Electronic Supplementary Information for:

Bioinspired Design for the Assembly of Glypromate® Neuropeptide Conjugates with Active Pharmaceutical Ingredients

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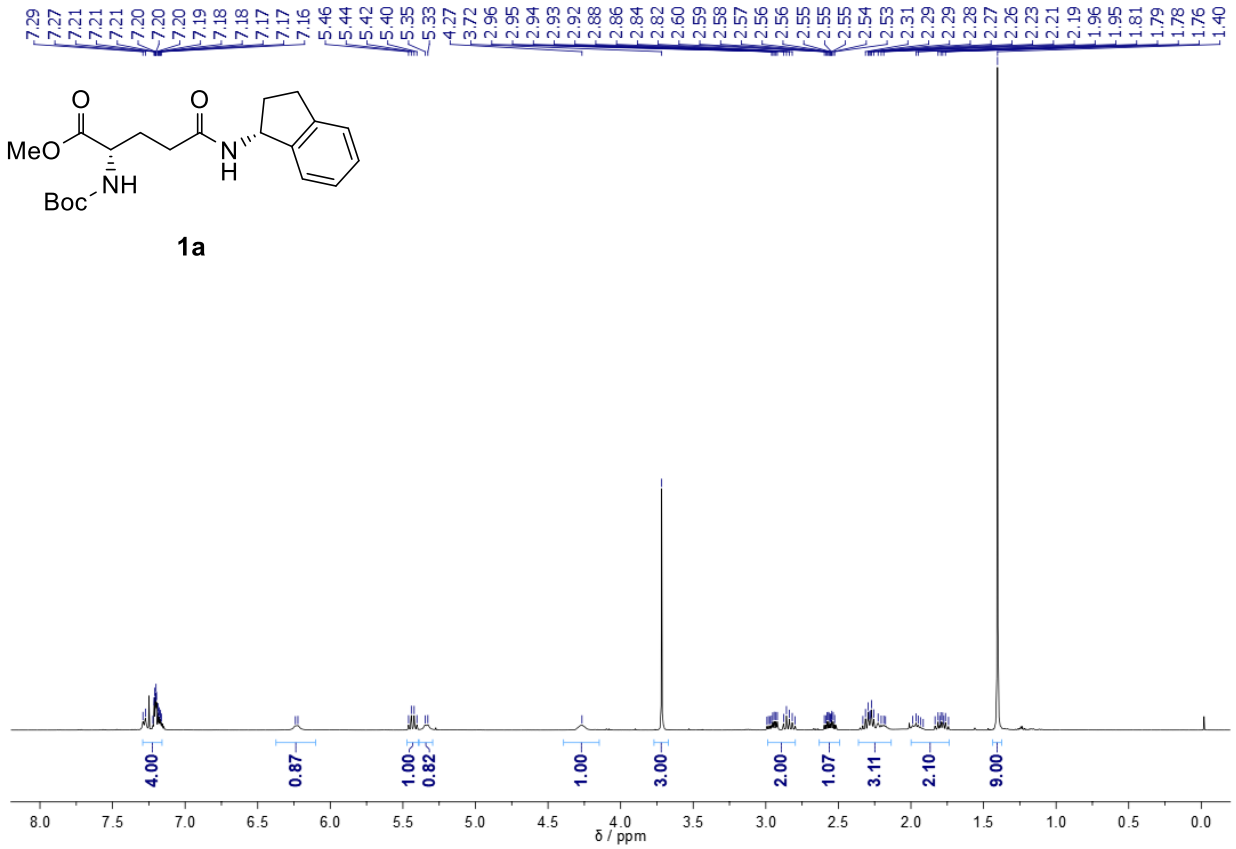
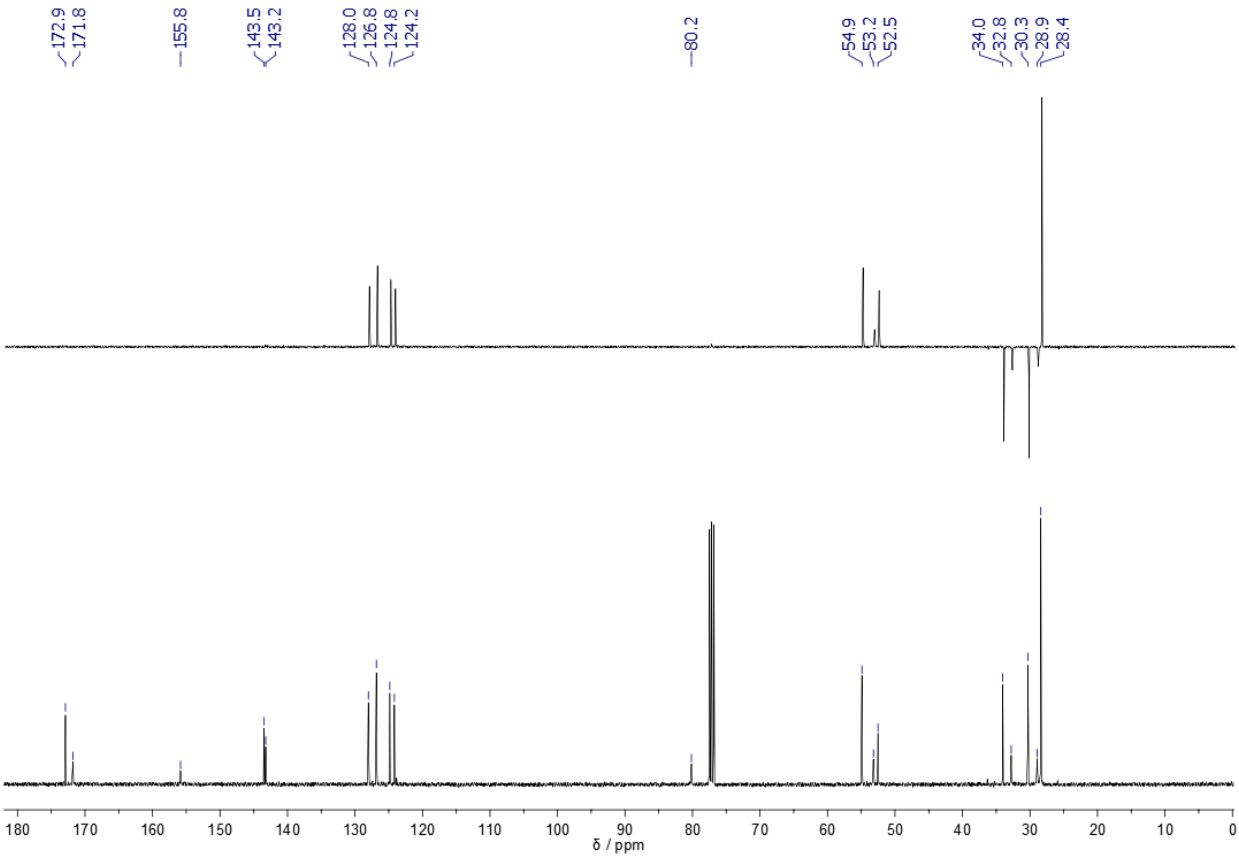


Figure S1. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **1a**.



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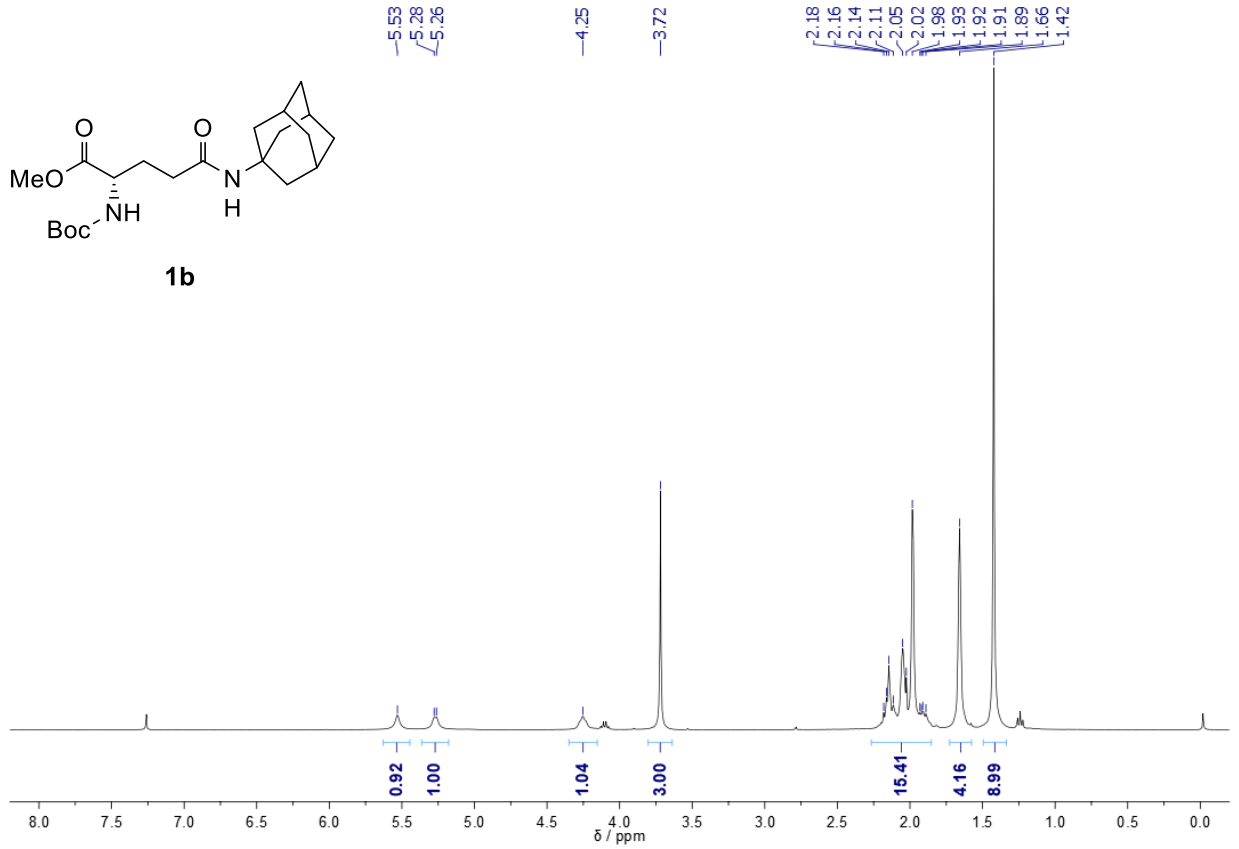

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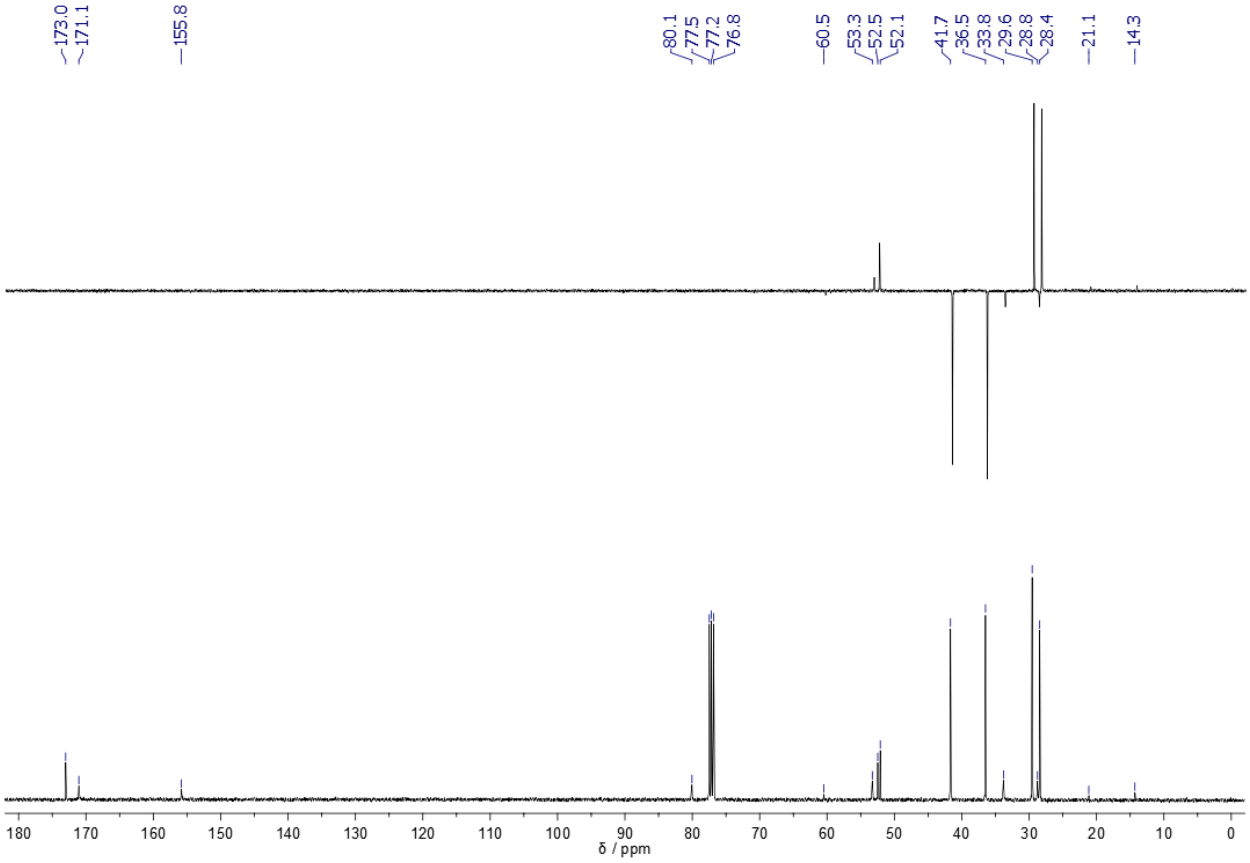

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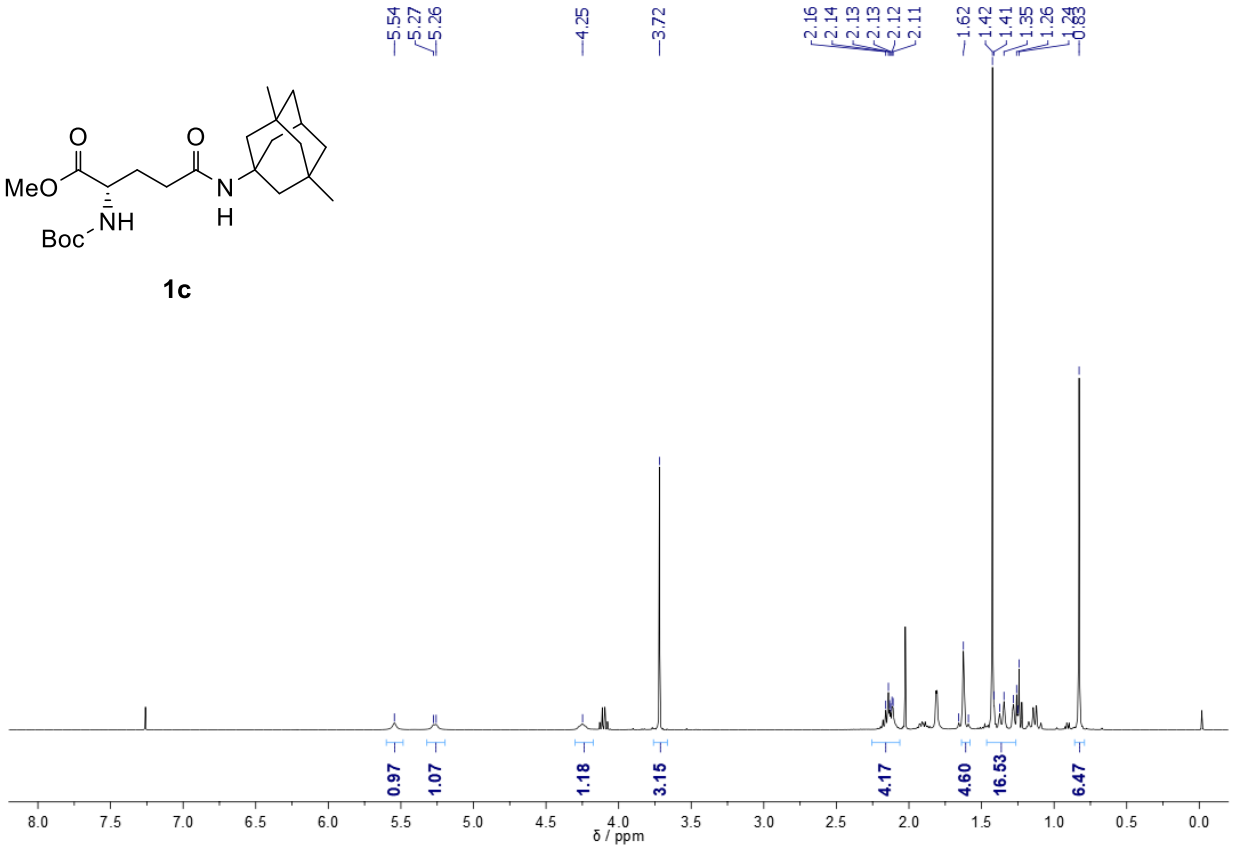

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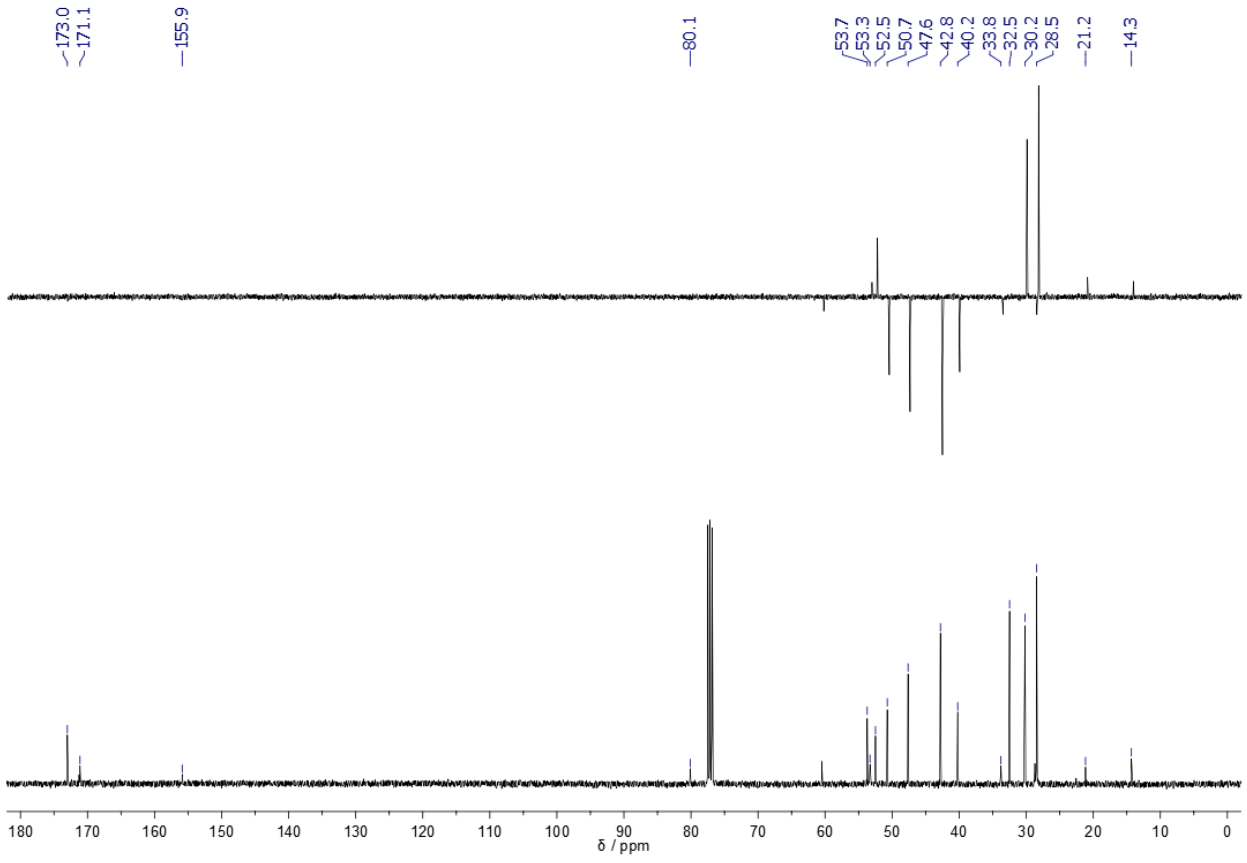

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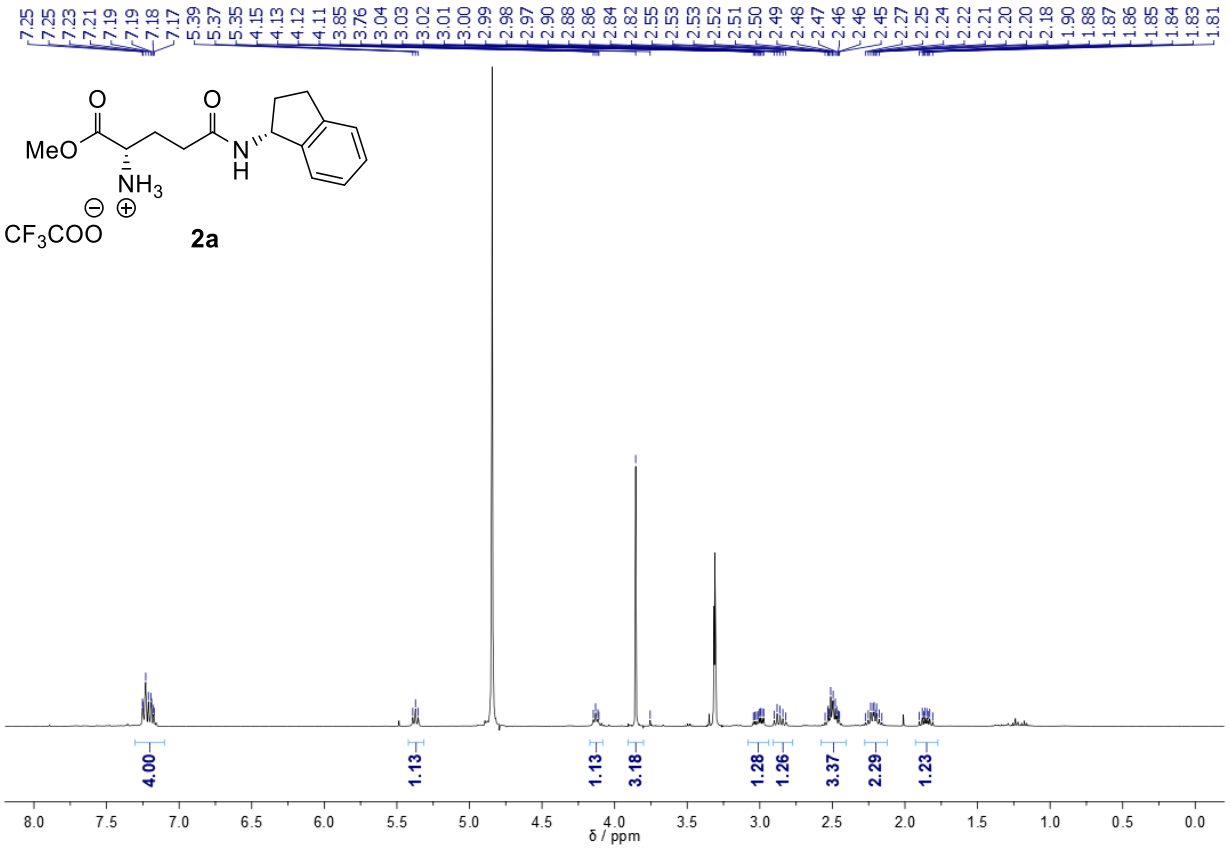
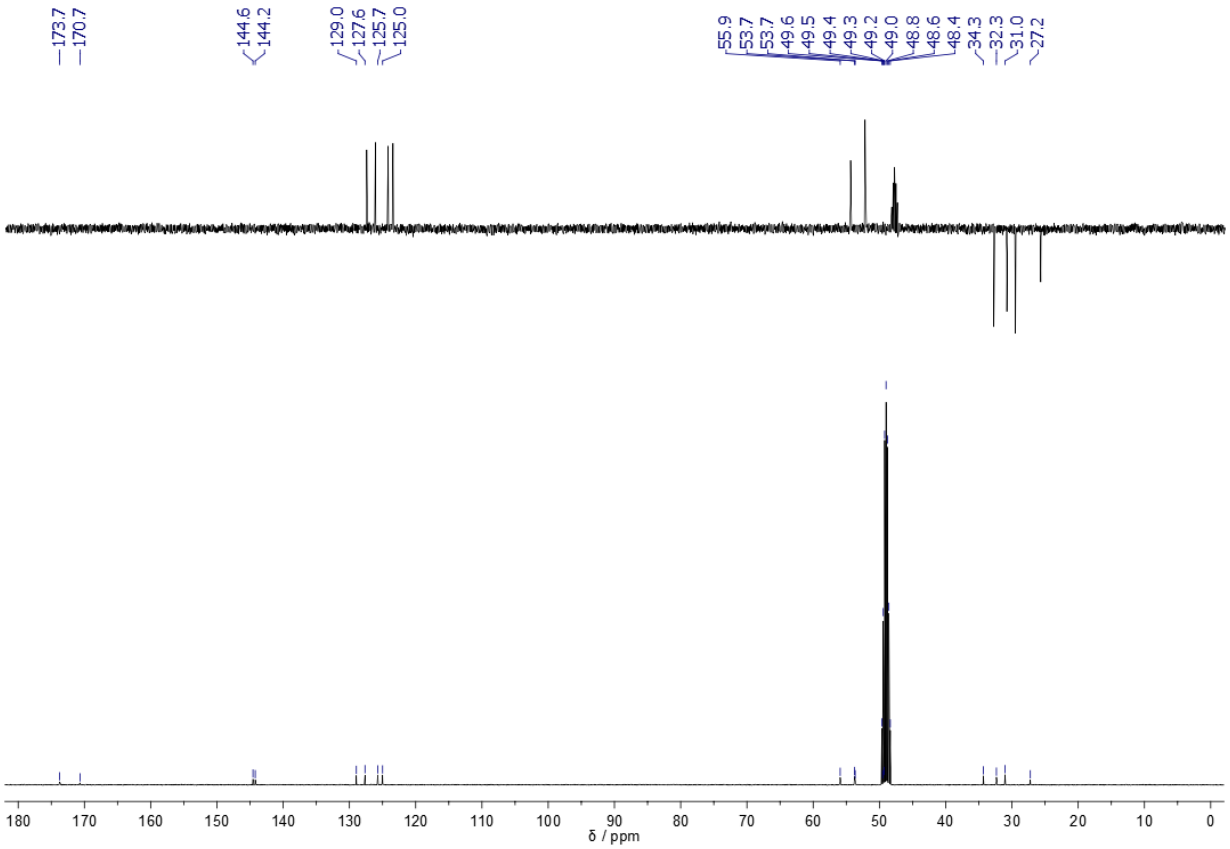


Figure S7. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **2a**.



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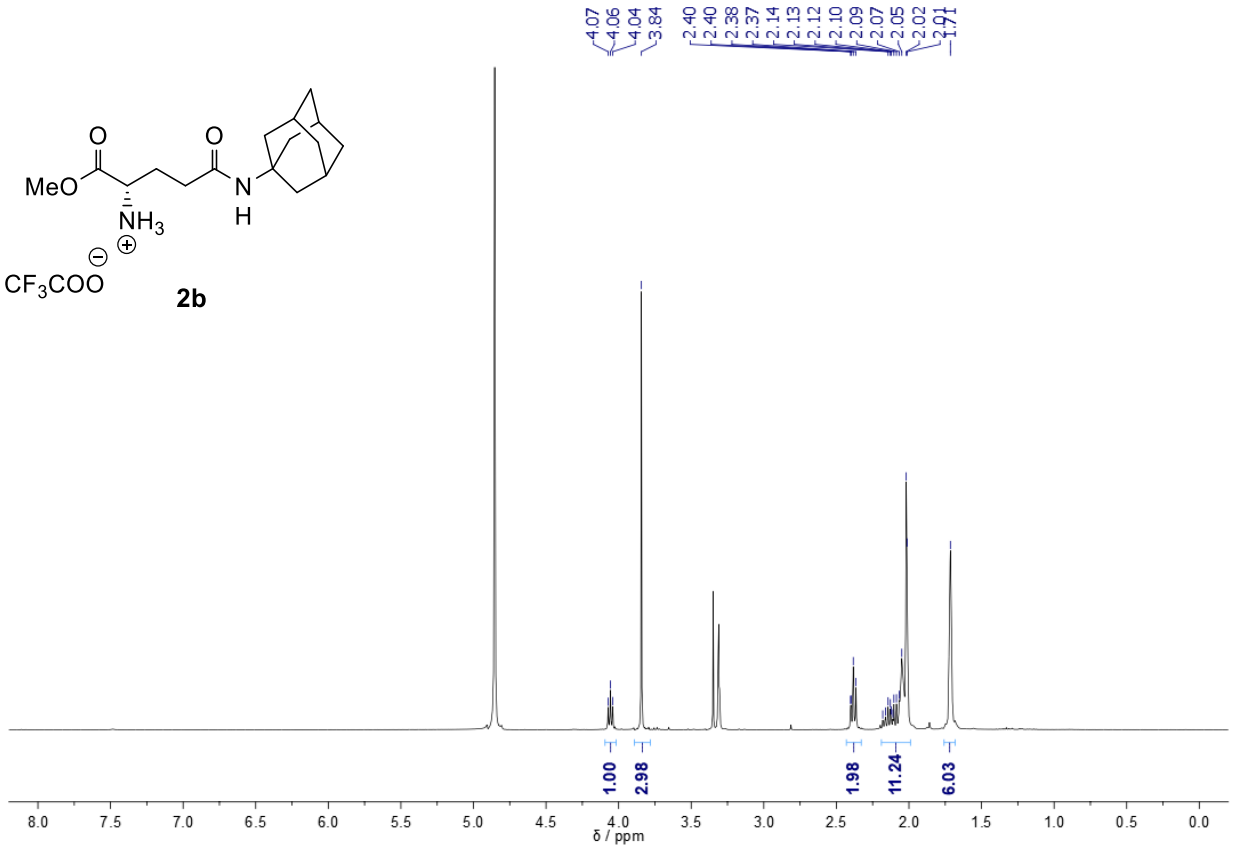

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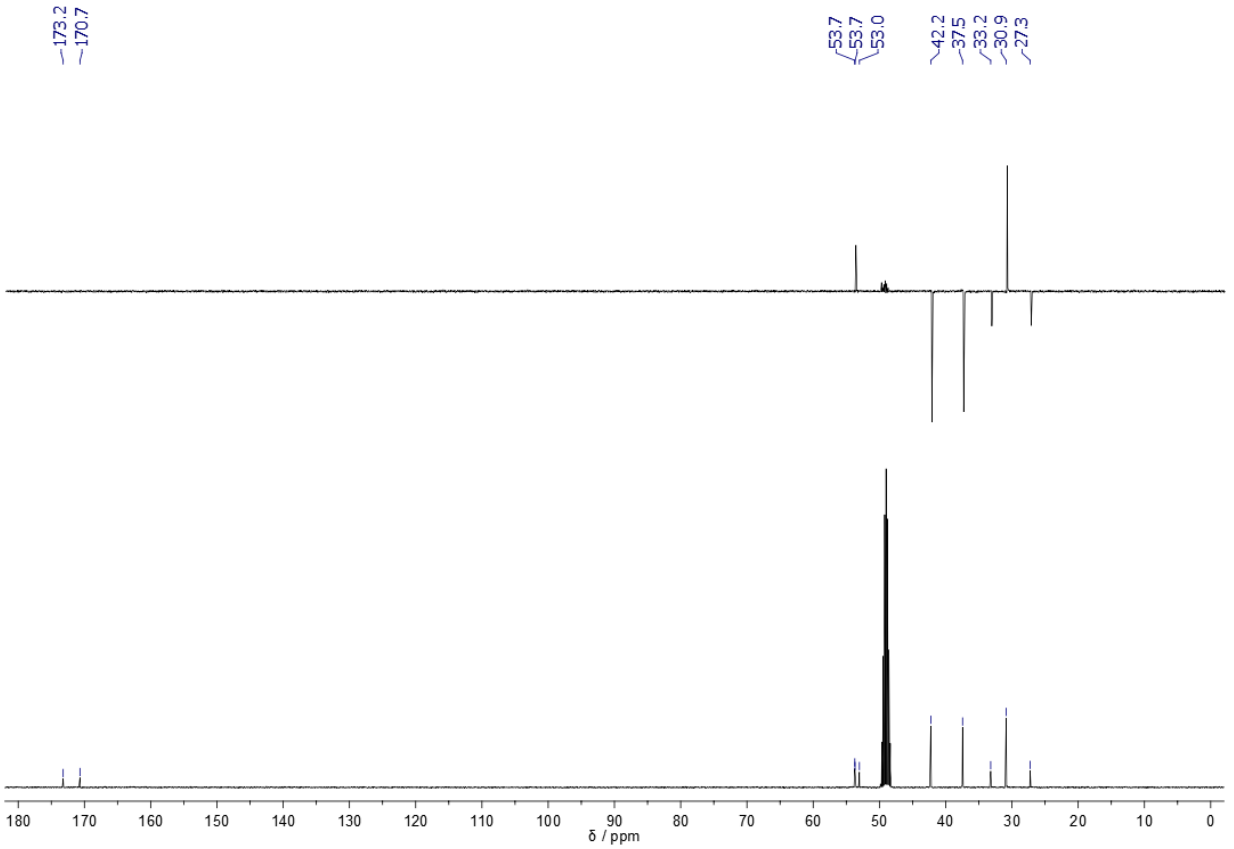

