Elaboration of the Effective Multi-Target Therapeutic Platform for the Treatment of Alzheimer's Disease Based on Novel Monoterpene-Derived Hydroxamic Acids

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[2] Department of Medicinal Chemistry, N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch, Russian Academy of Sciences, Lavrentiev Ave., 9, Novosibirsk 630090, Russia
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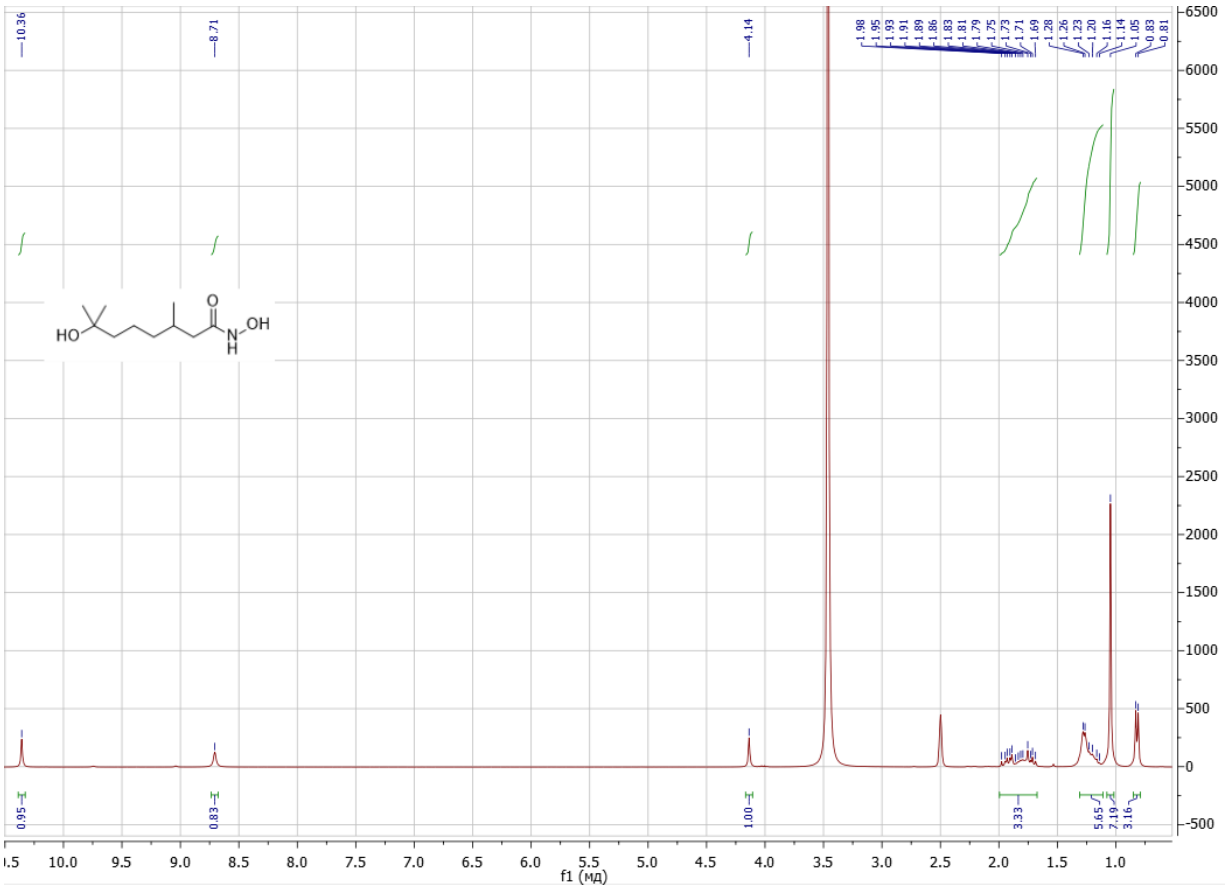
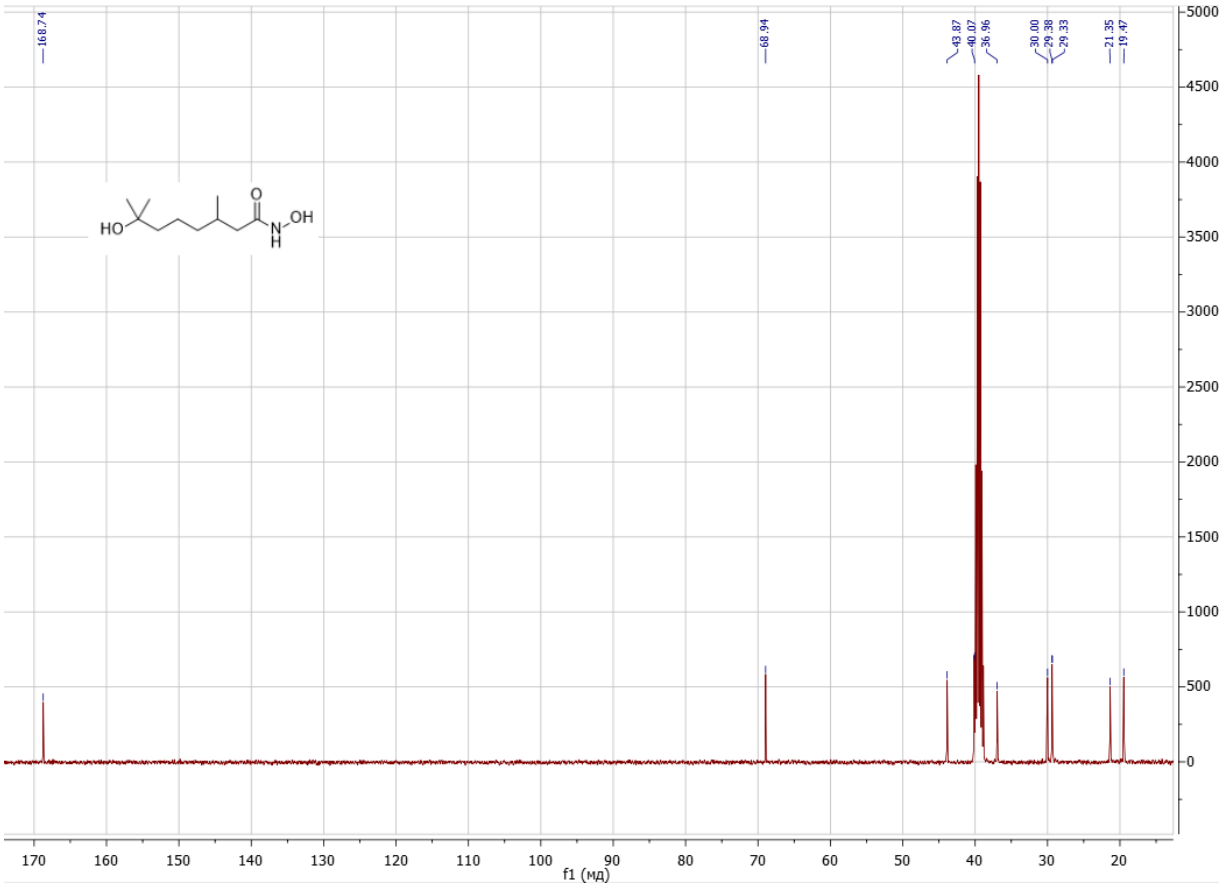
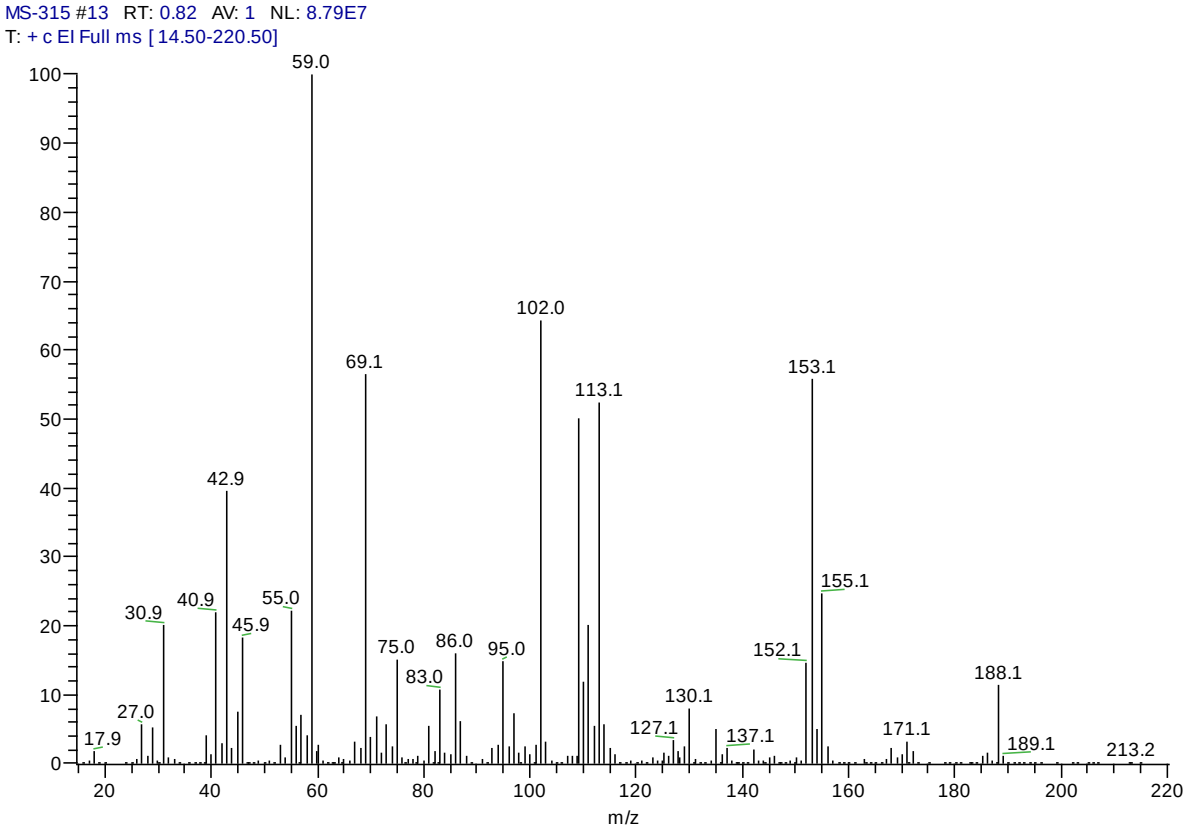
^{1}H NMR spectrum of compound **5**



