Supporting Information

Zn-Catalyzed Nicotinate-Directed Transamidations in Peptide Synthesis

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0 General Considerations

Unless stated otherwise, all commercial chemicals were used without further purification. Anhydrous 2-methyltetrahydrofuran was obtained by distillation over activated 3 Å molecular sieves. Anhydrous tetrahydrofuran was obtained using a PureSolv Innovative Technology system. Anhydrous 1,4-dioxane was obtained by drying over activated 4 Å molecular sieves for 24 h under argon atmosphere prior to use. Non-commercial starting materials were prepared based on literature procedures and are described below. ^{1}H and ^{13}C NMR spectra were recorded using different spectrometers. A Bruker Avance II 500 spectrometer was used at 500 MHz (^{1}H NMR) and 126 MHz (^{13}C NMR) at ambient temperature. Alternatively, A Bruker Avance 400 was used at 400 MHz (^{1}H NMR) and 101 MHz (^{13}C NMR) at 30°C. To obtain spectra at 250 MHz and 63 MHz, a Bruker Avance DRX 250 was used. The chemical shifts were reported in delta (δ) units in parts per million (ppm) relative to the signal of the deuterated solvent. For $CDCl_3$, the singlet in ^{1}H NMR was calibrated at 7.26 ppm and the central line of the triplet in ^{13}C NMR at 77.0 ppm. When recording in MeOD or DMSO-d_6, the calibration was performed at 3.31 ppm and 2.50 ppm for ^{1}H NMR and 49.0 ppm and 39.5 ppm for ^{13}C NMR, respectively. Assignments were made using one dimensional (1D) ^{1}H and ^{13}C spectra and two-dimensional (2D) HSQC, HMBC, and COSY spectra. Multiplicities were described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), broad (br), or a combination thereof. The corresponding coupling constants (*J* values) were reported in Hertz (Hz). Analytical RP-HPLC was performed on a VWR-Hitachi Chromaster HPLC with a Chromolith HighResolution RP-18C column from Merck (150 mm X 4.6 mm, 1.1 μm, 150 Å). The flow rate was 3 ml/min and UV detection was done at 214 nm. The solvent system used consisted of 0.1% TFA in ultrapure water (A) and 0.1% TFA in acetonitrile (B) with a gradient from 3% B to 100% B over a 6 minutes runtime. For LC-MS analysis, the HPLC unit used was a Waters 600 system combined with a Waters 2487 UV detector at 215 nm and as stationary phase a Vydac MS RP C18-column (150 mm x 2.1 mm, 3 μm, 300 Å). The solvent system used was 0.1 % formic acid in water (A) and 0.1 % formic acid in acetonitrile (B) with a gradient going from 3 % to 100 % B over 20 minutes with a flow rate of 0.3 ml/min. The MS unit, coupled to the HPLC system, was a Micromass QTOF-micro system. For the high resolution mass spectroscopy, the same MS system was used with reserpine (2.10^{-3} mg/ml) solution in H_2O:CH_3CN (1:1) as reference. Chiral HPLC was recored using a Kontron HPLC autosampler 465, Biotek system pump 522, a Jasco X-LC 3195 CD detector, Water Acquity PDA detector, and a Diacel Chiralpak IA column. Optical rotations were recorded with a Schmidt Haensch Polartronic M at a wavelength of 589.3 nm at a concentration between 5 and 15 mg/ml in chloroform and a cell of 5 cm. LC-MS samples to check for chiral purity were prepared by dissolving 2-4 mg of the compound in *n*-hexane/EtOH (80/20) and further diluted to a concentration of 10^{-4} M. From these samples 20 μL was injected and analyzed via a Kontron HPLC autosampler 465

equipped with a Kontron HPLC pump 522, a Chiralpak IA column, a Waters Photo Diode Array detector and a Jasco X-LC 3195CD system. Automated flash chromatography was performed using Grace® Reveleris X2 system equipped with an ELSD and UV detector (254 nm or 280 nm) or Biotage® Isolera One Normal Phase Silicagel Flash Chromatography associated with UV detection. The used normal phase columns for the systems were Grace® Silica Flash Cartridges of 40 g with a flow rate of 40 ml/min unless stated otherwise. Semi-preparative RP-HPLC-purifications were done using a Gilson HPLC system with Gilson 322 pump equipped with a Grace® Vydac 150HC C18 (250 mm x 22 mm, 10 μm) column and Waters UV/VIS-156 detector at 215 nm. The same solvent system was used as applied for the analytical RP-HPLC with a flow rate of 20 ml/min. The transamidations were performed in sealed microwave vials for a reaction volume of 0.5 ml – 2 ml (Figure S1) equiped with a triangle stirring bar.

Figure S1. Reaction vial (0.5 ml – 2 ml) used for the transamidation reactions

1 Optimization Data

1.1 General Procedure for the Optimization of the Transamidation

To a microwave vial was added Boc-L-Phe-NH-*t*Bu-nic **L-4a** (1 equiv, 110 mg, 0.25 mmol), H-L-Phe-OMe **L-5a**, additives, and solvent. The vial was sealed with a crimp cap, and stirred at the specified temperature and time. The mixture was then allowed to cool down to room temperature, decapped, and concentrated *in vacuo*. A known amount of 1,3,5-trimethoxybenzene, between 10 - 15 mg, was added to the crude mixture, which was then dissolved in MeOD or DMSO-d_6. Potential precipitating salts were removed by centrifugation. A ^{1}H NMR of the crude was recorded and signals were integrated in comparison to the internal standard. The mass balance was calculated based on the remaining starting material **L-4a** and *tert*-butyl 2-aminonicotinate **S2** by-product of the transamidation. Considering experimental and instrumental errors, a total measured mass balance in the 95-105% range was considered as a successful experiment. Reported values were subsequently recalculated to 100%. HPLC and LC-MS of the sample were subsequently recorded to confirm the formation of the desired peptide compound.

Procedure for the Desalting of H-L-Phe-OMe Hydrochloric Acid Salt ***L-5a.HCl***

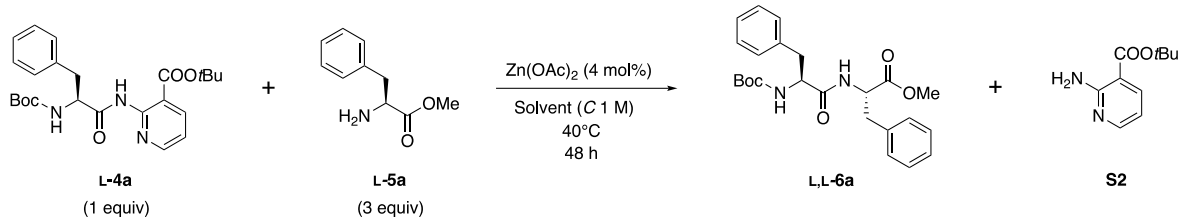
The desalting of the commercially available H-L-Phe-OMe hydrochloric acid salt **L-5a.HCl** was performed by adding DIPEA (1 equiv) to a stirring mixture of **L-5a.HCl** (1.1 equiv) in diethyl ether. The mixture was stirred for 30 minutes at room temperature, filtered and concentrated *in vacuo*. The purity of the H-L-Phe-OMe **L-5a** was confirmed by ^{1}H NMR.

1.2 Evaluation of the Reaction Parameters of the Transamidation

The transamidation on amino acid and peptide substrates was optimized using the synthesis of the dipeptide, Boc-L-Phe-L-Phe-OMe **L,L-6a** from Boc-L-Phe-NH-*t*Bu-nic **L-4a** and H-L-Phe-OMe hydrochloric acid salt **L-5a.HCl** or **L-5a** according to the general procedure.

As a starting point, the reaction conditions of the alcoholysis previously developed in our laboratories were evaluated using **L-5a** ($Zn(OAc)_2$ cat., 3 equiv. ROH in *t*BuOAc at 40°C).[1] The solvent screening was evaluated at a concentration of 1 M (Table S1). In *t*BuOAc a solubilty problem of the starting materials was observed (Table S1, entry 1). The solvents were chosen based on their frequent use for transformations on peptides and amino acids. A good solubility of both starting materials was observed in DMSO, DMF, THF, and 1,4-dioxane (Table S1, Entry 2, 3, 5, 6). The use of THF (Table S1, Entry 5) as solvent resulted in the best conversion and yield for the transamidation.

Table S1. Evaluation of the Solvent.

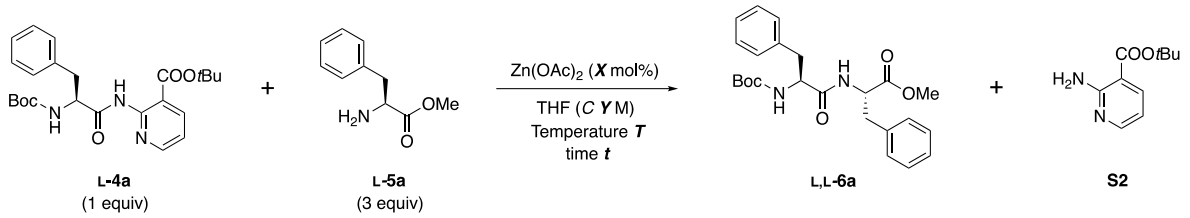


Entry (ELN-code)	Solvent	Solubility of starting materials[a]	Yield **L-4a** (%)[b]	Yield **L,L-6a** (%)[b]
1 (KH_98.1)	*t*BuOAc	✖	-	-
2 (KH_98.3)	DMSO	✓	78	22
3 (KH_98.5)	DMF	✓	23	77
4 (KH_131.1)	CH_2Cl_2	✖	-	-
5 (KH_131.2)	THF	✓	12	88
6 (KH_131.3)	1,4-dioxane	✓	24	76

[a] ✖ = No clear solution could be obtained when stirring the reaction mixture at 40°C, ✓ = A clear solution could be obtained when stirring the reaction mixture at 40°C. [b] ^{1}H NMR yield using 1,3,5-trimethoxybenzene as internal standard.

To anticipate possible solubility issues with amino acids and peptides, the concentration of the reaction mixture was subsequently evaluated (Table S2, Entry 1-3), showing no significant change in reaction by decreasing the concentration from 1 M (Table S2, Entry 1) to 0.5 M (Table S2, Entry 2). A further reduction in concentration however affected the conversion negatively (Table S2, Entry 3). To achieve full conversion within 24 h, rather than the currently used 48 h, a catalyst loading of 10 mol% at 60°C was required (Table S2, Entries 5-6).

Table S2. Effect of Catalyst Loading, Temperature, Reaction Time and Concentration.

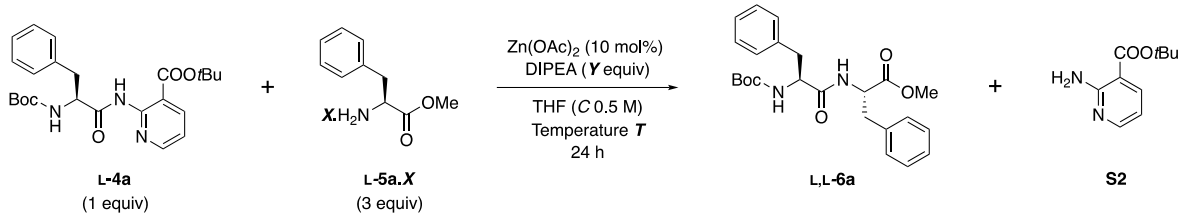


Entry (ELN-code)	$Zn(OAc)_2$ (***X*** mol%)	Concentration ***Y*** (M)[a]	Temperature ***T*** (°C)	Reaction Time ***t*** (h)	Yield **L-4a** (%)[b]	Yield **L,L-6a** (%)[b]
1 (KH_131.2)	4	1	40	48	12	88
2 (KH_143.3)	4	0.5	40	48	10	90
3 (KH_144.3)	4	0.2	40	48	29	71
4 (KH_466)	4	0.5	40	24	28	72
5 (KH_157.1)	10	0.5	40	24	23	77
6 (KH_182.1)	10	0.5	60	24	0	100

[a] Molar concentration of the limiting reactant. [b] ^{1}H NMR yield using 1,3,5-trimethoxybenzene as internal standard.

The commercial HCl-salt form of the amine **L-5a**, **L-5a.HCl**, required the liberation of the amine prior to transamidation. The *in situ* deprotonation of the amino acid using DIPEA was therefore tested. Both with **L-5a** and **L-5a.HCl**, full conversion was obtained at 60°C within 24 h using 10 mol% $Zn(OAc)_2$ in THF (Table S3, Entry 3, 6).

Table S3. Evaluation of Amine Form, **L-5a** versus **L-5a.HCl** and Temperature.



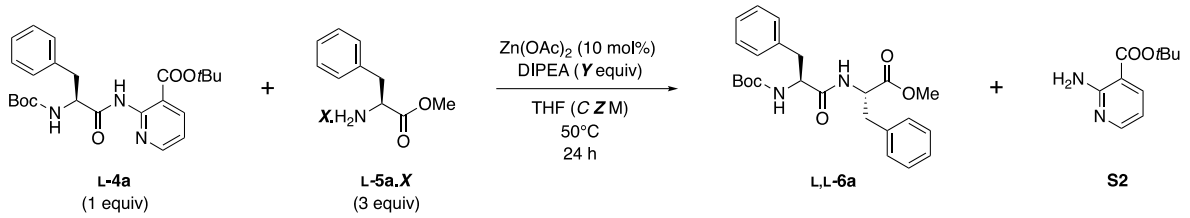
L-4a (1 equiv) + **L-5a.*X*** (3 equiv) → **L,L-6a** + **S2**

Entry (ELN-code)	Amine form ***X***	DIPEA (***Y*** equiv)	Temperature ***T*** (°C)	Yield **L-4a** (%)[a]	Yield **L,L-6a** (%)[a]
1 (KH_157.1)	**L-5a**[b]	0	40	23	77
2 (KH_183)	**L-5a**[b]	0	50	14	86
3 (KH_182.1)	**L-5a**[b]	0	60	0	100
4 (KH_157.3)	**L-5a.HCl**	3	40	33	67
5 (KH_184)	**L-5a.HCl**	3	50	17	83
6 (KH_182.3)	**L-5a.HCl**	3	60	0	100

[a] ^{1}H NMR yield using 1,3,5-trimethoxybenzene as internal standard. [b] Free amine obtained as described in the general procedure for desalting **L-5a.HCl**.

Due to the high concentration, the amount of DIPEA added could be considered as a co-solvent. Consequently, a possible dilution effect needed to be evaluated (Table S4). It was observed that no significant difference was found in either the case where DIPEA was considered as a co-solvent (Table S4, Entry 3), or as a reactant (Table S4, Entry 4).

Table S4. Effect of Dilution due to *in situ* Deprotonation with DIPEA.

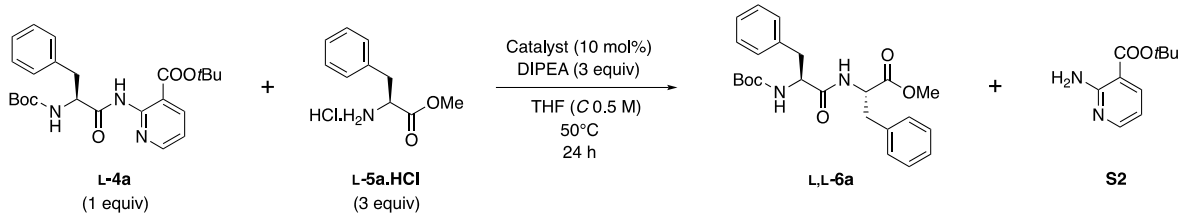


Entry (ELN-code)	Amine form ***X***	DIPEA (***Y*** equiv)	Concentration ***Z*** (M)	Yield **L-4a** (%)[a]	Yield **L,L-6a** (%)[a]
1 (KH_183)	**L-5a**	0	0.5[b]	14	86
2 (KH_187)	**L-5a**	0	0.39[b]	10	90
3 (KH_188)	**L-5a.HCl**	3	0.5[c]	19	81
4 (KH_184)	**L-5a.HCl**	3	0.39[c]	17	83

[a] ^{1}H NMR yield using 1,3,5-trimethoxybenzene as internal standard. [b] Concentration calculated based on the limiting reactant in the volume THF used. [c] Concentration calculated based on the limiting reactant in the total volume of THF and DIPEA used.

As a combination of catalyst and bases have not been screened in our esterification,[1] a selection of catalysts that performed well in the alcoholysis reaction was tested in the model system with DIPEA. The results showed that, compared to $Zn(OAc)_2$ (Table S5, Entry 1), Zn formate.$2H_2O$ (Table S5, Entry 4), $Ni(OAc)_2.H_2O$ (Table S5, Entry 7), and $Cu(OAc)_2.H_2O$ (Table S5, Entry 9) also gave good results, though a lower conversion was obtained.

Table S5. Evaluation of the Catalyst.



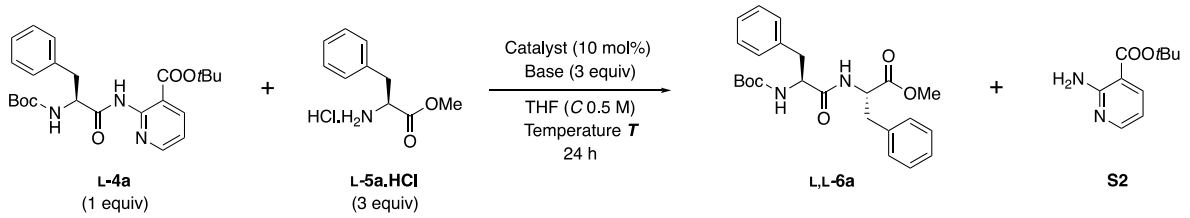
L-4a (1 equiv) + L-5a.HCl (3 equiv) → L,L-6a + S2

Entry (ELN-code)	Catalyst (10 mol%)[a]	Yield **L-4a** (%)[b]	Yield **L,L-6a** (%)[b]
1 (KH_184)	$Zn(OAc)_2$	17	83
2 (KH_235)	$Zn(OTf)_2.H_2O$	62	38
3 (KH_1121)	$Zn(acac)_2$	56	44
4 (KH_237)	Zn formate.$2H_2O$	29	71
5 (KH_1282)	$ZnCl_2$	49	51
6 (KH_241)	$Co(OAc)_2.4H_2O$	38	62
7 (KH_243)	$Ni(OAc)_2.H_2O$	31	69
8 (KH_246)	$Ni(acac)_2$ (4% water)	39	61
9 (KH_244)	$Cu(OAc)_2.H_2O$	31	69
10 (KH_245)	$Cu(OOCCF_3)_2$	44	56

[a] Hydrates determined by TGA analysis. [b] ^{1}H NMR yield using 1,3,5-trimethoxybenzene as internal standard.

The four best catalysts were then evaluated with different tertiary amine bases at both 40°C and 50°C (Table S6). Despite the fact that at 50°C multiple combinations resulted in full conversion (Table S6, Entry 3, 5, 8, 10), the corresponding experiments at 40°C revealed that $Zn(OAc)_2$ in combination with Et_3N is the most promising system.

Table S6. Evaluation of $Zn(OAc)_2$, Zn formate.$2H_2O$, $Ni(OAc)_2.H_2O$ and $Cu(OAc)_2.H_2O$ with Different Tertiary Amine Bases.



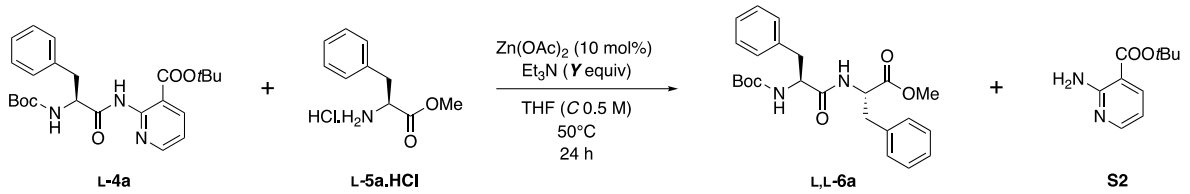
L-4a (1 equiv) + L-5a.HCl (3 equiv) → L,L-6a + S2

Entry (ELN-code)	Catalyst (10 mol%)[a]	Base (3 equiv)	Temperature ***T*** (°C)	Yield **L-4a** (%)[b]	Yield **L,L-6a** (%)[b]
1 (KH_184)	$Zn(OAc)_2$	DIPEA	50	17	83
2 (KH_267)	$Zn(OAc)_2$	Et_3N	40	8	92
3 (KH_257)	$Zn(OAc)_2$	Et_3N	50	0	100
4 (KH_270)	$Zn(OAc)_2$	NMM[c]	40	12	88
5 (KH_258)	$Zn(OAc)_2$	NMM[c]	50	0	100
6 (KH_237)	Zn formate.$2H_2O$	DIPEA	50	29	71
7 (KH_268)	Zn formate.$2H_2O$	Et_3N	40	18	82
8 (KH_259)	Zn formate.$2H_2O$	Et_3N	50	0	100
9 (KH_271)	Zn formate.$2H_2O$	NMM[c]	40	30	70
10 (KH_260)	Zn formate.$2H_2O$	NMM[c]	50	0	100
11 (KH_243)	$Ni(OAc)_2.H_2O$	DIPEA	50	31	69
12 (KH_263)	$Ni(OAc)_2.H_2O$	Et_3N	50	12	88
13 (KH_264)	$Ni(OAc)_2.H_2O$	NMM[c]	50	18	82
14 (KH_244)	$Cu(OAc)_2.H_2O$	DIPEA	50	31	69
15 (KH_265)	$Cu(OAc)_2.H_2O$	Et_3N	50	9	91
16 (KH_266)	$Cu(OAc)_2.H_2O$	NMM[c]	50	12	88

[a] Hydrates determined by TGA analysis. [b] ^{1}H NMR yield using 1,3,5-trimethoxybenzene as internal standard. [c] NMM = *N*-methylmorpholine.

Using the optimal catalyst/tertiary amine base system, the excess of **L-5a.HCl** and Et_3N was simultaneously stepwise reduced to 1.1 equivalents (Table S7, Entry 1-4). This had a significant effect on the conversion; 3 to 1.1 equiv. reduced conversion with 25%. The ratio **L-5a.HCl** and Et_3N was finally investigated (Table S7, Entries 4-6). With a loading of 1.1 equiv. **L-5a.HCl**, the use of more base inhibited conversion to a very small extend; 1.1 to 6 equiv. reduced conversion with only 10%.

Table S7. Evaluation of the Excess of **L-5a.HCl** and Et_3N



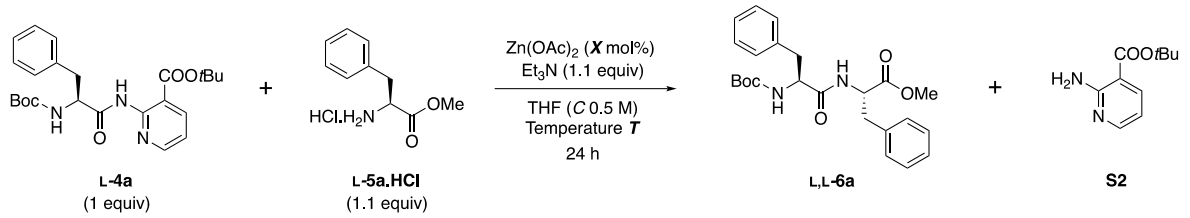
L-4a (1 equiv) + L-5a.HCl (*X* equiv) → L,L-6a + S2

Entry (ELN-code)	H-L-Phe-OMe.HCl **L-5a.HCl** (*X* equiv)	Et_3N (*Y* equiv)	Yield **L-4a** (%)[a]	Yield **L,L-6a** (%)[a]
1 (KH_257)	3	3	0	100
2 (KH_274)	2	2	7	93
3 (KH_273)	1.5	1.5	13	87
4 (KH_355)	1.1	1.1	25	75
5 (KH_349)	1.1	3	30	70
6 (KH_352)	1.1	6	35	65

[a] ^1H NMR yield using 1,3,5-trimethoxybenzene as internal standard.

To obtain full conversion using only 1.1 equivalents of **L-5a.HCl**, and 1.1 equivalents of Et_3N the catalyst loading was increased alongside with the temperature (Table S8). Here, the use of 20 mol% of catalyst at 70°C (Table S8, Entry 7), resulted in full conversion. Considering $Zn(OAc)_2$ is cheap, air-stable, non-toxic (E650) and aiming a general applicability of the developed transamidation protocol, a higher catalyst loading rather than an excess of **L-5a.HCl** was preferred as standard optimized conditions.

Table S8. Evaluation of $Zn(OAc)_2$ Loading and Temperature with 1.1 Equivalents of **L-5a.HCl** and 1.1 Equivalents of Et_3N.



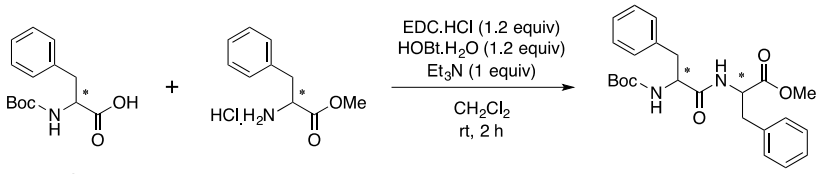
L-4a (1 equiv) + **L-5a.HCl** (1.1 equiv) → **L,L-6a** + **S2**

Entry (ELN-code)	$Zn(OAc)_2$ (***X*** mol%)	Temperature ***T*** (°C)	Yield **L-4a** (%)[a]	Yield **L,L-6a** (%)[a]
1 (KH_355)	10	50	25	75
2 (KH_356)	10	60	21	79
3 (KH_361)	10	70	14	86
4 (KH_420)	15	50	19	81
5 (KH_459)	15	70	12	88
6 (KH_421)	20	50	12	88
7 (KH_402)	20	70	0	100

[a] ^{1}H NMR yield using 1,3,5-trimethoxybenzene as internal standard.

Next, the effect of the transamidation reaction conditions on the chiral purity of both the *t*Bu-nicotinate activated amide **4a** moiety and the nucleophile **5a** was evaluated. Consequently, we synthesized the four stereoisomers of Boc-Phe-Phe-OMe **6a** by coupling the enantiomers of Boc-Phe-OH **S1** with those of H-Phe-OMe.HCl **5a.HCl** using EDC.HCl and $HOBt.H_2O$. These were then analyzed using chiral HPLC (Table S9) and used as references for the evaluation of epimerization under the optimal reaction conditions.

Table S9. Synthesis and Chiral Analysis of the Four Stereoisomers of Boc-Phe-Phe-OMe **6a**

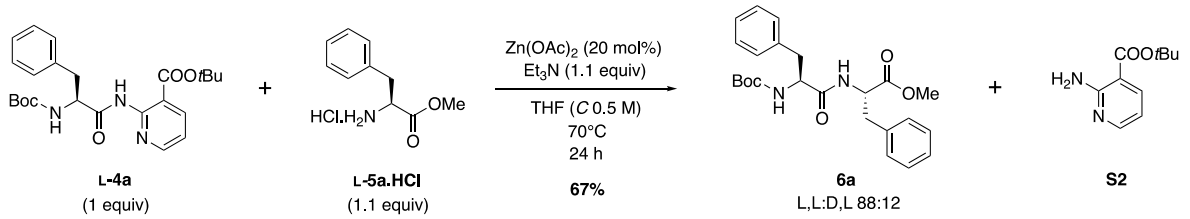


S1 (1 equiv) **5a.HCl** (1 equiv) **6a**

Entry (ELN-code)	Stereochemistry of **6a**	Isolated yield (%)	rt (min)[a]
1 (KH_1066)	L,L	75	3.85
2 (KH_873)	D,L	76	5.71
3 (KH_1067)	L,D	76	3.76
4 (KH_1068)	D,D	84	4.26

[a] %ee measured using HPLC with *n*-hexane:*i*-propanol on a Diacel Chiralpak IA column.

With the ability in hand to distinguish between the different steroisomers, we repeated the transamidation of Boc-L-Phe-NH-*t*Bu-nic **L-4a** with H-L-Phe-OMe.HCl **L-5a.HCl** under the optimized reaction conditions. Dipeptide **6a** was isolated with a yield of 67%, however, the chiral analysis showed that a mixture of **L,L-6a** and **D,L-6a** was present in a 88:12 ratio (Scheme S1).

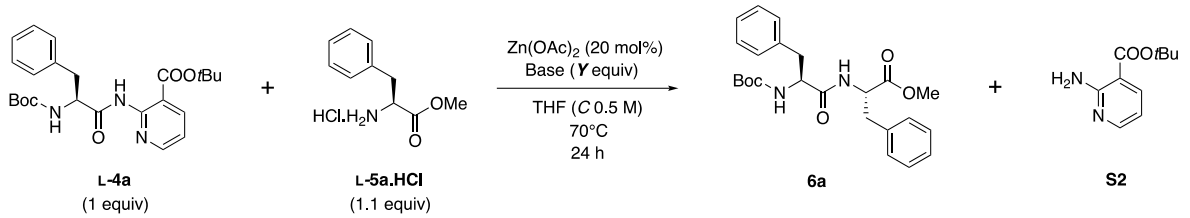


L-4a (1 equiv) **L-5a.HCl** (1.1 equiv) **6a** L,L:D,L 88:12 **S2**

Scheme S1. Transamidation of Boc-L-Phe-NH-*t*Bu-nic **L-4a** and H-L-Phe-OMe.HCl **L-5a.HCl** under optimized conditions.

As the chiral purity of the dipeptide is jeopardized under the optimal reaction conditions, we decided to further investigate the impact of base on the reaction. Besides, full retention of chiral information, full conversion and a high isolated yield were aimed for (Table S10).

Table S10. Evaluation of the Base on the Chiral Purity of **6a**.



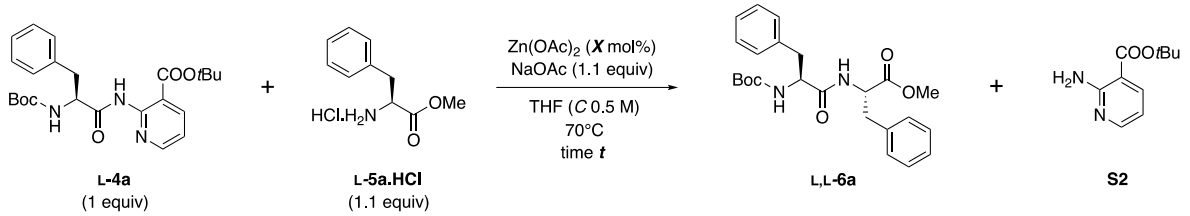
Entry (ELN-code)	Base	(***Y*** equiv)	Yield ***L*-4a** (%)[a]	Yield **L,L-6a** (%)[a]	Isolated yield **6a** (%)	Chiral Purity analysis of **6a**[b]	
						%L,L	%D,L
1 (KH_1070)	Et_3N	1.1	0	100	67	88	12
2 (KH_1080)	Pyridine	1.1	44	56	26	100	0
3 (KH_1081)	NMM	1.1	9	91	69	100	0
4 (KH_1082)	K_2CO_3	0.55	0	100	54	94	6
5 (KH_1092)	**NaOAc**	**1.1**	**0**	**100**	**79**	**100**	**0**
6 (KH_1093)	*N*,*N*-dimethylaniline	1.1	47	53	28	100	0
7 (KH_1096)	Bu_3N	1.1	0	100	38	91	9

[a] ^{1}H NMR yield using 1,3,5-trimethoxybenzene as internal standard. [b] %ee measured using HPLC with *n*-hexane:*i*-propanol on a Diacel Chiralpak IA column, corrected for chiral purity of the starting material.

Similar to Et_3N as base (Table S10, Entry 1), full conversion was obtained for K_2CO_3 (Table S10, Entry 4), NaOAc (Table S10, Entry 5) and Bu_3N (Table S10, Entry 7). However, in the chiral purity analysis, from these only NaOAc showed no epimerization during the transamidation. Therefore NaOAc was selected as the optimal base (Table S10, Entry 5).

With the optimized conditions in hand, the need for the catalyst was evaluated (Table S11). Table S11, Entry 1 shows the reaction does occur without catalyst revealing 82% conversion. Full conversion without catalyst can be achieved within 48 h. Chiral purity analysis, however, shows that the chiral purity is jeopardized under these conditions. The addition of $Zn(OAc)_2$ has a significant effect as it allows to achieve full conversion within 24 h and retains the enantiomeric purity of the product.

Table S11. Effect of $Zn(OAc)_2$.



L-4a (1 equiv) + L-5a.HCl (1.1 equiv) → L,L-6a + S2

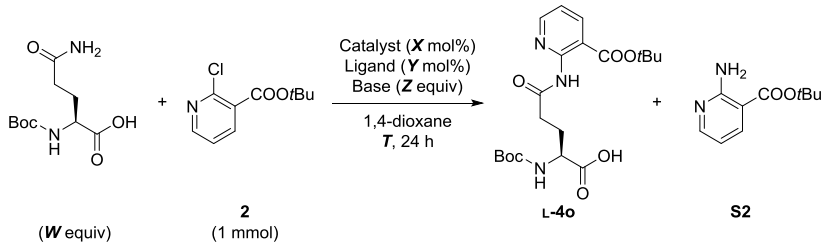
Entry (ELN-code)	$Zn(OAc)_2$ (***X*** mol%)	Reaction Time ***t*** (h)	Yield **L-4a** (%)[a]	Yield **L,L-6a** (%)[a]	Chiral Purity analysis of **6a**[b]	
					%L,L	%D,L
1 (KH_1195)	0	24	18	82	95	5
2 (KH_1195)	0	48	0	100	88	12
3 (KH_1092)	20	24	0	100	100	0

[a] ^{1}H NMR yield using 1,3,5-trimethoxybenzene as internal standard. [b] %ee measured using HPLC with *n*-hexane:*i*-propanol on a Diacel Chiralpak IA column, corrected for chiral purity of the starting material.

1.3 Optimization of the Synthesis of L-4o: *tert*-Butyl 2-Chloronicotinate Introduction On The Side Chain of Boc-L-Gln-OH

The introduction of *tert*-butyl 2-chloronicotinate **2** in the side chain of Boc-L-Gln-OH was evaluated. As starting point, two different reaction conditions previously reported in our lab were tested (Table S12, entries 1-2).[1] Since the combination of $Pd(OAc)_2$ and Xantphos (Table S12, Entry 2) afforded the formation of the desired product, a further optimization of that method was required to obtain higher yields. The best results were obtained in entry 6, where 5 mol% of $Pd(OAc)_2$, 10 mol% of Xantphos and 1.2 equiv. of Cs_2CO_3 in 1,4-dioxane at 90 °C were used. The addition of 1% of formic acid in water during the purification revealed to be a crucial factor to obtain good yields. Details about the chiral purity of the obtained compound will be discussed in a separate section.

Table S12. Optimization of DG introduction on the Gln side chain.



Entry (ELN code)	Catalyst (***X*** mol%)	Ligand (***Y*** mol%)	Base (***Z*** equiv)	***T*** (°C)	(***W*** equiv)	**2** (%)[a,b]	**L-4o** (%)[a]	**S2** (%)[a]	MB (%)[a,c]
1 (ER1310)	Pd-G3-dcpf (10 mol%)	-	Cs_2CO_3 (7.5 equiv)	40	1.1	93	0	0	93
2 (DM614)	$Pd(OAc)_2$ (5 mol%)	Xantphos (10 mol%)	K_2CO_3 (7.5 equiv)	90	1.1	38	10	46	94
3 (DM607)	$Pd(OAc)_2$ (5 mol%)	Xantphos (10 mol%)	K_2CO_3 (1.2 equiv)	90	1.5	32	0	58	90
4 (DM600)	$Pd(OAc)_2$ (5 mol%)	Xantphos (10 mol%)	Rb_2CO_3 (1.2 equiv)	90	1.5	26	0	24	50
5 (DM596)	$Pd(OAc)_2$ (5 mol%)	Xantphos (10 mol%)	Cs_2CO_3 (1.2 equiv)	90	1.5	0	50	5	55
6	$Pd(OAc)_2$	Xantphos	Cs_2CO_3	90	1.5	0	60[d]	9	69

(DM613)	(5 mol%)	(10 mol%)	(1.2 equiv)						
7 (DM598)	$Pd(OAc)_2$ (5 mol%)	Xantphos (10 mol%)	Cs_2CO_3 (1.0 equiv)	90	1.5	0	40	3	43
8 (DM601)	$Pd(OAc)_2$ (5 mol%)	Xantphos (10 mol%)	Cs_2CO_3 (3 equiv)	90	1.5	30	0	40	70
9 (DM511)	$Pd(OAc)_2$ (5 mol%)	Xantphos (10 mol%)	Cs_2CO_3 (1.2 equiv)	90	1.1	0	30	7	37
10 (DM599)	$Pd(OAc)_2$ (5 mol%)	Xantphos (10 mol%)	Cs_2CO_3 (1.2 equiv)	90	2.0	0	50	8	58

[a] Isolated yields after column chromatography. General work up: the mixture was acidified to pH = 5 with 1 M HCl [b] Recovered **2** [c] Mass balance. [d] No acidification in the work up. H_2O + 1% formic acid was used in the purification.

2 NMR Characterization of Compound L-4o

To demonstrate that the *t*Bu-nic directing group was selectively installed on the side chain primary amide of Boc-L-Gln-OH, full 2D NMR analysis of compound **L-4o** was performed. The ^{1}H-NMR of **L-4o** is given in Figure S2.

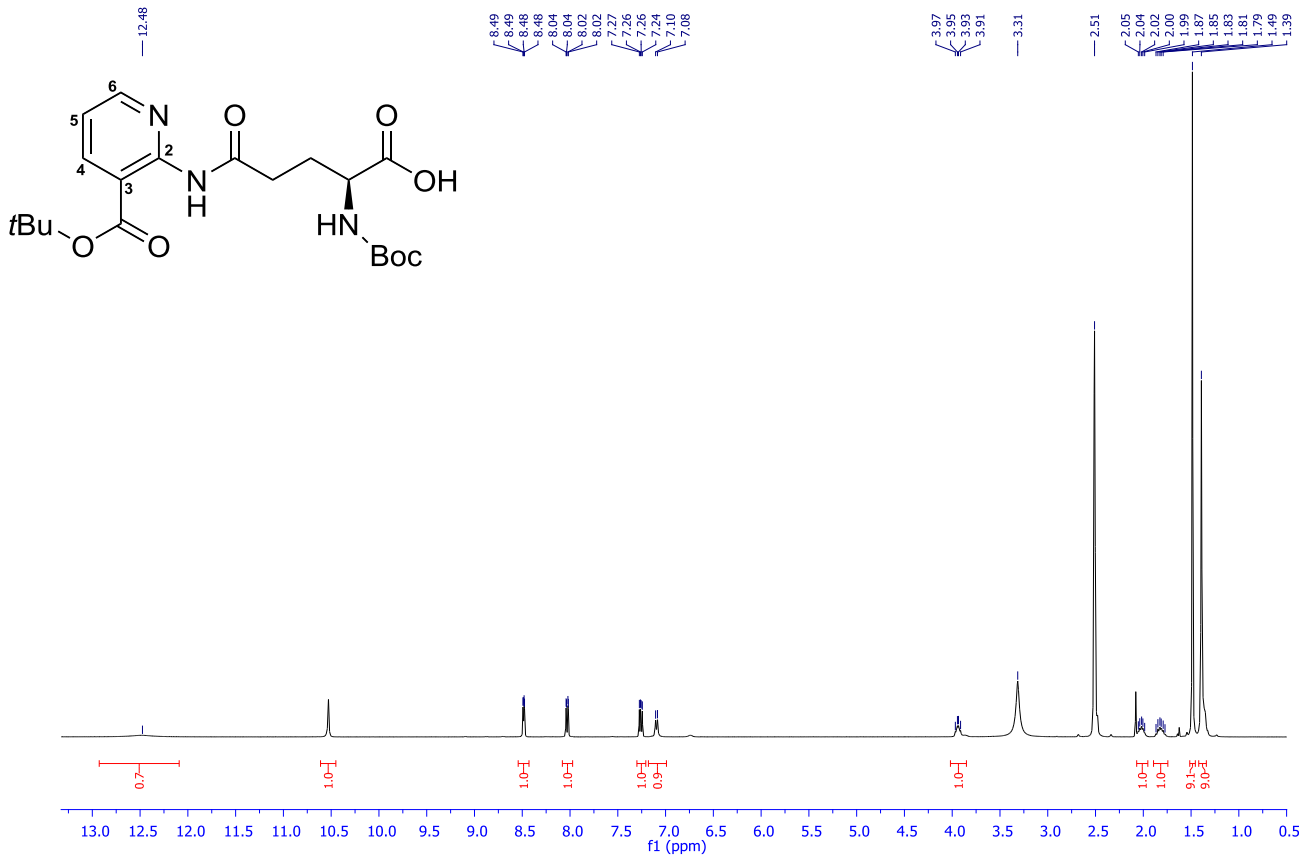


Figure S2. Full ^{1}H NMR spectrum (in DMSO-d_6) of **L-4o.**

2.1 COSY NMR Correlations in L-4o

The COSY spectrum showed the presence of two different spin systems, the first in the aromatic area of the proton NMR (spin system A, Figure S3) and the second in the aliphatic area (spin system B, Figure S4). The analysis of the spin system A (Figure S2) allowed to place the proton at 7.26 ppm (dd, J = 7.7, 4.8 Hz) in position 5 on the pyridine ring, since it both couples with the protons at 8.03 ppm (dd, J = 7.7, 1.7 Hz) and 8.48 ppm (dd, J = 4.7, 1.7 Hz). The latter proton could be placed in position 6 according to its higher chemical shift and, consequently, the proton at 8.03 ppm could be attributed to position 4.

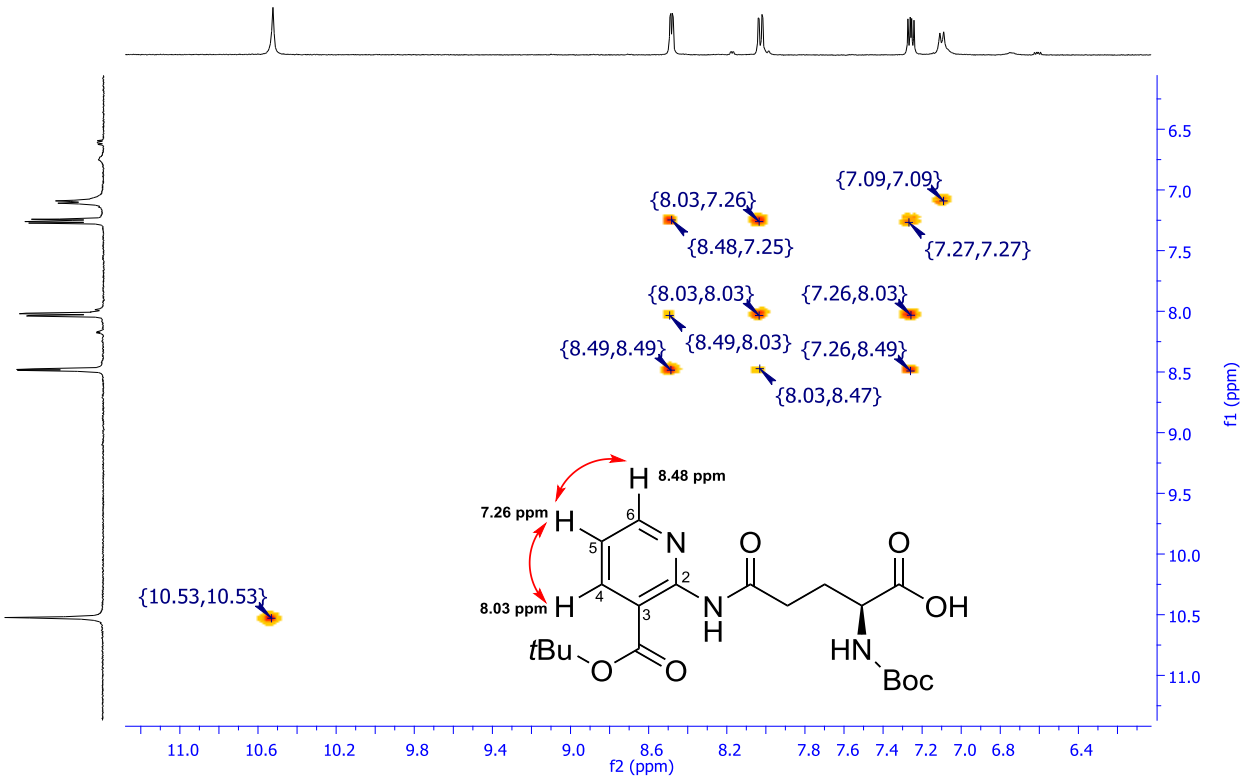


Figure S3. COSY correlations (in DMSO-d_6) in the aromatic spin system A of **L-4o.**

Regarding the spin system B, the analysis started from the proton at 7.09 ppm (d, J = 7.9 Hz), which corresponds to the amine group from the amino acid (see also section 2.2). This proton couples with the proton at 3.94 ppm (dd, J = 13.1, 8.7 Hz) (Figure S4, pink arrow) that in turn couples with the protons at 2.03 (m) and 1.83 ppm (td, J = 16.2, 7.8 Hz) (Figure S4, red arrows). Finally, a COSY correlation between the protons at 2.51 ppm (overlapping with DMSO signals) and the protons at 2.03 and 1.83 ppm was found (Figure S4, blue arrows).

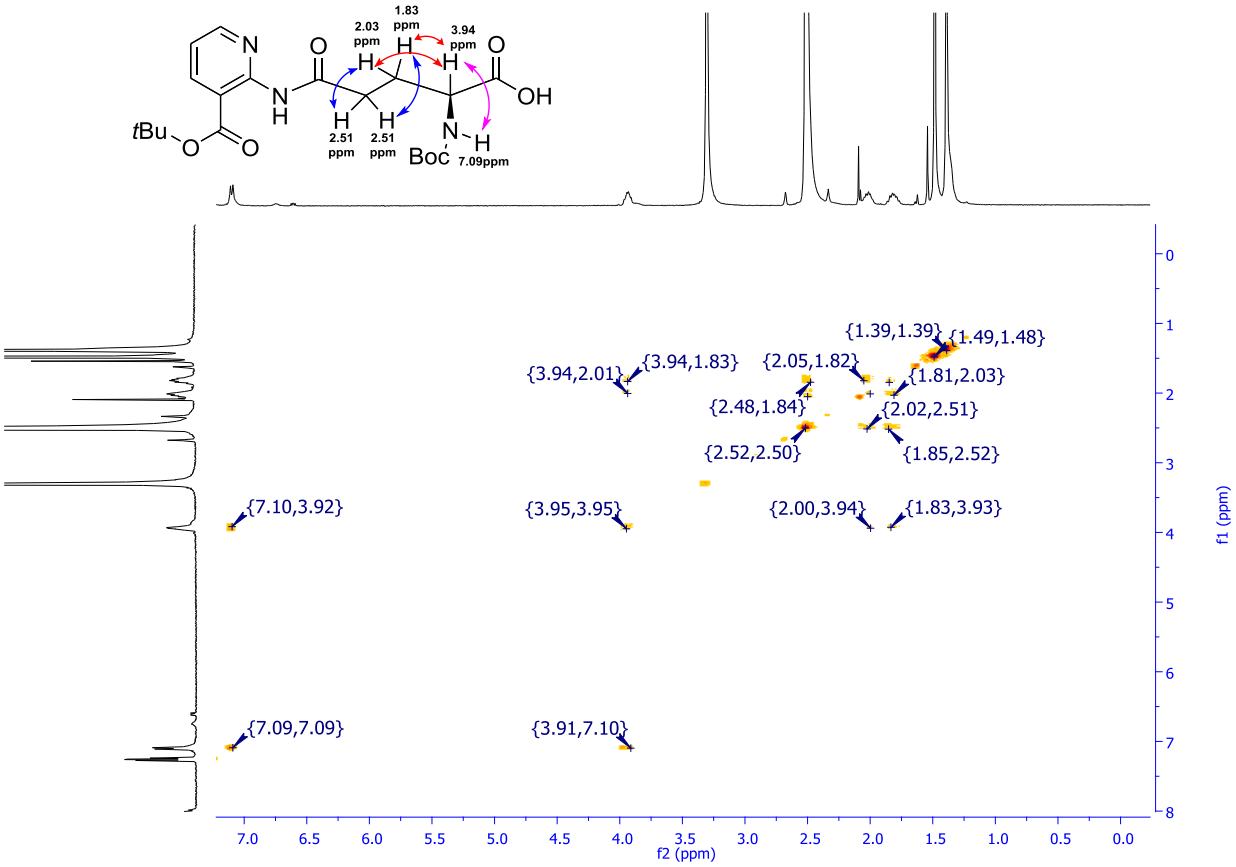


Figure S4. COSY correlations (in DMSO-d_6) in aliphatic spin system B of **L-4o.**

2.2 ^{15}N and ^{13}C HSQC NMR Correlations in L-4o

^{15}N HSQC revealed that the proton at 7.09 ppm is directly bound to a nitrogen atom (Figure S5). In combination with the COSY correlation (d, J = 7.9 Hz) to the aliphatic carbon chain of glutamine (Figure S4), allowed us to identify this proton as the Boc-NH. The proton at 10.53 ppm (s) also belongs to a nitrogen atom, however no proton coupling to the aliphatic carbon chain is observed, identifying it as the *t*Bu-nic-NH.

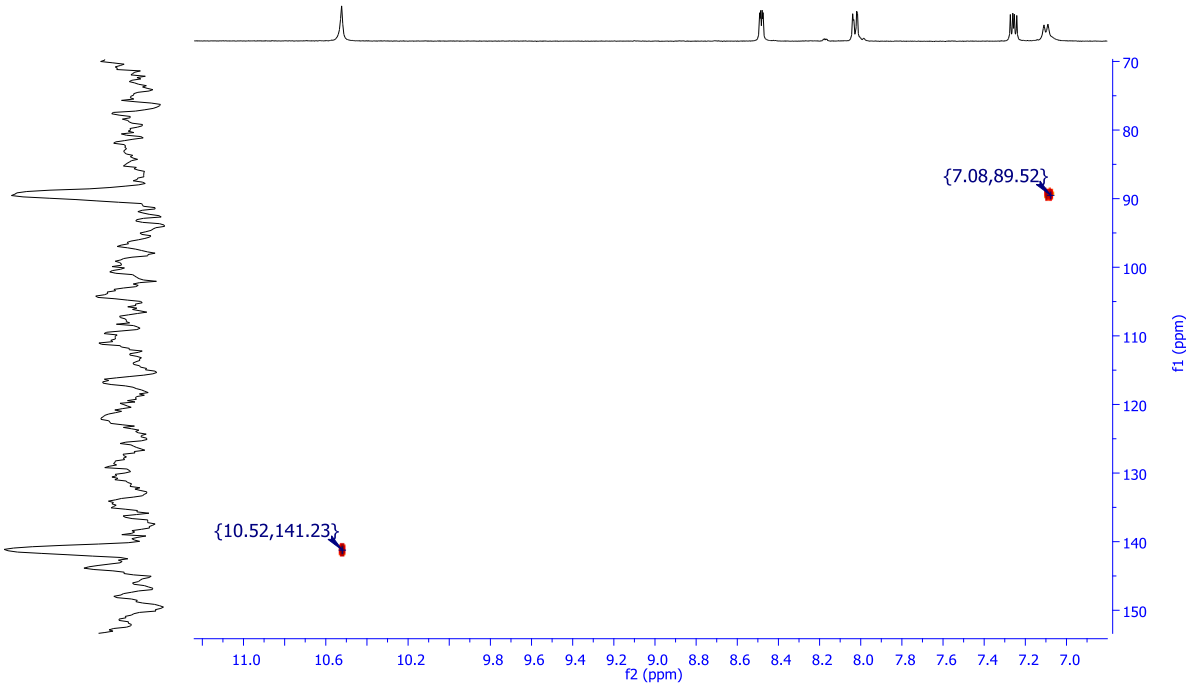


Figure S5. ^{15}N HSQC correlations in DMSO-d_6 of **L-4o.**

The analysis of the ^{13}C HSQC allowed us to assign the values of the carbons directly bound to protons (Figure S6). The proton at 3.94 ppm coupled with the carbon at 53.9 ppm. APT NMR revealed that this is the only aliphatic C-H, consequently, it could be unambiguously assigned as the chiral carbon of glutamine. The protons at 2.03 and 1.83 ppm both couple with the same carbon (27.0 ppm in ^{13}C NMR), indicating it belongs to a CH_2. Finally, the two protons at 2.51 ppm couple both with the carbon at 33.2 ppm, which also point to a CH_2. APT NMR confirmed the signals at 27.0 and 33.2 ppm are CH_2's. Regarding the HSQC NMR correlation of the pyridine ring, the protons at 8.48 ppm, 8.03 ppm and 7.26 ppm correlate with the carbons at 151.4 ppm, 139.6 ppm and 120.7 ppm respectively. APT NMR confirmed that the signals at 151.4 ppm, 139.6 ppm and 120.7 ppm are CH's.

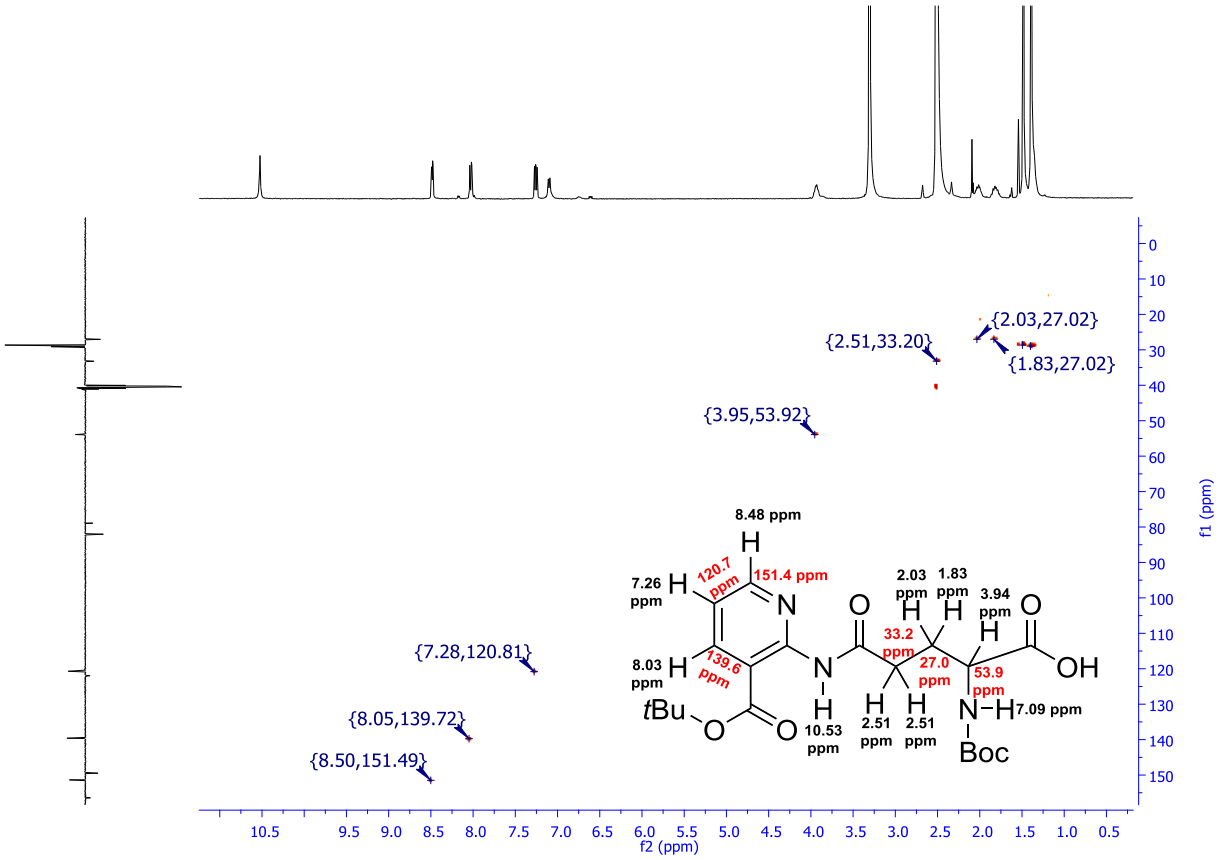


Figure S6. ^{13}C HSQC correlations in DMSO-d_6 of **L-4o.**

2.3 NOESY NMR Correlations in L-4o

The key NOESY correlations of the two N-H protons are reported in Figure S7. The N-H at 7.09 ppm couples with the proton at 3.94 ppm (the proton attached to the chiral carbon), the proton at 1.82 ppm and the two protons at 2.51 ppm (Figure S7, blue arrows). Furthermore, the proton at 7.09 ppm correlates with the signal at 1.39 ppm (s, 9H, see Figure 1) (Figure S7 purple arrow). The N-H proton at 10.53 ppm correlates with the two protons at 2.51 ppm on the side chain of the glutamine (Figure S7, red arrows) and with the protons at 1.49 ppm (s, 9H, see Figure 1) (Figure S7, green arrow). The signal at 1.49 ppm couples also with the proton at 8.03 ppm in position 4 on the pyridine ring, indicating that the *t*Bu group at 1.49 ppm can be linked to the pyridine ring, whereas the signal at 1.39 ppm correspond to the *t*Bu group on the amine nitrogen. Consequently, it can be stated that the N-H at 10.53 ppm is located in between the pyridine ring and the side chain of the glutamine.

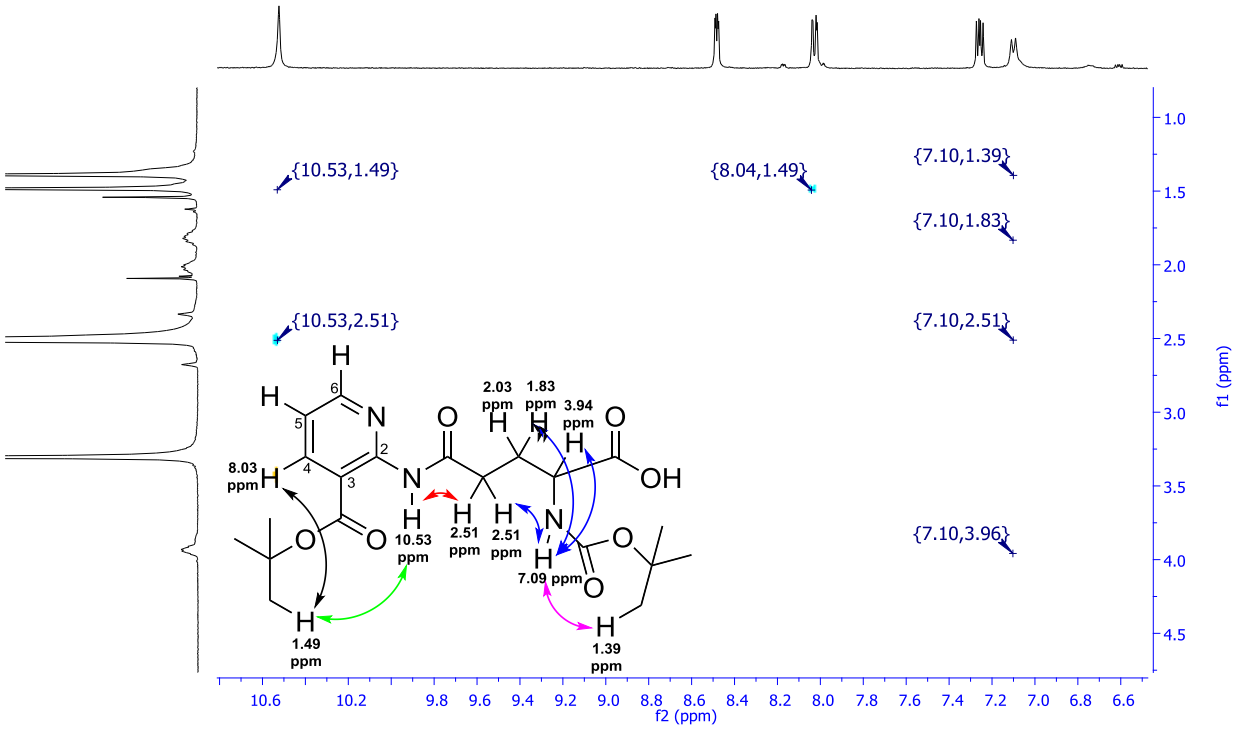


Figure S7. NOESY correlations in DMSO-d_6 of the N-H protons of **L-4o**.

2.4 HMBC NMR Correlations in L-4o

In order to assign the quaternary carbons of the pyridine ring and the carbonyls, the HMBC spectrum was analyzed. The protons at 8.48 and 8.03 ppm both coupled with the carbon at 149.5 ppm, identifying it as the carbon in position 2 of the pyridine ring (Figure S8 blue arrows). The correlation between the proton at 8.03 ppm and the carbon at 165.9 ppm allowed to assign that carbon as the carbonyl of the *t*Bu ester on the pyridine ring (Figure S8, pink arrow). The HMBC correlation between the proton at 7.26 ppm and the carbon at 121.9 ppm established the placement of the latter carbon in position 3 of the pyridine ring (Figure S8, red arrow).

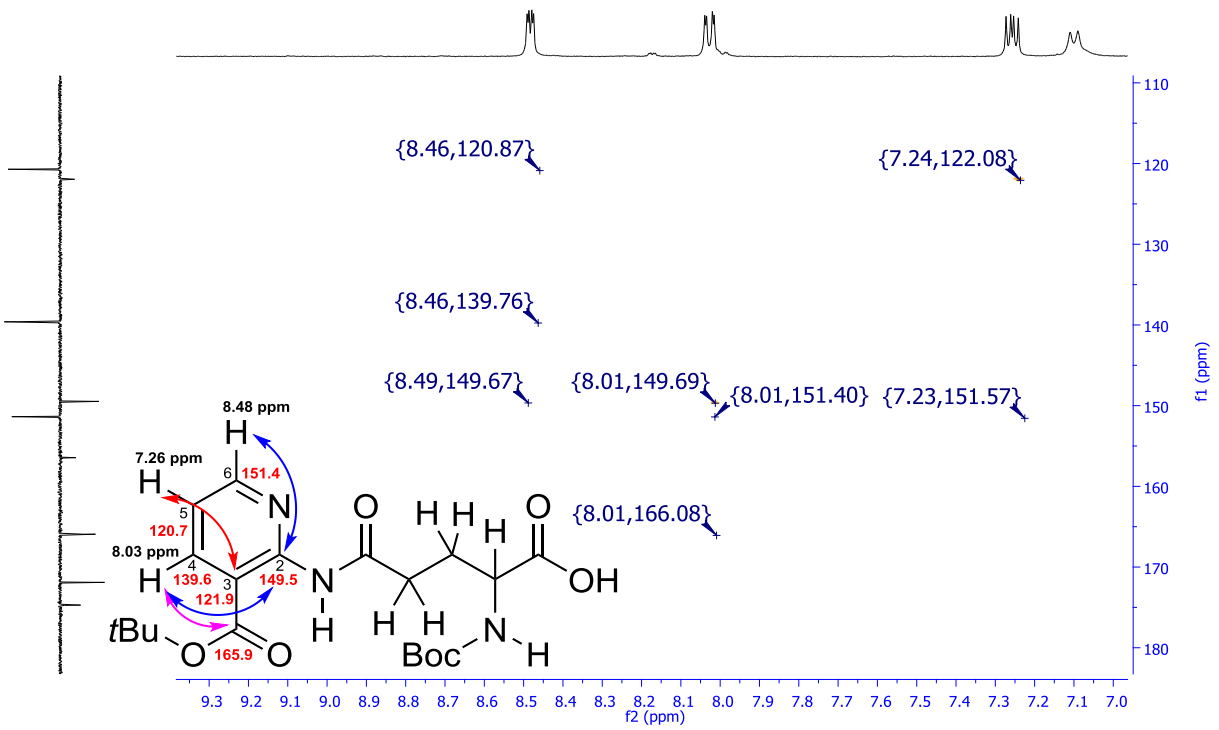


Figure S8: HMBC correlations in DMSO-d_6 of the pyridine ring in **L-4o**.

Regarding the HMBC correlations in the aliphatic chain, the two protons at 2.51 ppm couple with the carbonyl at 171.9 ppm and with the carbons at 27.0 ppm and 53.9 ppm, while the protons at 2.03 ppm and 1.83 ppm couple with the carbons at 33.2 ppm and 53.9 ppm, also confirming the HSQC of the side chain (Figure S9)

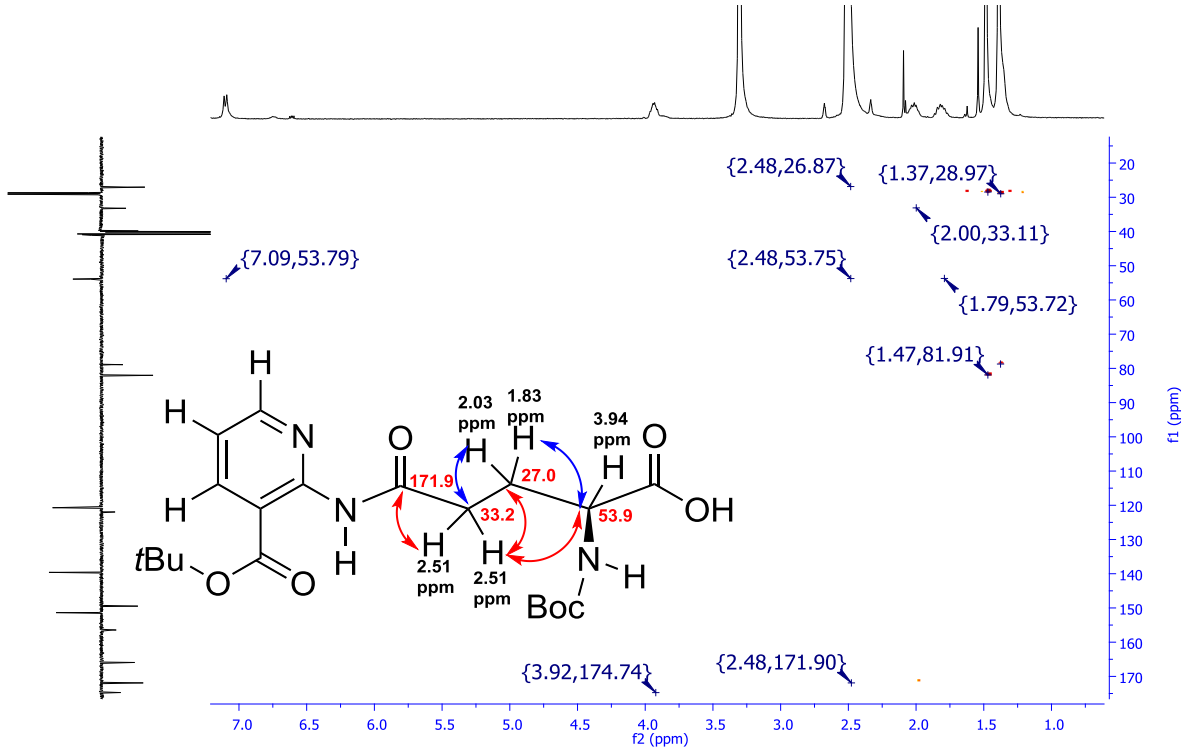


Figure S9: HMBC correlations in DMSO-d_6 of the aliphatic chain in **L-4o**.

The proton at 3.94 ppm showed an HMBC correlation with the carbonyl at 174.7 ppm, hereby identified as the carboxylic acid. Furthermore, a correlation between the N-H proton at 7.09 ppm and the carbon at 53.9 ppm was observed, further confirming it as the chiral carbon (Figure S10). The N-H proton at 10.56 ppm couples both with the carbon at 121.9 ppm (the C-3 of the pyridine ring) and the remaining carbonyl at 171.9 ppm. Interestingly, no HMBC correlation between the proton at 10.53 ppm and the carbon at 149.5 ppm were found, even when the relaxation time of carbon NMR was increased. Furthermore, the carbonyl at 171.9 ppm coupled also with the protons at 2.51 ppm. Those data, together with the information described in the section 2.3, unambiguously demonstrate that the *t*Bu-nic directing group was selectively installed on the side chain primary amide.

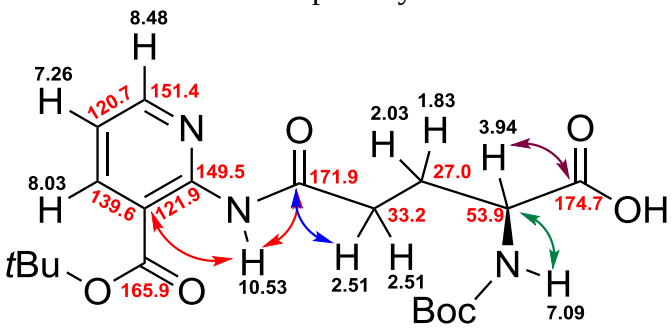
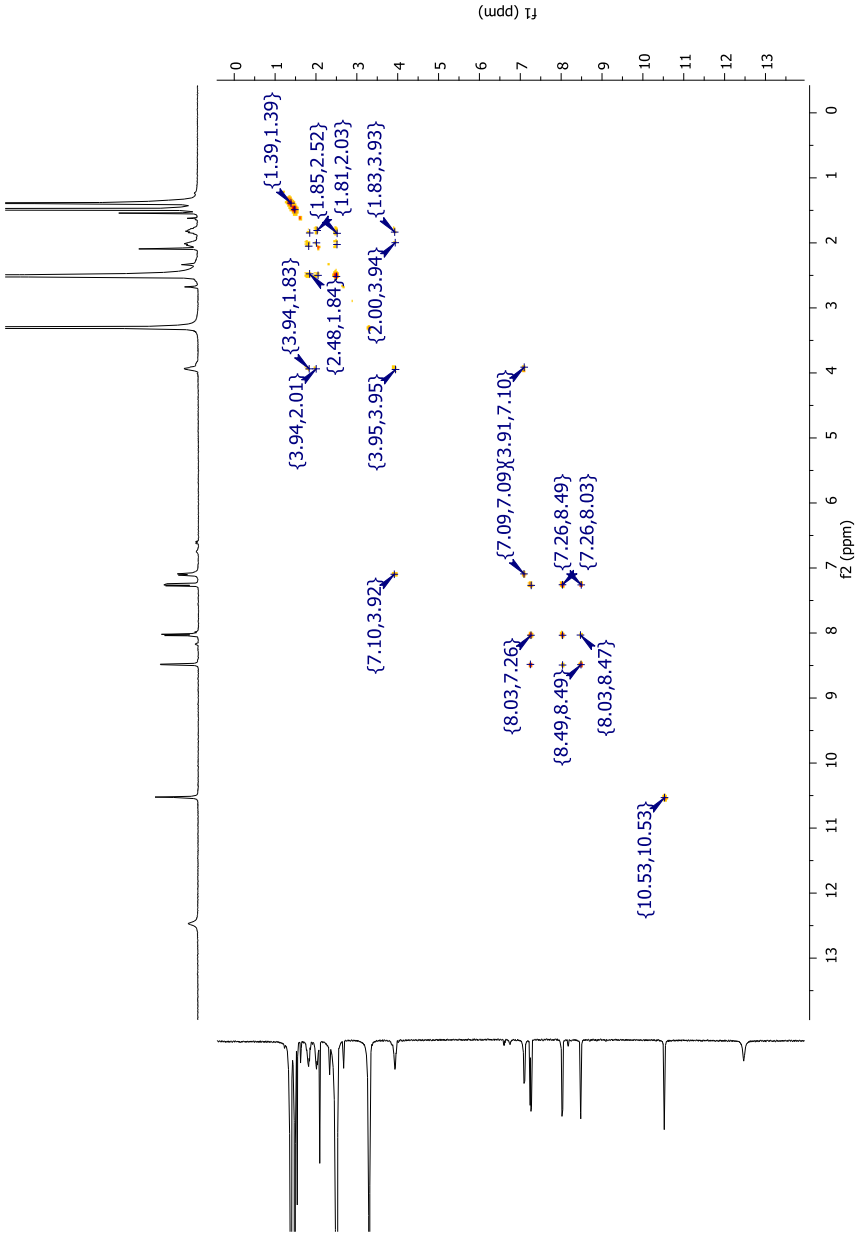
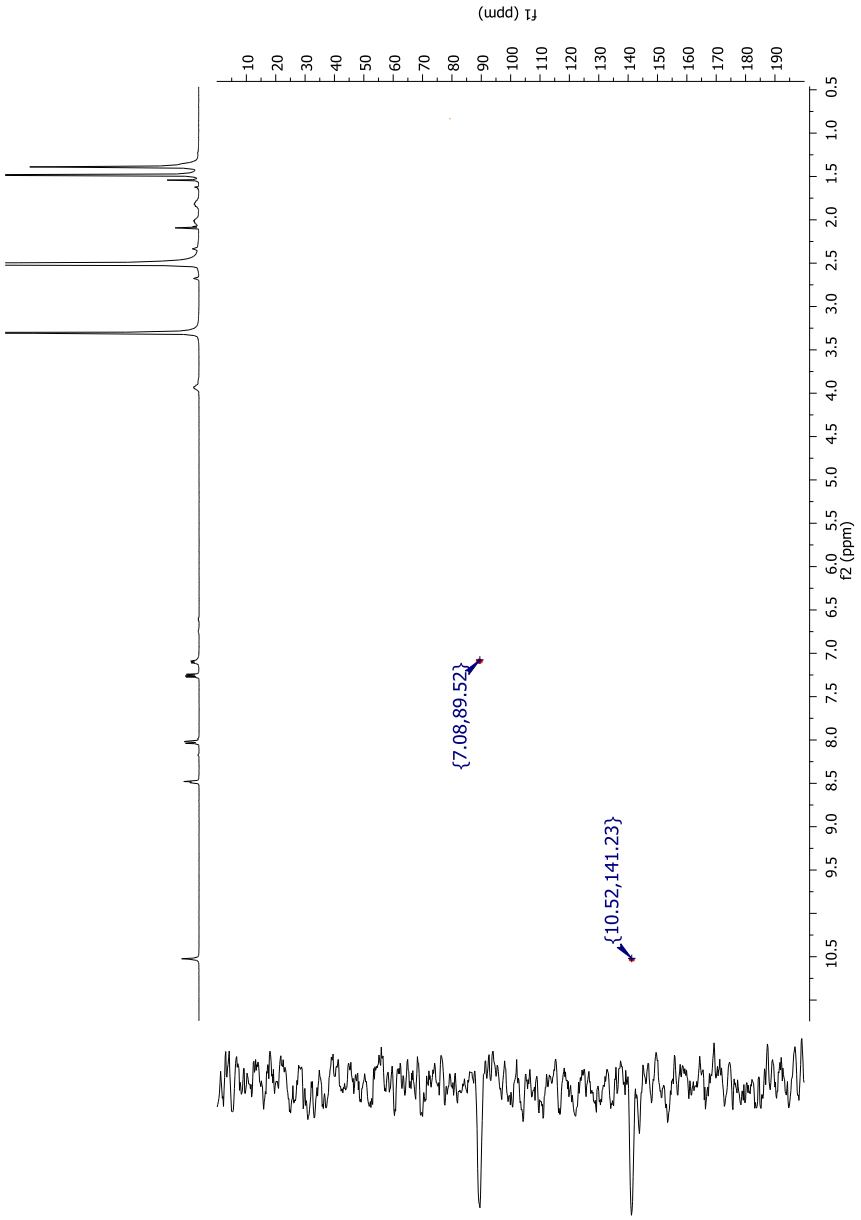


Figure S10. HMBC correlations in DMSO-d_6 distinguishing the position of the *t*Bu-nic group in **L-4o**.

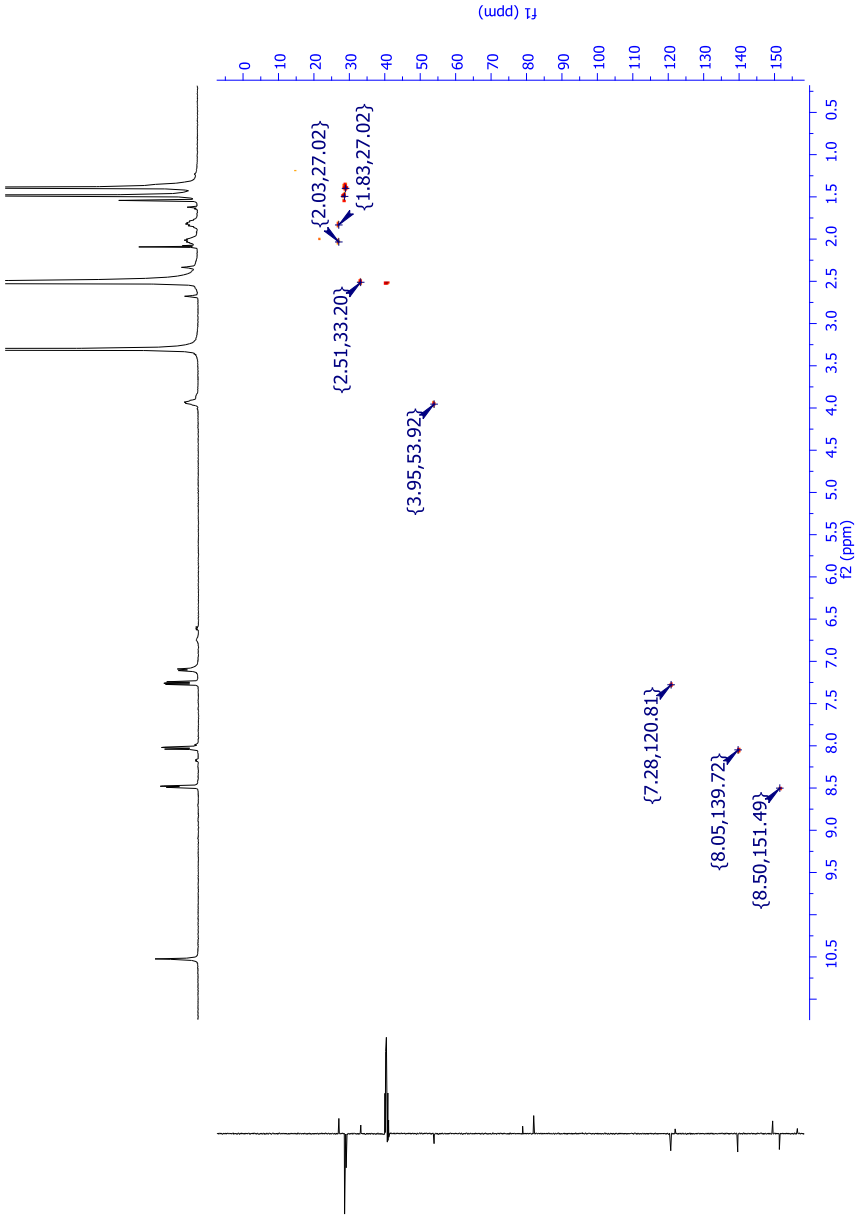
N^2-(*tert*-Butoxycarbonyl)-N^5-(3-(*tert*-butoxycarbonyl)pyridin-2-yl)-L-glutamine (Boc-L-Gln(NH-*t*Bu-nic)-OH, DM613) **L-4o - COSY NMR (400 MHz, DMSO-d_6)**



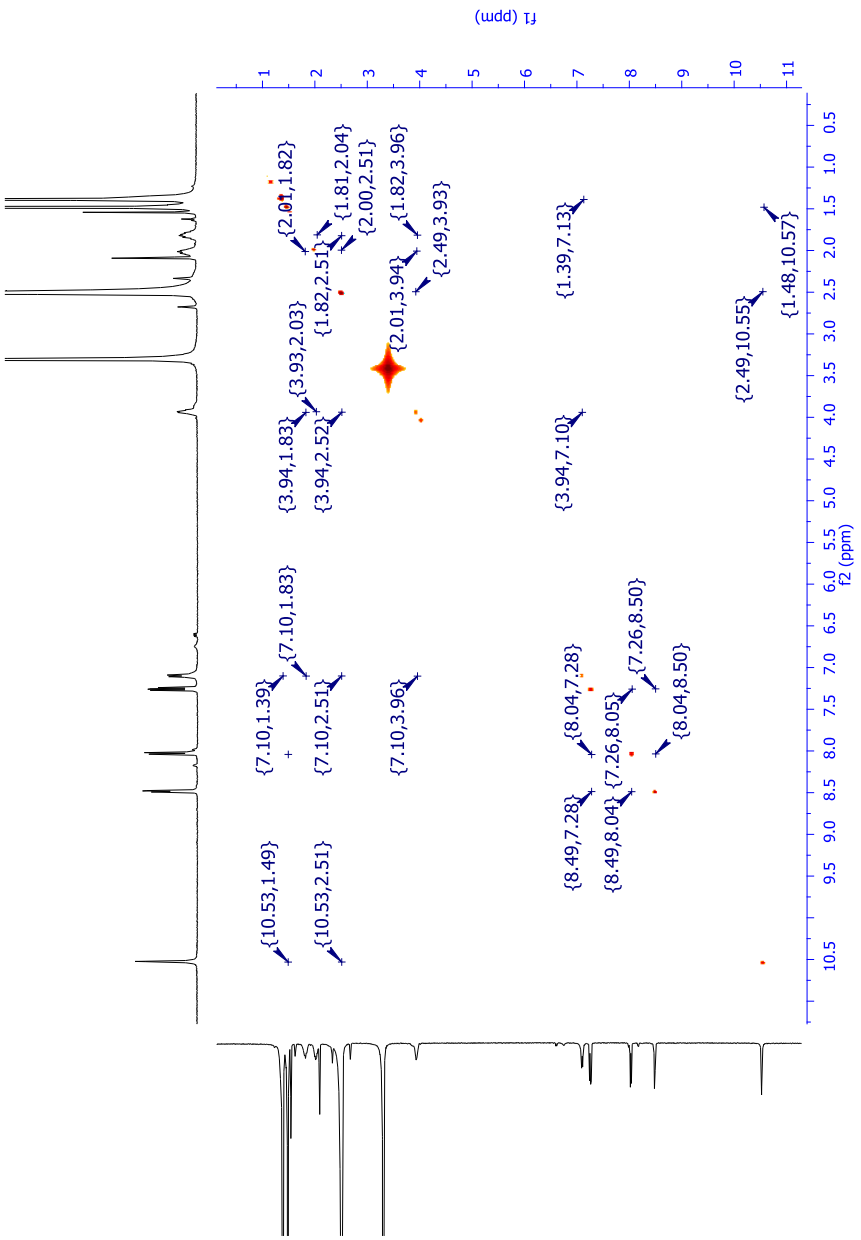
N^2-(*tert*-Butoxycarbonyl)-N^5-(3-(*tert*-butoxycarbonyl)pyridin-2-yl)-L-glutamine (Boc-L-Gln(NH-*t*Bu-nic)-OH, DM613) **L-4o** – **^{15}N HSQC NMR (400 MHz, DMSO-d_6)**



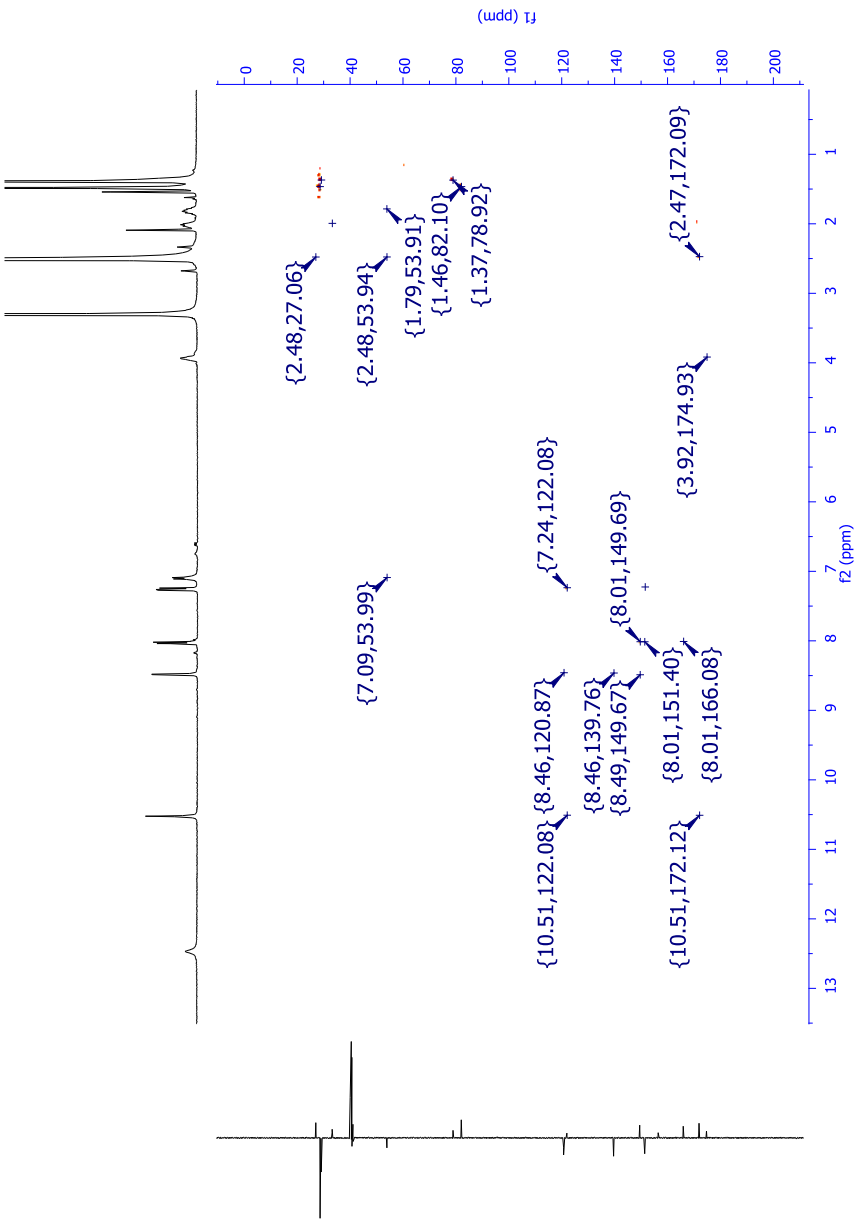
N^2-(*tert*-Butoxycarbonyl)-N^5-(3-(*tert*-butoxycarbonyl)pyridin-2-yl)-L-glutamine (Boc-L-Gln(NH-*t*Bu-nic)-OH, DM613) **L-4o - HSQC NMR (400 MHz, DMSO-d_6)**



N^2-(*tert*-Butoxycarbonyl)-N^5-(3-(*tert*-butoxycarbonyl)pyridin-2-yl)-L-glutamine (Boc-L-Gln(NH-*t*Bu-nic)-OH, DM613) **L-4o - NOESY NMR (400 MHz, DMSO-d_6)**

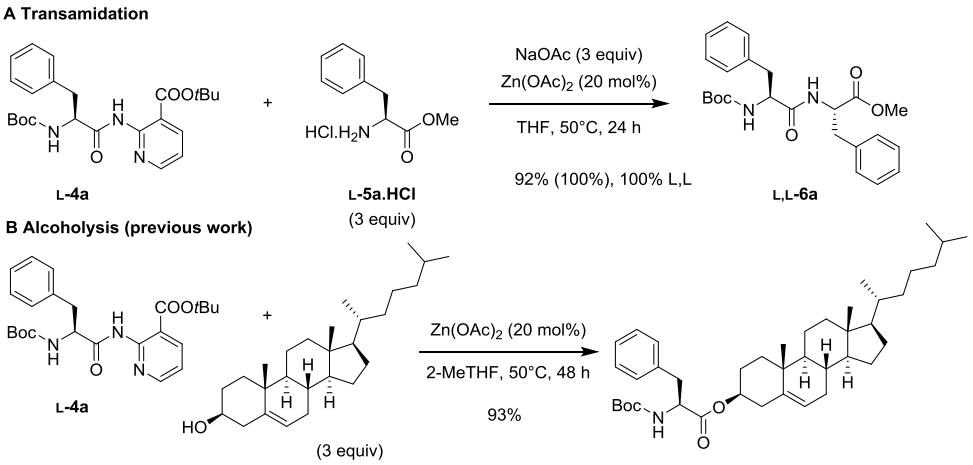


N^2-(*tert*-Butoxycarbonyl)-N^5-(3-(*tert*-butoxycarbonyl)pyridin-2-yl)-L-glutamine (Boc-L-Gln(NH-*t*Bu-nic)-OH, DM613) **L-4o - HMBC NMR (400 MHz, DMSO-d_6)**



3 Comparison of Transamidation and Alcoholysis

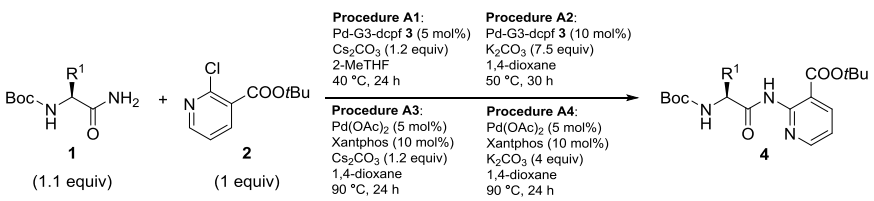
In the model system, the synthesis of Boc-L-Phe-L-Phe-OMe (**L,L-6a**) via transamidation of Boc-L-Phe-NH-*t*Bu-nic (**L-4a**) with H-L-Phe-OMe.HCl (**L-5a.HCl**), optimized conditions involved 1.1 equivalents **L-5a.HCl** and 1.1 equivalents NaOAc with 20 mol% $Zn(OAc)_2$ at 70 °C (see section 1.2). This reaction can also be performed at lower temperature, i.e. 50 °C, as used in the previously reported alcoholysis.[1] The standard amount of alcohol used in the alcoholysis is 3 equivalents (Scheme S2 - B). When the same excess of amine.HCl (3 equivalents **L-5a.HCl** requiring 3 equivalents NaOAc to *in situ* deprotonate) was used in the amide cleavage of the model substrate **L-4a** at 50 °C, full conversion and an excellent isolated yield was also obtained (Scheme S2 - A). Reactions can therefore be performed at a lower temperature provided a larger amount of reactant is used.



Scheme S2. A) Transamidation of Boc-L-Phe-NH-*t*Bu-nic **L-4a** with 3 equiv of H-L-Phe-OMe.HCl **L-5a.HCl** and 3 equiv NaOAc. ^{1}H NMR yield between brackets using 1,3,5-trimethoxybenzene as internal standard. B) Alcoholysis of Boc-L-Phe-NH-*t*Bu-nic **L-4a** with 3 equiv of cholesterol.

4 General procedures

General procedure A: Synthesis of *N*-Boc Protected *t*Bu-nicotinate Functionalized Amino Acid / Peptidic Amides 4



General procedure A1: A flame dried round bottomed flask was charged with Cs_2CO_3 (1.2 equiv), *N*-Boc protected amino acid amide **1** (1.1 equiv), Pd-G3-dcpf **3** (5 mol%) and *tert*-butyl 2-chloronicotinate **2** (1 equiv), dissolved in anhydrous 2-MeTHF (0.167 M). The vial was flushed with argon and then capped. The mixture was vigorously stirred at 40 °C for 24 h. After cooling down to room temperature, the mixture was filtered over celite® and concentrated *in vacuo*. The mixture was purified using automated normal phase flash chromatography and the chiral purity was confirmed using chiral HPLC. Following this procedure, compounds **L-4d**, **L-4f** – **4k**, **L-4m** and **L, L-4n** were obtained.

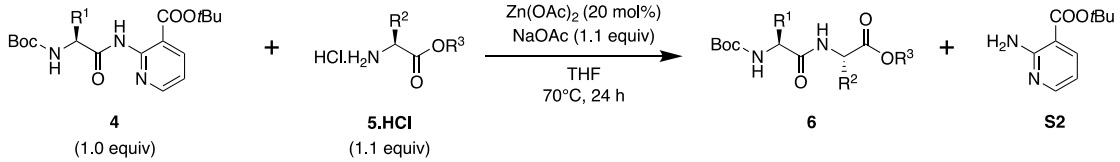
General procedure A2: A flame dried round bottomed flask was charged with K_2CO_3 (7.5 equiv), *N*-Boc protected amino acid amide **1** (1.1 equiv), Pd-G3-dcpf **3** (10 mol%) and *tert*-butyl 2-chloronicotinate **2** (1 equiv), dissolved in anhydrous 1,4-dioxane (0.167 M). The vial was flushed with argon and then capped. The mixture was vigorously stirred at 50°C for 30 h. After cooling down to room temperature, the mixture was filtered over celite® and concentrated *in vacuo*. The mixture was purified using automated normal phase flash chromatography and the chiral purity was confirmed using chiral HPLC. Following this procedure, compounds **L-4a** – **4c**, **L-4e**, and **L-4l** were obtained.

General procedure A3: An oven-dried microwave vial was charged with Boc-L-Gln-OH (1.5 equiv), $Pd(OAc)_2$ (5 mol%), Xantphos (10 mol%), *tert*-butyl 2-chloronicotinate **2** (1 equiv) and anhydrous 1,4-dioxane (0.167 M). While vigorous stirring, Cs_2CO_3 (1.2 equiv) was added and the resulting mixture was flushed with argon and then the vial was capped. The mixture was vigorously stirred at 90°C for 24 h. After cooling down to room temperature, the mixture was purified using automated reversed phase flash chromatography. Following this procedure, compound N^2-(*tert*-Butoxycarbonyl)-N^5-(3-(*tert*-butoxycarbonyl)pyridin-2-yl)-L-glutamine (Boc-L-Gln(NH-*t*Bu-nic)-OH, DM613) **L-4o** was obtained.

General procedure A4: An oven-dried microwave vial was charged with K_2CO_3 (4 equiv), *N*-Boc protected amino acid amide 1 (1.1 equiv), $Pd(OAc)_2$ (5 mol%), Xantphos (10 mol%), *tert*-butyl 2-chloronicotinate **2** (1 equiv) and anhydrous 1,4-dioxane (0.167 M). The vial was flushed with argon and

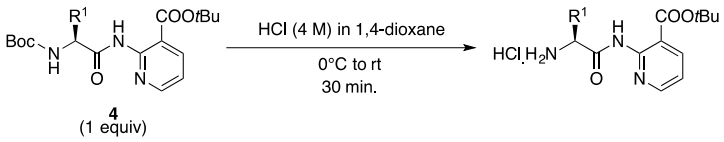
then capped. The mixture was vigorously stirred at 90°C for 24 h. After cooling down to room temperature, the mixture was filtered over celite® and concentrated *in vacuo*. The mixture was purified using automated normal phase flash chromatography and the chiral purity was confirmed using chiral HPLC. Following this procedure, compounds **L-4a** – **L-4k, L-4m** and **L,L-4n** were obtained.

General procedure B: Transamidation of *N*-Boc Protected *t*Bu Nicotinate Functionalized Amino Acid / Peptidic Amides 4



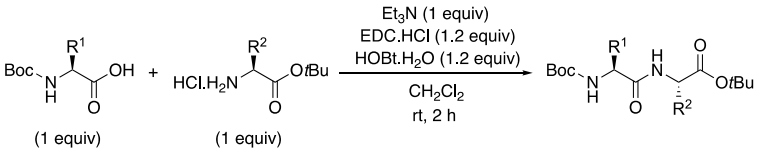
Unless stated otherwise, a microwave vial was charged with $Zn(OAc)_2$ (20 mol%, 0.1 mmol, 18 mg), *N*-Boc protected *t*Bu nicotinate functionalized amino acid amide **4** (1 equiv, 0.5 mmol), **5.HCl** (1.1 equiv, 0.55 mmol), NaOAc (1.1 equiv, 0.55 mmol, 46 mg) and dissolved in THF (1 ml). The mixture was sealed and stirred at 70°C for 24 h. Following, the mixture was concentrated, coated on silica and purified using automated normal phase flash chromatography.

General procedure C: Boc Deprotection of the *N*-Boc Protected *t*Bu Nicotinate Functionalized Amino Acid / Peptidic Amides 4



For the deprotection of the *N*-Boc protected *t*Bu nicotinate functionalized amino acids, a literature procedure was used allowing a Boc deprotection in the presence of *t*Bu ester.[2] In a round-bottom flask equipped with stirring bar, a solution of HCl in dioxane (4 ml, 4 M) was added and cooled down to 0°C. The *N*-Boc protected *t*Bu nicotinate functionalized amino acid **4** (0.2 mmol) was added at once. The mixture was allowed to warm up to room temperature and the mixture was stirred for 30 minutes. The solvent was removed *in vacuo* and the crude was triturated with diethyl ether.

General procedure D: Solution Peptide Synthesis



Unless stated otherwise, a round-bottom flask was charged with *N*-Boc protected amino acid (1 equiv), EDC.HCl (1.2 equiv) $HOBt.H_2O$ (1.2 equiv) in CH_2Cl_2. The solution was stirred at room temperature for 15 minutes. Alongside, *t*Bu amino acid ester hydrochloric acid salt (1 equiv) in CH_2Cl_2 was brought

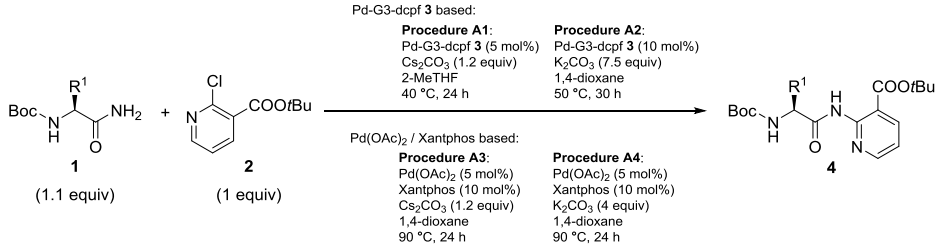
up to pH 9 with Et_3N (1 equiv). This solution was subsequently added to the pre-activated *N*-Boc protected amino acid mixture and the reaction was stirred for 2 h at room temperature. The solvent was removed *in vacuo* and the residue was redissolved in EtOAc. The organic phase was extracted with HCl (3x, 1 M) and $NaHCO_3$ (3 x, sat.), washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*.

5 Synthetic Procedures

5.1 Synthesis of the *N*-Boc Protected *t*Bu Nicotinate Functionalized Amino Acid / Peptidic Amides 4

The synthesis and characterisation of the *N*-Boc *t*Bu nicotinate functionalized amino acid / peptide amides **L-4a**, **L-4d**, **L-4e**, **L-4f**, **L-4g**, **L-4h**, **L-4i**, **L-4j**, **L-4k**, **L,L-4n** has previously been reported by our laboratories.[1] **L-4b**, **L-4c**, **L-4l**, **L-4m**, and **L-4o** have not been reported before. They are all accessed from the *N*-Boc amino acid / peptide amides through Pd-catalyzed coupling with *t*Bu 2-chloronicotinate **2** (see section 4). To increase the yield of Boc-L-Gln(NH-*t*Bu-nic)-OH (**L-4o**), featuring side chain DG introduction, a small optimization was performed (see section 1.3). There are generally two set of conditions, depending on the catalyst used [Pd-G3-dcpf **3** (A1 and A2) or $Pd(OAc)_2$/Xantphos (A3 and A4)]. Both catalysts were used with either Cs_2CO_3 (A1 and A3) or K_2CO_3 (A2 and A4). Generally, with some expections (**L-4d** and **L,L-4n**), conditions A4 based on $Pd(OAc)_2$/Xantphos gave epimerisation. All reaction conditions have been summarized in Table S13, also for those *N*-Boc *t*Bu-nicotinate functionalized amino acid / peptide amides **4** previously prepared. The *N*-Boc amino acid amides **1**, not commercially available, were synthesized based on the commercially available *N*-Boc amino acid precursors, using a literature protocol.[5] The spectroanalytical data and purity were checked and compared with literature characterisations.

Table S13. Synthesis of the *N*-Boc Protected *t*Bu Nicotinate Functionalized Amino Acid / Peptidic Amides **4**

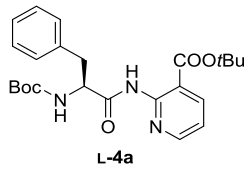


Entry (ELN-code)	Boc-AA-NH-*t*Bu-nic **4**	General Procedure A1 or A2	Yield **4** (%)[a]	%ee[b]	**$[\alpha]_D$**	ELN Code	General Procedure A3 or A4	Yield **4** (%)[a]	%ee[b]
1 (ER489)	Boc-L-Phe-NH-*t*Bu-nic **L-4a**	A2	93	99	-16 (*c* 10 mg/ml, $CHCl_3$, 25°C)	ER1557	A4	96	88
2 (ER804)	Boc-L-Ala-NH-*t*Bu-nic **L-4b**	A2	71	100	-26 (*c* 10 mg/ml, $CHCl_3$, 25°C)	ER1548	A4	96	4
3 (ER803)	Boc-L-Tyr(*t*Bu)-NH-*t*Bu-nic **L-4c**	A2	94	100	-13 (*c* 10 mg/ml, $CHCl_3$, 25°C)	ER1546	A4	99	42
4 (CW-1061)	Boc-L-Pro-NH-*t*Bu-nic **L-4d**	A1	80	100	-95 (*c* 10 mg/ml, $CHCl_3$, 25°C)	LVR0560	A4	91	98
5 (ER1558)	Boc-L-Met-NH-*t*Bu-nic **L-4e**	A2	93[c]	100	-22 (*c* 10 mg/ml, $CHCl_3$, 25°C)	ER1559	A4	94	4
6 (CW-1618)	Boc-βAla-NH-*t*Bu-nic **L-4f**	A1	99[d]	-	-	ER1549	A4	94	-

7 (CW-1124)	Boc-Gly-NH-*t*Bu-nic **L-4g**	A1	83	-	-	ER1559	A4	91	-
8 (ER1538)	Boc-L-Val-NH-*t*Bu-nic **L-4h**	A1	96[d]	96	-14 (*c* 10 mg/ml, $CHCl_3$, 25°C)	ER499	A4	94	93
9 (DM679)	Boc-L-Ile-NH-*t*Bu-nic **L-4i**	A1	82[d]	100[e]	-18 (*c* 10 mg/ml, $CHCl_3$, 27°C).	DM682	A4	79	84[e]
10 (LVR0603)	Boc-L-Ser(*t*Bu)-NH-*t*Bu-nic **L-4j**	A1	72[f]	99	-24 (*c* 10 mg/ml, $CHCl_3$, 27°C)	ER1561	A4	91	40
11 (ER1718)	Boc-L-Lys(Boc)-NH-*t*Bu-nic **L-4k**	A1	79	100	-15 (*c* 10 mg/ml, $CHCl_3$, 20°C)	ER1565	A4	89	48
12 (ER1676)	Boc-L-Cys(*t*Bu)-NH-*t*Bu-nic **L-4l**	A2	89	100	-33 (*c* 10 mg/ml, $CHCl_3$, 21°C)	ER1621	A4	Trace	-
13 (ER1738)	Boc-L-His(trt)-NH-*t*Bu-nic **L-4m**	A1	56[g]	98	-26 (*c* 10 mg/ml, $CHCl_3$, 19°C)	ER1703	A4	73	56
14 (CW-1843)	Boc-L-Pro-L-Leu-Gly-NH-*t*Bu-nic **L,L-4n**	A1	99[d]	100	-102 (*c* 10 mg/ml, $CHCl_3$, 21°C)	DM868	A4	25	100
15	Boc-L-Gln(NH-tBu-nic)-OH **L-4o**	-	-	-	+17 (*c* 10 mg/ml, $CHCl_3$, 25°C)	DM613	A3	60	100

[a] Isolated yield after column chromatography. [b] %ee measured using LC-CD analysis on a Chiralpak IA column, 250 nm, 1 ml/min. [c] T = 60°C. [d] Cs_2CO_3 (2 equiv). [e] %de. [f] K_2CO_3 (6 equiv). [g] 10 mol% Pd-G3-dcpf, 16h, 50v/v% DMF.

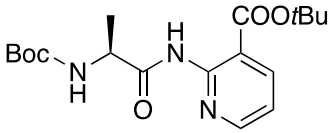
tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-L-phenylalanyl]amino}nicotinate (Boc-L-Phe-NH-*t*Bu-nic, ER489) **L-4a**



L-4a

The title compound was prepared using general procedure **A2,** from Boc-L-Phe-NH_2 (145 mg, 0.55 mmol, 1.1 equiv), K_2CO_3 (0.518 g, 3.75 mmol, 7.5 equiv), Pd-G3-dcpf **3** (52 mg, 0.05 mmol, 10 mol%) and *tert*-butyl 2-chloronicotinate **2** (107 mg, 0.5 mmol, 1 equiv) in anhydrous 1,4-dioxane (3 ml). This yielded, using Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 50:50 over 1 h), the desired compound as a white solid in 93% (207 mg, 0.469 mmol). M.p. 159 °C **^{1}H NMR (400 MHz, $CDCl_3$) δ** 11.28 (br s, 1H), 8.60 (d, *J* = 3.2 Hz, 1H), 8.22 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.26 (d, *J* = 4.3 Hz, 4H) 7.22-7.15 (m, 1H), 7.04 (dd, *J* = 7.7, 4.8 Hz, 1H), 5.18 (br d, *J* = 6.8 Hz, 1H), 4.98 (br s, 1H), 3.28 (dd, *J* = 13.9, 5.8 Hz, 1H), 3.09 (dd, *J* = 12.5, 6.7 Hz, 1H), 1.58 (s, 9H), 1.40 (s, 9H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$) δ** 170.6 (C), 165.8 (C), 155.4 (C), 152.7 (CH), 152.3 (C), 140.2 (CH), 136.8 (C), 129.6 (CH), 128.6 (CH), 126.9 (CH), 118.4 (CH), 112.8 (C), 83.4 (C), 80.0 (C), 56.9 (CH), 38.9 (CH_2), 28.4 (CH_3), 28.2 (CH_3) ppm. **HRMS** (ESI+) m/z calcd. for $C_{24}H_{32}N_3O_5$ $[M+H]^+$: 442.2336, found 442.2322. Spectroscopic data are reported in literature.[1] **$[\alpha]_D$** = -16 (*c* 10 mg/ml, $CHCl_3$, 25°C).
LC-CD analysis on a Chiralpak IA column (retention time = 3.94 min, 250 nm, 1.0 ml/min) revealed 99%ee.

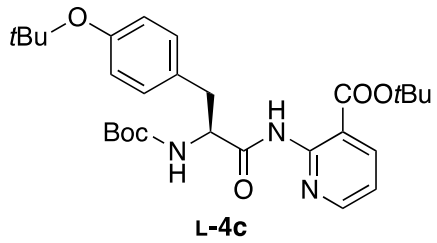
tert-Butyl (*S*)-2-(2-((*tert*-butoxycarbonyl)amino)propanamido)nicotinate (Boc-L-Ala-NH-*t*Bu-nic, ER804) **L-4b**



L-4b

The title compound was prepared using general procedure **A2,** from Boc-L-Ala-NH_2 (214 mg, 1.1 mmol, 1.1 equiv), K_2CO_3 (1.04 g, 7.5 mmol, 7.5 equiv), Pd-G3-dcpf **3** (104 mg, 0.1 mmol, 10 mol%) and *tert*-butyl 2-chloronicotinate **2** (214 mg, 1 mmol, 1 equiv) in anhydrous 1,4-dioxane (6 ml). This yielded, using Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 0:100 over 1 h), the desired compound as a white solid in 71% (260 mg, 0.7 mmol). **^{1}H NMR (500 MHz, $CDCl_3$) δ** 11.34 (br s, 1H), 8.56 (br s, 1H), 8.22 (d, *J* = 6.6 Hz, 1H), 7.02 (br s, 1H), 5.30-5.22 (m, 1H), 4.70-4.62 (m, 1H), 1.57 (s, 9H), 1.47 (d, *J* = 5 Hz, 3H), 1.43 (s, 9H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$) δ** 171.5 (C), 165.8 (C), 155.1 (C), 152.5 (CH), 152.2 (C), 140.0 (CH), 118.2 (CH), 112.7 (C), 83.3 (C), 79.6 (C), 51.4 (CH), 28.3 (CH_3), 28.0 (CH_3), 19.0 (CH_3) ppm. **HRMS** (ESI+) m/z calcd. for $C_{18}H_{28}N_3O_5$ $[M+H]^+$: 366.2024, found 366.2013. No spectroscopic data are reported in literature. **$[\alpha]_D$** = -26 (*c* 10 mg/ml, $CHCl_3$, 25°C).
LC-CD analysis on a Chiralpak IA column (retention time = 3.35 min, 250 nm, 1.0 ml/min) revealed 100%ee.

tert-Butyl (*S*)-2-(3-(4-(*tert*-butoxy)phenyl)-2-((*tert*-butoxycarbonyl)amino)propanamido)nicotinate (Boc-L-Tyr(*t*Bu)-NH-*t*Bu-nic, ER803) **L-4c**

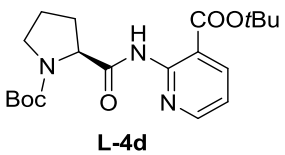


L-4c

The title compound was isolated using general procedure **A2**, from Boc-L-Tyr(*t*Bu)-NH_2 (370 mg, 1.1 mmol, 1.1 equiv), K_2CO_3 (1.03 g, 7.5 mmol, 7.5 equiv), Pd-G3-dcpf **3** (103 mg, 0.1 mmol, 10 mol%) and *tert*-butyl 2-chloronicotinate **2** (214 mg, 1 mmol, 1 equiv) in anhydrous 1,4-dioxane (6 ml). The reaction mixture was purified using the Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 0:100 over 1 h) to obtain a white solid in 94% (481 mg, 0.93 mmol) yield. **^{1}H NMR (500 MHz, $CDCl_3$) δ** 11.28 (br s, 1H), 8.59 (d, *J* = 4.2 Hz, 1H), 8.21 (dd, *J* = 1.3, 7.8 Hz, 1H), 7.14 (d, *J* = 8.5 Hz, 2H), 7.03 (dd, *J* = 4.8, 7.7 Hz, 1H), 6.87 (d, *J* = 8.3 Hz, 2H), 5.23-5.10 (m, 1H), 4.93 (br s, 1H), 3.24 (dd, *J* = 5.6, 14.2 Hz, 1H), 3.02 (dd, *J* = 7.1, 12.7 Hz, 1H), 1.58 (s, 9H), 1.40 (s, 9H), 1.28 (s, 9H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$) δ** 170.6 (C), 165.8 (C), 155.4 (C), 154.3 (C), 152.6 (CH), 152.2, (C) 140.1 (CH) , 131.5 (C), 129.9 (CH), 124.2 (CH), 118.4 (CH), 112.9 (C), 83.4 (C), 79.8 (C), 78.3 (C), 57.0 (CH), 38.3 (CH_2), 28.9 (CH_3), 28.4 (CH_3), 28.2 (CH_3) ppm. **HRMS** (ESI+) m/z calcd. for $C_{28}H_{40}N_3O_6$ $[M+H]^+$: 514.2911 found 514.2933. **$[\alpha]_D$** = -13 (*c* 10 mg/ml, $CHCl_3$, 25°C). No spectroscopic data are reported in literature.

LC-CD analysis on a Chiralpak IA column (retention time = 3.87 min, 250 nm, *n*-hexane:EtOH 80:20, 1.0 ml/min) revealed 100%ee.

tert-Butyl 2-{[1-(*tert*-butoxycarbonyl)-L-prolyl]amino}nicotinate (Boc-L-Pro-NH-*t*Bu-nic, CW-1061) **L-4d**



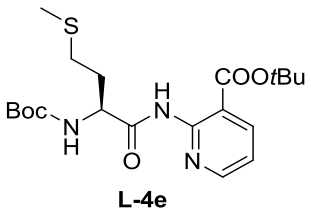
L-4d

The title compound was isolated using general procedure **A1**, from Boc-L-Pro-NH_2 (1.178 g, 5.5 mmol, 1.1 equiv), Cs_2CO_3 (1.955 g, 6.0 mmol, 1.2 equiv), Pd-G3-dcpf **3** (257 mg, 0.250 mmol, 5 mol%), and *tert*-butyl 2-chloronicotinate **2** (1.068 mg, 5.0 mmol, 1 equiv) in anhydrous 2-MeTHF (30.0 ml). The reaction mixture was purified using the Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 40:60 over 1 h) to obtain a brown solid in 80% (1.566 g, 4.00 mmol) yield. M.p. 98°C. **^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers) δ** 11.54 (br s, 0.6H), 11.46 (br s, 0.4H), 8.58 (br s, 1H), 8.22 (br s, 0.4H), 8.20 (br s, 0.6H), 7.01 (d, *J* = 4.8 Hz, 1H), 4.56 (br s, 0.3H), 4.36 (br s, 0.6H), 3.74-3.33 (m, 2H), 2.36-2.09 (m, 2H), 2.01-1.81 (m, 2H), 1.54 (s, 9H), 1.45 (s, 3H), 1.32 (s, 6H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$, mixture of rotamers) δ** [171.6, 171.1 (C)], 166.0 (C), [155.1, 154.2 (C)], [152.9, 152.7 (CH)], 152.2 (C), 140.0 (CH), [118.6, 118.1 (CH)], [113.0, 112.8 (C)], [83.5, 83.0 (C)], [80.3, 80.0 (C)], [62.9, 62.2 (CH)], [47.3, 46.9 (CH_2)], [31.6,

30.5 (CH_2)], [28.6, 28.3 (CH_3)], 28.1 (CH_3), [24.3, 23.8 (CH_2)] ppm. Spectroscopic data are reported in literature.[1] **HRMS** (ESI+) m/z calcd. for $C_{20}H_{30}N_3O_5$ $[M+H]^+$: 392.2180 found 392.2179 **$[\alpha]_D$** = -95 (*c* 10 mg/ml, $CHCl_3$, 25°C).

LC-CD analysis on a Chiralpak IA column (retention time = 3.33 min, 250 nm, 1.0 ml/min) revealed 100%ee.

tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-L-methionyl]amino}nicotinate (Boc-L-Met-NH-*t*Bu-nic, ER1558) **L-4e**

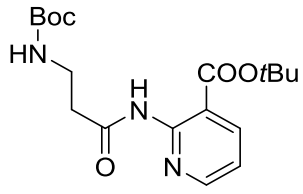


L-4e

The title compound was prepared using general procedure **A2,** from Boc-L-Met-NH_2 (273 mg, 1.1 mmol, 1.1 equiv), K_2CO_3 (1.037 g, 7.5 mmol, 7.5 equiv), Pd-G3-dcpf **3** (104 mg, 0.1 mmol, 10 mol%) and *tert*-butyl 2-chloronicotinate **2** (214 mg, 1.0 mmol, 1 equiv) in anhydrous 1,4-dioxane (6 ml). This yielded, using Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 50:50 over 1 h), the desired compound as a white solid in 93% (396 mg, 0.932 mmol). M.p. 117 °C **^{1}H NMR (400 MHz, $CDCl_3$) δ** 11.34 (br s, 1H), 8.56 (dd, *J* = 7.0, 1.6 Hz, 1H), 8.23 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.04 (dd, *J* = 7.8, 4.8 Hz, 1H), 5.38 (br d, *J* = 7.3 Hz, 1H), 4.86 (br s, 1H), 2.68-2.56 (m, 2H), 2.33-2.22 (m, 1H), 2.09 (s, 3H), 2.00-1.89 (m, 1H), 1.59 (s, 9H), 1.44 (s, 9H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$) δ** 170.9 (C), 166.0 (C), 155.6 (C), 152.6 (CH), 152.2 (C), 140.2 (CH), 118.5 (CH), 113.0 (C), 83.6 (C), 80.0 (C), 55.1 (CH), 32.8 (CH_2), 30.4 (CH_2), 28.4 (CH_3), 28.2 (CH_3), 15.4 (CH_3) ppm. **HRMS** (ESI+) m/z calcd. for $C_{26}H_{43}N_4O_7$ $[M+H]^+$: 523.3126, found 523.3126. Spectroscopic data are reported in literature.[1] **$[\alpha]_D$** = -22 (*c* 10 mg/ml, $CHCl_3$, 25°C).

LC-CD analysis on a Chiralpak IA column (retention time = 7.0 min, 250 nm, 1.0 ml/min) revealed 100%ee.

tert-Butyl 2-{3-[(*tert*-butoxycarbonyl)amino]propanamido}nicotinate (Boc-βAla-NH-*t*Bu-nic, CW-1618) **4f**

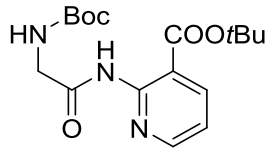


4f

The title compound was isolated using general procedure **A1**, from , Boc-βAla-NH_2 (1.035 g, 5.5 mmol, 1.1 equiv), Cs_2CO_3 (3.26 g, 10.0 mmol, 2.0 equiv), Pd-G3-dcpf **3** (257 mg, 0.250 mmol, 5 mol%), and *tert*-butyl 2-chloronicotinate **2** (1.068 mg, 5.0 mmol, 1 equiv) in anhydrous 2-MeTHF (30.0 ml). The reaction mixture was purified using the Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 25:75 over 1 h) to obtain a white solid in 99% (1.820 g, 4.99 mmol) yield. M.p. 99°C **^{1}H NMR (400 MHz, $CDCl_3$) δ** 10.93 (br s,

1H), 8.53 (dd, *J* = 4.8, 1.9 Hz, 1H), 8.23 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.02 (dd, *J* = 7.9, 4.8 Hz, 1H), 5.35 (br s, 1H), 3.50 (q, *J* = 5.8 Hz, 2H), 2.89 (t, *J* = 5.6 Hz, 2H), 1.59 (s, 9H), 1.41 (s, 9H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$) δ** 171.5 (C), 166.0 (C), 156.1 (C), 152.5 (CH), 152.4 (C), 140.3 (CH), 118.2 (CH), 112.6 (C), 83.6 (C), 79.1 (C), 38.4 (CH_2), 36.2 (CH_2), 28.5 (CH_3), 28.2 (CH_3) ppm. Spectroscopic data are reported in literature.[1] **HRMS** (ESI+) m/z calcd. for $C_{18}H_{28}N_3O_5$ $[M+H]^+$: 366.2023 found 366.2022.

