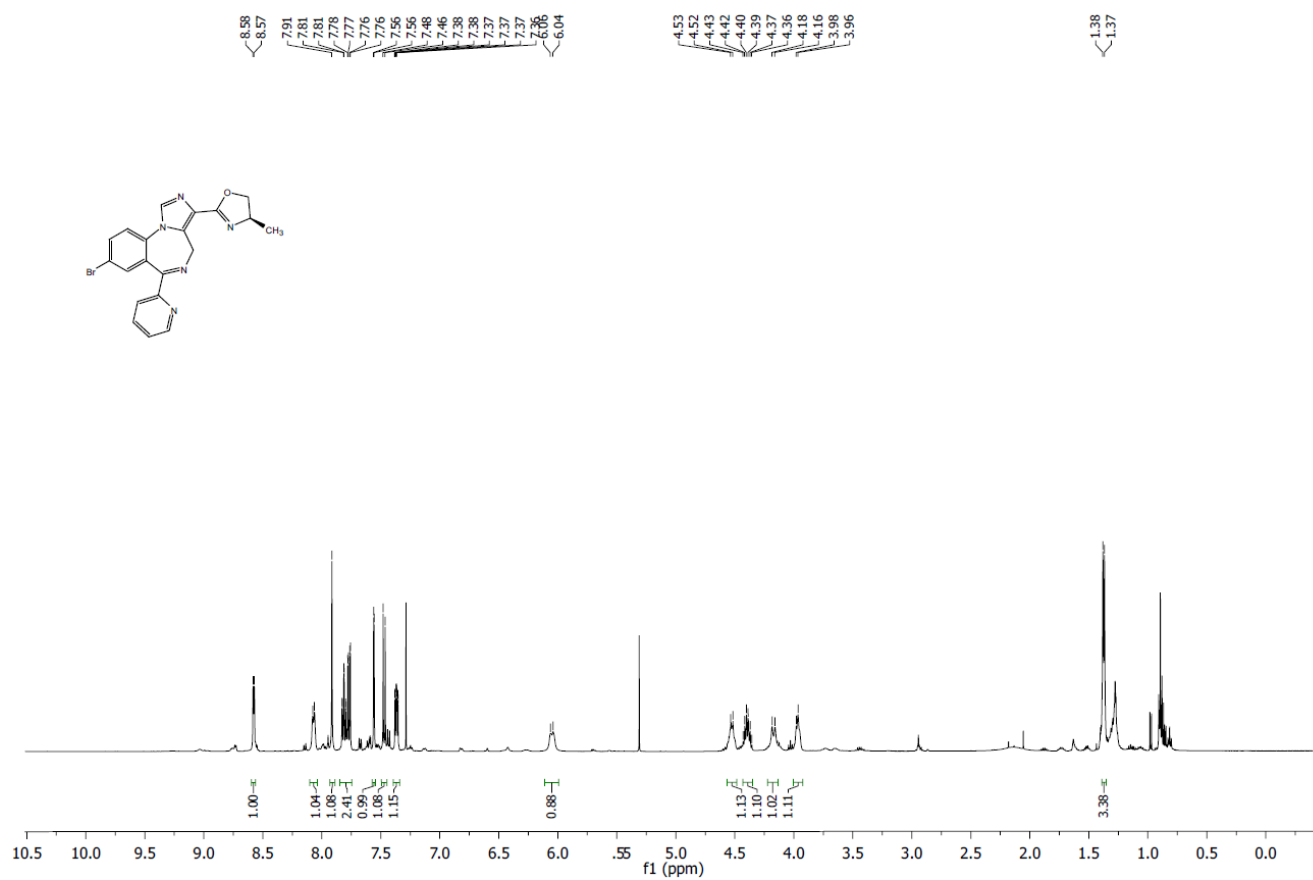
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| Total | | 100.000 |

