Supporting information

Determination of the amino linkage of D-Dab residue of occidiofungins A-D cyclic lipo-octapeptides and antifungal activity of their analogues

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Table S1. ^{1}H-NMR assignments of the tripeptides (**11a-b**, **12a-b**)

	Tyr-αDab-Gly (**11a**)	DTyr-αDab-Gly (**11b**)	Tyr-γDab-Gly (**12a**)	DTyr-γDab-Gly (**12b**)
$TyrNH_2$	8.09, d, *J*3.4	8.09, d, *J*3.4	8.25, d, *J*4.5	8.25, d, *J*4.5
2	3.94, m	3.96, m	3.80, m	3.81, m
3	2.92, dd, *J*14.3, 5.7	2.94, dd, *J*13.7, 5.7	2.92, dd, *J*14.0, 6.5	2.88, dd, *J*13.8, 6.8
3	2.79, dd, *J*14.3, 7.8	2.74, dd, *J*13.8, 8.3	2.88, dd, *J*14.0, 7.5	2.81, dd, *J*13.5, 7.5
Ph2,6	6.96, d, *J*8.6	7.01, d, *J*8.0	6.97, d, *J*8.0	6.96, d, *J*8.6
Ph3,5	6.64, d, *J*8.0	6.69, d, *J*8.6	6.67, d, *J*8.6	6.67, d, *J*9.0
OH	4.73, brs	4.73, brs	5.0x	5.0x
DabNH	8.79, d, *J*8.6	8.86, d, *J*7.7	8.84, t, *J*5.7	8.52, t, *J* 5.4
2	4.41, q, *J* 7.3	4.44, q, *J* 7.3	3.80, m	3.80, m
3	1.93, m	1.88, m	1.81, m	1.79, m
3	1.80, m	1.77, m	1.81, m	1.79, m
4	2.79, m	2.74, m	3.17, m	3.17, m
$5NH_2$	7.90, s	7.83, s	8.13, d, *J*4.5	8.13, d, *J*5.5
GlyNH	8.36, t, *J*6.0	8.51, t, *J*5.7	8.50, t, *J*5.7	8.84, t, *J*5.7
2	3.82, dd, *J*17.8, 6.3	3.78, dd, *J*17.5, 6.0	3.91, dd, *J*17.8, 6.3	3.90, dd, *J*17.8, 5.7
2	3.71, dd, *J*17.8, 5.7	3.74, dd, *J*17.0, 5.5	3.80, dd, *J*17.5, 5.5	3.80, dd, *J*17.5, 5.5
OH	9.38, brs	9.35, brs	9.38, brs	9.38, brs

Table S2. ^{1}H-NMR assignments of Ocf A (**5**), Ocf B (**6**), Bk-1119 (**5**)

	Ocf A (**5**)	Ocf B (**6**)	Bk-1119 (**10**)
TyrNH_2	8.00	8.00	8.05, m, 1H
2	4.42	4.42	4.13, m, 1H
3	5.16	5.16	5.03, brs, 1H
3			
Ph2,6	7.17	7.17	7.12, d, J8.0, 2H
Ph3,5	6.76	6.76	6.63, d, J8.0, 2H
OH	-	-	5.68, s, 1H
DabNH	8.04	8.04	7.69, m, 1H
2	4.39	4.39	4.35, m, 1H
3	1.96	1.96	1.86, m, 1H
3	2.15	2.15	2.03, m, 1H
4	2.90	2.90	2.86, m, 2H
5NH_2	7.49	7.49	
GlyNH	7.93	7.93	7.95, brs, 1H
2	3.72	3.72	3.63, m, 1H
2	3.94	3.94	3.72, m, 1H
OH			

Reference

1) Lin, Z.; Falkinham, J. O. Ⅲ; Tawfik, K. A.; Jeffs, P.; Bray, B.; Dubay, G.; Cox, J. E.; Schmidt, E. W. Burkholdines from Burkholderia: antifungal agents and possible virulence factors. *J. Nat. Prod.* **2012**, *75*, 1518-1523.
2) Lu, S.-E.; Novak, J.; Austin, F. W.; Gu, G.; Ellis, D.; Kirk, M.; Wilson-Stanford, S.; Tonelli, M.; Smith, L. *Biochemistry* **2009**, *48*, 8312-8321

Table S3. ^{1}H-and ^{13}C-NMR of Ocfs A (**5**), E (**9**), and isolated Bk-1119 (**5**)

AA		Ocf E (DMSO-d6)		Ocf A (**5**) (DMSO-d6)		Bk-1119 (**10**)[3] (DMSO-d6)		Δ E-Bk	Δ A-Bk
		^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C		
Tyr	1								
	NH	7.95		8.02		8.05, m		-0.1	-0.03
	2	4.14		4.18	63.1	4.13, m	60.8	0.01	0.05
	3	5.09		5.08	73.9	5.03, brs	71.7	0.06	0.05
	Ph1						131.0		
	Ph2,6	7.15				7.12, d (8.0)	128.0	0.03	
	Ph3,5	6.68				6.63, d (8.0)	115.4	0.05	
	Ph4								
	OH	5.73,9.33				5.68, s		0.05	
Dab	1				172.1				
	NH	7.65		7.71		7.69, brs		-0.04	0.02
	2	4.42		4.39	53.9	4.35, m	51.3	0.07	0.04
	3	2.11, 1.89		2.11. 1.91	32.8	2.03, m, 1,86, m	30.3	0.08 0.03	0.08 0.05
	4	2.92		2.92	32.8	2.86, m,	36.7	0.06	0.06
	NH_2	7.75							
Gly	1				170.9				
	NH	7.98		7.93		7.95, brs		0.03	-0.02
	2	3.81, 3.64		3.81, 3.64	45.1	3.72, m, 3.63, m	42.8	0.09 0.01	0.09 0.01
Asn (Asp)	1								
	NH	8.41		8.36		8.29, m		0.12	0.07
	2	4.57		4.58	58.7	4.52, m	50.4	0.05	0.06
	3	2.76, 2.50	38.6	2.63, 2.41	40.1	2.56, m, 2.37, m	37.5	0.2 0.13	0.07 0.04
	4								
	NH_2	7.41							
Ser I	1				169.6				
	NH	7.80		7.81		8.02, m		-0.22	-0.21
	2	4.23	58.3	4.20	58.7	4.18, m	56.4	0.05	0.02
	3	3.58	64.2	3.62	63.1	3.38, m, 3.29, m	61.9	0.20, 0.29	0.24,0.33

									0.33
	OH	4.83							
AsnII	1								
	1NH	8.09		8.13	172.7	8.04, m		0.05	0.09
	2	4.52		4.53	52.9	4.48, m	50.5	0.04	0.05
	3	2.52, 2.35		2.58, 2.36	40.1	2.48, m, 2.31, m	37.9	0.04 0.04	0.1 0.05
	4								
	NH_2 OH	7.26,6.86		7.23, 6.84					
ATHOD	1				170.9				
	2	2.40, 2.32		2.38	40.0	2.36, m, 2.29, m	41.4	0.04 0.03	0.02 0.09
	3	4.15	47.4	4.14	47.5	4.11, m	45.1	0.04	0.03
	NH	7.53		7.49		7.48, brs		0.05	0.01
	4	1.76, 1.35		1.77	41.3	1.72, m, 1.40, m	N.D	0.03 -0.05	0.05
	5	3.51				3.40, m	67.9	0.11	
	5OH	4.17							
	6	3.05				3.07, m	75.6	-0.02	
	6OH	4.08							
	7	3.75				3.68, m	77.8	0.07	
	8	1.36				1.51, m, 1.50, m	30.6	-0.15	
	9-17	1.31				1.24, m	23-32	0.07	
	18	0.86				0.82, t (6.5)	14.8	0.04	
SerII	1								
	NH	8.07		8.13		7.72, d (6.6)		0.35	0.41
	2	4.18		4.21	58.9	4.16, m	56.3	0.02	0.05
	3	3.42				3.55, m	61.9	-0.07	
	OH	4.97				4.78, brs		0.21	
Xyl	H1	4.18				4.14, m	102.7	0.04	
	H2	2.99				2.94, m	73.7	0.05	

	H3	3.28,4.94				3.06, m	77.2	0.22
	H4	3.10,4.93				3.26, m	70.2	-0.16
	H5	3.72, 3.06				3.67, m, 3.01, m	66.3	0.05 0.05

Fig. S1a. Difference between chemical shifts of Ocf E (**9**), Ocf A (**5**) and Bk-1119 (**5**)

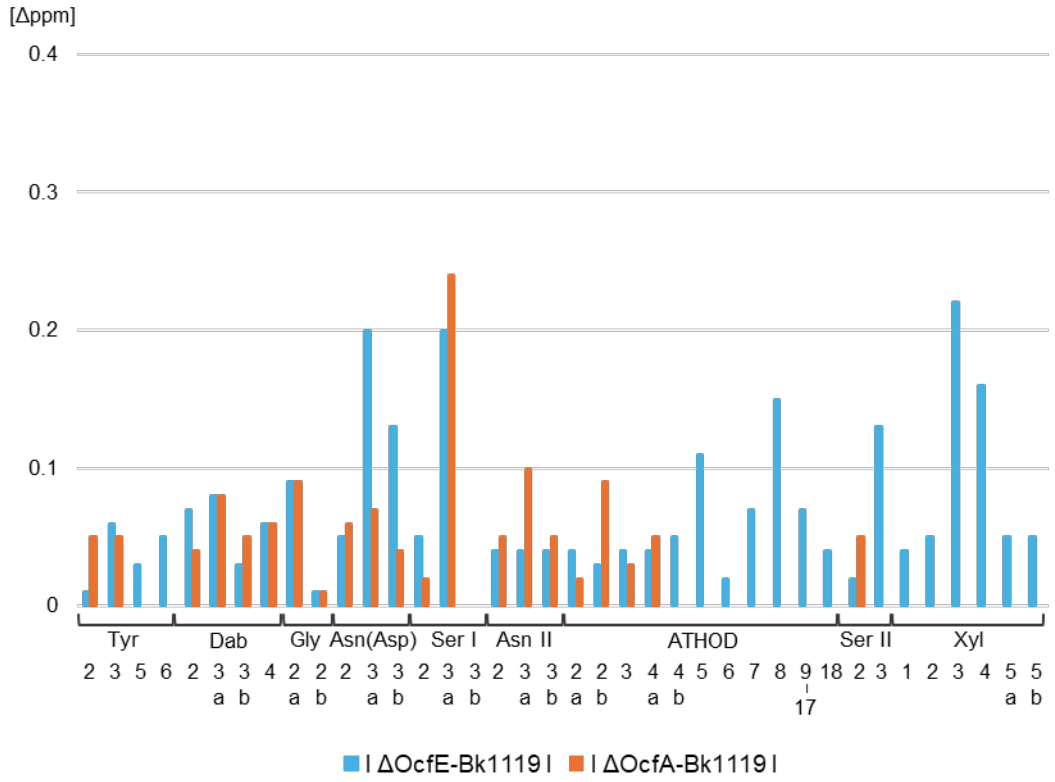


Fig. S1b. Difference in chemical shifts between Ocf E (**9**), OcfA (**5**) and Bk-1119(**5**) (revised)

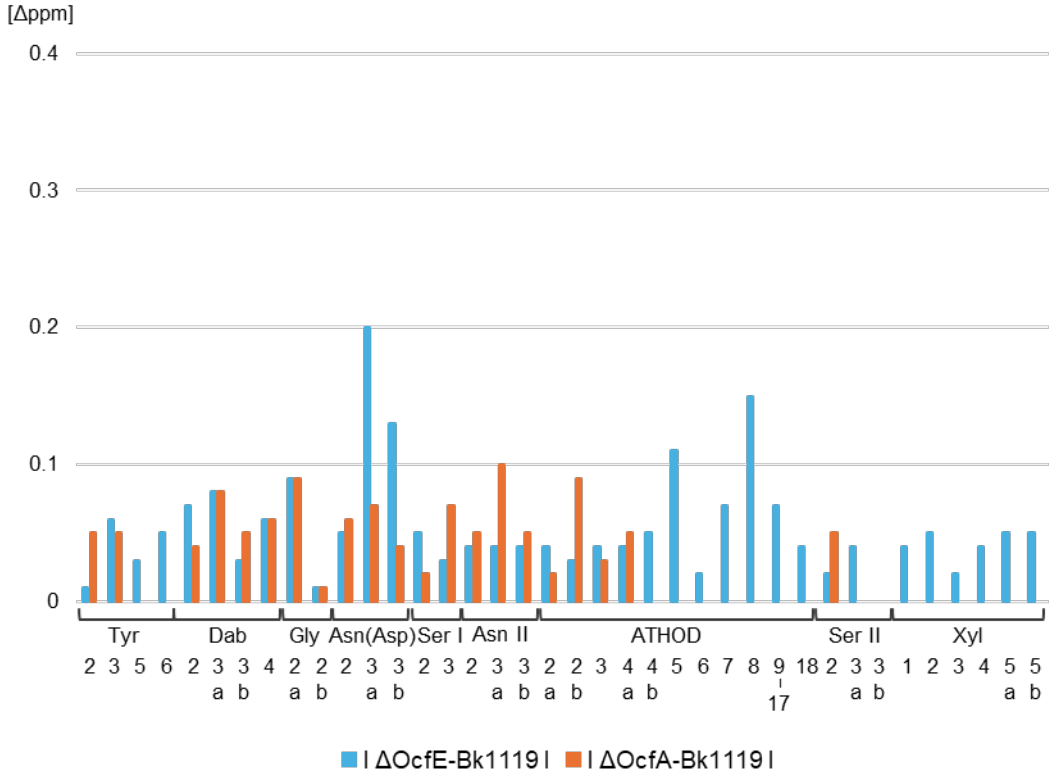


Table S4. Difference in ^{1}H-chemical shifts between the values of **5**, **6 11a-b**, **12a-b** and **13-18**.

entry	peptide	Hα	Ocf A (**5**) (Δ)	Ocf B (**6**) (Δ)	**11a** (Δ)	**11b** (Δ)	**12a** (Δ)	**12b** (Δ)
1	**13**	4.50	-0.11	-0.11	-0.08	-0.07	-0.60	-0.59
2	**14**	4.21	0.18	0.18	0.21	0.22	-0.31	-0.46
3	**15**	4.38	0.01	0.01	0.04	0.05	-0.48	-0.47
4	**16**	4.44	-0.05	-0.05	-0.02	-0.01	-0.54	-0.53
5	**17**	3.88	0.51	0.51	0.54	0.55	0.02	0.03
6	**18**	3.77	0.62	0.62	0.65	0.66	0.13	0.14

Hα (ppm) = chemical shift of α-proton of DAB residue of cyclic peptides

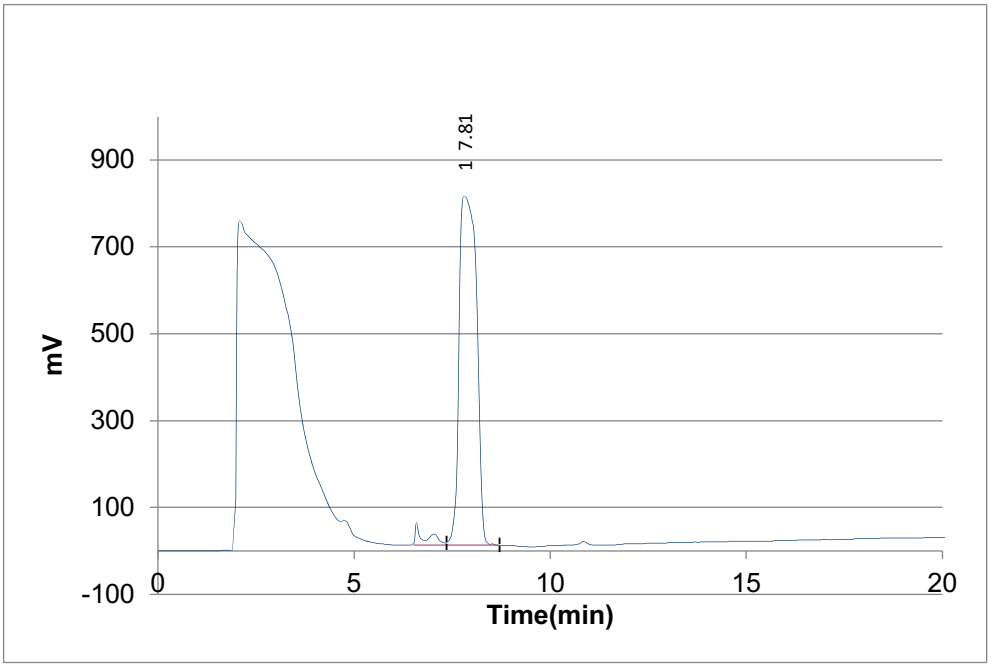
Ocf A (**5**) (Δ) = 4.39 ppm – Hα; Ocf B (**6**) (Δ) = 4.39 ppm – Hα; **11a** (Δ) = 4.42 ppm – Hα; **11b** (Δ) = 4.43 ppm – Hα; **12a** (Δ) = 3.90 ppm – Hα; **12b** (Δ) = 3.91 ppm – Hα.