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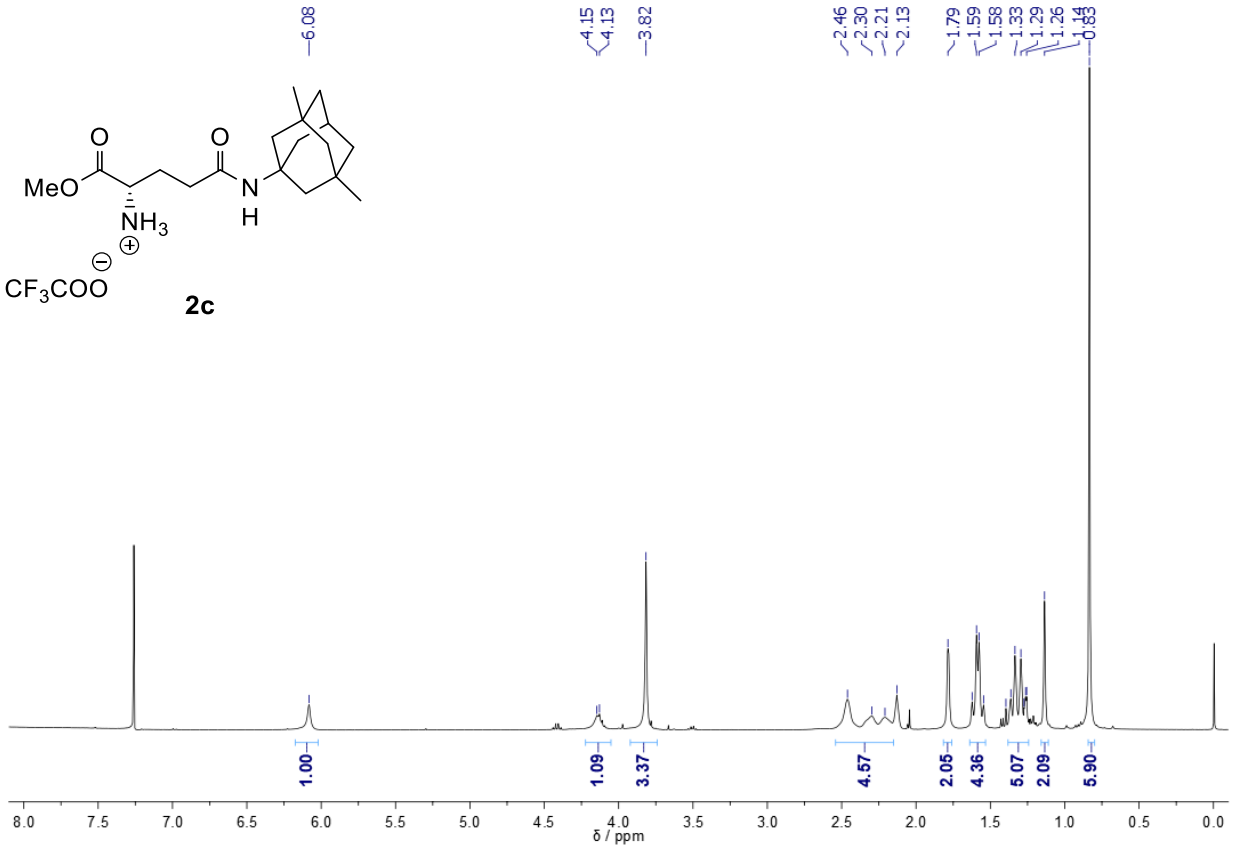

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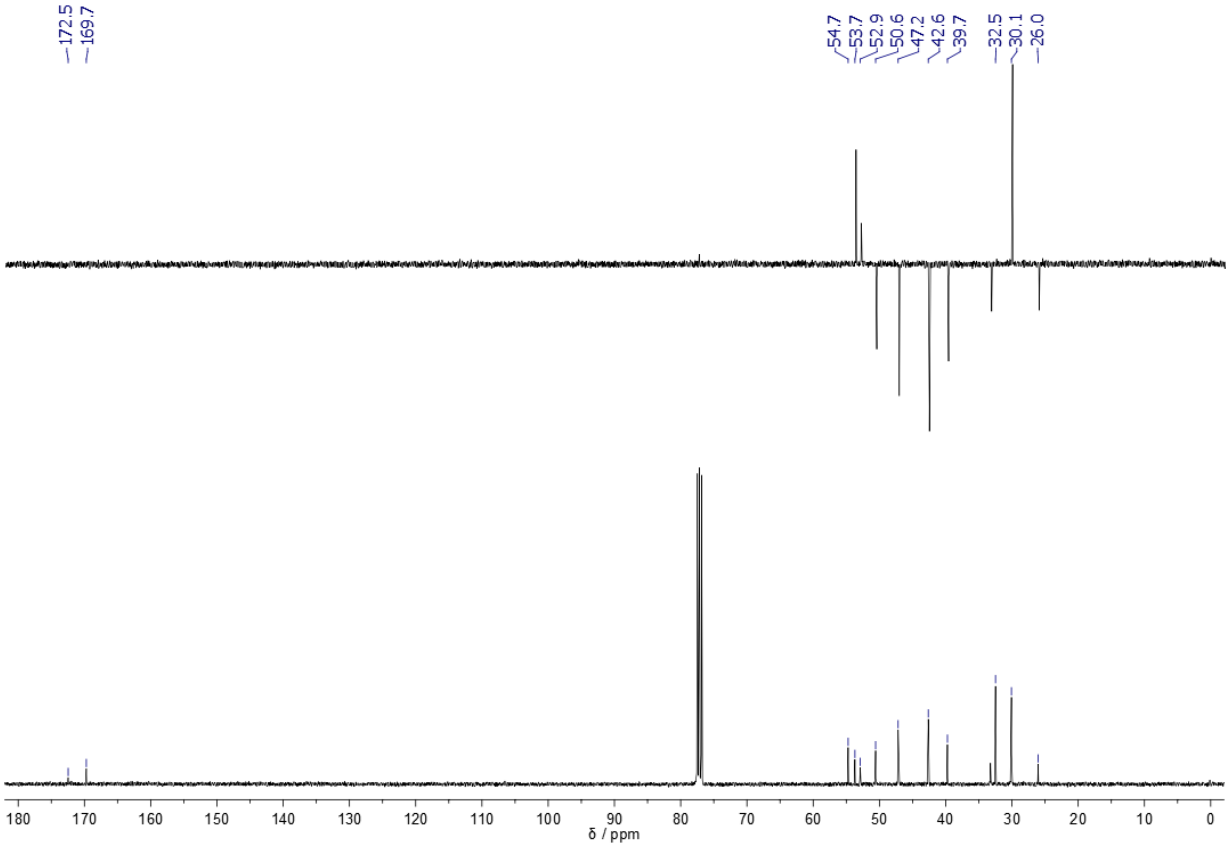

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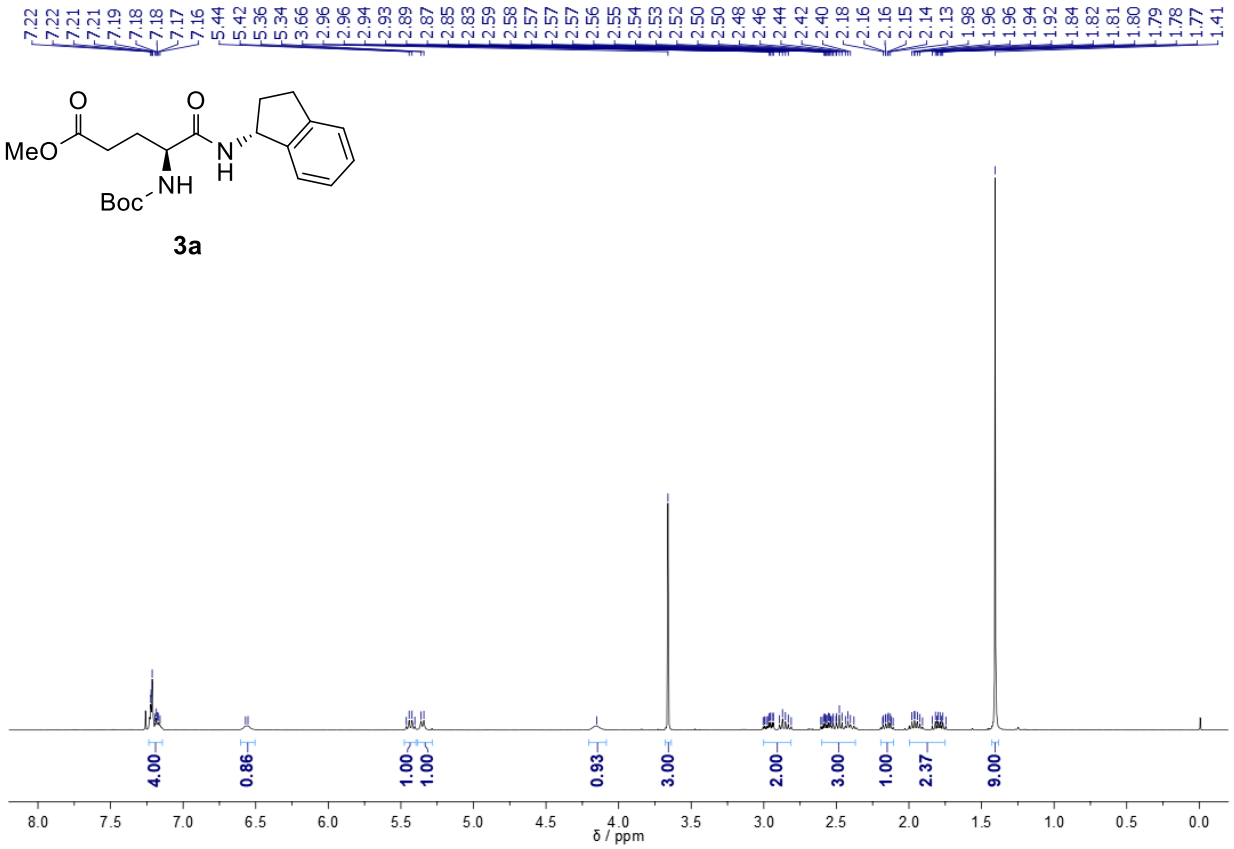


Figure S13. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **3a**.

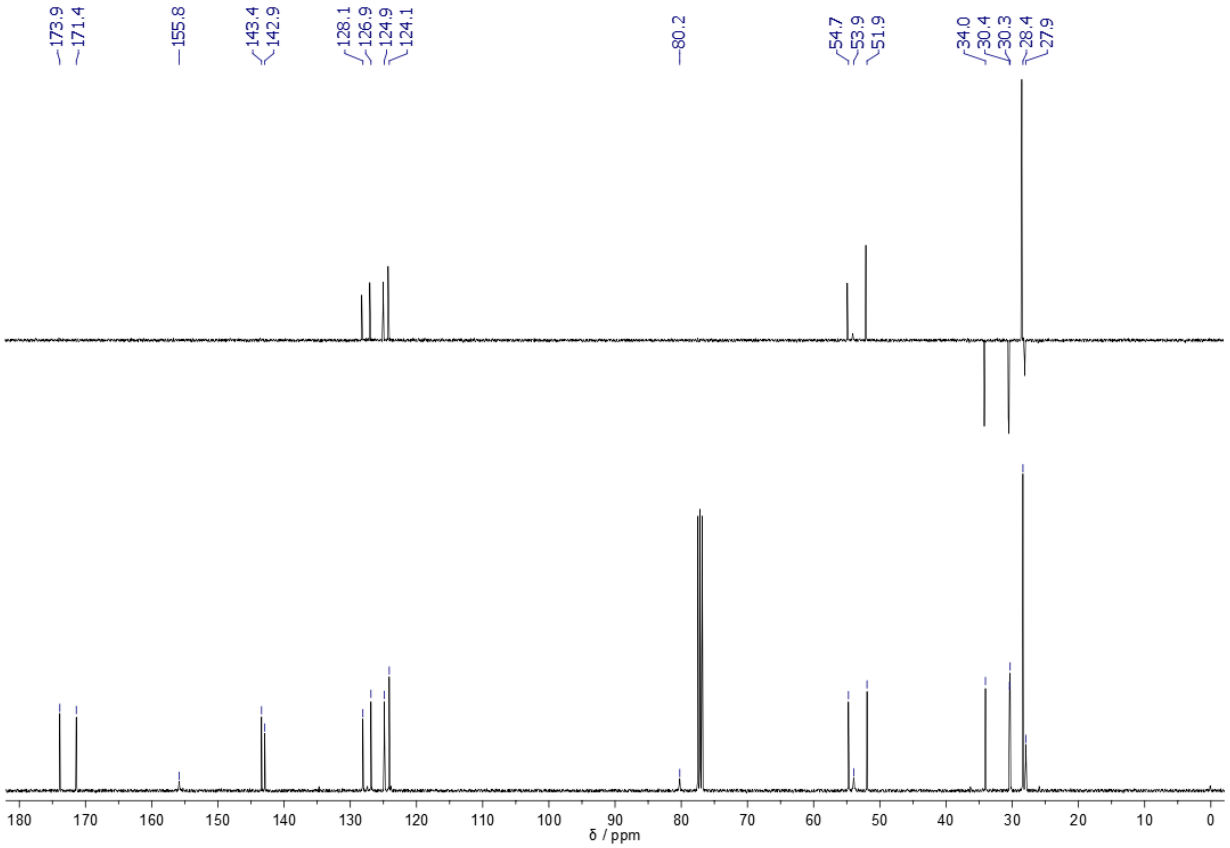


Figure S14. ^{13}C-NMR and DEPT-135 spectra (101 MHz, $CDCl_3$) of compound **3a**.

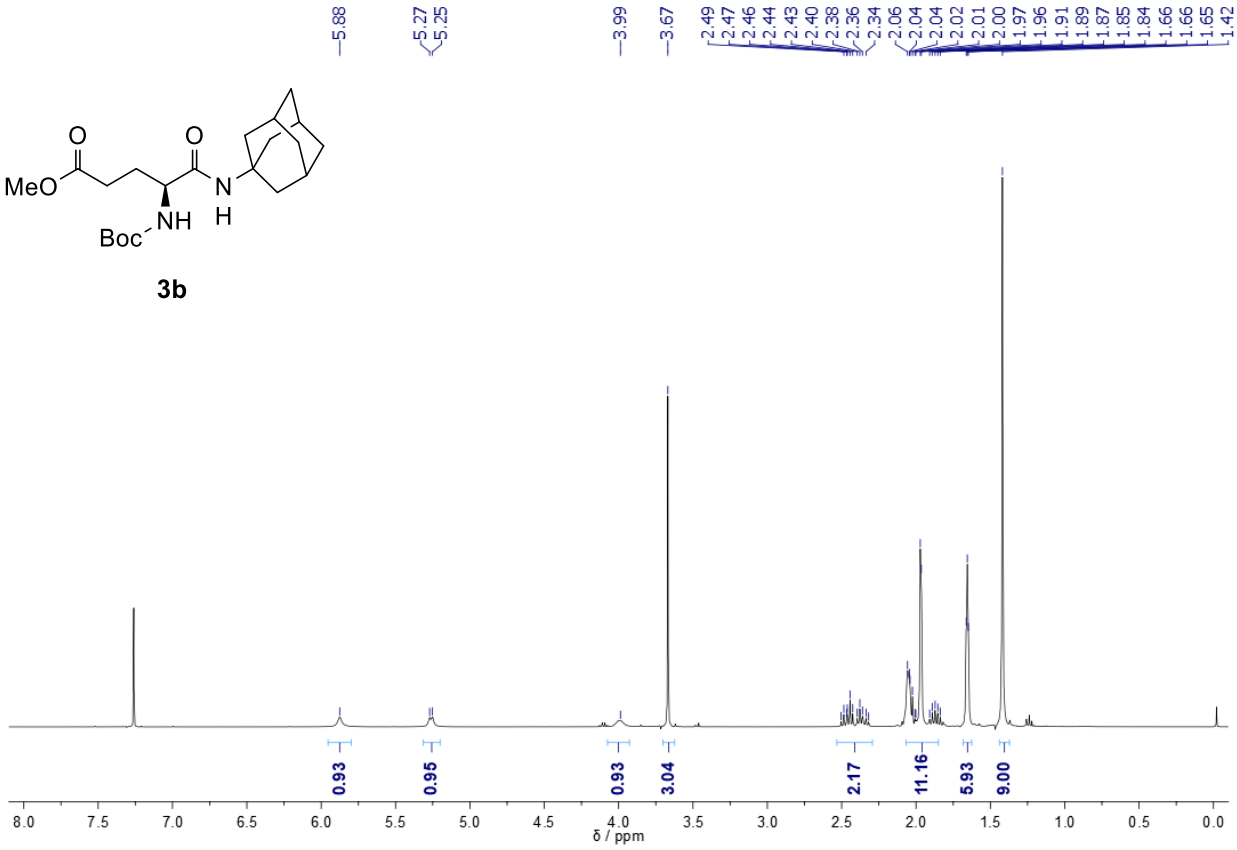
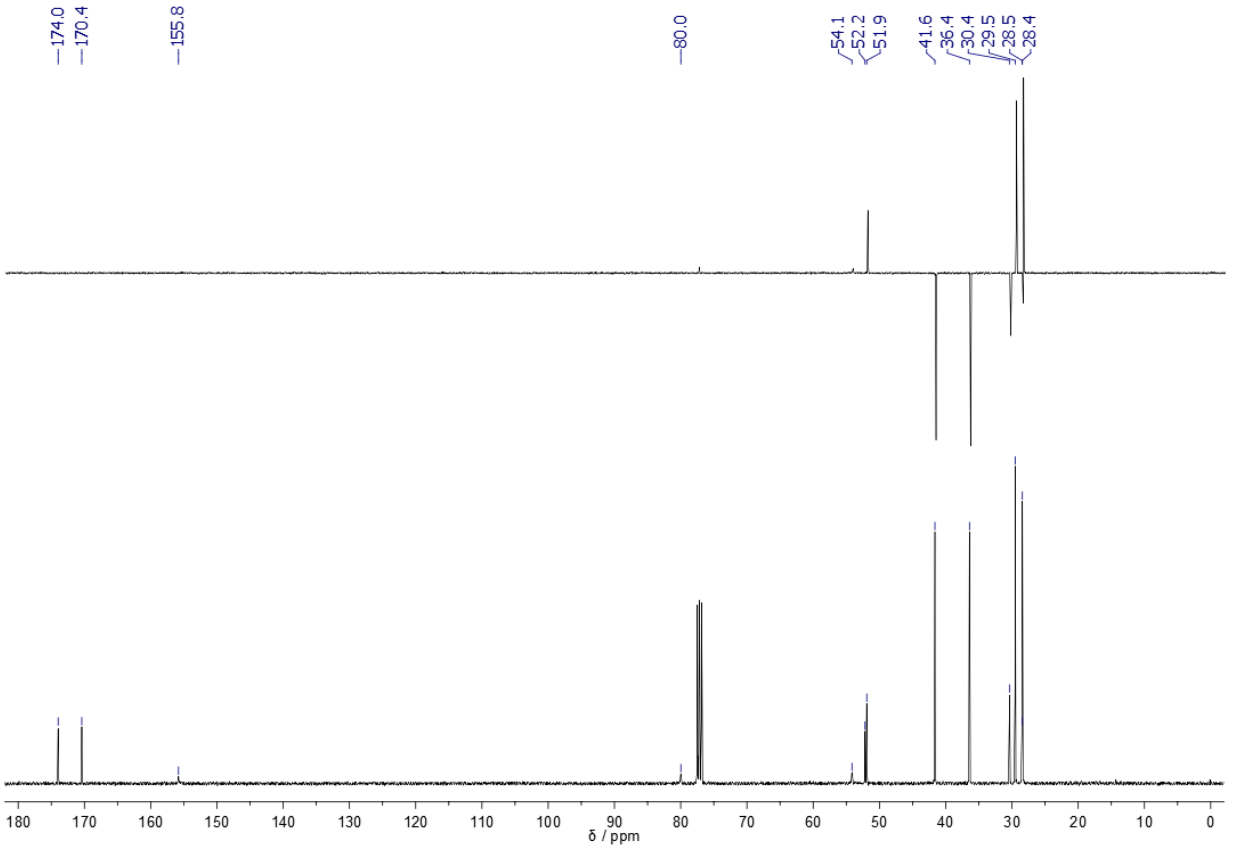


Figure S15. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **3b**.



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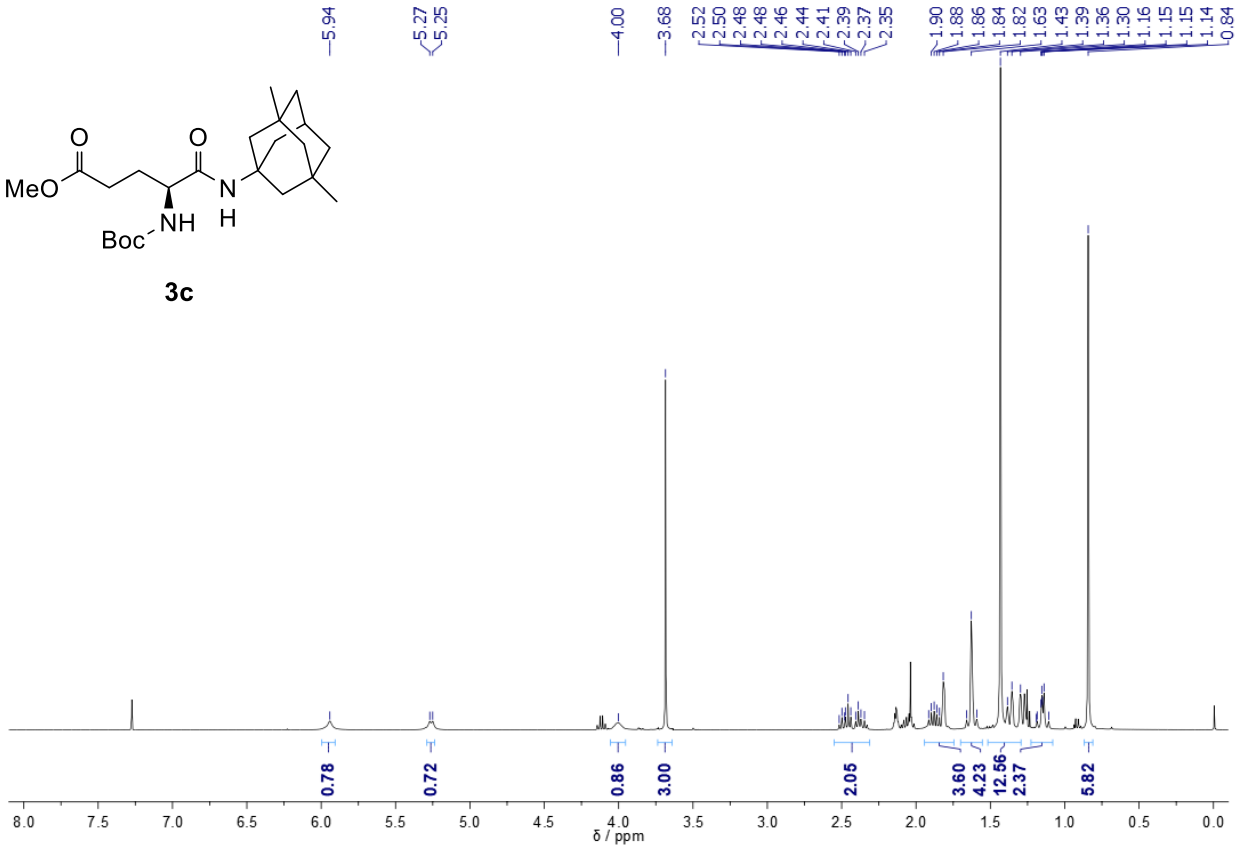


Figure S17. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **3c**.

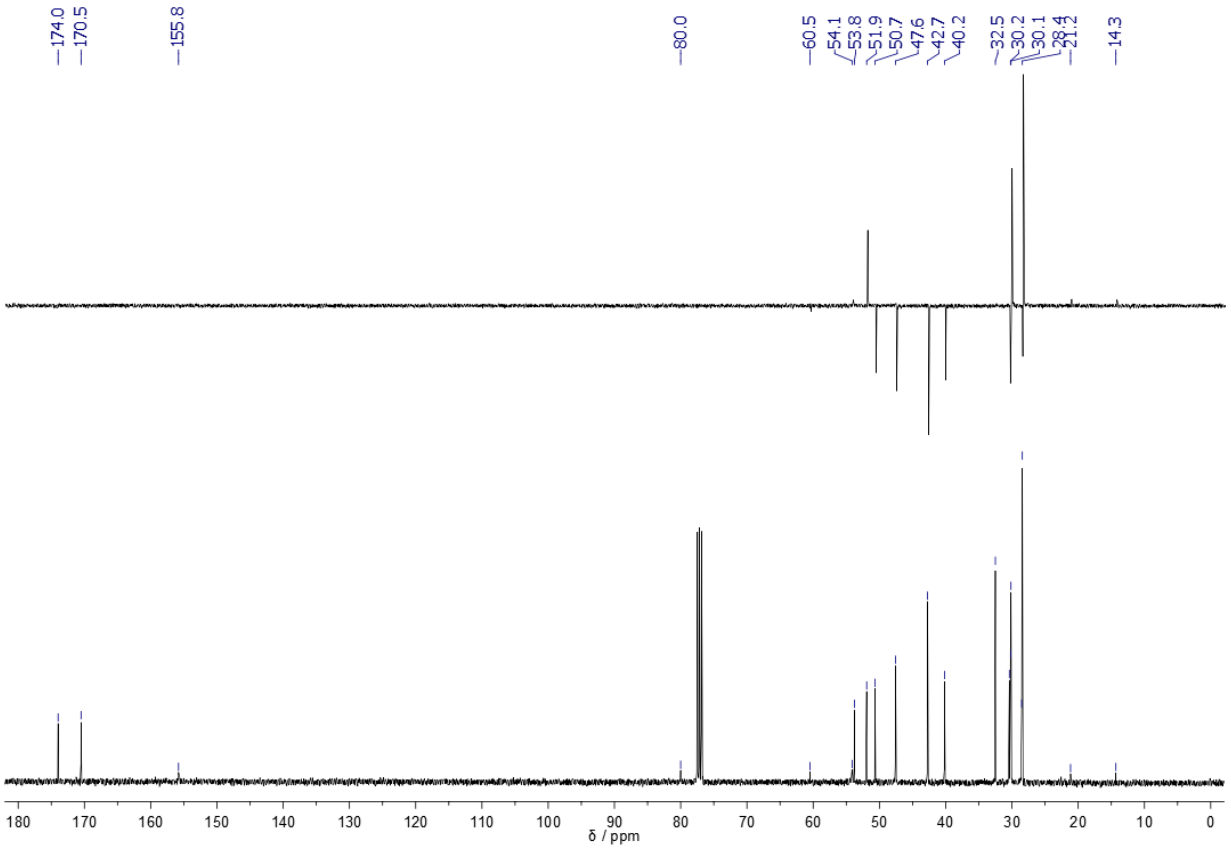


Figure S18. ^{13}C-NMR and DEPT-135 spectra (101 MHz, $CDCl_3$) of compound **3c**.

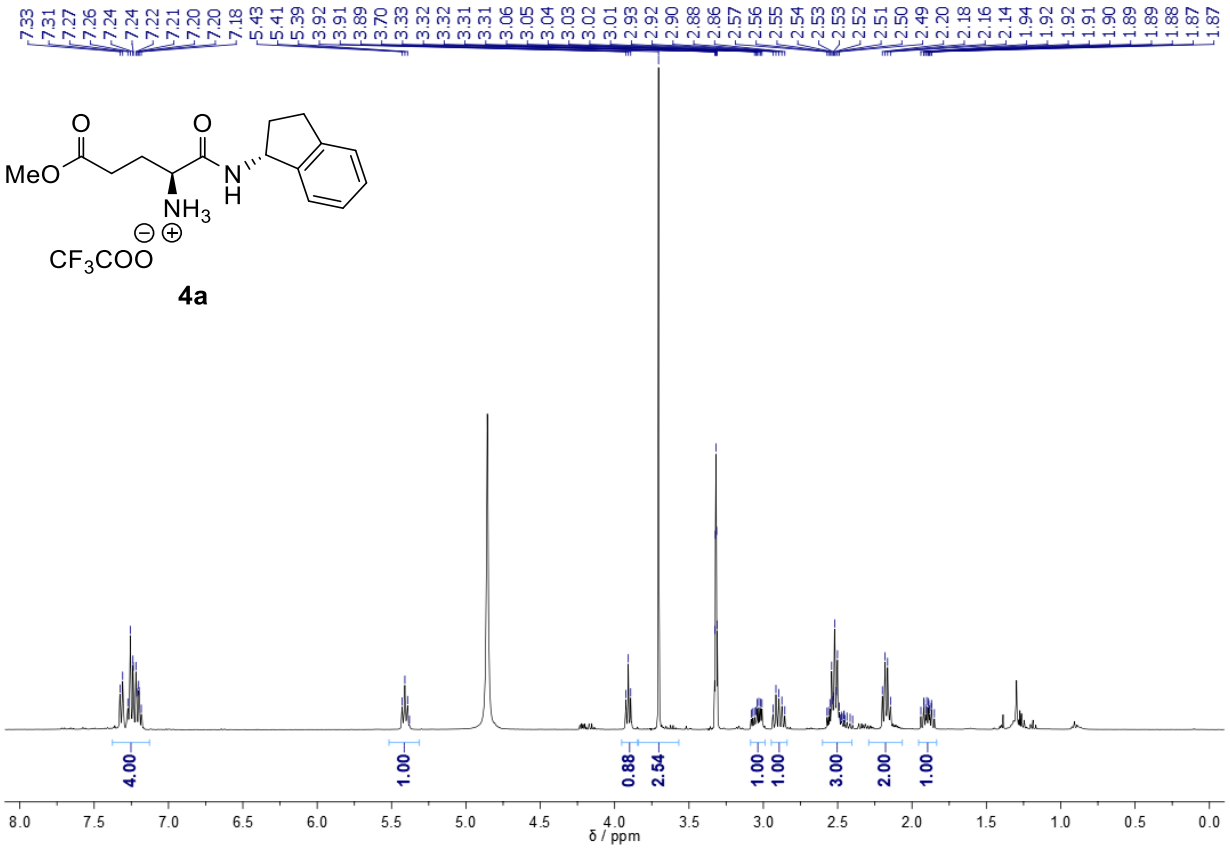


Figure S19. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **4a**.