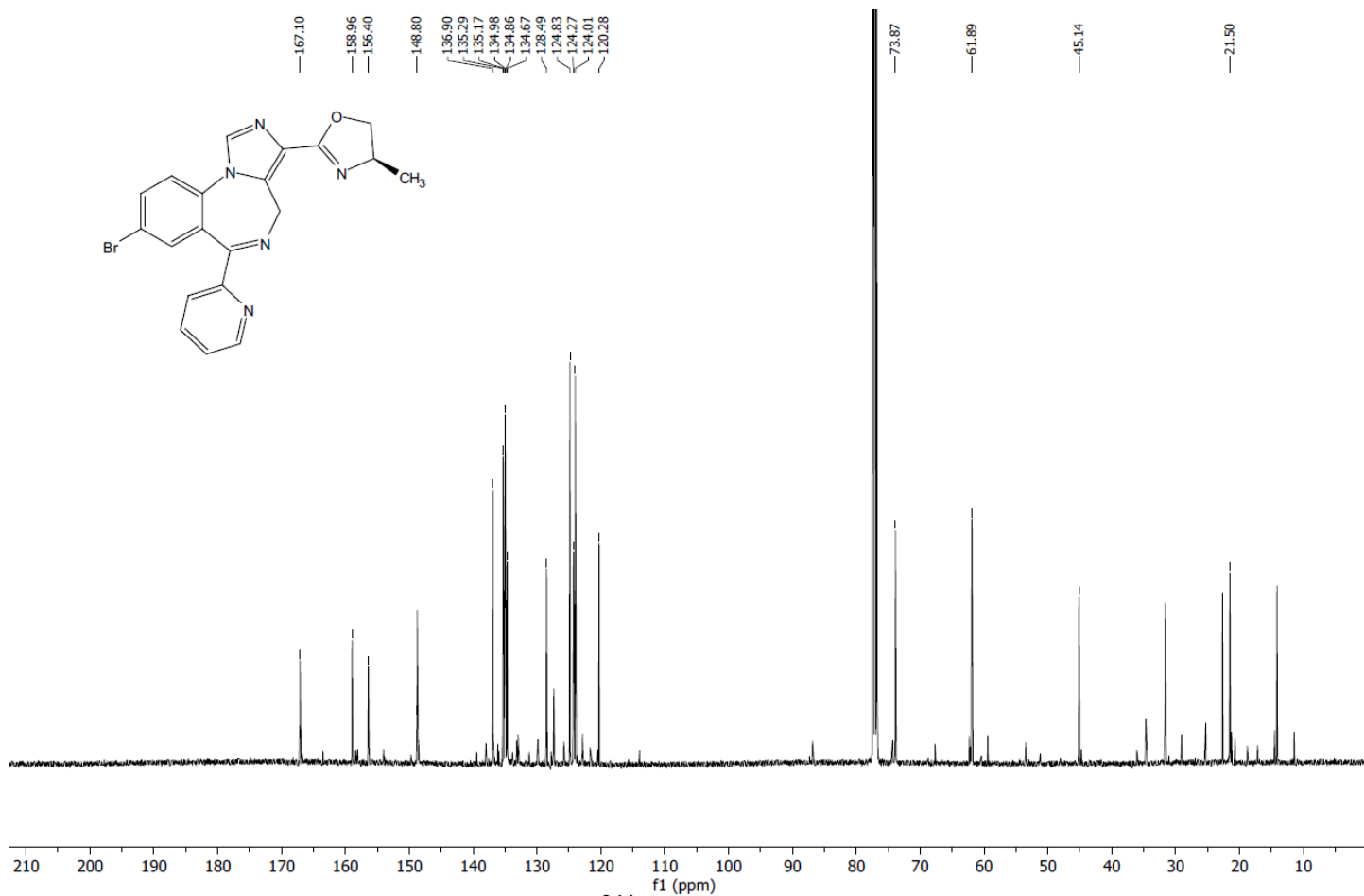
6. ^1H NMR of oxazoline 5 (CDCl₃)

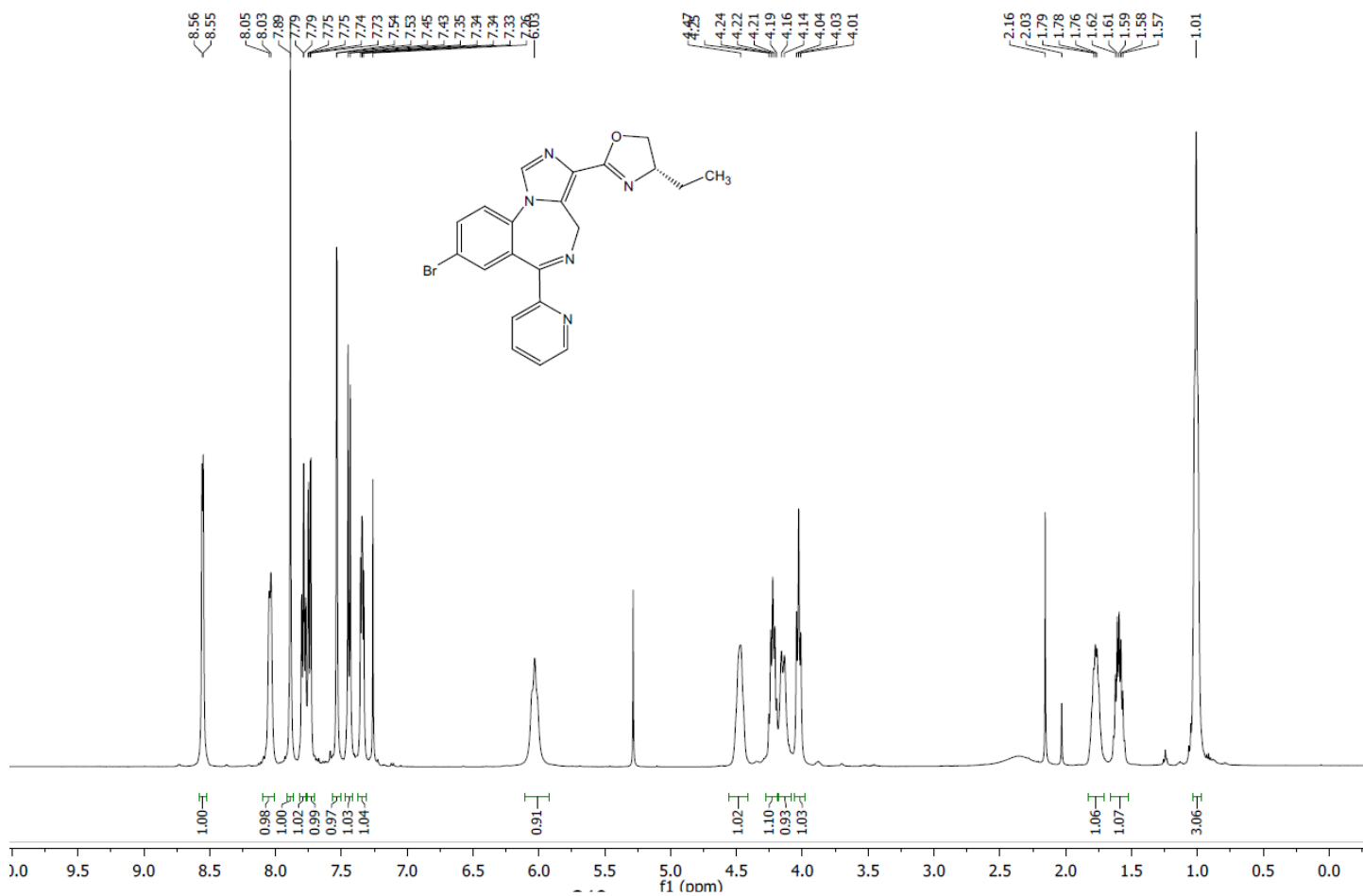
7. ^{13}C NMR of oxazoline 5 (CDCl_3)