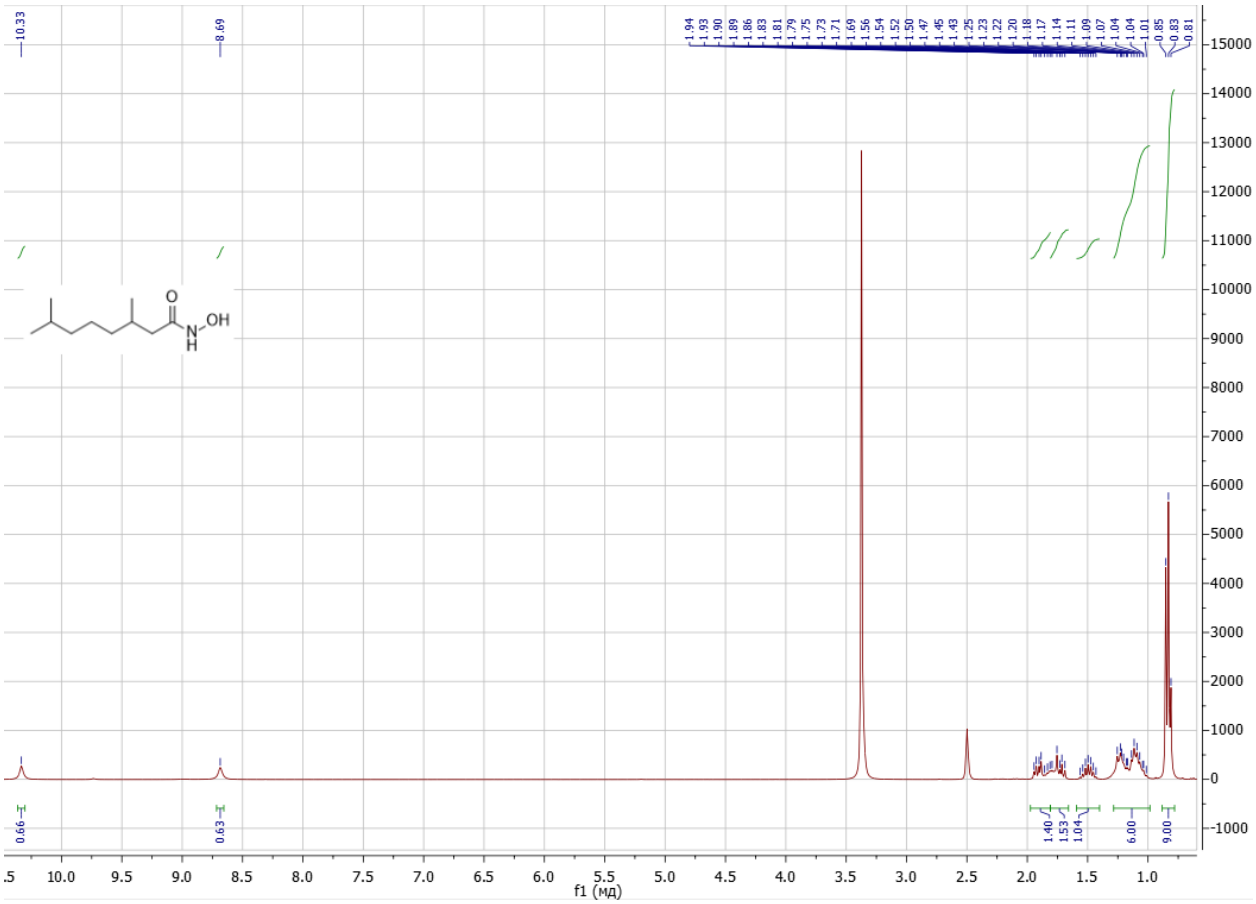
^{13}C NMR spectrum of compound **5**



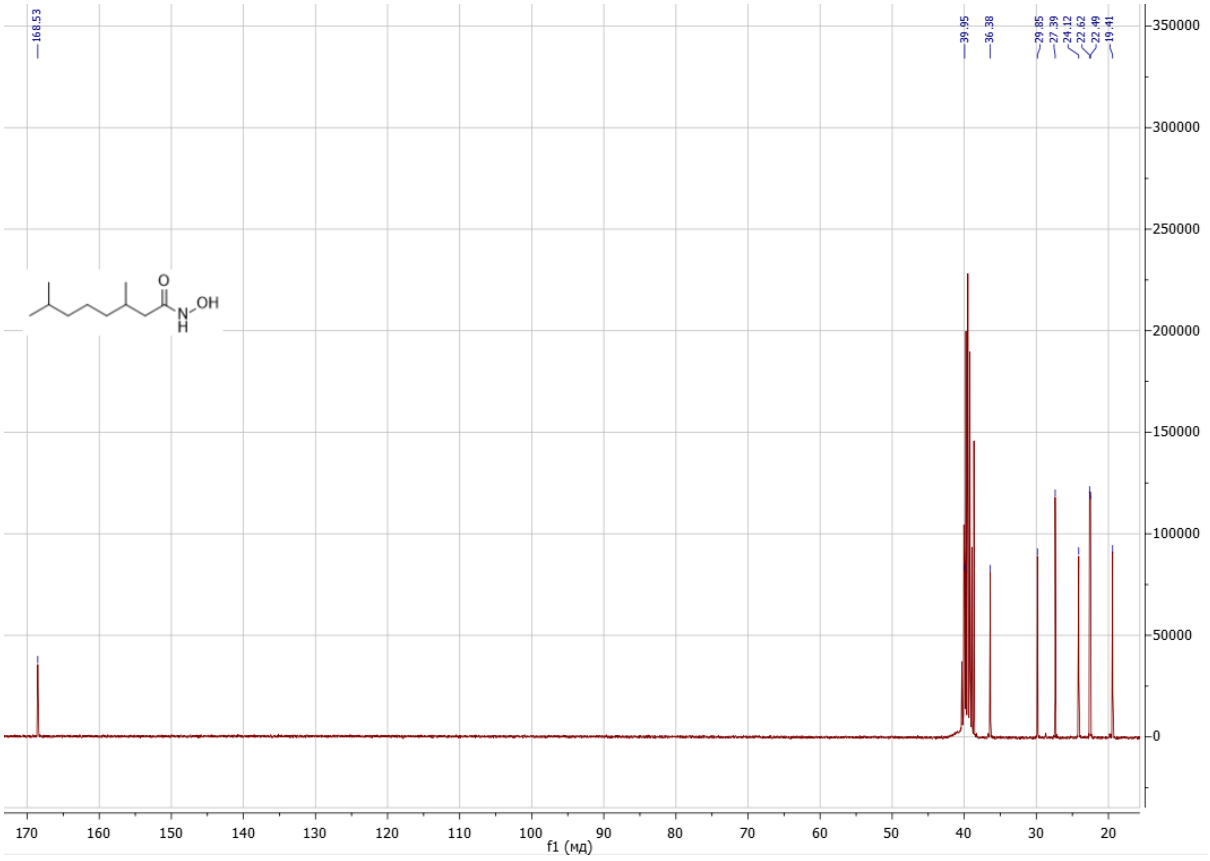
Mass-spectrum of compound **5**



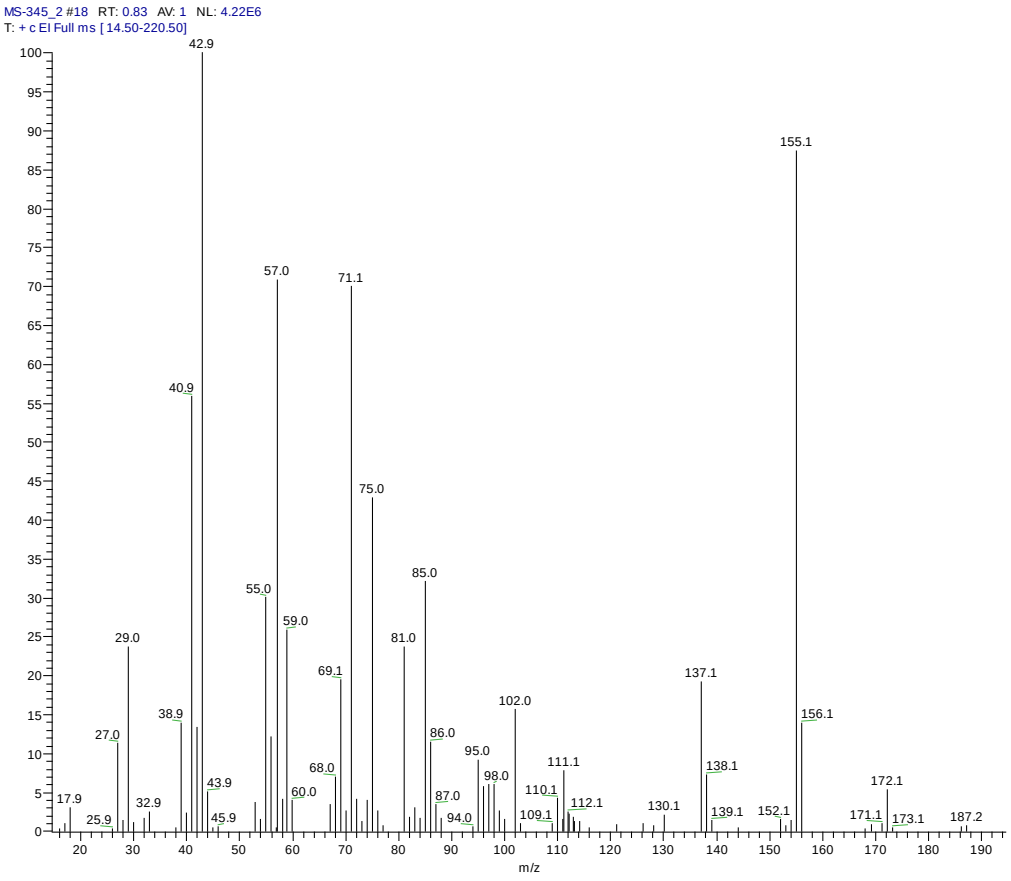
^{1}H NMR spectrum of compound **8**



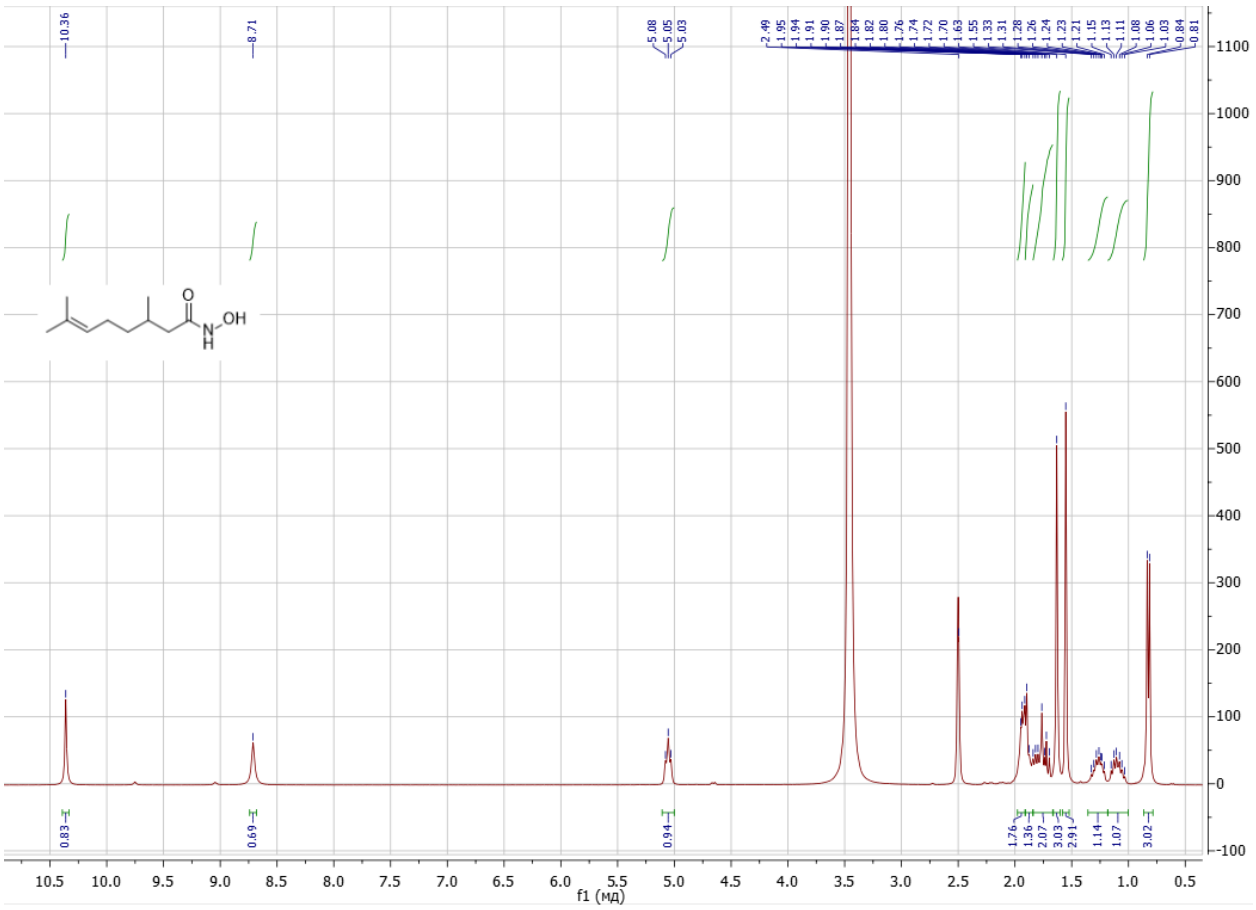
^{13}C NMR spectrum of compound **8**



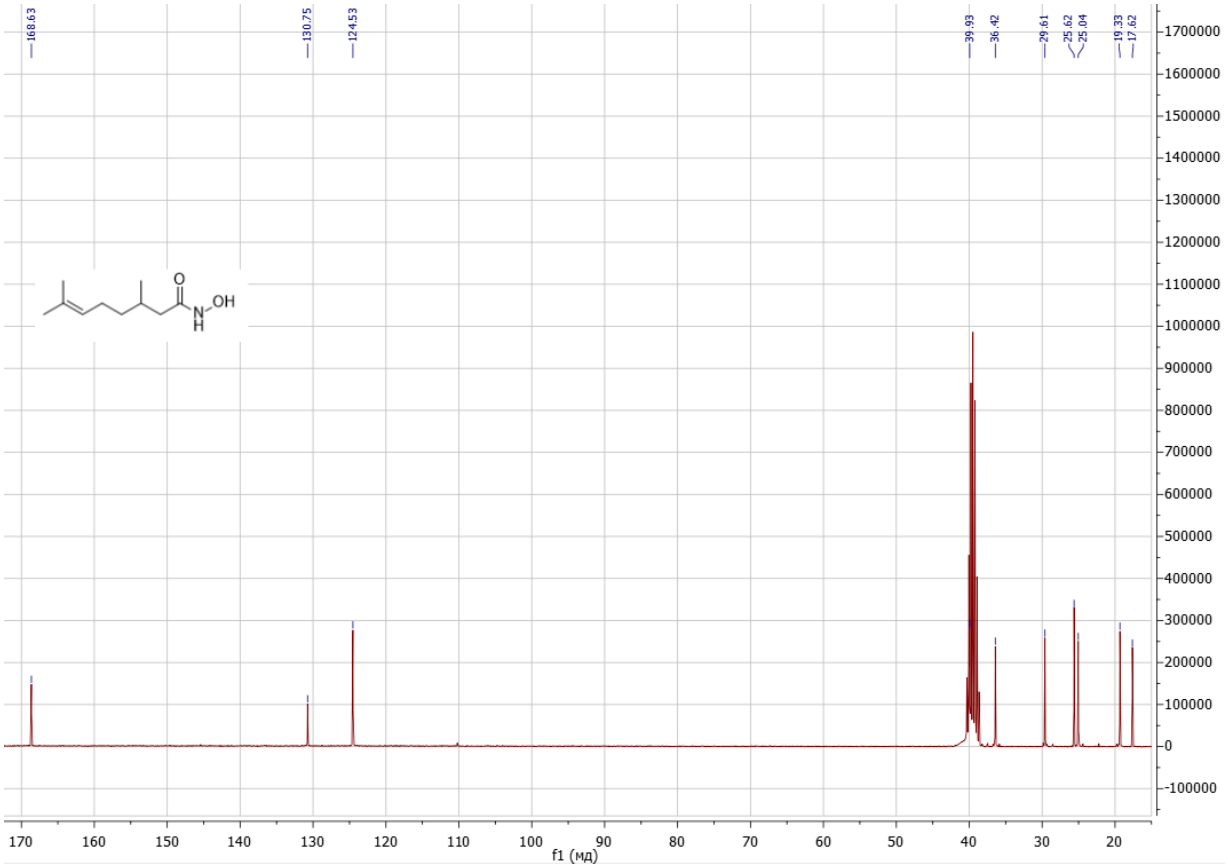
Mass-spectrum of compound **8**



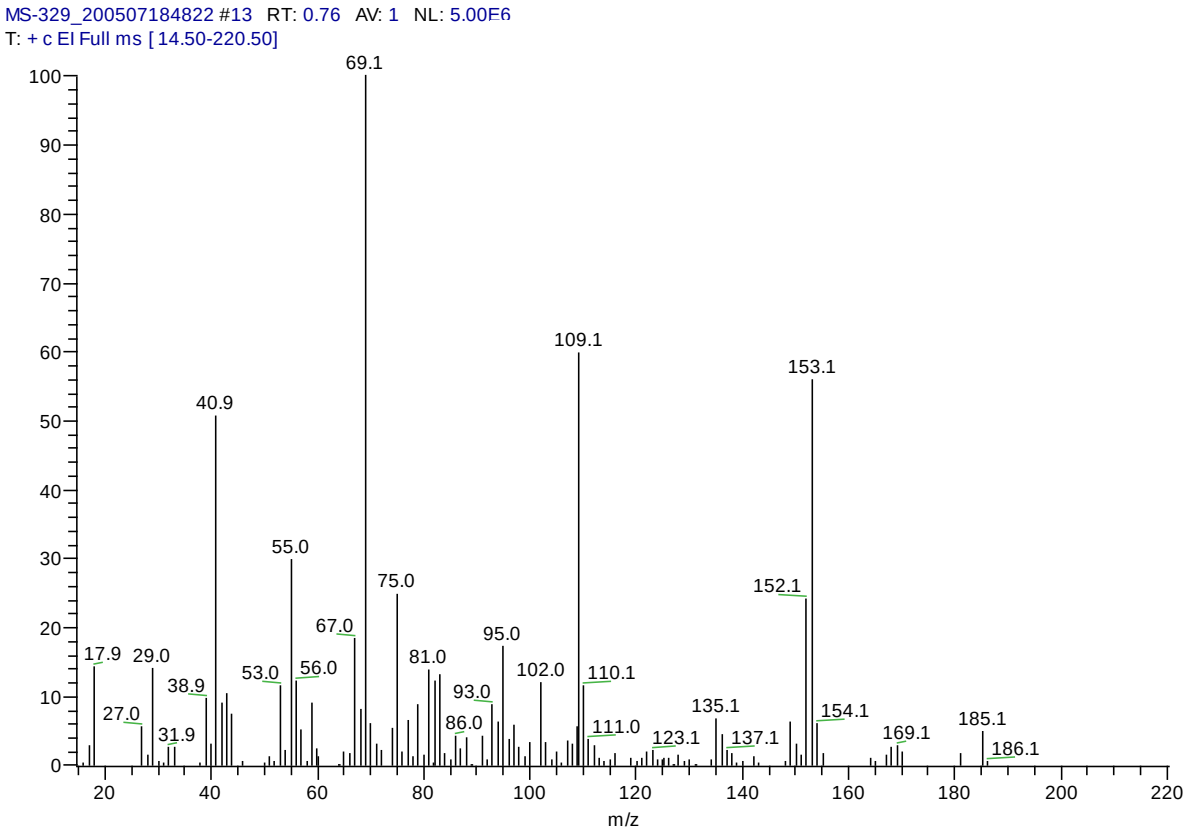
^{1}H NMR spectrum of compound **10**



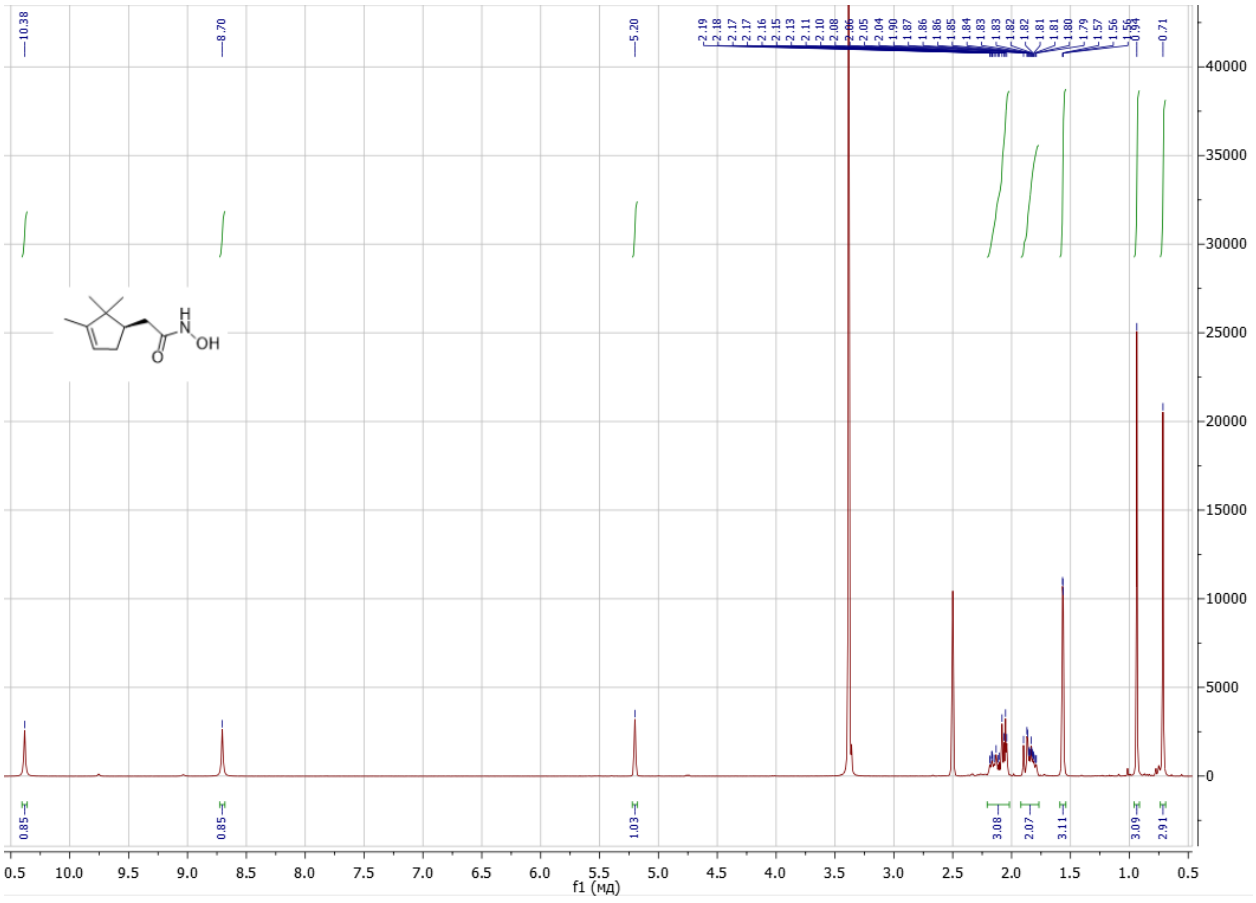
^{13}C NMR spectrum of compound **10**



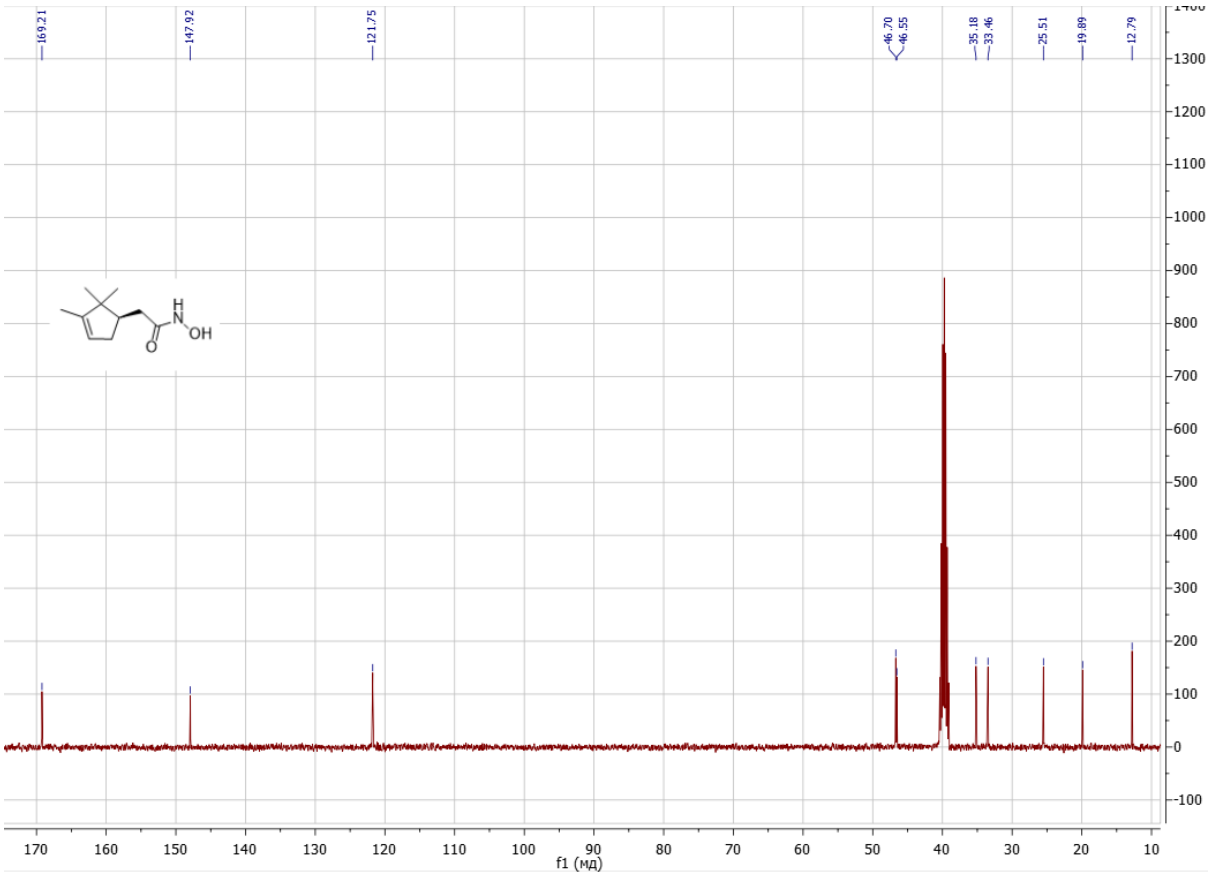
Mass-spectrum of compound **10**



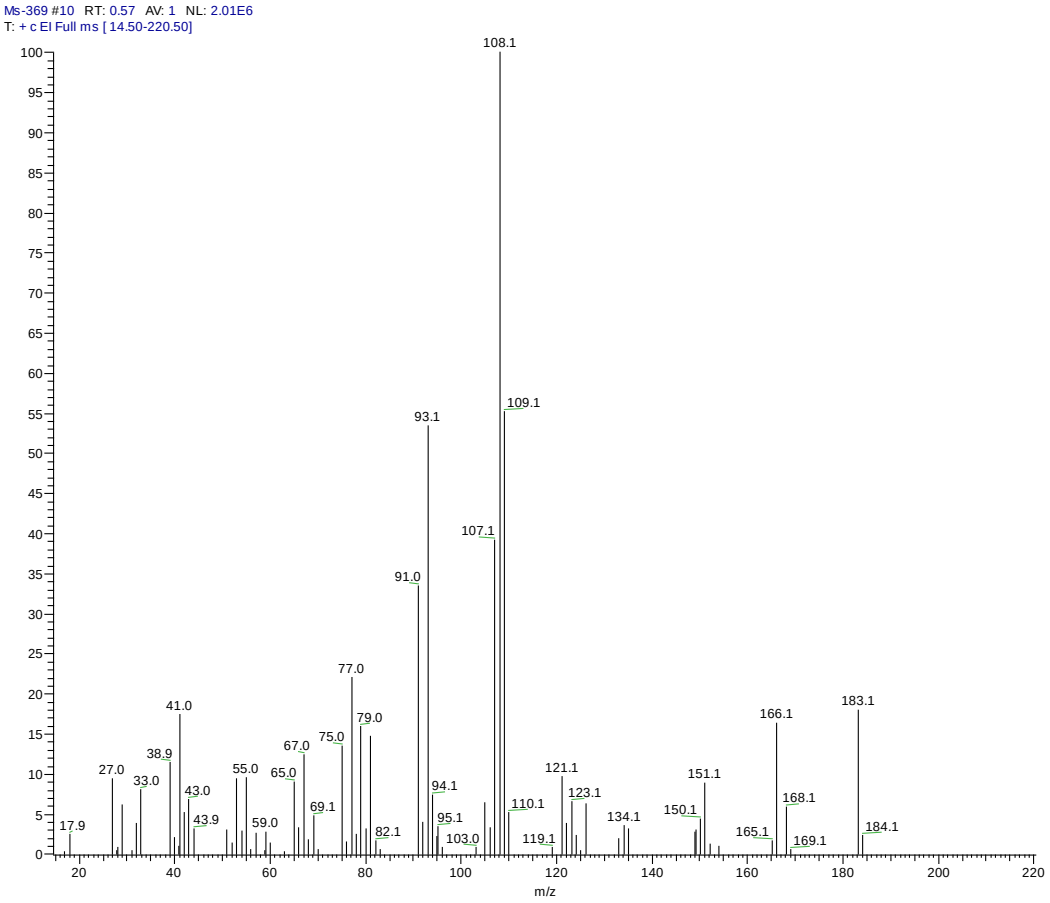
^{1}H NMR spectrum of compound (+)-**13**



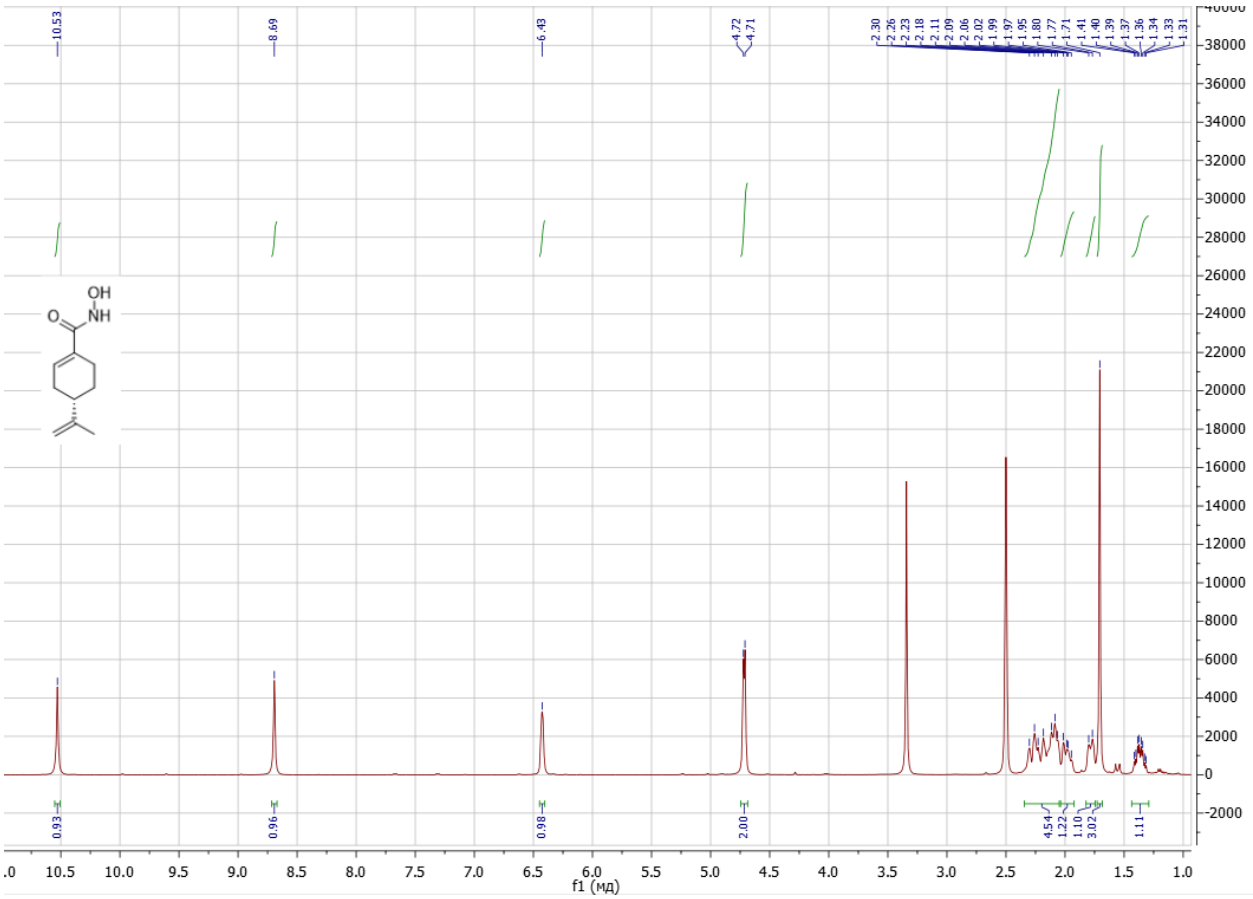
^{13}C NMR spectrum of compound (+)-**13**