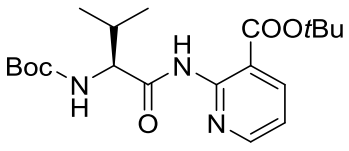
tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)glycyl]amino}nicotinate (Boc-Gly-NH-*t*Bu-nic, CW-1124) **4g**



4g

The title compound was isolated using general procedure **A1**, from , Boc-Gly-NH_2 (0.958 g, 5.5 mmol, 1.1 equiv), Cs_2CO_3 (1.955 g, 6.0 mmol, 1.2 equiv), Pd-G3-dcpf **3** (257 mg, 0.250 mmol, 5 mol%), and *tert*-butyl 2-chloronicotinate **2** (1.068 g, 5.0 mmol, 1 equiv) in anhydrous 2-MeTHF (30.0 ml). The reaction mixture was purified using the Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 30:70 over 1 h) to obtain a white solid in 83% (1.49 g, 4.25 mmol) yield. M.p. 129°C **^{1}H NMR (400 MHz, $CDCl_3$) δ** 11.19 (br s, 1H), 8.51 (dd, *J* = 4.8, 1.4 Hz, 1H), 8.24 (dd, *J* = 7.9, 1.9 Hz, 1 H), 7.02 (dd, *J* = 7.8, 4.8 Hz, 1H), 5.43 (br s, 1H), 4.45 (br d, *J* = 4.1 Hz, 2H), 1.60 (s, 9H), 1.47 (s, 9H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$) δ** 169.9 (C), 165.8 (C), 156.0 (C), 152.4 (CH), 152.2 (C), 140.4 (CH), 118.2 (CH), 112.3 (C), 83.6 (C), 79.9 (C), 46.8 (CH_2), 28.5 (CH_3), 28.2 (CH_3) ppm. Spectroscopic data are reported in literature.[1] **HRMS** (ESI+) m/z calcd. for $C_{17}H_{26}N_3O_5$ $[M+H]^+$: 352.1867 found 352.1859.

tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-L-valyl]amino}nicotinate (Boc-L-Val-NH-*t*Bu-nic, ER1538) **L-4h**

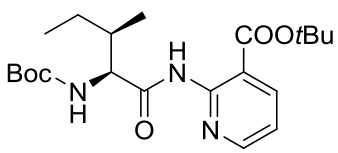


L-4h

The title compound was isolated using general procedure **A1**, from Boc-L-Val-NH_2 (1.190 g, 5.5 mmol, 1.1 equiv), Cs_2CO_3 (3.26 g, 10.0 mmol, 2.0 equiv), Pd-G3-dcpf **3** (257 mg, 0.250 mmol, 5 mol%), and *tert*-butyl 2-chloronicotinate **2** (1.068 g, 5.0 mmol, 1 equiv) in anhydrous 2-MeTHF (30.0 ml). The reaction mixture was purified using the Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 40:60 over 1 h) to obtain a white solid in 96% (1.896 g, 4.82 mmol) yield. M.p. 132°C. **^{1}H NMR (400 MHz, $CDCl_3$) δ** 11.30 (br s, 1H), 8.57 (dd, *J* = 4.4, 1.3 Hz, 1H), 8.22 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.02 (dd, *J* = 7.8, 4.8 Hz, 1H), 5.25 (br d, *J* = 8.5 Hz, 1H), 4.53 (br s, 1H), 2.37 – 2.24 (m, 1H), 1.58 (s, 9H), 1.44 (s, 9H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.94 (d, J = 6.9 Hz, 3H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$) δ** 170.6 (C), 166.0 (C), 156.0 (C), 152.7 (CH), 152.3 (C), 140.1 (CH), 118.4 (CH), 112.9 (C), 83.5 (C), 79.7 (C), 60.7 (CH), 31.1 (CH), 28.4 (CH_3), 28.2

(CH_3), 19.6 (CH_3), 17.2 (CH_3) ppm. Spectroscopic data are reported in literature.[1] **HRMS** (ESI+) m/z calcd. for $C_{20}H_{32}N_3O_5$ $[M+H]^+$: 394.2336 found 394.2339 **$[\alpha]_D$** = -14 (*c* 10 mg/ml, $CHCl_3$, 25°C).
LC-CD analysis on a Chiralpak IA column (retention time = 8.6 min, 250 nm, 1.0 ml/min) revealed 96%ee.

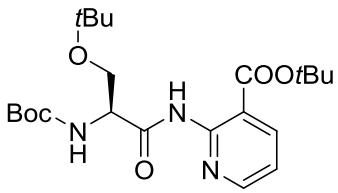
tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-L-isoleucyl]amino}nicotinate (Boc-L-Ile-NH-*t*Bu-nic, DM679) **L-4i**



L-4i

The title compound was isolated using general procedure **A1**, from Boc-L-Ile-NH_2 (0.760 g, 3.3 mmol, 1.1 equiv), Cs_2CO_3 (1.955 g, 6.0 mmol, 2.0 equiv), Pd-G3-dcpf **3** (143 mg, 0.150 mmol, 5 mol%), and *tert*-butyl 2-chloronicotinate **2** (0.641 g, 3.0 mmol, 1 equiv) in anhydrous 2-MeTHF (19.0 ml). The reaction mixture was purified using the Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 0:100 over 1 h) to obtain a colorless oil in 82% (1.00 g, 2.45 mmol) yield. **^{1}H NMR (400 MHz, $CDCl_3$) δ** 11.31 (br s, 1H), 8.56 (dd, *J* = 4.5, 1.4 Hz, 1H), 8.20 (dd, *J* = 7.9 Hz, 1.8 Hz, 1H), 7.01 (dd, *J* = 7.8, 4.8 Hz), 5.22 (br d, *J* = 8.6 Hz, 1H), 4.48 (br s, 1H), 2.09 - 1.95 (m, 1H), 1.56 (s, 9H), 1.54 – 1.47 (m, 1H) 1.42 (s, 9H), 1.19 - 1.07 (m, 1H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.89 (t, *J* = 7.4 Hz, 3H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$) δ** 170.4 (C), 166.0 (C), 155.9 (C), 152.7 (CH), 152.2 (C), 140.0 (CH), 118.4 (CH), 113.0 (C), 83.4 (C), 79.7 (C), 60.5 (CH), 37.8 (CH), 28.4 (CH_3), 28.1 (CH_3), 24.4 (CH_2), 15.8 (CH_3), 11.8 (CH_3) ppm. Spectroscopic data are reported in literature.[1] **HRMS** (ESI+) m/z calcd. for $C_{21}H_{34}N_3O_5$ $[M+H]^+$: 408.2493 found 408.2506. **$[\alpha]_D$** = -18 (*c* 10 mg/ml, $CHCl_3$, 27°C).

tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-*O*-*tert*-butyl-L-seryl]amino} nicotinate (Boc-L-Ser(*t*Bu)-NH-*t*Bu-nic, LVR0603) **L-4j**



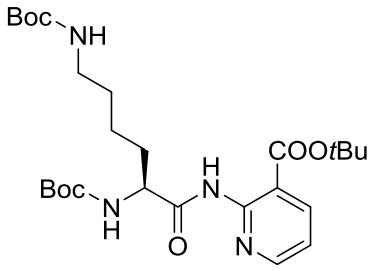
L-4j

The title compound was isolated using general procedure **A2**, from Boc-L-Ser(*t*Bu)-NH_2 (0.141 g, 0.55 mmol, 1.1 equiv), K_2CO_3 (0.416 g, 3.0 mmol, 6.0 equiv), Pd-G3-dcpf **3** (51 mg, 0.05 mmol, 10 mol%), and *tert*-butyl 2-chloronicotinate **2** (0.107 g, 0.5 mmol, 1 equiv) in anhydrous 1,4-dioxane (3 ml). The reaction mixture was purified using the Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 60:40 over 1 h) to obtain a brown oil in 72% (0.158 g, 0.36 mmol) yield. **^{1}H NMR (400 MHz, $CDCl_3$) δ** 11.44 (br s, 1H), 8.54 (dd, *J* = 3.0 Hz, 1H), 8.18 (d, *J* = 7.0 Hz, 1H), 6.98 (dd, *J* = 7.4, 4.9 Hz, 1H), 5.53 (br d, *J* = 5.2 Hz, 1H), 4.48 (br s, 1H), 3.87 (br s, 1H), 3.52 (br s, 1H), 1.54 (s, 9H), 1.42 (s, 9H), 1.10 (s, 9H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$) δ** 169.2 (C), 165.7 (C), 155.6 (C), 152.6 (CH), 152.2 (C), 139.9 (CH), 118.3 (CH),

113.2 (C), 83.0 (C), 79.8 (C), 73.6 (C), 62.0 (CH_2), 56.2 (CH), 28.4 (CH_3), 28.1 (CH_3), 27.3 (CH_3) ppm. Spectroscopic data are reported in literature.[1] **HRMS** (ESI+) m/z calcd. for $C_{22}H_{36}N_3O_6$ $[M+H]^+$: 438.2599 found 438.2588. **$[\alpha]_D$** = -24 (*c* 10 mg/ml, $CHCl_3$, 27°C).

LC-CD analysis on a Chiralpak IA column (retention time = 3.02 min, 250 nm, 1.0 mL/min) revealed 99% ee.

tert-Butyl 2-{[N^2,N^6-bis(*tert*-butoxycarbonyl)-L-lysyl]amino} nicotinate (Boc-L-Lys(Boc)-NH-*t*Bu-nic, ER1718) **L-4k**

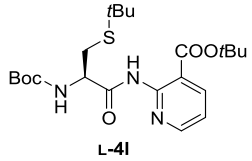


L-4k

The title compound was isolated using general procedure **A1**, from Boc-L-Lys(Boc)-NH_2 (0.380 g, 1.1 mmol, 1.1 equiv), Cs_2CO_3 (0.391 g, 1.2 mmol, 1.2 equiv), Pd-G3-dcpf **3** (52 mg, 0.050 mmol, 5 mol%), and and *tert*-butyl 2-chloronicotinate **2** (214 mg, 1.0 mmol, 1 equiv) in anhydrous 2-MeTHF (3.0 ml). The reaction mixture was purified using the Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 50:50 over 1 h) to obtain a white solid in 78% (0.406 g, 0.778 mmol) yield. M.p. 162°C. **^{1}H NMR (400 MHz, $CDCl_3$) δ** 11.31 (br s, 1H), 8.56 (d, *J* = 3.2 Hz, 1H), 8.23 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.03 (dd, J= 7.8, 4.8 Hz, 1H), 5.33 (br d, *J* = 4.7 Hz, 1H), 4.70 (br s, 1H), 4.62 (br s, 1H), 3.18-3.02 (m, 2H), 2.04-1.90 (m, 1H), 1.77 - 1.63 (m, 2H), 1.59 (s, 9H), 1.45 (s, 9H), 1.55 - 1.47 (m, 3H), 1.41 (s, 9H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$) δ** 171.3 (C), 166.0 (C), 156.2 (C), 155.8 (C), 152.7 (CH), 152.4 (C), 140.2 (CH), 118.4 (CH), 112.9 (C), 83.6 (C), 79.9 (C), 79.1 (C), 55.6 (CH), 40.3 (CH_2), 32.8 (CH_2), 29.6 (CH_2), 28.6 (CH_3), 28.5 (CH_3), 28.2 (CH_3), 22.6 (CH_2) ppm. Spectroscopic data are reported in literature.[1] **HRMS** (ESI+) m/z calcd. for $C_{26}H_{43}N_4O_7$ $[M+H]^+$: 523.3126 found 523.3126 **$[\alpha]_D$** = -15 (*c* 10 mg/ml, $CHCl_3$, 20°C).

LC-CD analysis on a Chiralpak IA column (retention time = 4.25 min, 250 nm, 1.0 mL/min) revealed 100% ee.

tert-Butyl (*R*)-2-(2-((*tert*-butoxycarbonyl)amino)-3-(*tert*-butylthio)propanamido)nicotinate (Boc-L-Cys(*t*Bu)-NH-*t*Bu-nic, ER1625/ER1676) **L-4l**



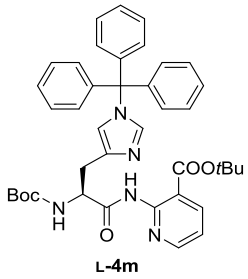
L-4l

The title compound was isolated using general procedure **A2**, from Boc-L-Cys(*t*Bu)-NH_2 (0.304 mg, 1.1 mmol, 1.1 equiv), K_2CO_3 (1.03 g, 7.5 mmol, 7.5 equiv), Pd-G3-dcpf **3** (103 mg, 0.1 mmol, 10 mol%) and *tert*-butyl 2-chloronicotinate **2** (214 mg, 1 mmol, 1 equiv) in anhydrous 1,4-dioxane (6 ml). The reaction mixture was purified using the Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 50:50 over 1 h) to obtain a brown oil in 89% (405 mg, 0.89 mmol) yield. **^{1}H NMR (400 MHz, $CDCl_3$) δ** 11.49 (br s, 1H), 8.59 (dd, *J* = 4.7, 1.8 Hz, 1H), 8.24

(dd, *J* = 7.9, 1.9 Hz, 1H), 7.04 (dd, *J* = 7.8, 4.8 Hz, 1H), 5.48 (br s, 1H), 4.79 (br s, 1H), 3.07 (d, *J* = 5.3 Hz, 2H), 1.60 (s, 9H), 1.4 (s, 9H), 1.33 (s, 9H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$) δ** 169.5 (C), 165.9 (C), 152.8 (CH), 152.3 (C), 140.1 (CH), 118.5 (CH), 113.2 (C), 83.4 (C), 80.1 (C), 55.8 (CH), 42.9 (C), 31.3 (CH_2), 31.0 (CH_3), 28.5 (CH_3), 28.2 (CH_3) ppm. **HRMS** (ESI+) m/z calcd. for $C_{28}H_{40}N_3O_6$ $[M+H]^+$: 454.2371 found 454.2376. **$[\alpha]_D$** = -33 (*c* 10 mg/ml, $CHCl_3$, 21°C).

LC-CD analysis on a Chiralpak IA column (retention time = 3.87 min, 250 nm, *n*-hexane:EtOH 80:20, 1.0 ml/min) revealed 100%ee.

tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-1-(triphenylmethyl)-L-histidyl]amino}pyridine-3-carboxylate (Boc-L-His(Trt)-NH-*t*Bu-nic, ER1738) **L-4m**

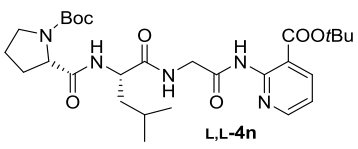


L-4m

The title compound was isolated using a slightly modified general procedure **A1**, from Boc- L-His(Trt)-NH_2 (0.273 g, 0.55 mmol, 1.1 equiv), Cs_2CO_3 (0.195 g, 0.6 mmol, 1.2 equiv), Pd-G3-dcpf **3** (52 mg, 0.05 mmol, 10 mol%), and *tert*-butyl 2-chloronicotinate **2** (107 mg, 0.5 mmol, 1 equiv) in a mixture of anhydrous 2-MeTHF and DMF (1:1 v/v, 3.13 ml). The reaction mixture was stirred at 40 °C for 16h. The reaction mixture was purified using the Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 0:100 over 1 h) to obtain a brown oil in 56% (188 mg, 0.28 mmol) yield. **^{1}H NMR (400 MHz, $CDCl_3$) δ** 11.48 (s, 1H), 8.56 (d, *J* = 2.8 Hz, 1H), 8.23 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.36 (s, 1H), 7.30 – 7.18 (m, 9H), 7.05 (d, *J* = 7.0 Hz, 7H), 6.68 (s, 1H), 6.47 (d, *J* = 5.9 Hz, 1H), 4.73 (s, 1H), 3.22 (dd, *J* = 9.4, 8.3 Hz, 1H), 3.10 (dd, *J* = 14.1, 4.0 Hz, 1H), 1.56 (s, 9H), 1.45 (s, 9H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$) δ** 170.3 (C), 165.5 (C), 155.8 (C), 152.5 (C), 152.2 (CH), 142.3 (C), 139.8 (CH), 138.5 (CH), 136.6 (C), 129.7 (CH), 127.9 (CH), 127.9 (CH), 119.7 (CH), 118.1 (CH), 113.2 (C), 82.9 (C), 79.5 (C), 75.2 (C), 56.3 (CH), 30.2 (CH_2), 28.4 (CH_3), 28.0 (CH_3) ppm. No spectroscopic data are reported in literature. **HRMS** (ESI+) m/z calcd. for $C_{40}H_{44}N_5O_5$ $[M+H]^+$: 674.3337 found 674.3347 **$[\alpha]_D$** = -26 (*c* 10 mg/ml, $CHCl_3$, 19°C).

LC-CD analysis on a Chiralpak IA column (retention time = 8.58 min, 250 nm, *n*-hexane:*i*PrOH 65:35, 1.0 ml/min) revealed 98% ee.

1-(*tert*-Butoxycarbonyl)-L-prolyl-L-leucyl-*N*-[3-*tert*-butyoxycarbonyl)pyridin-2-yl)]glycinamide (Boc-L-Pro-L-Leu-Gly-NH-*t*Bu-nic, CW-1843) **L,L-4n**

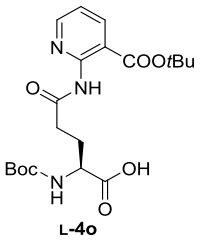


L,L-4n

The title compound was isolated using general procedure **A1**, from Boc-L-Pro-L-Leu-Gly-NH_2 (1.230 g, 3.20 mmol, 1.1 equiv), Cs_2CO_3 (7.11 g, 21.81mmol, 7.5 equiv), Pd-G3-dcpf **3** (299 mg, 0.291 mmol, 10 mol%), and *tert*-butyl 2-chloronicotinate **2** (621 mg, 2.91mmol, 1 equiv) in anhydrous 2-MeTHF (20.0 ml). The

reaction mixture was purified using the Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 0:100 over 1 h) to obtain a white solid in 99% (1.625 g, 2.90 mmol) yield. M.p. 182°C. **^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers) δ** 11.16 (br s, 1H), 8.54 (dd, *J* = 4.6, 1.0 Hz, 1H), 8.24 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.33 (br s, 0.6H), 7.08 (br s, 0.4H), 7.03 (dd, *J* = 7.8, 4.8 Hz, 1H), 6.86 (br s, 0.4H), 6.47 (br s, 0.5H), 4.59 (br, 1H), 4.49 (dd, *J* = 18.5, 5.1 Hz, 1H), 4.31 (br s, 2H), 3.42 (br s, 2H), 2.26 (br, 1H), 2.07 (br, 1H), 1.90 (br s, 3H), 1.69-1.63 (m, 1H), 1.61 (s, 9H), 1.43 (s, 9H), 0.93 (t, *J* = 6.1 Hz, 6H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$) δ** 172.7 (C), 172.3 (C), 168.6 (C), 165.8 (C), 156.3 (C), 152.6 (CH), 152.1 (C), 140.4 (CH), 118.3 (CH), 112.2 (C), 83.5 (C), 80.9 (C), 60.7 (CH), 51.7 (CH), 47.4 (CH_2), 45.4 (CH_2), 40.4 (CH_2), 32.0 (CH_2), 29.8 (CH_2), 29.4 (CH_2), 28.4 (CH_3), 28.2 (CH_3), 25.0 (CH_3), 21.5 (CH) ppm. Spectroscopic data are reported in literature.[1] **HRMS** (ESI+) m/z calcd. for $C_{28}H_{44}N_5O_7$ $[M+H]^+$: 562.3235 found 562.3221. **$[\alpha]_D$** = -102 (*c* 10 mg/ml, $CHCl_3$, 21°C).

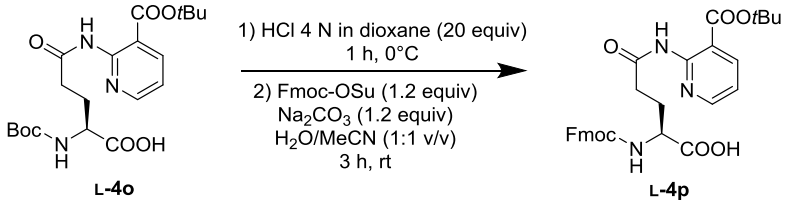
N^2-(*tert*-Butoxycarbonyl)-N^5-(3-(*tert*-butoxycarbonyl)pyridin-2-yl)-L-glutamine (Boc-L-Gln(NH-*t*Bu-nic)-OH, DM613) **L-4o**



L-4o

The title compound was isolated using general procedure **A3**, from Boc-L-Gln-OH (369 mg, 1.5 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol, 5 mol%), 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (58 mg, 0.1 mmol, 10 mol%), *tert*-butyl 2-chloronicotinate **2** (214 mg, 1 mmol) and anhydrous 1,4-dioxane (1.3 ml). While vigorous stirring, Cs_2CO_3 (391 mg, 1.2 mmol) was added and the resulting mixture was flushed with argon. The mixture was vigorously stirred at 90°C for 24 h. After cooling down to room temperature, EtOAc was added and the mixture was purified with Combiflash® RF200 reverse phase silica gel flash chromatography (Water + 1% formic acid:Acetonitrile, 100:0 to 0:100 in 80 min) (Chromabond®Flash RS25 C18 Cartridges, 25 g, 25/67mL; flow rate 18 mL/min, max. operating pressure 150 psi - 10 bar.), yielding the desired compound as a pale yellow solid in 60% isolated yield (214 mg, 0.5 mmol). **^{1}H NMR (400 MHz, DMSO-d_6) δ** 12.48 (s, 1H), 10.53 (s, 1H), 8.48 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.03 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.26 (dd, *J* = 7.7, 4.8 Hz, 1H), 7.09 (d, *J* = 7.9 Hz, 1H), 3.94 (dd, *J* = 13.1, 8.7 Hz, 1H), 2.12 – 1.95 (m, 1H), 1.82 (td, *J* = 16.2, 7.8 Hz, 1H), 1.49 (s, 9H), 1.39 (s, 9H) ppm. Two protons overlap with DMSO peak. **^{13}C NMR (101 MHz, DMSO-d_6) δ** 174.7 (C), 171.9 (C), 165.9 (C), 156.4 (C), 151.4 (CH), 149.5 (C), 139.6 (CH), 121.9 (C), 120.7 (CH), 82.0 (CH_2), 78.9 (CH_2), 53.9 (CH), 33.2 (C), 29.1 (CH_3), 28.7 (CH_3), 27.0 (C) ppm. **HRMS** (ESI+) m/z calcd. for $C_{20}H_{30}N_3O_7$ $[M+H]^+$: 424.2078, found 424.2069. **$[\alpha]_D$** = +17 (*c* 10 mg/ml, $CHCl_3$, 25°C). No spectroscopic data are reported in literature. The chiral purity was checked by transformation into a dipeptide (see section 5.2).

N-[3-(*tert*-butoxycarbonyl)pyridin-2-yl]-*N*-2-{[(9*H*-fluoren-9-yl)methoxy]carbonyl}-L-glutamine (Fmoc-L-Gln(NH-*t*Bu-nic)-OH, DM683) **L-4p**



L-4o **L-4p**

Step 1: N^2-(*tert*-butoxycarbonyl)-*N*-[3-(*tert*-butoxycarbonyl)pyridyn-2-yl]-L-glutamine [Boc-L-Gln(*t*Bu-nic)-OH] **L-4o** (1.12 g, 2.64 mmol) was cooled to 0°C and 4M Hydrochloric acid in dioxane

(13.22 ml, 52.9 mmol) was added dropwise. After 1h, the solvents were removed in vacuo to yield the corresponding ammonium chloride that was used directly in the subsequent reaction step.

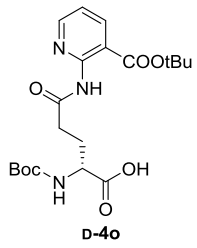
Step 2 : The amino acid coming from the previous step was dissolved in water (26.4 ml) and acetonitrile (26.4 ml). Then, Fmoc-OSu (1.071 g, 3.17 mmol) and sodium carbonate (0.336 g, 3.17 mmol) were added until a pH in the range between 8-10 was reached. After 3h, the solvent was removed and the crude was dissolved in EtOAc (100 ml), washed with 1 M HCl (50 ml). The organic phase was then dried over $MgSO_4$ and evaporated. The mixture was then purified by flash column chromatography using Combiflash® RF200 reverse phase silica gel flash chromatography (Water + 1% formic acid:Acetonitrile, 100:0 to 0:100 in 80 min), yielding *N*-[3-(*tert*-butoxycarbonyl)pyridin-2-yl]-*N*-2-{[(9*H*-fluoren-9-yl)methoxy]carbonyl}- L-glutamine [Fmoc-L-Gln(*t*Bu-nic)-OH] as a white crystals in 78% isolated yield (1.13 g, 2.01 mmol).**^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ** 10.56 (s, 1H), 8.47 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.03 (dd, J = 7.7, 1.7 Hz, 1H), 7.90 (d, *J* = 7.5 Hz, 2H), 7.73 (d, *J* = 7.4 Hz, 2H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 2H), 7.25 (dd, *J* = 7.7, 4.8 Hz, 1H), 4.33 – 4.18 (m, 3H), 4.02 (dd, *J* = 13.2, 8.8 Hz, 1H), 2.16 – 2.03 (m, 1H), 1.88 (td, *J* = 16.4, 7.9 Hz, 1H), 1.48 (s, 9H) pm. Two protons overlap with DMSO peak. **^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ** 174.0 (C), 171.5 (C), 165.5 (C), 156.6 (C), 151.0 (CH), 149.1 (C), 144.3 (C), 141.2 (C), 139.2 (CH), 128.1 (CH), 127.5 (CH), 125.7 (CH), 121.5 (C), 120.6 (CH), 120.3 (CH), 81.6 (C), 66.1 (CH_2), 53.9 (CH), 47.1 (CH), 32.8 (CH_2), 28.2 (CH_3), 26.7 (CH_2) ppm. **HRMS** (ESI+) m/z calcd. for $C_{30}H_{31}N_3O_7$ $[M+Na]^+$: 568.2054, found 568.2060. **$[\alpha]_D$** = +17 (*c* 10 mg/ml, $CHCl_3$, 21°C). No spectroscopic data are reported in literature.

Remark: Compounds **L-4e, L-4h, L-4i, L-4k** were synthesized starting from enantiopure peptidic amide starting material. In our previous publication,[1] the substrates were partially epimerized which explains the difference observed in comparison to the current data.

5.2 Effect of *tert*-butyl 2-chloronicotinate introduction on the chiral purity of Boc-L-Gln-OH

The evaluation of the *tert*-butyl 2-chloronicotinate introduction on the chiral purity of the Boc-L-Gln-OH side chain was performed by means of coupling Boc-L-Gln(*t*Bu-nic)-OH **L-4o** with H-L-Val-OMe. The diastereoisomer of Boc-L-Gln(*t*Bu-nic)-L-Val-OMe **L,L-21**, i.e. Boc-D-Gln(*t*Bu-nic)-L-Val-OMe **D,L-22**, was synthesized as reference. Boc-D-Gln(*t*Bu-nic)-OH **D-4o** was obtained by introducing the *t*Bu-nic directing group on the side chain of Boc-D-Gln-OH and then coupled with H-L-Val-OMe. The two diasteromeric dipeptides, Boc-L-Gln(*t*Bu-nic)-L-Val-OMe **L,L-21** and Boc-D-Gln(*t*Bu-nic)-L-Val-OMe **D,L-21** obtained, were subsequently analysed by LC.

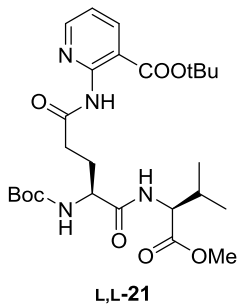
N^2-(*tert*-Butoxycarbonyl)-N^5-(3-(*tert*-butoxycarbonyl)pyridin-2-yl)-D-glutamine (Boc-D-Gln(*t*Bu-nic)-OH, DM602) **D-4o**



D-4o

The title compound was isolated using general procedure **A4.** An oven-dried microwave vial was charged with Boc-D-Gln-OH (369 mg, 1.5 mmol), $Pd(OAc)_2$ (11 mg, 0.05 mmol), 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (58 mg, 0.1 mmol), *tert*-butyl 2-chloronicotinate **2** (214 mg, 1 mmol) and anhydrous 1,4-dioxane (1.3 ml). While vigorous stirring, Cs_2CO_3 (391 mg, 1.2 mmol) was added and the resulting mixture was flushed with argon. The mixture was vigorously stirred at 90°C for 24 hours. After cooling down to room temperature, EtOAc was added and the mixture was purified with Combiflash® RF200 reverse phase silica gel flash chromatography (Water + 1% formic acid:Acetonitrile, 100:0 to 0:100 in 80 min) (Chromabond®Flash RS25 C18 Cartridges, 25 g, 25/67mL; flow rate 18 mL/min, max. operating pressure 150 psi - 10 bar.), yielding the desired compound as a pale yellow solid in 60% isolated yield (211 mg, 0.5 mmol) **^{1}H NMR (400 MHz, DMSO-d_6) δ** 12.48 (s, 1H), 10.53 (s, 1H), 8.48 (dd, *J* = 4.7, 1.7 Hz, 1H), 8.03 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.26 (dd, *J* = 7.7, 4.8 Hz, 1H), 7.09 (d, *J* = 7.9 Hz, 1H), 3.94 (dd, *J* = 13.1, 8.7 Hz, 1H), 2.12 – 1.95 (m, 1H), 1.82 (td, *J* = 16.2, 7.8 Hz, 1H), 1.49 (s, 9H), 1.39 (s, 9H) ppm. Two protons overlap with DMSO peak. **^{13}C NMR (101 MHz, DMSO-d_6) δ** 174.7 (C), 171.9 (C), 165.9 (C), 156.4 (C), 151.4 (CH), 149.5 (C), 139.6 (CH), 121.9 (C), 120.7 (CH), 82.0 (CH_2), 78.9 (CH_2), 53.9 (CH), 33.2 (C), 29.1 (CH_3), 28.7 (CH_3), 27.0 (C) ppm. **HRMS** (ESI+) m/z calcd. for $C_{20}H_{30}N_3O_7$ $[M+H]^+$: 424.2078, found 424.2069. **$[\alpha]_D$** = -14 (*c* 10 mg/ml, $CHCl_3$, 20°C). No spectroscopic data are reported in literature.

Methyl N^2-(*tert*-butoxycarbonyl)-*N*-[3-(*tert*-butoxycarbonyl)pyridin-2-yl]-L-glutaminyl-L-valinate (Boc-L-Gln(*t*Bu-nic)-L-Val-OMe, DM584) **L,L-21**

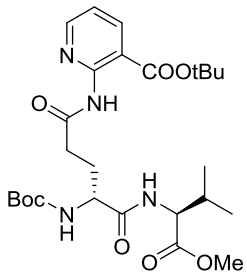


L,L-21

The title compound was obtained following general procedure **D**. A round-bottom flask was charged with Boc-L-Gln(*t*Bu-nic)-OH **L-4o** (190 mg, 0.45 mmol), EDC.HCl (103 mg, 0.54 mmol), $HOBt.H_2O$ (82 mg, 0.54 mmol) in CH_2Cl_2 (10 ml). The solution was stirred at room temperature for 15 minutes. Alongside, H-L-Val-OMe hydrochloric acid salt (75 mg, 0.45 mmol) in CH_2Cl_2 (10 ml) was brought up to pH 9 with Et_3N (33 µl, 0.45 mmol). This solution was subsequently added to the pre-activated *N*-Boc protected amino acid mixture and the reaction was stirred for 2 hours at room temperature. The solvent was removed in vacuo and the residue was redissolved in EtOAc. The organic phase was extracted with HCl (3x, 1 M) and $NaHCO_3$ (3 x, sat.),

washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified via Biotage®Isolera one automatic flash chromatography with Heptane:EtOAc (0% EtOAc to 100% EtOAc in 60 min, 20.0 ml/min) (Grace®Silica Flash Cartridges 12 g: GraceResolv Silica 12/20ml; flow rate 20 ml/min, max. operating pressure 150 psi - 10 bar.) affording the desired product as a pale yellow solid in 95% isolated yield (40 mg, 0.04 mmol). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 10.99 (s, 1H), 8.56 (d, *J* = 3.1 Hz, 1H), 8.24 (d, *J* = 6.4 Hz, 1H), 7.05 (dd, *J* = 7.8, 4.8 Hz, 1H), 6.86 (s, 1H), 5.83 (s, 1H), 4.53 (dd, *J* = 8.7, 5.0 Hz, 1H), 4.28 (s, 1H), 3.72 (s, 3H), 3.00 – 2.88 (m, 1H), 2.88 – 2.76 (m, 1H), 2.35 – 2.06 (m, 3H), 1.61 (s, 9H), 1.44 (s, 9H), 0.94 (dd, *J* = 16.7, 6.8 Hz, 6H) ppm. **^{13}C NMR (100 MHz, $CDCl_3$) δ** 172.3 (C), 172.0 (C), 171.8 (C), 165.8 (C), 152.2 (CH), 152.1 (C), 140.1 (CH), 118.1 (CH), 83.4 (C), 77.2 (C), 57.2 (CH), 52.0 (CH), 34.5 (CH_2), 31.1 (CH_2), 28.3 (CH_3), 28.1 (CH_3), 19.0 (CH_3), 17.7 (CH) ppm. **HRMS** (ESI+) m/z calcd for $C_{26}H_{41}N_4O_8$ $[M+H]^+$: 537.2919, found 537.2928. **$[\alpha]_D$** = +10 (*c* 10 mg/ml, $CHCl_3$, 20°C). No spectroscopic data are reported in literature**.** LC-CD analysis on a Chiralpak IA column (retention time = 6.43 min, 250 nm, *n*-hexane:EtOH 80:20**,** 1.0 ml/min) revealed 100%de and ee and indirectly 100% ee for **L-4o**.

Methyl N^2-(*tert*-butoxycarbonyl)-*N*-[3-(*tert*-butoxycarbonyl)pyridin-2-yl]-D-glutaminyl-L-valinate (Boc-D-Gln(*t*Bu-nic)-L-Val-OMe, DM593) **D,L-21**



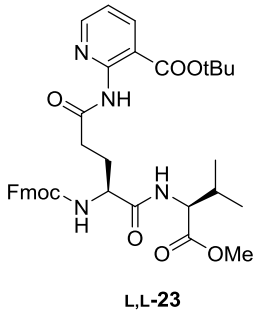
D,L-21

The title compound was obtained following general procedure **D**. A round-bottom flask was charged with Boc-D-Gln(*t*Bu-nic)-OH **D-4o** (100 mg, 0.24 mmol), EDC.HCl (54 mg, 0.28 mmol), HOBt.H_2O (43 mg, 0.28 mmol) in CH_2Cl_2 (5 ml). The solution was stirred at room temperature for 15 minutes. Alongside, H-L-Val-OMe hydrochloric acid salt (40 mg, 0.24 mmol) in CH_2Cl_2 (5 ml) was brought up to pH 9 with Et_3N (33 µl, 0.24 mmol). This solution was subsequently added to the pre-activated *N*-Boc protected amino acid mixture and the reaction was stirred for 2 hours at room temperature. The solvent was removed in vacuo and the residue was redissolved in EtOAc. The organic phase was extracted with HCl (3x, 1 M) and $NaHCO_3$ (3 x, sat.), washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified via Biotage®Isolera one automatic flash chromatography with Heptane:EtOAc (0% EtOAc to 100% EtOAc in 60 min, 20.0 ml/min) (Grace®Silica Flash Cartridges 12 g: GraceResolv Silica 12/20ml; flow rate 20 ml/min, max. operating pressure 150 psi - 10 bar.) affording the desired product as a pale yellow solid in 31% isolated yield (40 mg, 0.075 mmol). **^{1}H NMR (400 MHz, $CDCl_3$) δ**10.94 (s, 1H), 8.54 (dd, *J* = 4.7, 1.8 Hz, 1H), 8.23 (dd, *J* = 7.8, 1.9 Hz, 1H), 7.10 (d, *J* = 8.1 Hz, 1H), 7.04 (dd, *J* = 7.8, 4.8 Hz, 1H), 5.61 (s, 1H), 4.51 (dd, *J* = 8.7, 5.1 Hz, 1H), 4.30 (d, *J* = 6.0 Hz, 1H), 3.72 (s, 3H), 2.90 (qd, *J* = 15.7, 8.1 Hz, 2H), 2.27 – 2.06 (m, 3H), 1.61 (s, 9H), 1.42 (s, 9H), 0.93 (dd, *J* = 8.8, 7.0 Hz, 6H) ppm. **^{13}C NMR**

(100 MHz, $CDCl_3$) δ 172.4 (C), 172.1 (C), 171.9 (C), 165.8 (C), 152.2 (CH), 152.0 (C), 140.0 (CH), 118.2 (CH), 83.4 (C), 77.2 (C), 57.4 (CH), 52.0 (CH), 34.4 (CH_2), 31.0 (CH_2), 28.3 (CH_3), 28.1 (CH_3), 19.0 (CH_3), 17.8 (CH) ppm. **HRMS** (ESI+) m/z calcd for $C_{26}H_{41}N_4O_8$ $[M+H]^+$: 537.2919, found 537.2928. **$[\alpha]_D$** = -14 (*c* 5 mg/ml, $CHCl_3$, 20°C). No spectroscopic data are reported in literature**.** LC-CD analysis on a Chiralpak IA column (retention time = 7.48 min, 250 nm, 1.0 ml/min) revealed 100% de and ee and indirectly 100% ee for **D-4o**

As for **L-4o**, the chiral purity of **L-4p** was assessed by coupling with H-L-Val-OMe to obtain the dipeptide Fmoc-L-Gln(*t*Bu-nic)-**L**-Val-OMe **L,L-23**. The dipeptide **L,L-23** was converted into the dipeptide **L,L-21** by the interchanging of the Fmoc protecting group with Boc. Finally, the chiral purity of the so obtained dipeptide **L,L-21** was assessed by means of both NMR and LC analysis.

Methyl *N*-[3-(*tert*-butoxycarbonyl)pyridin-2-yl]-N^2~-{[(9*H*-fluoren-9-yl)methoxy]carbonyl}-L-glutaminyl-L-valinate (Fmoc-L-Gln(*t*Bu-nic)-L-Val-OMe **L, L-23**

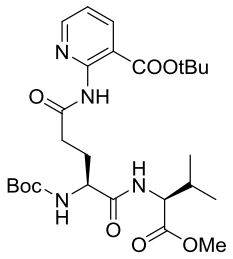


L,L-23

To a solution of Fmoc-L-Gln(*t*Bu-nic)-OH **L-4p** (0.136 g, 0.25 mmol) in DCM (4.17 ml), EDC (0.058 g, 0.300 mmol) and 1-hydroxybenzotriazolehydrate (0.046 g, 0.300 mmol) were added and the solution was stirred for 20 min. In parallel, to a flask containing H-L-Val-OMe (0.042 g, 0.250 mmol) dissolved in DCM (4.17 ml), *N*,*N*-di-isopropylethylamine (0.044 ml, 0.250 mmol) was added. This solution was then added to the activated carboxylic acid mixture and the reaction was stirred for 1h at room temperature. Then, the solvent was removed under vacuum and the crude was redissolved in EtOAc (50 ml). The organic layer was washed with 10% citric acid in water (3x30 ml), saturated $NaHCO_3$ (3x30 ml) and brine, dried over $MgSO_4$ and concentrated in vacuo. The brown oil was then purified via Biotage®Isolera one automatic flash chromatography with Heptane:EtOAc (50% EtOAc to 100% EtOAc in 60 min, 12.0 ml/min) (Grace®Silica Flash Cartridges 12 g: GraceResolv Silica 12/20 ml; flow rate 20 ml/min, max. operating pressure 150 psi - 10 bar.) affording the desired product as a pale yellow solid in 58% isolated yield (96 mg, 0.146 mmol). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 10.98 (s, 1H), 8.51 (dd, *J* = 4.8, 1.9 Hz, 1H), 8.22 (dd, *J* = 7.8, 1.9 Hz, 1H), 7.74 (d, *J* = 7.7 Hz, 2H), 7.59 (d, *J* = 5.8 Hz, 2H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 7.6 Hz, 2H), 7.03 (dd, *J* = 7.8, 4.8 Hz, 1H), 5.98 (d, *J* = 6.2 Hz, 1H), 4.51 (dd, *J* = 8.5, 5.0 Hz, 1H), 4.43 (dd, *J* = 13.0, 6.8 Hz, 1H), 4.36 (d, *J* = 7.1 Hz, 2H), 4.20 (t, *J* = 7.2 Hz, 1H), 3.72 (s, 3H), 3.04 – 2.86 (m, 2H), 2.28 – 2.11 (m, 3H), 1.56 (s, 9H), 0.94 (dd, *J* = 9.0, 7.0 Hz, 6H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$) δ** 172.6 (C), 172.1 (C), 171.7 (C), 165.8 (C), 152.2 (C), 151.9 (C), 143.8 (C), 141.8 (C), 141.3 (C), 140.0 (CH), 127.7 (CH), 127.1 (CH), 125.2 (CH), 119.9 (CH), 118.3 (CH), 83.5 (C), 57.6 (CH), 54.0 (CH), 52.1 (CH), 47.1 (CH_2),

34.3 (CH), 30.8 (CH_2), 29.7 (CH_2), 28.1 (CH_3), 19.0 (CH_3), 17.9 (CH_3) ppm. **HRMS** (ESI+) m/z calcd for $C_{36}H_{42}N_4O_8$ $[M+H]^+$: 658.3003, found 658.3012. $[\alpha]_D$ = +34 (*c* 1 mg/ml, $CHCl_3$, 20°C). No spectroscopic data are reported in literature.

Methyl N^2-(*tert*-butoxycarbonyl)-*N*-[3-(*tert*-butoxycarbonyl)pyridin-2-yl]-D-glutaminyl-L-valinate (Boc-L-Gln(*t*Bu-nic)-L-Val-OMe, DM758) **L,L-21** from **L,L-23**



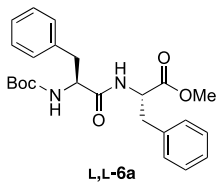
L,L-21

Fmoc-L-Gln(*t*Bu-nic)-L-Val-OMe **L,L-23** (0.096 g, 0.146 mmol) was dissolved in 20 mL of piperidine/DMF solution (1:4). Reaction was stirred for 30 min at room temperature. The solvent was evaporated and 25 ml of cold ether was added to precipitate the amino acid. The suspended mixture was filtrated over filter paper and rinsed with cold ether. The solid was dried at lyophilisator and used in the next step without purification.

The amino acid coming from the previous step was dissolved in acetonitrile (2.91 ml) and 4-dimethylaminopyridine (3.56 mg, 0.029 mmol) and di-*tert*-butyldicarbonate (0.038 g, 0.175 mmol) were added. After the reaction was completed (16 h), EtOAc (50 ml) was added and the mixture was washed first with 1 N HCl (20 ml) and then with brine (20 ml). The organic phase was then dried over $MgSO_4$ and evaporated. The crude product was purified via Biotage®Isolera one automatic flash chromatography with Heptane:EtOAc (0% EtOAc to 100% EtOAc in 60 min, 20.0 ml/min) (Grace®Silica Flash Cartridges 12 g: GraceResolv Silica 12/20ml; flow rate 20 ml/min, max. operating pressure 150 psi - 10 bar.) affording the desired product as a pale yellow solid in 83% isolated yield (65 mg, 0.12 mmol). **^{1}H NMR (400 MHz, $CDCl_3$) δ** 10.99 (s, 1H), 8.56 (d, *J* = 3.1 Hz, 1H), 8.24 (d, *J* = 6.4 Hz, 1H), 7.05 (dd, *J* = 7.8, 4.8 Hz, 1H), 6.86 (s, 1H), 5.83 (s, 1H), 4.53 (dd, *J* = 8.7, 5.0 Hz, 1H), 4.28 (s, 1H), 3.72 (s, 3H), 3.00 – 2.88 (m, 1H), 2.88 – 2.76 (m, 1H), 2.35 – 2.06 (m, 3H), 1.61 (s, 9H), 1.44 (s, 9H), 0.94 (dd, *J* = 16.7, 6.8 Hz, 6H) ppm. **^{13}C NMR (100 MHz, $CDCl_3$) δ** 172.3 (C), 172.0 (C), 171.8 (C), 165.8 (C), 152.2 (CH), 152.1 (C), 140.1 (CH), 118.1 (CH), 83.4 (C), 77.2 (C), 57.2 (CH), 52.0 (CH), 34.5 (CH_2), 31.1 (CH_2), 28.3 (CH_3), 28.1 (CH_3), 19.0 (CH_3), 17.7 (CH) ppm. **HRMS** (ESI+) m/z calcd for $C_{26}H_{41}N_4O_8$ $[M+H]^+$: 537.2919, found 537.2928. $[\alpha]_D$ = 10 (*c* 10 mg/ml, $CHCl_3$, 20°C). No spectroscopic data are reported in literature**.** LC-CD analysis on a Chiralpak IA column (retention time = 6.43 min, 250 nm, *n*-hexane:EtOH 80:20**,** 1.0 ml/min) revealed 100%de and ee and indirectly 100% ee for **L-4p**.

5.3 Dipeptide Synthesis using Transamidation of *N*-Boc Protected *t*Bu Nicotinate Functionalized Amino Acid Amides 4

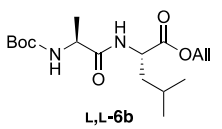
Methyl (*tert*-butoxycarbonyl)-L-phenylalanyl-L-phenylalaninate (Boc-L-Phe-L-Phe-OMe, KH_1160) **L,L-6a**



L,L-6a

The title compound was prepared using general procedure **B** from Boc-L-Phe-NH-*t*Bu-nic **L-4a** (221 mg, 0.5 mmol, 1 equiv), H-L-Phe-OMe hydrochloric acid salt **L-5a.HCl** (119 mg, 0.55 mmol, 1.1 equiv), NaOAc (46 mg, 0.55 mmol, 1.1 equiv) and $Zn(OAc)_2$ (18 mg, 0.1 mmol, 20 mol%) in THF (1 ml). This yielded, after Grace Reveleris® X2 Normal Phase silicagel flash chromatography (CH_2Cl_2:EtOAc, 100:0 to 70:30 over 10 CV), the desired compound as a white powder in 95% (203 mg, 0.477 mmol) yield. **^{1}H NMR (500 MHz, $CDCl_3$) δ** 7.21-7.09 (m, 8H), 6.91-6.90 (m, 2H), 6.29 (br s, 1H), 4.94 (br s, 1H), 4.72 (dd, *J* = 5.4, 11.5 Hz, 1H), 4.28 (br s, 1H), 3.58 (s, 3H), 3.01-2.92 (m, 4H), 1.32 (s, 9H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$) δ** 171.5 (C), 170.9 (C), 155.4 (C), 136.6 (C), 135.7 (C), 129.4 (CH), 129.3 (CH), 128.7 (CH), 128.6 (CH), 127.2 (CH), 127.0 (CH), 80.2 (C), 55.7 (CH), 53.4 (CH), 52.3 (CH_3), 38.3 (CH_2). 38.0 (CH_2), 28.3 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{24}H_{31}N_2O_5Na$ $[M+Na]^+$: 449.2047 found 449.2057. **$[\alpha]_D$** = +26 (*c* 10 mg/ml, $CHCl_3$, 25°C). The spectroscopic data were in accordance with those previously reported.[6]

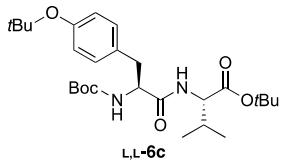
Prop-1-en-1-yl (*tert*-butoxycarbonyl)-L-alanyl-L-leucinate (Boc-L-Ala-L-Leu-OAll, KH_1197) **L,L-6b**



L,L-6b

The title compound was prepared using general procedure **B** from Boc-L-Ala-NH-*t*Bu-nic **L-4b** (183 mg, 0.5 mmol, 1 equiv), H-L-Leu-OAll hydrochloric acid salt **L-5b.HCl** (114 mg, 0.55 mmol, 1.1 equiv), NaOAc (46 mg, 0.55 mmol, 1.1 equiv) and $Zn(OAc)_2$ (18 mg, 0.1 mmol, 20 mol%) in THF (1 ml). This yielded, after Grace Reveleris® X2 Normal Phase silica gel flash chromatography (CH_2Cl_2:EtOAc, 100:0 to 0:100 over 20 CV), the desired compound as a colorless oil in 99% (170 mg, 0.496 mmol) yield. **^{1}H NMR (500 MHz, $CDCl_3$) δ** 6.52 (br s, 1H), 5.91 (ddt, *J* = 10.5, 17.1, 5.2 Hz, 1H), 5.33 (dd, *J* = 17.1, 1.0 Hz, 1H), 5.26 (dd, *J* = 10.5, 1.0 Hz, 1H), 5.00 (br s, 1H), 4.65-4.60 (m, 2H), 4.22-4.14 (m, 1H), 1.70-1.64 (m, 3H), 1.61-1.56 (m, 1H), 1.45 (s, 9H), 1.36 (d, *J* = 7.1 Hz, 3H), 0.94 (d, *J* = 6.1 Hz, 6H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$) δ** 172.5 (C), 172.5 (C), 155.7 (C), 131.7 (CH), 118.9 (CH_2), 80.3 (C), 66.0 (CH_2), 50.9 (CH), 50.0 (CH), 41.7 (CH_2), 28.4 (CH_3), 24.9 (CH), 23.0 (CH_3), 21.9 (CH_3), 18.0 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{17}H_{31}N_2O_5$ $[M+H]^+$: 343.2227 found 343.2221. **$[\alpha]_D$** = -37 (*c* 10 mg/ml, $CHCl_3$, 22°C). No spectroscopic data are reported in literature.

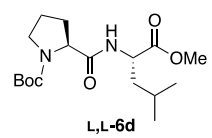
tert-Butyl ((*S*)-3-(4-(*tert*-butoxy)phenyl)-2-((*tert*-butoxycarbonyl)amino)propanoyl)-L-valinate (Boc-L-Tyr(tBu)-L-Val-O*t*Bu, KH_1245) **L,L-6c**



L,L-**6c**

The title compound was prepared using general procedure **B,** from Boc-L-Tyr(*t*Bu)-NH-*t*Bu-nic **L-4c** (256 mg, 0.5 mmol, 1 equiv), H-L-Val-O*t*Bu hydrochloric acid salt **L-5c.HCl** (116 mg, 0.55 mmol, 1.1 equiv), NaOAc (46 mg, 0.55 mmol, 1.1 equiv) and $Zn(OAc)_2$ (18 mg, 0.1 mmol, 20 mol%) in THF (1 ml). This yielded, after Grace Reveleris® X2 Normal Phase silicagel flash chromatography (Petroleum Ether:EtOAc, 100:0 to 0:100 over 20 CV), the desired compound as a colorless oil in 85% (210 mg, 0.426 mmol). **^{1}H (500 MHz, DMSO-*d*$_6$, mixture of rotamers) δ** 8.00-7.92 (m, 0.2H), 7.88 (d, *J* = 8.3 Hz, 0.8H), 7.21 (d, *J* = 7.2 Hz, 0.2H), 7.17 (d, *J* = 8.3 Hz, 1.8H), 6.92-6.82 (m, 2.9H), 6.4 (br s, 0.1H), 4.33-4.19 (m, 1H), 4.12-4.02 (m, 1H), 2.96-2.83 (m, 1H), 2.73-2.60 (m, 1H), 2.10-1.97 (m, 1H), 1.41 (s, 9H), 1.29 (s, 7.5H), 1.26 (s, 10.5H), 0.89 (dd, *J* = 6.8, 6.8 Hz, 5.6H), 0.82 (dd, *J* = 6.3, 6.3 Hz, 0.4H) ppm. **^{13}C (126 MHz, DMSO-*d*$_6$, mixture of rotamers) δ** 171.9 (C), 170.4 (C), 155.1 (C), 153.3 (C), 132.7 (C), 129.6 (CH), 123.1 (CH), 80.6 (C), 77.9 (C), 77.4 (C), 57.7 (CH), 55.4 (CH), 36.7 (CH_2), 30.1 (CH), 28.5 (CH_3), [28.0, 27.8] (CH_3), 27.6 (CH_3), 18.8 (CH_3), 17.9 (CH_3) ppm. NMR-data was acquired at elevated temperature so that peaks arising from hindered rotation coalesced. **^{1}H NMR (500 MHz, DMSO-d$_6$, 60°C) δ** 7.72 (d, *J* = 7.2 Hz, 1H), 7.15 (d, *J* = 8.2 Hz, 2H), 6.84 (d, *J* = 8.2 Hz, 2H), 6.76 (br s, 1H), 4.26 (ddd, *J* = 9.3, 9.3, 4.0 Hz, 1H), 4.10 (dd, *J* = 5.9, 8.2 Hz, 1H), 2.94 (dd, *J* = 14.0, 4.0 Hz, 1H), 2.71 (dd, *J* = 10.7, 13.1 Hz, 1H), 2.10-2.00 (m, 1H), 1.42 (s, 9H), 1.31 (s, 9H), 1.28 (s, 9H), 0.94-0.88 (m, 6H) ppm. **^{13}C (126 MHz, DMSO-*d*$_6$, 60°C) δ** 171.5 (C), 170.0 (C), 154.8 (C), 153.3 (C), 132.3 (C), 129.4 (CH), 122.8 (CH), 80.4 (C), 77.8 (C), 77.2 (C), 57.6 (CH), 55.3 (CH), 36.6 (CH_2), 30.0 (CH), 28.3 (CH_3), 27.8 (CH_3), 27.4 (CH_3), 18.5 (CH_3), 17.7 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{27}H_{44}N_2O_6Na$ $[M+Na]^+$: 515.3091 found 515.3090. **$[\alpha]_D$** = +5 (*c* 10 mg/ml, $CHCl_3$, 25°C). No spectroscopic data are reported in literature.

tert-Butyl (*S*)-2-(((*S*)-1-methoxy-4-methyl-1-oxopentan-2-yl)carbamoyl)pyrrolidine-1-carboxylate (Boc-L-Pro-L-Leu-OMe, KH_1196) **L,L-6d**

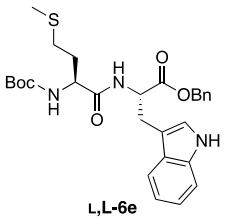


L,L-**6d**

The title compound was prepared using general procedure **B,** from Boc-L-Pro-NH-*t*Bu-nic **L-4d** (196 mg, 0.5 mmol, 1 equiv), H-L-Leu-OMe hydrochloric acid salt **L-5d.HCl** (100 mg, 0.55 mmol, 1.1 equiv), NaOAc (46 mg, 0.55 mmol, 1.1 equiv) and $Zn(OAc)_2$ (18 mg, 0.1 mmol, 20 mol%) in THF (1 ml). This yielded, after Grace Reveleris® X2 Normal Phase silicagel flash chromatography (Petroleum Ether:EtOAc, 100:0 to 0:100 over 20 CV), the desired compound as a colorless oil in 95% (162 mg, 0.474 mmol) yield. **^{1}H (500 MHz, DMSO-*d*$_6$, mixture of rotamers) δ** 8.20 (d, *J* = 7.8 Hz, 0.7H), 8.14 (d, *J* = 7.6 Hz, 0.3H), 4.32-4.24 (m, 1H), 4.17-4.10 (m,

1H), 3.61 (s, 2.1H), 3.60 (s, 0.9H), 3.40-3.32 (m, 1H), 3.29-3.20 (m, 1H), 2.17-2.07 (m, 0.7H), 2.05-1.97 (m, 0.3H), 1.82-1.70 (m, 3H), 1.69-1.64 (m, 1H), 1.60 (ddt, *J* = 5.0, 9.2, 8.9 Hz, 1H), 1.47 (ddd, *J* = 4.4, 9.3, 13.5 Hz, 1H), 1.38 (s, 2.6H), 1.32 (s, 6.4H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.84 (pseudo t, *J* = 5.4 Hz, 3H) ppm. **^{13}C (126 MHz, DMSO-*d*$_6$, mixture of rotamers) δ** 172.9 (C), [172.7, 172.3] (C), [153.5, 153.3] (C), [78.5, 78.3] (C), [59.2, 58.9] (CH), 51.7 (CH_3), [50.2, 50.0] (CH), [46.6, 46.4] (CH_2), 30.9 (CH_2), 29.6 (CH_2), [28.1, 27.9] (CH_3), [24.1, 23.8] (CH), 22.9 (CH_2), [22.8, 22.8] (CH_3), [21.3, 21.0] (CH_3) ppm. NMR-data was acquired at elevated temperature so that peaks arising from hindered rotation coalesced. **^{1}H NMR (500 MHz, DMSO-*d*$_6$, 60°C) δ** 8.00 (br s , 1H), 4.31 (ddd, *J* = 5.1, 8.0, 9.6 Hz, 1H), 4.15 (dd, *J* = 1.9, 8.7 Hz, 1H), 3.62 (s, 3H), 3.41-3.34 (m, 1H), 3.31-3.25 (m, 1H), 2.17-2.07 (m, 1H), 1.85-1.72 (m, 3H), 1.71-1.62 (m, 1H), 1.60 (ddd, *J* = 4.7, 9.7, 13.8 Hz, 1H) 1.50 (ddd, *J* = 4.9, 8.9, 13.7 Hz, 1H), 1.35 (s, 9H), 0.90 (d, *J* = 6.7 Hz, 3H), 0.86 (d, *J* = 6.4 Hz, 3H) ppm. **^{13}C (126 MHz, DMSO-*d*$_6$, 60°C) δ** 172.5 (C), 172.3 (C), 153.2 (C), 78.1 (C), 59.0 (CH), 51.4 (CH_3), 50.0 (CH), 46.3 (CH_2), 30.6 (CH_2), 29.3 (CH_2), 27.7 (CH_3), 23.9 (CH), 22.7 (CH_2), 22.4 (CH_3), 21.0 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{17}H_{31}N_2O_5$ $[M+H]^+$: 343.2227 found 343.2223. **[α]$_D$** = -67 (*c* 10 mg/ml, $CHCl_3$, 25°C). The spectroscopic data were in accordance with those previously reported.[7]

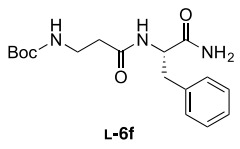
Benzyl (*tert*-butoxycarbonyl)-L-methionyl-L-tryptophanate (Boc-L-Met-L-Trp-OBn, DM769) **L,L-6e**



L,L-6e

The title compound was prepared using general procedure **B,** from Boc-L-Met-NH-*t*Bu-nic **L-4e** (213 mg, 0.5 mmol, 1 equiv), H-L-Trp-OBn hydrochloric acid salt **L-5e.HCl** (182 mg, 0.55 mmol, 1.1 equiv), NaOAc (46 mg, 0.55 mmol, 1.1 equiv) and $Zn(OAc)_2$ (18 mg, 0.1 mmol, 20 mol%) in THF (1 ml). This yielded, after Grace Reveleris® X2 Normal Phase silicagel flash chromatography (Petroleum Ether:EtOAc, 100:0 to 0:100 over 20 CV), the desired compound as a white powder in 80% (210 mg, 0.399 mmol) yield. **^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ** 10.90 (s, 1H), 8.29 (d, *J* = 7.2 Hz, 1H), 7.52 (d, *J* = 7.9 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.35 – 7.30 (m, 3H), 7.23 – 7.16 (m, 3H), 7.13 – 7.07 (m, 1H), 7.01 (dd, *J* = 11.0, 3.9 Hz, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 5.12 – 4.97 (m, 2H), 4.65 (dd, *J* = 13.6, 6.8 Hz, 1H), 4.13 (dd, *J* = 12.7, 7.9 Hz, 1H), 3.20 (qd, *J* = 14.7, 7.0 Hz, 2H), 2.45 (t, *J* = 7.0 Hz, 2H), 2.02 (s, 3H), 1.40 (s, 9H) ppm. **^{13}C (100 MHz, DMSO-*d*$_6$) δ** 172.3 (C), 172.1 (C), 172.1 (C), 155.8 (C), 136.6 (C), 136.1 (C), 128.8 (CH), 128.8 (CH), 128.4 (CH), 128.2 (CH), 127.6 (CH), 127.5 (C), 124.2 (CH), 121.5 (CH), 118.9 (CH), 118.5 (CH), 111.9 (CH), 109.7 (C), 78.6 (C), 66.5 (CH_2), 53.8 (CH), 53.7 (CH), 32.4 (CH_2), 30.14 (CH_2), 28.65 (CH_2), 27.55 (CH_3), 15.10 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{28}H_{35}N_3O_5SNa$ $[M+Na]^+$: 548.2190 found 548.2182. **[α]$_D$** = -9 (*c* 10 mg/ml, $CHCl_3$, 22°C). No spectroscopic data are reported in literature.

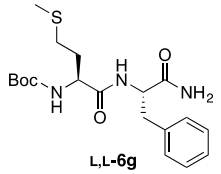
*tert-B*utyl (*S*)-(3-((1-amino-1-oxo-3-phenylpropan-2-yl)amino)-3-oxopropyl)carbamate (Boc-βAla-L-Phe-NH_2, DM332) **L-6f**



L-6f

The title compound was prepared using general procedure **B,** from Boc-βAla-NH-*t*Bu-nic **4f** (183 mg, 0.42 mmol, 1 equiv), H-L-Phe-NH_2 hydrochloric acid salt **L-5f.HCl** (110 mg, 0.55 mmol, 1.1 equiv), NaOAc (45 mg, 0.55 mmol, 1.1 equiv) and $Zn(OAc)_2$ (18 mg, 0.1 mmol, 20 mol%) in THF (1 ml), by stirring at 70°C for 48 h. This yielded, after Biotage® Isolera One Normal phase silicagel flash chromatography (n-Heptane:EtOAc, 100:0 to 0:100 for 40 min at a flow rate of 22 ml/min), the desired compound as a white powder in 72% (120 mg, 0.358 mmol) yield. **^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ** 8.01 (d, *J* = 8.27 Hz, 1H), 7.40 (br s, 1H), 7.30-7.17 (m, 5H), 7.03 (br s, 1H), 6.57 (br s, 1H), 4.43 (dt, *J* = 4.5, 4.3 Hz, 1H), 3.07-2.97 (m, 3H), 2.74 (dd, *J* = 10.0, 3.9 Hz, 1H), 2.28-2.12 (m, 2H), 1.37 (s, 9H) ppm. **^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ** 173.1 (C), 170.1 (C), 155.3 (C), 138.1 (C), 129.0 (CH), 127.9 (CH), 126.1 (CH), 77.5 (C), 53.6 (CH), 37.5 (CH_2), 36.5 (CH_2), 35.5 (CH_2), 28.2 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{17}H_{26}N_3O_4$ $[M+H]^+$: 336.1918 found 336.1923. **$[\alpha]_D$** = -11 (*c* 5 mg/ml, $CHCl_3$, 25°C). No spectroscopic data are reported in literature.

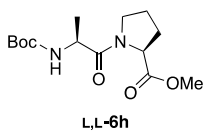
tert-Butyl ((*S*)-1-(((*S*)-1-amino-1-oxo-3-phenylpropan-2-yl)amino)-4-(methylthio)-1-oxobutan-2-yl)carbamate (Boc-L-Met-L-Phe-NH_2, DM770) **L,L-6g**



L,L-6g

The title compound was prepared using general procedure **B,** from Boc-L-Met-NH-*t*Bu-nic **L-4e** (213 mg, 0.5 mmol, 1 equiv), H-L-Phe-NH_2 hydrochloric acid salt **L-ff.HCl** (301 mg, 1.5 mmol, 3 equiv), NaOAc (123 mg, 1.5 mmol, 3 equiv) and $Zn(OAc)_2$ (18 mg, 0.1 mmol, 20 mol%) in THF (1 ml). This yielded, after Grace Reveleris® X2 Normal Phase silicagel flash chromatography (Petroleum Ether:EtOAc, 100:0 to 0:100 over 20 CV), the desired compound as a white powder in 89% (175 mg, 0.443 mmol) yield. **^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ** 7.77 (d, *J* = 8.3 Hz, 1H), 7.40 (s, 1H), 7.29 – 7.16 (m, 5H), 7.13 (s, 1H), 7.03 (d, *J* = 7.4 Hz, 1H), 4.49 (dd, *J* = 12.8, 8.1 Hz, 1H), 3.93 (dd, *J* = 13.4, 6.6 Hz, 1H), 3.04 (dd, *J* = 13.6, 4.5 Hz, 1H), 2.85 (dd, *J* = 13.7, 8.9 Hz, 1H), 2.33 (t, *J* = 6.5 Hz, 2H), 1.99 (s, 3H), 1.72 (dd, *J* = 13.9, 7.0 Hz, 2H), 1.38 (s, 9H), 1.29 (s, 1H) ppm. **^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ** 173.2 (C), 171.7 (C), 155.87 (C), 138.2 (C), 129.7 (CH), 128.4 (CH), 126.7 (CH), 78.8 (C), 54.5 (CH), 53.8 (CH), 38.0 (CH_2), 32.0 (CH_2), 30.0 (CH_2), 28.6 (CH_3), 15.0 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{19}H_{29}N_3O_4SNa$ $[M+Na]^+$: 418.1771 found 418.1754. **$[\alpha]_D$** = -33 (*c* 5 mg/ml, $CHCl_3$, 25°C). No spectroscopic data are reported in literature.

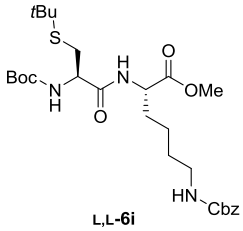
Methyl (*tert*-butoxycarbonyl)-L-alanyl-L-prolinate (Boc-L-Ala-L-Pro-OMe, KH_1204) **L,L-6h**



L,L-6h

The title compound was prepared using general procedure **B,** from Boc-L-Ala-NH-*t*Bu-nic **L-4b** (183 mg, 0.5 mmol, 1 equiv), H-L-Pro-OMe hydrochloric acid salt **L-5g.HCl** (mg, 1.5 mmol, 3 equiv), NaOAc (123 mg, 1.5 mmol, 3 equiv) and $Zn(OAc)_2$ (18 mg, 0.1 mmol, 20 mol%) in THF (1 ml), by stirring at 100°C for 24 h. This yielded, after Grace Reveleris® X2 Normal Phase silicagel flash chromatography (Petroleum Ether:EtOAc, 100:0 to 0:100 over 20 CV), the desired compound as a white powder in 68% (102 mg, 0.338 mmol) yield. **^{1}H NMR (500 MHz, $CDCl_3$) δ** 5.34 (d, *J* = 7.8 Hz, 1H), 4.53 (dd, *J* = 4.4, 7.0 Hz, 1H), 4.49-4.42 (m, 1H), 3.72 (s, 3H), 3.72-3.67 (m, 1H), 3.64-3.57 (m, 1H), 2.26-2.16 (m, 1H), 2.10-1.94 (m, 3H), 1.42 (s, 9H), 1.35 (d, *J* = 6.9 Hz, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$) δ** 172.5 (C), 171.8 (C), 155.4 (C), 79.7 (C), 58.8 (CH), 52.3 (CH_3), 47.9 (CH), 46.9 (CH_2), 29.0 (CH_2), 28.5 (CH_3), 25.0 (CH_2), 18.4 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{14}H_{24}N_2O_5Na$ $[M+Na]^+$: 323.1577 found 323.1556. **$[\alpha]_D$** = -119 (*c* 5 mg/ml, $CHCl_3$, 22°C). No spectroscopic data are reported in literature.

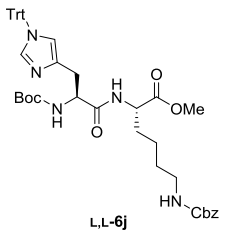
Methyl N^6-((benzyloxy)carbonyl)-N^2-(*N*-(*tert*-butoxycarbonyl)-*S*-(*tert*-butyl)-L-cysteinyl)-L-lysinate (Boc-L-Cys(*t*Bu)-L-Lys(Cbz)-OMe, KH_1315) **L,L-6i**



L,L-6i

The title compound was prepared using general procedure **B** from Boc-L-Cys(*t*Bu)-NH-*t*Bu-nic **L-4l** (226 mg, 0.5 mmol, 1 equiv), H-L-Lys(Cbz)-OMe hydrochloric acid salt **L-5h.HCl** (496 mg, 1.65 mmol, 3 equiv), NaOAc (124 mg, 1.65 mmol, 3 equiv) and $Zn(OAc)_2$ (18 mg, 0.1 mmol, 20 mol%) in THF (1 ml). The reaction mixture was concentrated *in vacuo* and redisolved in EtOAc. The organic phase was washed with HCl (3x, 1 M), $NaHCO_3$ (3x, sat.) and brine. The organic phase was dried over $MgSO_4$, filtrated and concentrated *in vacuo*. After Grace Reveleris® X2 Normal Phase silicagel flash chromatography (CH_2Cl_2:EtOAc, 100:0 to 70:30 over 10 CV), this yielded the desired compound as a white powder in 57% (157 mg, 0.285 mmol) yield. **^{1}H NMR (500 MHz, $CDCl_3$) δ** 7.38-7.27 (m, 4H), 6.99-6.90 (m, 1H), 6.07 (br s, 1H), 5.43 (d, *J* = 7.0 Hz, 1H), 5.14-5.07 (m, 2H), 4.96 (br s, 1H), 4.59 (dd, *J* = 16.1, 7.5 Hz, 1H), 4.32-4.25 (m, 1H), 3.73 (s, 3H), 3.22-3.13 (m, 2H), 2.99 (dd, *J* = 12.9, 5.58 Hz, 1H), 2.82 (dd, *J* = 12.7, 6.3 Hz, 1H), 1.91-1.83 (m, 1H), 1.74-1.65 (m, 1H), 1.57-1.49 (m, 2H), 1.45 (s, 9H), 1.40- 1.33 (m, 2H), 1.32 (s, 9H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$) δ** 172.2 (C), 170.8 (C), 156.6 (C), 155.5 (C), 136.5 (C), 128.5 (CH), 128.1 (CH), 80.5 (C), 66.7 (CH), 54.2 (CH), 52.4 (CH_3), 52.0 (CH), 42.9 (C), 40.6 (CH_2), 31.9 (CH_2), 30.8 (CH_3), 30.4 (CH_2), 29.1 (CH_2), 28.2 (CH_3), 22.1 (CH_2) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{27}H_{43}N_3O_7SNa$ $[M+Na]^+$: 576.2720 found 576.2776. **$[\alpha]_D$** = -6 (*c* 10 mg/ml, $CHCl_3$, 20°C). No spectroscopic data are reported in literature.

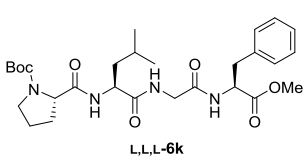
Methyl N^6-((benzyloxy)carbonyl)-N^2-(N'-(*tert*-butoxycarbonyl)-N^τ-trityl-L-histidyl)-L-lysinate (Boc-L-His(Trt)-L-Lys(Cbz)-OMe, KH_1308) **L,L-6j**



L,L-6j

The title compound was prepared using general procedure **B** from Boc-L-His(Trt)-NH-*t*Bu-nic **L,L-4m** (336 mg, 0.5 mmol, 1 equiv), H-L-Lys(Cbz)-OMe hydrochloric acid salt **L-5h.HCl** (496 mg, 1.65 mmol, 3 equiv), NaOAc (124 mg, 1.65 mmol, 3 equiv) and $Zn(OAc)_2$ (18 mg, 0.1 mmol, 20 mol%) in THF (1 ml). This yielded, after Grace Reveleris® X2 Normal Phase silicagel flash chromatography (CH_2Cl_2:EtOAc, 100:0 to 70:30 over 10 CV), the desired compound as a white powder in 72% (276 mg, 0.36 mmol) yield. **^{1}H NMR (500 MHz, MeOD) δ** 8.68 (br s, 1H), 7.51-7.40 (m, 10H), 7.38-7.30 (m, 3H), 7.29-723 (m, 3H), 7.22-7.17 (m, 6H), 5.05 (s, 2H), 4.43 (dd, *J* = Hz, 1H), 4.38 (dd, *J* = Hz, 1H), 3.57 (s, 3H), 3.16 (dd, *J* = 15.0, 4.3 Hz, 1H), 3.12-3.08 (m, 2H), 3.00 (dd, *J* = Hz, 1H), 1.90-1.80 (m, 1H), 1.73-1.65 (m, 1H), 1.56-1.45 (m, 4H), 1.40 (s, 9H) ppm. **^{13}C NMR (126 MHz, MeOD) δ** 174.2 (C), 173.8 (C), 158.9 (C), 157.5 (C), 143.6 (C), 138.4 (C), 137.6 (C), 130.9 (CH), 129.4 (CH), 129.3 (CH), 129.3 (CH), 128.9 (CH), 128.8 (CH), 121.6 (CH), 80.6 (C), 67.3 (C), 55.8 (CH), 53.5 (CH), 52.7 (CH_3), 41.4 (CH_2), 32.3 (CH_2), 31.6 (CH_2), 30.3 (CH_2), 28.8 (CH_3), 23.8 (CH_2) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{45}H_{52}N_5O7$ $[M+H]^+$: 774.3867 found 774.3804. **$[\alpha]_D$** = -5 (*c* 10 mg/ml, $CHCl_3$, 20°C). No spectroscopic data are reported in literature.

tert-Butyl (*S*)-2-(((*S*)-1-((2-(((*S*)-1-methoxy-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethyl)amino)-4-methyl-1-oxopentan-2-yl)carbamoyl)pyrrolidine-1-carboxylate (Boc-L-Pro-L-Leu-Gly-L-Phe-OMe, KH_1265) **L,L,L-6k**



L,L,L-6k

The title compound was prepared using general procedure **B,** from Boc-L-Pro-L-Leu-Gly-NH-*t*Bu-nic **L-4n** (281 mg, 0.5 mmol, 1 equiv), H-L-Phe-OMe hydrochloric acid salt **L-5a.HCl** (119 mg, 0.55 mmol, 1.1 equiv), NaOAc (45 mg, 0.55 mmol, 1.1 equiv) and $Zn(OAc)_2$ (18 mg, 0.1 mmol, 20 mol%) in THF (1 ml). This yielded, after Grace Reveleris® X2 Normal Phase silicagel flash chromatography (Petroleum Ether:EtOAc, 100:0 to 0:100 over 20 CV), the desired compound as a yellow oil in 88% (240 mg, 0.439 mmol) yield. **^{1}H (500 MHz, DMSO-d_6, mixture of rotamers) δ** 8.26 (d, *J* = 7.6 Hz, 0.6H), 8.20 (d, *J* = 8.0 Hz, 0.4H), 8.09 (t, *J* = 5.0 Hz, 0.6H), 8.04 (t, *J* = 5.2 Hz, 0.4H), 7.98-7.92 (m, 1H), 7.30-7.24 (m, 2H), 7.23-7.16 (m, 3H), 4.50-4.43 (m, 1H), 4.31-4.19 (m, 1H), 4.13 (dd, *J* = 3.1, 8.6 Hz, 1H), 3.73 (dd, *J* = 6.1, 16.8 Hz, 1H), 3.68-3.60 (m, 1H), 3.57 (s, 3H), 3.34-3.29 (m, 1H), 3.28-3.22 (m, 1H), 3.00 (dd, *J* = 6.1, 13.8 Hz, 1H), 2.91 (dd, *J* = 8.9, 13.9 Hz, 1H), 2.12-1.96 (m, 1H), 1.81-1.68

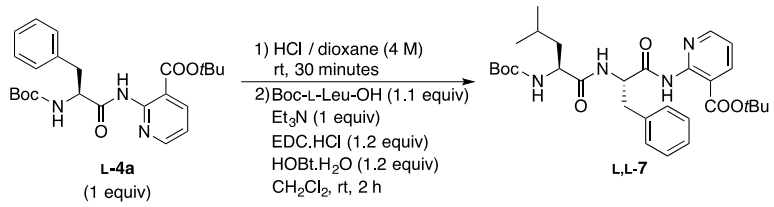
(m, 3H), 1.68-1.58 (m, 1H), 1.53-1.41 (m, 2H), 1.36 (s, 3H), 1.31 (s, 6H), 0.91-0.80 (m, 6H) ppm. **^{13}C (126 MHz, DMSO-*d*$_6$, mixture of rotamers) δ** 172.4 (C), 172.2 (C), 171.7 (C), 168.7 (C), 153.3 (C), 136.9 (C), 129.0 (CH), 128.2 (CH), 126.5 (CH), [78.7, 78.3] (C), [59.3, 59.2] (CH), 53.6 (CH), 51.8 (CH_3), [51.2, 51.0] (CH), [46.6, 46.4] (CH_2), 41.5 (CH_2), 40.8 (CH), 36.8 (CH_2), 30.9 (CH_2), 29.5 (CH_2), [28.0, 27.9] (CH_3), 24.0 (CH_2), [23.0, 22.9] (CH_3), 21.5 (CH_3) ppm. NMR-data was acquired at elevated temperature so that peaks arising from hindered rotation coalesced. **^{1}H (500 MHz, DMSO-*d*$_6$, 80°C) δ** 7.94 (d, *J* = 6.5 Hz, 1H), 7.79 (t, *J* = 5.3 Hz, 1H), 7.67 (d, *J* = 7.4 Hz, 1H), 7.30-7.25 (m, 2H), 7.23-7.18 (m, 3H), 4.57-4.51 (m, 1H), 4.33-4.26 (m, 1H), 4.13 (dd, *J* = 2.8, 8.1 Hz, 1H), 3.74 (dd, *J* = 5.7, 16.7 Hz, 1H, overlap with HDO), 3.67 (dd, *J* = 5.7, 16.7 Hz, 1H overlap with HDO), 3.60 (s, 3H overlap with HDO), 3.38-2.27 (m, 2H), 3.04 (dd, *J* = 13.8 , 6.0 Hz 1H), 2.92 (dd, *J* = 8.0, 13.8 Hz, 1H), 2.10-2.03 (m, 1H), 1.91-1.84 (m, 1H), 1.83-1.73 (m, 2H), 1.72-1.63 (m, 1H), 1.51 (dd, *J* = 6.7, 6.7 Hz, 2H), 1.38 (s, 9H), 0.89 (d, *J* = 6.7 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 3H) ppm. **^{13}C (126 MHz, DMSO-*d*$_6$, 80°C) δ** 171.9 (C), 171.8 (C), 171.1 (C), 168.2 (C), 153.4 (C), 136.6 (C), 128.6 (CH), 127.8 (CH), 126.1 (CH), 78.3 (C), 59.2 (CH), 53.2 (CH), 51.2 (CH_3), 51.1 (CH), 46.2 (CH_2), 41.6 (CH_2), 40.6 (CH), 36.7 (CH_2), 29.0 (CH_2), 27.7 (CH_3), 23.8 (CH_2), 23.0 (CH_2), 22.5 (CH_3), 21.2 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{27}H_{42}N_2O_6Na$ $[M+Na]^+$: 515.3091 found 515.3090. **$[\alpha]_D$** = -31 (*c* 5 mg/ml, $CHCl_3$, 22°C). No spectroscopic data are reported in literature.

Remark: Diastereomerical purity was checked on the target compounds. The diastereomerical excess (%de) was evaluated with HPLC (UV detector) on a Chiralpak IA column and/or ^{1}H NMR analysis.

5.4 Segment Coupling using Transamidation

Synthesis of the Directing Group Functionalized Peptide Segment

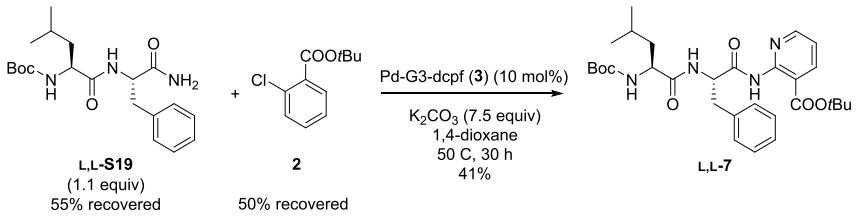
tert-Butyl 2-((*S*)-2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-4-methylpentanamido)-3-phenylpropanamido)nicotinate (Boc-L-Leu-L-Phe-NH-*t*Bu-nic, KH_549/ER1730) **L,L-7**



KH_549: The synthesis of Boc-L-Leu-L-Phe-NH-*t*Bu-nic **L,L-7** was started from Boc-L-Phe-NH-*t*Bu-nic **L-4a** (221 mg, 0.5 mmol, 1 equiv), initially deprotected following general procedure **C** with HCl/dioxane (10 ml, 4 M). After removal of the solvent under vacuum, the resulting crude solid material (L-Phe-NH-*t*Bu-nic.HCl) was used in the subsequent step without further purification.

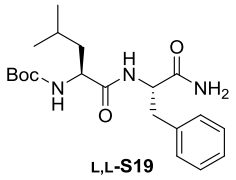
The next step was performed following general procedure **D**. The crude was dissolved in CH_2Cl_2 (20 ml) and Et_3N was added until the mixture reached pH 9. This was added to the pre-activated mixture of Boc-L-Leu-OH (137 mg, 0.55 mmol, 1.1 equiv), EDC.HCl (125 mg, 0.65 mmol, 1.2 equiv) and HOBt.H_2O (100 mg, 0.65 mmol, 1.2 equiv). The reaction mixture was stirred for 2 h. After extraction, the title compound **L,L-7** could be obtained as a white powder with 96% (266 mg, 0.48 mmol) over the two steps.

^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 10.82 (br s, 1H), 8.53 (br s, 1H), 8.06 (d, *J* = 7.7 Hz, 1H), 7.94 (d, *J* = 8.8 Hz, 1H), 7.32-7.28 (m, 3H), 7.26-7.20 (m, 2H), 7.20-7.15 (m, 1H), 6.83 (d, *J* = 8.9 Hz, 1H), 4.94-4.86 (m, 1H), 3.98-3.91 (m, 1H), 3.13 (d, *J* = 13.8 Hz, 1H), 2.83 (dd, *J* = 11.8, 11.8 Hz, 1H), 1.47 (s, 9H), 1.36 (s, 9H), 1.28-1.22 (m, 3H), 0.84-0.76 (m, 6H) ppm. **^{13}C NMR (126 MHz, DMSO-*d*$_6$) δ** 172.2 (C), 170.1 (C), 164.8 (C), 155.0 (C), 150.6 (CH), 148.3 (C), 138.8 (CH), 137.3 (C), 129.3 (CH), 127.9 (CH), 126.2 (CH), 120.8 (C), 120.1 (CH), 81.3 (C), 78.0 (C), 53.8 (CH), 52.9 (CH), 41.1 (CH_2), 37.4 (CH_2), 28.1 (CH_3), 27.7 (CH_3), 24.1 (CH), 22.8 (CH_3), 21.5 (CH_3) ppm. **HRMS** (ESI+) m/z calcd. for $C_{30}H_{43}N_4O_6$, $[M+H]^+$: 555.3177 found 555.3175. **$[\alpha]_D$** = -22 (*c* 10 mg/ml, $CHCl_3$, 25°C). No spectroscopic data are reported in literature.



ER1730: The title compound was synthesized using general procedure **A2**, from Boc-L-Leu-L-Phe-NH_2 **L,L-S19** (0.208 mg, 0.55 mmol, 1.1 equiv), K_2CO_3 (0.518 g, 3.75 mmol, 7.5 equiv), Pd-G3-dcpf **3** (52 mg, 0.05 mmol, 10 mol%) and *tert*-butyl 2-chloronicotinate **2** (107 mg, 0.5 mmol, 1 equiv) in anhydrous 1,4-dioxane (3.13 mL). The reaction mixture was purified using the Biotage® Isolera One Normal phase silicagel flash chromatography (*n*-Heptane:EtOAc, 100:0 to 50:50 over 45 min) to obtain white powder in 41% (114 mg, 0.2 mmol) yield. Boc-L-Leu-L-Phe-NH_2 and *tert*-butyl 2-chloronicotinate **2** were recoverd in 55% (113 mg, 0.3 mmol) and 50 % (54 mg, 0.25 mmol) yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ** 10.82 (br s, 1H), 8.53 (br s, 1H), 8.06 (d, *J* = 7.7 Hz, 1H), 7.94 (d, *J* = 8.8 Hz, 1H), 7.32-7.28 (m, 3H), 7.26-7.20 (m, 2H), 7.20-7.15 (m, 1H), 6.83 (d, *J* = 8.9 Hz, 1H), 4.94-4.86 (m, 1H), 3.98-3.91 (m, 1H), 3.13 (d, *J* = 13.8 Hz, 1H), 2.83 (dd, *J* = 11.8, 11.8 Hz, 1H), 1.47 (s, 9H), 1.36 (s, 9H), 1.28-1.22 (m, 3H), 0.84-0.76 (m, 6H) ppm. **^{13}C NMR (126 MHz, DMSO-*d*$_6$) δ** 172.2 (C), 170.1 (C), 164.8 (C), 155.0 (C), 150.6 (CH), 148.3 (C), 138.8 (CH), 137.3 (C), 129.3 (CH), 127.9 (CH), 126.2 (CH), 120.8 (C), 120.1 (CH), 81.3 (C), 78.0 (C), 53.8 (CH), 52.9 (CH), 41.1 (CH_2), 37.4 (CH_2), 28.1 (CH_3), 27.7 (CH_3), 24.1 (CH), 22.8 (CH_3), 21.5 (CH_3) ppm. **HRMS** (ESI+) m/z calcd. for $C_{30}H_{43}N_4O_6$, $[M+H]^+$: 555.3177 found 555.3175. **$[\alpha]_D$** = -22 (*c* 10 mg/ml, $CHCl_3$, 25°C). No spectroscopic data are reported in literature.

tert-Butyl 2-((*S*)-2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-4-methylpentanamido)-3-phenylpropanamido)nicotinate (Boc-L-Leu-L-Phe-NH_2, KH_1281) **L,L-S19**

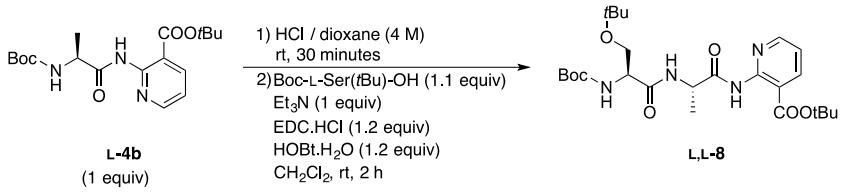


The synthesis of Boc-L-Leu-L-Phe-NH_2 **L,L-S19** was performed following general procedure **D** from Boc-L-Leu-OH.H_2O 499 mg, 2 mmol, 1 equiv), H-Phe-NH_2.HCl (328 mg, 2 mmol, 1 equiv), EDC.HCl (460 mg, 2.4 mmol, 1.2 equiv) and HOBt.H_2O (368 mg, 2.4 mmol, 1.2 equiv), Et_3N (0.279 ml, 2 mmol, 1 equiv) in CH_2Cl_2 (50 ml). This yielded, after extraction, the title compound as a colourless oil with 94% (706 mg, 1.87 mmol).

^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 7.68 (d, *J* = 8.3 Hz, 1H), 7.39 (br s , 1H), 7.25-7.15 (m, 5H), 7.10 (br s, 1H), 6.96 (d , *J* = 8.05 Hz, 1H), 4.50-4.42 (m, 1H), 3.91-3.77 (m, 1H), 3.00 (dd, *J* = 14.1, 4.8 Hz, 1H), 2.82 (dd, 14.2, 8.9 Hz, 1H), 1.52-1.41 (m, 1H), 1.37 (s, 9H), 1.33-1.26 (m, 1H), 1.26-1.20 (m, 1H), 0.81 (d, *J* = 6.7 Hz, 3H), 0.77 (d, *J* = 6.5 Hz, 3H) ppm. **^{13}C NMR (126 MHz, DMSO-*d*$_6$) δ** 172.7 (C), 172.0 (C), 155.3 (C), 137.7 (C), 129.2 (CH), 127.9 (CH), 126.1 (CH), 78.2 (C), 53.3 (CH), 53.1 (CH),

40.7 (CH_2), 37.6 (CH_2), 28.2 (CH_3), 24.1 (CH), 22.8 (CH_3), 21.6 (CH_3) ppm. **HRMS** (ESI+) m/z calcd. $C_{20}H_{32}N_3O_4$ for $[M+H]^+$: 378.2393 found 378.2347. No spectroscopic data are reported in literature.

tert-Butyl 2-((*S*)-2-((*S*)-3-(*tert*-butoxy)-2-((*tert* butoxycarbonyl)amino)propanamido)propanamido) nicotinate (Boc-L-Ser(*t*Bu)-L-Ala-NH-*t*Bu-nic, KH_635) **L,L-8**



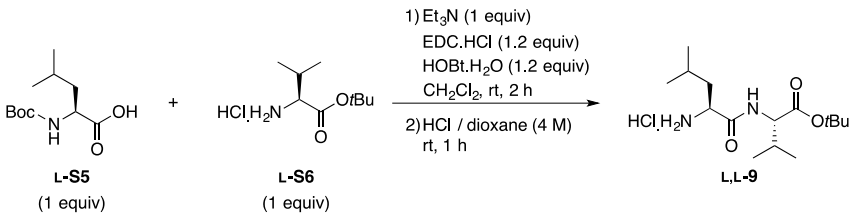
For the synthesis of Boc-L-Ser(*t*Bu)-L-Ala-NH-*t*Bu-nic **L,L-8** was started from Boc-L-Ala-NH-*t*Bu-nic **L-4b** (512 mg, 1.4 mmol, 1 equiv) that was deprotected following general procedure **C** with HCl/dioxane (20 ml, 4 M). After removal of the solvent under vacuum, the resulting crude solid material (L-Ala-NH-*t*Bu-nic.HCl) was used in the subsequent step without further purification.

The next step was performed following general procedure **D**. The crude was dissolved in CH_2Cl_2 (30 ml) and Et_3N was added until the mixture reached pH 9. This was added to the pre-activated mixture of Boc-L-Ser(*t*Bu)-OH (366 mg, 1.4 mmol, 1 equiv), EDC.HCl (322 mg, 1.68 mmol, 1.2 equiv) and HOBt.H_2O (257 mg, 1.68 mmol, 1.2 equiv). The reaction mixture was stirred for 2 h. After extraction the title compound **L,L-8** could be obtained as a white powder with quantitive yield (748 mg, 1.4 mmol) over the two steps.

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.22 (s, 1H), 8.58 (dd, *J* = 2.1, 4.8 Hz, 1H), 8.23 (dd, *J* = 2.1, 7.9 Hz, 1H), 7.67 (br s, 1H), 7.04 (dd, *J* = 4.8, 7.9 Hz, 1H), 5.47-5.39 (m, 1H), 4.93 (br s, 1H), 4.27-4.21 (m, 1H), 3.80 (d, *J* = 6.0 Hz, 1H), 3.48 (dd, *J* = 7.4, 8.6 Hz, 1H), 1.59 (s, 9H), 1.51 (d, *J* = 7.0 Hz, 3H), 1.44 (s, 9H), 1.20 (s, 9H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$) δ** 171.0 (C), 170.6 (C), 166.1 (C), 155.8 (C), 152.7 (CH), 152.3 (C), 140.2 (CH), 118.5 (CH), 113.0 (C), 83.7 (C), 80.0 (C), 74.2 (C), 61.8 (CH_2), 54.4 (CH), 50.7 (CH), 28.5 (CH_3), 28.2 (CH_3), 27.6 (CH_3), 19.0 (CH_3) ppm. **HRMS** (ESI+) m/z calcd. for $C_{25}H_{41}N_4O_7$, $[M+H]^+$: 509.2970, found 509.2971. **$[\alpha]_D$** = -2 (*c* 20 mg/ml, $CHCl_3$, 22°C). No spectroscopic data are reported in literature.

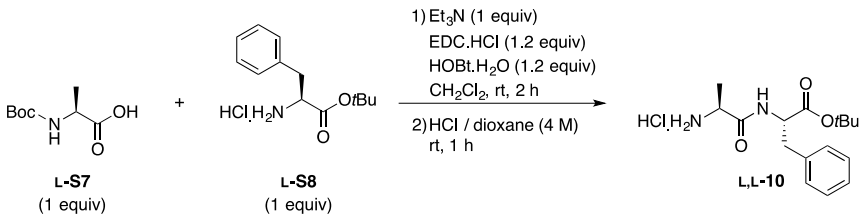
Synthesis of Amine Peptide Segment Hydrochloric Acid Salts

tert-Butyl L-leucyl-L-valinate hydrochloric acid salt (H-L-Leu-L-Val-O*t*Bu.HCl, KH_562) **L,L-9.HCl**



The title compound was obtained by means of a two-step synthesis. The amide coupling was performed following general procedure **D** from Boc-L-Leu-OH **L-S5** (578 mg, 2.5 mmol, 1 equiv), H-L-Val-O*t*Bu hydrochloric acid salt **L-S6** (524 mg, 2.5 mmol, 1 equiv), EDC.HCl (575 mg, 3 mmol, 1.2 equiv), HOBt.H_2O (459 mg, 3 mmol, 1.2 equiv) and Et_3N (0.35 ml, 2.5 mmol, 1 equiv). After extraction, the *N*-Boc protected dipeptide was obtained in a 97% (936 mg, 2.4 mmol) yield. Without intermediate purification, the product was deprotected following general procedure **C** from Boc-L-Leu-L-Val-O*t*Bu (387 mg, 1 mmol, 1 equiv) in HCl in dioxane (20 ml, 4 M) by stirring 30 min at room temperature. After removal of solvent and lyophilisation, the desired compound **L,L-9.HCl** was obtained in nearly quantitative yield (320 mg, 0.99 mmol) as a white powder. **^{1}H NMR (500 MHz, DMSO-d_6) δ** 8.66 (d, *J* = 7.8 Hz, 1H), 8.32 (br s, 2H), 4.04 (dd, *J* = 6.2, 7.9 Hz, 1H), 3.90 (dd, *J* = 7.2, 7.2 Hz, 1H), 2.04 (qdd, *J* = 6.6, 13.1, 13.1 Hz, 1H), 1.68 (qdt, *J* = 6.6, 6.6, 6.6 Hz, 1H), 1.56 (ddd, *J* = 7.2, 7,2, 2.1 Hz, 2H), 1.40 (s, 9H), 0.94-0.86 (m, 12H) ppm. **^{13}C NMR (126 MHz, DMSO-d_6) δ** 169.9 (C), 169.2 (C), 80.8 (C), 58.4 (CH), 50.5 (CH), 40.3 (CH_2), 29.8 (CH), 27.6 (CH_3), 23.5 (CH_3), 22.6 (CH), 22.2 (CH_3), 18.9 (CH_3), 18.2 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{15}H_{31}N_2O_3$, $[M+H]^+$: 287.2329 found 287.2311. **$[\alpha]_D$** = 8 (*c* 10 mg/ml, $CHCl_3$, 19°C). No spectroscopic data are reported in literature.

tert-Butyl L-alanyl-L-phenylalaninate hydrochloride (H-L-Ala-L-Phe-O*t*Bu.HCl, KH_782) **L,L-10.HCl**

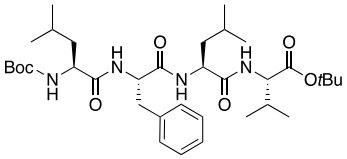


The title compound was obtained by means of a two step synthesis. The peptide synthesis was performed following general procedure **D** from Boc-L-Ala-OH **L-S7** (473 mg, 2.5 mmol, 1 equiv), H-L-Phe-O*t*Bu hydrochloric acid salt **L-S8** (644 mg, 2.5 mmol, 1 equiv), EDC.HCl (575 mg, 3 mmol, 1.2 equiv), HOBt.H_2O (459 mg, 3 mmol, 1.2 equiv) and Et_3N (0.35 ml, 2.5 mmol, 1 equiv). After extraction, the *N*-Boc protected dipeptide was obtained in a 95 % (930 mg, 2.37 mmol) yield. Without

intermediate purification, the product was deprotected following general procedure **C**, from Boc-L-Ala-L-Phe-O*t*Bu (903 mg, 2.3 mmol, 1 equiv) in HCl/dioxane (50 ml, 4 M) by stirring 1 h at room temperature. After removal of solvent and lyophilisation, the desired compound **L,L-10.HCl** was obtained in nearly quantitive yield (749 mg, 2.27 mmol) as a white powder. **^{1}H NMR (500 MHz, $CDCl_3$) δ** 8.27 (br s, 2H), 7.95 (br s, 1H), 7.21-7.18 (m, 4H), 7.15-7.12 (m, 1H), 4.58 (q, *J* = 6.2 Hz, 1H), 4.45 (br s, 1H), 3.14 (dd, *J* = 4.9, 13.3 Hz, 1H), 2.99 (dd, *J* = 7.8, 13.0 Hz, 1H), 1.59 (d, *J* = 5.1 Hz, 3H), 1.29 (s, 9H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$) δ** 170.2 (C), 169.8 (C), 136.4 (C), 129.7 (CH), 128.5 (CH), 126.9 (CH), 82.2 (C), 55.2 (CH), 49.7 (CH), 37.6 (CH_2), 28.0 (CH_3), 17.8 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{16}H_{25}N_2O_3$, $[M+H]^+$: 293.1860 found 293.1838. **$[\alpha]_D$** = 24 (*c* 10 mg/ml, $CHCl_3$, 19°C). No spectroscopic data are reported in literature.

Segment Condensation using Transamidation of N-Boc Protected tert-Butyl Nicotinate Functionalized Dipeptides

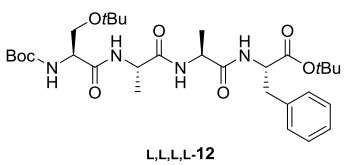
tert-Butyl (*tert*-butoxycarbonyl)-L-leucyl-L-phenylalanyl-L-leucyl-L-valinate (Boc-L-Leu-L-Phe-L-Leu-L-Val-O*t*Bu, KH_1224) **L,L,L,L-11**



L,L,L,L-11

The title compound was prepared using general procedure **B,** from Boc-L-Leu-L-Phe-NH-*t*Bu-nic **L,L-7** (277 mg, 0.5 mmol, 1 equiv), H-L-Leu-L-Val-O*t*Bu hydrochloric acid salt **L,L-9.HCl** (178 mg, 0.55 mmol, 1.1 equiv), NaOAc (46 mg, 0.55 mmol, 1.1 equiv) and $Zn(OAc)_2$ (18 mg, 0.1 mmol, 20 mol%) in THF (1 ml). This yielded, after Grace Reveleris® X2 Normal Phase silica gel flash chromatography (Petroleum Ether:EtOAc, 100:0 to 50:50 over 25 CV to 0:100 in 2 CV), the desired compound **L,L,L,L-11** as a white powder in 83% (269 mg, 0.415 mmol) yield. **^{1}H NMR (500 MHz, $CDCl_3$) δ** 7.29-7.25 (m, 2H), 7.24-7.20 (m, 1H), 7.19-7.16 (m, 2H), 6.87-6.81 (m, 2H), 6.72 (d, *J* = 6.9 Hz, 1H), 4.93 (d, *J* = 6.0 Hz, 1H), 4.71 (dt, *J* = 6.7, 6.8 Hz, 1H), 4.57-4.52 (m, 1H), 4.36 (dd, *J* = 5.4, 8.7 Hz, 1H), 4.00 (td, *J* = 5.0, 9.9 Hz, 1H), 3.17 (dd, *J* = 5.4, 13.1 Hz, 1H), 3.04 (dd, *J* = 6.0, 13.9 Hz, 1H), 2.15 (dq, *J* = 6.7, 13.1 Hz, 1H), 1.75-1.68 (m, 1H), 1.66-1.54 (m, 2H), 1.47 (s, 9H), 1.45-1.40 (m, 1H), 1.36 (s, 9H), 0.94-0.85 (m, 20H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$) δ** 172.8 (C), 171.8 (C), 170.8 (C), 170.7 (C), 156.1 (C), 136.3 (C), 129.4 (CH), 128.9 (CH), 127.2 (CH), 81.8 (C), 80.6 (C), 58.0 (CH), 54.3 (CH), 54.0 (CH) 52.0 (CH), 41.1 (CH_2), 40.9 (CH_2), 37.4 (CH_2), 31.2 (CH), 28.4 (CH_3), 28.1 (CH_3), 24.9 (CH_3), 24.6 (CH_3), 23.1 (CH_3), 23.0 (CH_3), 21.9 (CH), 19.1 (CH_3), 18.1 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{35}H_{58}N_4O_7Na$ $[M+Na]^+$: 669.4198 found 669.4222. **$[\alpha]_D$** = -46 (*c* 5 mg/ml, $CHCl_3$, 25°C).No spectroscopic data are reported in literature.

tert-Butyl *N*-(*tert*-butoxycarbonyl)-*O*-(*tert*-butyl)-L-seryl-L-alanyl-L-alanyl-L-phenylalaninate (Boc-L-Ser(*t*Bu)-L-Ala-L-Ala-L-Phe-O*t*Bu, KH_1229), **L,L,L,L-12**



L,L,L,L-12

The title compound was prepared using general procedure **B,** from Boc-L-Ser(*t*Bu)-L-Ala-NH-*t*Bu-nic **L,L-8** (254 mg, 0.5 mmol, 1 equiv), H-L-Ala-L-Phe-O*t*Bu hydrochloric acid salt **L,L-10.HCl** (181 mg, 0.55 mmol, 1.1 equiv), NaOAc (46 mg, 0.55 mmol, 1.1 equiv) and $Zn(OAc)_2$ (18 mg, 0.1 mmol, 20 mol%) in THF (1 ml). This yielded, after Grace Reveleris® X2 Normal Phase silicagel flash chromatography (Petroleum Ether:EtOAc, 100:0 to 50:50 over 25 CV to 0:100 in 2 CV), the desired compound **L,L,L,L-12** as a white powder in 74% (224 mg, 0.37 mmol) yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ** 8.11 (d, *J* = 7.0 Hz, 1H), 7.95 (d, *J* = 7.7 Hz, 1H), 7.83 (d, *J* = 7.4 Hz, 1H), 7.29-7.25 (m, 2H), 7.23-7.18 (m, 3H), 6.66 (d, *J* = 8.3 Hz, 1H), 4.34-4.27 (m, 3H), 4.02-3.96 (m, 1H), 3.47-3.44 (m, 1H), 3.42-3.38 (m, 1H), 2.99-2.90 (m, 2H), 1.38 (s, 9H), 1.31 (s, 9H), 1.20-1.14 (m, 6H), 1.10 (s, 9H) ppm. **^{13}C NMR (126 MHz, DMSO-*d*$_6$) δ** 171.9 (C), 171.3 (C), 170.2 (C), 169.6 (C), 155.2 (C), 137.1 (C), 129.1 (CH), 128.1 (CH), 126.4 (CH), 80.5 (C), 78.2 (C), 72.8 (C), 61.8 (CH_2), 55.0 (CH), 54.1 (CH), 47.9 (CH), 47.6 (CH), 36.7 (CH_2), 28.1 (CH_3), 27.4 (CH_3), 27.1 (CH_3), 18.4 (CH_3), 18.3 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{31}H_{50}N_4O_8Na$ $[M+Na]^+$: 629.3521 found 629.3542. **$[\alpha]_D$** = 6 (*c* 10 mg/ml, $CHCl_3$, 25°C). No spectroscopic data are reported in literature.

*HPLC Analysis of the Peptide **11** and **12** obtained by transamidation*

To confirm the NMR analysis indicating peptide **L,L,L,L-11** and **L,L,L,L-12** are diasteriomerically pure tetrapeptides, HPLC analysis was performed. Initially, a mixture of **L,L,L,L-** and **L,D,L,L**-diastereomers, obtained through classical peptide synthesis, was prepared for both peptides. The mixture was fully resolved on a Diacel Chiralpak IA column with an isocratic gradient of heptane/ethanol (80:20) (cf. Figure S11 for peptide **11** and Figure S13 for peptide **12**). Subsequently, the analysis of peptide **11** (KH_1224) and peptide **12** (KH_1229) obtained through transamidation was performed. Herein, peptide **11** (KH_1224; Figure S12) lacked any sign of the **L,D,L,L-11**. For peptide **12** (KH_1229; Figure S14), the analysis revealed less than 2% of the **L,D,L,L-12**.

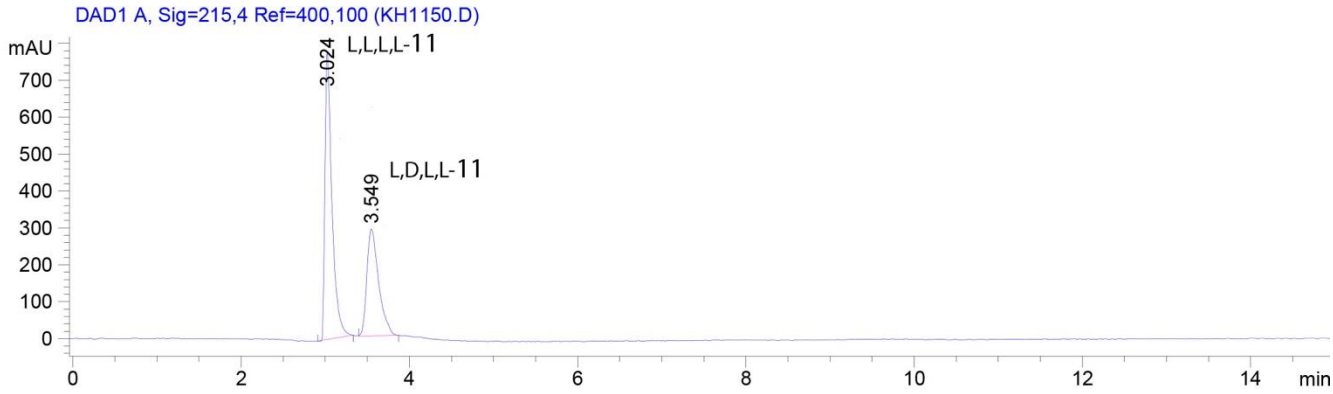


Figure S11. Chromatogram obtained at 215 nm by HPLC analysis with heptane/ethanol (80:20) of a mixture of **L,L,L,L-11** and **L,D,L,L-11**.

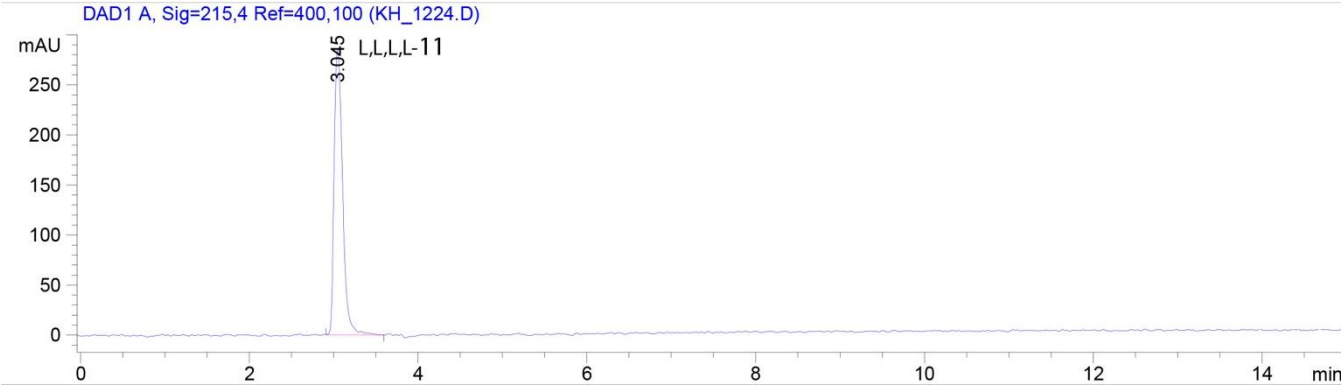


Figure S12. Chromatogram obtained of peptide **11** (KH_1224) synthesized via transamidation at 215 nm by HPLC analysis with heptane/ethanol (80:20) revealing **L,L,L,L-11** purity.

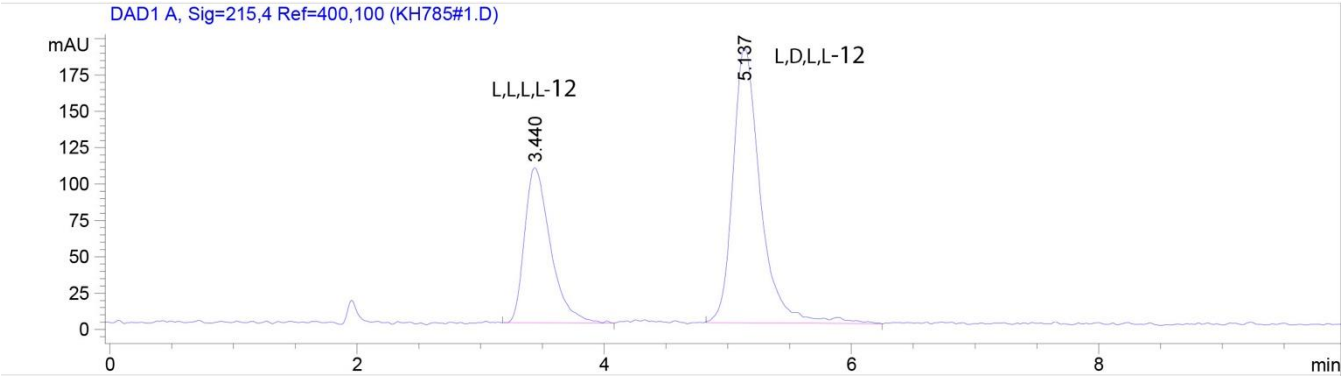


Figure S13. Chromatogram obtained at 215 nm by HPLC analysis with heptane/ethanol (80:20) of a mixture of **L,L,L,L-12** and **L,D,L,L-12**.

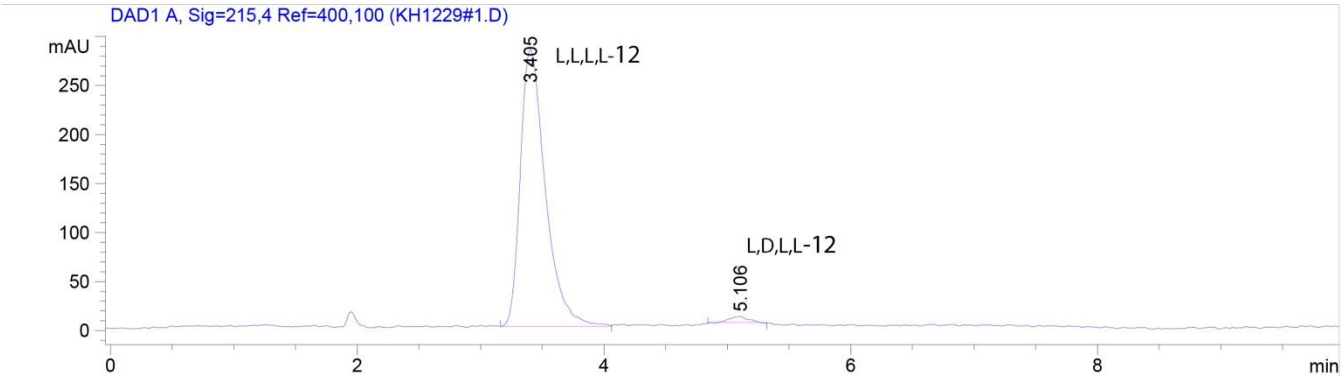
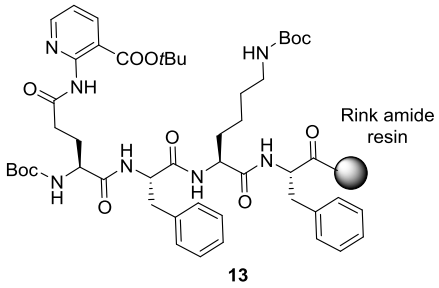


Figure S14. Chromatogram obtained of peptide **12** (KH_1229) synthesized via transamidation at 215 nm by HPLC analysis with heptane/ethanol (80:20) revealing **L,L,L,L-12** purity.

5.5 Transamidation on Solid Support

Fmoc rink amide resin =
4-(2',4'-Dimethoxyphenyl-Fmoc-aminomethyl)phenoxyacetamidoaminomethyl resin

*Assemble of the peptide sequence Boc-Gln(tBu-nic)-Phe-Lys(Boc)-Phe **13** on the solid support*



13

Into an SPPS reactor, Fmoc rink amide resin (303 mg, 0.1 mmol 0.33 mmol/g, 1 equiv) was weighted and swollen in CH_2Cl_2 for 15 minutes under constant shaking. The solvent was removed by filtration and the deprotection of the Fmoc protection group was achieved by treatment of the resin with a solution of 4-methylpiperidine (20%) in DMF (5 and 15 minutes of shaking). In the meantime, a mixture of *N*-Fmoc protected amino acid (3 equiv), HBTU (114 mg, 0.3 mmol, 3 equiv) and DIPEA (87 µl, 0.5 mmol, 5 equiv) was stirred for 15 minutes in DMF (1 ml). The resin was washed with DMF (3x) and CH_2Cl_2 (3x) before the pre-stirred mixture was added. After 40 minutes of shaking, the excess of reagents was removed by filtration and the resin was washed with DMF (3x) and CH_2Cl_2 (3x). The Kaiser test was applied to determine if the peptide coupling was finished. The same deprotection and coupling strategy was applied for the coupling of the following amino acids. Coupling of the Boc-L-Gln(*t*Bu-nic)-OH **L-4o** was achieved overnight.

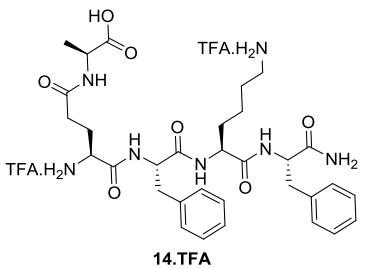
Kaiser test

For this test, some beats were transferred in a glass tube. Then two droplets of each of the following solutions were added:

1) a solution of ninhydrin (2.5 g) in EtOH (50 ml);
2) a solution of phenol (40 g) in EtOH (10 ml)
3) a solution of KCN (1 ml, 0.001M, aqueous) in pyridine (49 ml).

The glass tube was heated at 110˚C in a sand bath for approximately 5 min. A pale yellow colored mixture indicates less than 1% free amine present on the resin, while a dark blue color reveals that the coupling was incomplete. In that case, the coupling was repeated.

N-[(1*S*)-1-carboxyethyl]-L-glutaminyl-L-phenylalanyl-L-lysyl-L-phenylalanine **14.TFA** from **13**

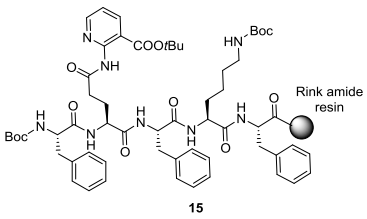


14.TFA

In the SPPS reactor, the resin with the assembled peptide **13** was rinsed with DMF (3x), CH_2Cl_2 (3x) and THF (3x). The resin is swollen in THF for 5 min, then carefully transferred in round-bottom shape microwave vial equipped with a magnet. Remaining beads in the SPPS reactor were recovered using additional THF. Subsequently, the beads were allowed

to deposit at the bottom of the vial and the excess of THF supernatant was carefully removed by pipette to reduce the solvent to a minimal volume. $Zn(OAc)_2$ (3.6 mg, 0.02 mmol, 20 mol%, 0.02 mmol), NaOAc (41 mg, 0.5 mmol, 5 equiv) and H-L-Ala-O*t*Bu.HCl **L-5i.HCl** (91 mg, 0.5 mmol, 5 equiv) were added and the vial was sealed with a crimp cap. The reaction was stirred over 48 h at 90°C. After it was allowed to cool down to room temperature, the reacting mixture was diluted with THF and CH_2Cl_2 and then transferred to the SPPS syringe reactor. The resin is thoroughly washed with THF and CH_2Cl_2. The resin is then cleaved using TFA/TIS/H_2O (95:2.5:2.5) cocktail for 2 hours at room temperature. After filtration, the solvent is removed *in vacuo* and the crude cleaved product is lyophilized and purified using semi-preparative HPLC (H_2O:CH_3CHN 80:20 to 45:55 over 20 min). This yielded, after lyophilization, the title compound **14.TFA** with 59% (51 mg, 0.059 mmol) yield. **HPLC** rt = 2.69 min. **HRMS** (ESI+) m/z: 640.3459 found 640.3411. **$[\alpha]_D$** = -8 (c 5 mg/ml, CH_3OH, 21°C).

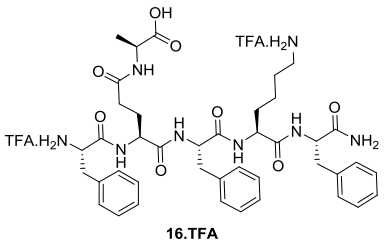
Assemble of the peptide sequence Boc-Phe-Gln(tBu-nic)-Phe-Lys(Boc)-Phe **15** *on the solid support*



15

Into an SPPS reactor, Fmoc rink amide resin (151 mg, 0.1 mmol 0.67 mmol/g, 1 equiv) was weighted and swollen in CH_2Cl_2 for 15 minutes under constant shaking. The solvent was removed by filtration and the deprotection of the Fmoc protection group was achieved by treatment of the resin with a solution of 4-methylpiperidine (20%) in DMF (5 and 15 minutes of shaking). In the meantime, a mixture of *N*-Fmoc protected amino acid (3 equiv), HBTU (114 mg, 0.3 mmol, 3 equiv) and DIPEA (87 µl, 0.5 mmol, 5 equiv) was stirred for 15 minutes in DMF (1 ml). The resin was washed with DMF (3x) and CH_2Cl_2 (3x) before the pre-stirred mixture was added. After 40 minutes of shaking, the excess of reagents was removed by filtration and the resin was washed with DMF (3x) and CH_2Cl_2 (3x). The Kaiser test was applied to determine if the peptide coupling was finished. The same deprotection and coupling strategy was applied for the coupling of the following amino acids. Coupling of the Fmoc-L-Gln(*t*Bu-nic)-OH **L-4p** was achieved overnight.

