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1. General Information

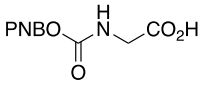
Unless otherwise specified, starting materials were purchased from commercial suppliers and used as received. ß-methyl-vinyl-phosphate was purchased from AK Scientifics, other molecules were purchased from Merck, TCI, Alfa Aesar, Fluorochem. All air and water sensitive reactions were performed under argon atmosphere. Solvents were purchased from commercial sources. If stated as dry, the solvents were distilled using standard methods or received already dried from suppliers. For the organic syntheses, the reactions were monitored by thin layer chromatography (TLC): precoated silica gel thin layer sheets 60 F254 (Merck, Darmstadt, Germany). The detection was performed by using a UV lamp (254 nm) or by staining with phosphomolybdic acid (PMA), KMnO4 or ninhydrin when appropriate. Small scale reactions were performed using a Grant-Bio thermoshaker plate (Dutscher, Brumath, France). Purifications were carried out using silica gel (60 Å, 180-240 mesh from Merck, Darmstadt, Germany). Final compounds were purified using a HPLC system with a reverse phase C18 column (Agilent, 250 mm x 21.2 mm, 5 µm) using a solvent system consisting of H_2O and acetonitrile (linear gradient, 0 to 100% over 45 minutes) at a flow rate of 12 $mL.min^{-1}$ and UV detection at 299 nm. The purity of final compounds (>95%) was established by analytical HPLC, which was performed on a Vydac C18 (250 mm x 4.6 mm, 5 µm) at a flow rate of 1.3 $mL.min^{-1}$ with UV detection at 299 nm. NMR spectra were recorded using Bruker spectrometers Bruker Advance II 500, and Bruker Advance III HD 4000 (Bruker Biospin, Fällanden, Switzerland). Chemical shifts (δ) are reported in parts per million (ppm) and referenced to the residual proton or carbone resonance of the solvents: $CDCl_3$ (δ 7.26), CD_3OD (δ 3.31), $(CD_3)_2SO$ (δ 2.50) or D_2O (δ 4.79) for ^1H and $CDCl_3$ (δ 77.16), CD_3OD (δ 49.00), $(CD_3)_2SO$ (δ 39.52) for ^{13}C. Coupling constants (J) are reported in Hz and splitting patterns are indicated as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, bs = broad signal. High-resolution mass spectroscopy (HRMS) was recorded using LTQ Orbitrap XL (Thermo Scientific, Illkirch, France). Low-resolution mass spectroscopy was also used for chemical intermediates (LCQ Deca XPMax, Thermo Scientific, Illkirch, France). Compounds **14**, **17**, **21**, **22**, and carbapenems **2** and **2'** were synthetized following described procedures.[1-4]

2. Organic syntheses

2-1. Synthesis of compounds 3-26

General procedure for the *N*-CO_2PNB protection of *N*-terminal amine: Amino acid or aminoalkyl acid (1.0 equiv.) was dissolved in a mixture of H_2O:dioxane (1:1) and treated with $NaHCO_3$ (2.0 equiv.). The reaction mixture was stirred for 5 minutes at 0 ˚C. 4-Nitrobenzyl chloroformate (1.2 equiv.) was added in one portion and the reaction mixture was stirred for 2 hours at 0 ˚C and then 18 hours at room temperature. The mixture was washed with diethyl ether (x2), the aqueous phase was acidified to pH = 1.0 with a solution of 1 M HCl and the resulting solution was extracted with EtOAc (x3). The combined organic layers were washed with H_2O, brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford the expected compound used in next step without further purification.

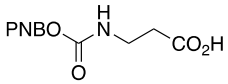
(((4-Nitrobenzyl)oxy)carbonyl)glycine (3)



3

Following the general procedure for the *N*-CO_2PNB protection, glycine (1.0 g, 13.3 mmol) and 4-nitrobenzyl chloroformate (3.4 g, 16.0 mmol) were reacted in presence of $NaHCO_3$ (2.2 g, 26.6 mmol) to afford compound **3** as a white foam (3.3 g, 98%). The analytical data correspond to the ones found in the literature.[5] **^{1}H NMR (500 MHz, DMSO):** δ 8.19 (d, J = 8.7 Hz, 2H), 7.68 (t, J = 6.2 Hz, 1H), 7.59 (d, J = 8.7 Hz, 2H), 5.19 (s, 2H), 3.71 (d, J = 6.3 Hz, 2H). **^{13}C NMR (126 MHz, DMSO):** δ 171.7, 156.4, 147.1, 145.1, 128.2 (2C), 123.6 (2C), 64.5, 42.3. **HRMS (ESI):** *m/z* calcd for $C_{10}H_{10}N_2O_6Na$ $[M + Na]^+$ 277.0431; found: 277.0428.

3-((((4-Nitrobenzyl)oxy)carbonyl)amino)propanoic acid (4)

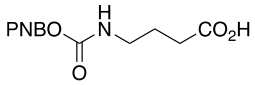


4

Following the general procedure for the *N*-CO_2PNB protection, ß-alanine (1.0 g, 11.2 mmol) and 4-nitrobenzyl chloroformate (2.9 g, 13.4 mmol) were reacted in presence of $NaHCO_3$ (1.8 g, 22.4 mmol) to afford compound **4** as a white foam (1.5 g, 99%). The analytical data correspond to the ones found in the literature.[6] **^{1}H NMR (500 MHz, DMSO):** δ 12.20 (s, 1H), 8.21 (d, J = 8.8 Hz, 2H), 7.58 (d, J = 8.5 Hz, 2H), 7.41 (t, J = 5.6 Hz, 1H), 5.16 (s, 2H), 3.24

(q, J = 6.6 Hz, 2H), 2.41 (t, J = 6.9 Hz, 2H).**^{13}C NMR (126 MHz, DMSO):** δ 172.8, 155.8, 147.0, 145.2, 128.1 (2C), 123.6 (2C), 66.4, 36.7, 34.2. **HRMS (ESI):** *m/z* calcd for $C_{11}H_{13}N_2O_6$ $[M + H]^+$ 269.0768; found: 269.0762.

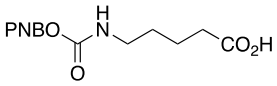
4-((((4-Nitrobenzyl)oxy)carbonyl)amino)butanoic acid (5)



5

Following the general procedure for the *N*-CO_2PNB protection, 4-aminobutyric acid (1.0 g, 9.7 mmol) and 4-nitrobenzyl chloroformate (2.5 g, 11.6 mmol) were reacted in presence of $NaHCO_3$ (1.6 g, 19.4 mmol) to afford compound **5** as a white foam (1.7 g, 63%). The analytical data correspond to the ones found in the literature.[7] **^{1}H NMR (500 MHz, DMSO):** δ 12.03 (s, 1H), 8.21 (d, J = 8.8 Hz, 2H), 7.59 (d, J = 8.5 Hz, 2H), 7.41 (t, J = 5.8 Hz, 1H), 5.15 (s, 2H), 3.03 (q, J = 6.7 Hz, 2H), 2.23 (t, J = 7.4 Hz, 2H), 1.65 (p, J = 7.2 Hz, 2H). **^{13}C NMR (126 MHz, DMSO):** δ 174.2, 155.9, 147.0, 145.3, 128.1 (2C), 123.6 (2C), 64.0, 39.8, 30.9, 24.8. **HRMS (ESI):** *m/z* calcd for $C_{12}H_{14}N_2NaO_6$ $[M + Na]^+$ 305.0744; found: 305.0737.

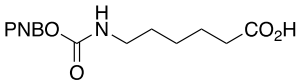
5-((((4-Nitrobenzyl)oxy)carbonyl)amino)pentanoic acid (6)



6

Following the general procedure for the *N*-CO_2PNB protection, 5-aminopentanoic acid (1.0 g, 8.5 mmol) and 4-nitrobenzyl chloroformate (2.2 g, 10.3 mmol) were reacted in presence of $NaHCO_3$ (14.3 g, 17.0 mmol) to afford compound **6** as a white foam (2.0 g, 79%). **^{1}H NMR (500 MHz, DMSO):** δ 8.22 (d, J = 8.8 Hz, 2H), 7.59 (d, J = 8.6 Hz, 2H), 7.38 (t, J = 5.8 Hz, 1H), 5.15 (s, 2H), 3.00 (q, J = 6.4 Hz, 2H), 2.21 (t, J = 7.2 Hz, 2H), 1.51-1.47 (m, 2H), 1.46-1.35 (m, 2H).**^{13}C NMR (126 MHz, DMSO):** δ 174.4, 155.8, 146.9, 145.4, 128.1 (2C), 123.5 (2C), 63.9, 40.0, 33.3, 28.9, 21.8. **HRMS (ESI):** *m/z* calcd for $C_{13}H_{16}N_2NaO_6$ $[M + Na]^+$ 319.0901; found: 319.0893.

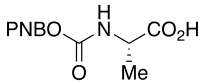
6-((((4-Nitrobenzyl)oxy)carbonyl)amino)hexanoic acid (7)



7

Following the general procedure for the *N*-CO_2PNB protection, 6-aminohexanoic acid (1.0 g, 7.6 mmol) and 4-nitrobenzyl chloroformate (1.9 g, 9.1 mmol) were reacted in presence of $NaHCO_3$ (14.3 g, 17.0 mmol) to afford compound **7** as a whitish foam (2.3 g, 98%). **^{1}H NMR (500 MHz, DMSO):** δ 11.95 (s, 1H), 8.22 (d, *J* = 8.5 Hz, 2H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.37 (t, *J* = 5.9 Hz, 1H), 5.15 (s, 2H), 2.99 (q, *J* = 6.6 Hz, 2H), 2.18 (t, *J* = 7.4 Hz, 2H), 1.49 (p, *J* = 7.5 Hz, 2H), 1.41 (p, *J* = 7.2 Hz, 2H), 1.26 (p, *J* = 7.6, 7.1 Hz, 2H). **^{13}C NMR (126 MHz, DMSO):** δ 174.5, 155.8, 146.9, 145.4, 128.1 (2C), 123.5 (2C), 63.9, 40.0, 33.6, 29.1, 25.8, 24.2. **HRMS (ESI):** *m/z* calcd for $C_{14}H_{18}N_2NaO_6$ $[M + Na]^+$ 333.1057; found: 333.1049.

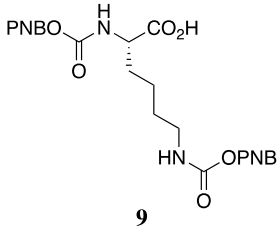
(*S*)-2-((((4-Nitrobenzyl)oxy)carbonyl)amino)propanoic acid (8)



8

Following the general procedure for the *N*-CO_2PNB protection, L-alanine (1.0 g, 11.2 mmol) and 4-nitrobenzyl chloroformate (2.9 g, 13.4 mmol) were reacted in presence of $NaHCO_3$ (18.8 g, 22.4 mmol) to afford compound **8** as a white foam (2.6 g, 88%). The analytical data correspond to the ones found in the literature.[8] $[\alpha]_D^{25}$: – 6.2 (c = 1.2, EtOH). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 10.87 (bs, 1H), 8.19 (d, *J* = 8.7 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 5.45 (t, *J* = 6.9 Hz, 1H), 5.2 (d, *J* = 3.9 Hz, 2H), 4.49-4.25 (m, 1H), 1.48 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 177.6, 155.6, 147.8, 143.7, 128.3 (2C), 123.9 (2C), 65.7, 49.7, 18.3. **HRMS (ESI):** *m/z* calcd for $C_{11}H_{12}N_2O_6Na$ $[M + Na]^+$ 291.0588; found: 291.0584.

***N*^{2},*N*^{6}-bis(((4-Nitrobenzyl)oxy)carbonyl)-*L*-lysine (9)**

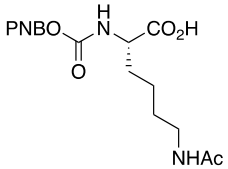


9

Following the general procedure for the *N*-CO_2PNB protection, L-lysine (1.0 g, 6.8 mmol) and 4-nitrobenzyl chloroformate (3.5 g, 16.3 mmol) were reacted in presence of $NaHCO_3$

(22.8 g, 27.2 mmol) to afford compound **9** as a yellowish foam (1.4 g, 81%). $[\alpha]_D^{25}$: + 1.63 (c = 1.4, DMSO). **^{1}H NMR (500 MHz, DMSO):** δ 12.58 (s, 1H), 8.22 (d, J = 7.8 Hz, 4H), 7.70 (d, J = 8.0 Hz, 1H), 7.63-7.51 (m, 4H), 7.38 (d, J = 6.2 Hz, 1H), 5.18 (s, 2H), 5.15 (s, 2H), 3.94-3.89 (m, 1H), 3.06-2.97 (m, 2H), 1.72-1.67 (m, 1H), 1.6-1.52 (m, 1H), 1.43-1.26 (m, 4H). **^{13}C NMR (126 MHz, DMSO):** δ 173.8, 155.9, 155.8, 146.9, 146.9, 145.3, 145.0, 128.1 (4C), 123.5 (4C), 64.2, 63.9, 53.9, 40.0, 30.4, 28.9, 22.8. **HRMS (ESI):** *m/z* calcd for $C_{22}H_{24}N_4NaO_{10}$ $[M + Na]^+$ 527.1385; found: 527.1378.

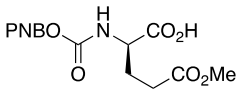
N^6-Acetyl-N^2-(((4-nitrobenzyl)oxy)carbonyl)-*L*-lysine (10)



10

Following the general procedure for the *N*-CO_2PNB protection, *N*-acetyl-L-lysine (1.0 g, 5.3 mmol) and 4-nitrobenzyl chloroformate (1.4 g, 6.4 mmol) were reacted in presence of $NaHCO_3$ (0.9 g, 10.6 mmol) to afford compound **10** as a whitish foam (1.8 g, 91%). $[\alpha]_D^{25}$: + 1.8 (c = 0.3, EtOH). **^{1}H NMR (500 MHz, DMSO):** δ 8.22 (d, J = 8.5 Hz, 2H), 7.78 (t, J = 5.8 Hz, 1H), 7.68 (d, J = 8.1 Hz, 1H), 7.61 (d, J = 8.5 Hz, 2H), 5.18 (s, 2H), 3.95-3.91 (m, 1H), 3.00 (q, J = 6.4 Hz, 2H), 1.78 (s, 3H), 1.74-1.67 (m, 1H), 1.63-1.56 (m, 1H), 1.41-1.30 (m, 4H). **^{13}C NMR (126 MHz, DMSO):** δ 173.9, 169.1, 156.0, 147.0, 145.1, 128.1 (2C), 123.6 2C), 64.3, 54.0, 38.4, 30.5, 28.8, 23.1, 22.6. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{21}N_3NaO_7$ $[M + Na]^+$ 390.1272; found: 390.1272.

(*R*)-5-Methoxy-2-((((4-nitrobenzyl)oxy)carbonyl)amino)-5-oxopentanoic acid (11)

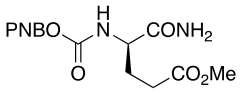


11

According to the procedure described in literature,[7] D-glutamic acid (1.0 g, 6.8 mmol) in dry MeOH (20 mL) was treated dropwise over 5 minutes with TMSCl (1.7 mL, 13.6 mmol) at room temperature. The mixture was stirred for additional 10 minutes and then concentrated under reduced pressure to afford the crude monoprotected D-glutamic acid. The crude product was dissolved in H_2O:dioxane (1:1) (20 mL) and treated with $NaHCO_3$ (1.1 g, 13.6 mmol) and 4-nitrobenzyl chloroformate (1.8 g, 8.2 mmol) at 0 ˚C. The reaction mixture was stirred for 18 hours at room temperature. Dioxane was removed under reduced pressure, and the

crude mixture was dissolved in H_2O (80 mL). The aqueous phase was washed with Et_2O (2 x 50 mL) and then acidified to pH = 2.0 using a solution of HCl 1 M. The product was extracted from the aqueous phase with EtOAc (3 x 100 mL). The combined organic layers were washed with H_2O (100 mL), brine (100 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford compound **11** as a white foam (1.6 g, 69%). $[\alpha]_D^{25}$: – 29.5 (c = 3.75, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 10.15 (bs, 1H), 8.17 (d, J = 8.7 Hz, 2H), 7.48 (d, J = 8.6 Hz, 2H), 5.82 (d, J = 8.1 Hz, 1H), 5.29-5.17 (m, 2H), 4.45-4.11 (m, 1H), 3.66 (s, 3H), 2.52-2.40 (m, 2H), 2.29-2.21 (m, 1H), 2.08-2.01 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 175.7, 173.7, 155.9, 147.8, 143.7, 128.2 (2C), 123.9 (2C), 65.8, 53.5, 52.1, 30.2, 27.8. **HRMS (ESI):** *m/z* calcd for $C_{14}H_{17}N_2O_8$ $[M + H]^+$ 341.0979; found: 341.0976.

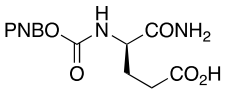
Methyl (*R*)-5-amino-4-((((4-nitrobenzyl)oxy)carbonyl)amino)-5-oxopentanoate (12)



12

To a mixture of compound **11** (0.5 g, 1.5 mmol) and ethyl chloroformate (164 µL, 2.1 mmol) in dry THF (15 mL), NEt_3 (300 µL, 2.1 mmol) was added dropwise at – 15 ˚C. The reaction mixture was stirred for 30 minutes at – 15 ˚C. NH_4OH 28% (1 mL) was added dropwise, and the reaction mixture was warmed up to room temperature and left stirring for 1 hour. The crude mixture was dissolved in EtOAc (75 mL) and washed with a sat. solution of NH_4Cl (75 mL), sat. solution of $NaHCO_3$ (75 mL), brine (75 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was then purified by silica gel chromatography (cyclohexane:EtOAc 1:9) to afford compound **12** as a white foam (353 mg, 71%). $[\alpha]_D^{25}$: – 10.7 (c = 1.5, DMSO). **^{1}H NMR (500 MHz, CD_3OD):** δ 8.23 (d, J = 8.8 Hz, 2H), 7.61 (d, J = 8.4 Hz, 2H), 5.22 (s, 2H), 4.15 (dd, J = 9.4, 5.1 Hz, 1H), 3.66 (s, 3H), 2.44 (t, J = 7.6 Hz, 2H), 2.17-2.09 (m, 1H), 1.96-1.88 (m, 1H). **^{13}C NMR (126 MHz, CD_3OD):** δ 176.7, 175.0, 158.0, 149.0, 145.9, 129.2 (2C), 124.6 (2C), 66.3, 55.5, 52.2, 31.2, 28.5. **HRMS (ESI):** *m/z* calcd for $C_{14}H_{18}N_3O_7$ $[M + H]^+$ 340.1139; found: 340.1136.

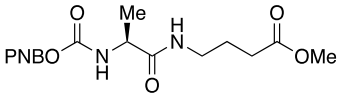
(*R*)-5-Amino-4-((((4-nitrobenzyl)oxy)carbonyl)amino)-5-oxopentanoic acid (13)



13

LiOH 1 M (1.8 mL, 1.8 mmol) was added dropwise to a solution of compound **12** (300 mg, 0.9 mmol) in THF (10 mL) and the reaction mixture was stirred for 1 hour at room temperature. THF was removed under reduced pressure, and the crude mixture was diluted with H_2O (50 mL). After washing the mixture with Et_2O (50 mL), the aqueous layer was acidified to pH = 2.0 – 3.0 using a solution of HCl 1 M. The product was extracted with EtOAc (3 x 75 mL). The combined organic layers were washed with H_2O, brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The obtained solid was dissolved in a minimal volume of H_2O and lyophilized to afford compound **13** as a white foam (250 mg, 87%). $[\alpha]_D^{25}$: + 2.5 (c = 0.4, MeOH). **^{1}H NMR (500 MHz, CD_3OD):** δ 8.21 (d, *J* = 8.7 Hz, 2H), 7.59 (d, *J* = 8.6 Hz, 2H), 5.27-5.18 (m, 2H), 4.19 (dd, *J* = 9.3, 4.9 Hz, 1H), 2.35 (t, *J* = 7.7 Hz, 2H), 2.23-2.16 (m, 1H), 2.01-1.90 (m, 1H). **^{13}C NMR (126 MHz, CD_3OD):** δ 177.8, 175.3, 158.2, 148.9, 146.0, 129.1 (2C), 124.6 (2C), 66.2, 55.0, 32.7, 28.51. **HRMS (ESI):** *m/z* calcd for $C_{13}H_{16}N_3O_7$ $[M + H]^+$ 326.0982; found: 326.0980.

Methyl (*S*)-4-(2-((((4-nitrobenzyl)oxy)carbonyl)amino)propanamido)butanoate (15)

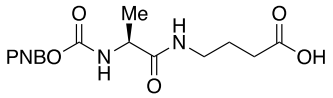


15

Methyl 4-aminobutanoate hydrochloride **14** (618 mg, 4.0 mmol) in dry DCM (20 mL) was treated with DIPEA (1.2 mL, 6.7 mmol) at 0 ˚C. After 5 minutes, protected L-Ala **8** (900 mg, 3.4 mmol), K-oxyma® (901 mg, 5.0 mmol), and EDC (959 mg, 5.0 mmol) were added. The reaction mixture was stirred at room temperature for 4 hours. The crude mixture was diluted in EtOAc (50 mL) and washed with a solution of 10% $NaHCO_3$ (50 mL), 10% citric acid (50 mL), H_2O (50 mL), brine (50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by silica gel chromatography (cyclohexane:EtOAc 3:7) afforded compound **15** as a white foam (1.1 g, 86%). $[\alpha]_D^{25}$: – 1.7 (c = 1.0, DCM). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.15 (d, *J* = 8.8 Hz, 2H), 7.44 (d, *J* = 8.8 Hz, 2H), 6.10 (bs, 1H), 5.38 (d, *J* = 4.5 Hz, 1H), 5.13 (s, 2H), 4.19 (p, *J* = 7.0 Hz, 1H), 3.61 (s, 3H), 3.30 (q, *J* = 6.8 Hz, 2H), 2.30 (t, *J* = 7.1 Hz, 2H), 1.77 (p, *J* = 6.8 Hz, 2H), 1.33 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 173.8, 172.1, 155.1, 147.7, 143.7, 128.1 (2C), 123.8 (2C), 65.4, 51.8, 50.7, 39.1,

31.4, 24.4, 18.9. **HRMS (ESI):** *m/z* calcd for $C_{16}H_{21}N_3NaO_7$ $[M + Na]^+$ 390.1271; found: 390.1264.

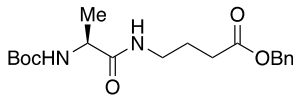
(*S*)-4-(2-((((4-Nitrobenzyl)oxy)carbonyl)amino)propanamido)butanoic acid (16)



16

A solution of LiOH 1 M (5 mL, 2.5 mmol) was added dropwise to compound **15** (900 mg, 2.5 mmol) in THF (10 mL) and the reaction mixture was stirred for 1 hour at room temperature. THF was removed under reduced pressure, and the crude mixture was diluted in H_2O (50 mL). After washing the mixture with Et_2O (50 mL), the aqueous layer was acidified to pH = 2.0 – 3.0 using a solution of HCl 1 M. The product was extracted with EtOAc (3 x 75 mL). The combined organic layers were washed with H_2O, brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The obtained oil was dissolved in a minimal volume of H_2O and lyophilized to afford compound **16** as a yellowish foam (545 mg, 63%). $[\alpha]_D^{25}$: – 4.8 (c = 0.65, MeOH). **^{1}H NMR (500 MHz, CD_3OD):** δ 8.12 (d, *J* = 8.8 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 5.11 (s, 2H), 4.00 (q, *J* = 7.1 Hz, 1H), 3.13 (t, *J* = 5.5 Hz, 2H), 2.21 (t, *J* = 7.3 Hz, 2H), 1.68 (t, *J* = 7.0 Hz, 2H), 1.24 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR (126 MHz, CD_3OD):** δ 177.1, 175.6, 157.8, 149.0, 146.0, 129.2 (2C), 124.6 (2C), 66.3, 52.3, 39.8, 32.2, 25.8, 18.4. **HRMS (ESI):** *m/z* calcd for $C_{15}H_{20}N_3O_7$ $[M + H]^+$ 354.3347; found: 354.1291.

Benzyl (*S*)-4-(2-((tert-butoxycarbonyl)amino)propanamido)butanoate (18)

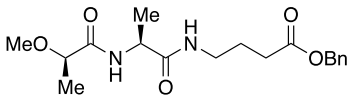


18

Benzyl 4-aminobutanoate **17** (1.0 g, 5.2 mmol) in dry DCM (20 mL) was treated with DIPEA (1.8 mL, 10.4 mmol) at 0 ˚C. After stirring for 5 minutes at 0 ˚C, Boc-L-Ala-OH (1.5 g, 7.8 mmol) and TBTU (2.5 g, 7.8 mmol) were added to the mixture at 0 ˚C. The reaction mixture was stirred for 18 hours at room temperature and dissolved in EtOAc (100 mL). The organic phase was washed with H_2O (100 mL), sat. solution of $NaHCO_3$ (100 mL), brine (100 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude solid was then purified by silica gel chromatography (cyclohexane:EtOAc 6:4) to afford compound **18** as a colorless oil (1.53 g, 81%). $[\alpha]_D^{25}$: – 8.6 (c = 0.5, DCM). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.32-7.25 (m, 5H), 6.87 (bs, 1H), 5.42 (bs, 1H), 5.06 (s, 2H), 4.13 (bs, 1H), 3.28-3.20 (m,

2H), 2.35 (t, J = 7.4 Hz, 2H), 1.80 (p, J = 7.2 Hz, 2H), 1.37 (s, 9H), 1.28 (d, J = 7.0 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 175.6, 173.1, 155.7, 135.9, 128.6 (3C), 128.2 (2C), 80.0, 66.3, 50.1, 38.8, 31.5, 28.3 (3C), 24.6, 18.5. **HRMS (ESI):** *m/z* calcd for $C_{19}H_{29}N_2O_5$ [M + H]$^+$ 365.2071; found: 365.2067.

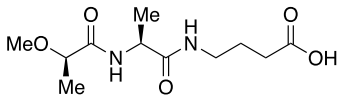
Benzyl 4-((*S*)-2-((*R*)-2-methoxypropanamido)propanamido)butanoate (19)



19

Compound **18** (700 mg, 1.9 mmol) was stirred in a mixture of 50% of TFA in DCM (5 mL) for 2 hours. The solvents were removed under a stream of air and co-evaporation with acetonitrile was performed to remove the excess of TFA. The salt was then dissolved in dry DCM (10 mL) and DIPEA (1.7 mL, 9.5 mmol) was added at 0 ˚C. After stirring for 5 minutes, (2*R*)-2-methoxy propanoic acid (237 mg, 2.3 mmol), and TBTU (915 mg, 2.9 mmol) were added at 0 ˚C. The reaction mixture was stirred for 24 hours at room temperature. DCM was removed under reduced pressure and the crude solid was dissolved in EtOAc (100 mL). The solution was washed with H_2O (100 mL), sat. solution of $NaHCO_3$ (100 mL), brine (100 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (cyclohexane:EtOAc 2:8) to afford compound **19** as a white foam (474 mg, 71%). $[\alpha]_D^{25}$: – 32.6 (c = 1.2, CH_2Cl_2). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.38-7.29 (m, 5H), 7.07 (d, J = 8.0 Hz, 1H), 6.68 (s, 1H), 5.10 (s, 2H), 4.45 (p, J = 7.1 Hz, 1H), 3.74 (q, J = 6.7 Hz, 1H), 3.37 (s, 3H), 3.32-3.24 (m, 2H), 2.39 (t, J = 7.3 Hz, 2H), 1.84 (p, J = 7.0 Hz, 2H), 1.37 (d, J = 7.0 Hz, 3H), 1.33 (d, J = 6.8 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 173.4, 173.1, 172.1, 136.0, 128.7 (2C), 128.4 (3C), 78.0, 66.5, 57.4, 48.4, 38.9, 31.7, 24.7, 18.3, 17.9. **HRMS (ESI):** *m/z* calcd for $C_{18}H_{27}N_2O_5$ [M + H]$^+$ 351.1914; found: 351.1910.

4-((*S*)-2-((*R*)-2-Methoxypropanamido)propanamido)butanoic acid (20)

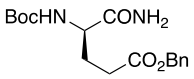


20

Compound **19** (450 mg, 1.3 mmol) was hydrogenated in dry MeOH (5 mL) using 10% wt. Pd/C (70 mg, 0.6 mmol) for 18 hours at room temperature. The catalyst was removed by

filtration through celite® and the filtrate was concentrated under reduced pressure to afford compound **20** in mixture with its methyl ester **20'** (330 mg, ratio: 0.77(**20**):0.23(**20'**); yield determined by NMR: 76%). The crude mixture was used without further purification. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.36-7.27 (m, 2H), 4.46 (p, J = 7.2 Hz, 1H), 3.68 (q, J = 6.7 Hz, 1H), 3.29 (s, 3H), 3.20 (p, J = 6.7 Hz, 2H), 2.27 (td, J = 7.3, 3.0 Hz, 2H), 1.82-1.67 (m, 2H), 1.30 (d, J = 7.0 Hz, 3H), 1.25 (d, J = 6.8 Hz, 3H). **HRMS (ESI):** *m/z* calcd for $C_{11}H_{21}N_2O_5$ $[M + H]^+$ 261.1445; found: 261.1439.

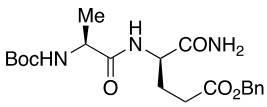
Benzyl (*R*)-5-amino-4-((*tert*-butoxycarbonyl)amino)-5-oxopentanoate (23)



23

To a mixture of compound **22** (1.3 g, 3.0 mmol) and ethyl chloroformate (360 µL, 4.6 mmol) in dry THF (20 mL), NEt_3 (64 µL, 4.6 mmol) was added dropwise at – 15 ˚C. The reaction mixture was stirred for 30 minutes at – 15 ˚C. NH_4OH 28% (1.5 mL) was added dropwise, and the reaction mixture was warmed up to room temperature and left stirring for 1 hour. The crude mixture was dissolved in EtOAc (100 mL) and washed with a sat. solution of NH_4Cl (100 mL), sat. solution of $NaHCO_3$ (100 mL), brine (100 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was then purified by silica gel chromatography (cyclohexane:EtOAc 2:8) to afford compound **23** as a white foam (1.2 g, 96%). $[\alpha]_D^{25}$: + 5.0 (c = 1.0, DCM). **^{1}H NMR (500 MHz, CD_3OD):** δ 7.38-7.28 (m, 5H), 5.13 (s, 2H), 4.14-4.04 (m, 1H), 2.47 (t, J = 7.5 Hz, 2H), 2.14-2.04 (m, 1H), 1.92-1.84 (m, 1H), 1.44 (s, 9H). **^{13}C NMR (126 MHz, CD_3OD):** δ 177.2, 174.3, 157.8, 137.6, 129.5 (2C), 129.2 (3C), 80.7, 67.4, 55.0, 31.4, 28.7 (3C), 28.6. **LRMS (ESI):** *m/z* calcd for $C_{17}H_{24}N_2NaO_5$ $[M + Na]^+$ 359.3; found: 359.3.

Benzyl (*R*)-5-amino-4-((*S*)-2-((tert-butoxycarbonyl)amino)propanamido)-5-oxo pentanoate (24)

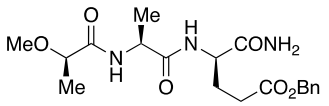


24

Compound **23** (1.2 g, 3.6 mmol) was stirred in a mixture of 50% of TFA in DCM (5 mL) for 2 hours. The solvents were removed under a stream of air and co-evaporation with acetonitrile

was performed to remove the excess of TFA. The amine TFA salt intermediate was dissolved in dry DCM (30 mL) and DIPEA (3.6 mL, 21.4 mmol) was added at 0 ˚C. After stirring for 5 minutes, Boc-Ala-OH (810 mg, 4.3 mmol), EDC (1.0 g, 5.4 mmol) and K-oxyma® (770 mg, 4.3 mmol) were added at 0 ˚C. The reaction mixture was stirred for 24 hours at room temperature. DCM was removed under reduced pressure and the crude solid was dissolved in EtOAc (100 mL). The mixture was washed with water (100 mL), sat. solution of $NaHCO_3$ (100 mL), brine (100 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (DCM:MeOH 99:1) to afford compound **24** as a white foam (1.0 g, 70%). $[\alpha]_D^{25}$**:** + 1.6 (c = 1.0, DCM). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.41 (d, J = 6.6 Hz, 1H), 7.31-7.21 (m, 5H), 6.83 (bs, 1H), 6.01 (s, 1H), 5.34 (d, J = 6.8 Hz, 1H), 5.03 (d, J = 2.9 Hz, 2H), 4.42 (q, J = 7.4, 7.0 Hz, 1H), 4.05 (t, J = 7.2 Hz, 1H), 2.52-2.34 (m, 2H), 2.25-2.18 (m, 1H), 2.03-1.96 (m, 1H), 1.39 (s, 9H), 1.30 (d, J = 7.0 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 173.8, 173.6, 173.3, 155.9, 135.7, 128.6 (2C), 128.3 (2C), 128.2, 80.3, 66.6, 52.3, 50.6, 30.6, 28.3 (3C), 26.9, 17.9. **HRMS (ESI):** *m/z* calcd for $C_{20}H_{30}N_3O_6$ $[M + H]^+$ 408.2129; found: 408.2126.

Benzyl (*R*)-5-amino-4-((*S*)-2-((*R*)-2-methoxypropanamido)propanamido)-5-oxopentanoate (25)

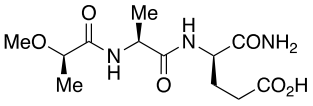


25

Compound **24** (350 mg, 0.9 mmol) was stirred in a mixture of 50% of TFA in DCM (5 mL) for 2 hours. The solvents were removed under a stream of air and co-evaporation with acetonitrile was performed to remove the excess of TFA. The TFA salt intermediate was dissolved in dry DCM (10 mL) followed by the addition of DIPEA (827 µL, 4.9 mmol) at 0 ˚C. The reaction mixture was allowed to stir for 15 minutes at 0 ˚C. (2*R*)-2-Methoxy propanoic acid (123 mg, 1.2 mmol) and TBTU (472 mg, 1.5 mmol) were added consecutively at 0 ˚C. The reaction mixture was stirred for 24 hours at room temperature and then quenched with a sat. solution of $NaHCO_3$ (100 mL). Extraction with EtOAc (3 x 100 mL) was proceed; the combined organic layers were washed with H_2O (100 mL), brine (100 mL) dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (DCM:MeOH 95:5) to afford compound **25** as a white foam (240 mg, 72%). $[\alpha]_D^{25}$: + 6.8 (c = 1.0, MeOH). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.60 (d, J = 8.1 Hz,

1H), 7.36-7.27 (m, 5H), 7.23 (d, *J* = 7.2 Hz, 1H), 6.85 (bs, 1H), 6.20 (bs, 1H), 5.09 (d, *J* = 2.8 Hz, 2H), 4.50-4.43 (m, 2H), 3.72 (q, *J* = 6.7 Hz, 1H), 3.34 (s, 3H), 2.57-2.38 (m, 2H), 2.24-2.16 (m, 1H), 2.01-1.93 (m, 1H), 1.36 (d, *J* = 7.0 Hz, 3H), 1.31 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 173.7, 173.6, 173.2, 172.7, 135.7, 128.6 (2C), 128.3 (2C), 128.2, 77.9, 66.6, 57.3, 52.3, 48.8, 30.6, 27.0, 18.1, 17.7. **HRMS (ESI):** *m/z* calcd for $C_{19}H_{28}N_3O_6$ [M + H]$^+$ 394.1973; found: 394.1969.

(*R*)-5-Amino-4-((*S*)-2-((*R*)-2-methoxypropanamido)propanamido)-5-oxopentanoic acid (26)



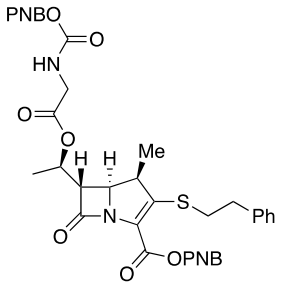
26

Compound **25** (240 mg, 0.6 mmol) was hydrogenated in dry MeOH (5 mL) using 10% wt. Pd/C (32 mg, 0.3 mmol) for 18 hours at room temperature. The catalyst was removed by filtration through celite® and the filtrate was concentrated under reduced pressure to afford compound **26** as a whitish foam (185 mg, 99%). $[\alpha]_D^{25}$: + 25.1 (c = 2.5, MeOH). **^{1}H NMR (500 MHz, CD_3OD):** δ 4.38-4.31 (m, 2H), 3.75 (q, *J* = 6.7 Hz, 1H), 3.32 (s, 3H), 2.36 (t, *J* = 7.5 Hz, 2H), 2.18-2.13 (m, 1H), 1.92-1.85 (m, 1H), 1.36 (d, *J* = 7.1 Hz, 3H), 1.28 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR (126 MHz, CD_3OD):** δ 176.7, 176.2, 175.8, 175.0, 78.7, 57.8, 53.7, 50.4, 31.4, 28.1, 18.5, 18.0. **HRMS (ESI):** *m/z* calcd for $C_{12}H_{22}N_3O_6$ [M + H]$^+$ 304.1503; found: 304.1500.

2-2. Synthesis of protected peptido-carbapenems 27a-n

General procedure for carbapenem esterification: Carbapenem **2** (1 equiv.) in presence of peptidoglycan mimetic (4 equiv. up to 8 equiv.) was treated with DMAP (0.9 equiv.) and then with small portions of EDC (8 equiv. up to 16 equiv.) at – 20 ˚C. The reaction mixture was stirred for 1 – 24 hours while maintaining a temperature between – 30 to – 15 ˚C. After the completion of the reaction, EtOAc was added to dissolve the crude. The organic layer was washed with a sat. solution of $NaHCO_3$, brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (cyclohexane:EtOAc or DCM:MeOH as eluent systems) to afford the desired peptido-carbapenem derivatives.[9]

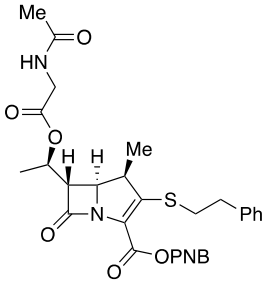
4-Nitrobenzyl (4*R*,5*S*)-4-methyl-6-((*R*)-1-(((((4-nitrobenzyl)oxy)carbonyl)glycyl)-oxy) ethyl)-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (27a)



27a

Following the general procedure of esterification, carbapenem **2** (45 mg, 0.09 mmol) and compound **3** (101.7 mg, 0.4 mmol) were reacted in presence of EDC (153.4 mg, 0.8 mmol) and DMAP (12 mg, 0.09 mmol) to afford compound **27a** as a yellowish foam (64 mg, 89%) after silica gel chromatography purification (cyclohexane:EtOAc 1:1). Completion of esterification was observed after 2 hours of reaction. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.14-8.11 (m, 4H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.41 (d, *J* = 8.7 Hz, 2H), 7.25-7.10 (m, 5H), 5.41 (d, *J* = 13.8 Hz, 1H), 5.32-5.27 (m, 2H), 5.17 (d, *J* = 13.8 Hz, 1H), 5.13 (s, 2H), 3.96-3.89 (m, 3H), 3.31 (dd, *J* = 7.6, 2.6 Hz, 1H), 3.24-3.15 (m, 1H), 3.05-2.96 (m, 2H), 2.93-2.81 (m, 2H), 1.36 (d, *J* = 6.3 Hz, 3H), 1.12 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 170.4, 169.2, 160.3, 156.0, 153.0, 147.8, 147.7, 143.7, 143.1, 139.2, 128.8 (2C), 128.7 (2C), 128.3 (2C), 128.2 (2C), 127.0, 123.9 (4C) 123.3, 70.1, 65.7, 65.4, 56.9, 56.0, 43.3, 43.0, 36.3, 33.1, 18.6, 16.7. **HRMS (ESI):** *m/z* calcd for $C_{35}H_{35}N_5O_{11}S$ $[M + H]^+$ 719.2017; found: 719.2028.

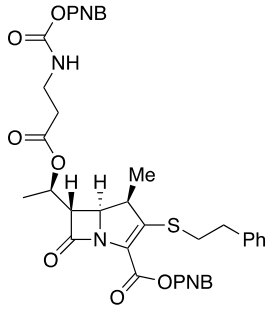
4-Nitrobenzyl (4*R*,5*S*,6*S*)-6-((*R*)-1-((acetylglycyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (27b)



27b

Following the general procedure of esterification, carbapenem **2** (50 mg, 0.1 mmol) and *N*-acetyl-glycine (100 mg, 0.8 mmol) were reacted in presence of EDC (153.4 mg, 0.8 mmol) and DMAP (12 mg, 0.09 mmol) to afford compound **27b** as a yellowish foam (54 mg, 93%) after silica gel chromatography purification (cyclohexane:EtOAc 1:9). Completion of esterification was observed after 4 hours of reaction. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.14 (d, *J* = 8.6 Hz, 2H), 7.57 (d, *J* = 8.8 Hz, 2H), 7.27-7.09 (m, 5H), 6.02 (t, *J* = 5.4 Hz, 1H), 5.42 (d, *J* = 13.8 Hz, 1H), 5.30-5.25 (m, 1H), 5.18 (d, *J* = 13.8 Hz, 1H), 4.01-3.93 (m, 2H), 3.90-3.86 (m, 1H), 3.30 (dd, *J* = 7.9, 2.7 Hz, 1H), 3.26-3.20 (m, 1H), 3.09-2.95 (m, 2H), 2.94-2.81 (m, 2H), 1.96 (s, 3H), 1.36 (d, *J* = 6.3 Hz, 3H), 1.13 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 170.5 (2C), 169.4, 160.4, 153.2, 147.7, 143.2, 139.2, 128.8 (2C), 128.7 (2C), 128.3 (2C), 127.0, 123.9 (2C), 123.3, 70.0, 65.3, 57.0, 56.8, 43.3, 41.7, 36.3, 33.1, 23.0, 18.6, 16.7. **HRMS (ESI):** *m/z* calcd for $C_{29}H_{31}N_3NaO_8S$ $[M + Na]^+$ 604.1724; found: 604.1714.

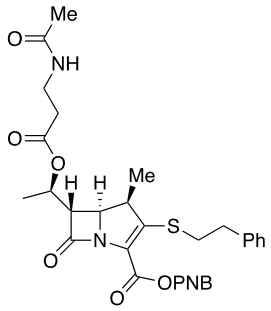
4-Nitrobenzyl (4*R*,5*S*,6*S*)-4-methyl-6-((*R*)-1-((3-((((4-nitrobenzyl)oxy)carbonyl)amino) propanoyl)oxy)ethyl)-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (27c)



27c

Following the general procedure of esterification, carbapenem **2** (50 mg, 0.1 mmol) and compound **4** (110 mg, 0.4 mmol) were reacted in presence of EDC (153.4 mg, 0.8 mmol) and DMAP (12 mg, 0.09 mmol) to afford compound **27c** as a yellowish foam (70 mg, 96%) after silica gel chromatography purification (cyclohexane:EtOAc 6:4). Completion of esterification was observed after 2 hours of reaction. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.12-8.08 (m, 4H), 7.55 (d, *J* = 8.6 Hz, 2H), 7.44-7.37 (m, 2H), 7.23-7.11 (m, 5H), 5.47 (bs, 1H), 5.40 (d, *J* = 13.8 Hz, 1H), 5.24 (p, *J* = 6.3 Hz, 1H), 5.19-5.06 (m, 3H), 3.93 (dd, *J* = 9.0, 2.5 Hz, 1H), 3.41-3.37 (m, 2H), 3.33 (dd, *J* = 6.5, 2.5 Hz, 1H), 3.22-3.15 (m, 1H), 3.06-2.97 (m, 2H), 2.93-2.80 (m, 2H), 2.54-2.45 (m, 2H), 1.31 (d, *J* = 6.4 Hz, 3H), 1.12 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$)**: δ 171.2, 171.0, 160.3, 155.9, 152.9, 147.8, 147.7, 144.1, 143.1, 139.2, 128.8 (2C), 128.7 (2C), 128.3 (2C), 128.1 (2C), 127.0, 123.8 (4C), 123.3, 68.5, 65.3, 65.2, 56.8, 56.2, 43.4, 37.0, 36.3, 34.8, 33.1, 18.4, 16.7. **HRMS (ESI):** *m/z* calcd for $C_{36}H_{37}N_4O_{11}S$ $[M + H]^+$ 733.2174; found: 733.2179.

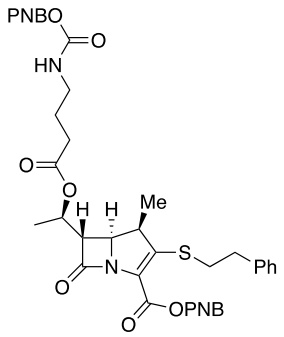
4-Nitrobenzyl (4*R*,5*S*,6*S*)-6-((*R*)-1-((3-acetamidopropanoyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (27d)



27d

Following the general procedure of esterification, carbapenem **2** (50 mg, 0.1 mmol) and *N*-acetyl-ß-alanine (52.5 mg, 0.4 mmol) were reacted in presence of EDC (153 mg, 0.8 mmol) and DMAP (12 mg, 0.09 mmol) to afford compound **27d** as a yellowish foam (52 mg, 87%) after silica gel chromatography purification (DCM:MeOH 95:5). Completion of esterification was observed after 3 hours of reaction. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.18-8.10 (m, 2H), 7.56 (d, *J* = 8.3 Hz, 2H), 7.26-7.09 (m, 5H), 6.19 (bs, 1H), 5.42 (d, *J* = 13.8 Hz, 1H), 5.23 (q, *J* = 7.3, 6.9 Hz, 1H), 5.18 (d, *J* = 13.7 Hz, 1H), 3.94 (dd, *J* = 8.9, 2.6 Hz, 1H), 3.50-3.42 (m, 1H), 3.40-3.33 (m, 1H), 3.34 (dd, *J* = 6.6, 2.6 Hz, 1H), 3.24-3.15 (m, 1H), 3.07-2.96 (m, 2H), 2.93-2.83 (m, 2H), 2.53-2.43 (m, 2H), 1.87 (s, 3H), 1.32 (d, *J* = 6.2 Hz, 3H), 1.14 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 171.5, 171.2, 160.4, 152.9, 152.9, 147.8, 143.1, 139.2, 128.8 (2C), 128.7 (2C), 128.3 (2C), 127.05, 123.9 (2C), 123.4, 68.4, 65.4, 56.8, 56.3, 43.4, 36.3, 35.3, 34.6, 33.1, 23.3, 18.3, 16.8. **HRMS (ESI):** *m/z* calcd for $C_{30}H_{33}N_3NaO_8S$ $[M + Na]^+$ 618.1881; found: 618.1880.

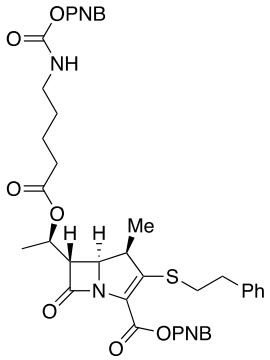
4-Nitrobenzyl (4*R*,5*S*,6*S*)-4-methyl-6-((*R*)-1-((4-((((4-nitrobenzyl)oxy)carbonyl)amino) butanoyl)oxy)ethyl)-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (27e)



27e

Following the general procedure of esterification, carbapenem **2** (50 mg, 0.1 mmol) and compound **5** (113 mg, 0.4 mmol) were reacted in presence of EDC (153 mg, 0.8 mmol) and DMAP (12 mg, 0.09 mmol) to afford compound **27e** as a yellowish foam (74 mg, 99%) after silica gel chromatography purification (cyclohexane:EtOAc 1:1). Completion of esterification was observed after 1 hour of reaction. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.20-8.05 (m, 4H), 7.56 (d, *J* = 8.7 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.32-7.11 (m, 5H), 5.41 (d, *J* = 13.7 Hz, 1H), 5.22 (p, *J* = 6.4 Hz, 1H), 5.16 (d, *J* = 13.8 Hz, 1H), 5.07 (s, 2H), 3.96 (dd, *J* = 9.1, 2.5 Hz, 1H), 3.31 (dd, *J* = 6.6, 2.5 Hz, 1H), 3.25-3.18 (m, 1H), 3.18-3.12 (m, 2H), 3.07-2.95 (m, 2H), 2.94-2.81 (m, 2H), 2.35-2.27 (m, 2H), 1.83-1.73 (m, 2H), 1.30 (d, *J* = 6.4 Hz, 3H), 1.12 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 172.3, 171.0, 160.4, 156.1, 152.8, 147.8, 147.7, 144.1, 143.1, 139.2, 128.8 (2C), 128.7 (2C), 128.3 (2C), 128.2 (2C), 127.0, 123.9 (4C), 123.4, 68.3, 65.4, 65.2, 57.0, 56.4, 43.4, 40.5, 36.3, 33.1, 31.7, 25.2, 18.5, 16.8. **HRMS (ESI):** *m/z* calcd for $C_{37}H_{39}N_5O_{11}S$ $[M + H]^+$ 747.2330; found: 747.2334.

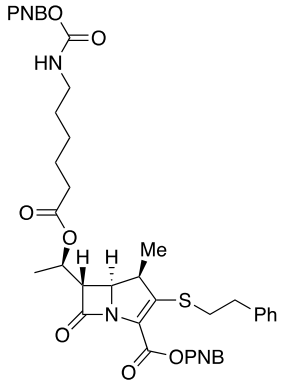
4-Nitrobenzyl (4*R*,5*S*,6*S*)-4-methyl-6-((*R*)-1-((5-((((4-nitrobenzyl)oxy)carbonyl)amino) pentanoyl)oxy)ethyl)-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (27f)



27f

Following the general procedure of esterification, carbapenem **2** (70 mg, 0.15 mmol) and compound **6** (215 mg, 0.8 mmol) were reacted in presence of EDC (306 mg, 1.6 mmol) and DMAP (12 mg, 0.09 mmol) to afford compound **27f** as a yellowish foam (74 mg, 97%) after silica gel chromatography purification (cyclohexane:EtOAc 3:7). Completion of esterification was observed after 24 hours of reaction. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.13-8.10 (m, 4H), 7.56 (d, *J* = 8.7 Hz, 2H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.24-7.10 (m, 5H), 5.41 (d, *J* = 13.7 Hz, 1H), 5.21 (q, *J* = 6.4 Hz, 1H), 5.17 (d, *J* = 13.7 Hz, 1H), 5.08 (s, 2H), 4.95 (t, *J* = 6.1 Hz, 1H), 3.96 (dd, *J* = 9.2, 2.6 Hz, 1H), 3.30 (dd, *J* = 6.8, 2.6 Hz, 1H), 3.23-3.14 (m, 1H), 3.12 (q, *J* = 6.7 Hz, 2H), 3.06-2.95 (m, 2H), 2.92-2.81 (m, 2H), 2.27 (dt, *J* = 7.2, 1.7 Hz, 2H), 1.58 (q, *J* = 7.3 Hz, 2H), 1.51-1.43 (m, 2H), 1.30 (d, *J* = 6.3 Hz, 3H), 1.13 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 172.5, 171.0, 160.4, 156.0, 152.6, 147.8, 147.7, 144.3, 143.1, 139.2, 128.8 (2C), 128.7 (2C), 128.3 (2C), 128.2 (2C), 127.0, 123.8 (4C), 123.5, 68.2, 65.4, 65.2, 57.1, 56.5, 43.4, 40.8, 36.3, 33.1, 30.3, 27.0, 22.1, 18.5, 16.8. **HRMS (ESI):** *m/z* calcd for $C_{38}H_{40}N_4NaO_{11}S$ $[M + Na]^+$ 783.2307; found: 783.2291.

