## 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 ${ }^{a} *$<br>${ }^{a}$ Department of Chemistry and Biochemistry, University of Berne, Freiestrasse 3, 3012 Berne Switzerland; jean-louis.reymond@dcb.unibe.ch<br>${ }^{b}$ Department of Biotechnology and Biosciences, University of Milano-Bicocca, Piazza della Scienza 2, 20126 Milan, Italy<br>${ }^{c}$ Department of Microbiology and Molecular Medicine, University of Geneva, and Service of Infectious Diseases, University Hospital of Geneva, Geneva, Switzerland

Table of Contents

1. AMBP Libraries 2
2. Antimicrobial activity 5
2.1 Broth Microdilution Method 5
2.2 Pseudomonas aeruginosa Biofilm Inhibition and Dispersal on Polystyrene Microtiter Plates 7
3. Membrane interaction experiment 13
4. TEM Transmission Electron Microscopy 15
5. Selective synthesis 16
6. Crystallization 17
7. Molecular Dynamics 19
8. FTIR 25
9. HPLC and MS Data 26

## 1. AMBP Libraries

Table S1: First library of bicyclic peptides

| N | Sequence ${ }^{\text {a }}$ | MS calc/obs [M] | $\begin{gathered} \text { MIC BR } \\ 151 \end{gathered}$ | $\begin{gathered} \text { MIC } \\ \text { PAO1 } \end{gathered}$ | $\mathbf{H}^{\text {b) }}$ | + ${ }^{\text {c) }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 1a | ${ }^{2} K\left({ }^{1}\right) \mathrm{K} Z^{1} \mathrm{KLZ}{ }^{2} \mathrm{~L}$ | 914.19/914.19 | >256 | >256 | 2 | 2 |
| 1b | ${ }^{1} K\left({ }^{2}\right) \mathrm{K} Z^{1} \mathrm{KL} Z^{2} \mathrm{~L}$ | 914.19/914.19 | 128 | >256 | 2 | 2 |
| 2a | $\mathrm{L}^{2} K\left(\mathrm{~L}^{1}\right) \mathrm{LKKZ}{ }^{1} \mathrm{~K} Z^{2}$ | 1154.67/1154.66 | >256 | >256 | 3 | 3 |
| 2b | $\mathrm{L}^{1} K\left(\mathrm{~L}^{2}\right) \mathrm{LKKZ}^{1} \mathrm{~K} Z^{2}$ | 1154.67/1154.66 | >256 | >256 | 3 | 3 |
| 3a | $\mathrm{K}^{2} K\left(\mathrm{~K}^{1}\right) \mathrm{LLLZ}^{1} \mathrm{LZ}^{2} \mathrm{~K}$ | 1267.65/1267.65 | >256 | >256 | 4 | 3 |
| 3b | $\mathrm{K}^{1} K\left(\mathrm{~K}^{2}\right) \mathrm{LLL}^{1}{ }^{1} Z^{2} \mathrm{~K}$ | 1267.65/1267.65 | 256 | >256 | 4 | 3 |
| 4 | $\mathrm{L}^{12} K\left(\mathrm{~L}^{12}\right) \mathrm{KKZ}{ }^{21} \mathrm{KLL}^{12}$ | 1282.76/1282.76 | 128 | >256 | 3 | 4 |
| 5a | $\mathrm{K}^{2} K\left(\mathrm{~K}^{1}\right) \mathrm{LKLZ}^{1} \mathrm{LKZ}^{2}$ | 1282.76/1282.76 | >256 | >256 | 3 | 4 |
| 5b | $\mathrm{K}^{1} K\left(\mathrm{~K}^{2}\right) \mathrm{LKLZ}{ }^{1} \mathrm{LKZ}^{2}$ | 1282.76/1282.76 | >256 | >256 | 3 | 4 |
| 6a | $\mathrm{K}^{2} K\left(\mathrm{~K}^{1}\right) \mathrm{LKLL}^{1} \mathrm{LLKZ}^{2} \mathrm{~L}$ | 1508.93/1508.93 | >256 | >256 | 5 | 4 |
| 6b | $\mathrm{K}^{1} K\left(\mathrm{~K}^{2}\right) \mathrm{LKLZ}^{1} \mathrm{KLLZ}^{2} \mathrm{~L}$ | 1508.93/1508.93 | >256 | >256 | 5 | 4 |
| 7 | $\mathrm{K}^{12} K\left(\mathrm{~K}^{12}\right) \mathrm{LLKZ}^{21} \mathrm{KLLZ}^{12} \mathrm{~L}$ | 1508.93/1508.93 | >256 | >256 | 5 | 4 |
| 8a | $\mathrm{K}^{1} \mathrm{~L} K\left(\mathrm{~K}^{2} \mathrm{~L}\right) \mathrm{KKK} Z^{2} \mathrm{LLZ}{ }^{1}$ | 1523.94/1523.94 | >256 | >256 | 4 | 5 |
| 8b | $\mathrm{K}^{1} \mathrm{~L} K\left(\mathrm{~K}^{2} \mathrm{~L}\right) \mathrm{KKKZ}{ }^{1} \mathrm{LLZ} Z^{2}$ | 1523.94/1523.94 | >256 | >256 | 4 | 5 |
| 9a | $\mathrm{L}^{1} \mathrm{~L} K\left(\mathrm{~L}^{2} \mathrm{~L}\right) \mathrm{KK} Z^{2} \mathrm{KKL} Z^{1} \mathrm{~L}$ | 1622.01/1622.01 | 128 | >256 | 6 | 4 |
| 9b | $\mathrm{L}^{1} \mathrm{~L} K\left(\mathrm{~L}^{2} \mathrm{~L}\right) \mathrm{KK} Z^{1} \mathrm{KKL} Z^{2} \mathrm{~L}$ | 1622.01/1622.01 | 128 | >256 | 6 | 4 |
| 10a | $\mathrm{K}^{1} \mathrm{~L} K\left(\mathrm{~K}^{2} \mathrm{~L}\right) \mathrm{KLLZ}^{2} \mathrm{KLLZ}{ }^{1} \mathrm{~K}$ | 1750.11/1750.11 | 32 | >256 | 6 | 5 |
| 10b | $\mathrm{K}^{1} \mathrm{~L} K\left(\mathrm{~K}^{2} \mathrm{~L}\right) \mathrm{KLLZ} Z^{1} \mathrm{KLL} Z^{2} \mathrm{~K}$ | 1750.11/1750.11 | 32 | >256 | 6 | 5 |
| 11a | $\mathrm{L}^{1} \mathrm{~L} K\left(\mathrm{~L}^{2} \mathrm{~L}\right) \mathrm{KLK} Z^{2} \mathrm{KKLZ}{ }^{1} \mathrm{~K}$ | 1750.11/1750.11 | 64 | >256 | 6 | 5 |
| 11b | $\mathrm{L}^{1} \mathrm{~L} K\left(\mathrm{~L}^{2} \mathrm{~L}\right) \mathrm{KLK} Z^{1} \mathrm{KKLZ}{ }^{2} \mathrm{~K}$ | 1750.11/1750.11 | 16 | >256 | 6 | 5 |
| 12 | $\mathrm{K}^{12} \mathrm{LK} K\left(\mathrm{~K}^{12} \mathrm{LK}\right) \mathrm{LLZ}^{21} \mathrm{KLLZ}^{12}$ | 1750.11/1750.11 | 64 | >256 | 6 | 5 |
| 13a | $\mathrm{K}^{2} \mathrm{LL} K\left(\mathrm{~K}^{1} \mathrm{LL}\right) \mathrm{KLZ}{ }^{1} \mathrm{KKLZ}^{2}$ | 1750.11/1750.11 | 16 | >256 | 6 | 5 |
| 13b | $\mathrm{K}^{1} \mathrm{LL} K\left(\mathrm{~K}^{2} \mathrm{LL}\right) \mathrm{KL} Z^{1} \mathrm{KKLZ}{ }^{2}$ | 1750.11/1750.11 | 16 | >256 | 6 | 5 |
| 14a | $\mathrm{K}^{2} \mathrm{LL} K\left(\mathrm{~K}^{1} \mathrm{LL}\right) \mathrm{KK} Z^{1} \mathrm{KLZ}^{2} \mathrm{~L}$ | 1750.11/1750.11 | 64 | >256 | 6 | 5 |
| 14b | $\mathrm{K}^{1} \mathrm{LL} K\left(\mathrm{~K}^{2} \mathrm{LL}\right) \mathrm{KK} Z^{1} \mathrm{KLZ}{ }^{2} \mathrm{~L}$ | 1750.11/1750.11 | 64 | >256 | 6 | 5 |
| 15 | $\mathrm{L}^{12} \mathrm{~K} K\left(\mathrm{~L}^{12} \mathrm{~K}\right) \mathrm{KLKZ}{ }^{21} \mathrm{LLKZ}^{12} \mathrm{~L}$ | 1750.11/1750.11 | 16 | >256 | 6 | 5 |
| 16a | $\mathrm{K}^{2} \mathrm{~L} K\left(\mathrm{~K}^{1} \mathrm{~L}\right) \mathrm{LKL} Z^{1} \mathrm{KKLZ}{ }^{2} \mathrm{~K}$ | 1765.12/1765.12 | >256 | >256 | 4 | 6 |
| 16b | $\mathrm{K}^{1} \mathrm{~L} K\left(\mathrm{~K}^{2} \mathrm{~L}\right) \mathrm{LKL} Z^{1} \mathrm{KKLZ}{ }^{2} \mathrm{~K}$ | 1765.12/1765.12 | >256 | >256 | 4 | 6 |
| 17a | $\mathrm{K}^{2} \mathrm{KL} K\left(\mathrm{~K}^{1} \mathrm{KL}\right) \mathrm{KK} Z^{1} \mathrm{LLLZ}^{2} \mathrm{~K}$ | 1893.21/1893.22 | 128 | >256 | 5 | 7 |
| 17b | $\mathrm{K}^{1} \mathrm{KL} K\left(\mathrm{~K}^{2} \mathrm{KL}\right) \mathrm{KK} Z^{1} \mathrm{LLLZ}^{2} \mathrm{~K}$ | 1893.21/1893.22 | 128 | >256 | 5 | 7 |
| 18a | $\mathrm{K}^{1} \mathrm{LK} K\left(\mathrm{~K}^{2} \mathrm{LK}\right) \mathrm{LKKZ}{ }^{2} \mathrm{LLLL} Z^{1} \mathrm{~L}$ | 1991.29/1992.29 | 32 | >256 | 7 | 6 |
| 18b | $\mathrm{K}^{1} \mathrm{LK} K\left(\mathrm{~K}^{2} \mathrm{LK}\right) \mathrm{LKK} Z^{1} \mathrm{LLLL}^{2} \mathrm{~L}$ | 1991.29/1992.29 | 32 | >256 | 7 | 6 |
| 19 | $\mathrm{K}^{12} \mathrm{LK} K\left(\mathrm{~K}^{12} \mathrm{LK}\right) \mathrm{LLLZ}^{21} \mathrm{KLKZ}^{12} \mathrm{~L}$ | 1991.29/1991.29 | 8 | >256 | 7 | 6 |

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

Table S2: Second library of bicyclic peptides.

