Supplementary Information

2-Methoxy-4-methylsulfinylbenzyl alcohol (Mmsb) as a Safety-Catch Linker for the Fmoc/*t*Bu Solid-Phase Peptide Synthesis Strategy

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Note

Mmsb linker was already fully characterized in our previous publication[1].

All the model peptides used in this study are already published. The Fmoc-tripeptide for DKP study,[2] the peptide for beta-lactam formation study,[3-6] and somatostatin peptide for heterodetic cyclization study.[7]

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Characterization of the peptides

LCMS

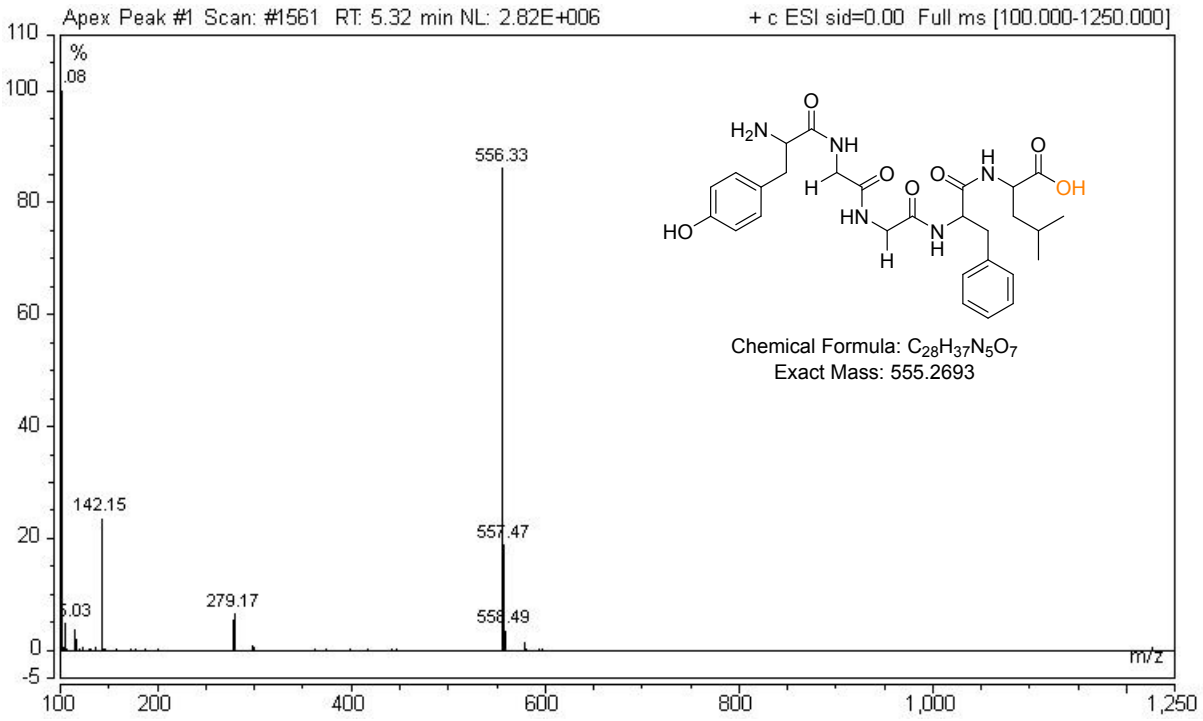

Figure S1: LCMS spectrum of H-Tyr-Gly-Gly-Phe-Leu-OH, m/z calcd. [M+H] = 555.26; found [M+H] = 556.33

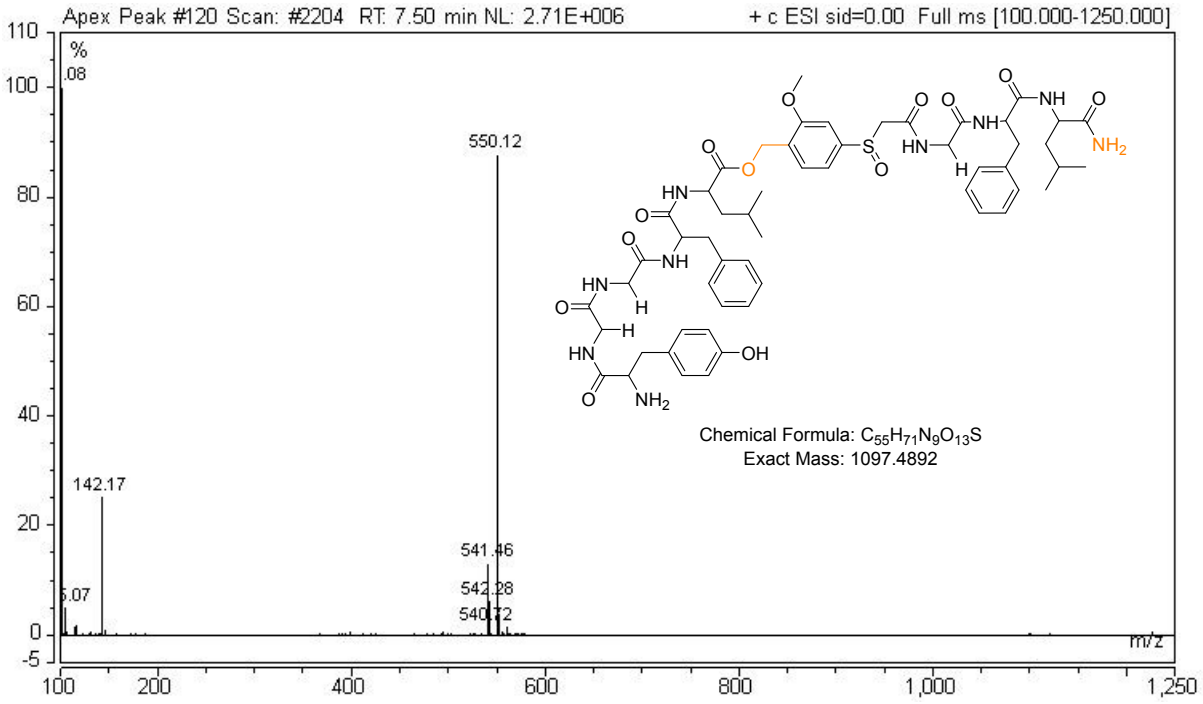

Figure S2: LCMS spectrum of H-Tyr-Gly-Gly-Phe-Leu-O-**Mmsb**-Gly-Phe-Leu-NH_2, m/z calcd. $[M+2H]^+/2$ = 549.75; found $[M+2H]^+/2$ = 550.12

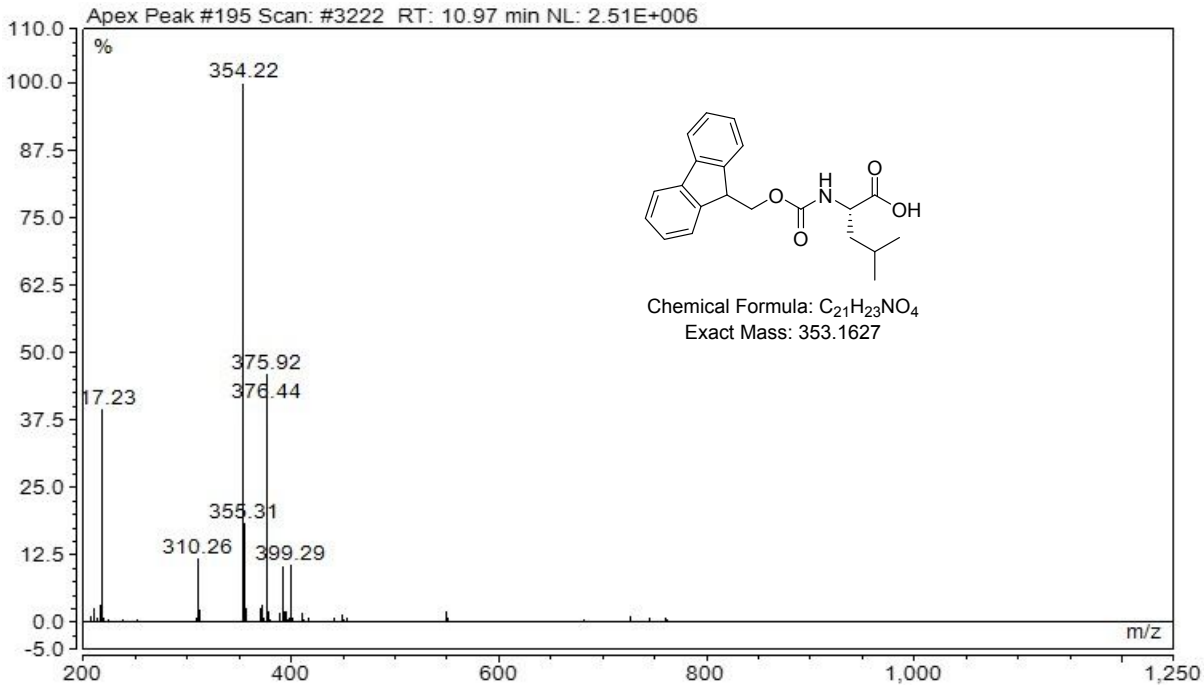

Figure S3: LCMS spectrum of Fmoc-Leu-OH, m/z calcd. $[M+H]^+ = 353.16$; found $[M+H]^+ = 354.22$.

