Supplementary Material

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

Kamal P. Pandey,[a] Md Zubair Ahmed Khan,[a] Lalit K. Golani,[a] Prithu Mondal, Md Yeunus Mian, Farjana Rashid, V. V. N. Phani Babu Tiruveedhula, Daniel E. Knutson, Dishary Sharmin, Taukir Ahmed, Sepideh Rezvanian, Nicolas M. Zahn, Leggy A. Arnold, Jeffrey M. Witkin, and James M. Cook*

[a] These authors contributed equally to this research
Department of Chemistry and Biochemistry, Milwaukee Institute for Drug Discovery, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin 53211, USA
E-mail: capncook@uwm.edu

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1. Figure S1. Showing halogen bond interactions

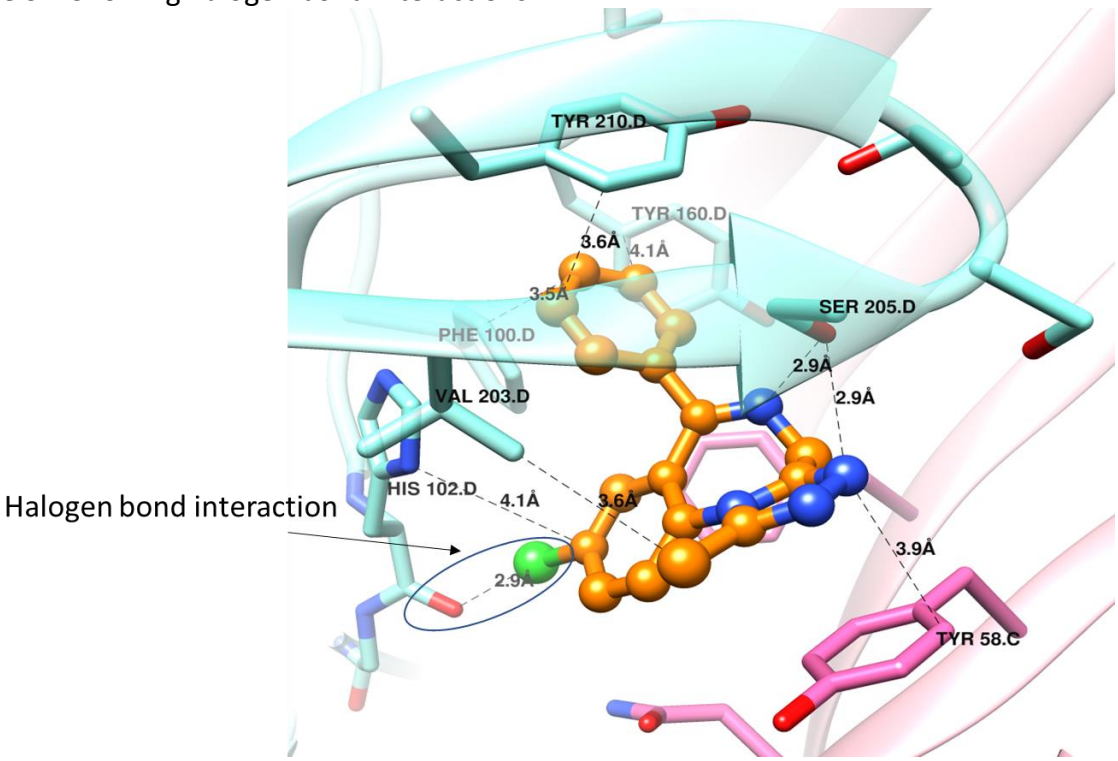

Figure S1. Showing halogen bond interaction in complex of alprazolam (orange) with α1β3γ2L $GABA_A$ receptor (PDB: 6HUO) at $\alpha^{+}\gamma^{-}$ interface benzodiazepine binding site [α1 (represented as chain D, color: aquamriane) and γ2 (represented as chain C, color: orchid)], dashed lines indicate 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 α1β3γ2L $GABA_A$ 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)

SHIMADZU LabSolutions Analysis Report

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Sample ID	:		
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Method Filename	: chiral 3-11-2020.lcm		
Batch Filename	: 10-12-20.lcb		
Vial #	: Vial 2	Sample Type	: Unknown
Injection Volume	: 5 uL	Level	: 1
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Date Processed	: 10/12/2020 7:42:38 PM	Processed by	: Kamal Pandey

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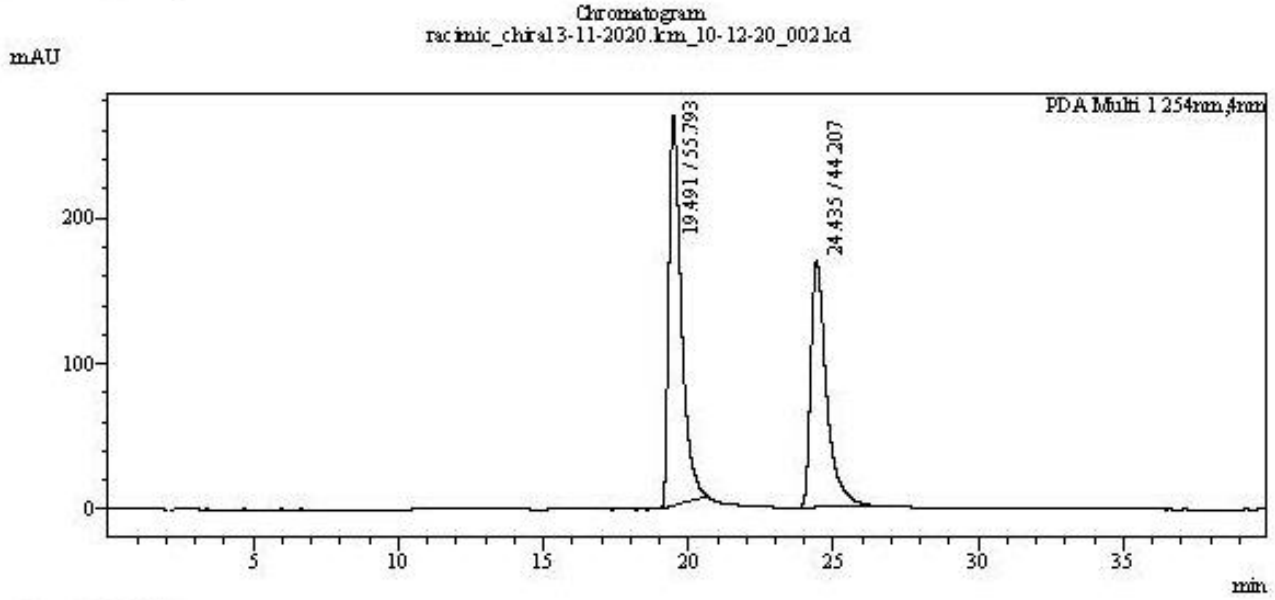

<Peak Table>

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)

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

Sample Name	: KPP-III-96B		
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Method Filename	: chiral 3-11-2020.lcm		
Batch Filename	: 10-12-20.lcb		
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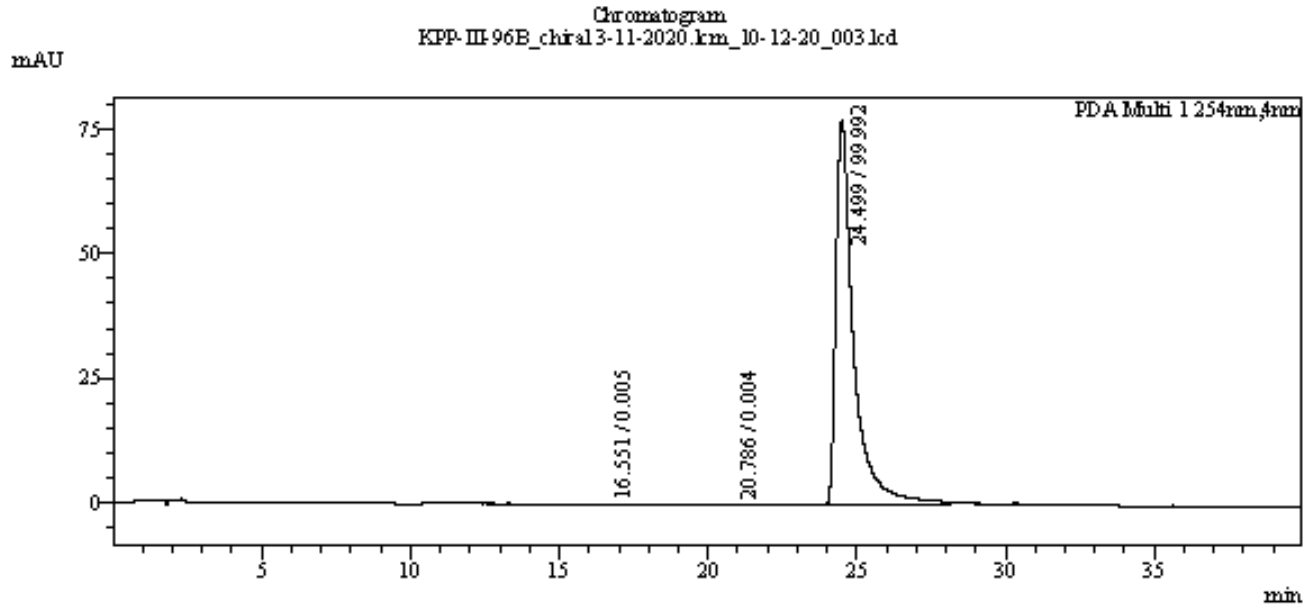