| N | Sequence | MS calc/obs [M] | $\begin{gathered} \text { MIC BR } \\ 151 \end{gathered}$ | $\begin{gathered} \text { MIC } \\ \text { PAO1 } \end{gathered}$ | MBIC | Dispersal | H | + |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 20 | ${ }^{12} \mathrm{LLK} K\left(\mathrm{~L}^{12} \mathrm{LK}\right) \mathrm{LLL} Z^{21} \mathrm{KLKZ}^{12} \mathrm{~L}$ | 1961.27/1961.27 | 4 | 128 | 32 | 60 \% | 9 | 4 |
| 21a | ${ }^{2} \mathrm{KLK} K\left(\mathrm{~K}^{1} \mathrm{LK}\right) \mathrm{LLLZ}{ }^{1} \mathrm{LLLZ}{ }^{2} \mathrm{~L}$ | 1961.27/1961.27 | 4 | 128 |  |  | 9 | 4 |
| 21b | ${ }^{1} \mathrm{KLK} K\left(\mathrm{~K}^{2} \mathrm{LK}\right) \mathrm{LLLZ}{ }^{1} \mathrm{LLLZ}^{2} \mathrm{~L}$ | 1961.27/1961.27 | 4 | 64 | >32 |  | 9 | 4 |
| 22 | ${ }^{12} \mathrm{KLLK}\left(\mathrm{K}^{12} \mathrm{LL}\right) \mathrm{KLLZ}^{21} \mathrm{KLLZ}^{12} \mathrm{~L}$ | 1961.27/1961.28 | 4 | >256 |  |  | 9 | 4 |
| 23 | ${ }^{12} \mathrm{LLK} K\left(\mathrm{~L}^{12} \mathrm{LK}\right) \mathrm{KLLZ}{ }^{21} \mathrm{KLKZ}^{12} \mathrm{~L}$ | 1976.28/1976.29 | 4 | 128 |  |  | 8 | 5 |
| 24 | ${ }^{12} \mathrm{LLK} K\left(\mathrm{~L}^{12} \mathrm{LK}\right) \mathrm{KLKZ}{ }^{21} \mathrm{LLKZ}^{12} \mathrm{~L}$ | 1976.28/1976.28 | 4 | 128 | 16 | $50 \%$ | 8 | 5 |
| 25a | ${ }^{2} \mathrm{LLK} K\left(\mathrm{~L}^{1} \mathrm{LK}\right) \mathrm{KLKZ}{ }^{1} \mathrm{KLLZ}{ }^{2} \mathrm{~K}$ | 1991.29/1991.30 | 64 | >256 |  |  | 7 | 6 |
| 25b | ${ }^{1} \mathrm{LLK}$ K( $\left.\mathrm{L}^{2} \mathrm{LK}\right) \mathrm{KLKZ}{ }^{1} \mathrm{KLLZ}{ }^{2} \mathrm{~K}$ | 1991.29/1991.30 | 16 | 64 | >32 |  | 7 | 6 |
| 26a | ${ }^{1} \mathrm{KLLL} K\left(\mathrm{~K}^{2} \mathrm{LL}\right) \mathrm{KLLZ}{ }^{2} \mathrm{KLKZ}{ }^{1} \mathrm{~K}$ | 1991.29/1991.30 | 32 | >256 |  |  | 7 | 6 |
| 26b | ${ }^{1} \mathrm{KLLLK}\left(\mathrm{K}^{2} \mathrm{LL}\right) \mathrm{KLLZ}{ }^{1} \mathrm{KLKZ}{ }^{2} \mathrm{~K}$ | 1991.29/1991.30 | 1 | 128 | 32 | $36 \%$ | 7 | 6 |
| 27a | ${ }^{2} \mathrm{KLKK}\left(\mathrm{K}^{1} \mathrm{LK}\right) \mathrm{KLLZ}{ }^{1} \mathrm{LLLZ}{ }^{2} \mathrm{~K}$ | 1991.29/1991.30 | 32 | 256 |  |  | 7 | 6 |
| 27b | ${ }^{1} \mathrm{KLKK}$ ( $\left.\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{KLLZ}{ }^{1} \mathrm{LLLZ}{ }^{2} \mathrm{~K}$ | 1991.29/1991.30 | 1 | 32 | 32 | 12 \% | 7 | 6 |
| 28 a | ${ }^{2} \mathrm{KLL} K\left(\mathrm{~K}^{1} \mathrm{LL}\right) \mathrm{KLKZ}{ }^{1} \mathrm{KKL} Z^{2} \mathrm{~L}$ | 1991.29/1991.29 | 64 | >256 |  |  | 7 | 6 |
| 28b | ${ }^{1} \mathrm{KLLL} K\left(\mathrm{~K}^{2} \mathrm{LL}\right) \mathrm{KLKZ}{ }^{1} \mathrm{KKLZ} Z^{2} \mathrm{~L}$ | 1991.29/1991.29 | 64 | >256 | >32 |  | 7 | 6 |
| 29a | ${ }^{2} \mathrm{KLLL}$ ( $\left.\mathrm{K}^{1} \mathrm{LL}\right) \mathrm{KLLZ}{ }^{1} \mathrm{KKKZ}{ }^{2} \mathrm{~L}$ | 1991.29/1991.29 | 16 | >256 | 32 | No disp. | 7 | 6 |
| 29b | ${ }^{1} \mathrm{KLLL}$ ( $\left.\mathrm{K}^{2} \mathrm{LL}\right) \mathrm{KLLZ}{ }^{1} \mathrm{KKKZ}{ }^{2} \mathrm{~L}$ | 1991.29/1991.29 | 2 | 256 | 8 | 100\% | 7 | 6 |
| 30a | ${ }^{2} \mathrm{KLLK}\left(\mathrm{K}{ }^{1} \mathrm{LL}\right) \mathrm{LK} Z^{1} \mathrm{KLKZ}{ }^{2} \mathrm{~L}$ | 1863.19/1863.19 | 128 | >256 |  |  | 7 | 5 |
| 30b | ${ }^{1} \mathrm{KLL} K\left(\mathrm{~K}^{2} \mathrm{LL}\right) \mathrm{LK} Z^{1} \mathrm{KLKZ}{ }^{2} \mathrm{~L}$ | 1863.19/1863.19 | 128 | >256 |  |  | 7 | 5 |
| 31a | ${ }^{2} \mathrm{KLK} K\left(\mathrm{~K}^{1} \mathrm{LK}\right) \mathrm{KKLZ}{ }^{1} \mathrm{LLK} Z^{2} \mathrm{~L}$ | 1878.20/1878.21 | 128 | >256 |  |  | 6 | 6 |
| 31b | ${ }^{1} \mathrm{KLK} K\left(\mathrm{~K}^{2} \mathrm{LK}\right) \mathrm{KKLZ}{ }^{1} \mathrm{LLK} Z^{2} \mathrm{~L}$ | 1878.20/1878.21 | 128 | >256 |  |  | 6 | 6 |
| 32a | ${ }^{2} \mathrm{KLK} K\left(\mathrm{~K}^{1} \mathrm{LK}\right) \mathrm{LLZ}{ }^{1} \mathrm{LKLZ}{ }^{2} \mathrm{~K}$ | 1878.20/1878.20 | 32 | >256 |  |  | 6 | 6 |
| 32b | ${ }^{1} \mathrm{KLK} K\left(\mathrm{~K}^{2} \mathrm{LK}\right) \mathrm{LLZ}{ }^{1} \mathrm{LKLZ} Z^{2} \mathrm{~K}$ | 1878.20/1878.20 | 16 | >256 |  |  | 6 | 6 |
| 33a | ${ }^{2} \mathrm{KLLK}\left(\mathrm{K}^{1} \mathrm{LL}\right) \mathrm{KLK} Z^{1} \mathrm{KKKZ}{ }^{2} \mathrm{~L}$ | 2006.30/2006.31 | 64 | >256 |  |  | 6 | 7 |
| 33b | ${ }^{1} \mathrm{KLLK}\left(\mathrm{K}^{2} \mathrm{LL}\right) \mathrm{KLKZ}{ }^{1} \mathrm{KKKZ}{ }^{2} \mathrm{~L}$ | 2006.30/2006.31 | 32 | >256 | >32 |  | 6 | 7 |
| 34a | ${ }^{2} \mathrm{LLK} K\left(\mathrm{~L}^{1} \mathrm{LK}\right) \mathrm{KKKZ}{ }^{1} \mathrm{KLKZ}{ }^{2} \mathrm{~L}$ | 2006.30/2006.31 | 8 | >256 |  |  | 6 | 7 |
| 34b | ${ }^{1} \mathrm{LLKK}\left(\mathrm{L}^{2} \mathrm{LK}\right) \mathrm{KKKZ}{ }^{1} \mathrm{KLKZ}{ }^{2} \mathrm{~L}$ | 2006.30/2006.31 | 8 | >256 | >32 |  | 6 | 7 |
| 35a | ${ }^{2} \mathrm{KLKK}$ ( $\left.\mathrm{K}^{1} \mathrm{LK}\right) \mathrm{LLLZ}{ }^{1} \mathrm{KKKZ}{ }^{2} \mathrm{~L}$ | 2006.30/2006.31 | 16 | >256 |  |  | 6 | 7 |
| 35b | ${ }^{1} \mathrm{KLKK}$ ( $\left.\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{LLLZ}{ }^{1} \mathrm{KKKZ}{ }^{2} \mathrm{~L}$ | 2006.30/2006.31 | 16 | >256 |  |  | 6 | 7 |
| 36a | ${ }^{2} \mathrm{KLK} K\left(\mathrm{~K}^{1} \mathrm{LK}\right) \mathrm{KLLZ}{ }^{1} \mathrm{LLKZ}{ }^{2} \mathrm{~K}$ | 2006.30/2006.30 | 32 | >256 | >32 | No disp. | 6 | 7 |
| 36b | ${ }^{1} \mathrm{KLK} K\left(\mathrm{~K}^{2} \mathrm{LK}\right) \mathrm{KLLZ}{ }^{1} \mathrm{LLKZ}{ }^{2} \mathrm{~K}$ | 2006.30/2006.30 | 16 | 64 | 8 | 100 \% | 6 | 7 |
| 37a | ${ }^{2} \mathrm{KLK} K\left(\mathrm{~K}^{1} \mathrm{LK}\right) \mathrm{KLLZ}{ }^{1} \mathrm{KLKZ}{ }^{2} \mathrm{~L}$ | 2006.30/2006.30 | 32 | >256 | 16 | $30 \%$ | 6 | 7 |
| 37b | ${ }^{1} \mathrm{KLKK}$ ( $\left.\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{KLLZ}{ }^{1} \mathrm{KLK} Z^{2} \mathrm{~L}$ | 2006.30/2006.30 | 32 | 256 | 16 | $100 \%$ | 6 | 7 |
| 38 | ${ }^{12} \mathrm{KKK} K\left(\mathrm{~K}^{12} \mathrm{KK}\right) \mathrm{KKKZ}{ }^{21} \mathrm{LLLZ}^{12} \mathrm{~L}$ | 2036.32/2036.33 | 16 | >256 |  |  | 4 | 9 |

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

Table S3: Third library of bicyclic peptides

| N | Sequence | MS calc/obs [M] | $\begin{gathered} \text { MIC BR } \\ 151 \end{gathered}$ | $\begin{gathered} \text { MIC } \\ \text { PAO1 } \end{gathered}$ | MBIC | Dispersal | H | + |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 39a | ${ }^{1} \mathrm{LLKK}\left(\mathrm{L}^{2} \mathrm{LK}\right) \mathrm{KKLZ}{ }^{2} \mathrm{LLLZ}{ }^{1} \mathrm{~K}$ | 1976.28/1976.28 | 16 | 128 |  |  | 8 | 5 |
| 39b | ${ }^{2} \mathrm{LLKK}\left(\mathrm{L}^{1} \mathrm{LK}\right) \mathrm{KKLZ}{ }^{2} \mathrm{LLLZ}{ }^{1} \mathrm{~K}$ | 1976.28/1976.28 | 4 | 64 | >32 |  | 8 | 5 |
| 40a | ${ }^{2} \mathrm{KLKK}\left(\mathrm{K}^{1} \mathrm{LK}\right) L K L Z^{1} L L L Z^{2} K$ | 1991.29/1991.28 | >64 | >256 |  |  | 7 | 6 |
| 40b | ${ }^{1} \mathrm{KLKK}\left(\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{LKLZ}{ }^{1} \mathrm{LLLZ}{ }^{2} \mathrm{~K}$ | 1991.29/1991.28 | 64 | >256 |  |  | 7 | 6 |
| 41a | ${ }^{2} \mathrm{KLKK}\left(\mathrm{K}^{1} \mathrm{LK}\right) \mathrm{KKK} Z^{1} \mathrm{LLLZ}{ }^{2} \mathrm{~K}$ | 2006.30/2006.30 | >64 | >256 |  |  | 7 | 6 |
| 41b | ${ }^{1} \mathrm{KLKK}\left(\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{KKKZ}{ }^{1} \mathrm{LLLZ}{ }^{2} \mathrm{~K}$ | 2006.30/2006.30 | >64 | $>256$ |  |  | 7 | 6 |
| 42a | ${ }^{1} \mathrm{KLKK}\left(\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{LLLZ}{ }^{2} \mathrm{LKL} Z^{1} \mathrm{~K}$ | 1991.29/1991.29 | 16 | >256 |  |  | 7 | 6 |
| 42b | ${ }^{2} \mathrm{KLKK}\left(\mathrm{K}^{1} \mathrm{LK}\right) \mathrm{LLLZ}{ }^{2} \mathrm{LKL} Z^{1} \mathrm{~K}$ | 1991.29/1991.29 | 4 | 256 |  |  | 7 | 6 |
| 43 | ${ }^{12} \mathrm{KLKK}\left(\mathrm{K}^{21} \mathrm{LK}\right) \mathrm{KLLZ}{ }^{12} \mathrm{LKLZ}^{21} \mathrm{~K}$ | 2006.30/2006.30 | >64 | >256 |  |  | 6 | 7 |
| 44a | ${ }^{1} \mathrm{KLKK}\left(\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{LKLZ}{ }^{2} \mathrm{LLK} Z^{1} \mathrm{~K}$ | 2006.30/2006.30 | >64 | $>256$ |  |  | 6 | 7 |
| 44b | ${ }^{2} \mathrm{KLKK}\left(\mathrm{K}^{1} \mathrm{LK}\right) \mathrm{LKL} Z^{2} \mathrm{LLK} Z^{1} \mathrm{~K}$ | 2006.30/2006.30 | 64 | $>256$ |  |  | 6 | 7 |
| 45a | ${ }^{1} \mathrm{KLKK}\left(\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{LLL} Z^{2} \mathrm{LKK} Z^{1} \mathrm{~K}$ | 2006.30/2006.30 | 8 | >256 |  |  | 6 | 7 |
| 45b | ${ }^{1} \mathrm{KLKK}\left(\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{LLLZ}{ }^{1} \mathrm{LKK} Z^{2} \mathrm{~K}$ | 2006.30/2006.30 | 4 | 256 |  |  | 6 | 7 |
| 46 | ${ }^{12} \mathrm{KLKK}\left(\mathrm{K}^{21} \mathrm{LK}\right) \mathrm{LKLZ}{ }^{21} \mathrm{LKLZ}{ }^{12} \mathrm{~K}$ | 2006.30/2006.30 | $>64$ | >256 |  |  | 6 | 7 |
| 47a | ${ }^{2} \mathrm{KLKK}\left(\mathrm{K}^{1} \mathrm{LK}\right) \mathrm{LKK} Z^{1} \mathrm{LLL} Z^{2} \mathrm{~K}$ | 2006.30/2006.30 | >64 | $>256$ |  |  | 6 | 7 |
| 47b | ${ }^{1} \mathrm{KLKK}\left(\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{LKK} Z^{1} \mathrm{LLLZ}{ }^{2} \mathrm{~K}$ | 2006.30/2006.30 | >64 | >256 |  |  | 6 | 7 |
| 48a | ${ }^{1} \mathrm{KLKK}\left(\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{LKLZ}{ }^{2} \mathrm{KLL} Z^{1} \mathrm{~K}$ | 2006.30/2006.30 | >64 | $>256$ |  |  | 6 | 7 |
| 48b | ${ }^{2} \mathrm{KLKK}\left(\mathrm{K}^{1} \mathrm{LK}\right) \mathrm{LKL} Z^{2} \mathrm{KLL} Z^{1} \mathrm{~K}$ | 2006.30/2006.30 | 64 | $>256$ |  |  | 6 | 7 |
| 49a | ${ }^{1} \mathrm{KLKK}\left(\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{KLK} Z^{2} \mathrm{LLK} Z^{1} \mathrm{~K}$ | 2021.31/2021.31 | >64 | >256 |  |  | 5 | 8 |
| 49b | ${ }^{2} \mathrm{KLKK}\left(\mathrm{K}^{1} \mathrm{LK}\right) \mathrm{KLK} Z^{2} \mathrm{LLK} Z^{1} \mathrm{~K}$ | 2021.31/2021.31 | 16 | 256 |  |  | 5 | 8 |
| 50 | ${ }^{21} \mathrm{KLKK}\left(\mathrm{K}^{12} \mathrm{LK}\right) \mathrm{KLLZ}{ }^{21} \mathrm{KLK} Z^{12} \mathrm{~K}$ | 2021.31/2021.31 | $>64$ | >256 |  |  | 5 | 8 |
| 51a | ${ }^{2} \mathrm{KLKK}\left(\mathrm{K}^{1} \mathrm{LK}\right) \mathrm{KLK} Z^{1} \mathrm{KLL} Z^{2} \mathrm{~K}$ | 2021.31/2021.31 | $>64$ | $>256$ |  |  | 5 | 8 |
| 51b | ${ }^{1} \mathrm{KLKK}\left(\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{KLK} Z^{1} \mathrm{KLLZ}{ }^{2} \mathrm{~K}$ | 2021.31/2021.31 | >64 | $>256$ |  |  | 5 | 8 |
| 52 | ${ }^{12} \mathrm{KLKK}\left(\mathrm{K}^{21} \mathrm{LK}\right) \mathrm{KKLZ}{ }^{12} \mathrm{LLK} Z^{21} \mathrm{~K}$ | 2021.31/2021.31 | >64 | $>256$ |  |  | 5 | 8 |
| 53a | ${ }^{2} \mathrm{KLKK}\left(\mathrm{K}^{1} \mathrm{LK}\right) \mathrm{KLLZ}{ }^{1} \mathrm{LKK} Z^{2} \mathrm{~K}$ | 2021.31/2021.31 | >64 | $>256$ |  |  | 5 | 8 |
| 53b | ${ }^{1} \mathrm{KLKK}\left(\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{KLLZ}{ }^{1} \mathrm{LKK} Z^{2} \mathrm{~K}$ | 2021.31/2021.31 | 32 | $>256$ |  |  | 5 | 8 |
| 54 | ${ }^{12} \mathrm{KLKK}\left(\mathrm{K}^{21} \mathrm{LK}\right) \mathrm{KKKZ}{ }^{12} \mathrm{LLL} Z^{21} \mathrm{~K}$ | 2021.31/2021.31 | $>64$ | $>256$ |  |  | 5 | 8 |
| 55a | ${ }^{1} \mathrm{KLKK}\left(\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{KLK} Z^{2} \mathrm{LKLZ}{ }^{1} \mathrm{~K}$ | 2021.31/2021.31 | $>64$ | >256 |  |  | 5 | 8 |
| 55b | ${ }^{2} \mathrm{KLKK}\left(\mathrm{K}^{1} \mathrm{LK}\right) \mathrm{KLK} Z^{2} \mathrm{LKLZ}{ }^{1} \mathrm{~K}$ | 2021.31/2021.31 | >64 | >256 |  |  | 5 | 8 |
| 56 a | ${ }^{1} \mathrm{KKKK}\left(\mathrm{K}^{2} \mathrm{KK}\right) \mathrm{KLLZ}{ }^{2} \mathrm{LLLZ}^{1} \mathrm{~K}$ | 2021.31/2021.31 | 4 | 128 | >32 | No disp. | 5 | 8 |
| 56b | ${ }^{2} \mathrm{KKKK}\left(\mathrm{K}^{1} \mathrm{KK}\right) \mathrm{KLLZ}{ }^{2} \mathrm{LLLZ}^{1} \mathrm{~K}$ | 2021.31/2022.31 | 2 | 32 | 32 | $75 \%$ | 5 | 8 |
| 57a | ${ }^{1} \mathrm{KLKK}\left(\mathrm{K}^{2} \mathrm{LK}\right) \mathrm{LKLZ}{ }^{2} \mathrm{KLK} Z^{1} \mathrm{~K}$ | 2021.31/2021.31 | >64 | >256 |  |  | 5 | 8 |
| 57b | ${ }^{2} \mathrm{KLKK}\left(\mathrm{K}^{1} \mathrm{LK}\right) \mathrm{LKLZ}{ }^{2} \mathrm{KLKZ}^{1} \mathrm{~K}$ | 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 $\mu \mathrm{g} / \mathrm{mL}$. 27b was tested against MRSA and MSSA and the activity was $>128 \mu \mathrm{~g} / \mathrm{mL}$.

| 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.

