Supporting information for

Synthesis and antimicrobial evaluation of (+)-neoisopulegol-based amino and thiol adducts

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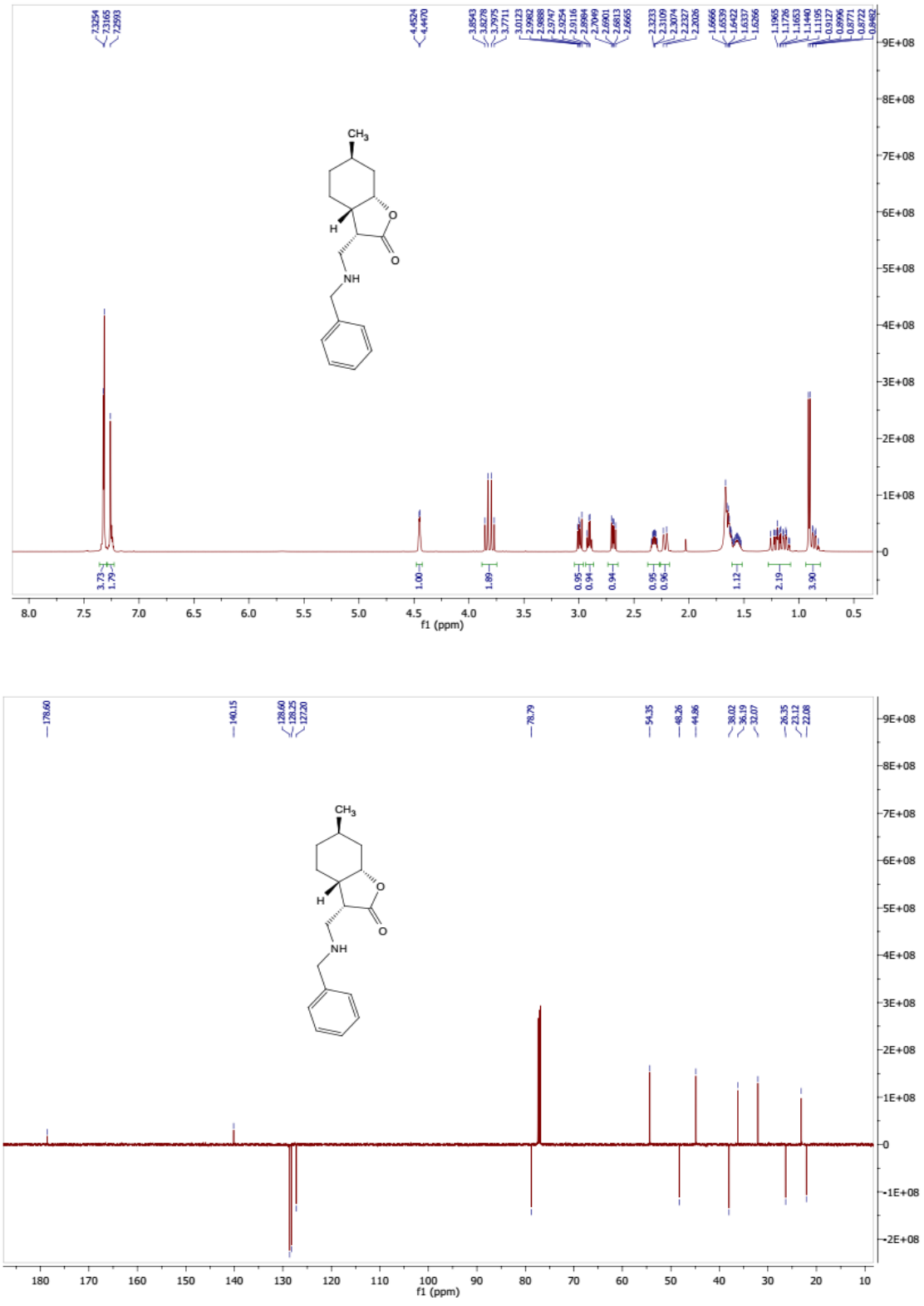
1. NMR spectra of new compounds



Figures S1-S2. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **23.**

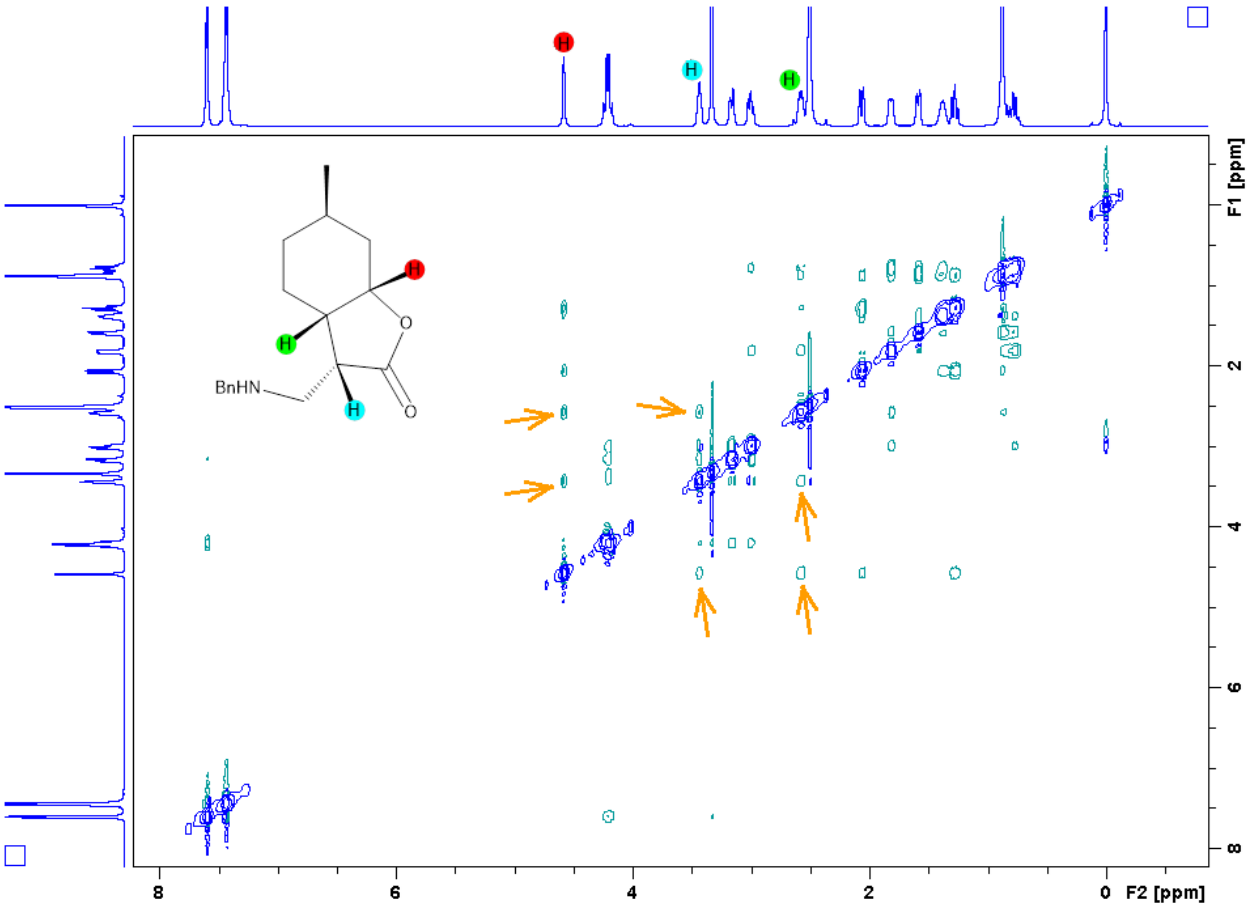
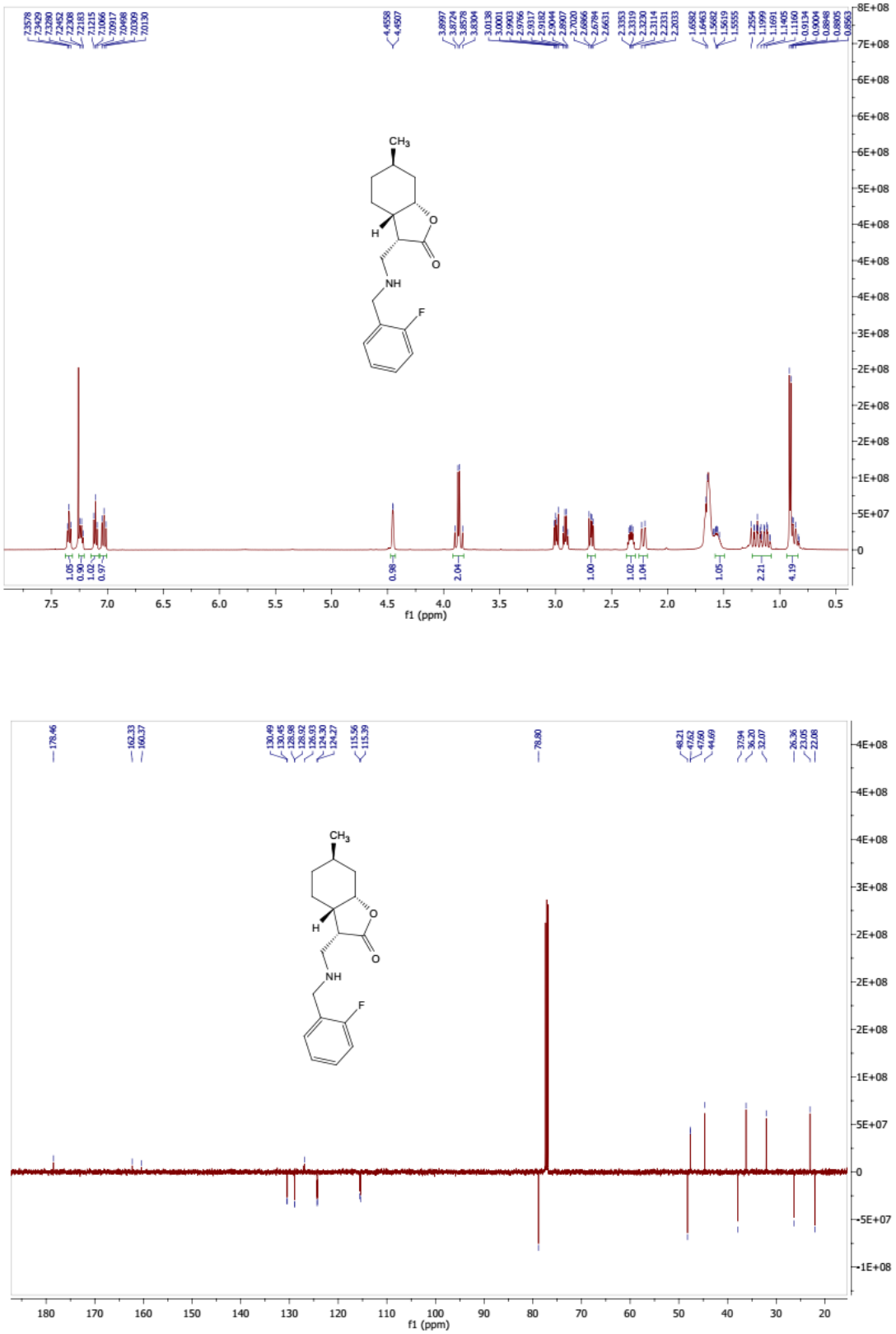


Figure S3. NOESY (500 MHz, DMSO-d_6) spectra of **23.**



Figures S4-S5. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **24.**

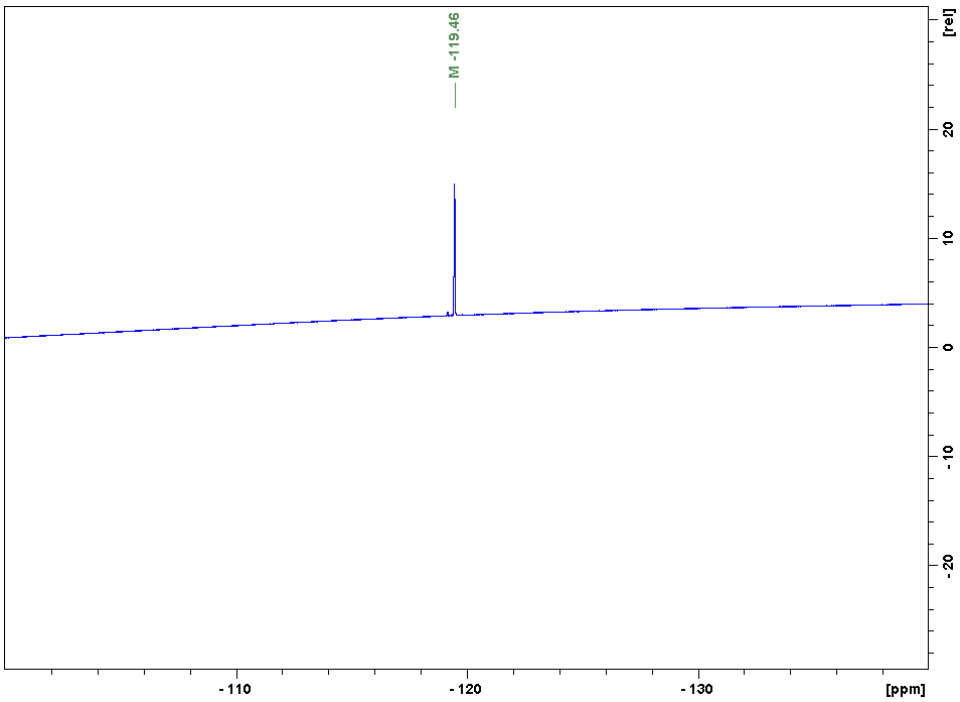
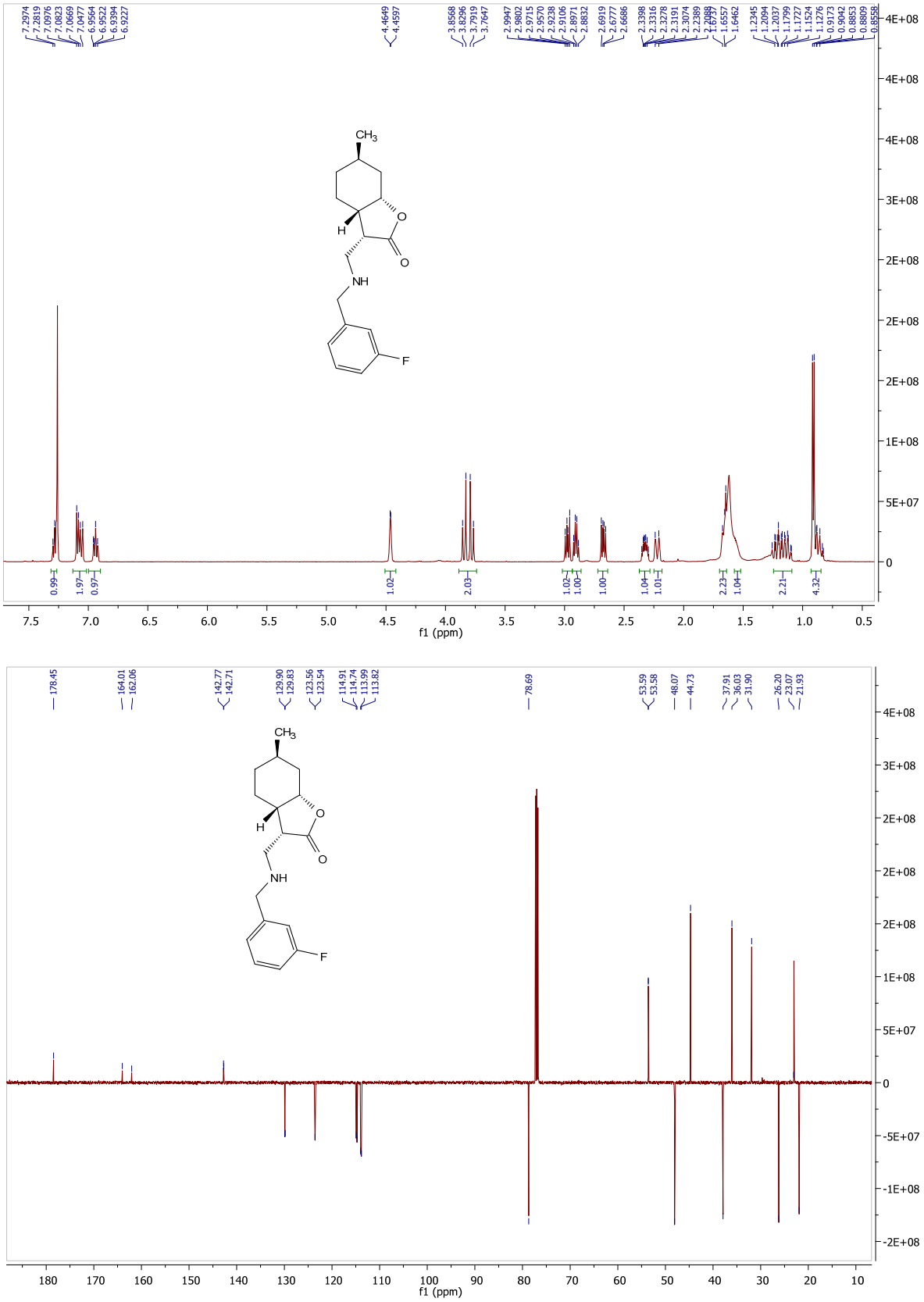


Figure S6. ^{19}F (471 MHz, $CDCl_3$) NMR spectra of **24.**



Figures S7-S8. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **25.**

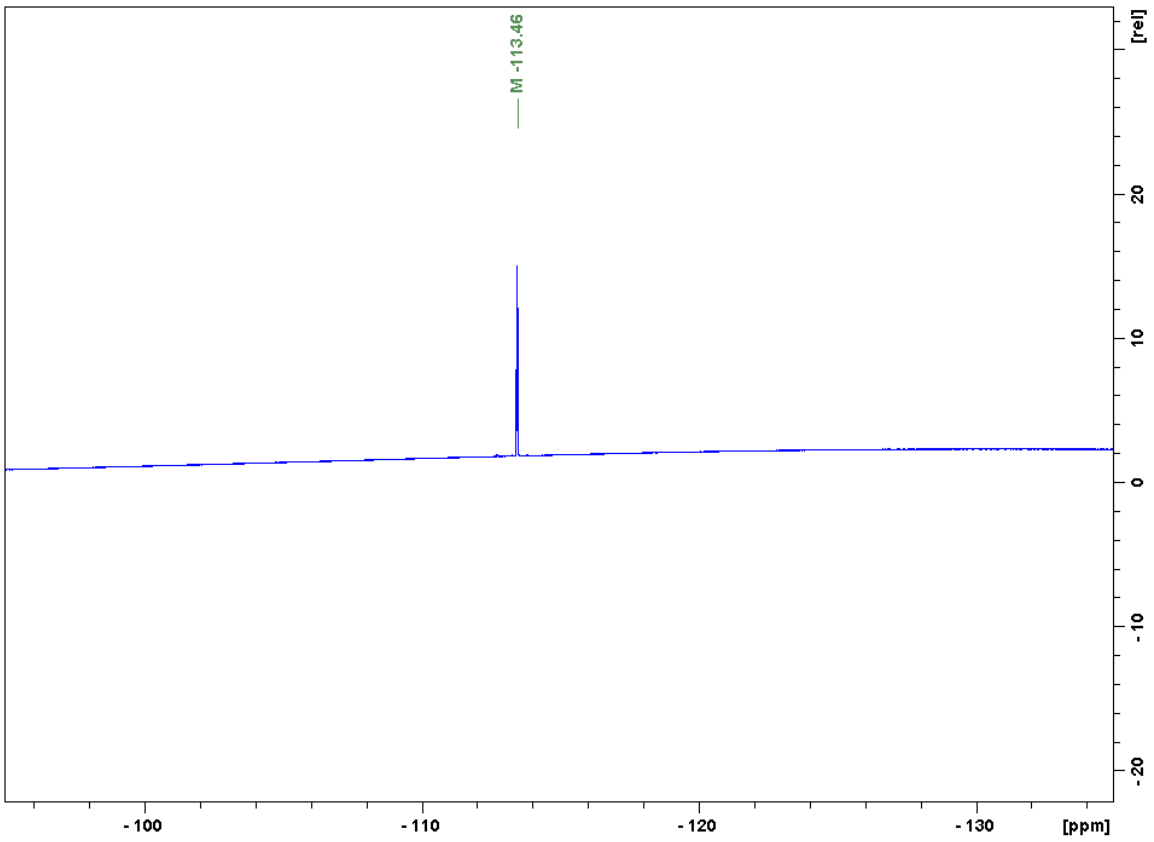
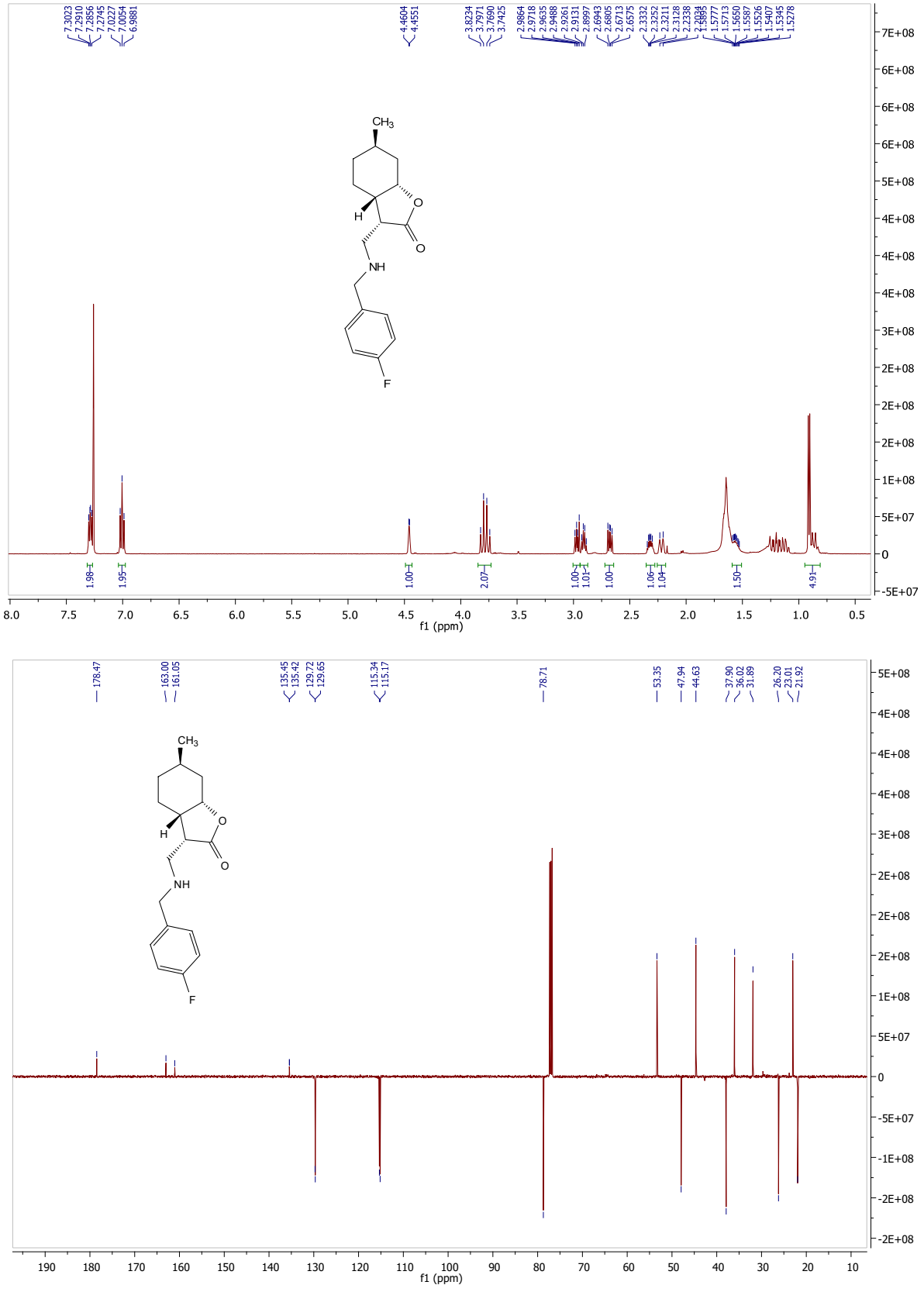