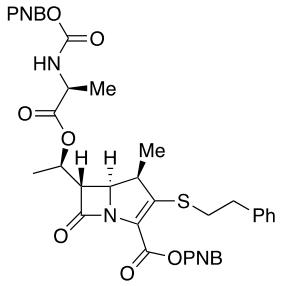
4-Nitrobenzyl (4*R*,5*S*,6*S*)-4-methyl-6-((*R*)-1-((6-((((4-nitrobenzyl)oxy)carbonyl)amino) hexanoyl)oxy)ethyl)-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (27g)



27g

Following the general procedure of esterification, carbapenem **2** (70 mg, 0.15 mmol) and compound **7** (125 mg, 0.4 mmol) were reacted in presence of EDC (153.4 mg, 0.8 mmol) and DMAP (12 mg, 0.09 mmol) to afford compound **27g** as a yellowish foam (52 mg, 68%) after silica gel chromatography purification (cyclohexane:EtOAc 3:7). Completion of esterification was observed after 24 hours of reaction. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.12 (d, *J* = 8.7 Hz, 4H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.25-7.09 (m, 5H), 5.41 (d, *J* = 13.8 Hz, 1H), 5.22-5.16 (m, 2H), 5.13-5.09 (m, 3H), 3.96 (dd, *J* = 9.1, 2.7 Hz, 1H), 3.30 (dd, *J* = 6.9, 2.7 Hz, 1H), 3.22-3.15 (m, 1H), 3.16-3.09 (m, 2H), 3.07-2.96 (m, 2H), 2.90-2.83 (m, 2H), 2.24 (t, *J* = 7.4 Hz, 2H), 1.56 (p, *J* = 7.5 Hz, 2H), 1.44 (p, *J* = 7.2 Hz, 2H), 1.33-1.25 (m, 5H), 1.13 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 172.7, 171.0, 160.4, 156.0, 152.6, 147.7 (2C), 144.3, 143.2, 139.2, 128.8 (2C), 128.7 (2C), 128.2 (2C), 128.2 (2C), 127.0, 123.8 (4C), 123.5, 68.2, 65.3, 65.1, 57.1, 56.5, 43.3, 41.0, 36.8, 34.3, 33.1, 29.6, 26.2, 24.6, 18.5, 16.8. **HRMS (ESI):** *m/z* calcd for $C_{39}H_{42}N_4NaO_{11}S$ $[M + Na]^+$ 797.2463; found: 797.2456.

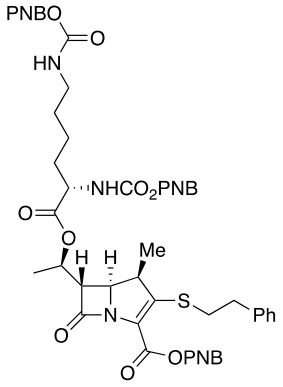
(4*R*,5*S*,6*S*)-4-Nitrobenzyl 4-methyl-6-(1-(((*S*)-2-((((4-nitrobenzyl)oxy)carbonyl)amino) propanoyl)oxy)ethyl)-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (27h)



27h

Following the general procedure of esterification, carbapenem **2** (50 mg, 0.1 mmol) and compound **8** (107 mg, 0.4 mmol) were reacted in presence of EDC (153.4 mg, 0.8 mmol) and DMAP (12 mg, 0.09 mmol) to afford compound **27h** as a yellowish foam (72 mg, 98%) after silica gel chromatography purification (cyclohexane:EtOAc 7:3). Completion of esterification was observed after 1 hour of reaction. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.12 (d, *J* = 8.4 Hz, 2H), 8.09 (d, *J* = 8.4 Hz, 2H), 7.56 (d, *J* = 8.6 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.24-7.08 (m, 5H), 5.41 (d, *J* = 13.8 Hz, 1H), 5.34 (d, *J* = 7.4 Hz, 1H), 5.32-5.23 (m, 1H), 5.17 (d, *J* = 13.8 Hz, 1H), 5.08 (s, 2H), 4.24 (p, *J* = 7.2 Hz, 1H), 3.91 (dd, *J* = 8.9 Hz, 1.8 Hz, 1H), 3.30 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.24-3.15 (m, 1H), 3.05-2.94 (m, 2H), 2.92-2.82 (m, 2H), 1.35 (d, *J* = 7.1 Hz, 6H), 1.12 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 172.3, 170.4, 160.3, 155.3, 153.2, 147.7 (2C), 143.7, 143.1, 139.2, 128.8 (2C), 128.7 (2C), 128.2 (2C), 128.0 (2C), 127.0, 123.8 (4C), 123.2, 70.1, 65.4, 65.3, 56.9, 56.9, 49.9, 43.3, 36.3, 33.1, 18.6, 18.3, 16.7. **HRMS (ESI):** *m/z* calcd for $C_{36}H_{37}N_4O_{11}S$ $[M + H]^+$ 733.2174; found: 733.2184.

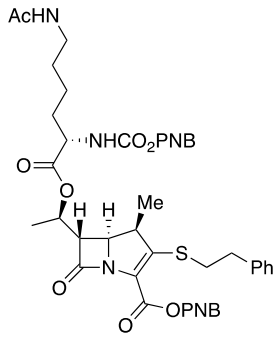
4-Nitrobenzyl (4*R*,5*S*,6*S*)-4-methyl-6-((*R*)-1-((*N*^{2}-(((4-nitrobenzoyl)oxy)methyl)-*N*^{6}-(((4-nitrobenzyl)oxy)carbonyl)-*L*-lysyl)oxy)ethyl)-7-oxo-3-(phenethylthio)-1-azabicyclo [3.2.0]hept-2-ene-2-carboxylate (27i)



27i

Following the general procedure of esterification, carbapenem **2** (50 mg, 0.1 mmol) and compound **9** (201.8 mg, 0.4 mmol) were reacted in presence of EDC (153.4 mg, 0.8 mmol) and DMAP (12 mg, 0.09 mmol) to afford compound **27i** as a yellowish foam (87 mg, 90%) after silica gel chromatography purification (cyclohexane:EtOAc 3:7). Completion of esterification was observed after 1 hour of reaction. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.12-8.06 (m, 6H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.42-7.35 (m, 4H), 7.24-7.07 (m, 5H), 5.46 (d, *J* = 7.5 Hz, 1H), 5.40 (d, *J* = 13.9 Hz, 1H), 5.27 (p, *J* = 6.5 Hz, 1H), 5.16 (d, *J* = 13.8 Hz, 1H), 5.12 (d, *J* = 3.8 Hz, 1H), 5.07 (s, 4H), 4.22-4.18 (m, 1H), 3.91 (dd, *J* = 9.0, 2.5 Hz, 1H), 3.31 (dd, *J* = 7.9, 2.5 Hz, 1H), 3.23 (q, *J* = 7.8 Hz, 1H), 3.16-3.08 (m, 2H), 3.05-2.95 (m, 2H), 2.90-2.81 (m, 2H), 1.82-1.73 (m, 1H), 1.70-1.61 (m, 1H), 1.52-1.42 (m, 2H), 1.40-1.26 (m, 5H), 1.13 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 171.6, 170.4, 160.3, 156.2, 155.7, 153.2, 147.7, 144.1 (2C), 143.7 (2C), 143.1, 139.2, 128.8 (4C), 128.7 (2C), 128.2 (2C), 128.2 (2C), 127.0, 124.0 (2C), 123.8 (4C), 123.2, 70.0, 65.7, 65.5, 65.3, 65.2, 56.8, 54.0, 43.3, 40.6, 36.3, 33.1, 31.8, 29.5, 22.3, 18.5, 16.7. **HRMS (ESI):** *m/z* calcd for $C_{47}H_{48}N_6NaO_{15}S$ $[M + Na]^+$ 991.2791; found: 991.2774.

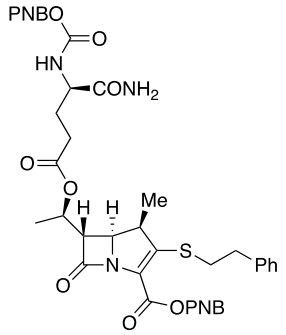
4-Nitrobenzyl (4*R*,5*S*,6*S*)-6-((*R*)-1-((*N*^{6}-acetyl-*N*^{2}-(((4-nitrobenzyl)oxy)carbonyl)-*D*-lysyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (27j)



27j

Following the general procedure of esterification, carbapenem **2** (50 mg, 0.1 mmol) and compound **10** (150 mg, 0.4 mmol) were reacted in presence of EDC (153 mg, 0.8 mmol) and DMAP (12 mg, 0.09 mmol) to afford compound **27j** as a yellowish foam (70 mg, 84%) after silica gel chromatography purification (DCM:MeOH 96:4). Completion of esterification was observed after 1 hour of reaction. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.18-8.07 (m, 4H), 7.56 (d, *J* = 8.7 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.25-7.09 (m, 5H), 5.81-5.71 (m, 1H), 5.60 (d, *J* = 7.8 Hz, 1H), 5.41 (d, *J* = 13.7 Hz, 1H), 5.32-5.23 (m, 1H), 5.17 (d, *J* = 13.9 Hz, 1H), 5.08 (d, *J* = 2.1 Hz, 2H), 4.20-4.16 (m, 1H), 3.93 (dd, *J* = 9.0, 2.5 Hz, 1H), 3.31 (dd, *J* = 7.9, 2.5 Hz, 1H), 3.27-3.20 (m, 1H), 3.20-3.09 (m, 2H), 3.06-2.95 (m, 2H), 2.89-2.83 (m, 2H), 1.88 (s, 3H), 1.80-1.73 (m, 1H), 1.68-1.62 (m, 1H), 1.48-1.40 (m, 2H), 1.37-1.28 (m, 5H), 1.13 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 171.7, 170.6, 170.5, 160.3, 155.8, 153.3, 147.7, 143.8, 143.8, 143.1, 139.2, 128.8 (2C), 128.7 (2C), 128.2 (2C), 128.0 (2C), 127.0, 123.8 (4C), 123.2, 69.9, 65.7, 65.4, 65.3, 56.9, 54.1, 43.3, 39.0, 36.3, 33.1, 31.6, 29.2, 23.3, 22.4, 18.6, 16.7. **HRMS (ESI):** *m/z* calcd for $C_{41}H_{46}N_5O_{12}S$ $[M + H]^+$ 832.2858; found: 832.2865.

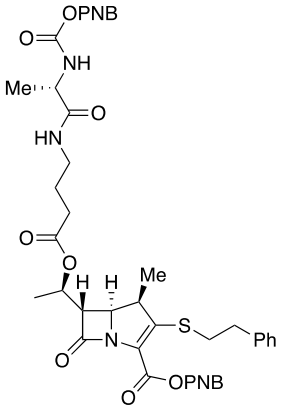
4-Nitrobenzyl (4*R*,5*S*,6*S*)-6-((*S*)-1-(((*R*)-5-amino-4-((((4-nitrobenzyl)oxy)carbonyl) amino)-5-oxopentanoyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0] hept-2-ene-2-carboxylate (27k)



27k

Following the general procedure of esterification, carbapenem **2** (50 mg, 0.1 mmol) and compound **13** (150 mg, 0.4 mmol) were reacted in presence of EDC (153 mg, 0.8 mmol) and DMAP (12 mg, 0.09 mmol) to afford compound **27k** as a yellowish foam (65 mg, 82%) after silica gel chromatography purification (cyclohexane:EtOAc 2:8). Completion of esterification was observed after 4 hours of reaction. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.13-8.11 (m, 4H), 7.54 (d, *J* = 7.9 Hz, 2H), 7.41 (d, *J* = 7.7 Hz, 2H), 7.26-7.09 (m, 5H), 6.05 (bs, 1H), 5.94 (d, *J* = 6.8 Hz, 1H), 5.42 (d, *J* = 8.3 Hz, 1H), 5.37 (d, *J* = 13.9 Hz, 1H), 5.31 (p, *J* = 6.4 Hz, 1H), 5.20 (d, *J* = 13.6 Hz, 1H), 5.11 (s, 2H), 4.27-4.21 (m, 1H), 4.03 (d, *J* = 7.6 Hz, 1H), 3.40-3.35 (m, 1H), 3.28-3.22 (m, 1H), 3.07-2.98 (m, 2H), 2.93-2.83 (m, 2H), 2.25-2.13 (m, 2H), 2.08-1.99 (m, 2H), 1.31 (d, *J* = 5.8 Hz, 3H), 1.13 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 171.2, 171.0, 160.4, 155.8, 155.7, 152.7, 147.8 (2C), 143.8, 142.9, 139.1, 128.9 (2C), 128.7 (2C), 128.4 (2C), 128.2 (2C), 127.1, 123.9 (4C), 123.4, 68.8, 65.6 (2C), 56.9, 55.7, 53.9, 43.4, 36.3, 33.2, 31.2, 27.8, 18.3, 16.8. **HRMS (ESI):** *m/z* calcd for $C_{38}H_{40}N_5O_{12}S$ $[M + H]^+$ 790.2388; found: 790.2383.

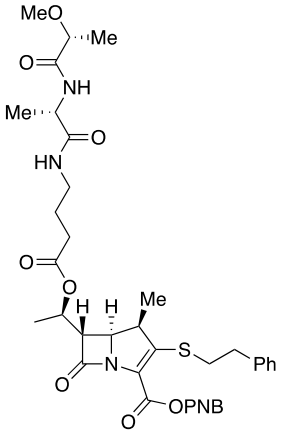
4-Nitrobenzyl (4*R*,5*S*,6*S*)-4-methyl-6-((5*R*,13*R*)-5-methyl-1-(4-nitrophenyl)-3,6,11-trioxo-2,12-dioxa-4,7-diazatetradecan-13-yl)-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (27l)



27l

Following the general procedure of esterification, carbapenem **2** (50 mg, 0.1 mmol) and compound **16** (141 mg, 0.4 mmol) were reacted in presence of EDC (306 mg, 1.6 mmol) and DMAP (12 mg, 0.09 mmol) to afford compound **27l** as a yellowish foam (70 mg, 86%) after silica gel chromatography purification (cyclohexane:EtOAc 3:7). Completion of esterification was observed after 3 hours of reaction. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.13-8.11 (m, 4H), 7.56 (d, *J* = 7.9 Hz, 2H), 7.41 (d, *J* = 7.7 Hz, 2H), 7.26-7.09 (m, 5H), 6.41 (bs, 1H), 5.56 (d, *J* = 5.9 Hz, 1H), 5.42 (d, *J* = 13.7 Hz, 1H), 5.24 (p, *J* = 6.3 Hz, 1H), 5.18 (d, *J* = 13.5 Hz, 1H), 5.11 (s, 2H), 4.15-4.12 (m, 1H), 3.98 (d, *J* = 8.9 Hz, 1H), 3.33-3.32 (m, 1H), 3.26-3.22 (m, 2H), 3.18-3.11 (m, 1H), 3.08-2.98 (m, 2H), 2.92-2.83 (m, 2H), 2.31-2.23 (m, 2H), 1.77-1.74 (m, 2H), 1.28 (d, *J* = 6.2 Hz, 6H), 1.13 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 172.4, 172.3, 171.2, 160.5, 155.5, 152.6, 147.7 (2C) 143.9, 143.0, 139.1, 128.8 (2C), 128.7 (2C), 128.3 (2C), 128.1 (2C), 127.0, 123.8 (4C), 123.5, 68.0, 65.5, 65.4, 57.1, 56.3, 50.7, 43.4, 38.8, 36.3, 33.1, 31.8, 24.7, 19.1, 18.4, 16.8. **HRMS (ESI):** *m/z* calcd for $C_{40}H_{44}N_5O_{12}S$ $[M + H]^+$ 818.2701; found: 818.2697.

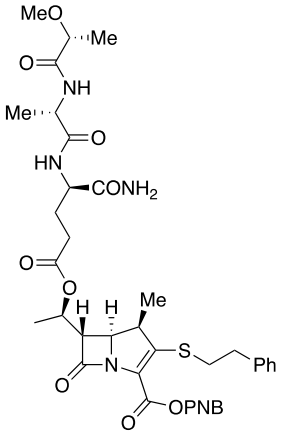
4-Nitrobenzyl (4*R*,5*S*)-6-((3*R*,6*S*,14*R*)-3,6-dimethyl-4,7,12-trioxo-2,13-dioxa-5,8-diaza pentadecan-14-yl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (27m)



27m

Following the general procedure of esterification, carbapenem **2** (50 mg, 0.1 mmol) and compound **20** (104 mg, 0.4 mmol) were reacted in presence of EDC (306 mg, 1.6 mmol) and DMAP (12 mg, 0.09 mmol) to afford, after silica gel chromatography (cyclohexane:EtOAc 1:9), compound **27m** in a mixture with peptide **20** (25 mg, ratio: 0.72(**27m**):0.28(**20**); yield determined by NMR: 35%). The mixture was engaged without further purification.

4-Nitrobenzyl (4*R*,5*S*)-6-((3*S*,6*R*,9*R*,14*R*)-9-carbamoyl-3,6-dimethyl-4,7,12-trioxo-2,13-dioxa-5,8-diazapentadecan-14-yl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0] hept-2-ene-2-carboxylate (27n)



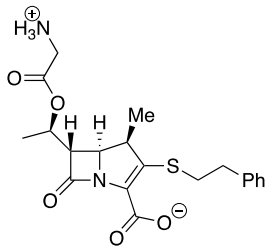
27n

Following the general procedure of esterification, carbapenem **2** (50 mg, 0.1 mmol) and compound **26** (121 mg, 0.4 mmol) were reacted in presence of EDC (306 mg, 1.6 mmol) and DMAP (12 mg, 0.09 mmol) to afford compound **27n** as a yellowish foam (67 mg, 87%) after silica gel chromatography purification (DCM:MeOH 95:5). Completion of esterification was observed after 20 hours of reaction. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.13 (d, J = 8.7 Hz, 2H), 7.56 (d, J = 8.5 Hz, 2H), 7.29-7.10 (m, 5H), 7.04 (d, J = 7.1 Hz, 1H), 6.72 (bs, 1H), 5.83 (bs, 1H), 5.41 (d, J = 13.9 Hz, 1H), 5.24-5.15 (m, 3H), 4.49-4.32 (m, 2H), 3.94 (dd, J = 9.1, 2.6 Hz, 1H), 3.67 (q, J = 6.8 Hz, 1H), 3.38 (dd, J = 6.9, 2.6 Hz, 1H), 3.30 (s, 3H), 3.27-3.20 (m, 1H), 3.09-2.97 (m, 2H), 2.92-2.84 (m, 2H), 2.45-2.32 (m, 2H), 2.18-2.07 (m, 1H), 1.91-1.84 (m, 1H), 1.34-1.31 (m, 6H), 1.26 (d, J = 6.6 Hz, 3H), 1.14 (d, J = 7.3 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 173.8, 173.6, 172.5, 172.3, 171.2, 160.4, 153.0, 147.7, 143.1, 139.2, 128.9 (2C), 128.7 (2C), 128.3 (2C), 127.0, 123.8 (2C), 123.3, 77.9, 68.6, 65.4, 57.4, 56.8, 56.4, 52.0, 48.9, 43.4, 36.2, 33.1, 30.7, 27.4, 18.3, 18.1, 17.8, 16.8. **HRMS (ESI):** *m/z* calcd for $C_{37}H_{46}N_5O_{11}S$ $[M + H]^+$ 768.2909; found: 768.2909.

2-3. Synthesis of peptido-carbapenems 28a-n

General procedure for final carbapenem deprotection: The corresponding carbapenem derivative (1 equiv.) was treated with Pt/C 10% wt. (1 equiv. mass.) in a mixture of THF:triethylammonium bicarbonate buffer (1 M, pH = 8.5) (2:1) and the reaction mixture was hydrogenated under 3.5 bars for 2 hours at room temperature using the PARR apparatus. The crude mixture was filtered through a celite pack to remove the catalyst. THF was removed under reduced pressure, and H_2O was added. The crude mixture were purified using a HPLC system with a reverse phase C18 column (Agilent, 250 mm x 21.2 mm, 5 µm) using a solvent system consisting of H_2O and acetonitrile (linear gradient, 0 to 100% over 45 minutes) and the selected fractions were collected and lyophilized to afford the corresponding deprotected carbapenem derivative.

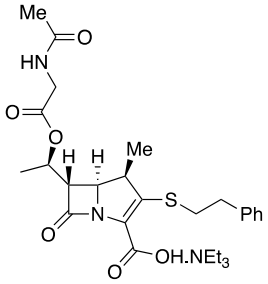
(4*R*,5*S*)-6-((*R*)-1-(2-Ammonioacetoxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-aza bicyclo[3.2.0]hept-2-ene-2-carboxylate (28a)



28a

Following the general procedure of deprotection, treating carbapenem **27a** (55 mg, 0.08 mmol) with Pt/C (55 mg, 1 equiv. mass.) afforded compound **28a** as a white foam (6.5 mg, 21%) after HPLC purification. **^{1}H NMR (500 MHz, D_2O):** δ 7.45-7.33 (m, 5H), 5.50-5.46 (m, 1H), 4.06-3.93 (m, 3H), 3.63 (dd, J = 4.0, 2.6 Hz, 1H), 3.27-3.16 (m, 2H), 3.08-3.01 (m, 2H), 3.01-2.92 (m, 1H), 1.40 (d, J = 6.5 Hz, 3H), 1.13 (d, J = 7.2 Hz, 3H). **HRMS (ESI):** *m/z* calcd for $C_{20}H_{25}N_2O_5S$ $[M + H]^+$ 405.1478; found 405.1471. **HPLC purity:** 95.2%. **HPLC retention time:** 18.6 min.

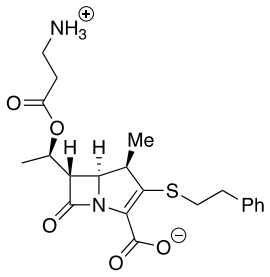
(4*R*,5*S*,6*S*)-6-((*R*)-1-((Acetylglycyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (28b)



28b

Following the general procedure of deprotection, treating carbapenem **27b** (50 mg, 0.09 mmol) with Pt/C (50 mg, 1 equiv. mass.) afforded compound **28b** as a white foam (12.3 mg, 26%) after HPLC purification. **^{1}H NMR (500 MHz, D_2O):** δ 7.46-7.32 (m, 5H), 5.35 (q, J = 9.0, 6.1 Hz, 1H), 4.14-3.98 (m, 2H), 3.87 (d, J = 8.8 Hz, 1H), 3.58 (d, J = 4.7 Hz, 1H), 3.24 (q, J = 7.3 Hz, 6H), 3.22-2.88 (m, 5H), 2.12 (s, 3H), 1.39 (s, 3H), 1.33 (td, J = 7.4, 1.0 Hz, 9H), 1.13 (d, J = 6.8 Hz, 3H). **HRMS (ESI):** *m/z* calcd for $C_{22}H_{26}N_2NaO_6S$ $[M + Na]^+$ 469.1404; found: 469.1393. **HPLC purity:** 90.4%. **HPLC retention time:** 19.9 min.

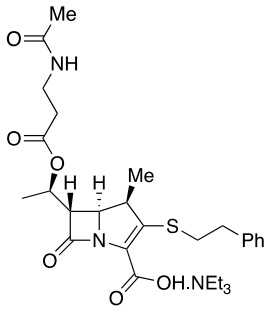
(4*R*,5*S*)-6-((*R*)-1-((3-Ammoniopropanoyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (28c)



28c

Following the general procedure of deprotection, treating carbapenem **27c** (70 mg, 0.1 mmol) with Pt/C (70 mg, 1 equiv. mass.) afforded compound **28c** as a white foam (2.4 mg, 6%) after HPLC purification. **^{1}H NMR (500 MHz, D_2O):** δ 7.43-7.33 (m, 5H), 5.42-5.37 (m, 1H), 3.93 (dd, *J* = 8.9, 2.4 Hz, 1H), 3.63-3.58 (m, 1H), 3.36 (t, *J* = 6.5 Hz, 2H), 3.25-3.16 (m, 2H), 3.09-3.05 (m, 2H), 3.01-2.85 (m, 3H), 1.37 (d, *J* = 6.4 Hz, 3H), 1.12 (d, *J* = 7.3 Hz, 3H). **HRMS (ESI):** *m/z* calcd for $C_{21}H_{27}N_2O_5S$ $[M + H]^+$ 419.1635; found: 419.1641. **HPLC purity:** 99.6%. **HPLC retention time:** 19.4 min.

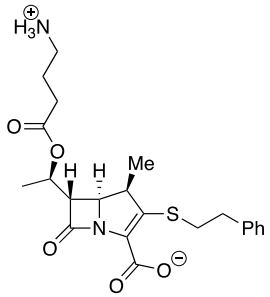
(4*R*,5*S*,6*S*)-6-((*R*)-1-((3-Acetamidopropanoyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid (28d)



28d

Following the general procedure of deprotection, treating carbapenem **27d** (50 mg, 0.09 mmol) with Pt/C (50 mg, 1 equiv. mass.) afforded compound **28d** as a white foam (19 mg, 40%) after HPLC purification. **^{1}H NMR (500 MHz, D_2O):** δ 7.45-7.31 (m, 5H), 5.40-5.26 (m, 1H), 3.85 (d, *J* = 8.7 Hz, 1H), 3.60-3.46 (m, 3H), 3.24 (q, *J* = 7.3 Hz, 6H), 3.22 -3.02 (m, 4H), 2.97 (q, *J* = 16.6, 12.5 Hz, 1H), 2.71 (bs, 2H), 2.02 (s, 3H), 1.35 (d, *J* = 12.5 Hz, 3H), 1.32 (d, *J* = 7.3 Hz, 9H), 1.17-1.06 (m, 3H). **HRMS (ESI):** *m/z* calcd for $C_{23}H_{28}N_2NaO_6S$ $[M + H]^+$ 483.1560; found: 483.1547. **HPLC purity:** 87.7%. **HPLC retention time:** 20.3 min.

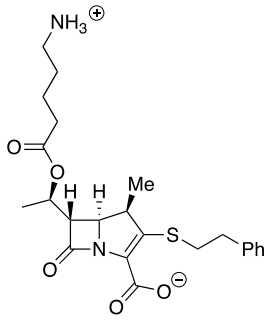
(4*R*,5*S*)-6-((*R*)-1-((4-Ammoniobutanoyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (28e)



28e

Following the general procedure of deprotection, treating carbapenem **27e** (40 mg, 0.05 mmol) with Pt/C (40 mg, 1 equiv. mass.) afforded compound **28e** as a white foam (8.7 mg, 40%) after HPLC purification. **NMR (500 MHz, D_2O):** δ 7.43-7.33 (m, 5H), 5.39-5.34 (m, 1H), 3.92 (dd, *J* = 8.8, 2.3 Hz, 1H), 3.59-3.58 (t, *J* = 3.2 Hz, 1H), 3.27-3.14 (m, 2H), 3.08-3.02 (m, 4H), 2.99-2.93 (m, 1H), 2.70-2.64 (m, 1H), 2.58-2.52 (m, 1H), 2.08-2.02 (m, 2H), 1.35 (d, *J* = 6.4 Hz, 3H), 1.12 (d, *J* = 7.2 Hz, 3H). **HRMS (ESI):** *m/z* calcd for $C_{22}H_{29}N_2O_5S$ $[M + H]^+$ 433.1791; found: 433.1796. **HPLC purity:** 99.7%. **HPLC retention time:** 19.2 min.

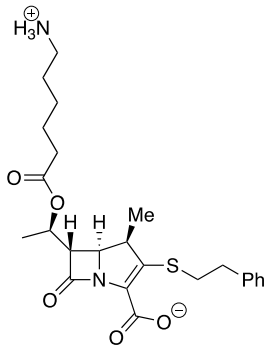
(4*R*,5*S*,6*S*)-6-((*R*)-1-((5-Ammoniopentanoyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (28f)



28f

Following the general procedure of deprotection, treating carbapenem **27f** (50 mg, 0.07 mmol) with Pt/C (50 mg, 1 equiv. mass.) afforded compound **28f** as a white foam (1.7 mg, 6%) after HPLC purification. **^{1}H NMR (500 MHz, D_2O):** δ 7.43-7.34 (m, 5H), 5.39-5.34 (m, 1H), 3.93-3.89 (m, 1H), 3.58 (t, J = 2.9 Hz, 1H), 3.23-3.19 (m, 1H), 3.17-3.14 (m, 1H), 3.10-3.03 (m, 4H), 3.00-2.94 (m, 1H), 2.60-2.55 (m, 1H), 2.53-2.46 (m, 1H), 1.79-1.70 (m, 4H), 1.33 (d, J = 6.3 Hz, 3H), 1.12 (d, J = 7.2 Hz, 3H). **HRMS (ESI):** *m/z* calcd for $C_{23}H_{31}N_2O_5S$ $[M + H]^+$ 447.1948; found: 447.1952. **HPLC purity:** 98.9%. **HPLC retention time:** 19.6 min.

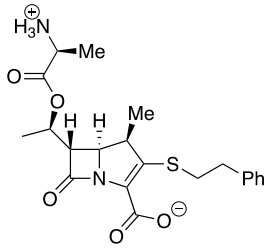
(4*R*,5*S*,6*S*)-6-((*R*)-1-((6-Ammoniohexanoyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (28g)



28g

Following the general procedure of deprotection, treating carbapenem **27g** (50 mg, 0.07 mmol) with Pt/C (50 mg, 1 equiv. mass.) afforded compound **28g** as a white foam (4.6 mg, 17%) after HPLC purification. **^{1}H NMR (500 MHz, D_2O):** δ 7.46-7.33 (m, 5H), 5.37-5.32 (m, 1H), 3.91 (dd, *J* = 8.9, 2.6 Hz, 1H), 3.59 (t, *J* = 2.7, 1H), 3.27-3.19 (m, 1H), 3.17-3.09 (m, 2H), 3.09-3.03 (m, 3H), 3.01-2.93 (m, 1H), 2.59-2.53 (m, 1H), 2.52-2.44 (m, 1H), 1.74 (p, *J* = 7.4 Hz, 4H), 1.47-1.42 (m, 2H), 1.35 (d, *J* = 6.3 Hz, 3H), 1.13 (d, *J* = 7.2 Hz, 3H). **HRMS (ESI):** *m/z* calcd for $C_{24}H_{33}N_2O_5S$ $[M + H]^+$ 461.2105; found: 461.2096. **HPLC purity:** 99.4%. **HPLC retention time:** 20.2 min.

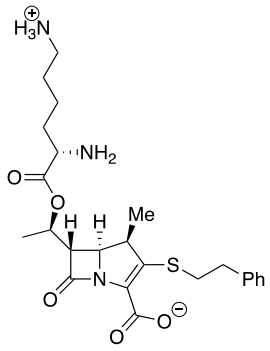
(4*R*,5*S*)-6-((*R*)-1-(((*S*)-2-Ammoniopropanoyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethyl thio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (28h)



28h

Following the general procedure of deprotection, treating carbapenem **27h** (74 mg, 0.1 mmol) with Pt/C (74 mg, 1 equiv. mass.) afforded compound **28h** as a white foam (3.3 mg, 8%) after HPLC purification. **^{1}H NMR (500 MHz, D_2O):** δ 7.43-7.33 (m, 5H), 5.46 (p, J = 6.1 Hz, 1H), 4.30 (q, J = 6.8 Hz, 1H), 3.94 (d, J = 8.9 Hz, 1H), 3.63 (bs, 1H), 3.24-3.18 (m, 2H), 3.09-3.02 (m, 2H), 2.99-2.93 (m, 1H), 1.64 (d, J = 6.9 Hz, 3H), 1.40 (d, J = 6.1 Hz, 3H), 1.13 (d, J = 7.1 Hz, 3H). **HRMS (ESI):** *m/z* calcd for $C_{21}H_{27}N_2O_5S$ $[M + H]^+$ 419.1635; found: 419.1629. **HPLC purity:** 98.2%. **HPLC retention time:** 19.0 min.

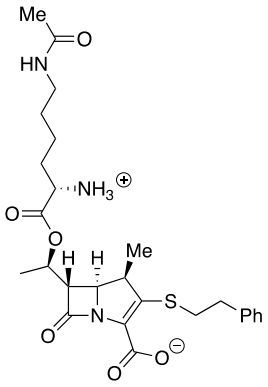
(4*R*,5*S*,6*S*)-6-((*R*)-1-(((*S*)-2,6-Diammoniohexanoyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (28i)



28i

Following the general procedure of deprotection, treating carbapenem **27i** (83 mg, 0.09 mmol) with Pt/C (83 mg, 1 equiv. mass.) afforded compound **28i** as a white foam (3.8 mg, 9%) after HPLC purification. **^{1}H NMR (500 MHz, D_2O):** δ 7.46-7.32 (m, 5H), 5.49-5.33 (m, 1H), 3.96 (dd, J = 9.0, 2.5 Hz, 1H), 3.76 (t, J = 6.4 Hz, 1H), 3.63 (t, J = 3.2 Hz, 1H), 3.27-3.13 (m, 2H), 3.12-3.02 (m, 4H), 3.01-2.95 (m, 1H), 1.92-1.80 (m, 2H), 1.77 (p, J = 7.5 Hz, 2H), 1.57-1.44 (m, 2H), 1.38 (d, J = 6.4 Hz, 3H), 1.14 (d, J = 7.3 Hz, 3H). **HRMS (ESI):** *m/z* calcd for $C_{24}H_{34}N_3O_5S$ $[M + H]^+$ 476.2214; found: 476.2203. **HPLC purity:** 92.7%. **HPLC retention time:** 17.9 min.

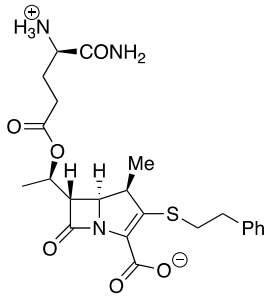
(4*R*,5*S*,6*S*)-6-((*R*)-1-(((*S*)-6-Acetamido-2-ammoniohexanoyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (28j)



28j

Following the general procedure of deprotection, treating carbapenem **27j** (50 mg, 0.06 mmol) with Pt/C (50 mg, 1 equiv. mass.) afforded compound **28j** as a white foam (9.7 mg, 32%) after HPLC purification. **^{1}H NMR (500 MHz, D_2O):** δ 7.45-7.29 (m, 5H), 5.50-5.46 (m, 1H), 4.22 (t, *J* = 6.4 Hz, 1H), 3.93 (dd, *J* = 9.1, 2.4 Hz, 1H), 3.63 (t, *J* = 3.2 Hz, 1H), 3.23-3.13 (m, 4H), 3.09-3.01 (m, 2H), 3.00-2.93 (m, 1H), 2.09-1.95 (m, 5H), 1.70-1.60 (m, 2H), 1.60-1.51 (m, 1H), 1.50 (d, *J* = 7.1 Hz, 1H), 1.41 (d, *J* = 6.4 Hz, 3H), 1.13 (d, *J* = 7.4 Hz, 3H). **HRMS (ESI):** *m/z* calcd for $C_{26}H_{36}N_3O_6S$ $[M + H]^+$ 518.2319; found: 518.2310. **HPLC purity:** 97.2%. **HPLC retention time:** 18.8 min.

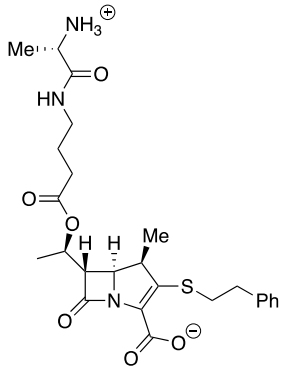
(4*R*,5*S*)-6-((*R*)-1-(((*R*)-5-Amino-4-ammonio-5-oxopentanoyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (28k)



28k

Following the general procedure of deprotection, treating carbapenem **27k** (40 mg, 0.05 mmol) with Pt/C (40 mg, 1 equiv. mass.) afforded compound **28k** as a white foam (3.4 mg, 14%) after HPLC purification. **^{1}H NMR (500 MHz, D_2O):** δ 7.43-7.32 (m, 5H), 5.51-5.46 (m, 1H), 4.26 (t, J = 6.4 Hz, 1H), 3.87 (dd, J = 9.0, 2.4 Hz, 1H), 3.66-3.62 (m, 1H), 3.22-3.17 (m, 1H), 3.14-3.02 (m, 3H), 2.98-2.94 (m, 1H), 2.58 (t, J = 7.6 Hz, 2H), 2.28 (q, J = 7.2 Hz, 2H), 1.40 (d, J = 6.4 Hz, 3H), 1.12 (d, J = 7.2 Hz, 3H). **HRMS (ESI):** *m/z* calcd for $C_{23}H_{30}N_3O_6S$ $[M + H]^+$ 476.1849; found: 476.1844. **HPLC purity:** 91.5%. **HPLC retention time:** 18.5 min.

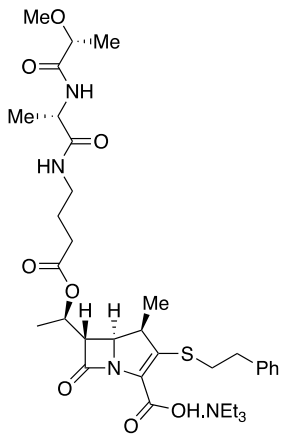
(4*R*,5*S*)-6-((*R*)-1-((4-((S)-2-Ammoniopropanamido)butanoyl)oxy)ethyl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylate (28l)



28l

Following the general procedure of deprotection, treating carbapenem **27l** (110 mg, 0.13 mmol) with Pt/C (110 mg, 1 equiv. mass.) afforded compound **28l** as a white foam (10.1 mg, 15%) after HPLC purification. **^{1}H NMR (500 MHz, D_2O):** δ 7.42-7.32 (m, 5H), 5.38-5.29 (m, 1H), 4.06 (q, *J* = 7.0 Hz, 1H), 3.83 (dd, *J* = 8.9, 2.3 Hz, 1H), 3.58-3.52 (m, 1H), 3.39-3.24 (m, 2H), 3.24-3.15 (m, 1H), 3.14-3.00 (m, 3H), 3.00-2.91 (m, 1H), 2.58-2.44 (m, 2H), 1.96-1.85 (m, 2H), 1.54 (d, *J* = 7.1 Hz, 3H), 1.34 (d, *J* = 6.4 Hz, 3H), 1.10 (d, *J* = 7.2 Hz, 3H). **HRMS (ESI):** *m/z* calcd for $C_{25}H_{34}N_3O_6S$ $[M + H]^+$ 504.2162; found: 504.2164. **HPLC purity:** 97.9%. **HPLC retention time:** 19.4 min.

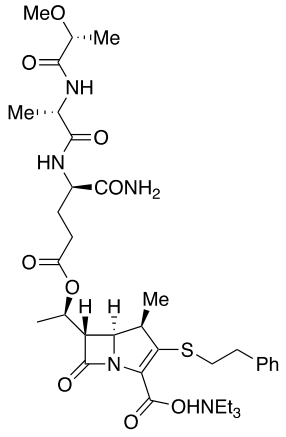
(4*R*,5*S*)-6-((3*R*,6*S*,14*R*)-3,6-Dimethyl-4,7,12-trioxo-2,13-dioxa-5,8-diazapentadecan-14-yl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid (28m)



28m

Following the general procedure of deprotection, treating the mixture of **27m:20** (25 mg, with 18 mg of **27m**) with Pt/C (18 mg, 1 equiv. mass.) afforded compound **28m** as a white foam (3.9 mg, 31%) after HPLC purification. **^{1}H NMR (500 MHz, D_2O):** δ 7.42-7.32 (m, 5H), 5.31 (p, *J* = 6.3 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 1H), 3.95 (q, *J* = 6.8 Hz, 1H), 3.82 (dd, *J* = 9.1, 2.5 Hz, 1H), 3.56 (dd, *J* = 5.0, 2.5 Hz, 1H), 3.39 (s, 3H), 3.37-3.32 (m, 2H), 3.27-3.22 (m, 2H), 3.15-3.09 (m, 2H), 3.01-2.91 (m, 1H), 2.50-2.46 (m, 2H), 1.88 (p, *J* = 7.2 Hz, 2H), 1.43 (d, *J* = 7.2 Hz, 3H), 1.37 (d, *J* = 6.7 Hz, 3H), 1.35 (d, *J* = 6.4 Hz, 3H), 1.11 (d, *J* = 7.2 Hz, 3H). **HRMS (ESI):** *m/z* calcd for $C_{29}H_{40}N_3O_8S$ $[M + H]^+$ 590.2530; found: 590.2531. **HPLC purity:** 93.7%. **HPLC retention time:** 21.0 min.

(4*R*,5*S*)-6-((3*R*,6*S*,9*R*,14*R*)-9-Carbamoyl-3,6-dimethyl-4,7,12-trioxo-2,13-dioxa-5,8-diaza pentadecan-14-yl)-4-methyl-7-oxo-3-(phenethylthio)-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid (28n)



28n

Following the general procedure of deprotection, treating the mixture of **27n** (65 mg, 0.09 mmol) with Pt/C (65 mg, 1 equiv. mass.) afforded compound **28n** as a white foam (11.3 mg, 21%) after HPLC purification. **^{1}H NMR (500 MHz, D_2O):** δ 7.42-7.31 (m, 5H), 5.31 (p, *J* = 6.2 Hz, 1H), 4.41-4.34 (m, 2H), 3.95 (q, *J* = 6.8 Hz, 1H), 3.85 (dd, *J* = 8.9, 2.5 Hz, 1H), 3.57 (dd, *J* = 5.1, 2.5 Hz, 1H), 3.38 (s, 3H), 3.22-3.14 (m, 2H), 3.11-3.06 (m, 2H), 3.00-2.92 (m, 1H), 2.65-2.49 (m, 2H), 2.34-2.25 (m, 1H), 2.06-1.99 (m, 1H), 1.47 (d, *J* = 7.2 Hz, 3H), 1.36 (d, *J* = 6.3, 3H), 1.35 (d, *J* = 5.3 Hz, 3H), 1.12 (d, *J* = 7.2 Hz, 3H). **HRMS (ESI):** *m/z* calcd for $C_{30}H_{41}N_4O_9S$ $[M + H]^+$ 633.2588; found: 633.2587. **HPLC purity:** 98.4%. **HPLC retention time:** 20.1 min.

3. Acylation of 2' and compounds 28a-n monitored by MS

In a 1.5 mL Eppendorf, 1.0 µL of 1.0 M ammonium acetate (pH = 7.4), 10.0 µL of 1.0 mM **2'** or **28a-n** (C_f = 500 µM), 1.55 µL of 646 µM Ldt_{fm} (dom II) (C_f = 50 µM) and 7.45 µL of H_2O were mixed. After 1 minute of incubation at 25 ˚C, the mixture was diluted 1/10 (5 µM of Ldt_{fm}). 2.5 µL of this diluted solution was injected in mass spectroscopy (flowrate 10 $\mu L.min^{-1}$ in 50% ACN + 0.1% acetic acid).

4. Enzymatic studies

Determination of kinetic constants for inactivation of Ldt_{fm}. Acylation of Ldt_{fm} (10 µM) by various concentrations (50 to 300 µM) of meropenem or peptido-carbapenem was detected by stopped-flow spectrofluorimetry at 20 °C in 100 mM phosphate buffer (pH = 6.0), using a stopped-flow apparatus (RX-2000, Applied Biophysics) coupled to a spectrofluorimeter (Cary Eclipse; Varian). At least three concentrations were used for each carbapenem. Excitation was performed at 224 nm with a 5 nm slit and a 2 mm optical path. Fluorescence emission was determined at 335 nm with a 5 nm slit and a 10 mm optical path. Excitation was performed at 224 nm to avoid any confusing effect arising from the decrease in the absorbance at the usual excitation wavelength of 284 nm caused by β-lactam ring opening. Kinetics were recorded for 2 minutes. The reaction was completed in less than 10 seconds. Kinetic constants k_1, k_{-1} , and k_2 were determined by simultaneously fitting differential equations to the kinetics obtained with a minimum of three concentrations of carbapenems using the DynaFit software (BioKin Ltd).[10] The differential equations were $d[E]/dt = - k_1 [E][C] + k_{-1} [E_{anh}]$; $d[E_{anh}]/dt = k_1 [E][C] - k_2 [E_{anh}]$; $d[EI^*]/dt = k_2[E_{anh}]$ according to the reaction pass appearing in Scheme 5 of the main text in which [E], $[E_{anh}]$, and [EI*] are the concentrations of apo Ldt_{fm}, amine anion intermediate, and acylenzyme, respectively. The fluorescence of the sample was considered to be additively contributed by the fluorescence of [E], $[E_{anh}]$, and [EI*] according to relative fluorescence intensities that were introduced as variables in the DynaFit software.

5. References

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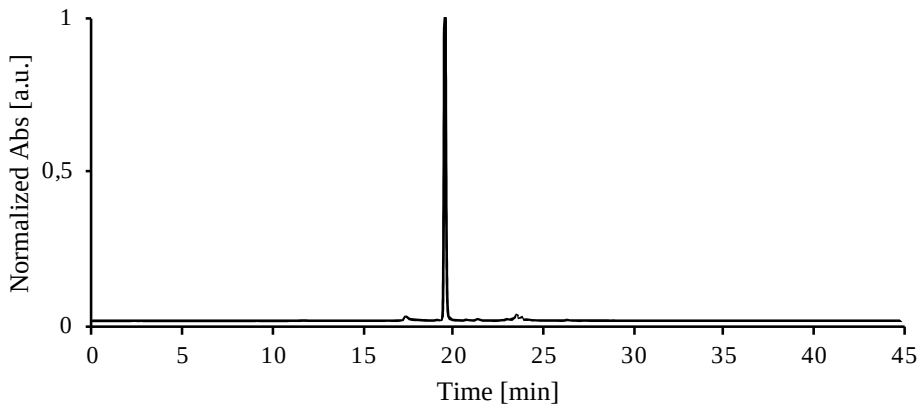
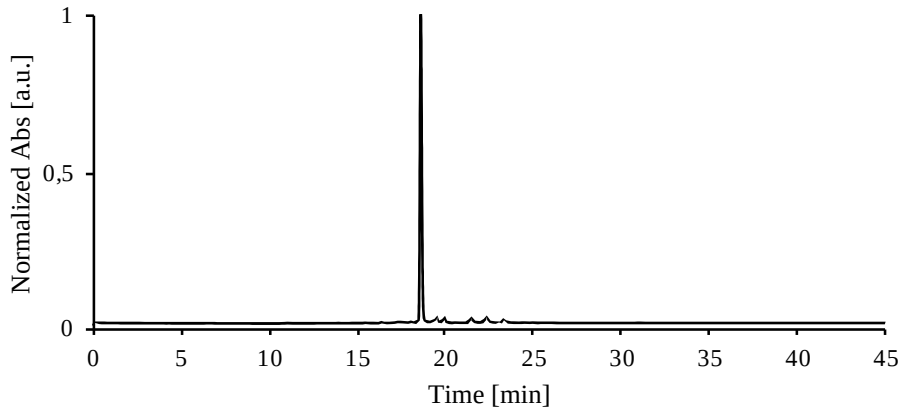
6. Analytical HPLC spectra of compounds 2’ and 28a-n.

Analytical HPLC was performed on a Vydac C_{18} (250 mm x 4.6 mm, 5 µm). Detection at 299 nm, flow 1.3 mL.min^{-1}. **Solvent A:** H_2O + 0.1% TFA; **Solvent B:** ACN + 0.1% TFA. Gradient 0 to 100% of Solvent B over 45 minutes.