## $2^{\text {nd }}$ Library



Figure S2: Broth Microdilution Method to determine the MIC values of 27a and 27b against Bacillus subtilis; 2-fold dilution series starting from $256 \mu \mathrm{~g} / \mathrm{mL}$ (left side). Polymyxin B (dilution starting from $64 \mu \mathrm{~g} / \mathrm{mL}$ ) 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 $256 \mu \mathrm{~g} / \mathrm{mL}$ (right side).


Figure S3: Broth Microdilution Method to determine the MIC values of $\mathbf{6 2 b}$, 56b, 39b against Pseudomonas aeruginosa; 2-fold dilution series starting from $256 \mu \mathrm{~g} / \mathrm{mL}$ (left side). Polymyxin B (dilution starting from $64 \mu \mathrm{~g} / \mathrm{mL}$ ) was used as a reference (raw A-B). Raw 11 is used as growing control without compound ( $\mathrm{w} / \mathrm{o}$ ) 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 $\pm$ 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 $\pm$ 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 $\pm$ 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 $\pm$ 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 $\pm$ 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 $\pm$ 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 $\pm$ 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 $\pm$ 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 $\pm$ 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 $\pm$ 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 $\pm$ 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 $\pm$ SD.


Figure S16: Inhibition of Pseudomonas aeruginosa strain PA01 biofilms by 36b, 29b and $\mathbf{2 2}$ in synergy with 0.05 $\mu \mathrm{g} / \mathrm{mL}$ Tobramycin and $0.04 \mu \mathrm{~g} / \mathrm{mL}$ 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 $\pm$ SD.


Figure S17:Inhibition of Pseudomonas aeruginosa strain PA01 biofilms by 36b, 29b and $\mathbf{2 2}$ in synergy with $1.5 \mu \mathrm{~g} / \mathrm{mL}$
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 $\pm$ 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 $\pm$ 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 27 a ( $200 \mu \mathrm{~g} / \mathrm{mL}$ ). Time in seconds (x-axis) and absorbance intensity ( y -axis).


Figure S21 :Membrane PC interaction experiment of 27b ( $200 \mu \mathrm{~g} / \mathrm{mL}$ ). 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 ( $20 \mu \mathrm{~g} / \mathrm{ml}$ : 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 $20 \mu \mathrm{~g} / \mathrm{ml}$ of polymyxin B. C. Treatment with $32 \mu \mathrm{~g} / \mathrm{ml}$ of 62b. D. Treatment with $128 \mu \mathrm{~g} / \mathrm{ml}$ of $\mathbf{2 7 b}$.


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. $\mathbf{6 2 b}$ 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, $\mathrm{X}=$ 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( ( ${ }_{\text {a }}$ ) | 1.000040 | 1.000040 | 0.999990 |
| Resolution( A ) | 48.16-2.13 | 48.27-1.89 | 47.23-1.17 |
| Cell dimension |  |  |  |
| Space group | P 1211 | P 1211 | C 121 |
| Unit cell(Å) | $\begin{gathered} 48.31,79.36,52.58,90 \\ 94.46,90 \end{gathered}$ | $\begin{gathered} 48.42,79.20,52.63 \\ 90,94.52,90 \end{gathered}$ | $\begin{gathered} 94.41,45.77,88.06 \\ 90,94.24,90 \end{gathered}$ |
| 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/ $/ \mathrm{I}$ () | 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 ( A ) | 48.16-2.13 | 48.27-1.89 | 47.23-1.17 |
| $R_{\text {work }}$ (\%) | 0.174 | 0.176 | 0.132 |
| Rfree (\%) | 0.223 | 0.222 | 0.157 |
| Average Biso ( ${ }^{2}$ ) | 19.0 | 16.0 | 16.5 |
| All atoms | 3655 | 3757 | 3890 |
| Solvent atoms | 240 | 328 | 456 |
| RMSD from ideality angles ( ${ }^{\circ}$ ) | 0.832 | 0.884 | 1.160 |
| Bonds (Å) | 0.004 | 0.006 | 0.009 |
| Protein Data Bank deposition code | 518 M | 518 X | 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 $10 \mathrm{~A}^{0}$ 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. Ace 1 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 $\mathbf{1}^{\text {st }}$ cluster | \# of clusters | \# struct. in $\mathbf{1}^{\text {st }}$ 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 (backbonebackbone) 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 |

RMS fluctuation 27A


RMS fluctuation 27B


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 ]