L-phenylalanyl-*N*-[(1*S*)-1-carboxyethyl]-L-glutaminyl-L-phenylalanyl-L-lysyl-L-phenylalanine **16.TFA** from **15**



16.TFA

In the SPPS reactor, the resin with the assembled peptide **15** was rinsed with DMF (3x), CH_2Cl_2 (3x) and THF (3x). The resin is swollen in THF for 5 min, then carefully transferred in round-bottom shape microwave vial equipped with a magnet. Remaining beads in the SPPS reactor were recovered using additional THF. Subsequently, the beads were allowed to deposit at the bottom of the vial and the excess of THF supernatant was carefully removed by pipette to reduce the solvent to a minimal volume. $Zn(OAc)_2$ (3.6 mg, 0.02 mmol, 20

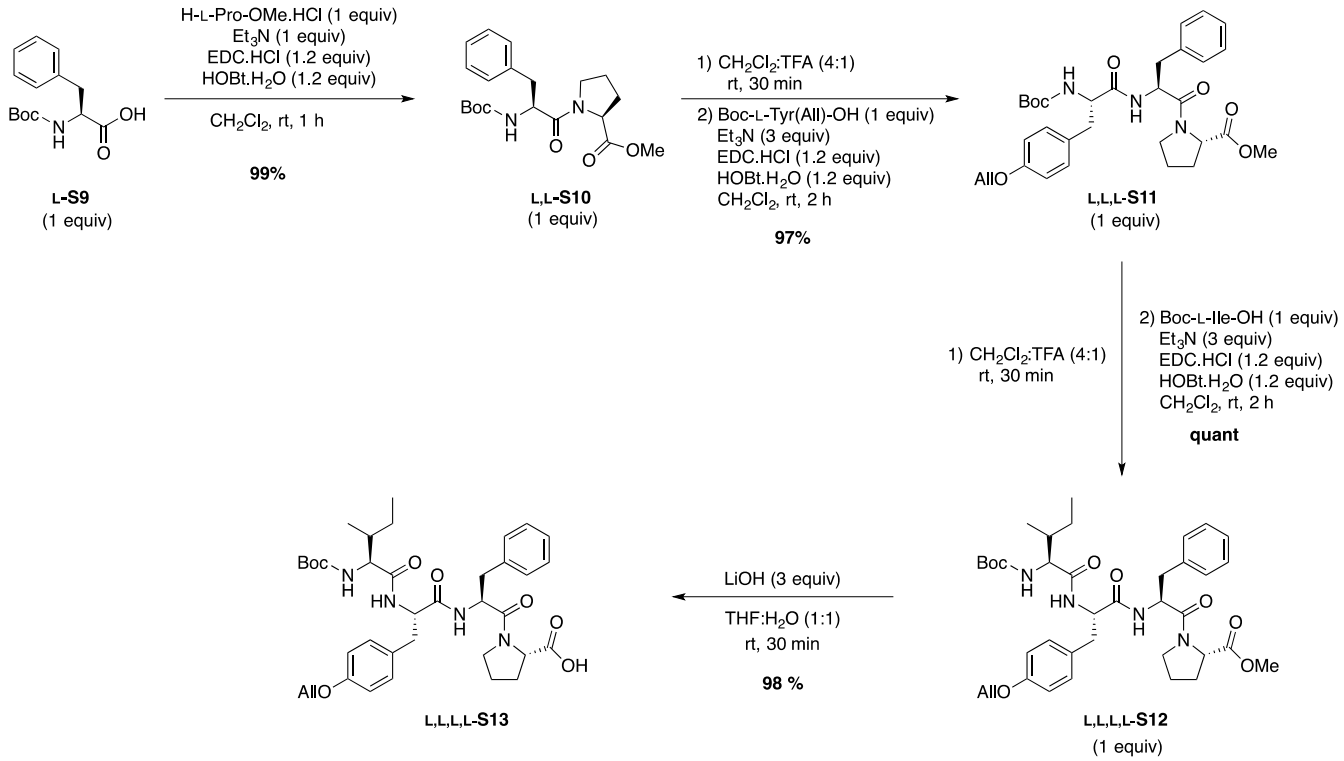
mol%, 0.02 mmol), NaOAc (41 mg, 0.5 mmol, 5 equiv) and H-L-Ala-O*t*Bu.HCl **L-5i** (91 mg, 0.5 mmol, 5 equiv) were added and the vial was sealed with crimp cap. The reaction was stirred over 48 h at 90°C. After it was allowed to cool down to room temperature, the reacting mixture was diluted with THF and CH_2Cl_2 and then transferred to the SPPS syringe reactor. The resin is thoroughly washed with THF and CH_2Cl_2. The resin is then cleaved using TFA/TIS/H_2O (95:2.5:2.5) cocktail for 2 hours at room temperature. After filtration, the solvent is removed *in vacuo* and the crude cleaved product is lyophilized and purified using semi-preparative HPLC (H_2O:CH_3CHN 80:20 to 45:55 over 20 min). This yielded, after lyophilization, the title compound **16.TFA** with 50% (50 mg, 0.049 mmol) yield. **HPLC** rt = 2.90 min. **HRMS** (ESI+) m/z calc for $C_{41}H_{54}N_8O_8Na$ $[M+Na]^+$: 809.3962 found 809.4008. $\mathbf{[\alpha]_D}$ = -23 (c 5 mg/ml, CH_3OH, 21°C).

5.6 Cyclization using Transamidation of *t*Bu-nicotinate Linear Heptapeptide: Synthesis and Cyclization

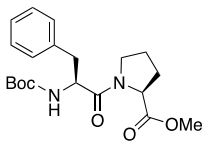
*Synthesis of the tBu nicotinate bearing linear heptapeptide **17.HCl***

For the synthesis of the linear heptapeptide 17.HCl, a covergent strategy assembeling fragment **L,L,L,L-S13** and **L,L,L-S15** was used.

*Synthesis of fragment **L,L,L,L-S13***



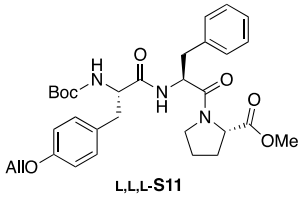
(*S*)-Methyl 1-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-phenylpropanoyl)pyrrolidine-2-carboxylate (Boc-L-Phe-L-Pro-OMe, KH_983) **L,L-S10**



L,L-**S10**

The title compound was prepared using general procedure **D** from Boc-L-Phe-OH **L-S9** (796 mg, 3 mmol, 1 equiv), Pro-OMe.HCl (387 mg, 3 mmol, 1 equiv), EDC.HCl (690 mg, 3.6 mmol, 1.2 equiv), HOBt.H_2O (551 mg, 3.6 mmol, 1.2 equiv) and Et_3N (0.418 ml, 3 mmol, 1 equiv). The reaction mixture was stirred for 1 h. This yielded after extraction the title compound as a white powder with 99% yield (1.118 g, 2.97 mmol). **^{1}H NMR (500 MHz, DMSO-*d*$_6$, mixture of rotamers) δ** 7.35-7.22 (m, 4H), 7.22-7.17 (m, 1H), 7.08 (d, *J* = 8.4Hz, 0.8H), 6.93 (d, *J* = 8.8 Hz, 0.1H), 6.71 (d, *J* = 7.7 Hz, 0.1H), 4.39-4.31 (m, 1.6H), 4.29-4.22 (m, 0.3H), 4.14 (dd, *J* = 2.5, 7.9 Hz, 0.1H), 3.73-3.64 (m, 1H), 3.63 (s, 0.4H), 3.61 (s, 2.6H), 3.54-3.47 (m, 0.7H), 3.45-3.37 (m, 0.2H), 3.32-3.25 (m, 0.1H), 2.89 (dd, *J* = 4.5, 14.2 Hz, 0.9H), 2.83 (dd, *J* = 4.1, 13.6 Hz, 0.1H), 2.74 (dd, *J* = 9.8, 14.1 Hz, 1H), 2.23-2.10 (m, 1H), 1.95-1.89 (m, 1.8H), 1.85-1.78 (m, 1H), 1.74-1.66 (m, 0.2H), 1.29 (s, 6.3H), 1.28 (s, 1.4H), 1.22 (s, 1.3H) ppm. **^{13}C NMR (126 MHz, DMSO-*d*$_6$, mixture of rotamers) δ** [172.4, 172.3, 172.2] (C), [170.5, 170.4, 170.2] (C), [155.3, 154.7, 154.2] (C), [137.9, 137.6] (C), [129.9, 129.6, 129.4] (CH), [128.6, 128.1] (CH), [127.4, 126.4] (CH), [78.3, 78.1, 78.0] (C), [59.0, 58.7, 58.5] (CH), [55.2, 53.8, 53.4] (CH), [52.2, 52.0, 51.8] (CH_3), [46.6, 46.5, 46.3, 46.1] (CH_2), [38.2, 36.9, 36.4, 36.2] (CH_2), 30.8 (CH_2), [28.6, 28.2, 27.9, 27.7] (CH_3), 24.8 (CH_2) ppm. NMR-data was acquired at elevated temperature so that peaks arising from hindered rotation coalesced. **^{1}H NMR (500 MHz, DMSO-*d*$_6$, 60°C, mixture of rotamers) δ** 7.32-7.24 (m, 3.7H), 7.23-7.18 (m, 1.3H), 6.80 (br s, 1H) 4.48-4.38 (m, 0.7H), 4.35 (dd, *J* = 4.8, 8.7 Hz, 1H), 4.33-4.25 (m, 0.3H), 3.93 (br s, 1H), 3.63 (s, 3H), 3.49-3.42 (m, 0.8H), 3.42-3.37 (m, 0.2H), 2.96-2.87 (m, 1H), 2.78 (dd, *J* = 9.3, 13.5 Hz, 1H), 2.27 (td, *J* = 7.7, 20.1 Hz, 1H), 1.92 (td, *J* = 6.8, 13.7 Hz, 2H), 1.87-1.79 (m, 1H), 1.31 (s, 9H) ppm. **HRMS** (ESI+) m/z: calcd. $C_{20}H_{28}N_2O_5Na$ for $[M+Na]^+$: 399.1891 found 399.1867. No spectroscopic data are reported in literature.

Methyl ((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-*L*-phenylalanyl-*L*-prolinate (Boc-L-Tyr(All)-L-Phe-L-Pro-OMe, KH_985) **L,L,L-S11**

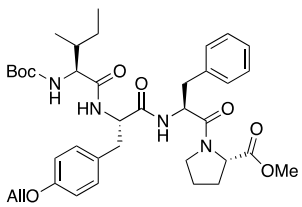


L,L,L-S11

The title compound was obtained by means of a two step synthesis. To a solution of Boc-L-Phe-L-Pro-OMe **L,L-S10** (1.118 g, 2.97 mmol, 1 equiv) in CH_2Cl_2 (20 ml) was trifluoroacetic acid (5 ml) added and the mixture was stirred at room temperature for 30 minutes. After evaporation of the solvent *in vacuo*, the resulting crude solid material was used in the subsequent step without further purification. The peptide synthesis was performed following general procedure **D** forming the pre-activated mixture using Boc-L-Tyr(All)-OH (964 mg, 3 mmol, 1 equiv), EDC.HCl (690 mg, 3 mmol, 1.2 equiv) and HOBt.H_2O (551 mg, 3.6 mmol, 1.2 equiv) in CH_2Cl_2 (20 ml). In parallel, to a flask containing the crude H-L-Phe-L-Pro-OMe.TFA from the previous step, dissolved in CH_2Cl_2 (20 ml), was Et_3N added until the mixture reached pH 9. The two mixture were combined and allowed to stirred for 2 h at roomtemperature. This yielded, after extraction, the title compound as a white powder with 97% (1.686 g, 2.91 mmol) yield over the two steps. **^{1}H NMR (500 MHz, DMSO-d_6, mixture of rotamers) δ** 8.26 (d, *J* = 7.9 Hz, 0.1H), 8.14 (d, *J* = 8.0 Hz, 0.8H), 8.03 (d, *J* = 8.4 Hz, 0.1H), 7.31-7.25 (m, 4H), 7.23-7.18 (m, 1H), 7.12 (d, *J* = 8.3 Hz, 0.5H), 7.07 (d, *J* = 8.5 Hz, 1.5H), 6.86-6.77 (m, 3H), 6.02 (ddt, *J* = 5.0 Hz, 10.5 Hz, 17.2 Hz, 1H), 5.37 (dd, *J* = 1.5, 17.2 Hz, 1H), 5.23 (dd, *J* = 1.3 Hz, 10.6 Hz, 1H), 4.70 (ddd, J = 7.9, 7.9, 6.1 Hz, 0.9H), 4.57 (ddd, *J* = 7.8, 7.8, 7.8 Hz, 0.1H), 4.51 (d, *J* = 5.0 Hz, 2H), 4.29 (dd, *J* = 4.8, 8.6 Hz, 1H), 4.07 (ddd, *J* = 4.9, 4.9, 13.9 Hz, 1H), 3.61 (s, 2.5H), 3.59 (s, 0.5H), 3.60-2.56 (m, 1H), 3.41-3.35 (m, 1H), 3.01 (dd, *J* = 5.9, 14.1 Hz, 0.9H), 2.89 (dd, *J* = 7.8, 12.8 Hz, 0.1H), 2.84-2.72 (m, 2H), 2.56 (dd, *J* = 10.3, 13.5 Hz, 1H), 2.17-2.09 (m, 1H), 1.92-1.84 (m, 2H), 1.84-1.76 (m, 1H), 1.29 (s, 8H), 1.16 (s, 1H) ppm. **^{13}C NMR (126 MHz, DMSO-d_6, mixture of rotamers) δ** [172.1, 171.8] (C), 171.3 (C), [169.6, 169.4] (C), 156.7 (C), 155.0 (C), 137.2 (C), 136.7 (C), 133.9 (CH), [130.1, 130.0] (CH), [129.4, 129.2] (CH), [128.3, 128.1] (CH), [126.7, 126.4] (CH), 117.2 (CH_2), 114.2 (CH), 78.0 (C), 68.1 (CH_2), [58.6, 58.4] (CH), 55.9 (CH), 51.8 (CH), [51.7, 51.5] (CH_3), [46.5, 45.9] (CH_2), 37.0 (CH_2), 36.7 (CH_2), 28.6 (CH_2), [28.1, 27.8] (CH_3), 24.6 (CH_2) ppm. NMR-data was acquired at elevated temperature so that peaks arising from hindered rotation coalesced. **^{1}H NMR (500 MHz, DMSO-d_6, 60°C, mixture of rotamers) δ** 7.97 (br s, 0.9H), 7.84 (br s, 0.1H), 7.31-7.24 (m, 4H), 7.23-7.18 (m, 1H), 7.10 (d, *J* = 8.0 Hz, 0.3H), 7.01 (d, *J* = 8.2 Hz, 1.7H), 6.84-6.78 (m, 2H), 6.60 (br s, 1H), 6.02 (ddt, *J* = 5.0, 10.5 Hz, 17.2 Hz, 1H), 5.37 (dd, J = 1.5, 17.2 Hz, 1H), 5.23 (dd, *J* = 1.3, 10.6 Hz, 1H), 4.74 (dd, *J* = 7.7, 14.4 Hz, 0.9H), 4.61 (dd, *J* = 7.5, 15.2 Hz, 0.1H), 4.51 (d, *J* = 5.2 Hz, 2H), 4.31 (dd, *J* = 4.7, 8.6 Hz, 1H), 4.13-4.07 (m, 1H), 3.62 (s, 3H), 3.61-3.58 (m, 1H), 3.40-3.33 (m, 1H), 3.02 (dd, *J* = 6.0, 13.8 Hz, 1H), 2.81 (ddd, *J* = 14.2, 14.2, 6.3 Hz, 2H), 2.60 (dd, *J* = 10.3, 13.2 Hz, 1H),

2.19-2.09 (m, 1H), 1.92-1.76 (m, 3H),1.30 (s, 9H) ppm. **HRMS** (ESI+) m/z: calcd. $C_{32}H_{42}N_3O_7$ for $[M+H]^+$: 580.3017 found 580.3020. No spectroscopic data are reported in literature.

Methyl ((*S*)-2-((2*S*,3*R*)-2-((*tert*-butoxycarbonyl)amino)-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenylalanyl-L-prolinate (Boc-L-Ile-L-Tyr(All)-L-Phe-L-Pro-OMe, KH_987) **L,L,L,L-S12**

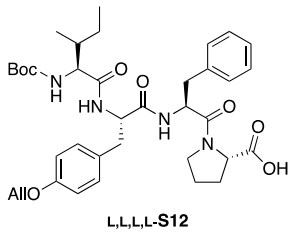


L,L,L,L-**S12**

The title compound was obtained by means of a two step synthesis. To a solution of Boc-L-Tyr(All)-L-Phe-L-Pro-OMe **L,L,L-S11** (1.686 g, 2.91 mmol, 1 equiv) in CH_2Cl_2 (20 ml), trifluoroacetic acid (5 ml) was added and the mixture was stirred at room temperature for 30 minutes. After evaporation of the solvent *in vacuo*, the resulting crude solid material was used in the subsequent step without further purification. The peptide synthesis was performed following general procedure **D** forming the pre-activated mixture using Boc-L-Ile-OH.0.5H_2O (671 mg, 2.9 mmol, 1 equiv), EDC.HCl (667 mg, 3.5 mmol, 1.2 equiv) and HOBt.H_2O (533 mg, 3.5 mmol, 1.2 equiv) in CH_2Cl_2 (20 ml). In parallel, to a flask containing the crude H-L-Tyr(All)-L-Phe-L-Pro-OMe.TFA from the previous step, dissolved in CH_2Cl_2 (20 ml), was Et_3N added until the mixture reached pH 9. The two mixture were combined and allowed to stirred for 2 h at roomtemperature.This yielded, after extraction, the title compound as a white powder with 99% (1.987 g, 2.87 mmol) yield over the two steps. **^{1}H NMR (500 MHz, DMSO-*d*$_6$, mixture of rotamers) δ** 8.44 (br s, 0.1H), 8.33 (d, *J* = 7.8 Hz, 0.8H), 8.21 (d, *J* = 8 Hz, 0.1H), 7.78-7.70 (m, 1H), 7.29-7.22 (m, 4H), 7.21-7.17 (m, 1H), 7.12 (d, *J* = 8.2 Hz, 0.2H), 7.09 (d, *J* = 8.4 Hz, 1.8H), 6.77 (d, *J* = 8.4 Hz, 2H), 6.69 (d, *J* = 9.2 Hz, 1H), 6.02 (ddt, *J* = 5.0, 10.5, 17.2 Hz, 1H), 5.36 (dd, *J* = 1.5, 17.2 Hz, 1H), 5.23 (dd, *J* = 1.5, 10.5 Hz, 1H), 4.65 (q, *J* = 7.2 Hz, 1H), 4.56-4.51 (m, 1H), 4.49 (d, *J* = 5.0 Hz, 2H), 4.30-4.25 (m, 1H), 3.84-3.82 (m, 0.1H), 3.74 (t, *J* = 8.5 Hz, 0.9H), 3.60 (s, 2.6H), 3.58 (s, 0.4H), 3.53-3.49 (m, 1H), 3.30-3.24 (m, 1H), 2.99 (dd, *J* = 6.3, 13.9 Hz, 1H), 2.82 (dd, *J* = 4.8, 13.7 Hz, 1H), 2.78 (dd, *J* = 7.4, 13.8 Hz, 1H), 2.66 (dd, *J* = 9.4, 13.7 Hz, 1H), 2.15-2.08 (m, 1H), 1.84-1.77 (m, 2.7H), 1.67-1.64 (m, 0.3H), 1.57-1.52 (m, 1H), 1.37 (s, 9H), 1.27-1.22 (m, 1H), 0.99-0.92 (m, 1H), 0.73 (t, *J* = 7.4 Hz, 3H), 0.61 (d, *J* = 6.7 Hz, 3H) ppm. **^{13}C NMR (126 MHz, DMSO-*d*$_6$, mixture of rotamers) δ** [172.2, 171.9] (C), 170.9 (C), [170.7, 170.4] (C), [169.5, 169.3] (C), 156.8 (C), 155.3 (C), 137.3 (C), 136.7 (C), 134.0 (CH), 130.3 (CH), [129.6, 129.3, 129.2] (CH), [128.4, 128.2] (CH), [126.8, 126.4] (CH), 117.2 (CH_2), 114.2 (CH), 78.1 (C), 68.1 (CH_2), 59.0 (CH), [58.7, 58.4] (CH), 53.5 (CH), [52.4, 51.9] (CH), 51.9 (CH_3), [46.5, 46.0] (CH_2), 37.0 (CH_2), 37.0 (CH_2), 36.6 (CH), [30.5, 28.7] (CH_2), [28.2, 28.0] (CH_3), [24.6] (CH_2), 24.3 (CH_2), [21.9] (CH_2), 15.3 (CH_3), 10.9 (CH_3) ppm. NMR-data was acquired at elevated temperature so that peaks arising from hindered rotation coalesced. **^{1}H NMR (500 MHz, DMSO-*d*$_6$, 60°C, mixture of rotamers) δ** 8.11 (d, *J*

= 5.9 Hz, 0.9H), 7.93 (d, *J* = 8.1 Hz, 0.1H), 7.69 (d, *J* = 8.4 Hz, 0.1H), 7.64 (d, *J* = 8.4 Hz, 0.9H), 7.30-7.22 (m, 4H), 7.21-7.15 (m, 1H), 7.12 (d, *J* = 8.4 Hz, 0.3H), 7.08 (d, *J* = 8.5 Hz, 1.7H), 6.78 (d, *J* = 8.4 Hz, 2H), 6.47 (br s, 1H), 6.02 (ddt, *J* = 5.1, 10.5, 17.3 Hz, 1H), 5.36 (dd, *J* = 1.5, 17.3 Hz, 1H), 5.23 (dd, *J* = 1.5, 10.5 Hz, 1H), 4.69 (dd, *J* = 7.2, 14.6 Hz, 1H) 4.61-4.51 (m, 1H), 4.50 (d, *J* = 5.1 Hz, 2H), 4.29 (dd, *J* = 4.0, 8.4 Hz, 1H), 3.86-3.83 (m, 0.1H), 3.80-3.74 (m, 0.9H), 3.61 (s, 2.7H), 3.59 (s, 0.3H), 3.58-3.49 (m, 1H), 3.30-3.23 (m, 1H), 3.01 (dd, *J* = 6.6, 13.9 Hz, 1H), 2.86 (dd, *J* = 5.1, 14.1 Hz, 1H), 2.80 (dd, *J* = 6.9, 13.9 Hz, 1H), 2.70 (dd, *J* = 8.7, 13.9 Hz, 1H), 2.17-2.07 (m, 1H), 1.89-1.77 (m, 3H), 1.63-1.56 (m, 1H), 1.37 (s, 9H), 1.34-1.23 (m, 1H), 1.06-0.97 (m, 1H), 0.76 (t, *J* = 7.4 Hz, 3H), 0.66 (d, *J* = 6.7 Hz, 3H) ppm. **HRMS** (ESI+) m/z: calcd. $C_{38}H_{52}N_4O_8Na$ for $[M+Na]^+$: 715.3677 found 715.3718. No spectroscopic data are reported in literature.

((*S*)-2-((2*S*,3*R*)-2-((*tert*-Butoxycarbonyl)amino)-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenyl-alanyl-L-proline (Boc-L-Ile-L-Tyr(All)-L-Phe-L-Pro-OH, KH_988) **L,L,L,L-S12**

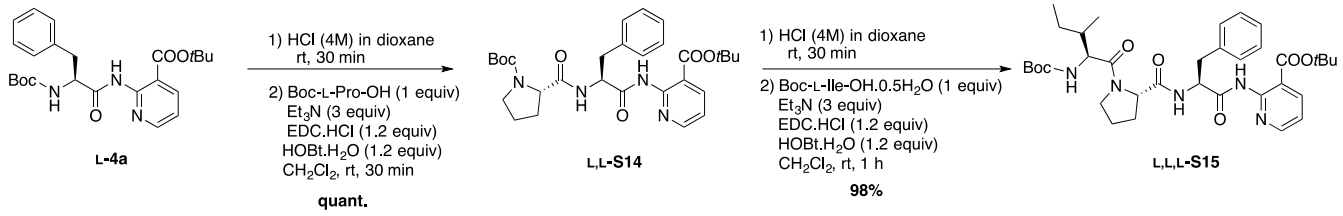


L,L,L,L-S12

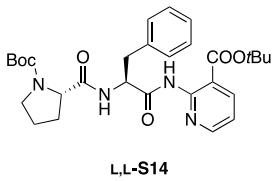
The title compound was obtained starting from Boc-L-Ile-L-Tyr(All)-L-Phe-L-Pro-OMe **L,L,L,L-S11** (2.0 g, 2.99 mmol) solubilized in THF (22 ml). A solution of LiOH (0.119 g, 8.7 mmol, 3 equiv) in water (22 ml) was added and the mixture was stirred at rt for 30 minutes and quenched with HCl 1 N until pH 4 was reached. The aqueous layer was then extracted with CH_2Cl_2 (3x). The resulting organic layer was finally dried over $MgSO_4$ and concentrated *in vacuo* giving a colorless oil in 98% (1.93 g, 2.84 mmol) yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$, mixture of rotamers) δ** 12.52 (br s, 1H), 8.43 (d, *J* = 7.1 Hz, 0.1H), 8.33 (d, *J* = 8.0 Hz, 0.8H), 8.05 (d, *J* = 8.0 Hz, 0.1H), 7.82 (d, *J* = 8.9 Hz, 0.1H), 7.76 (d, *J* = 8.3 Hz, 0.8H), 7.70 (d, *J* = 8.0 Hz, 0.1H), 7.30-7.21 (m, 4H), 9.19-7.14 (m, 1H), 7.09 (d, *J* = 8.6 Hz, 2H), 6.80-6.75 (m, 2H), 6.73-6.65 (m, 1H), 6.02 (ddt, *J* = 5.1, 10.5, 17.2 Hz, 1H), 5.36 (dd, *J* = 1.5, 17.2 Hz, 1H), 5.23 (dd, *J* = 1.5, 10.5 Hz, 1H), 4.64 (dd, *J* = 7.3, 14.0 Hz, 1H), 4.58-4.51 (m, 1H), 4.48 (d, *J* = 5.1 Hz, 2H), 4.22 (dd, *J* = 3.4, 8.3 Hz, 1H), 3.77-3.69 (m, 1H), 3.54-3.45 (m, 1H), 3.42-3.30 (m, 1H, overlap with HDO), 3.00 (dd, *J* = 5.7, 14.0 Hz, 1H), 2.83 (dd, *J* = 4.5, 13.7 Hz, 1H), 2.77 (dd, *J* = 7.7, 13.9 Hz, 1H), 2.65 (dd, *J* = 9.3, 13.9 Hz, 1H), 2.13-2.05 (m, 1H), 1.87-1.78 (m, 2.7H), 1.68-1.61 (m, 0.3H), 1.57-1.47 (m, 1H), 1.36 (s, 8H), 1.26 (s, 1H), 1.25-1.19 (m, 1H), 1.00-0.91 (m, 1H), 0.75-0.70 (m, 3H), 0.63-0.58 (m, 3H) ppm. **^{13}C NMR (126 MHz, DMSO-*d*$_6$, mixture of rotamers) δ** [173.1, 172.8] (C), [171.0, 170.8] (C), [170.7, 170.3] (C), 169.0 (C), 156.7 (C), 155.2 (C), 137.3 (C), 136.7 (C), 133.9 (CH), 130.2 (CH), [129.5, 129.3] (CH), [128.3, 128.1] (CH), [126.7, 126.3] (CH), 117.2 (CH_2), 114.1 (CH), 78.0 (C), 68.0 (CH_2), 58.9 (CH), [58.6, 58.4] (CH), [53.5, 53.4] (CH), [52.1, 51.8] (CH), [46.4, 45.8] (CH_2), 37.0 (CH_2), 36.8 (CH_2), 36.6 (CH), [30.5, 28.6] (CH_2), [28.2,

27.9] (CH_3), [24.5] (CH_2), 24.2 (CH_2), [21.7] (CH_2), 15.2 (CH_3), 10.9 (CH_3) ppm. NMR-data was acquired at elevated temperature so that peaks arising from hindered rotation coalesced. **^{1}H NMR (500 MHz, DMSO-*d*$_6$, 60°C, mixture of rotamers) δ** 12.32 (br s, 1H), 8.08 (d, *J* = 6.5 Hz, 0.9H), 7.77 (d, *J* = 7.6 Hz, 0.1H), 7.73 (d, *J* = 8.3 Hz, 0.1H), 7.63 (d, *J* = 8.3 Hz, 0.9H), 7.30-7.20 (m, 4H), 7.19-7.14 (m, 1H), 7.08 (d, *J* = 8.1 Hz, 2H), 6.77 (d, *J* = 7.8 Hz, 2H), 6.47 (br s, 1H), 6.02 (ddt, *J* = 5.1, 10.5, 17.2 Hz, 1H), 5.36 (dd, *J* = 1.5, 17.2 Hz, 1H), 5.23 (dd, *J* = 1.5, 10.5 Hz, 1H), 4.68 (dd, *J* = 6.8, 14.6 Hz, 1H), 4.57-4.51 (m, 1H), 4.50 (d, *J* = 5.5 Hz, 2H), 4.25 (dd, *J* = 3.2, 8.4 Hz, 1H), 3.79-3.71 (m, 1H), 3.55-3.49 (m, 1H), 3.35-3.26 (m, 1H), 3.03 (dd, *J* = 6.3, 13.9 Hz, 1H), 2.86 (dd, *J* = 5.2, 13.9 Hz, 1H), 2.79 (dd, *J* = 7.2, 13.9 Hz, 1H), 2.70 (dd, *J* = 8.8, 13.9 Hz, 1H), 2.15-2.05 (m, 1H), 1.91-1.67 (m, 3H), 1.63-1.55 (m, 1H), 1.37 (s, 9H), 1.33-1.26 (m, 1H), 1.05-0.96 (m, 1H), 0.76 (t, *J* = 7.2 Hz, 3H), 0.70-0.64 (m, 3H) ppm. **HRMS** (ESI+) m/z: calcd. $C_{37}H_{50}N_4O_8Na$ for $[M+Na]^+$: 701.3521 found 701.3553. No spectroscopic data are reported in literature.

Synthesis of Fragment ***L,L,L-S15***



tert-Butyl 2-((2*S*)-2-(1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxamido)-3-phenylpropanamido) nicotinate (Boc-L-Pro-L-Phe-NH-*t*Bu-nic, KH_1214) **L,L-S14**

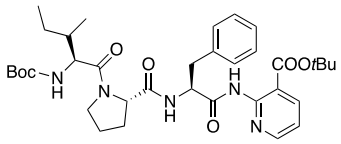


For the synthesis of Boc-L-Pro-L-Phe-NH-*t*Bu-nic **L,L-S14** was started from Boc-L-Phe-NH-*t*Bu-nic **L-4a** (442 mg, 1 mmol, 1 equiv) that was deprotected following general procedure **C** with HCl/dioxane (40 ml, 4 M). After removal of the solvent under vacuum, the resulting crude solid material (H-L-Phe-NH-*t*Bu-nic.HCl) was used in the subsequent step without further purification.

The next step was performed following general procedure **D**. The crude was dissolved in CH_2Cl_2 (20 ml) and Et_3N was added until the mixture reached pH 9. This was added to the pre-activated mixture of Boc-L-Pro-OH (215 mg, 1 mmol, 1 equiv), EDC.HCl (230 mg, 0.65 mmol, 1.2 equiv) and HOBt.H_2O (184 mg, 1.2 mmol, 1.2 equiv). The reaction mixture was stirred for 30 minutes. After extraction, the title compound could be obtained as a white powder in quantitive yield (545 mg, 1 mmol) over the two steps. **^{1}H NMR (500 MHz, $CDCl_3$, mixture of rotamers) δ** 11.42 (br s, 0.5H), 11.11 (br s, 0.5H), 8.64-8.50 (m, 1H), 8.23 (dd, *J* = 1.5, 7.8 Hz, 1H), 7.60 (br s, 0.5H), 7.25-7.19 (m, 4H), 7.18-7.14 (m, 1H), 7.06 (dd, *J* = 4.8, 7.5 Hz, 1H), 6.78 (br s, 0.5H), 5.54-4.99 (m, 1H), 4.51-4.11 (m, 1H), 3.45- 3.16 (m,

3H), 3.02 (dd, *J* = 8.6, 13.9 Hz, 1H), 2.58-2.25 (m, 1H), 2.07-1.88 (m, 1H), 1.85-1.67 (m, 2H), 1.57 (s, 9H), 1.45 (s, 9H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$, mixture of rotamers) δ** 172.3 (C), 170.0 (C), 165.7 (C), 152.2 (CH), 151.9 (C), 140.6 (CH), 137.0 (C), 129.5 (CH), 128.5 (CH), 126.8 (CH), 118.5 (CH), 113.3 (C), 83.7 (C), 80.6 (C), [61.0, 59.9] (CH), [55.5, 55.2] (CH), 47.0 (CH_2), [38.8, 38.1] (CH_2), 30.5 (C), [28.5] (CH_3), 28.3 (CH_3), [27.7] (CH_3), 24.6 (CH_2), 23.5 (CH_2) ppm. NMR-data was acquired at elevated temperature so that peaks arising from hindered rotation coalesced. **^{1}H NMR (500 MHz, DMSO-*d*$_6$, 80°C) δ** 10.38 (br s, 1H), 8.61 (br s, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.89 (d, *J* = 7.2 Hz, 1H), 7.34-7.21 (m, 5H), 7.20-7.15 (m, 1H), 5.00-4.89 (m, 1H), 4.19-4.05 (m, 1H), 3.33-3.24 (m, 2H), 3.20 (dd, *J* = 14.0, 3.8 Hz, 1H), 2.95 (dd, *J* = 14.1, 9.6 Hz, 1H), 2.05-1.92 (m, 1H), 1.80-1.72 (m, 1H), 1.71-1.61 (m, 2H), 1.54 (s, 9H), 1.29 (s, 9H) ppm. **HRMS** (ESI+) m/z: calcd. $C_{29}H_{39}N_4O_6$ for $[M+H]^+$: 539.2864 found 539.2861. The spectroscopic data were in accordance with those previously reported.[1]

tert-Butyl 2-((*S*)-2-((*S*)-1-((2*S*,3*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methylpentanoyl)pyrrolidine-2-carboxamido)-3-phenylpropan-amido)nicotinate (Boc-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic, KH_1039) **L,L,L-S15**



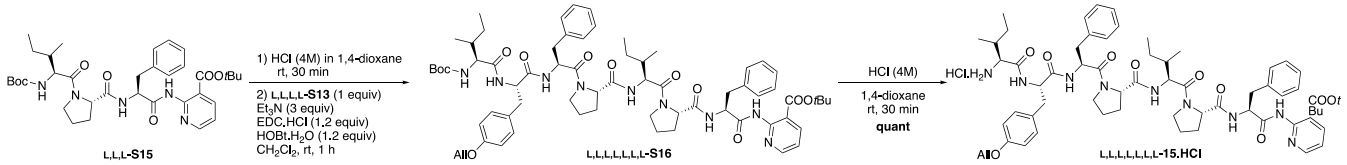
L,L,L-S15

For the synthesis of Boc-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic **L,L,L-S15** was started from Boc-L-Pro-L-Phe-NH-*t*Bu-nic **L,L-S14** (442 mg, 1 mmol, 1 equiv) that was deprotected following general procedure **C** with HCl/dioxane (40 ml, 4 M). After removal of the solvent under vacuum, the resulting crude solid material (H-L-Pro-L-Phe-*t*Bu-nic.HCl) was used in the subsequent step without further purification.

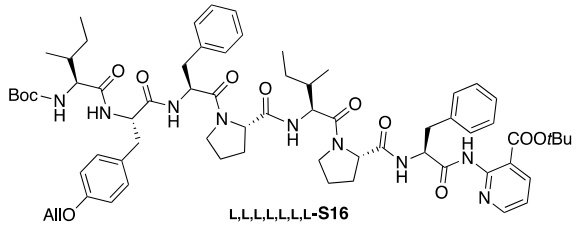
The next step was performed following general procedure **D**. The crude was dissolved in CH_2Cl_2 (20 ml) and Et_3N was added until the mixture reached pH 9. This was added to the pre-activatede mixture of Boc-L-Ile-OH.0.5H_2O (231 mg, 1 mmol, 1 equiv), EDC.HCl (230 mg, 1.2 mmol, 1.2 equiv) and HOBt.H_2O (184 mg, 1.2 mmol, 1.2 equiv). The reaction mixture was stirred for 1 h. After extraction, the title compound could be obtained as a white powder in 98% yield (639 mg, 0.98 mmol) over the two steps. **^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ** 10.73 (s, 1H), 8.52 (dd, *J* = 1.8, 4.8 Hz, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 8.06 (dd, *J* = 1.8, 7.7 Hz, 1H), 7.33 (d, *J* = 7.5 Hz, 2H) 7.31-7.23 (m, 3H), 7.18 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.81 (d, *J* = 8.7 Hz, 1H), 4.82-4.74 (m, 1H), 4.42-4.37 (m, 1H), 4.00 (dd, *J* = 8.7, 8.7 Hz, 1H), 3.72-3.66 (m, 1H), 3.53-3.46 (m, 1H), 3.11 (dd, *J* = 3.8, 13.9 Hz, 1H), 2.90 (dd, *J* = 9.2, 13.8 Hz, 1H), 2.01-1.94 (m, 1H), 1.84-1.76 (m, 3H), 1.71-1.61 (m, 1H), 1.49 (s, 9H), 1.36 (s, 9H), 1.12-1.02 (m, 1H), 0.84-0.80 (m, 4H), 0.78 (t, *J* = 7.3 Hz, 3H) ppm **^{13}C NMR (126 MHz, DMSO-*d*$_6$) δ** 171.6 (C), 170.5 (C), 170.1 (C), 164.9 (C), 155.4 (C), 150.7 (CH), 148.6 (C), 138.8 (CH), 137.5 (C), 129.2 (CH),

128.0 (CH), 126.2 (CH), 120.3 (C), 120.0 (CH), 81.4 (C), 77.8 (C), 59.1 (CH), 55.9 (CH), 54.5 (CH), 47.0 (CH_2), 36.9 (CH_2), 35.9 (CH), 28.9 (CH_2) , 28.1 (CH_3), 27.7 (CH_3), 24.3 (CH_2), 24.2 (CH_2), 14.9 (CH_3), 10.7 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. $C_{35}H_{49}N_5O_7Na$ for $[M+Na]^+$: 674.3524 found 674.3534. No spectroscopic data are reported in literature.

Assembling of the Fragments ***L,L,L,L-S13*** *and* ***L,L,L-S15*** *and Deprotection to Access Linear Heptamer* ***L,L,L,L,L,L,L-15***



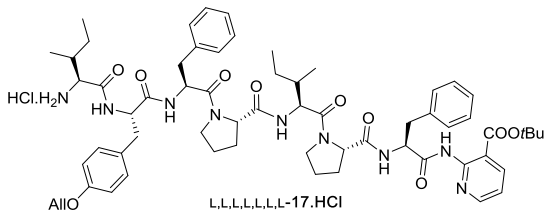
tert-Butyl 2-((*S*)-2-((*S*)-1-(((*S*)-2-((2*S*,3*R*)-2-((*tert*-butoxycarbonyl)amino)-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl) propanoyl)-L-phenylalanyl-L-prolyl-L-isoleucyl)pyrrolidine-2-carboxamido)-3-phenylpropanamido)nicotinate (Boc-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic, KH_1042) **L,L,L,L,L,L,L-S16**



The title compound was obtained by means of a two step synthesis from Boc-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic **L,L,L-S15** (433 mg, 0.664 mmol, 1 equiv) was deprotected following general procedure **C** with HCl/dioxane (40 ml, 4 M). After removal of the solvent under vacuum, the resulting crude solid material (H-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic.HCl) was used in the subsequent step without further purification. The peptide synthesis was performed following general procedure **D** forming the pre-activated mixture using Boc-L-Ile-L-Tyr(All)-L-Phe-L-Pro-OH **L,L,L,L-S13** (461 mg, 0.66 mmol, 1 equiv), EDC.HCl (153 mg, 0.797 mmol, 1.2 equiv) and HOBt.H_2O (122 mg, 0.797 mmol, 1.2 equiv) in CH_2Cl_2 (20 ml). In parallel, to a flask containing the crude H-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic.HCl from the previous step, dissolved in CH_2Cl_2 (20 ml), was Et_3N added until the mixture reached pH 9. The two mixture were combined and allowed to stirred for 1 h at roomtemperature. This yielded, after extraction and Grace Reveleris® X2 Reverse Phase silicagel flash chromatography (H_2O:CH_3CN, 97:3 to 0:100), the title compound as a white powder with 48% (385 mg, 0.318 mmol) yield over the two steps. **^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ** 10.74 (br s, 1H), 8.52 (dd, *J* = 1.6, 4.8 Hz, 1H), 8.34-8.29 (m, 1H), 8.11 (d, *J* = 8.6 Hz, 1H), 8.06 (dd, *J* = 1.5, 7.7 Hz, 1H), 7.93 (d, *J* = 8.3 Hz, 1H), 7.70 (d, *J* = 8.6 Hz, 1H), 7.34 (d, *J* = 7.4 Hz, 2H), 7.31-7.20 (m, 7H), 7.19-7.13 (m, 2H), 7.10-7.06 (m, 2H), 6.77 (d, *J* = 8.3 Hz, 2H), 6.68 (d, *J* = 9.5 Hz, 1H), 6.02 (ddt, *J* = 5.1, 10.5, 17.2 Hz, 1H), 5.36 (dd, *J* = 1.5, 17.2 Hz, 1H), 5.23 (dd, *J* = 1.5, 10.5 Hz, 1H), 4.82-4.75 (m, 1H), 4.67-4.61 (m, 1H), 4.56-4.50 (m, 1H), 4.48

(d, *J* = 5.1 Hz, 2H), 4.42-4.35 (m, 3H), 3.76-3.63 (m, 3H), 3.55-3.47 (m, 1H), 3.44-3.38 (m, 1H), 3.20-3.08 (m, 1H), 3.03-2.96 (m, 1H), 2.89 (dd, *J* = 9.6, 14.4 Hz, 1H), 2.83 (dd, *J* = 3.5, 13.5, Hz, 1H), 2.76 (dd, *J* = 7.9, 14.2 Hz, 1H), 2.64 (dd, *J* = 9.6, 13.6 Hz, 1H), 2.04-1.91 (m, 2H), 1.86-1.70 (m, 6H), 1.57-1.51 (m, 1H), 1.50 (s, 9H), 1.36 (s, 9H), 1.27-1.20 (m, 3H), 1.12-1.05 (m, 1H), 0.90-0.88 (m, 1H), 0.88-0.82 (m, 3H), 0.80 (t, *J* = 7.3 Hz, 3H), 0.72 (t, *J* = 7.3 Hz, 3H), 0.59 (d, *J* = 6.6 Hz, 3H) ppm. **^{13}C NMR (126 MHz, DMSO-*d*$_6$) δ** 171.6 (C), 171.1 (C), 170.8 (C), 170.7 (C), 170.2 (C), 169.9 (C), 169.3 (C), 164.9 (C), 156.7 (C), 155.2 (C), 150.7 (CH), 148.6 (C), 138.8 (CH), 137.5 (C), 137.5 (C), 133.9 (CH), 130.2 (CH), 129.5 (C), 129.3 (CH), 129.3 (CH), 128.1 (CH), 128.0 (CH), 126.3 (CH), 126.3 (CH), 120.6 (C), 120.1 (CH), 117.2 (CH_2), 114.0 (CH), 81.4 (C), 78.0 (C), 68.0 (CH_2), 59.2 (CH), 59.1 (CH), 59.0 (CH), 54.5 (CH), 54.4 (CH), 53.3 (CH), 51.9 (CH), 47.1 (CH_2), 46.8 (CH_2), 37.0 (CH_2), 37.0 (CH_2), 36.8 (CH_2), 36.5 (CH), 36.3 (CH), 29.0 (CH_2), 28.2 (CH_3), 27.7 (CH_3), 24.5 (CH_2), 24.4 (CH_2), 24.3 (CH_2), 24.2 (CH_2), 24.0 (CH_2), 15.2 (CH_3), 15.1 (CH_3), 10.9 (CH_3), 10.8 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. $C_{67}H_{89}N_9O_{12}Na$ for $[M+Na]^+$: 1234.6523 found 1234.6475. No spectroscopic data are reported in literature.

tert-Butyl 2-((*S*)-2-((*S*)-1-(((*S*)-2-((2*S*,3*R*)-2-amino-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenyl-alanyl-L-prolyl-L-isoleucyl)pyrrolidine-2-carboxamido)-3-phenylpropanamido)nicotinate hydrochloride acid salt (H-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic.HCl, KH_1046) **L,L,L,L,L,L,L-17.HCl**

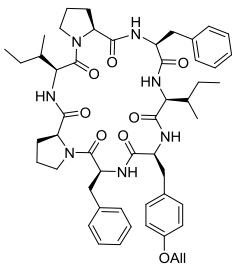


The title compound was prepared following general procedure **D** from Boc-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic **L,L,L,L,L,L,L-S16** (340 mg, 0.28 mmol, 1 equiv) in HCl/dioxane (10 ml, 4 M) by stirring 30 minutes at room temperature. After removal of solvent and lyophilisation, the desired compound **L,L,L,L,L,L,L-17.HCl** was obtained in nearly quantitive yield (327 mg, 0.28 mmol) as a white powder. **^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ** 10.8 (br s, 1H), 8.55- 8.45 (m, 2H), 8.16-8.10 (m, 2H), 8.08-8.04 (m, 1H), 7.95 (d, *J* = 8.8 Hz, 1H), 7.34 (d, *J* = 7.5 Hz, 1H), 7.30-7.11 (m, 12H), 6.81 (d, *J* = 8.5 Hz, 2H), 6.02 (ddt, *J* = 5.1, 10.5, 17.2 Hz, 1H), 5.36 (d, *J* = 17.2 Hz, 1H), 5.23 (d, *J* = 10.5 Hz, 1H), 4.84-4.75 (m, 1H), 4.69-4.61 (m, 1H), 4.59-4.53 (m, 1H), 4.52-4.47 (m, 3H), 4.43-4.30 (m, 3H), 3.89 (br s, 3H), 3.73-3.57 (m, 3H), 3.53-3.40 (m, 3H), 3.11 (dd, *J* = 3.5, 14.0 Hz, 1H), 2.98 (dd, *J* = 4.8, 13.7 Hz, 1H), 2.93-2.84 (m, 2H), 2.81-2.70 (m, 2H), 2.03-1.89 (m, 2H), 1.85-1.67 (m, 6H), 1.49 (s, 9H), 1.44-1.34 (m, 2H),1.14-0.96 (m, 2H), 0.91-0.71 (m, 12H) ppm. **^{13}C NMR (126 MHz, DMSO-*d*$_6$) δ** 171.6 (C), 171.1 (C), 170.2 (C), 169.9 (C), 169.2 (C), 167.5 (C), 164.9 (C), 156.8 (C), 150.6 (CH), 148.5 (C), 138.9 (CH), 137.6 (C), 137.5 (C), 133.9 (CH), 130.3 (CH), 129.3

(CH), 129.3 (C), 129.2 (CH) 128.1 (CH), 128.0 (CH), 126.3 (CH), 126.2 (CH), 120.6 (C), 120.1 (CH), 117.3 (CH_2), 114.2 (CH), 81.4 (C), 68.1 (CH_2), 59.1 (CH), 59.1 (CH), 56.3 (CH), 54.5 (CH), 54.4 (CH), 53.9 (CH), 51.9 (CH), 47.1 (CH_2), 46.8 (CH_2), 37.0 (CH_2), 36.8 (CH_2), 36.7 (CH_2), 36.3 (CH), 36.3 (CH), 29.0 (CH_2), 27.7 (CH_3), 24.5 (CH_2), 24.4 (CH_2) 24.3 (CH_2), 24.0 (CH_2), 23.6 (CH_2), 15.1 (CH_3), 14.6 (CH_3), 11.2 (CH_3), 10.9 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. $C_{62}H_{82}N_9O_{10}$ for $[M+H]^+$: 1112.6179 found 1112.6151. No spectroscopic data are reported in literature.

Cyclization of ***L,L,L,L,L,L,L-17.HCl*** *by means of Transamidation*

(6*S*,9*S*,12*S*,15*S*,17a*S*,23*S*,25a*S*)-6,15-Dibenzyl-12,23-di((*S*)-sec-butyl)-9-(4-(((*E*)-prop-1-en-1-yl)oxy)benzyl)octadecahydro-*5H*-dipyrrolo[1,2-a:1',2'-g][1,4,7,10,13,16,19]heptaazacyclohenicosine-5,8,11,14,17,22,25-heptaone (c[-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-], KH_1236) **L,L,L,L,L,L,L-18**



L,L,L,L,L,L,L-18

The title compound was prepared using general procedure **B** from H-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic **L,L,L,L,L,L,L-17.HCl** (120 mg, 0.105 mmol, 1 equiv), NaOAc (9 mg, 0.15 mmol, 1 equiv) and $Zn(OAc)_2$ (4 mg, 0.02 mmol, 20 mol%) in THF (0.3 ml). This yielded, after semi-preparative HPLC (H_2O:CH_3CH 70:30 to 40:60 over 10 min followed by 0:100 over 20 min), the desired compound as a white powder in 26% (25 mg, 0.027 mmol) yield.

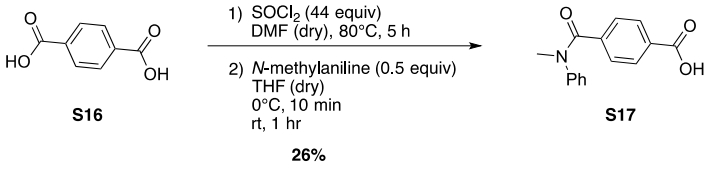
^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 9.39 (d, *J* = 8.6 Hz, 1H), 8.93 (d, *J* = 8.6 Hz, 1H), 8.76 (br s, 1H), 7.39 (d, *J* = 10.3 Hz, 1H), 7.36 (d, *J* = 8.6 Hz, 2H), 7.33 (d, *J* = 7.5 Hz, 2H), 7.30-7.28 (m, 1H), 7.27-7.21 (m, 7H), 7.20-7.16 (m, 1H), 6.89 (d, *J* = 8.6 Hz, 2H), 6.04 (ddt, *J* = 5.0, 10.5, 17.2 Hz, 1H), 5.40 (dd, *J* = 1.5, 17.2 Hz, 1H), 5.24 (dd, *J* = 1.5, 10.5 Hz, 1H), 4.56 (d, *J* = 5.0 Hz, 2H), 4.27-4.24 (m, 2H), 4.21-4.17 (m, 2H), 4.12-4.10 (m, 1H), 4.10-4.06 (m, 1H), 4.04 (dd, *J* = 4.6, 11.4 Hz, 1H), 3.52 (td, *J* = 7.7, 9.5 Hz, 1H), 3.44 (d, *J* = 7.7 Hz, 1H), 3.39 (dd, *J* = 2.3, 14.0 Hz, 1H), 3.29 (td, *J* = 9.3, 11.5 Hz, 1H), 3.23-3.17 (m, 1H), 3.15 (dd, *J* = 2.1, 13.2 Hz, 1H), 2.89 (dd, *J* = 4.5, 12.2 Hz, 1H), 2.73 (dd, *J* = 9.5, 13.2 Hz, 1H), 2.70-2.62 (m, 2H), 2.04-1.94 (m, 2H), 1.93-1.86 (m, 1H), 1.83-1.76 (m, 1H), 1.75-1.67 (m, 1H), 1.65-1.57 (m, 1H), 1.48-1.37 (m, 2H), 1.36-1.29 (m, 1H), 1.28-1.20 (m, 1H), 1.09-1.00 (m, 1H), 0.98 (m, 6H), 0.83 (d, *J* = 6.7 Hz, 2H), 0.75-0.73 (m, 6H), 0.62-0.57 (m, 1H) ppm. **^{13}C NMR (126 MHz, DMSO-*d*$_6$) δ** 171.9 (C), 170.6 (C), 170.1 (C), 169.9 (C), 169.0 (C), 168.3 (C), 157.0 (C), 138.6 (C), 135.2 (C), 133.9 (CH), 131.3 (CH), 129.6 (CH), 128.8 (CH), 128.8 (C), 128.5 (CH), 128.1 (CH), 127.2 (CH), 126.2 (CH), 117.2 (CH_2), 114.1 (CH), 68.1 (CH_2), 60.5 (CH), 60.0 (CH), 59.4 (CH), 55.2 (CH), 54.5 (CH), 54.1 (CH), 53.8 (CH), 48.1 (CH_2), 45.6 (CH_2), 37.1 (CH_2), 36.6 (CH_2), 35.3 (CH_2), 34.8 (CH), 29.4 (CH_2), 28.9 (CH_2), 24.5 (CH_2), 24.0 (CH), 21.6 (CH_2), 17.8 (CH_3), 14.6 (CH_2), 14.5 (CH_2), 12.1 (CH_3), 9.8 (CH_3), 9.7 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. $C_{52}H_{66}N_7O_8Na$ for

$[M+Na]^+$: 940.4943 found 940.4918. $\mathbf{[\alpha]_D}$ = -185 (*c* 1 mg/ml, $CHCl_3$, 27°C). No spectroscopic data are reported in literature.

5.7 Synthesis of the Chemoselectivity Building Block L,L-15 and Transamidation

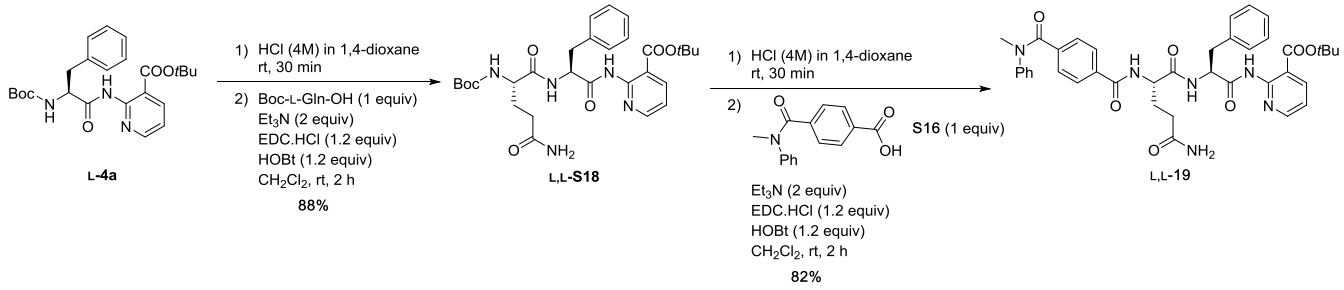
Starting from the Boc-L-Phe-NH-*t*Bu-nic amide **L-4a**, oligoamide *tert*-butyl 2-{[(3*S*)-3-{[(3*S*)-6-amino-3-4-[methyl(phenyl)carbamoyl]-benzamido}-6-oxohex-1-en-2-yl]amino-4-phenylbut-1-en-2yl]amino}pyridine-3-carboxylate **L,L-15** was built up using a convergent strategy assembling 4-[methyl(phenyl)carbamoyl]benzoic acid **S17** and Boc-L-Gln-L-Phe-NH-*t*Bu-nic amide **L,L-S18**.

Synthesis of 4-[methyl(phenyl)carbamoyl]benzoic acid (KH_808) ***S17***

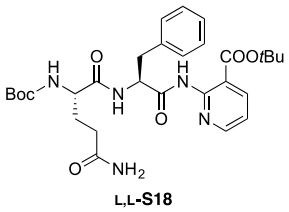


The synthesis of 4-[methyl(phenyl)carbamoyl]benzoic acid **S17** was done following a literature procedure.[8] A flame-dried microwave vial, charged with terephthalic acid **S16** (0.498 g, 3.0 mmol, 2.0 equiv), thionylchloride (9.60 ml, 132.0 mmol, 44.0 equiv) and anhydrous DMF (0.50 ml) was stirred at 80°C for 5 h under argon atmosphere. After removal of the solvent under vacuum, the resulting crude solid material was used in the subsequent step without further purification. To a flask containing the crude material from the previous step was added anhydrous THF (30.0 ml). The mixture was then cooled to 0°C and *N*-methylaniline (0.164 ml, 1.50 mmol, 1.0 equiv) was added dropwise and the mixture was stirred for another 15 min at 0°C, before being allowed to warm up to room temperature, followed by stirring for 2 h at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ (50 mL) and extracted with EtOAc (3 x 50 ml). Subsequently, the resulting aqueous layer was acidified with 37% HCl (aq.) until pH = 3 and extracted with DCM (3 x 50 ml). The organic layer was dried over $MgSO_4$ and the solvent was removed under vacuum. Purification via Grace® Reveleris X2 Normal Phase Silicagel Flash Chromatography (Petroleum ether (1% AcOH):EtOAc (1% AcOH), 100:0 to 70:30, 40.0 mL/min), yielded the title compound **S17** in 26% (0.196 g, 0.769 mmol) yield as white crystals. **^{1}H NMR (400 MHz, $CDCl_3$) δ** 11.47 (br s, 1H), 7.86 (d, *J* = 8.2 H, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.02 (d, *J* = 7.1 Hz, 2H), 3.50 (s, 3H) ppm. **^{13}C NMR (100 MHz, $CDCl_3$) δ** 170.6 (C), 170.0 (C), 144.1 (C), 140.7 (C), 130.4 (C), 129.6 (CH), 129.4 (CH), 128.7 (CH), 127.1 (CH), 127.0 (CH), 38.5 (CH_3) ppm. **HRMS** (ESI+) m/z: calcd for $C_{15}H_{13}NO_3$ $[M+H]^+$: 256.0968, found 256.0962 The spectroscopic data were in accordance with those previously reported.[1]

tert-Butyl 2-{[(3*S*)-3-{[(3*S*)-6-amino-3-{4-[methyl(phenyl)carbamoyl]-benzamido}-6-oxo-hex-1-en-2-yl] amino}-4-phenylbut-1-en-2yl]amino} pyridine-3-carboxylate **L,L-19**



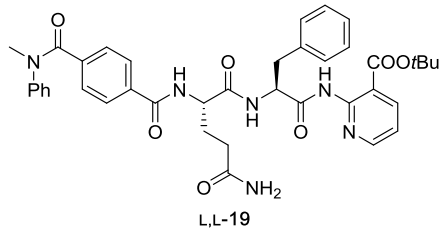
tert-Butyl 2-{[(3*S*)-3-({[(3*S*)-6-amino-3-[{*tert*-butoxycarbonyl)amino)-6-oxohex-1-en-2-yl]amino}pyridine-3-carboxylate (Boc-L-Gln-L-Phe-NH-*t*Bu-nic, KH_905) **L,L-S18**



For the synthesis of Boc-L-Gln-L-Phe-NH-*t*Bu-nic **L,L-S18** was started from Boc-L-Phe-NH-*t*Bu-nic **L-4a** (1.14 g, 2.58 mmol, 1 equiv) that was deprotected following general procedure **C** with HCl/dioxane (50 ml, 4 M). After removal of the solvent under vacuum, the resulting crude solid material (H-L-Phe-NH-*t*Bu-nic.HCl) was used in the subsequent step without further purification. The next step was performed following general procedure **D**. The crude was dissolved in CH_2Cl_2 (20 ml) and Et_3N was added until the mixture reached pH 9. This was added to the pre-activatede mixture of Boc-L-Gln-OH (635 mg, 2.58 mmol, 1 equiv), EDC.HCl (584 mg, 3.1 mmol, 1.2 equiv) and HOBt.H_2O (423 mg, 3.1 mmol, 1.2 equiv). The reaction mixture was stirred for 2 h. After extraction with citric acid in water (3 x 50 ml, 10%) and $NaHCO_3$ (3 x 50 ml, satuerated), the title compound could be obtained as a white powder in 84% yield (1.24 g, 2.18 mmol) over the two steps. **^{1}H NMR (500 MHz, DMSO-d_6, mixture of rotamers) δ** 10.83 (s, 1H), 8.53 (dd, *J* = 4.9, 1.8 Hz, 1H), 8.10-8.04 (m, 2H), 7.33-7.28 (m, 3H), 7.24 (t, *J* = 7.4 Hz, 2H), 7.20-7.15 (m, 2H), 6.83 (d, *J* = 8.4 Hz, 1H), 6.73 (br s, 1H), 4.91-4.85 (m, 1H), 3.94-3.87 (m, 1H), 3.14 (dd, *J* = 13.9, 3.7 Hz, 1H), 2.84 (dd, *J* = 13.9, 10.1 Hz, 1H), 2.08-1.92 (m, 2H), 1.78-1.70 (m, 1H), 1.62-1.55 (m, 1H), 1.48 (s, 8H), 1.36 (s, 8H), 1.23 (s, 1H), 1.18 (s, 1H) ppm. **^{13}C NMR (126 MHz, DMSO-d_6) δ** 173.8 (C), 171.6 (C), 170.2 (C), 164.9 (C), 155.1 (C), 150.6 (CH), 148.4 (C), 138.8 (CH), 137.4 (C), 129.3 (CH), 128.0 (CH), 126.3 (CH), 121.0 (C), 120.2 (CH), 81.4 (C), 78.1 (C), 54.1 (CH), 54.0 (CH), 37.4 (CH_2), 31.5 (CH_2), 28.2 (CH_2), 28.1 (CH_3), 27.7 (CH_3) ppm. NMR-data were also acquired at elevated temperature so that peaks arising from hindered rotation around the amide bond coalesced. **^{1}H NMR (500 MHz, DMSO-d_6, 60°C) δ** 10.60 (s, 1H), 8.51 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.08 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.92 (d, *J* = 8.3 Hz, 1H), 7.30-7.26 (m, 3H), 7.23 (t, *J* = 7.4 Hz, 2H), 7.18-7.15 (m, 1H), 7.02 (br s, 1H), 6.64 (br s, 1H), 6.55 (br s, 1H), 4.93 (td, *J* = 8.9 Hz, 4.1 Hz, 1H), 3.92 (dd, *J* = 8.5, 7.9 Hz, 1H), 3.20-3.17 (m, 1H, overlap with HDO), 2.89 (dd, *J* = 14.0, 9.5 Hz, 1H), 2.10-1.97 (m, 2H), 1.82-1.75 (m, 1H), 1.68-1.60 (m, 1H), 1.51 (s, 9H), 1.35 (s, 9H) ppm.

HRMS (ES+) m/z: calc for $C_{29}H_{40}N_5O_7$ $[M+H]^+$ 570.2922, found 570.2927. The spectroscopic data were in accordance with those previously reported.[1]

tert-Butyl 2-{[(3*S*)-3-{[(3*S*)-6-amino-3-{4-[methyl(phenyl)carbamoyl]-benzamido}-6-oxo-hex-1-en-2-yl]amino}-4-phenylbut-1-en-2yl] amino} pyridine-3-carboxylate (KH_907) **L,L-19**

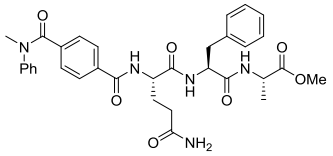


L,L-19

For the synthesis of **L,L-19** was started from Boc-L-Gln-L-Phe-*t*Bu-nic **L-S18** (1.14 g, 2 mmol, 1 equiv) that was deprotected following general procedure **C** with HCl/dioxane (40 ml, 4 M). After removal of the solvent under vacuum, the resulting crude solid material (H-L-Gln-L-Phe-NH-*t*Bu-nic.HCl) was used in the subsequent step without further purification. The next step was performed following general procedure **D**. The crude was dissolved in CH_2Cl_2 (20 ml) and Et_3N was added until the mixture reached pH 9. This was added to the pre-activated mixture of **S17** (511 mg, 2 mmol, 1 equiv), EDC.HCl (460 mg, 2.4 mmol, 1.2 equiv) and HOBt.H_2O (368 mg, 2.4 mmol, 1.2 equiv). The reaction mixture was stirred for 2 h. After extraction with citric acid in water (3 x 70 ml, 10%) and $NaHCO_3$ (3 x 70 ml, saturated), the title compound was obtained as a white powder in 95% yield (1.34 g, 1.89 mmol) over the two steps. **^{1}H-NMR (500 MHz, DMSO-*d*$_6$) δ** 10.78 (s, 1H), 8.54 (d, *J* = 7.8 Hz, 1H), 8.52 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.14 (d, *J* = 8.3 Hz, 1H), 8.06 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 7.9 Hz, 2H), 7.31-7.15 (m, 9H), 7.14-7.10 (m, 3H), 6.77 (br s, 1H), 4.83 (td, *J* = 10.4, 3.5 Hz, 1H), 4.38-4.34 (m, 1H), 3.39 (s, 3H), 3.12 (dd, *J* = 13.9, 3.7 Hz, 1H), 2.84 (dd, *J* = 13.9 Hz, 10.0 Hz, 1H), 2.13-2.00 (m, 2H), 1.92-1.86 (m, 1H), 1.81-1.73 (m, 1H), 1.45 (s, 9H) ppm. **^{13}C-NMR (126 MHz, DMSO-*d*$_6$) δ** 174.1 (C), 171.4 (C), 170.2 (C), 169.0 (C), 165.7 (C), 165.0 (C), 150.7 (CH), 148.4 (C), 144.3 (C), 139.1 (C), 138.9 (CH), 137.4 (C), 134.4 (C), 129.3 (CH), 129.3 (CH), 128.1 (CH), 128.0 (CH), 127.2 (CH), 127.1 (CH), 126.8 (CH), 126.4 (CH), 120.9 (C), 120.3 (CH), 81.5 (C), 54.3 (CH), 53.2 (CH), 37.9 (CH_3), 37.2 (CH_2), 31.6 (CH_2), 27.8 (CH_3), 26.9 (CH_2) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{39}H_{42}N_6O_7Na$ $[M+Na]^+$: 729.3007, found 729.3035. **$[\alpha]_D$** = 16 (*c* 5 mg/ml, $CDCl_3$, 20°C).The spectroscopic data were in accordance with those previously reported.[1]

Transamidation of L,L-19

Methyl (4-(methyl(phenyl)carbamoyl)benzoyl)-L-glutaminyl-L-phenylalanyl-L-alaninate (KH_1234) **L,L,L-20**



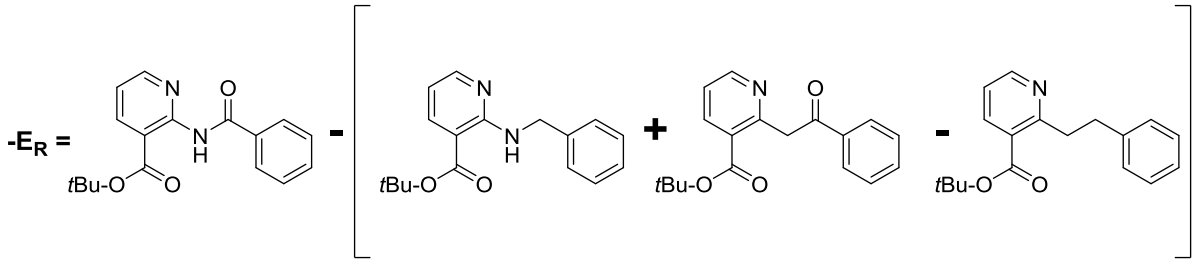
L,L,L-**20**

The title compound was prepared using general procedure **B,** from compound **L,L-19** (353 mg, 0.5 mmol, 1 equiv), H-L-Ala-OMe hydrochloric acid salt **L-5j.HCl** (80 mg, 0.55 mmol, 1.1 equiv), NaOAc (46 mg, 0.55 mmol, 1.1 equiv) and $Zn(OAc)_2$ (18 mg, 0.1 mmol, 20 mol%) in THF (1 ml). This yielded, after Grace Reveleris® X2 Normal Phase silicagel flash chromatography (CH_2Cl_2:MeOH, 100:0 to 90:10 over 17 CV), the desired compound **L,L,L-20** as a white powder in 93% (288 mg, 0.467 mmol) yield. **^{1}H NMR (500 MHz, DMSO-*d*$_6$, mixture of diastereomers 94:6 (L,L,L: L,D,L), mixture of rotamers) δ** 8.70 (d, *J* = 6.6 Hz, 0.1H), 8.65 (d, *J* = 7.1 Hz, 0.1H), 8.61 (d, *J* = 7.2 Hz, 0.8H), 8.31 (d, *J* = 7.0 Hz, 0.8H), 8.29-8.22 (m, 0.2H), 7.98-7.91 (m, 1H), 7.72-7.66 (m, 2H), 7.33 (d, *J* = 7.9 Hz, 2H), 7.30-7.24 (m, 3H), 7.21-7.08 (m, 8H), 6.80 (br s, 1H), 4.51 (ddd, *J* = 8.7, 8.7 4.3 Hz, 1H), 4.30- 4.21 (m, 2H), 3.63 (s, 0.4H), 3.61 (s, 2.3H), 3.58 (s, 0.3H), 3.39 (s, 3H), 3.03 (dd, *J* = 4.2, 14.0 Hz, 0.9H) 2.96 (dd, *J* = 5.0, 13.8 Hz, 0.1H), 2.82-1.72 (m, 1H), 2.16-2.02 (m, 2H), 1.92-1.82 (m, 1H), 1.81-1.71 (m, 1H), 1.27 (d, *J* = 7.3 Hz, 2.2H), 1.23 (d, *J* = 7.4 Hz, 0.4H), 1.21 (d, *J* = 7.4 Hz, 0.4H) ppm. **^{13}C NMR (126 MHz, DMSO-*d*$_6$, mixture of diastereomer 94:6 (L,L,L: L,D,L), mixture of rotamers) δ** [174.1, 173.9] (C), [172.8, 172.7] (C), 171.0 (C), 170.8 (C), 168.8 (C), [165.8, 165.7] (C), 144.2 (C), 139.1 (C), 137.6 (C), 134.3 (C), 129.2 (CH), 127.9 (CH), 127.9 (CH), 127.1 (CH), 126.9 (CH), 126.8 (CH), 126.7 (CH), [126.2, 126.1] (CH), 53.5 (CH), 53.3 (CH), 51.8 (CH_3), [47.6, 47.5] (CH), [37.8, 37.6] (CH_3), 37.2 (CH_2), 31.5 (CH_2), 26.8 (CH_2), [17.0, 16.8] (CH_3) ppm. NMR-data was acquired at elevated temperature so that peaks arising from hindered rotation coalesced. **^{1}H NMR (500 MHz, DMSO-*d*$_6$, 80°C, mixture of diastereomer 94:6 (L,L,L: L,D,L)) δ** 8.47 (d, *J* = 7.2 Hz, 0.06H), 8.45-8.8.37 (m, 0.94H), 8.06-7.94 (m, 1H), 7.74-7.66 (m, 3H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.31-7.24 (m, 2H), 7.23-7.07 (m, 8H), 7.00 (br s, 1H), 6.56 (br s, 1H), 4.58-4.52 (m, 1H), 4.35-4.26 (m, 2H), 3.63 (s, 2.8H), 3.60 (s, 0.2H), 3.39 (s, 3H), 3.09-3.04 (m, 1H), 2.84 (dd, *J* = 8.8, 13.8 Hz, 1H), 2.17-2.04 (m, 2H), 1.97-1.96 (m, 1H), 1.89-1.80 (m, 1H), 1.28-1.22 (m, 3H) ppm. **^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80°C, mixture of diastereomer 94:6 (L,L,L: L,D,L)) δ** 173.7 (C), 172.2 (C), 170.5 (C), 170.2 (C), 168.5 (C), 165.5 (C), 143.9 (C), 138.8 (C), 137.1 (C), 134.2 (C), 128.7 (CH), 127.5 (CH), 127.5 (CH), 126.7 (CH), 126.5 (CH), 126.4 (CH), 126.2 (CH), 125.7 (CH), 53.3 (CH), 53.1 (CH), 51.3 (CH_3), 47.3 (CH), 37.4 (CH_3), 37.0 (CH_2), 31.2 (CH_2), 26.5 (CH_2), [16.6, 16.5] (CH_3) ppm. **HRMS** (ESI+) m/z: calcd. for $C_{33}H_{37}N_5O_7Na$ $[M+Na]^+$: 638.2585 found 638.2584. **$[\alpha]_D$** = -44 (*c* 5 mg/ml, DMSO, 21°C). No spectroscopic data are reported in literature

LC-CD analysis on a Chiralpak IA column of the batch Boc-L-Phe-NH-*t*Bu-nic **L-4a** (retention time = 3.94 min, 250 nm, *n*-hexane:EtOH 65:35, 1.0 mL/min) used in this synthesis, showed to contain 6% Boc-D-Phe-NH-*t*Bu-nic **D-4a.**

6 Amide resonance energy calculations

Amide resonance energies (E_R) were computed using the density functional theory (DFT) methodology reported by Greenberg and Venanzi by computing the isodesmic equation in Scheme S3.[9] To this end, the electronic energies of the most stable amide conformation and corresponding amine, ketone and hydrocarbon low-energy gas phase conformation were computed. In the initial phase of the calculations, conformational analyses were performed using the MMFF force field. Subsequently, for all conformations obtained in a 7.5 kcal mol^{-1} cut-off window, an intermediate geometry optimization at the QM level was performed in the gas phase at the B3LYP/6-31G* level. Finally, for all conformations obtained in a 1.0 kcal mol^{-1} cut-off window, a full geometry optimization at the QM level was performed in the gas phase at the B3LYP/6-311++G(d,p) level of theory as recommended by Szostak et al.[10]

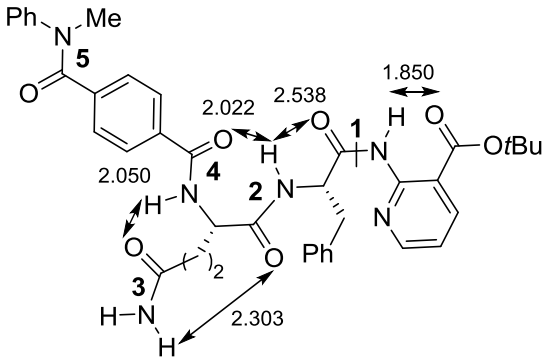


Scheme S3. Computation of the amide resonance energy (E_R) of e.g. *tert*-butyl 2-benzamidonicotinate using an isodesmic reaction.

Conformational analyses were performed using PCmodel version 10.[11] Density functional calculations were performed using Gaussian16.[12] For all DFT calculations, the default ultrafine grid having 99 radial shells and 590 angular points per shell was used. For the most stable conformations of the compounds studied, the Cartesian coordinates of the equilibrium geometry, the B3LYP/ 6-311++G(d,p) energy, the lowest frequencies obtained by diagonalizing the Hessian, and the thermodynamic properties derived from them are given below. For the most stable amide conformation, the resonance energies estimated from the isodesmic equation are compared with the NBO based second-order perturbation energies[13,14] involving the nitrogen lone pair and the CO π^* orbital. While the isodesmic equation resonance energies were in accordance with the observed experimental results, NBO based second-order perturbation energies were not.

Cartesian coordinates for the optimized structures

Oligoamide L,L-19



1: 9.8 kJ/mol **2**: 72.2 kJ/mol **3**: 64.1 kJ/mol
4: 67.9 kJ/mol **5**: 62.4 kJ/mol

Stoichiometry C39H42N6O7
Framework group C1[X(C39H42N6O7)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-7.253891	-0.246185	1.687467
2	C	0	-5.970709	-0.274757	0.901850
3	C	0	-3.496354	-0.160041	-0.424336
4	C	0	-5.482865	0.940790	0.411544
5	C	0	-5.199215	-1.430421	0.741626
6	C	0	-3.970534	-1.368955	0.096064
7	C	0	-4.267366	0.999342	-0.260363
8	O	0	-7.485280	0.684811	2.448035
9	N	0	-8.126490	-1.312880	1.578841
10	C	0	-9.291548	-1.295841	2.474604
11	C	0	-8.198217	-2.170755	0.433249
12	C	0	-8.392281	-3.868868	-1.782732
13	C	0	-8.285784	-1.639180	-0.855801
14	C	0	-8.224659	-3.558140	0.607662
15	C	0	-8.325226	-4.401197	-0.495148
16	C	0	-8.370051	-2.487147	-1.958294
17	C	0	-2.160578	-0.191183	-1.116476
18	O	0	-1.462183	-1.208238	-1.106259
19	N	0	-1.763804	0.943909	-1.742846
20	C	0	-0.549039	1.013152	-2.564247
21	C	0	-0.738748	2.020193	-3.714406
22	C	0	-0.705441	3.537495	-3.396598
23	C	0	-1.450162	3.920010	-2.125609
24	O	0	-2.667331	3.763994	-2.013844
25	N	0	-0.684454	4.428541	-1.129340
26	C	0	0.723125	1.268114	-1.707491
27	N	0	1.033645	0.250983	-0.874483
28	O	0	1.382786	2.302017	-1.800340
29	C	0	2.174940	0.296134	0.020923
30	C	0	3.049500	-0.934878	-0.236621
31	O	0	2.565137	-1.966530	-0.658498

32	C	0	1.742762	0.287853	1.515530
33	C	0	0.912916	1.487793	1.915400
34	C	0	-0.620617	3.718334	2.681225
35	C	0	1.512839	2.739011	2.105462
36	C	0	-0.466716	1.375215	2.111884
37	C	0	-1.230165	2.479545	2.491761
38	C	0	0.756039	3.844580	2.485639
39	N	0	4.416578	-0.927993	0.052048
40	C	0	5.308833	0.054169	0.448542
41	C	0	7.057204	2.041252	1.229087
42	C	0	6.707929	-0.237168	0.496837
43	N	0	4.831388	1.256549	0.785316
44	C	0	5.680109	2.214310	1.154506
45	C	0	7.562686	0.792178	0.896761
46	C	0	7.258218	-1.576502	0.141634
47	O	0	6.571693	-2.528417	-0.190597
48	O	0	8.592161	-1.611750	0.232614
49	C	0	9.381418	-2.838728	-0.067778
50	C	0	10.814660	-2.369771	0.179901
51	C	0	9.182537	-3.237337	-1.531125
52	C	0	8.996148	-3.954285	0.905381
53	H	0	-6.062323	1.841955	0.570335
54	H	0	-5.548884	-2.377280	1.132784
55	H	0	-3.357068	-2.253728	-0.018093
56	H	0	-3.934674	1.962186	-0.632318
57	H	0	-8.983450	-0.952064	3.459999
58	H	0	-10.067323	-0.618988	2.100900
59	H	0	-9.701855	-2.302228	2.542176
60	H	0	-8.462889	-4.526689	-2.641182
61	H	0	-8.284415	-0.564422	-0.992806
62	H	0	-8.152226	-3.971818	1.607323
63	H	0	-8.339424	-5.475387	-0.349164
64	H	0	-8.428582	-2.063960	-2.954620
65	H	0	-2.375707	1.750503	-1.762809
66	H	0	-0.424497	0.020242	-3.008350
67	H	0	0.039030	1.828924	-4.457690
68	H	0	-1.691538	1.769459	-4.188413
69	H	0	-1.198933	4.064978	-4.217917
70	H	0	0.326342	3.875999	-3.343493
71	H	0	0.307432	4.230529	-1.143659
72	H	0	-1.116904	4.539945	-0.222327
73	H	0	0.450129	-0.583625	-0.895751
74	H	0	2.726826	1.207284	-0.188154
75	H	0	2.649358	0.250664	2.125001
76	H	0	1.182527	-0.632195	1.705717
77	H	0	-1.209516	4.574962	2.990943
78	H	0	2.582368	2.840613	1.956232
79	H	0	-0.949152	0.413491	1.972959
80	H	0	-2.297846	2.368013	2.644341
81	H	0	1.240229	4.803207	2.639226
82	H	0	4.857711	-1.824948	-0.156064
83	H	0	7.704339	2.851511	1.538675
84	H	0	5.229848	3.170428	1.407714
85	H	0	8.625050	0.595139	0.939988
86	H	0	11.070712	-1.540494	-0.483243
87	H	0	11.510778	-3.190174	-0.009149
88	H	0	10.941515	-2.041371	1.213900
89	H	0	9.404294	-2.394527	-2.190680
90	H	0	9.873110	-4.048485	-1.776848
91	H	0	8.166221	-3.578644	-1.720035
92	H	0	7.978603	-4.301927	0.735585

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     93          H          0        9.087863   -3.609347    1.938436
     94          H          0        9.678815   -4.797385    0.769814
 ---------------------------------------------------------------------

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done:  E(RB3LYP) =  -2367.30946018     A.U. after    1 cycles
            NFock=  1  Conv=0.41D-08     -V/T= 2.0042


 Full mass-weighted force constant matrix:
 Low frequencies ---   -0.0013   -0.0003    0.0003    0.7993    1.7110    3.3320
 Low frequencies ---    6.7484    8.5881    8.6743