2’



28a



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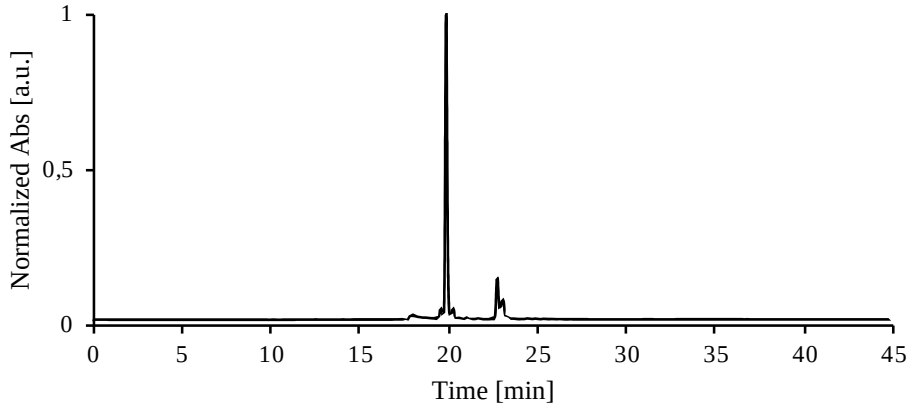

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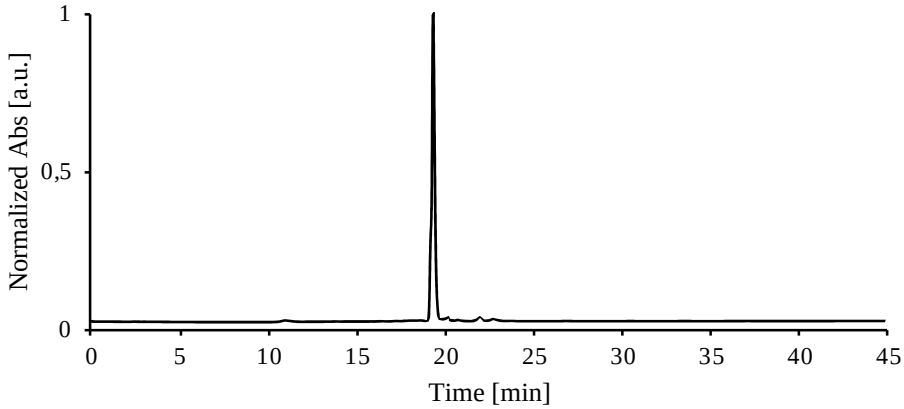
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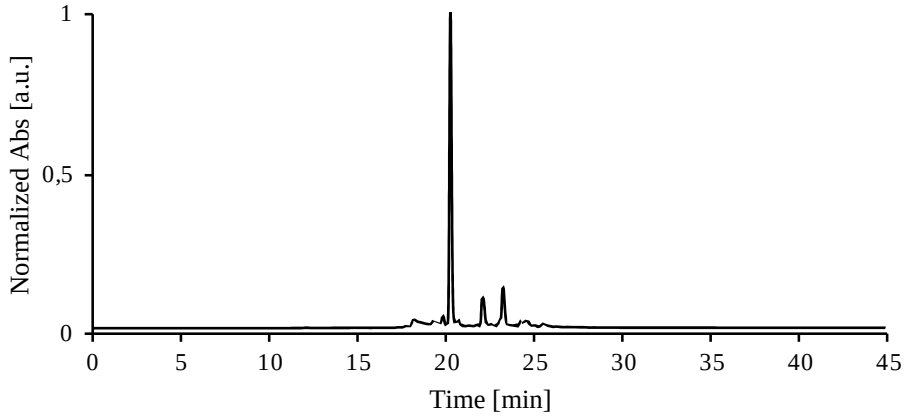
35
40
45
Time [min]

28d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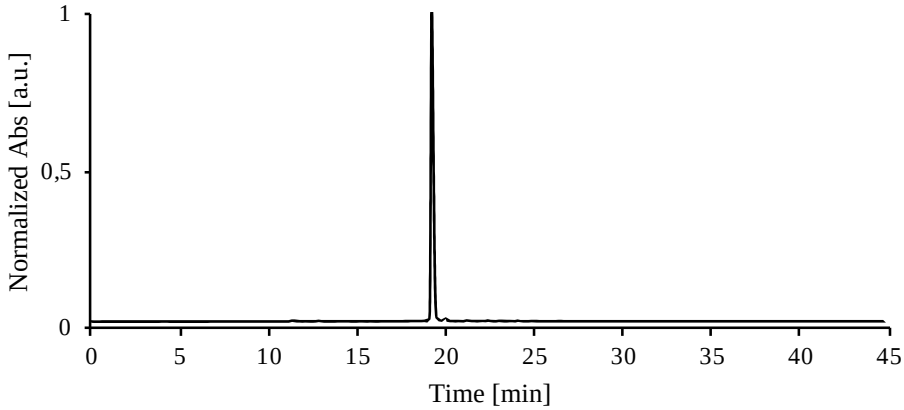
28e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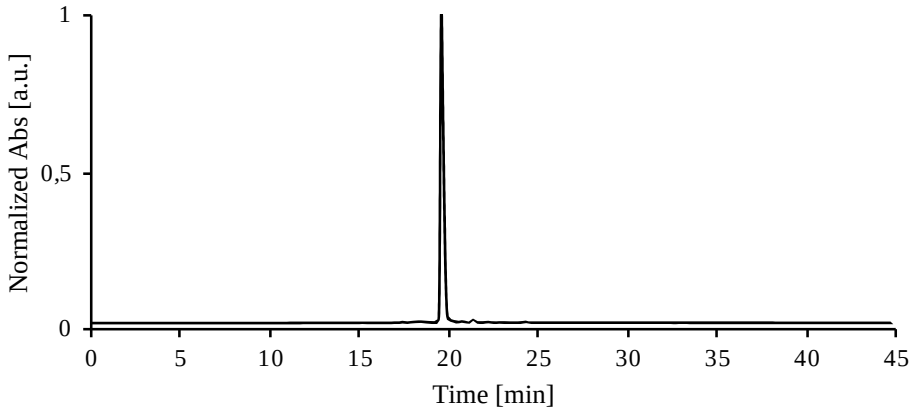
Time [min]

28f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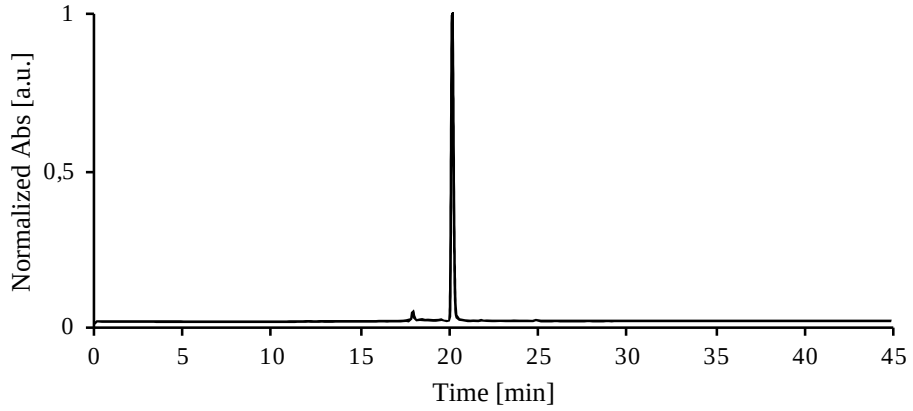
Time [min]

28g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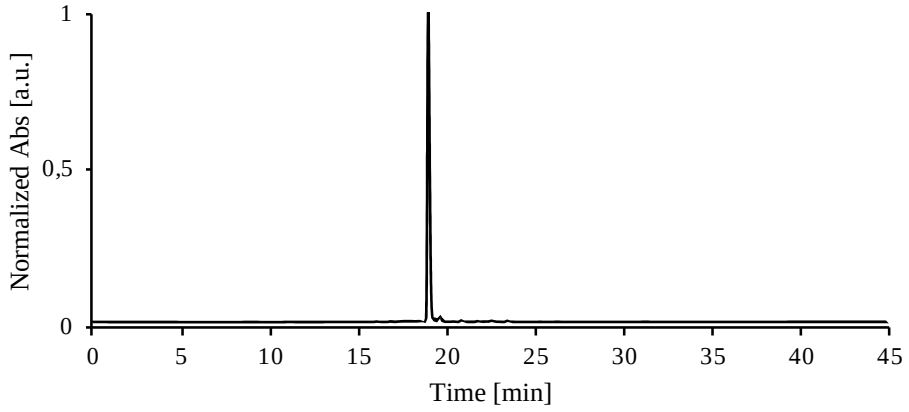
Time [min]

28h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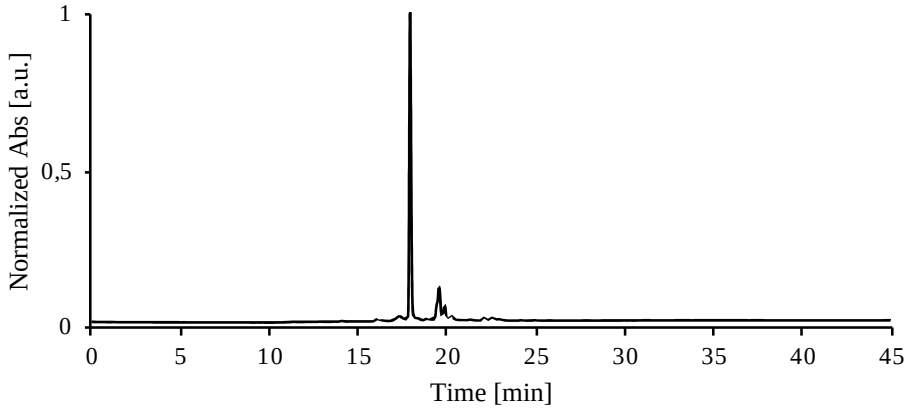
Time [min]

28i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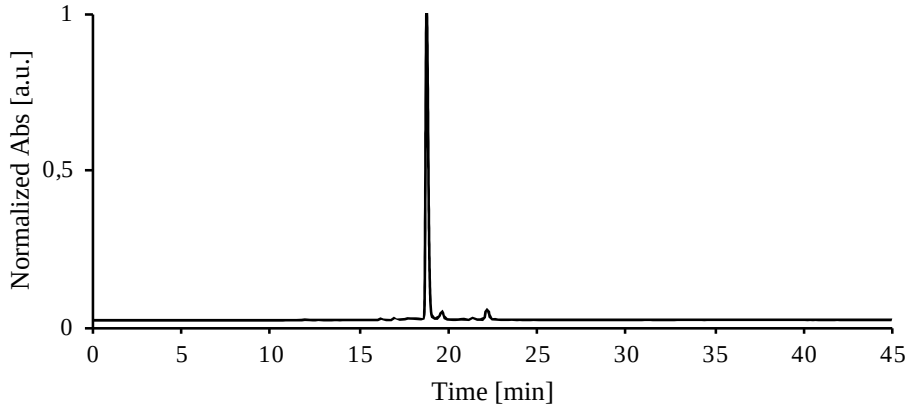
28j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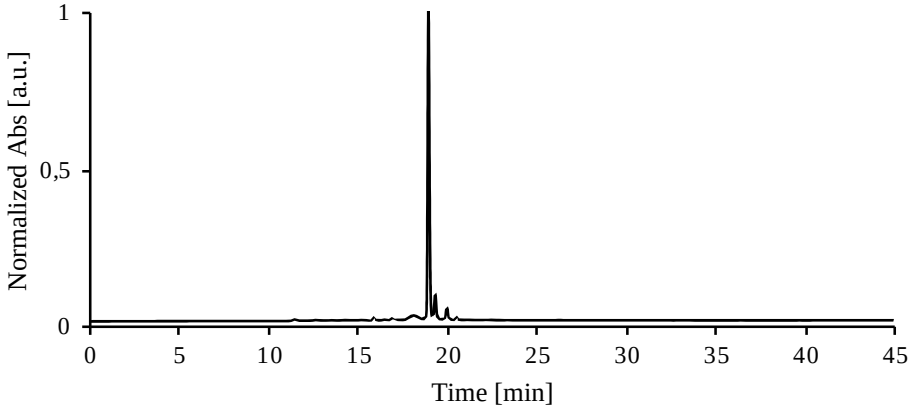
28k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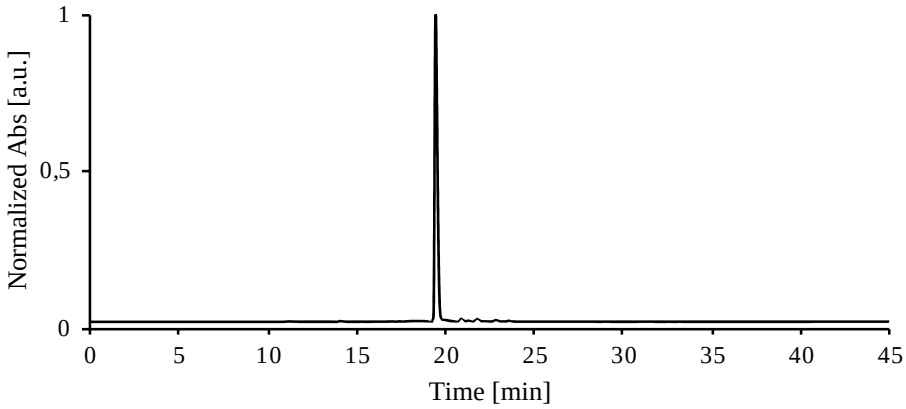
Time [min]

28l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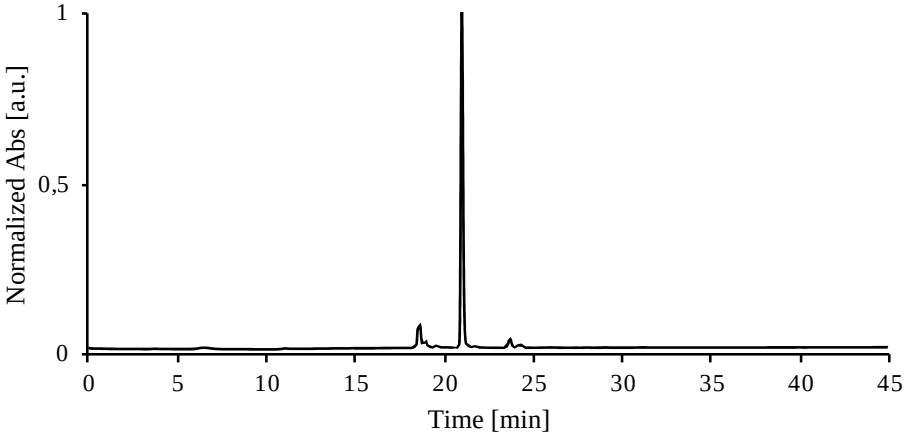
Time [min]

28m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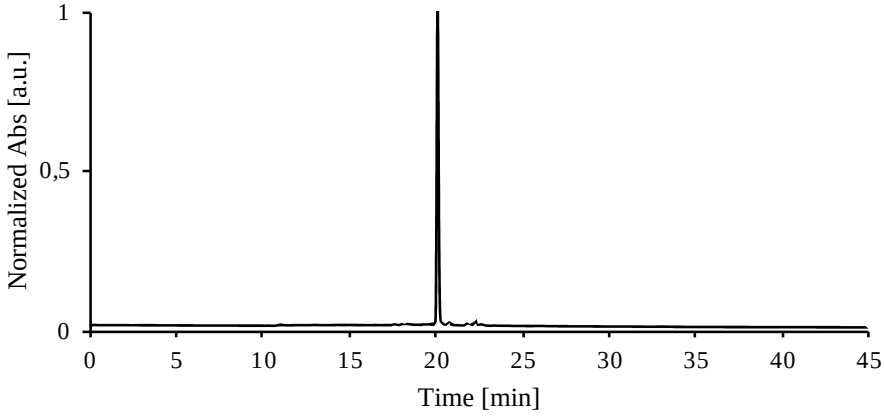
Time [min]

28n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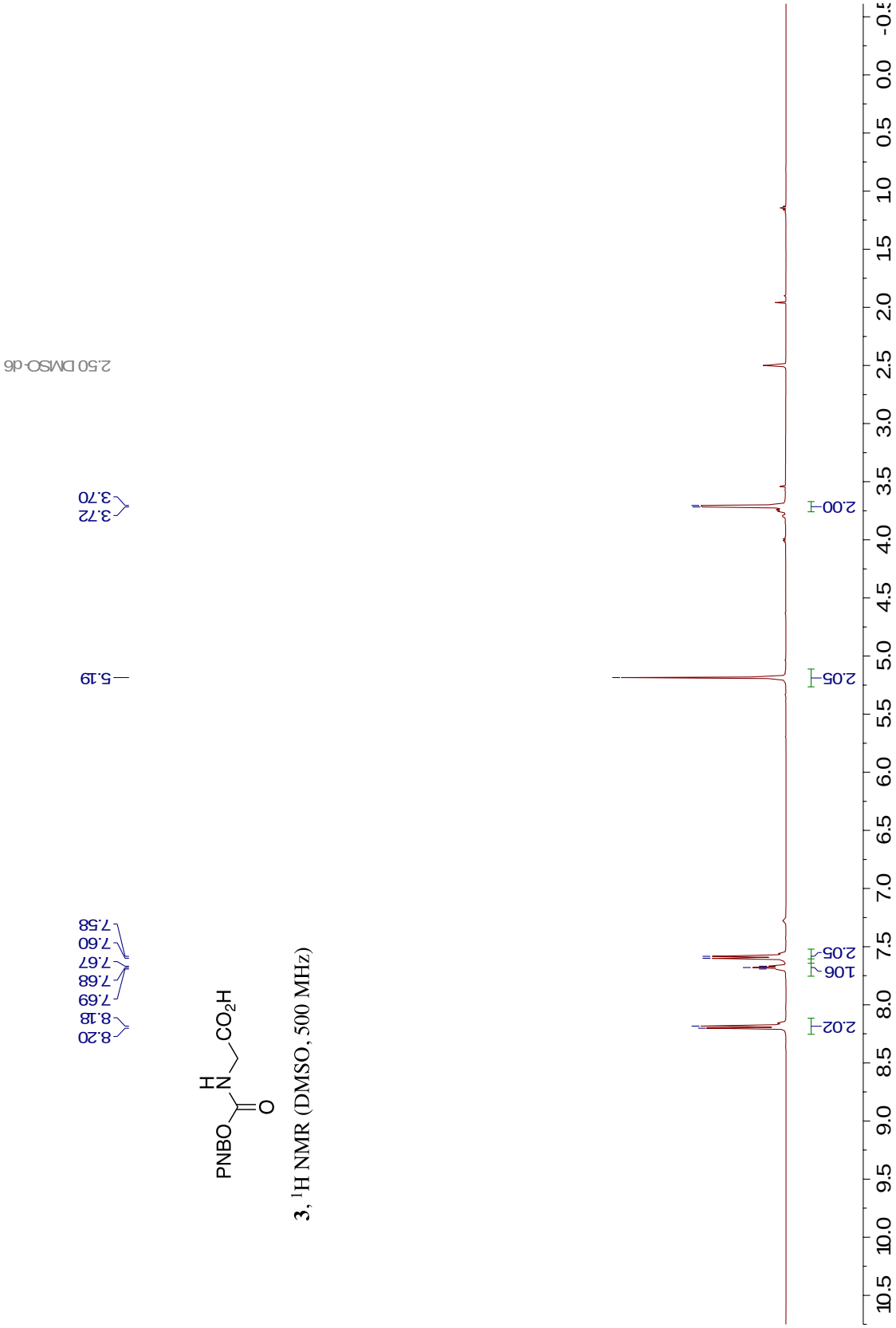
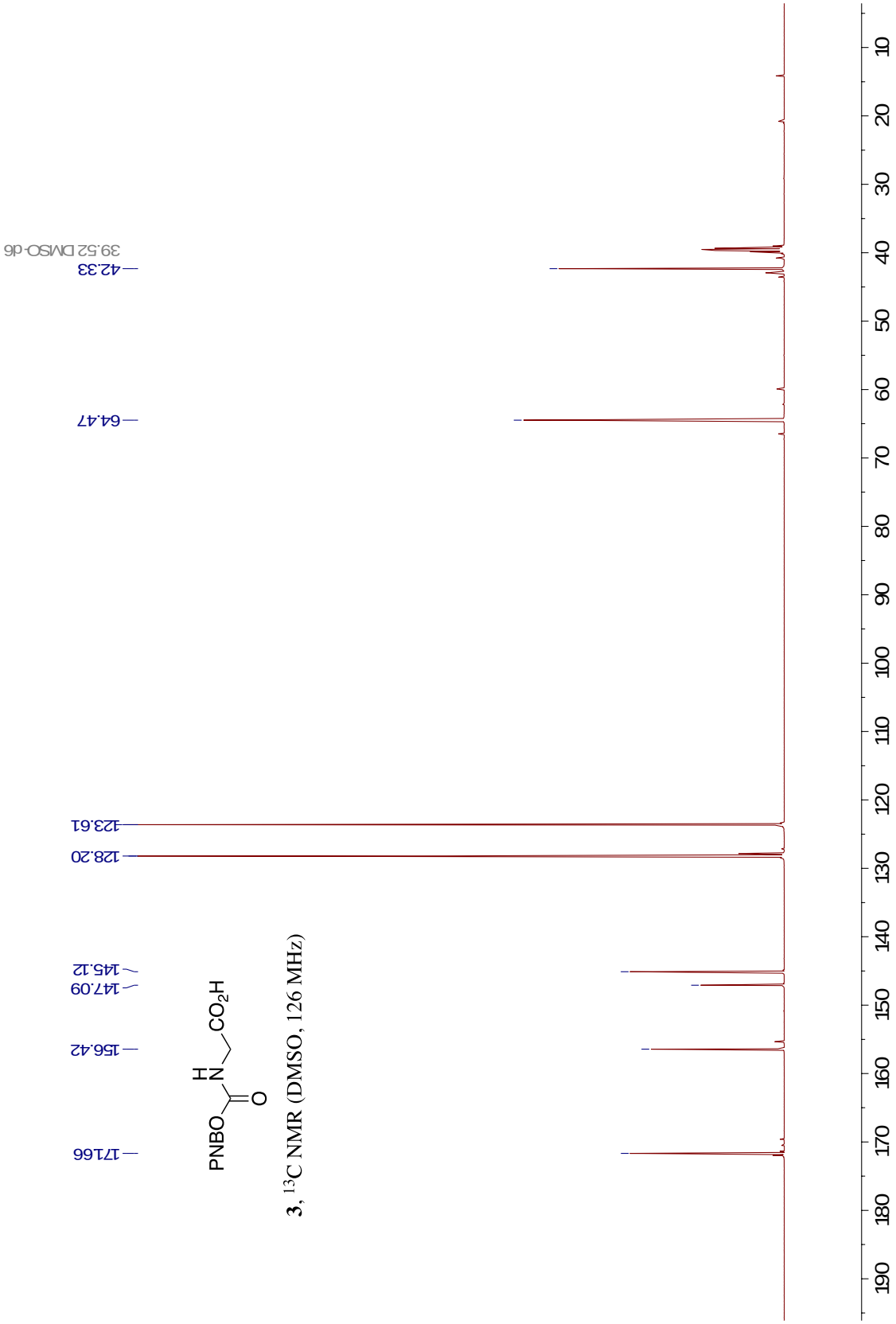
Time [min]

7. ^{1}H NMR and ^{13}C NMR spectra

7-1. ^{1}H and ^{13}C NMR spectra of compounds 3-26.



3, ^{1}H NMR (DMSO, 500 MHz)


171.66
156.42
147.09
145.12
128.20
123.61
64.47
42.33
39.52 DMSO-d6
PNBO
O
H
N
CO2H
O
3, 13C NMR (DMSO, 126 MHz)
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150
140
130
120
110
100
90
80
70
60
50
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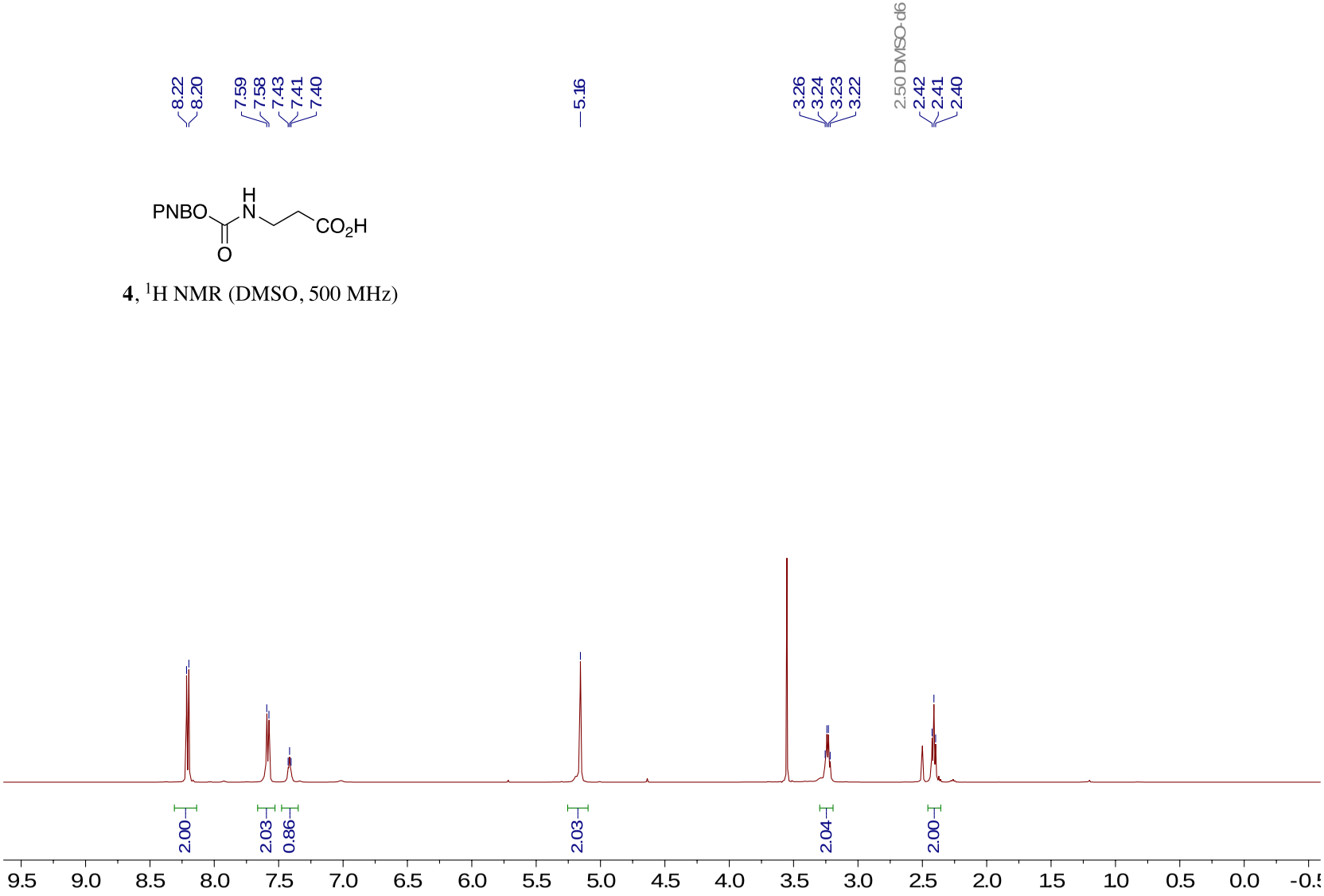
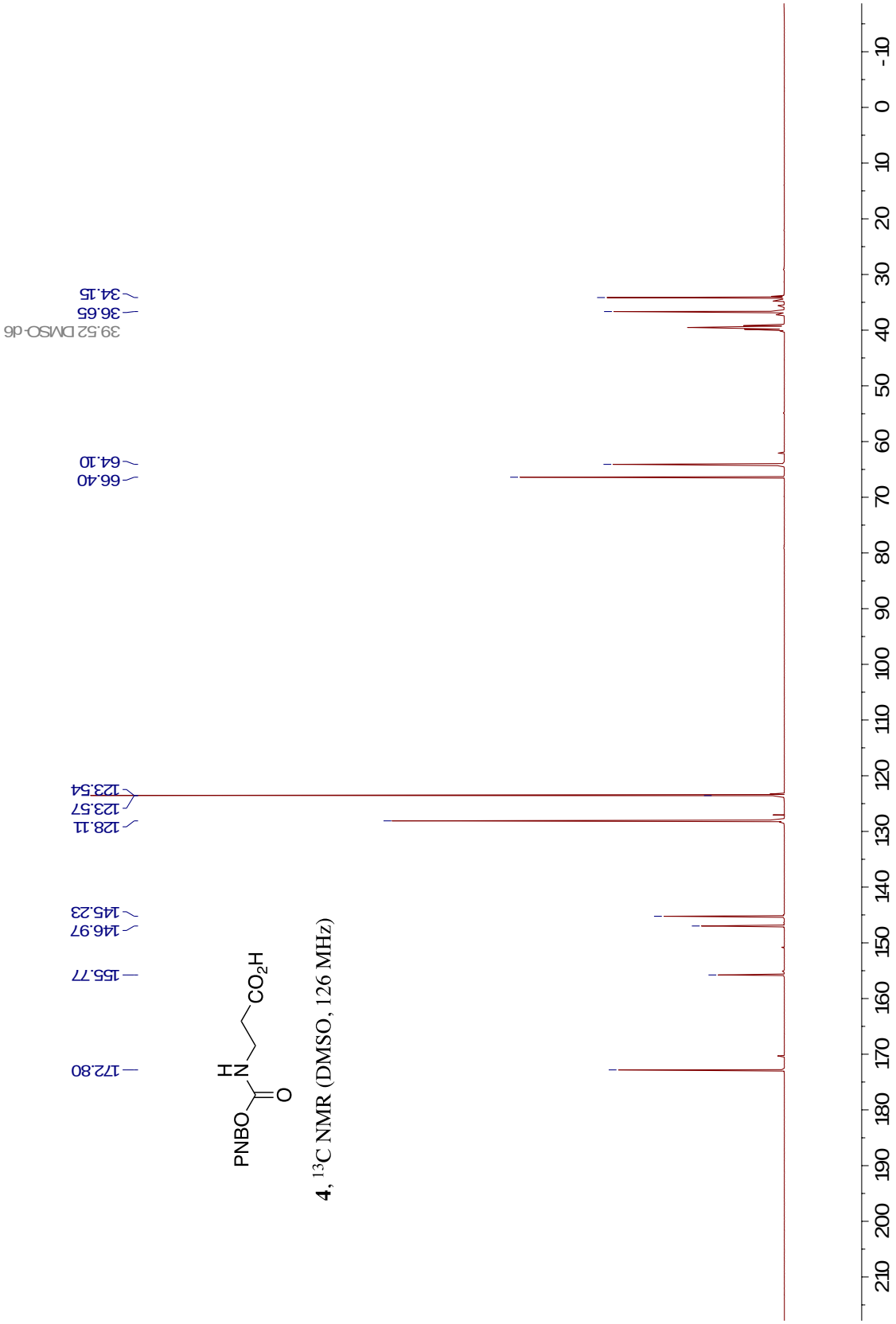
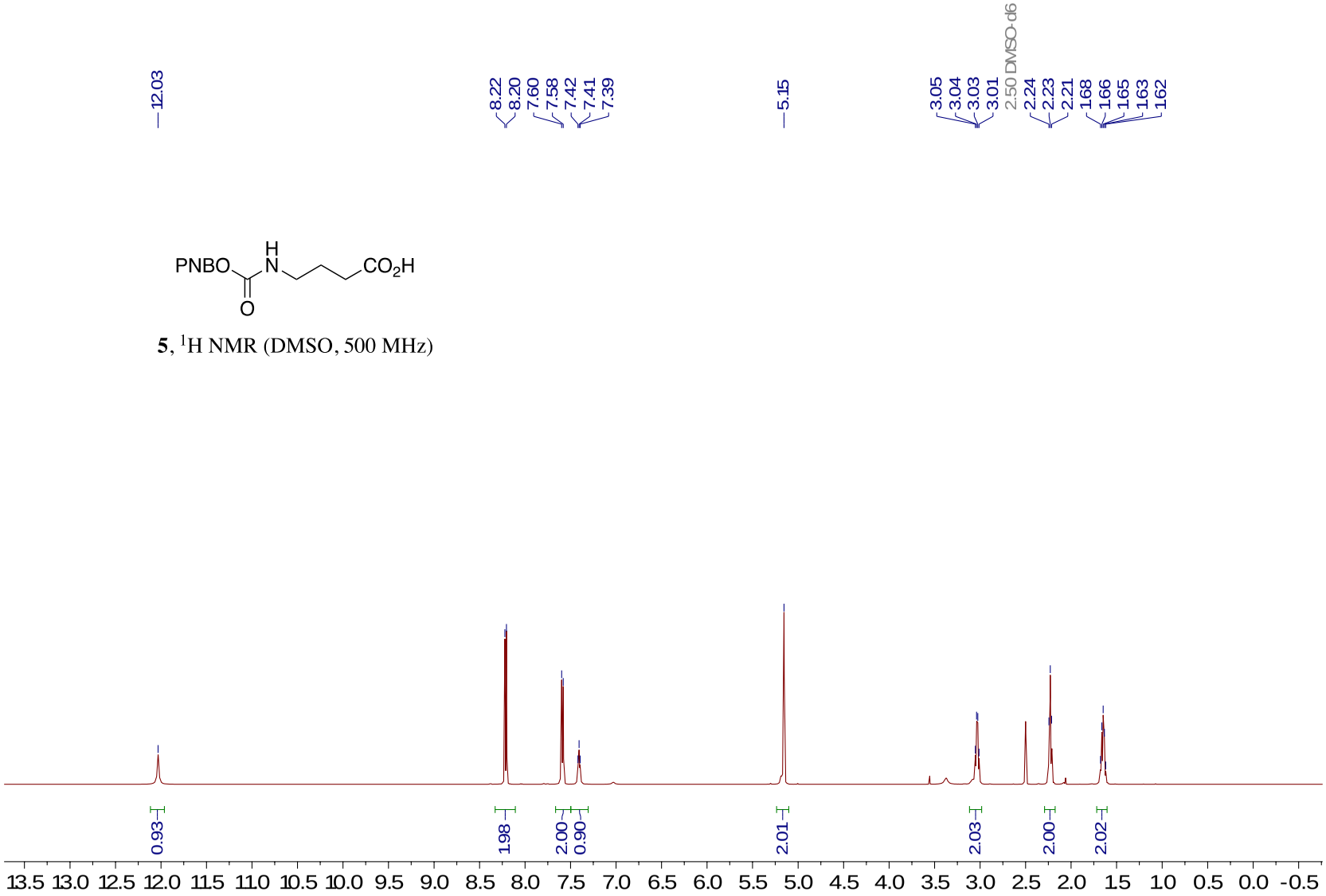
20
10



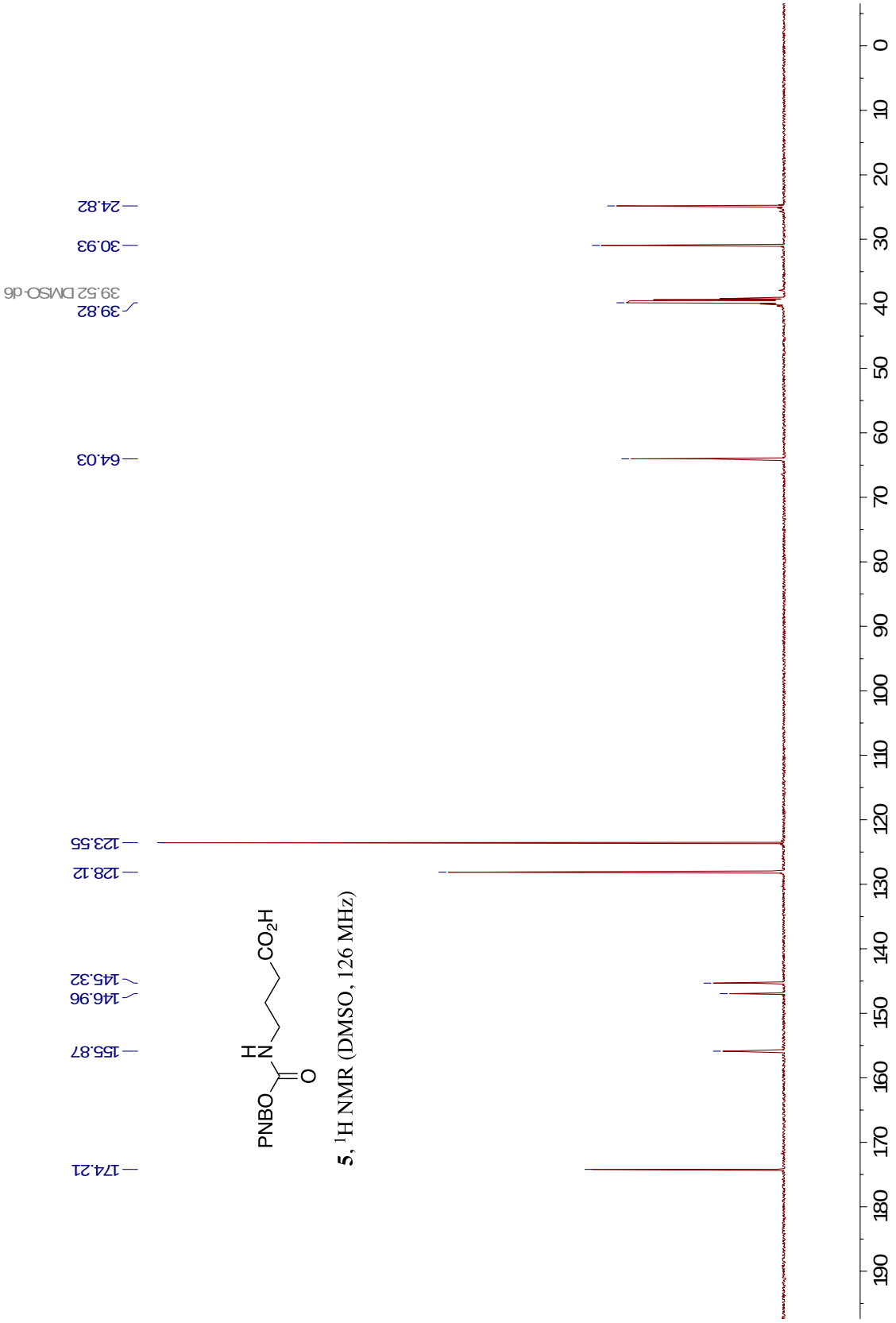
4, ^{1}H NMR (DMSO, 500 MHz)



4, ^{13}C NMR (DMSO, 126 MHz)

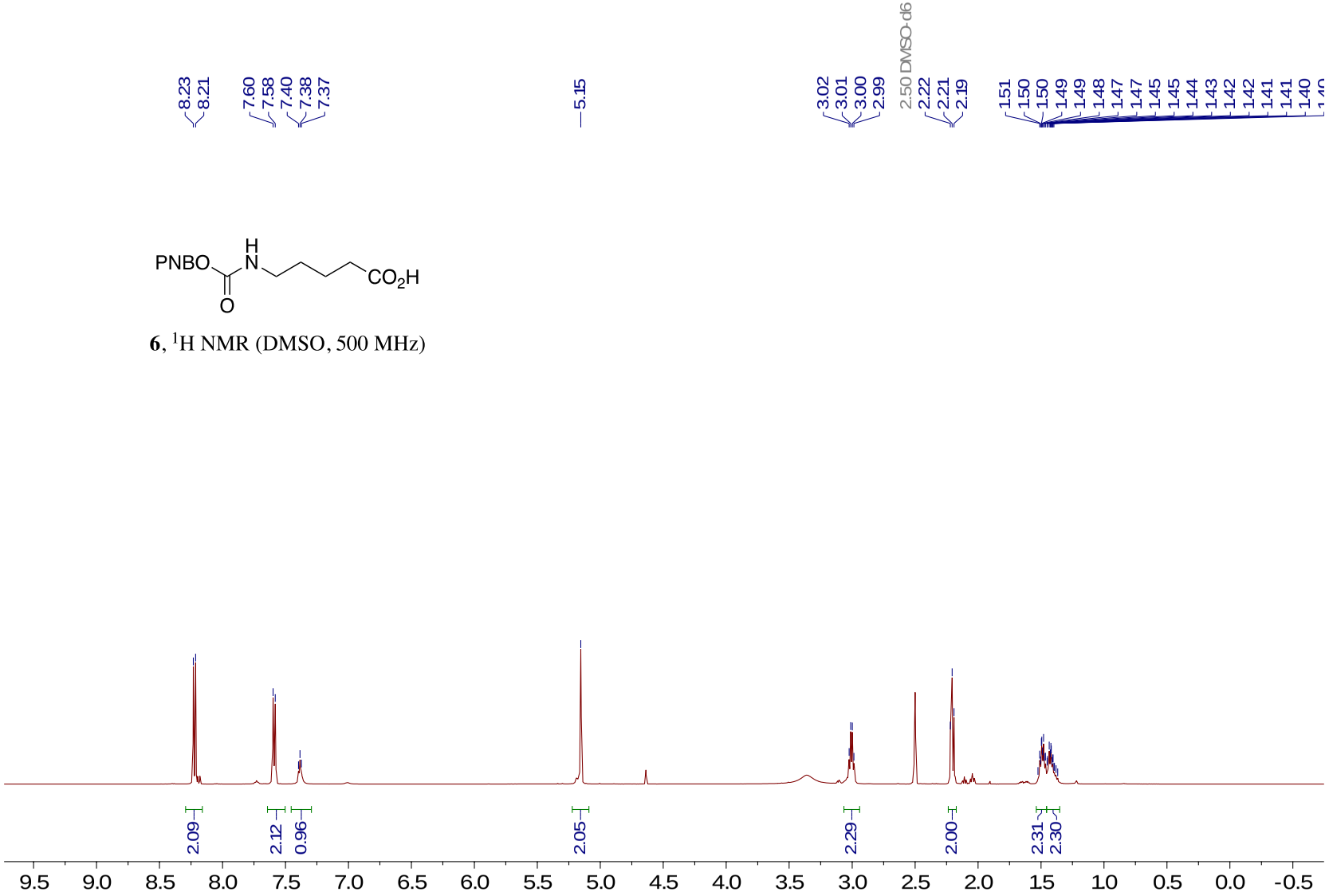


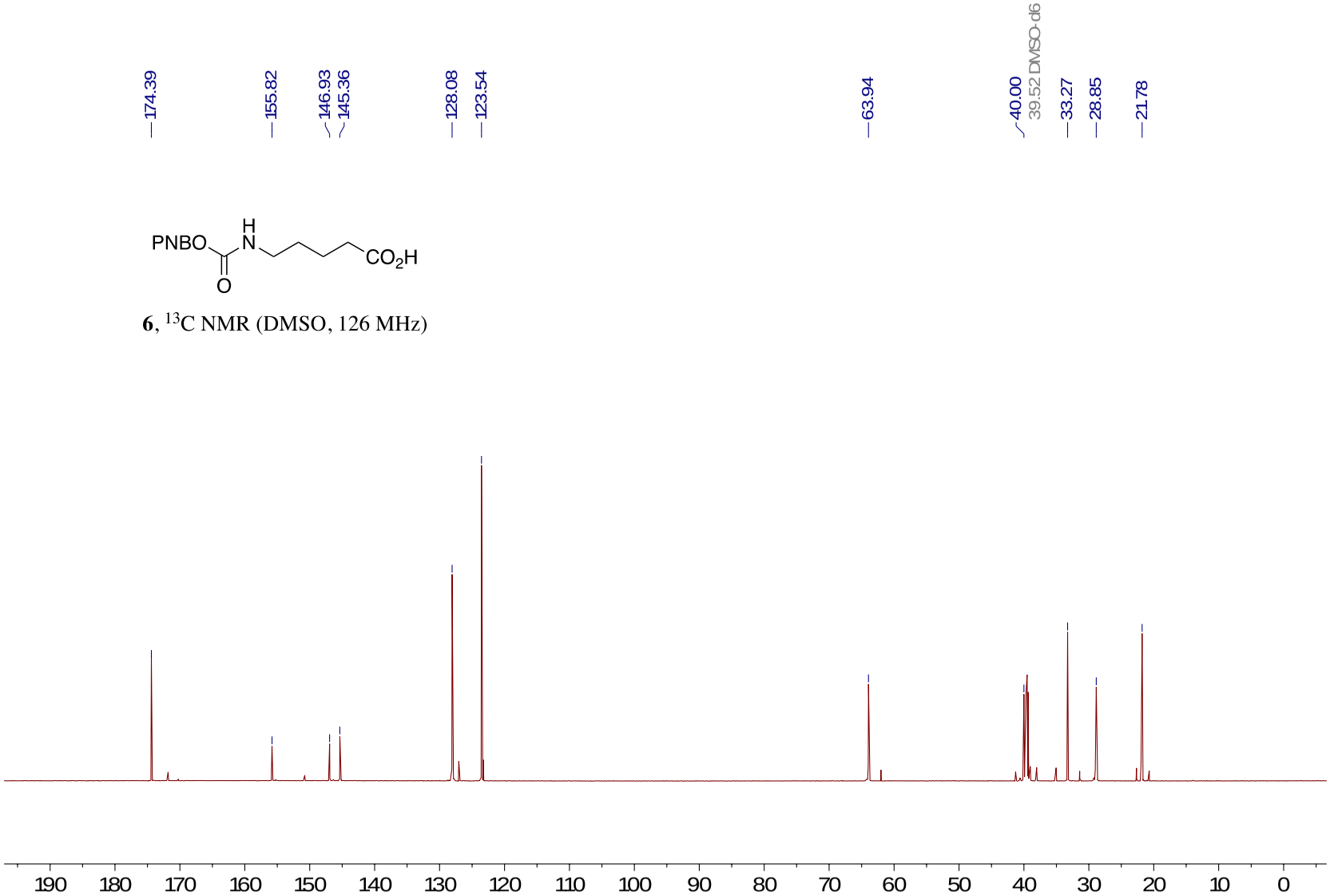
5, ^{1}H NMR (DMSO, 500 MHz)



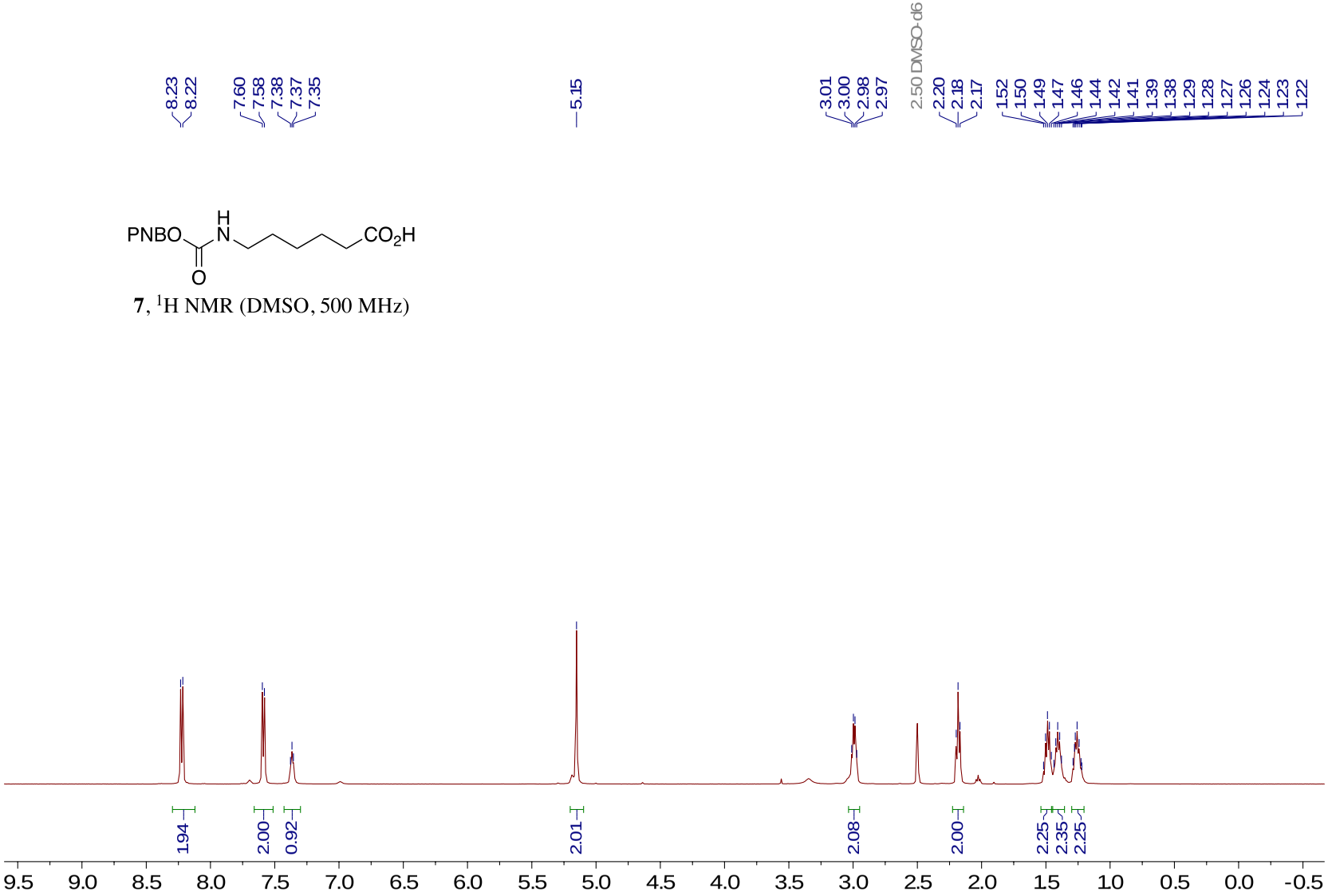
5, ^{1}H NMR (DMSO, 126 MHz)

6, ^{1}H NMR (DMSO, 500 MHz)

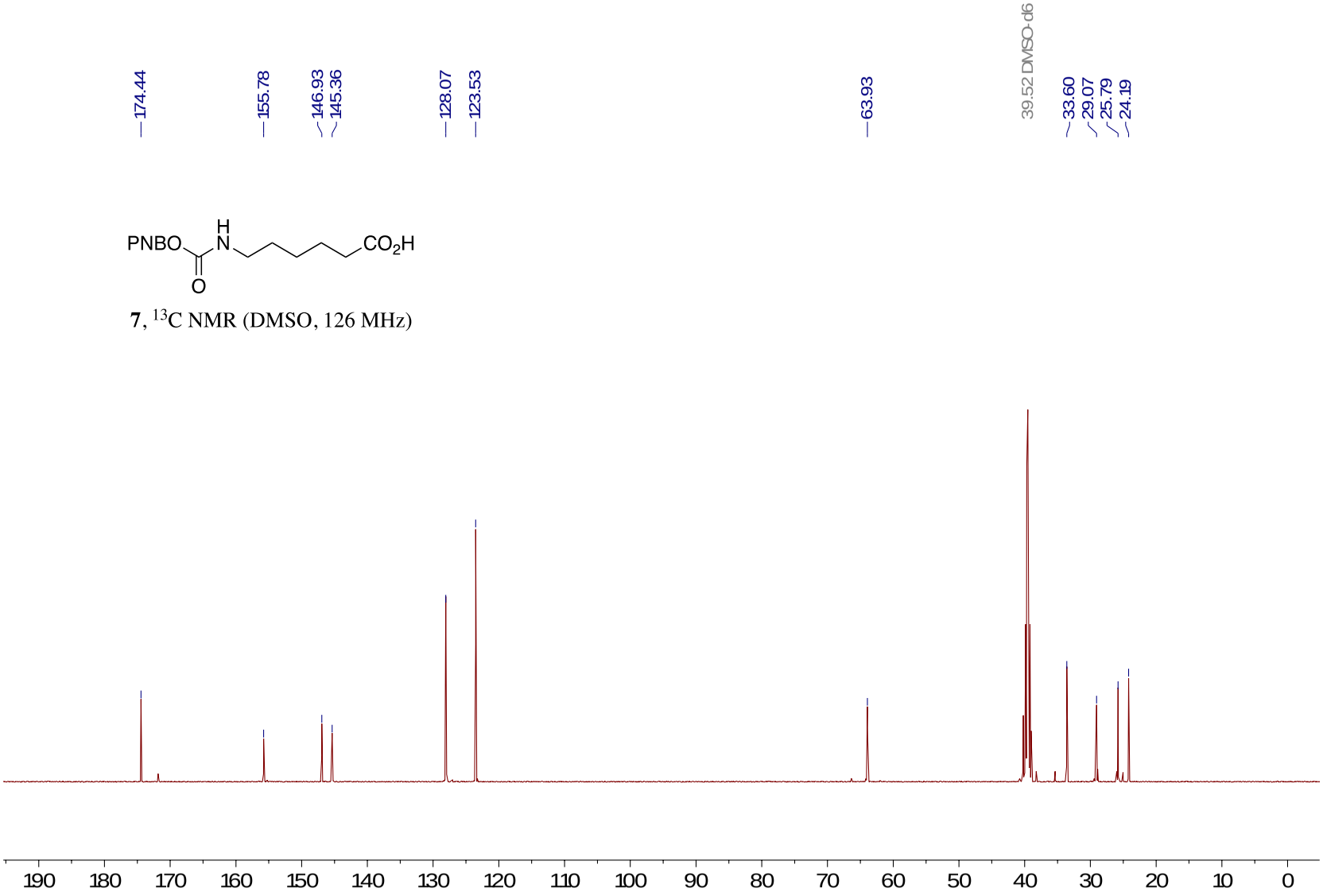




6, ^{13}C NMR (DMSO, 126 MHz)