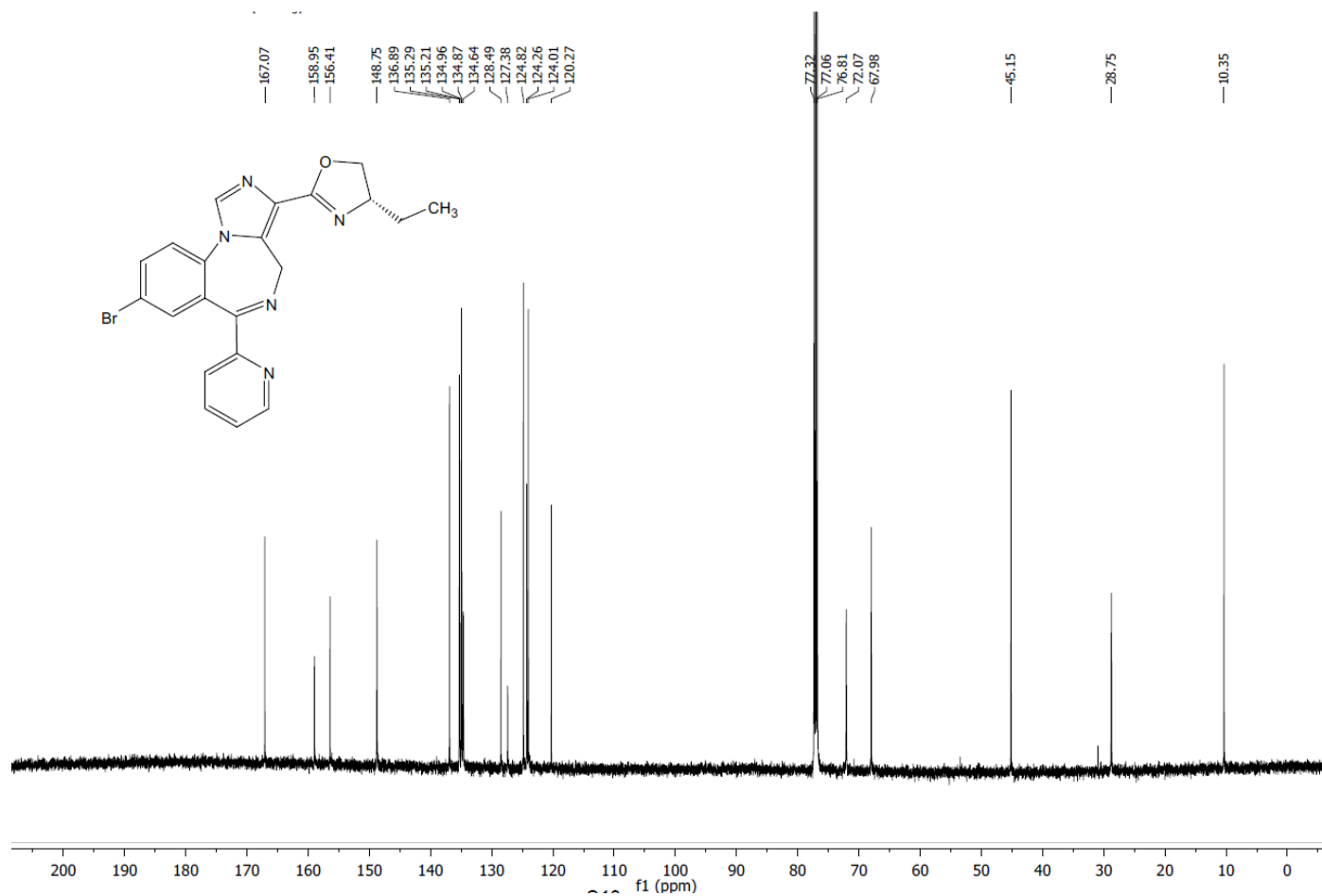
8. ^1H NMR of oxazoline **5a** (CDCl_3)

