Supplementary Information

Convenient route to Fmoc-homotyrosine via metallaphotoredox catalysis and its use in the total synthesis of anabaenopeptin cyclic peptides

Christopher Bérubé,[a,b] Louis-David Guay,[a,b] Tommy Fraser,[c] Victor Lapointe,[a,b] Sébastien Cardinal,[c] and Éric Biron[a,b,*]

[a] Faculté de pharmacie, Université Laval, Québec, Québec, Canada, G1V 0A6
[b] Laboratory of Medicinal Chemistry, Centre de recherche du CHU de Québec-Université Laval, 2705 Boulevard Laurier, Québec, Québec, Canada, G1V 0A6
[c] Departement de biologie, chimie et géographie, Université de Rimouski, 300 allée des Ursulines, Rimouski, Québec, Canada, G5L 3A1

Corresponding author: Eric.Biron@pha.ulaval.ca

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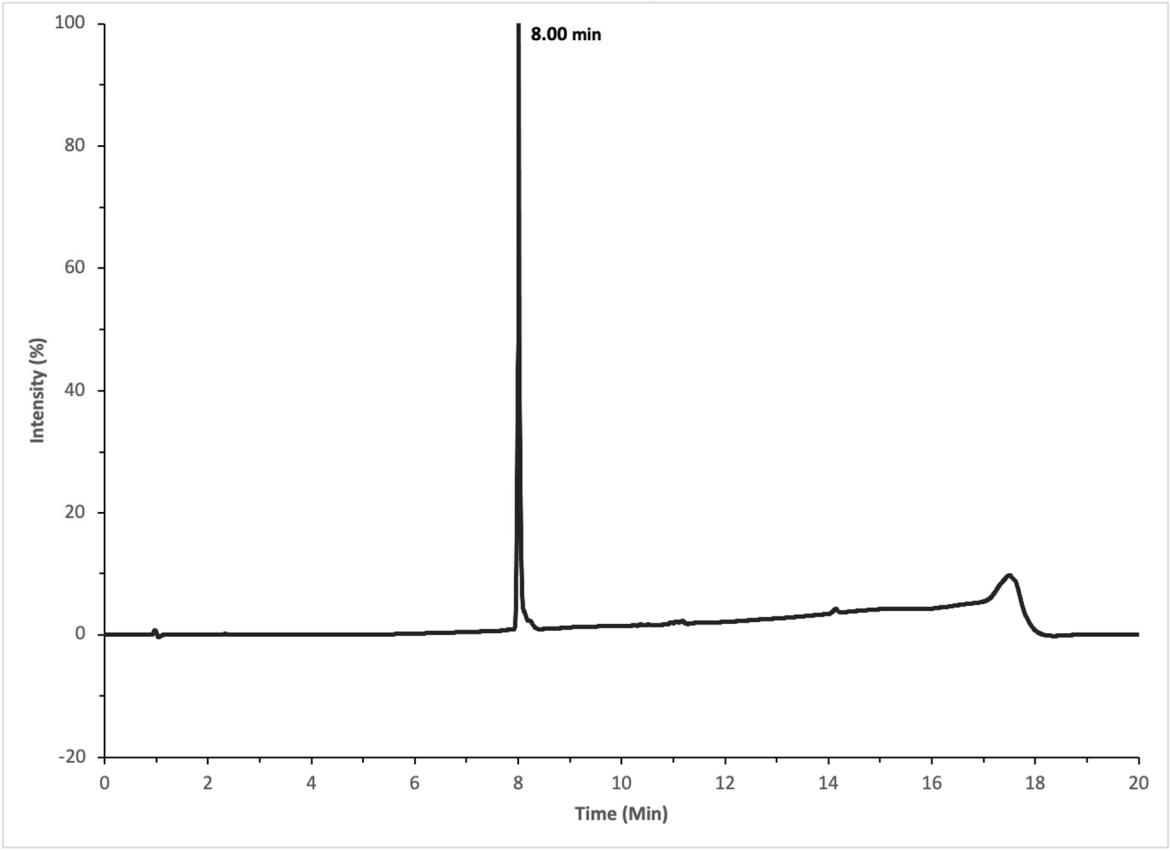
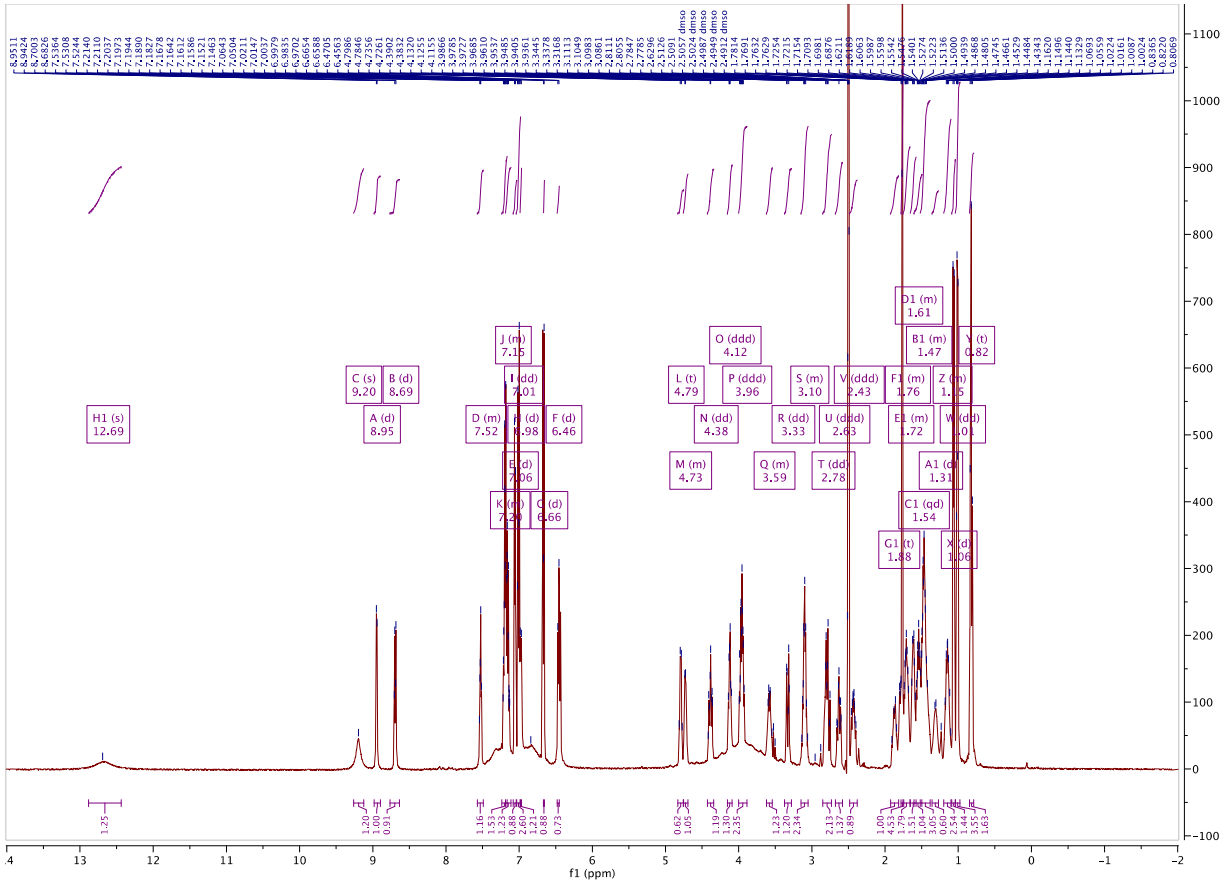
Figure S1. Characterization of anabaenopeptin F (**1**).

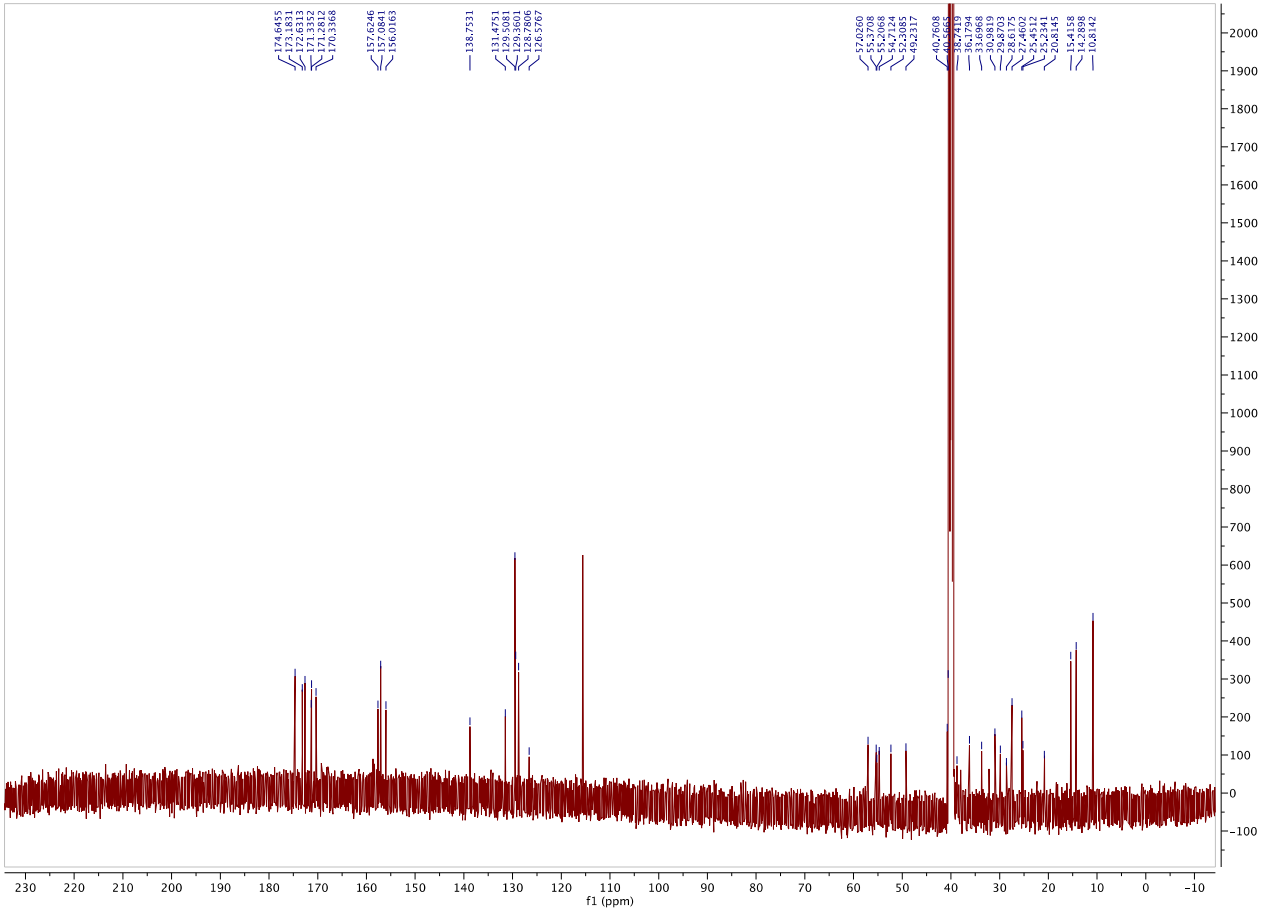
a) HPLC profile of purified anabaenopeptin F (**1**) (λ =220nm)



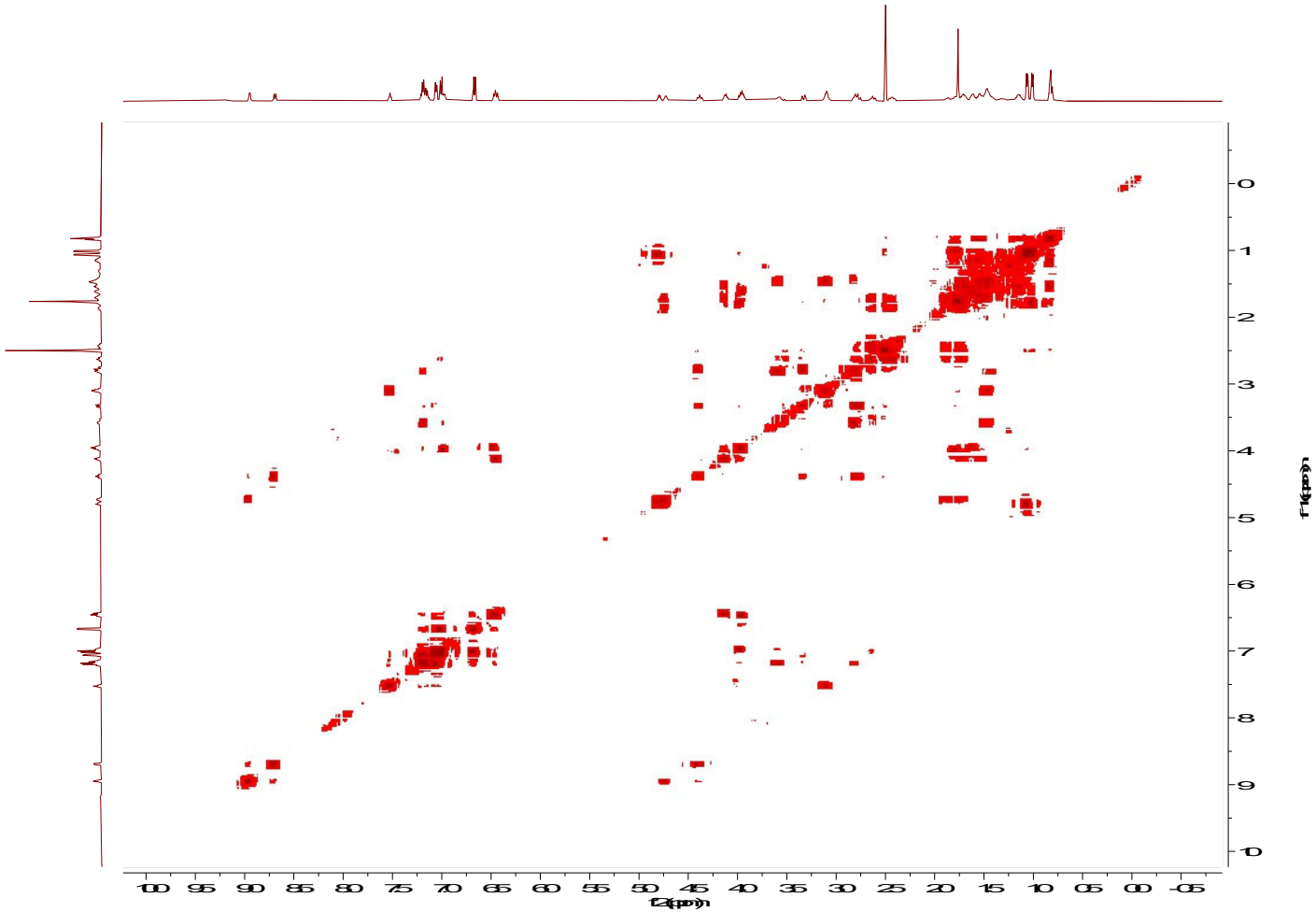
b) ^{1}H NMR spectrum of anabaenopeptin F (**1**) in DMSO-d6



