Supporting Information

Chemical Space Guided Discovery of Antimicrobial Bridged Bicyclic Peptides Against *Pseudomonas aeruginosa* and its Biofilms

*Ivan Di Bonaventura,[a] Xian Jin,[a] Ricardo Visini,[a] Daniel Probst,[a] Sacha Javor,[a] Bee-Ha Gan,[a] Gaëlle Michaud,[a] Antonino Natalello,[b] Silvia Maria Doglia,[b] Thilo Köhler,[c] Christian van Delden,[c] Achim Stocker,[a] Tamis Darbre[a] and Jean-Louis Reymond[a]**

[a]*Department of Chemistry and Biochemistry, University of Berne, Freiestrasse 3, 3012 Berne Switzerland; jean-louis.reymond@dcb.unibe.ch*

[b]*Department of Biotechnology and Biosciences, University of Milano-Bicocca, Piazza della Scienza 2, 20126 Milan, Italy*

[c]*Department of Microbiology and Molecular Medicine, University of Geneva, and Service of Infectious Diseases, University Hospital of Geneva, Geneva, Switzerland*

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1. AMBP Libraries

Table S1: First library of bicyclic peptides

N	Sequence[a)]	MS calc/obs [M]	MIC BR 151	MIC PAO1	H[b)]	+[c)]
1a	$^{2}K(^{1})KZ^{1}KLZ^{2}L$	914.19/914.19	>256	>256	2	2
1b	$^{1}K(^{2})KZ^{1}KLZ^{2}L$	914.19/914.19	128	>256	2	2
2a	$L^{2}K(L^{1})LKKZ^{1}KZ^{2}$	1154.67/1154.66	>256	>256	3	3
2b	$L^{1}K(L^{2})LKKZ^{1}KZ^{2}$	1154.67/1154.66	>256	>256	3	3
3a	$K^{2}K(K^{1})LLLZ^{1}LZ^{2}K$	1267.65/1267.65	>256	>256	4	3
3b	$K^{1}K(K^{2})LLLZ^{1}LZ^{2}K$	1267.65/1267.65	256	>256	4	3
4	$L^{12}K(L^{12})KKZ^{21}KLLZ^{12}$	1282.76/1282.76	128	>256	3	4
5a	$K^{2}K(K^{1})LKLZ^{1}LKZ^{2}$	1282.76/1282.76	>256	>256	3	4
5b	$K^{1}K(K^{2})LKLZ^{1}LKZ^{2}$	1282.76/1282.76	>256	>256	3	4
6a	$K^{2}K(K^{1})LKLZ^{1}LLKZ^{2}L$	1508.93/1508.93	>256	>256	5	4
6b	$K^{1}K(K^{2})LKLZ^{1}KLLZ^{2}L$	1508.93/1508.93	>256	>256	5	4
7	$K^{12}K(K^{12})LLKZ^{21}KLLZ^{12}L$	1508.93/1508.93	>256	>256	5	4
8a	$K^{1}LK(K^{2}L)KKKZ^{2}LLZ^{1}$	1523.94/1523.94	>256	>256	4	5
8b	$K^{1}LK(K^{2}L)KKKZ^{1}LLZ^{2}$	1523.94/1523.94	>256	>256	4	5
9a	$L^{1}LK(L^{2}L)KKZ^{2}KKLZ^{1}L$	1622.01/1622.01	128	>256	6	4
9b	$L^{1}LK(L^{2}L)KKZ^{1}KKLZ^{2}L$	1622.01/1622.01	128	>256	6	4
10a	$K^{1}LK(K^{2}L)KLLZ^{2}KLLZ^{1}K$	1750.11/1750.11	32	>256	6	5
10b	$K^{1}LK(K^{2}L)KLLZ^{1}KLLZ^{2}K$	1750.11/1750.11	32	>256	6	5
11a	$L^{1}LK(L^{2}L)KLKZ^{2}KKLZ^{1}K$	1750.11/1750.11	64	>256	6	5
11b	$L^{1}LK(L^{2}L)KLKZ^{1}KKLZ^{2}K$	1750.11/1750.11	16	>256	6	5
12	$K^{12}LKK(K^{12}LK)LLZ^{21}KLLZ^{12}$	1750.11/1750.11	64	>256	6	5
13a	$K^{2}LLK(K^{1}LL)KLZ^{1}KKLZ^{2}$	1750.11/1750.11	16	>256	6	5
13b	$K^{1}LLK(K^{2}LL)KLZ^{1}KKLZ^{2}$	1750.11/1750.11	16	>256	6	5
14a	$K^{2}LLK(K^{1}LL)KKZ^{1}KLZ^{2}L$	1750.11/1750.11	64	>256	6	5
14b	$K^{1}LLK(K^{2}LL)KKZ^{1}KLZ^{2}L$	1750.11/1750.11	64	>256	6	5
15	$L^{12}KK(L^{12}K)KLKZ^{21}LLKZ^{12}L$	1750.11/1750.11	16	>256	6	5
16a	$K^{2}LK(K^{1}L)LKLZ^{1}KKLZ^{2}K$	1765.12/1765.12	>256	>256	4	6
16b	$K^{1}LK(K^{2}L)LKLZ^{1}KKLZ^{2}K$	1765.12/1765.12	>256	>256	4	6
17a	$K^{2}KLK(K^{1}KL)KKZ^{1}LLLZ^{2}K$	1893.21/1893.22	128	>256	5	7
17b	$K^{1}KLK(K^{2}KL)KKZ^{1}LLLZ^{2}K$	1893.21/1893.22	128	>256	5	7
18a	$K^{1}LKK(K^{2}LK)LKKZ^{2}LLLZ^{1}L$	1991.29/1992.29	32	>256	7	6
18b	$K^{1}LKK(K^{2}LK)LKKZ^{1}LLLZ^{2}L$	1991.29/1992.29	32	>256	7	6
19	$K^{12}LKK(K^{12}LK)LLLZ^{21}KLKZ^{12}L$	1991.29/1991.29	8	>256	7	6

[a)] Sequences are given using standard one-letter codes for amino acids, capitals = L-amino acids, lower case = D-amino acids, *K* = branching lysine, the peptide extended on the side chain is in parentheses, *Z* = γ-thia-homoglutamic acid, formed by ClAc ligation at cysteine, [1] and [2] indicate cyclization points using the SMILES formalism, [b)] H = number of hydrophobic residues, including fatty acid side chains. [c)] + = number of positive charges. All MIC values reported in µg/mL. MIC indicated in µg/mL. MS calc/obs calculated in Dalton. For **1a** and **1b** the mass is considered $[M+H]^{+}$.

Table S2: Second library of bicyclic peptides.

N	Sequence	MS calc/obs [M]	MIC BR 151	MIC PAO1	MBIC	Dispersal	H	+
20	^{12}LLK*K*(L^{12}LK)LLL*Z*^{21}KLK*Z*^{12}L	1961.27/1961.27	4	128	32	60 %	9	4
21a	^{2}KLK*K*(K^{1}LK)LLL*Z*^{1}LLL*Z*^{2}L	1961.27/1961.27	4	128			9	4
21b	^{1}KLK*K*(K^{2}LK)LLL*Z*^{1}LLL*Z*^{2}L	1961.27/1961.27	4	64	>32		9	4
22	^{12}KLL*K*(K^{12}LL)KLL*Z*^{21}KLL*Z*^{12}L	1961.27/1961.28	4	>256			9	4
23	^{12}LLK*K*(L^{12}LK)KLL*Z*^{21}KLK*Z*^{12}L	1976.28/1976.29	4	128			8	5
24	^{12}LLK*K*(L^{12}LK)KLK*Z*^{21}LLK*Z*^{12}L	1976.28/1976.28	4	128	16	50 %	8	5
25a	^{2}LLK*K*(L^{1}LK)KLK*Z*^{1}KLL*Z*^{2}K	1991.29/1991.30	64	>256			7	6
25b	^{1}LLK*K*(L^{2}LK)KLK*Z*^{1}KLL*Z*^{2}K	1991.29/1991.30	16	64	>32		7	6
26a	^{1}KLL*K*(K^{2}LL)KLL*Z*^{2}KLK*Z*^{1}K	1991.29/1991.30	32	>256			7	6
26b	^{1}KLL*K*(K^{2}LL)KLL*Z*^{1}KLK*Z*^{2}K	1991.29/1991.30	1	128	32	36 %	7	6
27a	^{2}KLK*K*(K^{1}LK)KLL*Z*^{1}LLL*Z*^{2}K	1991.29/1991.30	32	256			7	6
27b	^{1}KLK*K*(K^{2}LK)KLL*Z*^{1}LLL*Z*^{2}K	1991.29/1991.30	1	32	32	12 %	7	6
28a	^{2}KLL*K*(K^{1}LL)KLK*Z*^{1}KKL*Z*^{2}L	1991.29/1991.29	64	>256			7	6
28b	^{1}KLL*K*(K^{2}LL)KLK*Z*^{1}KKL*Z*^{2}L	1991.29/1991.29	64	>256	>32		7	6
29a	^{2}KLL*K*(K^{1}LL)KLL*Z*^{1}KKK*Z*^{2}L	1991.29/1991.29	16	>256	32	No disp.	7	6
29b	^{1}KLL*K*(K^{2}LL)KLL*Z*^{1}KKK*Z*^{2}L	1991.29/1991.29	2	256	8	100%	7	6
30a	^{2}KLL*K*(K^{1}LL)LK*Z*^{1}KLK*Z*^{2}L	1863.19/1863.19	128	>256			7	5
30b	^{1}KLL*K*(K^{2}LL)LK*Z*^{1}KLK*Z*^{2}L	1863.19/1863.19	128	>256			7	5
31a	^{2}KLK*K*(K^{1}LK)KKL*Z*^{1}LLK*Z*^{2}L	1878.20/1878.21	128	>256			6	6
31b	^{1}KLK*K*(K^{2}LK)KKL*Z*^{1}LLK*Z*^{2}L	1878.20/1878.21	128	>256			6	6
32a	^{2}KLK*K*(K^{1}LK)LLZ^{1}LKLZ^{2}K	1878.20/1878.20	32	>256			6	6
32b	^{1}KLK*K*(K^{2}LK)LLZ^{1}LKLZ^{2}K	1878.20/1878.20	16	>256			6	6
33a	^{2}KLL*K*(K^{1}LL)KLK*Z*^{1}KKK*Z*^{2}L	2006.30/2006.31	64	>256			6	7
33b	^{1}KLL*K*(K^{2}LL)KLK*Z*^{1}KKK*Z*^{2}L	2006.30/2006.31	32	>256	>32		6	7
34a	^{2}LLK*K*(L^{1}LK)KKK*Z*^{1}KLK*Z*^{2}L	2006.30/2006.31	8	>256			6	7
34b	^{1}LLK*K*(L^{2}LK)KKK*Z*^{1}KLK*Z*^{2}L	2006.30/2006.31	8	>256	>32		6	7
35a	^{2}KLK*K*(K^{1}LK)LLL*Z*^{1}KKK*Z*^{2}L	2006.30/2006.31	16	>256			6	7
35b	^{1}KLK*K*(K^{2}LK)LLL*Z*^{1}KKK*Z*^{2}L	2006.30/2006.31	16	>256			6	7
36a	^{2}KLK*K*(K^{1}LK)KLL*Z*^{1}LLK*Z*^{2}K	2006.30/2006.30	32	>256	>32	No disp.	6	7
36b	^{1}KLK*K*(K^{2}LK)KLL*Z*^{1}LLK*Z*^{2}K	2006.30/2006.30	16	64	8	100 %	6	7
37a	^{2}KLK*K*(K^{1}LK)KLL*Z*^{1}KLK*Z*^{2}L	2006.30/2006.30	32	>256	16	30 %	6	7
37b	^{1}KLK*K*(K^{2}LK)KLL*Z*^{1}KLK*Z*^{2}L	2006.30/2006.30	32	256	16	100 %	6	7
38	^{12}KKK*K*(K^{12}KK)KKK*Z*^{21}LLL*Z*^{12}L	2036.32/2036.33	16	>256			4	9

AMBP activities reported in µg/mL. All Dispersal values are referred to a concentration of 32 µg/mL. For 29-b, dispersal with Polymyxin 1.5 µg/mL is equal to 8 µg/mL (100% dispersal); for 36-b, dispersal with Polymyxin 1.5 µg/mL is equal to 8 µg/mL (100% dispersal). MS calc/obs calculated in Dalton.

Table S3: Third library of bicyclic peptides

N	Sequence	MS calc/obs [M]	MIC BR 151	MIC PAO1	MBIC	Dispersal	H	+
39a	^{1}LLKK(L^{2}LK)KKLZ^{2}LLLZ^{1}K	1976.28/1976.28	16	128			8	5
39b	^{2}LLKK(L^{1}LK)KKLZ^{2}LLLZ^{1}K	1976.28/1976.28	4	64	>32		8	5
40a	^{2}KLKK(K^{1}LK)*LKLZ^{1}LLLZ^{2}K*	1991.29/1991.28	>64	>256			7	6
40b	^{1}KLKK(K^{2}LK)LKLZ^{1}LLLZ^{2}K	1991.29/1991.28	64	>256			7	6
41a	^{2}KLKK(K^{1}LK)KKKZ^{1}LLLZ^{2}K	2006.30/2006.30	>64	>256			7	6
41b	^{1}KLKK(K^{2}LK)KKKZ^{1}LLLZ^{2}K	2006.30/2006.30	>64	>256			7	6
42a	^{1}KLKK(K^{2}LK)LLLZ^{2}LKLZ^{1}K	1991.29/1991.29	16	>256			7	6
42b	^{2}KLKK(K^{1}LK)LLLZ^{2}LKLZ^{1}K	1991.29/1991.29	4	256			7	6
43	^{12}KLKK(K^{21}LK)KLLZ^{12}LKLZ^{21}K	2006.30/2006.30	>64	>256			6	7
44a	^{1}KLKK(K^{2}LK)LKLZ^{2}LLKZ^{1}K	2006.30/2006.30	>64	>256			6	7
44b	^{2}KLKK(K^{1}LK)LKLZ^{2}LLKZ^{1}K	2006.30/2006.30	64	>256			6	7
45a	^{1}KLKK(K^{2}LK)LLLZ^{2}LKKZ^{1}K	2006.30/2006.30	8	>256			6	7
45b	^{1}KLKK(K^{2}LK)LLLZ^{1}LKKZ^{2}K	2006.30/2006.30	4	256			6	7
46	^{12}KLKK(K^{21}LK)LKLZ^{21}LKLZ^{12}K	2006.30/2006.30	>64	>256			6	7
47a	^{2}KLKK(K^{1}LK)LKKZ^{1}LLLZ^{2}K	2006.30/2006.30	>64	>256			6	7
47b	^{1}KLKK(K^{2}LK)LKKZ^{1}LLLZ^{2}K	2006.30/2006.30	>64	>256			6	7
48a	^{1}KLKK(K^{2}LK)LKLZ^{2}KLLZ^{1}K	2006.30/2006.30	>64	>256			6	7
48b	^{2}KLKK(K^{1}LK)LKLZ^{2}KLLZ^{1}K	2006.30/2006.30	64	>256			6	7
49a	^{1}KLKK(K^{2}LK)KLKZ^{2}LLKZ^{1}K	2021.31/2021.31	>64	>256			5	8
49b	^{2}KLKK(K^{1}LK)KLKZ^{2}LLKZ^{1}K	2021.31/2021.31	16	256			5	8
50	^{21}KLKK(K^{12}LK)KLLZ^{21}KLKZ^{12}K	2021.31/2021.31	>64	>256			5	8
51a	^{2}KLKK(K^{1}LK)KLKZ^{1}KLLZ^{2}K	2021.31/2021.31	>64	>256			5	8
51b	^{1}KLKK(K^{2}LK)KLKZ^{1}KLLZ^{2}K	2021.31/2021.31	>64	>256			5	8
52	^{12}KLKK(K^{21}LK)KKLZ^{12}LLKZ^{21}K	2021.31/2021.31	>64	>256			5	8
53a	^{2}KLKK(K^{1}LK)KLLZ^{1}LKKZ^{2}K	2021.31/2021.31	>64	>256			5	8
53b	^{1}KLKK(K^{2}LK)KLLZ^{1}LKKZ^{2}K	2021.31/2021.31	32	>256			5	8
54	^{12}KLKK(K^{21}LK)KKKZ^{12}LLLZ^{21}K	2021.31/2021.31	>64	>256			5	8
55a	^{1}KLKK(K^{2}LK)KLKZ^{2}LKLZ^{1}K	2021.31/2021.31	>64	>256			5	8
55b	^{2}KLKK(K^{1}LK)KLKZ^{2}LKLZ^{1}K	2021.31/2021.31	>64	>256			5	8
56a	^{1}KKKK(K^{2}KK)KLLZ^{2}LLLZ^{1}K	2021.31/2021.31	4	128	>32	No disp.	5	8
56b	^{2}KKKK(K^{1}KK)KLLZ^{2}LLLZ^{1}K	2021.31/2022.31	2	32	32	75 %	5	8
57a	^{1}KLKK(K^{2}LK)LKLZ^{2}KLKZ^{1}K	2021.31/2021.31	>64	>256			5	8
57b	^{2}KLKK(K^{1}LK)LKLZ^{2}KLKZ^{1}K	2021.31/2021.31	64	>256			5	8

2. Antimicrobial activity

2.1 Broth Microdilution Method

Bicyclic peptides cytotoxicity was assayed against *Pseudomonas aeruginosa* PAO1, *P. aeruginosa* ZEM 1.A, *P. aeruginosa* ZEM 9.A, *P. aeruginosa* PEJ 2.6, *P. aeruginosa* PEJ 9.1, *Acinetobacter baumanii* (ATCC19606), *Staphylococcus aureus* (clinical isolate of MRSA), *Staphylococcus aureusNewman* (MSSA) and *Bacillus Subtilis* BR151.

Table S4: MIC of **62b** and Polymyxin B against multidrug resistant *P. aeruginosa* clinical isolates, and *Acinetobacter baumanii* reported in µg/mL. **27b** was tested against MRSA and MSSA and the activity was >128 µg/mL.

Strain	**62b**	**Polymyxin**
ZEM1.A	16	0.12
ZEM9.A	64	4
PEJ2.6	8	1
PEJ9.1	16	0.5
A. baumannii ATCC19606	8	1
MRSA	64	>32
MSSA	64	>32

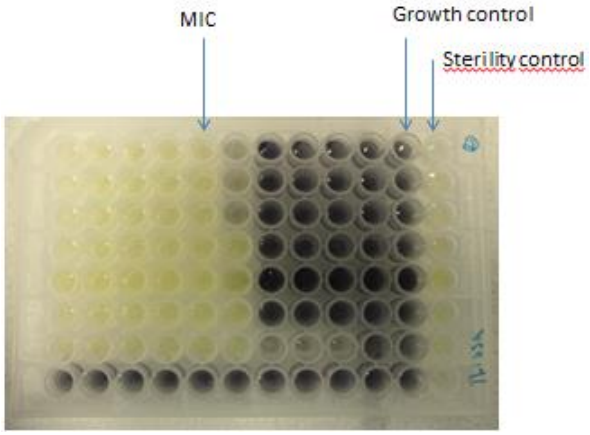


Figure S1: Broth Microdilution Method to determine the MIC values, raw 11 is used as growing control without compound (w/o) and raw 12 is used as a negative. All measurements were performed in duplicates, repeated three times and for the best compound repeated nine times.

2nd Library

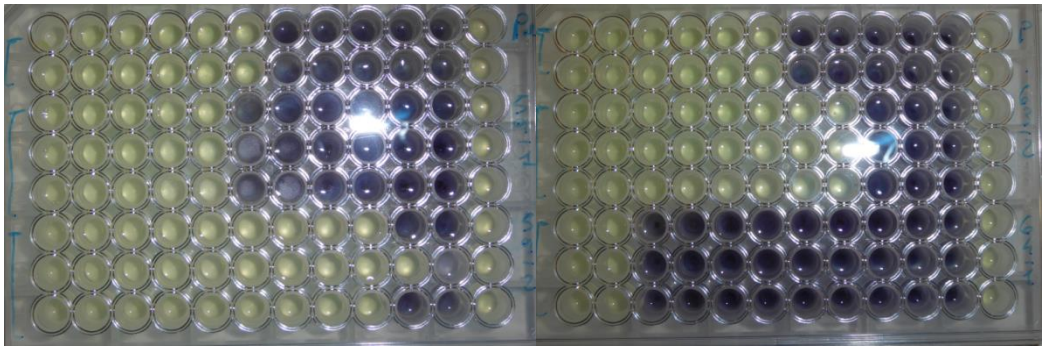


Figure S2: Broth Microdilution Method to determine the MIC values of **27a** and **27b** against *Bacillus subtilis*; 2-fold dilution series starting from 256 µg/mL(left side). Polymyxin B (dilution starting from 64 µg/mL) was used as a reference (raw A-B). Raw 11 is used as growing control without compound (w/o) and raw 12 is used as a negative. All measurements were performed in triplicates in this case; Broth Microdilution Method to determine the MIC values of **29b** and **30a** against *Bacillus subtilis*; 2-fold dilution series starting from 256 µg/mL (right side).

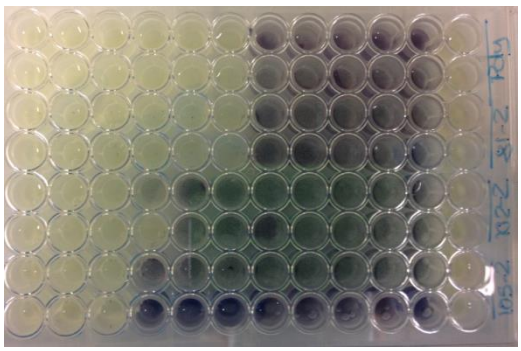


Figure S3: Broth Microdilution Method to determine the MIC values of **62b**, **56b**, **39b** against *Pseudomonas aeruginosa*; 2-fold dilution series starting from 256 µg/mL(left side). Polymyxin B (dilution starting from 64 µg/mL) was used as a reference (raw A-B). Raw 11 is used as growing control without compound (w/o) and raw 12 is used as a negative. All measurements were performed in duplicates after many repetitions.

2.2 *Pseudomonas aeruginosa* Biofilm Inhibition and Dispersal on Polystyrene Microtiter Plates

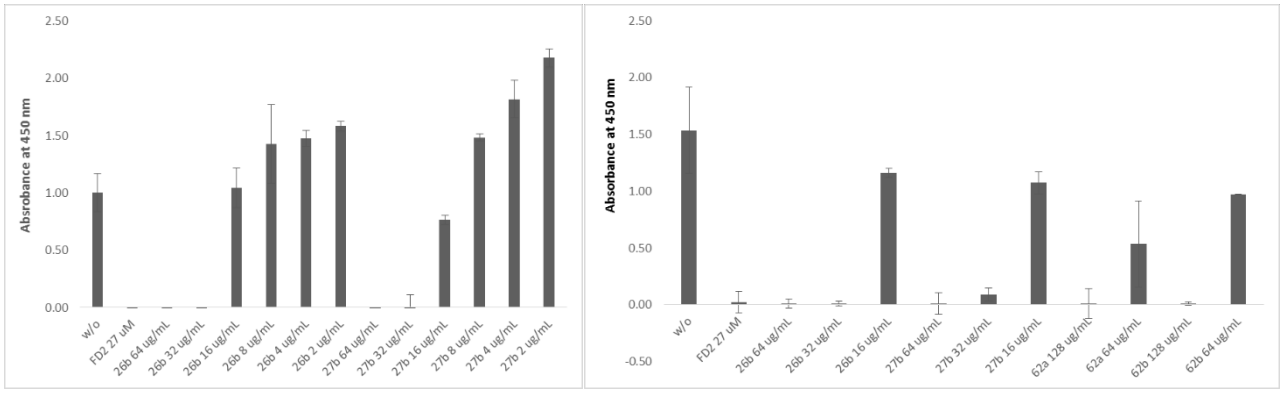


Figure S4: Inhibition of *Pseudomonas aeruginosa* strain PA01 biofilms by bicyclic peptides. **26b**, **27b**, **62a**, **62b**. All measurements were performed in triplicates. The minimum inhibition concentration (MBIC) is defined as the lowest concentration causing complete biofilm inhibition. Data are mean ± SD.

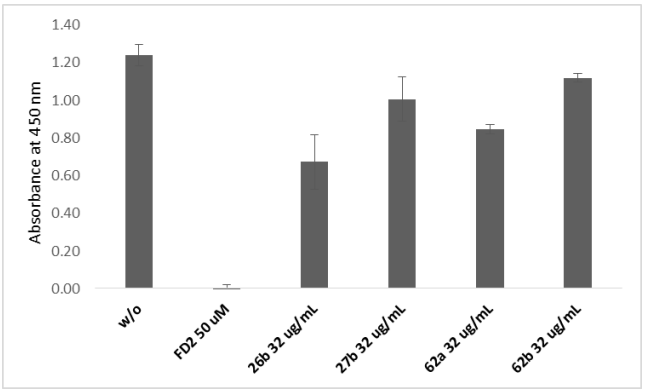


Figure S5: Dispersal of *Pseudomonas aeruginosa* strain PA01 biofilms. All measurements were performed in triplicates. Dispersal efficiency of the compounds was calculated in relation to the control. Data are mean ± SD.

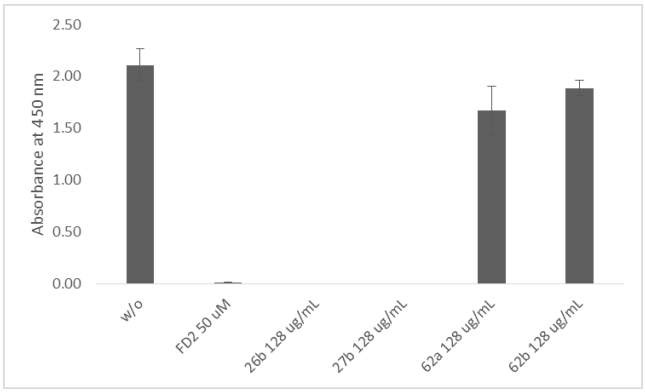


Figure S6: Dispersal of *Pseudomonas aeruginosa* strain PA01 biofilms. All measurements were performed in triplicates. Dispersal efficiency of the compounds was calculated in relation to the control. Data are mean ± SD.

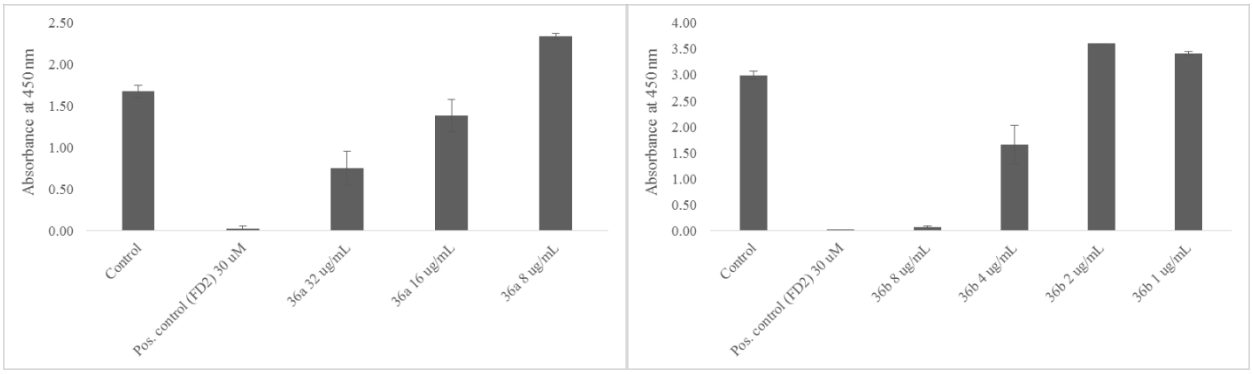


Figure S7: Inhibition of *Pseudomonas aeruginosa* strain PA01 biofilms by bicyclic peptides **36a** and **36b**. All measurements were performed in triplicates. The minimum inhibition concentration (MBIC) is defined as the lowest concentration causing complete biofilm inhibition. Data are mean ± SD.

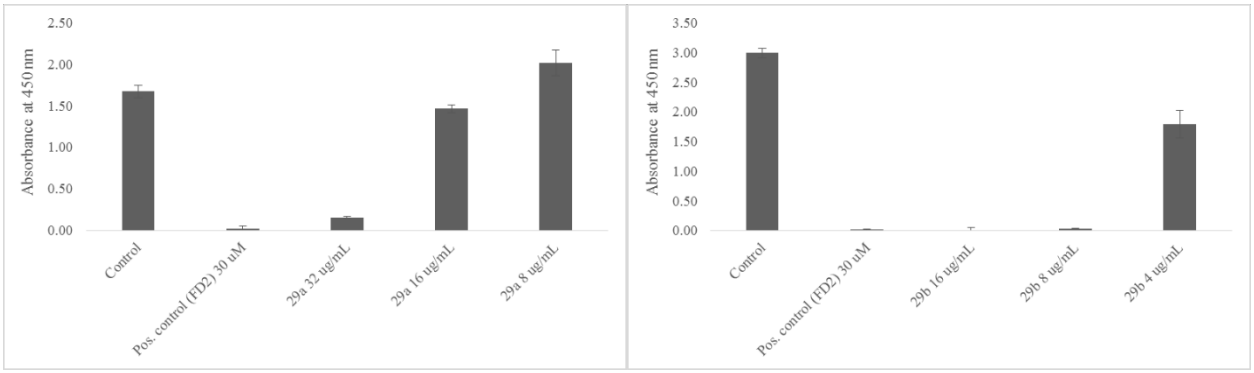


Figure S8: Inhibition of *Pseudomonas aeruginosa* strain PA01 biofilms by bicyclic peptides **29a** and **29b**.All measurements were performed in triplicates. The minimum inhibition concentration (MBIC) is defined as the lowest concentration causing complete biofilm inhibition. Data are mean ± SD.

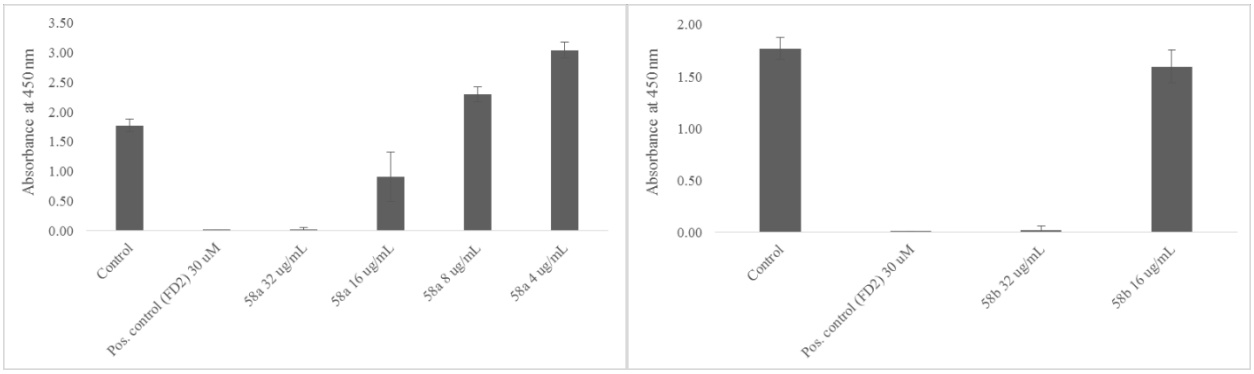


Figure S9: Inhibition of *Pseudomonas aeruginosa* strain PA01 biofilms by **58a** and **58b**. All measurements were performed in triplicates. The minimum inhibition concentration (MBIC) is defined as the lowest concentration causing complete biofilm inhibition. Data are mean ± SD.

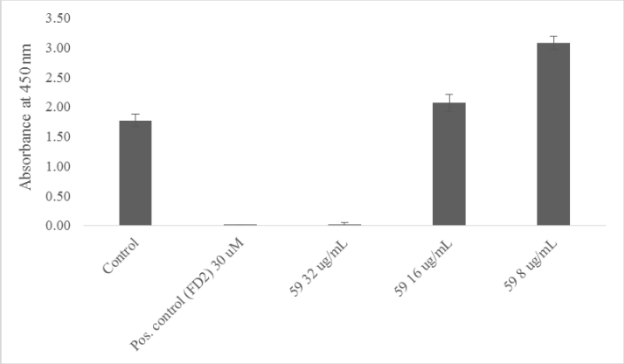


Figure S10: Inhibition of *Pseudomonas aeruginosa* strain PA01 biofilms by **59**. All measurements were performed in triplicates. The minimum inhibition concentration (MBIC) is defined as the lowest concentration causing complete biofilm inhibition. Data are mean ± SD.

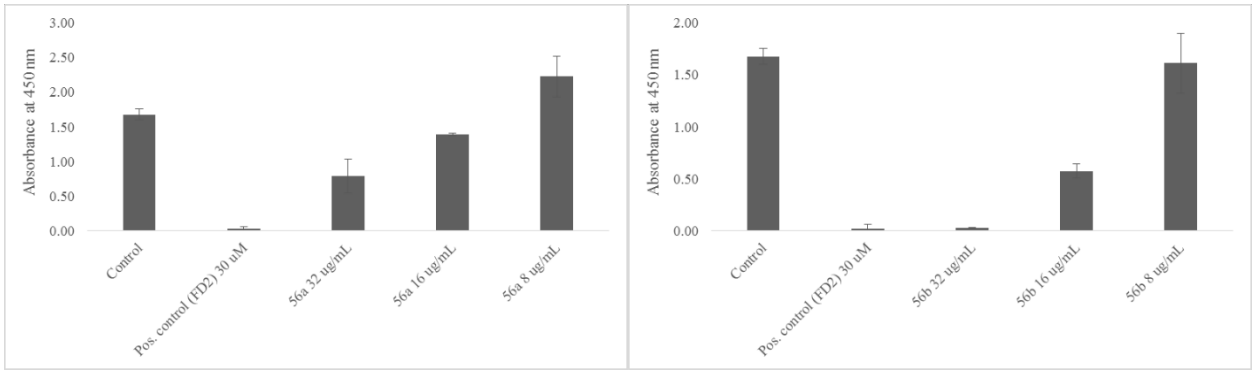


Figure S11: Inhibition of *Pseudomonas aeruginosa* strain PA01 biofilms by **56a** and **56b**. All measurements were performed in triplicates. The minimum inhibition concentration (MBIC) is defined as the lowest concentration causing complete biofilm inhibition. Data are mean ± SD.

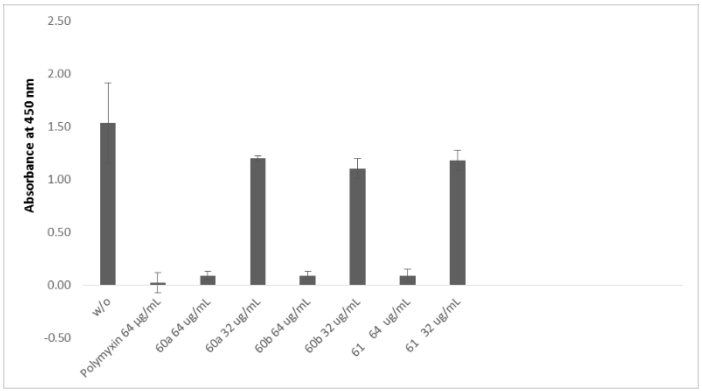


Figure S12: Inhibition of *Pseudomonas aeruginosa* strain PA01 biofilms by **60a**, **60b and 61**. All measurements were performed in triplicates. The minimum inhibition concentration (MBIC) is defined as the lowest concentration causing complete biofilm inhibition. Data are mean ± SD.

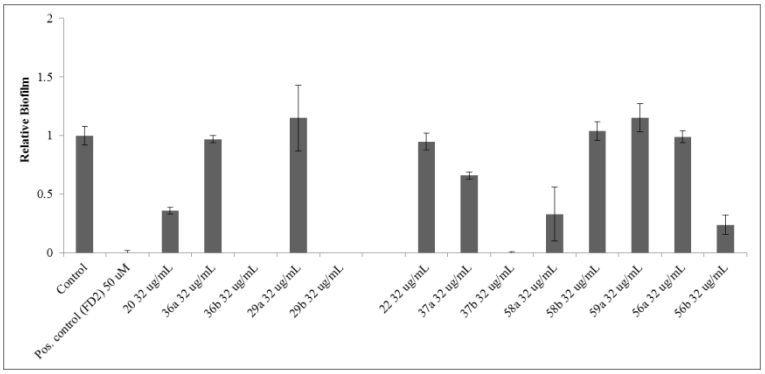


Figure S13: Dispersal of *Pseudomonas aeruginosa* strain PA01 biofilms. All measurements were performed in triplicates. The control was set up to a value of 1. Dispersal efficiency of the compounds was calculated in relation to the control. Data are mean ± SD.

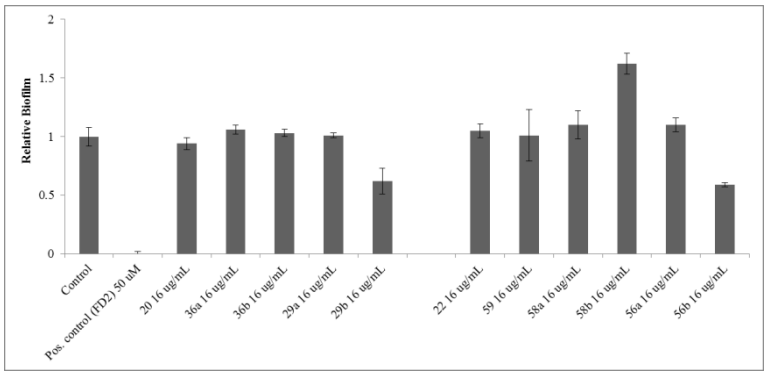


Figure S14: Dispersal of Pseudomonas aeruginosa strain PA01 biofilms. All measurements were performed in triplicates. The control was set up to a value of 1. Dispersal efficiency of the compounds was calculated in relation to the control. Data are mean ± SD.

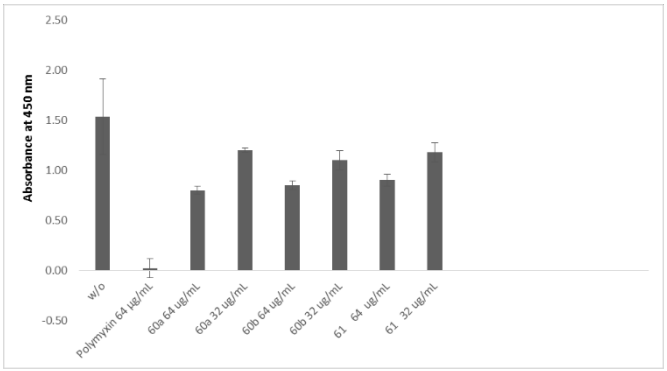


Figure S15: Dispersal of *Pseudomonas aeruginosa* strain PA01 biofilms. All measurements were performed in triplicates. Dispersal efficiency of the compounds was calculated in relation to the control. Data are mean ± SD.

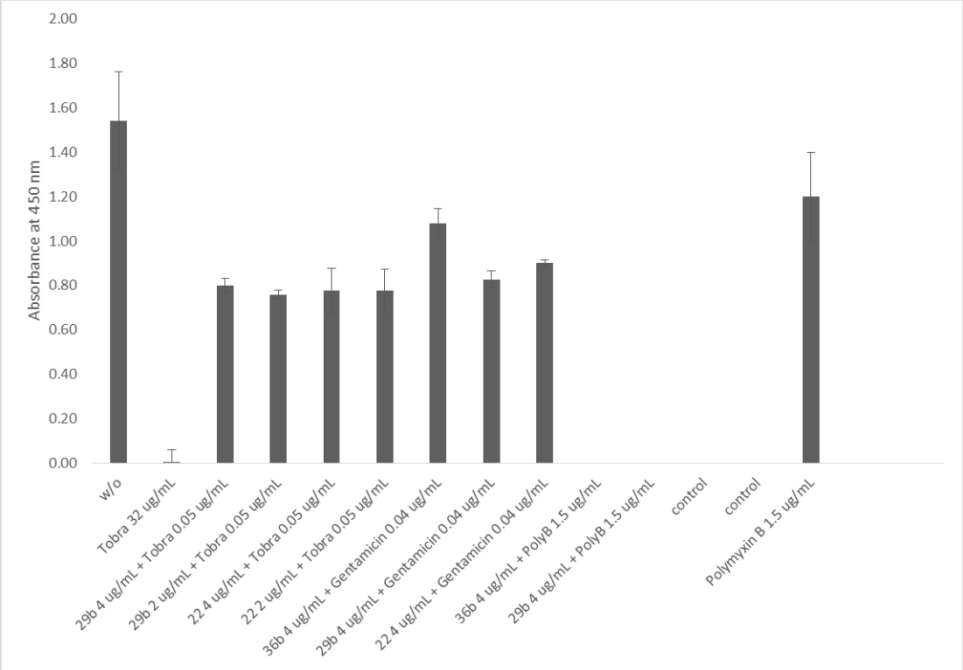


Figure S16: Inhibition of *Pseudomonas aeruginosa* strain PA01 biofilms by **36b**, **29b** and **22** in synergy with 0.05 µg/mL **Tobramycin** and 0.04 µg/mL **Gentamicin** or **Polymyxin B**. All measurements were performed in triplicates. The minimum inhibition concentration (MBIC) is defined as the lowest concentration causing complete biofilm inhibition. Data are mean ± SD.

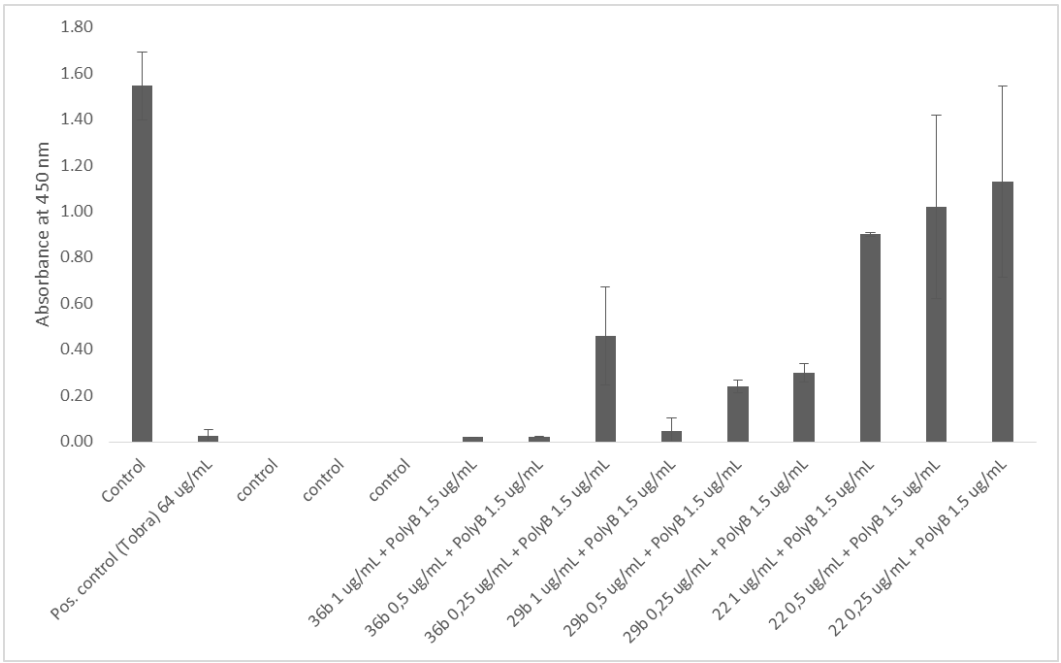


Figure S17: Inhibition of *Pseudomonas aeruginosa* strain PA01 biofilms by **36b**, **29b** and **22** in synergy with 1.5µg/mL **Polymyxin B**. All measurements were performed in triplicates. The minimum inhibition concentration (MBIC) is defined as the lowest concentration causing complete biofilm inhibition. Data are mean ± SD.

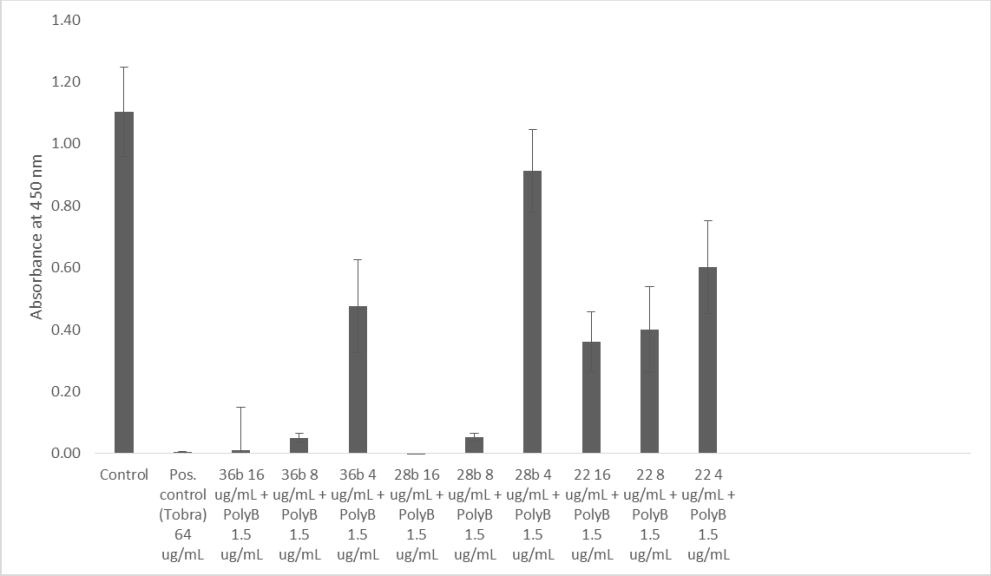


Figure S18: Dispersal of *Pseudomonas aeruginosa* strain PA01 biofilms. All measurements were performed in triplicates. Dispersal efficiency of the compounds was calculated in relation to the control. Data are mean ± SD

3. *Membrane interaction experiment*

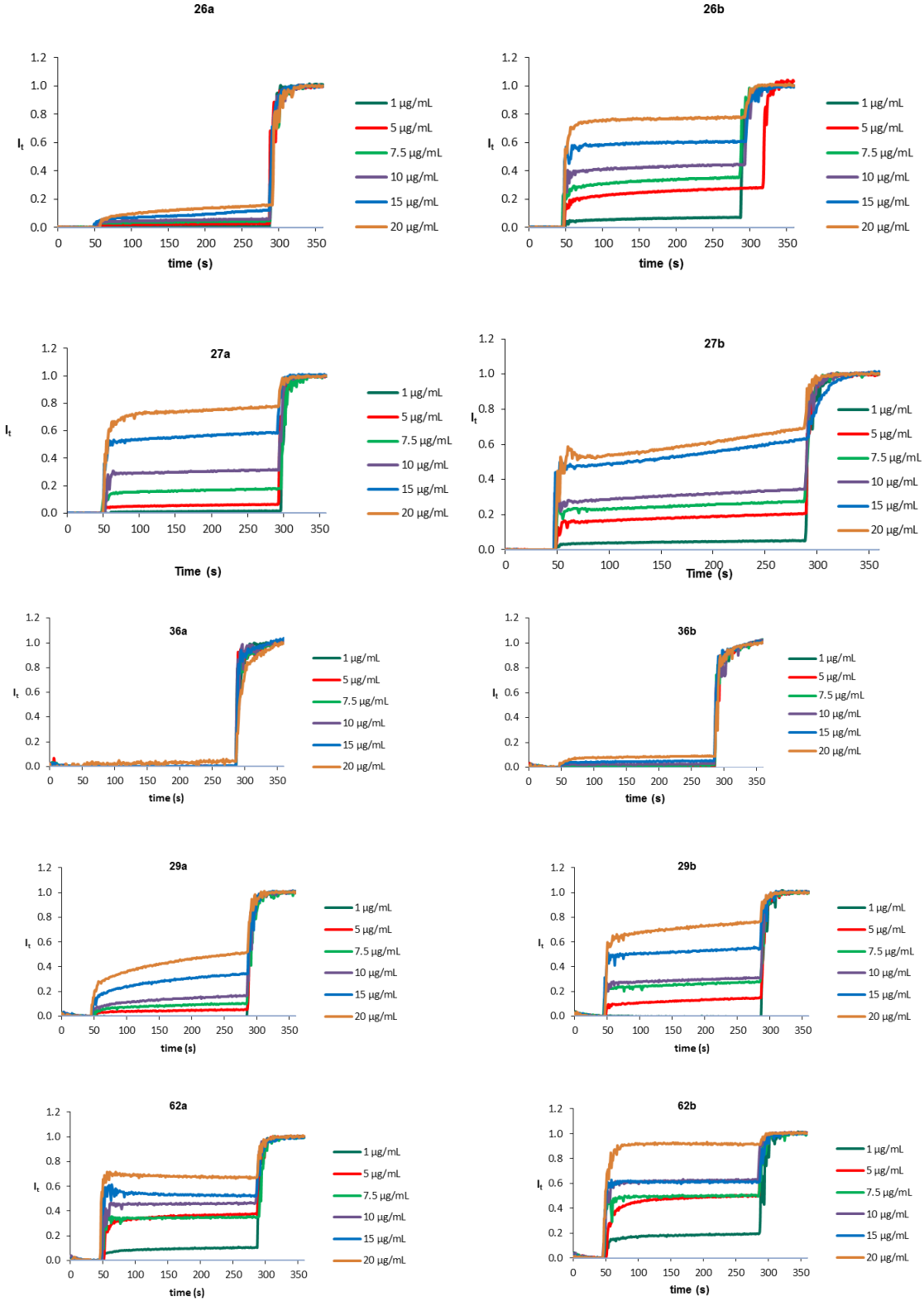


Figure S19: Membrane PG interaction experiment. Time in seconds (x-axis) and absorbance intensity (y-axis).

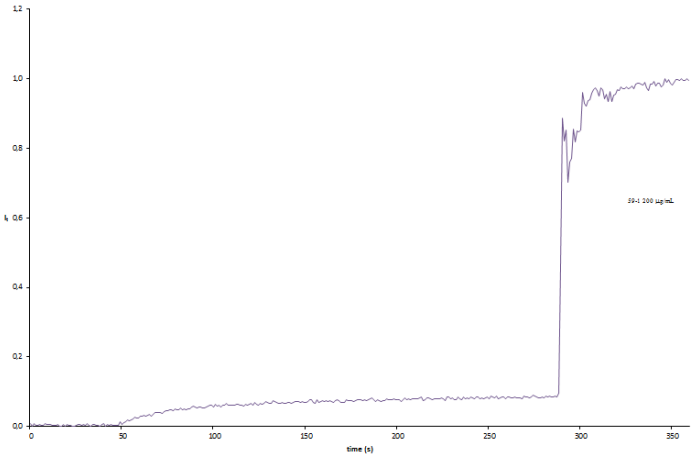


Figure S20: Membrane PC interaction experiment of **27a** (200µg/mL). Time in seconds (x-axis) and absorbance intensity (y-axis).

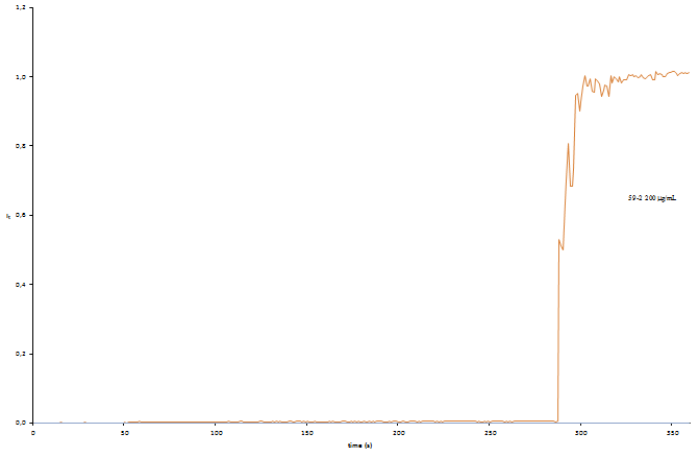


Figure S21 : Membrane PC interaction experiment of **27b** (200µg/mL). Time in seconds (x-axis) and absorbance intensity (y-axis).

4. TEM Transmission Electron Microscopy

The effects of the active compounds studied on the cell morphology of *Pseudomonas aeruginosa* were observed via transmission electron microscopy (TEM). Untreated *Pseudomonas aeruginosa* in M63 minimal medium showed a normal cell shape and undamaged structure of the inner and outer membrane. When *Pseudomonas aeruginosa* was incubated with polymyxin B as a control (20 µg/ml: 10x MIC for 30 min.), protrusions were observed at the outer cell membrane (figure S26B). Similarly, **62b** and **27b** induced notable protrusions of the bacterial cell membranes (figure S26C and figure S26D). The formation of blebs on the bacterial surface was similar to those induced by polymyxin B. Additionally, TEM images showed some alterations in the internal structures with a collapsed cytoplasm.

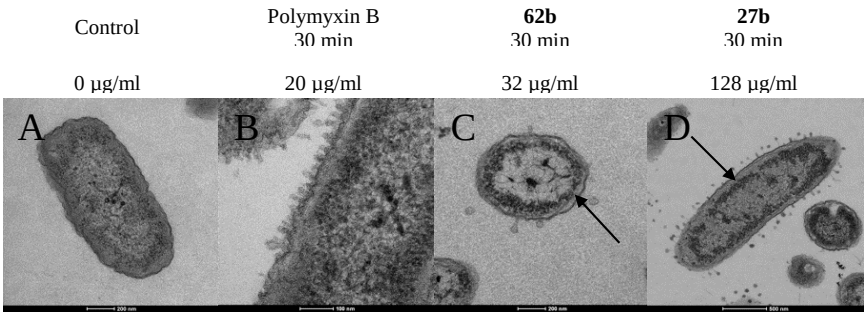


Figure S22: Morphology of *Pseudomonas aeruginosa* after treatment with the active compounds. A. Untreated *Pseudomonas aeruginosa* B. Treatment with 20 µg/ml of polymyxin B. C. Treatment with 32 µg/ml of **62b**. D. Treatment with 128 µg/ml of **27b**.

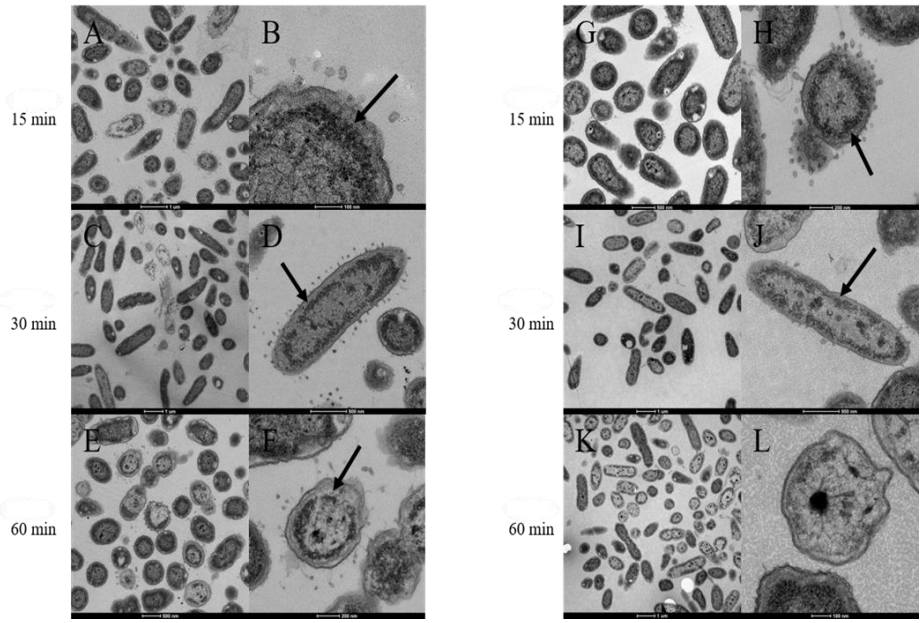
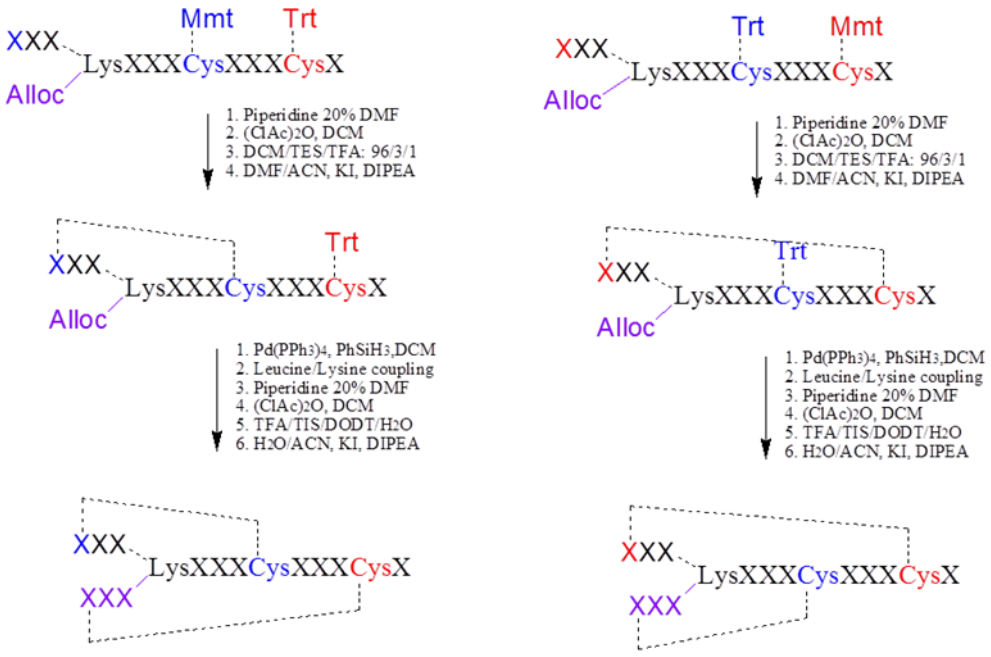


Figure S23: 27b (left) and **62b** (right) as Membrane Disruptive Compounds at different times. TEM pictures of treated *Pseudomonas aeruginosa*. Perturbations were observed on bacterial surfaces. Distinction of the outer and inner membrane was also observed probably due to leakage of cellular material from the cytoplasm (arrows). A and B. **27b** treatment for 15 min. C and D.**27b** treatment for 30 min. E and F. **27b** treatment for 60 min. G and H. 62b (bold) treatment for 15 min. I and J.**62b** treatment for 30 min. K and L.**62b** treatment for 60 min. A clear deformation at the bacterial cell membranes was observed.

5. Selective synthesis



Scheme S1: Scheme of the selective synthesis. In violet the side chain of the branching lysine, X= leucine/lysine

6. Crystallization

Table S5. Crystallographic Data.

Structural data	**63a.**LecB	**63b.**LecB	**64a.**LecB
Beam line	PX-III	PX-III	PX-III
Wavelength(Å)	1.000040	1.000040	0.999990
Resolution(Å)	48.16 - 2.13	48.27 – 1.89	47.23 – 1.17
Cell dimension			
Space group	P 1 21 1	P 1 21 1	C 1 2 1
Unit cell(Å)	48.31, 79.36, 52.58, 90, 94.46, 90	48.42, 79.20, 52.63, 90, 94.52, 90	94.41, 45.77, 88.06, 90, 94.24, 90
Measured reflection/unique	75055/21998	104989/31514	388462/125097
Average multiplicity	3.41	3.33	3.10
Completeness (%)	94.24	94.6	97.2
Average I/σ(I)	7.66	6.13	17.74
Correlation CC (1/2) (%)	98.9	98.3	99.9
Wilson B-factor	16.9	13.5	11.6
Refinement			
Resolution range (Å)	48.16 - 2.13	48.27 – 1.89	47.23 – 1.17
R_{work} (%)	0.174	0.176	0.132
R_{free} (%)	0.223	0.222	0.157
Average Biso (Å^2)	19.0	16.0	16.5
All atoms	3655	3757	3890
Solvent atoms	240	328	456
RMSD from ideality angles (°)	0.832	0.884	1.160
Bonds (Å)	0.004	0.006	0.009
Protein Data Bank deposition code	5I8M	5I8X	5NGQ

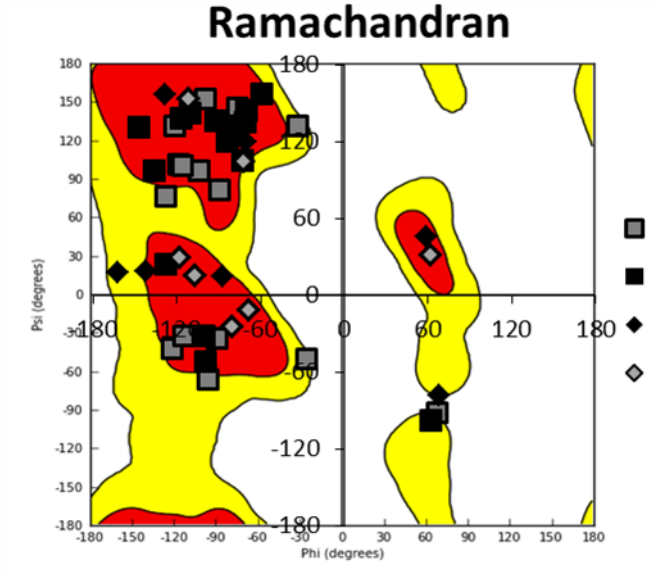


Figure S24. Ramachandran plot of **63a** and **63b** crystal structures and averaged MD structures of **27a** and **27b** (see below). The majority of the points is located in the most preferred regions (red) for beta-sheets and for alpha-helices.

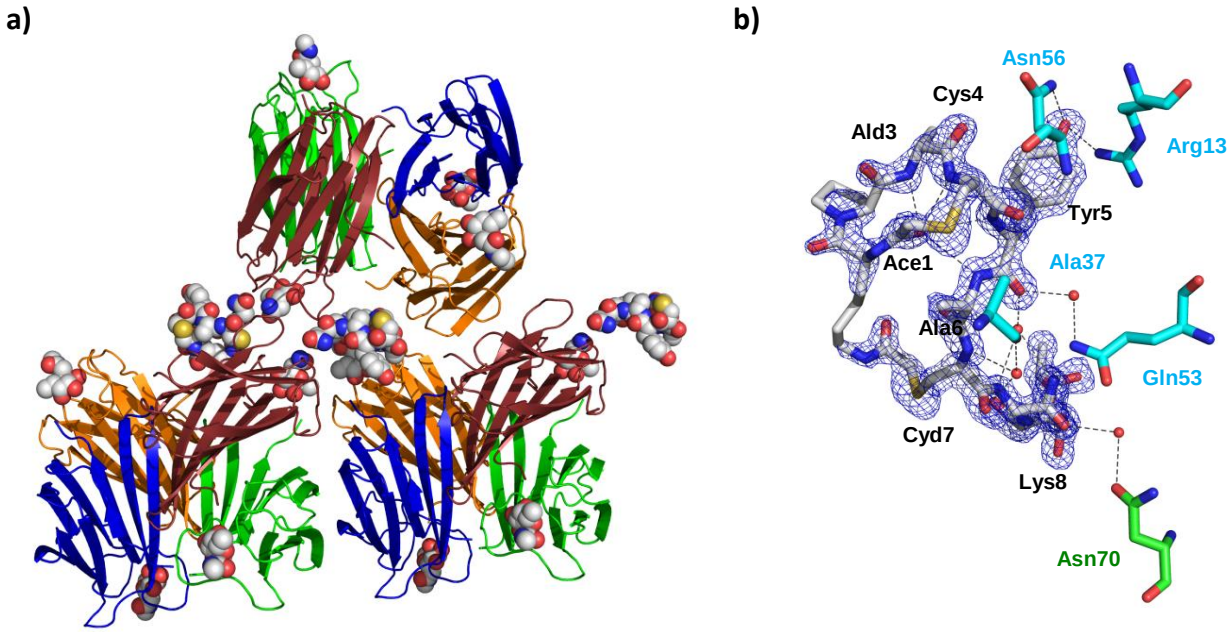


Figure S25. a) **64a.**LecB overview of several tetramers .The two symmetric copies of the bicycles are 10 A^0 distance with no contact between the two copies. Every tetramer contains also in this case just one copy of the bicycle. b) **64a.**LecB with all contacts. In this case hydrogen bridges are formed to the different monomers of the crystal. Ace1 is forming hydrogen bridges with the backbone of Ald3, Cys4 and Ala6. Additionally internal hydrogen bonds over 2 crystallographic waters are formed from Tyr5 to Lys8.

7. Molecular Dynamics

Table S6. Clustering of MD structures of **27a** and **27b**.

27a	10001 structures total	**27b**	10001 structures total
# of clusters	**# struct. in 1st cluster**	**# of clusters**	**# struct. in 1st cluster**
495	7679	707	7220
384	9078	333	8865
831	5294	235	8562
544	8347	1217	6390
423	9026	659	8488

Table S7. RMSD statistics. For each isomer, one of the five structures (middle of the main cluster for each SA-MD run) was chosen as a representative structure for that isomer. The chosen conformers were **27a** conformer 4 and **27b** conformer 3. As a quantitative measurement of the dissimilarity between the two isomers, the RMSD (backbone-backbone) of all the structures were computed against each of the two representative structures. For each isomer, the conformations at 300 K are closely related while being clearly distinct from the conformations adopted by the other isomer.

27a representative		**27b representative**	
RMSD vs **27a**	RMSD vs **27b**	RMSD vs **27a**	RMSD vs **27b**
0.1605170	0.6448520	0.5800744	0.1698346
0.0553145	0.7565612	0.5519930	0.3689211
0.4356027	0.5503745	0.6090052	N/A
N/A	0.7526465	0.5503745	0.3541467
0.0490695	0.6932683	0.5526662	0.3039081
Average RMSD (nm)			
0.175	**0.680**	**0.569**	**0.299**

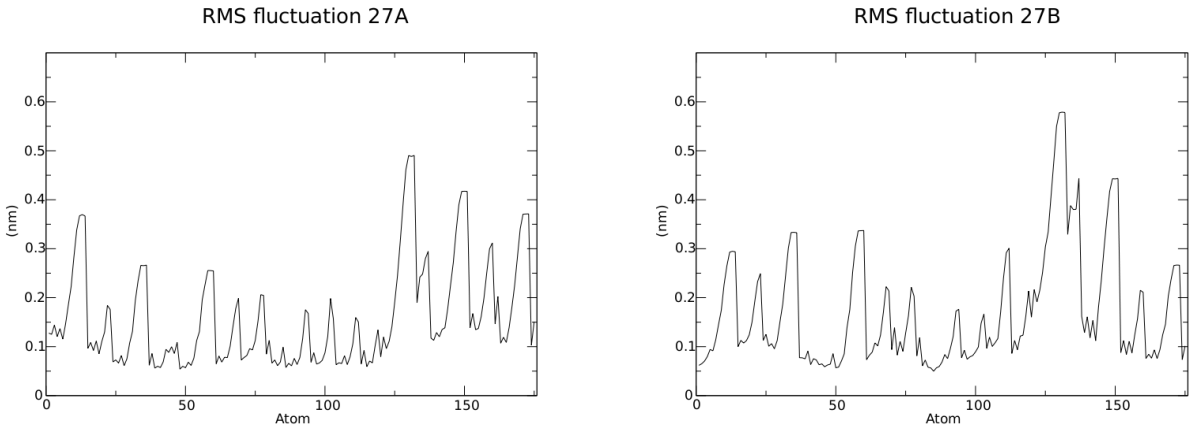


Figure S26. Analysis of backbone flexibility. The root mean square fluctuation over the last 100 ns of the trajectory is shown for each atom in the molecule for the representative conformer. The seesaw shape of the graphs derives from the more flexible atoms of the side chains alternating with the comparatively rigid backbone in the structure.

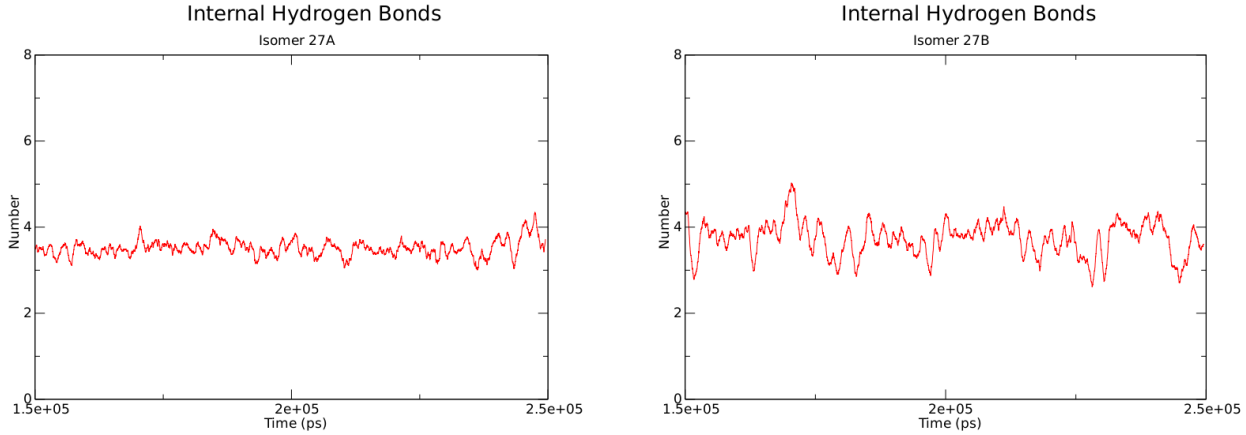


Figure S27. Analysis of internal H-bonds. Several stable internal hydrogen bonds contribute to the stability of the backbone structure. Approximately, four H-bonds are found along the SA-MD trajectories all of the conformers of **27a** and **27b**.

Parameters for non-natural amino acids

The model for the bicyclic peptide was built by merging the topologies of two peptides of identical sequence with different connectivity at the branching lysine. In the first peptide, the lysine had a normal connectivity (LSA) while the in the second peptide the chain was extended using the side chain nitrogen of the lysine (LSB). After merging the files, a branched peptide was obtained and bonds were added between the alkylated cysteine residues (CYX) and the corresponding acetyl residues (ACC) leading to the final desired topology. The parameters for the four non-natural residues of the Gromos53a6 force field (aminoacids.rtp) were derived from the existing amino acids. They were defined as follows.

```
[ LSA ] ; based on LYS, corrected for 53a6 FF

[ atoms ]

   N     N    -0.31000     0
   H     H     0.31000     0
  CA   CH1     0.00000     1
  CB   CH2     0.00000     1
  CG   CH2     0.00000     2
  CD   CH2     0.00000     2
  CE   CH2     0.00000     2 ; charge group 2
  NZ     N    -0.31000     3 ; NZ is now a peptide N
  HZ     H     0.31000     3 ; only one H
   C     C       0.450     4
   O     O      -0.450     4
 [ bonds ] ;
   N     H    gb_2
   N    CA    gb_21
  CA     C    gb_27
   C     O    gb_5
   C    +N    gb_10
  CA    CB    gb_27
  CB    CG    gb_27
  CG    CD    gb_27
  CD    CE    gb_27
  CE    NZ    gb_21   ; no change CHn - Nitrogen (all)
  NZ    HZ    gb_2
 [ angles ] ;
;  ai    aj    ak   gromos type
  -C     N     H     ga_32
   H     N    CA     ga_18
  -C     N    CA     ga_31
   N    CA     C     ga_13
  CA     C    +N     ga_19
```

```
   CA     C     O     ga_30
    O     C    +N     ga_33
    N    CA    CB     ga_13
    C    CA    CB     ga_13
   CA    CB    CG     ga_15
   CB    CG    CD     ga_15
   CG    CD    CE     ga_15
   CD    CE    NZ     ga_13 ; CHn - CHn - N
   CE    NZ    HZ     ga_18 ; H - N - CHn
 [ impropers ] ; no change in LSA, has to be defined in LSB
;  ai    aj    ak    al   gromos type
    N    -C    CA     H     gi_1
    C    CA    +N     O     gi_1
   CA     N     C    CB     gi_2
 [ dihedrals ]
;  ai    aj    ak    al   gromos type
  -CA    -C     N    CA     gd_14 ;     -C-N,NT,NE,NZ,NR-
   -C     N    CA     C     gd_39 ;         -CHn-N,NE-
    N    CA     C    +N     gd_40 ;        -CHn-C,NR (ring), CR1-
    N    CA    CB    CG     gd_34 ;      -CHn,SI-CHn-
   CA    CB    CG    CD     gd_34 ;
   CB    CG    CD    CE     gd_34 ;
   CG    CD    CE    NZ     gd_34 ;
   CD    CE    NZ    HZ     gd_39   ; - CHn - N -

[ LSB ] ; based on LYS, corrected for 53a6 FF
 [ atoms ]
   NZ     N    -0.31000     3 ; ex-N, charge standard N
   HZ     H     0.31000     3 ; only one H
   CE   CH1     0.00000     2 ; ex-CA charge group 2
   CD   CH2     0.00000     2 ; ex-CB
   CG   CH2     0.00000     2
   CB   CH2     0.00000     1 ; ex-CD
   CA   CH2     0.00000     1 ; ex-CE
    N     N    -0.31000     0 ; ex-NZ
    H     H     0.31000     0 ; ex-HZ
    C     C       0.450     4
    O     O      -0.450     4
 [ bonds ] ;
    N     H    gb_2
    N    CA    gb_21
   CE     C    gb_27   ; ex-CA
    C     O    gb_5
    C    +N    gb_10
   CA    CB    gb_27
   CB    CG    gb_27
   CG    CD    gb_27
   CD    CE    gb_27
   CE    NZ    gb_21   ; all Nitrogens
   NZ    HZ    gb_2    ; only one H
```

```
 [ angles ]
;  ai    aj    ak   gromos type
   -C     N     H     ga_32
    H     N    CA     ga_18
   -C     N    CA     ga_31
   NZ    CE     C     ga_13   ; CA->CE, N->NZ
   CE     C    +N     ga_19   ; CA -> CE
   CE     C     O     ga_30   ; CA -> CE
    O     C    +N     ga_33
    N    CA    CB     ga_13
   NZ    CE    CD     ga_13   ;
   CA    CB    CG     ga_15
   CB    CG    CD     ga_15
   CG    CD    CE     ga_15
   CD    CE     C     ga_13
   CE    NZ    HZ     ga_18   ; NZ type N
 [ impropers ]
;  ai    aj    ak    al   gromos type
    N    -C    CA     H     gi_1
    C    CE    +N     O     gi_1    ; C is next to CE in LSB
   CE    NZ     C    CG     gi_2    ; tetrahedral
 [ dihedrals ]
;  ai    aj    ak    al   gromos type
  -CA    -C     N    CA     gd_14
   -C     N    CA    CB     gd_39   ; C -> CB
    N    CA    CB    CG     gd_34
   CA    CB    CG    CD     gd_34
   CB    CG    CD    CE     gd_34
   CG    CD    CE    NZ     gd_34
   CD    CE    NZ    HZ     gd_39   ;
   CD    CE     C    +N     gd_40   ; - CHn - C - ,missing in the next AA
   CE     C    +N   +CA     gd_14    ; - C - N - , missing in the next AA since it looks for a CA in both
residues

[ CYX ]  ; derived from CYS1 and MET topologies
 [ atoms ]
    N     N    -0.31000     0
    H     H     0.31000     0
   CA   CH1     0.00000     1
   CB   CH2     0.24100     2
   SG     S    -0.48200     3
    C     C       0.450     4
    O     O      -0.450     4
 [ bonds ]
    N     H    gb_2
    N    CA    gb_21
   CA    CB    gb_27
   CA     C    gb_27
   CB    SG    gb_32
    C     O    gb_5
```

```
    C    +N    gb_10
 [ angles ]
;  ai    aj    ak   gromos type
   -C     N     H     ga_32
   -C     N    CA     ga_31
    H     N    CA     ga_18
    N    CA    CB     ga_13
    N    CA     C     ga_13
   CB    CA     C     ga_13
   CA    CB    SG     ga_16
   CA     C     O     ga_30
   CA     C    +N     ga_19
    O     C    +N     ga_33
 [ impropers ]
;  ai    aj    ak    al   gromos type
    N    -C    CA     H     gi_1
   CA     N     C    CB     gi_2
    C    CA    +N     O     gi_1
 [ dihedrals ]
;  ai    aj    ak    al   gromos type
  -CA    -C     N    CA     gd_14
   -C     N    CA     C     gd_39
    N    CA    CB    SG     gd_34
    N    CA     C    +N     gd_40

[ ACC ] ;
[ atoms ]
    CA   CH2   0.241     0
     C     C   0.450     1
     O     O  -0.450     1
 [ bonds ]
     C    CA   gb_27
     C     O   gb_5
     C    +N   gb_10
 [ angles ]
   CA     C     O    ga_30
   CA     C    +N    ga_19
    O     C    +N    ga_33
 [ impropers ]
    C    CA    +N     O    gi_1
```

8. FTIR

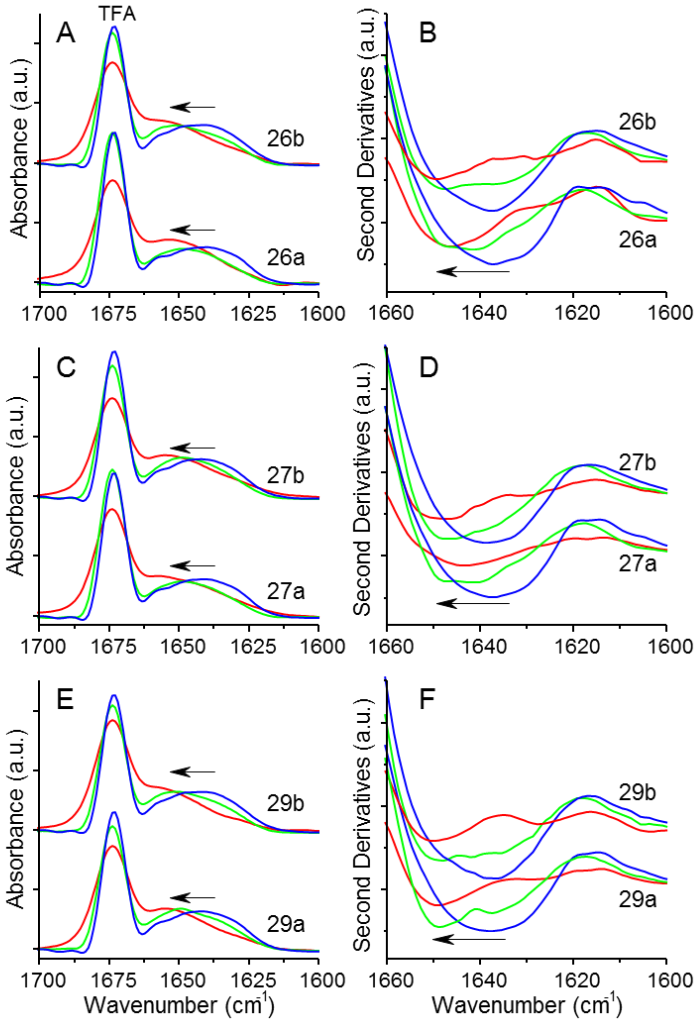
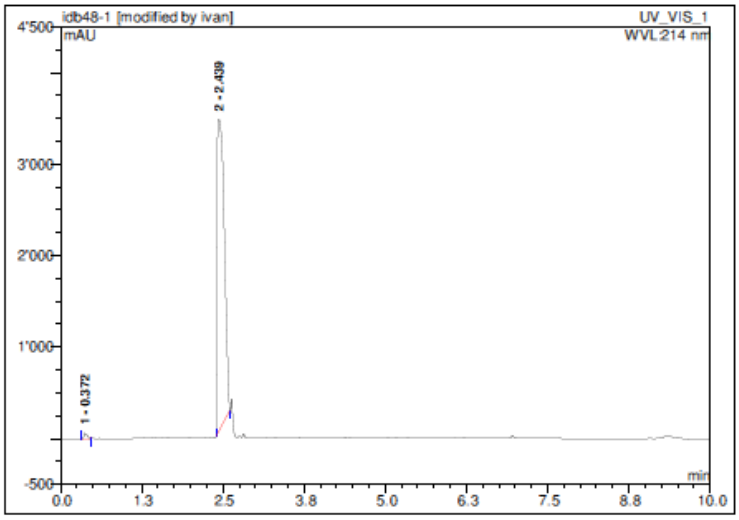
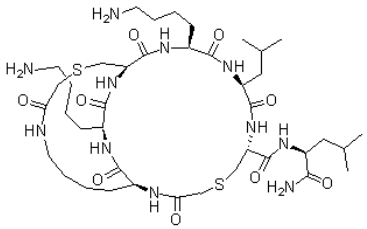


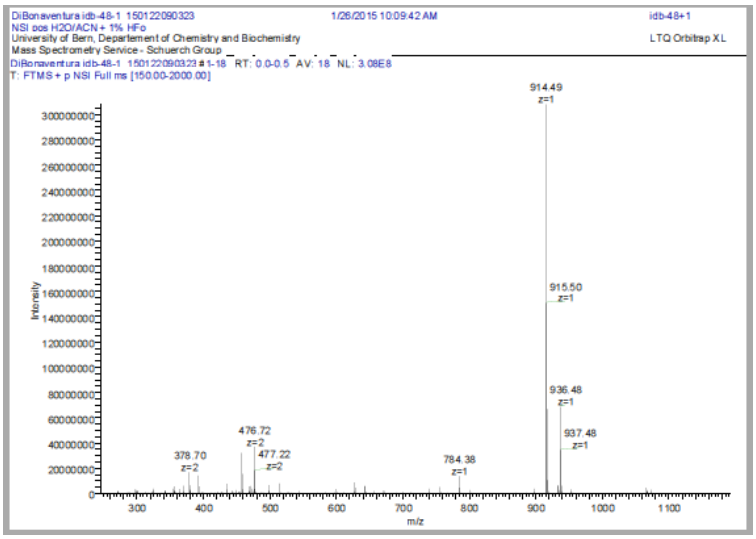
Figure S28: FTIR characterization of bridged bicyclic peptides **26a, 26b, 27a, 27b, 29a and 29b**. Fourier self-deconvoluted (A, C), and second derivative (B, D,) spectra of the bridged bicyclic peptides in D_2O/PBS at TFE concentrations of 0% (blue lines), 50% (green lines), and 90% (red lines).

9. HPLC and MS Data

$^{2}K(^{1})KZ^{1}KLZ^{2}L$ (1a) was obtained as foamy white solid after preparative RP-HPLC (24.4 mg, 18.5 %). Analytical RP-HPLC: t_R = 2.440 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{40}H_{71}N_{11}O_9S_2$ calc./obs. 914.49/914.49 Da $[M+H]^+$.

