

Supplementary Material

Isolation and Total Synthesis of PM170453, a New Cyclic Depsipeptide Isolated from *Lyngbya* sp

Rogelio Fernández,* Marta Pérez, Alejandro Losada, Silvia Reboredo, Asier Gómez-San Juan, María Jesús Martín,* Andrés Francesch, Simon Munt and Carmen Cuevas

Research and Development, PharmaMar S.A., Avda. de los Reyes 1, Pol. In. La Mina, 28770 - Colmenar Viejo, Madrid, Spain.

*Corresponding autor: *rfernandez@pharmamar.com; mjmartin@pharmamar.com*

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21. Spectra of synthetic vs natural PM170453

Figure S51. ^1H NMR spectra of synthetic vs. natural **PM170453**.....**55**

Figure S1. ^1H NMR spectrum of **PM170453**, (500 MHz, CD_3OD).

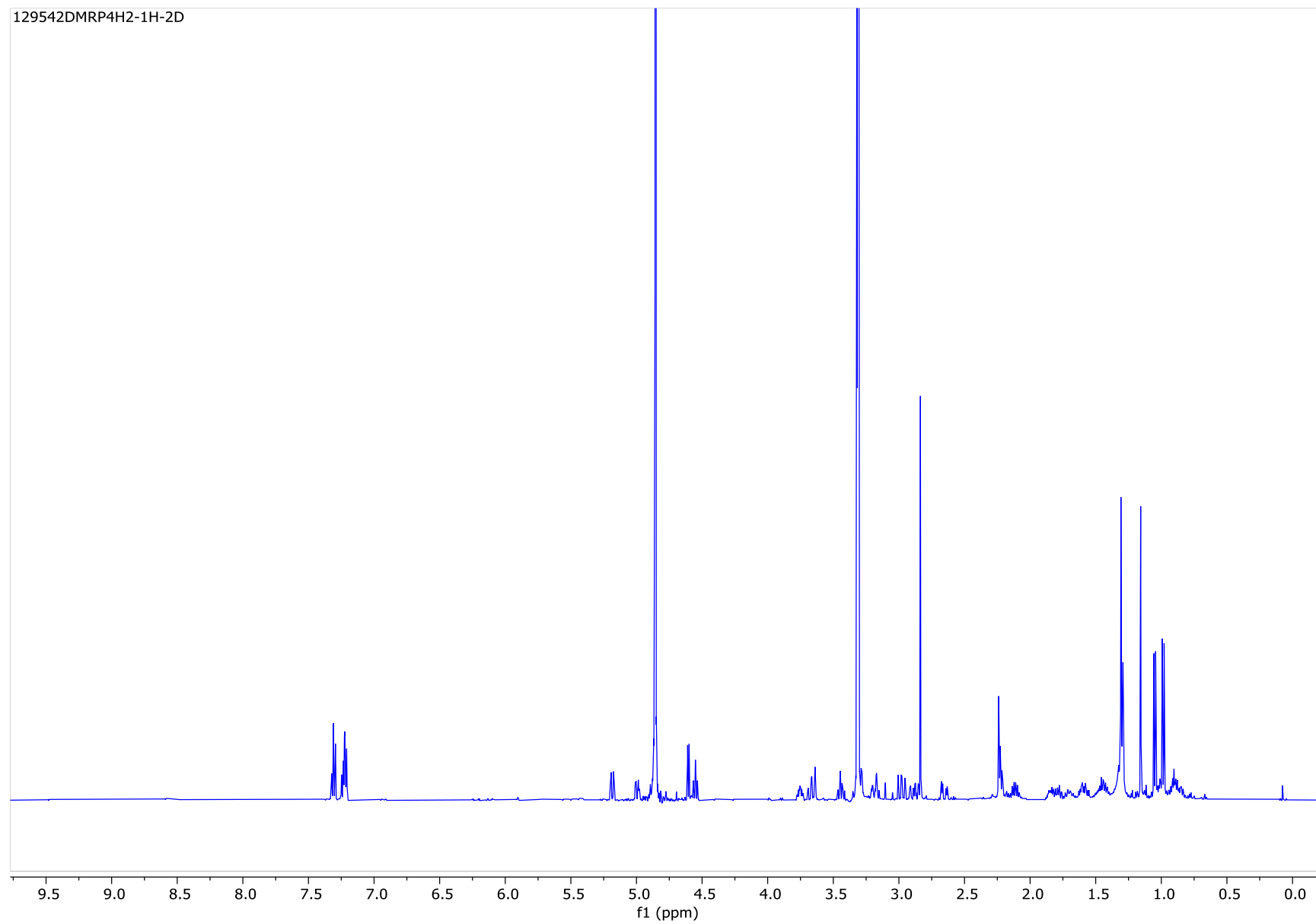


Figure S2. ^1H NMR spectrum of **PM170453**, (500 MHz, CD_3OH).

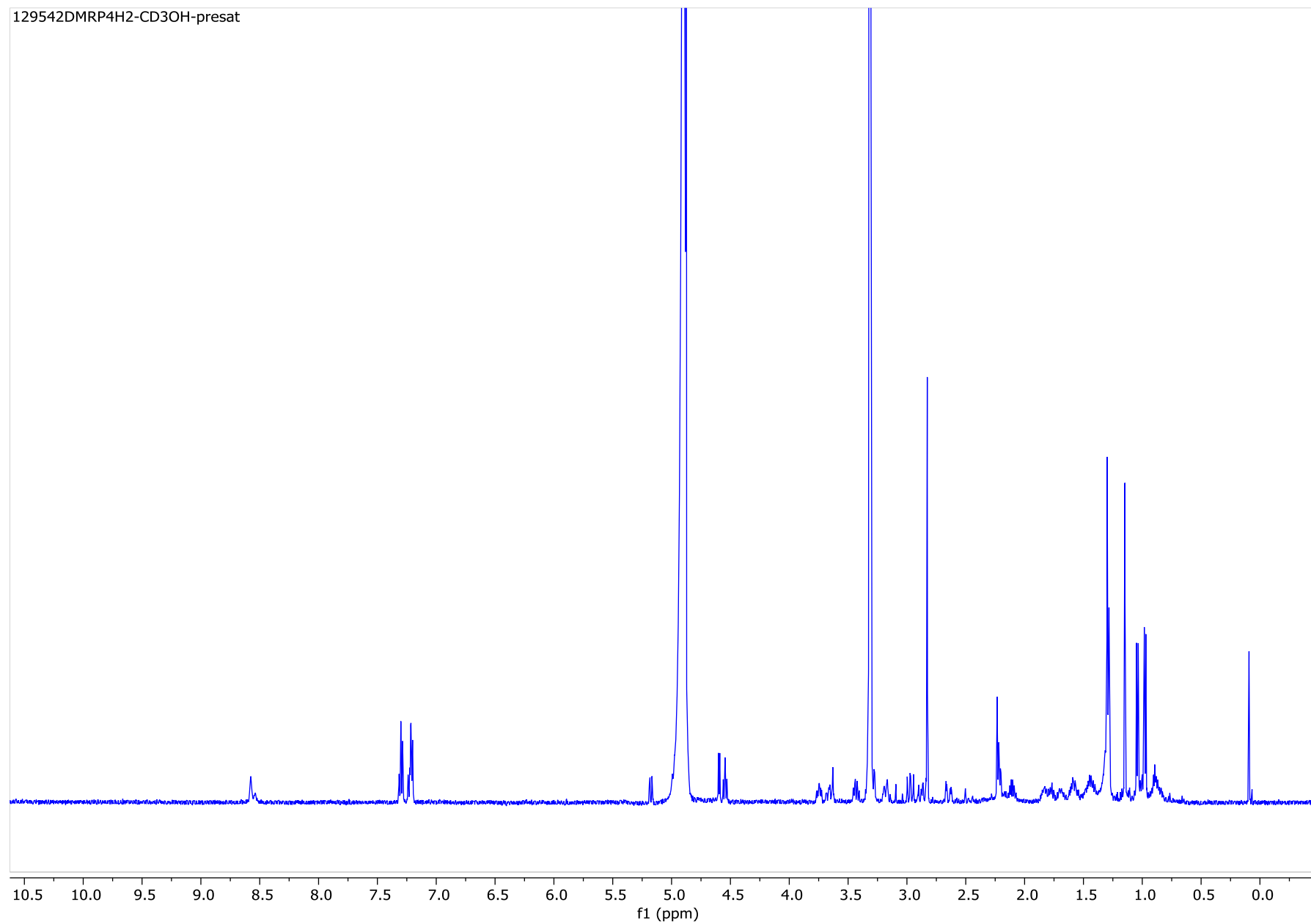


Figure S3. ^{13}C NMR spectrum of **PM170453**, (125 MHz, CD_3OD).

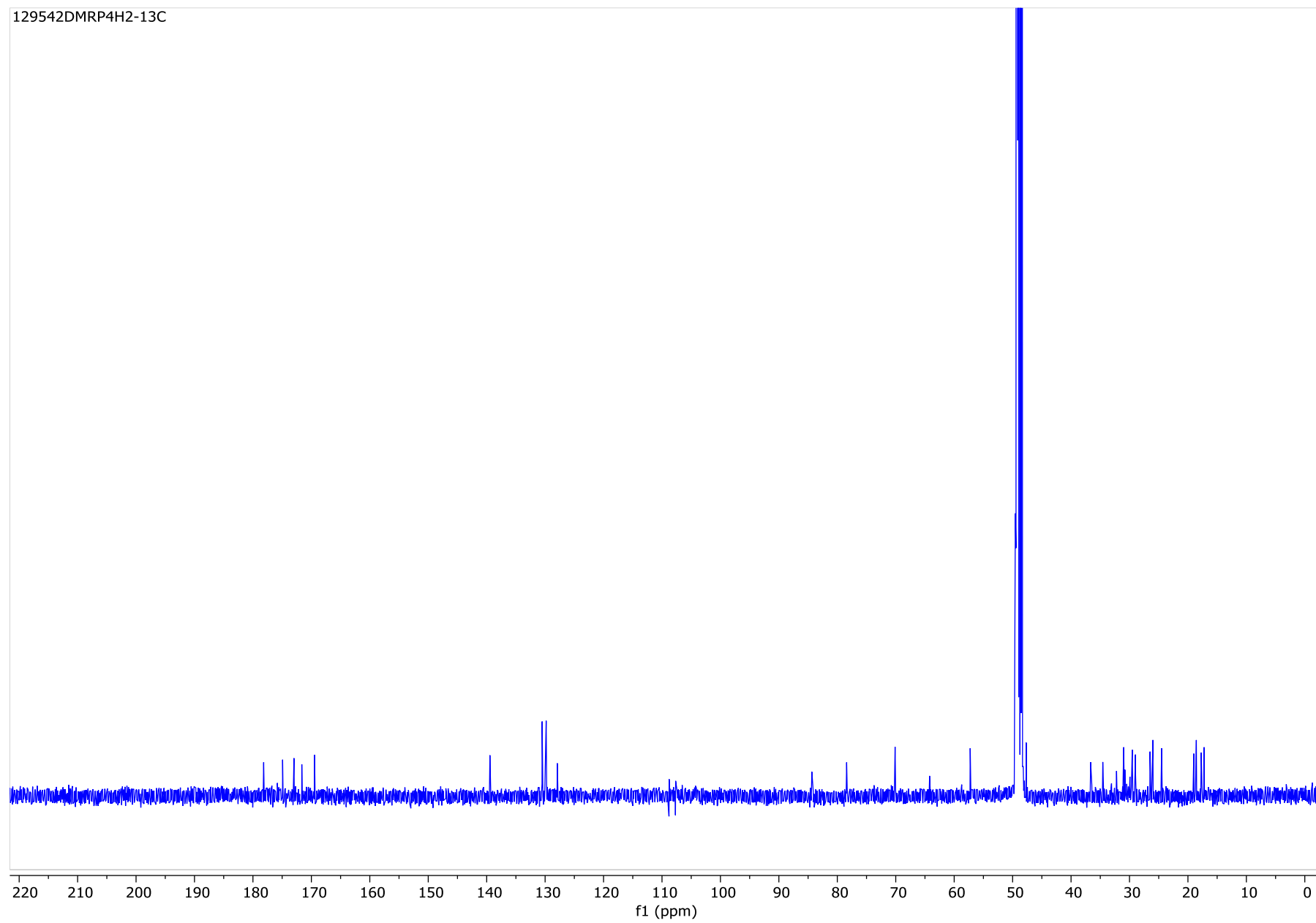


Figure S4. g-COSY spectrum of **PM170453**.

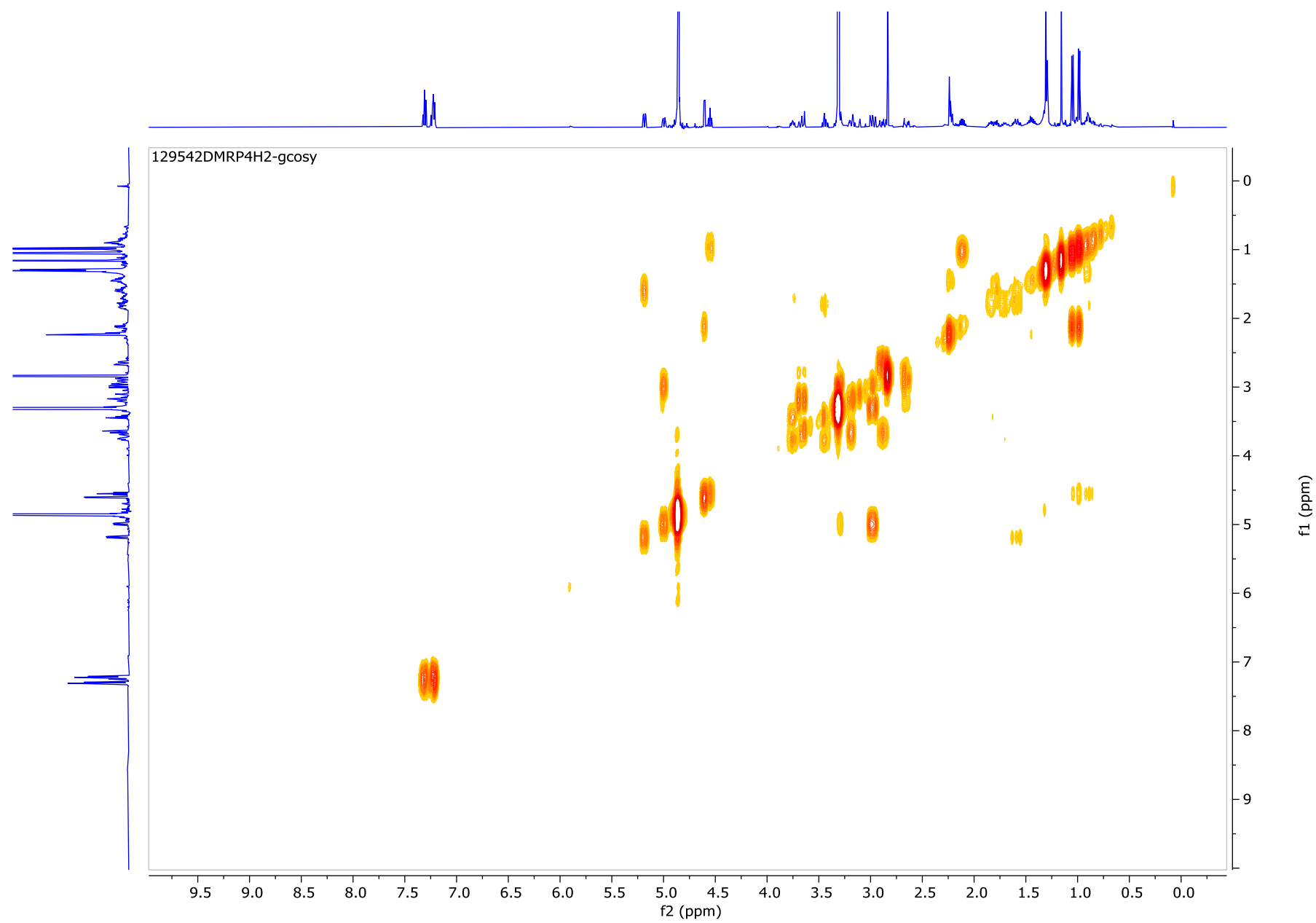


Figure S5. g-HSQC spectrum of **PM170453**

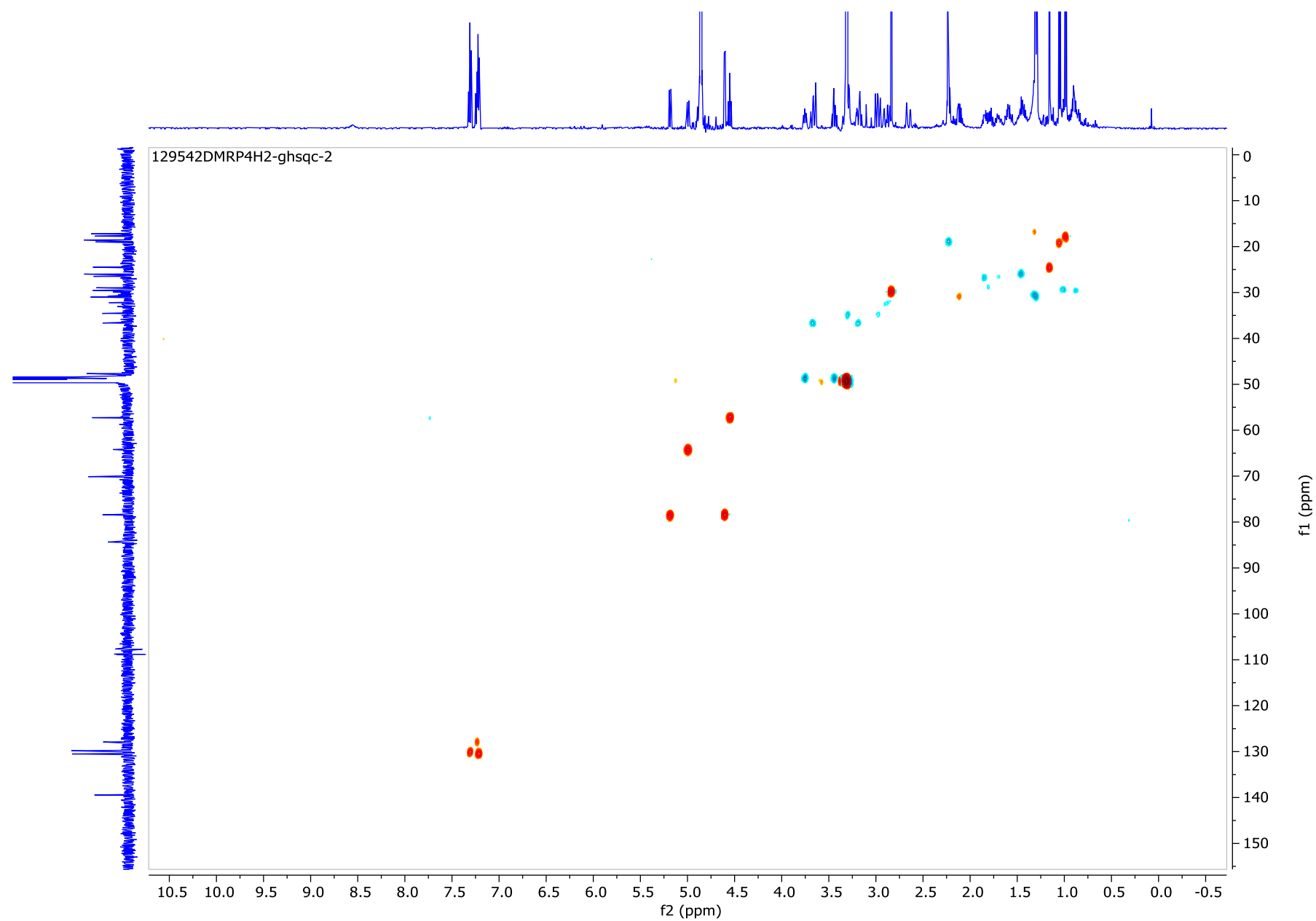


Figure S6. *g*-HSQC ($J = 250$ Hz) spectrum of **PM170453**.

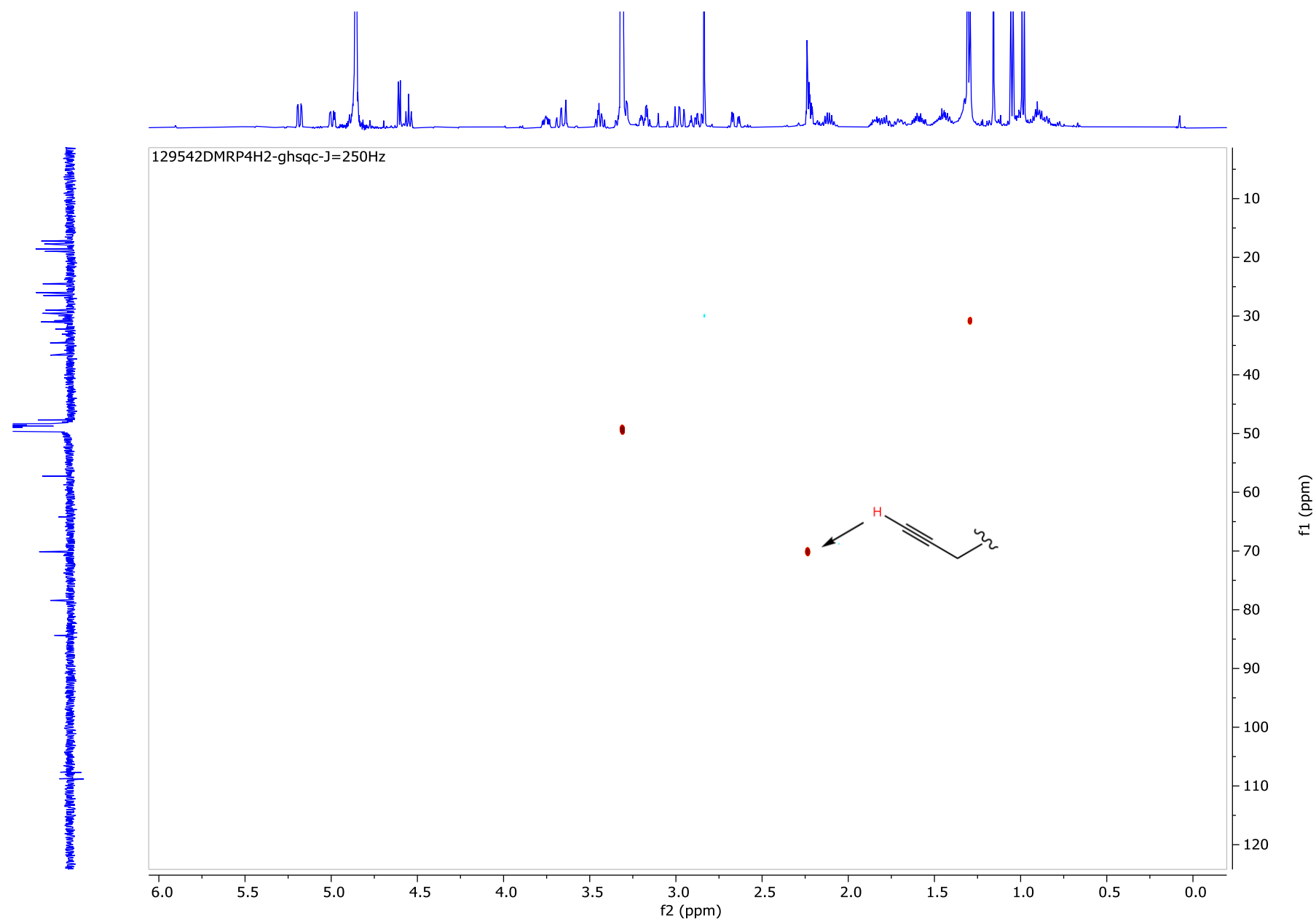


Figure S7. gHMBC spectrum of **PM170453**.