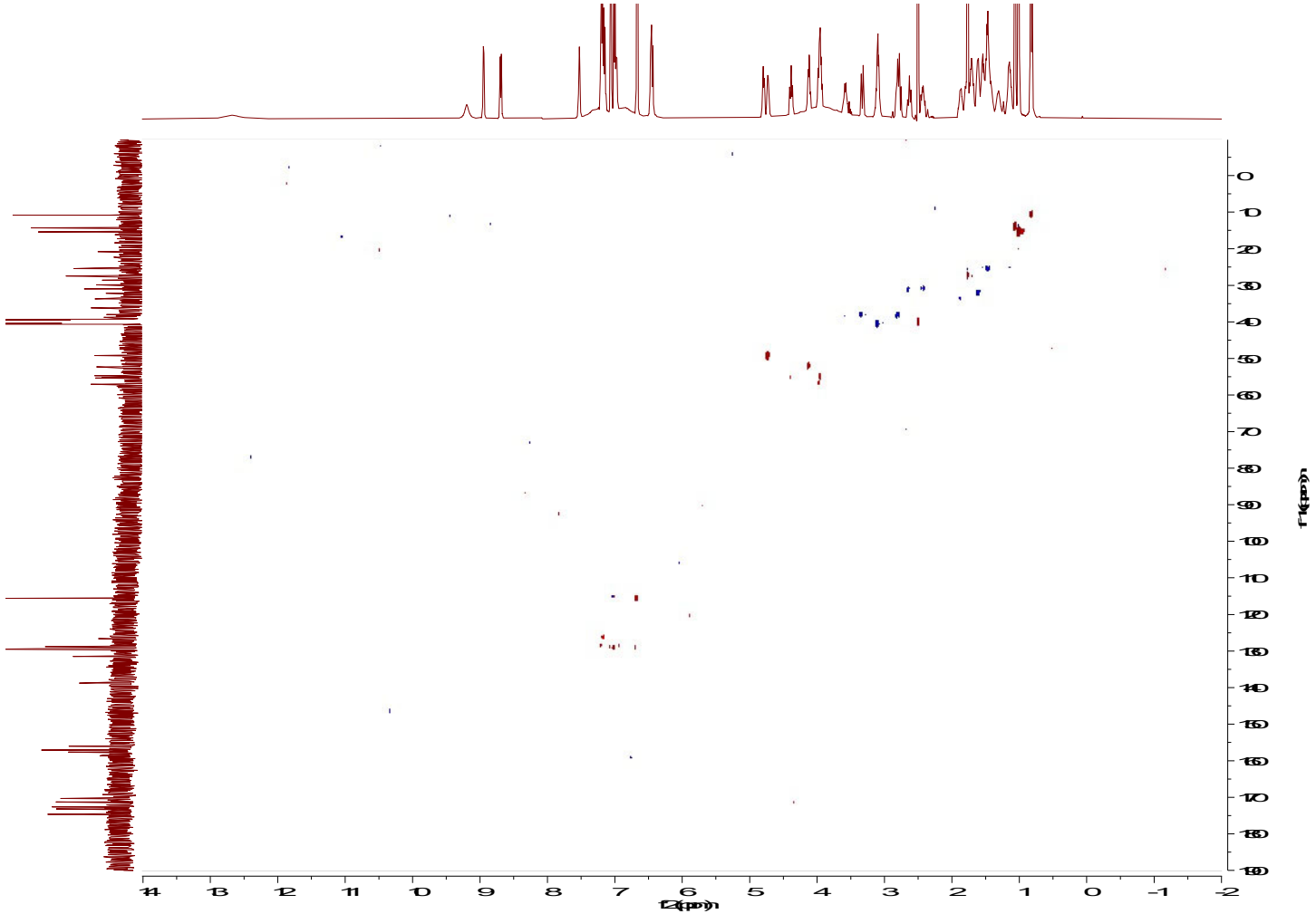
c) ^{13}C NMR spectrum of anabaenopeptin F (**1**) in DMSO-d6



d) ^{1}H-^{1}H COSY spectrum of anabaenopeptin F (**1**) in DMSO-d6



e) HSQC spectrum of anabaenopeptin F (**1**) in DMSO-d6

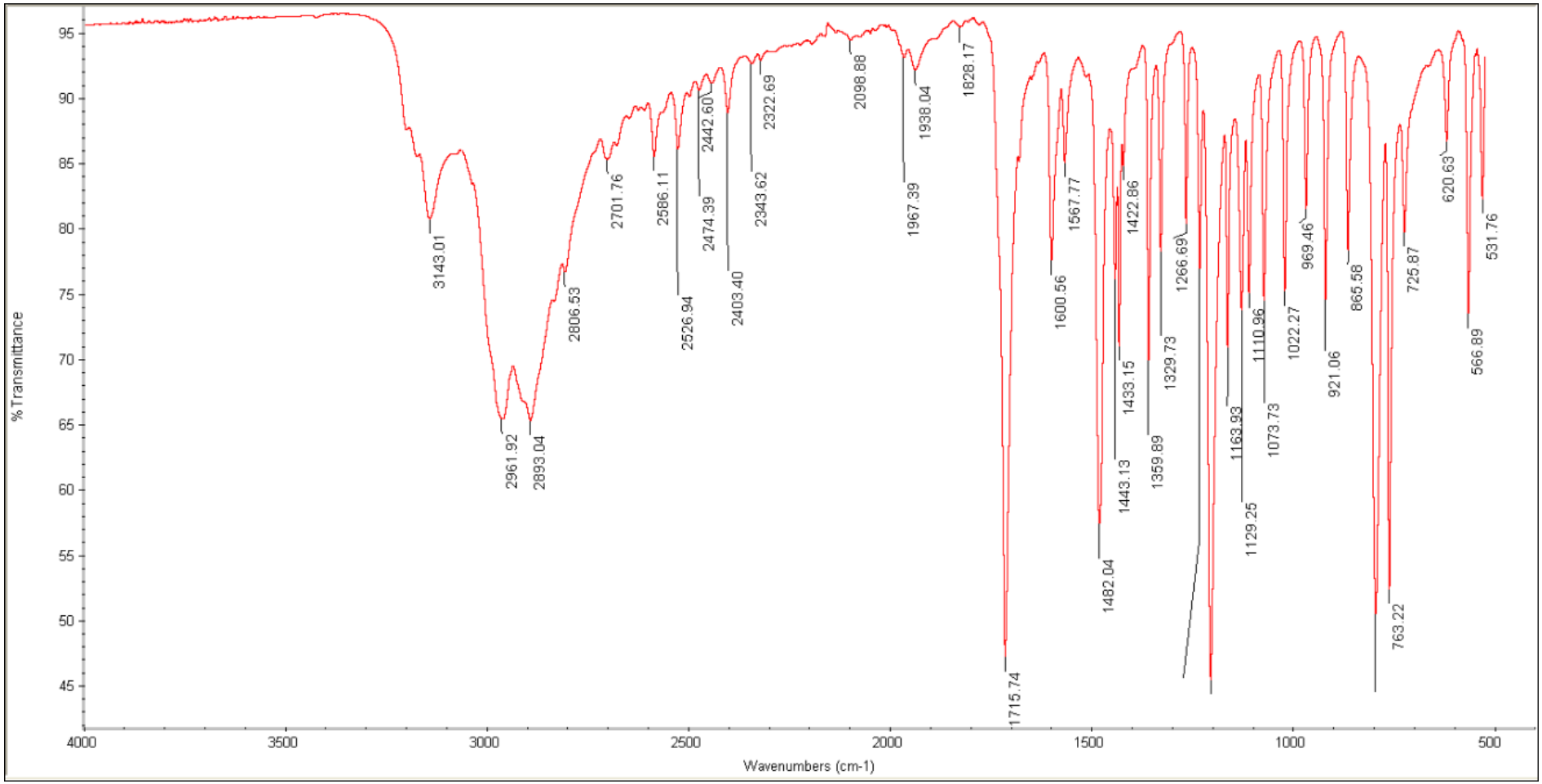


f) HRMS spectrum of anabaenopeptin F (**1**)

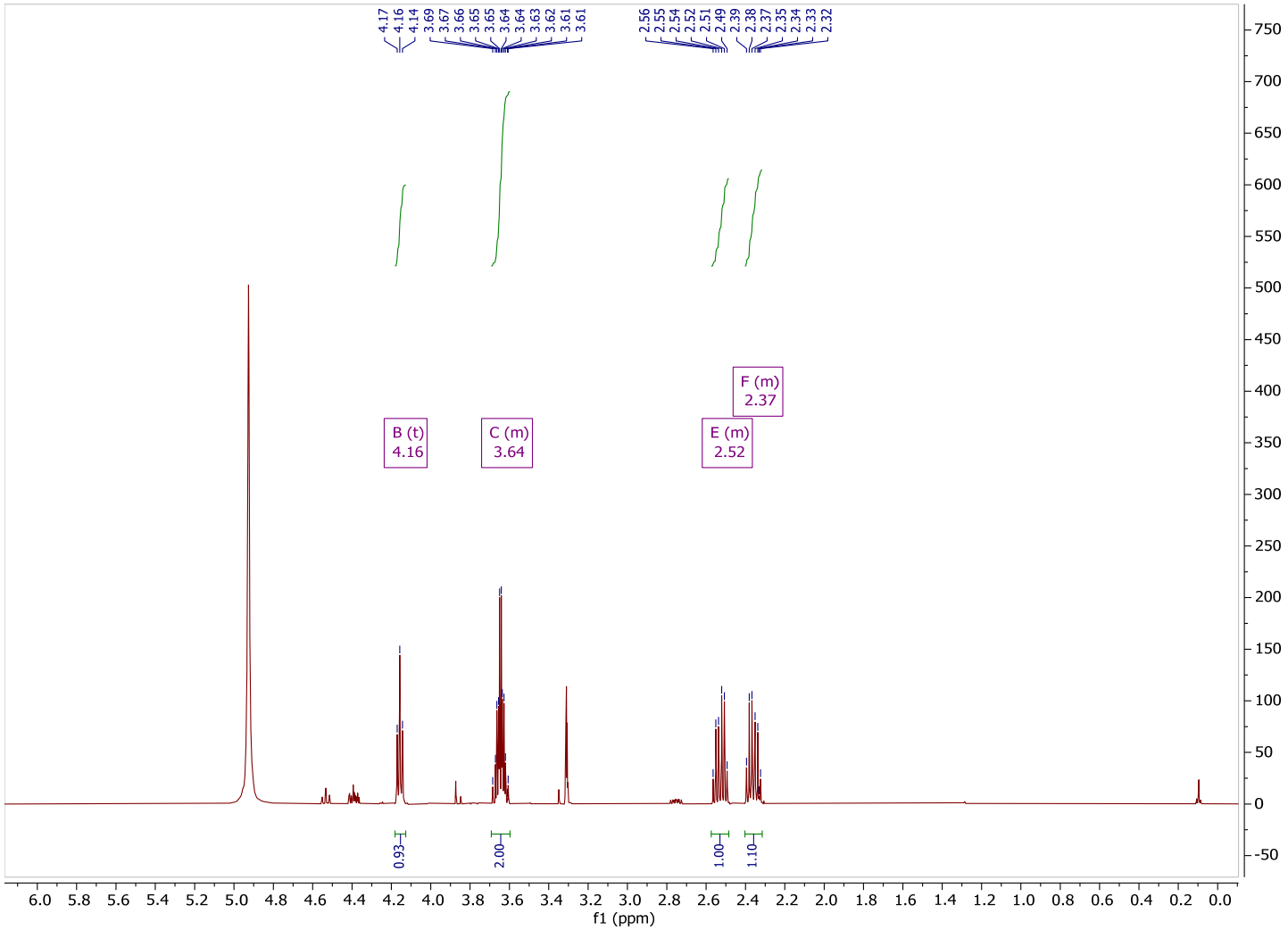
$[M + H]^+$ calculated mass for $C_{42}H_{62}N_{10}O_9$: 851.4744, found 851.4854.

Figure S2. Characterization of (2*S*)-2-amino-4-bromobutanoic acid hydrobromide compounds (**4**).

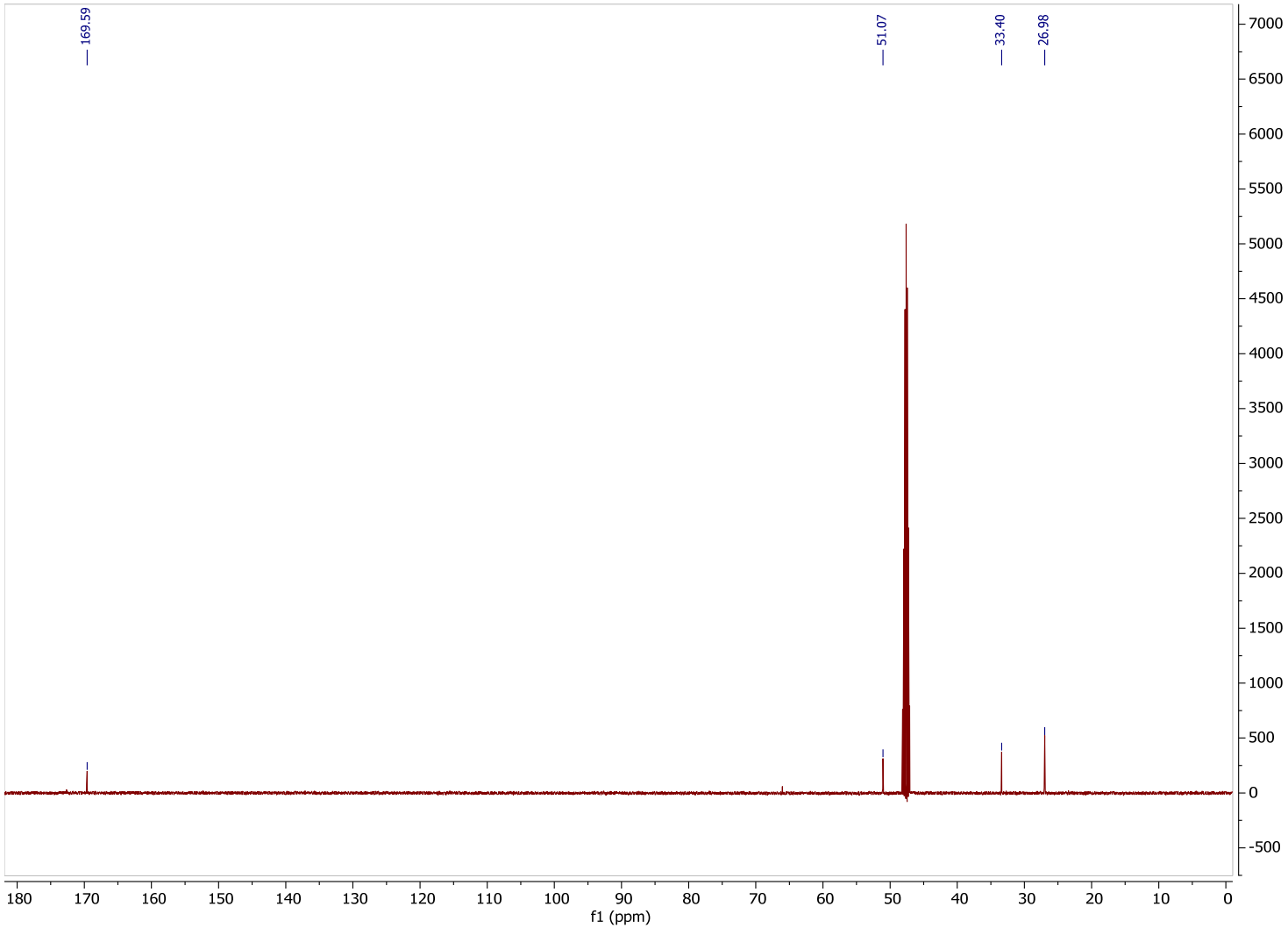
a) IR spectrum of H-L-Hser(Br)-OH (4)



b) ^{1}H NMR spectrum H-L-Hser(Br)-OH (**4**) in $CDCl_3$



c) ^{13}C NMR-APT spectrum H-L-Hser(Br)-OH (**4**) in $CDCl_3$



d) HRMS spectrum H-L-Hser(Br)-OH (**4**)

$[M+TFA-H]^+$ calculated for $C_4H_9Br_2NO_2$: 373.8856, found 373.6090.