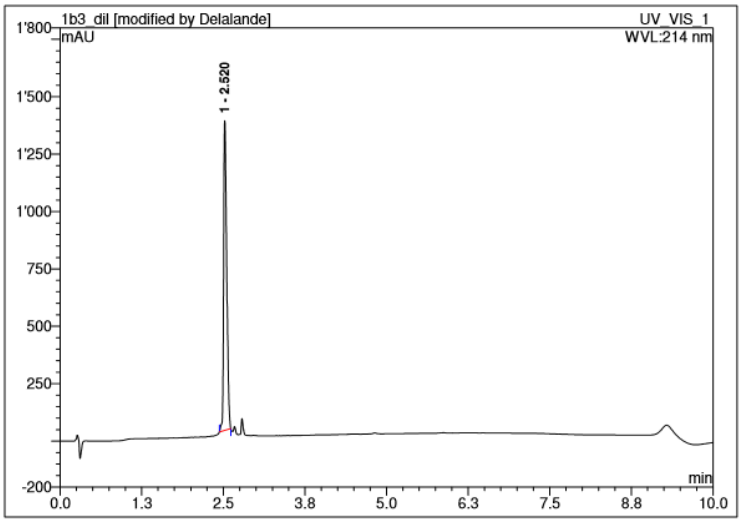


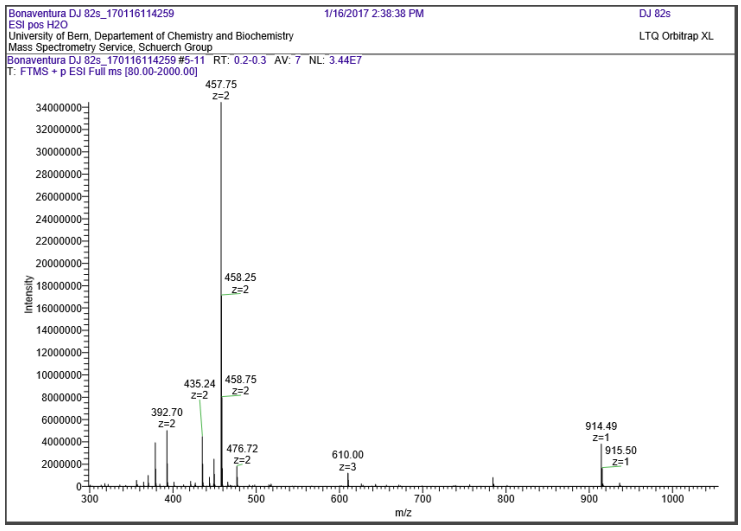




$^{2}K(^{1})KZ^{1}KLZ^{2}L$ (1a) was also obtained from the selective synthesis procedure as foamy white solid after preparative RP-HPLC (4.2 mg, 3.1 %). Analytical RP-HPLC: t_R = 2.540 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{40}H_{71}N_{11}O_9S_2$ calc./obs. 914.49/914.49 Da $[M+H]^+$.

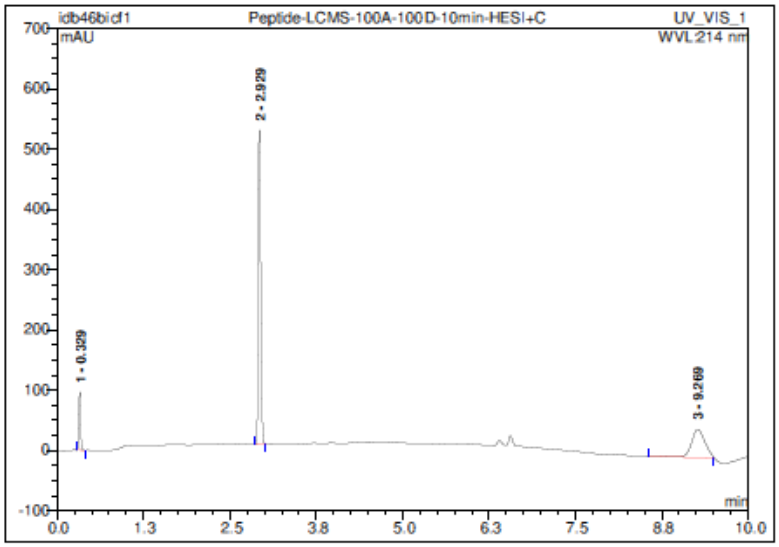
$^{1}K(^{2})KZ^{1}KLZ^{2}L$ (1b) was obtained as foamy white solid after preparative RP-HPLC (7.7 mg, 5.8 %). Analytical RP-HPLC: t_R = 2.520 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{40}H_{71}N_{11}O_9S_2$ calc./obs. 914.19/914.49 Da $[M+H]^+$.

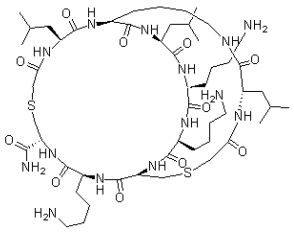


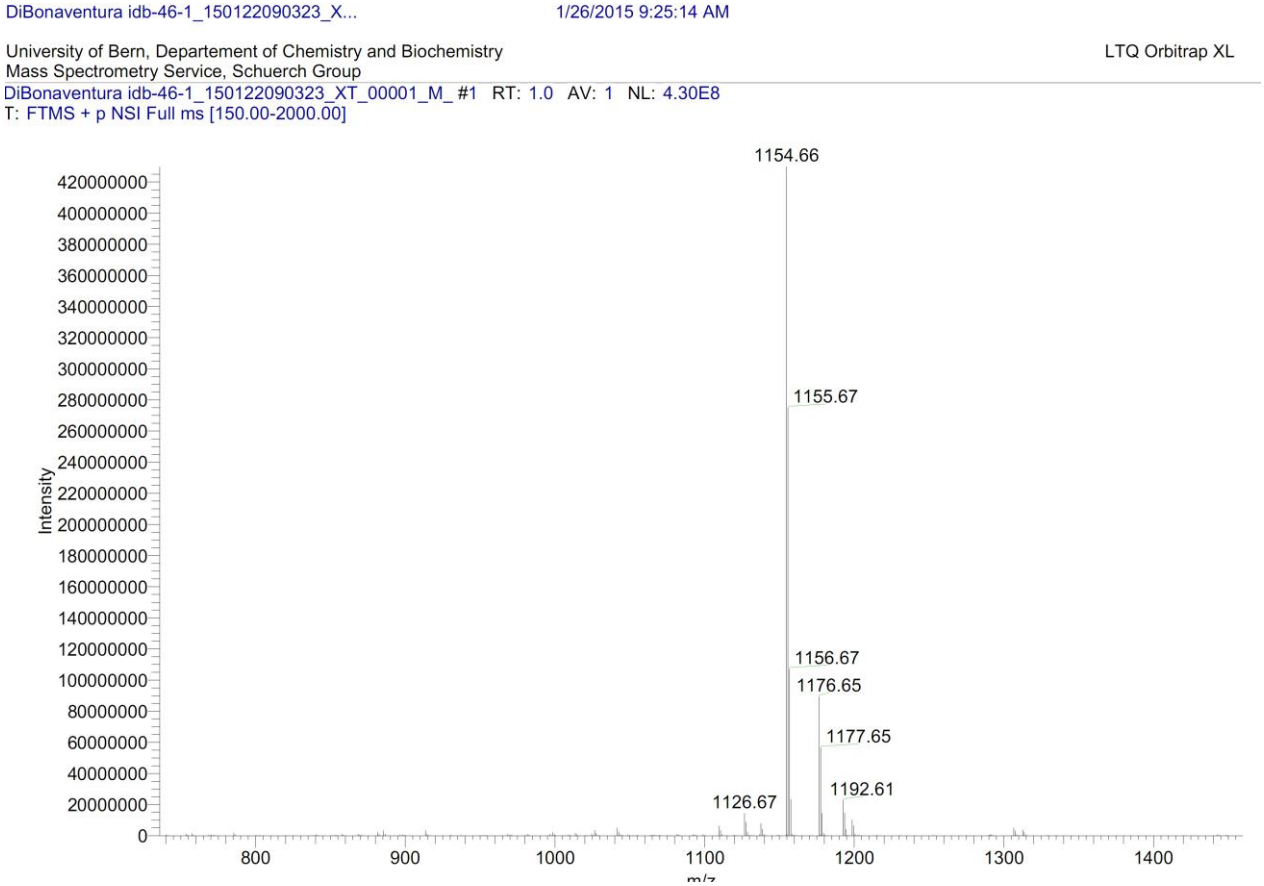


$^{1}K(^{2})KZ^{1}KLZ^{2}L$ (1b) was also obtained from the selective synthesis as foamy white solid after preparative RP-HPLC (6.4 mg, 4.5 %). Analytical RP-HPLC: t_R = 2.570 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{40}H_{71}N_{11}O_9S_2$ calc./obs. 914.19/914.49 Da $[M+H]^+$.

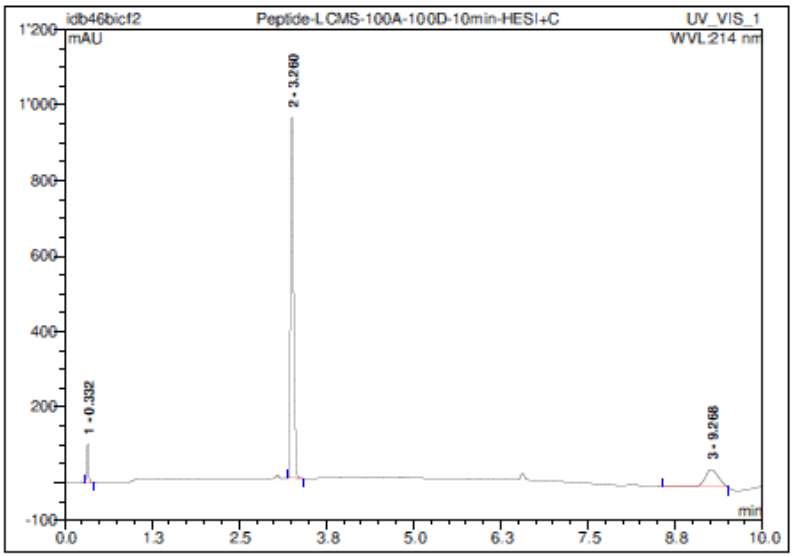
L^2*K*(L^1)LKK*Z*^{1}K*Z*^{2} (2a) was obtained as foamy white solid after preparative RP-HPLC (10.6 mg, 6.3 %). Analytical RP-HPLC: t_R = 2.930 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{52}H_{94}N_{14}O_{11}S_2$ calc./obs.1154.67/1554.66 Da [M].

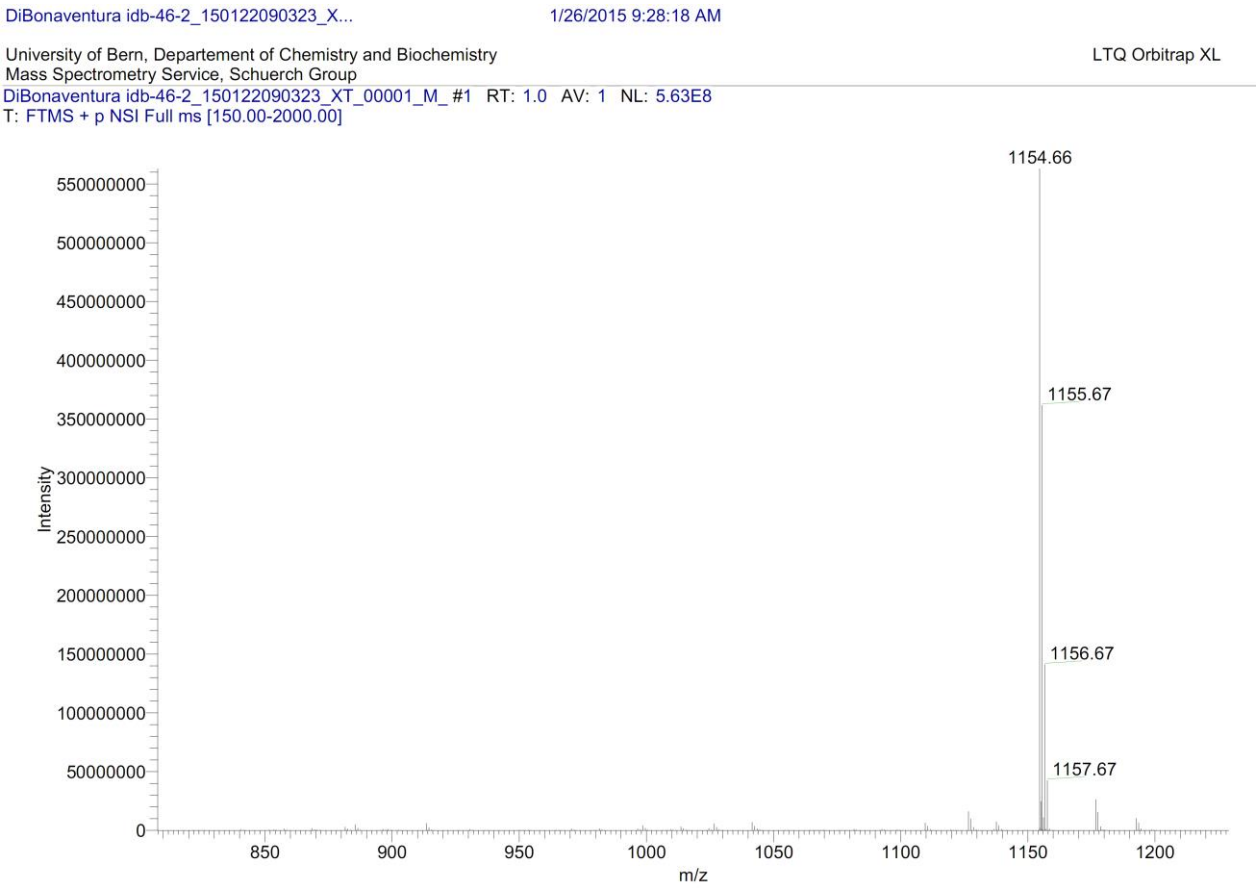




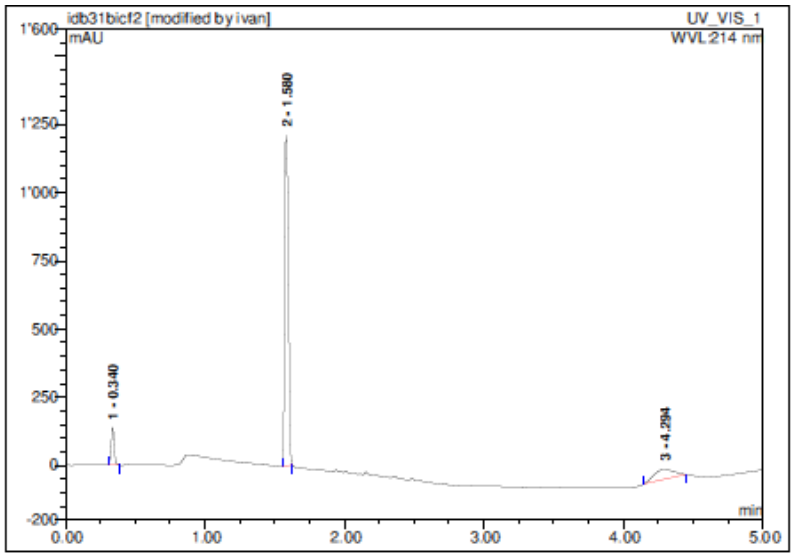


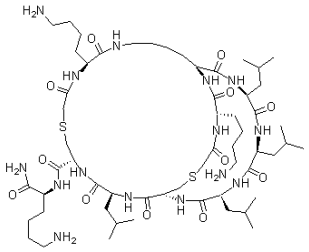
L[1]*K*(L[2])LKKZ[1]KZ[2] (2b) was obtained as foamy white solid after preparative RP-HPLC (38.0 mg, 22.8 %). Analytical RP-HPLC: t_R = 3.260 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{52}H_{94}N_{14}O_{11}S_2$ calc./obs.1154.67/1154.66 Da [M].

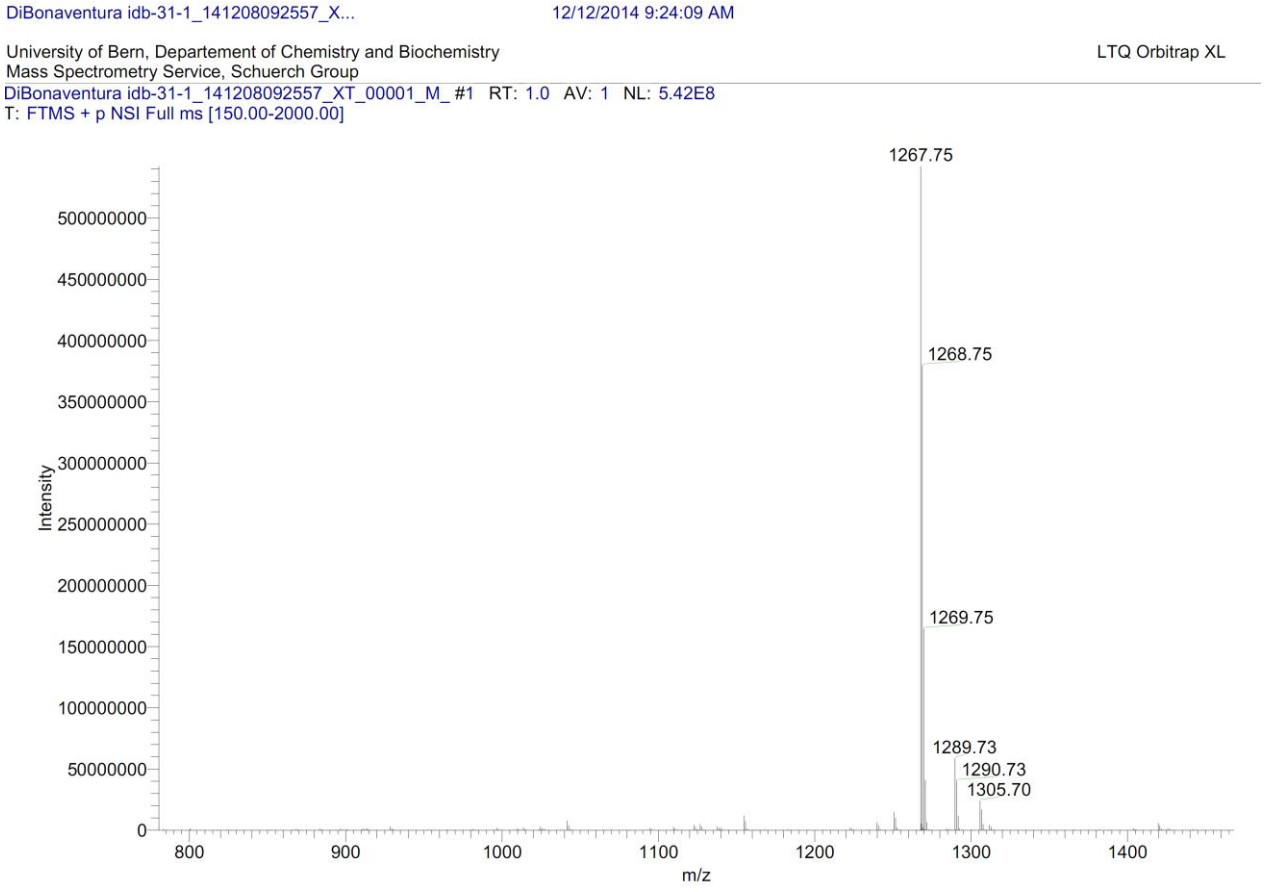




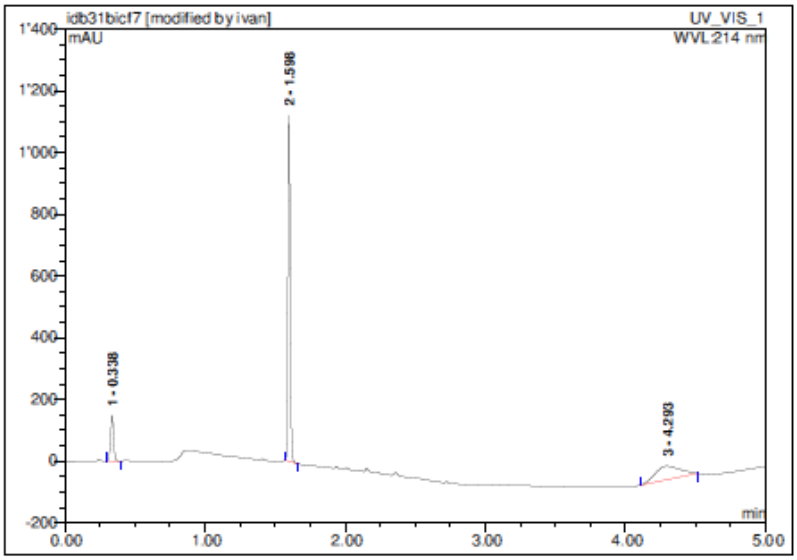
K^2*K*(K^1)LLL*Z*^{1}L*Z*^{2}K (3a) was obtained as foamy white solid after preparative RP-HPLC (17.9 mg, 9.8 %). Analytical RP-HPLC: t_R = 1.580 min (A/D 100:0 to 0:100 in 5.00 min, λ = 214 nm). MS (ESI+): $C_{58}H_{105}N_{15}O_{12}S_2$ calc./obs. 1267.75/1267.75 Da [M].

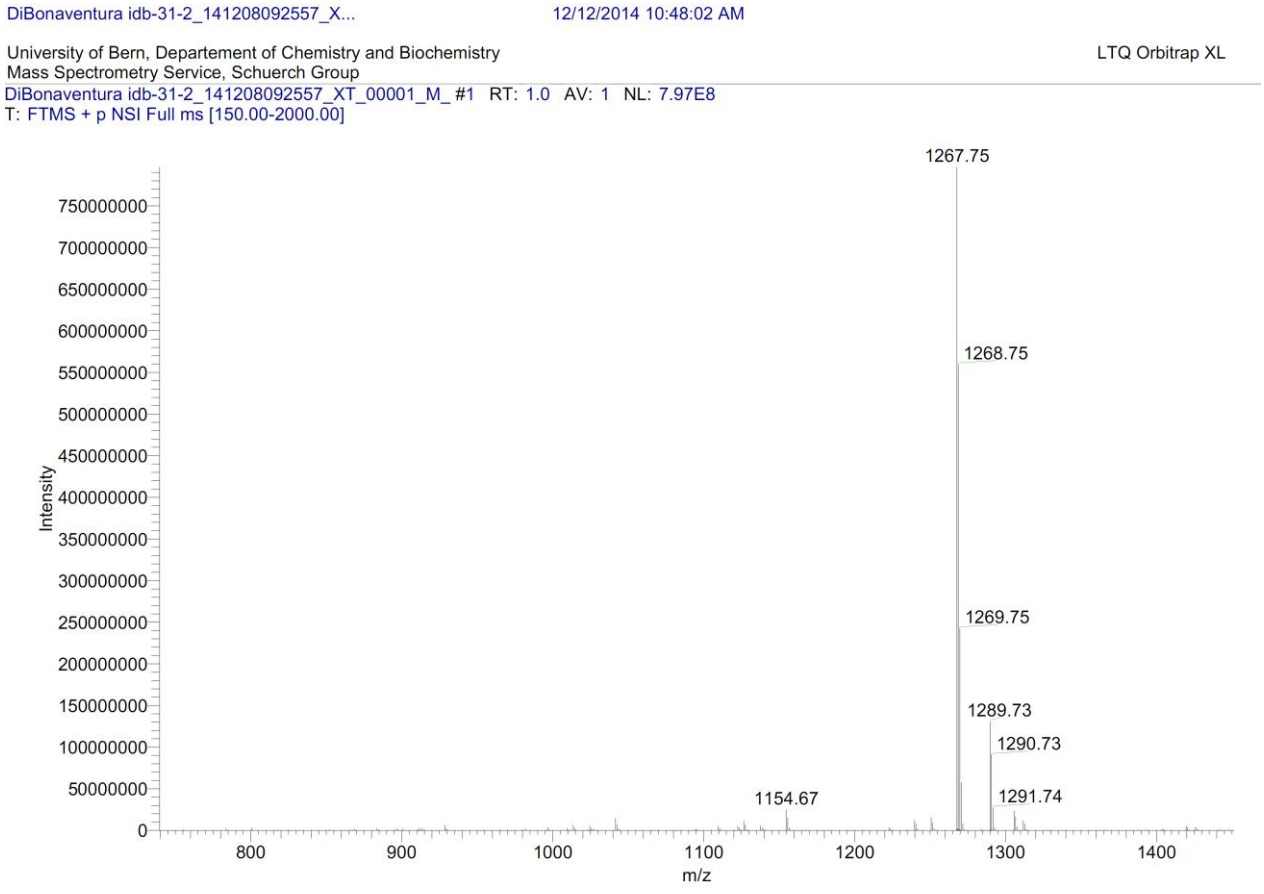




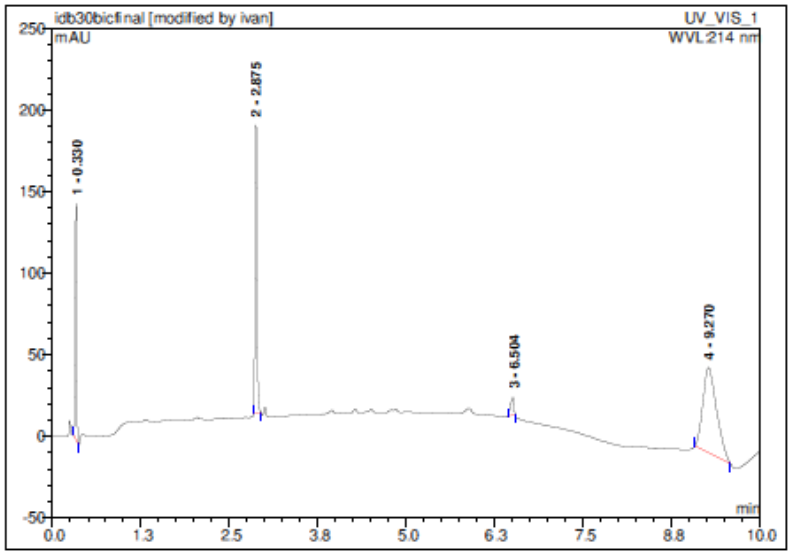


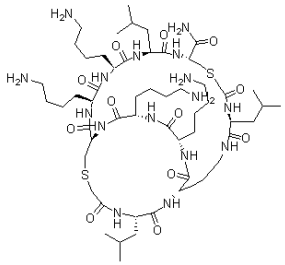
K[1]*K*(K[2])LLLZ[1]LZ[2]K (3b) was obtained as foamy white solid after preparative RP-HPLC (7.6 mg, 4.1 %). Analytical RP-HPLC: t_R = 1.600 min (A/D 100:0 to 0:100 in 5.00 min, λ = 214 nm). MS (ESI+): $C_{58}H_{105}N_{15}O_{12}S_2$ calc./obs. 1267.75/1267.75 Da [M].

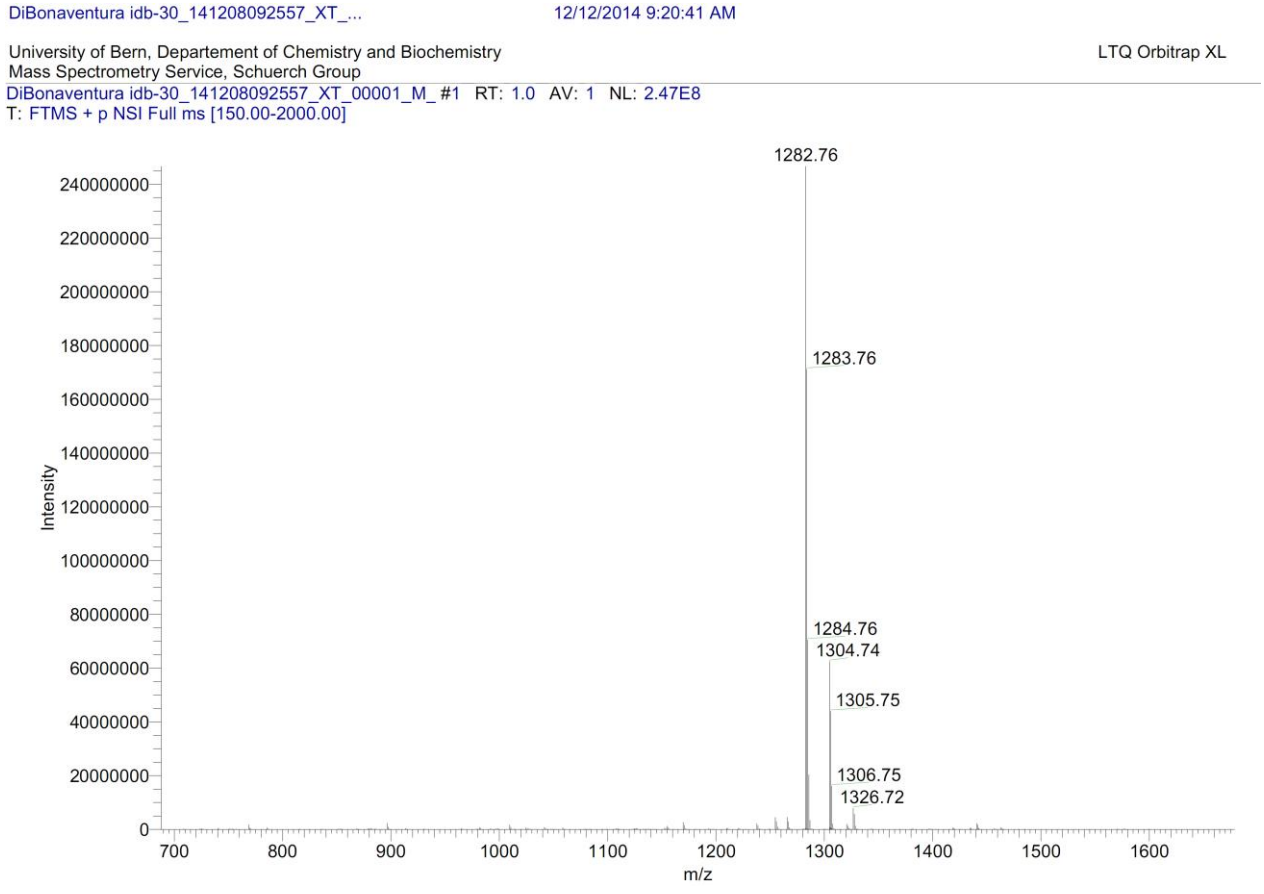




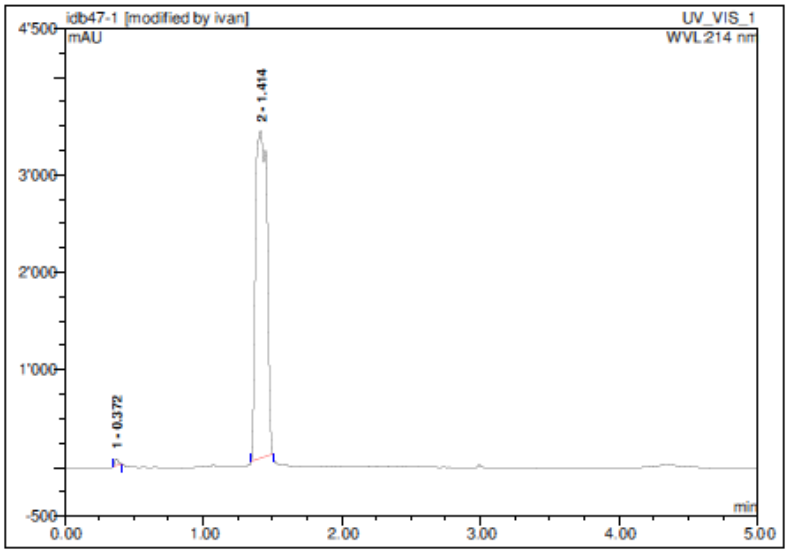
L^{12}*K*(L^{12})KK*Z*^{21}KLL*Z*^{12} (4) was obtained as foamy white solid after preparative RP-HPLC (36.0 mg, 19.7 %). Analytical RP-HPLC: t_R = 2.880 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214 nm). MS (ESI+): $C_{58}H_{106}N_{16}O_{12}S_2$ calc./obs. 1282.76/1282.76 Da [M].

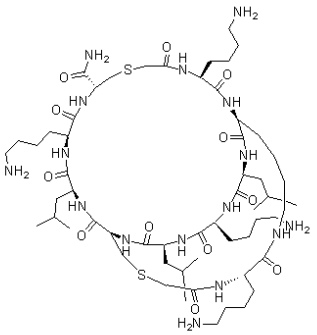


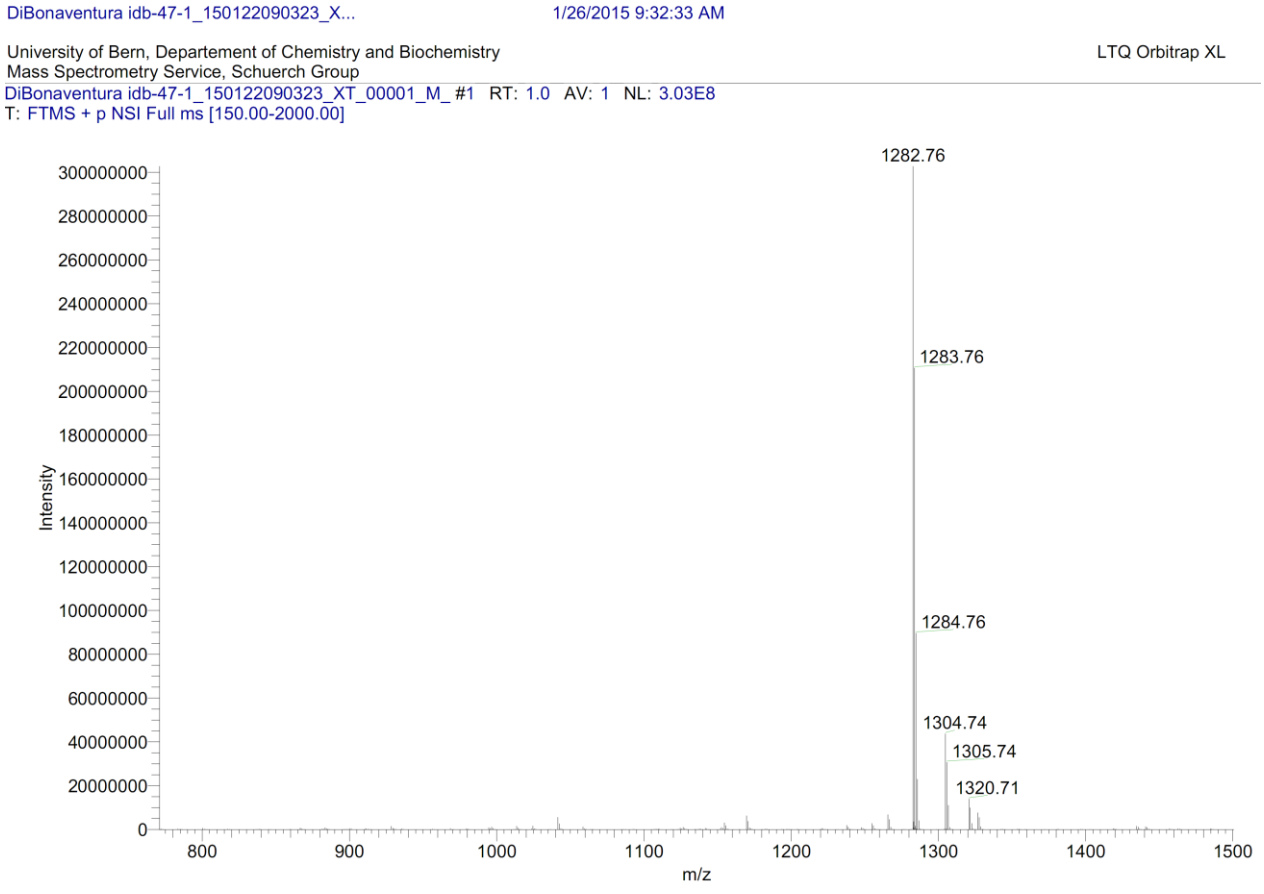




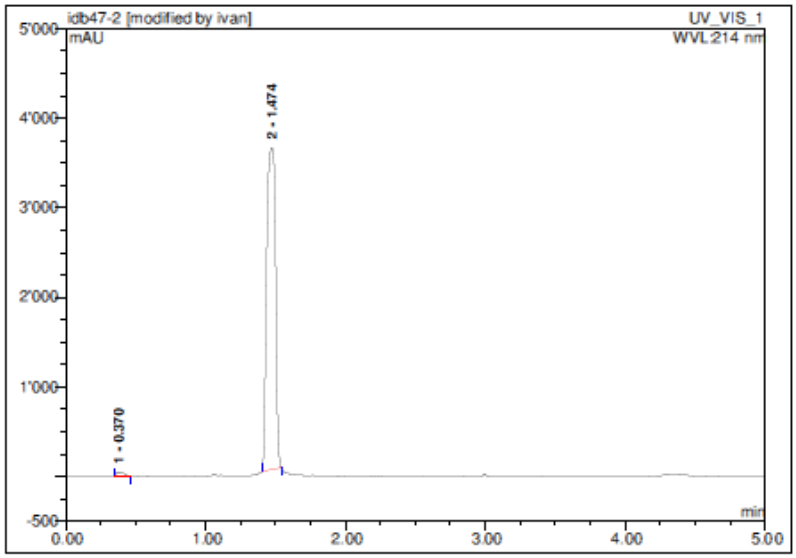
K²*K*(K¹)LKL*Z*¹LK*Z*² (5a) was obtained as foamy white solid after preparative RP-HPLC (13.8 mg, 7.4 %). Analytical RP-HPLC: t_R = 1.410 min (A/D 100:0 to 0:100 in 5.00 min, λ = 214nm). MS(ESI+): $C_{56}H_{106}N_{16}O_{12}S_2$calc./obs.1282.76/1282.76 Da [M].

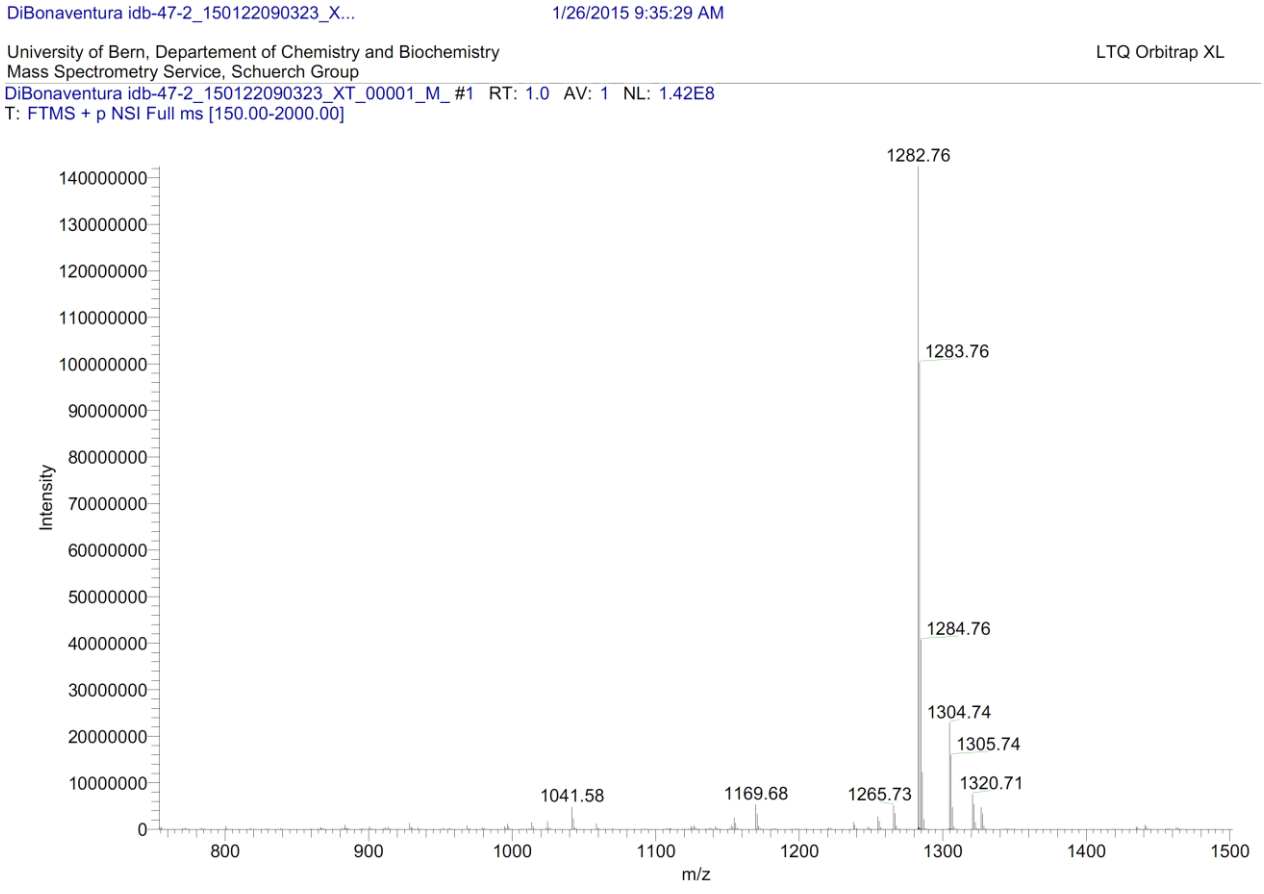




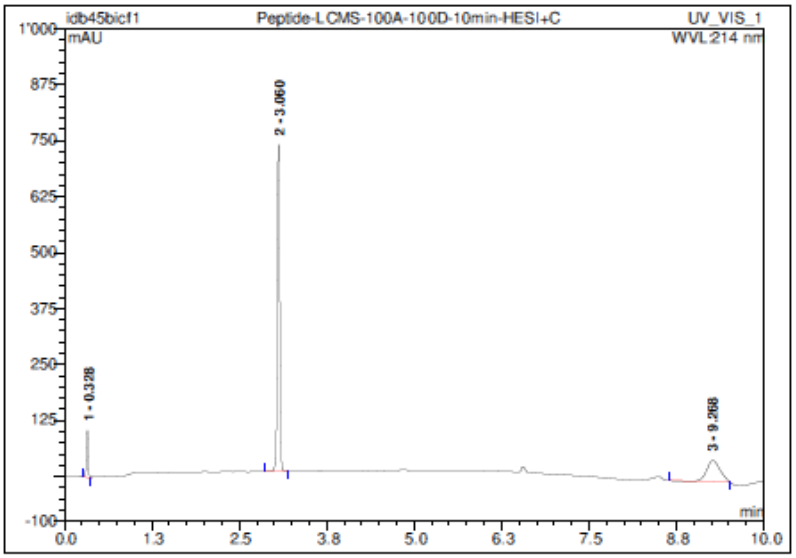


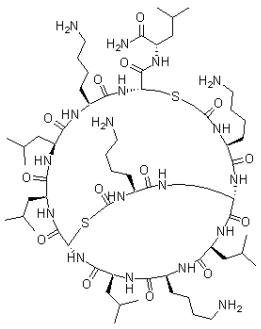
K^1*K*(K^2)LKL*Z*^{1}LK*Z*^{2} (5b) was obtained as foamy white solid after preparative RP-HPLC (19.5 mg, 10.5 %). Analytical RP-HPLC: t_R = 1.470 min (A/D 100:0 to 0:100 in 5.00 min, λ = 214nm). MS(ESI+): $C_{56}H_{106}N_{16}O_{12}S_2$ calc./obs.1282.76/1282.76 Da [M].

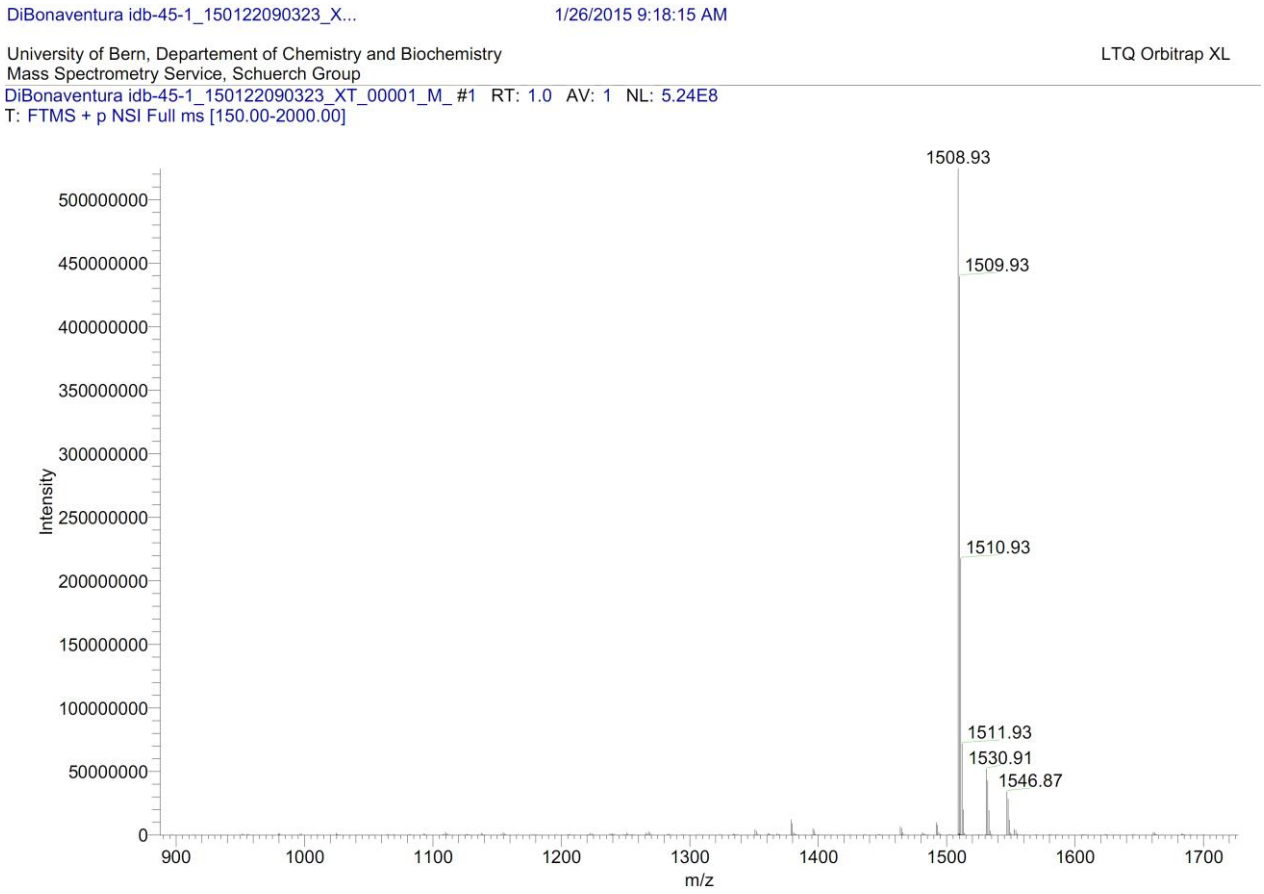




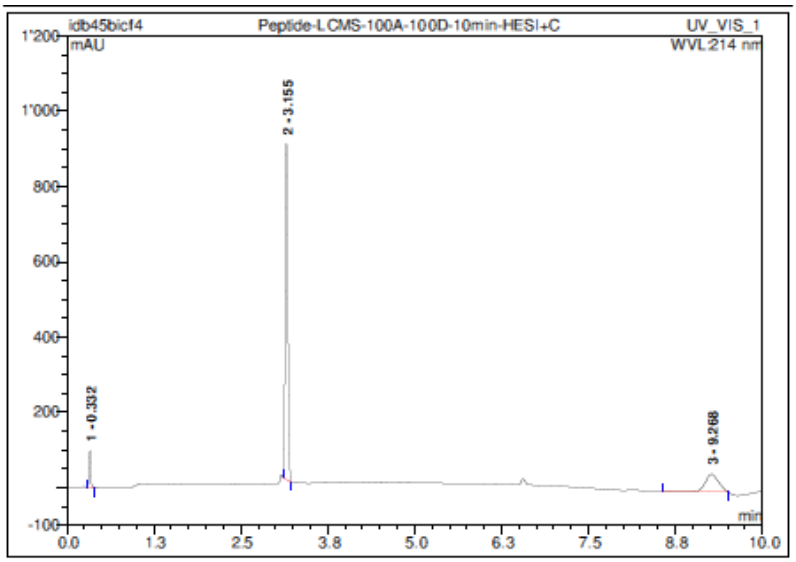
+K^2*K*(K^1)LKL*Z*^{1}LLK*Z*^{2}L (6a) was obtained as foamy white solid after preparative RP-HPLC (9.0 mg, 4.1 %). Analytical RP-HPLC: t_R = 3.060 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{70}H_{128}N_{18}O_{14}S_2$ calc./obs.1508.93/1508.93 Da [M].

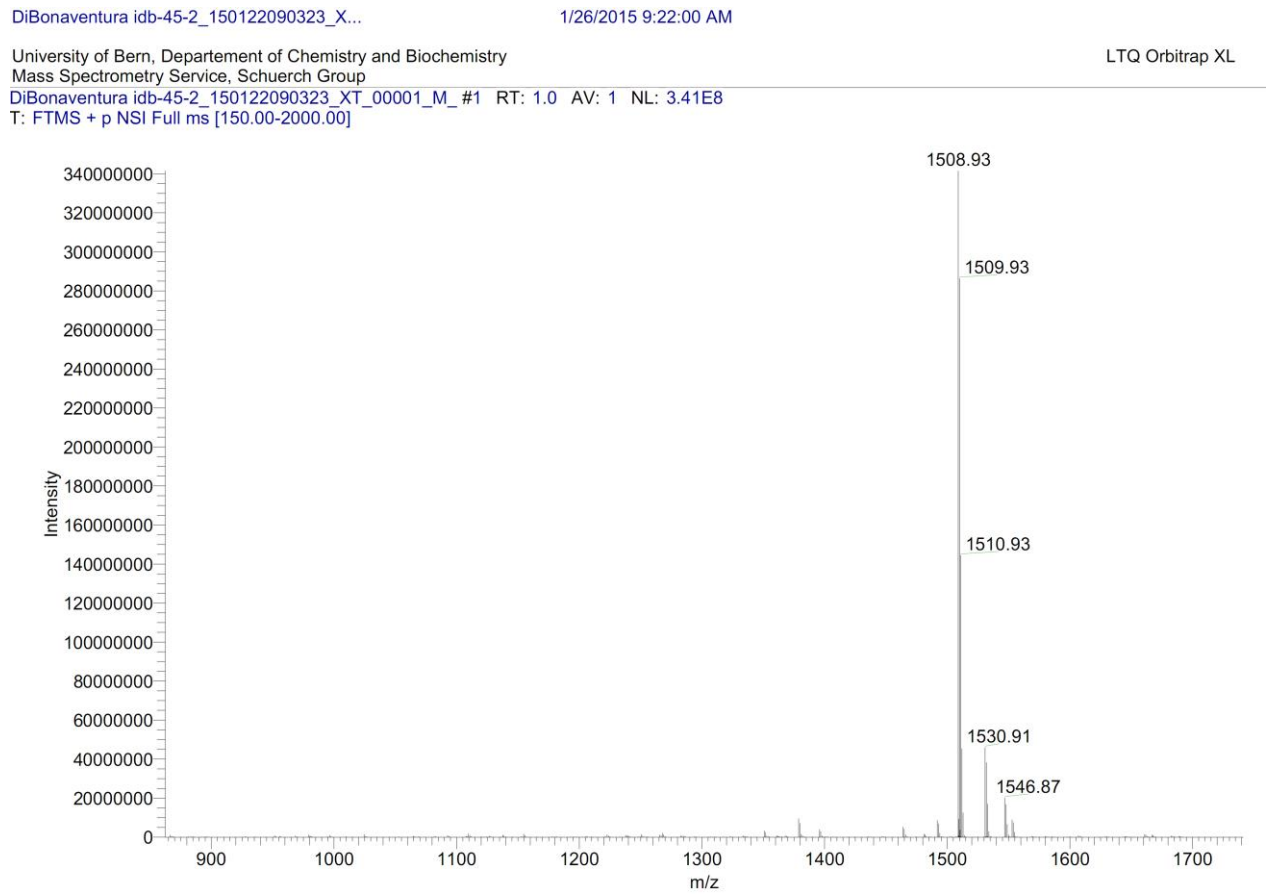




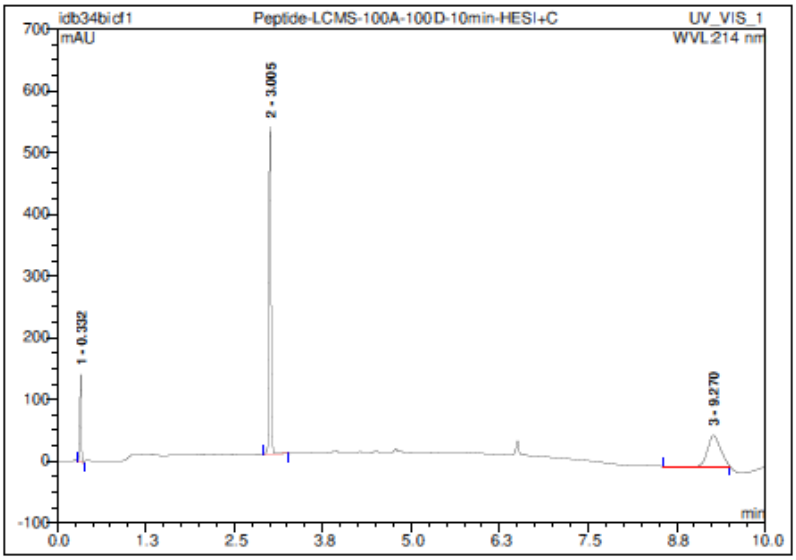


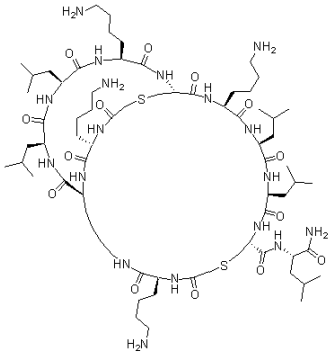
K[1]*K*(K[2])LKL*Z*[1]KLL*Z*[2]L (6b) was obtained as foamy white solid after preparative RP-HPLC (20.0 mg, 9.1 %). Analytical RP-HPLC: t_R = 3.160 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{70}H_{128}N_{18}O_{14}S_2$ calc./obs.1508.93/1508.93 Da [M].

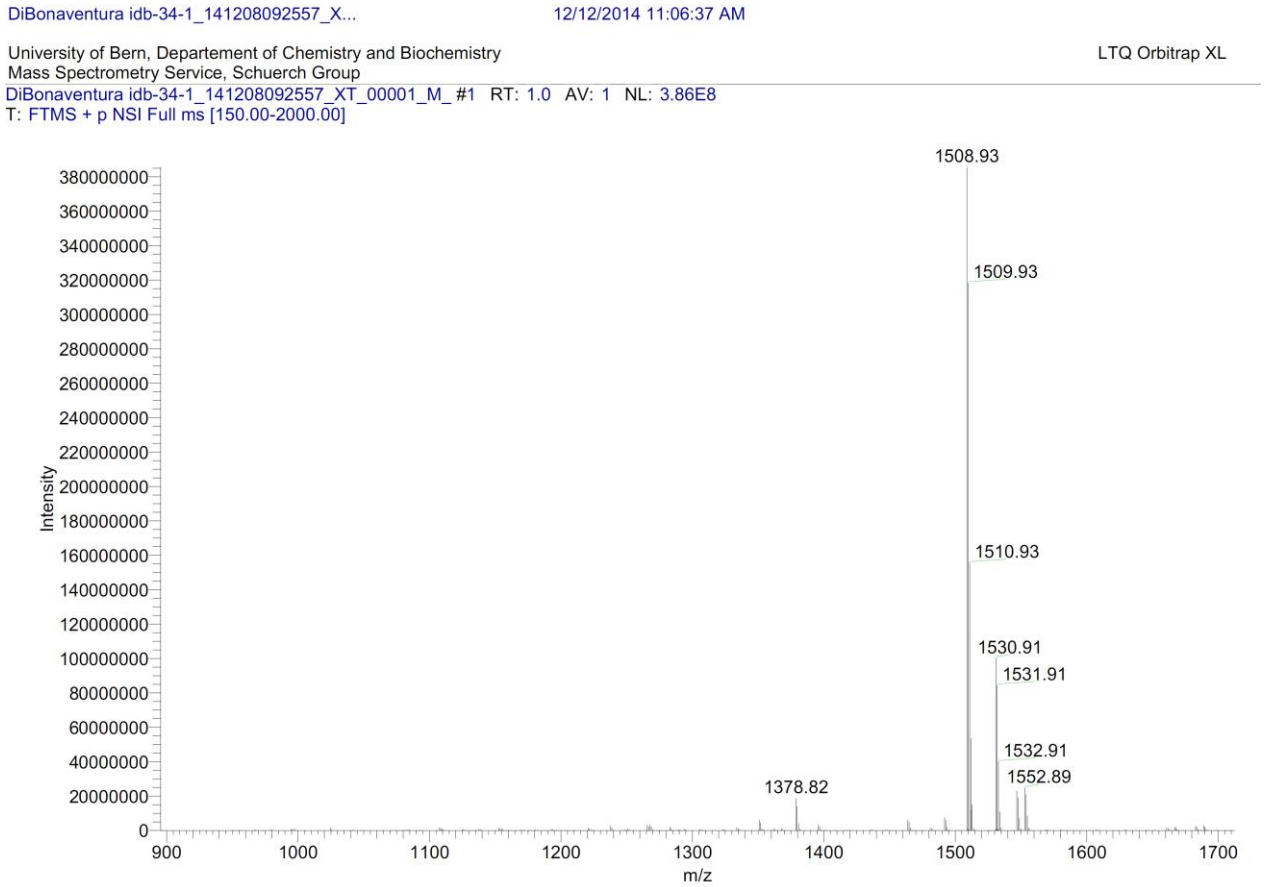




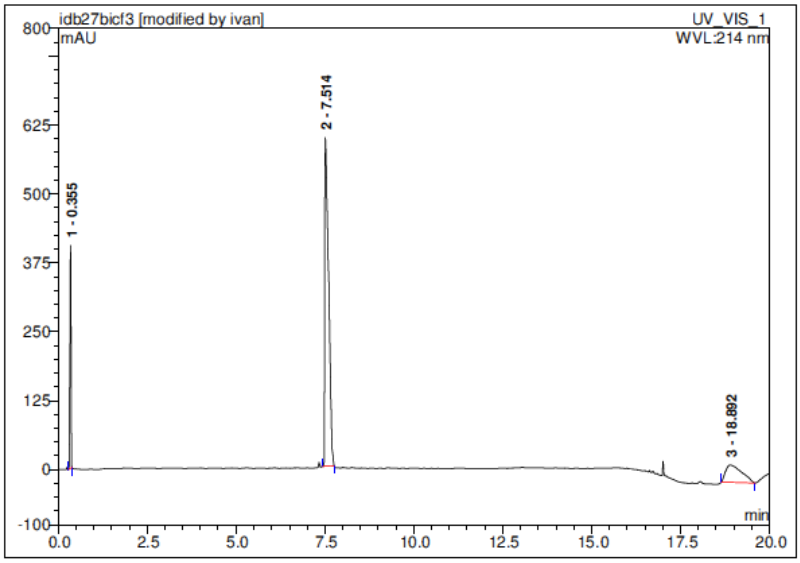
K^{12}*K*(K^{12})LLKZ^{21}KLL*Z*^{12}L (7) was obtained as foamy white solid after preparative RP-HPLC (6.3 mg, 2.9 %). Analytical RP-HPLC: t_R = 3.010 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{70}H_{128}N_{18}O_{14}S_2$ calc./obs.1508.93/1508.93 Da [M].

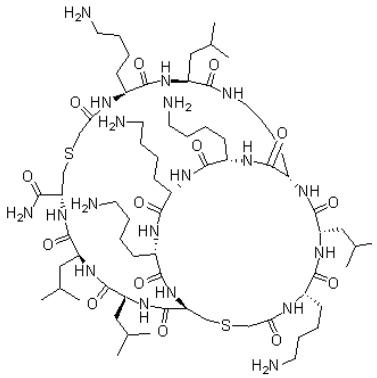


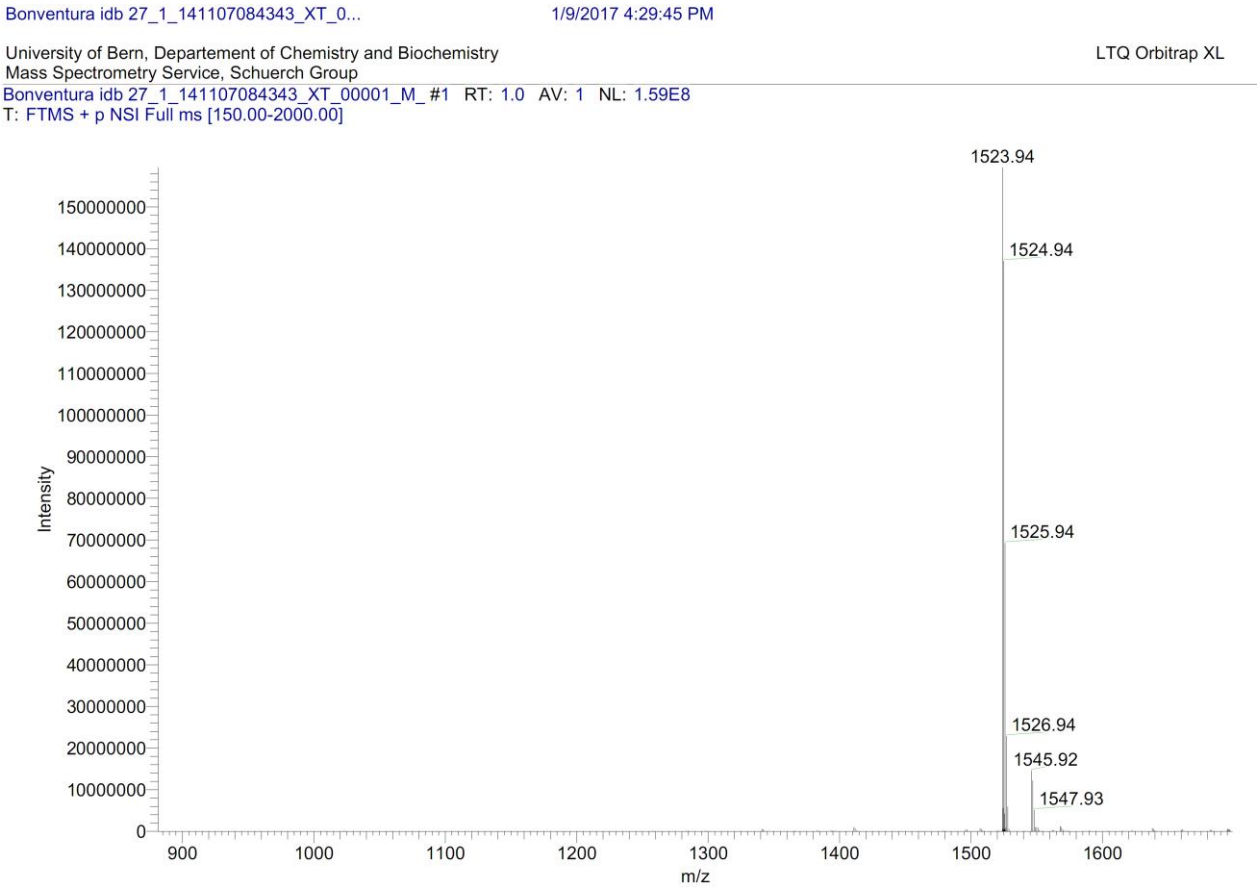




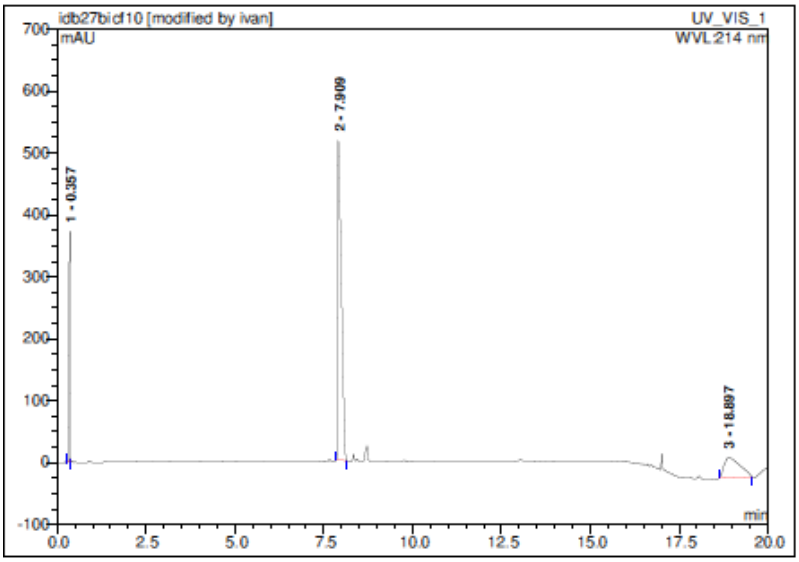
K[1]L*K*(K[2]L)KKKZ[2]LLZ[1] (8a) was obtained as foamy white solid after preparative RP-HPLC (8.4 mg, 3.8 %). Analytical RP-HPLC: t_R = 7.510 min (A/D 100:0 to 0:100 in 20.00 min, λ = 214 nm). MS (ESI+): $C_{70}H_{129}N_{19}O_{14}S_2$ calc./obs. 1523.94/1523.94 Da [M].

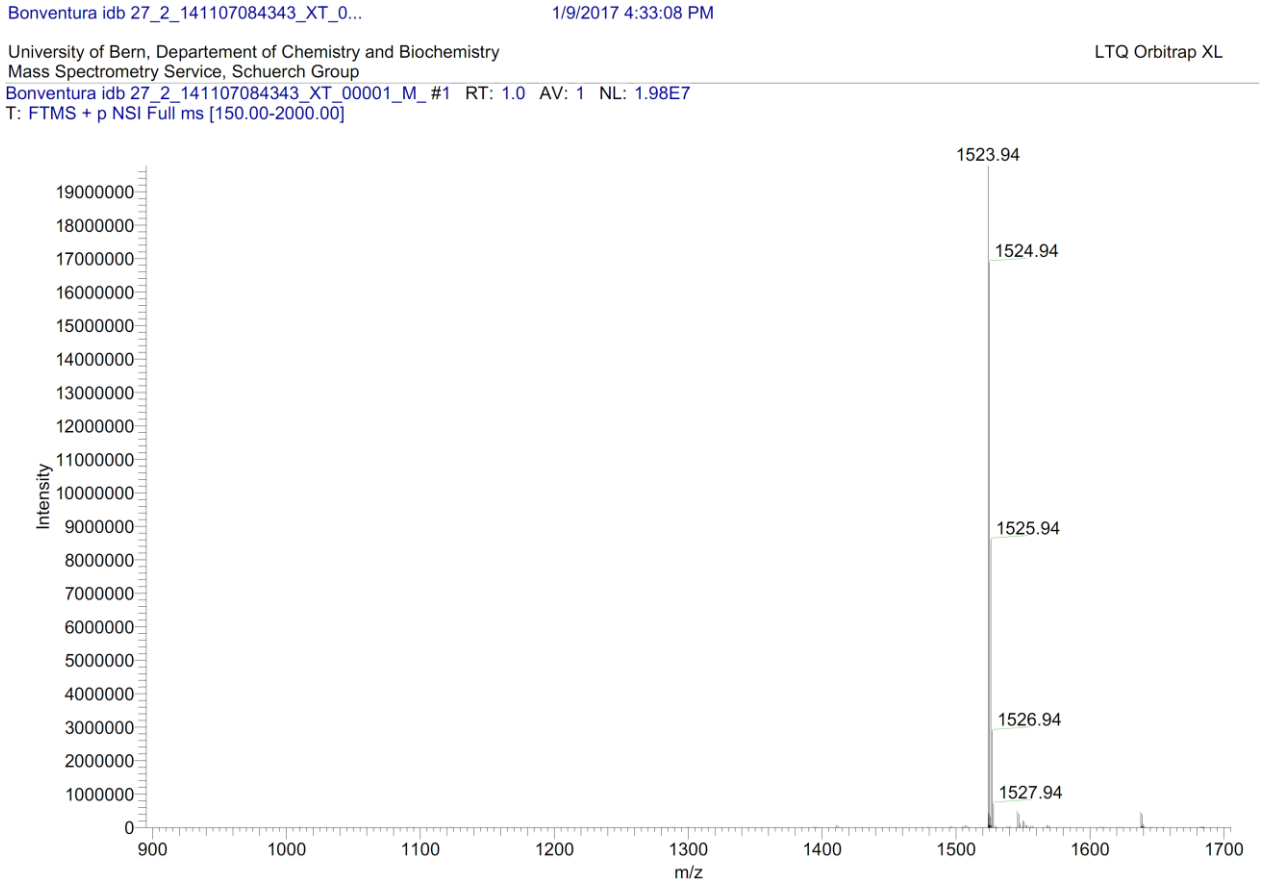




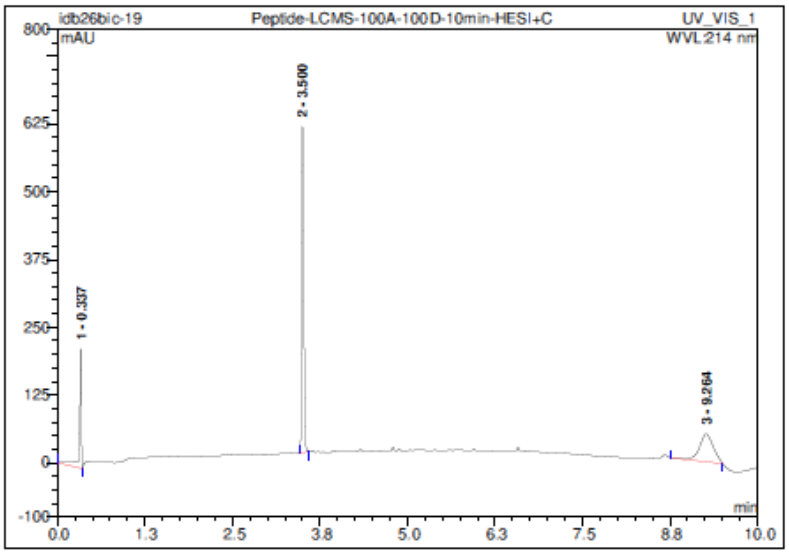


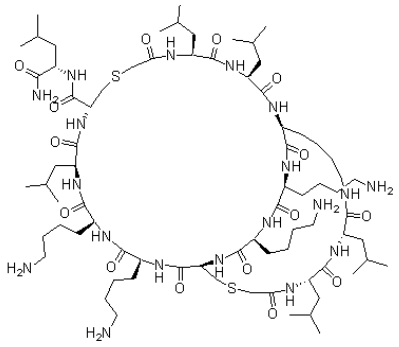
K[1]L*K*(K[2]L)KKKZ[1]LLZ[2](8b) was obtained as foamy white solid after preparative RP-HPLC (29.4 mg, 13.4 %). Analytical RP-HPLC: t_R = 7.910 min (A/D 100:0 to 0:100 in 20.00 min, λ = 214 nm). MS (ESI+): $C_{70}H_{129}N_{19}O_{14}S_2$ calc./obs. 1523.94/1523.94 Da [M].

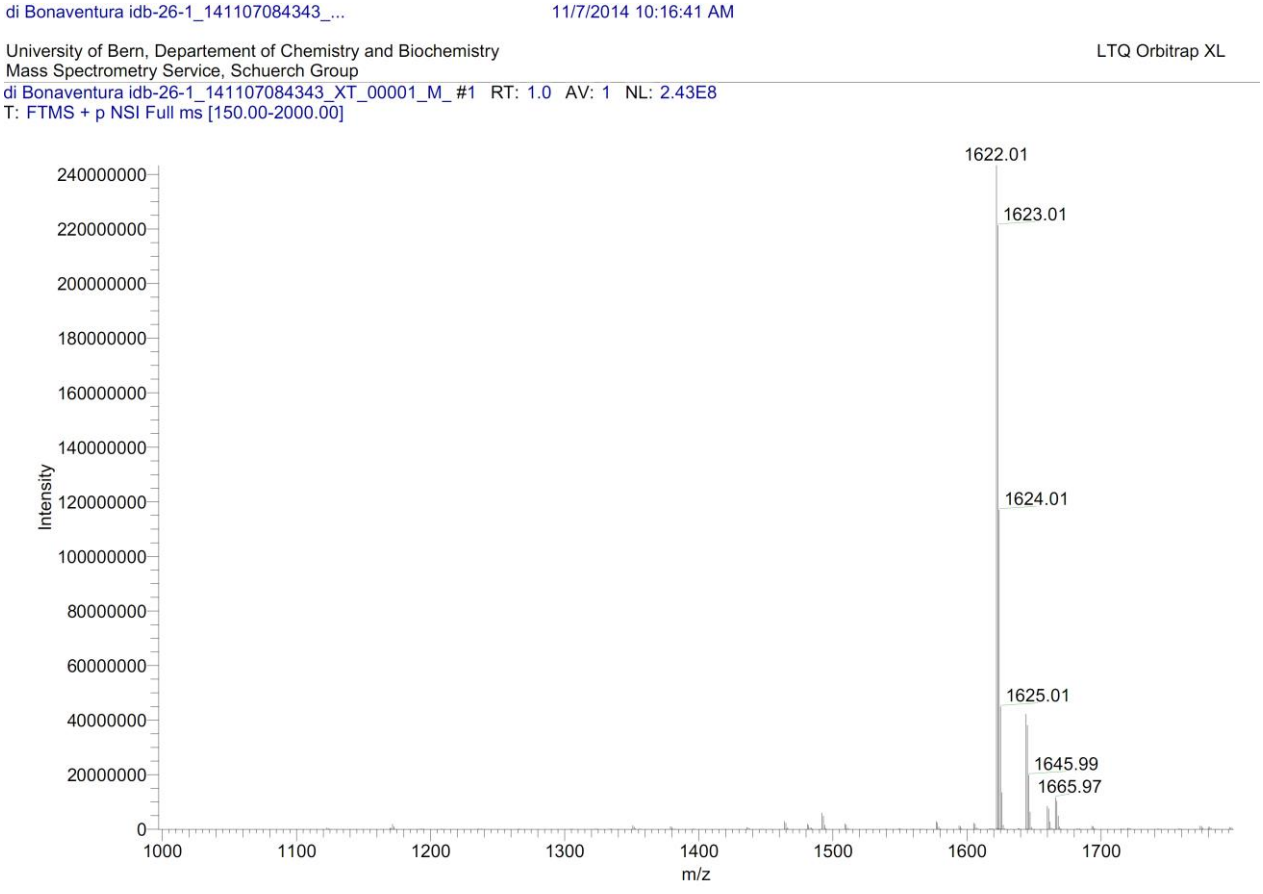




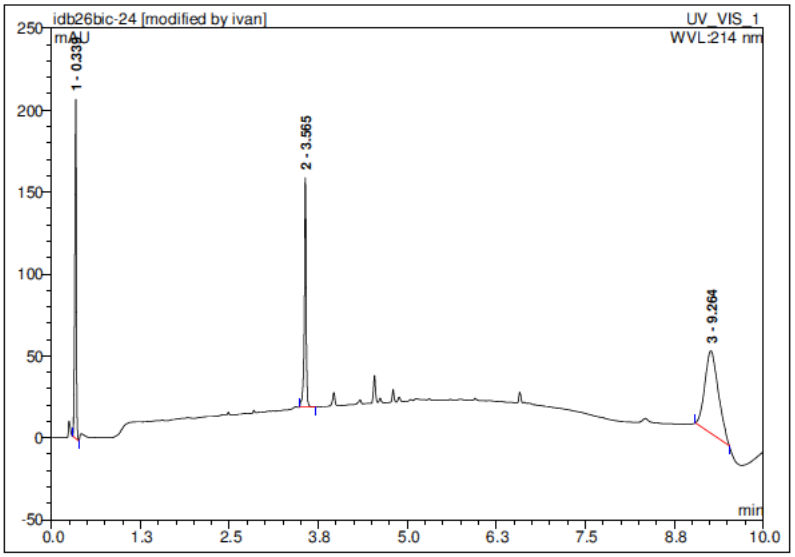
L[1]L*K*(L[2]L)KK*Z*[2]KKL*Z*[1]L (9a) was obtained as foamy white solid after preparative RP-HPLC (5.7 mg, 2.4 %). Analytical RP-HPLC: t_R = 3.500 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214 nm). MS (ESI+): $C_{76}H_{139}N_{19}O_{15}S_2$ calc./obs. 1622.01/1622.01 Da [M].

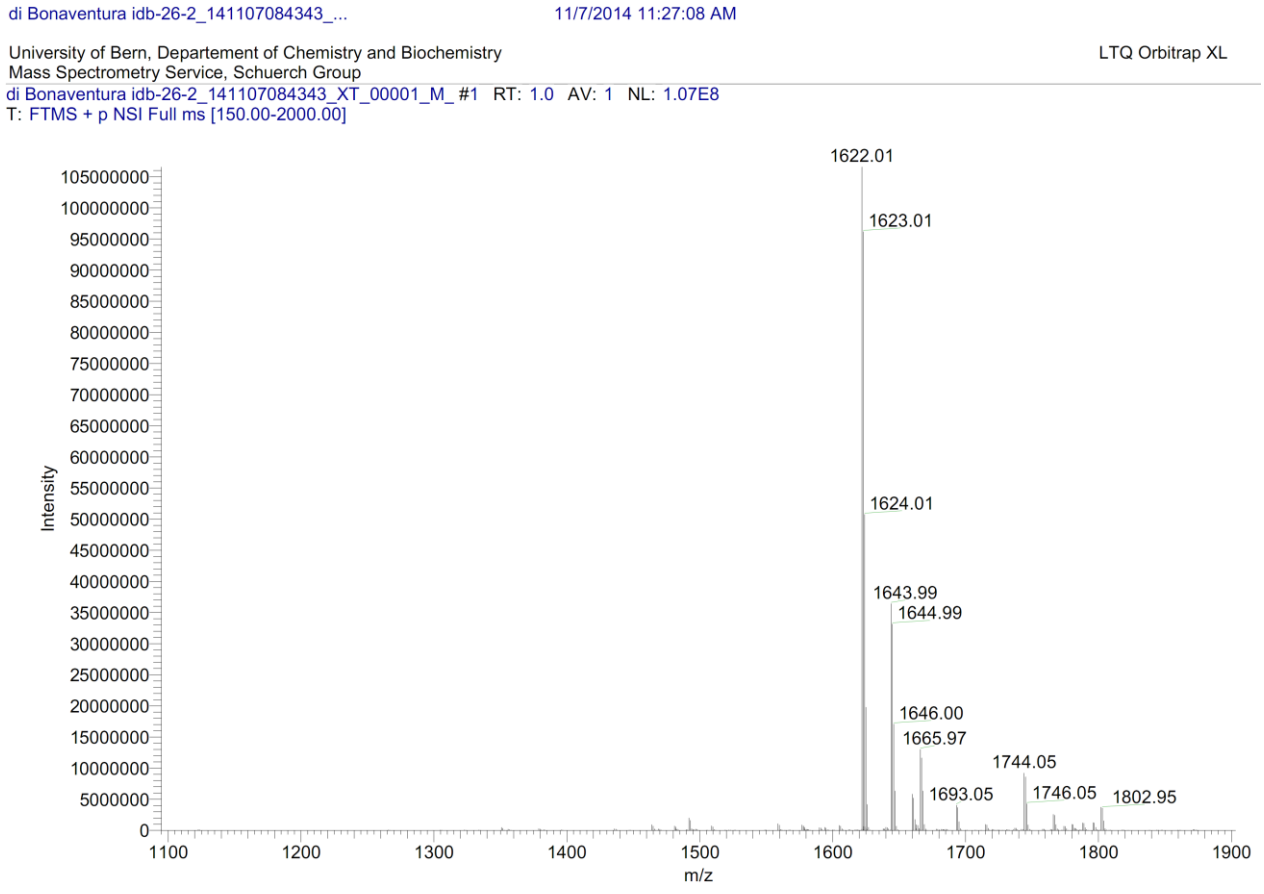




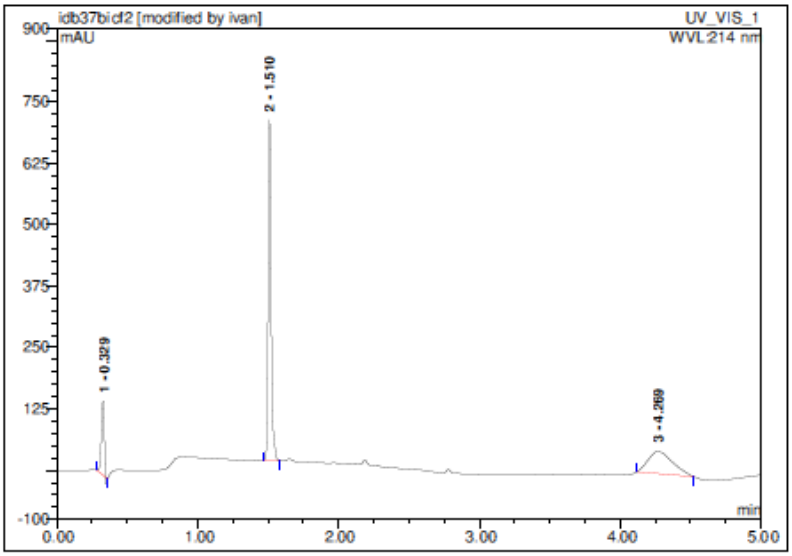


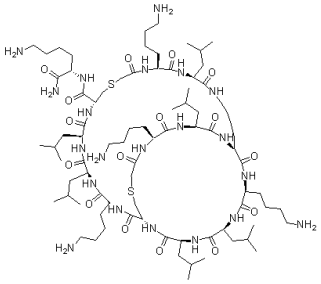
L^{1}L*K*(L^{2}L)KK*Z*^{1}KKL*Z*^{2}L (9b) was obtained as foamy white solid after preparative RP-HPLC (2.1 mg, 0.9 %). Analytical RP-HPLC: t_R = 3.570 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214 nm). MS (ESI+): $C_{76}H_{139}N_{19}O_{15}S_2$ calc./obs. 1622.01/1622.01 Da [M].