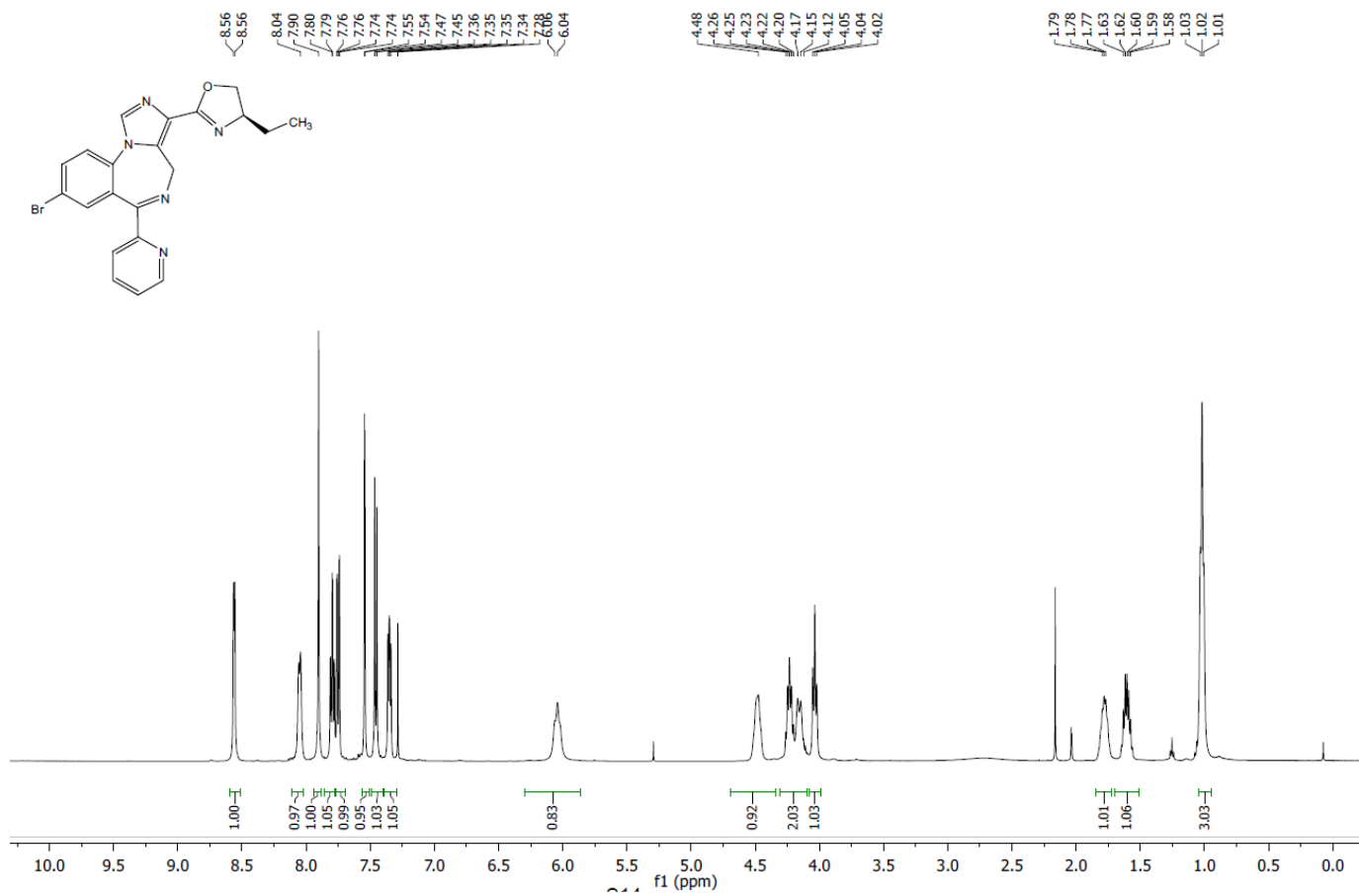
9. ^{13}C NMR of oxazoline **5a** (CDCl_3)

