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SUPPLEMENTARY MATERIAL

An Efficient Chemical Synthesis of Lassomycin Enabled by an On-Resin Lactamisation/Off-Resin Methanolysis Strategy and Preparation of Chemical Variants

Paul W. R. Harris,[A,B,E] Gregory M. Cook,[B,D] Ivanhoe K. H. Leung,[A] and Margaret A. Brimble[A,B,C]

[A]School of Biological Sciences, The University of Auckland, 3A Symonds Street, Auckland 1010, New Zealand.

[B]Maurice Wilkins Centre for Molecular Biodiscovery, The University of Auckland, 3A Symonds Street, Auckland 1010, New Zealand.

[C]School of Chemical Sciences, The University of Auckland, 23 Symonds Street, Auckland 1010, New Zealand.

[D]Department of Microbiology and Immunology, School of Medical Sciences, University of Otago, 720 Cumberland Street, Dunedin 9054, New Zealand.

[E]Corresponding author. Email: paul.harris@auckland.ac.nz

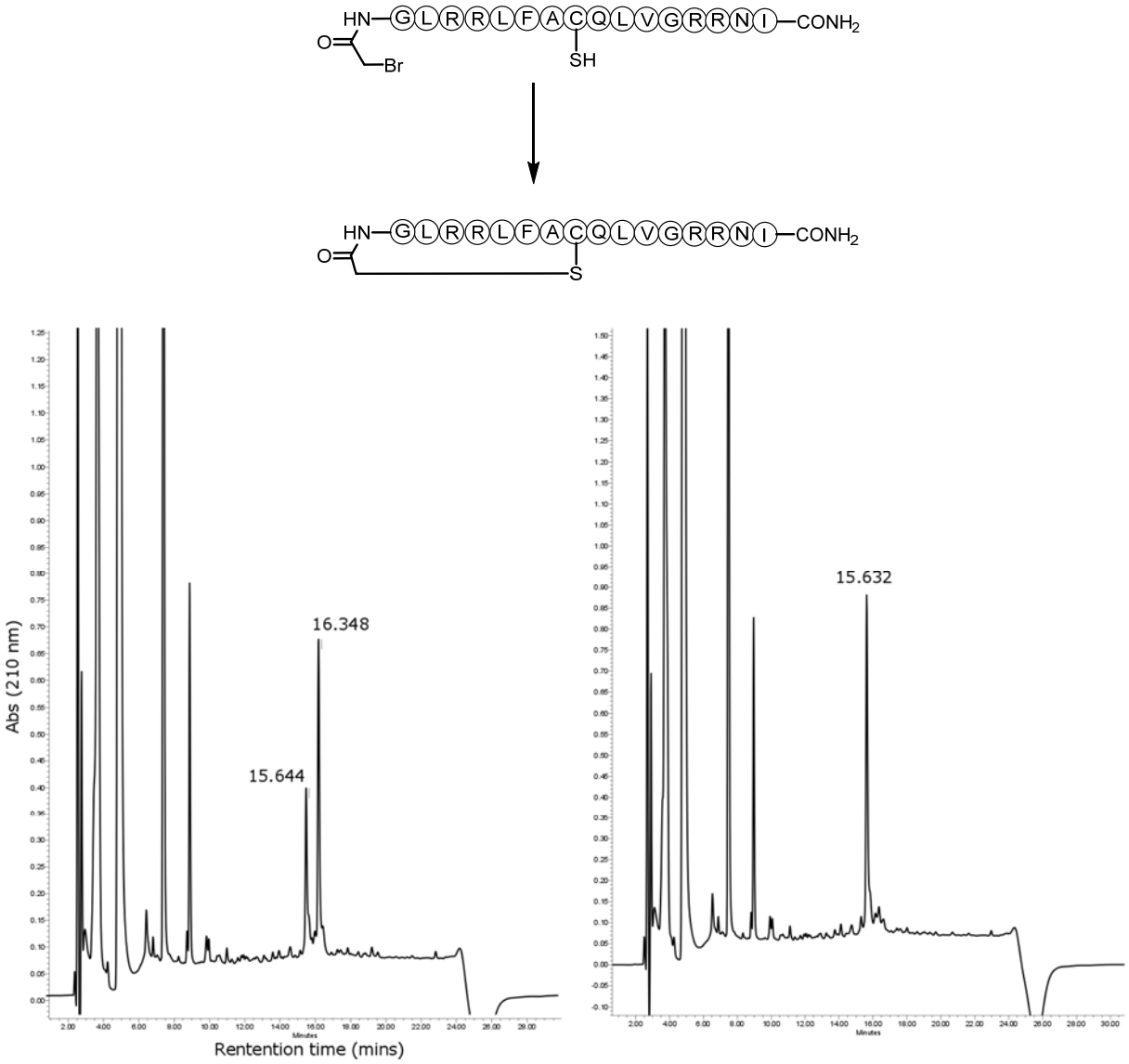

Figure S1. HPLC monitoring (214 nm) of the thioetherification reaction for the preparation of Lassomycin [^{1}Gly-COCH$_2$-^{8}Cys] **12,** left T = 0, right T =30 mins. At T = 0 the reaction is *ca.* 40% complete. The earlier eluting material from 0-9 mins are buffer components.