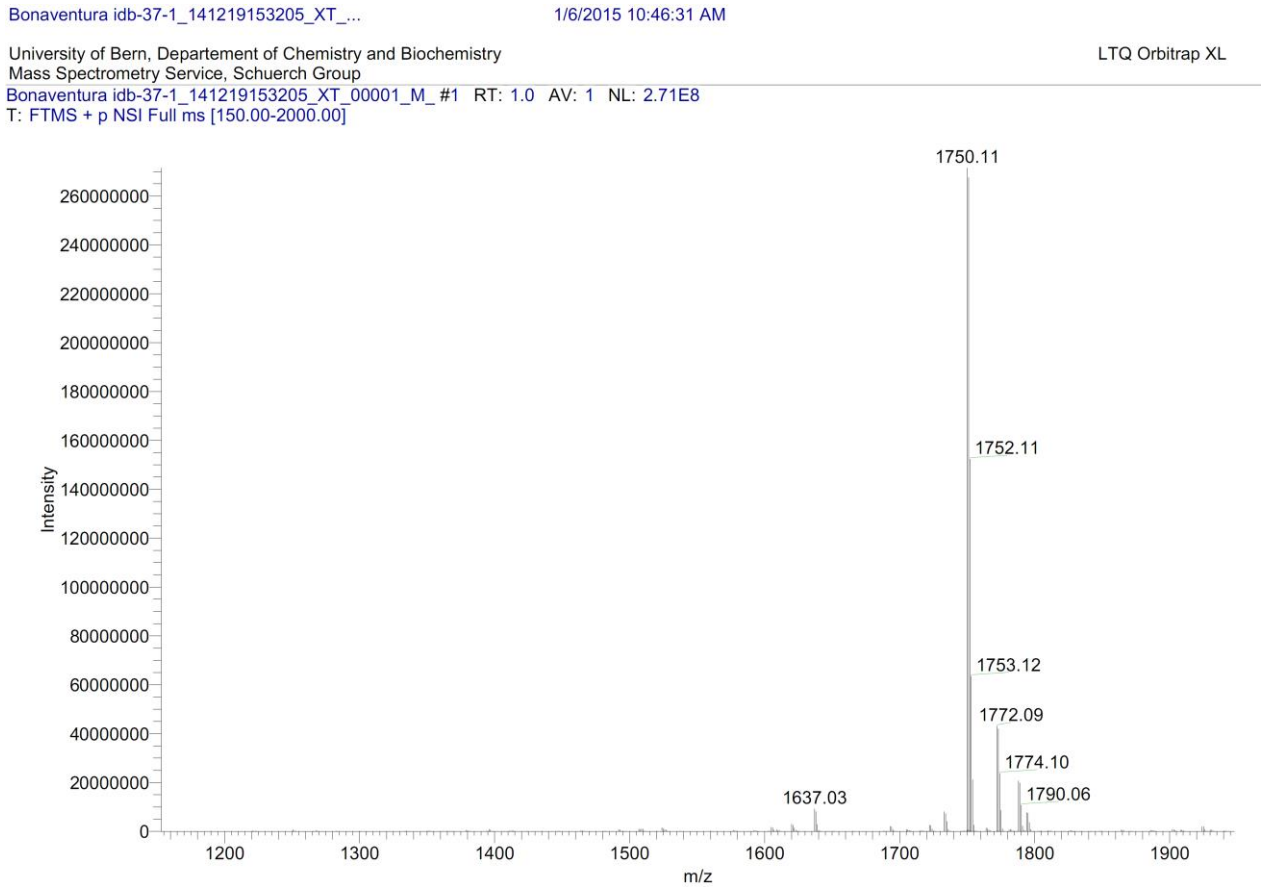




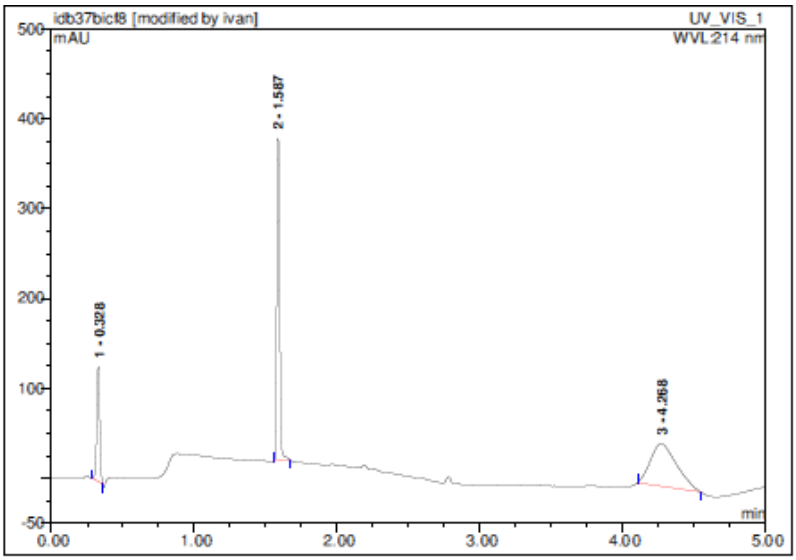
K[1]L*K*(K[2]L)KLL*Z*[2]KLL*Z*[1]K (10a) was obtained as foamy white solid after preparative RP-HPLC (11.5 mg, 4.5 %). Analytical RP-HPLC: t_R = 3.120 min (A/D 100:0 to 0:100 in 5.00 min, λ = 214nm). MS (ESI+): $C_{82}H_{151}N_{21}O_{16}S_2$ calc./obs.1750.11/1750.11 Da [M].

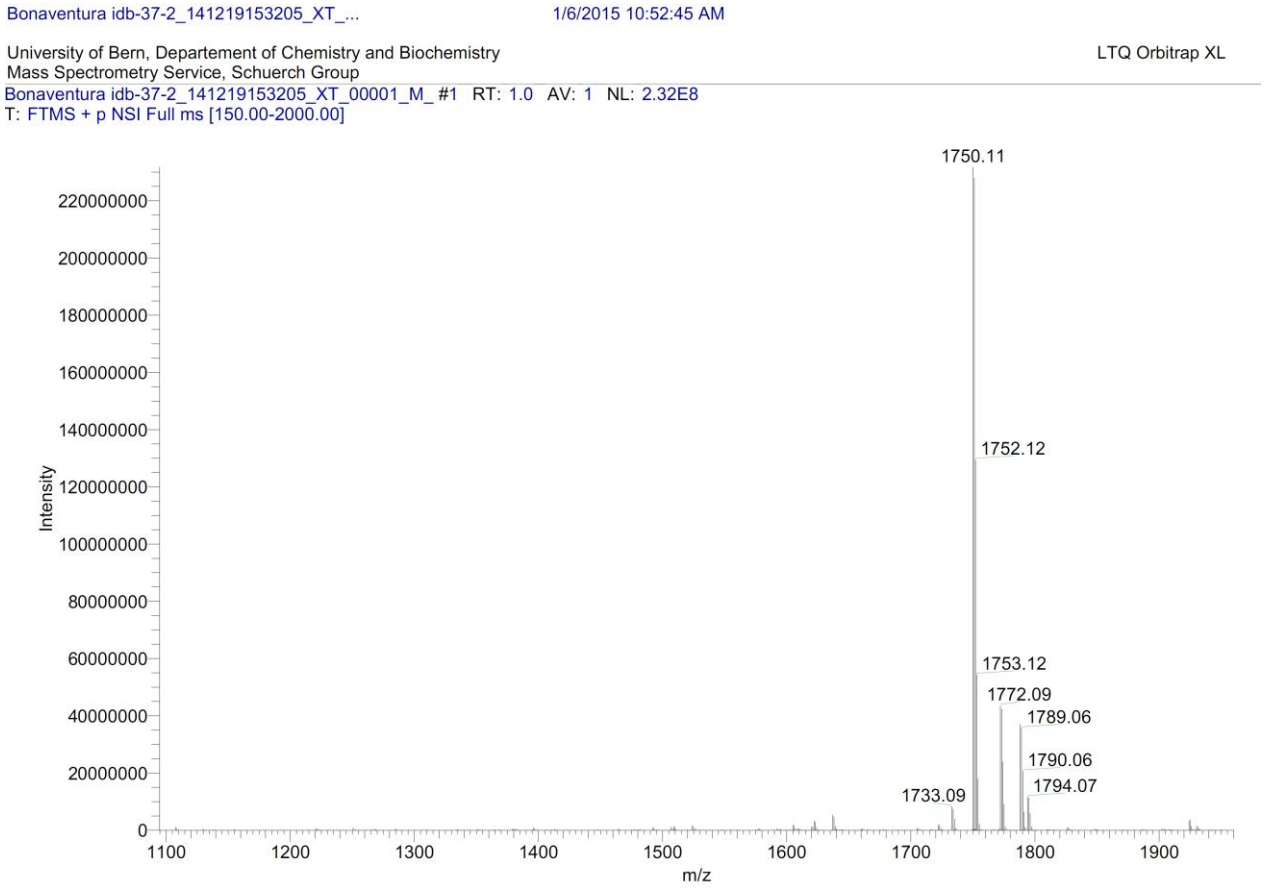




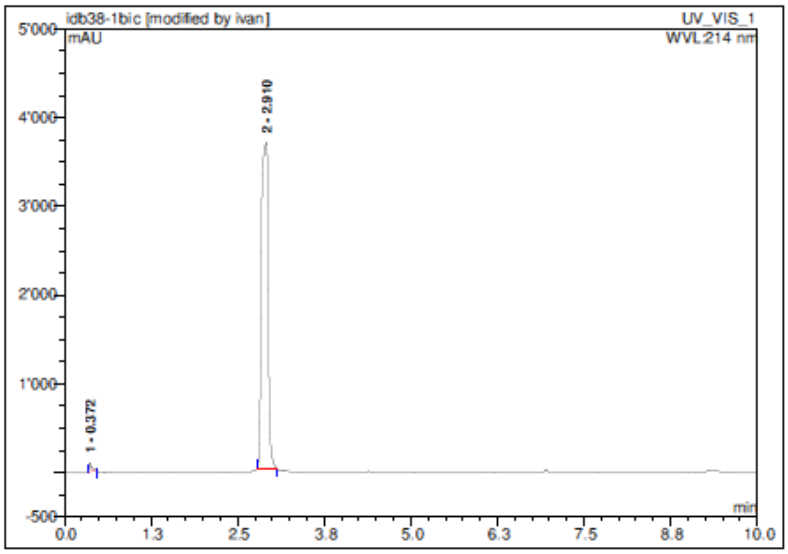


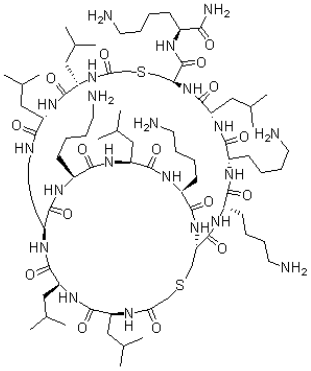
K[1]L*K*(K[2]L)KLL*Z*[1]KLL*Z*[2]K (10b) was obtained as foamy white solid after preparative RP-HPLC (2.9 mg, 1.1 %). Analytical RP-HPLC: t_R = 3.590 min (A/D 100:0 to 0:100 in 5.00 min, λ = 214nm). MS (ESI+): $C_{82}H_{151}N_{21}O_{16}S_2$ calc./obs.1750.11/1750.11 Da [M].

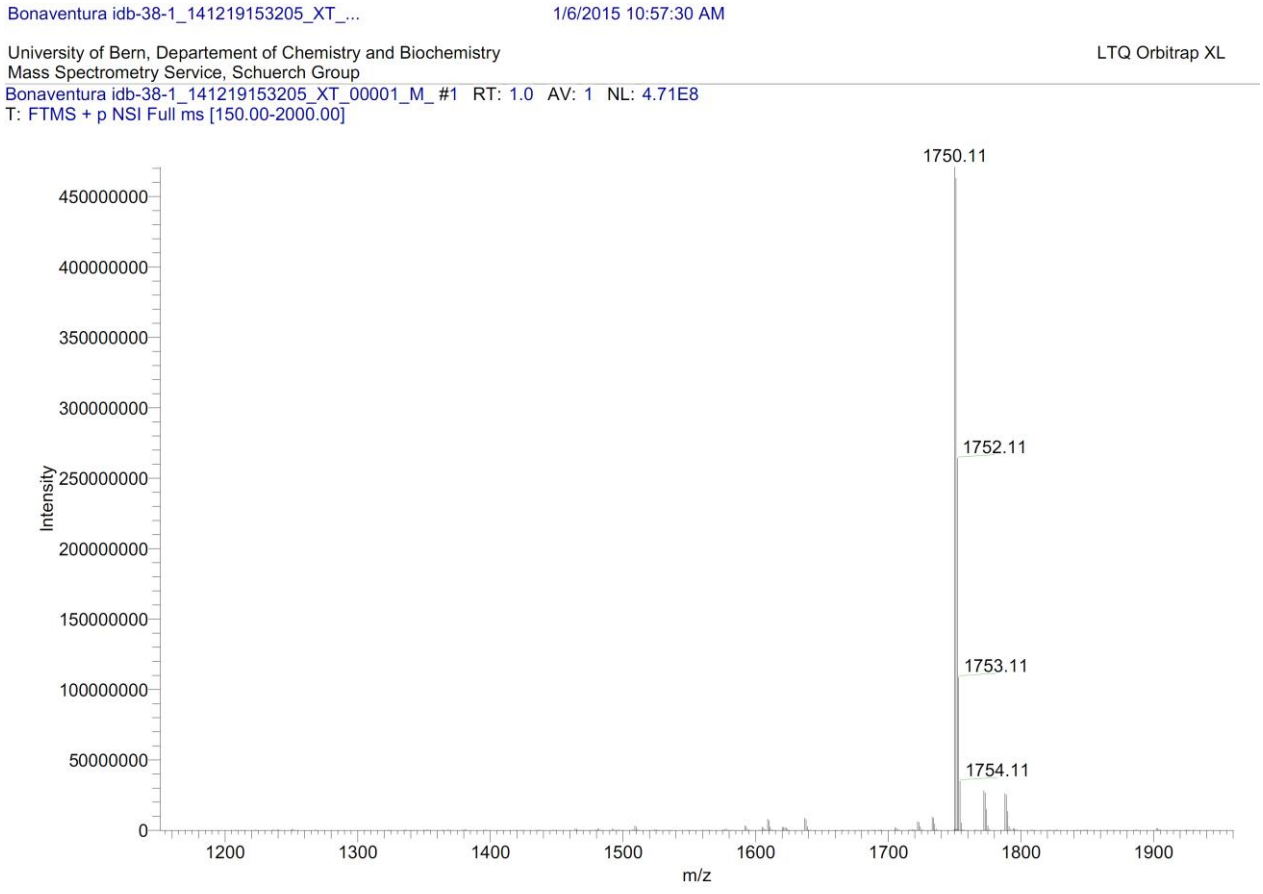




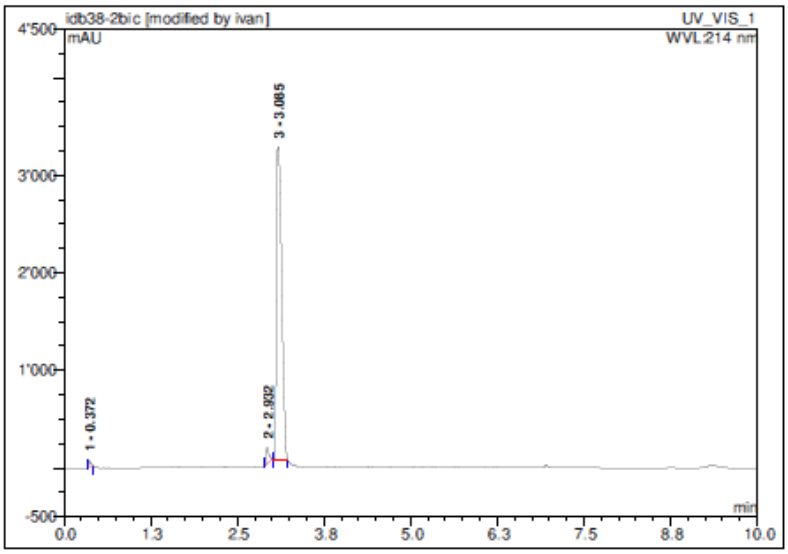
L[1]L*K*(L[2]L)KLKZ[2]KKLZ[1]K (11a) was obtained as foamy white solid after preparative RP-HPLC (37.3 mg, 14.7 %). Analytical RP-HPLC: t_R = 2.910 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{82}H_{151}N_{21}O_{16}S_2$ calc./obs.1750.11/1750.11 Da [M].

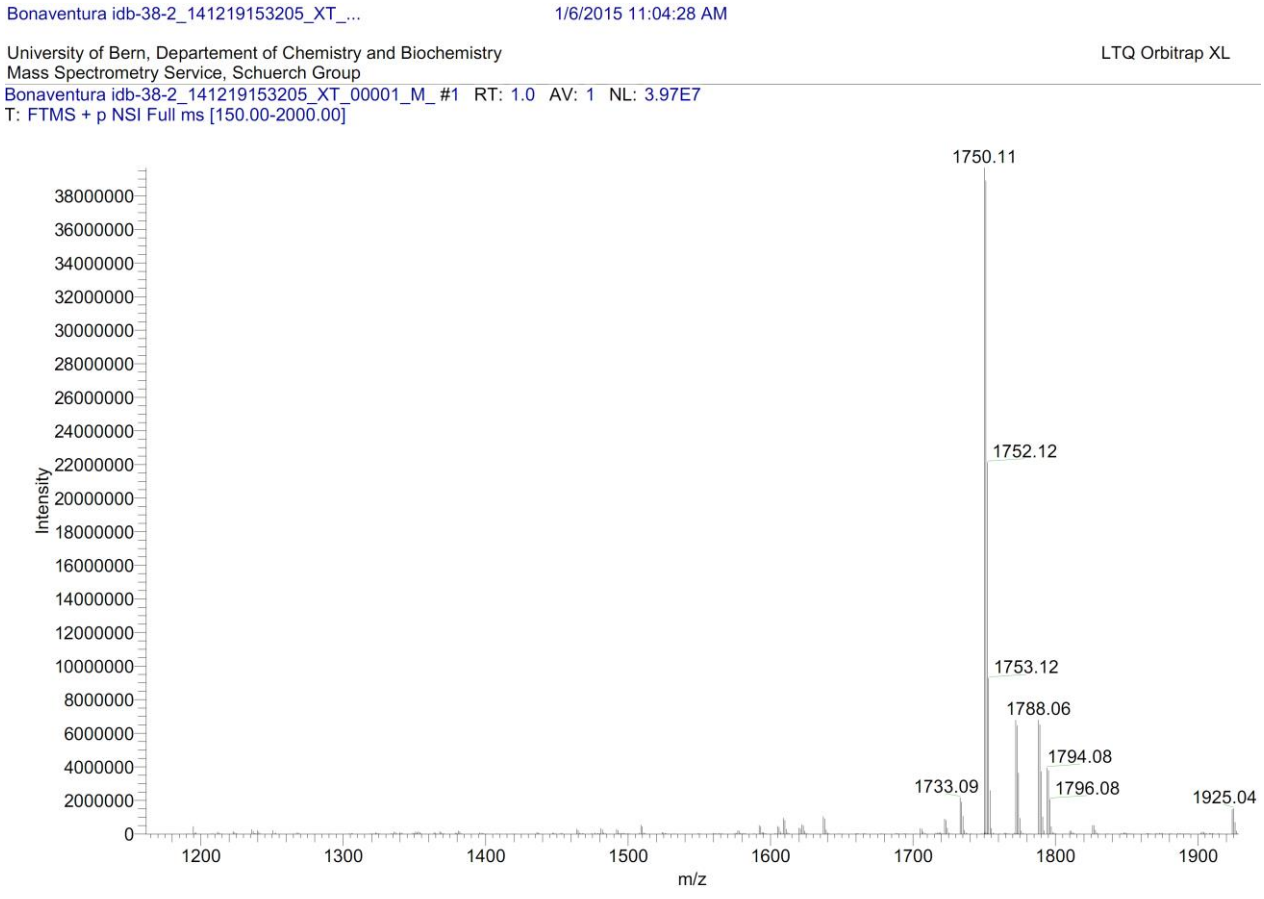




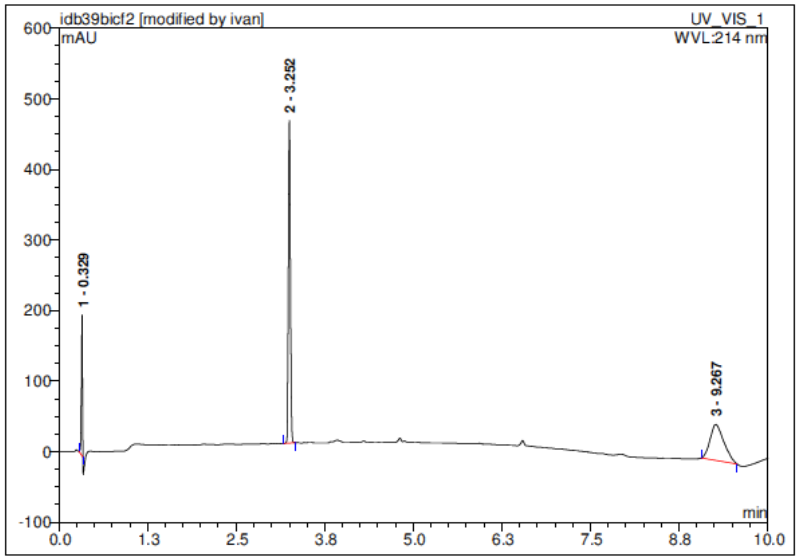


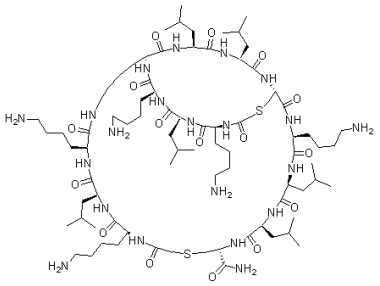
L[1]L*K*(L[2]L)KLK*Z*[1]KKL*Z*[2]K (11b) was obtained as foamy white solid after preparative RP-HPLC (11.5 mg, 4.5 %). Analytical RP-HPLC: t_R = 3.090 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{82}H_{151}N_{21}O_{16}S_2$ calc./obs.1750.11/1750.11 Da [M].

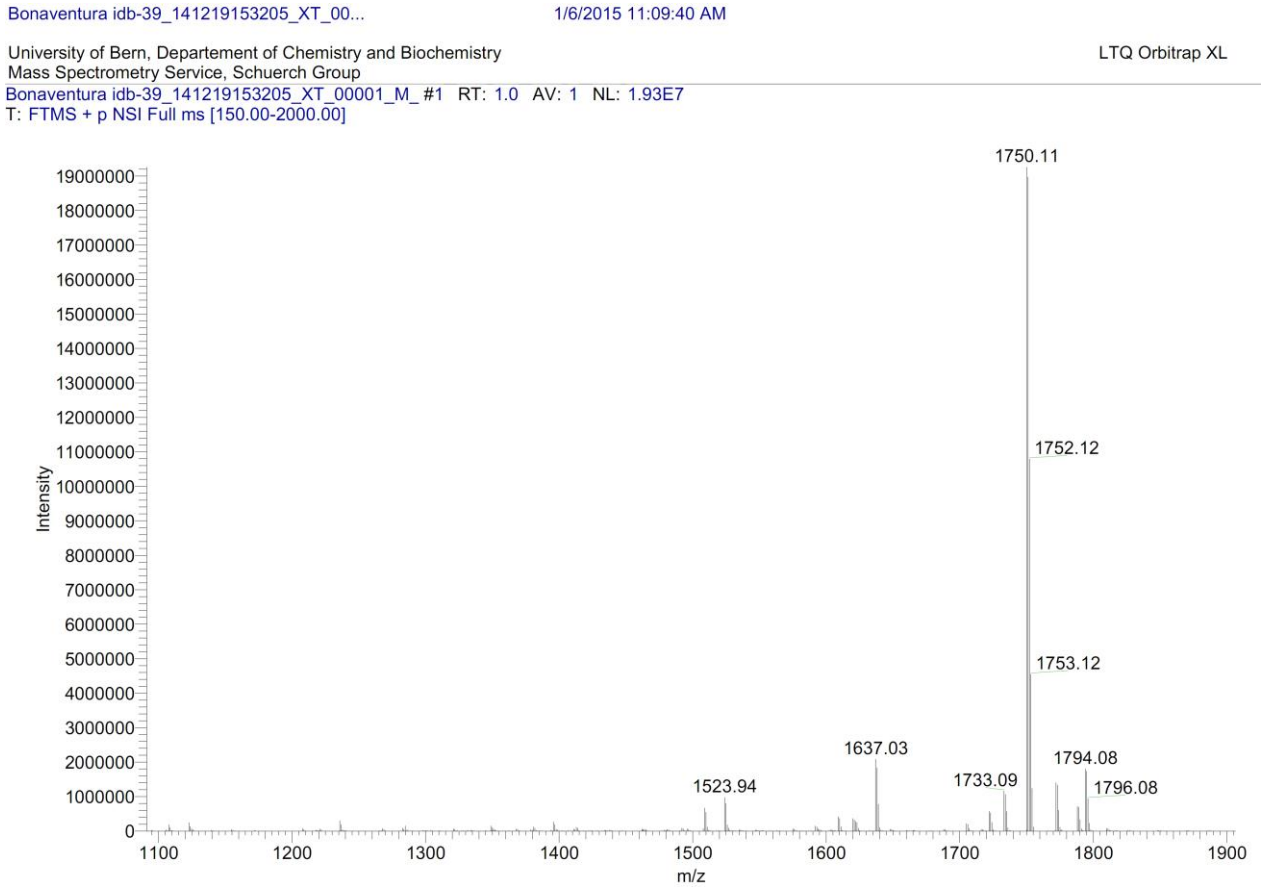




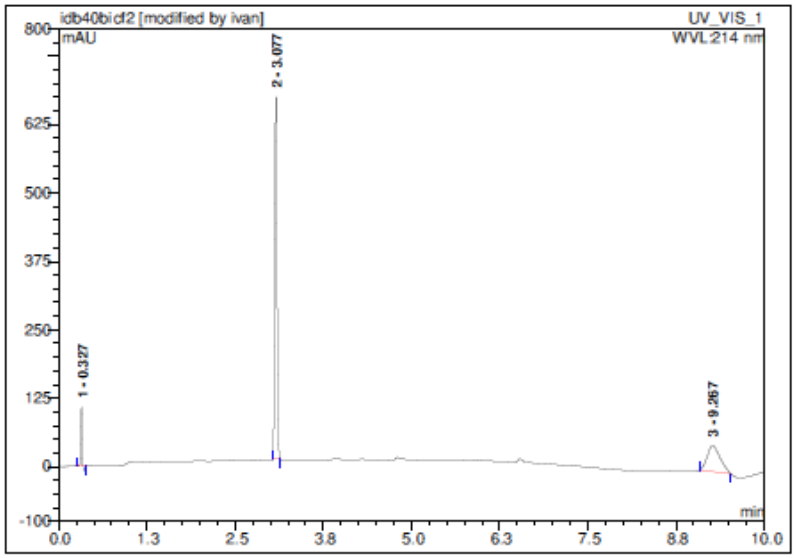
K[12]LK*K*(K[12]LK)LL*Z*[21]KLL*Z*[12] (12) was obtained as foamy white solid after preparative RP-HPLC (6.9 mg, 2.7 %). Analytical RP-HPLC: t_R = 3.250 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{82}H_{151}N_{21}O_{16}S_2$ calc./obs.1750.11/1750.11 Da [M].

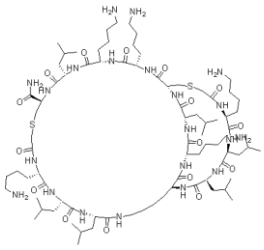


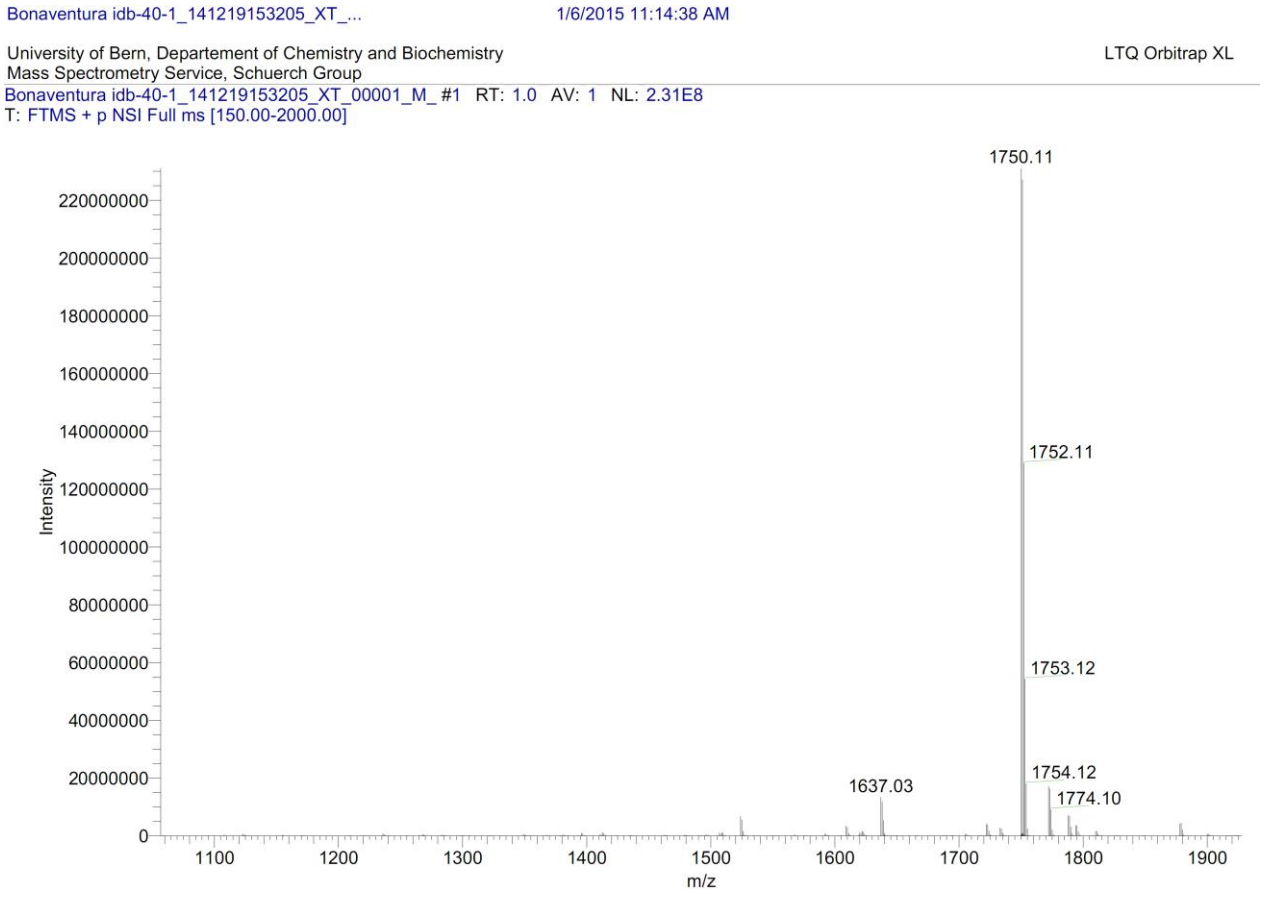




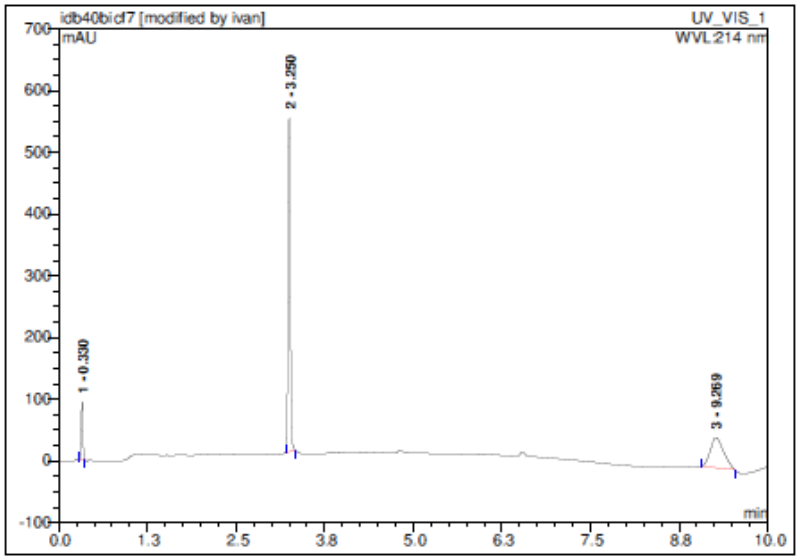
K²LL*K*(K¹LL)KL*Z*¹KKL*Z*² (13a) was obtained as foamy yellow solid after preparative RP-HPLC (12.7 mg, 5.0 %). Analytical RP-HPLC: t_R = 3.080 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{82}H_{151}N_{21}O_{16}S_2$calc./obs.1750.11/1750.11 Da [M].

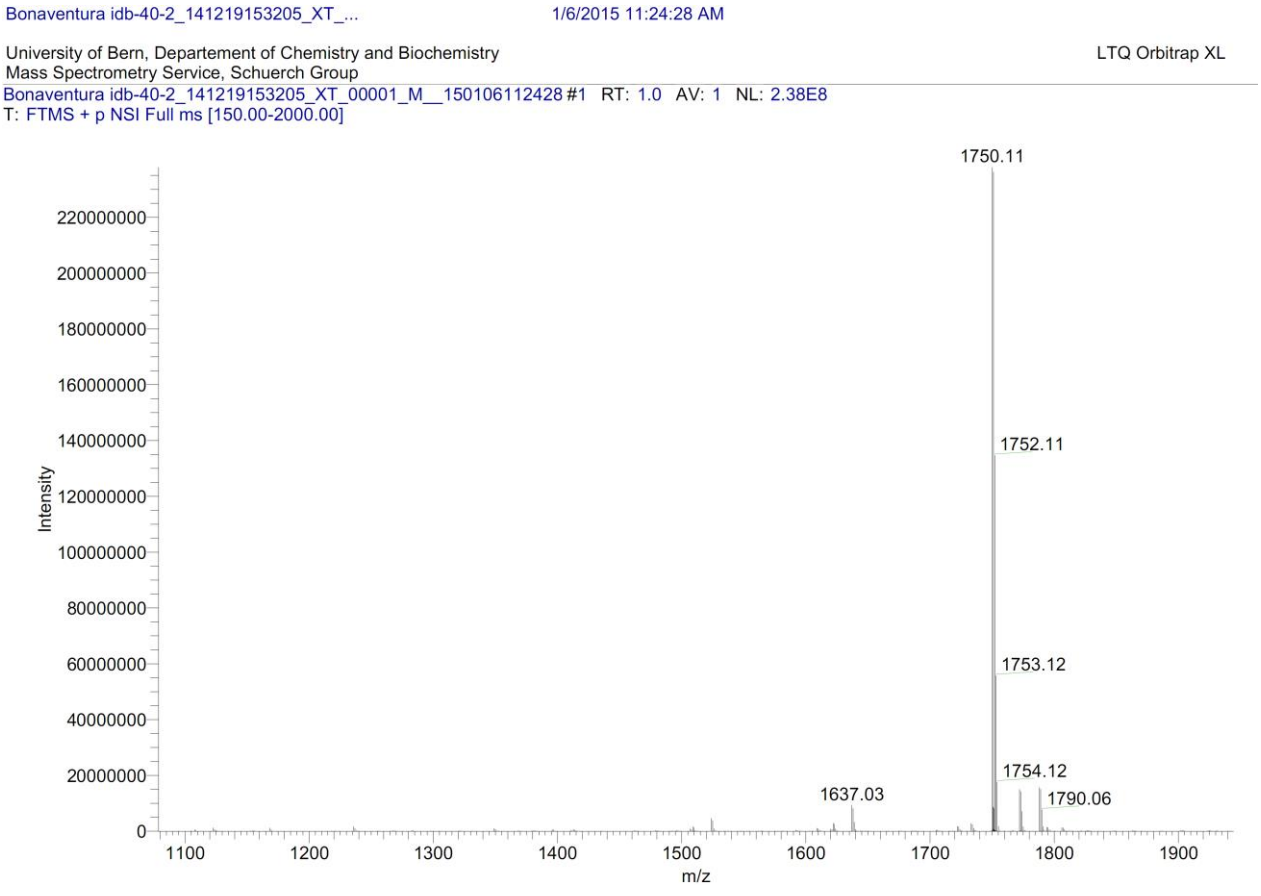




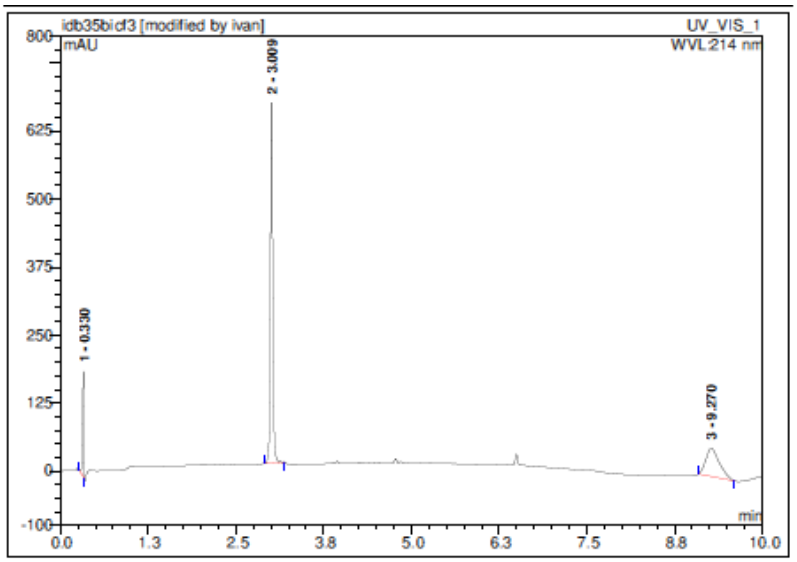


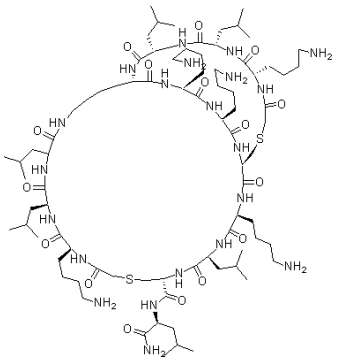
K[1]LL*K*(K[2]LL)KL*Z*[1]KKL*Z*[2] (13b) was obtained as foamy white solid after preparative RP-HPLC (7.9 mg, 3.1 %). Analytical RP-HPLC: t_R = 3.250 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{82}H_{151}N_{21}O_{16}S_2$calc./obs.1750.11/1750.11 Da [M].

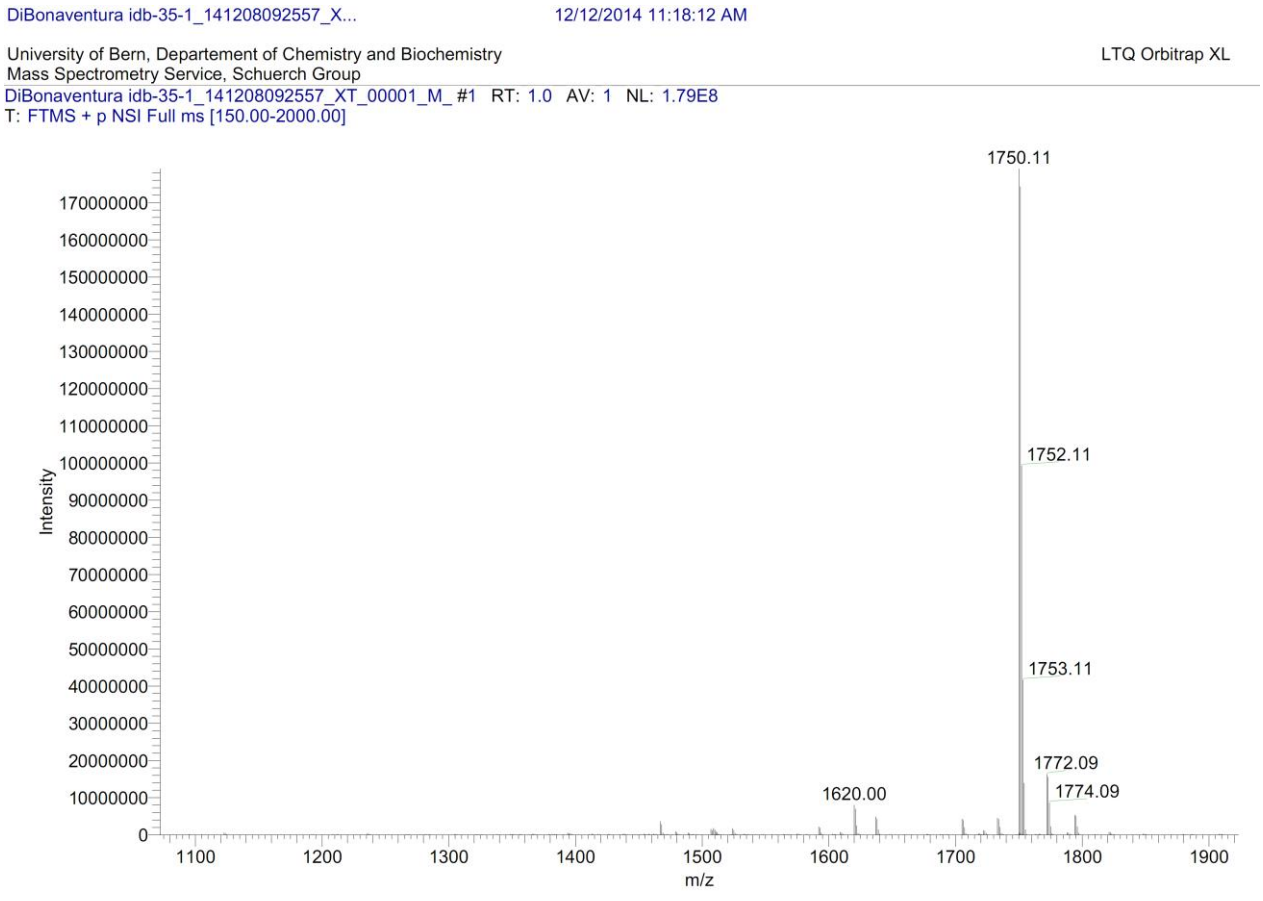




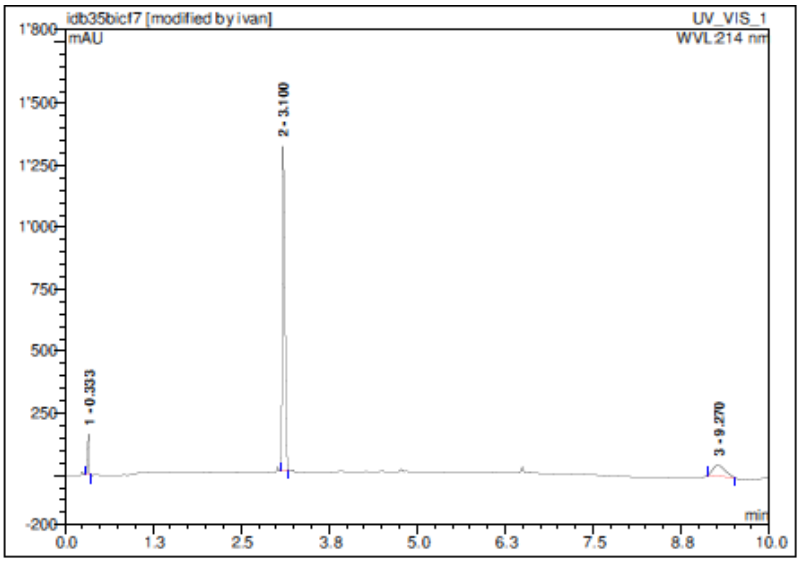
K²LL*K*(K¹LL)KK*Z*¹KL*Z*²L (14a) was obtained as foamy white solid after preparative RP-HPLC (10.6 mg, 4.2 %). Analytical RP-HPLC: t_R = 3.010 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{82}H_{151}N_{21}O_{16}S_2$calc./obs.1750.11/1750.11 Da [M].

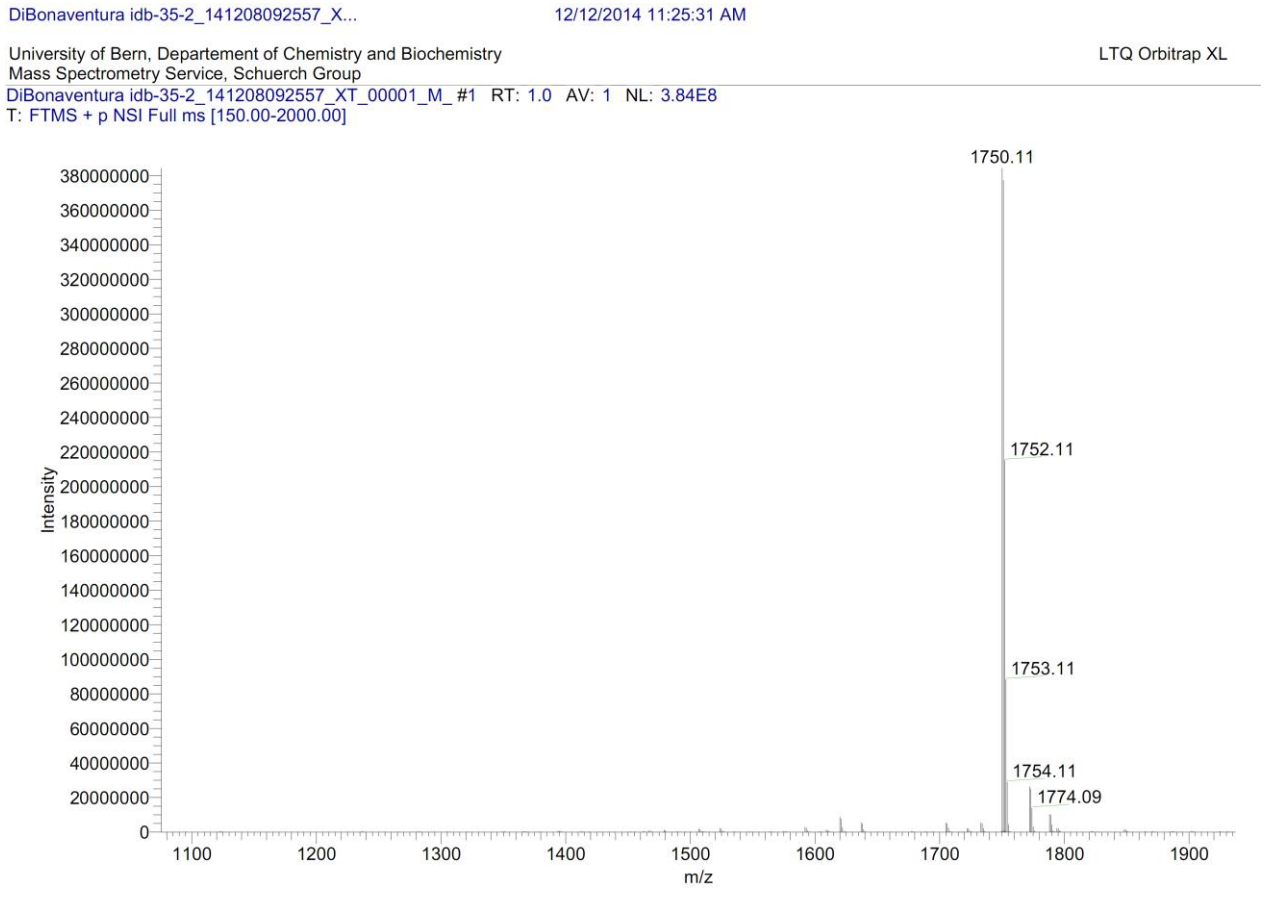




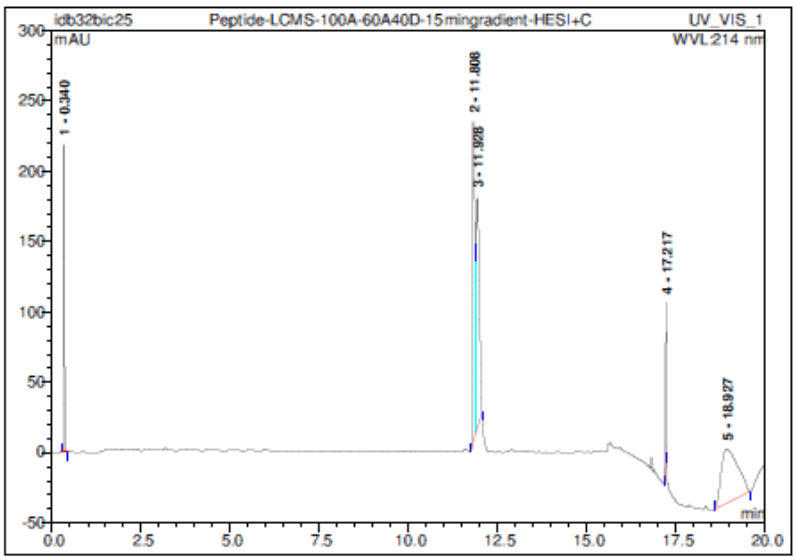


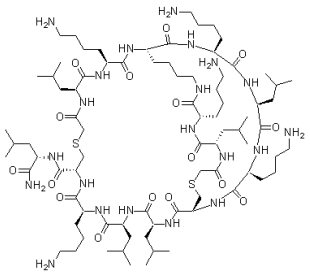
K[1]LL*K*(K[2]LL)KK*Z*[1]KL*Z*[2]L (14b) was obtained as foamy white solid after preparative RP-HPLC (31.8 mg, 12.6 %). Analytical RP-HPLC: t_R = 3.100 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{82}H_{151}N_{21}O_{16}S_2$ calc./obs.1750.11/1750.11 [M].

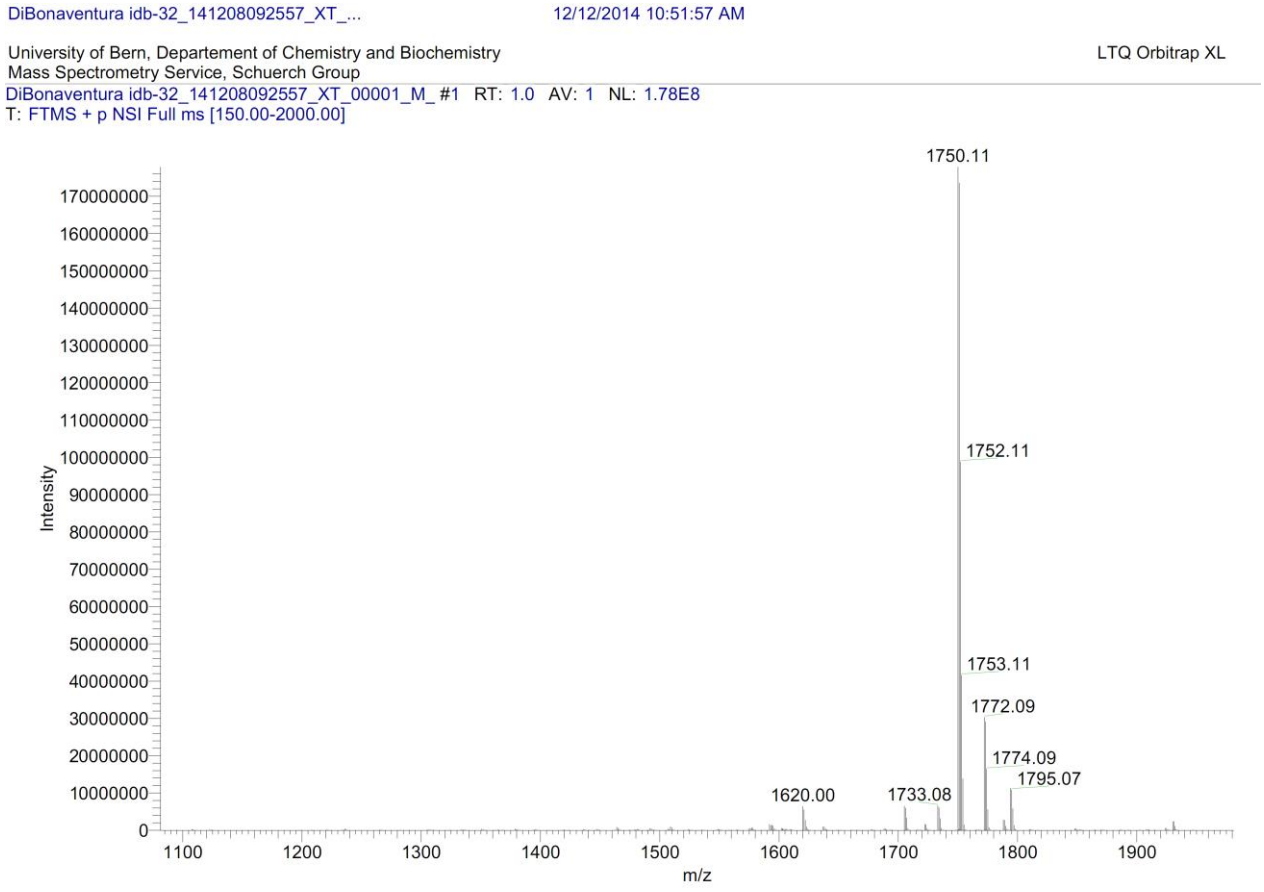




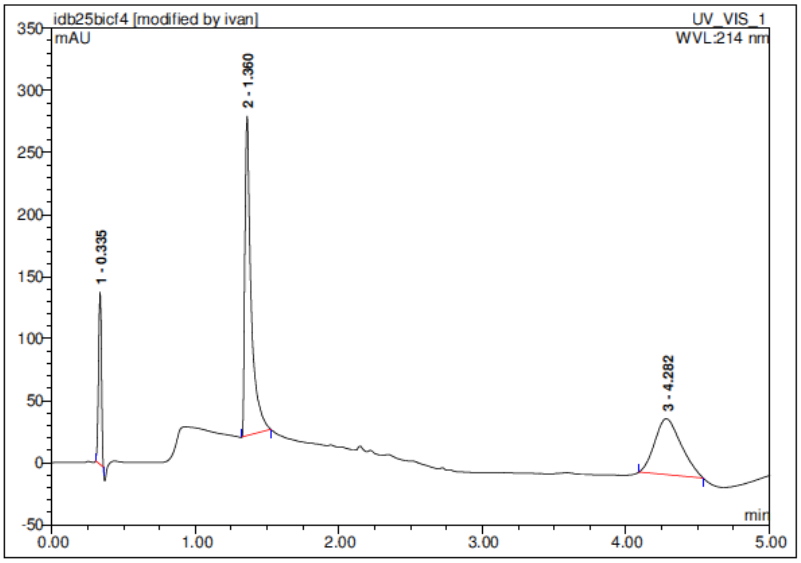
L^{12}K*K*(L^{12}K)KLK*Z*^{21}LLK*Z*^{12}L (15) was obtained, like a mixture of isomers, as foamy white solid after preparative RP-HPLC (13.4 mg, 5.3 %). Analytical RP-HPLC: t_R = 11.810 min, 11.930 min (A/D 100:0 to 0:100 in 20.00 min, λ = 214 nm). MS (ESI+): $C_{82}H_{151}N_{21}O_{16}S_2$ calc./obs. 1750.11/1750.11 Da [M].

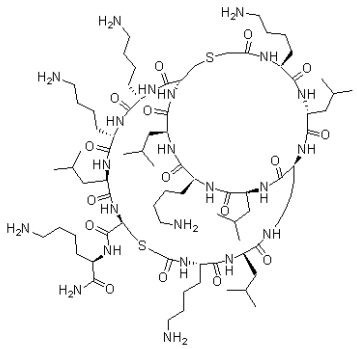


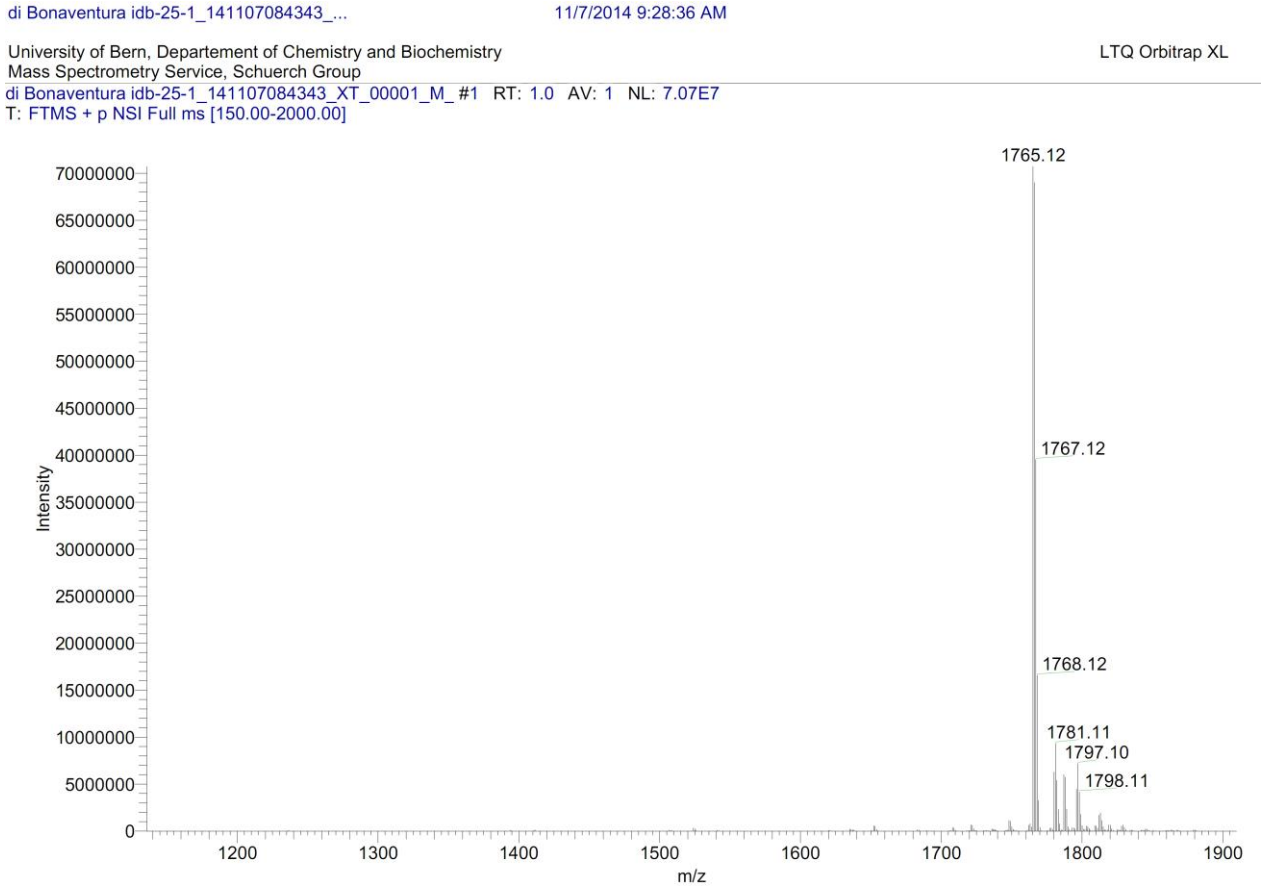




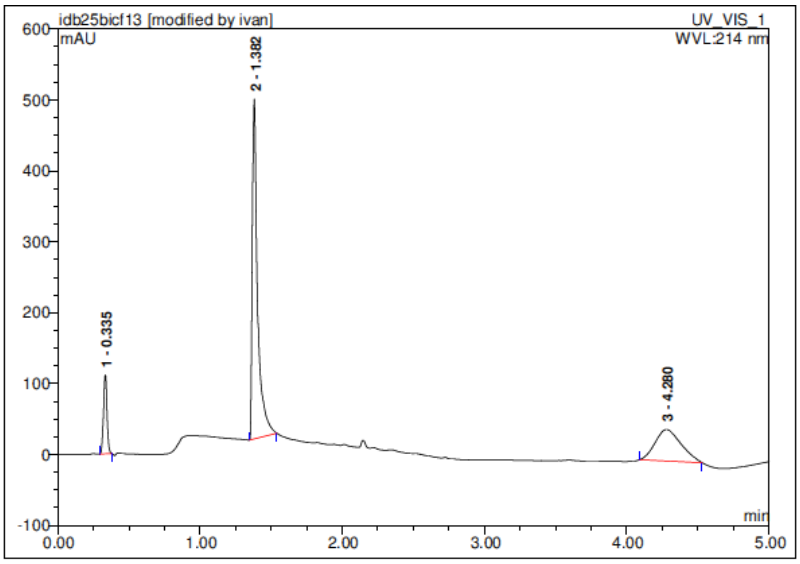
K^{2}L*K*(K^{1}L)LKL*Z*^{1}KKL*Z*^{2}K (16a) was obtained as foamy white solid after preparative RP-HPLC (24.8 mg, 9.0%). Analytical RP-HPLC: t_R = 1.360 min (A/D 100:0 to 0:100 in 5.0 min, λ = 214 nm). MS (ESI+): $C_{82}H_{152}N_{22}O_{16}S_2$ calc./obs. 1765.12/176512 Da [M].

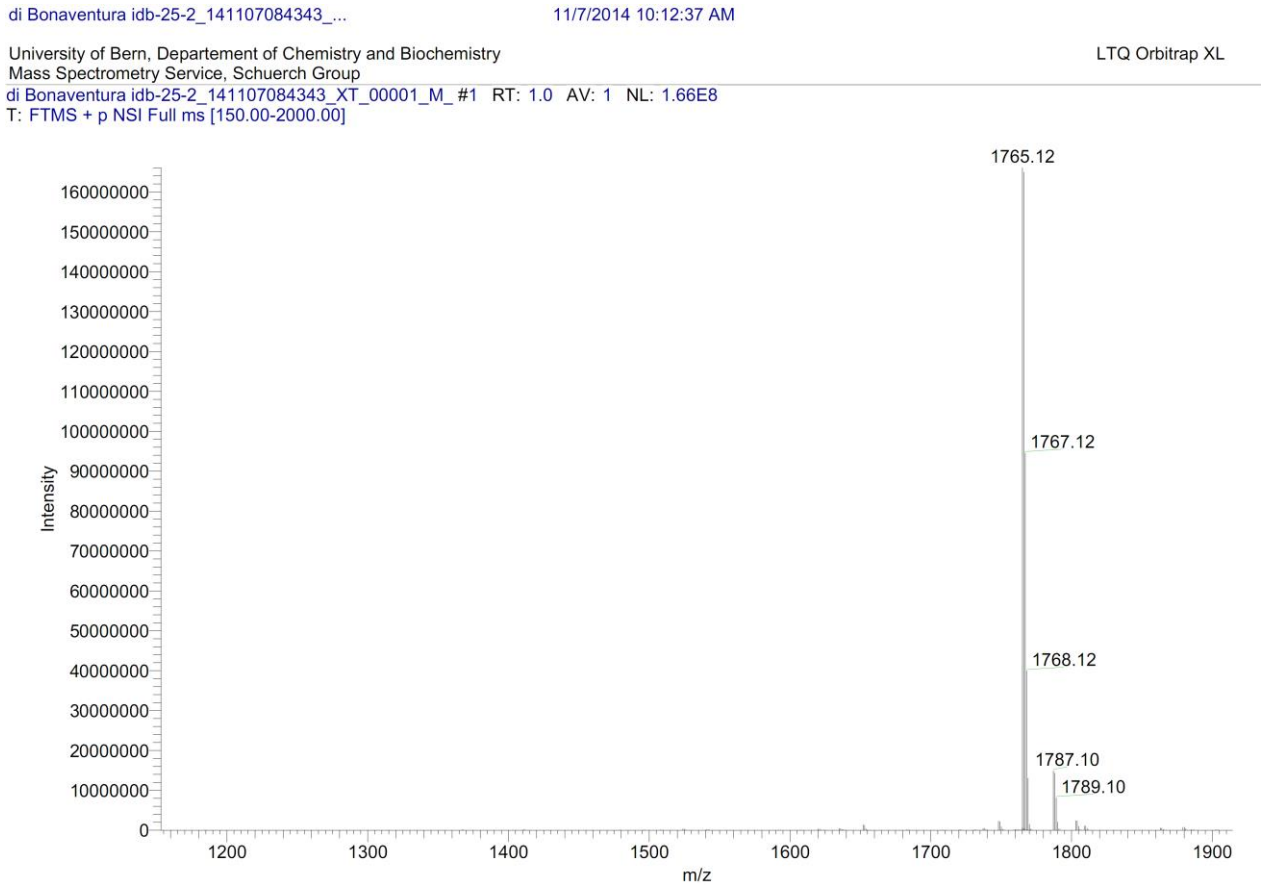




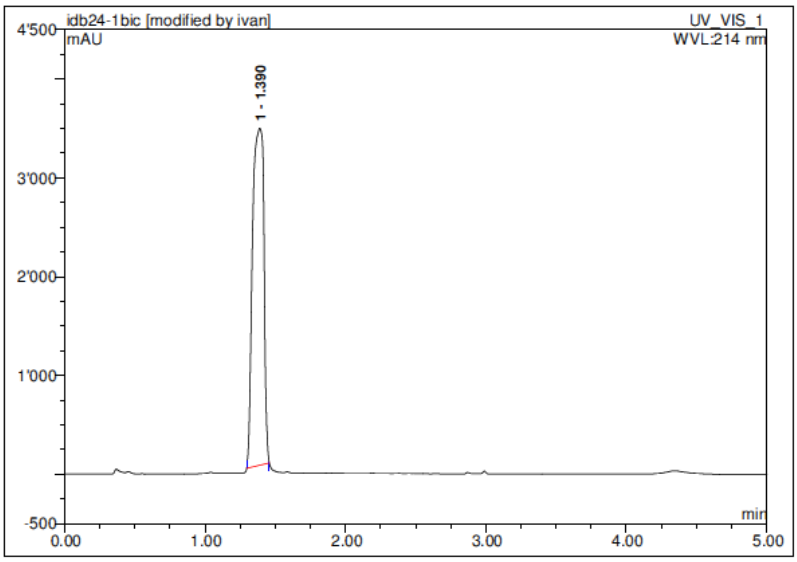


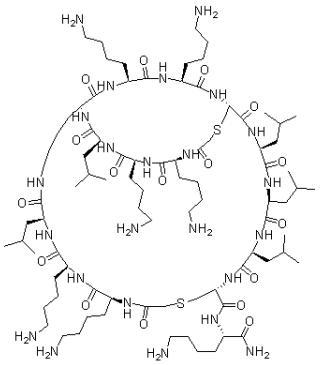
K[1]L*K*(K[2]L)LKL*Z*[1]KKL*Z*[2]K (16b) was obtained as foamy white solid after preparative RP-HPLC (4.4 mg, 1.7 %). Analytical RP-HPLC: t_R = 1.380 min (A/D 100:0 to 0:100 in 5.0 min, λ = 214 nm). MS (ESI+): $C_{82}H_{152}N_{22}O_{16}S_2$ calc./obs. 1765.12/176512 Da [M].

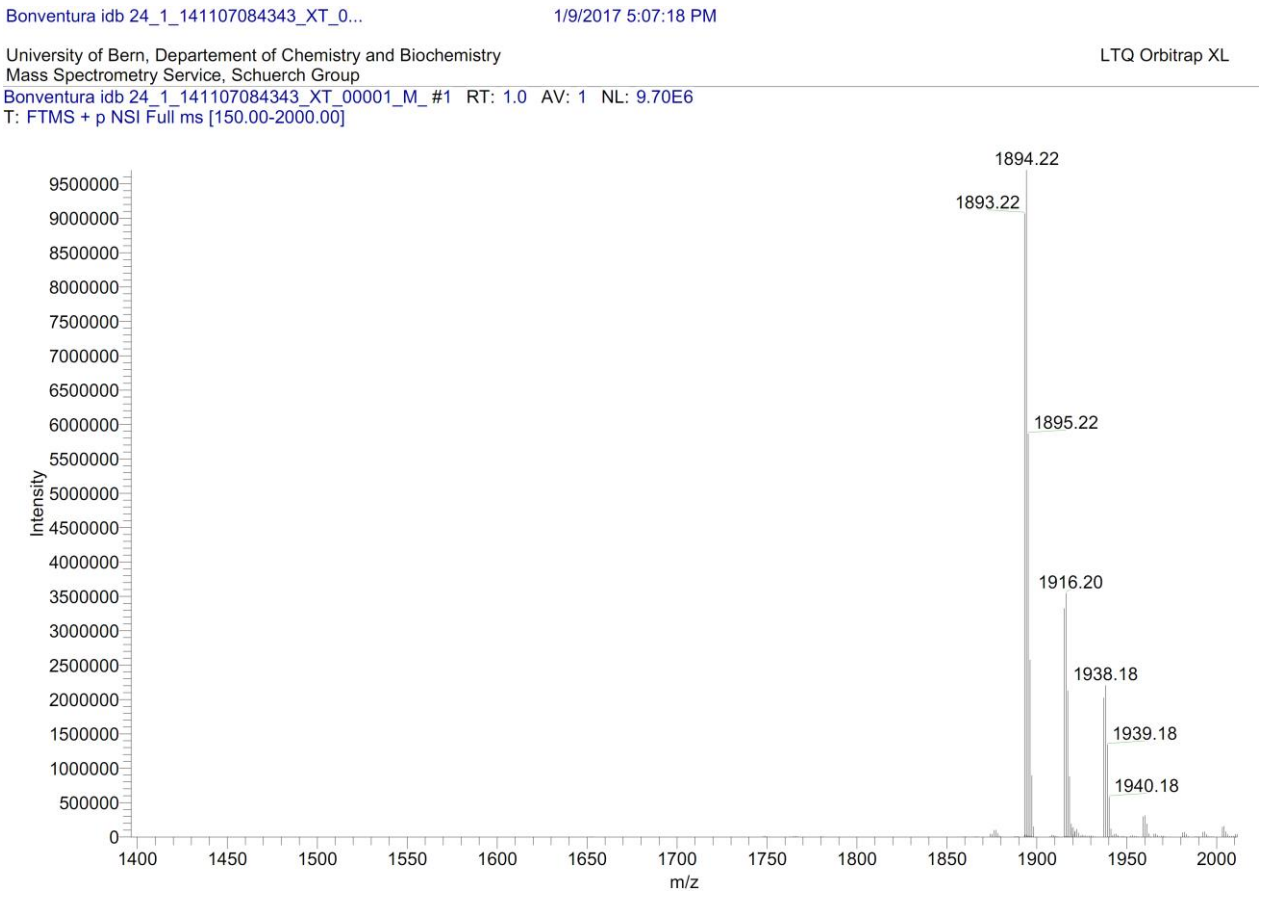




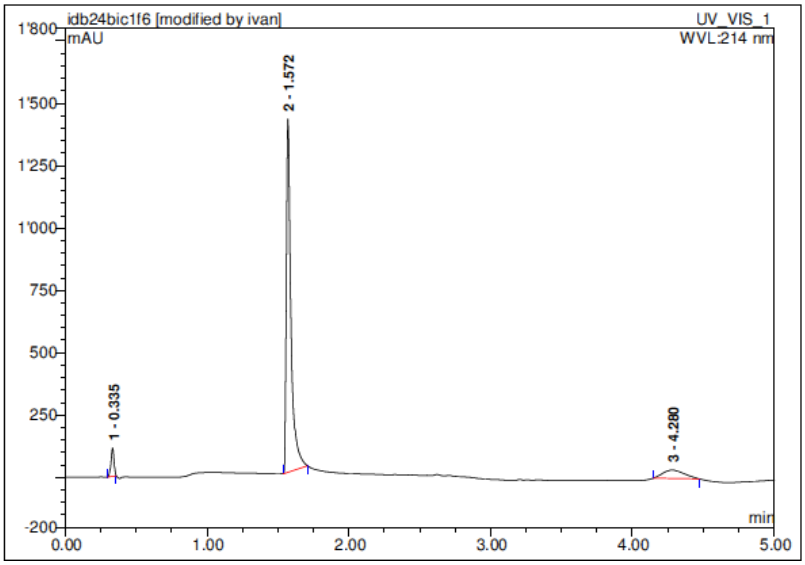
K^{2}KL*K*(K^{1}KL)KK*Z*^{1}LLL*Z*^{2}K (17a) was obtained as foamy white solid after preparative RP-HPLC (24.8 mg, 9.0%). Analytical RP-HPLC: t_R = 1.390 min (A/D 100:0 to 0:100 in 5.0 min, λ = 214 nm). MS (ESI+): $C_{88}H_{164}N_{24}O_{17}S_2$ calc./obs. 1893.21/1893.22 Da [M].

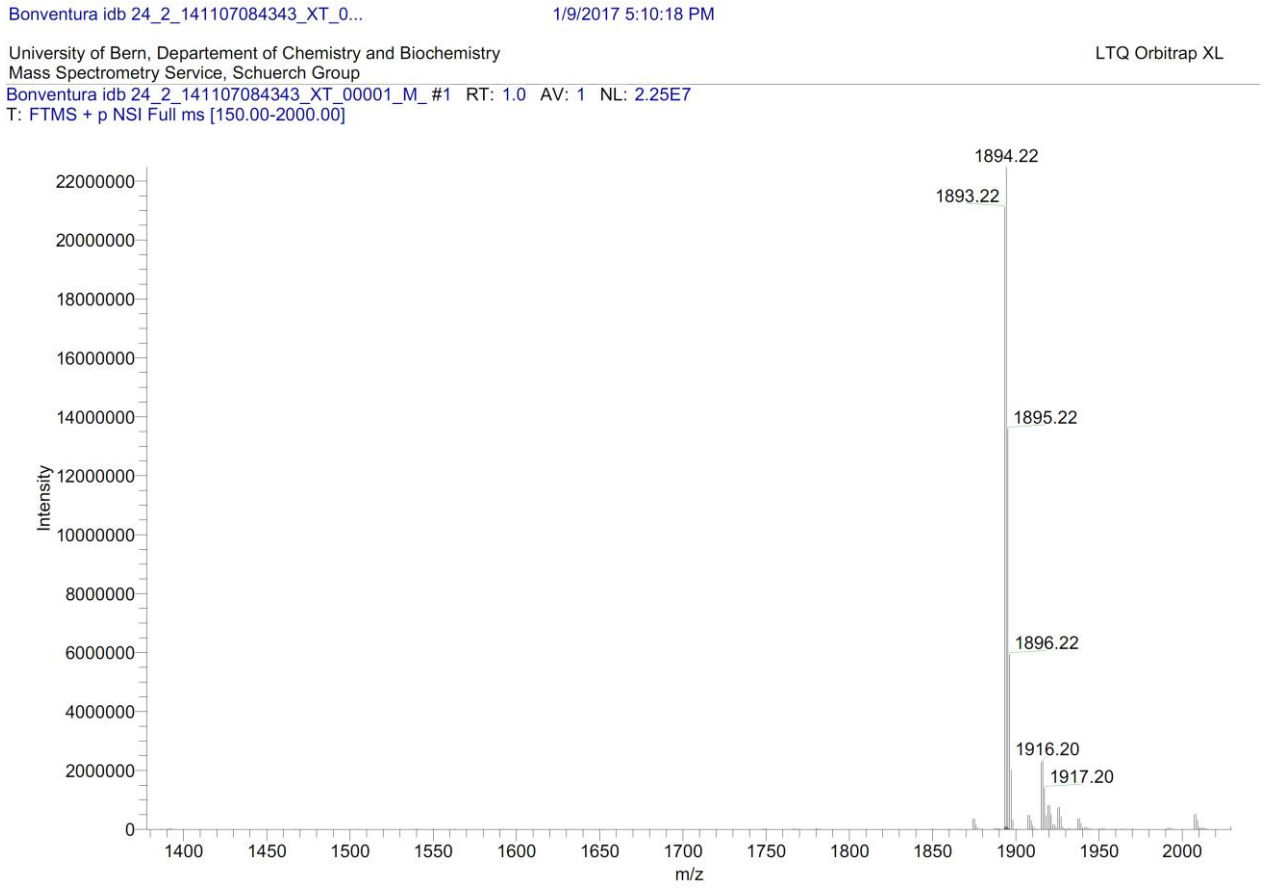




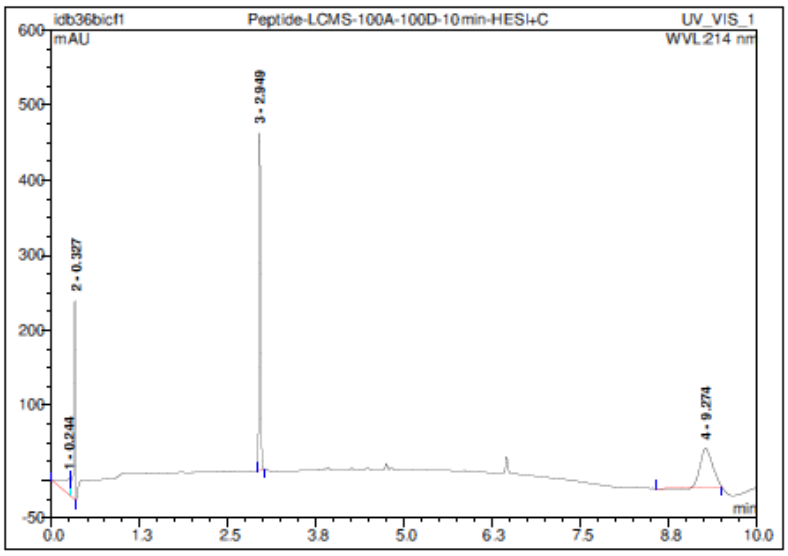


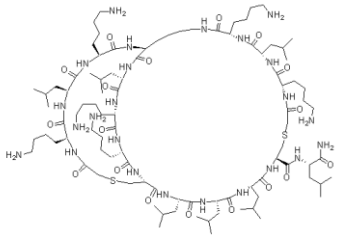
K[1]KL*K*(K[2]KL)KK*Z*[1]LLL*Z*[2]K (17b) was obtained as foamy white solid after preparative RP-HPLC (20.9 mg, 7.6%). Analytical RP-HPLC: t_R = 1.570 min (A/D 100:0 to 0:100 in 5.0 min, λ = 214 nm). MS (ESI+): $C_{88}H_{164}N_{24}O_{17}S_2$ calc./obs. 1893.21/1893.22 Da [M].

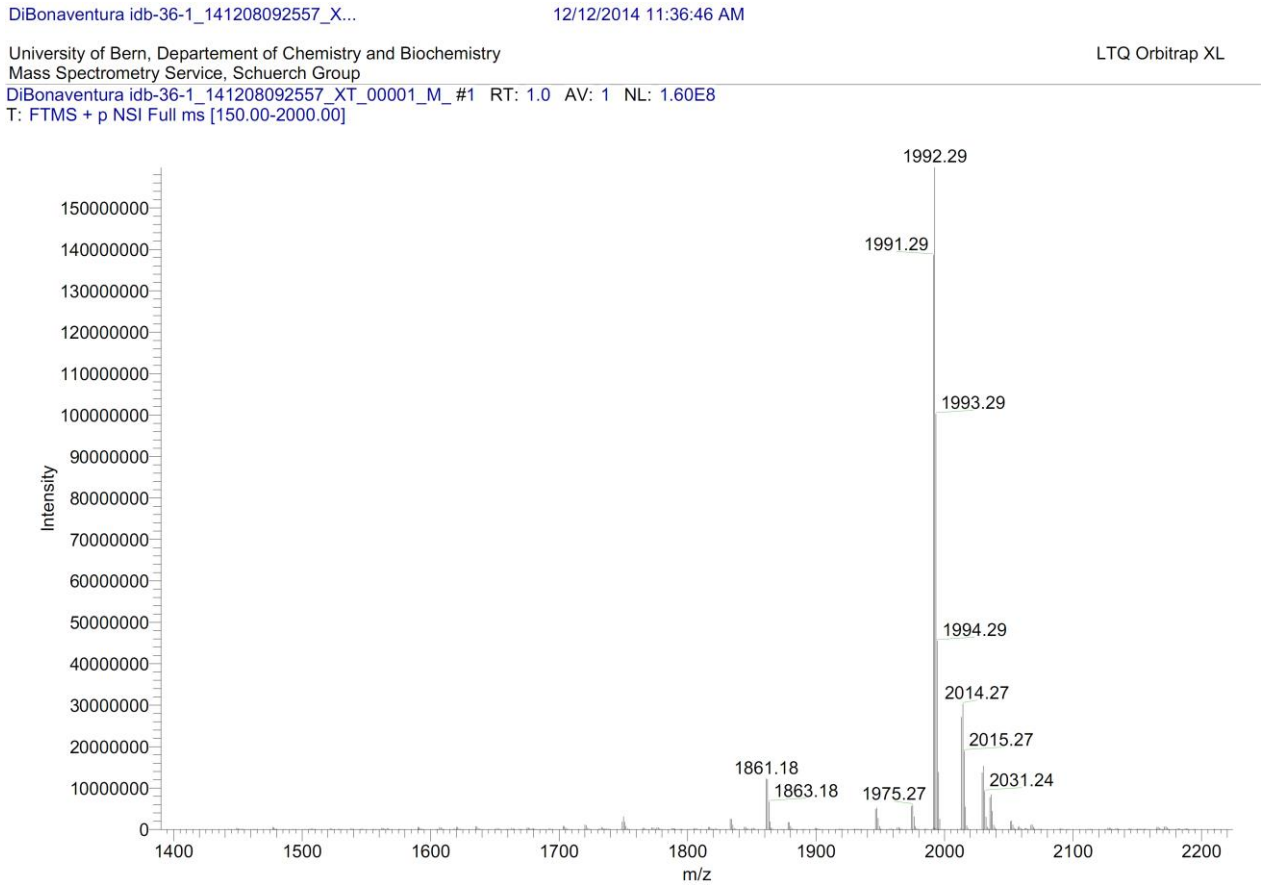




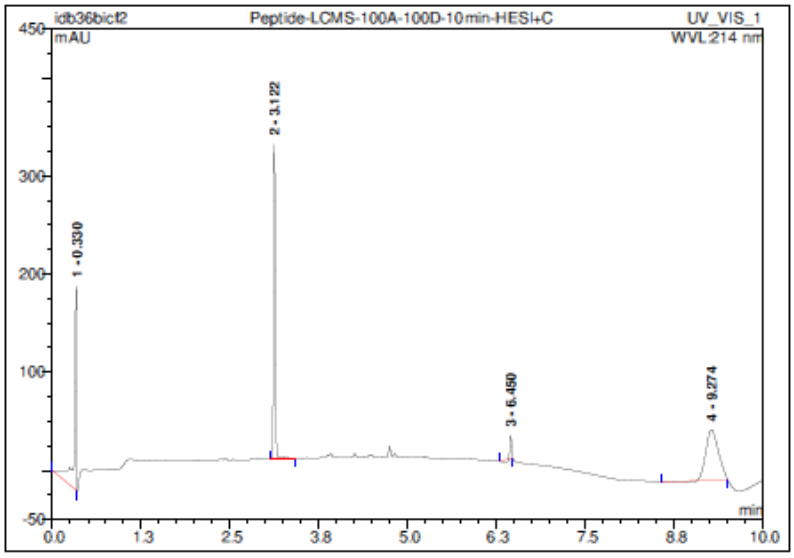
K[1]LK*K*(K[2]LK)LKK*Z*[2]LLL*Z*[1]L (18a) was obtained as foamy white solid after preparative RP-HPLC (4.4 mg, 1.6 %). Analytical RP-HPLC: t_R = 2.950 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs.1991.29/1991.29 Da [M].