; 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

[ LSB ] ; based on LYS, corrected for 53a6 FF
[ atoms]
$\mathrm{NZ} \quad \mathrm{N} \quad-0.31000 \quad 3$; ex- N , charge standard N
HZ H $0.31000 \quad 3$; only one H
CE CH1 0.00000 2; ex-CA charge group 2
CD CH2 0.00000 2; ex-CB
CG CH2 $0.00000 \quad 2$
CB CH2 0.00000 1; ex-CD
CA CH2 0.00000 1;ex-CE
N N -0.31000 0 ; ex-NZ
H H $0.31000 \quad 0$; ex-HZ
C $\quad$ C $0.450 \quad 4$
$\begin{array}{llll}\mathrm{O} & \mathrm{O} & -0.450 & 4\end{array}$
[ 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
$\mathrm{N} \quad-\mathrm{C} \quad \mathrm{CA} \quad \mathrm{H} \quad$ gi_1
C $\quad \mathrm{CE}+\mathrm{N} \quad \mathrm{O}$ 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 ]
$\begin{array}{llll}\mathrm{N} & \mathrm{N} & -0.31000 & 0\end{array}$
H $\quad \mathrm{H} \quad 0.31000 \quad 0$
CA CH1 $0.00000 \quad 1$
CB CH2 $0.24100 \quad 2$
$\begin{array}{llll}\text { SG } & \mathrm{S} & -0.48200 & 3\end{array}$
$\begin{array}{llll}\text { C } & \mathrm{C} & 0.450 & 4\end{array}$
$\begin{array}{llll}\mathrm{O} & \mathrm{O} & -0.450 & 4\end{array}$
[ 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
    \(\mathrm{O} \quad \mathrm{C}+\mathrm{N} \quad\) ga_33
    [ impropers ]
; ai aj ak al gromos type
    \(\mathrm{N} \quad-\mathrm{C} \quad \mathrm{CA} \quad \mathrm{H} \quad\) gi_1
    CA \(\mathrm{N} \quad \mathrm{C}\) 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 \(\quad\) gd_39
    N CA CB SG gd_34
    \(\mathrm{N} \quad \mathrm{CA} \quad \mathrm{C} \quad+\mathrm{N} \quad\) gd_40
```

[ ACC ] ;
[ atoms]
CA CH2 $0.241 \quad 0$
C $\quad$ C $\quad 0.450 \quad 1$
O O $\quad-0.450 \quad 1$
[ 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 $\mathrm{CA}+\mathrm{N} \quad \mathrm{O}$ gi_1

## 8. FTIR



Figure S28: FTIR characterization of bridged bicyclic peptides 26a, 26b, 27a, 27b, 29a and 29b. Fourier selfdeconvoluted ( $\mathrm{A}, \mathrm{C}$ ), and second derivative ( $\mathrm{B}, \mathrm{D}$, ) spectra of the bridged bicyclic peptides in $\mathrm{D}_{2} \mathrm{O} / \mathrm{PBS}$ at TFE concentrations of $0 \%$ (blue lines), $50 \%$ (green lines), and $90 \%$ (red lines).

## 9. HPLC and MS Data

${ }^{2} \mathbf{K}\left({ }^{1}\right) \mathbf{K} \boldsymbol{Z}^{1} \mathbf{K L} Z^{2} \mathbf{L}$ (1a) was obtained as foamy white solid after preparative RP-HPLC ( 24.4 mg , $18.5 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.440 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm})$. MS(ESI+): $\mathrm{C}_{40} \mathrm{H}_{71} \mathrm{~N}_{11} \mathrm{O}_{9} \mathrm{~S}_{2}$ calc./obs. 914.49/914.49 Da $[\mathrm{M}+\mathrm{H}]^{+}$.



${ }^{2} K\left({ }^{1}\right) \mathbf{K} \boldsymbol{Z}^{1} \mathbf{K L} Z^{2} \mathbf{L}(\mathbf{1 a )}$ was also obtained from the selective synthesis procedure as foamy white solid after preparative RP-HPLC ( $4.2 \mathrm{mg}, 3.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.540 \mathrm{~min}$ (A/D 100:0 to $0: 100$ in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm})$. $\mathrm{MS}(\mathrm{ESI}+)$ : $\mathrm{C}_{40} \mathrm{H}_{71} \mathrm{~N}_{11} \mathrm{O}_{9} \mathrm{~S}_{2}$ calc./obs. $914.49 / 914.49 \mathrm{Da}$ $[\mathrm{M}+\mathrm{H}]^{+}$.
${ }^{1} \mathbf{K}\left({ }^{2}\right) \mathbf{K} \boldsymbol{Z}^{1} \mathbf{K L} Z^{\mathbf{2}} \mathbf{L} \mathbf{( 1 b )}$ was obtained as foamy white solid after preparative RP-HPLC ( $7.7 \mathrm{mg}, 5.8$ $\%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.520 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). MS(ESI+): $\mathrm{C}_{40} \mathrm{H}_{71} \mathrm{~N}_{11} \mathrm{O}_{9} \mathrm{~S}_{2}$ calc./obs. 914.19/914.49 Da $[\mathrm{M}+\mathrm{H}]^{+}$.


${ }^{1} K\left({ }^{2}\right) K Z^{1} \mathbf{K L} Z^{2} \mathbf{L}$ (1b) was also obtained from the selective synthesis as foamy white solid after preparative RP-HPLC ( $6.4 \mathrm{mg}, 4.5 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.570 \mathrm{~min}$ (A/D 100:0 to 0:100 in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm})$. $\mathrm{MS}\left(\mathrm{ESI}+\right.$ ): $\mathrm{C}_{40} \mathrm{H}_{71} \mathrm{~N}_{11} \mathrm{O}_{9} \mathrm{~S}_{2}$ calc./obs. 914.19/914.49 Da $[\mathrm{M}+\mathrm{H}]^{+}$.
$\mathbf{L}^{2} \mathbf{K}\left(\mathbf{L}^{\mathbf{1}}\right) \mathbf{L K K} \boldsymbol{Z}^{1} \mathbf{K} \boldsymbol{Z}^{\mathbf{2}} \mathbf{( 2 a )}$ was obtained as foamy white solid after preparative RP-HPLC ( 10.6 mg , $6.3 \%)$. Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.930 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm})$. MS (ESI+): $\mathrm{C}_{52} \mathrm{H}_{94} \mathrm{~N}_{14} \mathrm{O}_{11} \mathrm{~S}_{2}$ calc./obs.1154.67/1554.66 Da [M].



DiBonaventura idb-46-1_150122090323_X...
1/26/2015 9:25:14 AM
Mass Spectrometry Service, Schuerch Group
DiBonaventura idb-46-1_150122090323_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 4.30E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.\mathbf{L}^{1} \mathbf{K}\left(\mathbf{L}^{\mathbf{2}}\right) \mathbf{L K K} \boldsymbol{Z}^{1} \mathbf{K} \boldsymbol{Z}^{\mathbf{2}} \mathbf{( 2 b}\right)$ was obtained as foamy white solid after preparative RP-HPLC ( 38.0 mg , $22.8 \%)$. Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.260 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ).

MS(ESI+): $\mathrm{C}_{52} \mathrm{H}_{94} \mathrm{~N}_{14} \mathrm{O}_{11} \mathrm{~S}_{2}$ calc./obs.1154.67/1154.66 Da [M].


DiBonaventura idb-46-2_150122090323_X...
1/26/2015 9:28:18 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura idb-46-2_150122090323_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 5.63E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.\mathbf{K}^{\mathbf{2}} \mathbf{K}\left(\mathbf{K}^{\mathbf{1}}\right) \mathbf{L L L} \mathbf{L} \mathbf{Z}^{\mathbf{1}} \mathbf{L} \boldsymbol{Z}^{\mathbf{2}} \mathbf{K} \mathbf{( 3 a}\right)$ was obtained as foamy white solid after preparative RP-HPLC (17.9 $\mathrm{mg}, 9.8 \%)$. Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=1.580 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in $5.00 \mathrm{~min}, \lambda=214 \mathrm{~nm})$. MS (ESI+): $\mathrm{C}_{58} \mathrm{H}_{105} \mathrm{~N}_{15} \mathrm{O}_{12} \mathrm{~S}_{2}$ calc./obs. $1267.75 / 1267.75 \mathrm{Da}$ [M].



DiBonaventura idb-31-1_141208092557_X...
12/12/2014 9:24:09 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
DiBonaventura idb-31-1 141208092557 XT 00001_M_\#1 RT: 1.0 AV: 1 NL: 5.42E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.\mathbf{K}^{\mathbf{1}} \mathbf{K}\left(\mathbf{K}^{2}\right) \mathbf{L L L} Z^{1} \mathbf{L} Z^{\mathbf{2}} \mathbf{K} \mathbf{( 3 b}\right)$ was obtained as foamy white solid after preparative RP-HPLC ( 7.6 mg , $4.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=1.600 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $5.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{58} \mathrm{H}_{105} \mathrm{~N}_{15} \mathrm{O}_{12} \mathrm{~S}_{2}$ calc./obs. $1267.75 / 1267.75 \mathrm{Da}[\mathrm{M}]$.


DiBonaventura idb-31-2_141208092557_X...
12/12/2014 10:48:02 AM
University of Bern, Departement of Chemistry and Biochemistry
DiBonaventura idb-31-2_141208092557_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 7.97E8 T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{L}^{\mathbf{1 2}} \mathbf{K}\left(\mathbf{L}^{\mathbf{1 2}}\right) \mathbf{K} \mathbf{K} \boldsymbol{Z}^{\mathbf{2 1}} \mathbf{K} \mathbf{L} \mathbf{L} \boldsymbol{Z}^{\mathbf{1 2}} \mathbf{( 4 )}$ was obtained as foamy white solid after preparative RP-HPLC (36.0 $\mathrm{mg}, 19.7 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.880 \mathrm{~min}(\mathrm{~A} / \mathrm{D} \mathrm{100:0}$ to 0:100 in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{58} \mathrm{H}_{106} \mathrm{~N}_{16} \mathrm{O}_{12} \mathrm{~S}_{2}$ calc./obs. 1282.76/1282.76 Da [M].



DiBonaventura idb-30_141208092557_XT_...
12/12/2014 9:20:41 AM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
DiBonaventura idb-30_141208092557_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 2.47E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{K}^{\mathbf{2}} \mathbf{K}\left(\mathbf{K}^{\mathbf{1}}\right) \mathbf{L K L} \mathbf{Z}^{\mathbf{1}} \mathbf{L K} \mathbf{Z}^{\mathbf{2}} \mathbf{( 5 a )}$ was obtained as foamy white solid after preparative RP-HPLC (13.8 $\mathrm{mg}, 7.4 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=1.410 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $5.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). $\mathrm{MS}(\mathrm{ESI}+)$ : $\mathrm{C}_{56} \mathrm{H}_{106} \mathrm{~N}_{16} \mathrm{O}_{12} \mathrm{~S}_{2}$ calc./obs. 1282.76/1282.76 Da [M].



DiBonaventura idb-47-1_150122090323_X...
1/26/2015 9:32:33 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura idb-47-1_150122090323_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 3.03E8 T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.\mathbf{K}^{\mathbf{1}} \mathbf{K}\left(\mathbf{K}^{\mathbf{2}}\right) \mathbf{L K} \mathbf{L} \mathbf{Z}^{\mathbf{1}} \mathbf{L K} \mathbf{Z}^{\mathbf{2}} \mathbf{( 5 b}\right)$ was obtained as foamy white solid after preparative RP-HPLC (19.5 $\mathrm{mg}, 10.5 \%)$. Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=1.470 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $5.00 \mathrm{~min}, \lambda=214 \mathrm{~nm})$. MS(ESI+): $\mathrm{C}_{56} \mathrm{H}_{106} \mathrm{~N}_{16} \mathrm{O}_{12} \mathrm{~S}_{2}$ calc./obs.1282.76/1282.76 Da [M].


DiBonaventura idb-47-2_150122090323_X...
1/26/2015 9:35:29 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura idb-47-2_150122090323_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.42E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$+\mathbf{K}^{\mathbf{2}} \mathbf{K}\left(\mathbf{K}^{\mathbf{1}}\right) \mathbf{L K L} Z^{\mathbf{1}} \mathbf{L L K} Z^{\mathbf{2}} \mathbf{L}(\mathbf{6 a})$ was obtained as foamy white solid after preparative RP-HPLC (9.0 $\mathrm{mg}, 4.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.060 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{70} \mathrm{H}_{128} \mathrm{~N}_{18} \mathrm{O}_{14} \mathrm{~S}_{2}$ calc./obs.1508.93/1508.93 Da [M].



DiBonaventura idb-45-1_150122090323_X...
1/26/2015 9:18:15 AM
University of Bern, Departement of Chemistry and Biochemistry
DiBonaventura idb-45-1_150122090323_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 5.24E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{K}^{1} \mathbf{K}\left(\mathbf{K}^{2}\right) \mathbf{L K L} Z^{1} \mathbf{K L L} Z^{\mathbf{2}} \mathbf{L} \mathbf{( 6 b )}$ was obtained as foamy white solid after preparative RP-HPLC (20.0 $\mathrm{mg}, 9.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.160 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{70} \mathrm{H}_{128} \mathrm{~N}_{18} \mathrm{O}_{14} \mathrm{~S}_{2}$ calc./obs.1508.93/1508.93 Da [M].


DiBonaventura idb-45-2_150122090323_X...
1/26/2015 9:22:00 AM
University of Bern, Departement of Chemistry and Biochemistry

T: FTMS + p NSI Full ms [150.00-2000.00]

 ( $6.3 \mathrm{mg}, 2.9 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.010 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{70} \mathrm{H}_{128} \mathrm{~N}_{18} \mathrm{O}_{14} \mathrm{~S}_{2}$ calc./obs.1508.93/1508.93 Da [M].


12/12/2014 11:06:37 AM
DiBonaventura idb-34-1_141208092557_X...
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
DiBonaventura idb-34-1_141208092557_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 3.86E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{K}^{\mathbf{1}} \mathbf{L K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L}\right) \mathbf{K K K} \mathbf{Z}^{\mathbf{2}} \mathbf{L L} \mathbf{Z}^{\mathbf{1}}$ (8a) was obtained as foamy white solid after preparative RP-HPLC (8.4 $\mathrm{mg}, 3.8 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=7.510 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $20.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{70} \mathrm{H}_{129} \mathrm{~N}_{19} \mathrm{O}_{14} \mathrm{~S}_{2}$ calc./obs. $1523.94 / 1523.94 \mathrm{Da}[\mathrm{M}]$.



Bonventura idb 27_1_141107084343_XT_0...
1/9/2017 4:29:45 PM
LTQ Orbitrap XL
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonventura idb 27_1_141107084343_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.59E8
T: FTMS + p NSI Full ms [150.00-2000.00

$\left.\mathbf{K}^{\mathbf{1}} \mathbf{L} \boldsymbol{K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L}\right) \mathbf{K K K} \mathbf{Z}^{\mathbf{1}} \mathbf{L} \mathbf{L} \mathbf{Z}^{\mathbf{2}} \mathbf{( 8 b}\right)$ was obtained as foamy white solid after preparative RP-HPLC (29.4 $\mathrm{mg}, 13.4 \%)$. Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=7.910 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in $20.00 \mathrm{~min}, \lambda=214 \mathrm{~nm})$. MS (ESI+): $\mathrm{C}_{70} \mathrm{H}_{129} \mathrm{~N}_{19} \mathrm{O}_{14} \mathrm{~S}_{2}$ calc./obs. $1523.94 / 1523.94 \mathrm{Da}[\mathrm{M}]$.


Bonventura idb 27_2_141107084343_XT_0...
1/9/2017 4:33:08 PM
University of Bern, Departement of Chemistry and Biochemistry
Bonventura idb 27_2_141107084343_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.98E7
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{L}^{\mathbf{1}} \mathbf{L} \mathbf{K}\left(\mathbf{L}^{\mathbf{2}} \mathbf{L}\right) \mathbf{K K} \mathbf{Z}^{\mathbf{2}} \mathbf{K} \mathbf{K} \mathbf{L} \mathbf{Z}^{\mathbf{1}} \mathbf{L} \mathbf{( 9 a )}$ was obtained as foamy white solid after preparative RP-HPLC (5.7 $\mathrm{mg}, 2.4 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.500 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{76} \mathrm{H}_{139} \mathrm{~N}_{19} \mathrm{O}_{15} \mathrm{~S}_{2}$ calc./obs. $1622.01 / 1622.01 \mathrm{Da}[\mathrm{M}]$.


di Bonaventura idb-26-1_141107084343_..
11/7/2014 10:16:41 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
di Bonaventura idb-26-1_141107084343_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 2.43E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.\mathbf{L}^{\mathbf{1}} \mathbf{L K}\left(\mathbf{L}^{\mathbf{2}} \mathbf{L}\right) \mathbf{K K} \boldsymbol{Z}^{\mathbf{1}} \mathbf{K} \mathbf{K} \mathbf{L} \mathbf{Z}^{\mathbf{2}} \mathbf{L} \mathbf{( 9 b}\right)$ was obtained as foamy white solid after preparative RP-HPLC (2.1 $\mathrm{mg}, 0.9 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.570 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{76} \mathrm{H}_{139} \mathrm{~N}_{19} \mathrm{O}_{15} \mathrm{~S}_{2}$ calc./obs. $1622.01 / 1622.01 \mathrm{Da}[\mathrm{M}]$.

di Bonaventura idb-26-2_141107084343_..
11/7/2014 11:27:08 AM
University of Bern, Departement of Chemistry and Biochemistry
di Bonaventura idb-26-2_141107084343_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.07E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{K}^{\mathbf{1}} \mathbf{L K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L}\right) \mathbf{K L L} \mathbf{Z}^{\mathbf{2}} \mathbf{K L L} \boldsymbol{Z}^{\mathbf{1}} \mathbf{K}$ (10a) was obtained as foamy white solid after preparative RP-HPLC ( $11.5 \mathrm{mg}, 4.5 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.120 \mathrm{~min}$ (A/D 100:0 to 0:100 in 5.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{82} \mathrm{H}_{151} \mathrm{~N}_{21} \mathrm{O}_{16} \mathrm{~S}_{2}$ calc./obs.1750.11/1750.11 Da [M].



Bonaventura idb-37-1_141219153205_XT_...
1/6/2015 10:46:31 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
Bonaventura idb-37-1_141219153205_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 2.71E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{K}^{\mathbf{1}} \mathbf{L} \boldsymbol{K}\left(\mathbf{K}^{2} \mathbf{L}\right) \mathbf{K L L} \mathbf{Z}^{1} \mathbf{K L L} Z^{\mathbf{2}} \mathbf{K}(\mathbf{1 0 b})$ was obtained as foamy white solid after preparative RP-HPLC ( $2.9 \mathrm{mg}, 1.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.590 \mathrm{~min}$ (A/D 100:0 to 0:100 in 5.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{82} \mathrm{H}_{151} \mathrm{~N}_{21} \mathrm{O}_{16} \mathrm{~S}_{2}$ calc./obs.1750.11/1750.11 Da [M].


Bonaventura idb-37-2_141219153205_XT_...
1/6/2015 10:52:45 AM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonaventura idb-37-2_141219153205_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 2.32E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{L}^{1} \mathbf{L} \boldsymbol{K}\left(\mathbf{L}^{\mathbf{2}} \mathbf{L}\right) \mathbf{K L K} \boldsymbol{Z}^{2} \mathbf{K K L} \mathbf{Z}^{\mathbf{1}} \mathbf{K}$ (11a) was obtained as foamy white solid after preparative RP-HPLC (37.3 mg, $14.7 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.910 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{82} \mathrm{H}_{151} \mathrm{~N}_{21} \mathrm{O}_{16} \mathrm{~S}_{2}$ calc./obs.1750.11/1750.11 Da [M].



Bonaventura idb-38-1_141219153205_XT_...
1/6/2015 10:57:30 AM
Mass Spectrometry Service, Schuerch Group
Bonaventura idb-38-1_141219153205_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 4.71E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{L}^{1} \mathbf{L K}\left(\mathbf{L}^{2} \mathbf{L}\right) \mathbf{K L K} \mathbf{Z}^{1} \mathbf{K K L} Z^{2} \mathbf{K}(\mathbf{1 1 b})$ was obtained as foamy white solid after preparative RP-HPLC ( $11.5 \mathrm{mg}, 4.5 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.090 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{82} \mathrm{H}_{151} \mathrm{~N}_{21} \mathrm{O}_{16} \mathrm{~S}_{2}$ calc./obs.1750.11/1750.11 Da [M].


Bonaventura idb-38-2_141219153205_XT_...
1/6/2015 11:04:28 AM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonaventura idb-38-2_141219153205_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 3.97E7
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{K}^{12} \mathbf{L K K}\left(\mathbf{K}^{12} \mathbf{L K}\right) \mathbf{L L} Z^{21} \mathbf{K L L} Z^{12}(\mathbf{1 2 )}$ was obtained as foamy white solid after preparative RPHPLC ( $6.9 \mathrm{mg}, 2.7 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.250 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{82} \mathrm{H}_{151} \mathrm{~N}_{21} \mathrm{O}_{16} \mathrm{~S}_{2}$ calc./obs.1750.11/1750.11 Da [M].



Bonaventura idb-39_141219153205_XT_00...
1/6/2015 11:09:40 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
Bonaventura idb-39_141219153205_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.93E7
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{K}^{\mathbf{2}} \mathbf{L L K}\left(\mathbf{K}^{1} \mathbf{L L}\right) \mathbf{K L} Z^{1} \mathbf{K K L Z} \mathbf{Z}^{\mathbf{2}}$ (13a) was obtained as foamy yellow solid after preparative RP-HPLC ( $12.7 \mathrm{mg}, 5.0 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.080 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{82} \mathrm{H}_{151} \mathrm{~N}_{21} \mathrm{O}_{16} \mathrm{~S}_{2}$ calc./obs.1750.11/1750.11 Da [M].



Bonaventura idb-40-1_141219153205_XT_...
1/6/2015 11:14:38 AM
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
Bonaventura idb-40-1_141219153205_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 2.31E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{K}^{\mathbf{1}} \mathbf{L L K}\left(\mathbf{K}^{2} \mathbf{L L}\right) \mathbf{K L} Z^{1} \mathbf{K K L} Z^{2}(\mathbf{1 3 b})$ was obtained as foamy white solid after preparative RP-HPLC ( $7.9 \mathrm{mg}, 3.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.250 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100 \mathrm{in} 10.00 \mathrm{~min}$, $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{82} \mathrm{H}_{151} \mathrm{~N}_{21} \mathrm{O}_{16} \mathrm{~S}_{2}$ calc./obs.1750.11/1750.11 Da [M].


Bonaventura idb-40-2_141219153205_XT_...
1/6/2015 11:24:28 AM
University of Bern, Departement of Chemistry and Biochemistry
Bonaventura idb-40-2_141219153205_XT_00001_M__150106112428 \#1 RT: 1.0 AV: 1 NL: 2.38E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{K}^{\mathbf{2}} \mathbf{L L K}\left(\mathbf{K}^{1} \mathbf{L L}\right) \mathbf{K K} \boldsymbol{Z}^{1} \mathbf{K L} Z^{2} \mathbf{L}$ (14a) was obtained as foamy white solid after preparative RP-HPLC ( $10.6 \mathrm{mg}, 4.2 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.010 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{82} \mathrm{H}_{151} \mathrm{~N}_{21} \mathrm{O}_{16} \mathrm{~S}_{2}$ calc./obs.1750.11/1750.11 Da [M].



DiBonaventura idb-35-1_141208092557_X...
12/12/2014 11:18:12 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura idb-35-1_141208092557_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.79E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{K}^{\mathbf{1}} \mathbf{L L K}\left(\mathbf{K}^{2} \mathbf{L L}\right) \mathbf{K K} \boldsymbol{Z}^{1} \mathbf{K L} \boldsymbol{Z}^{\mathbf{2}} \mathbf{L}(\mathbf{1 4 b})$ was obtained as foamy white solid after preparative RP-HPLC ( $31.8 \mathrm{mg}, 12.6 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.100 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{82} \mathrm{H}_{151} \mathrm{~N}_{21} \mathrm{O}_{16} \mathrm{~S}_{2}$ calc./obs.1750.11/1750.11 [M].


DiBonaventura idb-35-2_141208092557_X...
12/12/2014 11:25:31 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura idb-35-2_141208092557_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 3.84E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{L}^{\mathbf{1 2}} \mathbf{K} K\left(\mathbf{L}^{12} \mathbf{K}\right) \mathbf{K L K} Z^{\mathbf{2}} \mathbf{L} \mathbf{L K} Z^{12} \mathbf{L}(\mathbf{1 5})$ was obtained, like a mixture of isomers, as foamy white solid after preparative RP-HPLC ( $13.4 \mathrm{mg}, 5.3 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=11.810 \mathrm{~min}, 11.930 \mathrm{~min}$ (A/D 100:0 to 0:100 in $20.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{82} \mathrm{H}_{151} \mathrm{~N}_{21} \mathrm{O}_{16} \mathrm{~S}_{2}$ calc./obs. 1750.11/1750.11 Da [M].



DiBonaventura idb-32_141208092557_XT_...
12/12/2014 10:51:57 AM
Mass Spectrometry Service, Schuerch Group
DiBonaventura idb-32_141208092557_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.78E8
T: FTMS + p NSI Full ms [150.00-2000.00]

|  |  |  |  |  | 1750.11 |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 170000000 |  |  |  |  |  |  |  |  |
| 160000000 |  |  |  |  |  |  |  |  |
| 150000000 |  |  |  |  |  |  |  |  |
| 140000000 |  |  |  |  |  |  |  |  |
| 130000000 |  |  |  |  |  |  |  |  |
| 120000000 |  |  |  |  |  |  |  |  |
| 110000000 |  |  |  |  |  |  |  |  |
| 100000000 |  |  |  |  |  |  | 1752.11 |  |
|  |  |  |  |  |  |  |  |  |
| 70000000 |  |  |  |  |  |  |  |  |
| 60000000 |  |  |  |  |  |  |  |  |
| 50000000 |  |  |  |  |  |  | 1753.11 |  |
| 40000000 |  |  |  |  |  |  |  |  |