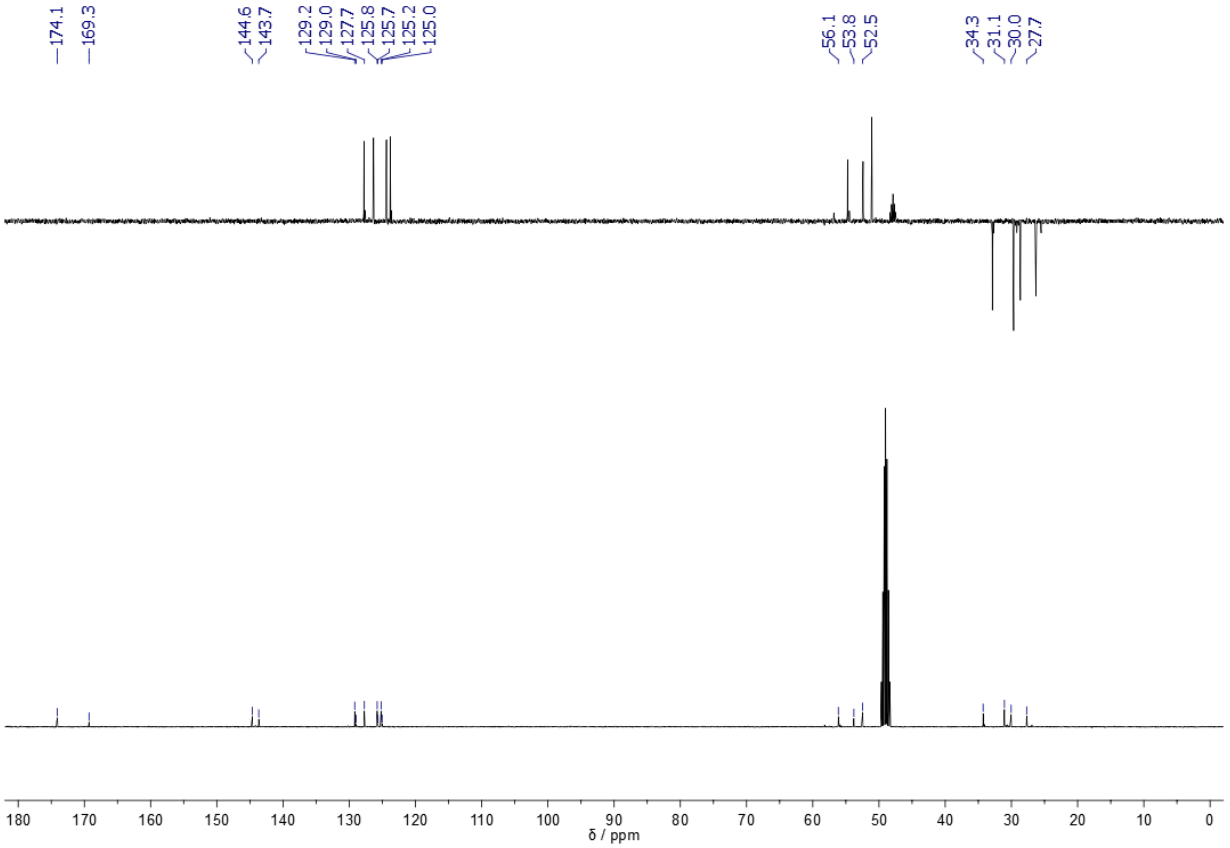


Figure S20. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **4a**.

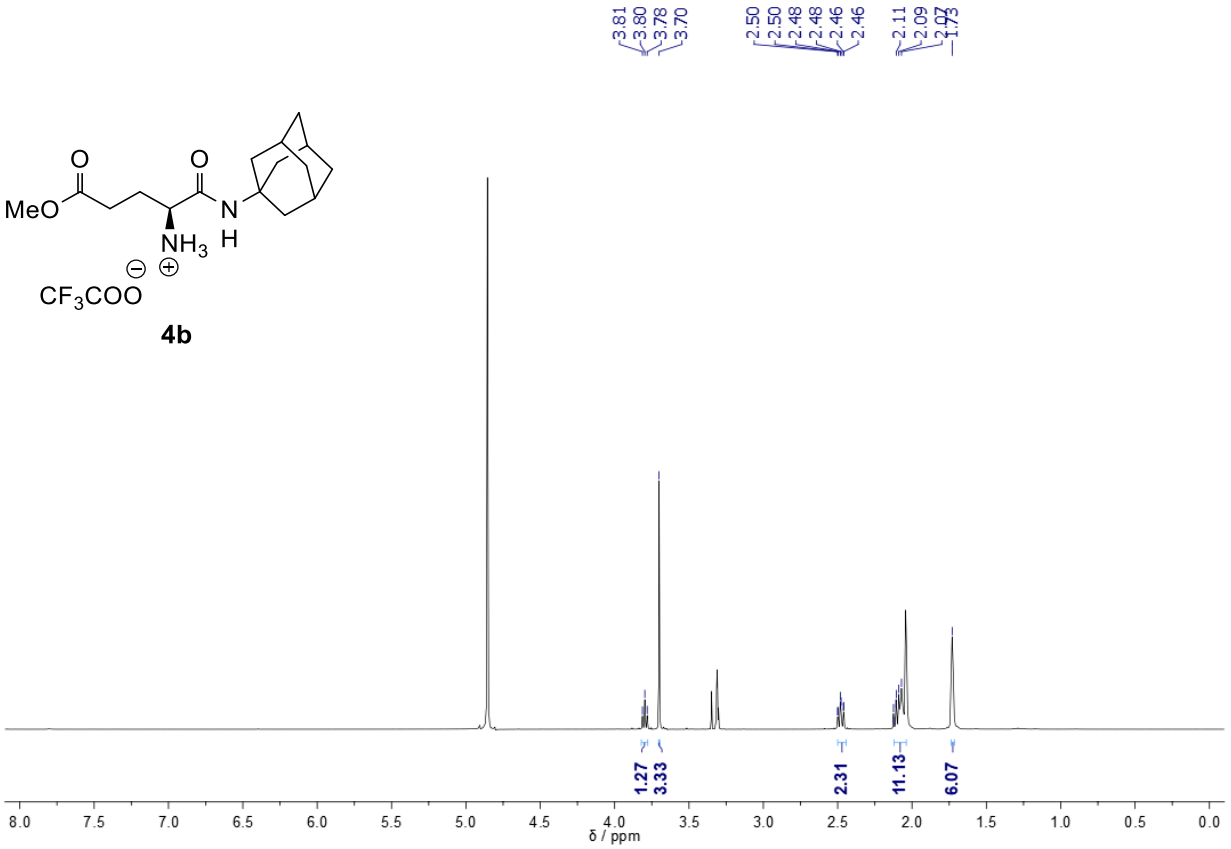
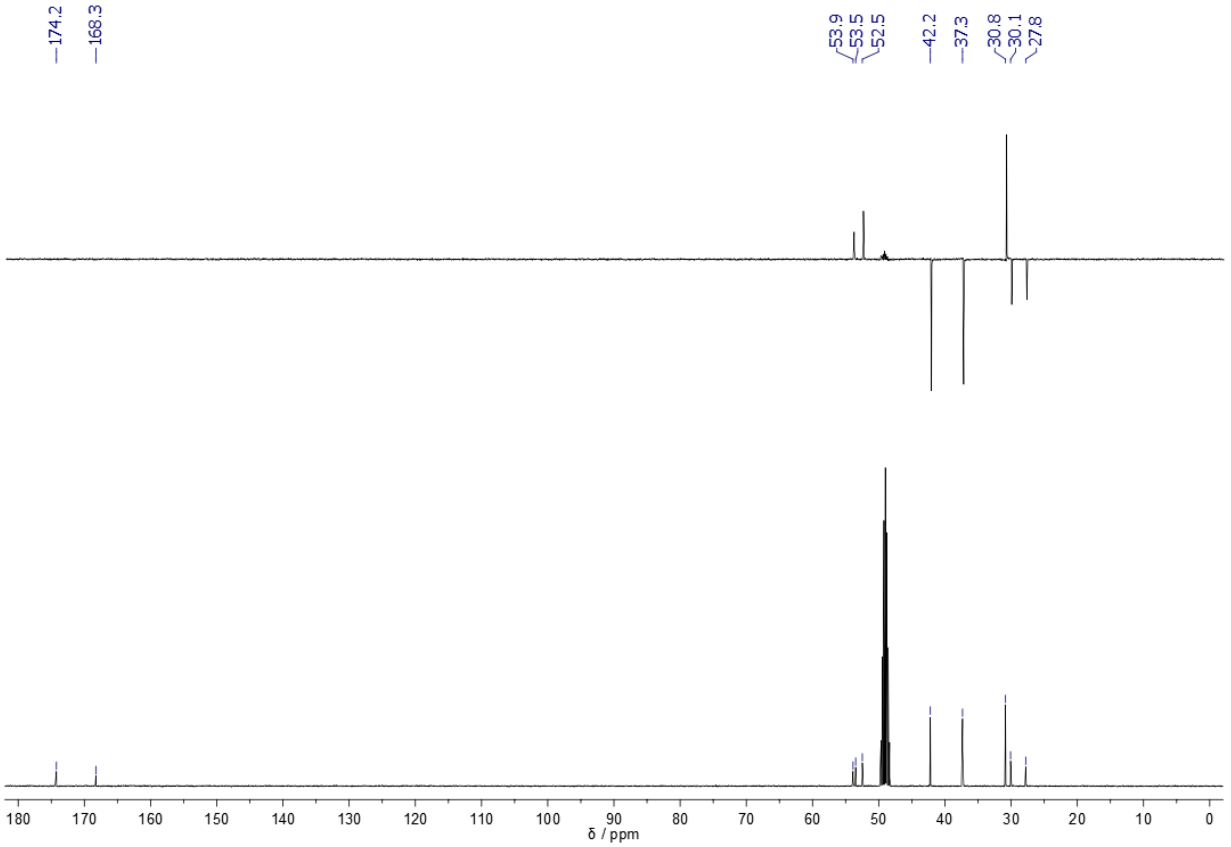


Figure S21. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **4b**.



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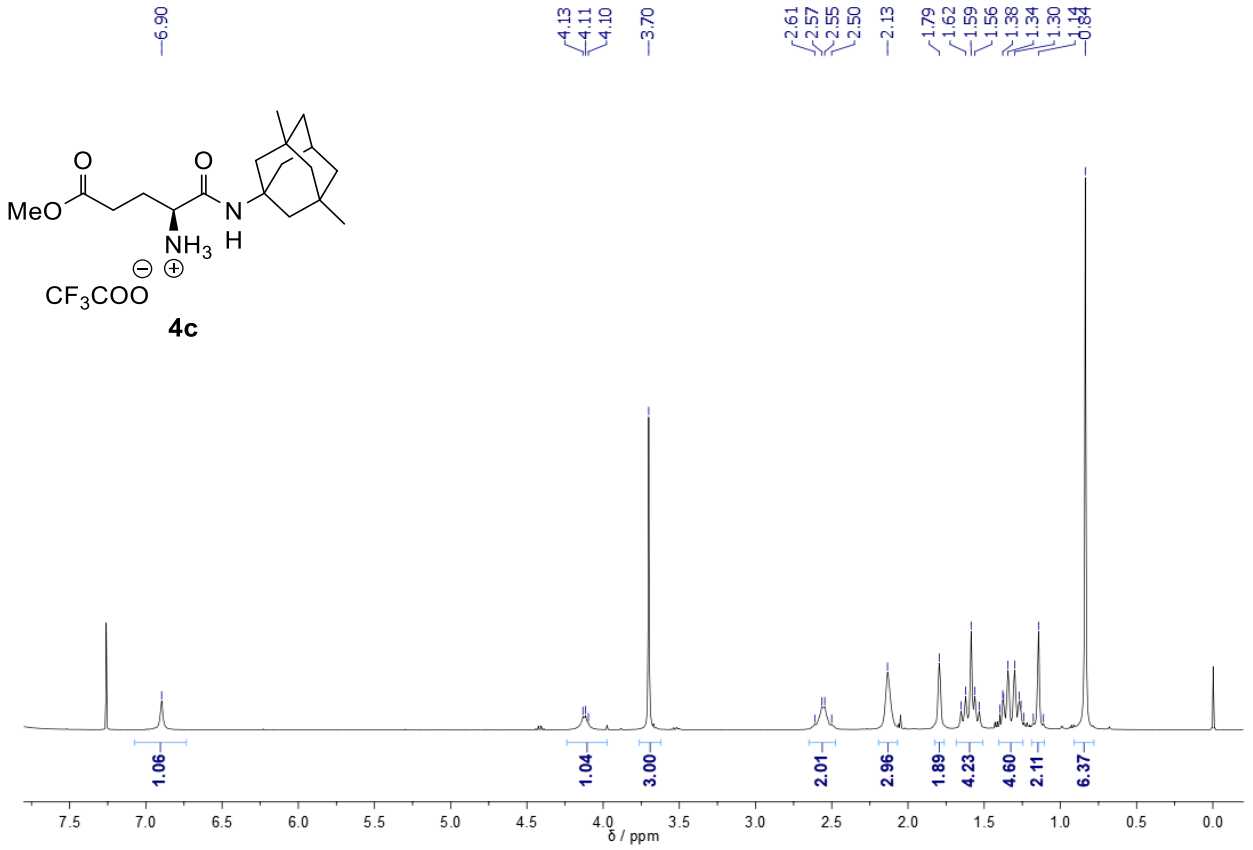


Figure S23. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **4c**.

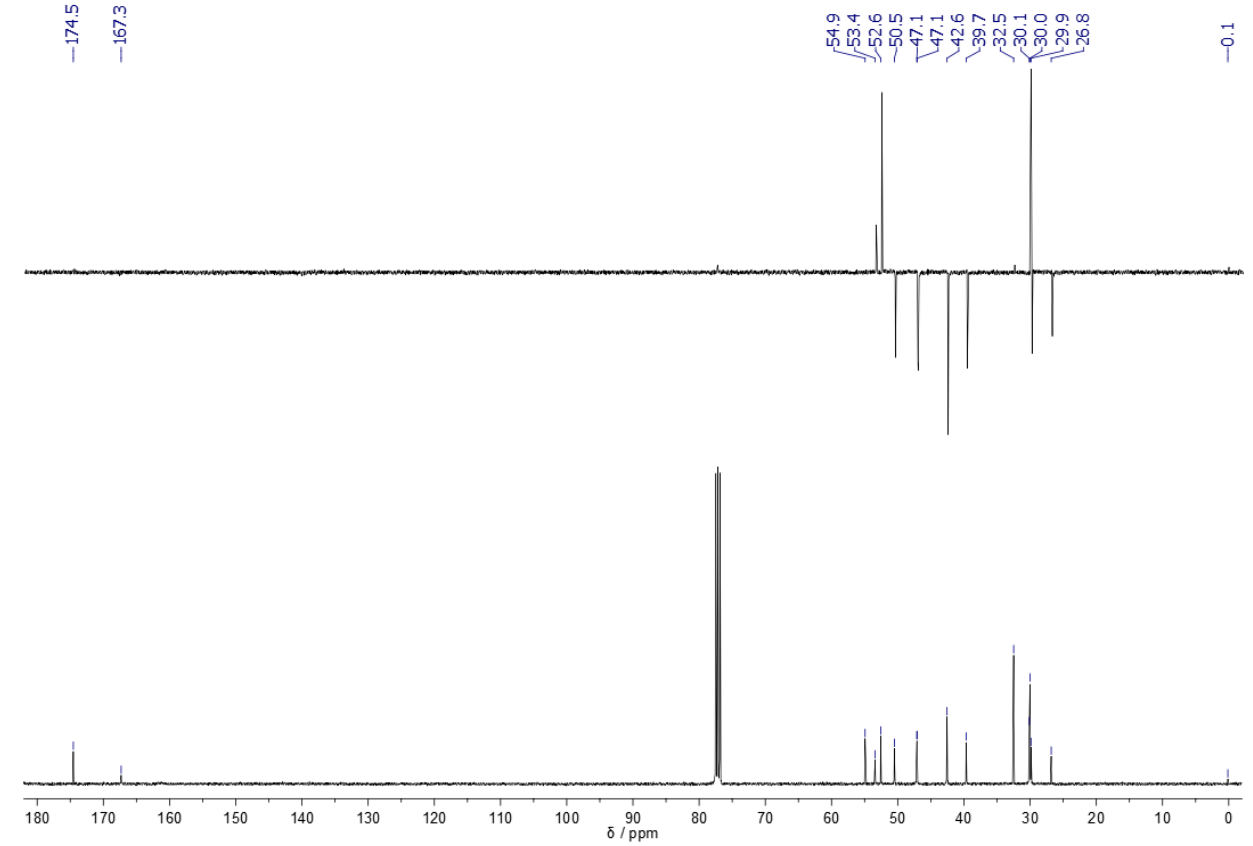


Figure S24. ^{13}C-NMR and DEPT-135 spectra (101 MHz, $CDCl_3$) of compound **4c**.

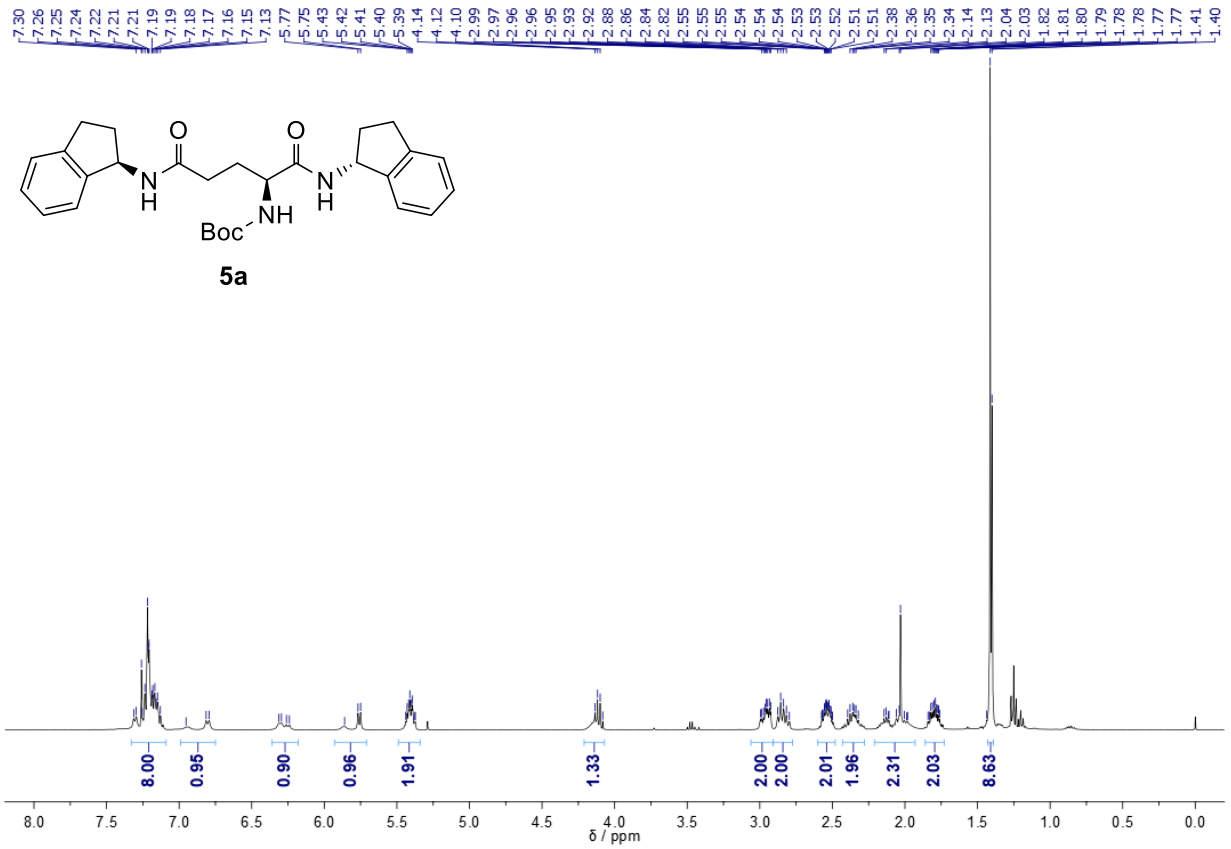


Figure S25. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **5a**.

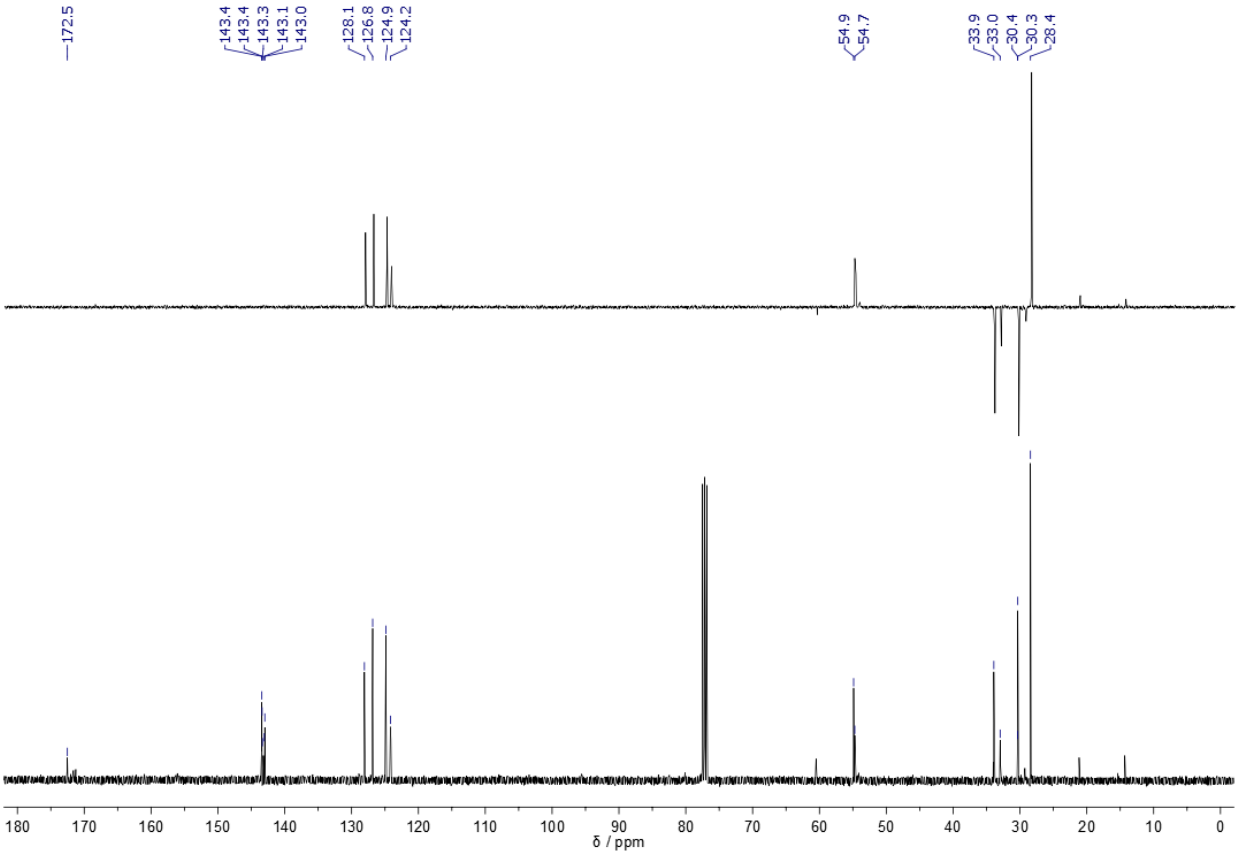


Figure S26. ^{13}C-NMR and DEPT-135 spectra (101 MHz, $CDCl_3$) of compound **5a**.

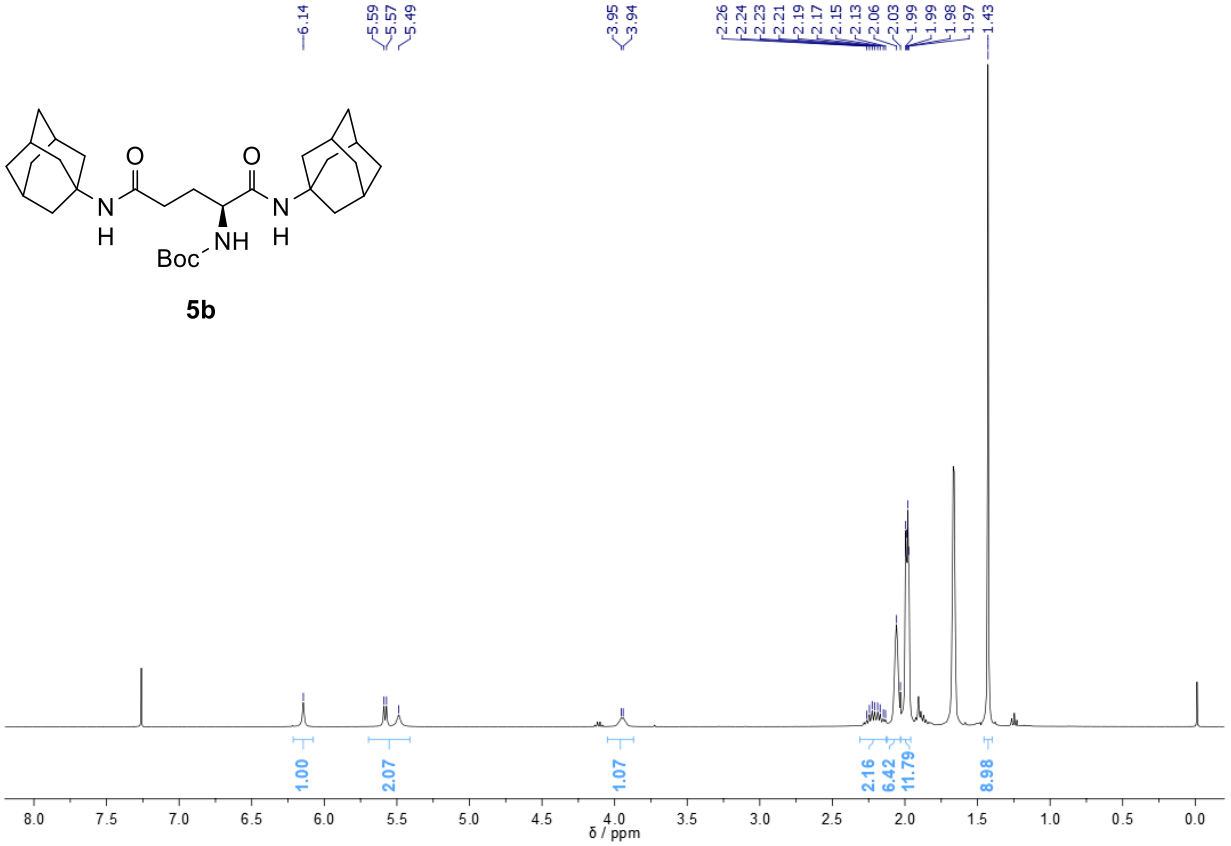


Figure S27. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **5b**.

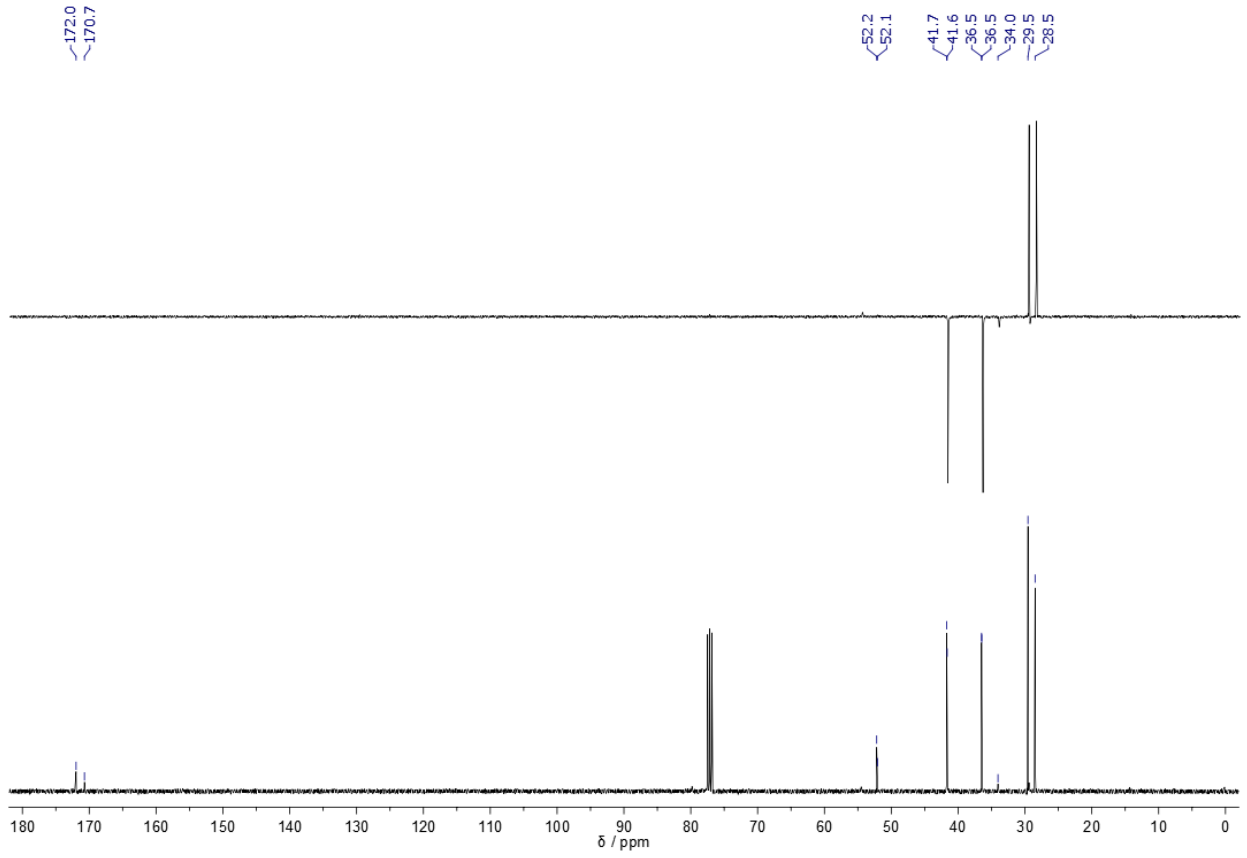
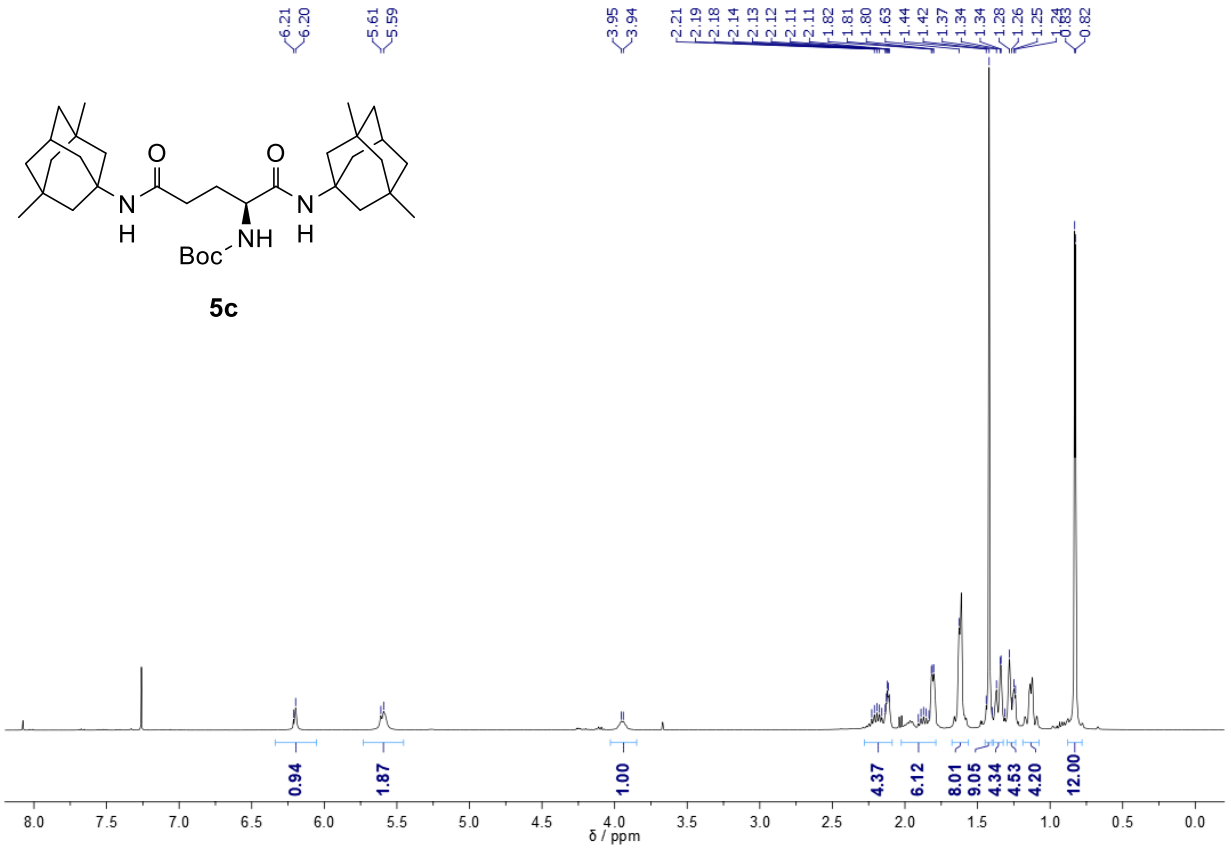


Figure S28. ^{13}C-NMR and DEPT-135 spectra (101 MHz, $CDCl_3$) of compound **5b**.