Figure S9. ^{19}F (471 MHz, $CDCl_3$) NMR spectra of **25.**



Figures S10-S11. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **26.**

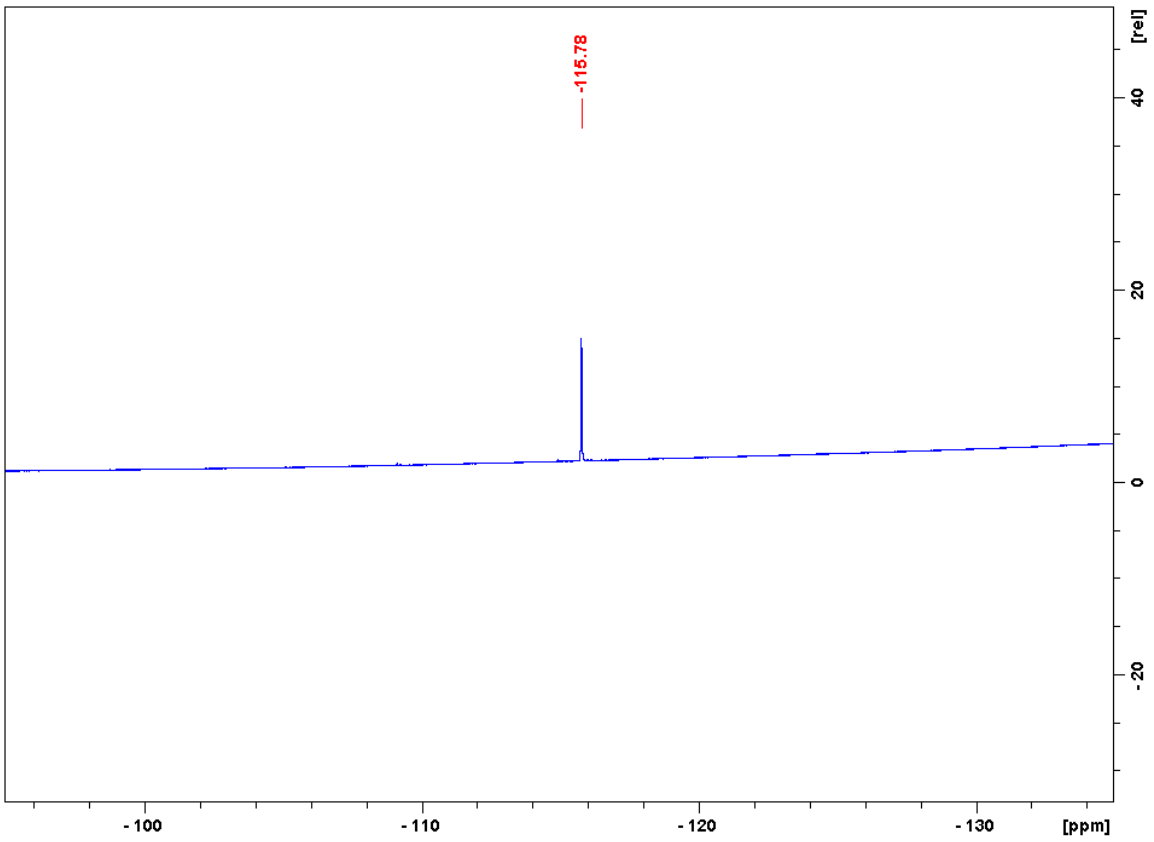
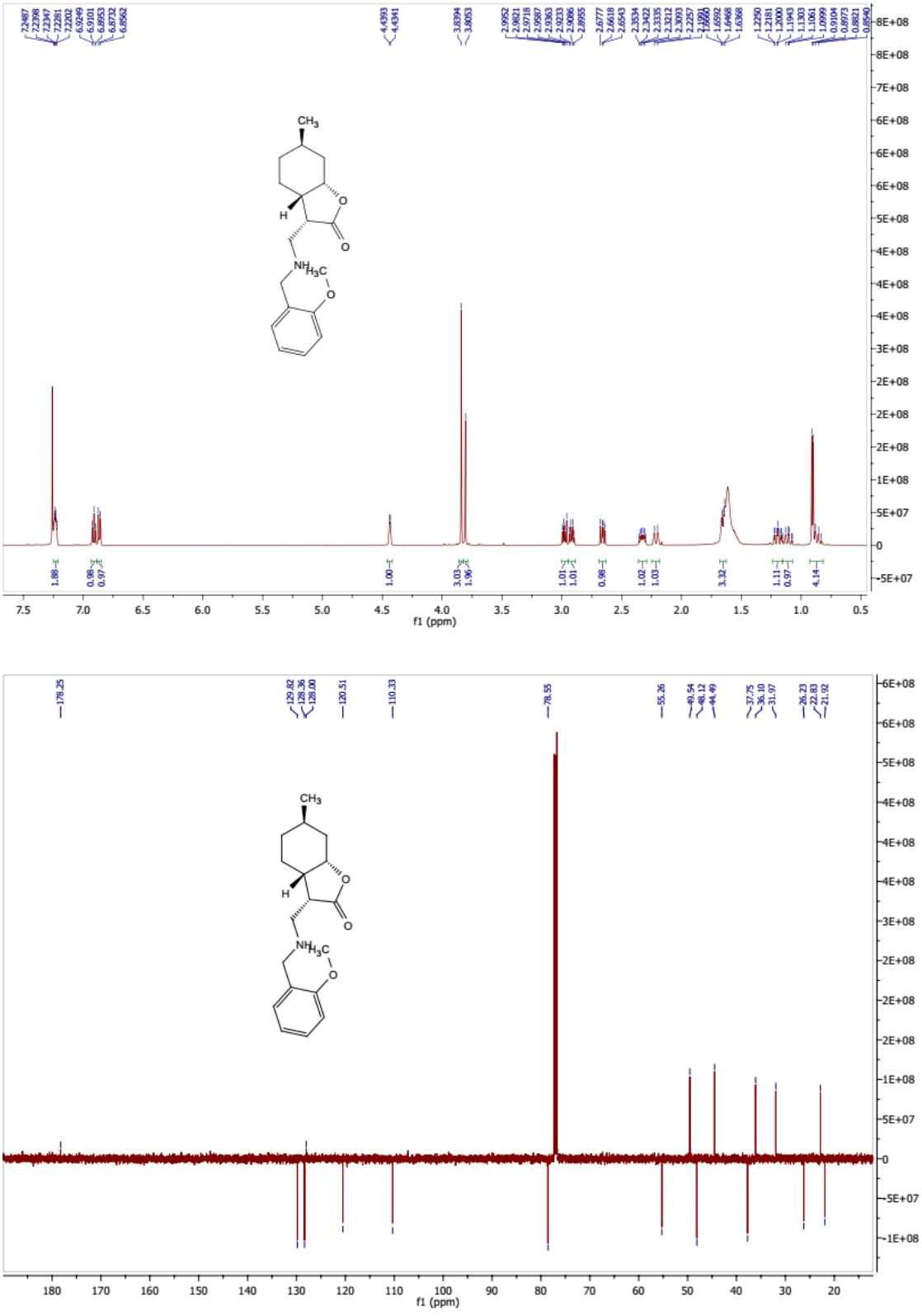
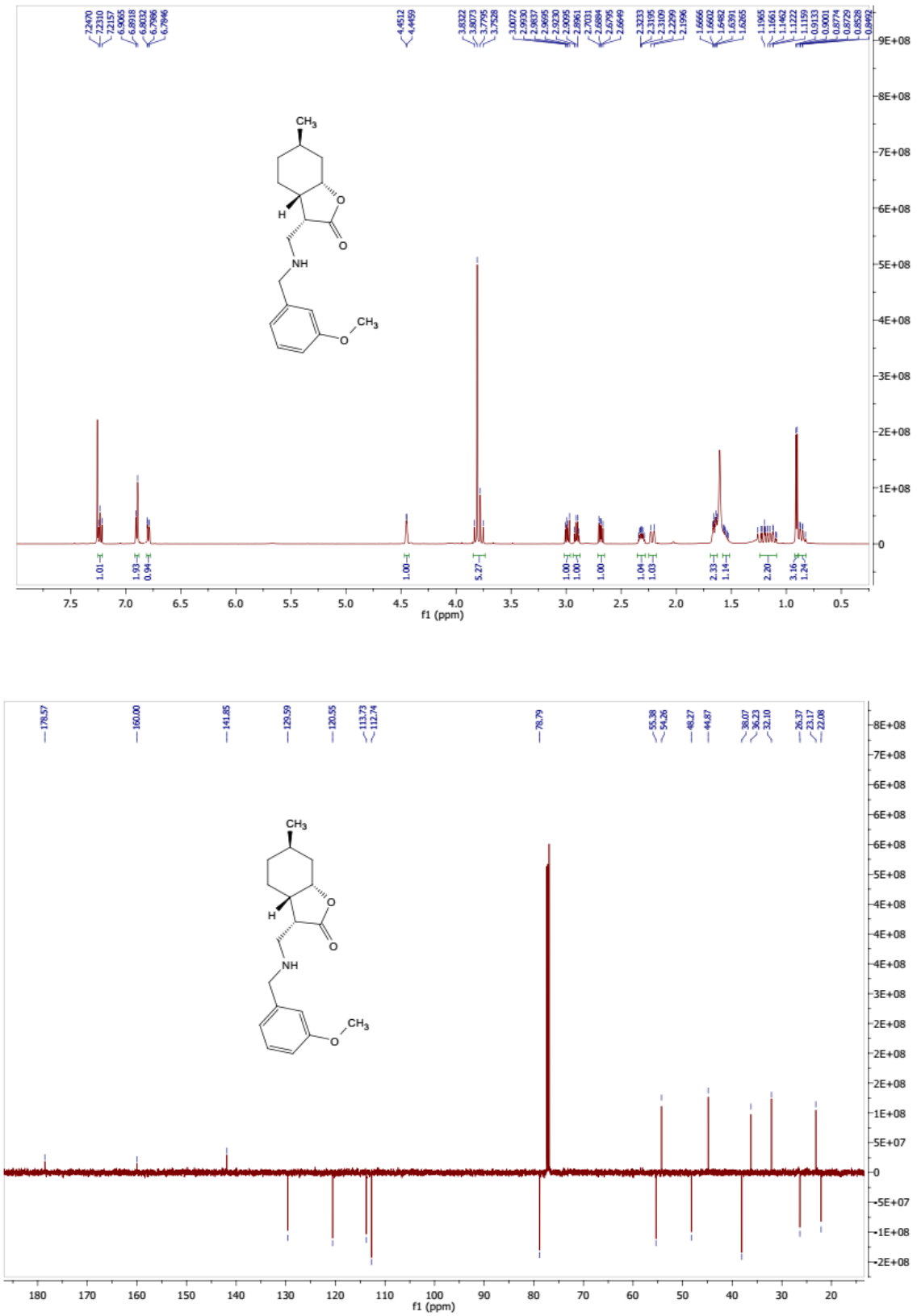


Figure S12. ^{19}F (471 MHz, $CDCl_3$) NMR spectra of **26.**



Figures S13-S14. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **27.**



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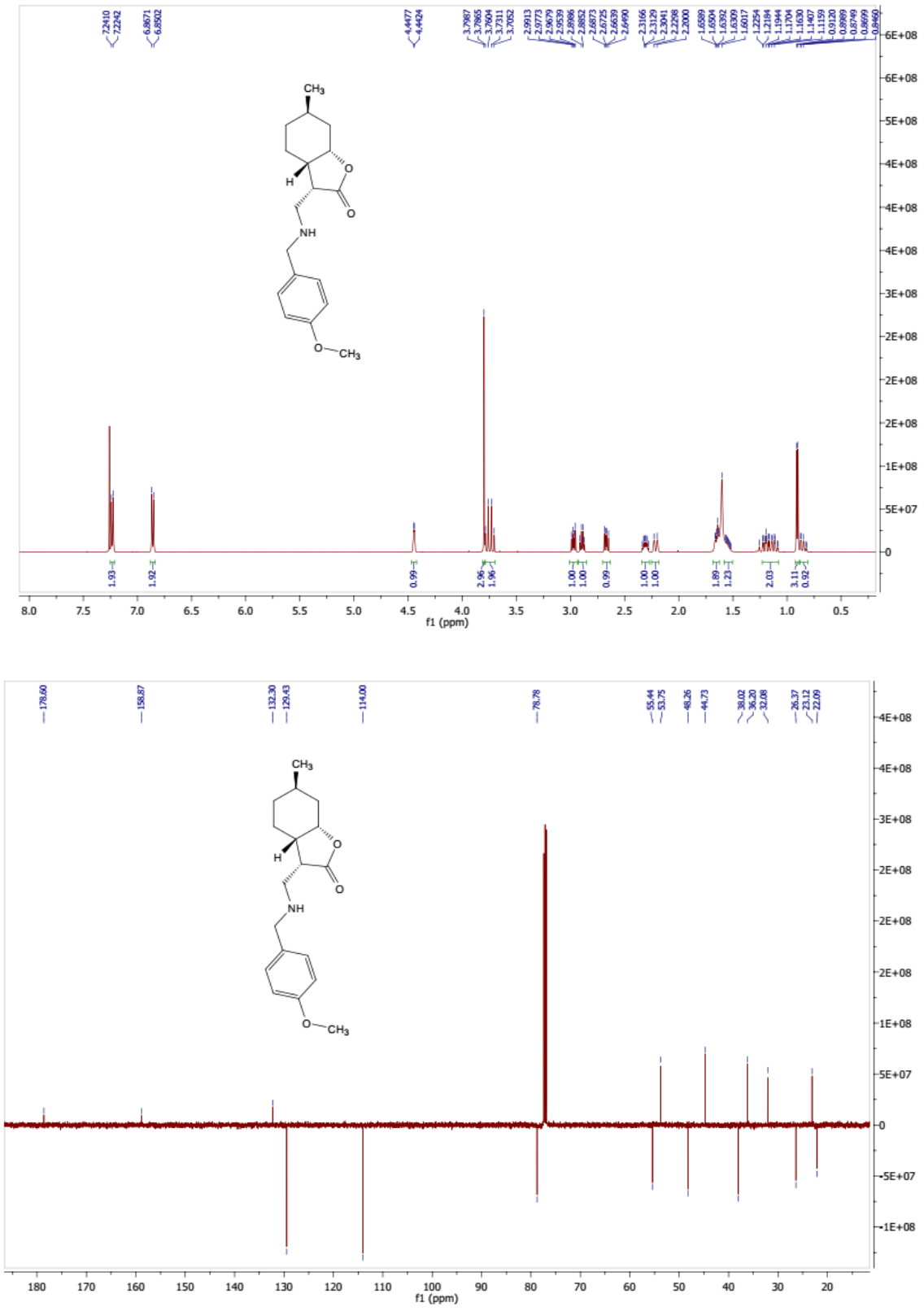
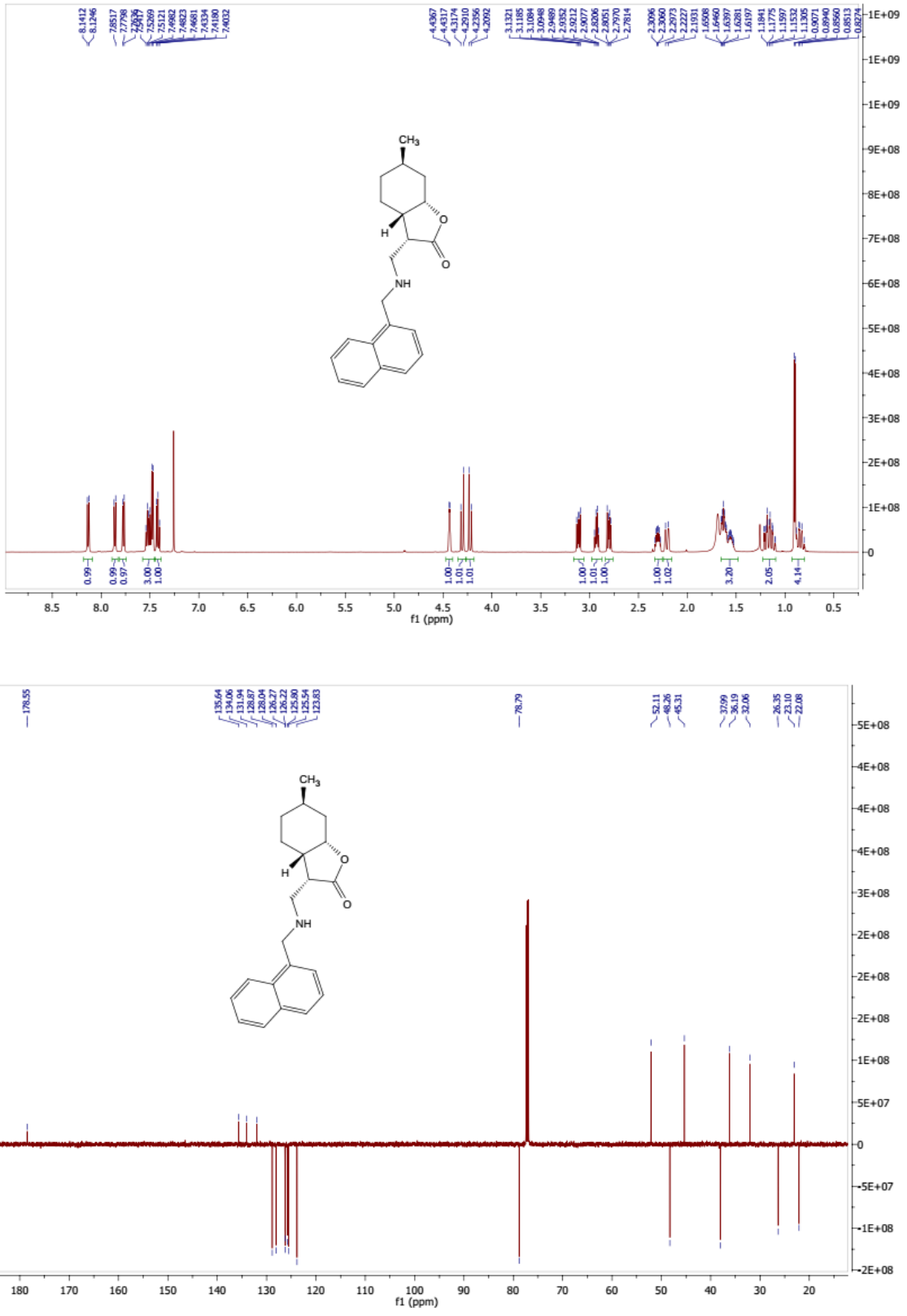
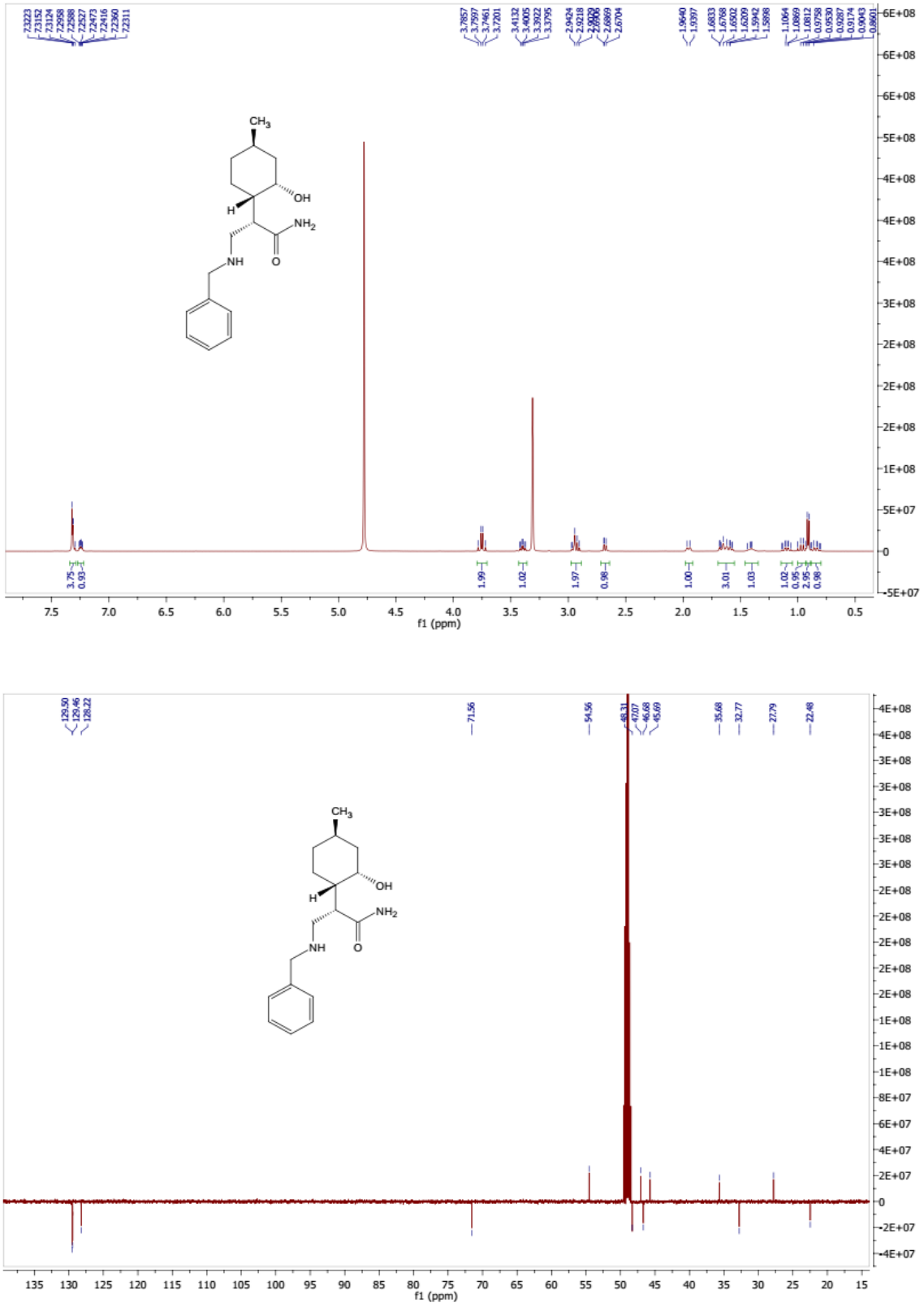