| 30000000 |  |  |  |  |  |  | 1772.09 |  |
| 20000000 |  |  |  |  |  |  | $\begin{aligned} & 1774.09 \\ & 1795.07 \end{aligned}$ |  |
| 10000000 |  |  |  |  | 1620.00 | 1733.08 |  |  |
|  |  |  |  |  |  |  |  |  |
| 1100 | 1200 | 1300 | 1400 | 1500 | 1600 | 1700 | 1800 | 1900 |
|  |  |  |  |  |  |  |  |  |

$\mathbf{K}^{\mathbf{2}} \mathbf{L K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L}\right) \mathbf{L K L} \boldsymbol{Z}^{\mathbf{1}} \mathbf{K K L} \boldsymbol{Z}^{\mathbf{2}} \mathbf{K}$ (16a) was obtained as foamy white solid after preparative RP-HPLC $(24.8 \mathrm{mg}, 9.0 \%)$. Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=1.360 \mathrm{~min}$ (A/D 100:0 to 0:100 in $5.0 \mathrm{~min}, \lambda=214$ $\mathrm{nm})$. MS (ESI+): $\mathrm{C}_{82} \mathrm{H}_{152} \mathrm{~N}_{22} \mathrm{O}_{16} \mathrm{~S}_{2}$ calc./obs. 1765.12/176512 Da [M].


di Bonaventura idb-25-1_141107084343_..
11/7/2014 9:28:36 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
di Bonaventura idb-25-1_141107084343_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 7.07E7
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{K}^{\mathbf{1}} \mathbf{L K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L}\right) \mathbf{L K L} \mathbf{Z}^{1} \mathbf{K K L} Z^{2} \mathbf{K}(\mathbf{1 6 b})$ was obtained as foamy white solid after preparative RP-HPLC ( $4.4 \mathrm{mg}, 1.7 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=1.380 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $5.0 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{82} \mathrm{H}_{152} \mathrm{~N}_{22} \mathrm{O}_{16} \mathrm{~S}_{2}$ calc./obs. 1765.12/176512 Da [M].

di Bonaventura idb-25-2_141107084343_..
11/7/2014 10:12:37 AM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
di Bonaventura idb-25-2_141107084343_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.66E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$K^{\mathbf{2}} \mathbf{K L K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{K L}\right) \mathbf{K K} Z^{1} \mathbf{L} L L Z^{\mathbf{2}} \mathbf{K}$ (17a) was obtained as foamy white solid after preparative RPHPLC ( $24.8 \mathrm{mg}, 9.0 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=1.390 \mathrm{~min}$ (A/D 100:0 to 0:100 in 5.0 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{88} \mathrm{H}_{164} \mathrm{~N}_{24} \mathrm{O}_{17} \mathrm{~S}_{2}$ calc./obs. 1893.21/1893.22 Da [M].


Bonventura idb 24_1_141107084343_XT_0...
1/9/2017 5:07:18 PM


LTQ Orbitrap XL
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonventura idb 24_1_141107084343_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 9.70E6
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{K}^{\mathbf{1}} \mathbf{K L K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{K L}\right) \mathbf{K K} Z^{\mathbf{1}} \mathbf{L} \mathbf{L L} Z^{\mathbf{2}} \mathbf{K}(\mathbf{1 7 b})$ was obtained as foamy white solid after preparative RPHPLC ( $20.9 \mathrm{mg}, 7.6 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=1.570 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in 5.0 min , $\lambda=214 \mathrm{~nm})$. MS (ESI+): $\mathrm{C}_{88} \mathrm{H}_{164} \mathrm{~N}_{24} \mathrm{O}_{17} \mathrm{~S}_{2}$ calc./obs. 1893.21/1893.22 Da [M].


Bonventura idb 24_2_141107084343_XT_0...
1/9/2017 5:10:18 PM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonventura idb 24_2_141107084343_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 2.25E7
T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{K}^{\mathbf{1}} \mathbf{L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{L K} \mathbf{L Z}^{\mathbf{2}} \mathbf{L L L} \mathbf{Z}^{1} \mathbf{L} \mathbf{( 1 8 a )}$ was obtained as foamy white solid after preparative RPHPLC ( $4.4 \mathrm{mg}, 1.6 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.950 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs.1991.29/1991.29 Da [M].



DiBonaventura idb-36-1_141208092557_X...
12/12/2014 11:36:46 AM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
DiBonaventura idb-36-1_141208092557_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.60E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.\mathbf{K}^{\mathbf{1}} \mathbf{L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{L K} \mathbf{K Z}^{\mathbf{1}} \mathbf{L L L} \mathbf{Z}^{\mathbf{2}} \mathbf{L} \mathbf{( 1 8 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $5.5 \mathrm{mg}, 1.9 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.120 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs.calc./obs.1991.29/1991.29 Da [M].


DiBonaventura idb-36-2_141208092557_X...
12/12/2014 11:40:04 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura idb-36-2_141208092557_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 2.92E8 T: FTMS + p NSI Full ms [150.00-2000.00]

$\mathbf{K}^{\mathbf{1 2}} \mathbf{L K K}\left(\mathbf{K}^{\mathbf{1 2}} \mathbf{L K}\right) \mathbf{L L L} \mathbf{Z}^{\mathbf{2 1}} \mathbf{K} \mathbf{L K} \mathbf{Z}^{\mathbf{1 2}} \mathbf{L}(\mathbf{1 9})$ was obtained as foamy white solid after preparative RPHPLC ( $7.9 \mathrm{mg}, 2.7 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=1.510 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 5.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.29 Da [M].



DiBonaventura idb-29-1 141208092557 X...
12/12/2014 9:13:07 AM
LTQ Orbitrap XL
University of Bern, Departement of Chemistry
Mass Spectrometry Service, Schuerch Group
Mass Spectrometry Service, Schuerch Group
T: FTMS $+\mathrm{p} \mathrm{NSI} \mathrm{Full} \mathrm{ms} \mathrm{[150.00-2000.00]}$

${ }^{12} \mathbf{L L K K}\left(\mathbf{L}^{\mathbf{1 2}} \mathbf{L K}\right) \mathbf{L L L} Z^{\mathbf{2}} \mathbf{K L K} \boldsymbol{Z}^{\mathbf{1 2}} \mathbf{L} \mathbf{( 2 0 )}$ was obtained as foamy white solid after preparative RPHPLC ( $11.6 \mathrm{mg}, 5.2 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=4.070 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}) . \mathrm{MS}(\mathrm{ESI}+): \mathrm{C}_{94} \mathrm{H}_{172} \mathrm{~N}_{22} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs.1961.27/1961.27 Da [M].



DiBonaventura IDB-49_XT_00001_M_
3/12/2015 9:29:59 AM

University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-49_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 6.15E7
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{1} \mathbf{L K}\right) \mathbf{L L L} Z^{1} \mathbf{L L L Z}{ }^{\mathbf{2}} \mathbf{L}$ (21a) was obtained, as foamy white solid after preparative RPHPLC ( $6.7 \mathrm{mg}, 3.0 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=4.280 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS(ESI+): $\mathrm{C}_{94} \mathrm{H}_{172} \mathrm{~N}_{22} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs.1961.27/1961.27 Da [M].


DiBonaventura IDB-50-1_XT_00001_M_
3/12/2015 8:31:49 AM
University of Bern, Departement of Chemistry and Biochemistry

$\left.{ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{L L L} \mathbf{Z}^{\mathbf{1}} \mathbf{L L L} \mathbf{Z}^{\mathbf{2}} \mathbf{L} \mathbf{( 2 1 b}\right)$ was obtained, as foamy white solid after preparative RPHPLC ( $3.7 \mathrm{mg}, 1.6 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=4.570 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}) . \mathrm{MS}\left(\mathrm{ESI}+\right.$ ): $\mathrm{C}_{94} \mathrm{H}_{172} \mathrm{~N}_{22} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs.1961.27/1961.27 Da [M].


DiBonaventura IDB-50-2_XT_00001_M_ 3/12/2015 8:36:57 AM
University of Bern, Departement of Chemistry and Biochemistry
DiBonaventura IDB-50-2_XT_00001_M \#1 RT: 1.0 AV: 1 NL: 2.87ET
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{12} \mathbf{K L L K}\left(\mathbf{K}^{12} \mathbf{L L}\right) \mathbf{K L L} Z^{\mathbf{2 1}} \mathbf{K L L} Z^{12} \mathbf{L}(\mathbf{2 2})$ was obtained as foamy white solid after preparative RPHPLC ( $8.9 \mathrm{mg}, 4.0 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.910 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm})$. MS(ESI+): $\mathrm{C}_{94} \mathrm{H}_{172} \mathrm{~N}_{22} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs.1961.27/1961.28 Da [M].



DiBonaventura IDB-51_XT_00001_M_
3/12/2015 8:40:38 AM
LTQ Orbitrap XL
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-51_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 2.32E7
$\mathrm{T}:$ FTMS +p NSI Full ms [ $\overline{150.00-\overline{2} 000.00]}$

$\left.{ }^{12} \mathbf{L} \mathbf{L K K}\left(\mathbf{L}^{\mathbf{1 2}} \mathbf{L K}\right) \mathbf{K L L} \mathbf{Z}^{\mathbf{2 1}} \mathbf{K} \mathbf{L K} Z^{\mathbf{1 2}} \mathbf{L} \mathbf{( 2 3}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $17.0 \mathrm{mg}, 7.6 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.540 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100 \mathrm{in} 10.00 \mathrm{~min}$, $\lambda=214 \mathrm{~nm})$. MS(ESI+): $\mathrm{C}_{94} \mathrm{H}_{173} \mathrm{~N}_{23} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs.1976.28/1976.29 Da [M].



DiBonaventura IDB-52_XT_00001_M_
3/12/2015 8:58:32 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-52_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 5.92E7
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{12} \mathbf{L} \mathbf{L K K}\left(\mathbf{L}^{\mathbf{1 2}} \mathbf{L K}\right) \mathbf{K} \mathbf{L K} \mathbf{Z}^{\mathbf{2 1}} \mathbf{L L K} \mathbf{Z}^{\mathbf{1 2}} \mathbf{L} \mathbf{( 2 4 )}$ was obtained as foamy white solid after preparative RPHPLC ( $4.8 \mathrm{mg}, 2.4 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.060 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS(ESI+): $\mathrm{C}_{94} \mathrm{H}_{173} \mathrm{~N}_{23} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1976.28/1976.28 Da [M].


Bonventura IDB 65_1_150601111542_XT_0...
6/1/2015 2:38:06 PM


University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonventura IDB 65_1_150601111542_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.57E8 T: FTMS $+\mathrm{p} \mathrm{NSI} \mathrm{Full} \mathrm{ms} \mathrm{[400.00-2000.00]}$

${ }^{2} \mathbf{L L K K}\left(\mathbf{L}^{\mathbf{1}} \mathbf{L K}\right) \mathbf{K L K} \mathbf{Z}^{1} \mathbf{K L L Z} \mathbf{Z}^{\mathbf{2}} \mathbf{K}$ (25a) was obtained as foamy white solid after preparative RPHPLC ( $7.4 \mathrm{mg}, 3.3 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.020 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.30 Da [M].



DiBonaventura IDB-57-1_XT_00001_M_
3/12/2015 1:05:02 PM
LTQ Orbitrap XL
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-57-1_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 2.40E7
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.{ }^{\mathbf{1}} \mathbf{L L K K}\left(\mathbf{L}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{K L K} \mathbf{Z}^{\mathbf{1}} \mathbf{K L L} Z^{\mathbf{2}} \mathbf{K} \mathbf{( 2 5 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $4.9 \mathrm{mg}, 2.8 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.120 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 n m$ ). MS(ESI + ): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.30 Da [M].


DiBonaventura IDB-57-2_XT_00001_M_
3/12/2015 1:08:30 PM
University of Bern, Departement of Chemistry and Biochemistry

T: FTMS $+p$ NSI Full ms [ $15 \overline{0} .00-20 \overline{0} 0 . \overline{0} 0$ ]

${ }^{1} \mathbf{K L L K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L L}\right) \mathbf{K L L Z} \mathbf{Z}^{\mathbf{2}} \mathbf{K L K} Z^{1} \mathbf{K}$ (26a) was obtained as foamy white solid after preparative RPHPLC ( $5.8 \mathrm{mg}, 2.6 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.340 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.30 Da [M].



DiBonaventura IDB-58-1_XT_00001_M_
3/12/2015 9:06:07 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-58-1_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 4.17E7
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{1} \mathbf{K L L K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L L}\right) \mathbf{K L L} Z^{1} \mathbf{K L K} Z^{\mathbf{2}} \mathbf{K}(\mathbf{2 6 b})$ was obtained as foamy white solid after preparative RPHPLC ( $23.0 \mathrm{mg}, 10.3 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.640 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.30 Da [M].


DiBonaventura IDB-58-2_XT_00001_M_
3/12/2015 9:09:55 AM
University of Bern, Departement of Chemistry and Biochemistry

T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L K}\right) \mathbf{K L L} Z^{1} \mathbf{L L L Z} \mathbf{Z}^{\mathbf{2}} \mathbf{K}$ (27a) was obtained as foamy white solid after preparative RPHPLC ( $19.9 \mathrm{mg}, 8.8 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.140 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.30 Da [M].


DiBonaventura IDB-59-1_XT_00001_M_ 3/12/2015 9:22:03 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-59-1_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 5.00E7
T: FTMS +p NSI Full ms [ $15 \overline{0} .00-20 \overline{0} 0 . \overline{0} 0$ ]

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{1} \mathbf{L K}\right) \mathbf{K L L Z}{ }^{1} \mathbf{L L L} Z^{\mathbf{2}} \mathbf{K}$ (27a) was also obtained from the selective synthesis procedure as foamy white solid after preparative RP-HPLC ( $0.3 \mathrm{mg}, 0.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.140$ $\min \left(\mathrm{A} / \mathrm{D} 100: 0\right.$ to $0: 100$ in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). $\mathrm{MS}\left(\mathrm{ESI}+\right.$ ): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.30 Da [M].
${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{K L L} Z^{1} \mathbf{L L L} Z^{\mathbf{2}} \mathbf{K}(\mathbf{2 7 b})$ was obtained as foamy white solid after preparative RPHPLC ( $13.2 \mathrm{mg}, 5.9 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.370 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.30 Da [M].


DiBonaventura IDB-59-2_XT_00001_M_ 3/12/2015 9:26:00 AM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Servie LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
RT: 1.0 AV: $1 \mathrm{NL}: 8.92 \mathrm{E} 7$
DiBonaventura IDB-59-2_XT_00001_M_\#1
T: FTMS +p NSI Full ms [150.00-2000.00]

${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{2} \mathbf{L K}\right) \mathbf{K L L Z} \mathbf{Z}^{1} \mathbf{L L L Z} \mathbf{Z}^{\mathbf{2}} \mathbf{K}$ (27b) was also obtained from the selective synthesis procedure as foamy white solid after preparative RP-HPLC ( $0.2 \mathrm{mg}, 0.09 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.370$ $\min \left(A / D 100: 0\right.$ to 0:100 in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.30 Da [M].
${ }^{2} \mathbf{K L L K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L L}\right) \mathbf{K L K} Z^{1} \mathbf{K K L Z} \mathbf{Z}^{\mathbf{2}} \mathbf{L} \mathbf{( 2 8 a )}$ was obtained as foamy white solid after preparative RPHPLC ( $17.5 \mathrm{mg}, 6.3 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.000 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100 \mathrm{in} 10.00 \mathrm{~min}$, $\lambda=214 \mathrm{~nm}$ ). MS(ESI + ): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.29 Da [M].



Bonventura idb 62_1_150330143207_XT_0...
3/30/2015 3:29:55 PM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
Bonventura idb 62_1_150330143207_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.21E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.{ }^{1} \mathbf{K L L K}\left(\mathbf{K}^{2} \mathbf{L L}\right) \mathbf{K L K} \mathbf{Z}^{1} \mathbf{K K L} Z^{2} \mathbf{L} \mathbf{( 2 8 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $7.0 \mathrm{mg}, 2.5 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.070 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 n m$ ). MS(ESI + ): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.29 Da [M].


Bonventura idb 62_2_150330143207_XT_O...
3/30/2015 3:32:52 PM
University of Bern, Departement of Chemistry and Biochemistry
Bonventura idb 62_2_150330143207_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 8.10E7
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.{ }^{2} \mathbf{K L L K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L L}\right) \mathbf{K L L Z} \mathbf{Z}^{1} \mathbf{K K K Z}{ }^{\mathbf{2}} \mathbf{L} \mathbf{( 2 9 a}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $9.8 \mathrm{mg}, 3.5 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.280 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS(ESI + ): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.29 Da [M].
Peptide-LCMS-100A-100D-10min-HESI+C


Bonventura idb 63_1_150330143207_XT_0...
3/30/2015 3:35:27 PM
LTQ Orbitrap XL
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonventura idb 63_1_150330143207_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.77E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.{ }^{1} \mathbf{K L L K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L L}\right) \mathbf{K L L} Z^{\mathbf{1}} \mathbf{K K K Z} \mathbf{Z}^{\mathbf{2}} \mathbf{L} \mathbf{( 2 9 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $27.7 \mathrm{mg}, 10.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.570 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in 10.00 min , $\lambda=214 \mathrm{~nm}) . \mathrm{MS}\left(\mathrm{ESI}+\right.$ ): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.29 Da [M].


Bonventura idb 63_2_150330143207_XT_0... 3/30/2015 3:38:35 PM
University of Bern, Departement of Chemistry and Biochemistry

T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.{ }^{2} \mathbf{K L L K}\left(\mathbf{K}^{1} \mathbf{L L}\right) \mathbf{L K} \boldsymbol{Z}^{1} \mathbf{K L K} \boldsymbol{Z}^{2} \mathbf{L} \mathbf{( 3 0 a}\right)$ was obtained as foamy white solid after preparative RP-HPLC ( $12.6 \mathrm{mg}, 4.9 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.140 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{88} \mathrm{H}_{162} \mathrm{~N}_{22} \mathrm{O}_{17} \mathrm{~S}_{2}$ calc./obs. 1863.19/1863.19 Da [M].


Bonventura idb 64_1_150420110031_XT_0...
4/20/2015 11:14:09 AM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonventura idb 64_1_150420110031_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.16E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.{ }^{1} \mathbf{K L L K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L L}\right) \mathbf{L K} Z^{1} \mathbf{K L K Z}{ }^{\mathbf{2}} \mathbf{L} \mathbf{( 3 0 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $2.9 \mathrm{mg}, 1.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.250 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{88} \mathrm{H}_{162} \mathrm{~N}_{22} \mathrm{O}_{17} \mathrm{~S}_{2}$ calc./obs. 1863.19/1863.19 Da [M].


Bonventura idb 64_2_150420110031_XT_O... 4/20/2015 3:39:55 PM
University of Bern, Departement of Chemistry and Biochemistry

T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L K}\right) \mathbf{K K L Z} \mathbf{Z}^{\mathbf{1}} \mathbf{L L K} Z^{\mathbf{2}} \mathbf{L}$ (31a) was obtained as foamy white solid after preparative RPHPLC ( $33.4 \mathrm{mg}, 15.8 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.830 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{88} \mathrm{H}_{163} \mathrm{~N}_{23} \mathrm{O}_{17} \mathrm{~S}_{2}$ calc./obs. 1878.20/1878.21 Da [M].



DiBonaventura IDB-56-1_XT_00001_M_
3/12/2015 9:14:19 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-56-1_XT_00001_M_\#1 RT: 1.0 AV: $1 \mathrm{NL}: 5.10 \mathrm{E} 7$
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.{ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{K K L Z} \mathbf{Z}^{\mathbf{1}} \mathbf{L L K} \mathbf{Z}^{\mathbf{2}} \mathbf{L} \mathbf{( 3 1 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $12.5 \mathrm{mg}, 5.9 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.880 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{88} \mathrm{H}_{163} \mathrm{~N}_{23} \mathrm{O}_{17} \mathrm{~S}_{2}$ calc./obs. 1878.20/1878.21 Da [M].


DiBonaventura IDB-56-2_XT_00001_M_
3/12/2015 9:17:57 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-56-2_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 2.54E7
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{1} \mathbf{L K}\right) \mathbf{L L Z} \mathbf{Z}^{1} \mathbf{L K L Z}{ }^{2} \mathbf{K}$ (32a) was obtained as foamy white solid after preparative RPHPLC ( $3.6 \mathrm{mg}, 1.4 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.090 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS(ESI + ): $\mathrm{C}_{88} \mathrm{H}_{163} \mathrm{~N}_{23} \mathrm{O}_{17} \mathrm{~S}_{2}$ calc./obs. $1878.20 / 1878.20 \mathrm{Da}$ [M].



Bonventura idb 67_1_150420110031_XT_0... 4/20/2015 3:47:28 PM
University of Bern, Departement of Chemistry and Biochemistry
Bonventura idb 67_1_150420110031_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.16E8
T: FTMS +p NSI Full ms [150.00-2000.0 $\overline{0}$ ]

${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{L L} Z^{1} \mathbf{L K L} Z^{2} \mathbf{K}(\mathbf{3 2 b})$ was obtained as foamy white solid after preparative RPHPLC ( $13.6 \mathrm{mg}, 5.2 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.240 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100 \mathrm{in} 10.00 \mathrm{~min}$, $\lambda=214 \mathrm{~nm})$. MS(ESI+): $\mathrm{C}_{88} \mathrm{H}_{163} \mathrm{~N}_{23} \mathrm{O}_{17} \mathrm{~S}_{2}$ calc./obs. 1878.20/1878.20 Da [M].


Bonventura idb 67_2_150420110031_XT_O...
4/20/2015 3:50:06 PM
University of Bern, Departement of Chemistry and Biochemistry

${ }^{2} \mathbf{K L L K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L L}\right) \mathbf{K L K} Z^{1} \mathbf{K K K Z}{ }^{\mathbf{2}} \mathbf{L}$ (33a) was obtained as foamy white solid after preparative RPHPLC ( $40.1 \mathrm{mg}, 17.7 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.810 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). $\mathrm{MS}\left(\mathrm{ESI}+\right.$ ): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.31 Da [M].



DiBonaventura IDB-53-1_XT_00001_M_
3/12/2015 12:58:21 PM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-53-1_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 7.86E7
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.{ }^{1} \mathbf{K L L K}\left(\mathbf{K}^{2} \mathbf{L L}\right) \mathbf{K L K} \mathbf{Z}^{1} \mathbf{K K K} \mathbf{Z}^{\mathbf{2}} \mathbf{L} \mathbf{( 3 3 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $15.1 \mathrm{mg}, 6.6 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.910 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100 \mathrm{in} 10.00 \mathrm{~min}$, $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.31 Da [M].


DiBonaventura IDB-53-2_XT_00001_M_