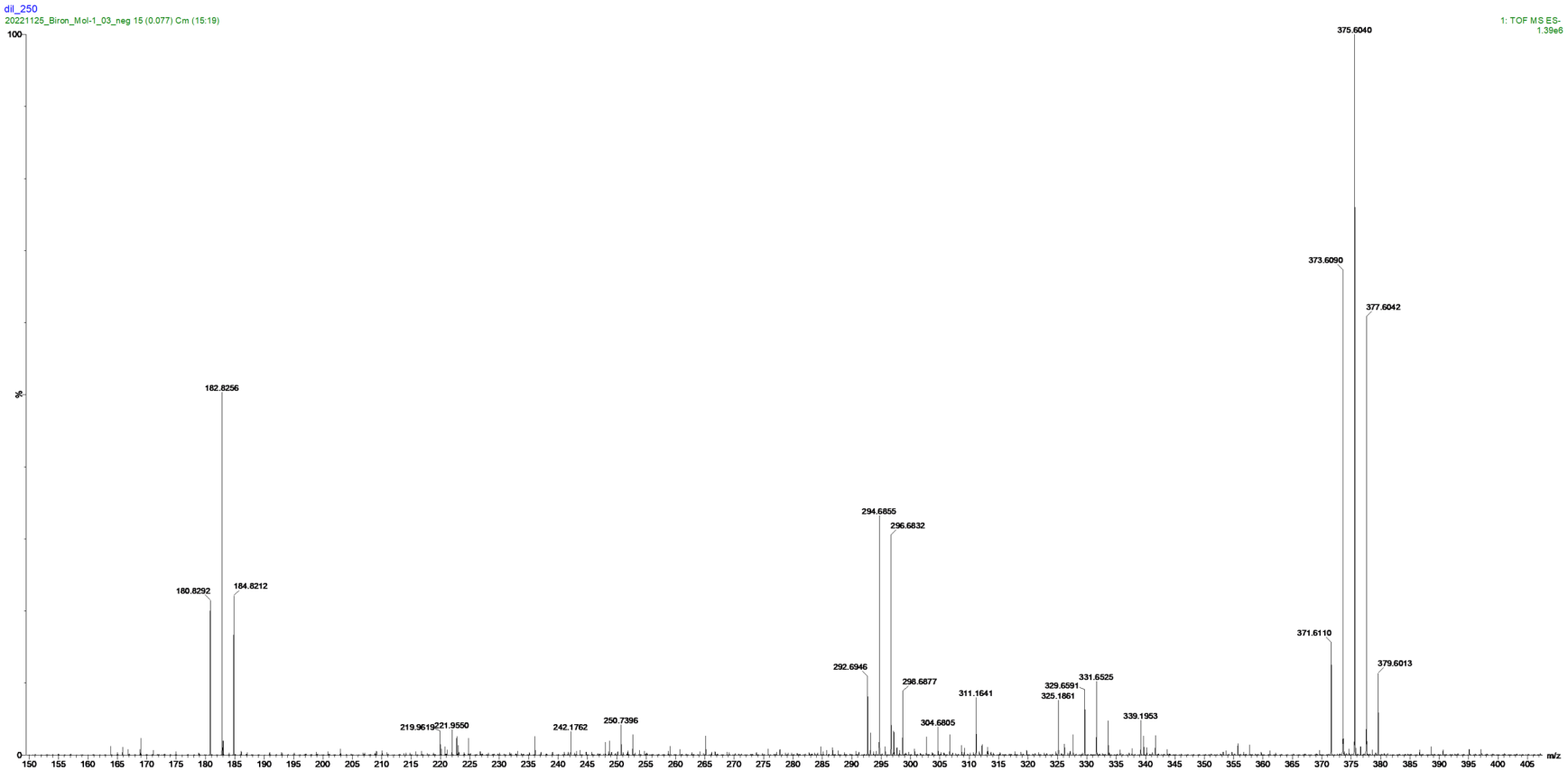
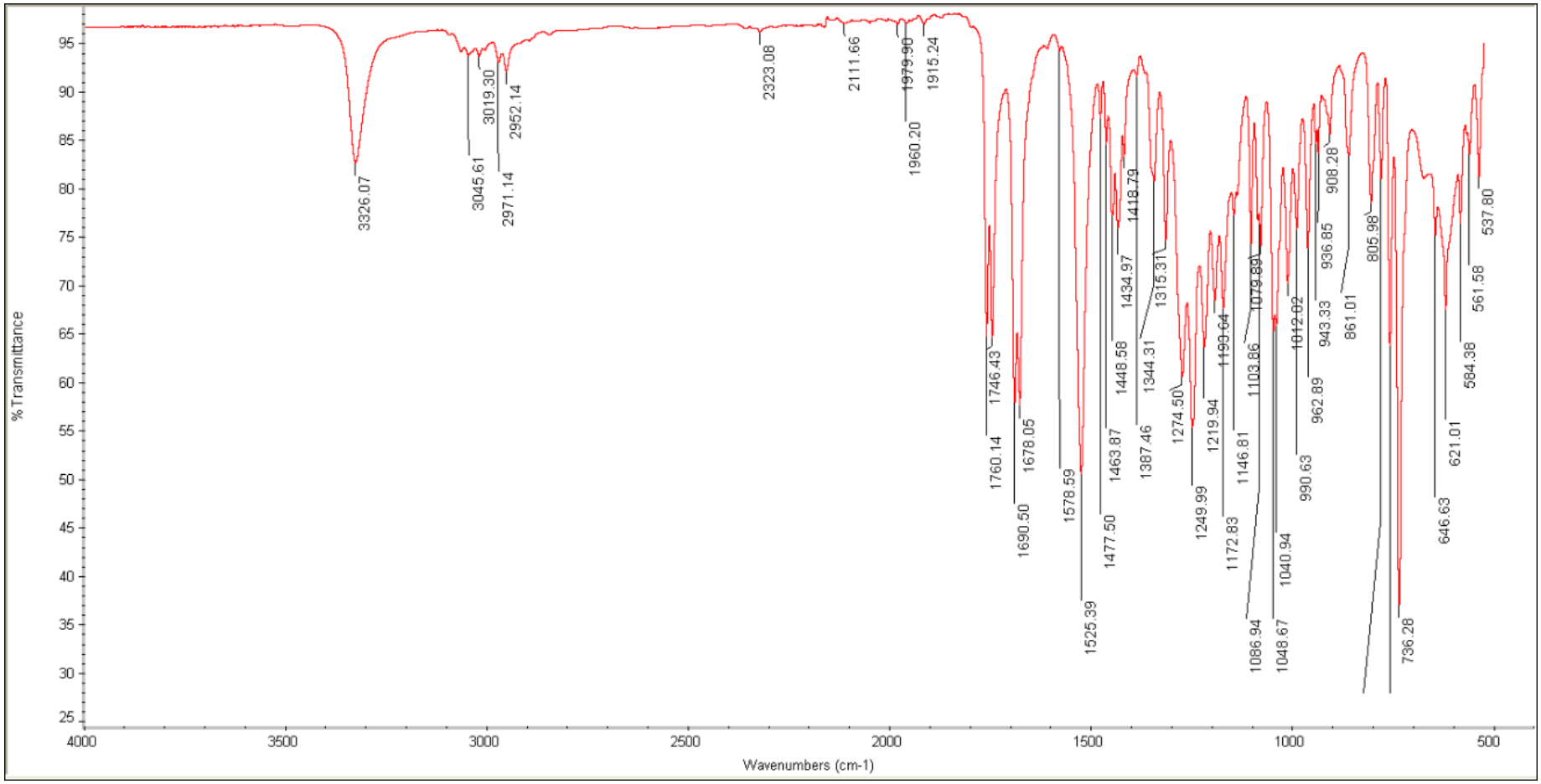
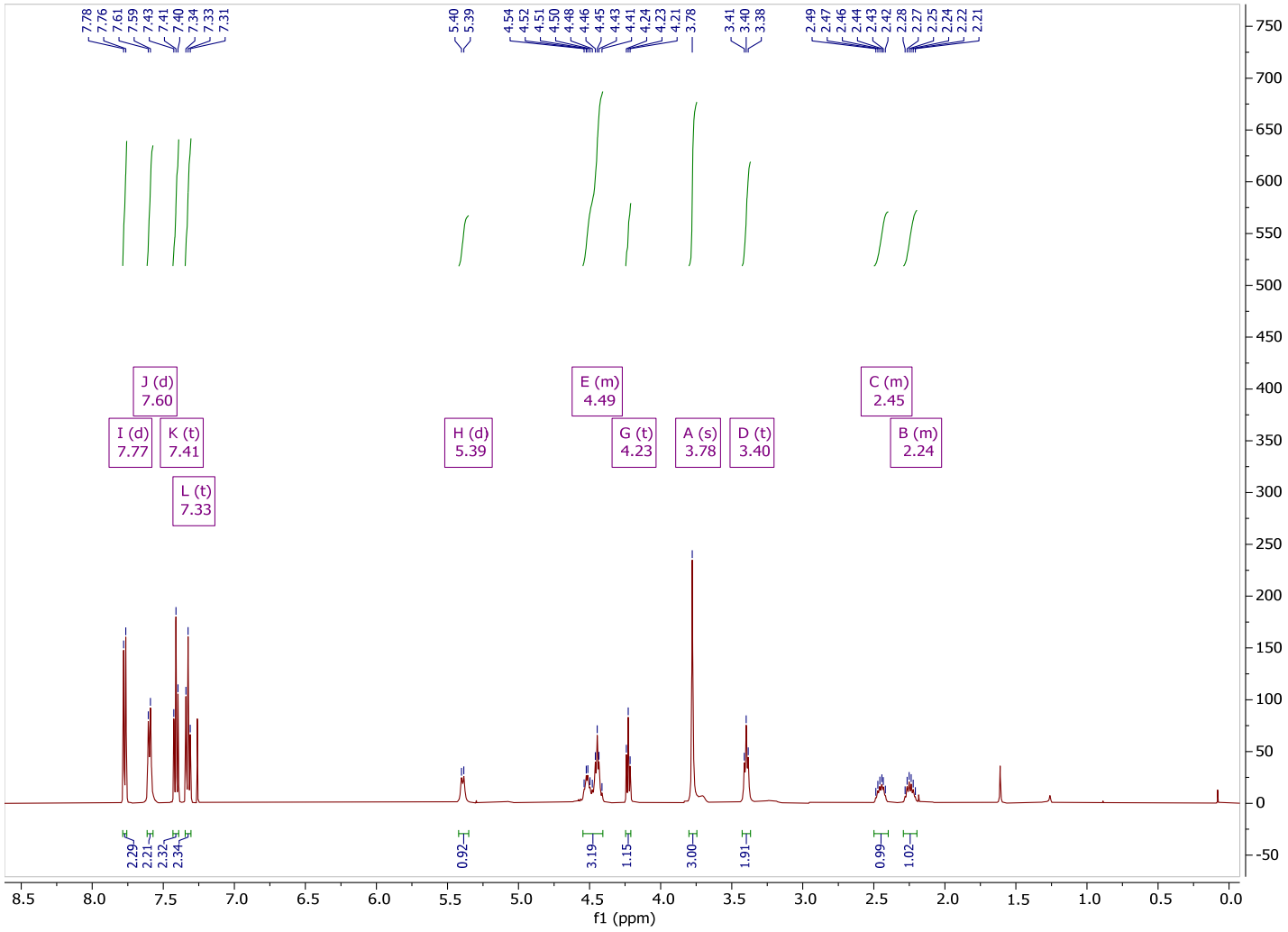


Figure S3. Characterization of methyl (2*S*)-4-bromo-2-([(9H-fluoren-9-ylmethoxy)carbonyl]amino)butanoate (**5**).

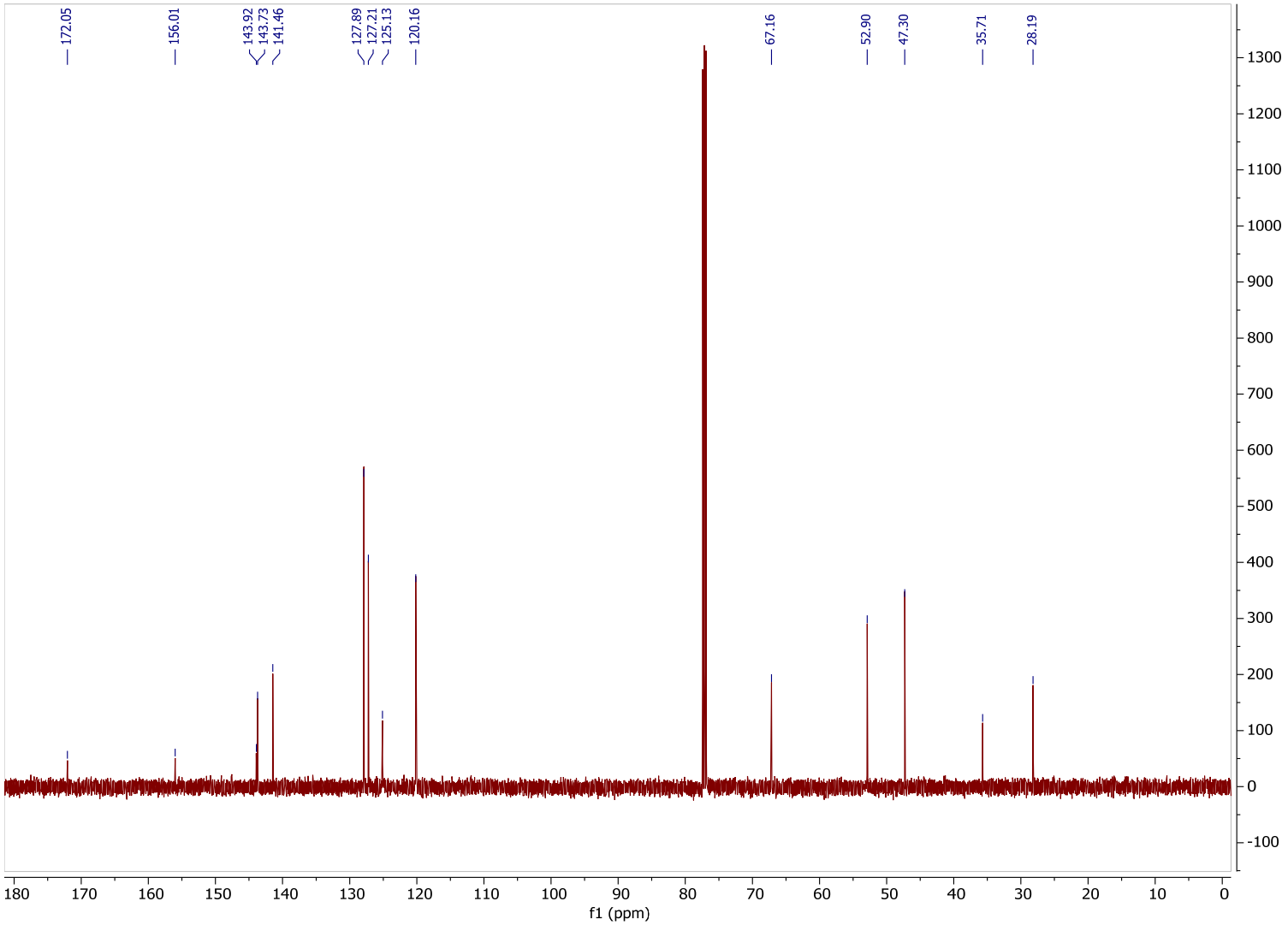
a) IR spectrum of Fmoc-L-Hser(Br)-OMe (**5**)



b) ^{1}H NMR spectrum Fmoc-L-Hser(Br)-OMe (**5**) in $CDCl_3$



c) ^{13}C NMR-APT spectrum Fmoc-L-Hser(Br)-OMe (**5**) in $CDCl_3$



d) HRMS spectrum of Fmoc-L-Hser(Br)-OMe (**5**)

$[M + Na]^+$ calculated for $C_{20}H_{20}BrNO_4Na$: 440.0468, found 440.0446.