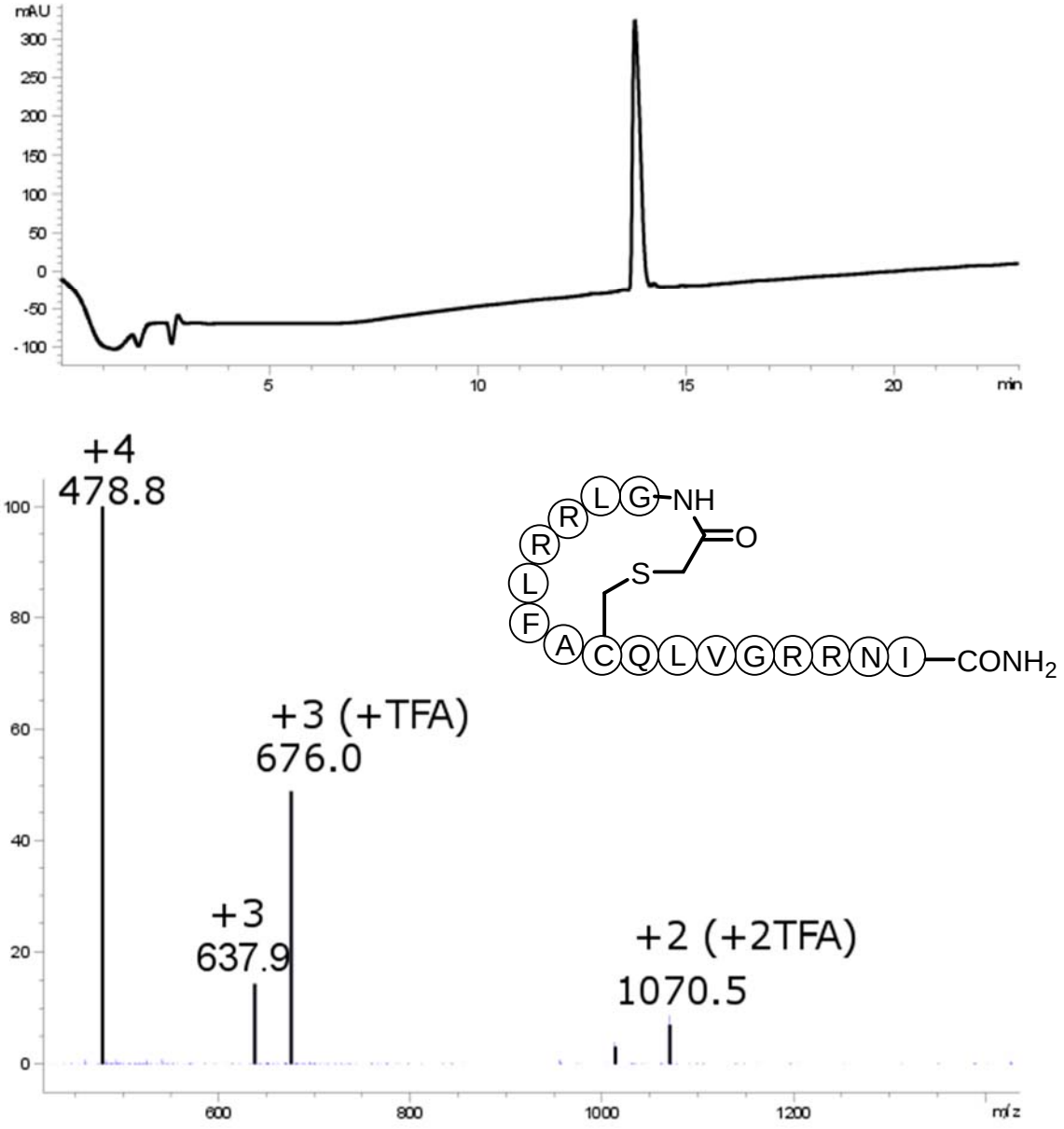

Figure S2. LC-MS of purified Lassomycin [^{1}Gly-COCH$_2$-^{8}Cys] **12**. Deconvolution yields a mass of 1911.0±0.4 Da. The calculated mass is 1911.28.

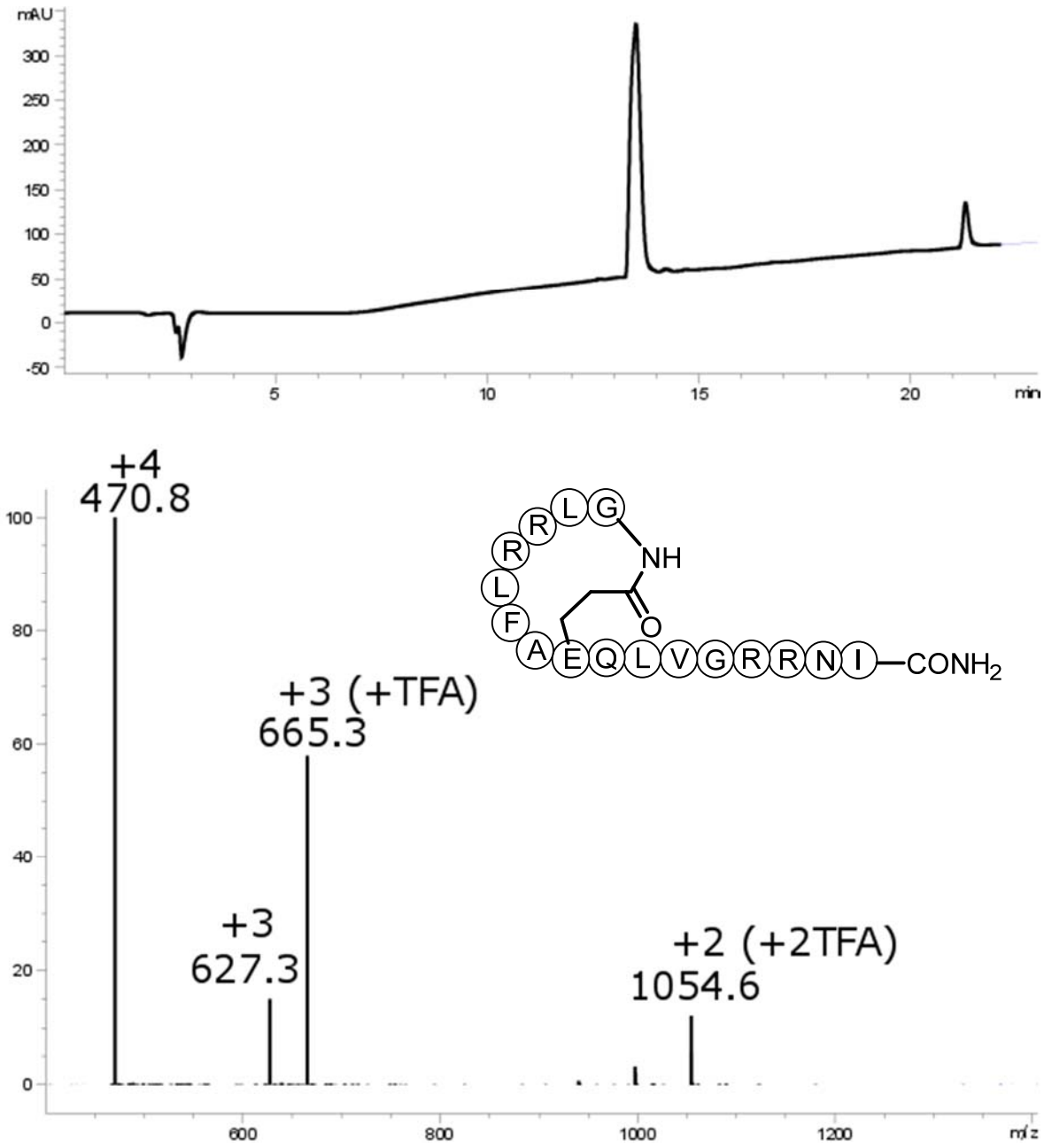

Figure S3. LC-MS of Lassomycin [^{1}Gly-^{8}Glu] **13**. Deconvolution yields a mass of 1865.8±0.2 Da. The calculated mass is 1866.2. The later eluting peak at *ca.* 21 mins is a non-peptide column contaminant.