3/12/2015 1:01:38 PM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-53-2_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 6.82E7
T: FTMS + p NSI Full ms [150.00-20000. 0 0]

${ }^{2} \mathbf{L L K K}\left(\mathbf{L}^{1} \mathbf{L K}\right) \mathbf{K K K} \boldsymbol{Z}^{1} \mathbf{K L K} \mathbf{Z}^{\mathbf{2}} \mathbf{L}$ (34a) was obtained as foamy white solid after preparative RPHPLC ( $26.5 \mathrm{mg}, 11.7 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.940 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.31 Da [M].



DiBonaventura IDB-54-1_XT_00001_M_
3/12/2015 11:54:27 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-54-1_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 9.45E7
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.{ }^{1} \mathbf{L L K K}\left(\mathbf{L}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{K K K} \boldsymbol{Z}^{1} \mathbf{K L K} \mathbf{Z}^{\mathbf{2}} \mathbf{L} \mathbf{( 3 4 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $20.6 \mathrm{mg}, 9.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.020 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100 \mathrm{in} 10.00 \mathrm{~min}$, $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.31 Da [M].


DiBonaventura IDB-54-2_XT_00001_M_
3/12/2015 11:58:03 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-54-2_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 6.80E7
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L K}\right) \mathbf{L L L Z} \mathbf{Z}^{1} \mathbf{K K K Z} \mathbf{Z}^{\mathbf{2}} \mathbf{L}(\mathbf{3 5 a})$ was obtained as foamy white solid after preparative RPHPLC ( $29.8 \mathrm{mg}, 13.2 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.850 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.31 Da [M].



DiBonaventura IDB-55-1_XT_00001_M_
3/12/2015 11:46:33 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-55-1_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 5.58E7
$\mathrm{T}:$ FTMS +p NSI Full ms $[24 \overline{0} .00-20 \overline{0} 0 . \overline{0} 0]$

$\left.{ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{L L L Z} \mathbf{Z}^{1} \mathbf{K K K Z} \mathbf{Z}^{\mathbf{2}} \mathbf{L} \mathbf{( 3 5 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $17.7 \mathrm{mg}, 7.8 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.890 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.31 Da [M].


DiBonaventura IDB-55-2_XT_00001_M_
3/12/2015 11:50:35 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-55-2 XT 00001 M \#1 RT: 1.0 AV: 1 NL: 8.36E7
T: FTMS +p NSI Full ms [ $24 \overline{0} .00-20 \overline{0} 0 . \overline{0} 0$ ]

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L K}\right) \mathbf{K L L Z} \mathbf{Z}^{1} \mathbf{L L K Z}{ }^{\mathbf{2}} \mathbf{K}$ (36a) was obtained as foamy white solid after preparative RPHPLC ( $11.2 \mathrm{mg}, 4.0 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.890 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100 \mathrm{in} 10.00 \mathrm{~min}$, $\lambda=214 \mathrm{~nm}$ ). $\mathrm{MS}\left(\mathrm{ESI}+\right.$ ): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].


3/30/2015 2:33:20 PM
LTQ Orbitrap XL
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonventura idb 60_1_150330143207_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.09E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.{ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{K L L} \boldsymbol{Z}^{1} \mathbf{L L K} \boldsymbol{Z}^{2} \mathbf{K} \mathbf{( 3 6 b}\right)$ was obtained as foamy white solid after preparative RPHPLC (11.8 mg, $4.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.970 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 [M].


Bonventura idb 60_2_150330143207_XT_O...
3/30/2015 2:36:28 PM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
Bonventura idb 60_2_150330143207_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.50E8
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{1} \mathbf{L K}\right) \mathbf{K L L} Z^{1} \mathbf{K L K} Z^{\mathbf{2}} \mathbf{L}$ (37a) was obtained as foamy white solid after preparative RPHPLC ( $11.0 \mathrm{mg}, 3.9 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.810 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].



Bonventura idb 66_1_150420110031_XT_0...
4/20/2015 3:42:31 PM
LTQ Orbitrap XL
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonventura idb 66_1_150420110031_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 4.93E6
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.{ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{K L L Z} \mathbf{1}^{1} \mathbf{K L K} Z^{\mathbf{2}} \mathbf{L} \mathbf{( 3 7 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $6.9 \mathrm{mg}, 2.5 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.860 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].


Bonventura idb 66_2_150420110031_XT_0... 4/20/2015 3:44:56 PM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
Bonventura idb 66_2_150420110031_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 2.43E8
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{12} \mathbf{K K K K}\left(\mathbf{K}^{12} \mathbf{K K}\right) \mathbf{K K K} Z^{21} \mathbf{L L L} Z^{12} \mathbf{L}(\mathbf{3 8})$ was obtained as foamy white solid after preparative RPHPLC ( $24.2 \mathrm{mg}, 10.5 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.570 / 2.620 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 $\min , \lambda=214 n m$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{177} \mathrm{~N}_{27} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2036.32/2036.33 Da [M].



DiBonaventura IDB-69_XT_00001_M_
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
DiBonaventura IDB-69_XT_00001 M \#1 RT: 1.0 AV: 1 NL: 4.25E7
T: FTMS + p NSI Full ms [ $\overline{1} 50.00-\overline{2} 00 \overline{0} .00$ ]

|  |  |  |  |  | 2037.33 |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $42000000 \pm$ - 2037 |  |  |  |  |  |  |  |  |
| 40000000 |  |  |  |  |  |  |  |  |
| $38000000{ }^{-1} 2036.33$ |  |  |  |  |  |  |  |  |
| 36000000 |  |  |  |  |  |  |  |  |
| 34000000 |  |  |  |  |  |  |  |  |
| 32000000 |  |  |  |  |  |  |  |  |
| 30000000 |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| 26000000 |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| 18000000 |  |  |  |  |  |  |  |  |
| 16000000 |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| 12000000 |  |  |  |  |  |  |  |  |
| 10000000 |  |  |  |  |  |  |  |  |
| 8000000 |  |  |  |  |  |  |  |  |
| $600000{ }^{-1}$ |  |  |  |  |  |  |  |  |
| $400000{ }^{-1}$ |  |  |  |  |  |  |  |  |
| $200000{ }^{-}=2059.31$ |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |
| 1400 | 1500 | 1600 | 1700 | $1800$ | 1900 | 2000 | 2100 | 2200 |

${ }^{1} \mathbf{L L K K}\left(\mathbf{L}^{2} \mathbf{L K}\right) \mathbf{K K L} Z^{2} \mathbf{L L L Z} \mathbf{Z}^{1} \mathbf{K}$ (39a) was obtained as foamy white solid after preparative RPHPLC ( $5.5 \mathrm{mg}, 2.9 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.350 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 7.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{173} \mathrm{~N}_{23} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1976.28/1976.28 Da [M].


Bonaventura 105_1_XT_00001_M_
9/17/2015 2:01:03 PM


University of Bern, Departement of Chemistry and Biochemistry

T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{2} \mathbf{L L K K}\left(\mathbf{L}^{1} \mathbf{L K}\right) \mathbf{K K L Z} \mathbf{Z}^{\mathbf{2}} \mathbf{L L L Z} \mathbf{Z}^{1} \mathbf{K}$ (39b) was obtained as foamy white solid after preparative RPHPLC ( $5.3 \mathrm{mg}, 2.8 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.410 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 7.00 min , $\lambda=214 \mathrm{~nm}$ ). MS(ESI + ): $\mathrm{C}_{94} \mathrm{H}_{173} \mathrm{~N}_{23} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1976.28/1976.28 Da [M].



Bonaventura 105_2_XT_00001_M_
1/10/2017 8:07:11 AM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonaventura 105_2_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.87E8
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{1} \mathbf{L K}\right) \mathbf{L K L Z}{ }^{1} \mathbf{L L L Z} \mathbf{Z}^{\mathbf{2}} \mathbf{K}$ (40a) was obtained as foamy white solid after preparative RPHPLC ( $9.3 \mathrm{mg}, 3.8 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.220 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs.1991.29/1991.28 Da [M].


beonaventura idb-86-1_XT_00001_M_
9/11/2015 8:03:47 AM
University of Bern, Departement of Chemistry and Biochemistry

T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{2} \mathbf{L K}\right) \mathbf{L K L Z}{ }^{1} \mathbf{L L L Z} \mathbf{Z}^{\mathbf{2}} \mathbf{K}(\mathbf{4 0 b})$ was obtained as foamy white solid after preparative RPHPLC ( $8.3 \mathrm{mg}, 3.3 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.300 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs.1991.29/1991.28 Da [M].

bonaventura idb-86-2_XT_00001_M_
9/11/2015 8:09:30 AM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
bonaventura idb-86-2 XT 00001 M \#1 RT: 1.0 AV: 1 NL: 1.14E8
T: FTMS +p NSI Full ms [150.00-20000.00]

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{1} \mathbf{L K}\right) \mathbf{K K K Z}{ }^{1} \mathbf{L L L Z} \mathbf{Z}^{2} \mathbf{K}$ (41a) was obtained as foamy white solid after preparative RPHPLC ( $9.9 \mathrm{mg}, 5.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.900 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 n m$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].



Bonaventura 87-1_XT_00001_M_
9/11/2015 3:49:53 PM
University of Bern, Departement of Chemistry and Biochemistry

${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{K K K} \mathbf{Z}^{\mathbf{1}} \mathbf{L L L} Z^{\mathbf{2}} \mathbf{K}(\mathbf{4 1 b})$ was obtained as foamy white solid after preparative RPHPLC ( $7.0 \mathrm{mg}, 3.6 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.970 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].



Bonaventura 87-2_XT_00001_M_ 9/11/2015 3:53:09 PM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonaventura 87-2_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.45E8
T: FTMS +p NSI F Full ms [150.00-2000.00]

${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{L L L} Z^{\mathbf{2}} \mathbf{L K L} Z^{1} \mathbf{K}$ (42a) was obtained as foamy white solid after preparative RPHPLC ( $3.0 \mathrm{mg}, 1.6 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.490 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.29 Da [M].


Bonaventura 89-1_XT_00001_M_
9/11/2015 3:57:02 PM
University of Bern, Departement of Chemistry and Biochemistry

T: FTMS $+\mathrm{p} \mathrm{NSI} \overline{\mathrm{Full}} \mathrm{ms}$ [150.00-2000.00]

$\left.{ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L K}\right) \mathbf{L L L} Z^{\mathbf{2}} \mathbf{L K} \mathbf{L} Z^{1} \mathbf{K} \mathbf{( 4 2 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $6.6 \mathrm{mg}, 3.4 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.650 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 n m$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1991.29/1991.29 Da [M].



Bonaventura 89-2_XT_00001_M_
9/11/2015 4:04:33 PM
University of Bern, Departement of Chemistry and Biochemistry

T: FTMS $+\mathrm{p} \mathrm{NSI} \overline{\mathrm{Full}} \mathrm{ms}$ [150.00-2000.00]

${ }^{\mathbf{1 2}} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2 1}} \mathbf{L K}\right) \mathbf{K L L} Z^{\mathbf{1 2}} \mathbf{L K L} Z^{\mathbf{2 1}} \mathbf{K}$ (43) was obtained, like one isomer, as foamy white solid after preparative RP-HPLC ( $16.5 \mathrm{mg}, 8.6 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.980 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].




Bonaventura 88_XT_00001_M_
University of Bern, Departement of Chemistry and Biochemistry
9/17/2015 4:05:26 PM
LTQ Orbitrap XL Mass Spectrometry Service, Schuerch Group
Bonaventura 88_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 2.22E8
$\mathrm{T}: \mathrm{FTMS}+\mathrm{p}$ NSI Full ms [150.00-2000.00]

${ }^{\mathbf{1}} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{L K L} \boldsymbol{Z}^{\mathbf{2}} \mathbf{L L K} \mathbf{Z}^{\mathbf{1}} \mathbf{K}$ (44a) was obtained as foamy white solid after preparative RPHPLC ( $8.9 \mathrm{mg}, 4.6 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.860 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].


Bonaventura 90-1_150914145155_XT_0000..
9/15/2015 8:48:12 AM
University of Bern, Departement of Chemistry and Biochemistry

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L K}\right) \mathbf{L K L} \boldsymbol{Z}^{\mathbf{2}} \mathbf{L L K} \mathbf{Z}^{1} \mathbf{K}(\mathbf{4 4 b})$ was obtained as foamy white solid after preparative RPHPLC ( $9.7 \mathrm{mg}, 5.0 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.980 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].


Bonaventura 90-2_150914145155_XT_0000..
9/15/2015 8:51:41 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
Bonaventura 90-2_150914145155_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.93E8
$\mathrm{T}:$ FTMS $+\mathrm{p} \mathrm{NSI} \overline{\text { Full }} \mathrm{ms}$ [150.00-2000.00]

${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{L L L Z} \mathbf{Z}^{\mathbf{2}} \mathbf{L K K} Z^{1} \mathbf{K}$ (45a) was obtained as foamy white solid after preparative RPHPLC ( $9.7 \mathrm{mg}, 5.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.270 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].



Bonaventura 93-1_XT_00001_M_
9/11/2015 4:07:29 PM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonaventura 93-1 XT 00001 M \#1 RT: 1.0 AV: 1 NL: 1.87E8
T: FTMS + p NSI Full $\overline{m s}$ [150.00-2000.00]

$\left.{ }^{\mathbf{1}} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{L L L} \mathbf{Z}^{\mathbf{1}} \mathbf{L K K} \mathbf{Z}^{\mathbf{2}} \mathbf{K} \mathbf{( 4 5 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $5.5 \mathrm{mg}, 2.8 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.300 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].



Bonaventura 93-2_XT_00001_M_
9/11/2015 4:10:09 PM
University of Bern, Departement of Chemistry and Biochemistry

T: FTMS +p NSI Full ms [150.00-2000.00]

${ }^{12} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2 1}} \mathbf{L K}\right) \mathbf{L K L} Z^{\mathbf{2 1}} \mathbf{L K} \mathbf{L} Z^{12} \mathbf{K}(\mathbf{4 6})$ was obtained, like one isomer, as foamy white solid after preparative RP-HPLC ( $10.3 \mathrm{mg}, 4.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.960 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].


bonaventura idb-99-2_XT_00001_M_
9/11/2015 8:36:33 AM
University of Bern, Departement of Chemistry and Biochemistry

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L K}\right) \mathbf{L K K} \boldsymbol{Z}^{1} \mathbf{L L L} Z^{2} \mathbf{K}$ (47a) was obtained as foamy white solid after preparative RPHPLC ( $9.7 \mathrm{mg}, 3.9 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.810 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].

bonaventura idb-100-1_XT_00001_M_
9/11/2015 9:21:39 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
bonaventura idb-100-1 XT $00001 \mathrm{M} \mathrm{\# 1} \mathrm{RT:} \mathrm{1.0} \mathrm{AV:} 1$ NL: 5.96E7
$\mathrm{T}:$ FTMS +p NSI Full $\overline{\mathrm{ms}}$ [ $\overline{150.00-2000} .00]$

${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{L K K} \mathbf{Z}^{1} \mathbf{L L L} Z^{2} \mathbf{K}(\mathbf{4 7 b})$ was obtained as foamy white solid after preparative RPHPLC ( $10.8 \mathrm{mg}, 4.3 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.860 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100 \mathrm{in} 10.00 \mathrm{~min}$, $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].


bonaventura idb-100-2_XT_00001_M_
9/11/2015 9:11:21 AM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
jonaventura idb-100-2_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 6.19E7
$\mathrm{T}: \mathrm{FTMS}+\mathrm{p}$ NSI Full ms [150.00- $\overline{2000} \mathbf{0} .00$ ]

${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{L K L} Z^{2} \mathbf{K L L} Z^{1} \mathbf{K}$ (48a) was obtained as foamy white solid after preparative RPHPLC ( $11.5 \mathrm{mg}, 6.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.960 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].



Bonaventura 103-1_150914145155_XT_000...
9/15/2015 9:08:49 AM
University of Bern, Departement of Chemistry and Biochemistry
Bonaventura 103-1_150914145155_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.09E8 T: FTMS +p NSI Fūll ms [150.00-2000.00]

$\left.{ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L K}\right) \mathbf{L K L} \boldsymbol{Z}^{\mathbf{2}} \mathbf{K L L} \mathbf{Z}^{1} \mathbf{K} \mathbf{( 4 8 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $6.5 \mathrm{mg}, 3.4 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.060 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{175} \mathrm{~N}_{25} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2006.30/2006.30 Da [M].



Bonaventura 103-2_150914145155_XT_000.
9/15/2015 9:11:37 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
Bonaventura 103-2_150914145155_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.20E8
T: FTMS +p NSI Füll ms [150.00-2000.00]

${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{2} \mathbf{L K}\right) \mathbf{K L K} \boldsymbol{Z}^{2} \mathbf{L L K} \mathbf{Z}^{1} \mathbf{K}$ (49a) was obtained as foamy white solid after preparative RPHPLC ( $7.1 \mathrm{mg}, 2.8 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.630 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2021.31 Da [M].

bonaventura idb-91-1_XT_00001_M_
9/11/2015 8:13:54 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
bonaventura idb-91-1_XT_00001_M \#1 RT: 1.0 AV: 1 NL: 1.61E8
T: FTMS +p NSI Full ms [150.00-2000.00]

${ }^{2}$ KLKK (K $\left.{ }^{1} \mathbf{L K}\right) K L K Z^{2} \mathbf{L L K Z}^{1} \mathbf{K}$ (49b) was obtained as foamy white solid after preparative RPHPLC ( $5.4 \mathrm{mg}, 2.2 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.780 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2021.31 Da [M].


bonaventura idb-91-2_XT_00001_M_
9/11/2015 8:21:23 AM
University of Bern, Departement of Chemistry and Biochemistry
bonaventura idb-91-2 XT 00001 M \#1 RT: 1.0 AV: 1 NL: 5.17E7
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{21} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{1 2}} \mathbf{L K}\right) \mathbf{K L L} \mathbf{Z}^{\mathbf{2 1}} \mathbf{K L K Z}{ }^{\mathbf{1 2}} \mathbf{K}$ (50) was obtained, like one isomer, as foamy white solid after preparative RP-HPLC ( $17.4 \mathrm{mg}, 6.2 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.740 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2021.31 Da [M].




Bonaventura 92_XT_00001_M_
9/17/2015 4:00:33 PM
University of Bern, Departement of Chemistry and Biochemistry
Bonaventura 92_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.27E8
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{1} \mathbf{L K}\right) K L K Z^{1} \mathbf{K L L Z} \mathbf{Z}^{\mathbf{2}} \mathbf{K}$ (51a) was obtained as foamy white solid after preparative RPHPLC ( $12.2 \mathrm{mg}, 6.3 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.510 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2021.31 Da [M].



Bonaventura 94-1_XT_00001_M_ 9/11/2015 4:14:10 PM
University of Bern, Departement of Chemistry and Biochemistry

${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{K L K} Z^{1} \mathbf{K L L Z} \mathbf{Z}^{\mathbf{2}} \mathbf{K}$ (51b) was obtained as foamy white solid after preparative RPHPLC ( $6.9 \mathrm{mg}, 3.5 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.570 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2021.31 Da [M].


Bonaventura 94-2_XT_00001_M_
9/11/2015 4:16:53 PM
University of Bern, Departement of Chemistry and Biochemistry
Bonaventura 94-2_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 7.35E7
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{12} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2 1}} \mathbf{L K}\right) \mathbf{K K L} Z^{\mathbf{1 2}} \mathbf{L L K Z}{ }^{\mathbf{2 1}} \mathbf{K}$ (52) was obtained as foamy white solid after preparative RPHPLC ( $25.0 \mathrm{mg}, 13.0 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.590 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2021.31 Da [M].


${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L K}\right) \mathbf{K L L} Z^{1} \mathbf{L K K} Z^{2} \mathbf{K}$ (53a) was obtained as foamy white solid after preparative RPHPLC ( $8.8 \mathrm{mg}, 4.5 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.700 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2021.31 Da [M], 2150.31/2150.31 Da [ $\mathrm{M}+6 \mathrm{Na}$ ].


Bonaventura 96-1_150914145155_XT_0000... 9/15/2015 8:58:45 AM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonaventura 96-1_150914145155_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.73E8
T: FTMS + p NSI Full ms [150.00-2000.00]

$\left.{ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{K L L Z} \mathbf{1}^{\mathbf{1}} \mathbf{L K K} \mathbf{Z}^{\mathbf{2}} \mathbf{K} \mathbf{( 5 3 b}\right)$ was obtained as foamy white solid after preparative RPHPLC (13.3 mg, $6.9 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.810 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2021.31 Da [M].



Bonaventura 96-2_150914145155_XT_0000... 9/15/2015 9:02:08 AM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonaventura 96-2_150914145155_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.78E8
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{12} \mathbf{K L K K}\left(\mathbf{K}^{21} \mathbf{L K}\right) \mathbf{K K K Z}{ }^{12} \mathbf{L L L Z}{ }^{21} \mathbf{K}(\mathbf{5 4})$ was obtained as foamy white solid after preparative RPHPLC ( $35.0 \mathrm{mg}, 18.0 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.580 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100$ in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2021.31 Da [M].




Bonaventura 97_150914145155_XT_00001_M_
9/15/2015 9:05:52 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
Bonaventura 97_150914145155_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 2.03E8
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{K L K} Z^{\mathbf{2}} \mathbf{L K L} \mathbf{Z}^{1} \mathbf{K}$ (55a) was obtained as foamy white solid after preparative RPHPLC ( $12.4 \mathrm{mg}, 10.0 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.570 \mathrm{~min}$ (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2021.31 Da [M].