 Zero-point correction=                           0.762219 (Hartree/Particle)
 Thermal correction to Energy=                    0.811884
 Thermal correction to Enthalpy=                  0.812828
 Thermal correction to Gibbs Free Energy=         0.668953
 Sum of electronic and zero-point Energies=          -2366.547241
 Sum of electronic and thermal Energies=             -2366.497576
 Sum of electronic and thermal Enthalpies=           -2366.496632
 Sum of electronic and thermal Free Energies=        -2366.640507
```

Amide 1 A
Stoichiometry C40H43N5O7
Framework group C1[X(C40H43N5O7)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-7.564158	1.009090	1.228072
2	C	0	-6.060571	0.973356	1.157032
3	C	0	-3.253882	0.930092	1.246723
4	C	0	-5.311463	1.810662	0.323364
5	C	0	-5.392705	0.139049	2.058972
6	C	0	-4.003962	0.103738	2.092735
7	C	0	-3.923305	1.799611	0.380268
8	O	0	-8.125366	0.925055	2.312823
9	N	0	-8.284490	1.196137	0.064005
10	C	0	-9.737054	1.362279	0.217191
11	C	0	-7.802689	0.844152	-1.239156
12	C	0	-6.915885	0.165485	-3.804939
13	C	0	-7.253886	-0.417074	-1.483788
14	C	0	-7.920836	1.758309	-2.290966
15	C	0	-7.482975	1.417603	-3.567402
16	C	0	-6.801601	-0.748057	-2.759585
17	C	0	-1.751063	0.958760	1.237662
18	O	0	-1.144067	1.938966	0.805180
19	N	0	-1.128327	-0.141316	1.735437
20	C	0	0.307342	-0.381409	1.659825
21	C	0	1.058757	0.082189	2.937159
22	C	0	1.241755	1.608590	3.044369
23	C	0	2.224710	2.118491	1.990790
24	O	0	3.434947	1.952121	2.119784
25	N	0	1.668676	2.731008	0.917245
26	C	0	0.512266	-1.890003	1.433991
27	C	0	1.891049	-2.402716	1.055631
28	O	0	-0.424457	-2.652788	1.576825
29	C	0	2.167666	-2.478884	-0.480160
30	C	0	2.164714	-1.079701	-1.084947
31	O	0	1.193903	-0.644817	-1.681240
32	C	0	1.199767	-3.409941	-1.245952
33	C	0	1.424993	-4.875118	-0.932450
34	C	0	1.874324	-7.594889	-0.363669
35	C	0	2.469263	-5.576681	-1.549013
36	C	0	0.608442	-5.561891	-0.026763
37	C	0	0.830546	-6.910086	0.254929
38	C	0	2.694720	-6.922517	-1.269209
39	N	0	3.260803	-0.227773	-0.931607
40	C	0	4.531117	-0.367660	-0.385369
41	C	0	7.053625	-0.695456	0.677558
42	C	0	5.420416	0.748695	-0.370229
43	N	0	4.887979	-1.555580	0.108789
44	C	0	6.108255	-1.710818	0.622226
45	C	0	6.688809	0.546049	0.174725
46	C	0	5.033878	2.094785	-0.879015
47	O	0	3.935994	2.360958	-1.348741
48	O	0	6.031726	2.972431	-0.774143
49	C	0	5.914711	4.392679	-1.204686
50	C	0	5.680742	4.452702	-2.714913
51	C	0	7.290226	4.951279	-0.840754
52	C	0	4.815602	5.096496	-0.407439

53	H	0	-5.810230	2.483319	-0.362316
54	H	0	-5.975101	-0.467293	2.741634
55	H	0	-3.514936	-0.545676	2.809730
56	H	0	-3.337113	2.460007	-0.246023
57	H	0	-9.938832	1.997341	1.077499
58	H	0	-10.138452	1.819072	-0.686015
59	H	0	-10.229870	0.397572	0.378147
60	H	0	-6.567591	-0.095460	-4.797483
61	H	0	-7.179388	-1.134474	-0.675237
62	H	0	-8.343305	2.738742	-2.101258
63	H	0	-7.574223	2.135381	-4.374767
64	H	0	-6.368160	-1.725818	-2.936172
65	H	0	-1.668424	-0.988017	1.869421
66	H	0	0.703630	0.148259	0.789002
67	H	0	2.049500	-0.376801	2.973863
68	H	0	0.501576	-0.282537	3.805026
69	H	0	0.280514	2.119151	2.970324
70	H	0	1.677717	1.835799	4.019717
71	H	0	2.273920	2.928215	0.131319
72	H	0	0.667449	2.654485	0.758528
73	H	0	2.673617	-1.793290	1.508671
74	H	0	1.974698	-3.415402	1.454772
75	H	0	3.181012	-2.872041	-0.551515
76	H	0	1.353307	-3.242680	-2.315342
77	H	0	0.164577	-3.132923	-1.042628
78	H	0	2.044803	-8.643612	-0.147140
79	H	0	3.106606	-5.065485	-2.264636
80	H	0	-0.200585	-5.032487	0.464100
81	H	0	0.184383	-7.425147	0.957558
82	H	0	3.504823	-7.448168	-1.763081
83	H	0	3.082589	0.703195	-1.308765
84	H	0	8.031965	-0.867782	1.106971
85	H	0	6.332898	-2.701004	1.009275
86	H	0	7.377837	1.378407	0.205183
87	H	0	6.461942	3.903347	-3.246448
88	H	0	4.709658	4.041007	-2.985597
89	H	0	5.718847	5.495376	-3.041630
90	H	0	7.465861	4.874244	0.234438
91	H	0	7.350047	6.004016	-1.126258
92	H	0	8.079587	4.406444	-1.363444
93	H	0	4.933268	4.905063	0.661325
94	H	0	4.892282	6.174518	-0.572875
95	H	0	3.823414	4.772940	-0.715776

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2351.24318025 A.U. after 2 cycles
NFock= 2 Conv=0.11D-08 -V/T= 2.0042

Full mass-weighted force constant matrix:
Low frequencies --- -2.2712 -1.3314 -0.8587 -0.0010 -0.0006 0.0007
Low frequencies --- 7.3346 9.3816 14.3196

Zero-point correction= 0.773134 (Hartree/Particle)
Thermal correction to Energy= 0.822802
Thermal correction to Enthalpy= 0.823747
Thermal correction to Gibbs Free Energy= 0.681208

Sum of electronic and zero-point Energies= -2350.470046
Sum of electronic and thermal Energies= -2350.420378
Sum of electronic and thermal Enthalpies= -2350.419434
Sum of electronic and thermal Free Energies= -2350.561972

Amide 1 B

Stoichiometry C39H44N6O6

Framework group C1[X(C39H44N6O6)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-5.493988	-3.115616	-0.464337
2	C	0	-4.699324	-1.879268	-0.783359
3	C	0	-3.241150	0.384177	-1.582040
4	C	0	-5.236191	-0.981475	-1.713319
5	C	0	-3.413874	-1.651257	-0.284033
6	C	0	-2.685786	-0.534232	-0.683599
7	C	0	-4.518834	0.141682	-2.100842
8	O	0	-6.129066	-3.683395	-1.343287
9	N	0	-5.442776	-3.627803	0.820568
10	C	0	-6.121278	-4.913468	1.035634
11	C	0	-5.167517	-2.836873	1.982868
12	C	0	-4.654703	-1.342066	4.293332
13	C	0	-4.243783	-3.293337	2.928590
14	C	0	-5.843291	-1.635001	2.209148
15	C	0	-5.577419	-0.886841	3.354139
16	C	0	-3.992847	-2.551016	4.078801
17	C	0	-2.524417	1.619260	-2.057726
18	O	0	-2.884406	2.184581	-3.096528
19	N	0	-1.508546	2.075484	-1.289373
20	C	0	-0.615393	3.176560	-1.663336
21	C	0	-1.030475	4.515556	-1.020457
22	C	0	-2.336989	5.125079	-1.563075
23	C	0	-2.155728	5.726436	-2.956947
24	O	0	-1.663242	6.837118	-3.111238
25	N	0	-2.569222	4.945943	-3.989259
26	C	0	0.814827	2.773028	-1.269162
27	N	0	0.916084	2.533793	0.173483
28	C	0	2.032641	1.696465	0.589544
29	C	0	1.702670	0.226361	0.291646
30	O	0	0.554109	-0.170928	0.213485
31	C	0	2.259416	1.831332	2.118799
32	C	0	2.604756	3.241699	2.547581
33	C	0	3.244612	5.866827	3.330608
34	C	0	1.702082	4.008062	3.292502
35	C	0	3.837104	3.813093	2.203121
36	C	0	4.154986	5.112161	2.589674
37	C	0	2.017679	5.310508	3.682162
38	N	0	2.713259	-0.723155	0.121778
39	C	0	4.098396	-0.676314	0.083637
40	C	0	6.854288	-0.555119	0.011323
41	C	0	4.831455	-1.846284	-0.288555
42	N	0	4.715732	0.464801	0.404945
43	C	0	6.046872	0.519149	0.363864
44	C	0	6.223905	-1.748158	-0.314649
45	C	0	4.162496	-3.134198	-0.636452
46	O	0	2.956248	-3.309302	-0.583527
47	O	0	5.039699	-4.070262	-1.008479
48	C	0	4.623443	-5.445887	-1.406929
49	C	0	5.962323	-6.106142	-1.732804
50	C	0	3.731396	-5.376610	-2.647251
51	C	0	3.942815	-6.142391	-0.227583
52	H	0	-6.214035	-1.183047	-2.133521

53	H	0	-2.963807	-2.354642	0.404760
54	H	0	-1.676910	-0.413507	-0.308123
55	H	0	-4.927353	0.841480	-2.818797
56	H	0	-5.926816	-5.569399	0.189402
57	H	0	-5.743918	-5.365166	1.951859
58	H	0	-7.204744	-4.779168	1.124574
59	H	0	-4.453846	-0.761758	5.186474
60	H	0	-3.714344	-4.222813	2.751401
61	H	0	-6.572596	-1.287328	1.487305
62	H	0	-6.102147	0.048063	3.515145
63	H	0	-3.270865	-2.911932	4.802679
64	H	0	-1.232231	1.571388	-0.455043
65	H	0	-0.653544	3.269181	-2.751213
66	H	0	-1.137235	4.363093	0.058097
67	H	0	-0.224008	5.242820	-1.166403
68	H	0	-2.634972	5.950869	-0.913869
69	H	0	-3.136035	4.380786	-1.554033
70	H	0	-2.393700	5.279784	-4.924918
71	H	0	-2.804112	3.967707	-3.838601
72	H	0	1.518388	3.541240	-1.624353
73	H	0	1.060159	1.844050	-1.790411
74	H	0	0.963151	3.414221	0.673346
75	H	0	2.969972	1.952100	0.084482
76	H	0	3.067277	1.153810	2.403169
77	H	0	1.349505	1.501567	2.627306
78	H	0	3.491779	6.878603	3.631231
79	H	0	0.745570	3.579697	3.574756
80	H	0	4.549400	3.229488	1.629601
81	H	0	5.114264	5.537341	2.315363
82	H	0	1.304127	5.887570	4.259798
83	H	0	2.333930	-1.649280	-0.083040
84	H	0	7.932228	-0.460457	-0.002976
85	H	0	6.487828	1.474915	0.634058
86	H	0	6.799040	-2.620042	-0.594489
87	H	0	5.798492	-7.139371	-2.047214
88	H	0	6.615217	-6.111905	-0.857129
89	H	0	6.468778	-5.575860	-2.542256
90	H	0	3.550471	-6.390766	-3.013039
91	H	0	4.225898	-4.814844	-3.443671
92	H	0	2.771641	-4.912202	-2.427505
93	H	0	2.984105	-5.684853	0.010409
94	H	0	3.772997	-7.191548	-0.483539
95	H	0	4.583464	-6.111122	0.657406

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2293.24522782 A.U. after 2 cycles
NFock= 2 Conv=0.77D-09 -V/T= 2.0042

Full mass-weighted force constant matrix:
Low frequencies --- -2.3342 -1.0289 -0.0009 -0.0008 -0.0005 0.8558
Low frequencies --- 4.5434 6.2745 9.2519

Zero-point correction= 0.780507 (Hartree/Particle)

Thermal correction to Energy=	0.829683
Thermal correction to Enthalpy=	0.830627
Thermal correction to Gibbs Free Energy=	0.686781
Sum of electronic and zero-point Energies=	-2292.464721
Sum of electronic and thermal Energies=	-2292.415545
Sum of electronic and thermal Enthalpies=	-2292.414600
Sum of electronic and thermal Free Energies=	-2292.558446

Amide 1 C

Stoichiometry C40H45N5O6

Framework group C1[X(C40H45N5O6)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-4.350882	0.960094	0.666157
2	C	0	-3.263421	-0.079035	0.666439
3	C	0	-1.137791	-1.908804	0.808088
4	C	0	-2.865643	-0.610617	1.898370
5	C	0	-2.576999	-0.456329	-0.490776
6	C	0	-1.514735	-1.352119	-0.418811
7	C	0	-1.832777	-1.535532	1.964421
8	O	0	-4.363931	1.834676	1.525150
9	N	0	-5.291529	0.935583	-0.343243
10	C	0	-6.266699	2.034608	-0.363334
11	C	0	-5.618401	-0.236902	-1.102459
12	C	0	-6.309926	-2.491706	-2.606338
13	C	0	-5.655614	-0.168311	-2.498386
14	C	0	-5.944655	-1.435303	-0.463485
15	C	0	-6.277259	-2.560409	-1.215337
16	C	0	-6.003471	-1.290216	-3.245218
17	C	0	-0.034610	-2.922010	0.959091
18	O	0	-0.011732	-3.670297	1.940843
19	N	0	0.904070	-2.955971	-0.016846
20	C	0	2.077503	-3.844065	-0.009442
21	C	0	1.854067	-5.074737	-0.910022
22	C	0	0.771063	-6.057452	-0.424420
23	C	0	1.248607	-6.909698	0.751680
24	O	0	1.930334	-7.910966	0.575153
25	N	0	0.870546	-6.479367	1.985059
26	C	0	3.318073	-3.051399	-0.455958
27	C	0	3.704303	-1.879642	0.480328
28	C	0	3.805147	-0.472607	-0.169944
29	C	0	2.434680	-0.014968	-0.648936
30	O	0	1.932638	-0.471644	-1.671763
31	C	0	4.822874	-0.428925	-1.337476
32	C	0	5.134362	0.973292	-1.817105
33	C	0	5.695006	3.594563	-2.673189
34	C	0	4.483937	1.518251	-2.930045
35	C	0	6.072405	1.764904	-1.142644
36	C	0	6.352128	3.063007	-1.564046
37	C	0	4.760698	2.817328	-3.354783
38	N	0	1.714504	0.954680	0.034206
39	C	0	1.847779	1.522569	1.295124
40	C	0	2.090731	2.571996	3.829277
41	C	0	1.094339	2.686018	1.629814
42	N	0	2.656932	0.926777	2.175359
43	C	0	2.777771	1.443173	3.397616
44	C	0	1.239135	3.190064	2.924042
45	C	0	0.175408	3.349675	0.658459
46	O	0	-0.081550	2.903389	-0.447511
47	O	0	-0.326359	4.486176	1.146840
48	C	0	-1.267814	5.346806	0.376475
49	C	0	-2.533219	4.564662	0.022992
50	C	0	-0.550440	5.899730	-0.856008
51	C	0	-1.577556	6.459846	1.376836
52	H	0	-3.376365	-0.291508	2.798947

53	H	0	-2.860545	-0.046175	-1.451396
54	H	0	-1.002695	-1.621813	-1.334769
55	H	0	-1.543330	-1.980572	2.907998
56	H	0	-7.068525	1.863918	0.362989
57	H	0	-6.701111	2.105544	-1.359360
58	H	0	-5.765800	2.966055	-0.108204
59	H	0	-6.573968	-3.366486	-3.189138
60	H	0	-5.398652	0.761012	-2.994494
61	H	0	-5.933559	-1.485650	0.618728
62	H	0	-6.520106	-3.488260	-0.710201
63	H	0	-6.024747	-1.228578	-4.327377
64	H	0	0.882421	-2.245722	-0.738020
65	H	0	2.209587	-4.168552	1.025363
66	H	0	2.798989	-5.618697	-1.005351
67	H	0	1.592120	-4.721812	-1.913802
68	H	0	-0.148847	-5.522205	-0.176914
69	H	0	0.544831	-6.757920	-1.230602
70	H	0	1.240488	-6.976218	2.781382
71	H	0	0.462946	-5.557951	2.119123
72	H	0	4.149210	-3.757731	-0.524185
73	H	0	3.141938	-2.691562	-1.473351
74	H	0	4.679031	-2.083339	0.933909
75	H	0	2.998682	-1.811640	1.312684
76	H	0	4.144668	0.203641	0.611299
77	H	0	4.454405	-1.028524	-2.171249
78	H	0	5.743946	-0.901644	-0.980408
79	H	0	5.913984	4.603098	-3.005806
80	H	0	3.753427	0.919772	-3.463508
81	H	0	6.596221	1.356877	-0.283197
82	H	0	7.087225	3.656674	-1.031480
83	H	0	4.247747	3.220092	-4.221378
84	H	0	0.935099	1.331995	-0.505883
85	H	0	2.212875	2.945455	4.837756
86	H	0	3.451160	0.914822	4.066981
87	H	0	0.674692	4.068763	3.204315
88	H	0	-2.336364	3.808456	-0.734931
89	H	0	-3.278809	5.263520	-0.367185
90	H	0	-2.953484	4.076056	0.904693
91	H	0	0.370199	6.413131	-0.567261
92	H	0	-1.200320	6.624521	-1.353739
93	H	0	-0.308951	5.108746	-1.564747
94	H	0	-2.253405	7.188077	0.922504
95	H	0	-2.058486	6.053616	2.269274
96	H	0	-0.663305	6.977311	1.676258

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2277.20641002 A.U. after 2 cycles
NFock= 2 Conv=0.36D-08 -V/T= 2.0043

Full mass-weighted force constant matrix:
Low frequencies --- -0.8607 -0.0008 -0.0001 0.0003 1.4635 2.2830
Low frequencies --- 7.7474 10.4313 13.6588

Zero-point correction=	0.791789 (Hartree/Particle)
Thermal correction to Energy=	0.841091
Thermal correction to Enthalpy=	0.842035
Thermal correction to Gibbs Free Energy=	0.699780
Sum of electronic and zero-point Energies=	-2276.414621
Sum of electronic and thermal Energies=	-2276.365319
Sum of electronic and thermal Enthalpies=	-2276.364375
Sum of electronic and thermal Free Energies=	-2276.506630

Amide 2 A

Stoichiometry C40H43N5O7
Framework group C1[X(C40H43N5O7)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-7.965294	2.411839	0.773085
2	C	0	-6.686735	1.646819	0.554564
3	C	0	-4.194315	0.384221	0.249987
4	C	0	-5.850416	1.450149	1.660835
5	C	0	-6.255411	1.230374	-0.707842
6	C	0	-5.017782	0.613211	-0.859271
7	C	0	-4.627832	0.813164	1.512557
8	O	0	-7.982615	3.360796	1.545571
9	N	0	-9.086223	2.060763	0.045207
10	C	0	-10.260881	2.931419	0.197373
11	C	0	-9.310013	0.751550	-0.492887
12	C	0	-9.803969	-1.790082	-1.554977
13	C	0	-9.726921	0.610559	-1.820456
14	C	0	-9.158531	-0.386208	0.303670
15	C	0	-9.393173	-1.651428	-0.231128
16	C	0	-9.976017	-0.653958	-2.345922
17	C	0	-2.860991	-0.298396	0.145252
18	O	0	-2.170924	-0.453851	1.137883
19	C	0	-2.404207	-0.799700	-1.217034
20	C	0	-1.023645	-1.463127	-1.203897
21	C	0	-0.752153	-2.170366	-2.552084
22	C	0	0.577708	-2.939353	-2.612568
23	C	0	0.600105	-4.120609	-1.643667
24	O	0	-0.256353	-4.993994	-1.682827
25	N	0	1.619751	-4.129698	-0.744042
26	C	0	0.057387	-0.406724	-0.946971
27	N	0	1.009070	-0.762756	-0.041477
28	C	0	2.120728	0.089097	0.314723
29	C	0	3.435436	-0.594320	-0.070528
30	O	0	3.497010	-1.796208	-0.283626
31	C	0	2.086090	0.471713	1.827610
32	C	0	2.056455	-0.700619	2.783729
33	C	0	1.995234	-2.891615	4.546415
34	C	0	0.837669	-1.274385	3.170924
35	C	0	3.240991	-1.240009	3.300243
36	C	0	3.213301	-2.325331	4.173417
37	C	0	0.808289	-2.362159	4.043224
38	N	0	4.623904	0.124510	-0.144128
39	C	0	4.914826	1.482573	-0.182662
40	C	0	5.443005	4.185758	-0.271496
41	C	0	6.259153	1.912179	-0.400315
42	N	0	3.916573	2.352303	-0.017624
43	C	0	4.173012	3.658355	-0.065511
44	C	0	6.489532	3.289803	-0.438074
45	C	0	7.384848	0.953191	-0.591076
46	O	0	7.252277	-0.259921	-0.588582
47	O	0	8.552950	1.578299	-0.765537
48	C	0	9.830524	0.843102	-0.985396
49	C	0	9.742919	0.027873	-2.276566
50	C	0	10.148628	-0.019277	0.237148
51	C	0	10.838586	1.982894	-1.126567

52	O	0	0.074606	0.656297	-1.556002
53	H	0	-6.171224	1.811597	2.630232
54	H	0	-6.877338	1.396733	-1.577847
55	H	0	-4.701359	0.314099	-1.850436
56	H	0	-3.982319	0.643782	2.365356
57	H	0	-10.793664	2.716031	1.129655
58	H	0	-10.934789	2.767515	-0.642019
59	H	0	-9.938792	3.970573	0.219310
60	H	0	-9.991800	-2.774580	-1.967381
61	H	0	-9.842033	1.492634	-2.440464
62	H	0	-8.855732	-0.278899	1.338433
63	H	0	-9.264516	-2.527995	0.393532
64	H	0	-10.294785	-0.752519	-3.377454
65	H	0	-3.152879	-1.507530	-1.591280
66	H	0	-2.391624	0.042805	-1.916626
67	H	0	-1.002375	-2.207335	-0.402926
68	H	0	-1.564242	-2.877999	-2.740467
69	H	0	-0.769553	-1.423741	-3.351848
70	H	0	0.691398	-3.361501	-3.615673
71	H	0	1.427054	-2.273590	-2.443507
72	H	0	1.673753	-4.906357	-0.102308
73	H	0	2.307769	-3.387569	-0.677169
74	H	0	0.903562	-1.638490	0.448267
75	H	0	2.021597	1.008729	-0.257790
76	H	0	1.188696	1.079924	1.962548
77	H	0	2.942338	1.114168	2.037696
78	H	0	1.971603	-3.734697	5.227892
79	H	0	-0.092937	-0.866677	2.789347
80	H	0	4.194988	-0.803185	3.021814
81	H	0	4.141992	-2.726188	4.564597
82	H	0	-0.144663	-2.791493	4.332386
83	H	0	5.432043	-0.472146	-0.328571
84	H	0	5.602928	5.255703	-0.300543
85	H	0	3.314827	4.310630	0.069246
86	H	0	7.498932	3.641326	-0.602013
87	H	0	10.727824	-0.389634	-2.501966
88	H	0	9.031877	-0.791628	-2.187275
89	H	0	9.448344	0.666438	-3.113176
90	H	0	9.440846	-0.839303	0.345428
91	H	0	11.152099	-0.438650	0.126159
92	H	0	10.135528	0.586549	1.146732
93	H	0	10.863291	2.592617	-0.220671
94	H	0	10.581564	2.624798	-1.972073
95	H	0	11.837807	1.574782	-1.294894

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2351.24730824 A.U. after 2 cycles
NFock= 2 Conv=0.16D-08 -V/T= 2.0042

Full mass-weighted force constant matrix:
Low frequencies --- -0.5246 -0.0013 -0.0008 0.0007 1.2485 2.6217
Low frequencies --- 4.6437 7.0435 8.1102

Zero-point correction= 0.772195 (Hartree/Particle)
Thermal correction to Energy= 0.822333

Thermal correction to Enthalpy=	0.823277
Thermal correction to Gibbs Free Energy=	0.677444
Sum of electronic and zero-point Energies=	-2350.475114
Sum of electronic and thermal Energies=	-2350.424976
Sum of electronic and thermal Enthalpies=	-2350.424031
Sum of electronic and thermal Free Energies=	-2350.569864

Amide 2 B

Stoichiometry C39H44N6O6

Framework group C1[X(C39H44N6O6)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-5.937452	3.589687	0.412677
2	C	0	-4.832937	2.842697	-0.283400
3	C	0	-2.660549	1.539901	-1.521338
4	C	0	-5.016774	2.131184	-1.474321
5	C	0	-3.546911	2.938997	0.253481
6	C	0	-2.478435	2.282117	-0.350770
7	C	0	-3.940727	1.499667	-2.086805
8	O	0	-5.723488	4.695159	0.895921
9	N	0	-7.196990	3.023681	0.459208
10	C	0	-8.257629	3.849527	1.052434
11	C	0	-7.450102	1.616592	0.338367
12	C	0	-7.977321	-1.119745	0.097099
13	C	0	-8.466778	1.168152	-0.511096
14	C	0	-6.715125	0.687251	1.078680
15	C	0	-6.964159	-0.678103	0.946575
16	C	0	-8.732270	-0.193966	-0.623758
17	C	0	-1.519608	0.756945	-2.145672
18	N	0	-1.591831	-0.707479	-1.959784
19	C	0	-1.562378	-1.181849	-0.571986
20	C	0	-2.295557	-2.540278	-0.486260
21	C	0	-2.323392	-3.218614	0.896077
22	C	0	-3.086102	-2.412464	1.946384
23	O	0	-4.304175	-2.492750	2.062476
24	N	0	-2.315521	-1.617955	2.734466
25	C	0	-0.114782	-1.301482	-0.058373
26	N	0	0.817777	-1.462250	-1.019023
27	C	0	2.238925	-1.534702	-0.744964
28	C	0	2.914279	-0.278246	-1.309935
29	O	0	2.438615	0.298985	-2.271116
30	C	0	2.885749	-2.784117	-1.399417
31	C	0	2.289199	-4.092544	-0.929093
32	C	0	1.193219	-6.532426	-0.059786
33	C	0	1.590253	-4.919414	-1.813195
34	C	0	2.430629	-4.508268	0.400394
35	C	0	1.887687	-5.715367	0.832678
36	C	0	1.046901	-6.131011	-1.385356
37	N	0	4.099192	0.216388	-0.771605
38	C	0	4.866908	-0.132405	0.329789
39	C	0	6.367042	-0.858071	2.526375
40	C	0	5.947261	0.710309	0.734149
41	N	0	4.576251	-1.263121	0.979266
42	C	0	5.299992	-1.606615	2.043845
43	C	0	6.685298	0.311733	1.850795
44	C	0	6.294955	1.967161	0.010233
45	O	0	5.723733	2.351701	-0.996898
46	O	0	7.306152	2.618157	0.592746
47	C	0	7.844361	3.902319	0.060772
48	C	0	8.412200	3.684084	-1.342591
49	C	0	8.958081	4.222782	1.056740
50	C	0	6.753856	4.974167	0.096705
51	O	0	0.135988	-1.280816	1.149354
52	H	0	-5.998699	2.073494	-1.926638

53	H	0	-3.396641	3.529577	1.149240
54	H	0	-1.489553	2.349520	0.091774
55	H	0	-4.101813	0.963005	-3.017468
56	H	0	-9.225911	3.451540	0.753823
57	H	0	-8.153509	4.876364	0.706948
58	H	0	-8.193641	3.847106	2.145842
59	H	0	-8.177551	-2.180581	-0.001430
60	H	0	-9.036247	1.886232	-1.090809
61	H	0	-5.938052	1.031856	1.750321
62	H	0	-6.359545	-1.386389	1.502088
63	H	0	-9.521541	-0.532052	-1.286280
64	H	0	-1.487051	0.936563	-3.223915
65	H	0	-0.563355	1.103872	-1.745686
66	H	0	-2.412942	-1.072426	-2.429487
67	H	0	-2.056692	-0.480233	0.110622
68	H	0	-1.834040	-3.228392	-1.202007
69	H	0	-3.327713	-2.374152	-0.813706
70	H	0	-2.849436	-4.169810	0.796015
71	H	0	-1.307946	-3.427803	1.236450
72	H	0	-1.355209	-1.420718	2.461447
73	H	0	-2.787455	-0.999202	3.376709
74	H	0	0.489880	-1.327869	-1.969906
75	H	0	2.364858	-1.581566	0.332643
76	H	0	2.783526	-2.701026	-2.485818
77	H	0	3.954788	-2.761116	-1.171685
78	H	0	0.771345	-7.472951	0.276267
79	H	0	1.472916	-4.615034	-2.848451
80	H	0	2.965974	-3.876851	1.101188
81	H	0	2.006238	-6.019932	1.866799
82	H	0	0.510613	-6.759225	-2.088198
83	H	0	4.419431	1.062967	-1.244831
84	H	0	6.926664	-1.182202	3.394065
85	H	0	5.010874	-2.533908	2.530748
86	H	0	7.507237	0.934005	2.177145
87	H	0	8.930685	4.591892	-1.662287
88	H	0	7.627472	3.461602	-2.063570
89	H	0	9.136806	2.865837	-1.339384
90	H	0	9.711785	3.432225	1.062932
91	H	0	8.555695	4.329135	2.066542
92	H	0	9.444594	5.160561	0.778926
93	H	0	6.328006	5.053508	1.100085
94	H	0	5.955966	4.759909	-0.612227
95	H	0	7.195600	5.940873	-0.159174

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2293.24571069 A.U. after 2 cycles
NFock= 2 Conv=0.29D-08 -V/T= 2.0042

Full mass-weighted force constant matrix:
Low frequencies --- -1.0194 -0.6559 -0.0013 -0.0010 0.0002 1.8308
Low frequencies --- 4.5480 6.7881 11.3031

Zero-point correction= 0.780621 (Hartree/Particle)
Thermal correction to Energy= 0.829689

Thermal correction to Enthalpy=	0.830634
Thermal correction to Gibbs Free Energy=	0.687150
Sum of electronic and zero-point Energies=	-2292.465090
Sum of electronic and thermal Energies=	-2292.416021
Sum of electronic and thermal Enthalpies=	-2292.415077
Sum of electronic and thermal Free Energies=	-2292.558561

Amide 2 C

Stoichiometry C40H45N5O6
Framework group C1[X(C40H45N5O6)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-6.730310	-1.106784	-0.901221
2	C	0	-5.621466	-1.064242	0.111220
3	C	0	-3.455636	-1.077300	1.924087
4	C	0	-4.424073	-1.707343	-0.212426
5	C	0	-5.747556	-0.476858	1.374970
6	C	0	-4.682324	-0.494316	2.267569
7	C	0	-3.352824	-1.701111	0.676317
8	O	0	-6.910955	-2.110980	-1.581102
9	N	0	-7.561128	-0.007983	-1.028584
10	C	0	-8.690974	-0.155935	-1.955700
11	C	0	-7.199496	1.324225	-0.639547
12	C	0	-6.521720	3.927278	0.132103
13	C	0	-5.964035	1.869606	-0.998507
14	C	0	-8.104799	2.100652	0.091387
15	C	0	-7.768583	3.398614	0.466739
16	C	0	-5.616527	3.158671	-0.597870
17	C	0	-2.273352	-0.993823	2.864946
18	C	0	-1.682934	0.428935	2.979165
19	C	0	-1.052346	0.979882	1.685517
20	C	0	-0.793677	2.497720	1.820954
21	C	0	-0.166983	3.167880	0.586718
22	C	0	-1.078445	3.127100	-0.636619
23	O	0	-2.197613	3.624755	-0.627689
24	N	0	-0.568162	2.492543	-1.727832
25	C	0	0.262736	0.252676	1.389382
26	N	0	0.369771	-0.306555	0.144217
27	C	0	1.609880	-0.906510	-0.310149
28	C	0	2.551196	0.177315	-0.862797
29	O	0	2.104780	1.165809	-1.430758
30	C	0	1.361681	-1.954063	-1.417880
31	C	0	0.489120	-3.120102	-1.000668
32	C	0	-1.104315	-5.325858	-0.286328
33	C	0	-0.632630	-3.470482	-1.758043
34	C	0	0.801662	-3.895331	0.122709
35	C	0	0.011947	-4.985975	0.478284
36	C	0	-1.423719	-4.565120	-1.407918
37	N	0	3.926102	0.069289	-0.754314
38	C	0	4.762804	-0.876923	-0.173862
39	C	0	6.389923	-2.782102	0.969407
40	C	0	6.144112	-0.574490	0.015037
41	N	0	4.245319	-2.057719	0.171240
42	C	0	5.034510	-2.974736	0.730310
43	C	0	6.939568	-1.562684	0.599117
44	C	0	6.739712	0.731568	-0.392978
45	O	0	6.125539	1.600342	-0.990195
46	O	0	8.021651	0.831110	-0.033453
47	C	0	8.846405	2.038095	-0.328708
48	C	0	8.954807	2.233496	-1.841728
49	C	0	10.199307	1.658891	0.271793
50	C	0	8.253223	3.254480	0.383623
51	O	0	1.167583	0.179858	2.210922

52	H	0	-4.342059	-2.207483	-1.170044
53	H	0	-6.677328	-0.003572	1.664434
54	H	0	-4.803154	-0.035366	3.243985
55	H	0	-2.426536	-2.192061	0.397480
56	H	0	-9.140666	-1.138673	-1.826368
57	H	0	-9.425200	0.620402	-1.747890
58	H	0	-8.361494	-0.064590	-2.996381
59	H	0	-6.255030	4.931747	0.440300
60	H	0	-5.265379	1.276477	-1.576027
61	H	0	-9.062094	1.679758	0.378323
62	H	0	-8.476609	3.990887	1.036062
63	H	0	-4.636260	3.549256	-0.846980
64	H	0	-2.582731	-1.312226	3.866420
65	H	0	-1.496322	-1.694070	2.544064
66	H	0	-2.474870	1.116741	3.292443
67	H	0	-0.919094	0.439201	3.762007
68	H	0	-1.750037	0.820691	0.856262
69	H	0	-0.136033	2.662937	2.679488
70	H	0	-1.747671	2.986097	2.036145
71	H	0	0.809303	2.733949	0.359014
72	H	0	-0.005490	4.226743	0.810998
73	H	0	-1.103592	2.523073	-2.582495
74	H	0	0.374912	2.117858	-1.740063
75	H	0	-0.339393	-0.084262	-0.538749
76	H	0	2.080512	-1.379206	0.546067
77	H	0	2.339294	-2.327581	-1.736431
78	H	0	0.916080	-1.455045	-2.284809
79	H	0	-1.720647	-6.172776	-0.007287
80	H	0	-0.890366	-2.883693	-2.634353
81	H	0	1.667841	-3.642469	0.724252
82	H	0	0.267242	-5.571835	1.354564
83	H	0	-2.290925	-4.817362	-2.007920
84	H	0	4.417453	0.898385	-1.093690
85	H	0	6.990392	-3.560065	1.422598
86	H	0	4.554484	-3.913946	0.990399
87	H	0	7.989471	-1.357137	0.756457
88	H	0	9.675216	3.029681	-2.047175
89	H	0	9.316672	1.320309	-2.321026
90	H	0	7.998093	2.510889	-2.280896
91	H	0	10.911008	2.474425	0.124613
92	H	0	10.107916	1.470170	1.343643
93	H	0	10.598843	0.762438	-0.207630
94	H	0	8.939895	4.098615	0.278661
95	H	0	8.129701	3.051074	1.450222
96	H	0	7.290270	3.537468	-0.038030

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2277.20942629 A.U. after 2 cycles
NFock= 2 Conv=0.35D-08 -V/T= 2.0043

Full mass-weighted force constant matrix:
Low frequencies --- -2.5557 -0.9252 -0.4490 -0.0011 -0.0007 0.0010
Low frequencies --- 5.2065 8.9061 13.4394

Zero-point correction= 0.791602 (Hartree/Particle)
Thermal correction to Energy= 0.840901

Thermal correction to Enthalpy=	0.841845
Thermal correction to Gibbs Free Energy=	0.699719
Sum of electronic and zero-point Energies=	-2276.417825
Sum of electronic and thermal Energies=	-2276.368525
Sum of electronic and thermal Enthalpies=	-2276.367581
Sum of electronic and thermal Free Energies=	-2276.509707

Amide 3 A

Stoichiometry C40H43N5O7
Framework group C1[X(C40H43N5O7)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	8.281751	1.588753	-1.285774
2	C	0	6.895030	1.413809	-0.725379
3	C	0	4.271169	1.307577	0.269938
4	C	0	6.644787	0.929013	0.562792
5	C	0	5.824273	1.874234	-1.498092
6	C	0	4.523566	1.806790	-1.014060
7	C	0	5.347845	0.892086	1.059639
8	O	0	8.554769	2.590575	-1.933749
9	N	0	9.241412	0.635618	-1.003749
10	C	0	10.607768	0.932710	-1.457738
11	C	0	8.941408	-0.730878	-0.692841
12	C	0	8.416693	-3.413739	-0.094874
13	C	0	9.556122	-1.342175	0.404633
14	C	0	8.075468	-1.475333	-1.497688
15	C	0	7.806456	-2.807719	-1.190719
16	C	0	9.297168	-2.677775	0.698247
17	C	0	2.894557	1.221318	0.865700
18	N	0	1.859123	1.241313	-0.011964
19	C	0	0.469205	0.987506	0.353165
20	C	0	-0.341126	2.285908	0.572659
21	C	0	0.030926	3.056982	1.853419
22	C	0	-0.459500	2.342965	3.113214
23	O	0	-1.644727	2.355615	3.431789
24	N	0	0.493106	1.706027	3.837787
25	C	0	-0.122020	0.119393	-0.782764
26	N	0	-1.372167	-0.348583	-0.578528
27	C	0	-2.004894	-1.264734	-1.518907
28	C	0	-3.512089	-0.992030	-1.662743
29	O	0	-4.277968	-1.885081	-1.943139
30	C	0	-1.674097	-2.753213	-1.237578
31	C	0	-1.958152	-3.222406	0.173504
32	C	0	-2.459978	-4.083883	2.806172
33	C	0	-3.220533	-3.705785	0.541592
34	C	0	-0.951889	-3.188088	1.146647
35	C	0	-1.197520	-3.612178	2.451614
36	C	0	-3.468864	-4.131644	1.845353
37	C	0	-4.017630	0.448557	-1.522359
38	C	0	-4.639400	0.662372	-0.154798
39	C	0	-5.532568	0.988687	2.430255
40	C	0	-6.021687	0.814708	0.071944
41	N	0	-3.759895	0.655220	0.861383
42	C	0	-4.186302	0.836429	2.114834
43	C	0	-6.454701	0.960658	1.396340
44	C	0	-7.031037	0.873052	-1.039993
45	O	0	-6.795343	1.261223	-2.163118
46	O	0	-8.233974	0.464315	-0.607862
47	C	0	-9.430497	0.446543	-1.490263
48	C	0	-9.755703	1.867241	-1.956167
49	C	0	-10.517499	-0.083017	-0.555296
50	C	0	-9.198274	-0.516563	-2.656084

51	O	0	0.536587	-0.130973	-1.789677
52	O	0	2.741676	1.145342	2.087297
53	H	0	7.463430	0.593744	1.186364
54	H	0	6.026437	2.299518	-2.473331
55	H	0	3.715176	2.180117	-1.631769
56	H	0	5.149029	0.540955	2.064226
57	H	0	10.719882	0.733413	-2.528777
58	H	0	11.308275	0.308042	-0.905729
59	H	0	10.825802	1.983885	-1.280288
60	H	0	8.211057	-4.451913	0.138641
61	H	0	10.225733	-0.764279	1.031812
62	H	0	7.613674	-1.010167	-2.360448
63	H	0	7.126832	-3.373809	-1.817452
64	H	0	9.775677	-3.141049	1.553685
65	H	0	2.047628	1.022128	-0.985121
66	H	0	0.456498	0.390255	1.270407
67	H	0	-0.185048	2.932233	-0.296568
68	H	0	-1.407380	2.050183	0.613760
69	H	0	1.105713	3.241133	1.896320
70	H	0	-0.476763	4.023919	1.833574
71	H	0	0.187559	1.162819	4.631502
72	H	0	1.407818	1.525980	3.432549
73	H	0	-1.925397	-0.038973	0.222381
74	H	0	-1.588175	-1.027605	-2.507540
75	H	0	-0.612855	-2.887750	-1.459775
76	H	0	-2.237788	-3.352111	-1.955405
77	H	0	-2.653344	-4.418981	3.819158
78	H	0	-4.009045	-3.747905	-0.200503
79	H	0	0.039487	-2.839022	0.875700
80	H	0	-0.401181	-3.581379	3.187368
81	H	0	-4.451831	-4.506818	2.108920
82	H	0	-3.193605	1.154799	-1.638278
83	H	0	-4.748765	0.617664	-2.307514
84	H	0	-5.841821	1.129091	3.458341
85	H	0	-3.418268	0.886202	2.878893
86	H	0	-7.513012	1.066204	1.594704
87	H	0	-10.711554	1.859665	-2.486975
88	H	0	-9.852029	2.538953	-1.099135
89	H	0	-8.989820	2.254380	-2.626145
90	H	0	-10.653985	0.584680	0.298521
91	H	0	-10.255026	-1.075127	-0.181878
92	H	0	-11.466525	-0.154406	-1.091891
93	H	0	-8.429603	-0.148189	-3.333267
94	H	0	-8.901165	-1.500485	-2.285226
95	H	0	-10.130333	-0.632103	-3.215915

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2351.24077207 A.U. after 2 cycles
NFock= 2 Conv=0.19D-0XBig12= 4.84D-14 4.83D-09.

Full mass-weighted force constant matrix:
Low frequencies --- -2.5988 -0.9715 -0.0016 -0.0010 0.0010 1.0734
Low frequencies --- 5.3837 6.5684 7.8196

Zero-point correction=	0.772715 (Hartree/Particle)
Thermal correction to Energy=	0.822526
Thermal correction to Enthalpy=	0.823470
Thermal correction to Gibbs Free Energy=	0.678227
Sum of electronic and zero-point Energies=	-2350.468057
Sum of electronic and thermal Energies=	-2350.418247
Sum of electronic and thermal Enthalpies=	-2350.417302
Sum of electronic and thermal Free Energies=	-2350.562545

Amide 3 B

Stoichiometry C39H44N6O6
Framework group C1[X(C39H44N6O6)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-8.352464	0.145950	-0.509286
2	C	0	-6.920887	-0.313505	-0.429485
3	C	0	-4.283253	-1.278114	-0.478285
4	C	0	-6.395958	-0.997906	0.671844
5	C	0	-6.124644	-0.144499	-1.566650
6	C	0	-4.814171	-0.605989	-1.586436
7	C	0	-5.096250	-1.487940	0.639919
8	O	0	-8.976621	0.017723	-1.554329
9	N	0	-8.956272	0.652295	0.625939
10	C	0	-10.392449	0.948604	0.521709
11	C	0	-8.240390	1.268921	1.703355
12	C	0	-6.896718	2.495572	3.829685
13	C	0	-8.525873	0.903689	3.022907
14	C	0	-7.290135	2.262860	1.456308
15	C	0	-6.613776	2.863532	2.516269
16	C	0	-7.859637	1.517668	4.079431
17	C	0	-2.881910	-1.820559	-0.432012
18	N	0	-2.006323	-1.299675	-1.325055
19	C	0	-0.572223	-1.566070	-1.334835
20	C	0	-0.177463	-2.662340	-2.352852
21	C	0	-0.650238	-4.079658	-1.981635
22	C	0	0.157694	-4.664559	-0.825046
23	O	0	1.304215	-5.070836	-0.993572
24	N	0	-0.468503	-4.696837	0.376576
25	C	0	0.107982	-0.226712	-1.699459
26	N	0	1.429996	-0.152404	-1.462546
27	C	0	2.217097	1.024150	-1.841725
28	C	0	3.686321	0.621174	-2.065655
29	C	0	2.037876	2.170551	-0.817648
30	C	0	2.636036	3.482697	-1.275763
31	C	0	3.744506	5.911085	-2.167687
32	C	0	2.017794	4.224753	-2.291478
33	C	0	3.815044	3.983324	-0.712494
34	C	0	4.366078	5.186898	-1.152931
35	C	0	2.565847	5.426117	-2.734740
36	N	0	4.470308	0.338768	-0.866904
37	C	0	4.599264	-0.886939	-0.293839
38	C	0	4.798373	-3.436397	0.763333
39	C	0	5.633072	-1.167103	0.659890
40	N	0	3.706580	-1.833353	-0.654585
41	C	0	3.816216	-3.066498	-0.151556
42	C	0	5.700772	-2.464720	1.172149
43	C	0	6.602728	-0.129575	1.074674
44	O	0	6.592878	1.022434	0.661055
45	O	0	7.499623	-0.592690	1.959413
46	C	0	8.577418	0.255618	2.524704
47	C	0	9.506492	0.734109	1.406719
48	C	0	9.303827	-0.717110	3.454032
49	C	0	7.969706	1.413576	3.319635
50	O	0	-0.550155	0.690036	-2.192318

51	O	0	-2.574453	-2.696286	0.381788
52	H	0	-7.005577	-1.163088	1.550792
53	H	0	-6.550508	0.337810	-2.437772
54	H	0	-4.225722	-0.466889	-2.485862
55	H	0	-4.690657	-2.039084	1.478785
56	H	0	-10.563224	1.894434	-0.003278
57	H	0	-10.885020	0.154185	-0.035406
58	H	0	-10.813482	1.017958	1.523442
59	H	0	-6.373937	2.968203	4.653066
60	H	0	-9.260557	0.129866	3.215567
61	H	0	-7.081359	2.562261	0.436153
62	H	0	-5.872601	3.627958	2.312643
63	H	0	-8.085372	1.224159	5.098391
64	H	0	-2.240009	-0.438831	-1.809789
65	H	0	-0.266417	-1.864480	-0.328205
66	H	0	0.910038	-2.676336	-2.465087
67	H	0	-0.596599	-2.384062	-3.324541
68	H	0	-0.478077	-4.737015	-2.836826
69	H	0	-1.719307	-4.084888	-1.762210
70	H	0	0.069365	-5.005695	1.172699
71	H	0	-1.310333	-4.146667	0.528624
72	H	0	1.960726	-0.959994	-1.128602
73	H	0	1.833011	1.369111	-2.806907
74	H	0	4.181461	1.451704	-2.571276
75	H	0	3.717526	-0.243291	-2.734164
76	H	0	2.480267	1.863757	0.133697
77	H	0	0.964266	2.294065	-0.657885
78	H	0	4.170236	6.847504	-2.510401
79	H	0	1.093429	3.860826	-2.729298
80	H	0	4.304096	3.431418	0.083989
81	H	0	5.279110	5.557991	-0.700313
82	H	0	2.069585	5.987534	-3.518861
83	H	0	5.173805	1.009766	-0.580678
84	H	0	4.840638	-4.448521	1.143270
85	H	0	3.075319	-3.786793	-0.488896
86	H	0	6.476459	-2.696546	1.889789
87	H	0	9.869512	-0.115584	0.822912
88	H	0	10.372323	1.234415	1.848937
89	H	0	9.003700	1.433022	0.740481
90	H	0	9.697145	-1.567136	2.892110
91	H	0	10.138613	-0.210653	3.944236
92	H	0	8.627191	-1.093283	4.224558
93	H	0	7.263395	1.036206	4.063517
94	H	0	7.456201	2.119344	2.669031
95	H	0	8.766743	1.942800	3.848938

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2293.27267065 A.U. after 2 cycles
NFock= 2 Conv=0.15D-08 -V/T= 2.0042

Full mass-weighted force constant matrix:
Low frequencies --- -1.2807 -0.5035 -0.0013 -0.0010 0.0009 1.9699
Low frequencies --- 5.6867 7.4965 12.4669
Diagonal vibrational polarizability:
230.2711108 284.5712477 229.2931176

Zero-point correction=	0.781331 (Hartree/Particle)
Thermal correction to Energy=	0.830161
Thermal correction to Enthalpy=	0.831105
Thermal correction to Gibbs Free Energy=	0.689730
Sum of electronic and zero-point Energies=	-2292.491340
Sum of electronic and thermal Energies=	-2292.442510
Sum of electronic and thermal Enthalpies=	-2292.441566
Sum of electronic and thermal Free Energies=	-2292.582941

Amide 3 C

Stoichiometry C40H45N5O6
Framework group C1[X(C40H45N5O6)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-7.219930	0.162420	1.741341
2	C	0	-5.794279	0.379382	1.308830
3	C	0	-3.073653	0.779923	0.735171
4	C	0	-4.826003	-0.492400	1.816727
5	C	0	-5.388070	1.460679	0.519529
6	C	0	-4.042001	1.657589	0.237581
7	C	0	-3.480684	-0.303954	1.523172
8	O	0	-7.460918	-0.207264	2.882979
9	N	0	-8.240207	0.446491	0.852931
10	C	0	-9.608271	0.354130	1.383056
11	C	0	-8.090856	0.413280	-0.571735
12	C	0	-7.861823	0.350096	-3.360250
13	C	0	-7.496853	-0.681279	-1.205001
14	C	0	-8.584613	1.469406	-1.344427
15	C	0	-8.473575	1.434537	-2.731319
16	C	0	-7.372986	-0.704573	-2.592715
17	C	0	-1.639042	1.045840	0.371769
18	N	0	-0.703536	0.524046	1.196283
19	C	0	0.725771	0.455132	0.915355
20	C	0	1.524775	1.577744	1.616870
21	C	0	1.265526	2.995199	1.072427
22	C	0	1.900341	3.221580	-0.298584
23	O	0	3.098093	3.471292	-0.417290
24	N	0	1.057657	3.125295	-1.354885
25	C	0	1.194254	-0.924286	1.435590
26	N	0	2.337846	-1.391889	0.897028
27	C	0	2.904889	-2.698975	1.237187
28	C	0	4.195187	-2.588571	2.074236
29	C	0	3.097549	-3.548771	-0.042864
30	C	0	1.813878	-3.840928	-0.788183
31	C	0	-0.590385	-4.368435	-2.151099
32	C	0	1.477646	-3.136298	-1.948702
33	C	0	0.924588	-4.817572	-0.324066
34	C	0	-0.266284	-5.080504	-0.996570
35	C	0	0.286215	-3.395416	-2.625912
36	C	0	5.373776	-1.800576	1.451265
37	C	0	5.405740	-0.326140	1.806990
38	C	0	5.683836	2.275851	2.683482
39	C	0	5.390954	0.726294	0.868444
40	N	0	5.542501	-0.079881	3.118640
41	C	0	5.663443	1.178336	3.540243
42	C	0	5.550235	2.040495	1.323656
43	C	0	5.154378	0.499938	-0.591557
44	O	0	4.309961	-0.264931	-1.030228
45	O	0	5.964832	1.248955	-1.333849
46	C	0	5.880665	1.313990	-2.820744
47	C	0	6.266345	-0.044661	-3.406763
48	C	0	6.928307	2.375006	-3.154896
49	C	0	4.485733	1.772598	-3.248133
50	O	0	0.543295	-1.504997	2.301348

51	O	0	-1.360964	1.729171	-0.619618
52	H	0	-5.139327	-1.315224	2.447323
53	H	0	-6.120391	2.157009	0.131879
54	H	0	-3.721395	2.490891	-0.374725
55	H	0	-2.761018	-1.022732	1.898959
56	H	0	-9.636528	0.779893	2.384050
57	H	0	-9.939028	-0.688204	1.442835
58	H	0	-10.280992	0.902444	0.725496
59	H	0	-7.769677	0.327489	-4.439893
60	H	0	-7.131321	-1.510076	-0.610547
61	H	0	-9.042566	2.321063	-0.853877
62	H	0	-8.855640	2.260512	-3.320538
63	H	0	-6.902536	-1.554970	-3.072964
64	H	0	-0.980588	-0.079929	1.961700
65	H	0	0.867189	0.509845	-0.166574
66	H	0	1.272178	1.551323	2.681115
67	H	0	2.592263	1.358418	1.539218
68	H	0	0.193786	3.201845	1.046128
69	H	0	1.731430	3.715640	1.748044
70	H	0	0.125006	2.732377	-1.237120
71	H	0	1.453576	3.196682	-2.279933
72	H	0	2.812954	-0.860648	0.171793
73	H	0	2.154578	-3.184549	1.863937
74	H	0	4.530295	-3.610954	2.277302
75	H	0	3.956944	-2.145729	3.044188
76	H	0	3.568312	-4.490747	0.257532
77	H	0	3.798321	-3.044313	-0.713483
78	H	0	-1.516191	-4.573361	-2.676966
79	H	0	2.158127	-2.380470	-2.327620
80	H	0	1.166944	-5.379911	0.572610
81	H	0	-0.939967	-5.843076	-0.621282
82	H	0	0.044678	-2.838142	-3.524509
83	H	0	5.414821	-1.943371	0.372362
84	H	0	6.299551	-2.215672	1.861606
85	H	0	5.791282	3.281026	3.072259
86	H	0	5.754201	1.313550	4.614843
87	H	0	5.521391	2.856852	0.614662
88	H	0	7.249664	-0.354579	-3.044024
89	H	0	5.534716	-0.810125	-3.151057
90	H	0	6.317254	0.034943	-4.496019
91	H	0	6.659504	3.334616	-2.708627
92	H	0	7.910485	2.079404	-2.779772
93	H	0	6.994186	2.502419	-4.238031
94	H	0	3.743613	0.989946	-3.096787
95	H	0	4.187875	2.655407	-2.677890
96	H	0	4.509483	2.030315	-4.310718

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2277.20772117 A.U. after 2 cycles

Full mass-weighted force constant matrix:
Low frequencies --- -1.4231 -0.0012 -0.0008 0.0009 0.7912 2.6005
Low frequencies --- 6.8167 8.5529 13.4800

Zero-point correction= 0.792103 (Hartree/Particle)
Thermal correction to Energy= 0.841250

Thermal correction to Enthalpy=	0.842195
Thermal correction to Gibbs Free Energy=	0.700825
Sum of electronic and zero-point Energies=	-2276.415618
Sum of electronic and thermal Energies=	-2276.366471
Sum of electronic and thermal Enthalpies=	-2276.365527
Sum of electronic and thermal Free Energies=	-2276.506896

Amide 4 A

Stoichiometry C40H43N5O7
Framework group C1[X(C40H43N5O7)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-7.538425	0.362590	0.420196
2	C	0	-6.112574	0.067407	0.793316
3	C	0	-3.460523	-0.612064	1.444389
4	C	0	-5.598218	-1.197326	0.475052
5	C	0	-5.278658	0.988823	1.439750
6	C	0	-3.967430	0.653569	1.754817
7	C	0	-4.292007	-1.539178	0.798073
8	O	0	-8.176374	-0.439739	-0.235709
9	C	0	-9.711490	1.552535	0.943451
10	C	0	-7.765245	2.822420	-0.067000
11	C	0	-7.083061	4.955277	-1.766000
12	C	0	-7.838879	2.679228	-1.457638
13	C	0	-7.347222	4.050290	0.456929
14	C	0	-7.009821	5.110056	-0.383170
15	C	0	-7.499331	3.736462	-2.299363
16	C	0	-2.029493	-0.885356	1.828362
17	O	0	-1.316922	0.007516	2.293407
18	N	0	-1.569364	-2.145038	1.637001
19	C	0	-0.243657	-2.581496	2.092989
20	C	0	-0.279282	-4.068875	2.492542
21	C	0	-0.330435	-5.144717	1.377291
22	C	0	-1.264138	-4.799749	0.226218
23	O	0	-2.478418	-4.669094	0.391121
24	N	0	-0.670000	-4.636617	-0.980986
25	C	0	0.873299	-2.230687	1.069720
26	N	0	1.072244	-0.903792	0.909992
27	O	0	1.516356	-3.094891	0.476798
28	C	0	2.065517	-0.368419	-0.003368
29	C	0	2.983527	0.579714	0.774282
30	O	0	2.575602	1.180196	1.749089
31	C	0	1.414547	0.427007	-1.171504
32	C	0	0.519808	-0.413700	-2.054941
33	C	0	-1.137928	-1.965300	-3.715962
34	C	0	-0.872334	-0.326534	-1.960091
35	C	0	1.069350	-1.294812	-2.994751
36	C	0	0.250998	-2.063066	-3.819108
37	C	0	-1.697109	-1.094948	-2.782197
38	N	0	4.296258	0.820394	0.362704
39	C	0	5.109104	0.276405	-0.618169
40	C	0	6.699498	-0.838482	-2.577958
41	C	0	6.494882	0.625294	-0.663657
42	N	0	4.567570	-0.561466	-1.507889
43	C	0	5.341228	-1.102649	-2.447446
44	C	0	7.269015	0.042352	-1.669088
45	C	0	7.113488	1.570839	0.309317
46	O	0	6.493868	2.142343	1.190947
47	O	0	8.425764	1.719754	0.099565
48	C	0	9.272906	2.614279	0.937111
49	C	0	10.653492	2.435126	0.306791
50	C	0	9.266751	2.125444	2.386491
51	C	0	8.793346	4.060307	0.799801

52	H	0	-6.244093	-1.906477	-0.027368
53	H	0	-5.637374	1.979410	1.685503
54	H	0	-3.313022	1.363150	2.244978
55	H	0	-3.940739	-2.530096	0.531941
56	H	0	-10.128661	1.291621	-0.029481
57	H	0	-9.997841	0.770628	1.651292
58	H	0	-10.150278	2.497937	1.270436
59	H	0	-6.817919	5.776603	-2.422084
60	H	0	-8.161981	1.736022	-1.884423
61	H	0	-7.290495	4.182024	1.533297
62	H	0	-6.689402	6.054288	0.043167
63	H	0	-7.559195	3.606458	-3.374302
64	H	0	-2.186519	-2.862200	1.274968
65	H	0	-0.026004	-1.999566	2.994346
66	H	0	-1.142023	-4.188959	3.153198
67	H	0	0.607282	-4.273269	3.097643
68	H	0	0.673410	-5.330596	1.003499
69	H	0	-0.709454	-6.070795	1.819140
70	H	0	-1.233492	-4.252411	-1.727262
71	H	0	0.319466	-4.428020	-0.999965
72	H	0	0.524964	-0.261629	1.480423
73	H	0	2.630281	-1.202425	-0.408189
74	H	0	2.220193	0.858000	-1.771382
75	H	0	0.843665	1.256869	-0.744992
76	H	0	-1.776894	-2.552556	-4.366674
77	H	0	-1.316833	0.354270	-1.241876
78	H	0	2.147948	-1.372139	-3.079031
79	H	0	0.695107	-2.731499	-4.549091
80	H	0	-2.774390	-1.007293	-2.695468
81	H	0	4.776792	1.480499	0.975842
82	H	0	7.284049	-1.301695	-3.362101
83	H	0	4.842841	-1.781300	-3.134492
84	H	0	8.320125	0.290614	-1.722440
85	H	0	11.385334	3.048481	0.837414
86	H	0	10.972349	1.391965	0.362933
87	H	0	10.643301	2.740657	-0.741850
88	H	0	10.000044	2.699189	2.959472
89	H	0	9.550703	1.071193	2.435858
90	H	0	8.289618	2.252406	2.849283
91	H	0	9.505530	4.721266	1.300931
92	H	0	8.748201	4.350129	-0.253078
93	H	0	7.812629	4.202944	1.250304
94	C	0	-8.181516	1.686569	0.865783
95	H	0	-7.805071	1.925447	1.864608

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2351.25809216 A.U. after 1 cycles
NFock= 1 Conv=0.67D-08 -V/T= 2.0042

Full mass-weighted force constant matrix:
Low frequencies --- -1.5721 -0.4060 -0.0006 0.0008 0.0024 2.6194
Low frequencies --- 5.0422 6.0461 9.4076

Zero-point correction=	0.773770 (Hartree/Particle)
Thermal correction to Energy=	0.823485
Thermal correction to Enthalpy=	0.824429
Thermal correction to Gibbs Free Energy=	0.679311
Sum of electronic and zero-point Energies=	-2350.484322
Sum of electronic and thermal Energies=	-2350.434607
Sum of electronic and thermal Enthalpies=	-2350.433663
Sum of electronic and thermal Free Energies=	-2350.578781

Amide 4 B

Stoichiometry C40H45N5O6

Framework group C1[X(C40H45N5O6)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-6.522497	-1.206867	-0.578745
2	C	0	-3.842533	-1.384603	0.302744
3	C	0	-6.217521	-1.385446	0.777495
4	C	0	-5.459386	-1.134730	-1.484493
5	C	0	-4.137819	-1.220549	-1.054866
6	C	0	-4.902138	-1.478316	1.212582
7	C	0	-7.933500	1.440510	-1.446501
8	C	0	-10.117151	0.228859	-0.990136
9	C	0	-12.891662	0.124644	-1.471547
10	C	0	-10.617574	0.071547	-2.289315
11	C	0	-11.035634	0.332784	0.059688
12	C	0	-12.409677	0.282432	-0.174520
13	C	0	-11.988740	0.019121	-2.529112
14	C	0	-2.446332	-1.490542	0.843244
15	O	0	-2.241497	-1.943395	1.973570
16	N	0	-1.448062	-1.076279	0.021827
17	C	0	-0.055479	-0.930244	0.428187
18	C	0	0.800437	-2.180970	0.119894
19	C	0	0.557522	-3.365050	1.072567
20	C	0	1.058277	-3.059425	2.483410
21	O	0	2.258890	-2.981609	2.732211
22	N	0	0.095177	-2.883336	3.421216
23	C	0	0.477480	0.325056	-0.305193
24	N	0	1.723116	0.707616	0.056806
25	O	0	-0.215840	0.911045	-1.128809
26	C	0	2.365945	1.903230	-0.457130
27	C	0	3.519996	1.652118	-1.442394
28	O	0	3.513390	2.230288	-2.512105
29	C	0	2.832599	2.857885	0.674973
30	C	0	1.690898	3.374702	1.522009
31	C	0	-0.446416	4.323827	3.081888
32	C	0	0.828233	4.361358	1.030170
33	C	0	1.465775	2.874281	2.807933
34	C	0	0.406419	3.343824	3.584235
35	C	0	-0.231135	4.832493	1.801173
36	N	0	4.640198	0.859236	-1.158823
37	C	0	5.075021	0.070306	-0.105629
38	C	0	5.918474	-1.534395	1.980468
39	C	0	6.405864	-0.451620	-0.127529
40	N	0	4.238542	-0.202729	0.903401
41	C	0	4.643979	-0.987842	1.907263
42	C	0	6.798817	-1.254367	0.946457
43	C	0	7.355210	-0.179185	-1.244179
44	O	0	7.067231	0.455595	-2.245757
45	O	0	8.559573	-0.715887	-1.021424
46	C	0	9.680435	-0.597410	-1.995063
47	C	0	10.055575	0.874361	-2.176894
48	C	0	9.297802	-1.275934	-3.311561
49	C	0	10.800904	-1.363005	-1.292281
50	H	0	-7.023413	-1.462681	1.500720
51	H	0	-5.666368	-1.018053	-2.543090
52	H	0	-3.346754	-1.183137	-1.794946

53	H	0	-4.671819	-1.629188	2.259790
54	H	0	-8.404795	2.391447	-1.186558
55	H	0	-6.875669	1.500575	-1.180004
56	H	0	-7.998703	1.323147	-2.532370
57	H	0	-13.958919	0.085150	-1.658066
58	H	0	-9.932808	-0.008823	-3.127005
59	H	0	-10.670709	0.457317	1.074631
60	H	0	-13.101246	0.367481	0.656602
61	H	0	-12.353111	-0.102781	-3.543374
62	H	0	-1.679228	-0.473969	-0.762535
63	H	0	-0.026964	-0.722529	1.502654
64	H	0	0.592871	-2.489326	-0.908883
65	H	0	1.860694	-1.921750	0.167449
66	H	0	-0.495935	-3.646934	1.081389
67	H	0	1.135661	-4.221826	0.717384
68	H	0	-0.855858	-2.679525	3.124260
69	H	0	0.393299	-2.593939	4.341196
70	H	0	2.306914	0.133783	0.659560
71	H	0	1.623404	2.412152	-1.069204
72	H	0	3.559685	2.342126	1.305733
73	H	0	3.350285	3.697042	0.199198
74	H	0	-1.270365	4.691179	3.683251
75	H	0	0.986792	4.764796	0.034865
76	H	0	2.129811	2.115154	3.208838
77	H	0	0.249694	2.944981	4.580507
78	H	0	-0.888124	5.597723	1.402910
79	H	0	5.331424	0.932748	-1.908447
80	H	0	6.197068	-2.171248	2.809335
81	H	0	3.900438	-1.215627	2.663119
82	H	0	7.801542	-1.659114	0.948179
83	H	0	10.966459	0.938570	-2.778070
84	H	0	10.257244	1.339975	-1.208865
85	H	0	9.267524	1.430423	-2.681722
86	H	0	8.504650	-0.736337	-3.826183
87	H	0	8.971936	-2.303557	-3.131648
88	H	0	10.174882	-1.309846	-3.963348
89	H	0	11.037773	-0.905059	-0.329386
90	H	0	11.701489	-1.351977	-1.910513
91	H	0	10.512241	-2.402613	-1.122172
92	C	0	-8.621692	0.276820	-0.713626
93	H	0	-8.500620	0.446016	0.362124
94	C	0	-7.958989	-1.094285	-1.035706
95	H	0	-8.551721	-1.879528	-0.555891
96	H	0	-8.016166	-1.274470	-2.113658

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2277.22458144 A.U. after 2 cycles
NFock= 2 Conv=0.12D-08 -V/T= 2.0043

Full mass-weighted force constant matrix:
Low frequencies --- -2.6647 -0.4784 -0.0012 -0.0008 0.0005 0.6836
Low frequencies --- 4.4125 8.0642 9.6585

Zero-point correction= 0.792199 (Hartree/Particle)
Thermal correction to Energy= 0.841338
Thermal correction to Enthalpy= 0.842282

Thermal correction to Gibbs Free Energy= 0.697789
Sum of electronic and zero-point Energies= -2276.432383
Sum of electronic and thermal Energies= -2276.383244
Sum of electronic and thermal Enthalpies= -2276.382300
Sum of electronic and thermal Free Energies= -2276.526792

Amide 4 C

Stoichiometry C39H44N6O6
Framework group C1[X(C39H44N6O6)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	5.441121	-1.437933	-0.467416
2	C	0	3.094247	-0.210841	-1.434150
3	C	0	4.250049	-2.161512	-0.584344
4	C	0	5.445580	-0.093975	-0.847153
5	C	0	4.287183	0.510918	-1.322565
6	C	0	3.088032	-1.561225	-1.057993
7	N	0	7.945306	-1.487429	-0.262040
8	C	0	8.512237	-1.925256	-1.526221
9	C	0	8.769620	-0.926381	0.716015
10	C	0	10.426264	0.266748	2.682066
11	C	0	8.222595	-0.349395	1.881928
12	C	0	10.169185	-0.879158	0.560196
13	C	0	10.975816	-0.286967	1.529206
14	C	0	9.041458	0.227260	2.845227
15	C	0	1.893894	0.522726	-1.964100
16	O	0	1.943392	1.710378	-2.261572
17	N	0	0.728817	-0.195971	-2.079181
18	C	0	-0.416879	0.366400	-2.784894
19	C	0	-1.201575	-0.723405	-3.555152
20	C	0	-2.111788	-1.641383	-2.724547
21	C	0	-1.400655	-2.568085	-1.743431
22	O	0	-0.221525	-2.900048	-1.882786
23	N	0	-2.164883	-3.036001	-0.732740
24	C	0	-1.391515	1.152465	-1.891942
25	N	0	-1.269385	0.966589	-0.558823
26	O	0	-2.269226	1.841073	-2.413371
27	C	0	-2.076138	1.591380	0.497133
28	C	0	-3.526650	1.067216	0.584306
29	O	0	-3.985971	0.733452	1.663438
30	C	0	-2.044187	3.146230	0.479872
31	C	0	-0.706907	3.706408	0.912071
32	C	0	1.785393	4.693054	1.756028
33	C	0	-0.478408	4.020243	2.257925
34	C	0	0.332754	3.896639	-0.004510
35	C	0	1.570487	4.382579	0.414835
36	C	0	0.755410	4.511840	2.678510
37	N	0	-4.237246	1.057234	-0.589253
38	C	0	-5.613950	0.811904	-0.714111
39	C	0	-8.332823	0.642609	-1.016623
40	C	0	-6.308097	-0.177602	0.012289
41	N	0	-6.220212	1.615072	-1.591550
42	C	0	-7.538569	1.515497	-1.753859
43	C	0	-7.697374	-0.213623	-0.126672
44	C	0	-5.628243	-1.258962	0.792322
45	O	0	-4.650485	-1.859691	0.388415
46	O	0	-6.293890	-1.532613	1.912399
47	C	0	-5.875713	-2.594751	2.866521
48	C	0	-4.469284	-2.301227	3.390308
49	C	0	-5.984702	-3.963288	2.191678
50	C	0	-6.910429	-2.452091	3.982313
51	H	0	4.228340	-3.211045	-0.306367

52	H	0	6.365913	0.473637	-0.773775
53	H	0	4.285140	1.552734	-1.617738
54	H	0	2.192203	-2.167335	-1.132351
55	H	0	7.699584	-2.107465	-2.231191
56	H	0	9.103709	-2.849868	-1.434937
57	H	0	9.149050	-1.147707	-1.952522
58	H	0	11.059099	0.722938	3.433733
59	H	0	7.149145	-0.322765	2.022785
60	H	0	10.636630	-1.316126	-0.311789
61	H	0	12.050036	-0.271163	1.378585
62	H	0	8.586478	0.665030	3.727322
63	H	0	0.748715	-1.209268	-2.015163
64	H	0	-0.044476	1.099303	-3.504437
65	H	0	-0.481961	-1.322447	-4.118180
66	H	0	-1.832615	-0.206777	-4.280535
67	H	0	-2.875496	-1.064095	-2.196563
68	H	0	-2.659143	-2.294828	-3.414269
69	H	0	-3.075213	-2.648822	-0.508199
70	H	0	-1.727197	-3.653928	-0.065914
71	H	0	-0.471299	0.418151	-0.269580
72	H	0	-1.634356	1.260381	1.436617
73	H	0	-2.310804	3.498508	-0.517516
74	H	0	-2.821149	3.490136	1.168477
75	H	0	2.746734	5.075550	2.080628
76	H	0	-1.277166	3.885601	2.981316
77	H	0	0.186314	3.660017	-1.051936
78	H	0	2.363904	4.513010	-0.311918
79	H	0	0.910817	4.756287	3.723703
80	H	0	-3.811845	1.542751	-1.384637
81	H	0	-9.406962	0.621428	-1.150722
82	H	0	-7.975926	2.174627	-2.498038
83	H	0	-8.263226	-0.936517	0.447283
84	H	0	-3.715264	-2.439004	2.617533
85	H	0	-4.250684	-2.979750	4.219502
86	H	0	-4.404254	-1.274196	3.753594
87	H	0	-6.990983	-4.117081	1.793450
88	H	0	-5.792231	-4.745300	2.931141
89	H	0	-5.264749	-4.069162	1.381398
90	H	0	-7.920517	-2.609030	3.597062
91	H	0	-6.719599	-3.192264	4.762974
92	H	0	-6.859699	-1.456289	4.426989
93	C	0	6.681721	-2.114693	0.097856
94	H	0	6.692365	-3.162311	-0.233341
95	H	0	6.602547	-2.154586	1.186909

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2293.25218619 A.U. after 1 cycles
NFock= 1 Conv=0.63D-08 -V/T= 2.0042

Full mass-weighted force constant matrix:
Low frequencies --- -0.8344 -0.0020 -0.0011 0.0007 1.0186 2.7248
Low frequencies --- 4.9502 7.7606 13.4875

Zero-point correction= 0.780695 (Hartree/Particle)
Thermal correction to Energy= 0.829491
Thermal correction to Enthalpy= 0.830435

Thermal correction to Gibbs Free Energy= 0.688727
Sum of electronic and zero-point Energies= -2292.471491
Sum of electronic and thermal Energies= -2292.422695
Sum of electronic and thermal Enthalpies= -2292.421751
Sum of electronic and thermal Free Energies= -2292.563459

Amide 5 A

Stoichiometry C39H44N6O6
Framework group C1[X(C39H44N6O6)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	7.602460	-1.384721	-1.917943
2	C	0	6.474954	-0.703494	-1.192028
3	C	0	4.231580	0.393813	0.099495
4	C	0	6.547275	-0.317010	0.150914
5	C	0	5.266026	-0.548143	-1.877695
6	C	0	4.160215	0.006992	-1.244179
7	C	0	5.436832	0.223659	0.787355
8	O	0	7.367285	-2.301811	-2.694392
9	N	0	8.903966	-0.999975	-1.647491
10	C	0	9.961759	-1.803743	-2.276120
11	C	0	9.270916	0.302960	-1.178451
12	C	0	10.048561	2.835825	-0.275535
13	C	0	8.781454	1.453973	-1.801115
14	C	0	10.165364	0.427928	-0.110401
15	C	0	10.554289	1.687974	0.334626
16	C	0	9.160605	2.713640	-1.341876
17	C	0	3.080892	1.005764	0.857624
18	O	0	3.268982	1.636758	1.895022
19	N	0	1.843425	0.818308	0.333088
20	C	0	0.637549	1.320064	0.976998
21	C	0	0.378618	2.789737	0.559608
22	C	0	-0.779249	3.535914	1.244032
23	N	0	-1.290618	2.470495	3.445679
24	C	0	-0.505820	0.384505	0.552131
25	N	0	-1.491013	0.255658	1.468140
26	O	0	-0.485942	-0.175472	-0.541270
27	C	0	-2.689718	-0.520954	1.221105
28	C	0	-3.908977	0.407237	1.257087
29	O	0	-3.923137	1.394227	1.976263
30	C	0	-2.891297	-1.629366	2.294305
31	C	0	-1.758322	-2.628905	2.344084
32	C	0	0.357709	-4.478076	2.417802
33	C	0	-0.785037	-2.563336	3.345421
34	C	0	-1.655025	-3.637895	1.379659
35	C	0	-0.607824	-4.554799	1.414299
36	C	0	0.265752	-3.479303	3.384246
37	N	0	-5.049588	0.143575	0.506322
38	C	0	-5.372907	-0.825736	-0.433338
39	C	0	-5.972136	-2.765281	-2.297956
40	C	0	-6.569094	-0.693570	-1.202603
41	N	0	-4.553211	-1.869048	-0.581715
42	C	0	-4.841259	-2.799554	-1.490134
43	C	0	-6.840805	-1.695159	-2.137780
44	C	0	-7.507513	0.452528	-1.032071
45	O	0	-7.362201	1.333523	-0.200484
46	O	0	-8.527807	0.397953	-1.894041
47	C	0	-9.606676	1.424830	-1.924410
48	C	0	-10.503823	0.917572	-3.052722
49	C	0	-9.011465	2.790362	-2.271838
50	C	0	-10.355972	1.429339	-0.590872

51	H	0	7.467581	-0.446954	0.705712
52	H	0	5.202975	-0.872210	-2.909259
53	H	0	3.249007	0.145803	-1.814687
54	H	0	5.483809	0.527976	1.825437
55	H	0	9.696364	-2.857548	-2.218843
56	H	0	10.086460	-1.537603	-3.331290
57	H	0	10.900076	-1.626723	-1.752750
58	H	0	10.345651	3.816571	0.077343
59	H	0	8.102240	1.360630	-2.640008
60	H	0	10.541971	-0.464271	0.377264
61	H	0	11.243749	1.773160	1.167008
62	H	0	8.766612	3.599804	-1.826316
63	H	0	1.682475	0.200879	-0.451364
64	H	0	0.780935	1.271673	2.057143
65	H	0	1.310151	3.327856	0.759790
66	H	0	0.227987	2.807475	-0.525177
67	H	0	-1.744757	3.095648	0.973870
68	H	0	-0.787973	4.550057	0.830287
69	H	0	-2.304188	2.492662	3.350381
70	H	0	-1.078949	2.481532	4.438518
71	H	0	-1.427459	0.842822	2.305703
72	H	0	-2.589696	-0.983816	0.243922
73	H	0	-3.006422	-1.147355	3.269988
74	H	0	-3.829934	-2.143224	2.071323
75	H	0	1.174799	-5.190207	2.444422
76	H	0	-0.849165	-1.788552	4.102578
77	H	0	-2.400839	-3.698322	0.594294
78	H	0	-0.543016	-5.328906	0.657479
79	H	0	1.012095	-3.410185	4.167957
80	H	0	-5.762768	0.866604	0.612735
81	H	0	-6.164294	-3.548677	-3.019440
82	H	0	-4.129651	-3.616755	-1.569225
83	H	0	-7.739612	-1.617087	-2.733867
84	H	0	-9.951798	0.868540	-3.993884
85	H	0	-11.351337	1.594078	-3.184702
86	H	0	-10.890054	-0.077929	-2.822774
87	H	0	-8.429234	2.730250	-3.194776
88	H	0	-8.373871	3.165683	-1.473237
89	H	0	-9.824481	3.503506	-2.431946
90	H	0	-9.729373	1.794827	0.220860
91	H	0	-11.230288	2.080203	-0.675401
92	H	0	-10.707144	0.423763	-0.345802
93	C	0	-0.693779	3.645747	2.776037
94	H	0	0.354573	3.712599	3.083133
95	H	0	-1.178020	4.579305	3.094089

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2293.24453695 A.U. after 1 cycles
NFock= 1 Conv=0.37D-08 -V/T= 2.0042

Full mass-weighted force constant matrix:
Low frequencies --- -3.2772 -0.4018 -0.0014 0.0008 0.0011 0.4510
Low frequencies --- 2.8332 5.2852 11.2137

Zero-point correction=	0.780404 (Hartree/Particle)
Thermal correction to Energy=	0.829810
Thermal correction to Enthalpy=	0.830754
Thermal correction to Gibbs Free Energy=	0.685173
Sum of electronic and zero-point Energies=	-2292.464133
Sum of electronic and thermal Energies=	-2292.414727
Sum of electronic and thermal Enthalpies=	-2292.413783
Sum of electronic and thermal Free Energies=	-2292.559364

Amide 5 B

Stoichiometry C40H43N5O7

Framework group C1[X(C40H43N5O7)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-7.412465	-1.210956	0.822659
2	C	0	-6.082047	-0.666218	0.379253
3	C	0	-3.508179	0.272055	-0.247541
4	C	0	-5.384432	0.149467	1.275904
5	C	0	-5.470499	-1.027375	-0.826013
6	C	0	-4.192615	-0.573127	-1.127455
7	C	0	-4.118727	0.629862	0.961289
8	O	0	-7.581636	-1.540648	1.989609
9	N	0	-8.410098	-1.387646	-0.118928
10	C	0	-9.633160	-2.056515	0.346731
11	C	0	-8.504270	-0.632507	-1.332920
12	C	0	-8.748268	0.821641	-3.711866
13	C	0	-8.406849	0.761171	-1.319738
14	C	0	-8.740483	-1.293111	-2.542857
15	C	0	-8.865686	-0.568243	-3.724369
16	C	0	-8.516680	1.481814	-2.507253
17	C	0	-2.133277	0.722374	-0.659601
18	O	0	-1.553902	0.186790	-1.610626
19	N	0	-1.570137	1.728629	0.050719
20	C	0	-0.314974	2.367936	-0.350511
21	C	0	-0.286478	3.854398	0.047871
22	C	0	-0.142504	4.234903	1.533850
23	C	0	-1.357380	4.134530	2.426533
24	O	0	-2.353831	3.492694	2.135228
25	C	0	0.948960	1.597234	0.124035
26	N	0	1.019123	0.323561	-0.321968
27	O	0	1.815712	2.122659	0.817064
28	C	0	2.171731	-0.514703	-0.055982
29	C	0	3.237008	-0.287260	-1.142578
30	O	0	2.924463	0.043998	-2.268425
31	C	0	1.771714	-2.010984	-0.049157
32	C	0	0.786936	-2.369133	1.043007
33	C	0	-1.033302	-3.027466	3.082184
34	C	0	1.209008	-2.473078	2.373848
35	C	0	-0.560238	-2.602078	0.751272
36	C	0	-1.465149	-2.927645	1.761630
37	C	0	0.309011	-2.799164	3.385445
38	N	0	4.597324	-0.483057	-0.879171
39	C	0	5.318972	-0.782440	0.262051
40	C	0	6.723468	-1.381194	2.562048
41	C	0	6.746860	-0.698026	0.242258
42	N	0	4.655725	-1.159637	1.360495
43	C	0	5.337647	-1.439862	2.469093
44	C	0	7.423827	-1.007793	1.423766
45	C	0	7.506610	-0.301915	-0.976814
46	O	0	6.990570	-0.068993	-2.057029
47	O	0	8.824356	-0.236219	-0.748696
48	C	0	9.800202	0.131789	-1.810030
49	C	0	11.131961	0.063419	-1.063158
50	C	0	9.522446	1.554252	-2.299893
51	C	0	9.754698	-0.899816	-2.938842
52	H	0	-5.840729	0.392828	2.227531

53	H	0	-5.983634	-1.675994	-1.524419
54	H	0	-3.702269	-0.863977	-2.047834
55	H	0	-3.614785	1.265542	1.678857
56	H	0	-10.273129	-1.365544	0.905926
57	H	0	-10.183447	-2.430095	-0.515459
58	H	0	-9.365069	-2.881600	1.003593
59	H	0	-8.838393	1.384317	-4.633790
60	H	0	-8.242104	1.277135	-0.381386
61	H	0	-8.811454	-2.375005	-2.555120
62	H	0	-9.043364	-1.090797	-4.657529
63	H	0	-8.430681	2.562286	-2.486475
64	H	0	-2.095000	2.211432	0.775031
65	H	0	-0.283260	2.326295	-1.445307
66	H	0	-1.180324	4.326689	-0.372058
67	H	0	0.570588	4.292398	-0.468498
68	H	0	0.224418	5.266086	1.601858
69	H	0	0.649818	3.628701	1.988945
70	H	0	0.323704	0.028690	-1.004040
71	H	0	2.578315	-0.242200	0.913487
72	H	0	2.685292	-2.597789	0.072784
73	H	0	1.353244	-2.263209	-1.028465
74	H	0	-1.735750	-3.281409	3.868169
75	H	0	2.252388	-2.296593	2.612326
76	H	0	-0.907583	-2.521170	-0.273387
77	H	0	-2.507040	-3.099783	1.515771
78	H	0	0.654661	-2.878431	4.410673
79	H	0	5.178553	-0.265188	-1.689149
80	H	0	7.230512	-1.623572	3.486919
81	H	0	4.739943	-1.733554	3.328064
82	H	0	8.503546	-0.949020	1.432173
83	H	0	11.143359	0.766757	-0.227550
84	H	0	11.950449	0.318488	-1.740285
85	H	0	11.306710	-0.942339	-0.674450
86	H	0	10.327732	1.864376	-2.971239
87	H	0	8.578600	1.616212	-2.838761
88	H	0	9.498328	2.250530	-1.457779
89	H	0	10.570937	-0.700026	-3.638259
90	H	0	9.891297	-1.908524	-2.540705
91	H	0	8.813209	-0.857369	-3.483669
92	C	0	-1.283764	4.882557	3.740163
93	H	0	-2.068825	4.538964	4.412458
94	H	0	-0.302803	4.765209	4.207736
95	H	0	-1.423167	5.952273	3.548398

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2351.23827423 A.U. after 2 cycles
NFock= 2 Conv=0.33D-08 -V/T= 2.0042

Full mass-weighted force constant matrix:
Low frequencies --- -1.1997 -0.0009 0.0013 0.0016 0.4116 2.4999
Low frequencies --- 3.9962 6.4787 7.5828

Zero-point correction= 0.770904 (Hartree/Particle)
Thermal correction to Energy= 0.821347
Thermal correction to Enthalpy= 0.822292
Thermal correction to Gibbs Free Energy= 0.674258
Sum of electronic and zero-point Energies= -2350.467370
Sum of electronic and thermal Energies= -2350.416927

Sum of electronic and thermal Enthalpies= -2350.415983
Sum of electronic and thermal Free Energies= -2350.564017

Amide 5 C

Stoichiometry C40H45N5O6
Framework group C1[X(C40H45N5O6)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	7.134471	-2.119132	-0.029975
2	C	0	5.887594	-1.283103	0.080478
3	C	0	3.442001	0.095259	0.186302
4	C	0	5.425587	-0.749693	1.288717
5	C	0	5.099099	-1.147613	-1.066576
6	C	0	3.896816	-0.452173	-1.019292
7	C	0	4.208083	-0.082160	1.342416
8	O	0	7.141882	-3.111980	-0.746418
9	N	0	8.236423	-1.782142	0.733099
10	C	0	9.367974	-2.719680	0.692341
11	C	0	8.508164	-0.455063	1.200589
12	C	0	9.098376	2.118804	2.127040
13	C	0	8.866439	-0.251247	2.537019
14	C	0	8.463251	0.634998	0.327925
15	C	0	8.745922	1.917251	0.794502
16	C	0	9.163435	1.028948	2.995241
17	C	0	2.143104	0.839630	0.322205
18	O	0	1.560298	0.917484	1.402107
19	N	0	1.663076	1.438777	-0.800536
20	C	0	0.435773	2.239256	-0.813958
21	C	0	0.530297	3.363859	-1.846124
22	C	0	1.585934	4.424243	-1.513243
23	C	0	-0.796143	1.332848	-1.070457
24	N	0	-1.120527	0.546090	-0.012124
25	O	0	-1.394877	1.337717	-2.136711
26	C	0	-2.257855	-0.353205	-0.028344
27	C	0	-3.305700	0.147325	0.974762
28	O	0	-2.973888	0.770106	1.964816
29	C	0	-1.858223	-1.800634	0.358095
30	C	0	-0.854642	-2.435132	-0.580933
31	C	0	0.993375	-3.665682	-2.307495
32	C	0	-1.164242	-2.643605	-1.930599
33	C	0	0.396517	-2.848541	-0.114318
34	C	0	1.314686	-3.461050	-0.967769
35	C	0	-0.250000	-3.251765	-2.786727
36	N	0	-4.665101	-0.126532	0.804413
37	C	0	-5.398850	-0.741380	-0.196167
38	C	0	-6.823122	-1.976241	-2.211045
39	C	0	-6.827462	-0.700699	-0.156214
40	N	0	-4.742835	-1.372028	-1.175385
41	C	0	-5.434330	-1.961412	-2.148829
42	C	0	-7.515033	-1.336221	-1.192666
43	C	0	-7.576916	-0.018146	0.936146
44	O	0	-7.047040	0.517535	1.895387
45	O	0	-8.900368	-0.064769	0.742818
46	C	0	-9.868445	0.542630	1.696515
47	C	0	-11.211693	0.224835	1.040396
48	C	0	-9.642636	2.053734	1.772820
49	C	0	-9.752257	-0.140629	3.060316
50	H	0	6.006606	-0.869447	2.194006

51	H	0	5.430134	-1.611821	-1.987400
52	H	0	3.296948	-0.388801	-1.920261
53	H	0	3.829967	0.309105	2.278606
54	H	0	8.991512	-3.740331	0.716804
55	H	0	10.009603	-2.538191	1.553162
56	H	0	9.954847	-2.590873	-0.223332
57	H	0	9.323233	3.116069	2.486908
58	H	0	8.897910	-1.096039	3.215987
59	H	0	8.205795	0.476782	-0.712596
60	H	0	8.700790	2.757161	0.110581
61	H	0	9.435100	1.176712	4.034321
62	H	0	2.171429	1.350060	-1.666331
63	H	0	0.337670	2.662114	0.190085
64	H	0	-0.455722	3.830476	-1.918541
65	H	0	0.715833	2.929007	-2.835196
66	H	0	2.573606	3.957506	-1.416638
67	H	0	1.362362	4.861978	-0.531992
68	H	0	-0.591910	0.655204	0.846465
69	H	0	-2.666971	-0.342714	-1.033870
70	H	0	-1.455701	-1.790657	1.375545
71	H	0	-2.771190	-2.402800	0.378235
72	H	0	1.704380	-4.143131	-2.972701
73	H	0	-2.126755	-2.321070	-2.312048
74	H	0	0.656315	-2.689642	0.927239
75	H	0	2.279908	-3.774045	-0.585554
76	H	0	-0.507772	-3.403861	-3.829347
77	H	0	-5.237210	0.283771	1.543402
78	H	0	-7.338682	-2.472918	-3.022644
79	H	0	-4.841960	-2.452459	-2.916126
80	H	0	-8.596190	-1.317468	-1.184300
81	H	0	-12.025657	0.624497	1.649641
82	H	0	-11.272446	0.673276	0.046298
83	H	0	-11.350271	-0.854430	0.944917
84	H	0	-10.445883	2.505418	2.361111
85	H	0	-9.667646	2.494971	0.773219
86	H	0	-8.690975	2.294322	2.243492
87	H	0	-9.852915	-1.223887	2.955152
88	H	0	-10.560838	0.211924	3.706236
89	H	0	-8.801769	0.082882	3.541669
90	C	0	2.705374	6.610619	-2.228311
91	H	0	2.732849	7.392677	-2.992103
92	H	0	2.489901	7.091070	-1.268744
93	H	0	3.707974	6.176103	-2.161647
94	C	0	1.659281	5.542495	-2.559614
95	H	0	0.673437	6.013202	-2.654201
96	H	0	1.881008	5.105234	-3.540798

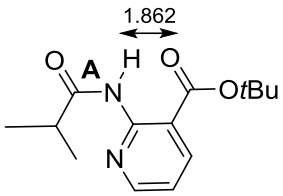
Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -2277.19574124 A.U. after 2 cycles
NFock= 2 Conv=0.37D-09 -V/T= 2.0043

Full mass-weighted force constant matrix:
Low frequencies --- -1.7036 -0.0009 0.0008 0.0019 1.2297 1.7771
Low frequencies --- 3.5469 6.8960 8.1273
Diagonal vibrational polarizability:
407.0984171 816.7210318 545.4044106

Zero-point correction=	0.789362 (Hartree/Particle)
Thermal correction to Energy=	0.839707
Thermal correction to Enthalpy=	0.840651
Thermal correction to Gibbs Free Energy=	0.692363
Sum of electronic and zero-point Energies=	-2276.406380
Sum of electronic and thermal Energies=	-2276.356035
Sum of electronic and thermal Enthalpies=	-2276.355091
Sum of electronic and thermal Free Energies=	-2276.503378

Model Fragment A



A: 27.4 kJ/mol

Stoichiometry C14H20N2O3
Framework group C1[X(C14H20N2O3)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	N	0	1.407509	-0.649817	-0.005082
2	C	0	0.949502	0.653171	-0.052673
3	C	0	0.069424	3.271535	-0.147949
4	C	0	-0.459177	0.912471	-0.050899
5	N	0	1.840756	1.650642	-0.093726
6	C	0	1.411966	2.909562	-0.142917
7	C	0	-0.866078	2.247698	-0.099209
8	C	0	-1.473248	-0.177596	0.002628
9	O	0	-2.725434	0.298250	-0.022140
10	C	0	-3.917092	-0.590454	0.025575
11	C	0	-3.931444	-1.371415	1.341114
12	C	0	-5.070495	0.411253	-0.025260
13	C	0	-3.934360	-1.503744	-1.201751
14	O	0	-1.198859	-1.364316	0.063403
15	C	0	2.678334	-1.250759	-0.066847
16	C	0	3.948344	-0.414458	-0.141408
17	C	0	5.068398	-1.209589	-0.821650
18	C	0	4.348314	0.014949	1.285545
19	O	0	2.706155	-2.466537	-0.030366
20	H	0	0.663194	-1.345168	0.047287
21	H	0	-0.227959	4.311468	-0.185611
22	H	0	2.189146	3.668797	-0.176271
23	H	0	-1.925237	2.465593	-0.098161
24	H	0	-3.851701	-0.689230	2.191372
25	H	0	-4.879838	-1.908491	1.427438
26	H	0	-3.118414	-2.093826	1.387912
27	H	0	-6.024785	-0.119824	0.002608
28	H	0	-5.029604	1.092178	0.827872
29	H	0	-5.030498	1.000998	-0.943812
30	H	0	-3.856906	-0.913487	-2.118394
31	H	0	-4.882734	-2.047048	-1.229559
32	H	0	-3.121164	-2.227002	-1.175350
33	H	0	3.733103	0.489638	-0.709824
34	H	0	5.301466	-2.119894	-0.266785
35	H	0	5.971070	-0.594923	-0.879668
36	H	0	4.790224	-1.502490	-1.837067
37	H	0	4.534865	-0.861091	1.913202
38	H	0	5.265667	0.608554	1.248609
39	H	0	3.573017	0.624553	1.752895

Standard basis: 6-311++G(d,p) (5D, 7F)

```
SCF Done:  E(RB3LYP) =  -881.011683052     A.U. after    1 cycles
           NFock=  1  Conv=0.69D-08     -V/T= 2.0042


Full mass-weighted force constant matrix:
Low frequencies ---   -3.0165   -0.0002    0.0004    0.0008    2.2965    3.1897
Low frequencies ---   13.3732   33.5635   50.3194



Zero-point correction=                          0.325403 (Hartree/Particle)
Thermal correction to Energy=                   0.345377
Thermal correction to Enthalpy=                 0.346321
Thermal correction to Gibbs Free Energy=        0.275889
Sum of electronic and zero-point Energies=           -880.686280
Sum of electronic and thermal Energies=              -880.666307
Sum of electronic and thermal Enthalpies=            -880.665362
Sum of electronic and thermal Free Energies=         -880.735794
```

Stoichiometry C15H23NO2
Framework group C1[X(C15H23NO2)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-0.989921	1.338233	0.336195
2	C	0	0.432221	3.572044	-0.458878
3	C	0	0.378506	1.203714	-0.002335
4	N	0	-1.602693	2.532511	0.271323
5	C	0	-0.917854	3.605165	-0.122265
6	C	0	1.083766	2.350775	-0.387653
7	C	0	1.081596	-0.119743	0.023394
8	O	0	2.418715	0.043173	0.069381
9	C	0	3.356137	-1.105204	0.059199
10	C	0	4.720362	-0.416159	0.102478
11	C	0	3.142535	-1.962842	1.308825
12	C	0	3.192983	-1.905595	-1.235250
13	O	0	0.525681	-1.195804	-0.005641
14	C	0	-3.544375	-1.617861	0.009517
15	C	0	-4.101911	-2.302969	-1.246417
16	C	0	-4.686384	-1.204688	0.949110
17	H	0	0.951499	4.472687	-0.763189
18	H	0	-1.475970	4.537051	-0.163813
19	H	0	2.134171	2.267403	-0.631853
20	H	0	4.814223	0.196848	1.001555
21	H	0	5.516150	-1.164841	0.108796
22	H	0	4.857749	0.225563	-0.770881
23	H	0	3.927154	-2.722524	1.362446
24	H	0	3.206868	-1.346552	2.209224
25	H	0	2.175451	-2.462447	1.289441
26	H	0	2.228178	-2.408277	-1.276117
27	H	0	3.982476	-2.659919	-1.292814
28	H	0	3.289474	-1.249701	-2.104414
29	H	0	-2.915992	-2.347839	0.537380
30	H	0	-4.732679	-1.614195	-1.819556
31	H	0	-4.713033	-3.172361	-0.985482
32	H	0	-3.296841	-2.643595	-1.904080
33	H	0	-5.325822	-0.451233	0.475529
34	H	0	-5.315435	-2.064414	1.199175
35	H	0	-4.317702	-0.784955	1.888271
36	C	0	-1.882127	0.207898	0.790659
37	H	0	-2.592706	0.644646	1.495096
38	H	0	-1.305771	-0.562538	1.302552
39	C	0	-2.643296	-0.433943	-0.387596
40	H	0	-1.910834	-0.784479	-1.120815
41	H	0	-3.250345	0.336214	-0.879543

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -790.901155082 A.U. after 1 cycles
NFock= 1 Conv=0.15D-08 -V/T= 2.0045

```
Full mass-weighted force constant matrix:
Low frequencies ---   -5.0703   -3.1626   -1.1254    0.0004    0.0005    0.0005
Low frequencies ---   17.9779   28.3952   35.1810
```

Zero-point correction=	0.354769 (Hartree/Particle)
Thermal correction to Energy=	0.374476
Thermal correction to Enthalpy=	0.375420
Thermal correction to Gibbs Free Energy=	0.305267
Sum of electronic and zero-point Energies=	-790.546386
Sum of electronic and thermal Energies=	-790.526679
Sum of electronic and thermal Enthalpies=	-790.525735
Sum of electronic and thermal Free Energies=	-790.595889

Stoichiometry C14H22N2O2
Framework group C1[X(C14H22N2O2)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	N	0	1.606962	-0.416747	-0.642196
2	C	0	1.100936	0.790524	-0.298755
3	C	0	0.180552	3.313374	0.376724
4	C	0	-0.303316	0.982691	-0.056900
5	N	0	1.975681	1.815075	-0.198702
6	C	0	1.520093	3.020163	0.121978
7	C	0	-0.728422	2.269219	0.282110
8	C	0	-1.262279	-0.135593	-0.162300
9	O	0	-2.526269	0.244382	0.100133
10	C	0	-3.666017	-0.700207	0.059408
11	C	0	-4.848712	0.198359	0.423120
12	C	0	-3.830164	-1.264759	-1.353942
13	C	0	-3.477066	-1.797179	1.110283
14	O	0	-0.950923	-1.282559	-0.454242
15	C	0	3.861666	-0.955675	0.355223
16	C	0	5.340495	-1.074334	-0.033228
17	C	0	3.375867	-2.206725	1.096179
18	H	0	0.932841	-1.169442	-0.703631
19	H	0	-0.129717	4.316503	0.638642
20	H	0	2.271940	3.803894	0.183088
21	H	0	-1.781392	2.433287	0.468578
22	H	0	-4.955541	1.007881	-0.302433
23	H	0	-5.772511	-0.385091	0.429163
24	H	0	-4.709894	0.636595	1.414005
25	H	0	-4.756111	-1.844249	-1.404632
26	H	0	-3.899340	-0.452862	-2.082493
27	H	0	-2.998216	-1.912825	-1.624057
28	H	0	-2.642558	-2.450043	0.860364
29	H	0	-4.387543	-2.399963	1.168972
30	H	0	-3.300425	-1.355295	2.094316
31	H	0	3.748419	-0.090533	1.017802
32	H	0	5.501862	-1.911670	-0.721976
33	H	0	5.965068	-1.248042	0.847503
34	H	0	5.698989	-0.164023	-0.522813
35	H	0	3.482668	-3.100126	0.469567
36	H	0	3.956740	-2.371794	2.008269
37	H	0	2.324693	-2.120742	1.383355
38	C	0	3.017497	-0.668438	-0.902755
39	H	0	3.432435	0.195185	-1.425286
40	H	0	3.069853	-1.528054	-1.580015

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -806.963378712 A.U. after 1 cycles
NFock= 1 Conv=0.39D-08 -V/T= 2.0044

Full mass-weighted force constant matrix:
Low frequencies --- 0.0004 0.0006 0.0007 1.5600 2.3300 5.1020
Low frequencies --- 26.5338 32.7997 48.4724

Zero-point correction=	0.343917 (Hartree/Particle)
Thermal correction to Energy=	0.363341
Thermal correction to Enthalpy=	0.364285
Thermal correction to Gibbs Free Energy=	0.295474
Sum of electronic and zero-point Energies=	-806.619462
Sum of electronic and thermal Energies=	-806.600038
Sum of electronic and thermal Enthalpies=	-806.599094
Sum of electronic and thermal Free Energies=	-806.667905

Stoichiometry C15H21NO3
Framework group C1[X(C15H21NO3)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-1.011142	1.531428	0.462634
2	C	0	0.384959	3.691864	-0.518068
3	C	0	0.370507	1.394204	0.207508
4	N	0	-1.655602	2.685331	0.240614
5	C	0	-0.974182	3.732869	-0.227277
6	C	0	1.059762	2.498878	-0.300676
7	C	0	1.105483	0.118815	0.492680
8	O	0	2.245723	0.052660	-0.213332
9	C	0	3.169212	-1.104852	-0.121804
10	C	0	2.453671	-2.376966	-0.581339
11	C	0	4.275362	-0.719778	-1.104367
12	C	0	3.721058	-1.221676	1.300904
13	O	0	0.730409	-0.725843	1.277286
14	C	0	-2.156027	-0.681085	-0.097793
15	C	0	-3.304082	-1.638241	0.231505
16	C	0	-3.003548	-3.060574	-0.251740
17	C	0	-4.597899	-1.084377	-0.401896
18	O	0	-1.516797	-0.776651	-1.121232
19	H	0	0.895627	4.565912	-0.903726
20	H	0	-1.546707	4.644161	-0.377005
21	H	0	2.116016	2.410428	-0.516716
22	H	0	1.672902	-2.670690	0.117984
23	H	0	2.005336	-2.227352	-1.566242
24	H	0	3.181027	-3.190065	-0.656288
25	H	0	5.033886	-1.505528	-1.137719
26	H	0	3.868398	-0.587498	-2.109113
27	H	0	4.757420	0.211984	-0.799271
28	H	0	4.499144	-1.989688	1.322367
29	H	0	2.941816	-1.496174	2.009994
30	H	0	4.171443	-0.276503	1.615383
31	H	0	-3.433302	-1.642533	1.320125
32	H	0	-2.837335	-3.071868	-1.330710
33	H	0	-3.841678	-3.724055	-0.021402
34	H	0	-2.108468	-3.463030	0.229262
35	H	0	-4.509865	-1.065752	-1.491309
36	H	0	-4.820144	-0.069375	-0.061778
37	H	0	-5.446720	-1.720602	-0.137762
38	C	0	-1.890881	0.408542	0.943977
39	H	0	-2.846138	0.836964	1.256754
40	H	0	-1.451647	-0.101696	1.805621

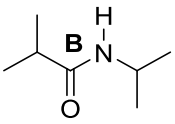
Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -864.939006781 A.U. after 1 cycles
NFock= 1 Conv=0.48D-08 -V/T= 2.0043

Full mass-weighted force constant matrix:
Low frequencies --- -4.4024 -3.2738 -1.2288 0.0005 0.0006 0.0008
Low frequencies --- 15.3575 17.9514 37.4215

Zero-point correction=	0.335510 (Hartree/Particle)
Thermal correction to Energy=	0.355965
Thermal correction to Enthalpy=	0.356910
Thermal correction to Gibbs Free Energy=	0.284411
Sum of electronic and zero-point Energies=	-864.603497
Sum of electronic and thermal Energies=	-864.583041
Sum of electronic and thermal Enthalpies=	-864.582097
Sum of electronic and thermal Free Energies=	-864.654595

Model Fragment B



B: 84.1 kJ/mol

Stoichiometry C7H15NO
Framework group C1[X(C7H15NO)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-2.568140	-1.144584	0.650670
2	C	0	-1.822229	0.189408	0.489904
3	C	0	-2.684338	1.230053	-0.241590
4	C	0	-0.523174	-0.040001	-0.290069
5	N	0	0.628513	0.269180	0.374323
6	C	0	1.964151	0.086137	-0.202416
7	C	0	2.898140	1.183738	0.310821
8	C	0	2.506778	-1.320713	0.079713
9	O	0	-0.527376	-0.464142	-1.437830
10	H	0	-1.970859	-1.875448	1.203208
11	H	0	-2.797497	-1.566907	-0.330029
12	H	0	-3.505908	-0.994055	1.192591
13	H	0	-1.577203	0.576458	1.486769
14	H	0	-2.914782	0.883490	-1.251261
15	H	0	-3.623950	1.391061	0.294121
16	H	0	-2.170236	2.191860	-0.322319
17	H	0	0.561926	0.566542	1.335947
18	H	0	1.832683	0.194967	-1.281196
19	H	0	3.018965	1.123592	1.398655
20	H	0	3.890244	1.079179	-0.134793
21	H	0	2.513959	2.175908	0.062040
22	H	0	2.636531	-1.481841	1.155073
23	H	0	1.820730	-2.077729	-0.304776
24	H	0	3.477687	-1.462417	-0.403852

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -405.908895155 A.U. after 1 cycles
NFock= 1 Conv=0.33D-08 -V/T= 2.0046

Full mass-weighted force constant matrix:
Low frequencies --- -2.3103 -0.0006 0.0006 0.0009 2.5254 6.0099
Low frequencies --- 22.2098 36.0468 83.6840

Zero-point correction= 0.214348 (Hartree/Particle)
Thermal correction to Energy= 0.225983
Thermal correction to Enthalpy= 0.226928
Thermal correction to Gibbs Free Energy= 0.176141
Sum of electronic and zero-point Energies= -405.694547
Sum of electronic and thermal Energies= -405.682912
Sum of electronic and thermal Enthalpies= -405.681967
Sum of electronic and thermal Free Energies= -405.732754

Stoichiometry C8H18
Framework group C1[X(C8H18)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	2.280338	-1.110860	0.904142
2	C	0	1.976208	-0.212345	-0.303491
3	C	0	3.087545	0.829977	-0.491578
4	C	0	-1.976208	0.212345	-0.303491
5	C	0	-3.087546	-0.829976	-0.491577
6	C	0	-2.280336	1.110860	0.904142
7	H	0	1.547168	-1.913338	1.015303
8	H	0	2.280510	-0.526789	1.831634
9	H	0	3.265589	-1.576514	0.806413
10	H	0	1.958504	-0.847816	-1.199954
11	H	0	3.148931	1.496224	0.376226
12	H	0	4.064522	0.352136	-0.611339
13	H	0	2.907572	1.450475	-1.374651
14	H	0	-1.958504	0.847816	-1.199954
15	H	0	-3.148930	-1.496225	0.376226
16	H	0	-4.064523	-0.352135	-0.611336
17	H	0	-2.907575	-1.450473	-1.374651
18	H	0	-2.280509	0.526789	1.831634
19	H	0	-1.547165	1.913337	1.015303
20	H	0	-3.265586	1.576516	0.806414
21	C	0	-0.601667	-0.476239	-0.195039
22	H	0	-0.594397	-1.095038	0.710935
23	H	0	-0.496408	-1.170725	-1.038781
24	C	0	0.601666	0.476239	-0.195037
25	H	0	0.594396	1.095036	0.710937
26	H	0	0.496408	1.170725	-1.038779

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -315.801664323 A.U. after 1 cycles
NFock= 1 Conv=0.30D-08 -V/T= 2.0054

Full mass-weighted force constant matrix:
Low frequencies --- -7.0637 -0.0004 -0.0000 0.0006 0.5386 2.2222
Low frequencies --- 37.9900 77.4015 121.3289

Zero-point correction= 0.243840 (Hartree/Particle)
Thermal correction to Energy= 0.254861
Thermal correction to Enthalpy= 0.255805
Thermal correction to Gibbs Free Energy= 0.207568
Sum of electronic and zero-point Energies= -315.557824
Sum of electronic and thermal Energies= -315.546804
Sum of electronic and thermal Enthalpies= -315.545859
Sum of electronic and thermal Free Energies= -315.594097

Stoichiometry C7H17N
Framework group C1[X(C7H17N)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-3.071192	0.643628	-0.612130
2	C	0	-1.904862	-0.281292	-0.240282
3	C	0	-2.112343	-0.908480	1.144171
4	N	0	0.579339	-0.413024	-0.169800
5	C	0	1.896714	0.227025	-0.294799
6	C	0	2.223642	1.051809	0.954713
7	C	0	2.953965	-0.854931	-0.524239
8	H	0	-2.955687	1.053848	-1.619862
9	H	0	-3.139392	1.485555	0.085693
10	H	0	-4.023977	0.107991	-0.575580
11	H	0	-1.872869	-1.093470	-0.981588
12	H	0	-2.197955	-0.129053	1.909861
13	H	0	-3.030356	-1.503223	1.171638
14	H	0	-1.273295	-1.551190	1.415419
15	H	0	0.511894	-1.157102	-0.858462
16	H	0	1.912456	0.909890	-1.165403
17	H	0	2.233686	0.408164	1.839011
18	H	0	3.205365	1.523564	0.854383
19	H	0	1.493454	1.846897	1.121888
20	H	0	2.973990	-1.553237	0.317661
21	H	0	2.747221	-1.425263	-1.435926
22	H	0	3.947522	-0.411904	-0.628362
23	C	0	-0.571023	0.475980	-0.332233
24	H	0	-0.532689	1.024041	-1.291981
25	H	0	-0.544155	1.233220	0.458999

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -331.838594977 A.U. after 1 cycles
NFock= 1 Conv=0.32D-08 -V/T= 2.0051

Alpha virt. eigenvalues -- 3.79743 3.81178 3.82697 3.84974 3.85776
Alpha virt. eigenvalues -- 3.87416 4.00651 4.03838 4.22087 4.28359
Alpha virt. eigenvalues -- 4.31035 4.34057 4.80972 4.93258 23.81265
Alpha virt. eigenvalues -- 23.83903 23.89418 23.96881 23.97772 23.98430
Alpha virt. eigenvalues -- 23.98961 35.59934
Condensed to atoms (all electrons):

		1	2	3	4	5	6
1	C	5.597953	-0.004353	-0.166679	-0.009634	-0.049176	-0.001062
2	C	-0.004353	5.814246	0.129014	-0.087312	-0.143585	0.062246
3	C	-0. 17	H	-0.033336	0.014528	-0.002887	0.000185	-0.007348	0.006558

Full mass-weighted force constant matrix:
Low frequencies --- -2.7421 -0.0002 0.0005 0.0006 2.5698 7.7496
Low frequencies --- 38.4055 71.1661 126.3518
Diagonal vibrational polarizability:
8.4307964 6.8694582 3.4472416

Zero-point correction=	0.232615 (Hartree/Particle)
Thermal correction to Energy=	0.243512
Thermal correction to Enthalpy=	0.244456
Thermal correction to Gibbs Free Energy=	0.196447
Sum of electronic and zero-point Energies=	-331.605980
Sum of electronic and thermal Energies=	-331.595083
Sum of electronic and thermal Enthalpies=	-331.594139
Sum of electronic and thermal Free Energies=	-331.642148

Stoichiometry C8H16O
Framework group C1[X(C8H16O)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	3.049727	-0.848497	0.151795
2	C	0	1.889836	-0.106791	-0.519496
3	C	0	2.173146	1.406675	-0.626497
4	C	0	0.575994	-0.300659	0.244945
5	C	0	-2.011585	-0.214767	0.169126
6	C	0	-2.199286	1.225046	0.667135
7	C	0	-3.196792	-0.656567	-0.700130
8	O	0	0.554927	-0.392043	1.454189
9	H	0	2.867092	-1.925743	0.187228
10	H	0	3.184364	-0.500967	1.177870
11	H	0	3.979326	-0.679530	-0.398603
12	H	0	1.746169	-0.495454	-1.534971
13	H	0	2.325020	1.836500	0.367164
14	H	0	3.078074	1.579531	-1.214889
15	H	0	1.353115	1.945840	-1.108875
16	H	0	-1.959866	-0.869251	1.045499
17	H	0	-1.379444	1.530728	1.320309
18	H	0	-2.250755	1.925840	-0.174411
19	H	0	-3.129690	1.321917	1.233926
20	H	0	-3.278809	-0.039364	-1.601969
21	H	0	-3.095558	-1.698983	-1.017641
22	H	0	-4.138916	-0.565380	-0.152033
23	C	0	-0.691560	-0.375311	-0.596532
24	H	0	-0.655147	-1.358096	-1.089775
25	H	0	-0.621269	0.353981	-1.414413

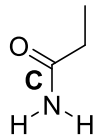
Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -389.839727583 A.U. after 1 cycles
NFock= 1 Conv=0.35D-08 -V/T= 2.0048

Full mass-weighted force constant matrix:
Low frequencies --- -4.9329 -1.5565 -0.0007 -0.0007 -0.0006 3.1098
Low frequencies --- 30.6891 48.5470 94.5766

Zero-point correction= 0.224839 (Hartree/Particle)
Thermal correction to Energy= 0.236570
Thermal correction to Enthalpy= 0.237514
Thermal correction to Gibbs Free Energy= 0.187061
Sum of electronic and zero-point Energies= -389.614889
Sum of electronic and thermal Energies= -389.603158
Sum of electronic and thermal Enthalpies= -389.602214
Sum of electronic and thermal Free Energies= -389.652666

Model Fragment C



C: 82.6 kJ/mol

Stoichiometry C3H7NO
Framework group C1[X(C3H7NO)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	1.966392	0.034042	0.192188
2	C	0	0.698705	-0.697356	-0.248738
3	C	0	-0.564208	0.136880	-0.048204
4	N	0	-1.711242	-0.582581	0.151768
5	O	0	-0.566076	1.354323	-0.084786
6	H	0	2.040676	1.001942	-0.304724
7	H	0	2.853450	-0.555425	-0.051692
8	H	0	1.962133	0.214144	1.269980
9	H	0	0.752380	-0.928375	-1.319792
10	H	0	0.600815	-1.657217	0.269357
11	H	0	-1.722038	-1.588282	0.162822
12	H	0	-2.585446	-0.084702	0.218485

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -248.613046929 A.U. after 1 cycles
NFock= 1 Conv=0.17D-08 -V/T= 2.0042

Full mass-weighted force constant matrix:
Low frequencies --- -3.6762 -0.0013 -0.0011 -0.0009 1.6358 3.4316
Low frequencies --- 38.4606 179.5365 207.9696

Stoichiometry C4H10
Framework group C1[X(C4H10)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-1.962432	-0.121045	-0.000004
2	C	0	-0.568390	0.514612	0.000001
3	H	0	-2.109650	-0.750712	-0.883198
4	H	0	-2.748776	0.639042	0.000012
5	H	0	-2.109650	-0.750715	0.883195
6	H	0	-0.463838	1.165399	-0.876739
7	H	0	-0.463848	1.165397	0.876740
8	C	0	0.568392	-0.514603	0.000002
9	H	0	0.463828	-1.165389	-0.876735
10	H	0	0.463829	-1.165390	0.876741
11	C	0	1.962428	0.121035	0.000000
12	H	0	2.748781	-0.639045	0.000005
13	H	0	2.109670	0.750699	-0.883200
14	H	0	2.109663	0.750718	0.883186

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -158.505539757 A.U. after 1 cycles
NFock= 1 Conv=0.28D-08 -V/T= 2.0055

Full mass-weighted force constant matrix:
Low frequencies --- -12.9339 -0.0005 -0.0004 -0.0004 7.4301 8.5293
Low frequencies --- 118.8223 221.1609 257.8792

Zero-point correction= 0.131280 (Hartree/Particle)
Thermal correction to Energy= 0.137084
Thermal correction to Enthalpy= 0.138028
Thermal correction to Gibbs Free Energy= 0.103234
Sum of electronic and zero-point Energies= -158.374260
Sum of electronic and thermal Energies= -158.368456
Sum of electronic and thermal Enthalpies= -158.367512
Sum of electronic and thermal Free Energies= -158.402306

Stoichiometry C4H8O
Framework group C1[X(C4H8O)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	2.023757	-0.020786	-0.043883
2	C	0	0.685651	-0.747563	0.053931
3	C	0	-0.529426	0.170040	0.017902
4	O	0	-0.424293	1.377319	0.020266
5	H	0	2.102239	0.532420	-0.982119
6	H	0	2.851667	-0.732189	0.006020
7	H	0	2.137618	0.699806	0.767857
8	H	0	0.573342	-1.487588	-0.748703
9	H	0	0.621506	-1.327823	0.984246
10	C	0	-1.885851	-0.509439	-0.030809
11	H	0	-2.030834	-0.957972	-1.019663
12	H	0	-1.951129	-1.319280	0.701316
13	H	0	-2.674853	0.220561	0.146074

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -232.543050999 A.U. after 1 cycles
NFock= 1 Conv=0.90D-09 -V/T= 2.0044

Full mass-weighted force constant matrix:
Low frequencies --- -0.4118 -0.0007 0.0005 0.0006 2.2267 3.6217
Low frequencies --- 50.9428 92.5757 199.5930

Zero-point correction= 0.111753 (Hartree/Particle)
Thermal correction to Energy= 0.118377
Thermal correction to Enthalpy= 0.119322
Thermal correction to Gibbs Free Energy= 0.081332
Sum of electronic and zero-point Energies= -232.431298
Sum of electronic and thermal Energies= -232.424674
Sum of electronic and thermal Enthalpies= -232.423729
Sum of electronic and thermal Free Energies= -232.461719

Stoichiometry C3H9N
Framework group C1[X(C3H9N)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	1.930685	0.117058	-0.000000
2	C	0	0.540389	-0.525866	0.000001
3	N	0	-1.961829	-0.027528	-0.000000
4	H	0	2.075263	0.747726	-0.882927
5	H	0	2.720762	-0.638397	-0.000002
6	H	0	2.075264	0.747725	0.882928
7	H	0	0.432065	-1.175192	-0.877807
8	H	0	0.432066	-1.175192	0.877808
9	H	0	-2.126567	-0.607422	0.816899
10	H	0	-2.126565	-0.607427	-0.816897
11	C	0	-0.597265	0.506322	-0.000000
12	H	0	-0.496169	1.157894	-0.875359
13	H	0	-0.496170	1.157896	0.875358

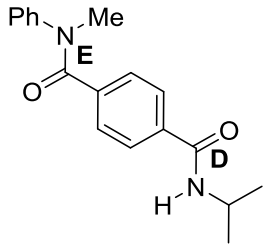
Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -174.545971426 A.U. after 1 cycles
NFock= 1 Conv=0.19D-08 -V/T= 2.0050

Full mass-weighted force constant matrix:
Low frequencies --- -12.6294 -5.7646 -5.1625 -0.0010 0.0006 0.0008
Low frequencies --- 129.6813 223.2346 265.6338

Zero-point correction= 0.120741 (Hartree/Particle)
Thermal correction to Energy= 0.126444
Thermal correction to Enthalpy= 0.127388
Thermal correction to Gibbs Free Energy= 0.092840
Sum of electronic and zero-point Energies= -174.425231
Sum of electronic and thermal Energies= -174.419528
Sum of electronic and thermal Enthalpies= -174.418583
Sum of electronic and thermal Free Energies= -174.453131

Model Fragments D and E



D: 84.3 kJ/mol
E: 58.2 kJ/mol

Stoichiometry C18H20N2O2
Framework group C1[X(C18H20N2O2)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	2.161484	-1.893613	-0.097961
2	C	0	0.845801	-1.162240	-0.098534
3	C	0	-1.718899	-0.012690	-0.133649
4	C	0	-0.164161	-1.655420	0.733423
5	C	0	0.558099	-0.093846	-0.955218
6	C	0	-0.710282	0.473562	-0.970784
7	C	0	-1.429189	-1.079121	0.726036
8	O	0	2.181333	-3.111845	0.024339
9	N	0	3.327330	-1.178712	-0.297253
10	C	0	4.559661	-1.968977	-0.430901
11	C	0	3.477412	0.210817	0.019865
12	C	0	3.831379	2.918323	0.632345
13	C	0	3.086089	0.708040	1.265406
14	C	0	4.062830	1.074152	-0.911774
15	C	0	4.241768	2.419637	-0.604019
16	C	0	3.252281	2.059065	1.563294
17	C	0	-3.063919	0.663195	-0.196128
18	N	0	-4.133246	-0.087800	0.200542
19	O	0	-3.176835	1.821250	-0.578621
20	C	0	-5.511374	0.412675	0.151681
21	C	0	-6.131418	0.216498	-1.237901
22	C	0	-6.332933	-0.255943	1.255440
23	H	0	0.054248	-2.495870	1.380760
24	H	0	1.320888	0.291521	-1.619324
25	H	0	-0.938554	1.303914	-1.627338
26	H	0	-2.179428	-1.453195	1.413846
27	H	0	4.920856	-2.305664	0.546688
28	H	0	5.326061	-1.353415	-0.899169
29	H	0	4.360984	-2.846508	-1.042943
30	H	0	3.963885	3.967916	0.867610
31	H	0	2.649985	0.037572	1.996317
32	H	0	4.363271	0.690114	-1.880250
33	H	0	4.691659	3.081556	-1.335331
34	H	0	2.936221	2.436288	2.529171
35	H	0	-4.001056	-1.079888	0.327256
36	H	0	-5.439805	1.484096	0.349358
37	H	0	-6.204982	-0.847329	-1.486827
38	H	0	-5.525856	0.711478	-1.999112
39	H	0	-7.138310	0.642421	-1.271652

```
    40          H          0       -6.391845   -1.339805    1.103474
    41          H          0       -5.895647   -0.069982    2.239248
    42          H          0       -7.354916    0.130433    1.255731
---------------------------------------------------------------------

Standard basis: 6-311++G(d,p) (5D, 7F)


SCF Done:  E(RB3LYP) =  -958.210260014     A.U. after    1 cycles
           NFock=  1  Conv=0.59D-08     -V/T= 2.0043


Full mass-weighted force constant matrix:
Low frequencies ---   -1.9476   -1.7214   -0.0003    0.0008    0.0008    1.6146
Low frequencies ---   17.9789   27.3663   41.6783




Zero-point correction=                           0.345865 (Hartree/Particle)
Thermal correction to Energy=                    0.367118
Thermal correction to Enthalpy=                  0.368062
Thermal correction to Gibbs Free Energy=         0.292976
Sum of electronic and zero-point Energies=           -957.864395
Sum of electronic and thermal Energies=              -957.843142
Sum of electronic and thermal Enthalpies=            -957.842198
Sum of electronic and thermal Free Energies=         -957.917284
```

Stoichiometry C18H22N2O
Framework group C1[X(C18H22N2O)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	2.189752	-1.822404	-0.158904
2	C	0	0.803922	-1.309312	0.113000
3	C	0	-1.871038	-0.564544	0.601138
4	C	0	0.203756	-0.281820	-0.624625
5	C	0	0.045454	-1.974736	1.080113
6	C	0	-1.270734	-1.596860	1.327826
7	C	0	-1.118219	0.078650	-0.388416
8	O	0	2.428604	-3.021478	-0.090233
9	N	0	3.172808	-0.926463	-0.547160
10	C	0	4.461041	-1.510652	-0.946429
11	C	0	3.176135	0.459543	-0.186720
12	C	0	3.251682	3.172833	0.500776
13	C	0	3.448810	1.427620	-1.158939
14	C	0	2.956593	0.858667	1.134343
15	C	0	2.983219	2.210331	1.471548
16	C	0	3.490117	2.775636	-0.814912
17	N	0	-4.082205	-0.021292	-0.346053
18	C	0	-5.503648	0.304001	-0.153667
19	C	0	-5.677424	1.770391	0.255622
20	C	0	-6.256463	0.006341	-1.451751
21	H	0	0.763650	0.230804	-1.396534
22	H	0	0.493926	-2.798978	1.621450
23	H	0	-1.843000	-2.119746	2.087591
24	H	0	-1.582367	0.859559	-0.979167
25	H	0	5.019777	-0.776476	-1.524923
26	H	0	4.282607	-2.400181	-1.547260
27	H	0	5.052954	-1.800161	-0.071388
28	H	0	3.278239	4.223315	0.766375
29	H	0	3.614793	1.120266	-2.185411
30	H	0	2.762865	0.110372	1.893473
31	H	0	2.804420	2.508342	2.498494
32	H	0	3.698393	3.517340	-1.577828
33	H	0	-4.005229	-0.888821	-0.868828
34	H	0	-5.937908	-0.325579	0.645427
35	H	0	-5.171463	1.996809	1.197156
36	H	0	-6.737200	2.004646	0.389785
37	H	0	-5.269692	2.428657	-0.516876
38	H	0	-5.859458	0.612641	-2.271116
39	H	0	-6.164066	-1.048085	-1.731488
40	H	0	-7.320701	0.228813	-1.342312
41	C	0	-3.297924	-0.145562	0.883959
42	H	0	-3.287653	0.829442	1.383415
43	H	0	-3.746126	-0.855617	1.600537

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -884.140209582 A.U. after 2 cycles
NFock= 2 Conv=0.62D-08 -V/T= 2.0045

```
Full mass-weighted force constant matrix:
Low frequencies ---   -4.5743   -2.1054   -1.6565   -0.0005    0.0003    0.0006
Low frequencies ---   13.4334   26.3183   39.7215

Zero-point correction=                          0.364165 (Hartree/Particle)
Thermal correction to Energy=                   0.384807
Thermal correction to Enthalpy=                 0.385751
Thermal correction to Gibbs Free Energy=        0.311743
Sum of electronic and zero-point Energies=           -883.776045
Sum of electronic and thermal Energies=              -883.755403
Sum of electronic and thermal Enthalpies=            -883.754459
Sum of electronic and thermal Free Energies=         -883.828467
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Stoichiometry C19H23NO
Framework group C1[X(C19H23NO)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	2.438369	-1.730221	-0.134816
2	C	0	0.972823	-1.457702	0.048141
3	C	0	-1.816612	-1.181228	0.401762
4	C	0	0.460992	-0.634856	1.056460
5	C	0	0.076628	-2.158553	-0.766326
6	C	0	-1.295234	-2.009005	-0.600100
7	C	0	-0.913651	-0.508426	1.232315
8	O	0	2.824292	-2.848954	-0.449433
9	N	0	3.347655	-0.714848	0.118251
10	C	0	4.767510	-1.092569	0.074105
11	C	0	3.045874	0.678379	-0.016114
12	C	0	2.525537	3.417464	-0.279565
13	C	0	2.401721	1.167676	-1.155688
14	C	0	3.441210	1.572613	0.984435
15	C	0	3.185696	2.934238	0.850174
16	C	0	2.133644	2.529399	-1.278962
17	C	0	-5.389623	0.343759	-0.220704
18	C	0	-5.877887	0.731876	1.182510
19	C	0	-5.848154	1.380902	-1.255852
20	H	0	1.132480	-0.105021	1.720024
21	H	0	0.471233	-2.830696	-1.518774
22	H	0	-1.973595	-2.556581	-1.247118
23	H	0	-1.291083	0.119679	2.033247
24	H	0	5.353402	-0.332103	0.588122
25	H	0	5.122734	-1.178733	-0.958477
26	H	0	4.899501	-2.056409	0.561694
27	H	0	2.322156	4.477280	-0.380586
28	H	0	2.109816	0.480670	-1.940881
29	H	0	3.937129	1.194683	1.871504
30	H	0	3.493802	3.617150	1.633945
31	H	0	1.627234	2.896019	-2.164713
32	H	0	-5.850132	-0.618542	-0.484494
33	H	0	-5.423262	1.675864	1.503964
34	H	0	-5.636011	-0.027488	1.930177
35	H	0	-6.963355	0.867186	1.193716
36	H	0	-5.412533	2.363490	-1.043262
37	H	0	-5.546539	1.095342	-2.267944
38	H	0	-6.936388	1.492905	-1.249359
39	C	0	-3.308240	-0.999068	0.564575
40	H	0	-3.534545	-0.826333	1.620573
41	H	0	-3.821350	-1.924447	0.279661
42	C	0	-3.861484	0.162126	-0.286597
43	H	0	-3.570378	-0.005883	-1.329919
44	H	0	-3.372940	1.096714	0.018084

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -868.104837741 A.U. after 1 cycles
NFock= 1 Conv=0.52D-08 -V/T= 2.0046

```
Full mass-weighted force constant matrix:
Low frequencies ---   -0.0005    0.0001    0.0003    0.5895    2.2386    3.9580
Low frequencies ---   15.7600   24.7513   34.8214

Zero-point correction=                           0.375393 (Hartree/Particle)
Thermal correction to Energy=                    0.396164
Thermal correction to Enthalpy=                  0.397108
Thermal correction to Gibbs Free Energy=         0.322994
Sum of electronic and zero-point Energies=           -867.729444
Sum of electronic and thermal Energies=              -867.708674
Sum of electronic and thermal Enthalpies=            -867.707730
Sum of electronic and thermal Free Energies=         -867.781844
```

Stoichiometry C19H21NO2
Framework group C1[X(C19H21NO2)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	2.334940	-1.863668	-0.041501
2	C	0	0.961317	-1.268933	0.125215
3	C	0	-1.684754	-0.377079	0.459759
4	C	0	-0.068665	-1.795412	-0.659932
5	C	0	0.654201	-0.308254	1.096663
6	C	0	-0.653924	0.123221	1.266336
7	C	0	-1.374245	-1.343330	-0.506664
8	O	0	2.456990	-3.063395	-0.251504
9	N	0	3.439787	-1.047911	0.107983
10	C	0	4.750120	-1.713794	0.077252
11	C	0	3.423093	0.367322	-0.117235
12	C	0	3.452870	3.130520	-0.557412
13	C	0	4.002151	1.225105	0.823416
14	C	0	2.874263	0.899957	-1.286329
15	C	0	2.879695	2.277343	-1.497586
16	C	0	4.019492	2.598867	0.601123
17	C	0	-3.080178	0.138274	0.687335
18	O	0	-3.295683	0.942150	1.575173
19	C	0	-5.557632	0.317294	-0.014585
20	C	0	-5.532319	1.737679	-0.596444
21	C	0	-6.682098	-0.514861	-0.646495
22	H	0	0.165515	-2.568775	-1.381119
23	H	0	1.434902	0.092978	1.729962
24	H	0	-0.902456	0.855049	2.024913
25	H	0	-2.149166	-1.760477	-1.137349
26	H	0	4.693452	-2.646779	0.634362
27	H	0	5.492406	-1.055725	0.526189
28	H	0	5.052069	-1.943592	-0.950079
29	H	0	3.461087	4.201084	-0.725943
30	H	0	4.425167	0.812819	1.732670
31	H	0	2.443826	0.235711	-2.026279
32	H	0	2.444164	2.680863	-2.404593
33	H	0	4.466375	3.255638	1.338857
34	H	0	-5.746804	0.397346	1.060645
35	H	0	-5.342447	1.713111	-1.675966
36	H	0	-4.760610	2.348089	-0.124216
37	H	0	-6.493452	2.236500	-0.442158
38	H	0	-6.526256	-0.639394	-1.724094
39	H	0	-6.743627	-1.512442	-0.200717
40	H	0	-7.651777	-0.028130	-0.508654
41	C	0	-4.206353	-0.390629	-0.193493
42	H	0	-3.894737	-0.346149	-1.244294
43	H	0	-4.308425	-1.460123	0.036109

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -942.142846854 A.U. after 1 cycles
NFock= 1 Conv=0.85D-08 -V/T= 2.0044

Full mass-weighted force constant matrix:
Low frequencies --- -1.2829 -0.0006 -0.0003 0.0001 1.7906 2.3425

```
Low frequencies ---   15.8940   29.0760   39.8904


Zero-point correction=                           0.356581 (Hartree/Particle)
Thermal correction to Energy=                    0.377902
Thermal correction to Enthalpy=                  0.378846
Thermal correction to Gibbs Free Energy=         0.303740
Sum of electronic and zero-point Energies=           -941.786266
Sum of electronic and thermal Energies=              -941.764945
Sum of electronic and thermal Enthalpies=            -941.764001
Sum of electronic and thermal Free Energies=         -941.839107
```

Stoichiometry C18H22N2O
Framework group C1[X(C18H22N2O)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-0.644217	-1.315120	-0.339994
2	C	0	2.120343	-0.808757	-0.120642
3	C	0	-0.176656	-0.247483	0.426076
4	C	0	0.289361	-2.137795	-0.982085
5	C	0	1.651685	-1.893593	-0.870803
6	C	0	1.190144	0.004499	0.533699
7	N	0	-2.999417	-0.957078	0.473035
8	C	0	-3.271414	-1.733100	1.671209
9	C	0	-3.846420	0.089890	0.108715
10	C	0	-5.536514	2.249549	-0.609379
11	C	0	-5.034556	0.355027	0.819355
12	C	0	-3.525063	0.944349	-0.967797
13	C	0	-4.362212	1.997057	-1.318174
14	C	0	-5.857124	1.420485	0.462182
15	C	0	3.609847	-0.609524	-0.037786
16	N	0	4.034191	0.651571	0.273355
17	O	0	4.389253	-1.533880	-0.236292
18	C	0	5.453980	1.011419	0.345960
19	C	0	6.012472	1.378783	-1.035111
20	C	0	5.641509	2.135302	1.366891
21	H	0	-0.888352	0.379745	0.949879
22	H	0	-0.054782	-2.983574	-1.570301
23	H	0	2.375872	-2.539761	-1.351496
24	H	0	1.520351	0.823189	1.163969
25	H	0	-3.459437	-1.075767	2.522782
26	H	0	-4.132305	-2.410049	1.558144
27	H	0	-2.392374	-2.333888	1.908734
28	H	0	-6.182540	3.074448	-0.884544
29	H	0	-5.330005	-0.277949	1.645054
30	H	0	-2.602274	0.804288	-1.516676
31	H	0	-4.082787	2.635216	-2.149720
32	H	0	-6.766340	1.592848	1.028295
33	H	0	3.362849	1.403818	0.244204
34	H	0	5.965089	0.112466	0.696297
35	H	0	5.513222	2.267597	-1.435186
36	H	0	5.869791	0.554040	-1.735572
37	H	0	7.083414	1.592139	-0.971472
38	H	0	5.108352	3.042299	1.059410
39	H	0	5.273655	1.837657	2.351654
40	H	0	6.699292	2.393031	1.459200
41	C	0	-2.132390	-1.593353	-0.506961
42	H	0	-2.291404	-2.678633	-0.468985
43	H	0	-2.443385	-1.289379	-1.510192

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -884.151433911 A.U. after 1 cycles
NFock= 1 Conv=0.58D-08 -V/T= 2.0045

```
Full mass-weighted force constant matrix:
Low frequencies ---   -2.6723   -0.0001    0.0007    0.0008    1.0589    1.9192
Low frequencies ---    8.1586   17.8000   34.1174
```

```
Zero-point correction=                           0.364476 (Hartree/Particle)
Thermal correction to Energy=                    0.385053
Thermal correction to Enthalpy=                  0.385997
Thermal correction to Gibbs Free Energy=         0.311277
Sum of electronic and zero-point Energies=           -883.786958
Sum of electronic and thermal Energies=              -883.766381
Sum of electronic and thermal Enthalpies=            -883.765436
Sum of electronic and thermal Free Energies=         -883.840157
```

Stoichiometry C19H23NO
Framework group C1[X(C19H23NO)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	-1.060067	-1.574984	-0.518339
2	C	0	1.697696	-1.069637	-0.161548
3	C	0	-0.405850	-0.595196	-1.270954
4	C	0	-0.303531	-2.308701	0.405070
5	C	0	1.053572	-2.067314	0.577879
6	C	0	0.952643	-0.343224	-1.096265
7	C	0	-4.874842	-1.672538	0.306322
8	C	0	-3.374442	0.373378	0.304607
9	C	0	-3.270725	3.186098	0.169384
10	C	0	-2.811639	1.124237	1.341133
11	C	0	-3.885287	1.061088	-0.804098
12	C	0	-3.834866	2.451377	-0.873365
13	C	0	-2.759034	2.516613	1.278131
14	C	0	3.168942	-0.863632	0.075381
15	N	0	3.670957	0.359227	-0.273320
16	O	0	3.870846	-1.748113	0.551515
17	C	0	5.074303	0.726020	-0.060457
18	C	0	5.505377	1.729558	-1.131863
19	C	0	5.309024	1.254233	1.360974
20	H	0	-0.962975	-0.025814	-2.006871
21	H	0	-0.783532	-3.088176	0.989184
22	H	0	1.639504	-2.649909	1.278228
23	H	0	1.429679	0.402087	-1.723478
24	H	0	-5.321346	-1.467101	-0.670910
25	H	0	-5.506281	-1.204468	1.065344
26	H	0	-4.899643	-2.755157	0.461637
27	H	0	-3.233434	4.268457	0.117672
28	H	0	-2.406721	0.612423	2.208245
29	H	0	-4.332027	0.508964	-1.624623
30	H	0	-4.239178	2.962186	-1.740635
31	H	0	-2.318192	3.076036	2.096051
32	H	0	3.020630	1.101497	-0.481964
33	H	0	5.639583	-0.200285	-0.181139
34	H	0	4.928557	2.658749	-1.058519
35	H	0	5.367425	1.317849	-2.134430
36	H	0	6.559842	1.988364	-1.009096
37	H	0	4.744029	2.176357	1.533718
38	H	0	4.999007	0.512227	2.098879
39	H	0	6.369214	1.472212	1.519367
40	C	0	-2.539625	-1.837559	-0.678596
41	H	0	-2.719756	-2.916144	-0.616263
42	H	0	-2.866889	-1.523522	-1.674720
43	C	0	-3.431374	-1.144892	0.390597
44	H	0	-3.032617	-1.426058	1.371483

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -868.122410774 A.U. after 2 cycles

```
          NFock=  2  Conv=0.68D-08     -V/T= 2.0046

Full mass-weighted force constant matrix:
Low frequencies ---   -3.4039   -2.0932   -0.0004   -0.0001    0.0003    1.2897
Low frequencies ---   14.6223   19.7786   31.0446


Zero-point correction=                           0.376009 (Hartree/Particle)
Thermal correction to Energy=                    0.396677
Thermal correction to Enthalpy=                  0.397621
Thermal correction to Gibbs Free Energy=         0.323248
Sum of electronic and zero-point Energies=           -867.746402
Sum of electronic and thermal Energies=              -867.725734
Sum of electronic and thermal Enthalpies=            -867.724790
Sum of electronic and thermal Free Energies=         -867.799163
```

Stoichiometry C19H21NO2
Framework group C1[X(C19H21NO2)]

Standard orientation:

Center Number	Atom	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	C	0	0.667306	-1.159088	-0.117152
2	C	0	-1.989944	-0.305895	-0.478672
3	C	0	0.364291	-0.124051	-1.011801
4	C	0	-0.380627	-1.767741	0.586993
5	C	0	-1.691873	-1.348559	0.408902
6	C	0	-0.949172	0.292622	-1.193513
7	C	0	4.401855	-2.090338	-0.749206
8	C	0	3.665564	0.255421	-0.133688
9	C	0	4.557432	2.722579	0.874996
10	C	0	3.894358	0.425734	1.236838
11	C	0	3.892500	1.338940	-0.988790
12	C	0	4.336358	2.563023	-0.491458
13	C	0	4.335276	1.649411	1.736509
14	C	0	-3.389219	0.194062	-0.735622
15	N	0	-4.292577	-0.006947	0.266982
16	O	0	-3.681995	0.742926	-1.790301
17	C	0	-5.681312	0.460103	0.185429
18	C	0	-6.579679	-0.477883	0.993622
19	C	0	-5.808689	1.921714	0.633849
20	H	0	1.150241	0.373396	-1.564143
21	H	0	-0.143920	-2.578203	1.265073
22	H	0	-2.484498	-1.863089	0.940761
23	H	0	-1.190113	1.083594	-1.892638
24	H	0	4.775582	-2.303557	0.252583
25	H	0	5.216451	-1.672248	-1.344823
26	H	0	4.089631	-3.036294	-1.198621
27	H	0	4.899735	3.674374	1.265109
28	H	0	3.726424	-0.402188	1.917006
29	H	0	3.727335	1.223358	-2.055789
30	H	0	4.508394	3.390099	-1.171390
31	H	0	4.504613	1.764129	2.801448
32	H	0	-3.951639	-0.304556	1.168594
33	H	0	-5.947815	0.398624	-0.871582
34	H	0	-6.311731	-0.464398	2.056312
35	H	0	-6.502217	-1.505975	0.632180
36	H	0	-7.623453	-0.164807	0.915416
37	H	0	-5.531121	2.033485	1.687178
38	H	0	-5.161842	2.563377	0.032975
39	H	0	-6.839041	2.269337	0.516661
40	C	0	3.230188	-1.095897	-0.697620
41	H	0	2.875342	-0.928219	-1.718694
42	C	0	2.062056	-1.667318	0.122072
43	O	0	2.262204	-2.520756	0.966224

Standard basis: 6-311++G(d,p) (5D, 7F)

SCF Done: E(RB3LYP) = -942.159052588 A.U. after 1 cycles
NFock= 1 Conv=0.32D-08 -V/T= 2.0044

Full mass-weighted force constant matrix:
Low frequencies --- -3.0075 -0.0005 -0.0001 0.0005 0.9323 0.9546

```
Low frequencies ---   13.0875   19.5289   34.2263

Zero-point correction=                           0.357464 (Hartree/Particle)
Thermal correction to Energy=                    0.378746
Thermal correction to Enthalpy=                  0.379690
Thermal correction to Gibbs Free Energy=         0.303920
Sum of electronic and zero-point Energies=           -941.801589
Sum of electronic and thermal Energies=              -941.780306
Sum of electronic and thermal Enthalpies=            -941.779362
Sum of electronic and thermal Free Energies=         -941.855133
```

**********Gaussian NBO Version 3.1**********
N A T U R A L A T O M I C O R B I T A L A N D
N A T U R A L B O N D O R B I T A L A N A L Y S I S
**********Gaussian NBO Version 3.1**********

Second Order Perturbation Theory Analysis of Fock Matrix in NBO Basis

Threshold for printing: 0.50 kcal/mol

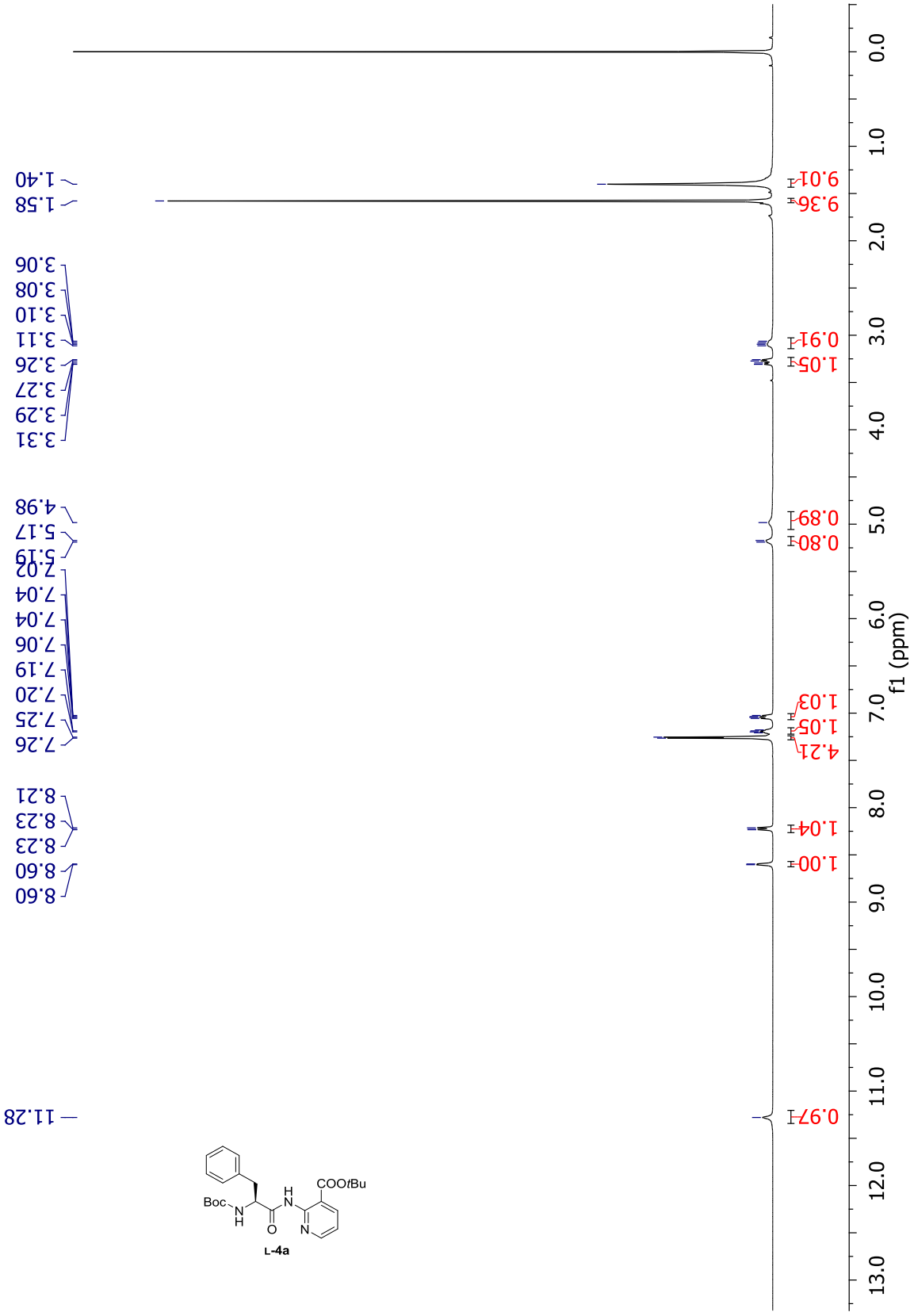
Donor NBO (i)	Acceptor NBO (j)	E(2) kcal/mol	E(j)-E(i) a.u.	F(i,j) a.u.	
170. LP (1) N 9	/***. BD*(2) C 1 - O 8	36.94	0.32	0.098	(E)
...					
173. LP (1) N 19	/***. BD*(2) C 17 - O 18	68.71	0.27	0.122	(D)
...					
176. LP (1) N 25	/***. BD*(2) C 23 - O 24	49.81	0.31	0.111	(C)
...					
177. LP (1) N 27	/***. BD*(2) C 26 - O 28	78.71	0.25	0.126	(B)
...					
182. LP (1) N 39	/***. BD*(2) C 30 - O 31	61.85	0.23	0.111	(A)

Comparison of the Resonance Energy (estimated from the isodesmic equation (REIE) and thee second-order pertubrbation energies (SOPE) involving the nitrogen lone pair and the CO π* orbital.