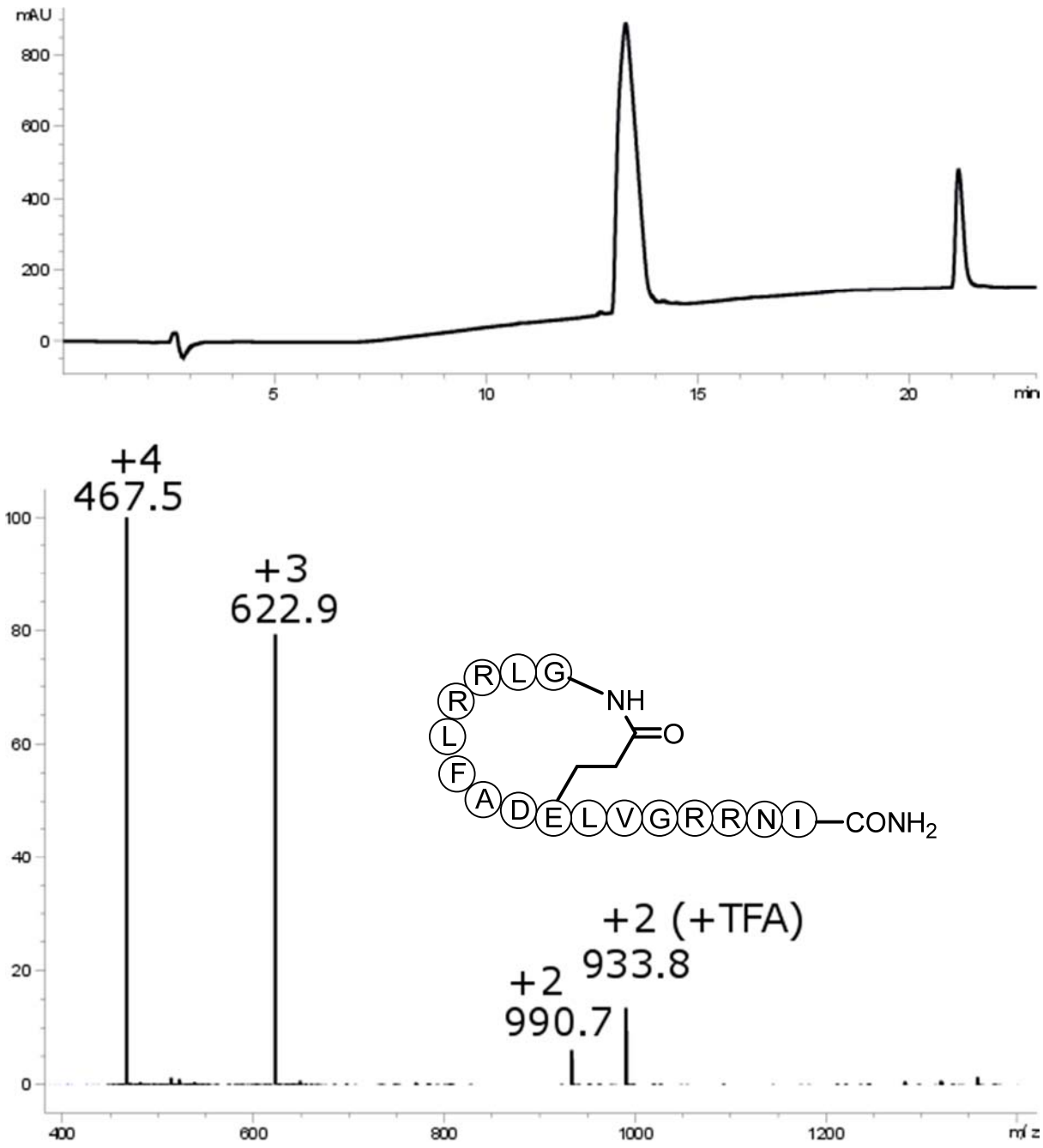

Figure S4. LC-MS of Lassomycin [^{1}Gly-^{9}Glu] **14.** Deconvolution yields a mass of 1879.1±0.2 Da. The calculated mass is 1879.2. The later eluting peak at *ca.* 21 mns is a non-peptide column contaminant. (LS-MS is wrong!)