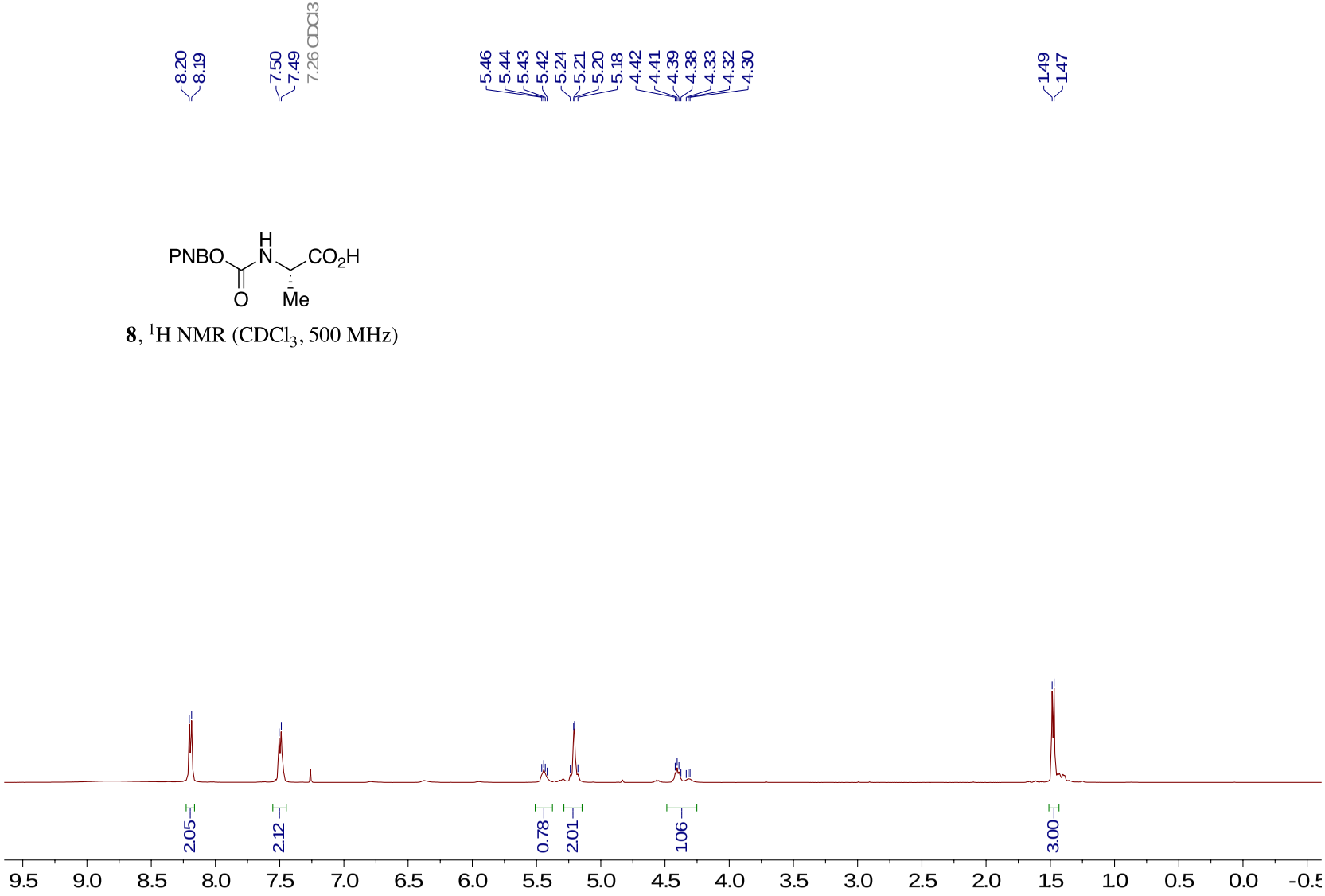


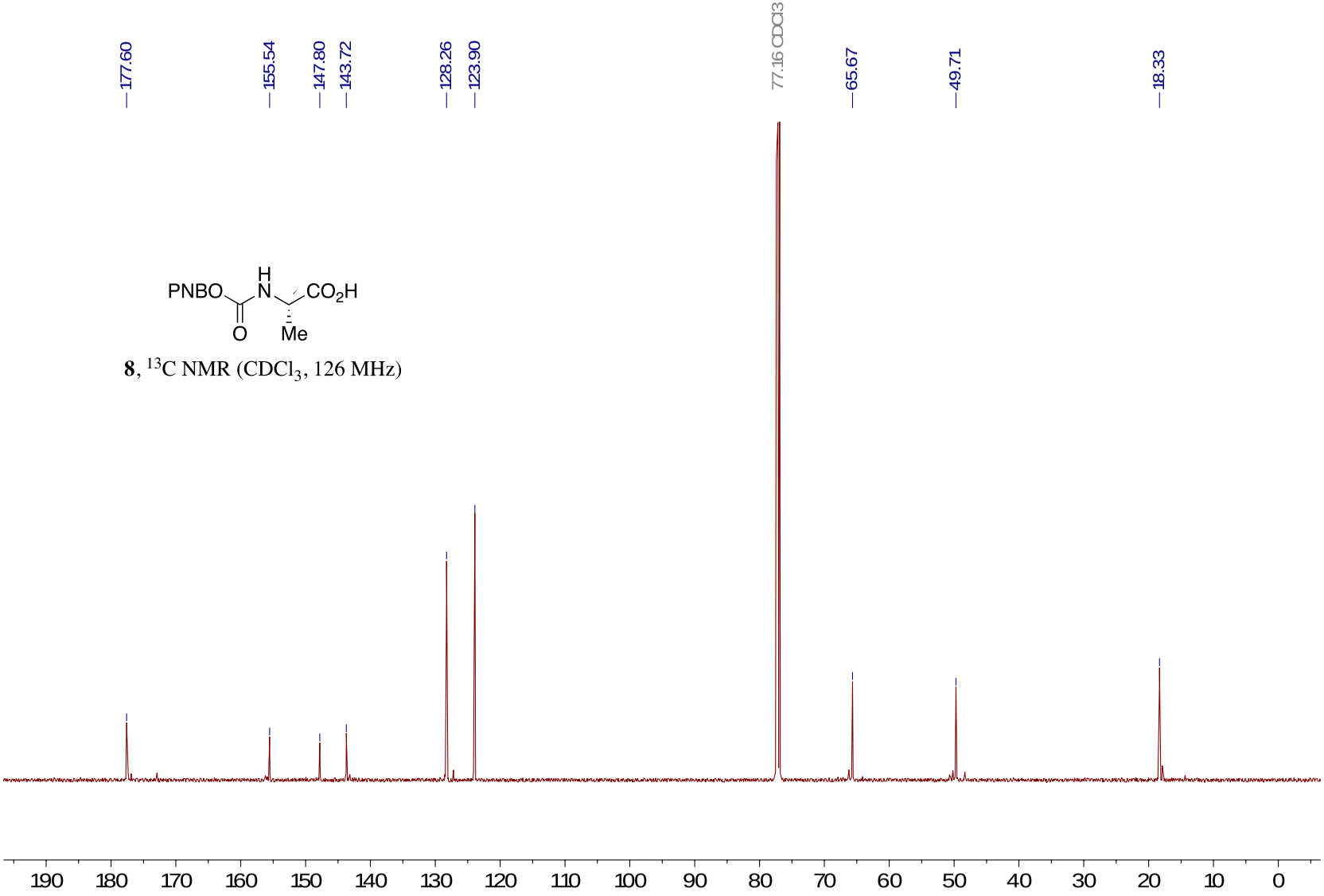
7, ^{1}H NMR (DMSO, 500 MHz)



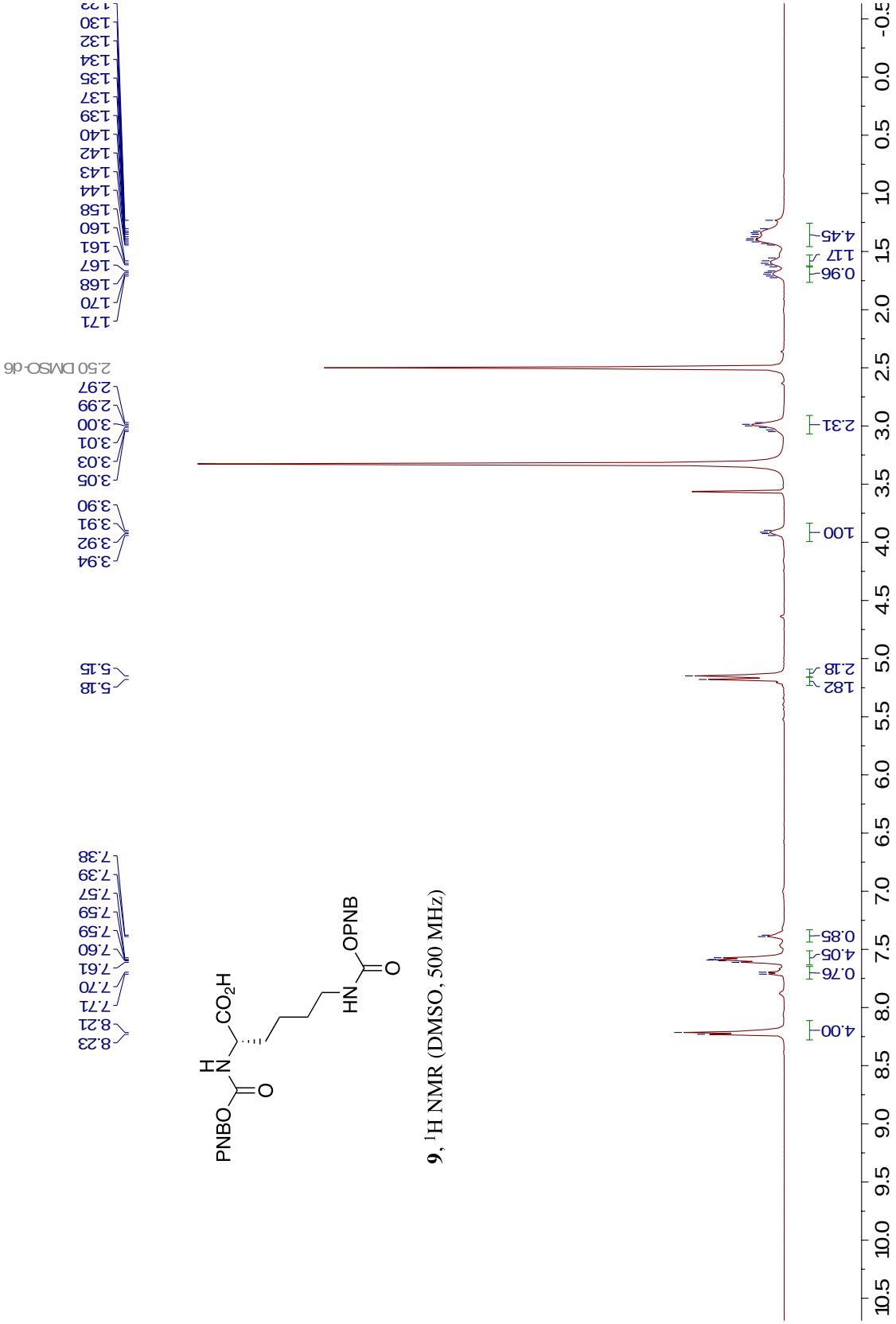
7, ^{13}C NMR (DMSO, 126 MHz)

8, ^{1}H NMR ($CDCl_3$, 500 MHz)

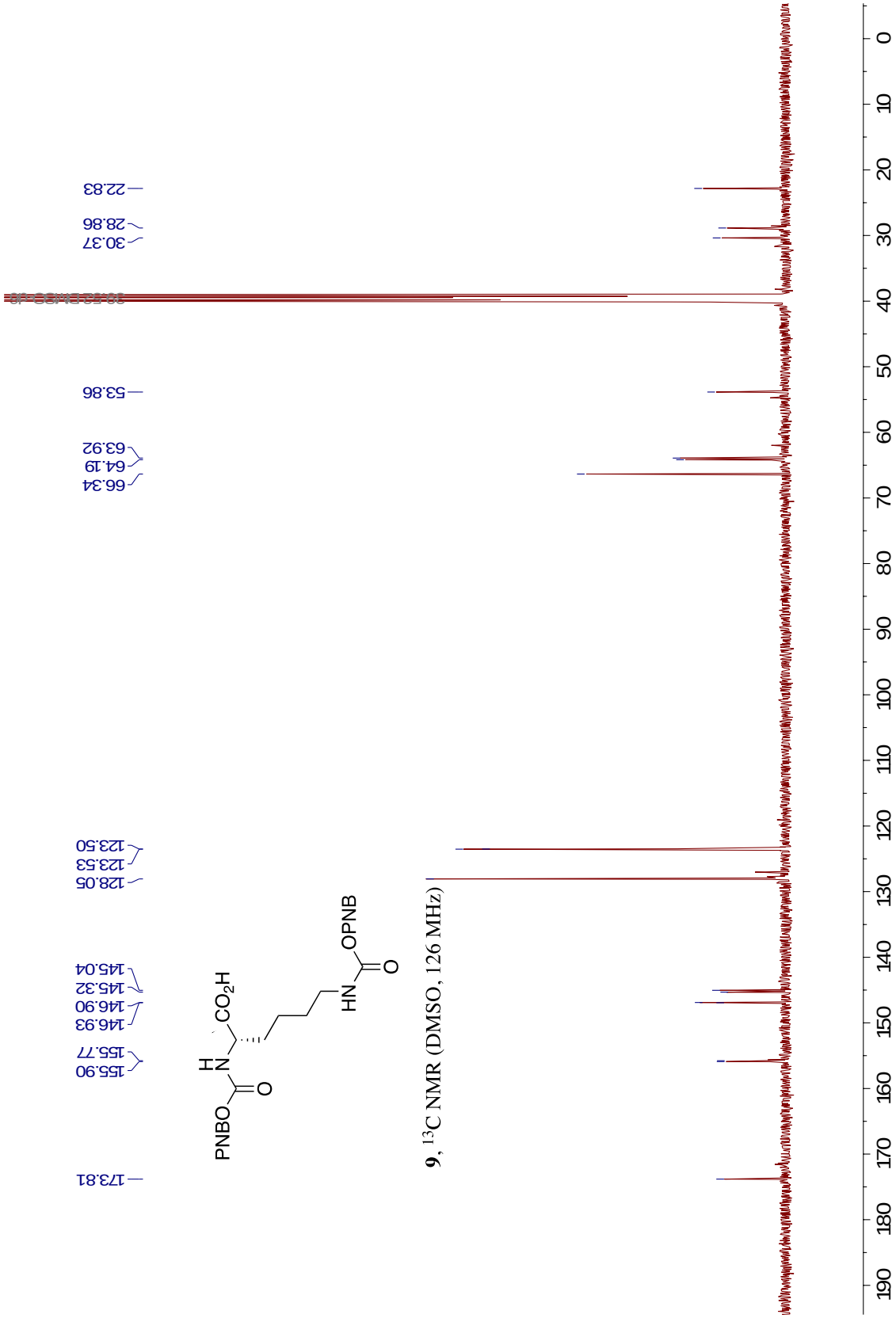




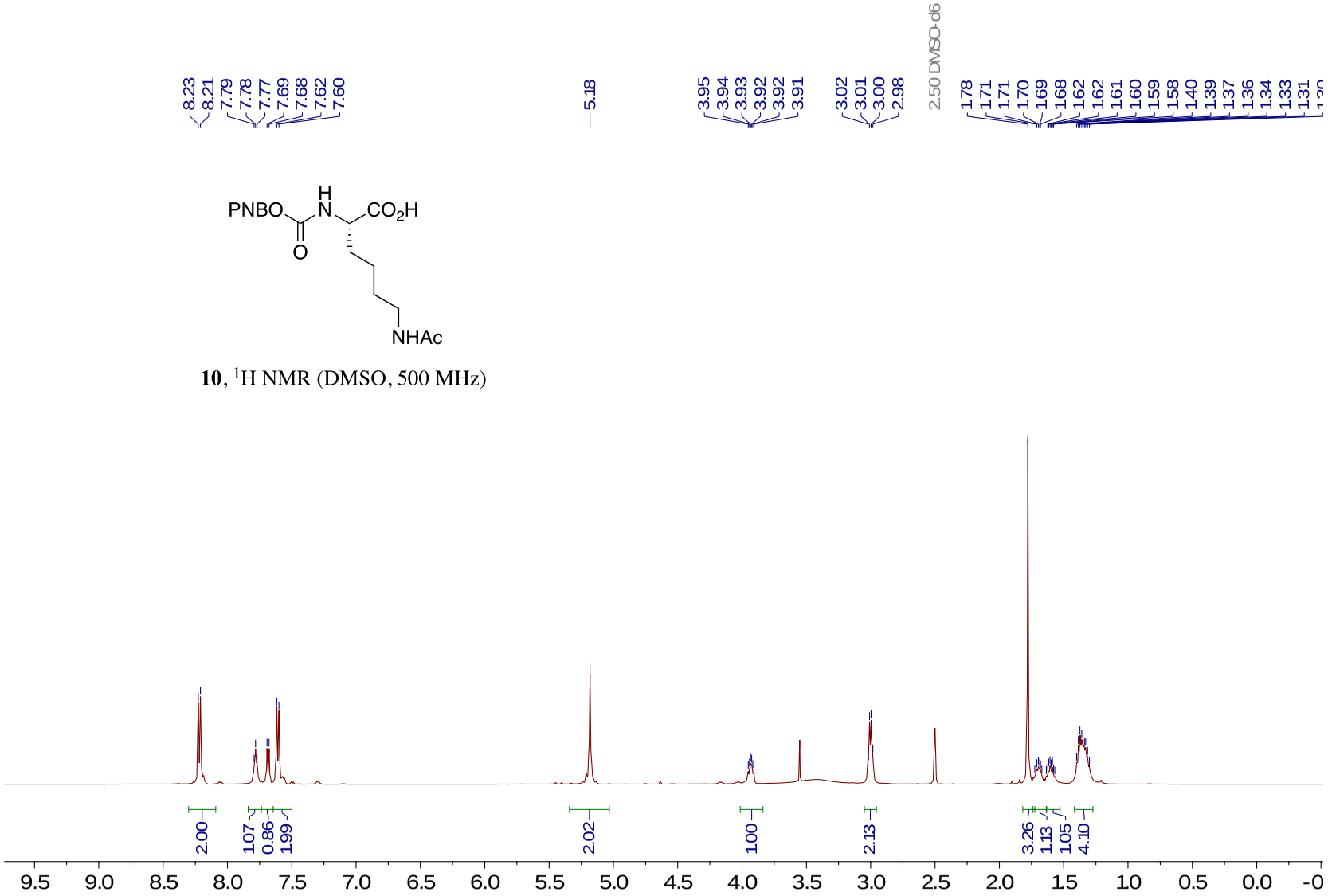
8, ^{13}C NMR ($CDCl_3$, 126 MHz)



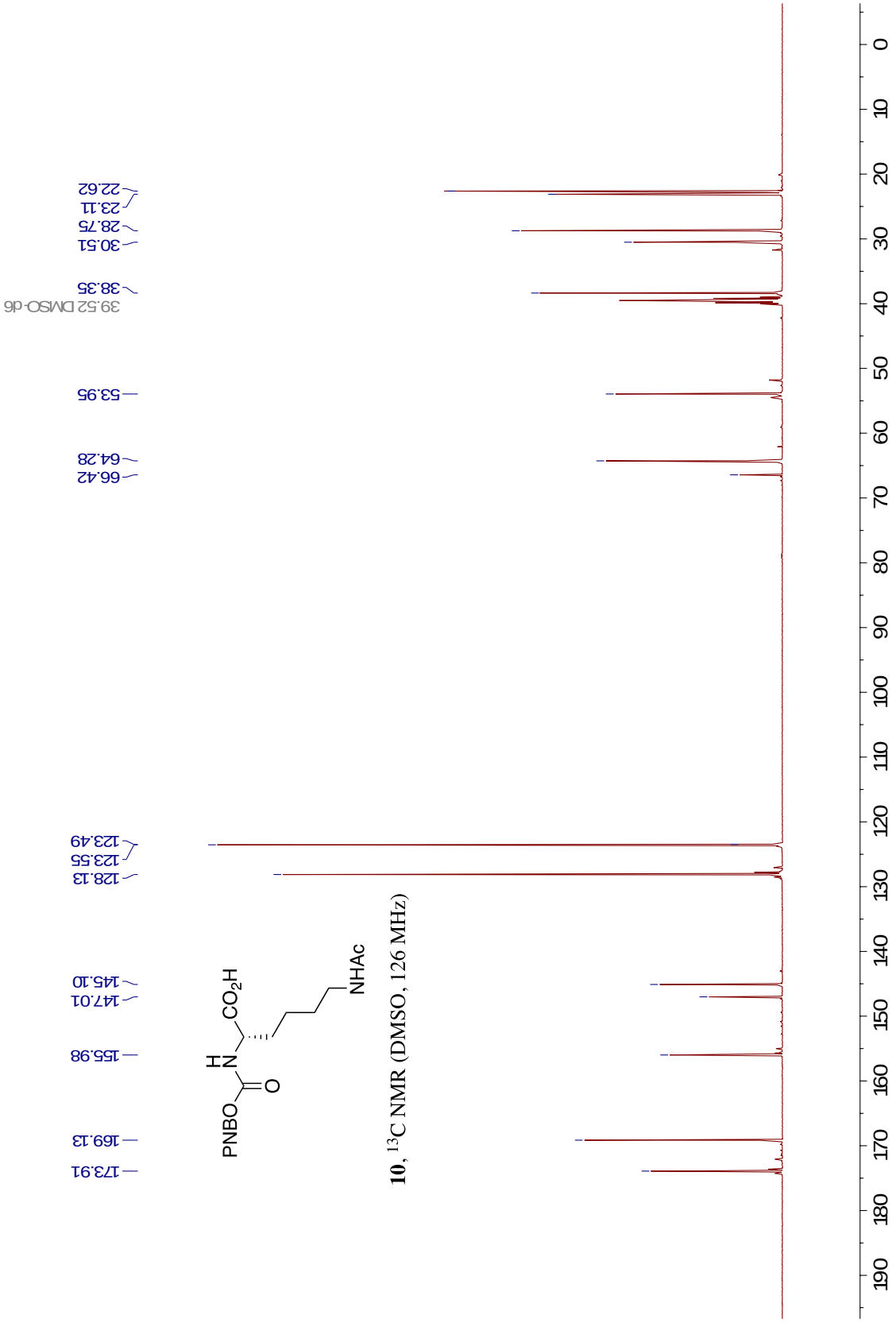
9, ^{1}H NMR (DMSO, 500 MHz)



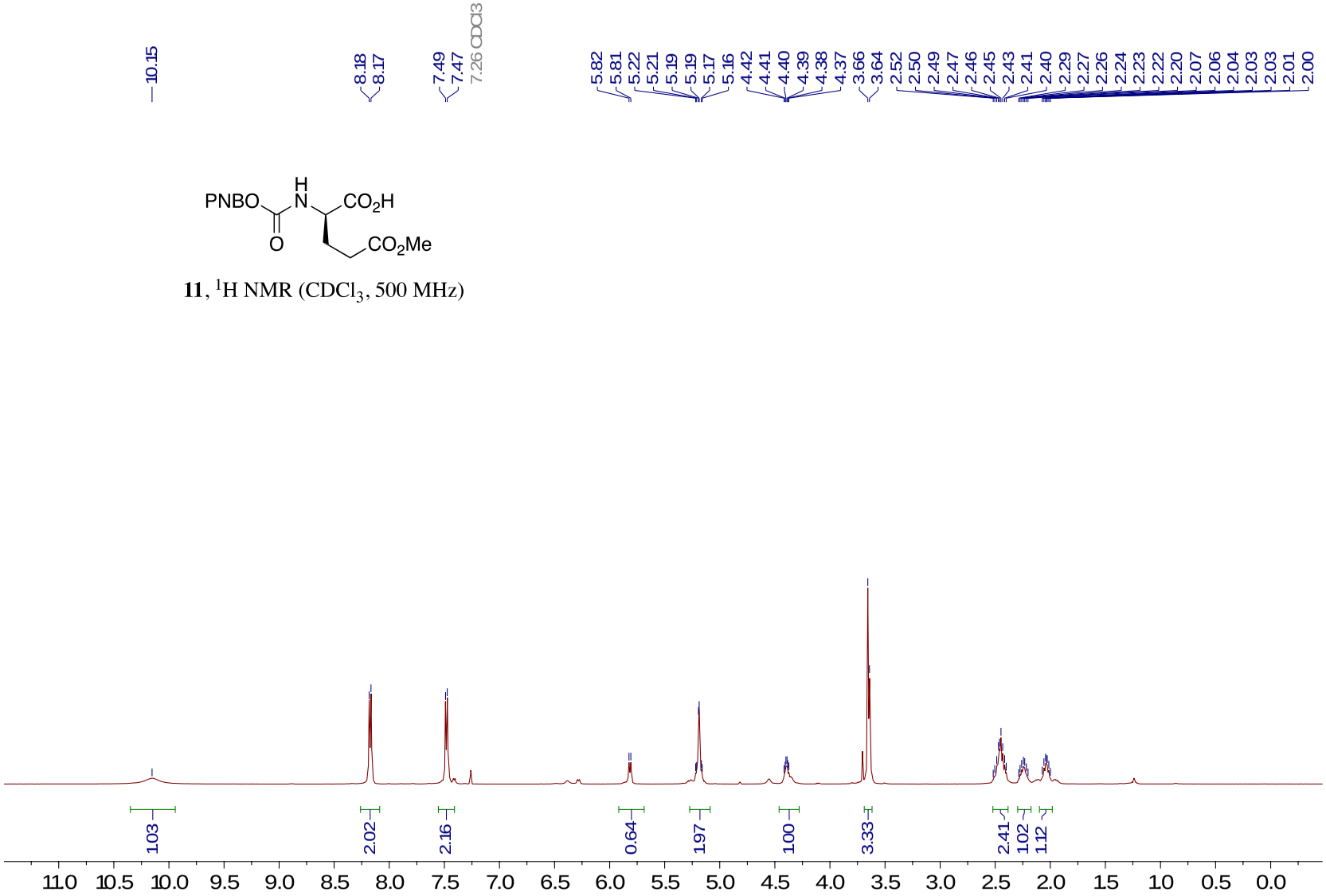
9, ^{13}C NMR (DMSO, 126 MHz)



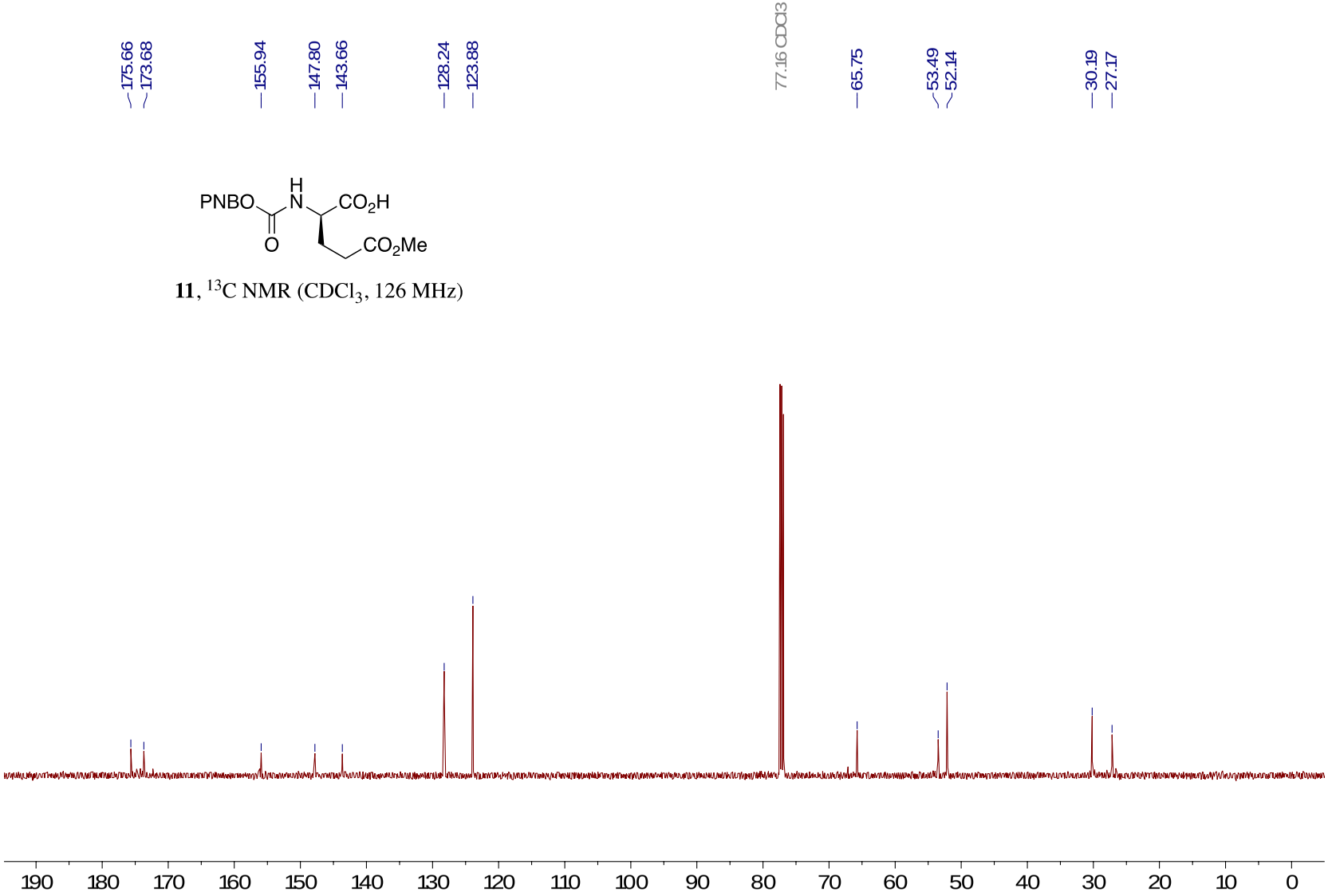
10, ^{1}H NMR (DMSO, 500 MHz)



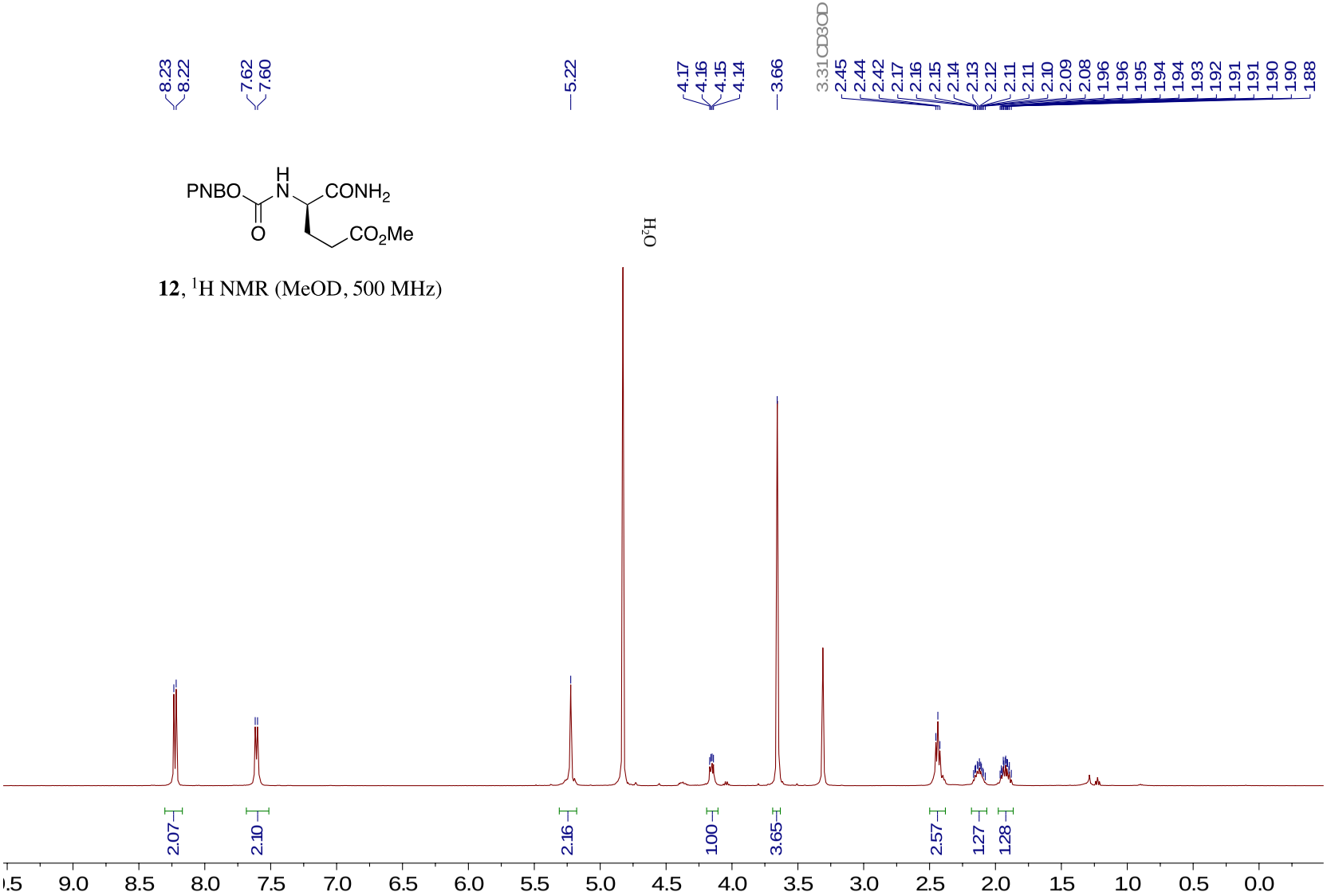
10, ^{13}C NMR (DMSO, 126 MHz)



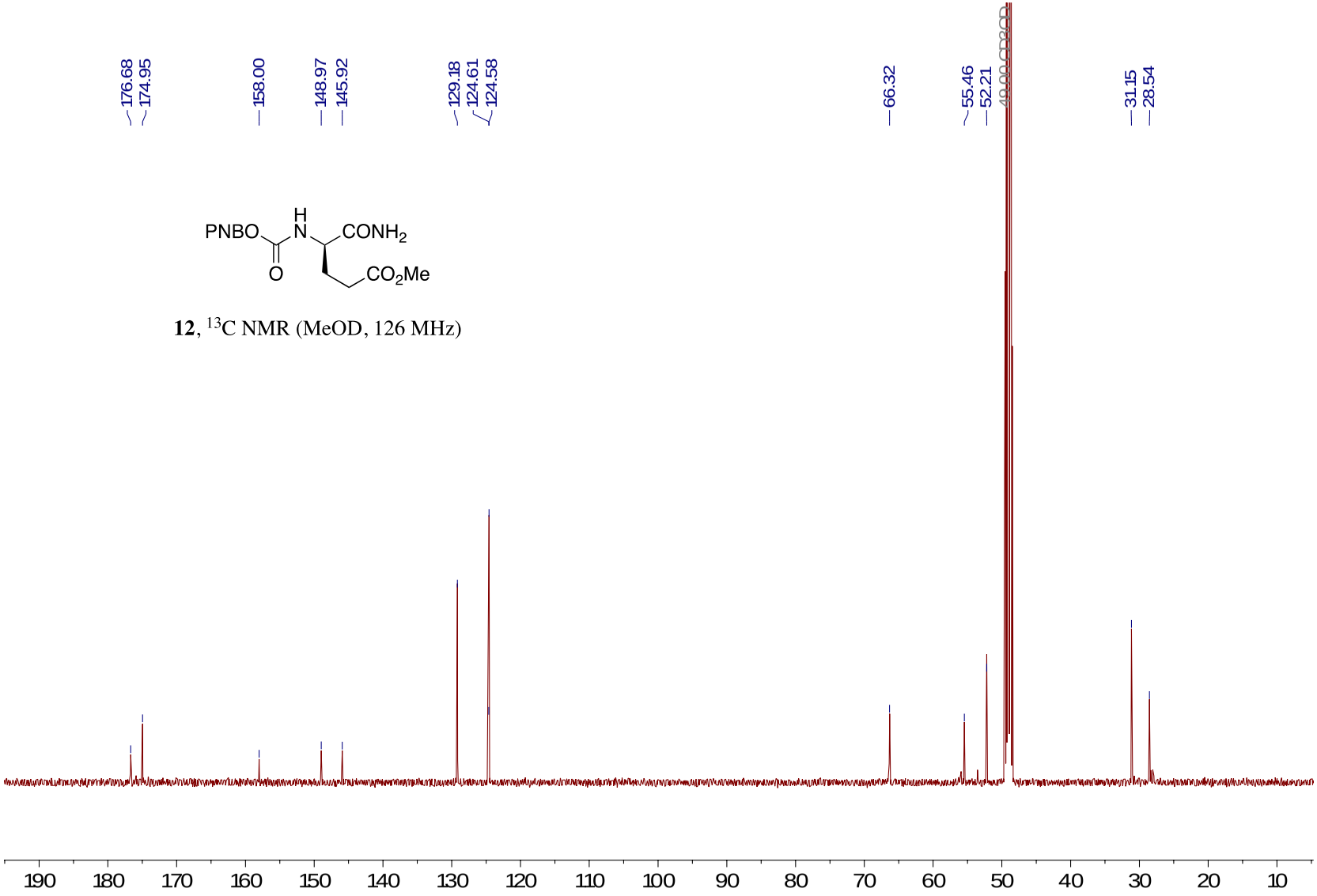
11, ^{1}H NMR ($CDCl_3$, 500 MHz)



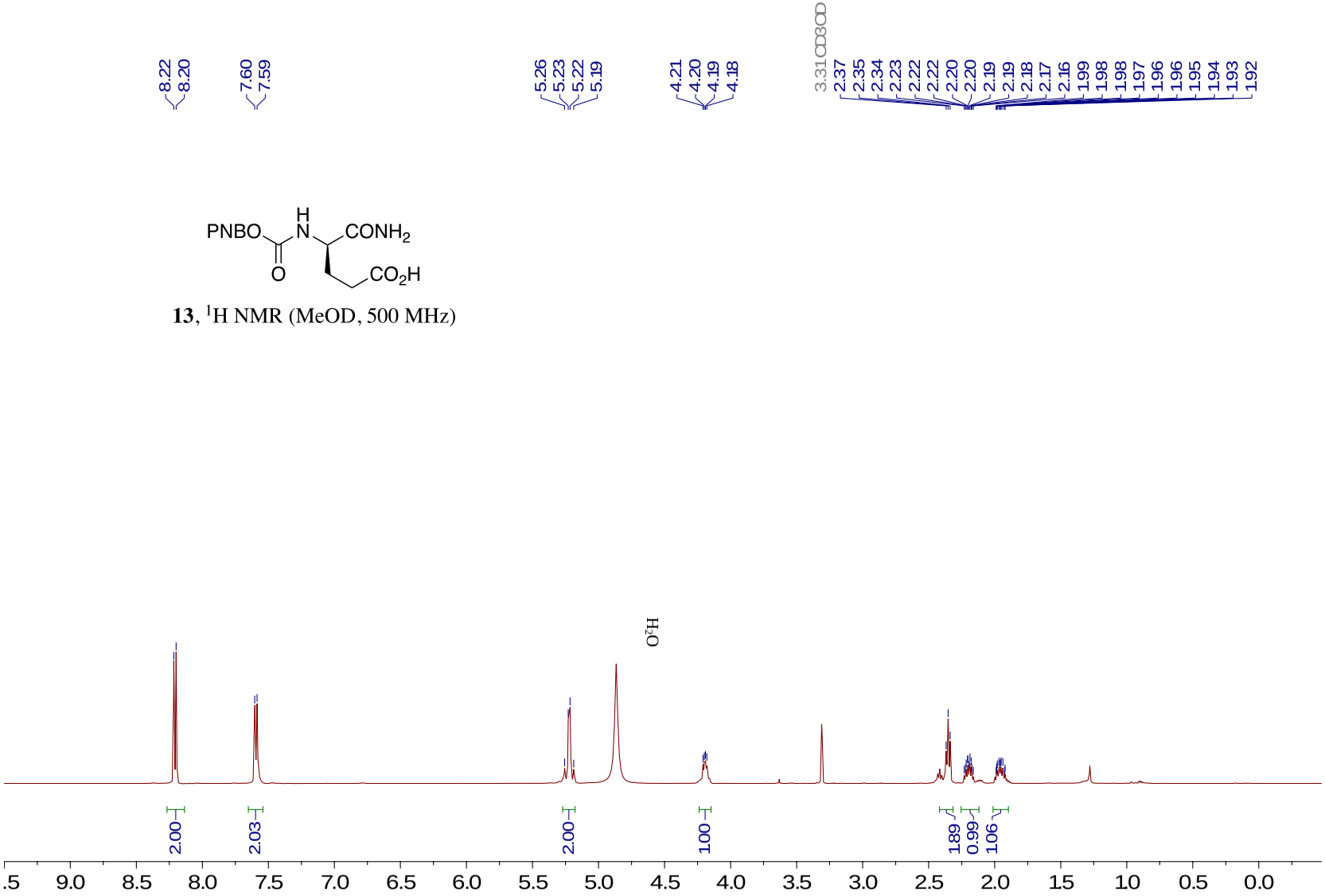
11, ^{13}C NMR ($CDCl_3$, 126 MHz)



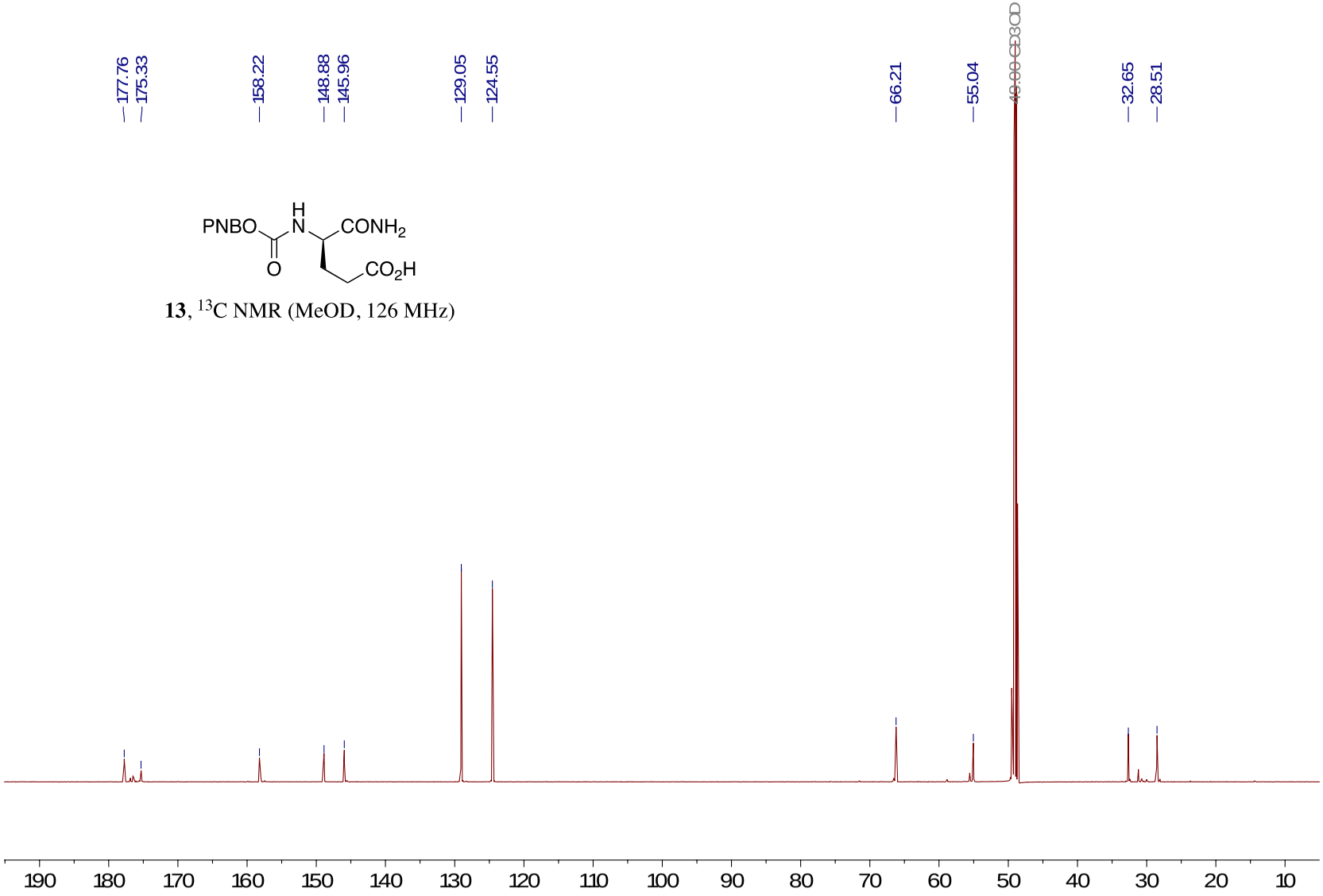
12, ^{1}H NMR (MeOD, 500 MHz)



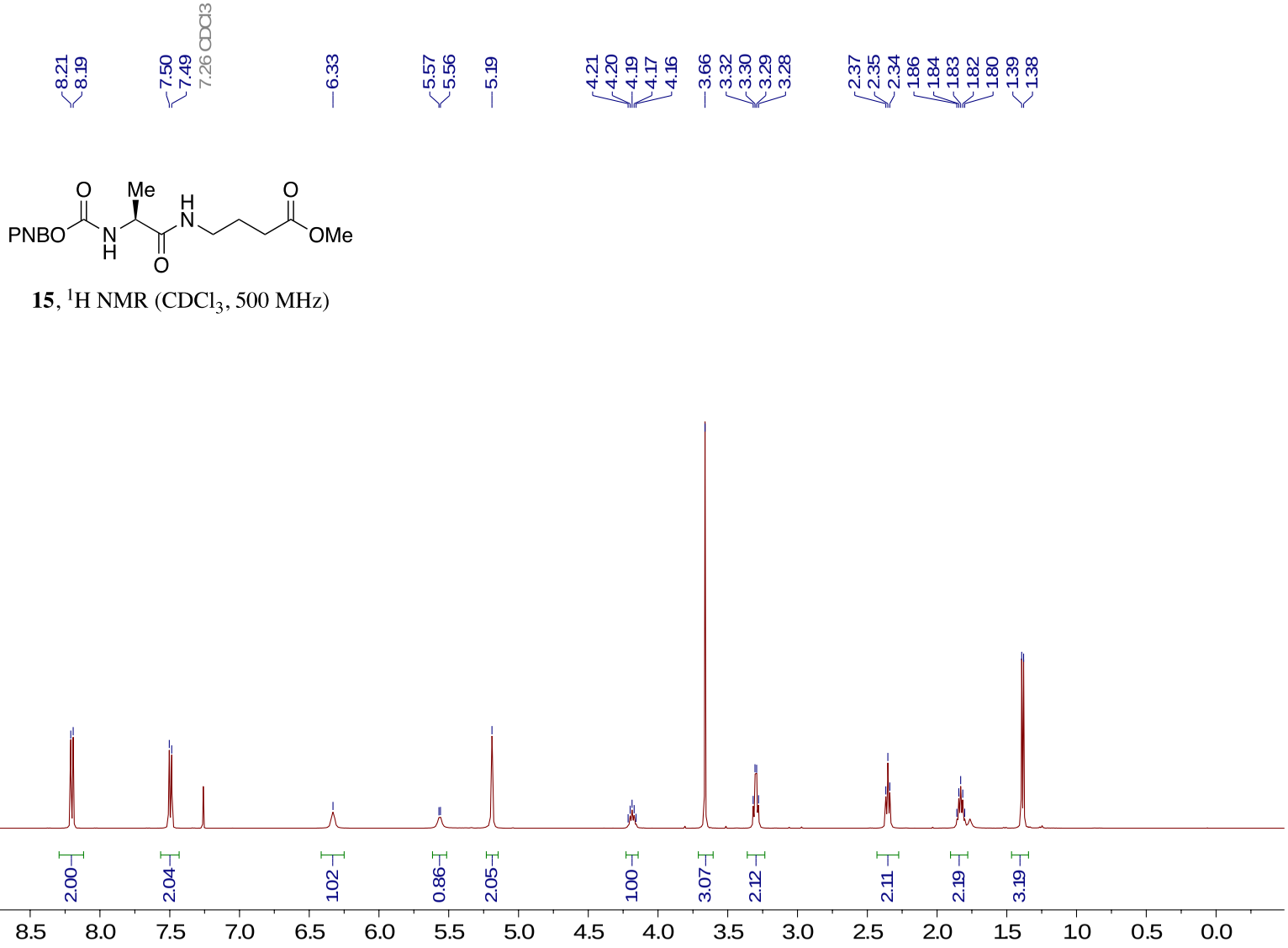
12, ^{13}C NMR (MeOD, 126 MHz)



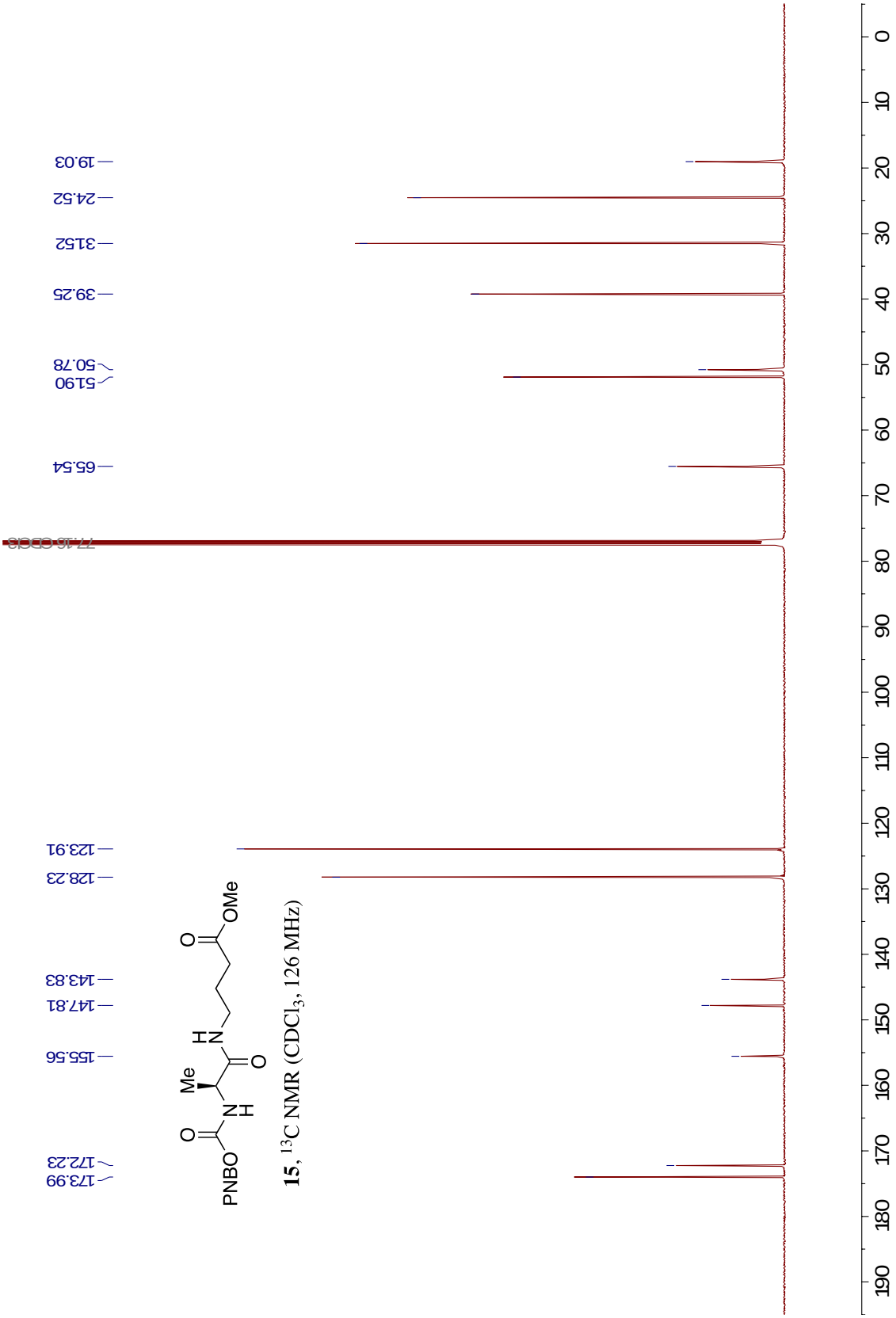
13, ^{1}H NMR (MeOD, 500 MHz)