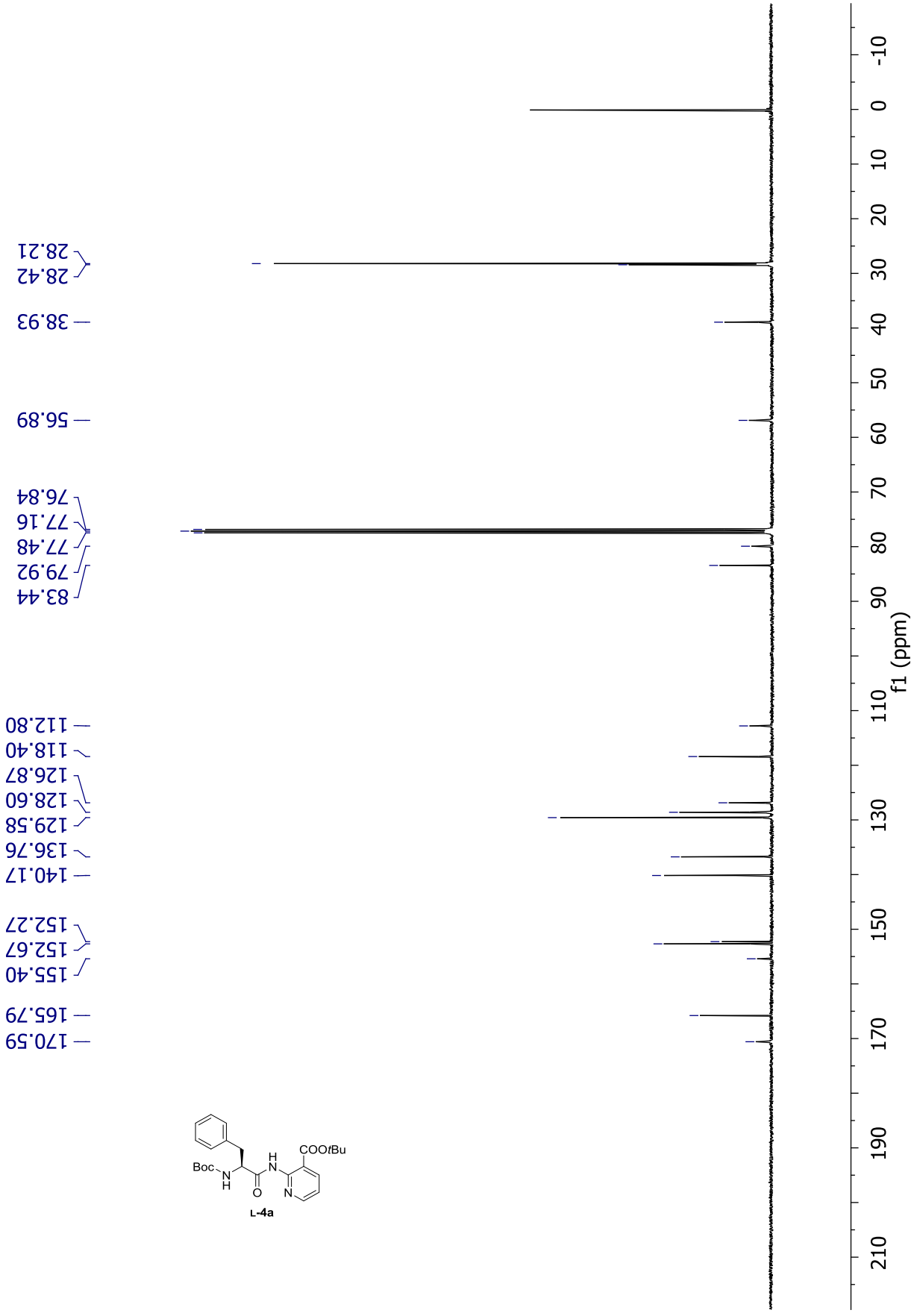
	REIE / kJ mol^{-1}	SOPE / kJ mol^{-1}
(A)	**9.8**	258.1
(B)	72.2	329.4
(C)	64.1	208.5
(D)	67.9	287.6
(E)	62.4	**154.6**

7 Copies of the NMR spectra

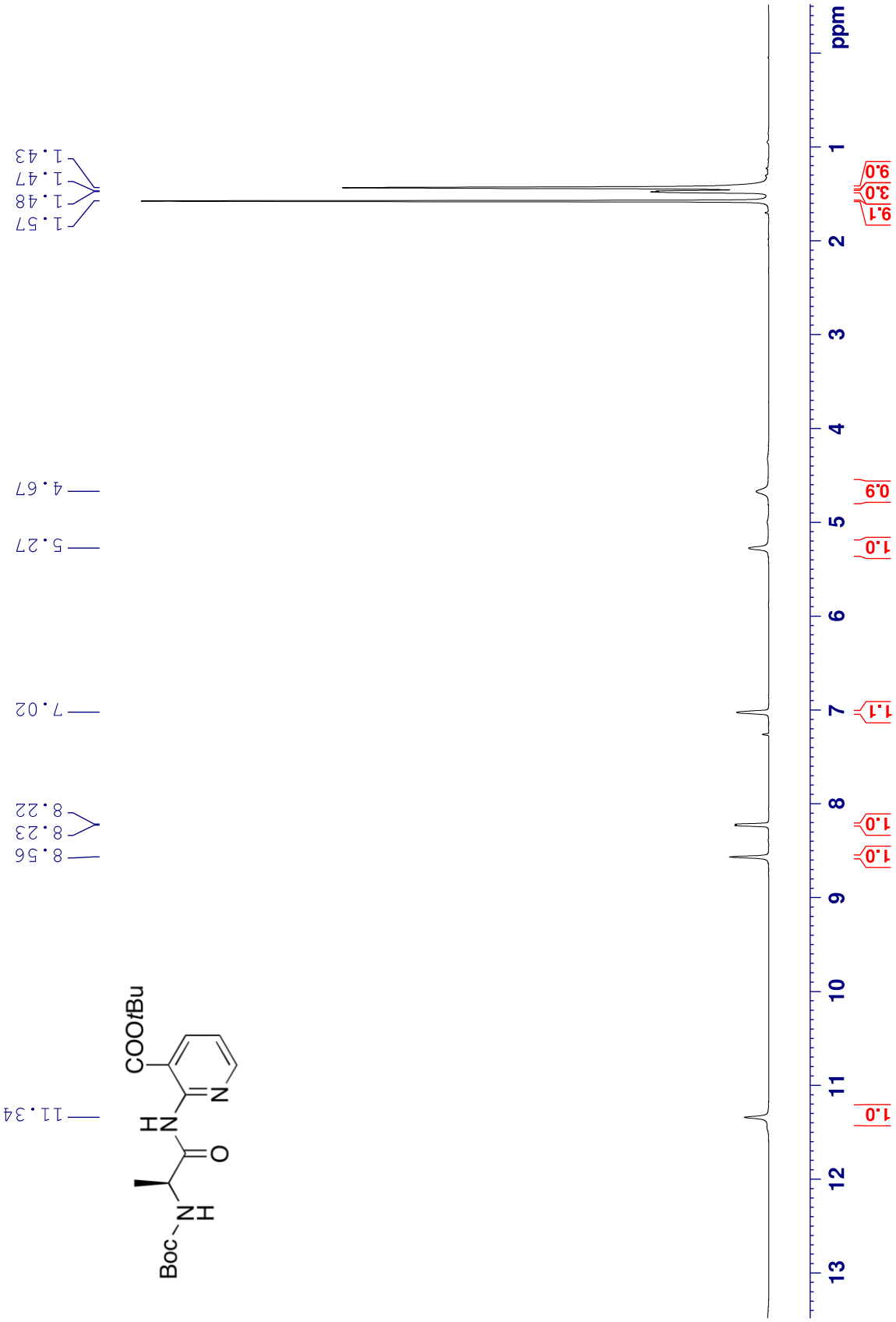
tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-L-phenylalanyl]amino}nicotinate (Boc-L-Phe-NH-*t*Bu-nic, ER489) **L-4a - ^{1}H NMR (400 MHz, $CDCl_3$)**



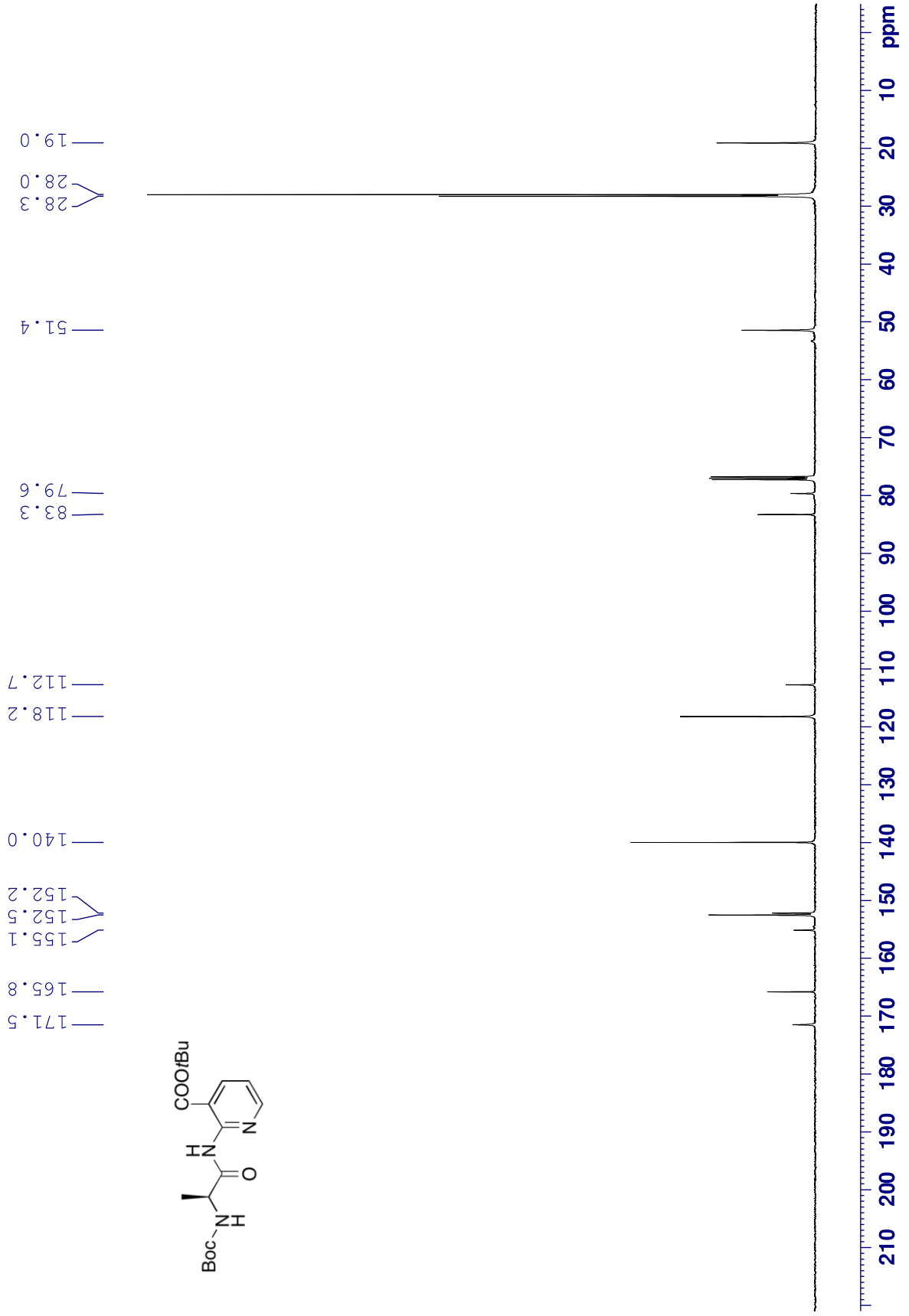
tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-L-phenylalanyl]amino}nicotinate (Boc-L-Phe-NH-*t*Bu-nic, ER489) **L-4a - ^{13}C NMR (101 MHz, $CDCl_3$)**



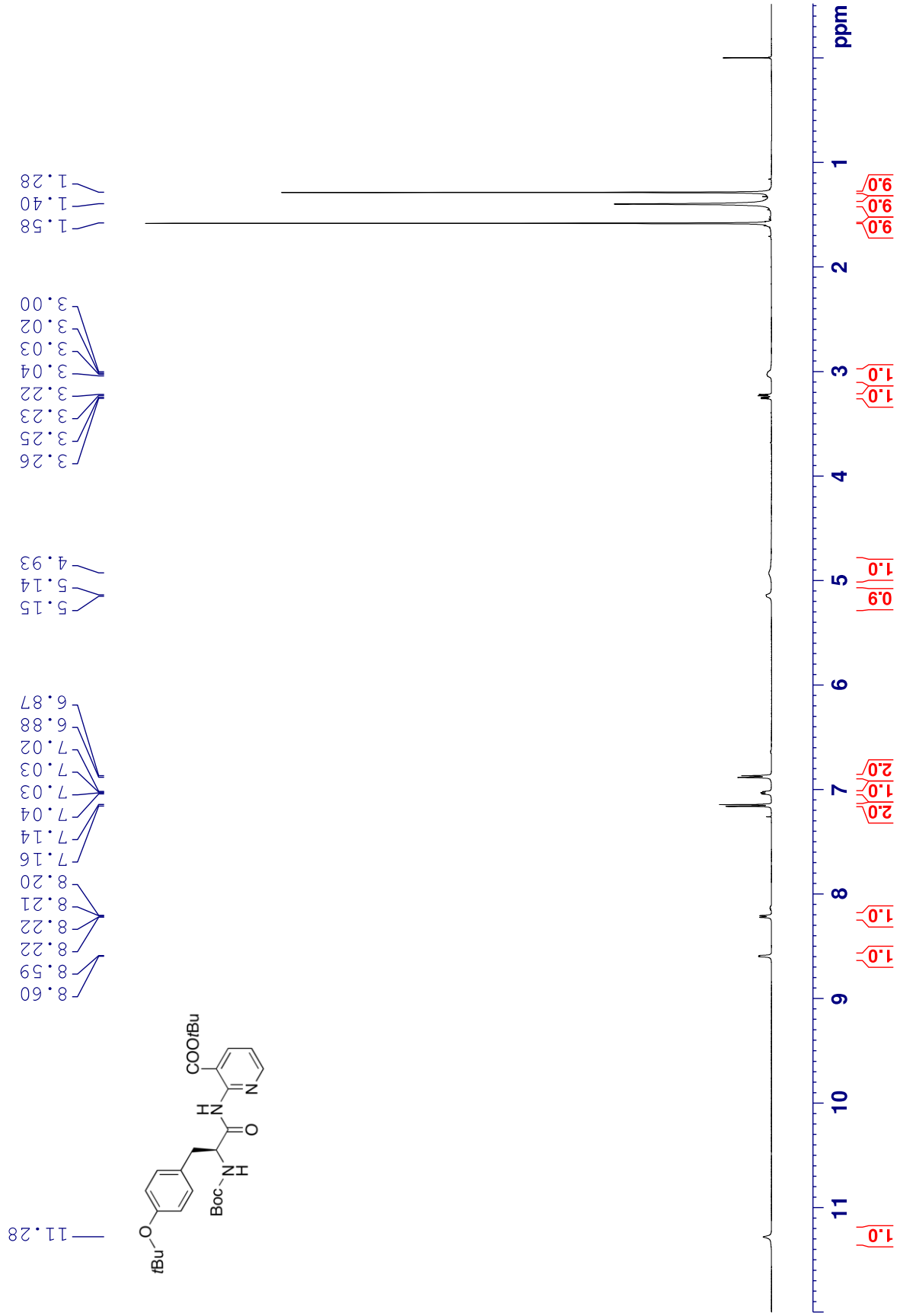
tert-Butyl (*S*)-2-(2-((*tert*-butoxycarbonyl)amino)propanamido)nicotinate (Boc-L-Ala-NH-*t*Bu-nic, ER804) **L-4b - ^{1}H NMR (500 MHz, $CDCl_3$)**



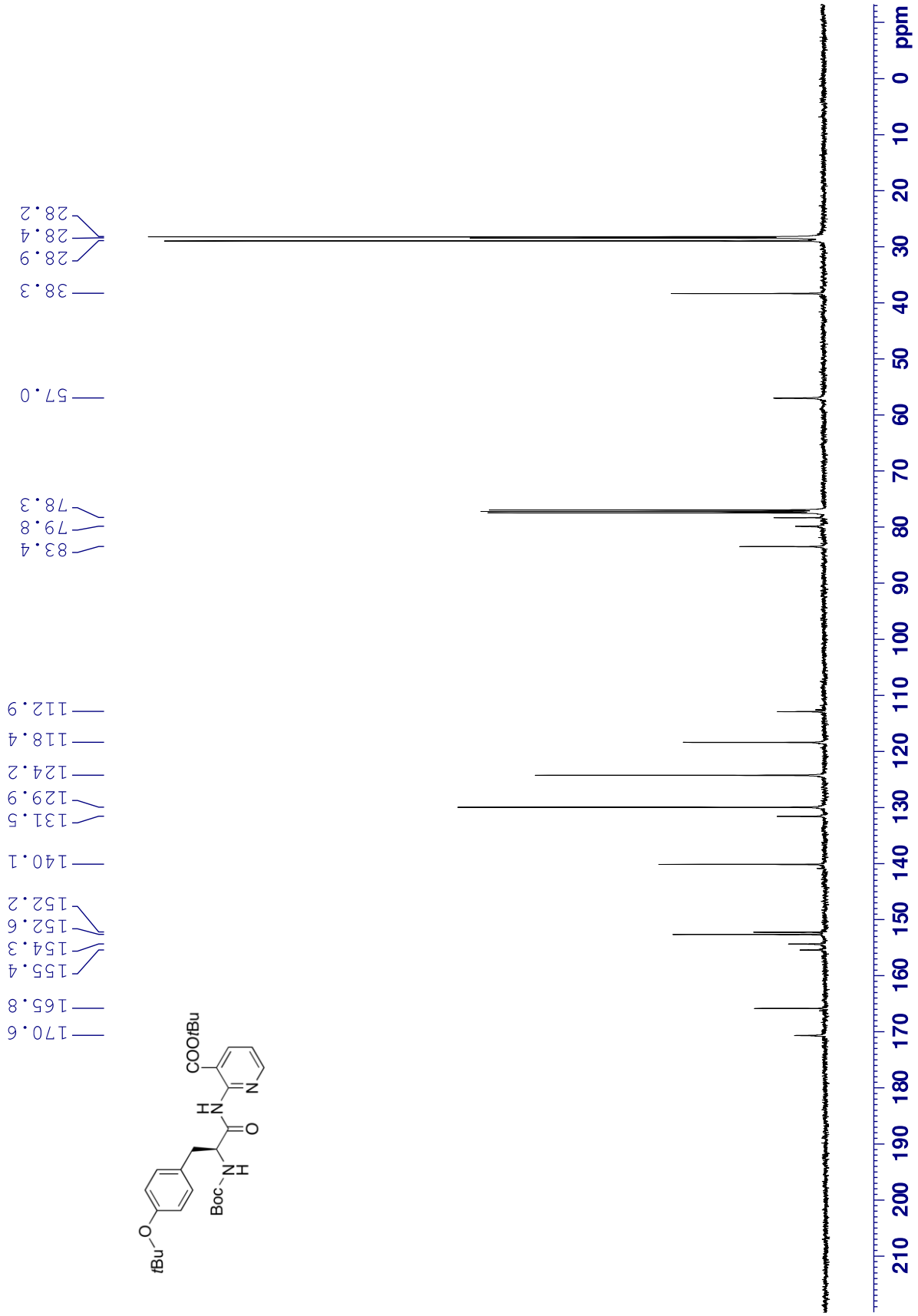
tert-Butyl (*S*)-2-(2-((*tert*-butoxycarbonyl)amino)propanamido)nicotinate (Boc-L-Ala-NH-*t*Bu-nic, ER804) **L-4b - ^{13}C NMR (126 MHz, $CDCl_3$)**



tert-Butyl (*S*)-2-(3-(4-(*tert*-butoxy)phenyl)-2-((*tert*-butoxycarbonyl)amino)propanamido)nicotinate (Boc-L-Tyr(*t*Bu)-NH-*t*Bu-nic, ER803) **L-4c - ^{1}H NMR (500 MHz, $CDCl_3$)**

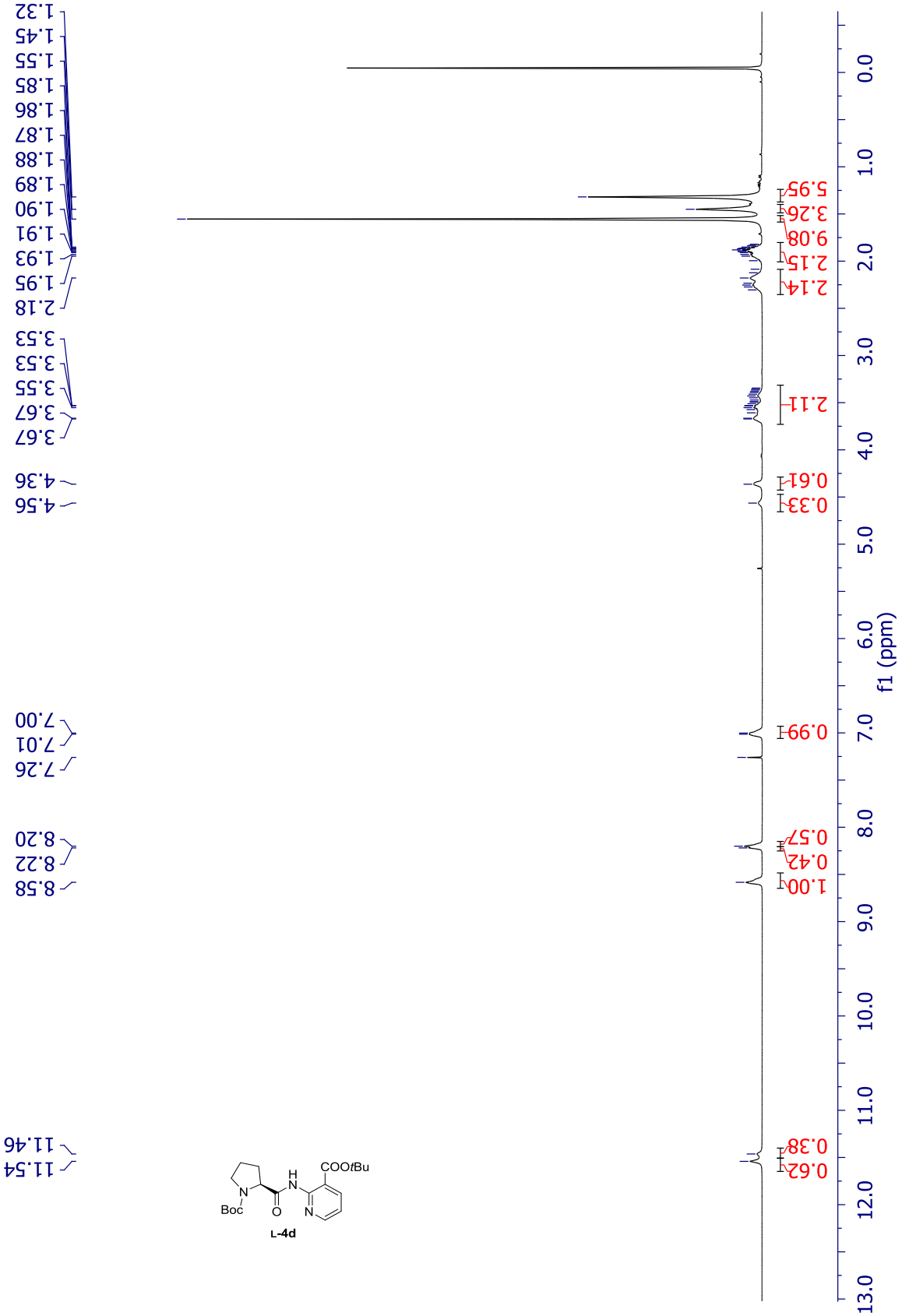


tert-Butyl (*S*)-2-(3-(4-(*tert*-butoxy)phenyl)-2-((*tert*-butoxycarbonyl)amino)propanamido)nicotinate (Boc-L-Tyr(*t*Bu)-NH-*t*Bu-nic, ER803) **L-4c - ^{13}C NMR (126 MHz, $CDCl_3$)**



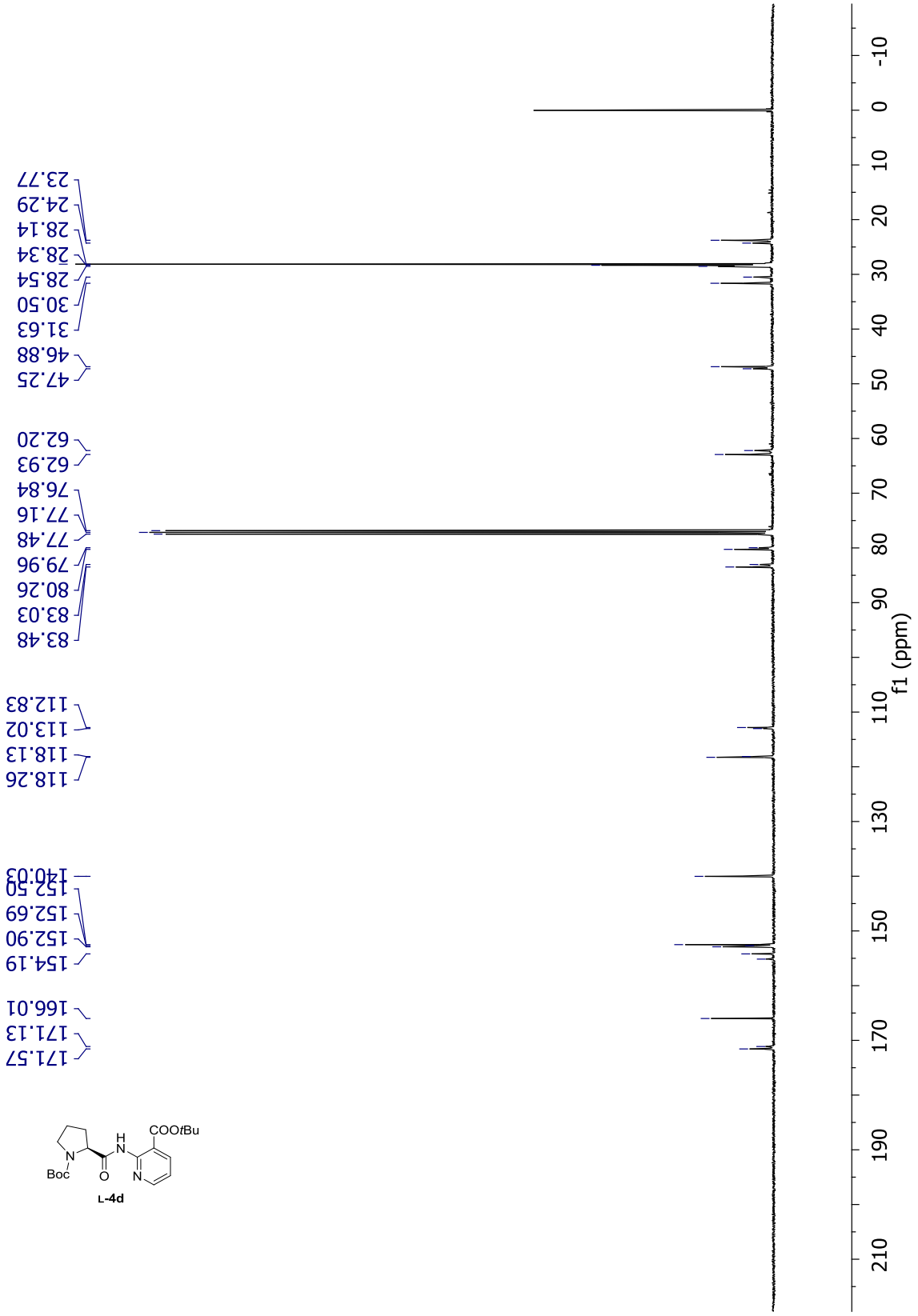
tert-Butyl 2-{[1-(*tert*-butoxycarbonyl)-L-prolyl]amino}nicotinate (Boc-L-Pro-NH-*t*Bu-nic, CW-1061)

L-4d L - ^{1}H NMR (400 MHz, $CDCl_3$)

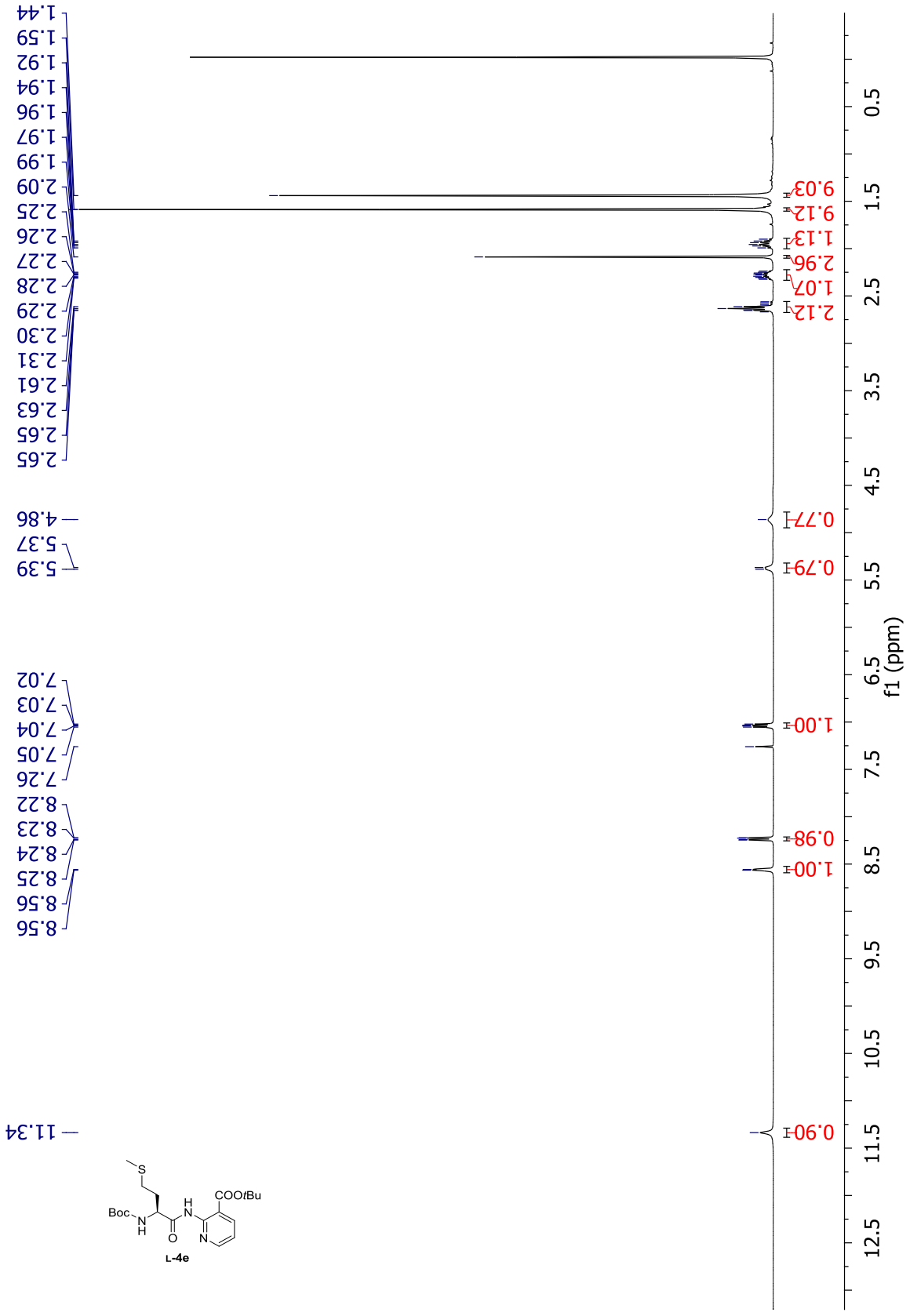


tert-Butyl 2-{[1-(*tert*-butoxycarbonyl)-L-prolyl]amino}nicotinate (Boc-L-Pro-NH-*t*Bu-nic, CW-1061)

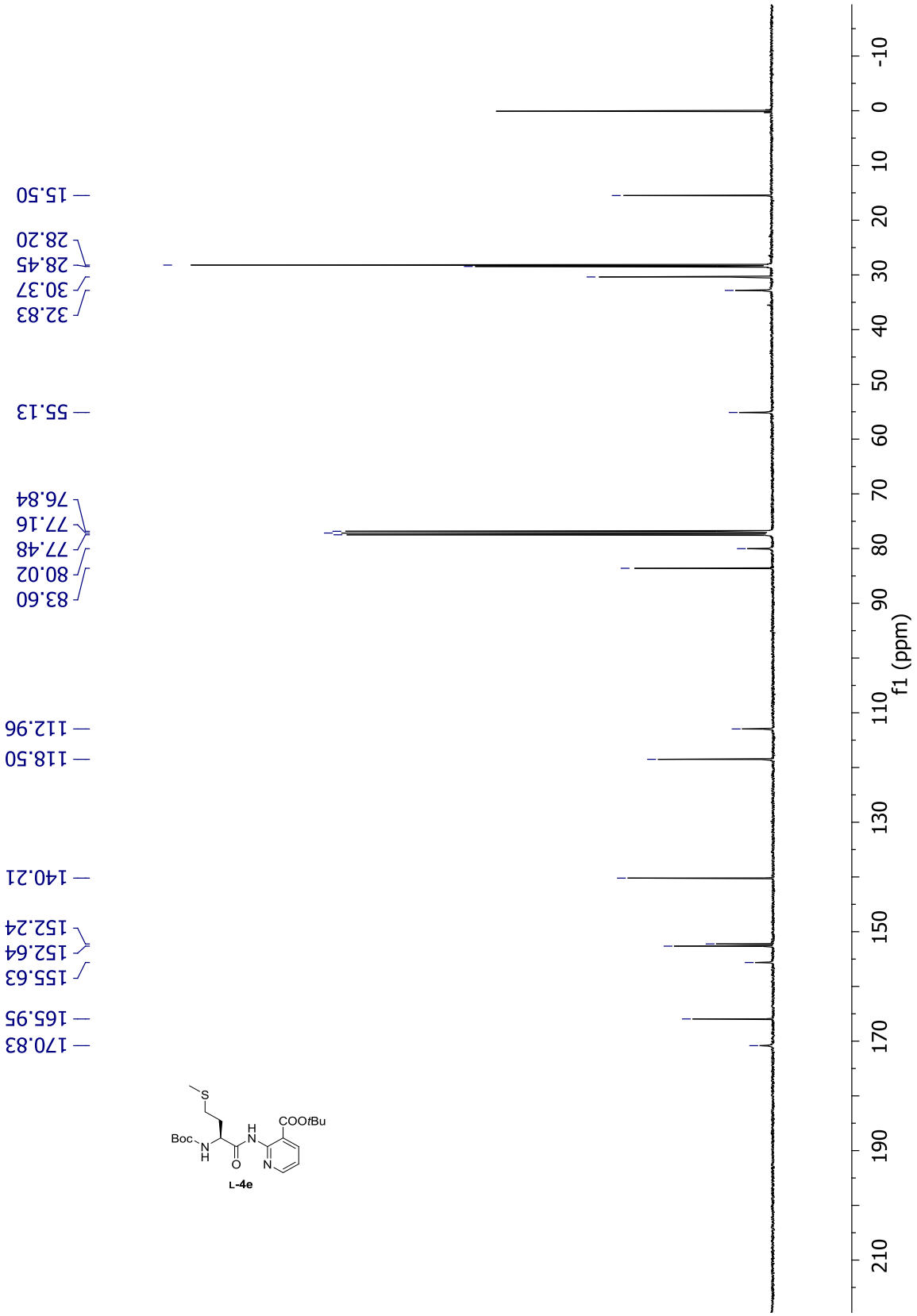
L-4d - ^{13}C NMR (101 MHz, $CDCl_3$)



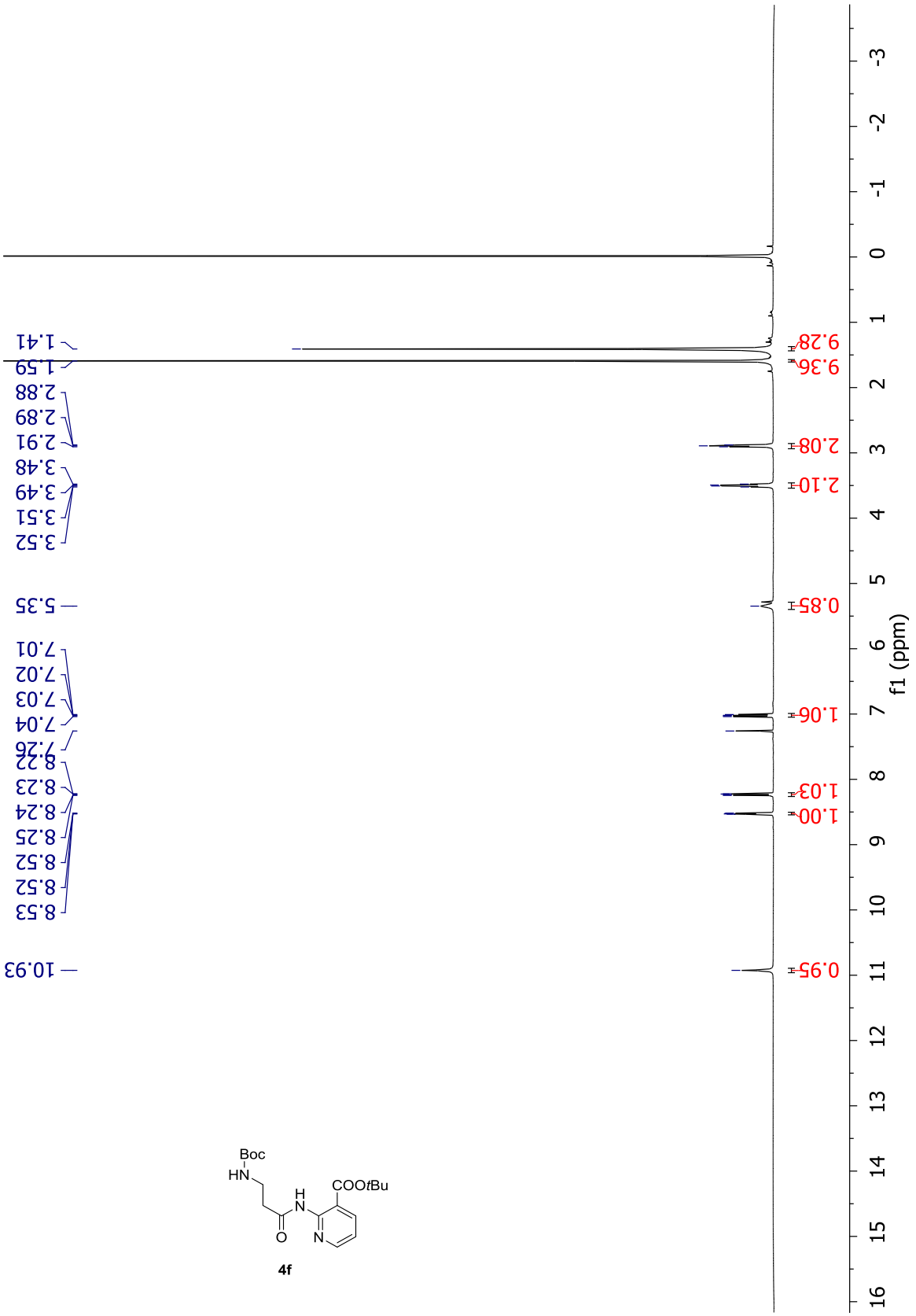
tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-L-methionyl]amino}nicotinate (Boc-L-Met-NH-*t*Bu-nic, ER1558) **L-4e - ^{1}H NMR (400 MHz, $CDCl_3$)**



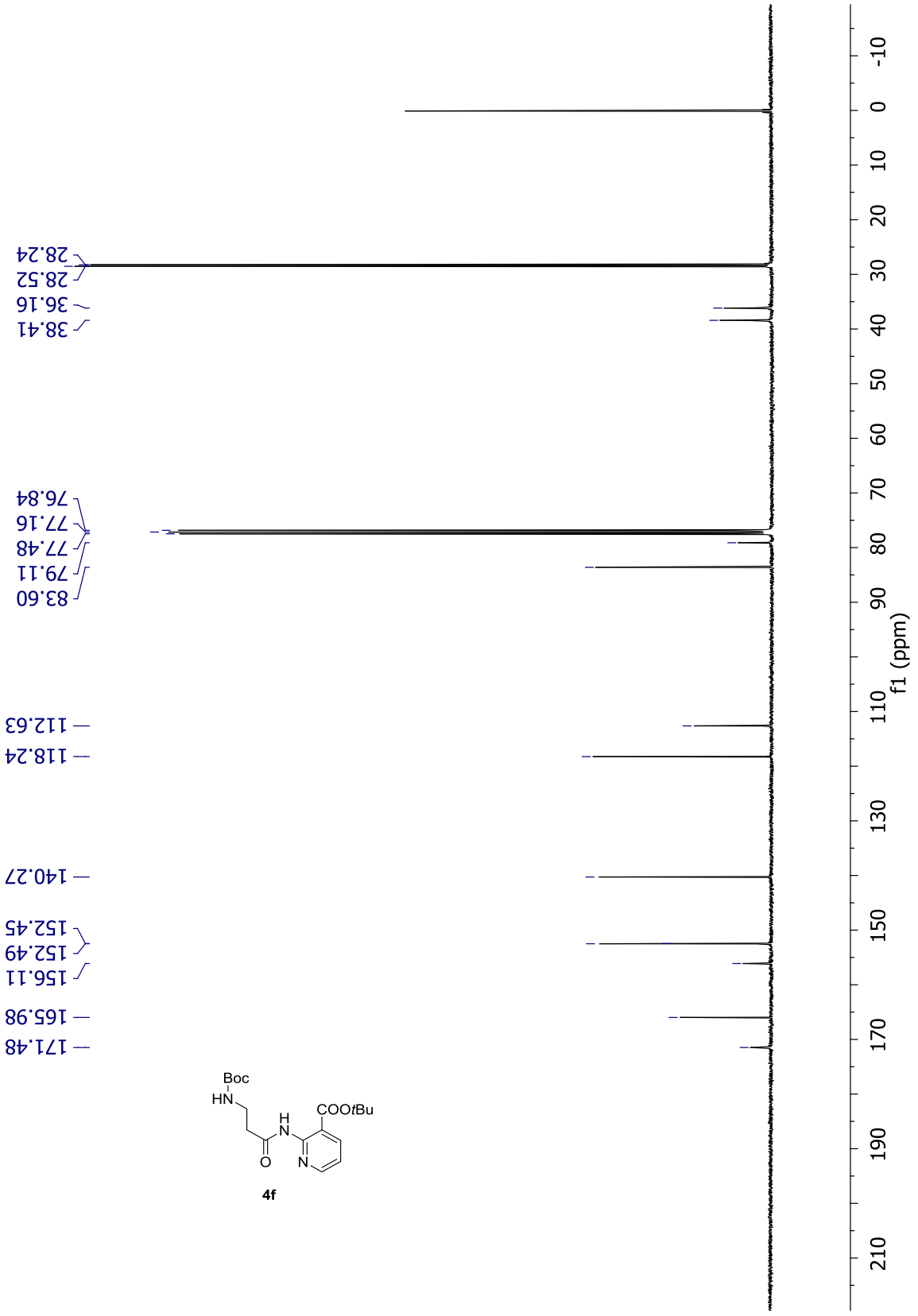
tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-L-methionyl]amino}nicotinate (Boc-L-Met-NH-*t*Bu-nic, ER1558) **L-4e - ^{13}C NMR (101 MHz, $CDCl_3$)**



tert-Butyl 2-{3-[(*tert*-butoxycarbonyl)amino]propanamido}nicotinate (Boc-βAla-NH-*t*Bu-nic, CW-1618) **4f** - **^{1}H NMR (400 MHz, CDCl$_3$)**

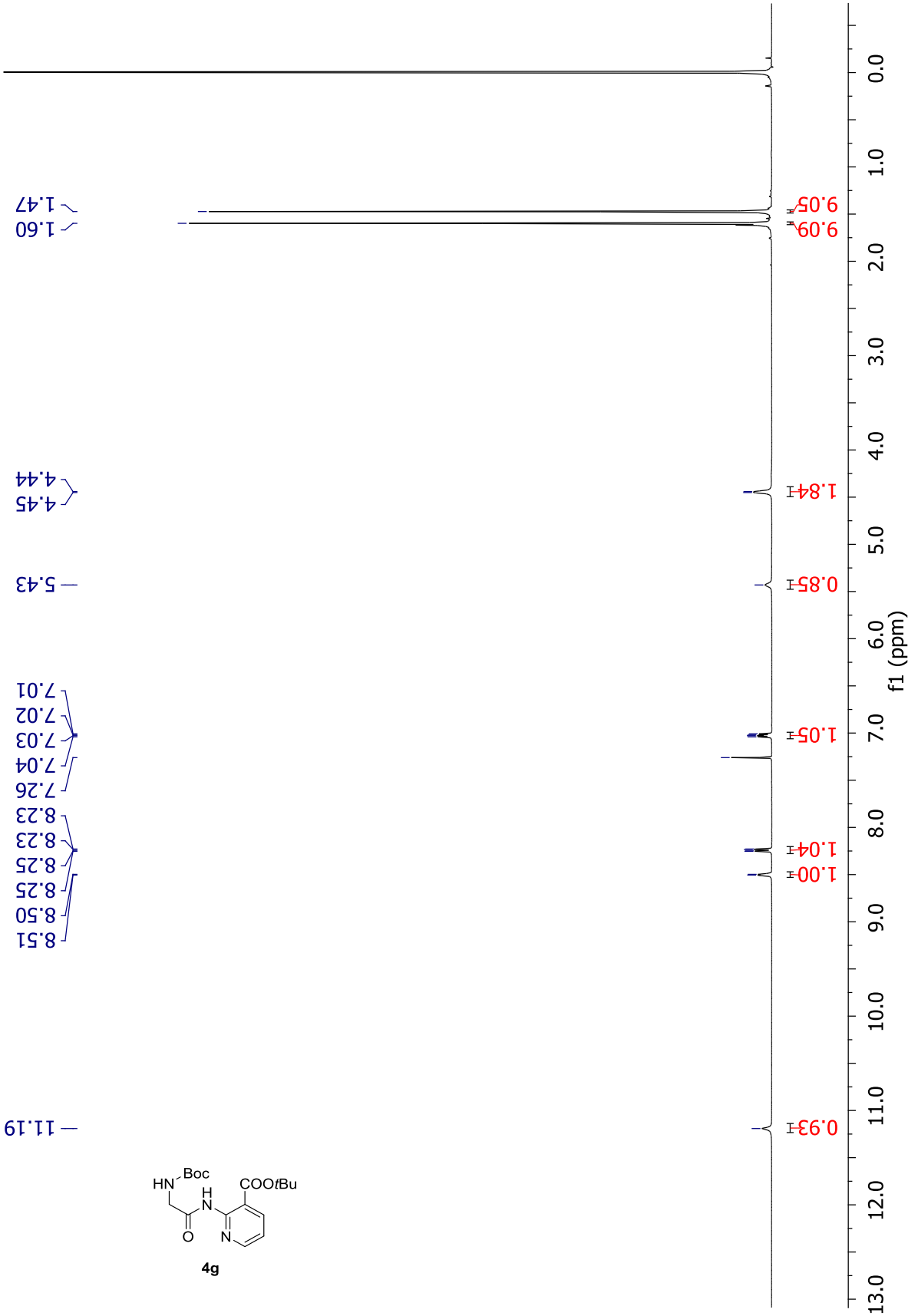


tert-Butyl 2-{3-[(*tert*-butoxycarbonyl)amino]propanamido}nicotinate (Boc-βAla-NH-*t*Bu-nic, CW-1618) **4f - ^{13}C NMR (101 MHz, CDCl$_3$)**



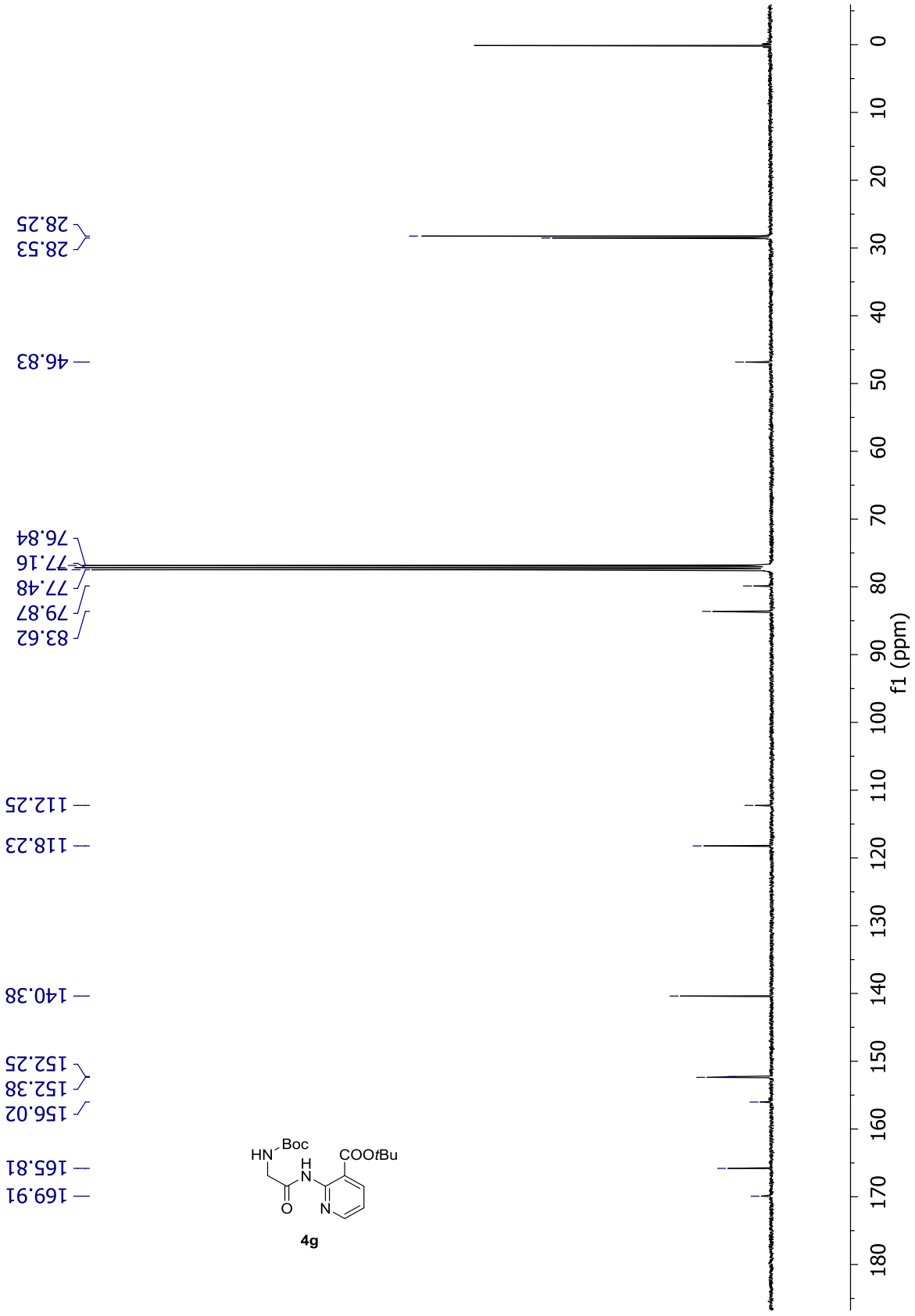
tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)glycyl]amino}nicotinate (Boc-Gly-NH-*t*Bu-nic, CW-1124) **4g** -

^{1}H NMR (400 MHz, $CDCl_3$)

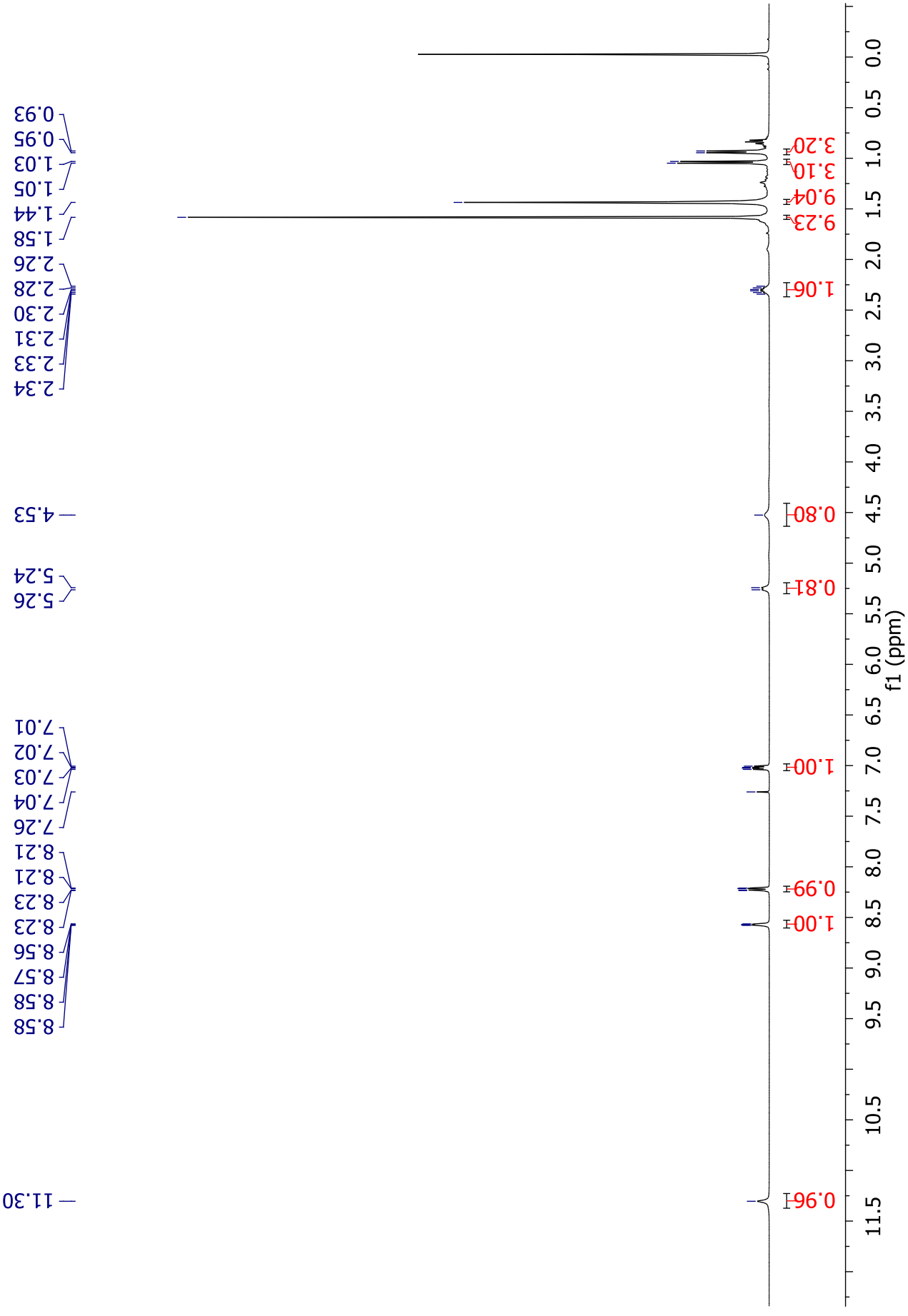


tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)glycyl]amino}nicotinate (Boc-Gly-NH-*t*Bu-nic, CW-1124) **4g** -

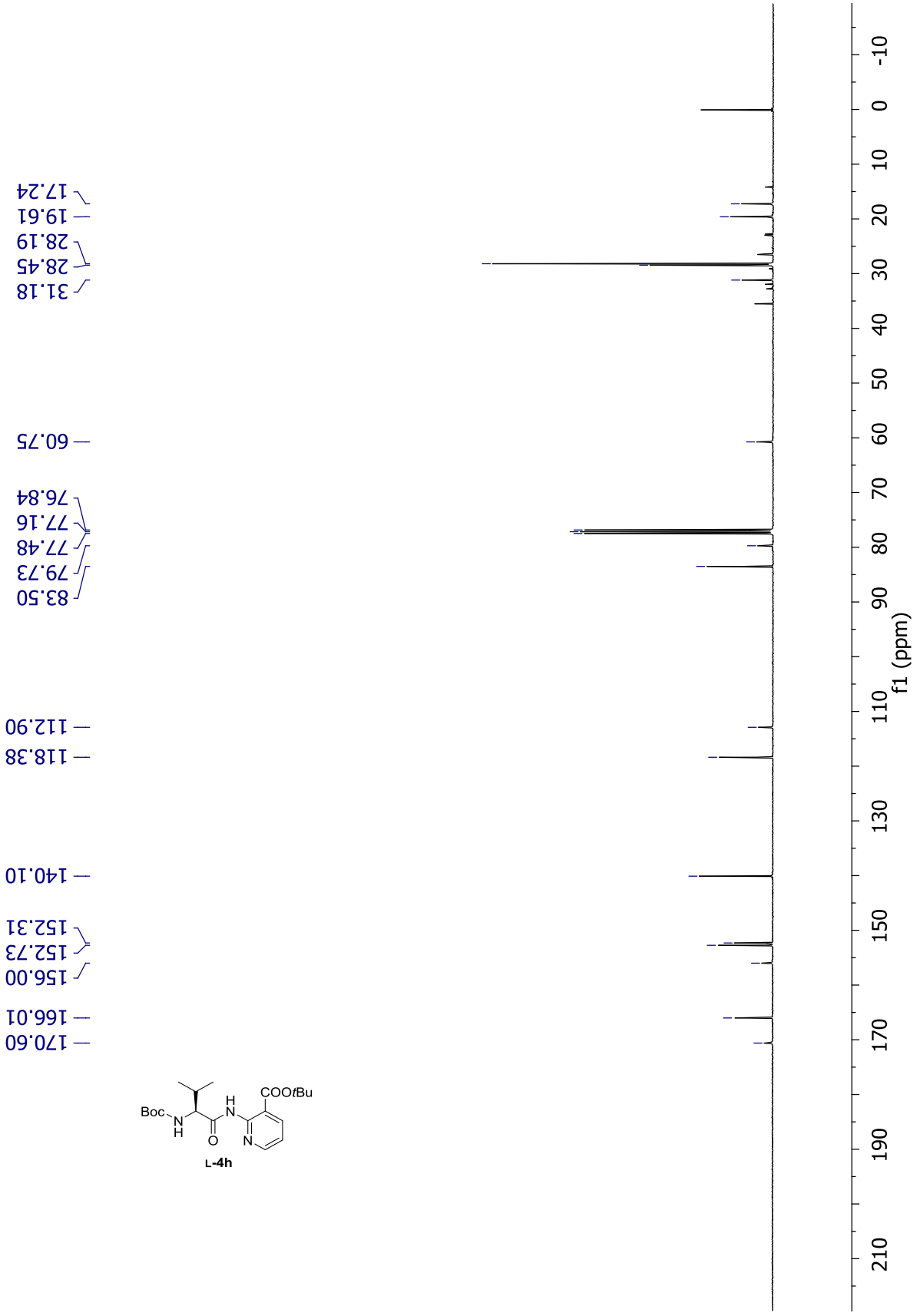
^{13}C NMR (101 MHz, $CDCl_3$)



tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-L-valyl]amino}nicotinate (Boc-L-Val-NH-*t*Bu-nic, ER1538) **L-4h - ^{1}H NMR (400 MHz, $CDCl_3$)**

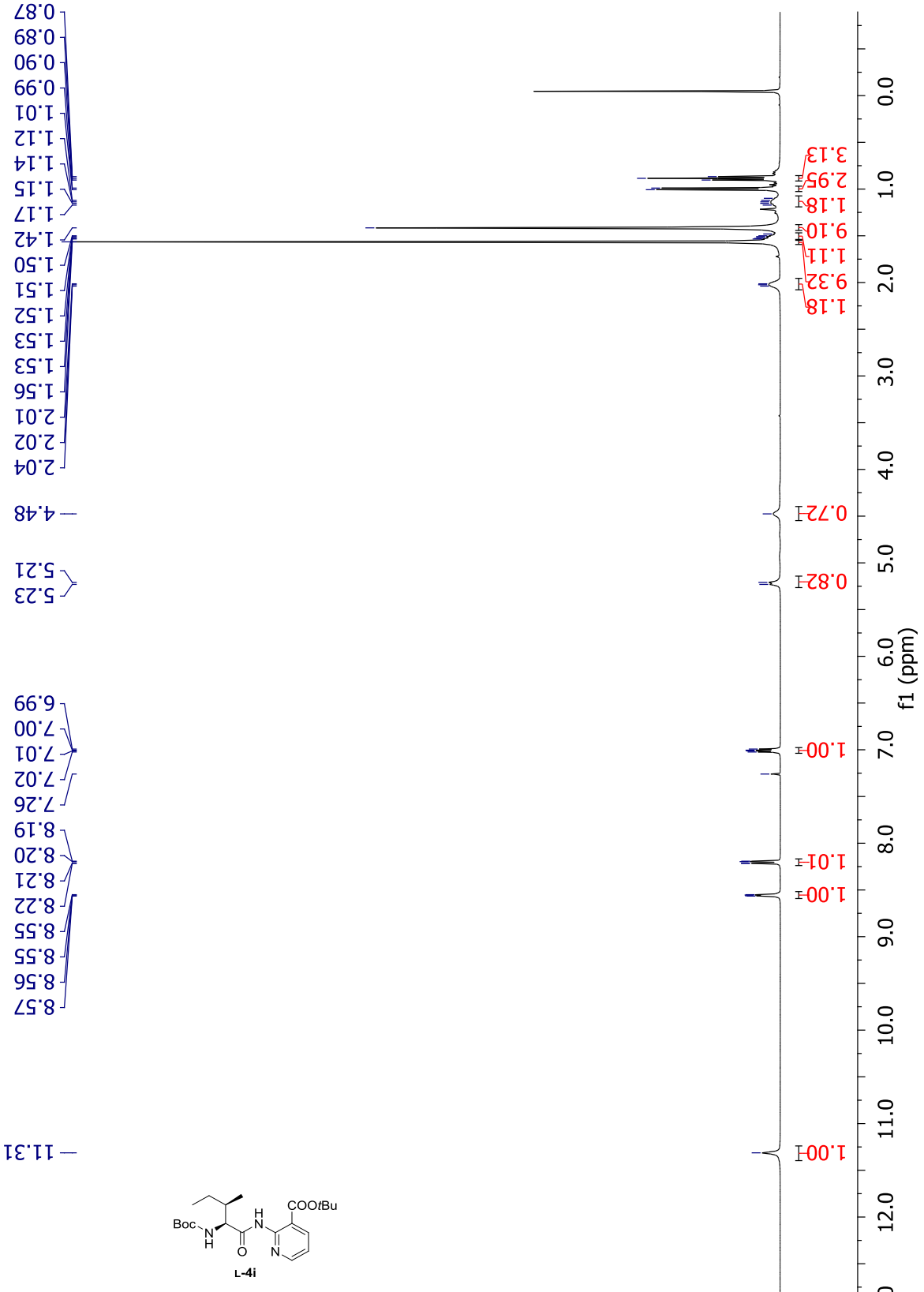


tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-L-valyl]amino}nicotinate (Boc-L-Val-NH-*t*Bu-nic, ER1538) **L-4h - ^{13}C NMR (101 MHz, $CDCl_3$)**



tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-L-isoleucyl]amino}nicotinate (Boc-L-Ile-NH-*t*Bu-nic, DM679)

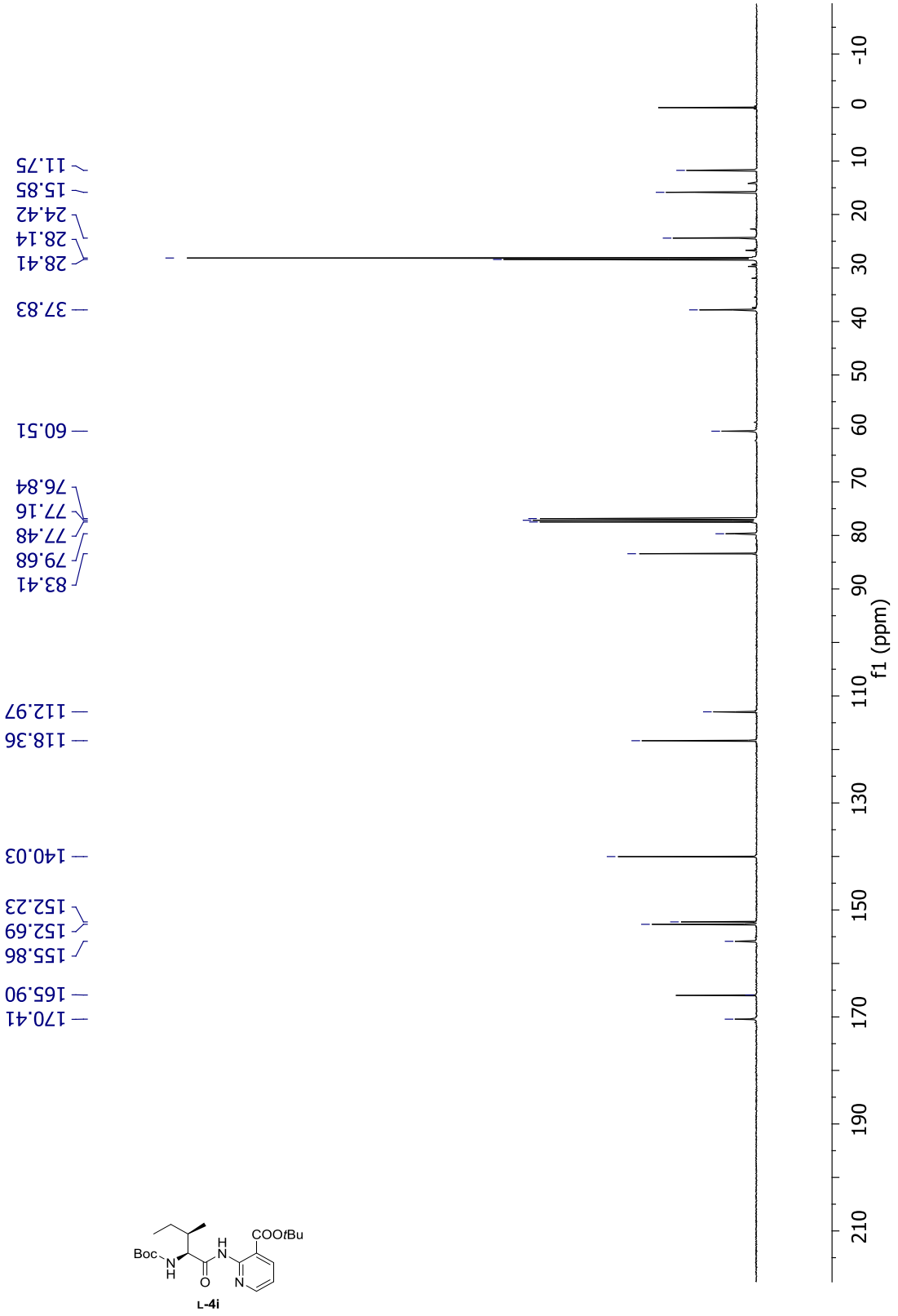
L-4i - ^{1}H NMR (400 MHz, $CDCl_3$)



L-4i

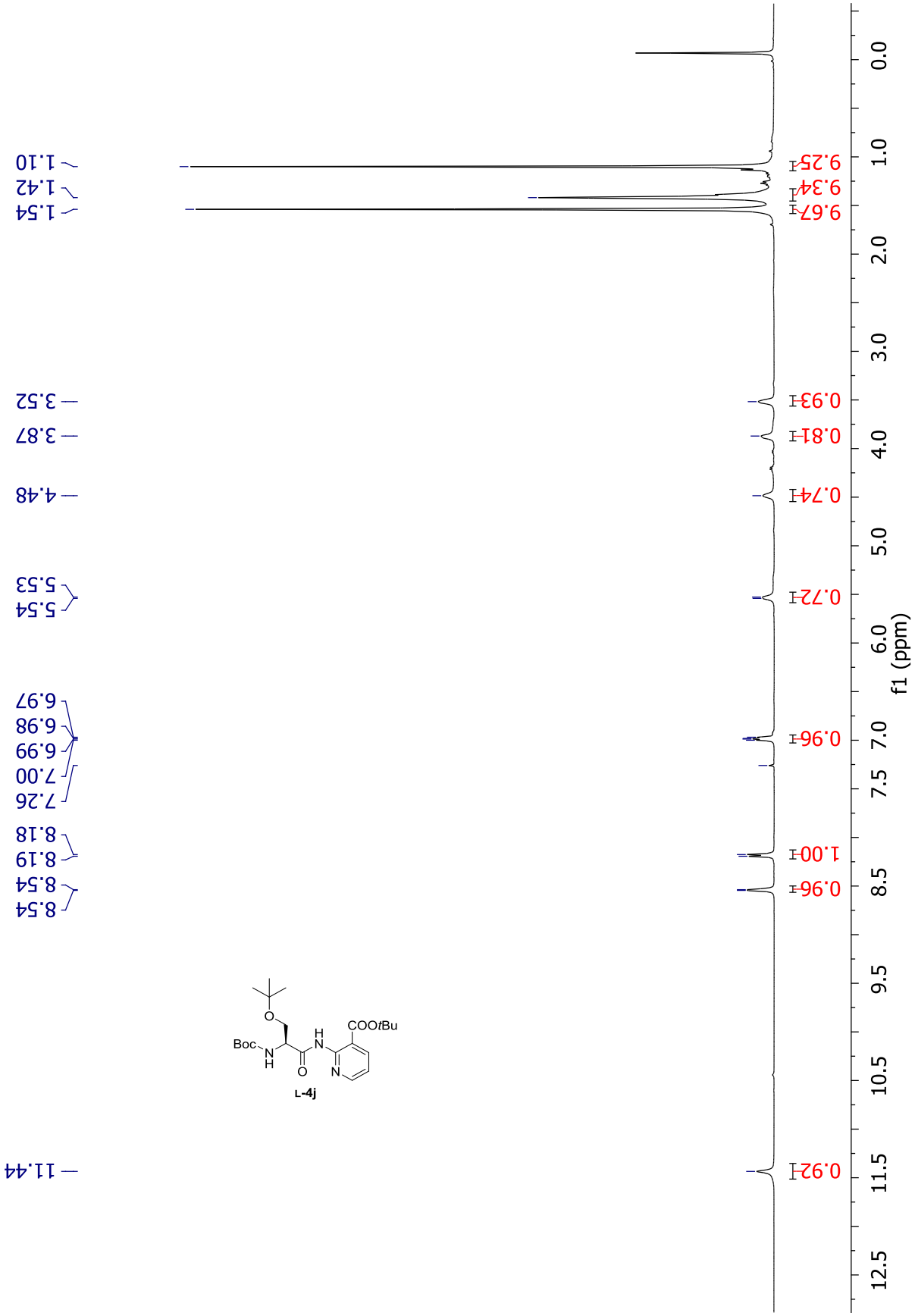
tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-L-isoleucyl]amino}nicotinate (Boc-L-Ile-NH-*t*Bu-nic, DM679)

L-4i - ^{13}C NMR (101 MHz, $CDCl_3$)

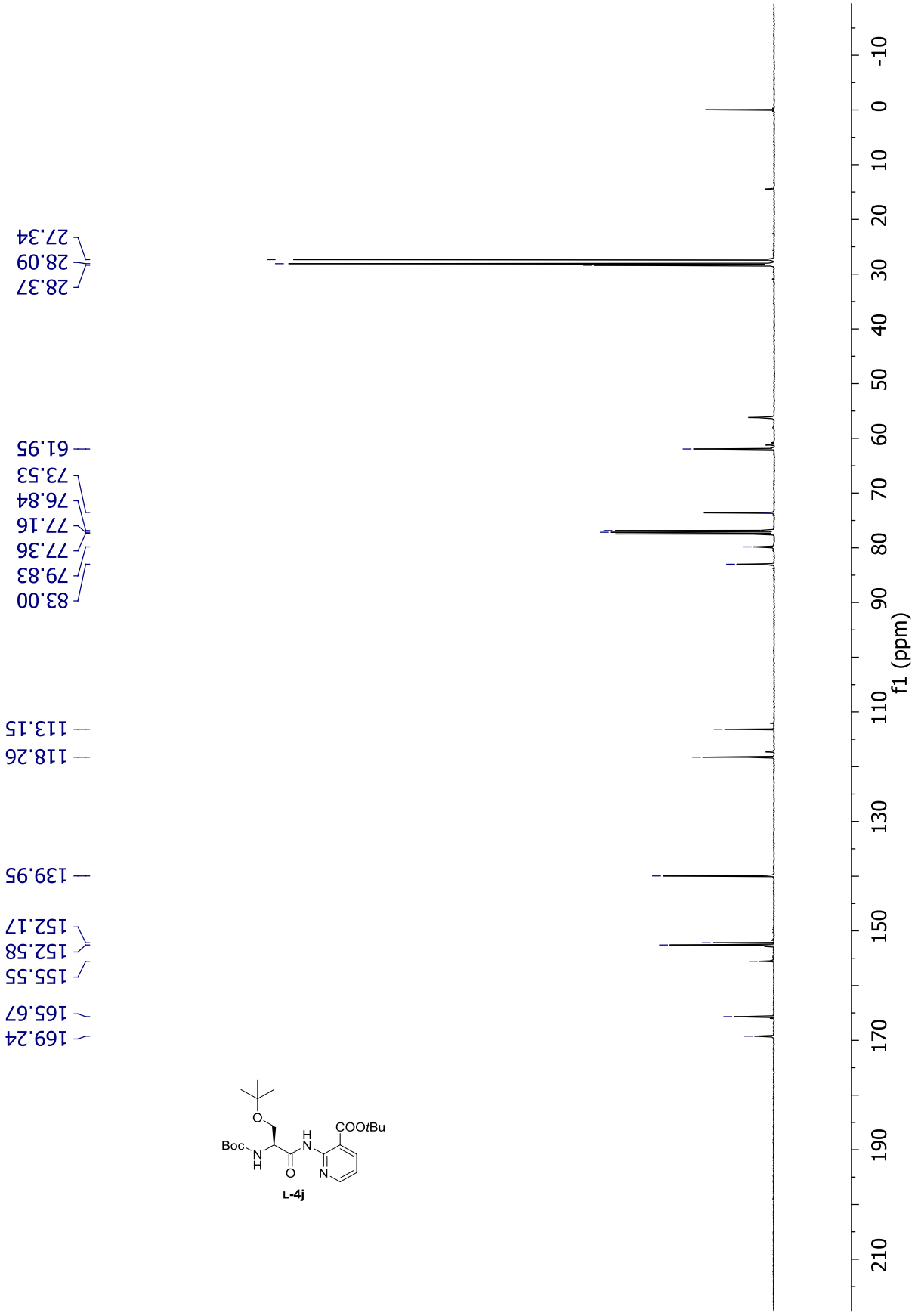


L-4i

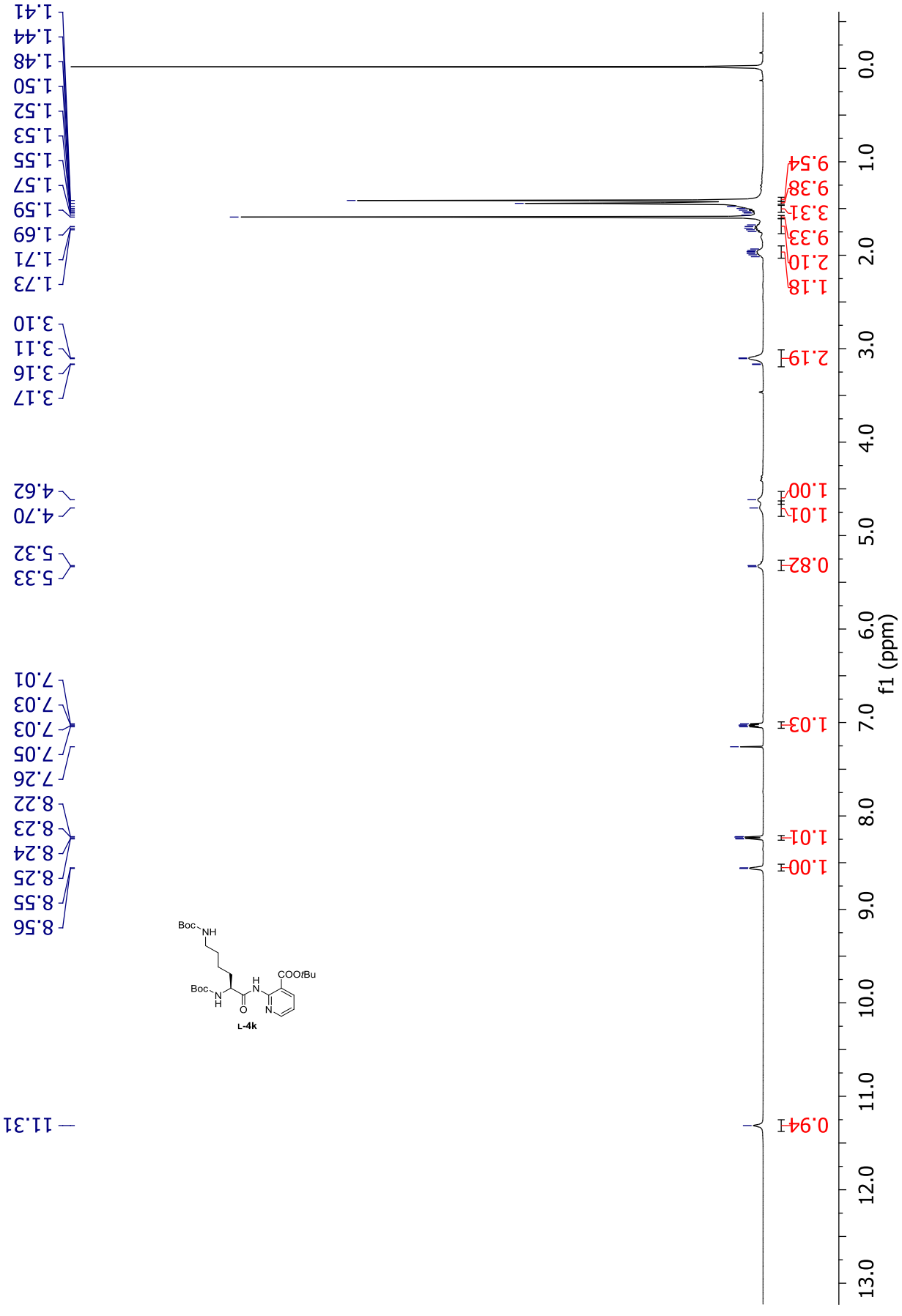
tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-O-*tert*-butyl-L-seryl]amino} nicotinate (Boc-L-Ser(*t*Bu)-NH-*t*Bu-nic, LVR0603) **L-4j - ^{1}H NMR (400 MHz, $CDCl_3$)**



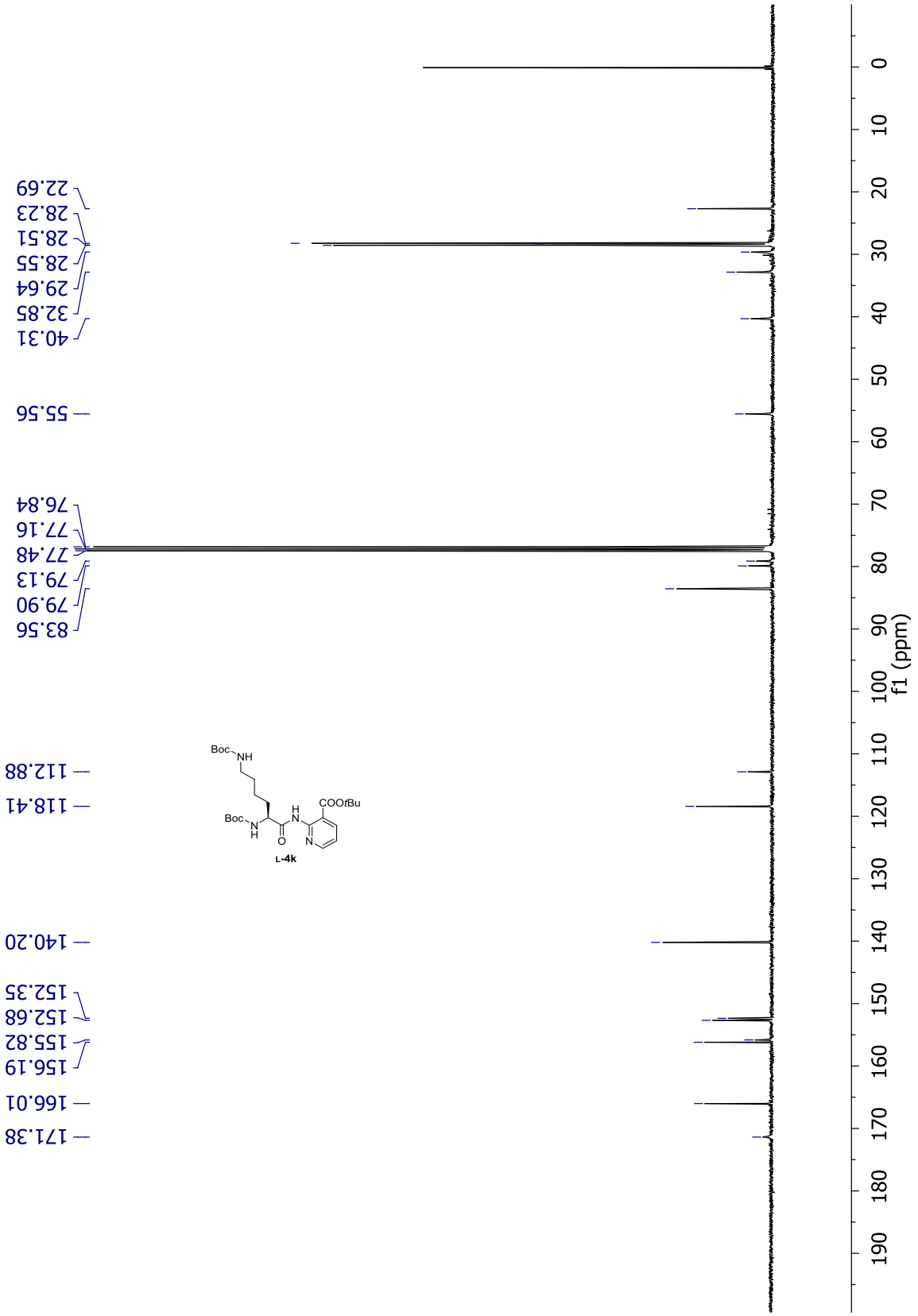
tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-*O*-*tert*-butyl-L-seryl]amino} nicotinate (Boc-L-Ser(*t*Bu)-NH-*t*Bu-nic, LVR0603) **L-4j – ^{13}C NMR (101 MHz, $CDCl_3$)**



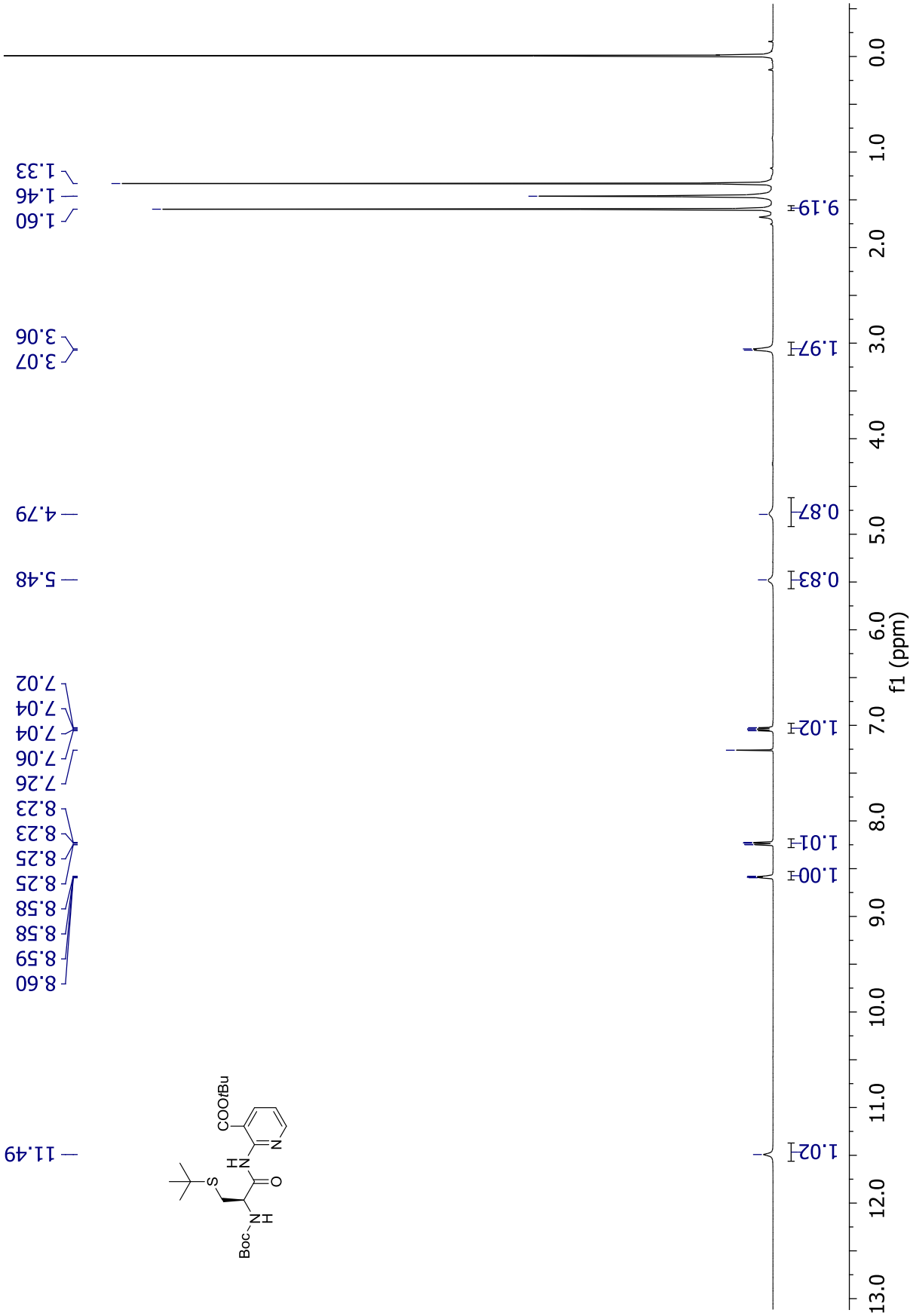
tert-Butyl 2-{[N^2,N^6-bis(*tert*-butoxycarbonyl)-L-lysyl]amino} nicotinate (Boc-L-Lys(Boc)-NH-*t*Bu-nic, ER1718) **L-4k - ^{1}H NMR (400 MHz, $CDCl_3$)**



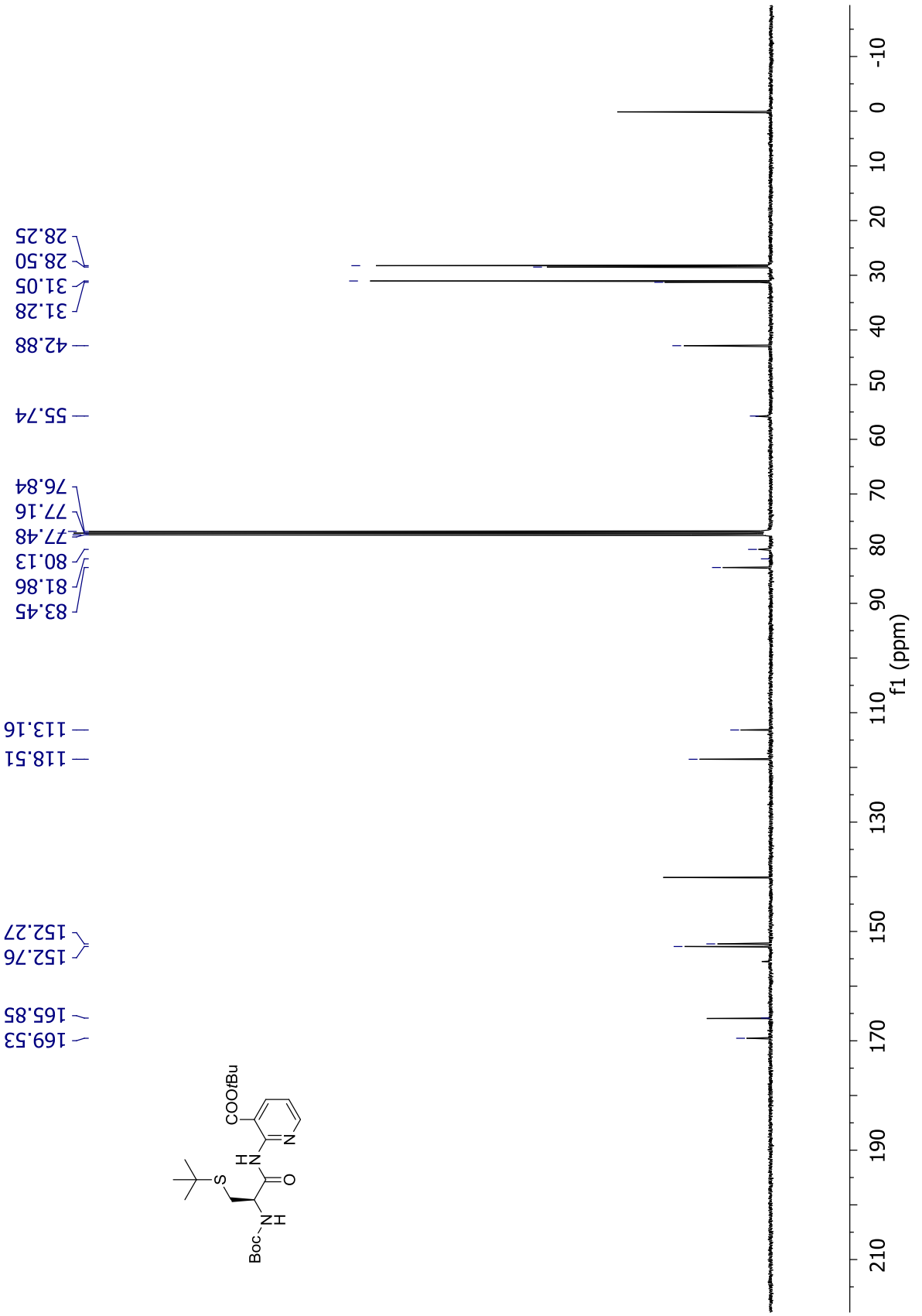
tert-Butyl 2-{[N^2,N^6-bis(*tert*-butoxycarbonyl) L-lysyl]amino} nicotinate (Boc-L-Lys(Boc)-NH-*t*Bu-nic, ER1718) **L-4k - ^{13}C NMR (101 MHz, $CDCl_3$)**



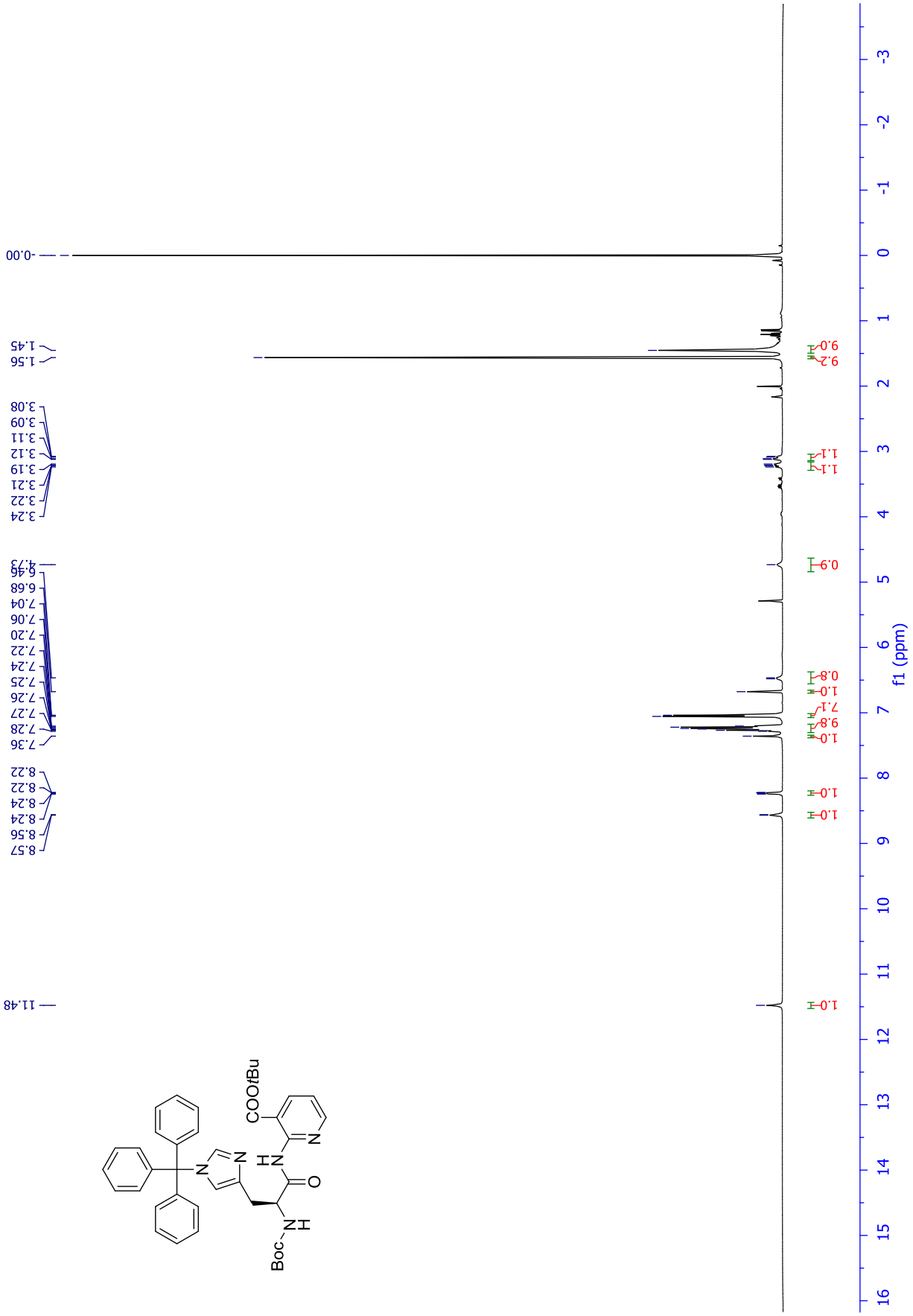
tert-Butyl (*R*)-2-(2-((*tert*-butoxycarbonyl)amino)-3-(*tert*-butylthio)propanamido)nicotinate (Boc-L-Cys(*t*Bu)-NH-*t*Bu-nic, ER1625/ER1676) **L-4l - ^{1}H NMR (400 MHz, $CDCl_3$)**



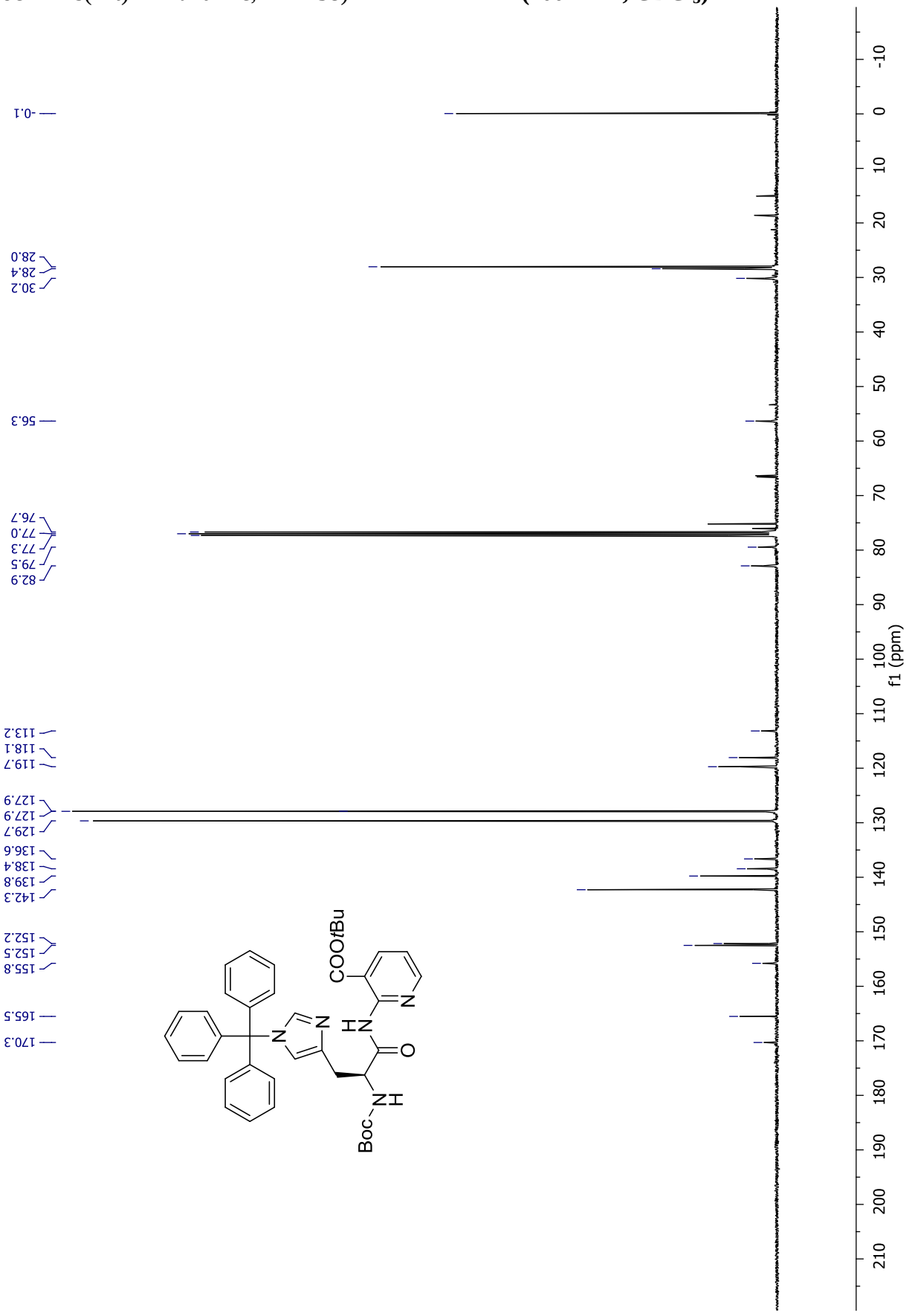
tert-Butyl (*R*)-2-(2-((*tert*-butoxycarbonyl)amino)-3-(*tert*-butylthio)propanamido)nicotinate (Boc-L-Cys(*t*Bu)-NH-*t*Bu-nic, ER1625/ER1676) **L-4l – ^{13}C NMR (101 MHz, $CDCl_3$)**



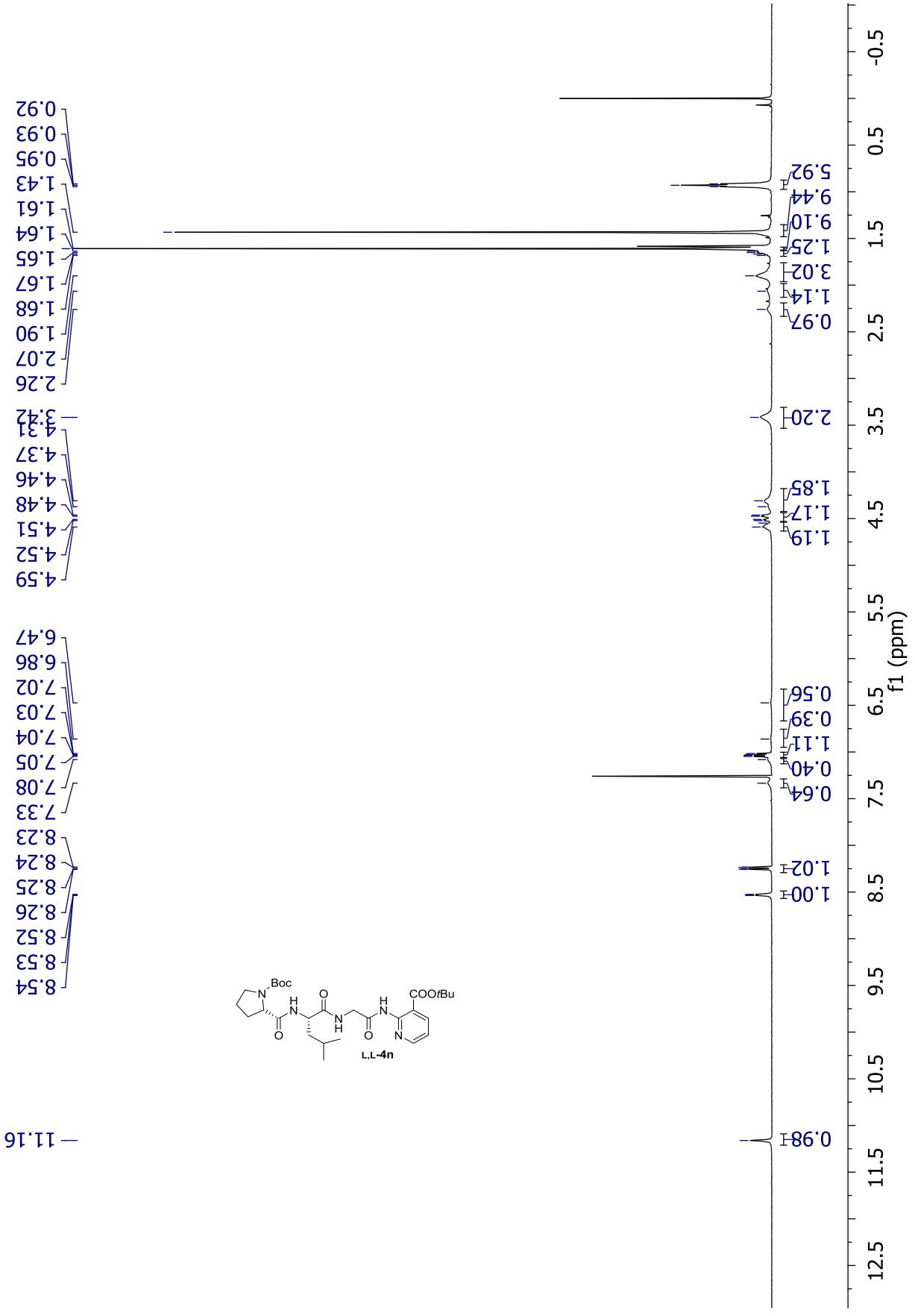
tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-1-(triphenylmethyl)-L-histidyl]amino}pyridine-3-carboxylate (Boc-L-His(Trt)-NH-*t*Bu-nic, ER1738) **L-4m - ^{1}H NMR (400 MHz, $CDCl_3$)**



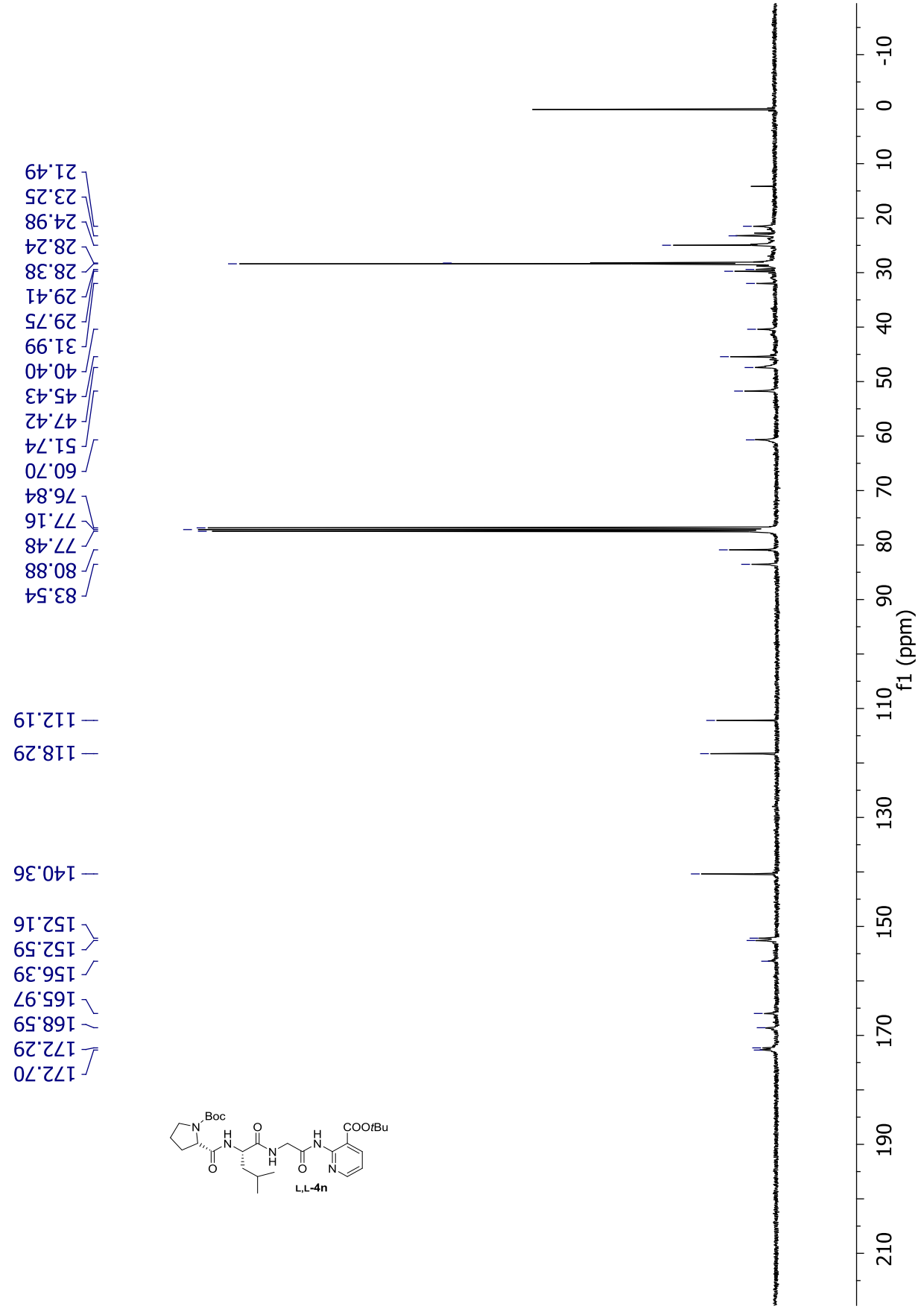
tert-Butyl 2-{[*N*-(*tert*-butoxycarbonyl)-1-(triphenylmethyl)-L-histidyl]amino}pyridine-3-carboxylate (Boc-L-His(Trt)-NH-*t*Bu-nic, ER1738) **L-4m - ^{1}H NMR (400 MHz, $CDCl_3$)**



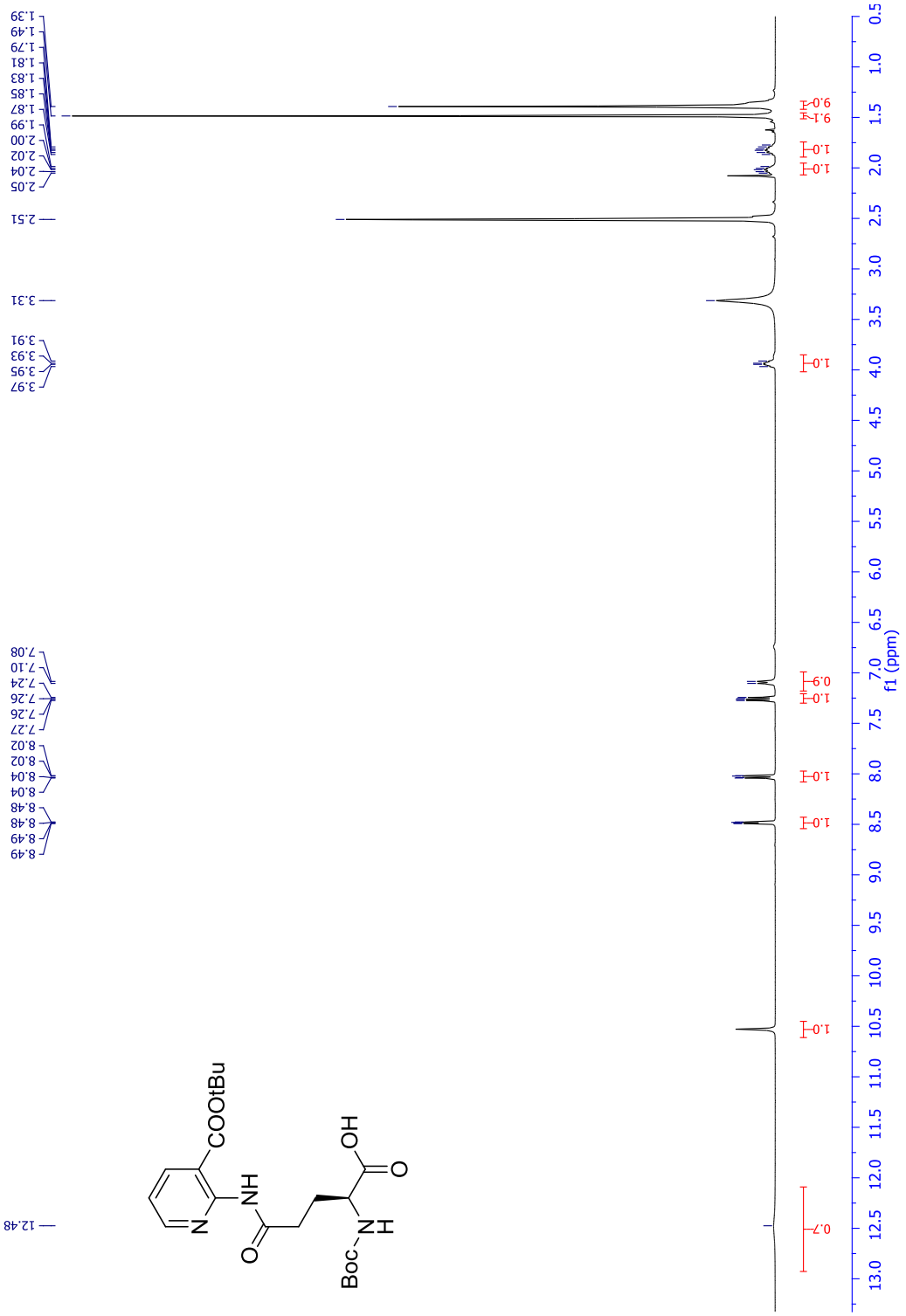
tert-Butoxycarbonyl)-L-prolyl-L-leucyl-*N*-[3-*tert*-butyoxycarbonyl)pyridin-2-yl)]glycinamide (Boc-L-Pro-L-Leu-Gly-NH-*t*Bu-nic, CW-1843) **L,L-4n- ^{1}H NMR (400 MHz, $CDCl_3$)**



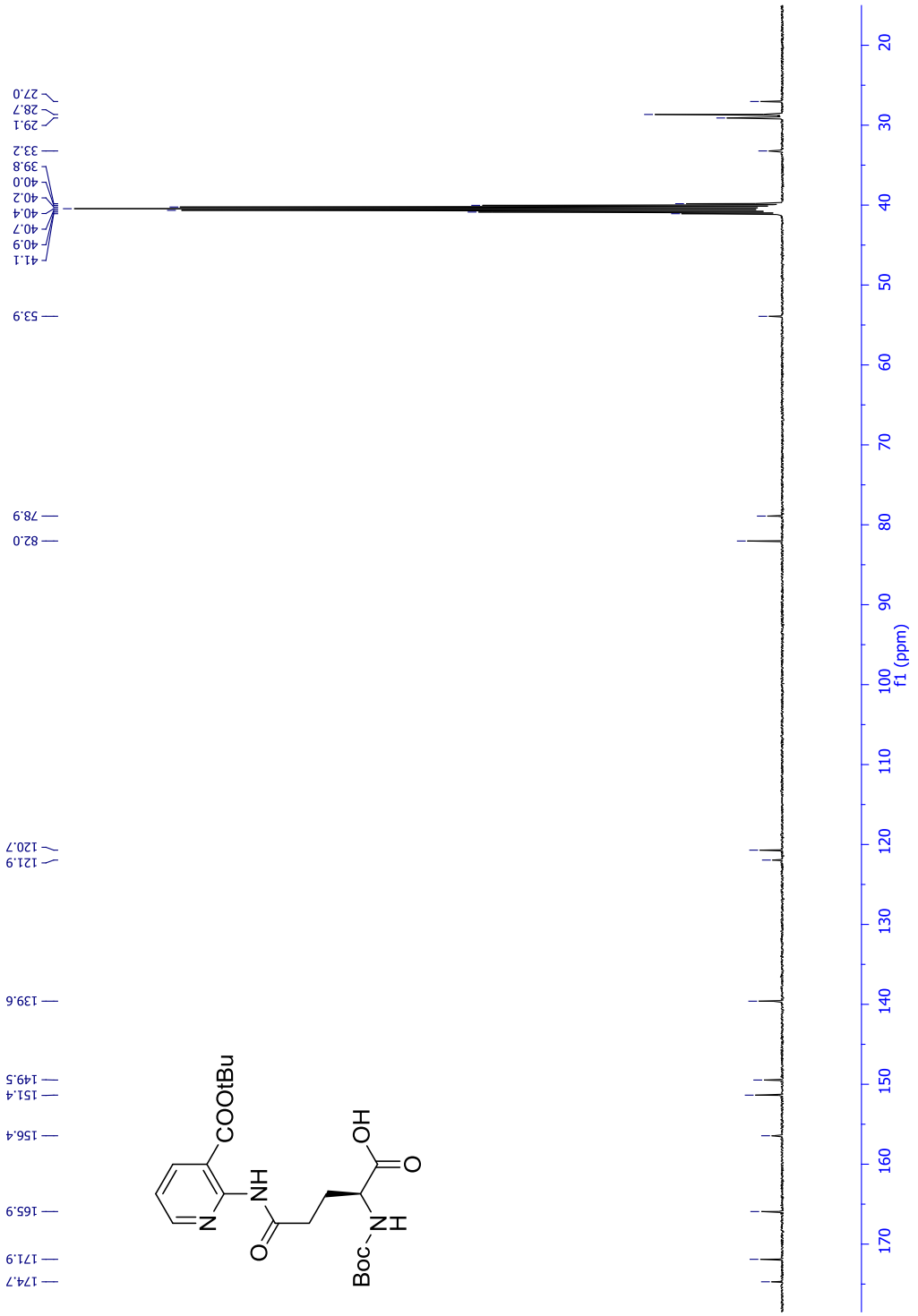
1-(*tert*-Butoxycarbonyl)-L-prolyl-L-leucyl-*N*-[3-*tert*-butyoxycarbonyl)pyridin-2-yl)]glycinamide (Boc-L-Pro-L-LEU-Gly-NH-*t*Bu-nic, CW-1843) **L,L-4n - ^{13}C NMR (101 MHz, $CDCl_3$)**



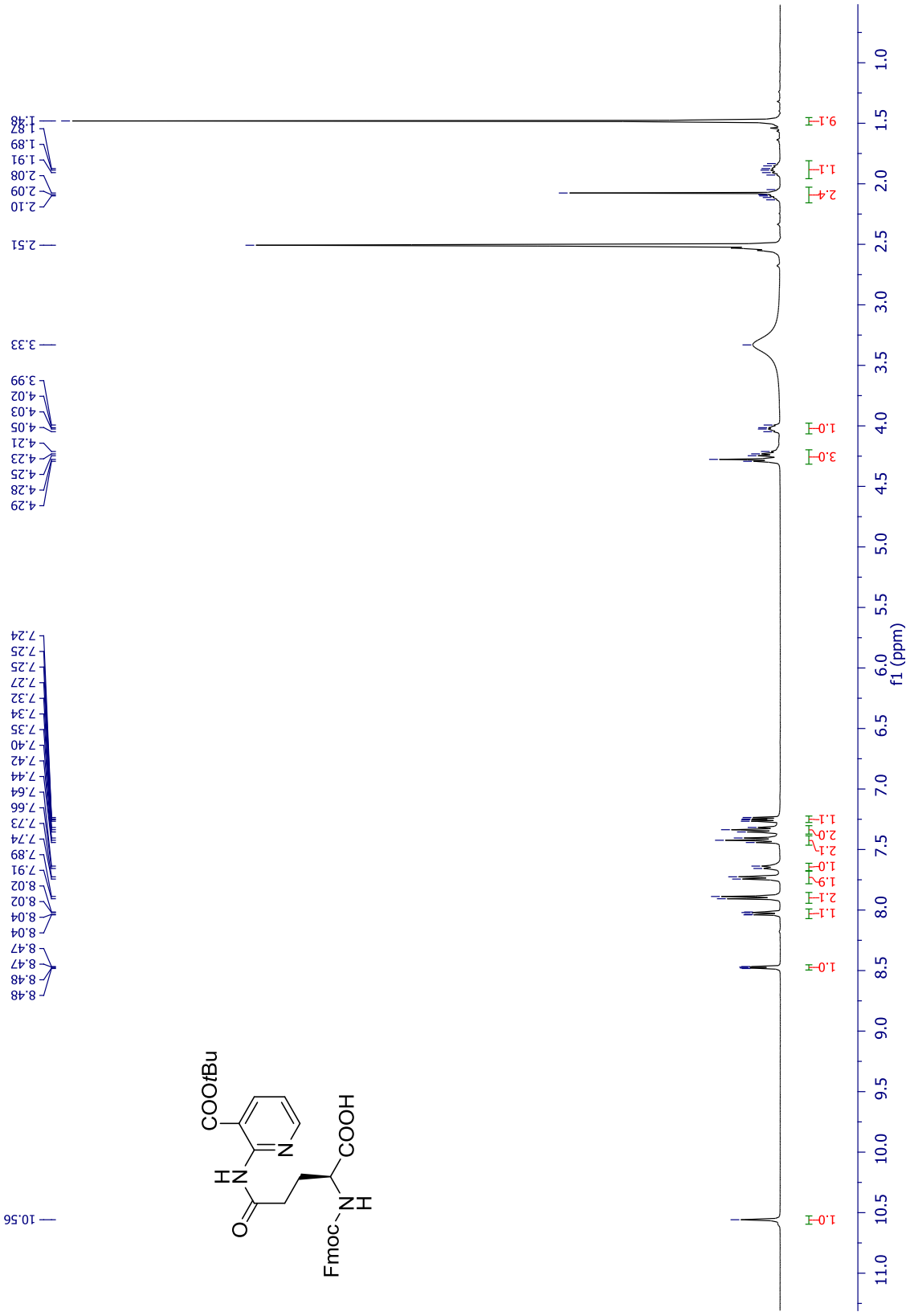
N^2-(*tert*-Butoxycarbonyl)-N^5-(3-(*tert*-butoxycarbonyl)pyridin-2-yl)-L-glutamine (Boc-L-Gln(NH-tBu-nic)-OH, DM613) **L-4o - ^{1}H NMR (400 MHz, DMSO-d_6)**



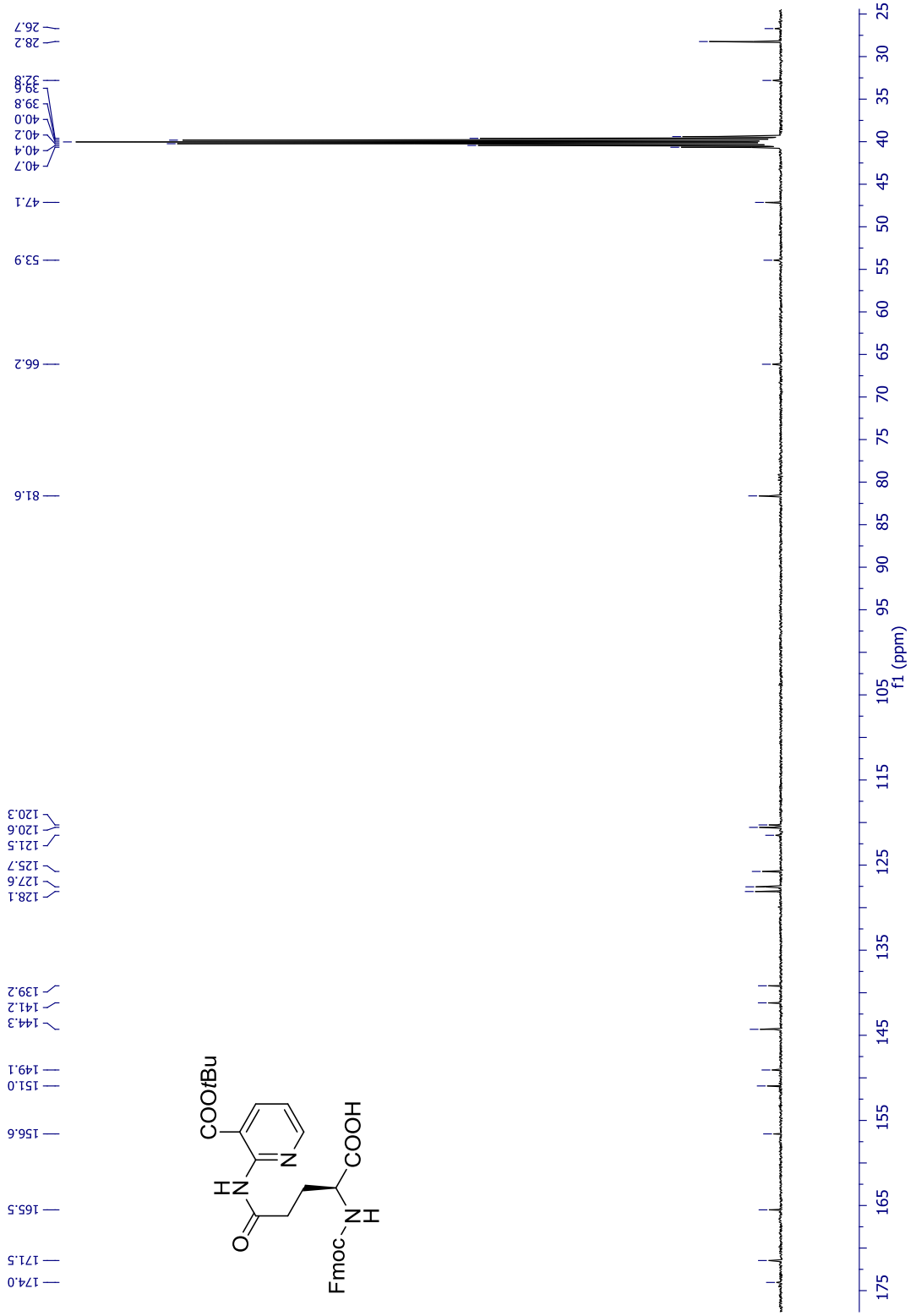
N^2-(*tert*-Butoxycarbonyl)-N^5-(3-(*tert*-butoxycarbonyl)pyridin-2-yl)-L-glutamine (Boc-L-Gln(NH-tBu-nic)-OH, DM613) **L-4o** – **^{13}C NMR (100 MHz, DMSO-d_6)**



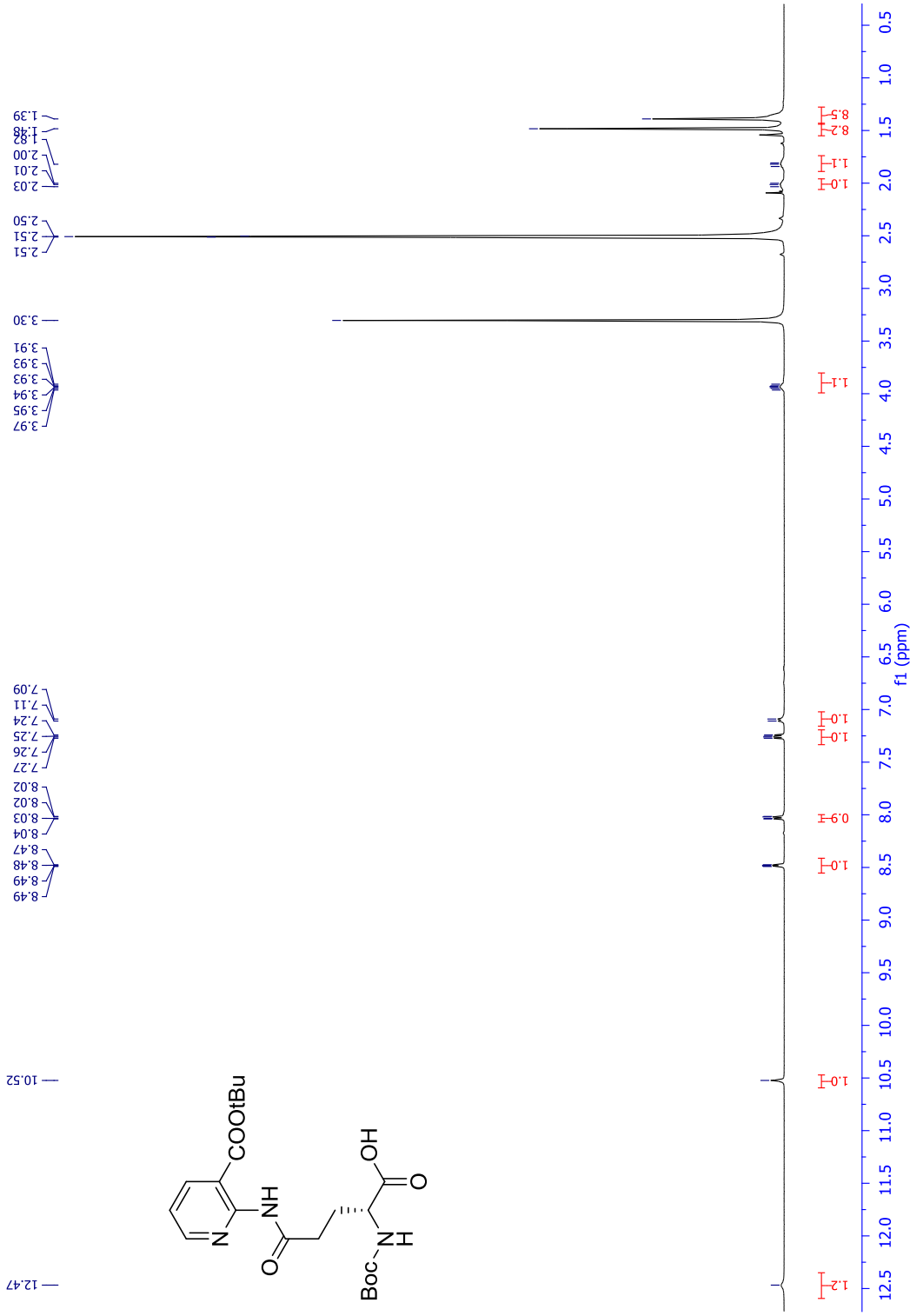
N-[3-(*tert*-butoxycarbonyl)pyridin-2-yl]-*N*-2-{[(9*H*-fluoren-9-yl)methoxy]carbonyl}-L-glutamine (Fmoc-L-Gln(*t*Bu-nic)-OH, DM674) **L-4p** – **^{1}H NMR (400 MHz, DMSO-*d*$_6$)**



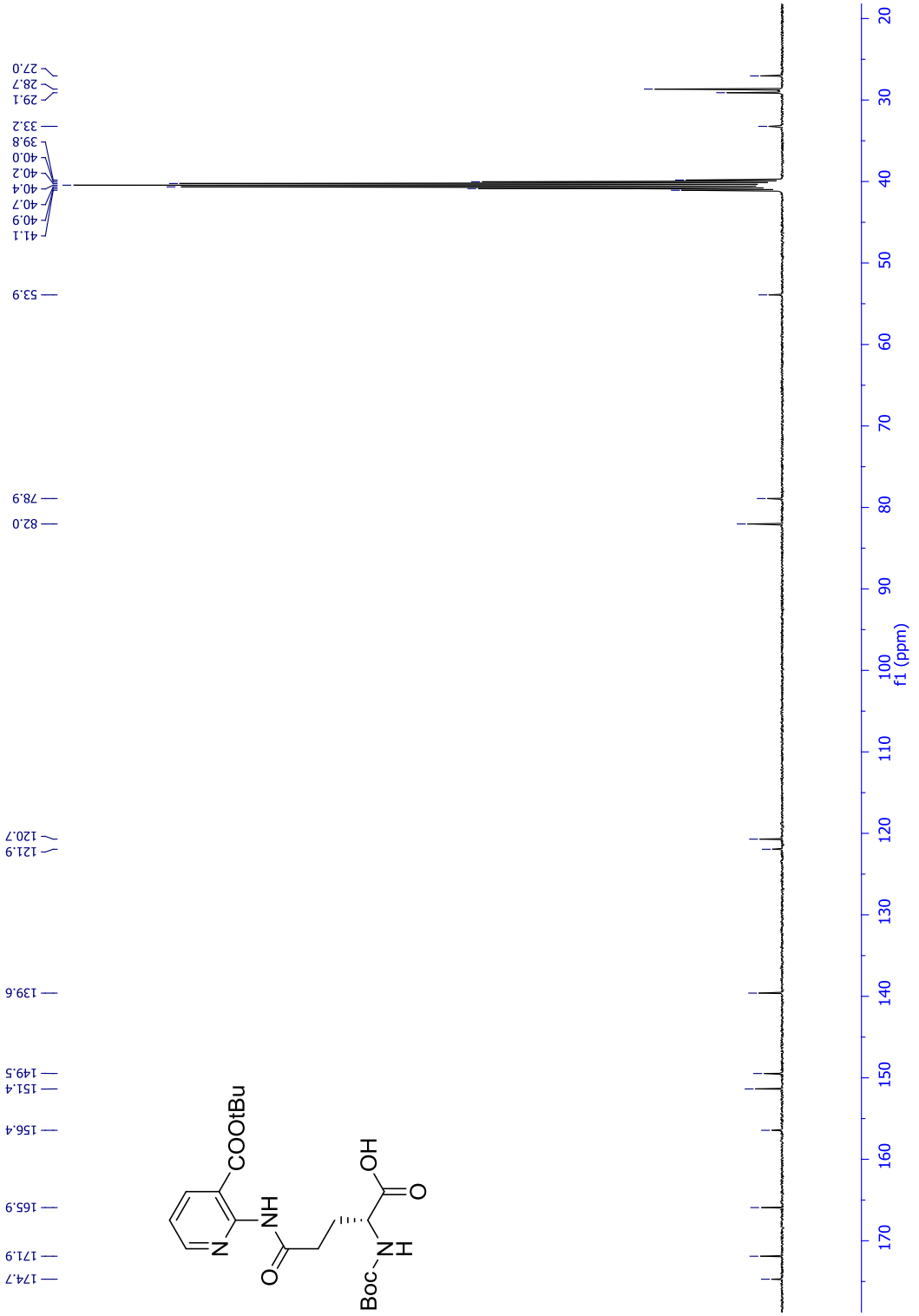
N-[3-(*tert*-butoxycarbonyl)pyridin-2-yl]-*N*-2-{[(9*H*-fluoren-9-yl)methoxy]carbonyl}-L-glutamine (Fmoc-L-Gln(*t*Bu-nic)-OH, DM674) **L-4p** – **^{13}C NMR (101 MHz, DMSO-*d*$_6$)**