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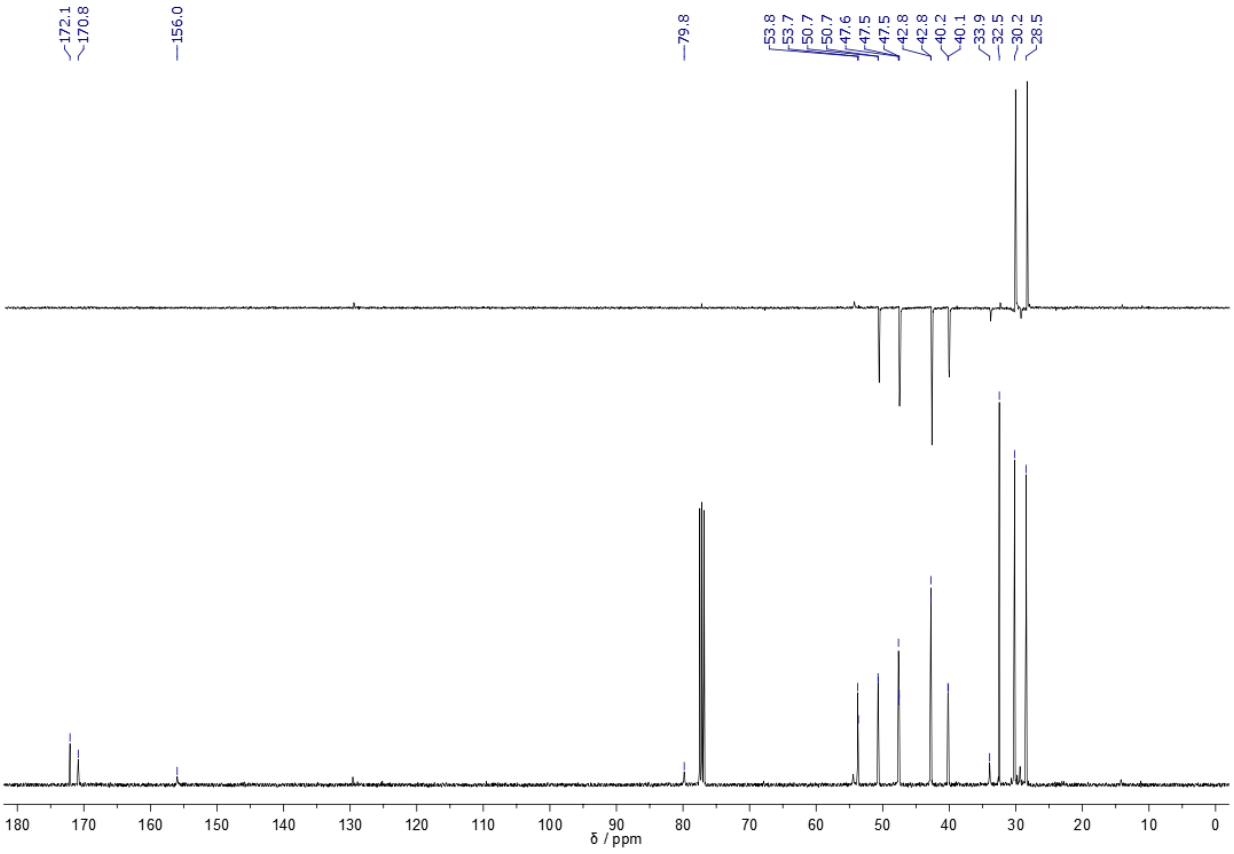

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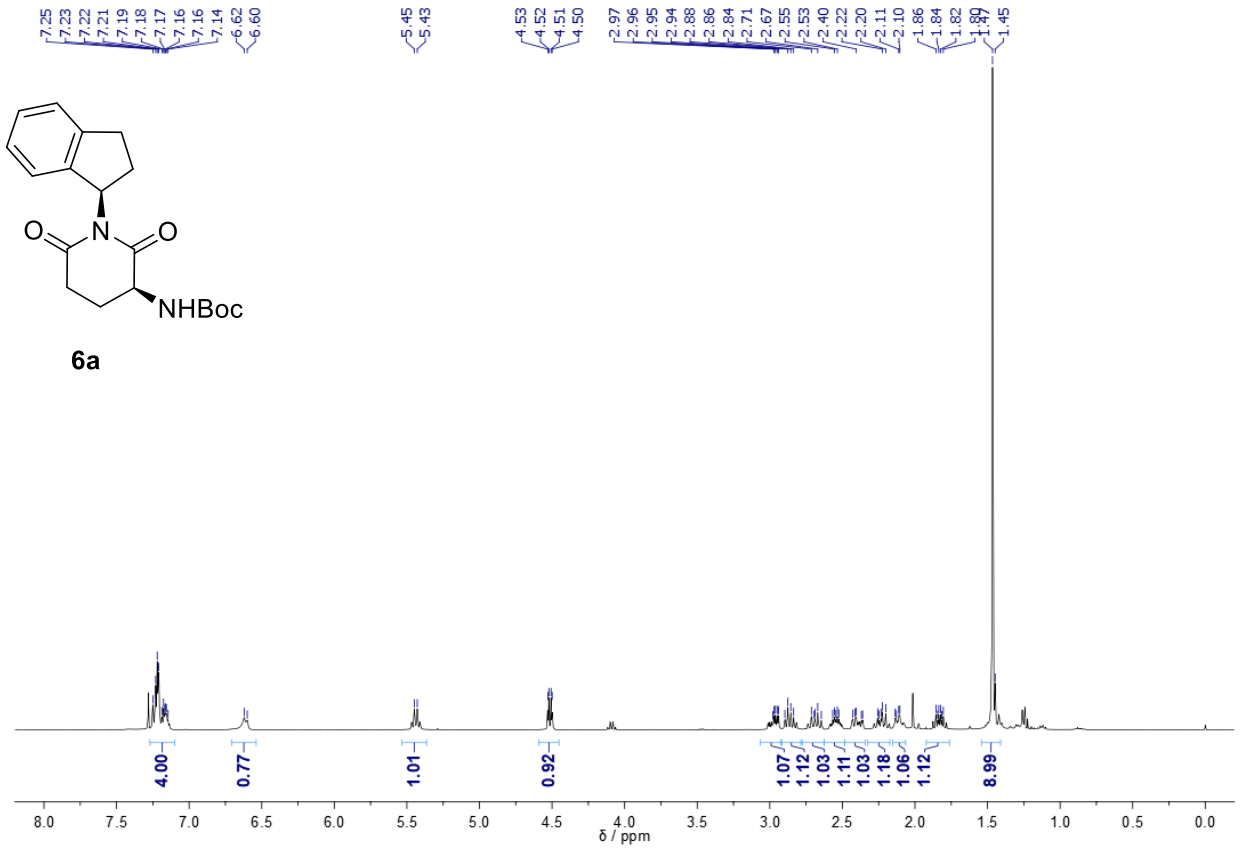

Figure S31. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **6a**.

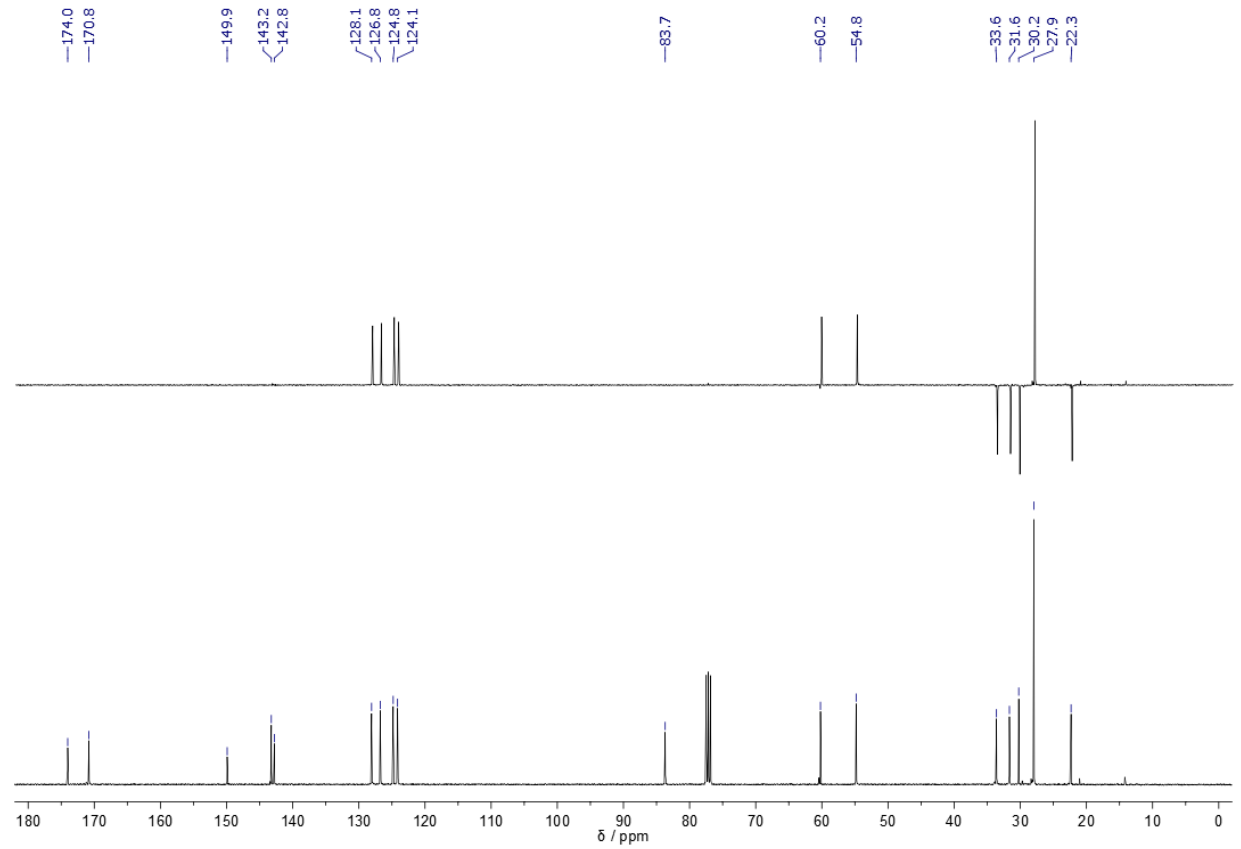

Figure S32. ^{13}C-NMR and DEPT-135 spectra (101 MHz, $CDCl_3$) of compound **6a**.

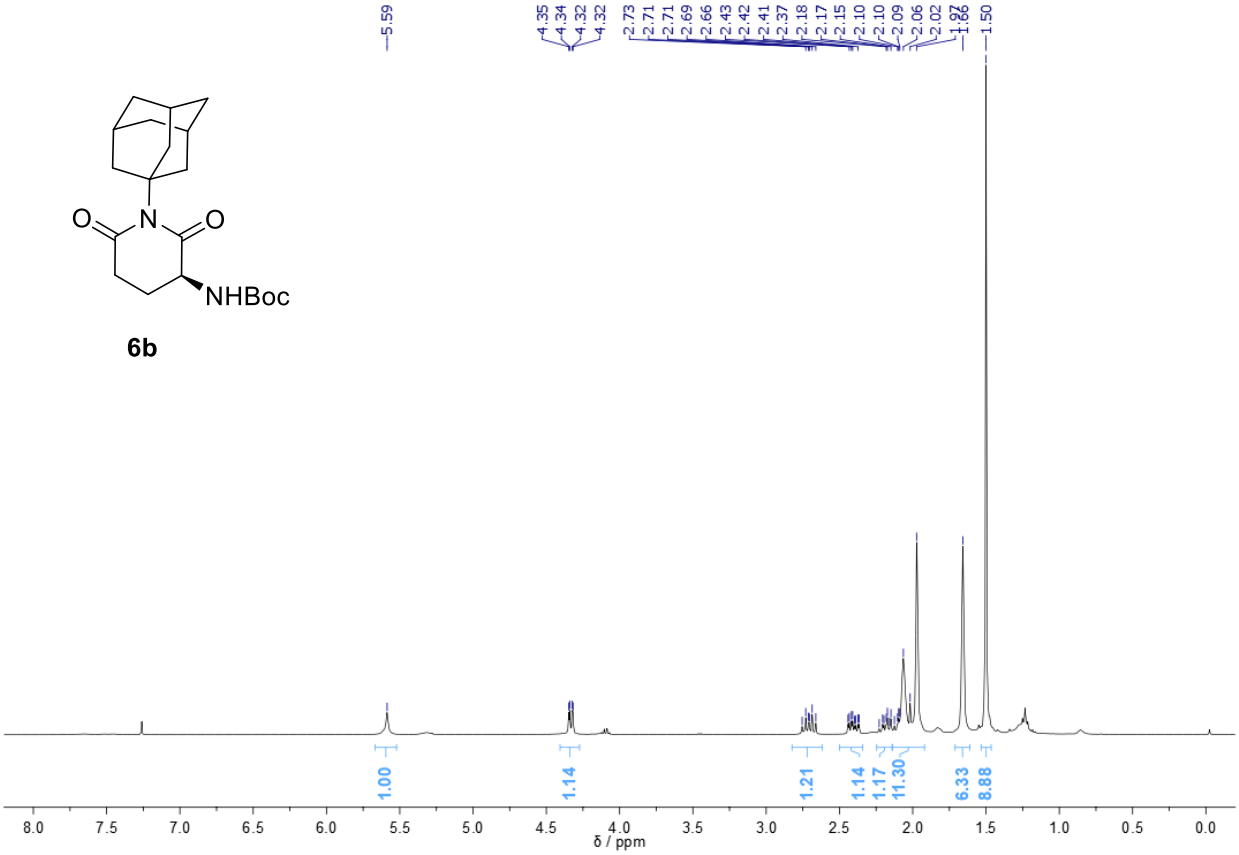

Figure S33. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **6b**.

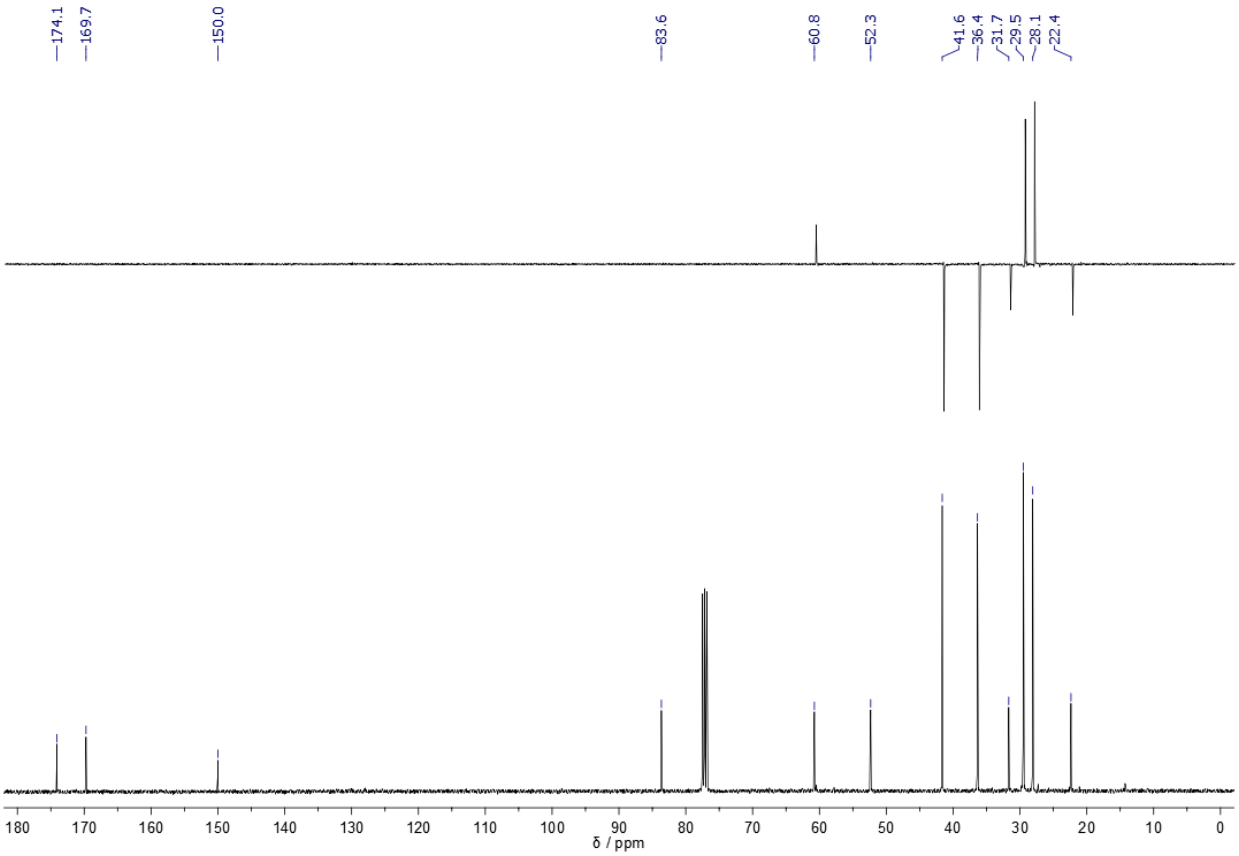

Figure S34. ^{13}C-NMR and DEPT-135 spectra (101 MHz, $CDCl_3$) of compound **6b**.

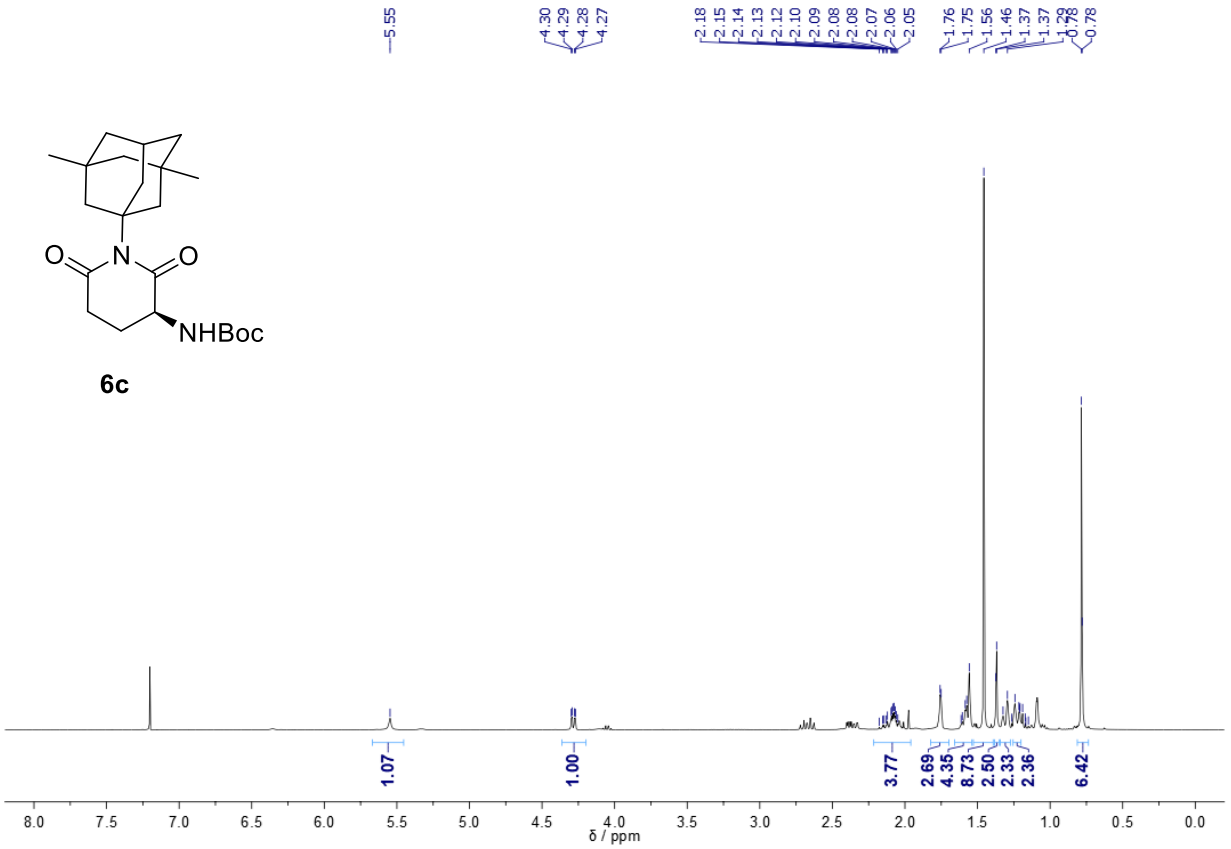

Figure S35. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **6c**.

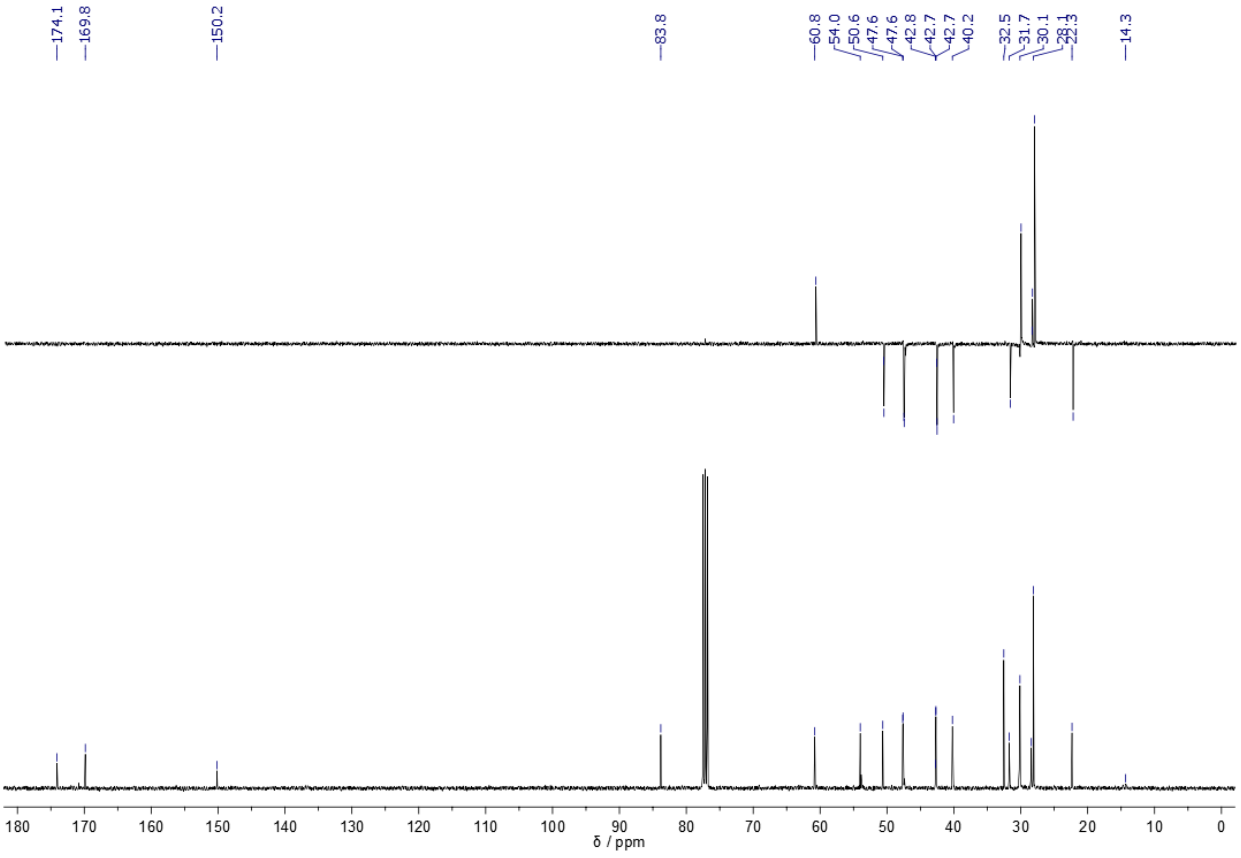

Figure S36. ^{13}C-NMR and DEPT-135 spectra (101 MHz, $CDCl_3$) of compound **6c**.

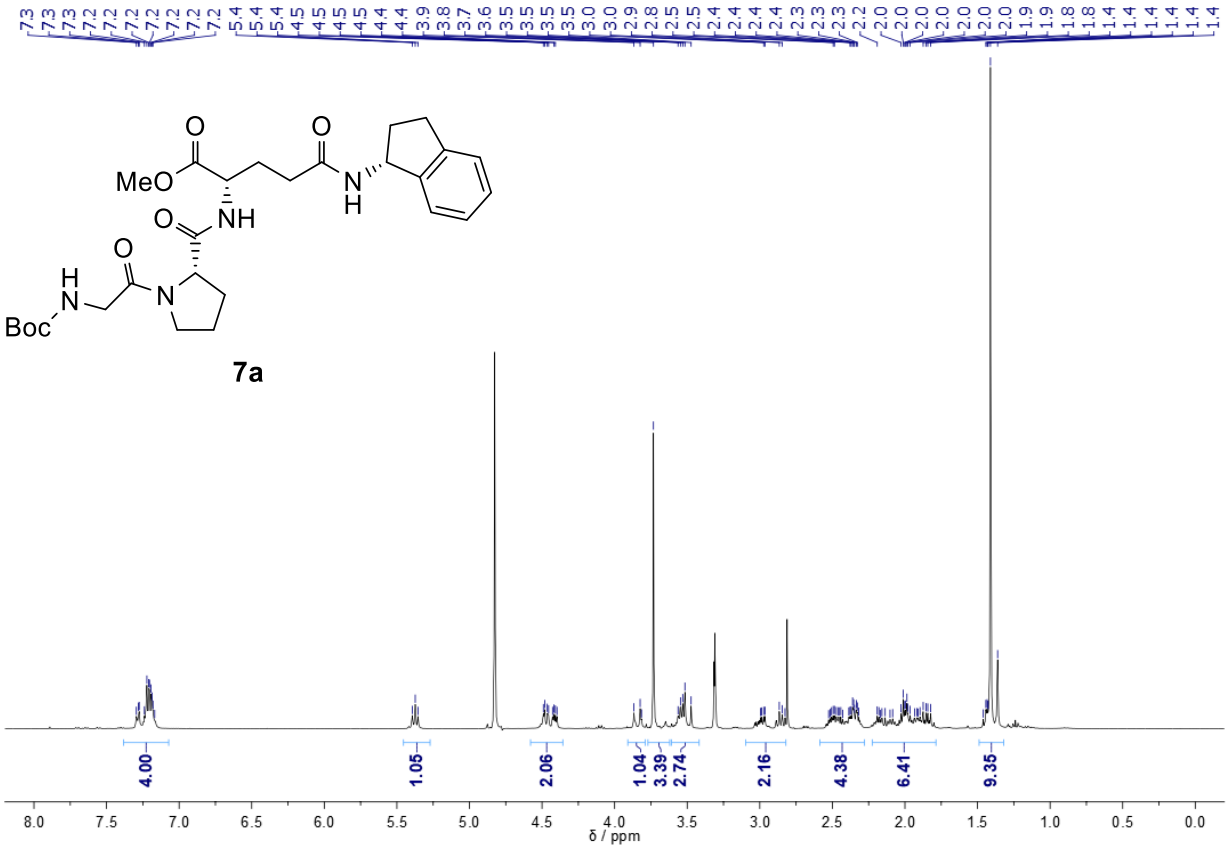

Figure S37. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **7a**.

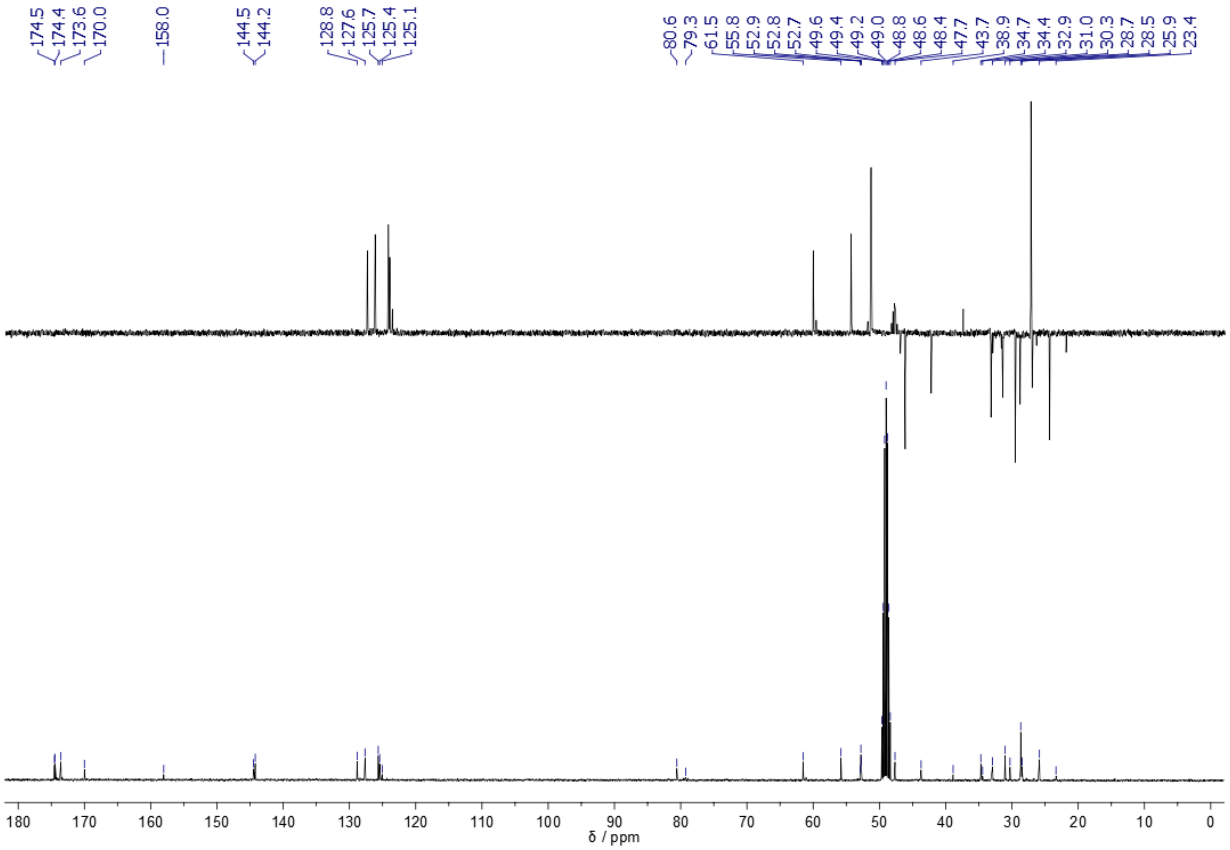

Figure S38. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **7a**.