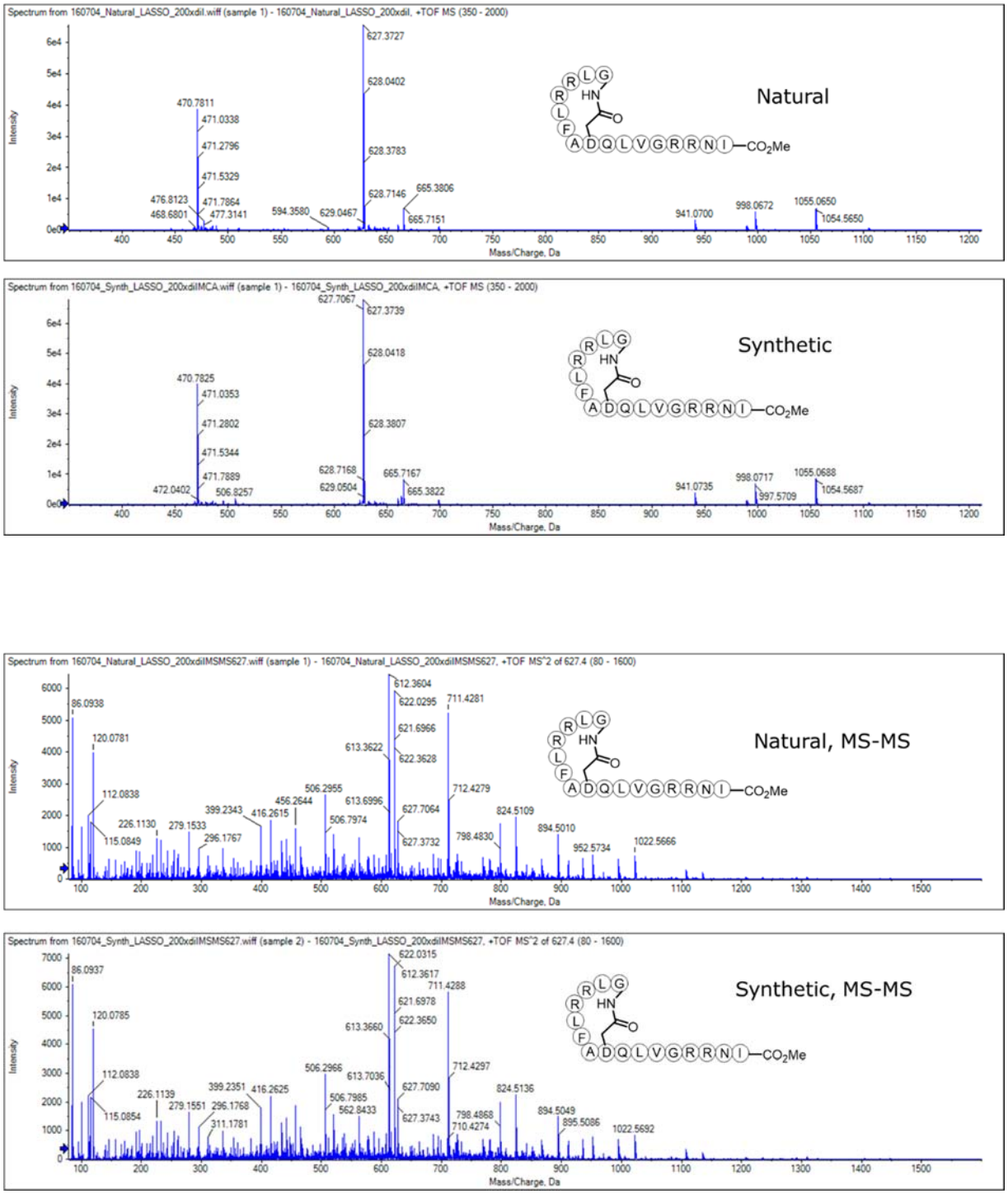

Figure S5. TOF-MS and MS/MS comparison of synthetic Lassomycin **1** and natural Lassomyin.