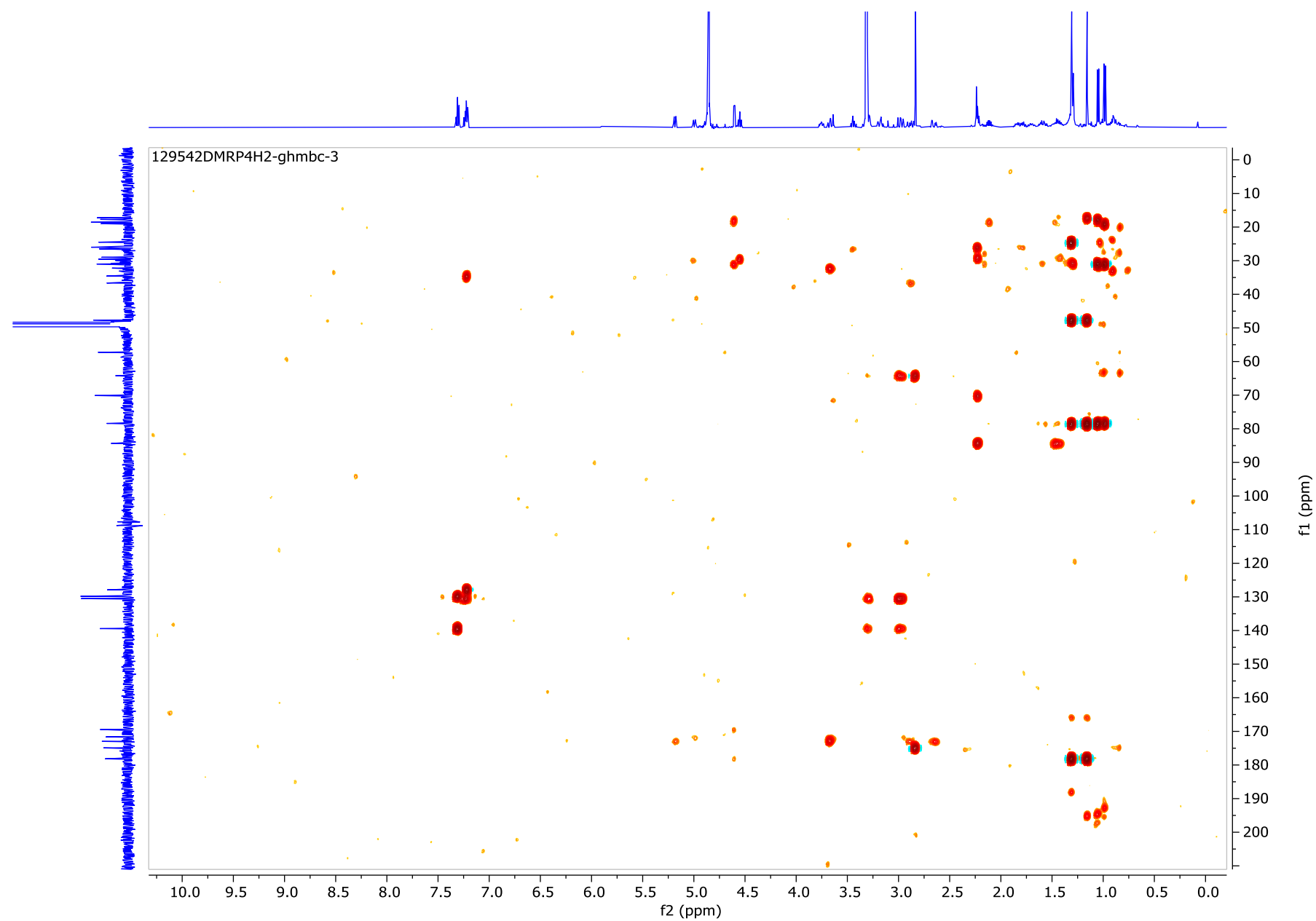


Figure S8. ROESY spectrum of **PM170453**.

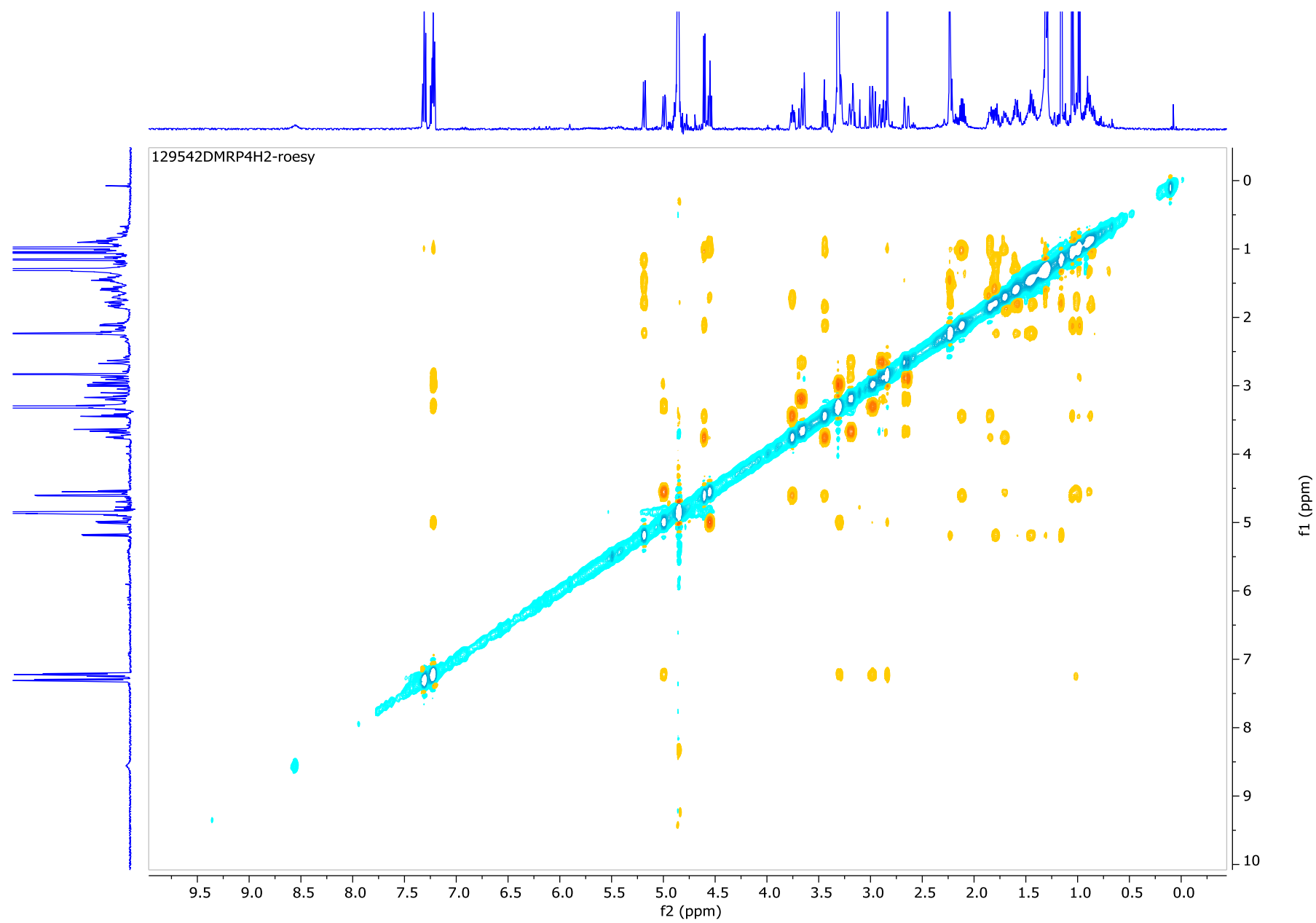


Figure S9. ROESY spectrum of **PM170453**. (CD₃OH).

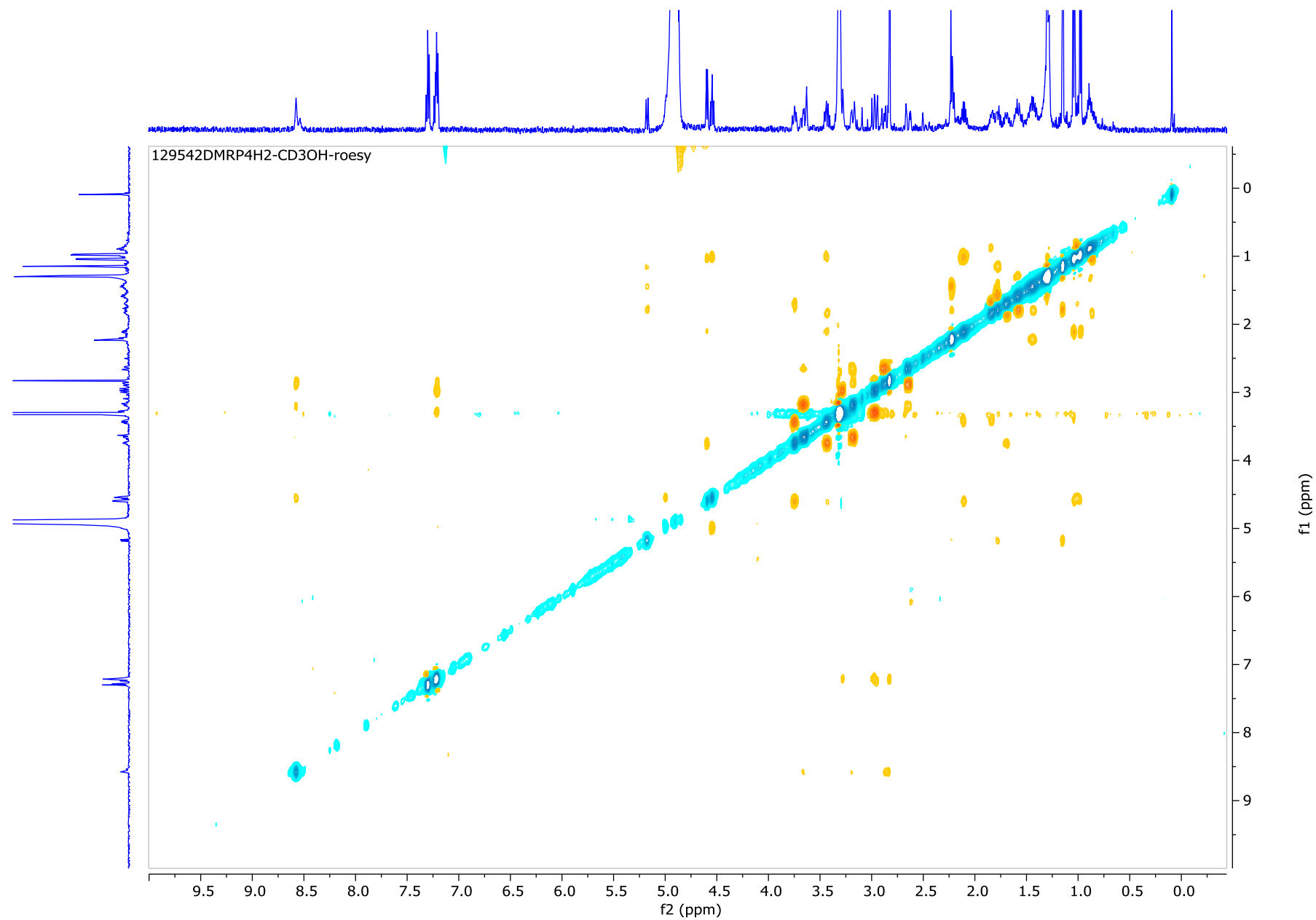


Figure S10. (+)-HRESITOFMS spectrum of **PM170453**.

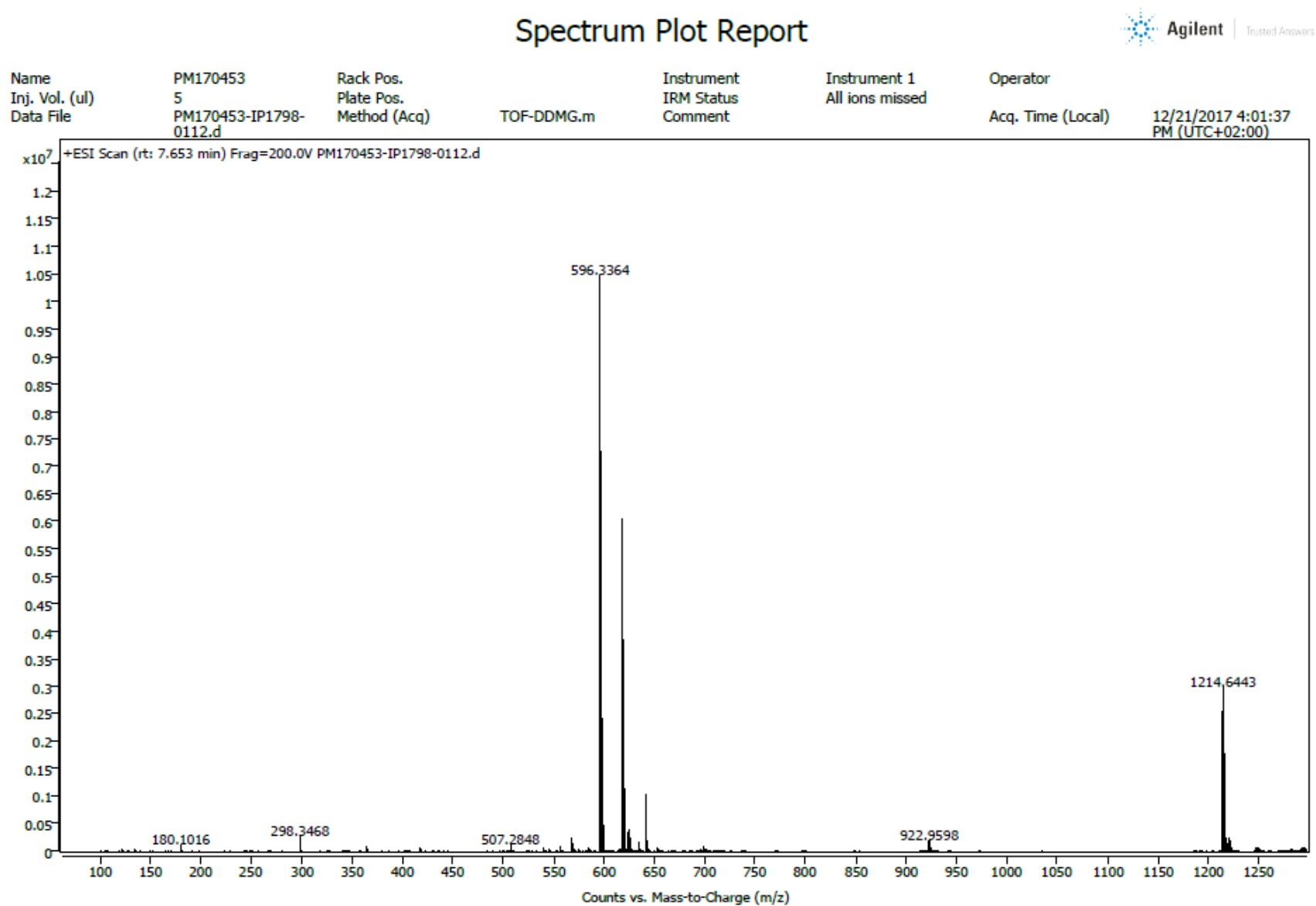


Figure S11. Dose-response curves for **1** in a panel of 4 tumour cell lines

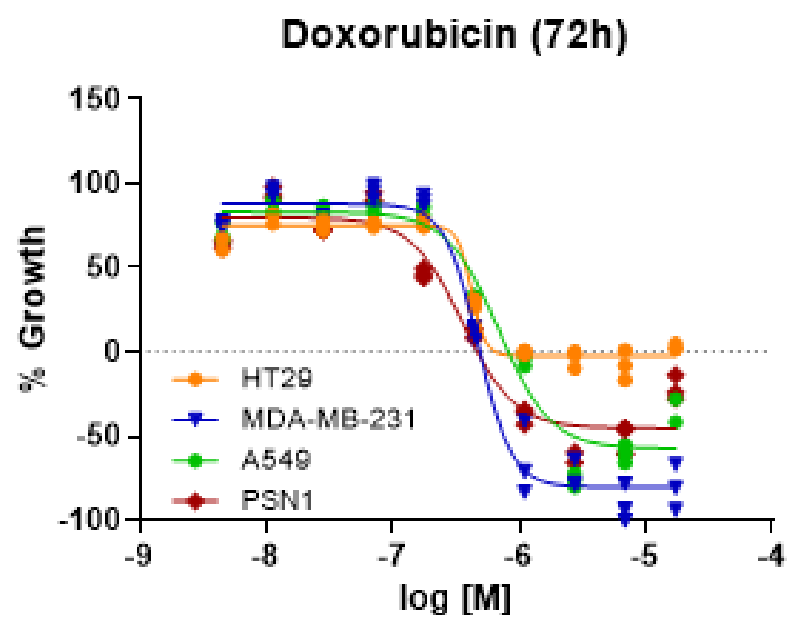
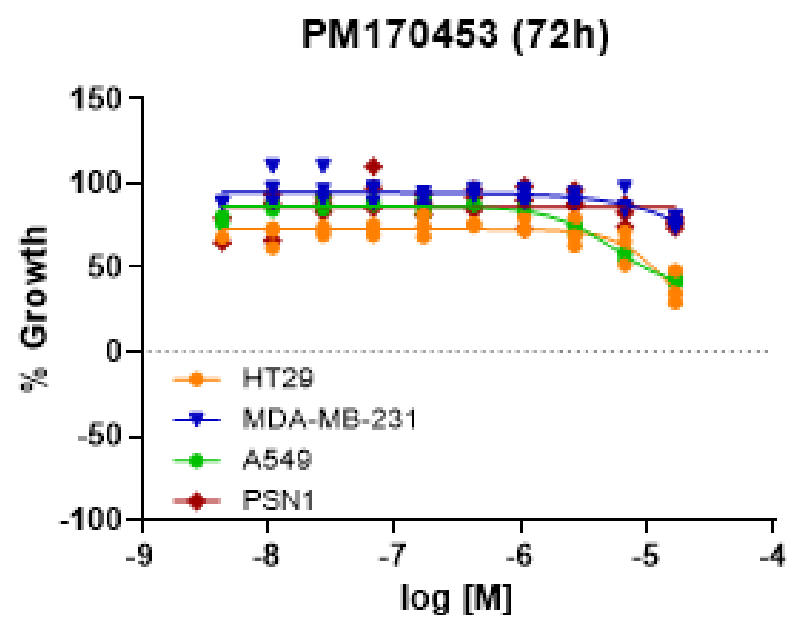


Figure S12. PD-1/PDL-1 interaction curves for **1**

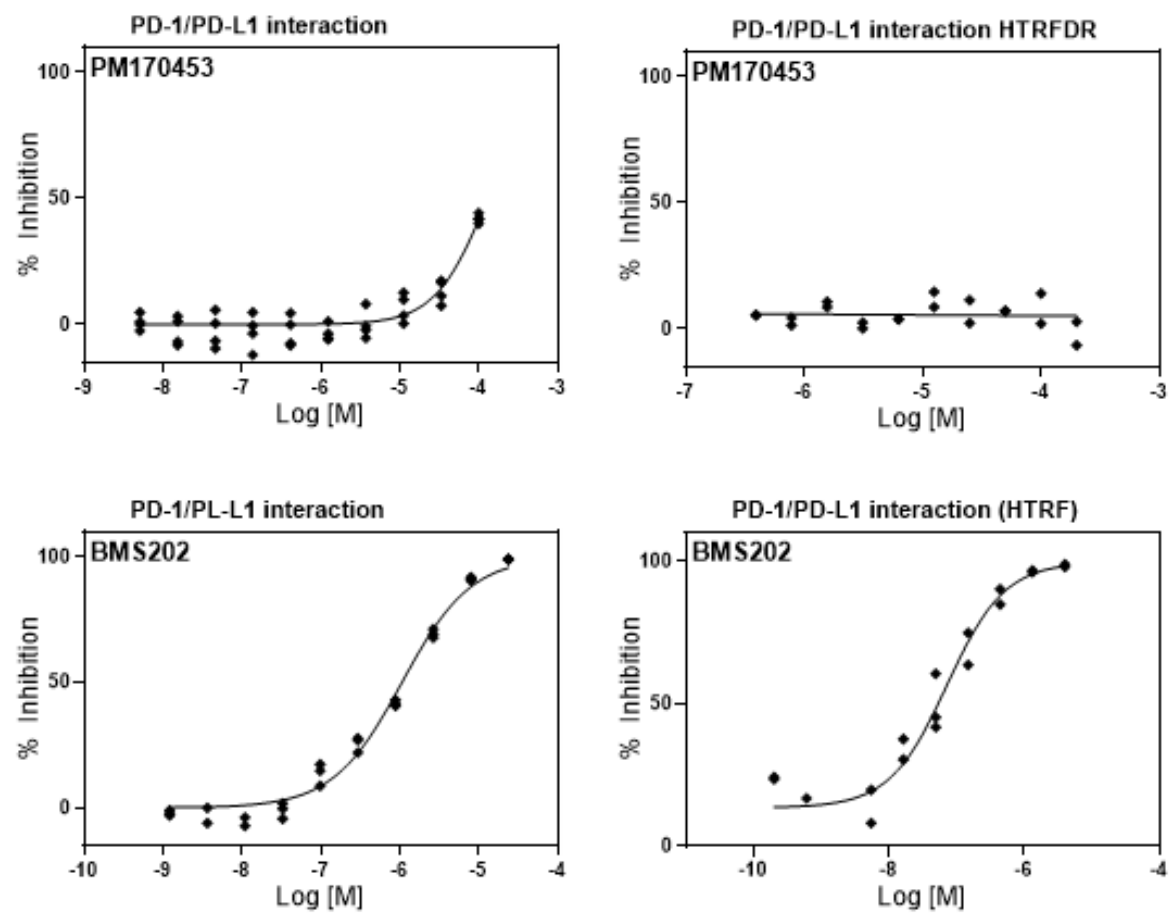


Figure S13. ^1H NMR spectrum of hex-5-ynal (**4**) (400 MHz, CDCl_3).