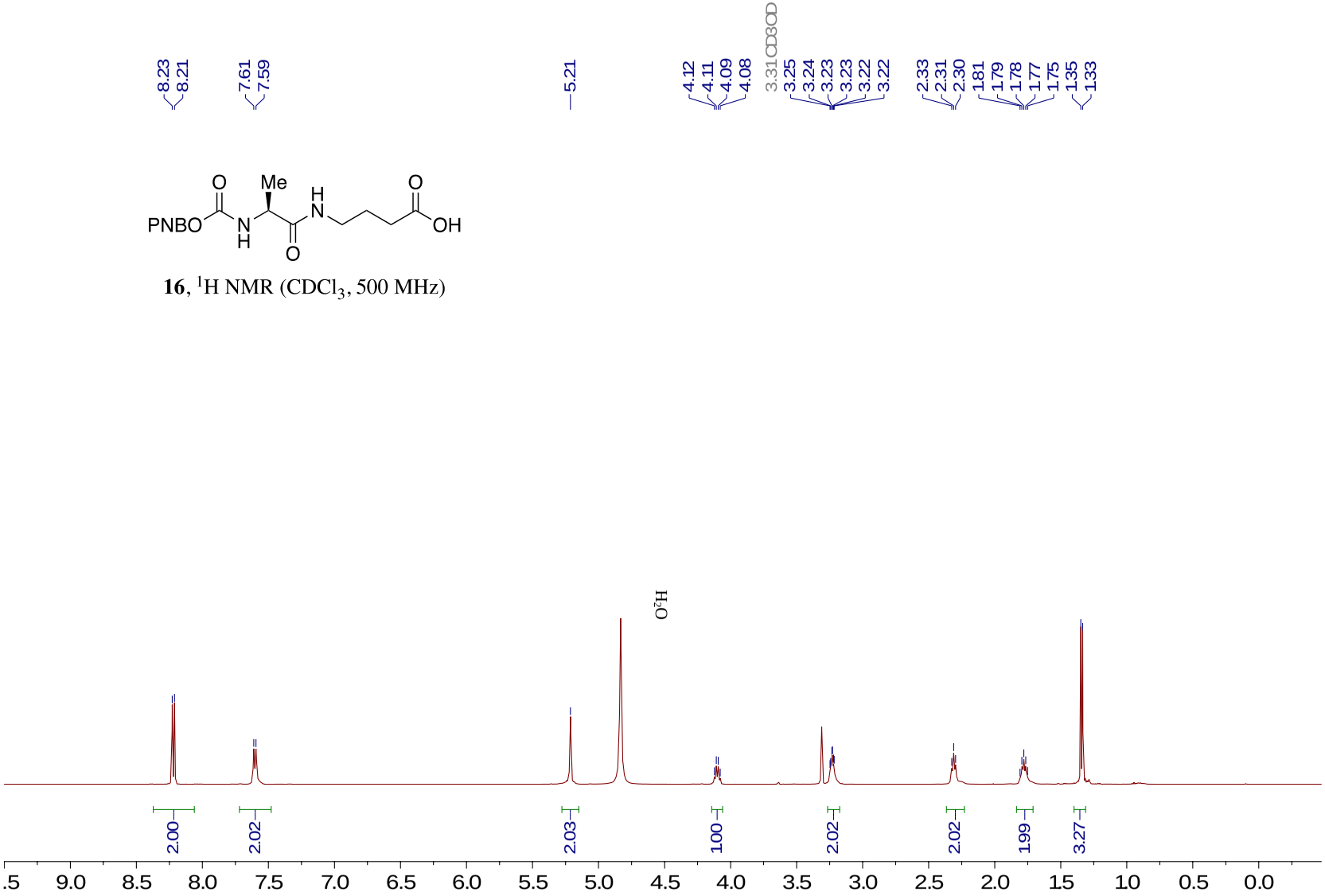
13, ^{13}C NMR (MeOD, 126 MHz)



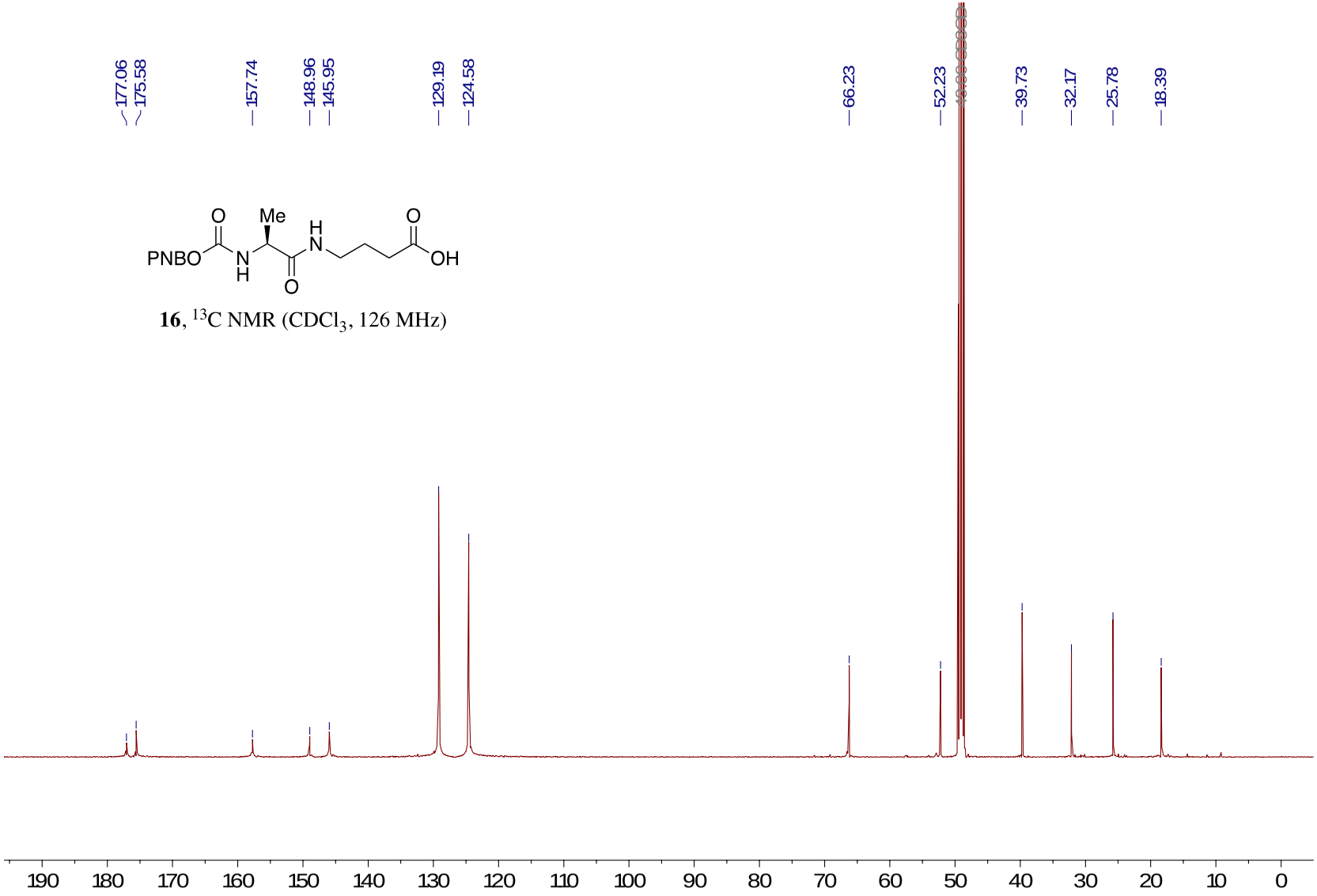
15, ^{1}H NMR ($CDCl_3$, 500 MHz)



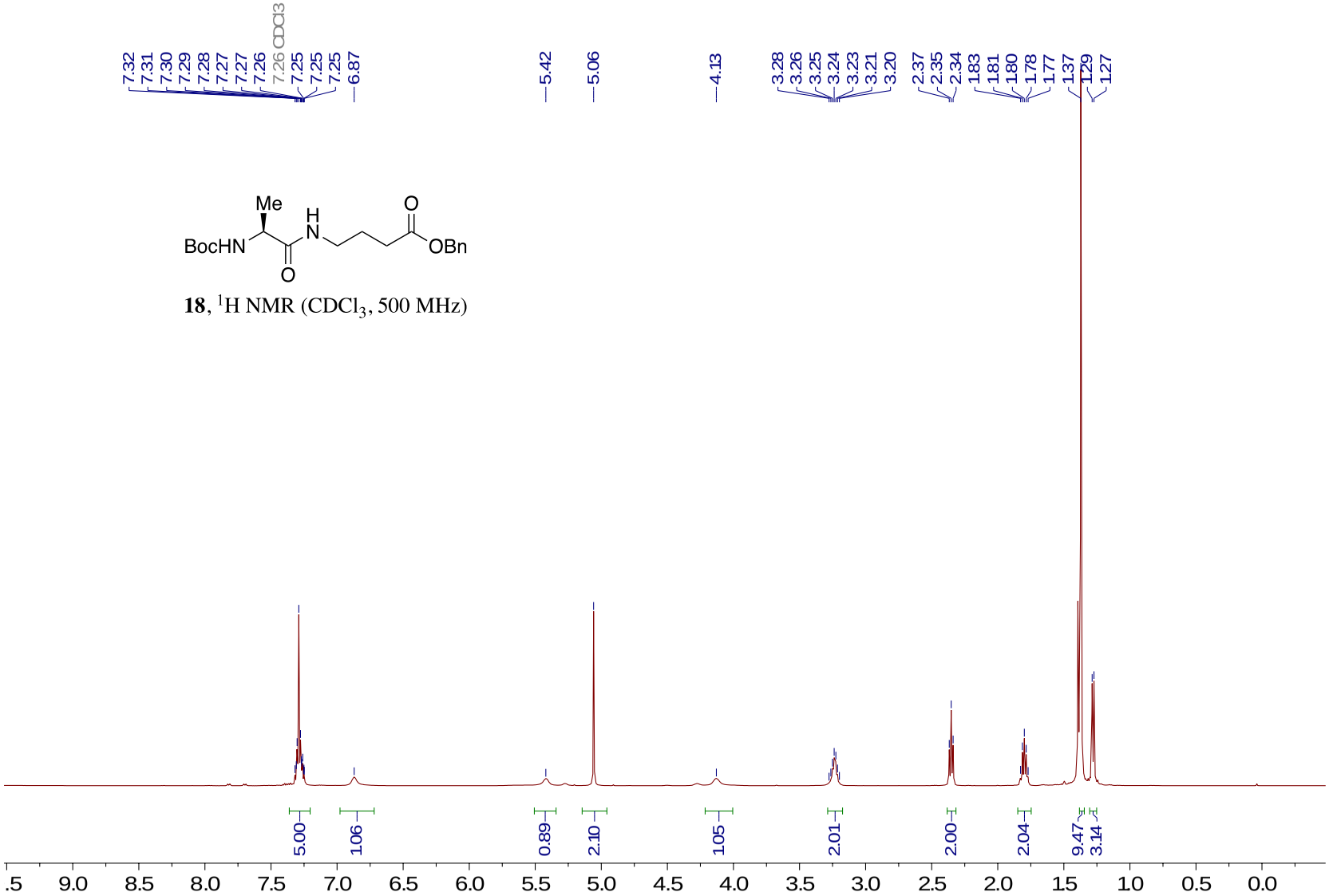
15, ^{13}C NMR ($CDCl_3$, 126 MHz)



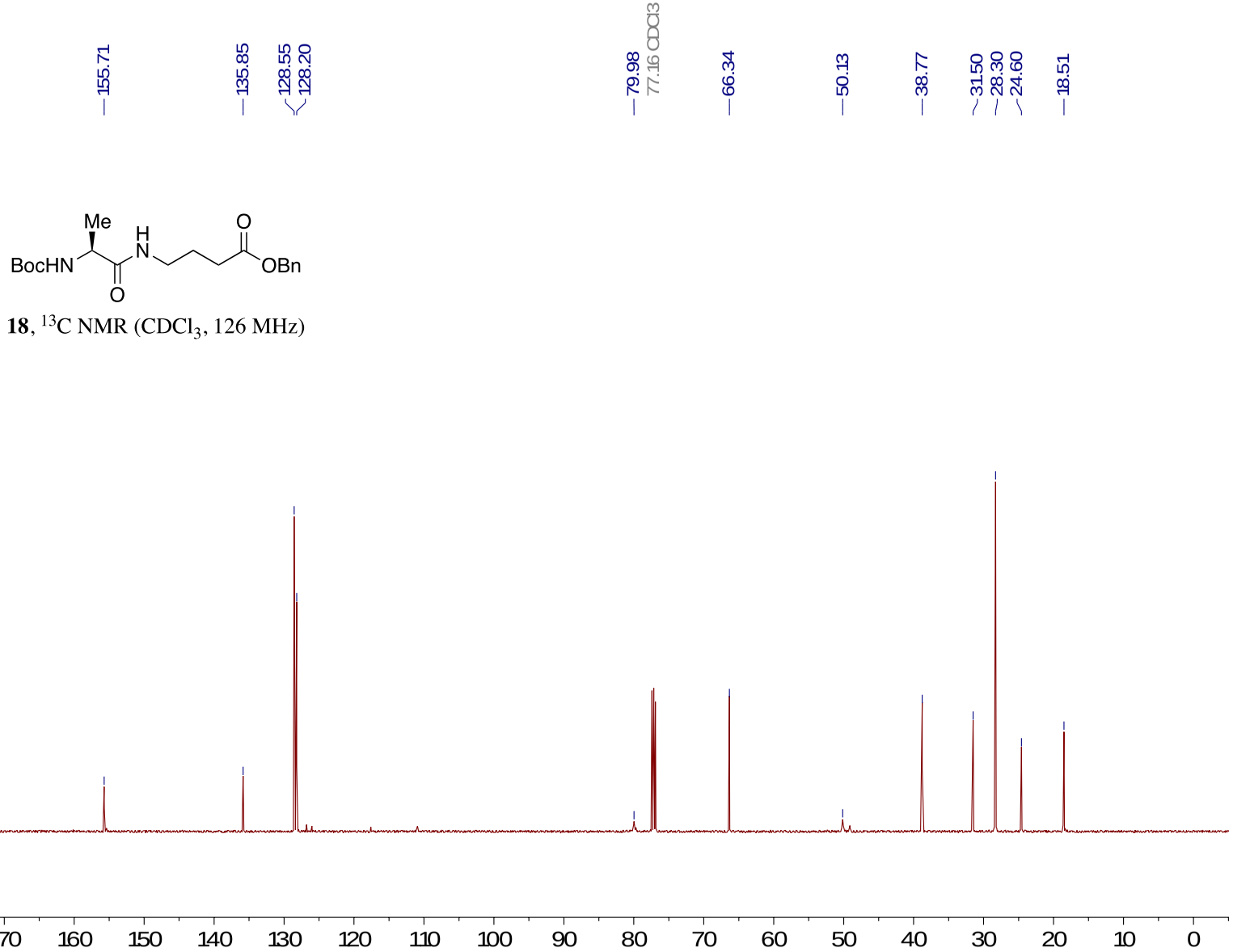
16, ^{1}H NMR ($CDCl_3$, 500 MHz)



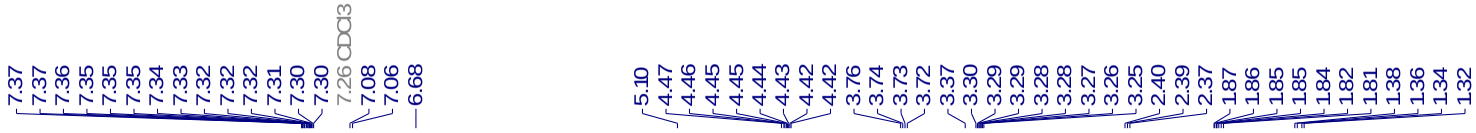
16, ^{13}C NMR ($CDCl_3$, 126 MHz)

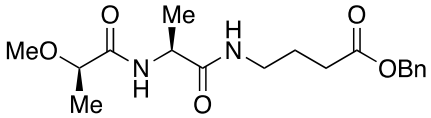


18, ^{1}H NMR ($CDCl_3$, 500 MHz)

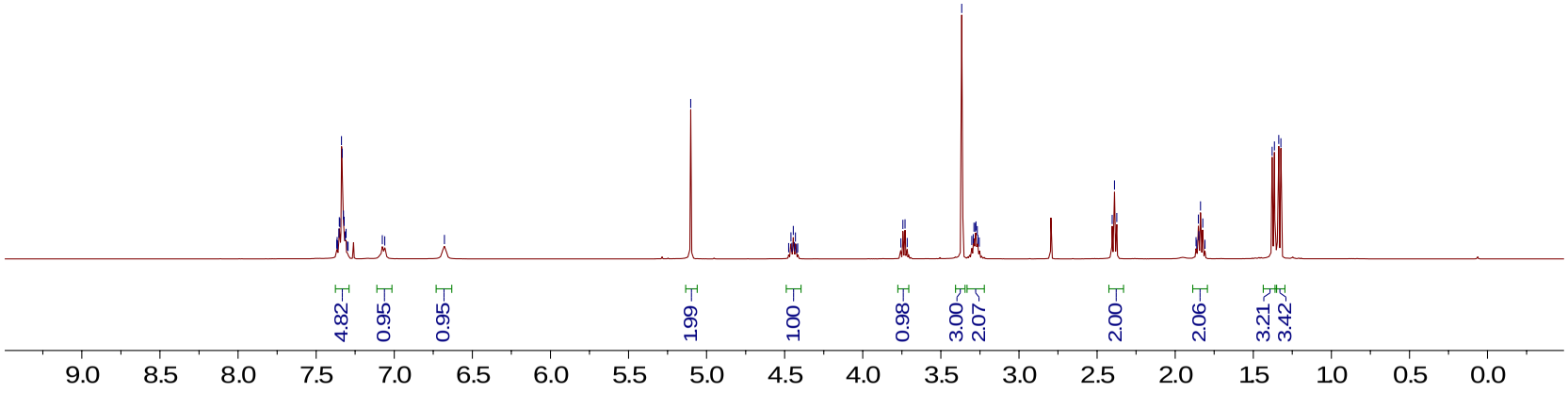


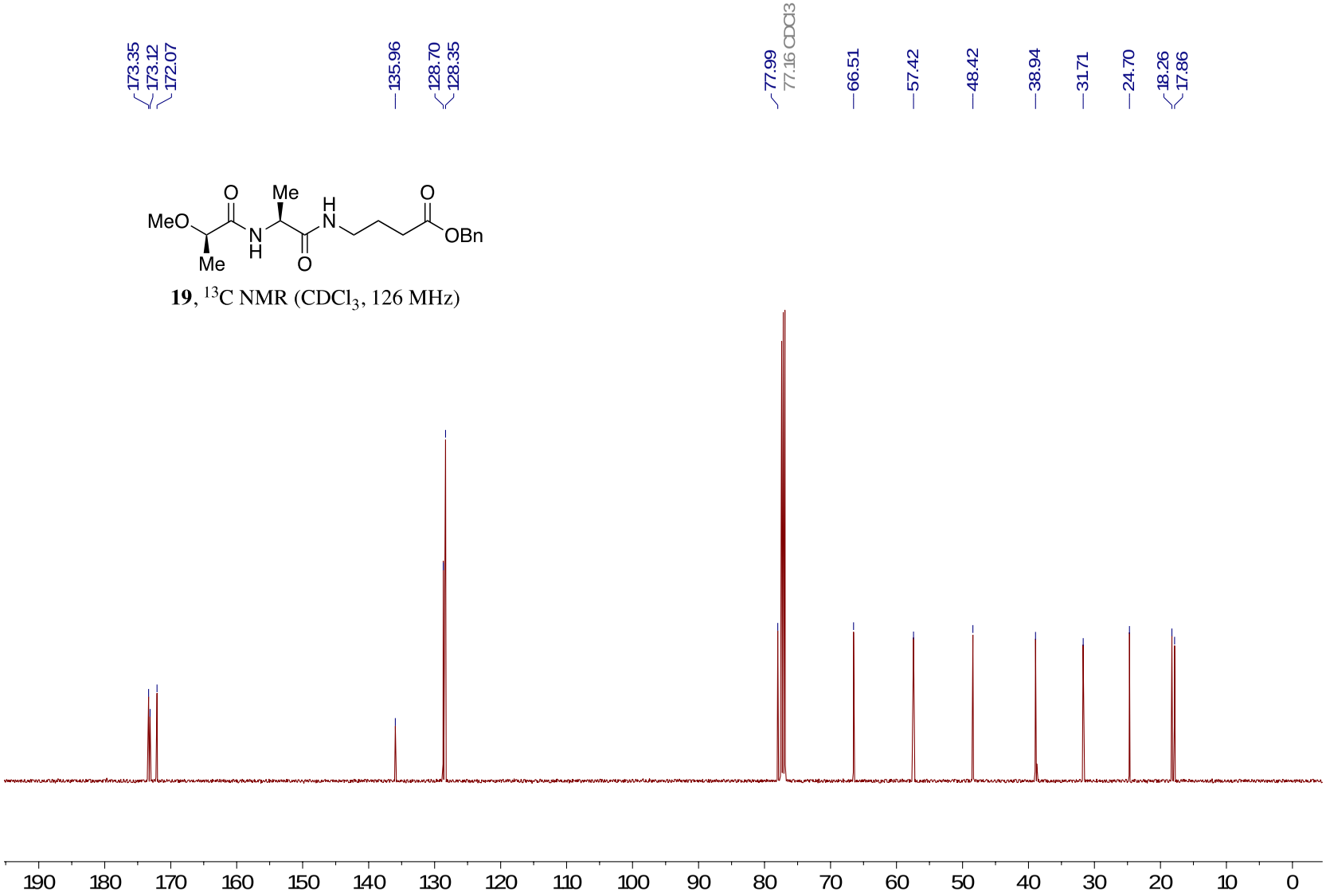
18, ^{13}C NMR ($CDCl_3$, 126 MHz)



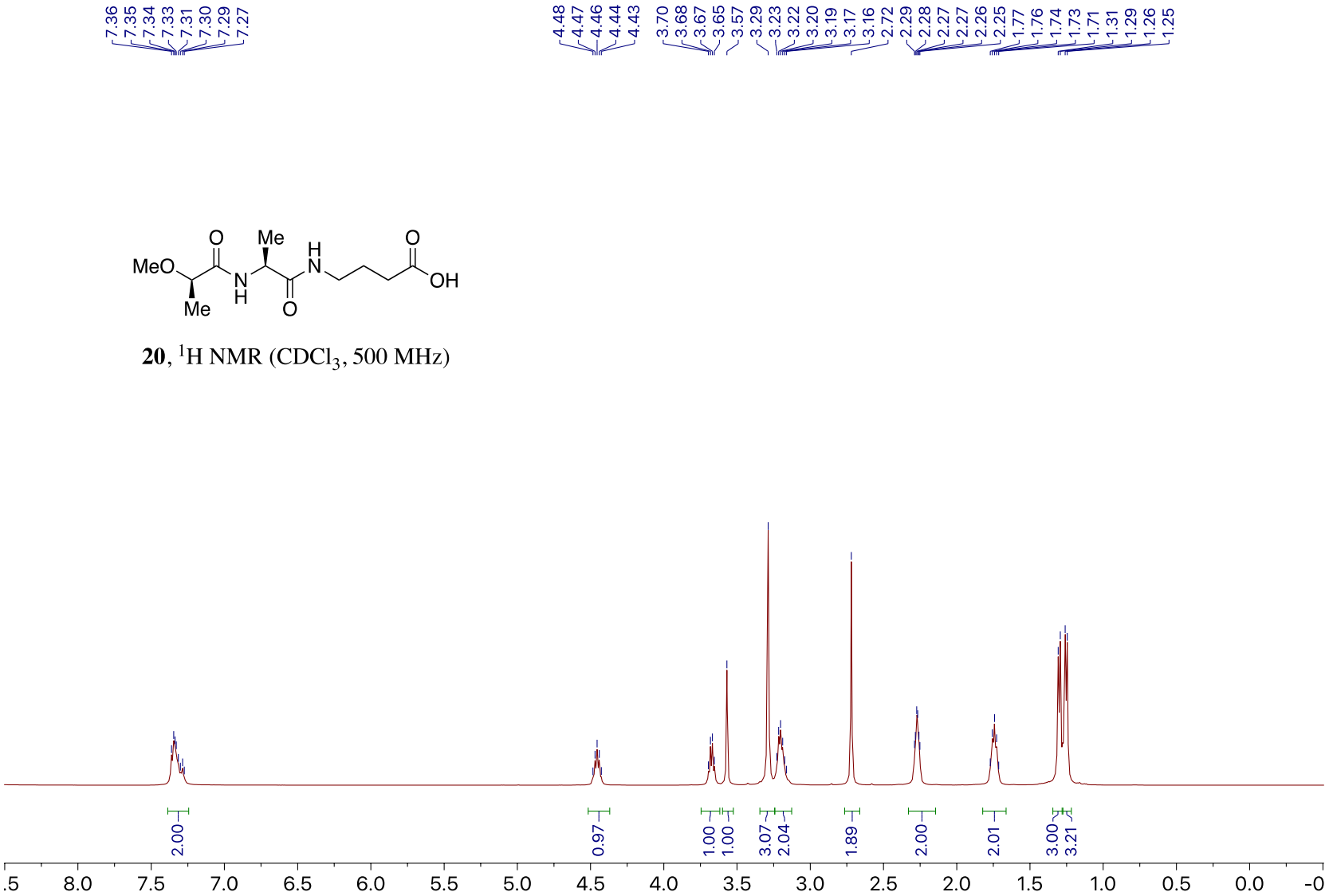


19, ^{1}H NMR ($CDCl_3$, 500 MHz)

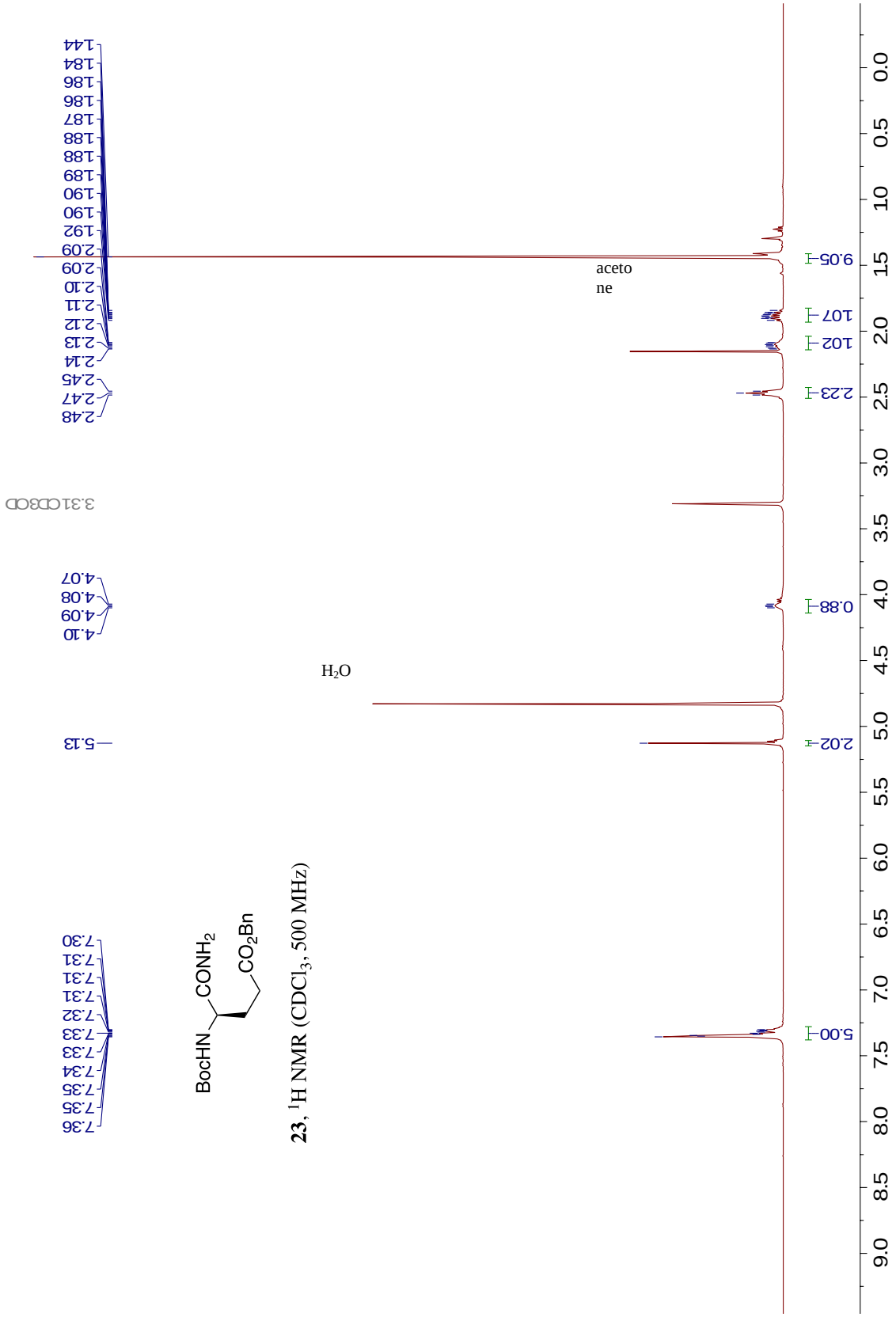




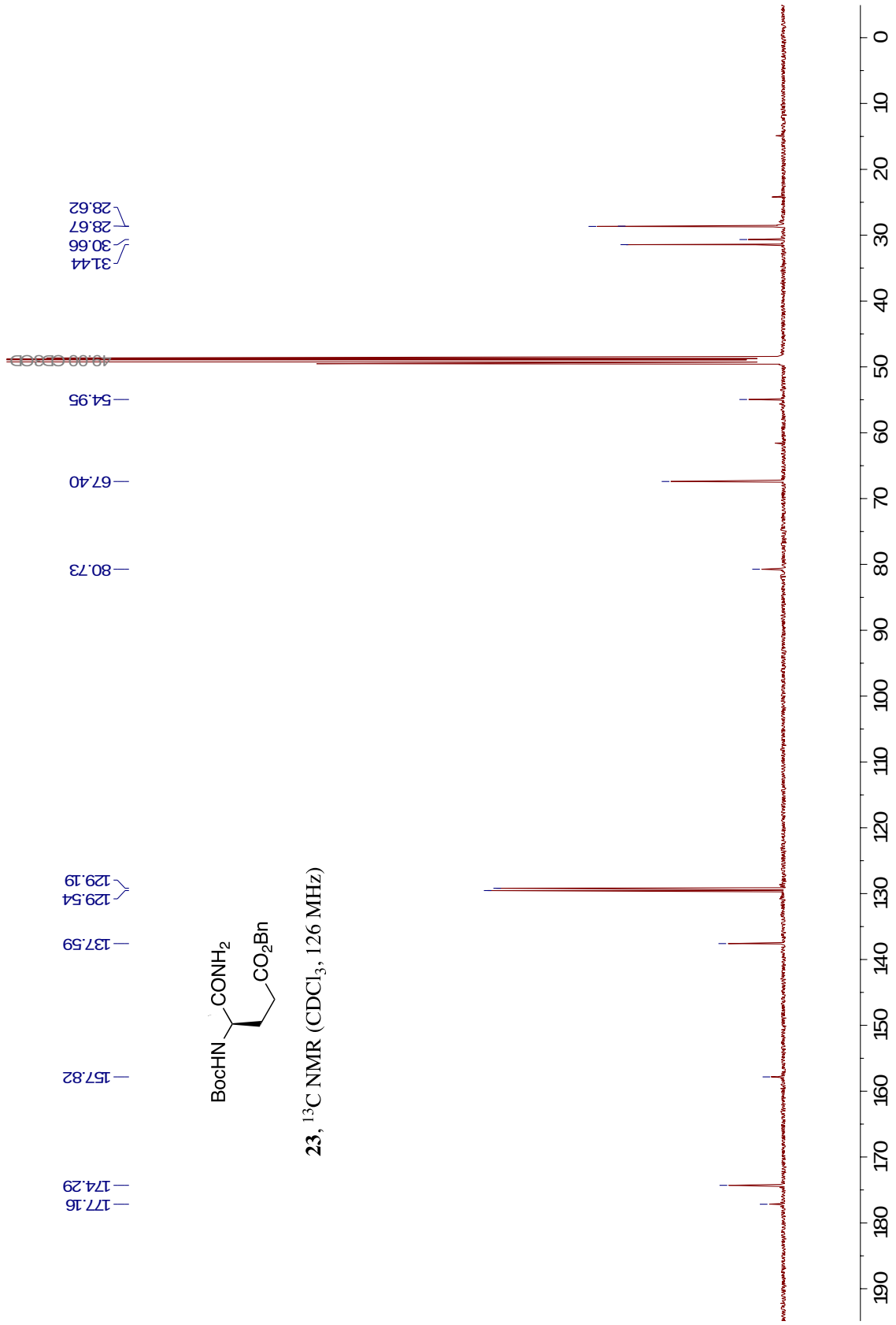
19, ^{13}C NMR ($CDCl_3$, 126 MHz)



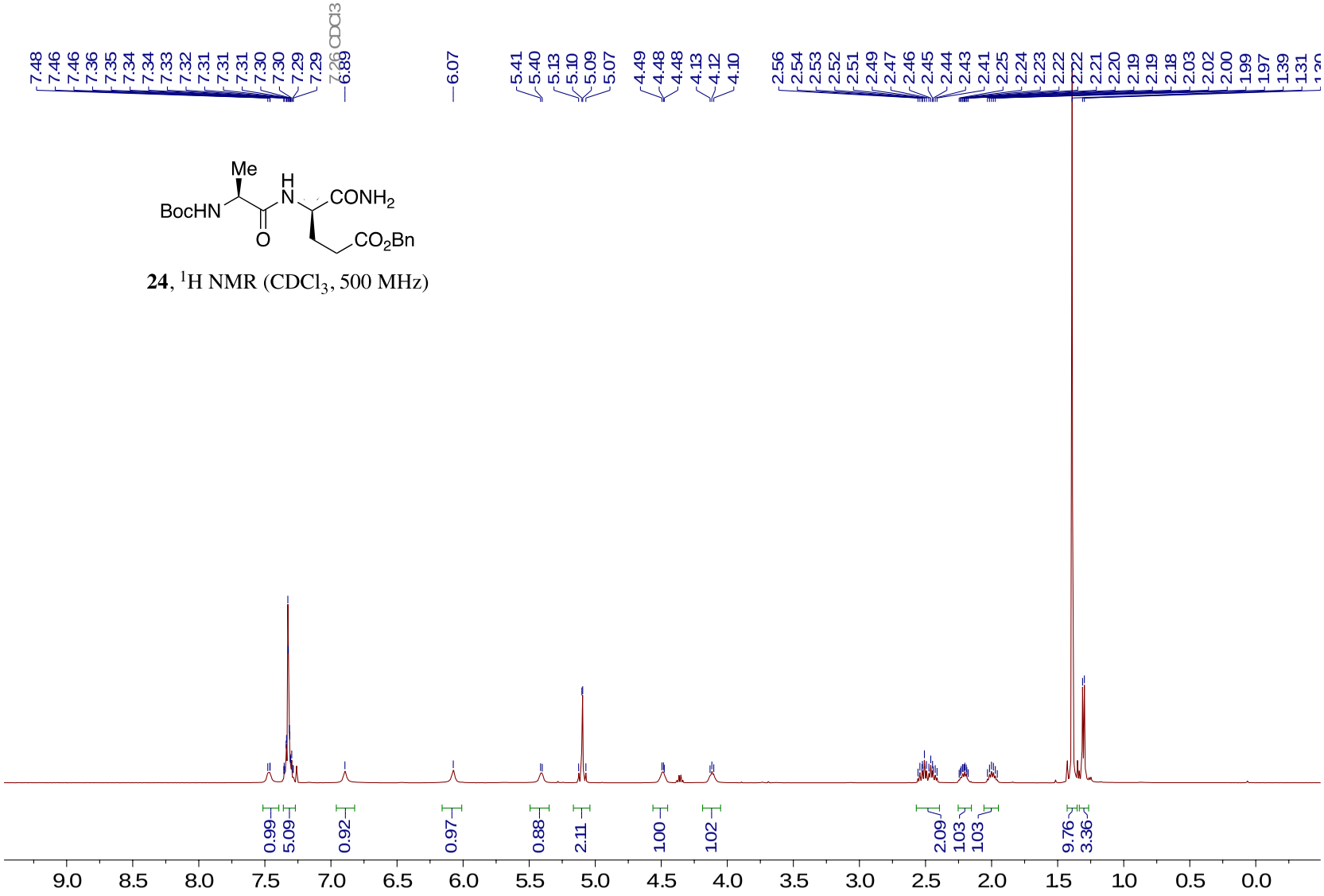
20, ^{1}H NMR ($CDCl_3$, 500 MHz)



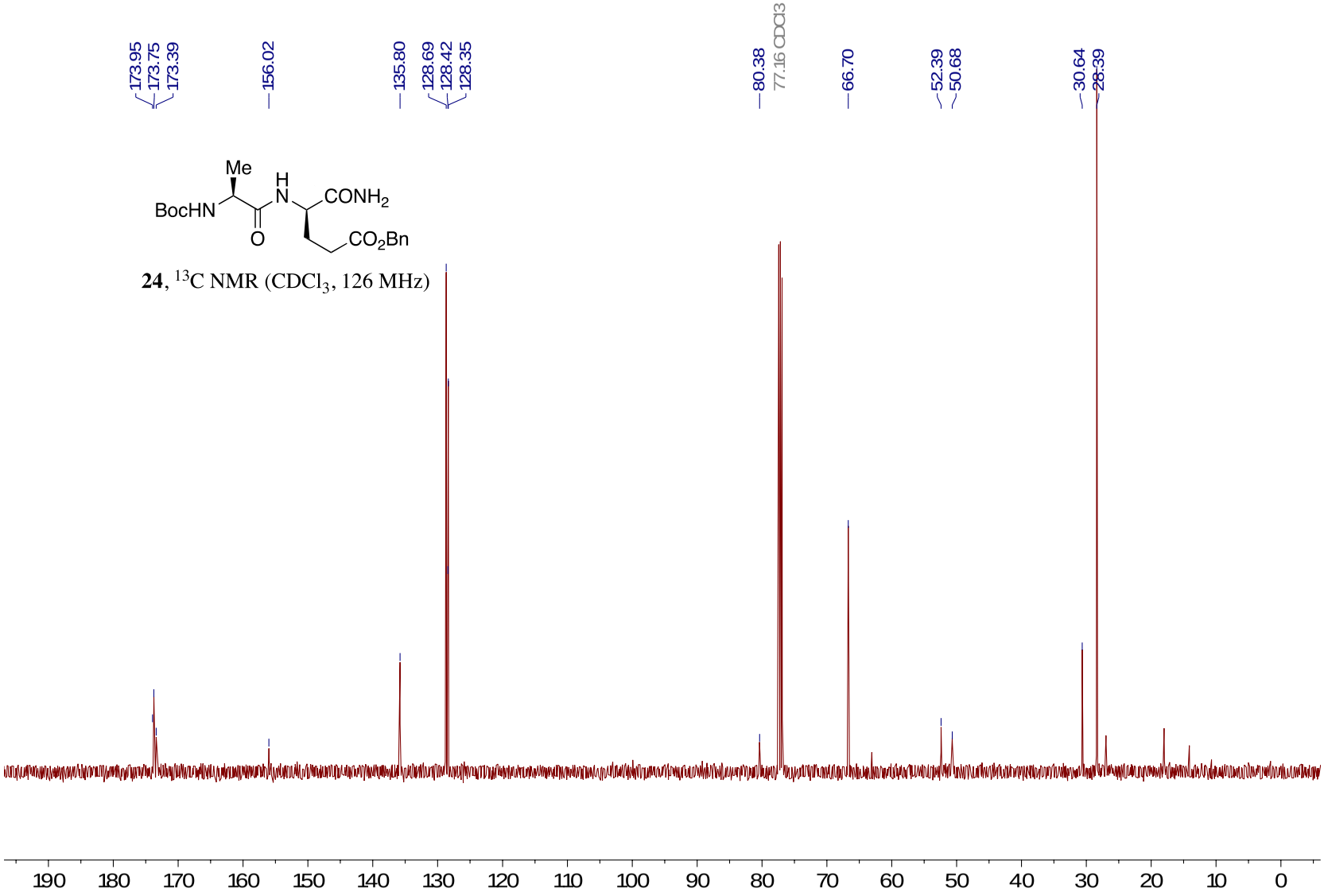
23, ^{1}H NMR ($CDCl_3$, 500 MHz)



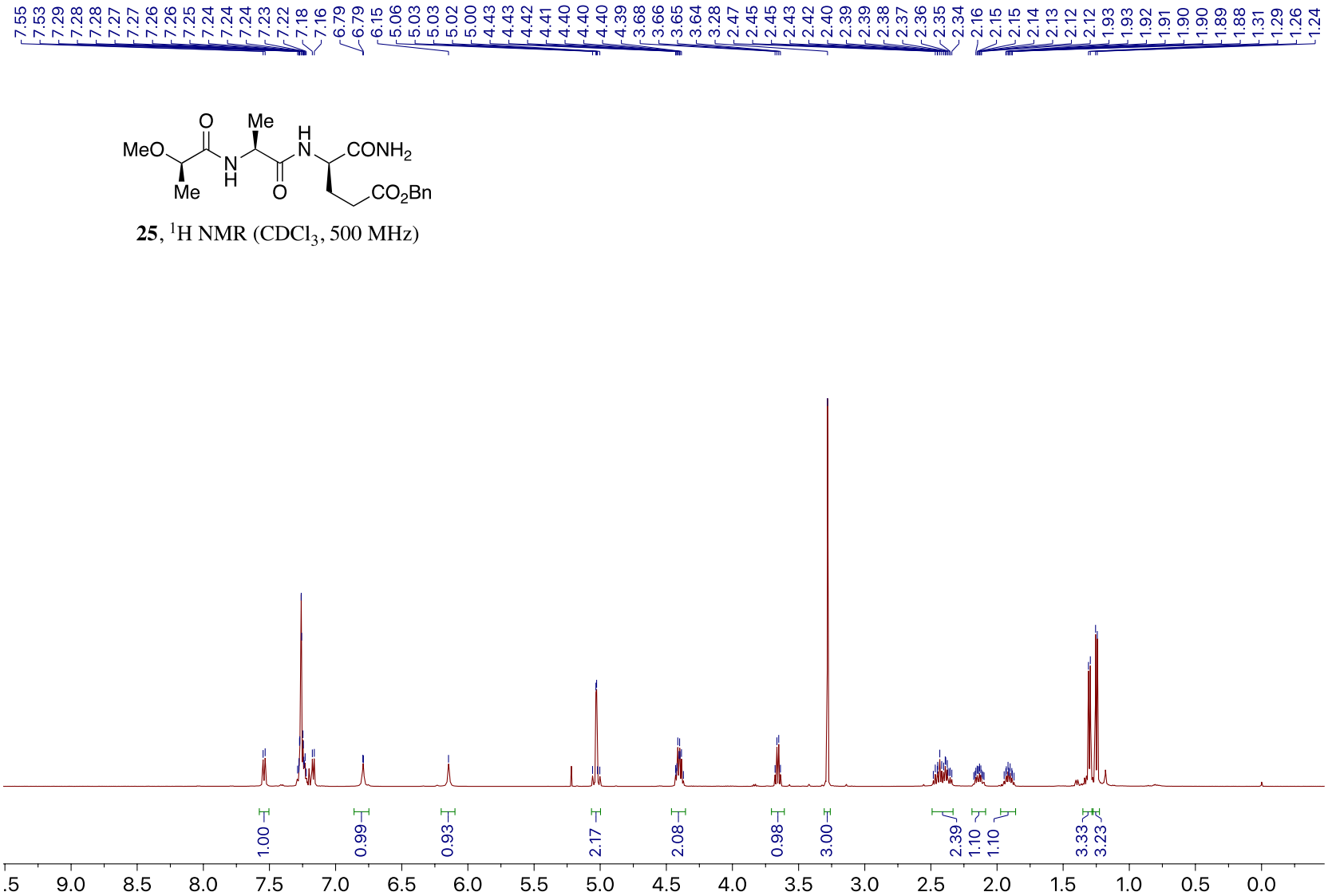
23, ^{13}C NMR ($CDCl_3$, 126 MHz)



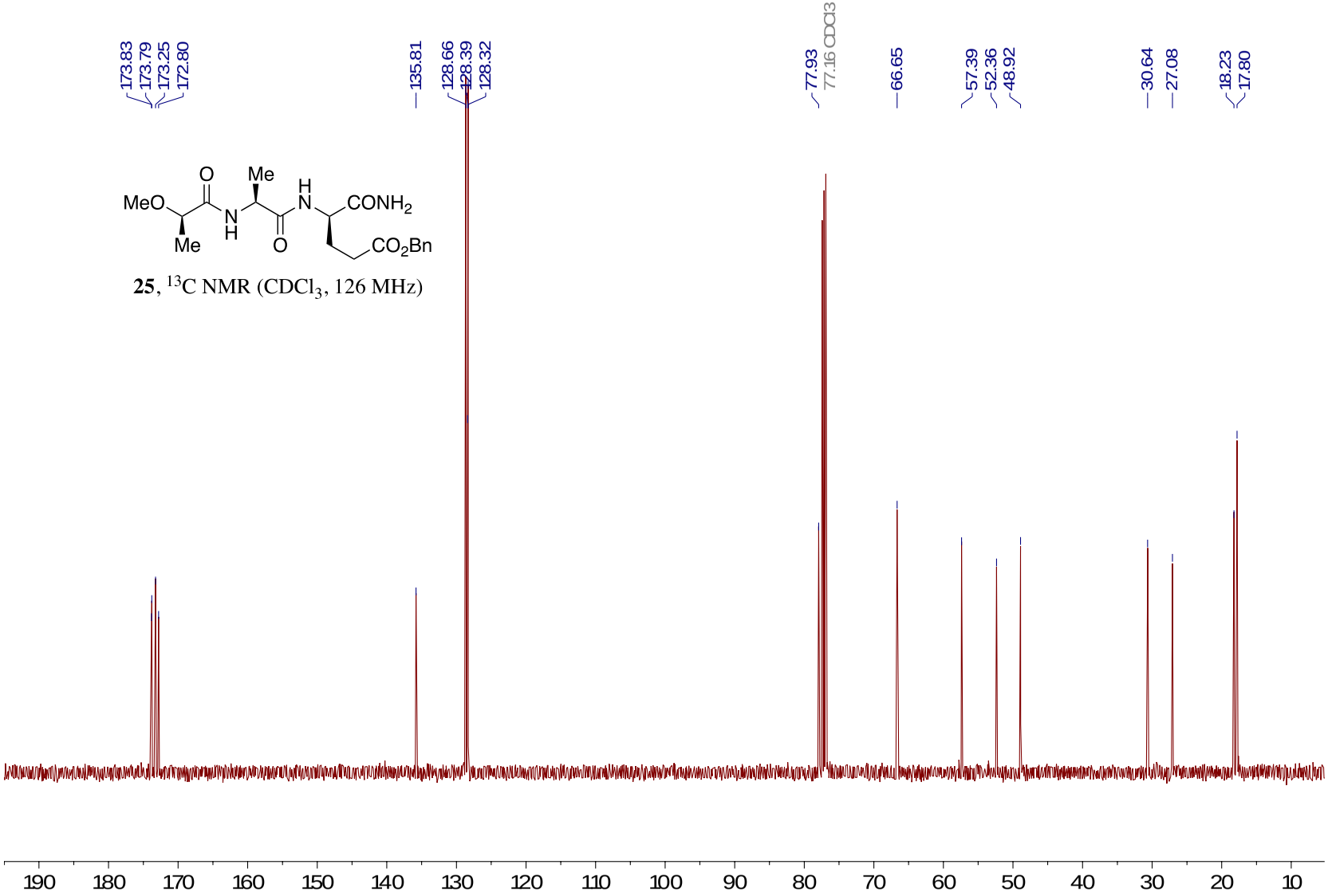
24, ^{1}H NMR ($CDCl_3$, 500 MHz)



24, ^{13}C NMR ($CDCl_3$, 126 MHz)