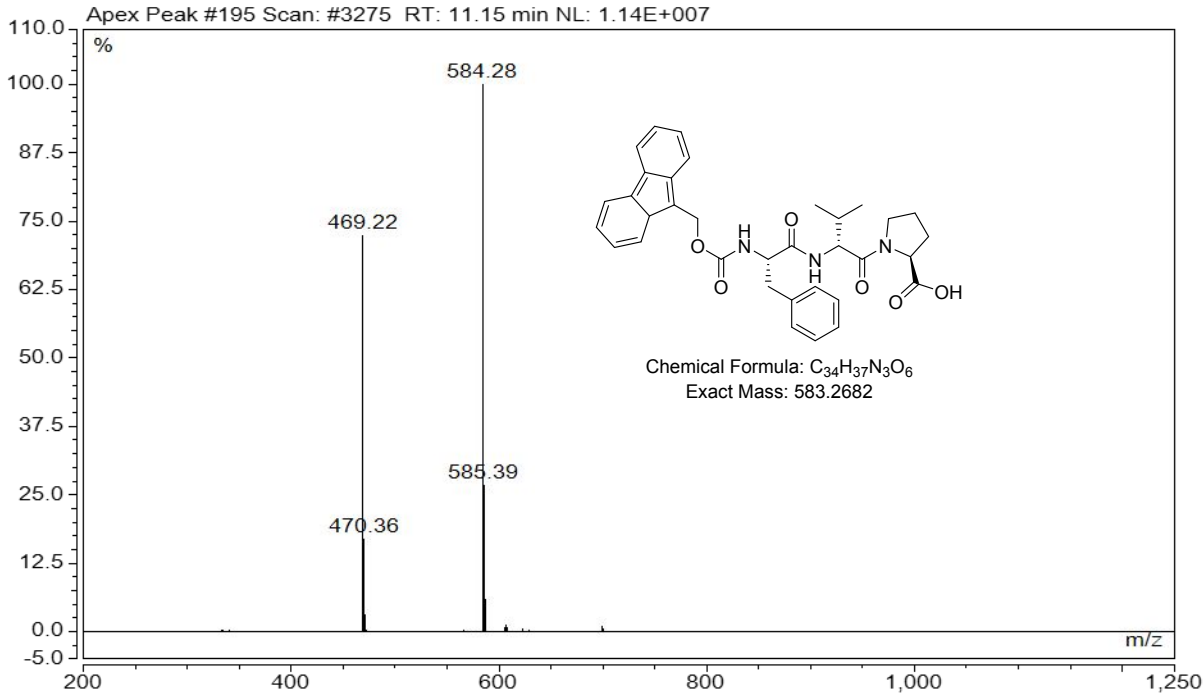

Figure S4: LCMS spectrum of Fmoc-Phe-DVal-Pro-OH, m/z calcd. $[M+H]^+ = 583.27$ and; found $[M+H]^+ = 584.28$. Mass 469.22 belongs to the same peptide with proline induced fragmentation in mass spectrometry.[8, 9]

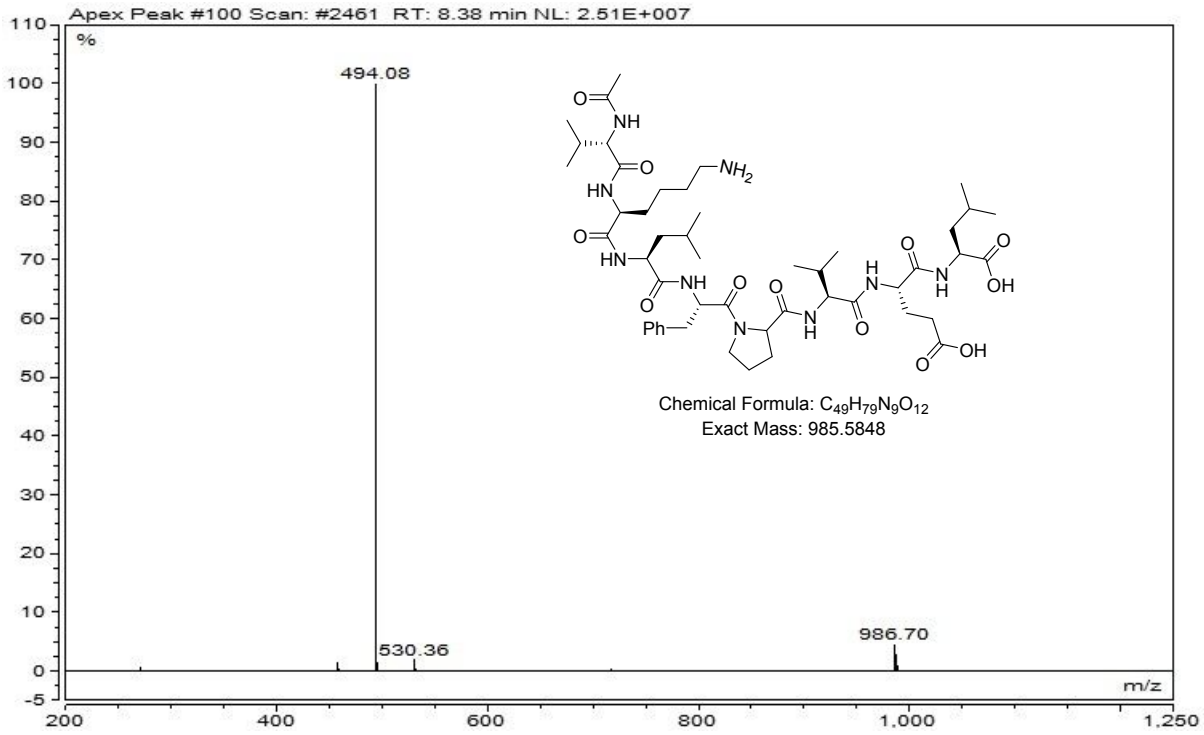

Figure S5: LCMS spectrum of linear model peptide Ac-Val-Lys-Leu-DPhe-Pro-Val-Glu-Leu-OH, m/z calcd. $[M+H]^+ = 985.58$ and $[M+2H]^+/2 = 493.79$; found $[M+H]^+ = 986.70$ and $[M+2H]^+/2 = 494.08$.