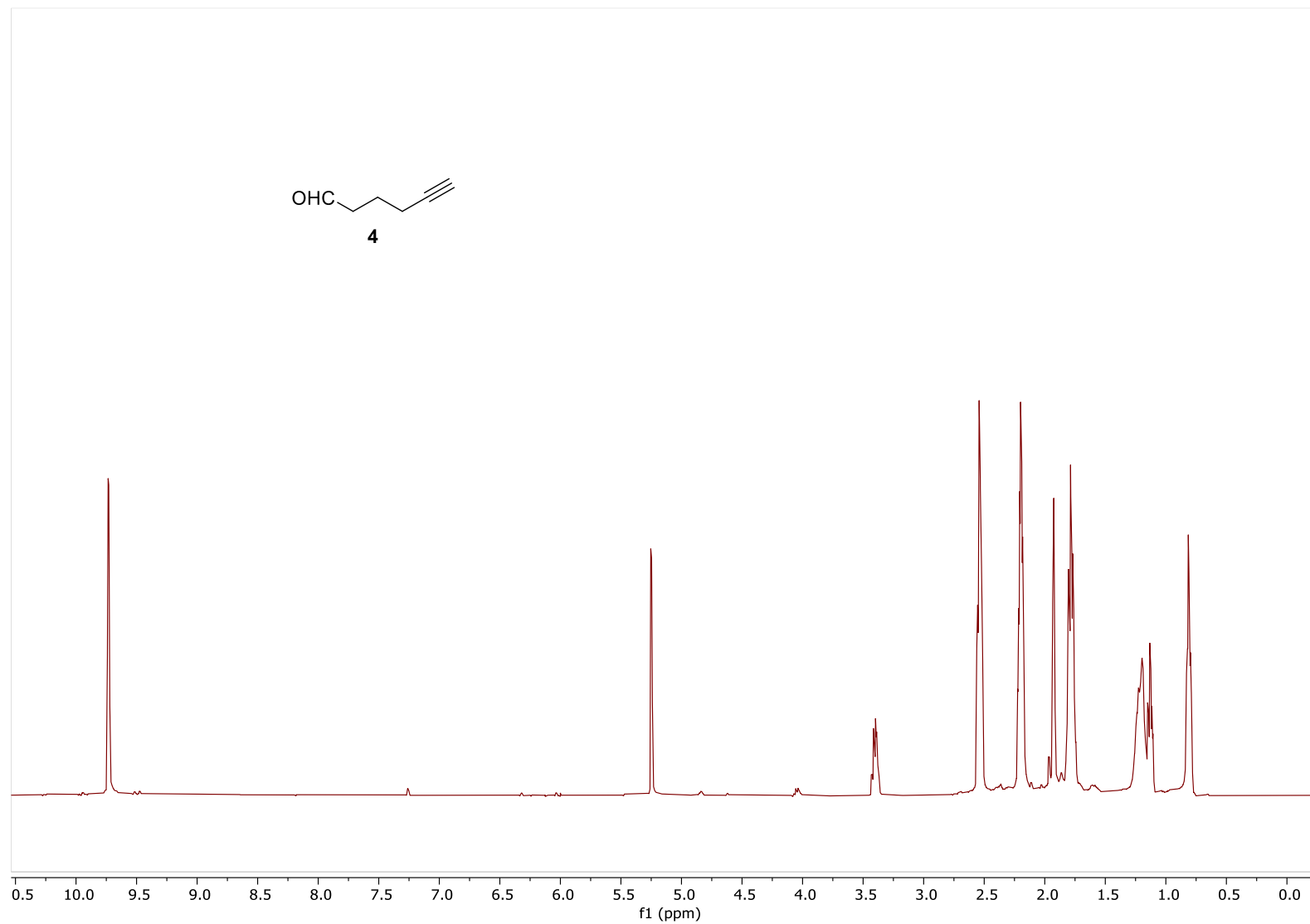


Figure S14. ^{13}C NMR spectrum of hex-5-ynal (**4**) (100 MHz, CDCl_3).

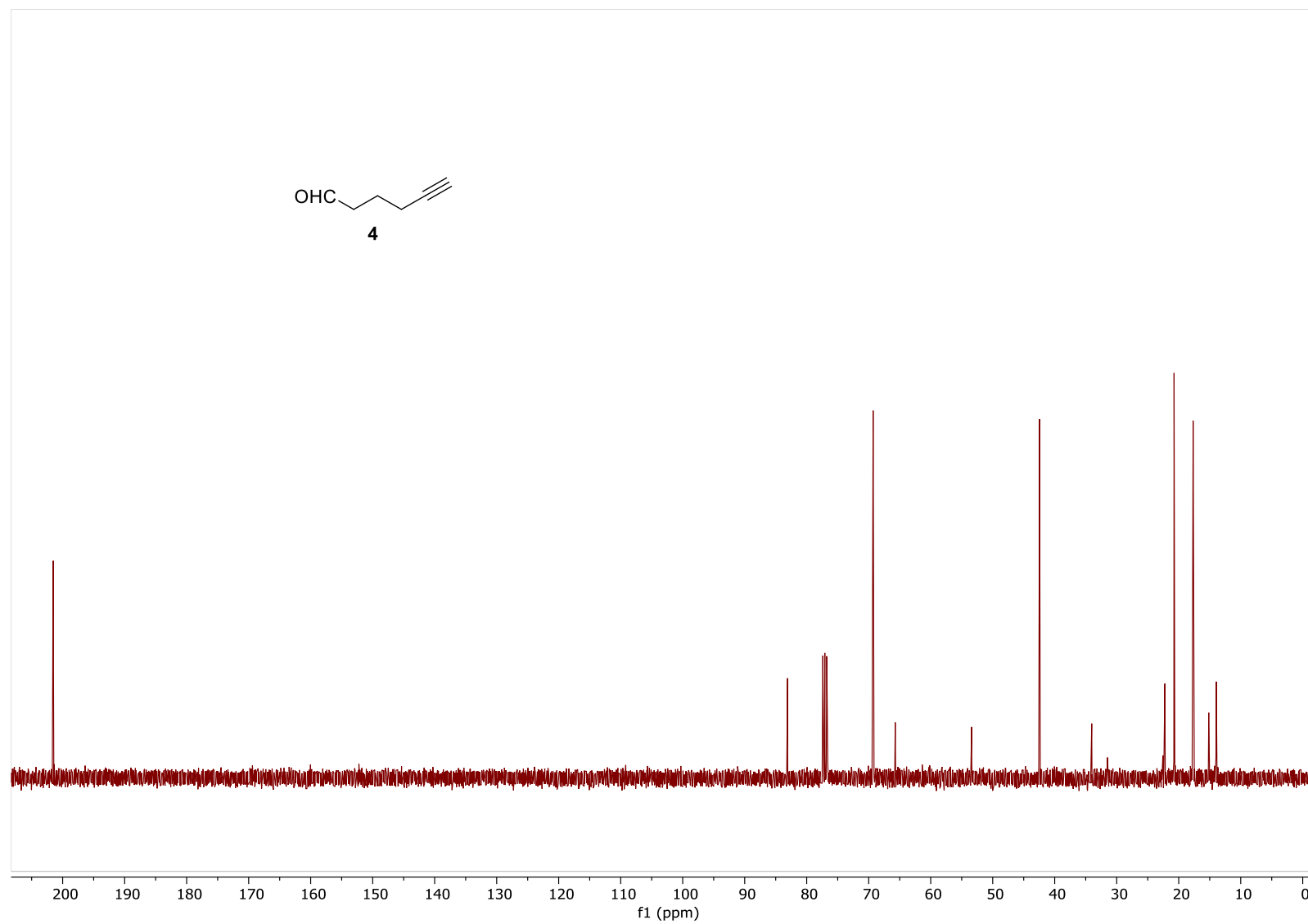


Figure S15. ^1H NMR spectrum of (*S*)-4-benzyl-3-isobutyryloxazolidin-2-one (**5**) (400 MHz, CDCl_3).

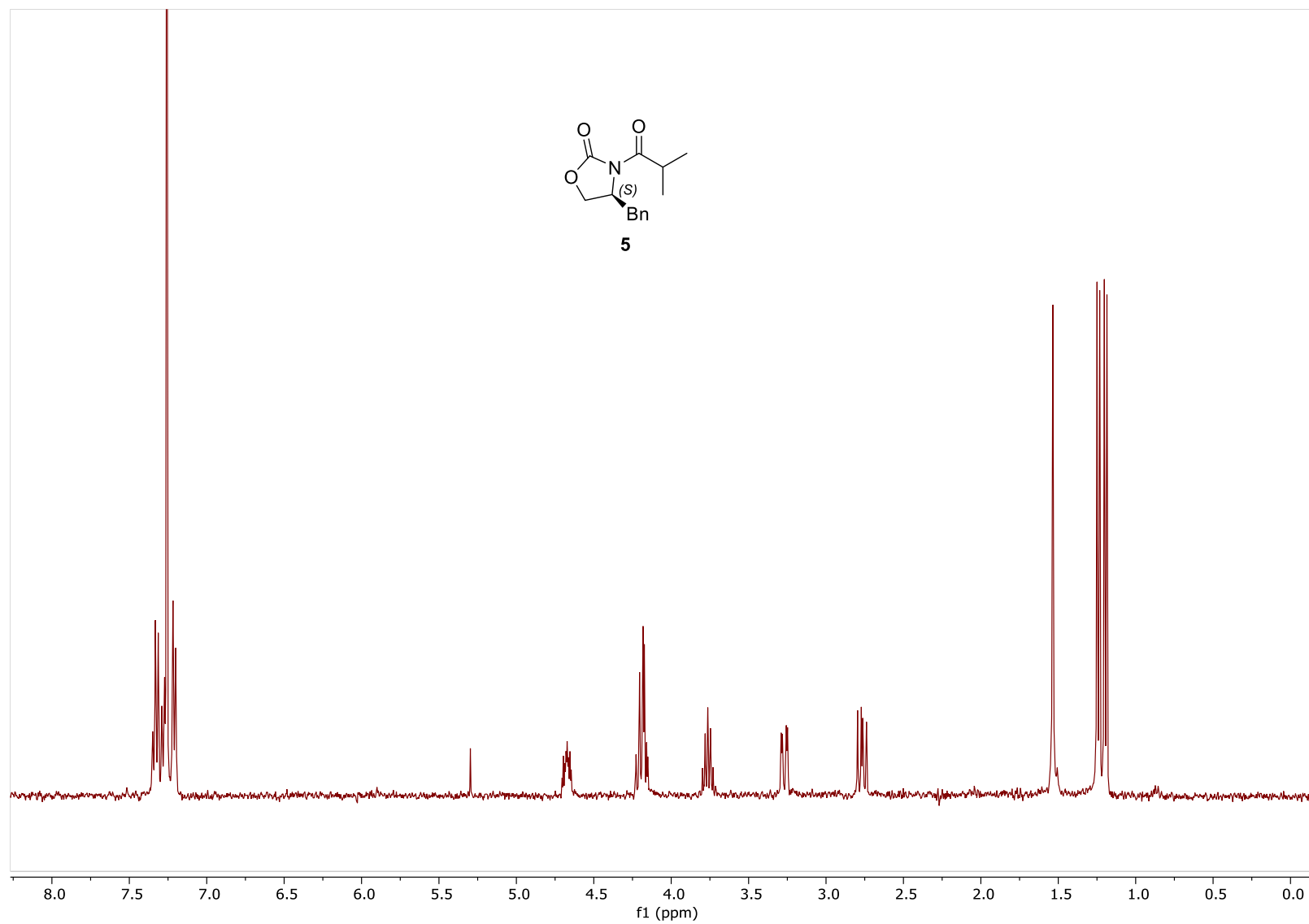


Figure S16. ^{13}C NMR spectrum of (*S*)-4-benzyl-3-isobutyryloxazolidin-2-one (**5**) (100 MHz, CDCl_3).

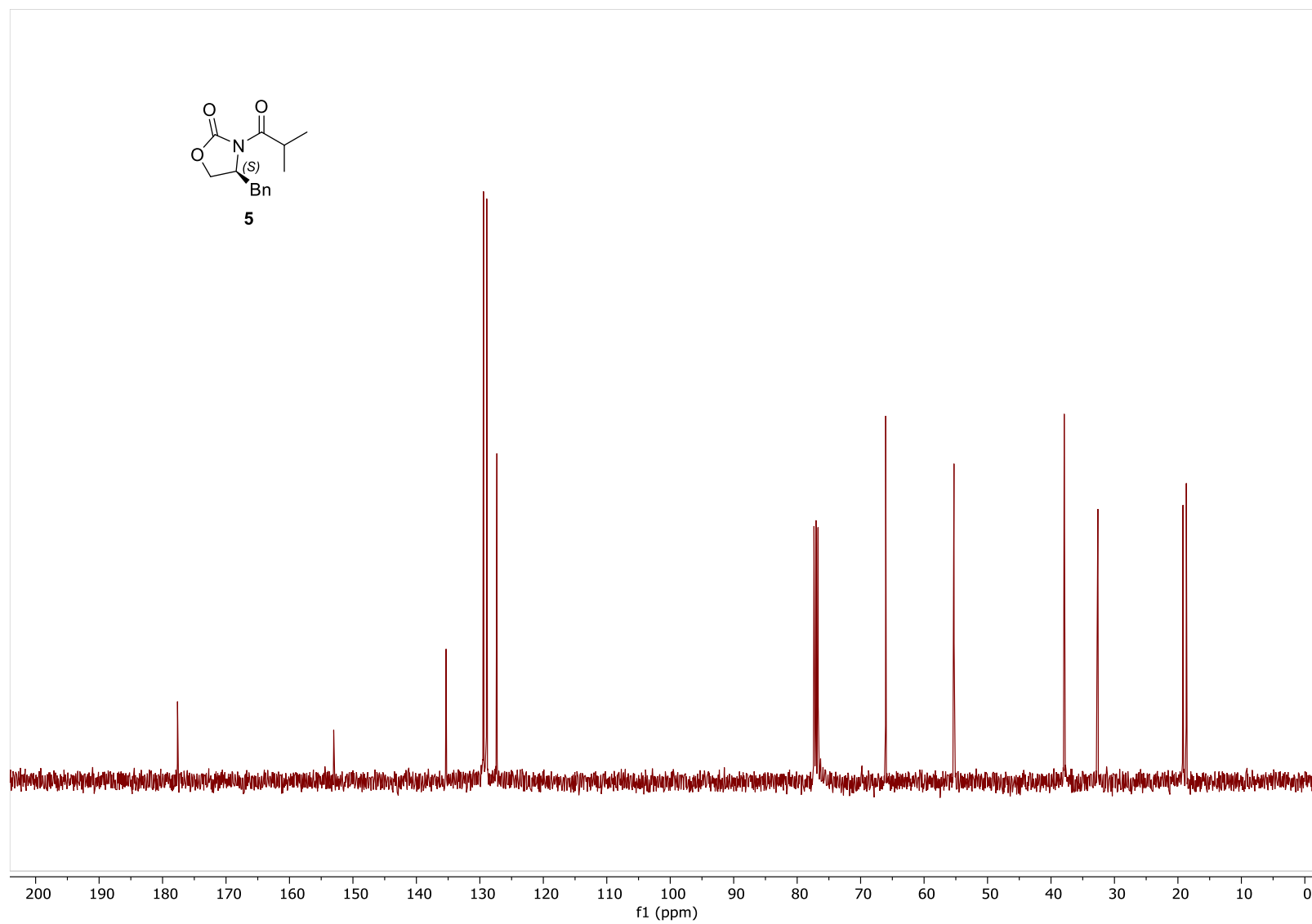


Figure S17. ^1H NMR spectrum of (*S*)-4-benzyl-3-((*S*)-3-hydroxy-2,2-dimethyloct-7-ynoyl)oxazolidin-2-one (**6**) (400 MHz, CDCl_3).

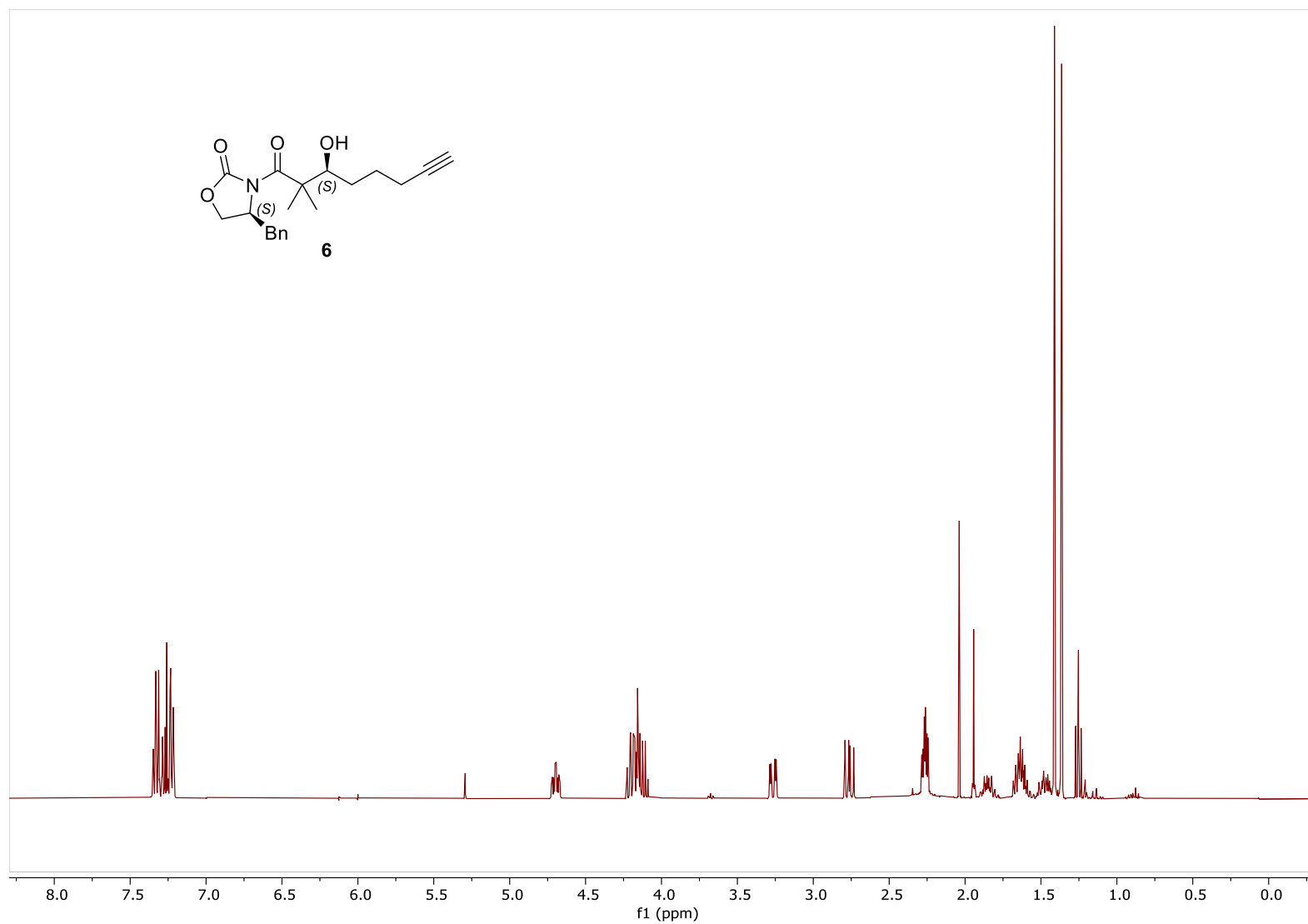


Figure S18. ^{13}C NMR spectrum of (*S*)-4-benzyl-3-((*S*)-3-hydroxy-2,2-dimethyloct-7-ynoyl)oxazolidin-2-one (**6**) (100 MHz, CDCl_3).

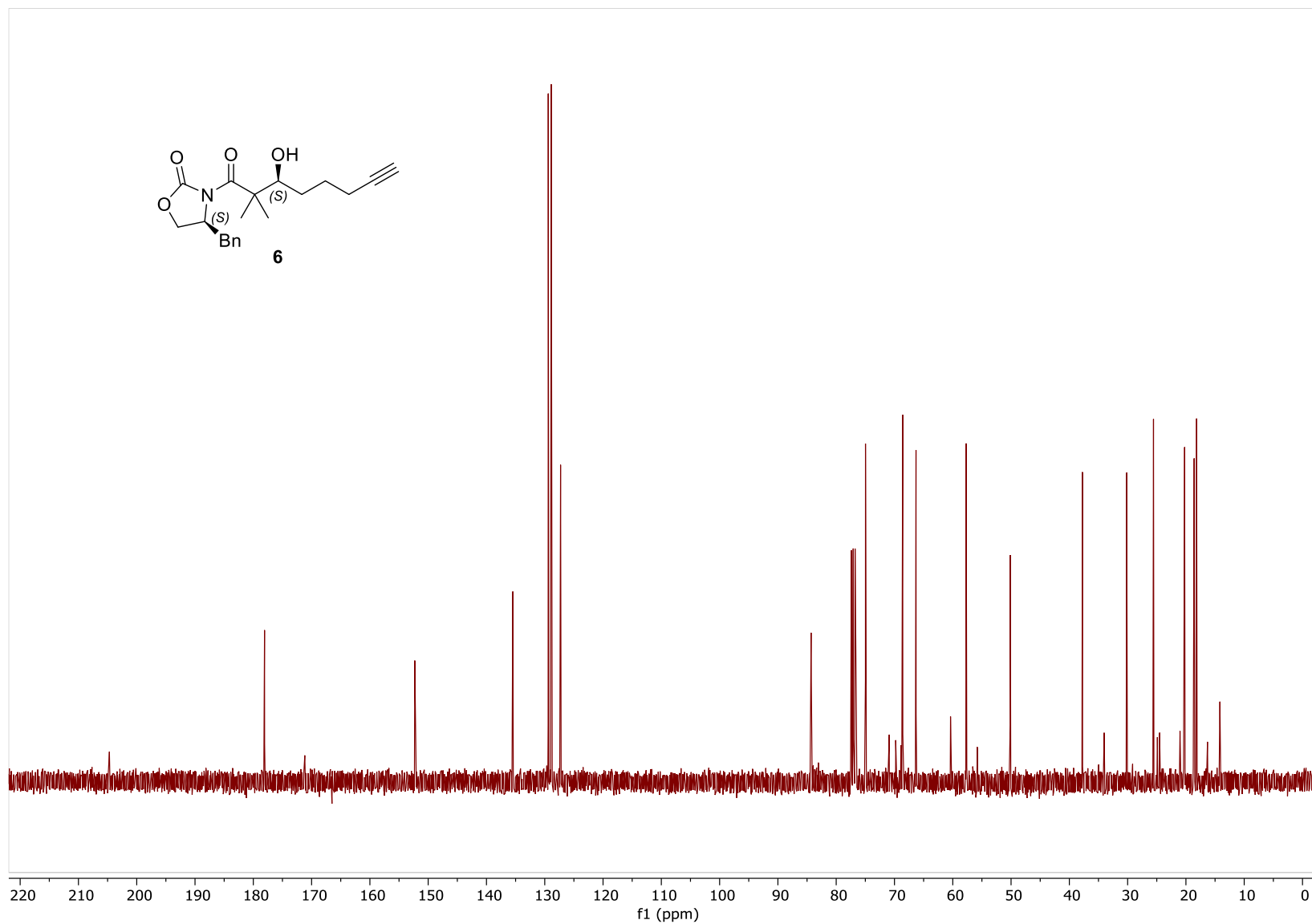


Figure S19. ^1H NMR spectrum of (*S*)-3-hydroxy-2,2-dimethyloct-7-ynoic acid (**7**) (400 MHz, CDCl_3).