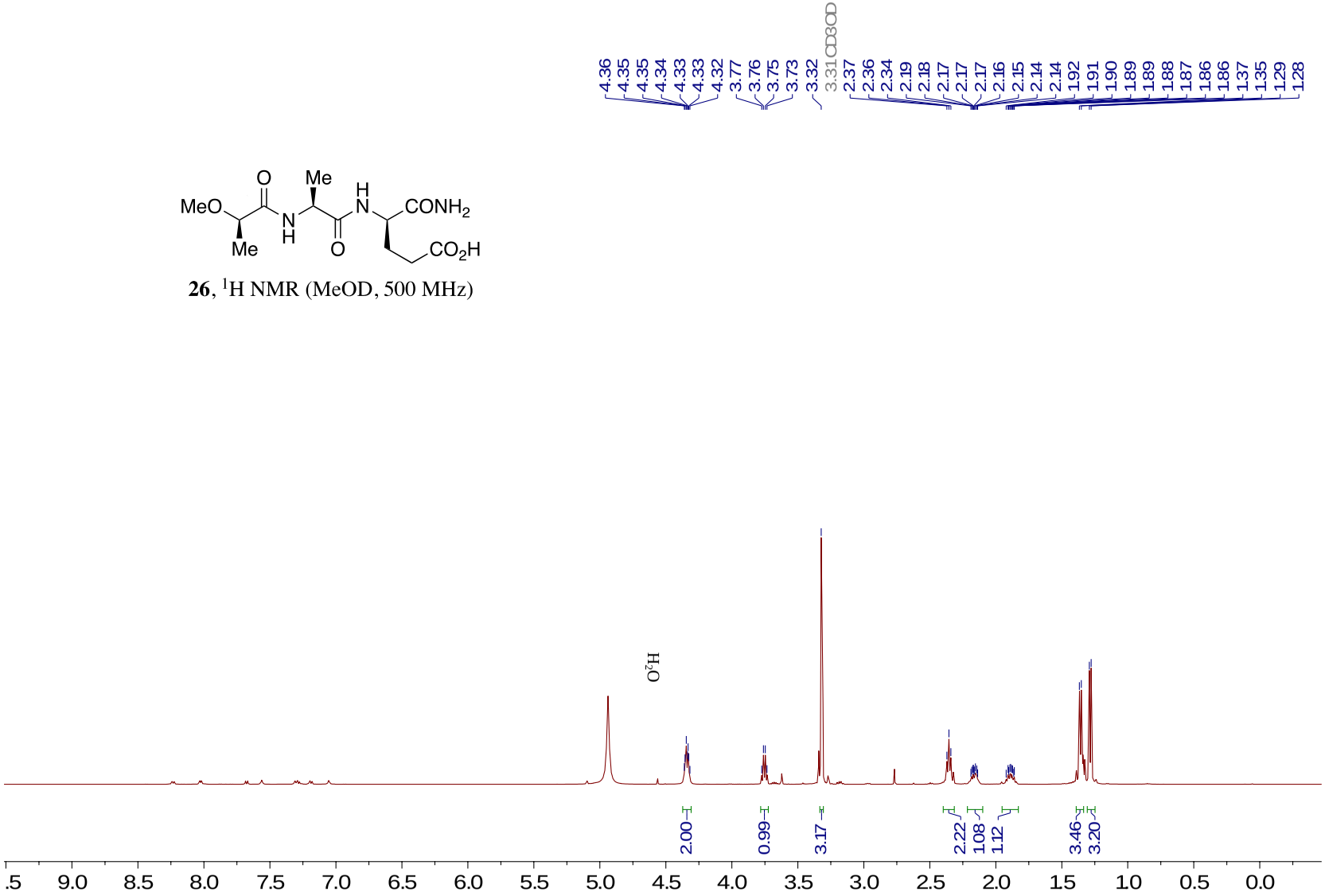


25, ^{1}H NMR ($CDCl_3$, 500 MHz)

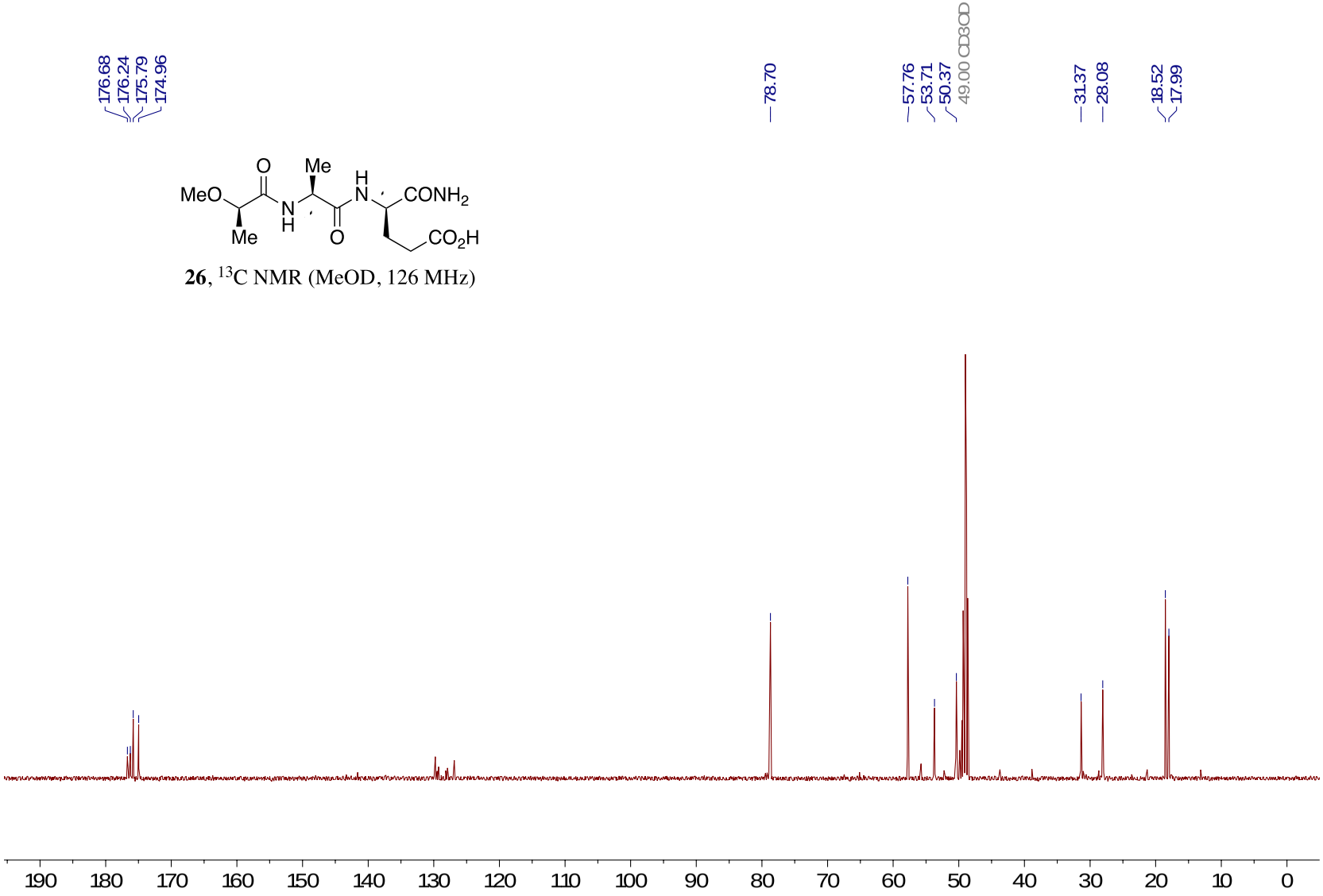


25, ^{13}C NMR ($CDCl_3$, 126 MHz)

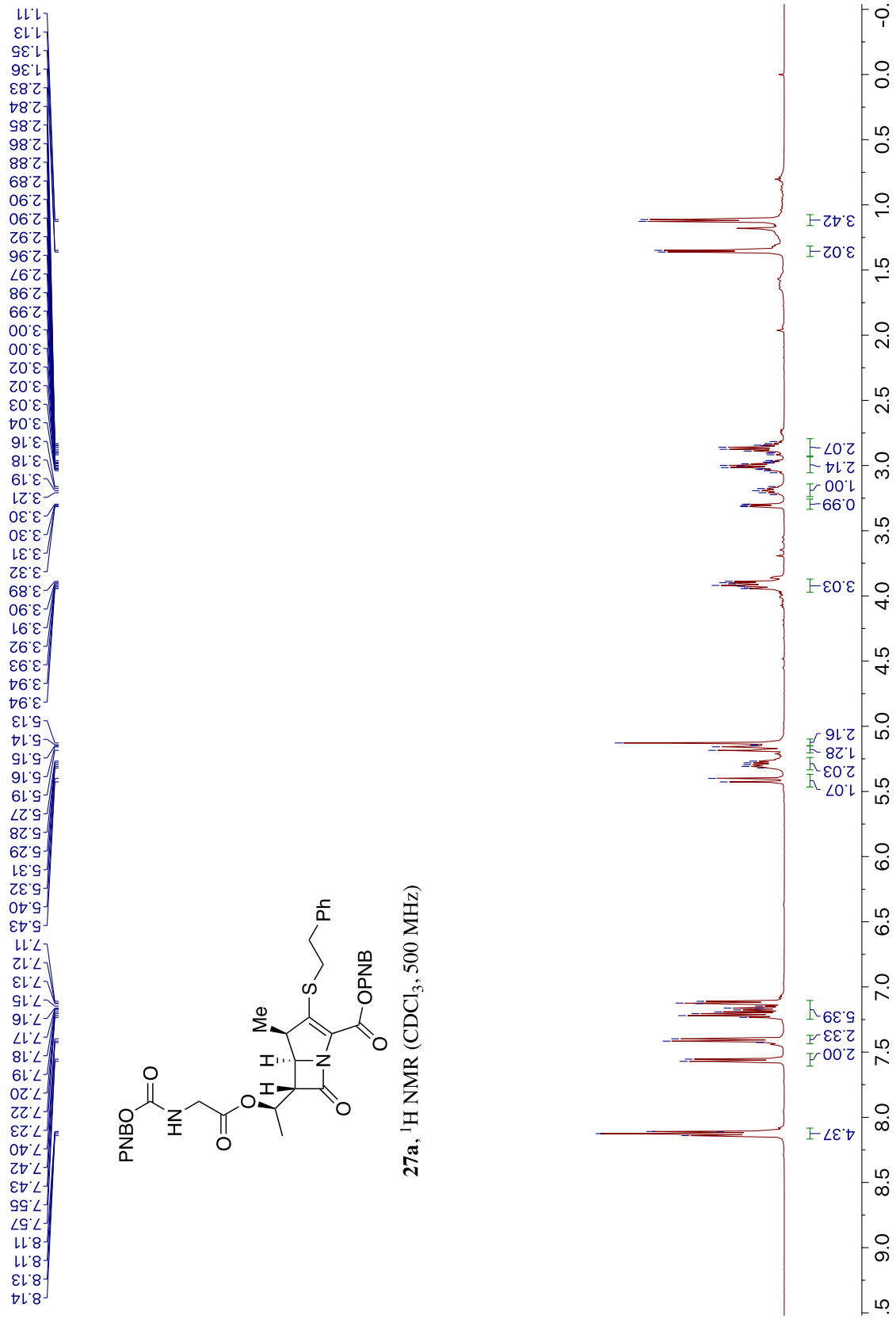
26, ^{1}H NMR (MeOD, 500 MHz)



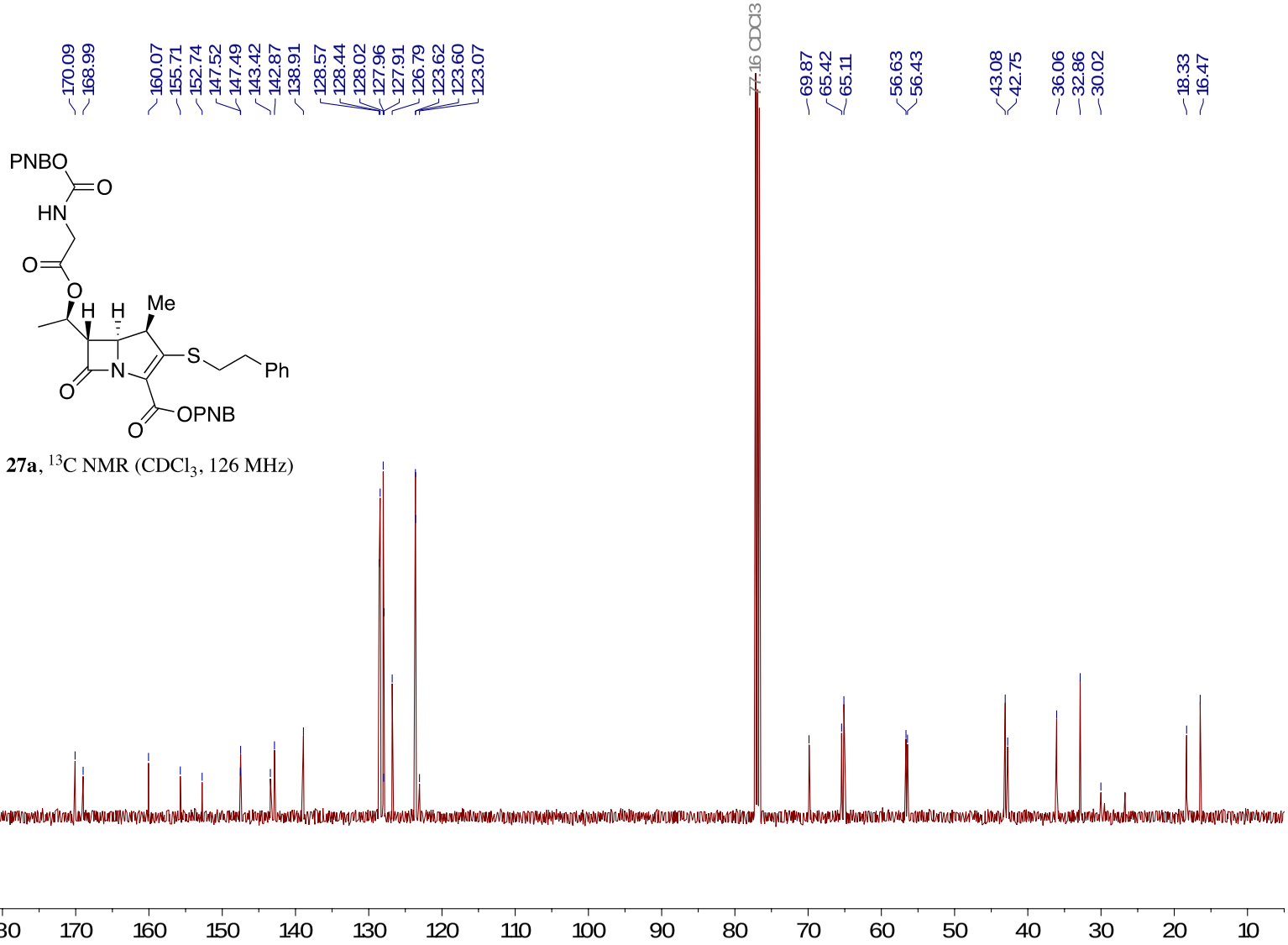
26, ^{13}C NMR (MeOD, 126 MHz)



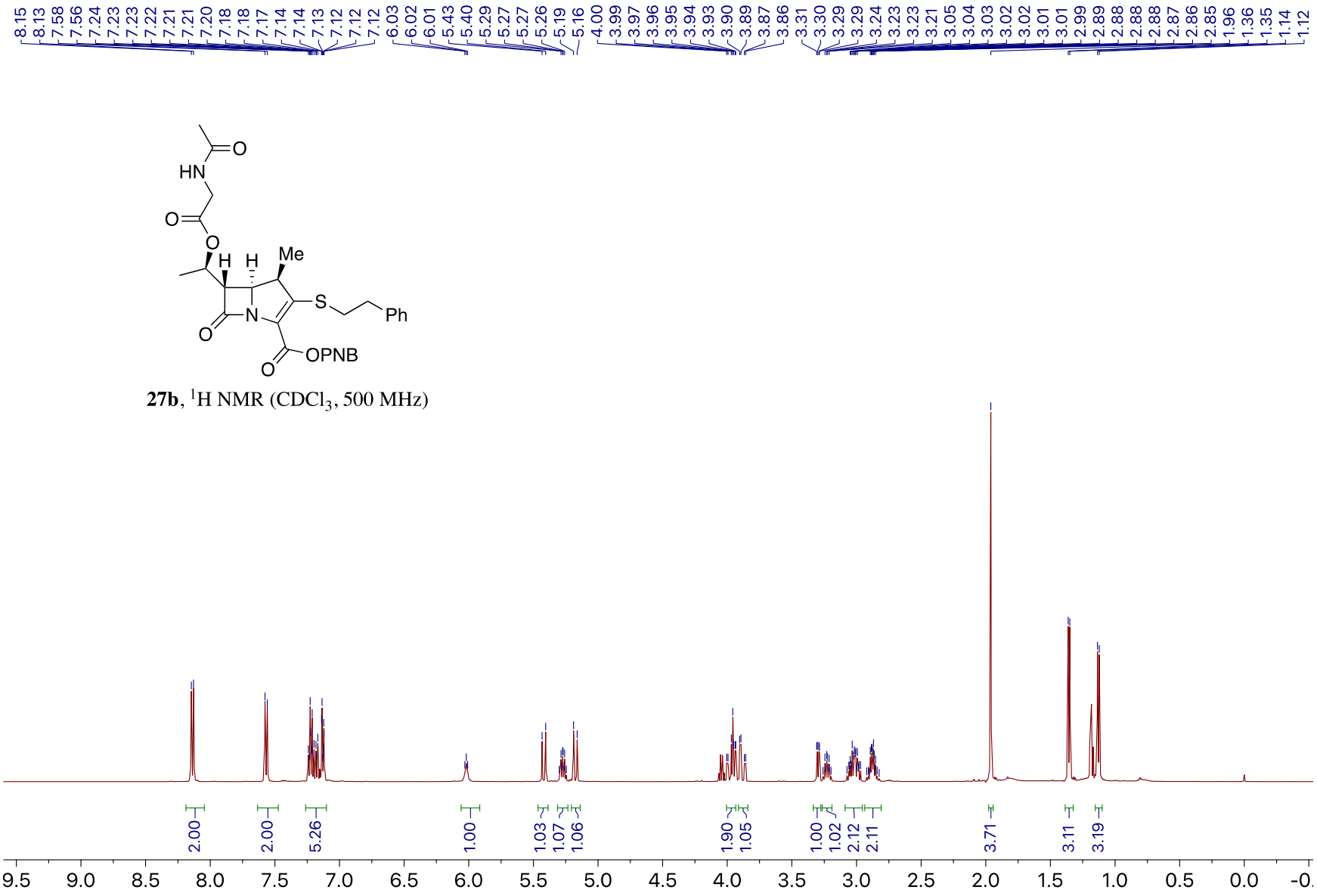
7-2. ^{1}H and ^{13}C NMR spectra of protected peptido-carbapenems 27a-n.



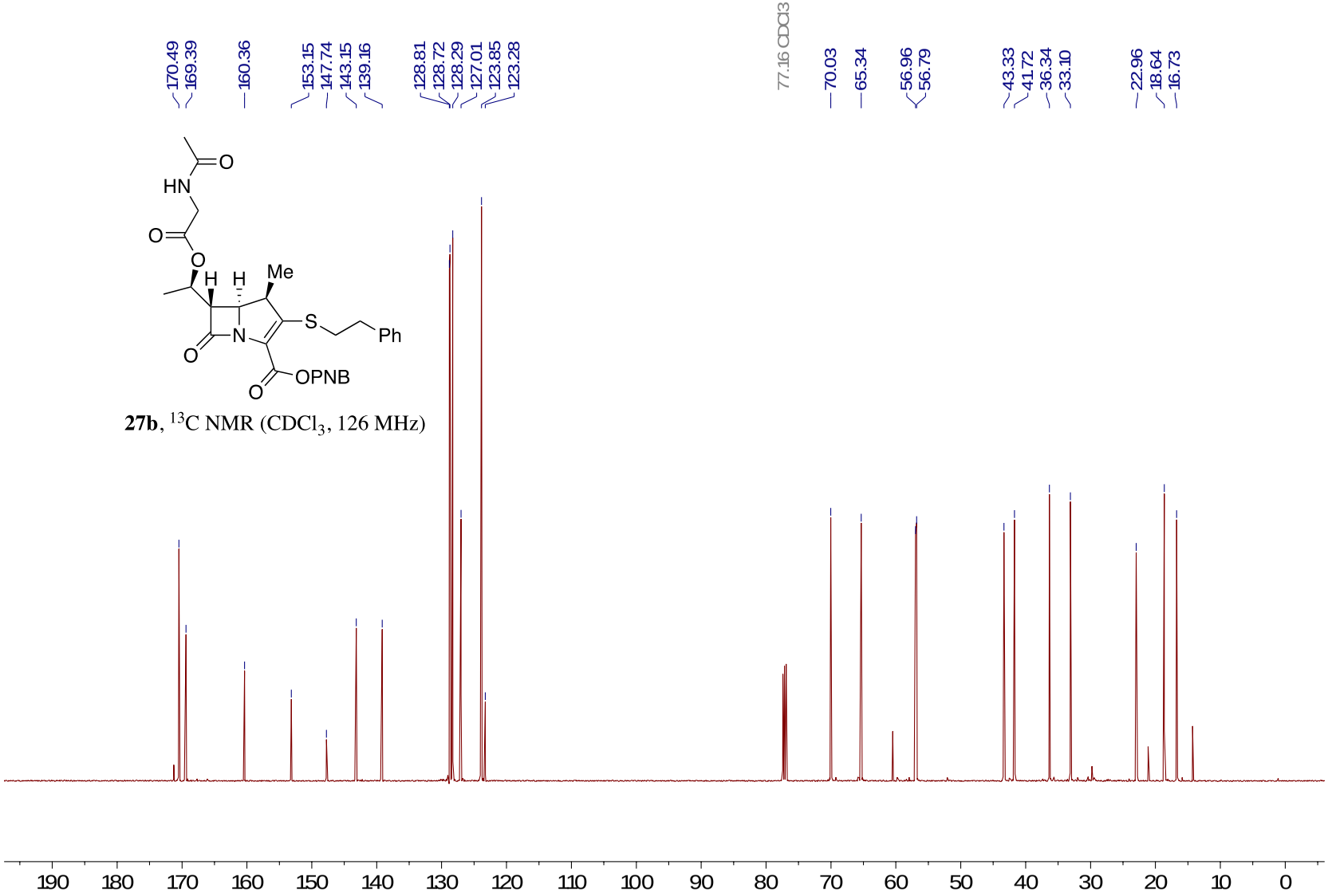
27a, ^{1}H NMR ($CDCl_3$, 500 MHz)



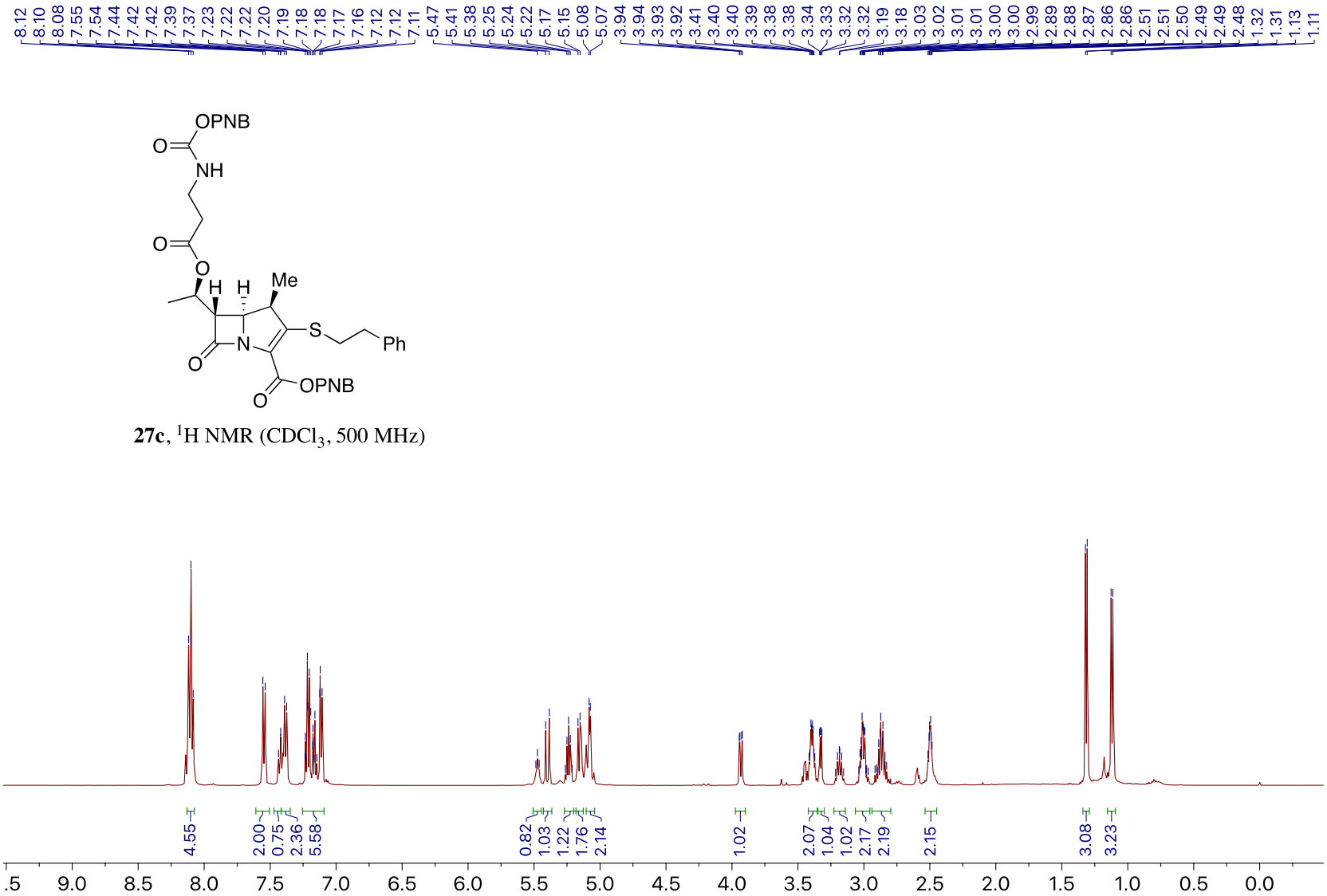
27a, ^{13}C NMR ($CDCl_3$, 126 MHz)



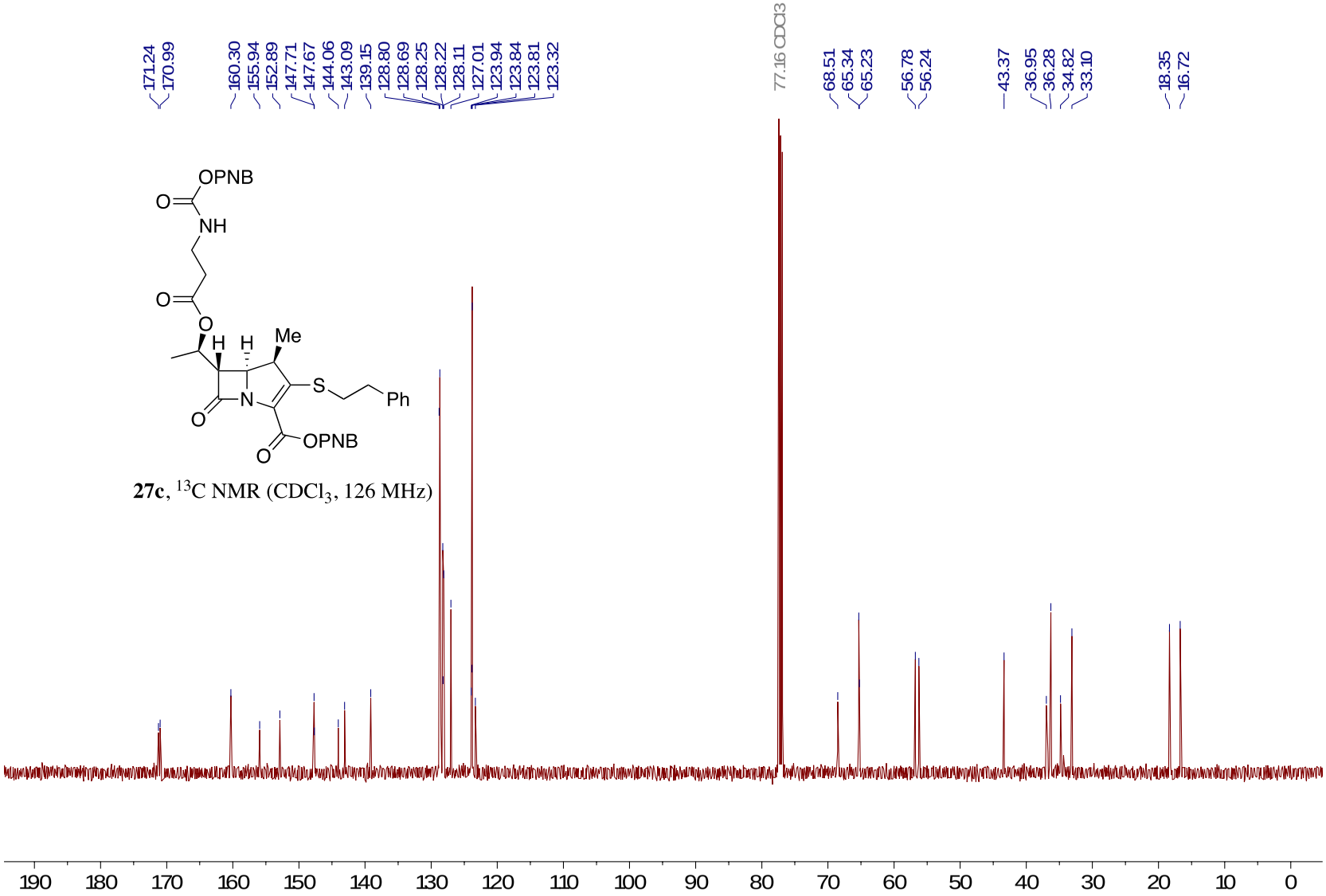
27b, ^{1}H NMR ($CDCl_3$, 500 MHz)



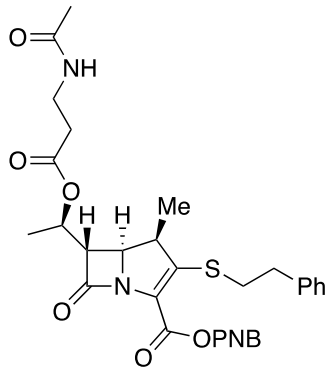
27b, ^{13}C NMR ($CDCl_3$, 126 MHz)



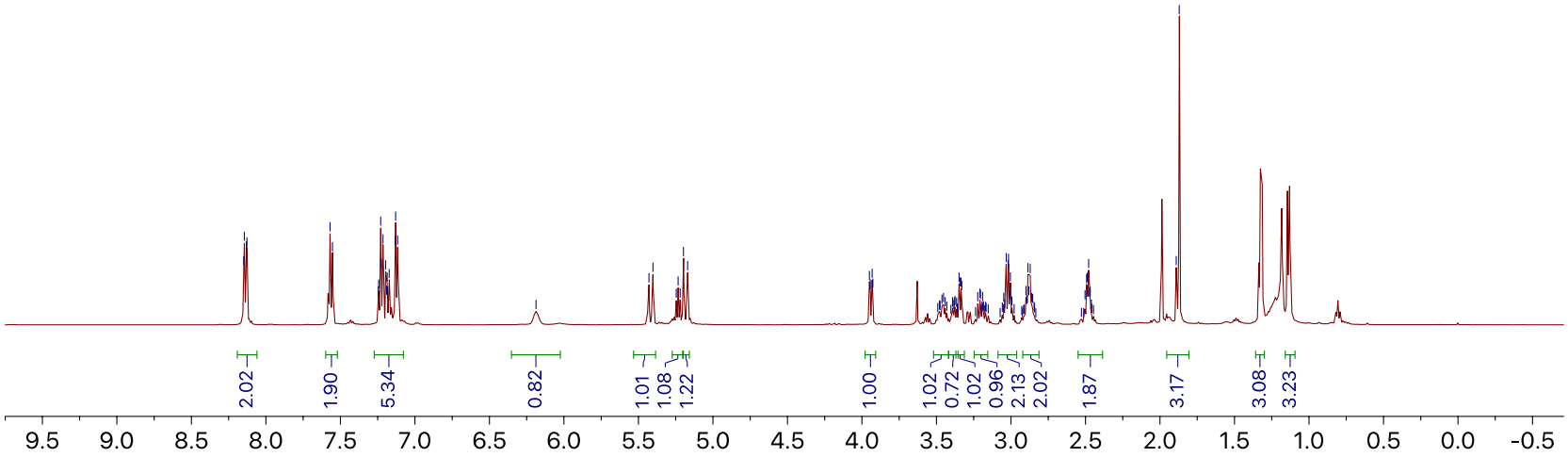
27c, ^{1}H NMR ($CDCl_3$, 500 MHz)

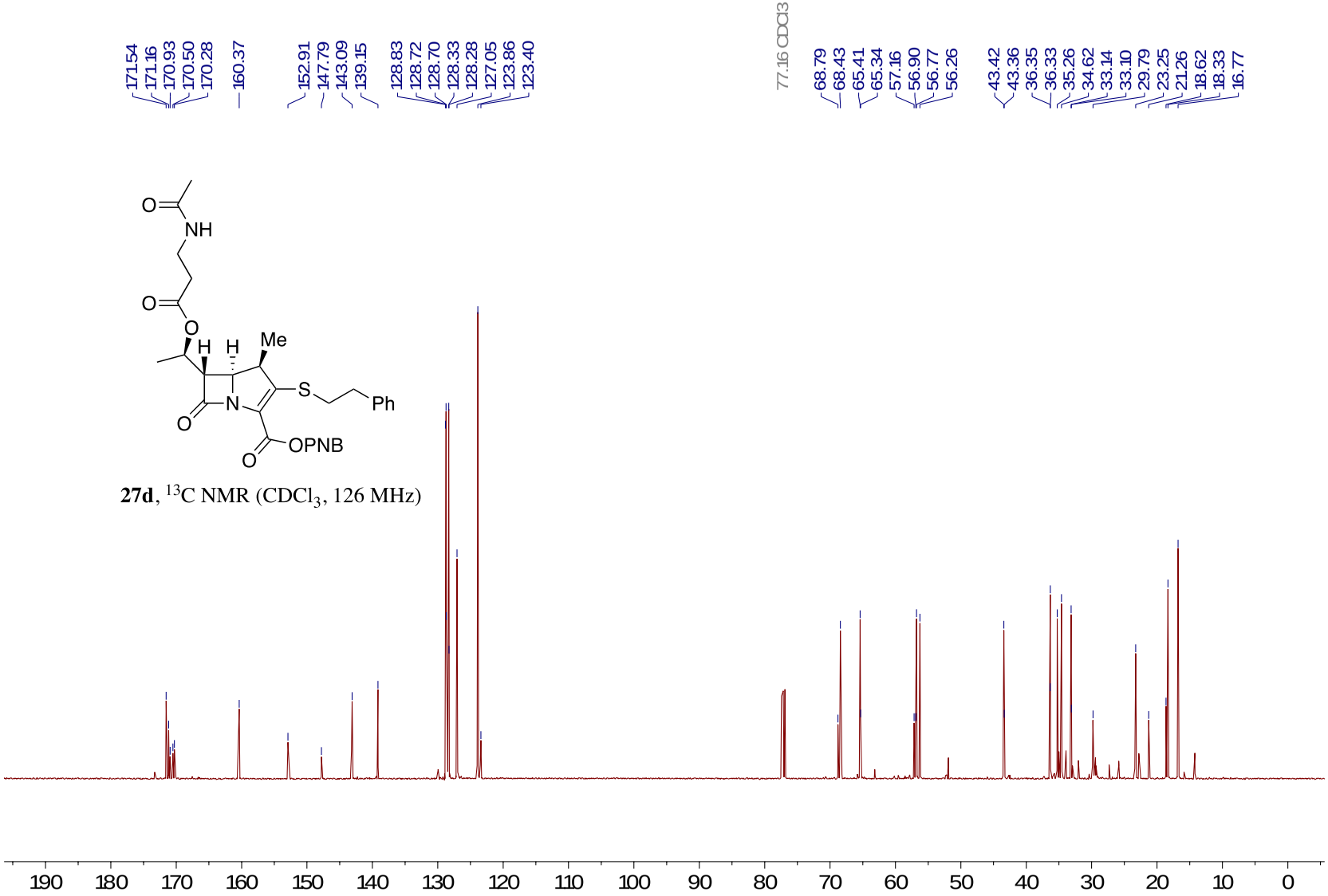


27c, ^{13}C NMR ($CDCl_3$, 126 MHz)

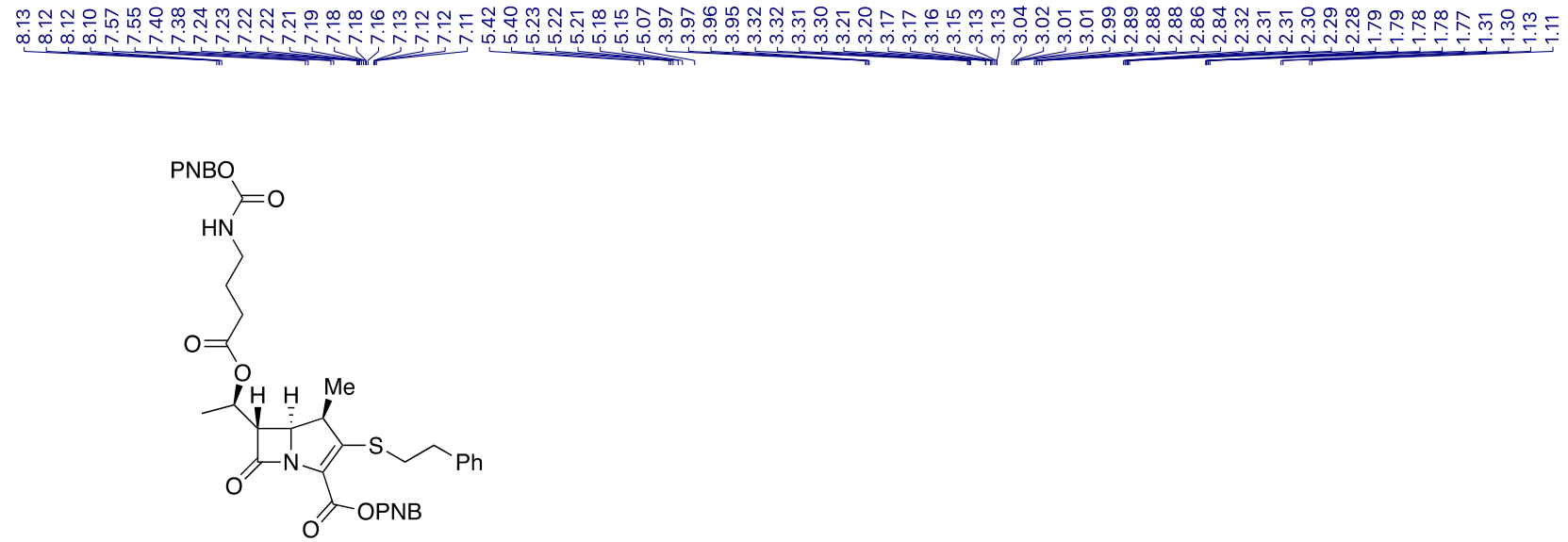


27d, ^{1}H NMR ($CDCl_3$, 500 MHz)

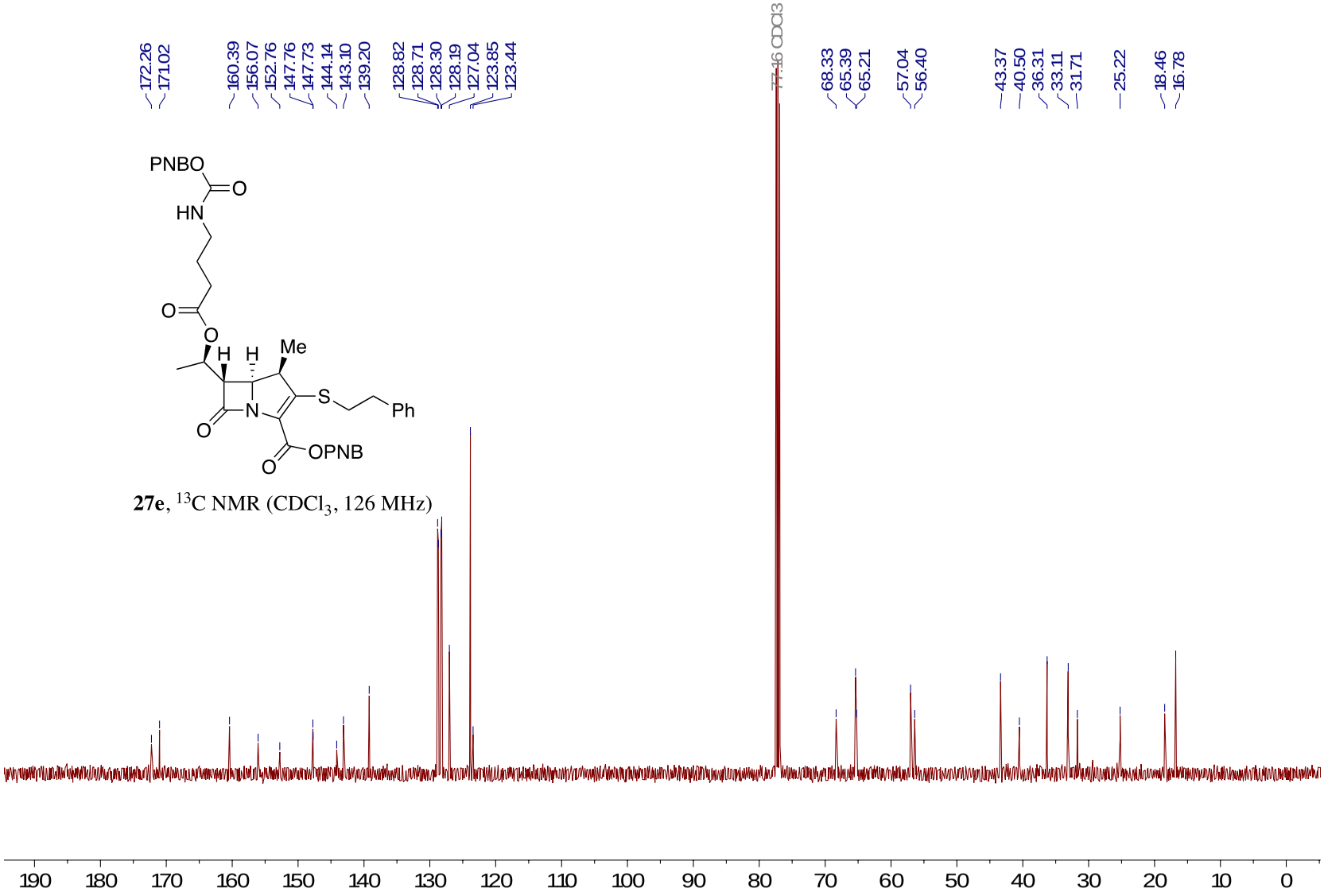




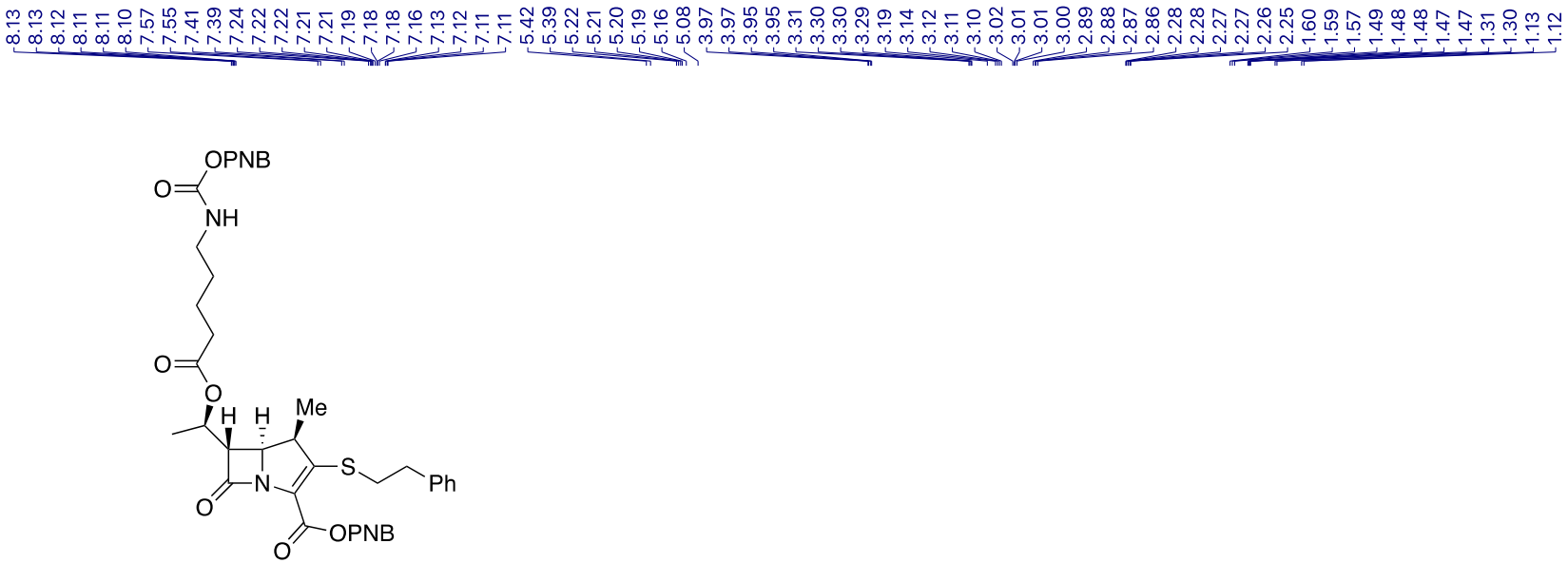
27d, ^{13}C NMR ($CDCl_3$, 126 MHz)



27e, ^{1}H NMR ($CDCl_3$, 500 MHz)

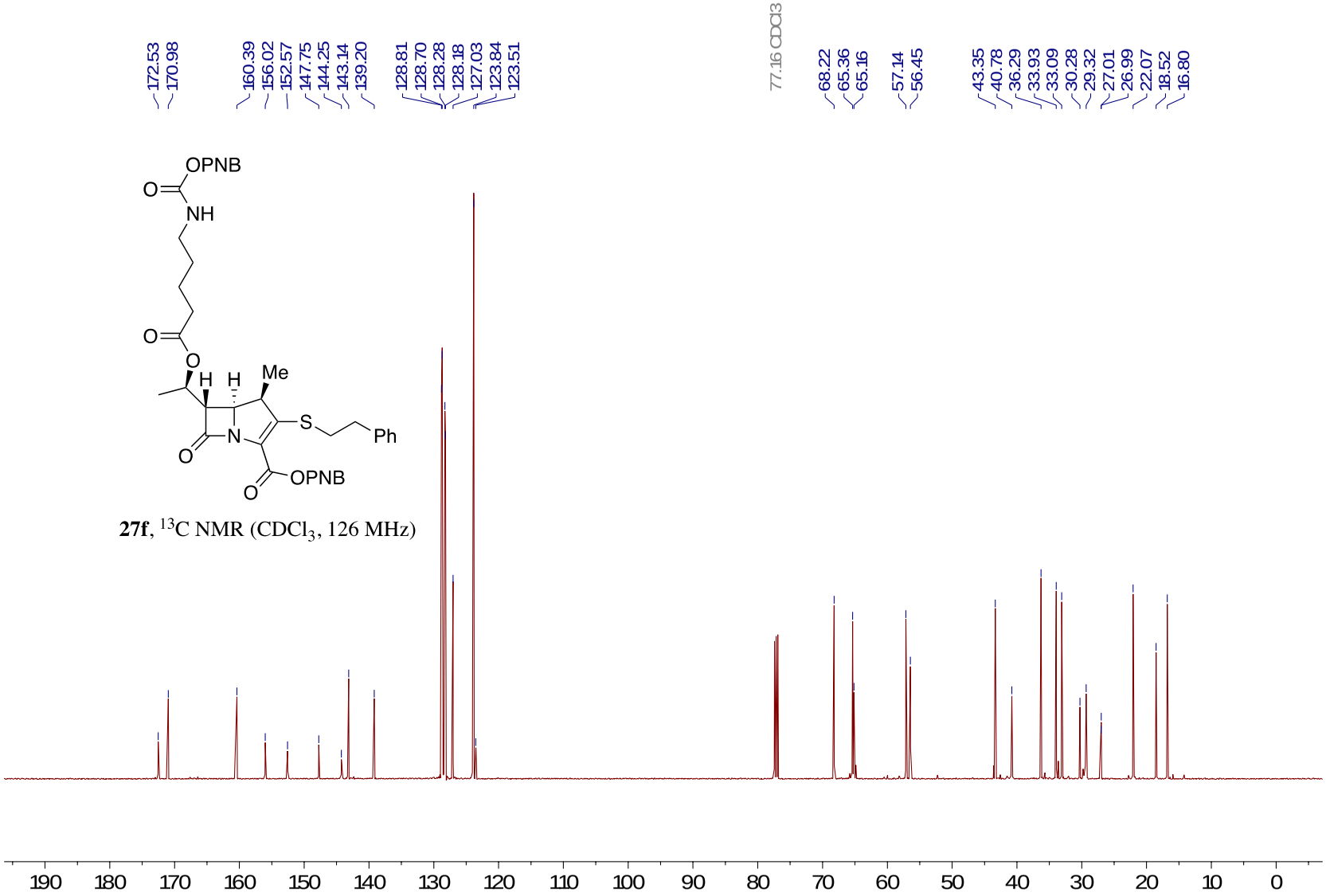


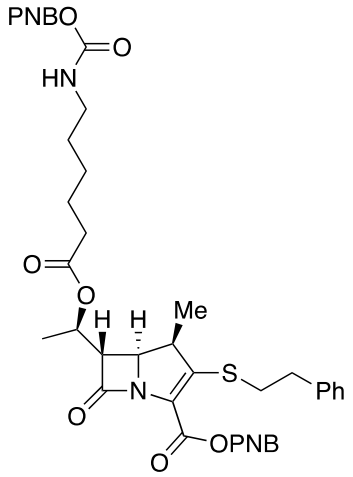
27e, ^{13}C NMR ($CDCl_3$, 126 MHz)



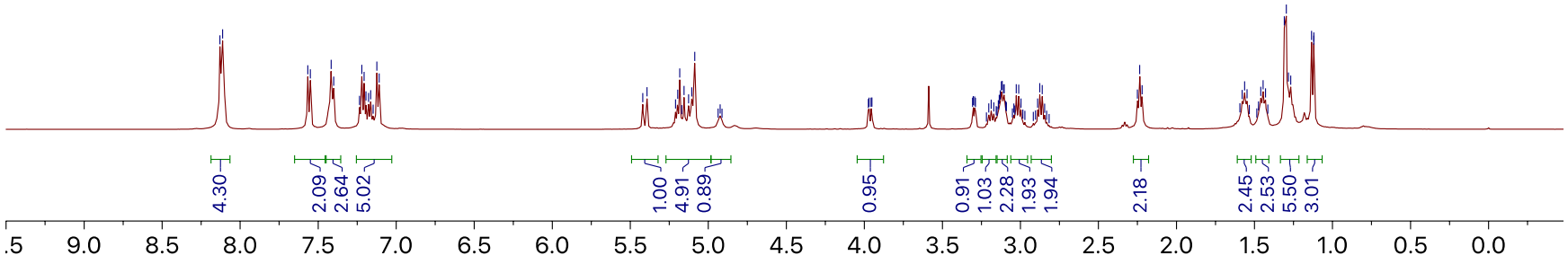
27f, ^{1}H NMR ($CDCl_3$, 500 MHz)

