Supporting information

First Total Synthesis and Stereochemical Revision of Laxaphycin B and Its Extension to Lyngbyacyclamide A.

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Used abbreviations for non standard amino acids:

Ada : 3-amino-décanoïc acid

Aoc : 3-amino-octanoïc acid

Hleu : 3-hydroxy-leucine

Hasn : 3-hydroxy asparagine

General procedures for solid-phase reactions

All peptides synthesis were carried out on an CEM Liberty One automated peptide synthesizer at a 0,1 mmol scale using standard Fmoc/tBu based solid-phase strategy and 278 mg of Rink amide MBHA LL resin at a 0.36 mmol/g substitution level. The first amino acid linked to the resin is Fmoc-3-OH-Asp(OAll) that generate the amide of the 3-OH-asparagin after cleavage of the peptide from resin. Stepwise coupling reactions were performed with enantiomerically pure Fmoc-protected amino acids provides by Novabiochem or Bachem, or synthesized in our lab. Amino acids were coupled with O-(7-Azabenzotriazol-1-yl)-N,N,NO, NO-tetramethyluronium-hexafluorophosphate (HATU), 1 mL, C=0.5 M, and diisopropyl-ethylamine(DIPEA), 0.5 mL, C=0.2 M, 70 °C, 25 W, 5 min. The coupling of Fmoc-Gln(trt)-OH with Fmoc-N-Me-Ileu-OH was performed by triple coupling, 70 °C, 25 W, 20 min. Deprotection of Fmoc-group was performed using 20% piperidine solution in DMF, initial deprotection 30 s, 40 W, 75 °C, second step 180 s, 40 W, 70 °C. The linear protected peptide linked to the resin was transferred into a batch reactor and the allyl protecting group was cleaved using $Pd[P(Ph_3)]_4$ (m= 0.35 g, 0.3 mmol, 3 eq) with a solution of $CHCl_3$/AcOH, NMM : 3.7/0.2/01 for 4 h at room temperature

Macrocyclization of linear precursor

Cyclisation was performed with diisopropylcarbodiimide (DIC) and Oxyma, 1 mL, C=0.5 M, 50°C 3 x 20 min, 120 s at 0 °C between each cycle. A Kaiser test was realized in order to check reaction completion.

Cleavage of protecting group and resin

The peptide was removed from the Rink amide MBHA resin with simultaneous side chains deprotection by treatment with a mixture of TFA/TIS/H_2O (9.5:2.5:2.5) for 3 h. After filtration, the resin was washed twice with the same solution and the filtrate concentrated under reduced pressure. The crude peptide was precipitated cold Et_2O and finally centrifuged. The precipitate was washed with cold ether extracted with water and lyophilized.

Analytical HPLC

The HPLC analysis was conducting by using ELSD detector on a Waters 2695 HPLC systems with a Phenomenex Luna 3 µM C-8 column (150 x 3 mm) using isocratic mixtures of water with 0.1 % formic acid (buffer A) and acetonitrile with 0.1% formic acid (buffer B). Standard conditions were a flow rate of 0.4 ml/min eluting with 40% B to 100% B in 35 min. Standard conditions were applied to all HPLC analysis unless otherwise stated.

Semi-preparative HPLC purification

Semi-preparative purification of cyclic peptides was performed using a Waters 1525 chromatography system fitted with a Waters 2487 tunable absorbance detector with detection at 214 nm. Purification was performed by eluting solvents A (water) and B (acetonitrile) on a UP50DB C-18 column (250 x 10 mm) at 3 ml/min.

LC-MS

LC/MS analyses were carried out using a Thermo Fisher Scientific LC/MS device, Accela HPLC coupled to a LCQ Fleet equipped with an electrospray ionisation source and a 3D ion-trap analyser. The analysis was performed with a Phenomenex Kinetex C-18 column (100 x 300 mm) using gradient mixture of water with 0.1 % formic acid (buffer A) and acetonitrile with 0.1 % formic acid (buffer B). Standard conditions were a flow rate of 0.5 ml/min eluting with 20% B to 100% B in 15 min. Standard conditions were applied to all HPLC/MS analysis unless otherwise stated.

NMR Spectroscopy

The samples for the NMR analysis were prepared by dissolving the peptide (0.5-2 mg) in 500 µL DMSO. 1D and 2D ^{1}H-NMR spectra were recorded on a JEOL EX-400 spectrometer. The NMR experiments were performed at 303K.

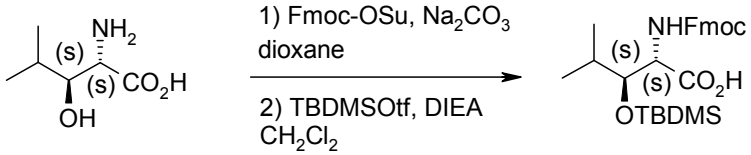
CD Spectroscopy

CD measurements were performed using a Jasco model J-815 spectropolarimeter. A stock solution of 1-2 mg of peptide was dissolved in 1 mL of methanol. A 100 µM of solution was then prepared from the stock solution. Spectra were recorded at 298K and at 328K with 0.1 cm Jasco quartz cell over the wavelength range 290-160 nm at 200 nm/min, response time of 1 s. Each spectrum represents the average of 2 scans. Spectra were analyzed using the spectral analysis software and smoothed using “adaptive smoothing” function.

*The synthesized laxaphicin B refers to the laxaphicin B with the hydroxyleucines of configuration (2S,3S) and (2R,3S) compound **2**. The revised laxaphicin B refers to the laxaphicin B with the hydroxyleucines of configuration (2R,3S) and (2R,3S) compound **3**.*

Experimental procedures

(2S,3S)-Fmoc-Leu(3-OTBDMS)-OH



To a suspension of Fmoc-(2S,3S)-OH-Leu (0.800 mg, 5.44 mmol) in 1,4-dioxane (19 mL) was added Na_2CO_3 0.5 M (21.7 mL, 10.88 mmol) following by Fmoc-Osu (1.83 g, 5.44 mmol) at room temperature. The reaction mixture was stirred at room temperature for 24 h and then Et_2O (20 mL) was added. The aqueous layer was extracted with Et_2O (3x20 mL). The aqueous layer was then cooled at 0 °C, acidified with HCl 1 M till pH 2-3 and AcOEt (50 mL) was then added. The aqueous layer was extracted with AcOEt (3x50 mL) and the combined organic layers were washed with brine and dried over Na_2SO_4. After filtration and removal of the solvents under reduced pressure the crude compound (1.12 g) was isolated and used in the next step without further purification. To a solution of this crude product (1.12 g, 3.03 mmol) in CH_2Cl_2 (40 mL) was added DIEA (2.11 mL, 10.60 mmol) and TBDMSOTf (2.44 mL, 10.60 mmol) at 0 °C. After 3 h at 0 °C, MeOH (2.0 mL), was added followed by NH_4Cl aq and Et_2O (300 mL). The aqueous phase was extracted with Et_2O (2x300 mL), the combined organic layers were washed with brine and dried over $MgSO_4$. After filtration and removal of the solvents under reduced pressure the crude product was dissolved in MeOH (55 mL) and treated with $NaHCO_3$ sat. (80 mL), water (8 mL) and K_2CO_3 (91 mg). After stirring the resulting suspension for 1 h at 25 °C, the reaction mixture was diluted with Et_2O. The aqueous layer was acidified with citric acid 1.0 M till pH 3-4 and then extracted with Et_2O (3x200 mL). The combined organic layers were washed with brine and dried over $MgSO_4$. After filtration and removal of the solvents under reduced pressure, the resulting crude product was purified by column chromatography (Cyclo/AcOEt 8:2 then 6:4) to afford (2S,3S)-Fmoc-Leu(3-OTBDMS)-OH (1.20 g, 82%) as a colorless oil.

^{1}H NMR ($CDCl_3$) : 7.75 (d, 2H, *J*=7.3 Hz) ; 7.59 (t, 2H, *J*=7.3 Hz) ; 7.31 (t, 2H *J*=7.3 Hz) ; 7.25 (t, 2H, *J*=7.7 Hz) ; 5.53 (d, 1H, NH, *J*=7.7 Hz) ; 4.57 (d, 1H *J*=7.7 Hz) ; 4.39 (d, 2H, *J*=7.0 Hz) ; 4.21 (t, 1H, *J*= 7.0 Hz) ; 3.62 (d, 2H, *J*=7.3 Hz) ; 2.0. (m, 1H) ; 1.02 (d, 3H, *J*=6.6 Hz) ; 0.96 (d, 3H, *J*= 6.6 Hz) ; 0.93 (s, 9H), 0.05 (s, 3H) ; -0.06 (s, 3H).

^{13}C NMR ($CDCl_3$) : 175.0 (C) ; 155.6 (C) ; 143.7 (CH) ; 141.4 (CH) ; 127.8 (CH) ; 127.2 (CH) ; 125.2 (CH) ; 120.1 (CH) ; 67.2 (CH_2) ; 57.2 (CH) ; 47.2 (CH) ; 31.6 (CH) ; 27.0 (CH_3) ; 19.5 (CH_3) ; 19.3 (C) ; -4.0 (CH_3) ; -4.1 (CH_3).

$[\alpha]^{20}$ = +7.1 (*c* 5.63 g/L in CH_2Cl_2).

HPLC Rt = 24.86 min.

(ESI^+) m/z $[M+H]^+$ calcd for $C_{27}H_{38}NO_5Si$ = 484.25, found 484.21.

(ESI^-) m/z $[M+H]^+$ calcd for $C_{27}H_{36}NO_5Si$ = 482.23, found 482.02.