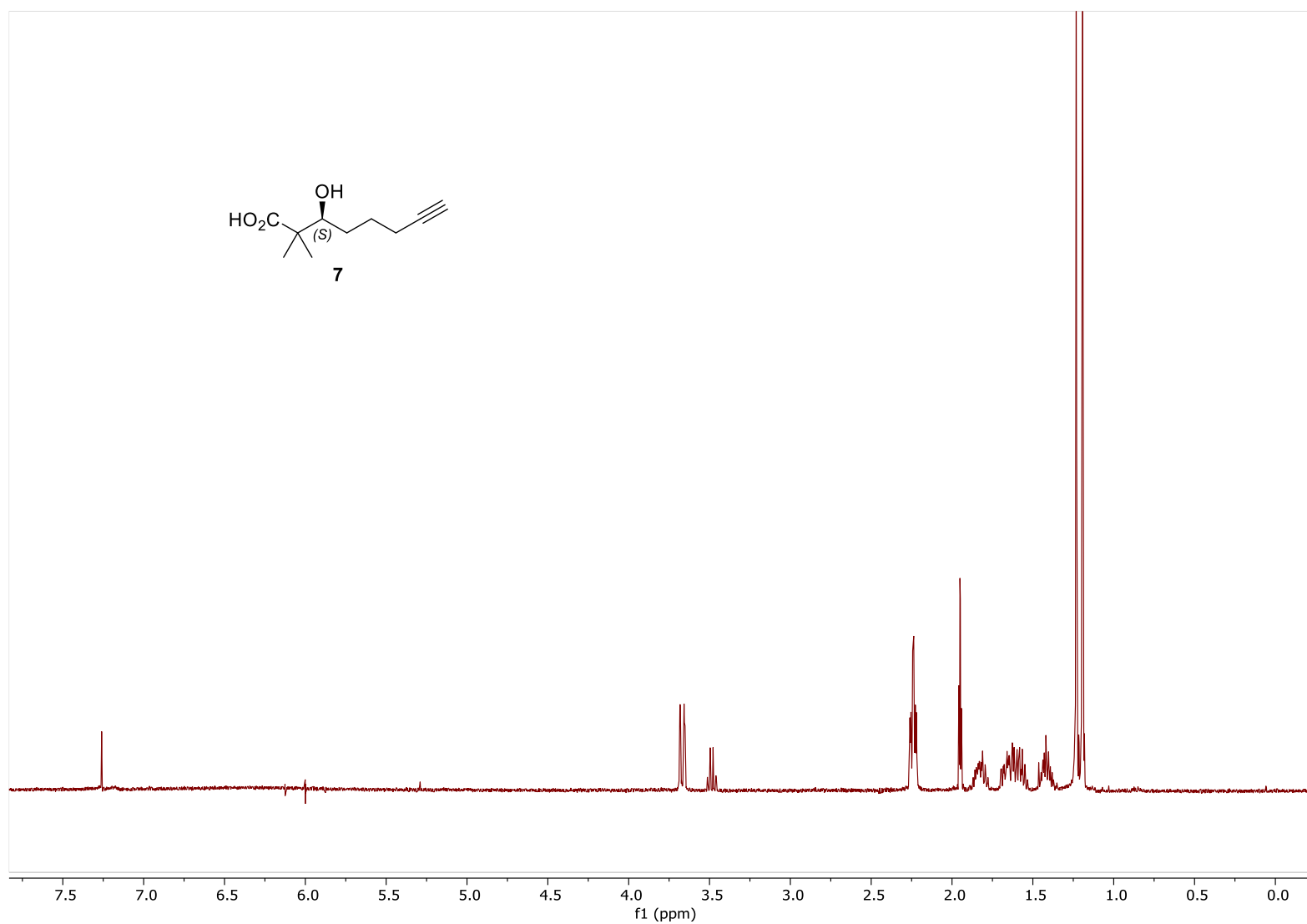


Figure S20. ^{13}C NMR spectrum of (*S*)-3-hydroxy-2,2-dimethyloct-7-ynoic acid (**7**) (100 MHz, CDCl_3).

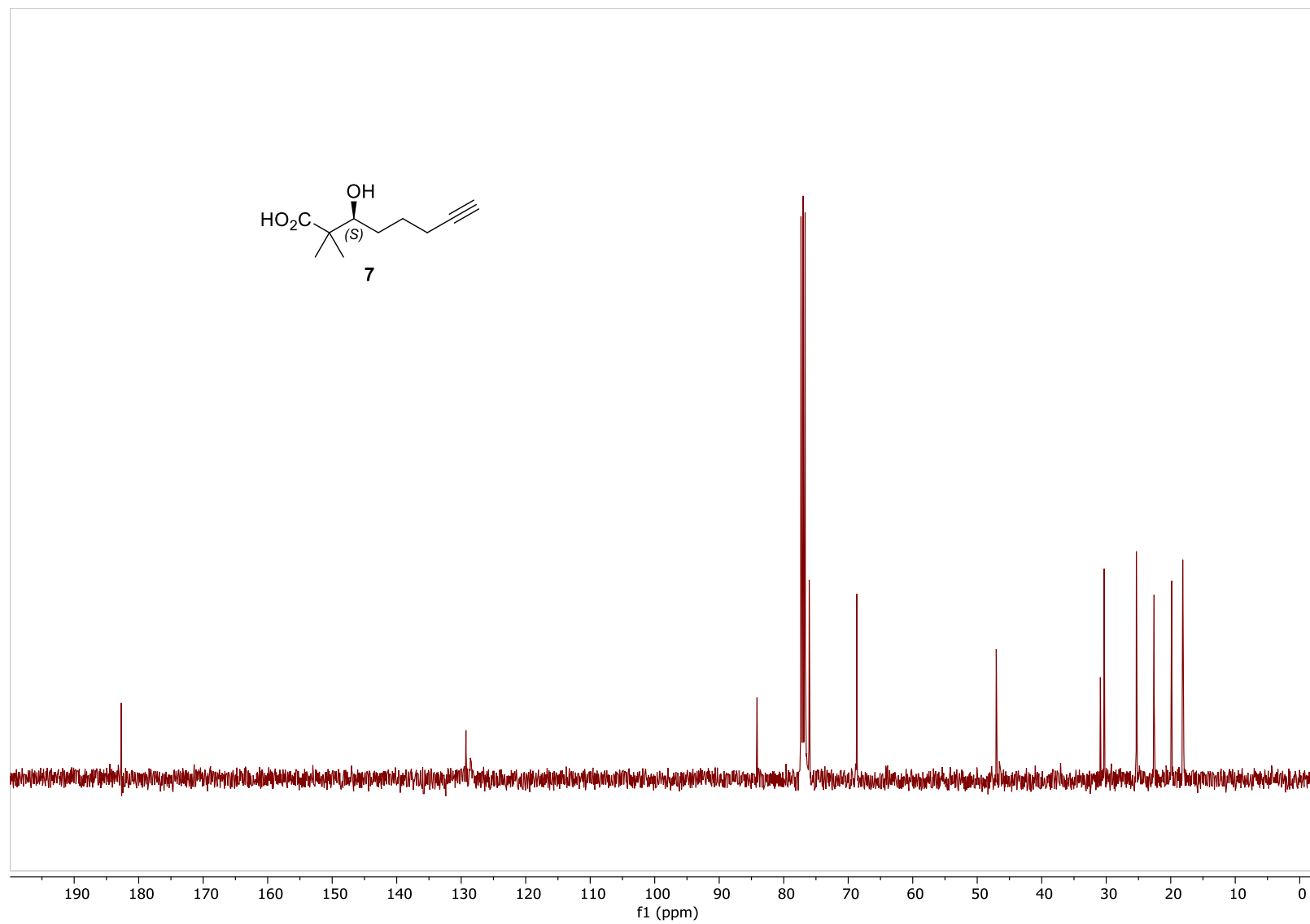


Figure S21. ^1H NMR spectrum of *tert*-butyldimethylsilyl (*S*)-3-((*tert*-butyldimethylsilyl)oxy)-2,2-dimethyloct-7-ynoate (**8**) (400 MHz, CDCl_3).

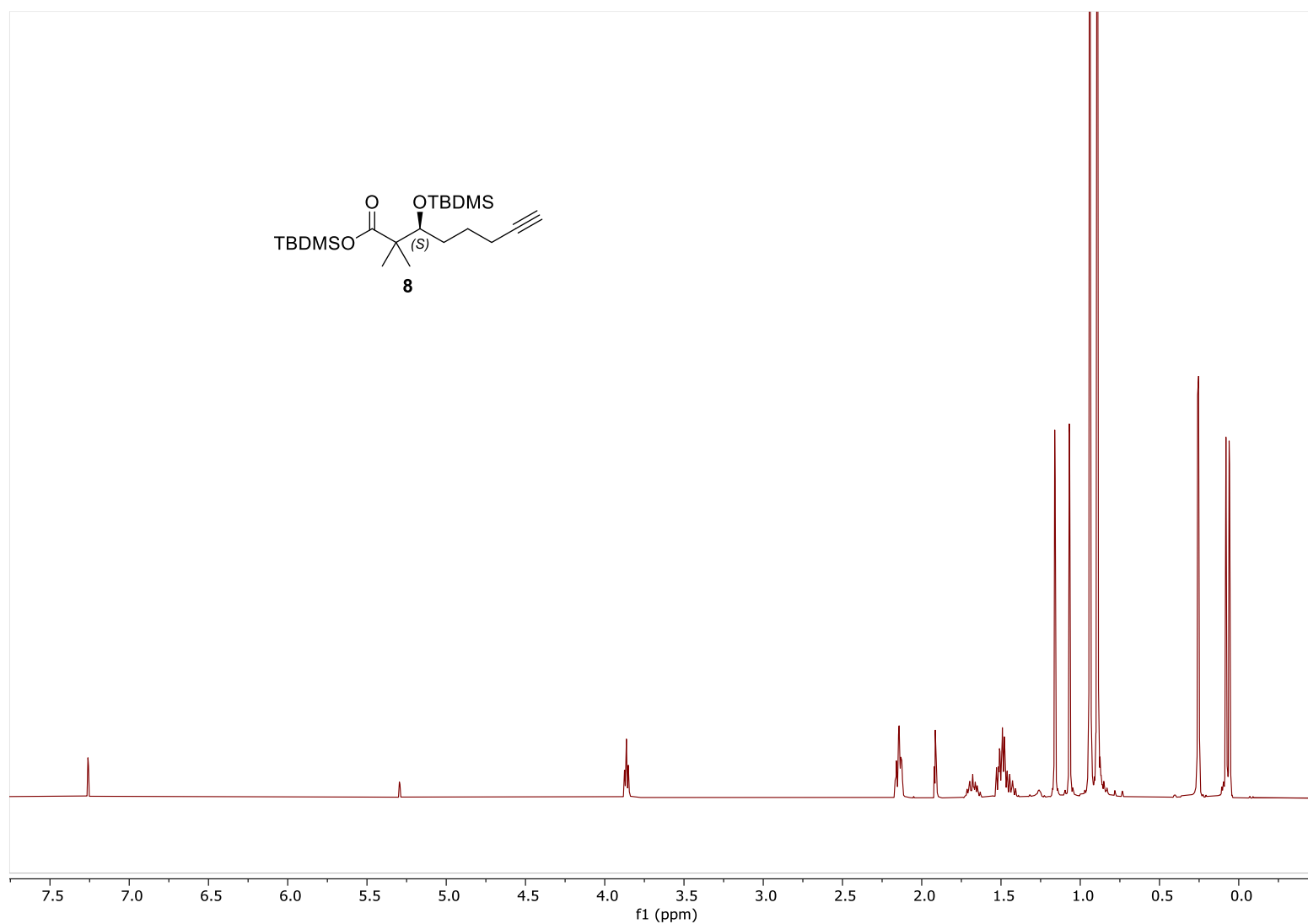
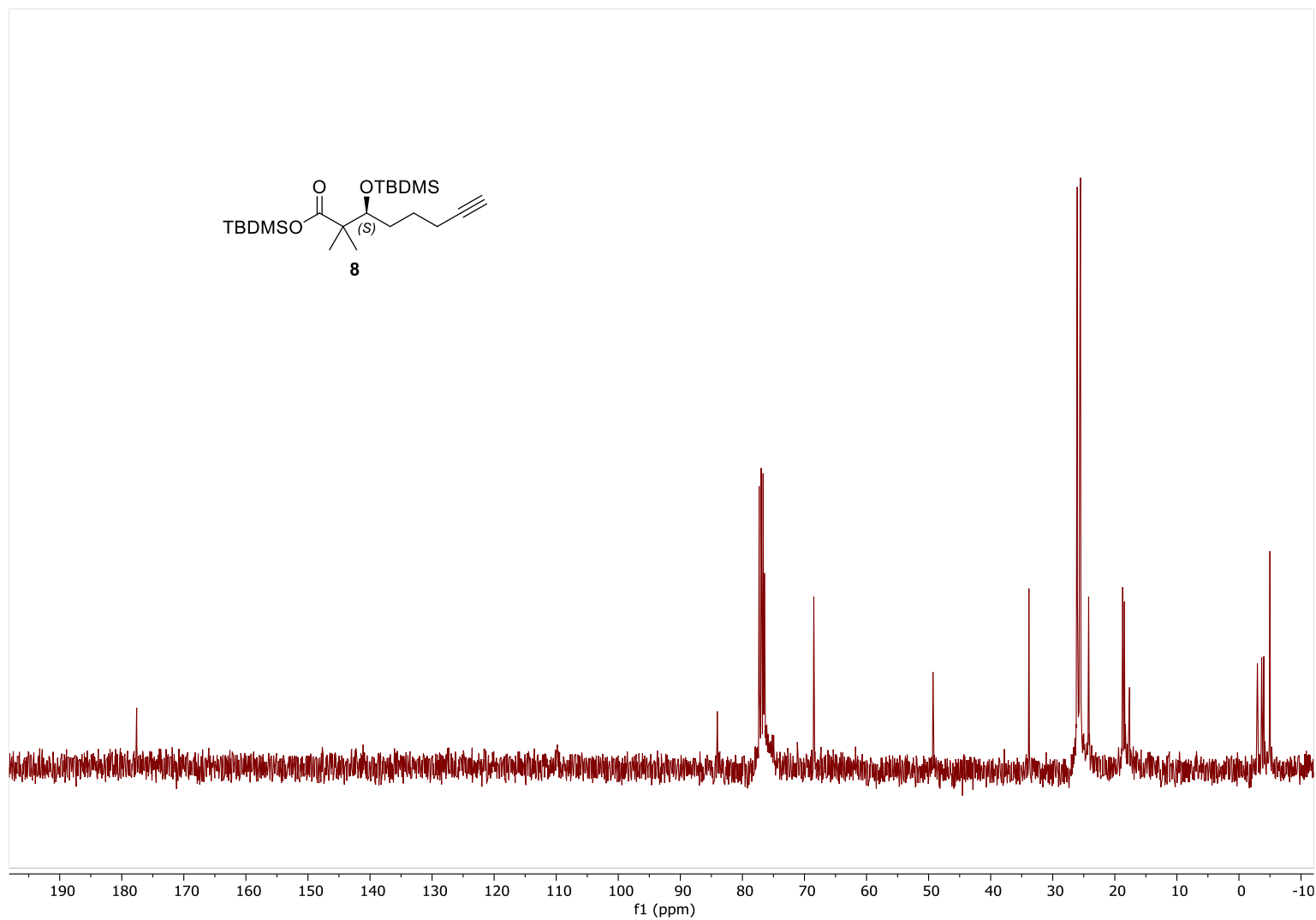


Figure S22. ^{13}C NMR spectrum of *tert*-butyldimethylsilyl (*S*)-3-((*tert*-butyldimethylsilyl)oxy)-2,2-dimethyloct-7-ynoate (**8**) (100 MHz, CDCl_3).



Chemical structure of compound **2** is shown above the spectrum. The structure is a substituted cyclohexane with a carboxylic acid group (HO₂C), a tert-butyldimethylsilyl ether (OTBDMS) group, and an ethynyl group (C≡CH).

Figure S24. ^{13}C NMR spectrum of (*S*)-3-((*tert*-butyldimethylsilyl)oxy)-2,2-dimethyloct-7-ynoic acid (**2**) (100 MHz, CD_3OD).

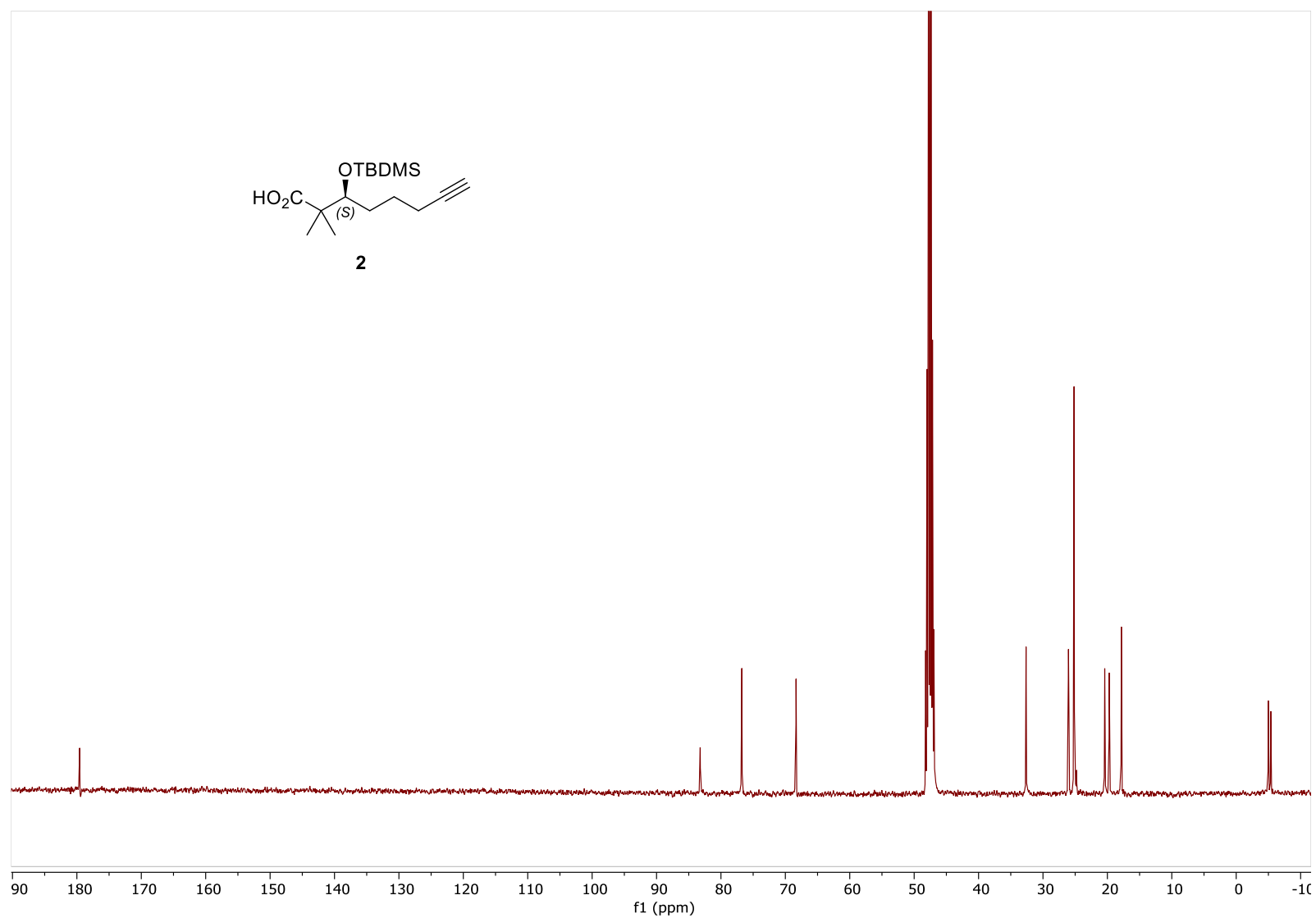


Figure S26. ^{13}C NMR spectrum of *tert*-butyldimethylsilyl (*S*)-2-((*tert*-butyldimethylsilyl)oxy)-3-methylbutanoate (**9**) (100 MHz, CDCl_3).

