2023
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Chemical Biology
LETTERS

Novel fluorinated piperazine based-amino acid derivatives as antiplasmodial agents: Synthesis, bioactivity and computational studies.

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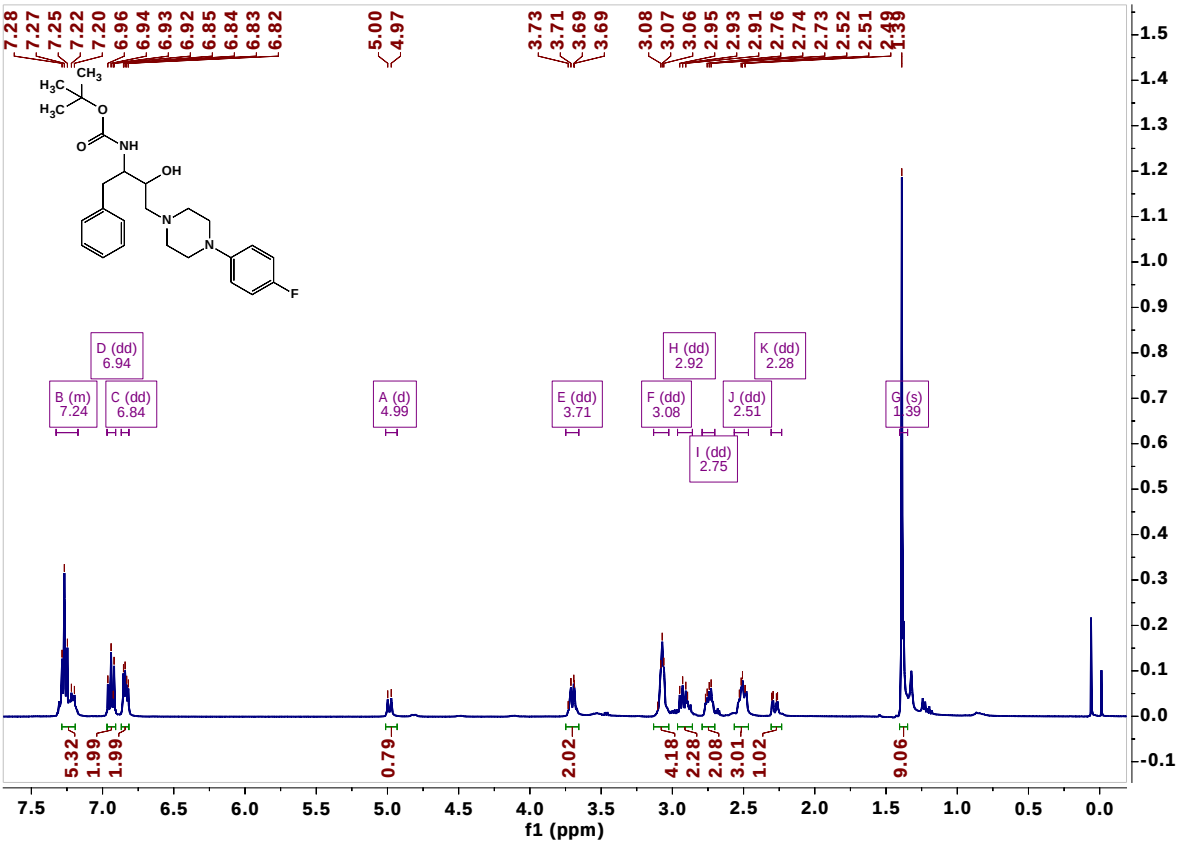

Figure S1. ^{1}H NMR spectrum of **4**.

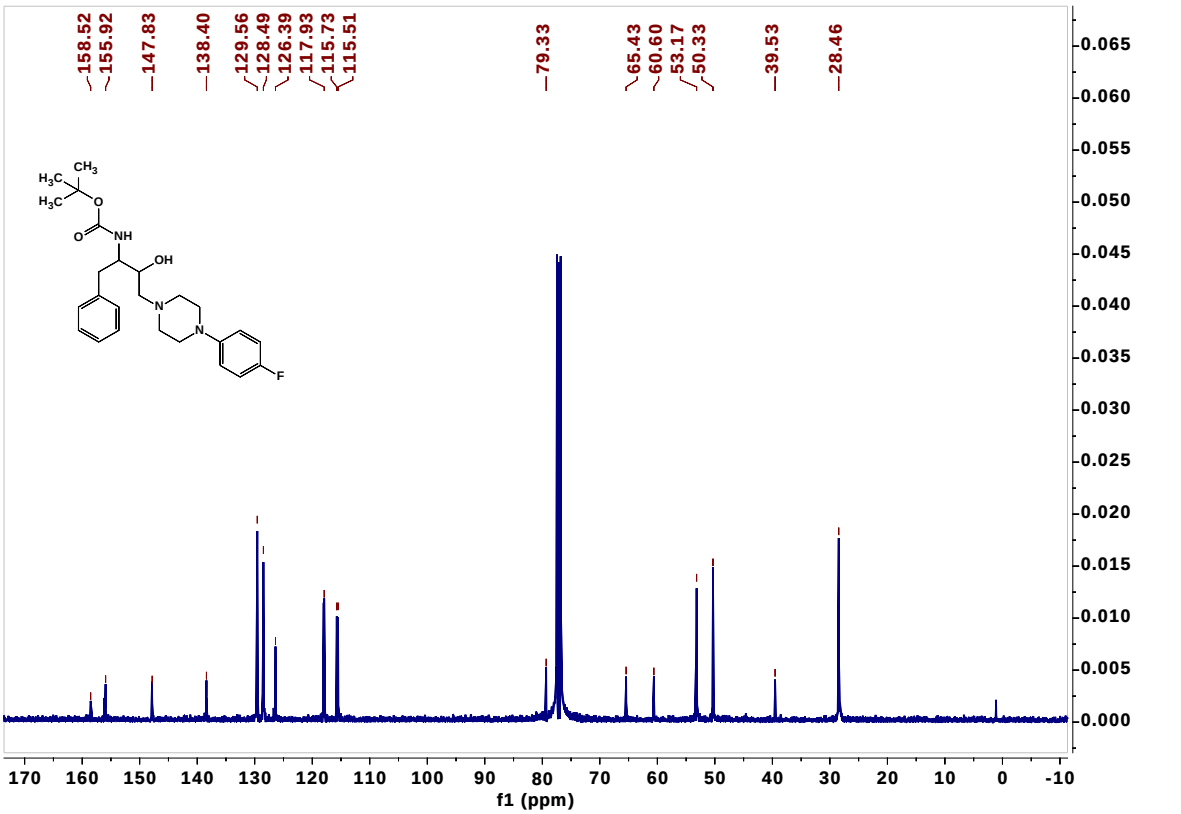

Figure S2. ^{13}C NMR spectrum of **4**.

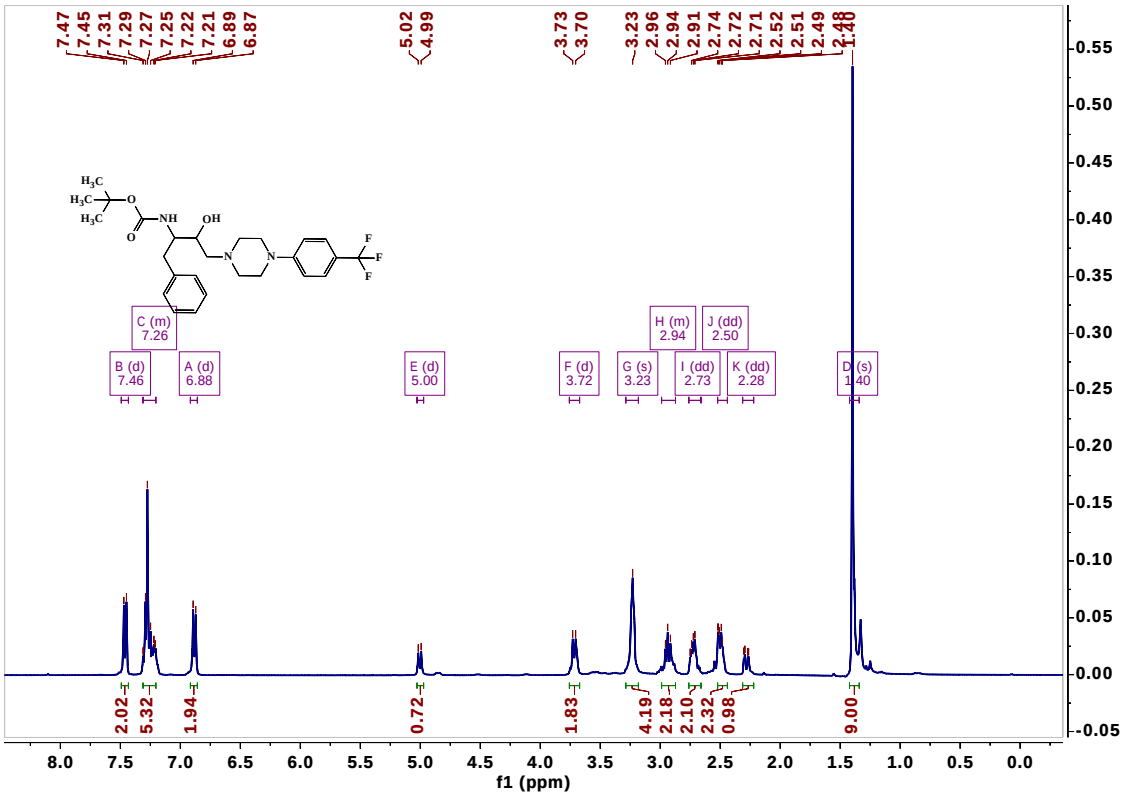

Figure S3. ^{1}H NMR spectrum of **5**.

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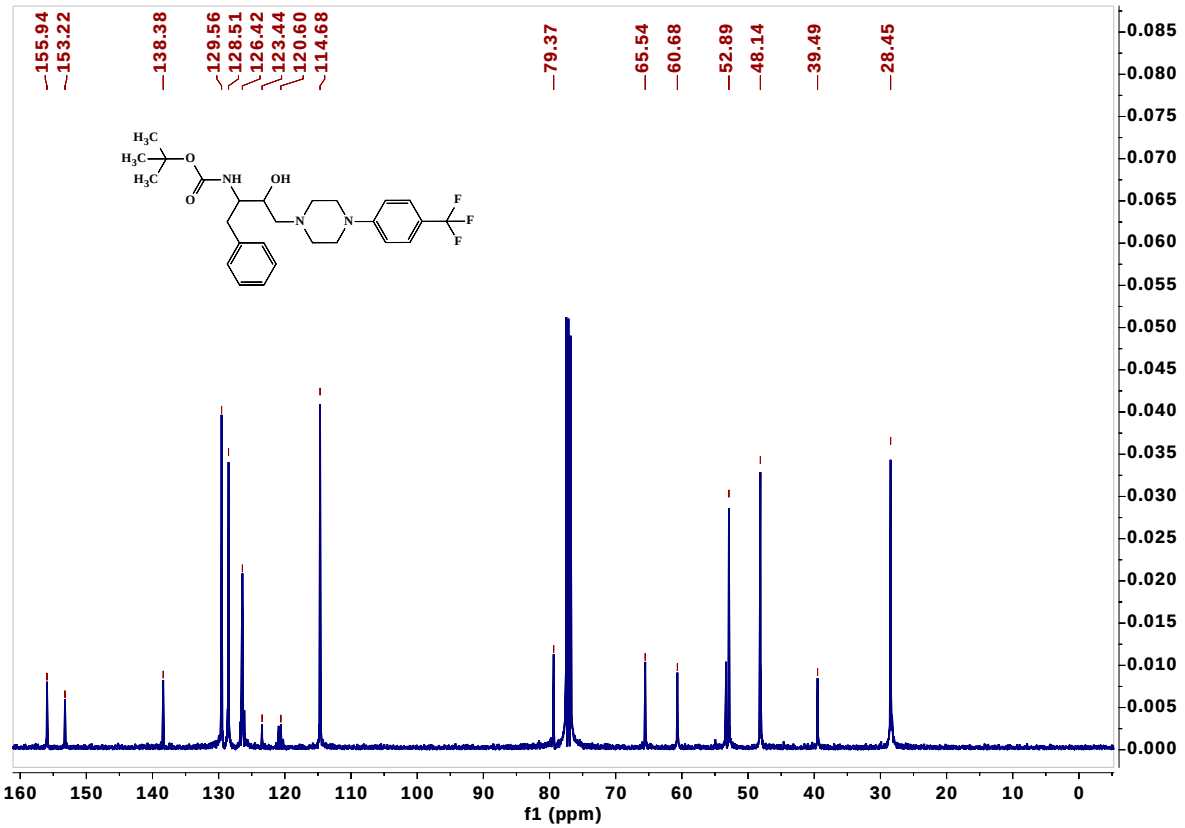


Figure S4. ^{13}C NMR spectrum of **5**.

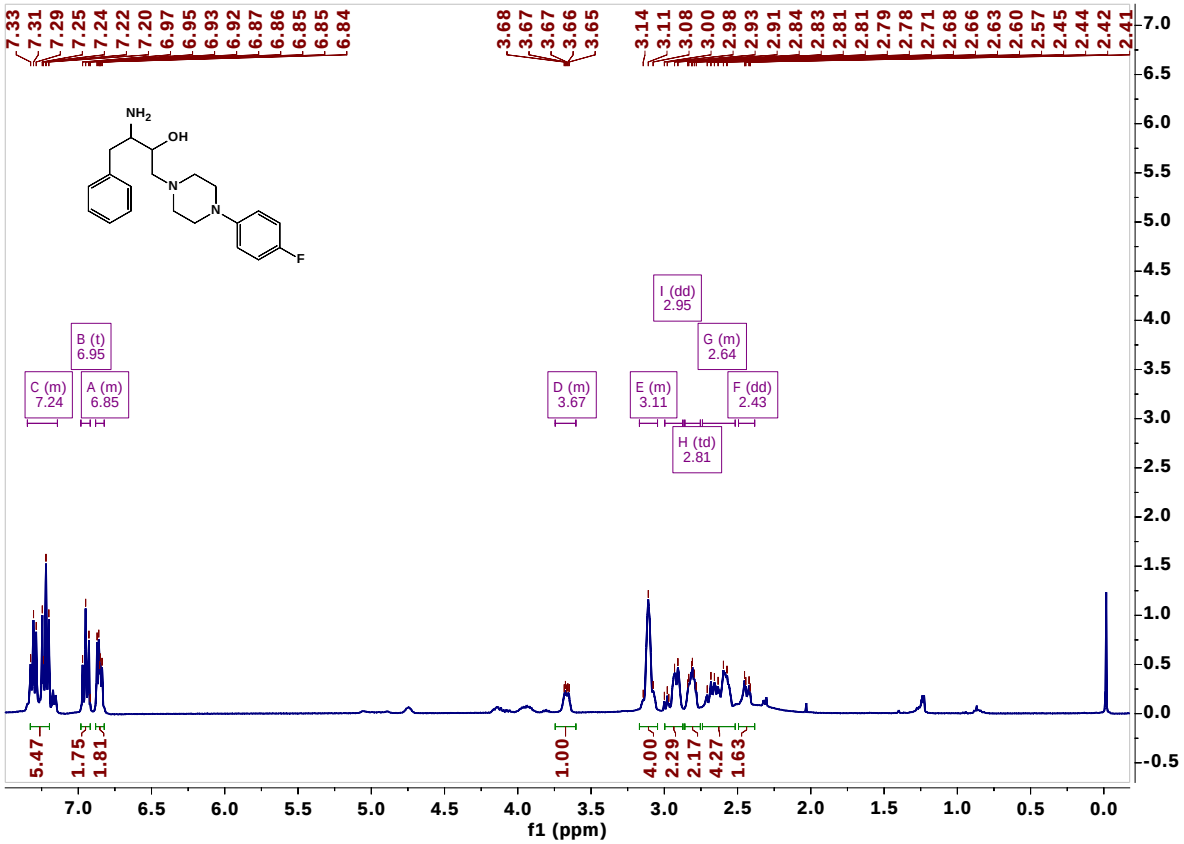


Figure S5. ^{1}H NMR spectrum of **6**.

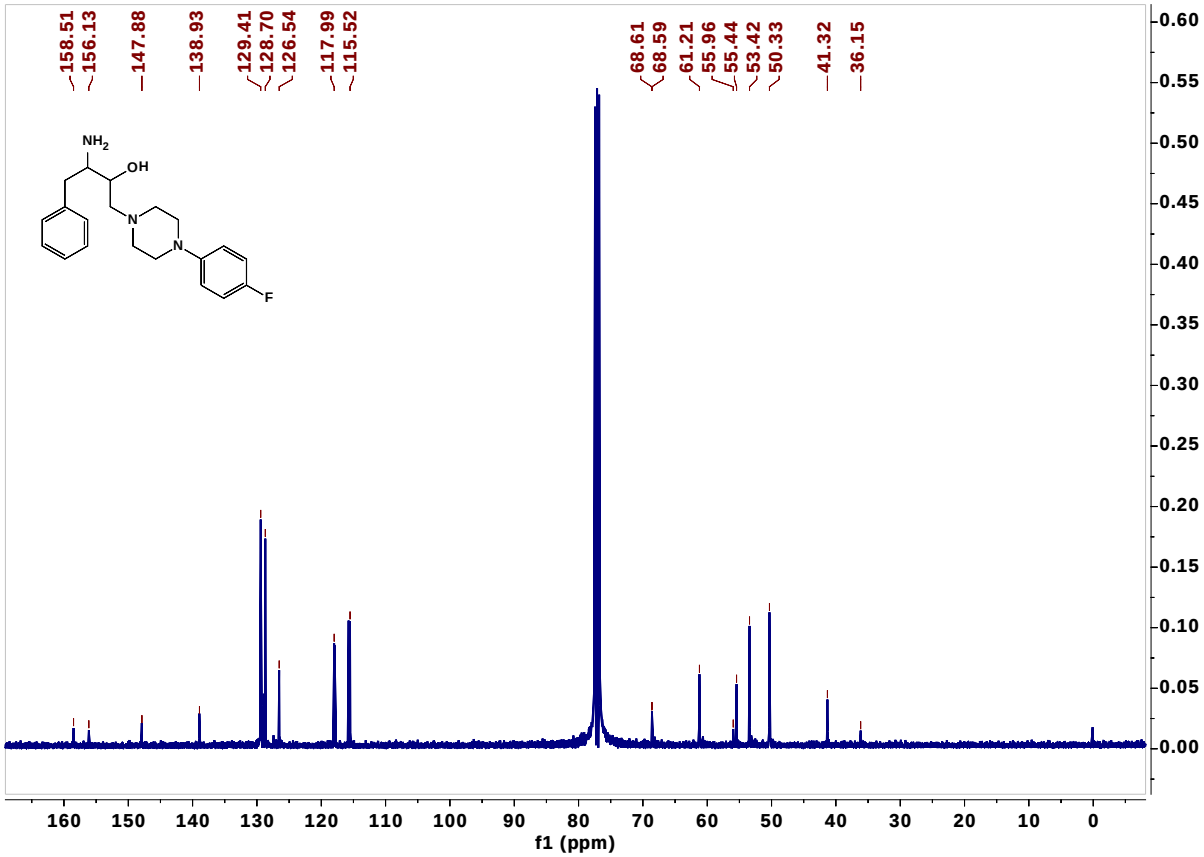


Figure S6. ^{13}C NMR spectrum of **6**.