<Peak Table>

KPP-III-96B_chiral 3-11-2020.lcm_10-12-20_003.lcd

(3D)DAD Ch1 254nm

Peak#	Ret. Time	Area%
1	16.551	0.005
2	20.786	0.004
3	24.499	99.992
Total		100.000

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

SHIMADZU LabSolutions **Analysis Report**

<Sample Information>

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Sample ID	:		
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Batch Filename	: 10-12-20.lcb		
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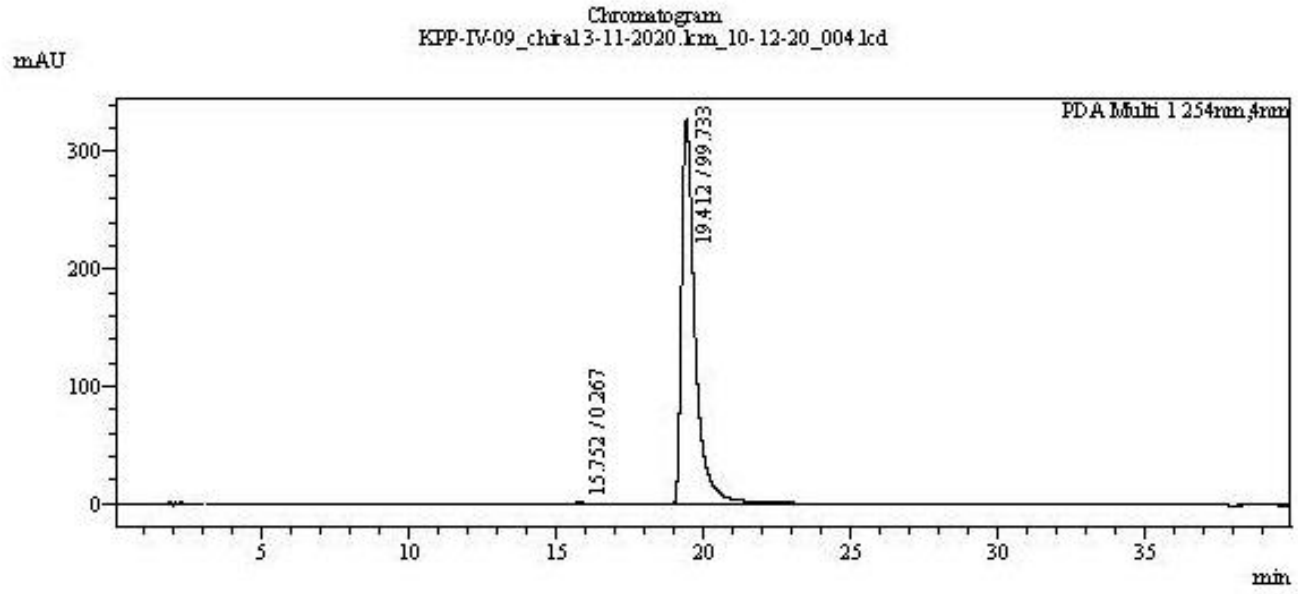

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(3D)DAD Ch1 254nm

Peak#	Ret. Time	Area%
1	15.752	0.267
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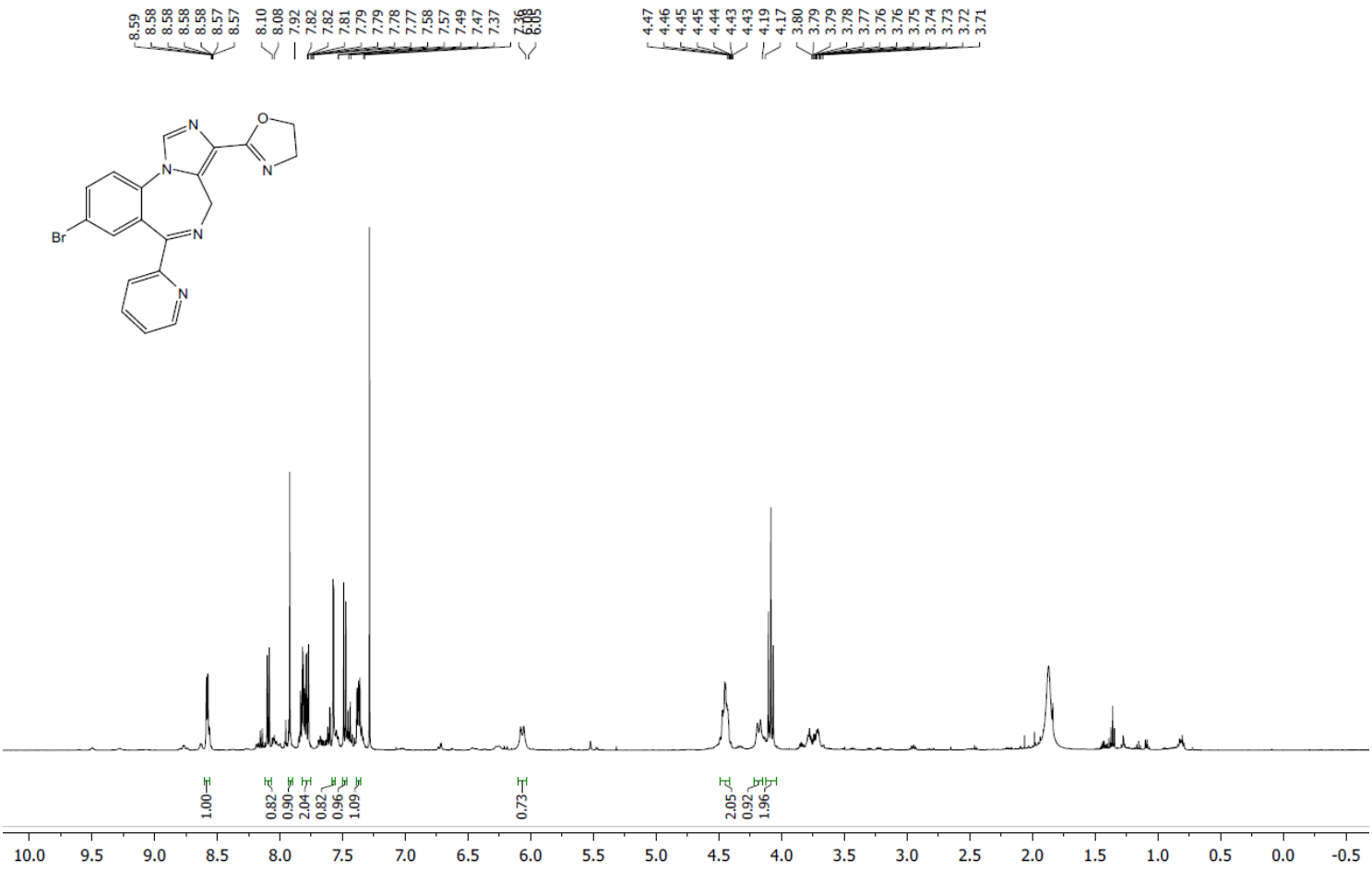
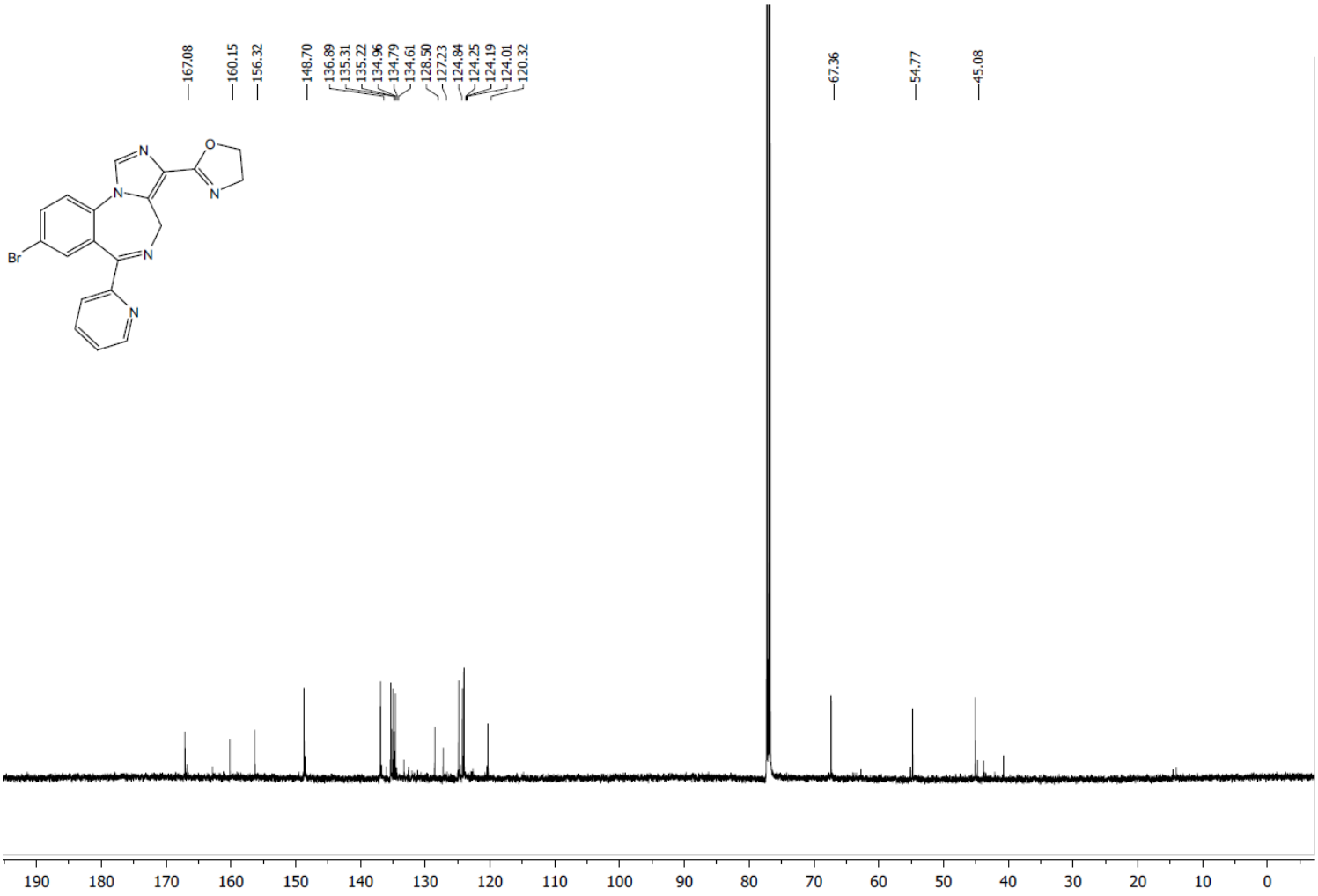
Total		100.000