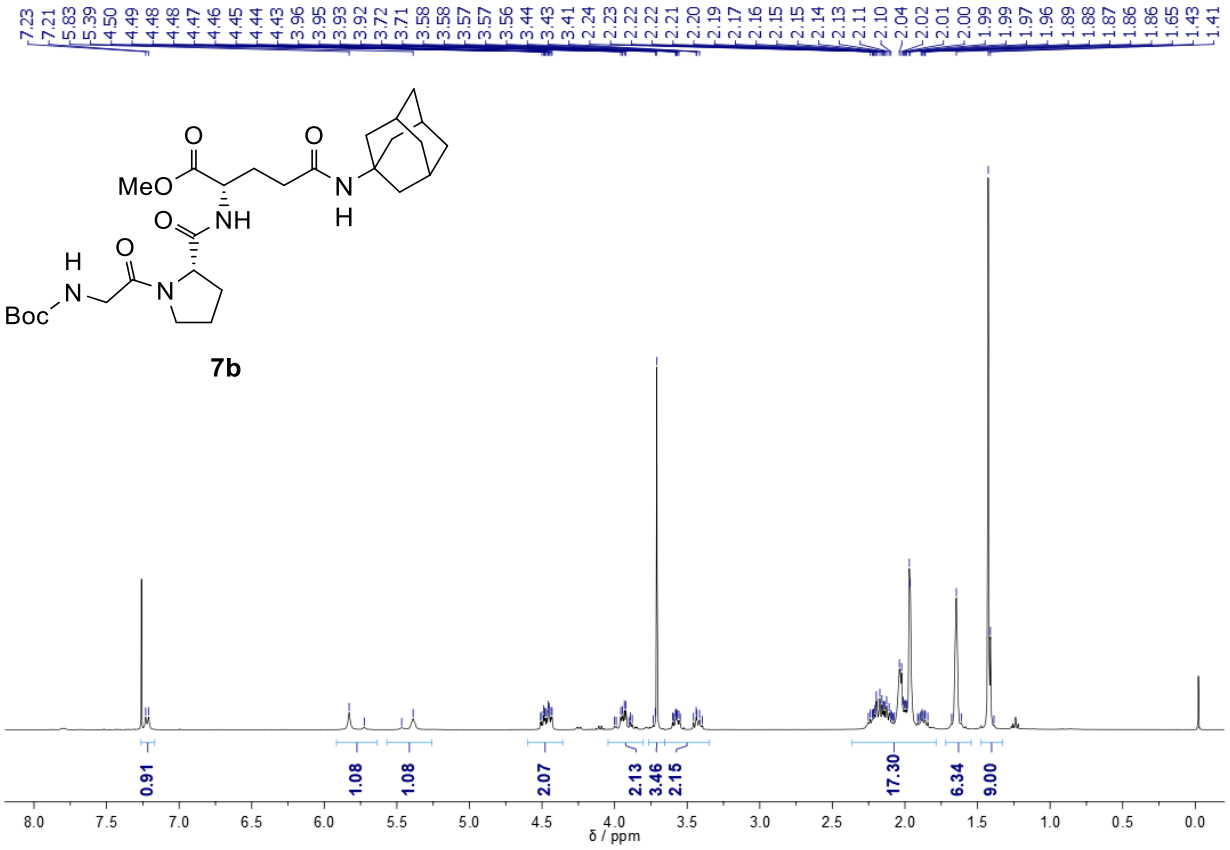

Figure S39. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **7b**.

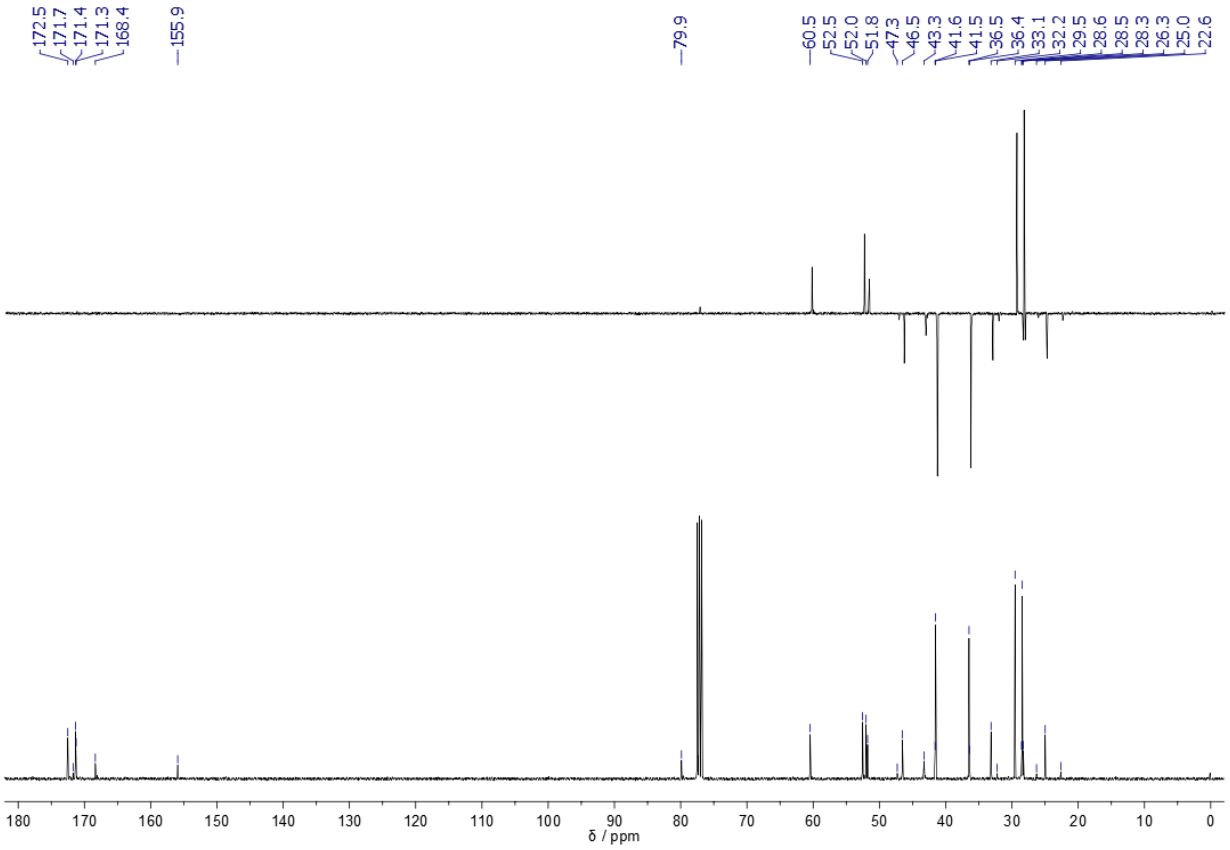

Figure S40. ^{13}C-NMR and DEPT-135 spectra (101 MHz, $CDCl_3$) of compound **7b**.

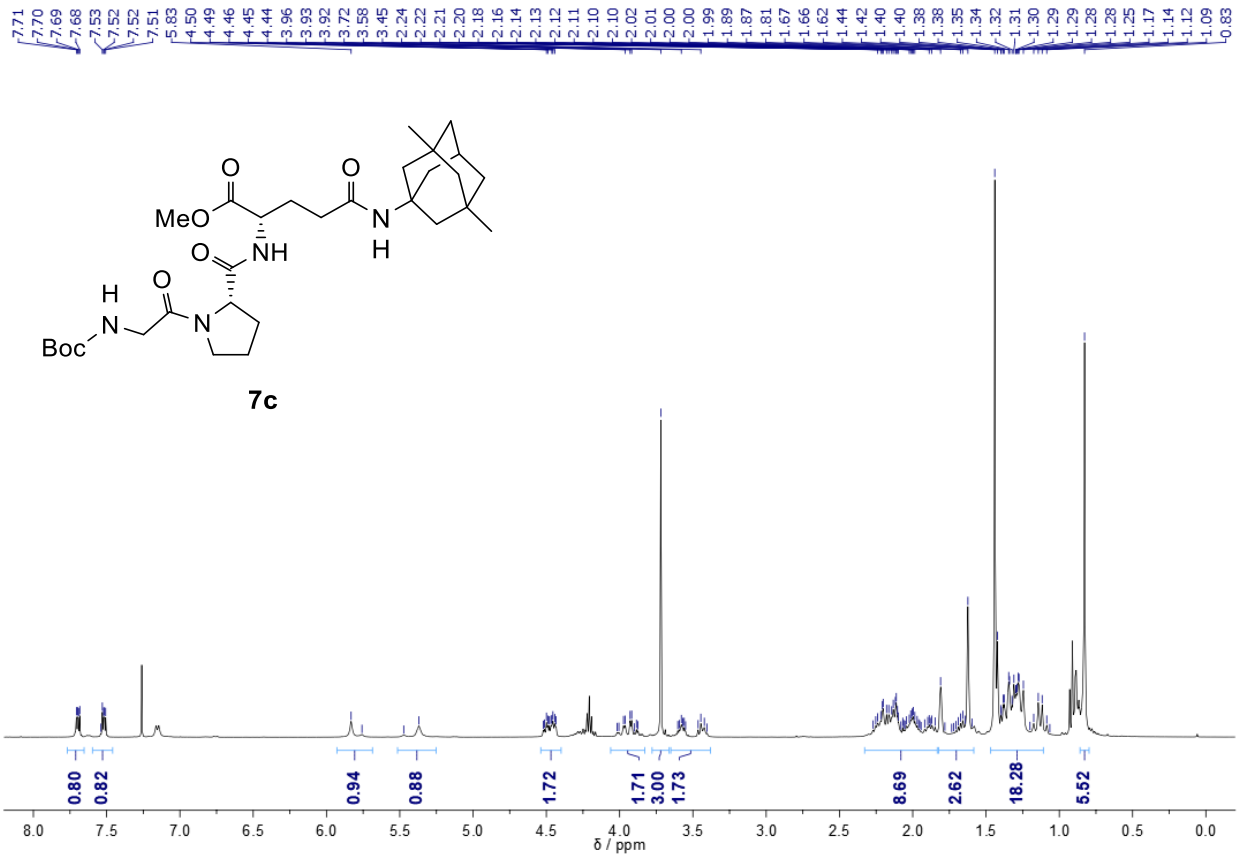

Figure S41. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **7c**.

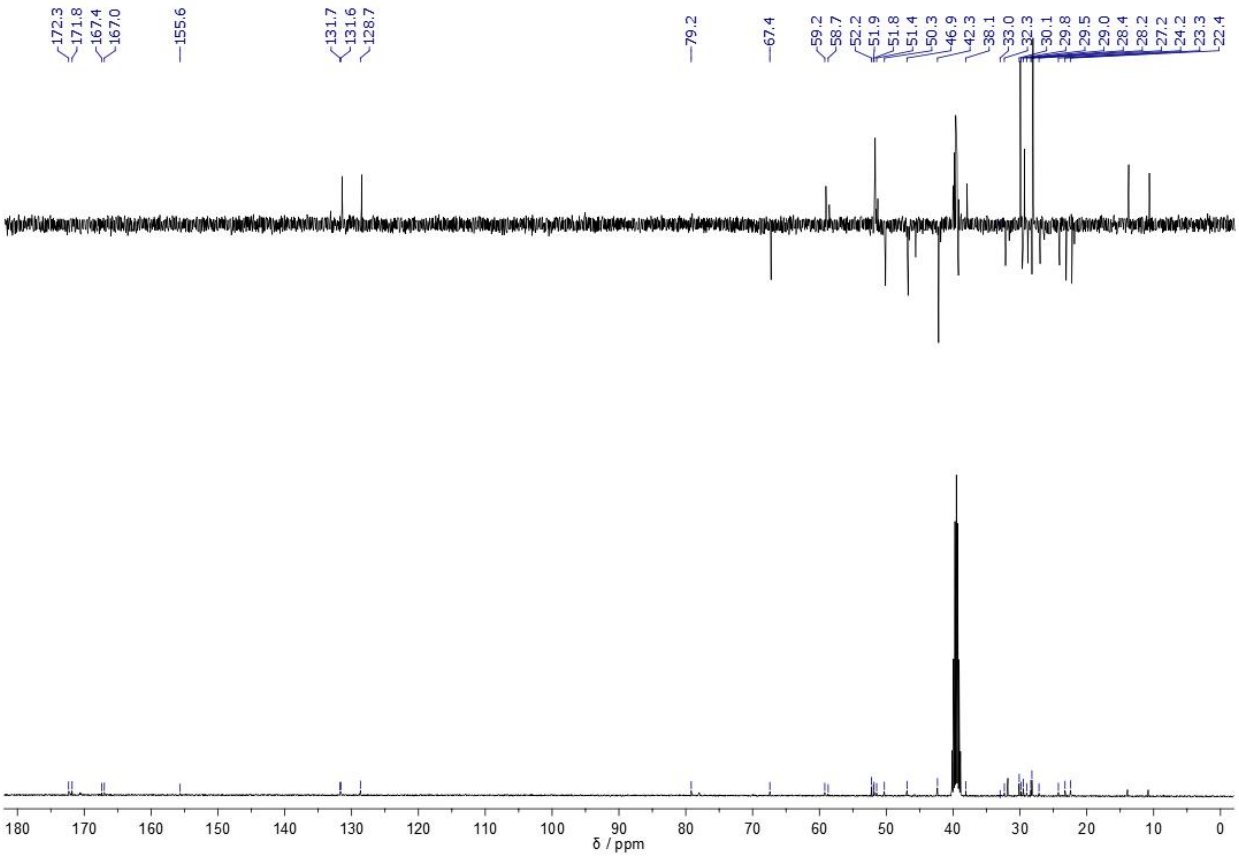

Figure S42. ^{13}C-NMR and DEPT-135 spectra (101 MHz, $CDCl_3$) of compound **7c**.

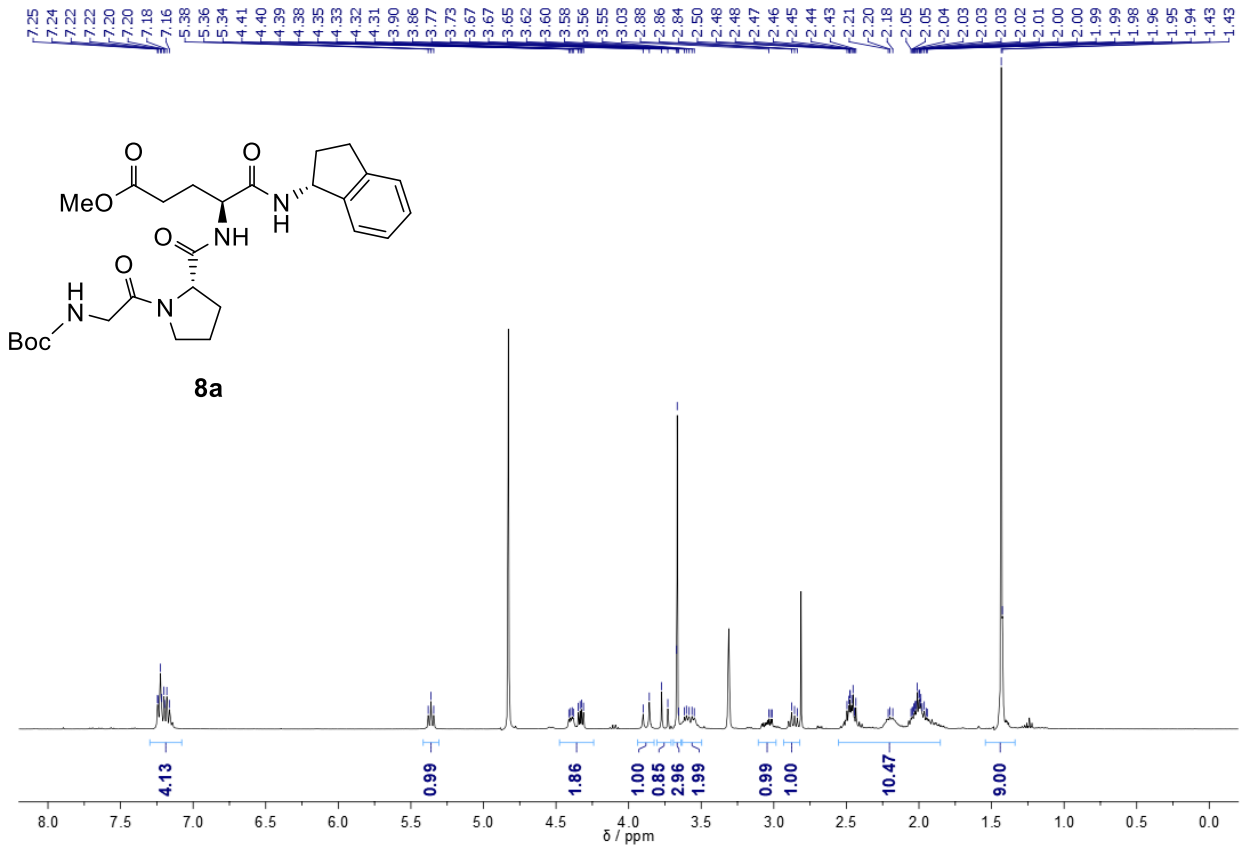

Figure S43. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **8a**.

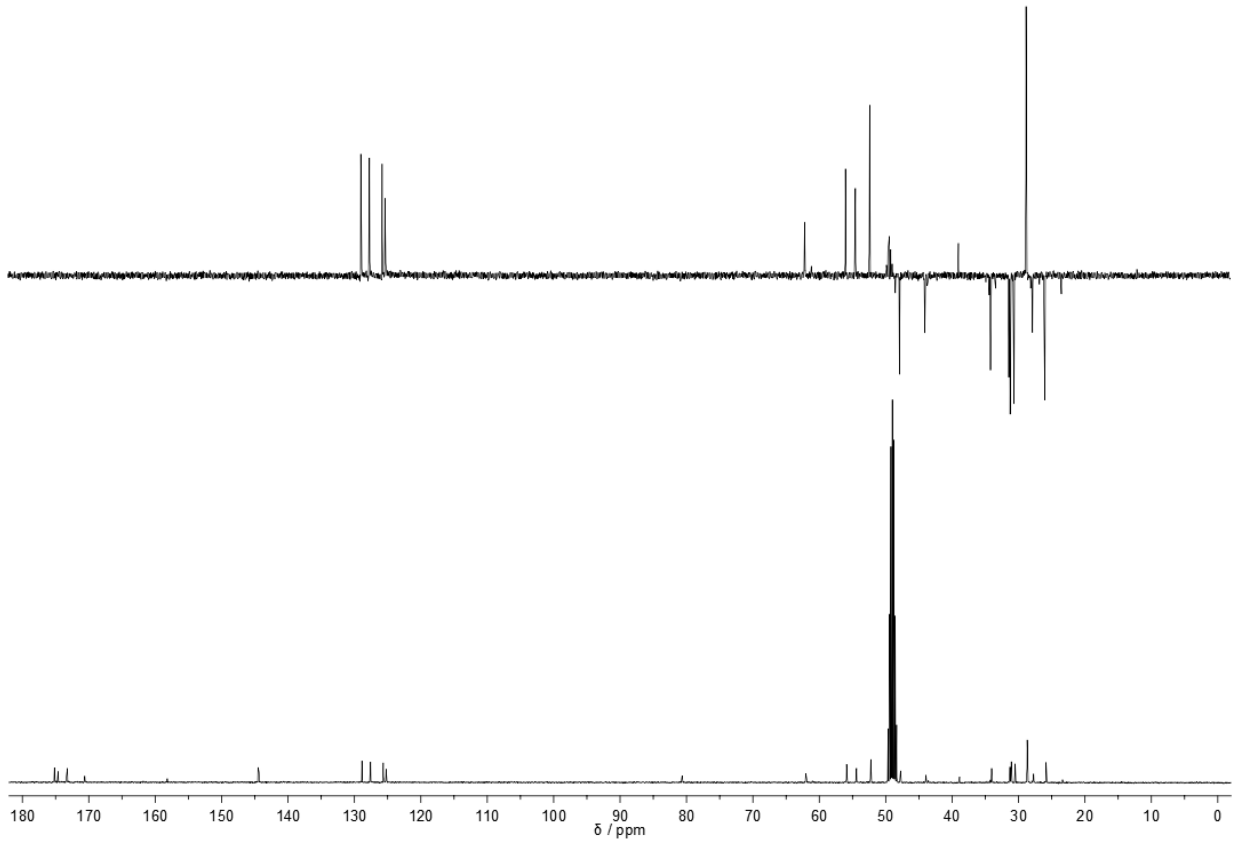

Figure S44. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **8a**.

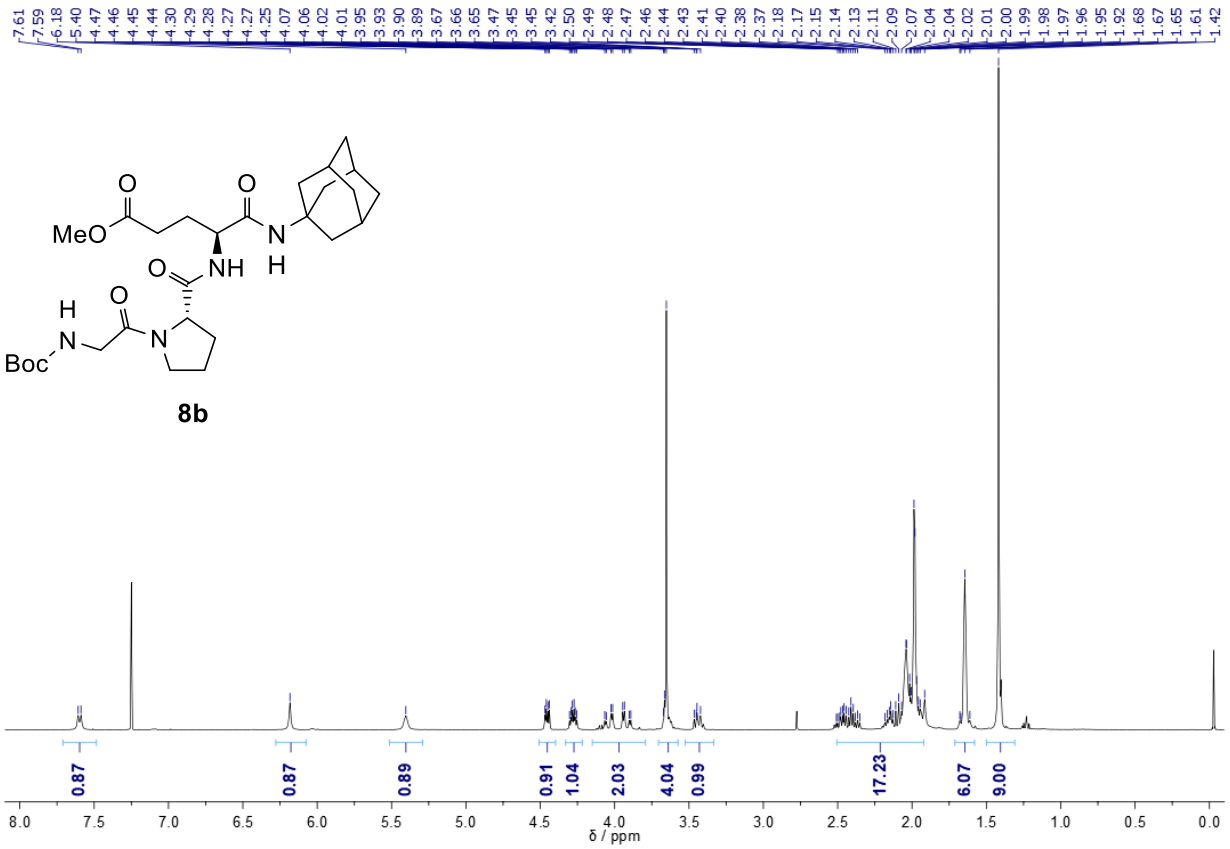

Figure S45. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **8b**.

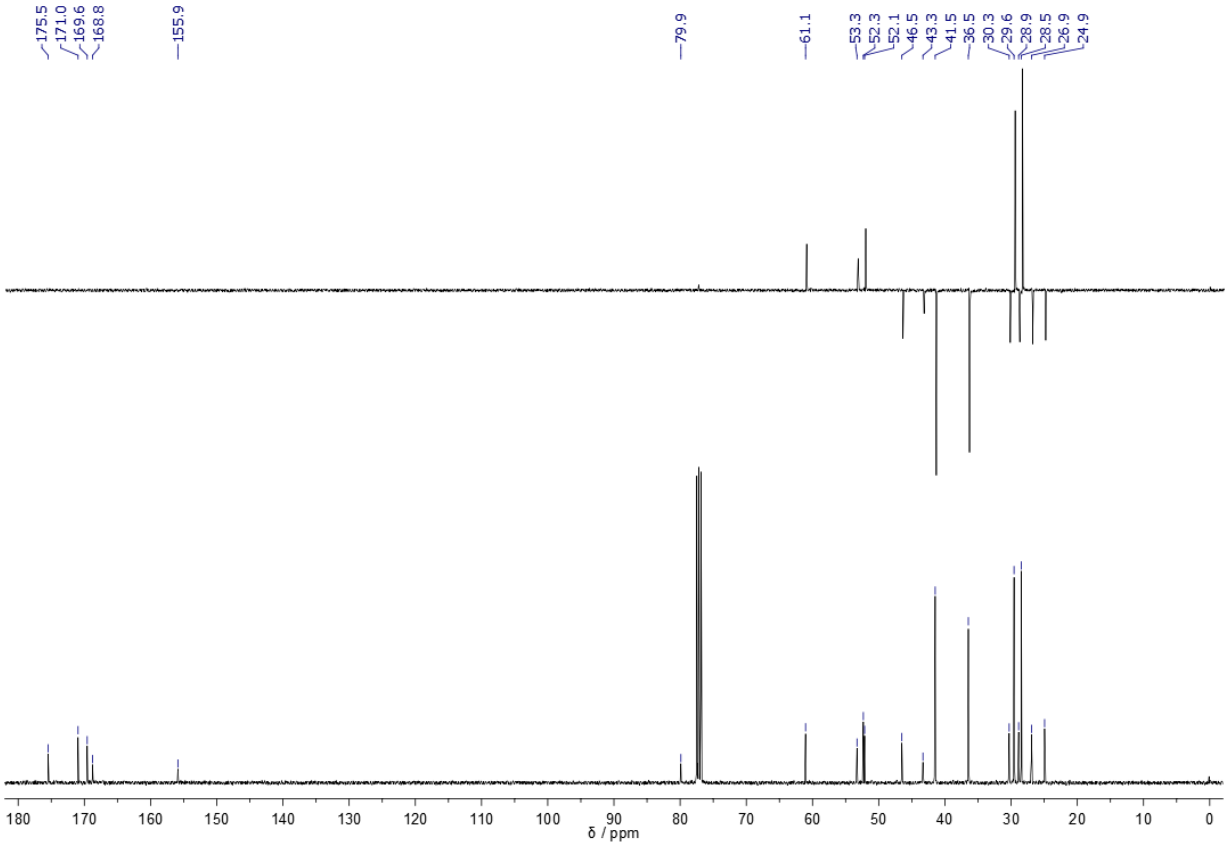

Figure S46. ^{13}C-NMR and DEPT-135 spectra (101 MHz, $CDCl_3$) of compound **8b**.

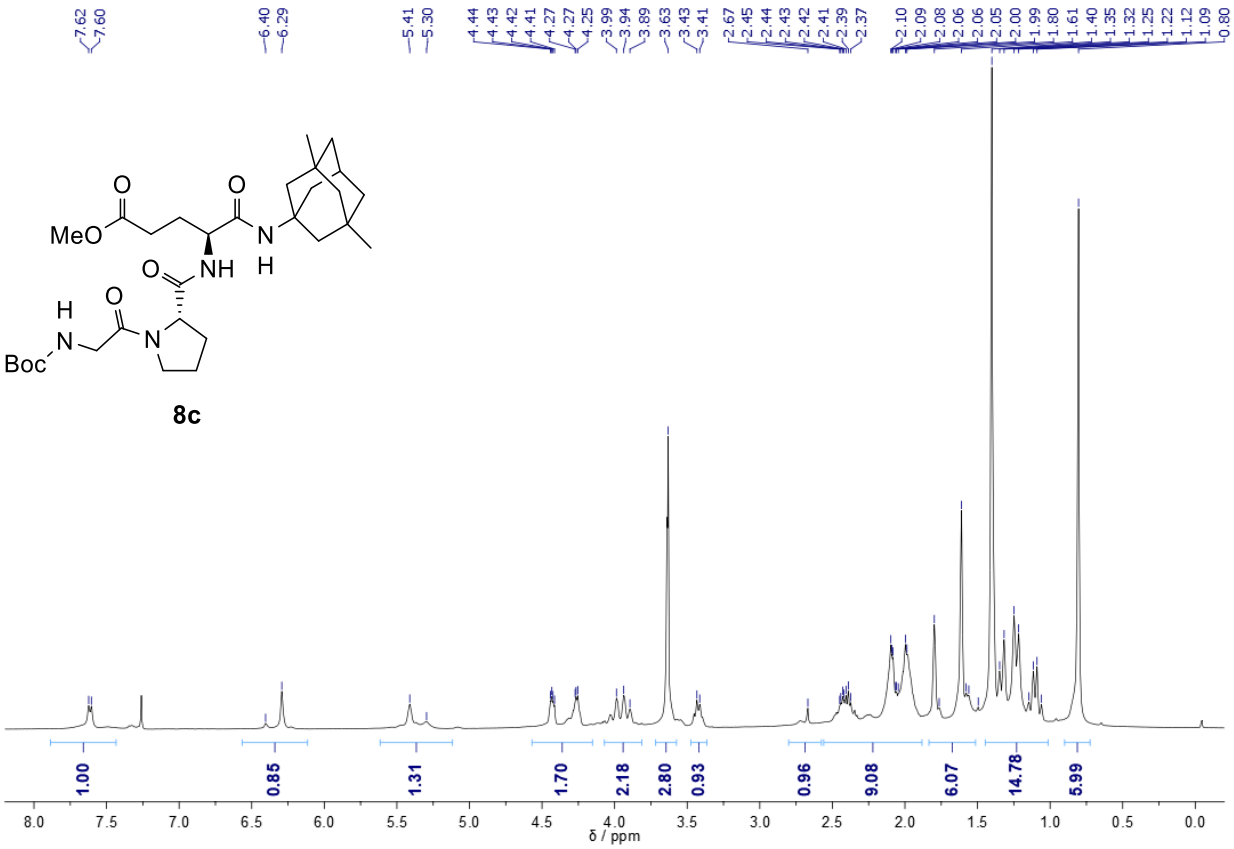

Figure S47. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **8c**.

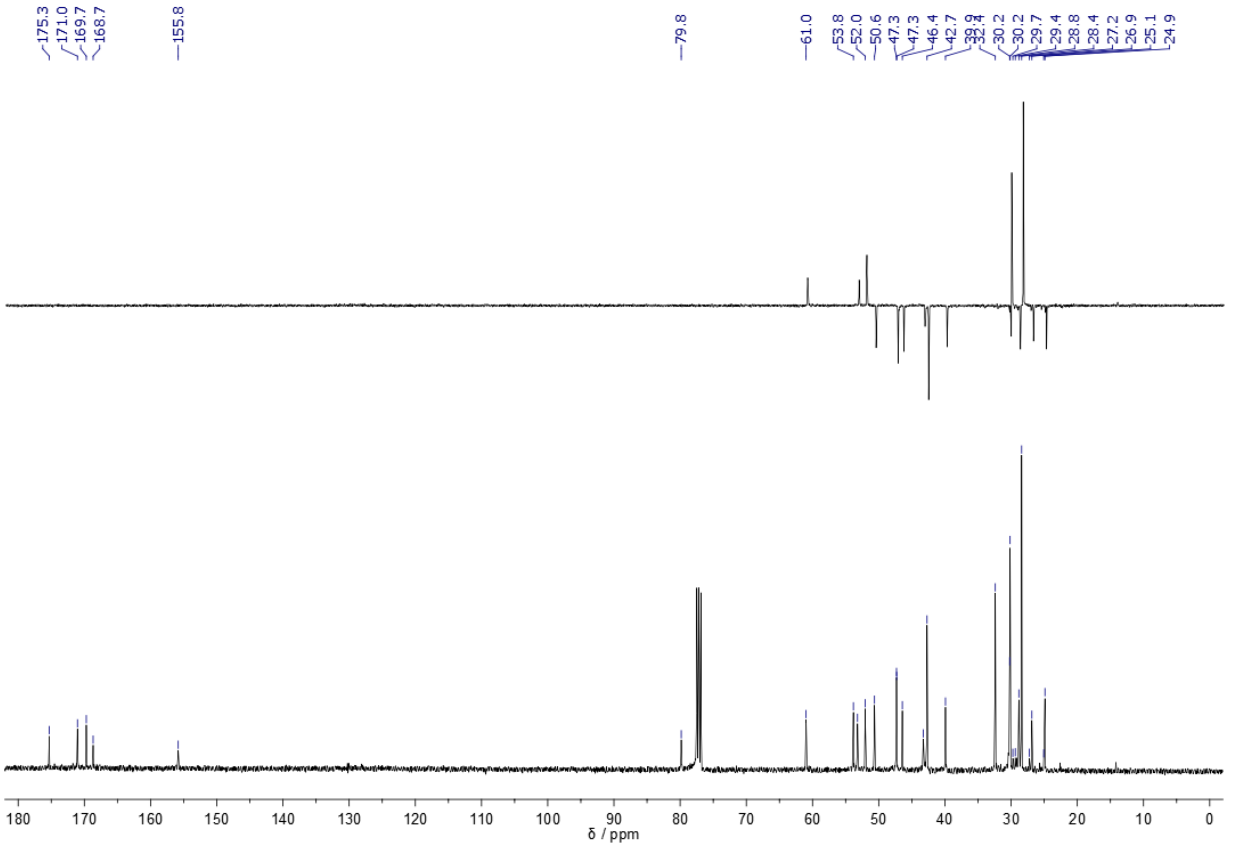

Figure S48. ^{13}C-NMR and DEPT-135 spectra (101 MHz, $CDCl_3$) of compound **8c**.