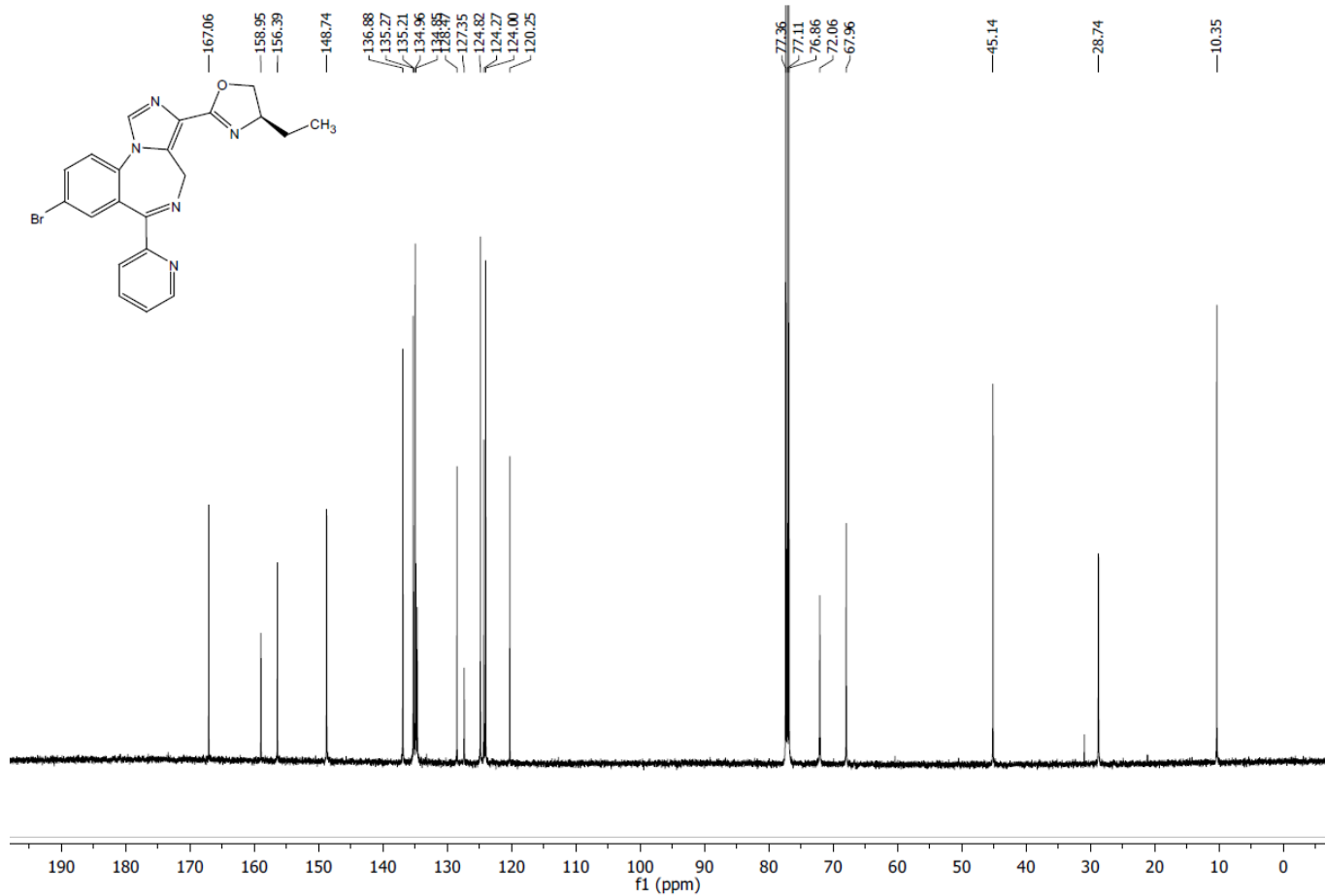
10. ^1H NMR of oxazoline **5b** (CDCl_3)