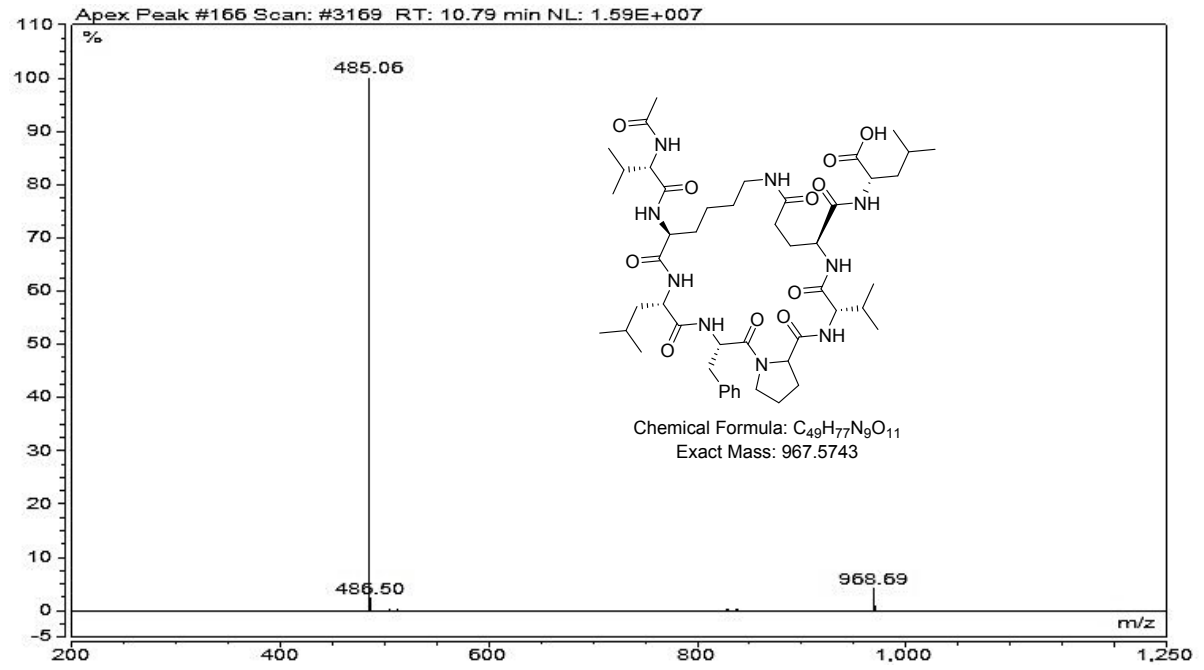

Figure S6: LCMS spectrum of cyclized model peptide Ac-Val-Lys-Leu-DPhe-Pro-Val-Glu-Leu-OH, m/z calcd. $[M+H]^+ = 967.57$ and $[M+2H]^+/2 = 484.79$; found $[M+H]^+ = 968.69$ and $[M+2H]^+/2 = 485.06$.

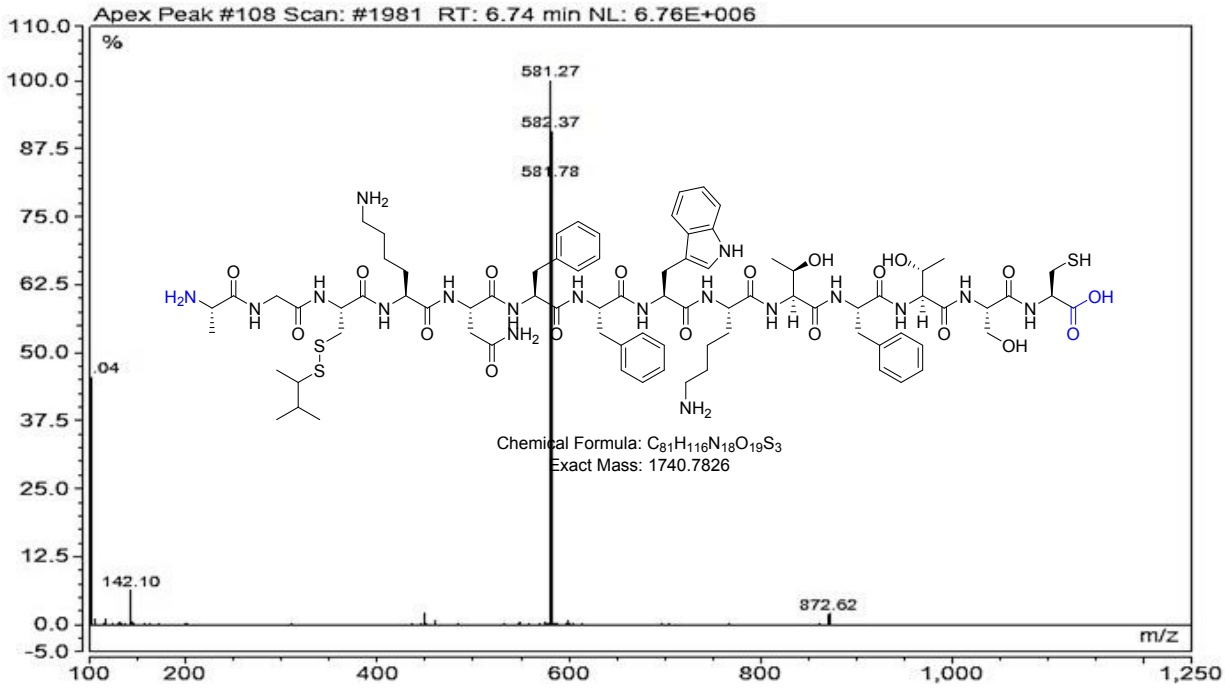

Figure S7: LCMS spectrum of Linear somatostatin-OH, m/z calcd. $[M+2H]^+/2$ = 871.39 and $[M+3H]^+/3$ = 581.26; found $[M+2H]^+/2$ = 872.62 and $[M+3H]^+/3$ = 581.27.

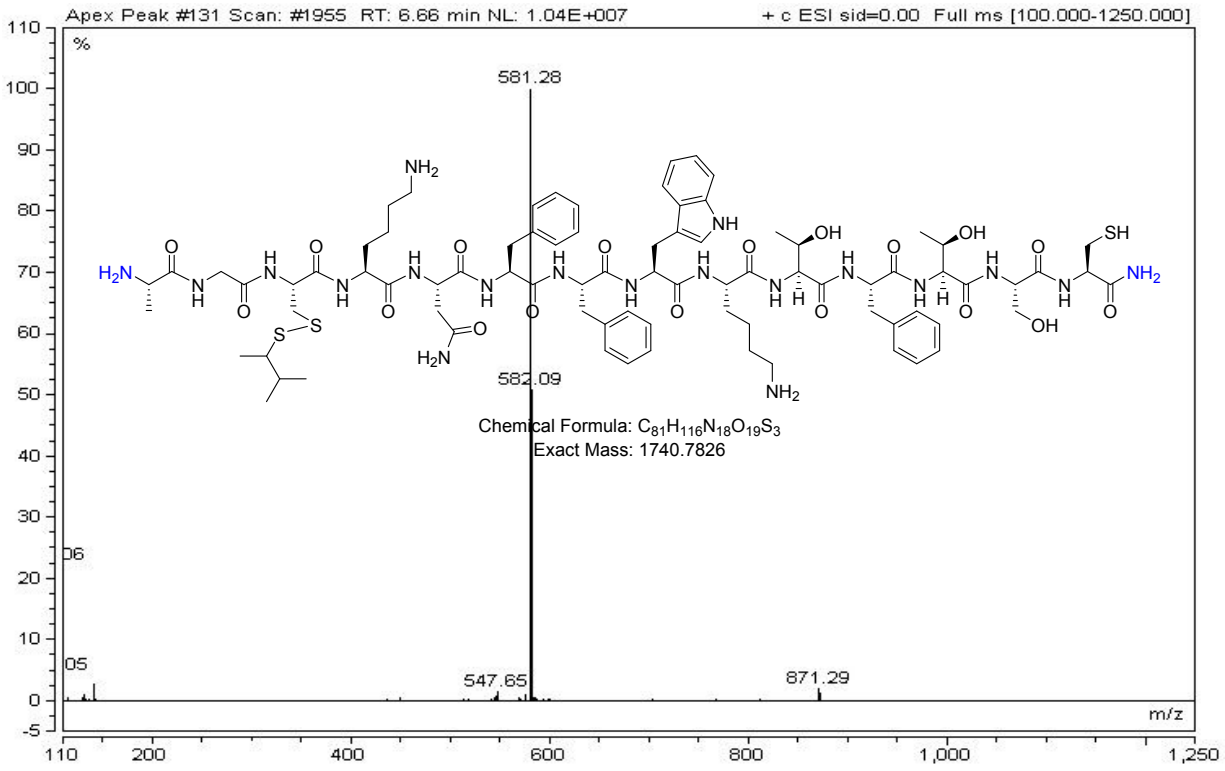

Figure S8: LCMS spectrum of linear somatostatin-NH_2, m/z calcd. $[M+2H]^+/2$ = 871.39 and $[M+3H]^+/3$ = 581.26; found $[M+2H]^+/2$ = 871.29 and $[M+3H]^+/3$ = 581.28.