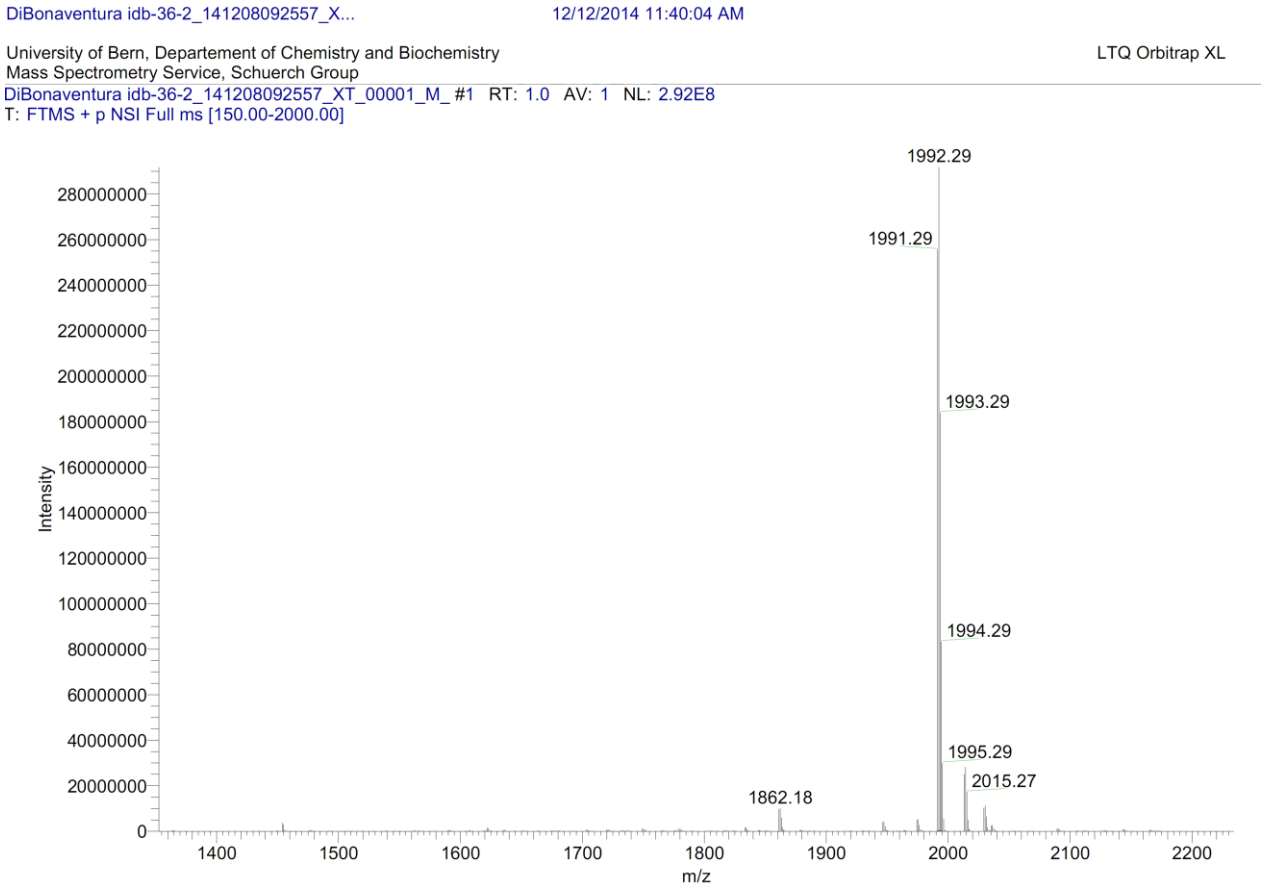




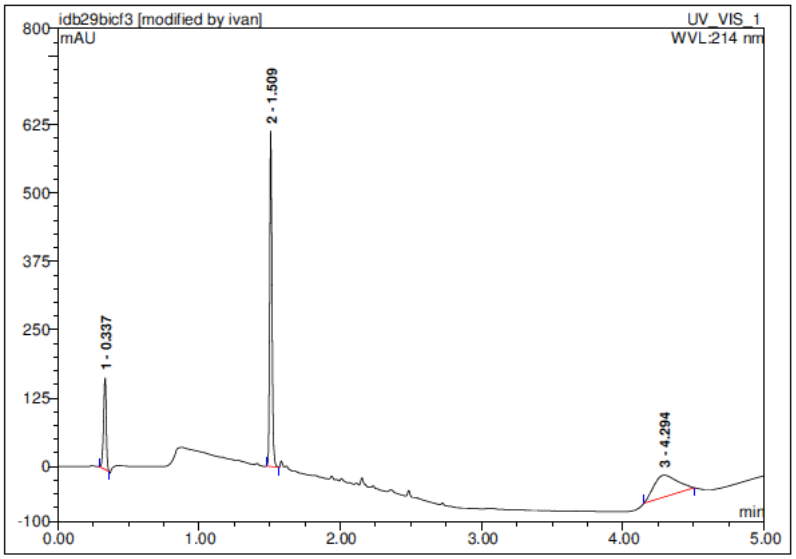


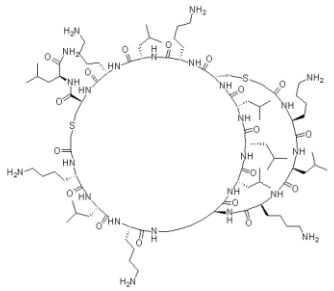
K[1]LK*K*(K[2]LK)LKK*Z*[1]LLL*Z*[2]L (18b) was obtained as foamy white solid after preparative RP-HPLC (5.5 mg, 1.9 %). Analytical RP-HPLC: t_R = 3.120 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$calc./obs.calc./obs.1991.29/1991.29 Da [M].

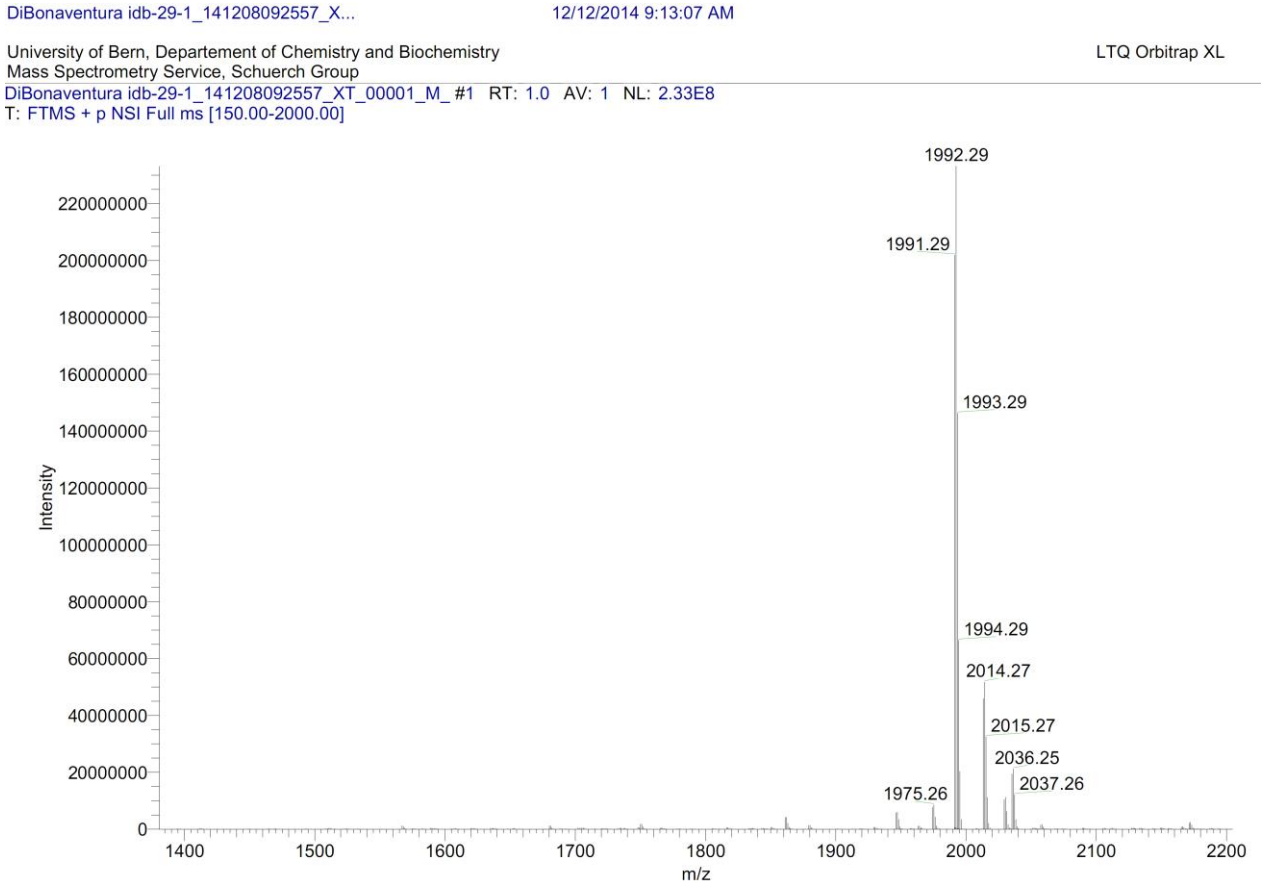




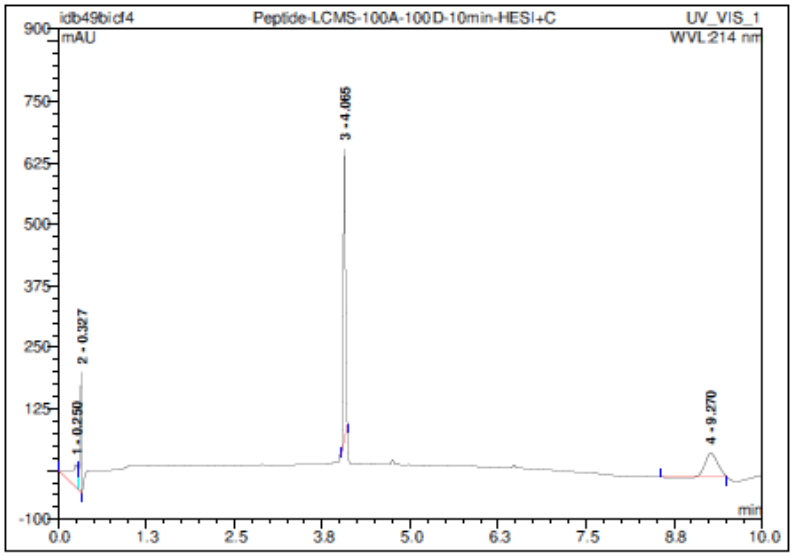
K^{12}LK*K*(K^{12}LK)LLLZ^{21}KLKZ^{12}L (19) was obtained as foamy white solid after preparative RP-HPLC (7.9 mg, 2.7 %). Analytical RP-HPLC: t_R = 1.510 min (A/D 100:0 to 0:100 in 5.00 min, λ = 214 nm). MS (ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs. 1991.29/1991.29 Da [M].

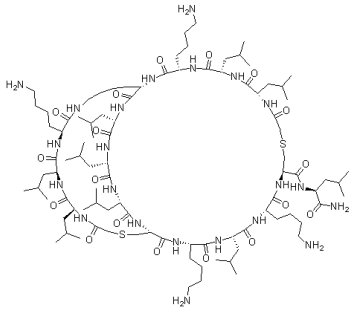


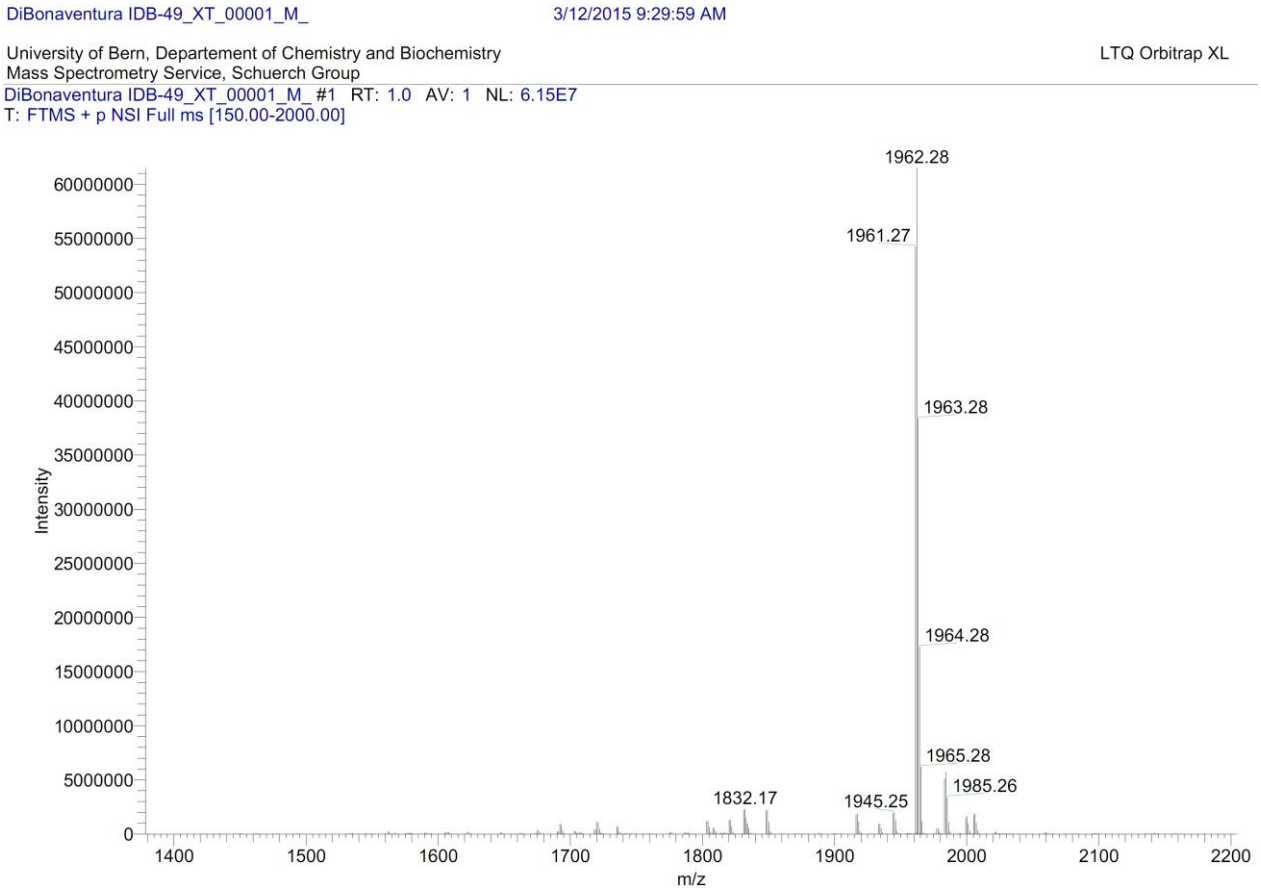




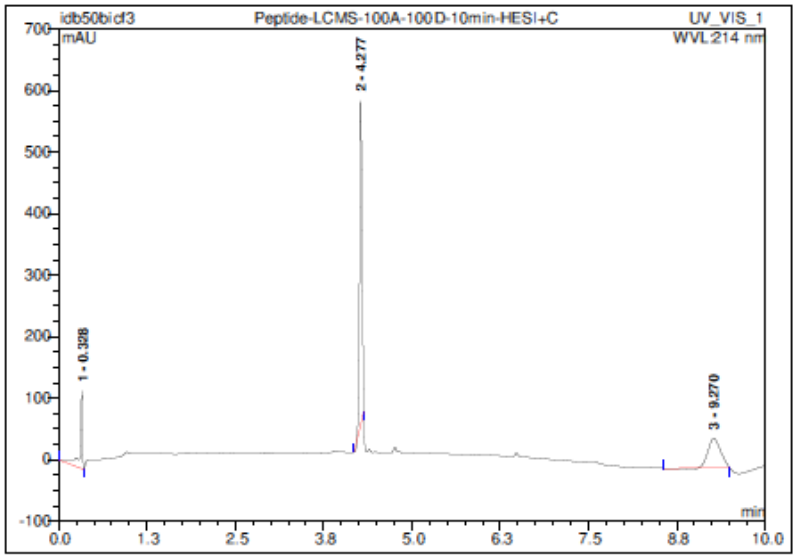
^{12}LLK*K*(L^{12}LK)LLL*Z*^{21}KLK*Z*^{12}L (20) was obtained as foamy white solid after preparative RP-HPLC (11.6 mg, 5.2 %). Analytical RP-HPLC: t_R = 4.070 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{172}N_{22}O_{18}S_2$ calc./obs.1961.27/1961.27 Da [M].

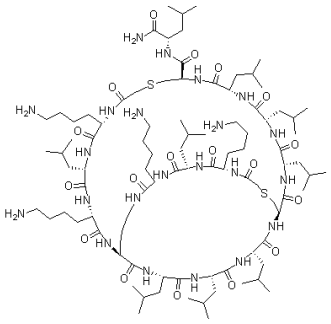


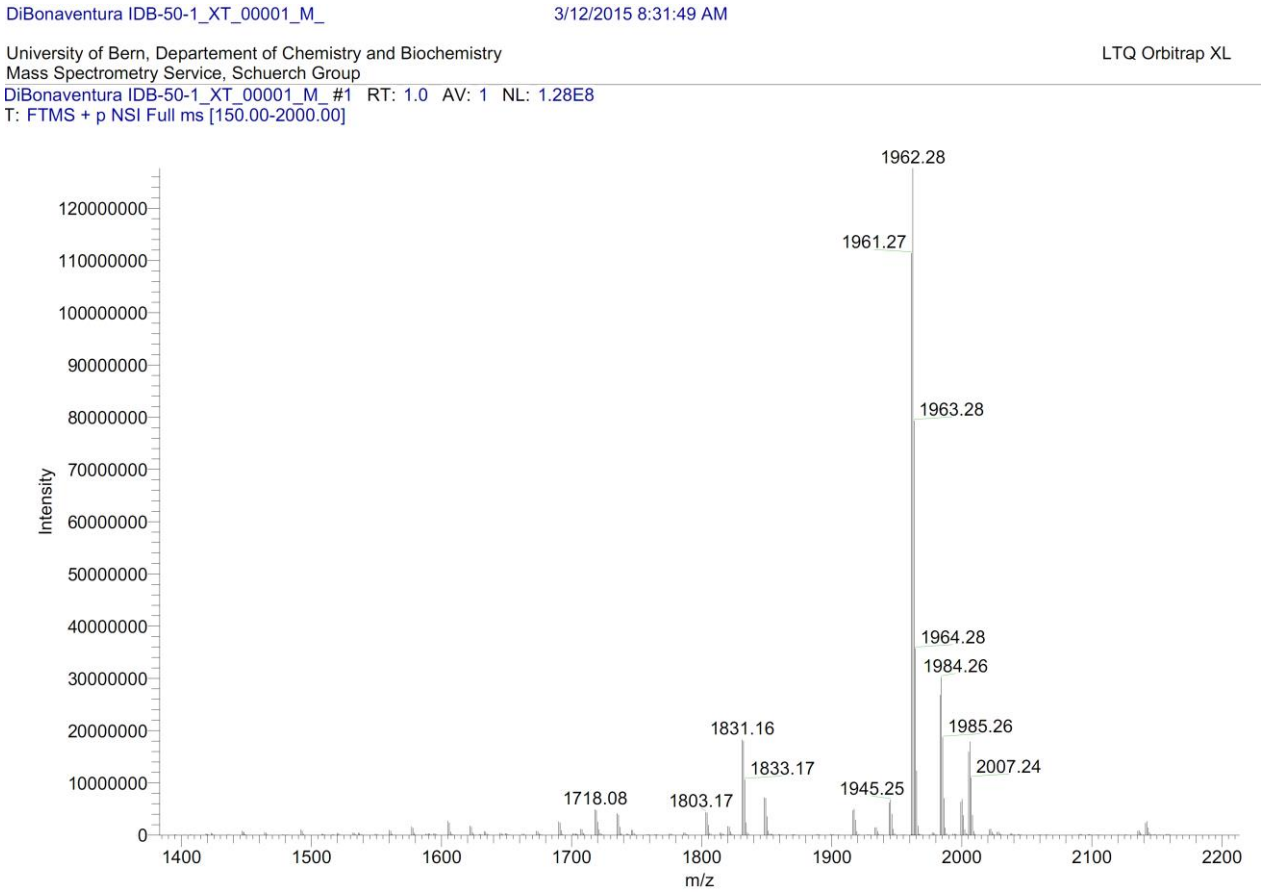




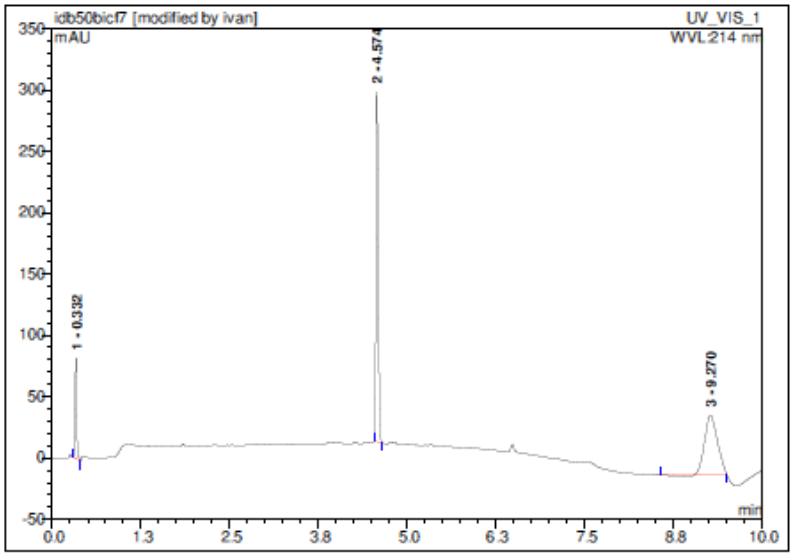
^{2}KLK*K*(K^{1}LK)LLL*Z*^{1}LLL*Z*^{2}L (21a) was obtained, as foamy white solid after preparative RP-HPLC (6.7 mg, 3.0 %). Analytical RP-HPLC: t_R = 4.280 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{172}N_{22}O_{18}S_2$ calc./obs.1961.27/1961.27 Da [M].

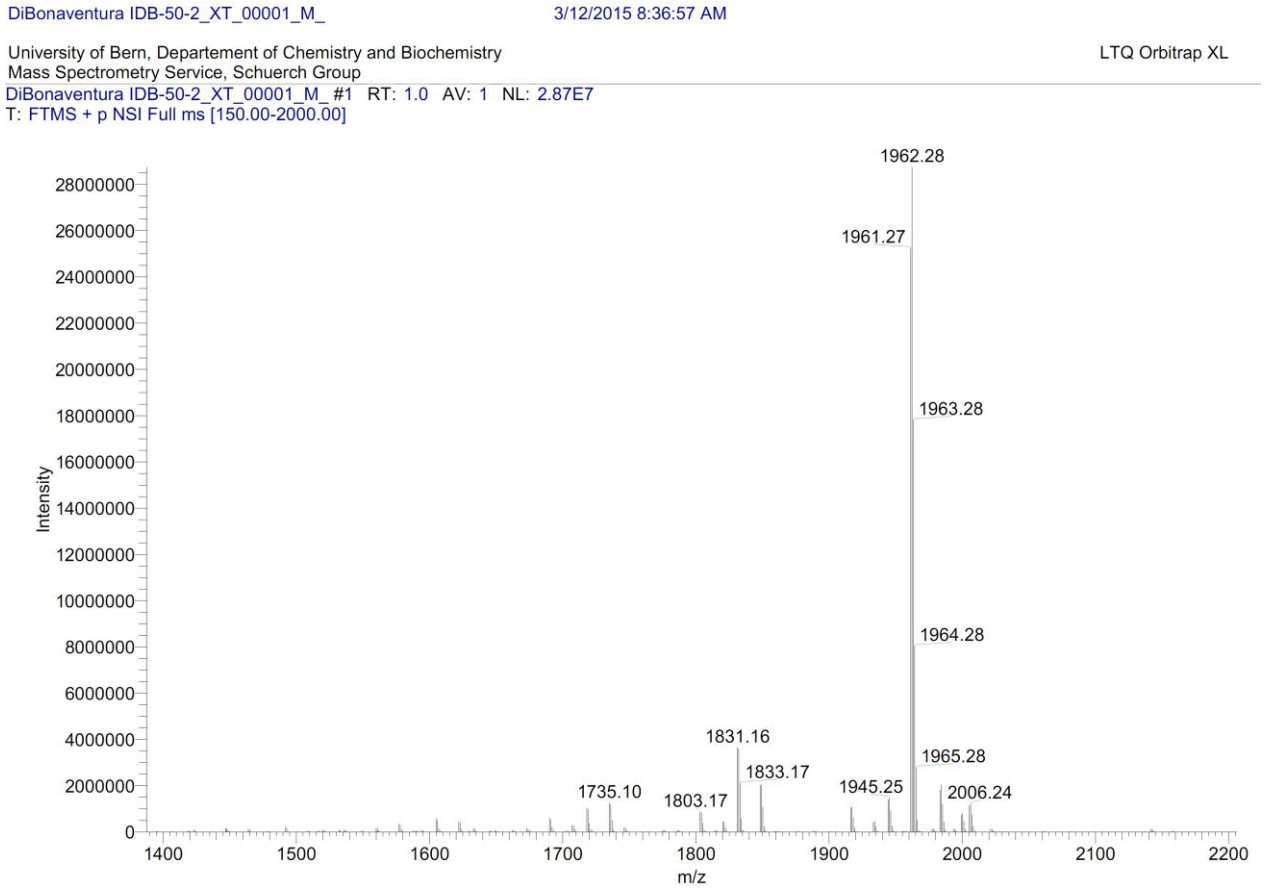




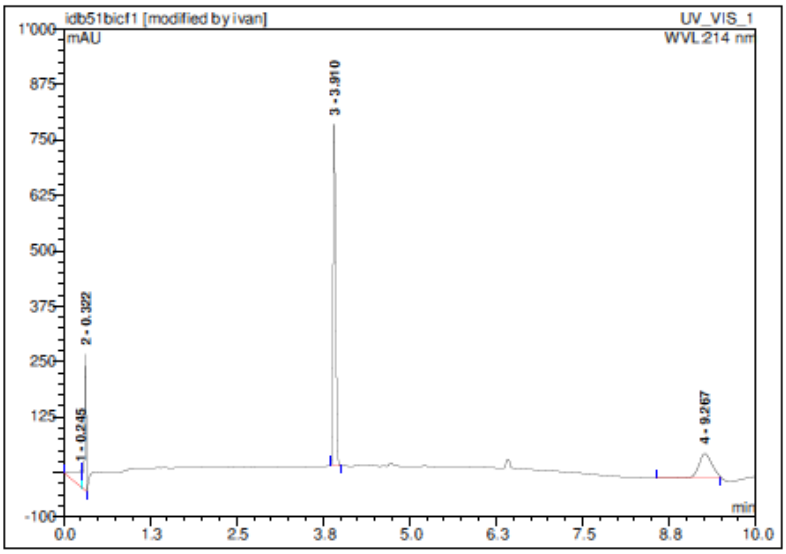


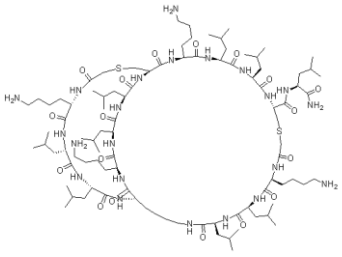
^{1}KLK*K*(K^{2}LK)LLL*Z*^{1}LLL*Z*^{2}L (21b) was obtained, as foamy white solid after preparative RP-HPLC (3.7 mg, 1.6 %). Analytical RP-HPLC: t_R = 4.570 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{172}N_{22}O_{18}S_2$ calc./obs.1961.27/1961.27 Da [M].

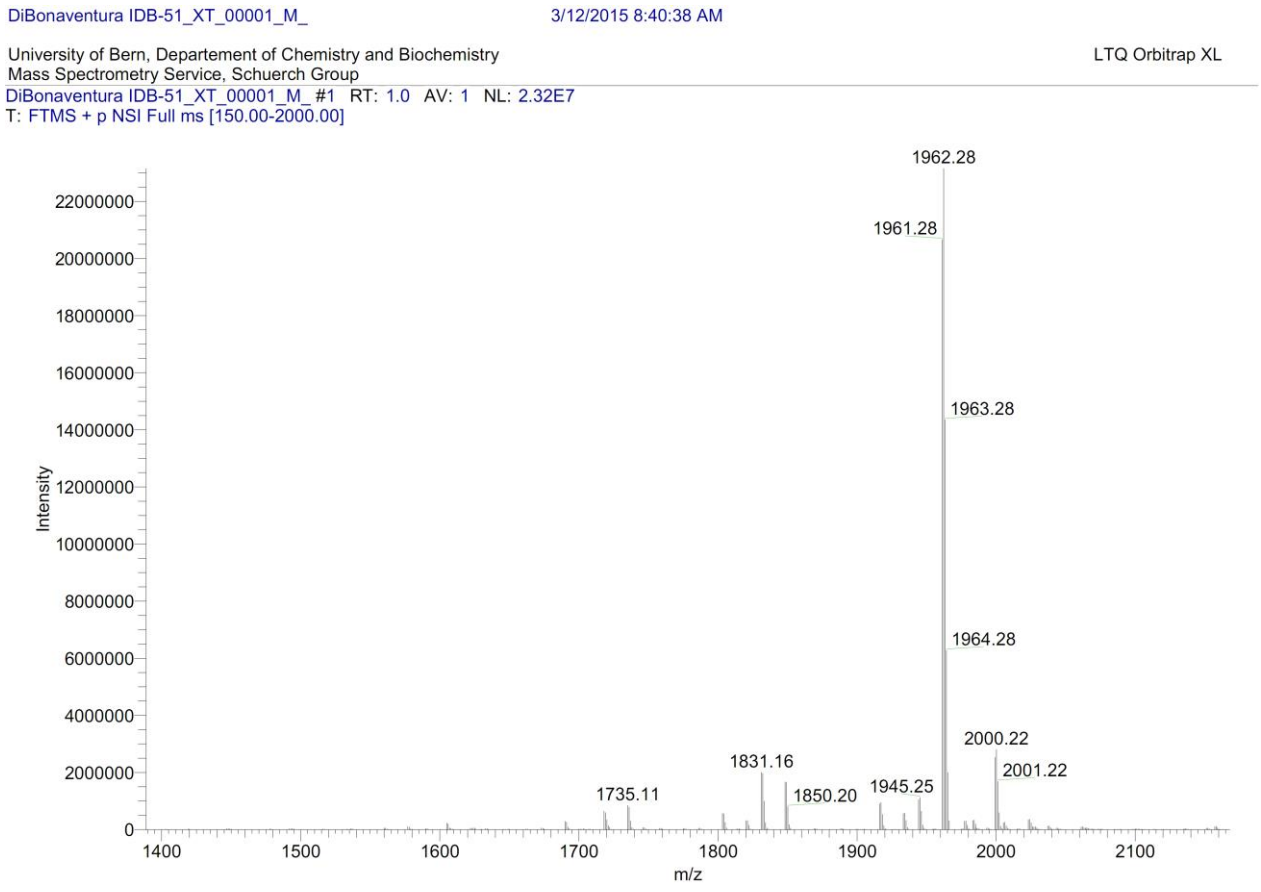




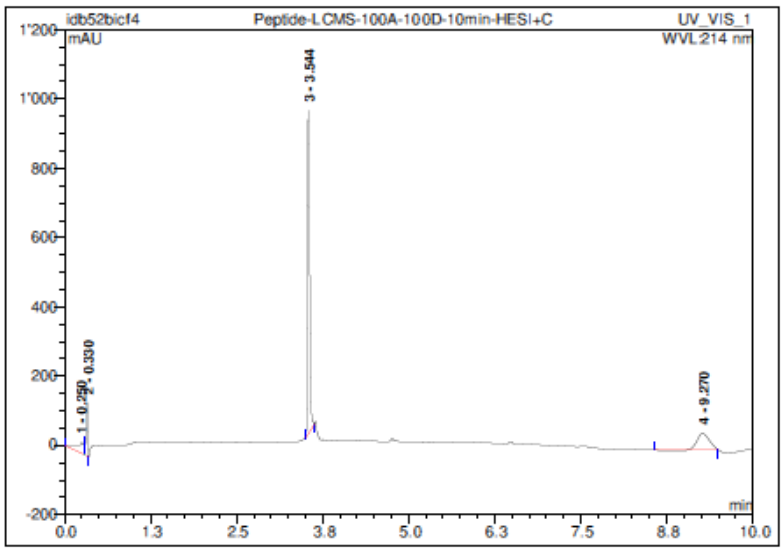
^{12}KLL*K*(K^{12}LL)KLL*Z*^{21}KLL*Z*^{12}L (22) was obtained as foamy white solid after preparative RP-HPLC (8.9 mg, 4.0 %). Analytical RP-HPLC: t_R = 3.910 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{172}N_{22}O_{18}S_2$calc./obs.1961.27/1961.28 Da [M].

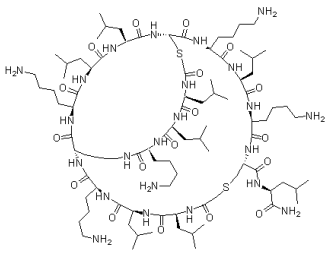


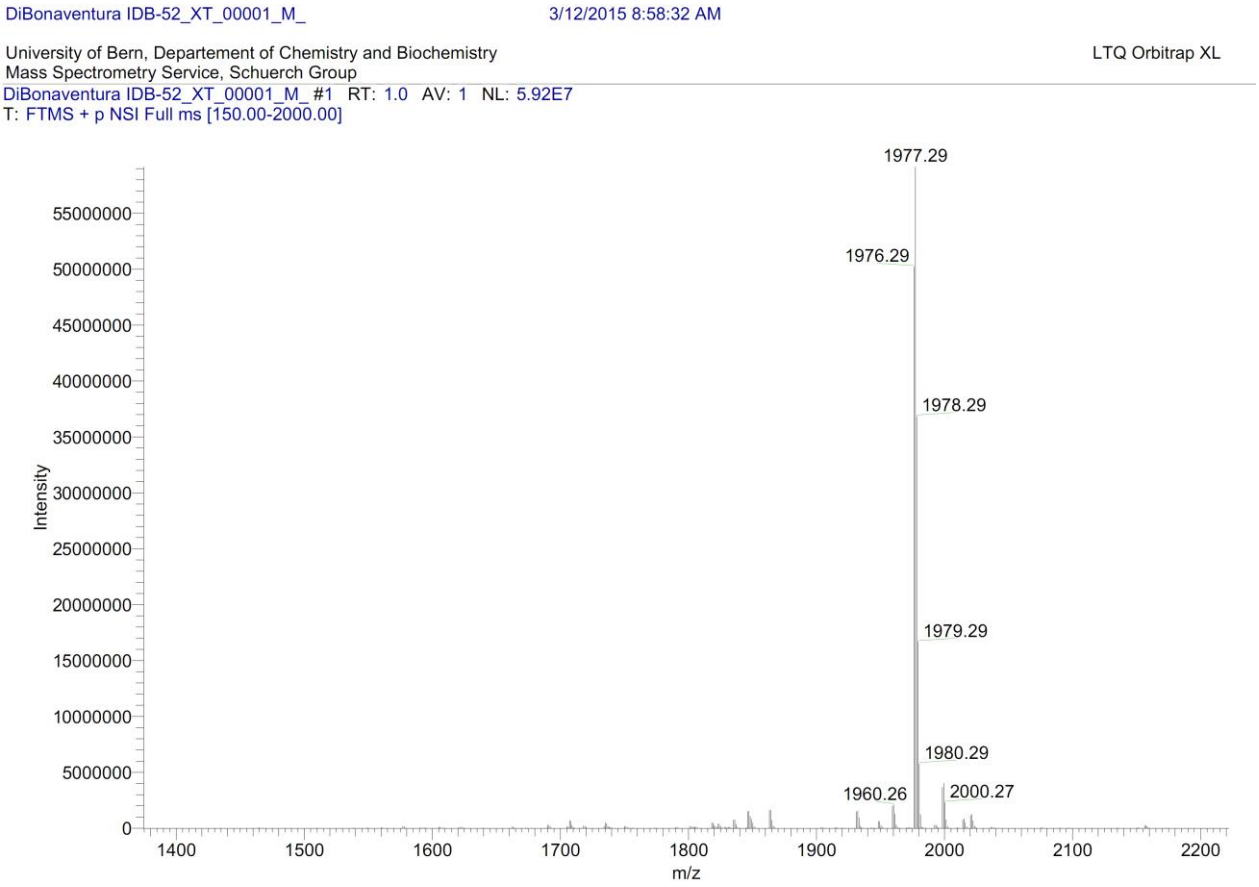




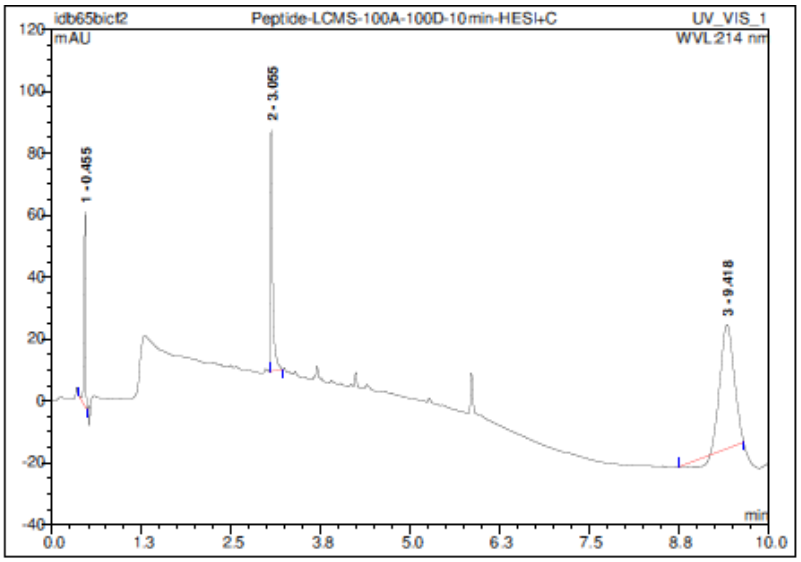
^{12}LLK*K*(L^{12}LK)KLL*Z*^{21}KLK*Z*^{12}L (23) was obtained as foamy white solid after preparative RP-HPLC (17.0 mg, 7.6 %). Analytical RP-HPLC: t_R = 3.540 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{173}N_{23}O_{18}S_2$calc./obs.1976.28/1976.29 Da [M].

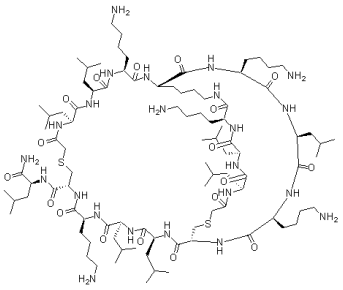


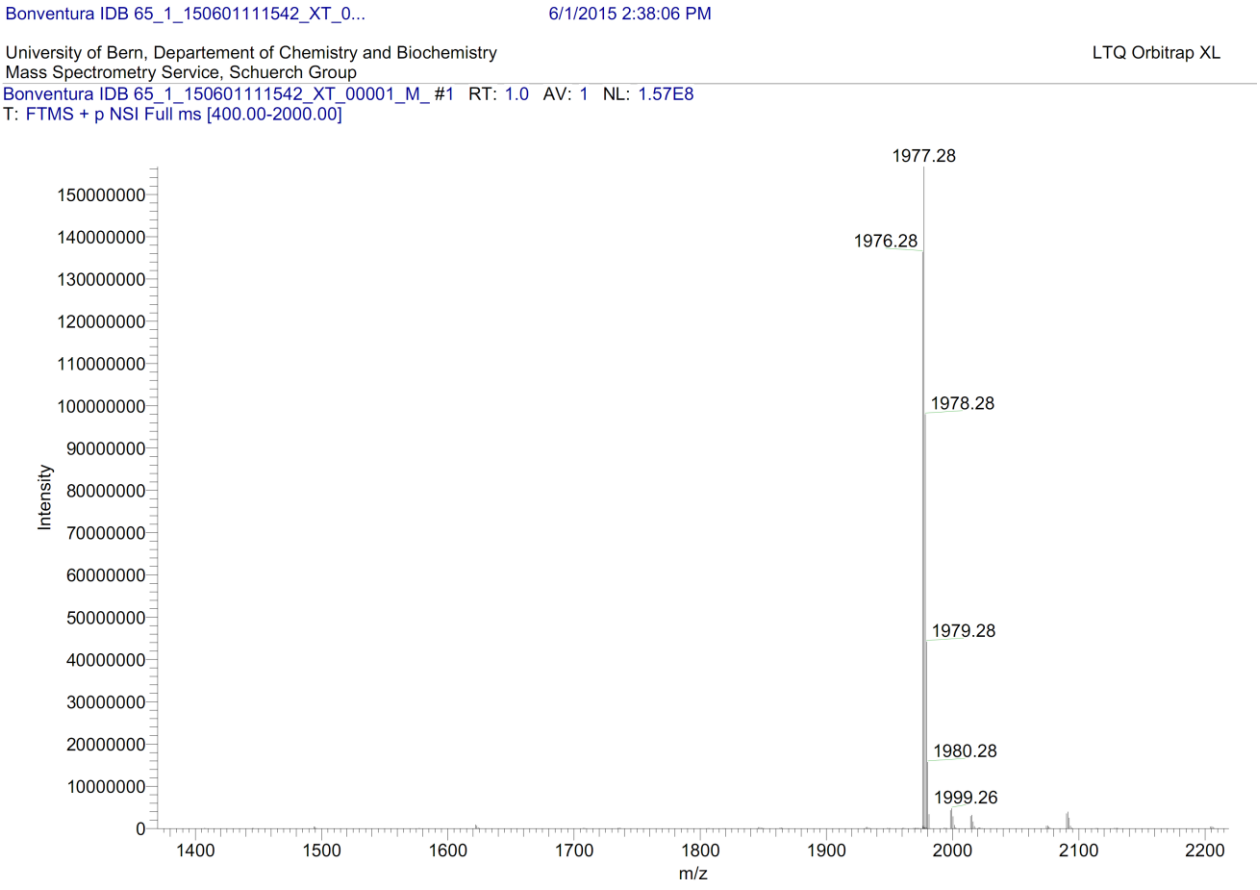




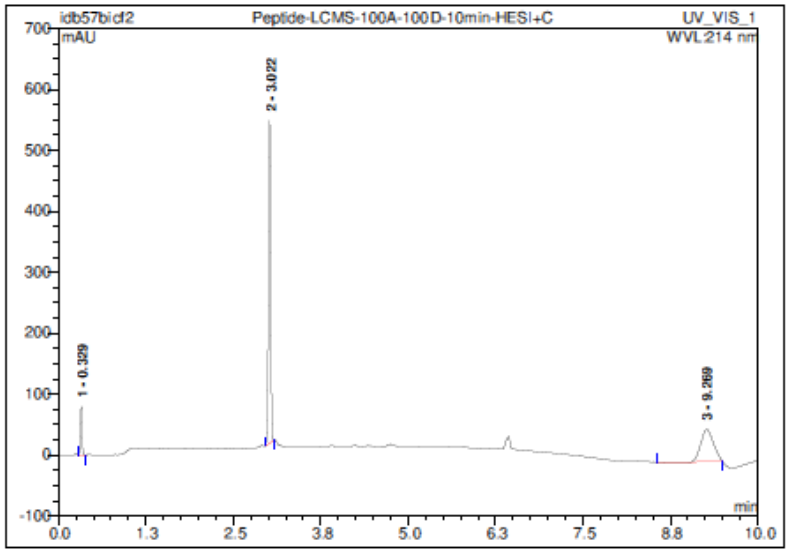
^{12}LLK*K*(L^{12}LK)KLK*Z*^{21}LLK*Z*^{12}L (24) was obtained as foamy white solid after preparative RP-HPLC (4.8 mg, 2.4 %). Analytical RP-HPLC: t_R = 3.060 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{173}N_{23}O_{18}S_2$ calc./obs. 1976.28/1976.28 Da [M].

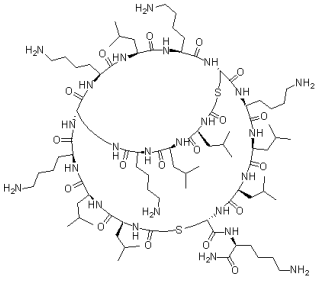


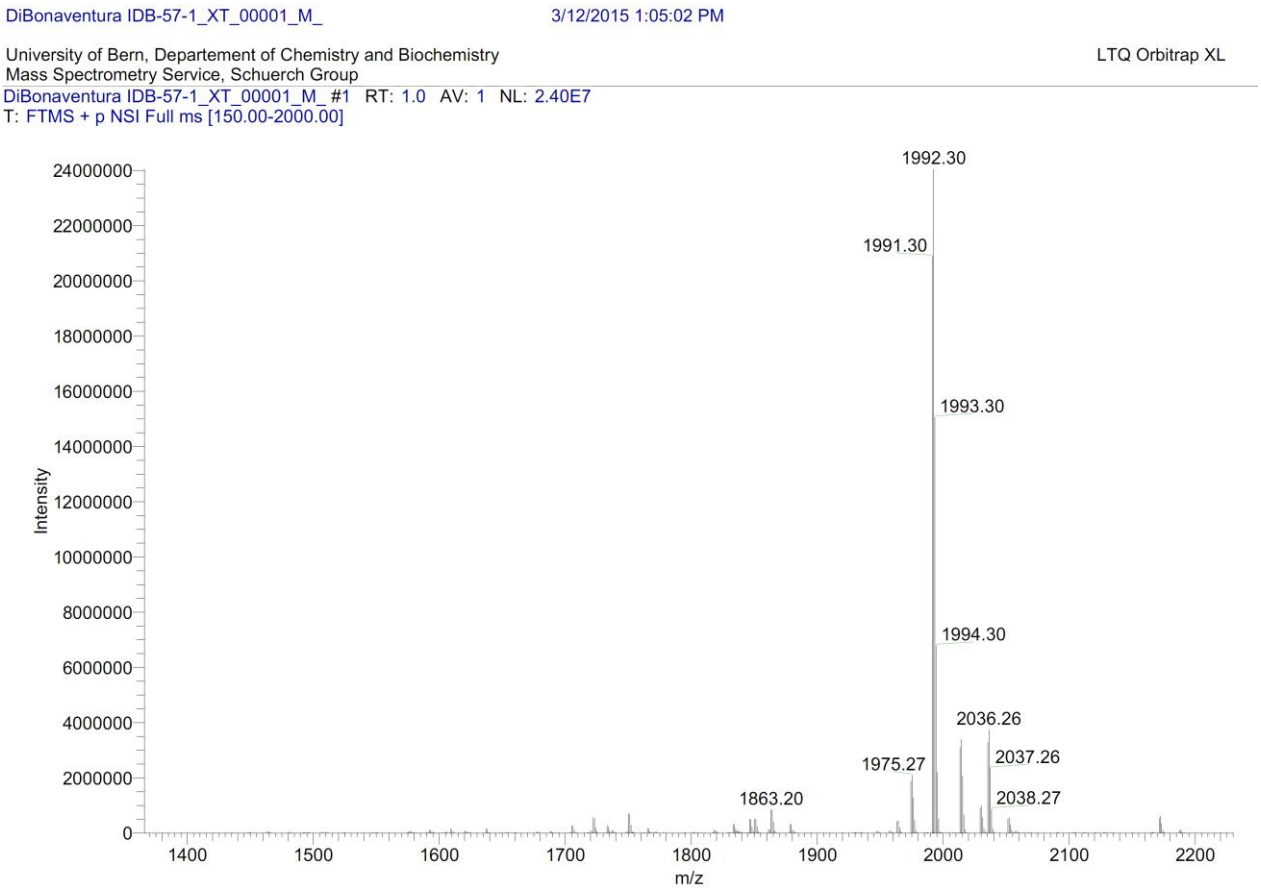




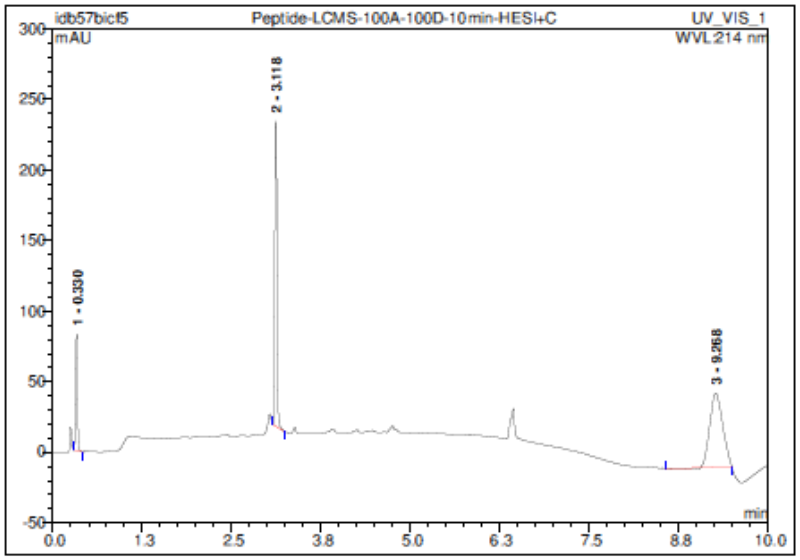
^{2}LLK*K*(L^{1}LK)KLKZ^{1}KLLZ^{2}K (25a) was obtained as foamy white solid after preparative RP-HPLC (7.4 mg, 3.3 %). Analytical RP-HPLC: t_R = 3.020 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs. 1991.29/1991.30 Da [M].

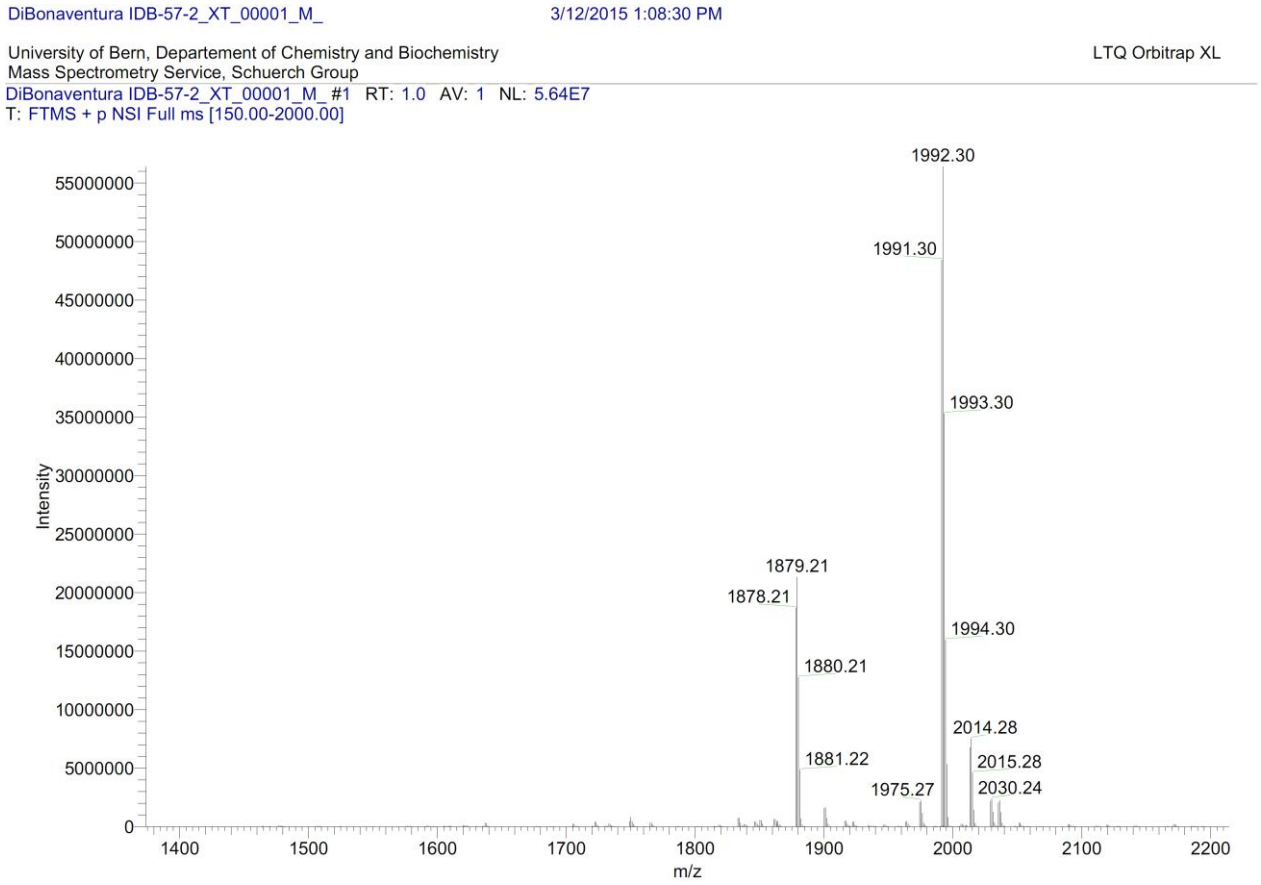




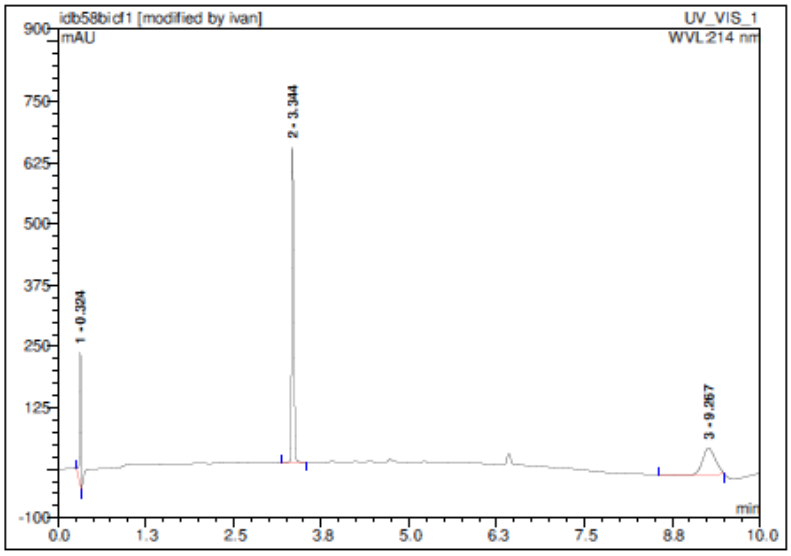


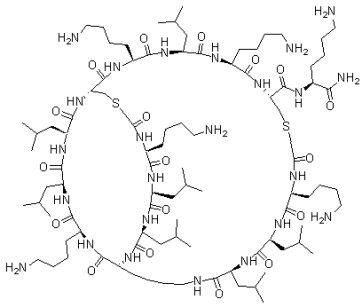
^{1}LLK*K*(L^{2}LK)KLK*Z*^{1}KLL*Z*^{2}K (25b) was obtained as foamy white solid after preparative RP-HPLC (4.9 mg, 2.8 %). Analytical RP-HPLC: t_R = 3.120 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs. 1991.29/1991.30 Da [M].

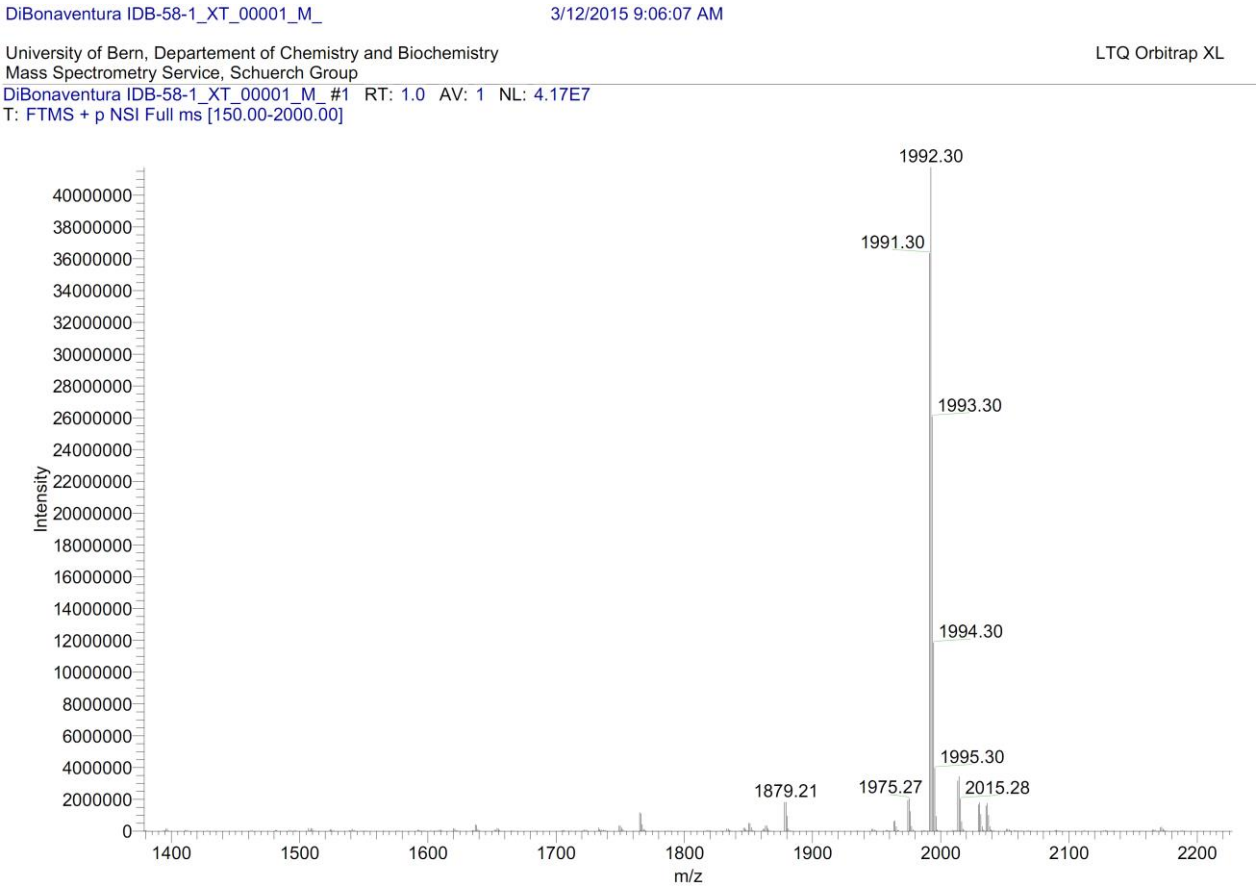




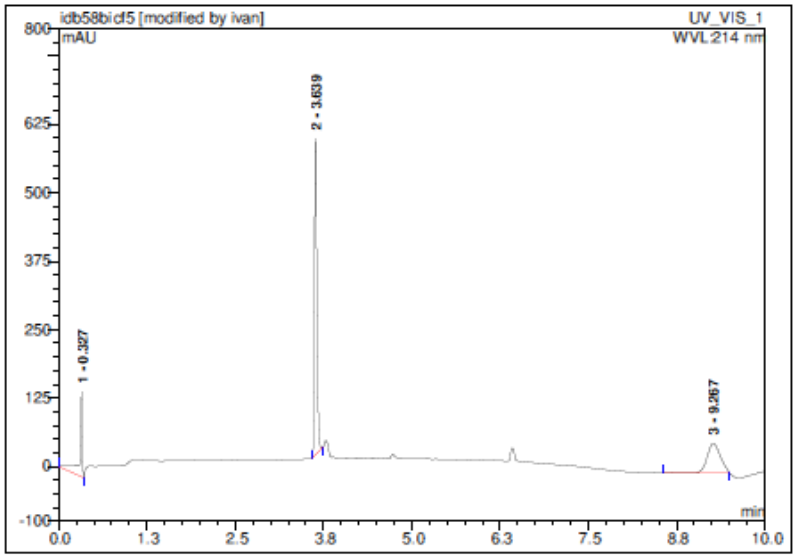
^{1}KLL*K*(K^{2}LL)KLL*Z*^{2}KLK*Z*^{1}K (26a) was obtained as foamy white solid after preparative RP-HPLC (5.8 mg, 2.6 %). Analytical RP-HPLC: t_R = 3.340 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs. 1991.29/1991.30 Da [M].

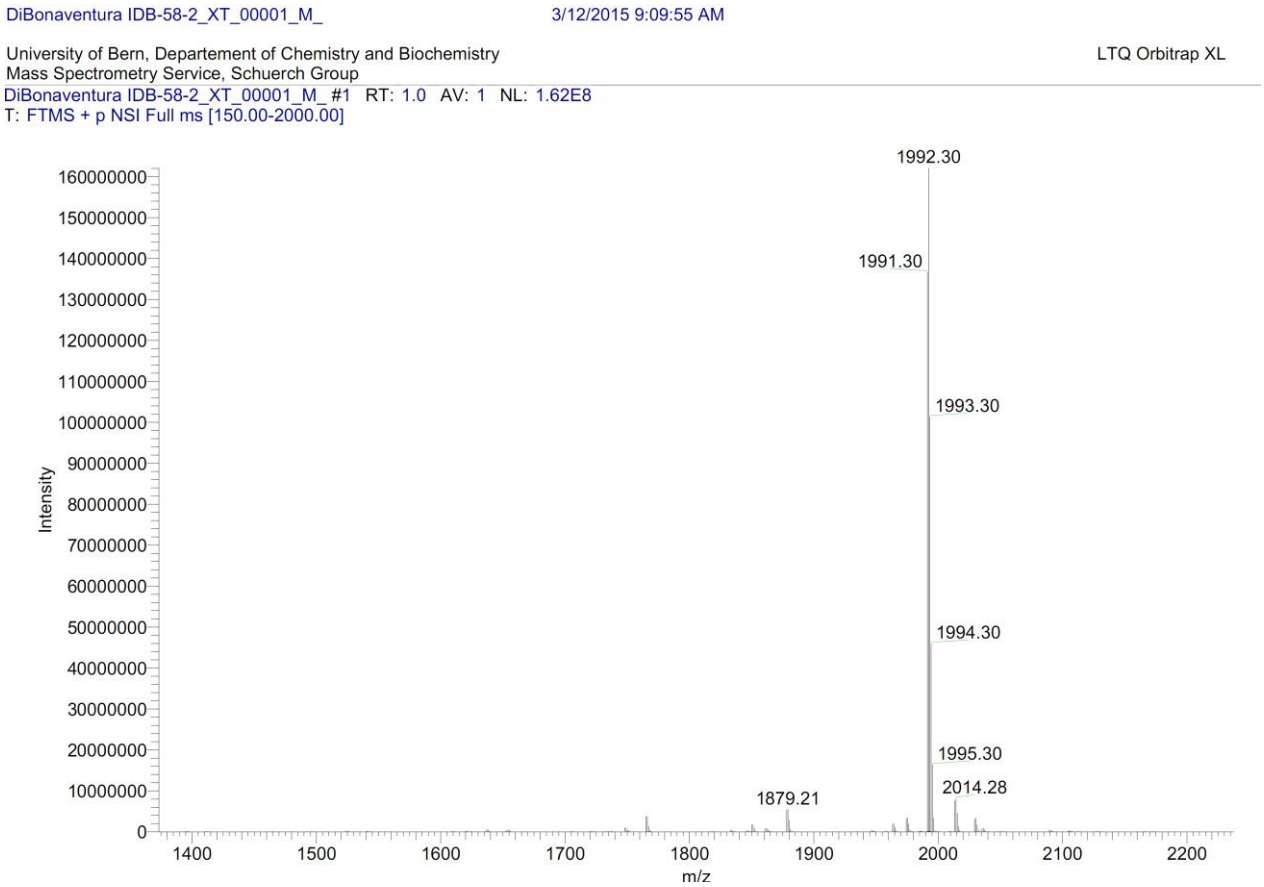




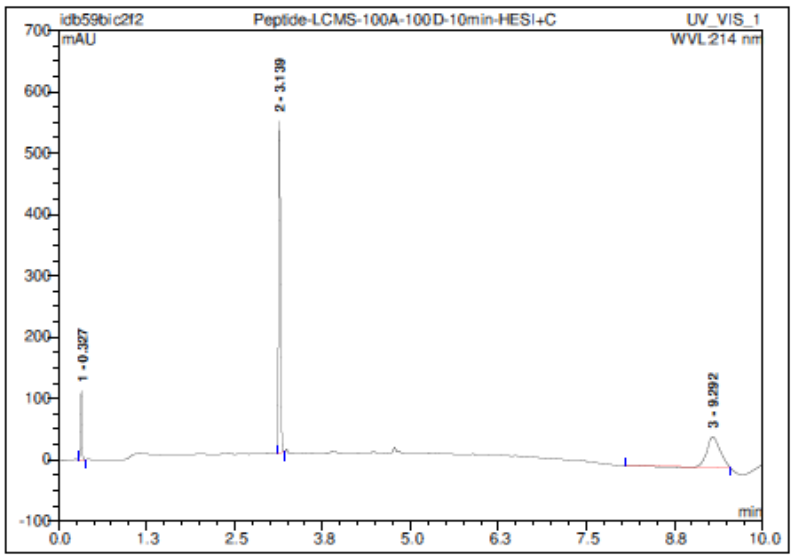


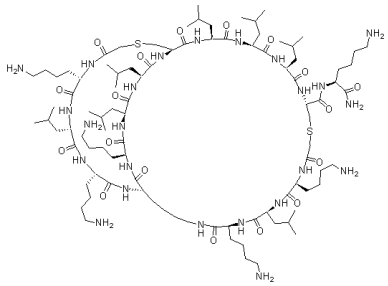
^{1}KLL*K*(K^{2}LL)KLL*Z*^{1}KLK*Z*^{2}K (26b) was obtained as foamy white solid after preparative RP-HPLC (23.0 mg, 10.3 %). Analytical RP-HPLC: t_R = 3.640 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$calc./obs. 1991.29/1991.30 Da [M].

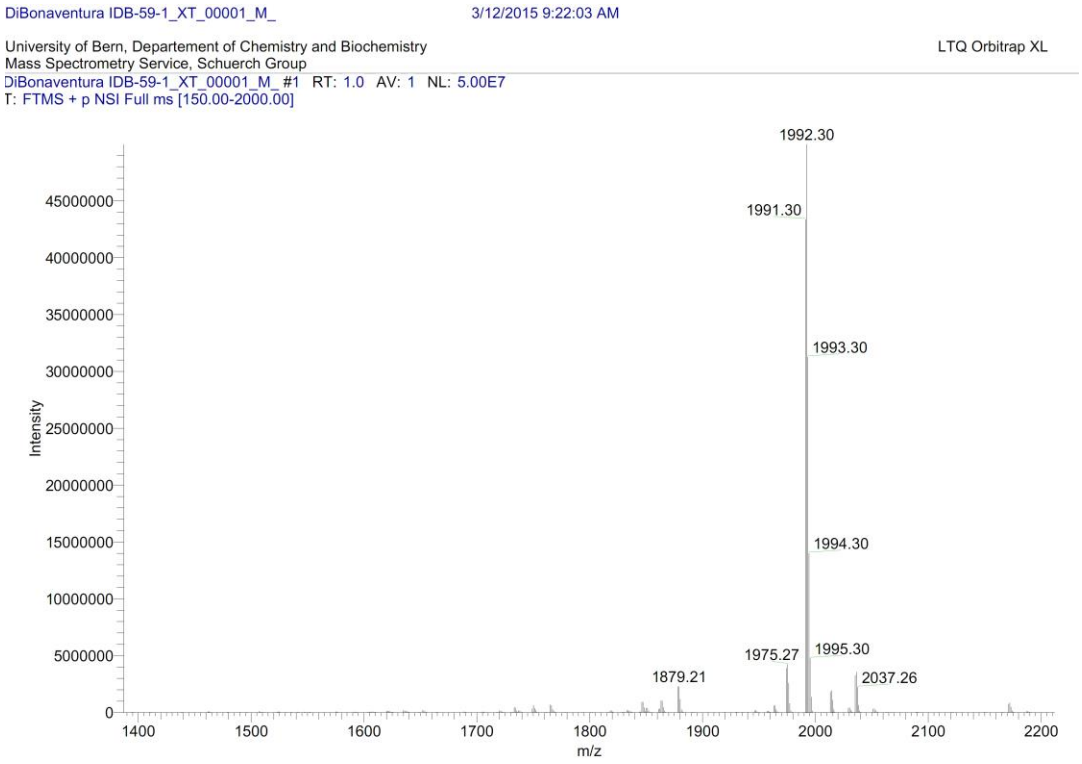




^{2}KLK*K*(K^{1}LK)KLL*Z*^{1}LLL*Z*^{2}K (27a) was obtained as foamy white solid after preparative RP-HPLC (19.9 mg, 8.8 %). Analytical RP-HPLC: t_R = 3.140 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs. 1991.29/1991.30 Da [M].

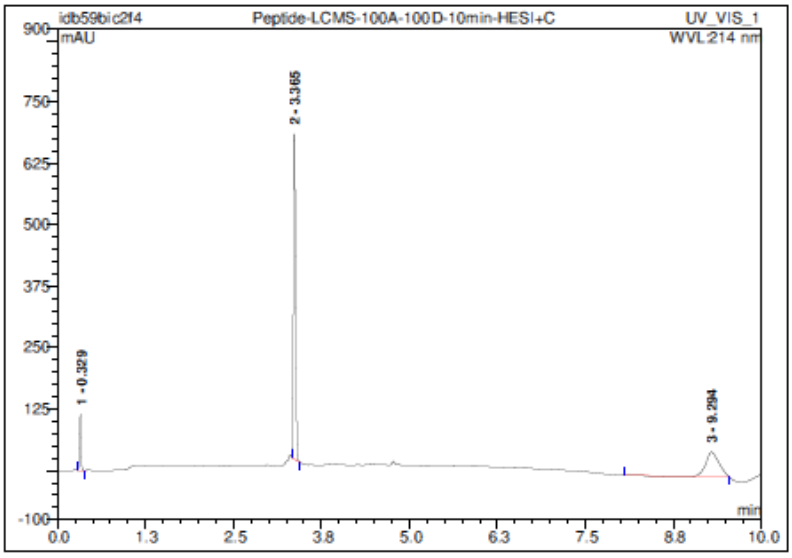


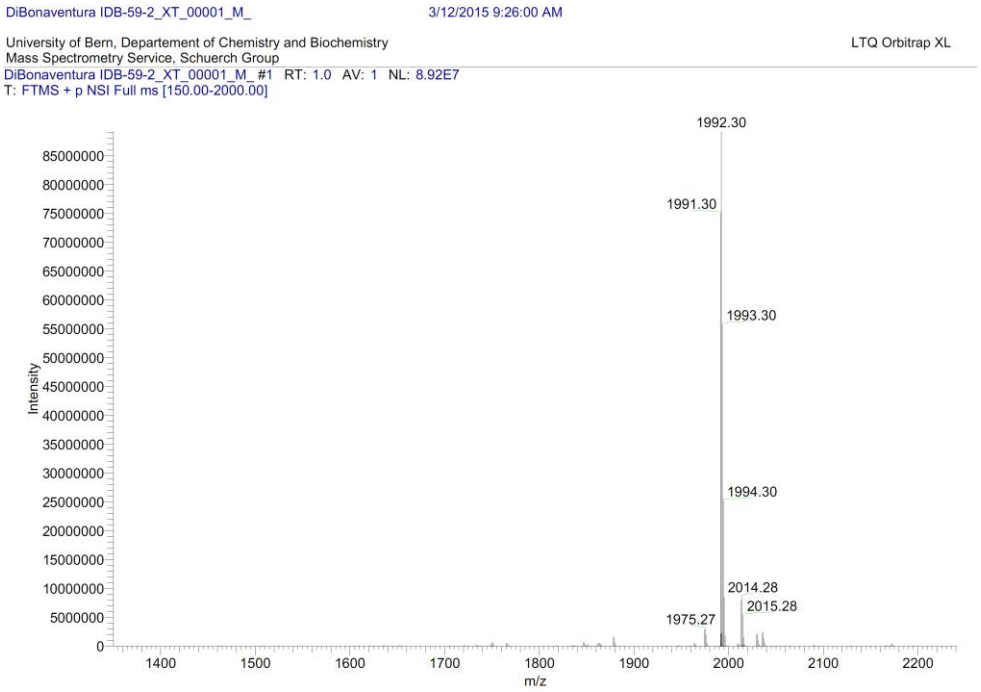




^{2}KLK*K*(K^{1}LK)KLL*Z*^{1}LLL*Z*^{2}K (27a) was also obtained from the selective synthesis procedure as foamy white solid after preparative RP-HPLC (0.3 mg, 0.1 %). Analytical RP-HPLC: t_R = 3.140 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs. 1991.29/1991.30 Da [M].

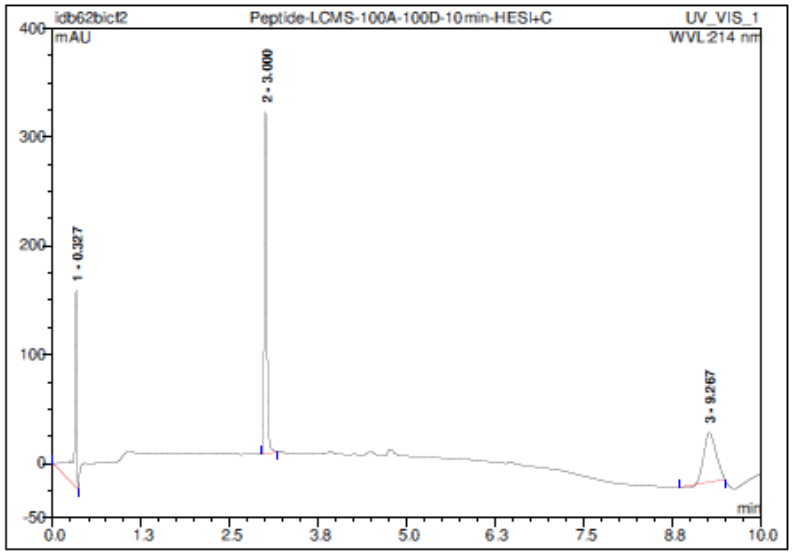
^{1}KLK*K*(K^{2}LK)KLL*Z*^{1}LLL*Z*^{2}K (27b) was obtained as foamy white solid after preparative RP-HPLC (13.2 mg, 5.9 %). Analytical RP-HPLC: t_R = 3.370 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs. 1991.29/1991.30 Da [M].

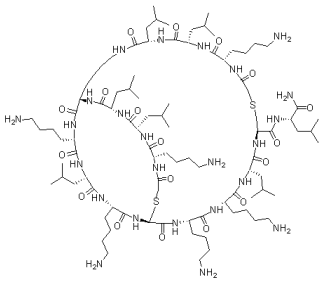


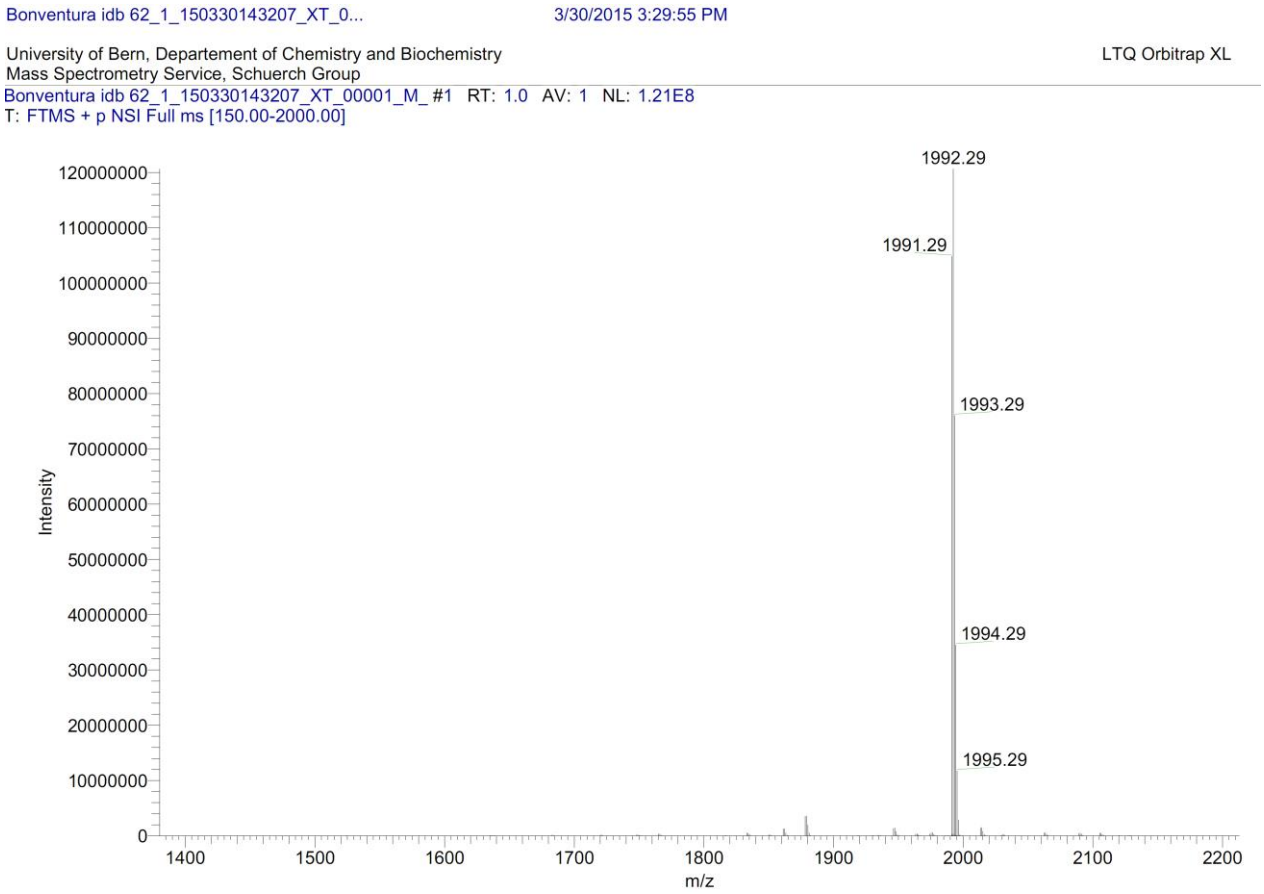


^{1}KLK*K*(K^{2}LK)KLL*Z*^{1}LLL*Z*^{2}K (27b) was also obtained from the selective synthesis procedure as foamy white solid after preparative RP-HPLC (0.2 mg, 0.09 %). Analytical RP-HPLC: t_R = 3.370 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs. 1991.29/1991.30 Da [M].

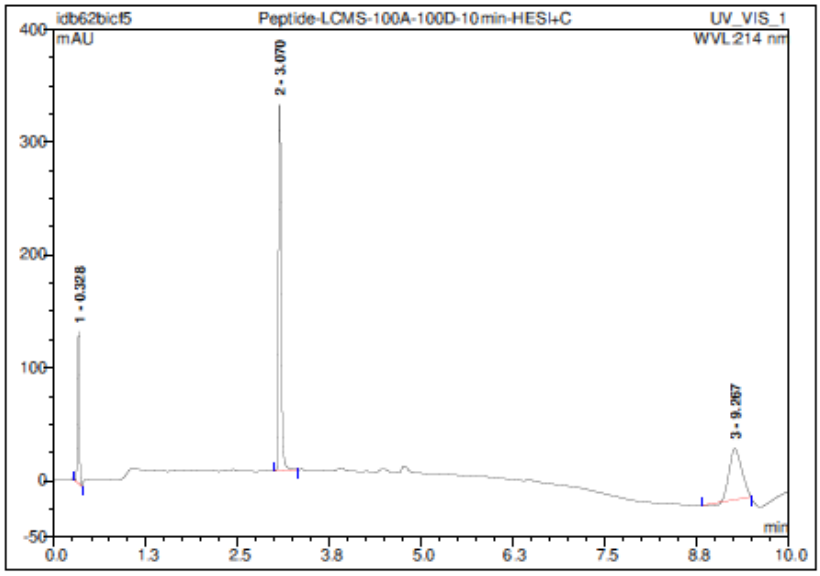
^{2}KLL*K*(K^{1}LL)KLK*Z*^{1}KKL*Z*^{2}L (28a) was obtained as foamy white solid after preparative RP-HPLC (17.5 mg, 6.3 %). Analytical RP-HPLC: t_R = 3.000 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs. 1991.29/1991.29 Da [M].

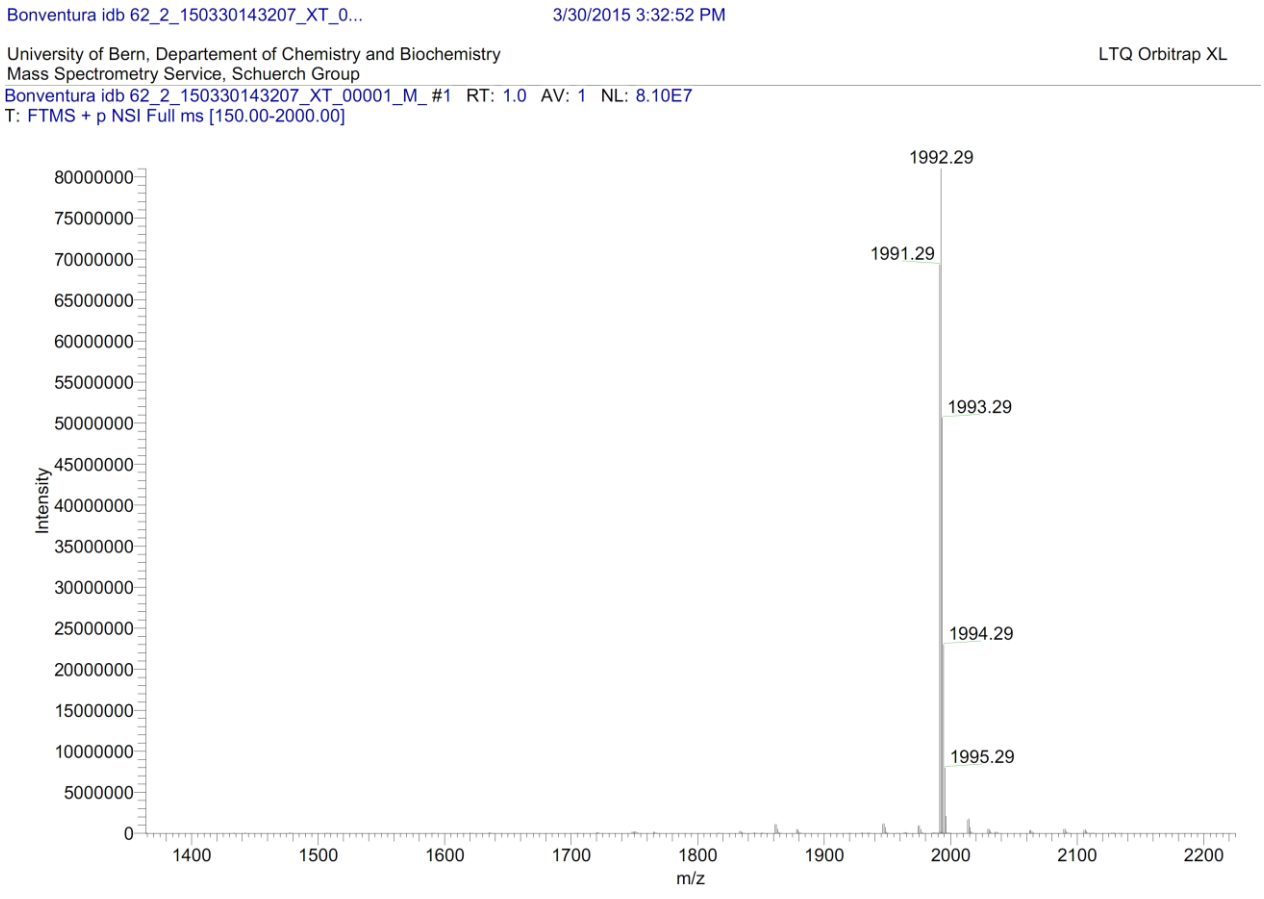




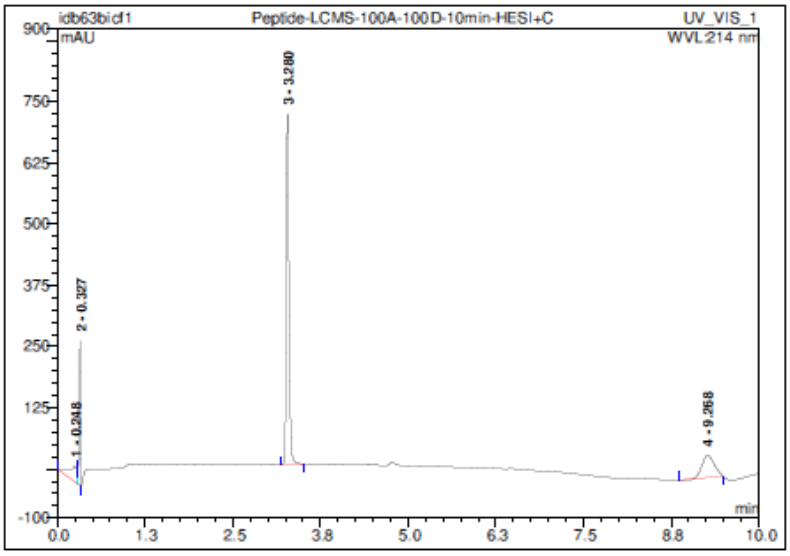


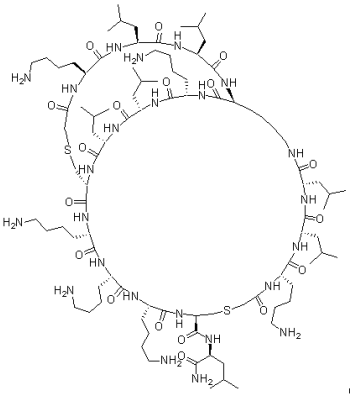
^{1}KLL*K*(K^{2}LL)KLK*Z*^{1}KKL*Z*^{2}L (28b) was obtained as foamy white solid after preparative RP-HPLC (7.0 mg, 2.5 %). Analytical RP-HPLC: t_R = 3.070 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs. 1991.29/1991.29 Da [M].