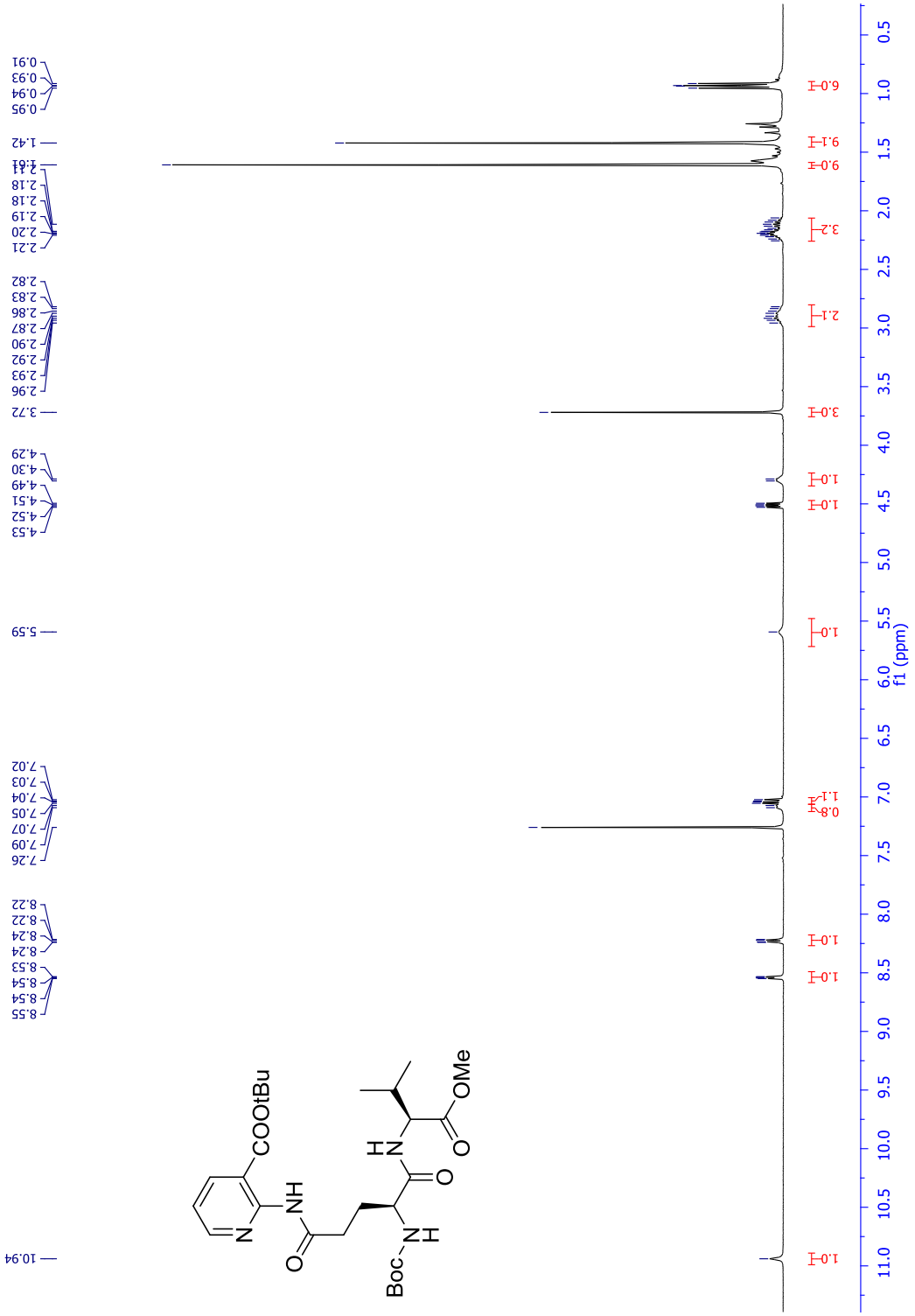
N^2-(*tert*-Butoxycarbonyl)-N^5-(3-(*tert*-butoxycarbonyl)pyridin-2-yl)-D-glutamine (Boc-D-Gln(NH-*t*Bu-nic)-OH, DM602) **D-4o - ^{1}H NMR (400 MHz, DMSO-d_6)**



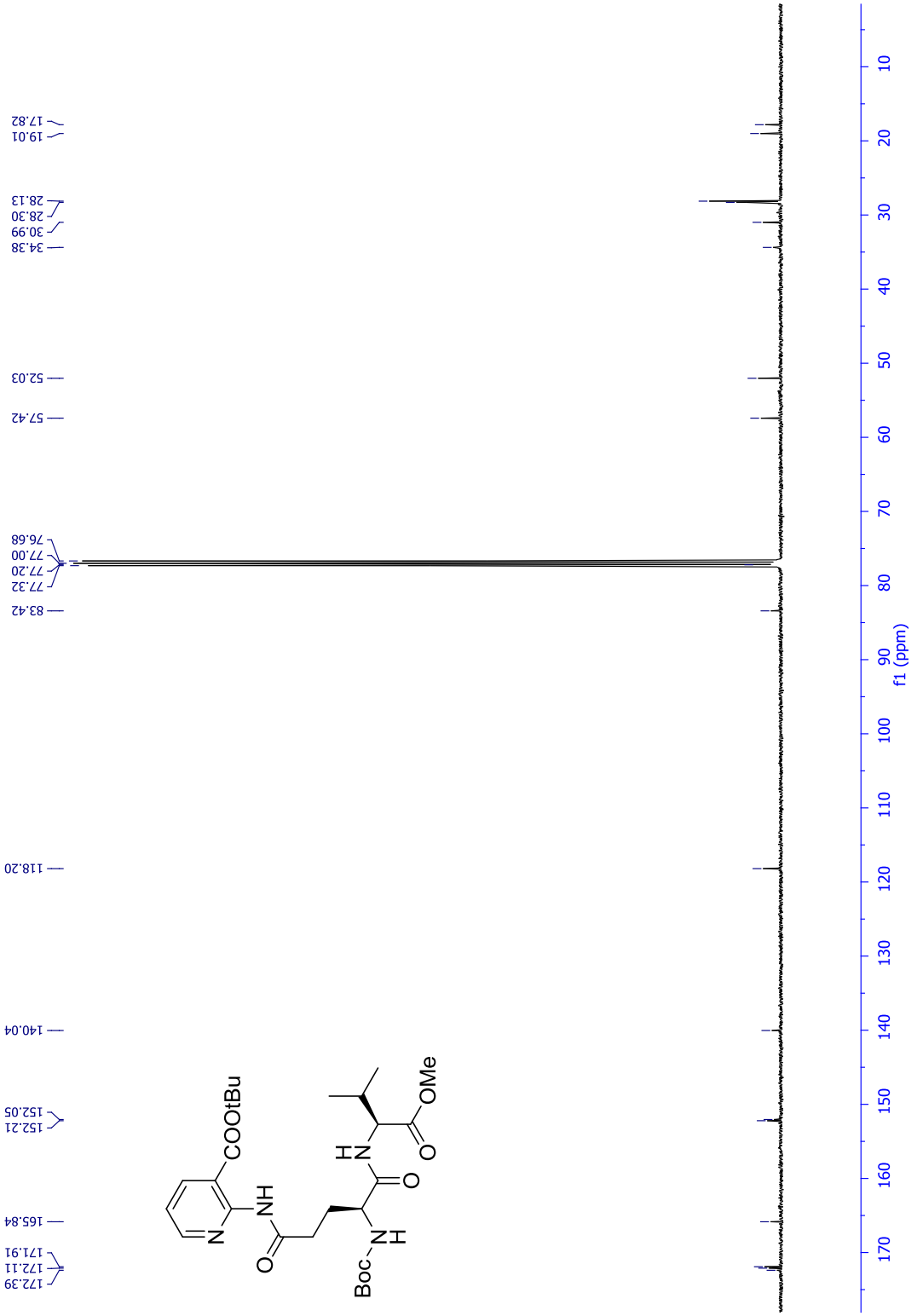
N^2-(*tert*-Butoxycarbonyl)-N^5-(3-(*tert*-butoxycarbonyl)pyridin-2-yl)-D-glutamine (Boc-D-Gln(NH-*t*Bu-nic)-OH, DM602) **D-4o** – **^{13}C NMR (100 MHz, DMSO-d_6)**



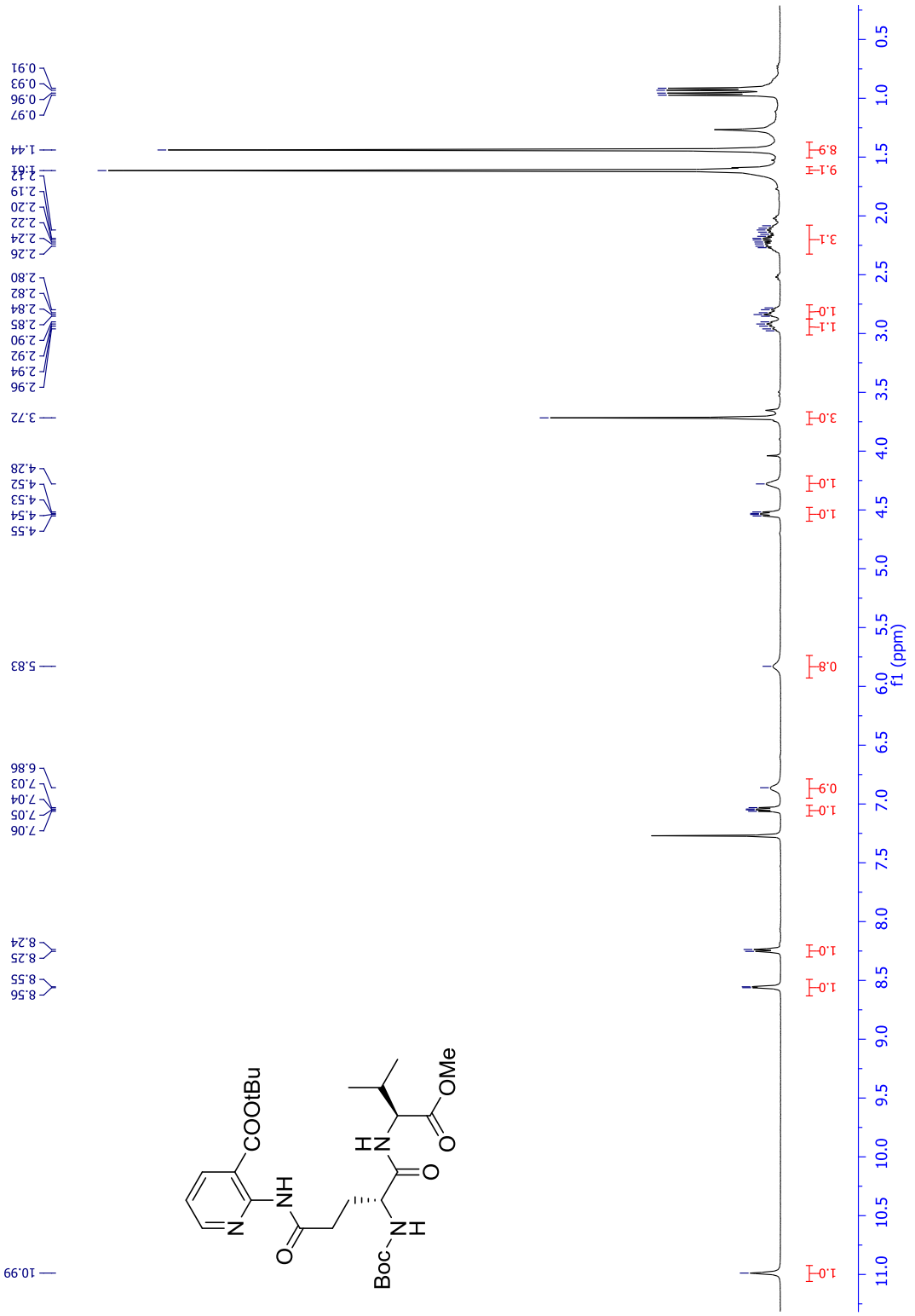
Methyl N^2-(*tert*-butoxycarbonyl)-*N*-[3-(*tert*-butoxycarbonyl)pyridin-2yl]-L-glutaminyl-L-valinate (Boc-L-Gln(*t*Bu-nic)-L-Val-OMe, DM58) **L,L-21 - ^{1}H NMR (400 MHz, $CDCl_3$)**



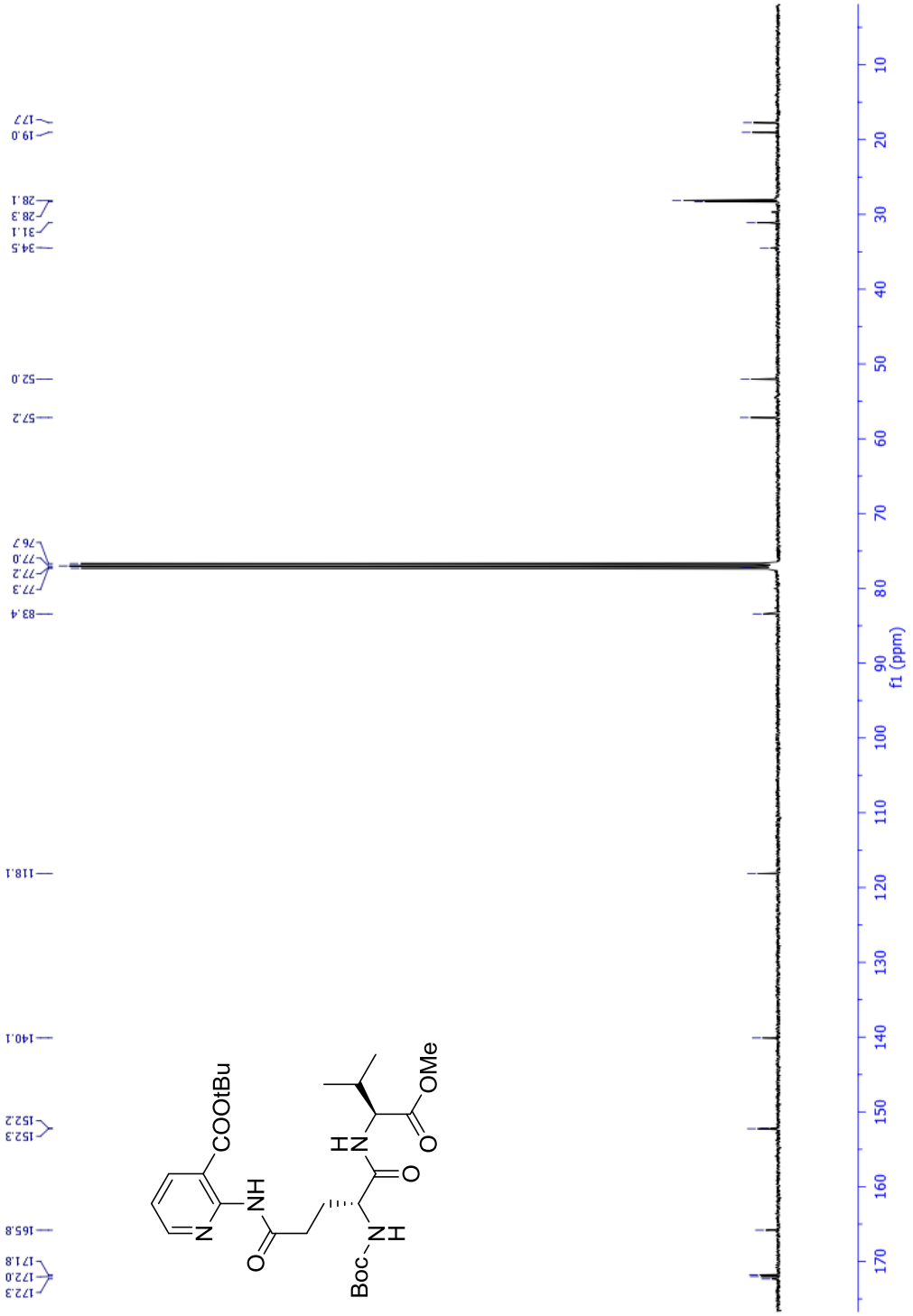
Methyl N^2-(*tert*-butoxycarbonyl)-*N*-[3-(*tert*-butoxycarbonyl)pyridin-2yl]-L-glutaminyl-L-valinate (Boc-L-Gln(*t*Bu-nic)-L-Val-OMe, DM584) **L,L-21 - ^{1}H NMR (400 MHz, $CDCl_3$)**



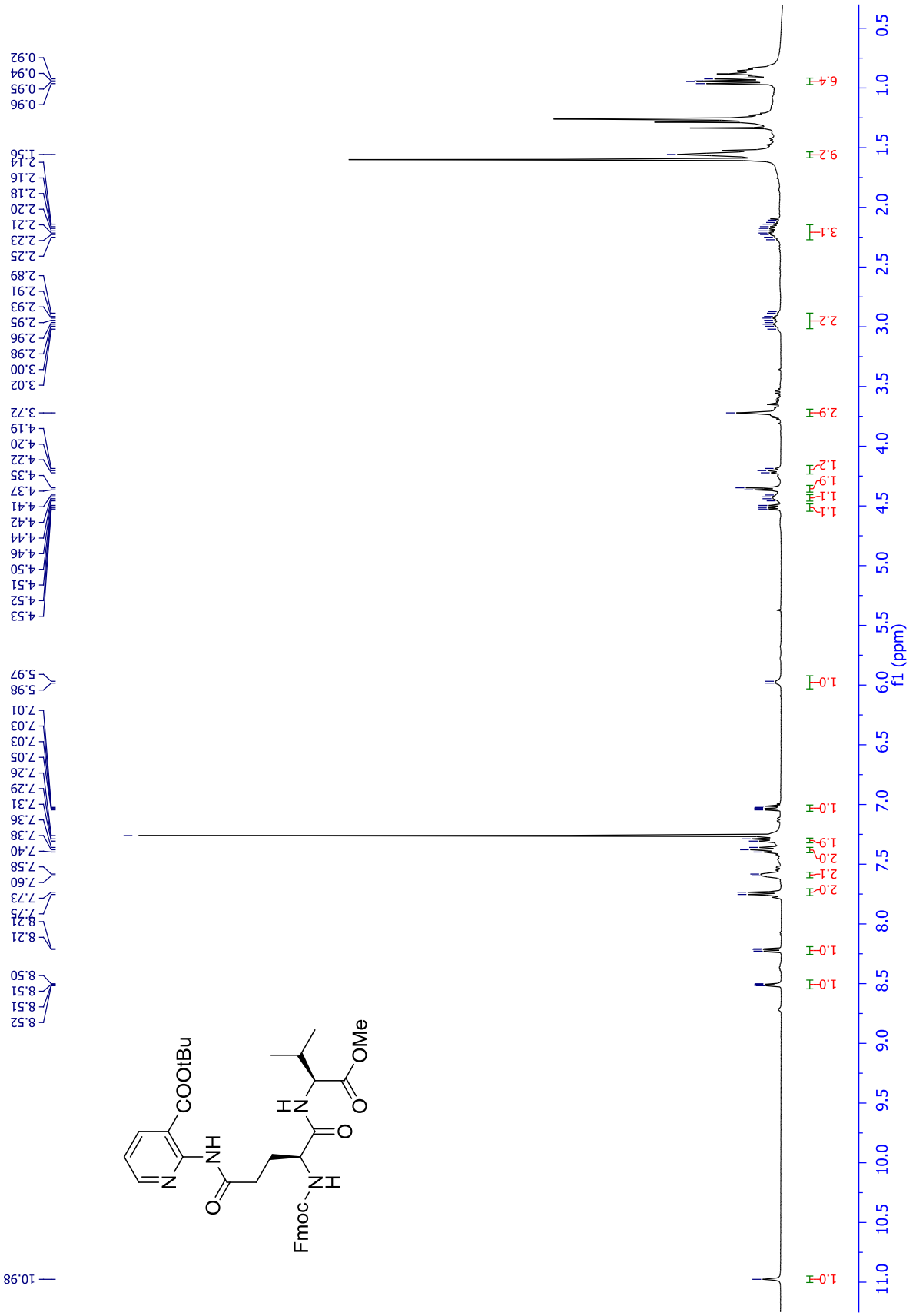
Methyl N^2-(*tert*-butoxycarbonyl)-*N*-[3-(*tert*-butoxycarbonyl)pyridin-2yl]-D-glutaminyl-L-valinate (Boc-D-Gln(*t*Bu-nic)-L-Val-OMe, DM593) **D,L-21 - ^{1}H NMR (400 MHz, $CDCl_3$)**



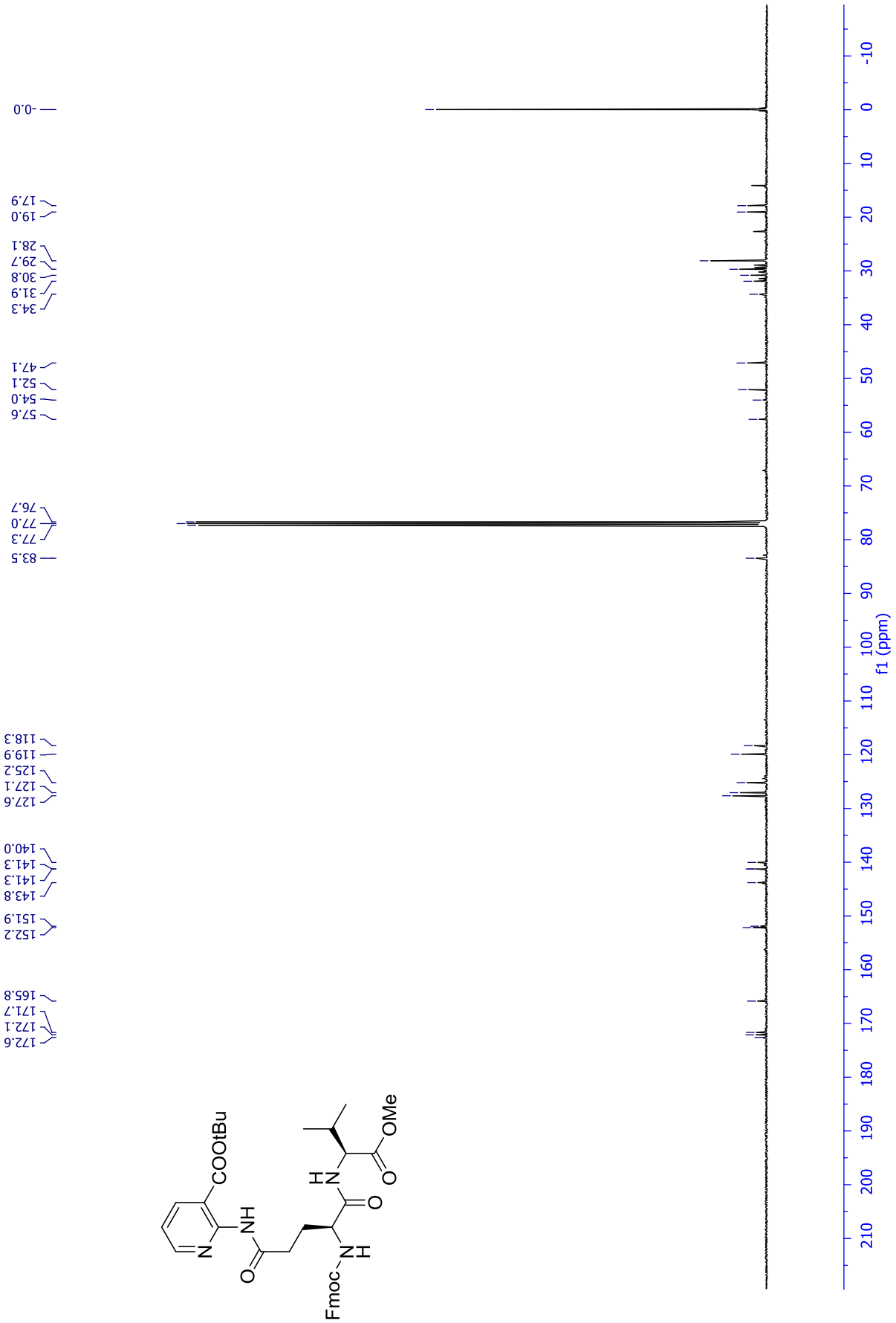
Methyl N^2-(*tert*-butoxycarbonyl)-*N*-[3-(*tert*-butoxycarbonyl)pyridin-2yl]-D-glutaminyl-L-valinate (Boc-D-Gln(*t*Bu-nic)-L-Val-OMe, DM593) **D,L-21 - ^{1}H NMR (400 MHz, $CDCl_3$)**



Methyl *N*-[3-(*tert*-butoxycarbonyl)pyridin-2-yl]-N^2~-{[(9*H*-fluoren-9-yl)methoxy]carbonyl}-L-glutaminyl-L-valinate (Fmoc-L-Gln(*t*Bu-nic)-L-Val-OMe) **L,L-23 - ^{1}H NMR (400 MHz, $CDCl_3$)**

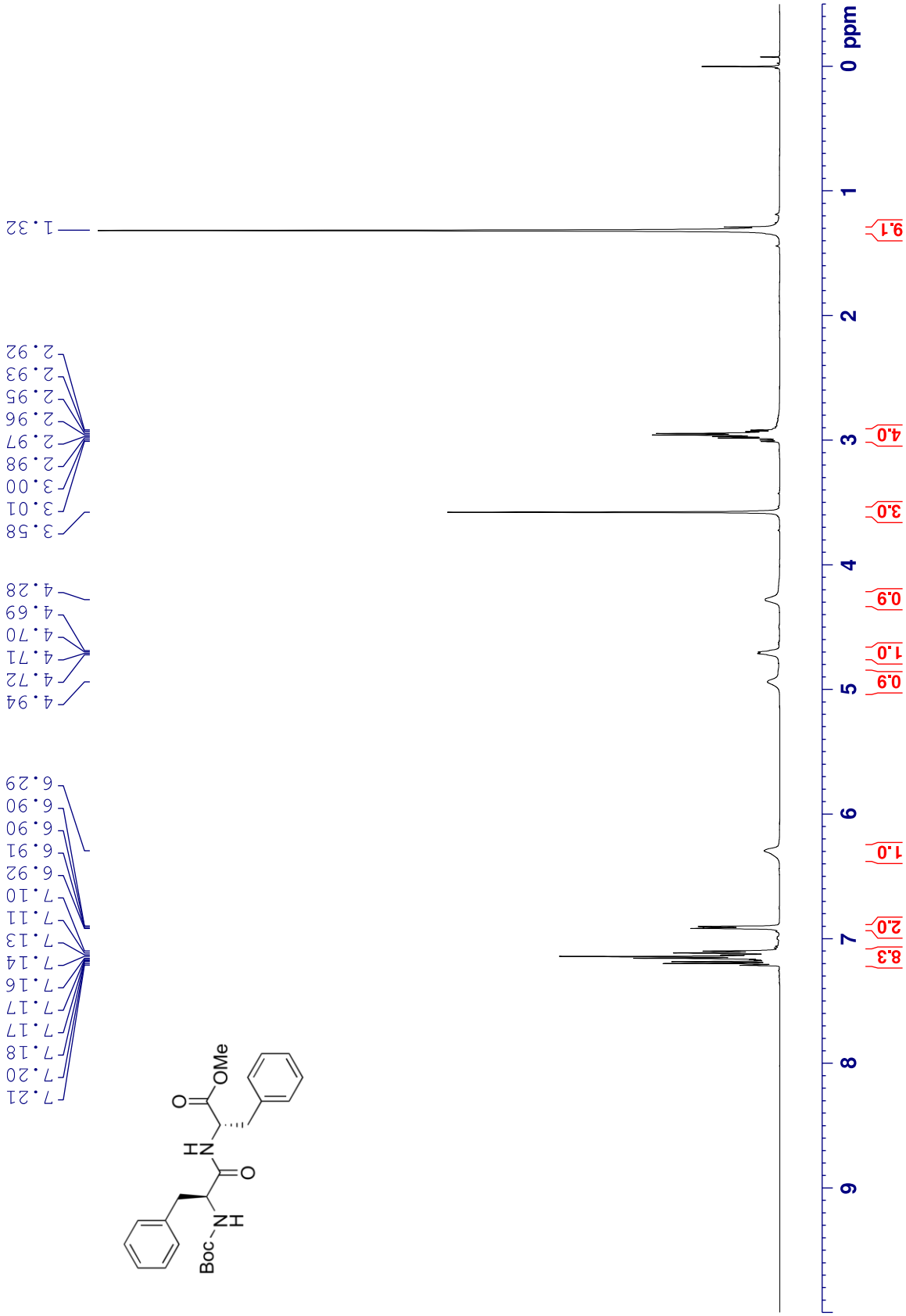


Methyl *N*-[3-(*tert*-butoxycarbonyl)pyridin-2-yl]-N^2~-{[(9*H*-fluoren-9-yl)methoxy]carbonyl}-L-glutaminyl-L-valinate (Fmoc-L-Gln(*t*Bu-nic)-L-Val-OMe) **L,L-23 – ^{13}C NMR (101 MHz, $CDCl_3$)**



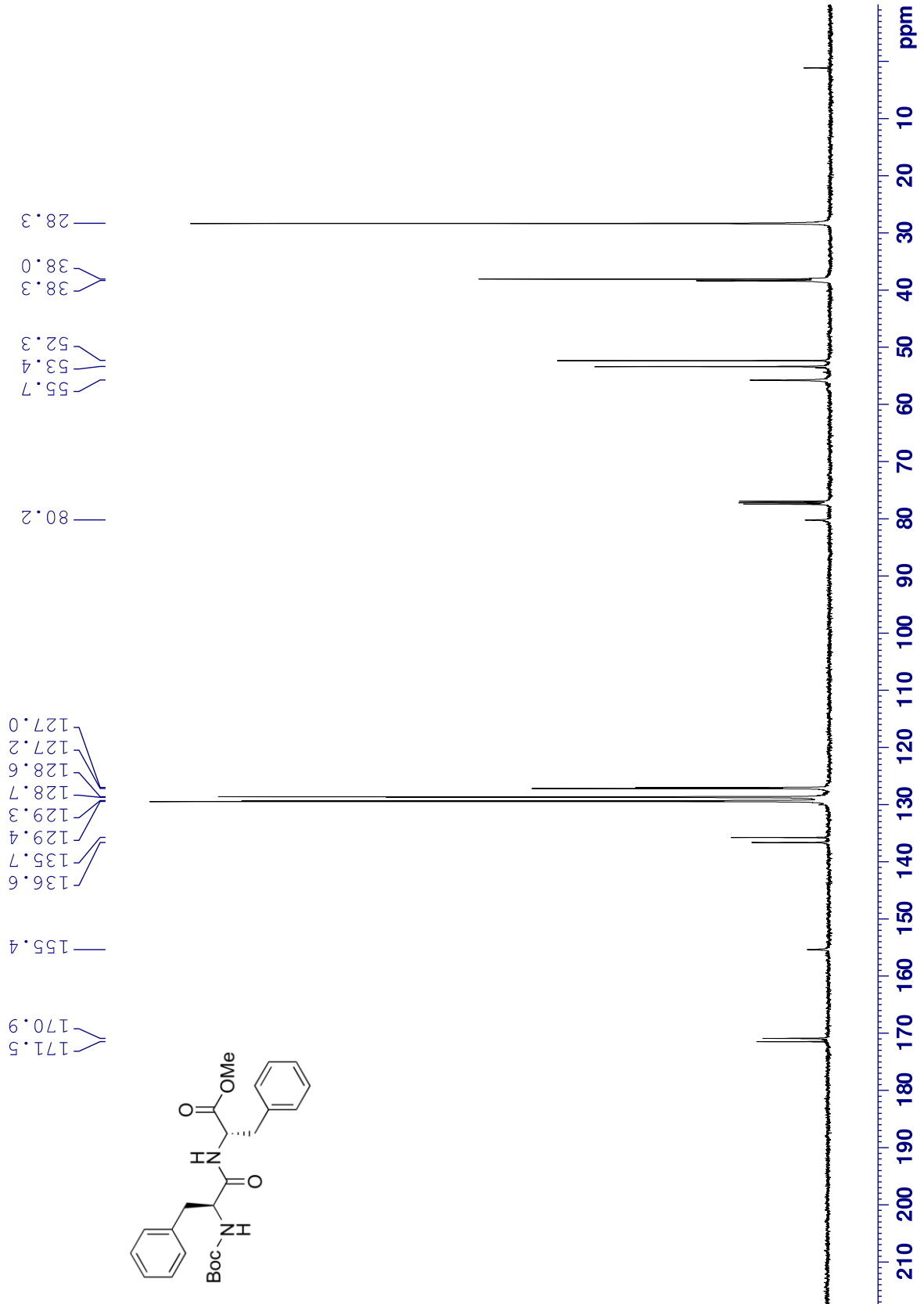
Methyl (*tert*-butoxycarbonyl)-L-phenylalanyl-L-phenylalaninate (Boc-L-Phe-L-Phe-OMe, KH_1160)

L,L-6a - ^{1}H NMR (500 MHz, $CDCl_3$)

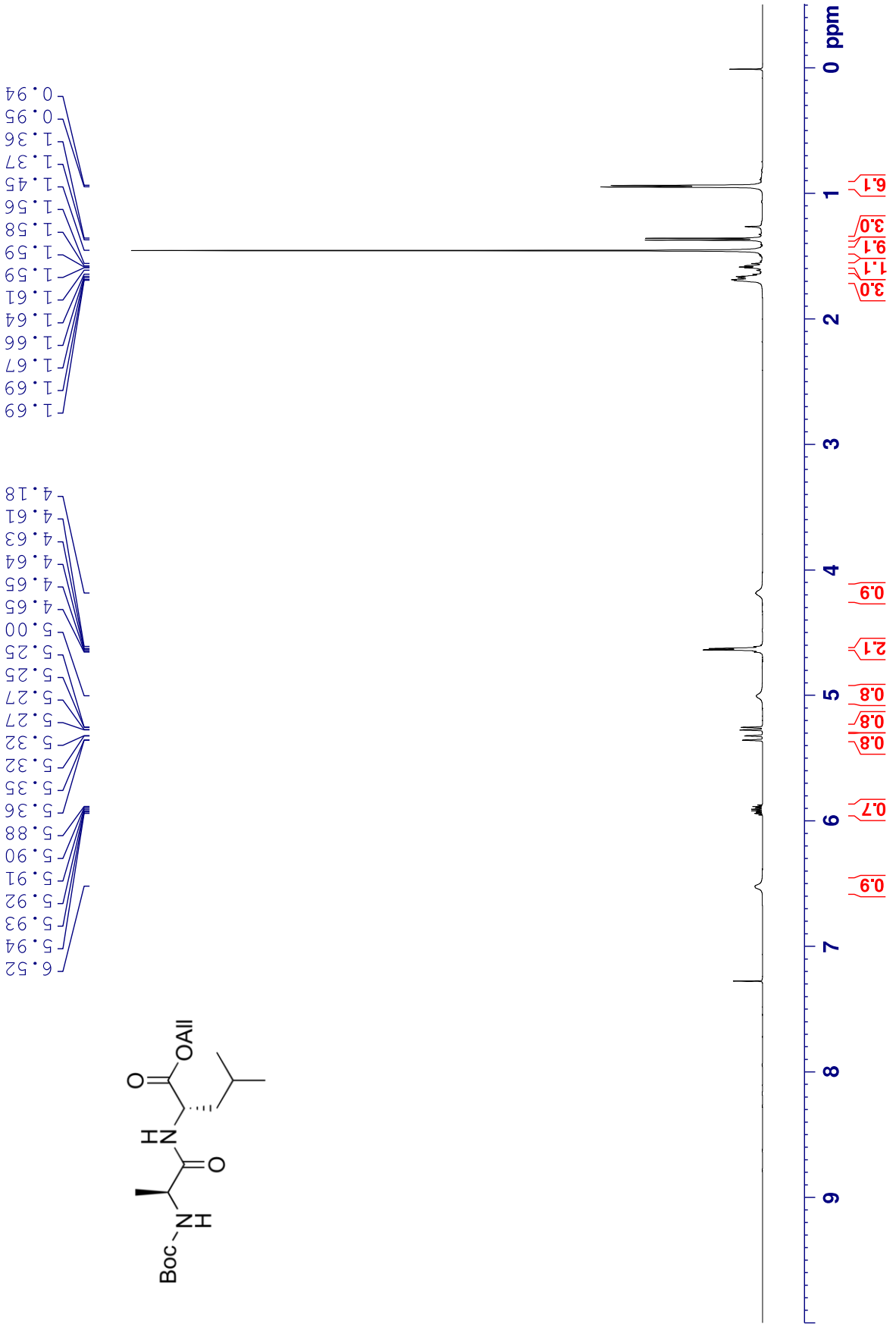


Methyl (*tert*-butoxycarbonyl)-L-phenylalanyl-L-phenylalaninate (Boc-L-Phe-L-Phe-OMe, KH_1160)

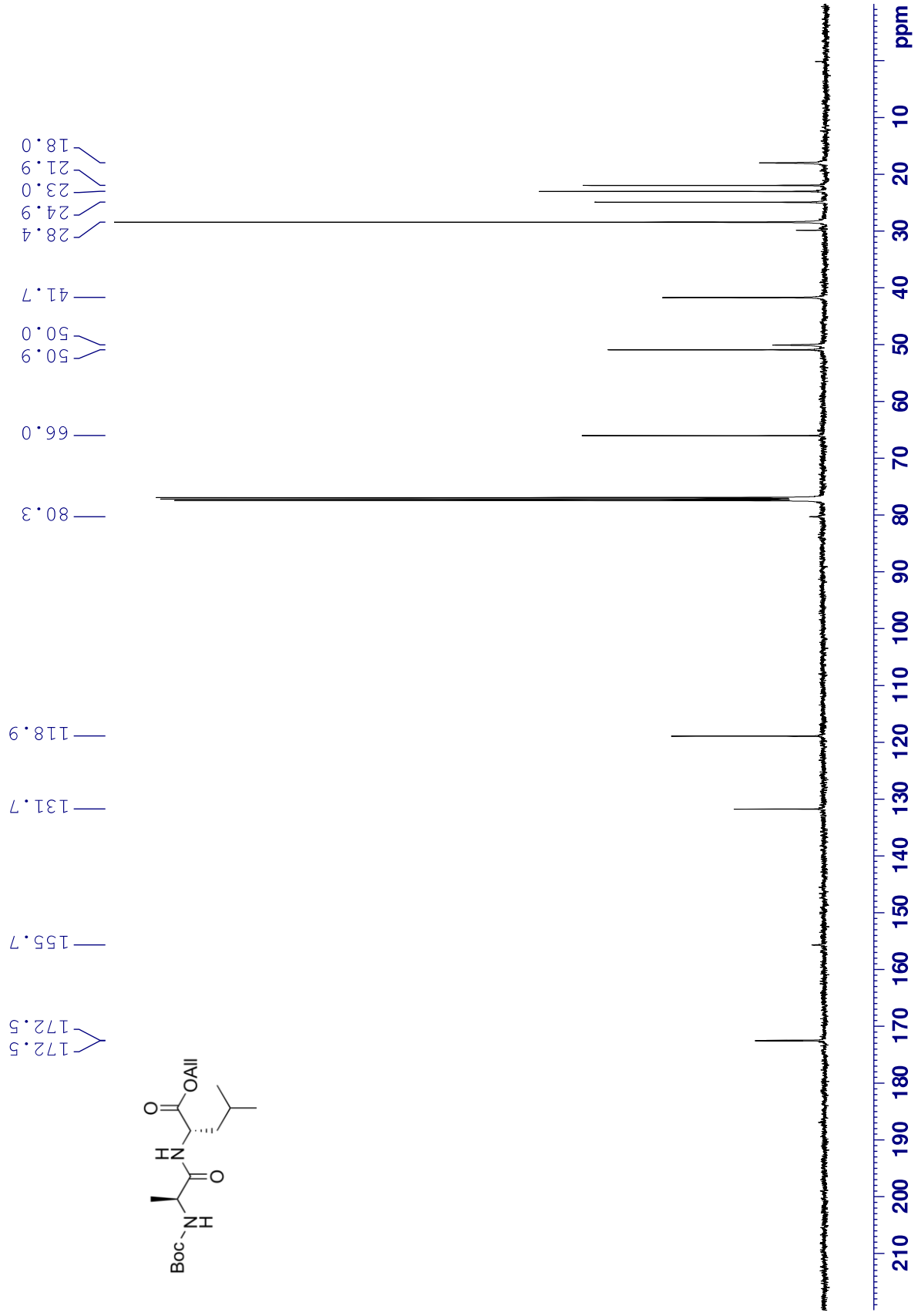
L,L-6a - ^{13}C NMR (126 MHz, $CDCl_3$)



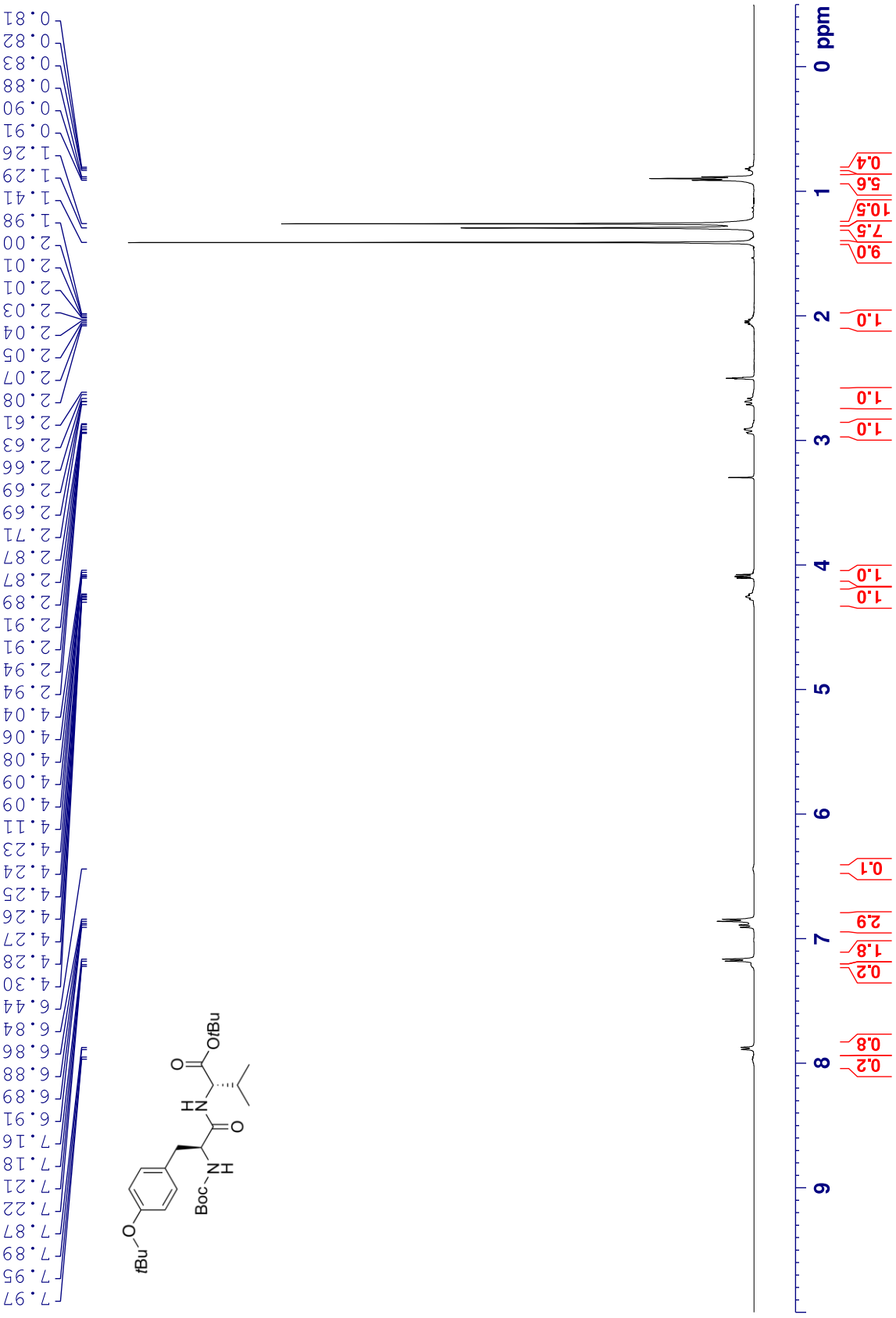
Prop-1-en-1-yl (*tert*-butoxycarbonyl)-L-alanyl-L-leucinate (Boc-L-Ala-L-Leu-OAll, KH_1197) **L,L-6b - ^{1}H NMR (500MHz, $CDCl_3$)**



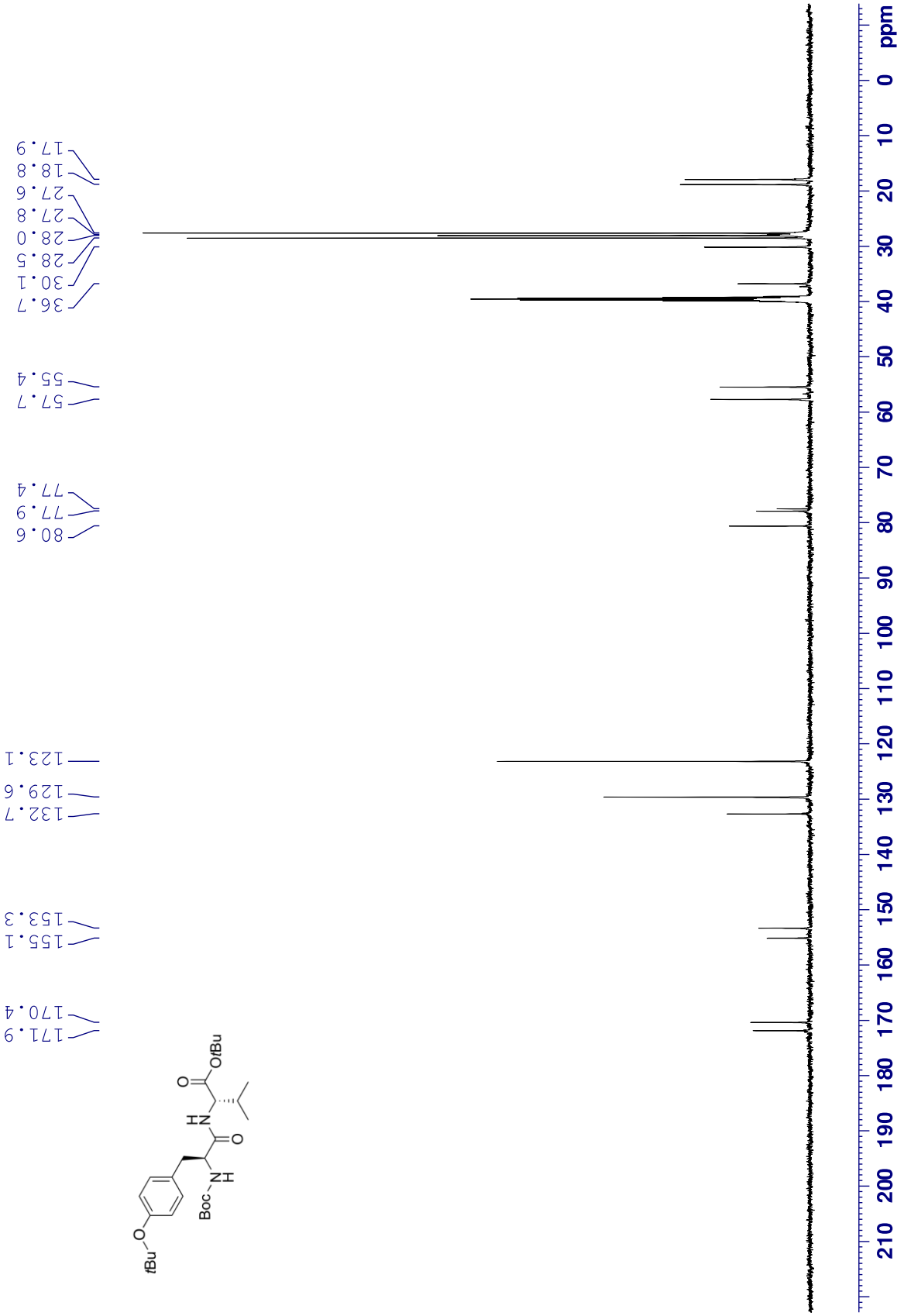
Prop-1-en-1-yl (*tert*-butoxycarbonyl)-L-alanyl-L-leucinate (Boc-L-Ala-L-Leu-OAll, KH_1197) **L,L-6b - ^{13}C NMR (126MHz, $CDCl_3$)**



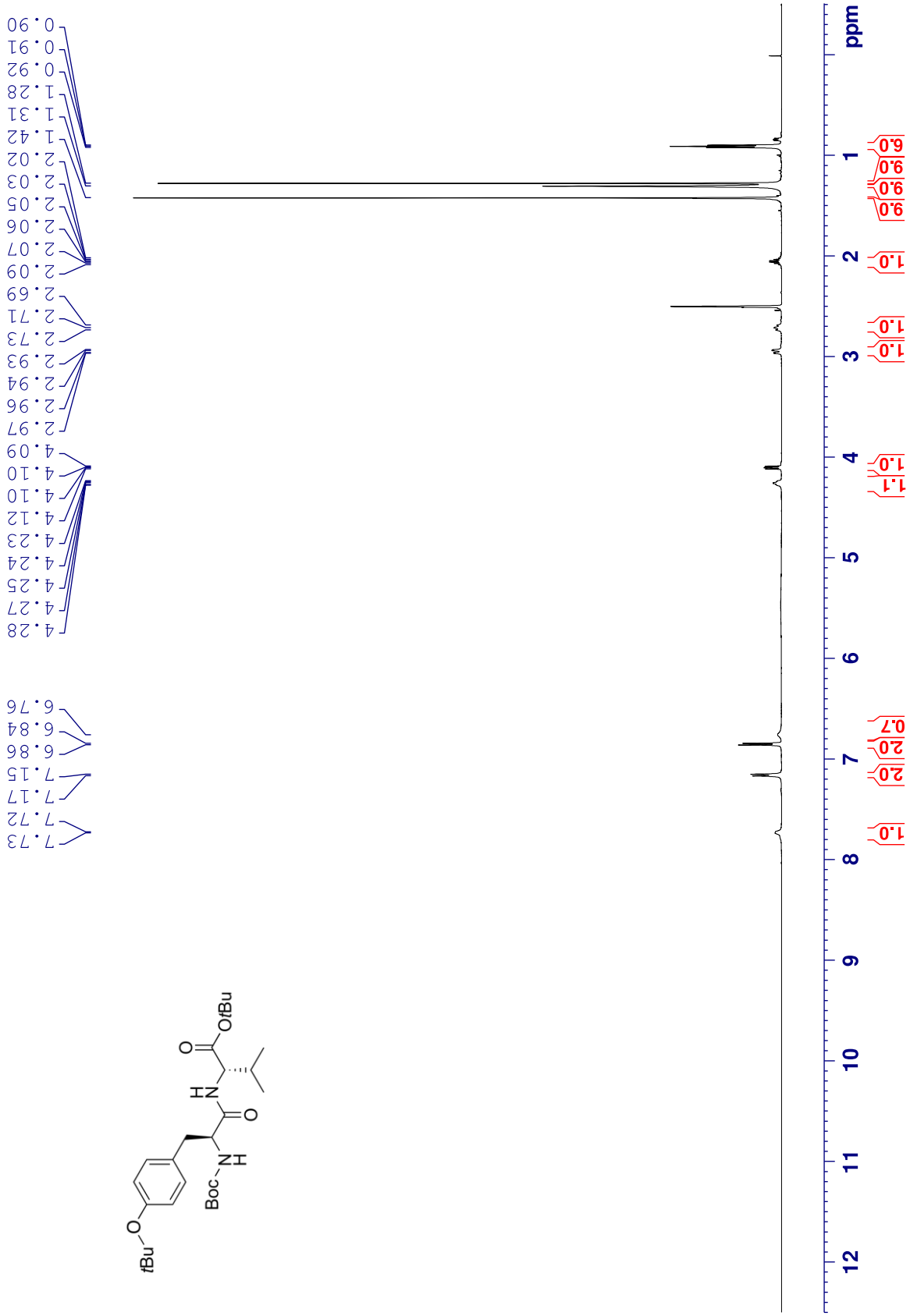
tert-Butyl ((*S*)-3-(4-(*tert*-butoxy)phenyl)-2-((*tert*-butoxycarbonyl)amino)propanoyl)-L-valinate (Boc-L-Tyr(*t*Bu)-L-Val-O*t*Bu, KH_1245) **L,L-6c - ^{1}H NMR (500 MHz, DMSO-*d*$_6$, mixture of rotamers)**



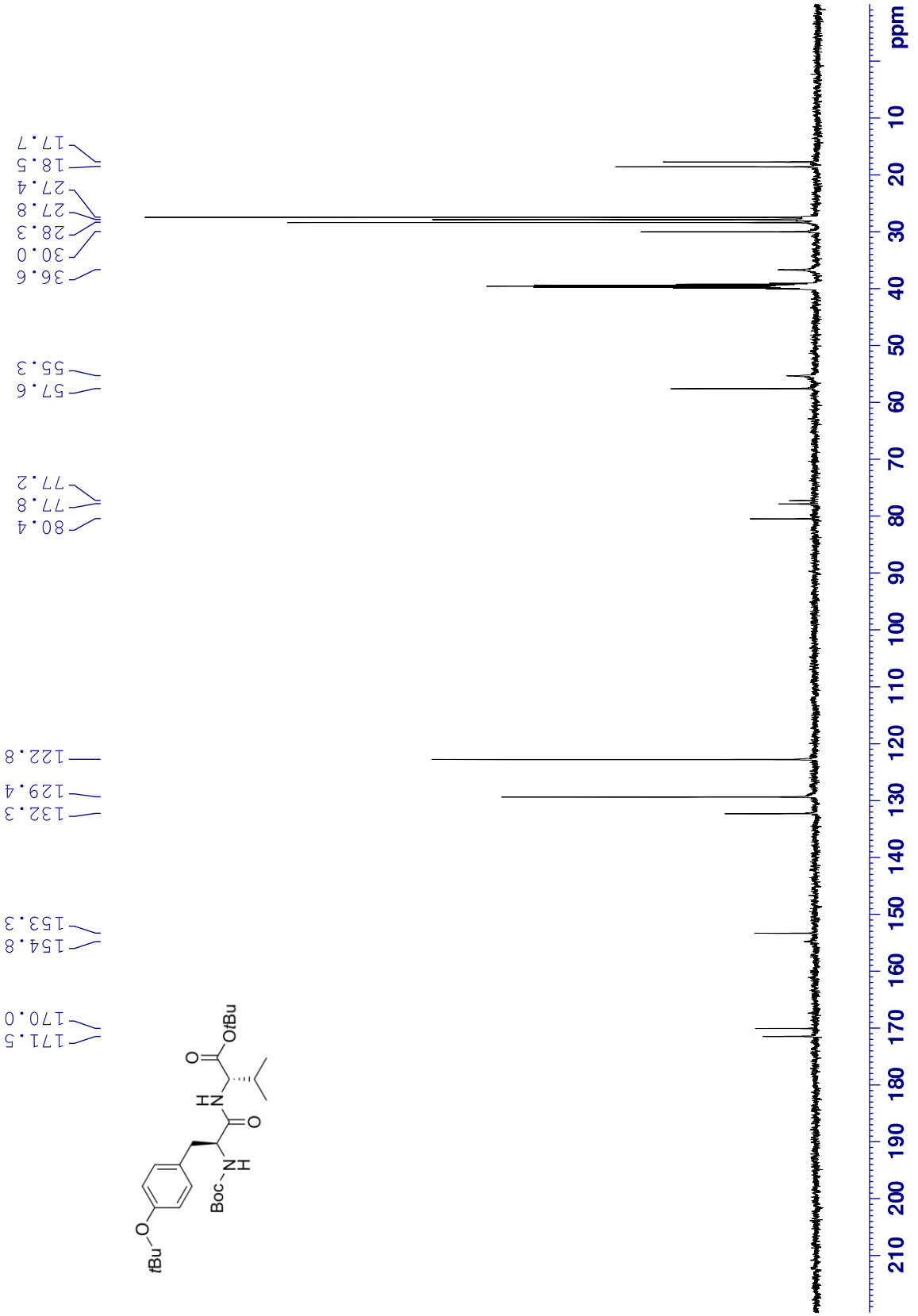
tert-Butyl ((*S*)-3-(4-(*tert*-butoxy)phenyl)-2-((*tert*-butoxycarbonyl)amino)propanoyl)-L-valinate (Boc-L-Tyr(*t*Bu)-L-Val-O*t*Bu, KH_1245) **L,L-6c - ^{13}C NMR (126 MHz, DMSO-d_6, mixture of rotamers)**



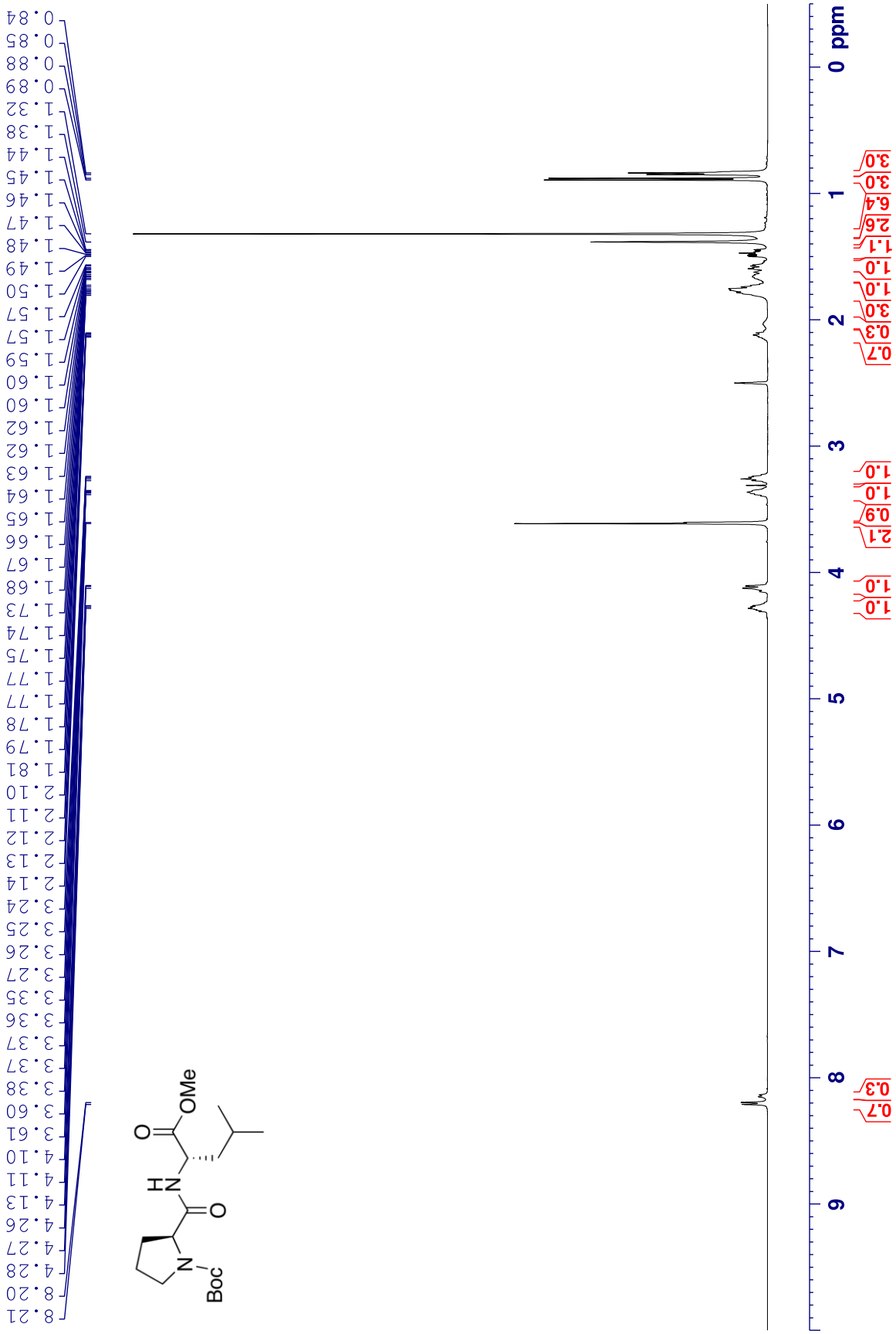
tert-Butyl ((*S*)-3-(4-(*tert*-butoxy)phenyl)-2-((*tert*-butoxycarbonyl)amino)propanoyl)-L-valinate (Boc-L-Tyr(*t*Bu)-L-Val-O*t*Bu, KH_1245) **L,L-6c - ^{1}H NMR (500 MHz, DMSO-d$_6$, 60°C)**



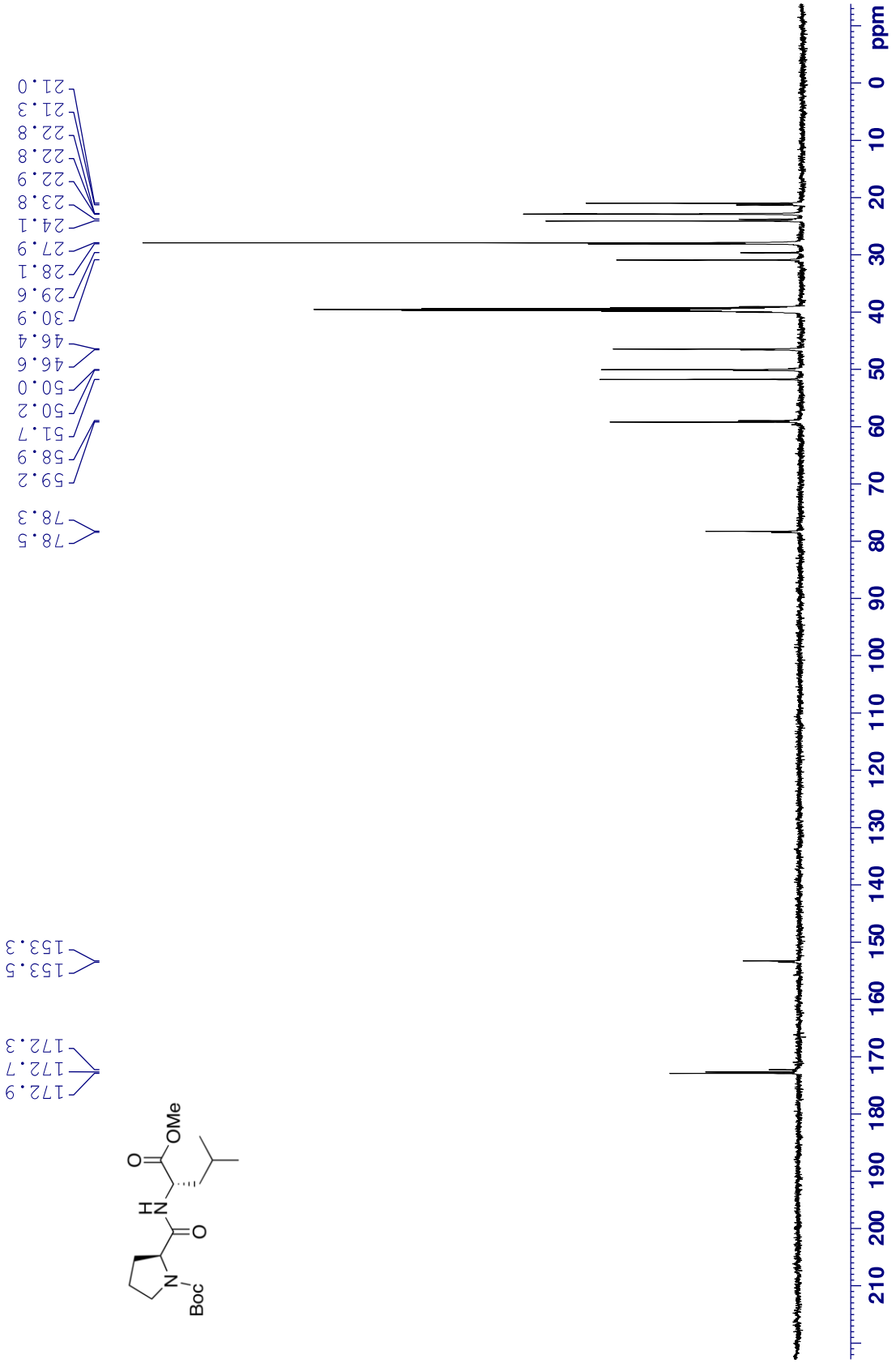
tert-Butyl ((*S*)-3-(4-(*tert*-butoxy)phenyl)-2-((*tert*-butoxycarbonyl)amino)propanoyl)-L-valinate (Boc-L-Tyr(*t*Bu)-L-Val-O*t*Bu, KH_1245) **L,L-6c - ^{13}C NMR (126 MHz, DMSO-*d*$_6$, 60°C)**



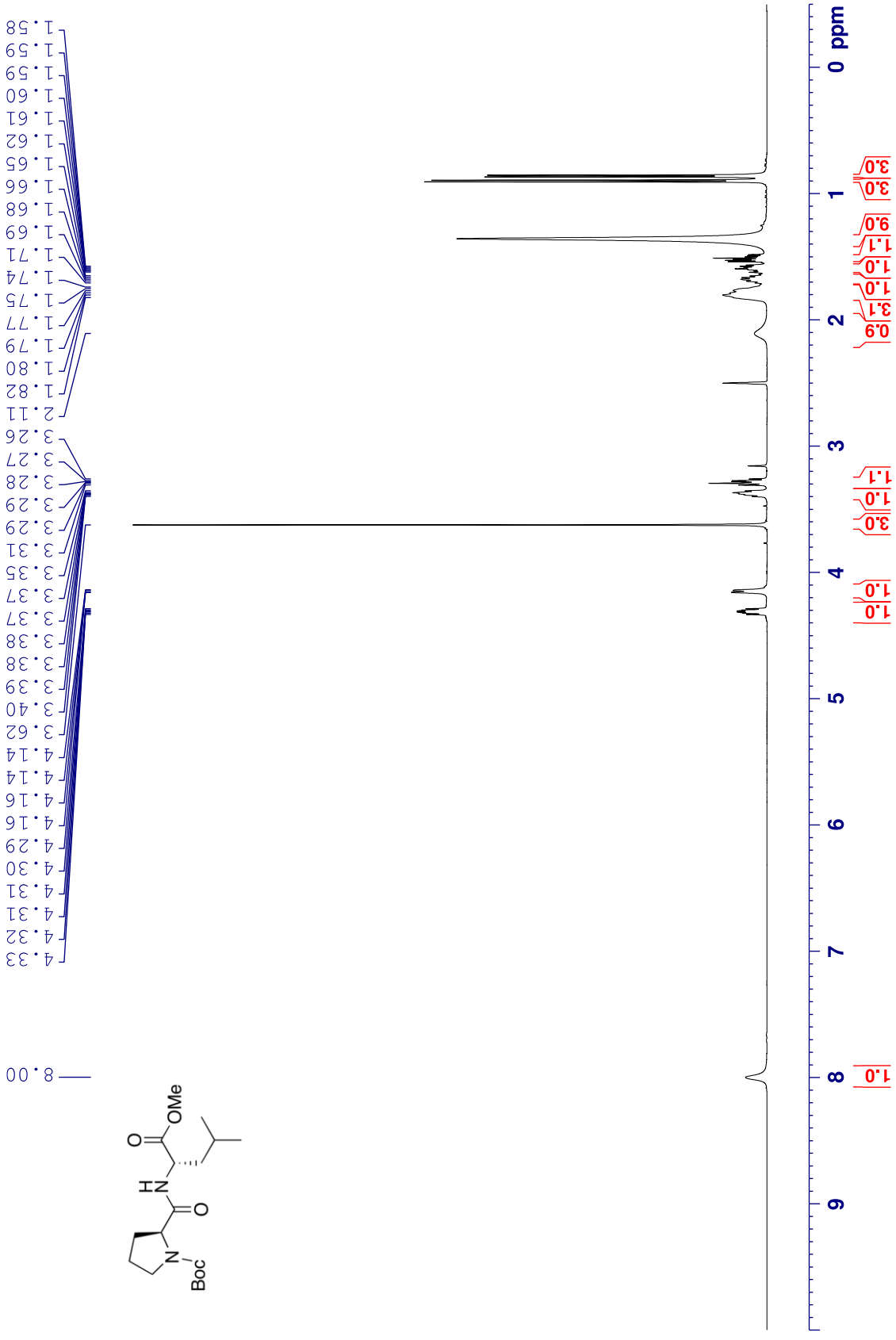
tert-Butyl (*S*)-2-(((*S*)-1-methoxy-4-methyl-1-oxopentan-2-yl)carbamoyl)pyrrolidine-1-carboxylate (Boc-L-Pro-L-Leu-OMe, KH_1196) **L,L-6d - ^{1}H NMR (500 MHz, DMSO-d_6, mixture of rotamers)**



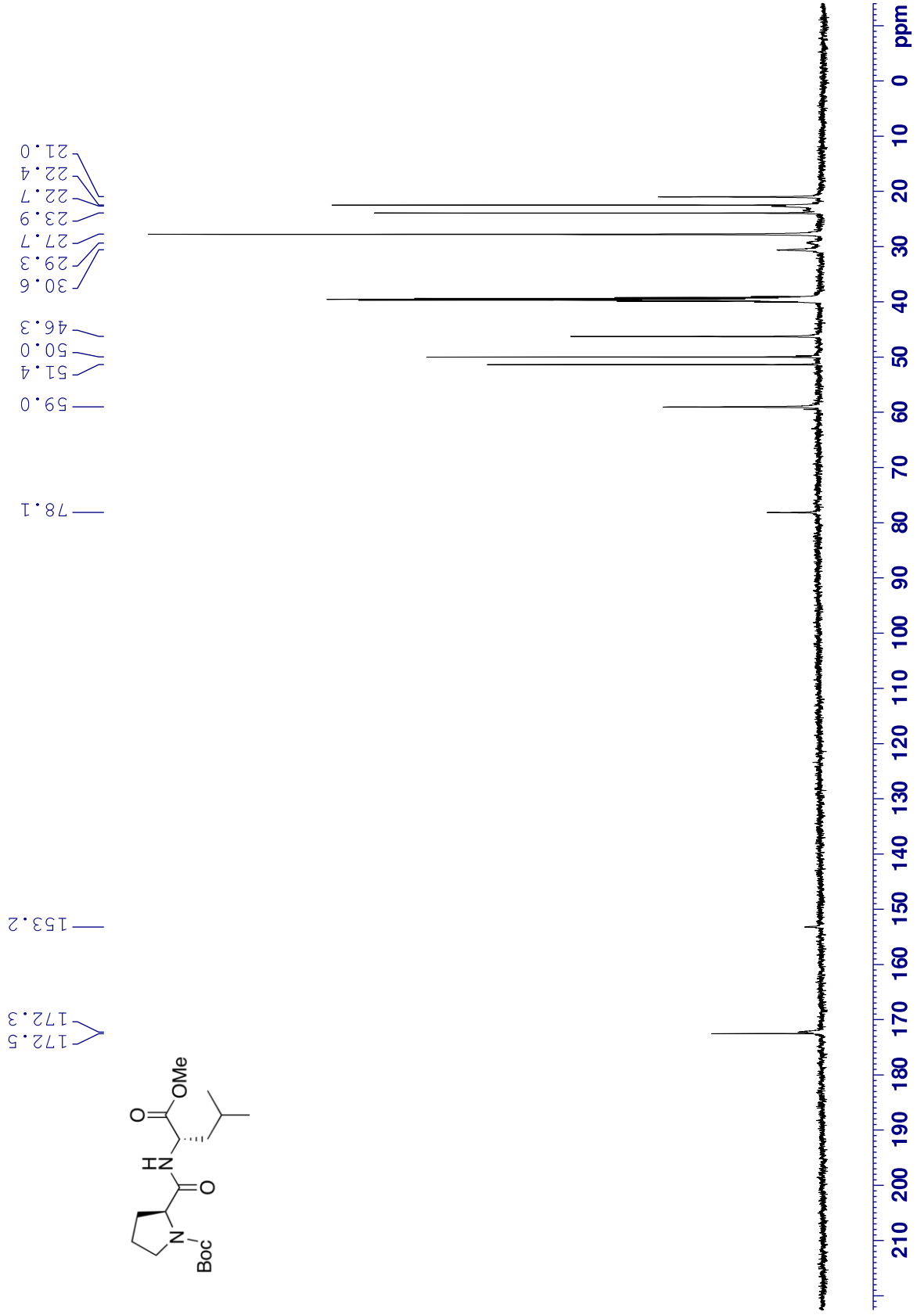
tert-Butyl (*S*)-2-(((*S*)-1-methoxy-4-methyl-1-oxopentan-2-yl)carbamoyl)pyrrolidine-1-carboxylate (Boc-L-Pro-L-Leu-OMe, KH_1196) **L,L-6d - ^{13}C NMR (126 MHz, DMSO-d_6, mixture of rotamers)**



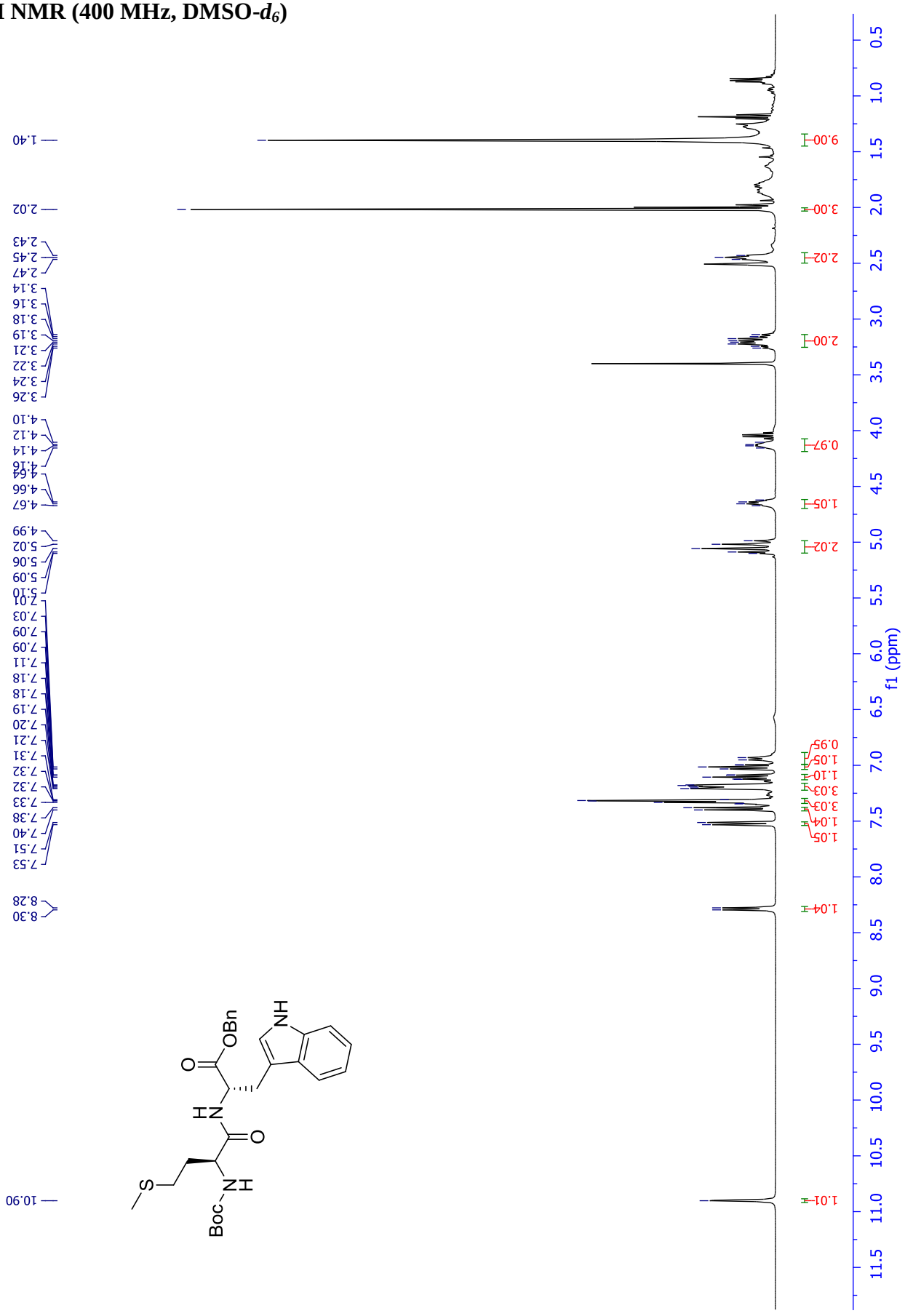
tert-Butyl (*S*)-2-(((*S*)-1-methoxy-4-methyl-1-oxopentan-2-yl)carbamoyl)pyrrolidine-1-carboxylate (Boc-L-Pro-L-Leu-OMe, KH_1196) **L,L-6d - ^{1}H NMR (500 MHz, DMSO-d_6, 60°C)**



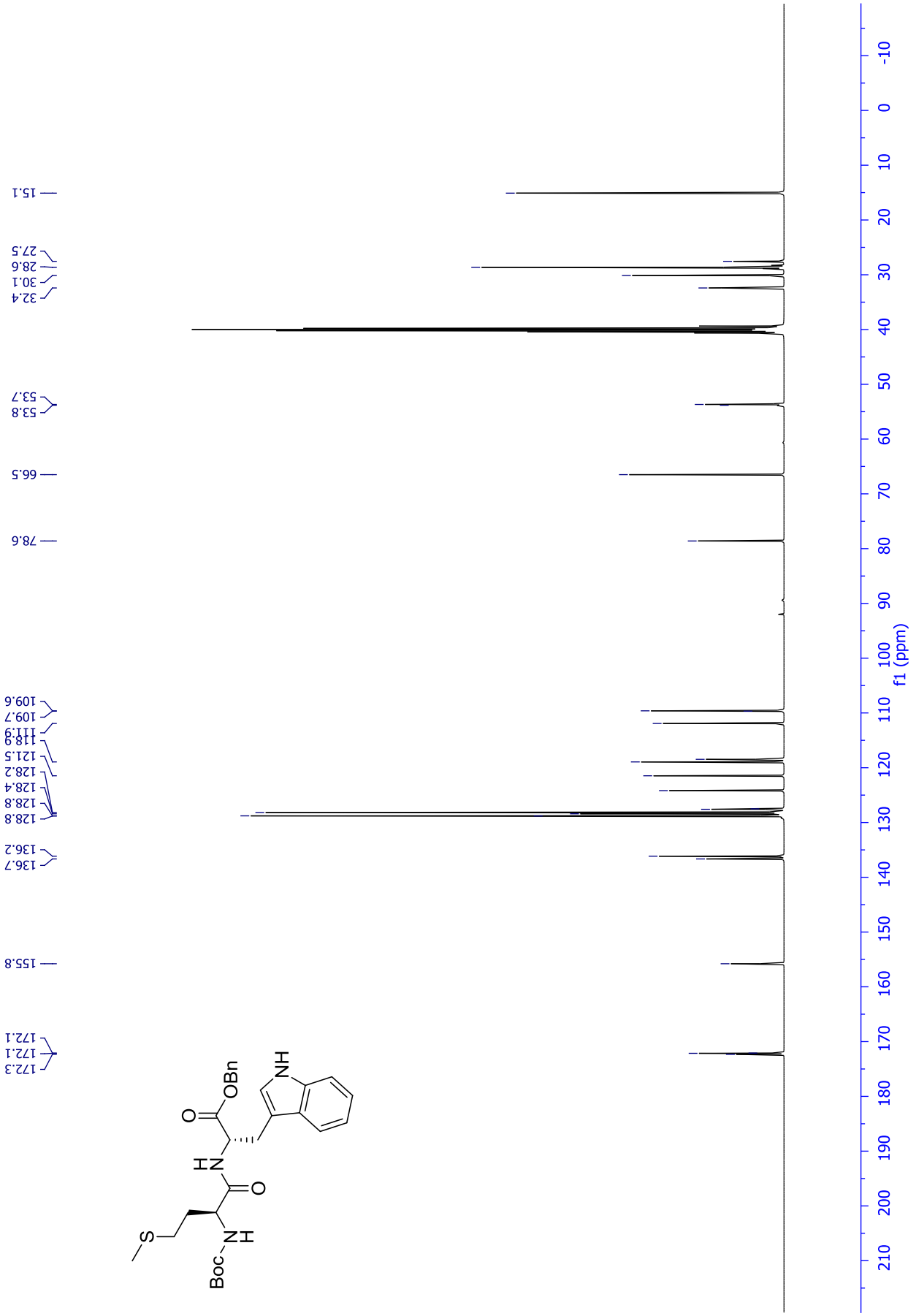
tert-Butyl (*S*)-2-(((*S*)-1-methoxy-4-methyl-1-oxopentan-2-yl)carbamoyl)pyrrolidine-1-carboxylate (Boc-L-Pro-L-Leu-OMe, KH_1196) **L,L-6d - ^{13}C NMR (126 MHz, DMSO-d_6, 60°C)**



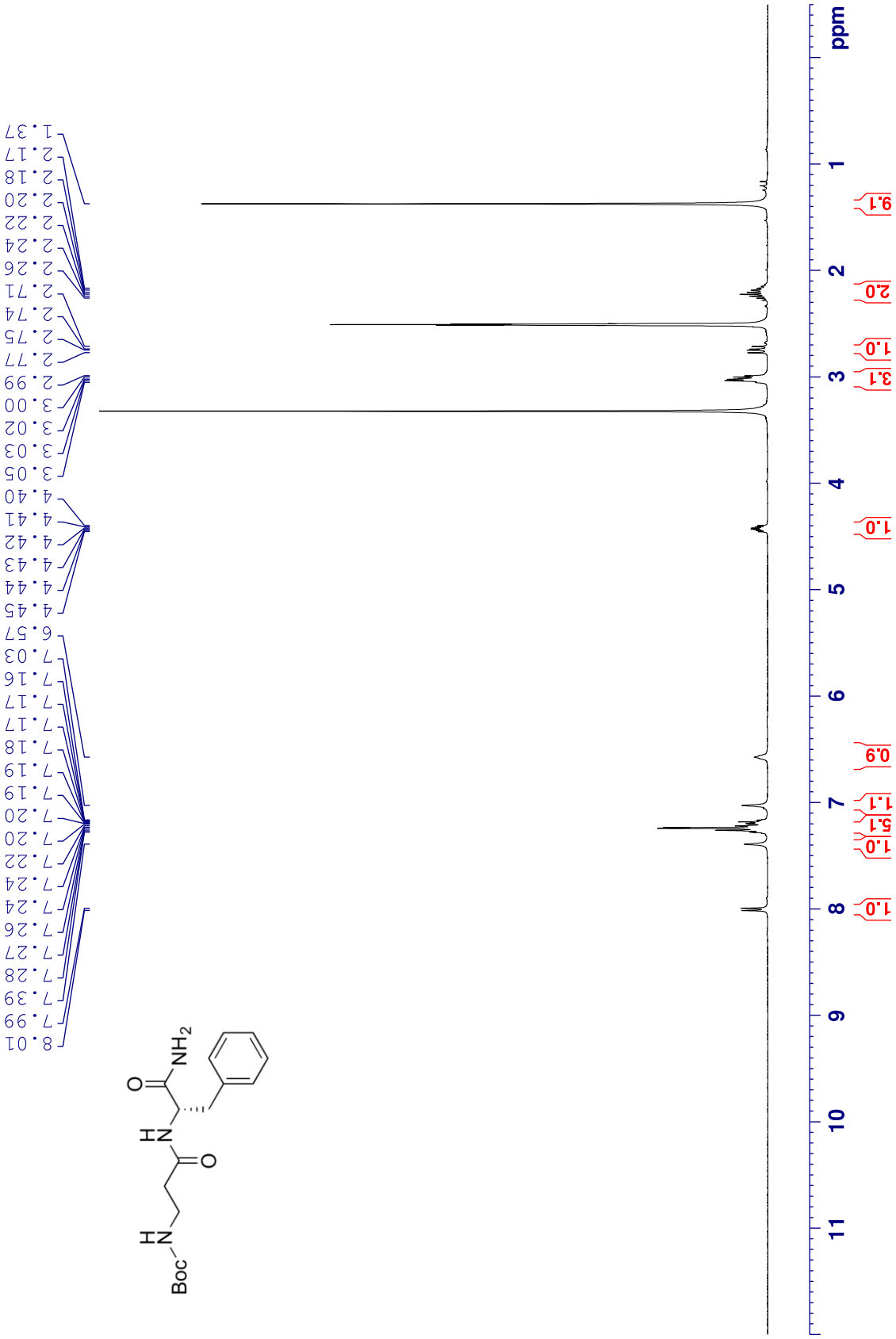
Benzyl (*tert*-butoxycarbonyl)-L-methionyl-L-tryptophanate (Boc-L-Met-L-Trp-OBn, DM769) **L,L-6e - ^{1}H NMR (400 MHz, DMSO-d_6)**



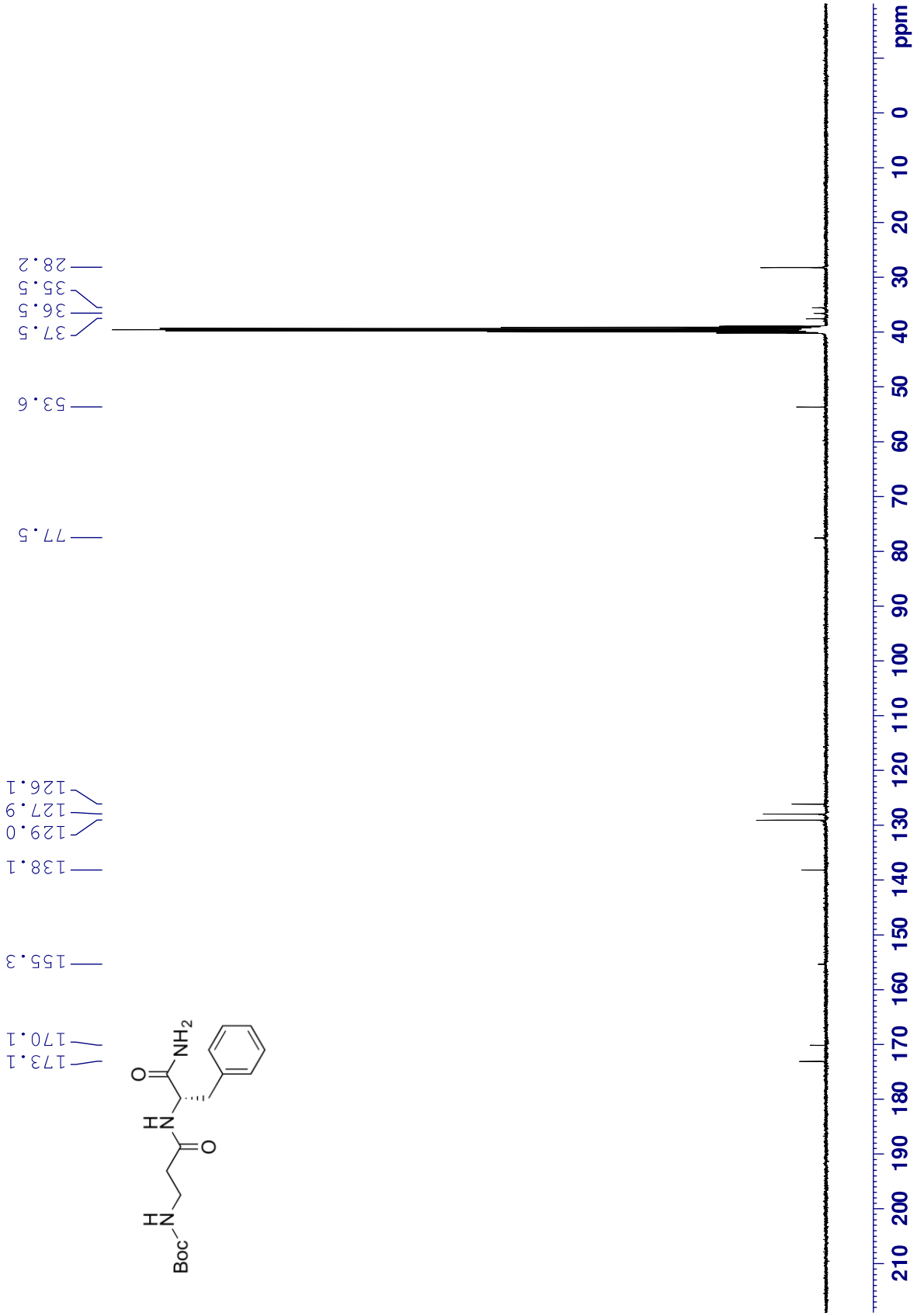
Benzyl (*tert*-butoxycarbonyl)-L-methionyl-L-tryptophanate (Boc-L-Met-L-Trp-OBn, DM769) **L,L-6e - ^{13}C NMR (400 MHz, DMSO-d_6,)**



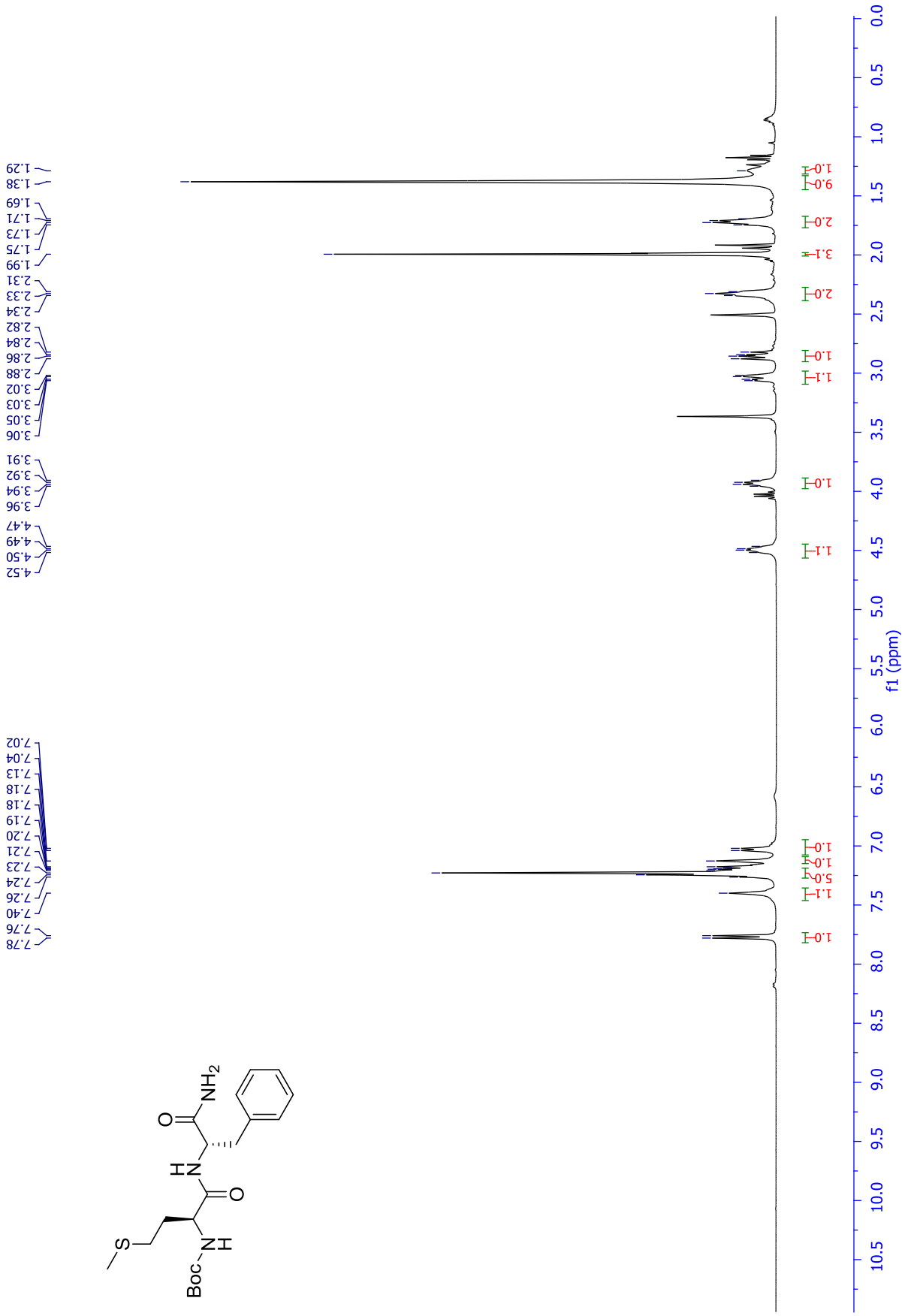
*tert-B*utyl (*S*)-(3-((1-amino-1-oxo-3-phenylpropan-2-yl)amino)-3-oxopropyl)carbamate (Boc-βAla-L-Phe-NH_2, DM332) **L-6f - ^{1}H NMR (400 MHz, DMSO-d_6)**



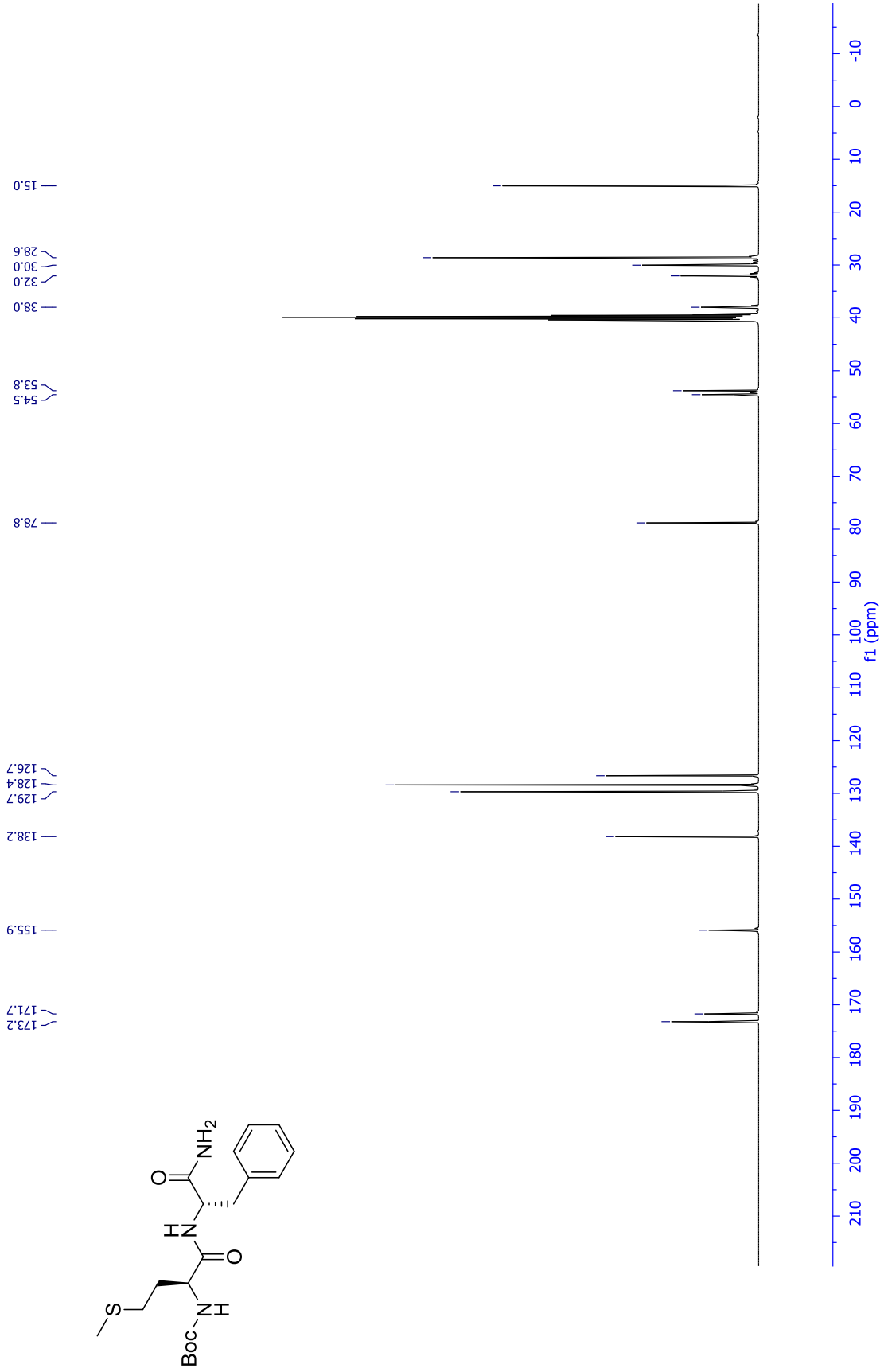
*tert-B*utyl (*S*)-(3-((1-amino-1-oxo-3-phenylpropan-2-yl)amino)-3-oxopropyl)carbamate (Boc-βAla-L-Phe-NH_2, DM332) **L-6f - ^{13}C NMR (100 MHz, DMSO-d_6)**



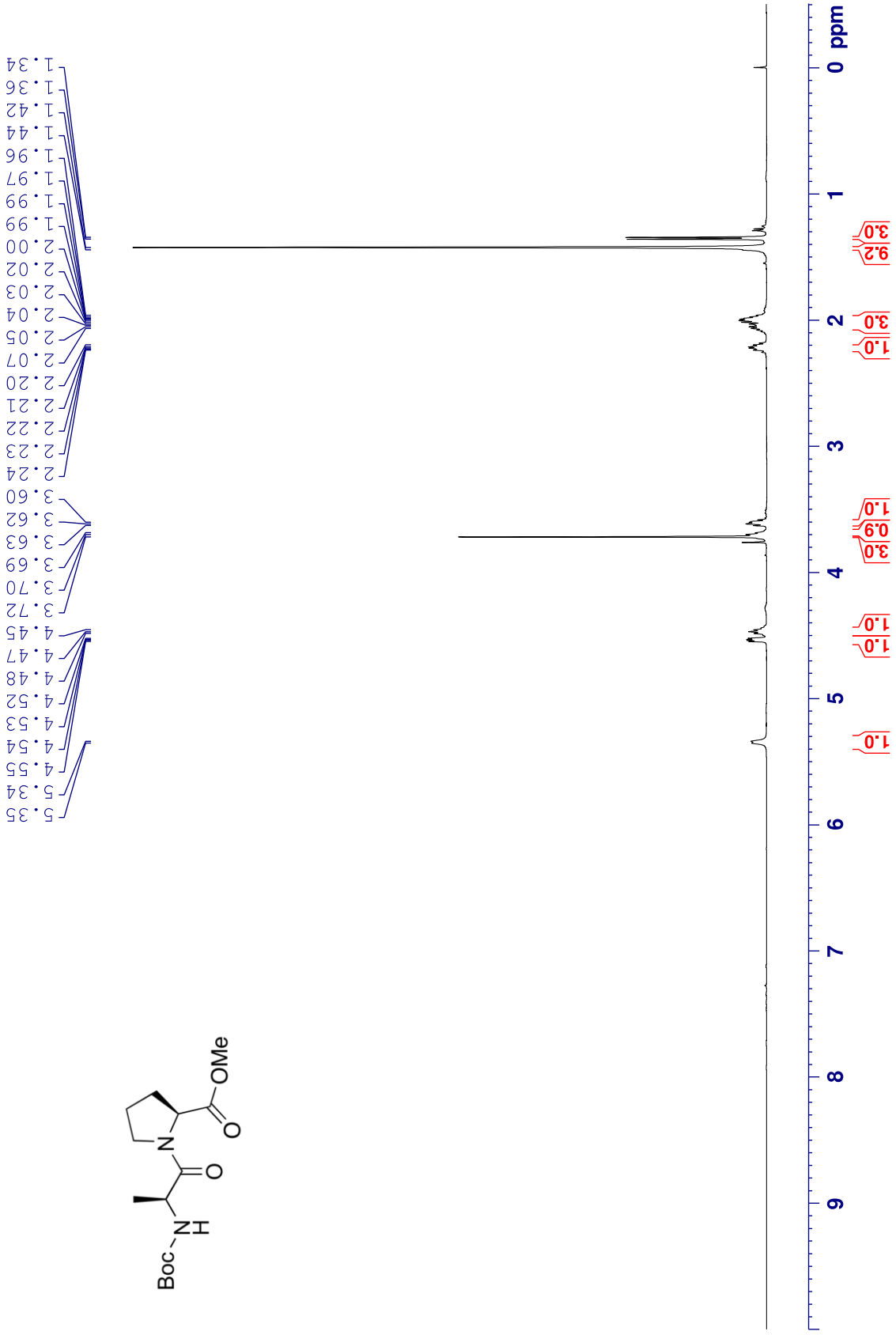
tert-Butyl ((*S*)-1-(((*S*)-1-amino-1-oxo-3-phenylpropan-2-yl)amino)-4-(methylthio)-1-oxobutan-2-yl)carbamate (Boc-L-Met-L-Phe-NH_2, DM770) **L,L-6g - ^{1}H NMR (400 MHz, DMSO-d_6)**



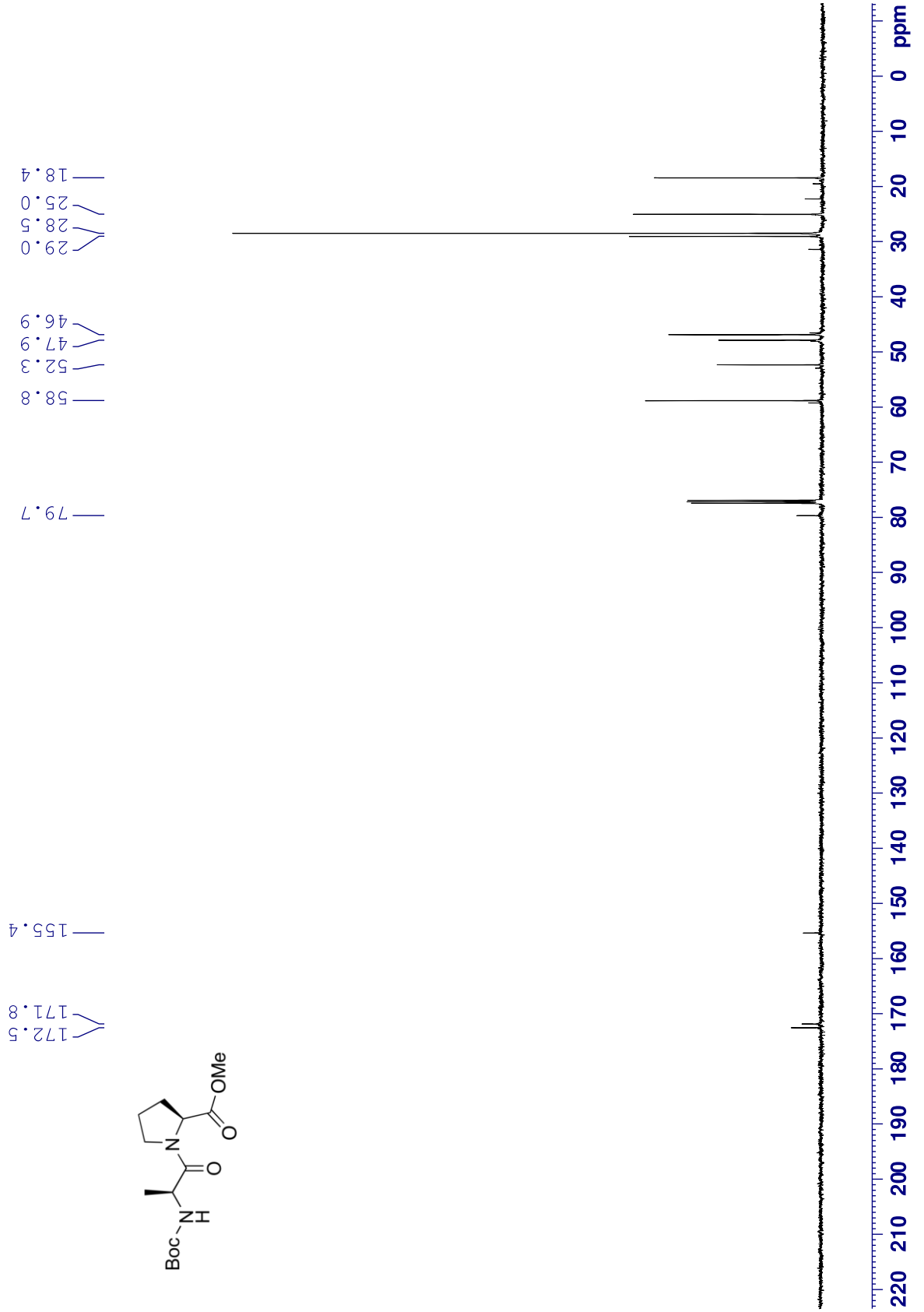
tert-Butyl ((*S*)-1-(((*S*)-1-amino-1-oxo-3-phenylpropan-2-yl)amino)-4-(methylthio)-1-oxobutan-2-yl)carbamate (Boc-L-Met-L-Phe-NH_2, DM770) **L,L-6g – ^{13}C NMR (100 MHz, DMSO-d_6)**



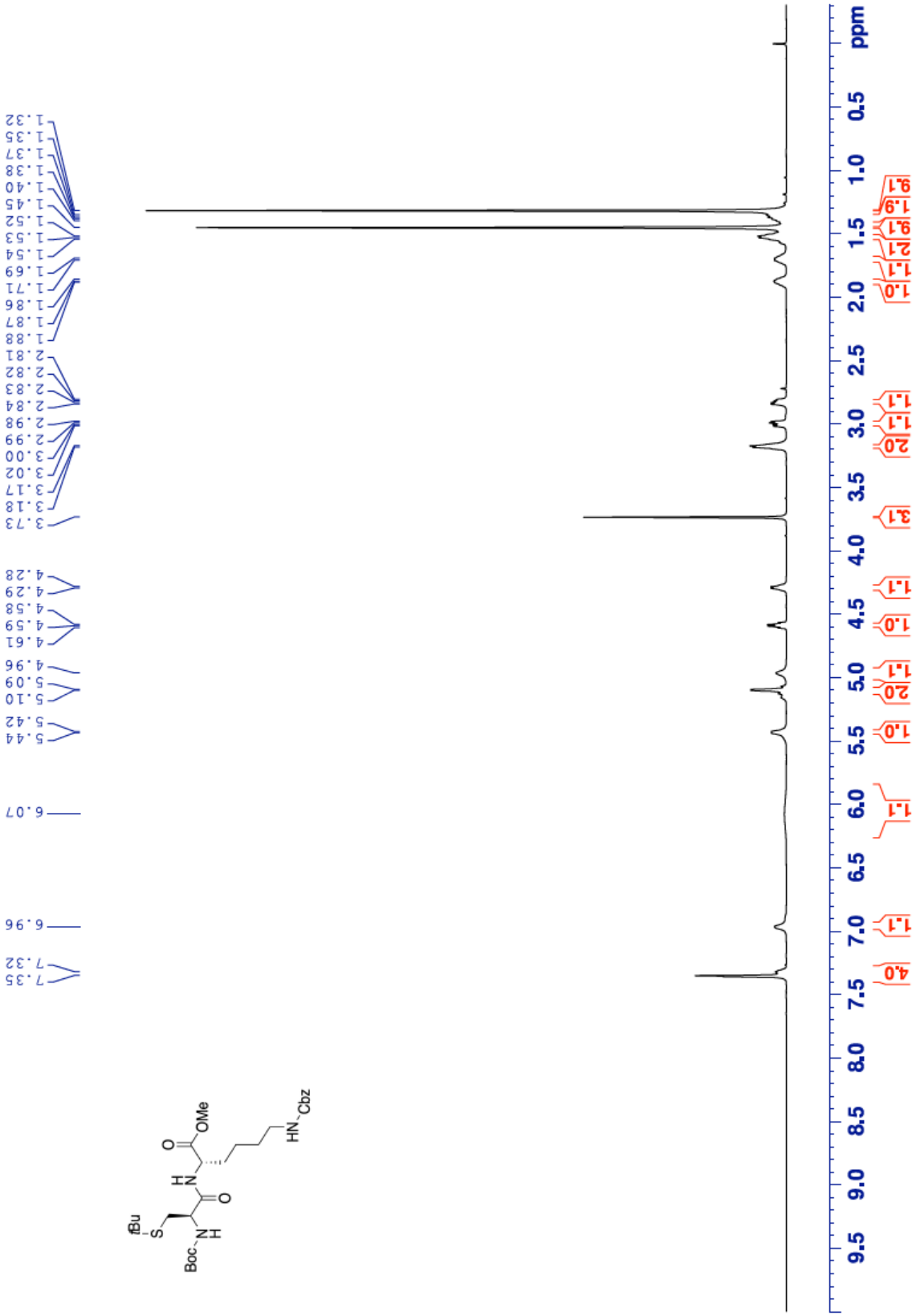
Methyl (*tert*-butoxycarbonyl)-L-alanyl-L-prolinate (Boc-L-Ala-L-Pro-OMe, KH_1204) **L,L-6h - ^{1}H NMR (500 MHz, $CDCl_3$)**



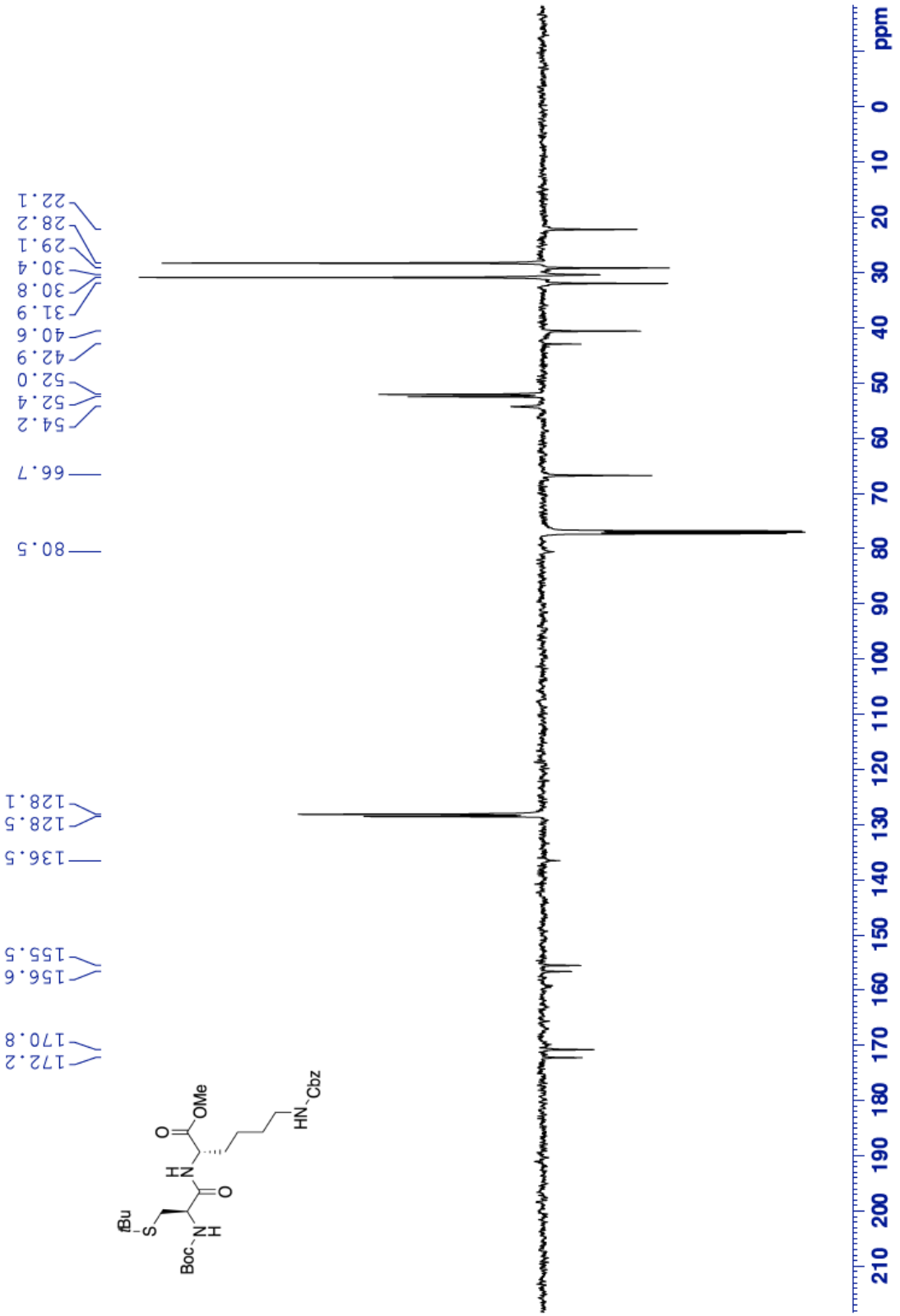
Methyl (*tert*-butoxycarbonyl)-L-alanyl-L-prolinate (Boc-L-Ala-L-Pro-OMe, KH_1204) **L,L-6h - ^{13}C NMR (126 MHz, $CDCl_3$)**



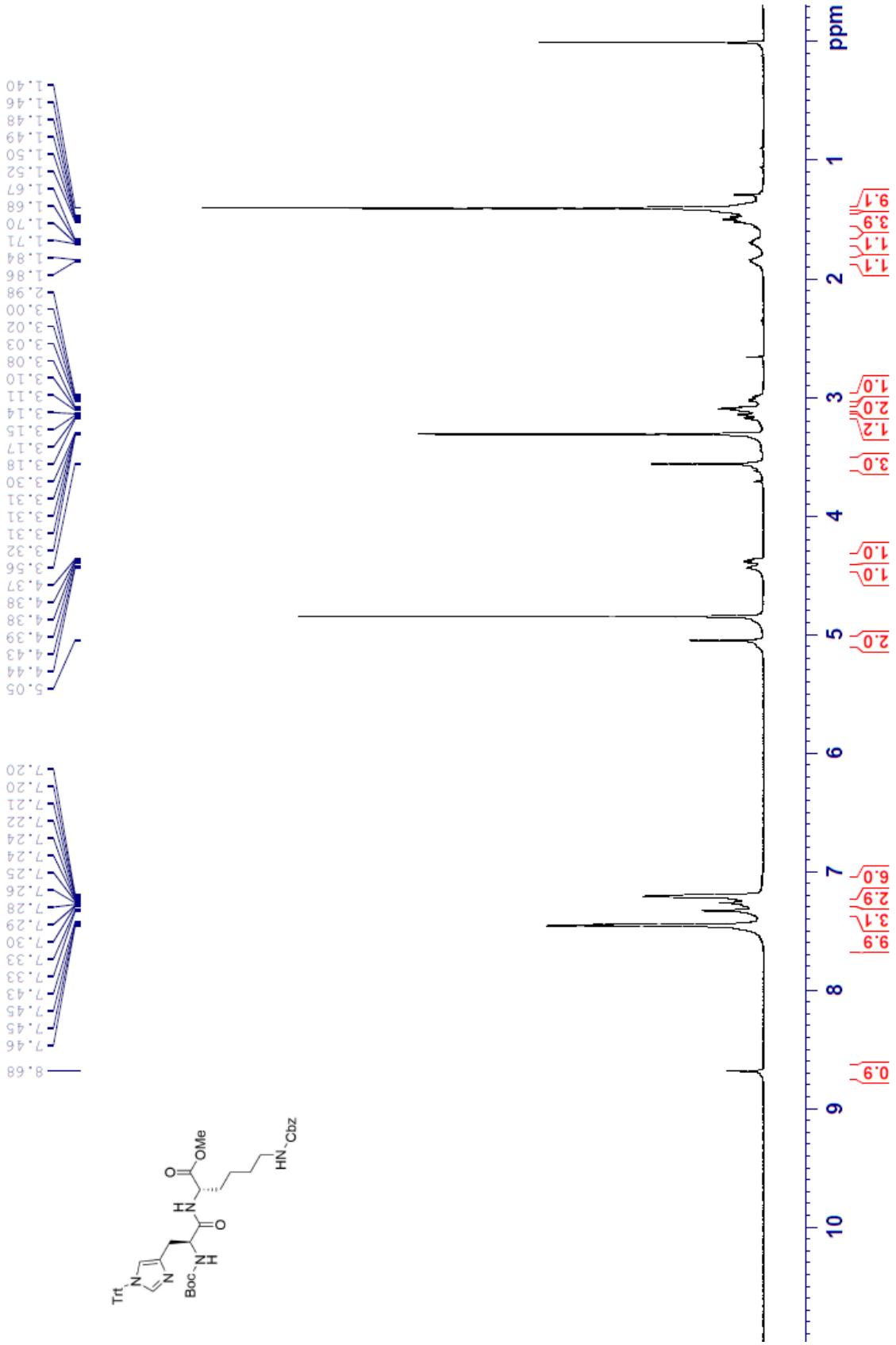
methyl N^6-((benzyloxy)carbonyl)-N^2-(*N*-(*tert*-butoxycarbonyl)-*S*-(*tert*-butyl)-L-cysteinyl)-L-lysinate (Boc-L-Cys(*t*Bu)-L-Lys(Cbz)-OMe, KH_1315) **L,L-6i** – **^{1}H NMR (500 MHz, $CDCl_3$)**



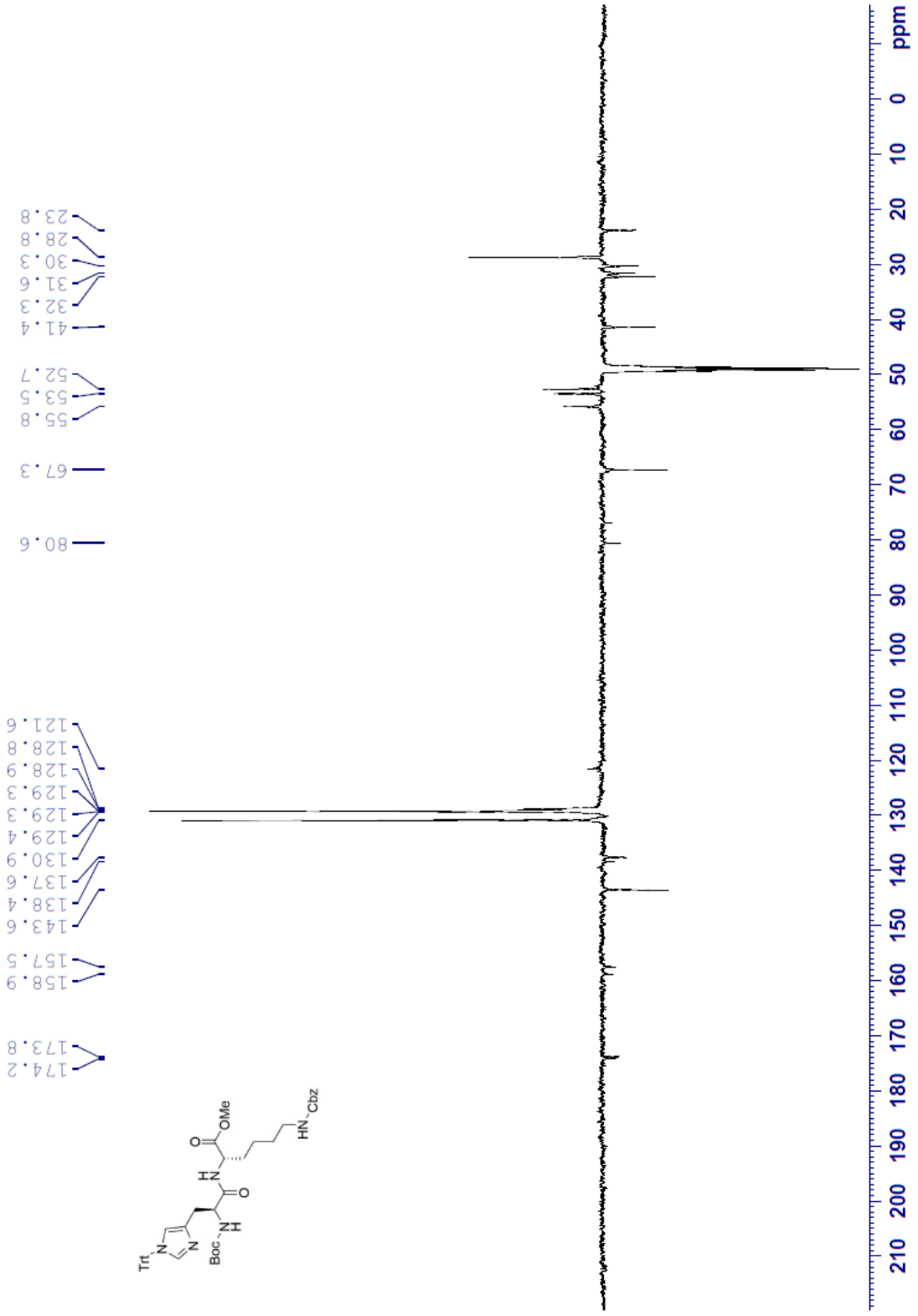
methyl N^6-((benzyloxy)carbonyl)-N^2-(*N*-(*tert*-butoxycarbonyl)-*S*-(*tert*-butyl)-L-cysteinyl)-L-lysinate (Boc-L-Cys(*t*Bu)-L-Lys(Cbz)-OMe, KH_1315) **L,L-6i** – **^{13}C APT NMR (126 MHz, $CDCl_3$)**