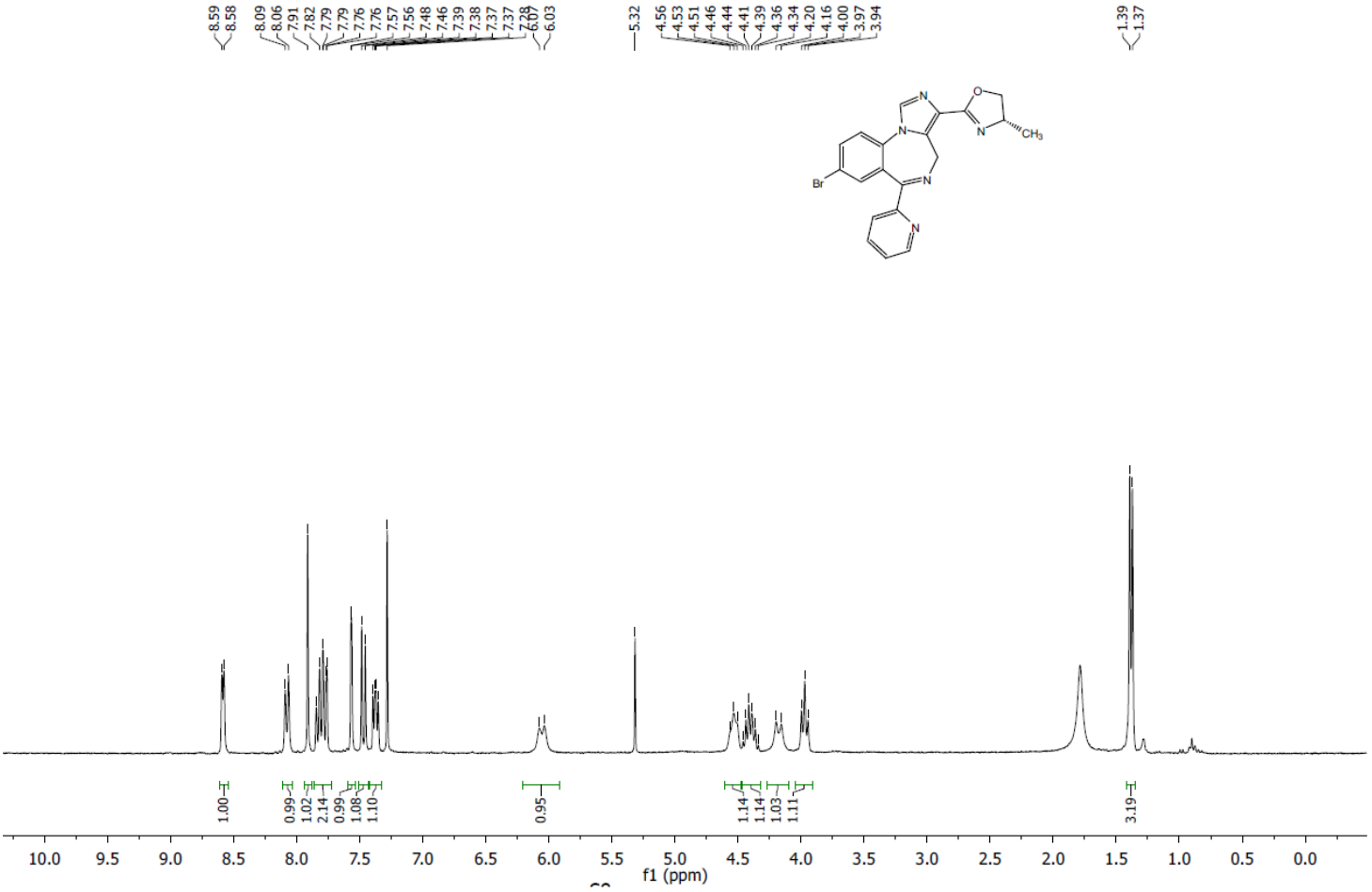
6. ^{1}H NMR of oxazoline **5** (CDCl3)



7. ^{13}C NMR of oxazoline **5** (CDCl3)



8. ^{1}H NMR of oxazoline **5a** (CDCl3)