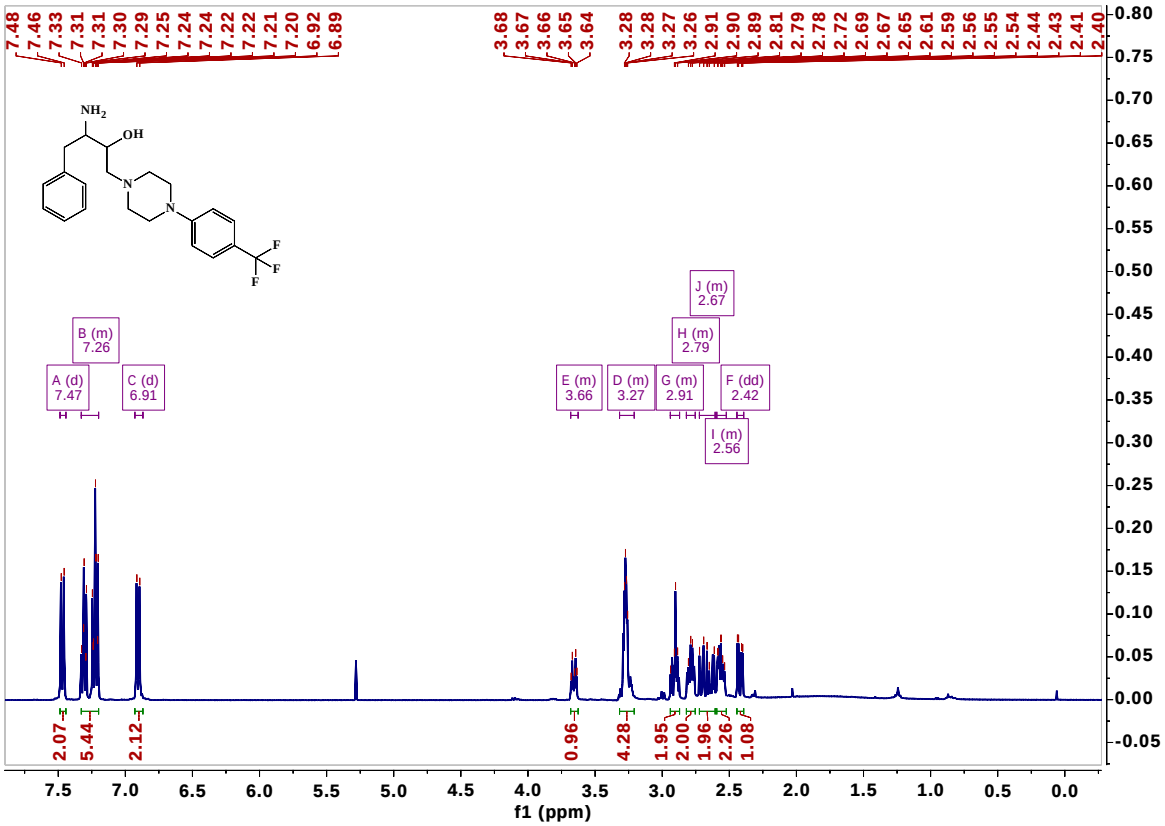


Figure S7. ^{1}H NMR spectrum of **9a**.

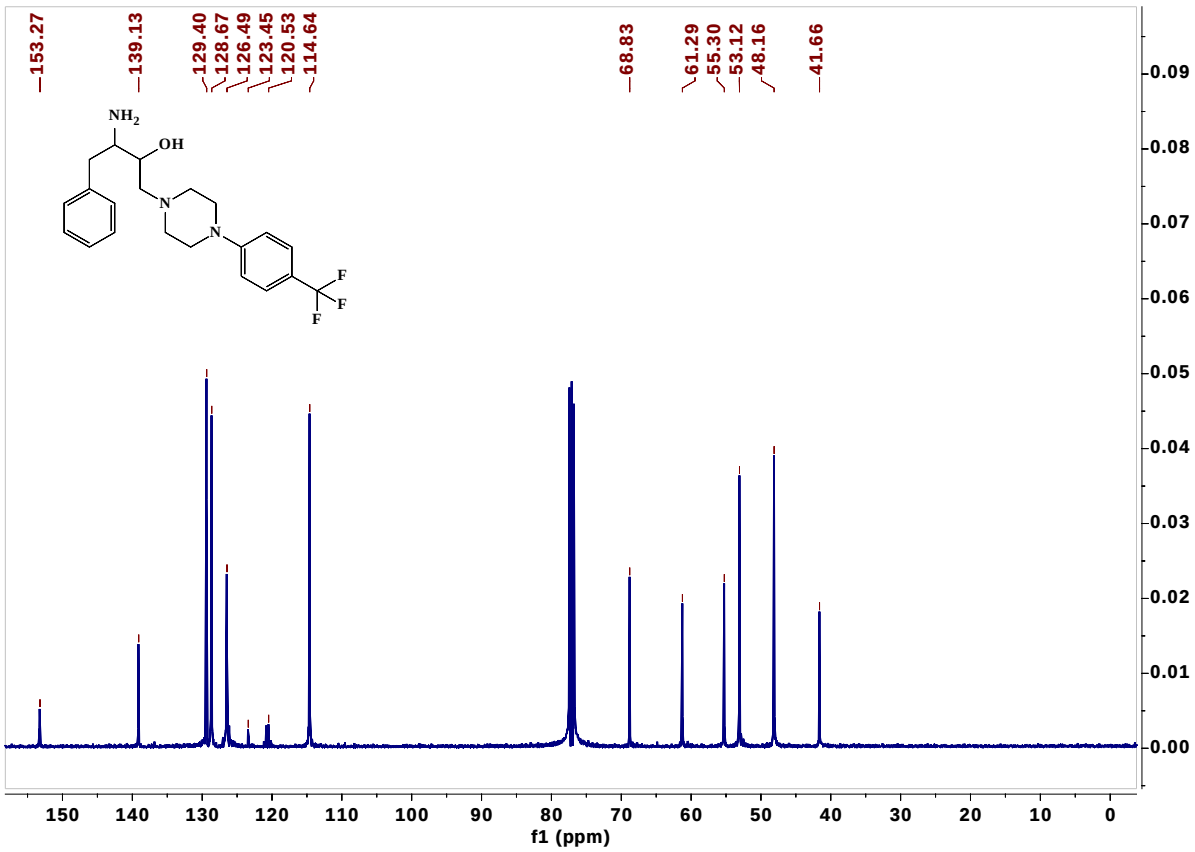


Figure S8. ^{13}C NMR spectrum of **9a**.

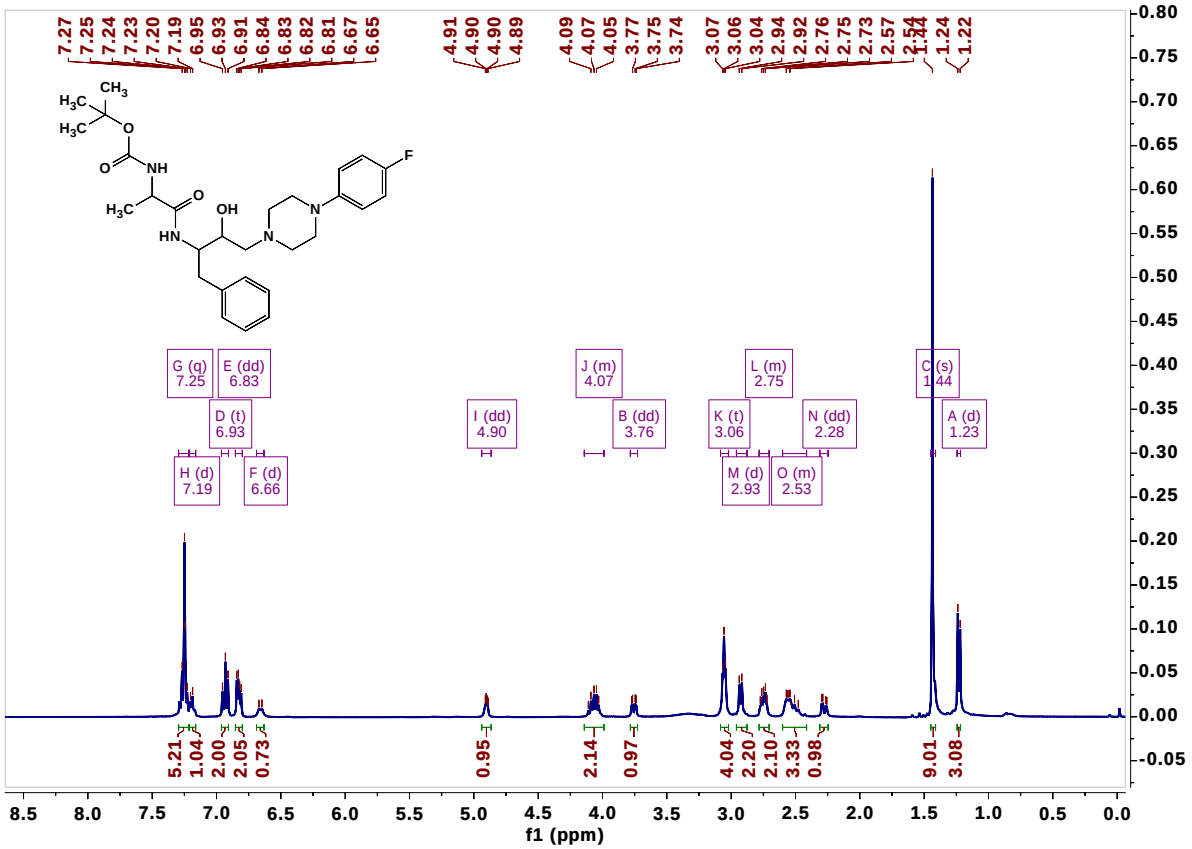


Figure S9. ^{1}H NMR spectrum of **9b**.

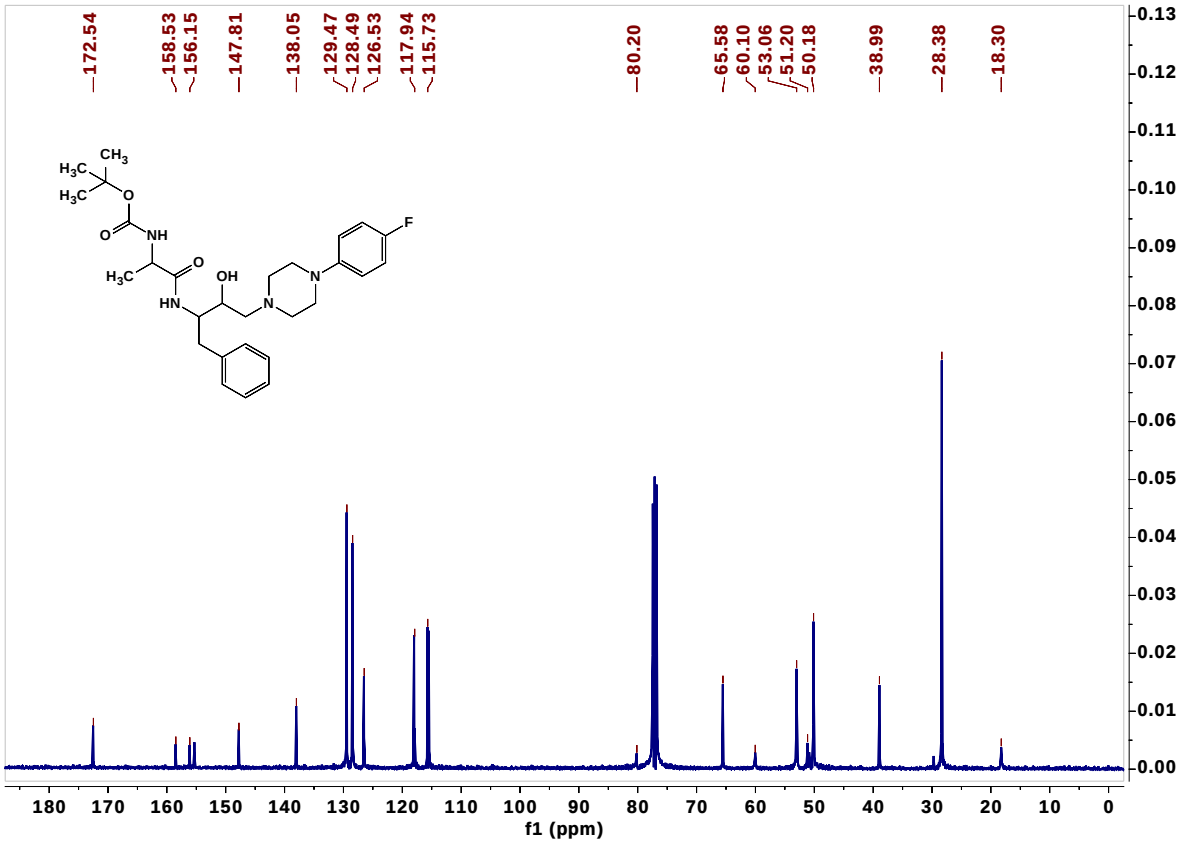


Figure S10. ^{13}C NMR spectrum of **9b.**

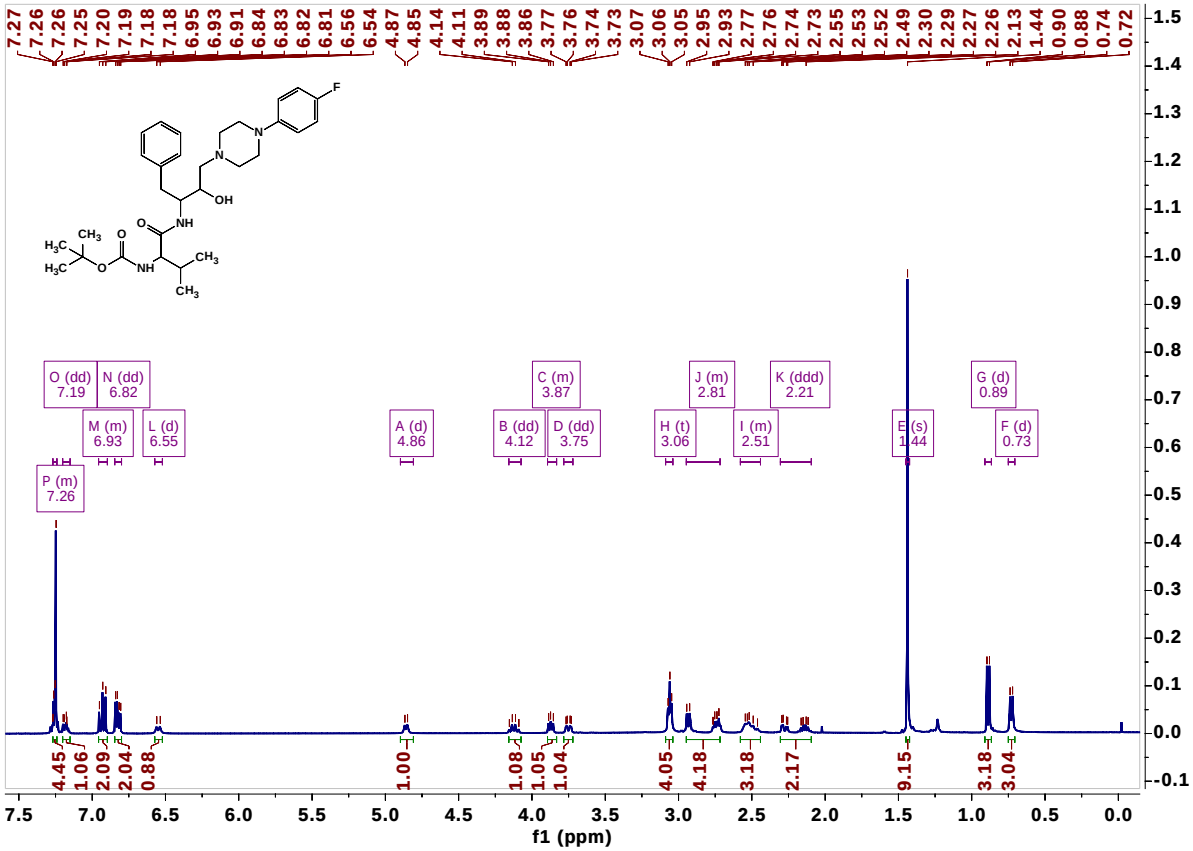


Figure S11. ^{1}H NMR spectrum of **9c**.

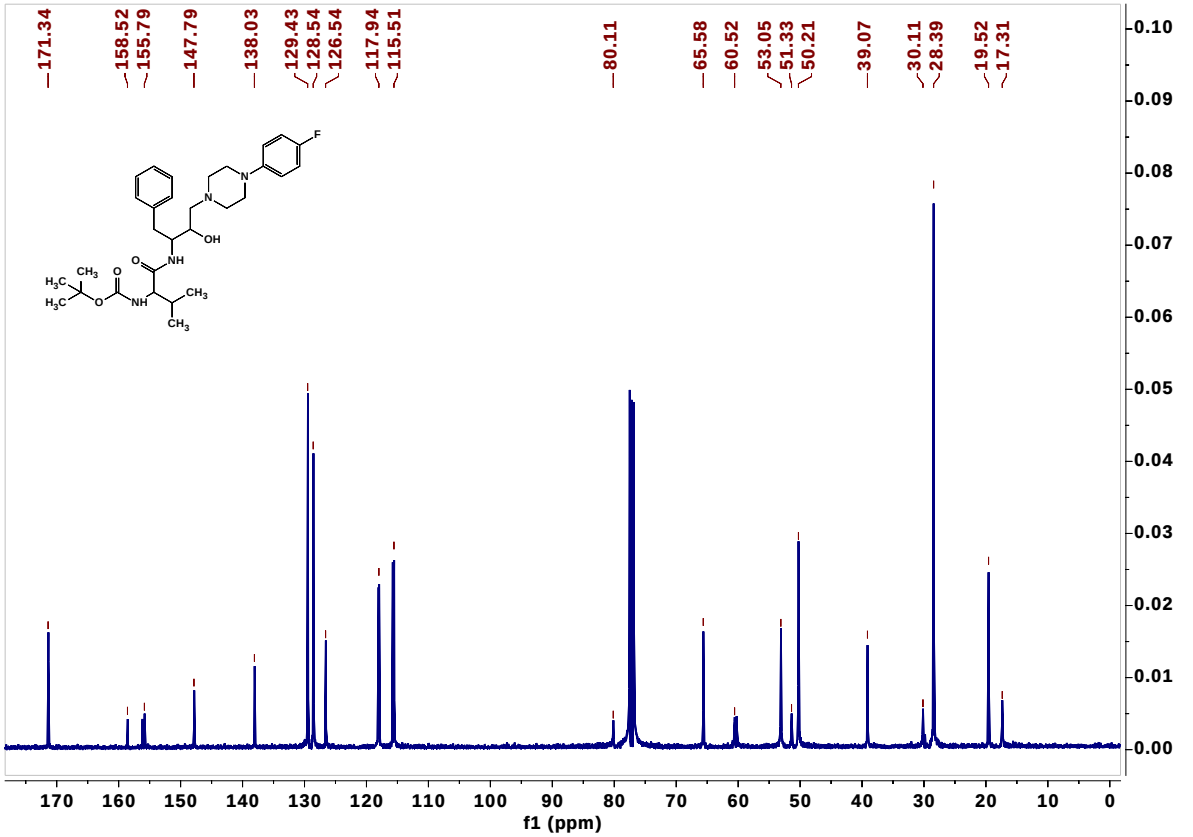


Figure S12. ^{13}C NMR spectrum of **9c**.

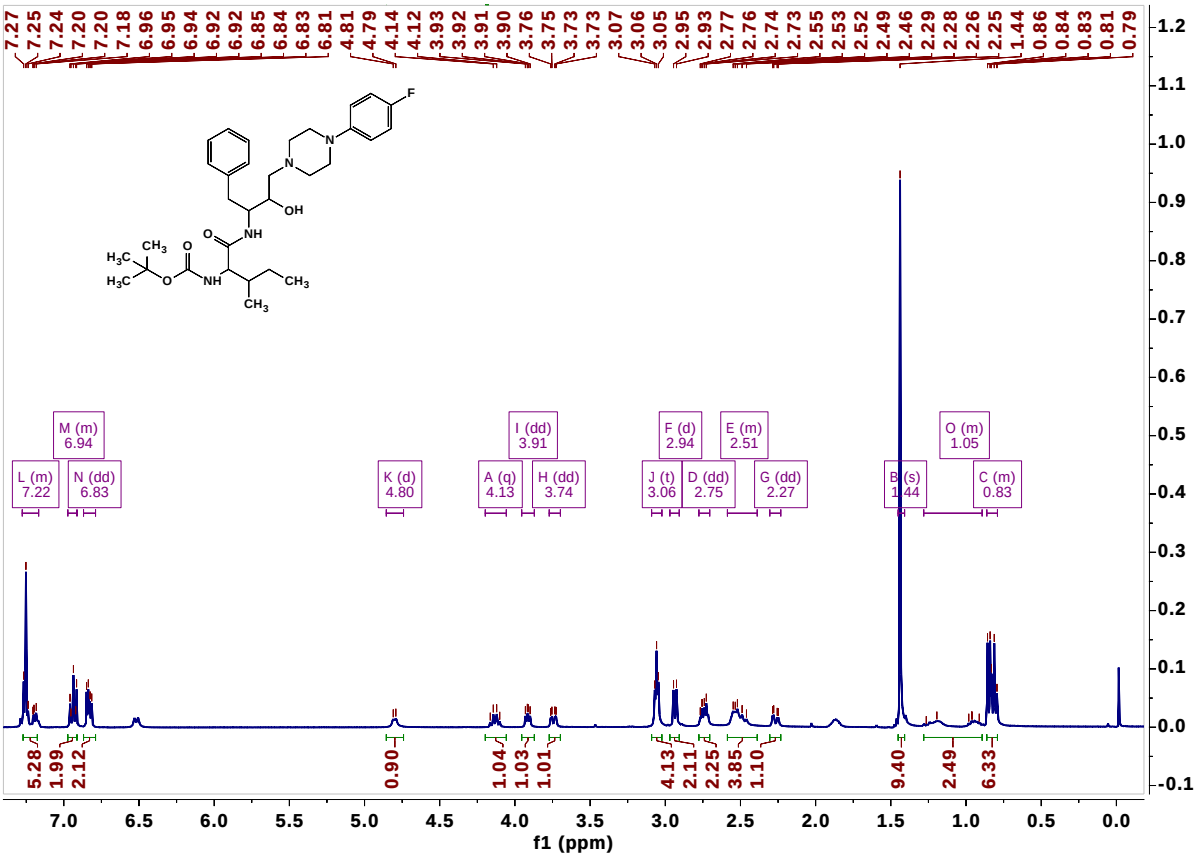


Figure S13. ^{1}H NMR spectrum of **9d**.