(2R,3S)-Fmoc-Leu(3-OTBDMS)-OH

Compound Fmoc-(2R,3S)-TBS-Leu was prepared according the same procedure as for compound Fmoc-(2S,3S)-TBS-Leu, scale: Fmoc-(2R,3S)-OHLeu (1.5 g, 4.406 mmol), 1,4-dioxane (16 mL), Na_2CO_3 0.5 M (21.7 mL, 10.88 mmol), Fmoc-Osu (1.83 g, 5.44 mmol).

Crude product (0.600 g, 1.62 mmol), CH_2Cl_2 (19 mL), DIEA (1.10 mL, 6.32 mmol), TBDMSOTf (1.49 mL, 6.48 mmol). MeOH (19 mL), $NaHCO_3$ sat. (67 mL), water (3 mL), K_2CO_3 (35 mg). After filtration and removal of the solvents under reduced pressure, the resulting crude product was purified by column chromatography (Cyclo/AcOEt 8:2 then 6:4) to afford (2R,3S)-Fmoc-Leu(3-OTBDMS)-OH (0.65 g, 31%) as a colorless oil.

^{1}H NMR ($CDCl_3$) : 7.75 (d, 2H, *J*=7.3 Hz,) ; 7.59 (t, 2H, *J*=7.7 Hz ,) ; 7.38 (t, 2H *J*=7.3 Hz) ; 7.24 (t, 2H, *J*=7.3 Hz,) ; 5.56 (d, NH, *J*= 6.5 Hz,) ; 4.41 (m, 1H) ; 4.39 (m, 2H) ; 4.24 (m, 1H) ; 4.03 (m, 2H) ; 1.84. (m, 1H) ; 0.94 (d, 3H, *J*=6.6 Hz) ; 0.90 (d, 3H, *J*=6.6 Hz) ; 0.88 (s, 9H), 0.07 (s, 3H) ; -0.01 (s, 3H).

^{13}C NMR ($CDCl_3$) : 177.2 (C) ; 156.3 (C) ; 144.1 (CH) ; 141.4 (CH) ; 127.8 (CH) ; 127.1 (CH) ; 125.3 (CH) ; 120.1 (CH) ; 67.4 (CH_2) ; 55.7 (CH) ; 53.5 (CH) ; 47.2 (CH) ; 32.9 (CH) ; 29.8 (CH_3) ; 26.0 (CH_3) ; 19.3 (CH_3) ; 18.4 (C) ; -4.16 (CH_3) ; -4.49 (CH_3).

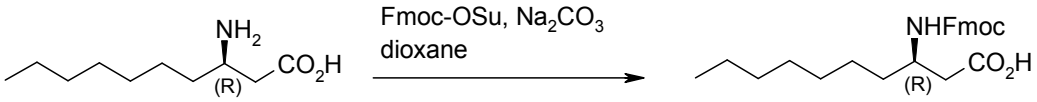
$[\alpha]^{20}$ = -27.8 (*c* 1.80 g/L in CH_2Cl_2).

HPLC Rt = 25.46 min.

(ESI^+) m/z $[M+H]^+$ calcd for $C_{27}H_{38}NO_5Si$ = 484.25, found 483.81.

(ESI^-) m/z $[M+H]^-$ calcd for $C_{27}H_{36}NO_5Si$ = 482.23, found 482.02.

(3R)-Fmoc-aminodecanoïc acid



To a suspension of aminodecanoïc acid (0.171, 0.91 mmol) in Na_2CO_3 10% (2 mL) was added at 0 °C a solution of Fmoc-Cl (0.235 g, 0.91 mmol) in dioxane (2 mL). The reaction mixture was stirred at room temperature for 3 h and then diluted with Et_2O (20 mL) and H_2O (20 mL). The aqueous layer was cooled, acidified with HCl 3M till pH 2-3 and AcOEt (50 mL) was added. The aqueous layer was extracted with AcOEt (3x50 mL) and the combined organic layers were washed with brine and dried over $MgSO_4$. After filtration and removal of the solvents under reduced pressure, the resulting crude product was purified by column chromatography (Cyclo/AcOEt 9:1 then 6:4) to afford Fmoc-(3R)-aminodecanoïc acid (0.281 g, 76%) as a white solid.

^{1}H NMR (DMSO): 7.89 (d, 2H, *J*=7.8 Hz) ; 7.69 (d, 2H, *J*=6.7 Hz) ; 7,40 (t, 2H, *J*=7.4 Hz) ; 7.32 (m, 2H) ; 7.21 (d, NH, *J*=5.6 Hz,) ; 4.28 (m, 2H) ; 4.22 (m, 1H) ; 3.77 (m, 1H) ; 2.28 (m, 2H) ; 1.39 (m, 2H) ; 1.22 (m, 10H) ; 0.84 (t, 3H, *J*=6.5 Hz).

^{13}C NMR (DMSO): 173.1 (C) ; 156.1 (C) ; 144.6 (CH) ; 141.3 (CH) ; 128.2 (CH) ; 127.6 (CH) ; 125.8 (CH) ; 120.7 (CH) ; 65.8 (CH_2) ; 49.4 (CH) ; 47.4 (CH) ; 39.5 (CH_2) ; 36.7 (CH_2) ; 31.8 (CH_2) ; 29.3 (CH_2) ; 29.2 (CH_2) ; 25.9 (CH_2) ; 22.7 (CH_2) ; 14.5 (CH_3).

$[\alpha]^{20}$ = +36.7 (*c* 1.64 g/L in CH_2Cl_2).

HPLC Rt = 20.90 min.

(ESI^+) m/z $[M+H]^+$ calcd for $C_{25}H_{32}NO_4$= 410.23, found 409.96.