```
Bonaventura 98-1_XT_00001_M_
```

9/11/20154:19:58 PM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL Mass Spectrometry Service- Schuerch Grqup
Boraventura $98-1$ XT coco1 $\mathrm{M} \neq 11 \mathrm{RT}: 1.0-\mathrm{AV}: 1{ }^{-} \mathrm{NL}: 1.14 \mathrm{~EB}$
T: FTMS $+p$ NSI Full ms [150.00-2000,00]

$\left.{ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L K}\right) \mathbf{K L K} Z^{\mathbf{2}} \mathbf{L K L Z} \mathbf{Z}^{1} \mathbf{K} \mathbf{( 5 5 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $7.8 \mathrm{mg}, 4.0 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.620 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2021.31 Da [M].


Bonaventura 98-2_XT_00001_M_
9/11/2015 4:24:01 PM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonaventura 98-2_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 2.35E8
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{\mathbf{1}} \mathbf{K K K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{K K}\right) \mathbf{K L L Z} \mathbf{Z}^{\mathbf{1}} \mathbf{L L L Z} \mathbf{Z}^{\mathbf{2}} \mathbf{K}$ (56a) was obtained as foamy white solid after preparative RPHPLC ( $10.8 \mathrm{mg}, 4.3 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.860 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100 \mathrm{in} 10.00 \mathrm{~min}$, $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2021.31 Da [M].

bonaventura idb-102-1_XT_00001_M_
9/11/2015 10:19:55 AM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL Mass Spectrometry Service, Schuerch Group
bonaventura idb-102-1_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 3.08E7
$\mathrm{T}:$ FTMS +p NSI Full $\overline{\mathrm{ms}}[\overline{1} 50.00-\overline{2} 00 \overline{0} .00$ ]

$\left.{ }^{2} \mathbf{K K K K}\left(\mathbf{K}^{1} \mathbf{K K}\right) \mathbf{K L L Z} \mathbf{Z}^{\mathbf{L}} \mathbf{L L L Z} \mathbf{Z}^{1} \mathbf{K} \mathbf{( 5 6 b}\right)$ was obtained as foamy white solid after preparative RPHPLC ( $7.4 \mathrm{mg}, 2.9 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.360 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2022.31 Da [M].


University of Bern, Departement of Chemistry and Biochemistry

T: FTMS +p NSI Full ms [ $\overline{150.00-2000.00]}$

${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{2} \mathbf{L K}\right) \mathbf{L K L Z}{ }^{2} \mathbf{K L K Z} \mathbf{Z}^{1} \mathbf{K}$ (57a) was obtained as foamy white solid after preparative RPHPLC ( $10.4 \mathrm{mg}, 5.4 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.570 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to $0: 100 \mathrm{in} 10.00 \mathrm{~min}$, $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2021.31 Da [M].



Bonaventura 104_1_XT_00001_M_
9/17/2015 2:07:11 PM
University of Bern, Departement of Chemistry and Biochemistry
Bonaventura 104_1_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.29E8 T : FTMS +p NSI Full ms [150.00-2000.00]

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{1} \mathbf{L K}\right) \mathbf{L K L Z} \mathbf{Z}^{2} \mathbf{K L K Z} \mathbf{Z}^{1} \mathbf{K}$ (57b) was obtained as foamy white solid after preparative RPHPLC ( $5.6 \mathrm{mg}, 2.9 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.700 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100: 0$ to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS (ESI+): $\mathrm{C}_{94} \mathrm{H}_{176} \mathrm{~N}_{26} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2021.31/2021.31 Da [M].



Bonaventura 104_2_XT_00001_M_
9/17/2015 3:55:13 PM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
Bonaventura 1042 XT 00001 M \#1 RT: 1.0 AV: 1 NL: 1.08E8 T: FTMS +p NSI Full ms [150.00-2000.00]

${ }^{2} \mathbf{K F K K}\left(\mathrm{~K}^{1} \mathbf{F K}\right) \mathbf{K F F Z}{ }^{1} \mathbf{F F F Z}{ }^{2} \mathbf{K}$ (58a) was obtained as foamy white solid after preparative RPHPLC ( $30.4 \mathrm{mg}, 13.62 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.350 \mathrm{~min}$. (A/D 100:0 to 0:100 in 10.00 $\min , \lambda=214 n m$ ). MS(ESI+): $\mathrm{C}_{115} \mathrm{H}_{160} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2229.18/2230.18 Da [M].



Bonaventura idb 78_1_150619153506_XT_..
6/25/2015 2:22:22 PM
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
Bonaventura idb 78_1_150619153506_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 9.67E7
T: FTMS + p NSI Fūll ms [150.00-2000.00]

${ }^{\mathbf{1}} \mathbf{K F K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{F K}\right) \mathbf{K F F} \mathbf{Z}^{1} \mathbf{F F F} \mathbf{Z}^{2} \mathbf{K}(\mathbf{5 8 b})$ was obtained as foamy white solid after preparative RPHPLC ( $20.2 \mathrm{mg}, 9.1 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.460 \mathrm{~min}$. (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm})$. MS(ESI+): $\mathrm{C}_{115} \mathrm{H}_{160} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2229.18/2229.18 Da [M].


Bonaventura idb 78_2_150619153506_XT_... 6/25/2015 2:25:15 PM
University of Bern, Departement of Chemistry and Biochemistry
Bonaventura idb 78_2_150619153506_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.53E8
T: FTMS +p NSI Full ms [150.00-2000.00]

${ }^{12} \mathbf{K W K K}\left(\mathbf{K}^{12} \mathbf{W K}\right) \mathbf{K W W Z}{ }^{\mathbf{2 1}} \mathbf{W} \mathbf{W W} \mathbf{Z}^{12} \mathbf{K}(\mathbf{5 9})$ was obtained, like one isomer, as foamy white solid after preparative RP-HPLC ( $11.0 \mathrm{mg}, 4.4 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=1.600 \mathrm{~min}$. (A/D 100:0 to 0:100 in $5.00 \mathrm{~min}, \lambda=214 \mathrm{~nm})$. MS(ESI+): $\mathrm{C}_{129} \mathrm{H}_{167} \mathrm{~N}_{31} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2502.25/2502.26 Da [M].



Bonaventura idb 79_150619153506_XT_00..
6/25/2015 2:50:49 PM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL Mass Spectrometry Service, Schuerch Group
Bonaventura idb 79_150619153506 XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 4.16E6
T: FTMS +p NSI Full ms [150.00-2000.00]

${ }^{2} \mathbf{B L B K}\left(\mathbf{B}^{1} \mathbf{L B}\right) \mathbf{B L L} Z^{1} \mathbf{L L L} Z^{2} \mathbf{B}(60 a)$ was obtained as foamy white solid after preparative RPHPLC ( $7.6 \mathrm{mg}, 3.2 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.840 \mathrm{~min}$. (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). $\mathrm{MS}\left(\mathrm{ESI}+\right.$ ): $\mathrm{C}_{82} \mathrm{H}_{150} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1823.10/1824.10 Da [M].