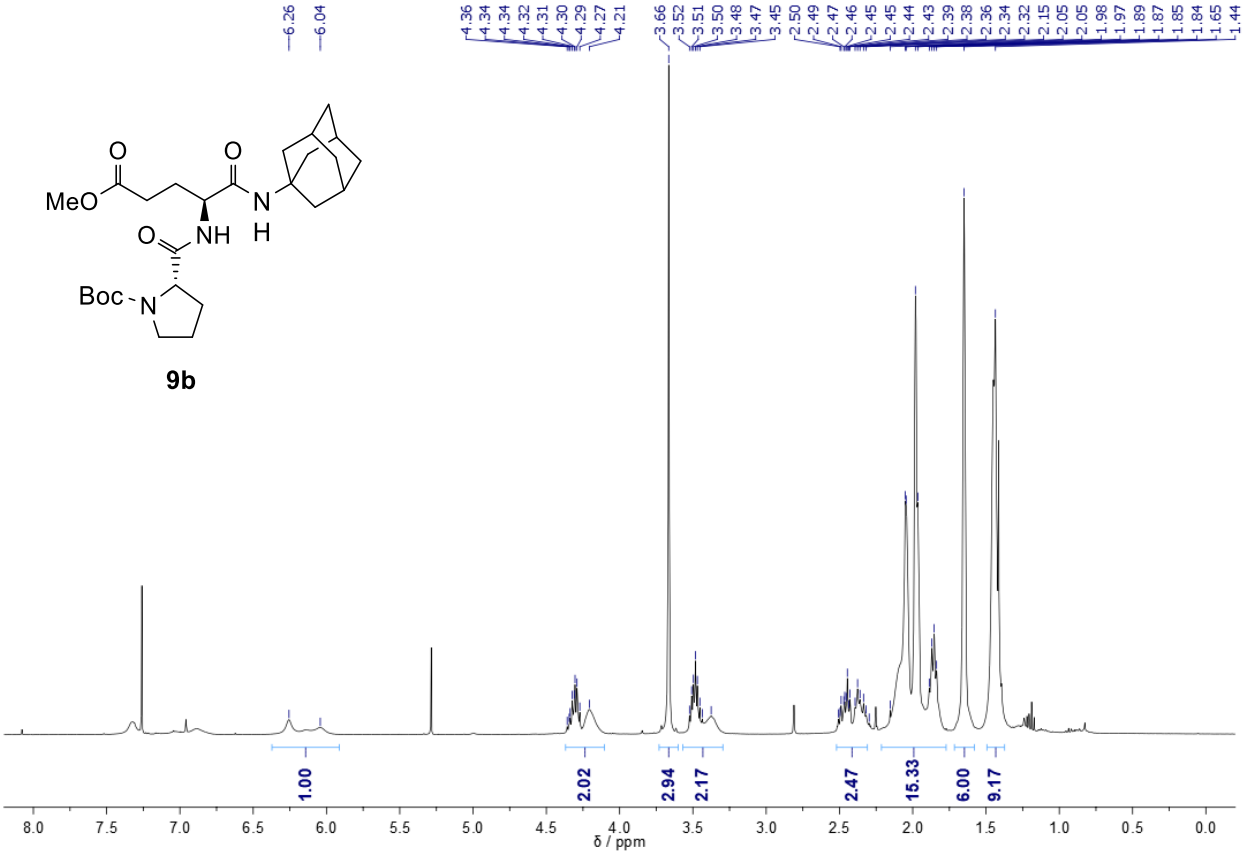

Figure S49. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **9b**.

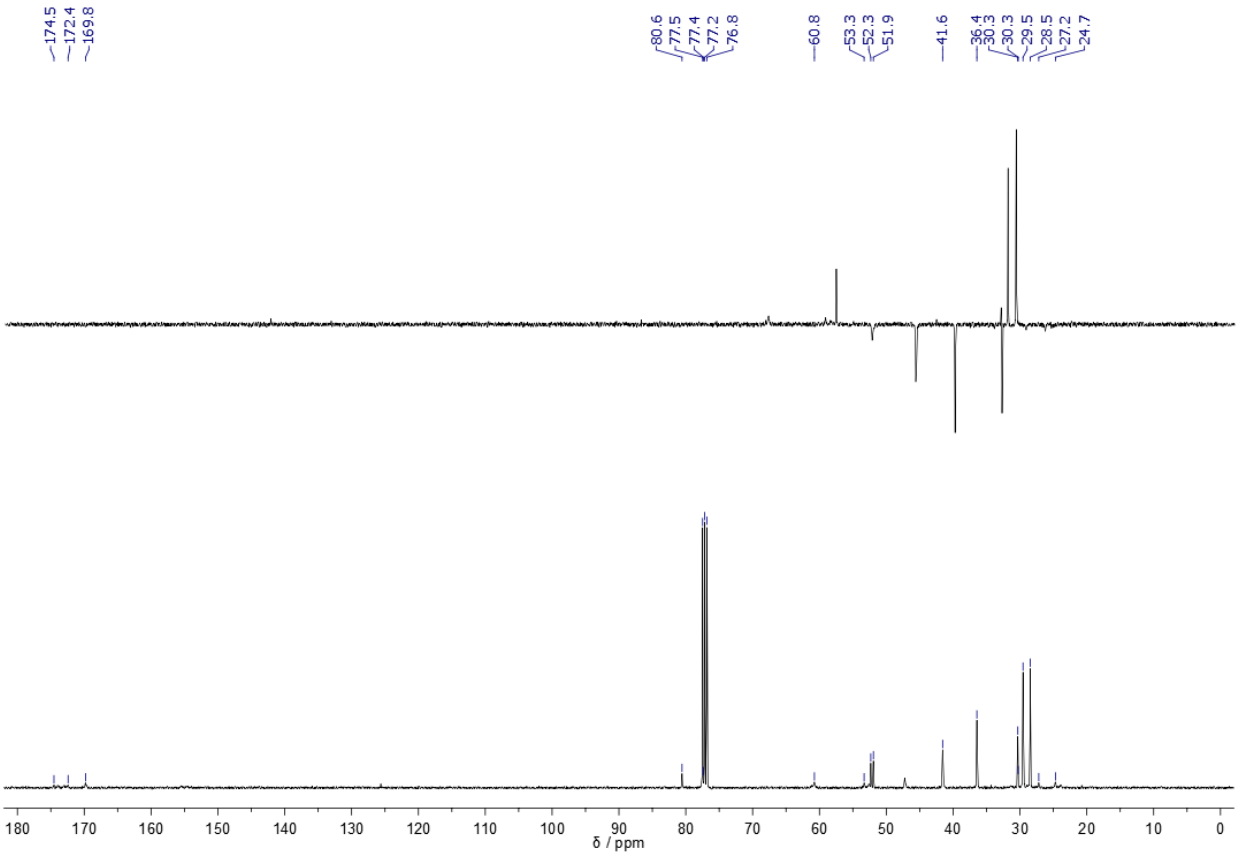

Figure S50. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **9b**.

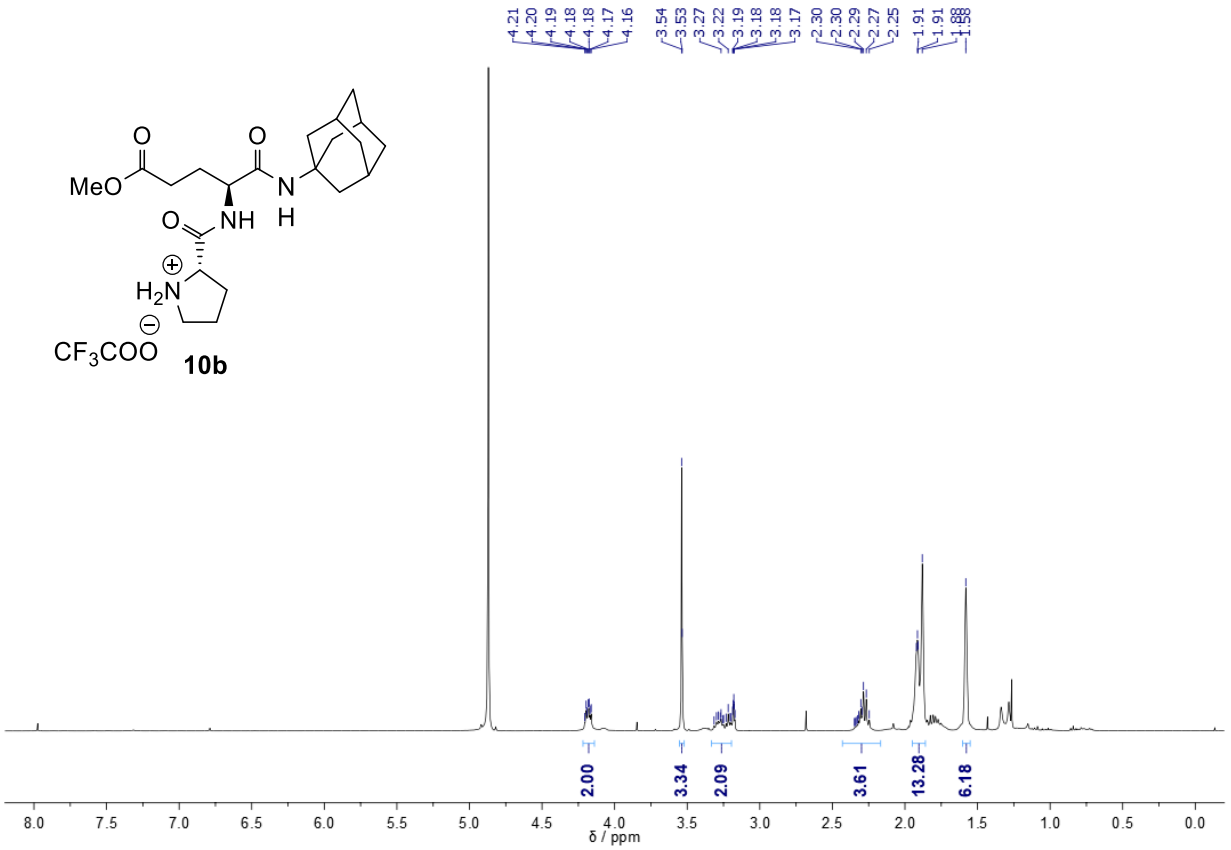

Figure S51. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **10b**.

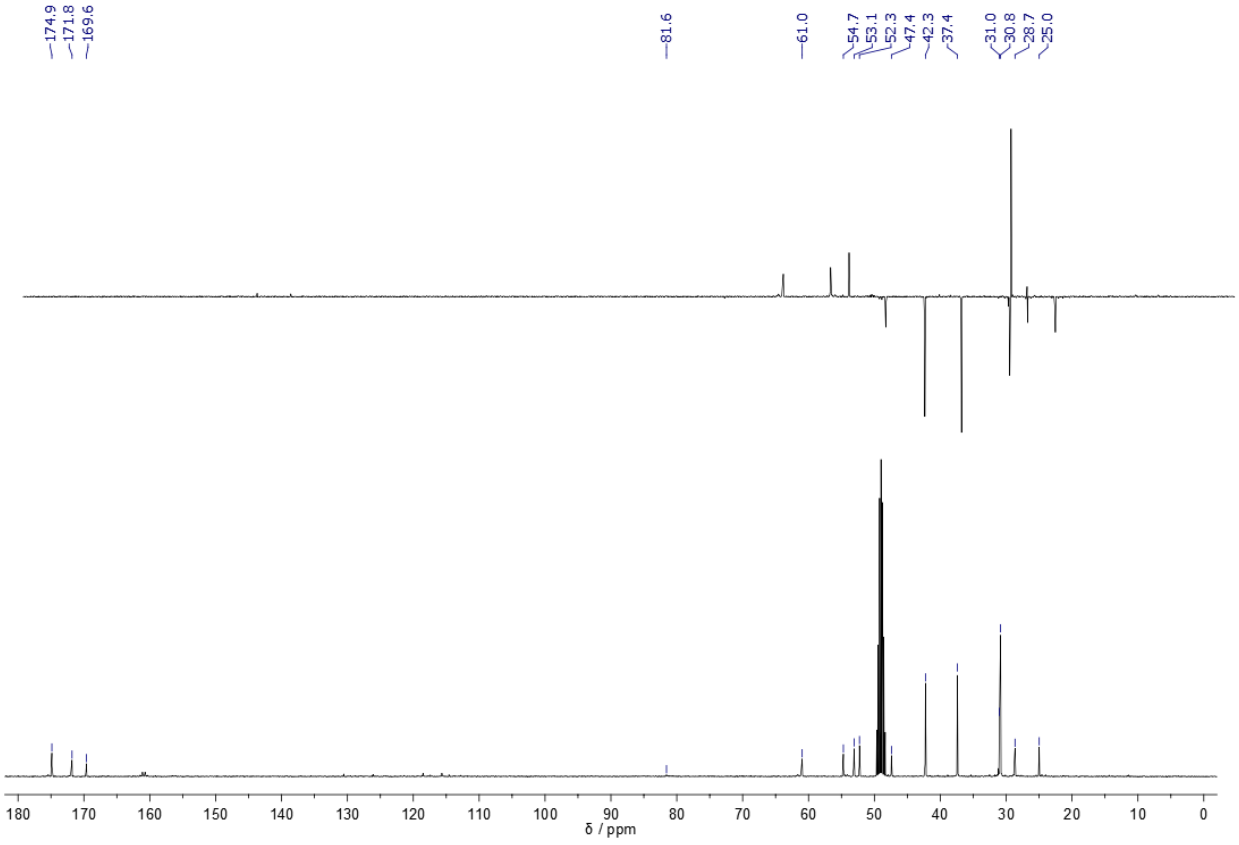

Figure S52. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **10b**.

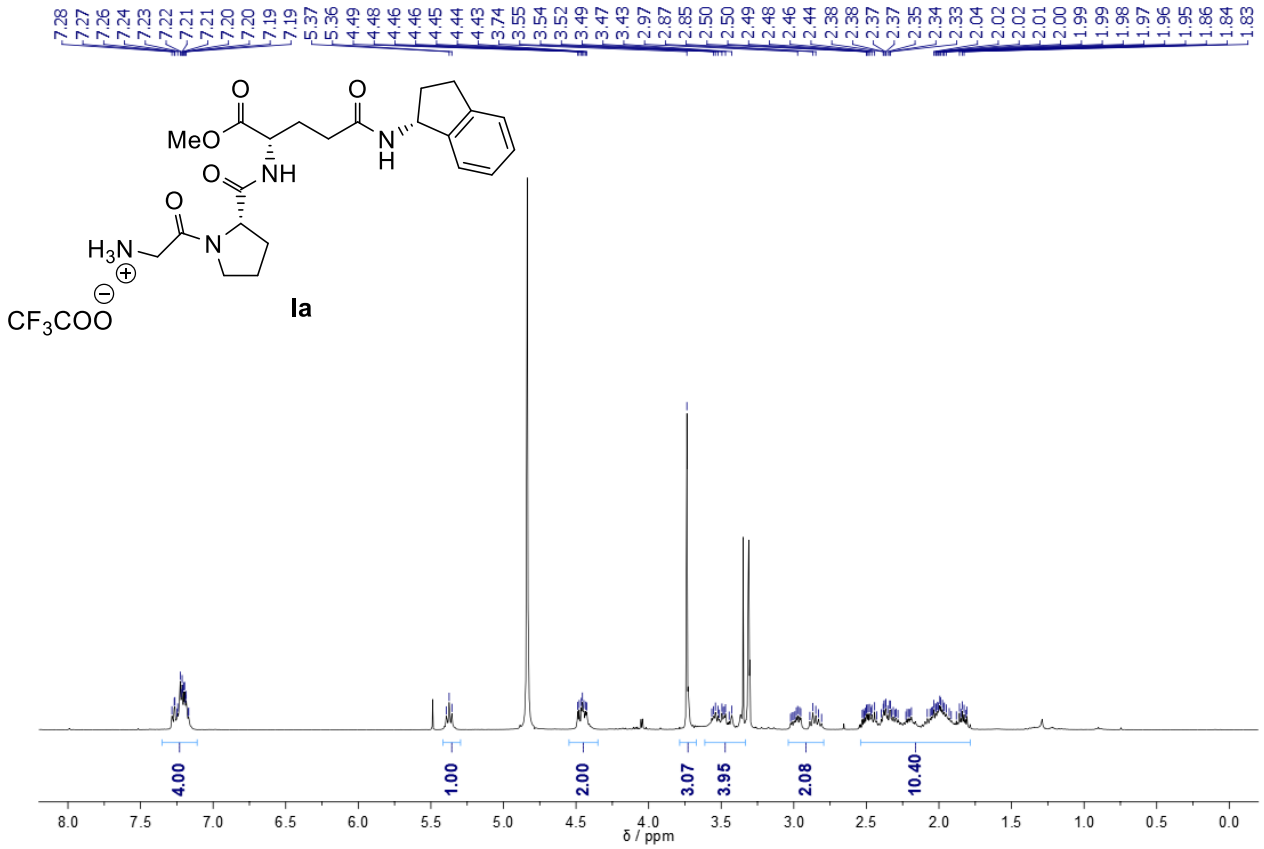

Figure S53. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **Ia**.

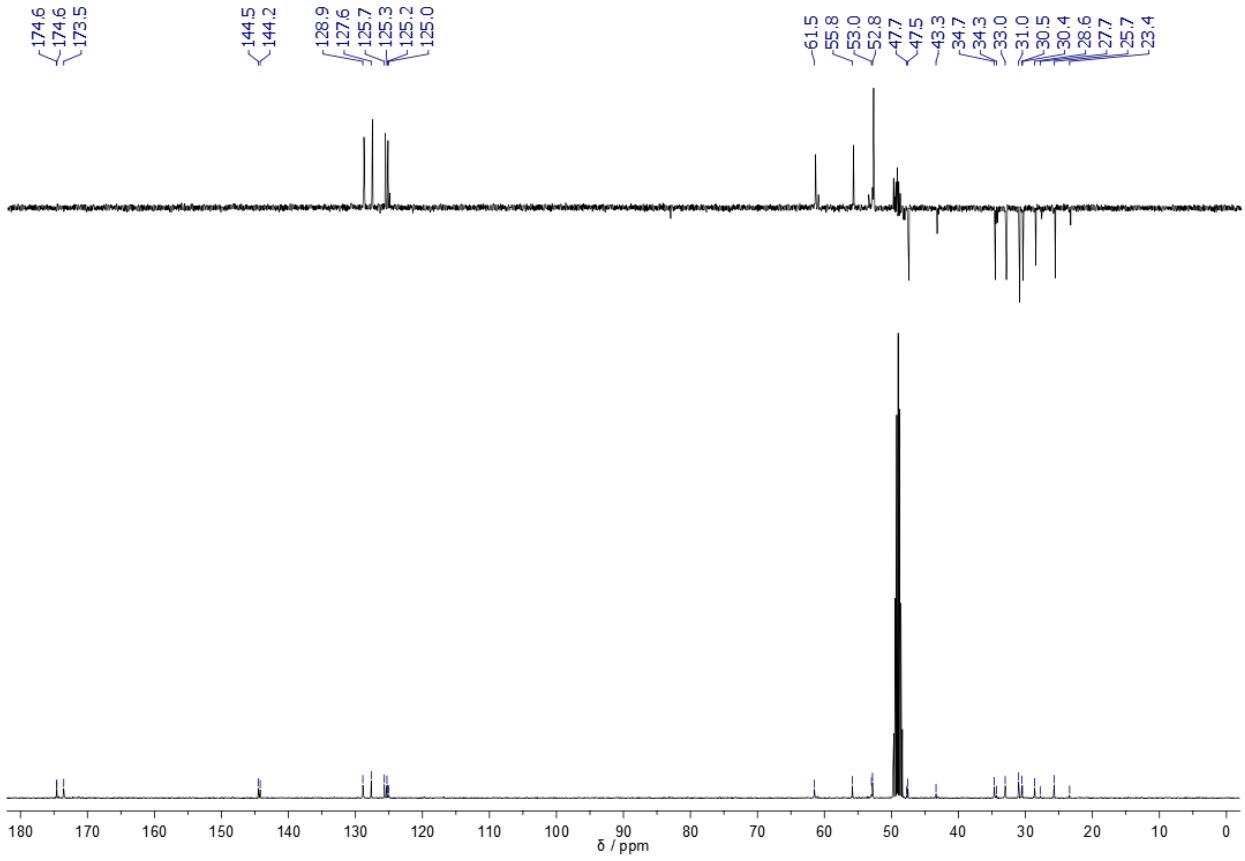

Figure S54. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **Ia**.

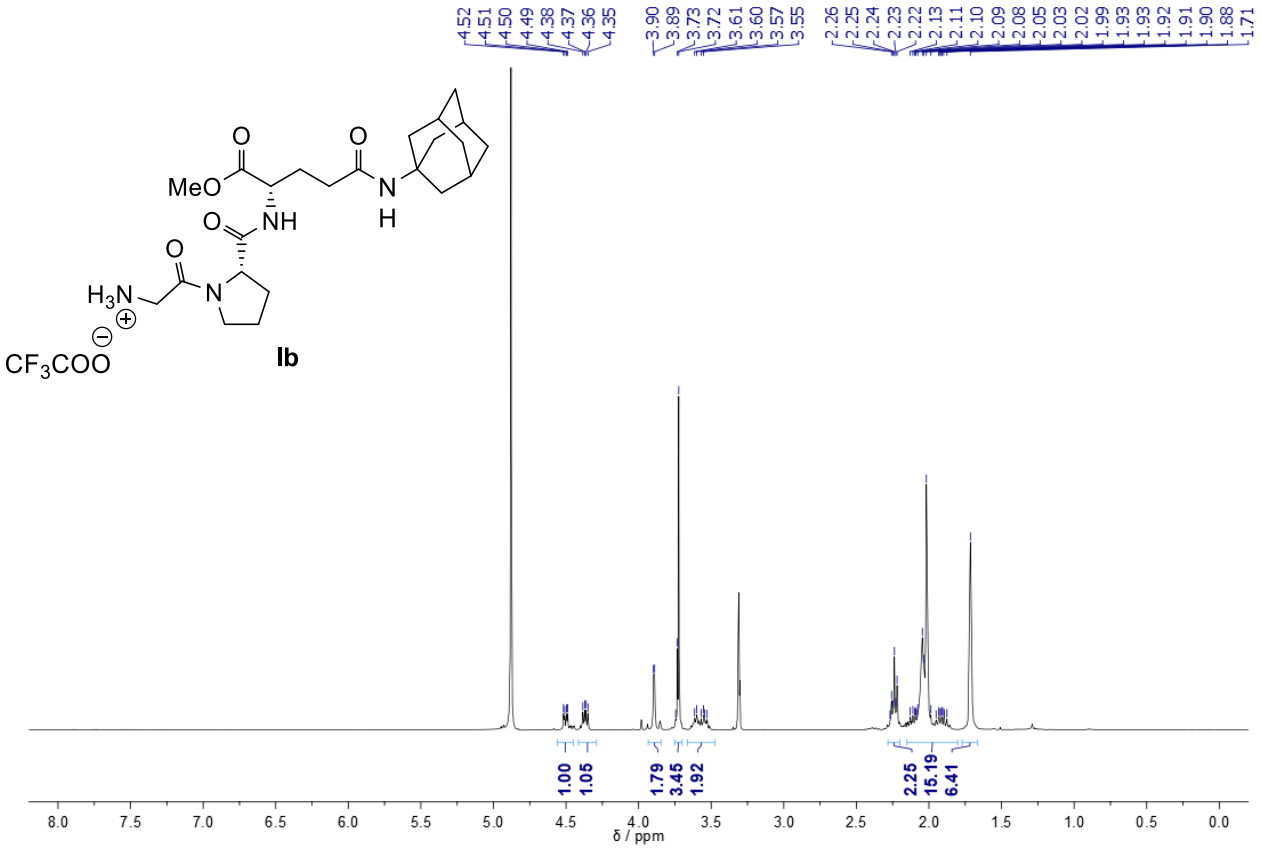

Figure S55. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **Ib**.

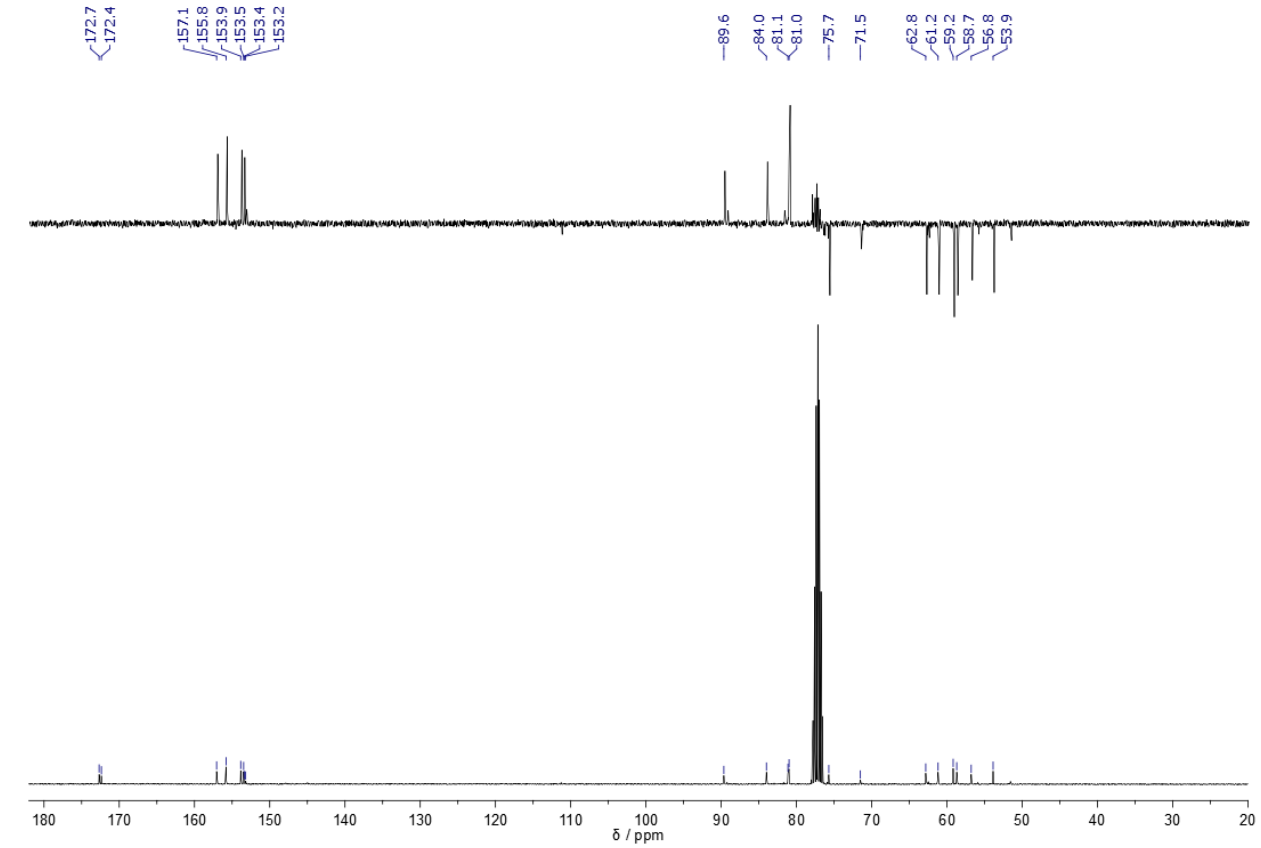

Figure S56. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **Ib**.

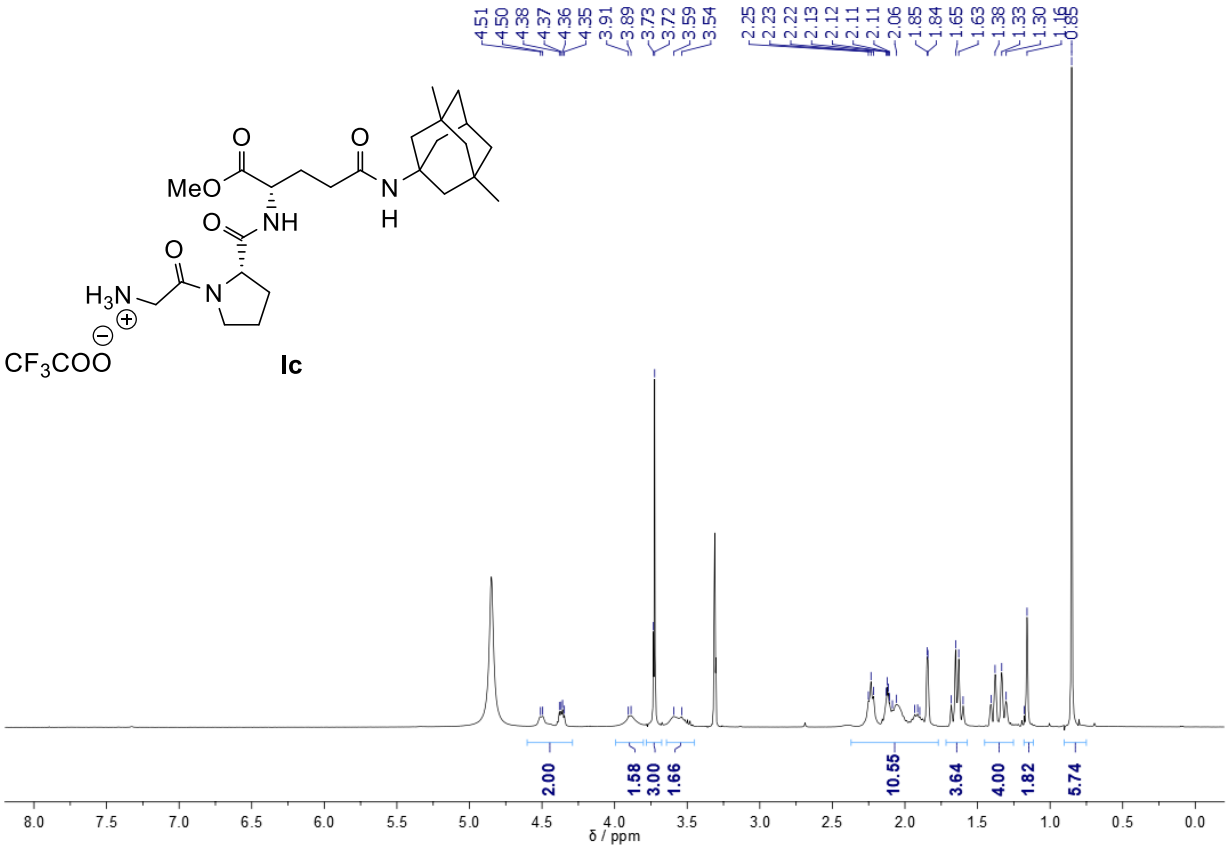

Figure S57. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **Ic**.