Appl. Environ. Microbiol. 2011, 77, 6189-6198.

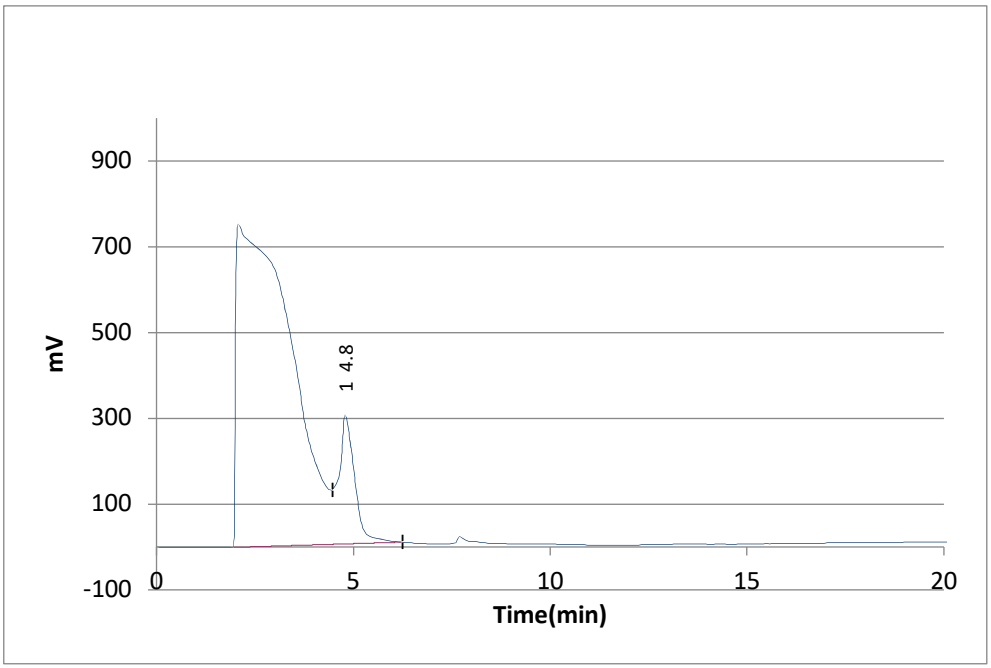
Appl. Environ. Microbiol. 2013, 79, 2899-2905.

HPLC spectra

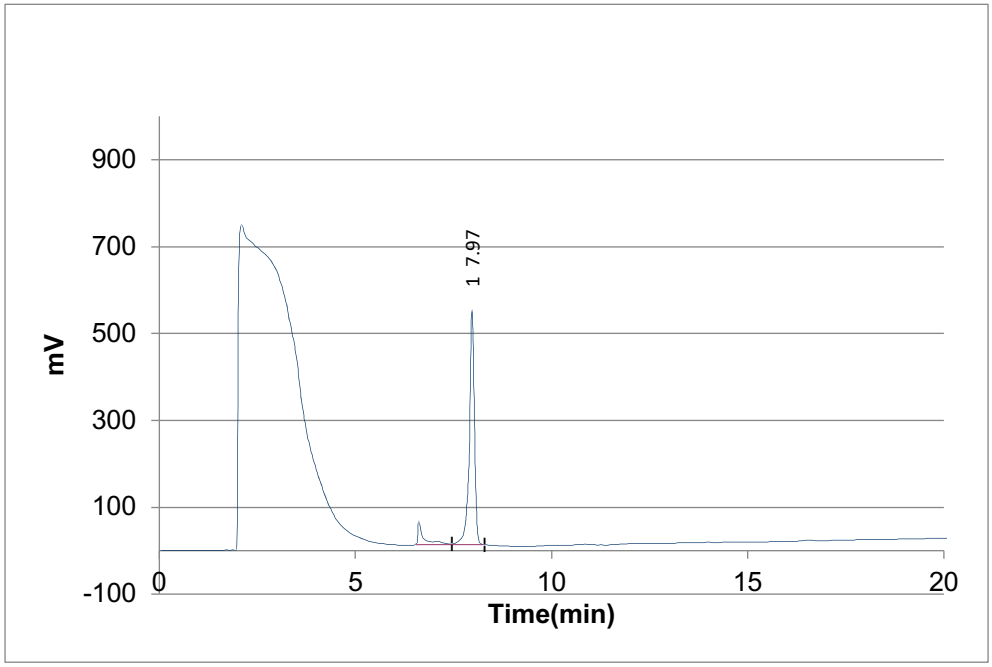
L-Tyr-L-αDab-Gly (**11a**)



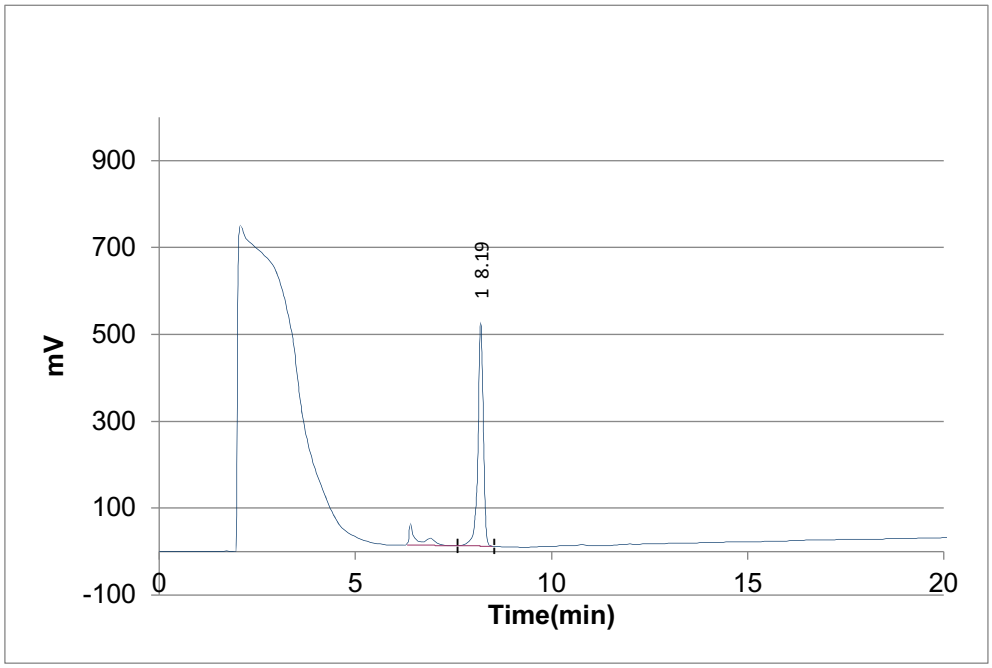
D-Tyr-L-αDab-Gly (**11b**)



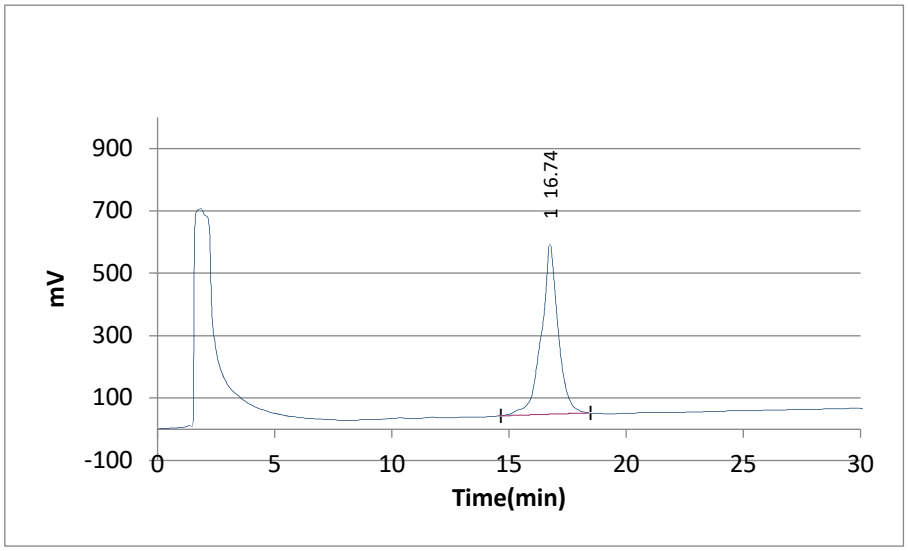
L-Tyr-L-γDab-Gly (**12a**)



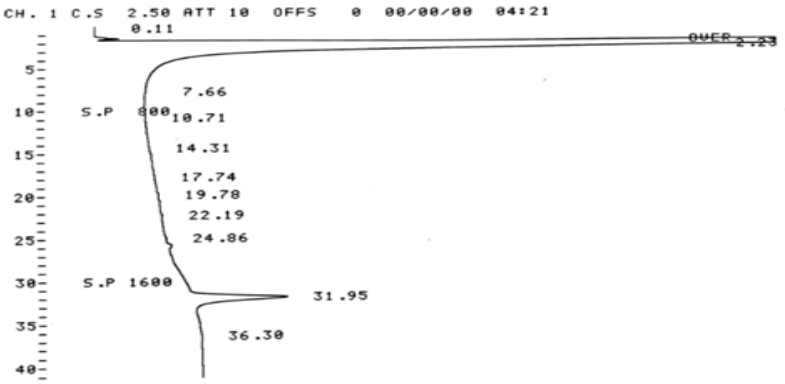
D-Tyr-L-γDab-Gly (**12b**)



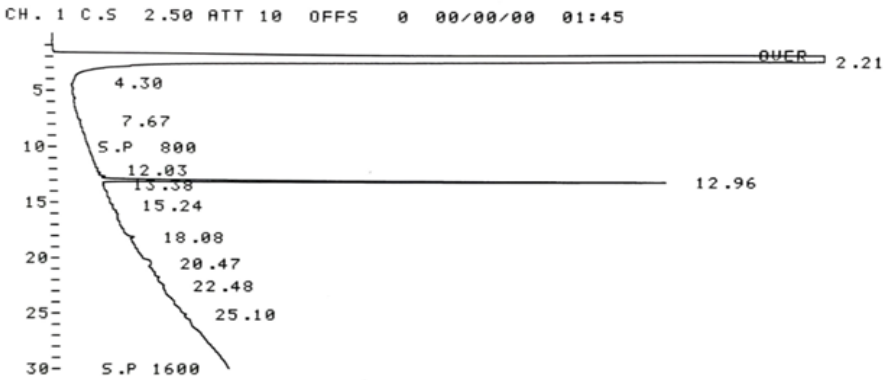
L-LAP-D-Ser(*t*Bu)-D-Tyr(*t*Bu)-D-αDab(Boc)-Gly-Asn(Trt)-Ser(*t*Bu)-Asn(Trt)



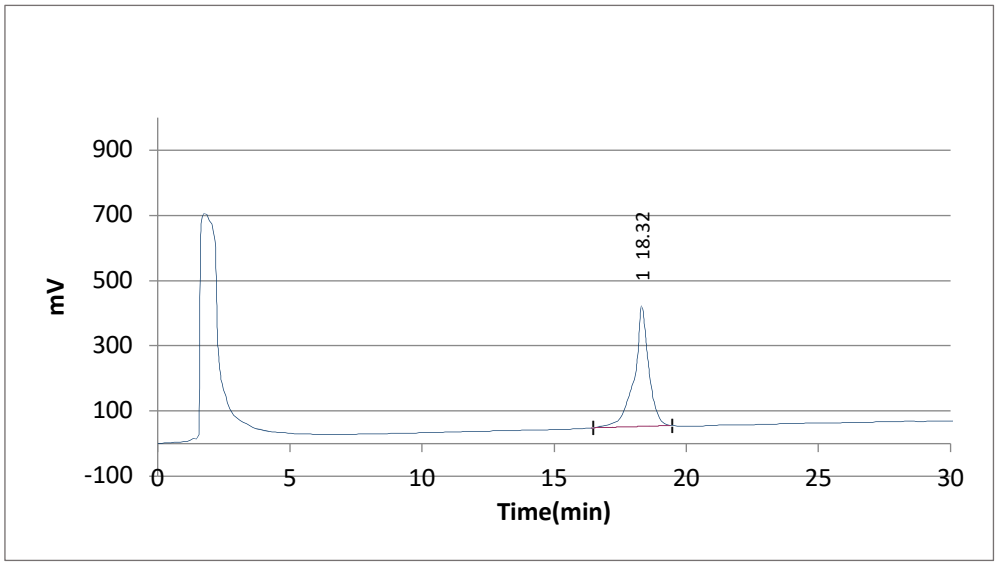
Cyclo-[L-LAP-D-Ser(*t*Bu)-D-Tyr(*t*Bu)-D-αDab(Boc)-Gly-Asn(Trt)-Ser(*t*Bu)-Asn(Trt)]



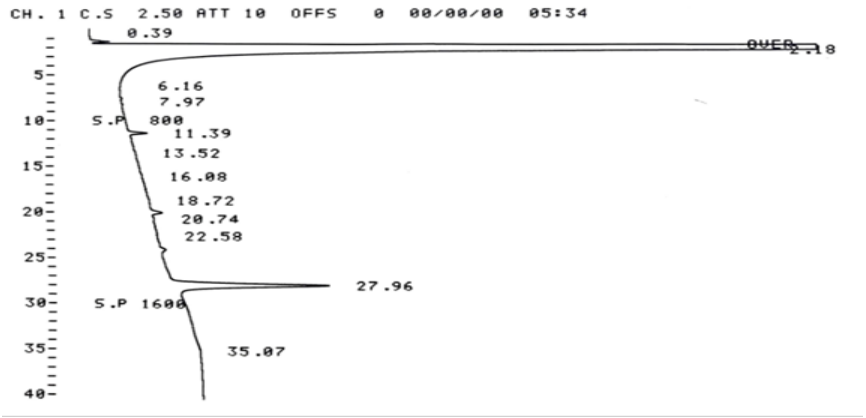
Cyclo-[L-LAP-D-Ser-D-Tyr-D-αDab-Gly-Asn-Ser-Asn] (**13**)