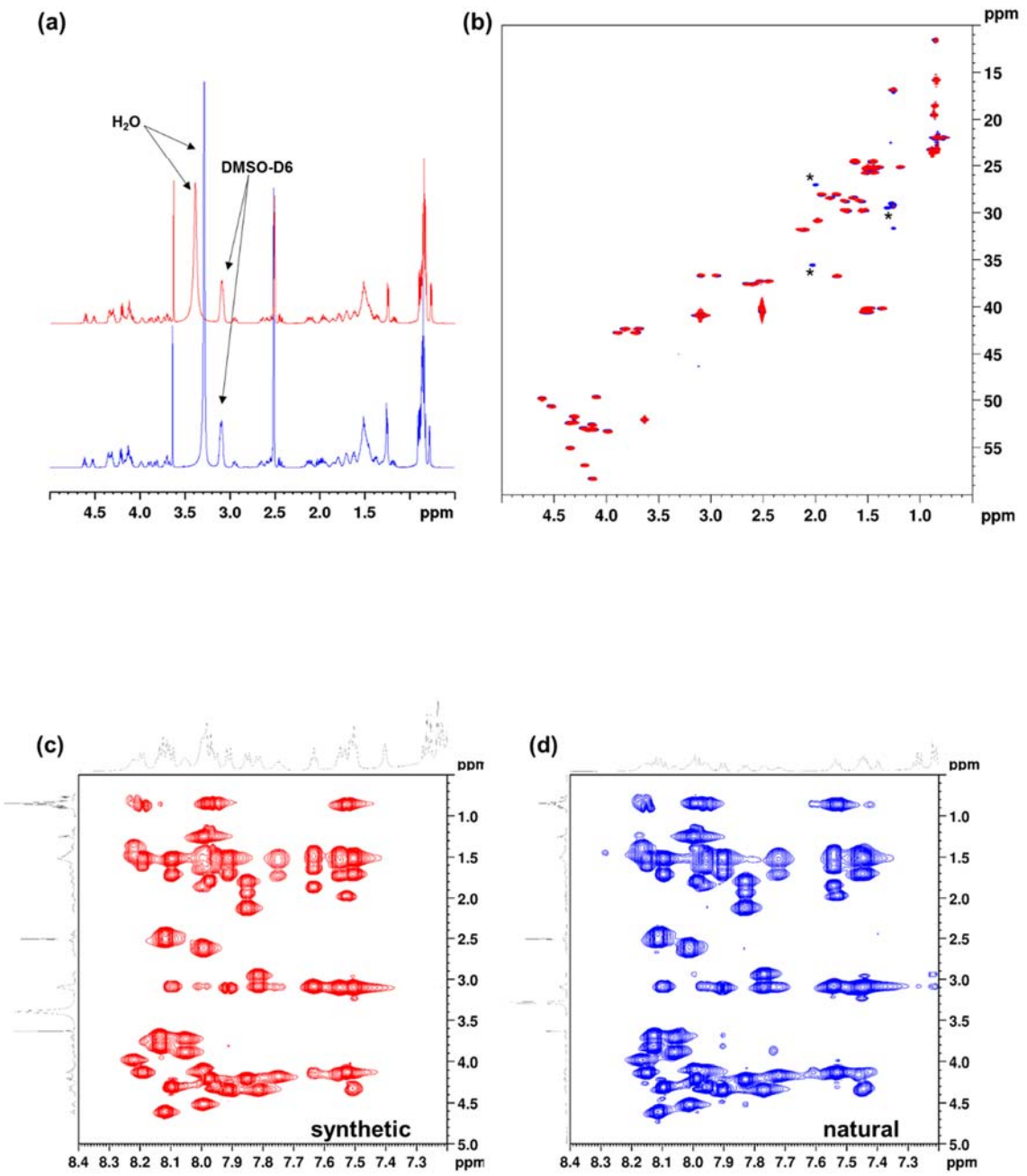

Figure S6. NMR comparison of synthetic Lassomycin **1** (red) and natural Lassomycin (blue); (a) ^{1}H NMR of the aliphatic region and (b) ^{1}H-^{13}C HSQC overlay of the same region. The asterisk (*) on (b) denotes impurities from the commercial obtained natural Lassomycin; (c) and (d) ^{1}H-^{1}H NMR TOSCY spectra of the NH fingerprint region of Lassomycin **1** (red) and natural Lassomycin (blue).