```
bonaventura 83_1_161010154940_XT_0000... 10/11/2016 8:06:39 AM
```

University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
bonaventura 831161010154940 XT 00001 M \#1 RT: 1.0 AV: 1 NL: 4.54E7
T: FTMS $+p$ NSI Full ms [150.00-2000.00]

${ }^{2} \mathbf{B L B K}\left(\mathbf{B}^{1} \mathbf{L B}\right) \mathbf{B L L} Z^{2} \mathbf{L L L} Z^{1} \mathbf{B}(60 b)$ was obtained as foamy white solid after preparative RPHPLC ( $3.5 \mathrm{mg}, 1.4 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=2.90 \mathrm{~min}$. (A/D 100:0 to 0:100 in 10.00 min , $\lambda=214 \mathrm{~nm}$ ). MS(ESI + ): $\mathrm{C}_{82} \mathrm{H}_{150} \mathrm{~N}_{24} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 1823.10/1823.10 Da [M].

| bonaventura 83_2_161011081204_XT_0000... | $10 / 11 / 2016$ 8:13:34 AM |  |
| :--- | :--- | :--- |
| University of Bern, Departement of Chemistry and Biochemistry |  | LTQ Orbitrap XL |
| Mass Spectrometry Service, Schuerch Group |  |  |
| bonaventura 83_216101081204_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.15E5 |  |  |
| T: FTMS + p NSI Full ms [150.00-2000.00] |  |  |


${ }^{12} \mathbf{R L R K}\left(\mathbf{R}^{\mathbf{2 1}} \mathbf{L R}\right) \mathbf{R L L} Z^{\mathbf{2 1}} \mathbf{L L L} Z^{12} \mathbf{R}$ (61) was obtained as foamy white solid, like a mixture of two isomers, after preparative RP-HPLC ( $9.5 \mathrm{mg}, 3.9 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=3.260 \mathrm{~min}$. (A/D 100:0 to 0:100 in $10.00 \mathrm{~min}, \lambda=214 \mathrm{~nm}$ ). $\mathrm{MS}\left(\mathrm{ESI}+\right.$ ): $\mathrm{C}_{94} \mathrm{H}_{174} \mathrm{~N}_{36} \mathrm{O}_{18} \mathrm{~S}_{2}$ calc./obs. 2159.52 $\mathrm{Da}[\mathrm{M}]$ found $2160.52[\mathrm{M}+\mathrm{H}]^{+}, 2274.32[\mathrm{M}+\mathrm{TFA}]^{+}, 2388.31[\mathrm{M}+2 \mathrm{TFA}]^{+}, 2502.30[\mathrm{M}+3 \mathrm{TFA}]^{+}$.
bonaventura 82_161010154940_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 1.04E7
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{1}} \mathbf{L K}\right) \mathbf{K L L} Z^{\mathbf{1}} \mathbf{L L L} Z^{\mathbf{2}} \mathbf{K K}\left(\mathbf{C 1 0}_{10}\right)(\mathbf{6 2 a})$ was obtained as foamy white solid after preparative RP-HPLC ( $11.3 \mathrm{mg}, 4.9 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=4.080 \mathrm{~min}$. (A/D 100:0 to 0:100 in 10.00 $\min , \lambda=214 \mathrm{~nm})$. $\mathrm{MS}\left(\mathrm{ESI}+\right.$ ): $\mathrm{C}_{110} \mathrm{H}_{204} \mathrm{~N}_{26} \mathrm{O}_{20} \mathrm{~S}_{2}$ calc./obs. 2273.52/2273.52 Da [M].



Bonaventura idb 81_1_150619153506_XT_..
6/25/2015 2:53:26 PM
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service, Schuerch Group
Bonaventura idb 81_1_150619153506_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 8.93E7
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{K L L} Z^{1} \mathbf{L L L Z} \mathbf{Z}^{\mathbf{2}} \mathbf{K K}\left(\mathbf{C}_{10}\right)(\mathbf{6 2 b})$ was obtained as foamy white solid after preparative RP-HPLC ( $8.5 \mathrm{mg}, 3.6 \%$ ). Analytical RP-HPLC: $\mathrm{t}_{\mathrm{R}}=4.240 \mathrm{~min}$. (A/D 100:0 to 0:100 in 10.00 $\min , \lambda=214 n m)$. MS(ESI+): $\mathrm{C}_{110} \mathrm{H}_{204} \mathrm{~N}_{26} \mathrm{O}_{20} \mathrm{~S}_{2}$ calc./obs. 2273.52/2273.52 Da [M].


Bonaventura idb 81_2_150619153506_XT_... 6/25/2015 2:56:04 PM
University of Bern, Departement of Chemistry and Biochemistry
LTQ Orbitrap XL
Mass Spectrometry Service, Schuerch Group
Bonaventura idb 81_2_150619153506_XT_00001_M_\#1 RT: 1.0 AV: 1 NL: 4.05E7
T: FTMS +p NSI Full ms [150.00-2000.00]

$\left.{ }^{2} \mathbf{K}^{( }{ }^{1}\right) \mathbf{K Z} \mathbf{Z}^{1} \mathbf{K L Z} \mathbf{Z}^{2} \mathbf{L K}(\mathbf{c F u c})(\mathbf{6 3 a})$ was obtained as a foamy white solid after preparative RP-HPLC ( $3.0 \mathrm{mg}, 2.6 \%$ ). Analytical RP-UHPLC: $\mathrm{t}_{\mathrm{R}}=1.47 \mathrm{~min}$ (A/D 100/0 to $0 / 100$ in 5.0 min , flow rate 1.2 $\mathrm{mL} \min ^{-1}, \lambda=214 \mathrm{~nm}$ ). MS ( $\mathrm{ESI}^{+}$) calc. for $\mathrm{C}_{54} \mathrm{H}_{95} \mathrm{~N}_{13} \mathrm{O}_{15} \mathrm{~S}_{2} 1229.65 \mathrm{Da}[\mathrm{M}]$, found: 1230.66 $[\mathrm{M}+\mathrm{H}]^{+}, 615.83[\mathrm{M}+\mathrm{H}]^{2+}$.


Robadey MRo 018 bic1_151008095655
NSI pos ACN H2O
University of Bern, Departement of Chemistry and Biochemistry
10/8/2015 10:15:09 AM
MRo 018 bic1
LTQ Orbitrap XL

Mass Spectrometry Service - Schuerch Group
Robadey MRo 018 bic1_151008095655 \#1-4 RT: 0.0-0.1 AV: 4 NL: 5.41E7
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{2} K\left({ }^{1}\right) \mathbf{K Z} \mathbf{Z}^{2} \mathbf{K L Z} \mathbf{Z}^{1} \mathbf{L K}(\mathbf{c F u c})(\mathbf{6 3 b})$ was obtained as a foamy white solid after preparative RP-HPLC ( $1.0 \mathrm{mg}, 0.9 \%$ ). Analytical RP-UHPLC: $\mathrm{t}_{\mathrm{R}}=1.48 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100 / 0$ to $0 / 100$ in 5.0 min , flow rate 1.2 $\mathrm{mL} \mathrm{min}-1, ~ \lambda=214 \mathrm{~nm}$ ). MS (ESI') calc. for $\mathrm{C}_{54} \mathrm{H}_{95} \mathrm{~N}_{13} \mathrm{O}_{15} \mathrm{~S}_{2}: 1229.65 \mathrm{Da}$ [M], found: 1230.66 $[\mathrm{M}+\mathrm{H}]^{+}, 1252.66[\mathrm{M}+\mathrm{Na}]^{+}, 615.84[\mathrm{M}+\mathrm{H}]^{2+}$.


Robadey MRo 018 bic2_151008095655
10/8/2015 10:18:33 AM
MRo 018 bic2
NSI pos ACN H2O
University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service - Schuerch Group
Robadey MRo 018 bic2_151008095655 \#1-13 RT: 0.0-0.4 AV: $13 \quad \mathrm{NL}: 2.55 \mathrm{E} 7$
T: FTMS + p NSI Full ms [150.00-2000.00]


## Structures of both isomers:



${ }^{1} \mathbf{K}\left({ }^{2}\right) \mathbf{P a Z} \mathbf{Z}^{\mathbf{2}} \mathbf{y A z}{ }^{1} \mathbf{K}$ (cFuc) (64a) was obtained as a foamy white solid after preparative RP-HPLC ( 0.6 $\mathrm{mg}, 0.5 \%$ ) Analytical RP-UHPLC: $\mathrm{t}_{\mathrm{R}}=2.39 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100 / 0$ to $0 / 100$ in 7.5 min , flow rate 1.2 $\mathrm{mLmin}^{-1}, \lambda=214 \mathrm{~nm}$ ). MS ( $\mathrm{ESI}^{+}$) calc. for $\mathrm{C}_{50} \mathrm{H}_{75} \mathrm{~N}_{11} \mathrm{O}_{16} \mathrm{~S}_{2}[\mathrm{M}+\mathrm{H}]^{+}: 1149.48$, found: 1150.5, $597.22[\mathrm{M}+\mathrm{Na}]^{2+}$.


${ }^{2} \mathbf{K}\left({ }^{(1)} \mathbf{P a Z} \mathbf{Z}^{\mathbf{y}} \mathbf{y} \mathbf{A z}{ }^{1} \mathbf{K}(\mathbf{c F u c})(\mathbf{6 4 b})\right.$ was obtained as a foamy white solid after preparative RP-HPLC (1.7 $\mathrm{mg}, 1.5 \%$ ) Analytical RP-UHPLC: $\mathrm{t}_{\mathrm{R}}=2.44 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100 / 0$ to $0 / 100$ in 7.5 min , flow rate 1.2 $\mathrm{mLmin}^{-1}, \lambda=214 \mathrm{~nm}$ ). MS ( $\mathrm{ESI}^{+}$) calc. for $\mathrm{C}_{50} \mathrm{H}_{75} \mathrm{~N}_{11} \mathrm{O}_{16} \mathrm{~S}_{2}[\mathrm{M}+\mathrm{H}]^{+}: 1149.48$, found: 1150.5, $575.75[\mathrm{M}+\mathrm{H}]^{2+}, 1172.48[\mathrm{M}+\mathrm{Na}]^{+}$.


${ }^{2} \mathbf{K L K K}\left(\mathbf{K}^{1} \mathbf{L K}\right) \mathbf{K L L Z} \mathbf{Z}^{1} \mathbf{L L L Z}^{2} \mathbf{K K}$ (cFuc) (65a) was obtained as a foamy white solid after preparative RP-HPLC ( $2.3 \mathrm{mg}, 1.2 \%$ ) Analytical RP-UHPLC: $\mathrm{t}_{\mathrm{R}}=2.35 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100 / 0$ to $0 / 100$ in 10.0 min , flow rate $\left.1.2 \mathrm{~mL} \mathrm{~min}^{-1}, \lambda=214 \mathrm{~nm}\right)$. $\mathrm{MS}\left(\mathrm{ESI}^{+}\right)$calc. for $\mathrm{C}_{108} \mathrm{H}_{198} \mathrm{~N}_{26} \mathrm{O}_{24} \mathrm{~S}_{2}$ 2307.48/2307.48 Da [M].


University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service - Schuerch Group
Robadey MRo 019 bic1_151008095655_XT_00001_M_ \#1 ${ }^{-}$RT: ${ }^{-} 1.0^{-}$AV: $1^{-}{ }^{-}$NL: ${ }^{-} 7.07 E 5$
T: FTMS + p NSI Full ms [150.00-2000.00]

${ }^{1} \mathbf{K L K K}\left(\mathbf{K}^{\mathbf{2}} \mathbf{L K}\right) \mathbf{K L L Z} \mathbf{Z}^{1} \mathbf{L L L Z}^{2} \mathbf{K K}(\mathbf{c F u c})(\mathbf{6 5 b})$ was obtained as a foamy white solid after preparative RP-HPLC ( $2.0 \mathrm{mg}, 1.0 \%$ ) Analytical RP-UHPLC: $\mathrm{t}_{\mathrm{R}}=2.63 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100 / 0$ to $0 / 100$ in 10.0 min , flow rate $1.2 \mathrm{~mL} \mathrm{~min}^{-1}, \lambda=214 \mathrm{~nm}$ ). MS ( $\mathrm{ESI}^{+}$) calc. for $\mathrm{C}_{108} \mathrm{H}_{198} \mathrm{~N}_{26} \mathrm{O}_{24} \mathrm{~S}_{2}$ 2307.48/2307.48 Da [M].


University of Bern, Departement of Chemistry and Biochemistry
Mass Spectrometry Service - Schuerch Group
Robadey MRo 019 bic2_151008095655_XT_00001_M_ \#1 RT: 1.0 AV: 1 NL: 3.92E5
T: FTMS + p NSI Full ms [150.00-2000.00]

vqwrairvrvir (DJK5) was obtained as a foamy white solid after preparative RP-HPLC ( 51.2 mg , 25.6 \%) Analytical RP-UHPLC: $\mathrm{t}_{\mathrm{R}}=1.20 \mathrm{~min}(\mathrm{~A} / \mathrm{D} 100 / 0$ to $0 / 100$ in 7.0 min , flow rate 1.2 $\left.\mathrm{mL}^{2} \mathrm{~min}^{-1}, \lambda=214 \mathrm{~nm}\right)$. $\mathrm{MS}\left(\mathrm{ESI}^{+}\right)$calc. for $\mathrm{C}_{70} \mathrm{H}_{123} \mathrm{~N}_{27} \mathrm{O}_{13} 1549.47 / 1549.97 \mathrm{Da}[\mathrm{M}]$.