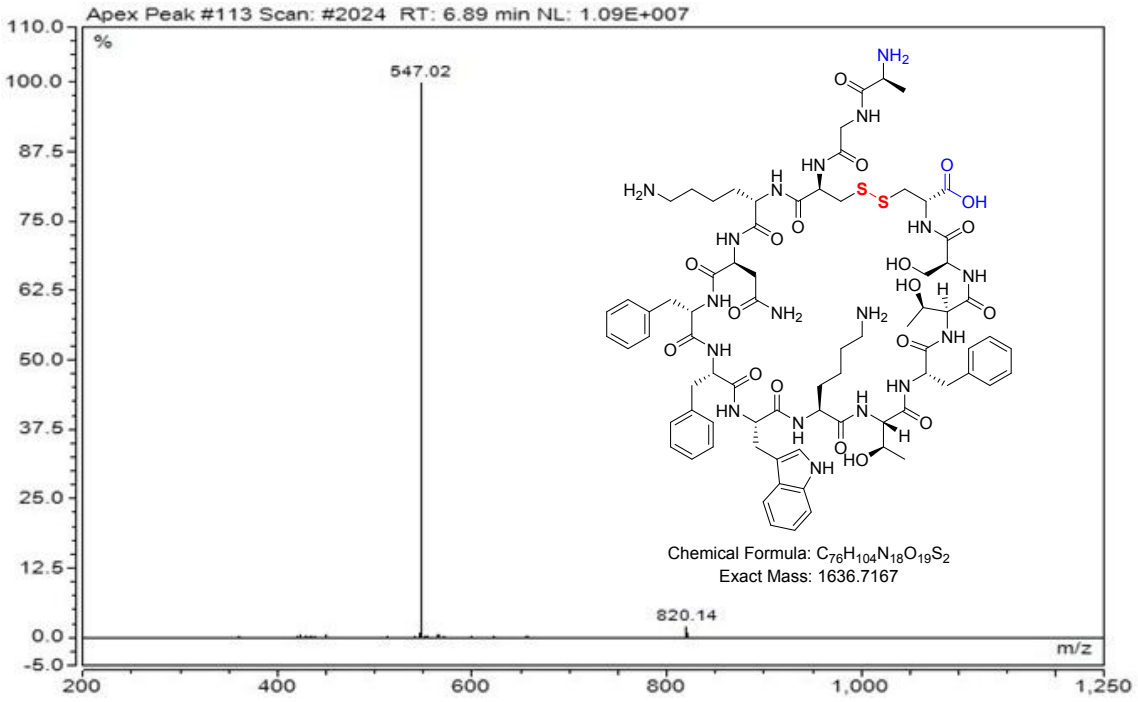

Figure S9: LCMS spectrum of Cyclized somatostatin-OH, m/z calcd. $[M+2H]^+/2$ = 819.36 and $[M+3H]^+/3$ = 546.57; found $[M+2H]^+/2$ = 820.14 and $[M+3H]^+/3$ = 547.02.

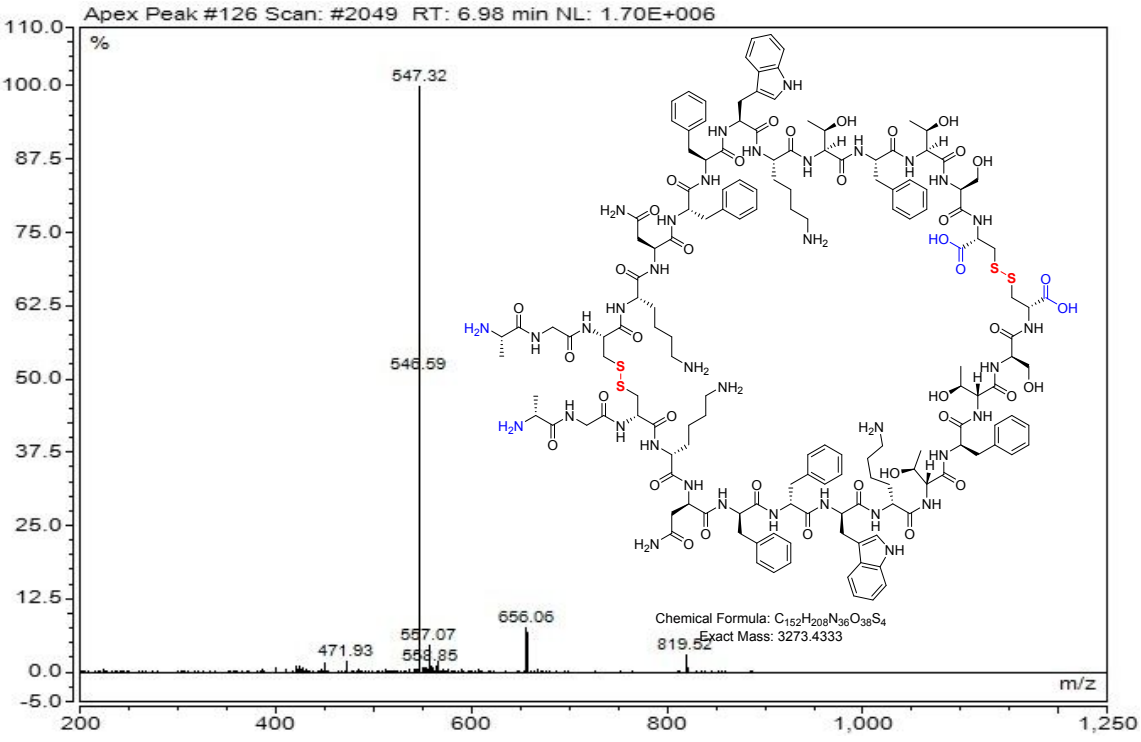

Figure S10: LCMS spectrum of Cyclic dimer I, m/z calcd. $[M+5H]^+/5$ = 655.67; found $[M+2H]^+/2$ = 656.06

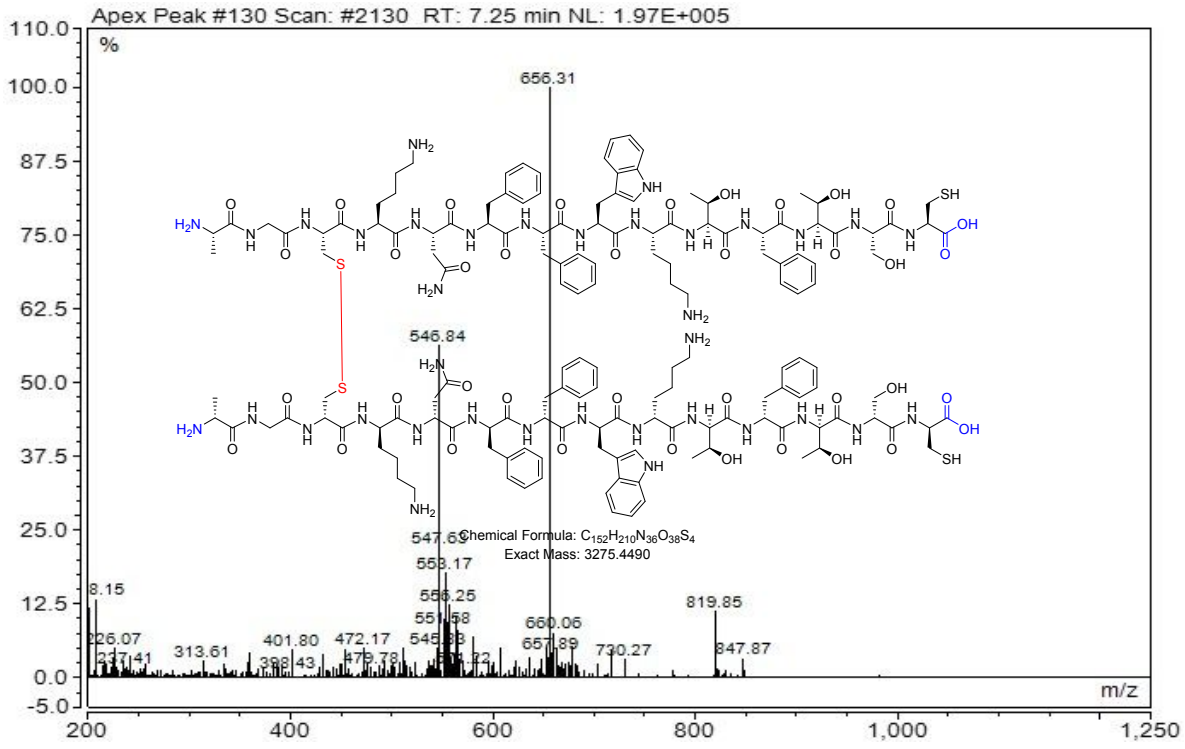

Figure S11: LCMS spectrum of Cyclic dimer II $[M+5H]^+/5$ = 656.09; found $[M+2H]^+/2$ = 656.31.