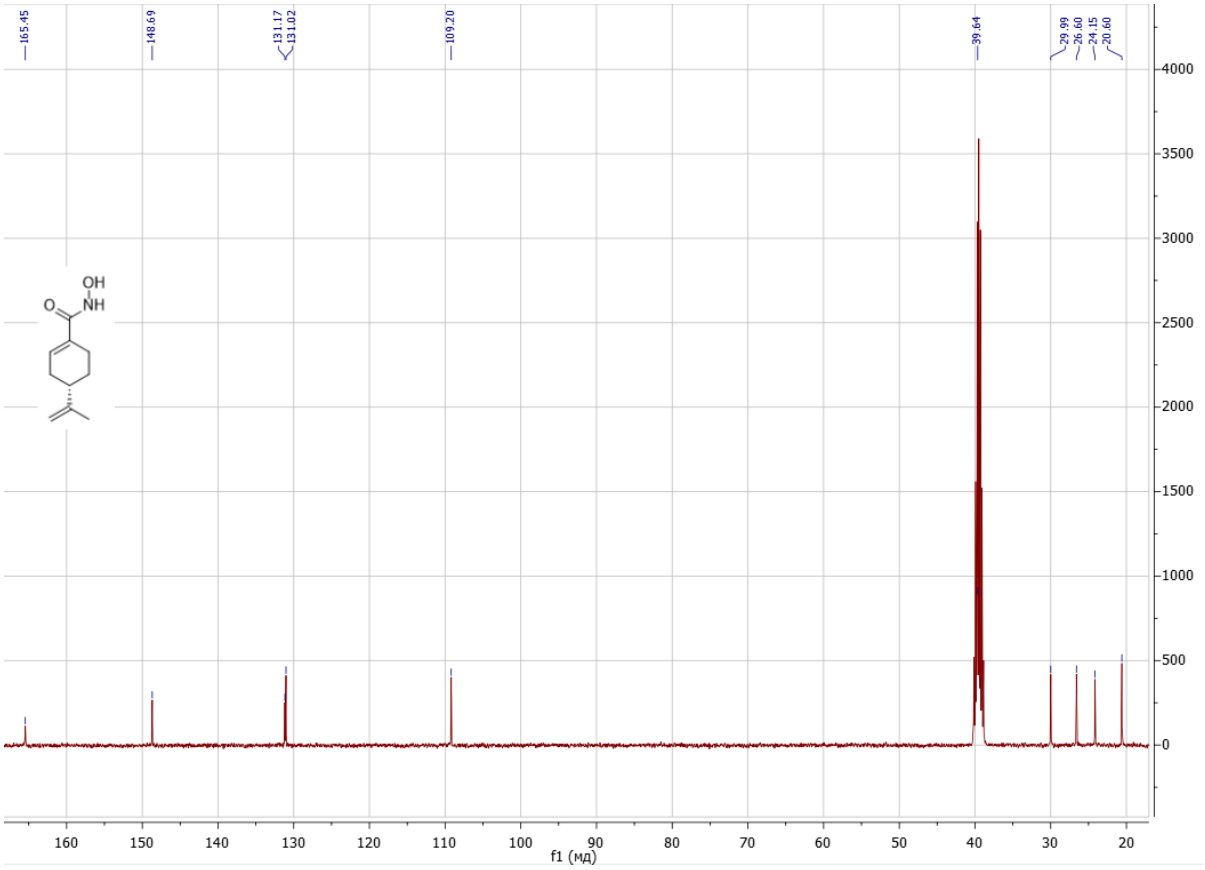
Mass-spectrum of compound (+)-**13**



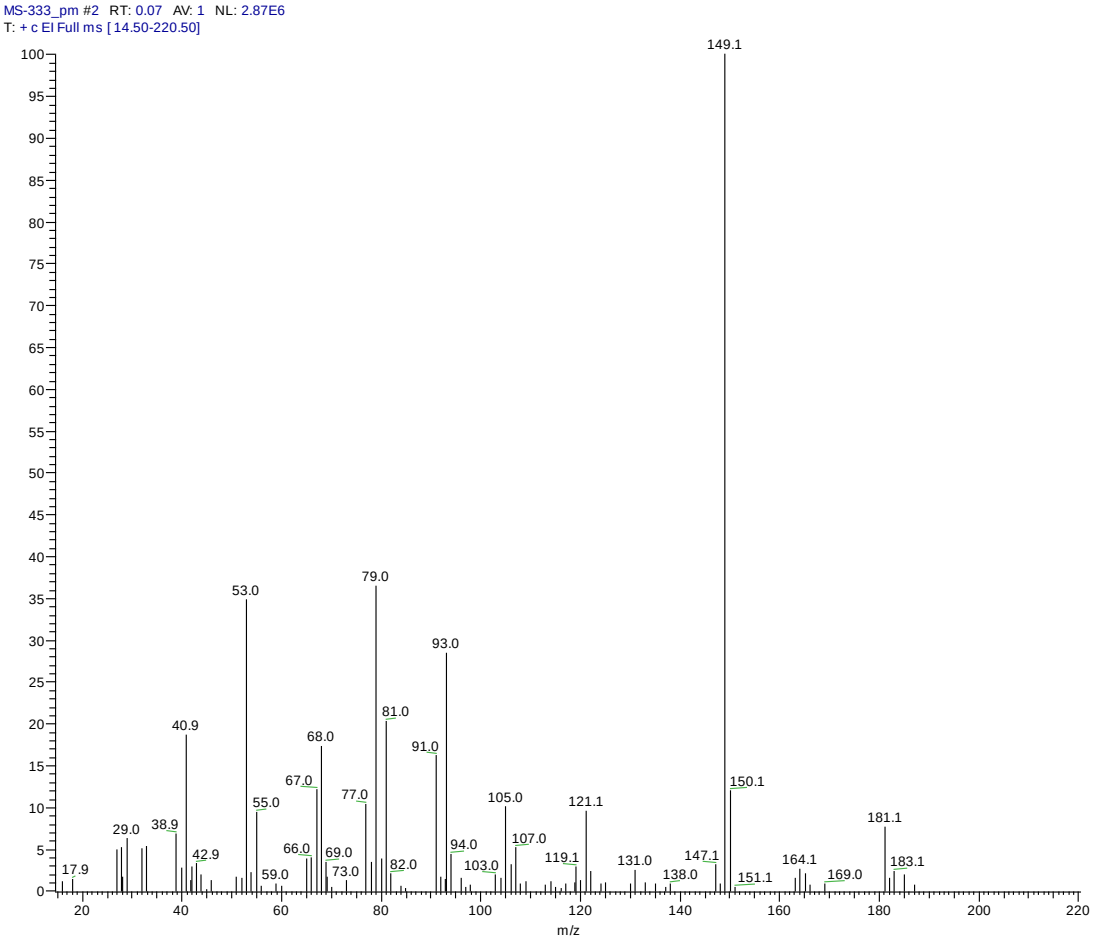
^{1}H NMR spectrum of compound **16**



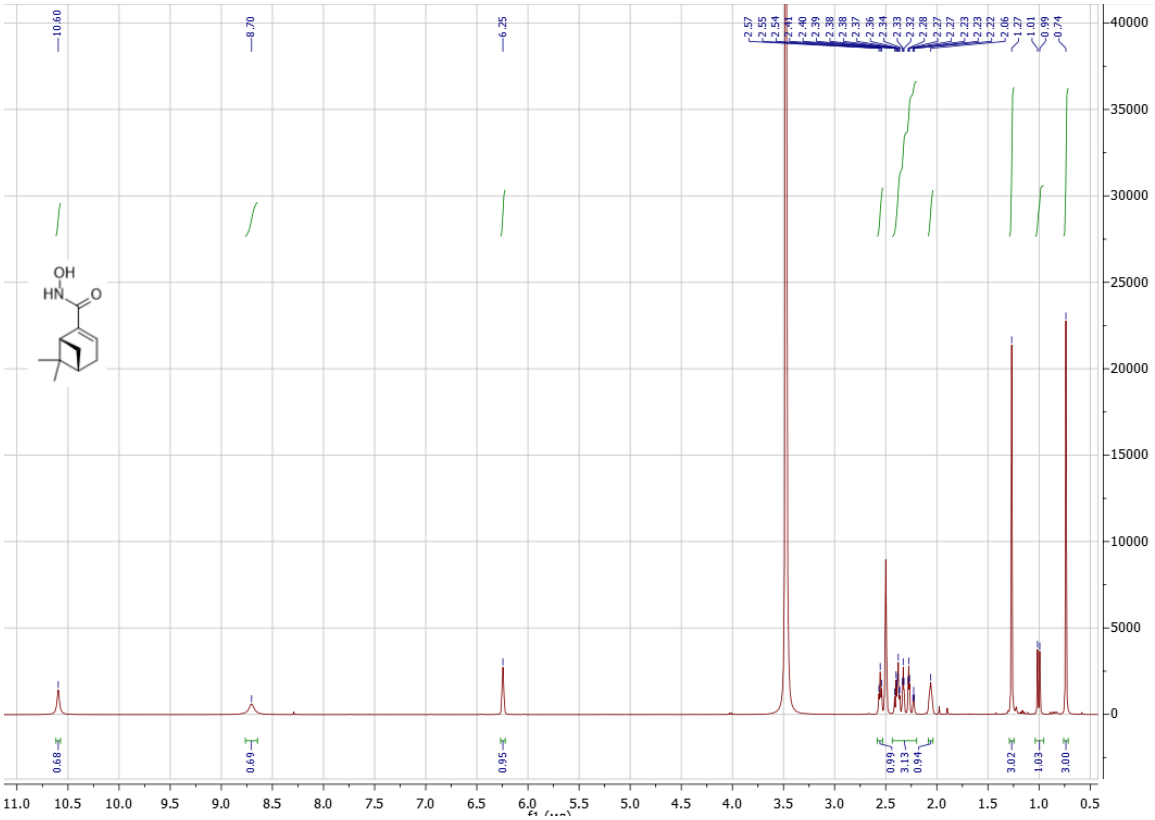
^{13}C NMR spectrum of compound **16**



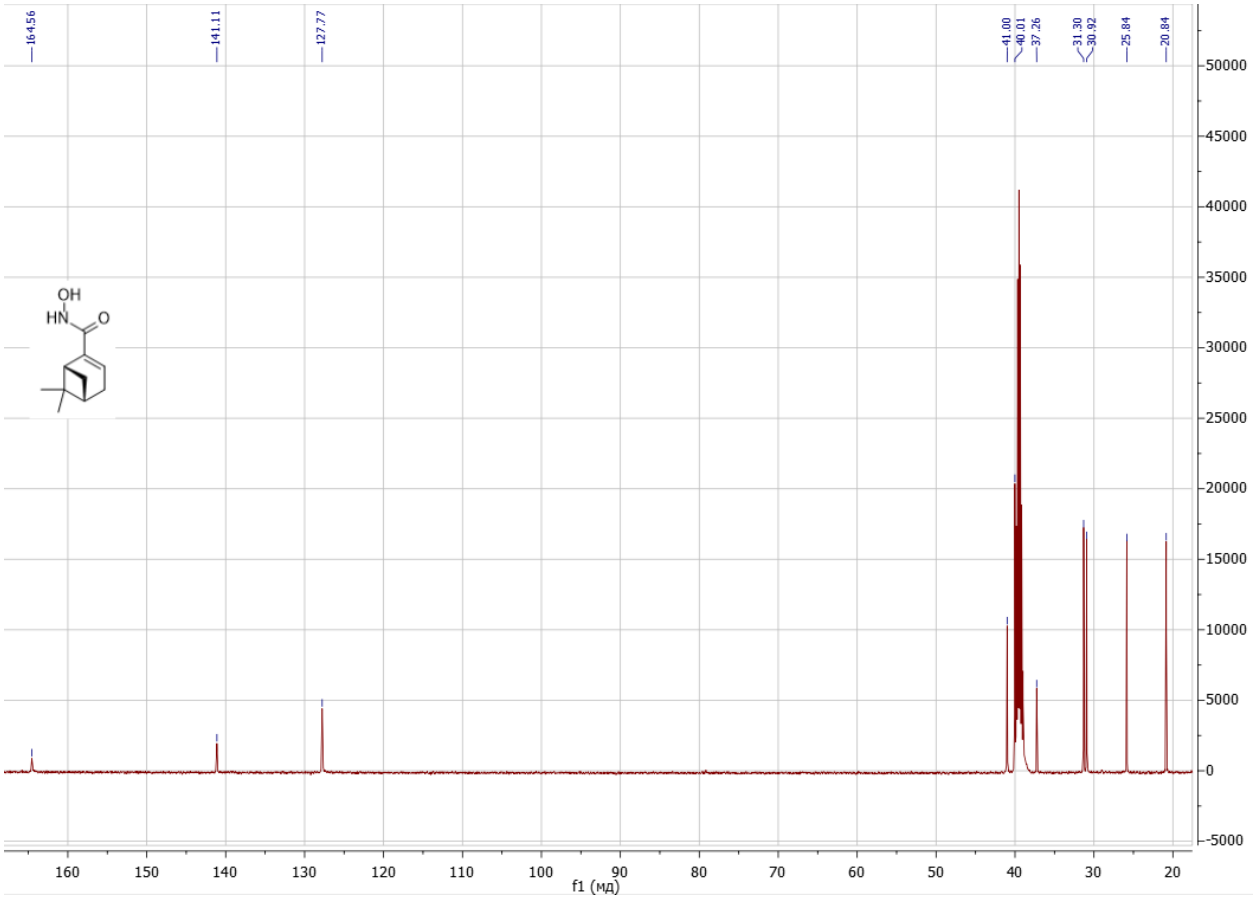
Mass-spectrum of compound **16**



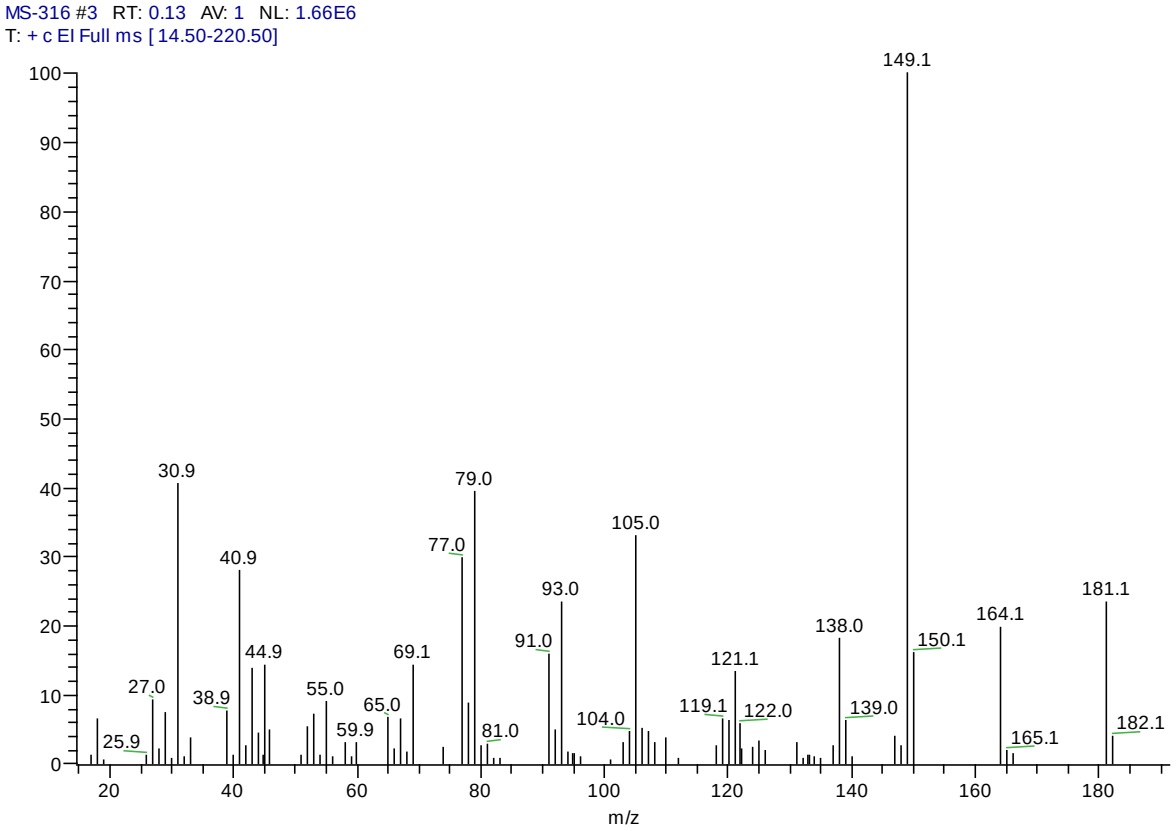
^{1}H NMR spectrum of compound (-)-**19**



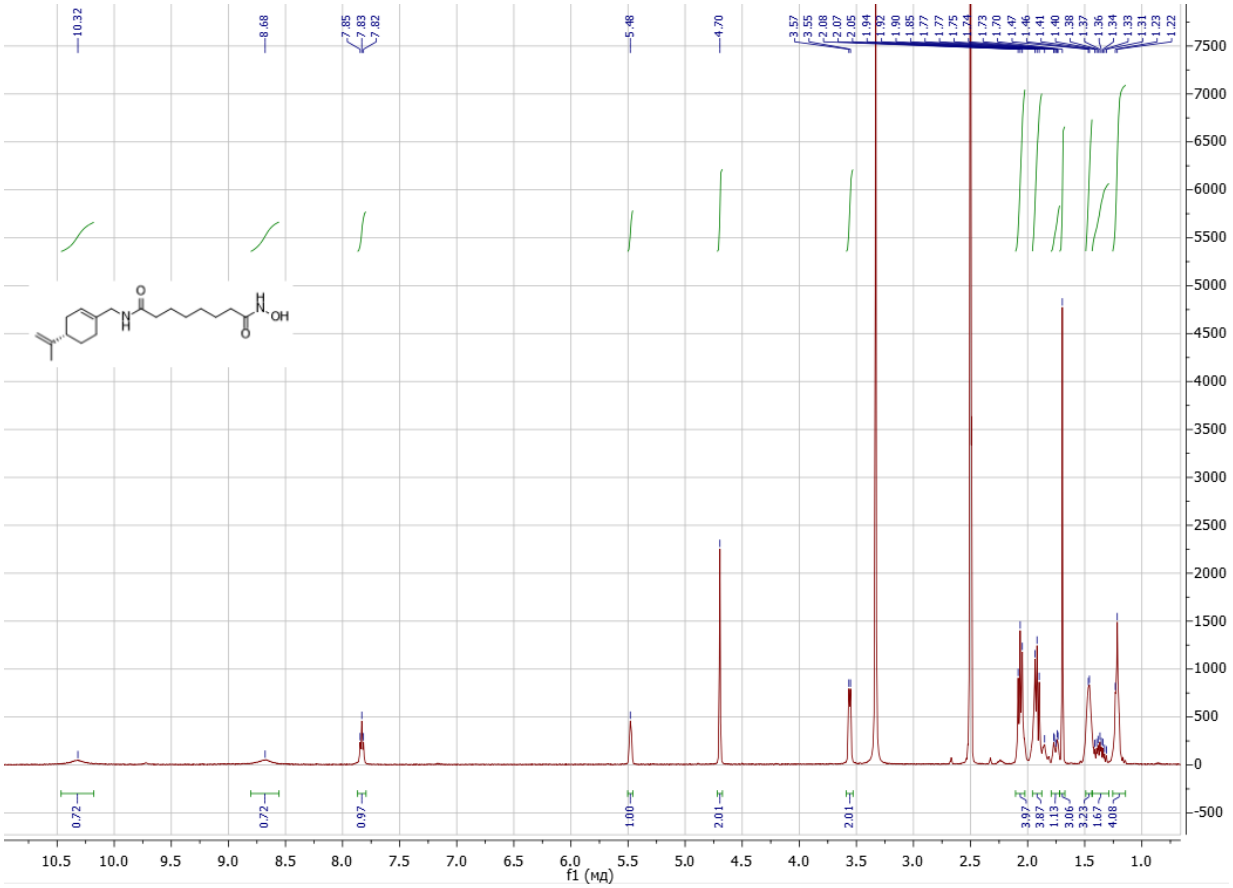
^{13}C NMR spectrum of compound (-)-**19**