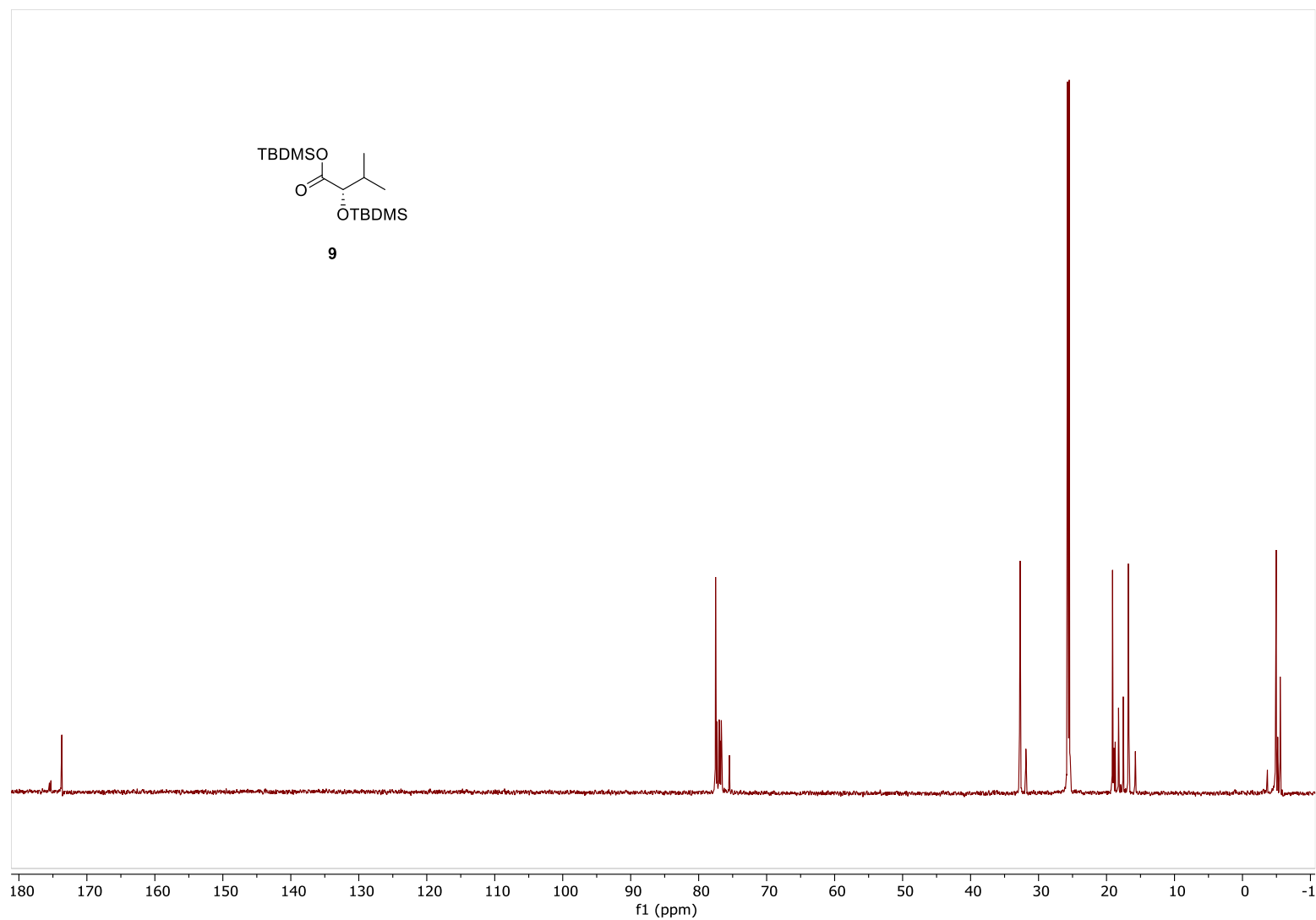


Figure S27. ^1H NMR spectrum of (*S*)-2-((*tert*-butyldimethylsilyl)oxy)-3-methylbutanoic acid (**10**) (400 MHz, CDCl_3).

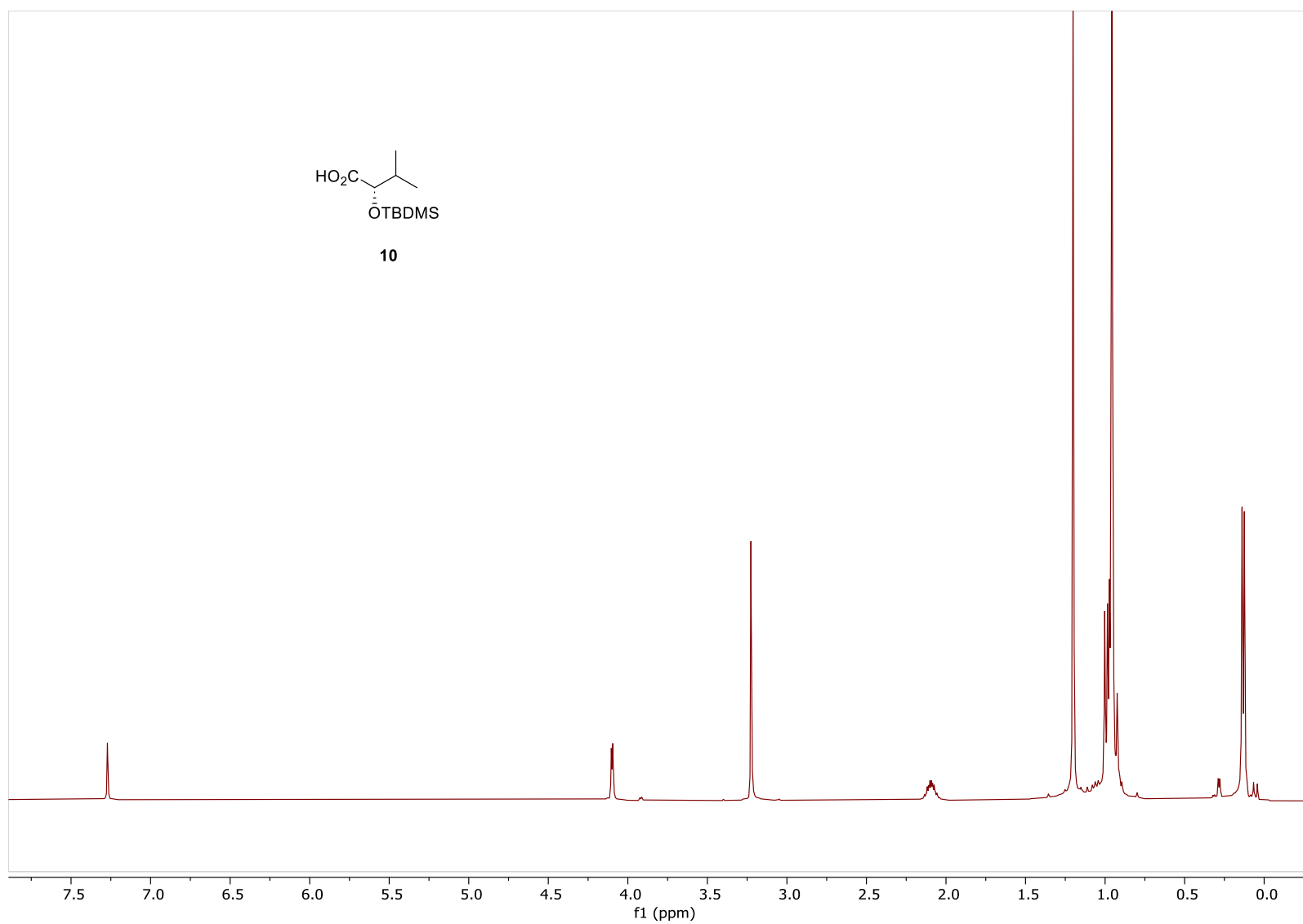


Figure S29. ^{13}C NMR spectrum of (*S*)-2-((*tert*-butyldimethylsilyl)oxy)-3-methylbutanoic acid (**10**) (100 MHz, CDCl_3).

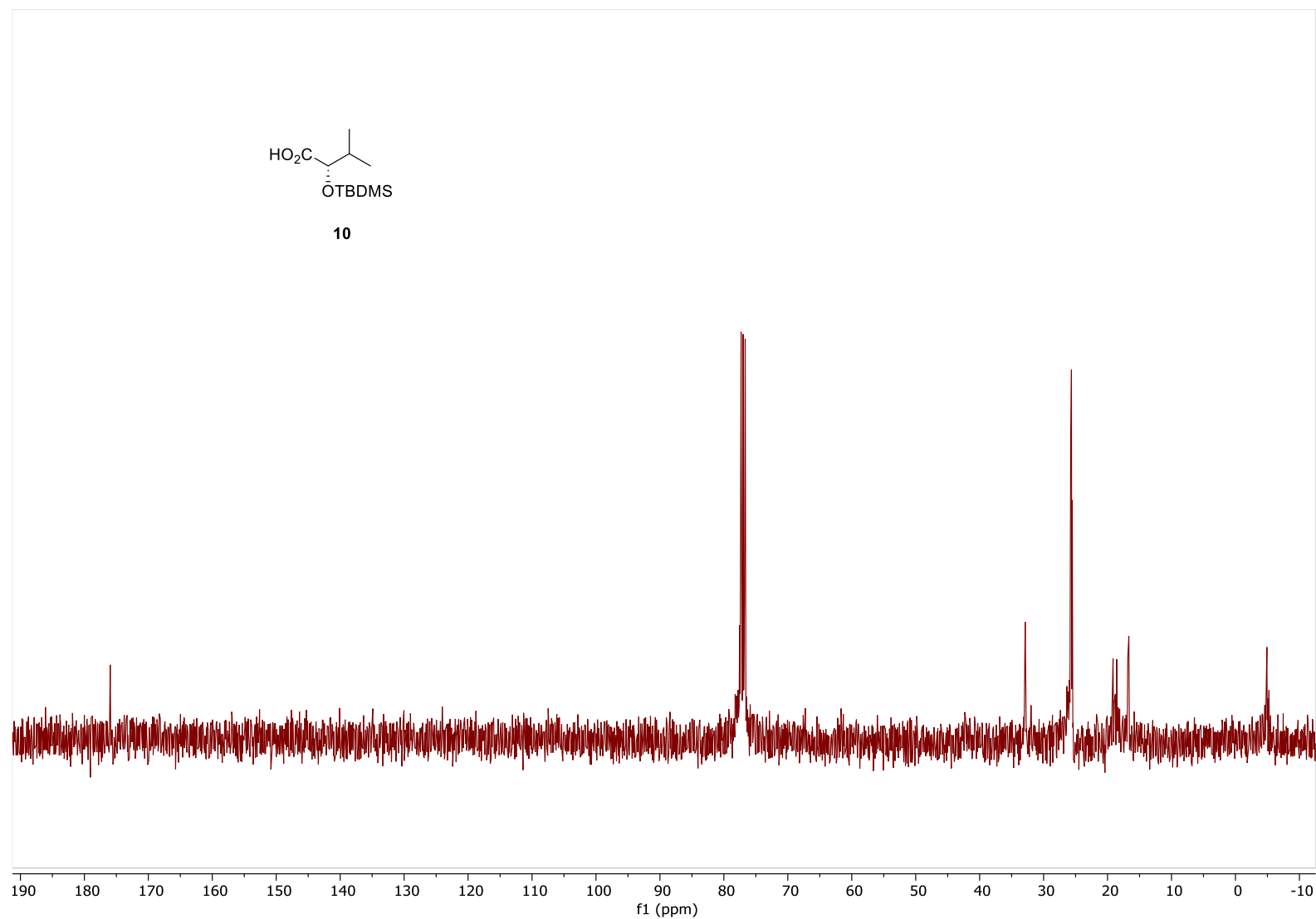


Figure S29. ^1H NMR spectrum of benzyl ((*S*)-2-((*tert*-butyldimethylsilyl)oxy)-3-methylbutanoyl)-L-prolinate (**11**) (400 MHz, CDCl_3).

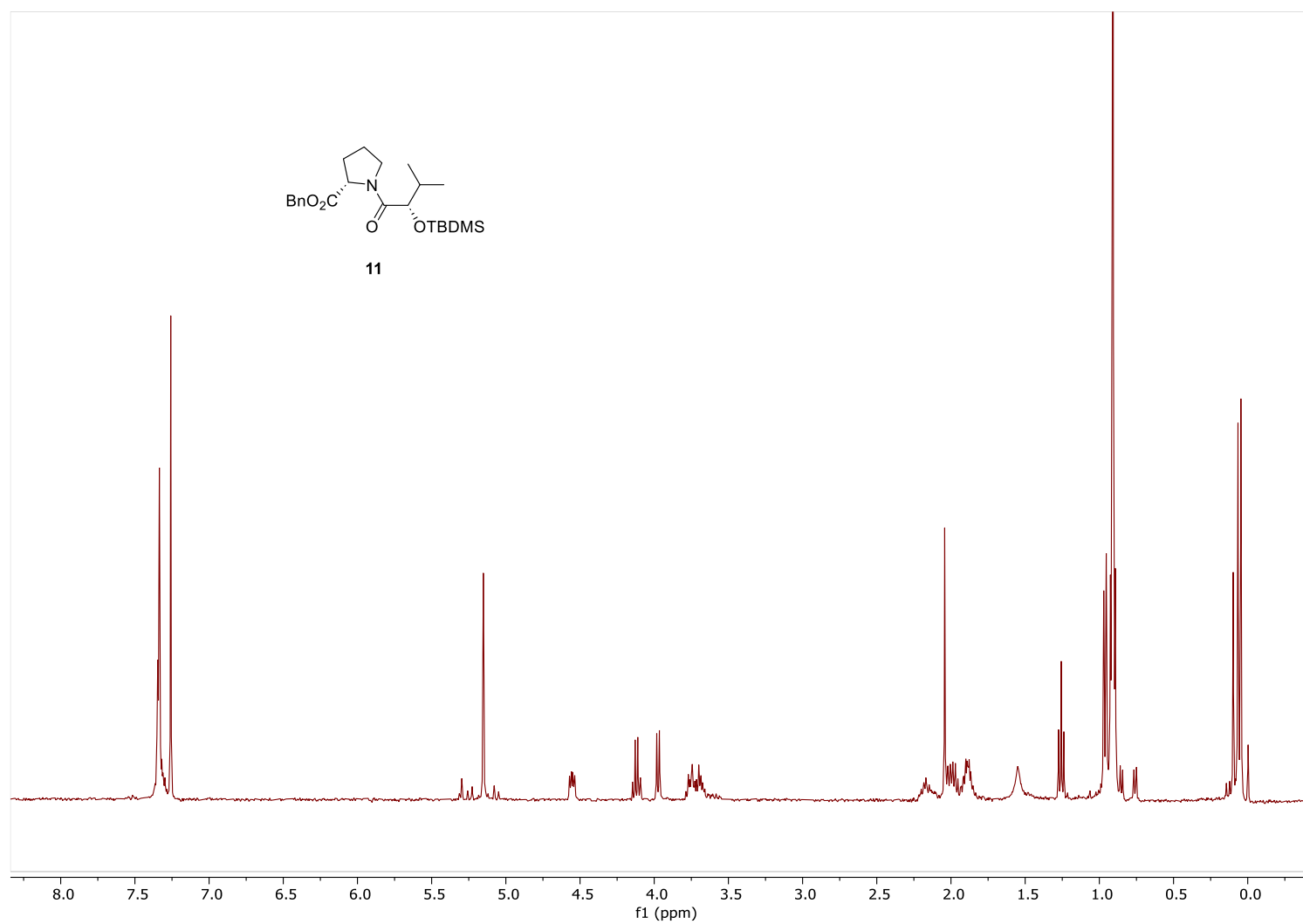


Figure S30. ^{13}C NMR spectrum of benzyl ((*S*)-2-((*tert*-butyldimethylsilyl)oxy)-3-methylbutanoyl)-L-prolinate (**11**) (100 MHz, CDCl_3).

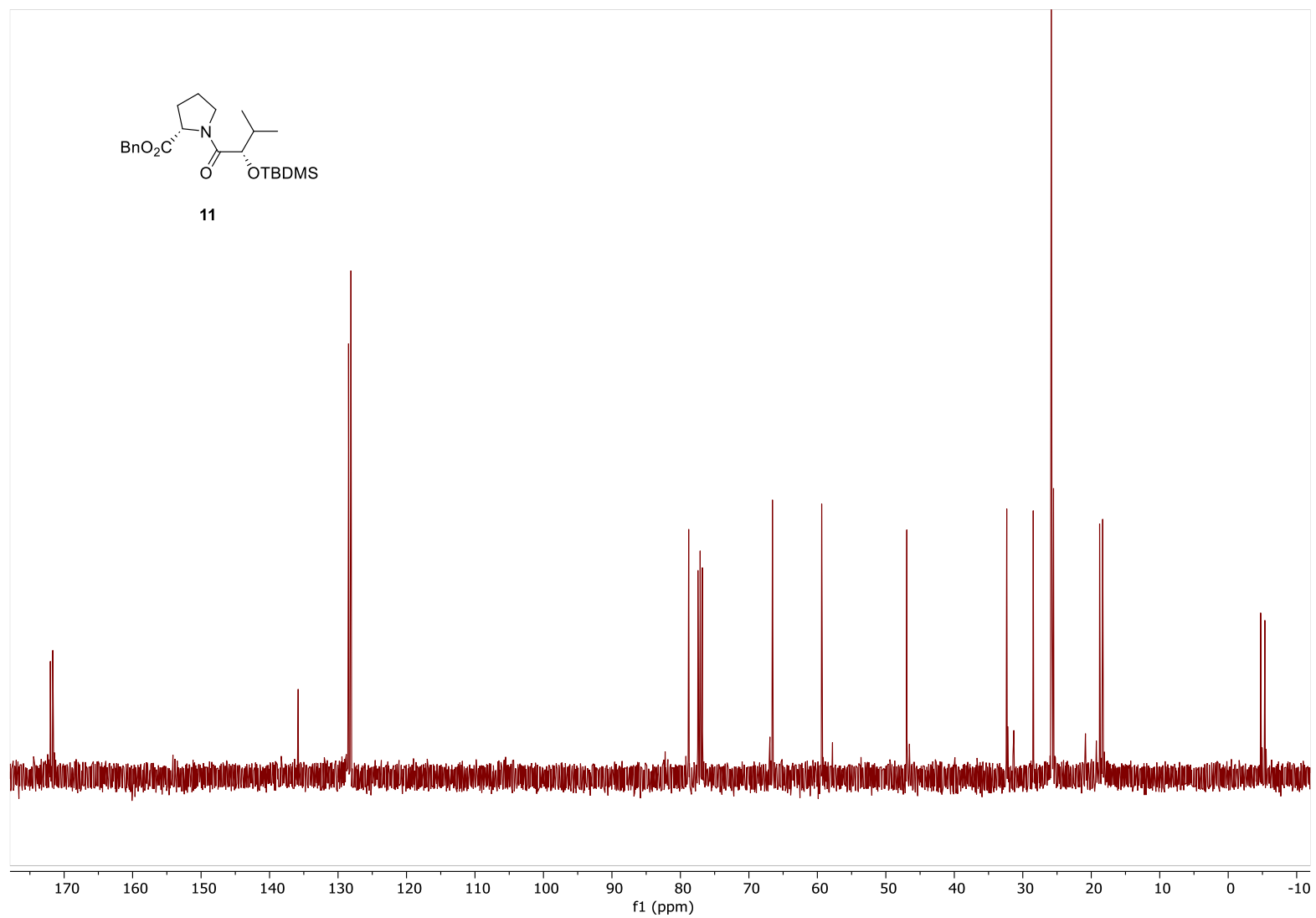


Figure S31. ^1H NMR spectrum of ((*S*)-2-((*tert*-butyldimethylsilyl)oxy)-3-methylbutanoyl)-L-proline (**12**) (400 MHz, CD_3OD).

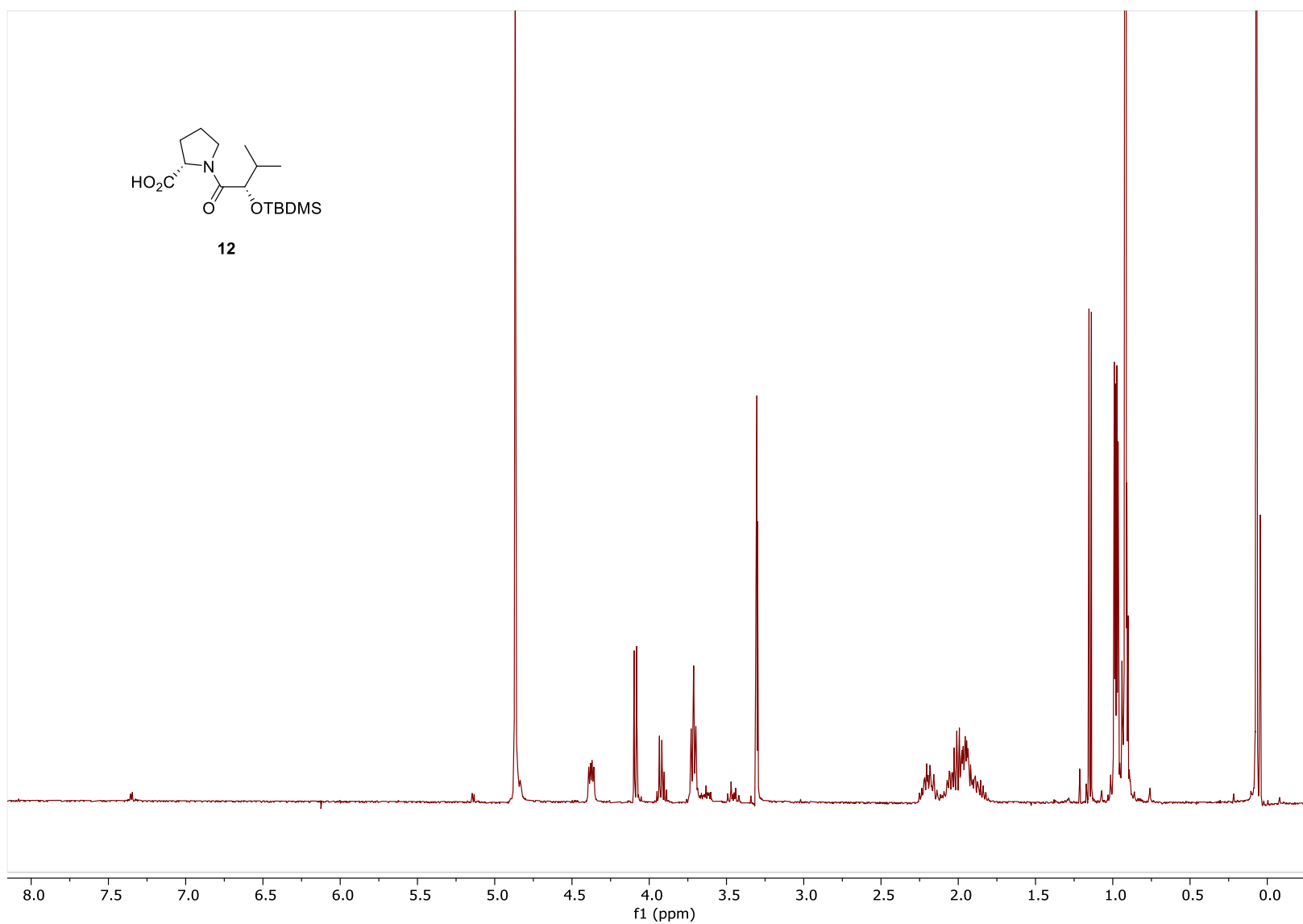


Figure S32. ^{13}C NMR spectrum of ((*S*)-2-((*tert*-butyldimethylsilyl)oxy)-3-methylbutanoyl)-L-proline (**12**) (100 MHz, CD_3OD).