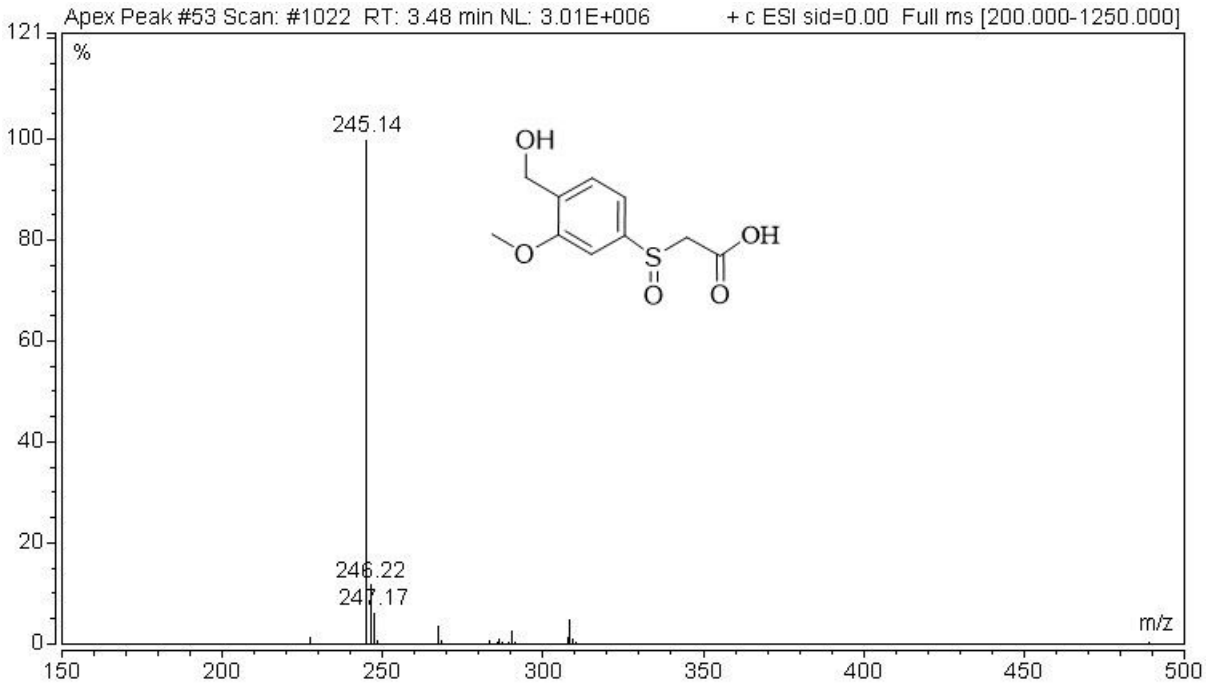

Figure S12: LCMS spectrum of Mmsb linker; $C_{10}H_{12}O_5S$; m/z calcd. $[M+H]^+$ = 244.04; found $[M+H]^+$ = 245.14.

Characterization of the peptides

HPLC

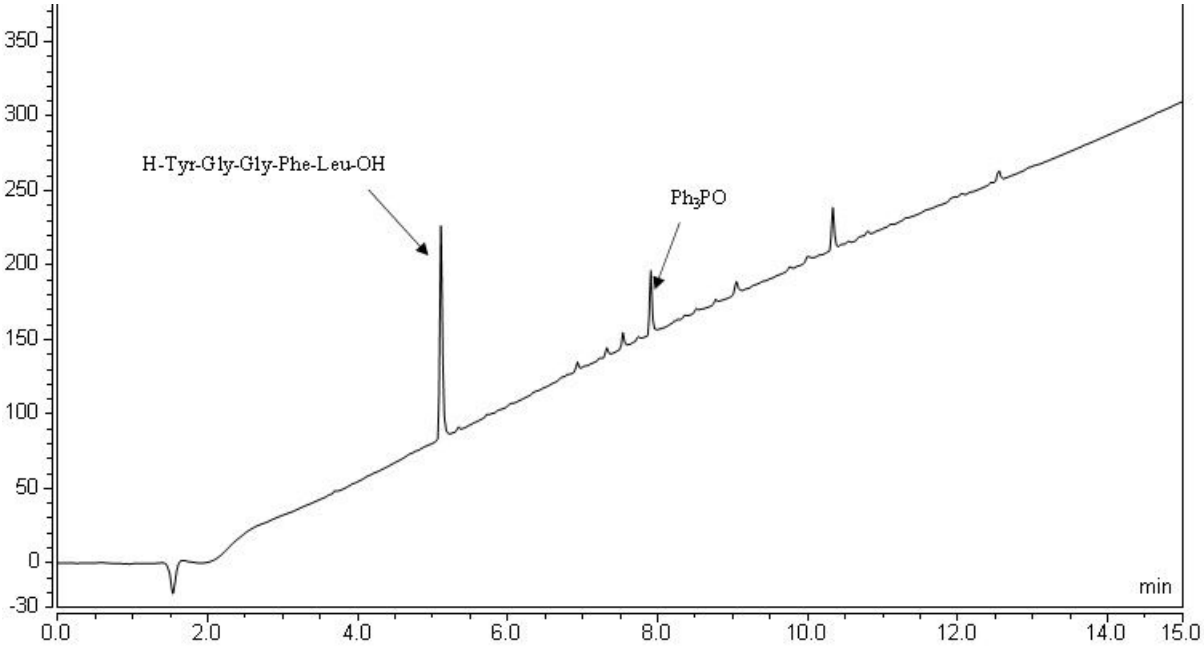

Figure S13: HPLC chromatogram for H-Tyr-Gly-Gly-Phe-Leu-OH.

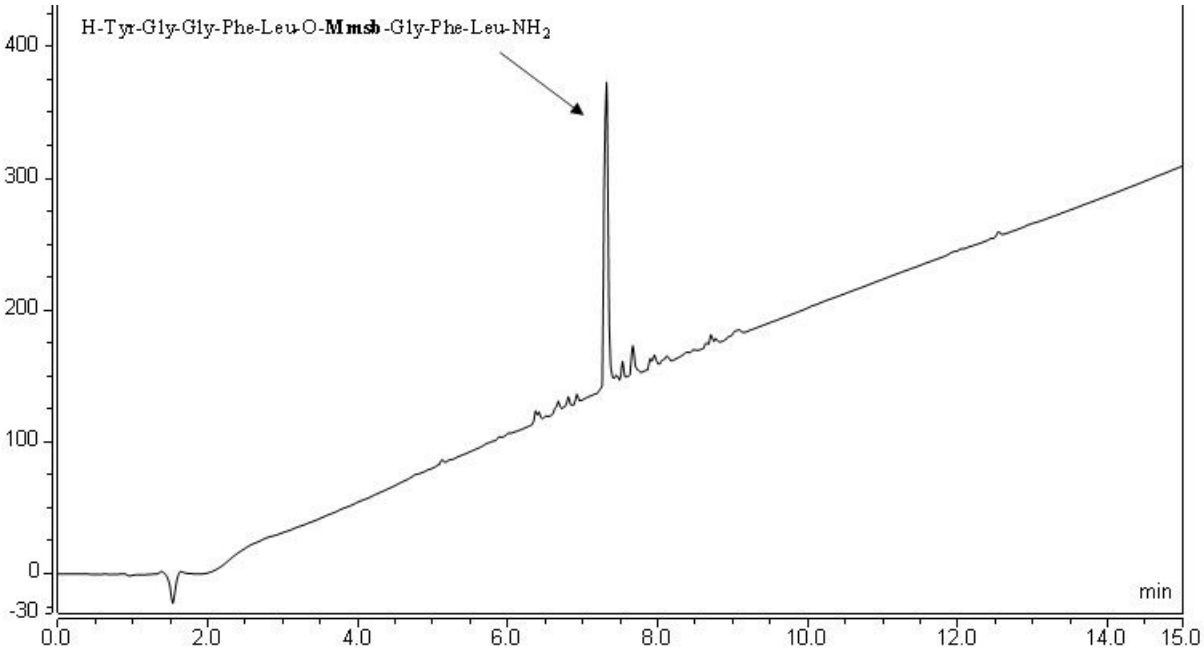

Figure S14: HPLC chromatogram for H-Tyr-Gly-Gly-Phe-Leu-O-Mmsb-Gly-Phe-Leu-NH_2.