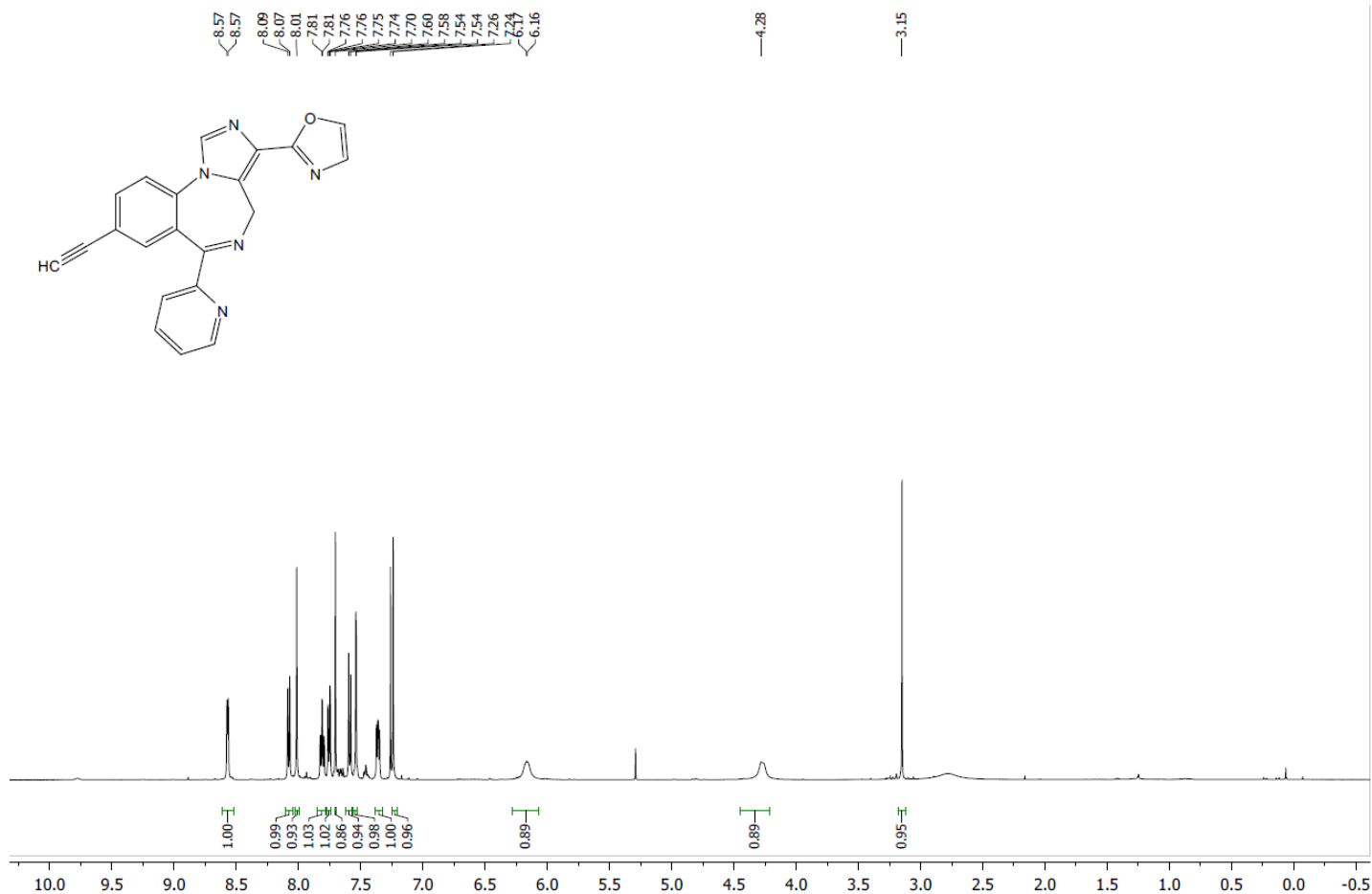
11. ^{13}C NMR of oxazoline **5b** (CDCl_3)

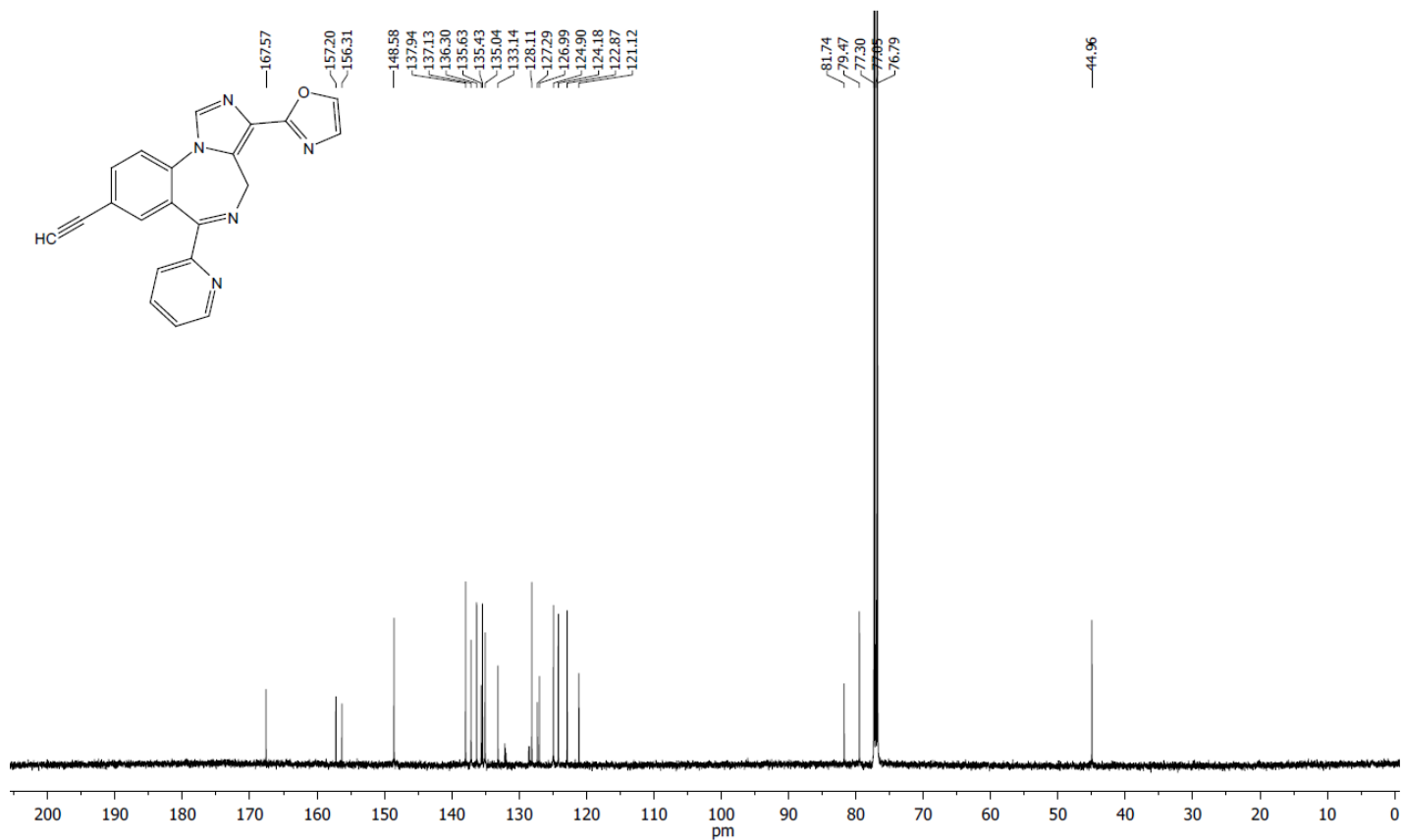
21. ^1H NMR of oxazoline **5c** (CDCl_3)