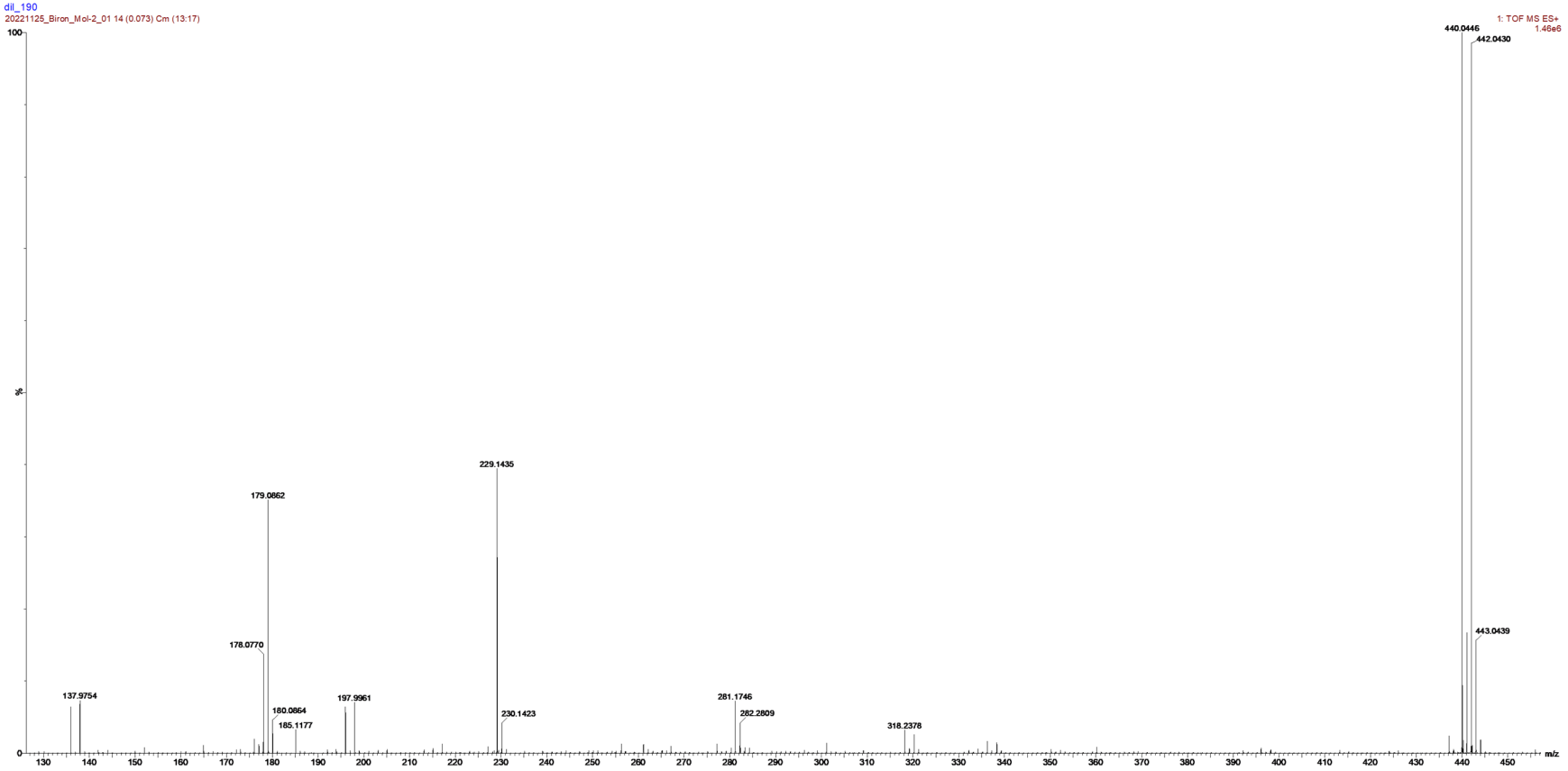
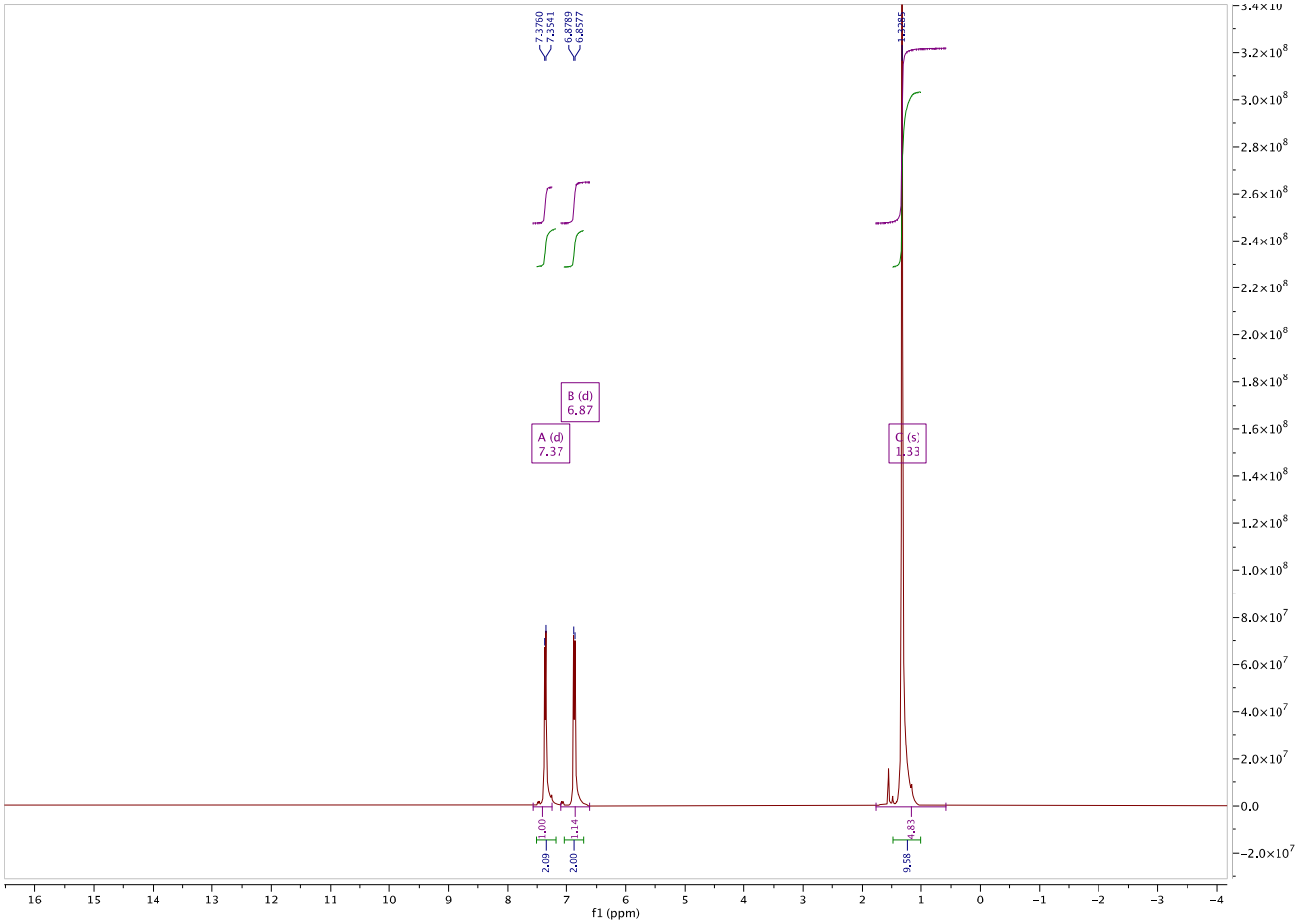


Figure S4. Characterization of 4-*tert*-butoxyphenyl bromide (**6**).

a) ^{1}H NMR spectrum of 4-*tert*-butoxyphenyl bromide (**6**) in $CDCl_3$



b) ^{13}C NMR-APT spectrum of 4-*tert*-butoxyphenyl bromide (**6**) in $CDCl_3$

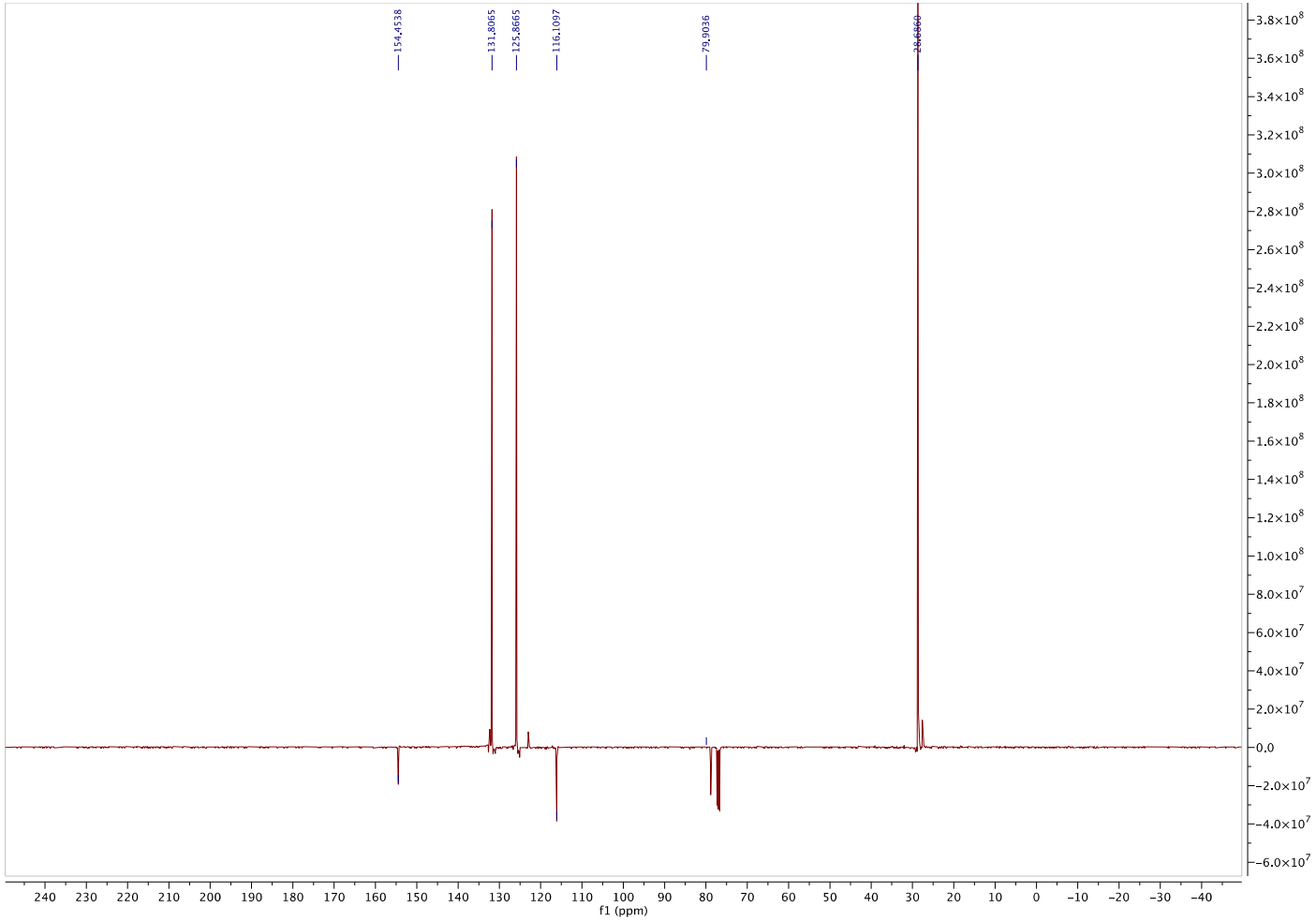
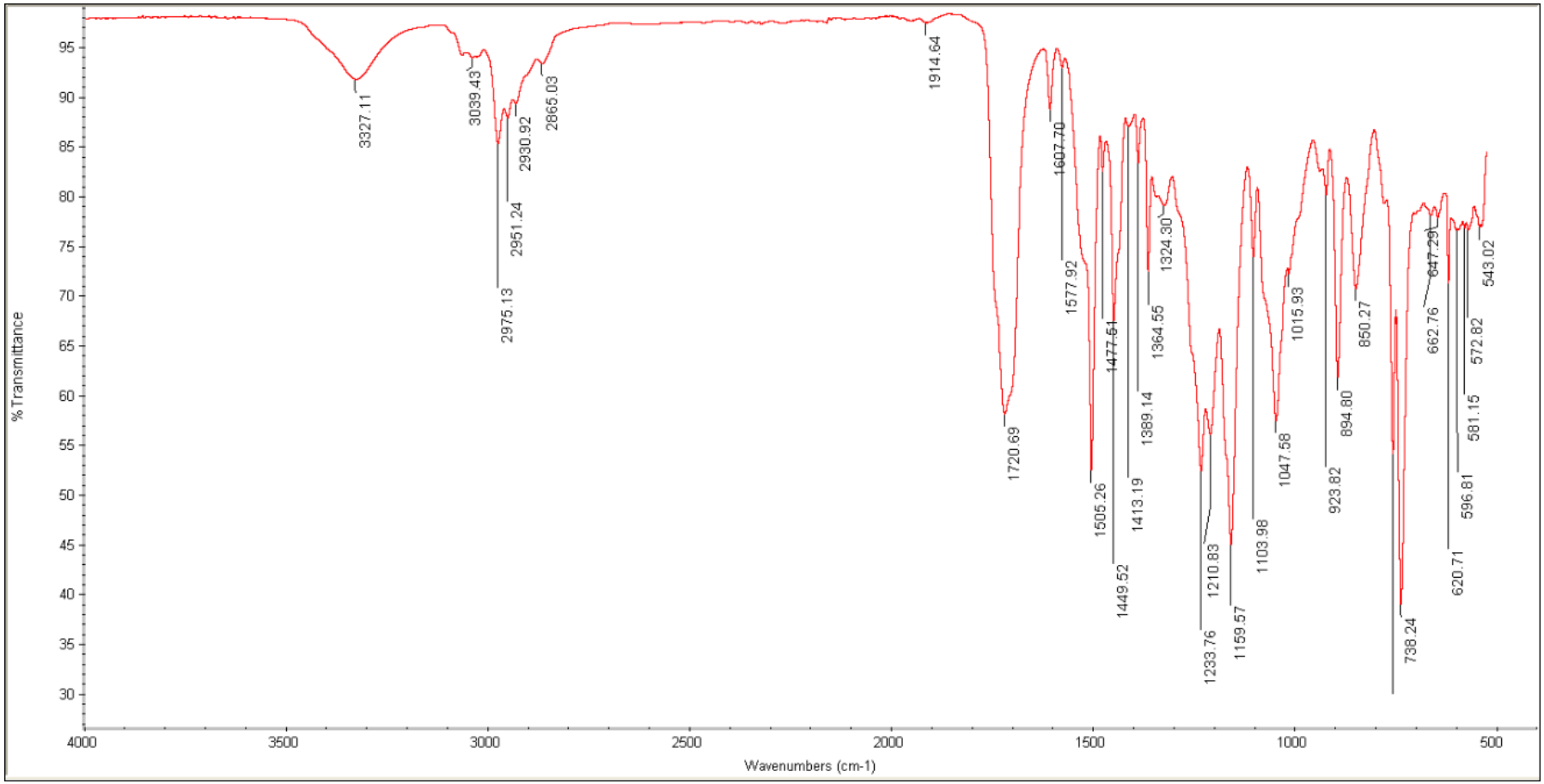
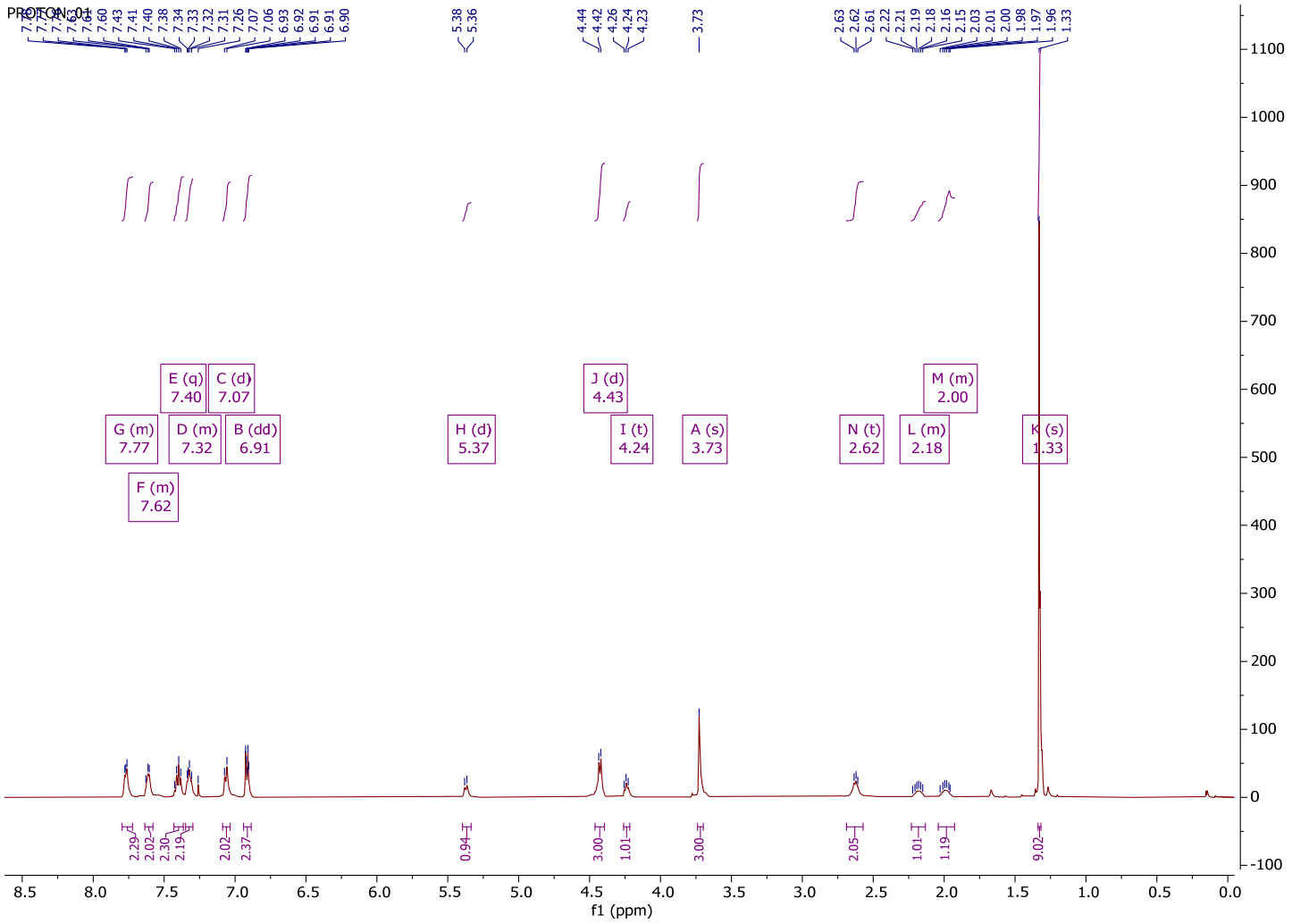