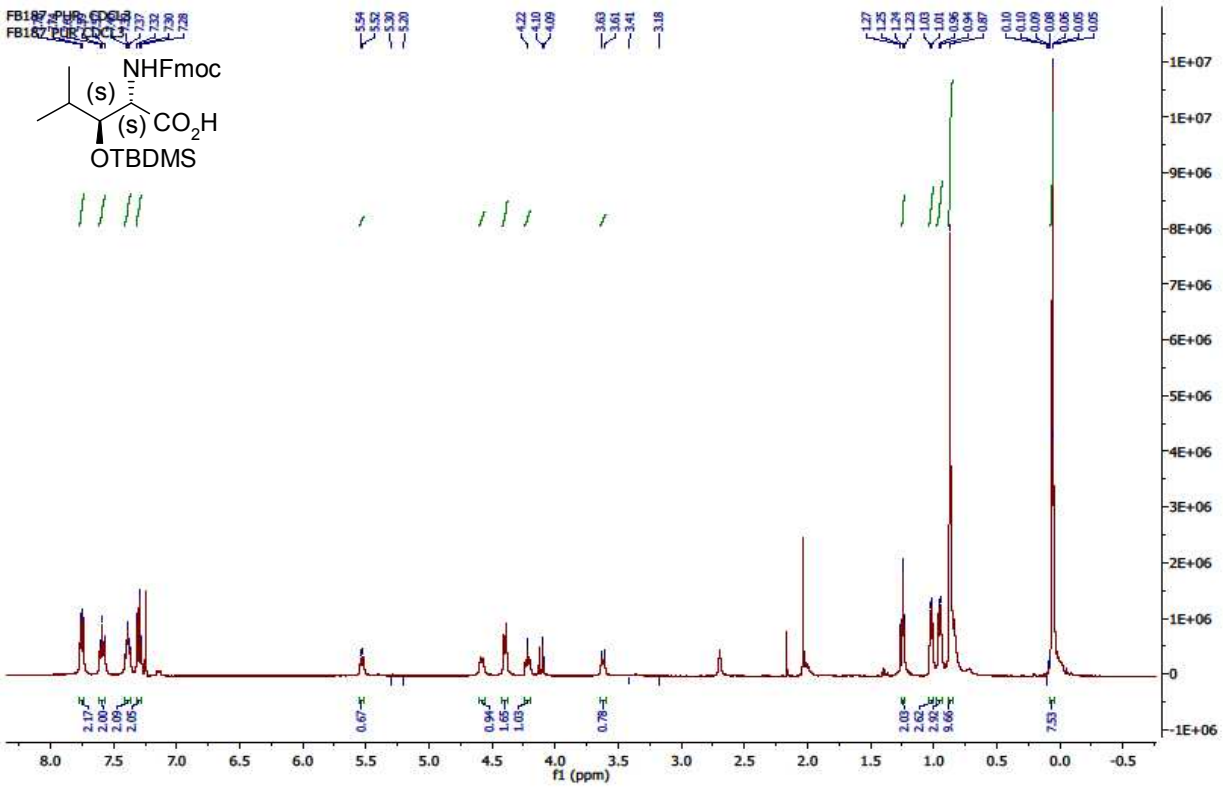


Figure S1: 1D NMR ^{1}H spectra of (2S,3S)-Fmoc-Leu(3-OTBDMS)-OH

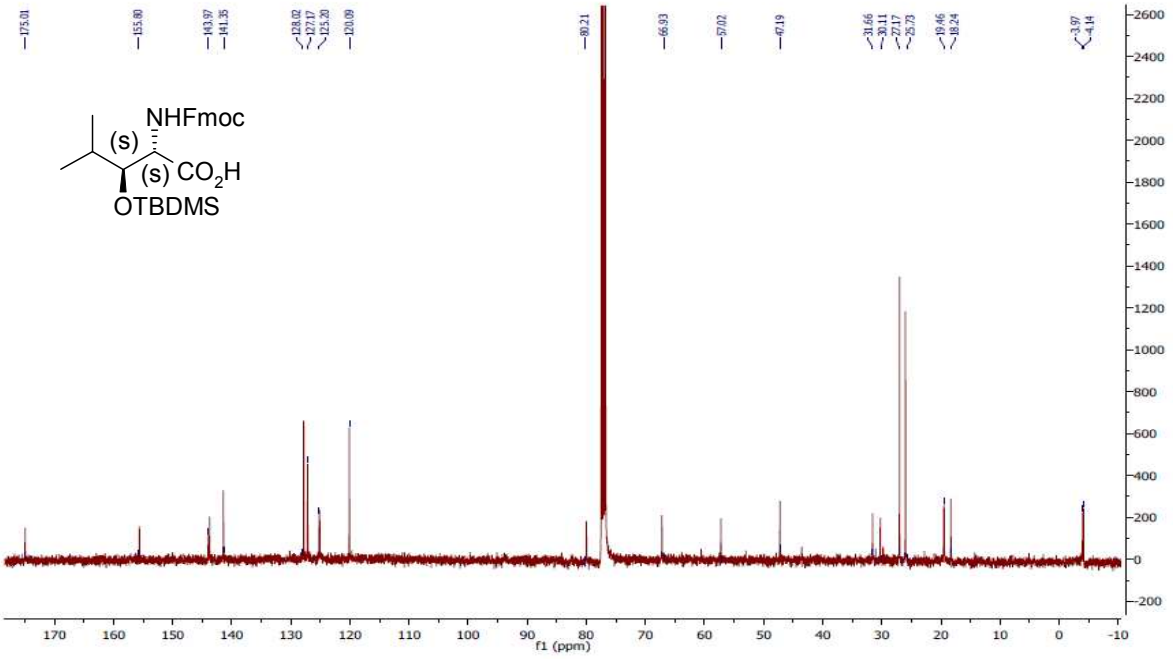


Figure S2: 1D NMR ^{13}C spectra of (2S,3S)-Fmoc-Leu(3-OTBDMS)-OH

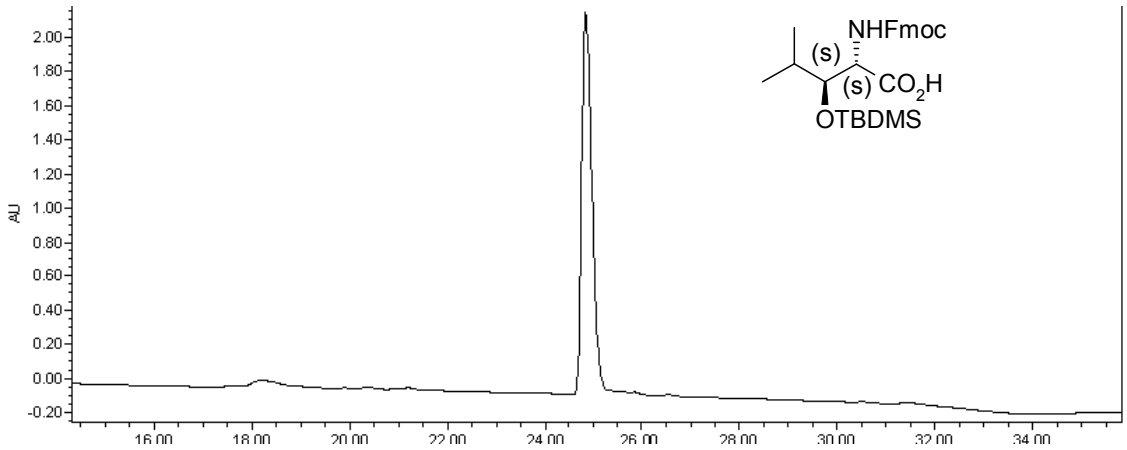


Figure S3: HPLC chromatogram of (2S,3S)-Fmoc-Leu(3-OTBDMS)-OH

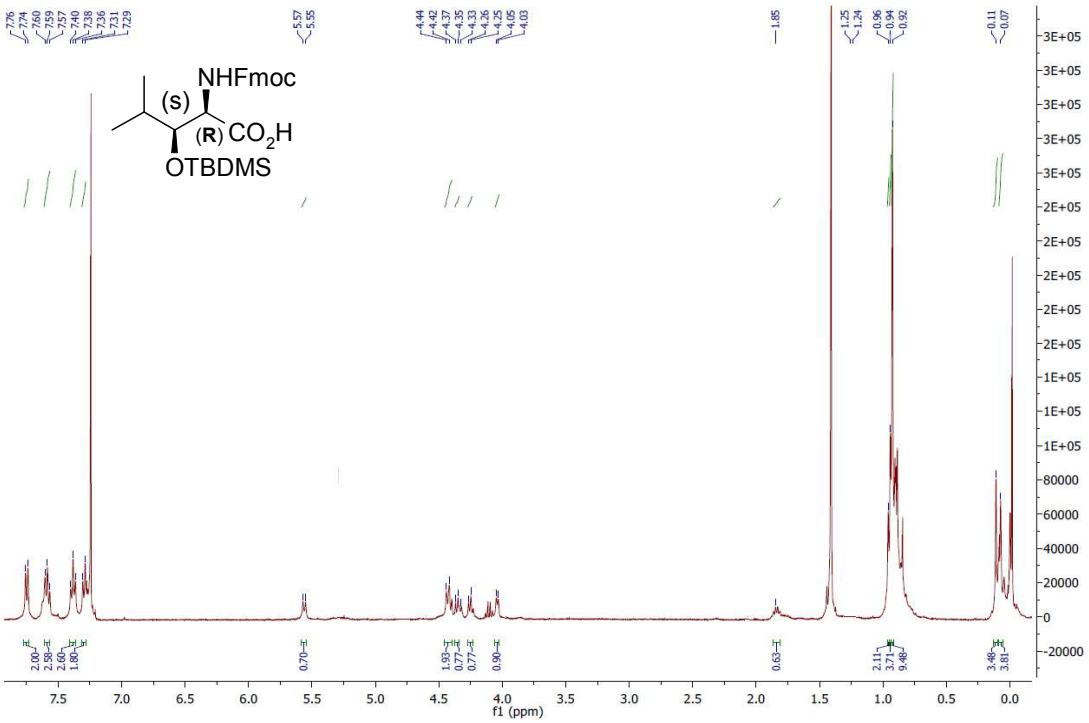


Figure S4: 1D NMR ^{1}H spectra of (2R,3S)-Fmoc-Leu(3-OTBDMS)-OH

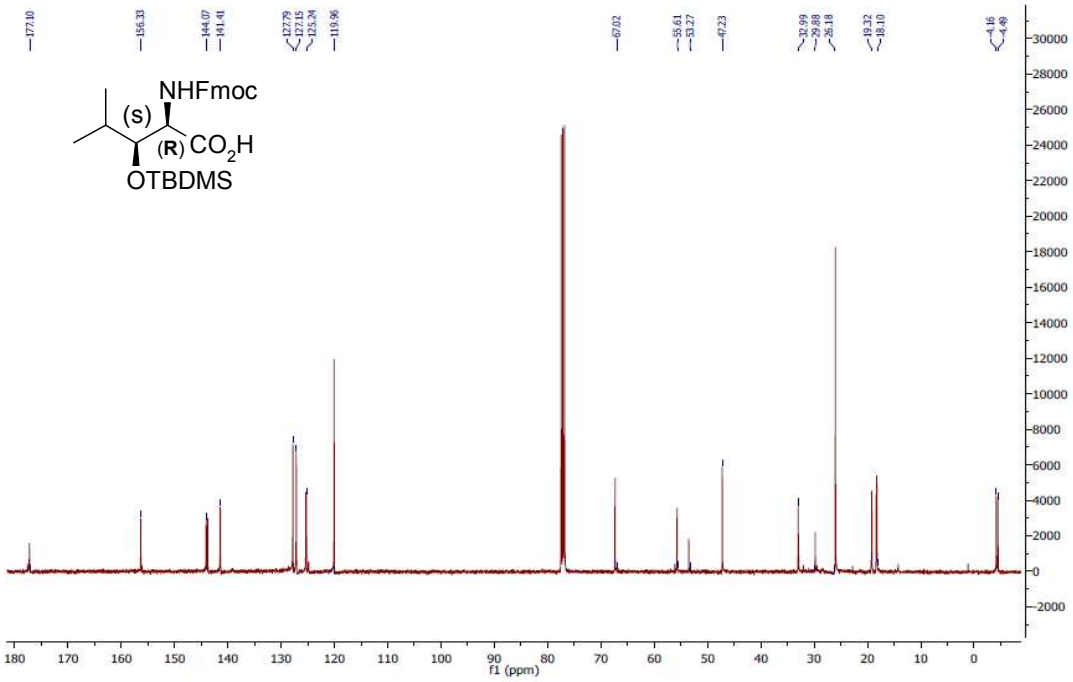


Figure S5: 1D NMR ^{13}C spectra of (2R,3S)-Fmoc-Leu(3-OTBDMS)-OH

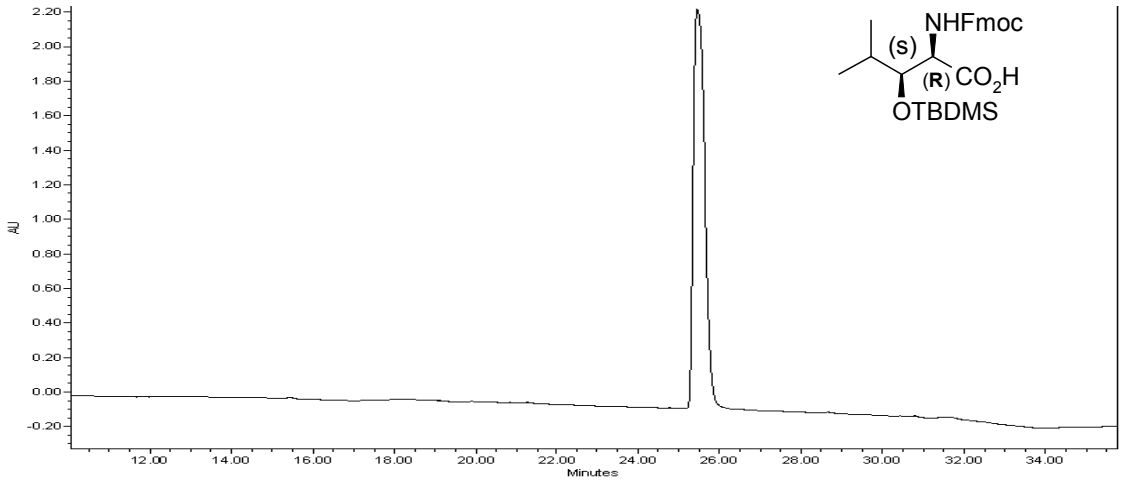


Figure S6: HPLC chromatogram of (2R,3S)-Fmoc-Leu(3-OTBDMS)-OH

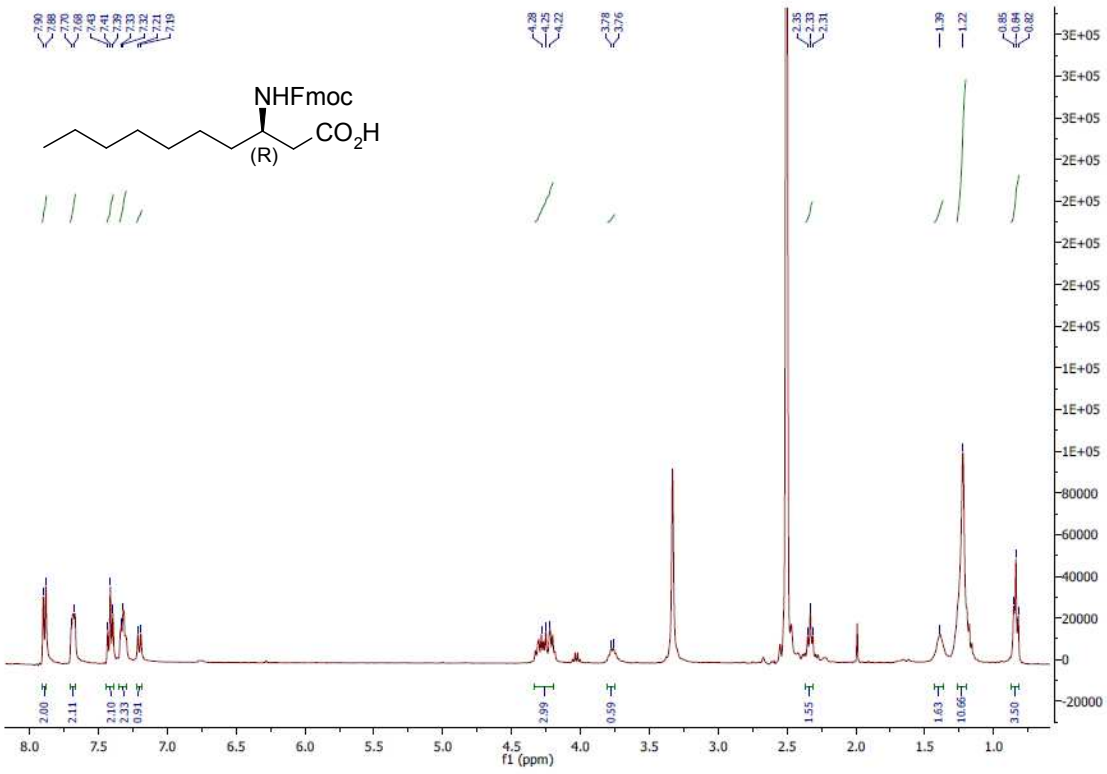