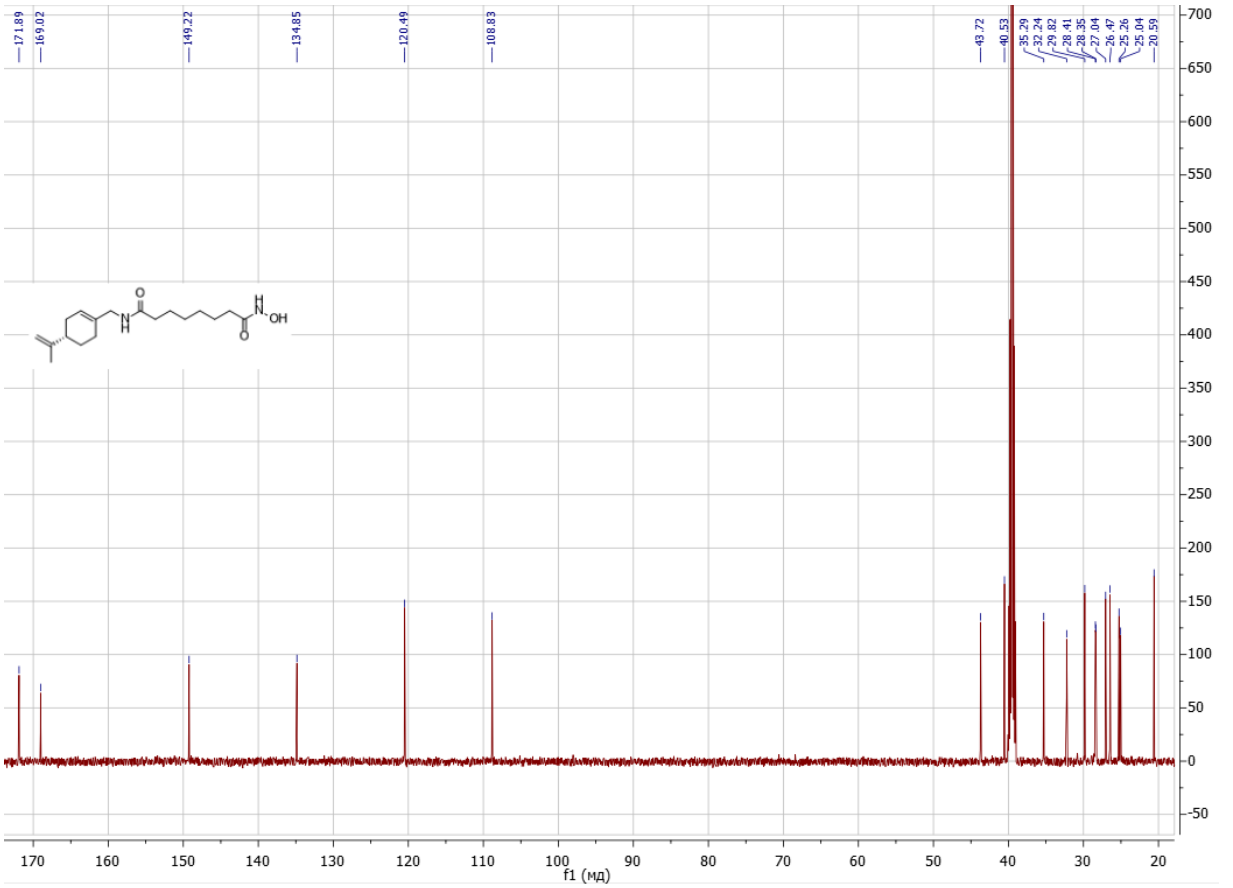
Mass-spectrum of compound (-)-**19**



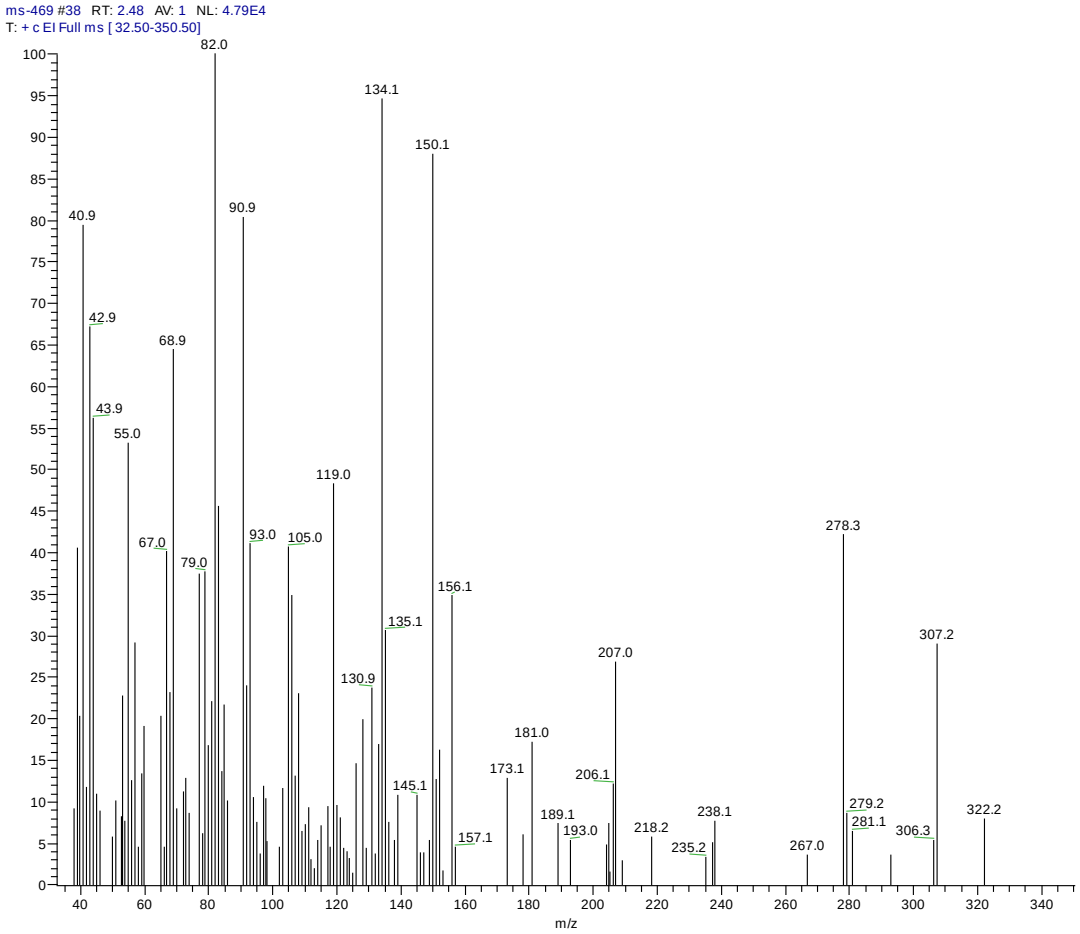
^{1}H NMR spectrum of compound **30**



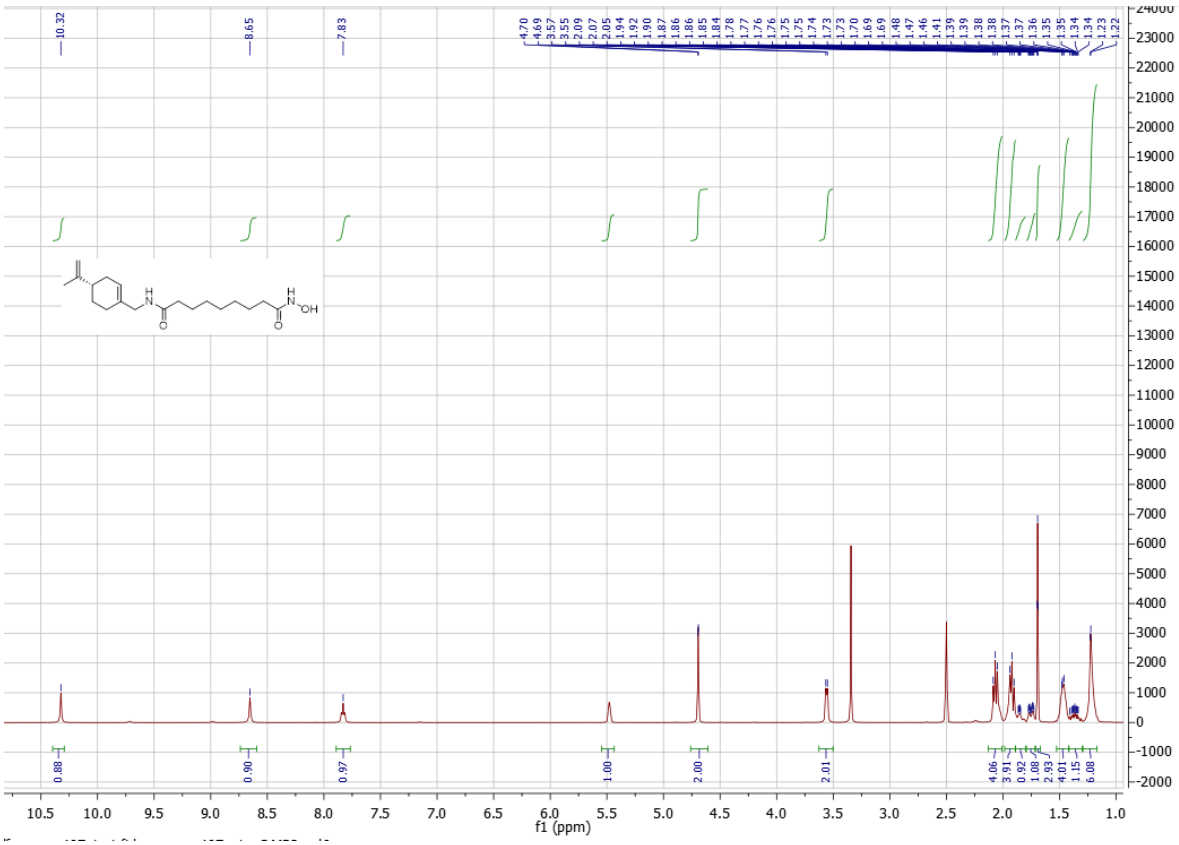
^{13}C NMR spectrum of compound **30**



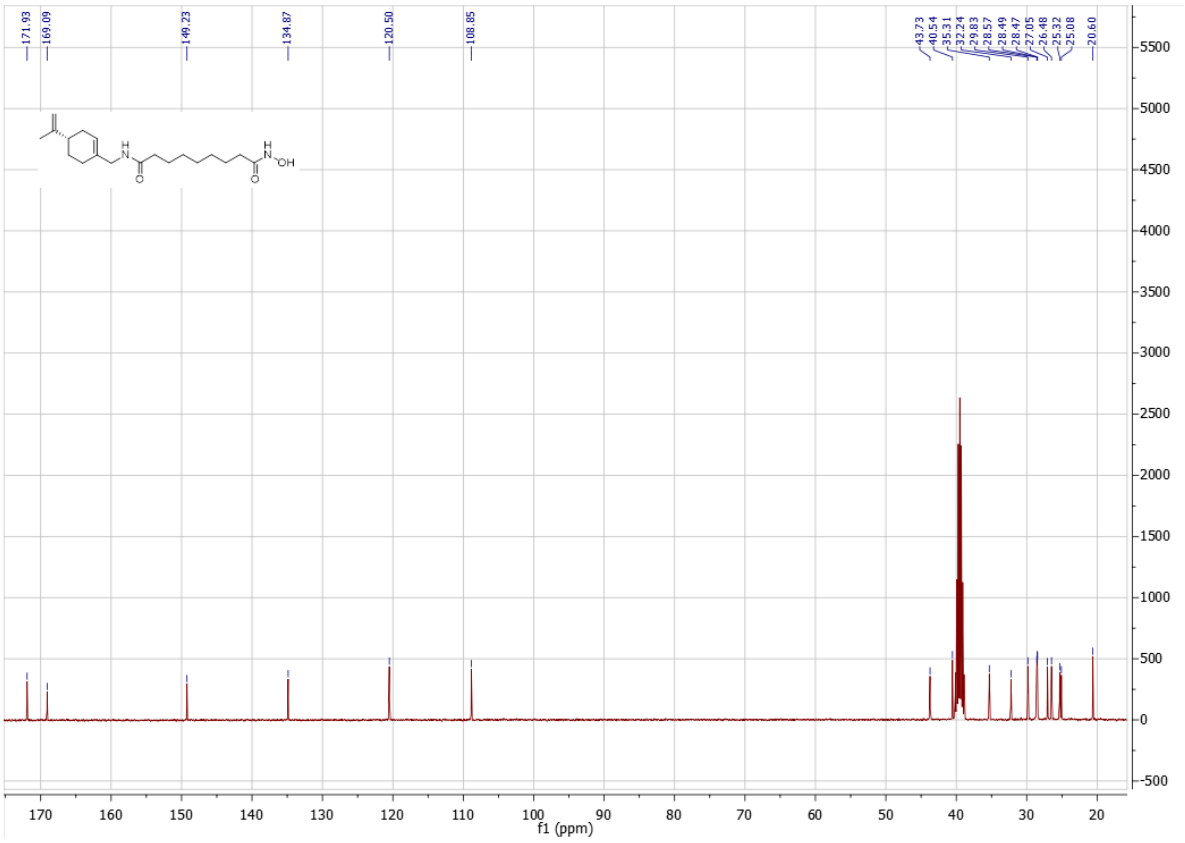
Mass-spectrum of compound **30**



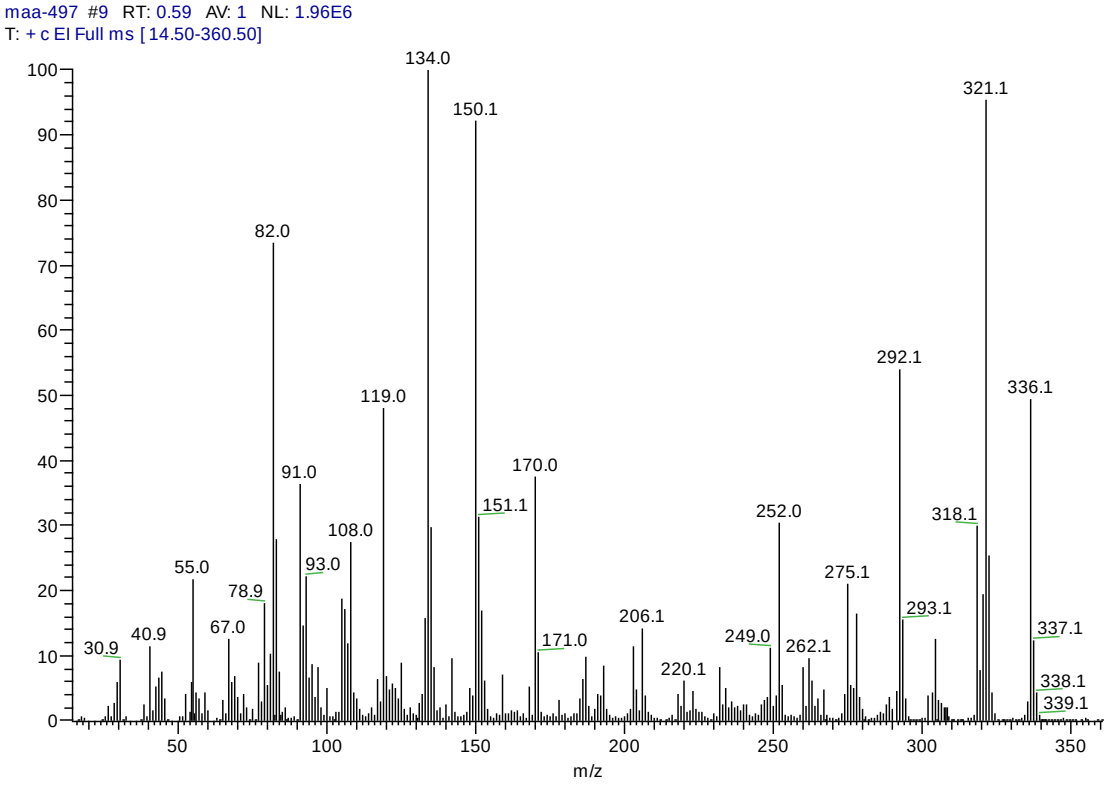
^{1}H NMR spectrum of compound **31**



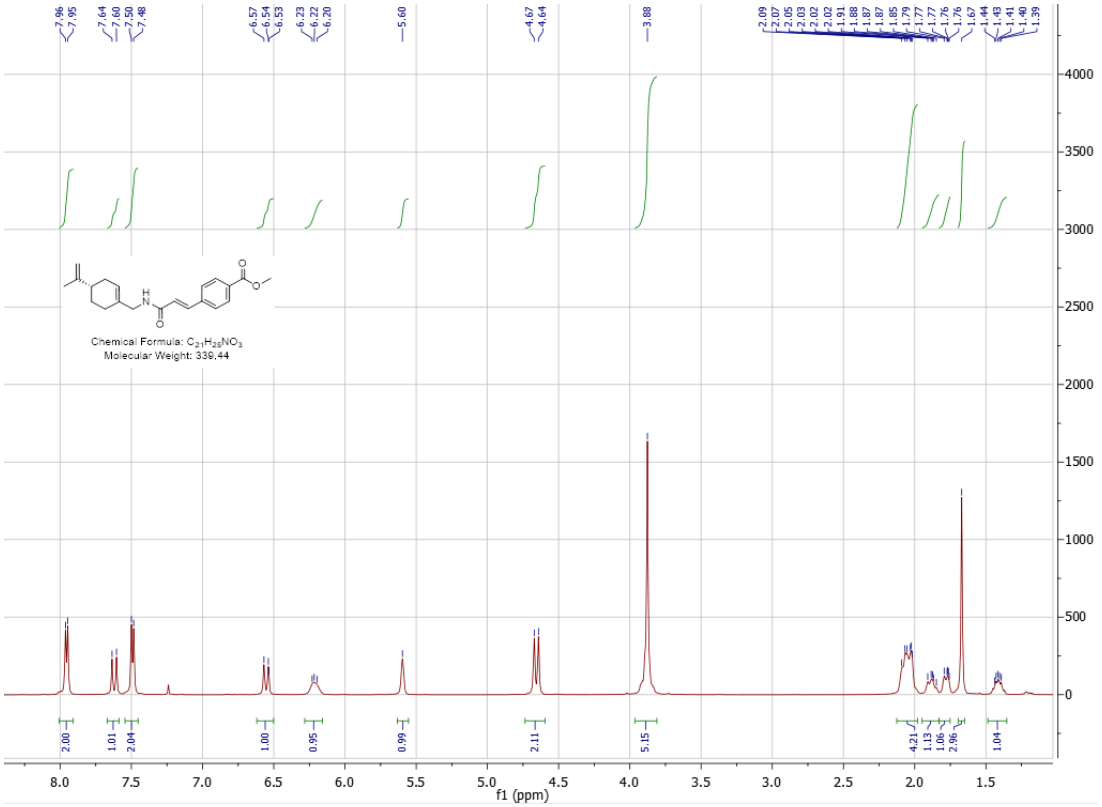
^{13}C NMR spectrum of compound **31**



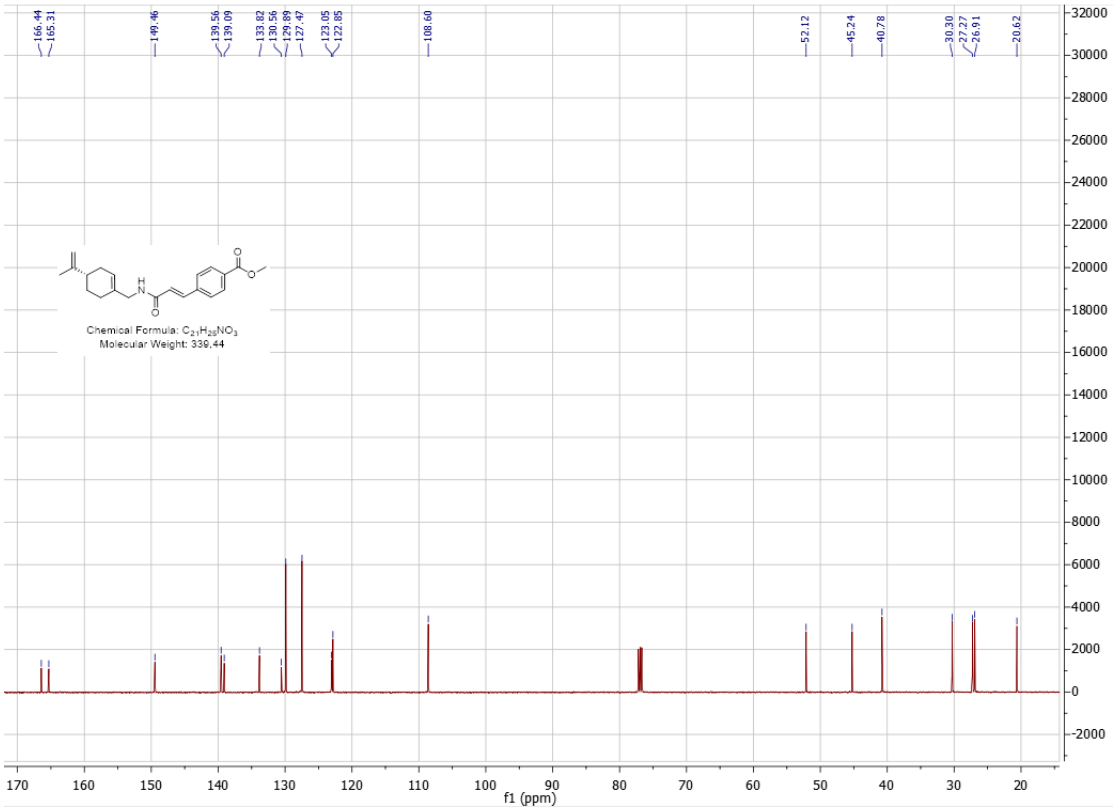
Mass-spectrum of compound **31**



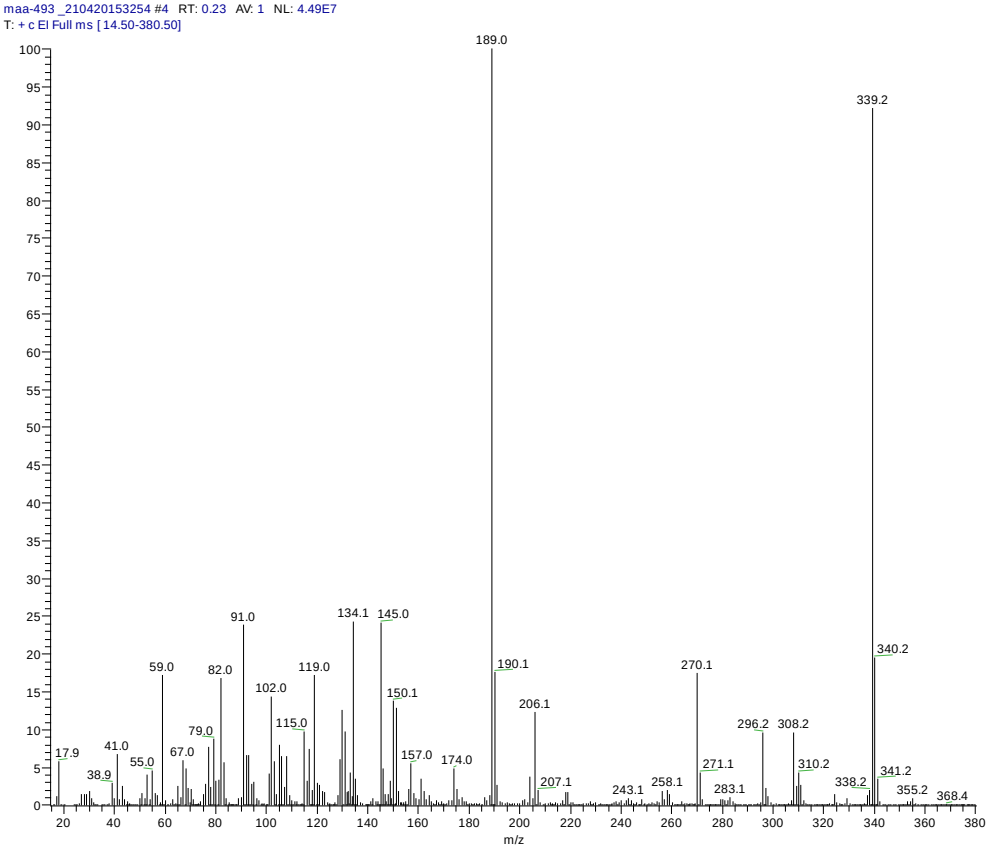