Figure S5. Characterization of methyl (2*S*)-4-(4-*tert*-butoxyphenyl)-2-([(9H-fluoren-9-ylmethoxy)carbonyl]amino)butanoate (Fmoc-L-Htyr(OtBu)-OMe) (**7**).

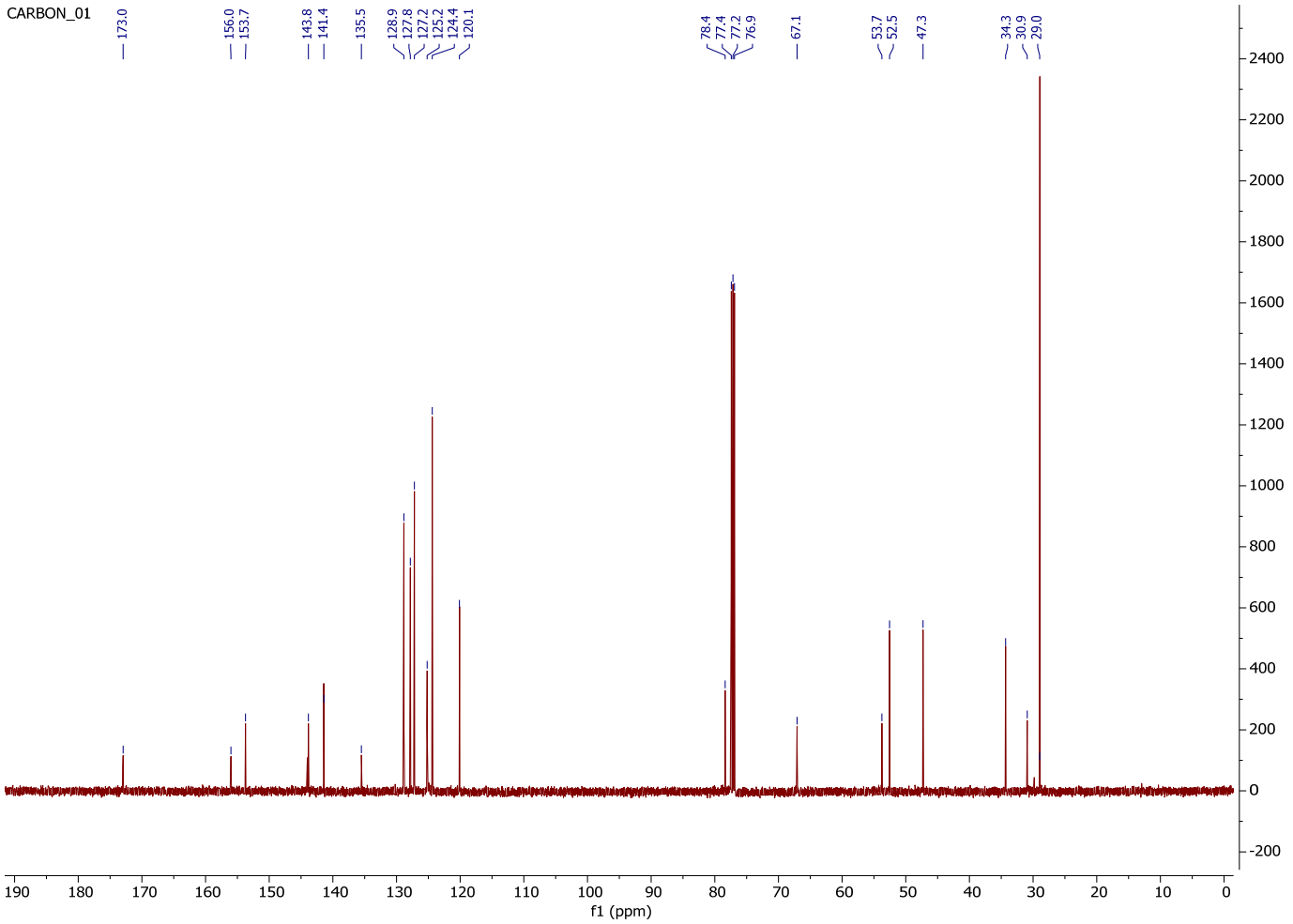
a) IR spectrum of Fmoc-L-Htyr(OtBu)-OMe (**7**)



b) ^{1}H NMR spectrum of Fmoc-L-Htyr(OtBu)-OMe (**7**) in $CDCl_3$



c) ^{13}C NMR-APT spectrum of Fmoc-L-Htyr(OtBu)-OMe (**7**) in $CDCl_3$



d) HRMS spectrum of Fmoc-L-Htyr(OtBu)-OMe (**7**)

$[M + Na]^+$ calculated for $C_{30}H_{33}NO_5Na$: 510.2256, found 510.2247.

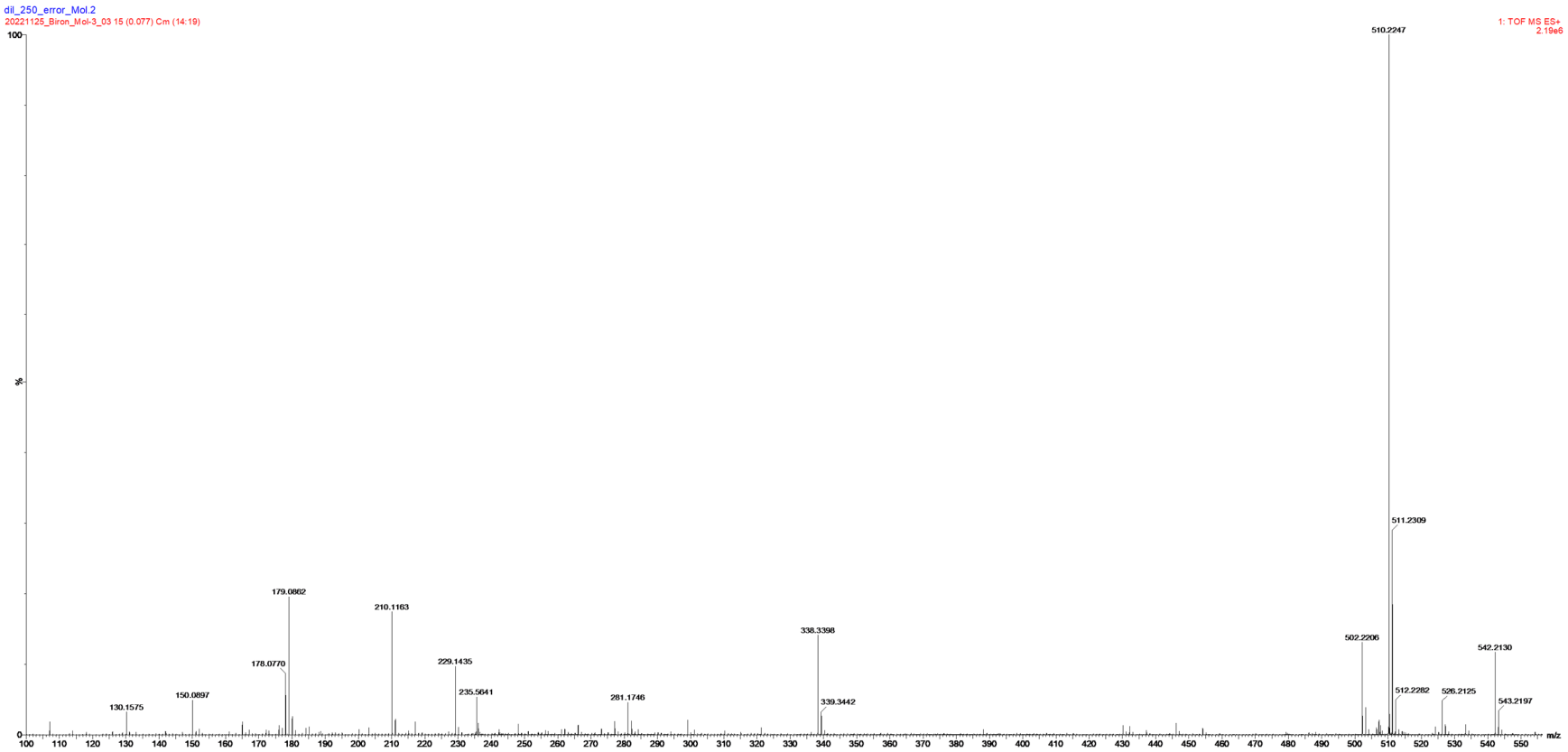
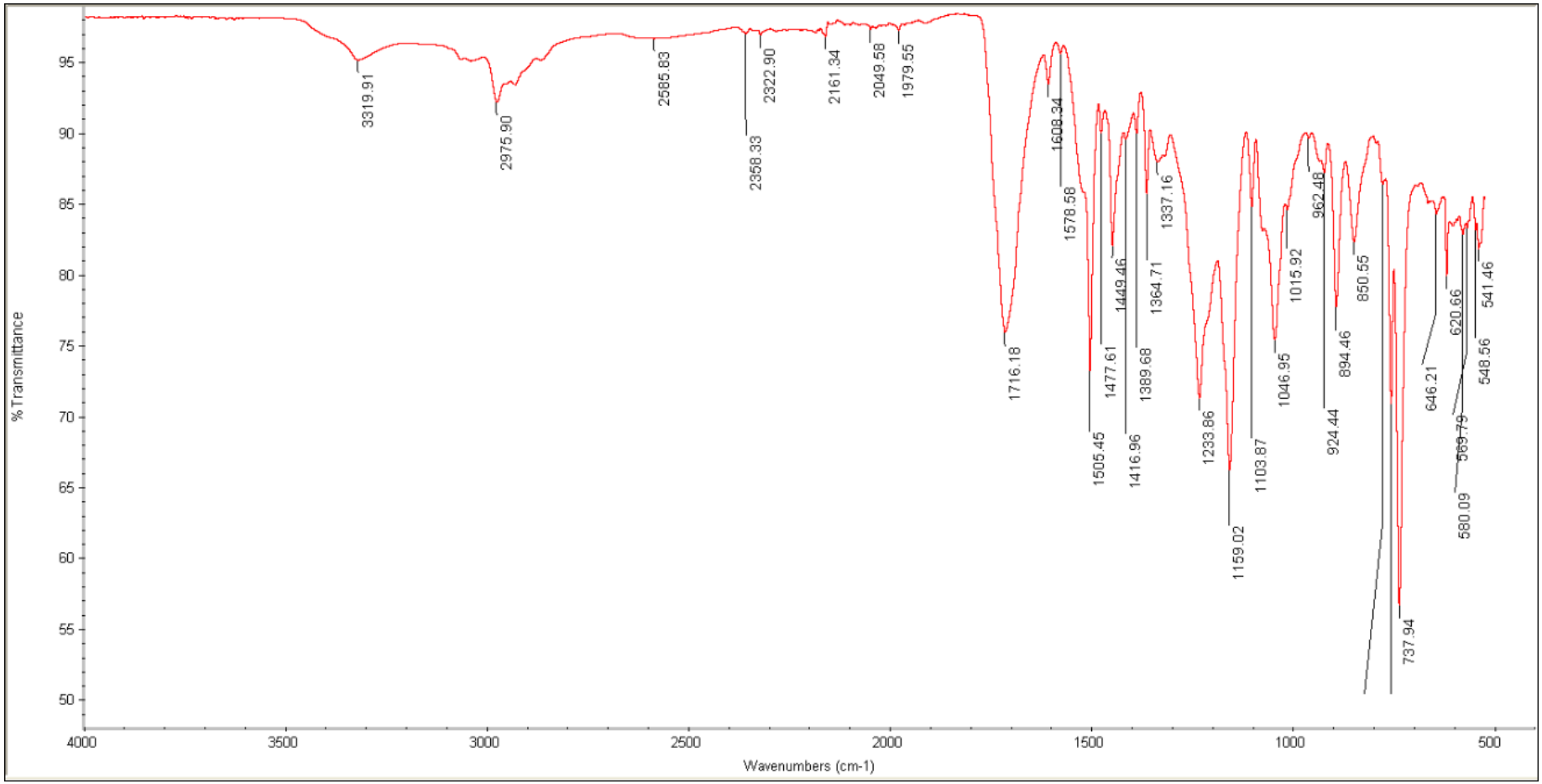
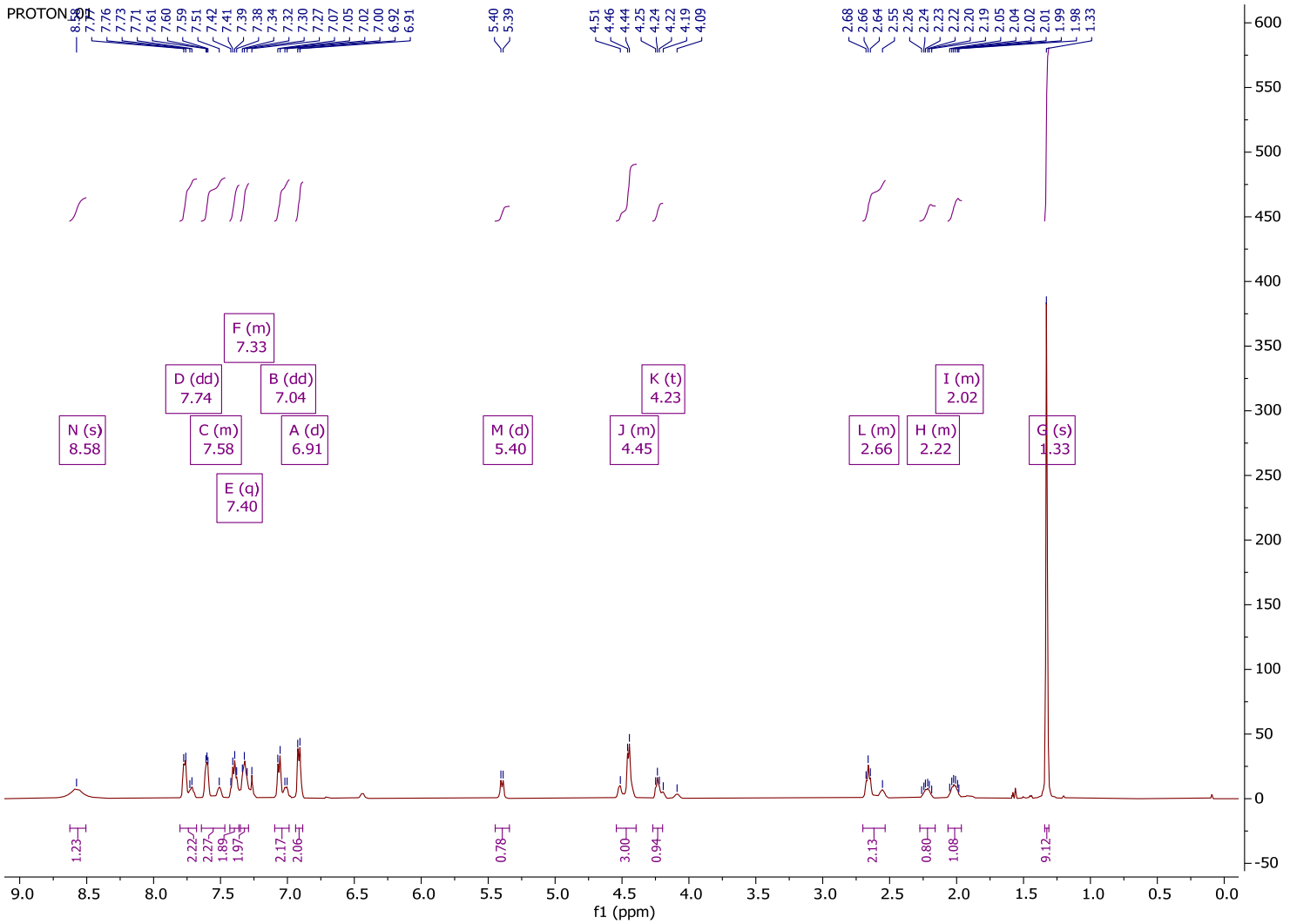