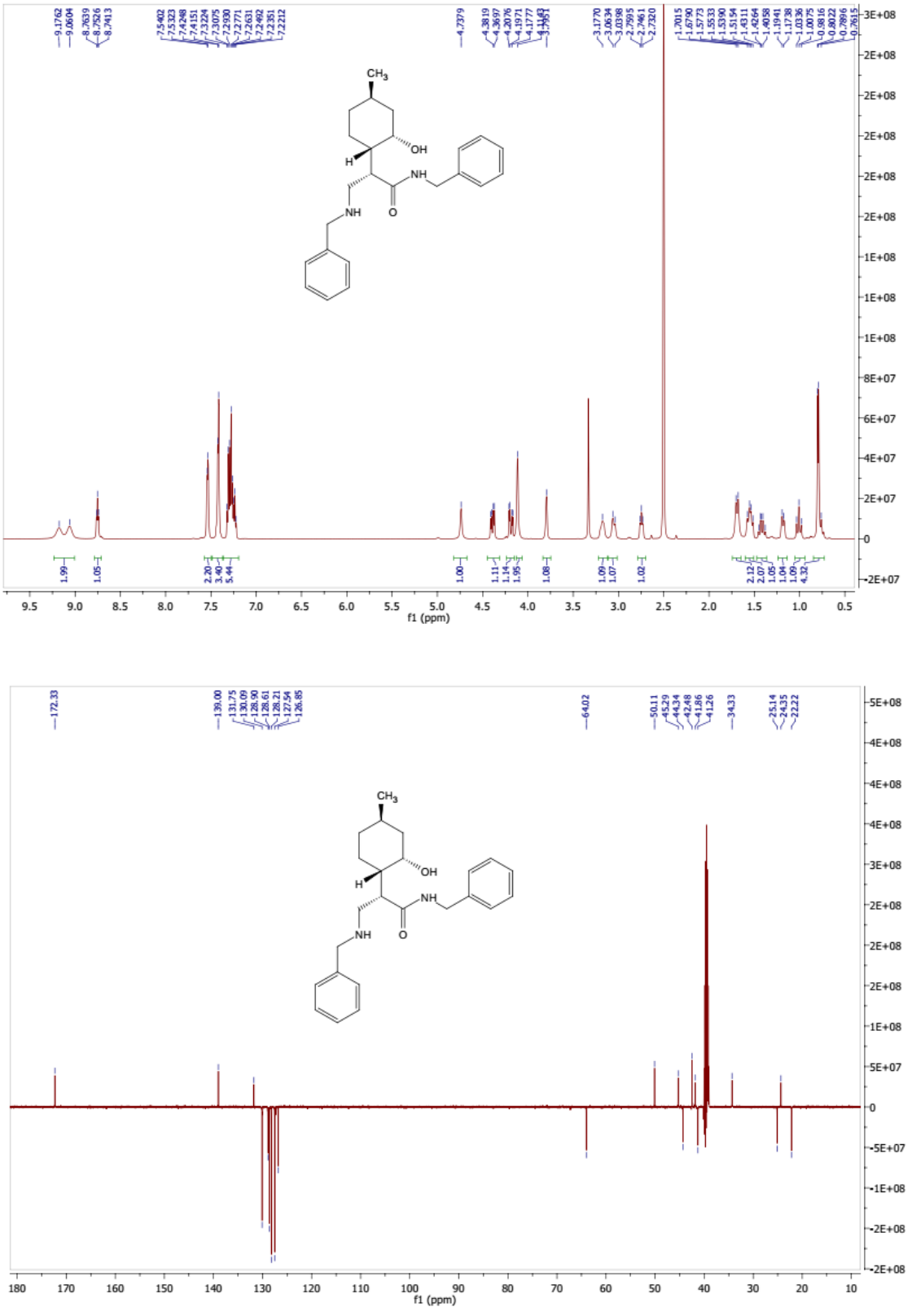
Figures S17-S18. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **29.**



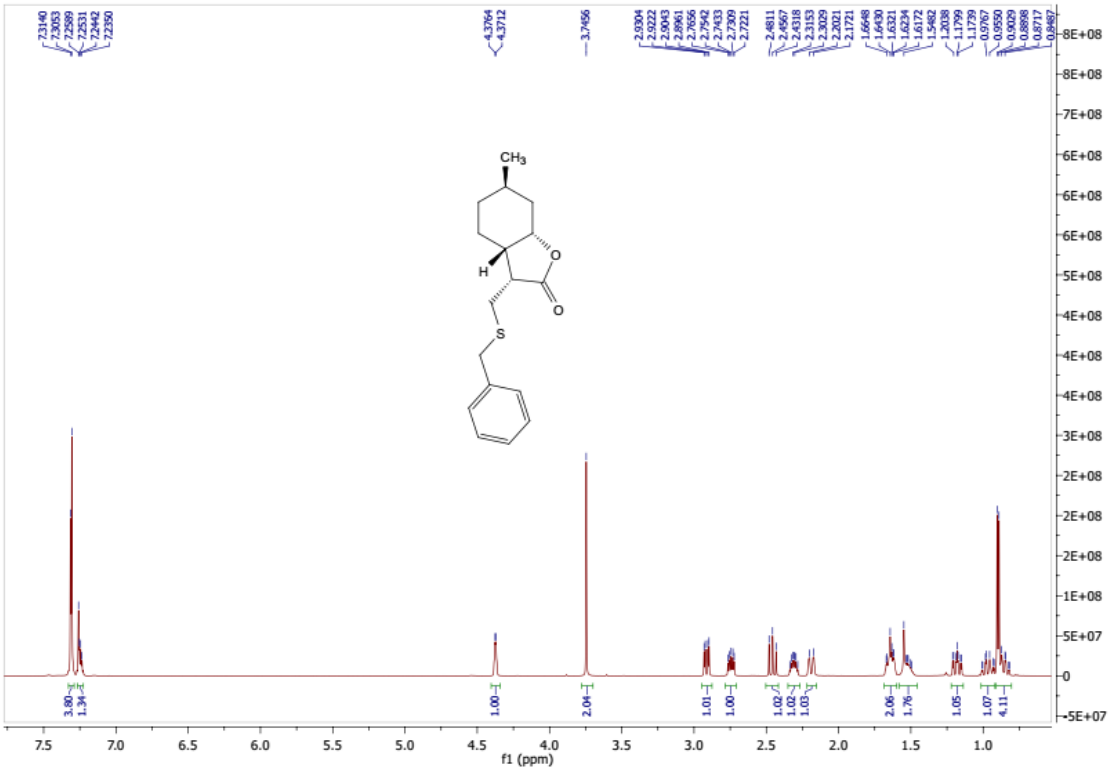
Figures S19-S20. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **30.**

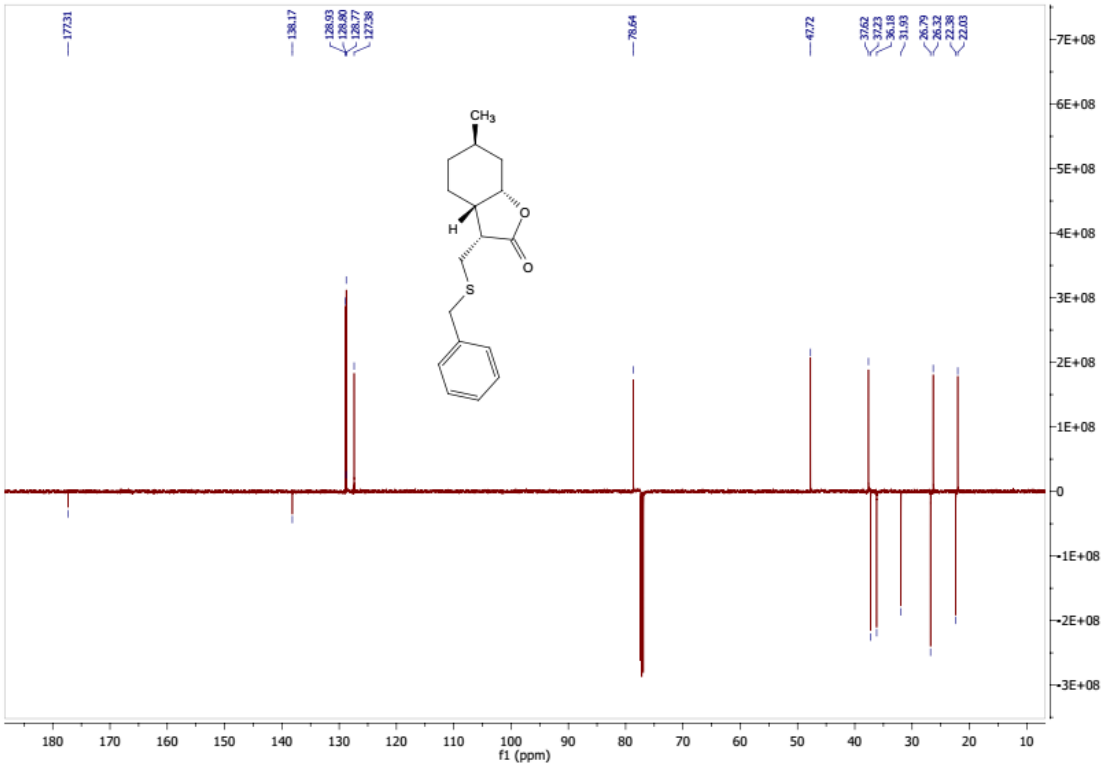


Figures S21-S22. ^{1}H (500 MHz, CD_3OD) and ^{13}C (125 MHz, CD_3OD) NMR spectra of **31.**



Figures S23-S24. ^{1}H (500 MHz, DMSO-d_6) and ^{13}C (125 MHz, DMSO-d_6) NMR spectra of **32.**





Figures S25-S26. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **33.**

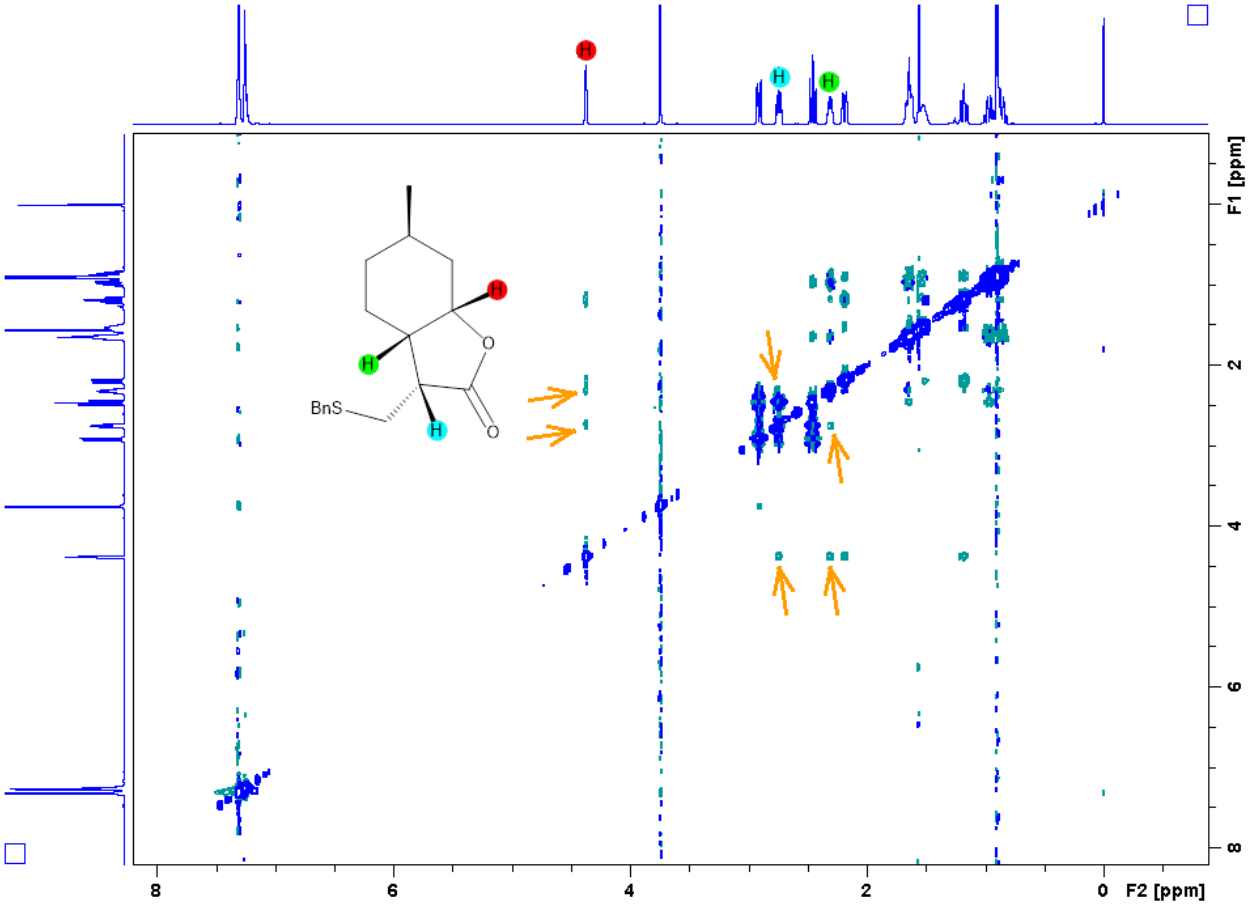
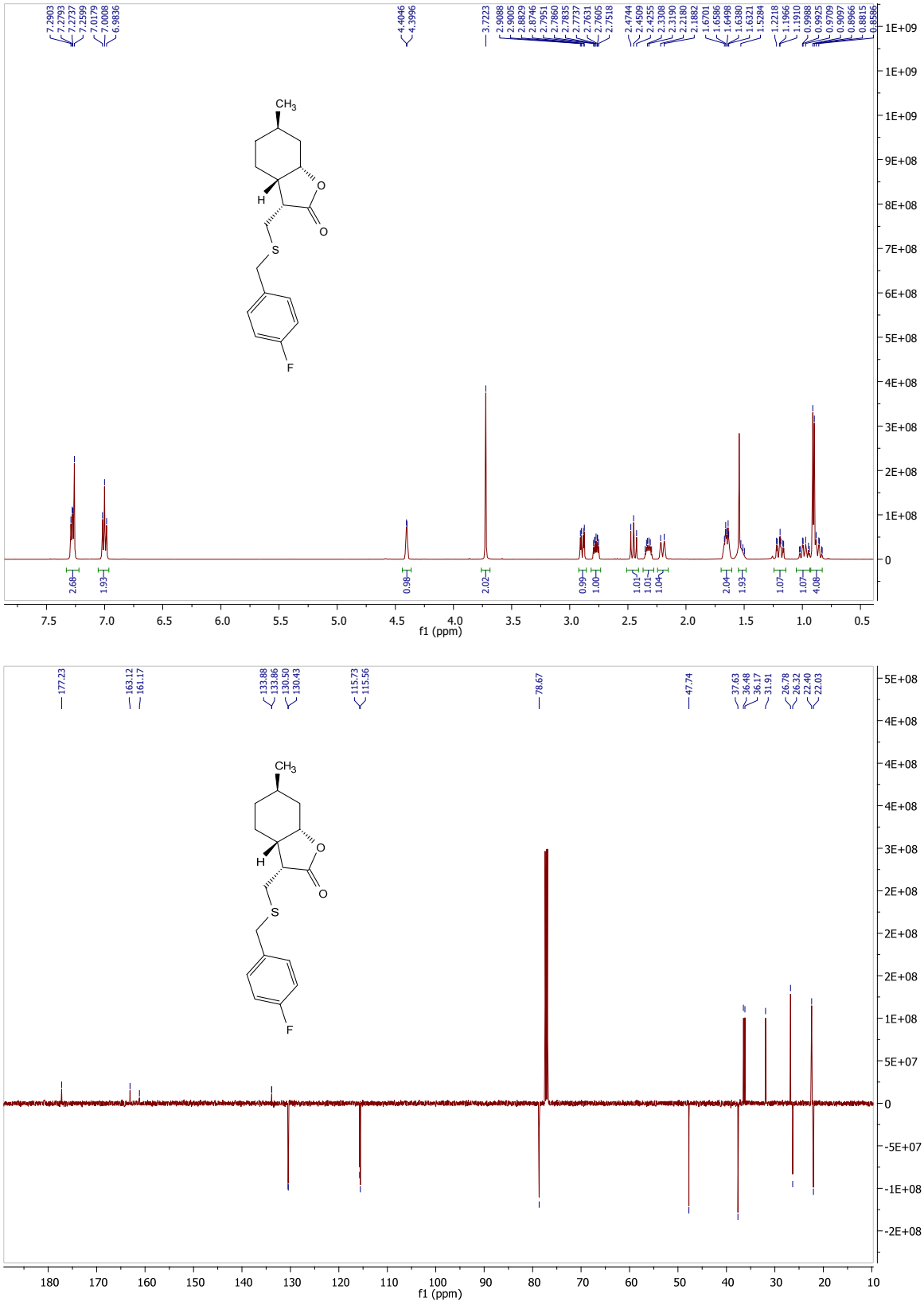


Figure S27. NOESY (500 MHz, $CDCl_3$) spectra of **33.**



Figures S28-S29. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **34.**

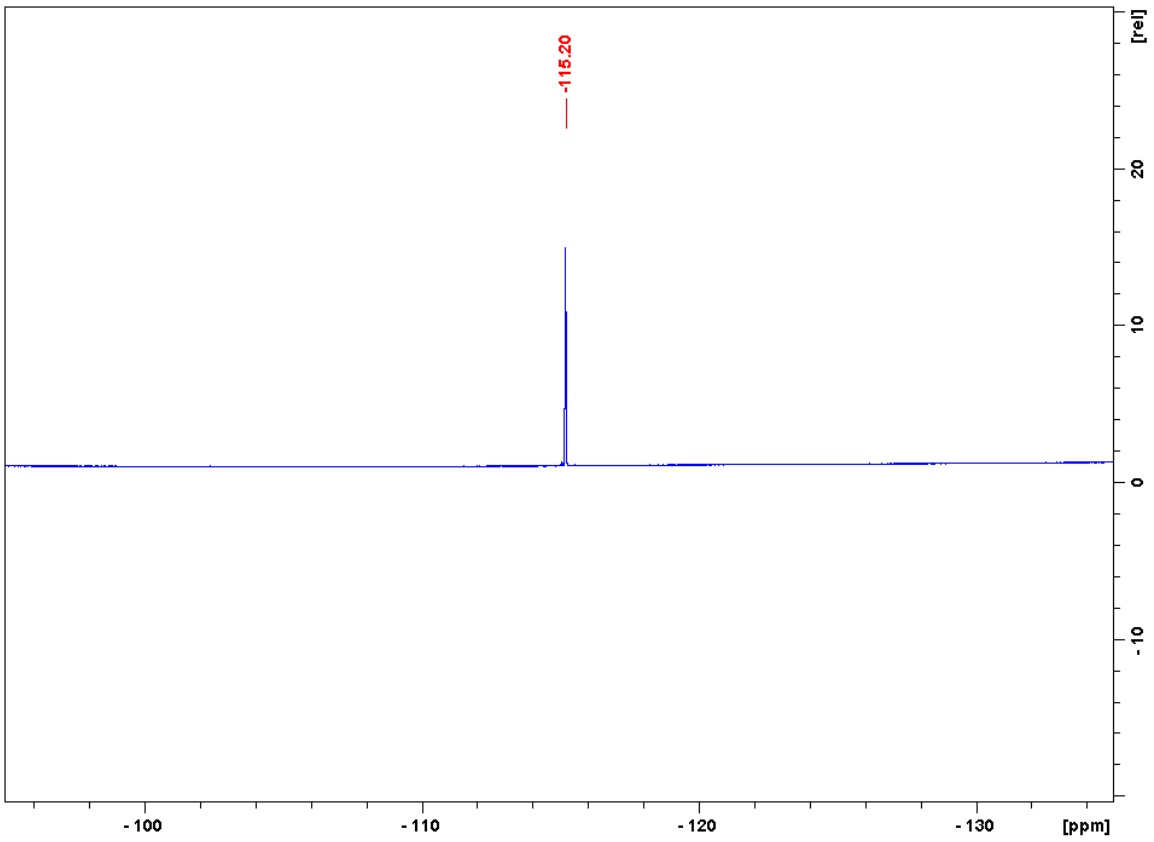
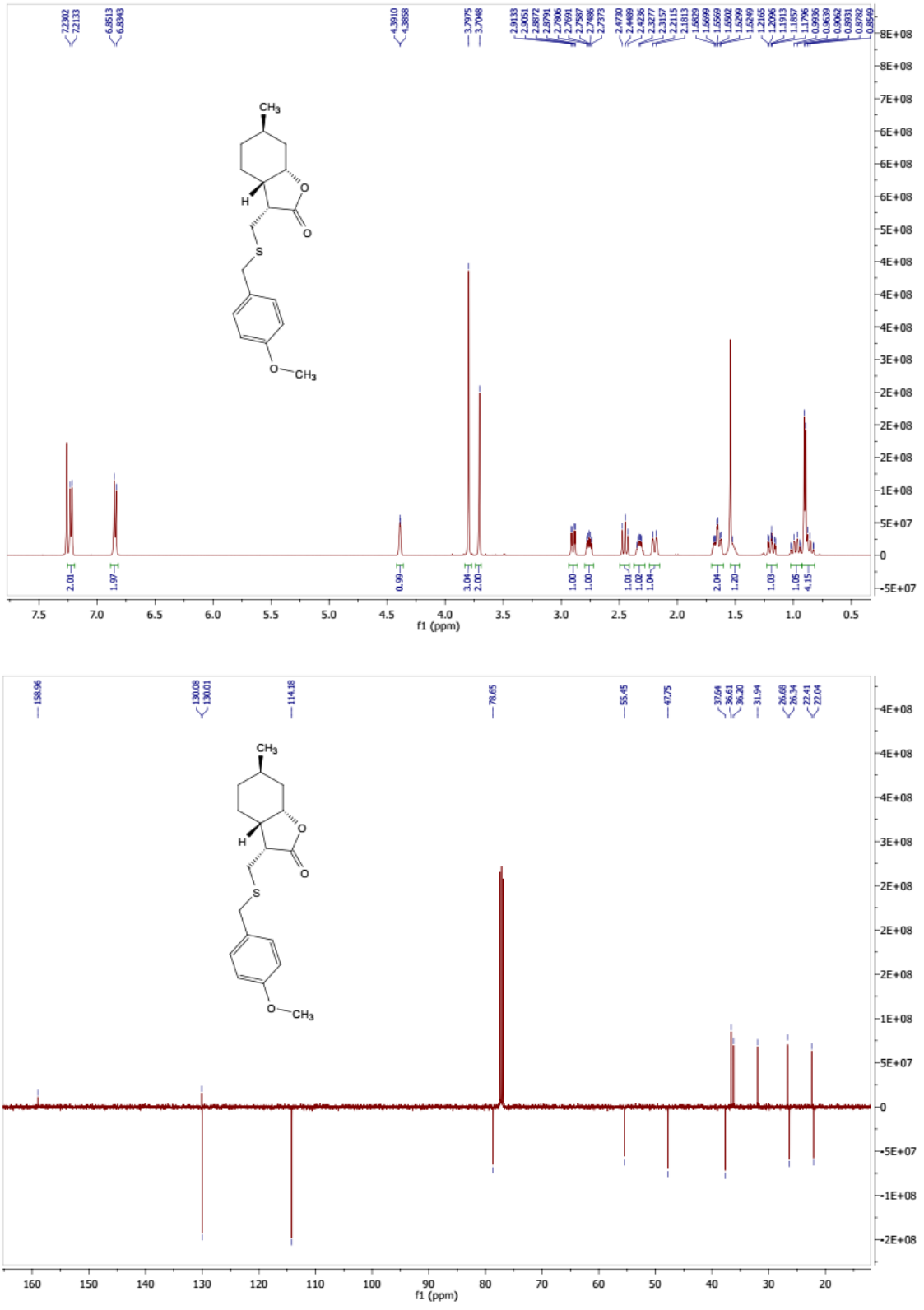
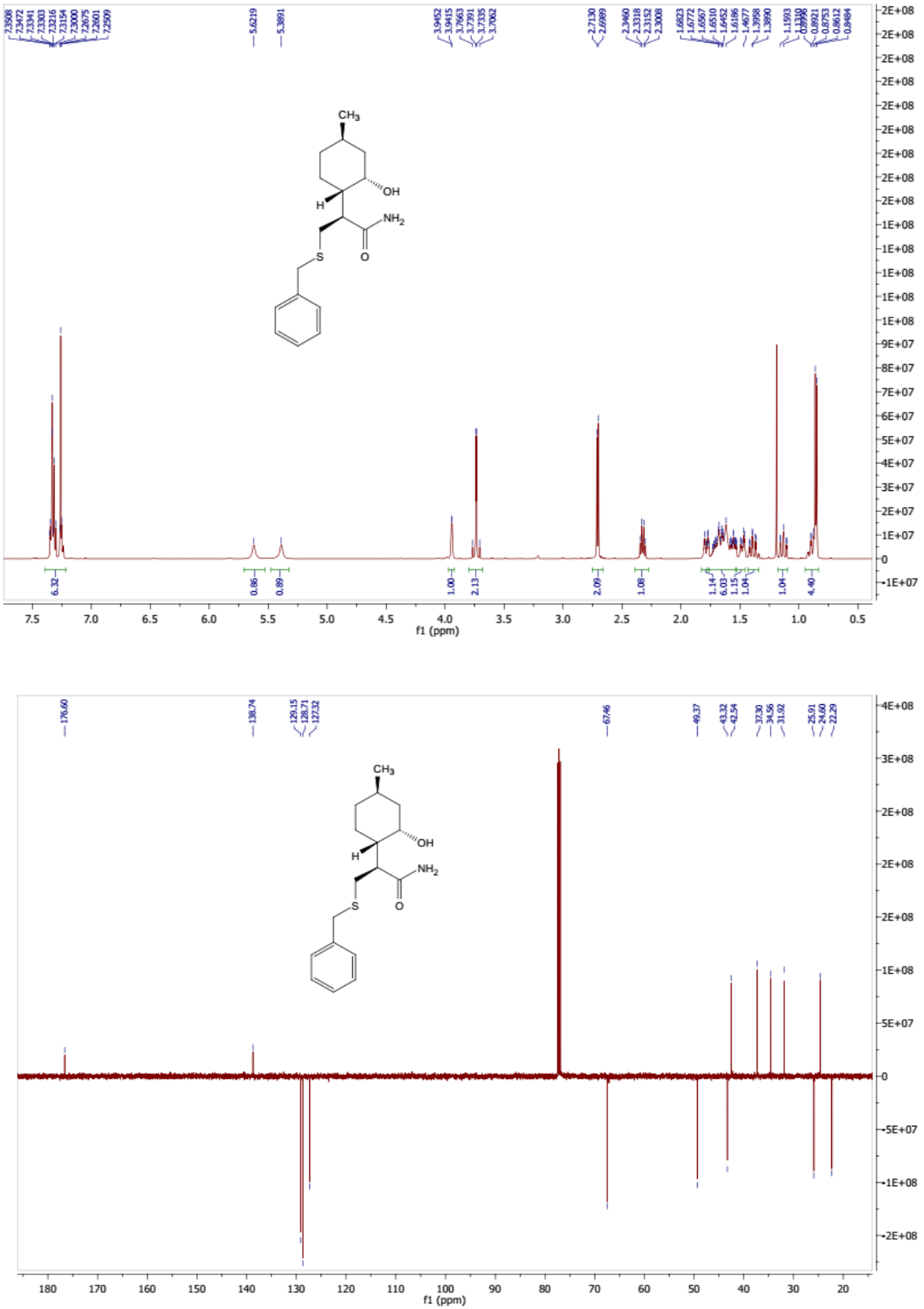