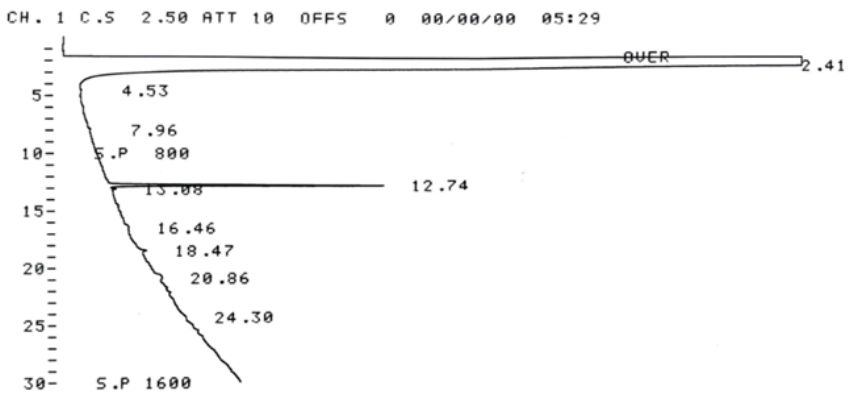
L-LAP-D-Ser(*t*Bu)-D-Tyr(*t*Bu)-L-αDab(Boc)-Gly-Asn(Trt)-Ser(*t*Bu)-Asn(Trt)



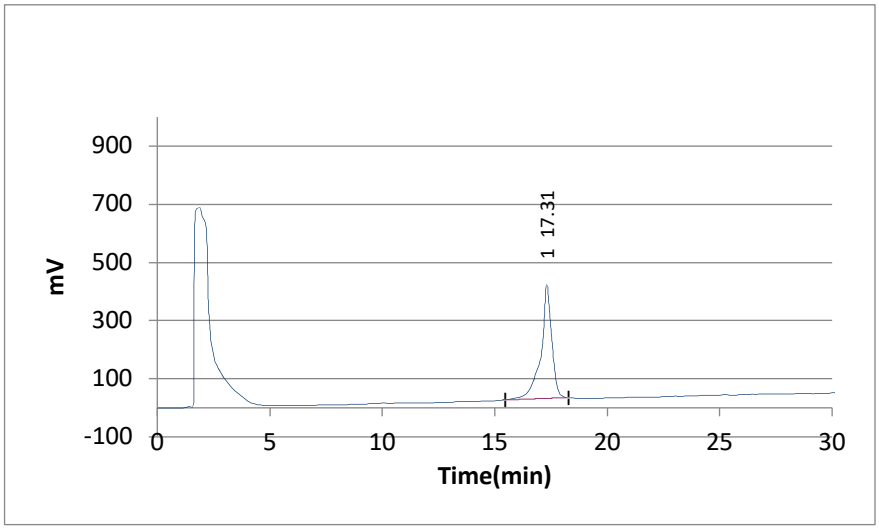
Cyclo-[L-LAP-D-Ser(*t*Bu)-D-Tyr(*t*Bu)-L-αDab(Boc)-Gly-Asn(Trt)-Ser(*t*Bu)-Asn(Trt)]



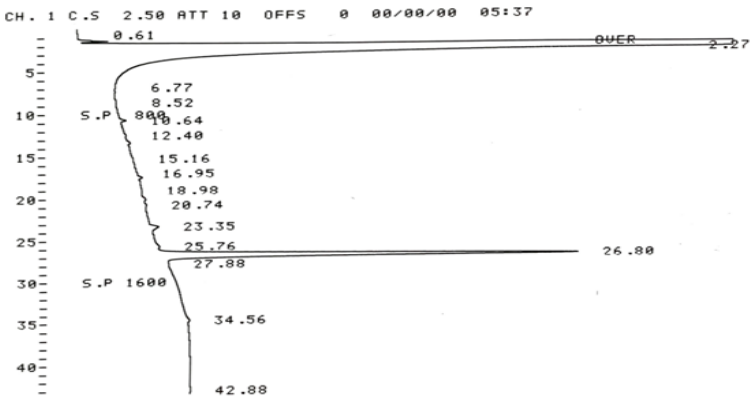
Cyclo-[L-LAP-D-Ser-D-Tyr-L-αDab-Gly-Asn-Ser-Asn] (**14**)



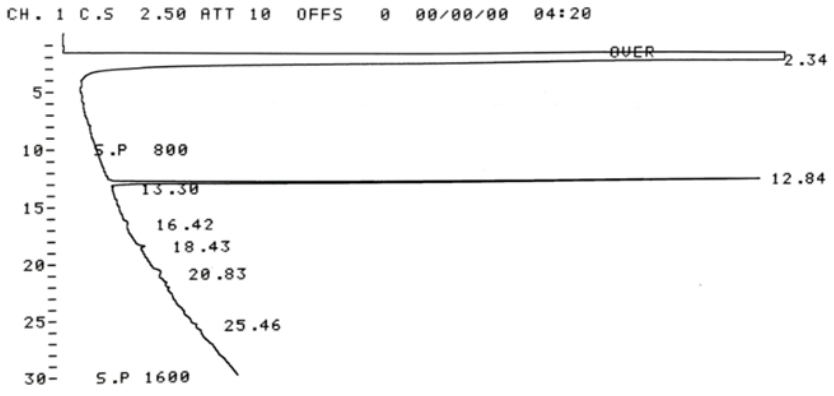
D-LAP-D-Ser(*t*Bu)-D-Tyr(*t*Bu)-D-αDab(Boc)-Gly-Asn(Trt)-Ser(*t*Bu)-Asn(Trt)



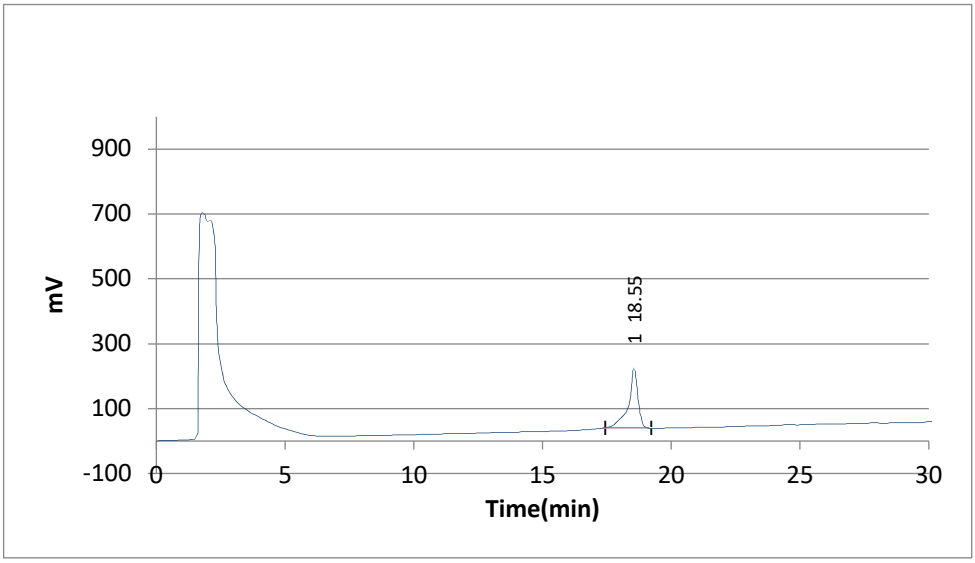
Cyclo-[D-LAP-D-Ser(*t*Bu)-D-Tyr(*t*Bu)-D-αDab(Boc)-Gly-Asn(Trt)-Ser(*t*Bu)-Asn(Trt)]



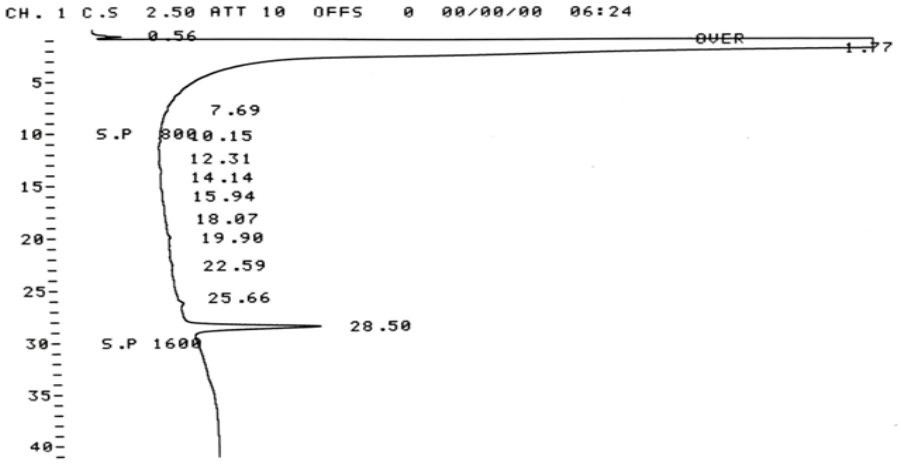
Cyclo-[D-LAP-D-Ser-D-Tyr-D-αDab-Gly-Asn-Ser-Asn] (**15**)



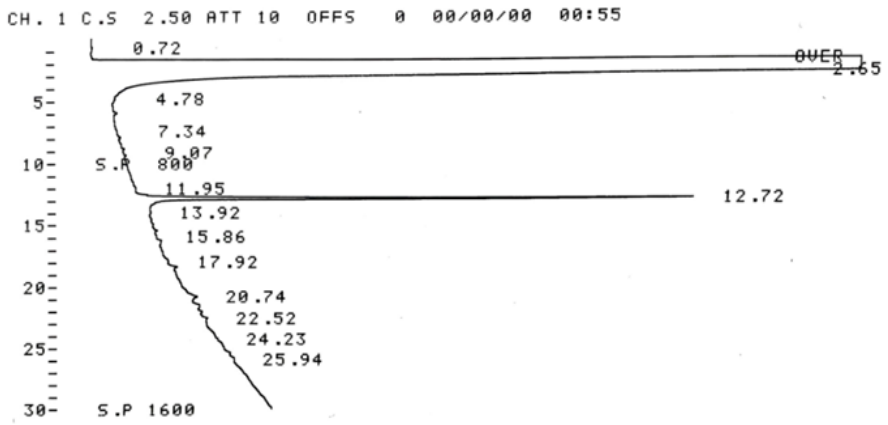
D-LAP-D-Ser(*t*Bu)-D-Tyr(*t*Bu)-L-αDab(Boc)-Gly-Asn(Trt)-Ser(*t*Bu)-Asn(Trt)



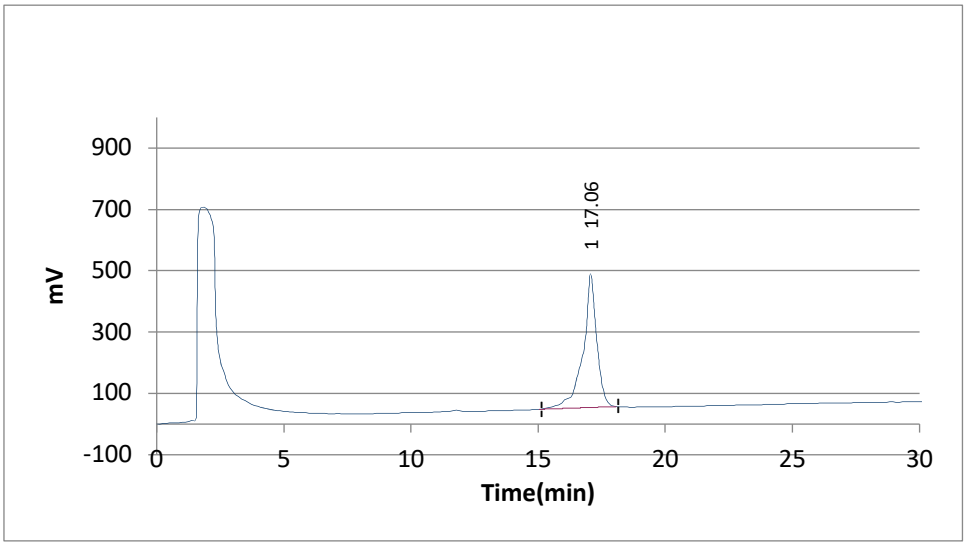
Cyclo-[D-LAP-D-Ser(*t*Bu)-D-Tyr(*t*Bu)-L-αDab(Boc)-Gly-Asn(Trt)-Ser(*t*Bu)-Asn(Trt)]



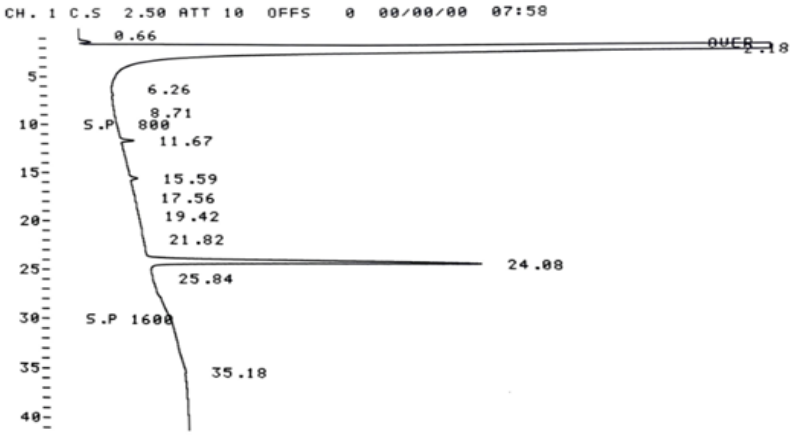
Cyclo-[D-LAP-D-Ser-D-Tyr-L-αDab-Gly-Asn-Ser-Asn] (**16**)



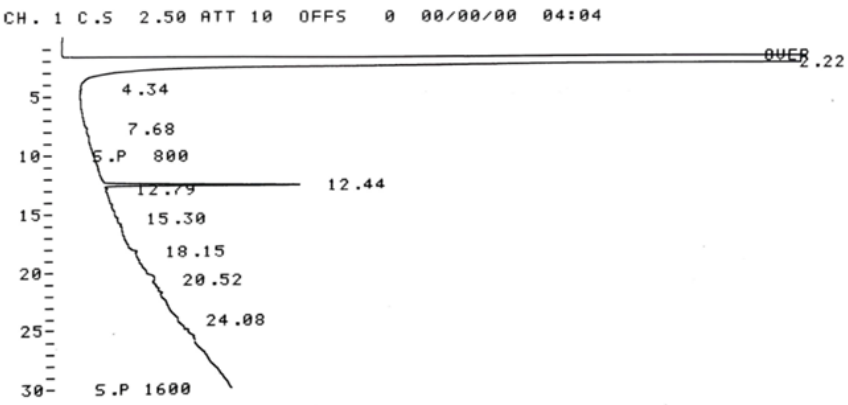
L-LAP-D-Ser(*t*Bu)-D-Tyr(*t*Bu)-L-γDab(Boc)-Gly-Asn(Trt)-Ser(*t*Bu)-Asn(Trt)



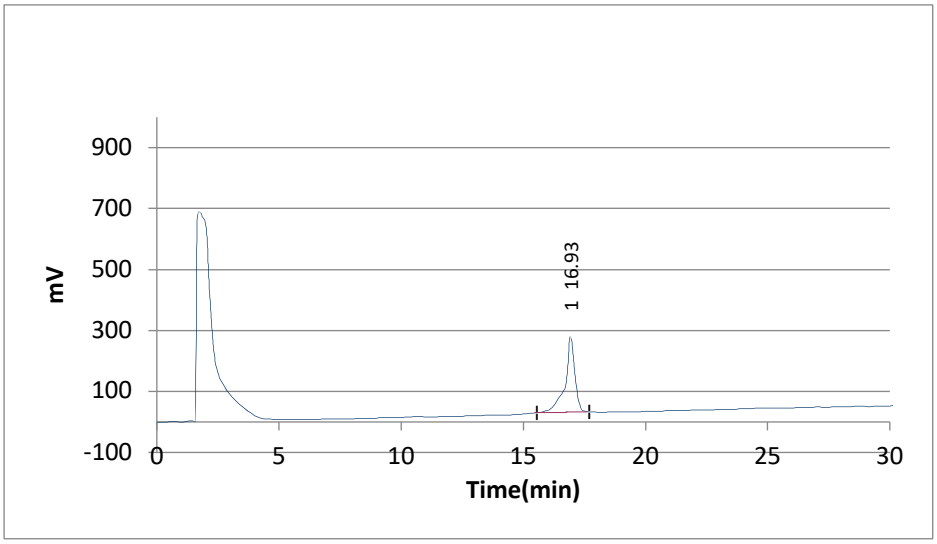
Cyclo-[L-LAP-D-Ser(*t*Bu)-D-Tyr(*t*Bu)-L-γDab(Boc)-Gly-Asn(Trt)-Ser(*t*Bu)-Asn(Trt)]