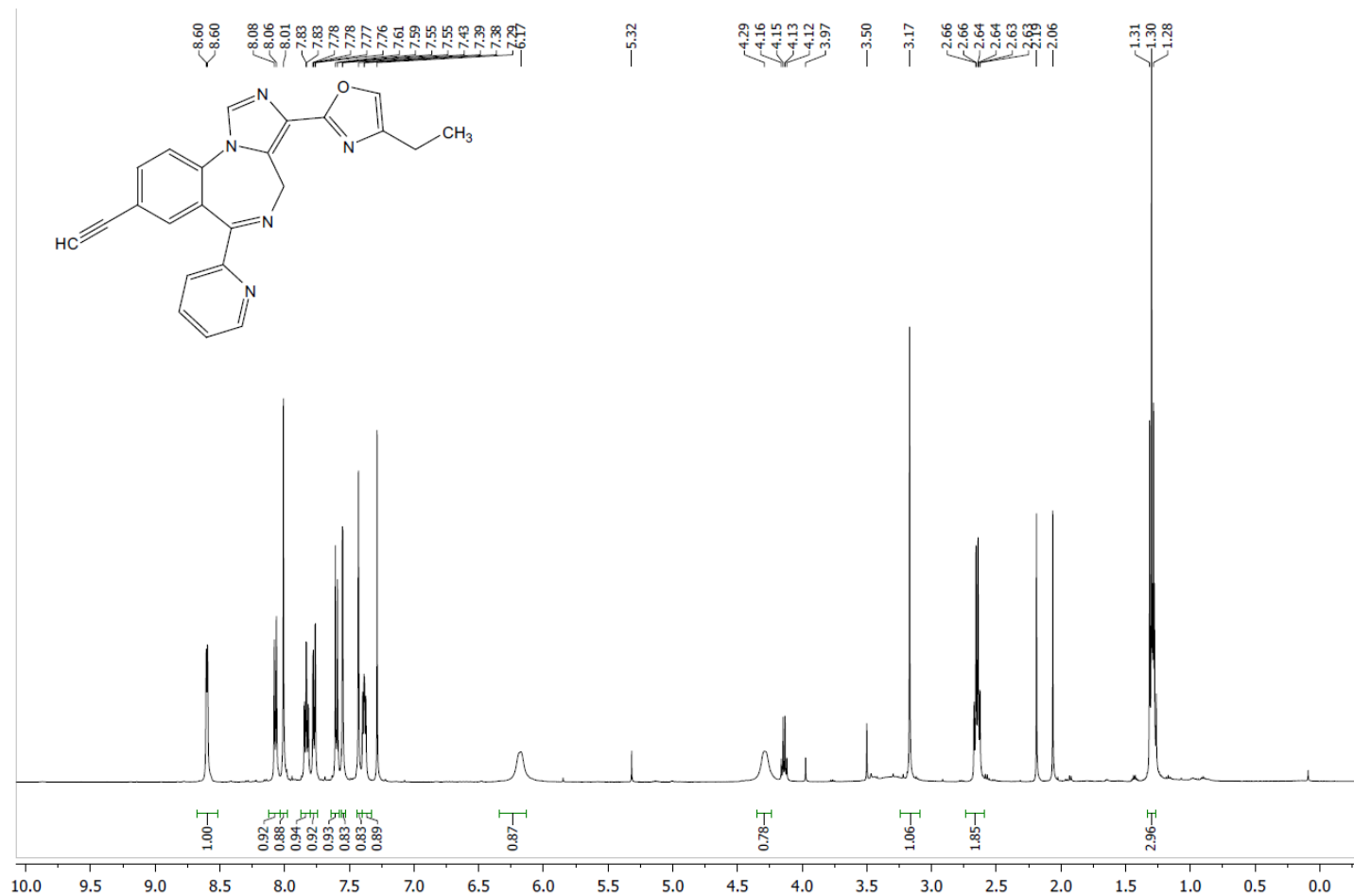
22. ^{13}C NMR of oxazoline 5c (CDCl_3)