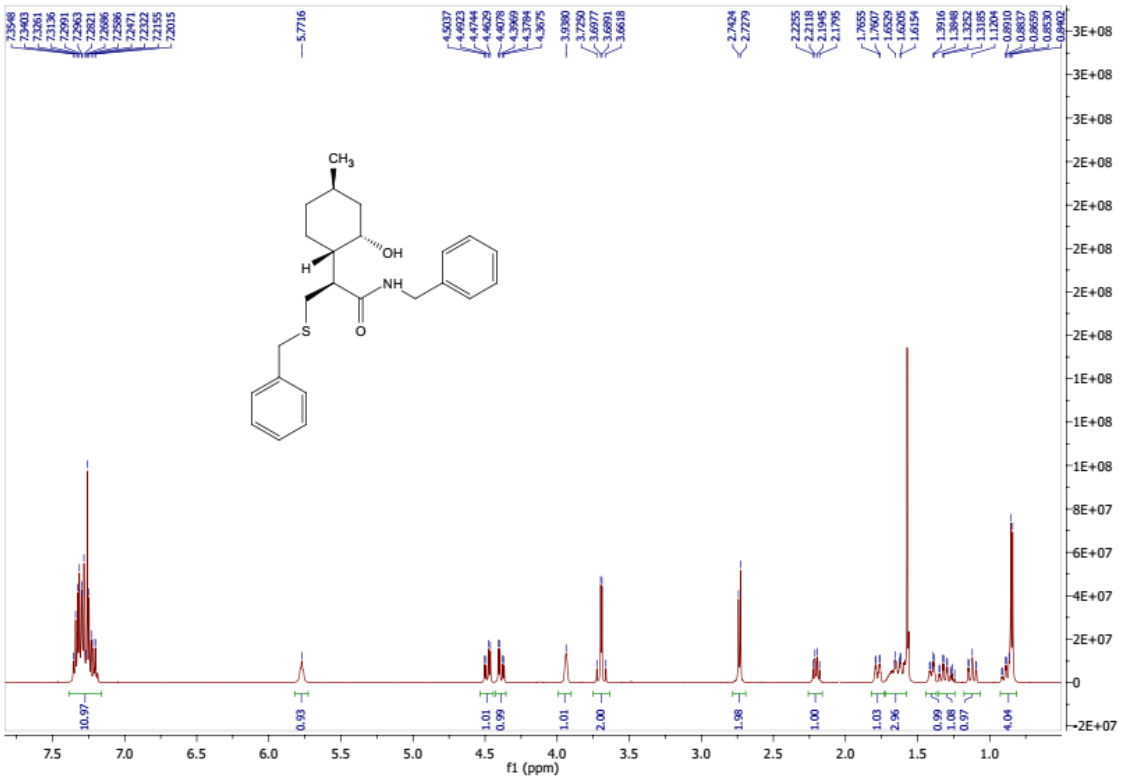
Figure S30. ^{19}F (471 MHz, $CDCl_3$) NMR spectra of **34.**

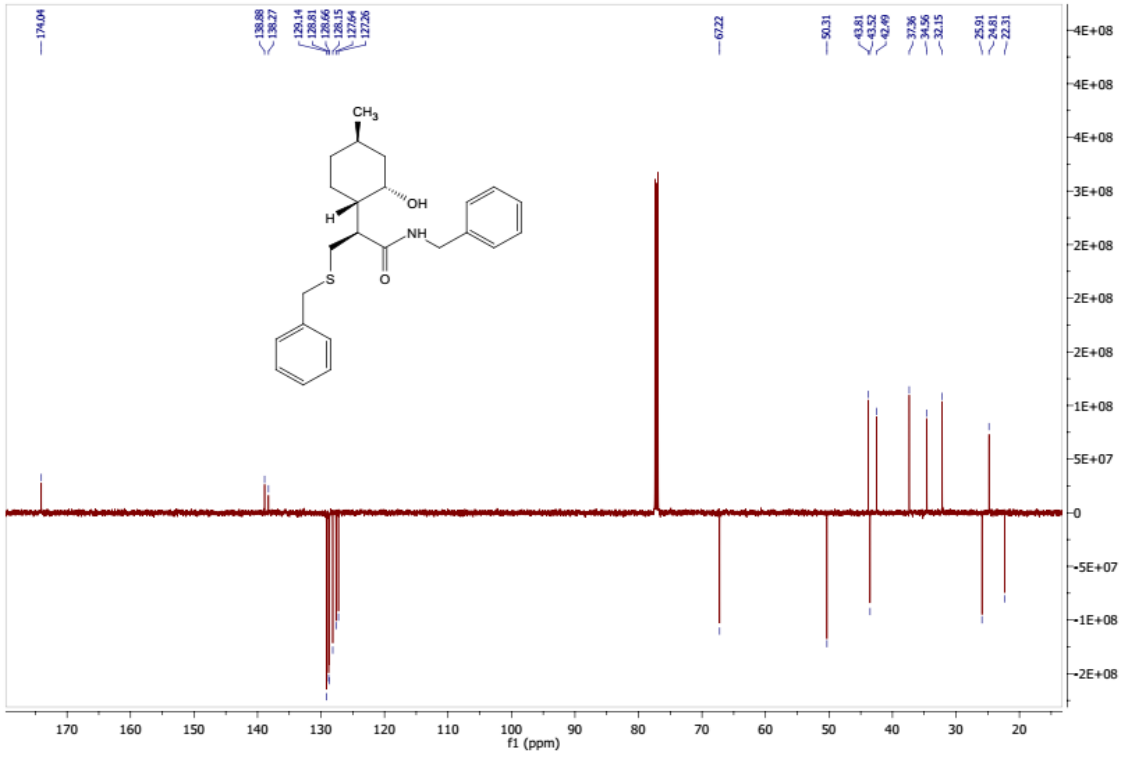


Figures S31-S32. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **35.**

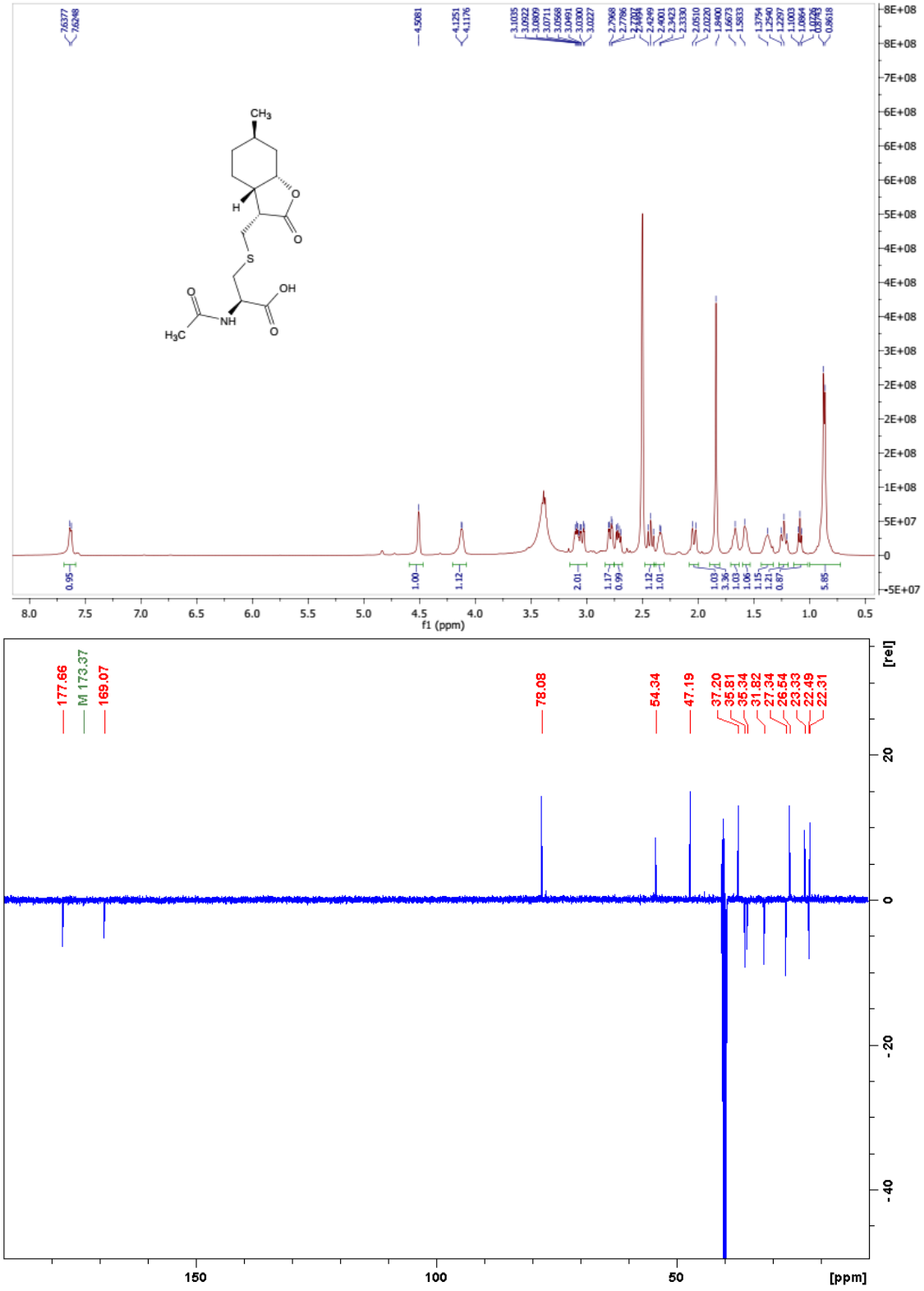


Figures S33-S34. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **36.**

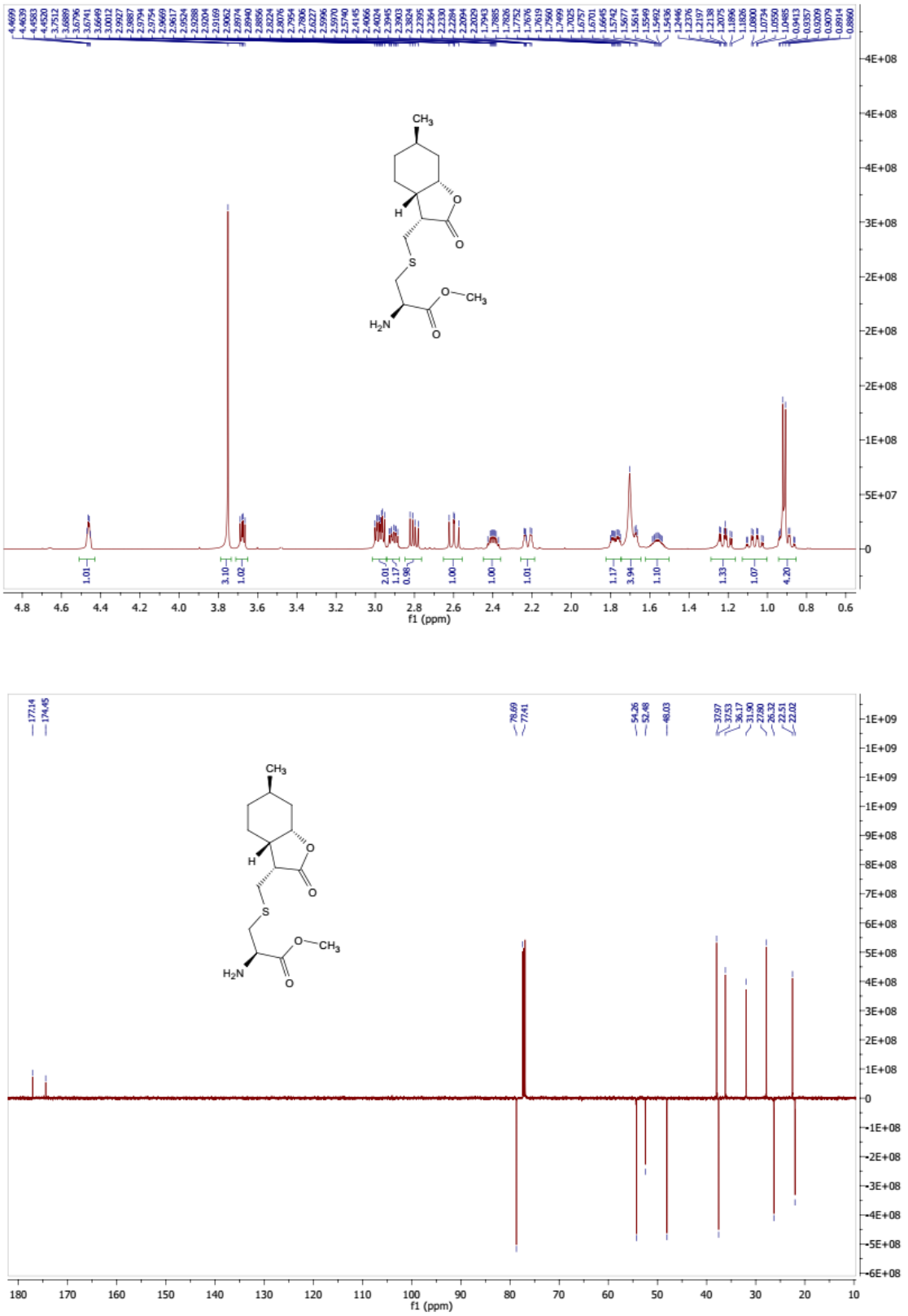




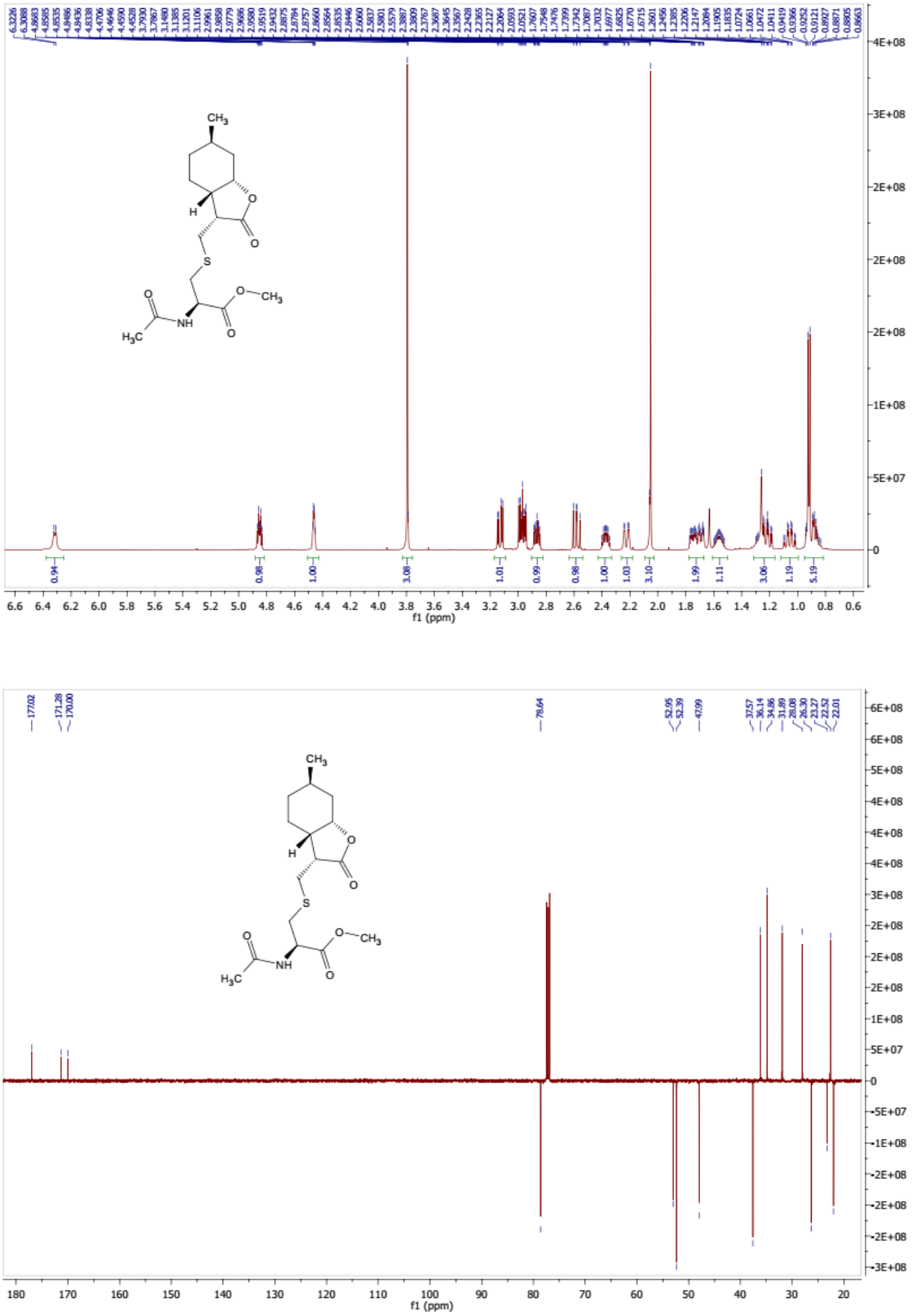
Figures S35-S36. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **37.**



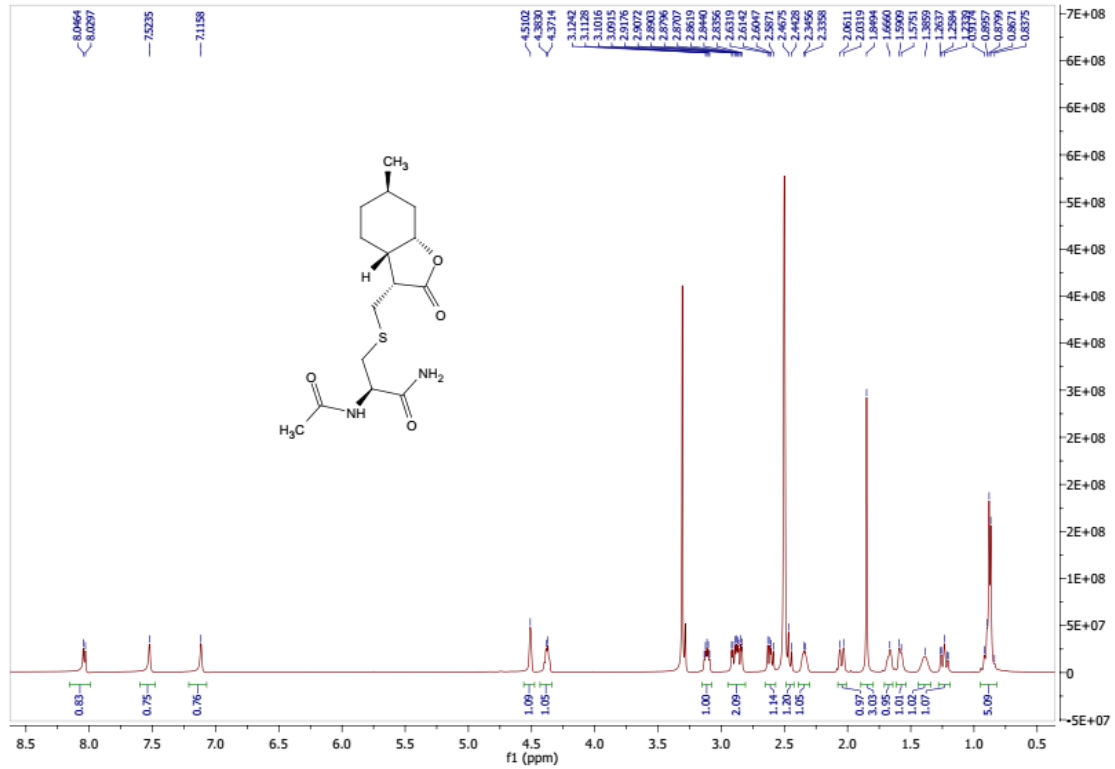
Figures S37-S38. ^{1}H (500 MHz, DMSO-*d*$_6$) and ^{13}C (125 MHz, DMSO-*d*$_6$) NMR spectra of **38.**