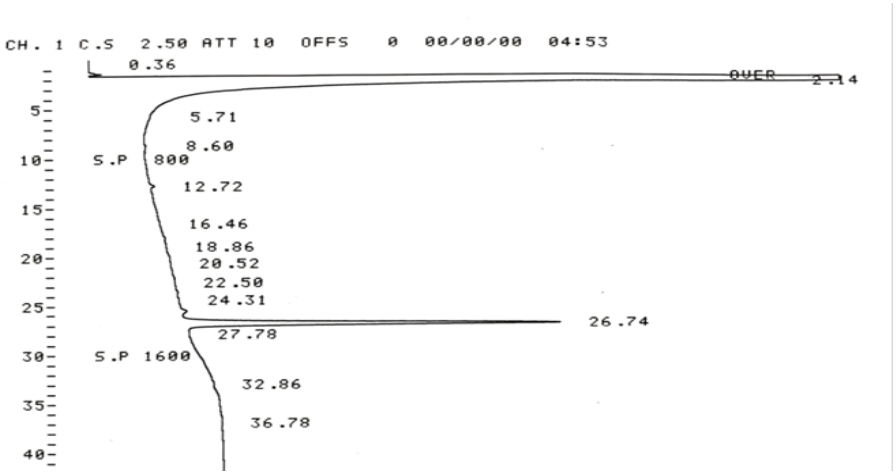
Cyclo-[L-LAP-D-Ser-D-Tyr-L-γDab-Gly-Asn-Ser-Asn] (**17**)



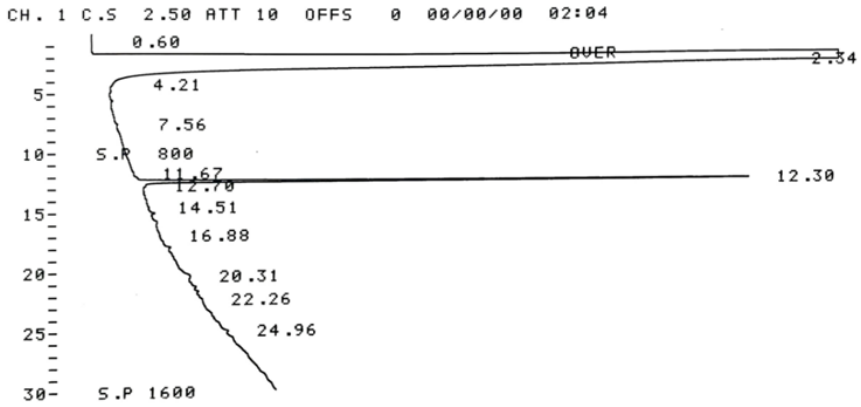
D-LAP-D-Ser(*t*Bu)-D-Tyr(*t*Bu)-L-γDab(Boc)-Gly-Asn(Trt)-Ser(*t*Bu)-Asn(Trt)



Cyclo-[D-LAP-D-Ser(*t*Bu)-D-Tyr(*t*Bu)-L-γDab(Boc)-Gly-Asn(Trt)-Ser(*t*Bu)-Asn(Trt)]

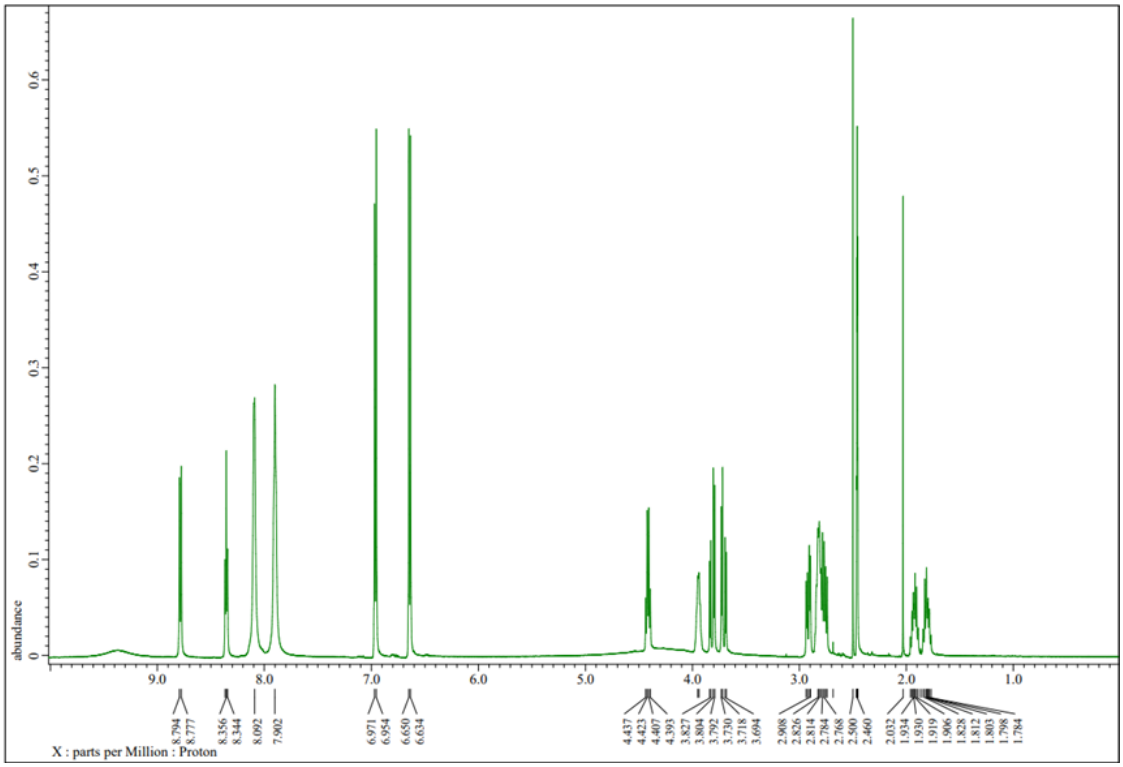


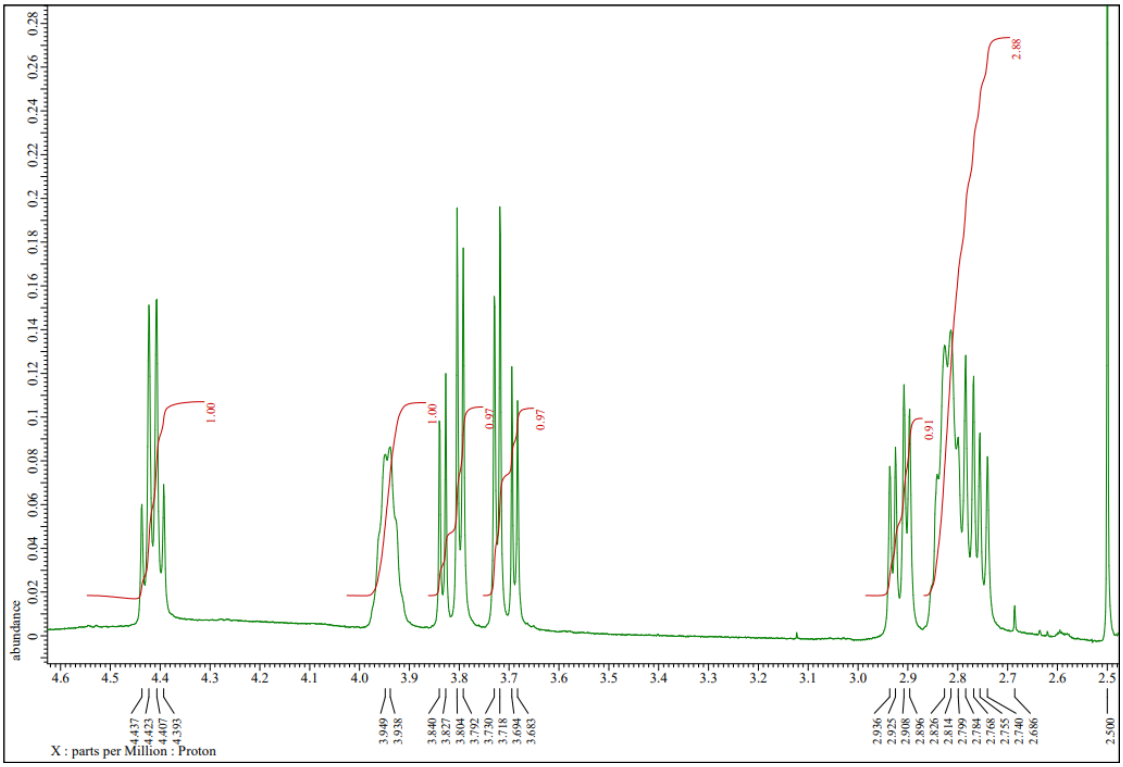
Cyclo-[D-LAP-D-Ser-D-Tyr-L-γDab-Gly-Asn-Ser-Asn] (**18**)