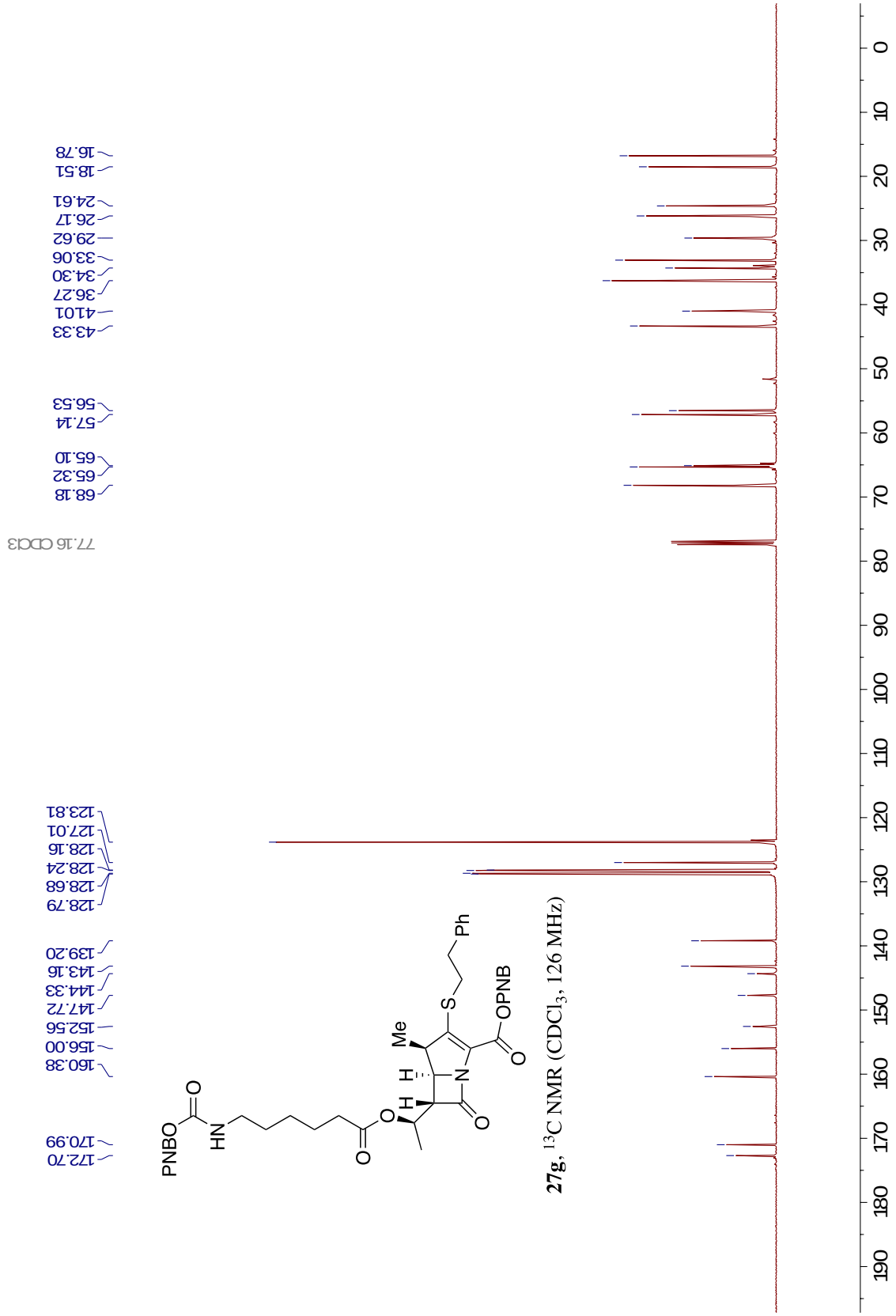
27f, ^{13}C NMR ($CDCl_3$, 126 MHz)



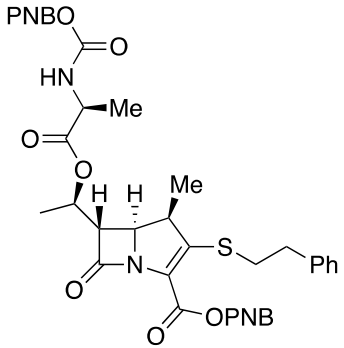


27g, ^{1}H NMR ($CDCl_3$, 500 MHz)

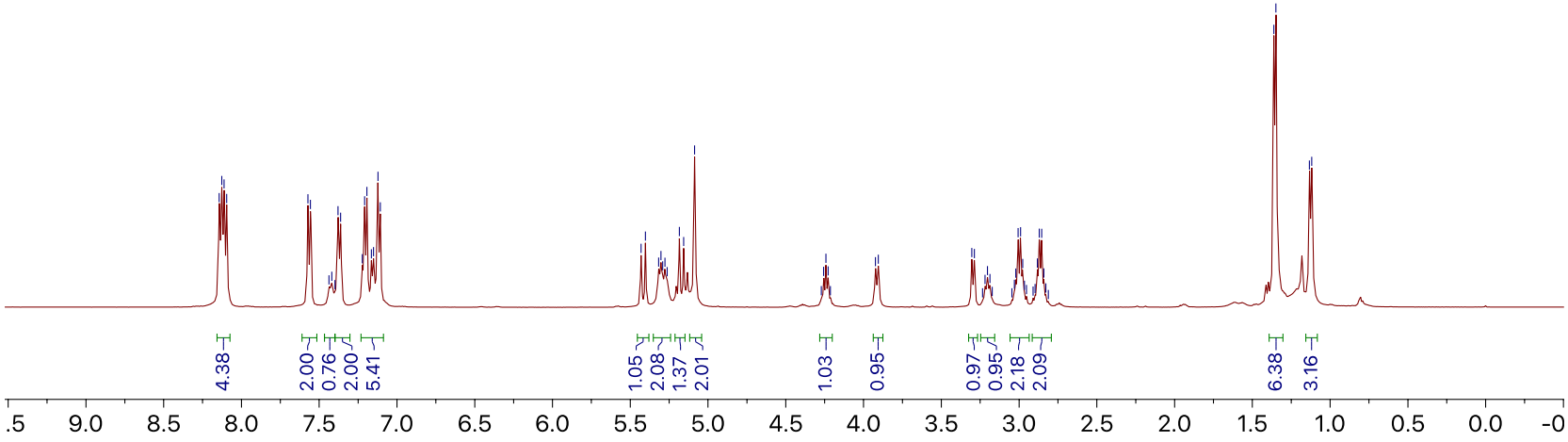


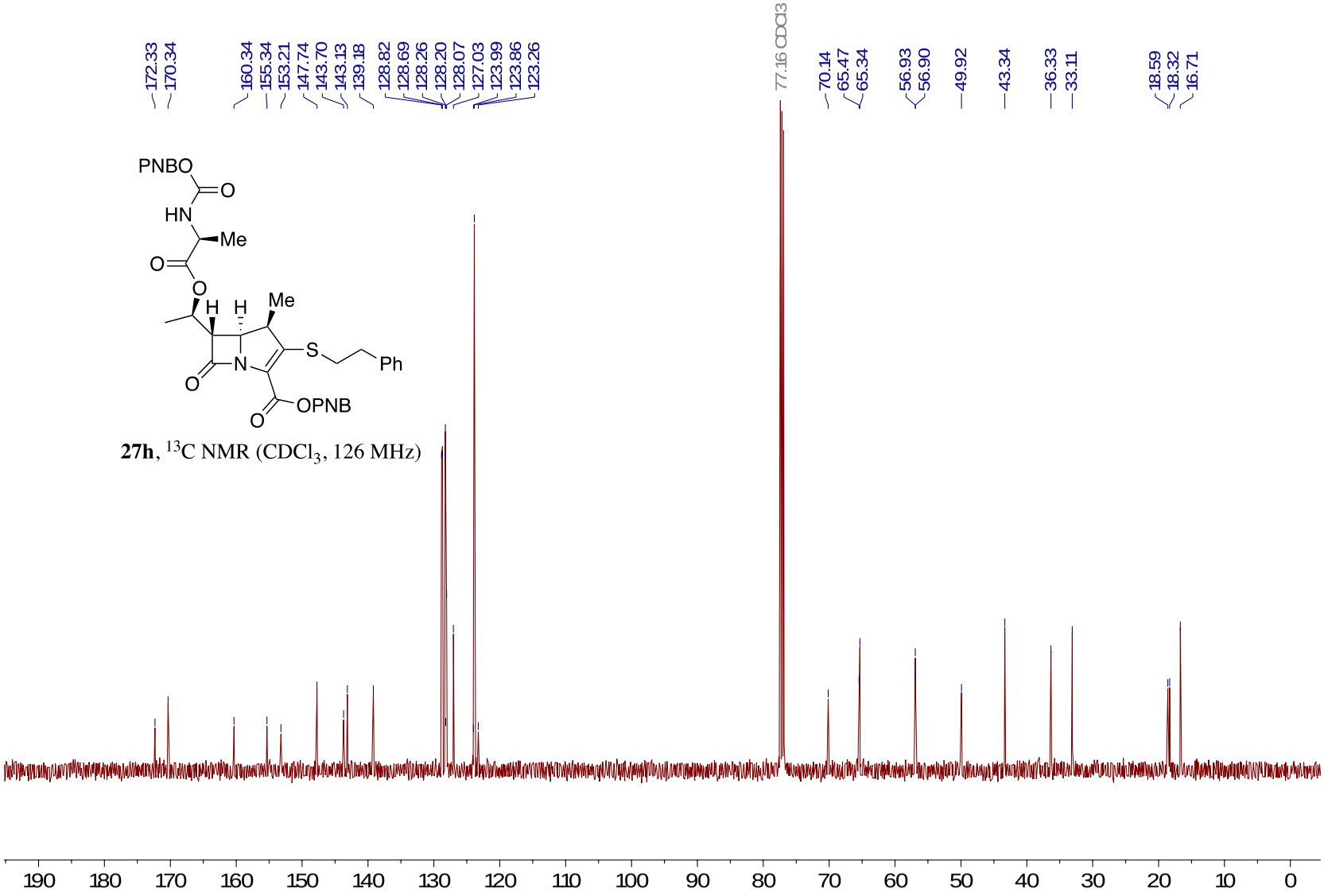


27g, ^{13}C NMR ($CDCl_3$, 126 MHz)

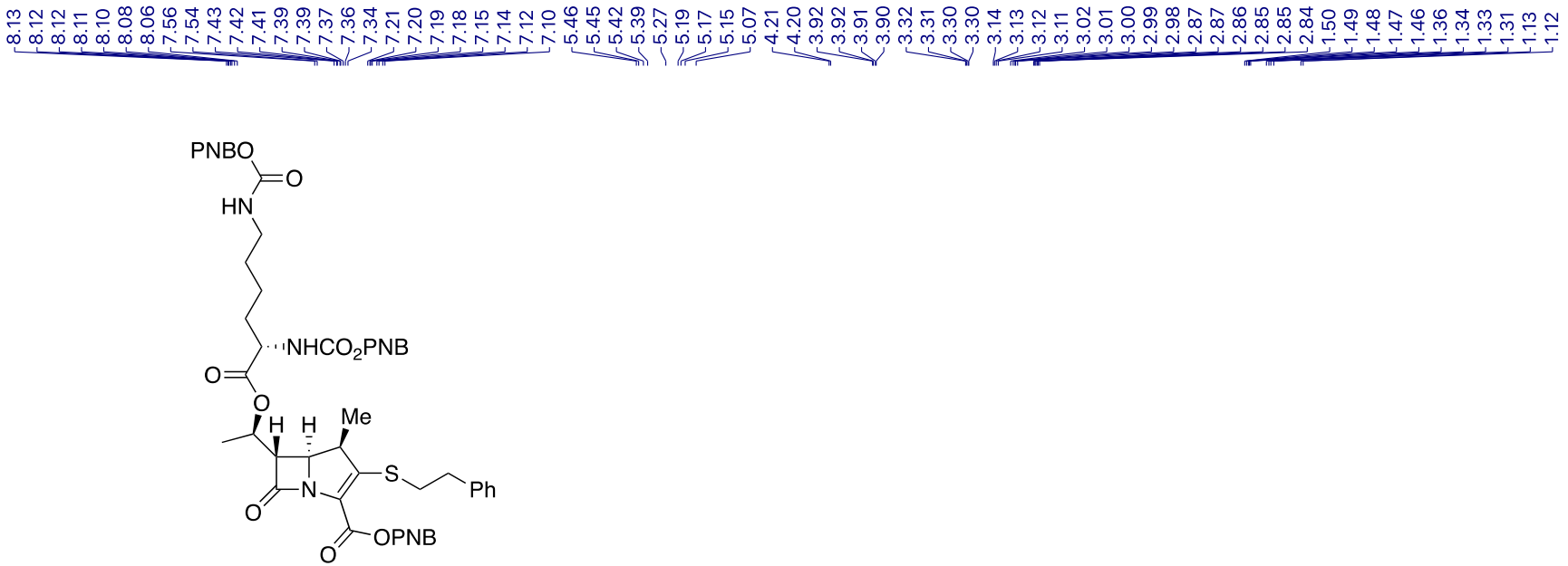


27h, ^{1}H NMR ($CDCl_3$, 500 MHz)

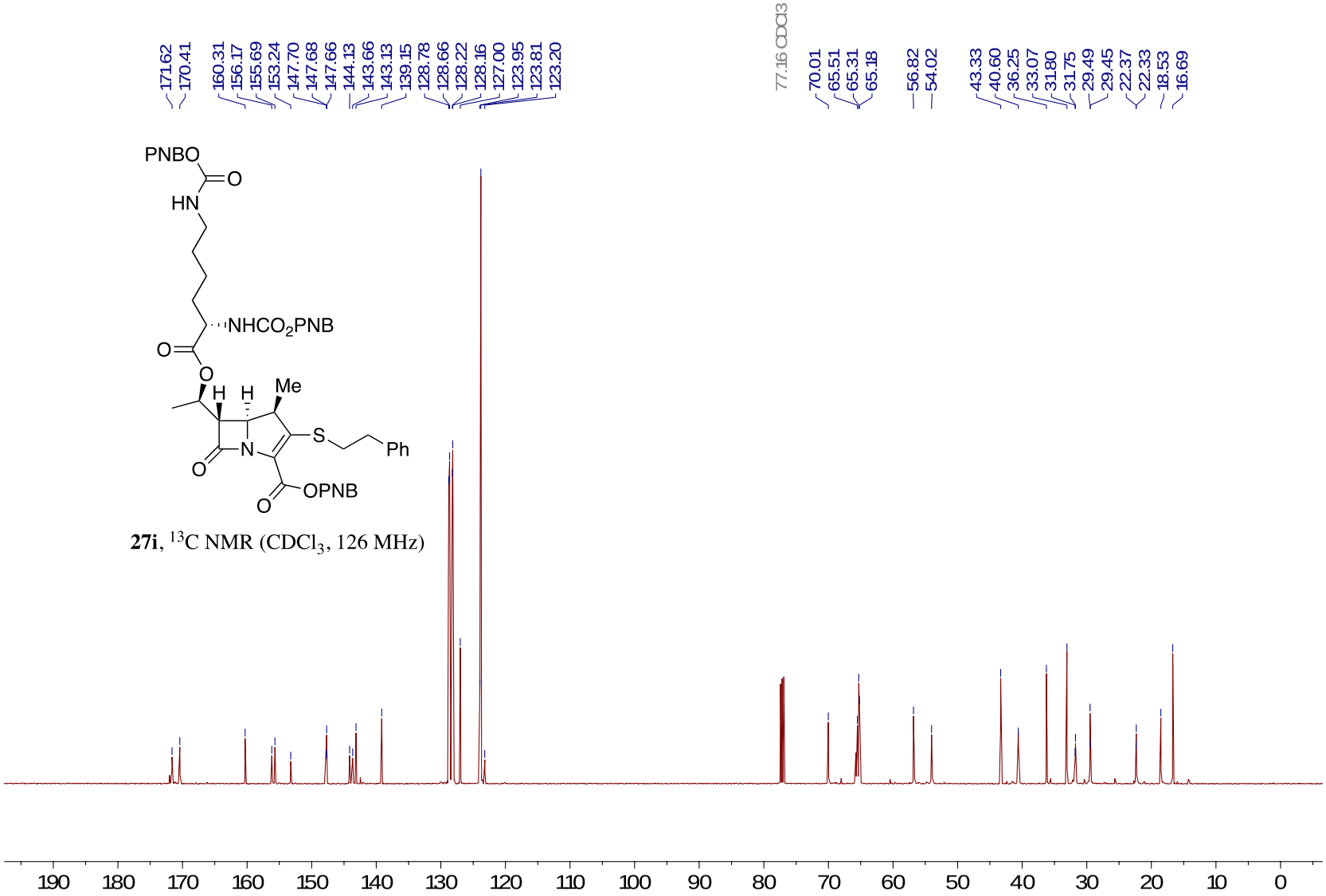




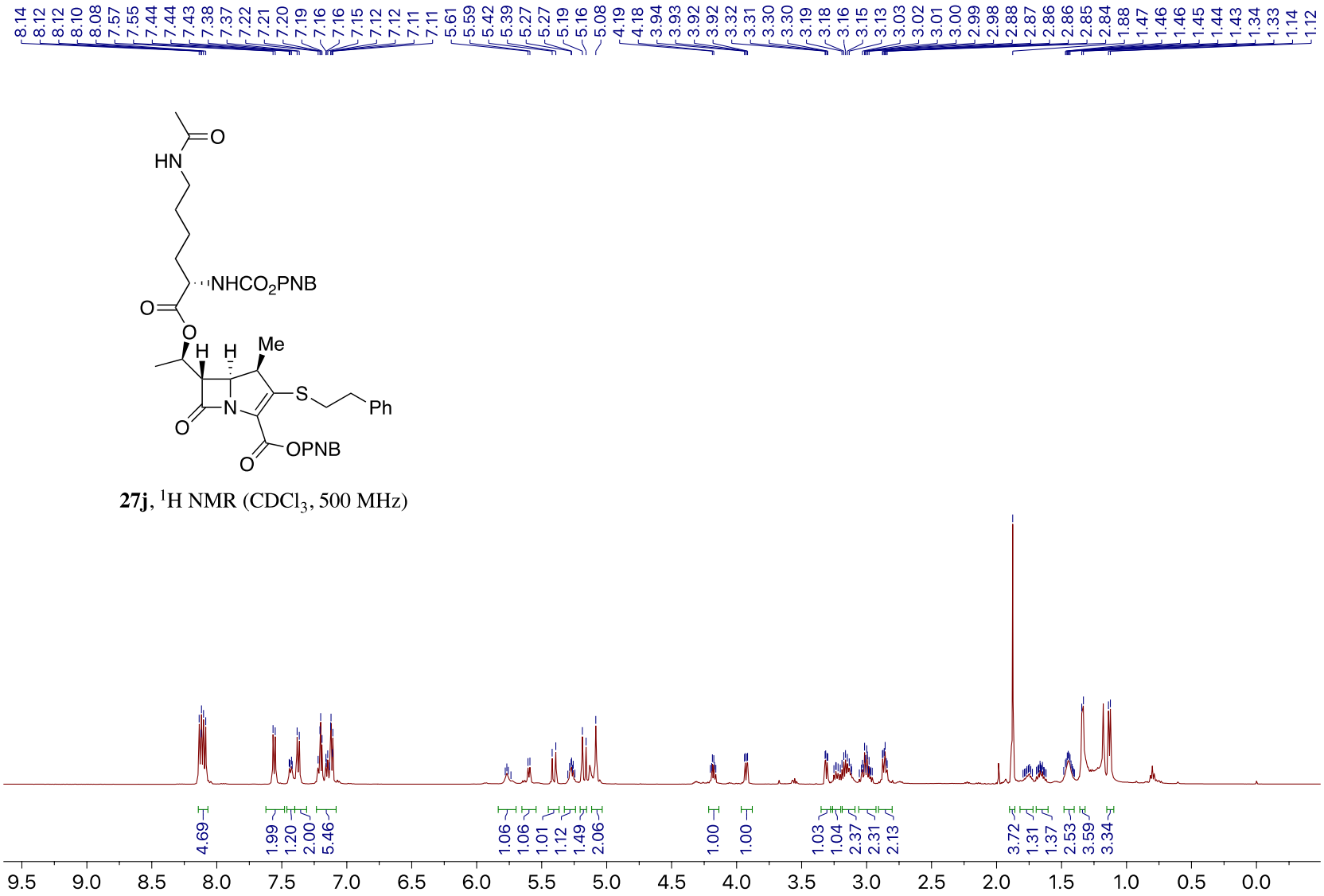
27h, ^{13}C NMR ($CDCl_3$, 126 MHz)



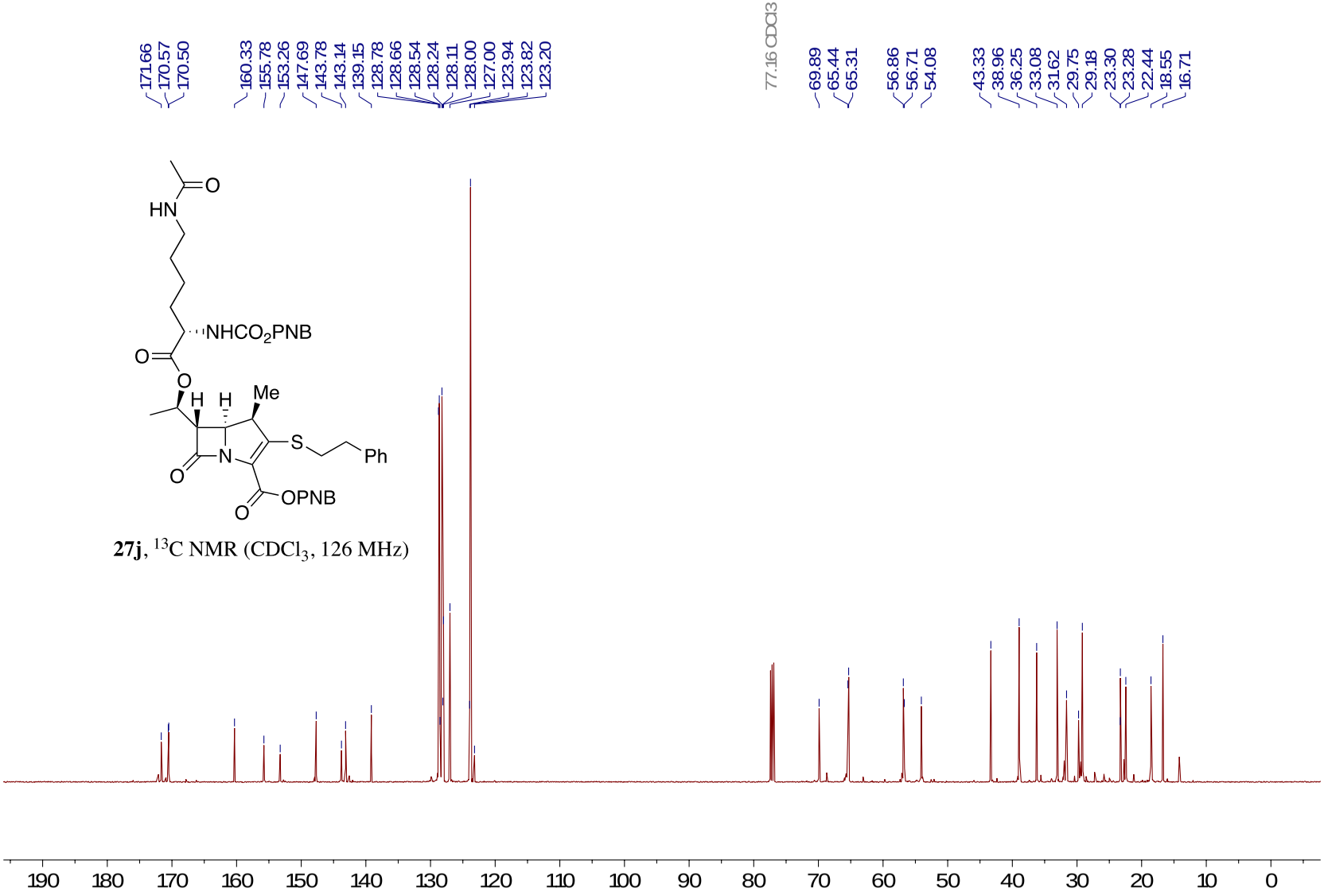
27i, ^{1}H NMR ($CDCl_3$, 500 MHz)



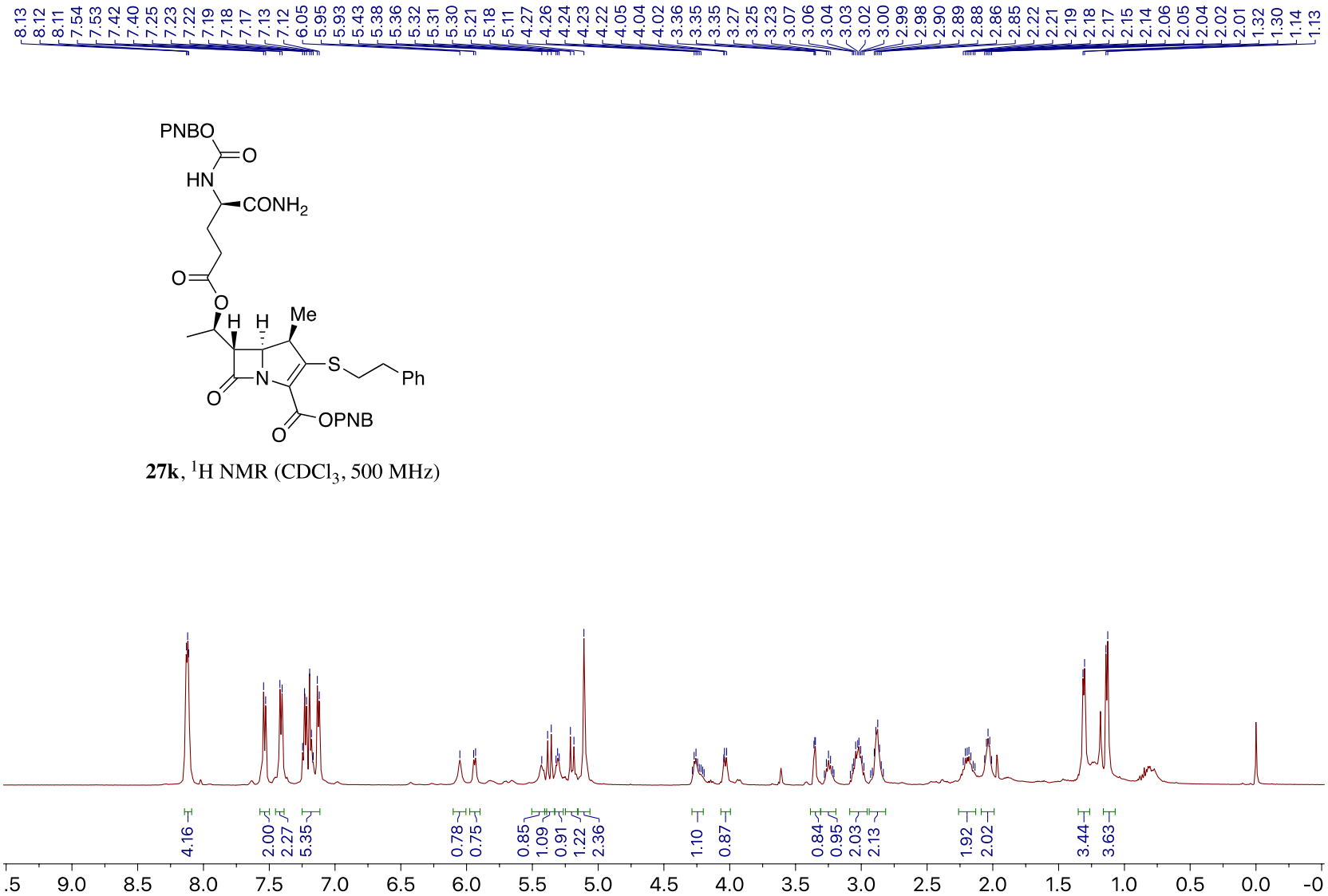
27i, ^{13}C NMR ($CDCl_3$, 126 MHz)



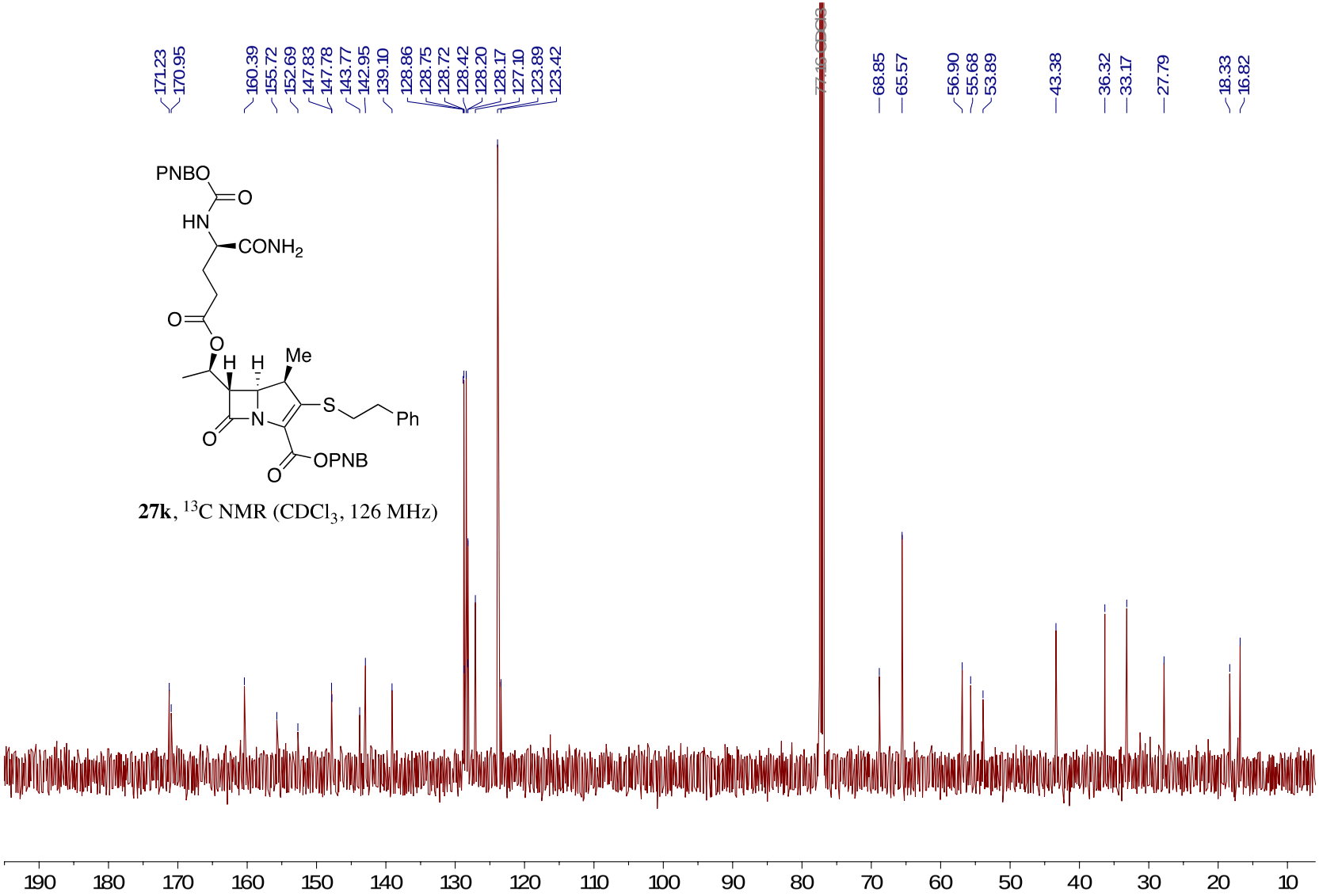
27j, ^{1}H NMR ($CDCl_3$, 500 MHz)



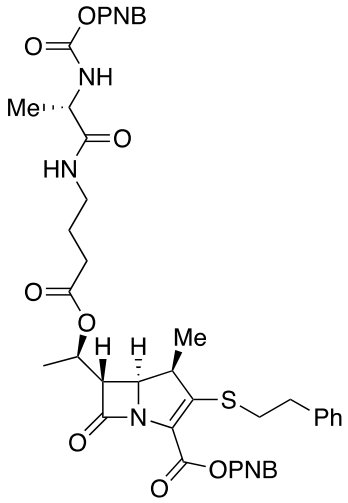
27j, ^{13}C NMR ($CDCl_3$, 126 MHz)



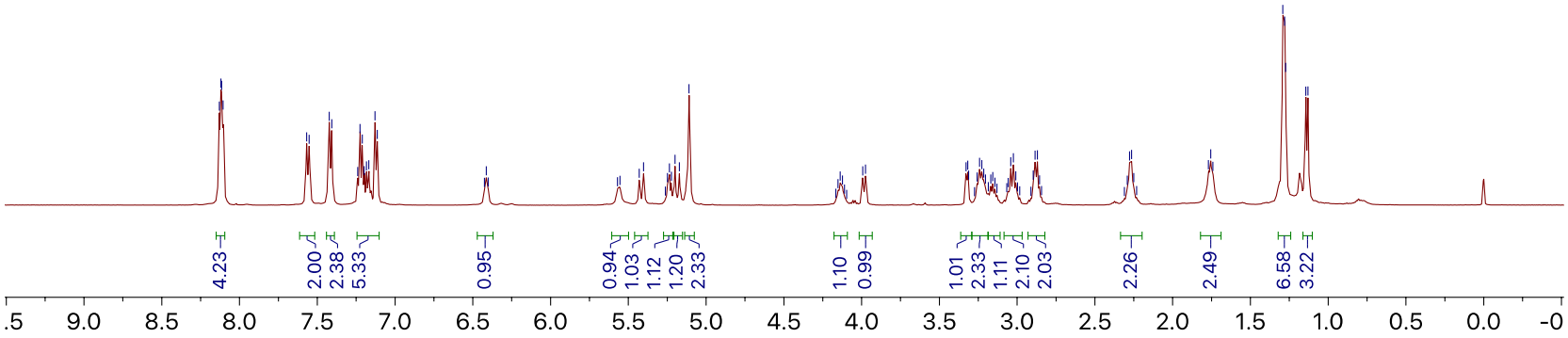
27k, ^{1}H NMR ($CDCl_3$, 500 MHz)

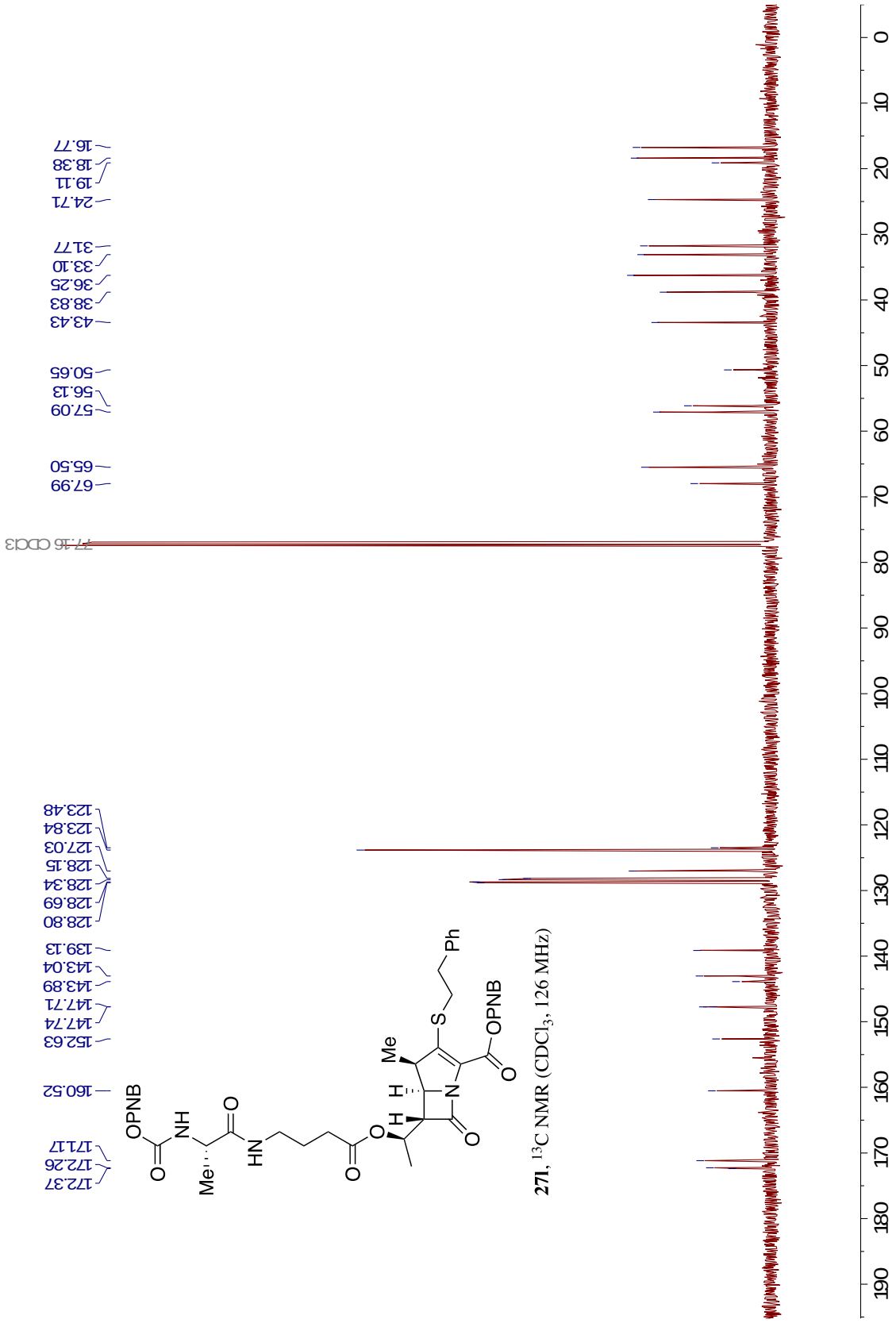


27k, ^{13}C NMR ($CDCl_3$, 126 MHz)

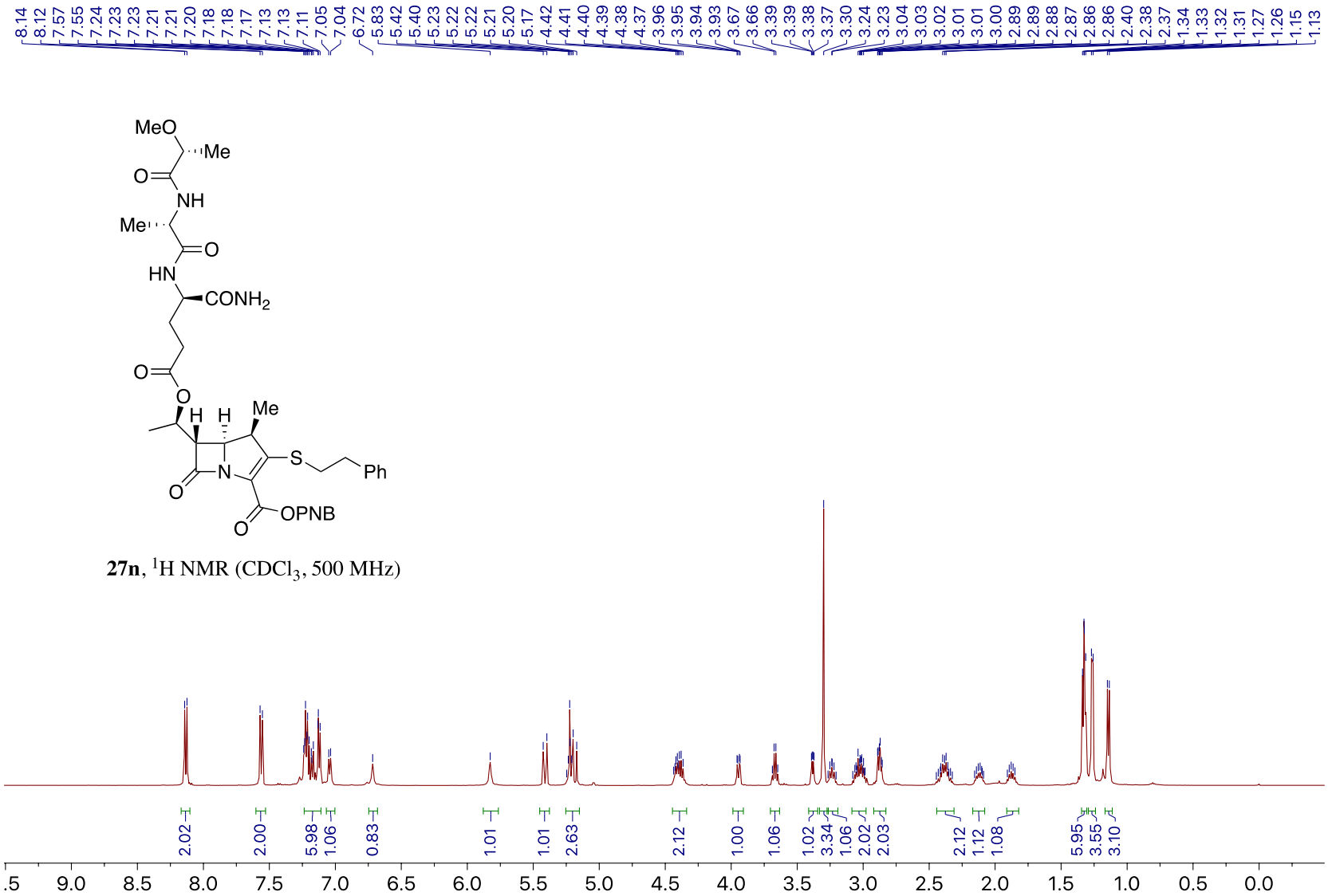


27l, ^{1}H NMR ($CDCl_3$, 500 MHz)

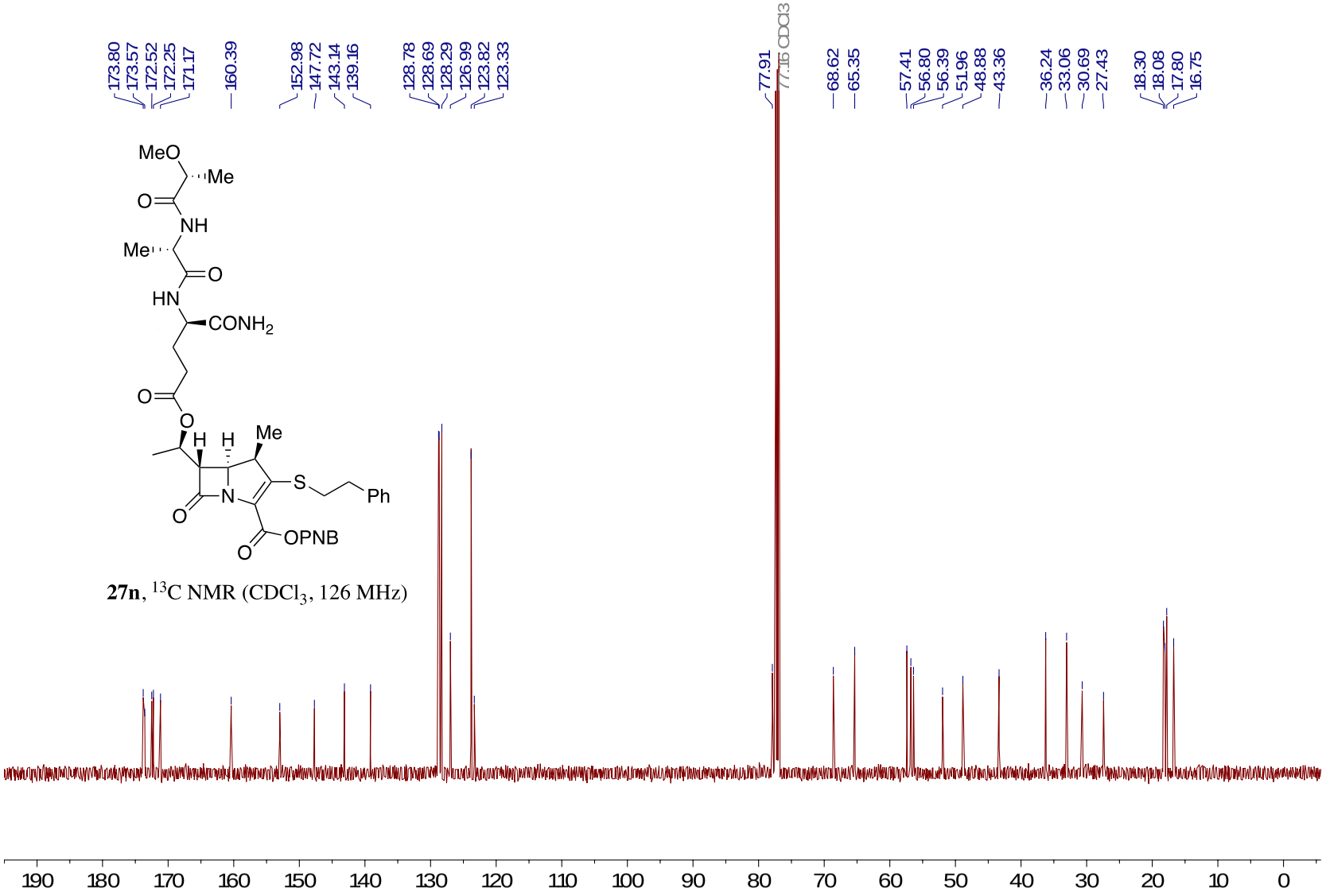




271, ^{13}C NMR ($CDCl_3$, 126 MHz)

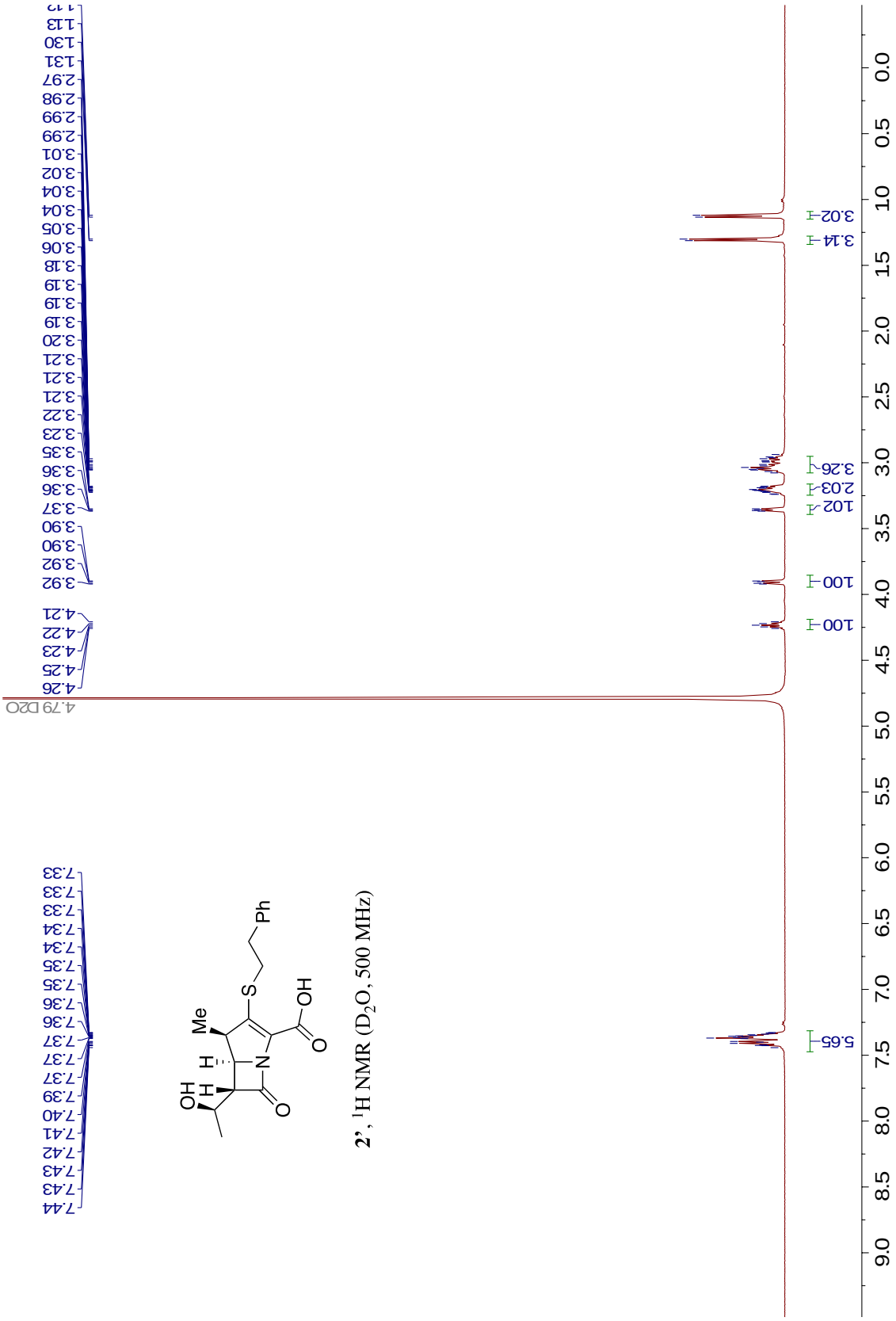


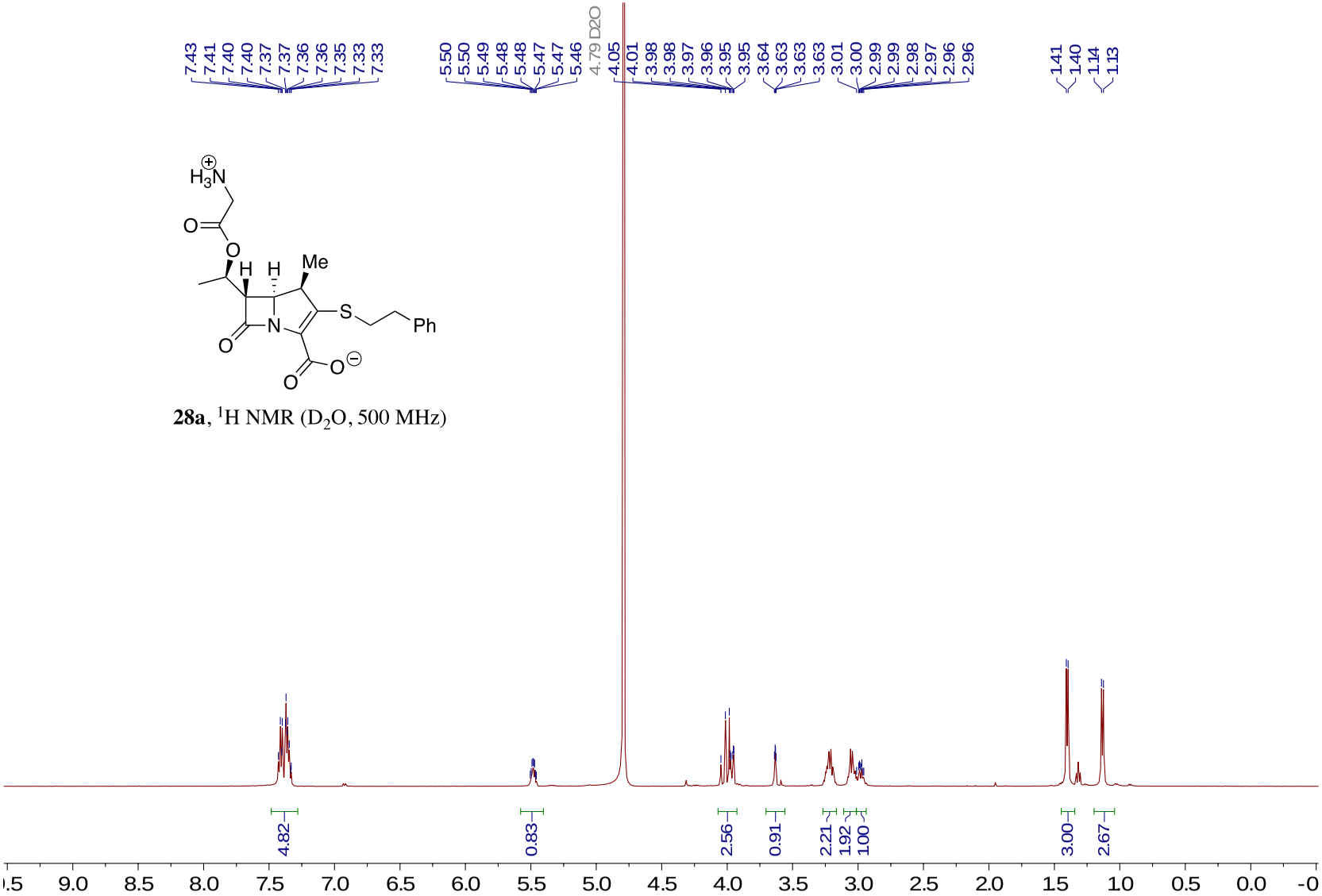
27n, ^{1}H NMR ($CDCl_3$, 500 MHz)



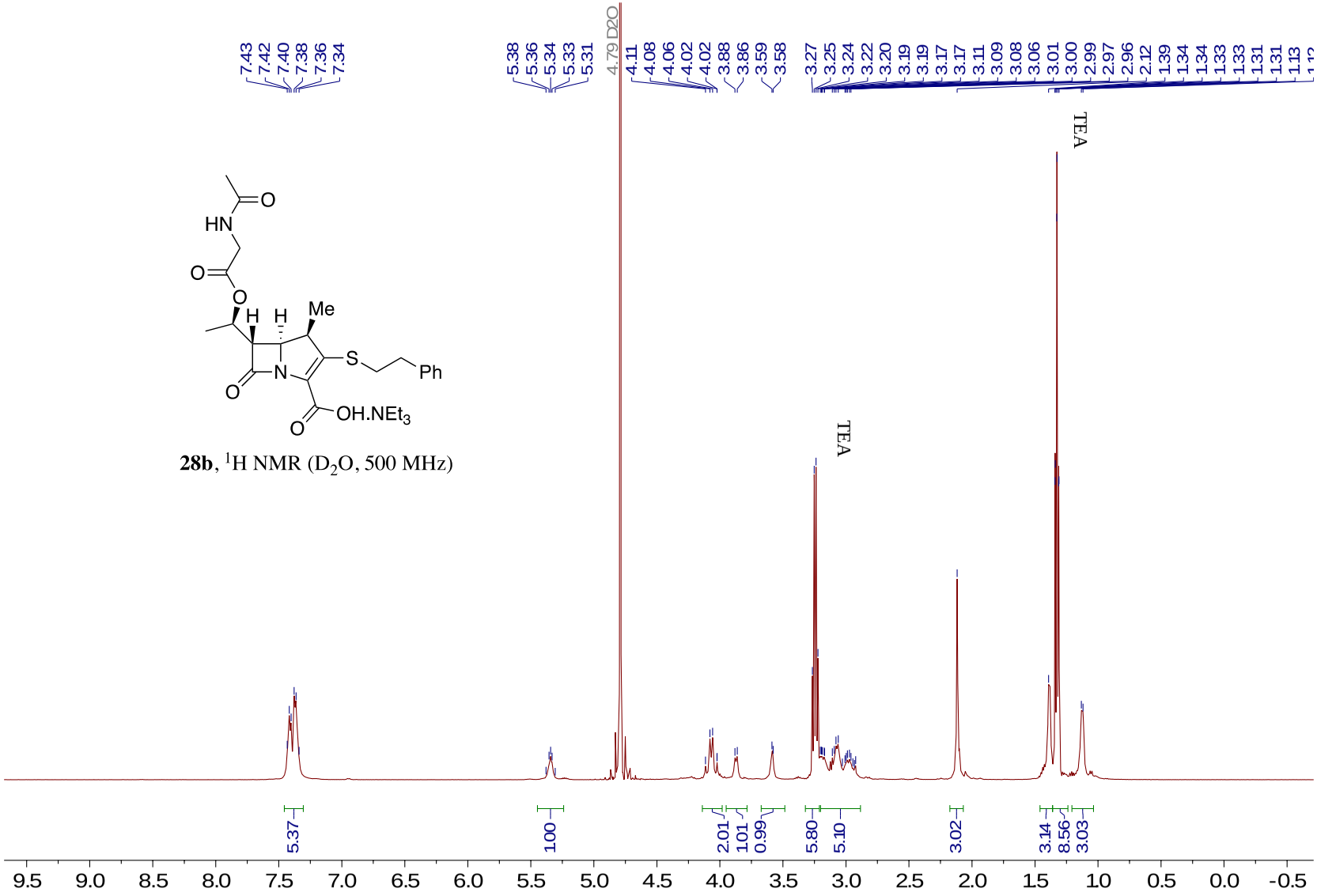
27n, ^{13}C NMR ($CDCl_3$, 126 MHz)

7-3. ^{1}H NMR spectra of carbapenem 2' and peptido-carbapenems 28a-n.