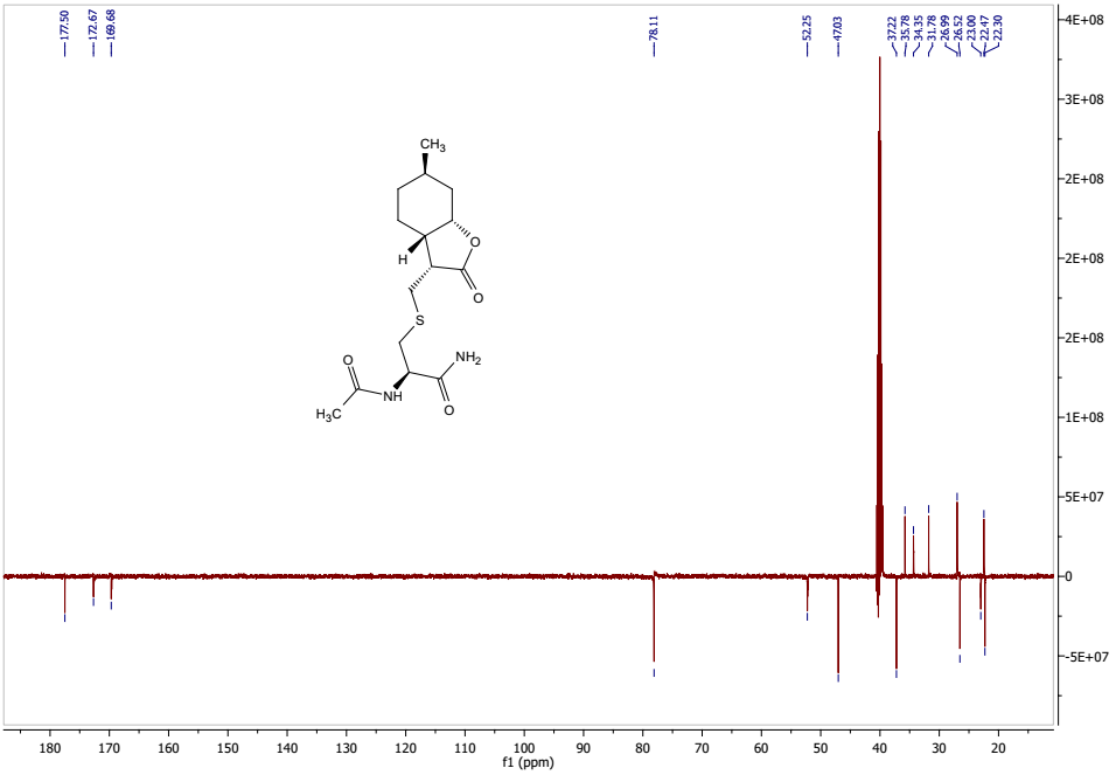


Figures S39-S40. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **39.**

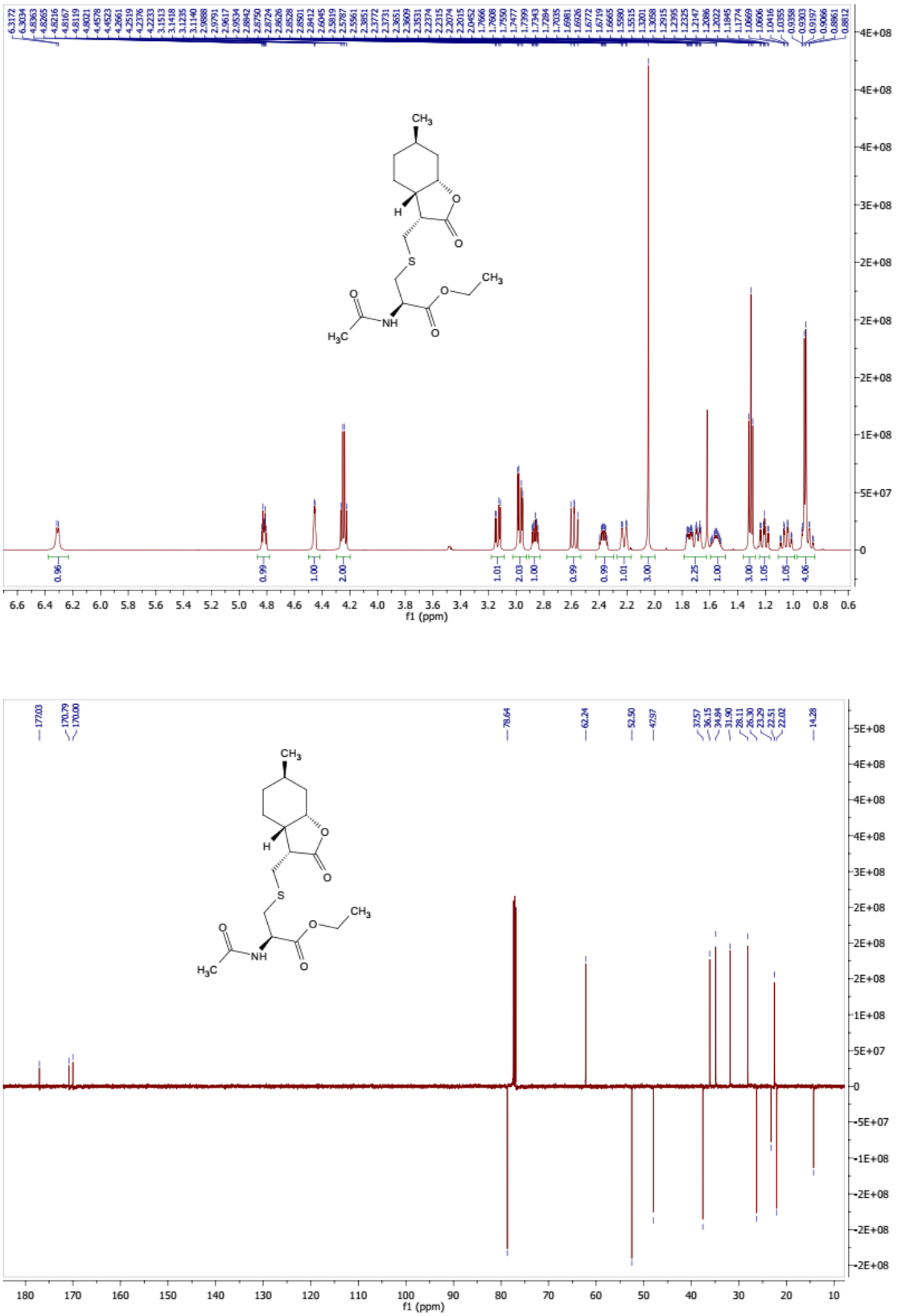


Figures S41-S42. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **40.**

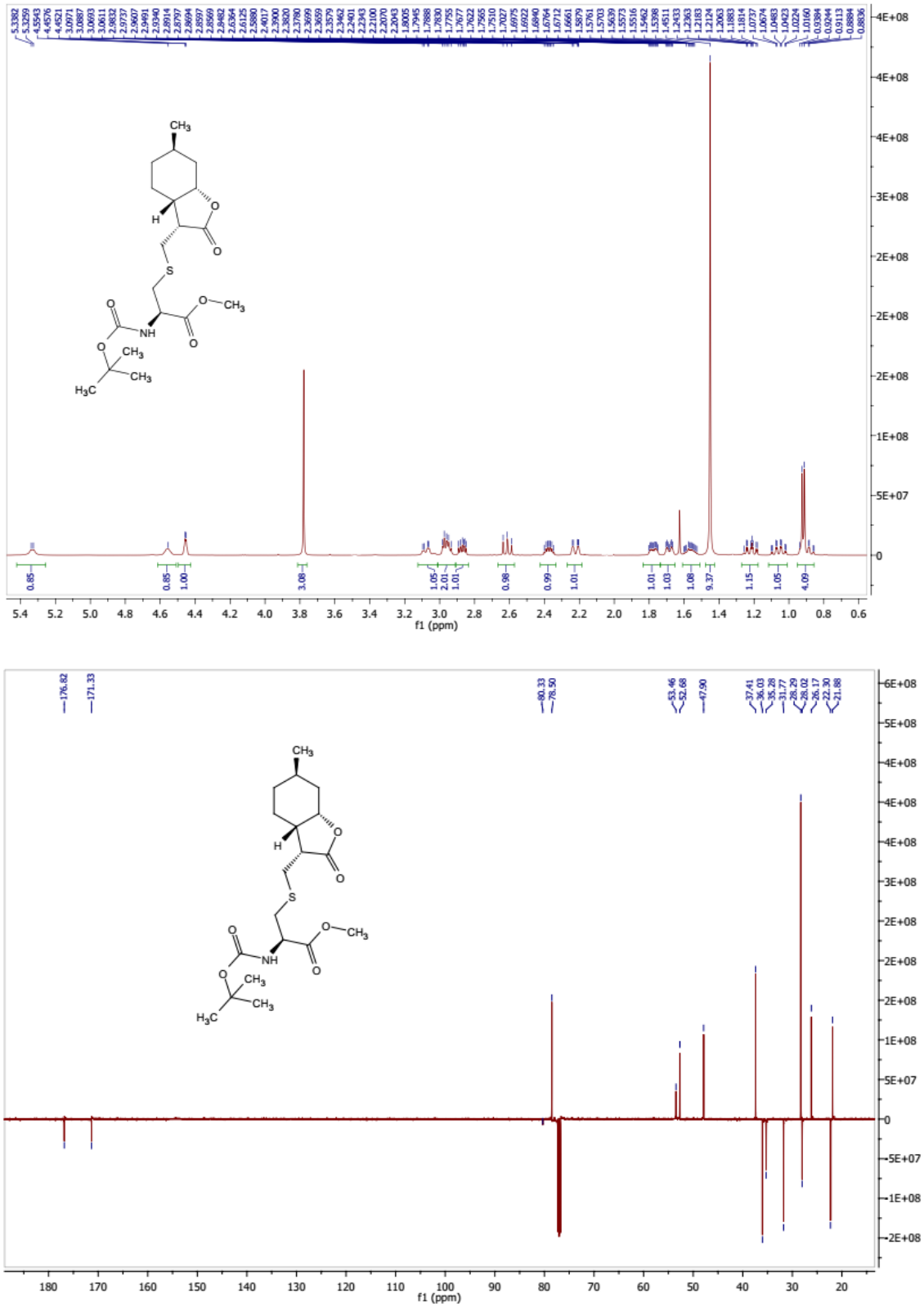




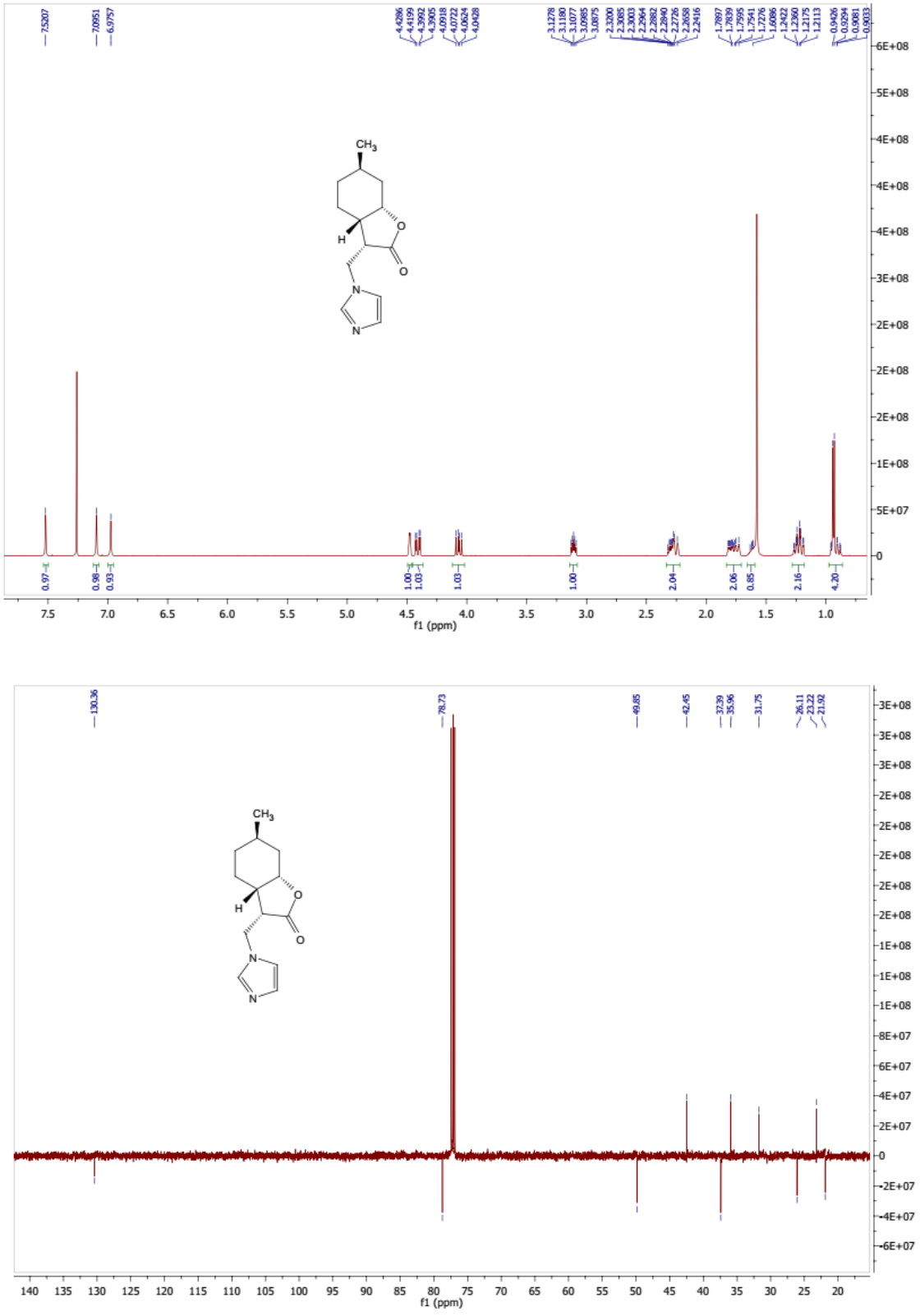
Figures S43-S44. ^{1}H (500 MHz, DMSO-d_6) and ^{13}C (125 MHz, DMSO-d_6) NMR spectra of **41.**



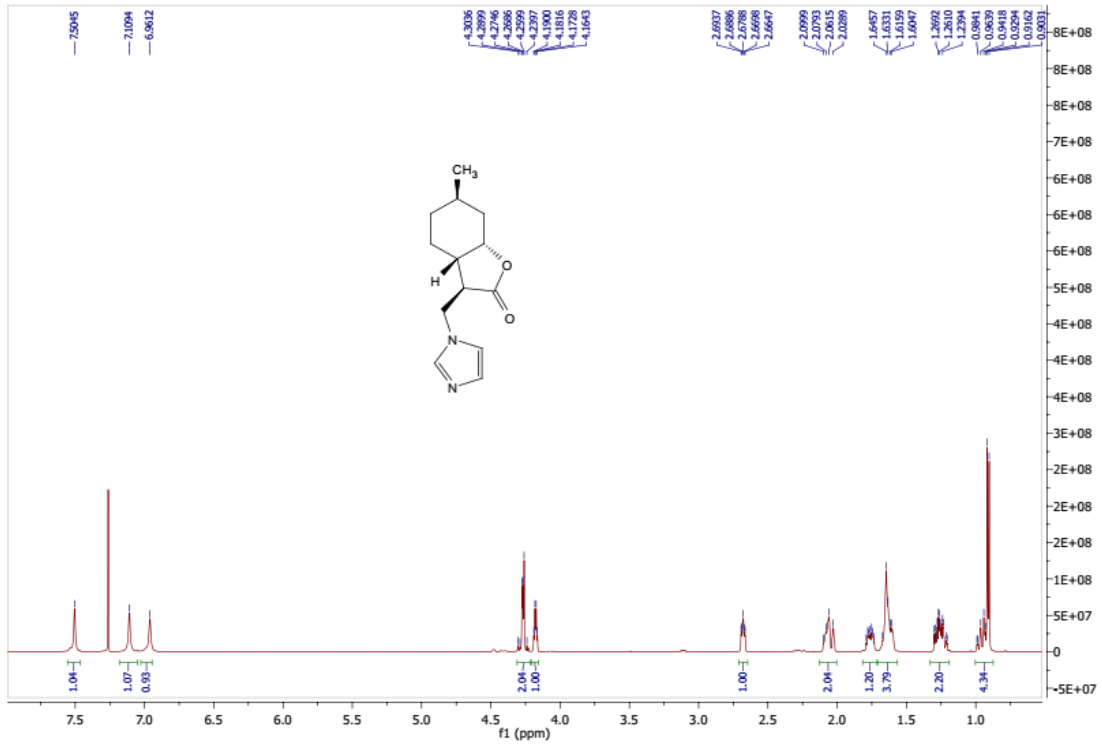
Figures S45-S46. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **42.**