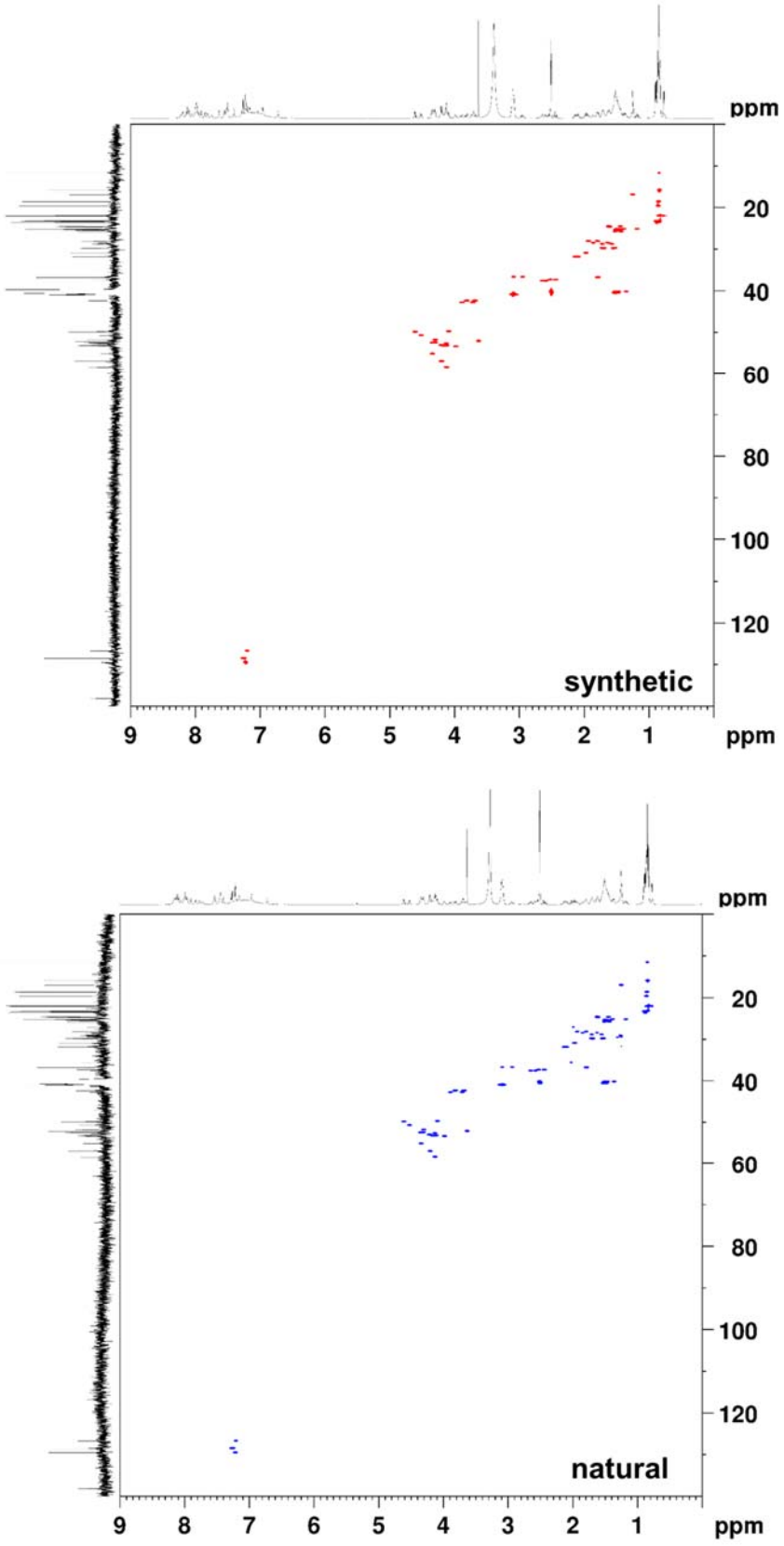

Figure S7. ^{1}H-^{13}C HSQC of synthetic Lassomycin (red) and natural Lassomycin (blue) indicating both peptides are effectively the same.