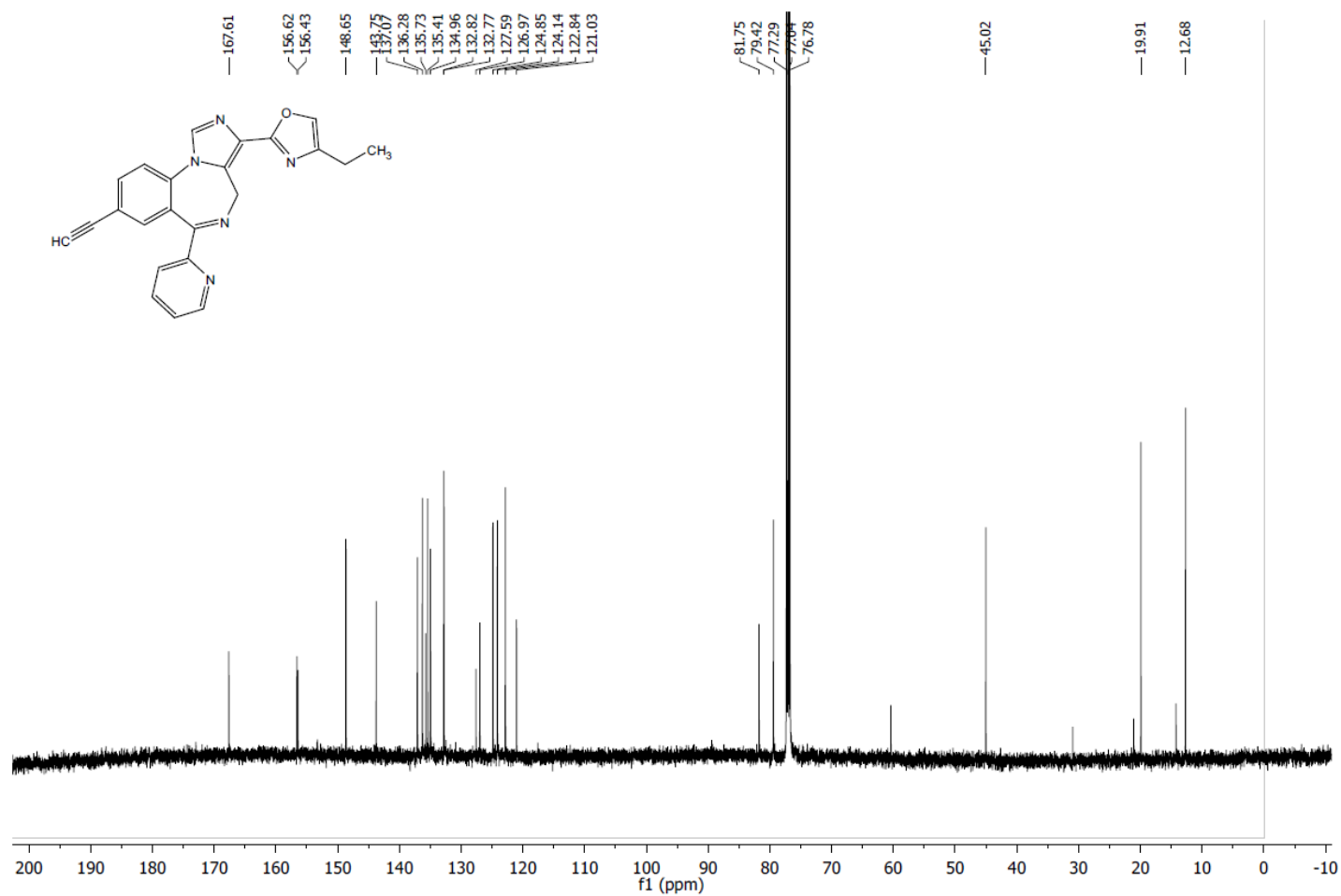
14. ^1H NMR of oxazoline **5d** (CDCl_3)

15. ^{13}C NMR of oxazoline **5d** (CDCl_3)

16. ^1H NMR of oxazole **6** (CDCl_3)

17. ^{13}C NMR of oxazole **6** (CDCl_3)

18. ^1H NMR of oxazole **6c** (CDCl_3)

19. ^{13}C NMR of oxazole **6c** (CDCl_3)

References

1. Pettersen, E. F.; Goddard, T. D.; Huang, C. C.; Couch, G. S.; Greenblatt, D. M.; Meng, E. C.; Ferrin, T. E. *J. Comput. Chem.* **2004**, *25*, 1605-1612.
<http://dx.doi.org/10.1002/jcc.20084>
2. Sanner, M. F. *J Mol Graph Model* **1999**, *17* (1), 57-61.