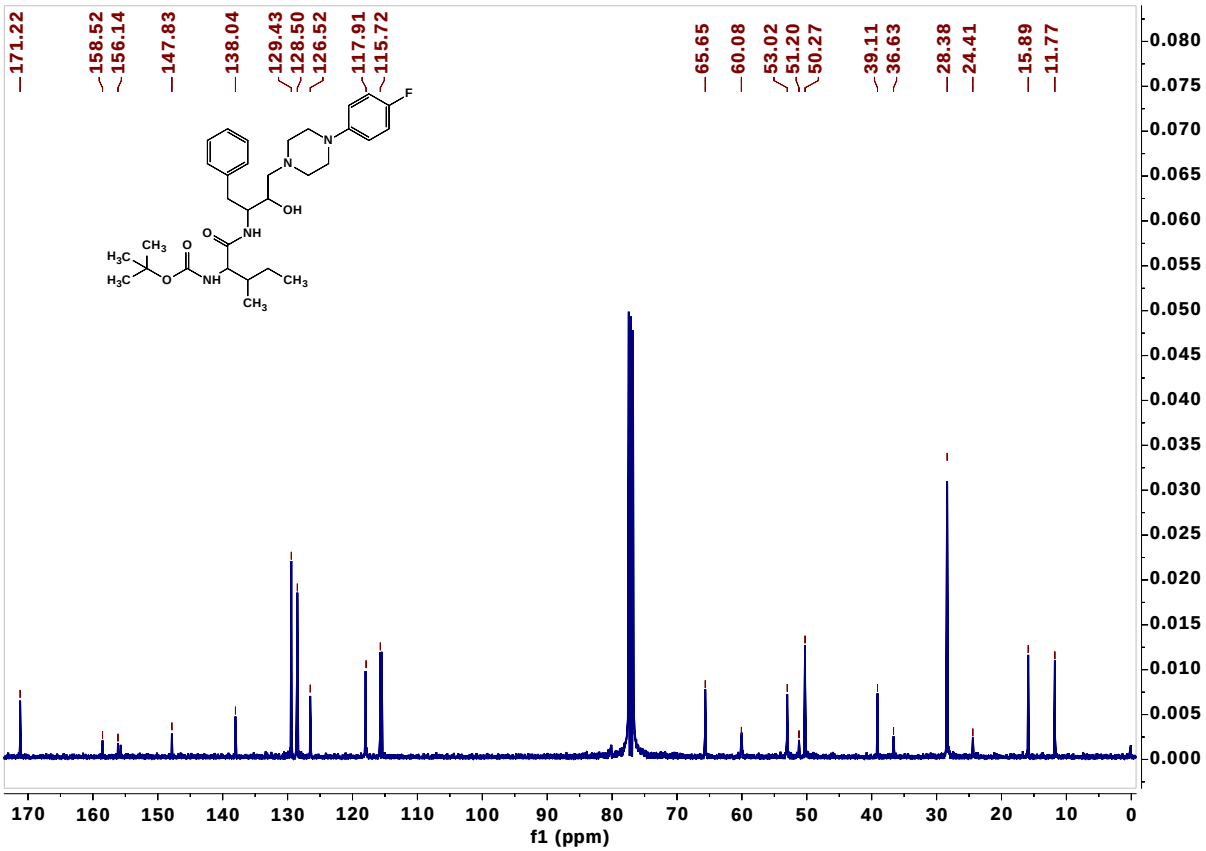


Figure S14. ^{13}C NMR spectrum of **9d**.

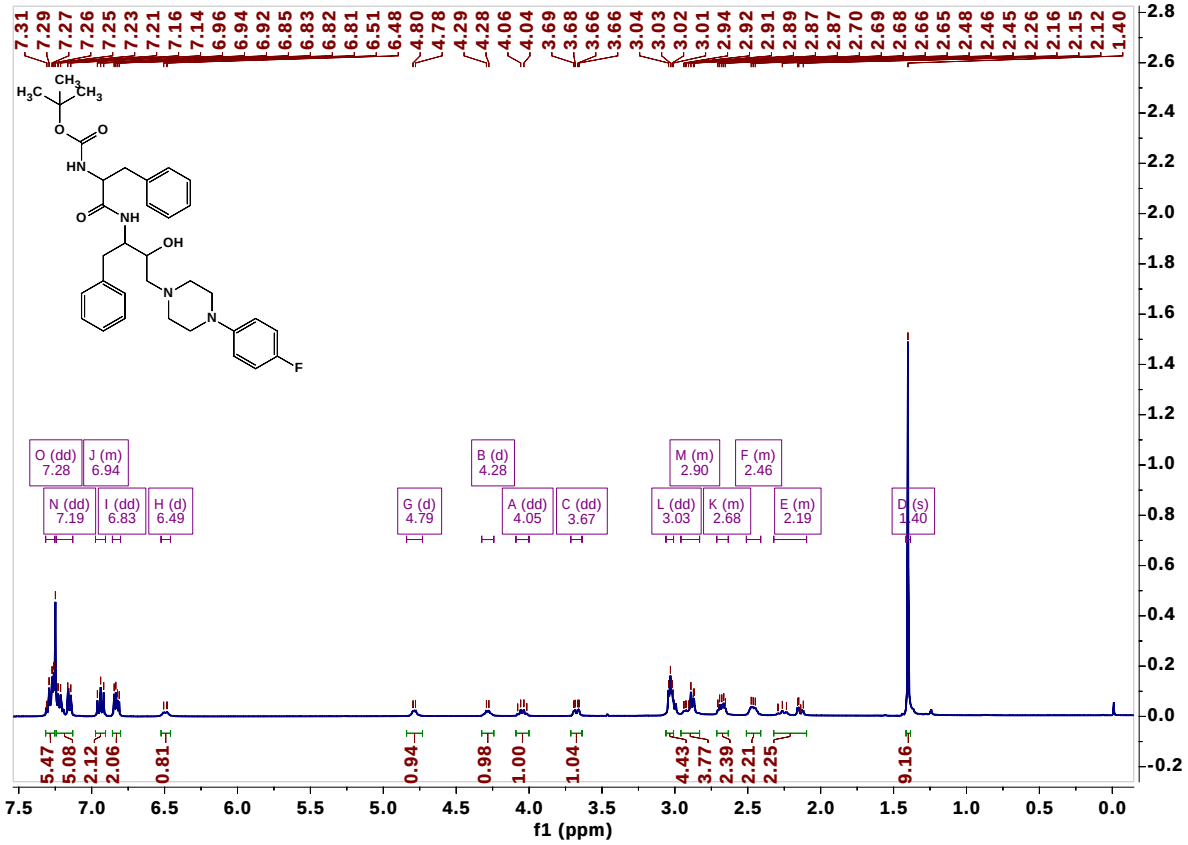


Figure S15. ^{1}H NMR spectrum of **9e**.

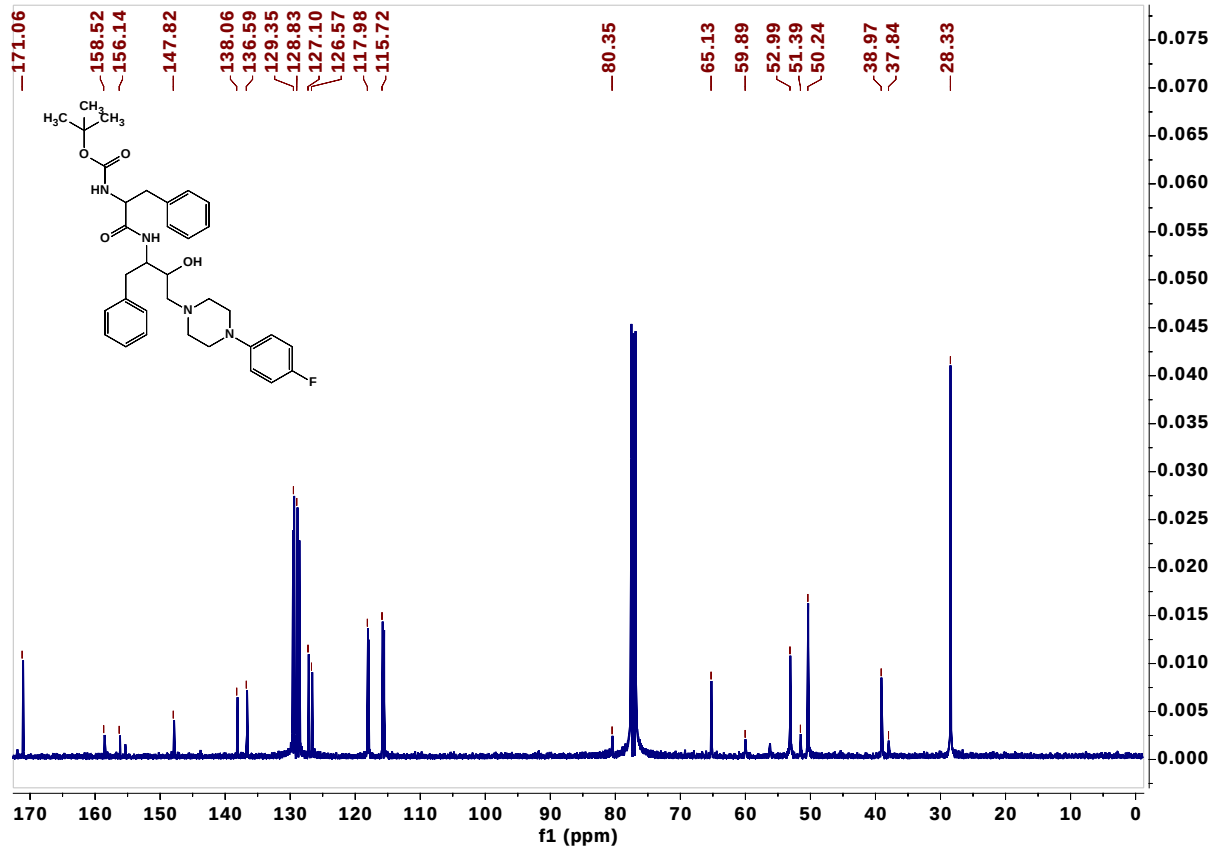


Figure S16. ^{13}C NMR spectrum of **9e**.

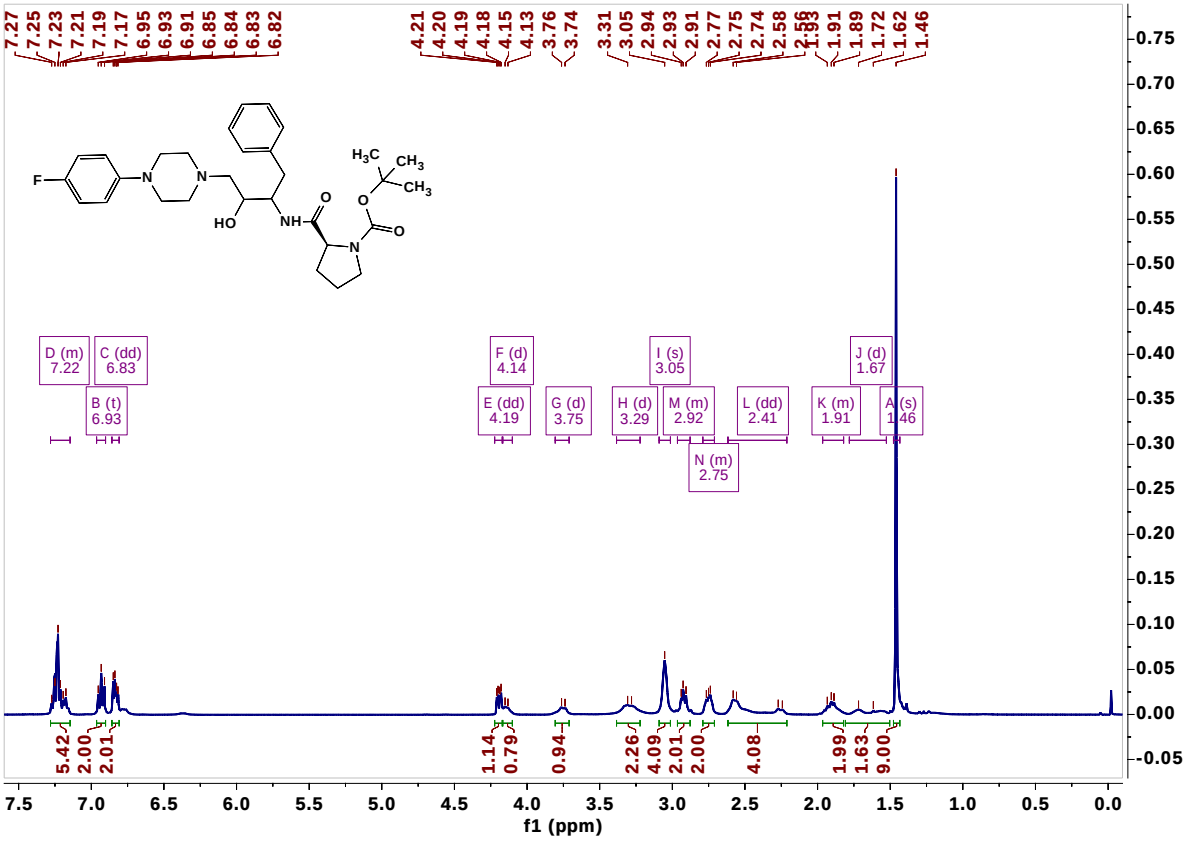


Figure S17. ^{1}H NMR spectrum of **10a**.

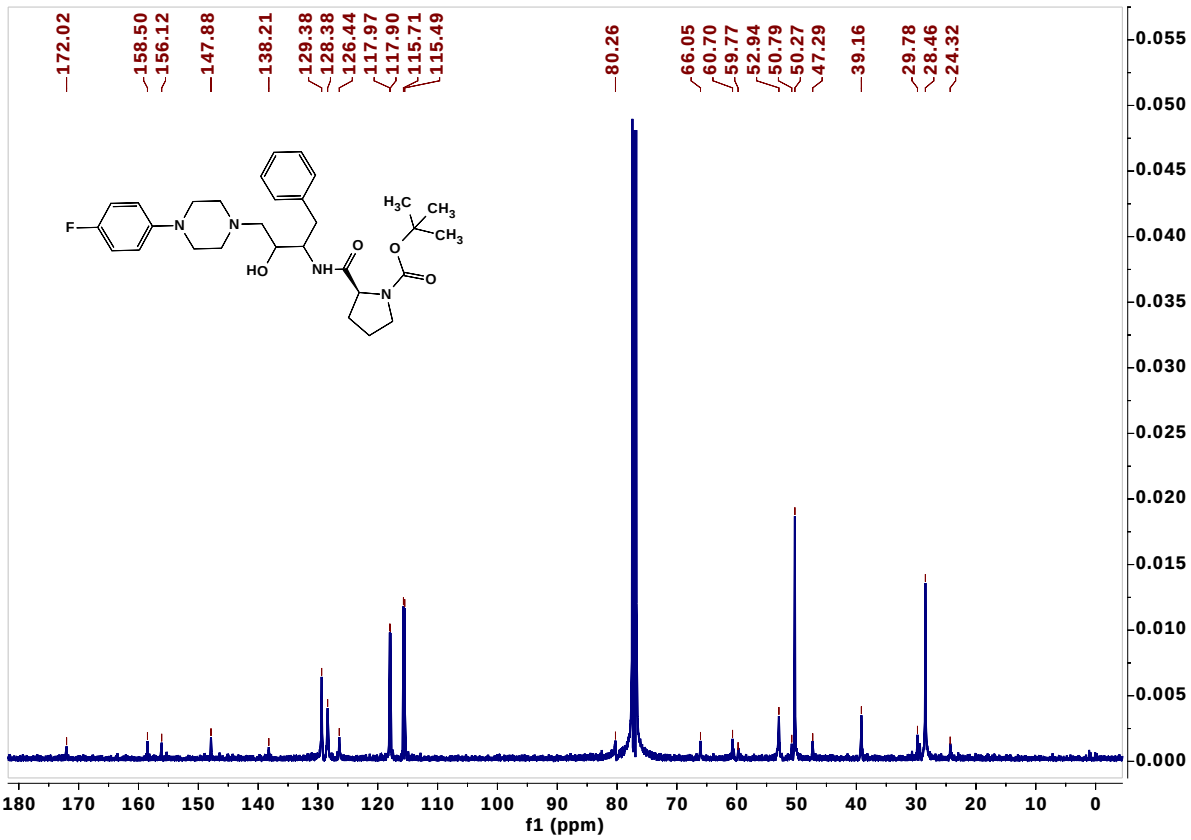


Figure S18. ^{13}C NMR spectrum of **10a**.

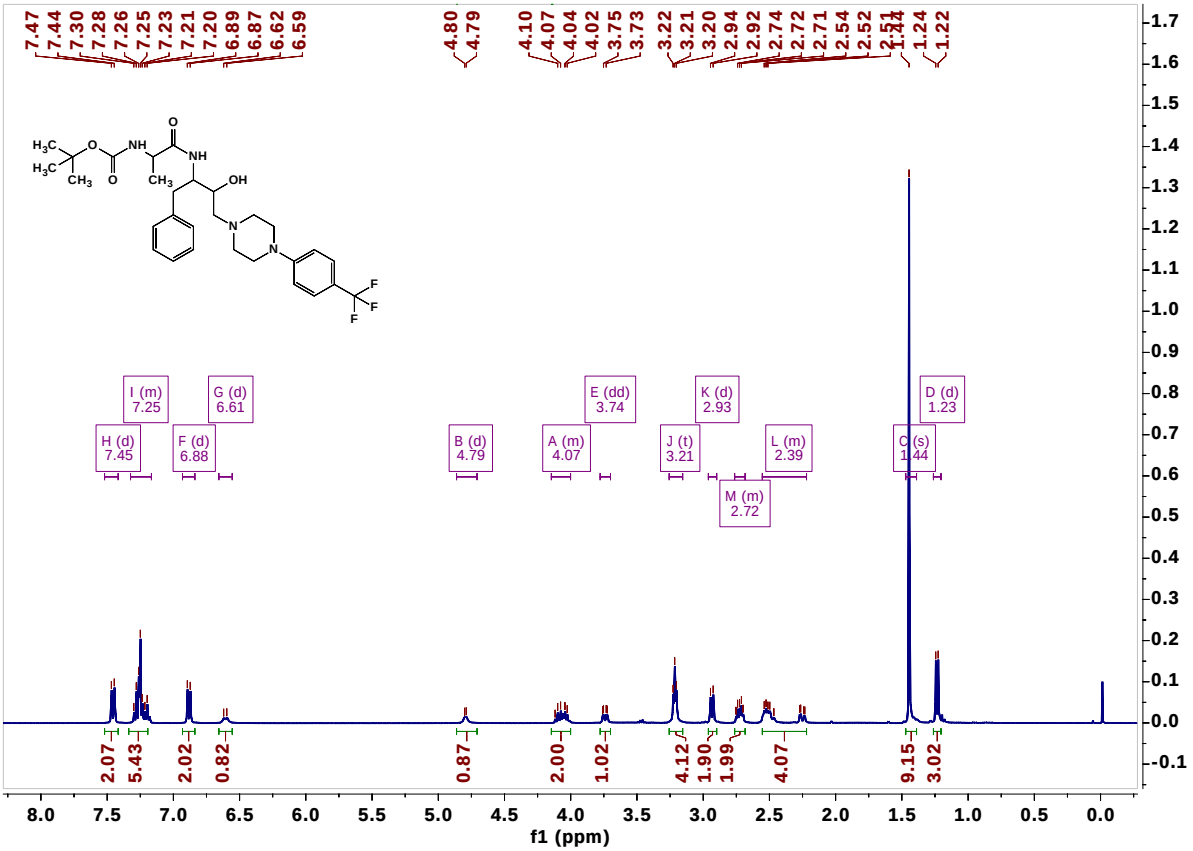


Figure S19. ^{1}H NMR spectrum of **10b**.