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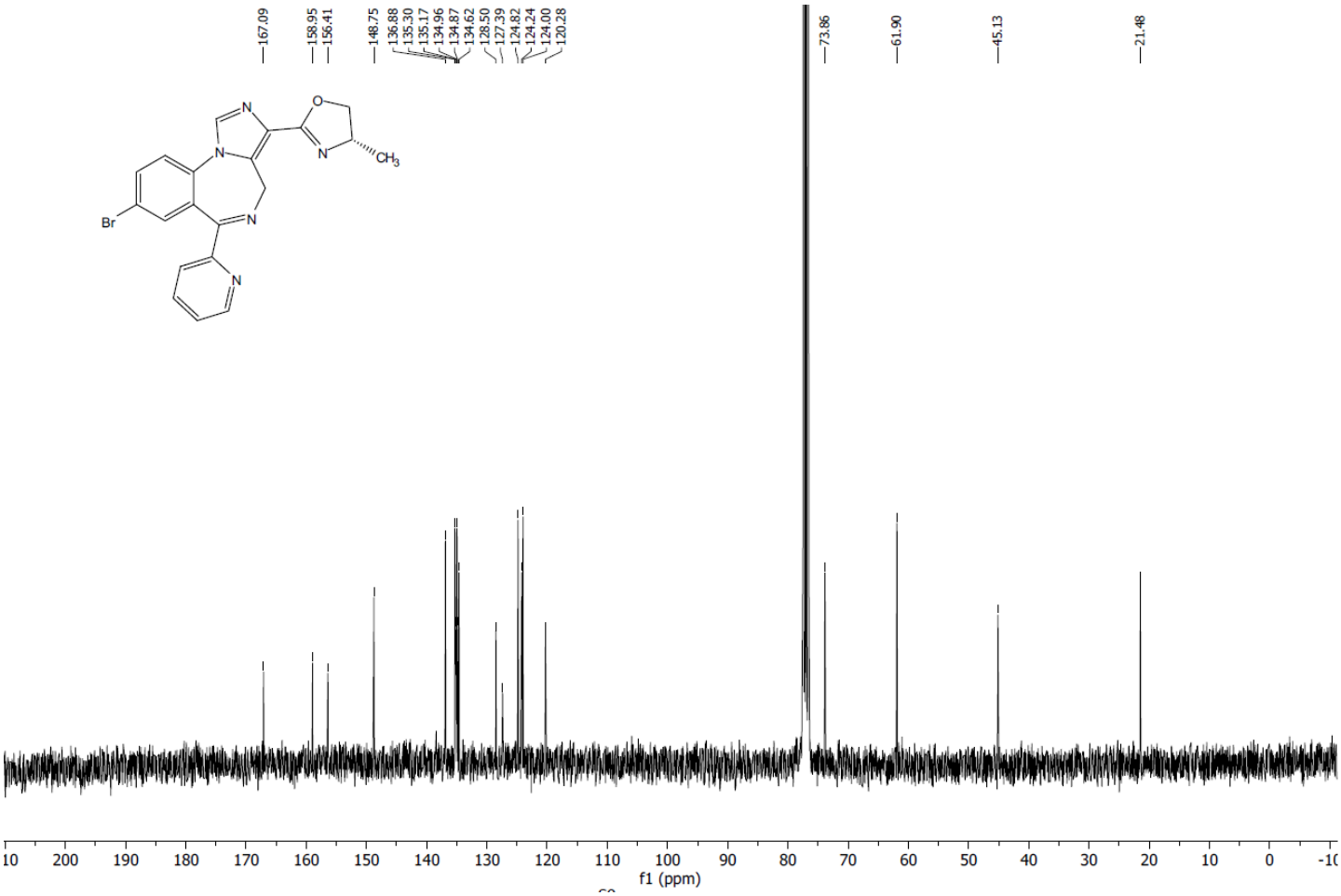
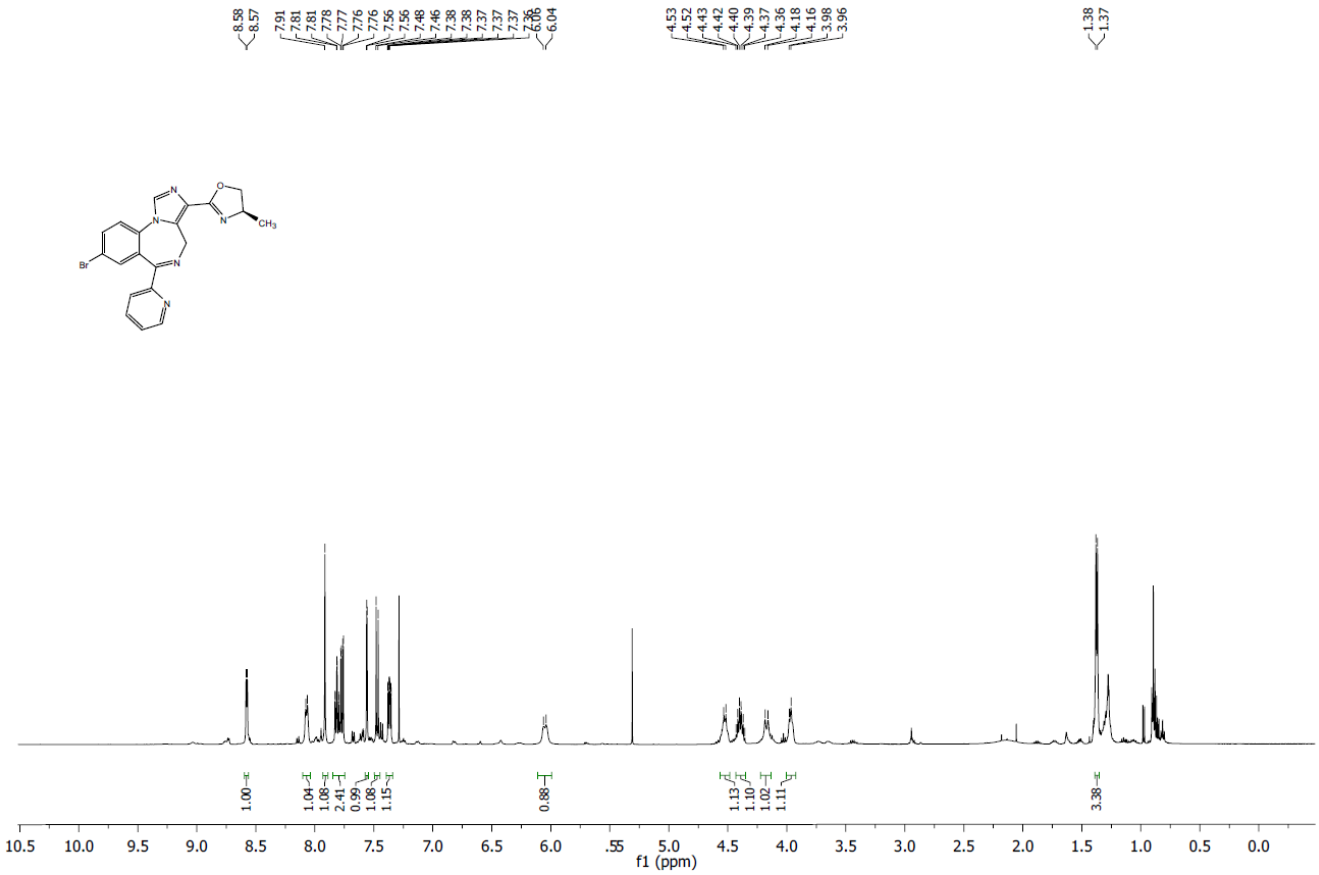
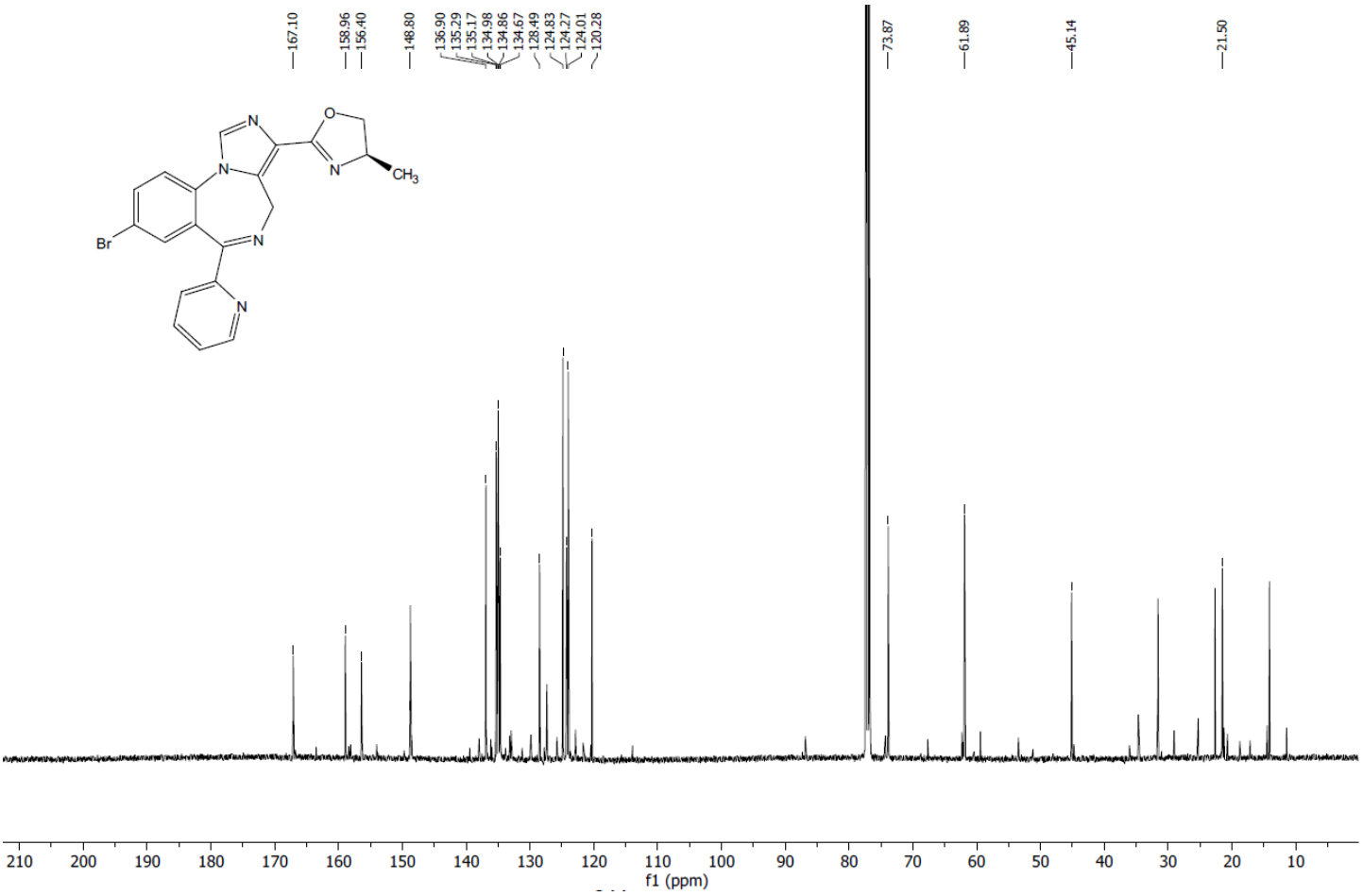