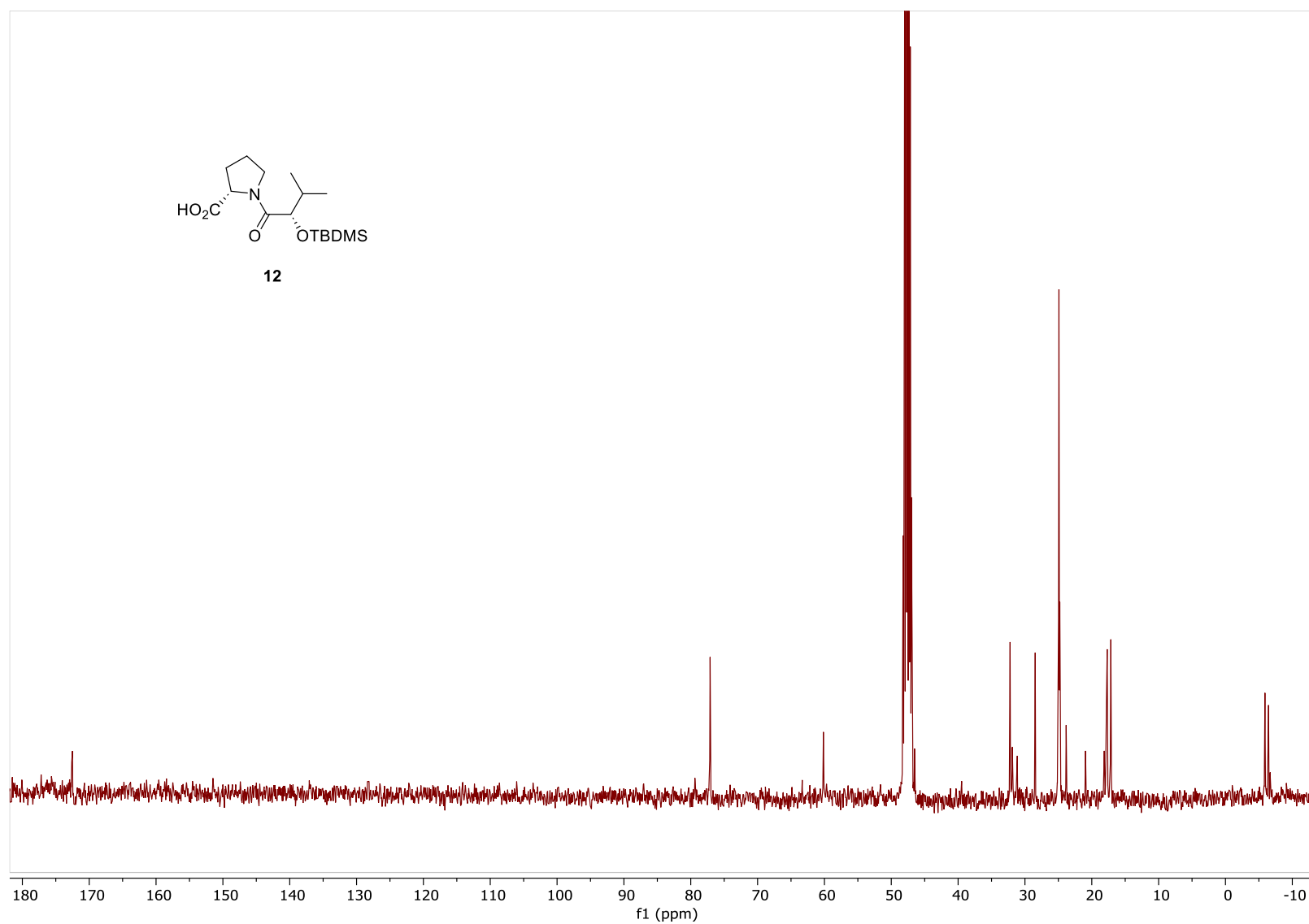


Figure S33. ^1H NMR spectrum of allyl *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-phenylalaninate (**13**) (400 MHz, CDCl_3).

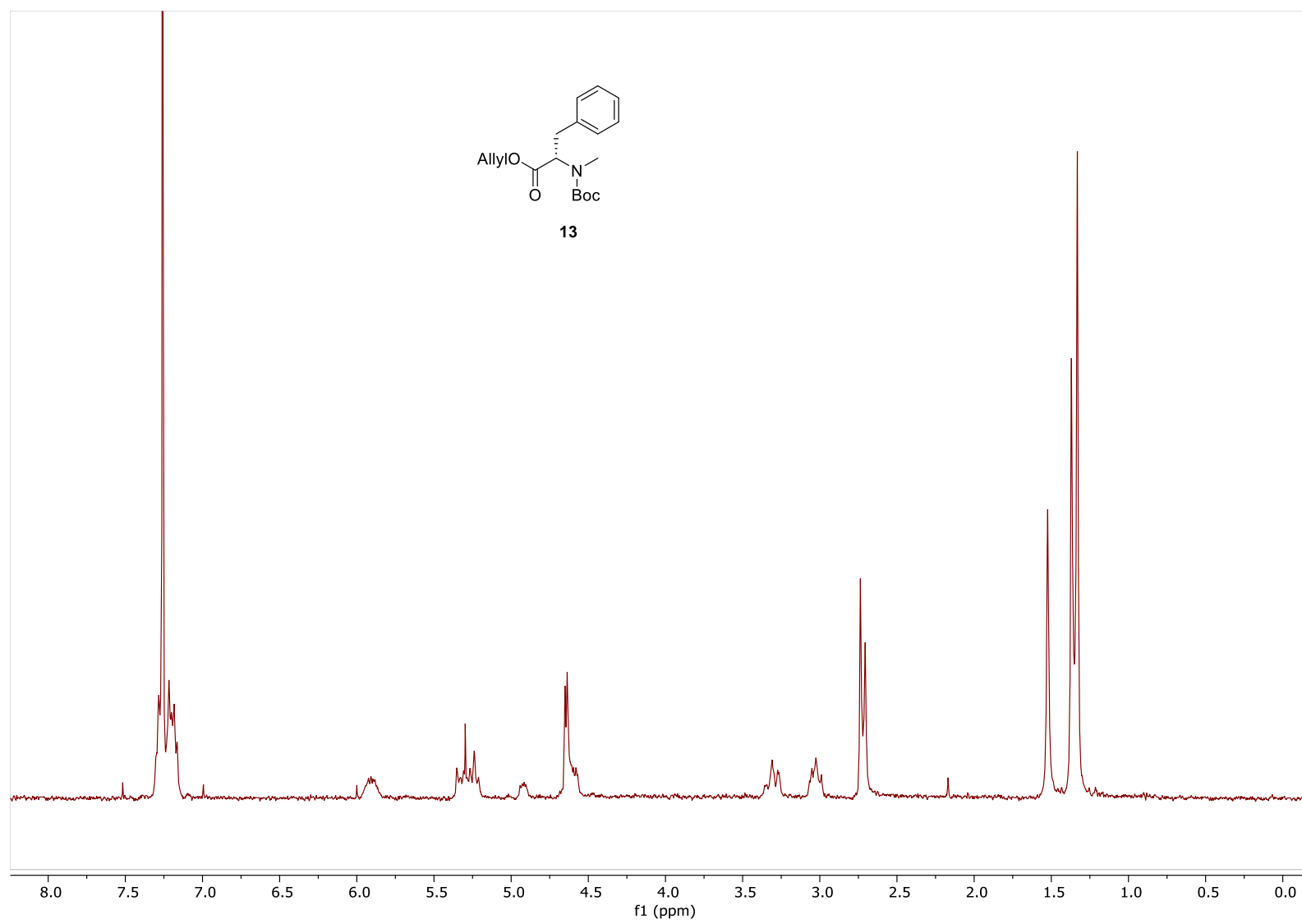


Figure S34. ^{13}C NMR spectrum of allyl *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-phenylalaninate (**13**) (100 MHz, CDCl_3).

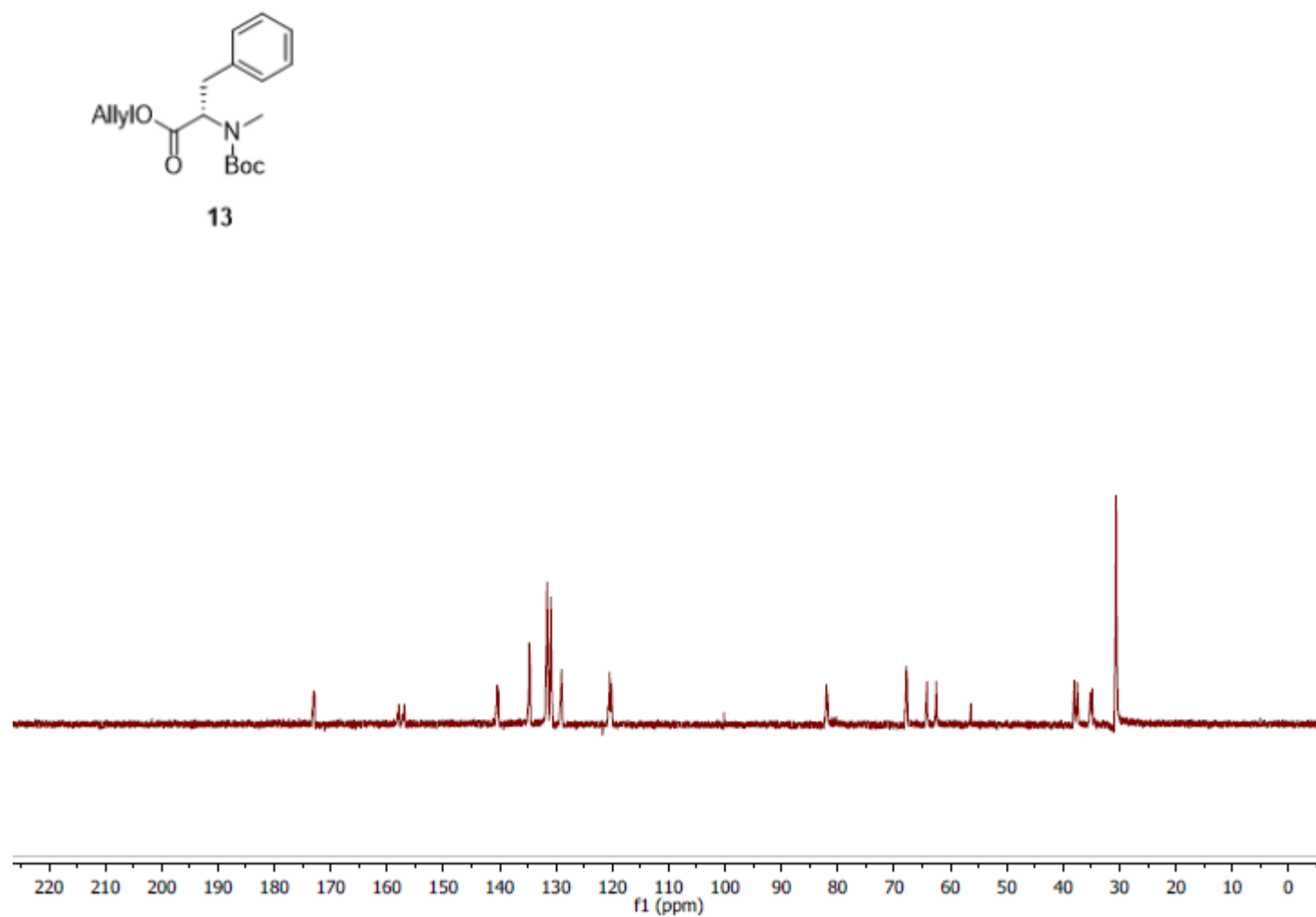


Figure S35. ^1H NMR spectrum of allyl methyl-L-phenylalaninate (**14**) (400 MHz, CDCl_3).

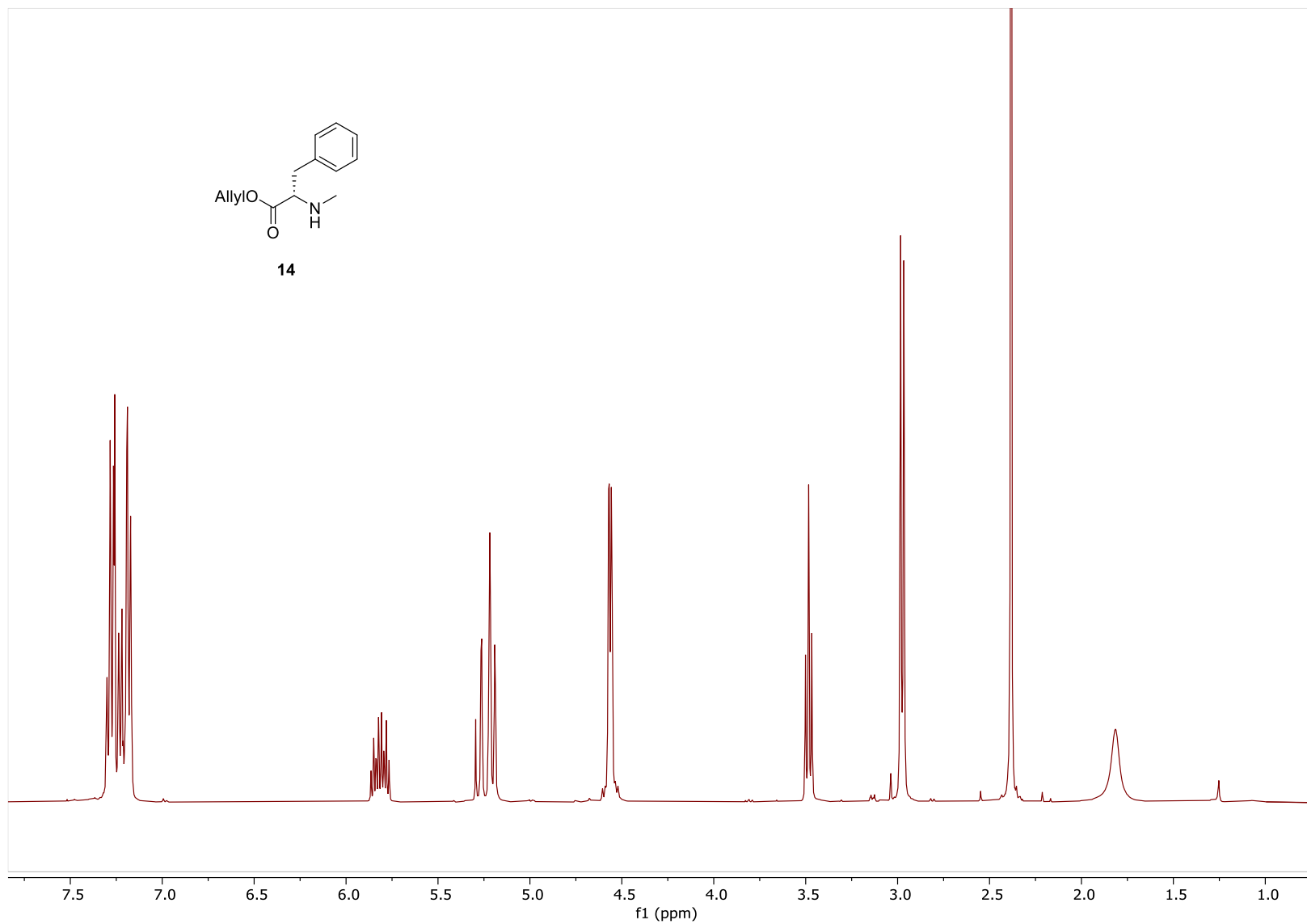


Figure S36. ^{13}C NMR spectrum of allyl methyl-L-phenylalaninate (**14**) (100 MHz, CDCl_3).

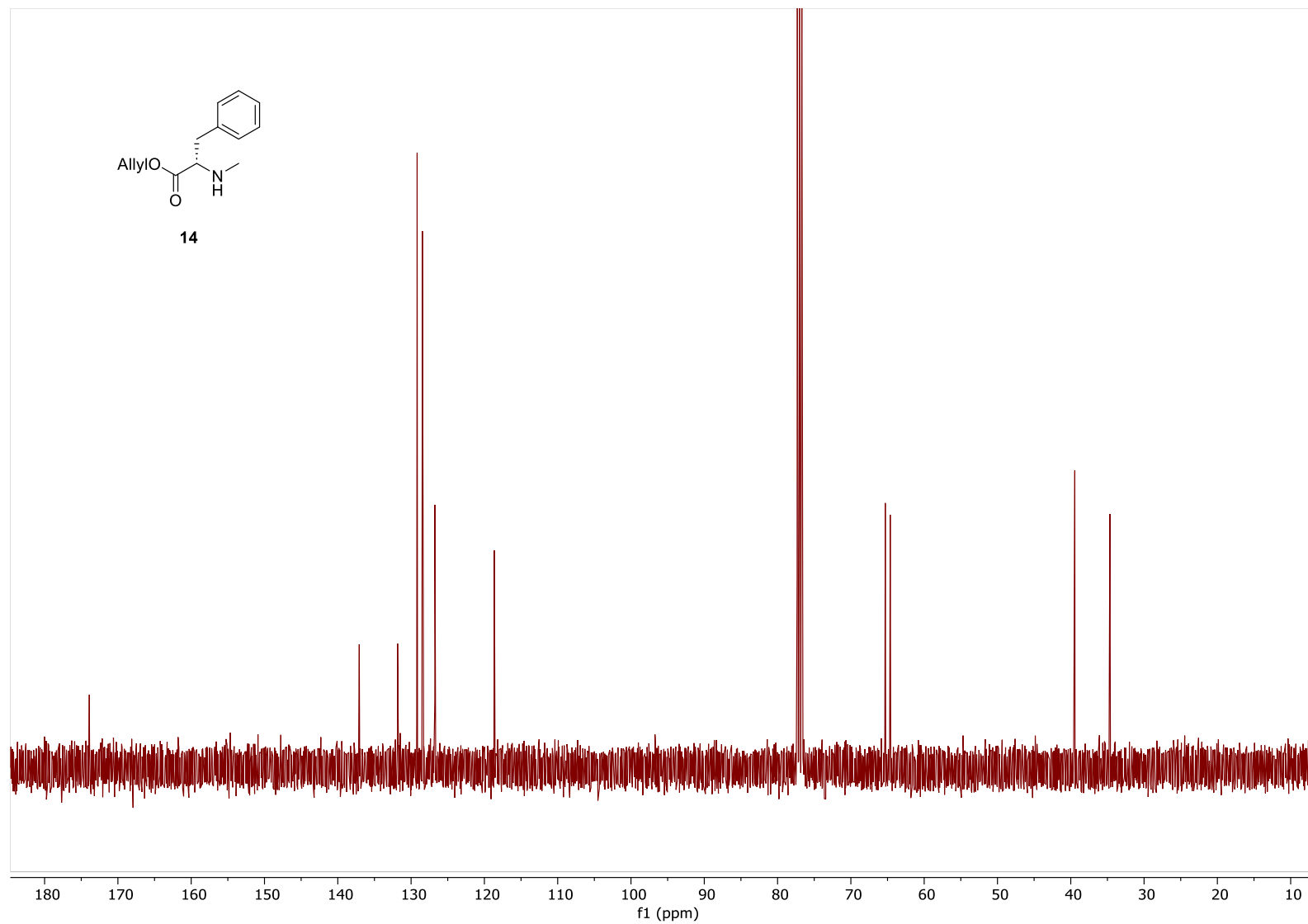


Figure S37. ^1H NMR spectrum of allyl *N*-(((*S*)-2-((*tert*-butyldimethylsilyl)oxy)-3-methylbutanoyl)-*L*-prolyl)-*N*-methyl-*L*-phenylalaninate (**15**) (500 MHz, CDCl_3).

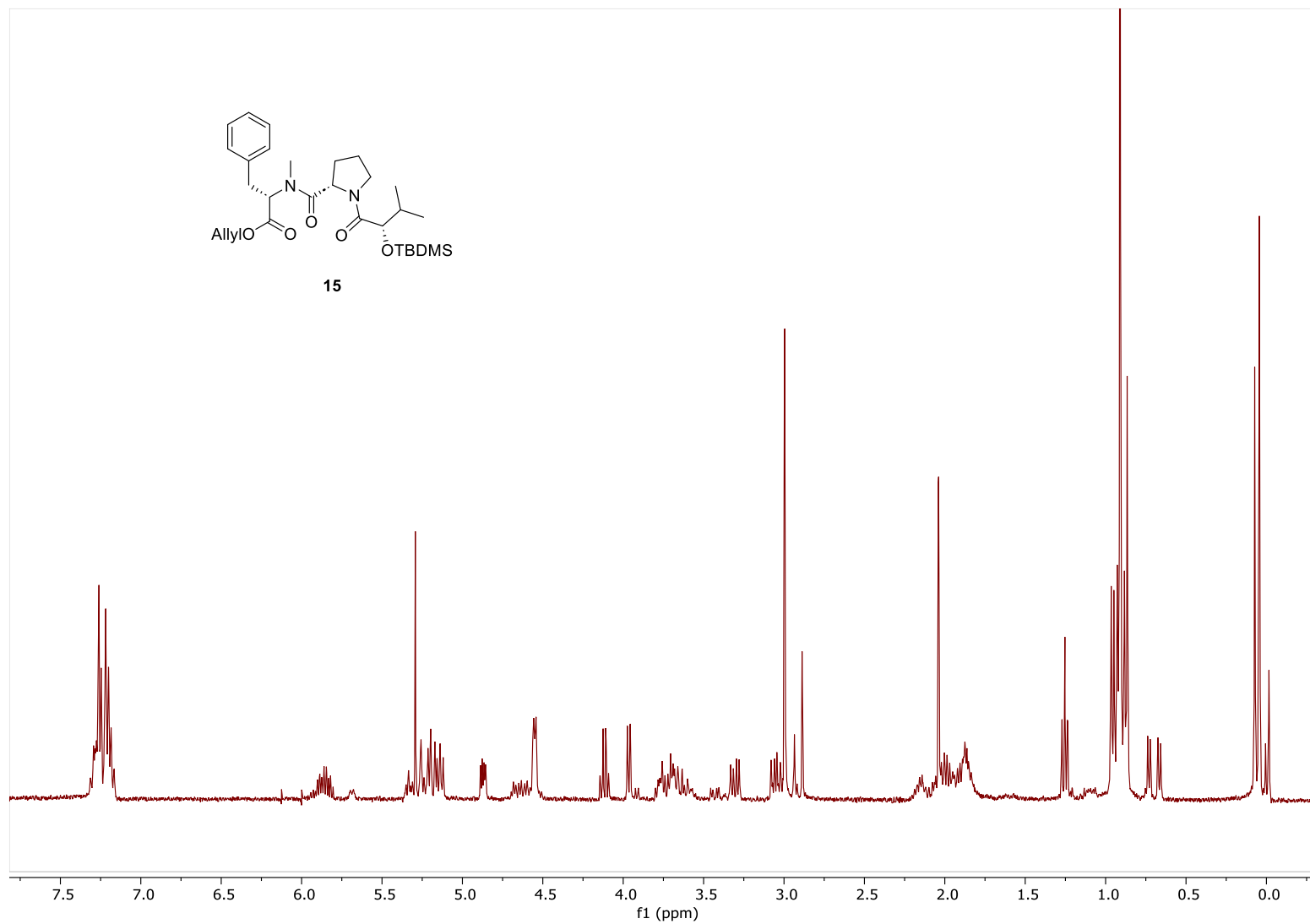


Figure S38. ^{13}C NMR spectrum of allyl *N*-(((*S*)-2-((*tert*-butyldimethylsilyl)oxy)-3-methylbutanoyl)-*L*-prolyl)-*N*-methyl-*L*-phenylalaninate (**15**) (100 MHz, CDCl_3).