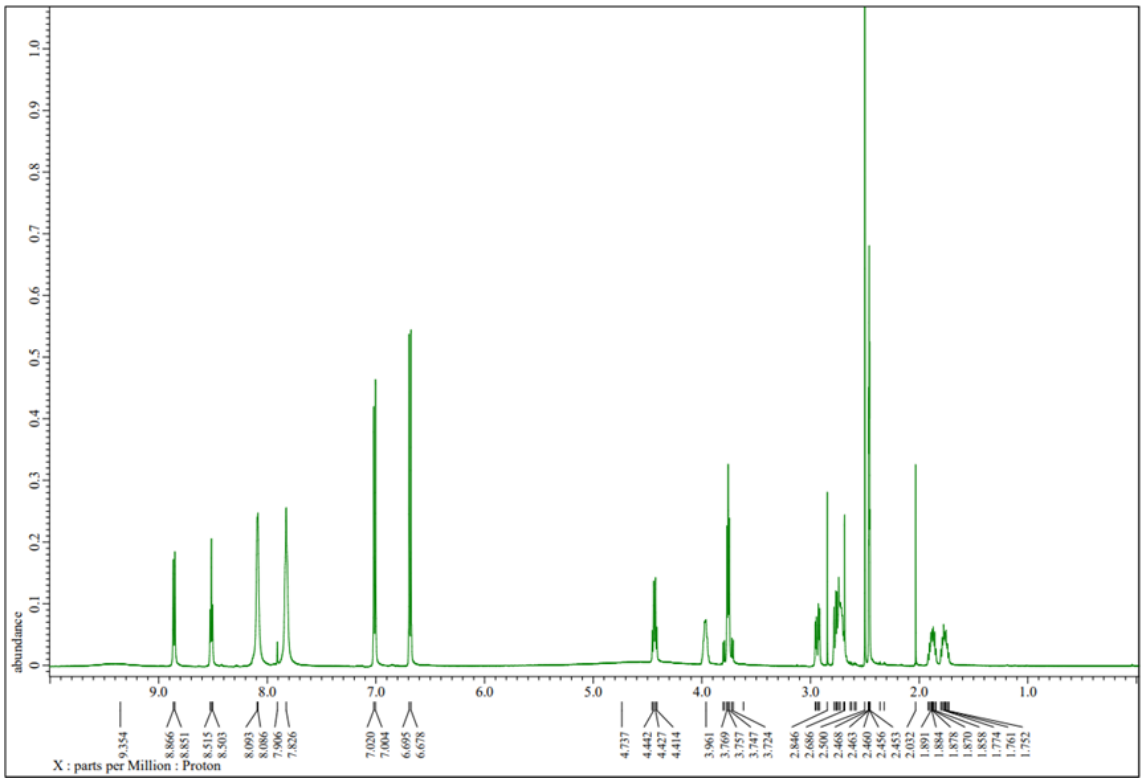
NMR spectra

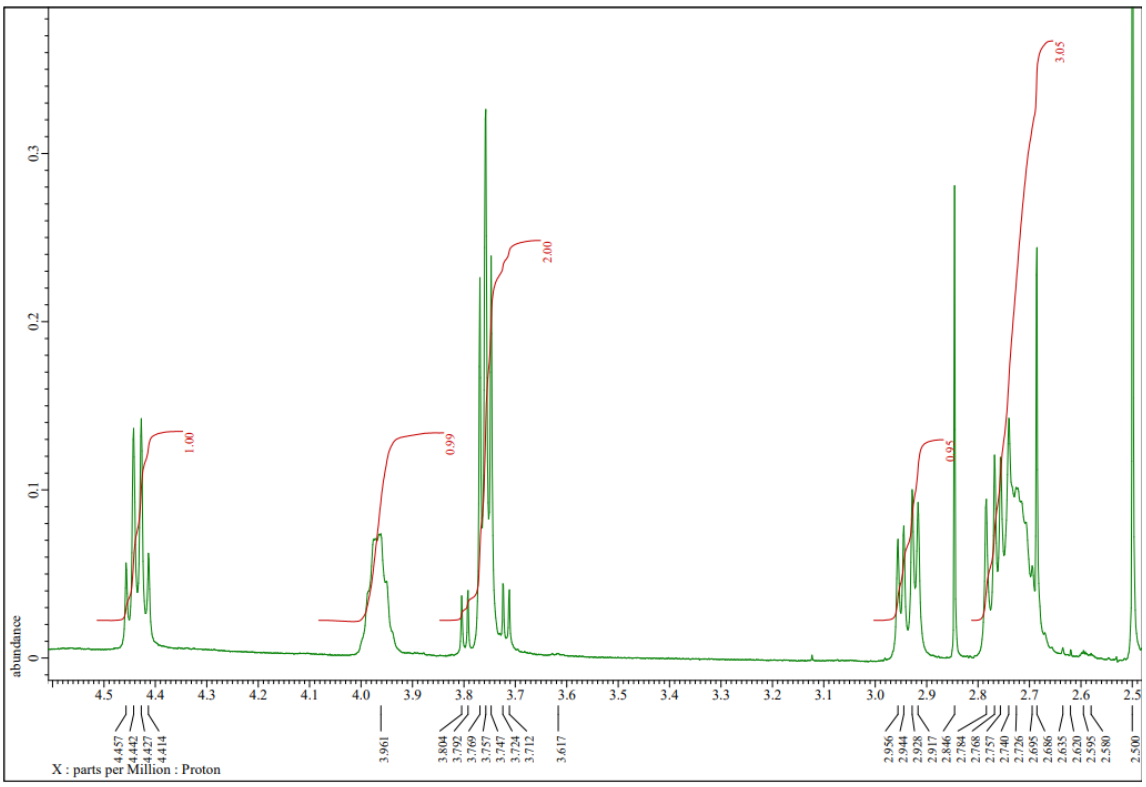
L-Tyr-L-αDab-Gly **(11a)**



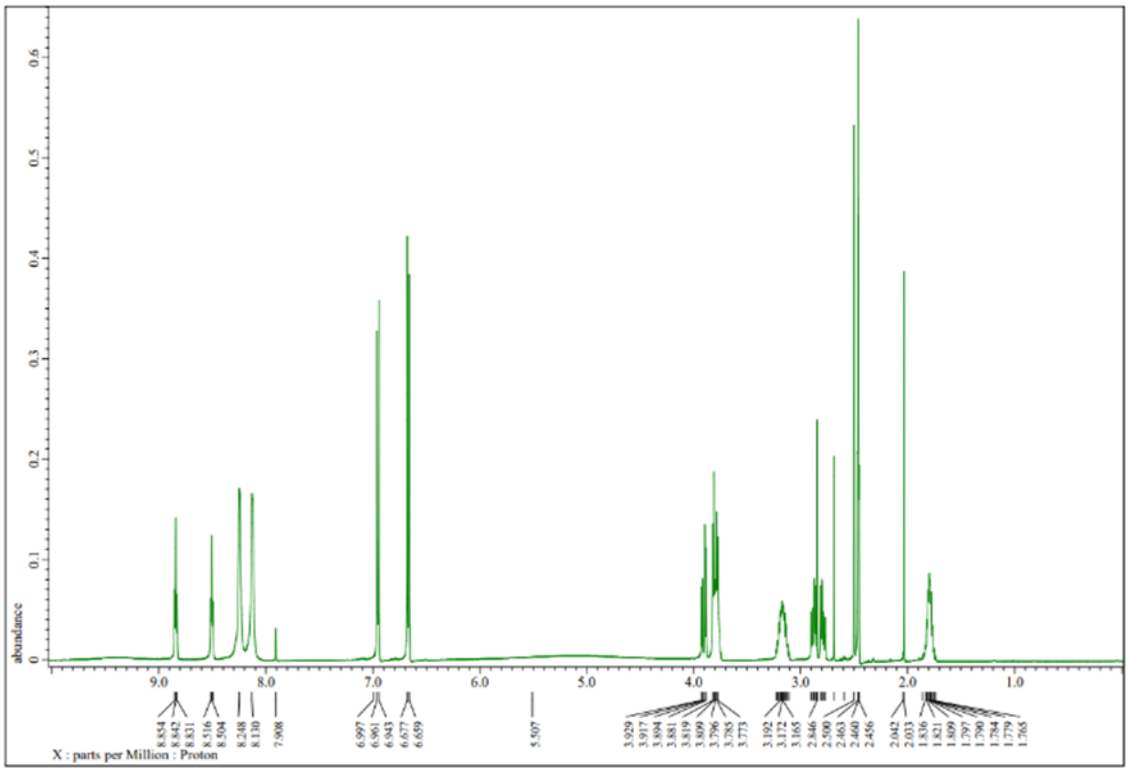


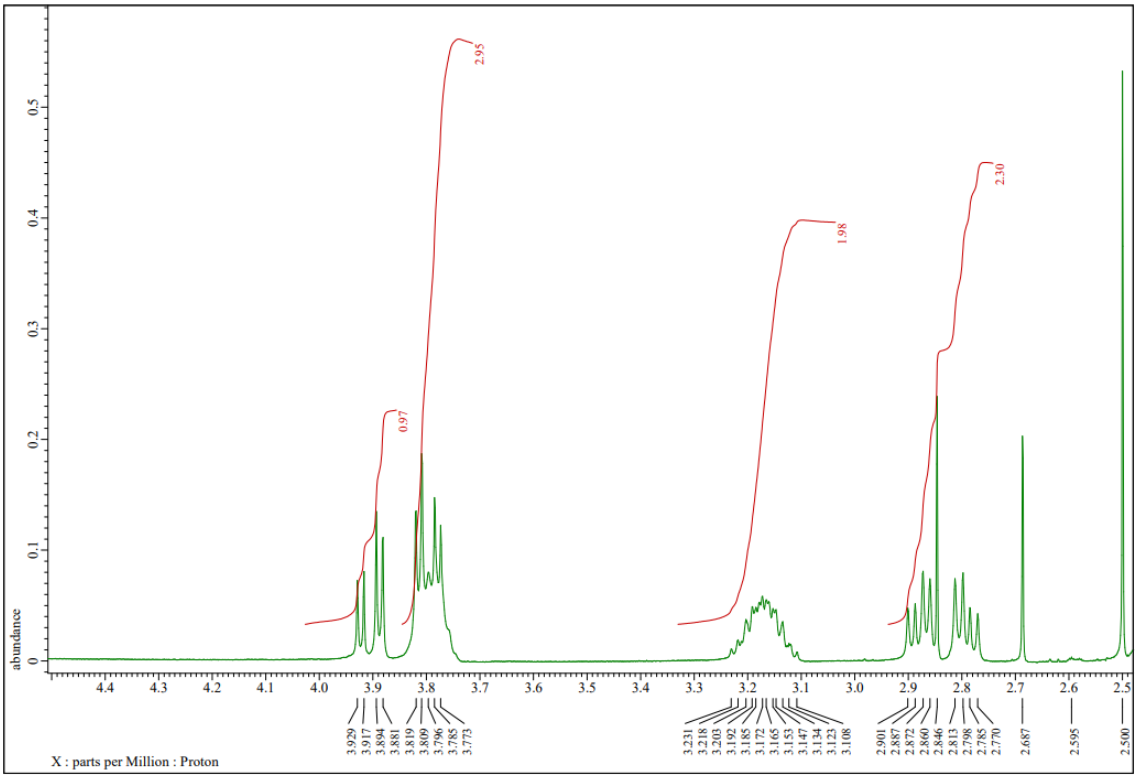
D-Tyr-L-αDab-Gly **(11b)**



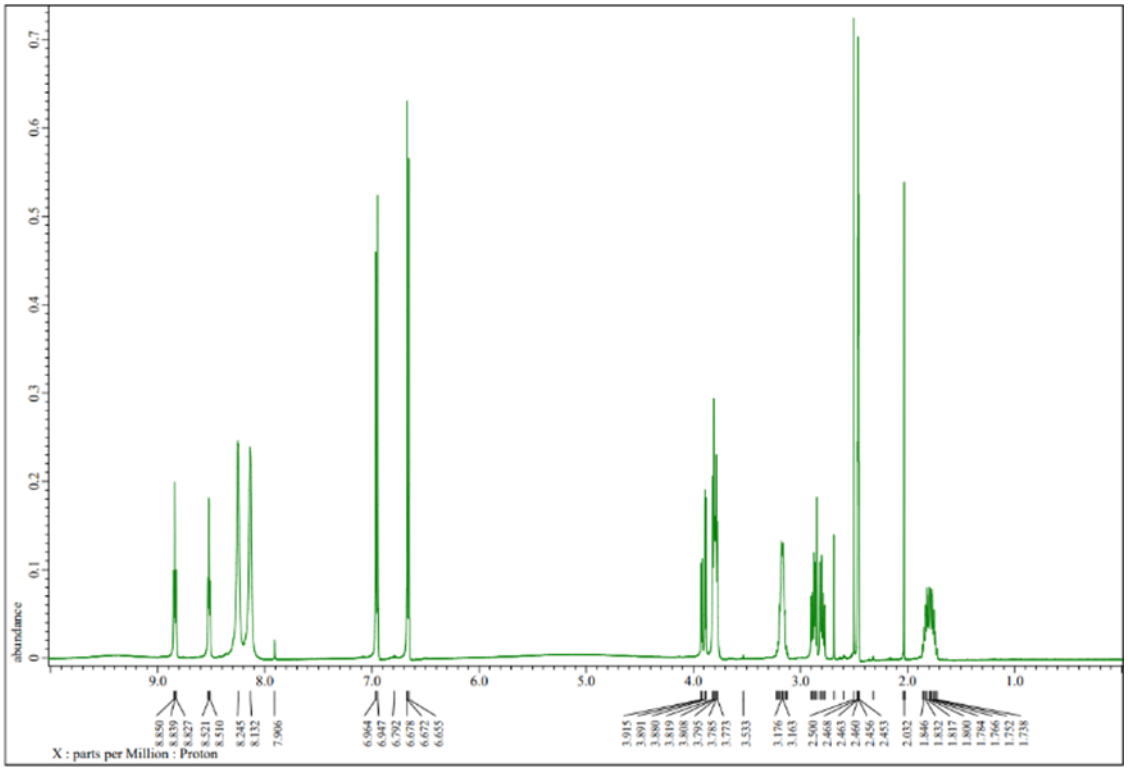


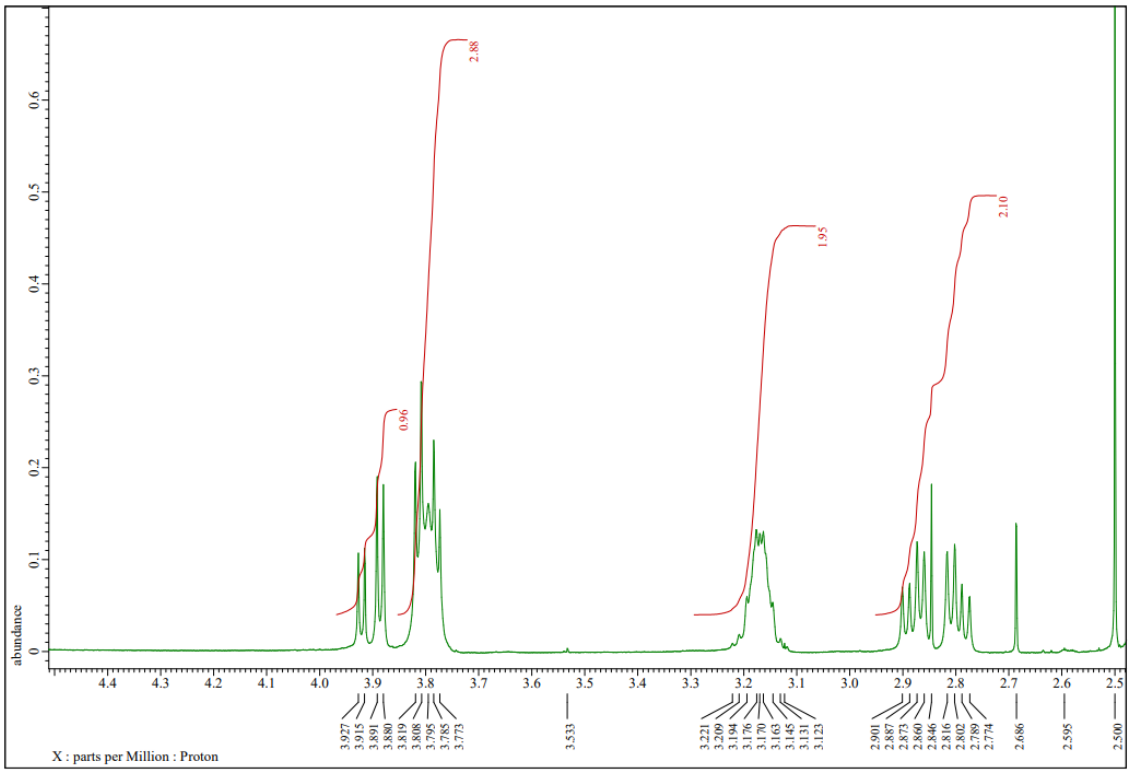
L-Tyr-L-γDab-Gly **(12a)**



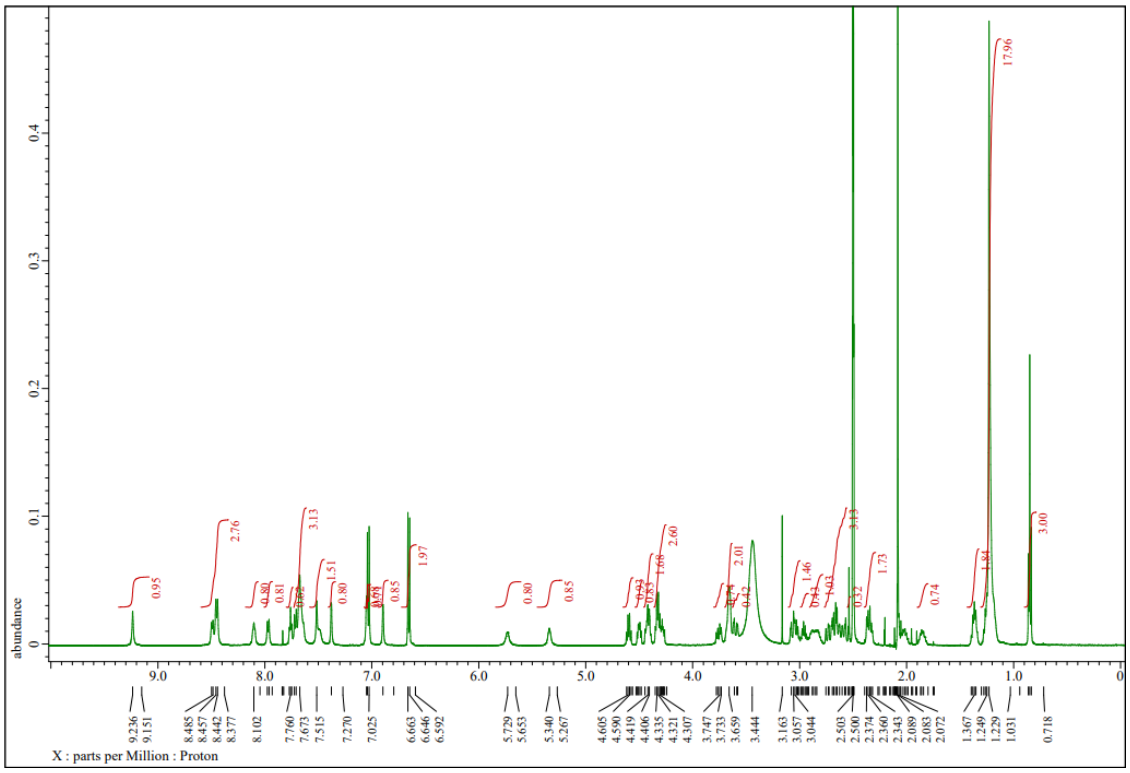