Figure S6. Characterization of (2S)-4-(4-tert-butoxyphenyl)-2-([(9H-fluoren-9-ylmethoxy)carbonyl]amino)butanoic acid (Fmoc-L-Htyr(OtBu)-OH) (**8**).

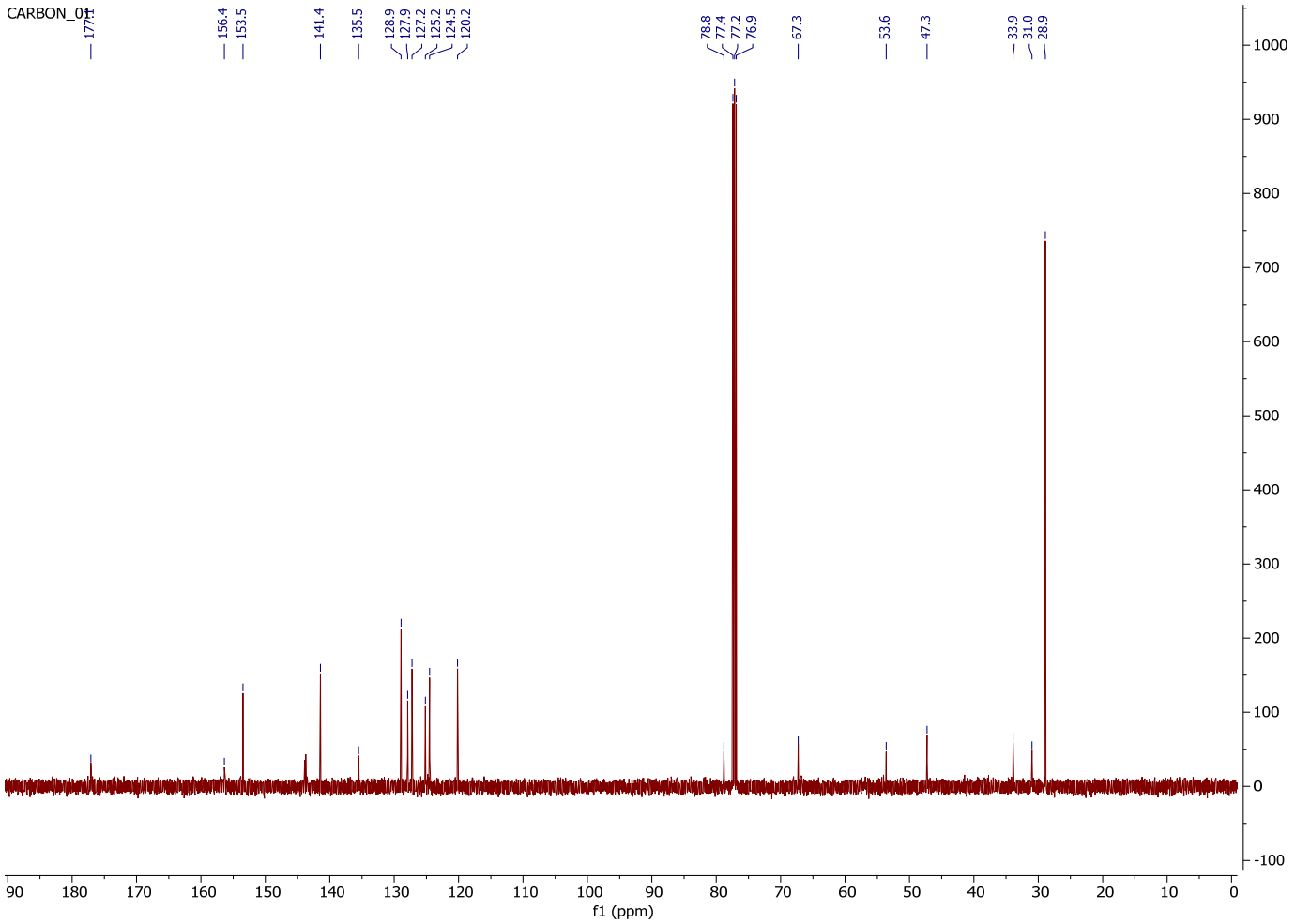
a) IR spectrum of Fmoc-L-Htyr(OtBu)-OH (**8**)



b) ^{1}H NMR spectrum of Fmoc-L-Htyr(OtBu)-OH (**8**) in $CDCl_3$



c) ^{13}C NMR-APT spectrum of Fmoc-L-Htyr(OtBu)-OH (**8**) in $CDCl_3$



d) HRMS spectrum of Fmoc-L-Htyr(OtBu)-OH (**8**)

$[M + Na]^+$ calculated for $C_{29}H_{31}NO_5Na$: 496.2094, found 496.2129.

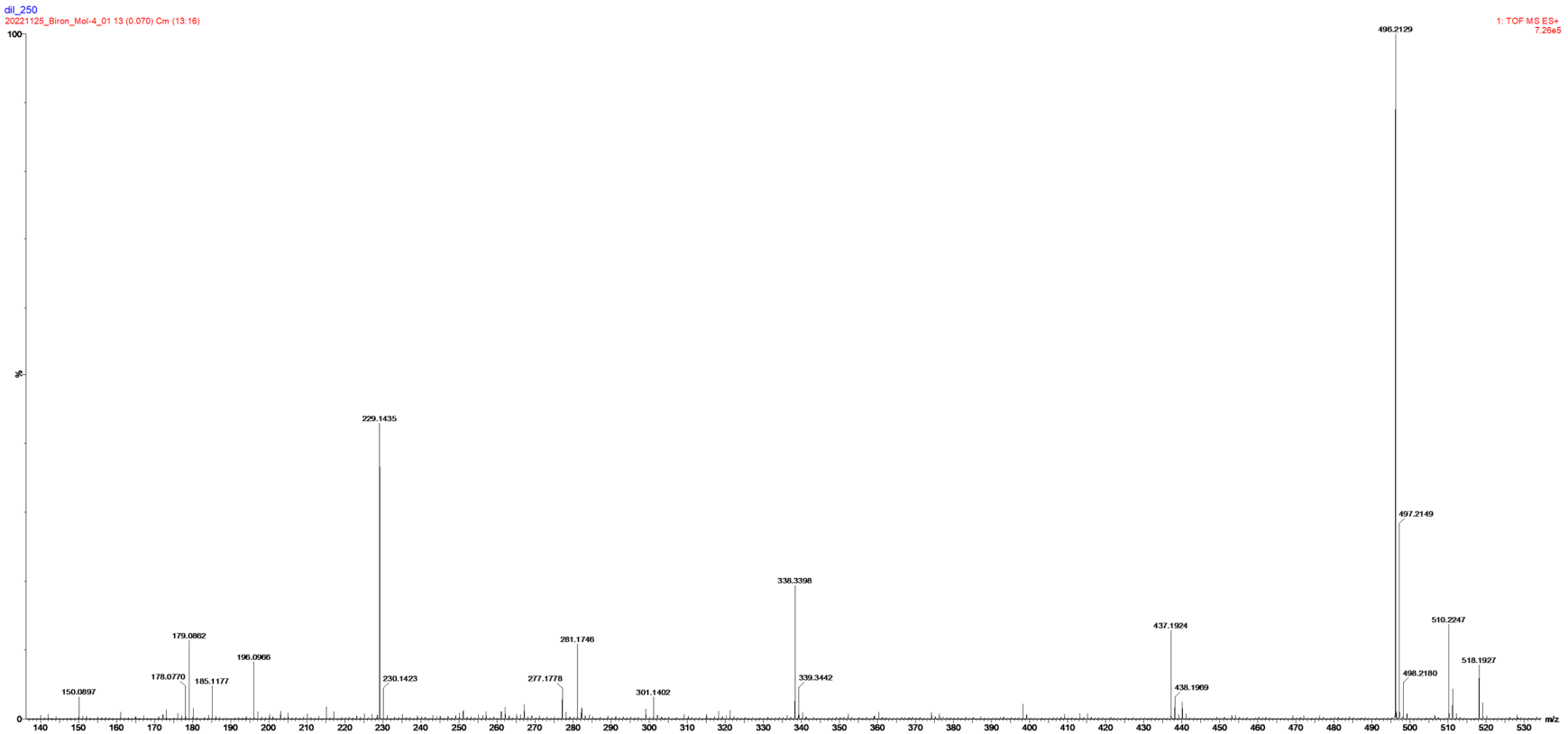
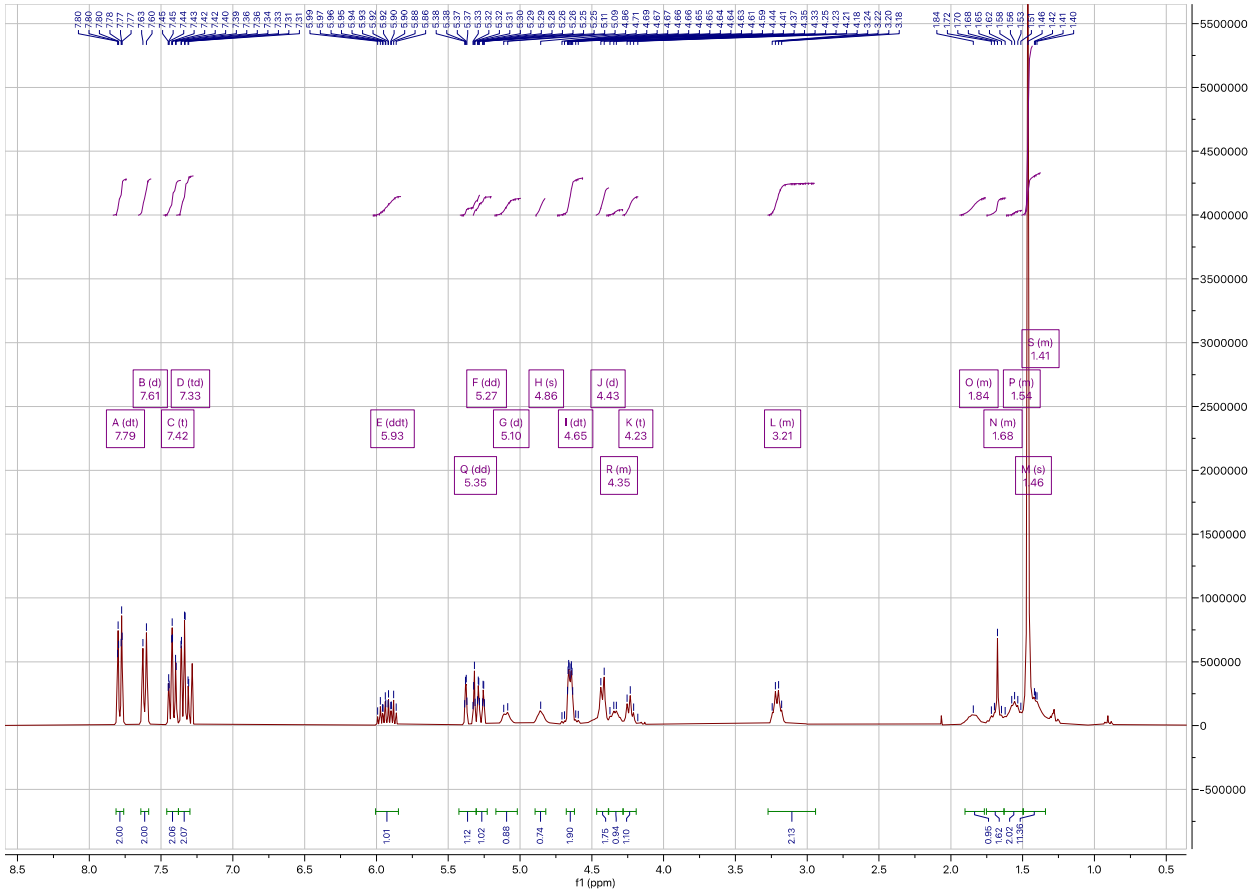
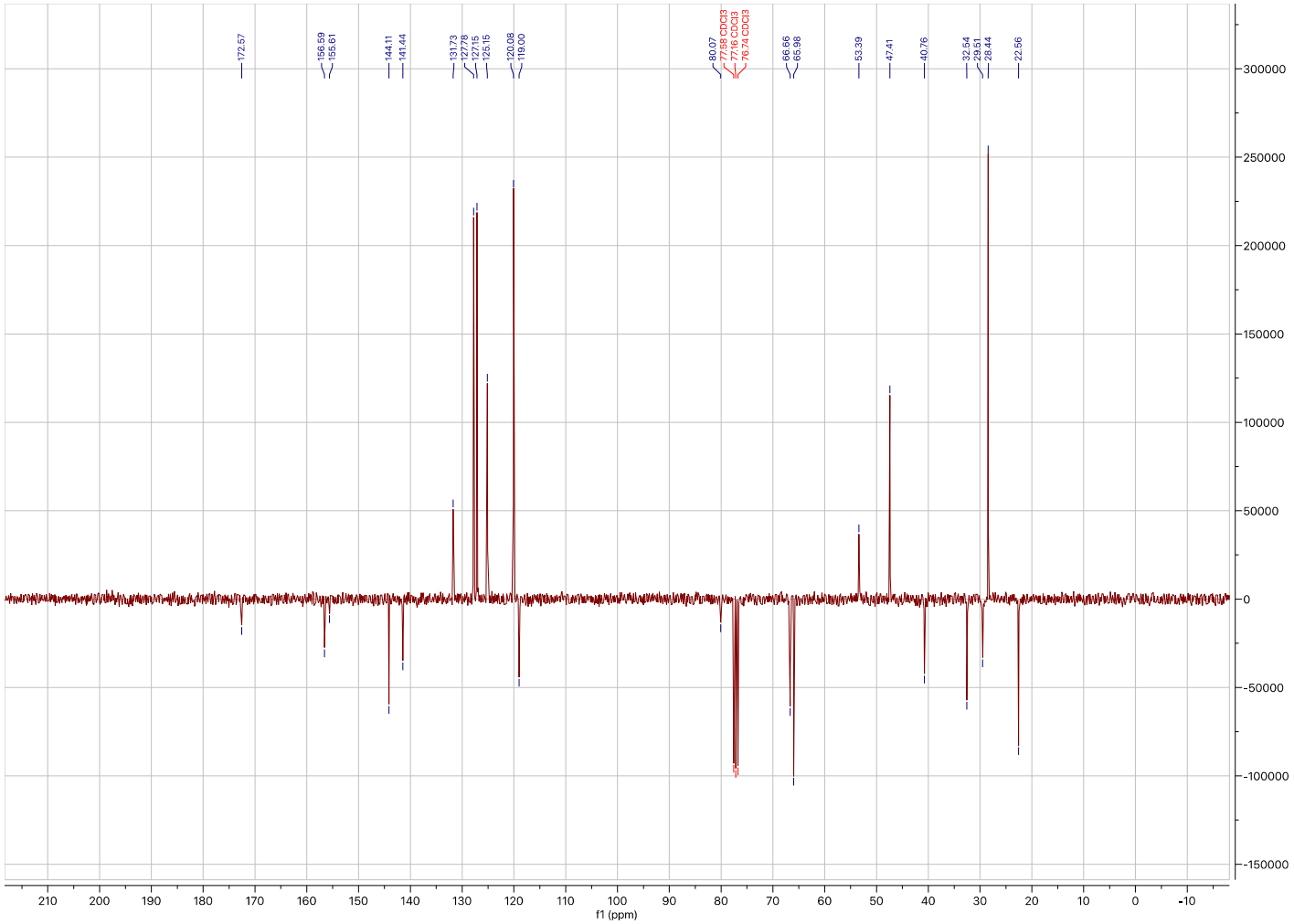