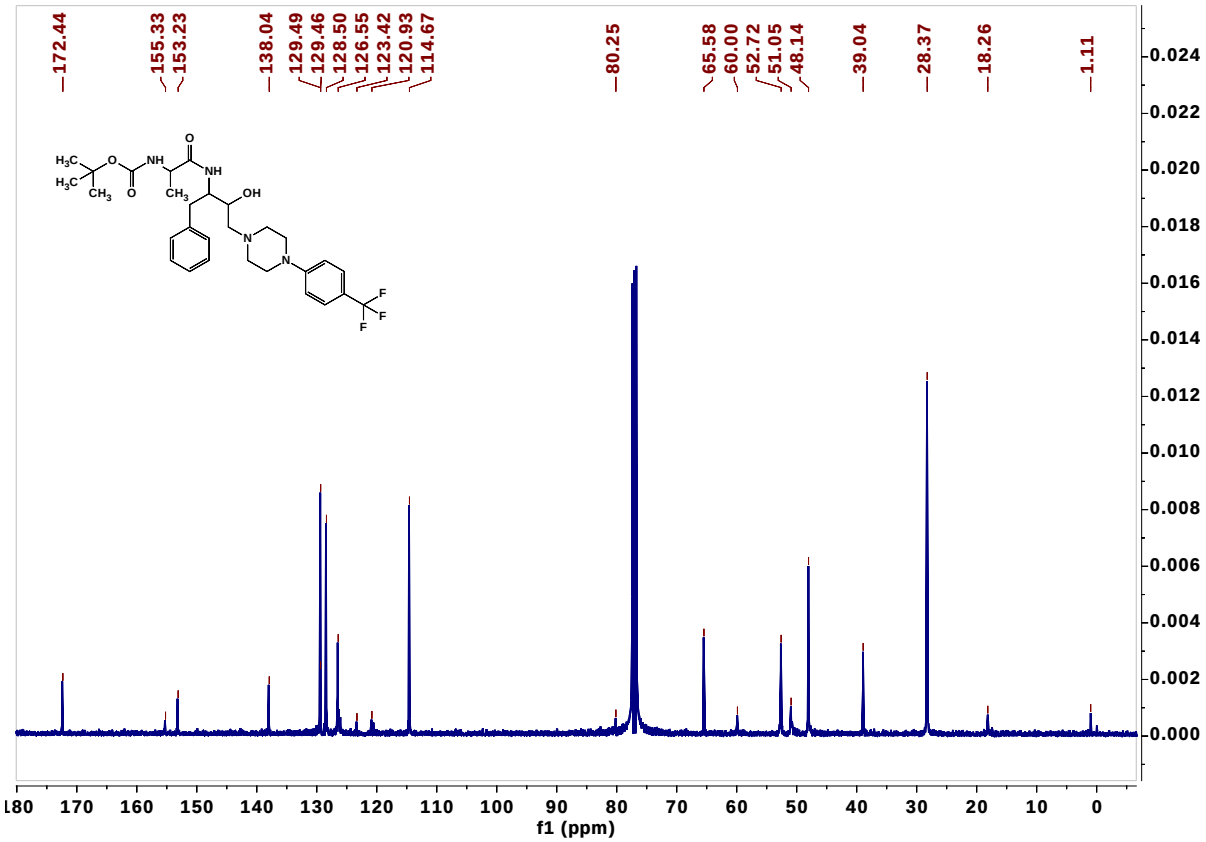


Figure S20. ^{13}C NMR spectrum of **10b**.

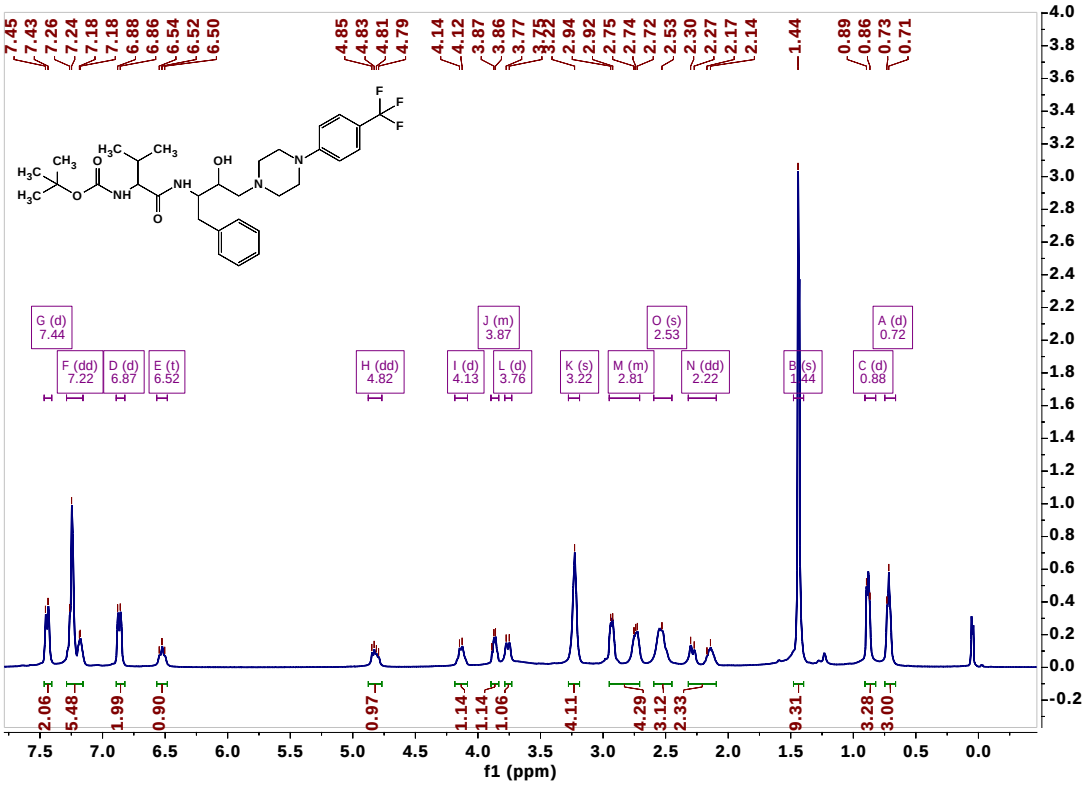


Figure S21. ^{1}H NMR spectrum of **10c**.

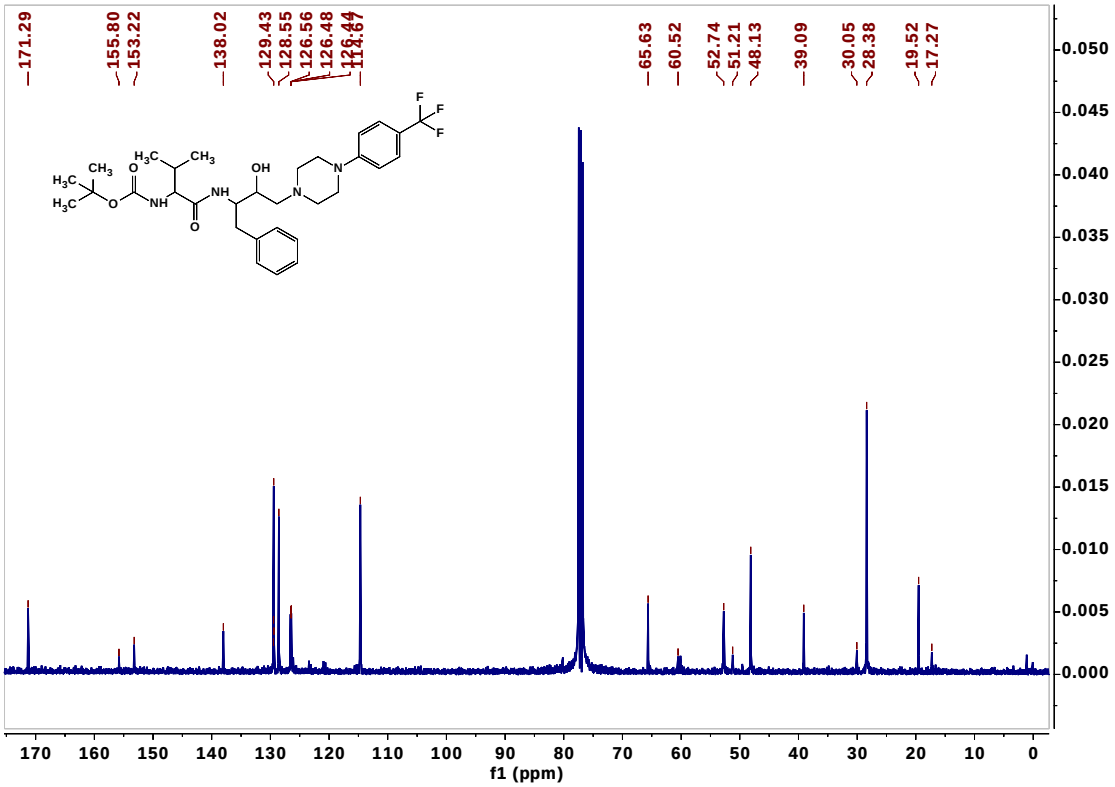


Figure S22. ^{13}C NMR spectrum of **10c**.

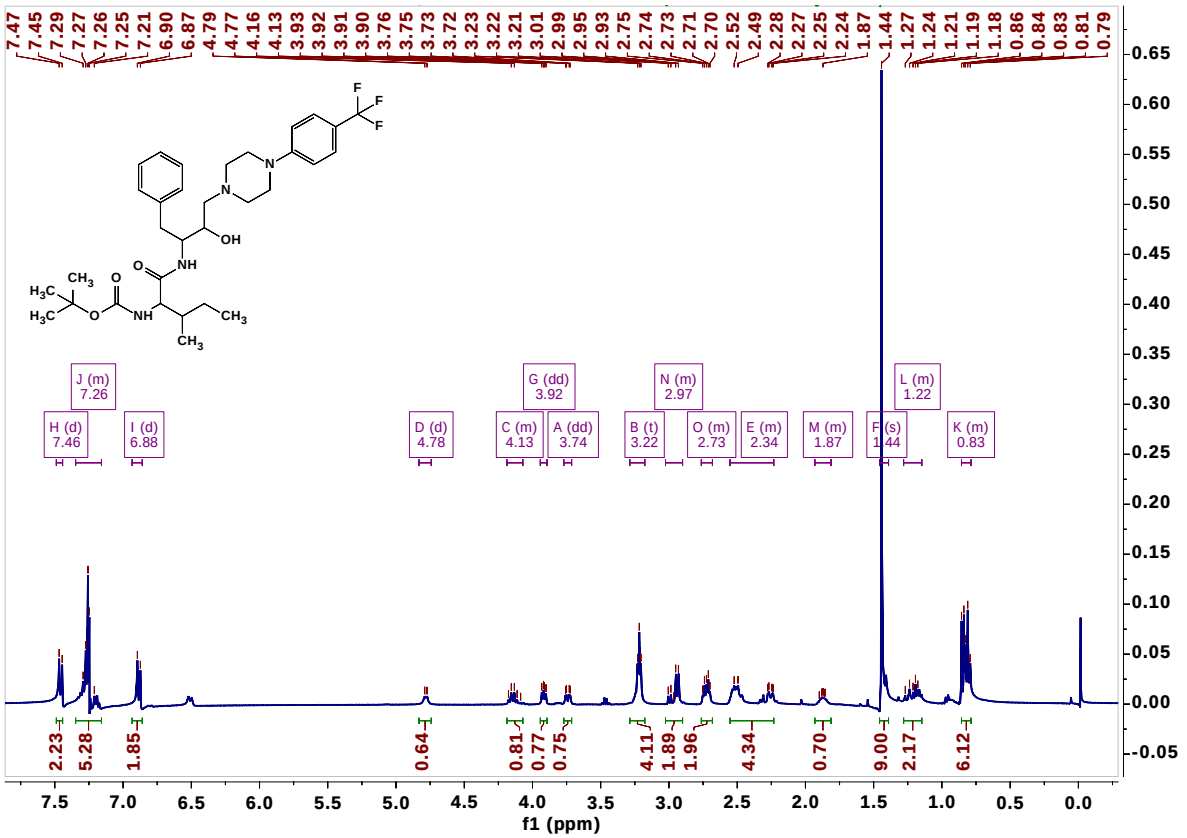


Figure S23. ^{1}H NMR spectrum of **10d**.

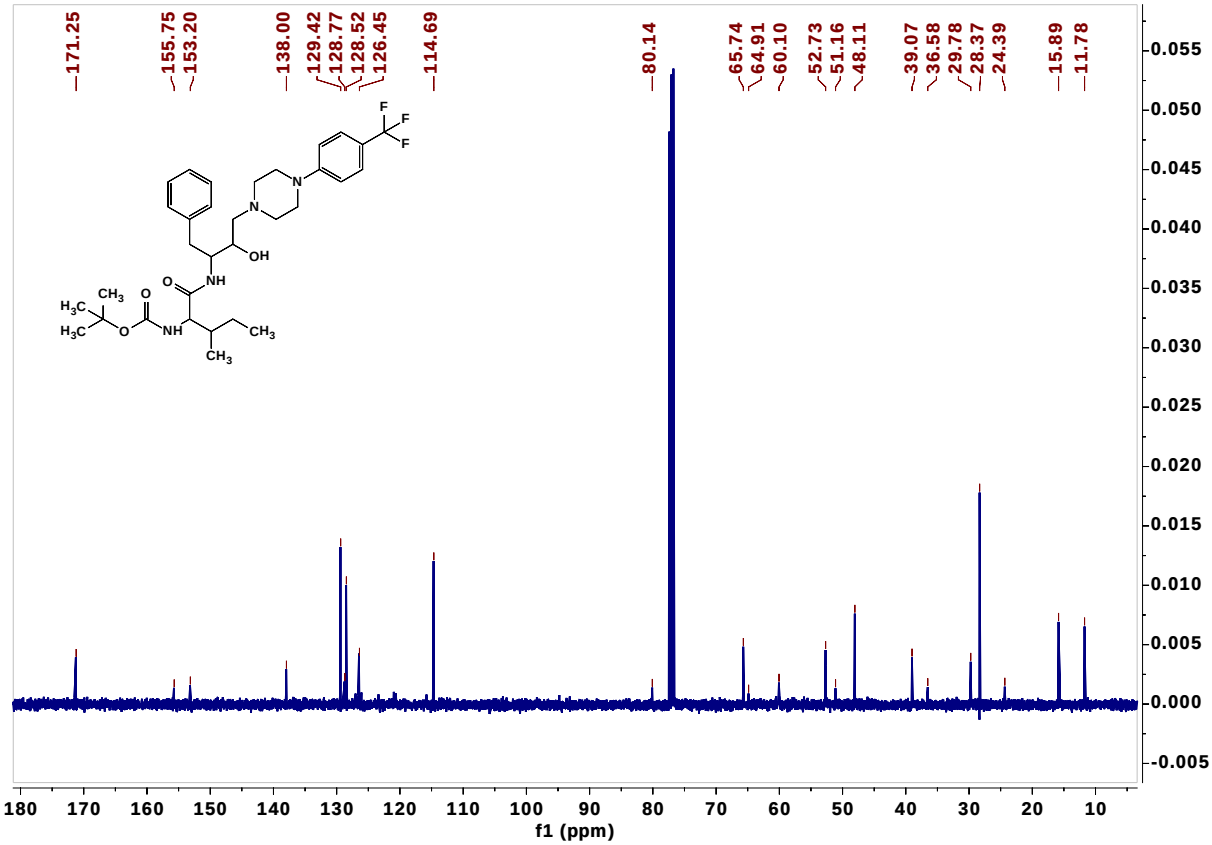


Figure S24. ^{13}C NMR spectrum of **10d**.

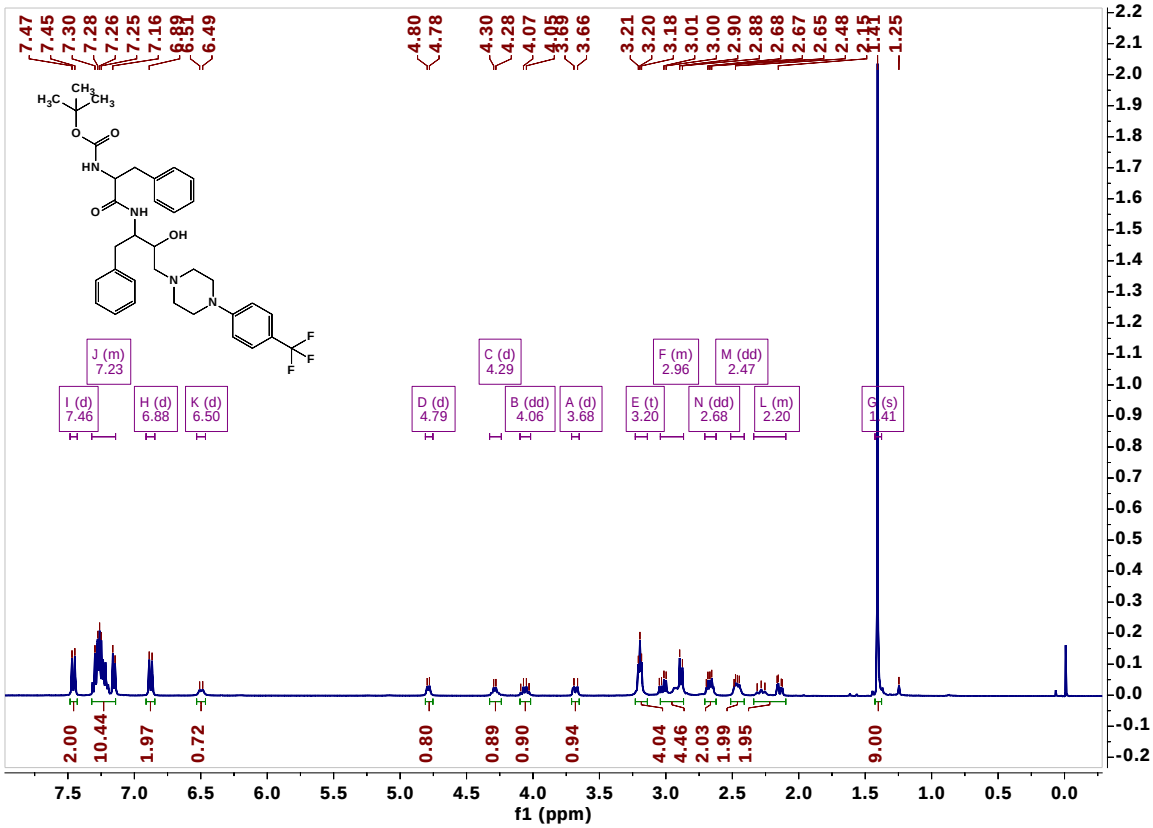


Figure S25. ^{1}H NMR spectrum of **10e**.