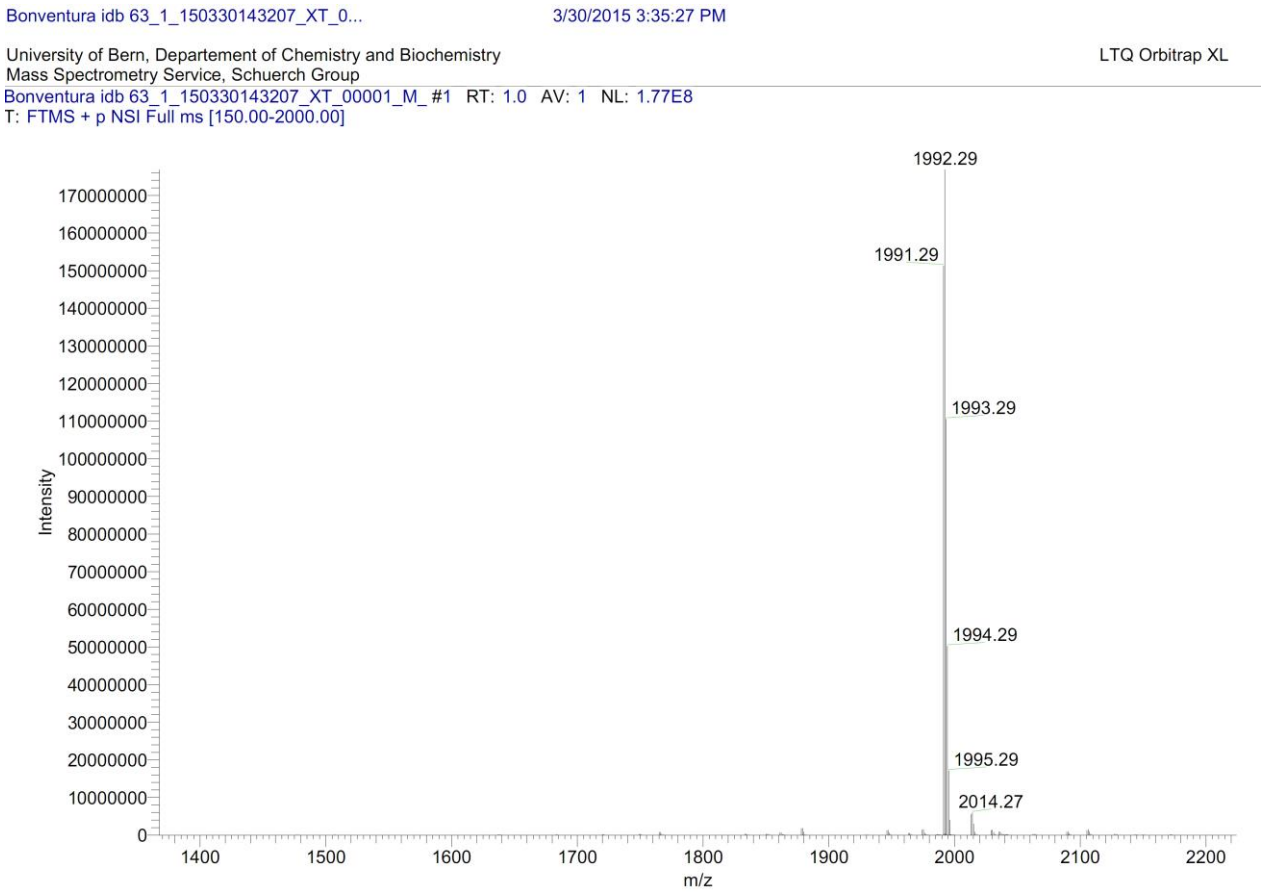




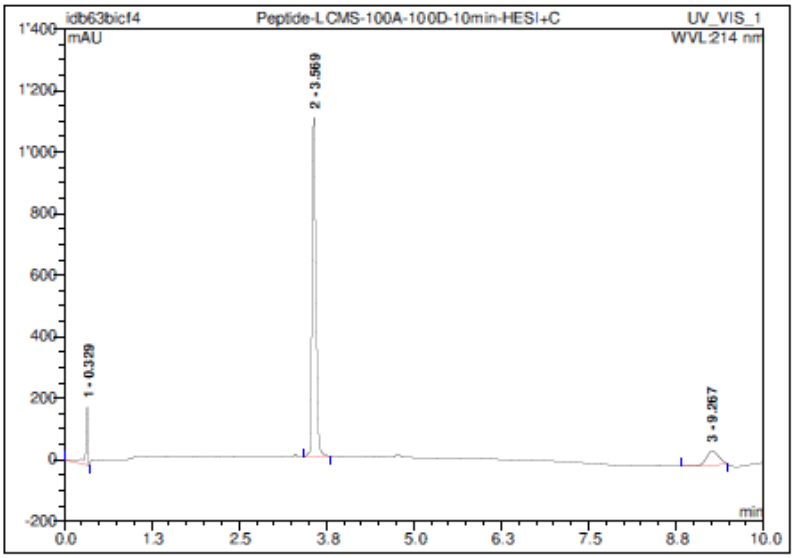
^{2}KLL*K*(K^{1}LL)KLL*Z*^{1}KKKZ^{2}L (29a) was obtained as foamy white solid after preparative RP-HPLC (9.8 mg, 3.5 %). Analytical RP-HPLC: t_R = 3.280 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs. 1991.29/1991.29 Da [M].

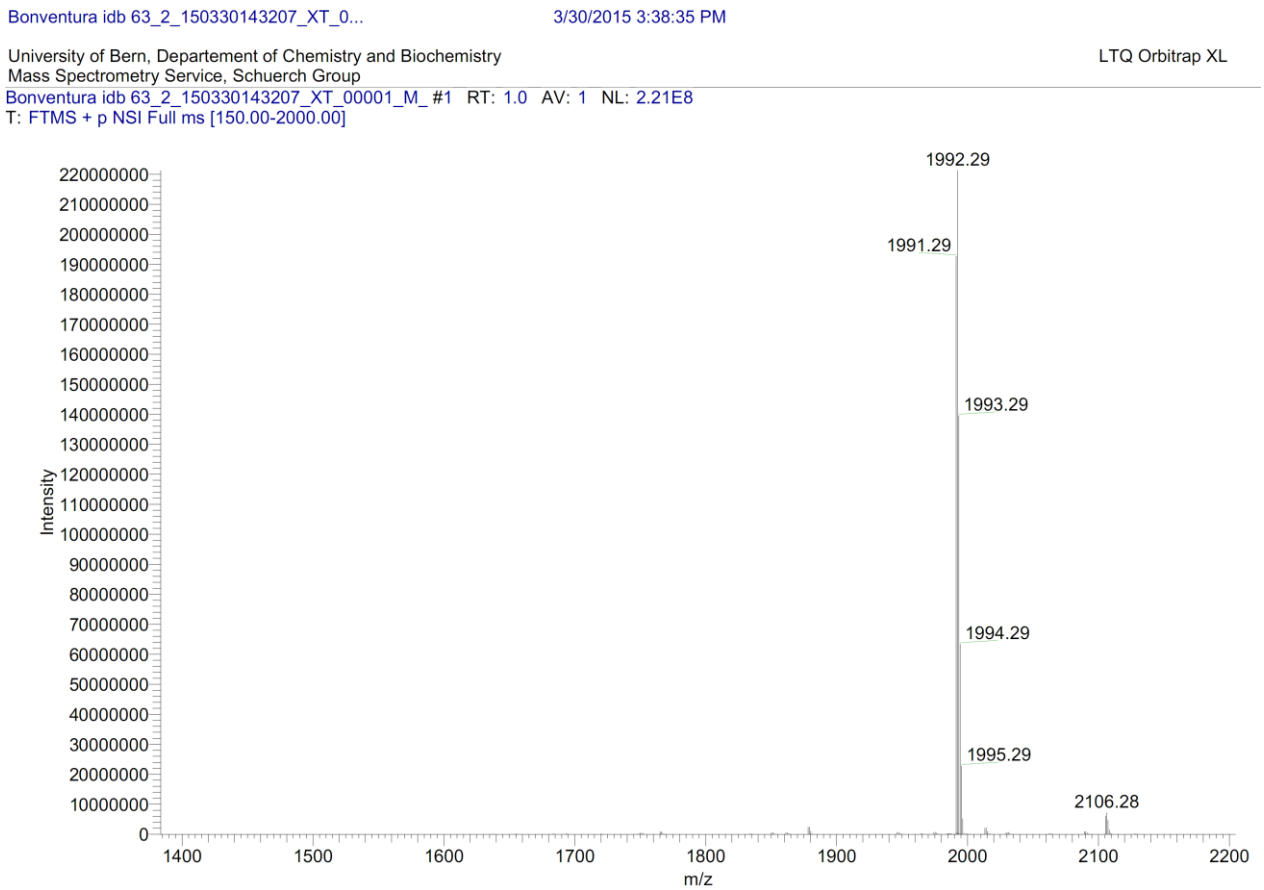




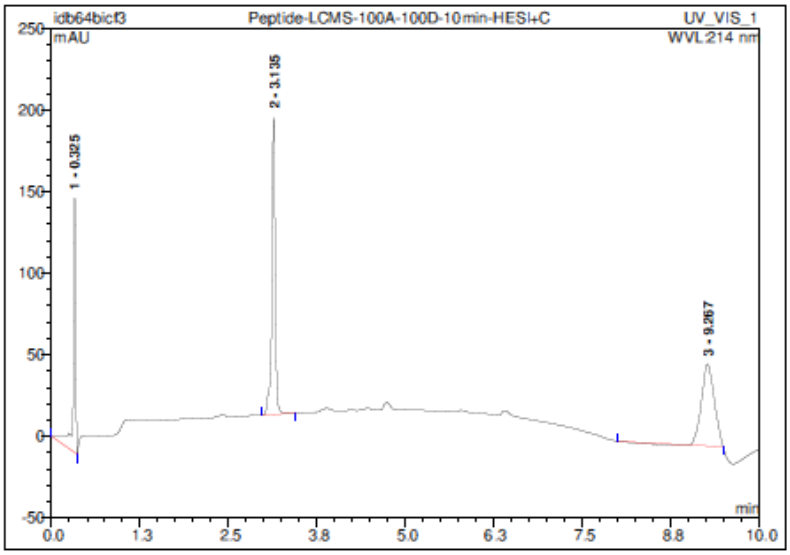


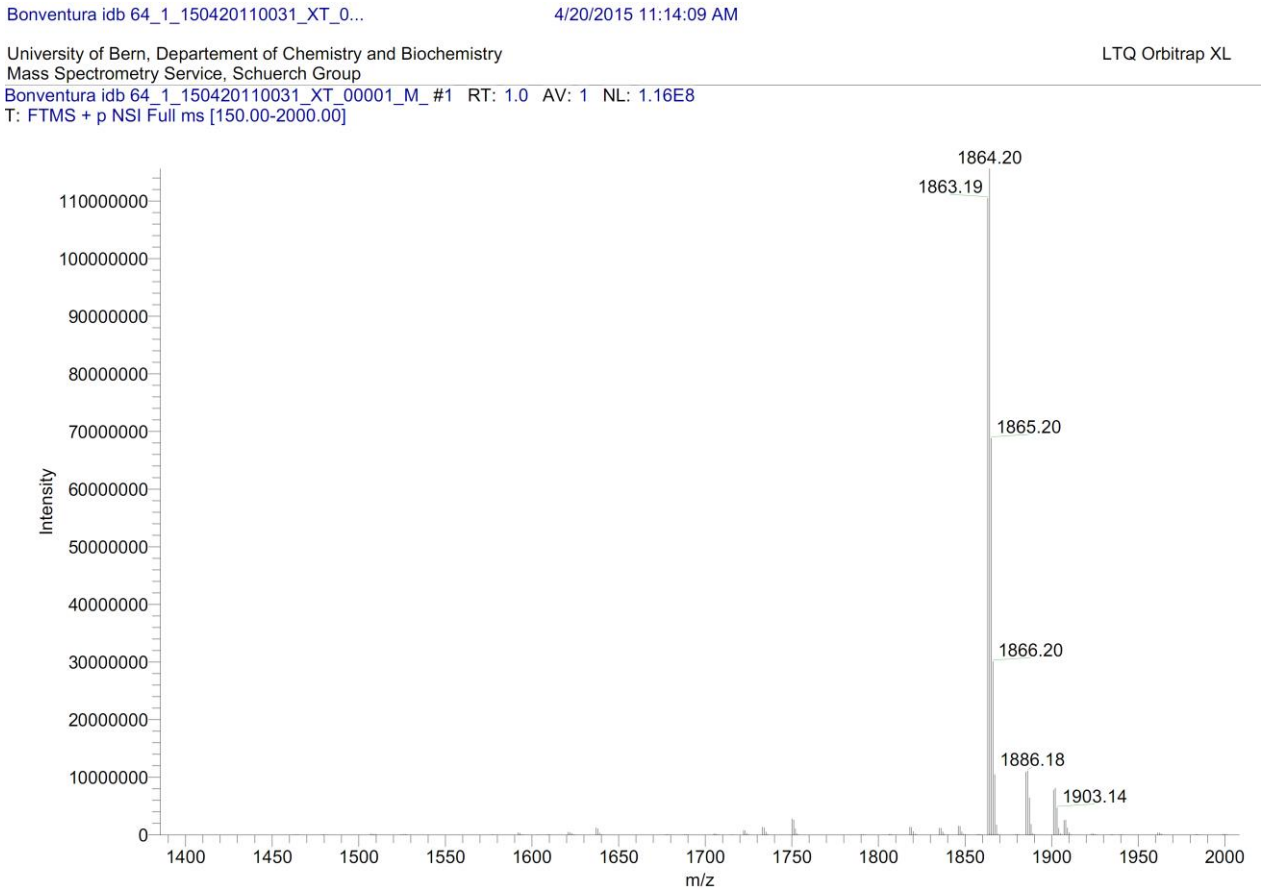
^{1}KLL*K*(K^{2}LL)KLL*Z*^{1}KKKZ^{2}L (29b) was obtained as foamy white solid after preparative RP-HPLC (27.7 mg, 10.1 %). Analytical RP-HPLC: t_R = 3.570 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs. 1991.29/1991.29 Da [M].



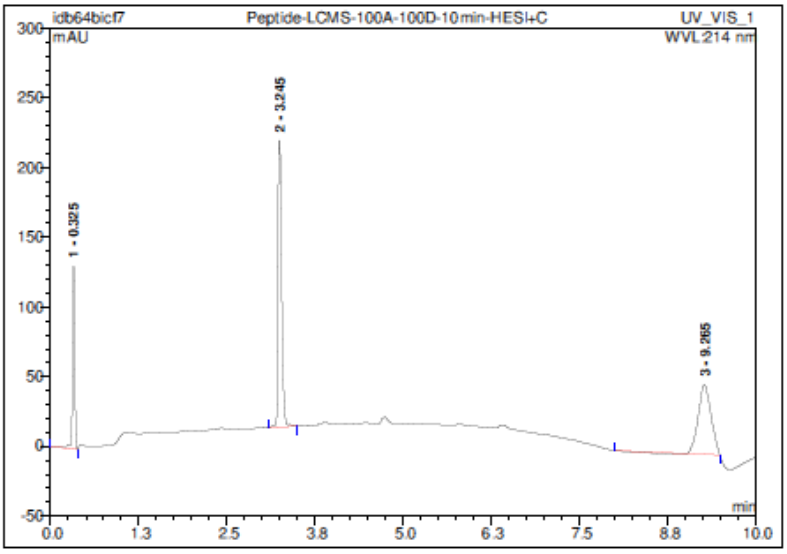


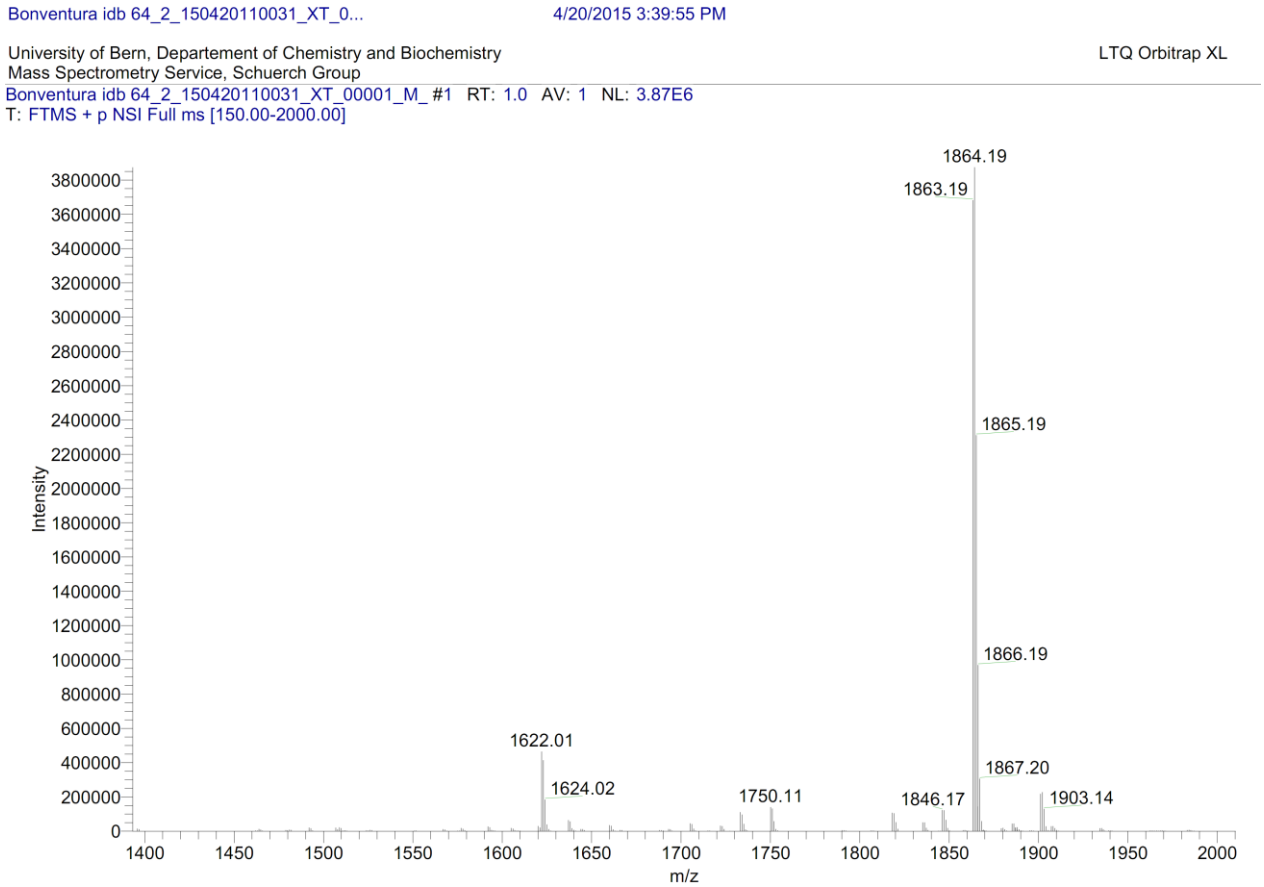
^{2}KLL*K*(K^{1}LL)LKZ^{1}KLKZ^{2}L (30a) was obtained as foamy white solid after preparative RP-HPLC (12.6 mg, 4.9 %). Analytical RP-HPLC: t_R = 3.140 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{88}H_{162}N_{22}O_{17}S_2$ calc./obs. 1863.19/1863.19 Da [M].



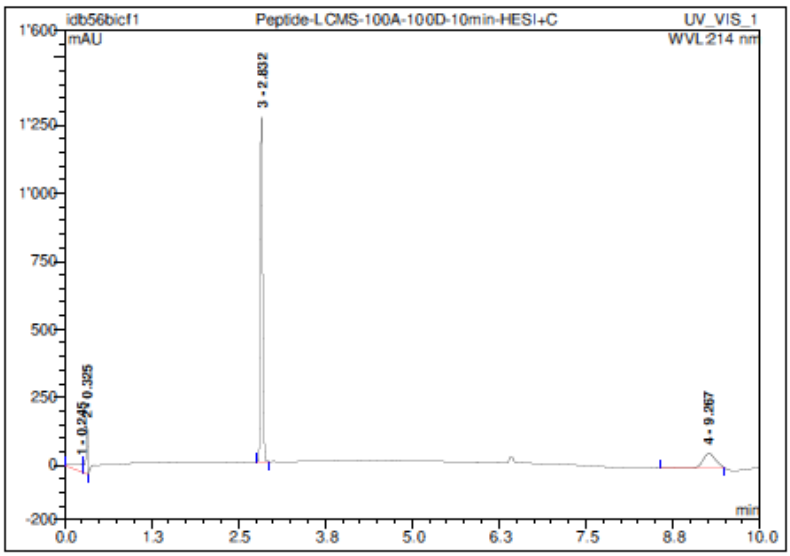


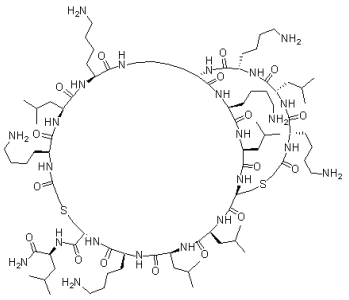
^{1}KLL*K*(K^{2}LL)LKZ^{1}KLKZ^{2}L (30b) was obtained as foamy white solid after preparative RP-HPLC (2.9 mg, 1.1 %). Analytical RP-HPLC: t_R = 3.250 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{88}H_{162}N_{22}O_{17}S_2$ calc./obs. 1863.19/1863.19 Da [M].

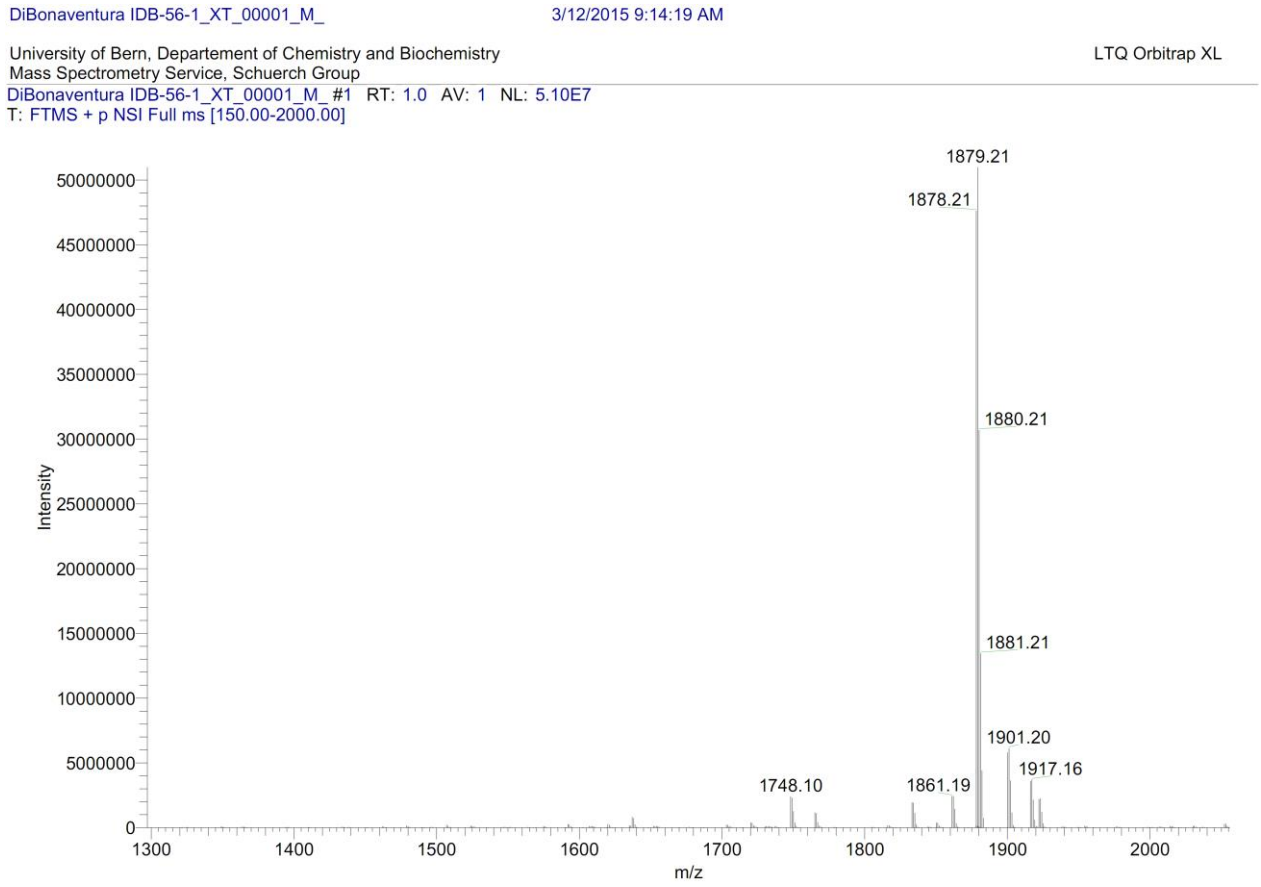




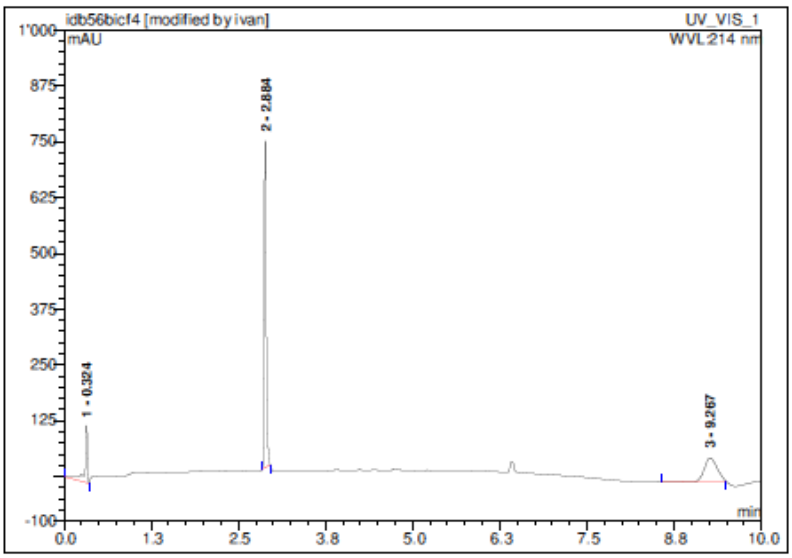
^{2}KLK*K*(K^{1}LK)KKL*Z*^{1}LLK*Z*^{2}L (31a) was obtained as foamy white solid after preparative RP-HPLC (33.4 mg, 15.8 %). Analytical RP-HPLC: t_R = 2.830 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{88}H_{163}N_{23}O_{17}S_2$ calc./obs. 1878.20/1878.21 Da [M].

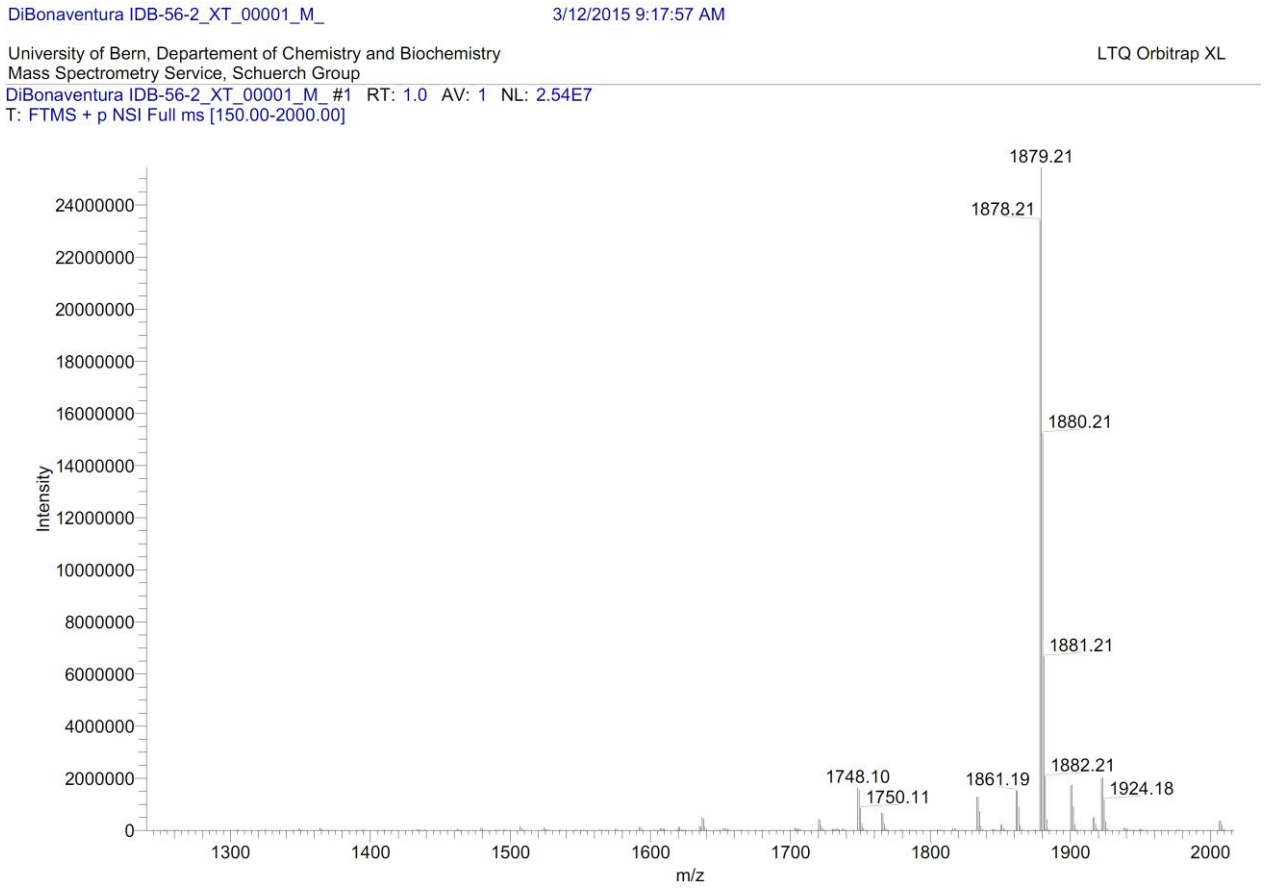




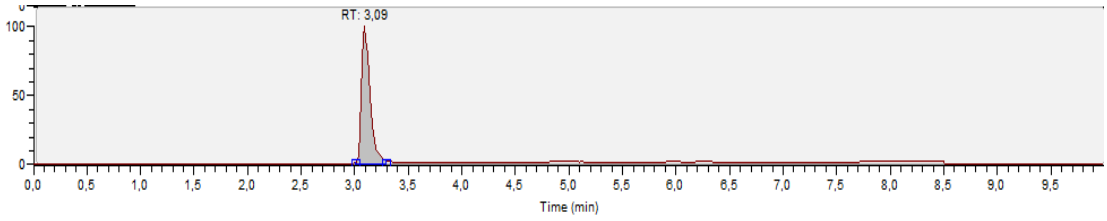


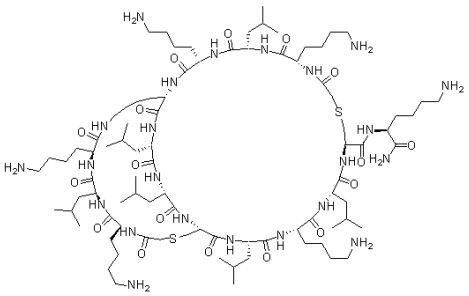
^{1}KLK*K*(K^{2}LK)KKL*Z*^{1}LLK*Z*^{2}L (31b) was obtained as foamy white solid after preparative RP-HPLC (12.5 mg, 5.9 %). Analytical RP-HPLC: t_R = 2.880 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{88}H_{163}N_{23}O_{17}S_2$ calc./obs.1878.20/1878.21 Da [M].

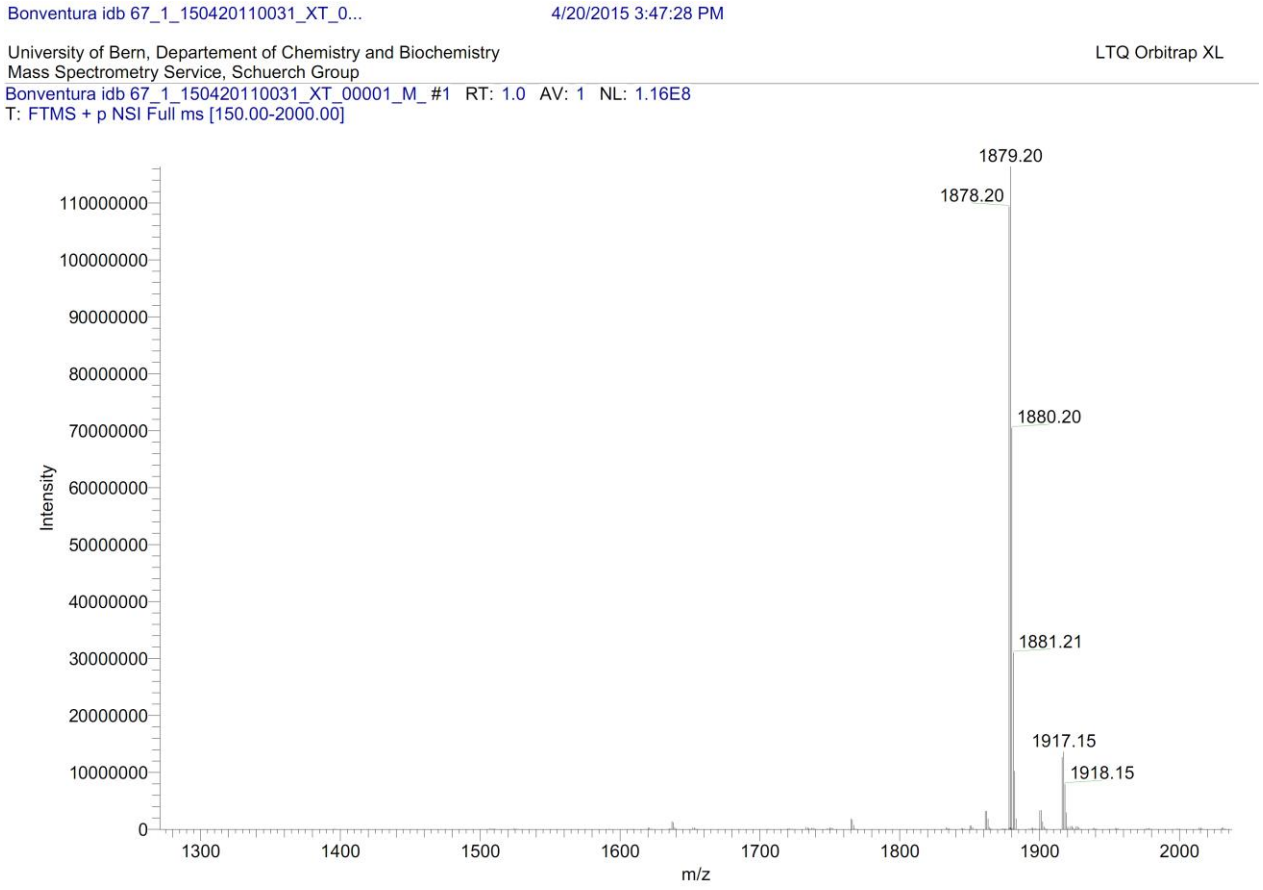




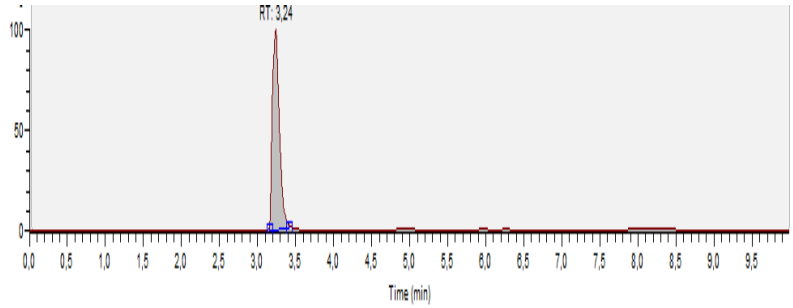
^{2}KLK*K*(K^{1}LK)LL*Z*^{1}LKL*Z*^{2}K (32a) was obtained as foamy white solid after preparative RP-HPLC (3.6 mg, 1.4 %). Analytical RP-HPLC: t_R = 3.090 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{88}H_{163}N_{23}O_{17}S_2$ calc./obs. 1878.20/1878.20 Da [M].

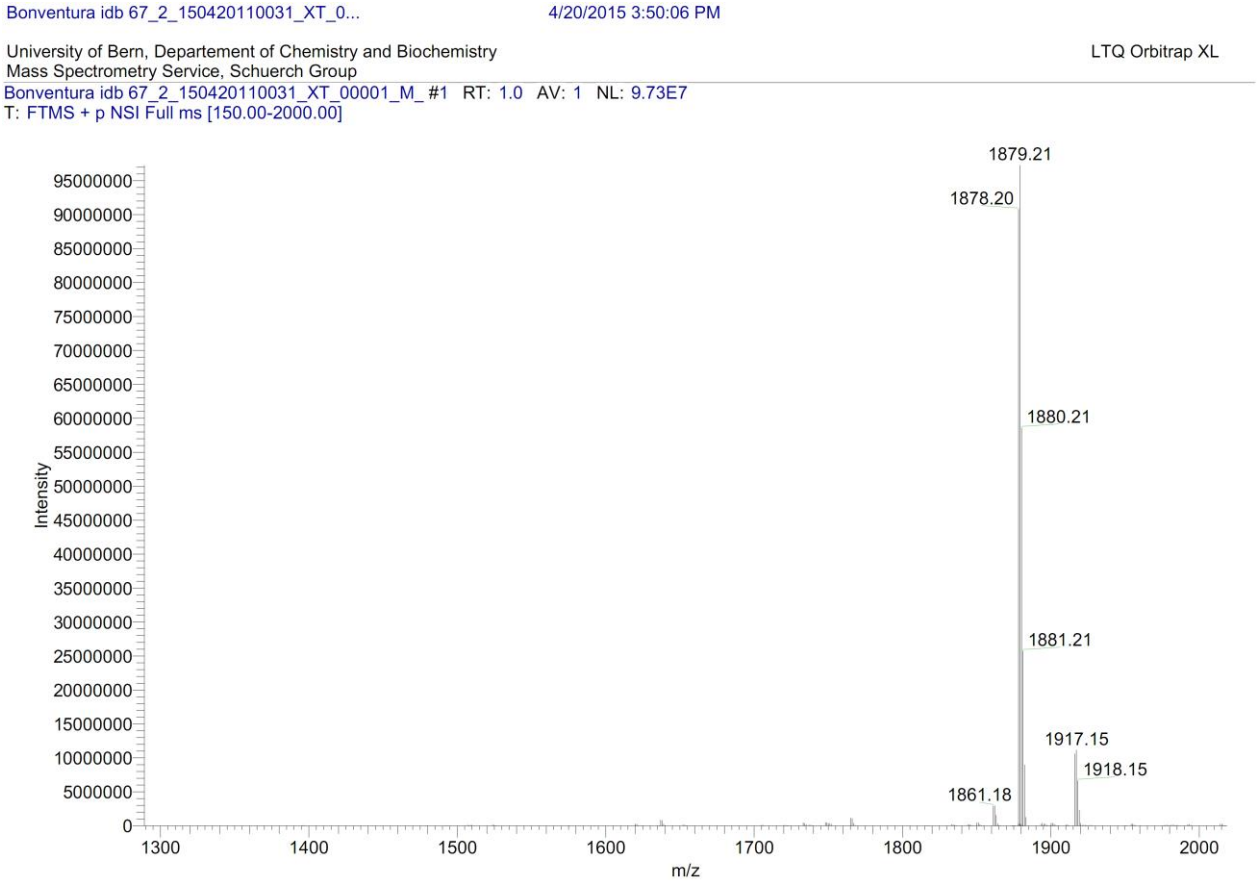




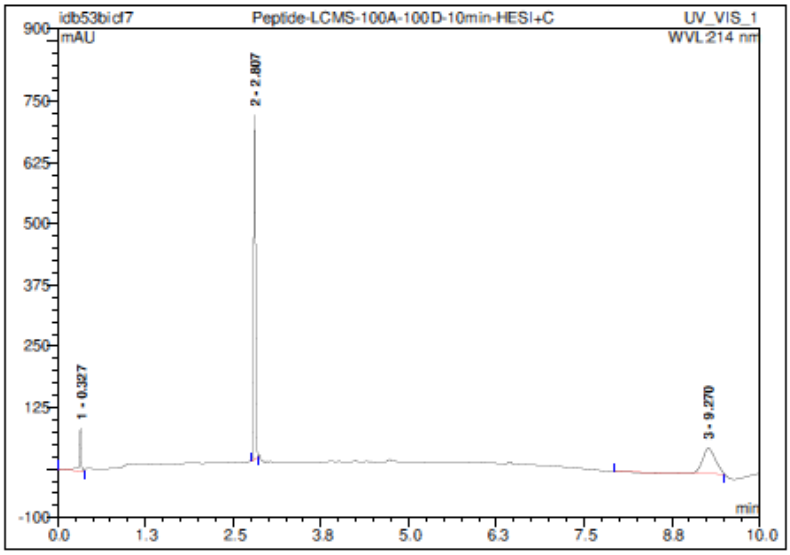


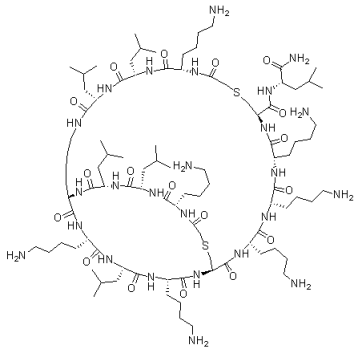
^{1}KLK*K*(K^{2}LK)LL*Z*^{1}LKL*Z*^{2}K (32b) was obtained as foamy white solid after preparative RP-HPLC (13.6 mg, 5.2 %). Analytical RP-HPLC: t_R = 3.240 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{88}H_{163}N_{23}O_{17}S_2$ calc./obs. 1878.20/1878.20 Da [M].

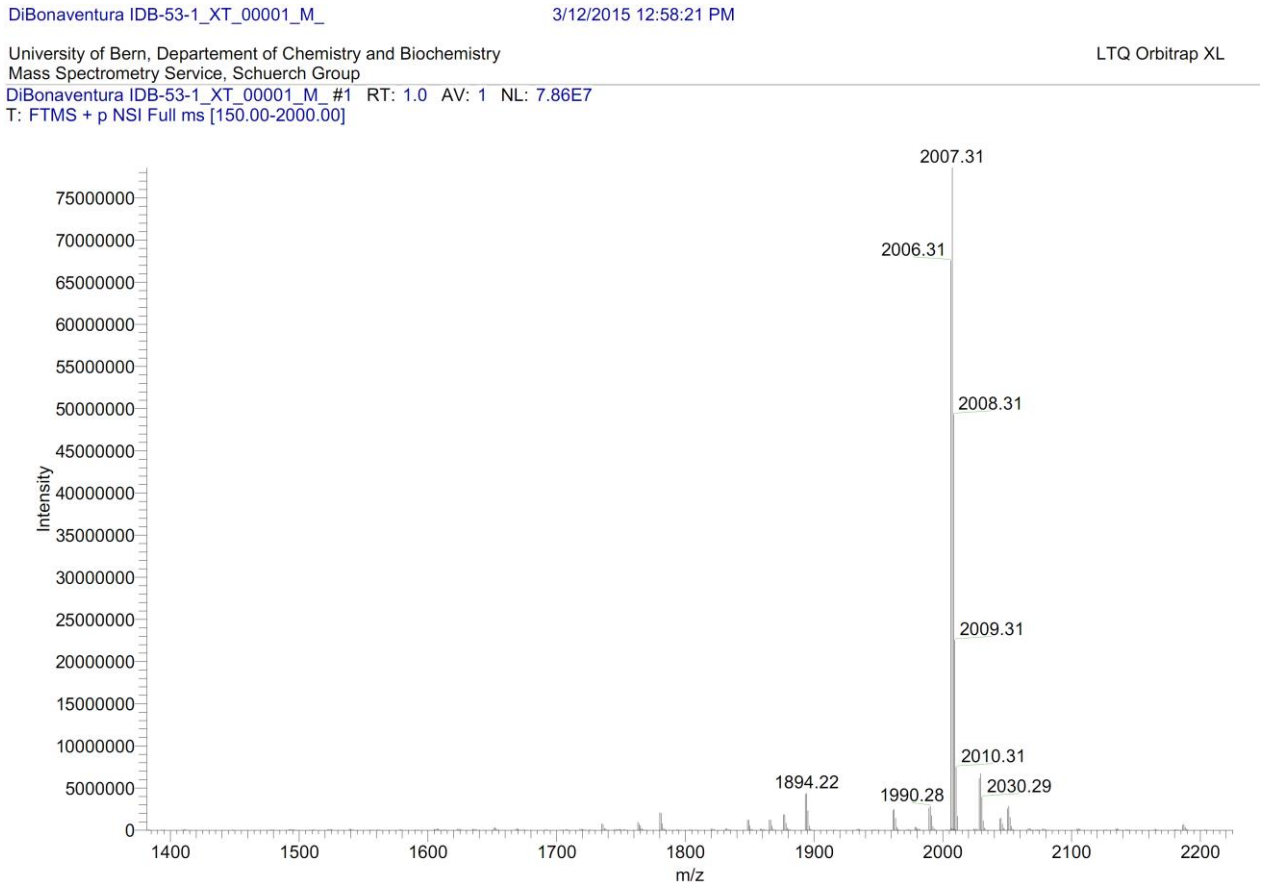




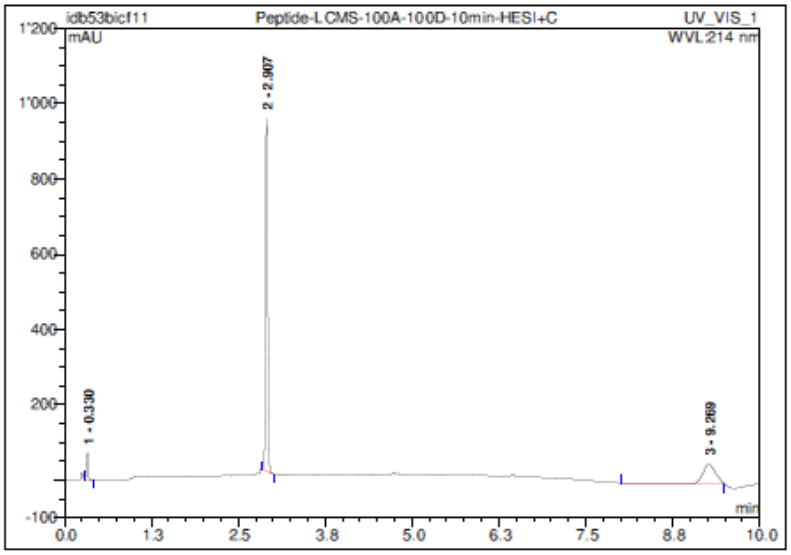
^{2}KLL*K*(K^{1}LL)KLK*Z*^{1}KKK*Z*^{2}L (33a) was obtained as foamy white solid after preparative RP-HPLC (40.1 mg, 17.7 %). Analytical RP-HPLC: t_R = 2.810 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.31 Da [M].

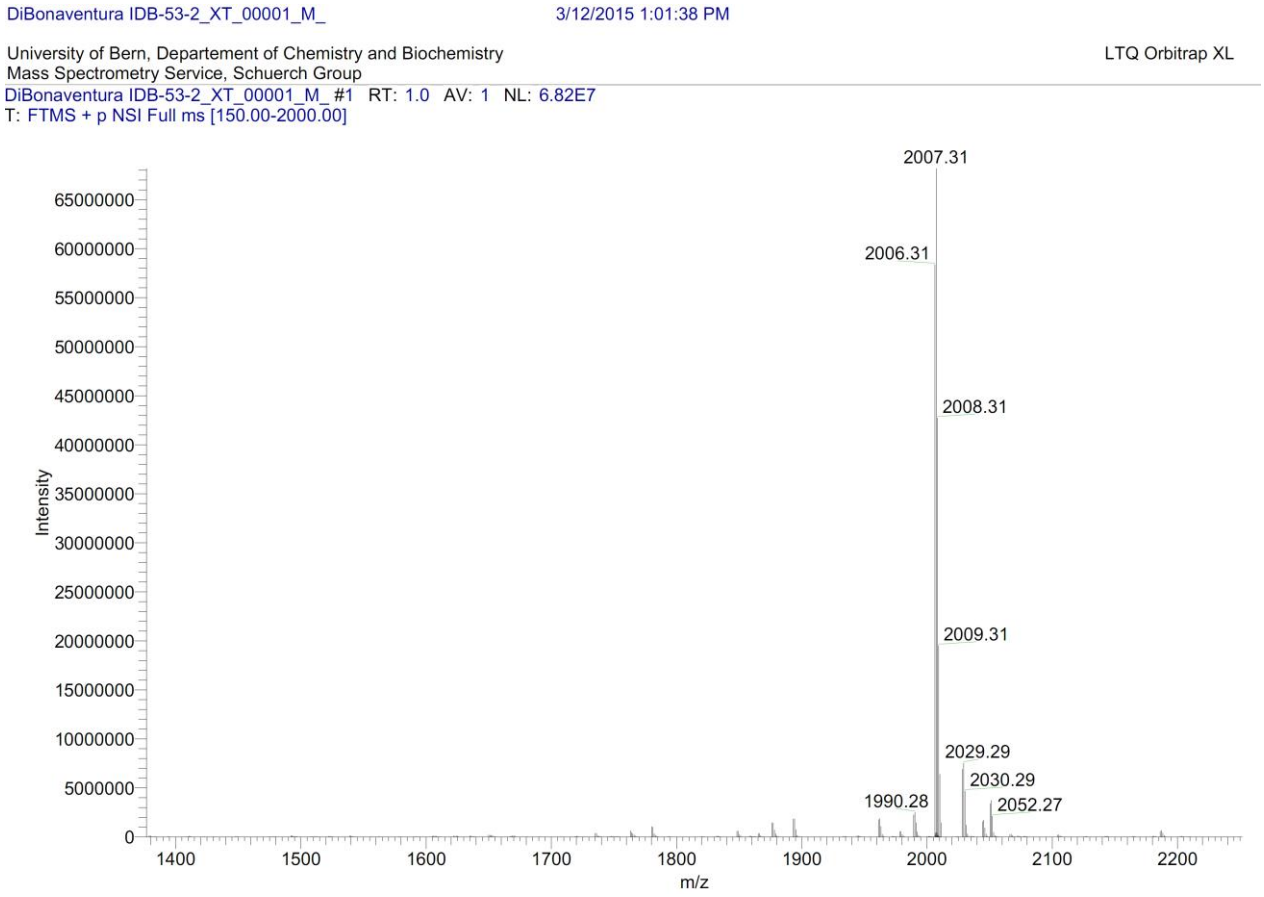




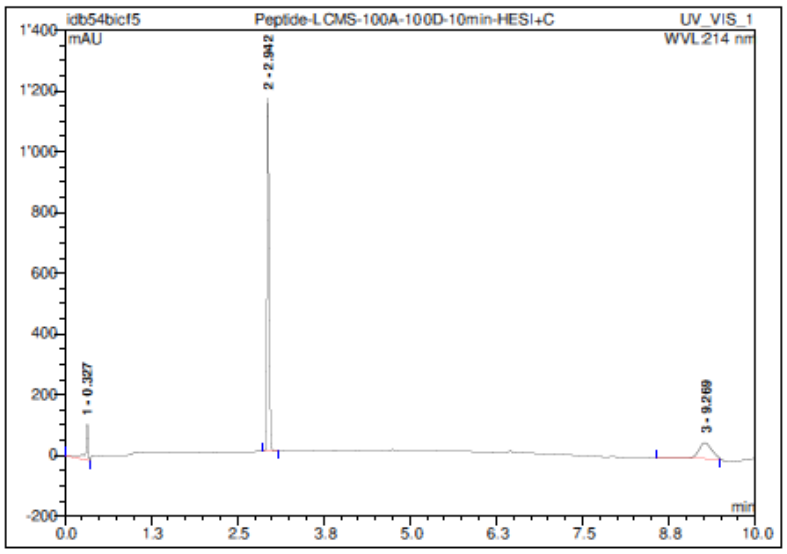


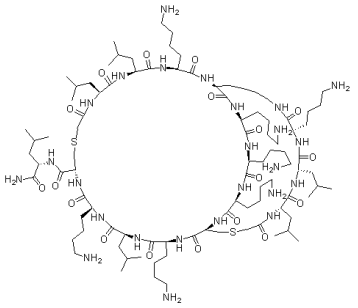
^{1}KLL*K*(K^{2}LL)KLK*Z*^{1}KKK*Z*^{2}L (33b) was obtained as foamy white solid after preparative RP-HPLC (15.1 mg, 6.6 %). Analytical RP-HPLC: t_R = 2.910 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.31 Da [M].

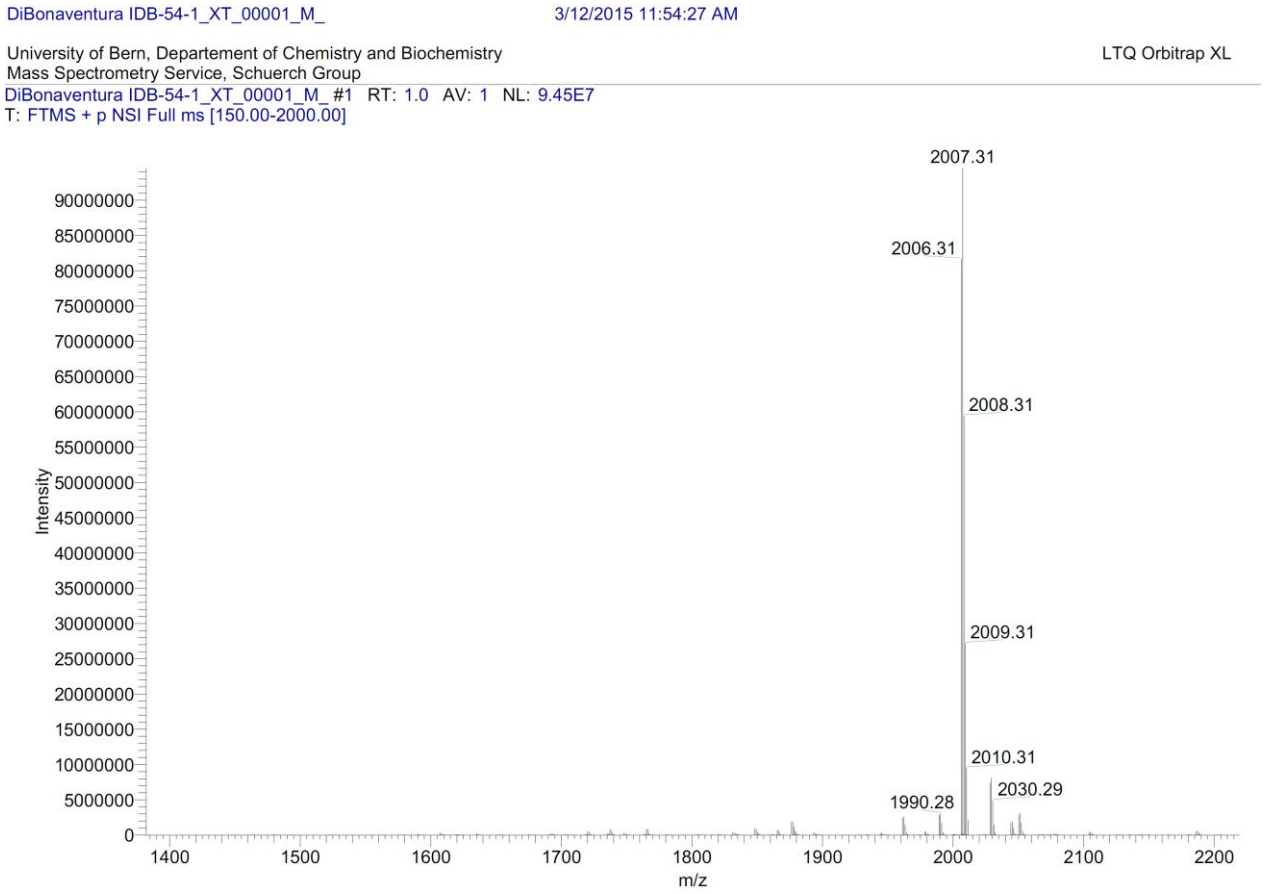




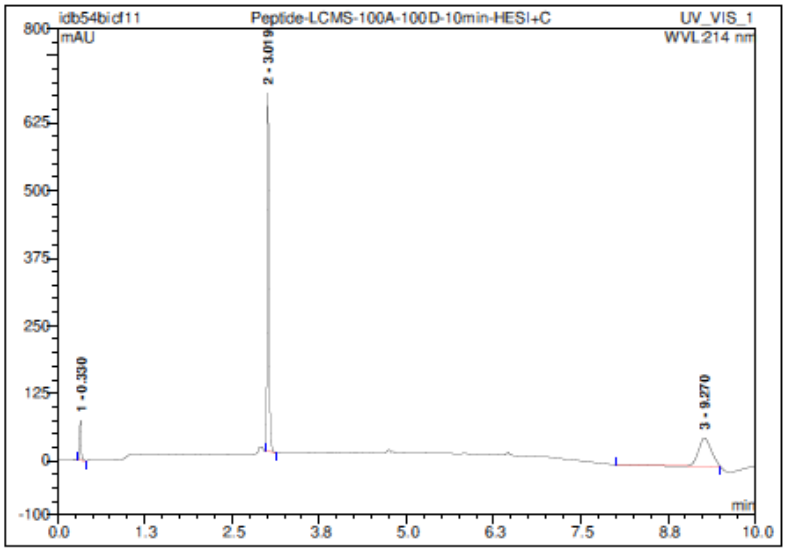
^{2}LLK*K*(L^{1}LK)KKKZ^{1}KLKZ^{2}L (34a) was obtained as foamy white solid after preparative RP-HPLC (26.5 mg, 11.7 %). Analytical RP-HPLC: t_R = 2.940 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.31 Da [M].

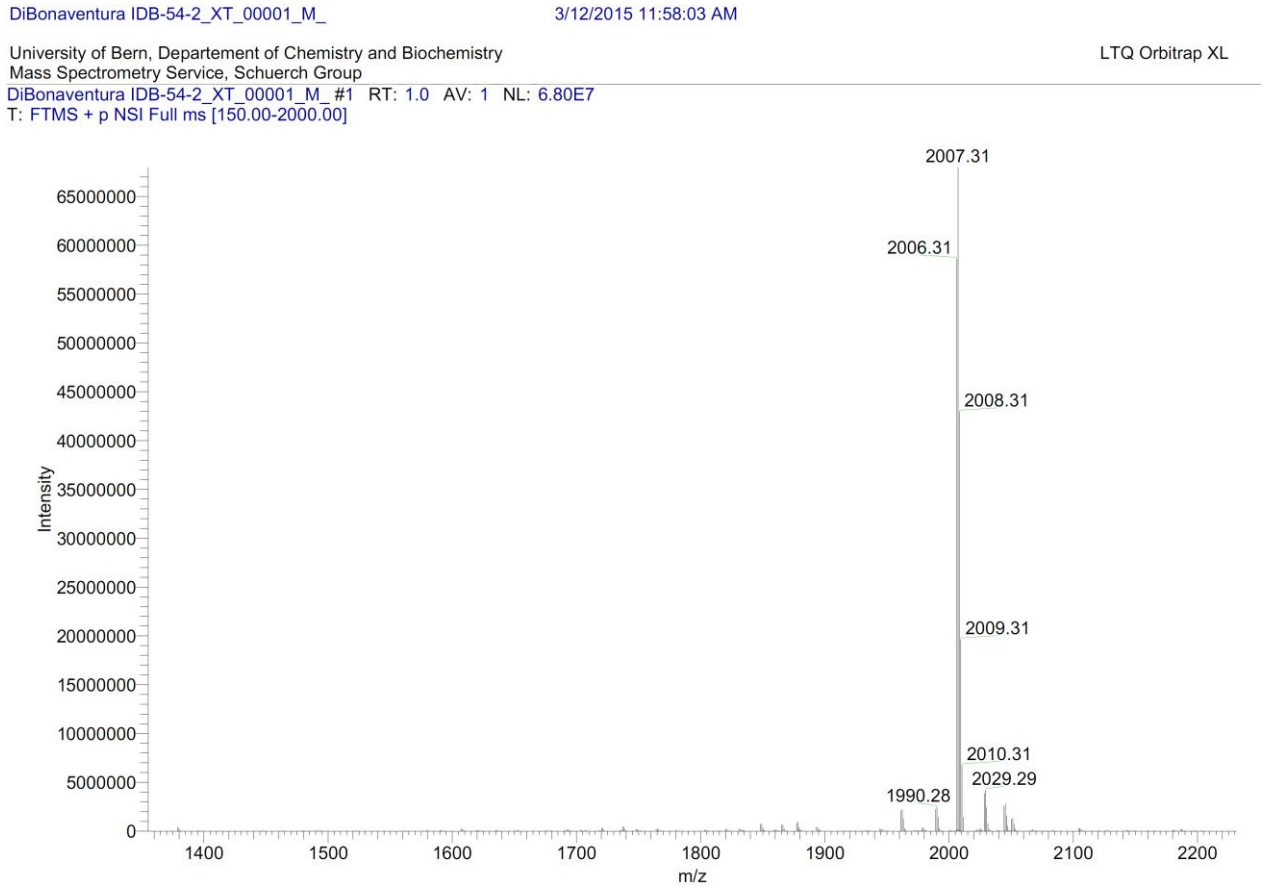




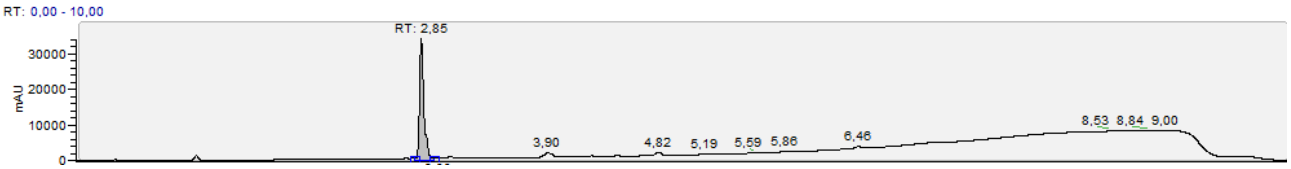


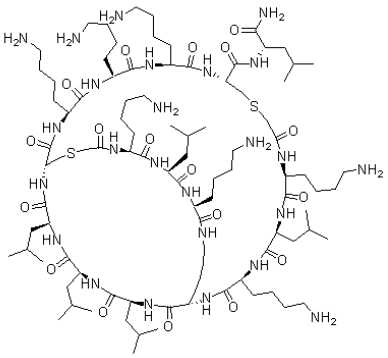
^{1}LLK*K*(L^{2}LK)KKKZ^{1}KLKZ^{2}L (34b) was obtained as foamy white solid after preparative RP-HPLC (20.6 mg, 9.1 %). Analytical RP-HPLC: t_R = 3.020 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.31 Da [M].

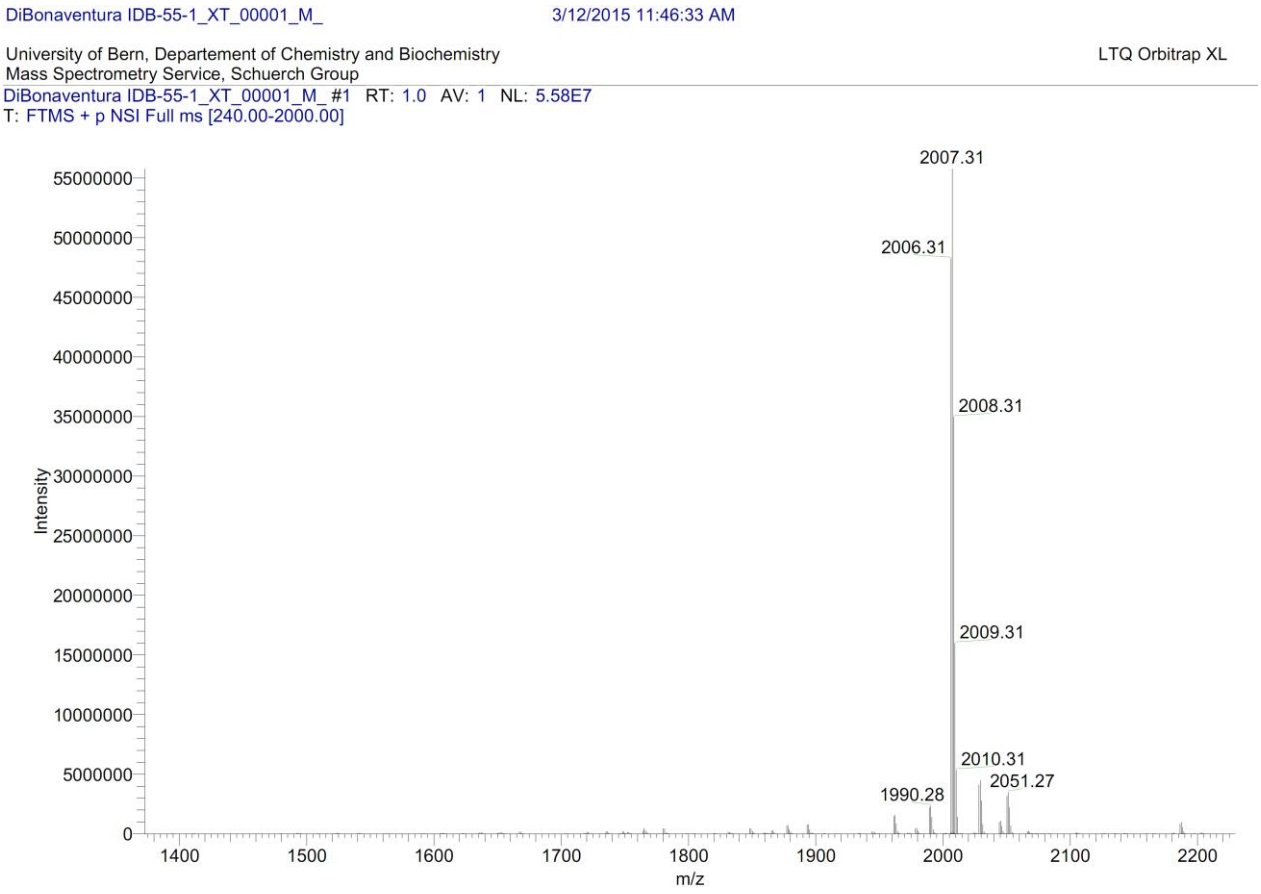




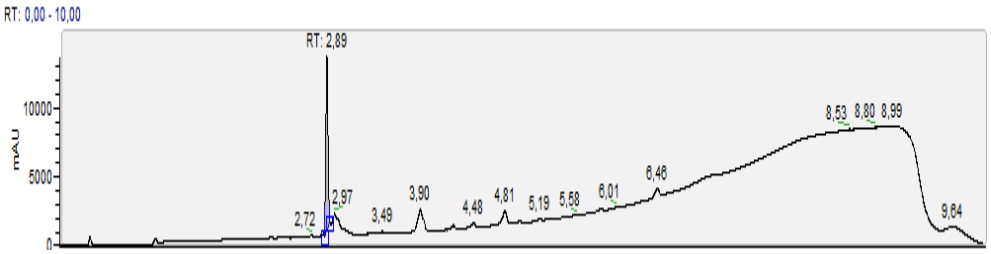
^{2}KLK*K*(K^{1}LK)LLL*Z*^{1}KKK*Z*^{2}L (35a) was obtained as foamy white solid after preparative RP-HPLC (29.8 mg, 13.2 %). Analytical RP-HPLC: t_R = 2.850 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.31 Da [M].

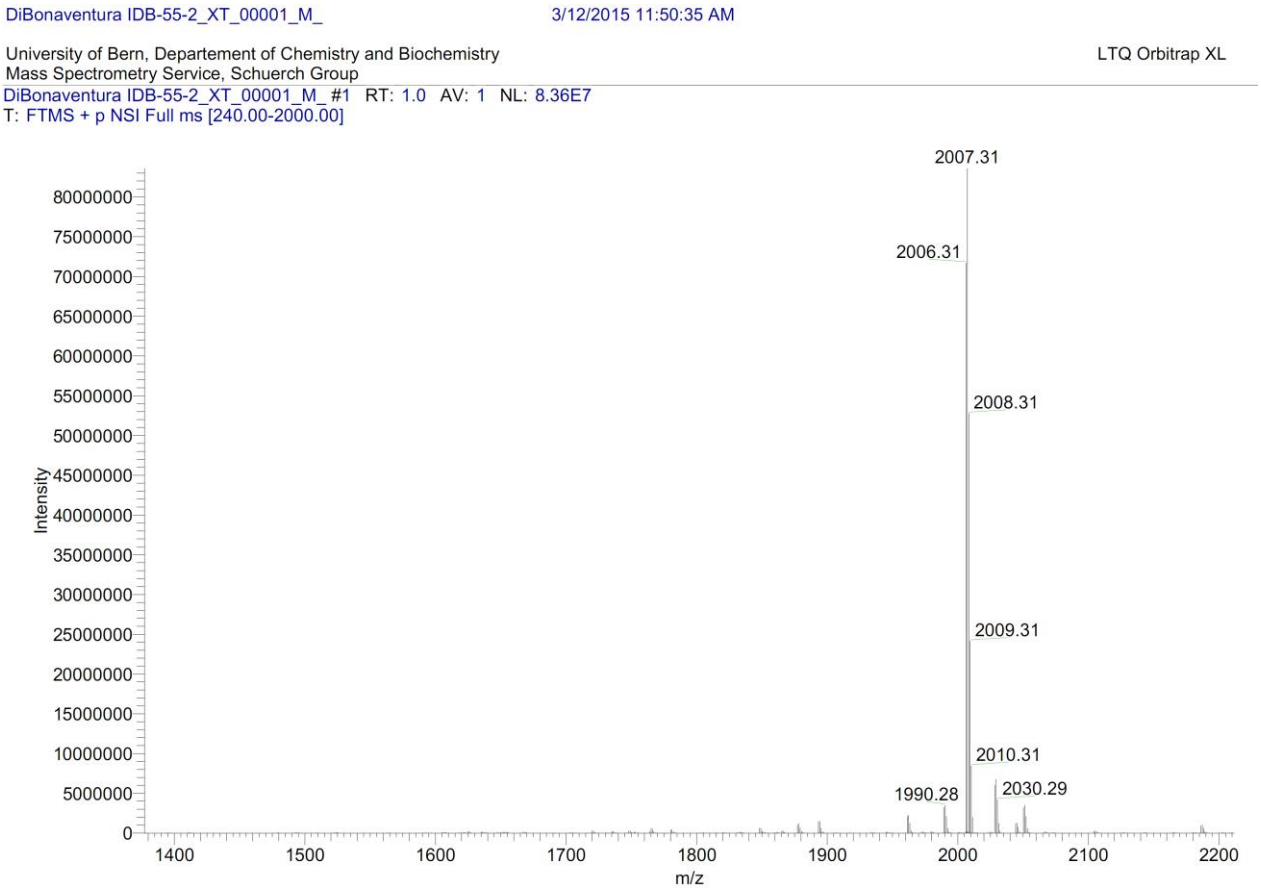




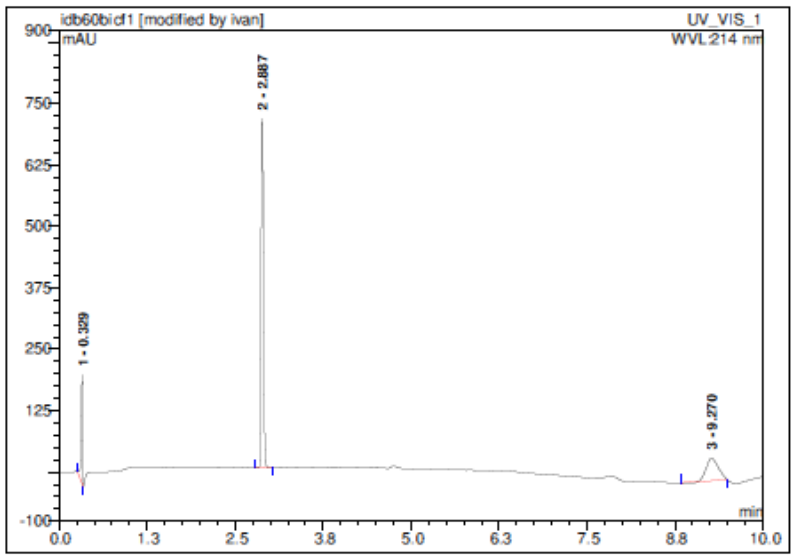


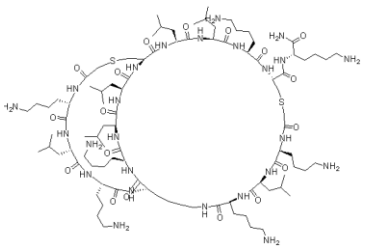
^{1}KLK*K*(K^{2}LK)LLL*Z*^{1}KKK*Z*^{2}L (35b) was obtained as foamy white solid after preparative RP-HPLC (17.7 mg, 7.8 %). Analytical RP-HPLC: t_R = 2.890 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.31 Da [M].

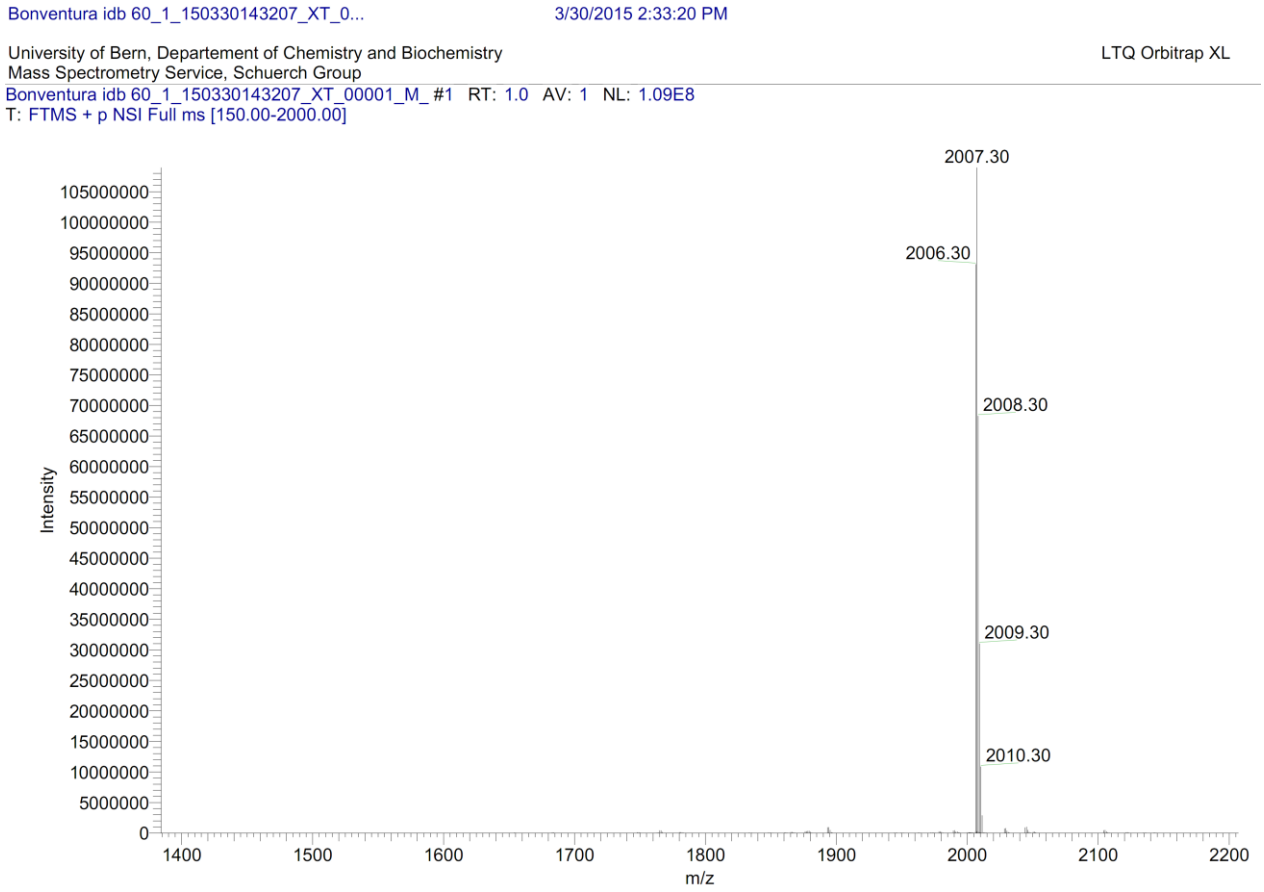




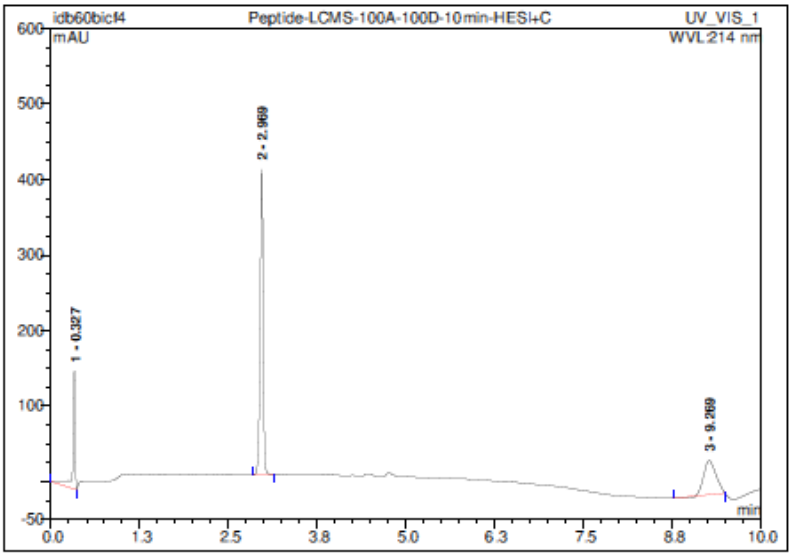
^{2}KLK*K*(K^{1}LK)KLLZ^{1}LLKZ^{2}K (36a) was obtained as foamy white solid after preparative RP-HPLC (11.2 mg, 4.0 %). Analytical RP-HPLC: t_R = 2.890 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].

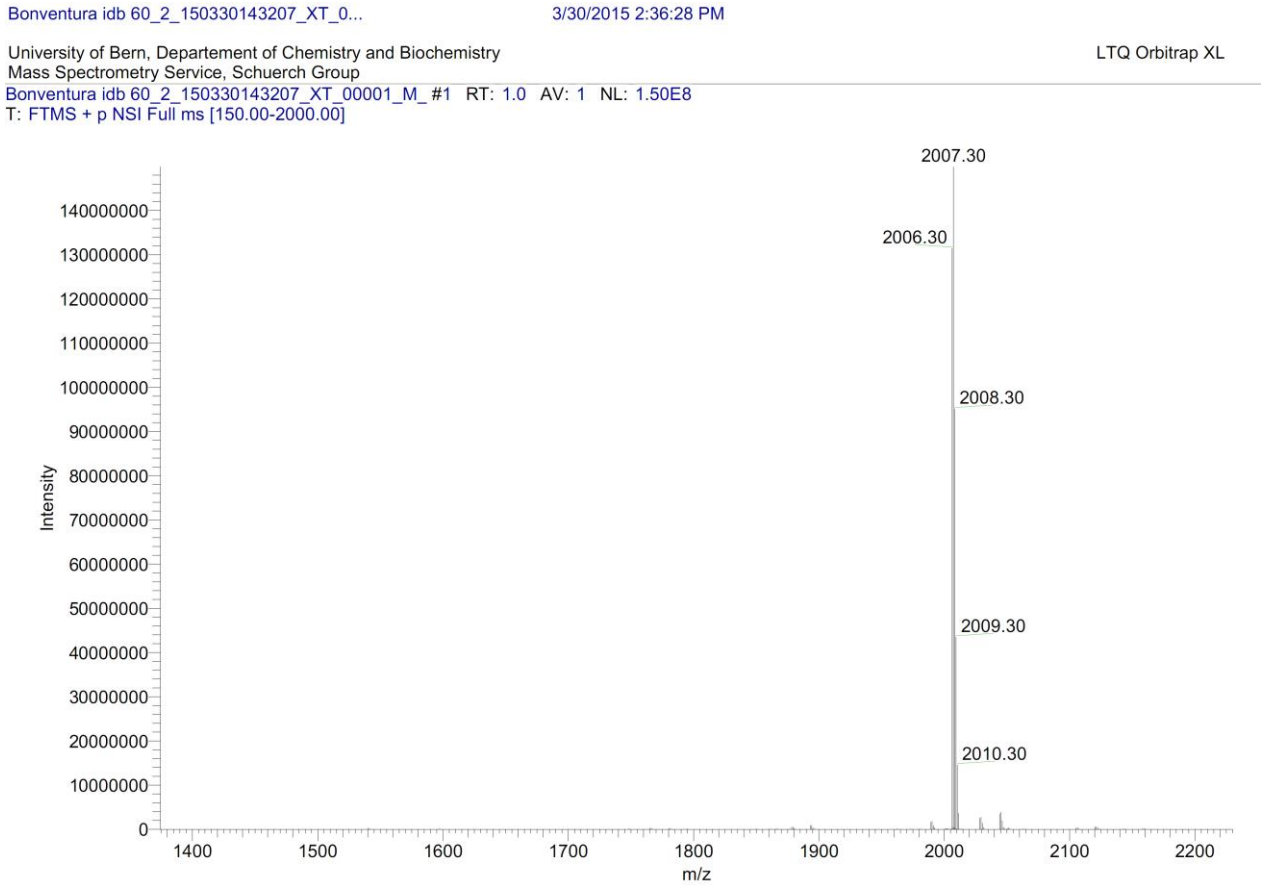




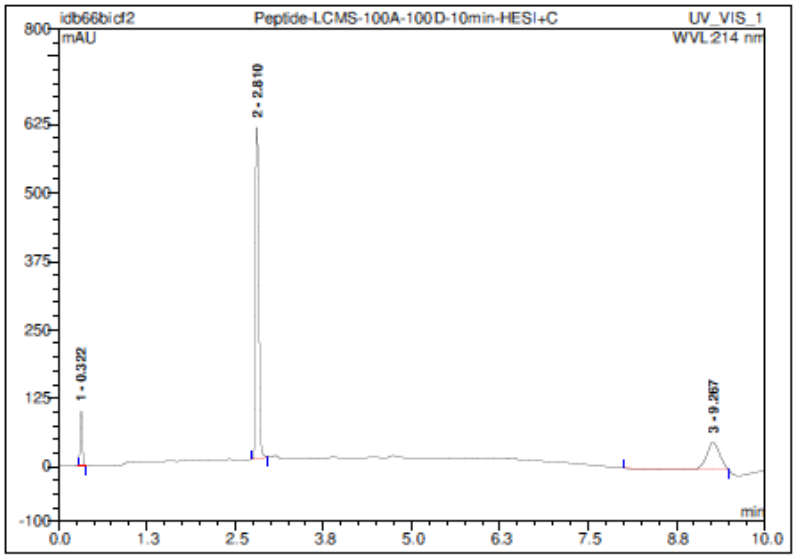


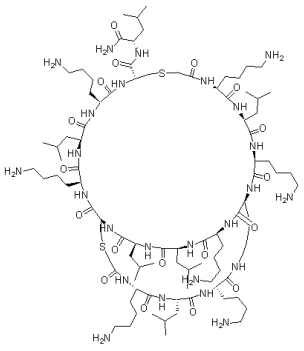
^{1}KLK*K*(K^{2}LK)KLLZ^{1}LLKZ^{2}K (36b) was obtained as foamy white solid after preparative RP-HPLC (11.8 mg, 4.1 %). Analytical RP-HPLC: t_R = 2.970 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 [M].