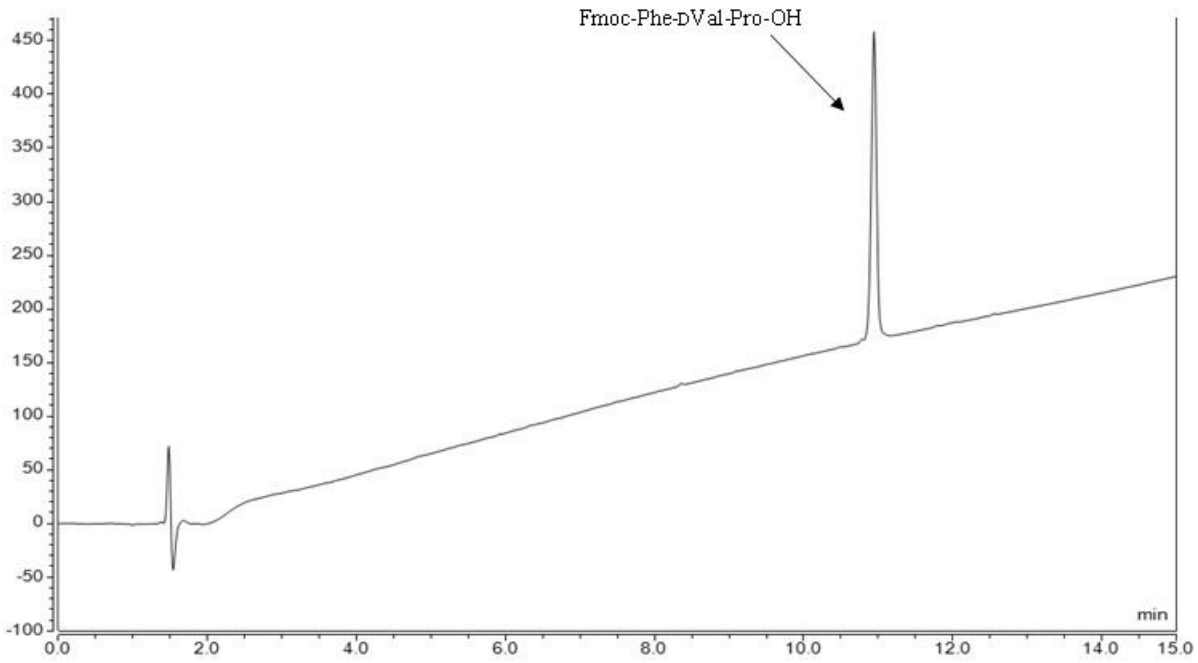

Figure S15: HPLC chromatogram for Fmoc-Phe-DVal-Pro-OH, Strategy **I** using Boc-DVal-OH **(a)** before Fmoc-Leu-OH addition.

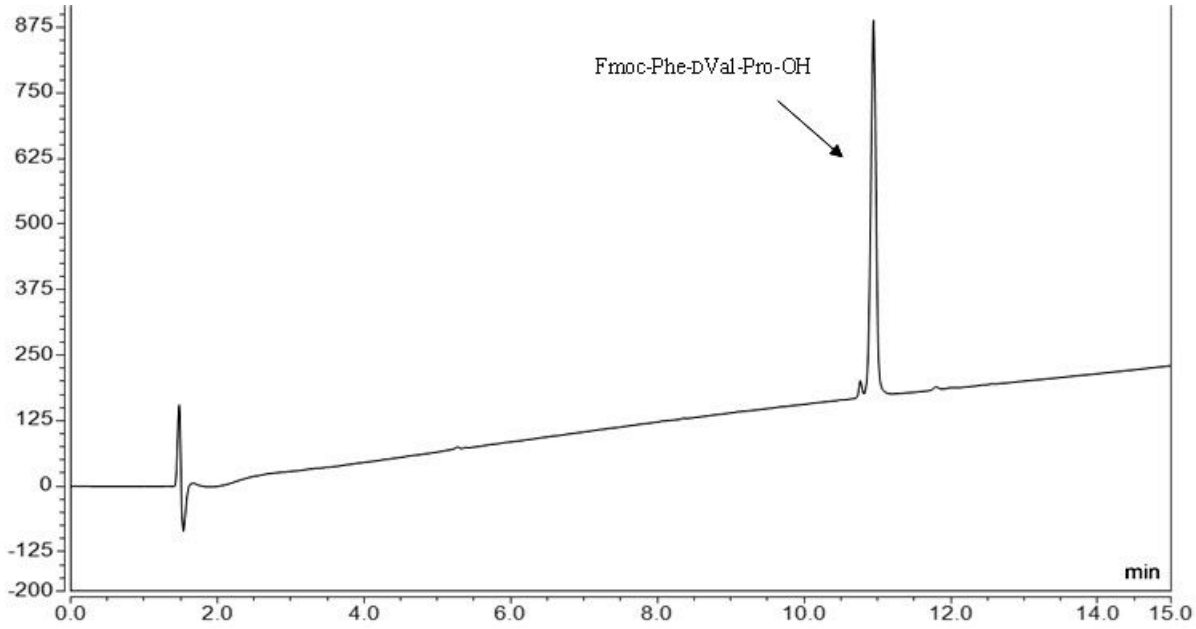

Figure S16: HPLC chromatogram for Fmoc-Phe-DVal-Pro-OH, Strategy **I** using Boc-DVal-OH **(b)** after Fmoc-Leu-OH addition.

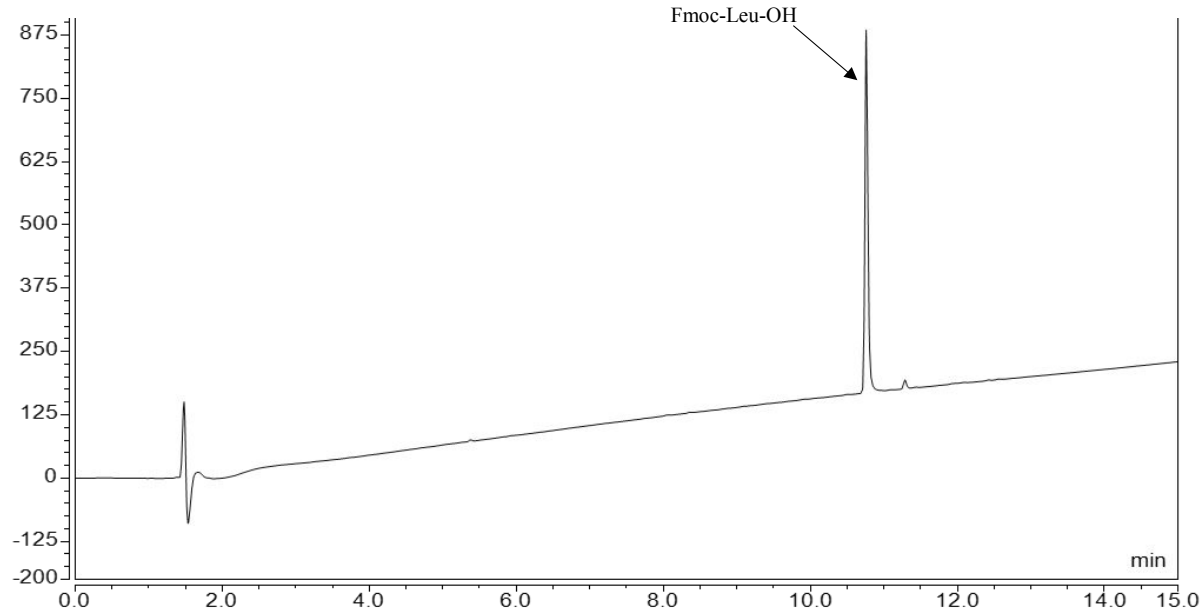

Figure S17: HPLC chromatogram for Fmoc-Leu-OH, Strategy **II** using Fmoc-DVal-OH.