Figure S7: 1D NMR ^{1}H spectra of (3R)-Fmoc-aminodecanoïc acid

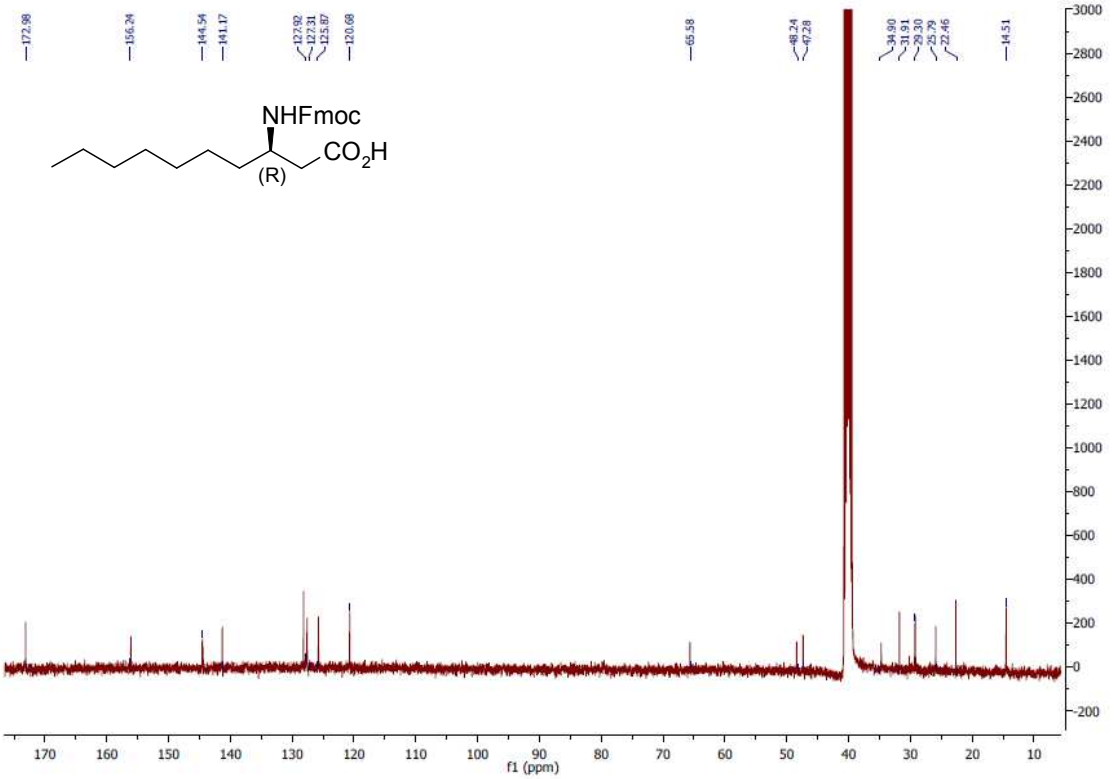


Figure S8: 1D NMR ^{13}C spectra of (3R)-Fmoc-aminodecanoïc acid

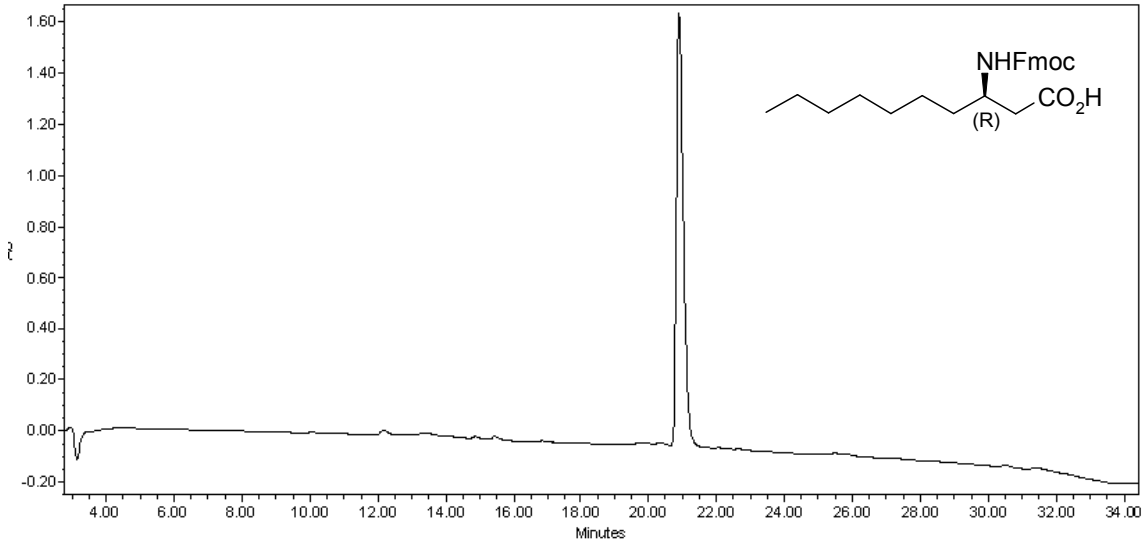


Figure S9: HPLC chromatogram of (3R)-Fmoc-aminodecanoïc acid

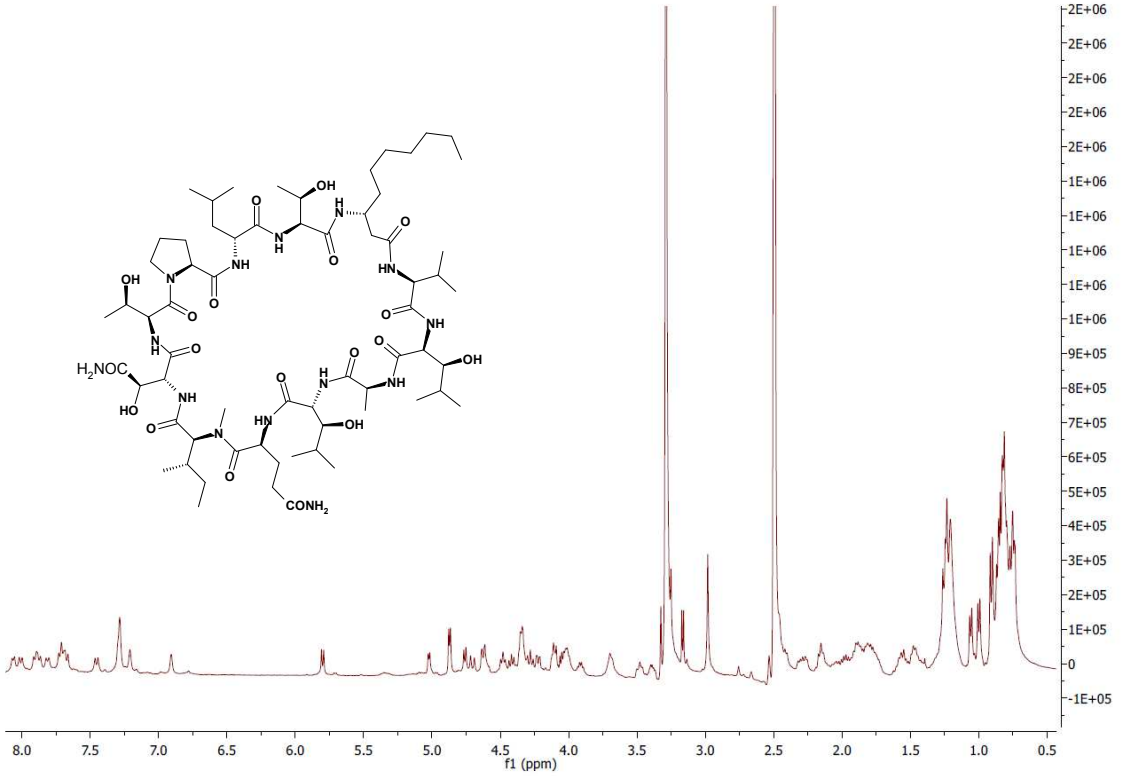


Figure S10: 1D NMR ^{1}H spectra of synthesized laxaphycin B (compound 2)

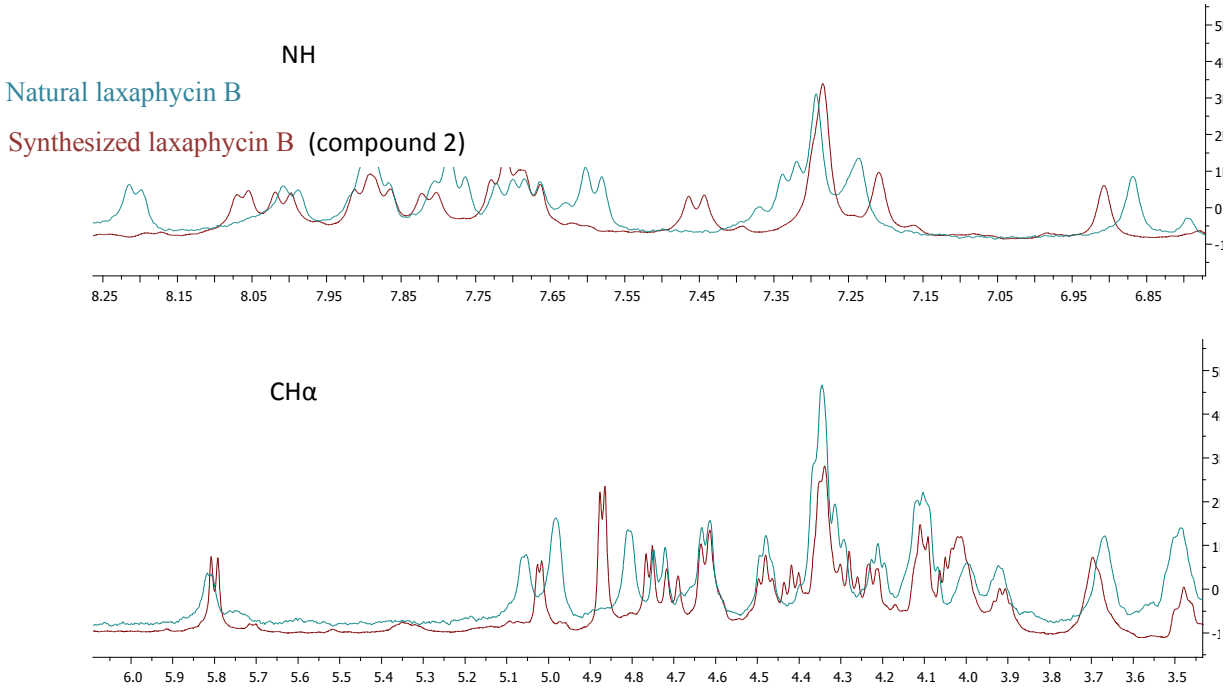


Figure S11: Superposition of 1D NMR ^{1}H spectra of compound **2** and natural laxaphycin B

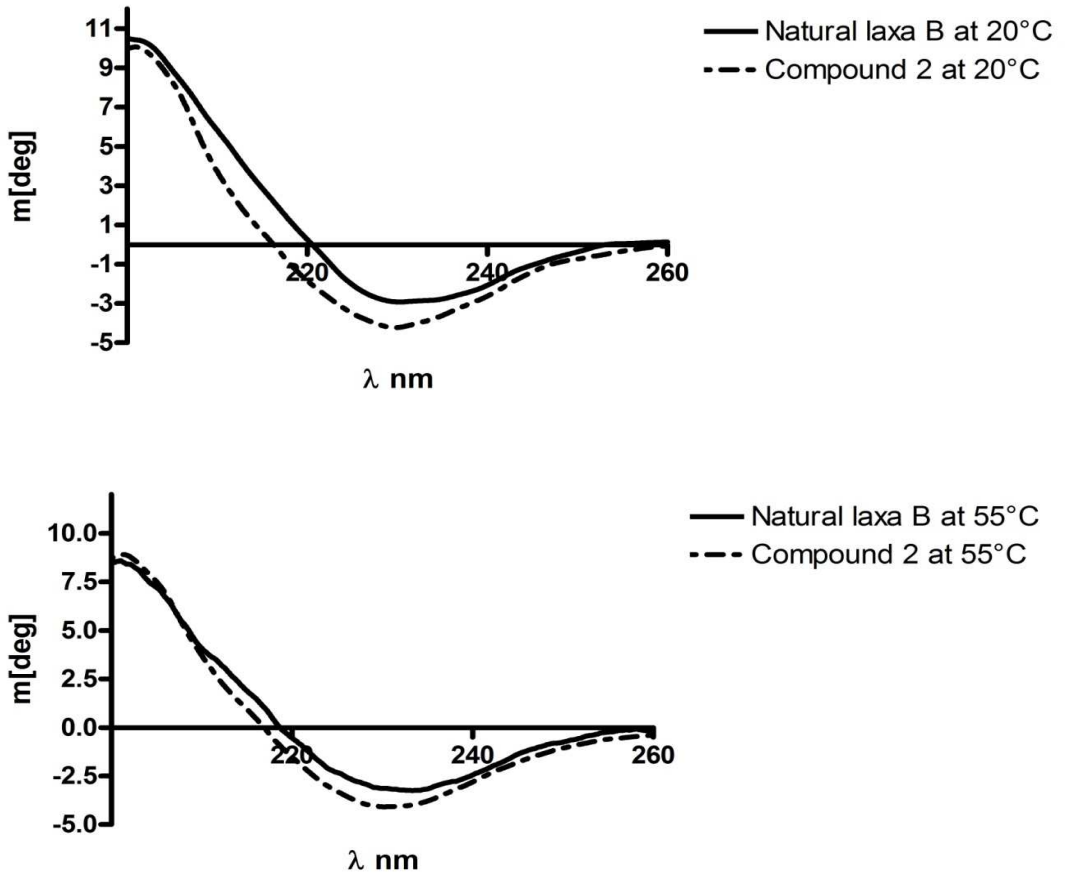


Figure S12: CD spectrum of compound **2** and natural laxaphycin B

CD spectra of compound 2 and laxaphycin B are similar and comparable to the one of lobocyclamide A that has also not been interpreted. The spectra showed a maximum 201 nm and a minimum at 230 nm. These data could be interpreted as the presence of a beta-sheet as secondary structure and let presume that the peptide has a definite three-dimensional structure. Nevertheless, this interpretation is only possible for peptide containing only alpha-amino acids, indeed in this case the maximum and minimum are respectively situated at 195 and 217 nm. But, in presence of a beta-amino acid these CD spectra need to be interpreted with caution because the maximum and minimum are shifted with respect to the ones observed for standard amino acids.