^{1}H NMR spectrum of compound **34a**



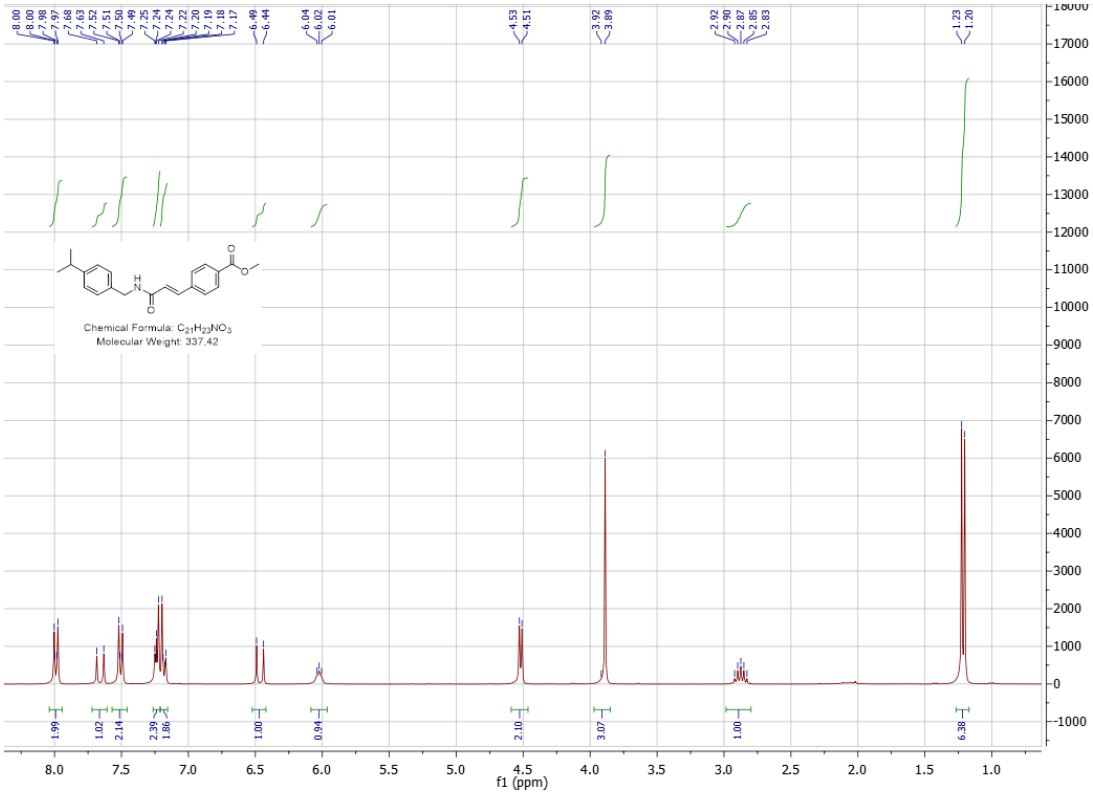
^{13}C NMR spectrum of compound **34a**



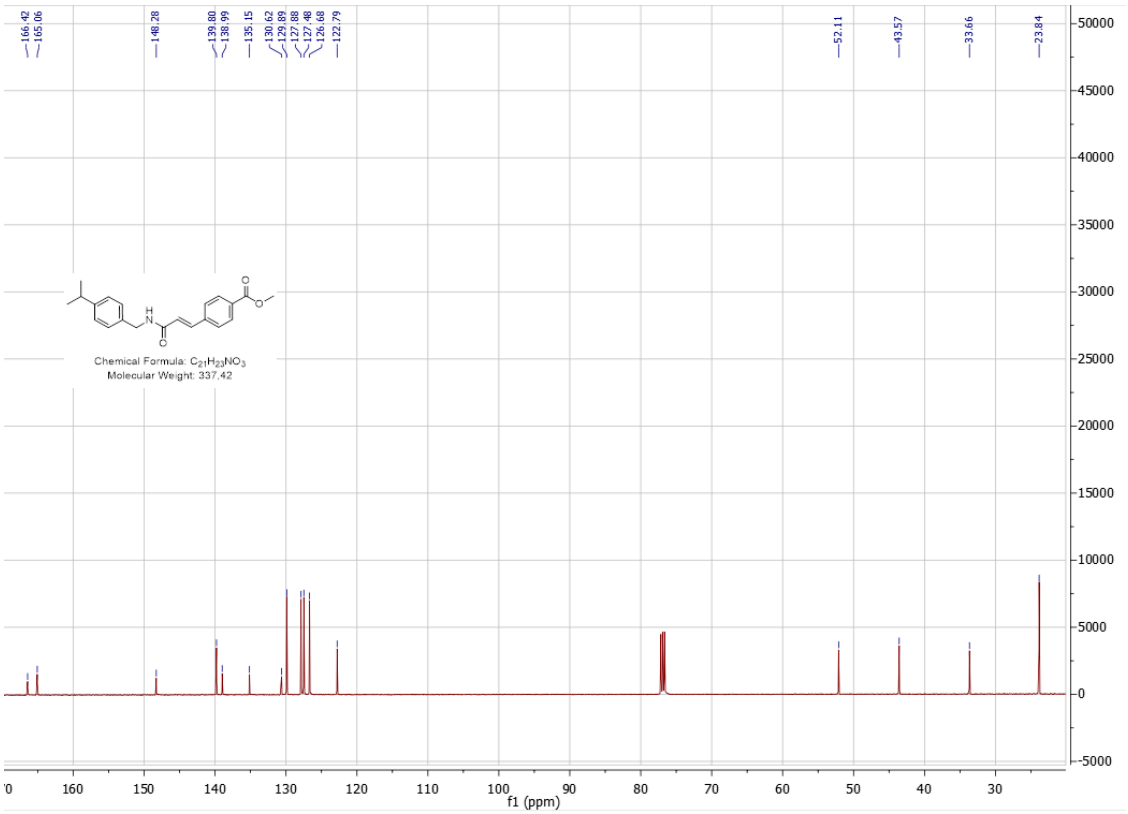
Mass-spectrum of compound **34a**



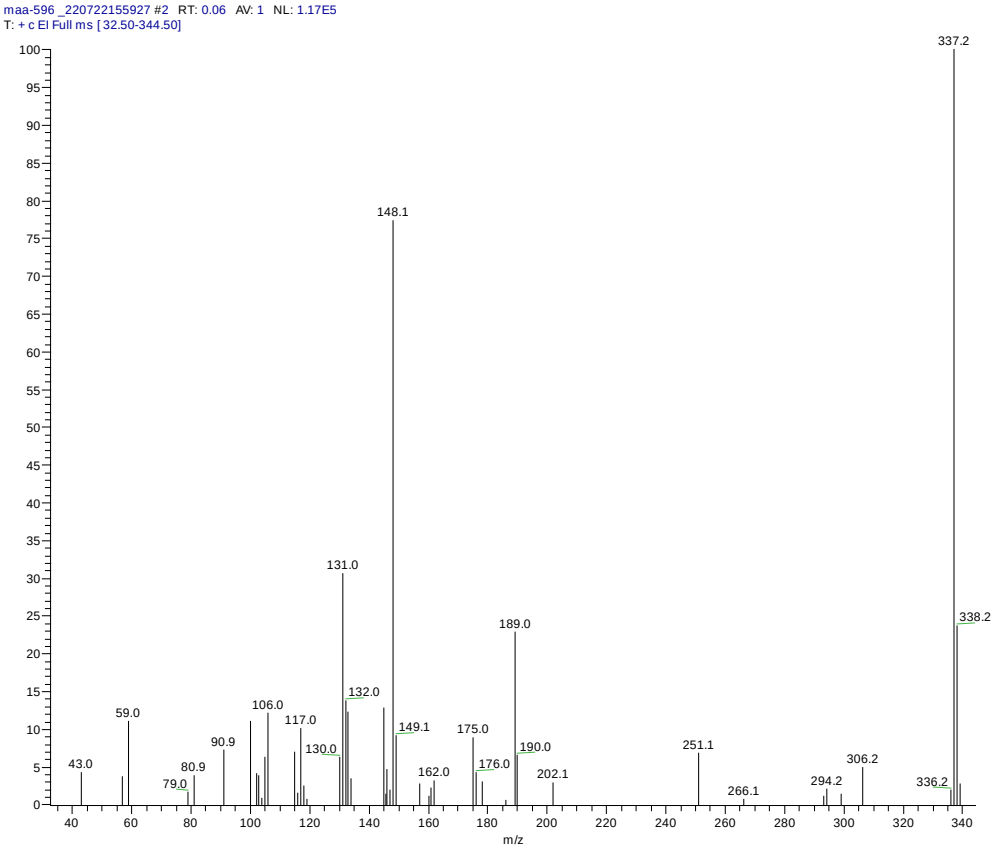
^{1}H NMR spectrum of compound **34b**



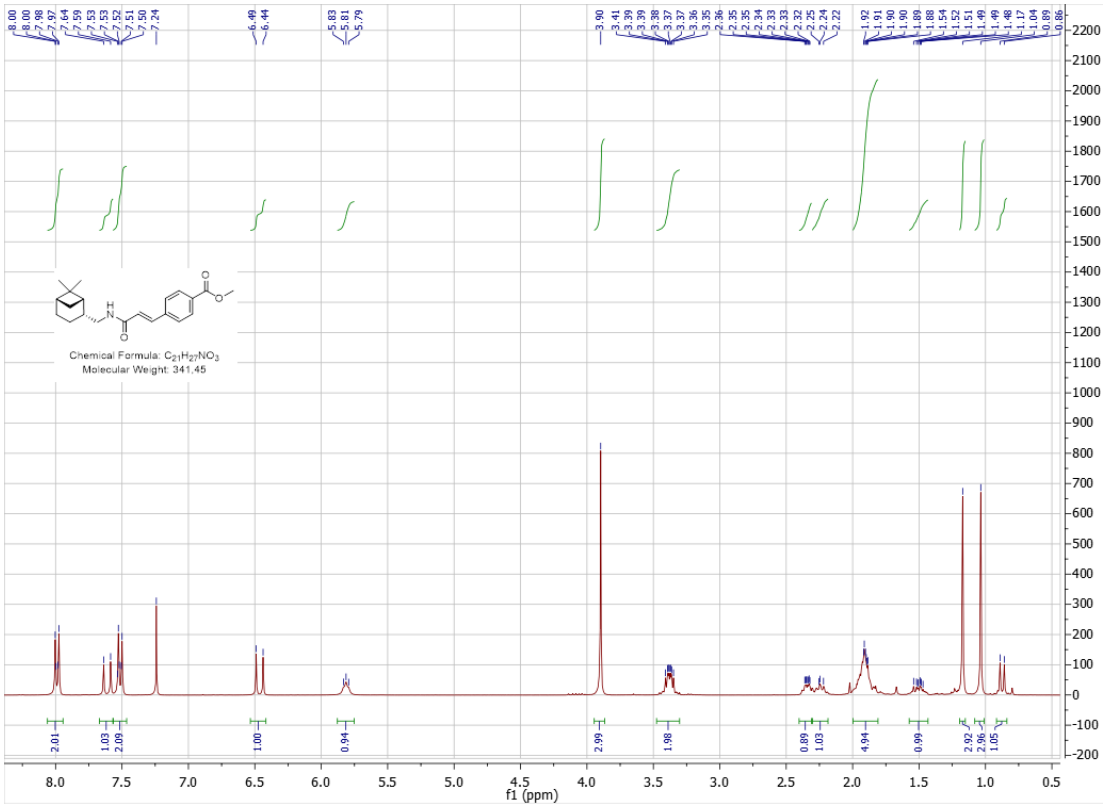
^{13}C NMR spectrum of compound **34b**



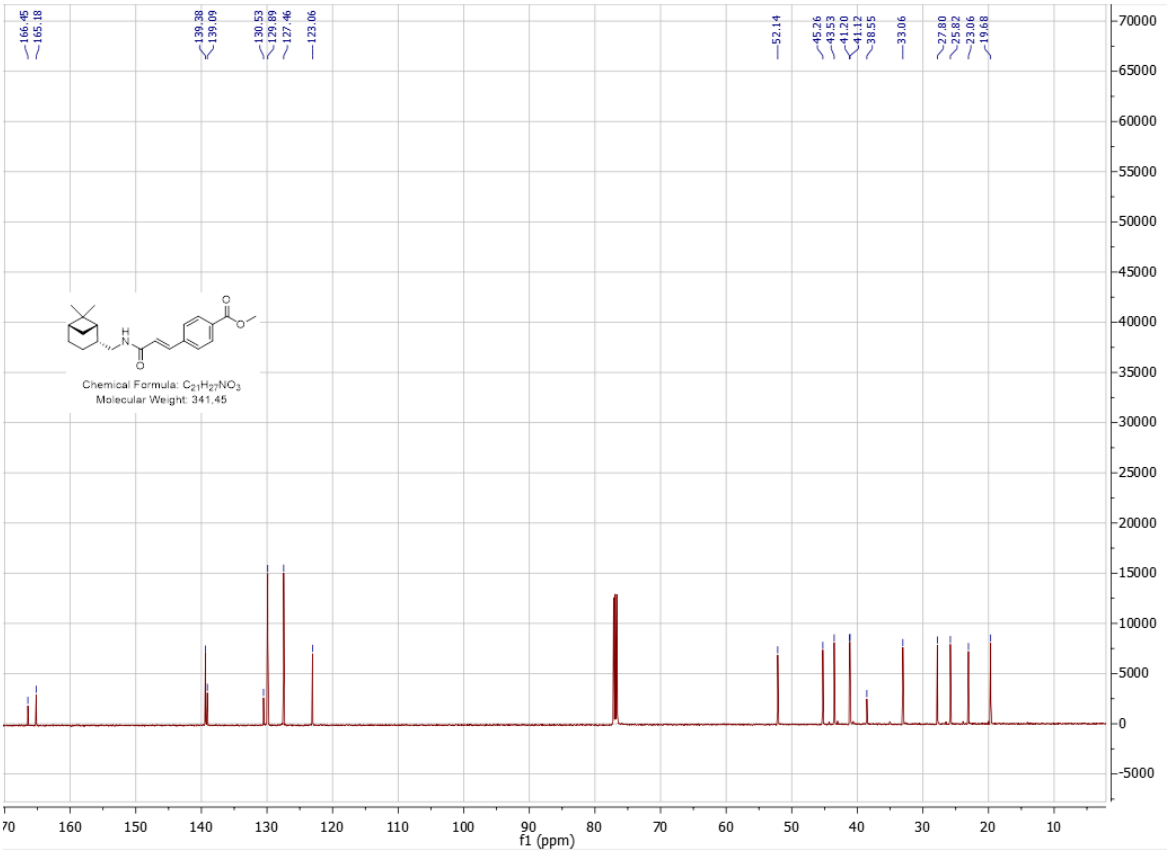
Mass-spectrum of compound **34b**



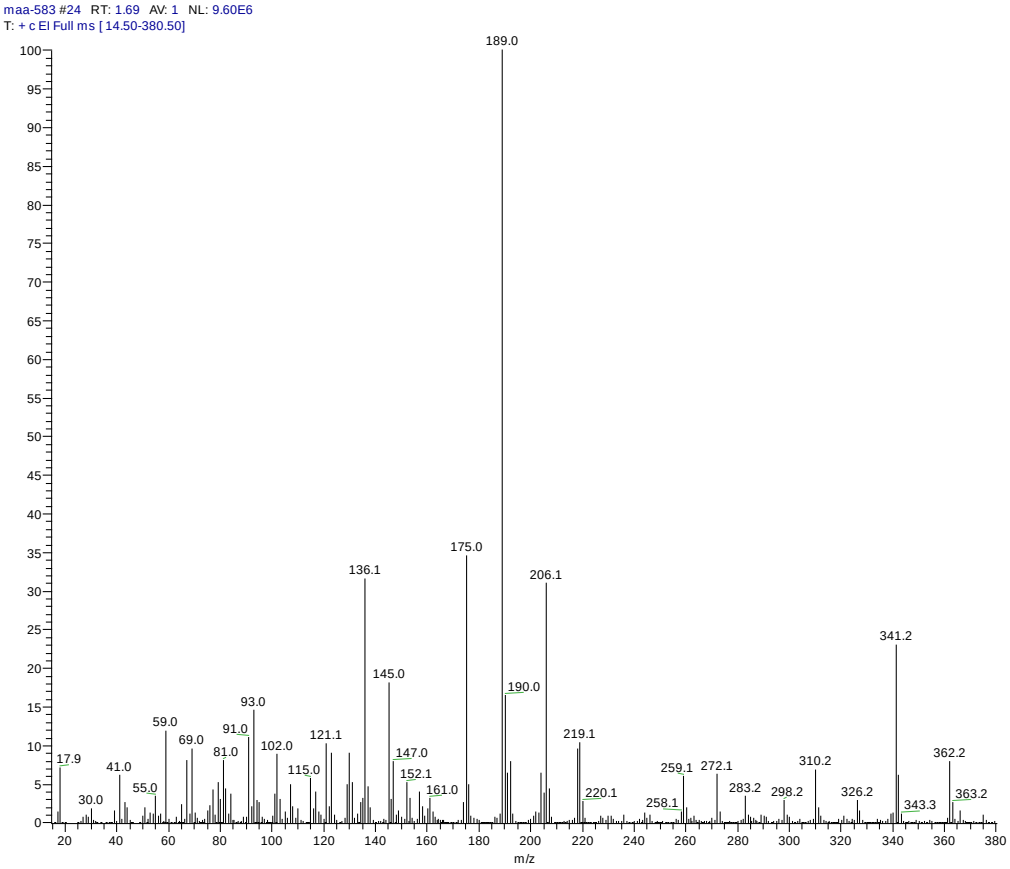
^{1}H NMR spectrum of compound **34c**



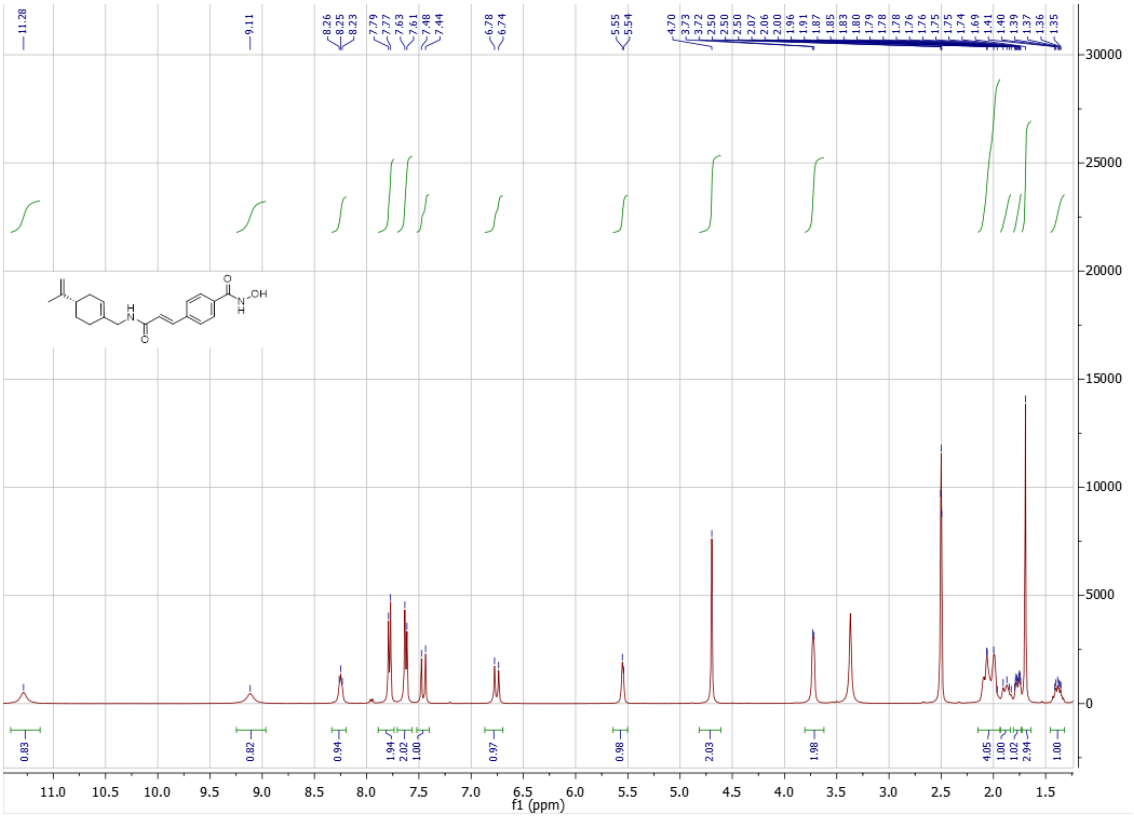
^{13}C NMR spectrum of compound **34c**