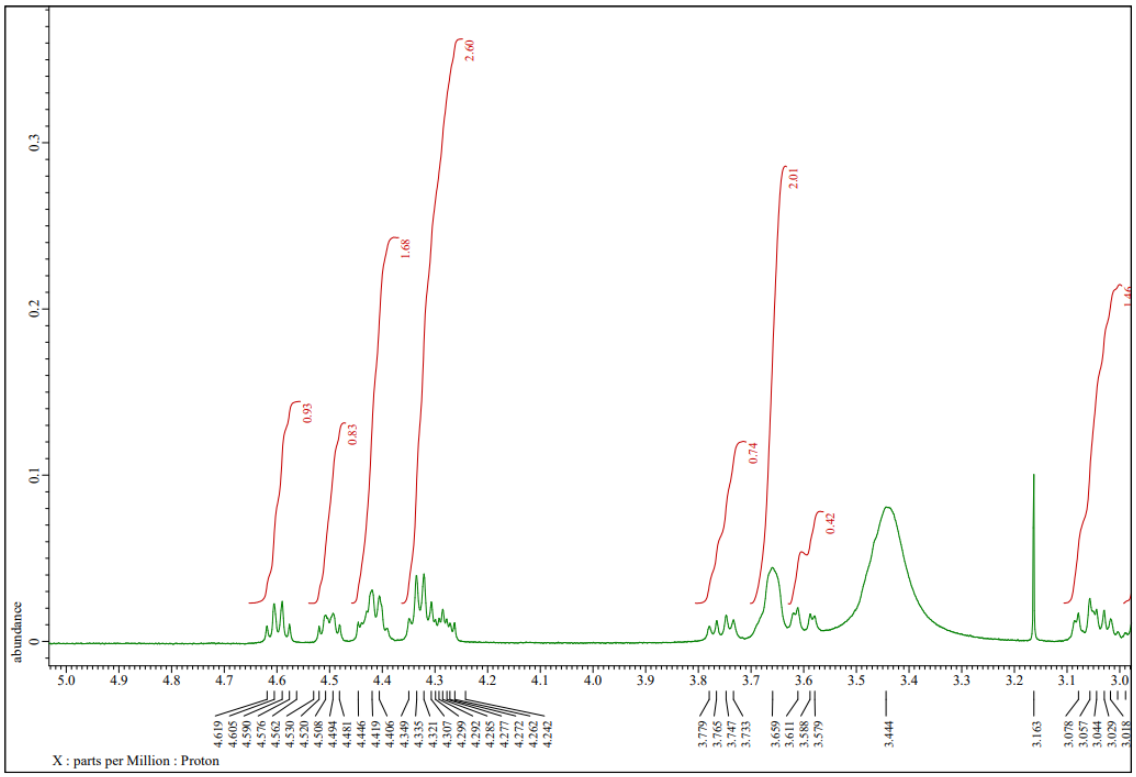
D-Tyr-L-γDab-Gly **(12b)**



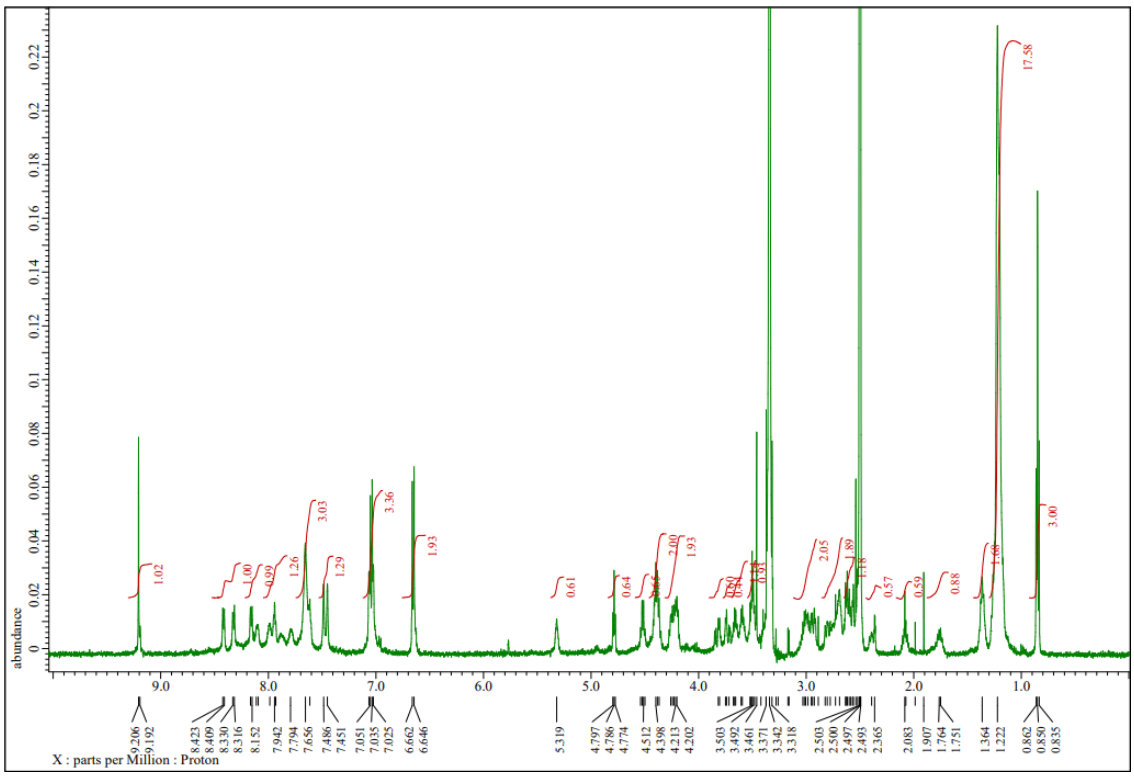


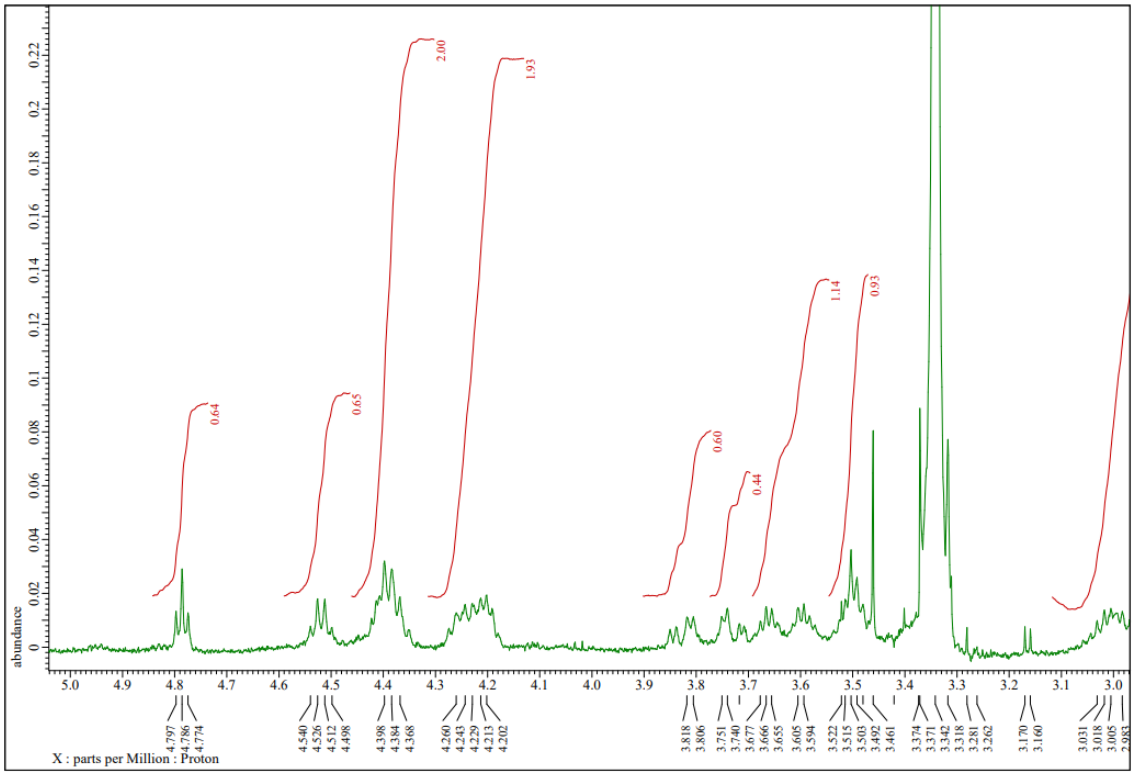
Cyclo-[L-LAP-D-Ser-D-Tyr-D-αDab-Gly-Asn-Ser-Asn] (**13**)



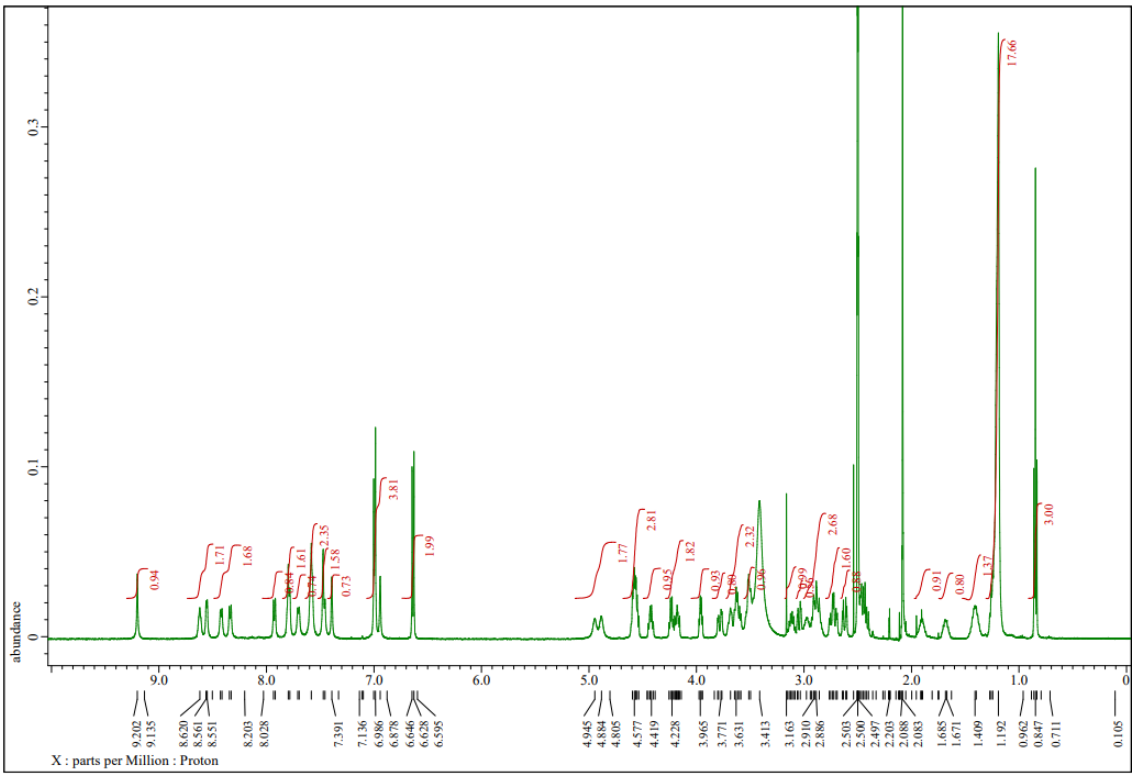


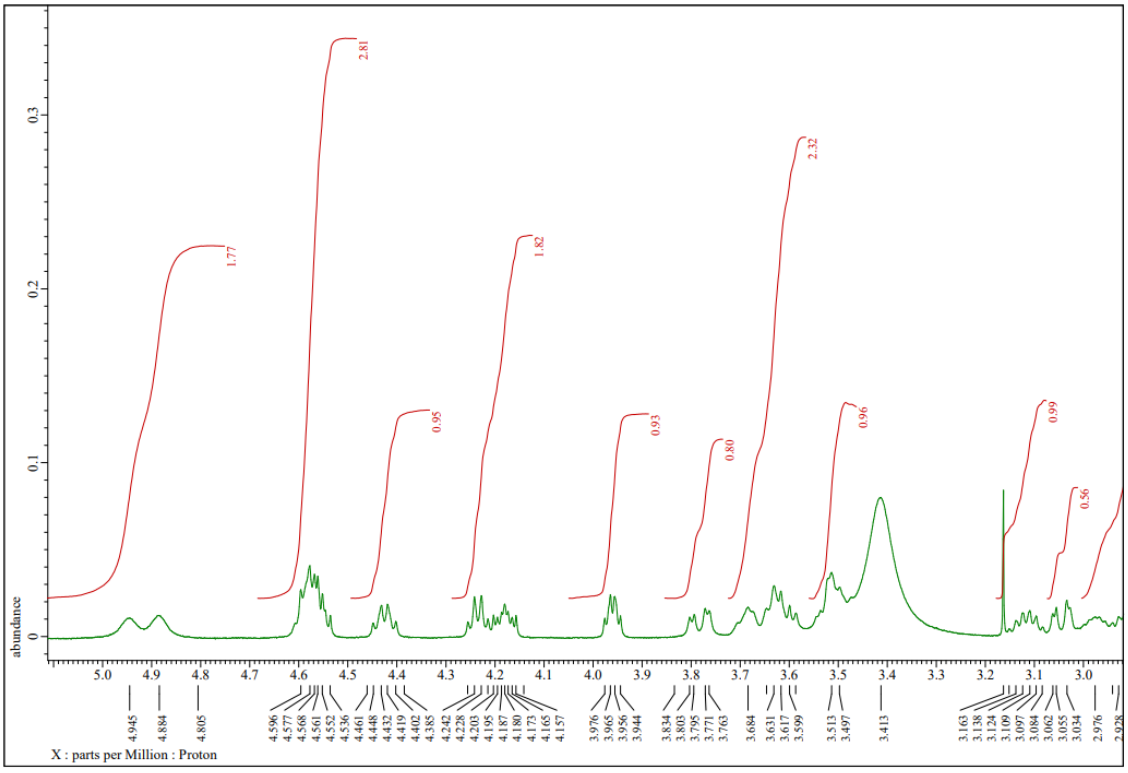
Cyclo-[L-LAP-D-Ser-D-Tyr-L-αDab-Gly-Asn-Ser-Asn] (**14**)