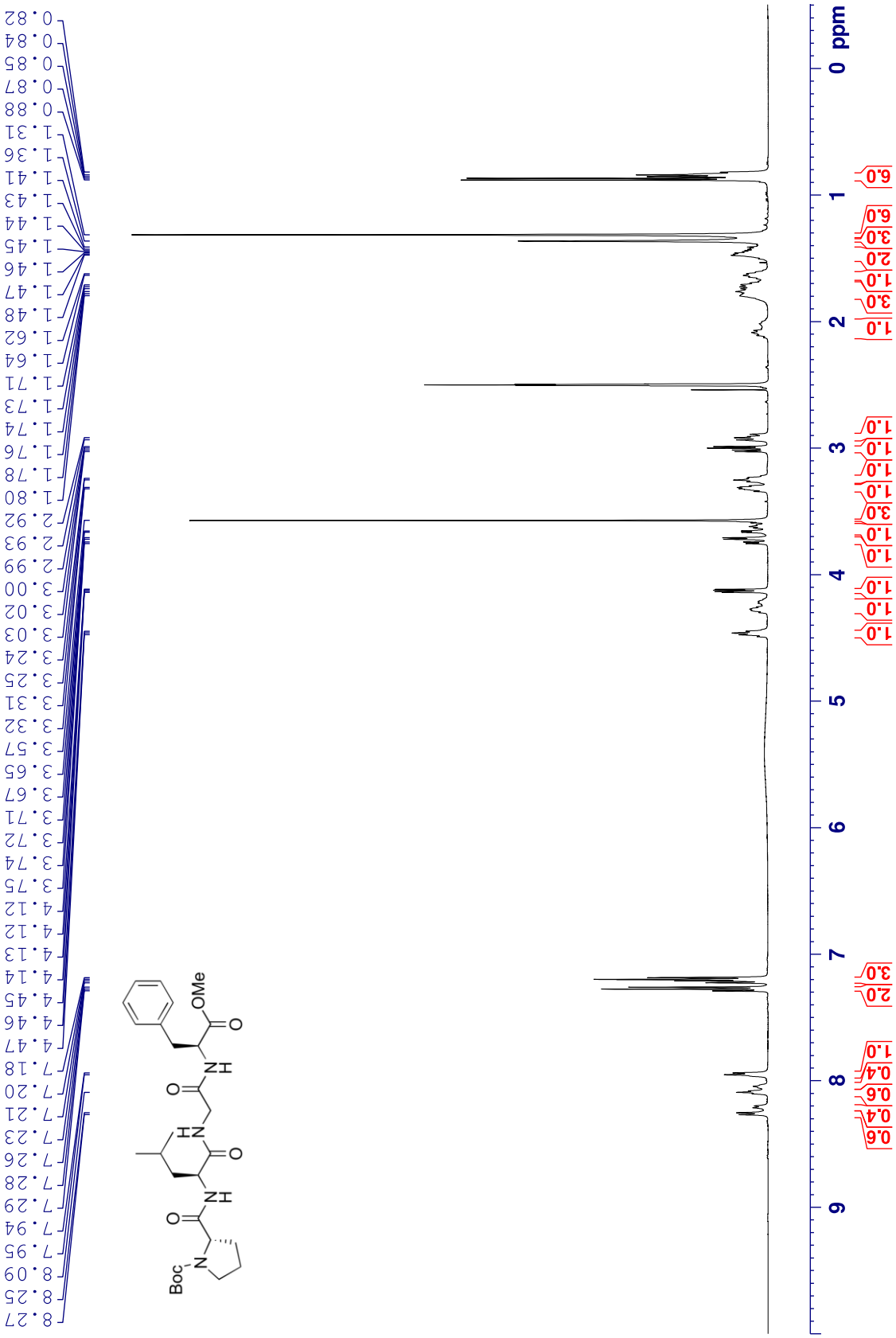
Methyl N^6-((benzyloxy)carbonyl)-N^2-(N'-(*tert*-butoxycarbonyl)-N^τ-trityl-L-histidyl)-L-lysinate (Boc-L-His(Trt)-L-Lys(Cbz)-OMe, KH_1308) **L,L-6j** – **^{1}H NMR (500 MHz, MeOD)**



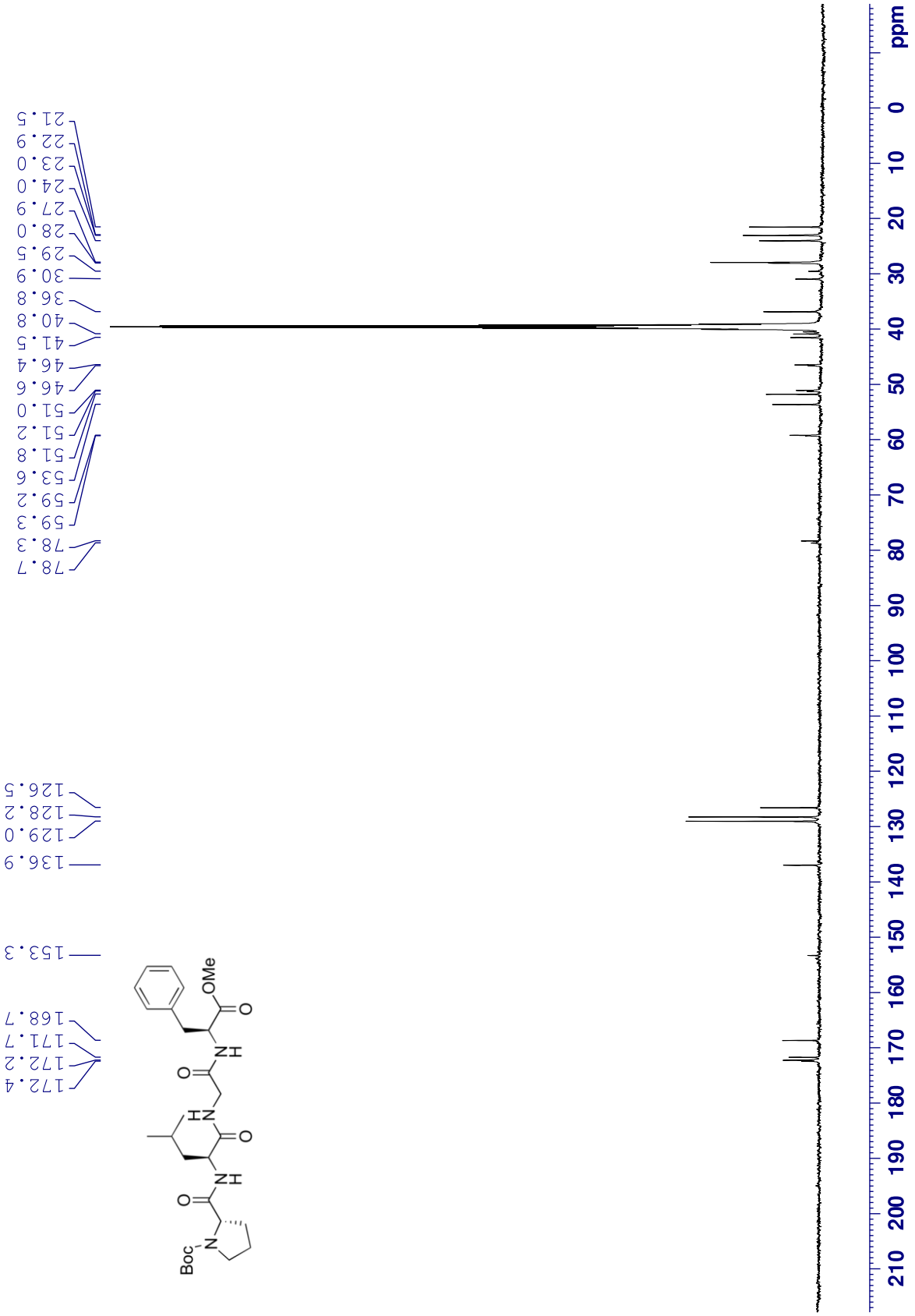
Methyl N^6-((benzyloxy)carbonyl)-N^2-($N^{'}$-(*tert*-butoxycarbonyl)-N^{τ}-trityl-L-histidyl)-L-lysinate (Boc-L-His(Trt)-L-Lys(Cbz)-OMe, KH_1308) **L,L-6j – ^{13}C APT NMR (126 MHz, MeOD)**



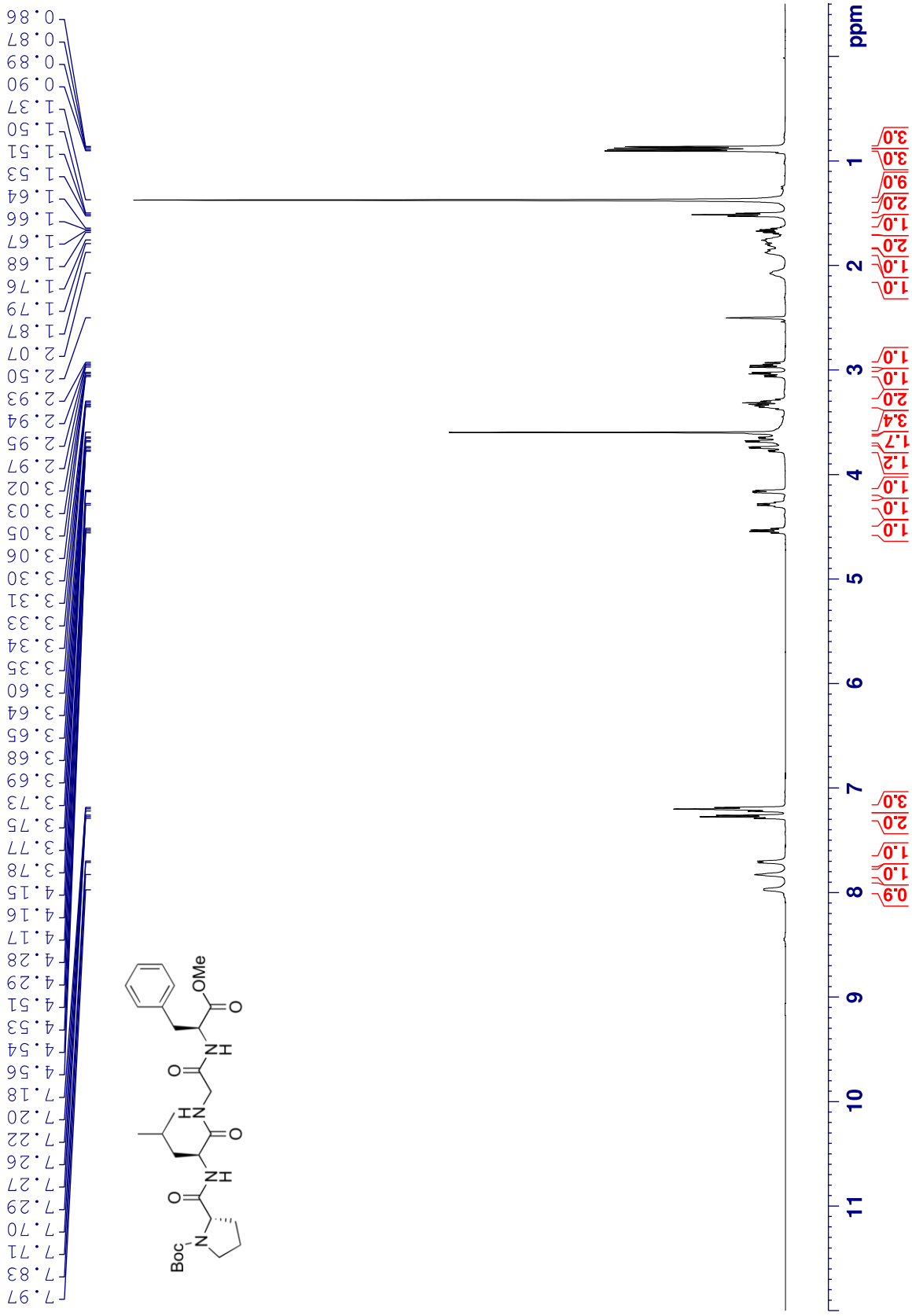
tert-Butyl (*S*)-2-(((*S*)-1-((2-(((*S*)-1-methoxy-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethyl)amino)-4-methyl-1-oxopentan-2-yl)carbamoyl)pyrrolidine-1-carboxylate (Boc-L-Pro-L-Leu-Gly-L-Phe-OMe, KH_1265) **L,L,L-6k - ^{1}H NMR (500 MHz, DMSO-d_6, mixture of rotamers)**



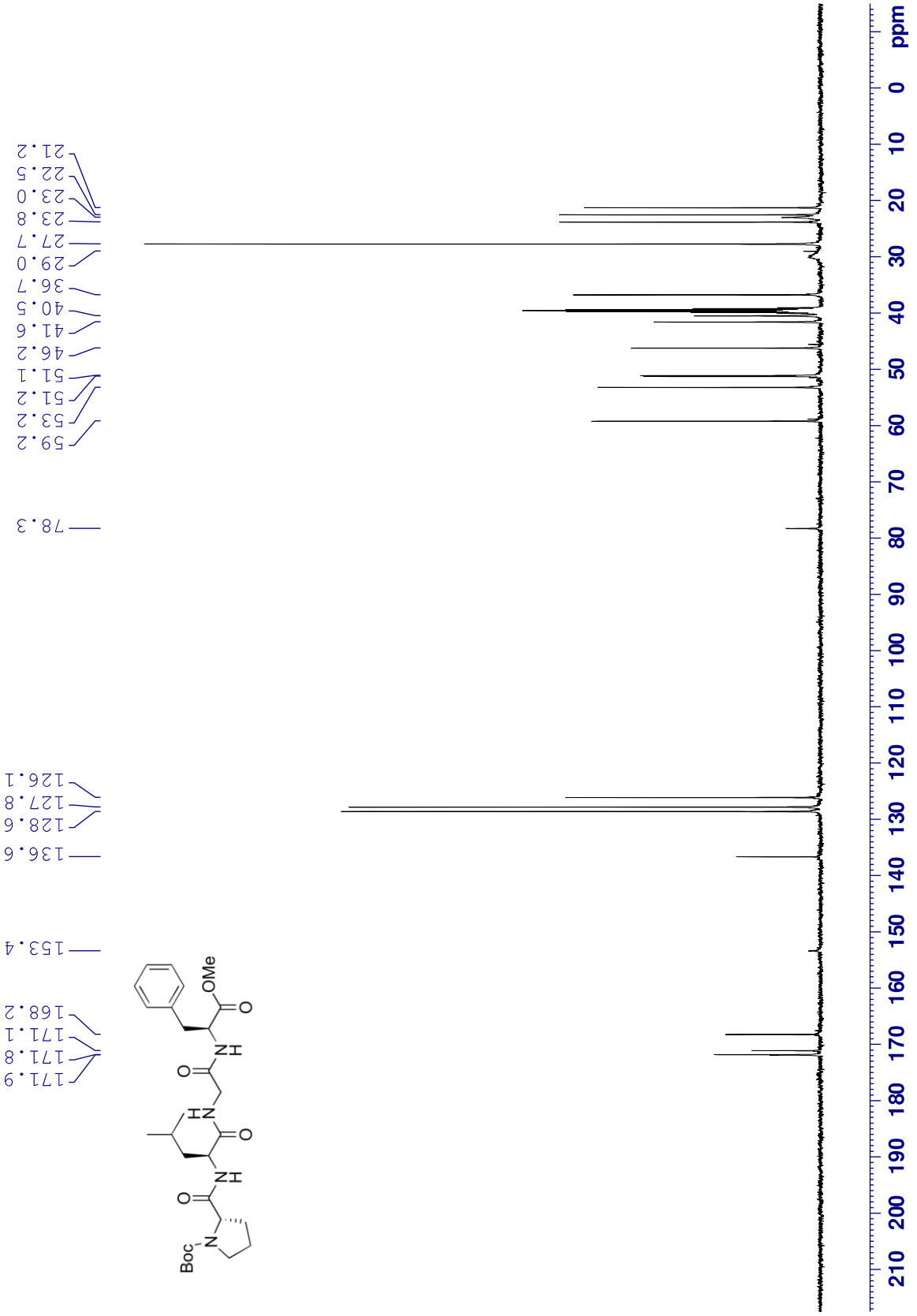
tert-Butyl (*S*)-2-(((*S*)-1-((2-(((*S*)-1-methoxy-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethyl)amino)-4-methyl-1-oxopentan-2-yl)carbamoyl)pyrrolidine-1-carboxylate (Boc-L-Pro-L-Leu-Gly-L-Phe-OMe, KH_1265) **L,L,L-6k – ^{13}C NMR (126 MHz, DMSO-*d*$_6$, mixture of rotamers)**



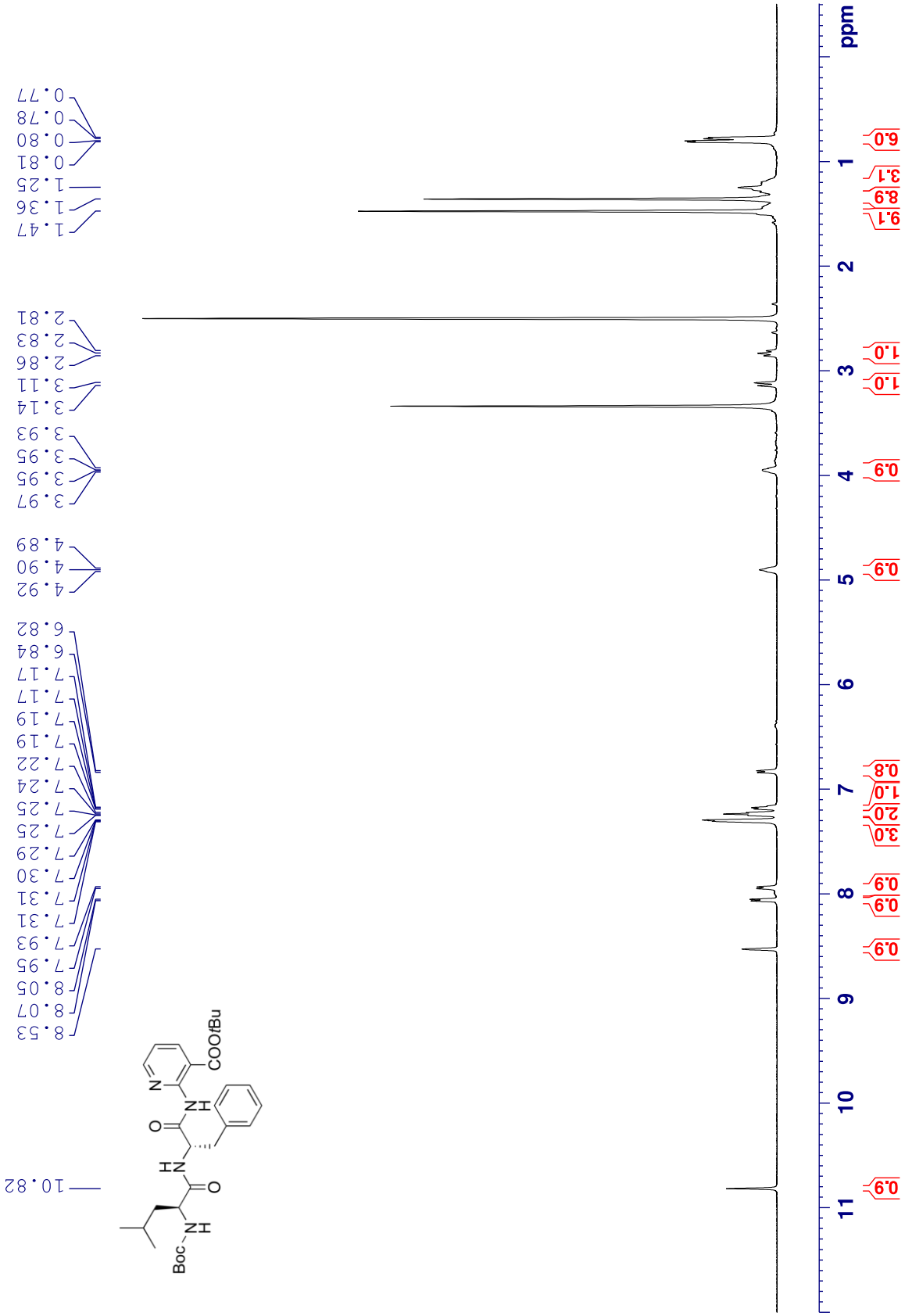
tert-Butyl (*S*)-2-(((*S*)-1-((2-(((*S*)-1-methoxy-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethyl)amino)-4-methyl-1-oxopentan-2-yl)carbamoyl)pyrrolidine-1-carboxylate (Boc-L-Pro-L-Leu-Gly-L-Phe-OMe, KH_1265) **L,L,L-6k- ^{1}H NMR (500 MHz, DMSO-d_6, 80°C)**



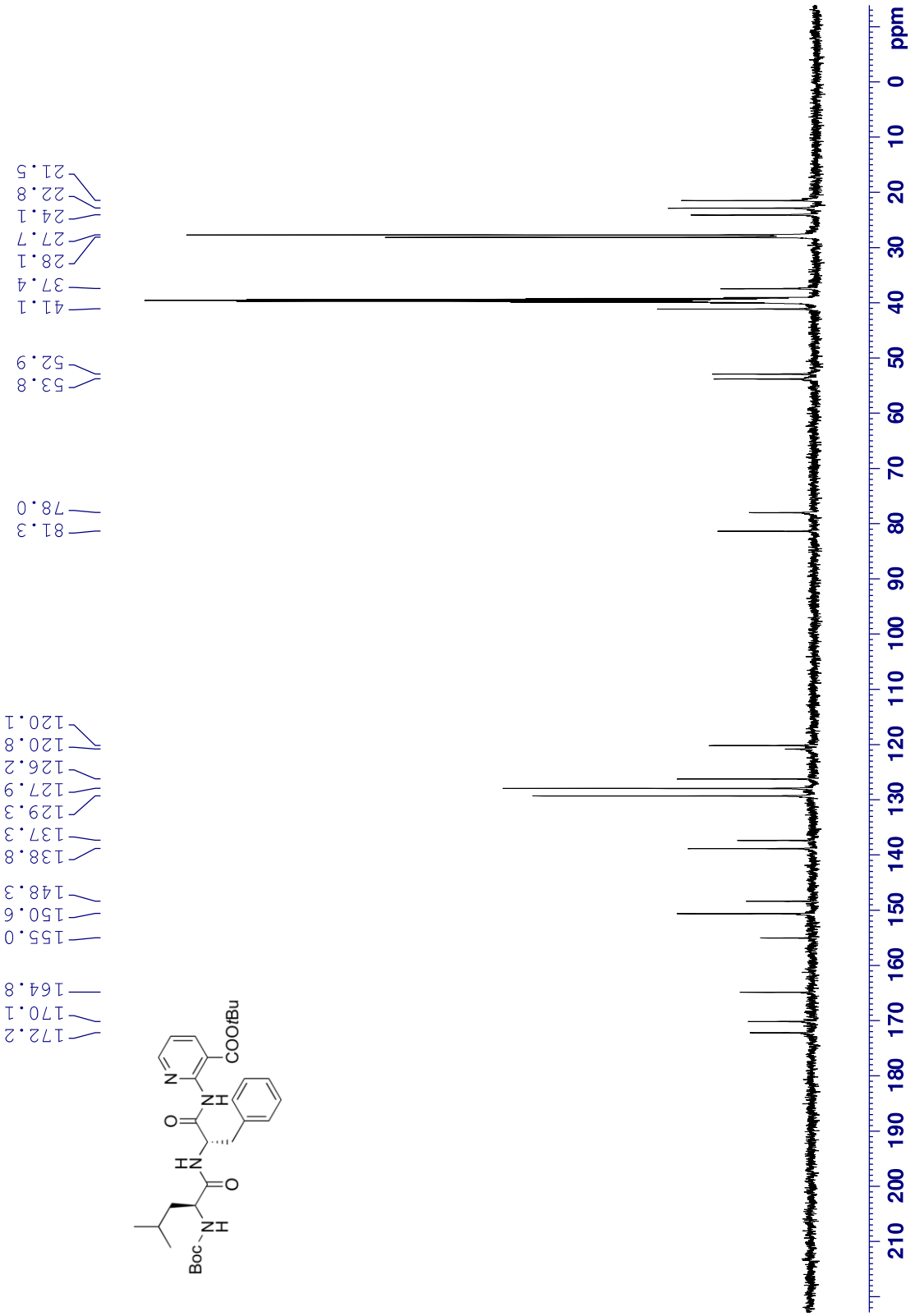
tert-Butyl (*S*)-2-(((*S*)-1-((2-(((*S*)-1-methoxy-1-oxo-3-phenylpropan-2-yl)amino)-2-oxoethyl)amino)-4-methyl-1-oxopentan-2-yl)carbamoyl)pyrrolidine-1-carboxylate (Boc-L-Pro-L-Leu-Gly-L-Phe-OMe, KH_1265) **L,L,L-6k – ^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80°C)**



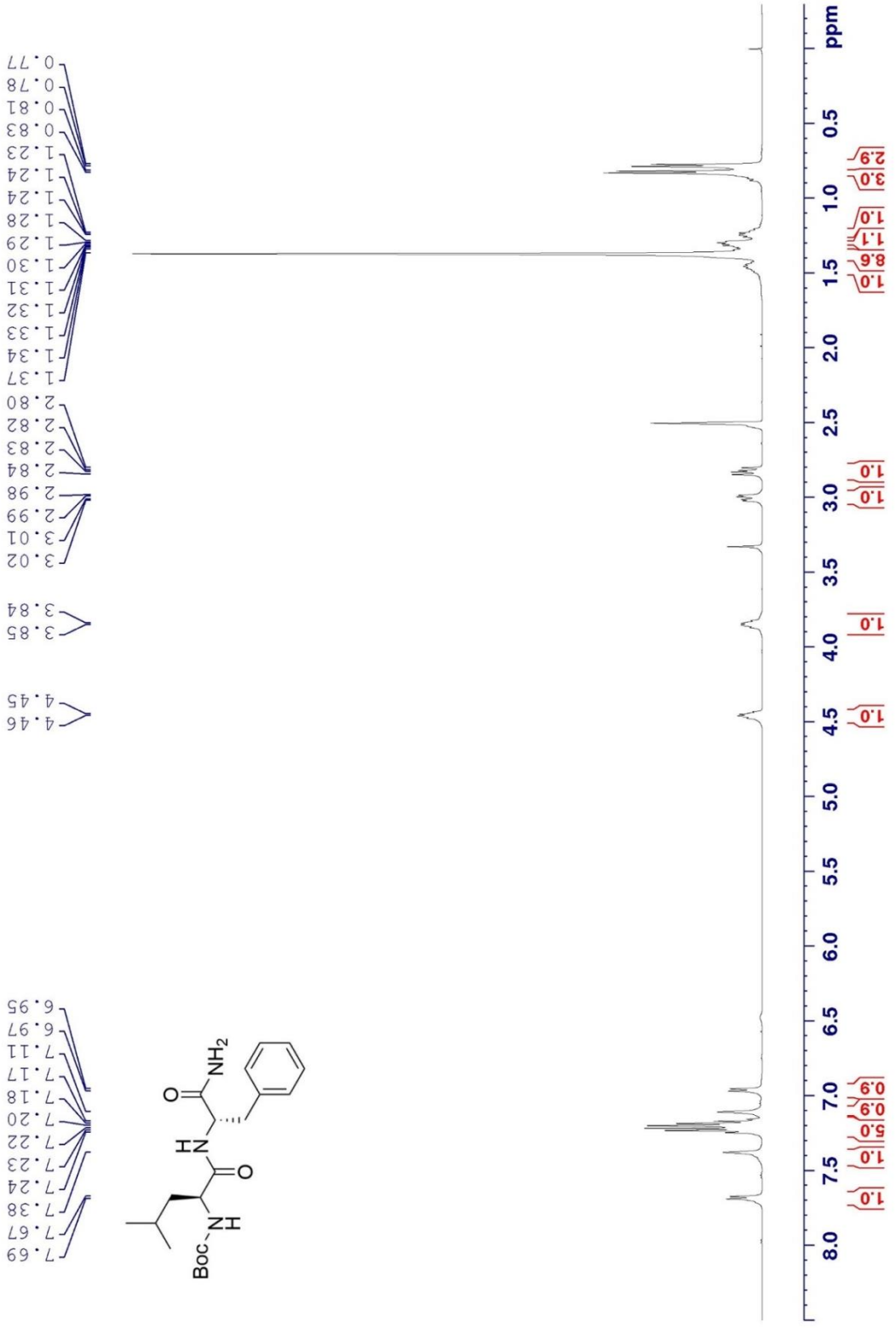
tert-Butyl 2-((*S*)-2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-4-methylpentanamido)-3-phenylpropanamido)nicotinate (Boc-L-Leu-L-Phe-NH-*t*Bu-nicn KH_549) **L,L-7 - ^{1}H NMR (500 MHz, DMSO-d_6)**



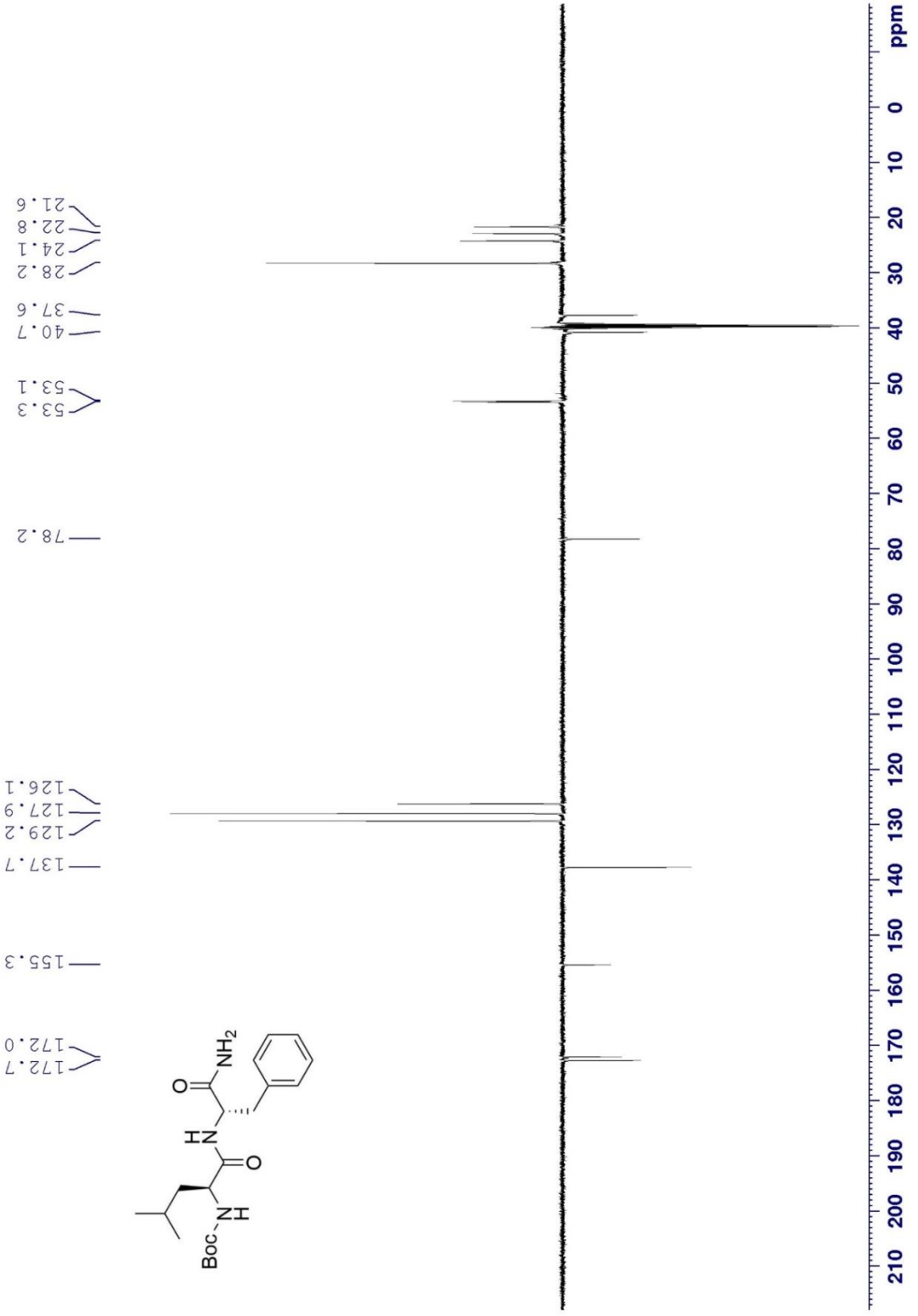
tert-Butyl 2-((*S*)-2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-4-methylpentanamido)-3-phenylpropanamido)nicotinate (Boc-L-Leu-L-Phe-NH-*t*Bu-nic, KH_549) **L,L-7 - ^{13}C NMR (126 MHz, DMSO-d_6)**



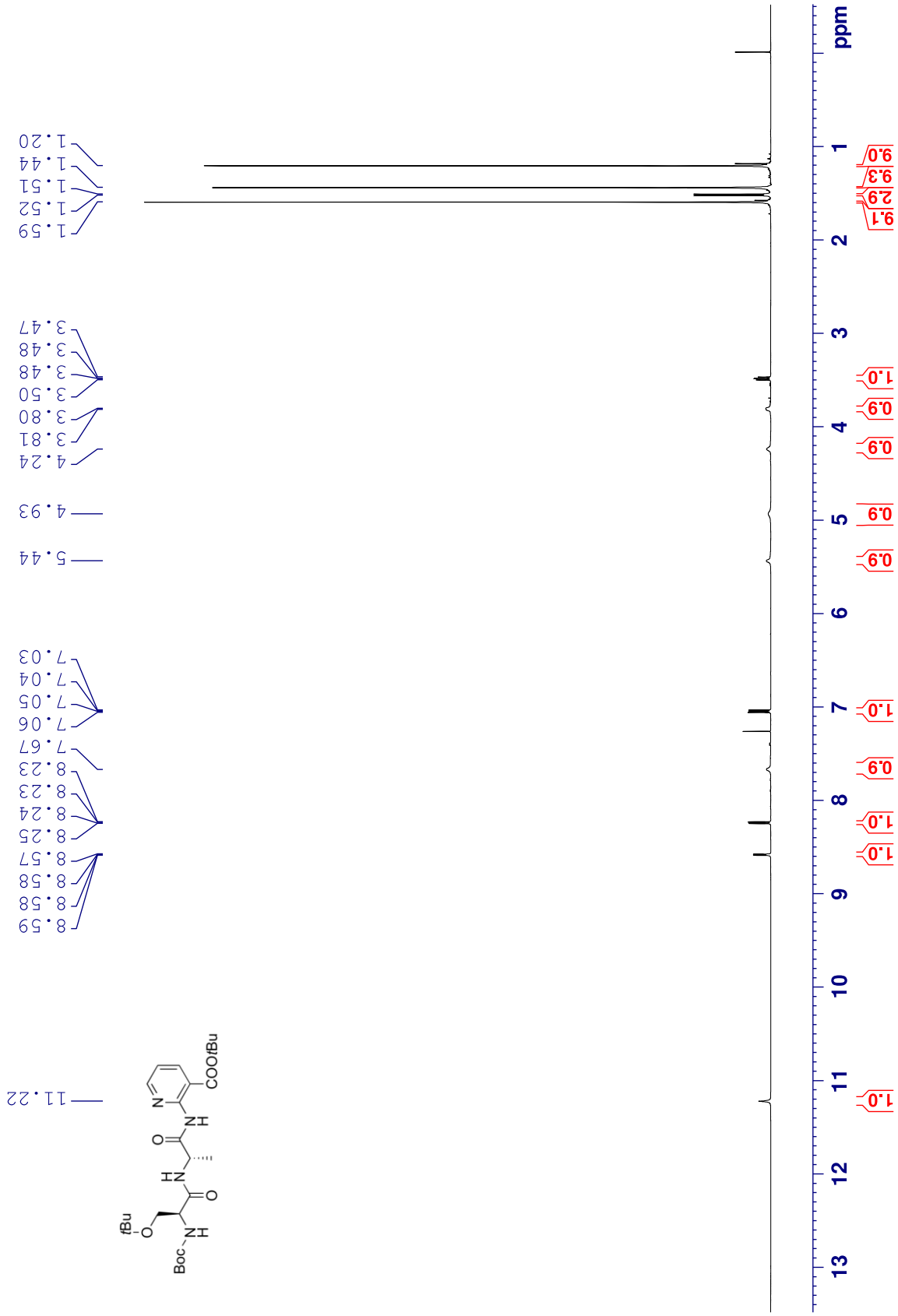
tert-Butyl 2-((*S*)-2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-4-methylpentanamido)-3-phenylpropanamido)nicotinate (Boc-L-Leu-L-Phe-NH_2, KH_1281) **L,L-S19 - ^{1}H NMR (500 MHz, DMSO-d_6)**



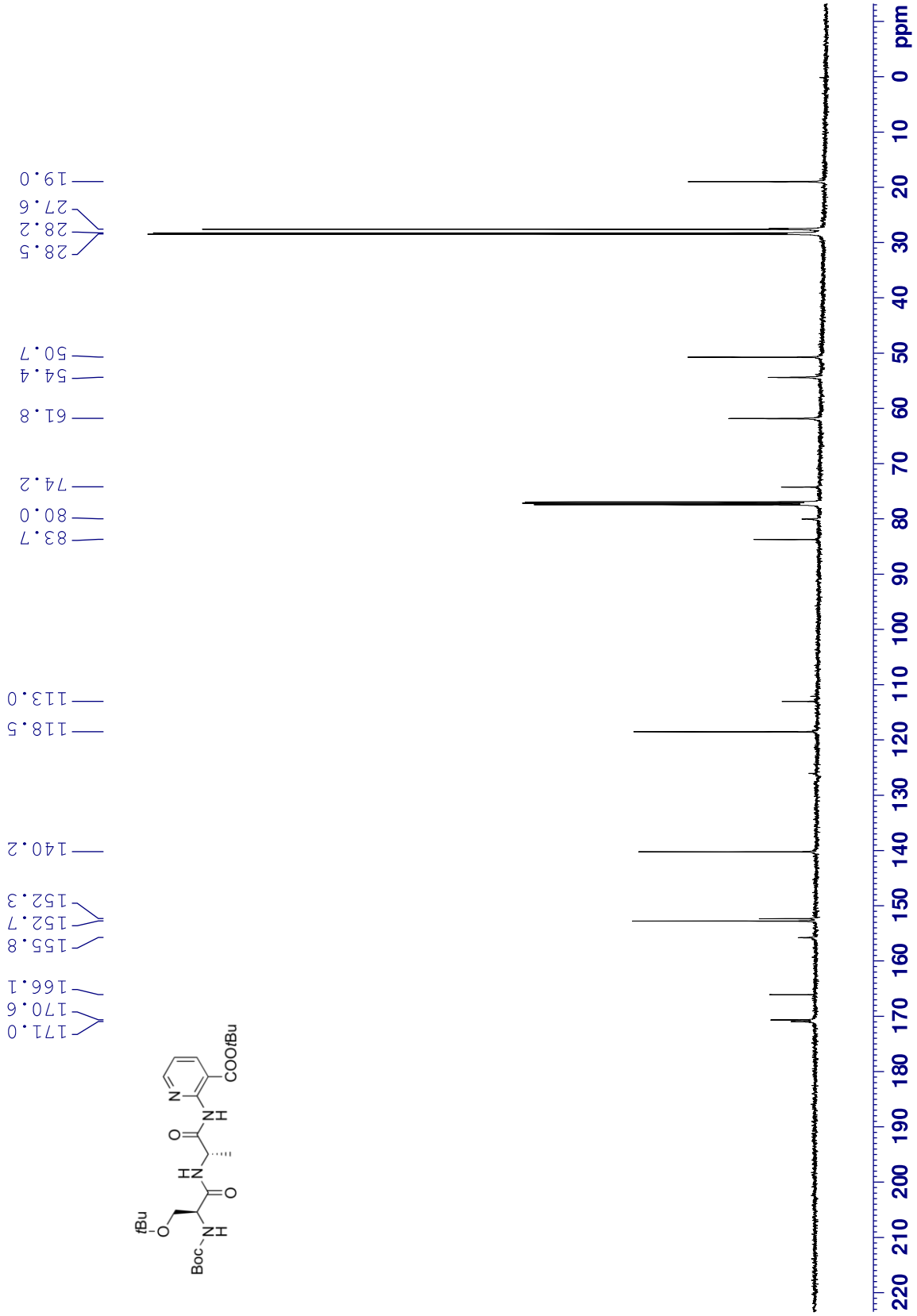
tert-Butyl 2-((*S*)-2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-4-methylpentanamido)-3-phenylpropanamido)nicotinate (Boc-L-Leu-L-Phe-NH_2, KH_1281)) **L,L-S19 ^{13}C APT NMR (126 MHz, DMSO-d_6)**



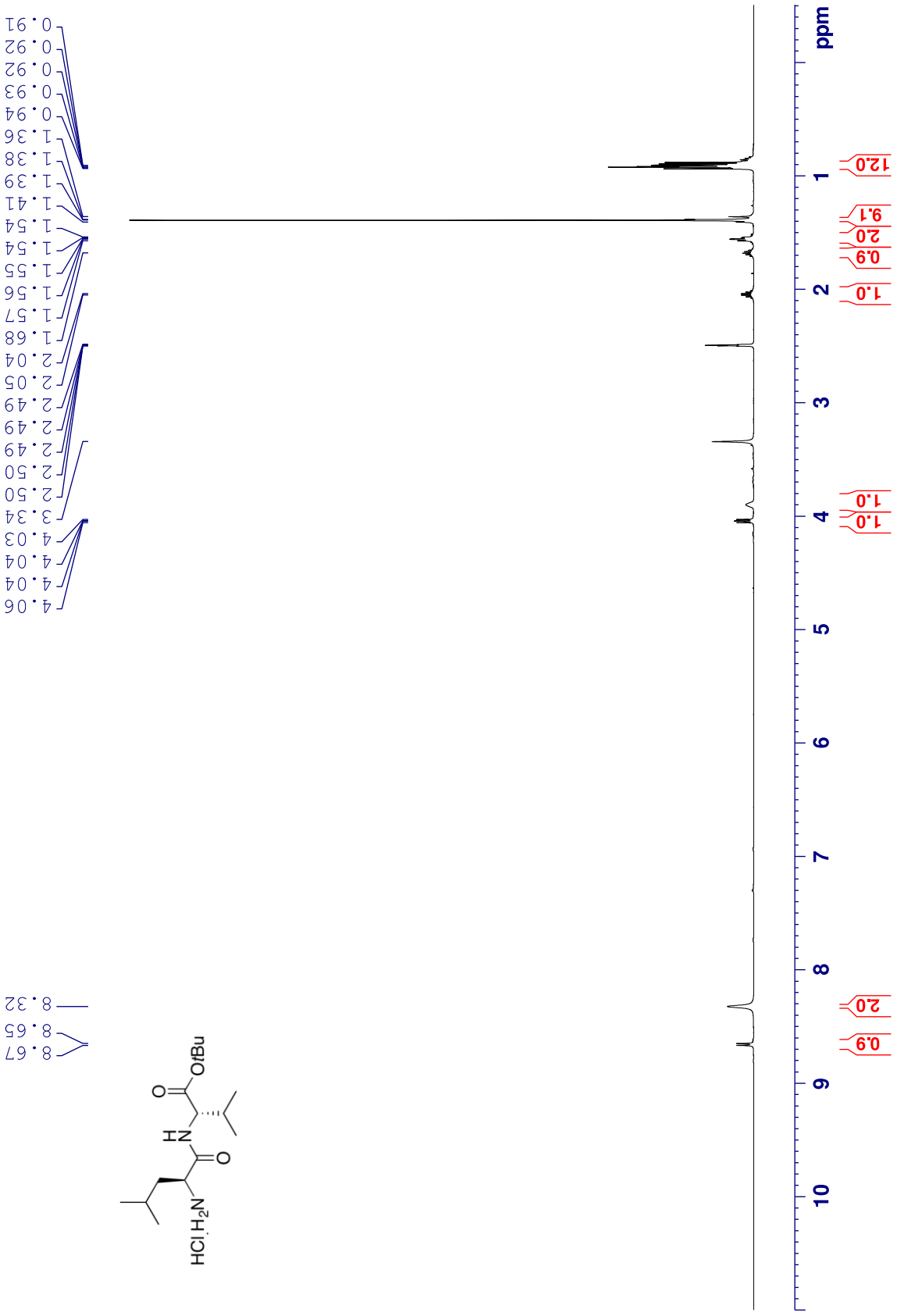
tert-Butyl 2-((*S*)-2-((*S*)-3-(*tert*-butoxy)-2-((*tert*-butoxycarbonyl)amino)propanamido)propanamido) nicotinate (Boc-L-Ser(*t*Bu)-L-Ala-NH-*t*Bu-nic, KH_635) **L,L-8 - ^{1}H NMR (500 MHz, $CDCl_3$)**



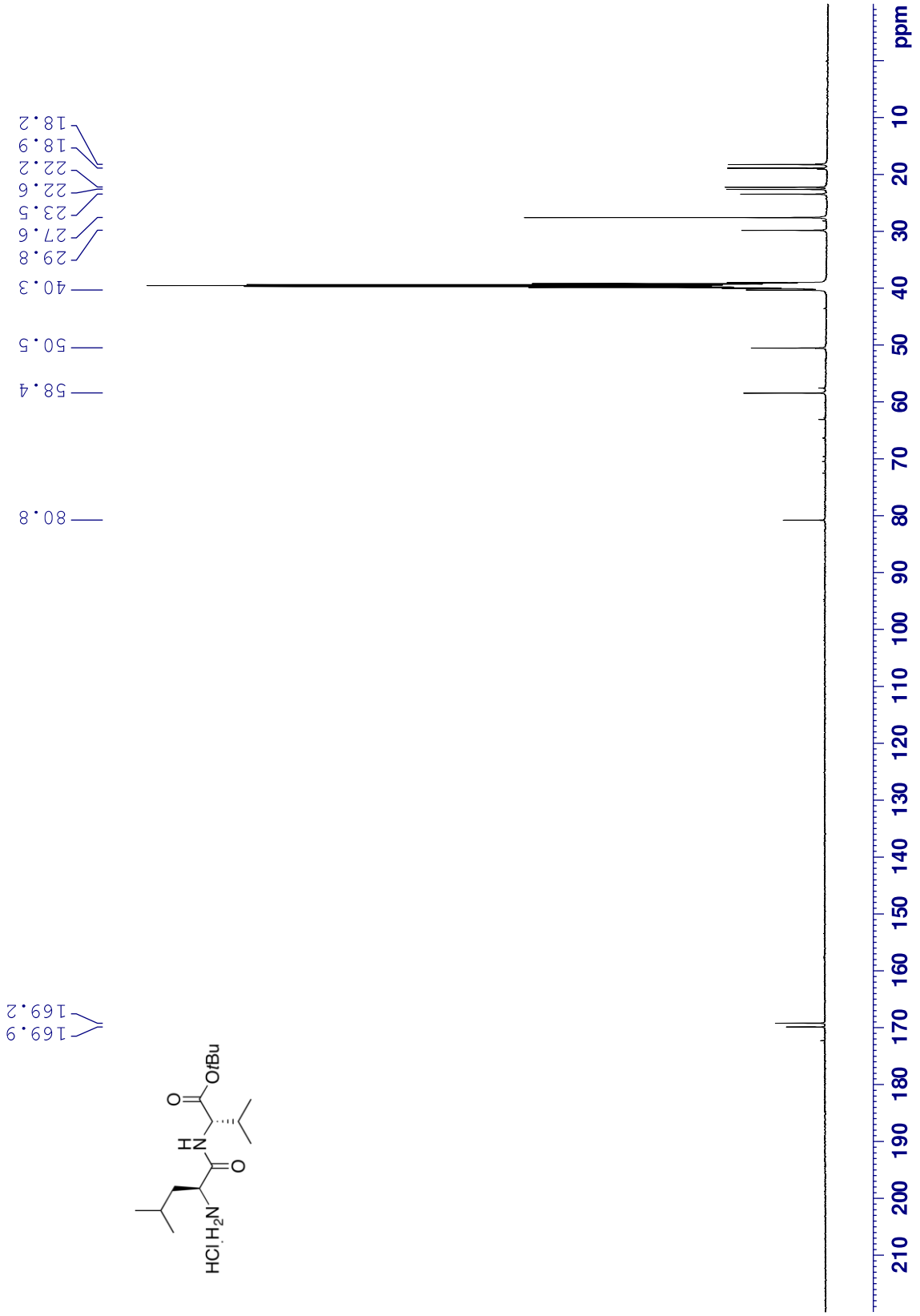
tert-Butyl 2-((*S*)-2-((*S*)-3-(*tert*-butoxy)-2-((*tert*-butoxycarbonyl)amino)propanamido)propanamido) nicotinate (Boc-L-Ser(*t*Bu)-L-Ala-NH-*t*Bu-nic, KH_635) **L,L-8 - ^{13}C NMR (126 MHz, $CDCl_3$)**



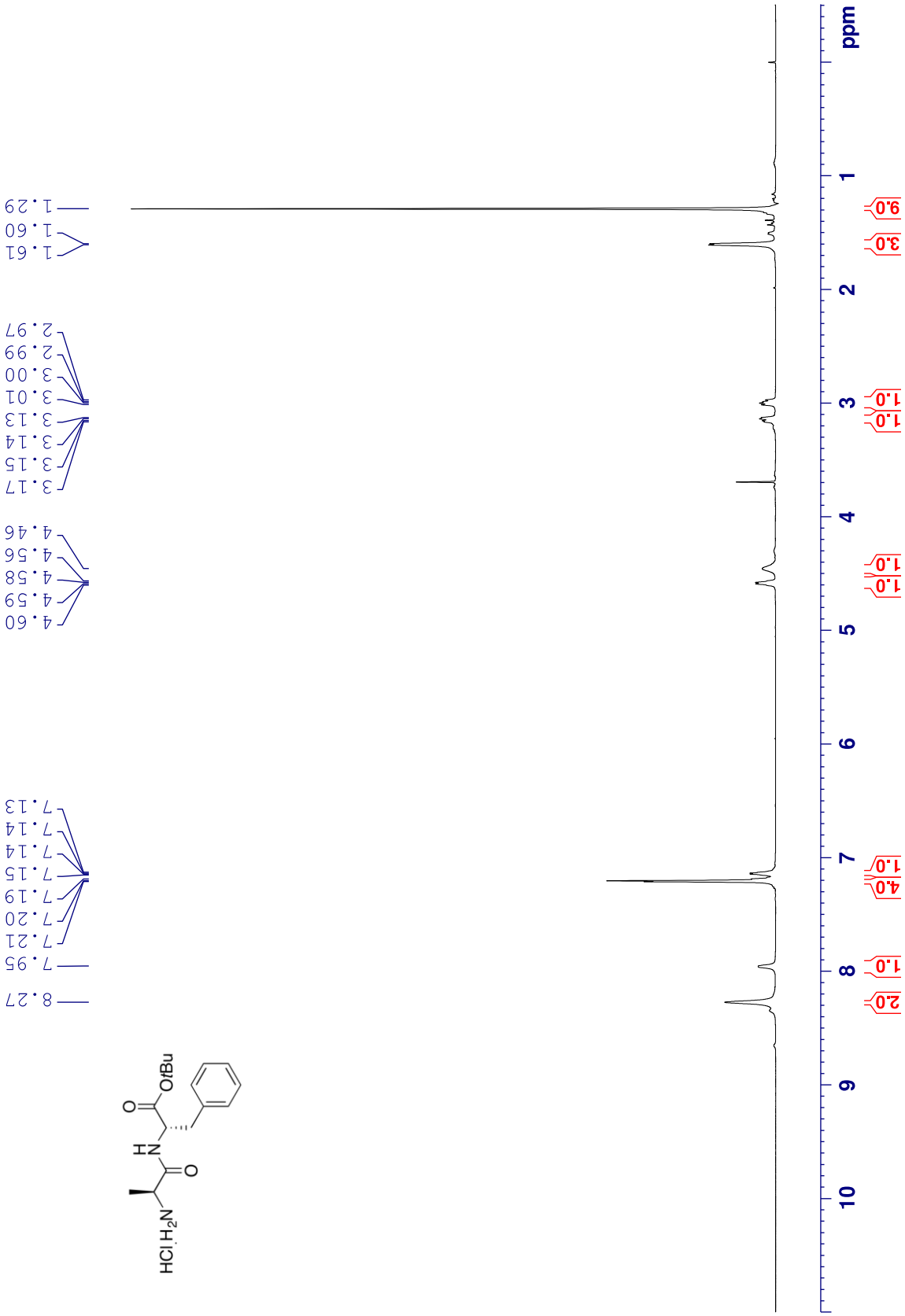
tert-Butyl L-leucyl-L-valinate hydrochloric acid salt (H-L-Leu-L-Val-O*t*Bu.HCl, KH_562) **L,L-9.HCl - ^{1}H NMR (500 MHz, DMSO-d_6)**



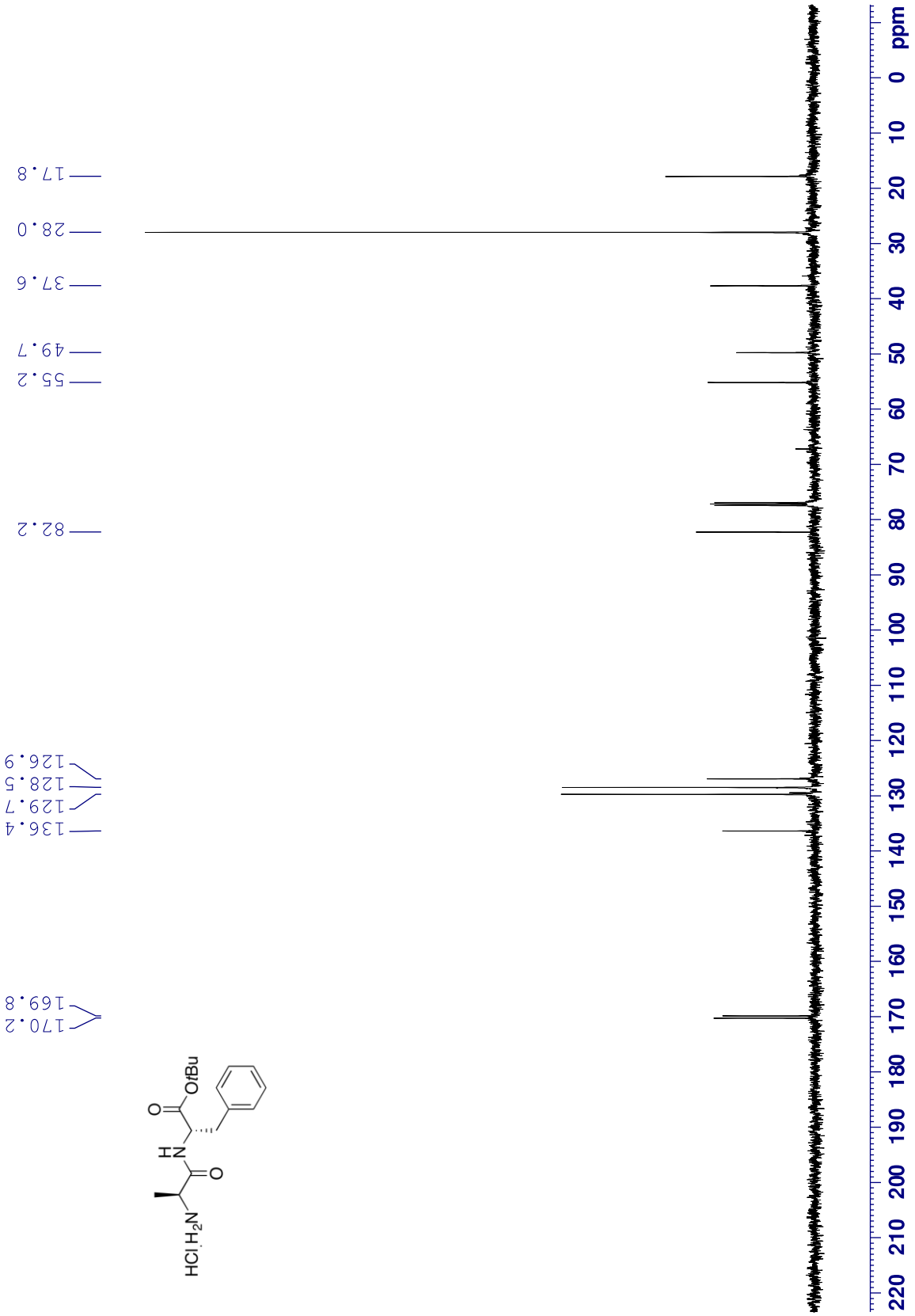
tert-Butyl L-leucyl-L-valinate hydrochloric acid salt (H-L-Leu-L-Val-O*t*Bu.HCl, KH_562) **L,L-9.HCl - ^{13}C NMR (126 MHz, DMSO-d_6)**



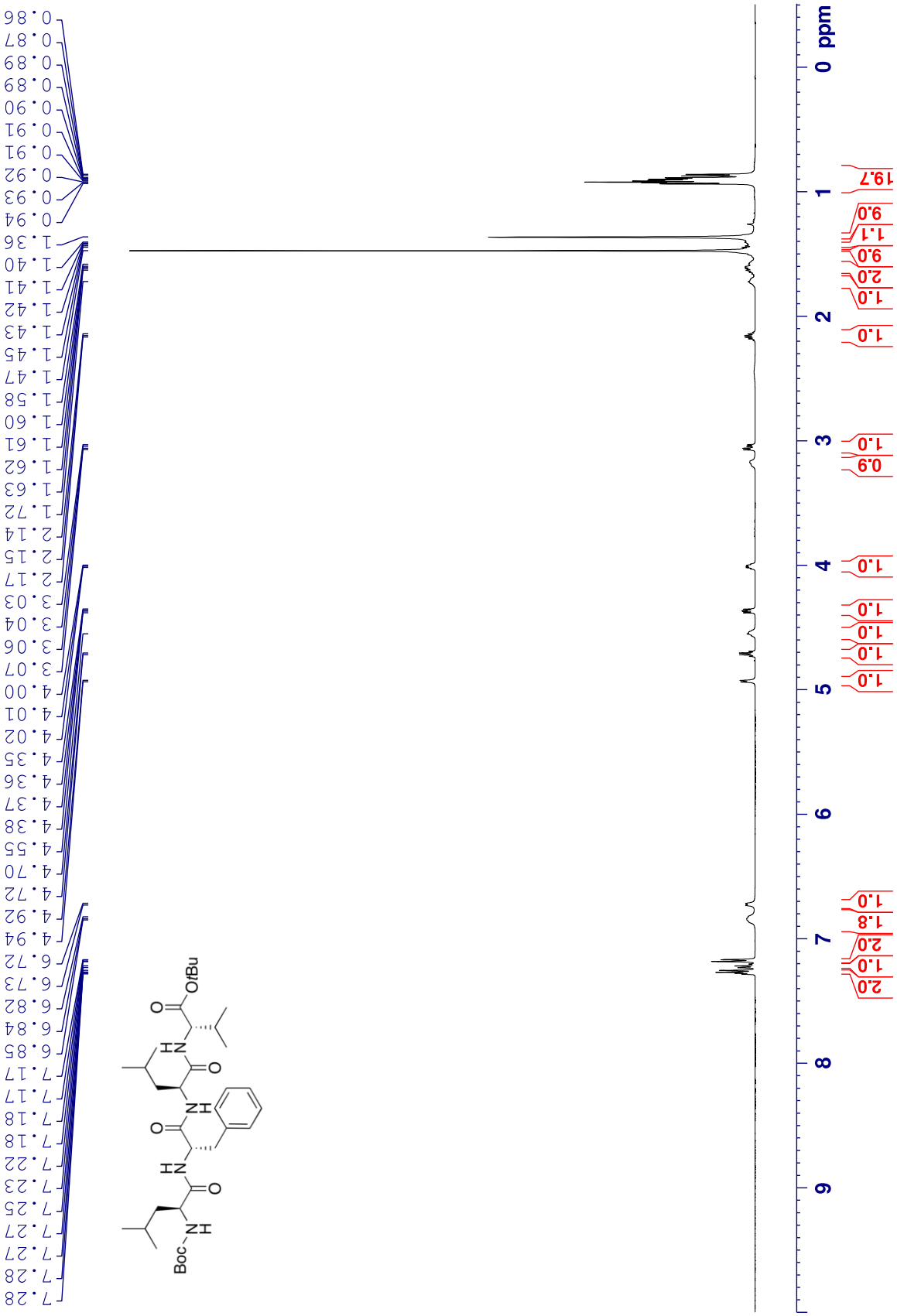
tert-Butyl L-alanyl-L-phenylalaninate hydrochloride (H-L-Ala-L-Phe-O*t*Bu.HCl, KH_782) **L,L-10.HCl - ^{1}H NMR (500 MHz, $CDCl_3$)**



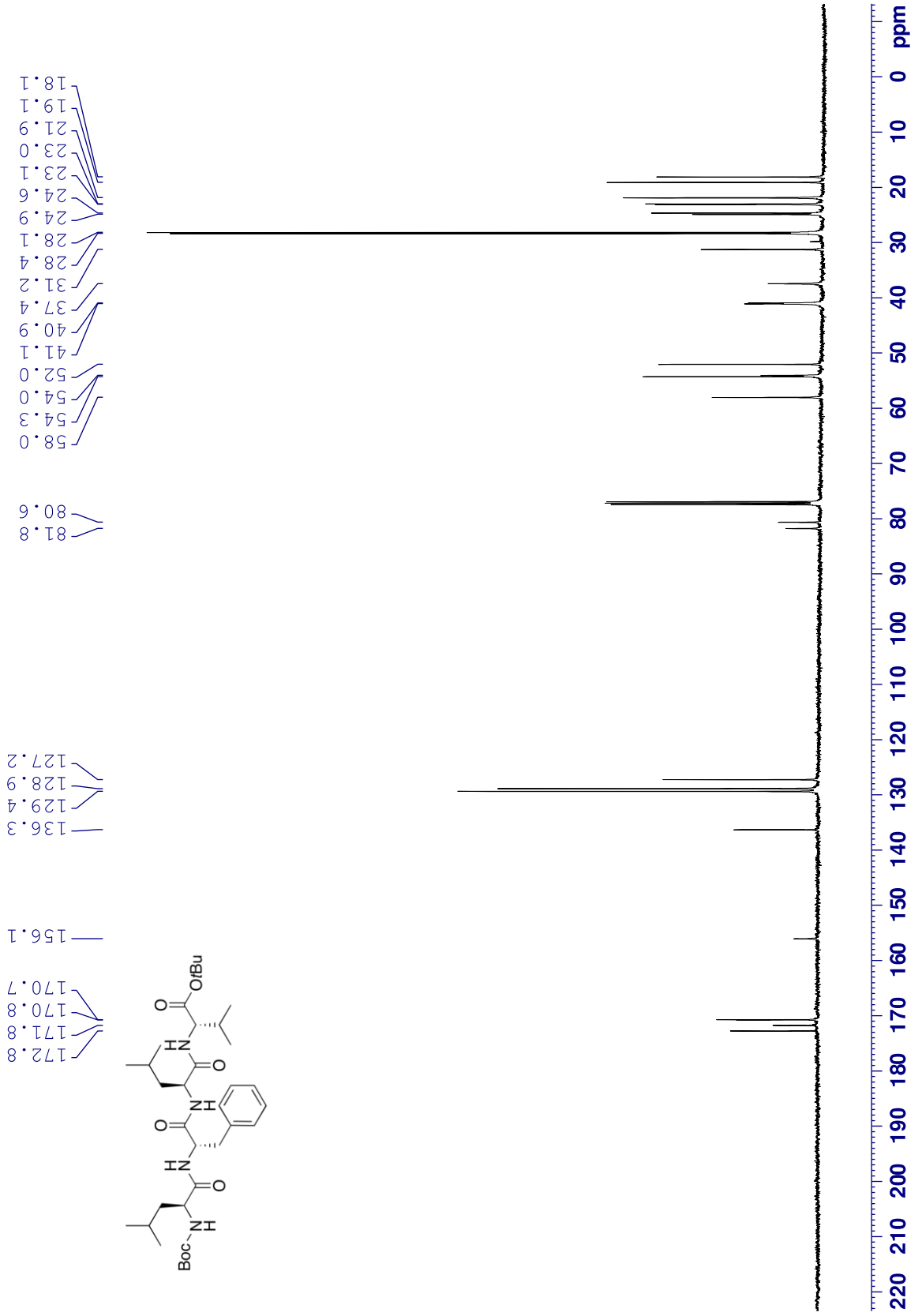
tert-Butyl L-alanyl-L-phenylalaninate hydrochloride (H-L-Ala-L-Phe-O*t*Bu.HCl, KH_782) **L,L-10.HCl - ^{13}C NMR (500 MHz, $CDCl_3$)**



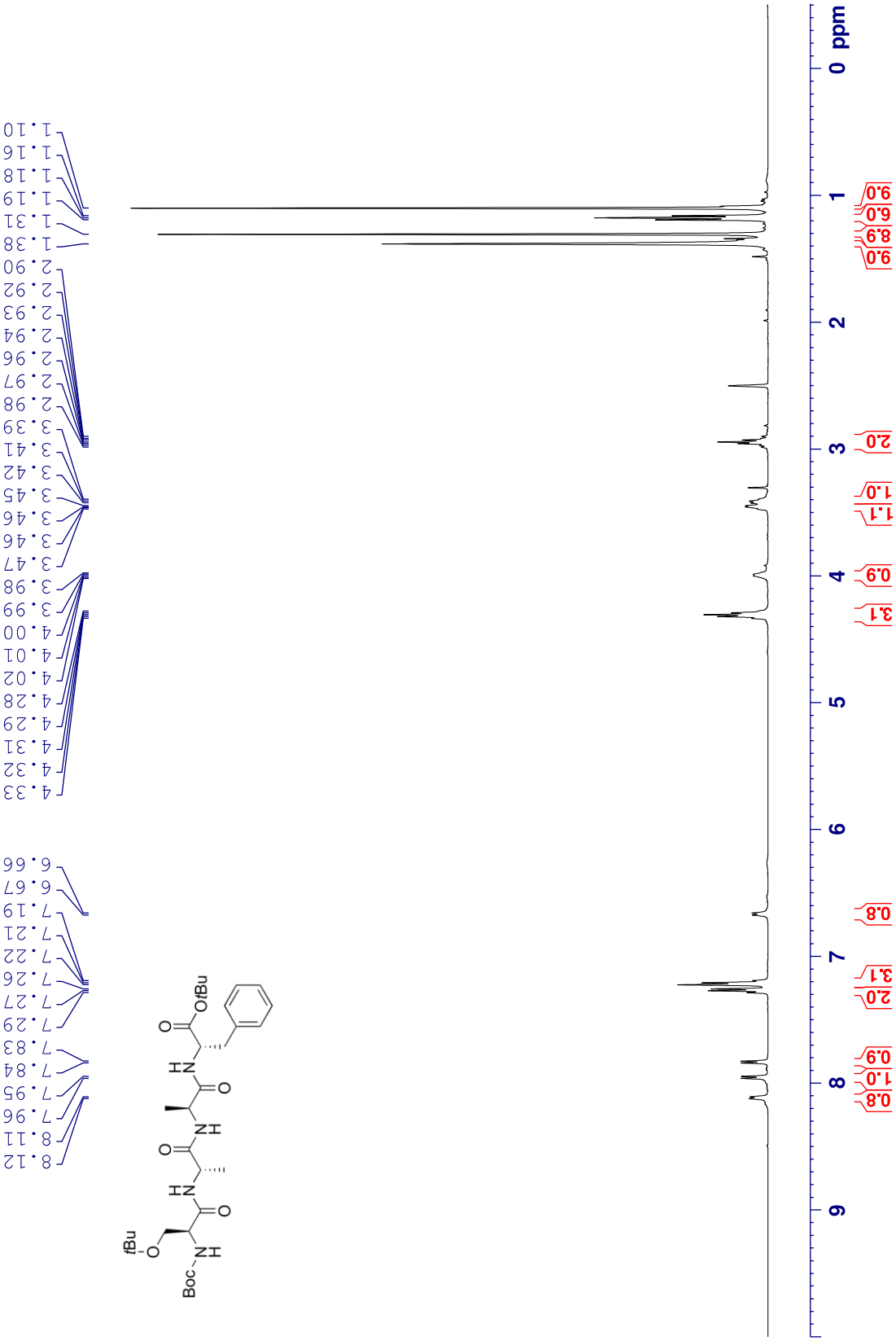
tert-Butyl (*tert*-butoxycarbonyl)-L-leucyl-L-phenylalanyl-L-leucyl-L-valinate (Boc-L-Leu-L-Phe-L-Leu-L-Val-O*t*Bu, KH_1224) **L,L,L,L-11- ^{1}H NMR (500 MHz, $CDCl_3$)**



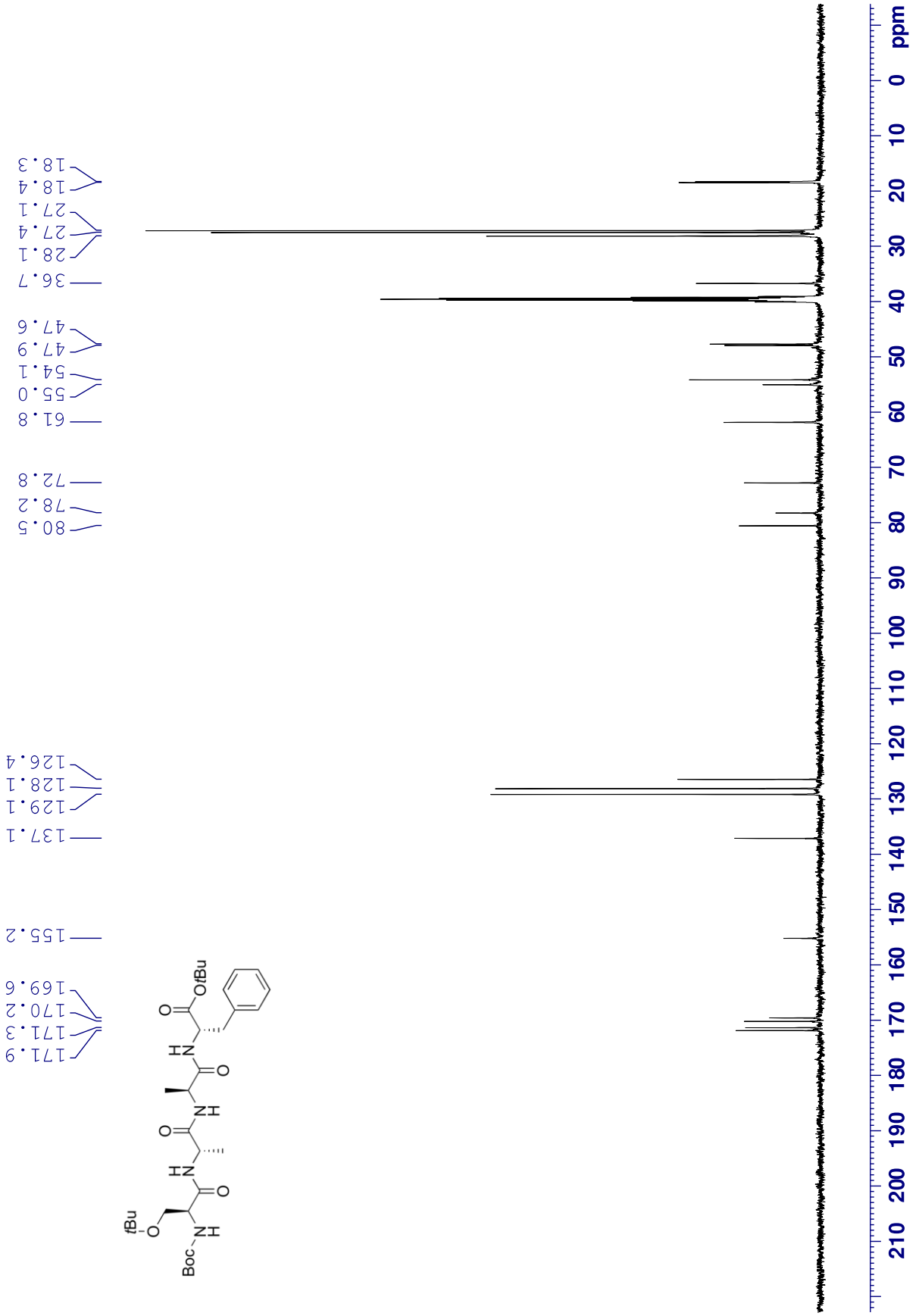
tert-Butyl (*tert*-butoxycarbonyl)-L-leucyl-L-phenylalanyl-L-leucyl-L-valinate (Boc-L-Leu-L-Phe-L-Leu-L-Val-O*t*Bu, KH_1224) **L,L,L,L-11-** ^{13}**C NMR (126 MHz, CDCl$_3$)**



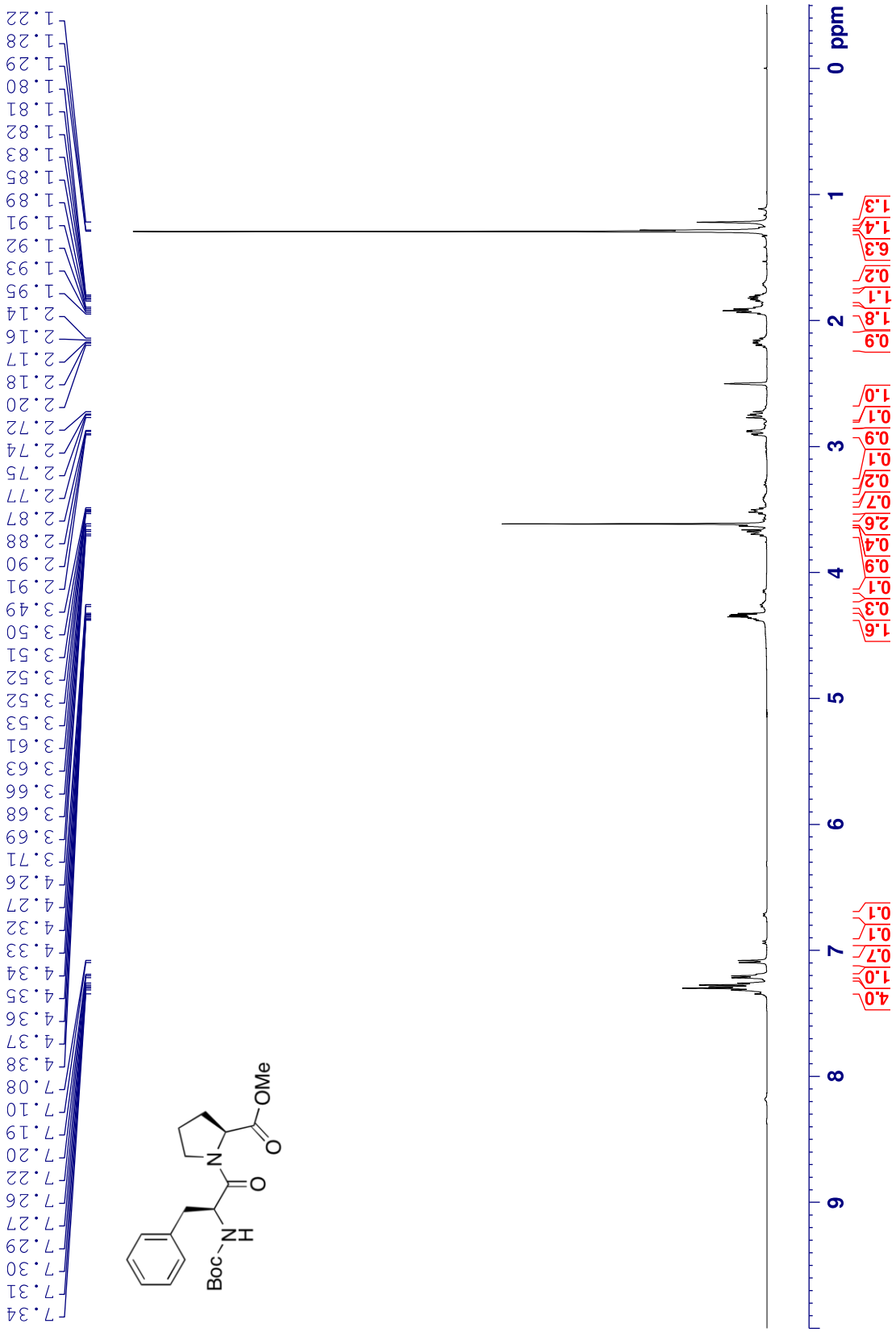
tert-Butyl *N*-(*tert*-butoxycarbonyl)-*O*-(*tert*-butyl)-L-seryl-L-alanyl-L-alanyl-L-phenylalaninate (Boc-L-Ser(*t*Bu)-L-Ala-L-Ala-L-Phe-O*t*Bu, KH_1229), **L,L,L,L-12 - ^{1}H NMR (500 MHz, DMSO-d_6)**



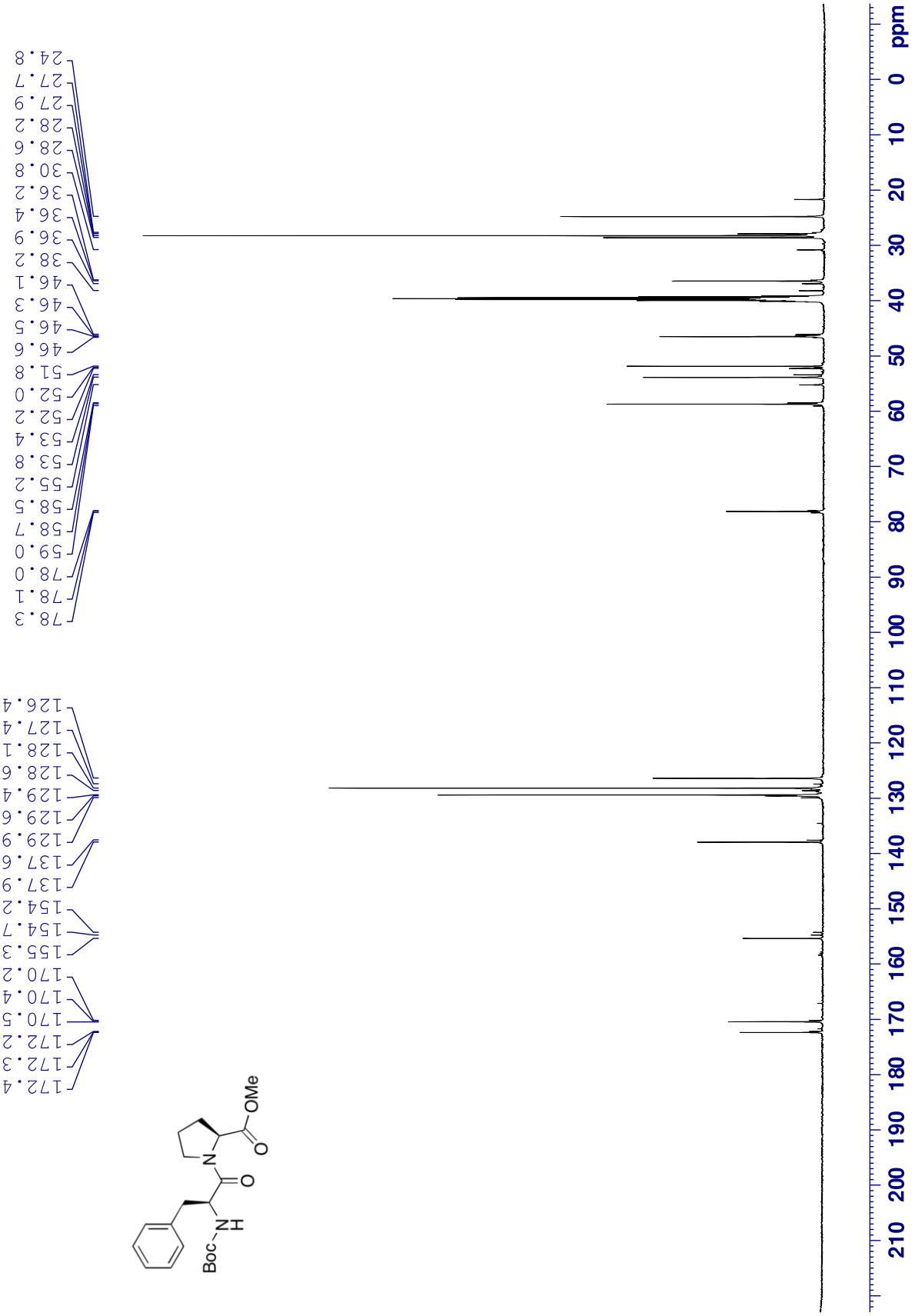
tert-Butyl *N*-(*tert*-butoxycarbonyl)-*O*-(*tert*-butyl)-L-seryl-L-alanyl-L-alanyl-L-phenylalaninate (Boc-L-Ser(*t*Bu)-L-Ala-L-Ala-L-Phe-O*t*Bu, KH_1229) **L,L,L,L-12 - ^{13}C NMR (126 MHz, DMSO-d_6)**



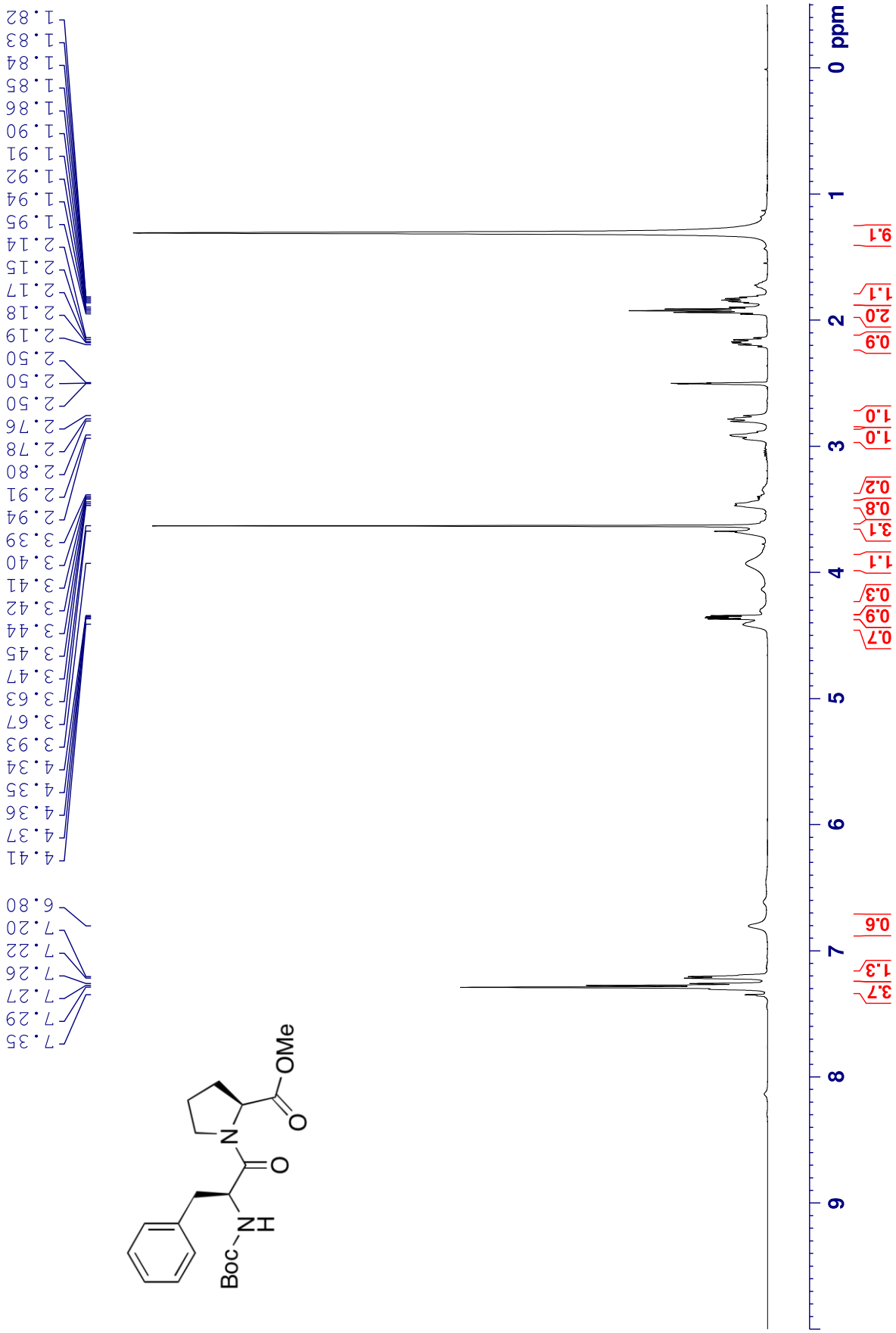
(*S*)-Methyl 1-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-phenylpropanoyl)pyrrolidine-2-carboxylate (Boc-L-Phe-L-Pro-OMe, KH_983) **L,L-S10 - ^{1}H NMR (500 MHz, DMSO-d_6, mixture of rotamers)**



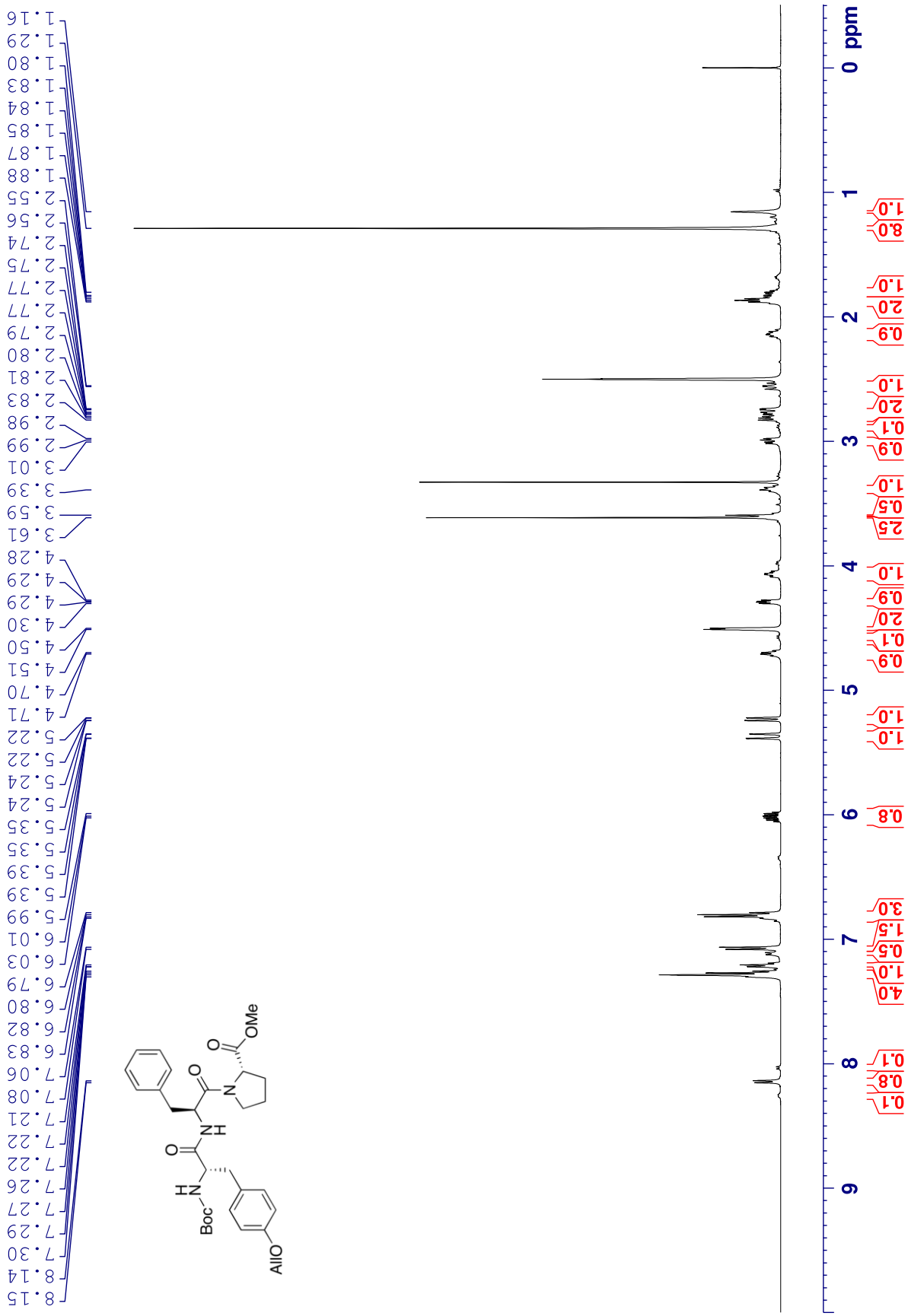
(*S*)-Methyl 1-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-phenylpropanoyl)pyrrolidine-2-carboxylate (Boc-L-Phe-L-Pro-OMe, KH_983) **L,L-S10 - ^{13}C NMR (126 MHz, DMSO-d_6, mixture of rotamers)**



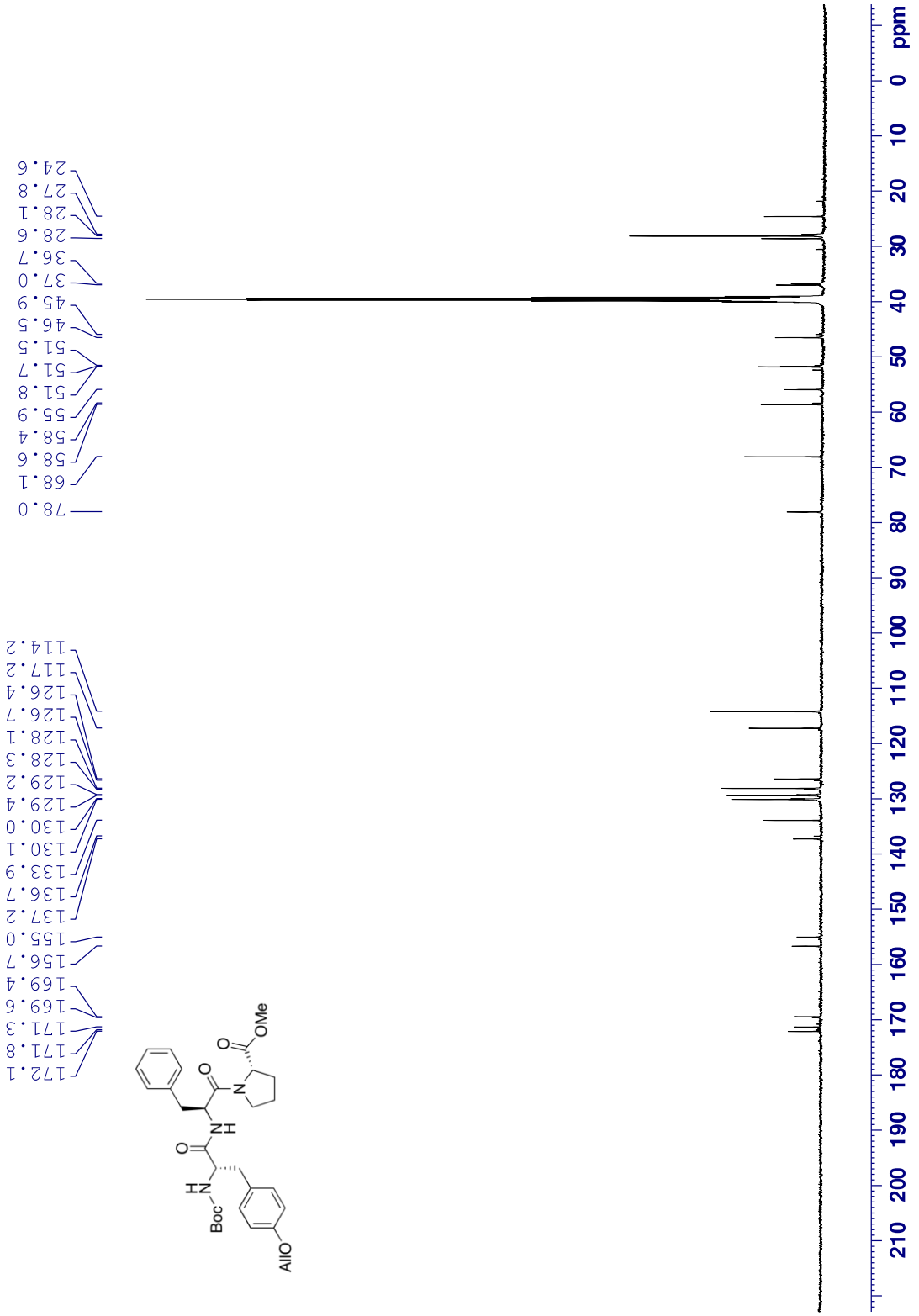
(*S*)-Methyl 1-((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-phenylpropanoyl)pyrrolidine-2-carboxylate (Boc-L-Phe-L-Pro-OMe, KH_983) **L,L-S10 - ^{1}H NMR (500 MHz, DMSO-d_6, 60°C, mixture of rotamers)**



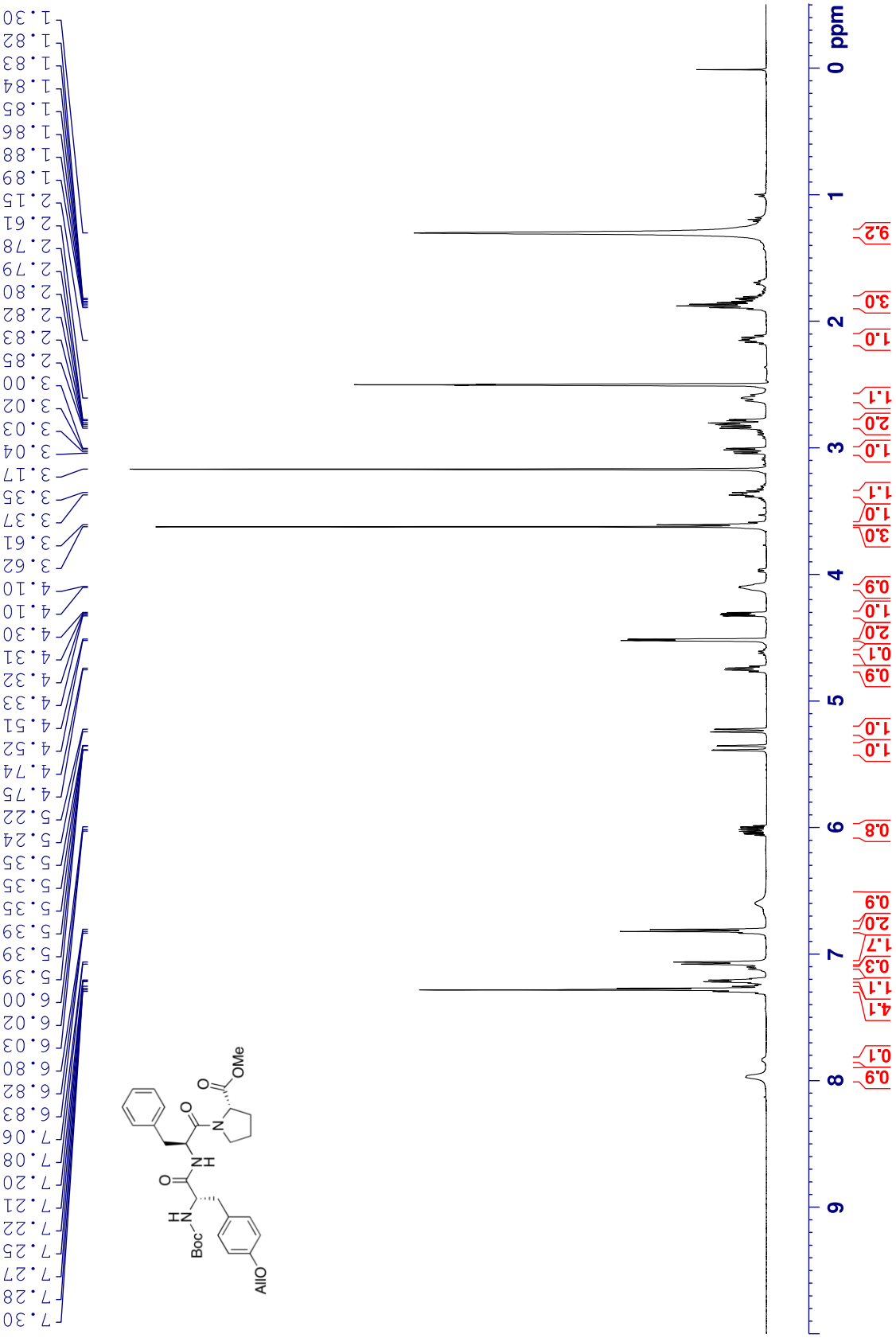
Methyl ((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenylalanyl-L-prolinate (Boc-L-Tyr(All)-L-Phe-L-Pro-OMe, KH_985) **L,L,L-S11 - ^{1}H NMR (500 MHz, DMSO-d_6, mixture of rotamers)**



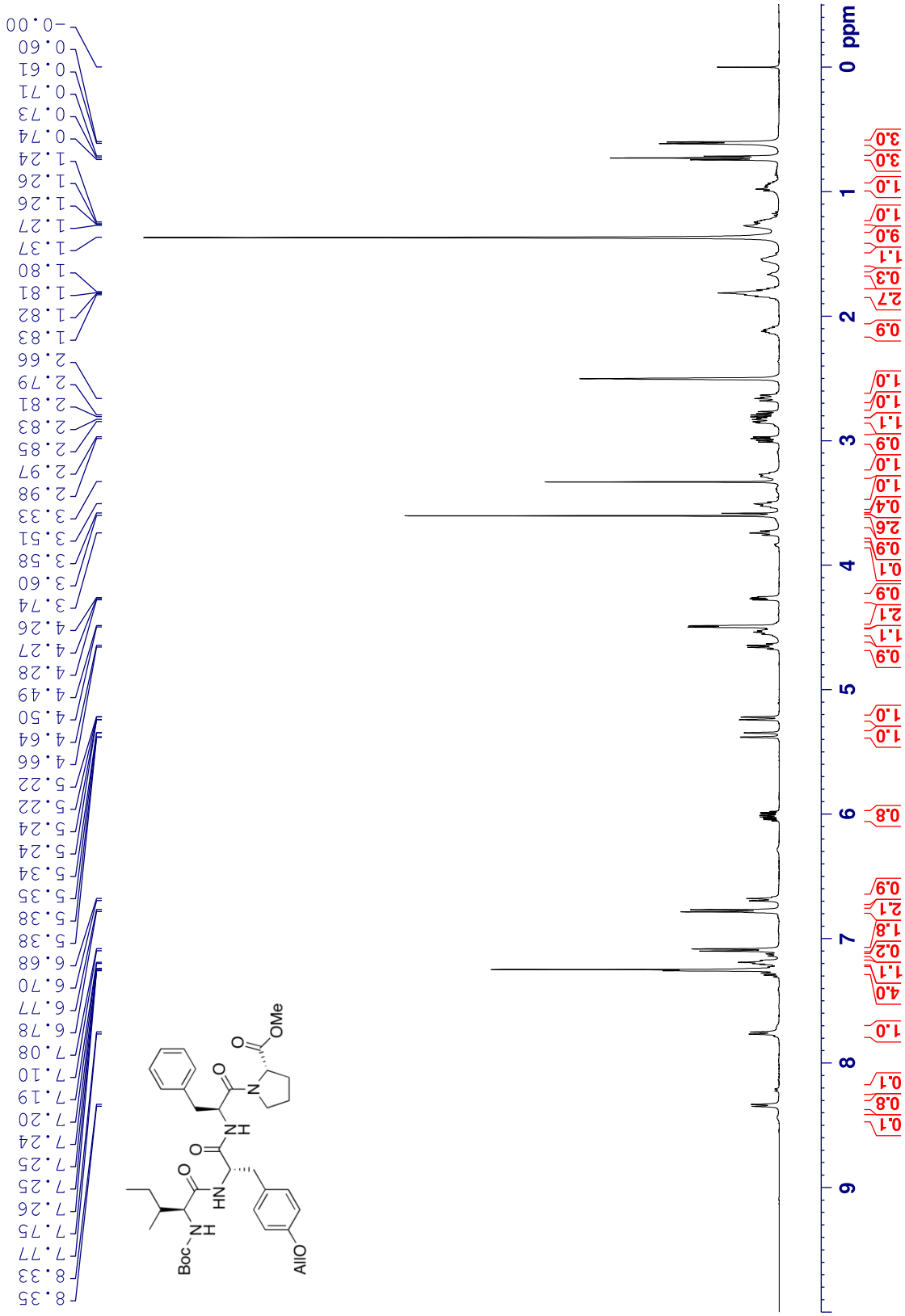
Methyl ((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenylalanyl-L-prolinate (Boc-L-Tyr(All)-L-Phe-L-Pro-OMe, KH_985) **L,L,L-S11 - ^{13}C NMR (126 MHz, DMSO-d_6, mixture of rotamers)**



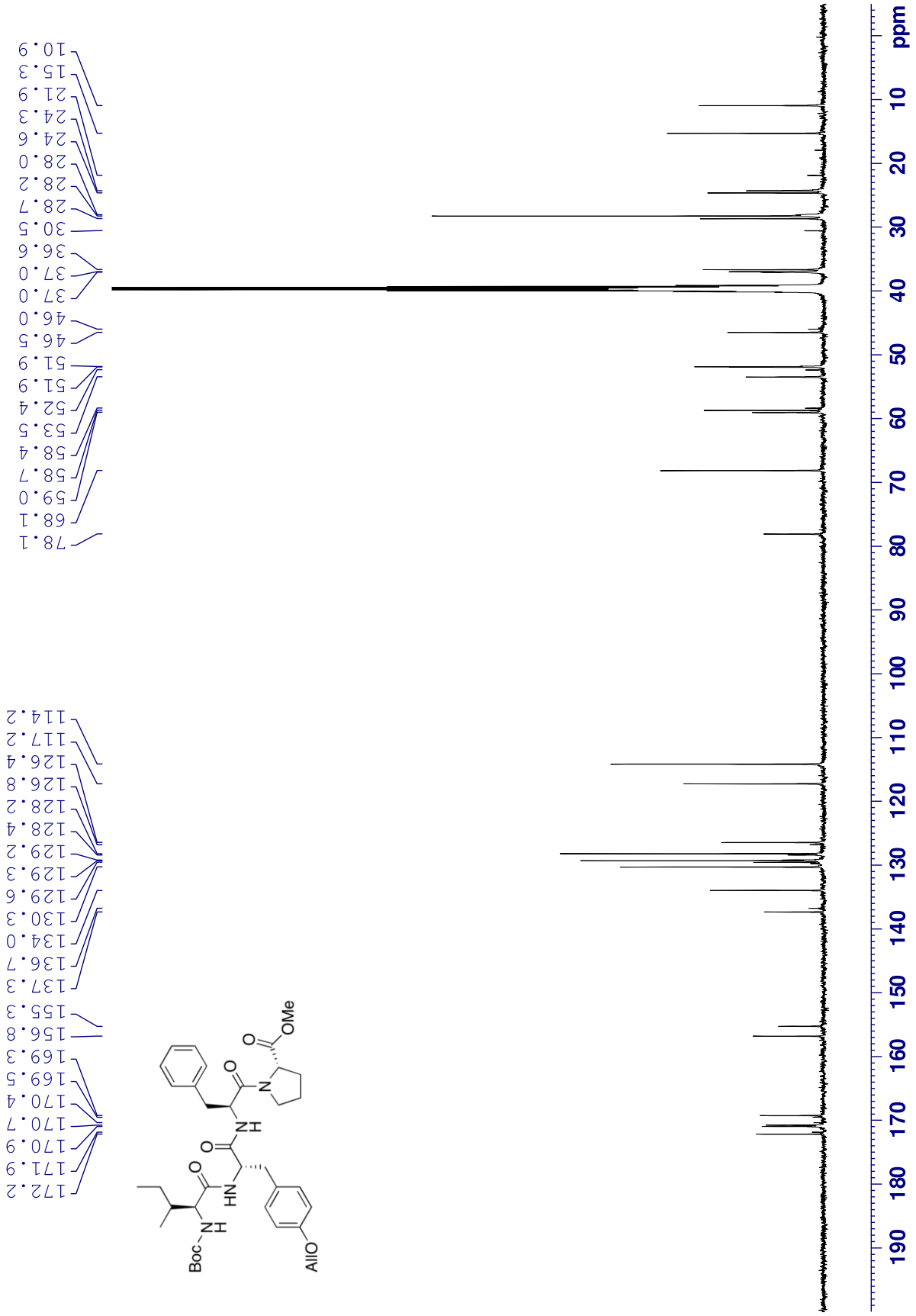
Methyl ((*S*)-2-((*tert*-butoxycarbonyl)amino)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenylalanyl-L-prolinate (Boc-L-Tyr(All)-L-Phe-L-Pro-OMe, KH_985) **L,L,L-S11 - ^{1}H NMR (500 MHz, DMSO-d_6, 60°C, mixture of rotamers)**



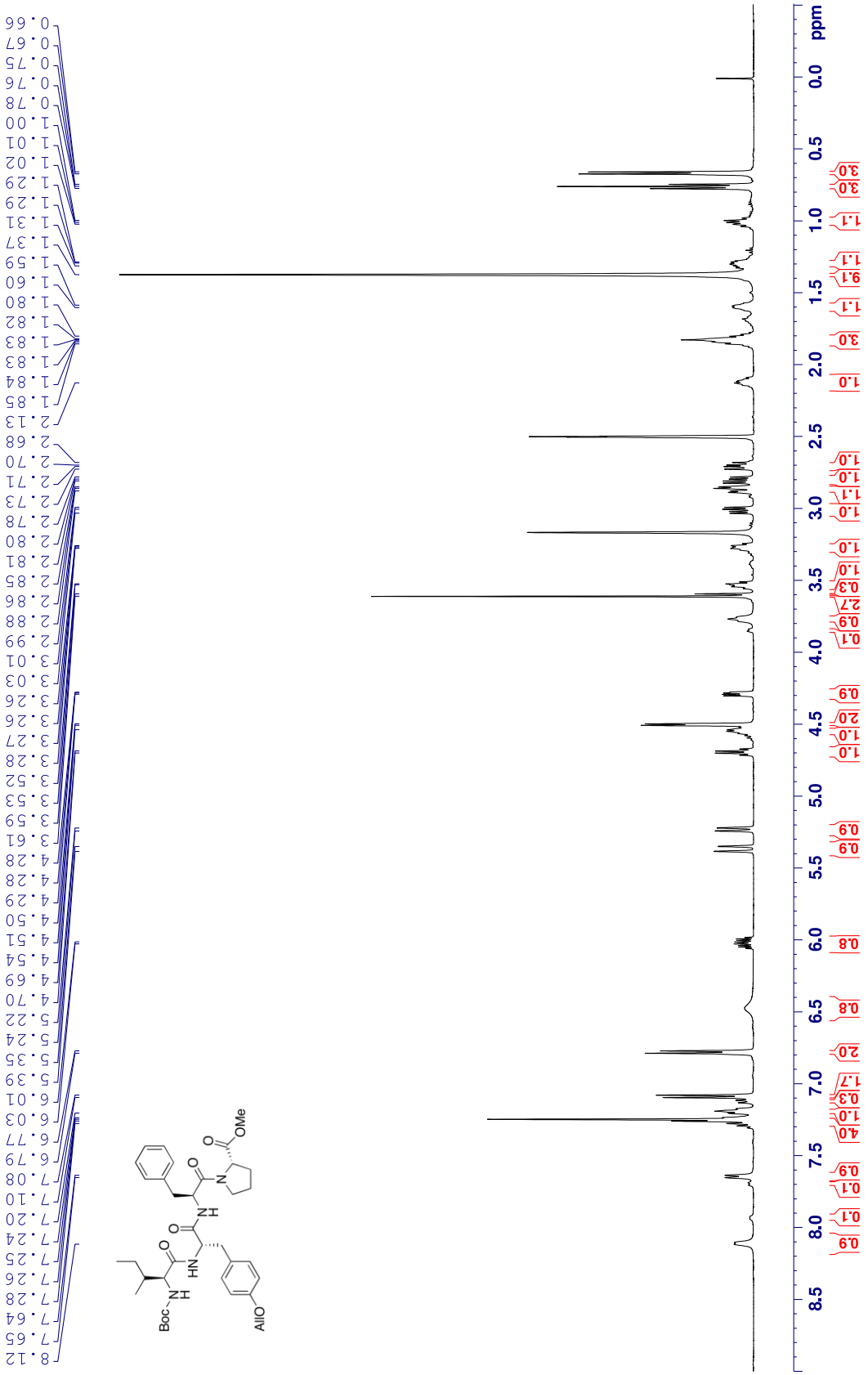
Methyl ((*S*)-2-((2*S*,3*R*)-2-((tert-butoxycarbonyl)amino)-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenylalanyl-L-prolinate (Boc-L-Ile-L-Tyr(All)-L-Phe-L-Pro-OMe, KH_987) **L,L,L,L-S12 - ^{1}H NMR (500 MHz, DMSO-*d*$_6$, mixture of rotamers)**



Methyl ((*S*)-2-((2*S*,3*R*)-2-((*tert*-butoxycarbonyl)amino)-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenylalanyl-L-prolinate (Boc-L-Ile-L-Tyr(All)-L-Phe-L-Pro-OMe, KH_987) **L,L,L,L-S12 - ^{13}C NMR (126 MHz, DMSO-d_6, mixture of rotamers)**

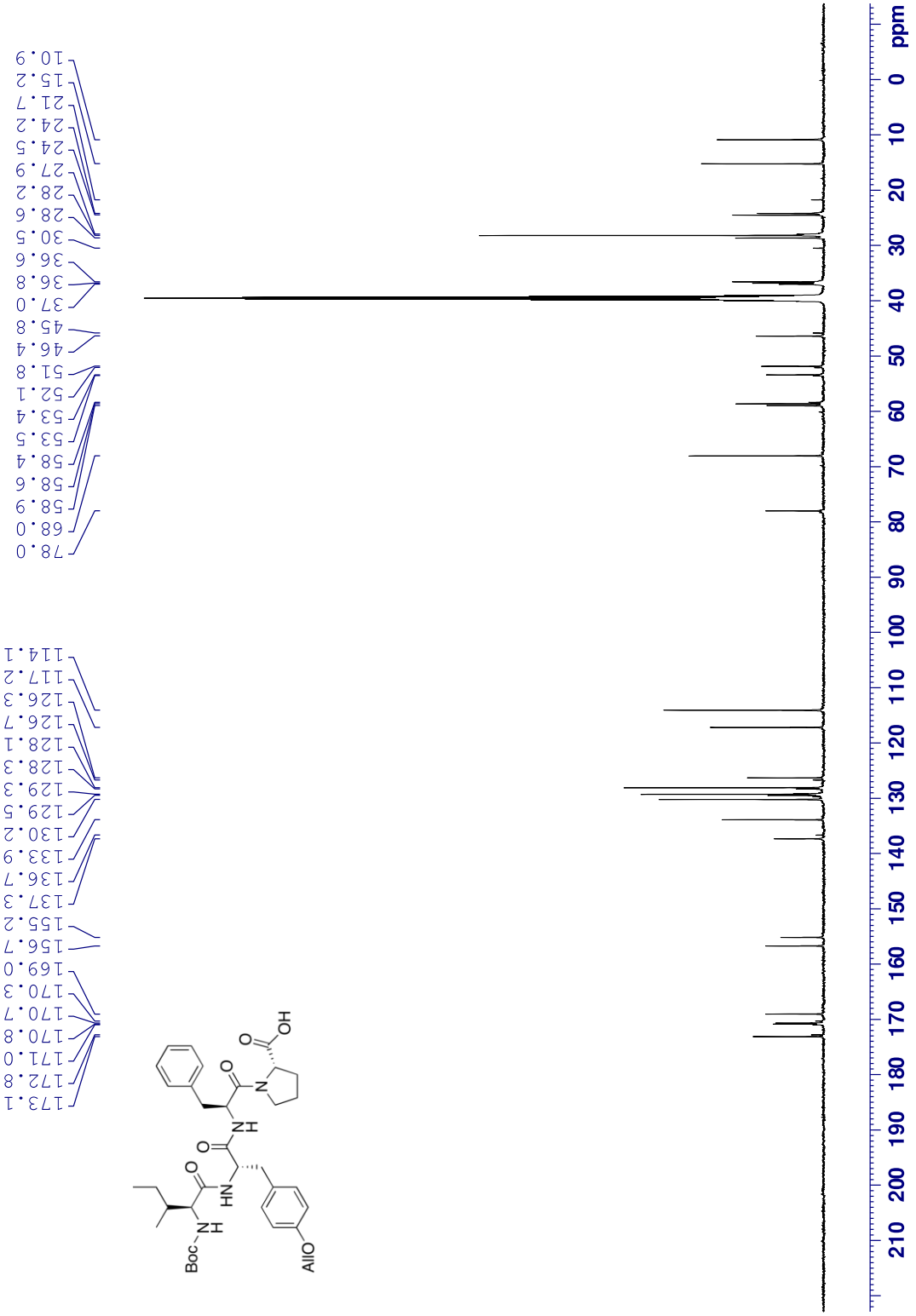


Methyl ((*S*)-2-((2*S*,3*R*)-2-((tert-butoxycarbonyl)amino)-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenylalanyl-L-prolinate (Boc-L-Ile-L-Tyr(All)-L-Phe-L-Pro-OMe, KH_987) **L,L,L,L-S12 - ^{1}H NMR (500 MHz, DMSO-*d*$_6$, 60°C, mixture of rotamers)**



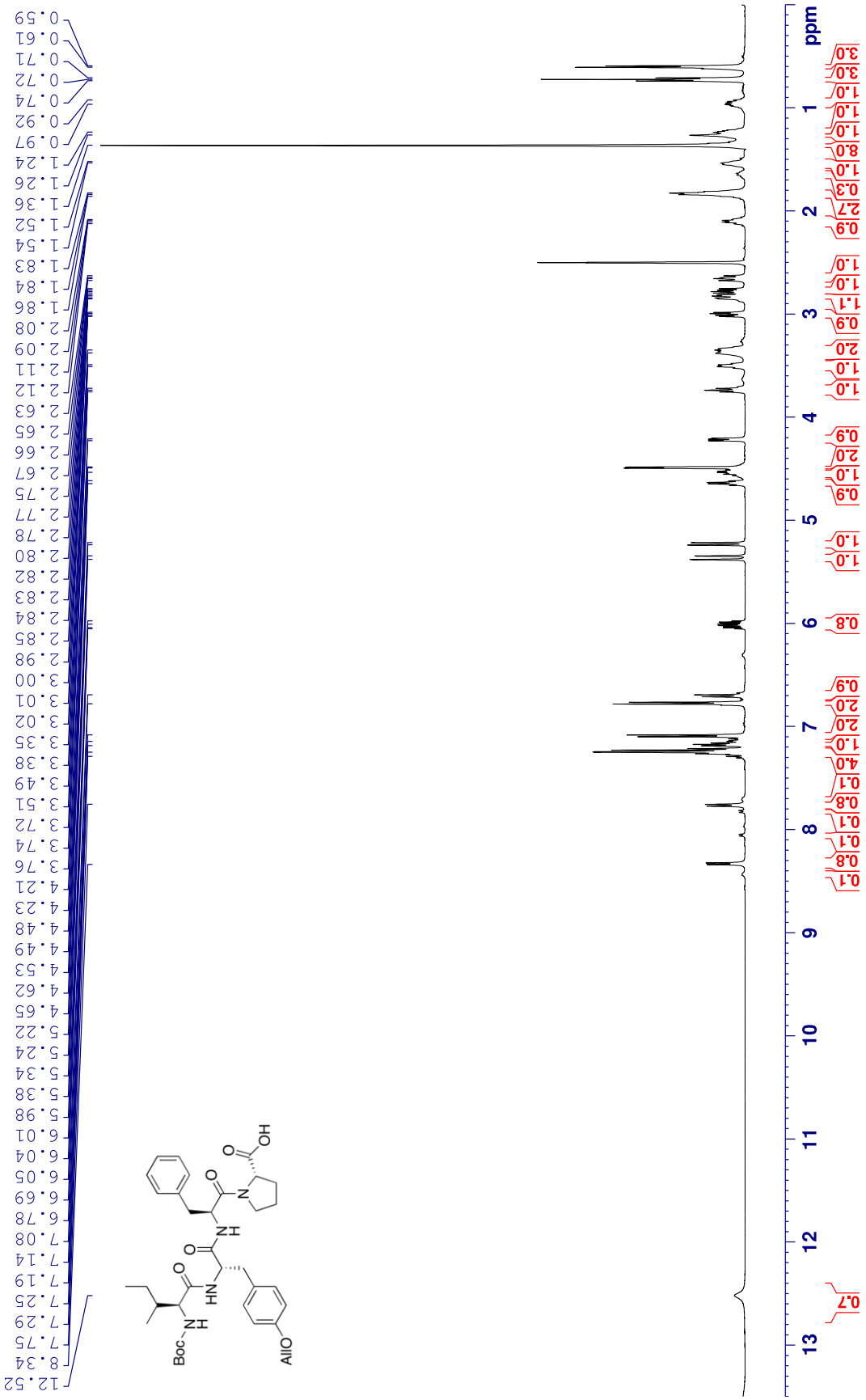
((*S*)-2-((2*S*,3*R*)-2-((*tert*-butoxycarbonyl)amino)-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenyl-alanyl-L-proline (Boc-L-Ile-L-Tyr(All)-L-Phe-L-Pro-OH, KH_988)

L,L,L,L-S13 - ^{1}H NMR (500 MHz, DMSO-d_6, mixture of rotamers)