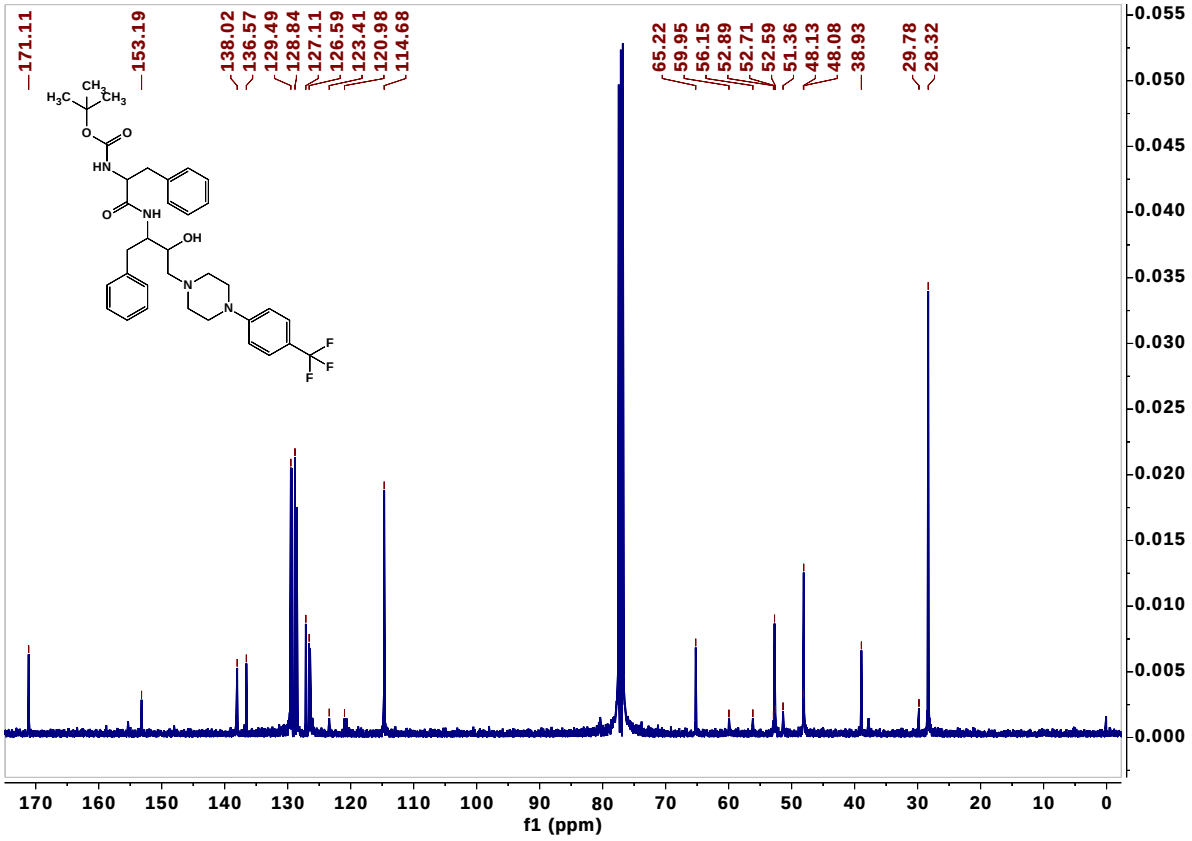


Figure S26. ^{13}C NMR spectrum of **10e**.

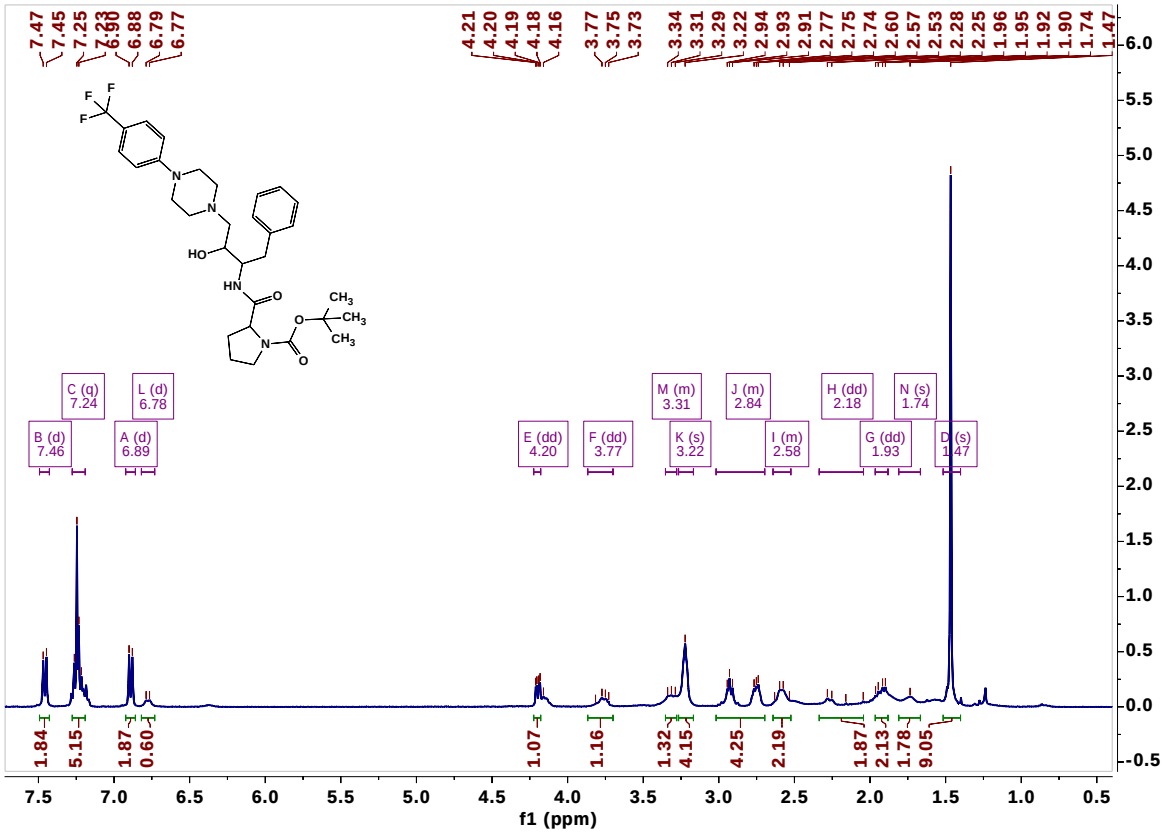


Figure S27. ^{1}H NMR spectrum of **11a**.

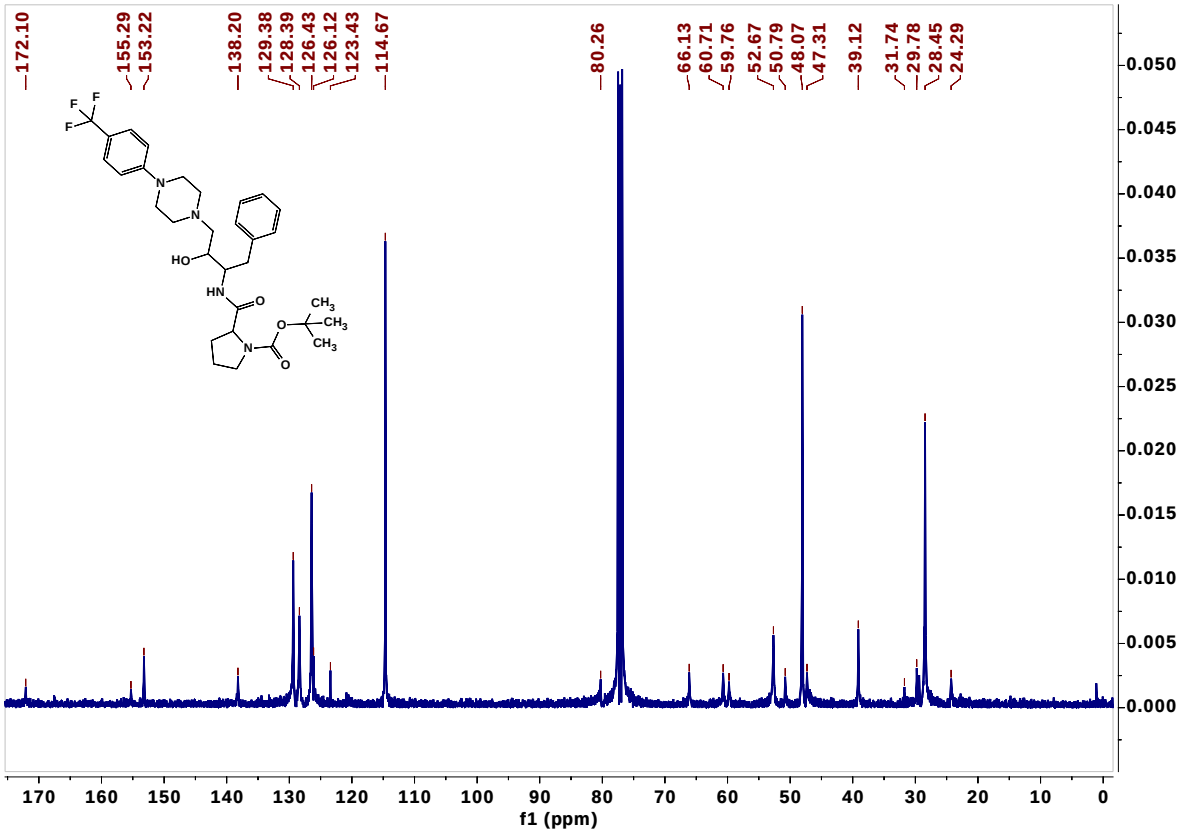


Figure S28. ^{13}C NMR spectrum of **11a**.

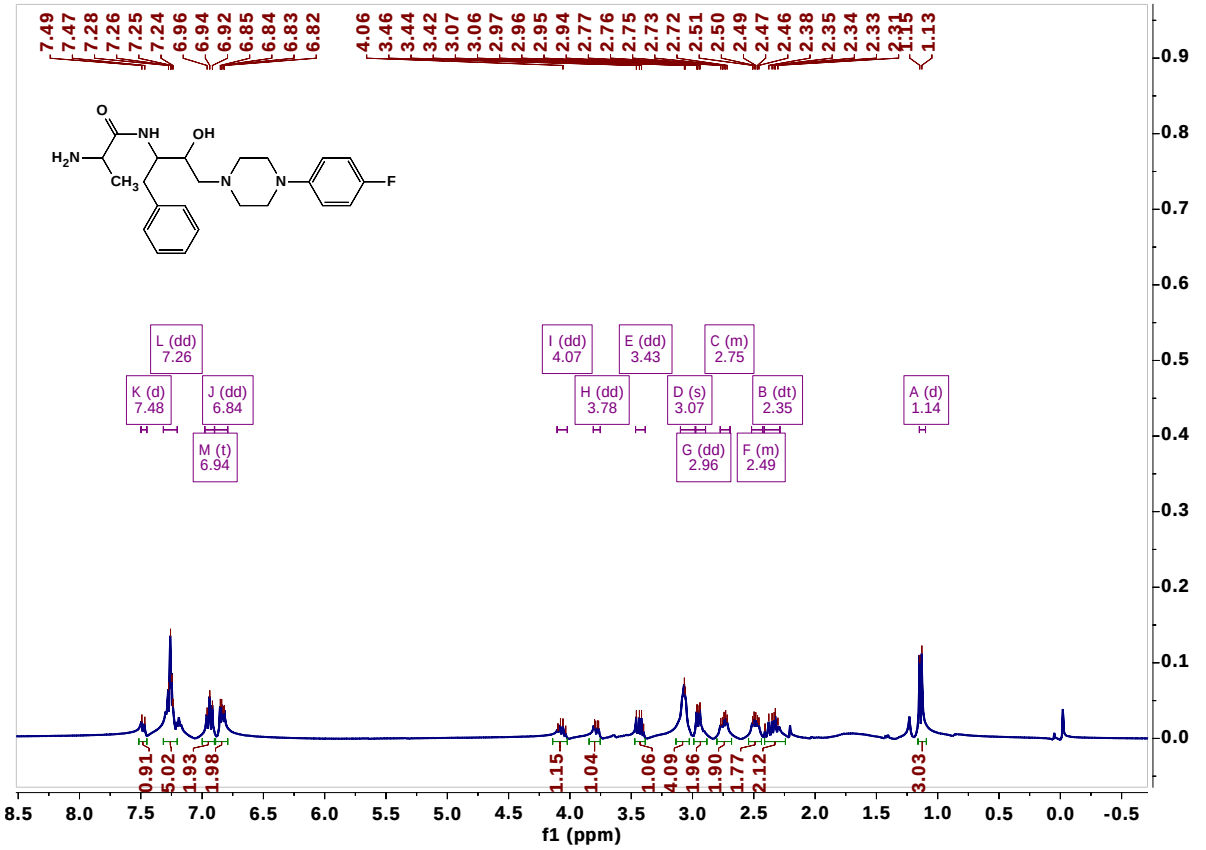


Figure S29. ^{1}H NMR spectrum of **11b**.

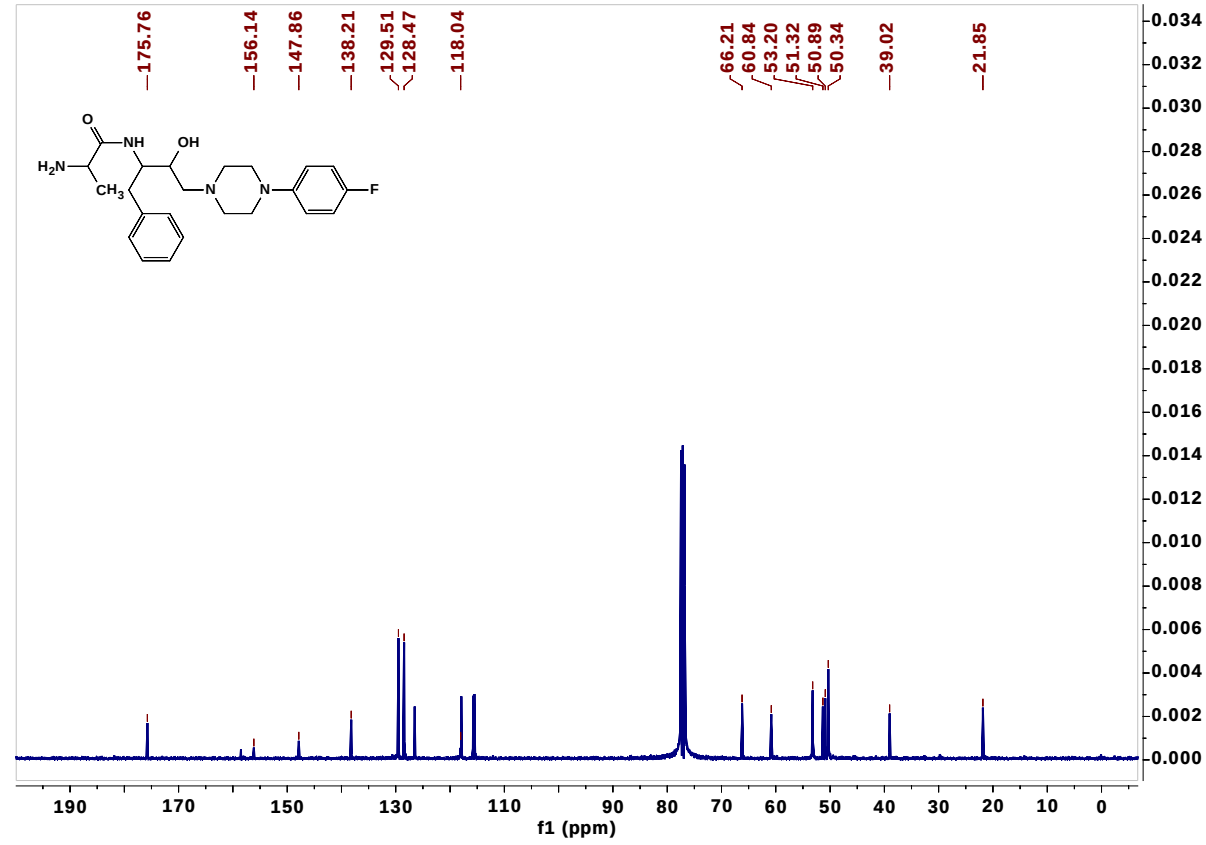


Figure S30. ^{13}C NMR spectrum of **11b**.

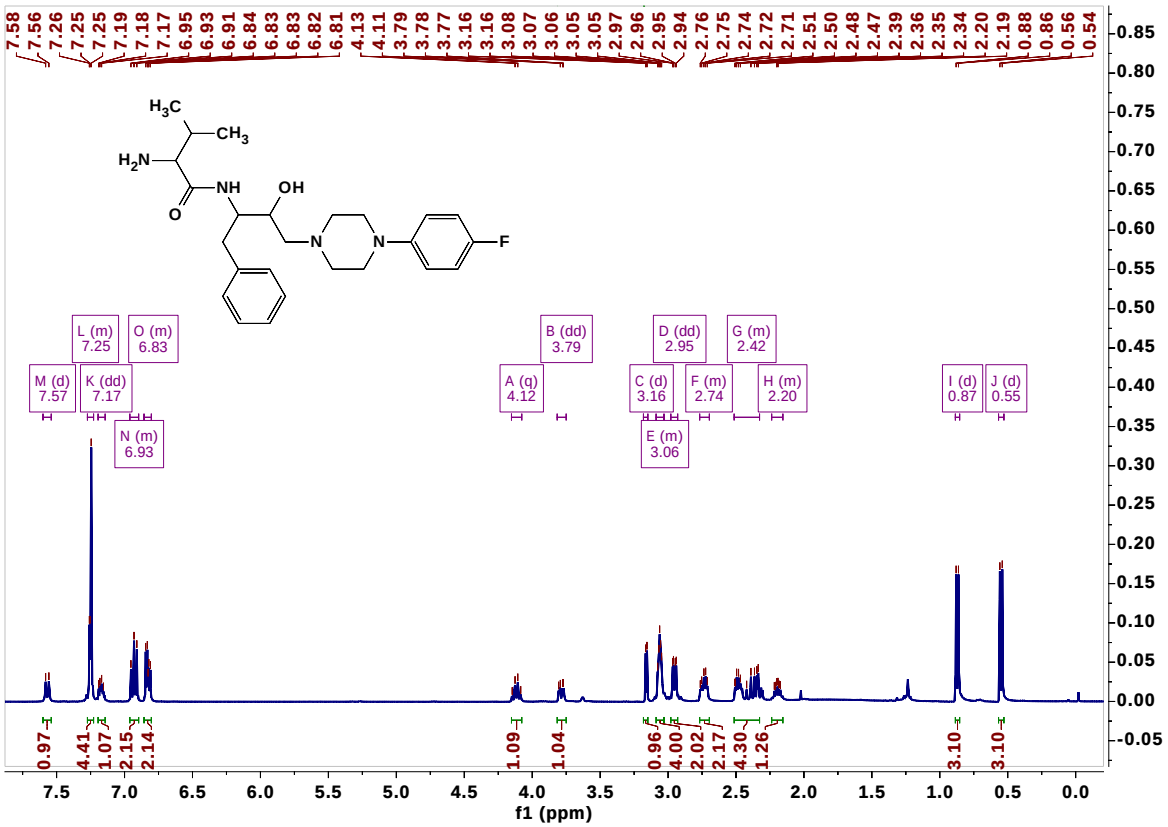


Figure S31. ^{1}H NMR spectrum of **11c**.

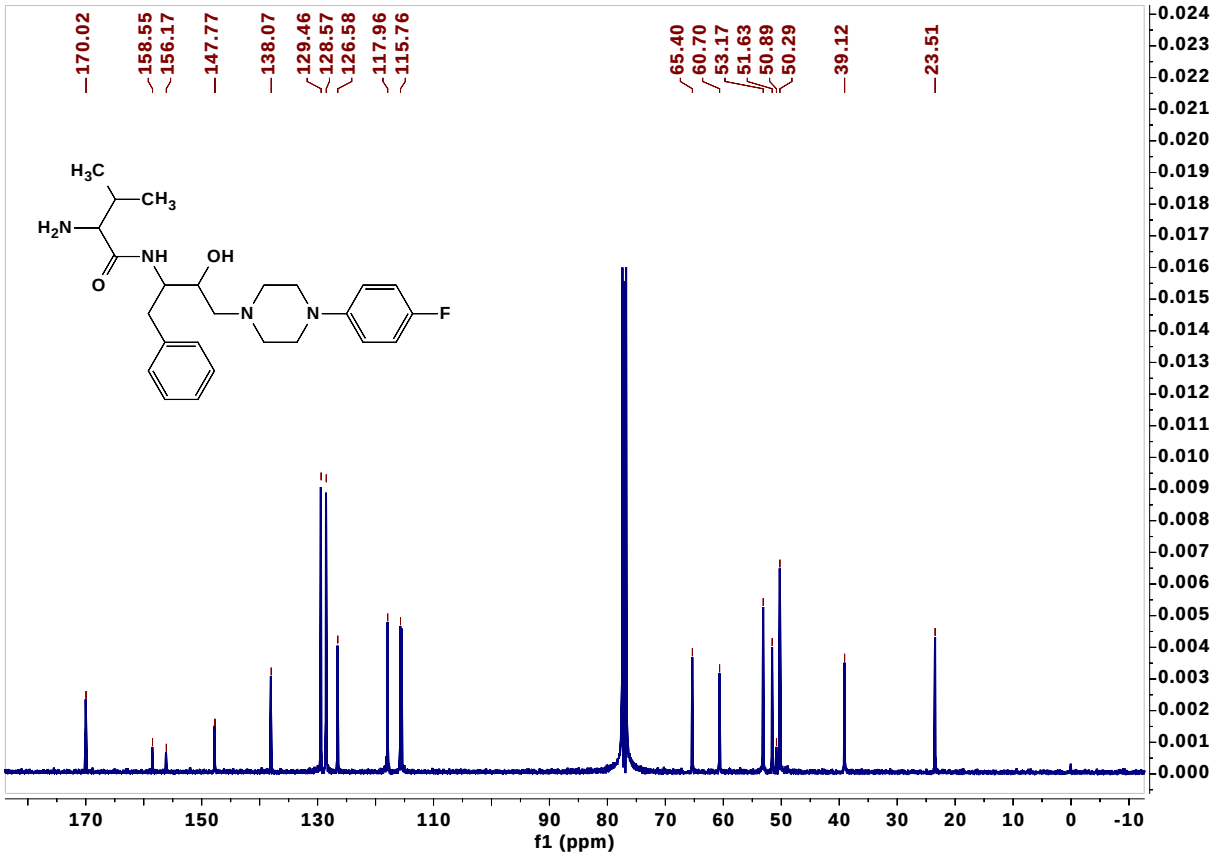


Figure S32. ^{13}C NMR spectrum of **11c**.