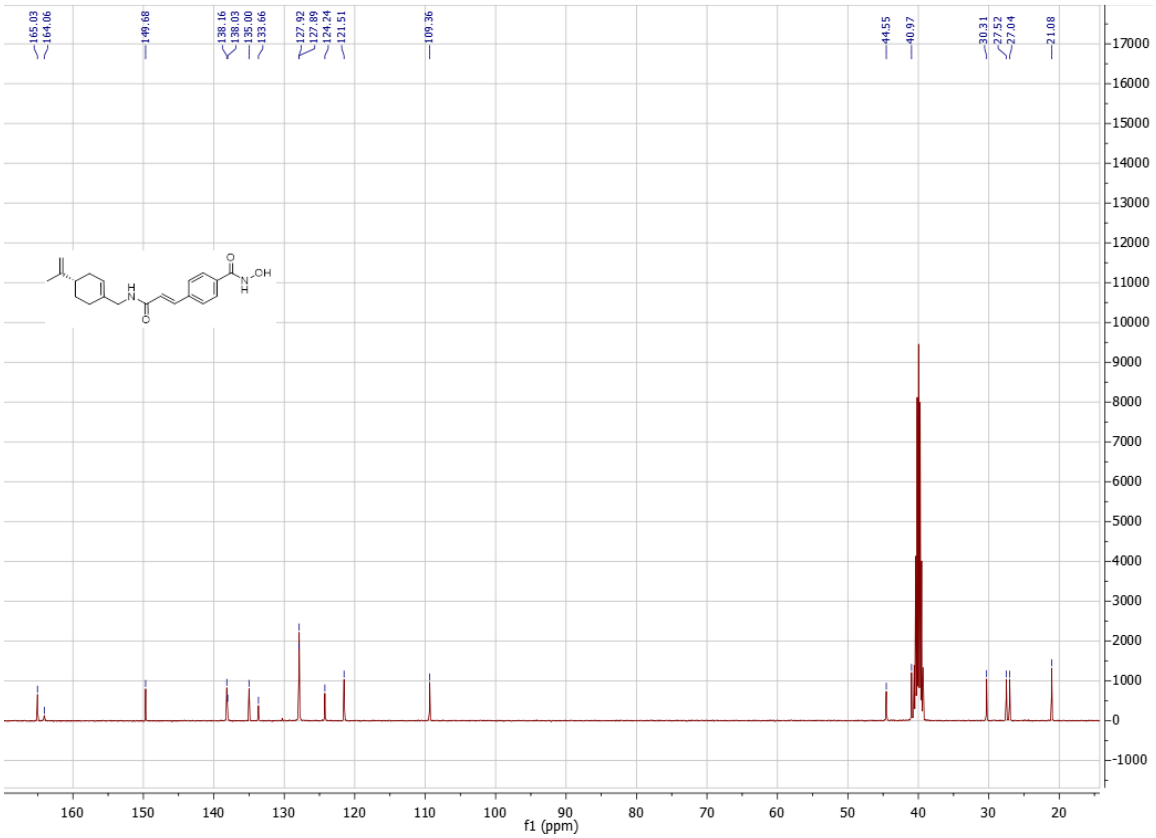
Mass-spectrum of compound **34c**



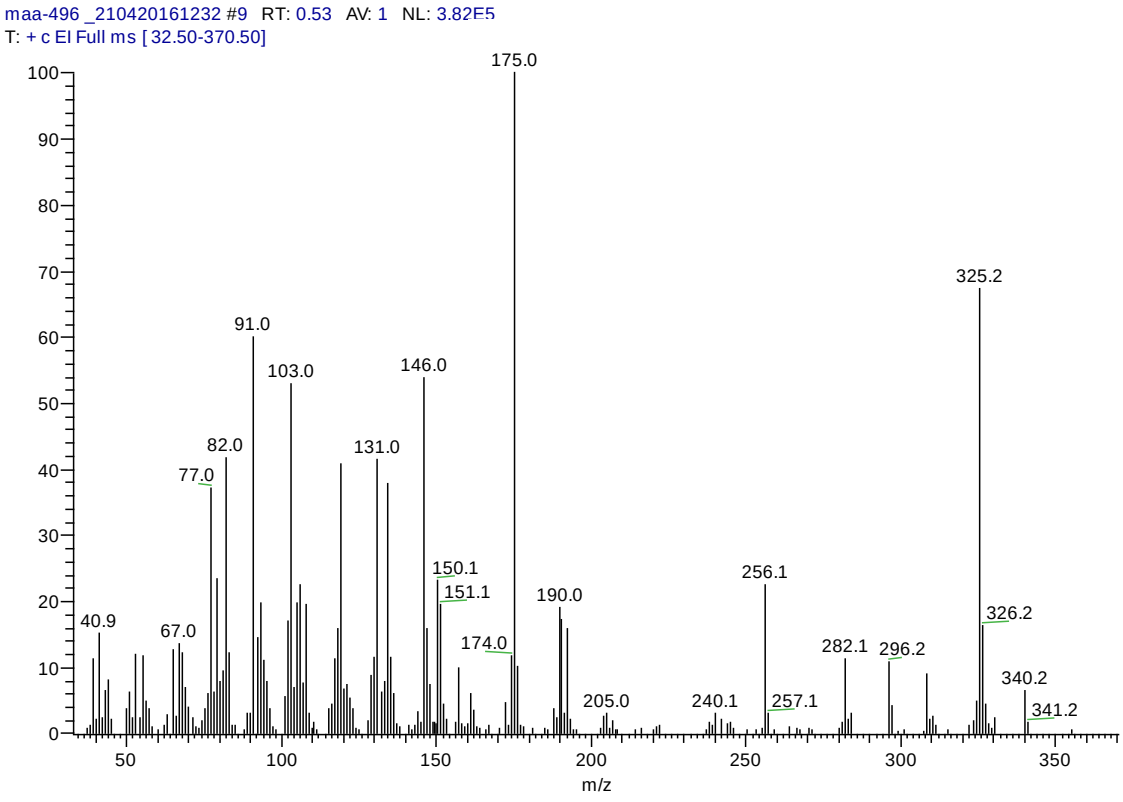
^{1}H NMR spectrum of compound **35a**



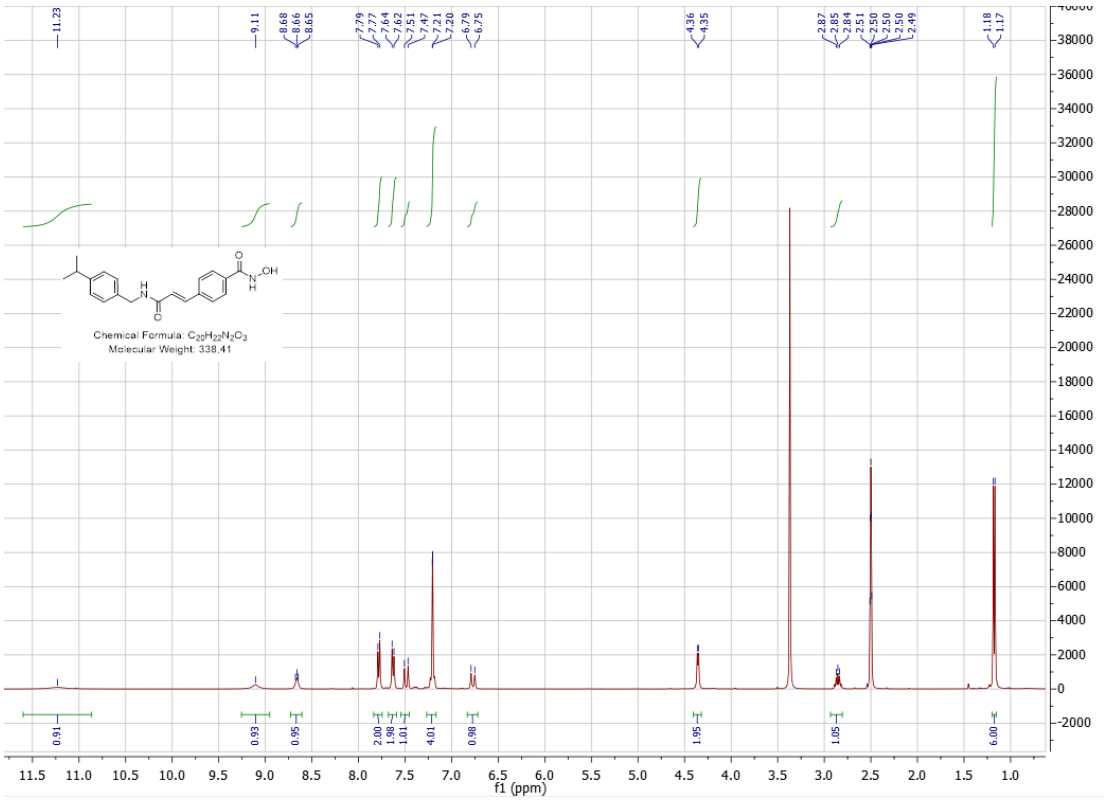
^{13}C NMR spectrum of compound **35a**



Mass-spectrum of compound **35a**



^{1}H NMR spectrum of compound **35b**



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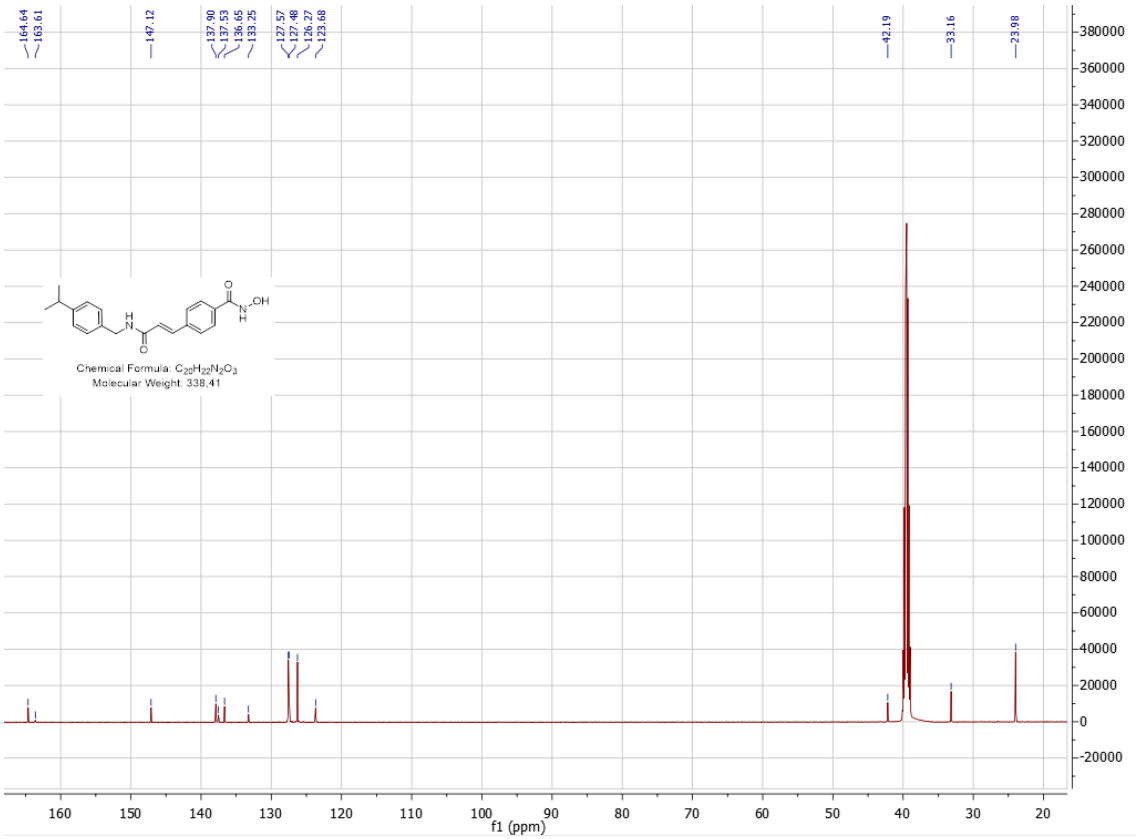

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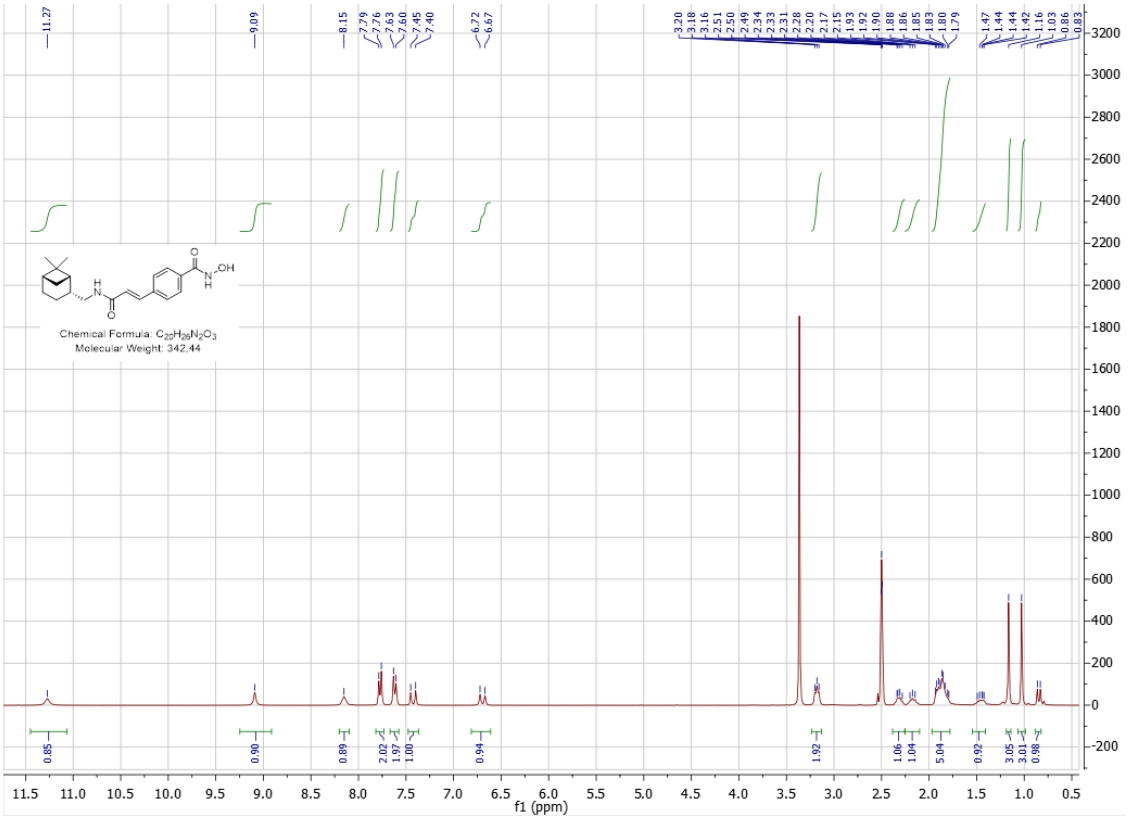
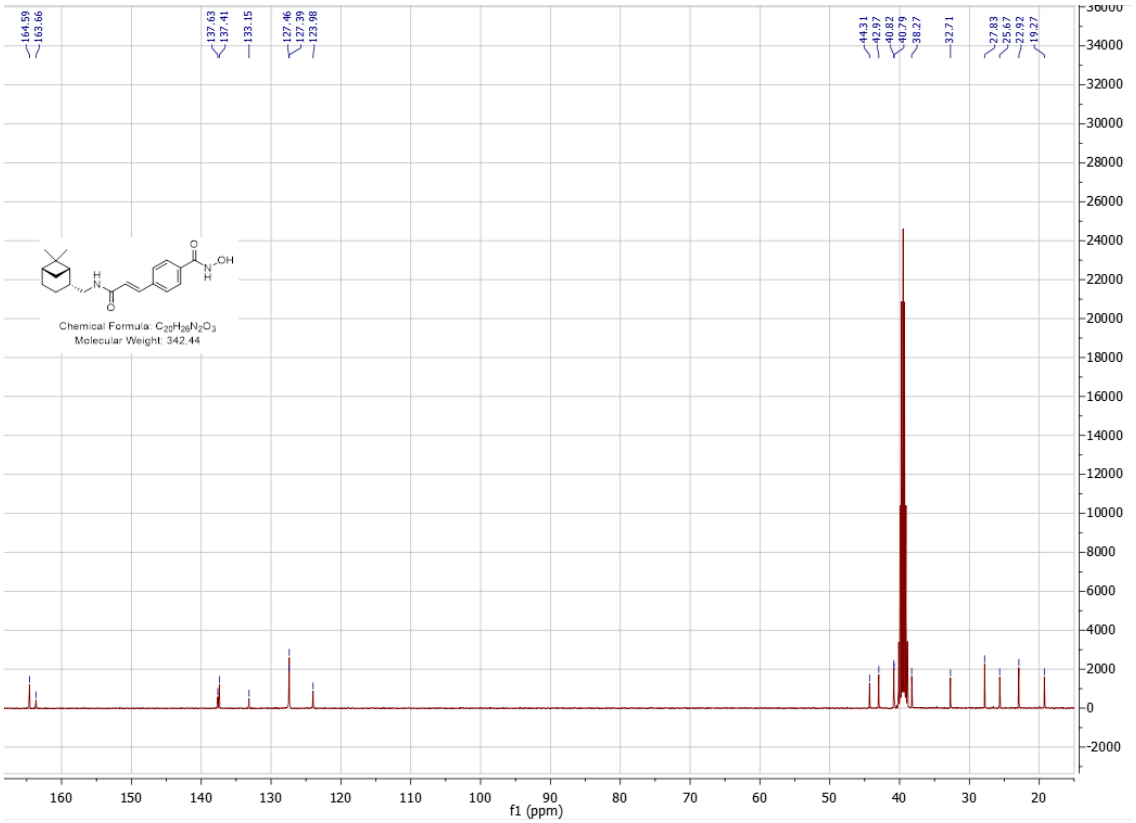
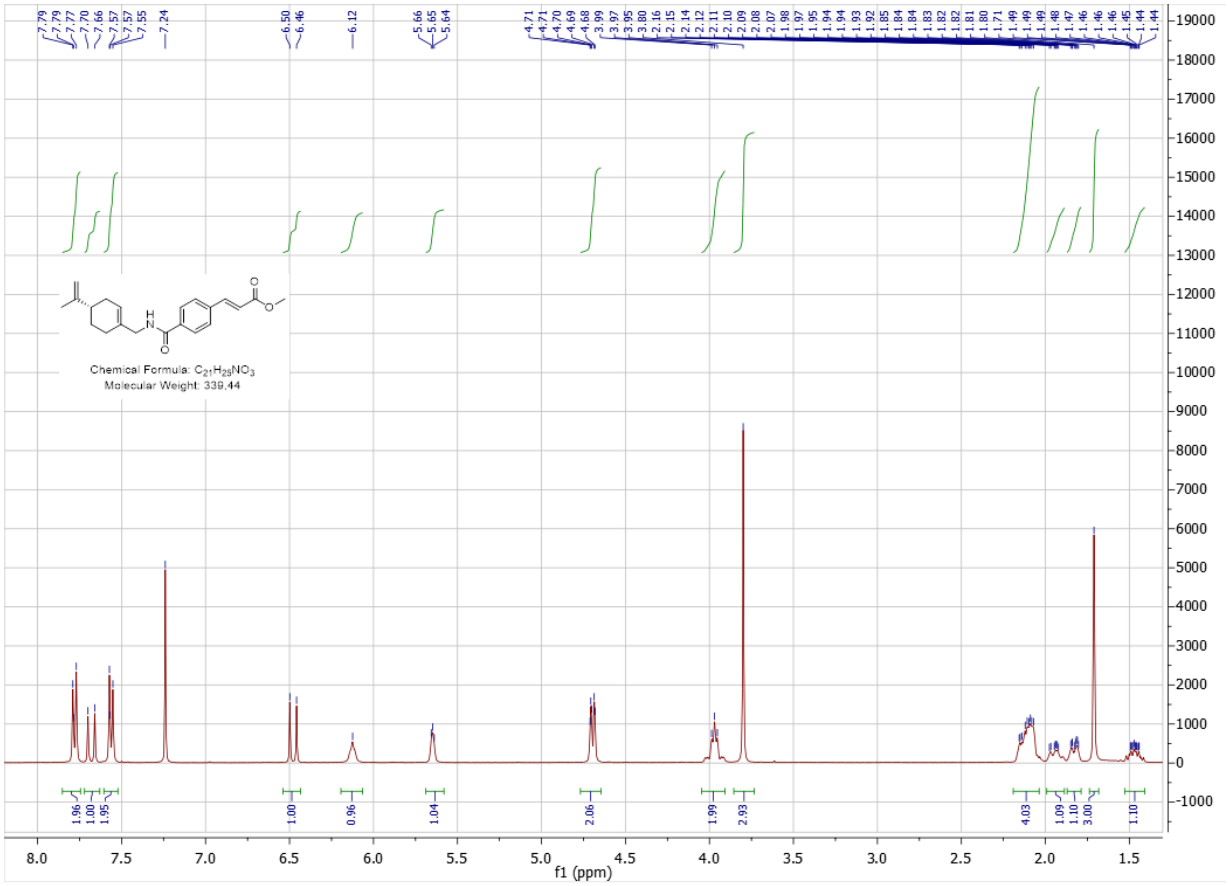