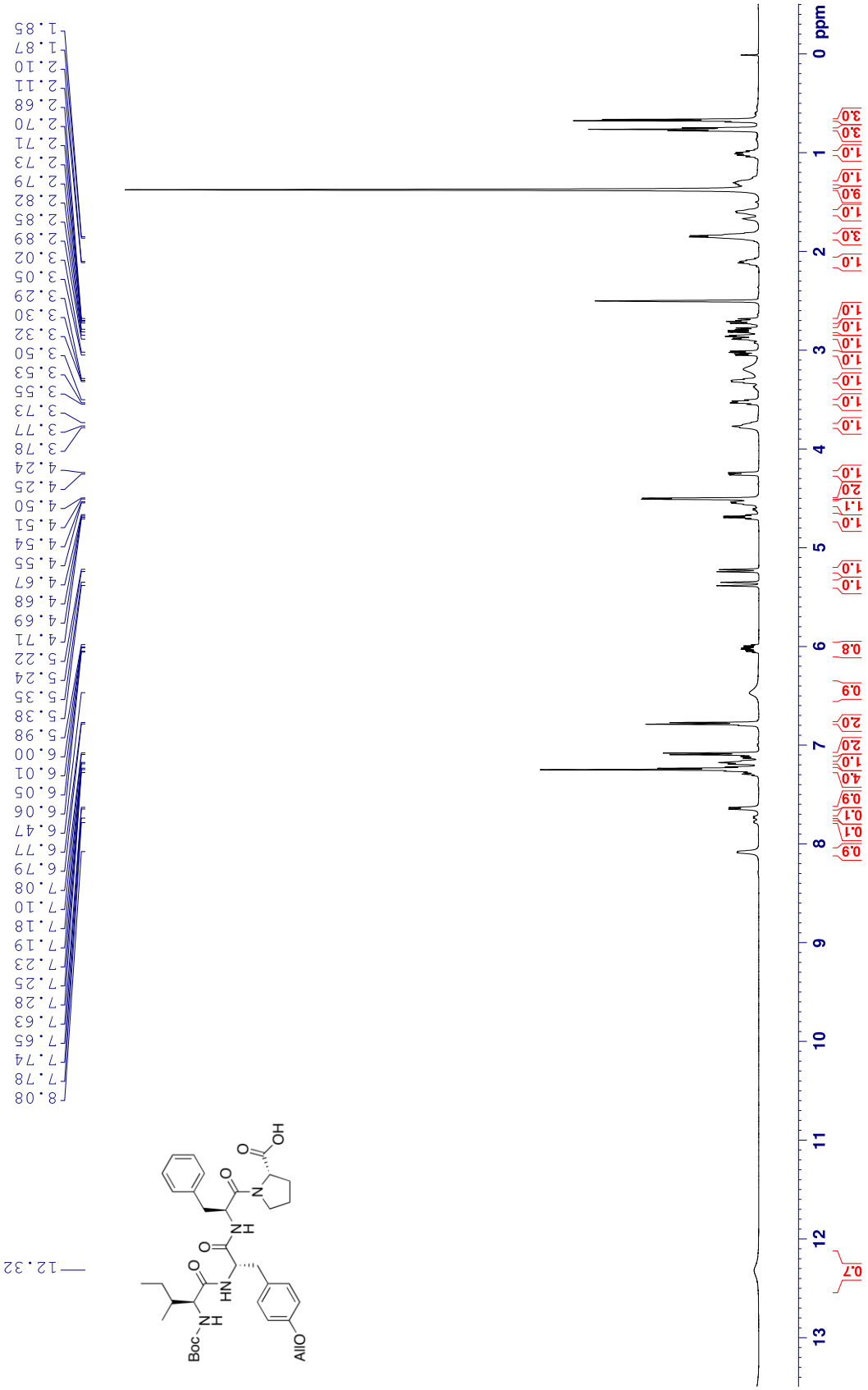
((*S*)-2-((2*S*,3*R*)-2-((*tert*-butoxycarbonyl)amino)-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenyl-alanyl-L-proline (Boc-L-Ile-L-Tyr(All)-L-Phe-L-Pro-OH, KH_988)

L,L,L,L-S13 - ^{13}C NMR (126 MHz, DMSO-d_6, mixture of rotamers)

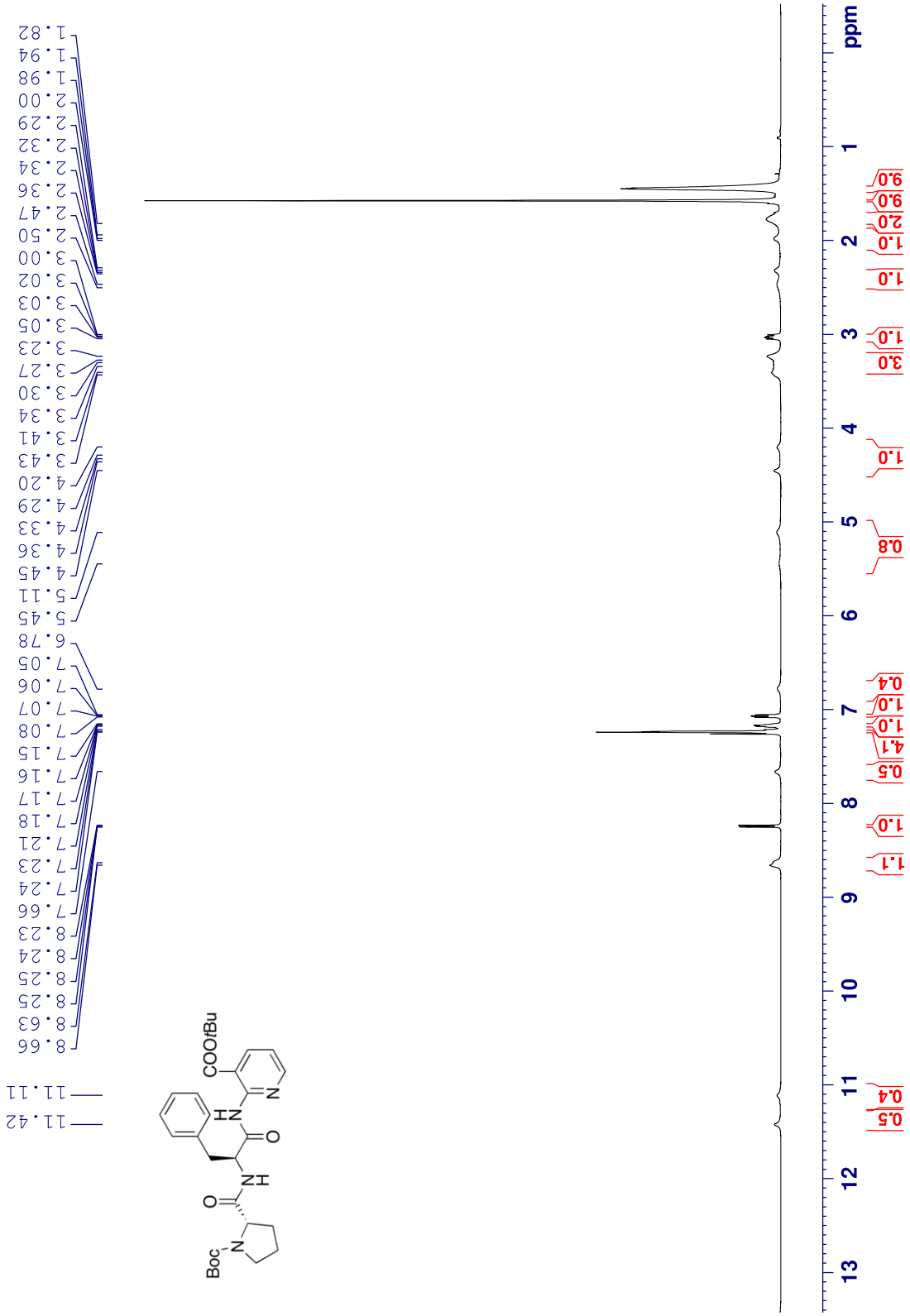


((*S*)-2-((2*S*,3*R*)-2-((*tert*-butoxycarbonyl)amino)-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenyl-alanyl-L-proline (Boc-L-Ile-L-Tyr(All)-L-Phe-L-Pro-OH, KH_988)

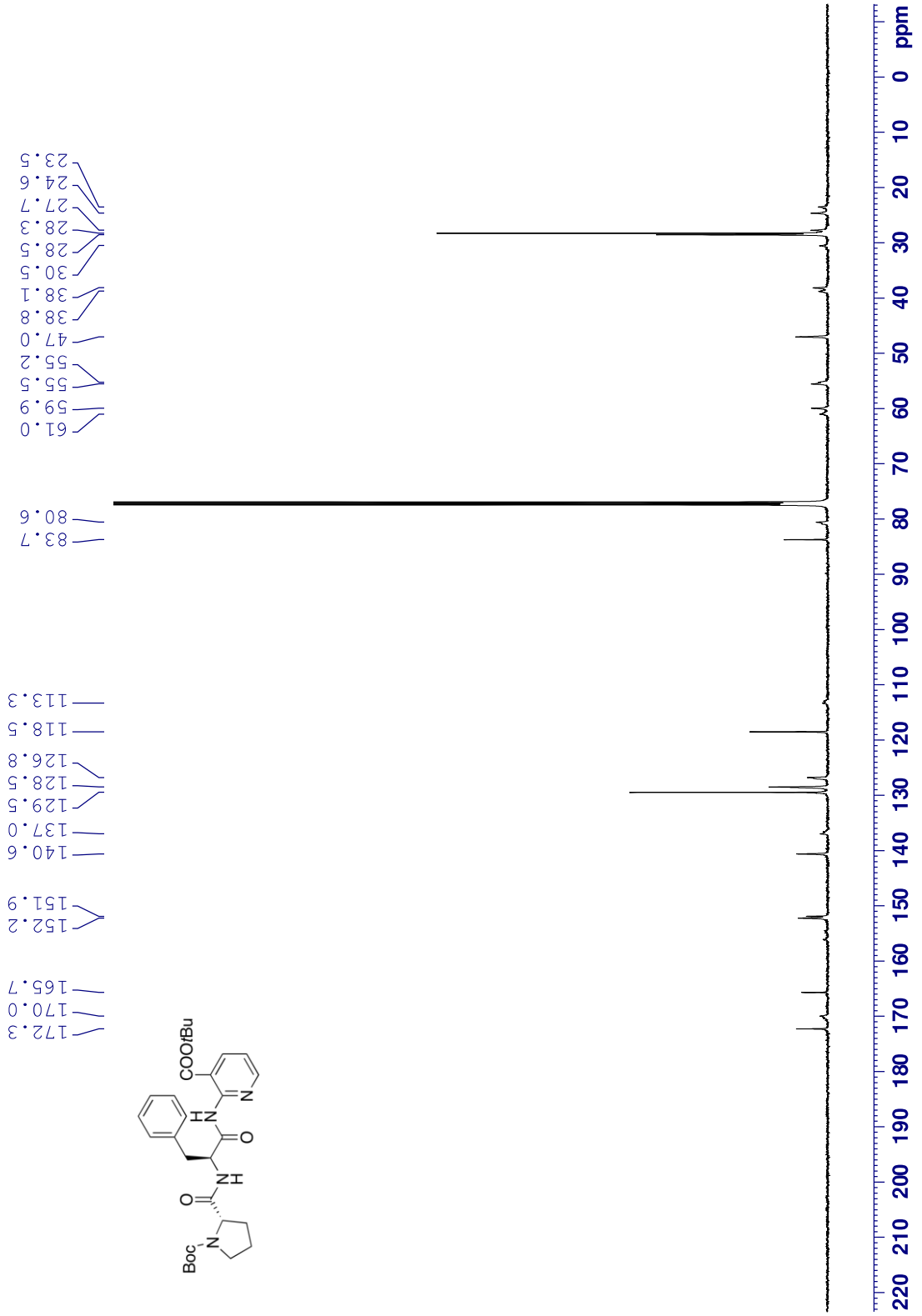
L,L,L,L-S13 - ^{1}H NMR (500 MHz, DMSO-d_6, 60°C, mixture of rotamers)



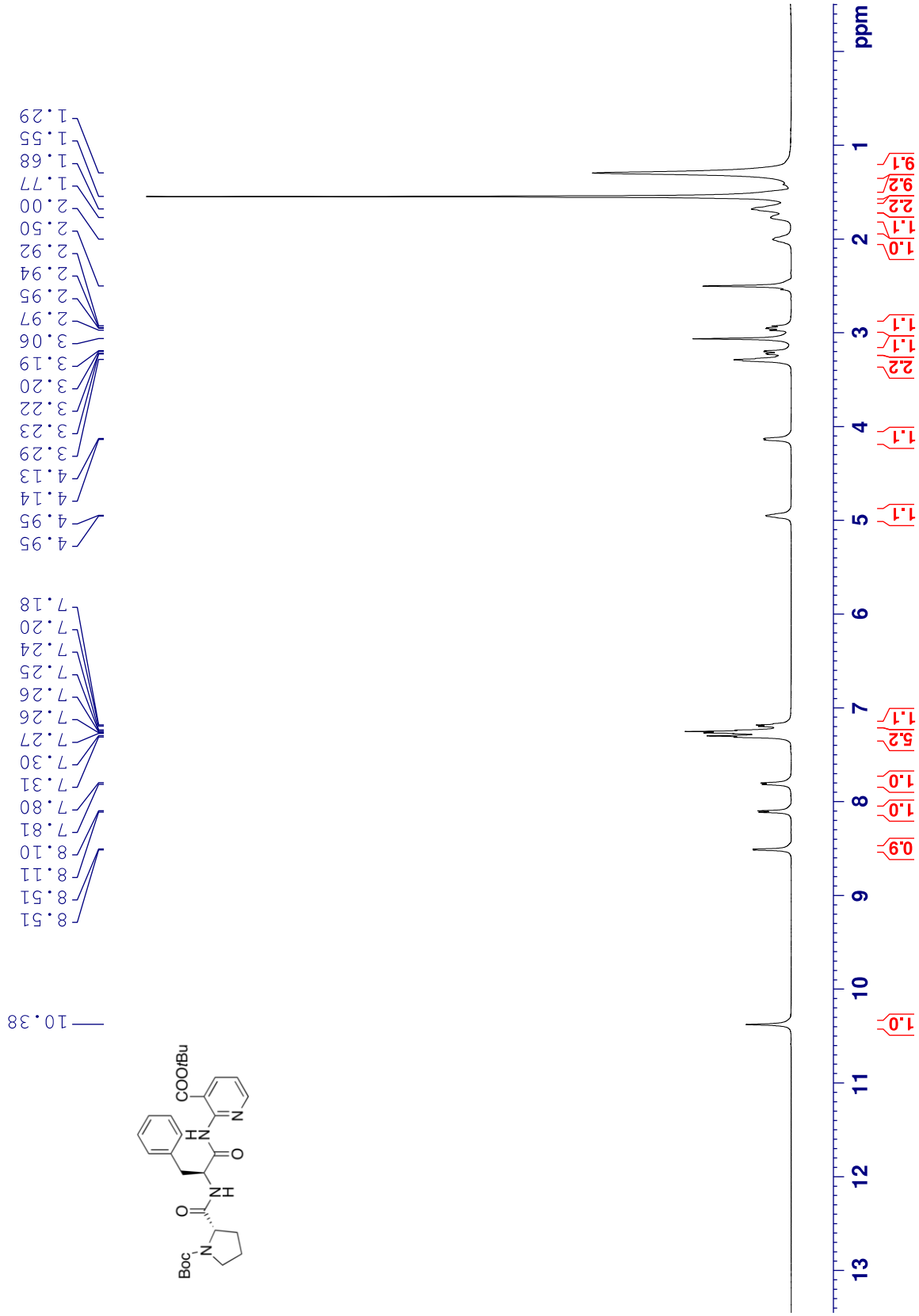
tert-Butyl 2-((2*S*)-2-(1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxamido)-3-phenylpropanamido)nicotinate (Boc-Pro-Phe-NH-*t*Bu-nic, KH_1214) **L,L-S14 - ^{1}H NMR (500 MHz, $CDCl_3$, mixture of rotamers)**



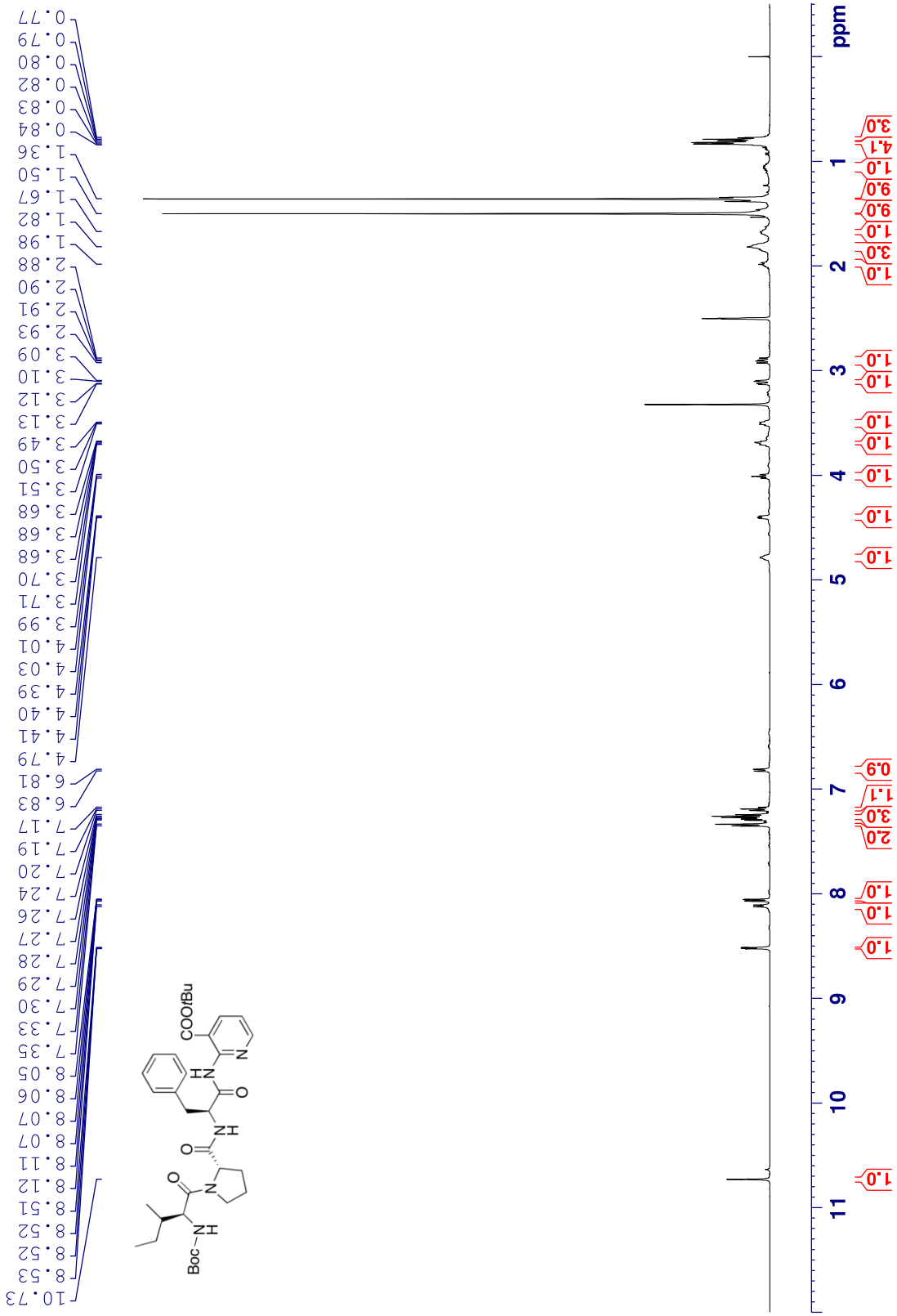
tert-Butyl 2-((2*S*)-2-(1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxamido)-3-phenylpropanamido)nicotinate (Boc-Pro-Phe-NH-*t*Bu-nic, KH_1214) **L,L-S14 - ^{13}C NMR (500 MHz, $CDCl_3$, mixture of rotamers)**



tert-Butyl 2-((2*S*)-2-(1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxamido)-3-phenylpropanamido)nicotinate (Boc-Pro-Phe-NH-*t*Bu-nic, KH_1214) **L,L-S14 - ^{1}H NMR (500 MHz, DMSO-d_6, 80°C)**

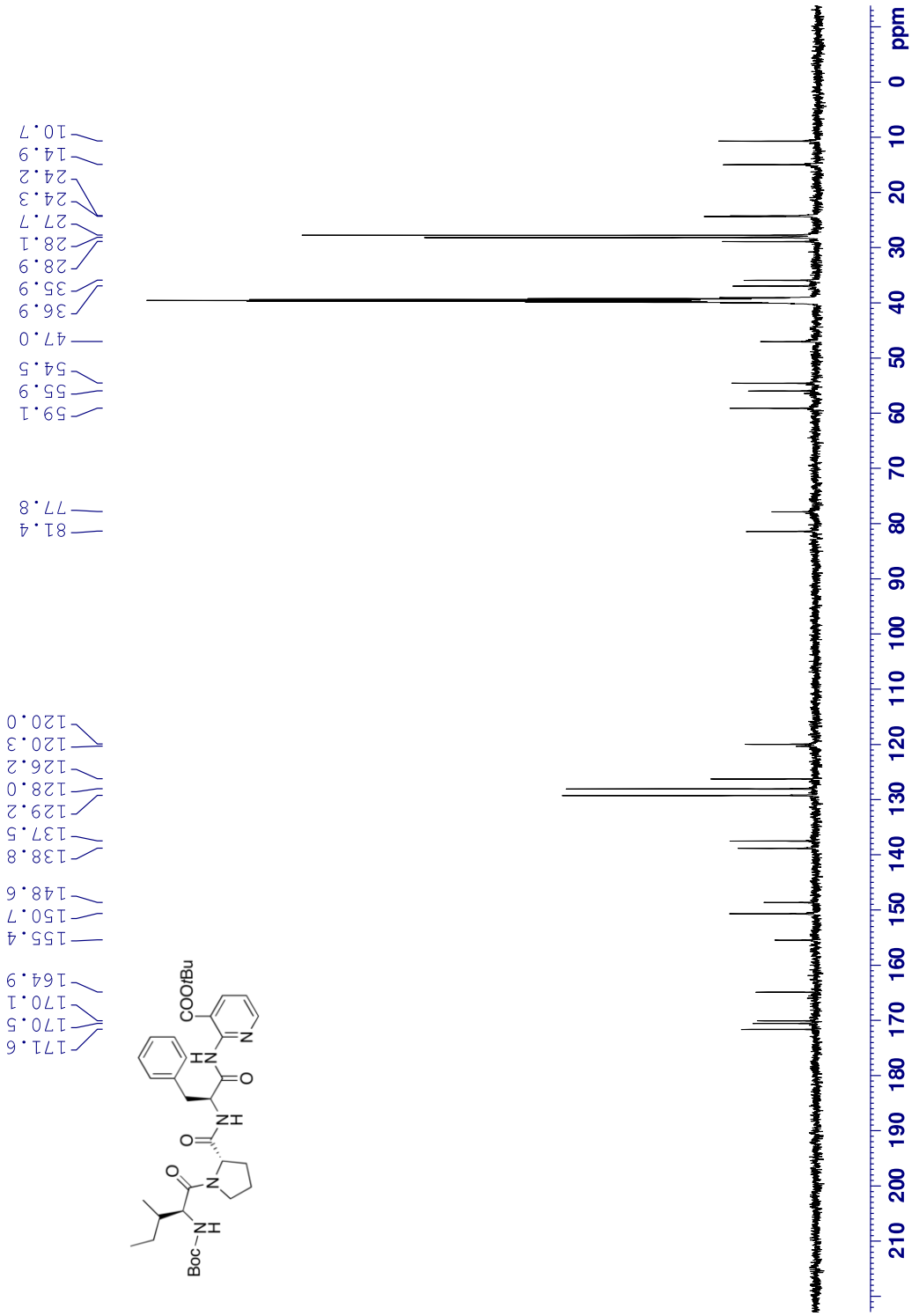


tert-Butyl 2-((*S*)-2-((*S*)-1-((2*S*,3*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methylpentanoyl)pyrrolidine-2-carboxamido)-3-phenylpropan-amido)nicotinate (Boc-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic, KH_1039) **L,L,L-S15 - ^{1}H NMR (500 MHz, DMSO-d_6)**

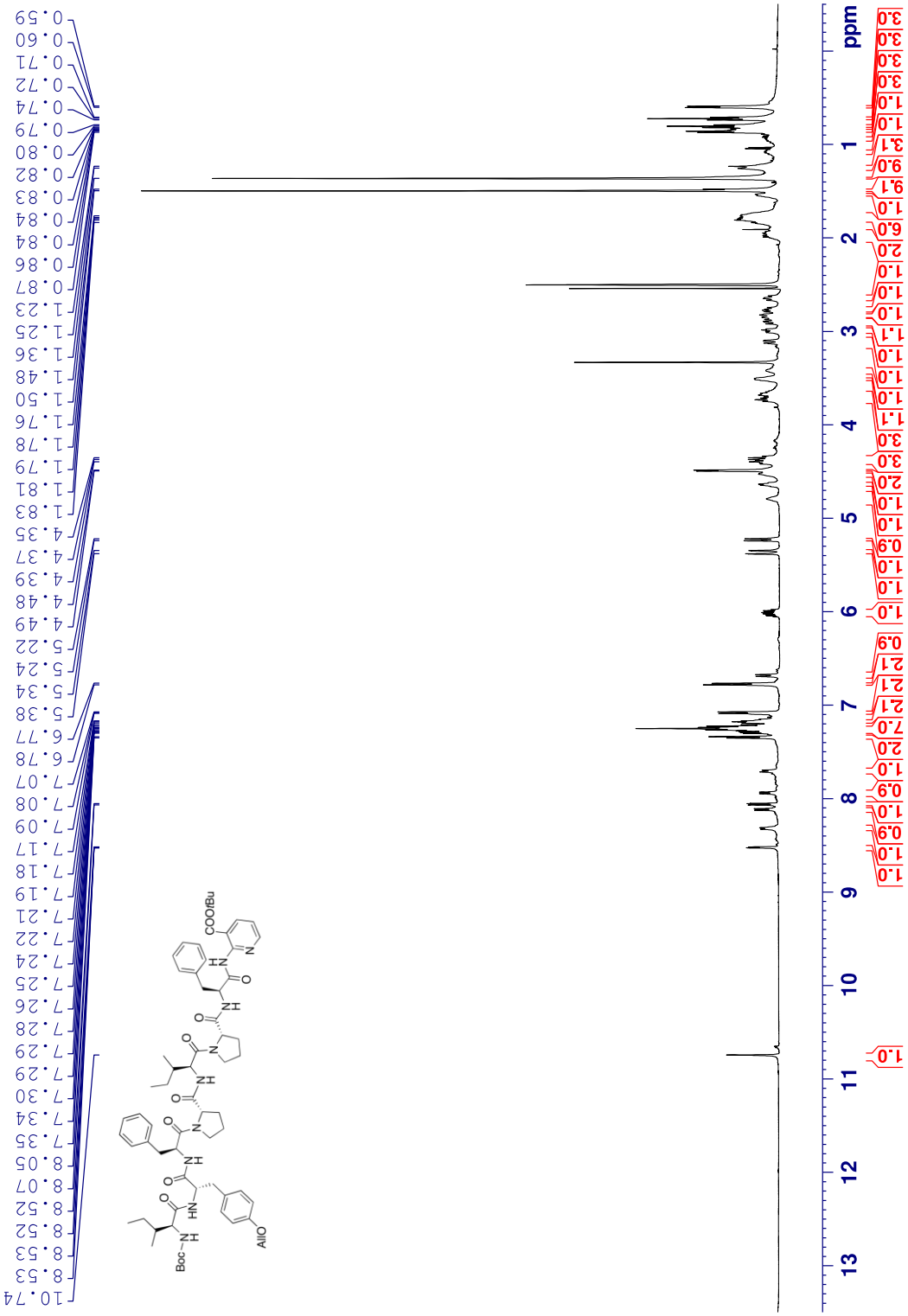


tert-Butyl 2-((*S*)-2-((*S*)-1-((2*S*,3*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methylpentanoyl)pyrrolidine-2-carboxamido)-3-phenylpropan-amido)nicotinate (Boc-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic, KH_1039) **L,L,L-**

S15 - ^{13}C NMR (126 MHz, DMSO-d_6)

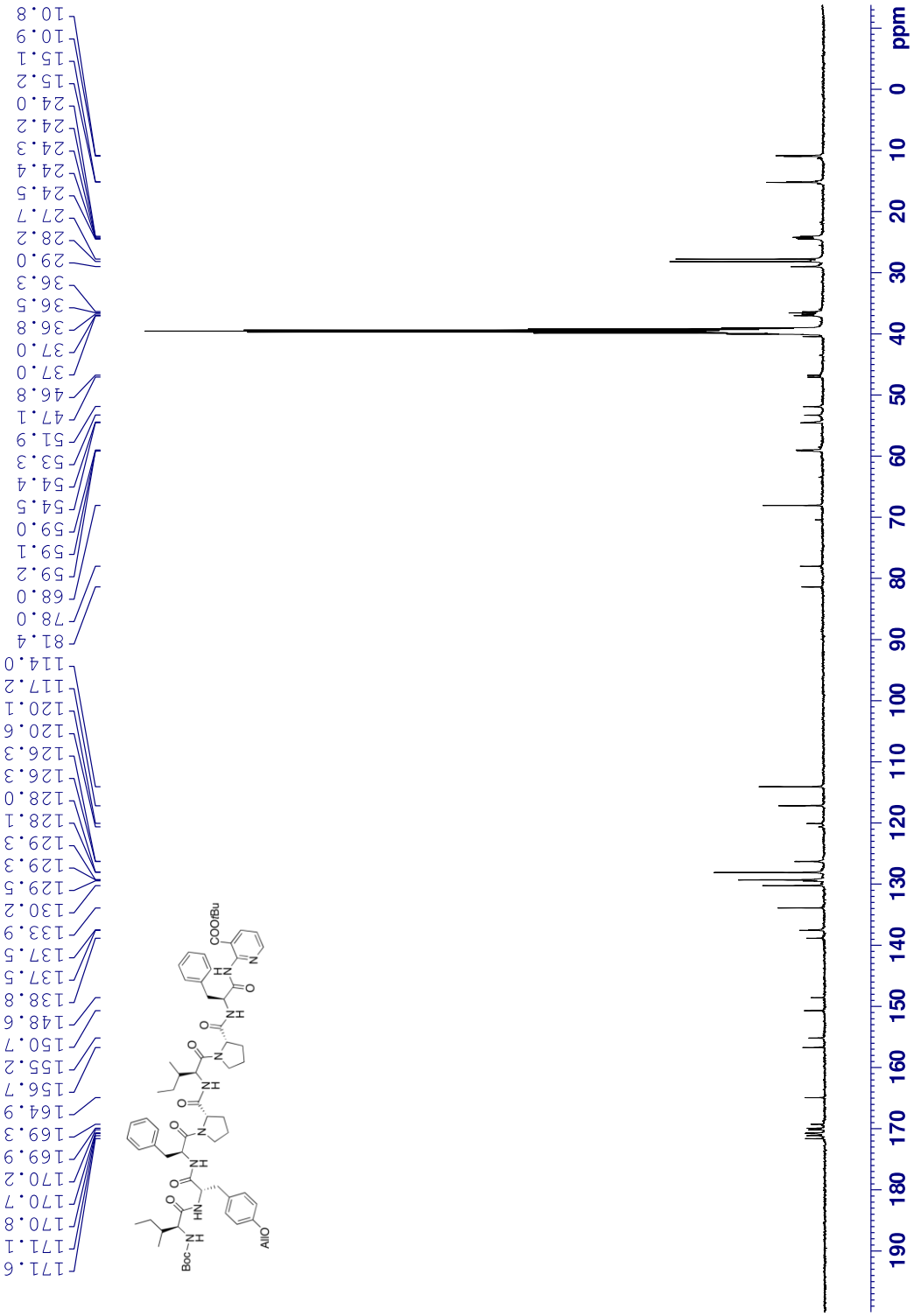


tert-Butyl 2-((*S*)-2-((*S*)-1-(((*S*)-2-((2*S*,3*R*)-2-((*tert*-butoxycarbonyl)amino)-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl) propanoyl)-L-phenylalanyl-L-prolyl-L-isoleucyl)pyrrolidine-2-carboxamido)-3-phenylpropanamido)nicotinate (Boc-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic, KH_1042) **L,L,L,L,L,L,L-S16 - ^{1}H NMR (500 MHz, DMSO-d_6)**

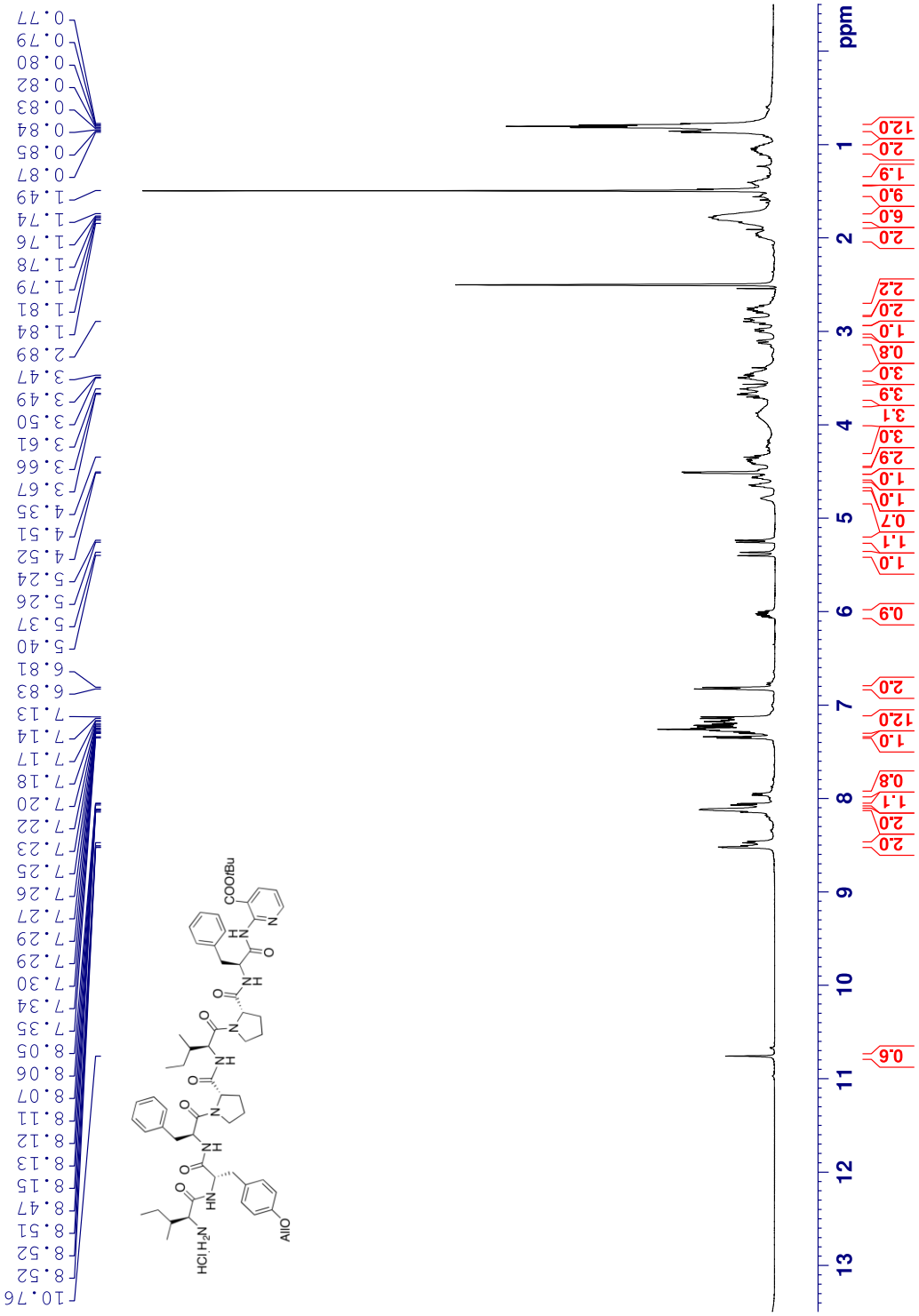


tert-Butyl 2-((*S*)-2-((*S*)-1-(((*S*)-2-((2*S*,3*R*)-2-((*tert*-butoxycarbonyl)amino)-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl) propanoyl)-L-phenylalanyl-L-prolyl-L-isoleucyl)pyrrolidine-2-carboxamido)-3-phenylpropanamido)nicotinate (Boc-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic, KH_1042)

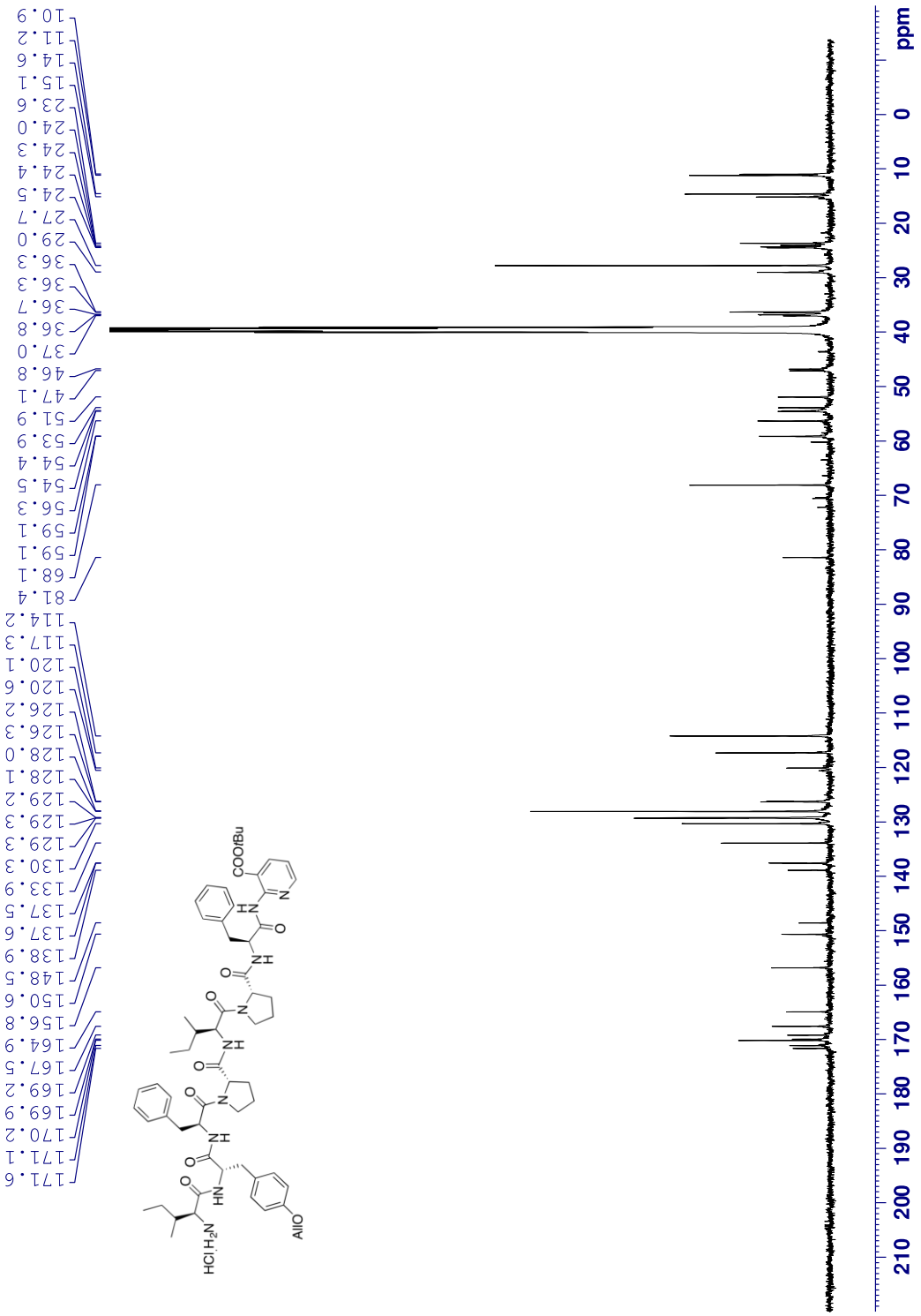
L,L,L,L,L,L,L-S16 - ^{13}C NMR (126 MHz, DMSO-d_6)



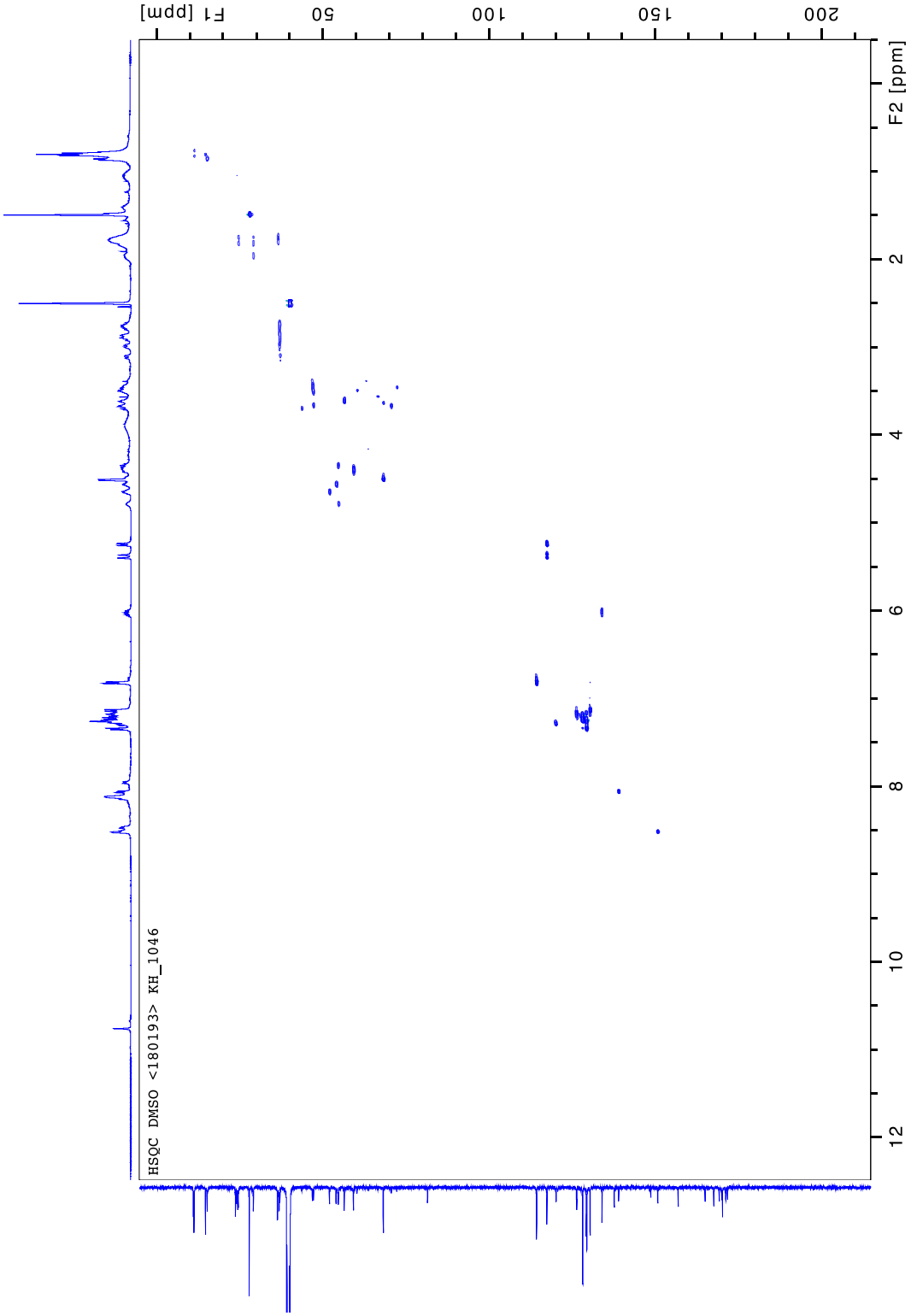
tert-Butyl 2-((*S*)-2-((*S*)-1-(((*S*)-2-((2*S*,3*R*)-2-amino-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenyl-alanyl-L-prolyl-L-isoleucyl)pyrrolidine-2-carboxamido)-3-phenylpropanamido)nicotinate hydrochloride acid salt (H-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic.HCl, KH_1046) **L,L,L,L,L,L-17.HCl - ^{1}H NMR (500 MHz, DMSO-d_6)**



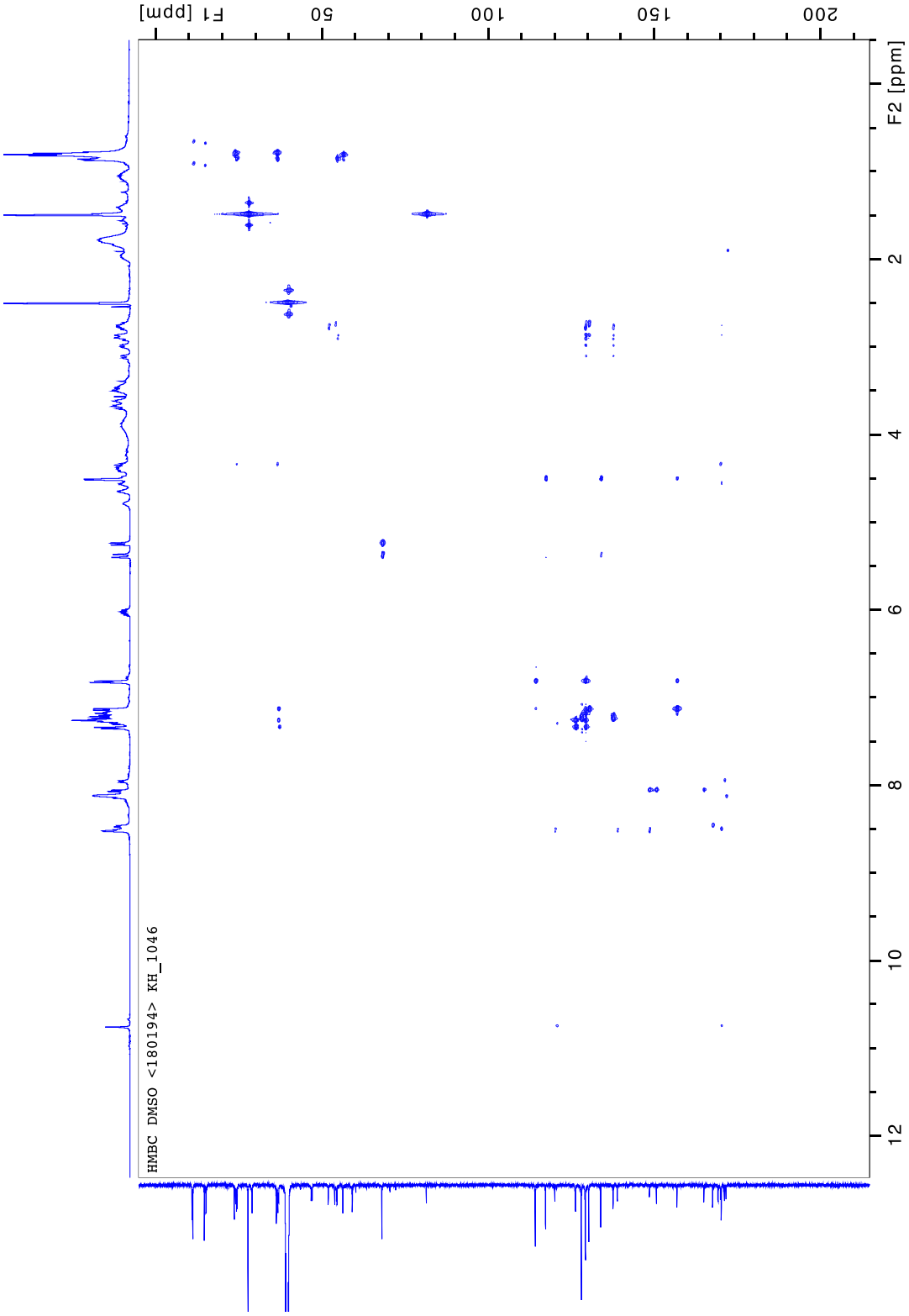
tert-Butyl 2-((*S*)-2-((*S*)-1-(((*S*)-2-((2*S*,3*R*)-2-amino-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenyl-alanyl-L-prolyl-L-isoleucyl)pyrrolidine-2-carboxamido)-3-phenylpropanamido)nicotinate hydrochloride acid salt (H-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic.HCl, KH_1046) **L,L,L,L,L,L-17.HCl - ^{13}C NMR (126 MHz, DMSO-d_6)**



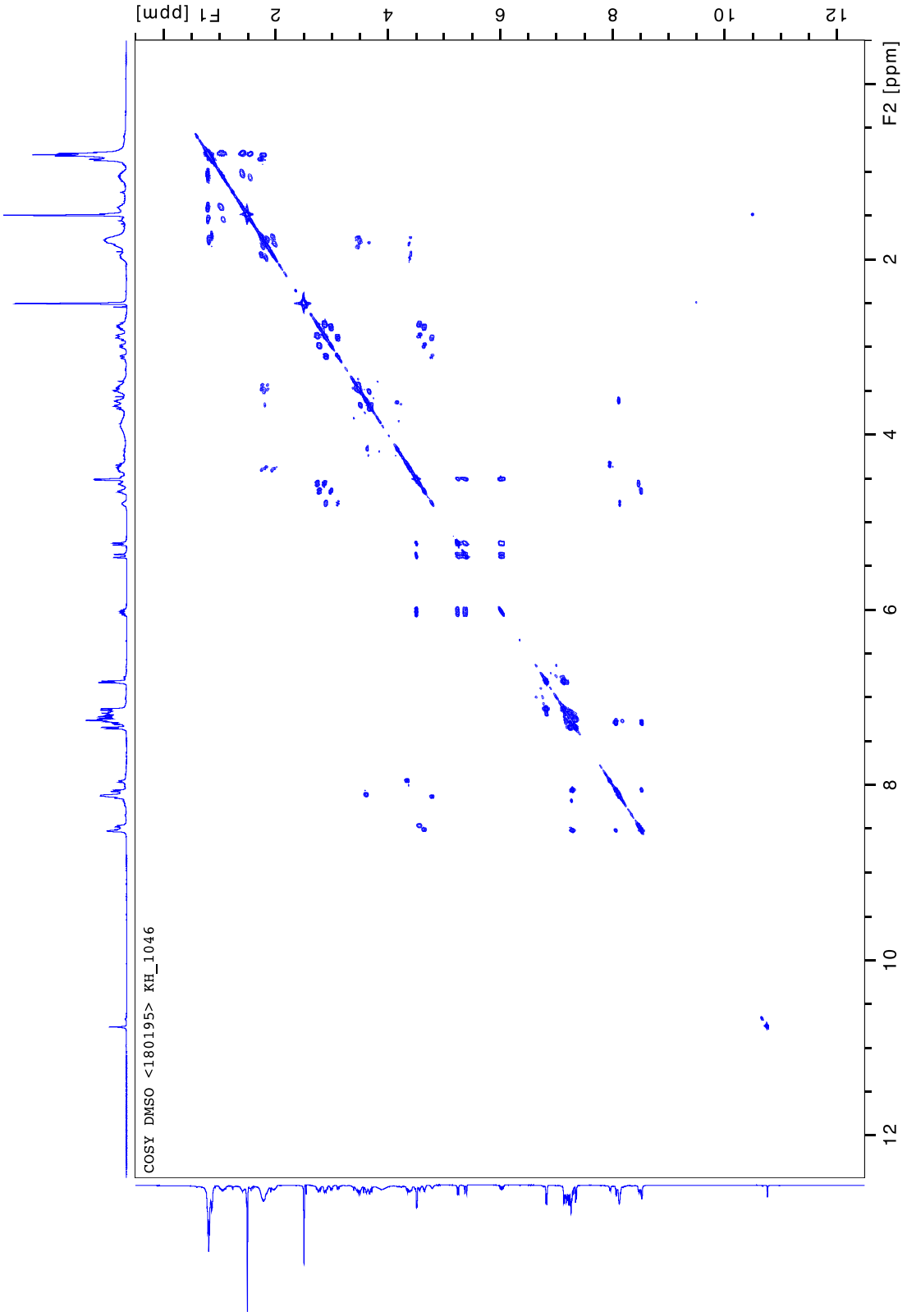
tert-Butyl 2-((*S*)-2-((*S*)-1-(((*S*)-2-((2*S*,3*R*)-2-amino-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenyl-alanyl-L-prolyl-L-isoleucyl)pyrrolidine-2-carboxamido)-3-phenylpropanamido)nicotinate hydrochloride acid salt (H-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic.HCl, KH_1046) **L,L,L,L,L,L-17.HCl – HSQC (DMSO-d_6)**



tert-Butyl 2-((*S*)-2-((*S*)-1-(((*S*)-2-((2*S*,3*R*)-2-amino-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenyl-alanyl-L-prolyl-L-isoleucyl)pyrrolidine-2-carboxamido)-3-phenylpropanamido)nicotinate hydrochloride acid salt (H-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic.HCl, KH_1046) **L,L,L,L,L,L-17.HCl – HMBC (DMSO-d_6)**

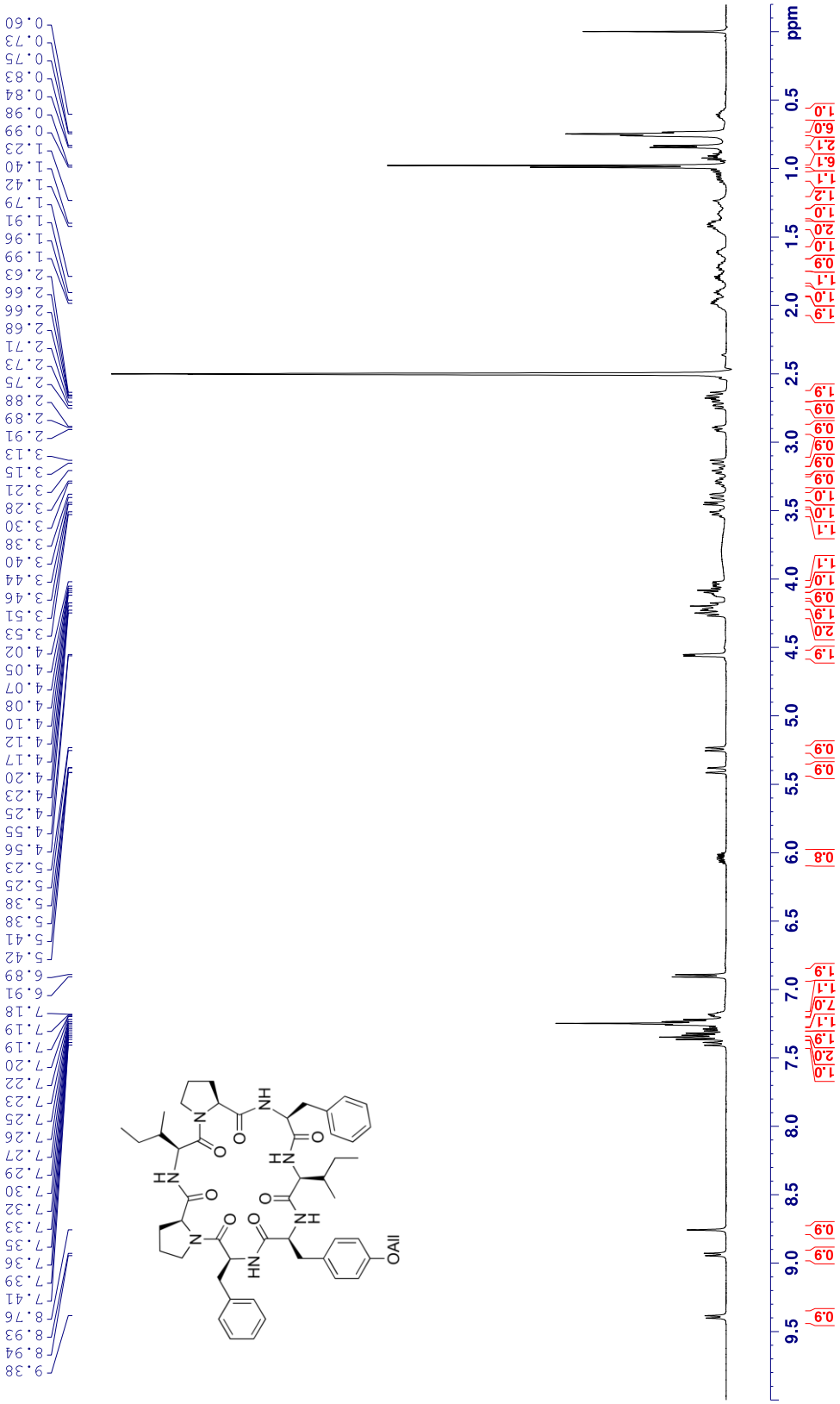


tert-Butyl 2-((*S*)-2-((*S*)-1-(((*S*)-2-((2*S*,3*R*)-2-amino-3-methylpentanamido)-3-(4-(((*E*)-prop-1-en-1-yl)oxy)phenyl)propanoyl)-L-phenyl-alanyl-L-prolyl-L-isoleucyl)pyrrolidine-2-carboxamido)-3-phenylpropanamido)nicotinate hydrochloride acid salt (H-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-NH-*t*Bu-nic.HCl, KH_1046) **L,L,L,L,L,L-17.HCl – COSY (DMSO-d_6)**



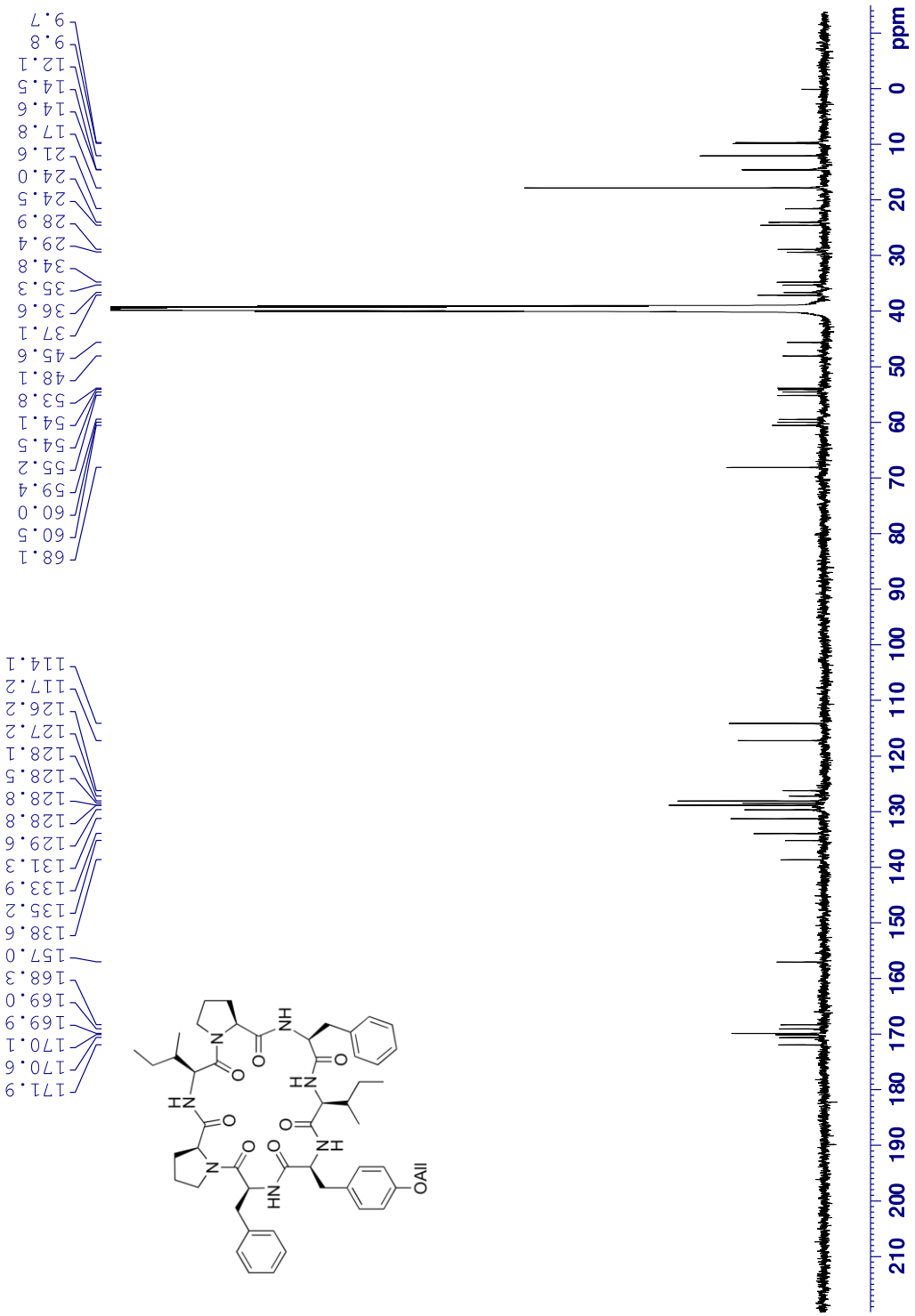
(6*S*,9*S*,12*S*,15*S*,17a*S*,23*S*,25a*S*)-6,15-dibenzyl-12,23-di((*S*)-*sec*-butyl)-9-(4-(((*E*)-prop-1-en-1-yl)oxy)benzyl)octadecahydro-5*H*-dipyrrolo[1,2-a:1',2'-g][1,4,7,10,13,16,19]heptaazacyclohenicosine-5,8,11,14,17,22,25-heptaone (c[-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-], KH_1236)

L,L,L,L,L,L,L-18 - ^{1}H NMR (500 MHz, DMSO-d_6)



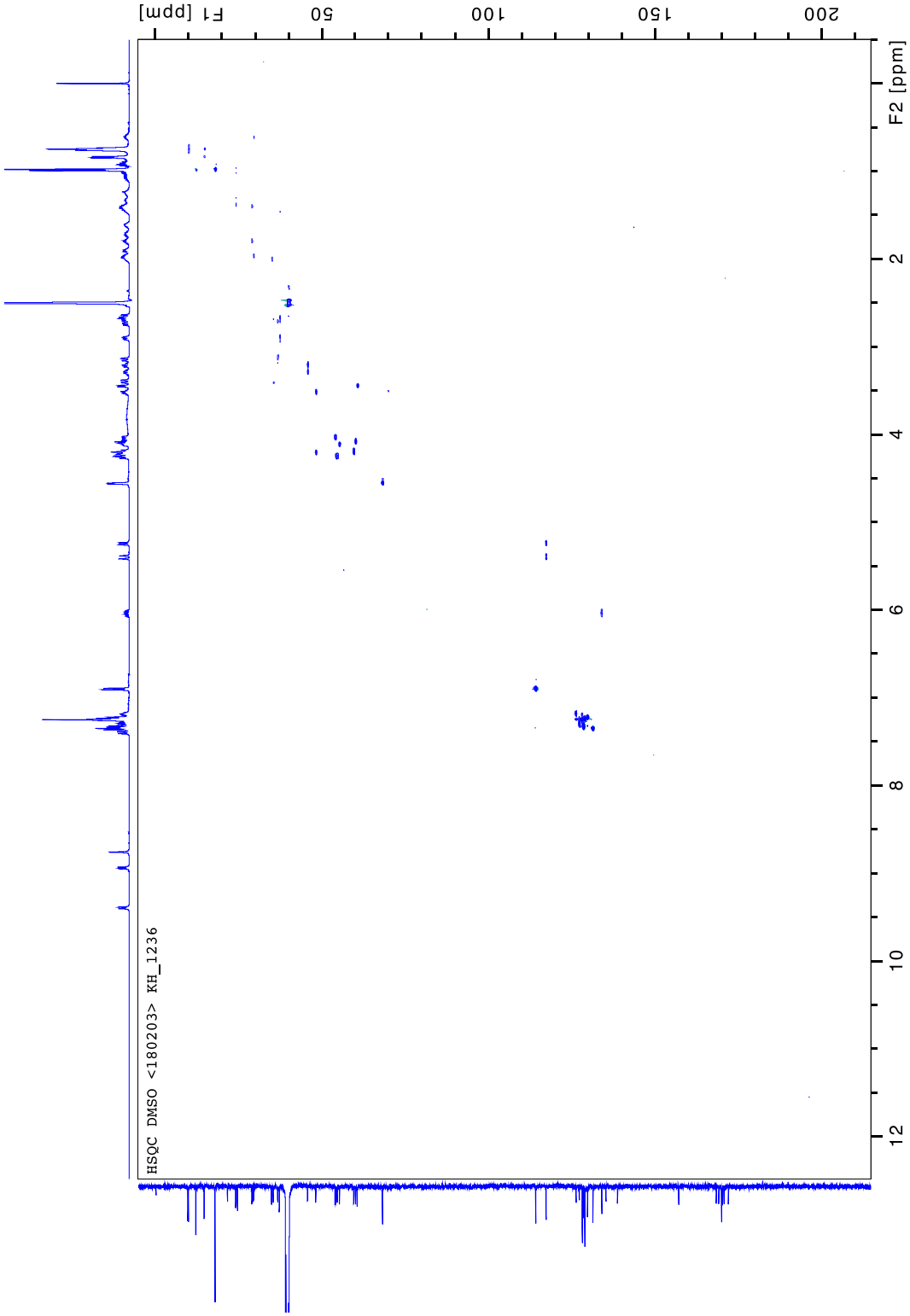
(6*S*,9*S*,12*S*,15*S*,17a*S*,23*S*,25a*S*)-6,15-dibenzyl-12,23-di((*S*)-*sec*-butyl)-9-(4-(((*E*)-prop-1-en-1-yl)oxy)benzyl)octadecahydro-5*H*-dipyrrolo[1,2-a:1',2'-g][1,4,7,10,13,16,19]heptaazacyclohenicosine-5,8,11,14,17,22,25-heptaone (c[-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-], KH_1236)

L,L,L,L,L,L,L-18- ^{13}C NMR (126 MHz, DMSO-d_6)



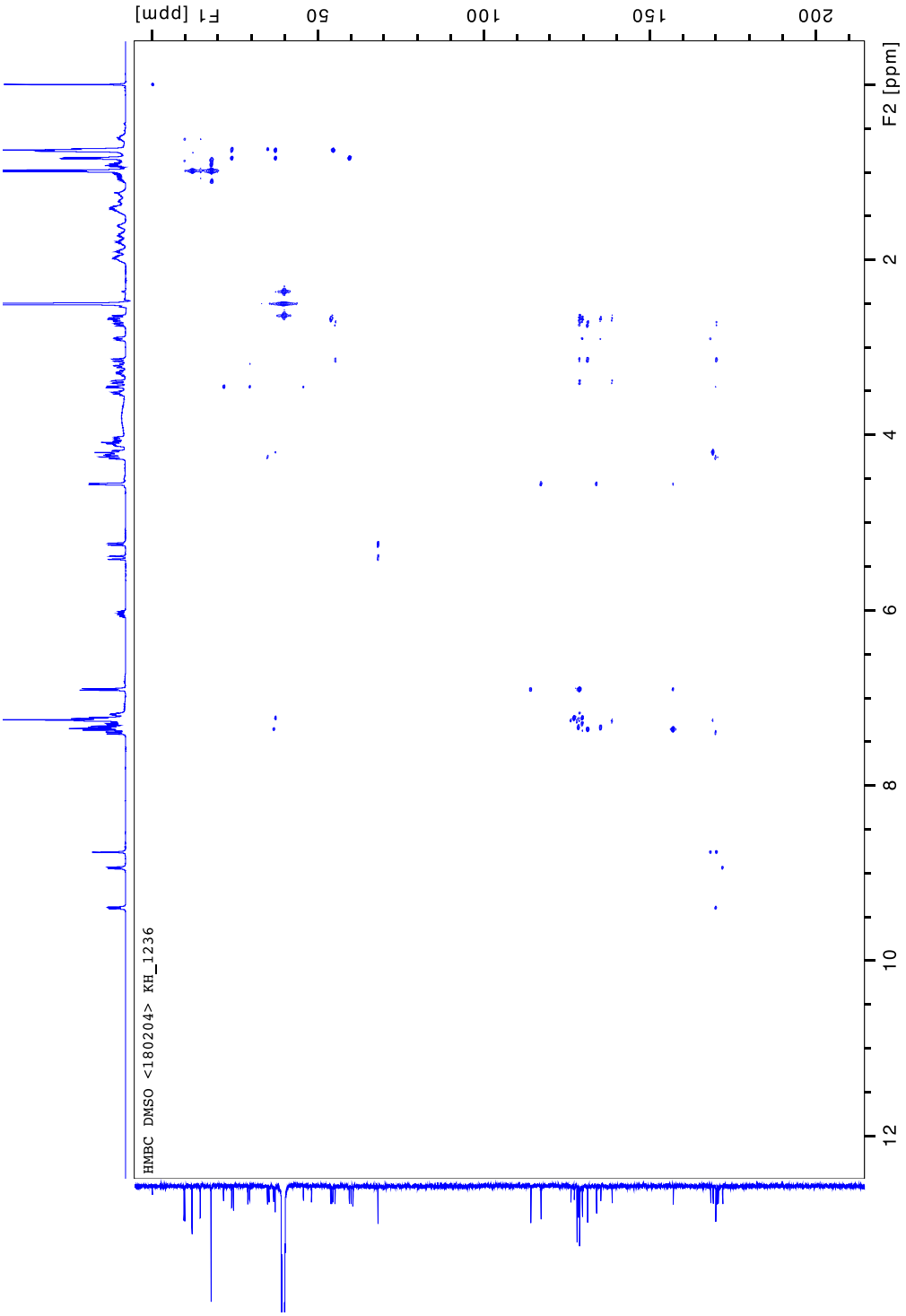
(6*S*,9*S*,12*S*,15*S*,17a*S*,23*S*,25a*S*)-6,15-dibenzyl-12,23-di((*S*)-*sec*-butyl)-9-(4-(((*E*)-prop-1-en-1-yl)oxy)benzyl)octadecahydro-5*H*-dipyrrolo[1,2-a:1',2'-g][1,4,7,10,13,16,19]heptaazacyclohenicosine-5,8,11,14,17,22,25-heptaone (c[-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-], KH_1236)

L,L,L,L,L,L,L-18 - HSQC (DMSO-d_6)



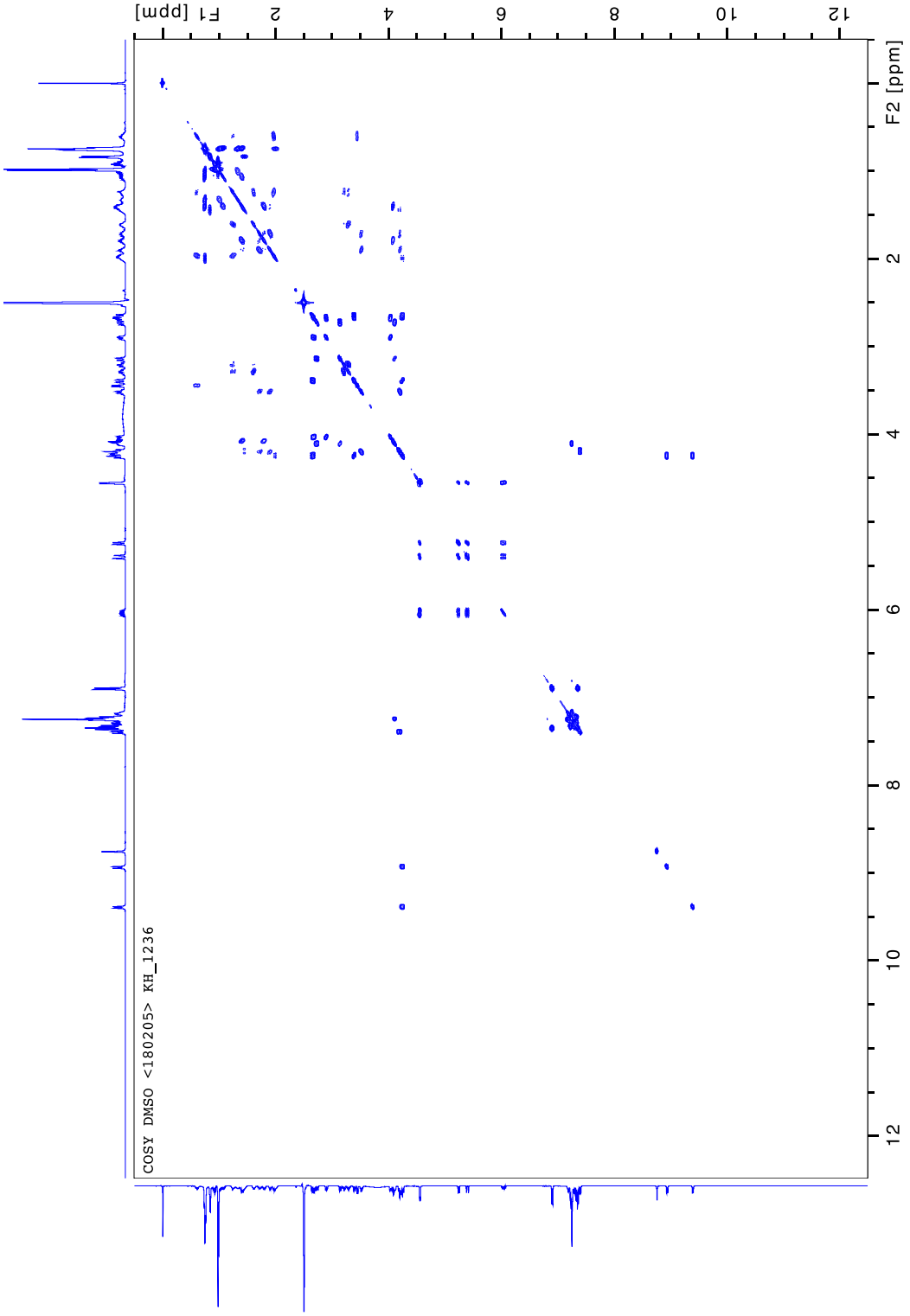
(6*S*,9*S*,12*S*,15*S*,17a*S*,23*S*,25a*S*)-6,15-dibenzyl-12,23-di((*S*)-*sec*-butyl)-9-(4-(((*E*)-prop-1-en-1-yl)oxy)benzyl)octadecahydro-5*H*-dipyrrolo[1,2-a:1',2'-g][1,4,7,10,13,16,19]heptaazacyclohenicosine-5,8,11,14,17,22,25-heptaone (c[-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-], KH_1236)

L,L,L,L,L,L,L-18 - HMBC (DMSO-*d*$_6$)

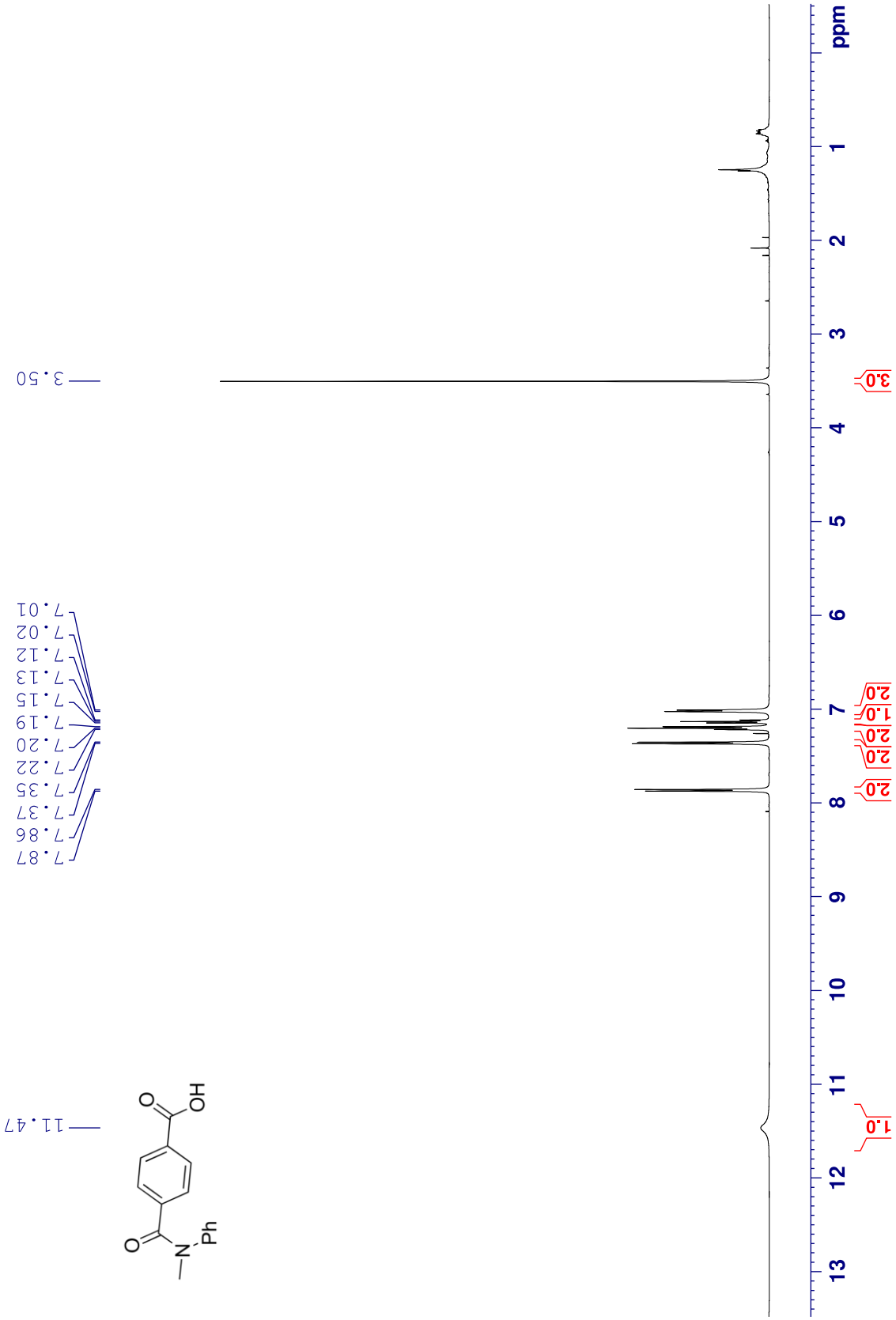


(6*S*,9*S*,12*S*,15*S*,17a*S*,23*S*,25a*S*)-6,15-dibenzyl-12,23-di((*S*)-*sec*-butyl)-9-(4-(((*E*)-prop-1-en-1-yl)oxy)benzyl)octadecahydro-5*H*-dipyrrolo[1,2-a:1',2'-g][1,4,7,10,13,16,19]heptaazacyclohenicosine-5,8,11,14,17,22,25-heptaone (c[-L-Ile-L-Tyr(All)-L-Phe-L-Pro-L-Ile-L-Pro-L-Phe-], KH_1236)

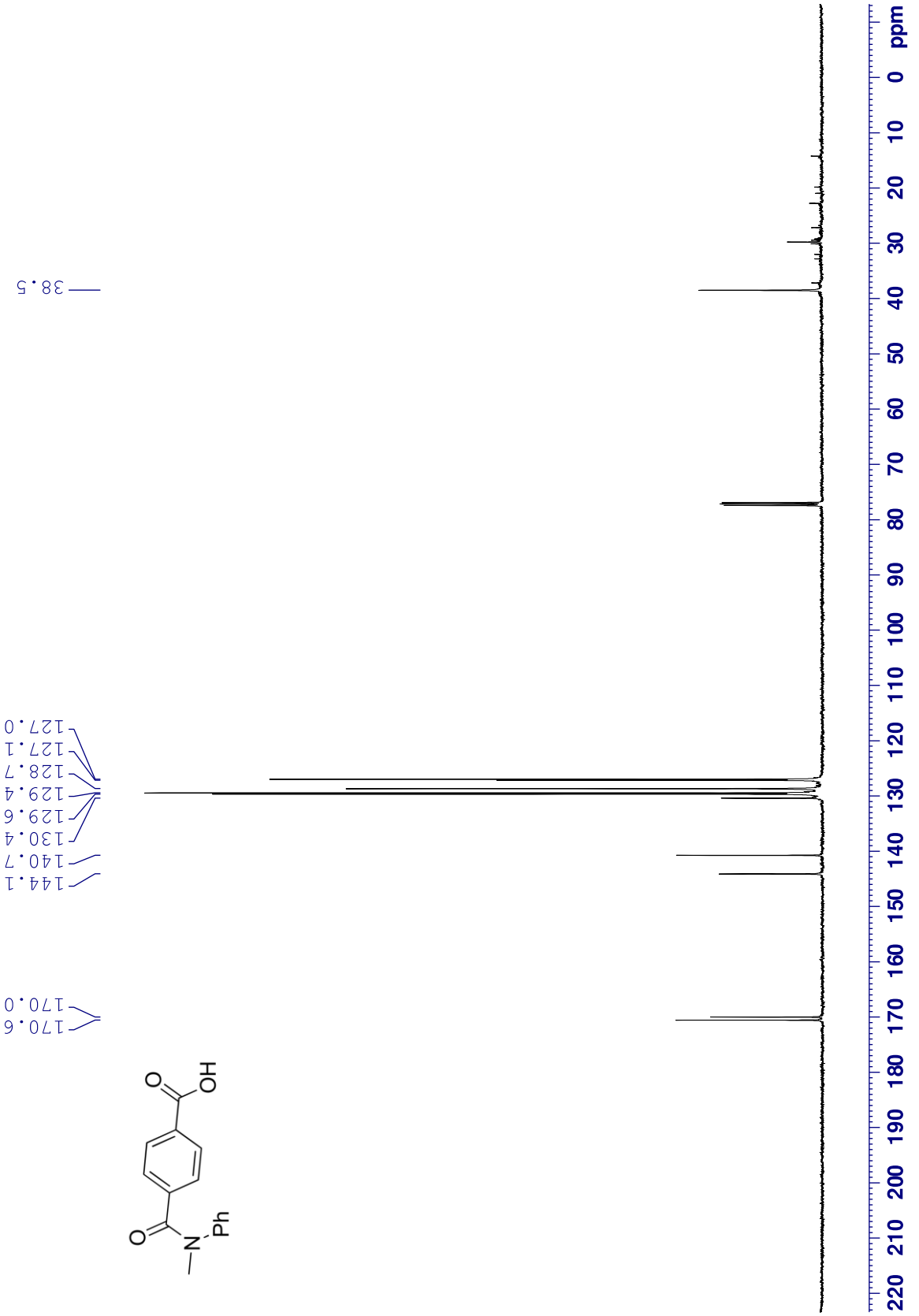
L,L,L,L,L,L,L-18- COSY (DMSO-*d*$_6$)



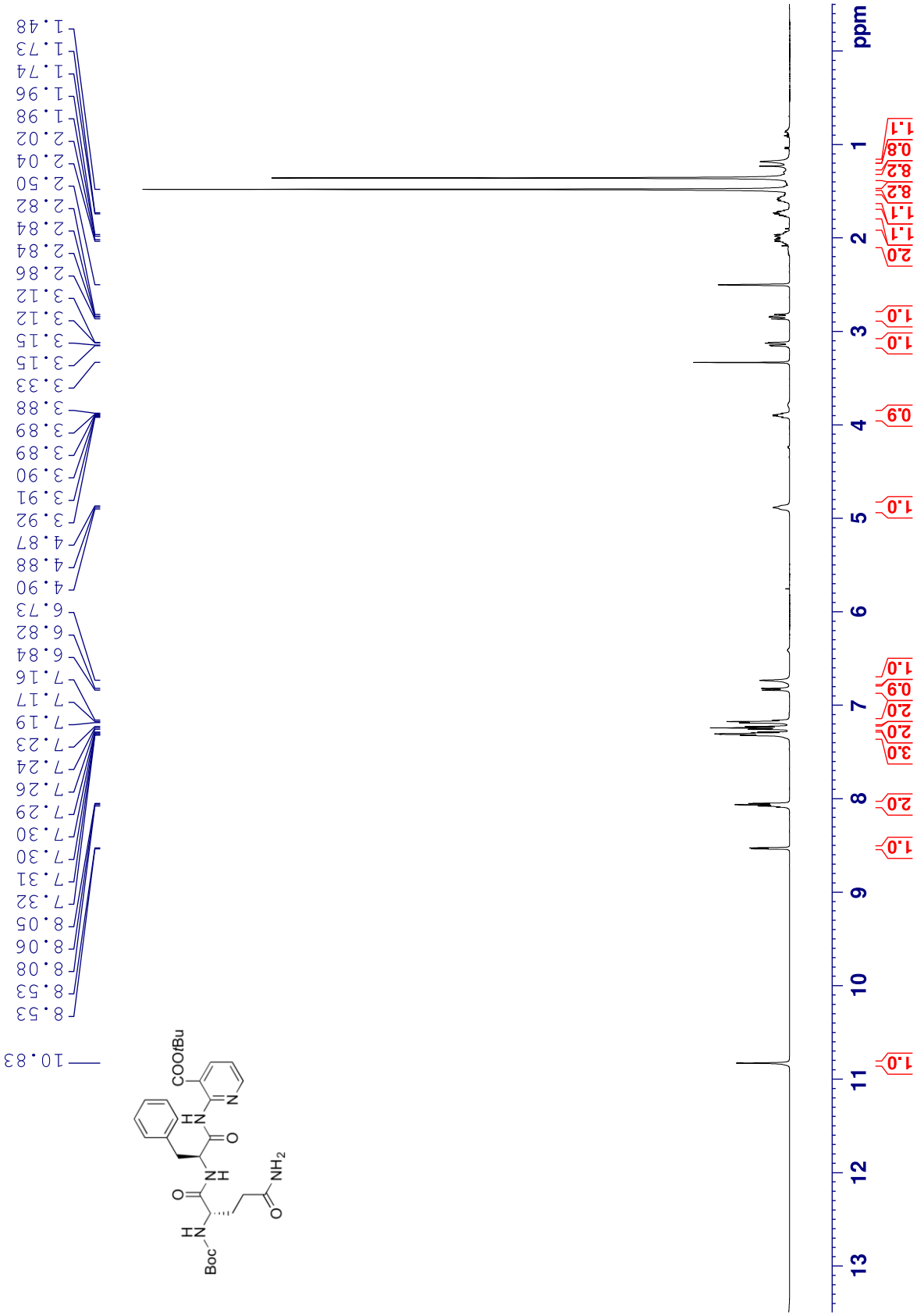
4-[methyl(phenyl)carbamoyl]benzoic acid (KH_808) **S17 - ^{1}H NMR (500 MHz, $CDCl_3$)**



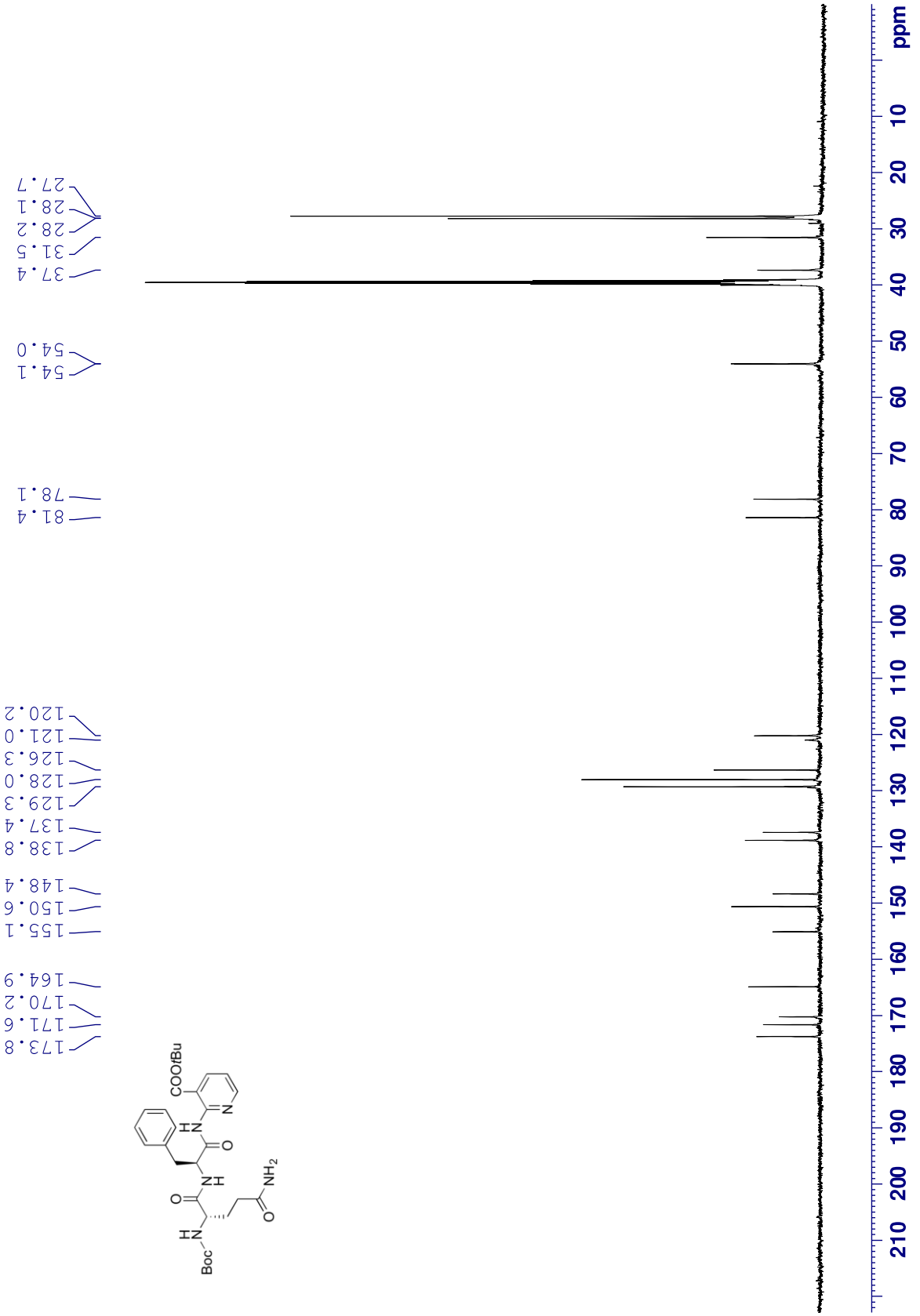
4-[methyl(phenyl)carbamoyl]benzoic acid (KH_808) **S17 - ^{13}C NMR (126 MHz, $CDCl_3$)**



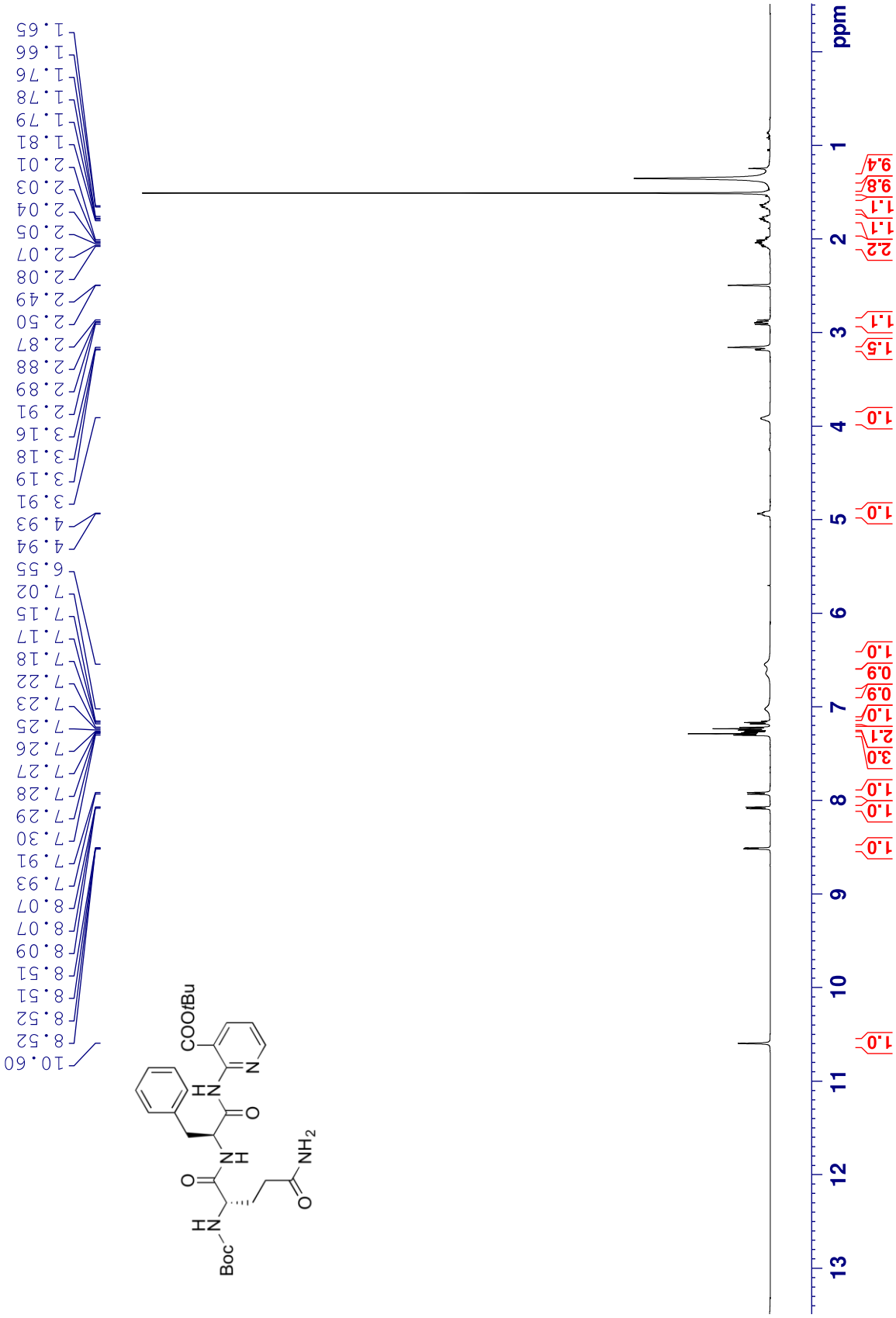
tert-Butyl 2-{[(3*S*)-3-({[(3*S*)-6-amino-3-[{*tert*-butoxycarbonyl)amino)-6-oxohex-1-en-2-yl]amino}pyridine-3-carboxylate (Boc-L-Gln-L-Phe-NH-*t*Bu-nic, KH_905) **L,L-S18 - ^{1}H NMR (500 MHz, DMSO-d_6, mixture of rotamers)**



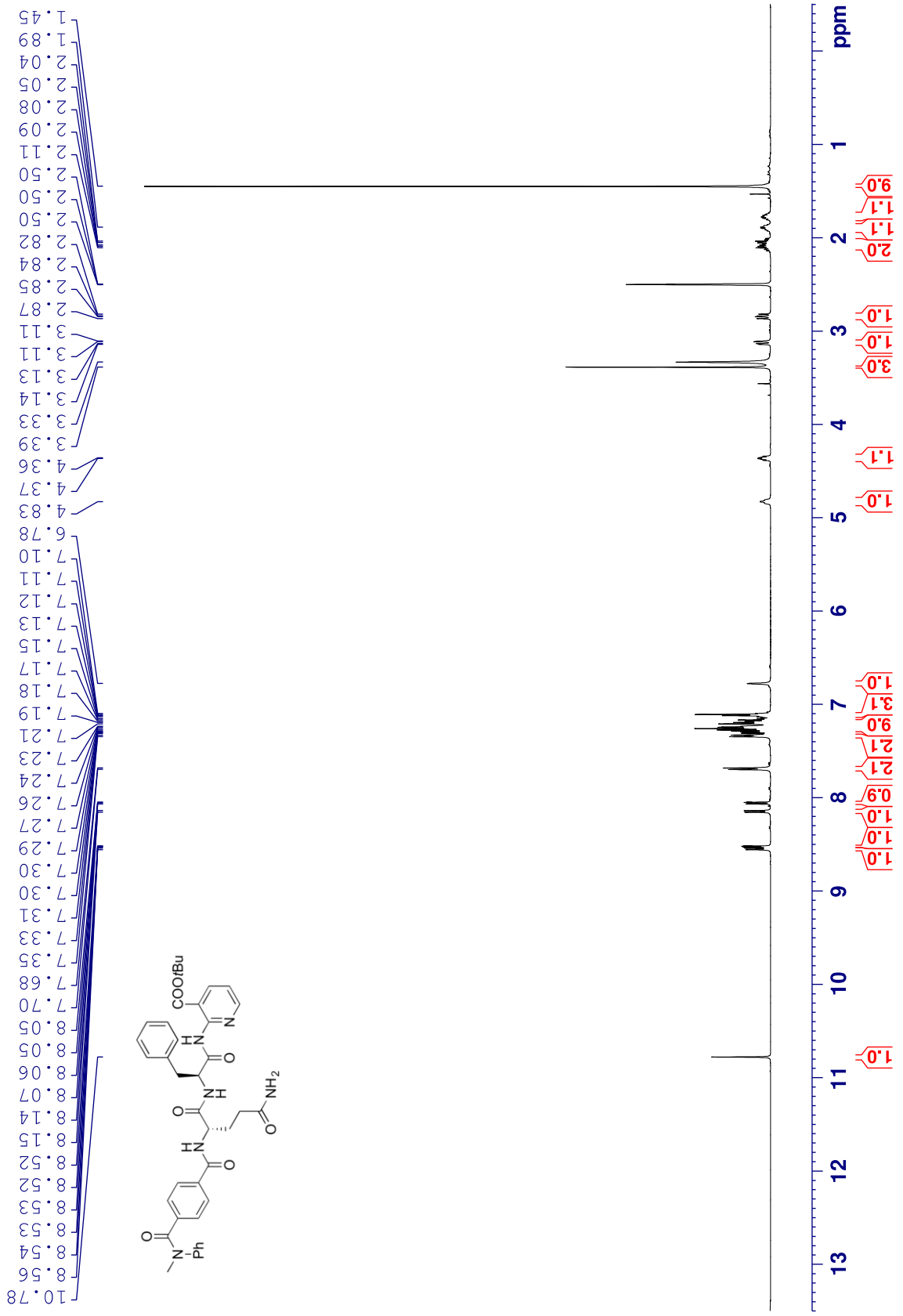
tert-Butyl 2-{[(3*S*)-3-({[(3*S*)-6-amino-3-[{*tert*-butoxycarbonyl)amino)-6-oxohex-1-en-2-yl]amino}pyridine-3-carboxylate (Boc-L-Gln-L-Phe-NH-*t*Bu-nic, KH_905) **L,L-S18 - ^{13}C NMR (126 MHz, DMSO-d_6, mixture of rotamers)**



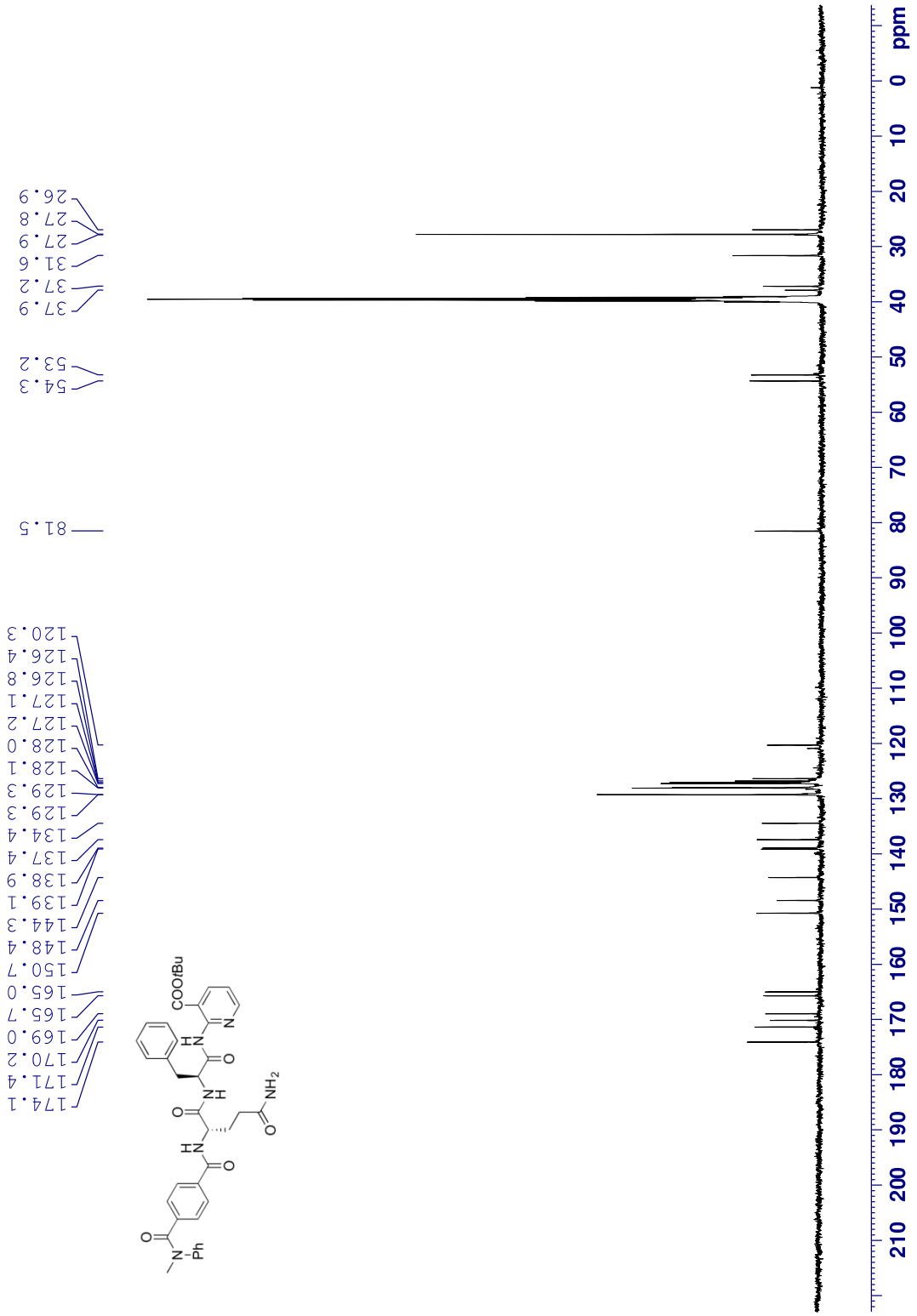
tert-Butyl 2-{[(3*S*)-3-({[(3*S*)-6-amino-3-[{*tert*-butoxycarbonyl)amino)-6-oxohex-1-en-2-yl]amino}pyridine-3-carboxylate (Boc-L-Gln-L-Phe-NH-*t*Bu-nic, KH_905) **L,L-S18 - ^{1}H NMR (500 MHz, DMSO-d_6, 60°C)**



tert-Butyl 2-{[(3*S*)-3-{[(3*S*)-6-amino-3-{4-[methyl(phenyl)carbamoyl]-benzamido}-6-oxo-hex-1-en-2-yl]amino}-4-phenylbut-1-en-2yl] amino} pyridine-3-carboxylate **L,L-19 - ^{1}H NMR (500 MHz, DMSO-d_6)**

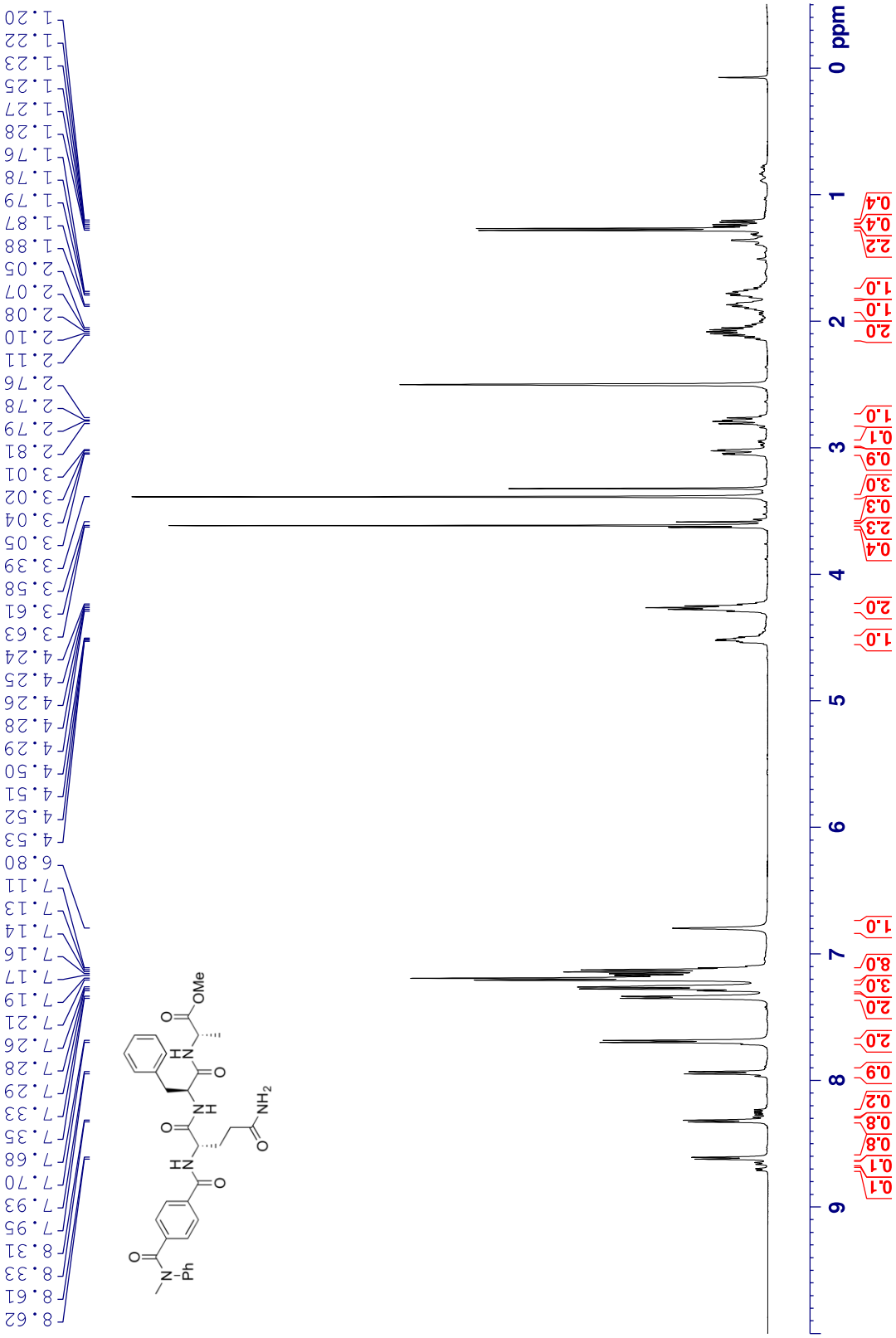


tert-Butyl 2-{[(3*S*)-3-{[(3*S*)-6-amino-3-{4-[methyl(phenyl)carbamoyl]-benzamido}-6-oxo-hex-1-en-2-yl]amino}-4-phenylbut-1-en-2yl] amino} pyridine-3-carboxylate **L,L-19 - ^{13}C NMR (126 MHz, DMSO-d_6)**



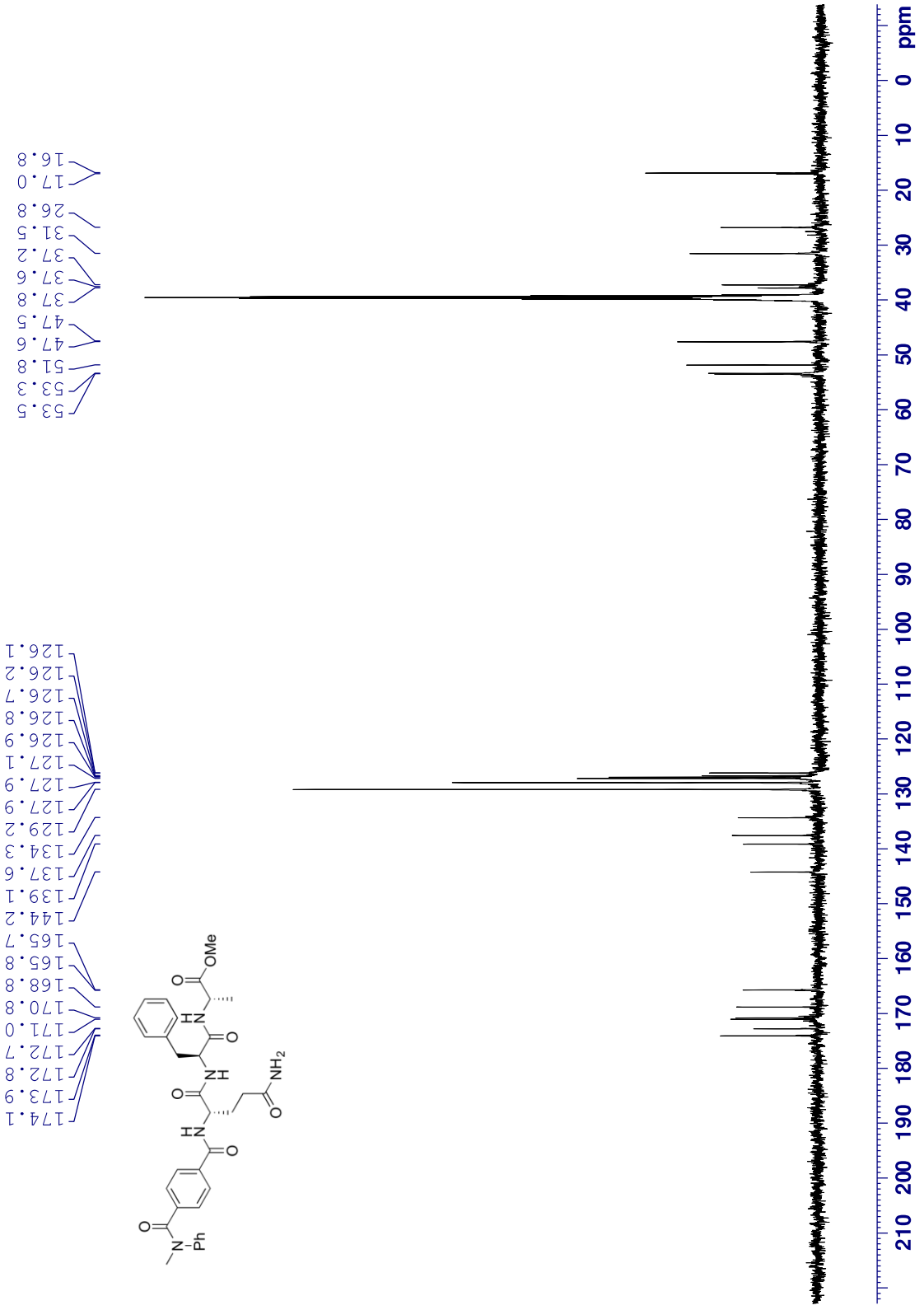
Methyl (4-(methyl(phenyl)carbamoyl)benzoyl)-L-glutaminyl-L-phenylalanyl-L-alaninate (KH_1234)

L,L,L-20 - ^{1}H NMR (500 MHz, DMSO-d_6, mixture of rotamers)



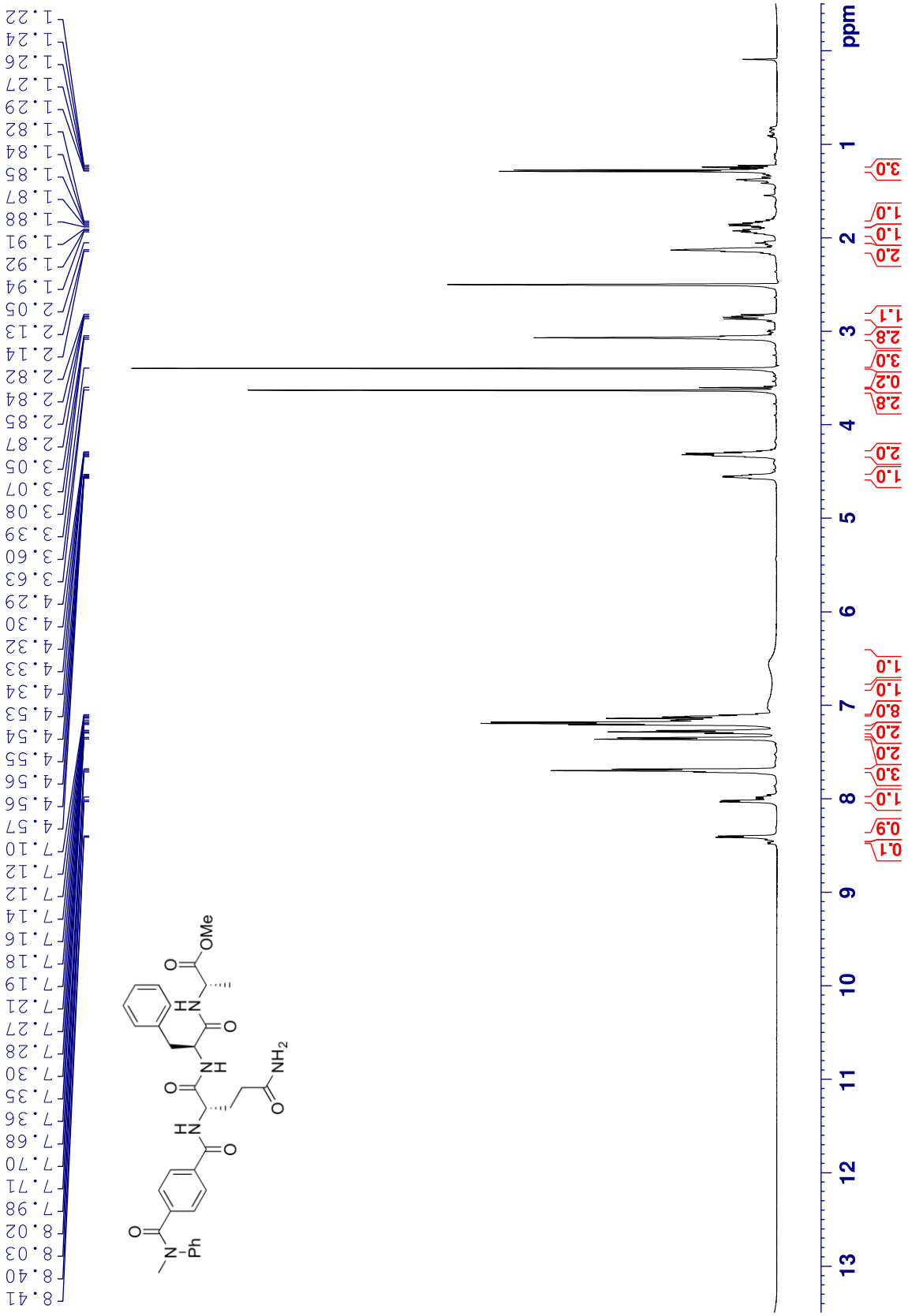
Methyl (4-(methyl(phenyl)carbamoyl)benzoyl)-L-glutaminyl-L-phenylalanyl-L-alaninate (KH_1234)

L,L,L-20 - ^{13}C NMR (126 MHz, DMSO-d_6, mixture of rotamers)



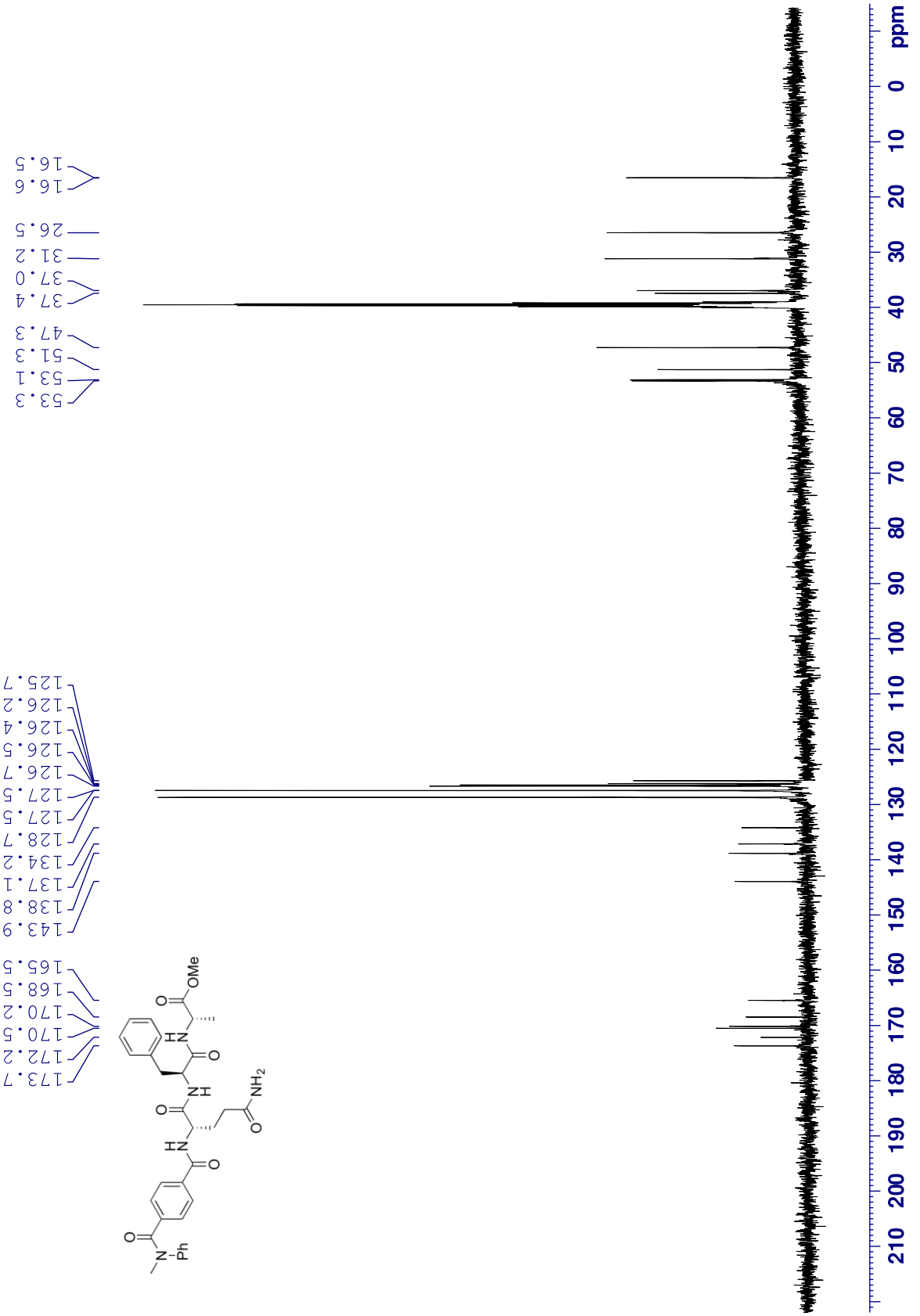
Methyl (4-(methyl(phenyl)carbamoyl)benzoyl)-L-glutaminyl-L-phenylalanyl-L-alaninate (KH_1234)

L,L,L-20 - ^{1}H NMR (500 MHz, DMSO-d_6, 80°C)



Methyl (4-(methyl(phenyl)carbamoyl)benzoyl)-L-glutaminyl-L-phenylalanyl-L-alaninate (KH_1234)

L,L,L-20 - ^{13}C NMR (126 MHz, DMSO-d_6, 80°C)



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