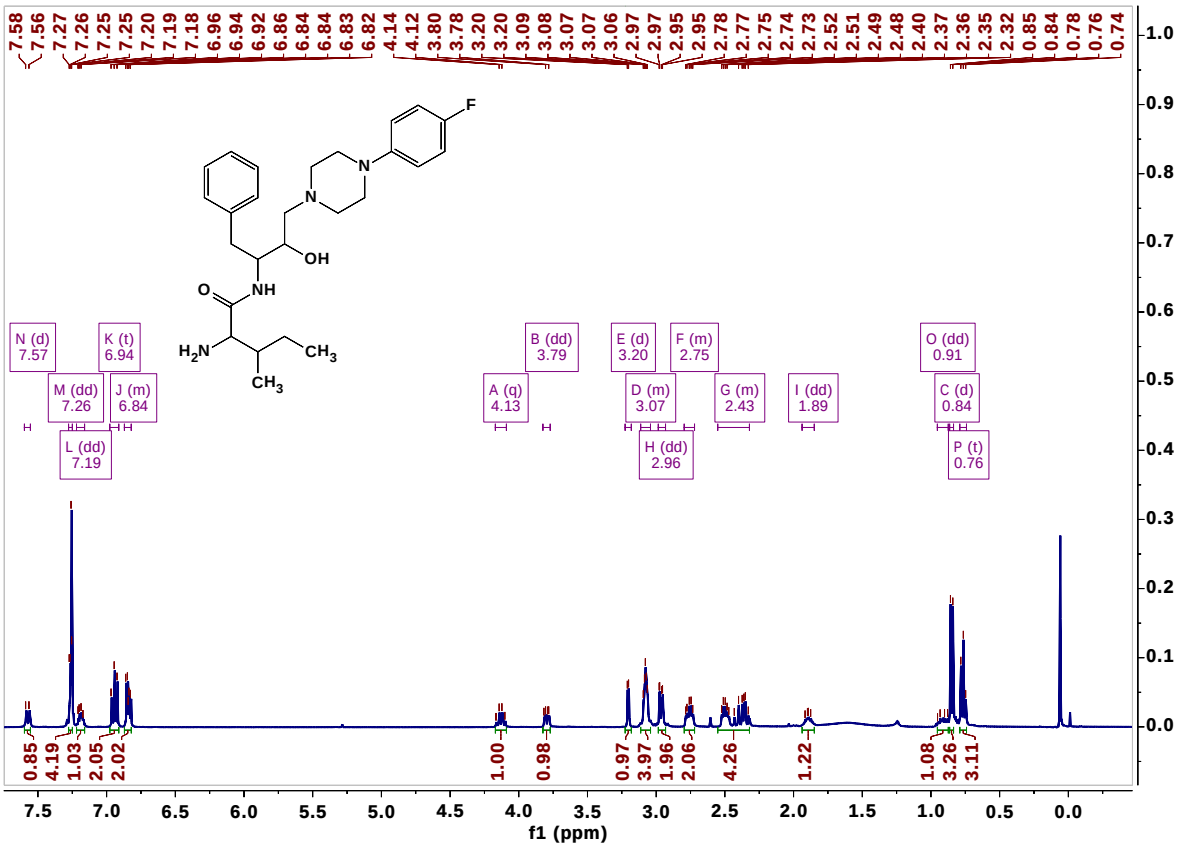


Figure S33. ^{1}H NMR spectrum of **11d**.

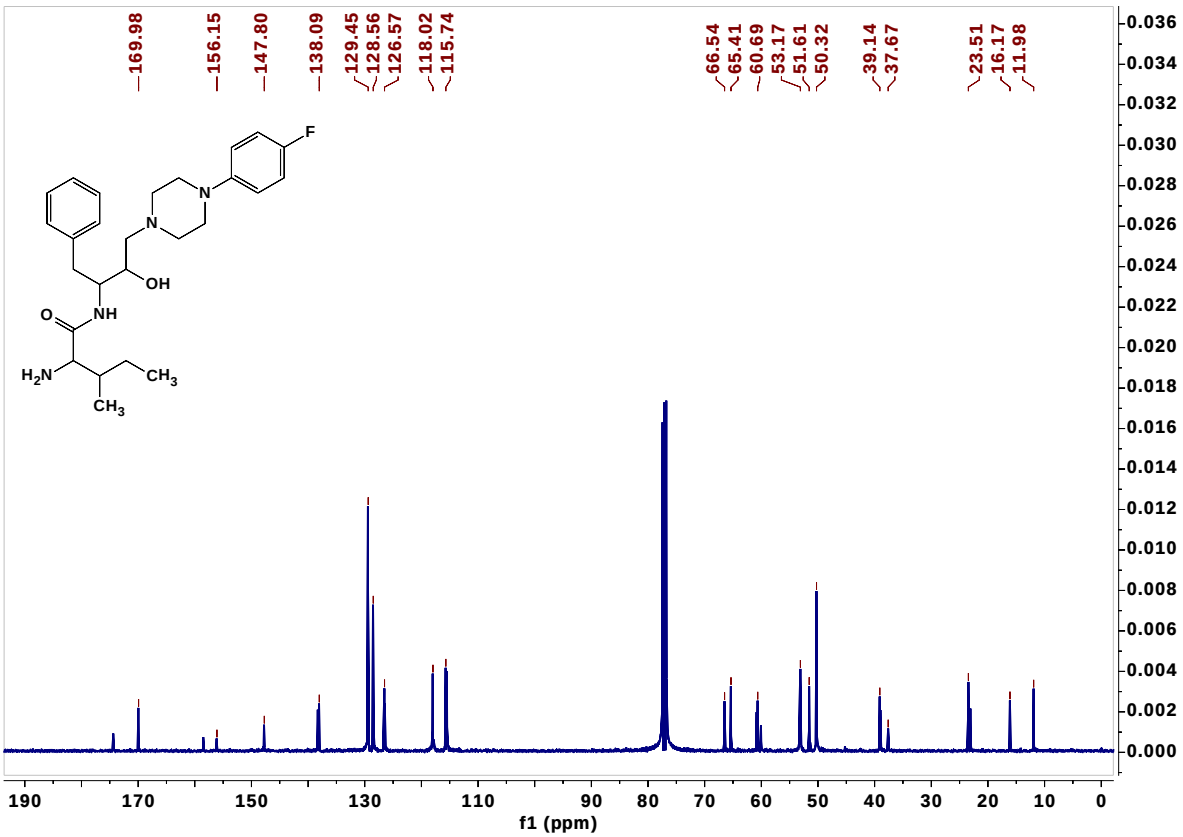


Figure S34. ^{13}C NMR spectrum of **11d**.

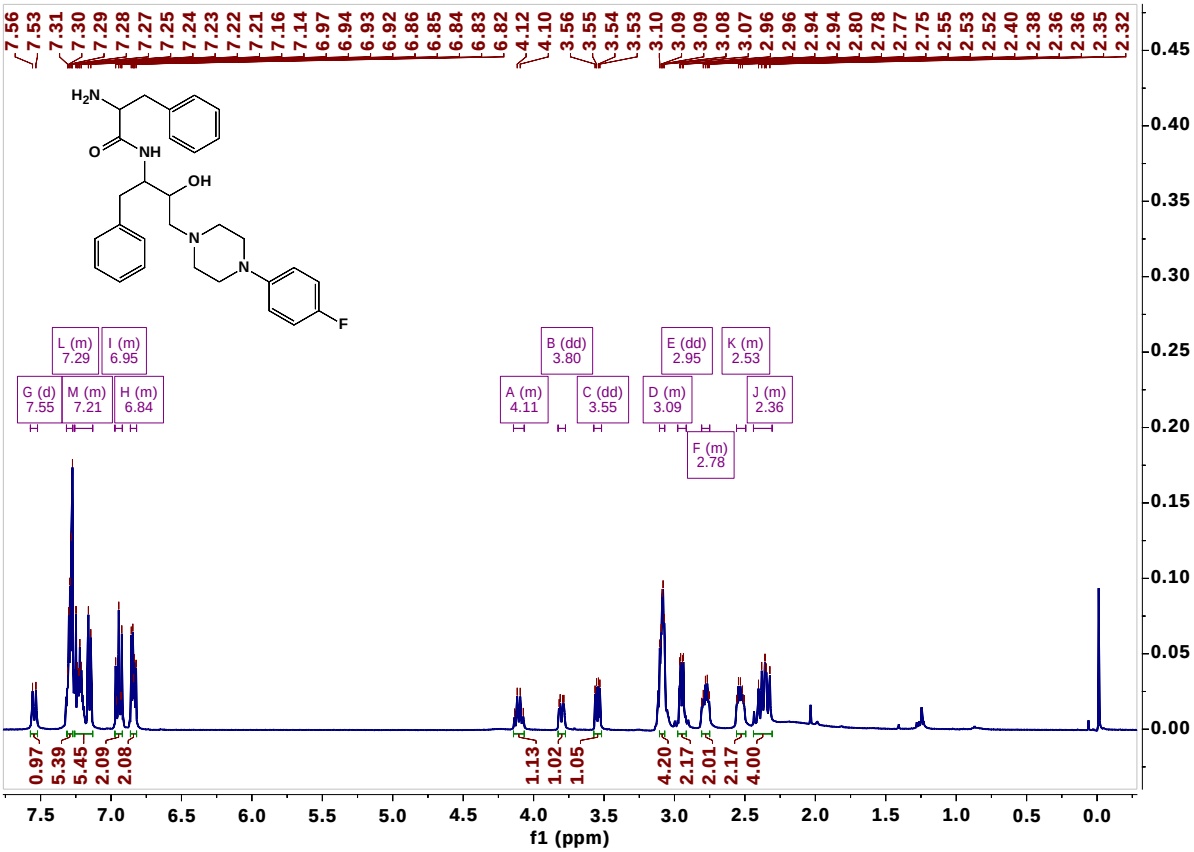


Figure S35. ^{1}H NMR spectrum of **11e**.

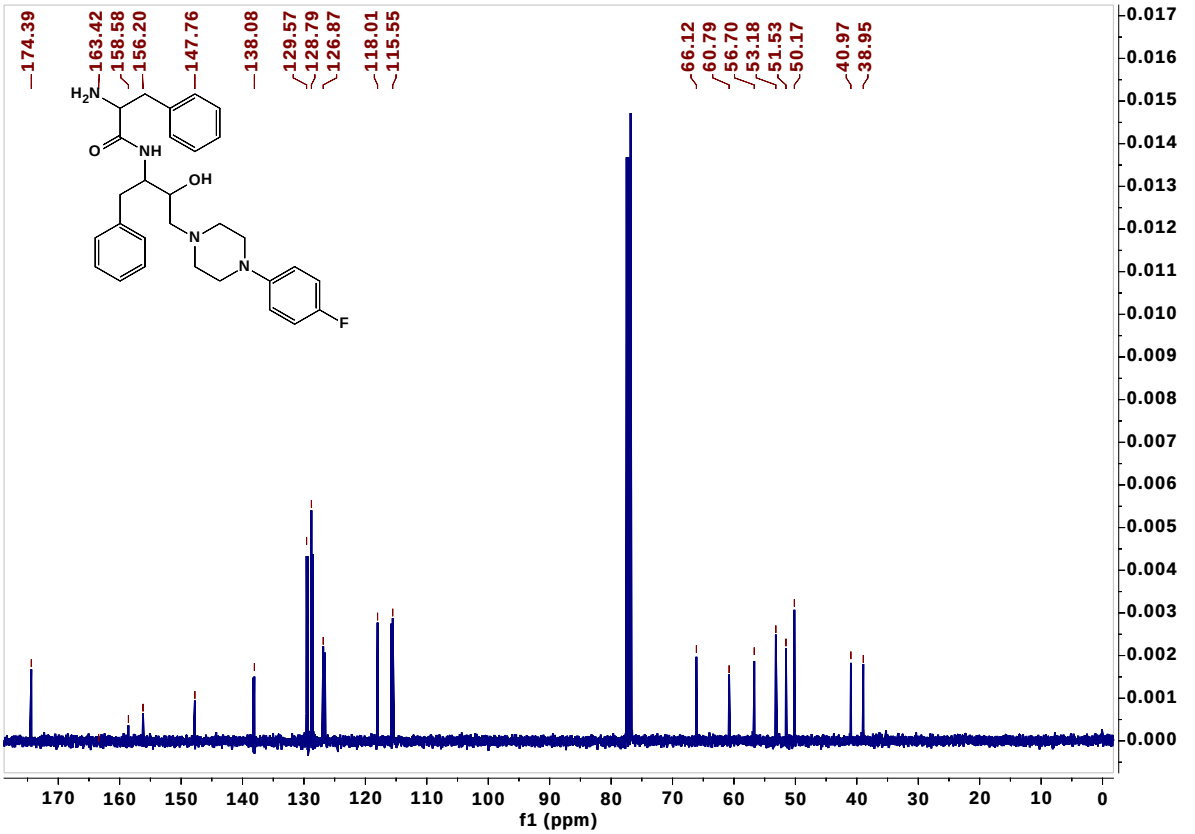


Figure S36. ^{13}C NMR spectrum of **11e**.

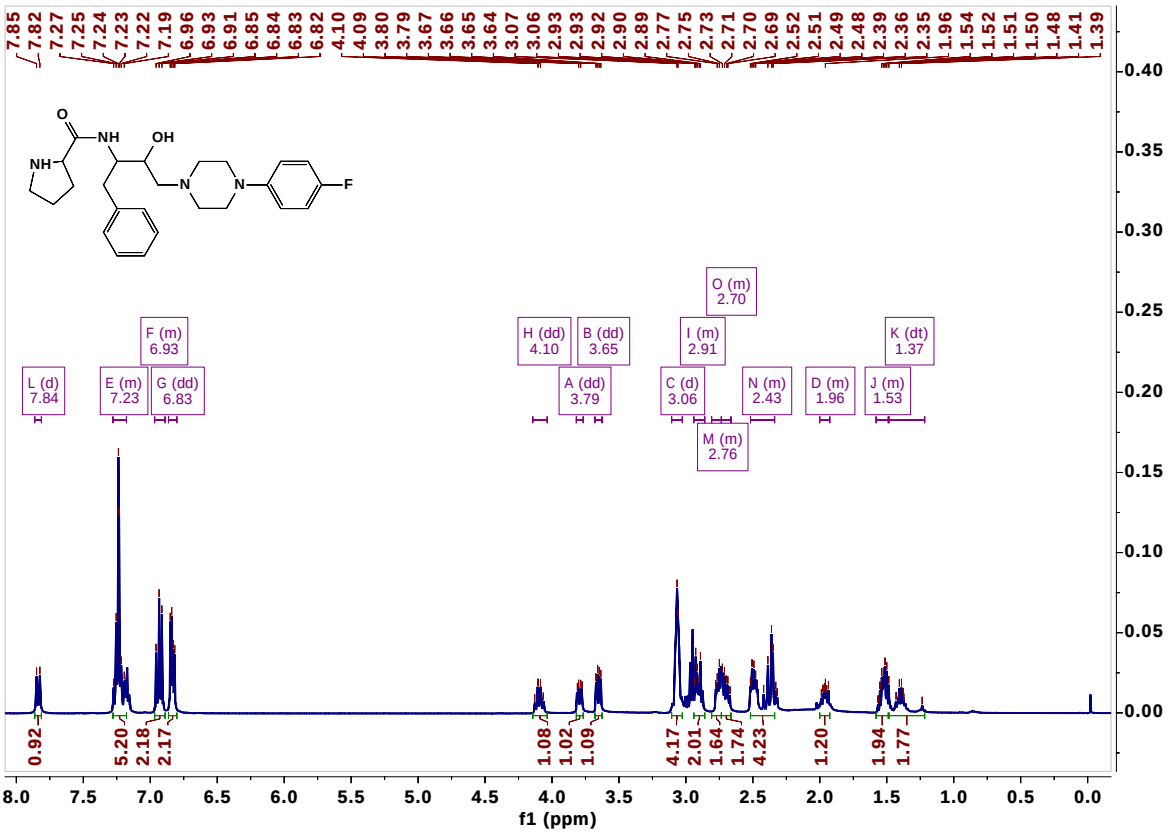


Figure S37. ^{1}H NMR spectrum of **11e**.

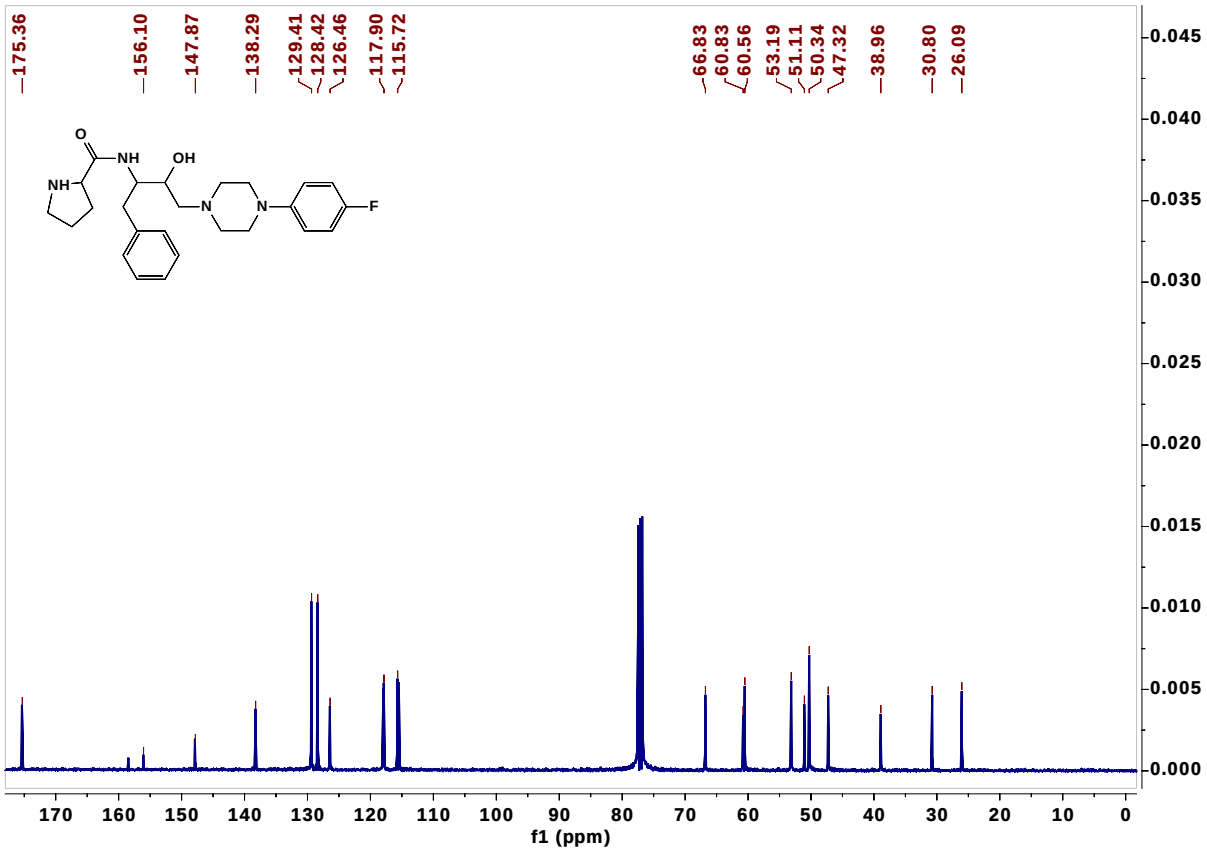


Figure S38. ^{13}C NMR spectrum of **11e**.