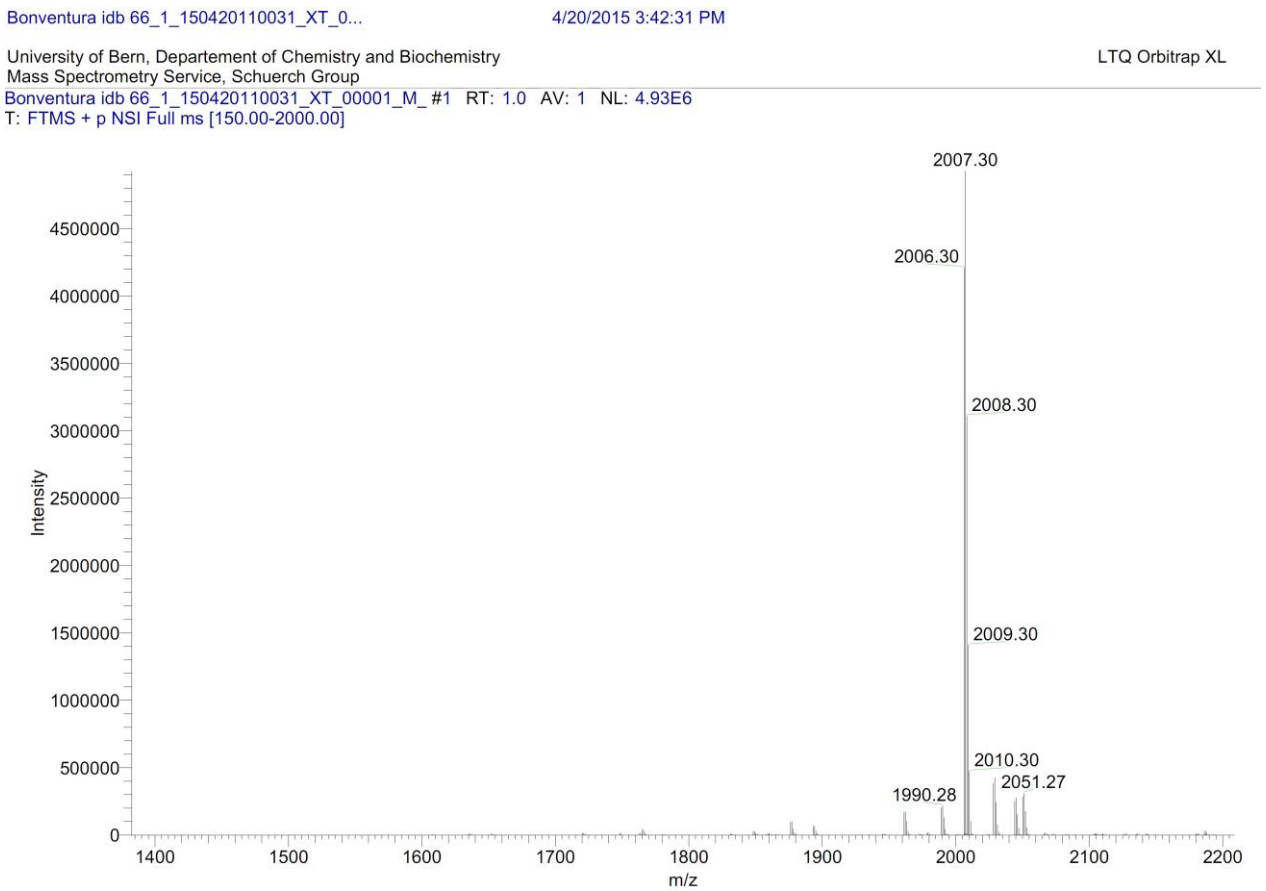




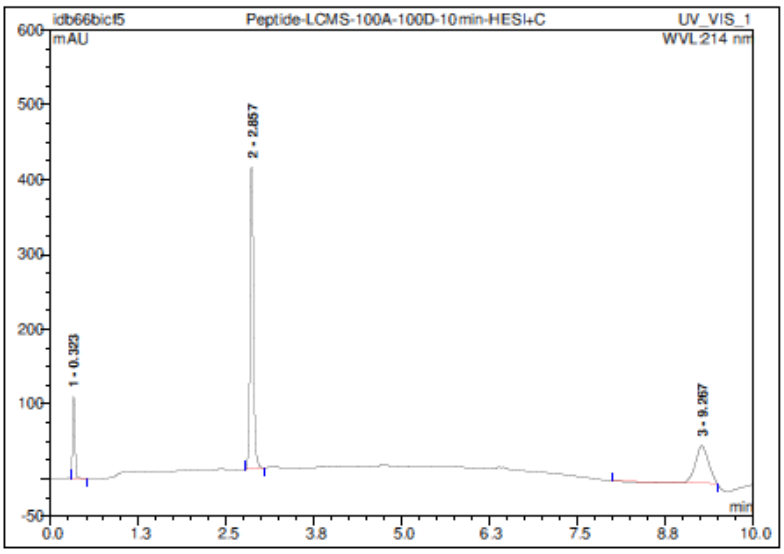
^{2}KLK*K*(K^{1}LK)KLL*Z*^{1}KLK*Z*^{2}L (37a) was obtained as foamy white solid after preparative RP-HPLC (11.0 mg, 3.9 %). Analytical RP-HPLC: t_R = 2.810 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].

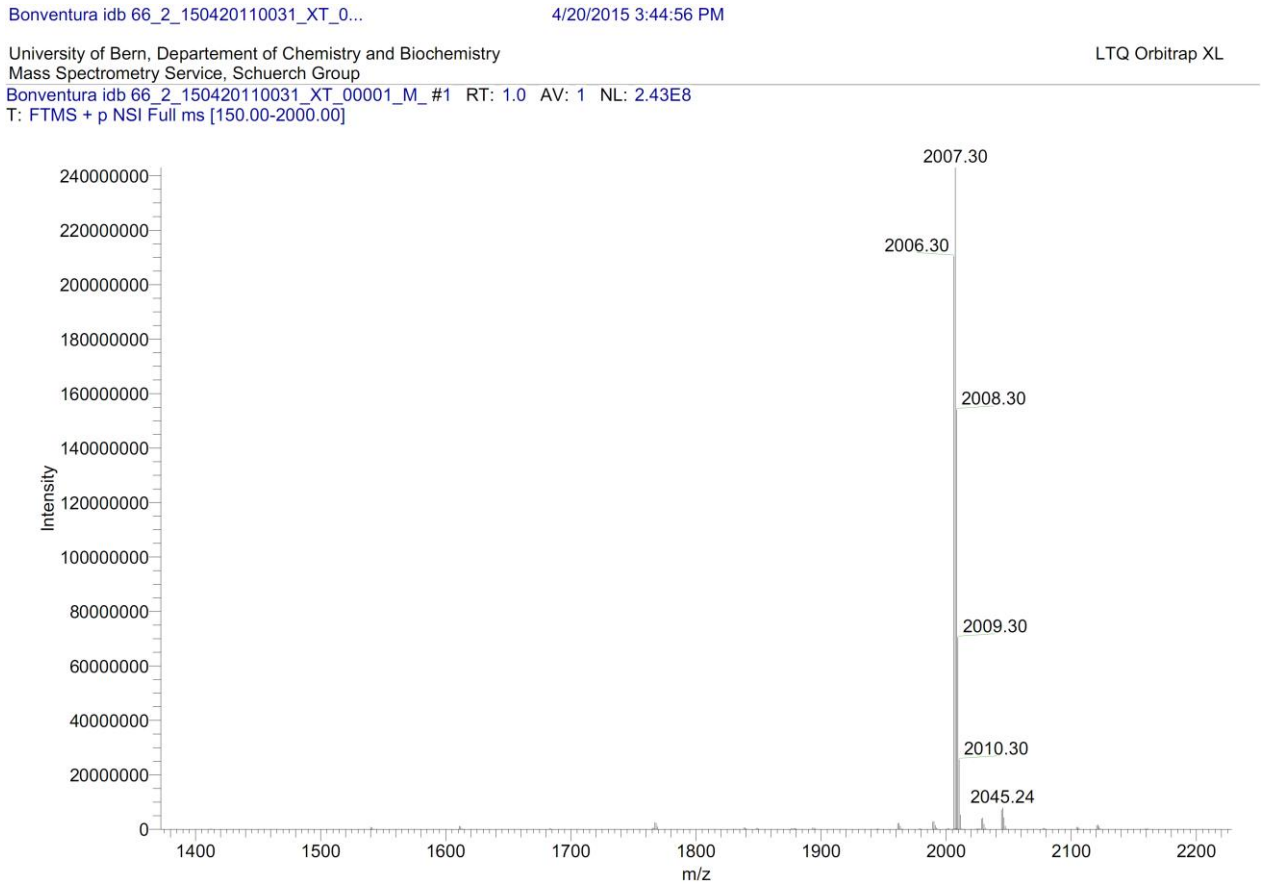




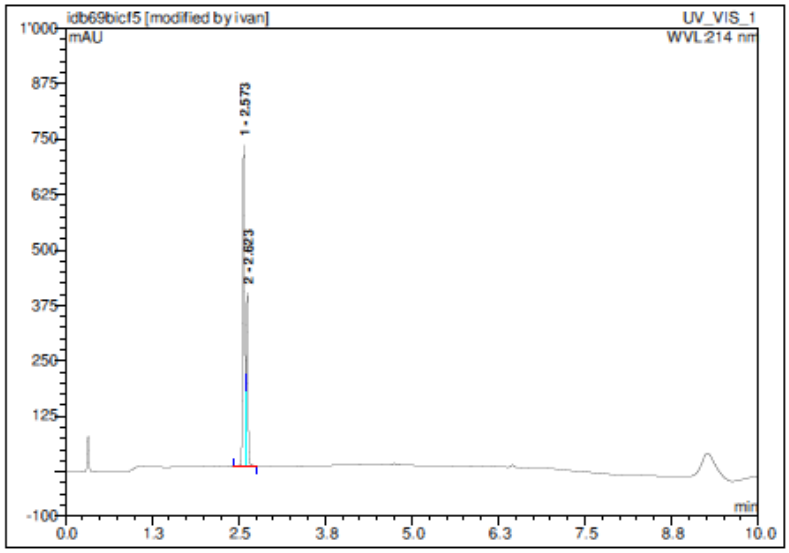


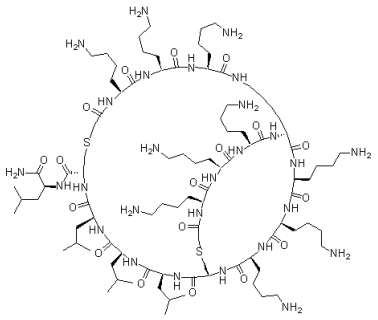
^{1}KLK*K*(K^{2}LK)KLLZ^{1}KLKZ^{2}L (37b) was obtained as foamy white solid after preparative RP-HPLC (6.9 mg, 2.5 %). Analytical RP-HPLC: t_R = 2.860 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].





^{12}KKK*K*(K^{12}KK)KKK*Z*^{21}LLL*Z*^{12}L (38) was obtained as foamy white solid after preparative RP-HPLC (24.2 mg, 10.5 %). Analytical RP-HPLC: t_R = 2.570/2.620 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{177}N_{27}O_{18}S_2$ calc./obs. 2036.32/2036.33 Da [M].





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University of Bern, Departement of Chemistry and Biochemistry LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
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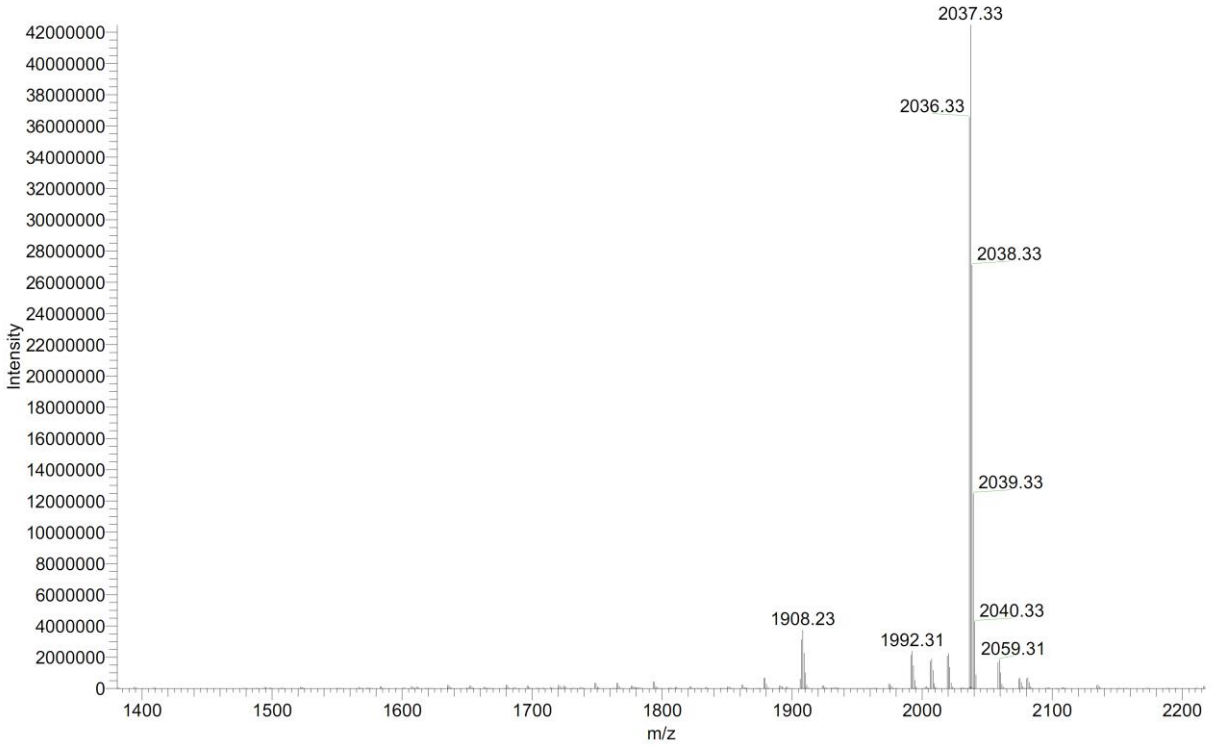
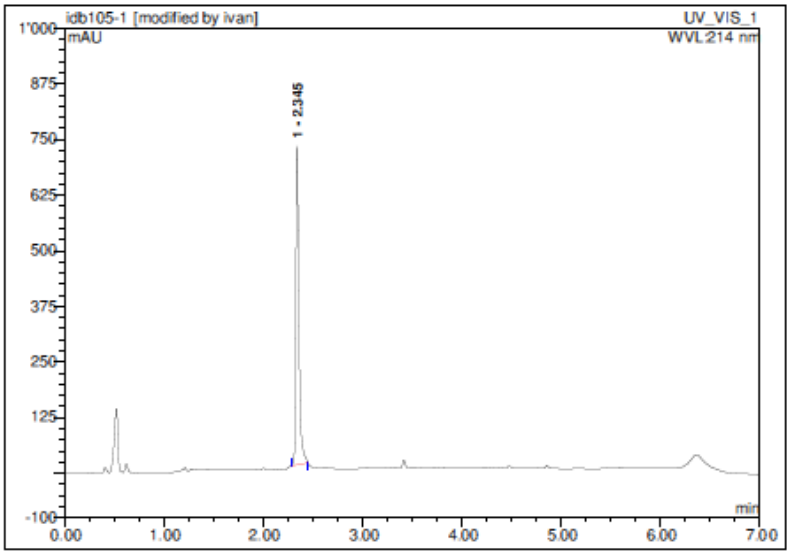
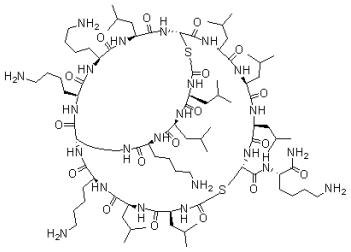
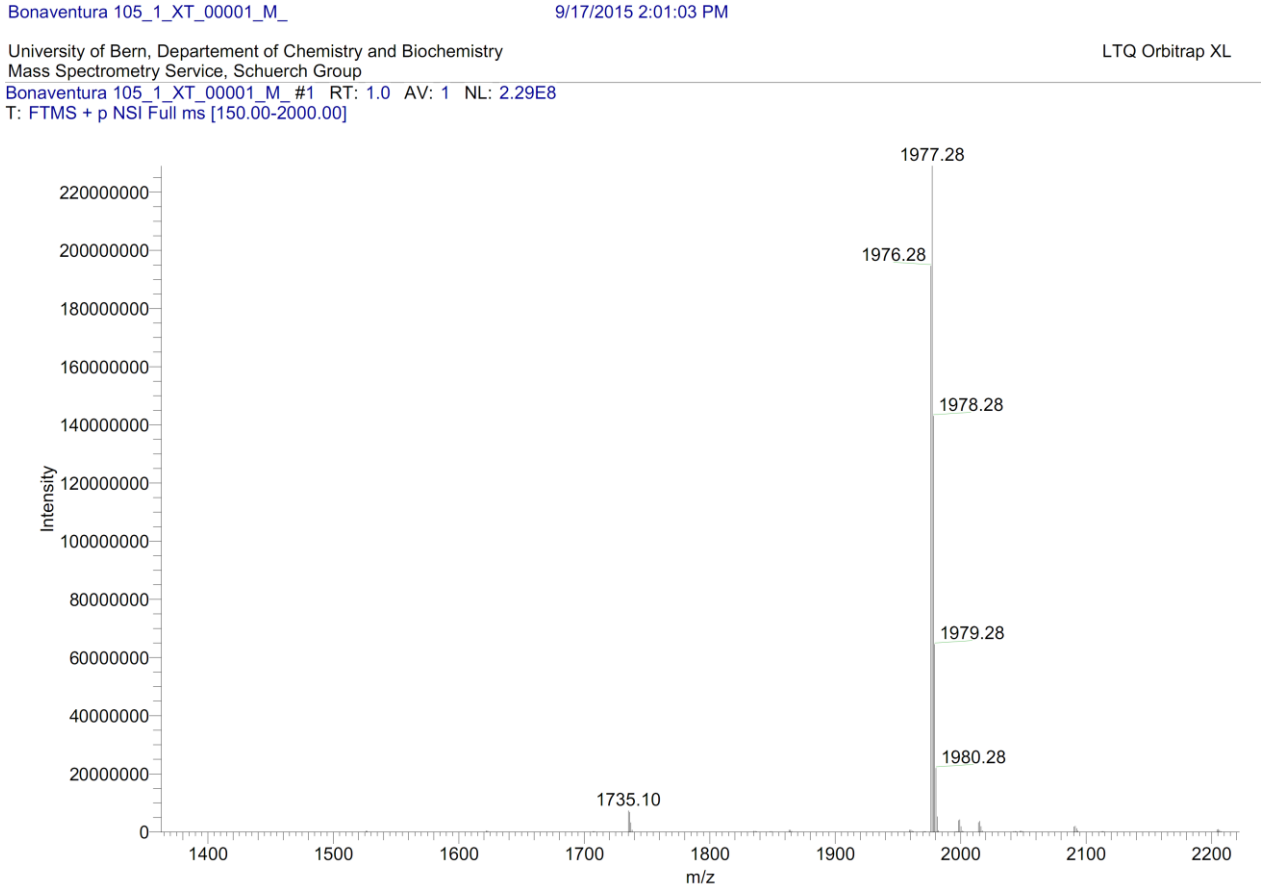


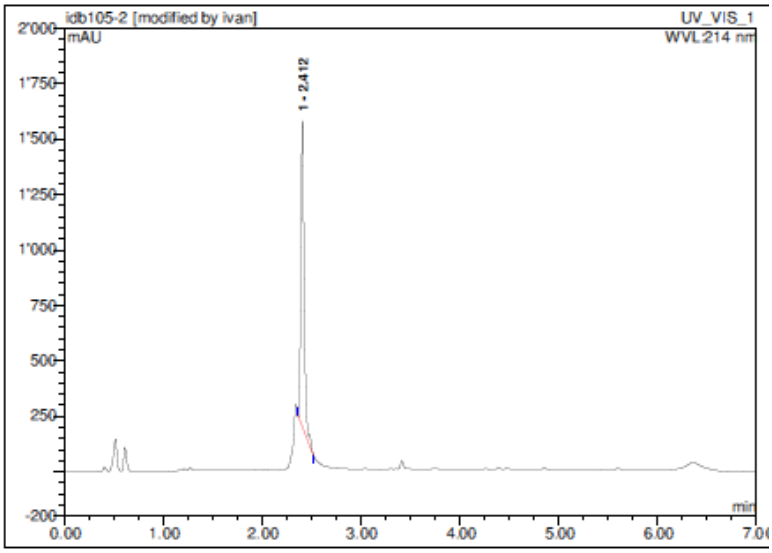
^{1}LLK*K*(L^{2}LK)KKL*Z*^{2}LLL*Z*^{1}K (39a) was obtained as foamy white solid after preparative RP-HPLC (5.5 mg, 2.9 %). Analytical RP-HPLC: t_R = 2.350 min (A/D 100:0 to 0:100 in 7.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{173}N_{23}O_{18}S_2$ calc./obs. 1976.28/1976.28 Da [M].

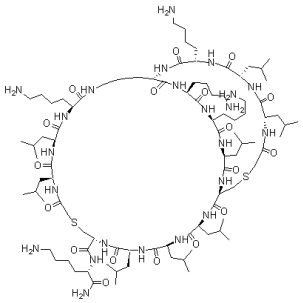


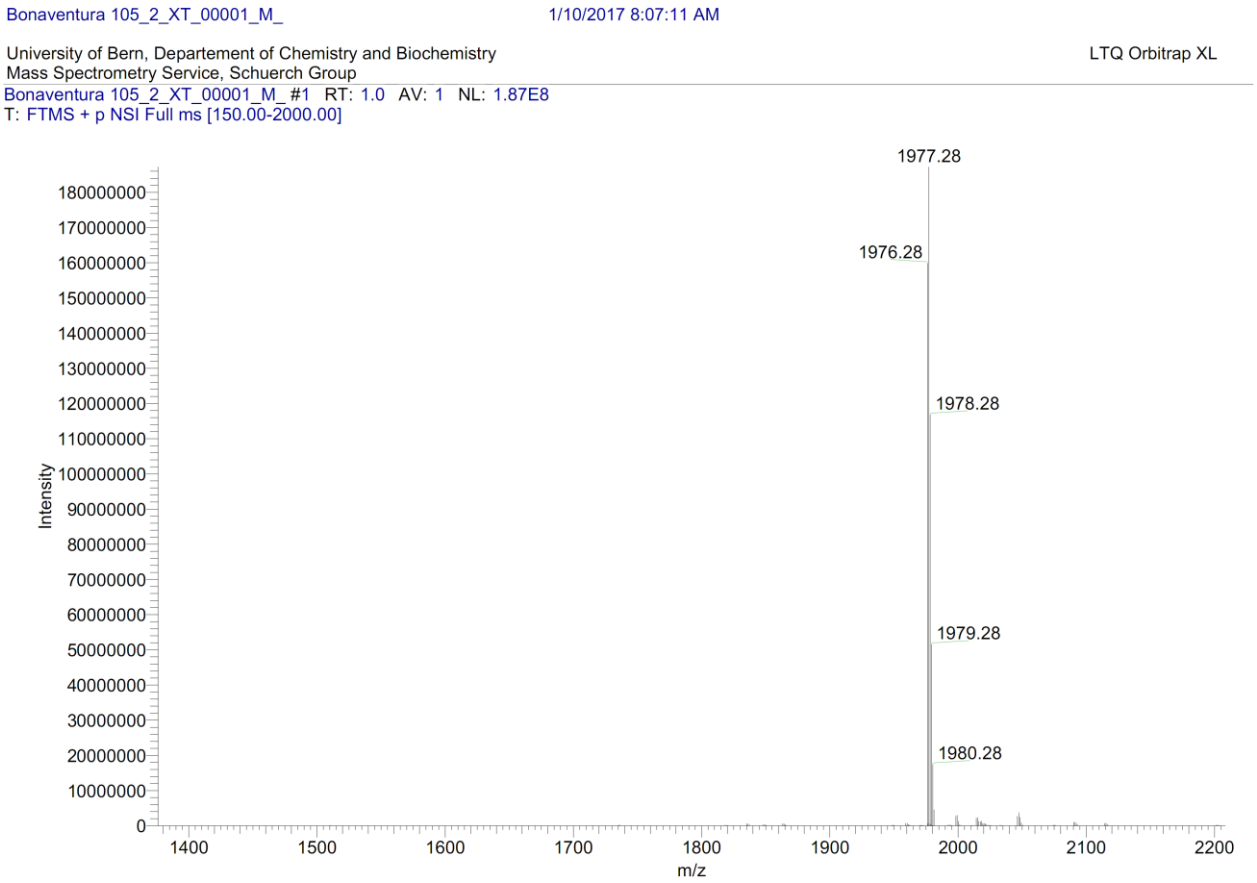




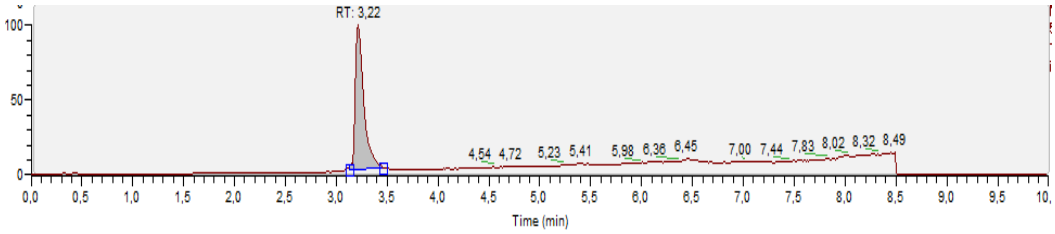
^{2}LLK*K*(L^{1}LK)KKL*Z*^{2}LLL*Z*^{1}K (39b) was obtained as foamy white solid after preparative RP-HPLC (5.3 mg, 2.8 %). Analytical RP-HPLC: t_R = 2.410 min (A/D 100:0 to 0:100 in 7.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{173}N_{23}O_{18}S_2$ calc./obs. 1976.28/1976.28 Da [M].

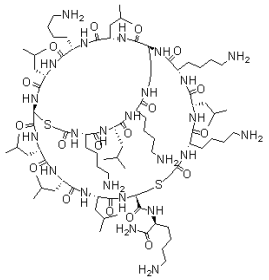


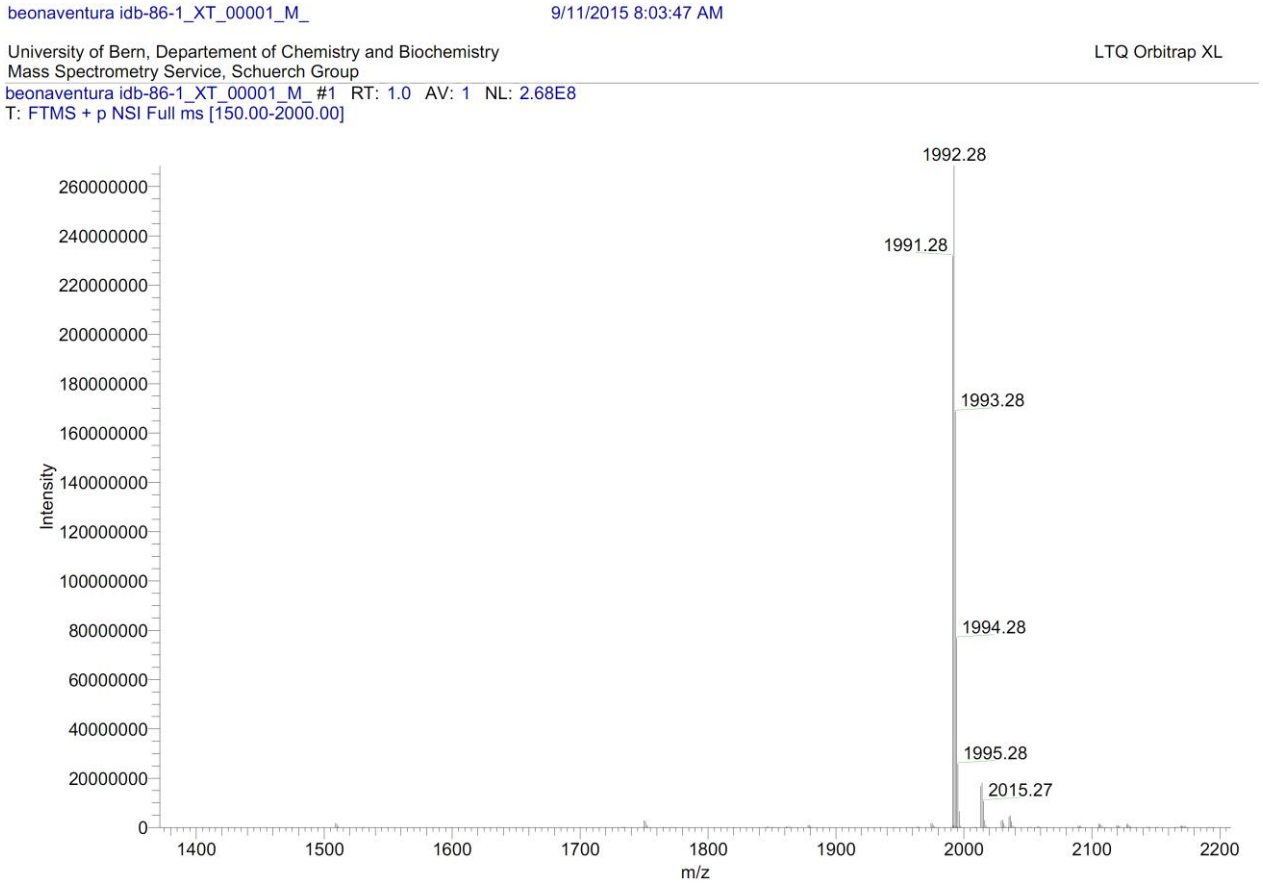




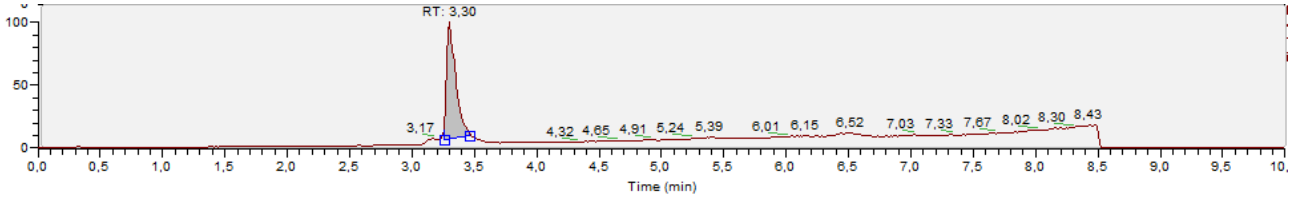
^{2}KLK*K*(K^{1}LK)LKL*Z*^{1}LLL*Z*^{2}K (40a) was obtained as foamy white solid after preparative RP-HPLC (9.3 mg, 3.8 %). Analytical RP-HPLC: t_R = 3.220 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$calc./obs.1991.29/1991.28 Da [M].

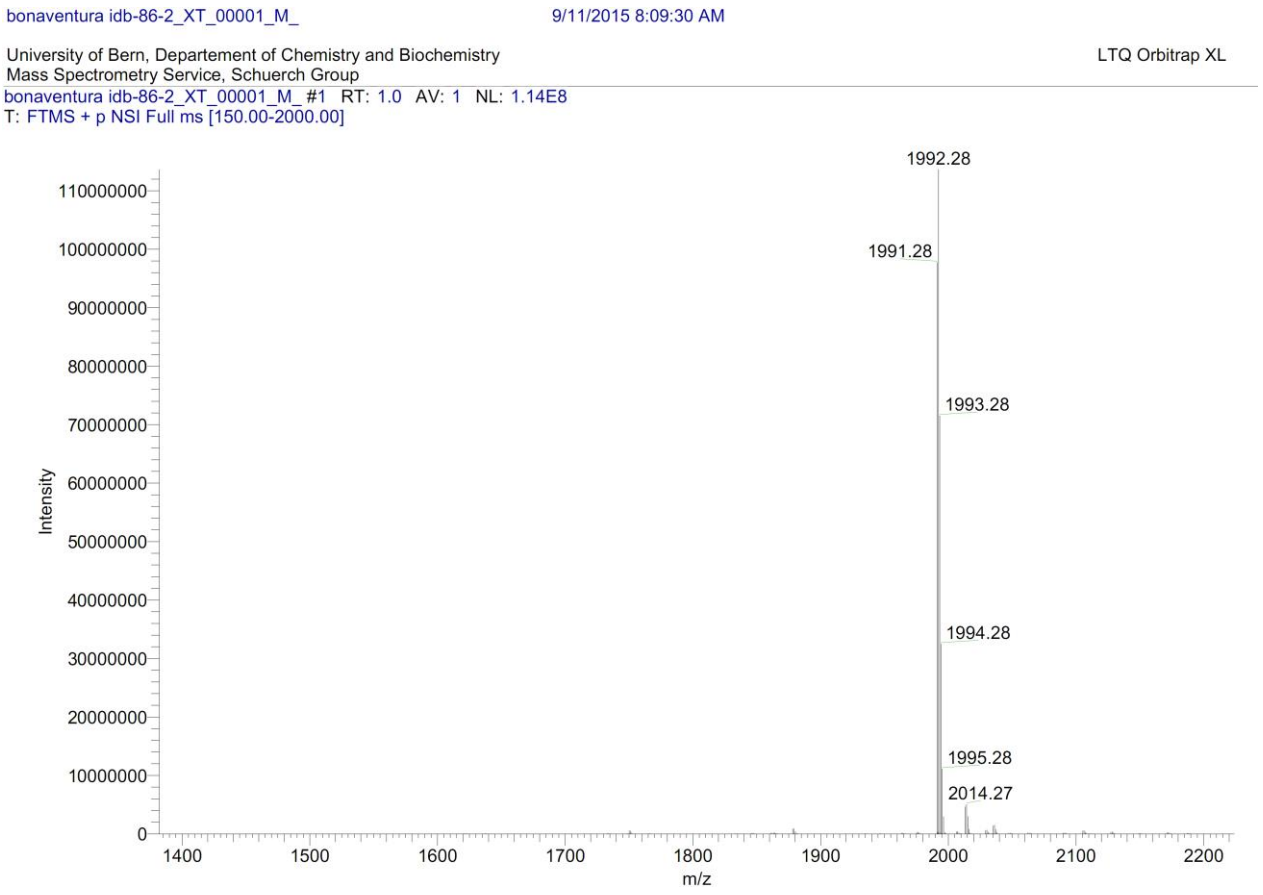




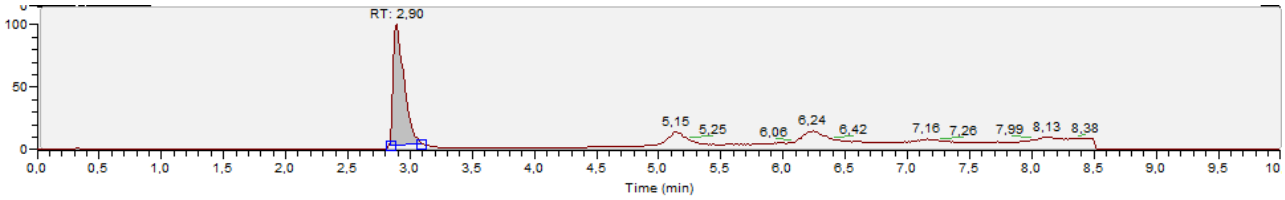


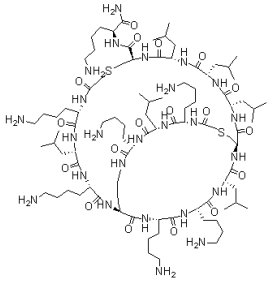
^{1}KLK*K*(K^{2}LK)LKL*Z*^{1}LLL*Z*^{2}K (40b) was obtained as foamy white solid after preparative RP-HPLC (8.3 mg, 3.3 %). Analytical RP-HPLC: t_R = 3.300 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$calc./obs.1991.29/1991.28 Da [M].

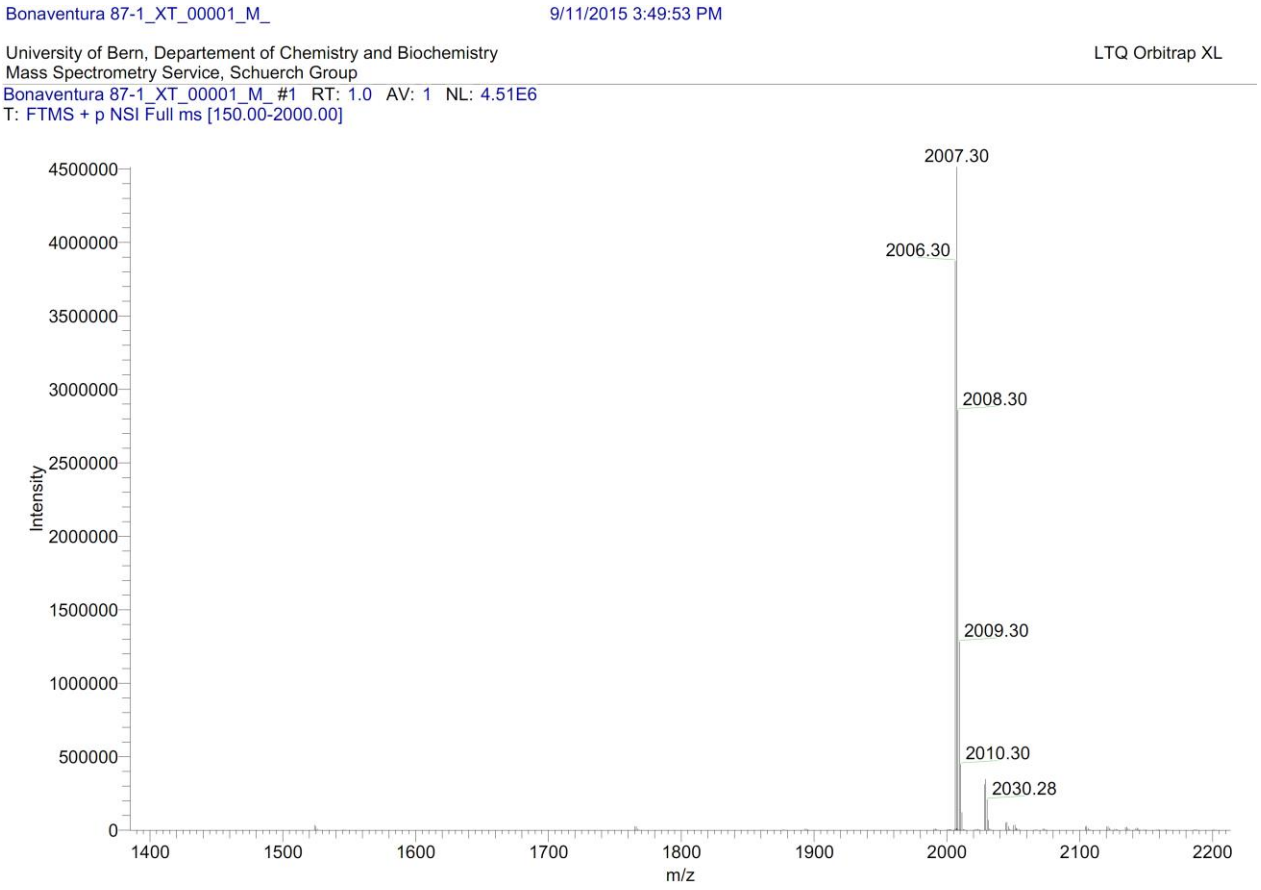




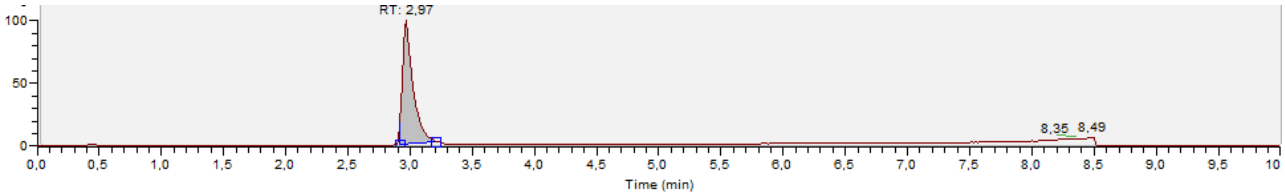
^{2}KLK*K*(K^{1}LK)KKK*Z*^{1}LLL*Z*^{2}K (41a) was obtained as foamy white solid after preparative RP-HPLC (9.9 mg, 5.1 %). Analytical RP-HPLC: t_R = 2.900 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].

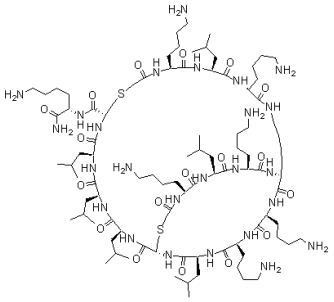


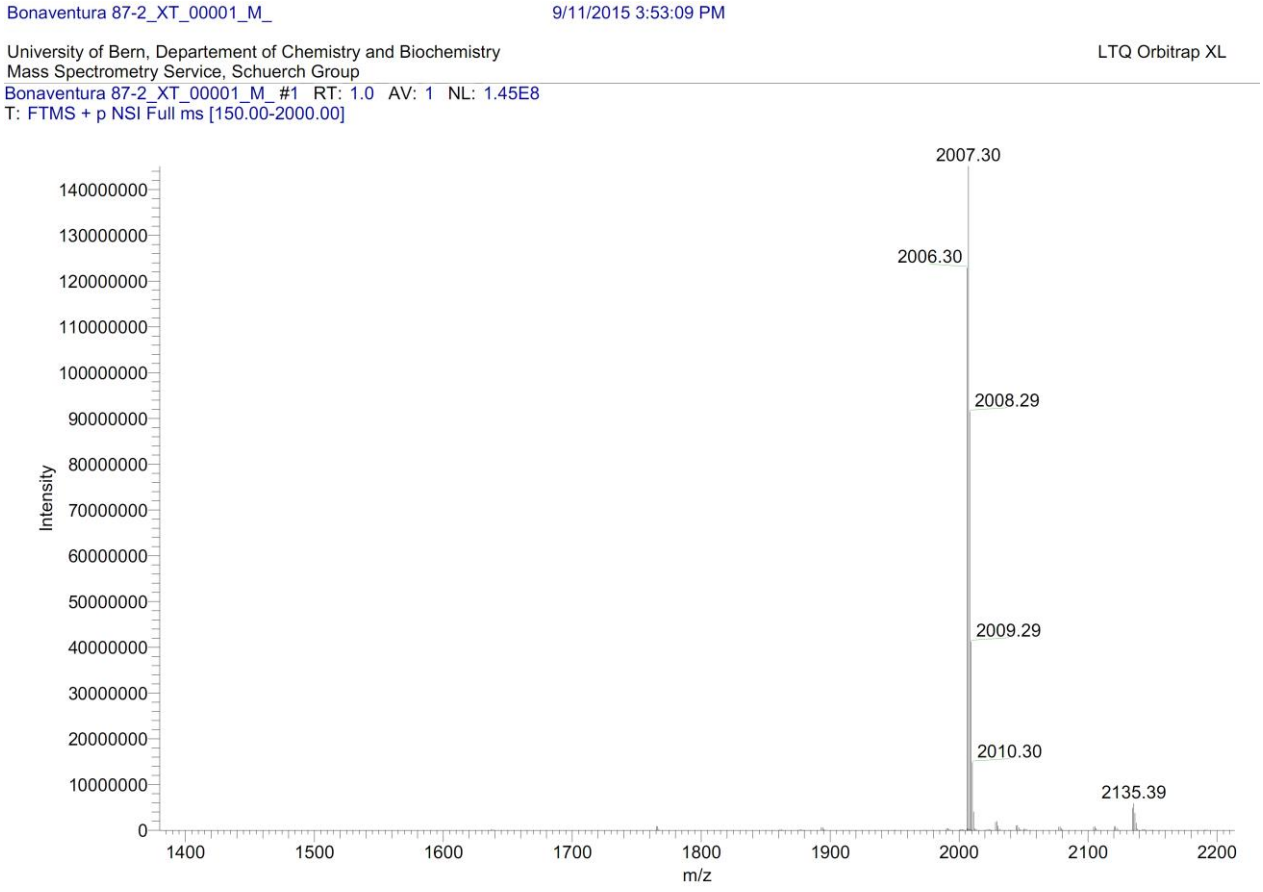




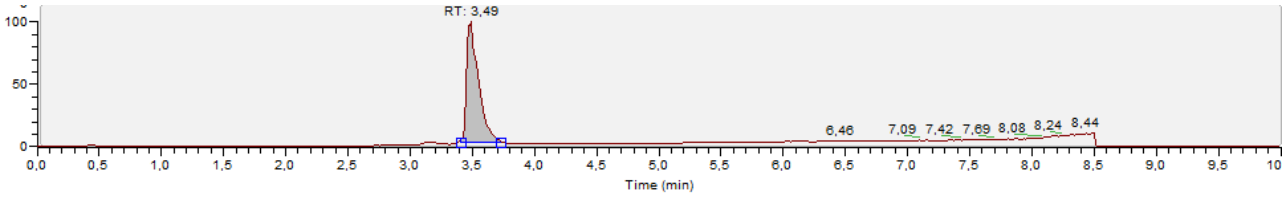
^{1}KLK*K*(K^{2}LK)KKK*Z*^{1}LLL*Z*^{2}K (41b) was obtained as foamy white solid after preparative RP-HPLC (7.0 mg, 3.6 %). Analytical RP-HPLC: t_R = 2.970 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].

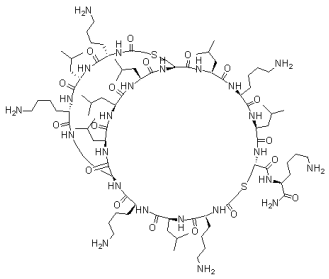


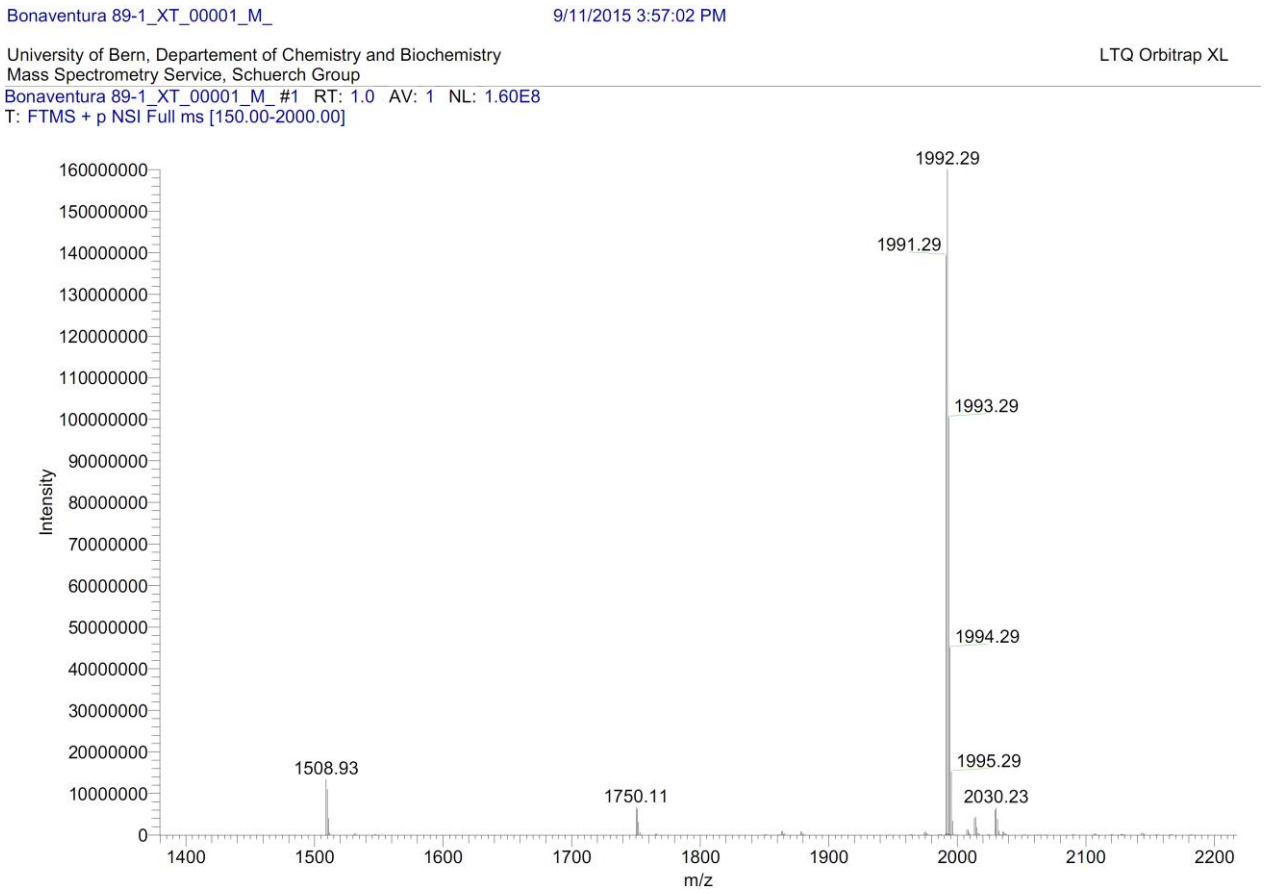




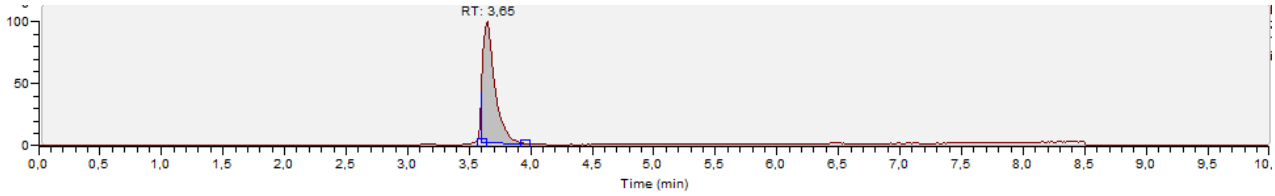
^{1}KLK*K*(K^{2}LK)LLL*Z*^{2}LKL*Z*^{1}K (42a) was obtained as foamy white solid after preparative RP-HPLC (3.0 mg, 1.6 %). Analytical RP-HPLC: t_R = 3.490 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+):$C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs. 1991.29/1991.29 Da [M].

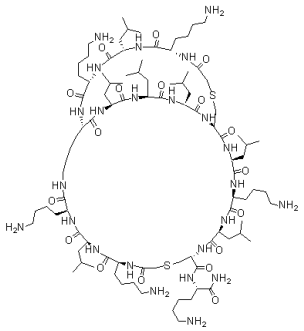


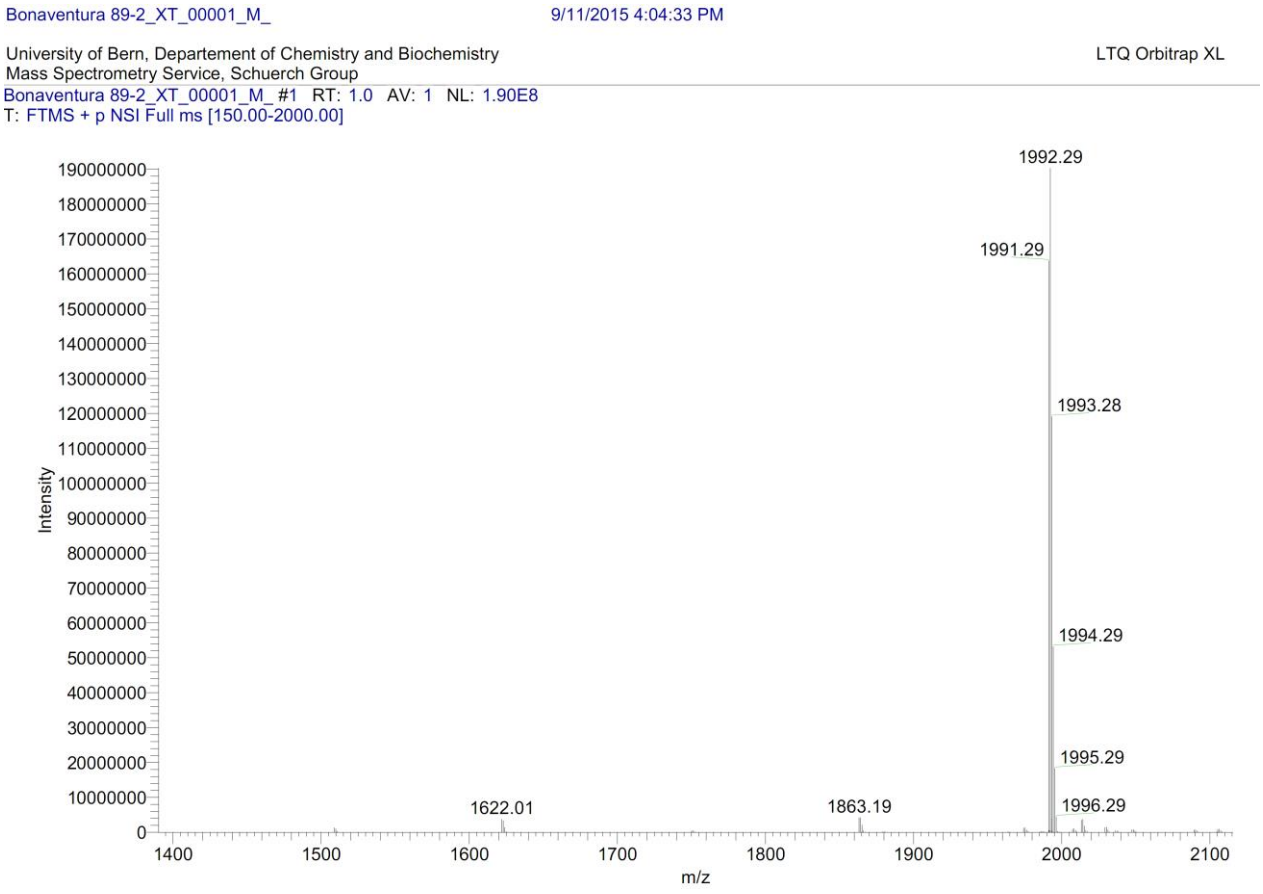




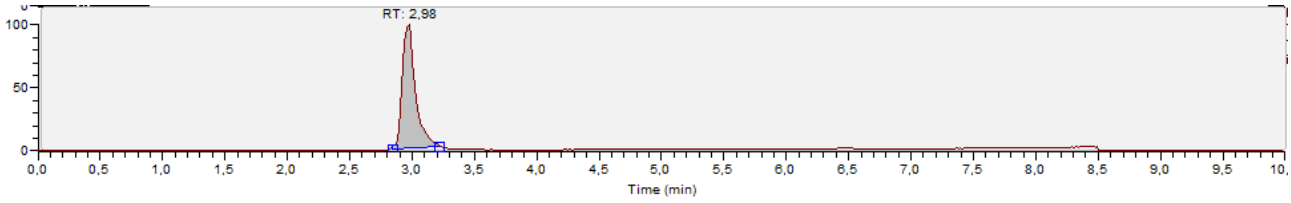
^{2}KLK*K*(K^{1}LK)LLL*Z*^{2}LKL*Z*^{1}K (42b) was obtained as foamy white solid after preparative RP-HPLC (6.6 mg, 3.4 %). Analytical RP-HPLC: t_R = 3.650 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{174}N_{24}O_{18}S_2$ calc./obs. 1991.29/1991.29 Da [M].

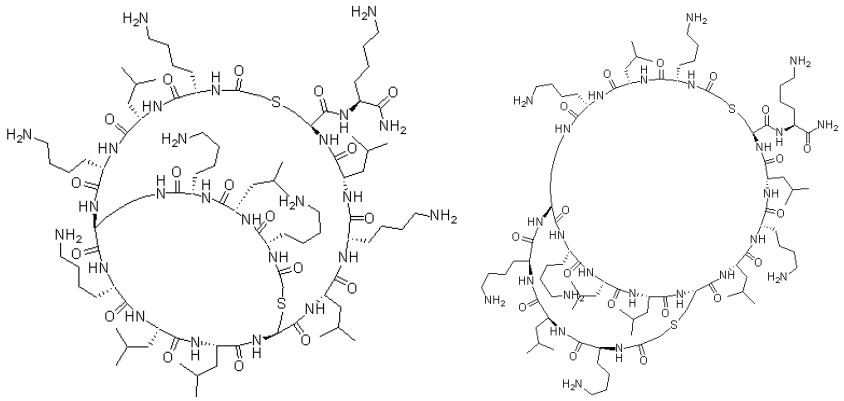


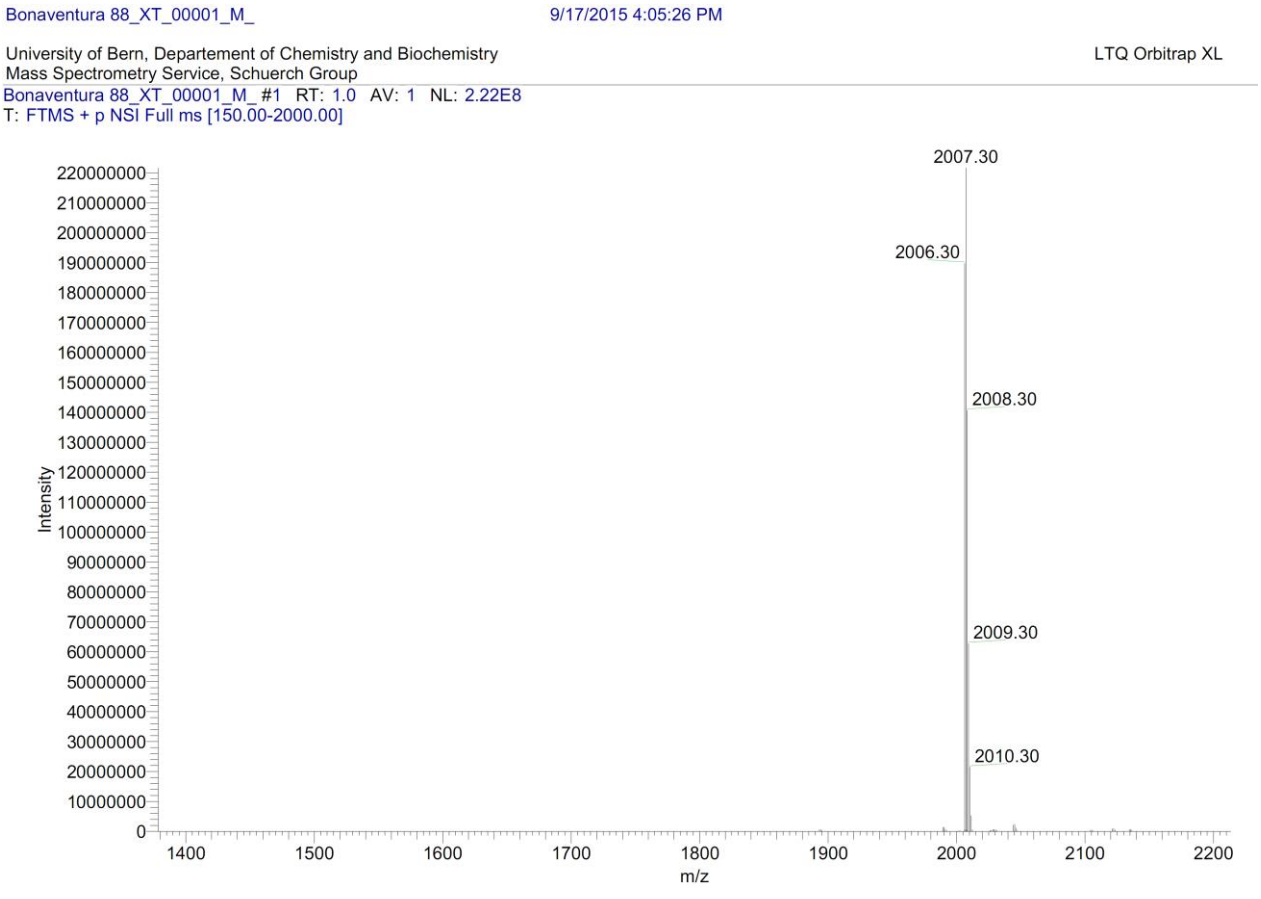




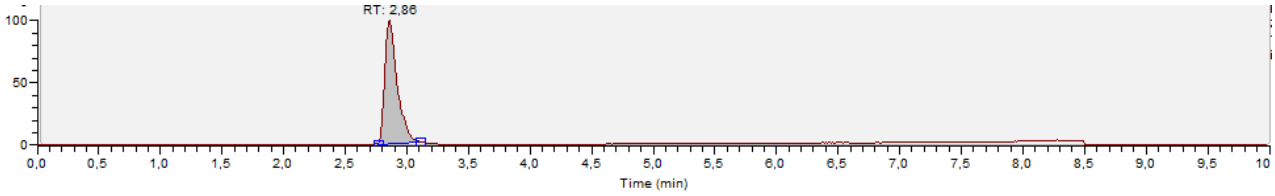
^{12}KLK*K*(K^{21}LK)KLL*Z*^{12}LKL*Z*^{21}K (43) was obtained, like one isomer, as foamy white solid after preparative RP-HPLC (16.5 mg, 8.6 %). Analytical RP-HPLC: t_R = 2.980 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].

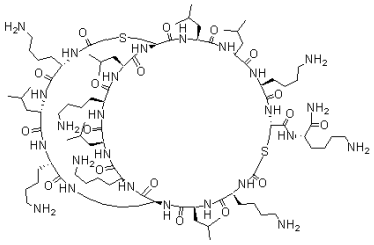


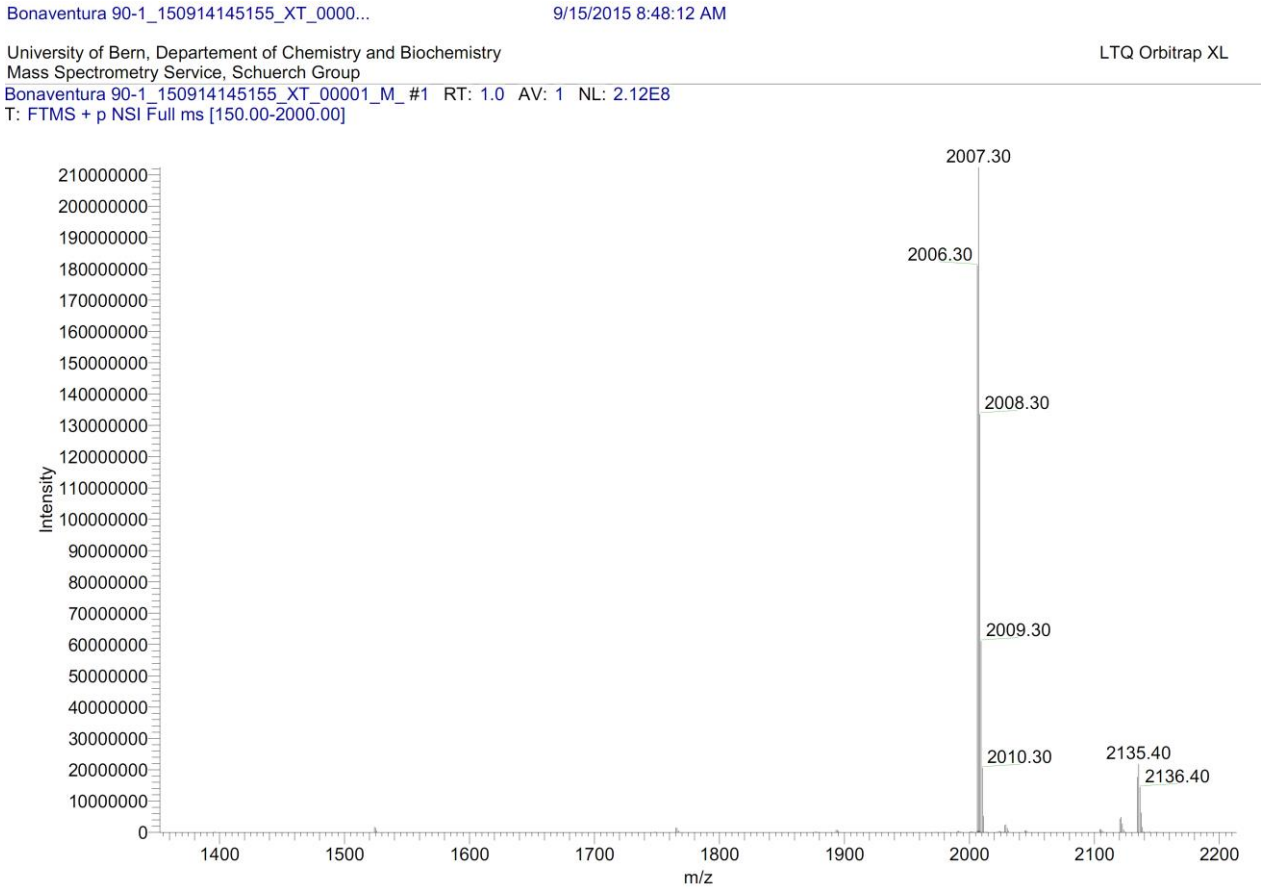




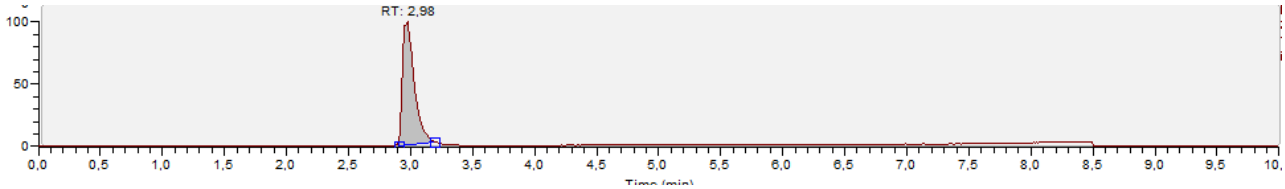
^{1}KLK*K*(K^{2}LK)LKLZ^{2}LLKZ^{1}K (44a) was obtained as foamy white solid after preparative RP-HPLC (8.9 mg, 4.6 %). Analytical RP-HPLC: t_R = 2.860 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].

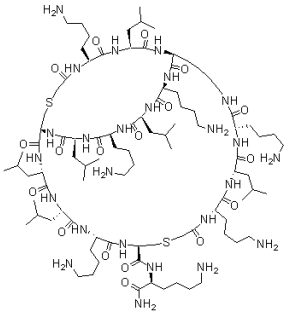


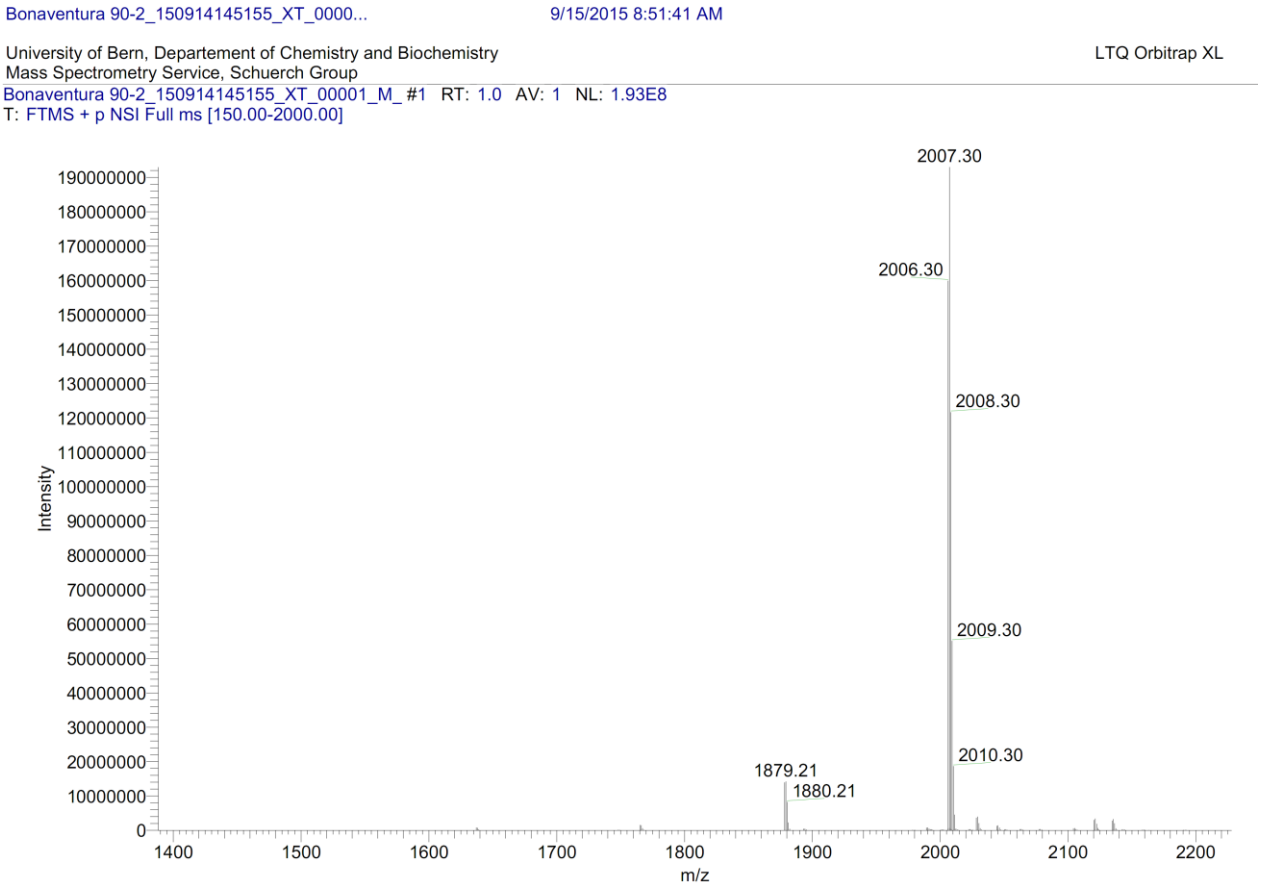




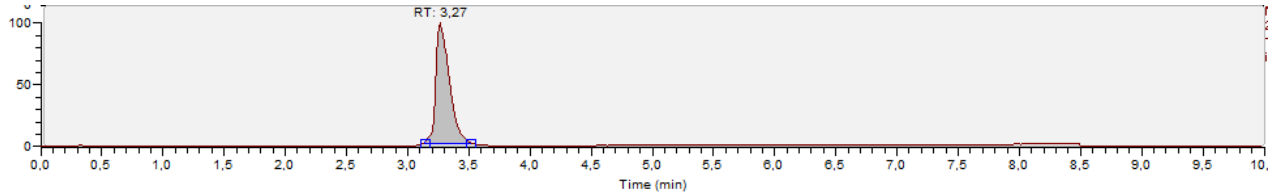
^{2}KLK*K*(K^{1}LK)LKLZ^{2}LLKZ^{1}K (44b) was obtained as foamy white solid after preparative RP-HPLC (9.7 mg, 5.0 %). Analytical RP-HPLC: t_R = 2.980 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].

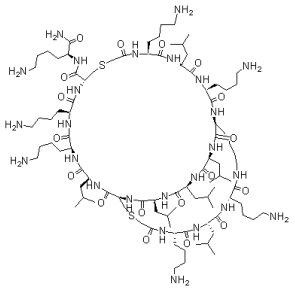


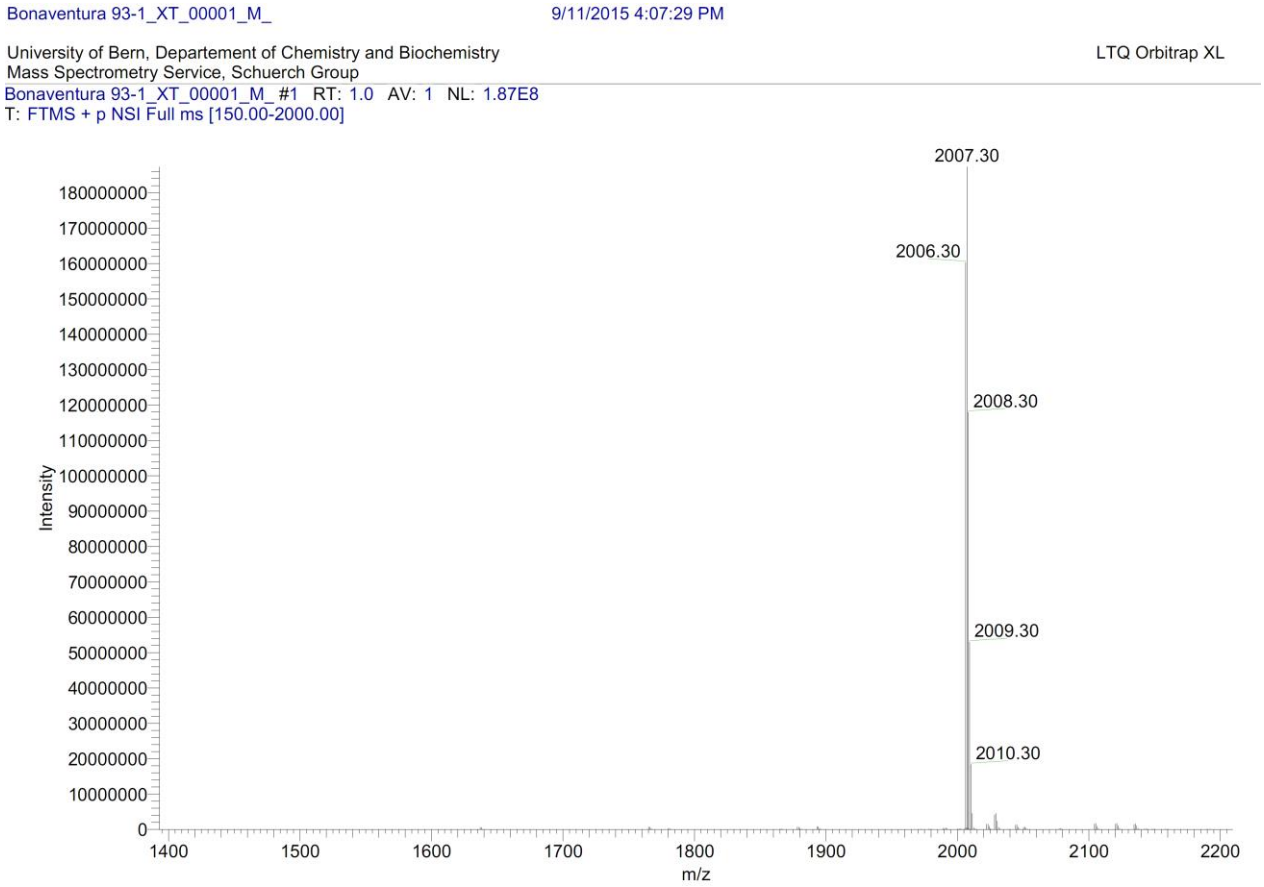




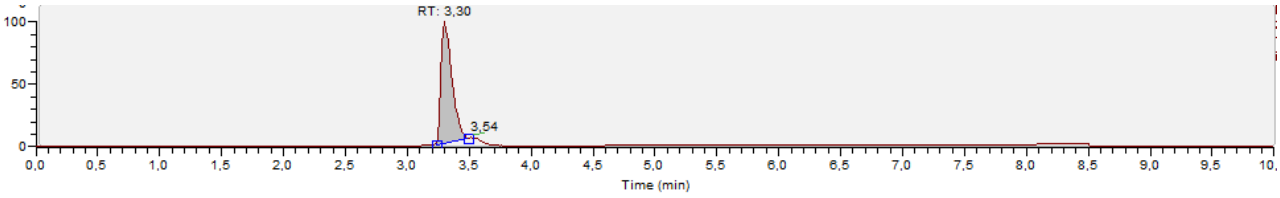
^{1}KLK*K*(K^{2}LK)LLL*Z*^{2}LKK*Z*^{1}K (45a) was obtained as foamy white solid after preparative RP-HPLC (9.7 mg, 5.1 %). Analytical RP-HPLC: t_R = 3.270 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].

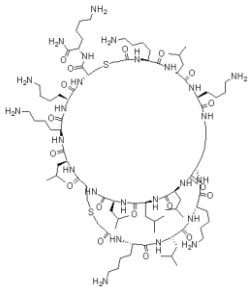


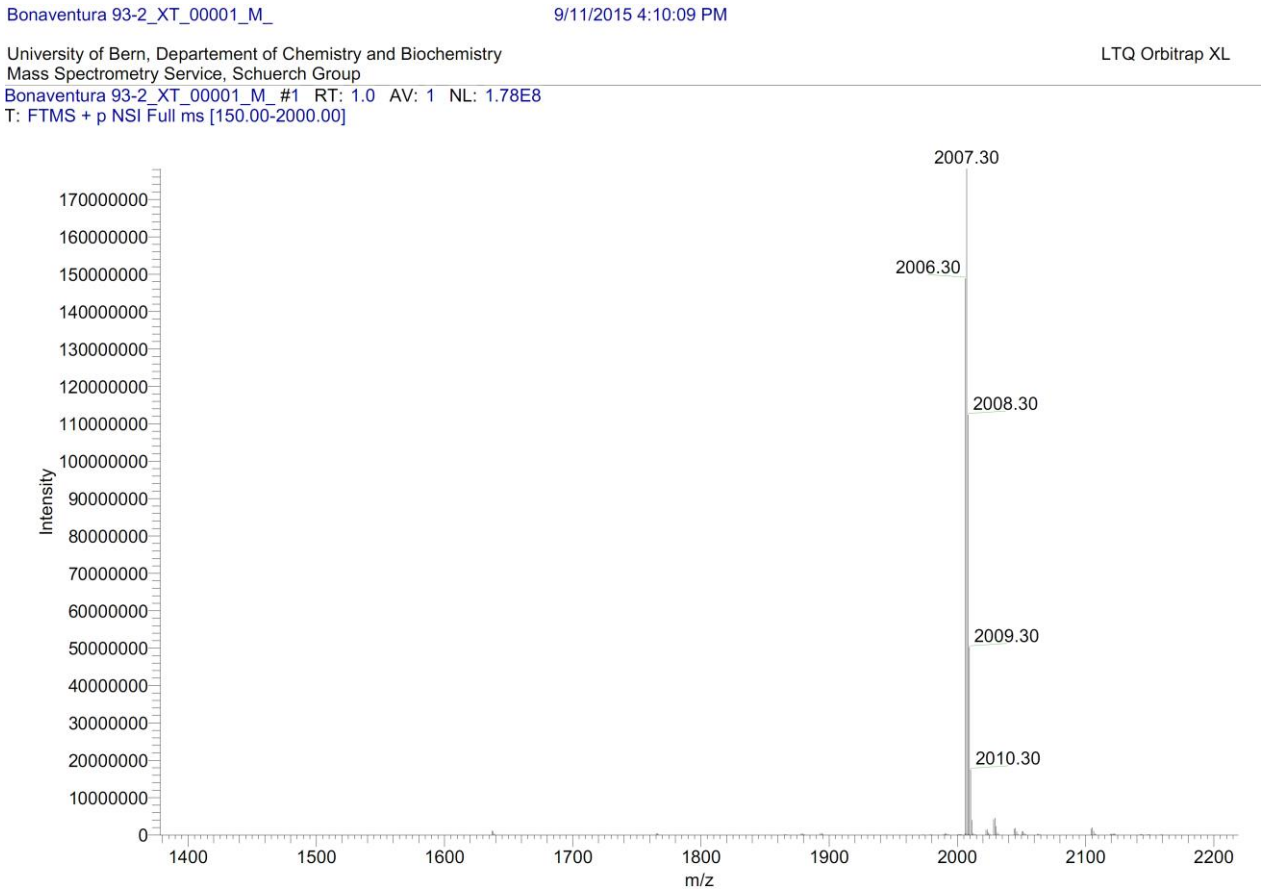




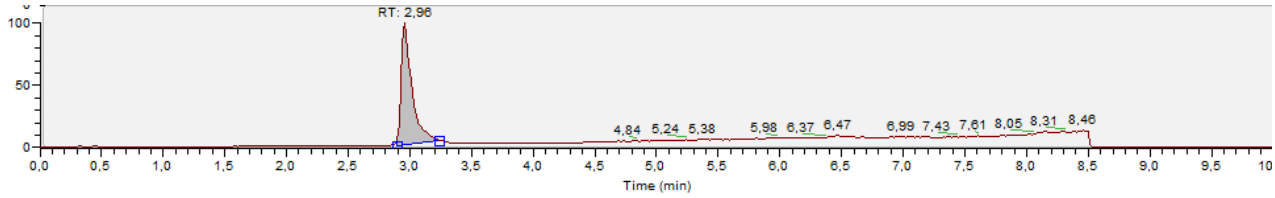
^{1}KLK*K*(K^{2}LK)LLL*Z*^{1}LKKZ^{2}K (45b) was obtained as foamy white solid after preparative RP-HPLC (5.5 mg, 2.8 %). Analytical RP-HPLC: t_R = 3.300 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].