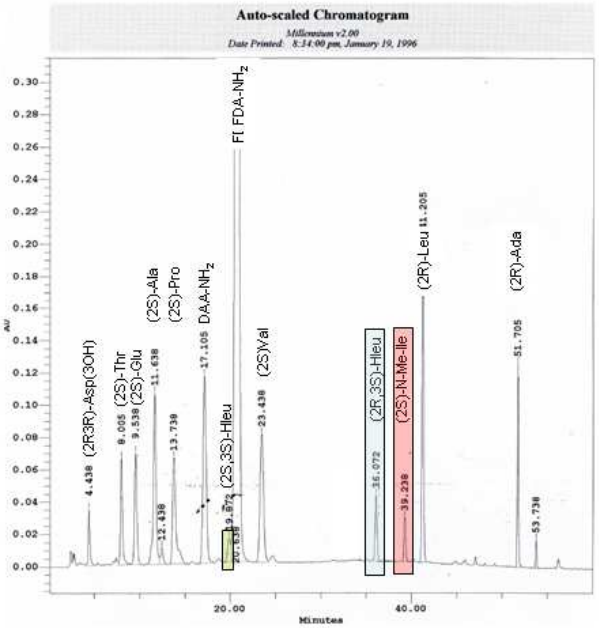
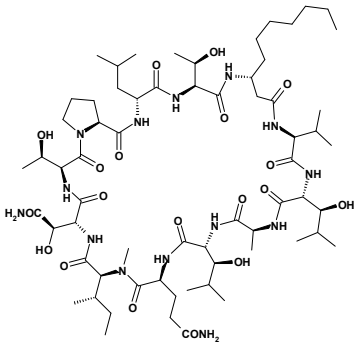


Figure S 13: Chromatogram of the amino acids derivatized with Marfey's reagent after Laxaphycine B acid hydrolysis.



Laxaphycin B (2)

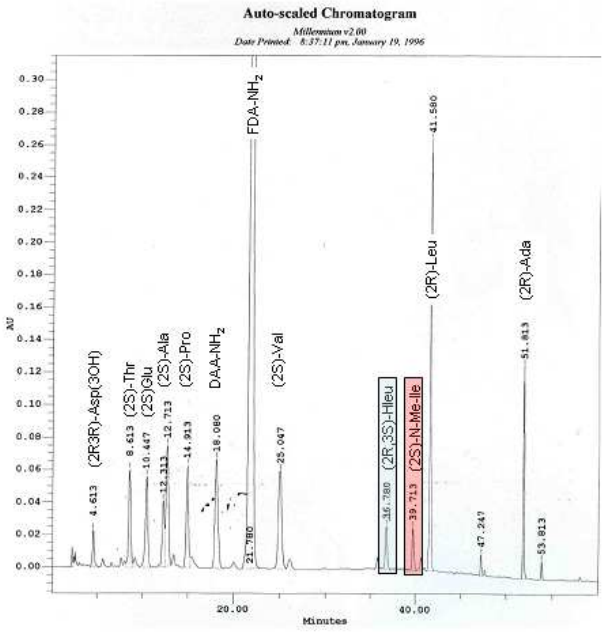
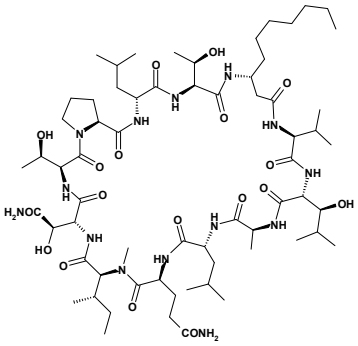


Figure S14: Chromatogram of the amino acids derivatized with Marfey's reagent after Laxaphycine B_2 acid hydrolysis.



Laxaphycin B_2

The relative intensity of the peak corresponding to the (2R,3S)-Hleu contained in laxaphycin B is 1.6 time greater than that observed in laxaphycin B_2 that contains only one Hleu. Hence, this indicated that laxaphycin B may contain two (2R, 3S)-Hleu and the small amount of the (2S, 3S)-Hleu that is detected could result of a racemization of the (2R,3S) isomer and was then considered as an artifact.

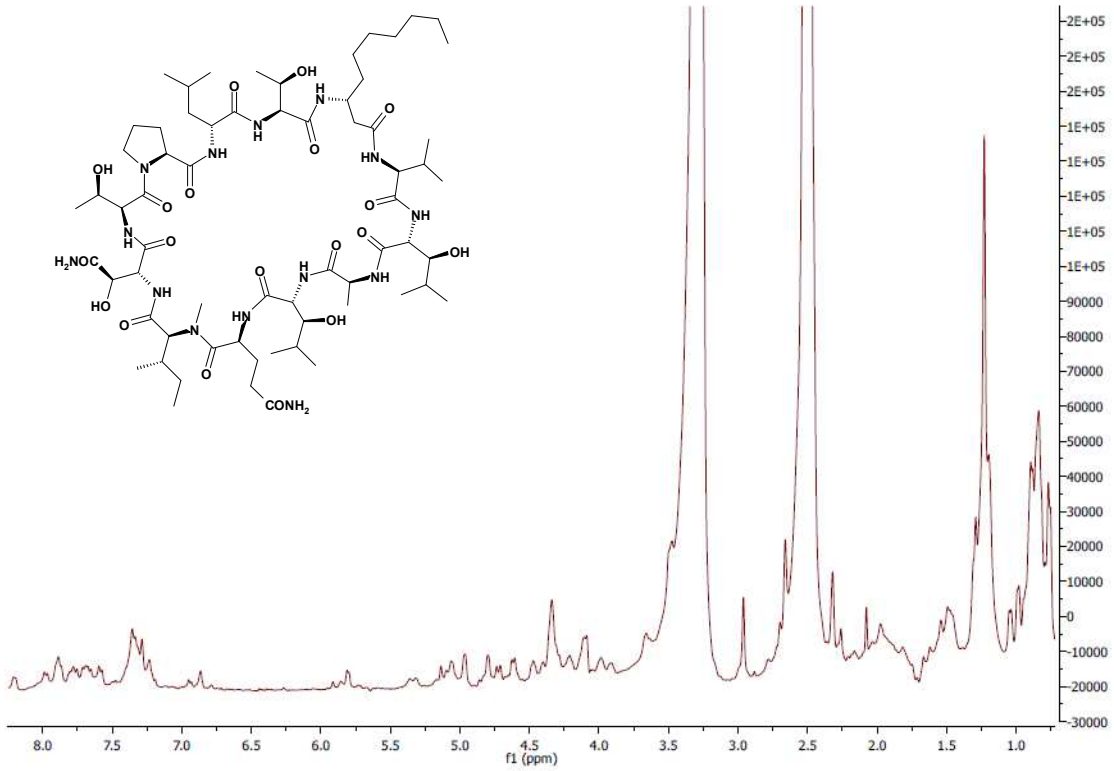


Figure S15: 1D NMR ^{1}H spectra of revised laxaphycin B (compound **3**)

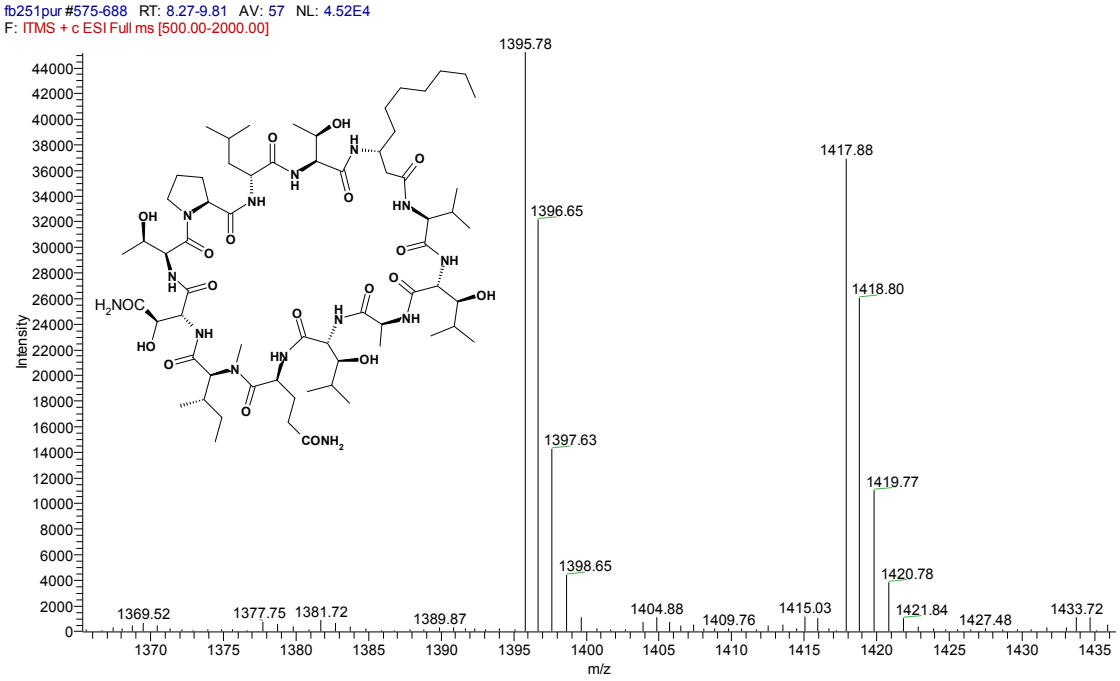


Figure S16: ESI^{+} MS of revised laxaphycin B (compound **3**). Calculated for: $[M+H]^{+}$ $C_{65}H_{115}N_{14}O_{19}$ 1395.84, found 1395.78 and $[M+Na]^{+}$ $C_{65}H_{114}N_{14}O_{19}Na$ 1417.82, found 1417.88.