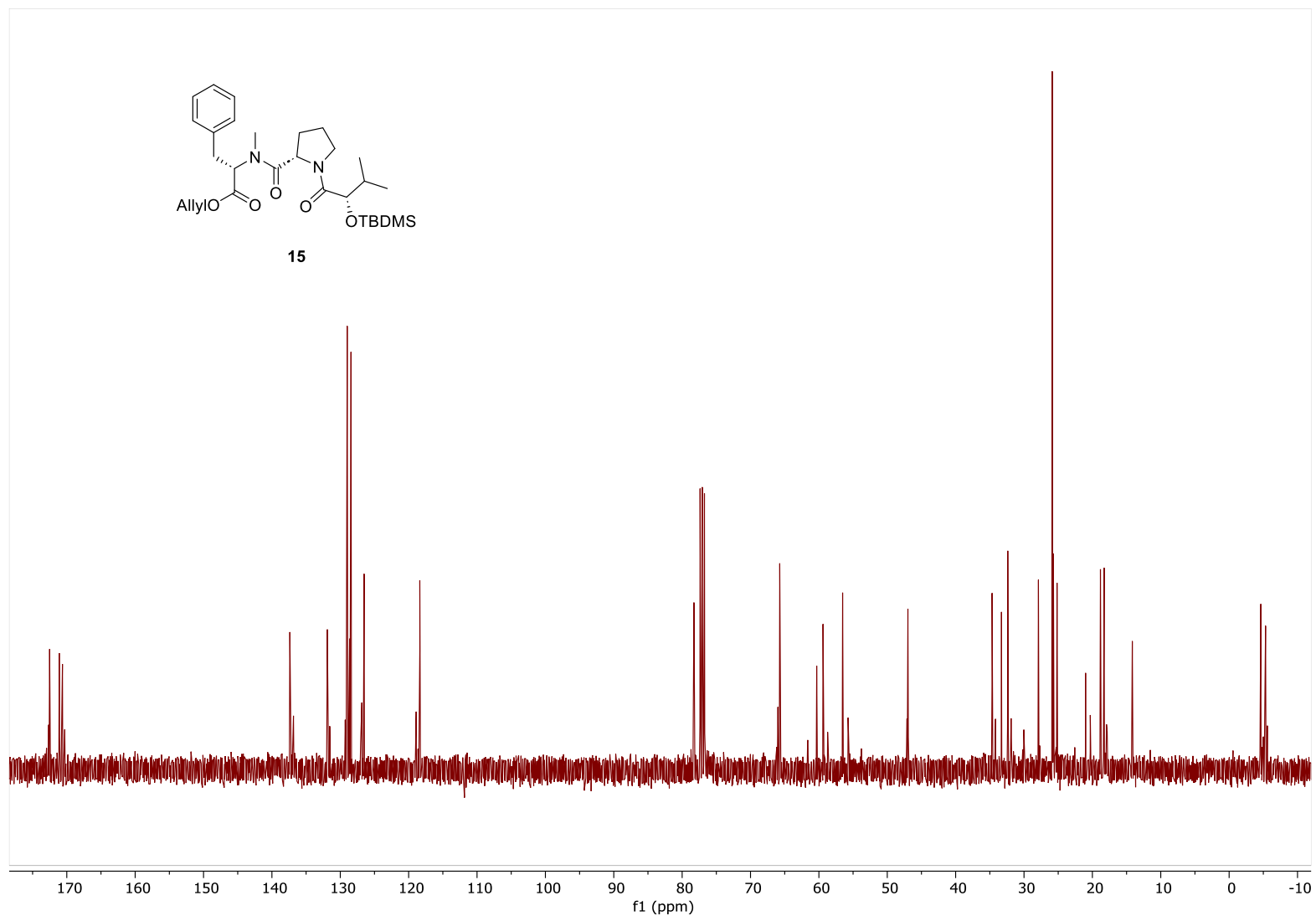


Figure S39. ^1H NMR spectrum of allyl *N*-(((*S*)-2-hydroxy-3-methylbutanoyl)-*L*-prolyl)-*N*-methyl-*L*-phenylalaninate (**3**) (500 MHz, CDCl_3).

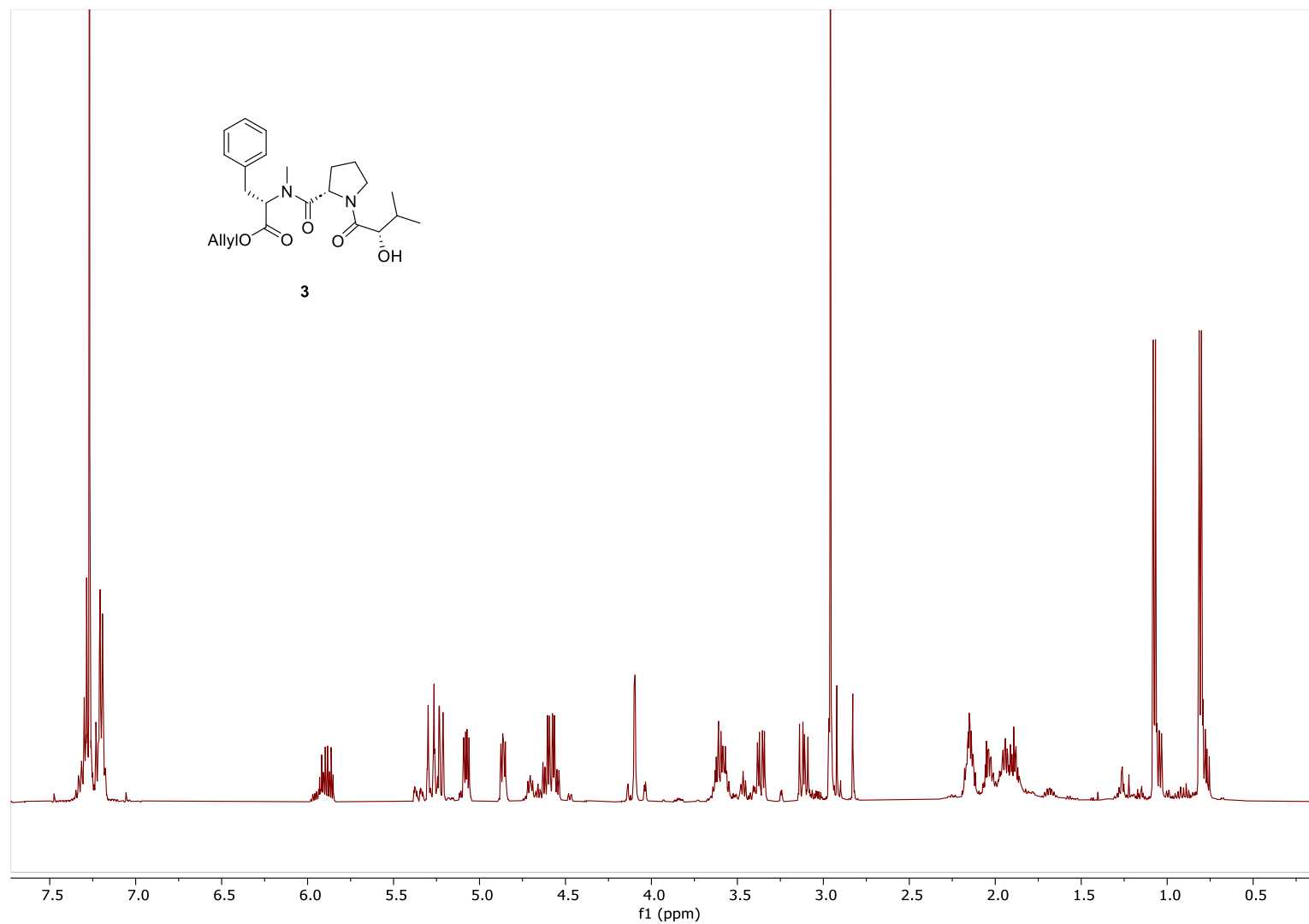


Figure S40. ^{13}C NMR spectrum of allyl *N*-(((*S*)-2-hydroxy-3-methylbutanoyl)-*L*-prolyl)-*N*-methyl-*L*-phenylalaninate (**3**) (100 MHz, CDCl_3).

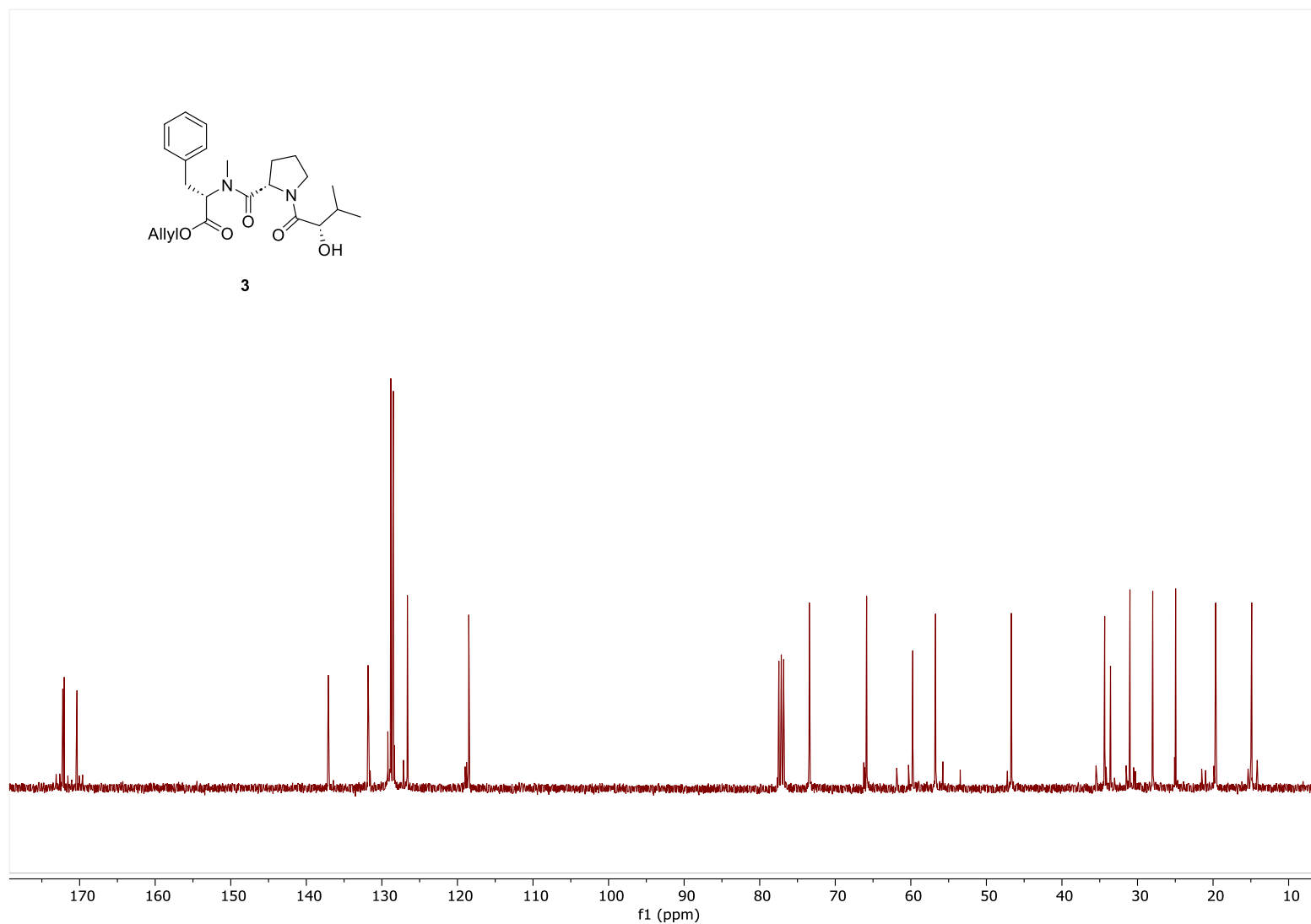


Figure S41. ^1H NMR spectrum of (*S*)-1-((*S*)-2-(((*S*)-1-(allyloxy)-1-oxo-3-phenylpropan-2-yl)(methyl)carbamoyl)pyrrolidin-1-yl)-3-methyl-1-oxobutan-2-yl (*S*)-3-((tert-butyldimethylsilyl)oxy)-2,2-dimethyloct-7-ynoate (**16**) (400 MHz, CDCl_3).

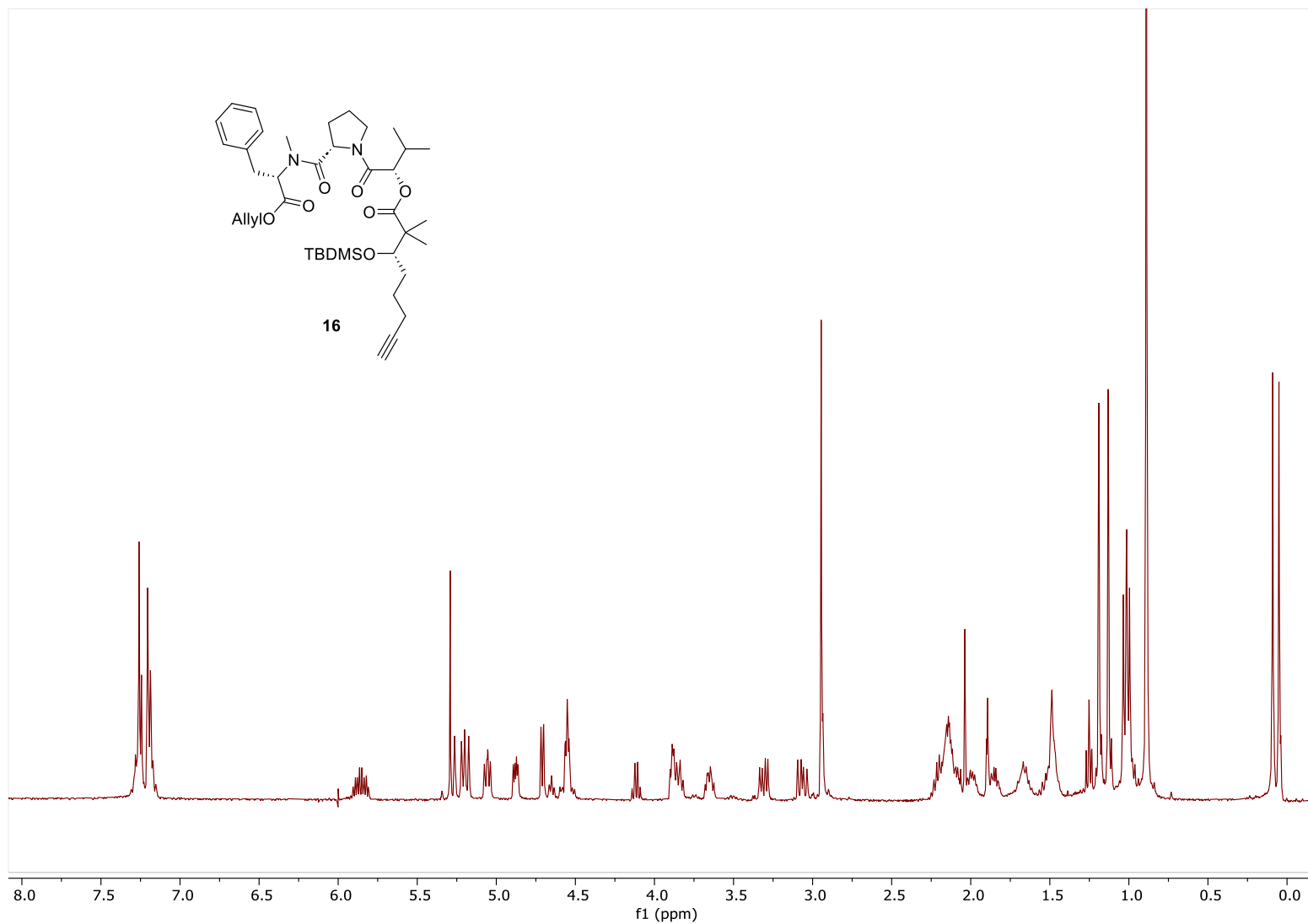


Figure S42. ^{13}C NMR spectrum of (*S*)-1-(((*S*)-2-(((*S*)-1-(allyloxy)-1-oxo-3-phenylpropan-2-yl)(methyl)carbamoyl)pyrrolidin-1-yl)-3-methyl-1-oxobutan-2-yl (*S*)-3-((tert-butyldimethylsilyl)oxy)-2,2-dimethyloct-7-ynoate (**16**) (100 MHz, CDCl_3).

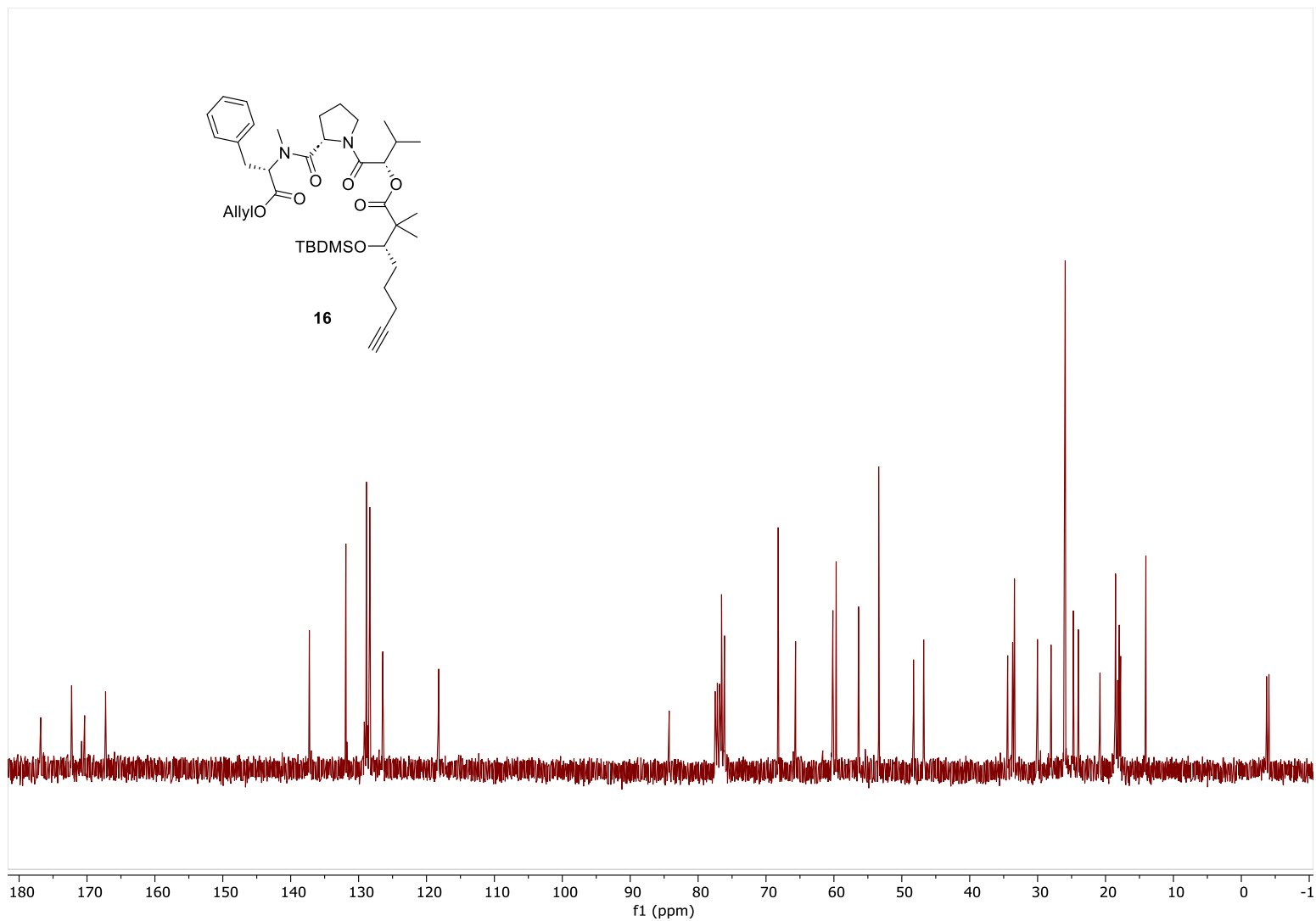


Figure S43. ^1H NMR spectrum of (*S*)-1-((*S*)-2-(((*S*)-1-(allyloxy)-1-oxo-3-phenylpropan-2-yl)(methyl)carbamoyl)pyrrolidin-1-yl)-3-methyl-1-oxobutan-2-yl (*S*)-3-hydroxy-2,2-dimethyloct-7-ynoate (**17**) (400 MHz, CDCl_3).