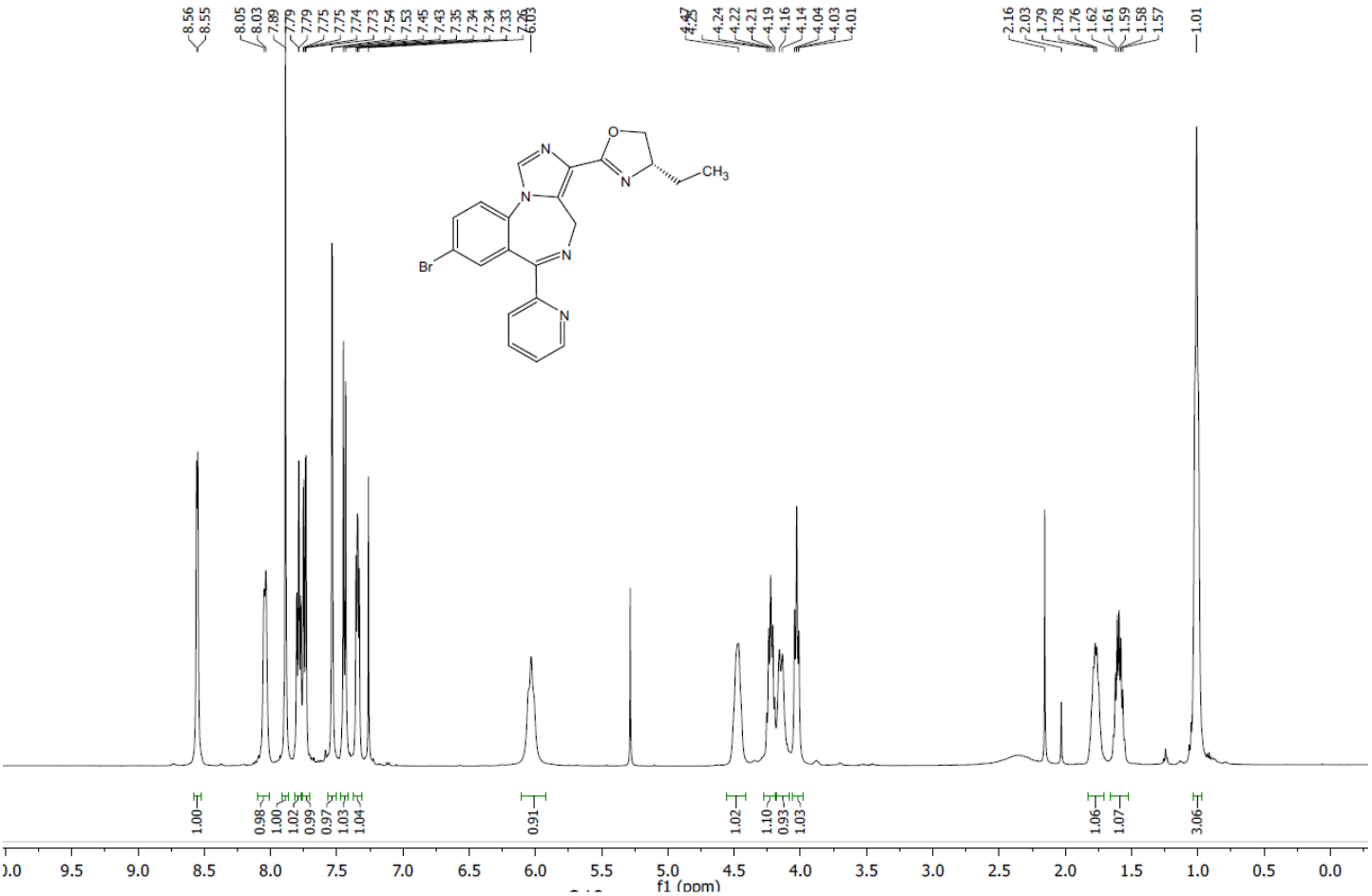
10. ^{1}H NMR of oxazoline **5b** (CDCl3)



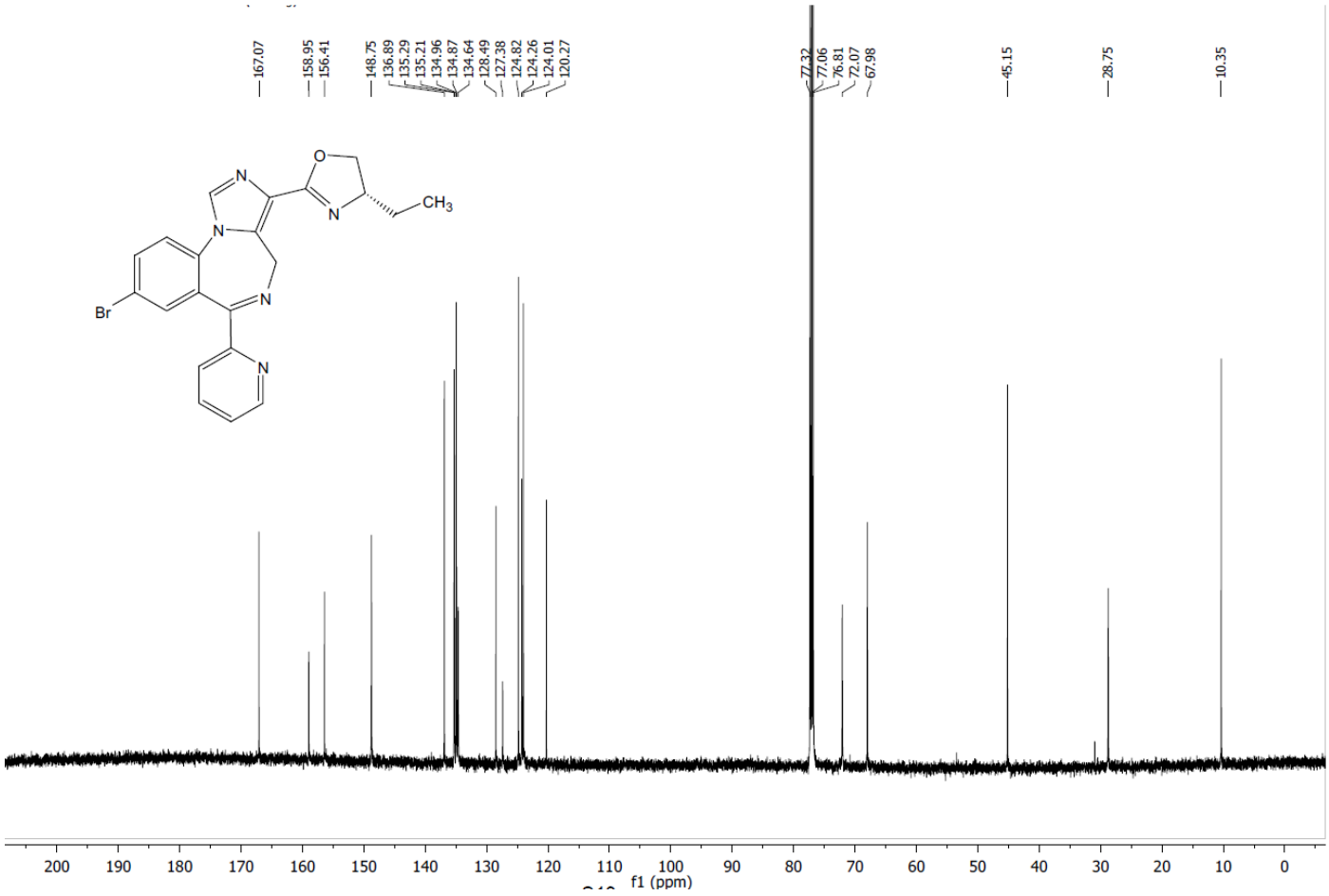
11. ^{13}C NMR of oxazoline **5b** (CDCl3)