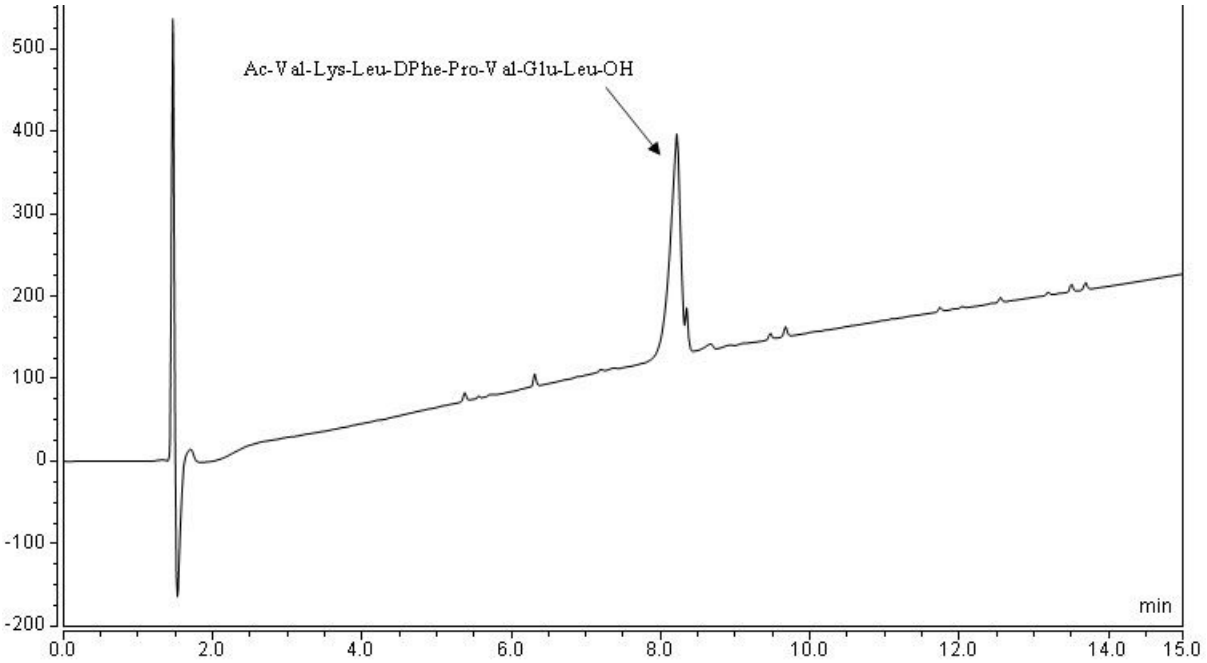

Figure S18: HPLC chromatogram for Ac-Val-Lys-DPhe-Pro-Val-Glu-Leu-OH.

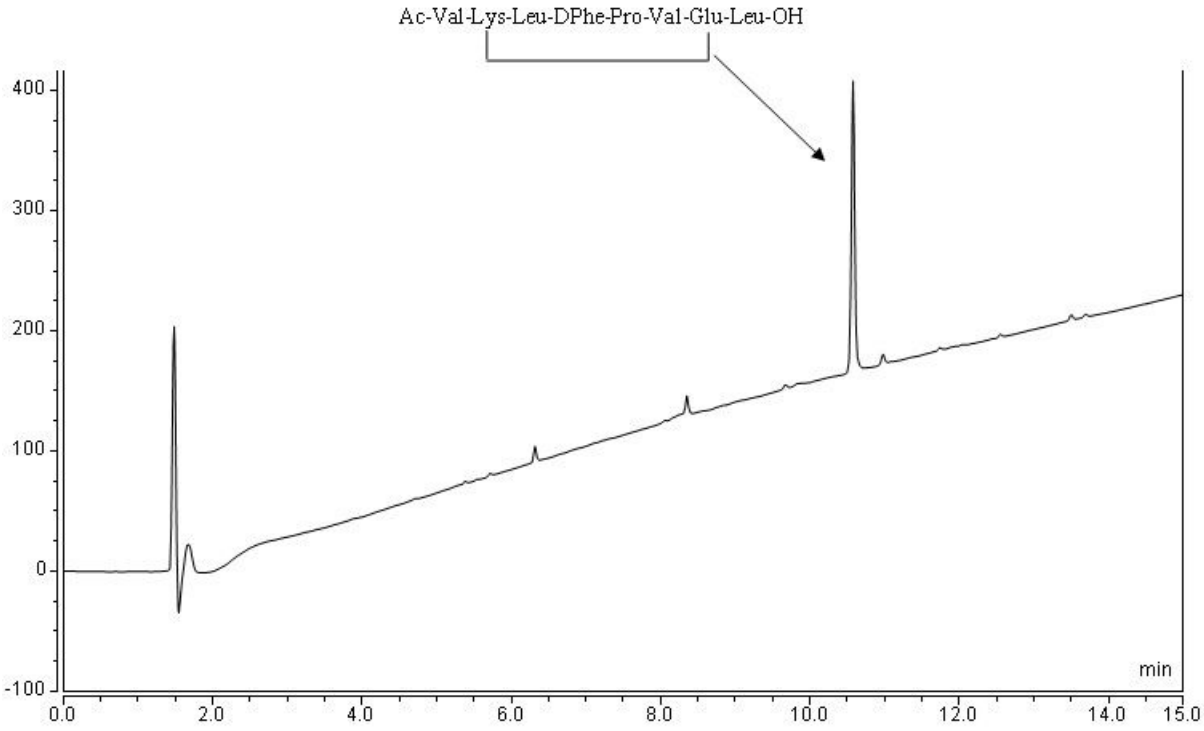

Figure S19: HPLC chromatogram for cyclized Ac-Val-Lys-DPhe-Pro-Val-Glu-Leu-OH.

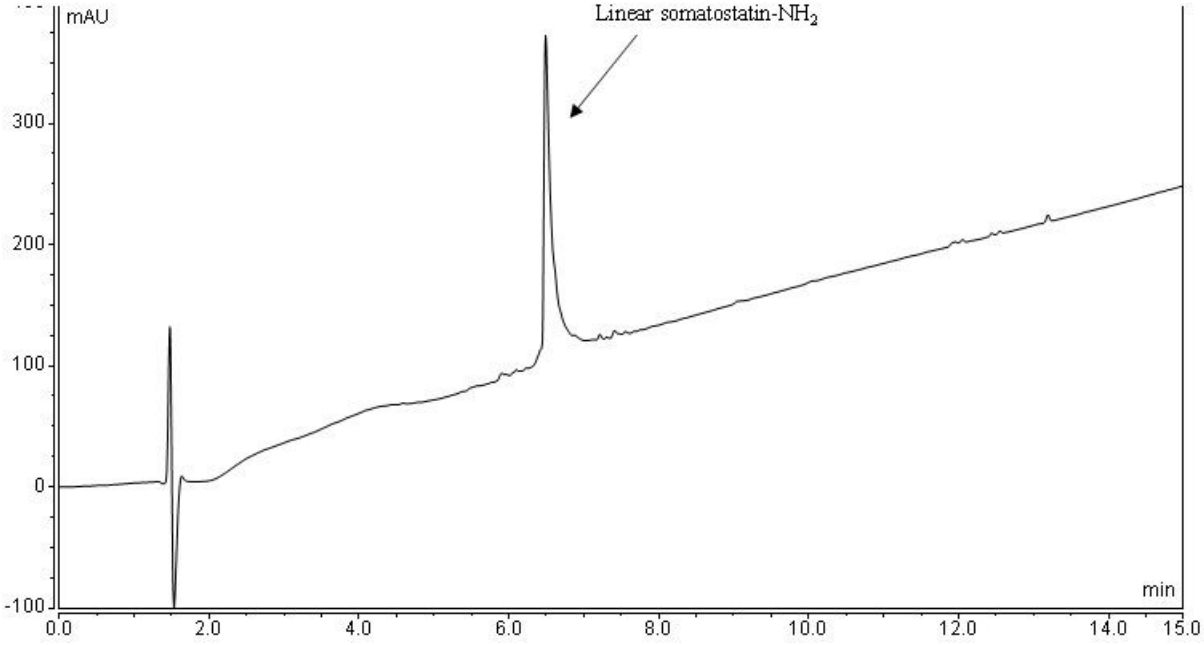

Figure S20: HPLC chromatogram for Linear somatostatin-NH_2.