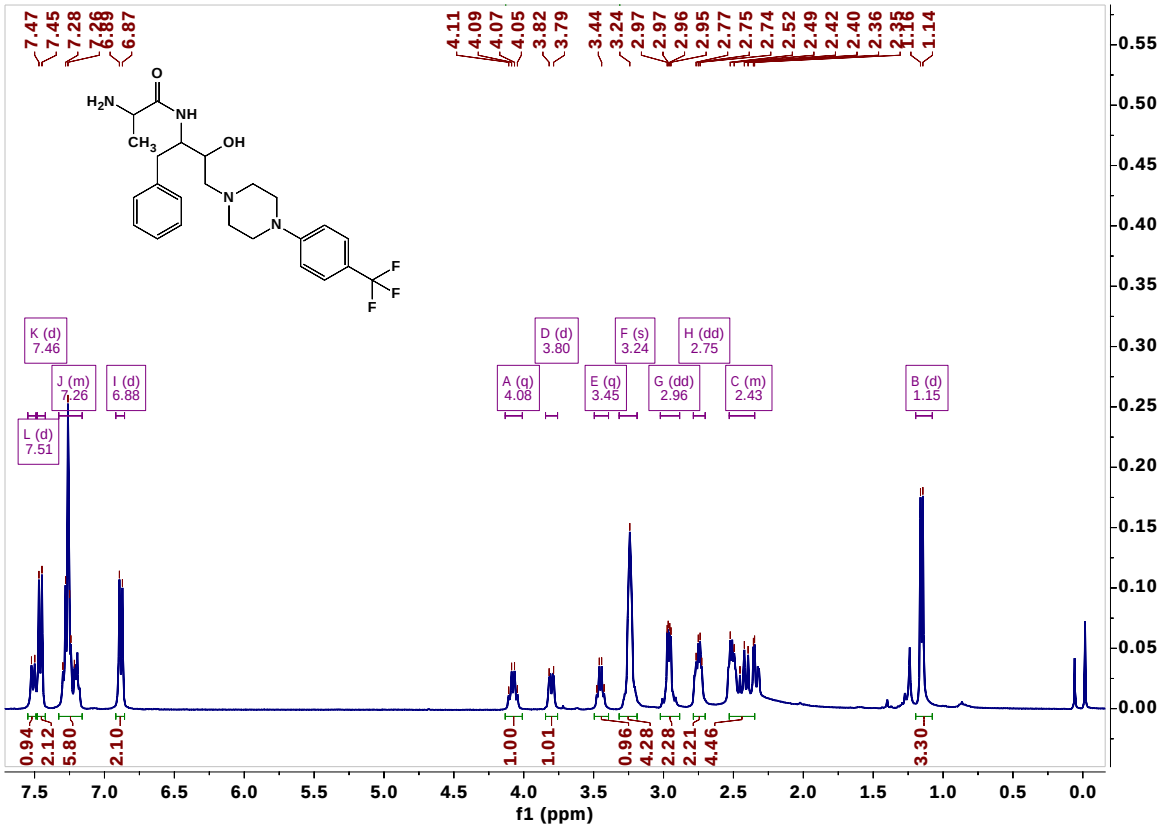


Figure S39. ^{1}H NMR spectrum of **12a**.

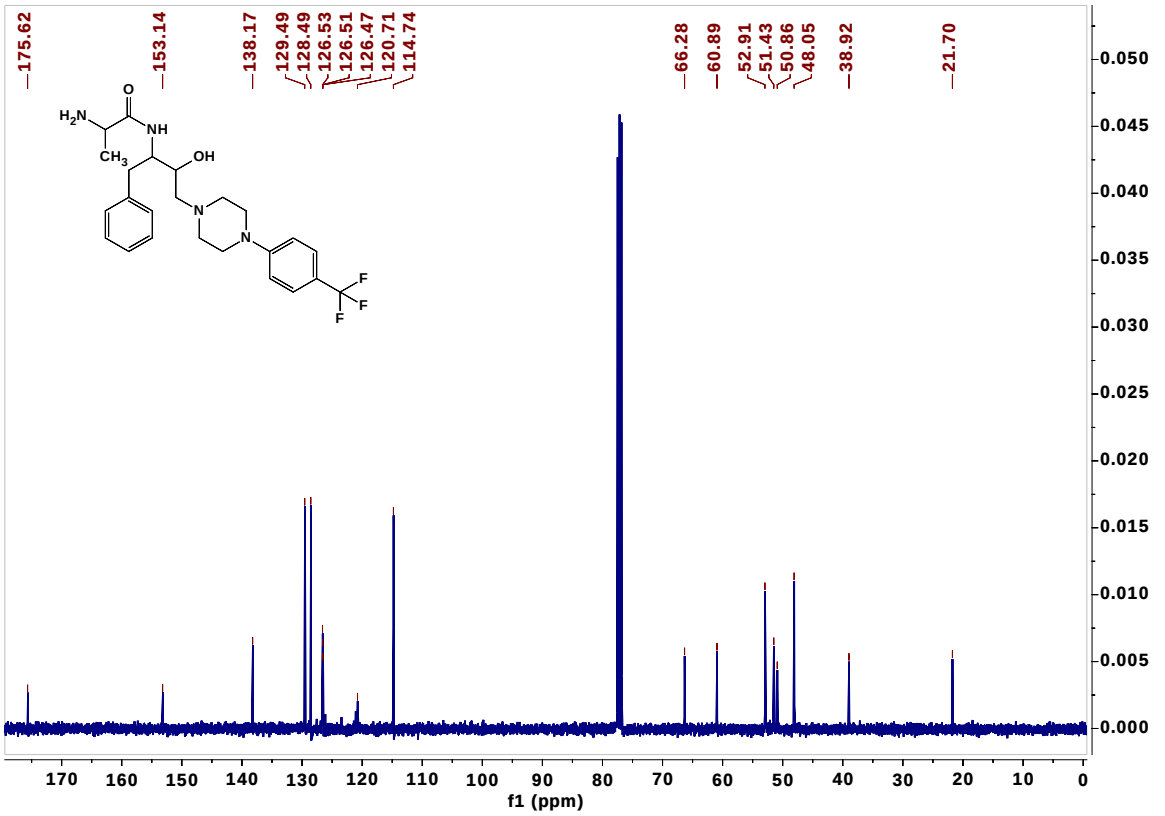


Figure S40. ^{13}C NMR spectrum of **12a**.

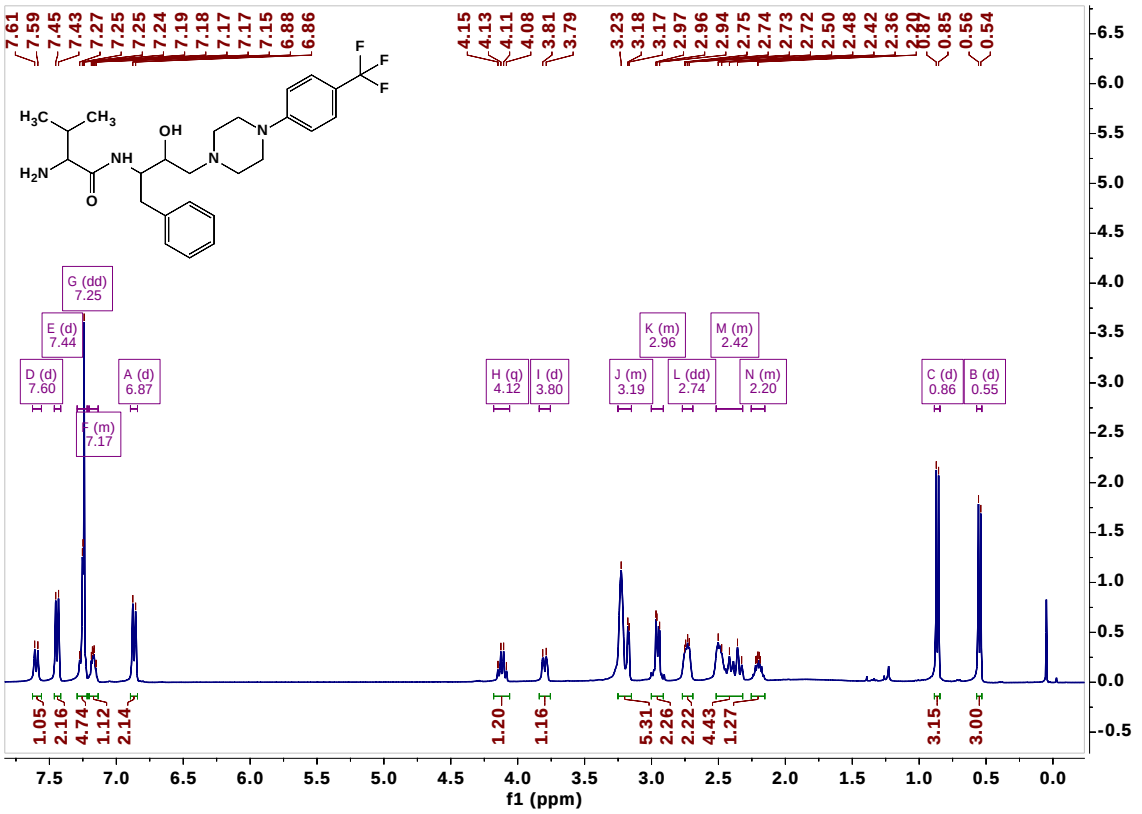


Figure S41. ^{1}H NMR spectrum of **12b**.

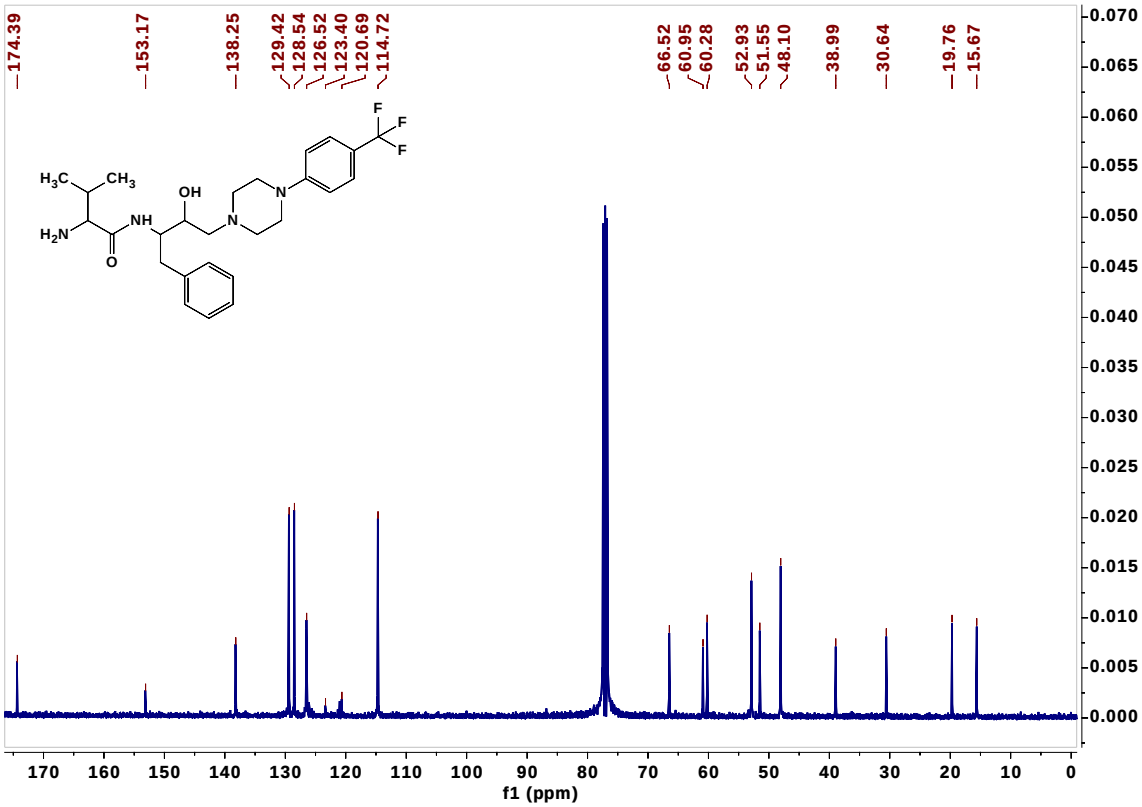


Figure S42. ^{13}C NMR spectrum of **12b**.

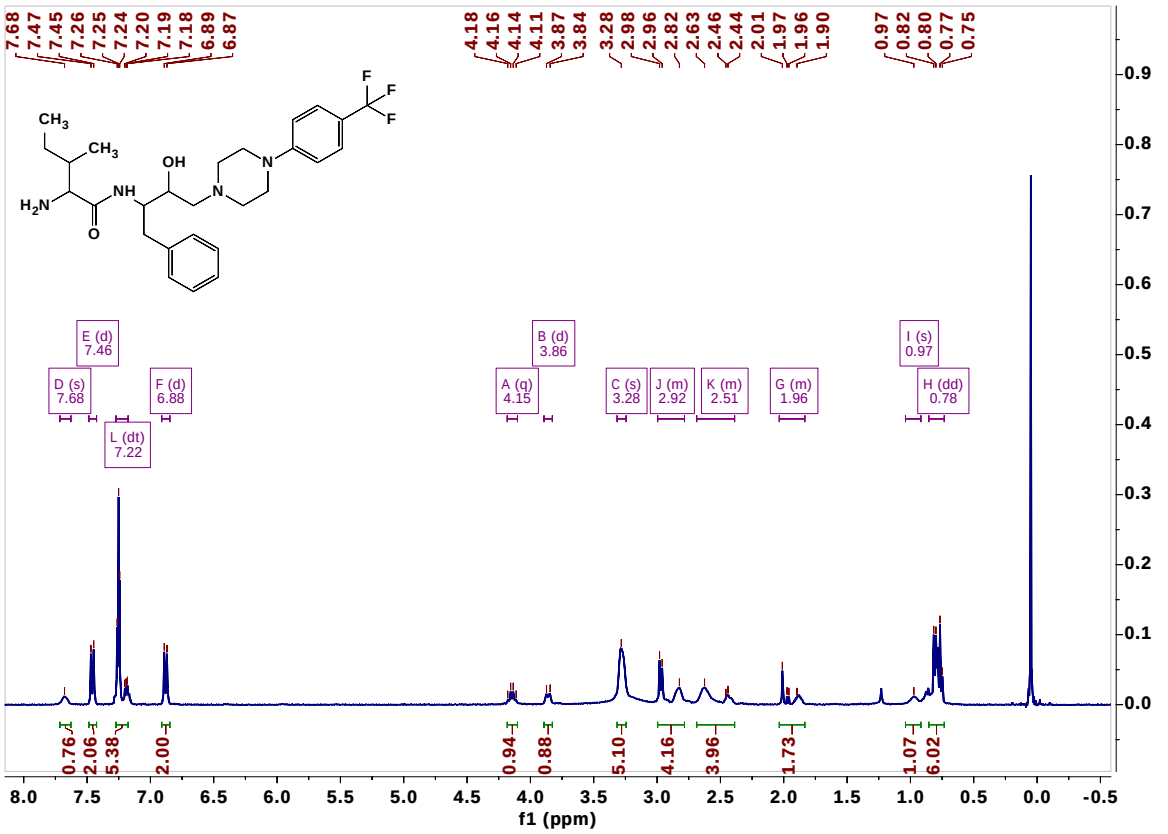


Figure S43. ^{1}H NMR spectrum of **12c**.

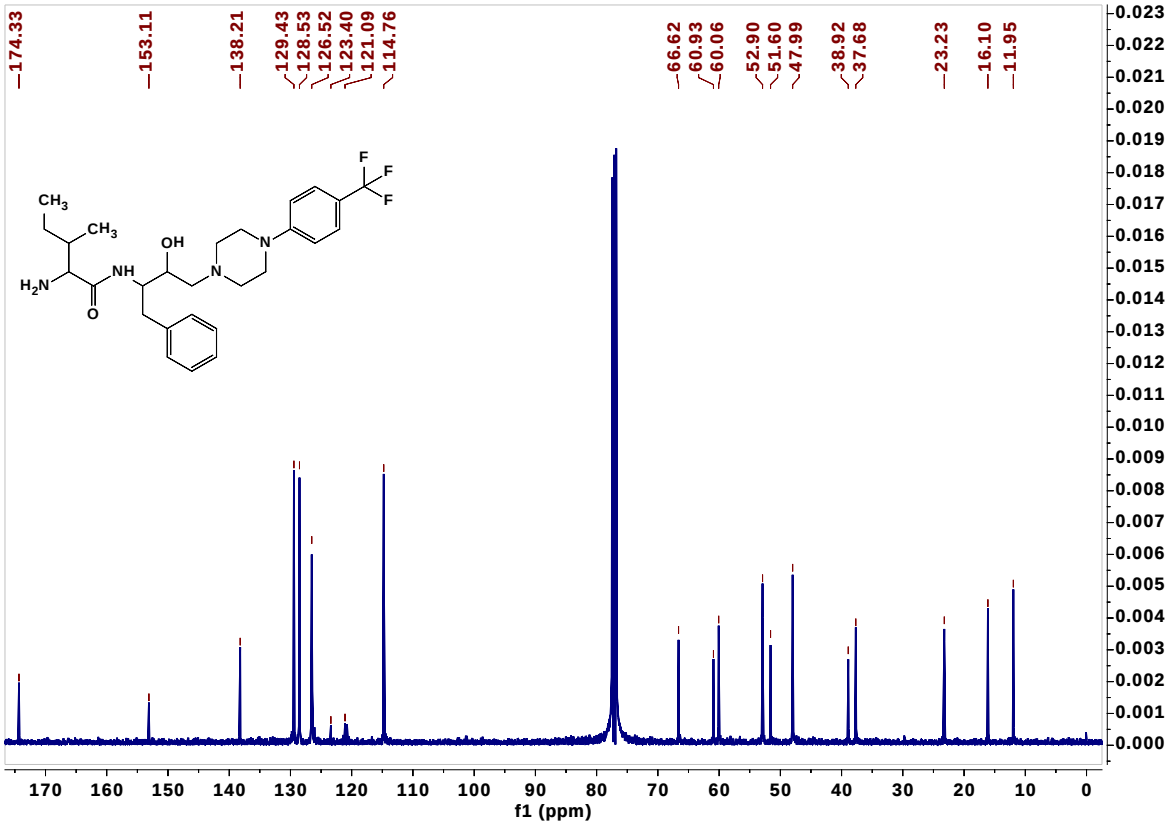


Figure S44. ^{13}C NMR spectrum of **12c**.