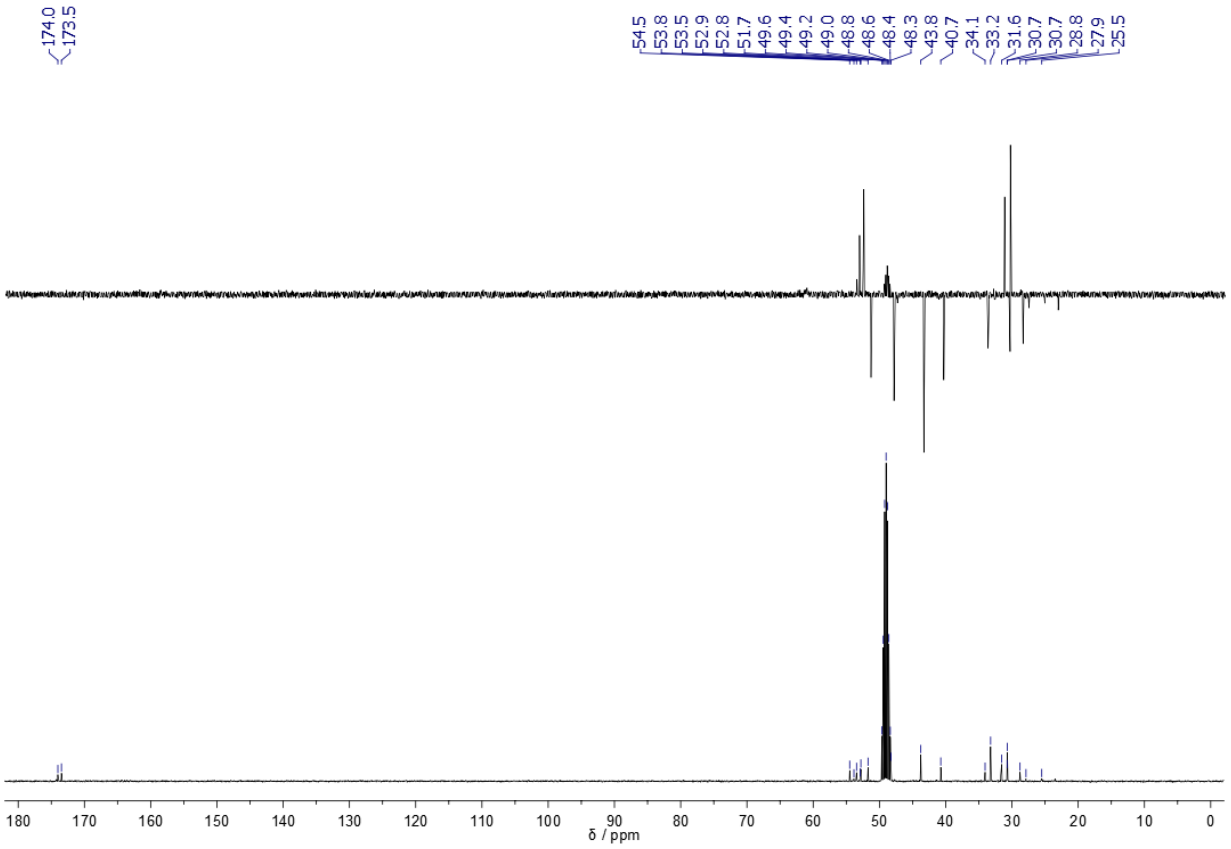

Figure S58. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **Ic**.

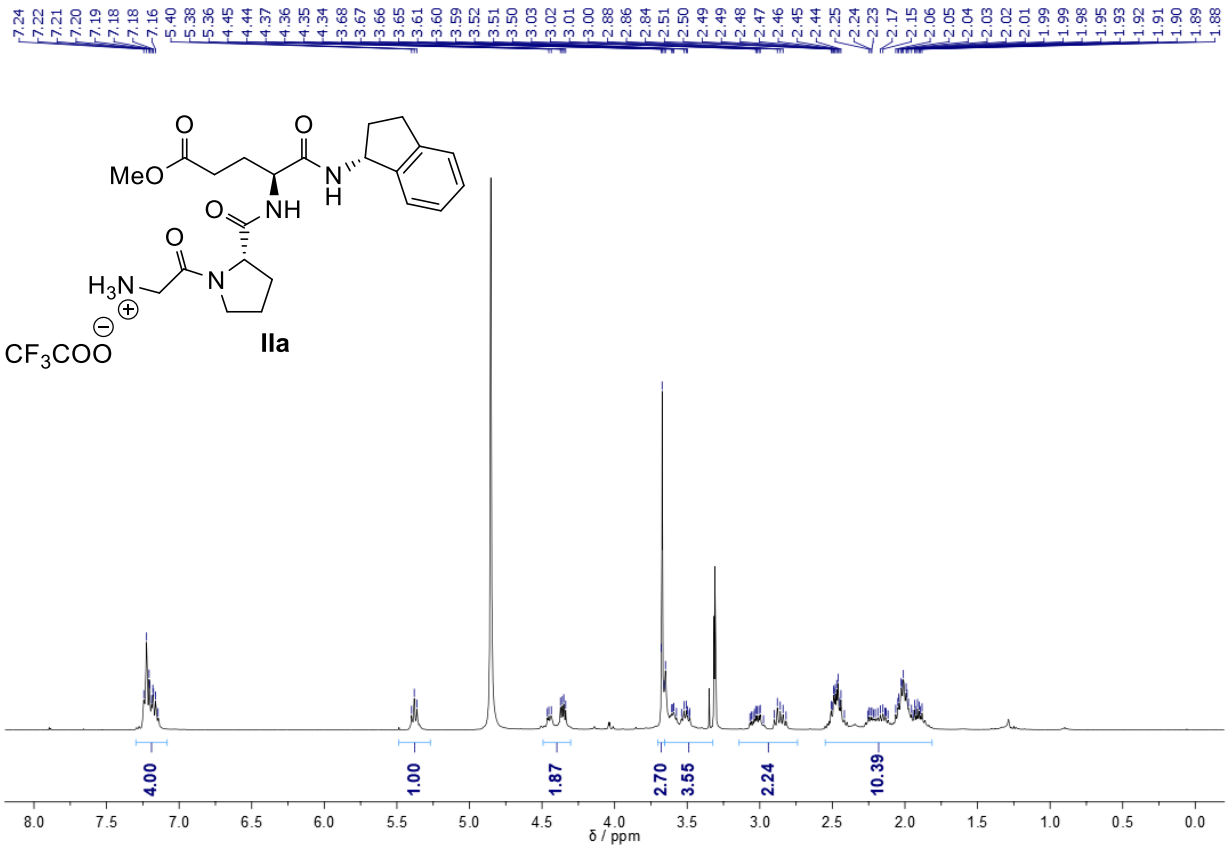

Figure S59. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **IIa**.

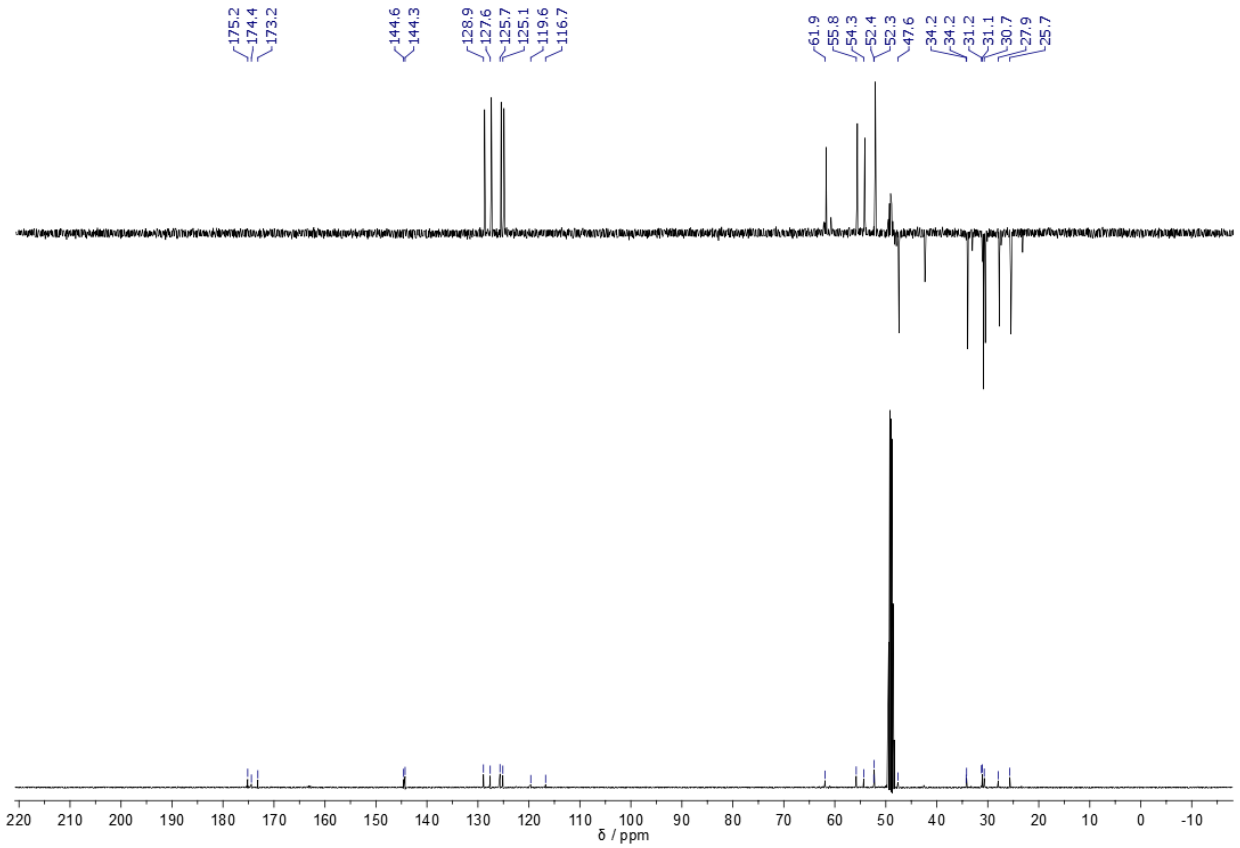

Figure S60. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **IIa**.

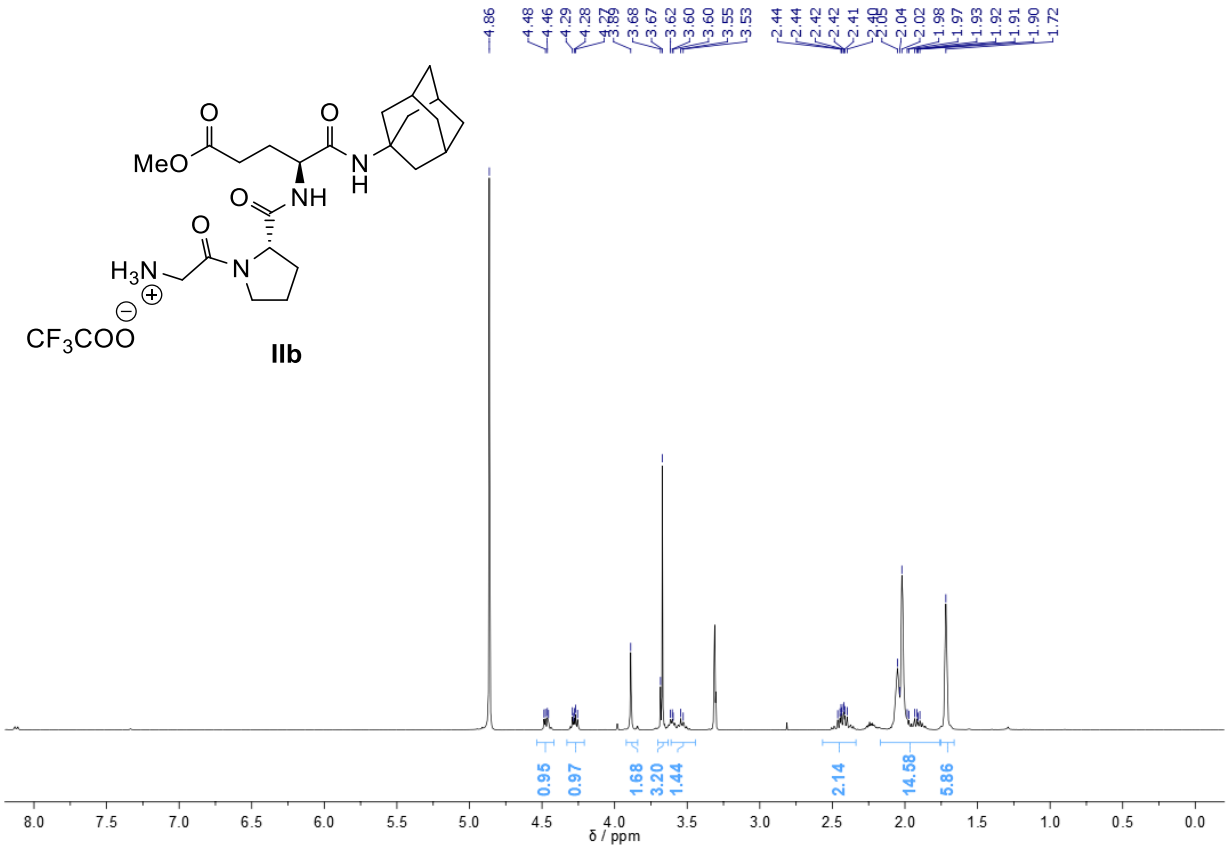

Figure S61. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **IIb**.

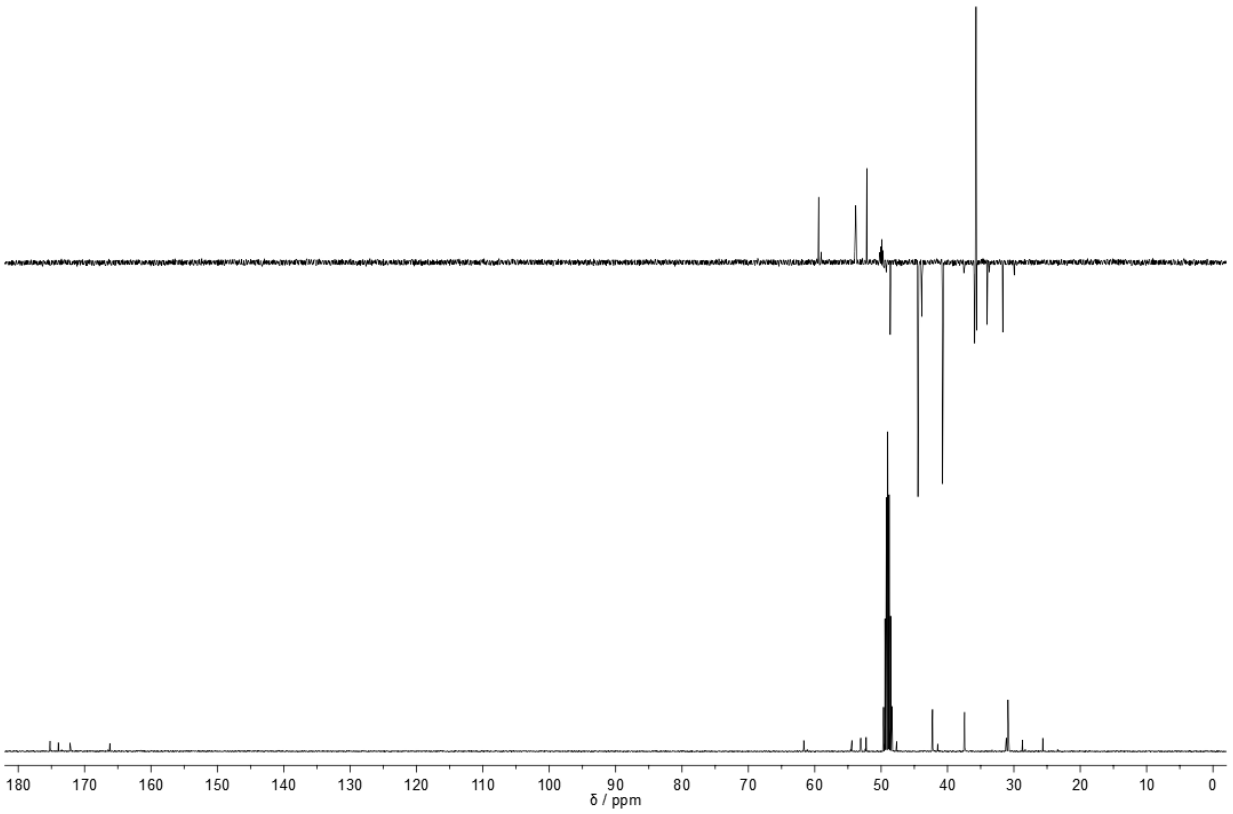

Figure S62. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **IIb**.

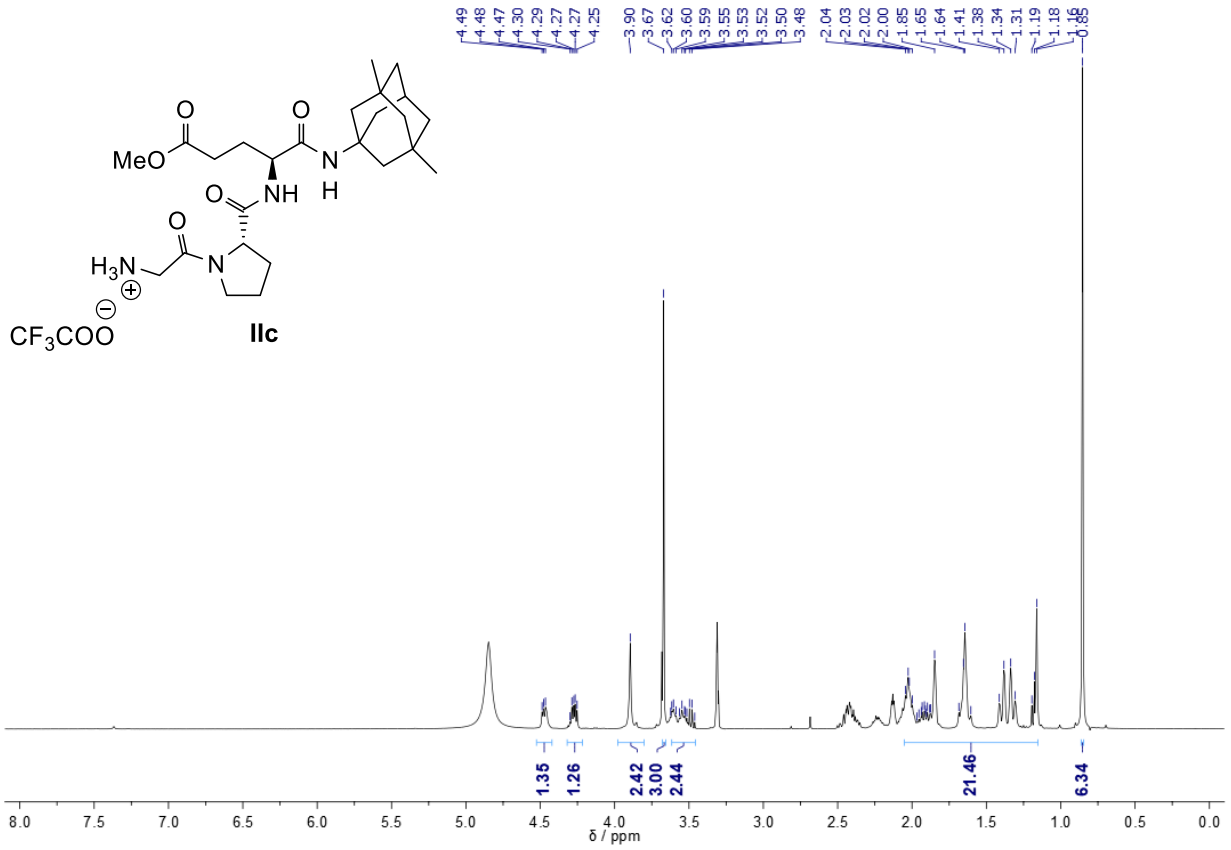

Figure S63. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **IIc**.

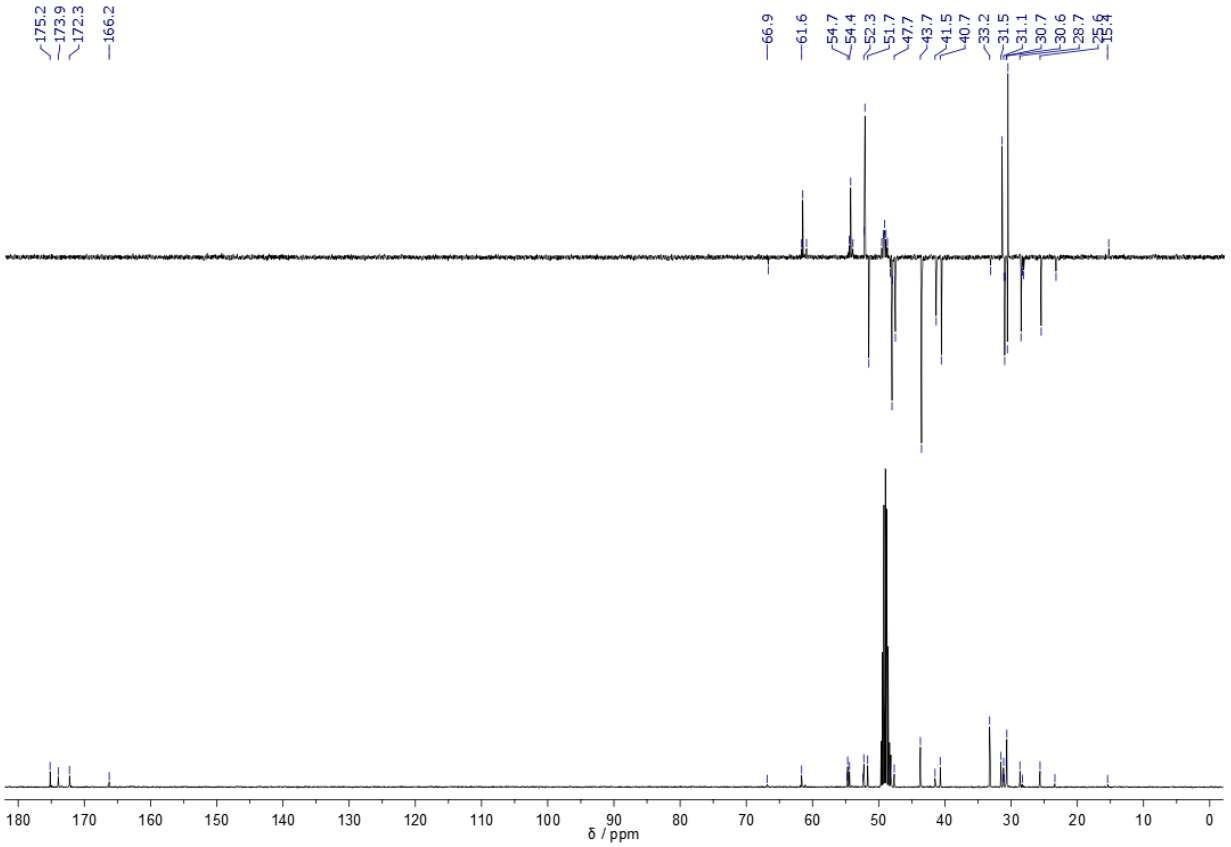

Figure S64. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **IIc**.

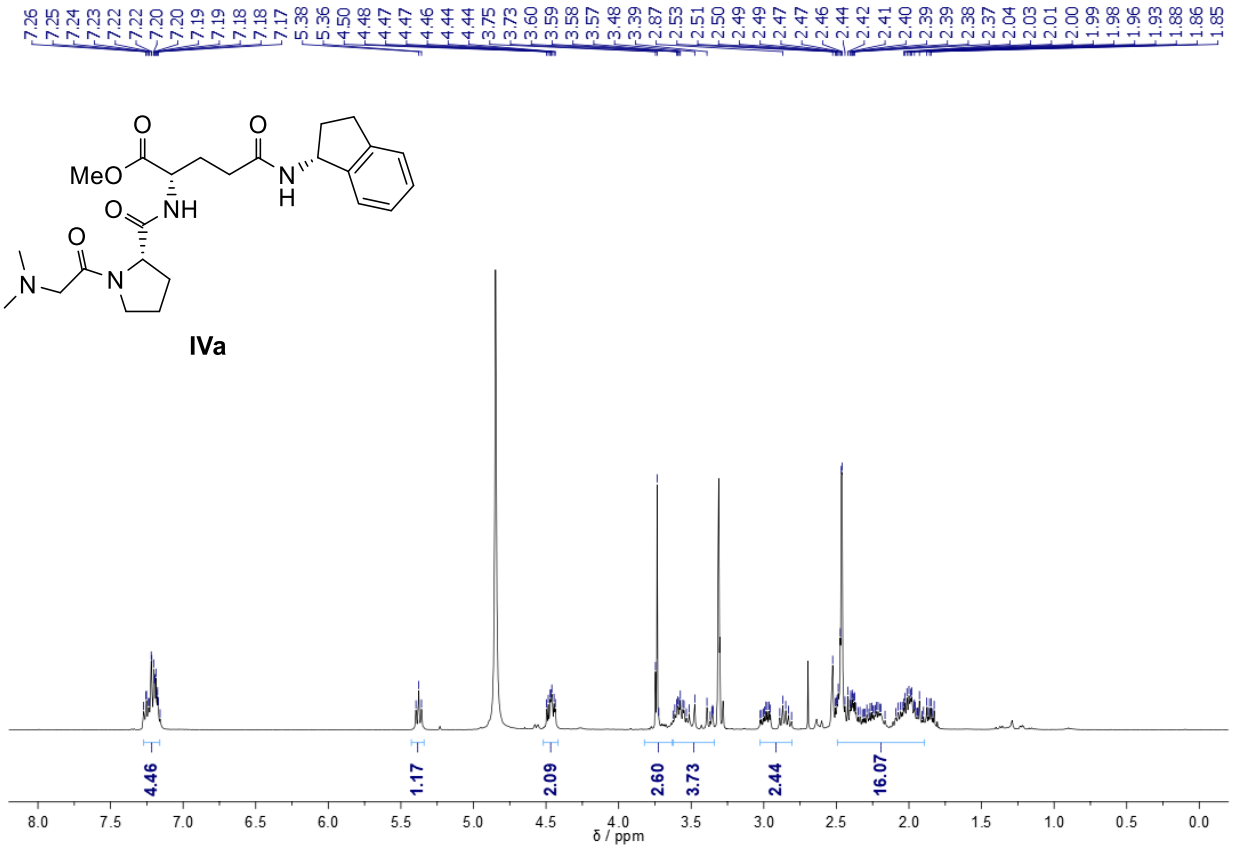

Figure S65. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **IVa**.

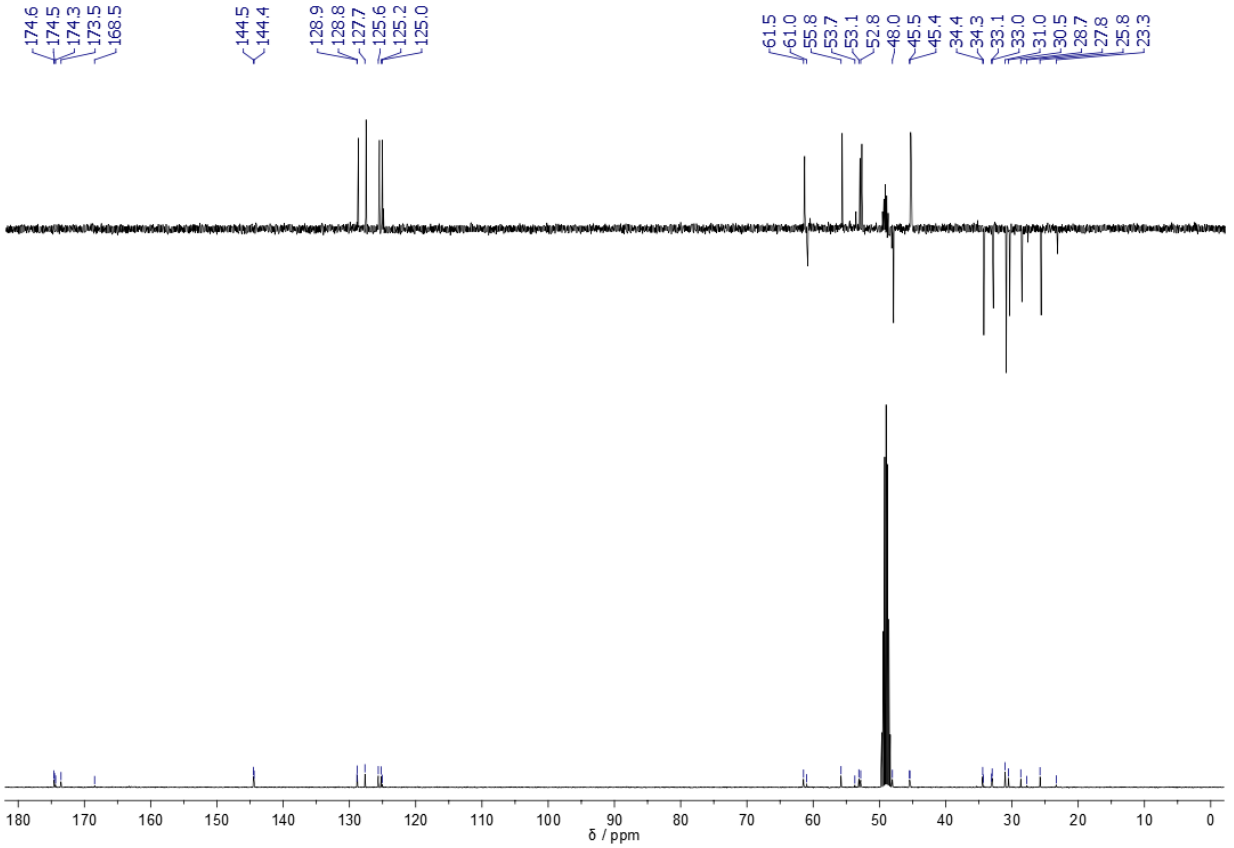

Figure S66. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **IVa**.

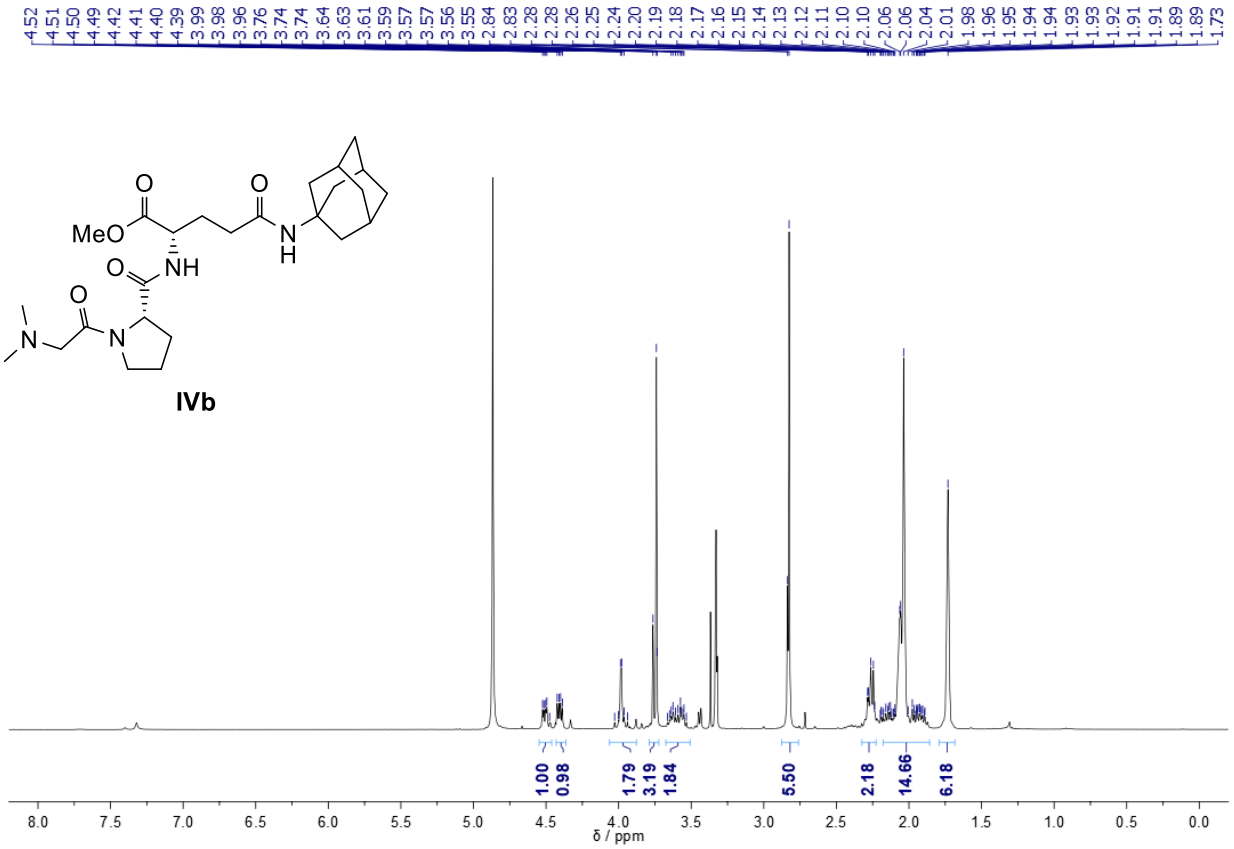

Figure S67. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **IVb**.