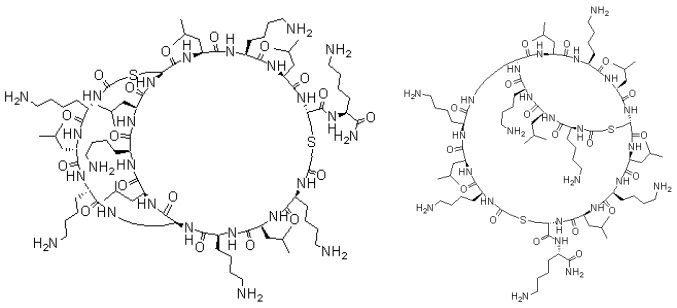


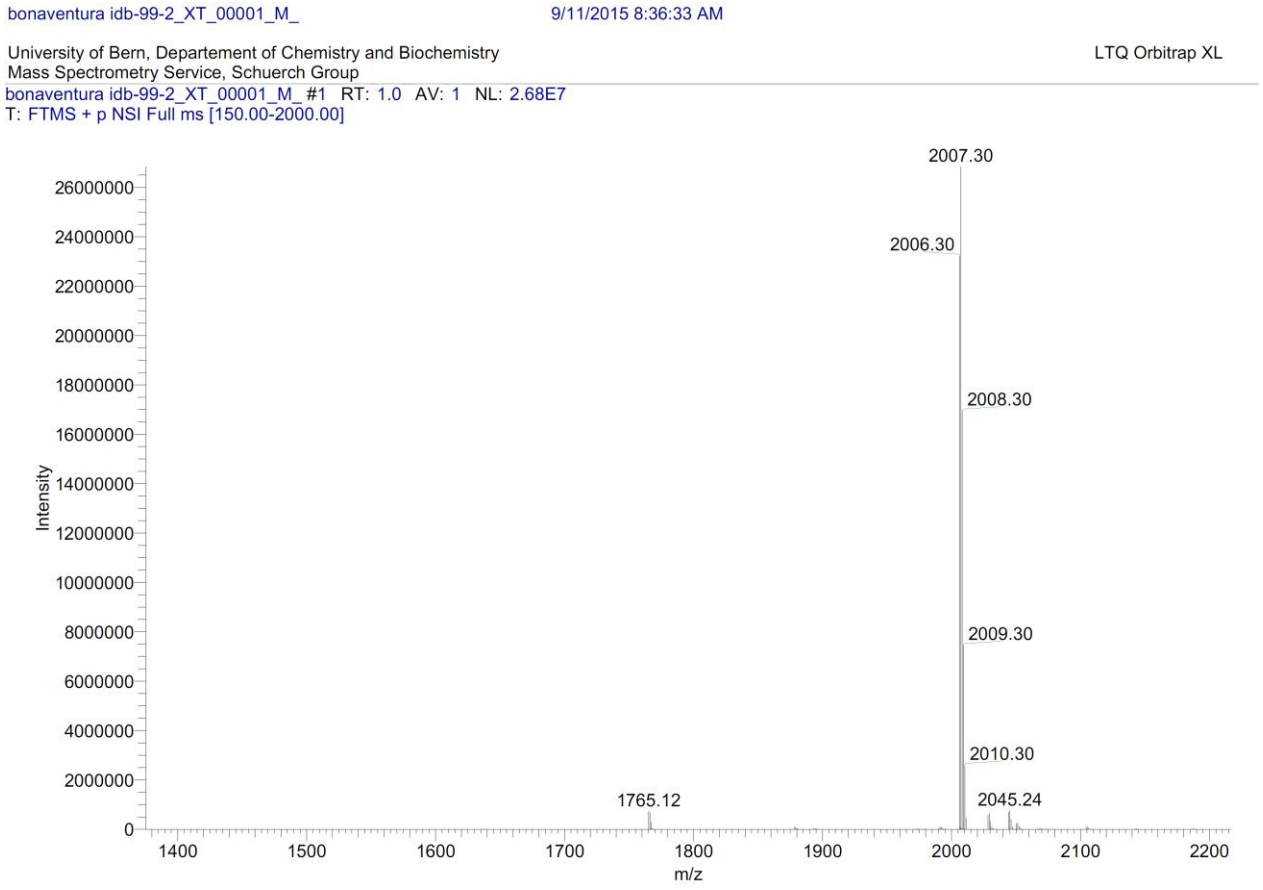




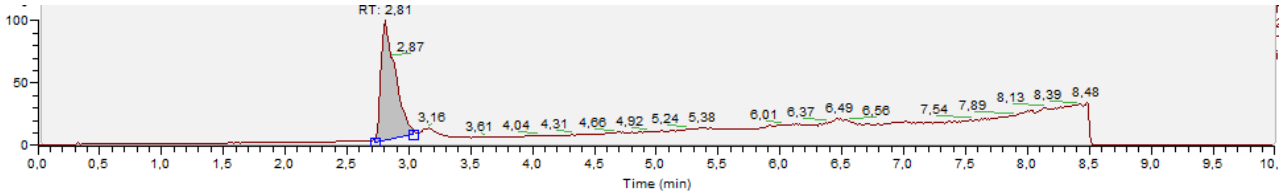
^{12}KLK*K*(K^{21}LK)LKL*Z*^{21}LKL*Z*^{12}K (46) was obtained, like one isomer, as foamy white solid after preparative RP-HPLC (10.3 mg, 4.1 %). Analytical RP-HPLC: t_R = 2.960 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].

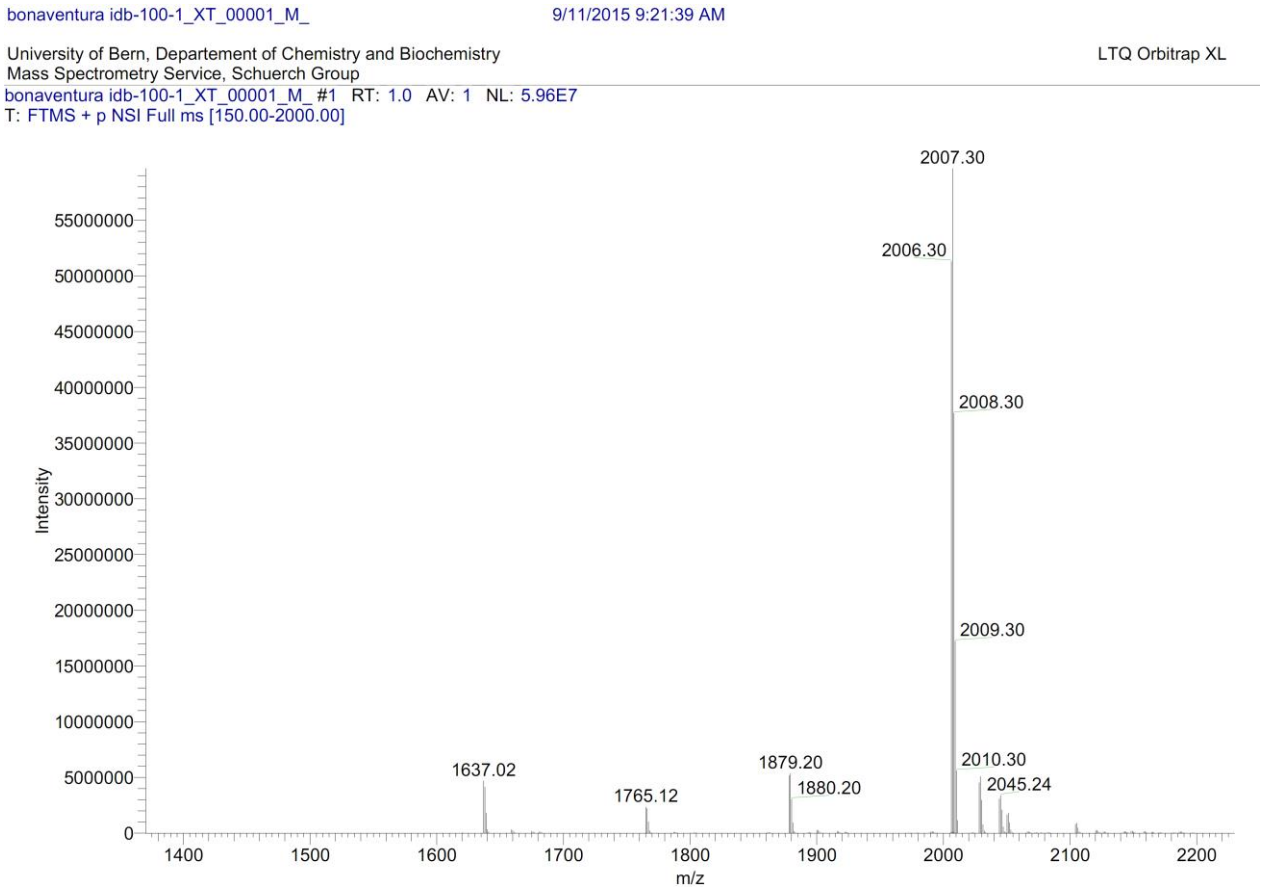




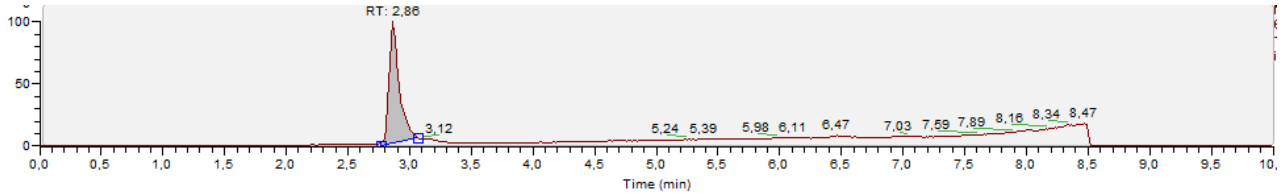


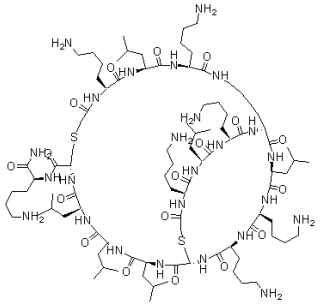
^{2}KLK*K*(K^{1}LK)LKK*Z*^{1}LLL*Z*^{2}K (47a) was obtained as foamy white solid after preparative RP-HPLC (9.7 mg, 3.9 %). Analytical RP-HPLC: t_R = 2.810 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].

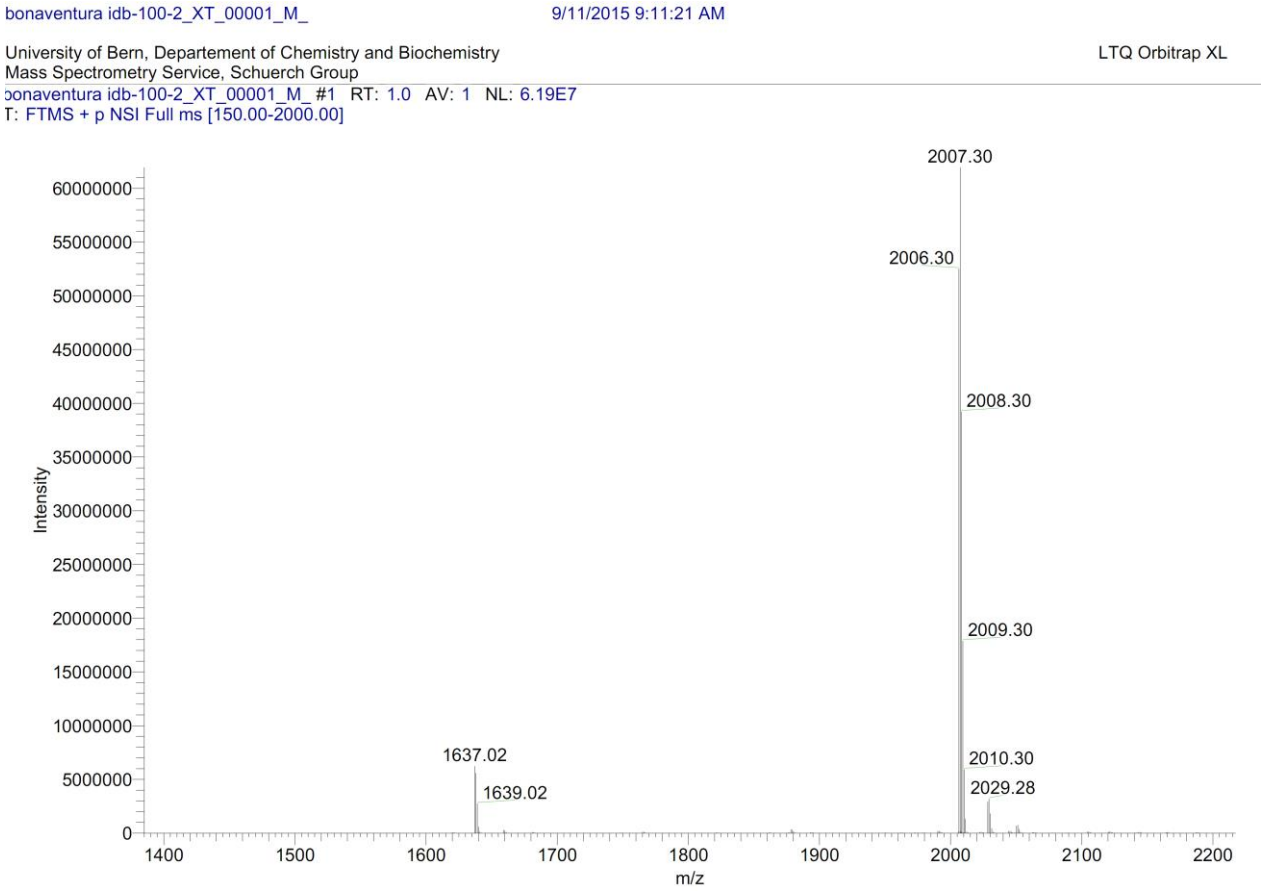




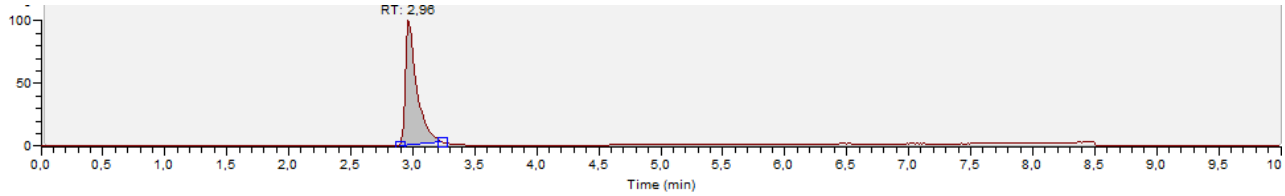
^{1}KLK*K*(K^{2}LK)LKK*Z*^{1}LLL*Z*^{2}K (47b) was obtained as foamy white solid after preparative RP-HPLC (10.8 mg, 4.3 %). Analytical RP-HPLC: t_R = 2.860 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].

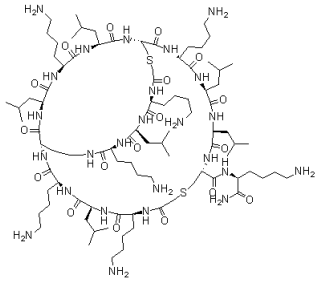


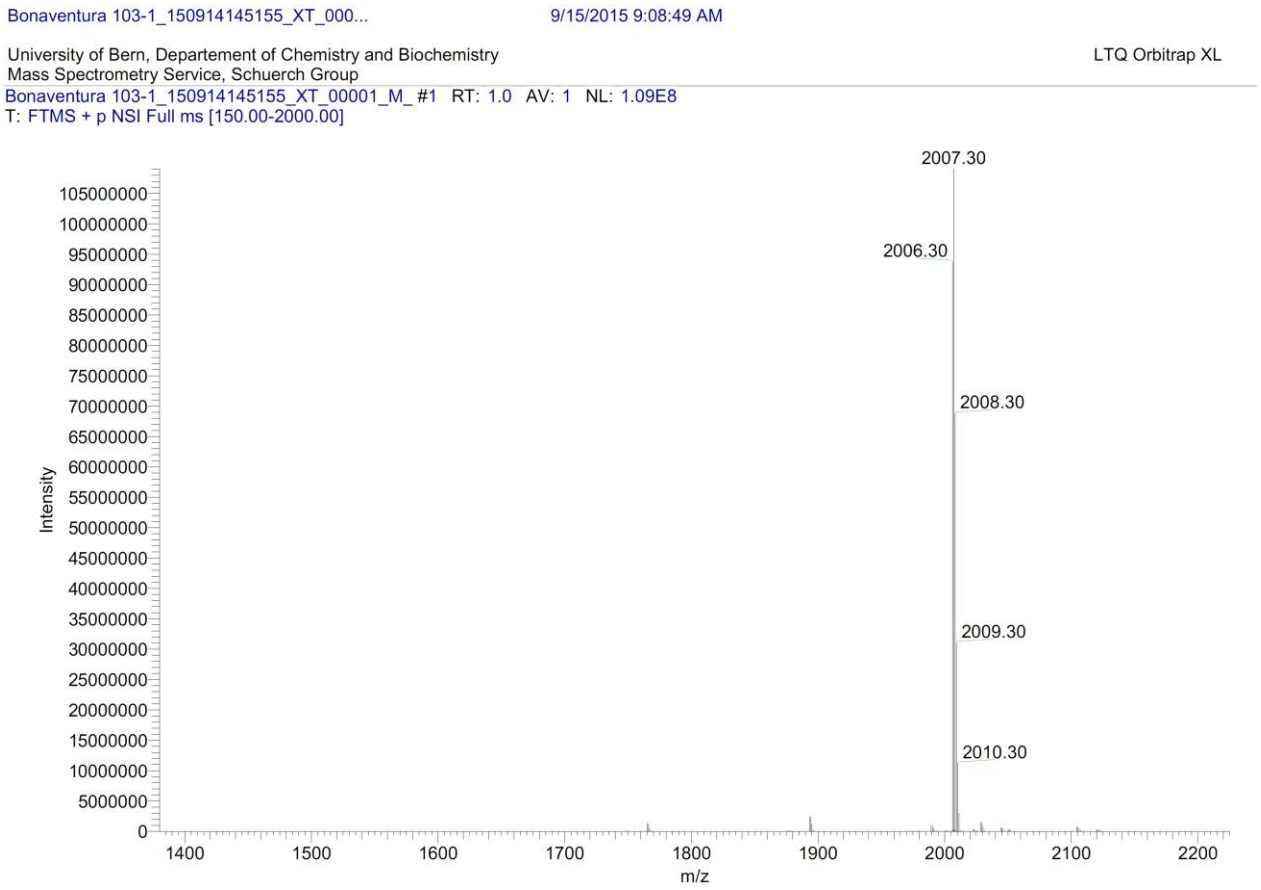




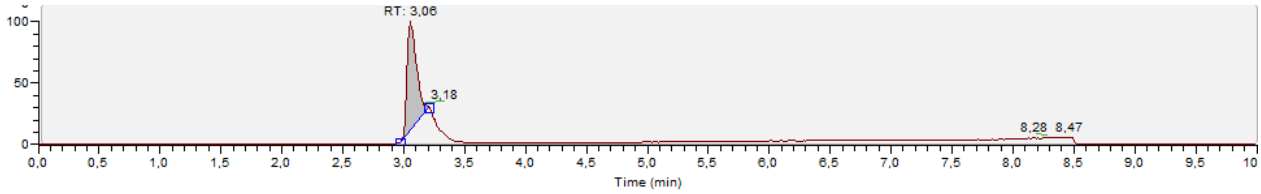
^{1}KLK*K*(K^{2}LK)LKLZ^{2}KLLZ^{1}K (48a) was obtained as foamy white solid after preparative RP-HPLC (11.5 mg, 6.1 %). Analytical RP-HPLC: t_R = 2.960 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].

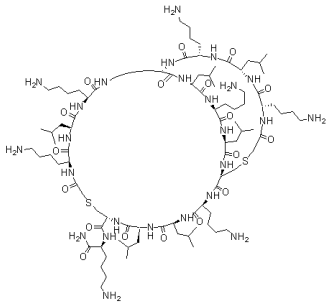


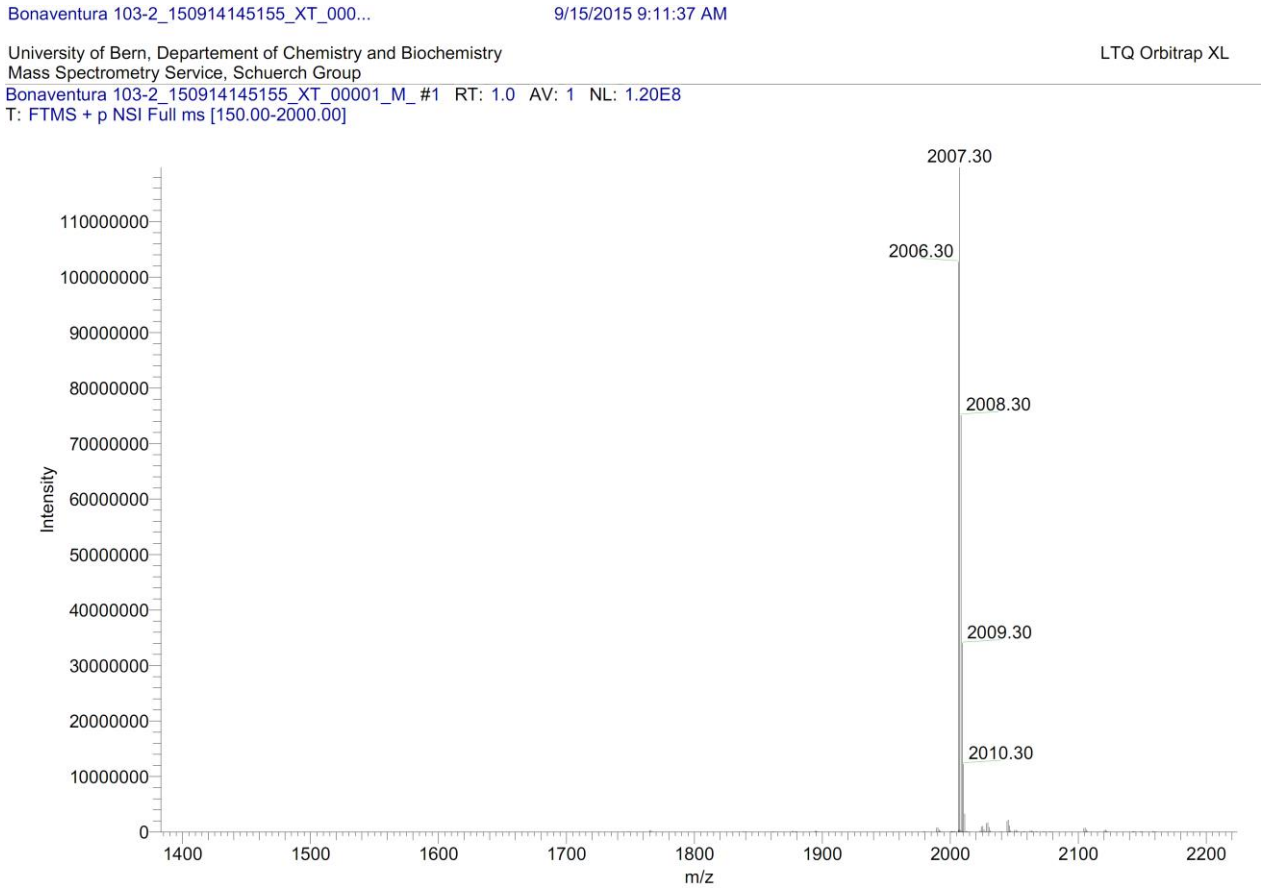




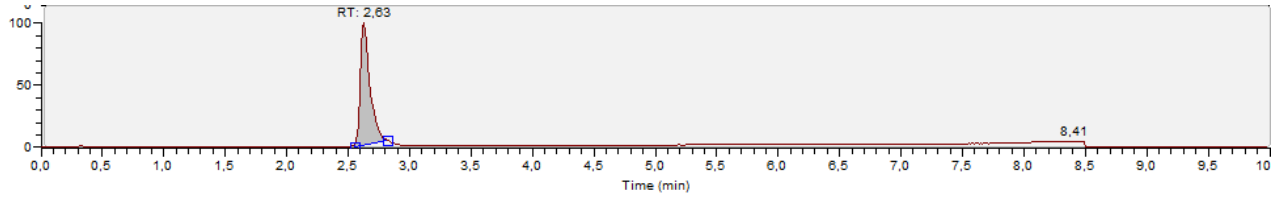
^{2}KLK*K*(K^{1}LK)LKLZ^{2}KLLZ^{1}K (48b) was obtained as foamy white solid after preparative RP-HPLC (6.5 mg, 3.4 %). Analytical RP-HPLC: t_R = 3.060 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{175}N_{25}O_{18}S_2$ calc./obs. 2006.30/2006.30 Da [M].

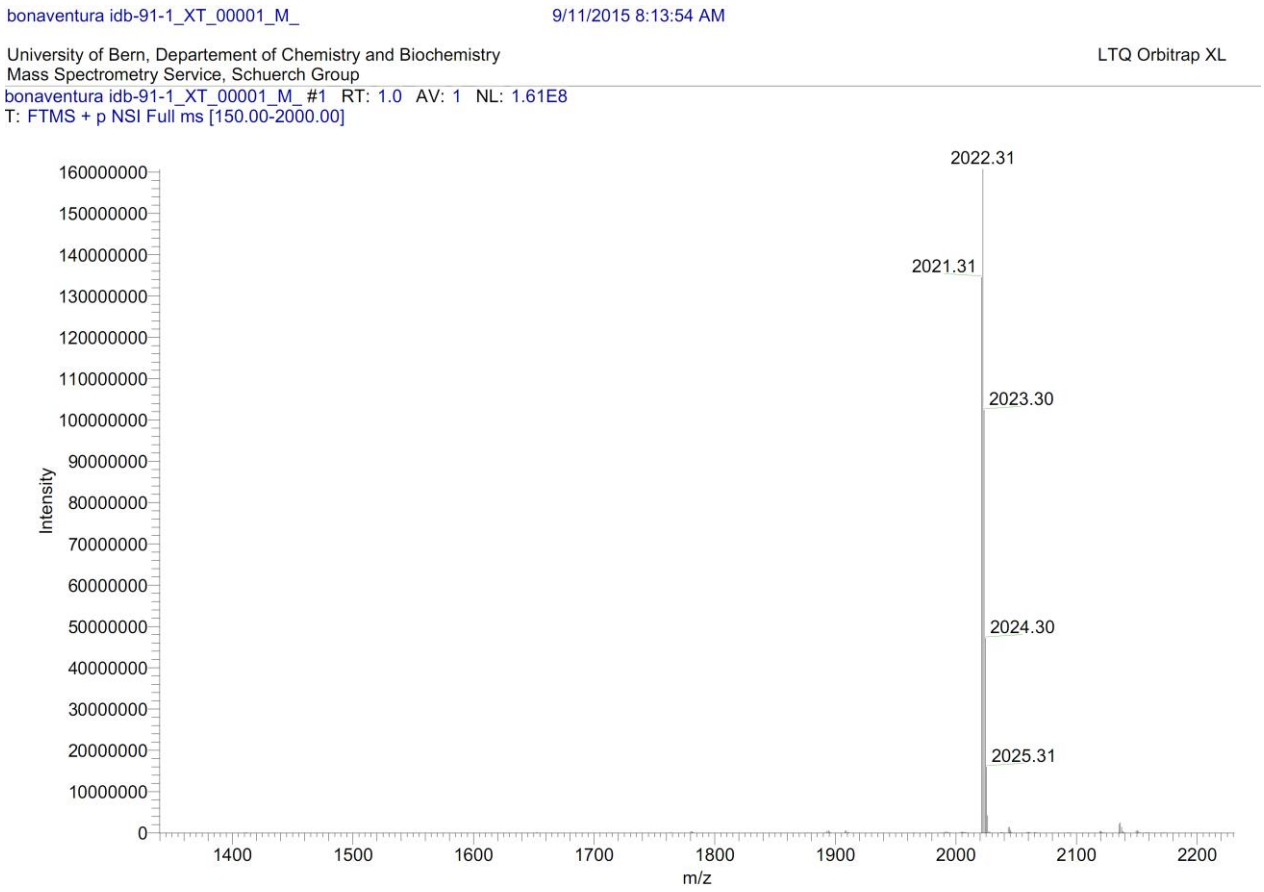




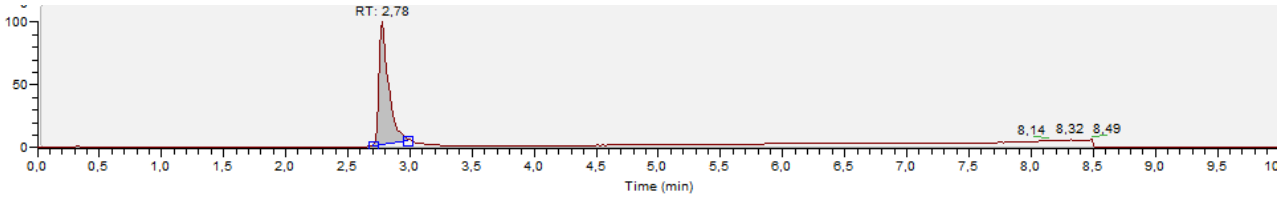


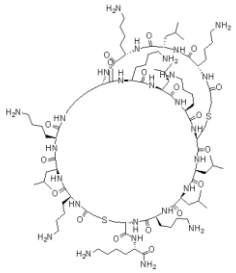
^{1}KLK*K*(K^{2}LK)KLK*Z*^{2}LLK*Z*^{1}K (49a) was obtained as foamy white solid after preparative RP-HPLC (7.1 mg, 2.8 %). Analytical RP-HPLC: t_R = 2.630 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2021.31 Da [M].

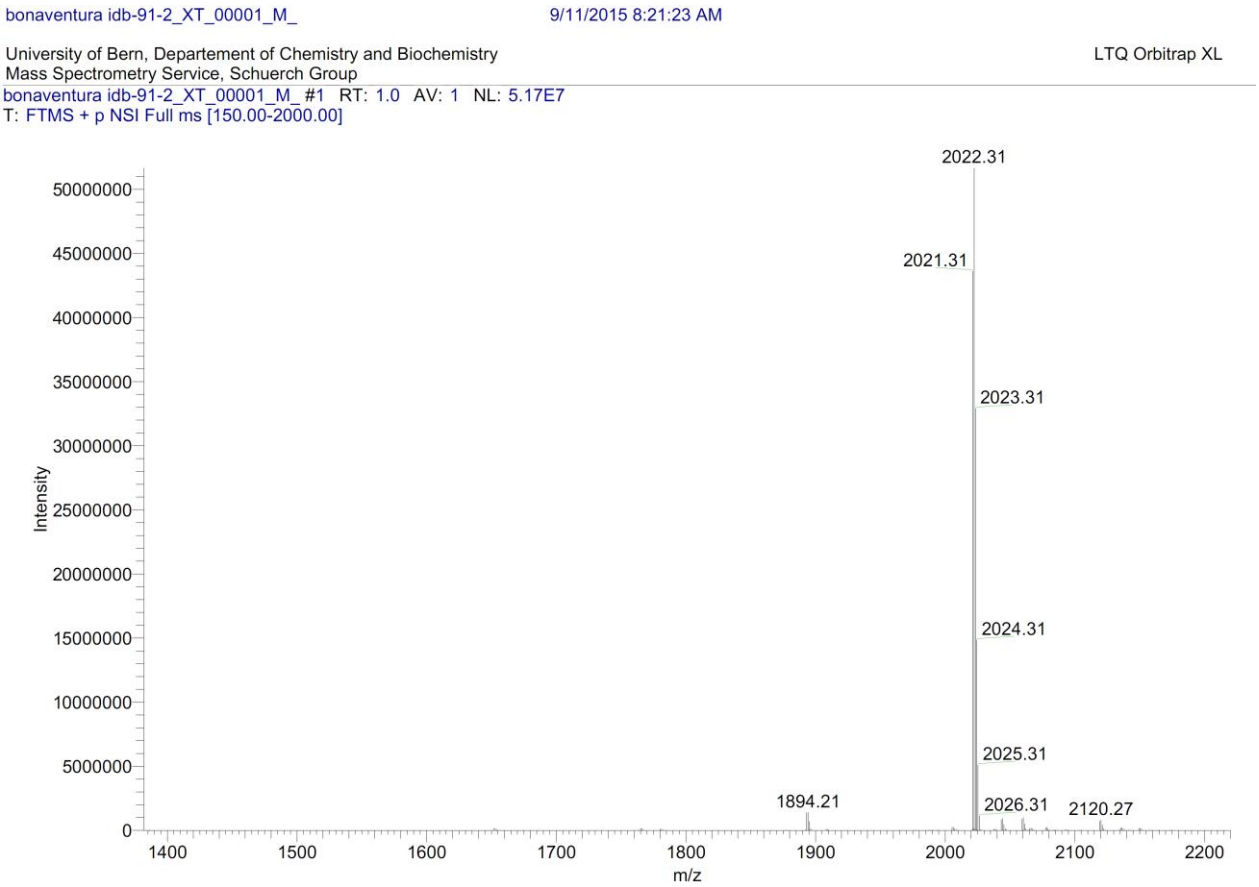




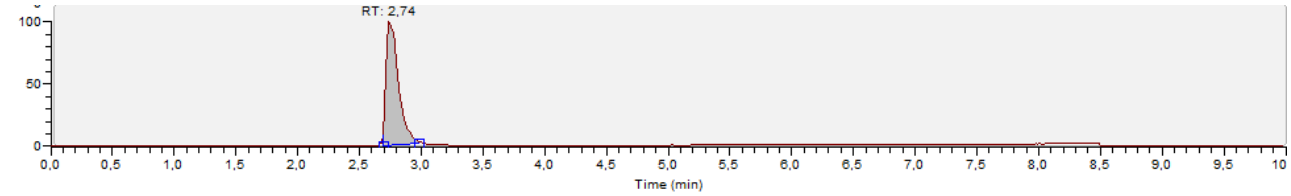
^{2}KLK*K*(K^{1}LK)KLK*Z*^{2}LLK*Z*^{1}K (49b) was obtained as foamy white solid after preparative RP-HPLC (5.4 mg, 2.2 %). Analytical RP-HPLC: t_R = 2.780 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2021.31 Da [M].

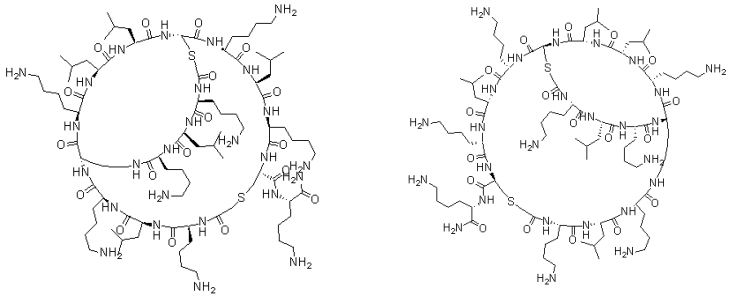


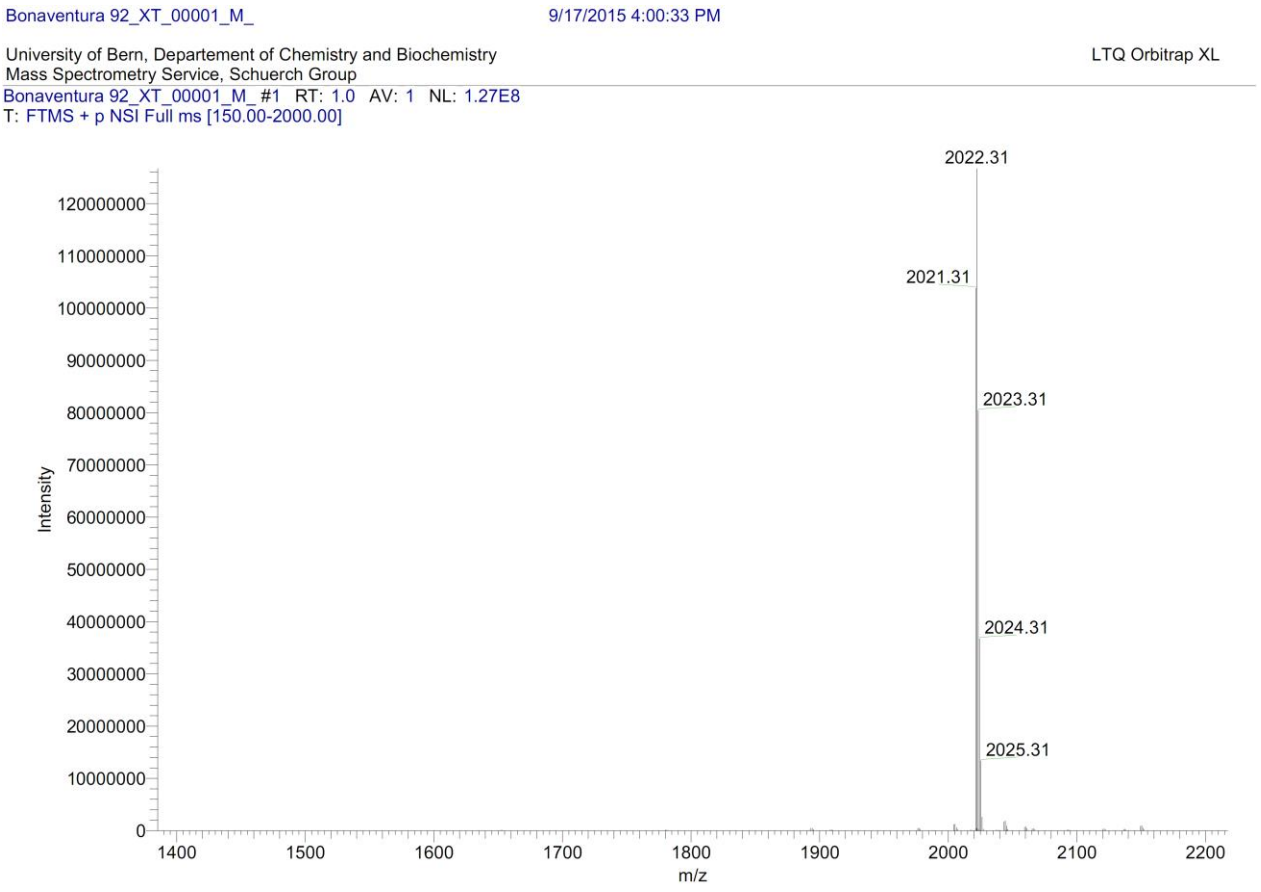




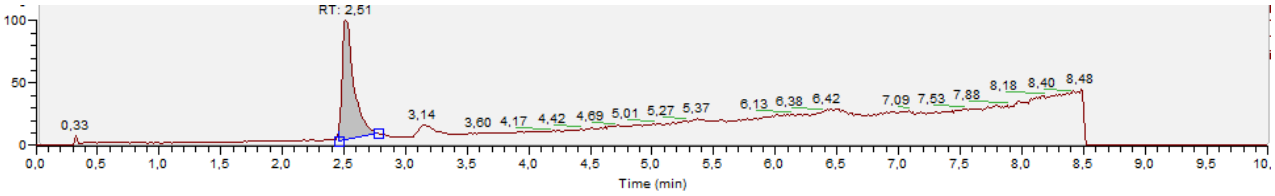
^{21}KLK*K*(K^{12}LK)KLL*Z*^{21}KLK*Z*^{12}K (50) was obtained, like one isomer, as foamy white solid after preparative RP-HPLC (17.4 mg, 6.2 %). Analytical RP-HPLC: t_R = 2.740 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2021.31 Da [M].

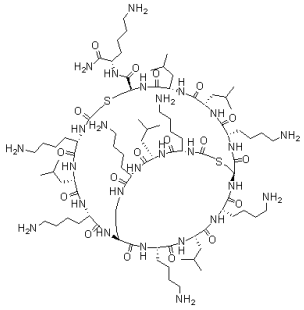


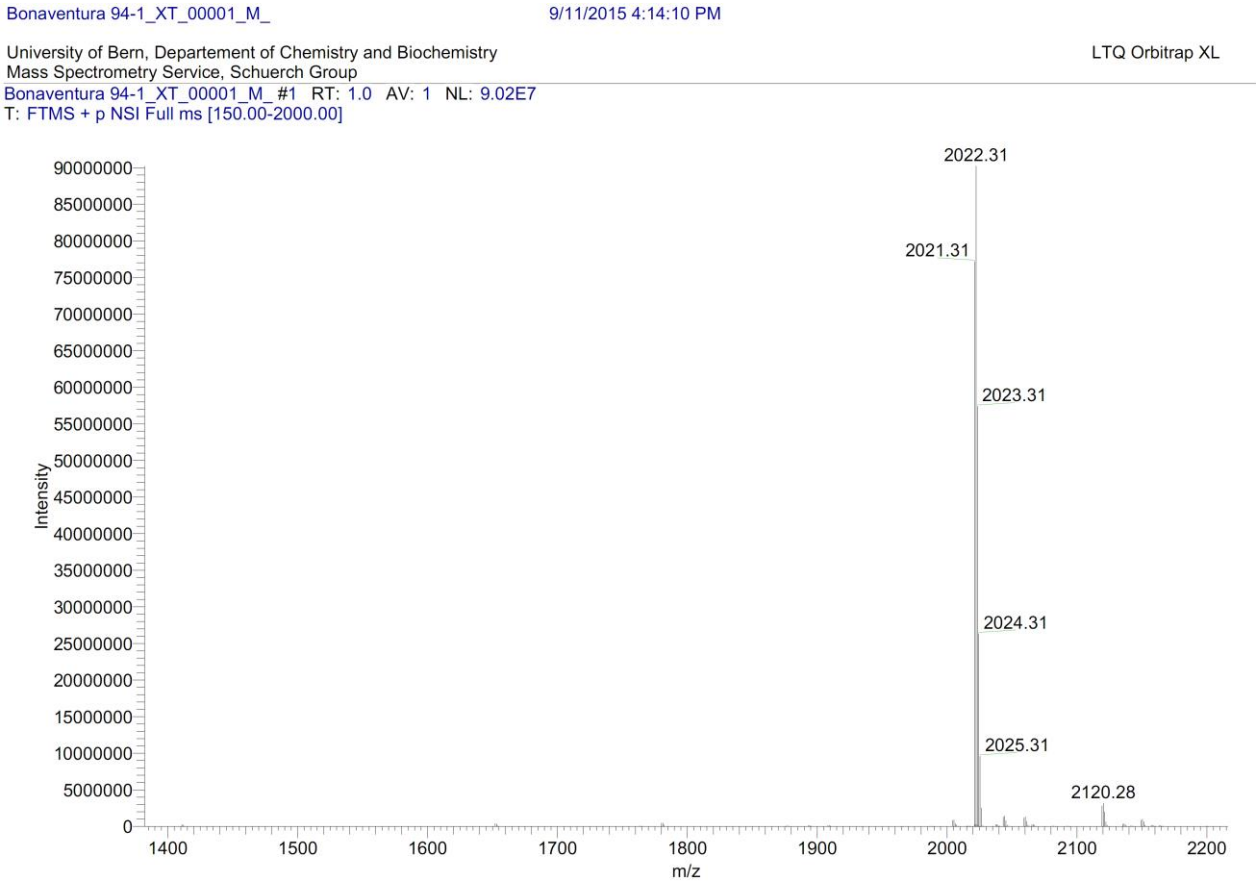




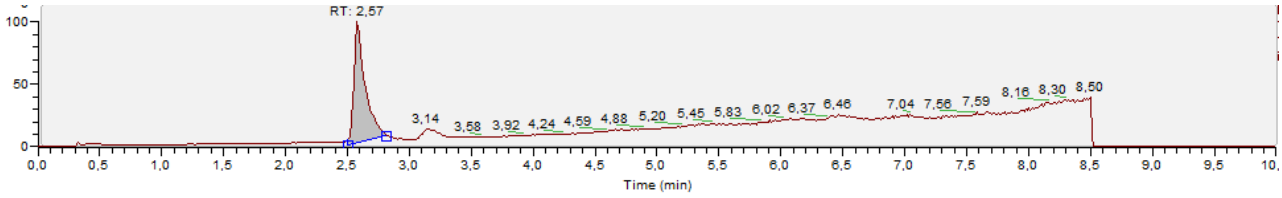
^{2}KLK*K*(K^{1}LK)KLK*Z*^{1}KLL*Z*^{2}K (51a) was obtained as foamy white solid after preparative RP-HPLC (12.2 mg, 6.3 %). Analytical RP-HPLC: t_R = 2.510 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2021.31 Da [M].

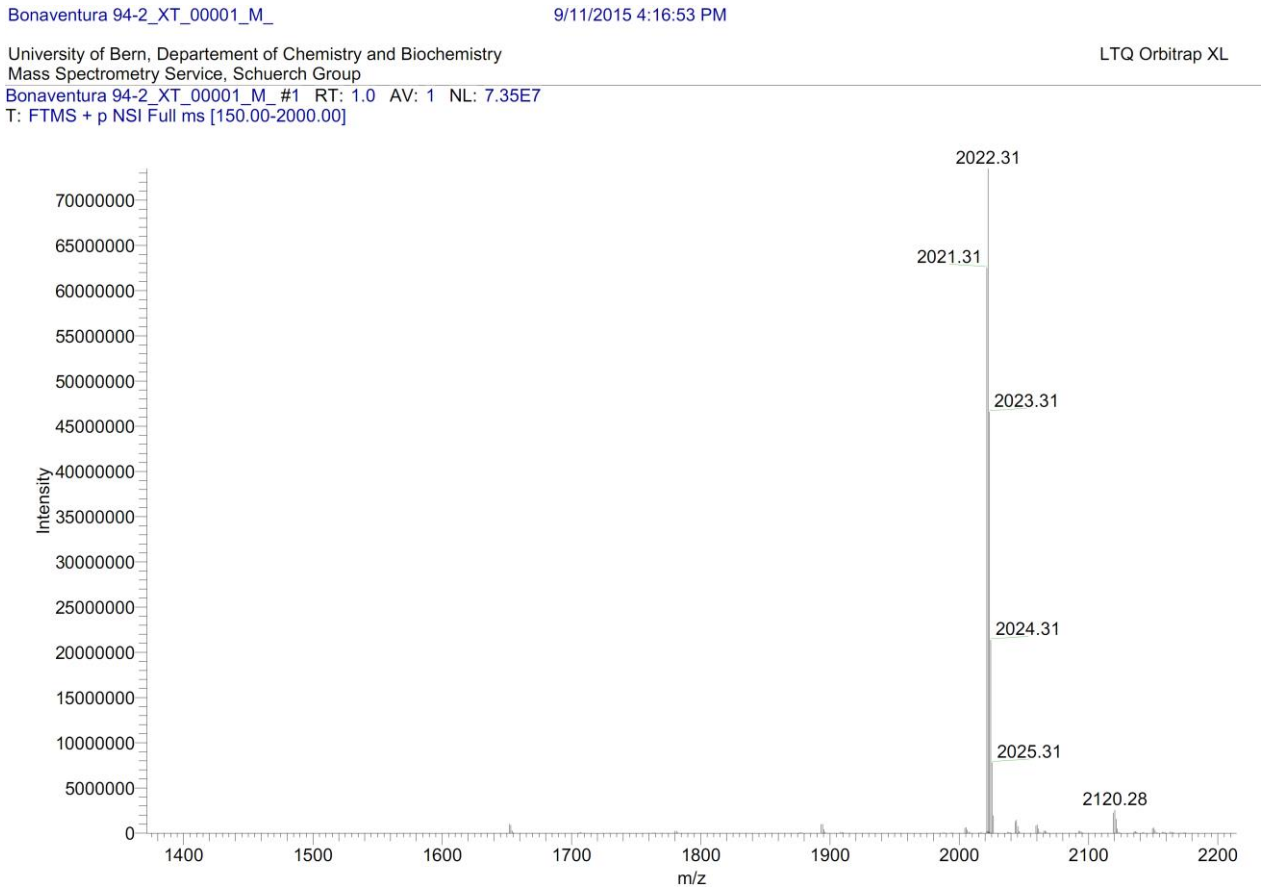




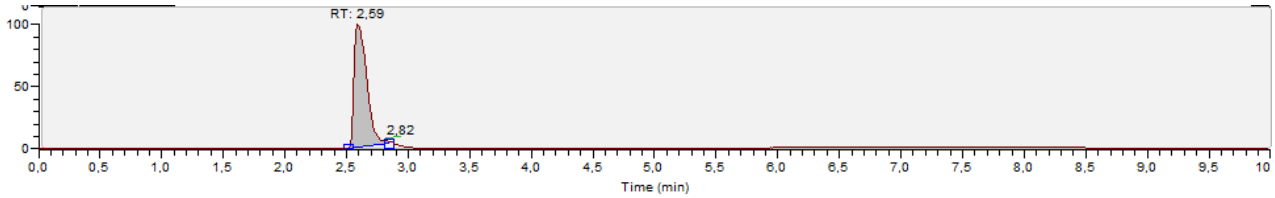


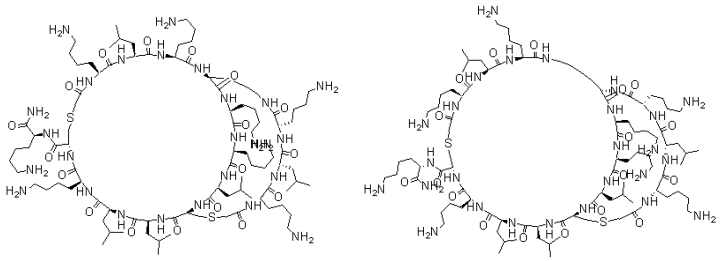
^{1}KLK*K*(K^{2}LK)KLK*Z*^{1}KLL*Z*^{2}K (51b) was obtained as foamy white solid after preparative RP-HPLC (6.9 mg, 3.5 %). Analytical RP-HPLC: t_R = 2.570 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2021.31 Da [M].

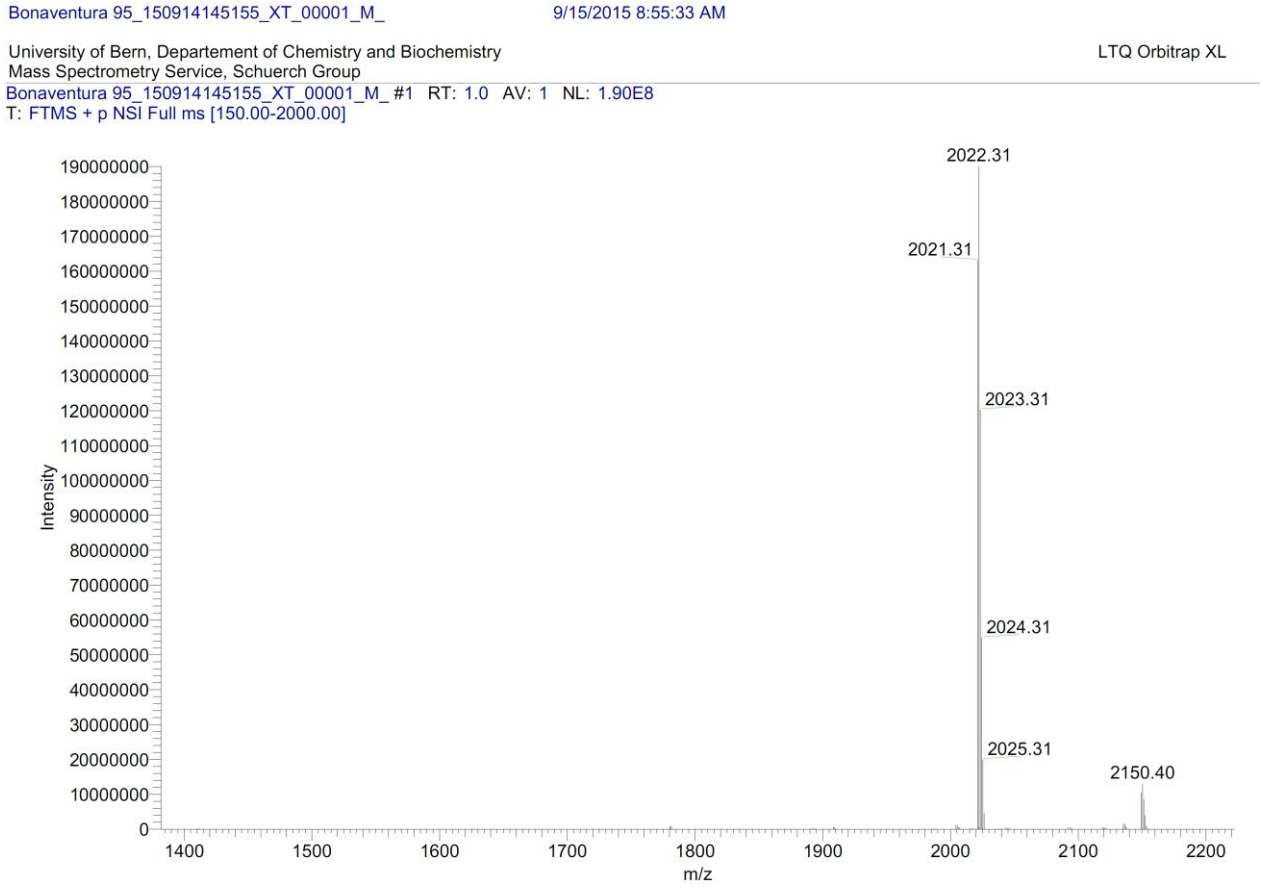




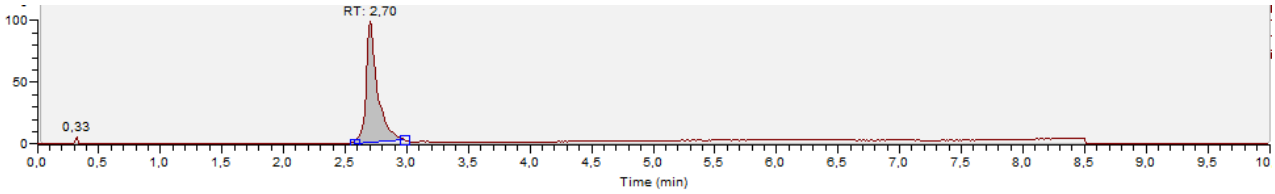
^{12}KLK*K*(K^{21}LK)KKL*Z*^{12}LLK*Z*^{21}K (52) was obtained as foamy white solid after preparative RP-HPLC (25.0 mg, 13.0 %). Analytical RP-HPLC: t_R = 2.590 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2021.31 Da [M].

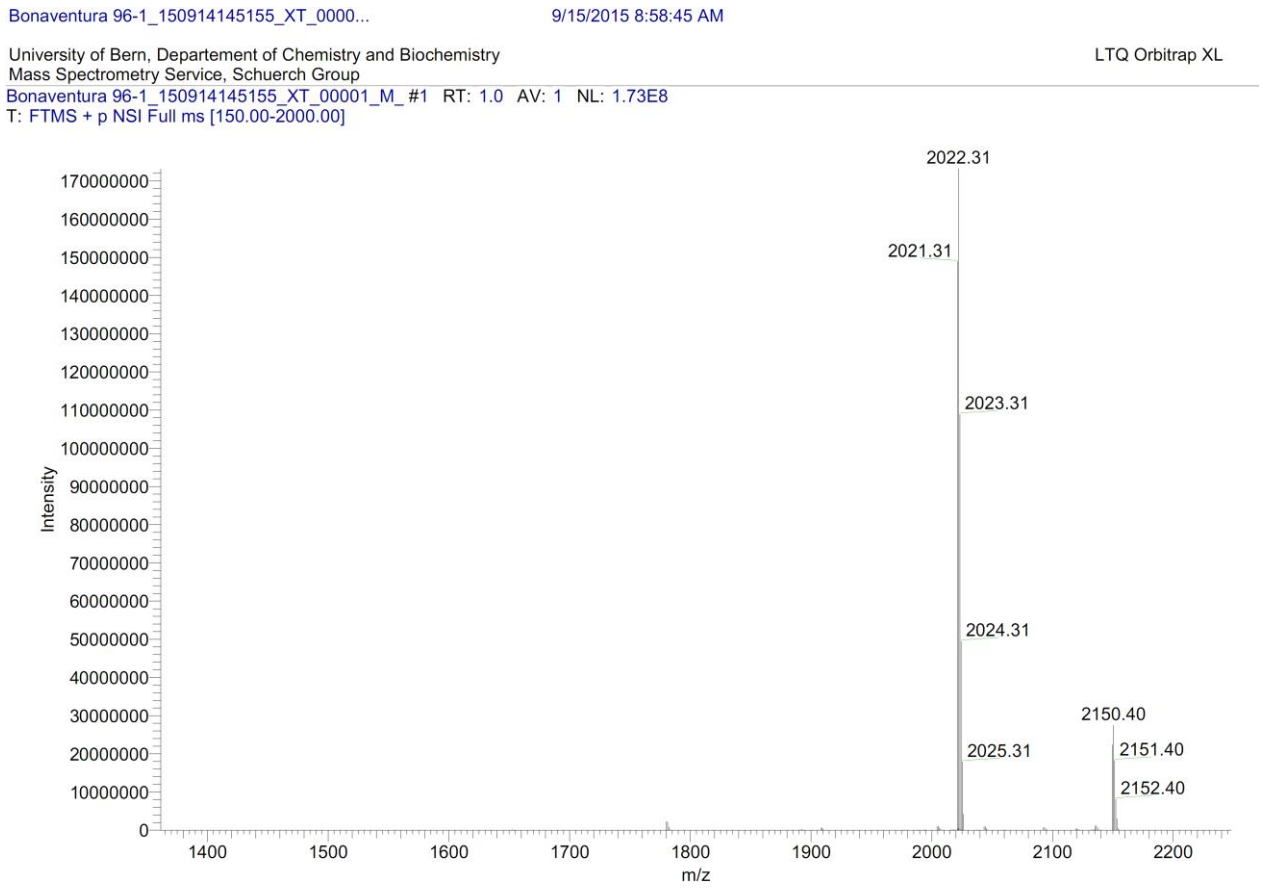




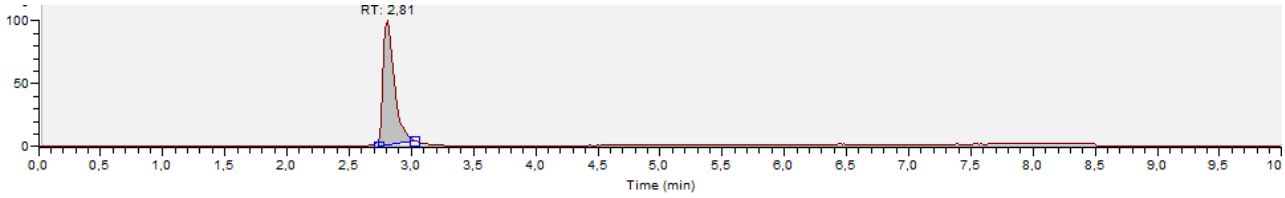


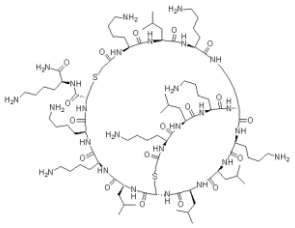
^{2}KLK*K*(K^{1}LK)KLL*Z*^{1}LKK*Z*^{2}K (53a) was obtained as foamy white solid after preparative RP-HPLC (8.8 mg, 4.5 %). Analytical RP-HPLC: t_R = 2.700 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2021.31 Da [M], 2150.31/2150.31 Da [M+6Na].

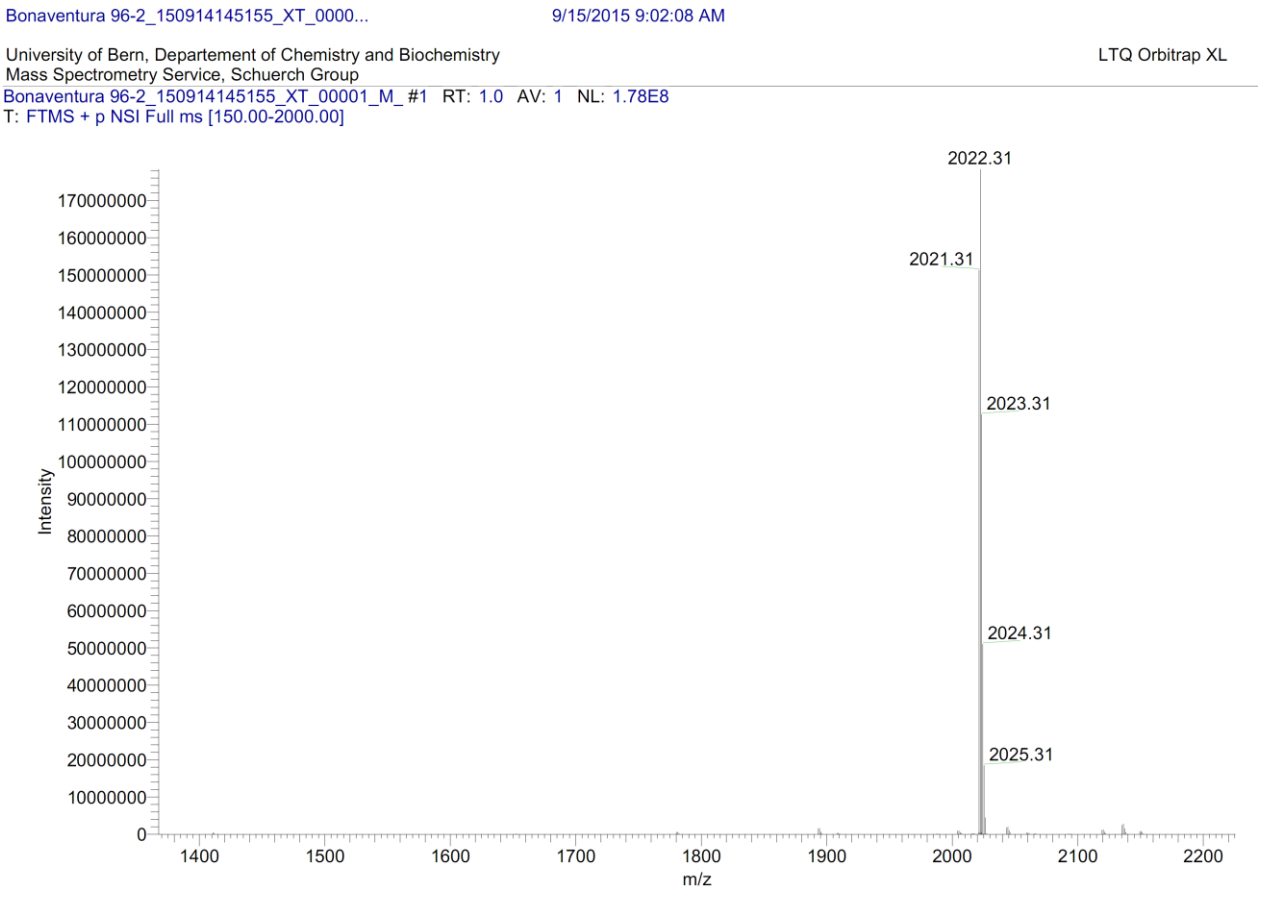




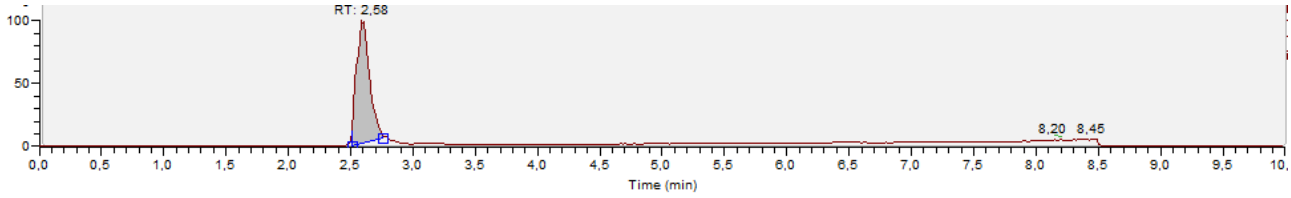
^{1}KLK*K*(K^{2}LK)KLL*Z*^{1}LKK*Z*^{2}K (53b) was obtained as foamy white solid after preparative RP-HPLC (13.3 mg, 6.9 %). Analytical RP-HPLC: t_R = 2.810 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2021.31 Da [M].

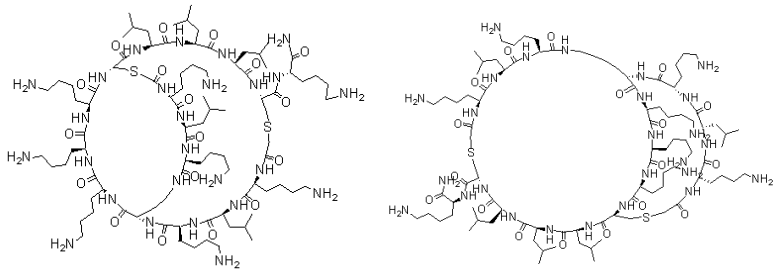


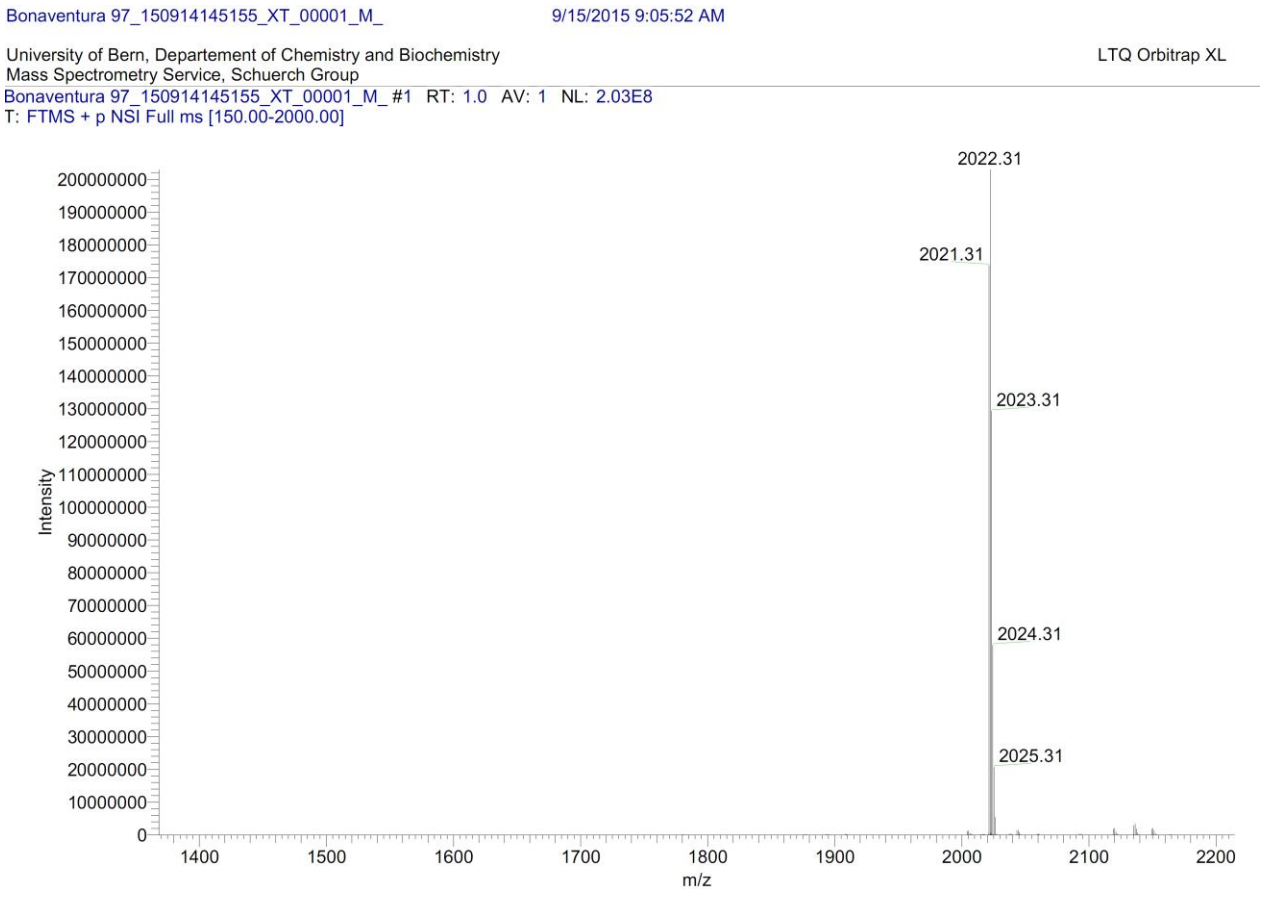




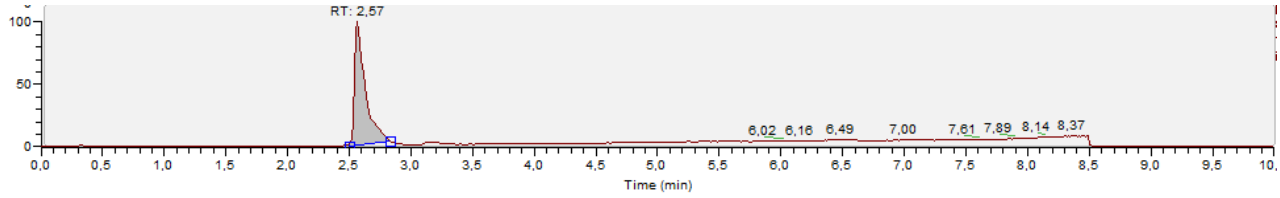
^{12}KLK*K*(K^{21}LK)KKKZ^{12}LLLZ^{21}K (54) was obtained as foamy white solid after preparative RP-HPLC (35.0 mg, 18.0 %). Analytical RP-HPLC: t_R = 2.580 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2021.31 Da [M].

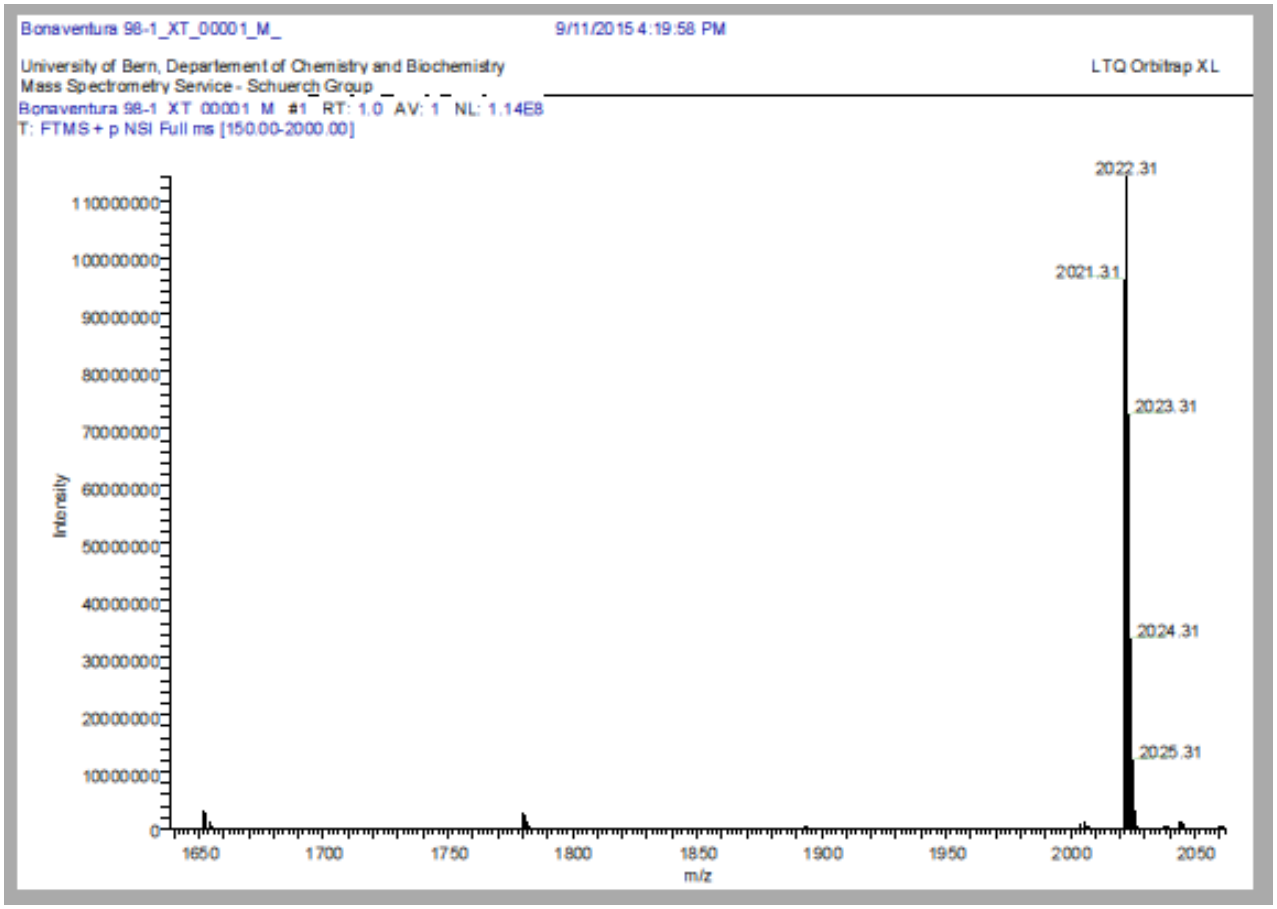




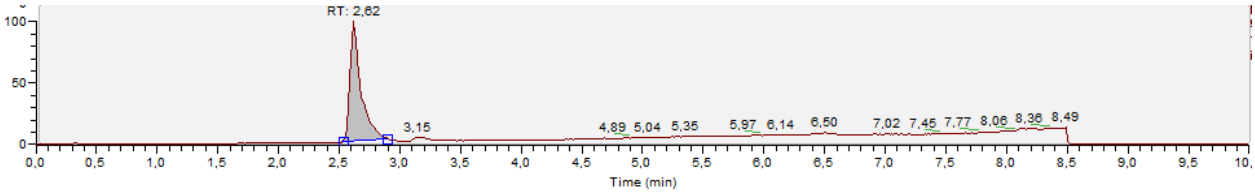


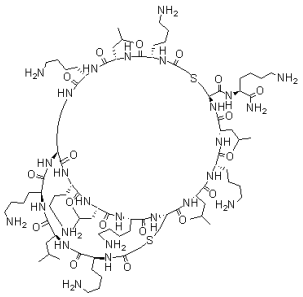
^{1}KLK*K*(K^{2}LK)KLK*Z*^{2}LKL*Z*^{1}K (55a) was obtained as foamy white solid after preparative RP-HPLC (12.4 mg, 10.0 %). Analytical RP-HPLC: t_R = 2.570 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2021.31 Da [M].

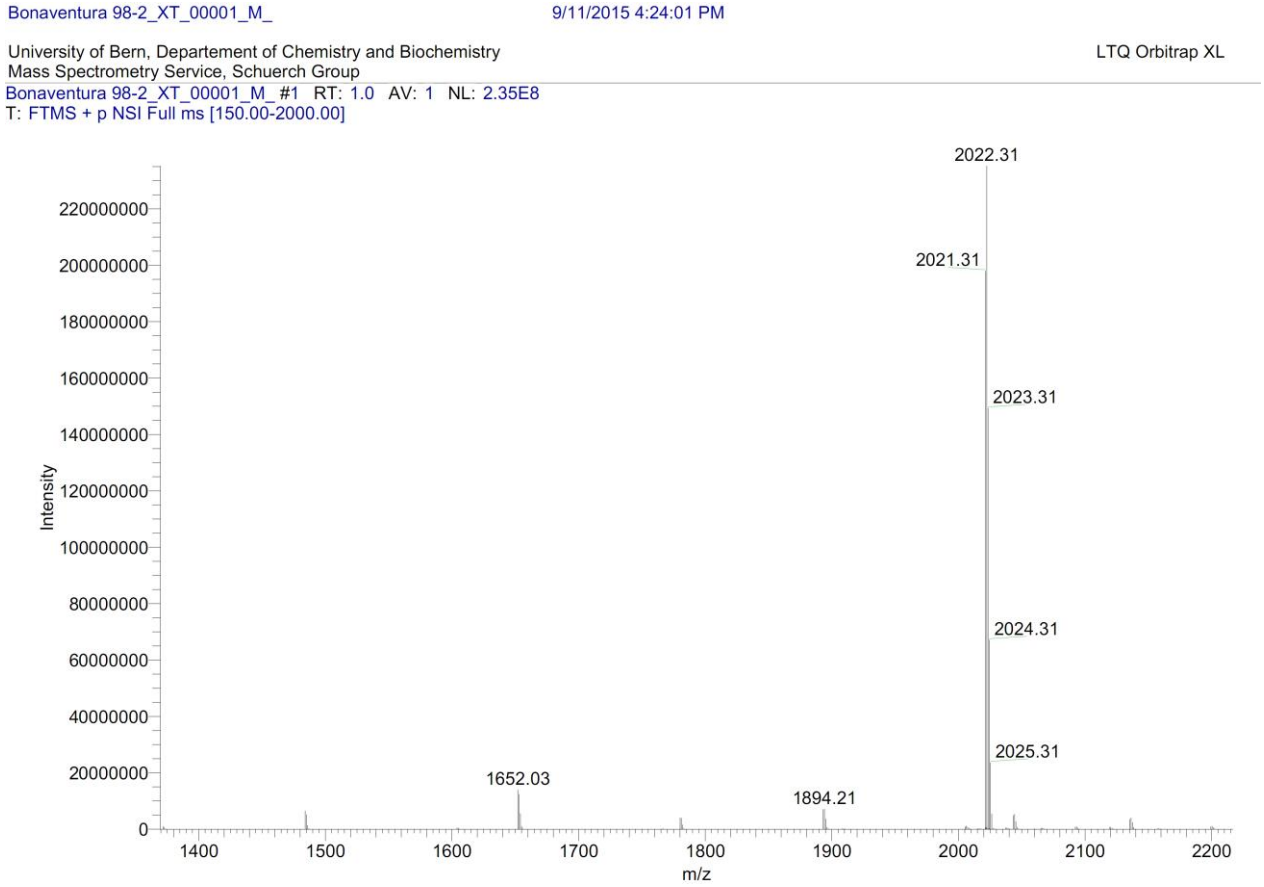




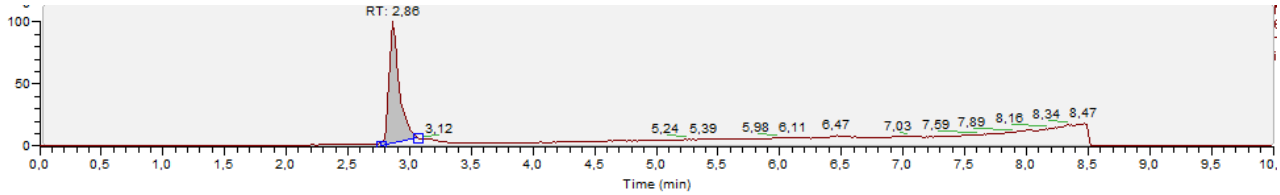
^{2}KLK*K*(K^{1}LK)KLK*Z*^{2}LKL*Z*^{1}K (55b) was obtained as foamy white solid after preparative RP-HPLC (7.8 mg, 4.0 %). Analytical RP-HPLC: t_R = 2.620 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2021.31 Da [M].

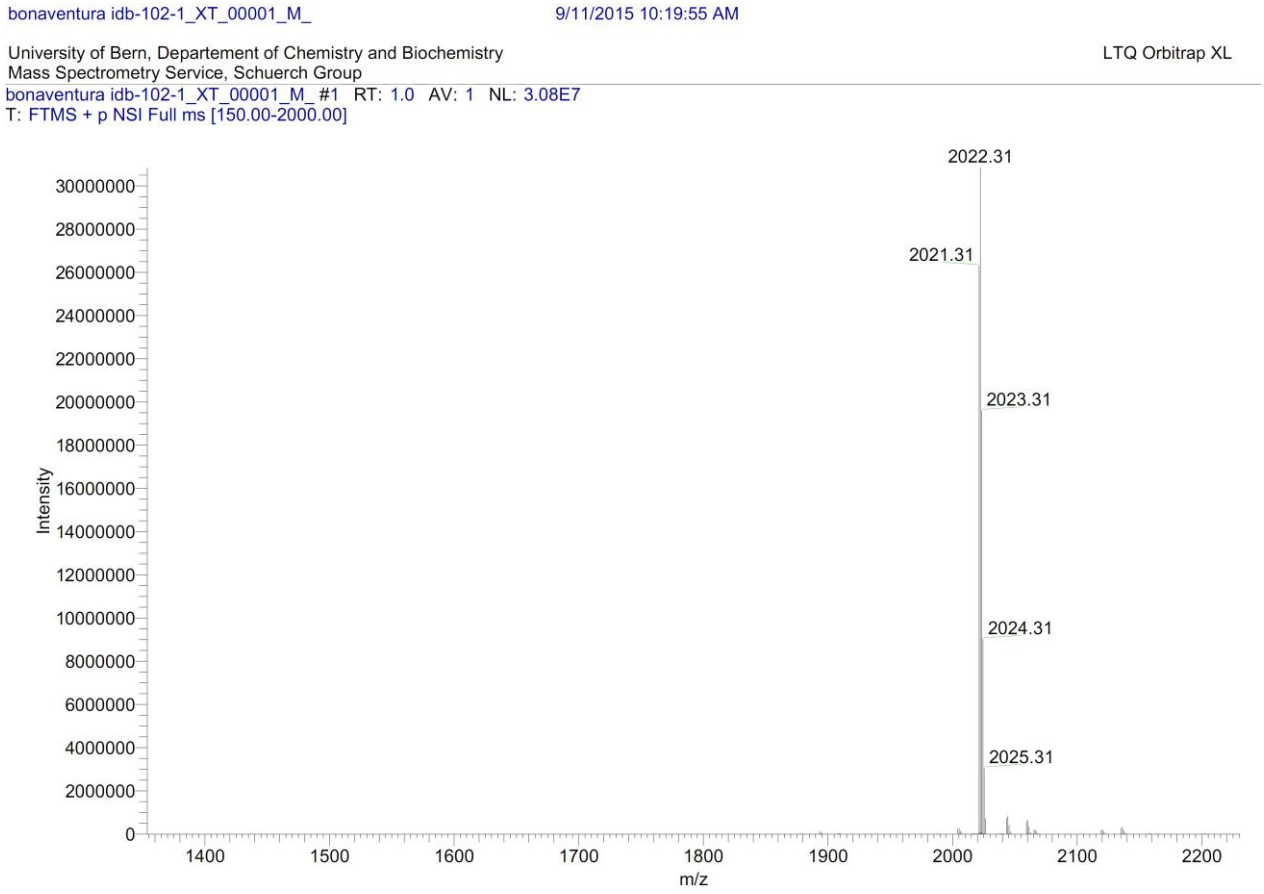




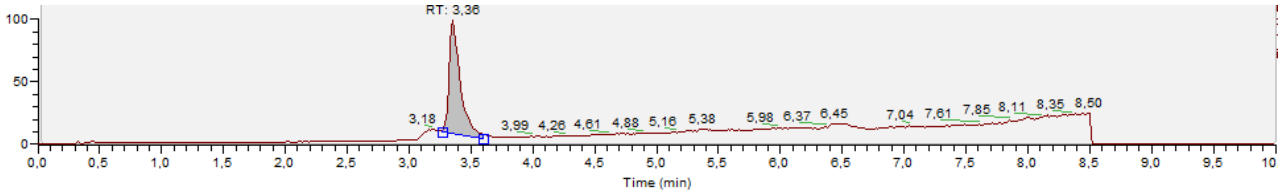


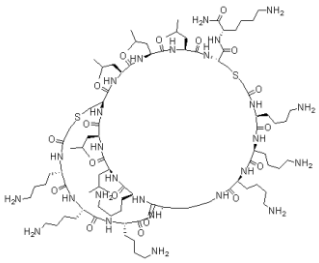
^{1}KKK*(K*^{2}KK)KLLZ*^{1}LLLZ*^{2}K (56a) was obtained as foamy white solid after preparative RP-HPLC (10.8 mg, 4.3 %). Analytical RP-HPLC: t_R = 2.860 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2021.31 Da [M].