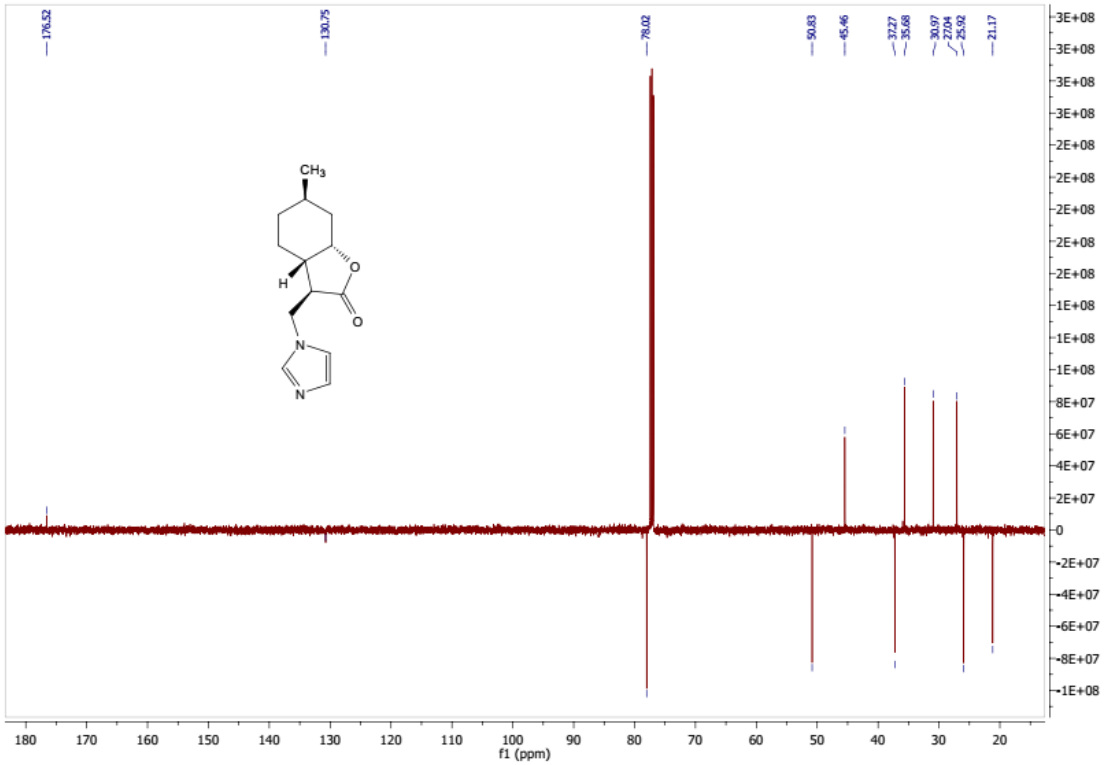


Figures S47-S48. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **43.**

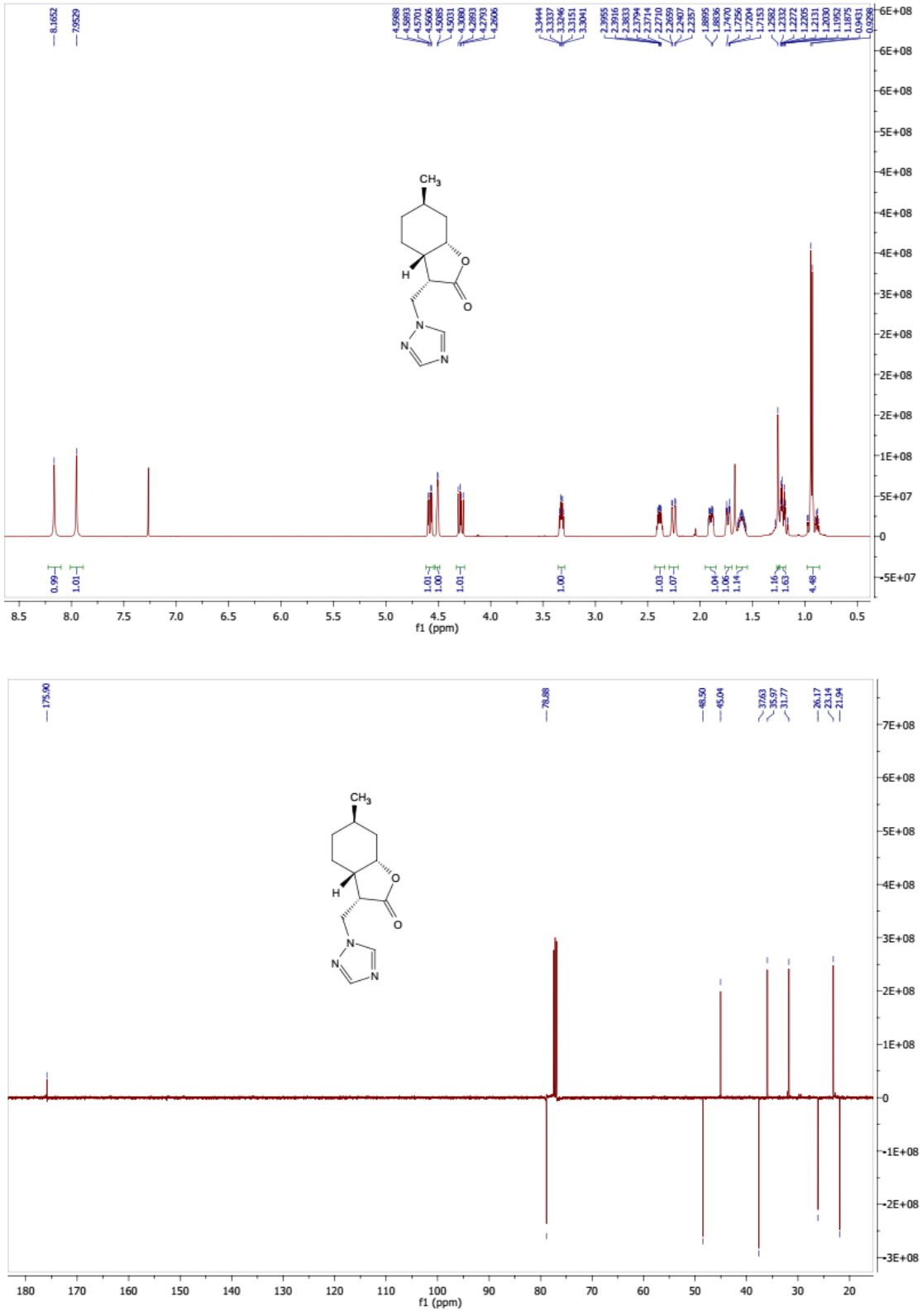


Figures S49-S50. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **44a.**

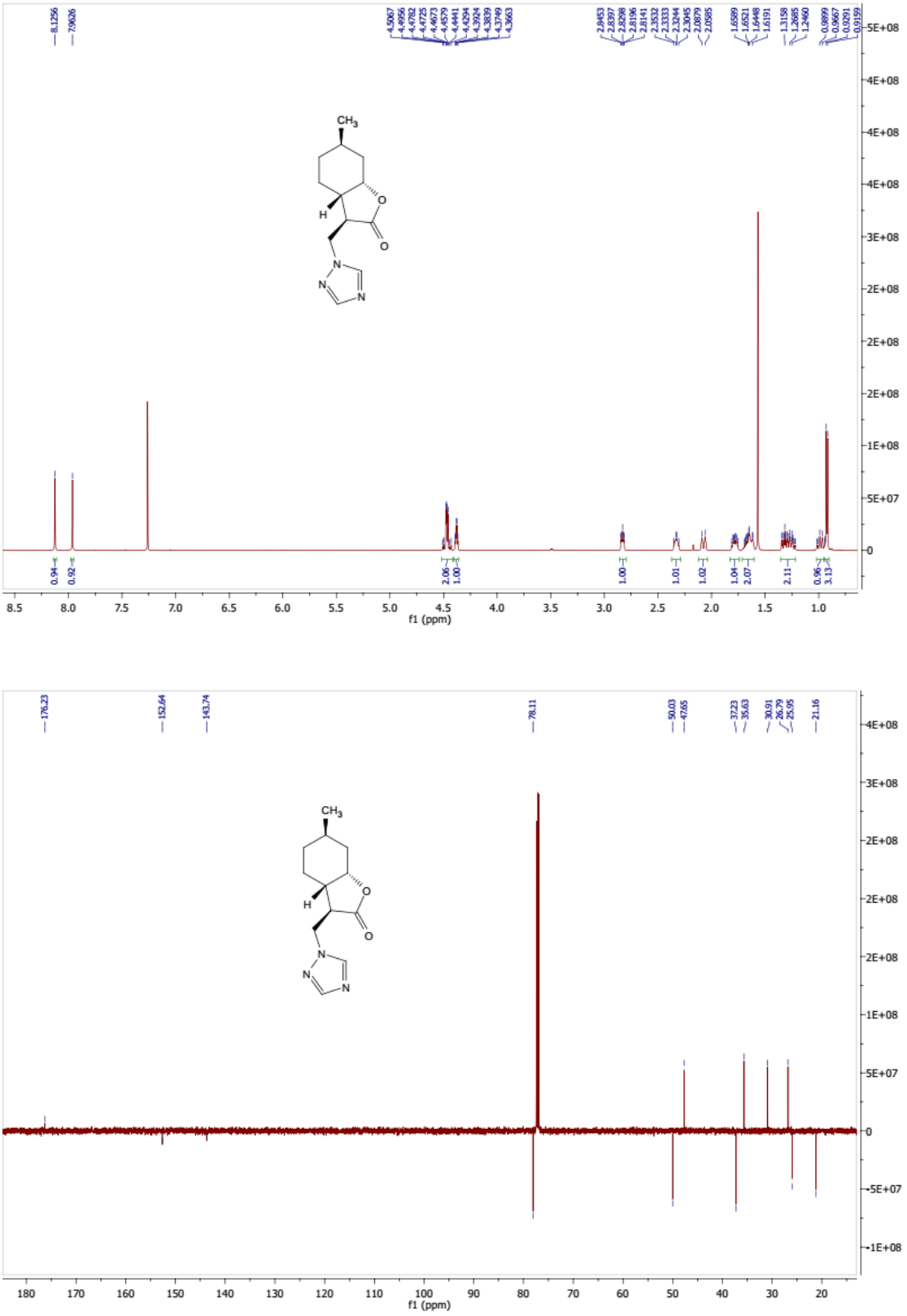




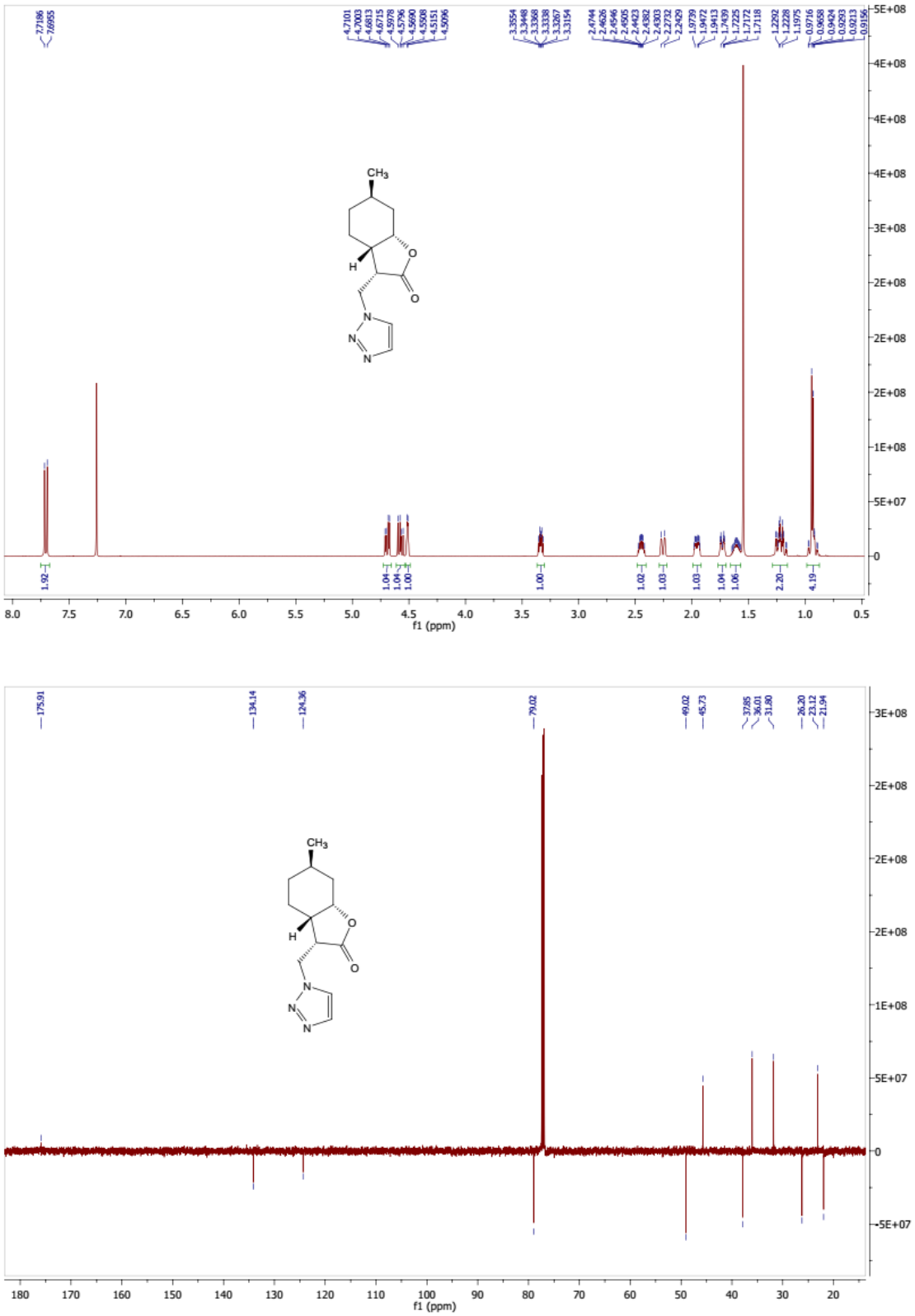
Figures S51-S52. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **44b.**



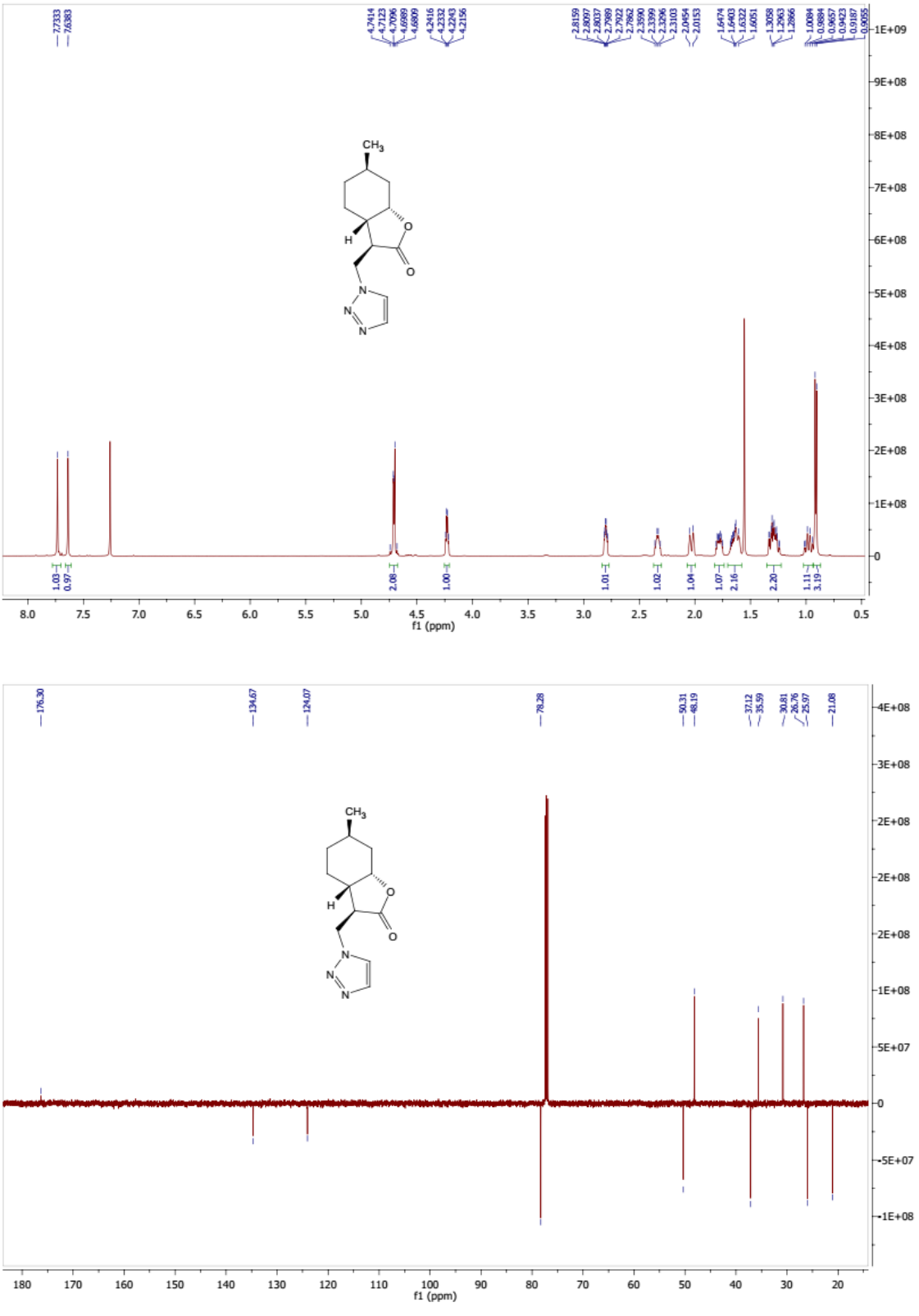
Figures S53-S54. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **45a.**



Figures S55-S56. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **45b.**



Figures S57-S58. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **46a.**



Figures S59-S60. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **46b.**

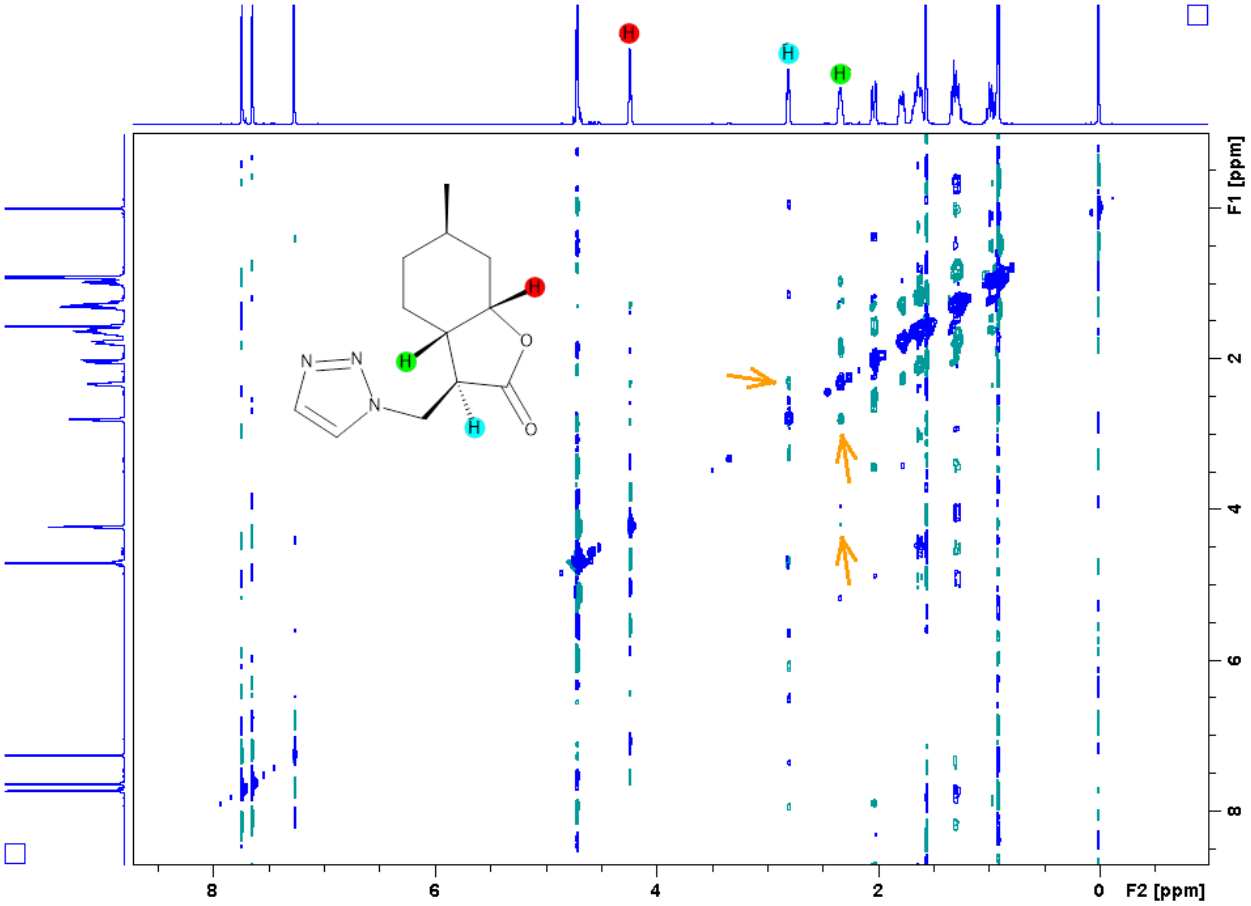
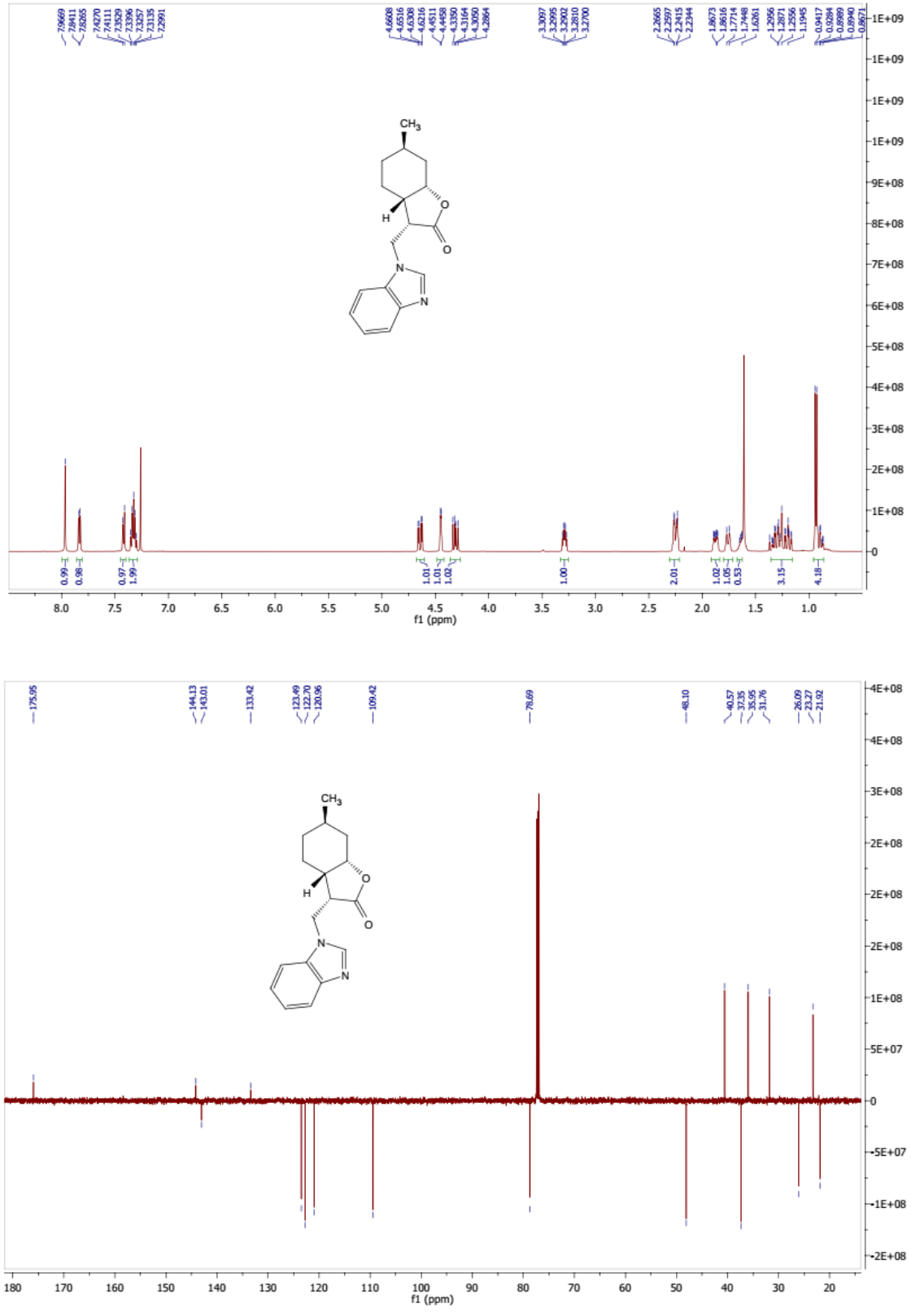


Figure S61. NOESY (500 MHz, $CDCl_3$) spectra of **46b.**



Figures S62-S63. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **47a.**

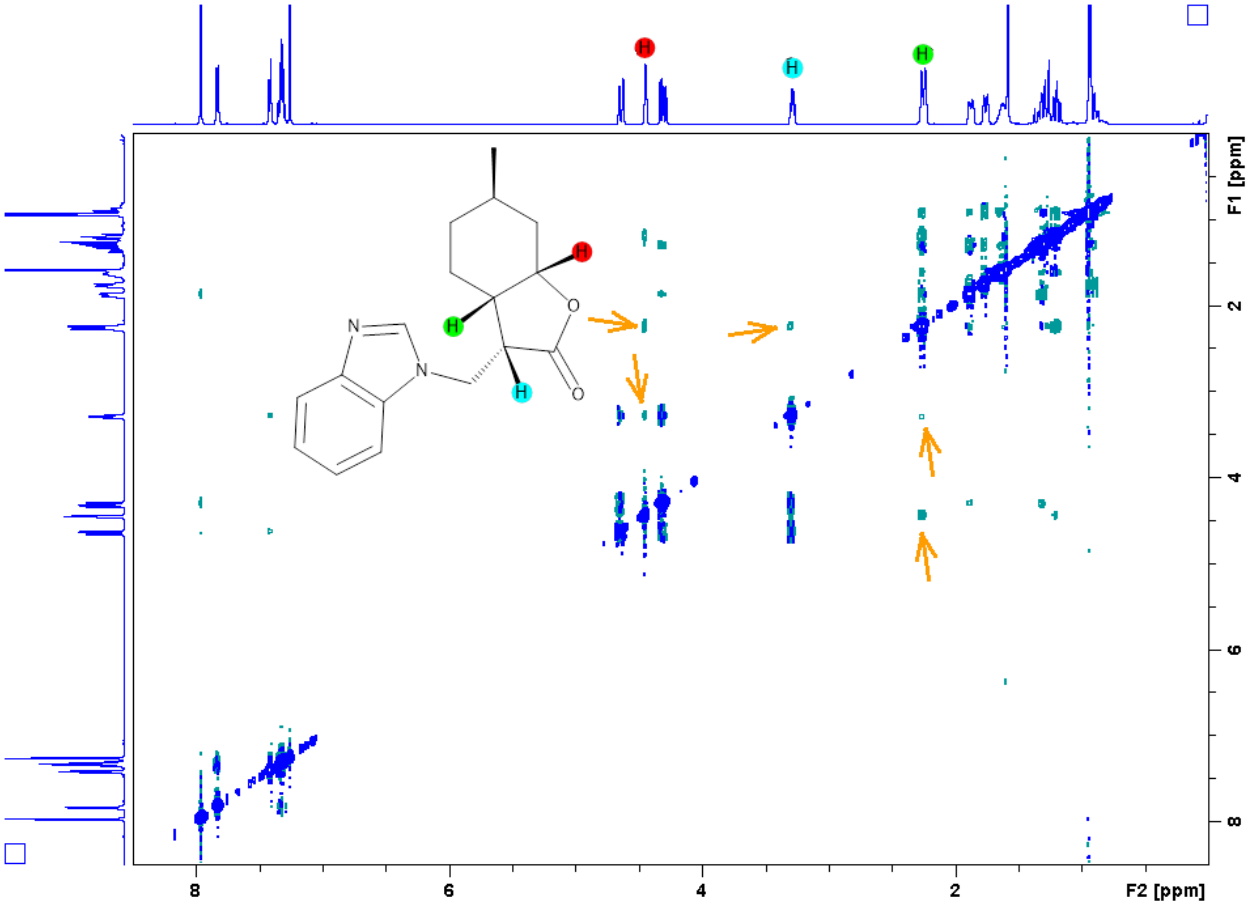
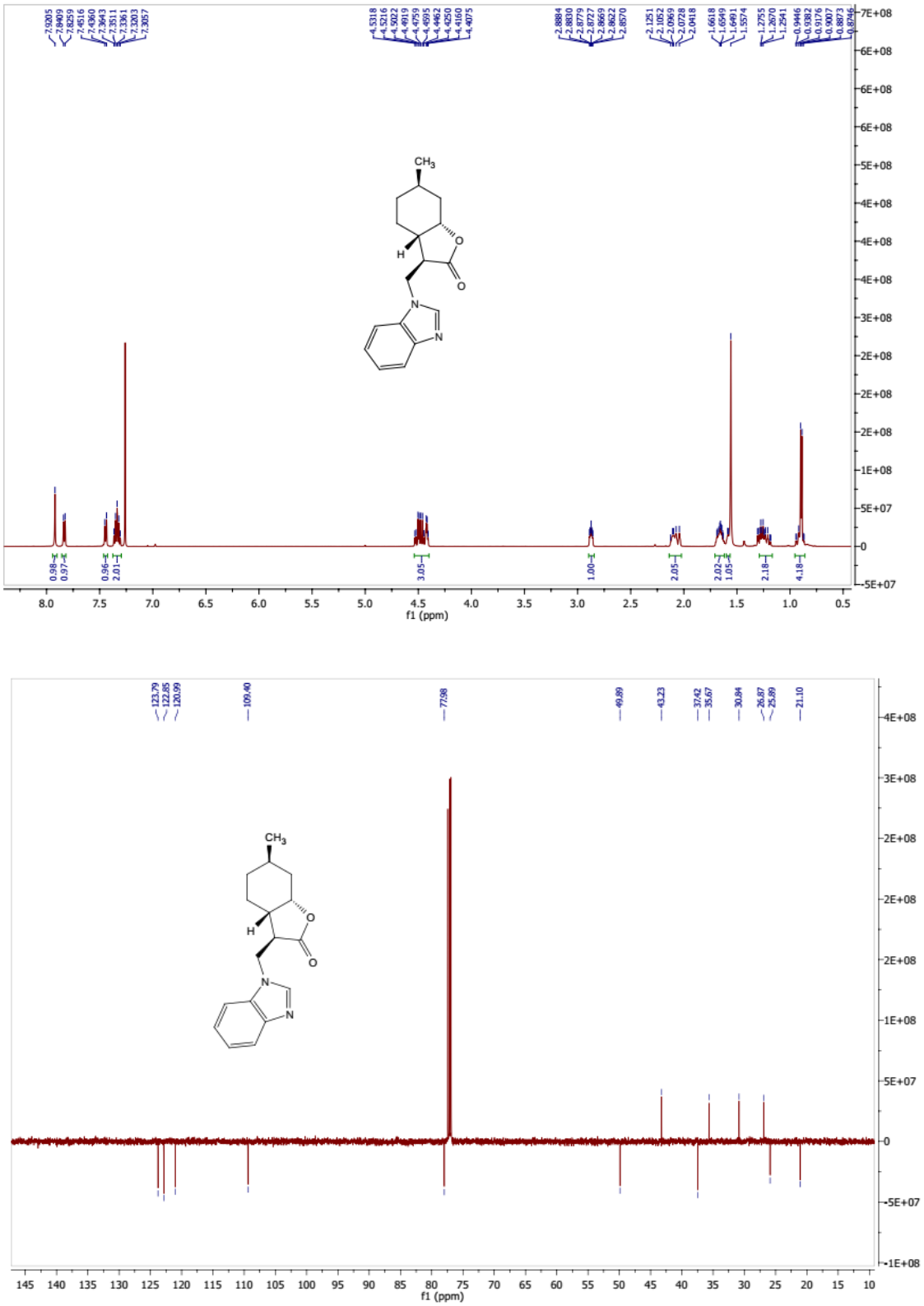