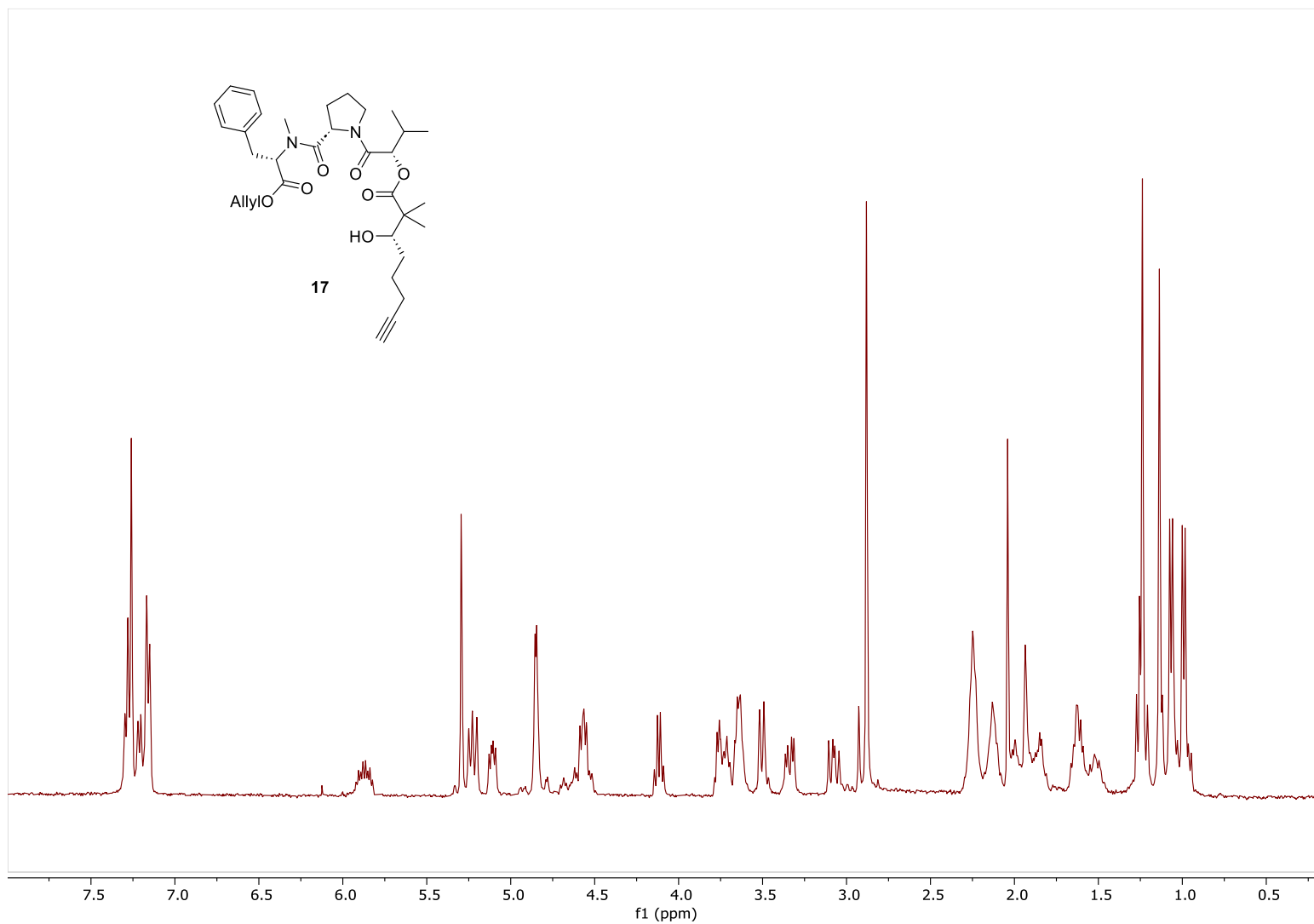


Figure S44. ^{13}C NMR spectrum of (*S*)-1-((*S*)-2-(((*S*)-1-(allyloxy)-1-oxo-3-phenylpropan-2-yl)(methyl)carbamoyl)pyrrolidin-1-yl)-3-methyl-1-oxobutan-2-yl (*S*)-3-hydroxy-2,2-dimethyloct-7-ynoate (**17**) (100 MHz, CDCl_3).

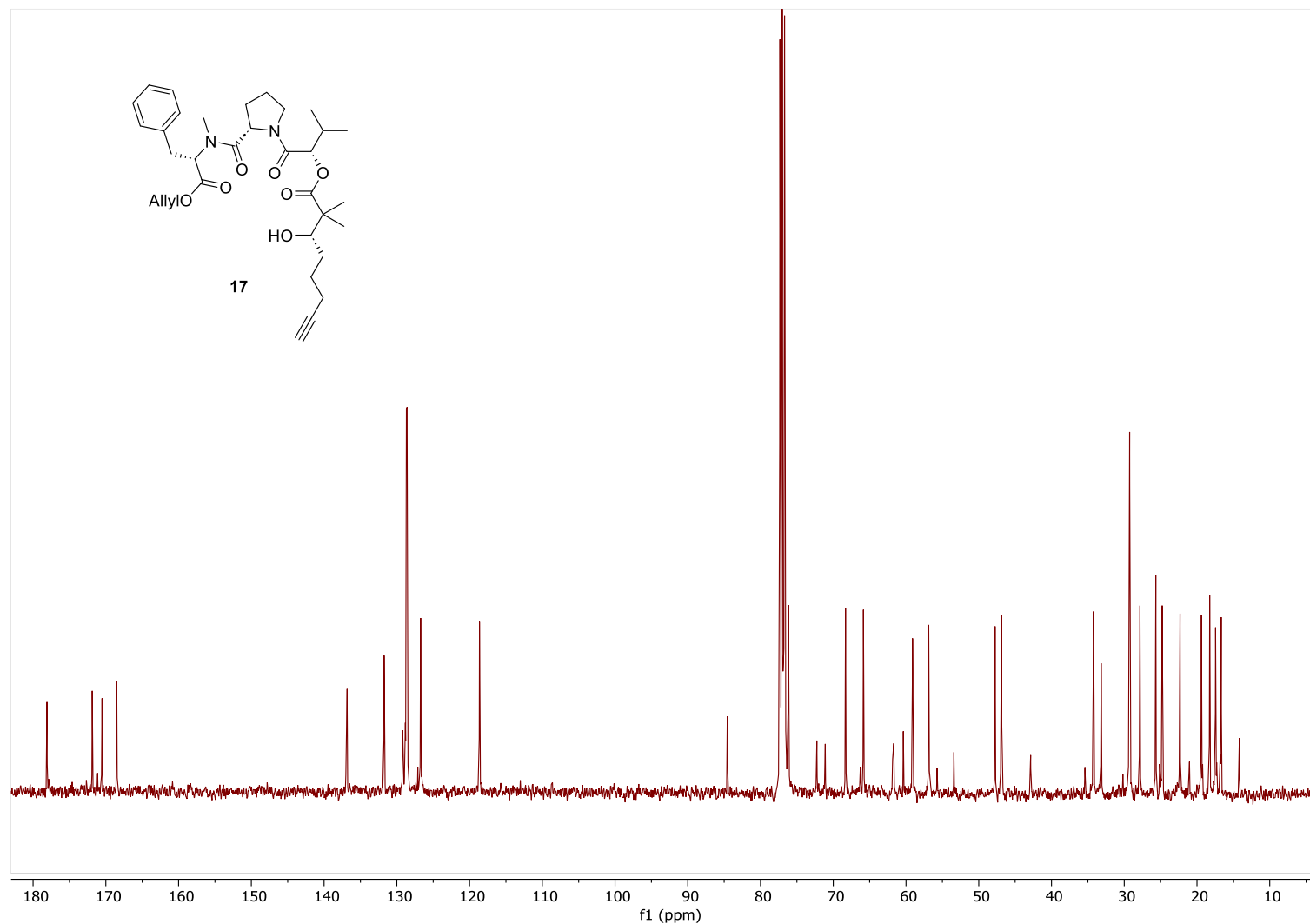


Figure S45. ^1H NMR spectrum of (*S*)-1-((*S*)-2-(((*S*)-1-(allyloxy)-1-oxo-3-phenylpropan-2-yl)(methyl)carbamoyl)pyrrolidin-1-yl)-3-methyl-1-oxobutan-2-yl (*S*)-3-((3-((*tert*-butoxycarbonyl)amino)propanoyl)oxy)-2,2-dimethyloct-7-ynoate (**18**) (400 MHz, CDCl_3).

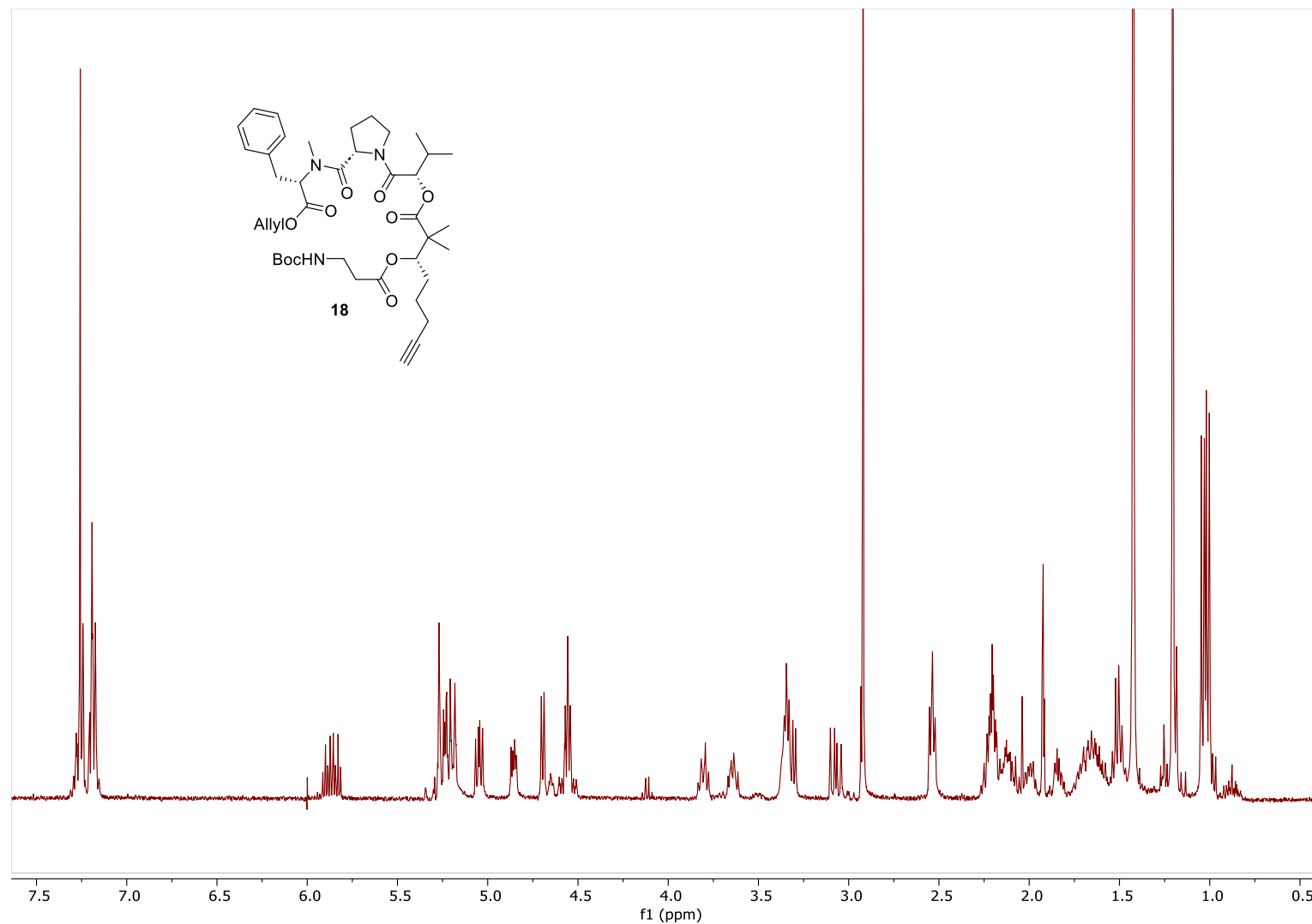


Figure S48. ^{13}C NMR spectrum of *N*-(((10*S*,14*S*)-14-isopropyl-2,2,11,11-tetramethyl-4,8,12-trioxo-10-(pent-4-yn-1-yl)-3,9,13-trioxa-5-azapentadecan-15-oyl)-*L*-prolyl)-*N*-methyl-*L*-phenylalanine (**19**) (100 MHz, CD_3OD).

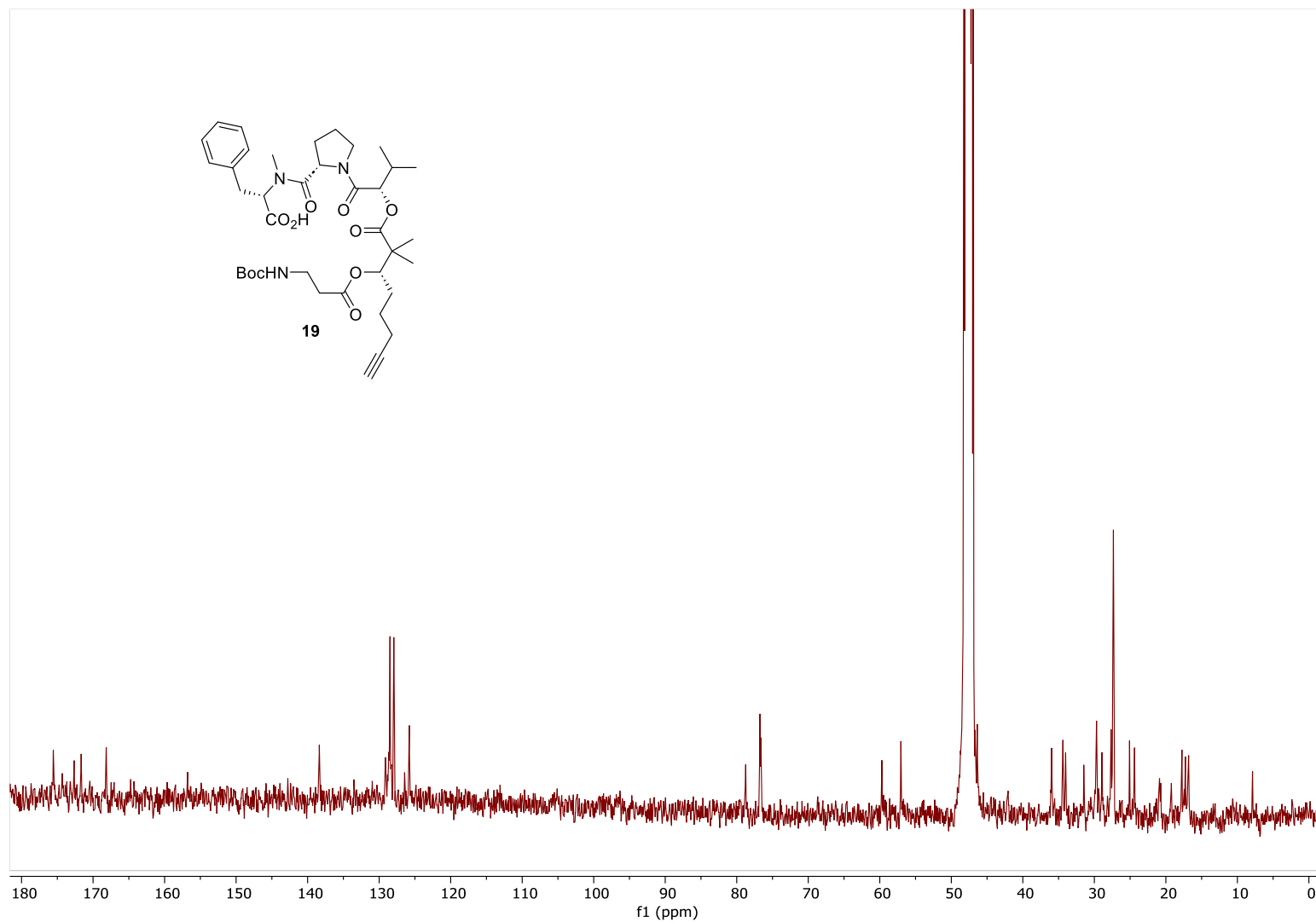


Figure S49. ^1H NMR spectrum of *N*-(((*S*)-2-(((*S*)-3-((3-aminopropanoyl)oxy)-2,2-dimethyloct-7-ynoyl)oxy)-3-methylbutanoyl)-*L*-prolyl)-*N*-methyl-*L*-phenylalanine (**20**) (400 MHz, CD_3OD).

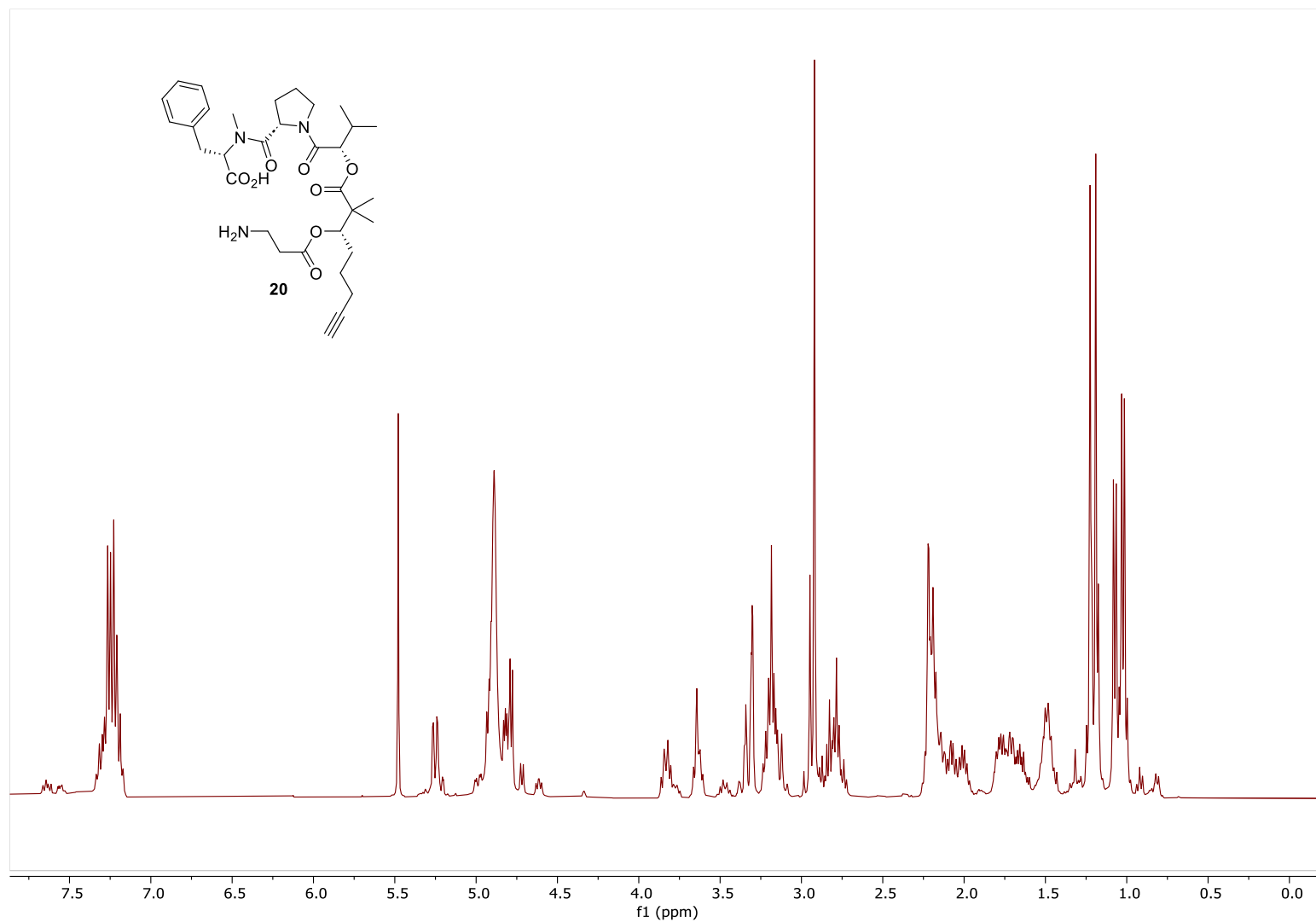


Figure S50. ^{13}C NMR spectrum of *N*-(((*S*)-2-(((*S*)-3-((3-aminopropanoyl)oxy)-2,2-dimethyloct-7-ynoyl)oxy)-3-methylbutanoyl)-L-prolyl)-*N*-methyl-L-phenylalanine (**20**) (100 MHz, CD_3OD).

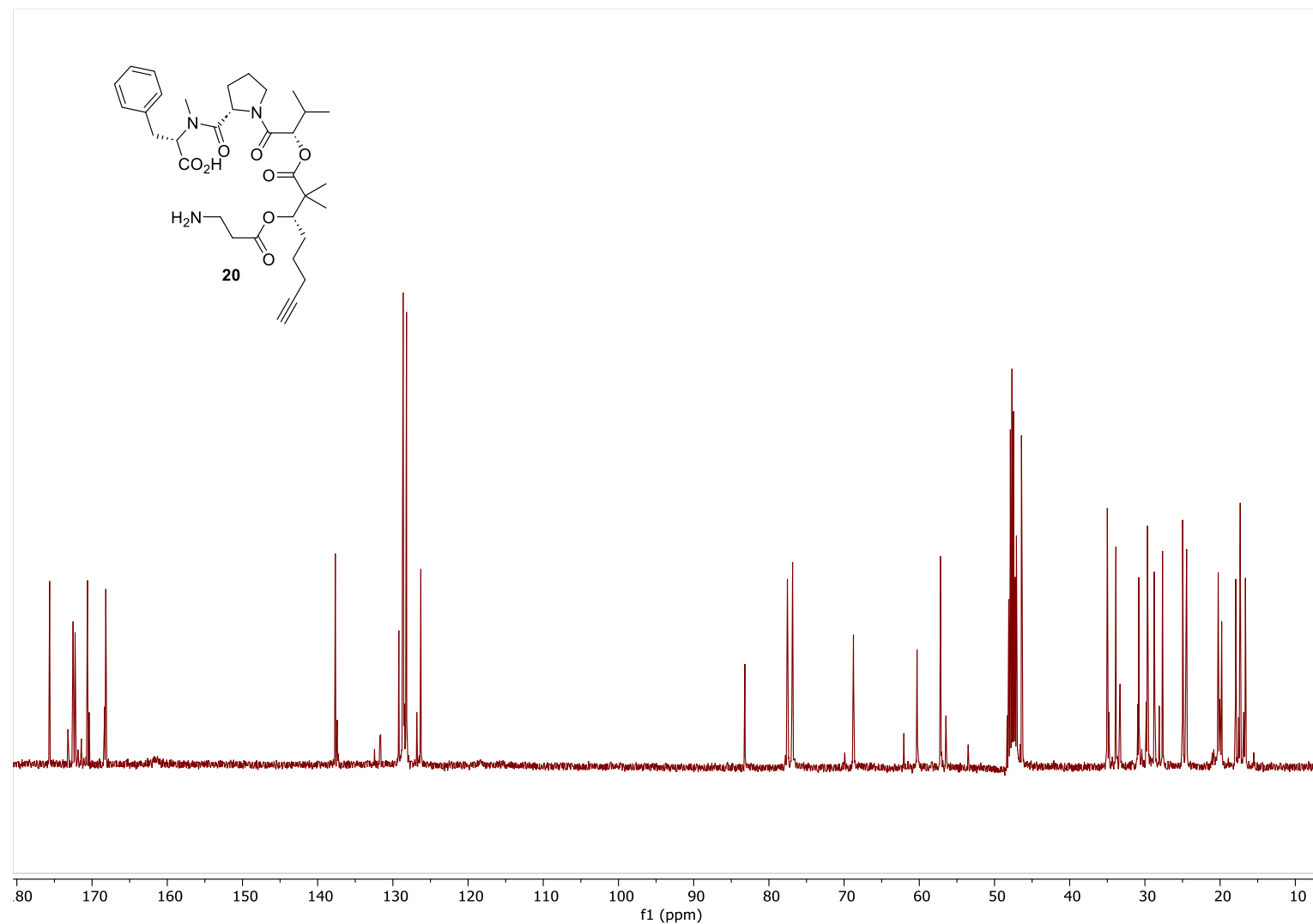


Figure S51. ^1H NMR spectra of synthetic vs. natural **PM170453**.