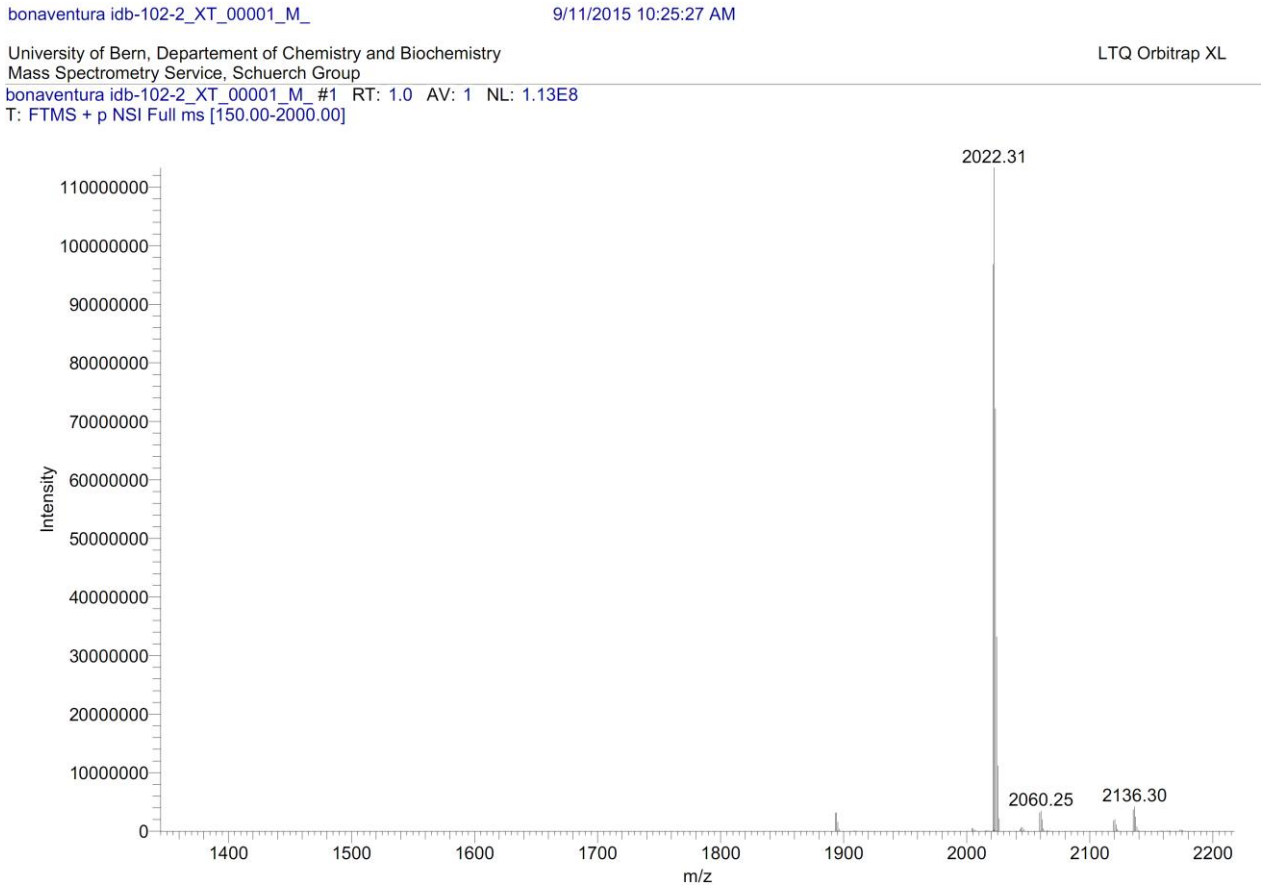




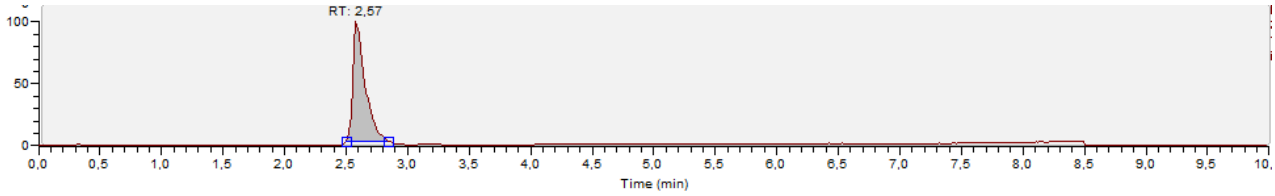
^{2}KKK*(K*^{1}KK)KLL*Z*^{2}LLL*Z*^{1}K (56b) was obtained as foamy white solid after preparative RP-HPLC (7.4 mg, 2.9 %). Analytical RP-HPLC: t_R = 3.360 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2022.31 Da [M].

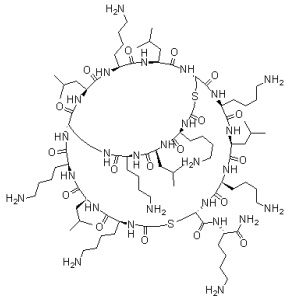


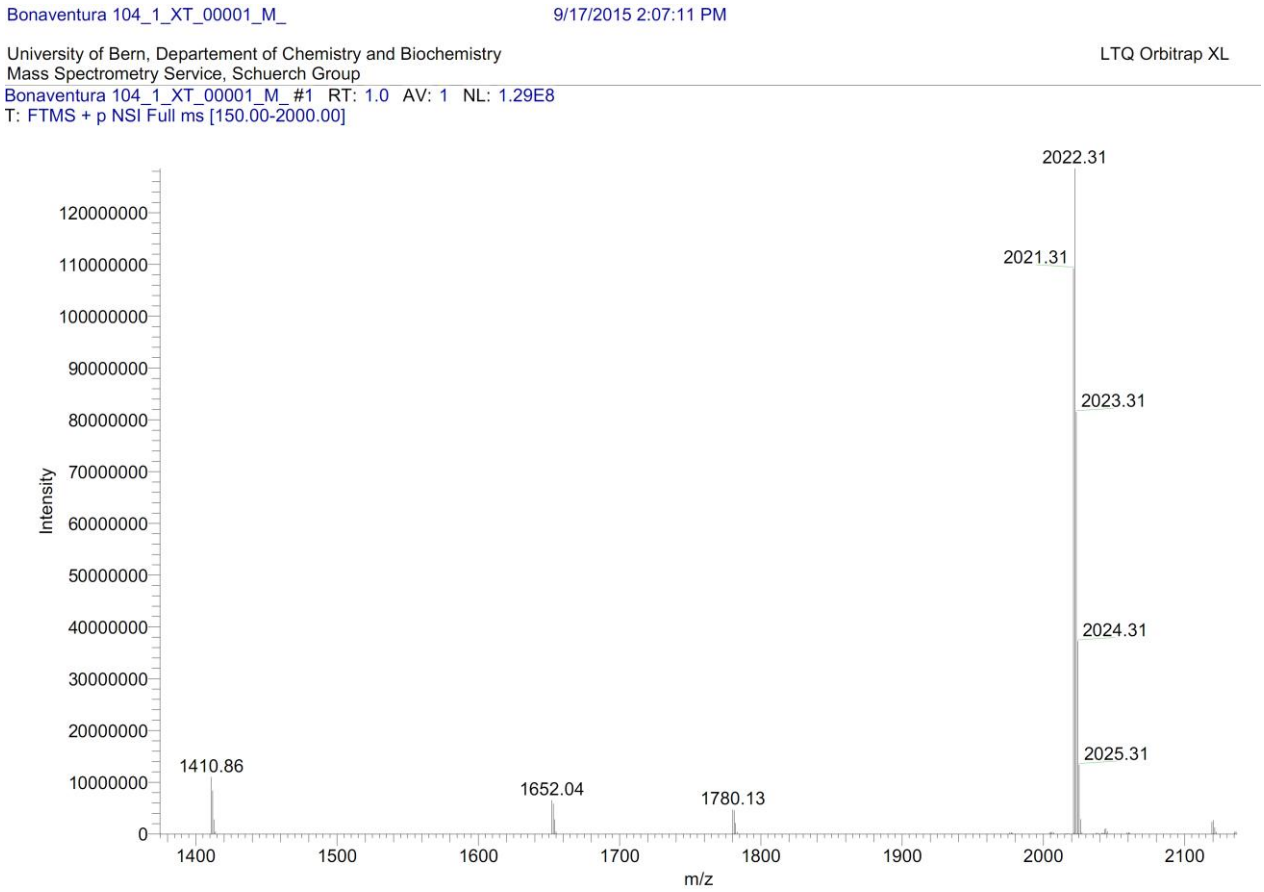




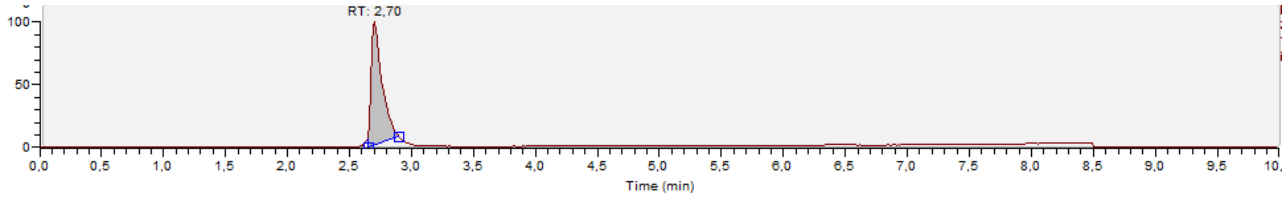
^{1}KLK*K*(K^{2}LK)LKL*Z*^{2}KLK*Z*^{1}K (57a) was obtained as foamy white solid after preparative RP-HPLC (10.4 mg, 5.4 %). Analytical RP-HPLC: t_R = 2.570 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2021.31 Da [M].

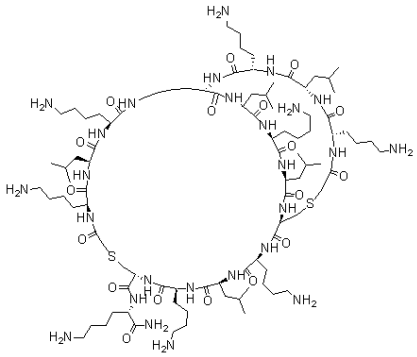


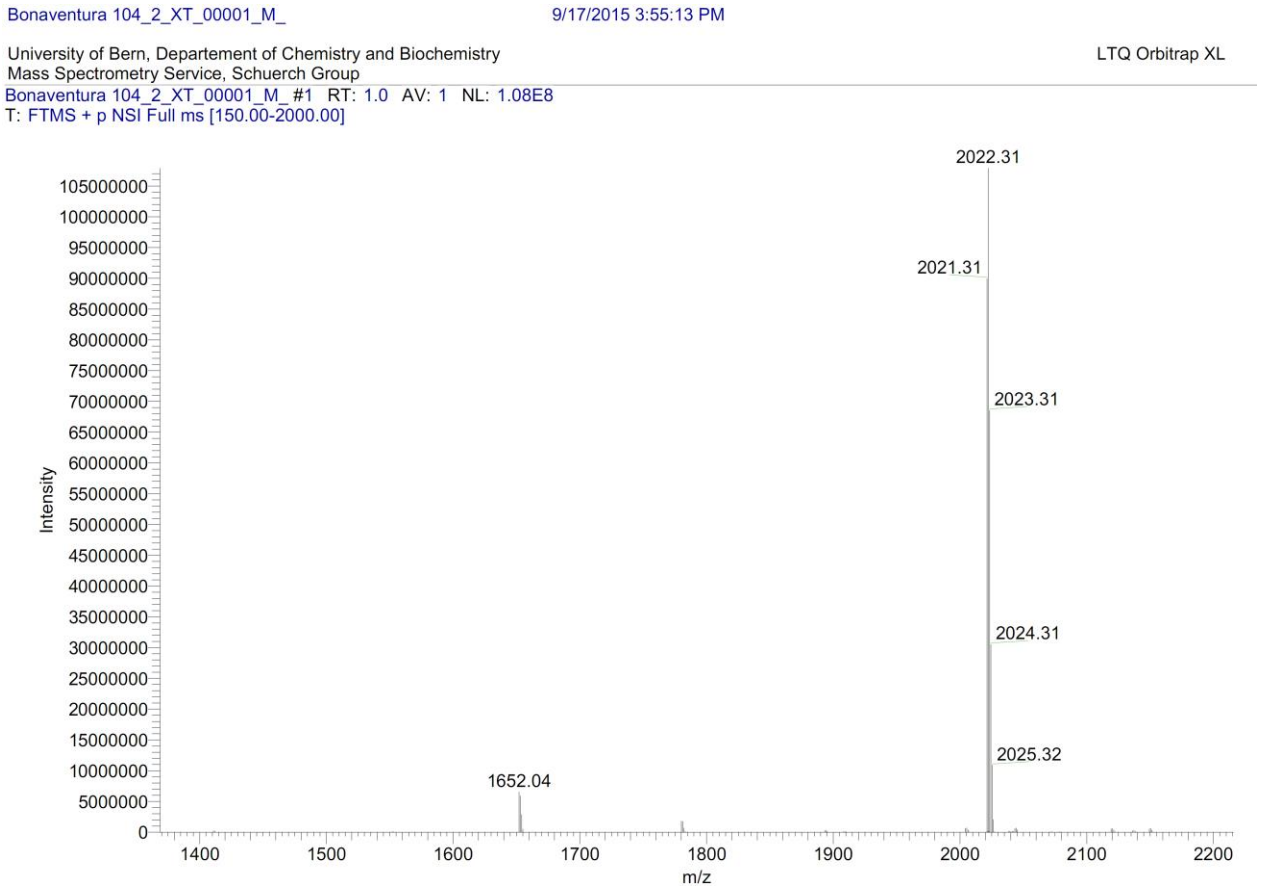




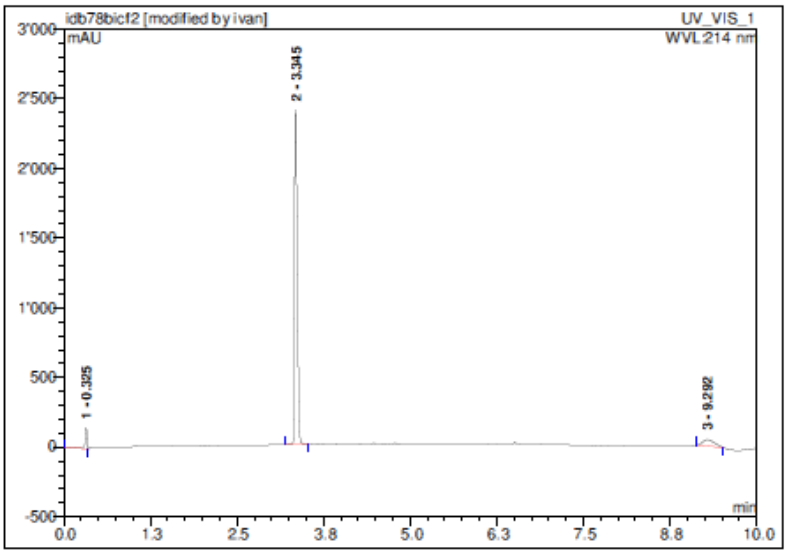
^{2}KLK*K*(K^{1}LK)LKL*Z*^{2}KLK*Z*^{1}K (57b) was obtained as foamy white solid after preparative RP-HPLC (5.6 mg, 2.9 %). Analytical RP-HPLC: t_R = 2.700 min (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS (ESI+): $C_{94}H_{176}N_{26}O_{18}S_2$ calc./obs. 2021.31/2021.31 Da [M].

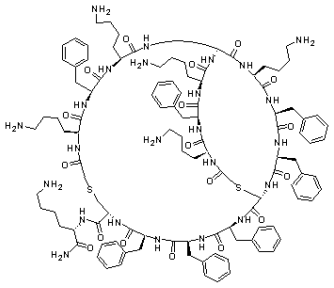


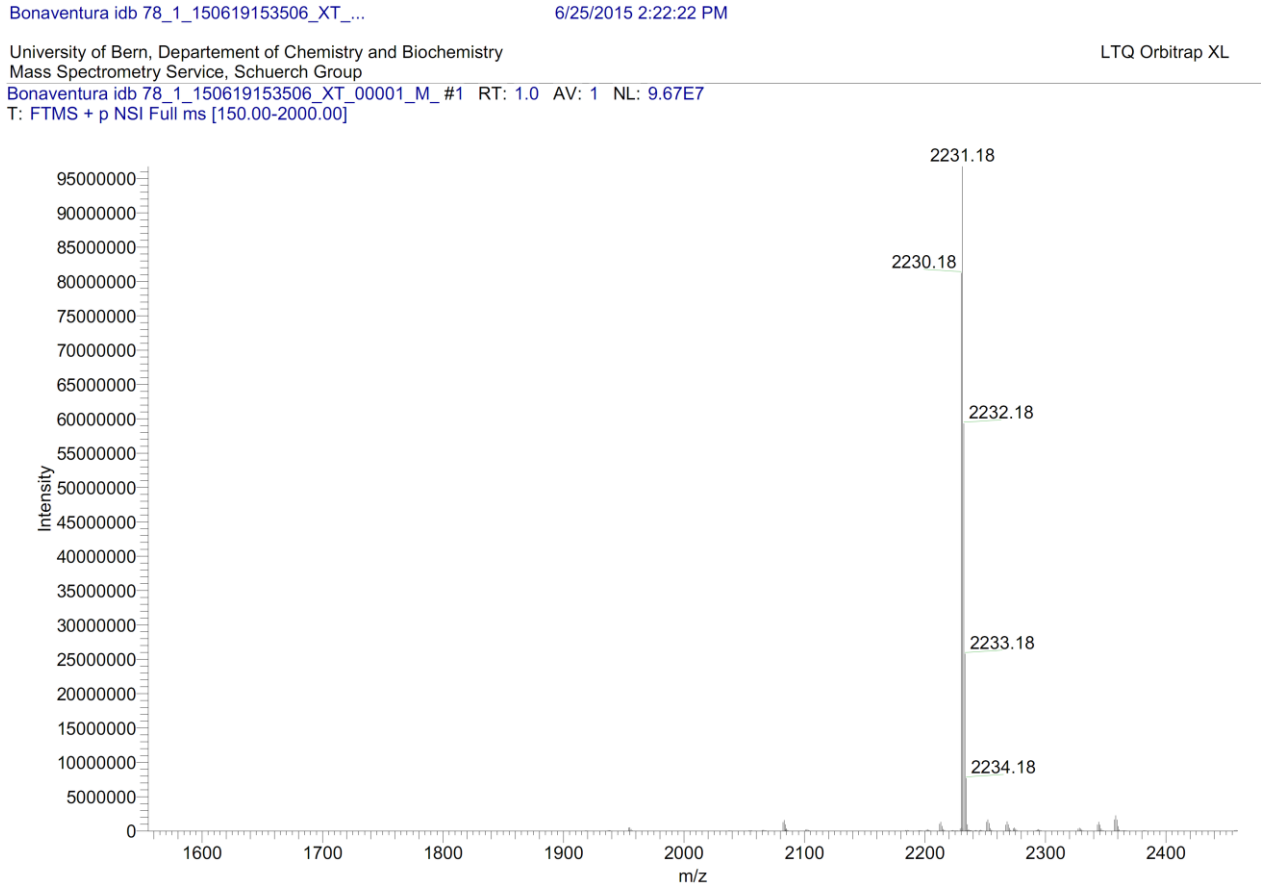




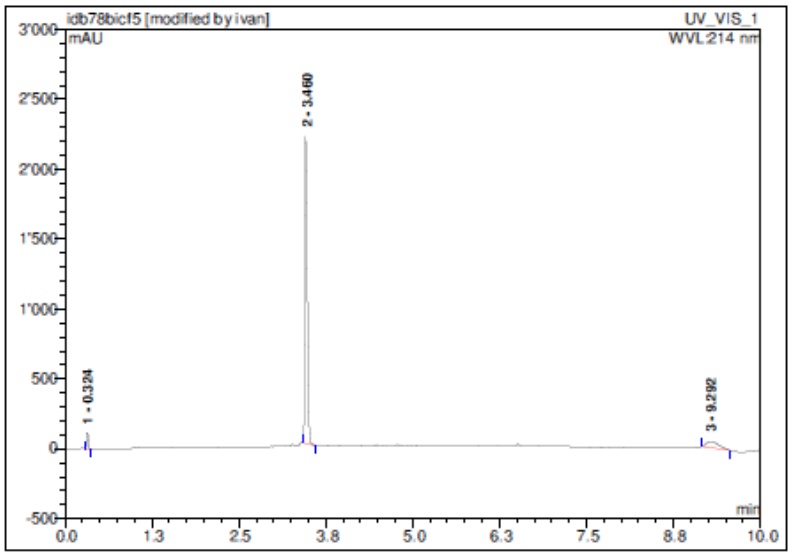
^{2}KFKK(K^{1}FK)KFFZ^{1}FFFZ^{2}K (58a) was obtained as foamy white solid after preparative RP-HPLC (30.4 mg, 13.62 %). Analytical RP-HPLC: t_R = 3.350 min. (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{115}H_{160}N_{24}O_{18}S_2$ calc./obs. 2229.18/2230.18 Da [M].

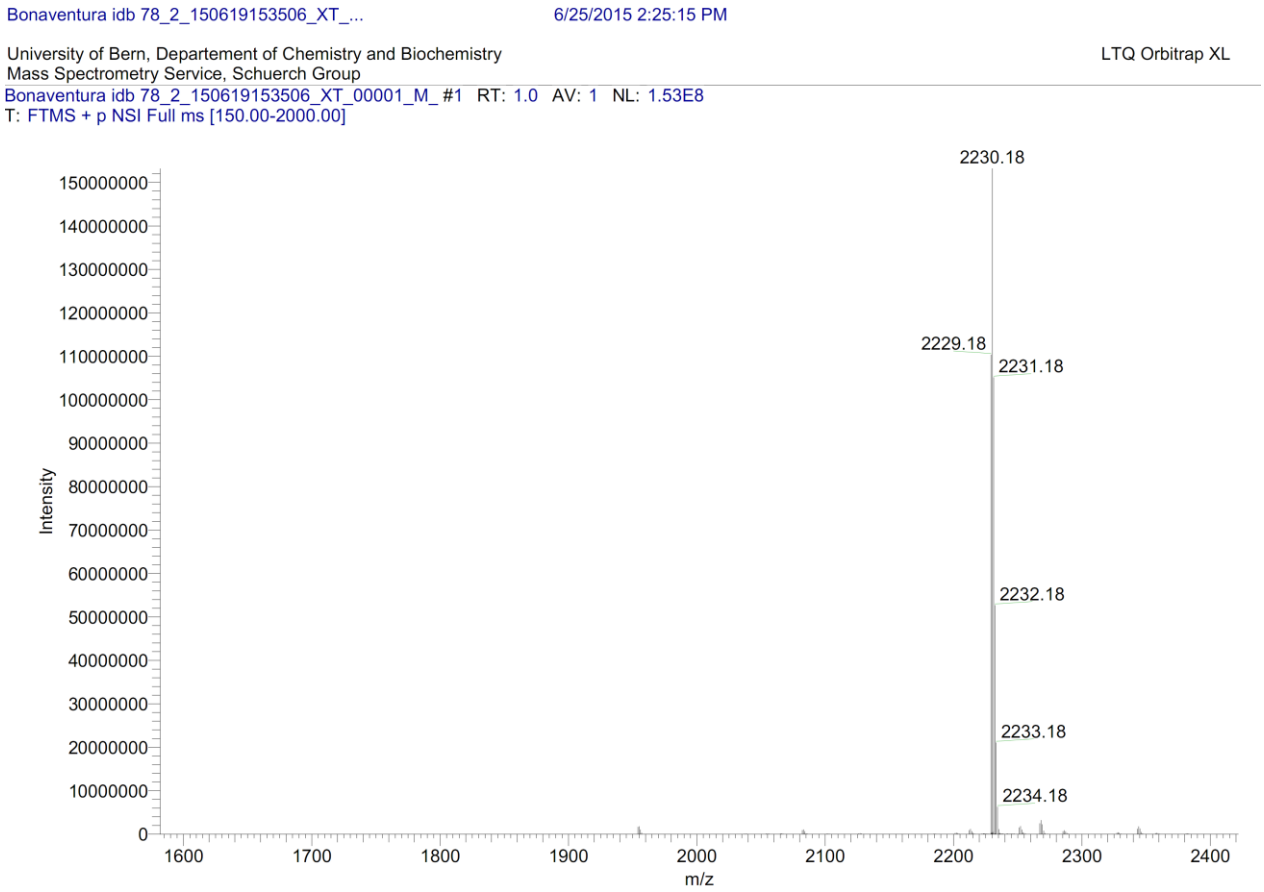




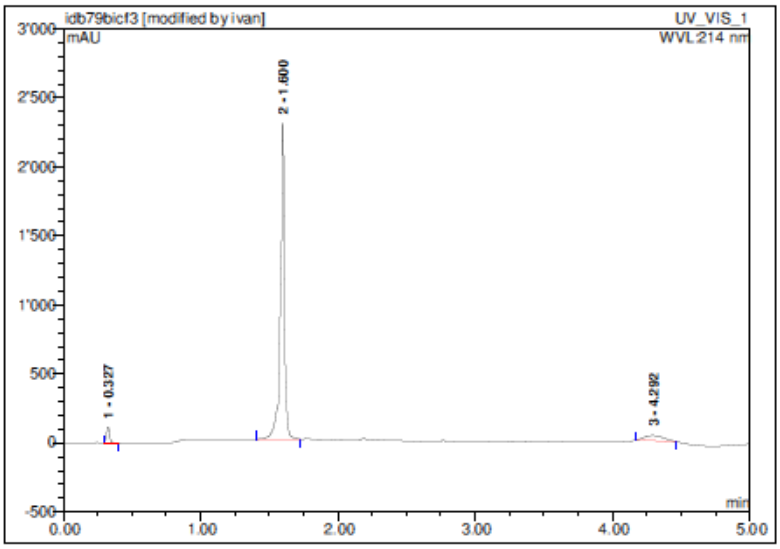


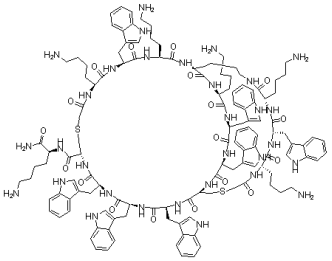
^{1}KFK*K*(K^{2}FK)KFFZ^{1}FFFZ^{2}K (58b) was obtained as foamy white solid after preparative RP-HPLC (20.2 mg, 9.1 %). Analytical RP-HPLC: t_R = 3.460 min. (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{115}H_{160}N_{24}O_{18}S_2$ calc./obs. 2229.18/2229.18 Da [M].





^{12}KWK*K*(K^{12}WK)KWWZ^{21}WWWZ^{12}K (59) was obtained, like one isomer, as foamy white solid after preparative RP-HPLC (11.0 mg, 4.4 %). Analytical RP-HPLC: t_R = 1.600 min. (A/D 100:0 to 0:100 in 5.00 min, λ = 214nm). MS(ESI+): $C_{129}H_{167}N_{31}O_{18}S_2$ calc./obs. 2502.25/2502.26 Da [M].





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University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group

LTQ Orbitrap XL

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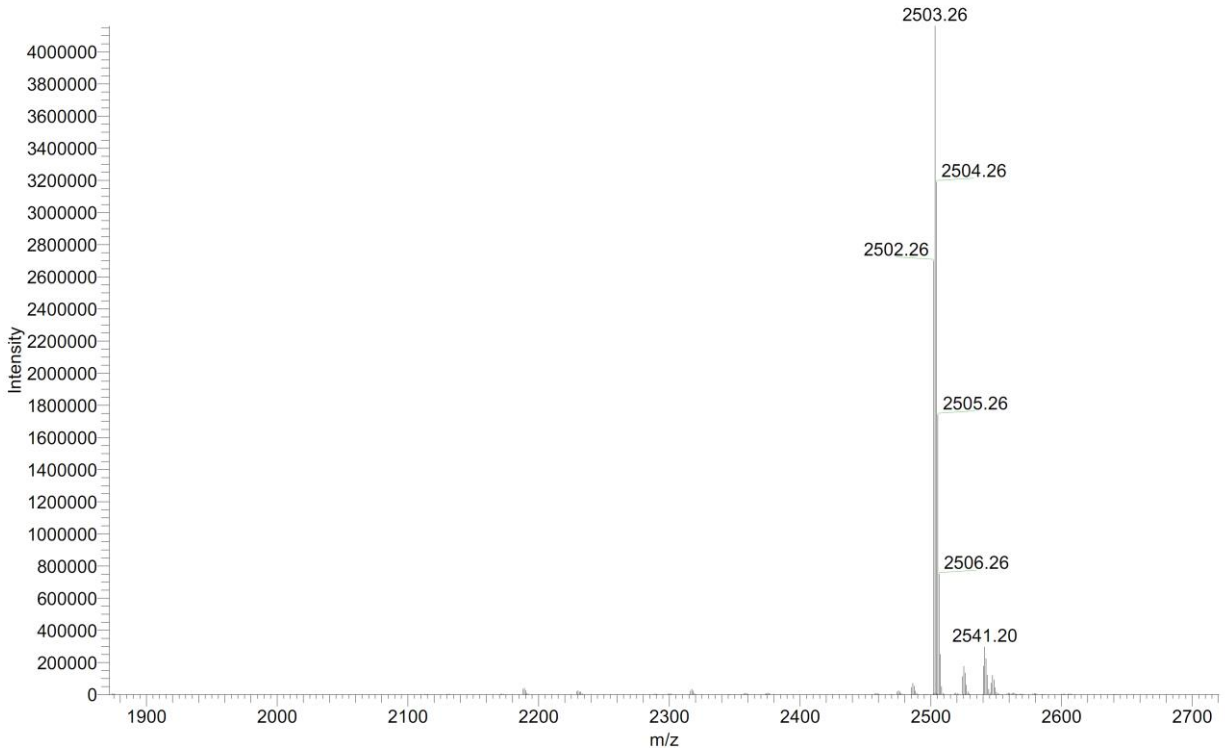
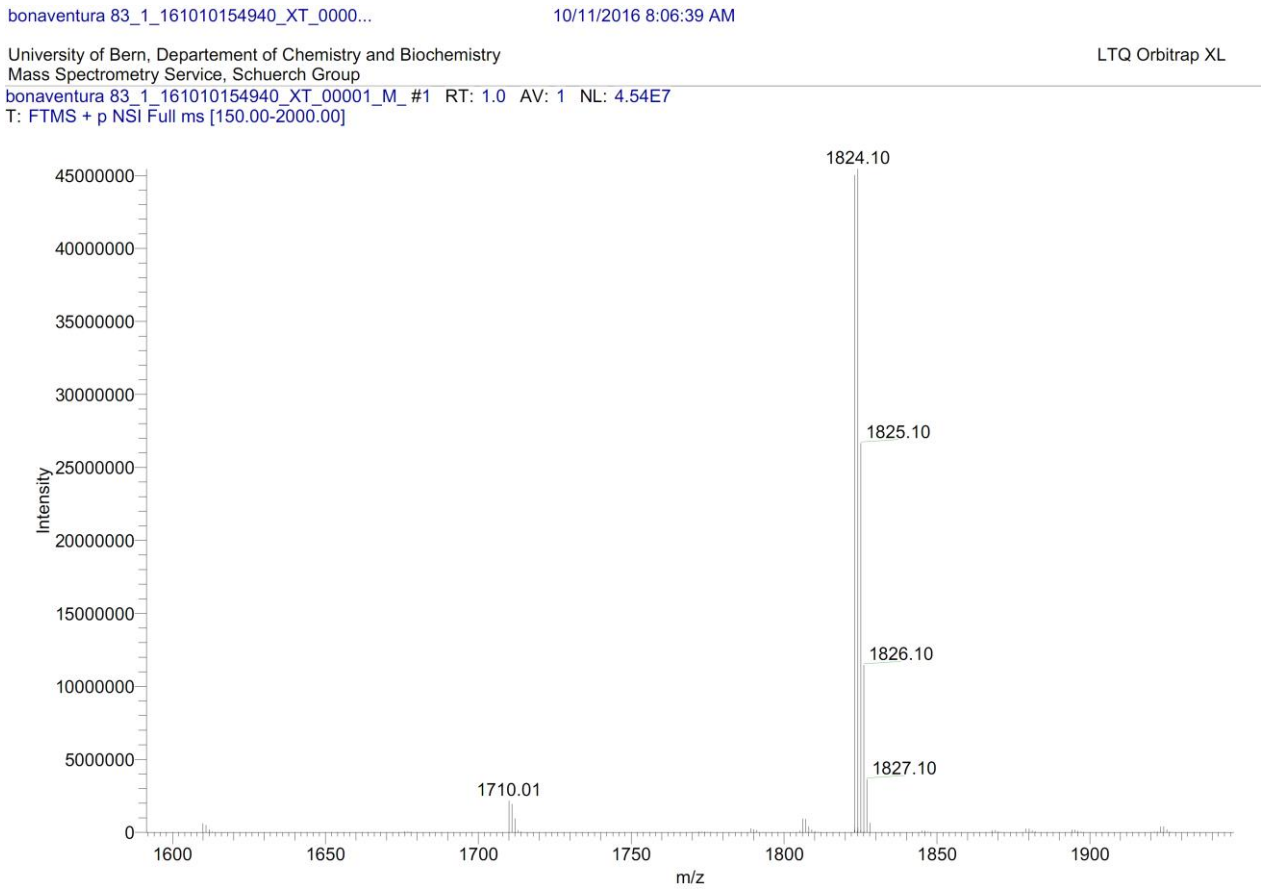
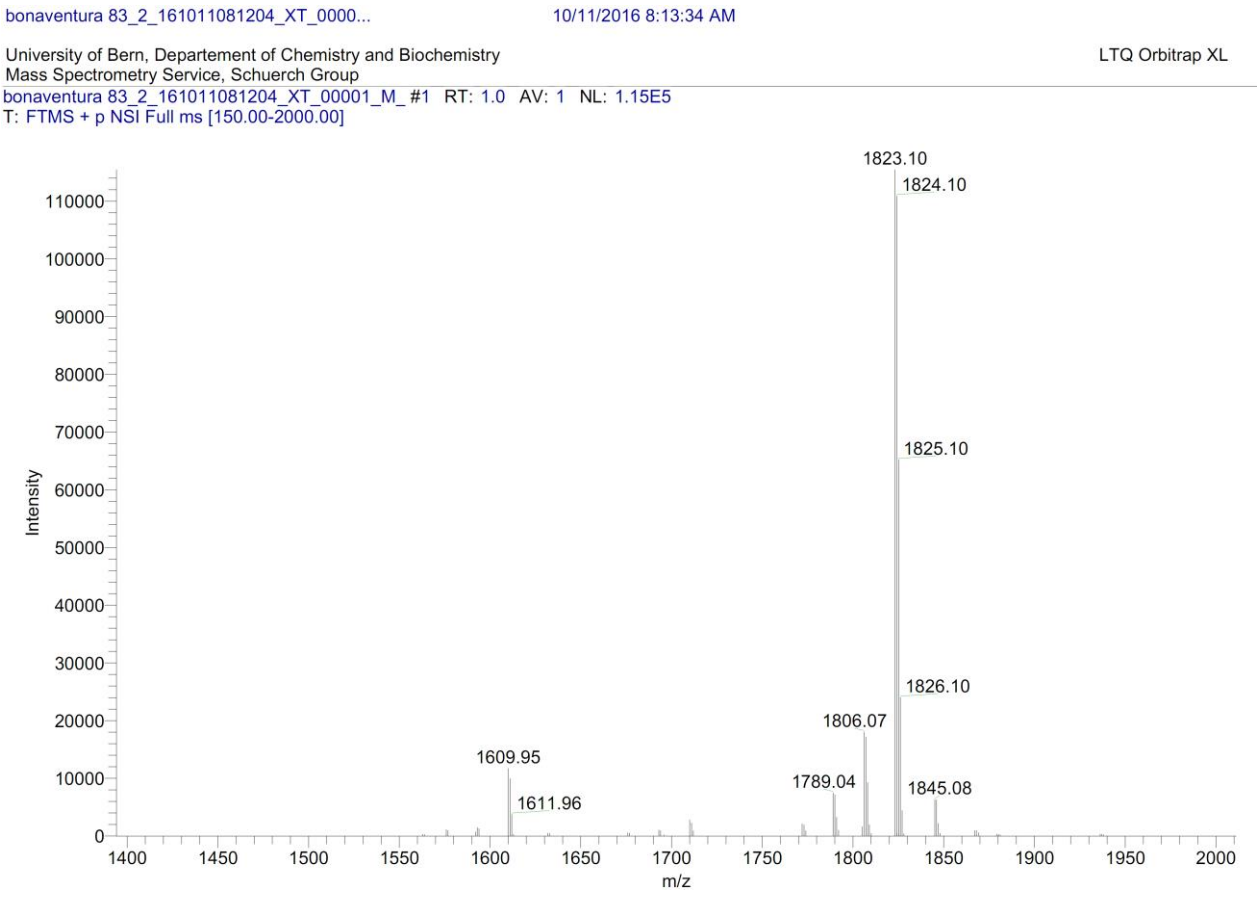


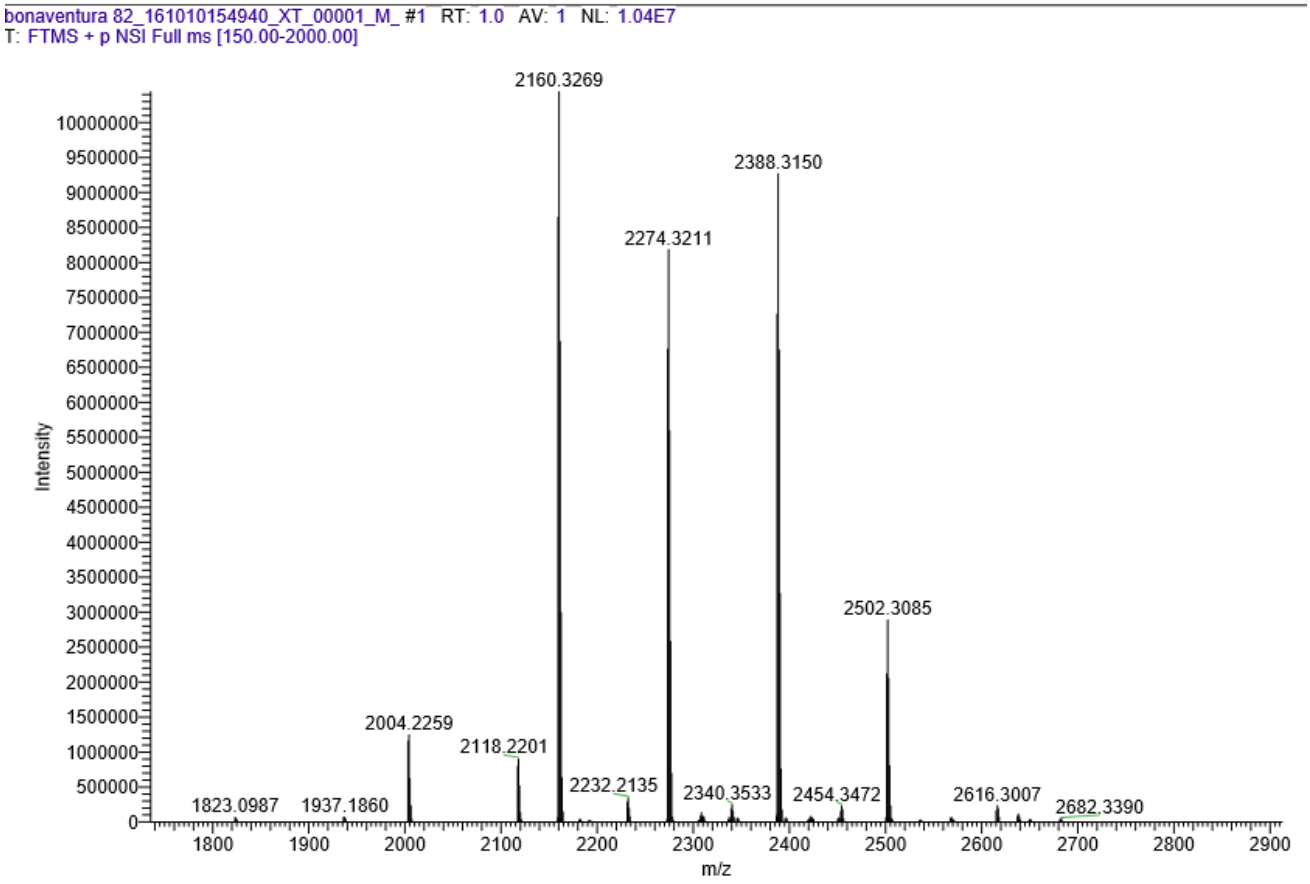
^{2}BLB*K*(B^{1}LB)BLL*Z*^{1}LLL*Z*^{2}B (60a) was obtained as foamy white solid after preparative RP-HPLC (7.6 mg, 3.2 %). Analytical RP-HPLC: t_R = 2.840 min. (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{82}H_{150}N_{24}O_{18}S_2$ calc./obs. 1823.10/1824.10 Da [M].



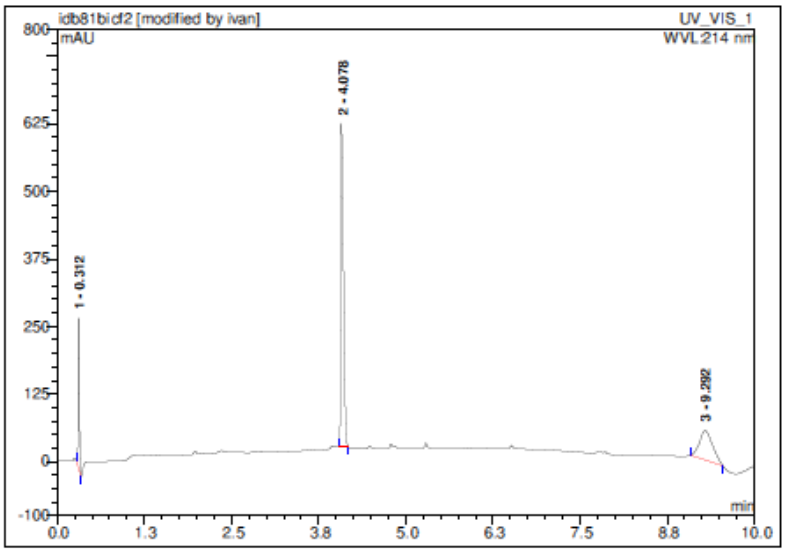
^{2}BLB*K*(B^{1}LB)BLL*Z*^{2}LLL*Z*^{1}B (60b) was obtained as foamy white solid after preparative RP-HPLC (3.5 mg, 1.4 %). Analytical RP-HPLC: t_R = 2.90 min. (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{82}H_{150}N_{24}O_{18}S_2$ calc./obs. 1823.10/1823.10 Da [M].

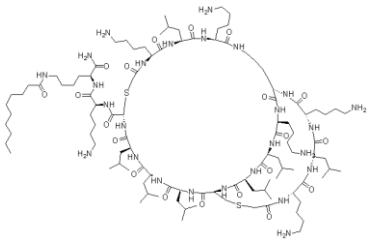


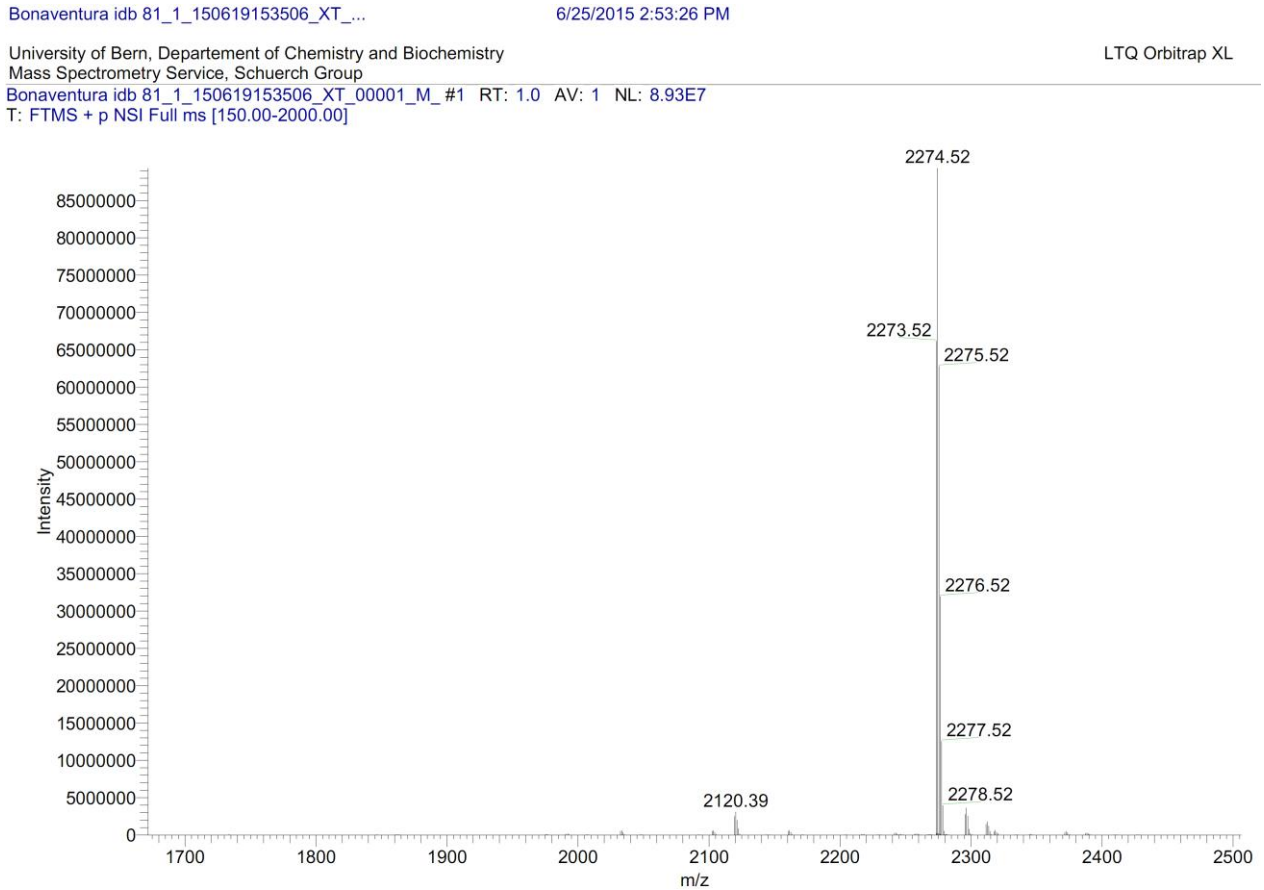
^{12}RLR*K*(R^{21}LR)RLL*Z*^{21}LLL*Z*^{12}R (61) was obtained as foamy white solid, like a mixture of two isomers, after preparative RP-HPLC (9.5 mg, 3.9 %). Analytical RP-HPLC: t_R = 3.260 min. (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{94}H_{174}N_{36}O_{18}S_2$ calc./obs. 2159.52 Da [M] found 2160.52 $[M+H]^+$, 2274.32 $[M+TFA]^+$, 2388.31$[M+2TFA]^+$, 2502.30 $[M+3TFA]^+$.



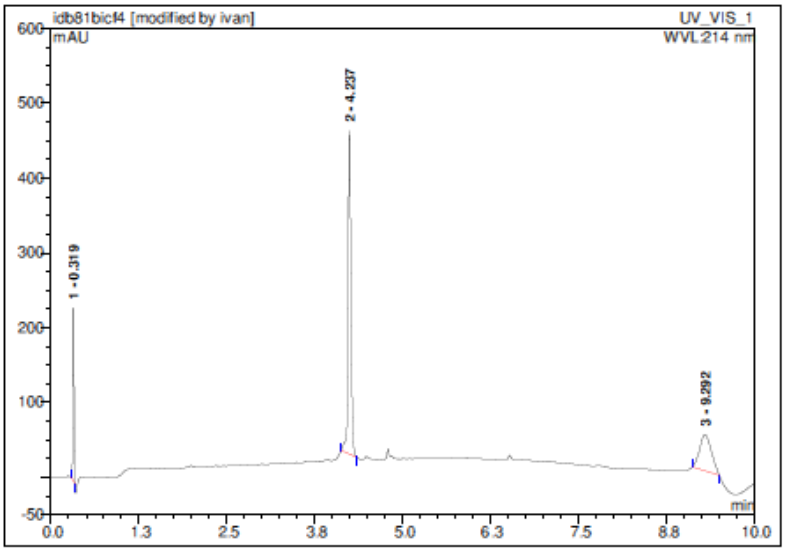
^{2}KLK*K*(K^{1}LK)KLL*Z*^{1}LLL*Z*^{2}KK(C_{10}) (62a) was obtained as foamy white solid after preparative RP-HPLC (11.3 mg, 4.9 %). Analytical RP-HPLC: t_R = 4.080 min. (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{110}H_{204}N_{26}O_{20}S_2$ calc./obs. 2273.52/2273.52 Da [M].

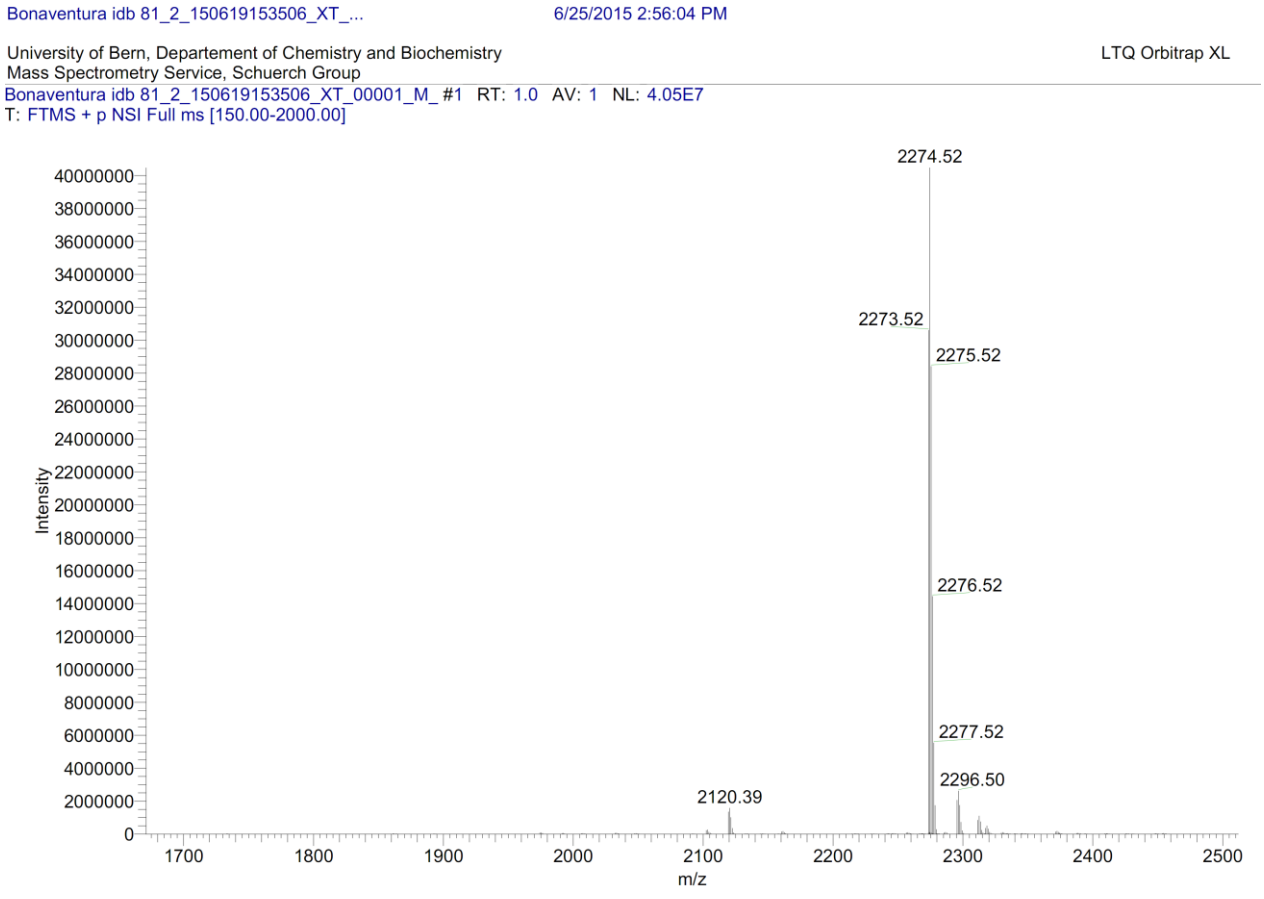




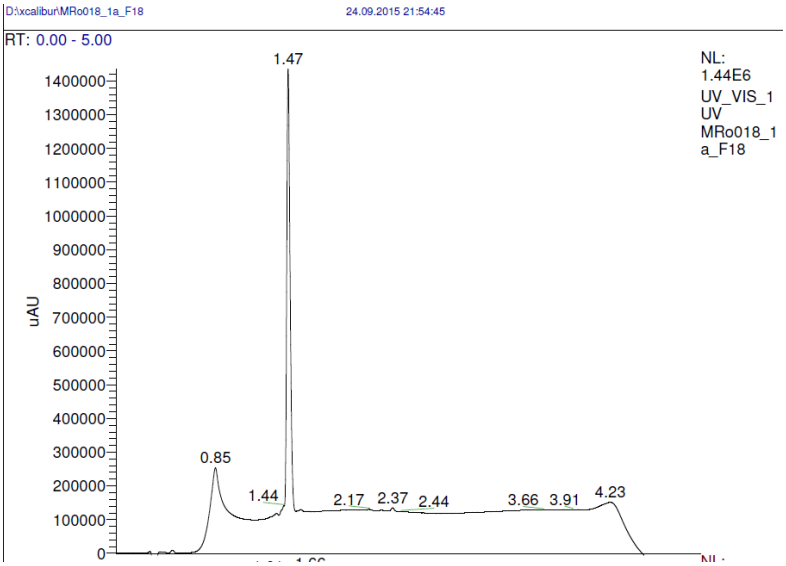


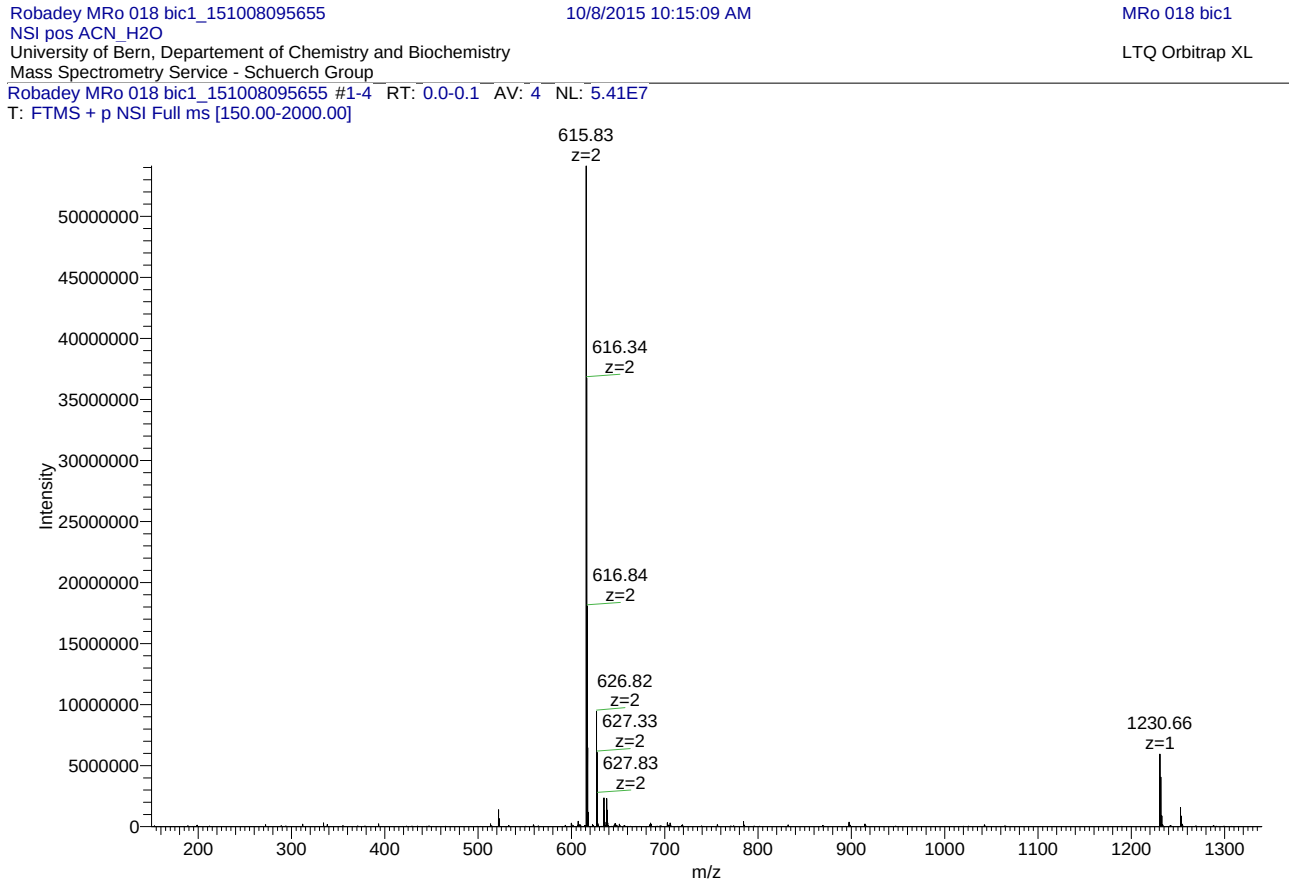
^{1}KLK*K*(K^{2}LK)KLL*Z*^{1}LLL*Z*^{2}KK(C_{10}) (62b) was obtained as foamy white solid after preparative RP-HPLC (8.5 mg, 3.6 %). Analytical RP-HPLC: t_R = 4.240 min. (A/D 100:0 to 0:100 in 10.00 min, λ = 214nm). MS(ESI+): $C_{110}H_{204}N_{26}O_{20}S_2$ calc./obs. 2273.52/2273.52 Da [M].



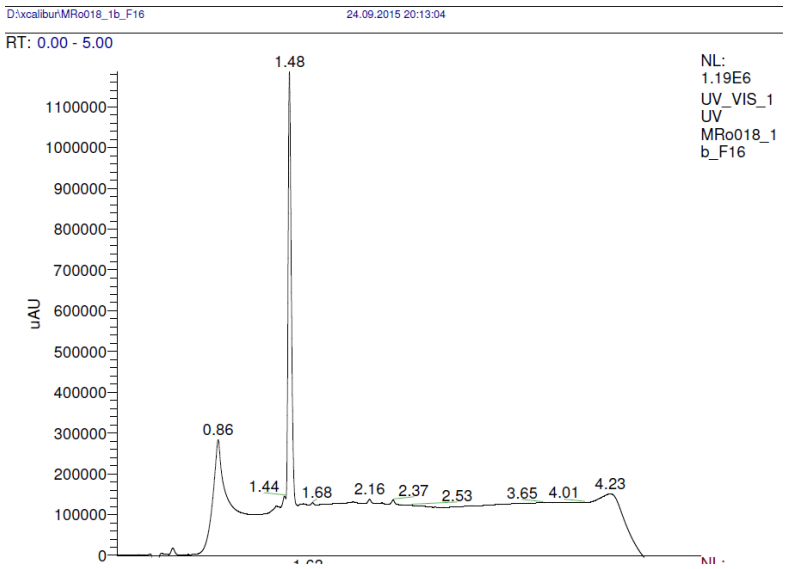


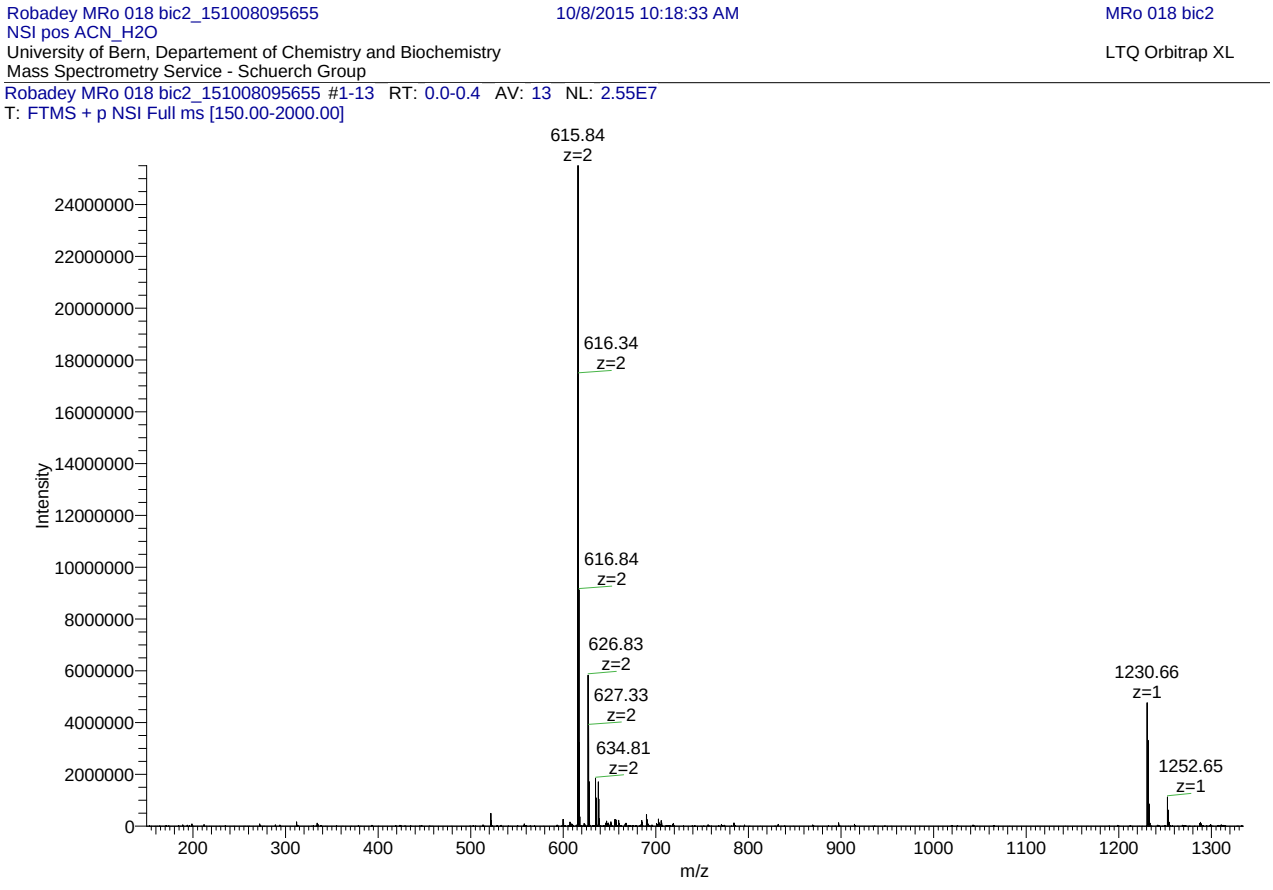
^{2}*K*(^{1})KZ^{1}KLZ^{2}LK(cFuc) (63a) was obtained as a foamy white solid after preparative RP-HPLC (3.0 mg, 2.6%). Analytical RP-UHPLC: t_R = 1.47 min (A/D 100/0 to 0/100 in 5.0 min, flow rate 1.2 mL·min^{-1}, λ = 214 nm). MS (ESI$^+$) calc. for $C_{54}H_{95}N_{13}O_{15}S_2$1229.65 Da [M], found: 1230.66 $[M+H]^+$, 615.83 $[M+H]^{2+}$.



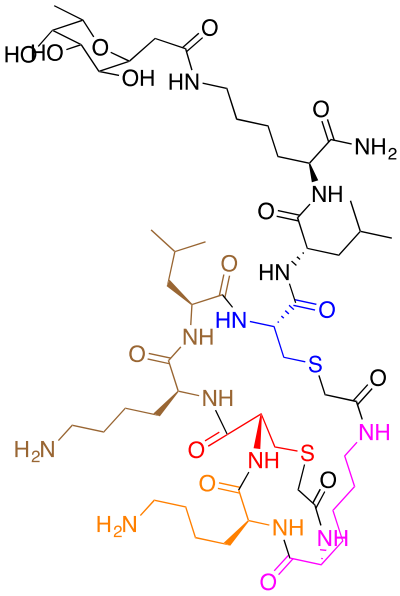


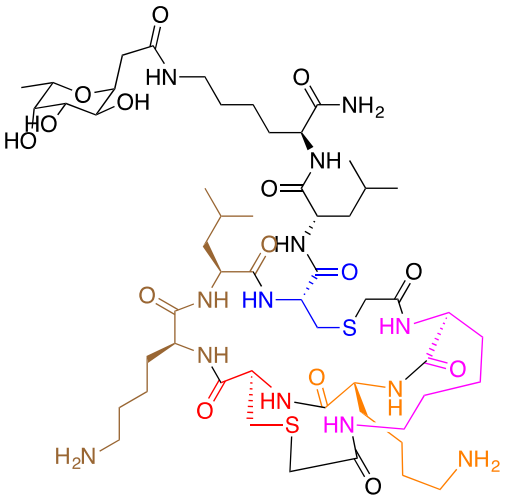
$^{2}K(^{1})KZ^{2}KLZ^{1}LK(cFuc)$ (63b) was obtained as a foamy white solid after preparative RP-HPLC (1.0 mg, 0.9%). Analytical RP-UHPLC: t_R = 1.48 min (A/D 100/0 to 0/100 in 5.0 min, flow rate 1.2 mL·min^{-1}, λ = 214 nm). MS (ESI$^+$) calc. for $C_{54}H_{95}N_{13}O_{15}S_2$: 1229.65 Da [M], found: 1230.66 $[M+H]^+$, 1252.66 $[M+Na]^+$, 615.84 $[M+H]^{2+}$.



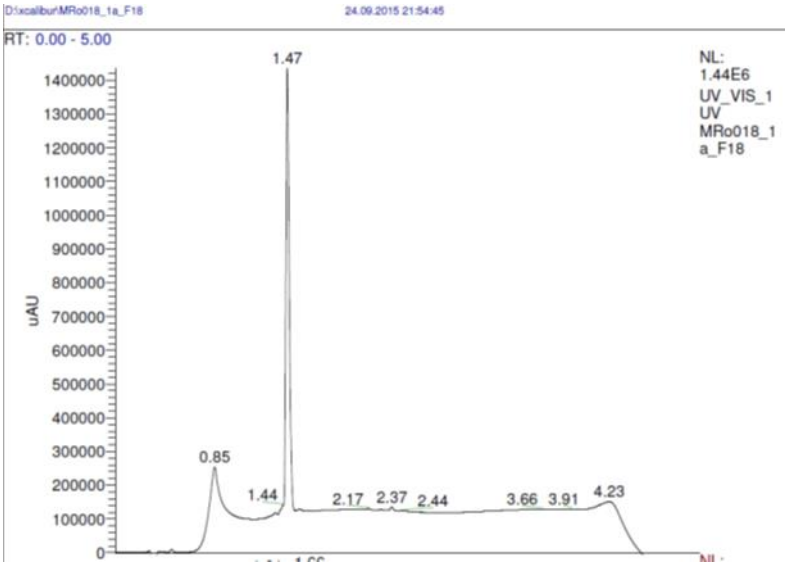


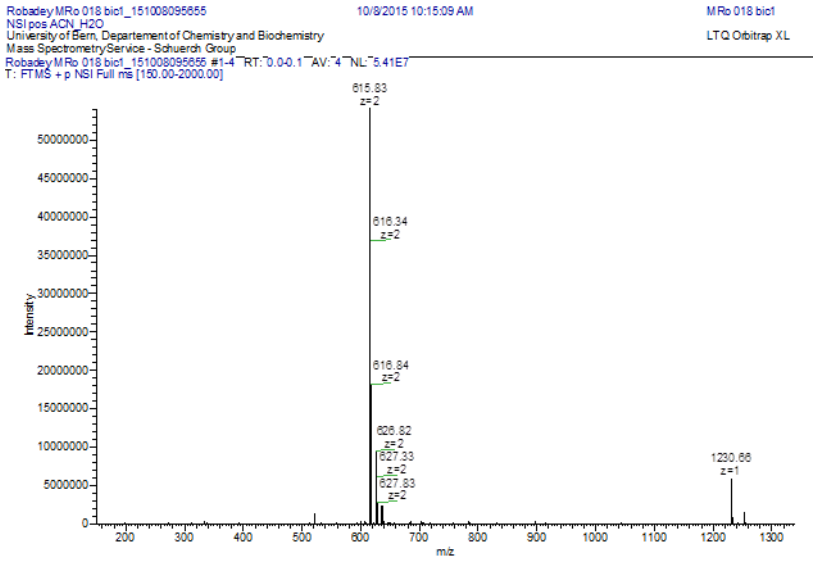
Structures of both isomers:



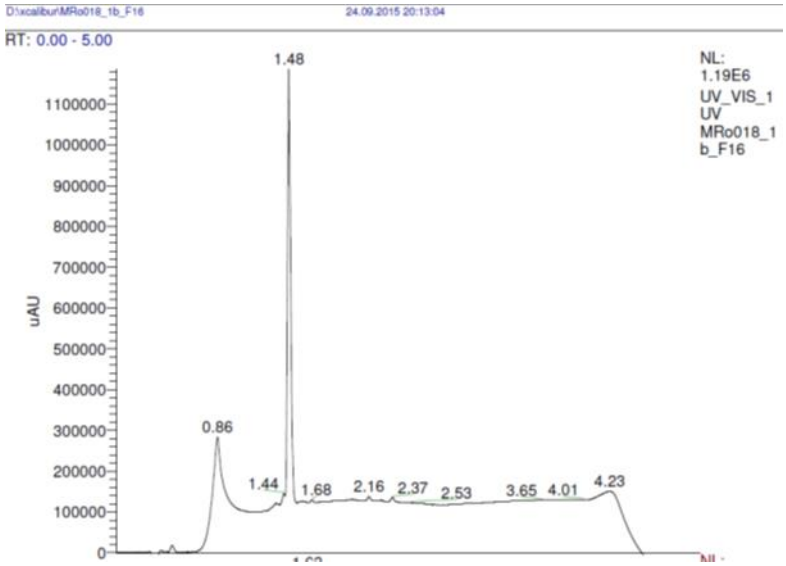


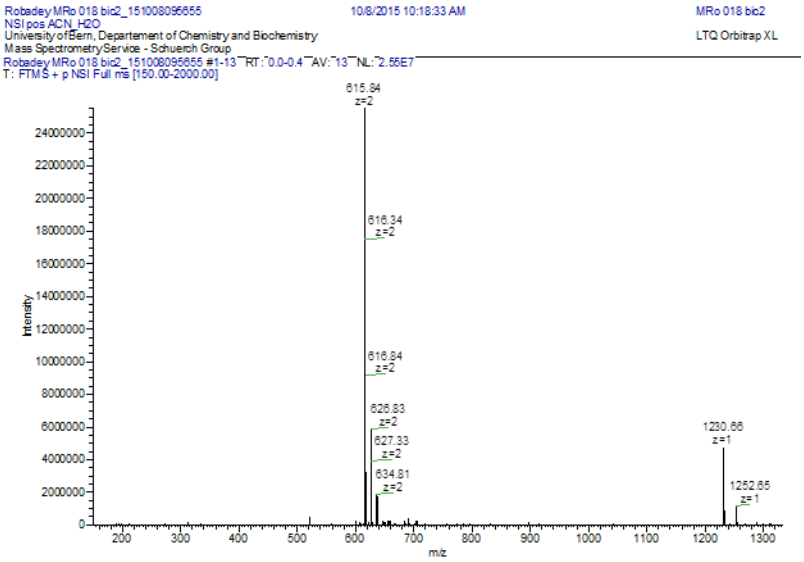
$^{1}K(^{2})PaZ^{2}yAz^{1}K(cFuc)$ (64a) was obtained as a foamy white solid after preparative RP-HPLC (0.6 mg, 0.5 %) Analytical RP-UHPLC: t_R = 2.39 min (A/D 100/0 to 0/100 in 7.5 min, flow rate 1.2 mL·min^{-1}, λ = 214 nm). MS (ESI$^+$) calc. for $C_{50}H_{75}N_{11}O_{16}S_2$ $[M+H]^+$: 1149.48, found: 1150.5, 597.22 $[M+Na]^{2+}$.



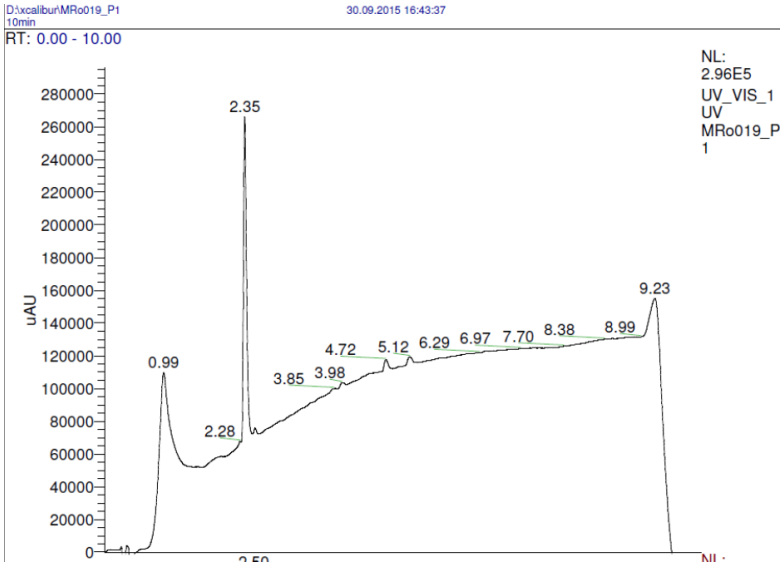


$^{2}K(^{1})PaZ^{2}yAz^{1}K(cFuc)$ (64b) was obtained as a foamy white solid after preparative RP-HPLC (1.7 mg, 1.5 %) Analytical RP-UHPLC: t_R = 2.44 min (A/D 100/0 to 0/100 in 7.5 min, flow rate 1.2 mL·min^{-1}, λ = 214 nm). MS (ESI$^+$) calc. for $C_{50}H_{75}N_{11}O_{16}S_2$ $[M+H]^+$: 1149.48, found: 1150.5, 575.75$[M+H]^{2+}$, 1172.48$[M+Na]^+$.





^{2}KLK*K*(K^{1}LK)KLLZ^{1}LLLZ^{2}KK(cFuc) (65a) was obtained as a foamy white solid after preparative RP-HPLC (2.3 mg, 1.2%) Analytical RP-UHPLC: t_R = 2.35 min (A/D 100/0 to 0/100 in 10.0 min, flow rate 1.2 mL·min^{-1}, λ = 214 nm). MS (ESI^{+}) calc. for $C_{108}H_{198}N_{26}O_{24}S_2$ 2307.48/2307.48 Da [M].



Robadey MRo 019 bic1_151008095655_XT_... 10/8/2015 10:22:11 AM

University of Bern, Departement of Chemistry and Biochemistry LTQ Orbitrap XL
Mass Spectrometry Service - Schuerch Group
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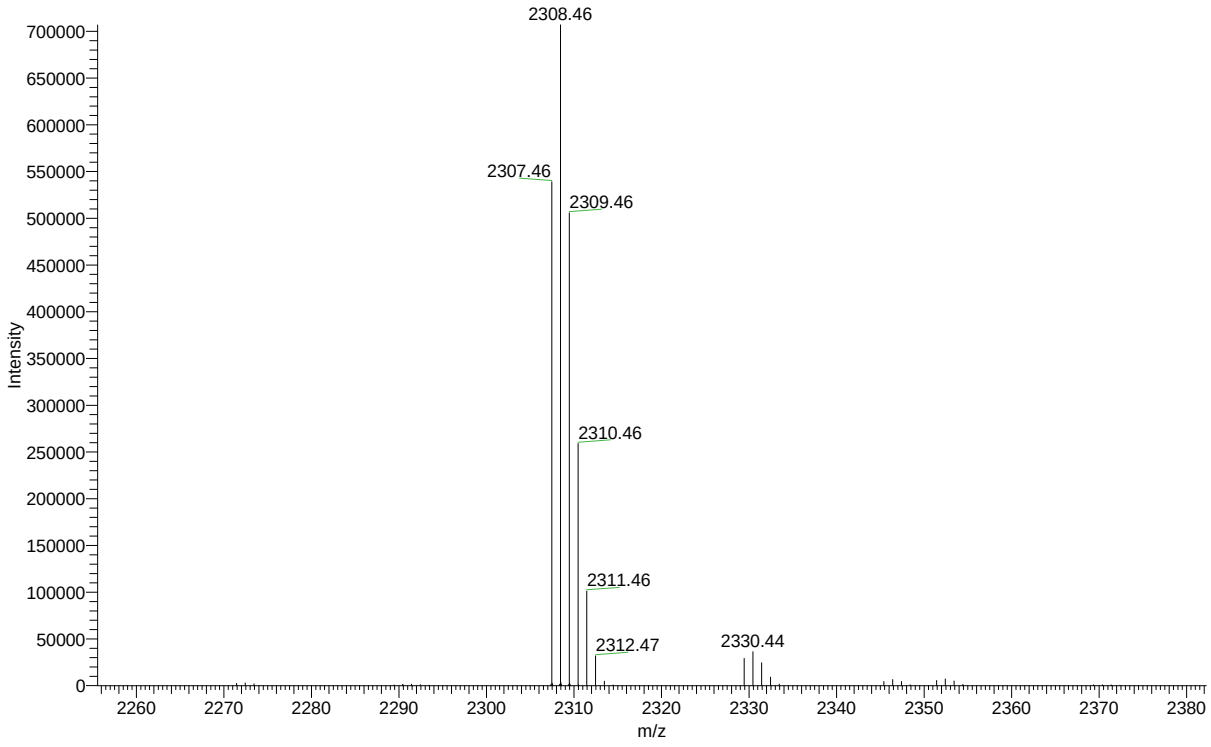
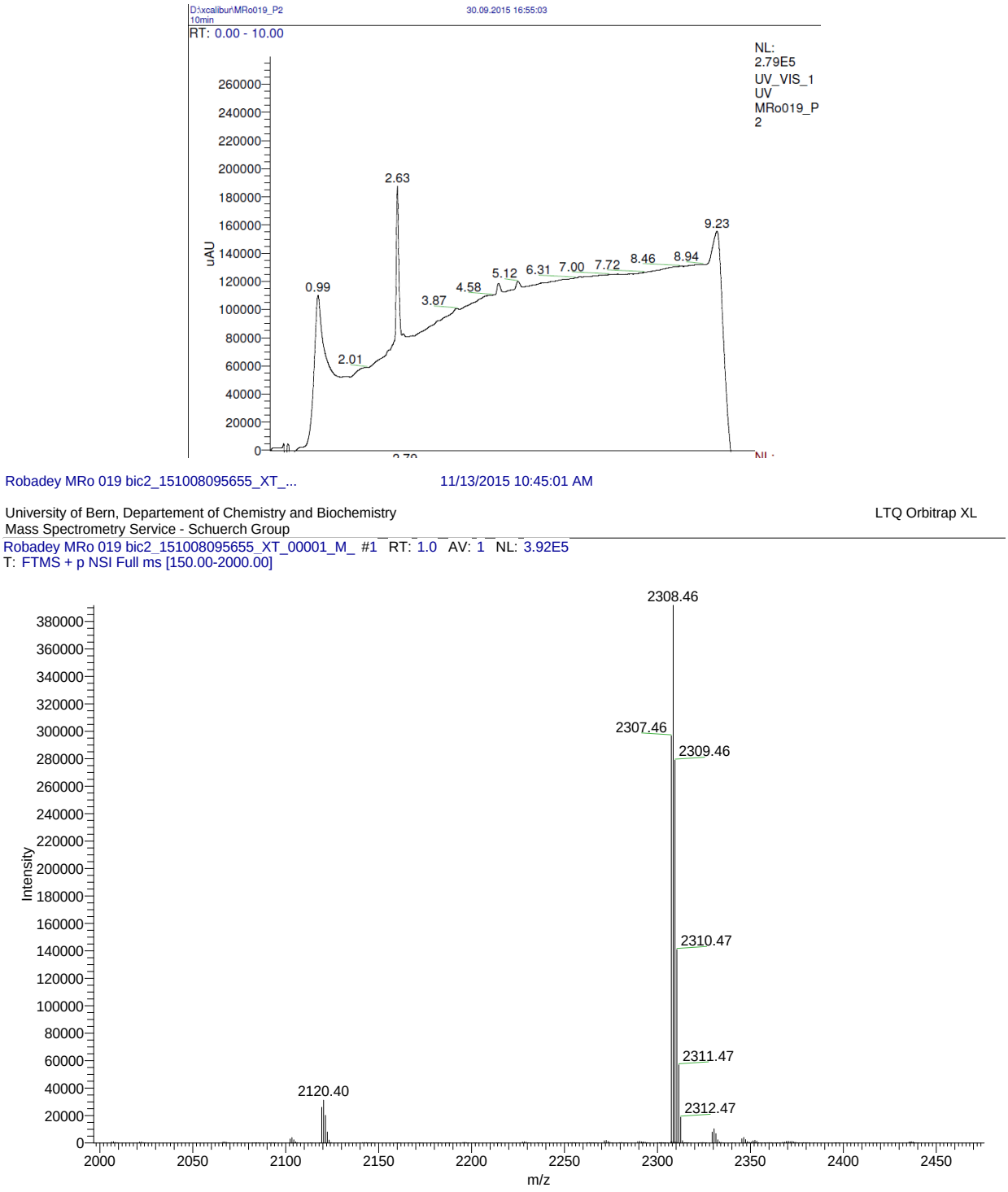


^{1}KLK*K*(K^{2}LK)KLLZ^{1}LLLZ^{2}KK(cFuc) (65b) was obtained as a foamy white solid after preparative RP-HPLC (2.0 mg, 1.0 %) Analytical RP-UHPLC: t_R = 2.63 min (A/D 100/0 to 0/100 in 10.0 min, flow rate 1.2 mL·min^{-1}, λ = 214 nm). MS (ESI^{+}) calc. for $C_{108}H_{198}N_{26}O_{24}S_2$ 2307.48/2307.48 Da [M].



vqwrairvrvir (DJK5) was obtained as a foamy white solid after preparative RP-HPLC (51.2 mg, 25.6 %) Analytical RP-UHPLC: t_R = 1.20 min (A/D 100/0 to 0/100 in 7.0 min, flow rate 1.2 $mL \cdot min^{-1}$, λ = 214 nm). MS (ESI^+) calc. for $C_{70}H_{123}N_{27}O_{13}$ 1549.47/1549.97 Da [M].