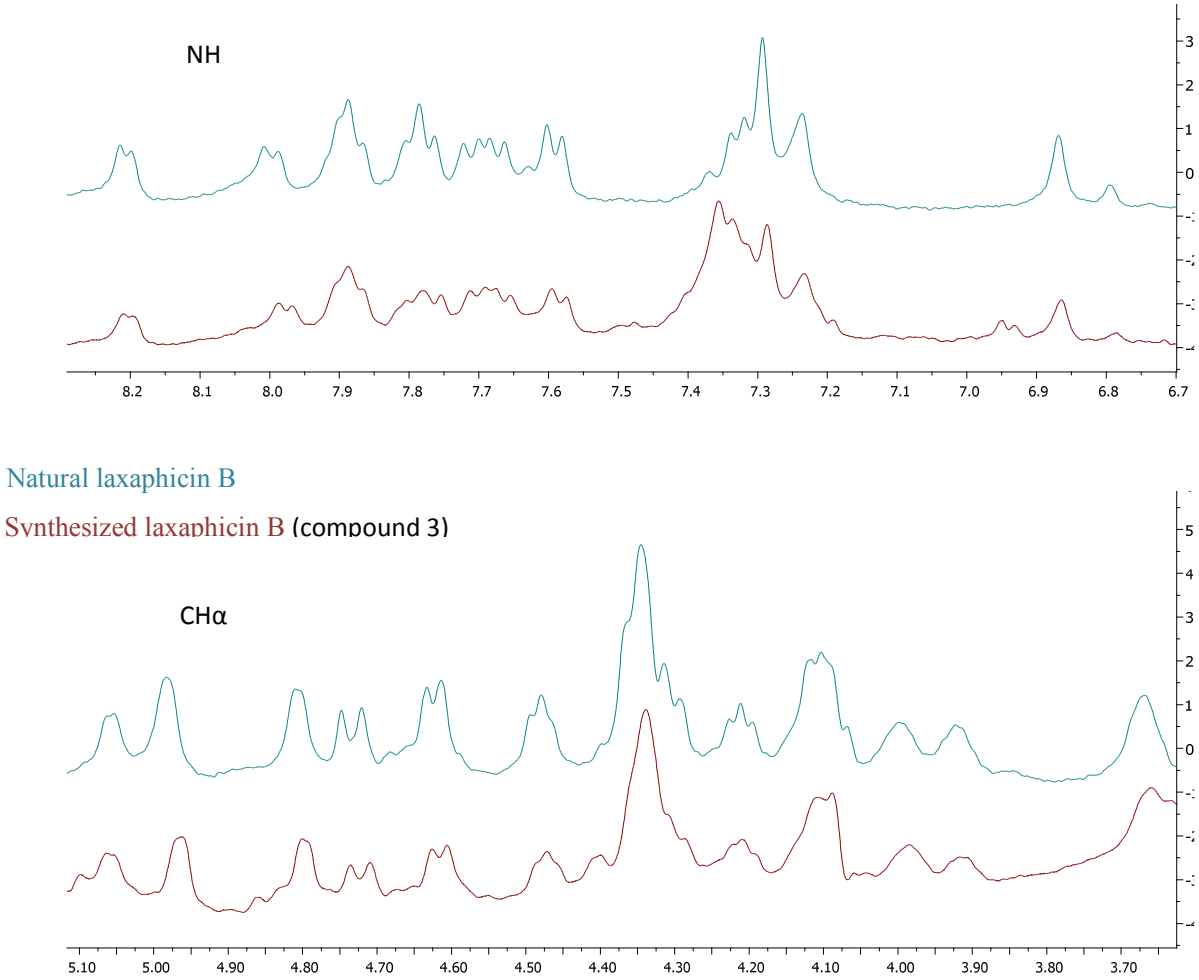


Figure S17: Superposition of 1D NMR ^{1}H spectra of compound **3** and natural laxaphycin B

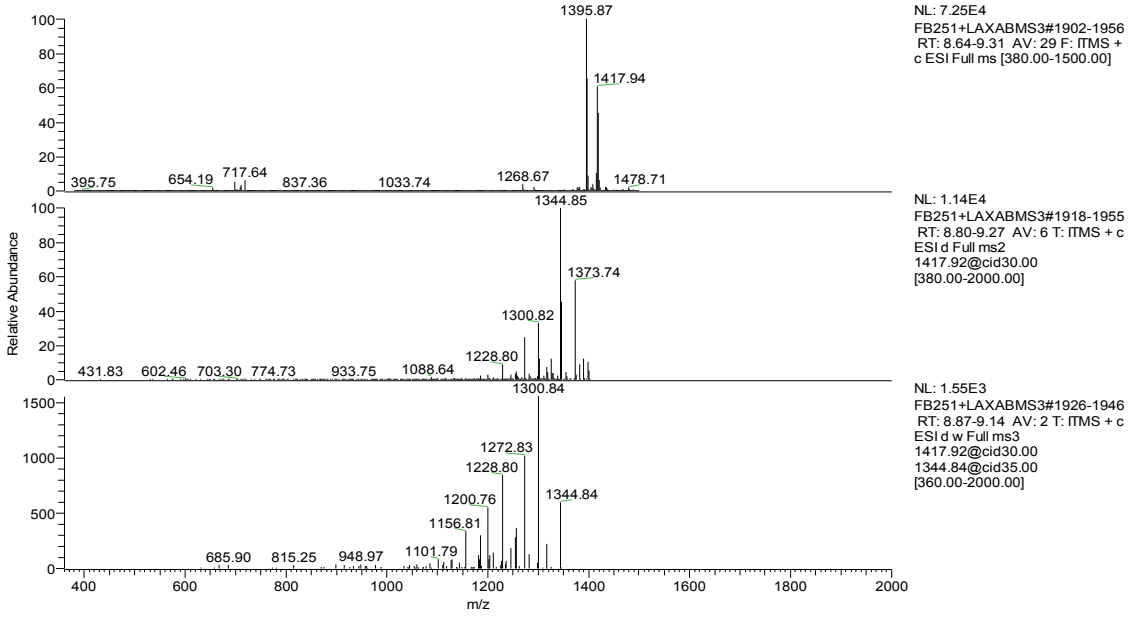


Figure S18: MS^{2} and MS^{3} spectra of compound **3**

Entry	Position	^{1}H multi (J, Hz) compound (**2**)	^{1}H multi (J, Hz) compound (**3**)
Ada	2	1.96-2.00	2.33-2.40
	3	4.11 m	4.11
	4	1.30 m	1.3-1.4
	5-9	1.20 m	1.24
	10	0.83 t	0.84
	NH	7.67 (d, 8.42)	7.58 (d, 8.58)
Val	2	4.43 m	4.09 d
	3	1.96 m	1.97 m
	4-5	0.87 m	0.91-0.85
	NH	8.06 (d, 6.5)	8.18 d (7.0)
hyLeu	2	4.21 (dd 8.4, 2.2)	4.34 (dd, 9.1, 2.0)
	3	3.48 m	3.49
	4	1.58 m	1.58
	5	0.91 d	0.89
	6	0.74 d	0.76
	OH	4.75 (d, 6.1)	4.94 (d, 4.4)
	NH	8.0 d (8.4)	7.94 (d, 8.05)
Ala	2	4.32 m	4.22
	3	1.47 m	1.31
	NH	7.90 m (d, 8.1)	7.86
HyLeu	2	4.28 m	4.28
	3	3.38 m	3.49
	4	1.75 m	1.56
	5	0.91 d	0.89
	6	0.81 d	0.76
	OH	4.87 (d, 4.9)	5.03 (d, 5.4)
	NH	7.86 (d, 8.2)	7.69 (d, 7.5)
Gln	2	4.58 m	4.63
	3	1.90-1.77 m	1.97 - 1.75
	4	2.15 m	2.04 - 2.10
	$CONH_2$	6.90 br s	6.85
	$CONH_2$	7.21 br s	7.22
	NH	7.71 (d, 7.6)	7.77 d (7.4)
NMeIle	2	4.71 (d, 11.0)	4.72 d (11.0)
	3	1.85 m	1.90
	4	1.25 m	1.29-0.89
	5	0.76 t	0.78
	6	0.74 d	0.76
	N-Me	2.98 s	2.97
HyAsn	2	4.62 m	4.63
	3	4.34 m	4.31
	$CONH_2$	7.28 br s	7.27
	OH	5.80 (d, 6.47)	5.79
	NH	7.71 (d, 7.8)	7.64 (d, 8.5)
Thr-1	2	4.45 m	4.49
	3	3.95 m	3.95
	4	1.06 (d, 5.9)	1.05 (d, 6.4)
	OH	5.02 (d, 4.4)	4.94 (d, 4.4)

	NH	7.28	7.33 (d, 8.0)
Pro	2	4.34	4.33
	3	1.95-1.80	1.82 - 2.04
	4	1.90	1.90 - 1.80
	5	3.60	3.68
Leu	2	4.1	4.31
	3	1.75	1.47
	4	1.50	1.53
	5	0.81	0.87
	5	0.81	0.82
	NH	7.80	7.89
Thr-2	2	4.00 m	4.11
	3	4.00 m	4.0
	4	0.99 d (6.2)	0.99
	OH	4.87 d (4.9)	4.78 d (5.2)
	NH	7.45 d (8.4)	7.74

Table S1: Assigned ^{1}H signal for compounds (**2**) and (**3**)