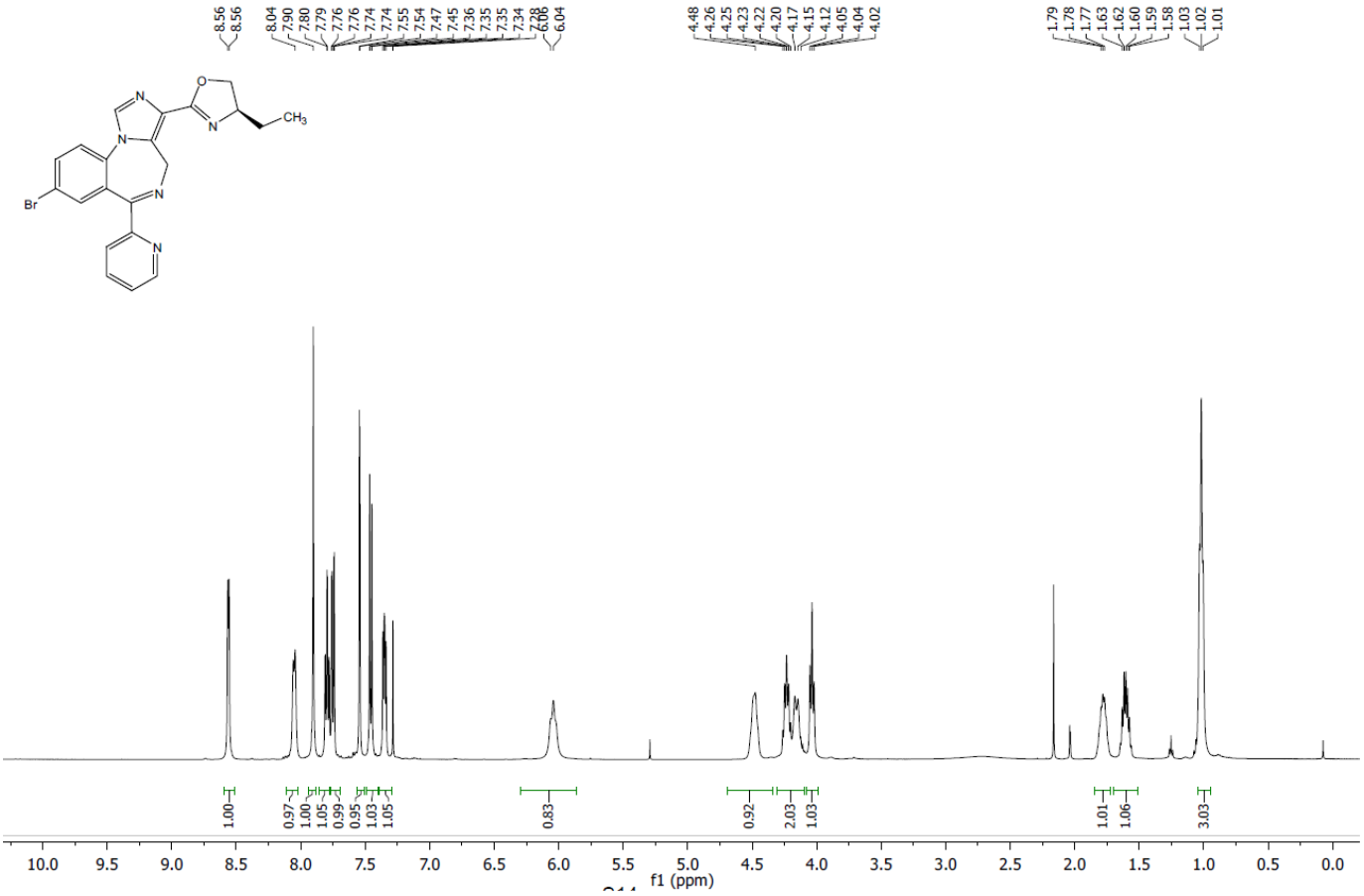
21. ^{1}H NMR of oxazoline **5c** (CDCl3)



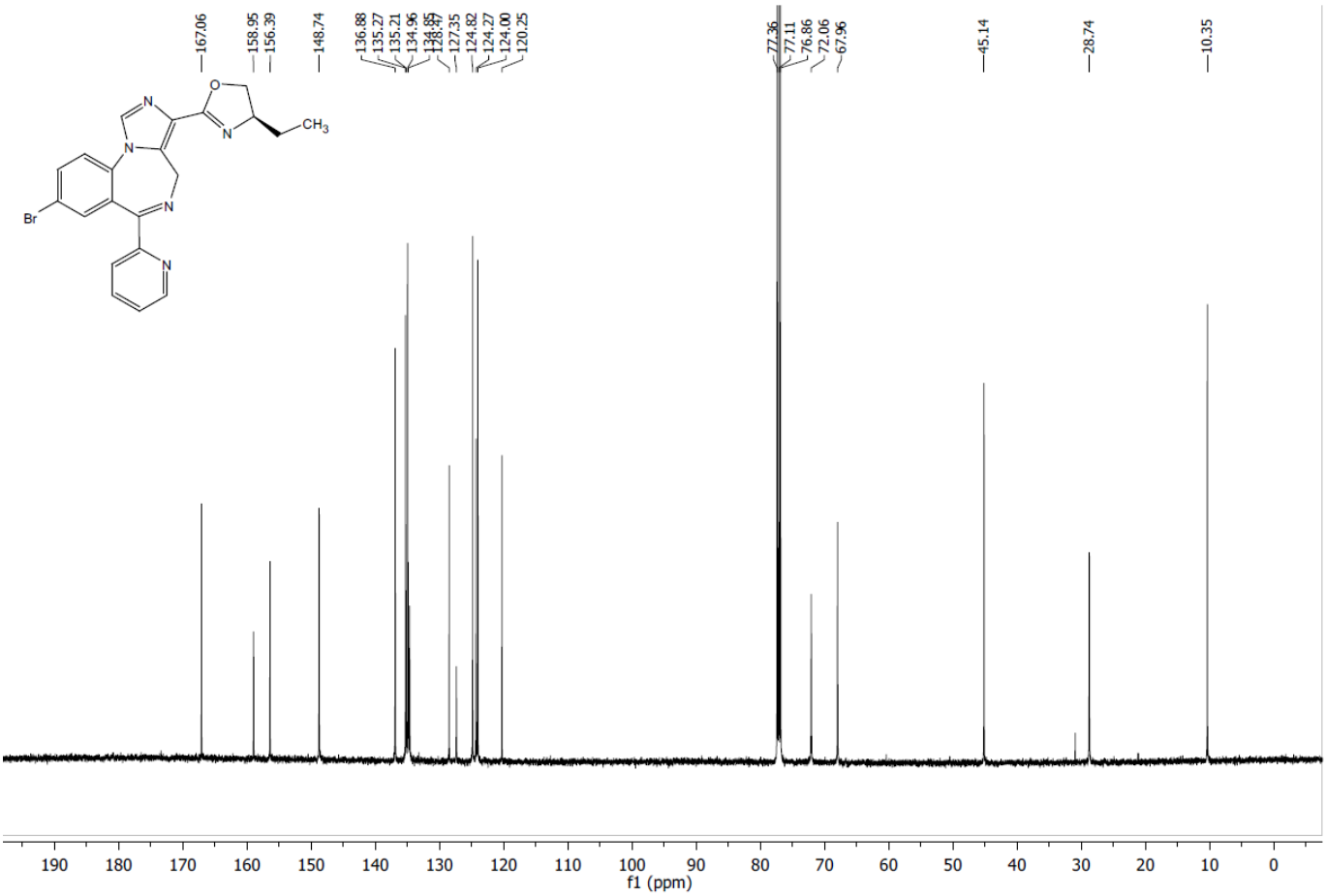
22. ^{13}C NMR of oxazoline **5c** ($CDCl_3$)