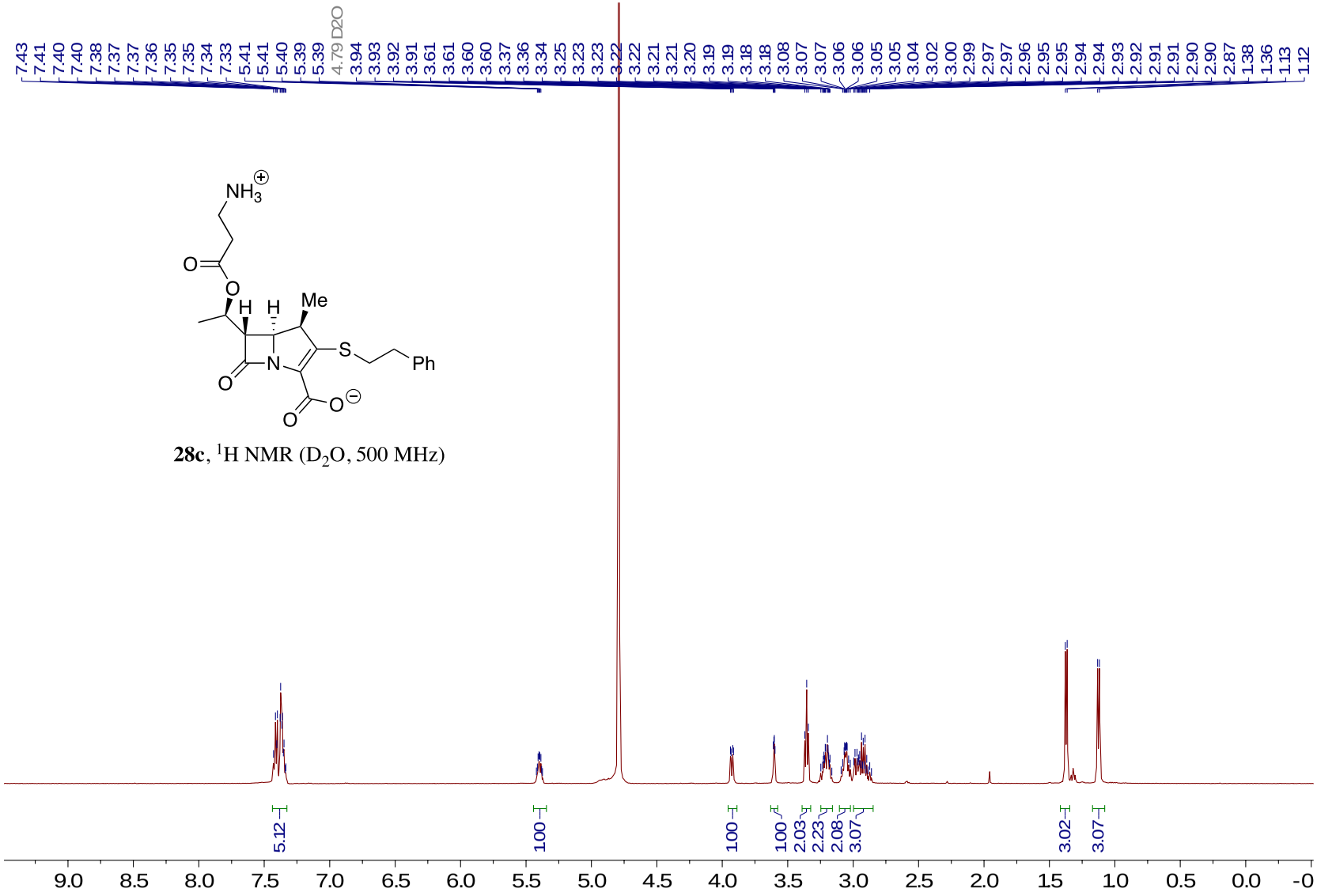




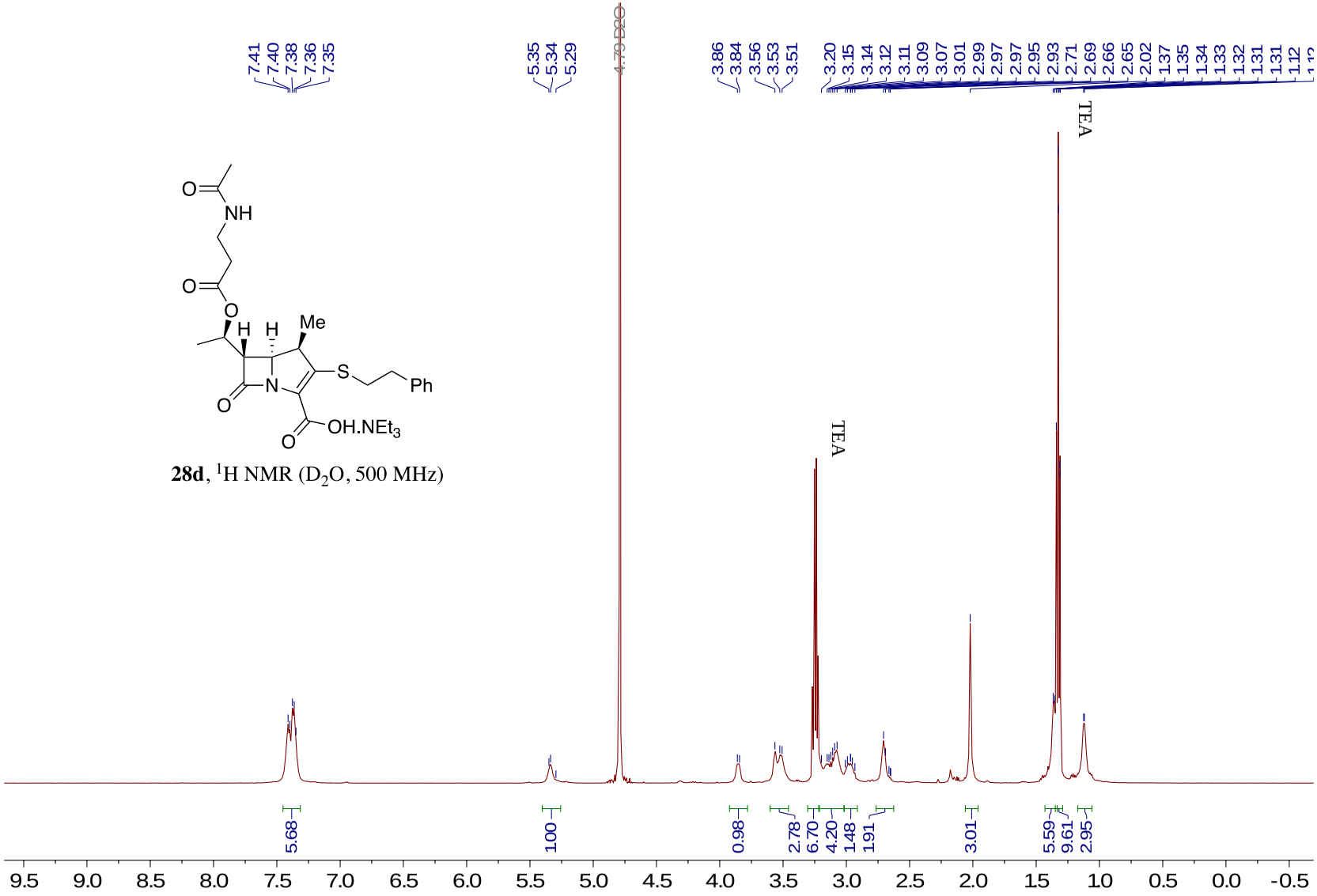
28a, ^{1}H NMR (D_2O, 500 MHz)



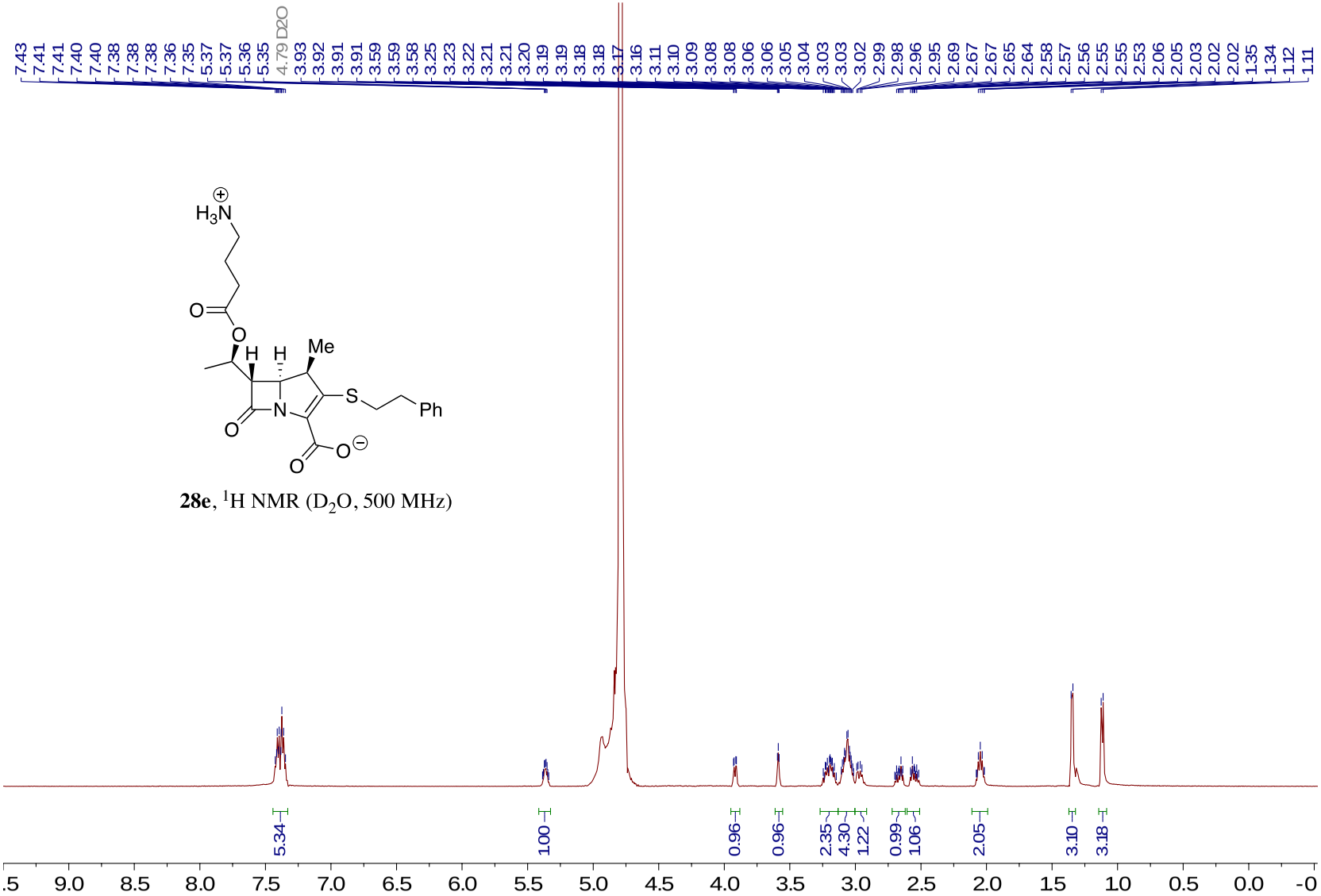
28b, ^{1}H NMR (D_2O, 500 MHz)



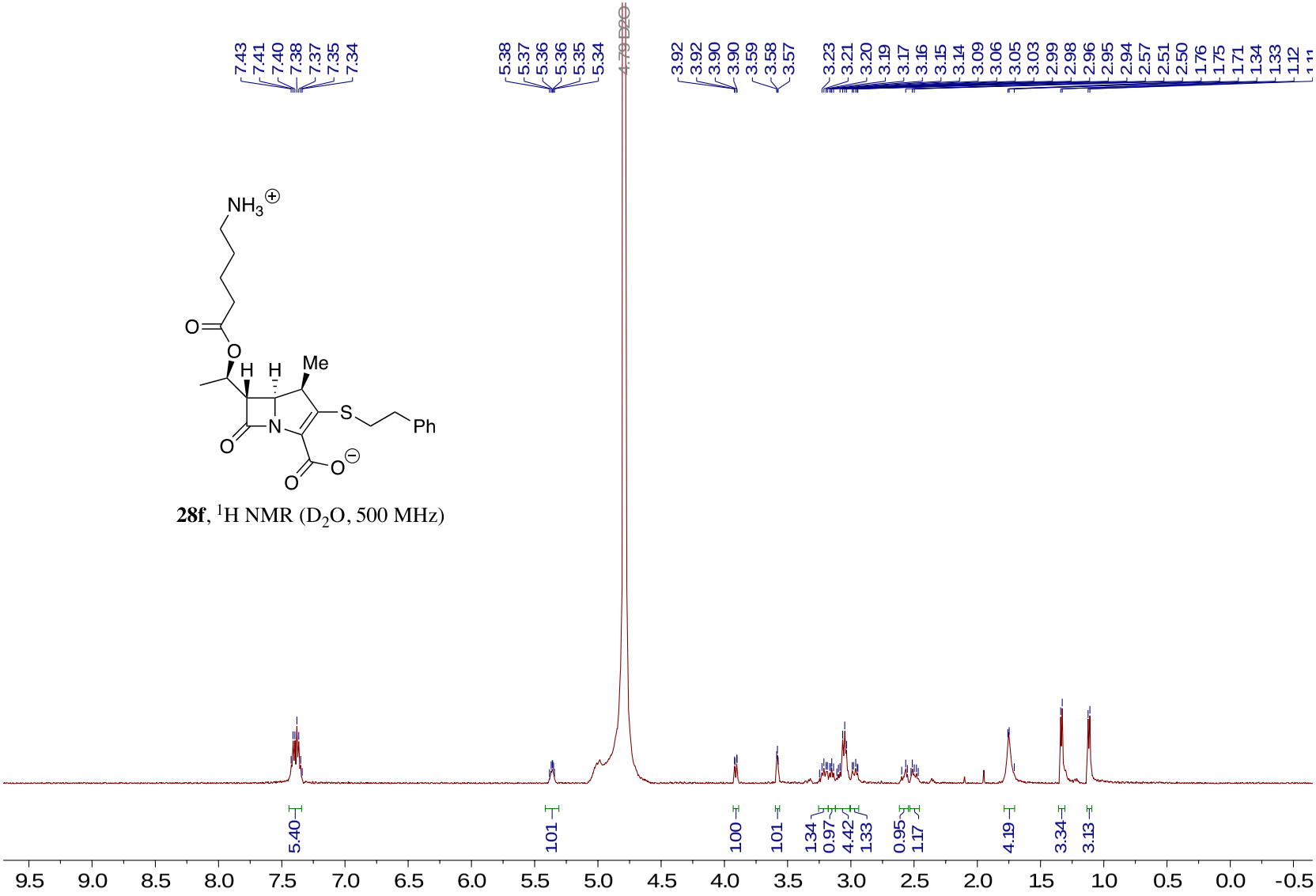
28c, ^{1}H NMR (D_2O, 500 MHz)



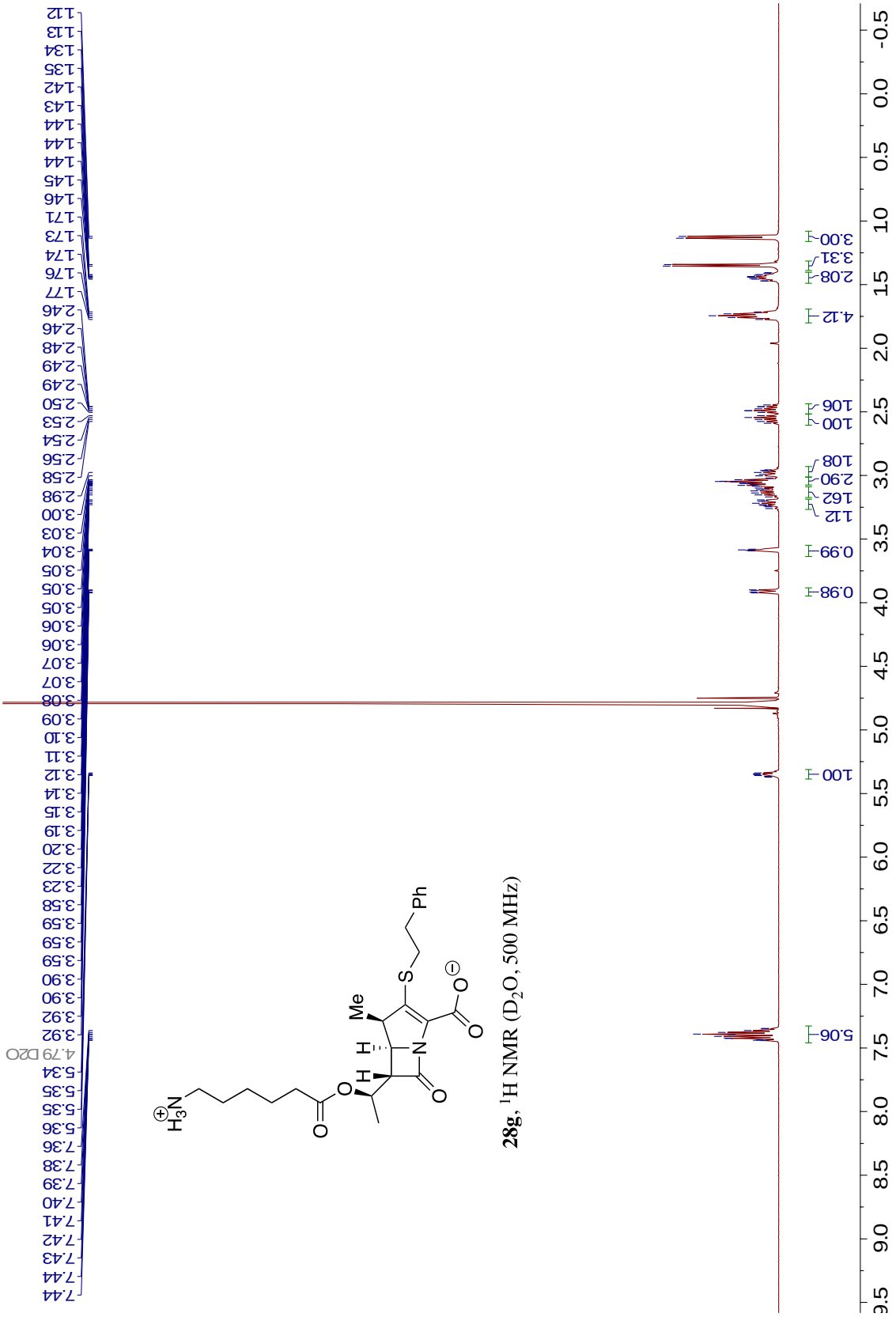
28d, ^{1}H NMR (D_2O, 500 MHz)



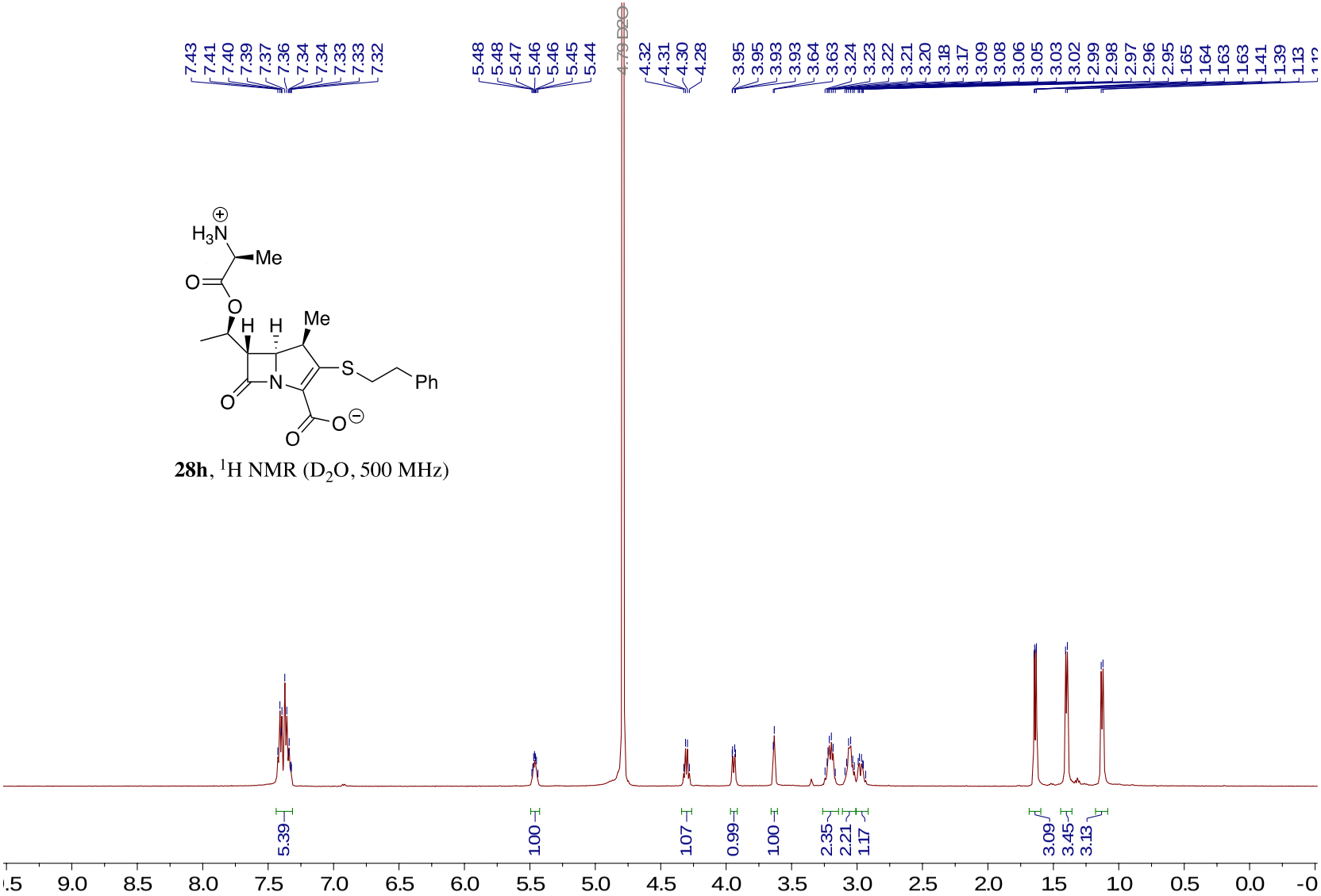
28e, ^{1}H NMR (D_2O, 500 MHz)



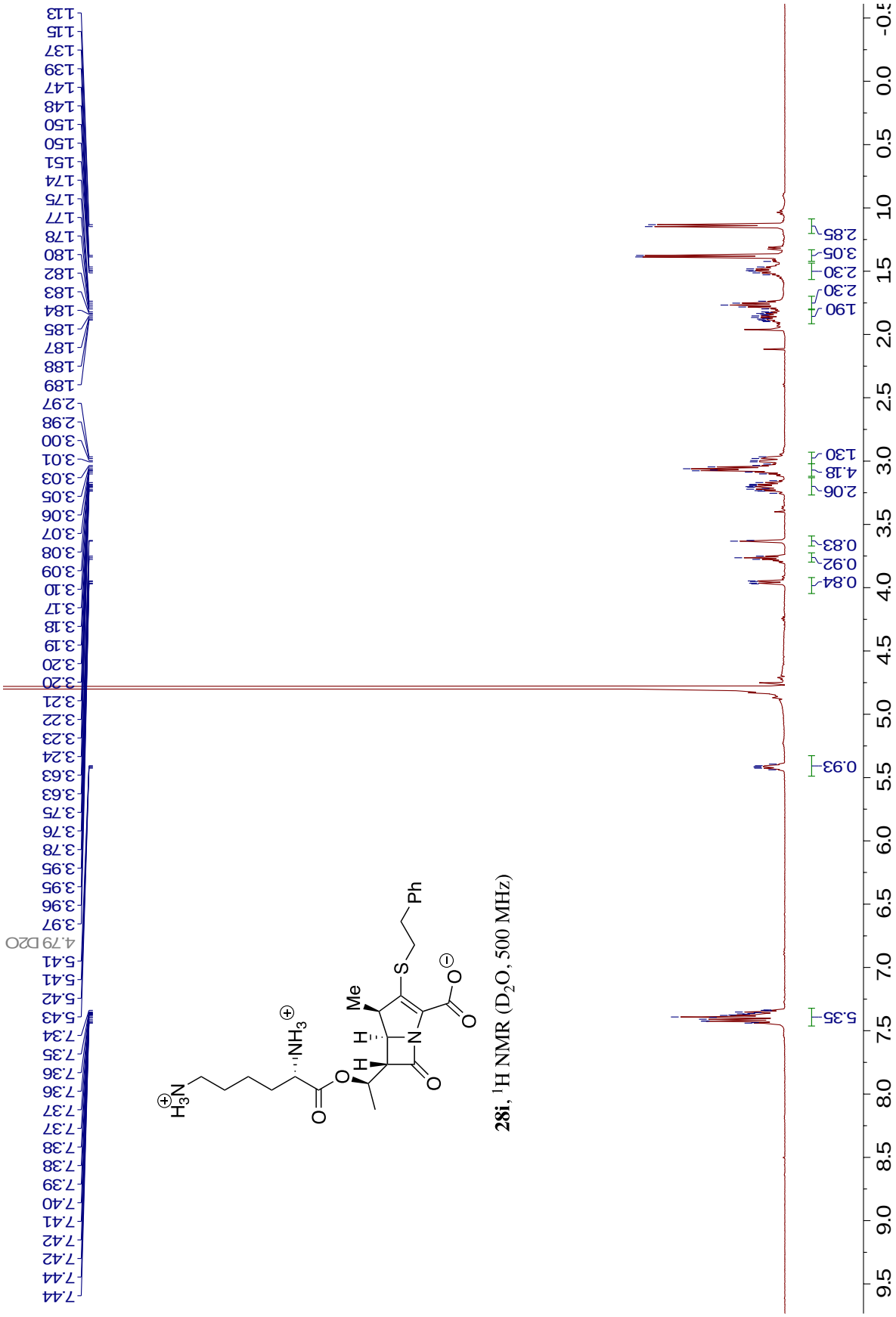
28f, ^{1}H NMR (D_2O, 500 MHz)



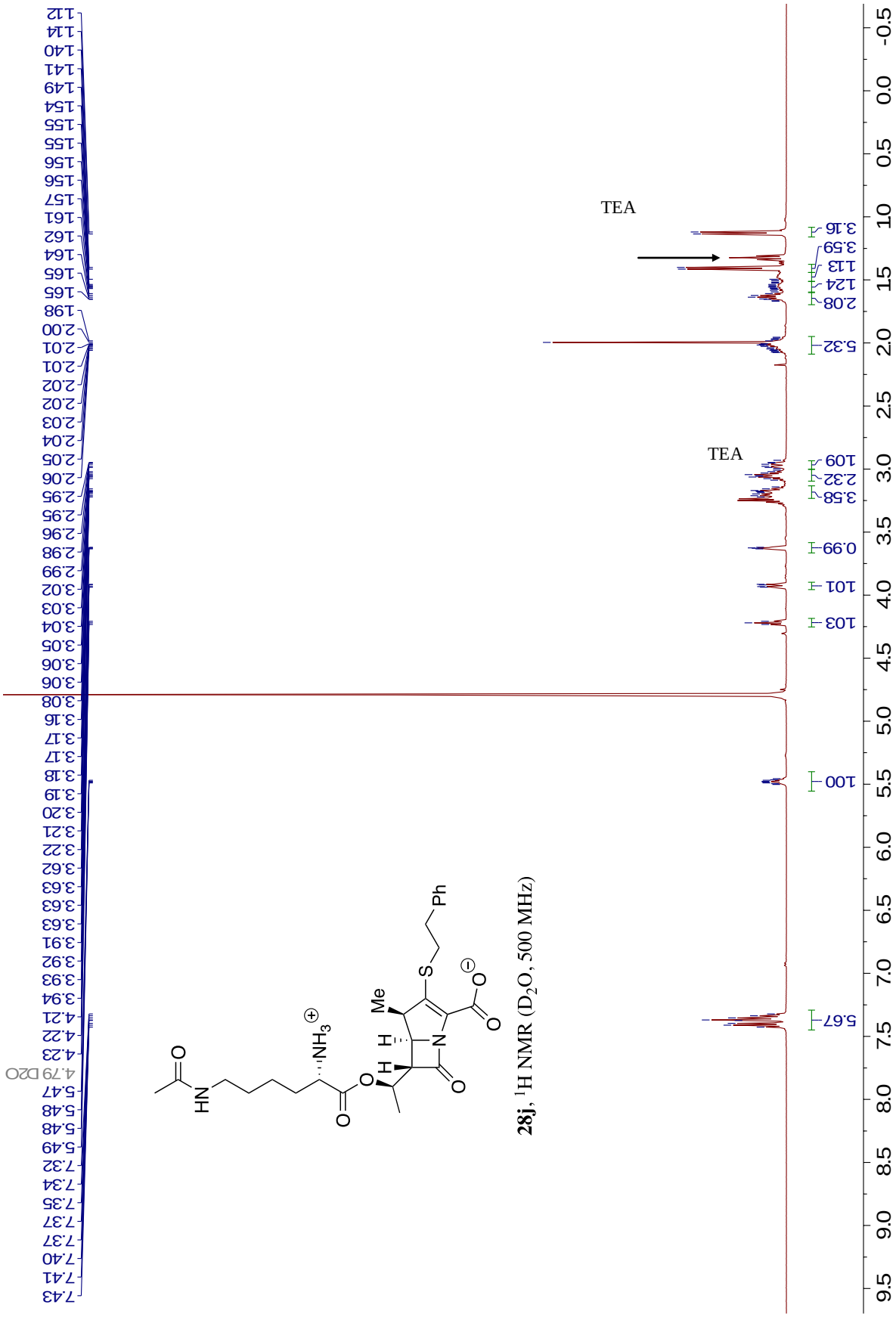
28g, ^{1}H NMR (D_2O, 500 MHz)



28h, ^{1}H NMR (D_2O, 500 MHz)

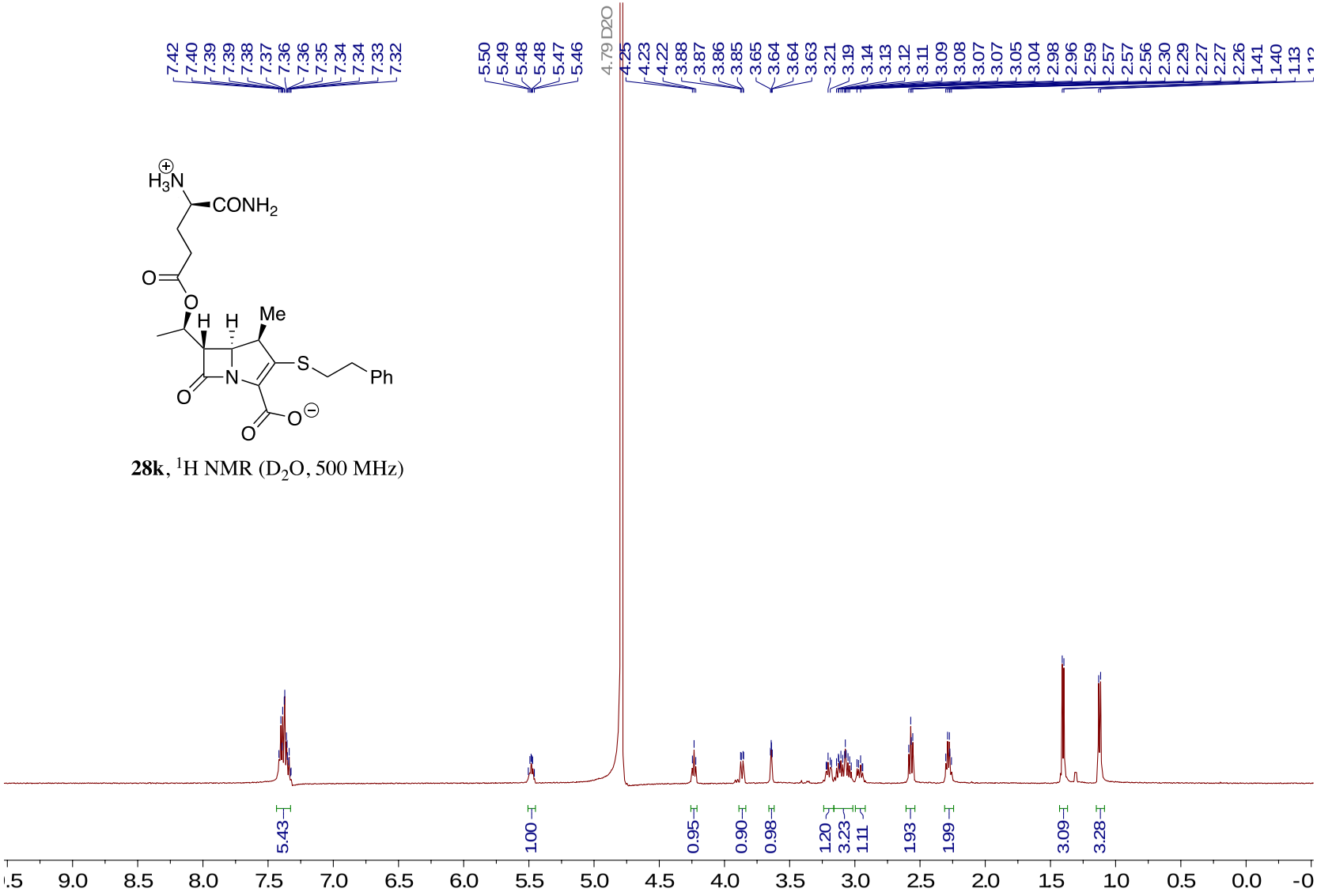


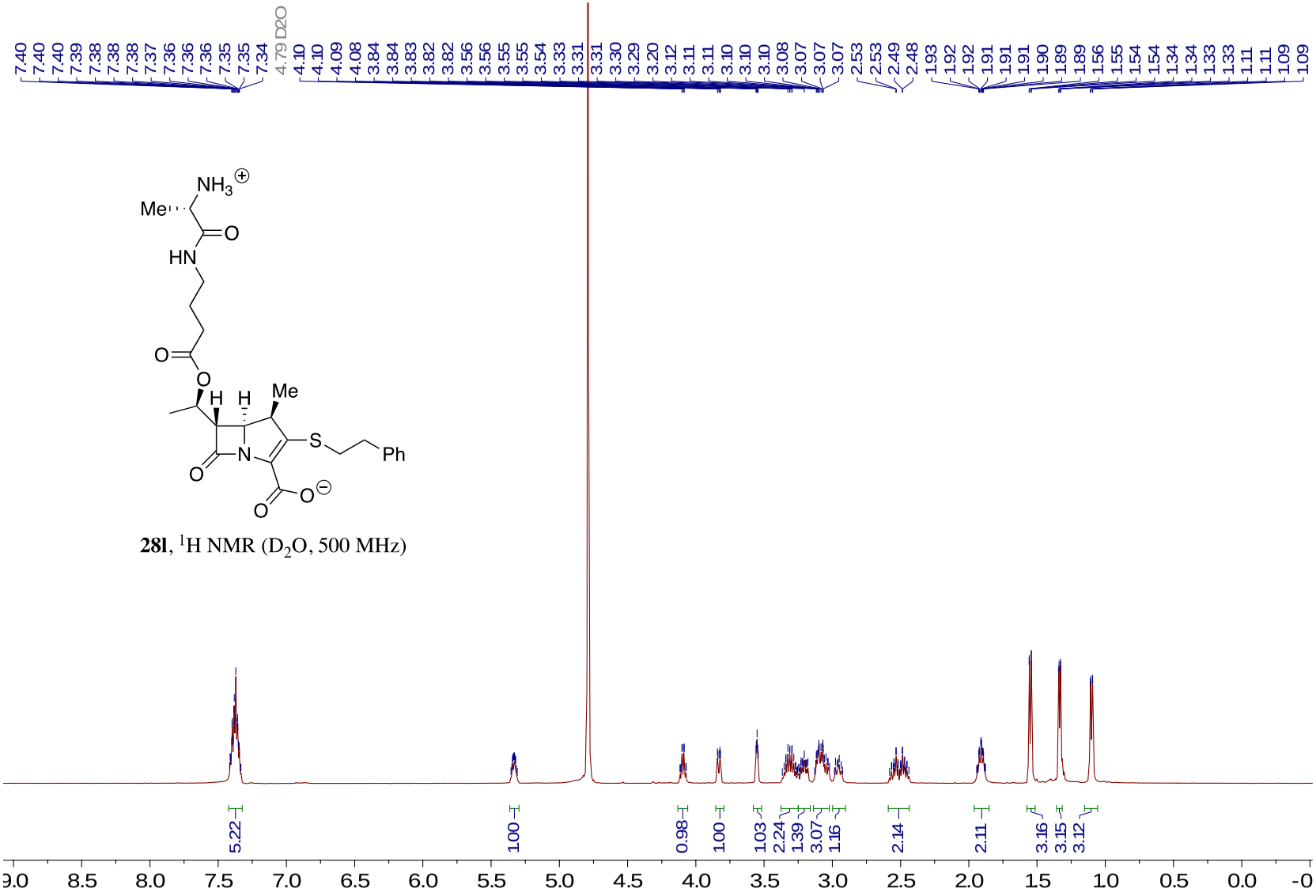
28i, ^{1}H NMR (D_2O, 500 MHz)



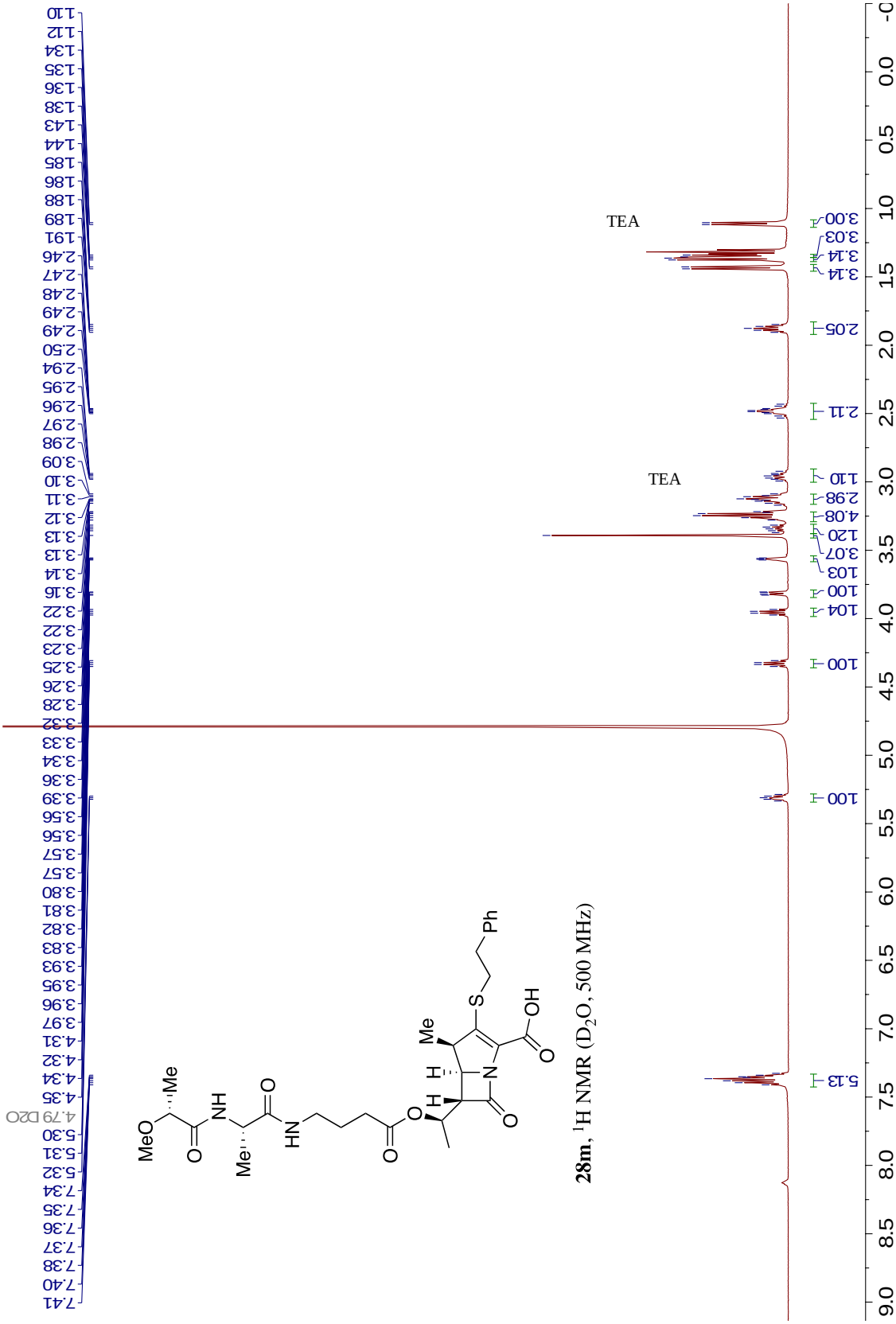
28j, ^{1}H NMR (D_2O, 500 MHz)

28k, ^{1}H NMR (D_2O, 500 MHz)

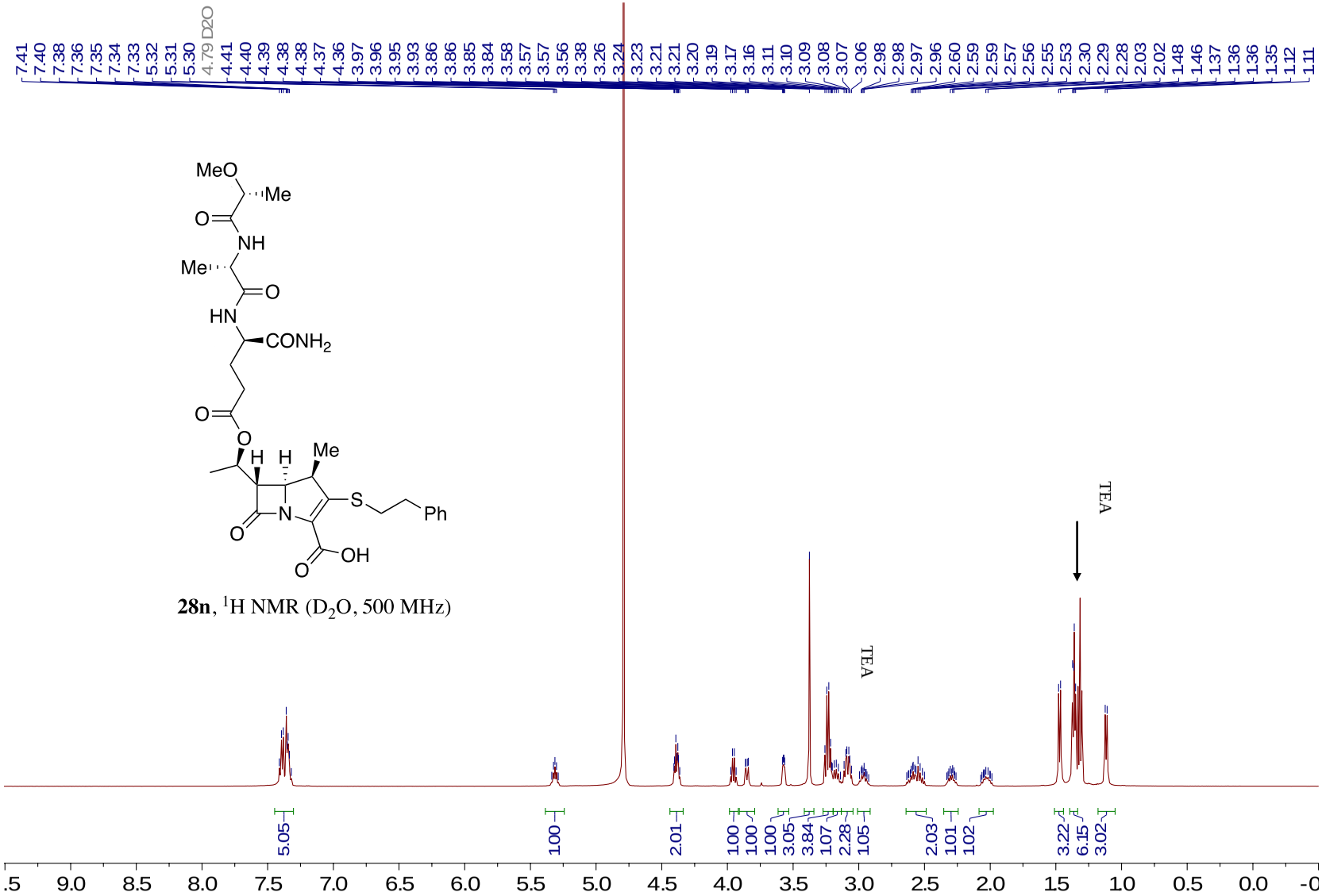




28l, ^{1}H NMR (D_2O, 500 MHz)



28m, ^{1}H NMR (D_2O, 500 MHz)



28n, ^{1}H NMR (D_2O, 500 MHz)