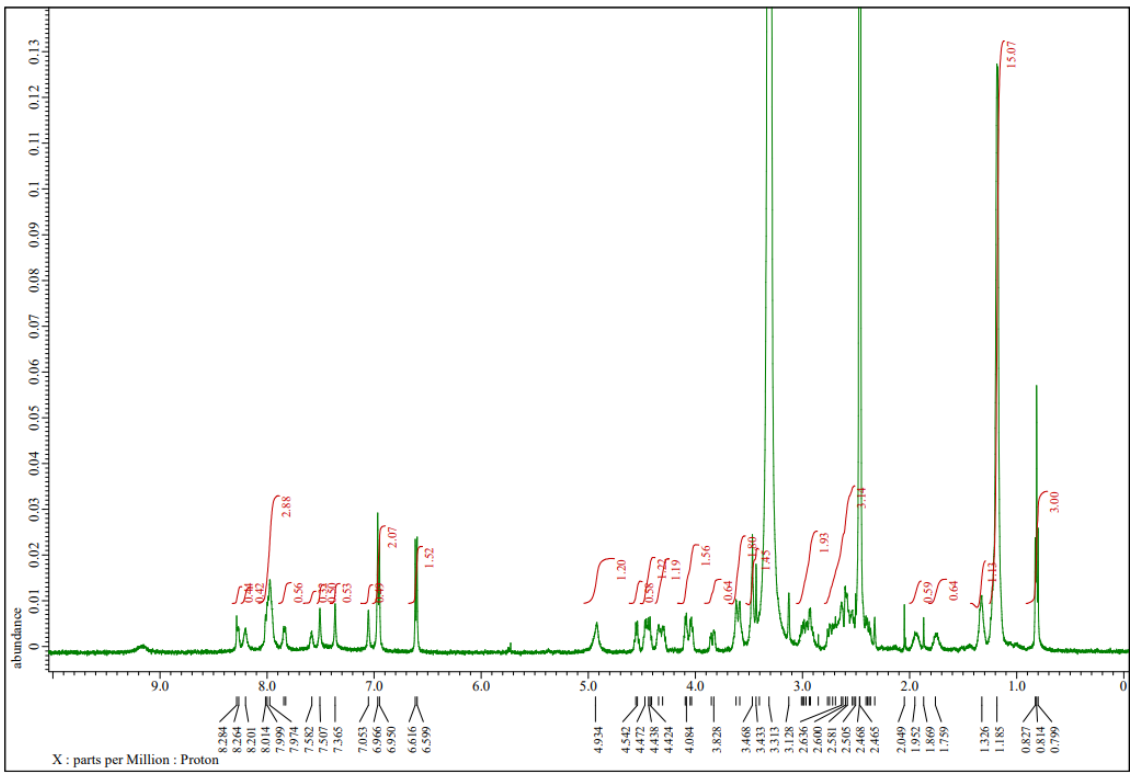


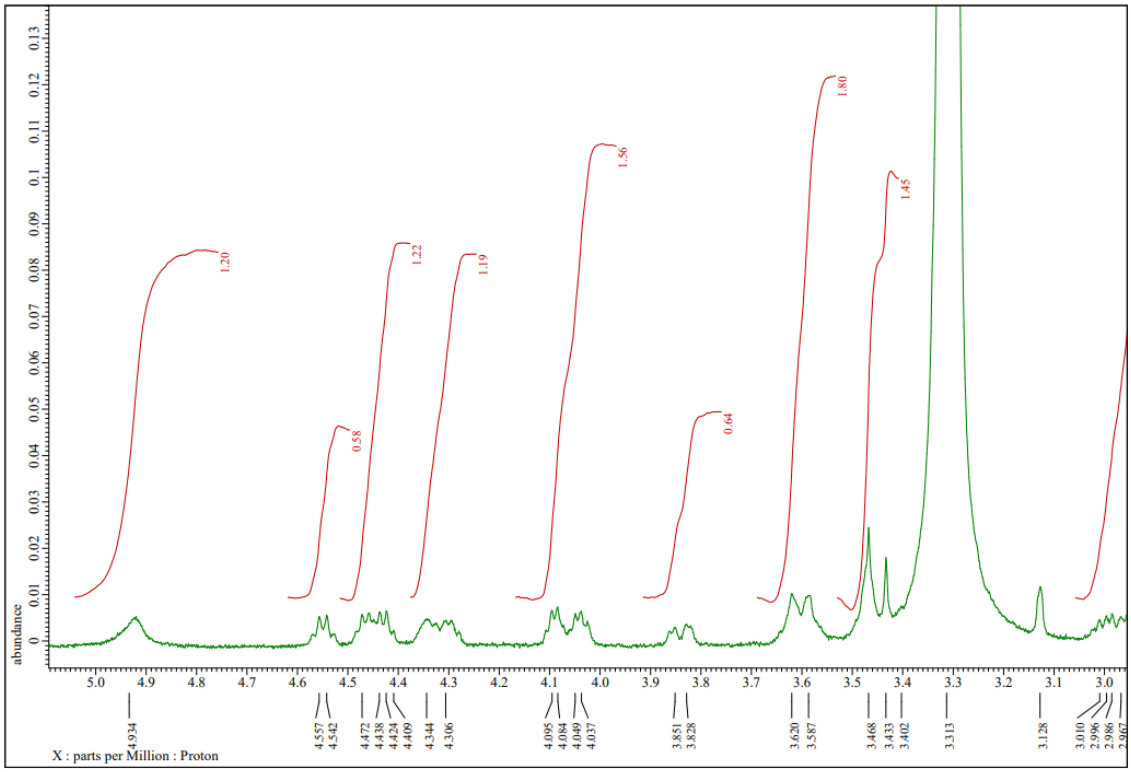
Cyclo-[D-LAP-D-Ser-D-Tyr-D-αDab-Gly-Asn-Ser-Asn] (**15**)



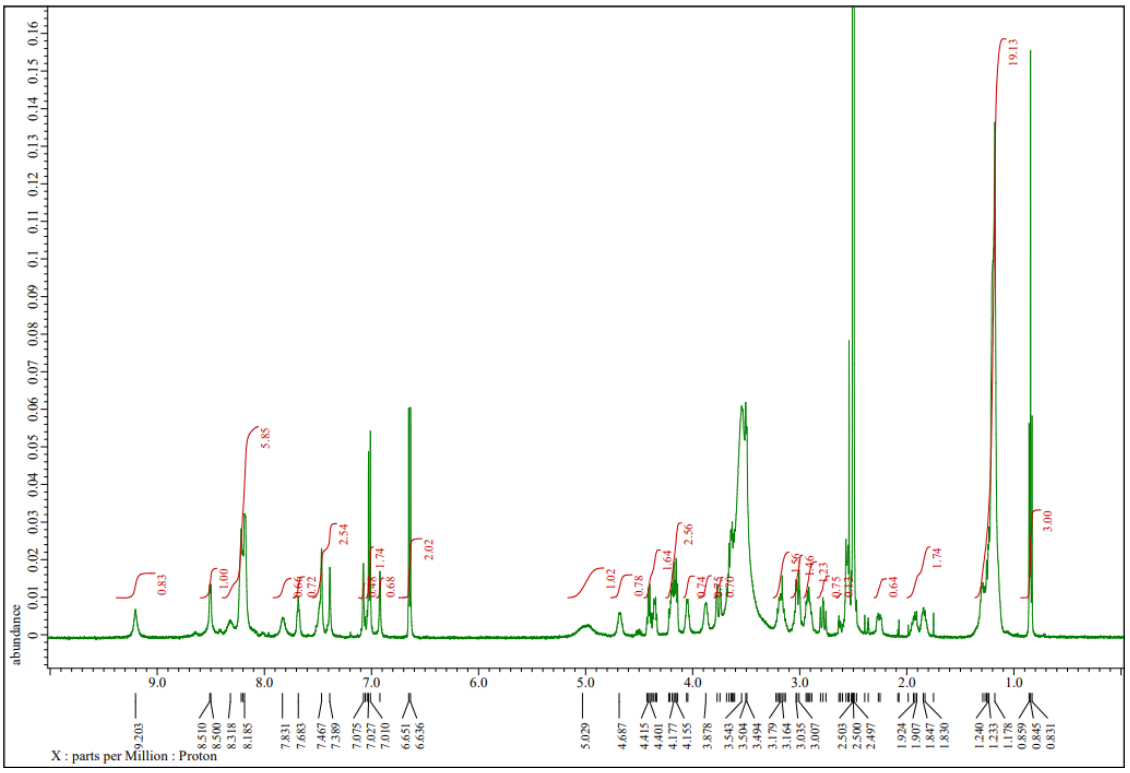


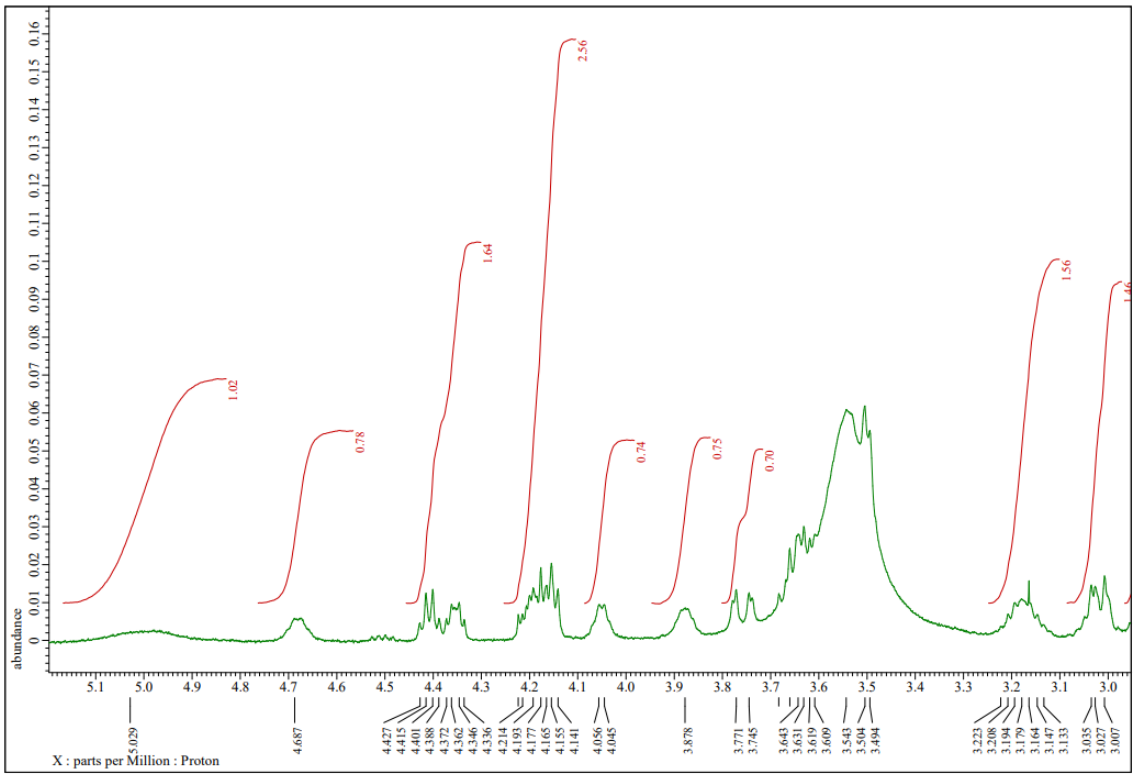
Cyclo-[D-LAP-D-Ser-D-Tyr-L-αDab-Gly-Asn-Ser-Asn] (**16**)



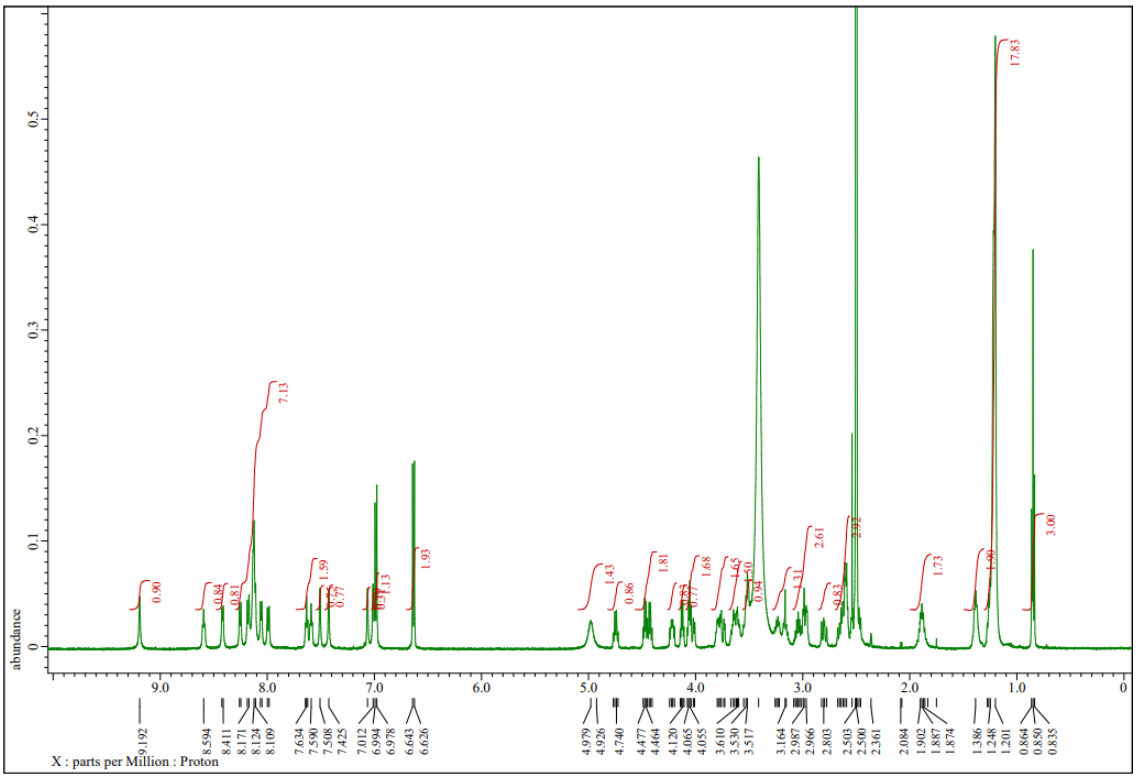


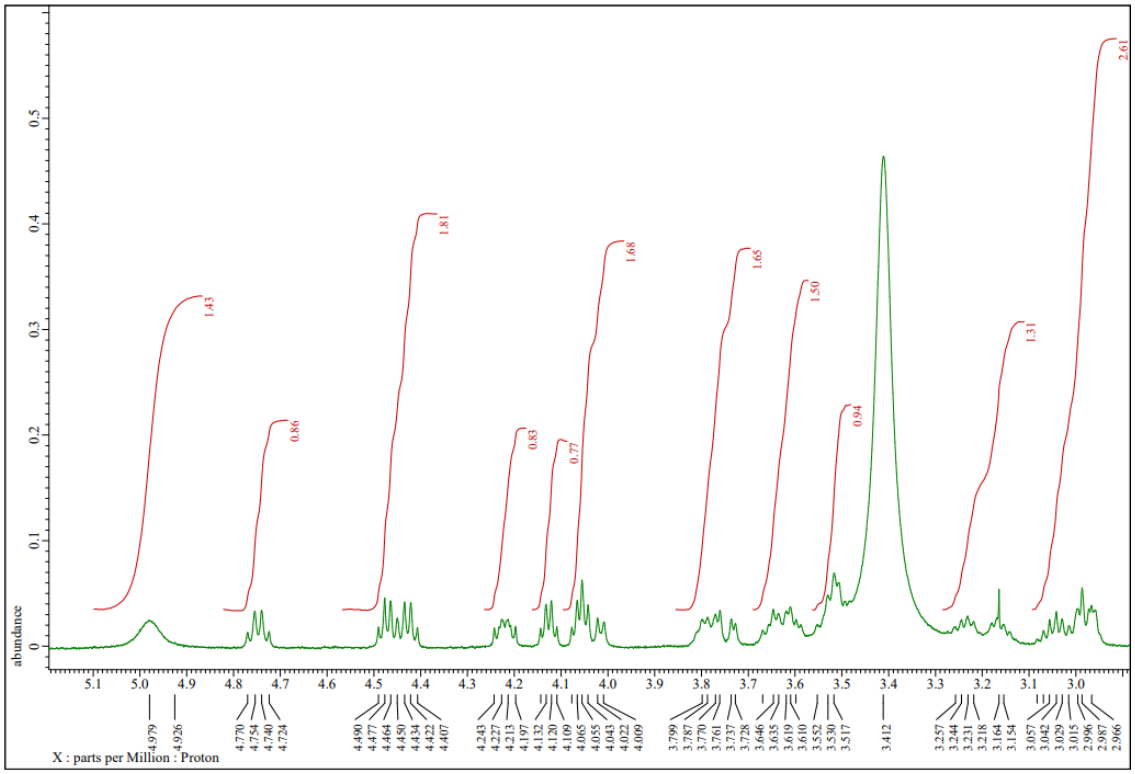
Cyclo-[L-LAP-D-Ser-D-Tyr-L-γDab-Gly-Asn-Ser-Asn] (**17**)





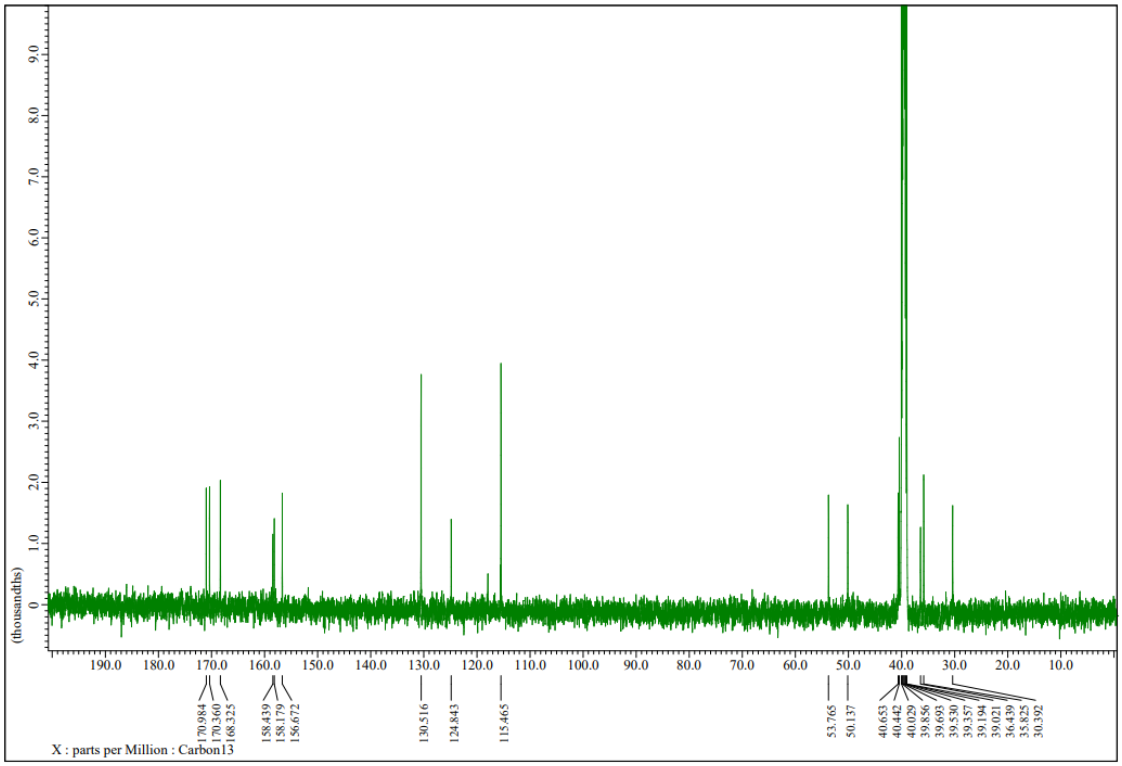
Cyclo-[D-LAP-D-Ser-D-Tyr-L-γDab-Gly-Asn-Ser-Asn] (**18**)