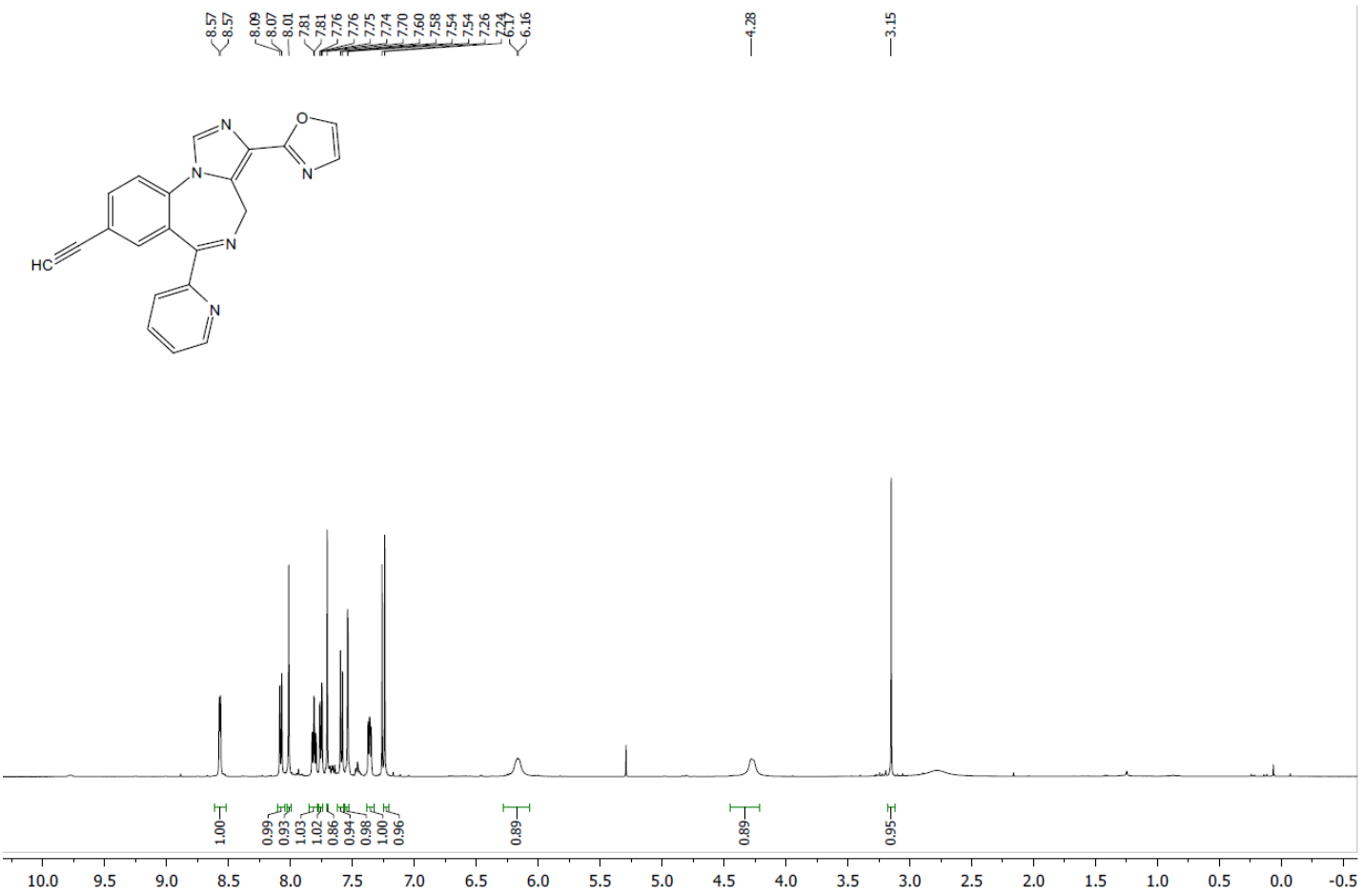
14. ^{1}H NMR of oxazoline **5d** ($CDCl_3$)



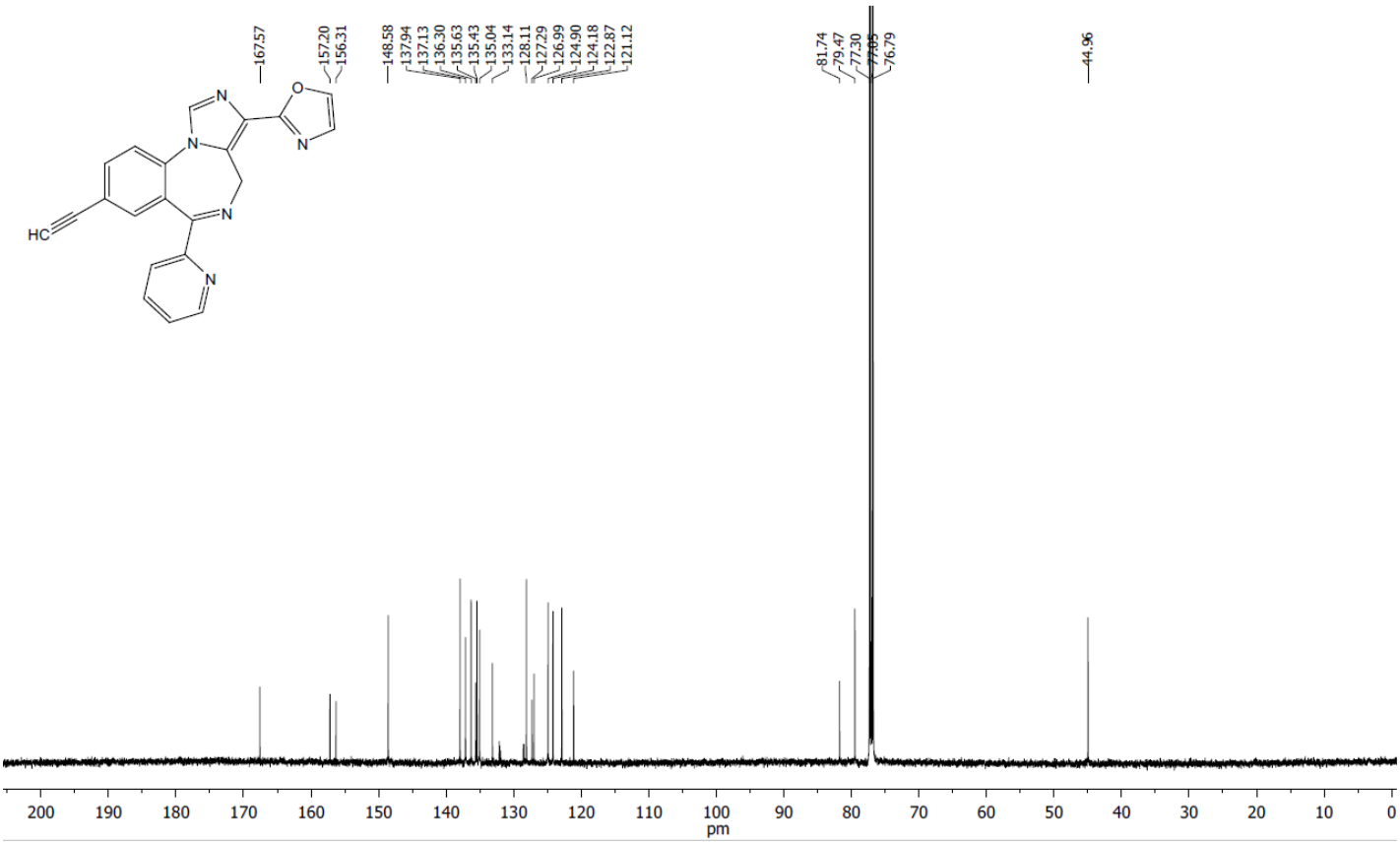
15. ^{13}C NMR of oxazoline **5d** ($CDCl_3$)