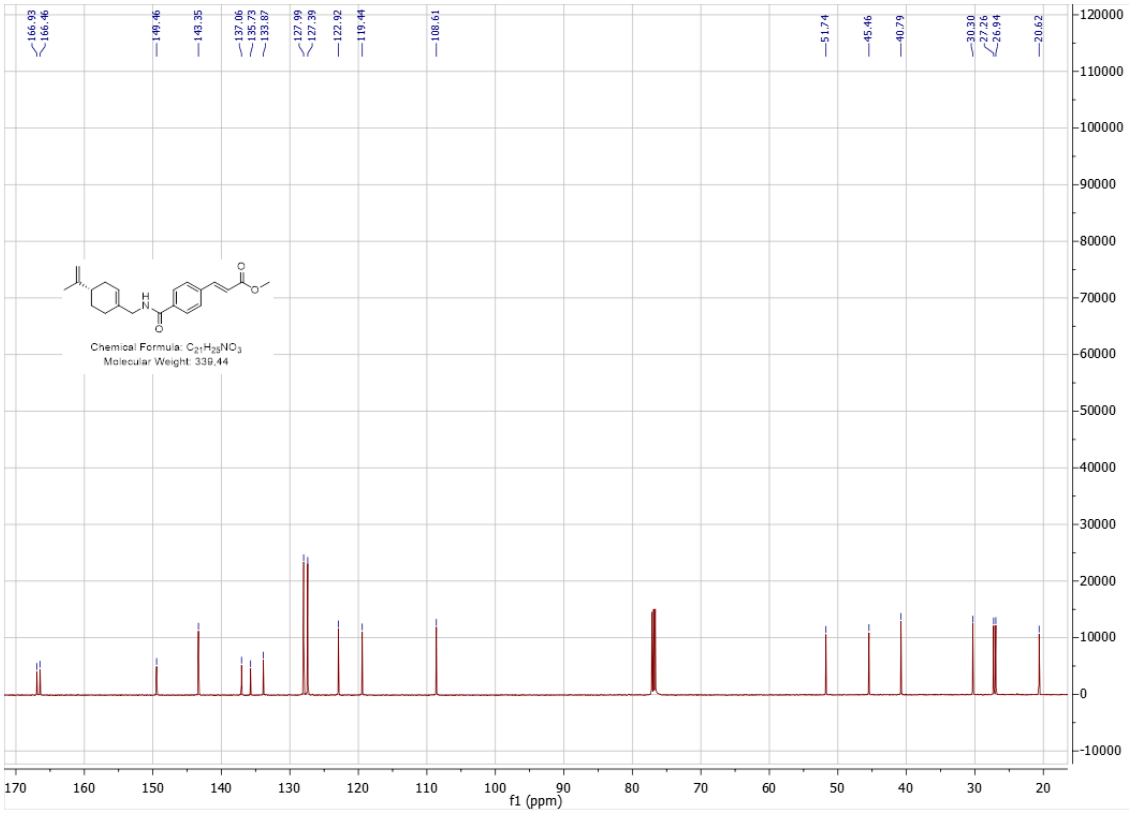
^{13}C NMR spectrum of compound **35c**



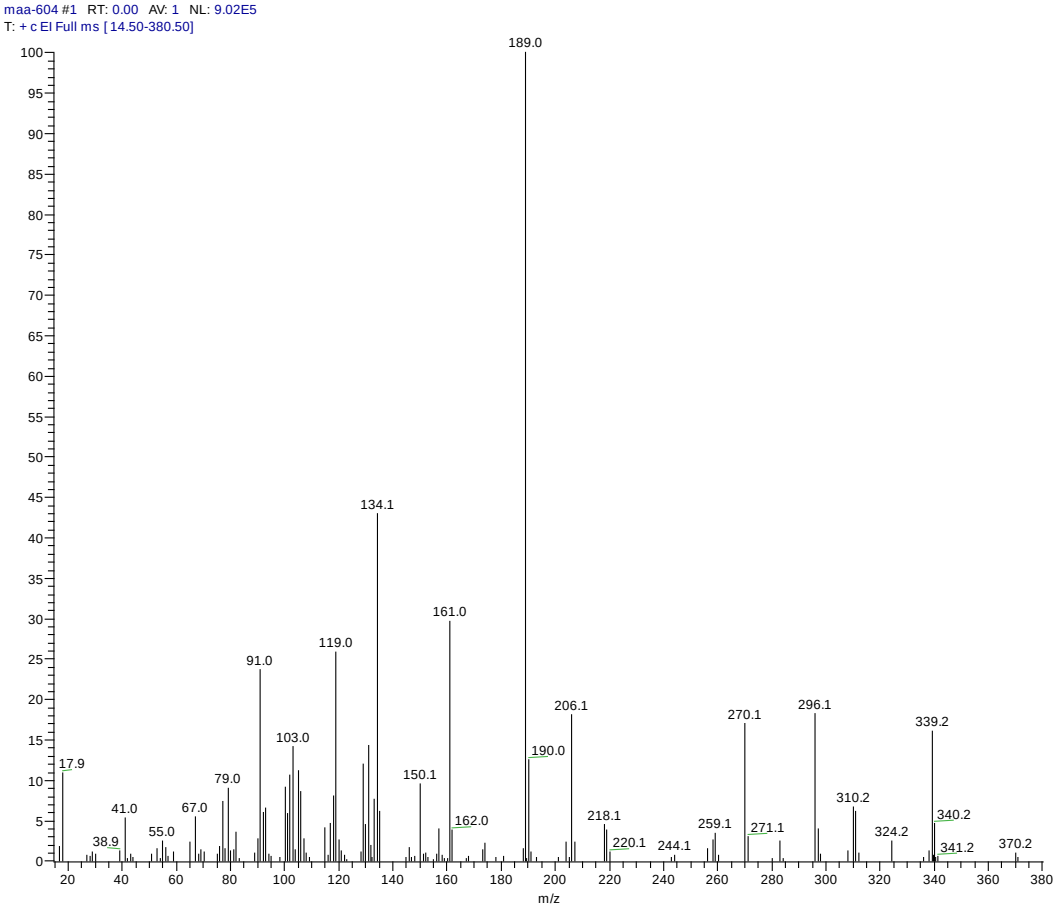
^{1}H NMR spectrum of compound **37a**



^{13}C NMR spectrum of compound **37a**



Mass-spectrum of compound **37a**



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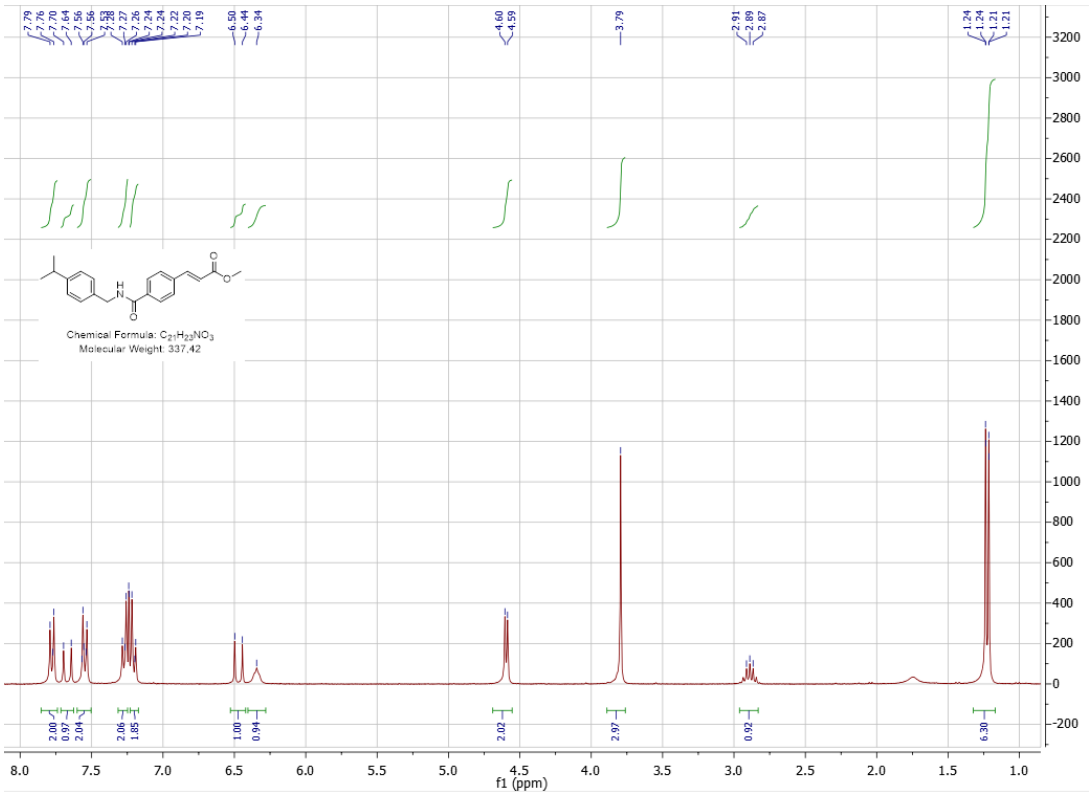
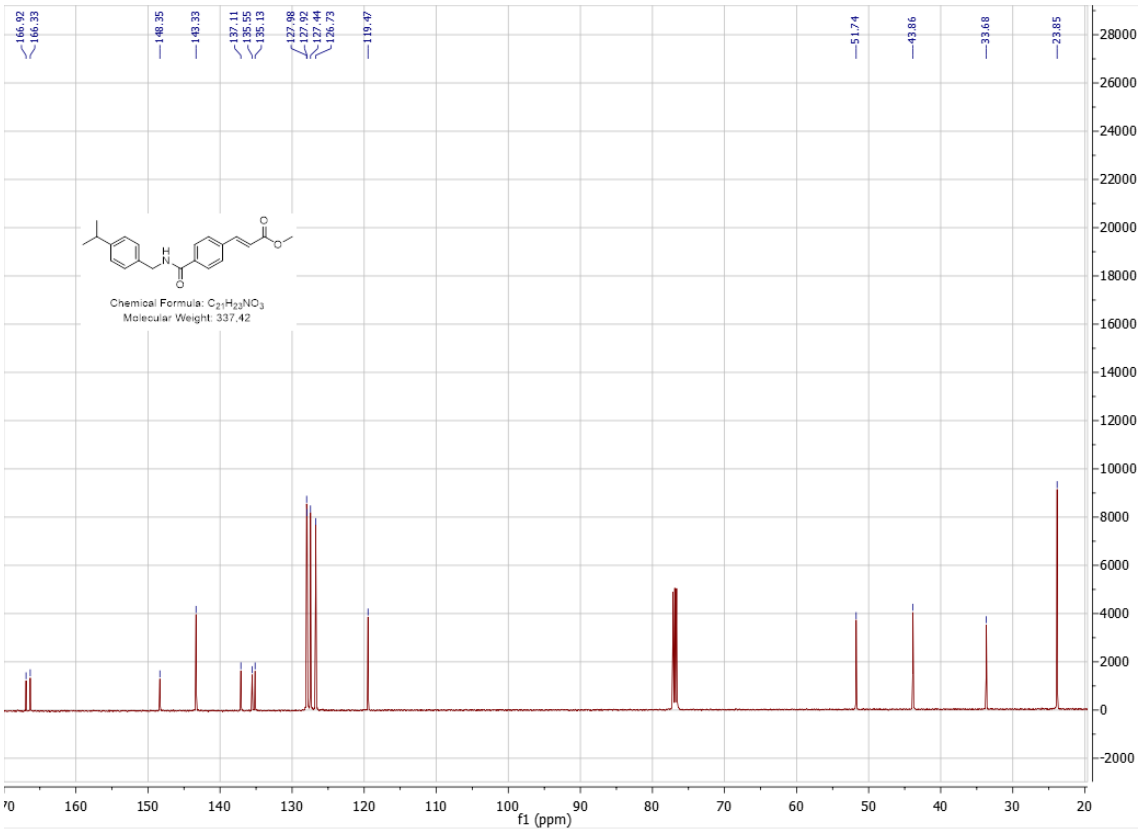
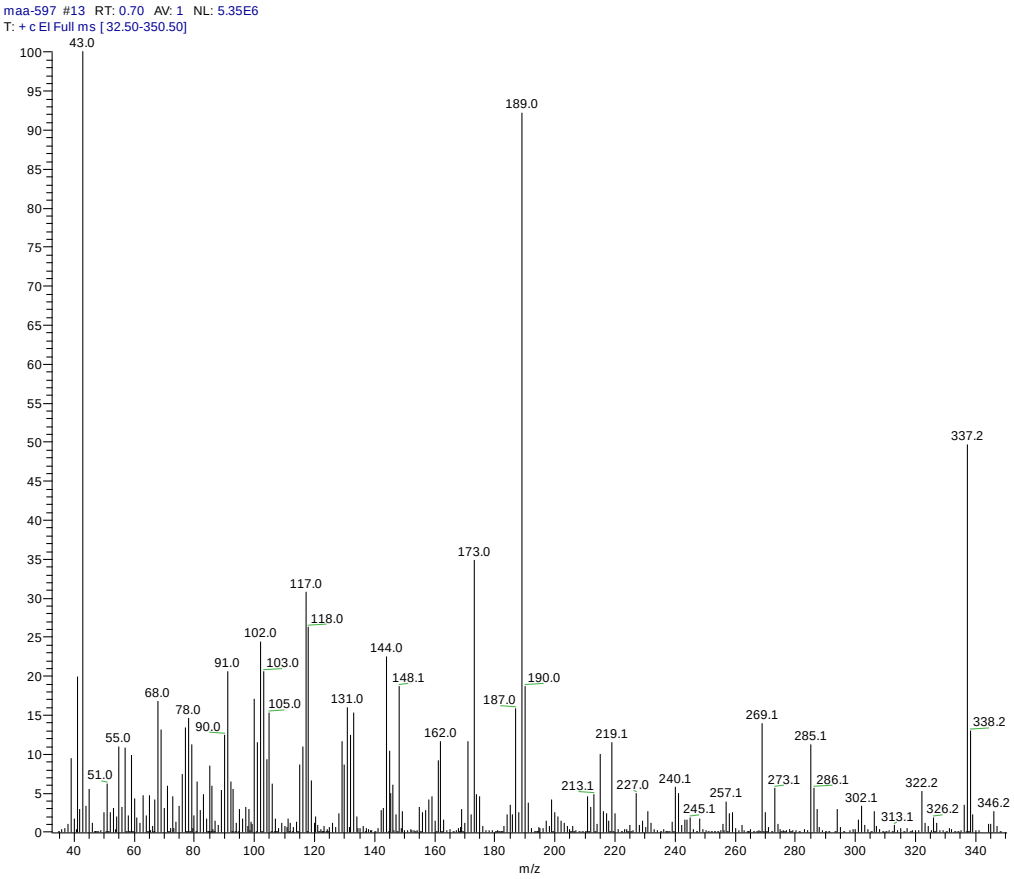


^{13}C NMR spectrum of compound **37b**



Mass-spectrum of compound **37b**



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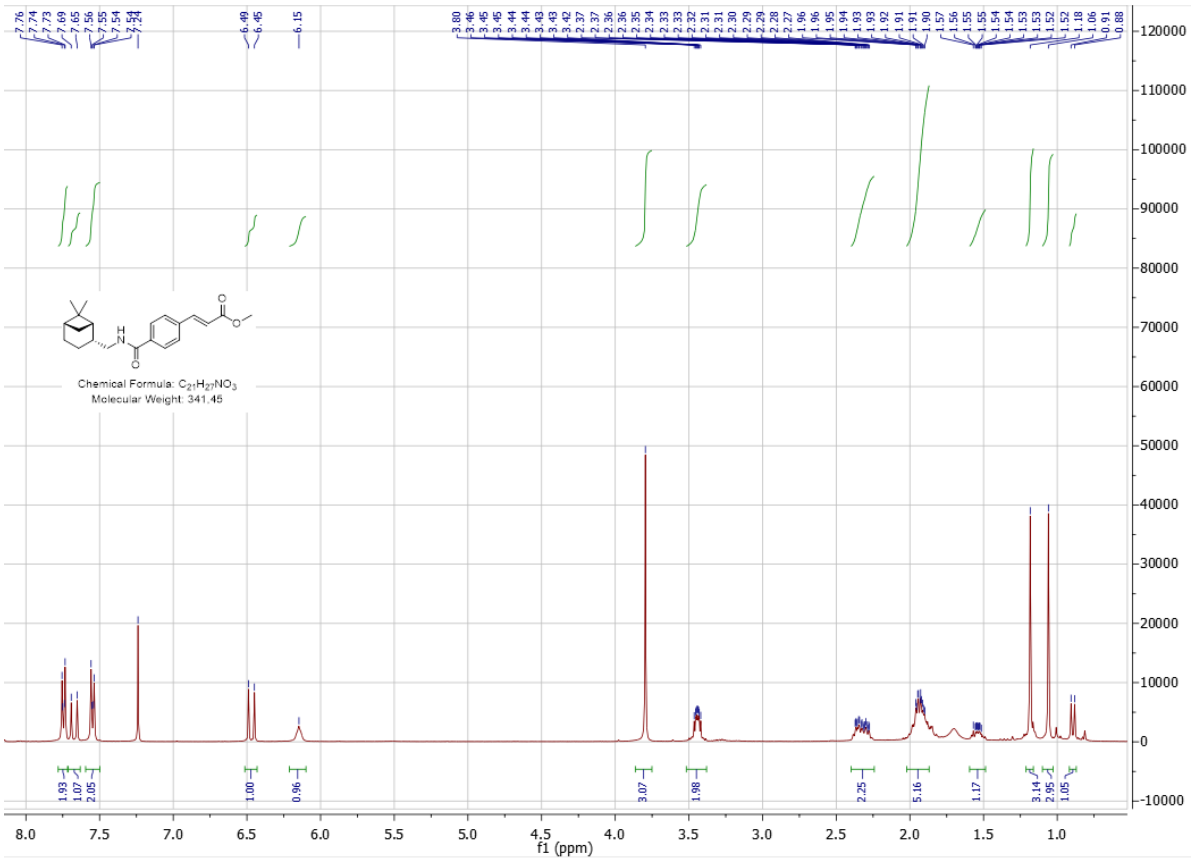
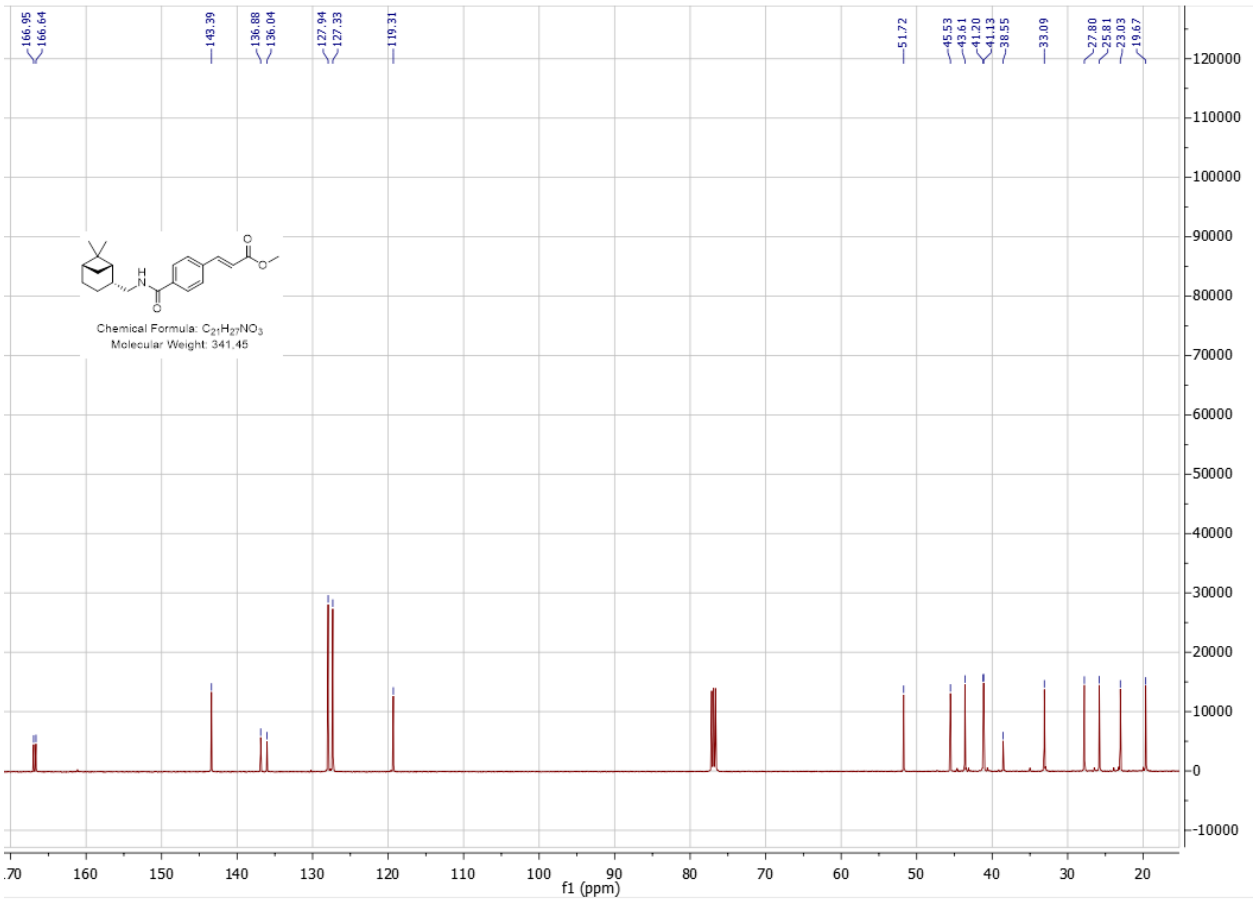
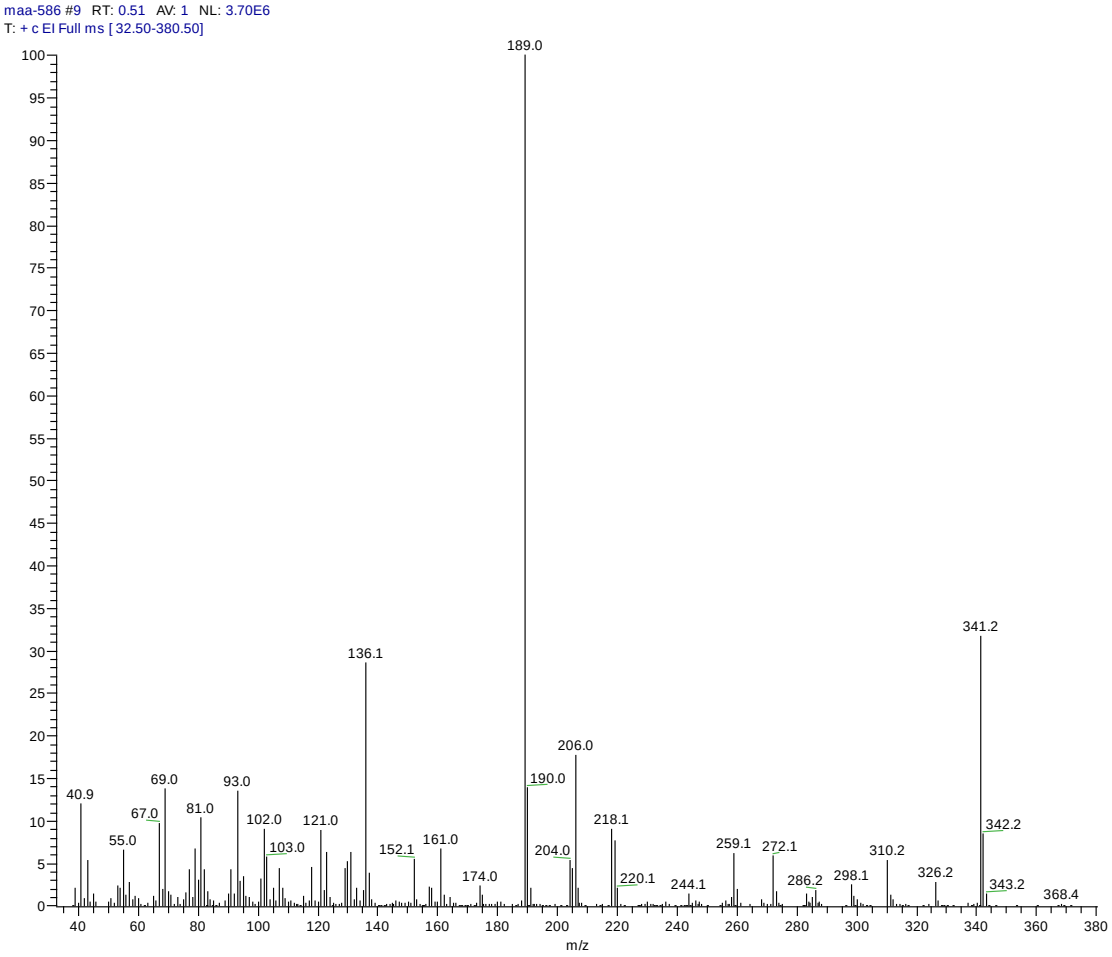