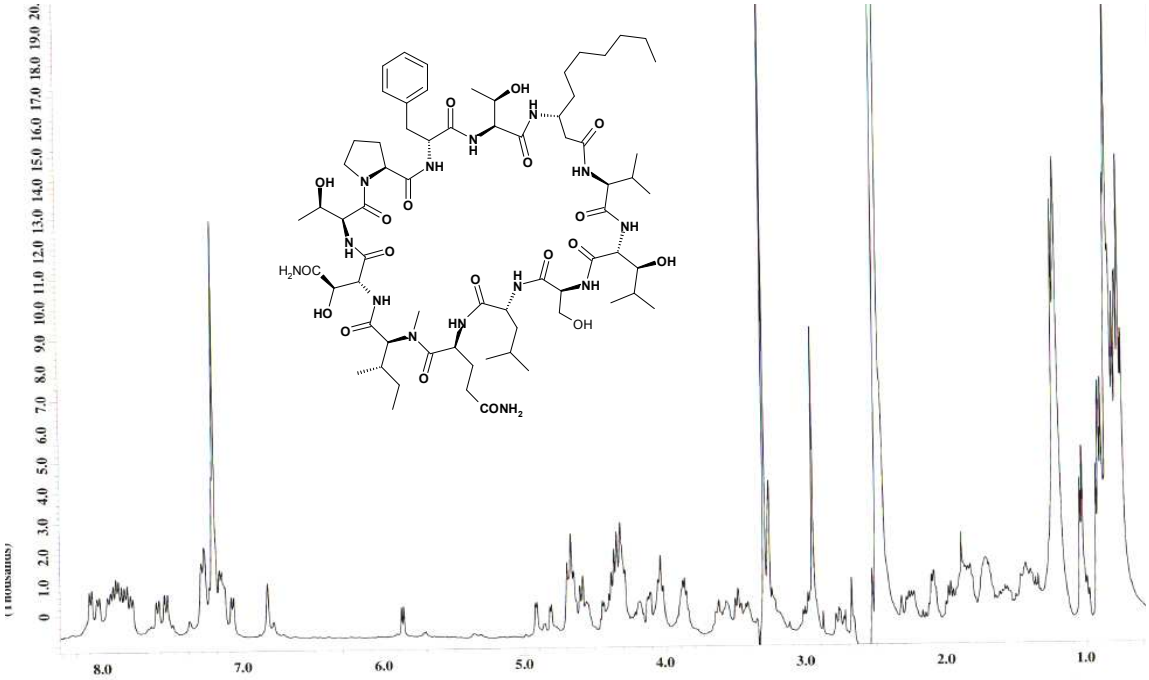


Figure S19: 1D ^{1}H NMR spectra of lyngbyacyclamide A (**5**)

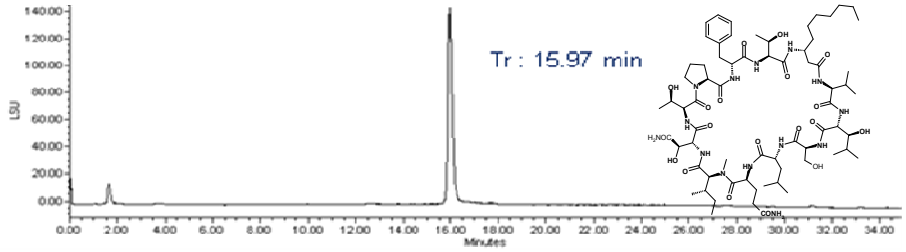


Figure S20: HPLC-ELSD chromatogram of synthesized lyngbyacyclamide A (**5**)

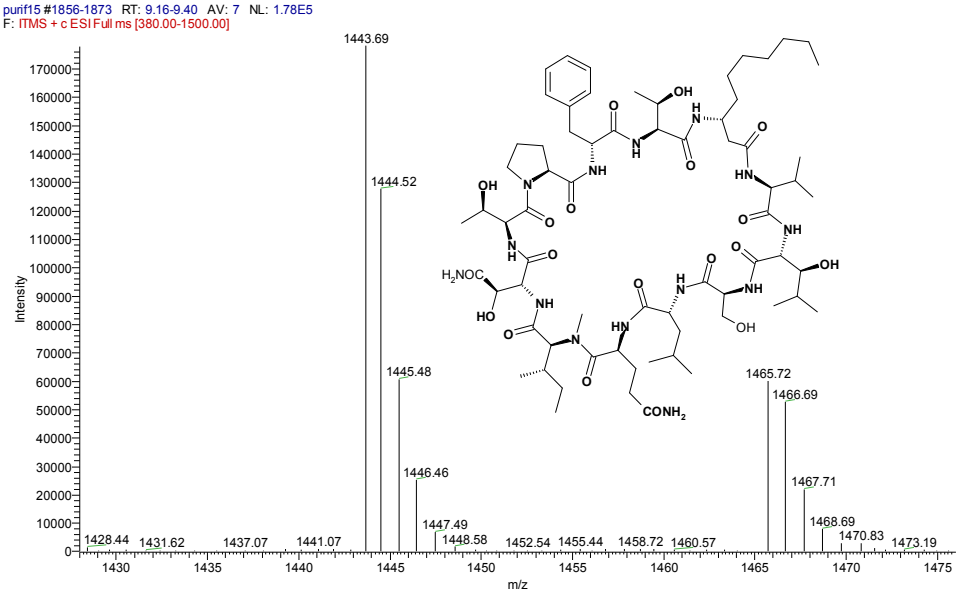


Figure S21: MS chromatogram ion trap ESI^{+} of lyngbyacyclamide A (5). Calculated for: $[M+H]^{+}$ $C_{69}H_{115}N_{14}O_{19}$ 1443.84, found 1343.69 and $[M+Na]^{+}$ $C_{69}H_{114}N_{14}O_{19}Na$ 1465.82 found 1465.72.

Entry	Position	^{1}H multi (J, Hz) natural lyngbyacyclamide	^{1}H multi (J, Hz) synthesized Lyngbyacyclamide **(5)**
Ada	2	2.25 dd (7.2, 14.0)	2.27 dd (7.2, 13.9)
	2	2.45 dd (6.0, 14.0)	2.45 m
	3	4.05 m	4.05 m
	4	1.30 m	1.30 m
	4	1.40 m	1.40 m
	5-9	1.20 m	1.20 m
	10	0.83 t (6.9)	0.83 t (6.2)
	NH	7.56 d (8.9)	7.56 d (8.6)
Val	2	4.03 t (7.4)	4.03 t (7.4)
	3	1.96 m	1.96 m
	4	0.90 d (6.9)	0.90 d (6.8)
	5	0.85 d (6.6)	0.85 d (6.2)
	NH	8.10 d (7.2)	8.09 d (7.3)
hyLeu	2	4.33 m	4.33 m
	3	3.47 t (8.6)	3.48 t (9.6)
	4	1.57 m	1.58 m
	5	0.77 d (6.6)	0.79 d (7.1)
	6	0.91 d (6.6)	0.91 d (6.8)
	OH	4.68 s	4.69 s
	NH	7.96 d (7.2)	7.95 d (8.5)
Hse	2	4.30 m	4.31 m
	3	1.70 m	1.74 m
	3	1.85 m	1.84 m
	4	3.30 m	3.35 m
	4	3.42 m	3.42 m
	OH	4.47 t (5.2)	4.5 t (4.9)
	NH	7.80 d (7.2)	7.80 d (7.2)
Leu	2	4.18 m	4.17 m
	3	1.33 m	1.39 m
	3	1.47 m	1.48 m
	4	1.58 m	1.57 m
	5	0.79 d (6.6)	0.77 d (6.7)
	6	0.84 d (6.9)	0.91 d (6.8)
	NH	7.84 d (7.8)	7.85 d (7.8)
Gln	2	4.54 m	4.57 m
	3	1.71 m	1.90 m
	3	1.88 m	1.74 m
	4	2.09 m	2.09 m
	$CONH_2$	6.85 br s	6.83 br s
	$CONH_2$	7.25 br s	7.22 br s
	NH	7.95 d (6.6)	7.92 d (8.1)
NMeIle	2	4.68 m	4.69 m
	3	1.90 m	1.90 m
	4	1.25 m	1.25 m
	5	0.75 t (7.2)	0.75 t (7.2)
	6	0.74 d (6.6)	0.74 d (6.7)
	N-Me	2.95 s	2.95 s
hyAsn	2	4.58 dd (1.8, 8.3)	4.59 d (8.7)

	3	4.64 d (1.8)	4.35 d (8.2)
	$CONH_2$	7.32 s	7.30 s
	OH	5.89 br	5.87 d (6.4)
	NH	7.64 d (8.3)	7.62 d (8.2)
Thr-1	2	4.35 m	4.38 d (6.6)
	3	3.86 m	3.86 m
	4	1.04 d (6.0)	1.03 d (6.1)
	OH	4.94 d (4.3)	4.92 d (4.5)
	NH	7.07 d (6.9)	7.08 d (7.1)
Pro	2	4.29 m	4.29 m
	3	1.36 m	1.40 m
	3	1.82 m	1.83 m
	4	1.63 m	1.63 m
	4	1.70 m	1.70 m
	5	3.53 m	3.53 m
	5	3.65 td (7.5, 9.4)	3.65 td (7.0, 9.0)
Phe	2	4.67 m	4.65 m
	3	2.74 dd (9.2, 13.5),	2.77 dd (9.2, 13.2)
	3	3.01 dd (5.8, 13.5)	2.99 dd (6.2, 14.2)
	5,9	7.21 m	7.23 m
	6,8	7.21 m	7.23 m
	7	7.16 m	7.13 m
	NH	8.04 d (7.7)	8.03 d (7.6)
Thr-2	2	4.12 dd (3.7, 8.1)	4.12 dd (3.5, 8.2)
	3	3.88 m	3.89 m
	4	0.82 d (6.9)	0.83 d (5.0)
	OH	4.84 d (4.9)	4.84 d (4.5)
	NH	7.92 d (8.1)	7.88 d (8.4)

Table S2: Assigned ^{1}H signal for lyngbyacyclamide A (**5**)