Figure S64. NOESY (500 MHz, $CDCl_3$) spectra of **47a.**



Figures S65-S66. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **47b.**

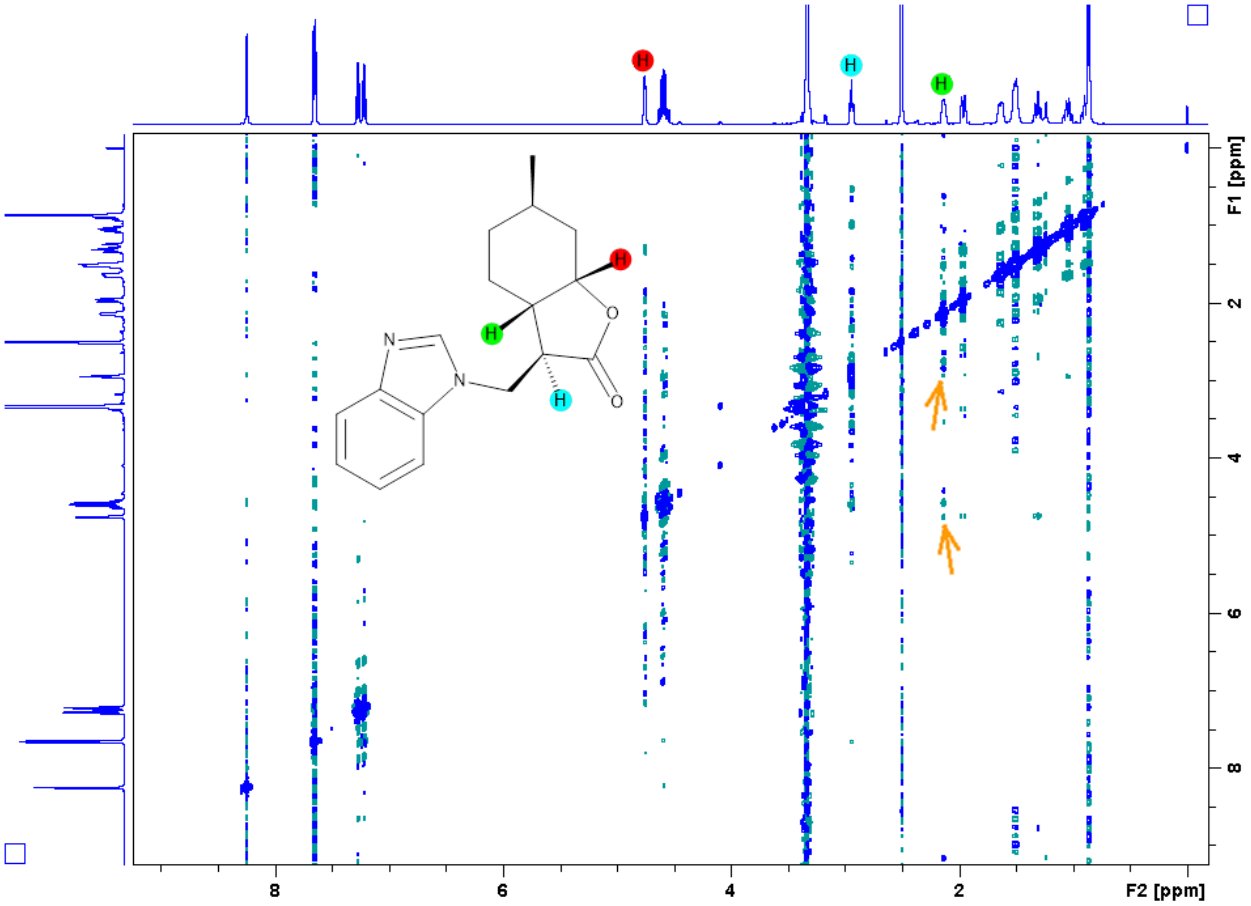
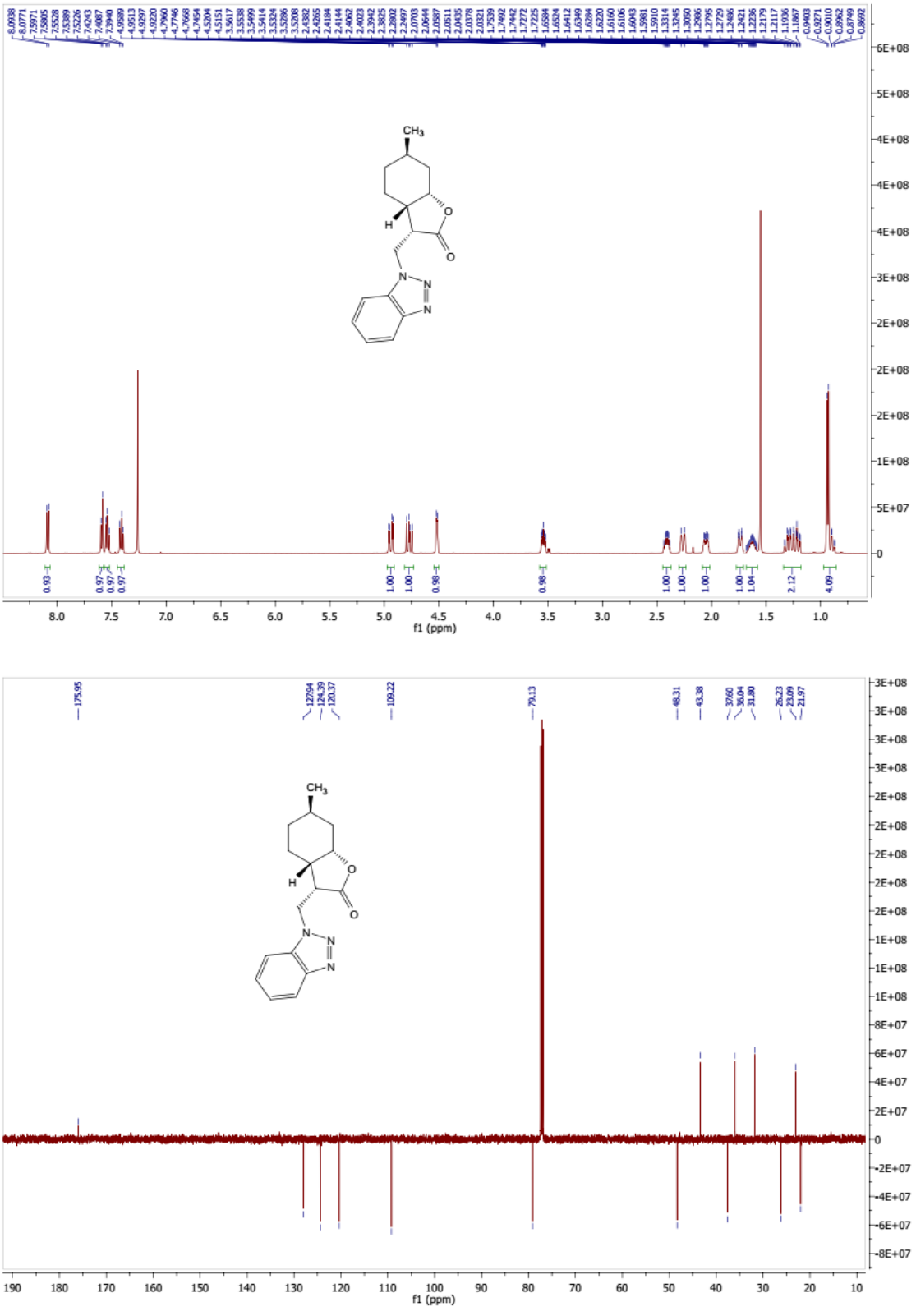
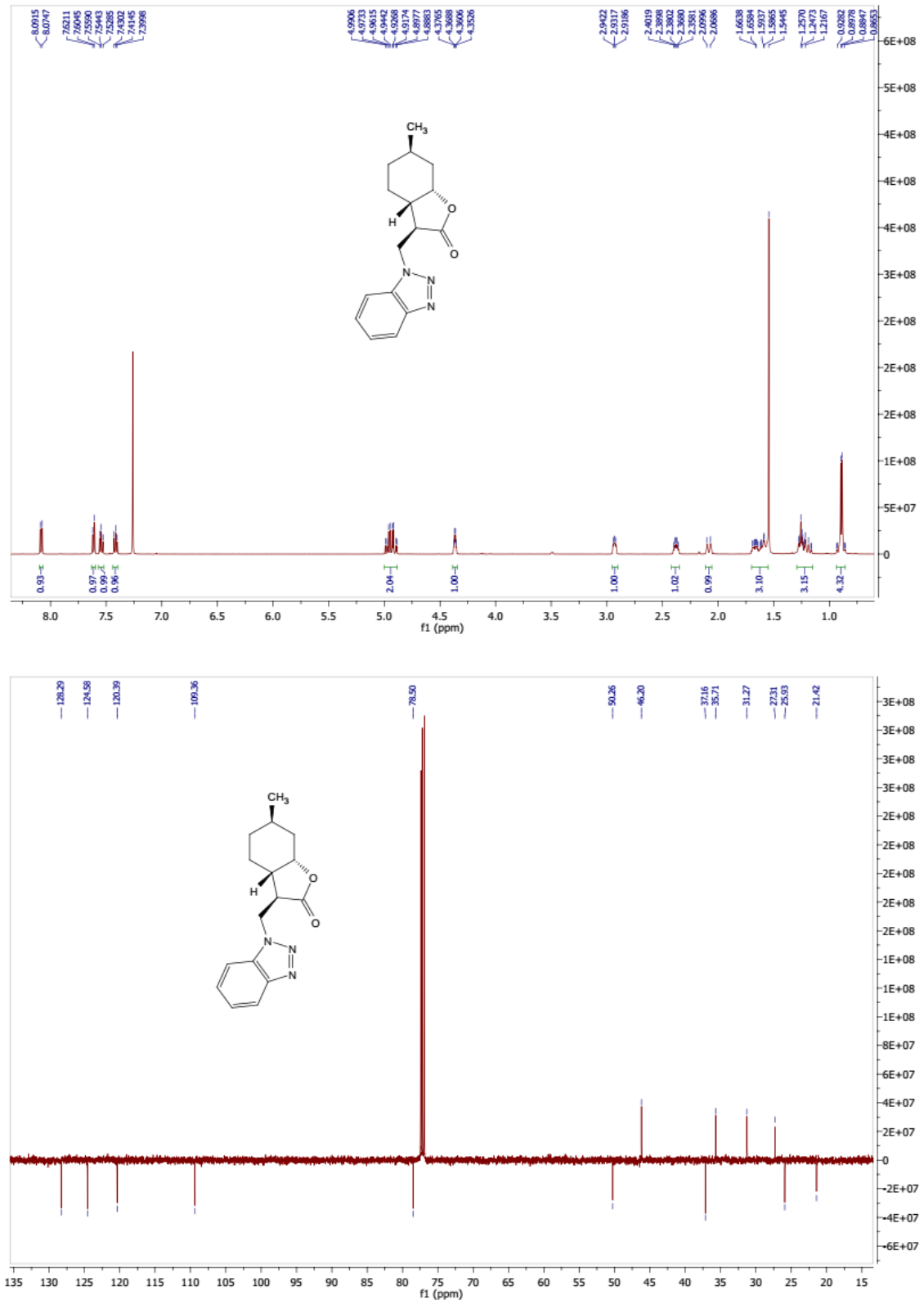


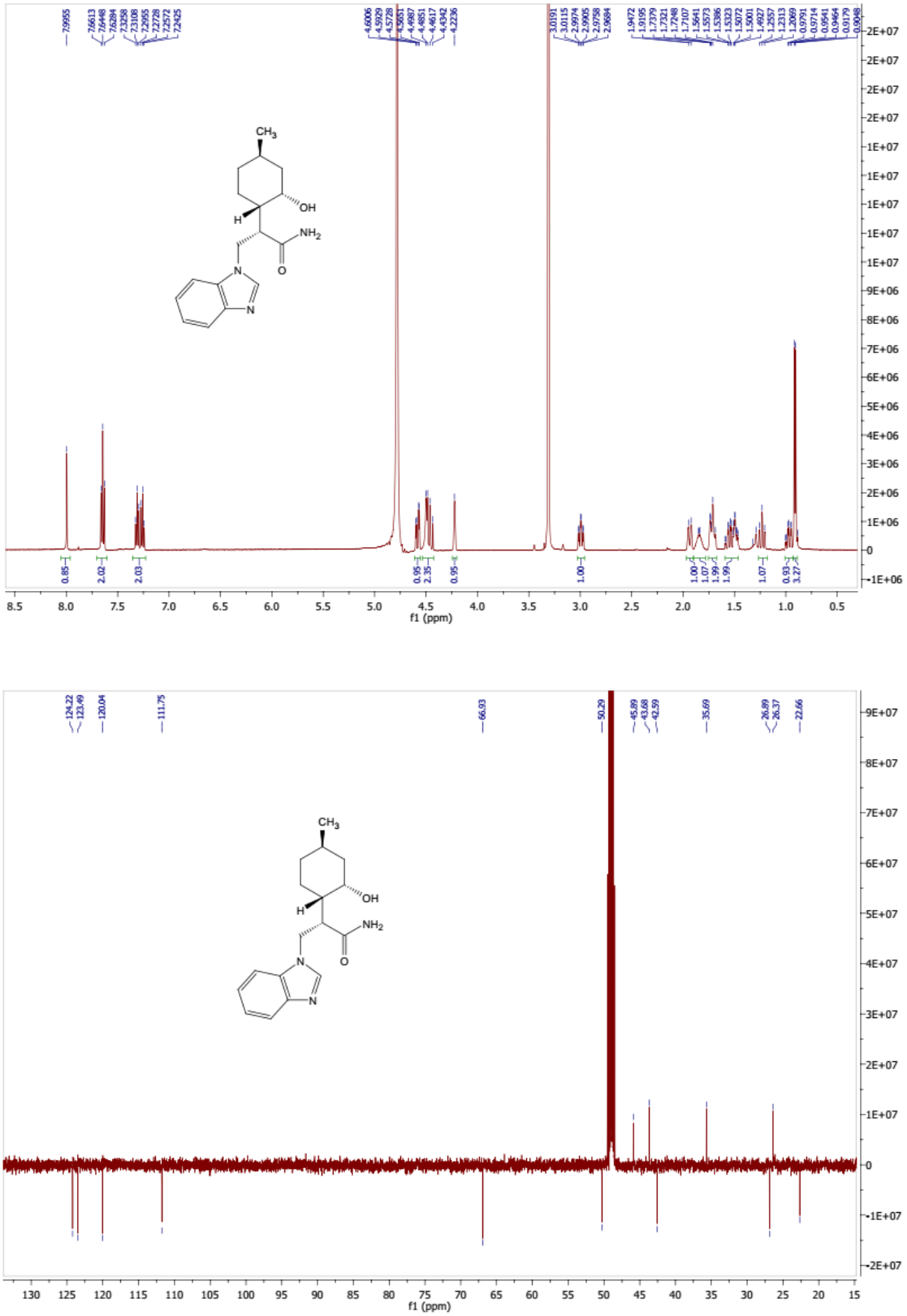
Figure S67. NOESY (500 MHz, DMSO-d_6) spectra of **47b.**



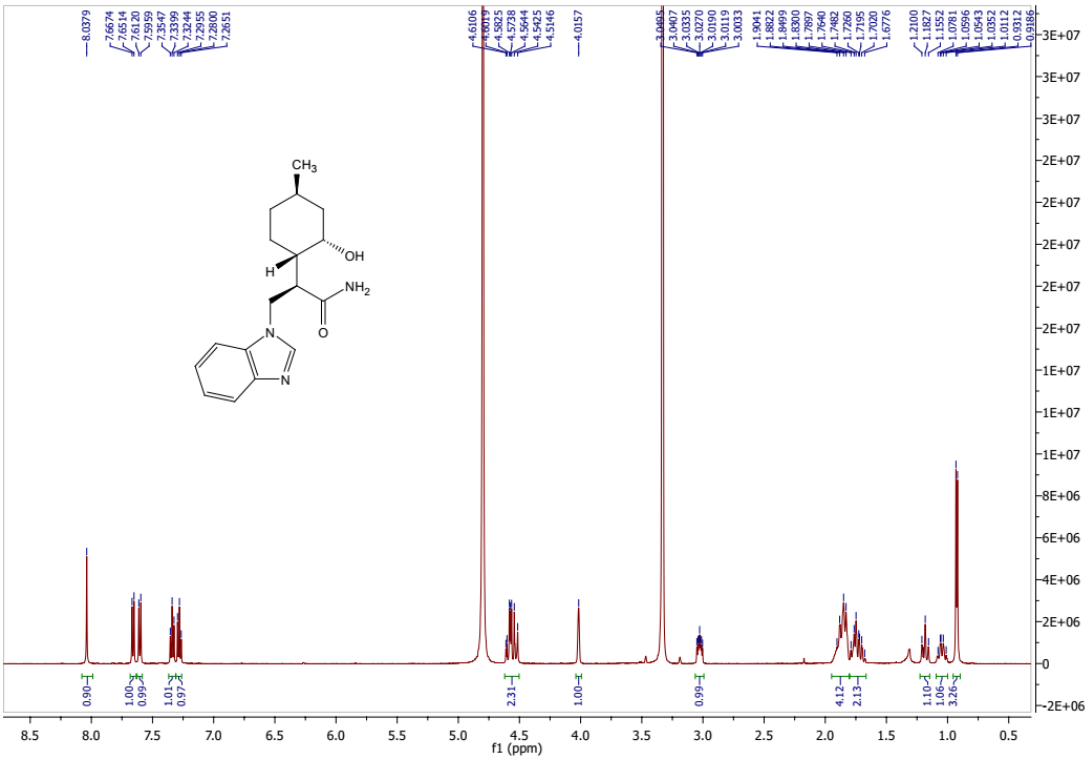
Figures S68-S69. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **48a.**

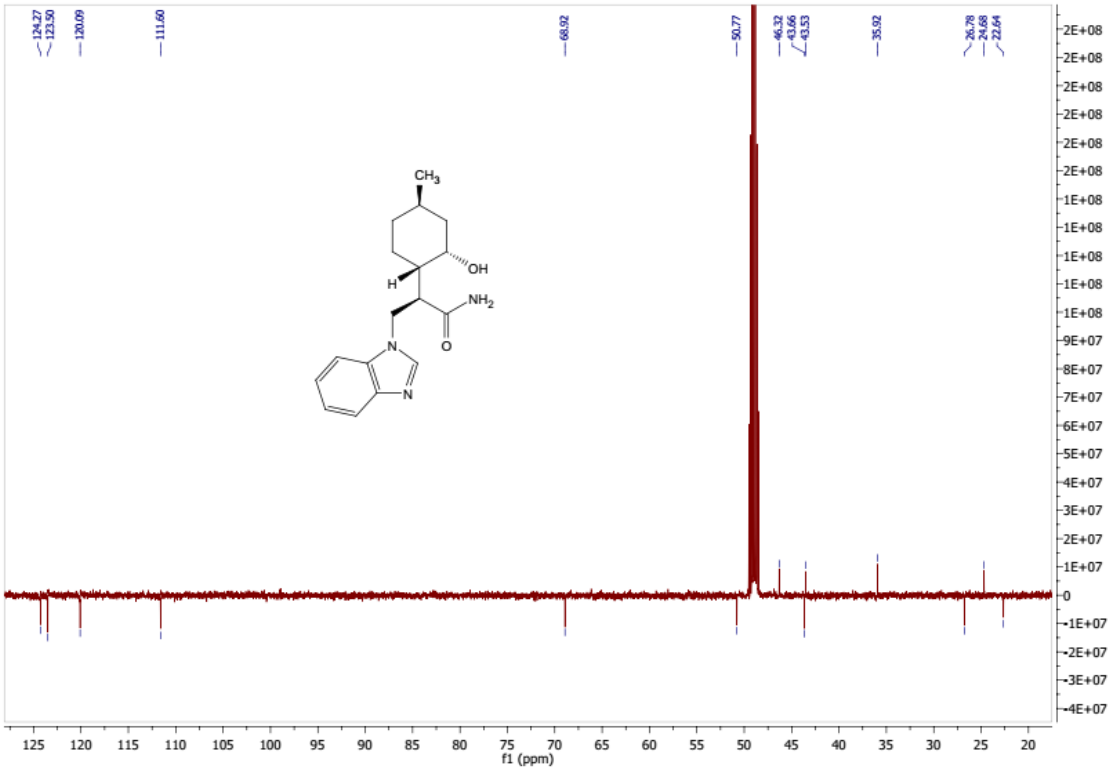


Figures S70-S71. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **48b.**

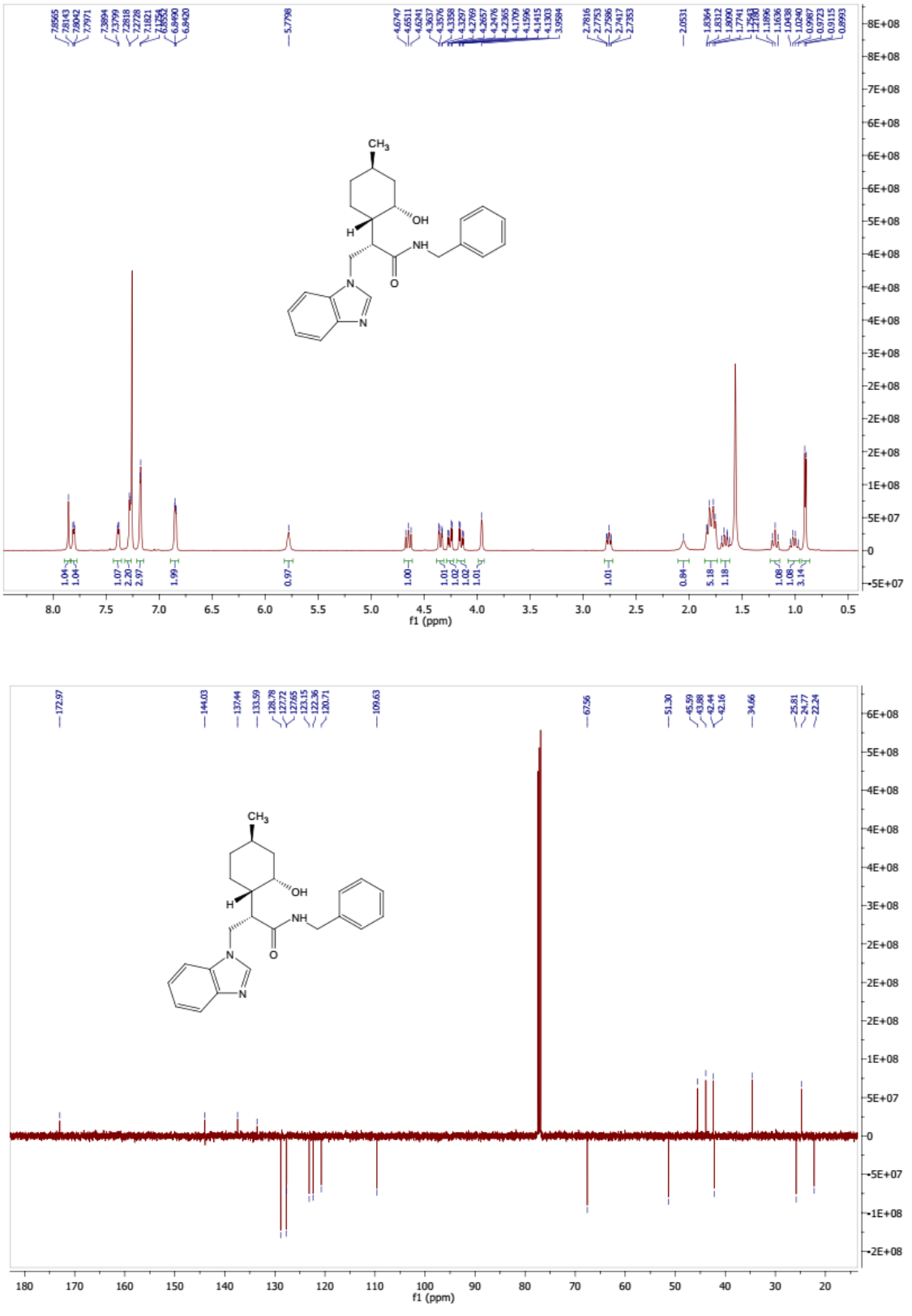


Figures S72-S73. ^{1}H (500 MHz, CD_3OD) and ^{13}C (125 MHz, CD_3OD) NMR spectra of **49a.**