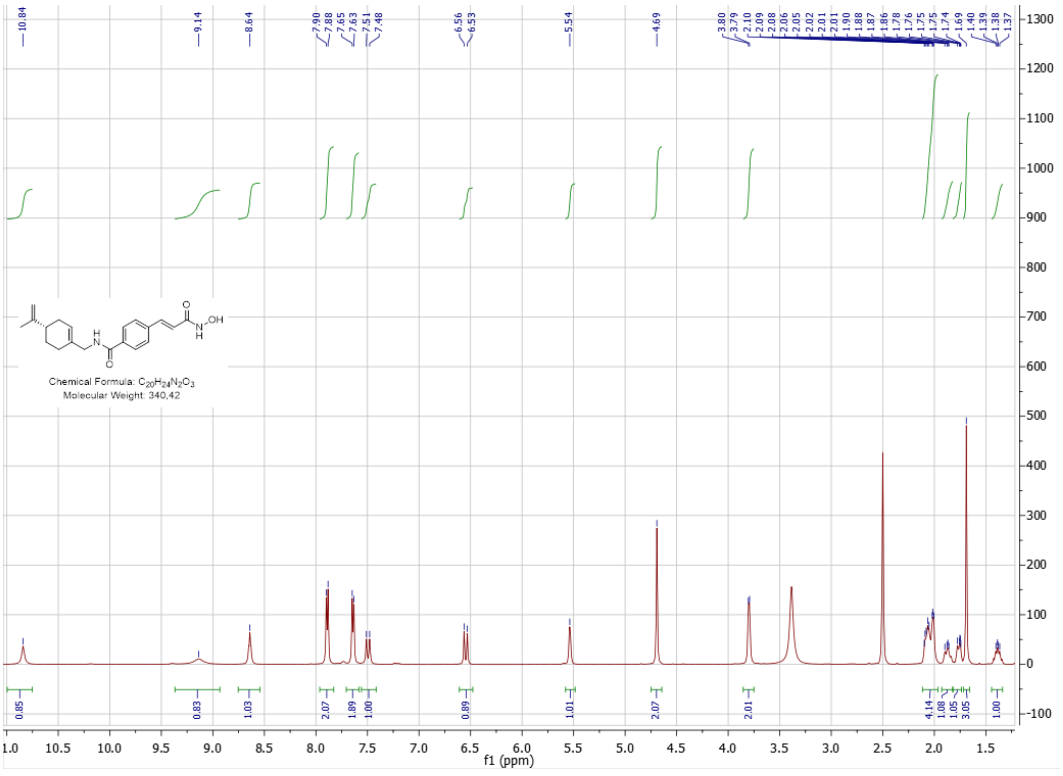
^{13}C NMR spectrum of compound **37c**



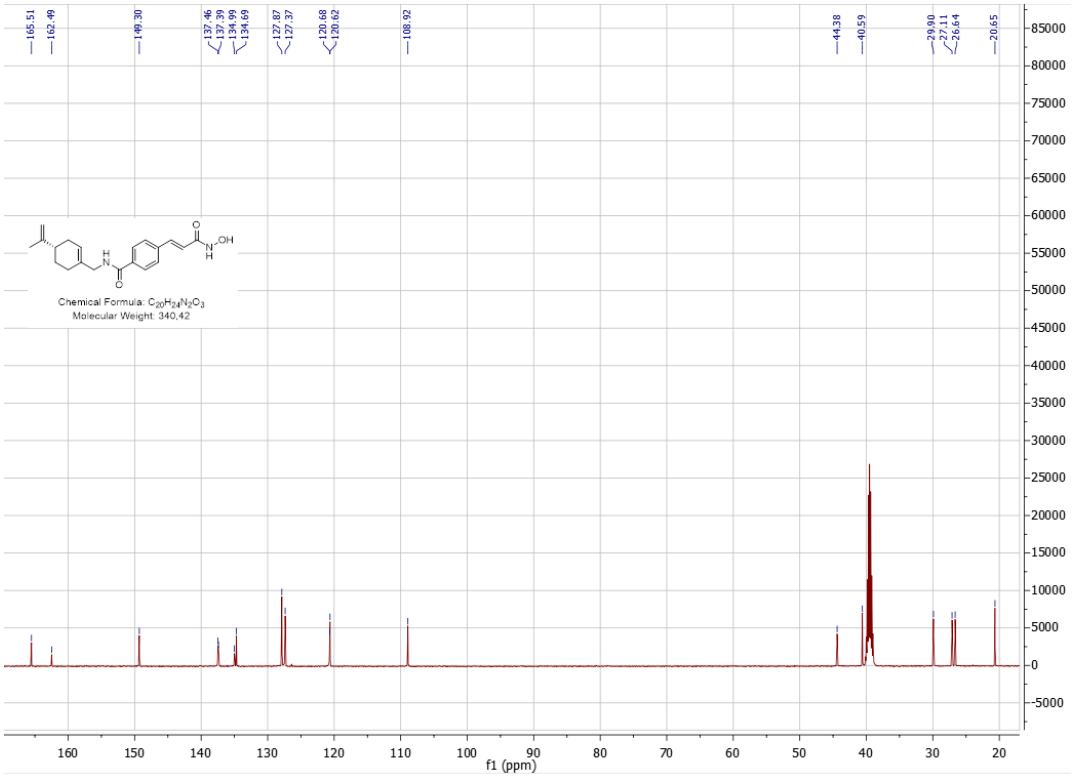
Mass-spectrum of compound **37c**



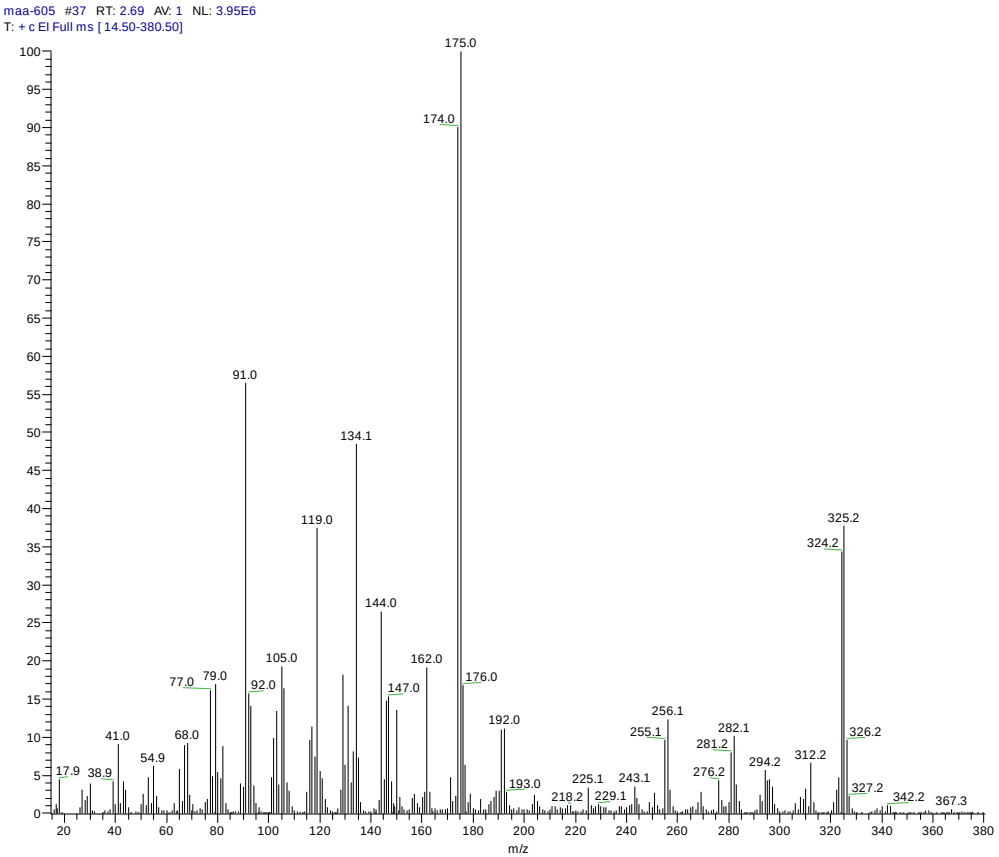
^{1}H NMR spectrum of compound **38a**



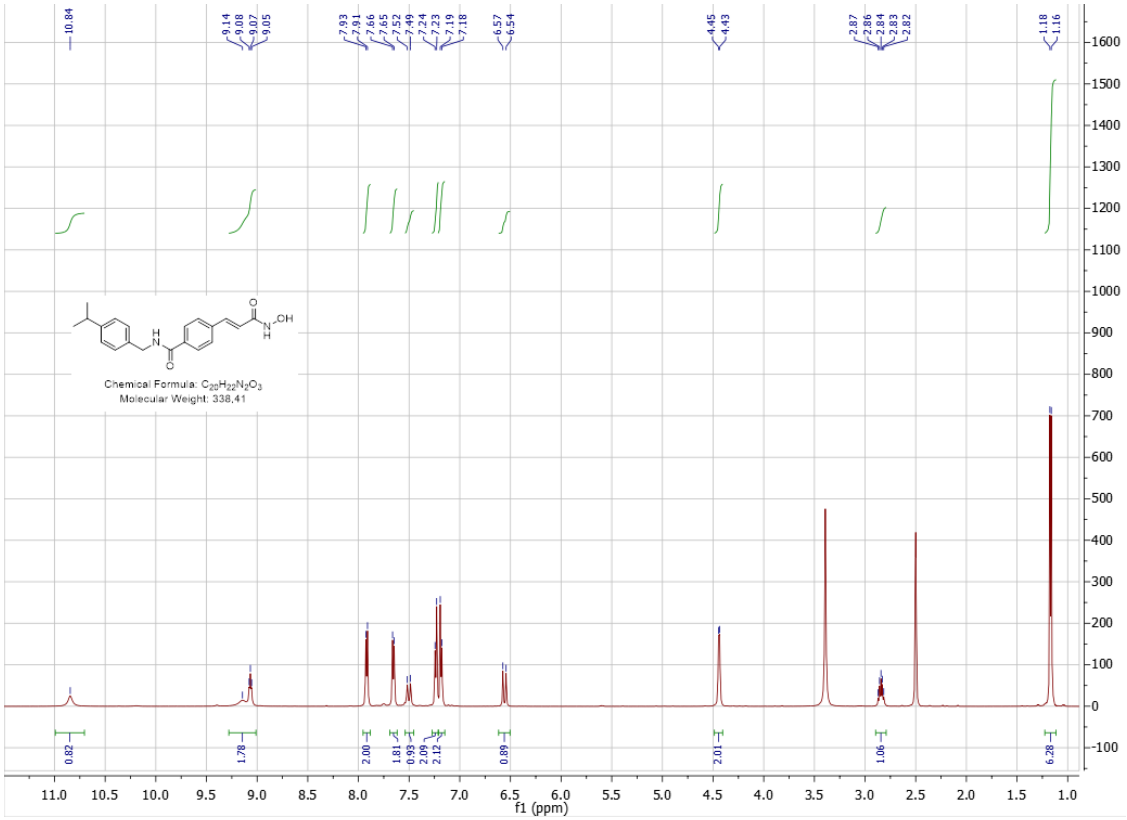
^{13}C NMR spectrum of compound **38a**



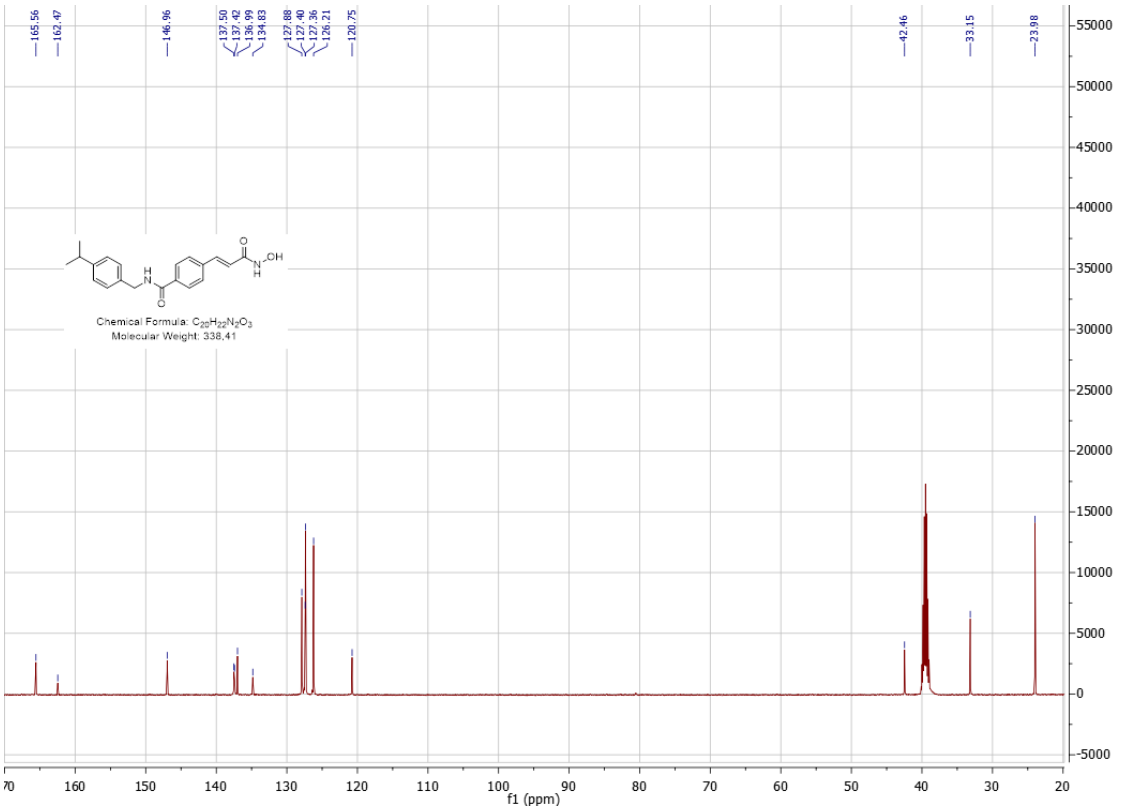
Mass-spectrum of compound **38a**



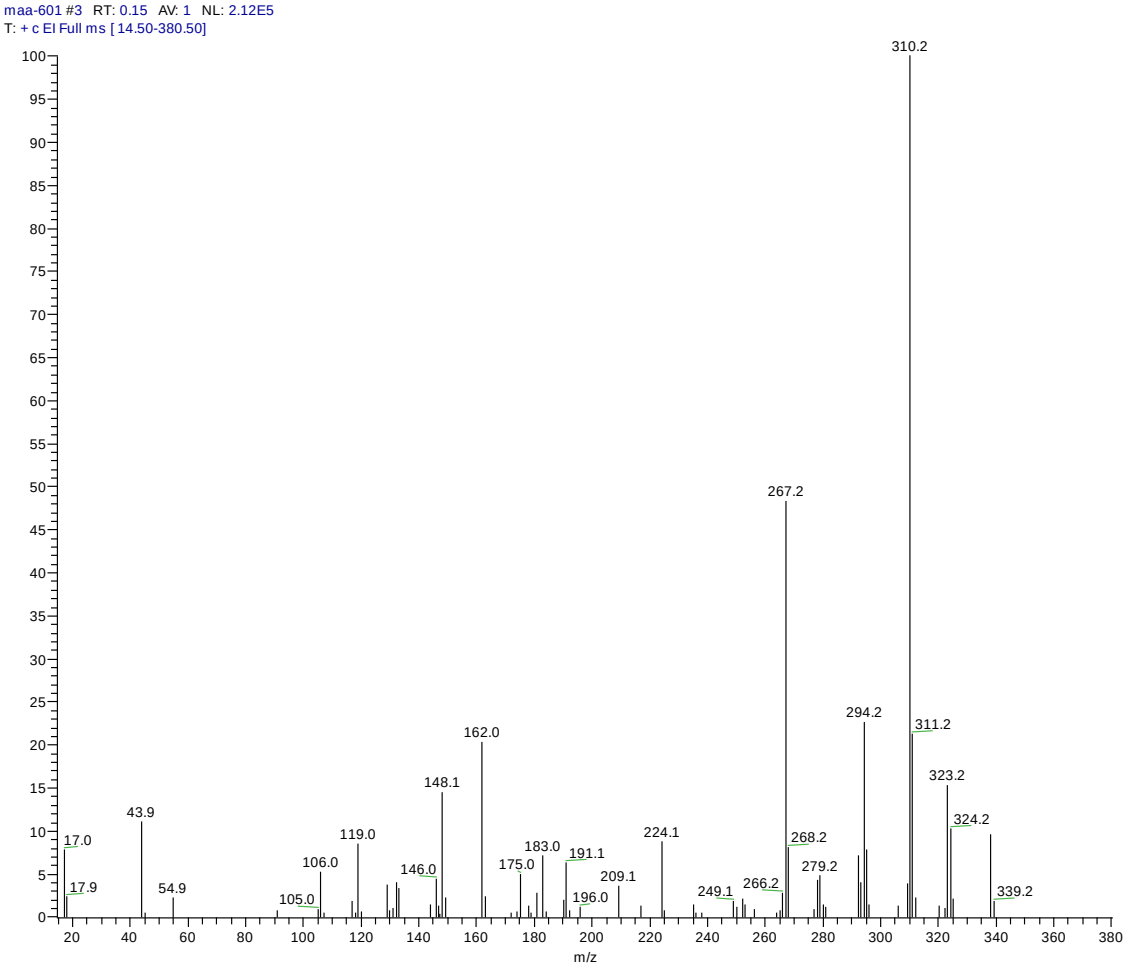
^{1}H NMR spectrum of compound **38b**



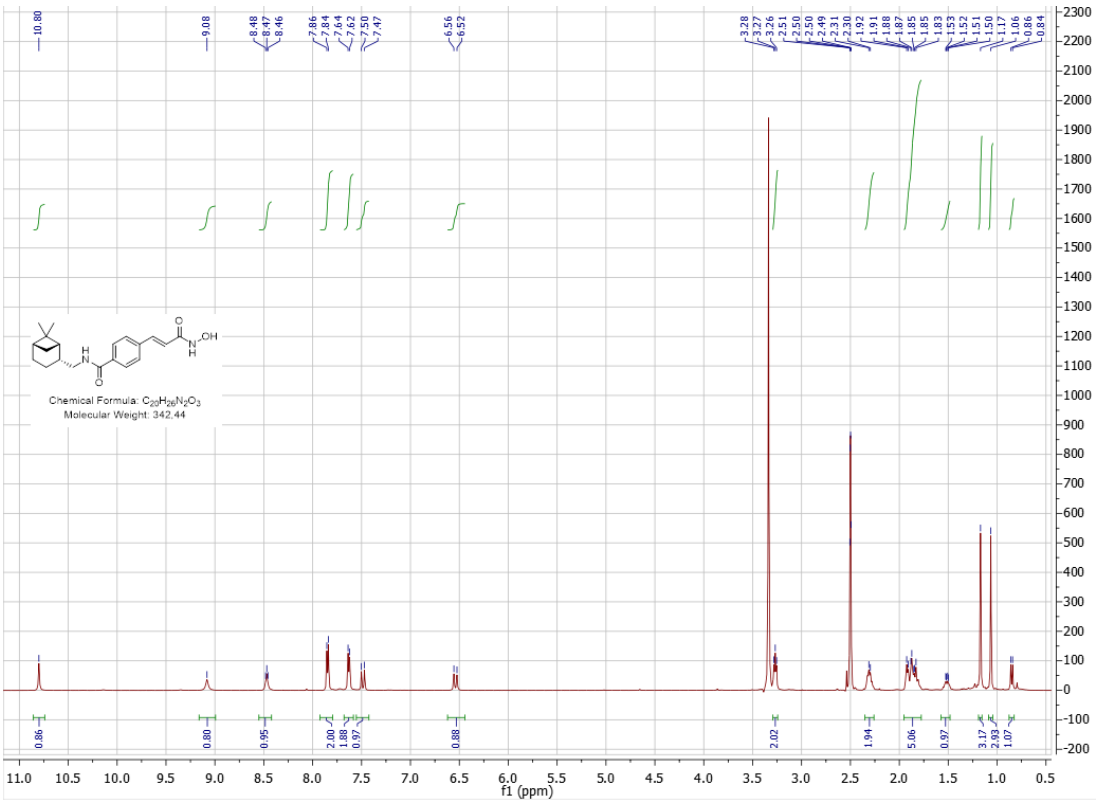
^{13}C NMR spectrum of compound **38b**



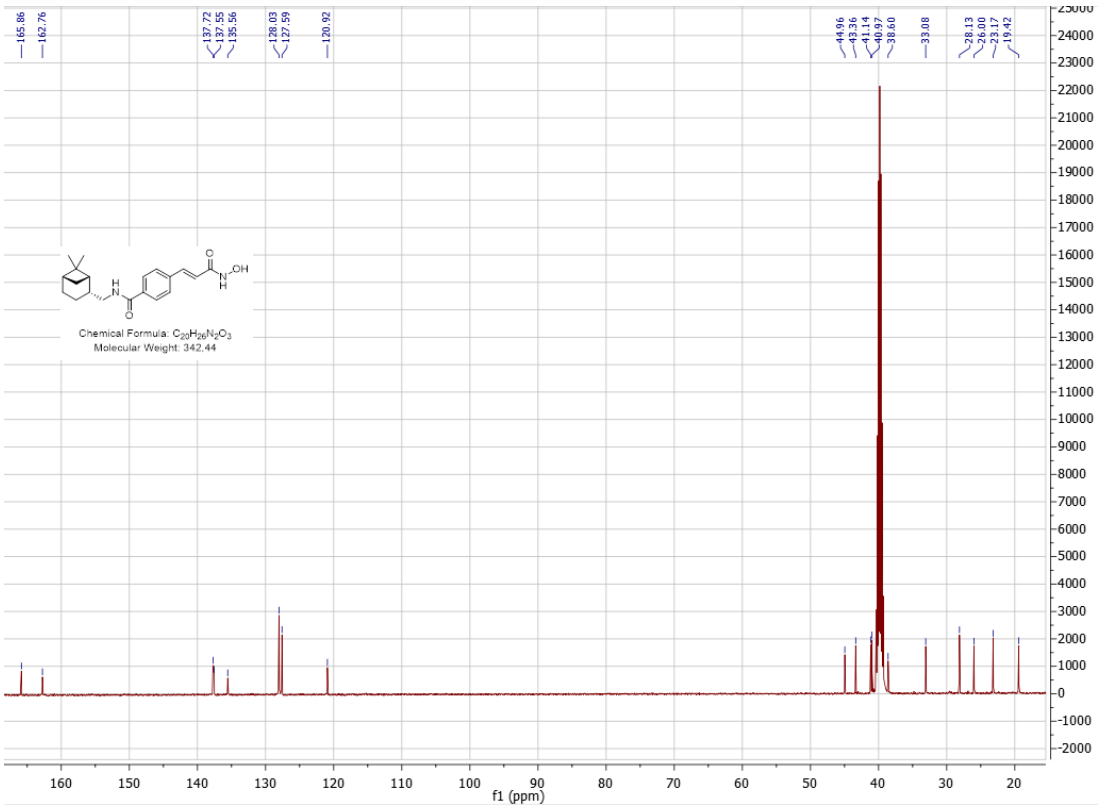
Mass-spectrum of compound **38b**



^{1}H NMR spectrum of compound **38c**



^{13}C NMR spectrum of compound **38c**



Mass-spectrum of compound **38c**

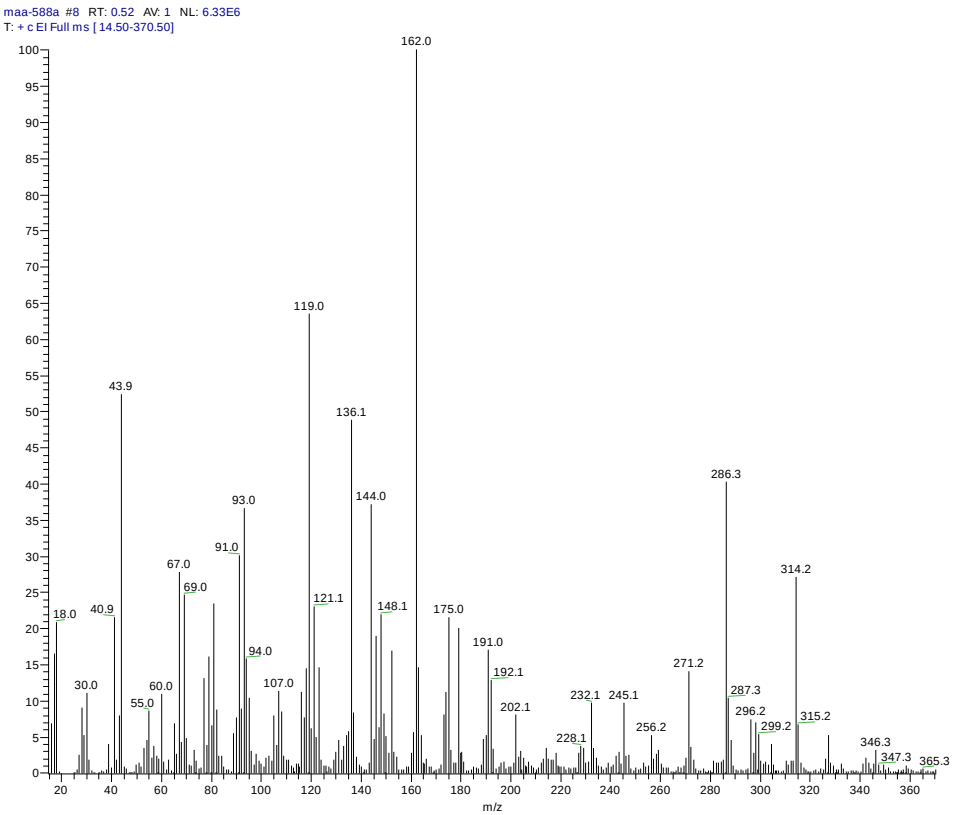


Table S1. Molecular docking of hydroxamic acids against HDAC6 (PDB ID: 5EDU) Hydrogen bonds are shown in the "H-bonds" column. Other interaction between peptide and ligand are shown in the "Other int-s".

Compound	H-bonds	Other interactions	Docking Score	IC_{50}, μM
Trichostatin A	HIS610	π-π stacking: HIE500	-8.798	
31	SER568 HIS610 TYR782	---	-9.547	0.66
30	SER568 GLY619 TYR782	---	-8.662	0.61
35a	HIE500 SER568 TYR782	π-π stacking: PHE620 HIE651	-8.120	3.87
38b	SER568	π-π stacking: PHE680	-7.125	4.81
38a	GLY619	π-π stacking: PHE680	-6.886	7.74
35b	HIE500 SER568 TYR782	π-π stacking: HIE500 PHE680	-6.689	8.23
35c	SER568 GLY619	π-π stacking: PHE620 HIE651 PHE680	-6.445	6.90
38c	TYR782	---	-6.210	8.03

Table S2. Results of docking procedures of molecules to the β-amyloid peptide (PDB ID: 1IYT). "C-term" corresponds to the C-terminus of the peptide (amino acids from 3 to 12, "N-term" corresponds to the fold in the vicinity of the N-terminus (amino acids from 22 to 30). Preferred position indicates the binding pocket with lower ΔG MM-GBSA. ΔG MM-GBSA is measured in kcal/mol. Hydrogen bonds are shown in the "H-bonds" columns. Other interaction between the β-amyloid and ligands are shown in the "Other int-s" columns.

Compound	Preferred position	$\Delta G\ bind_{pref.\ pos}$ (MM-GBSA)	H-bonds (C-term)	Other int-s (C-term)	H-bonds (N-term)	Other int-s (N-term)	ΔG C-term (MM-GBSA)	ΔG N-term (MM-GBSA)	Statistical distribution C-term:N-term (T = 298 K)
35b	C-term	-45.66	HIE6 GLU11	π-π stacking: TYR10 PHE4	ALA21 GLU22 SER26 LYS28	--	-45.66	-42.01	480:1
38a	C-term	-44.7	GLU3 ASP7 GLU 11	π-π stacking: TYR10	ALA21 GLU22 SER26	--	-44.7	-42.13	77:1

35c	N-term	-43.57	GLU3 ASP7 GLU 11	π-π stacking: TYR10	GLU22 GLY25 SER26	--	-38.89	-43.57	1:2700
38b	N-term	-41.05	GLU 11	π-π stacking: TYR10	ALA21 GLU22 LYS28	--	-37.84	-41.05	1:230
38c	C-term	-40.19	ASP7 GLU11	π-π stacking: TYR10	GLU22 LYS28	--	-40.19	-32.74	290000:1
35a	C-term	-38.14	GLU11 GIE14	π-π stacking: TYR10	ALA21 GLU22 LYS28	--	-38.14	-36.54	15:1