Figure S7. Characterization of Boc-D-Lys(Fmoc)-Oall.

a) ^{1}H NMR spectrum of Boc-D-Lys(Fmoc)-Oall in $CDCl_3$



b) ^{13}C NMR-APT spectrum of Boc-D-Lys(Fmoc)-Oall in $CDCl_3$



c) HRMS spectrum of Boc-D-Lys(Fmoc)-Oall

$[M + Na]^+$ calculated for $C_{29}H_{36}N_2O_6Na$ 531.2575; found 531.2510.

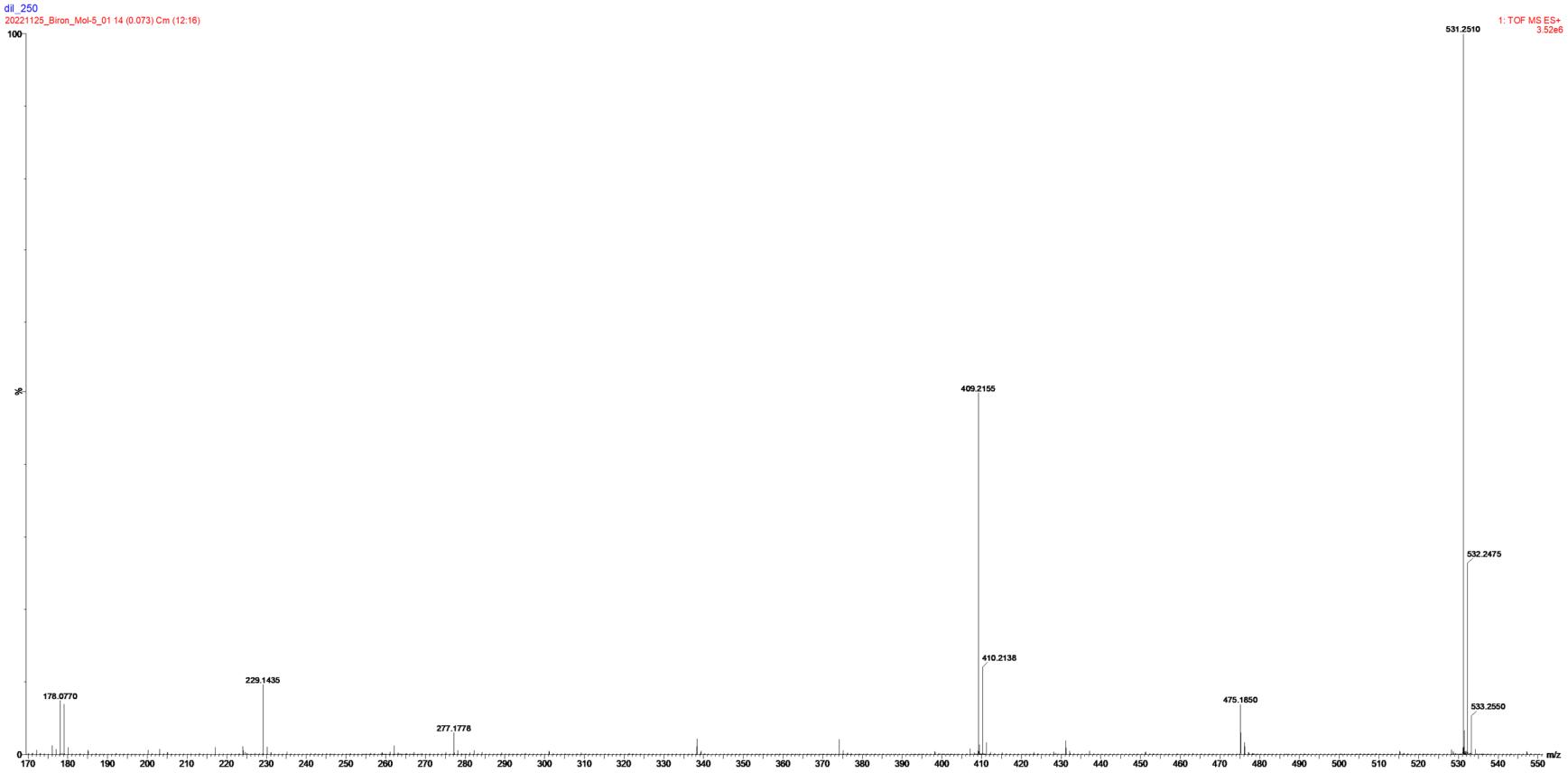
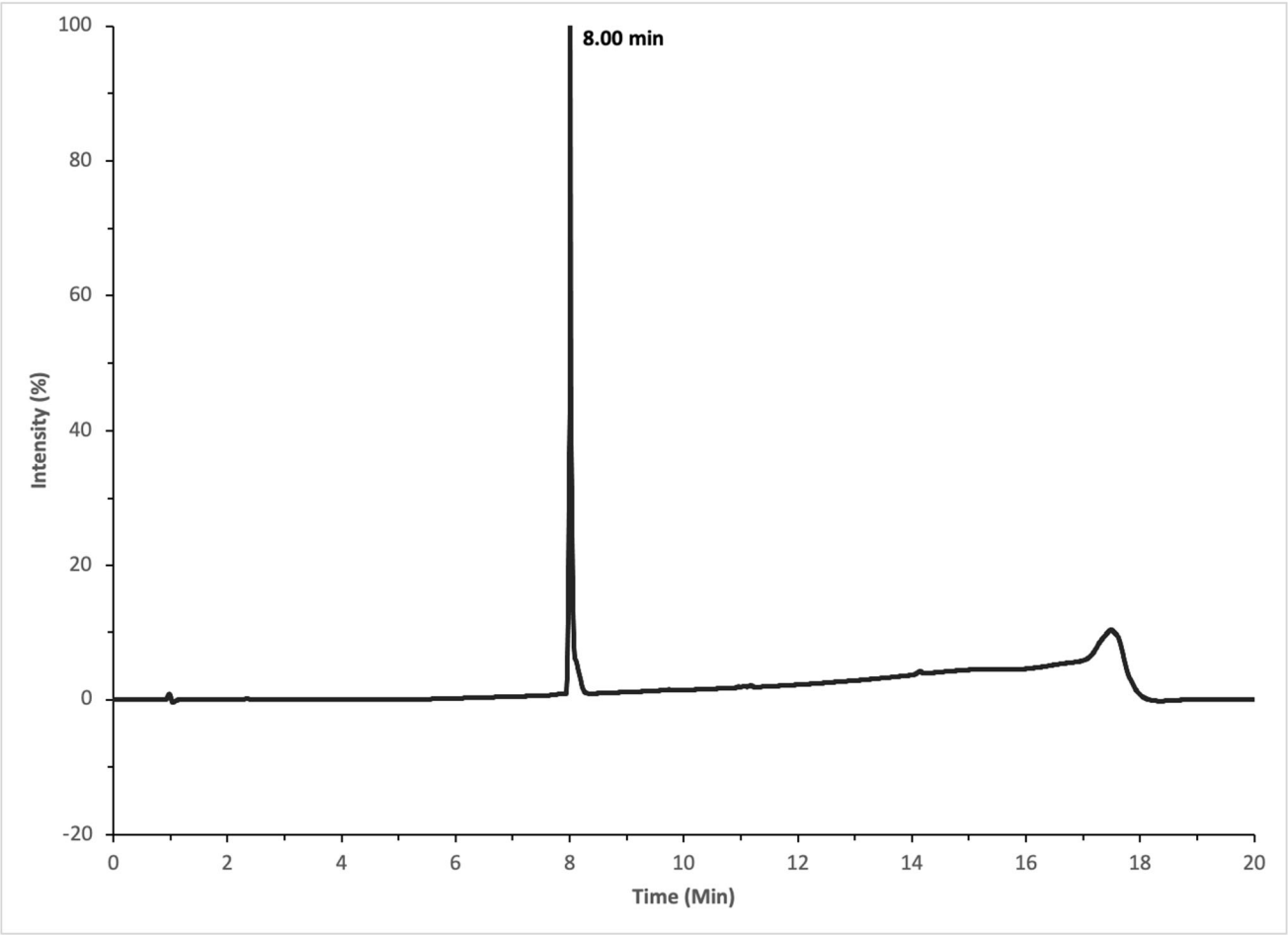
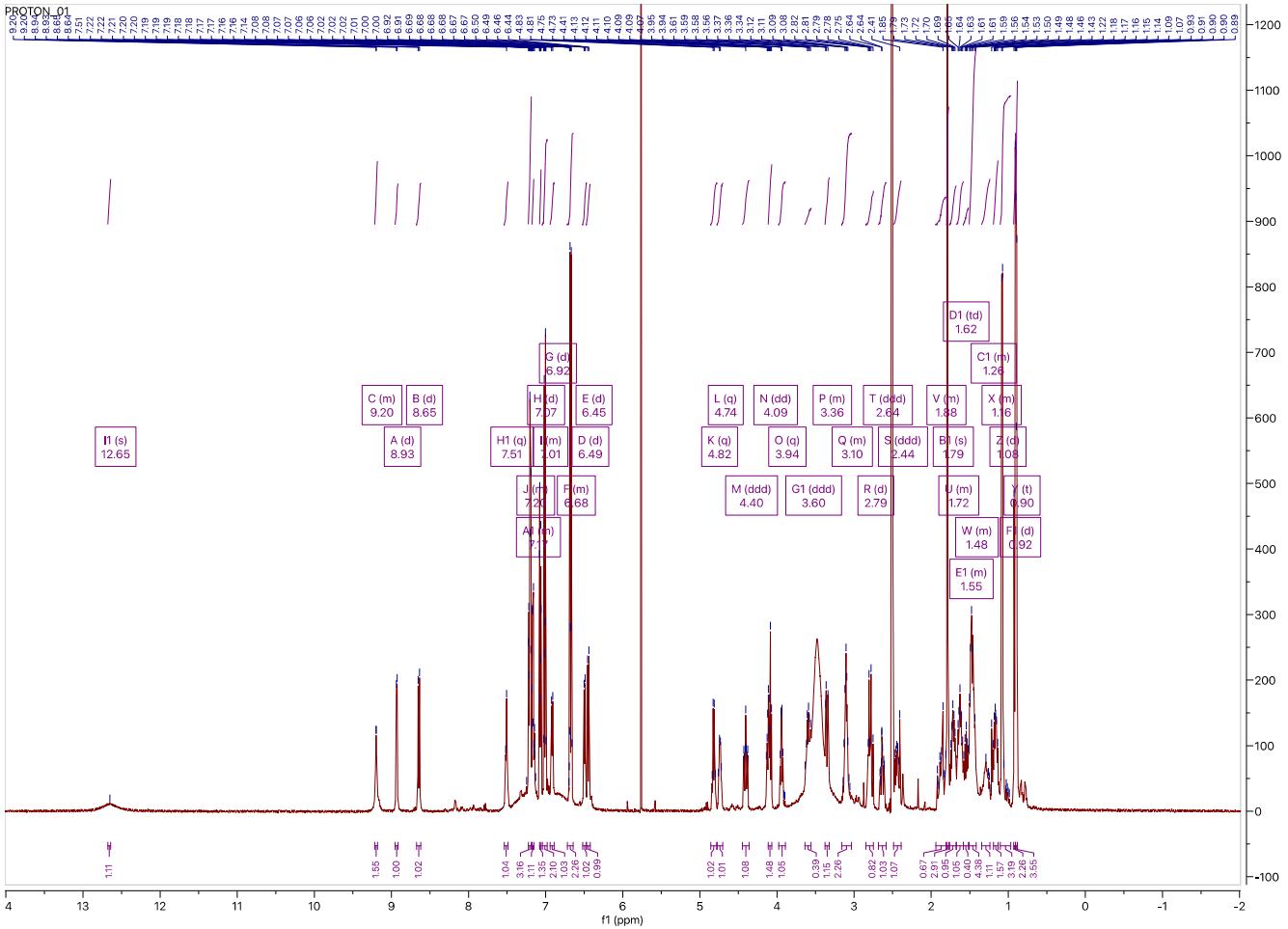


Figure S8. Characterization of anabaenopeptin F L-*allo*-Ile4 (**10**).