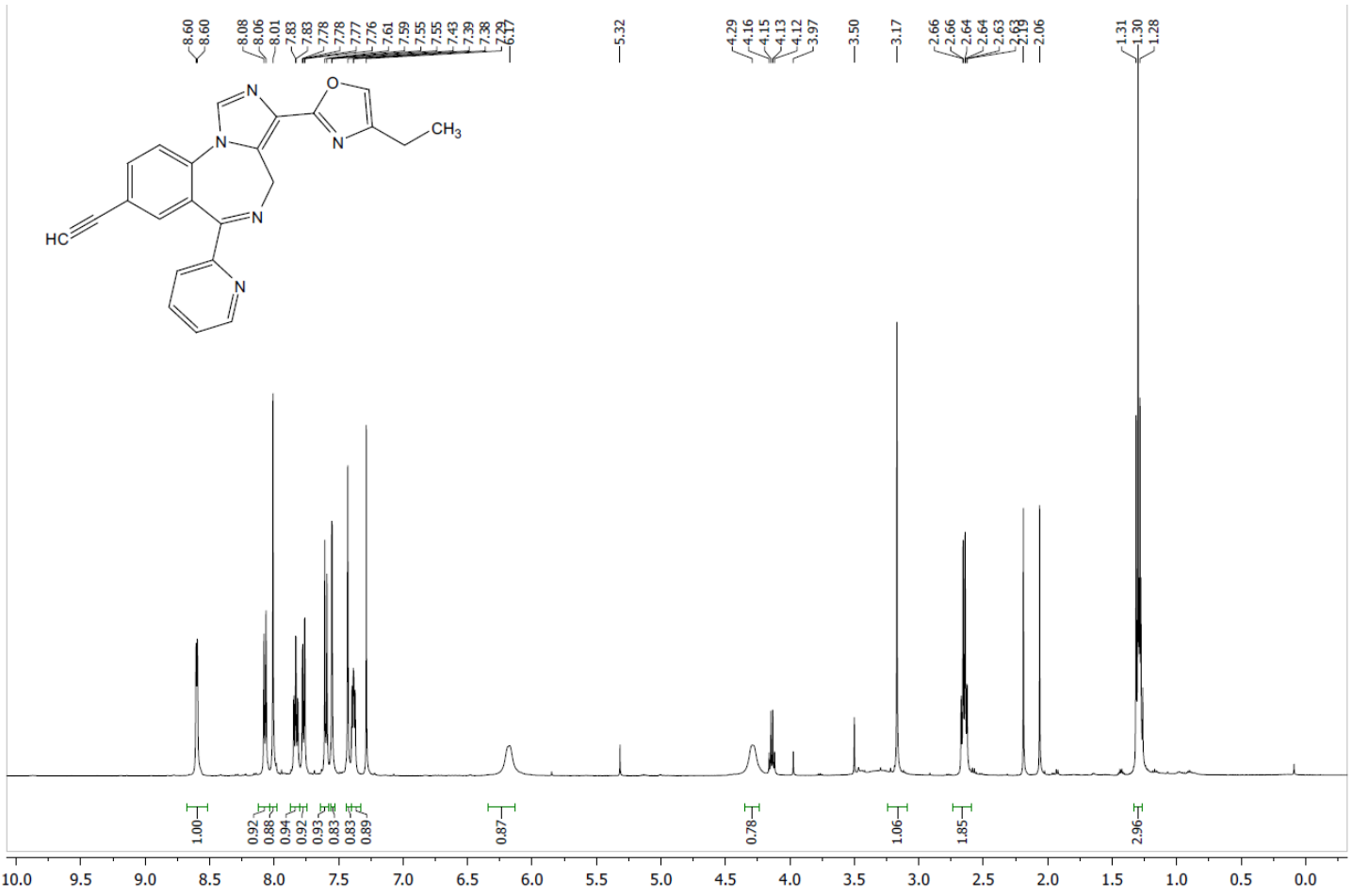
16. ^{1}H NMR of oxazole **6** ($CDCl_3$)



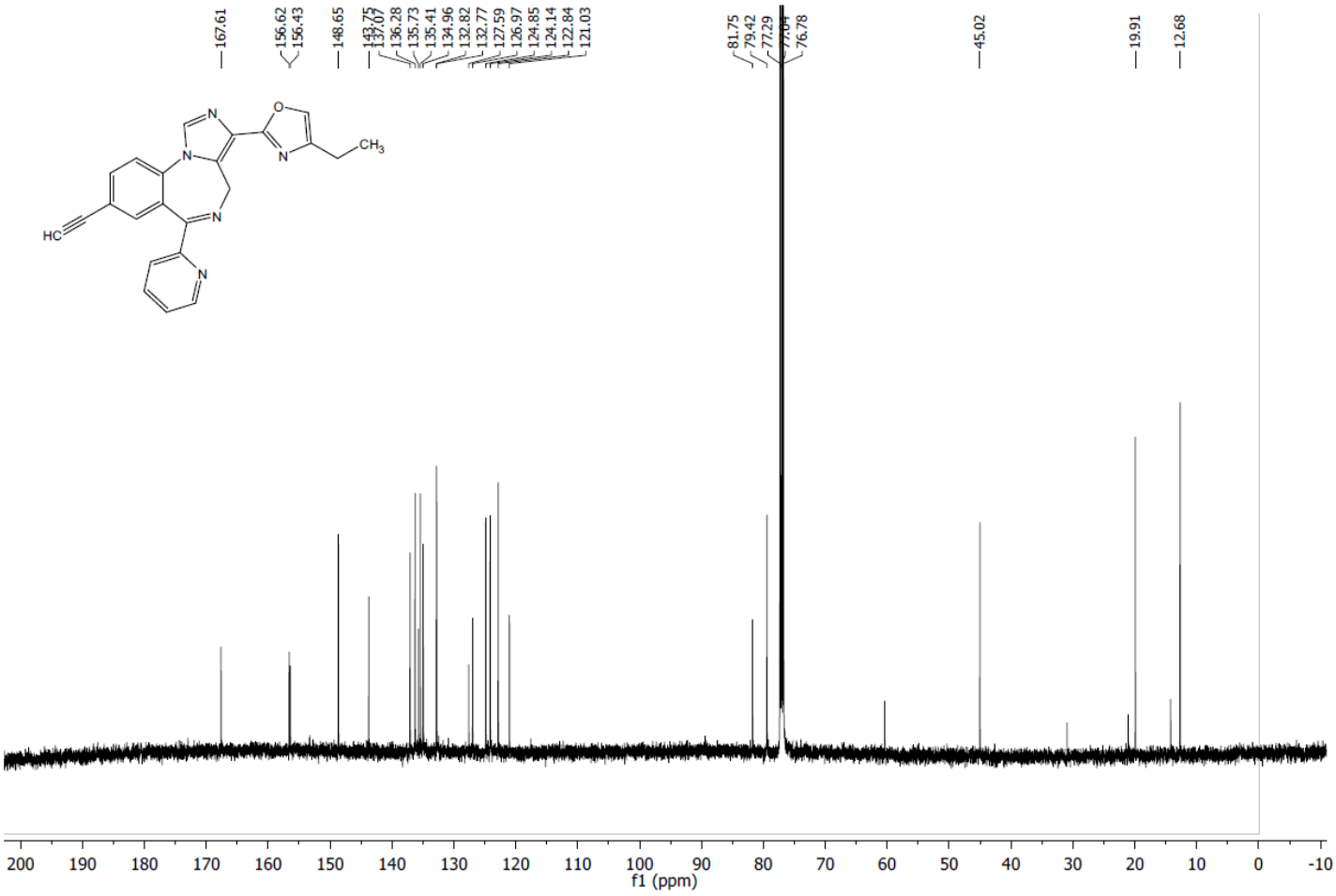
17. ^{13}C NMR of oxazole **6** (CDCl3)



18. ^{1}H NMR of oxazole **6c** (CDCl3)



19. ^{13}C NMR of oxazole **6c** (CDCl3)



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.