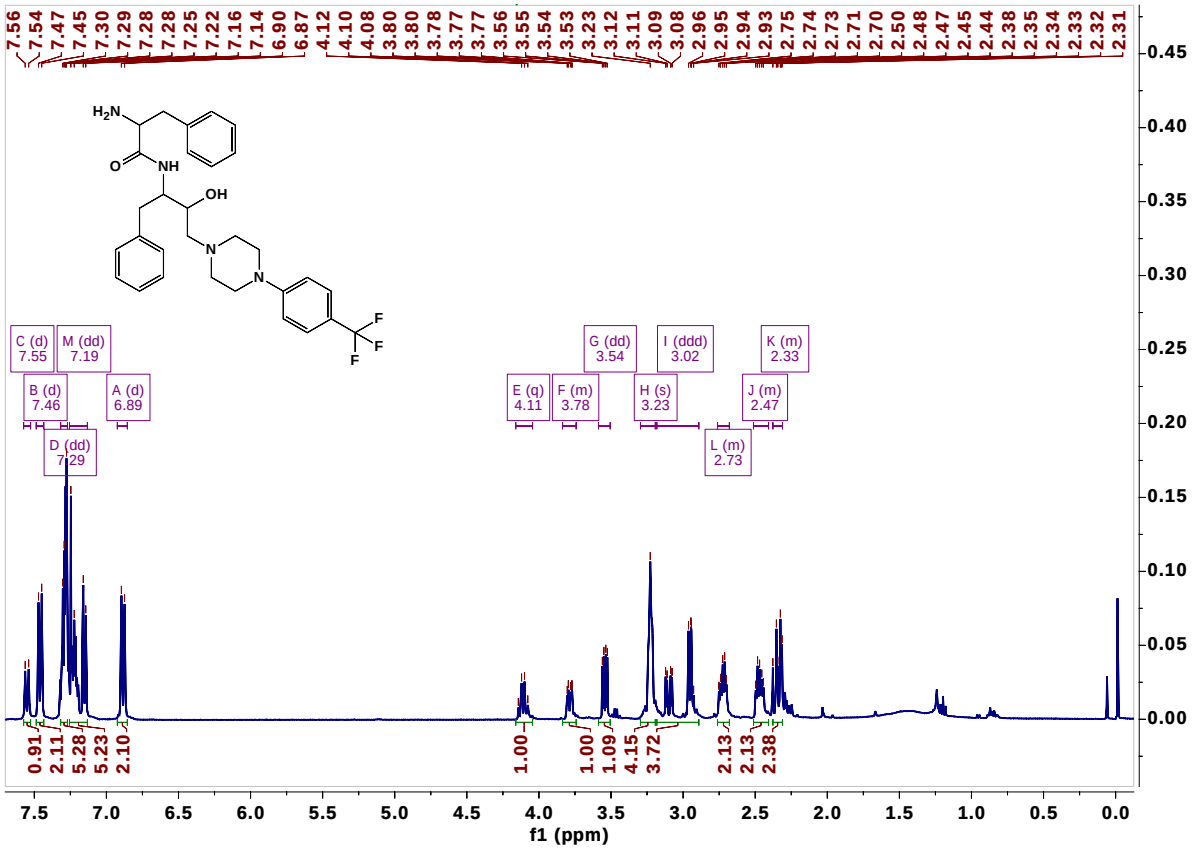


Figure S45. ^{1}H NMR spectrum of **12d**.

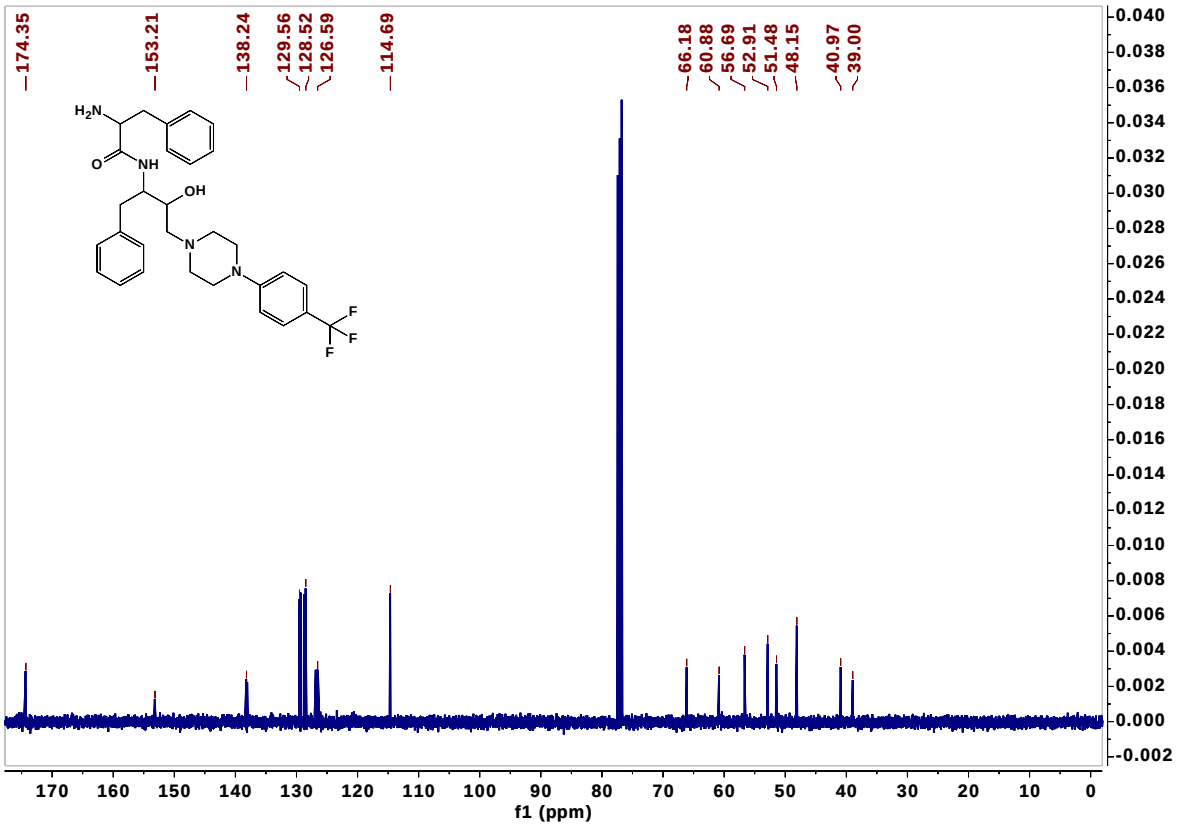


Figure S46. ^{13}C NMR spectrum of **12d**.

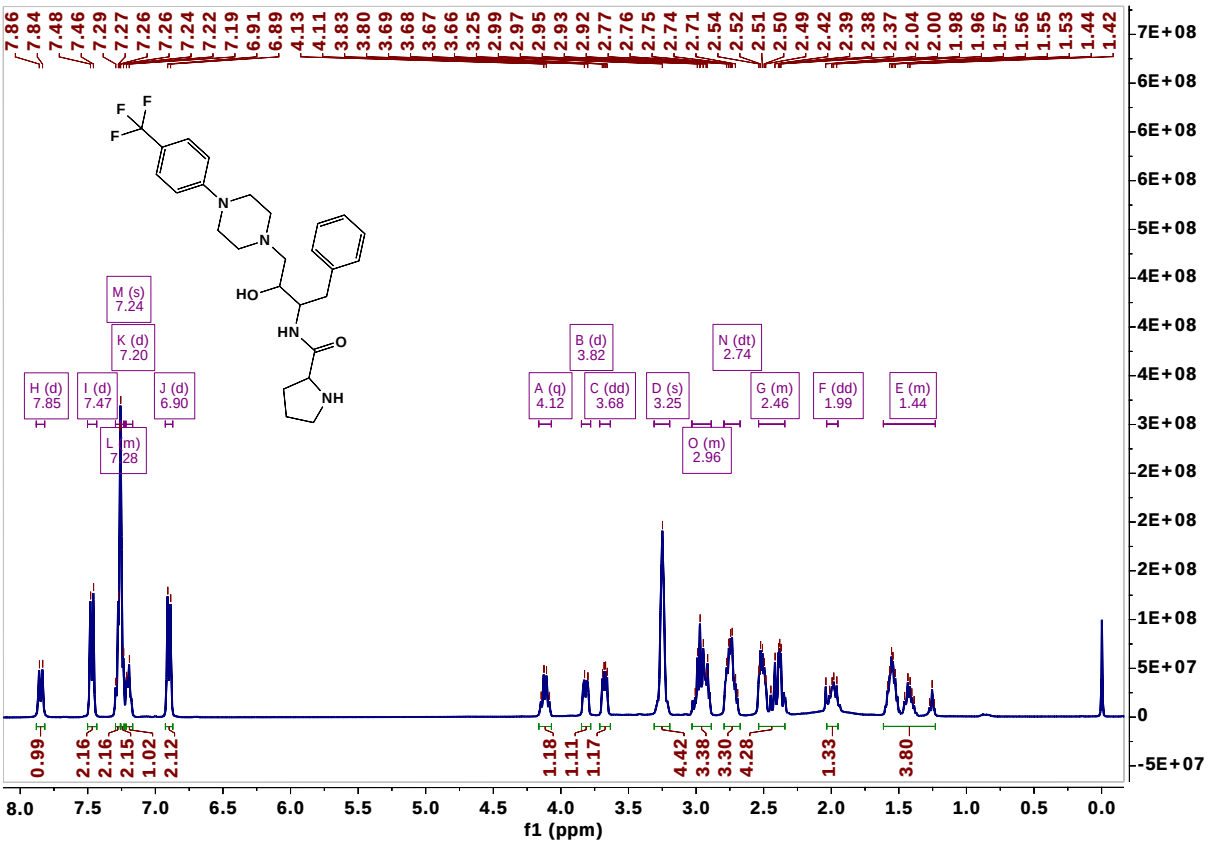


Figure S47. ^{1}H NMR spectrum of **12e**.

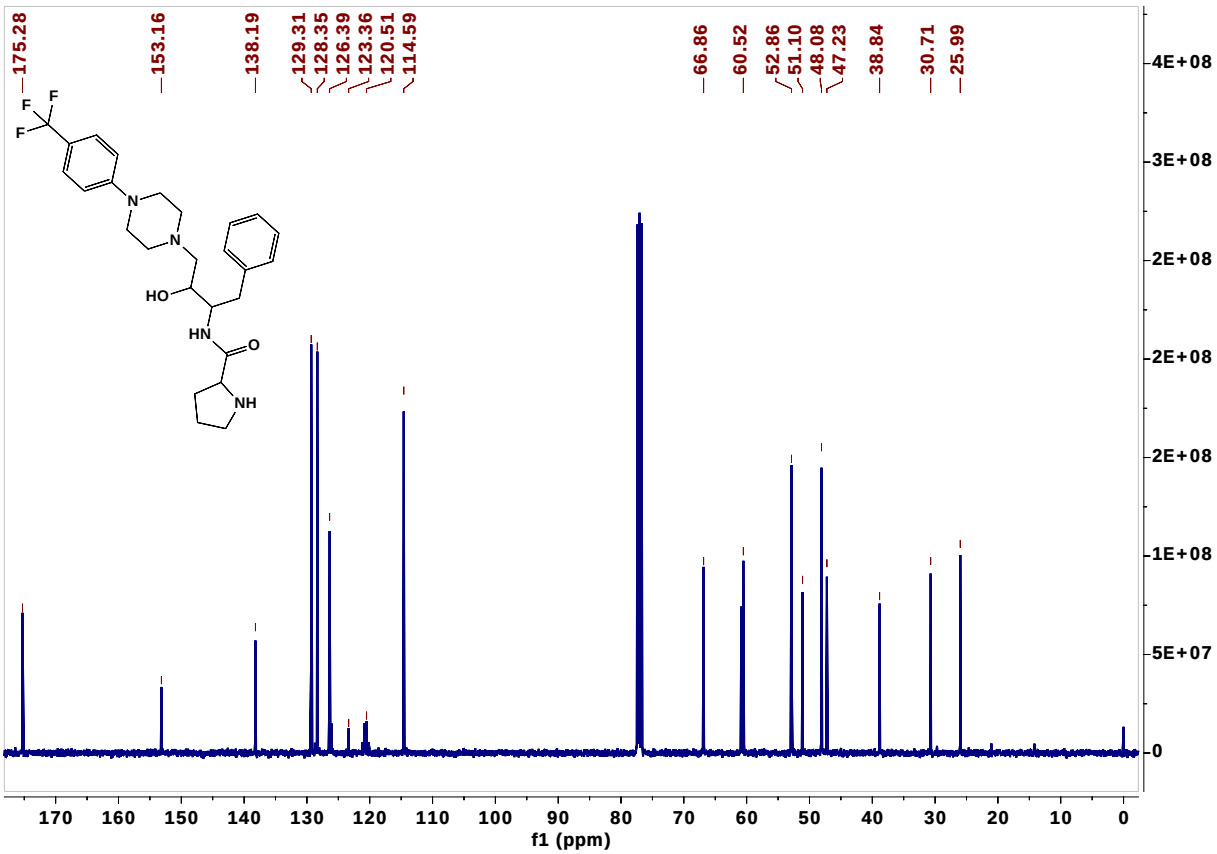
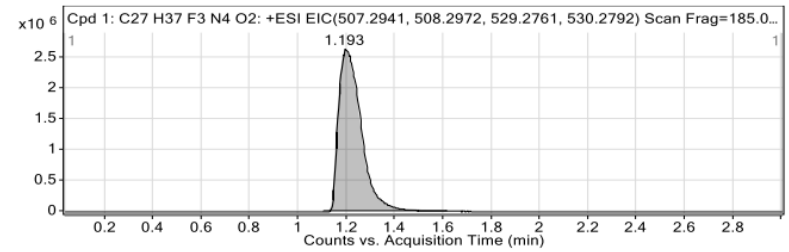


Figure S48. ^{13}C NMR spectrum of **12e**.

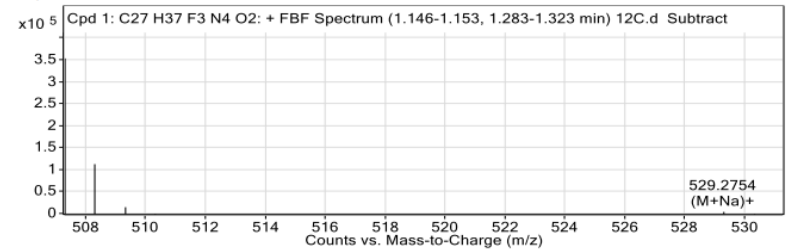
Compound Table

Compound Label	RT	Mass	Abund	Formula	Tgt Mass	Diff (ppm)	MFG Formula	DB Formula
Cpd 1: C27 H37 F3 N4 O2	1.193	506.2868	354577	C27 H37 F3 N4 O2	506.2869	-0.02	C27 H37 F3 N4 O2	C27 H37 F3 N4 O2

Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C27 H37 F3 N4 O2	507.2942	1.193	Find By Formula	506.2868



MS Spectrum



MS Zoomed Spectrum

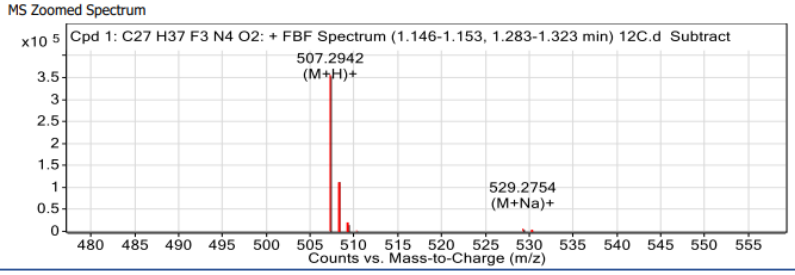


Figure S49. HRMS spectrum of **12c**.

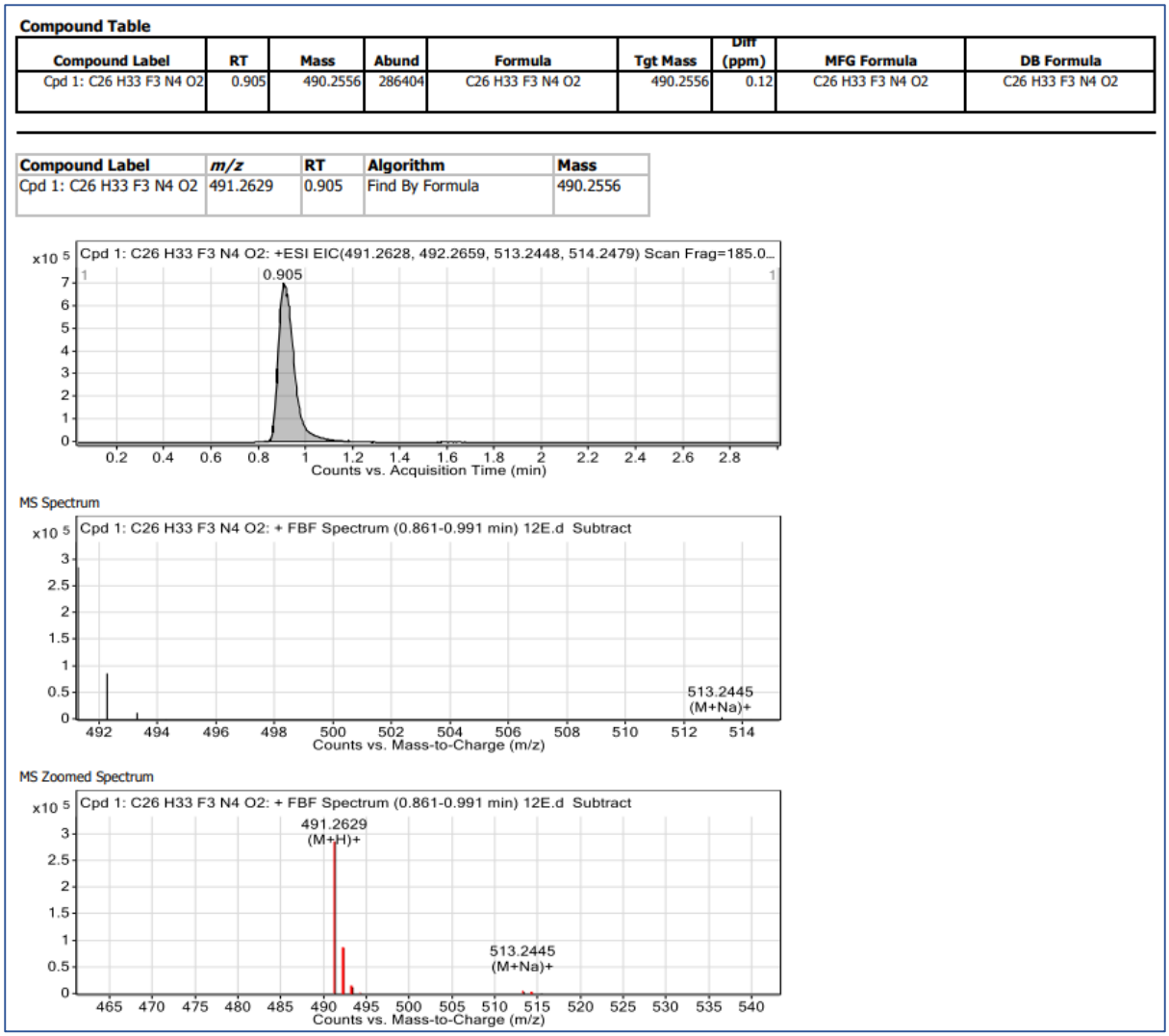


Figure S50. HRMS spectrum of **12e**.

Table S1. Physicochemical properties (ADME), Drug-likeness model score (DrugL Score); and Blood-Brain Barrier (BBB) Score of all the synthesized compounds

Entry No.	Cmpd.	MW	n ON	n OHNH	Nrot	TPSA	m LogP	DrugL Score	BBB Score	N Vio.
1	**9a**	514.63	6	3	13	94.14	2.29	-0.16	3.20	1
2	**9b**	542.69	6	3	14	94.14	2.67	-0.26	3.17	1
3	**9c**	556.71	6	3	15	94.14	2.86	-0.18	3.16	1
4	**9d**	590.73	6	3	15	94.14	3.19	-0.30	2.82	1
5	**9e**	540.67	6	2	12	85.35	2.67	0.54	3.55	1
6	**10a**	564.64	8	3	14	94.14	2.67	-0.46	3.18	1
7	**10b**	592.69	8	3	15	94.14	3.05	-0.56	3.17	1
8	**10c**	606.72	8	3	16	94.14	3.23	-0.47	3.17	1
9	**10d**	640.74	8	3	16	94.14	3.55	-0.60	2.72	1
10	**10e**	590.68	8	2	13	85.35	3.05	0.22	3.54	1
11	**11a**	414.52	5	3	9	81.83	1.72	1.09	3.71	0
12	**11b**	442.57	5	3	10	81.83	2.13	0.99	3.70	0
13	**11c**	456.6	5	3	11	81.83	2.34	1.06	3.69	0

14	**11d**	490.61	5	3	11	81.83	2.7	0.88	3.28	0
15	**11e**	440.55	5	3	9	67.84	2.13	1.12	4.11	0
16	**12a**	464.52	7	3	10	81.83	2.13	0.64	3.72	0
17	**12b**	492.58	7	3	11	81.83	2.54	0.54	3.70	0
18	**12c**	506.6	7	3	12	81.83	2.73	0.62	3.68	1
19	**12d**	540.62	7	3	12	81.83	3.08	0.44	3.26	1
20	**12e**	490.56	7	3	10	67.84	2.54	0.68	4.09	0

Cmpd. = Compound; MW = molecular weight (g/mol); nON = no. of hydrogen bond acceptor; nOHNH = no. of hydrogen bond donors; Nrot = no. of rotatable bonds; TPSA = total polar surface area; MLogP = Predicted octanol/water partition coefficient; DrugL. Score = Drug-likeness model score (0-2); BBB Score = The Blood-Brain Barrier (BBB) Score (6-High,0-Low); nVio. = no. of Lipinski violation.