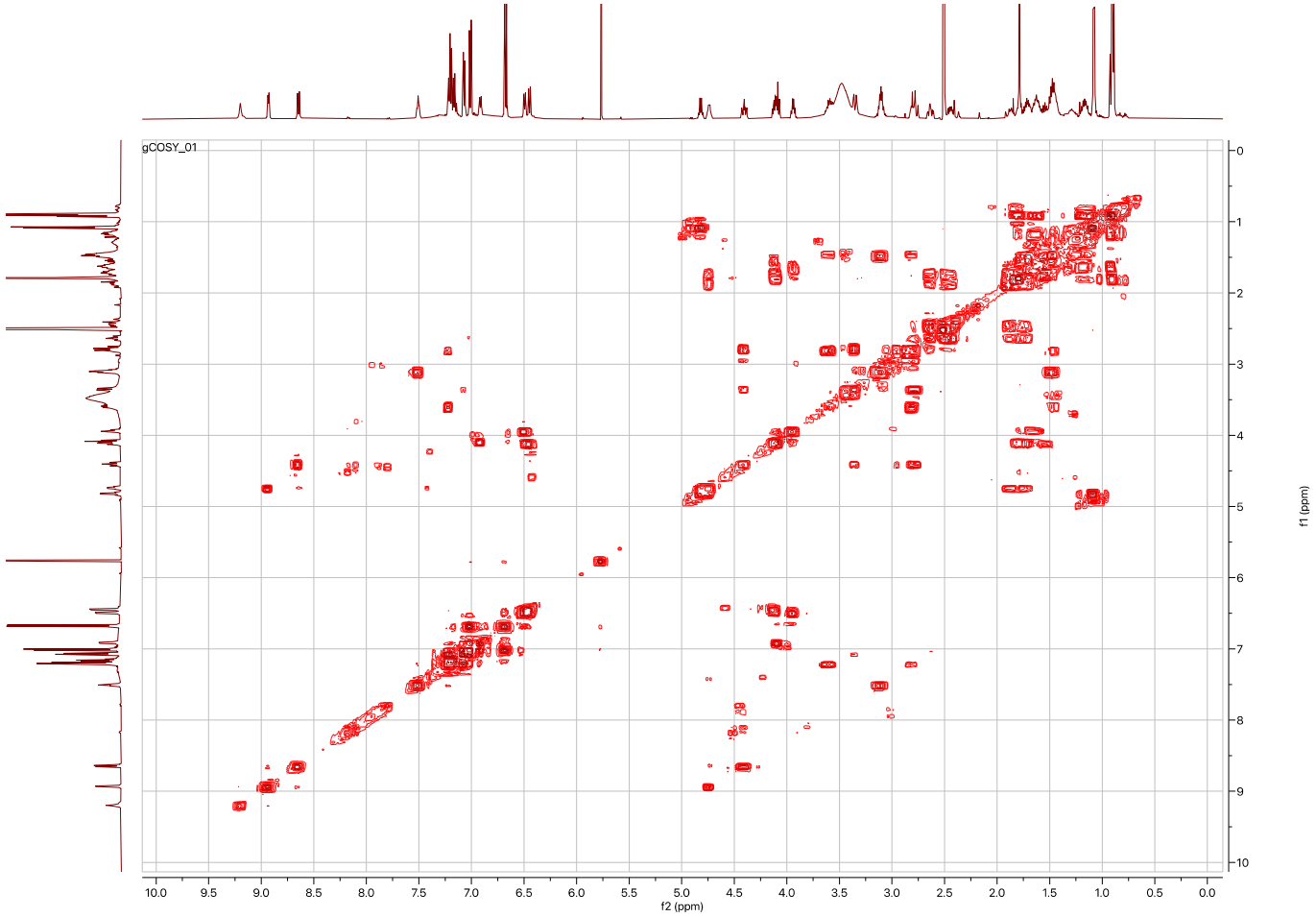
a) HPLC profile of purified anabaenopeptin F L-*allo*-Ile4 (**10**) (λ =220nm)



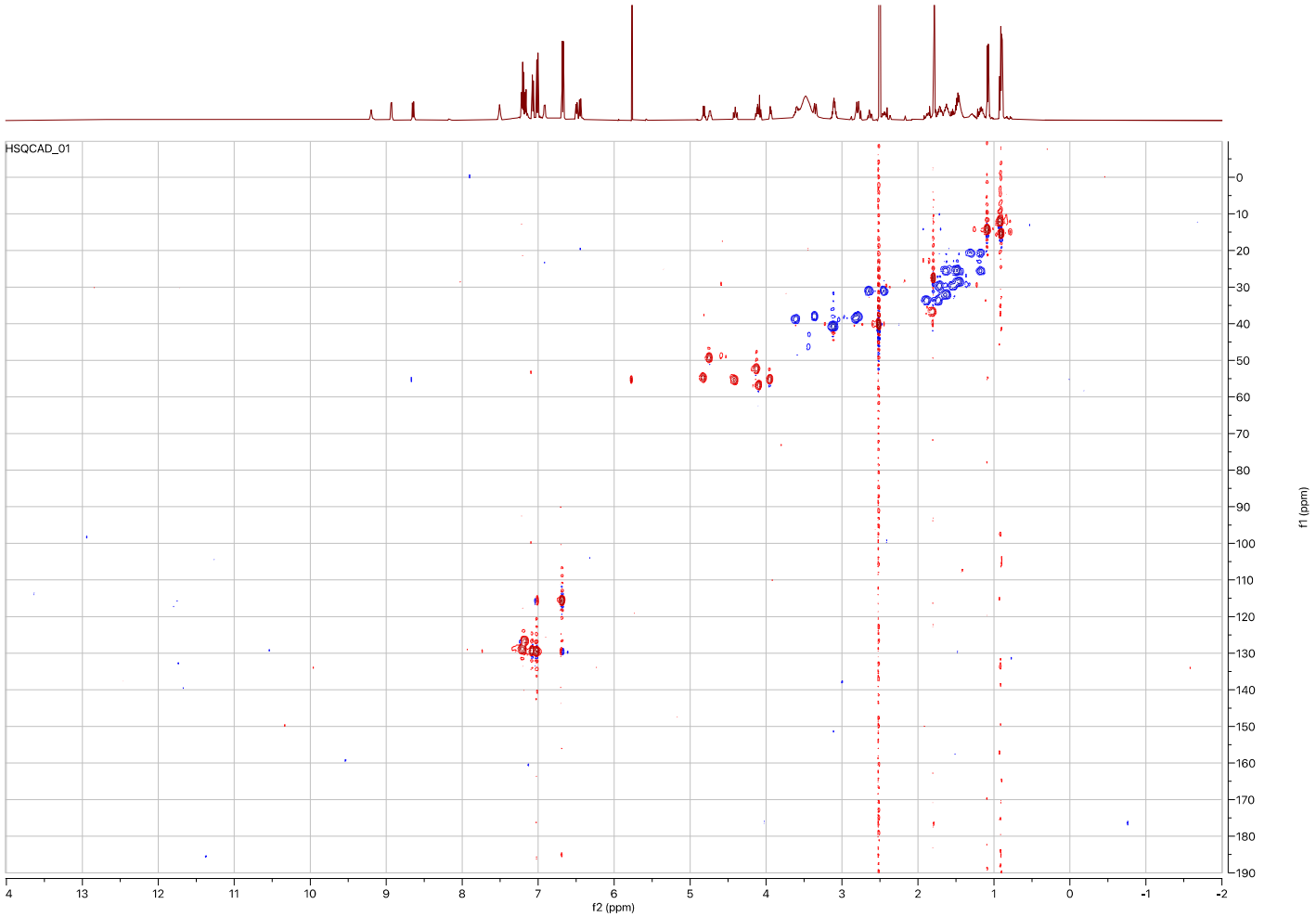
b) ^{1}H NMR spectrum of anabaenopeptin F L-*allo*-Ile4 (**10**) in DMSO-d6



c) ^{1}H-^{1}H COSY spectrum of anabaenopeptin F L-*allo*-Ile4 (**10**) in DMSO-d6



d) HSQC spectrum of anabaenopeptin F L-*allo*-Ile4 (**10**) in DMSO-d6



e) HRMS spectrum of anabaenopeptin F L-*allo*-Ile4 (**10**)

$[M + H]^+$ calculated for $C_{42}H_{63}N_{10}O_9$: 851.4744, found 851.4854.

Figure S9. Carboxypeptidase B inhibition assay of anabaenopeptin F (**1**) (left) and anabaenopeptin F L-*allo*-Ile4 (**10**) (right).

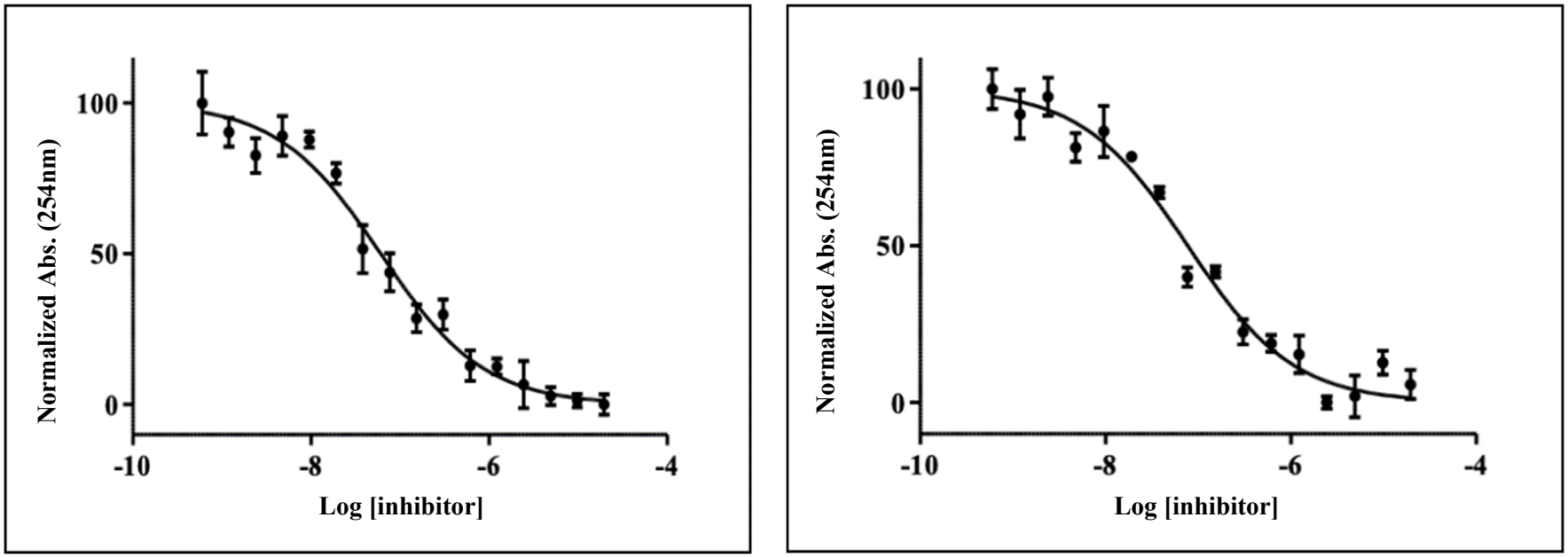


Table S1 – Chemical shift table of isolated and synthetic ABP F (**1**) and (**10**)

		Isolated ABP F *(Brönstrup, 2016)*	Synthetic ABP F **1**	Synthetic ABP F L-*allo*-Ile4 **10**
	Position	δ_H, mult., *J* (Hz)	δ_H, mult., *J* (Hz)	δ_H, mult., *J* (Hz)
Phe (1)	1	-	-	-
	2	4.38	4.38 (ddd, 12.5, 8.8, 3.4)	4.40 (ddd, 12.5, 8.9, 3.4)
	3	2.77	2.78 (dd, 13.9, 11.8)	2.79 (dd, 13.1, 10.3)
		3.31	3.33 (dd, 13.9, 3.4)	3.36 (dd, 13.9, 3.3)
	4	-	-	-
	5, 9	7.06	7.06 (d, 7.0)	7.07 (d, 6.8)
	6, 8	7.19	7.18 (m)	7.20 (m)
	7	7.15	7.14 (m)	7.17 (m)
	NH	8.62	8.69 (d, 8.8)	8.65 (8.9)
NMeAla (2)	1	-	-	-
	2	4.77	4.79 (q, 6.9)	4.82 (q, 6.4)
	3	1.06	1.06 (d, 6.7)	1.08 (d, 6.8)
	NMe	1.78	1.76 (s)	1.79 (s)
Htyr (3)	1	-	-	-
	2	4.71	4.72 (ddd 7.9, 5.4, 5.4)	4.74 (ddd 7.8, 5.4, 5.4)
	3	1.71	1.72 (m)	1.72 (m)
		1.87	1.88 (m)	1.88 (m)
	4	2.43	2.43 (ddd, 13.6, 11.0, 6.5)	2.44 (ddd, 13.6, 11.1, 6.4)
		2.63	2.63 (ddd, 13.6, 11.0, 4.4)	2.64 (ddd, 13.6, 11.0, 4.4)
	5	-	-	
	6, 10	7,00	6.98 (d, 8.0)	6.92 (d, 7.5)
	7, 9	6.67	6.66 (d, 8.0)	6.68 (d, 8.0)
	8	-	-	-
	NH	8.92	8.93 (d 4.3)	8.93 (d 4.6)
Ile (4)	1	-	-	-
	2	4.04	4.08 (dd, 7.7, 7.1)	4.09 (dd, 7.7, 7.1)
	3	1.76	1.76 (m)	1.78 (m)
	4	1.16	1.15 (m)	1.16 (m)
		1.62	1.61 (m)	1.62 (m)
	5	0.88	0.82 (t, 7.4)	0.90 (t, 7.5)
	6	0.89	0.88 (d, 6.5)	0.92 (d, 7.3)
	NH	6.93	6.92 (d, 7.0)	6.92 (d, 7.5)
Lys (5)	1	-	-	-
	2	3.92	3.94 (ddd, 6.7, 6.7, 4.2)	3.94 (ddd, 6.7, 6.7, 4.2)
	3	1.56	1.61 (m)	1.55 (m)
		1.61		
	4	1.18	1.15 (m)	1.17 (m)
		1.29	1.31 (m)	1.26 (m)
	5	1.44	1.47 (m)	1.48 (m)
	6	2.80	2.78 (m)	2.80 (m)
		3.56	3.59 (dddd, 13.6, 8.8, 8.8, 4.2)	3.57 (dddd, 13.5, 8.7, 8.8, 4.0)
	α-NH	6.62	6.46 (d, 7.1)	6.45 (d, 7.1)
	ε-NH	7.14	7.15 (m)	7.15 (m)
Arg (6)	1	-	-	-
	2	3.78	4.10 (ddd, 8.0, 7.9, 5.0)	4.09 (ddd, 8.1, 7.9, 4.8)
	3	1.55	1.54 (m)	1.54 (m)
			1.72 (m)	1.72 (m)
	4	1.36	1.47 (m)	1.48 (m)
		1.46		
	5	3.01	3.10 (m)	3.10 (m)
	6	-	-	-
	α-NH	broad	6.46 (d, 8.1)	6.49 (d, 8.0)
	ε-NH	broad	7.52 (t, 5.8)	7.51 (t, 6.1)
	COOH	n.a.	12.69	12.65 (s)