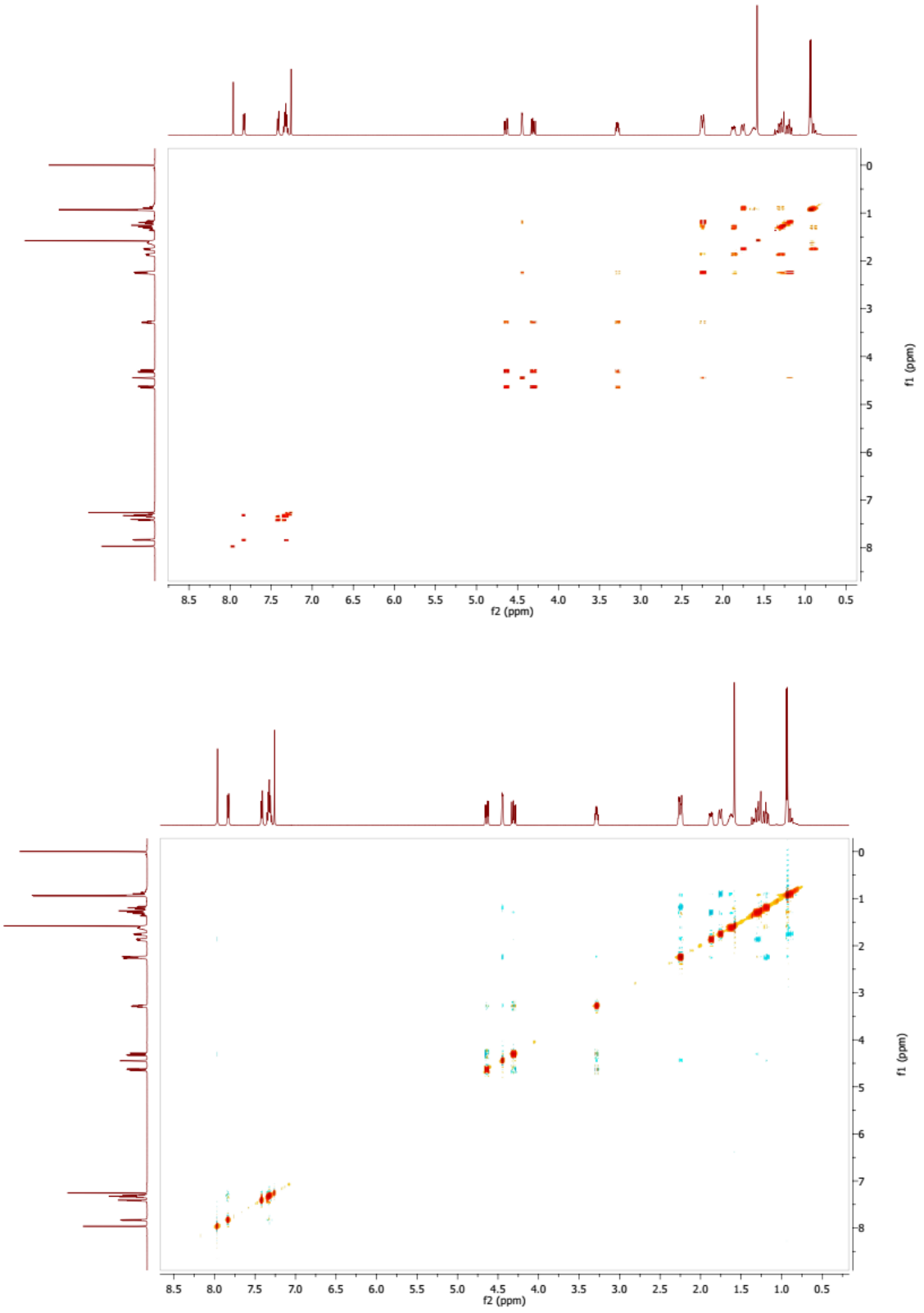




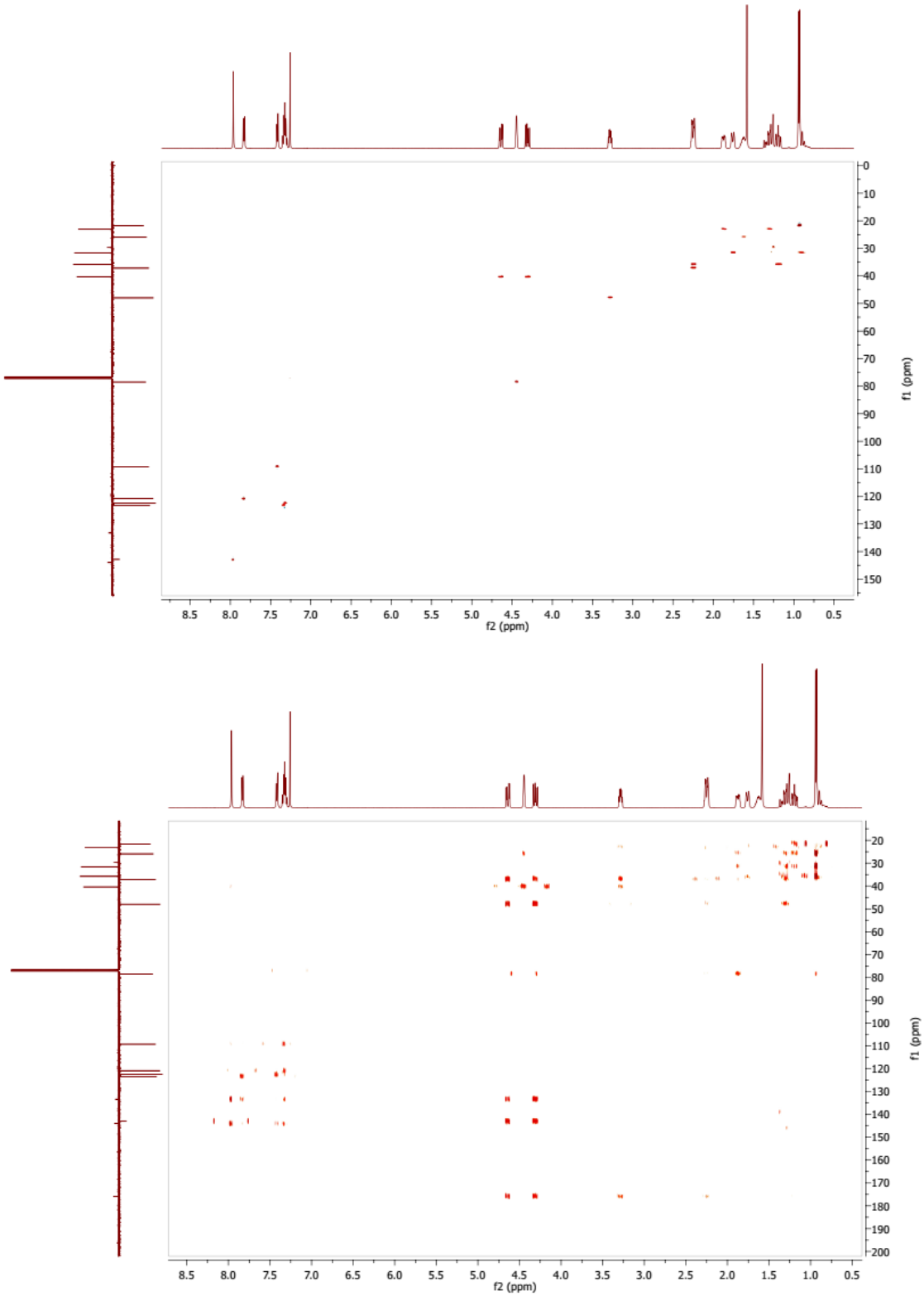
Figures S74-S75. ^{1}H (500 MHz, CD_3OD) and ^{13}C (125 MHz, CD_3OD) NMR spectra of **49b.**



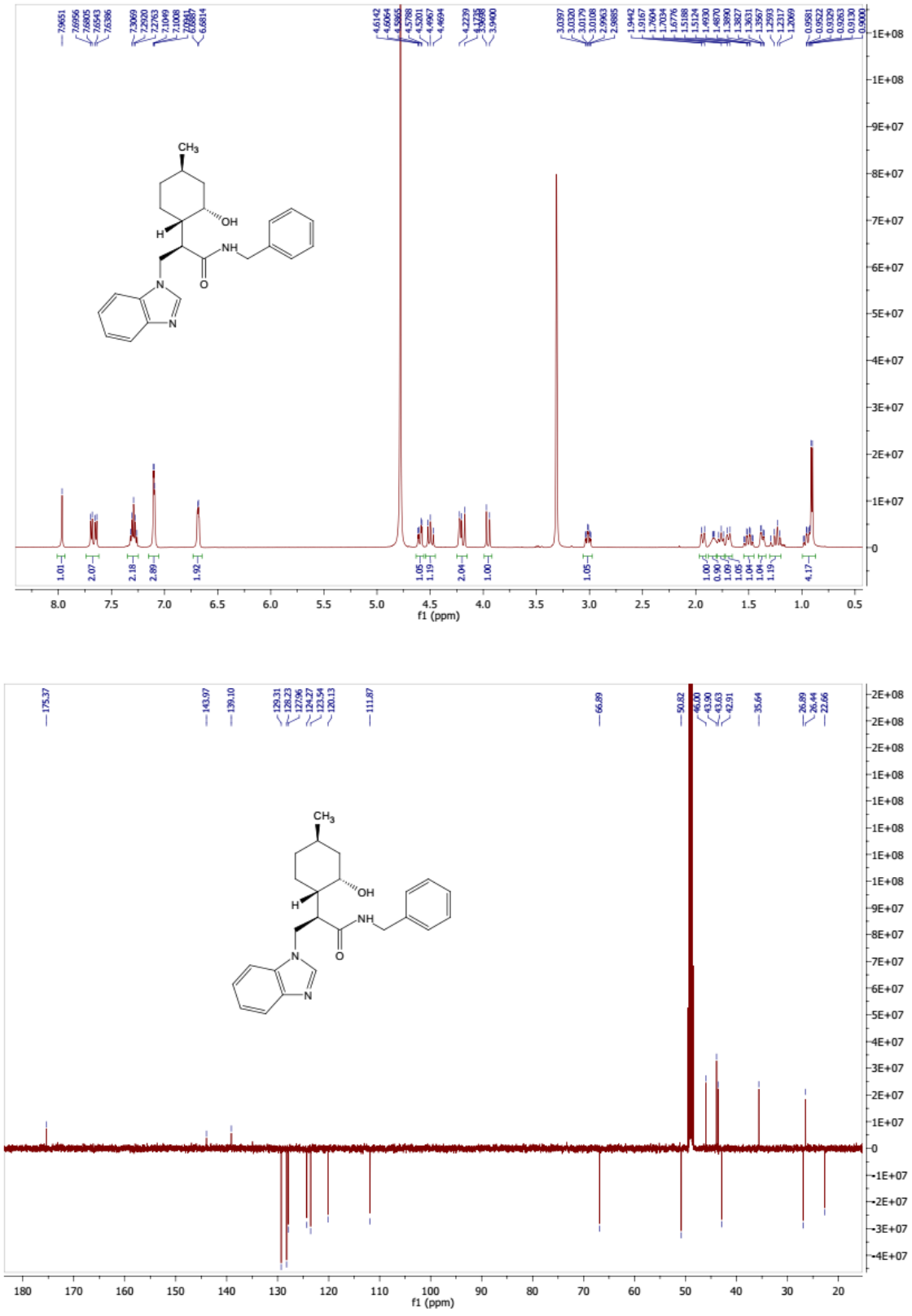
Figures S76-S77. ^{1}H (500 MHz, $CDCl_3$) and ^{13}C (125 MHz, $CDCl_3$) NMR spectra of **50a.**



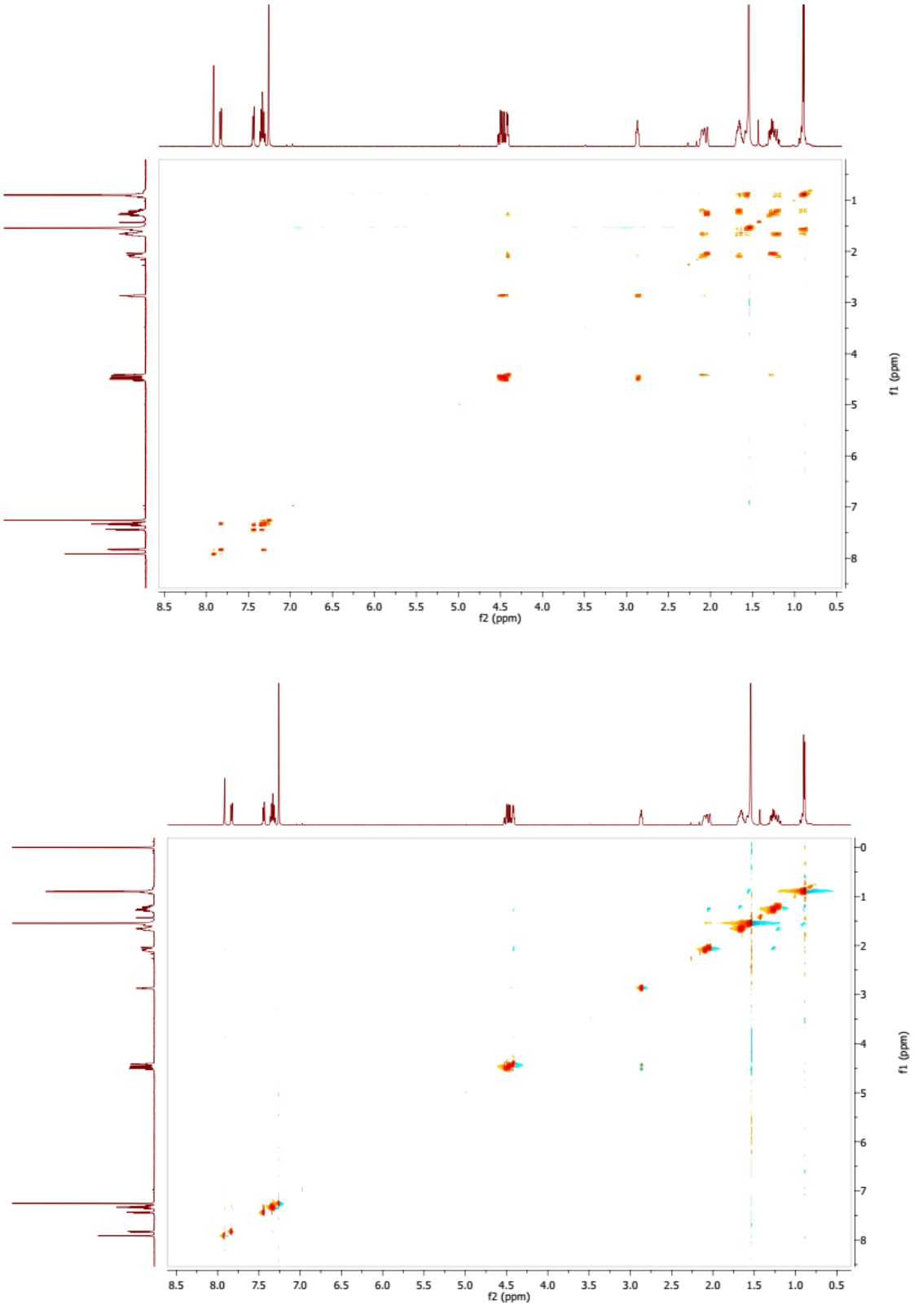
Figures S78-S79. COSY (500 MHz, $CDCl_3$) and NOESY (500 MHz, $CDCl_3$) NMR spectra of **50a.**



Figures S80-S81. HSQC (500 MHz, $CDCl_3$) and HMBC (500 MHz, $CDCl_3$) NMR spectra of **50a.**



Figures S82-S83. ^{1}H (500 MHz, CD_3OD) and ^{13}C (125 MHz, CD_3OD) NMR spectra of **50b.**



Figures S84-S85. COSY (500 MHz, $CDCl_3$) and NOESY (500 MHz, $CDCl_3$) NMR spectra of **50b.**

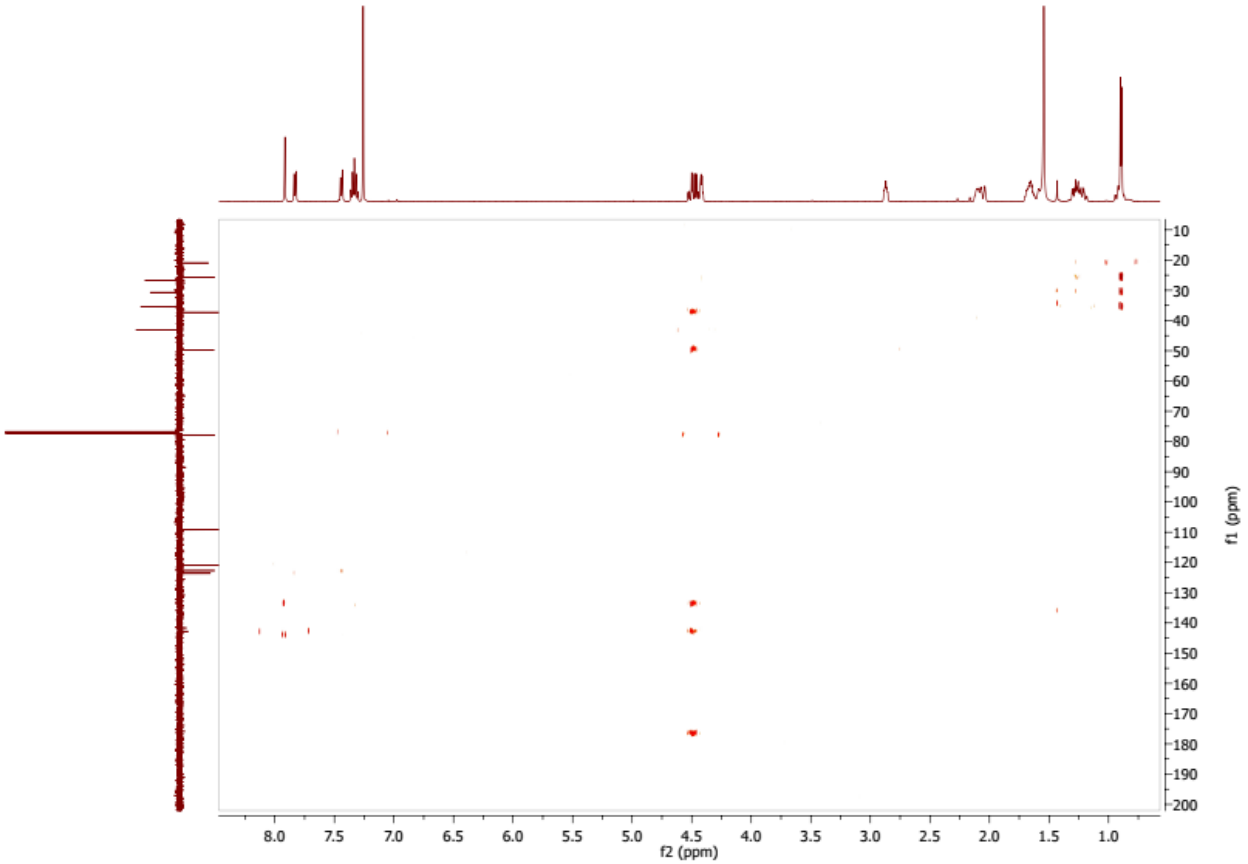


Figure S86. HMBC (500 MHz, $CDCl_3$) NMR spectra of **50b.**

2. Antimicrobial assay (results of all products)

Table S1. Biological screening data for every synthesized product (compounds **23**–**50**).

Entry	Compound	MIC (μM) on the following bacteria:		
		S. aureus ATCC 25923	*S. aureus* MRSA ATCC 43300	*E. coli* ATCC 25922
1	**23**	**100**	>100	>100
2	**24**	**100**	>100	>100
3	**25**	**100**	>100	>100
4	**26**	**100**	>100	>100
5	**27**	**100**	>100	>100
6	**28**	**50**	>100	>100
7	**29**	**100**	>100	>100
8	**30**	**12.5**	>100	>100
9	**31**	>100	>100	>100
10	**32**	>100	>100	>100
11	**33**	>100	>100	>100
12	**34**	>100	>100	>100
13	**35**	>100	>100	>100
14	**36**	>100	>100	>100
15	**37**	>100	>100	>100
16	**38**	>100	>100	>100
17	**39**	>100	>100	>100
18	**40**	>100	>100	>100
19	**41**	>100	>100	>100
20	**42**	>100	>100	>100
21	**43**	>100	>100	>100
22	**44a**	>100	>100	>100
23	**44b**	>100	>100	>100
24	**45a**	>100	>100	>100
25	**45b**	>100	>100	>100

Table S1. Biological screening data for every synthesized product (compounds **23–50**). [continued]

Entry	Compound	MIC (μM) on the following bacteria:		
		***S. aureus* ATCC 25923**	***S. aureus* MRSA ATCC 43300**	***E. coli* ATCC 25922**
26	**46a**	>100	>100	>100
27	**46b**	>100	>100	>100
28	**47a**	>100	>100	>100
29	**47b**	>100	>100	>100
30	**48a**	>100	>100	>100
31	**48b**	>100	>100	>100
32	**49a**	>100	>100	>100
33	**49b**	>100	>100	>100
34	**50a**	>100	>100	>100
35	**50b**	>100	>100	>100
36	**Ciprofloxacin**	4.2	4.2	2.1
37	**Tetracycline**	0.6	0.6	0.4

4. Molecular docking

Table S2. CDOCKER energy values for compounds **28** and **30.**

Compound	2W9S		4CJN		2ZCQ		3U2D	
	CDOCKER energy	NO. interactions	CDOCKER energy	NO. interactions	CDOCKER energy	NO. interactions	CDOCKER energy	NO. interactions
28	-8.9928	7	-8.72497	9	-33.7135	5	-23.3698	11
30	-1.28151	6	-3.79394	6	-24.8002	10	-15.5656	10

Table S3. In silico ADMET properties of compounds **28** and **30.**

Compound	Absorption level	Solubility level	BBB level	PPB level	CYP2D6 inhibition	Hepatotoxicity
28	0 (good)	3 (good)	2 (medium)	0 (<90%)	0 (non-inhibitor)	0 (nontoxic)
30	0 (good)	2 (low)	1 (high)	0 (<90%)	0 (non-inhibitor)	0 (nontoxic)

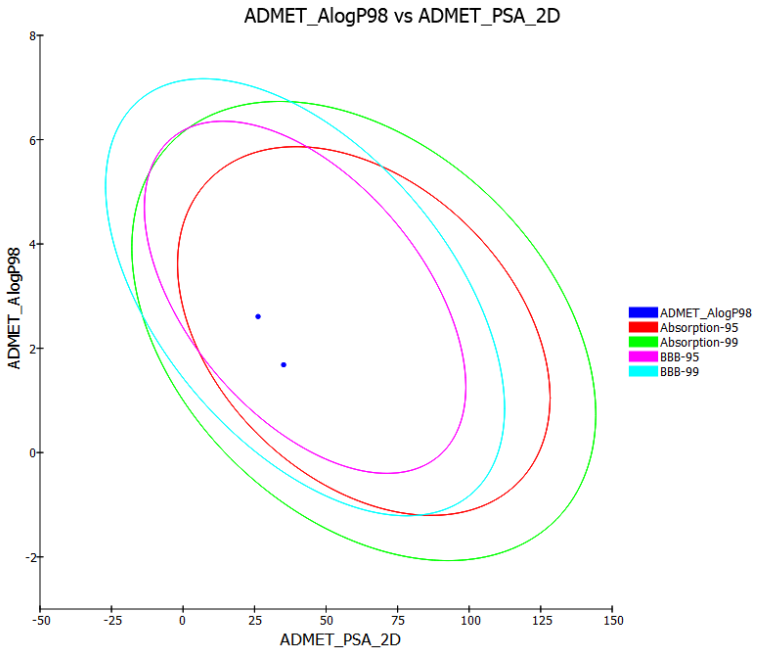


Figure S87. Plot of the Polar Surface Area (PSA) vs. LogP for a standard and test set showing the 95% and 99% confidence limit ellipses corresponding to the blood–brain barrier and intestinal absorption models of compounds **28** and **30.**