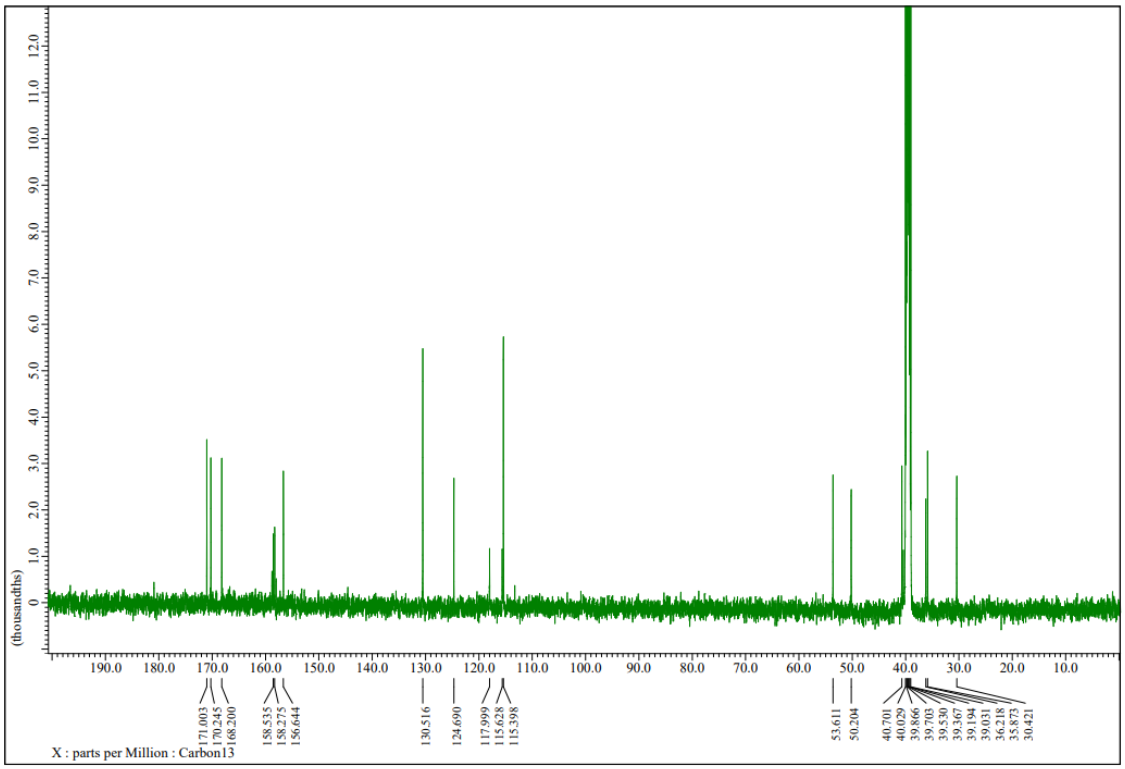


3. ^{13}C NMR spectra

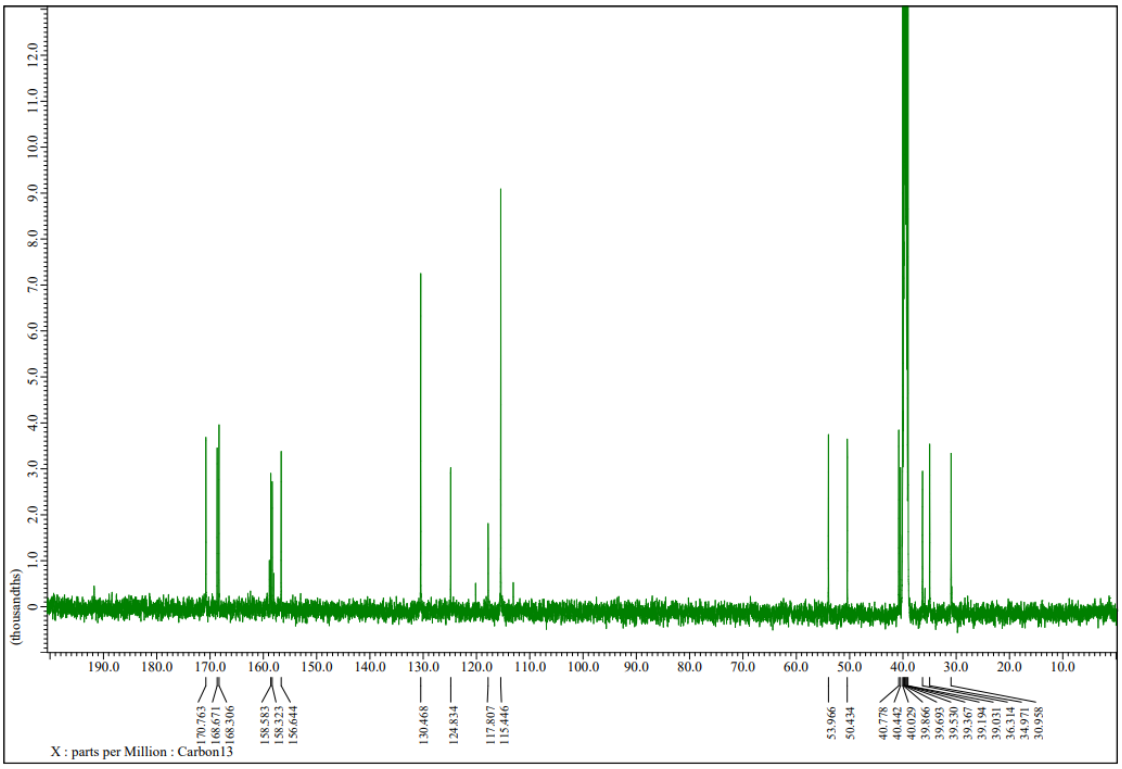
L-Tyr-L-αDab-Gly **(11a)**



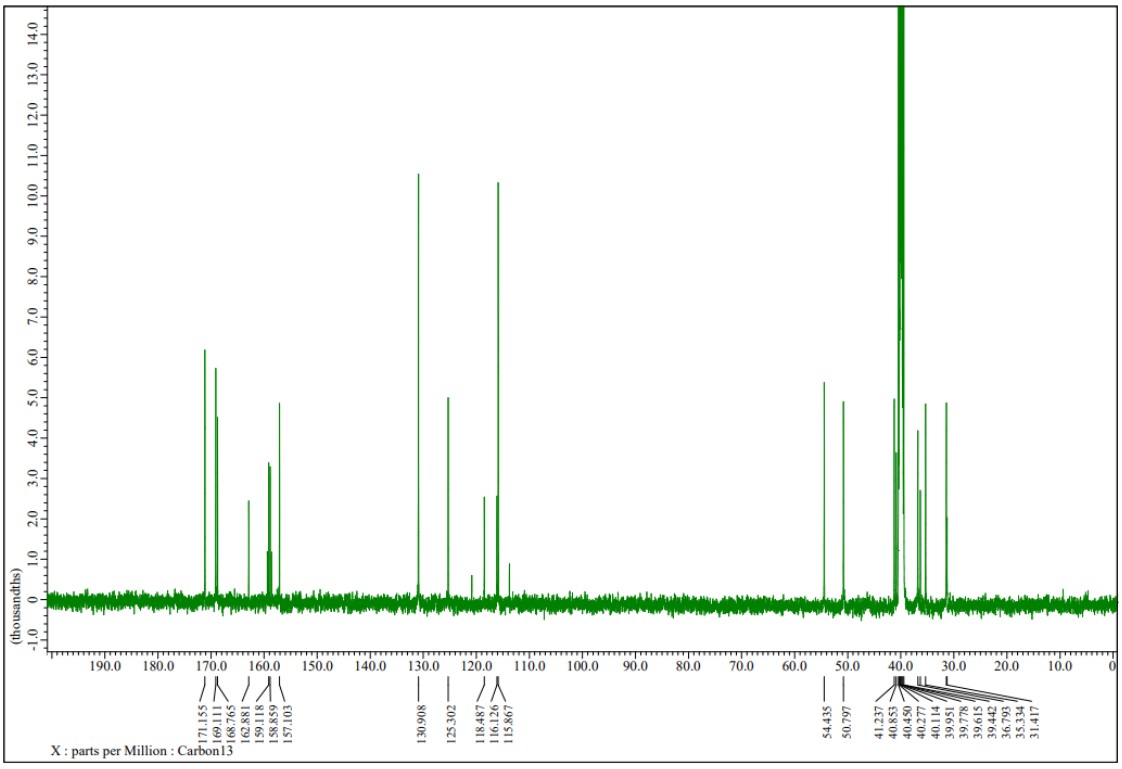
D-Tyr-L-αDab-Gly **(11b)**



L-Tyr-L-γDab-Gly **(12a)**

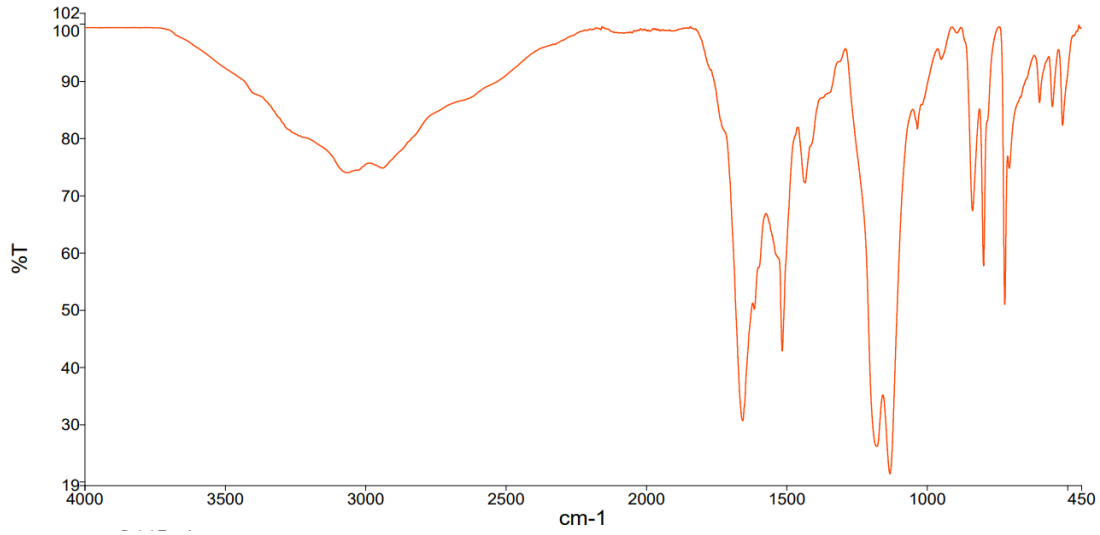


D-Tyr-L-γDab-Gly **(12b)**

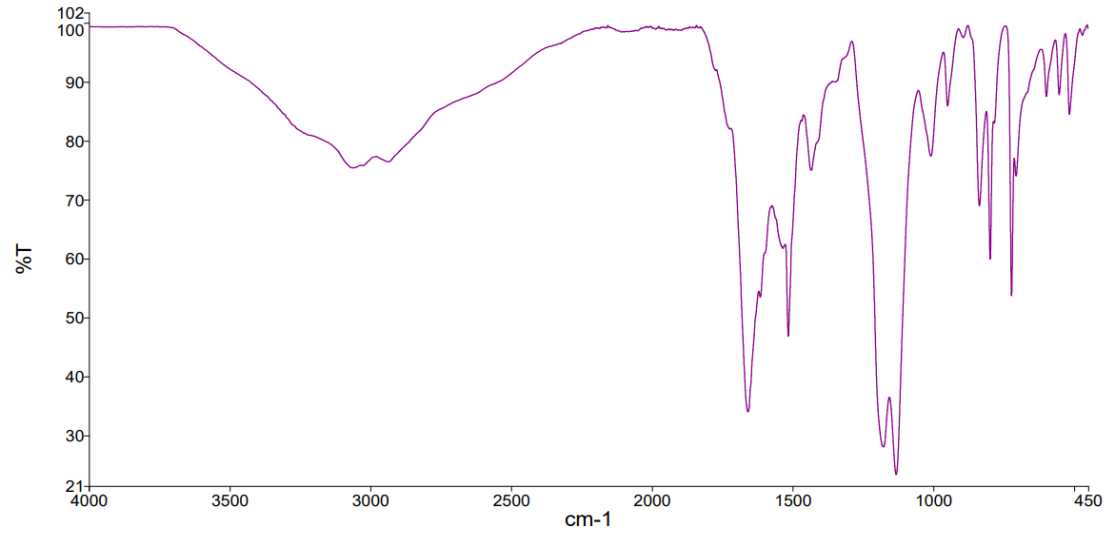


IR spectra

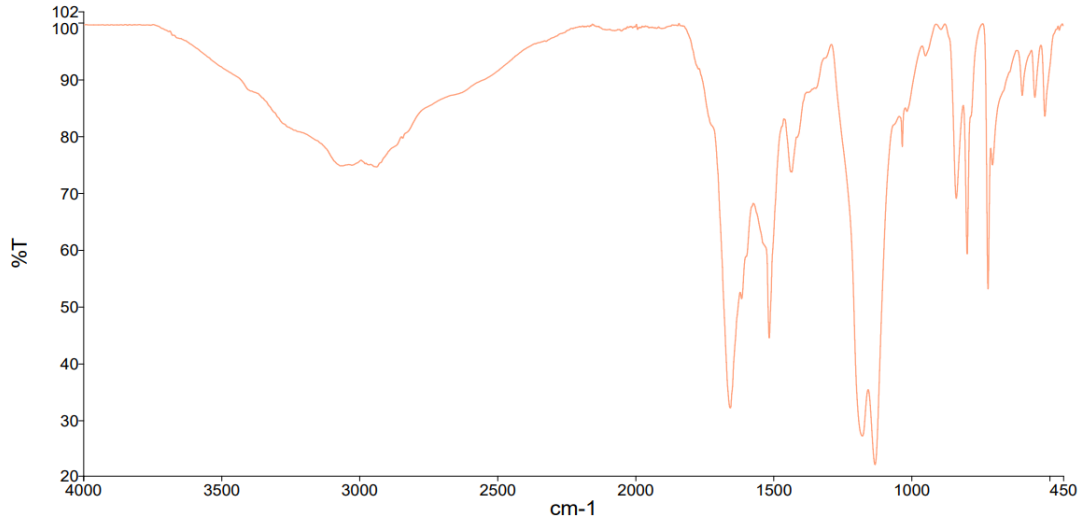
L-Tyr-L-αDab-Gly **(11a)**



D-Tyr-L-αDab-Gly **(11b)**



L-Tyr-L-γDab-Gly **(12a)**



D-Tyr-L-γDab-Gly **(12b)**