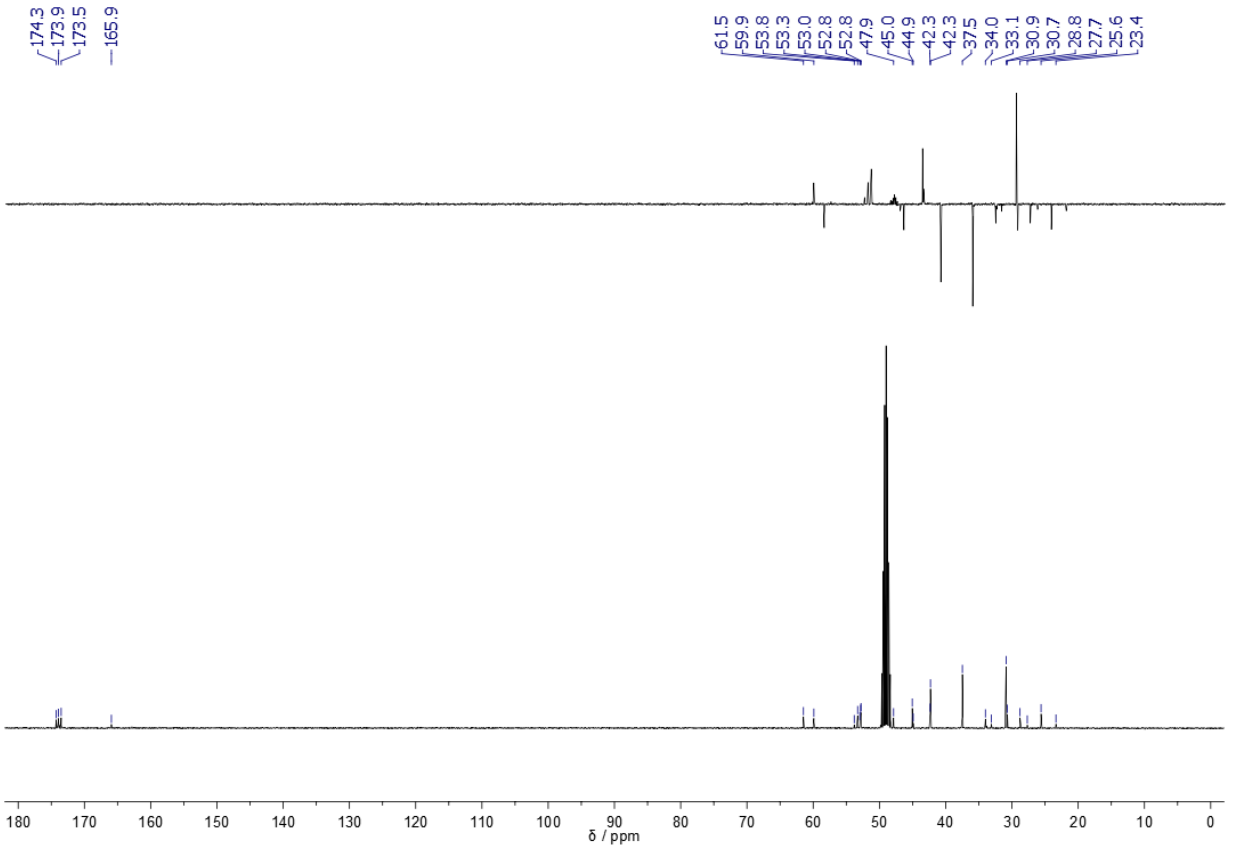

Figure S68. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **IVb**.

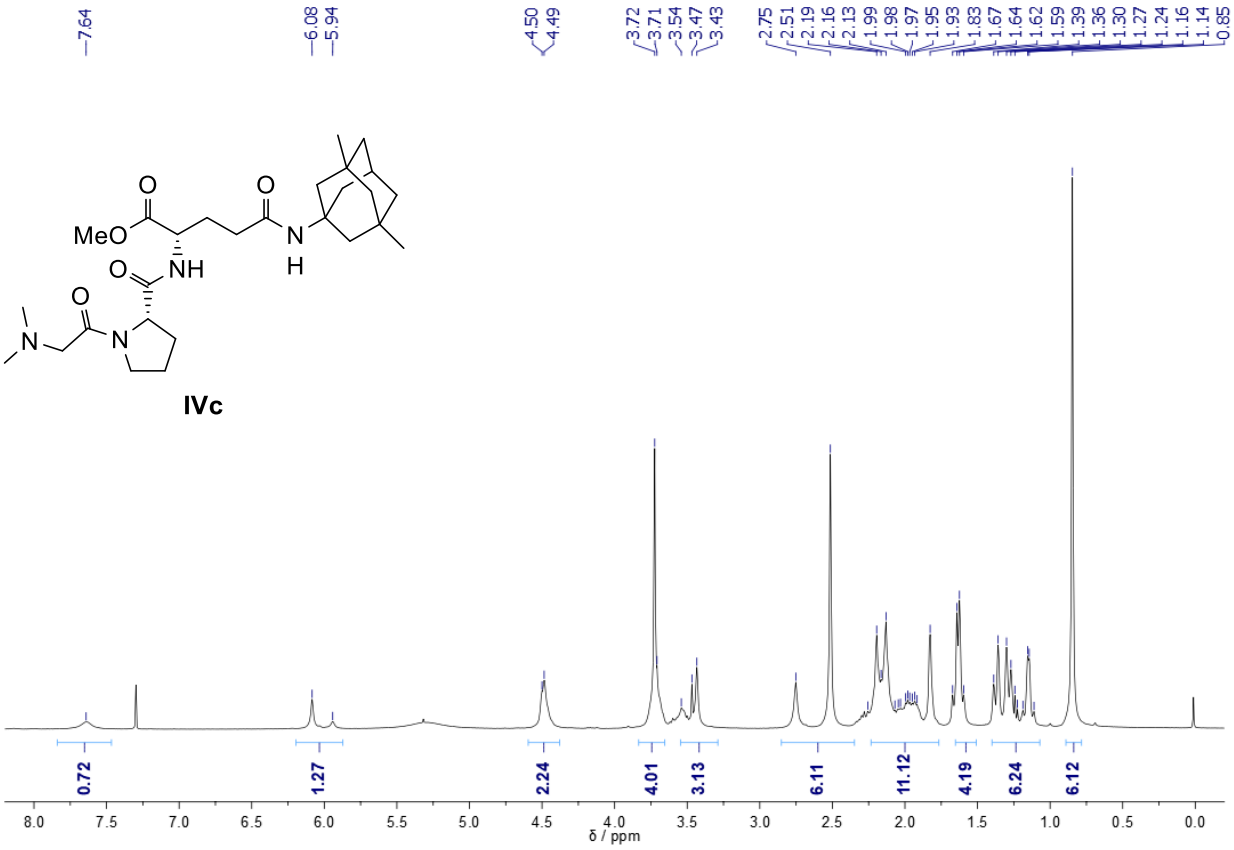

Figure S69. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **IVc**.

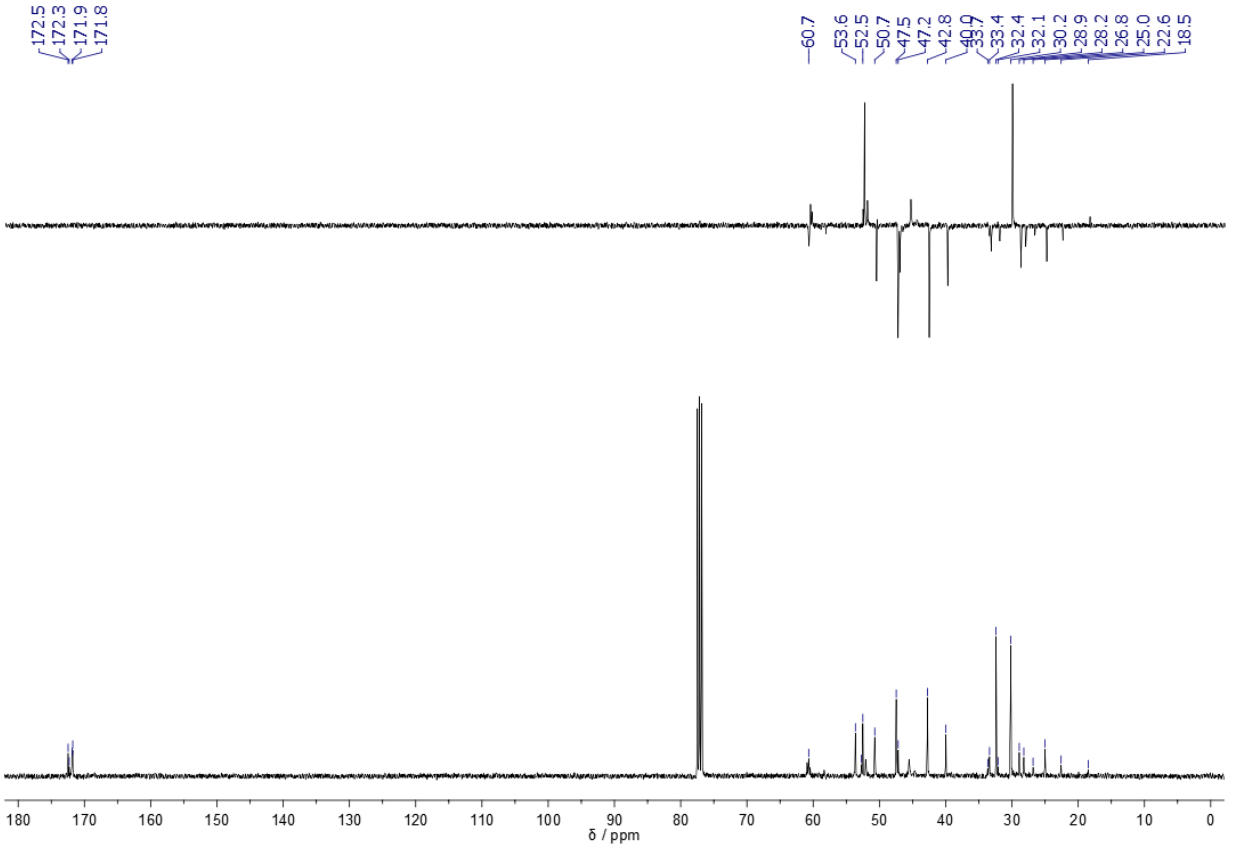

Figure S70. ^{13}C-NMR and DEPT-135 spectra (101 MHz, $CDCl_3$) of compound **IVc**.

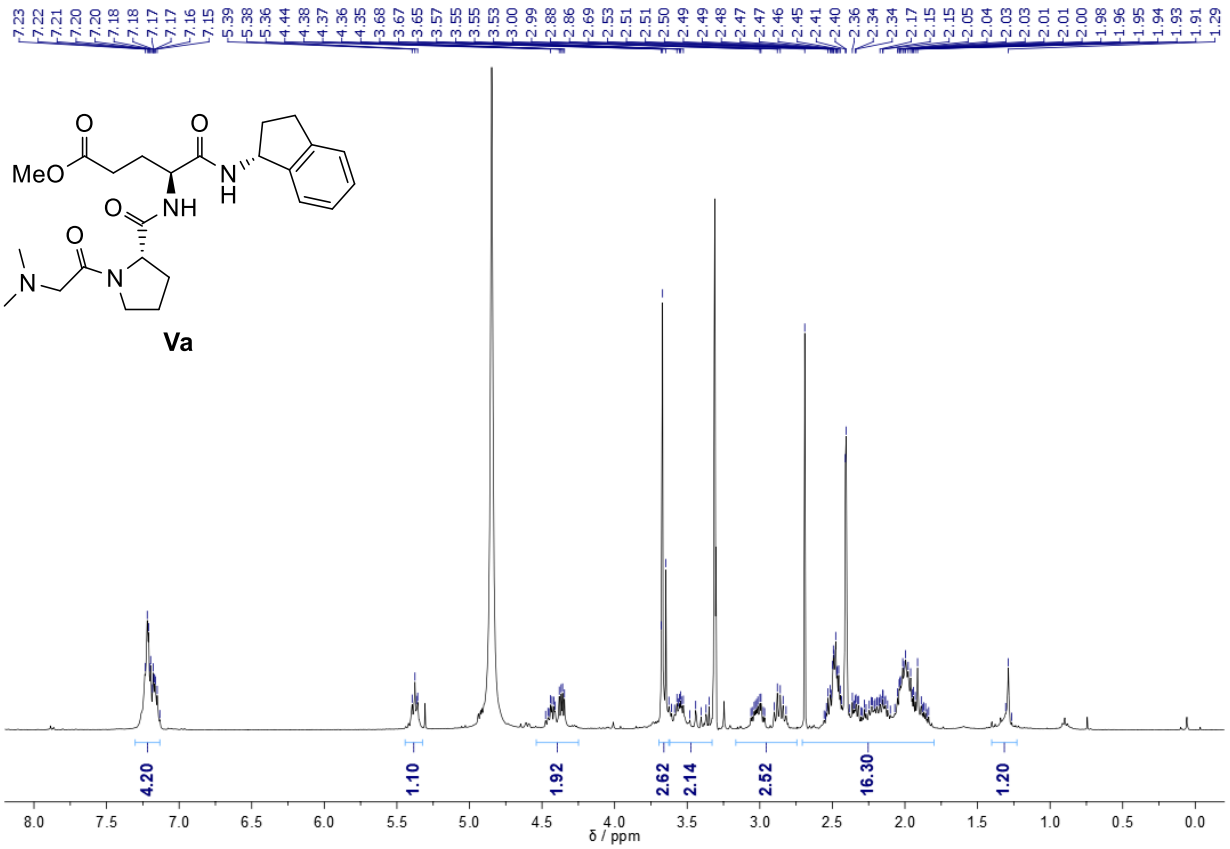

Figure S71. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **Va**.

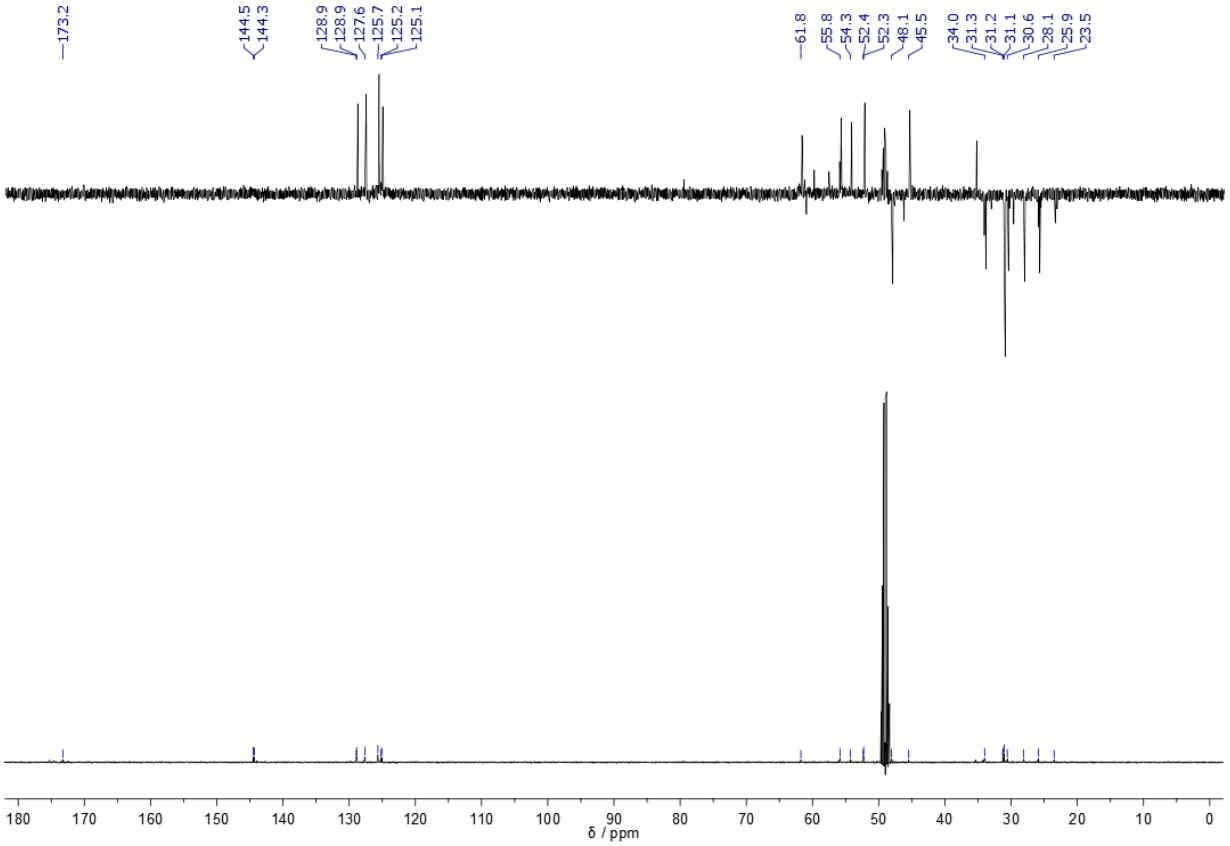

Figure S72. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **Va**.

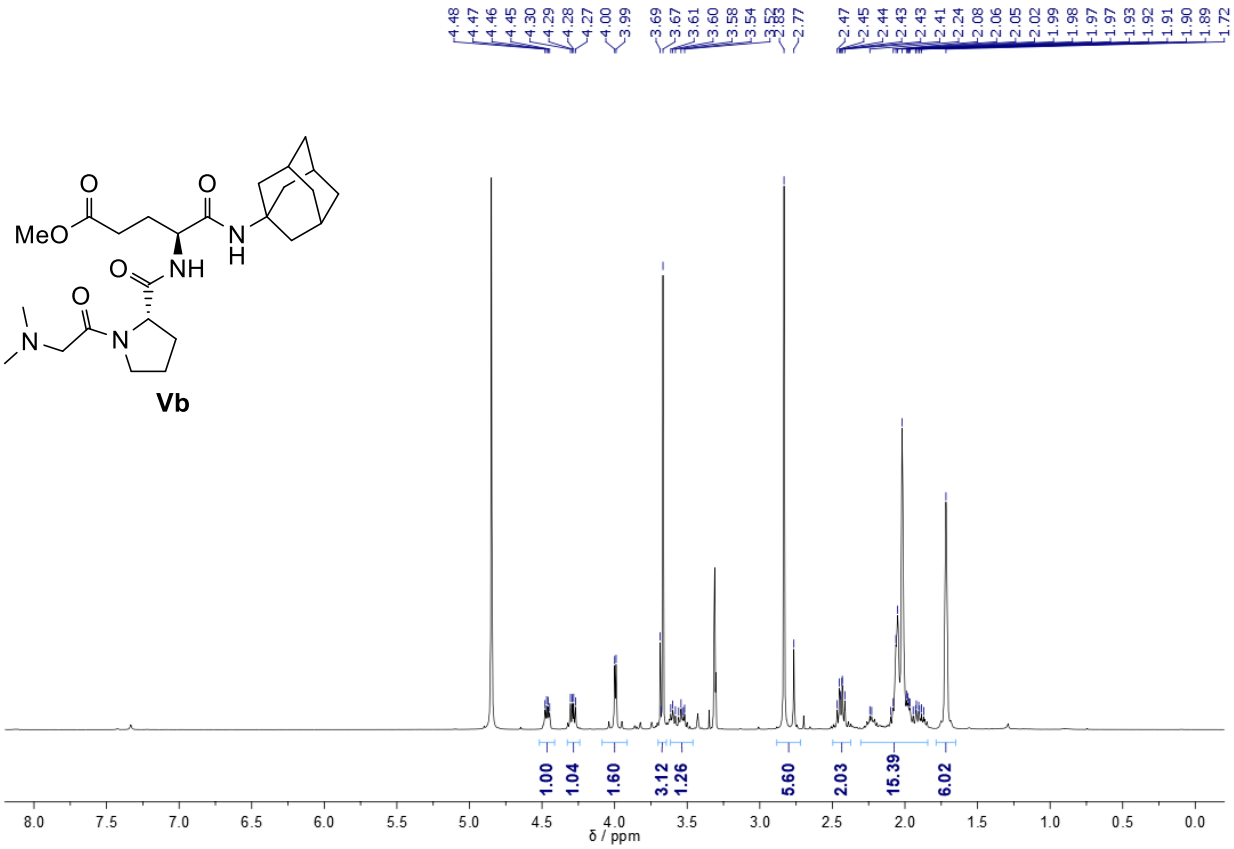

Figure S73. ^{1}H-NMR spectrum (400 MHz, CD_3OD) of compound **Vb**.

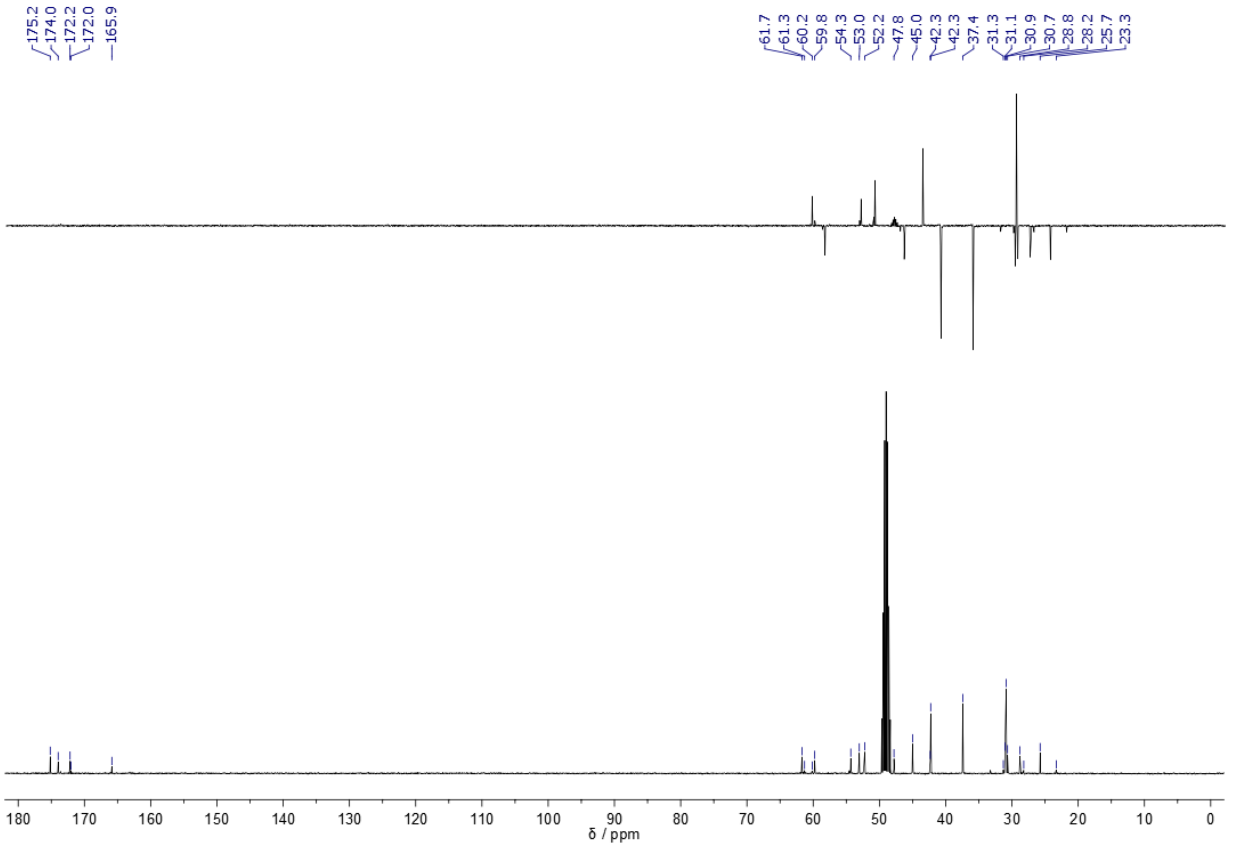

Figure S74. ^{13}C-NMR and DEPT-135 spectra (101 MHz, CD_3OD) of compound **Vb**.

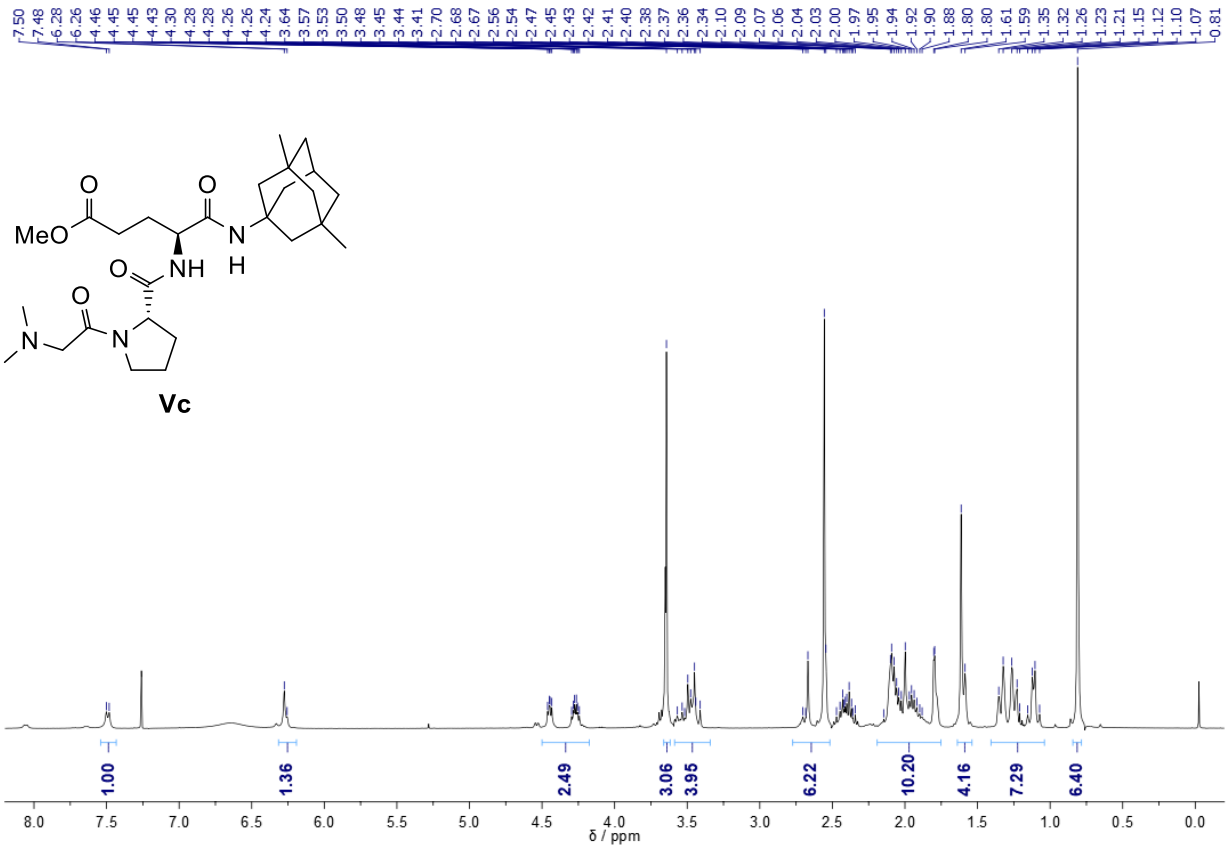

Figure S75. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of compound **Vc**.

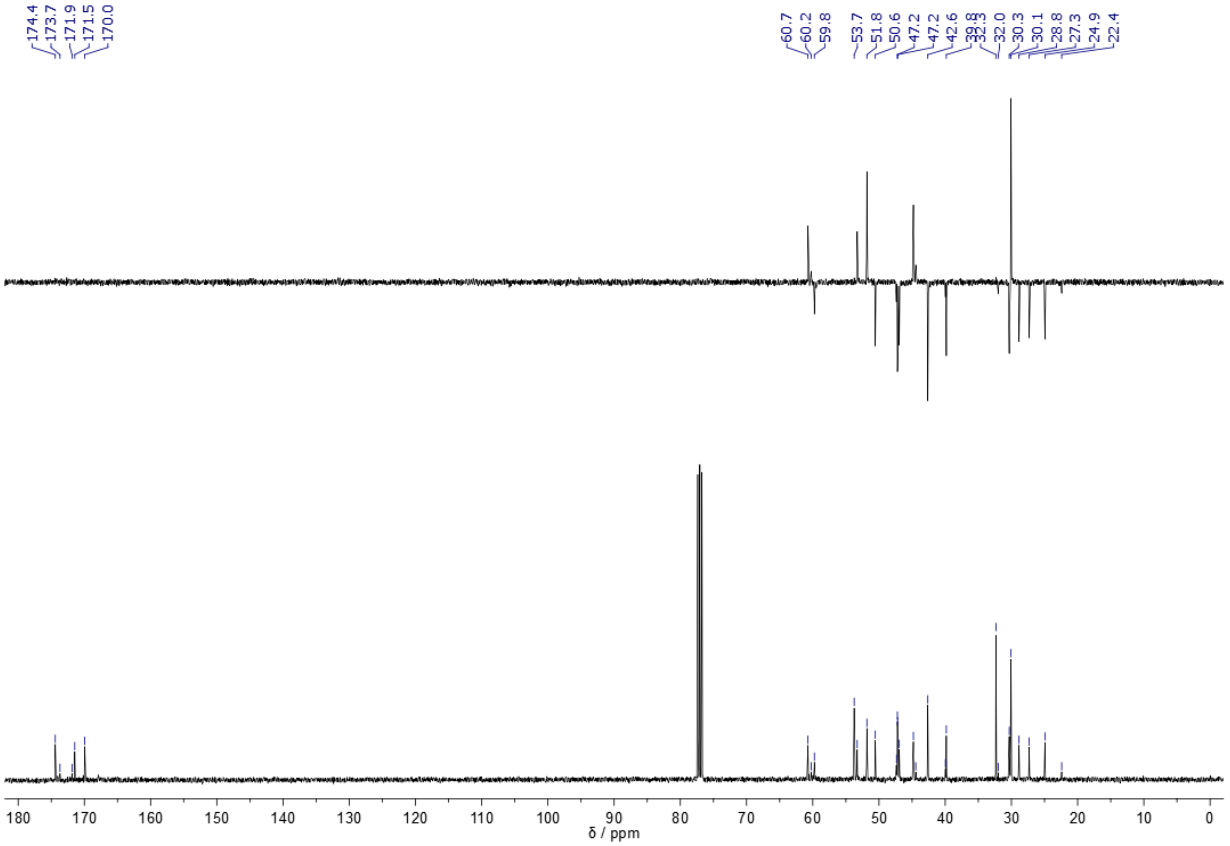

Figure S76. ^{13}C-NMR and DEPT-135 spectra (101 MHz, $CDCl_3$) of compound **Vc**.

Table S1. Calculated Druglike Properties for conjugates **III(a-c)** and **VI(a-c)**.

Conjugate	MW[a]	clogP[a]	HBA[a]	HBD[a]	n_{rotb}[a]	^{t}PSA[a] / Å^2	BB ratio[b]
IIIa	531.66	0.40	9	5	9	133.63	0.635
IIIb	567.68	2.55	9	5	9	133.63	0.710
IIIc	623.88	2.80	9	5	9	133.63	0.559
VIa	559.71	1.62	9	3	10	110.84	0.633
VIb	595.83	3.78	9	3	10	110.84	0.748
VIc	651.94	4.03	9	3	10	110.84	0.568

[a]Properties calculated using Cheminformatics software [http://www.molinspiration.com]: MW, molecular weight; N, number of heavy atoms; clogP, calculated logarithm of the octanol-water partition coefficient; HBA, number of hydrogen acceptors; HBD, number of hydrogen donors; n_{rotb}, number of rotatable bonds; ^{t}PSA, topological polar surface area. [b]*In silico* BBB permeability using Cheminformatics software [http://admet.scbdd.com/calcpre/index/], Category 0: BBB−; Category 1: BBB+; BB ratio ≥ 0.1: BBB+; BB ratio <0.1: BBB−.