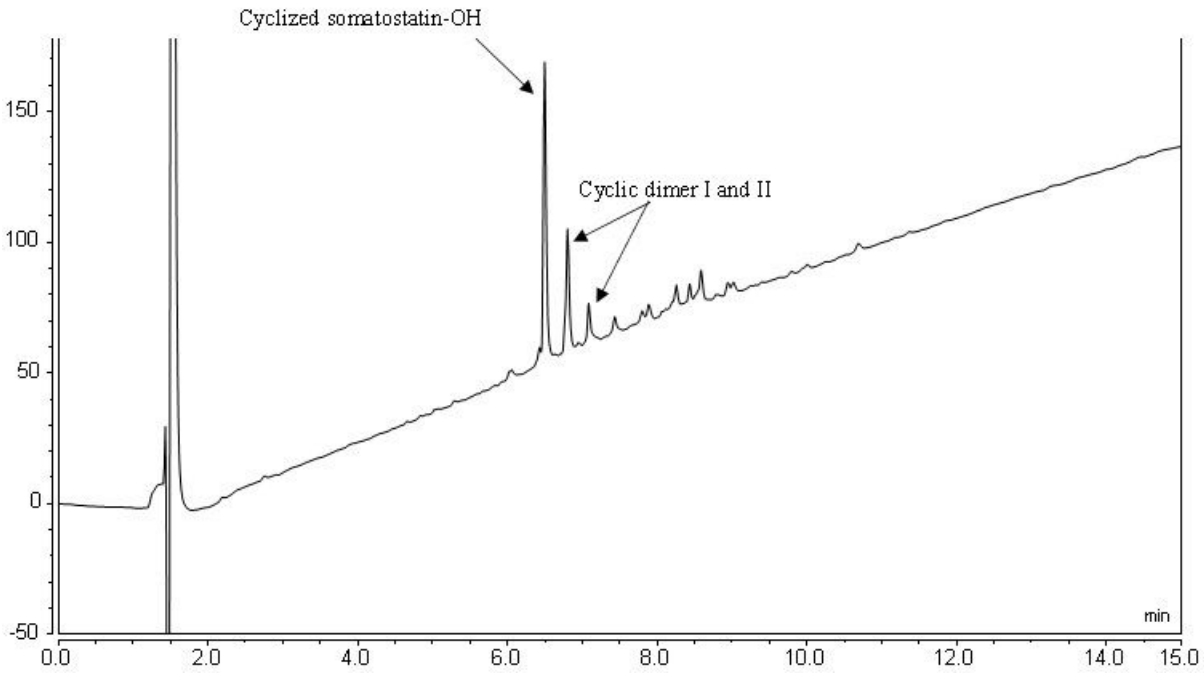

Figure S21: HPLC chromatogram for cyclized somatostatin-OH on-resin cyclization using HO-Mmsb-Resin.

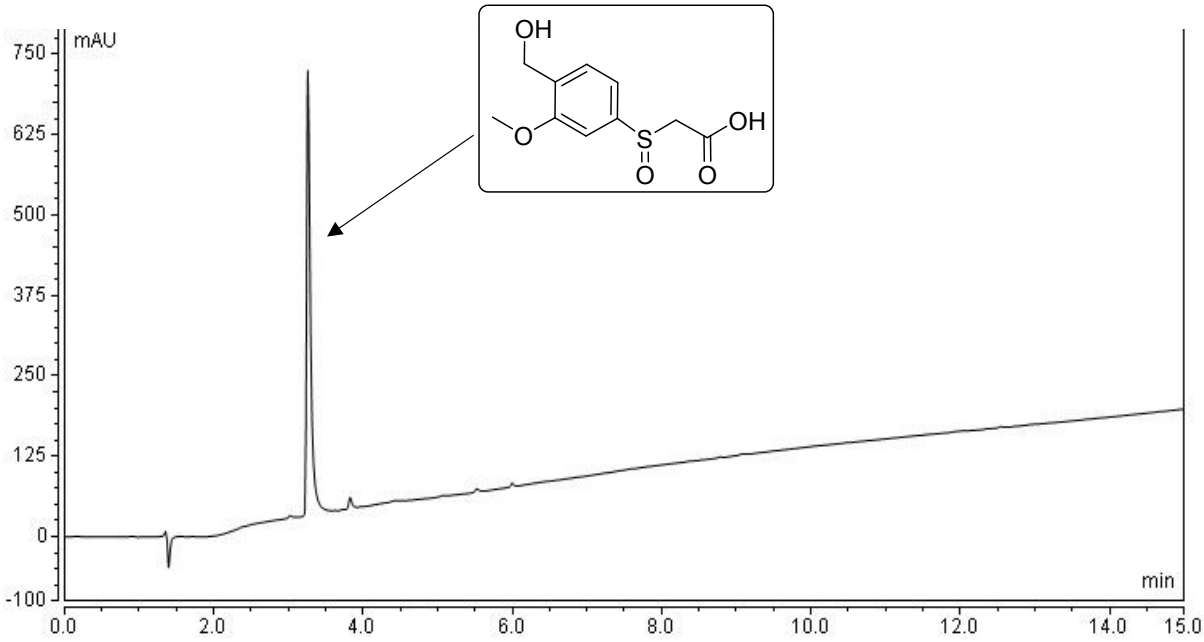

Figure S22: HPLC chromatogram for Mmsb linker.

NMR spectra for Mmsb linker

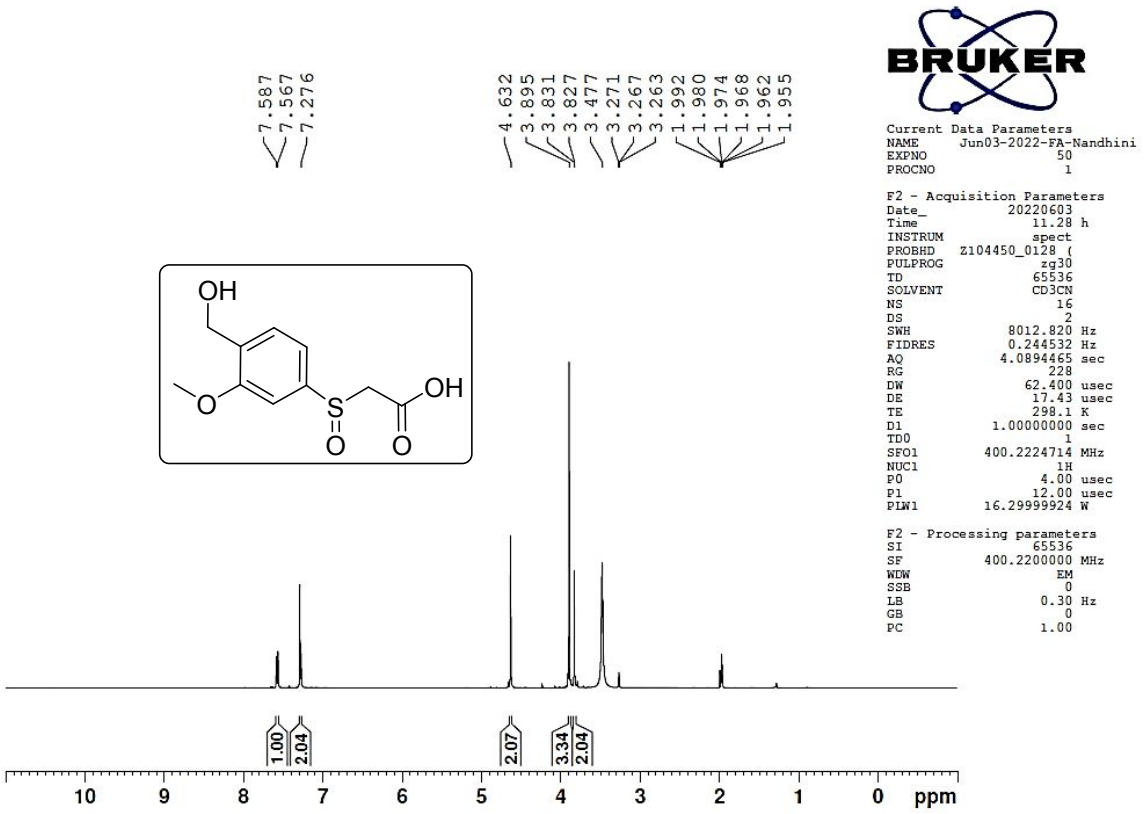

Figure S23: {^{1}H} NMR Spectra of Mmsb linker.

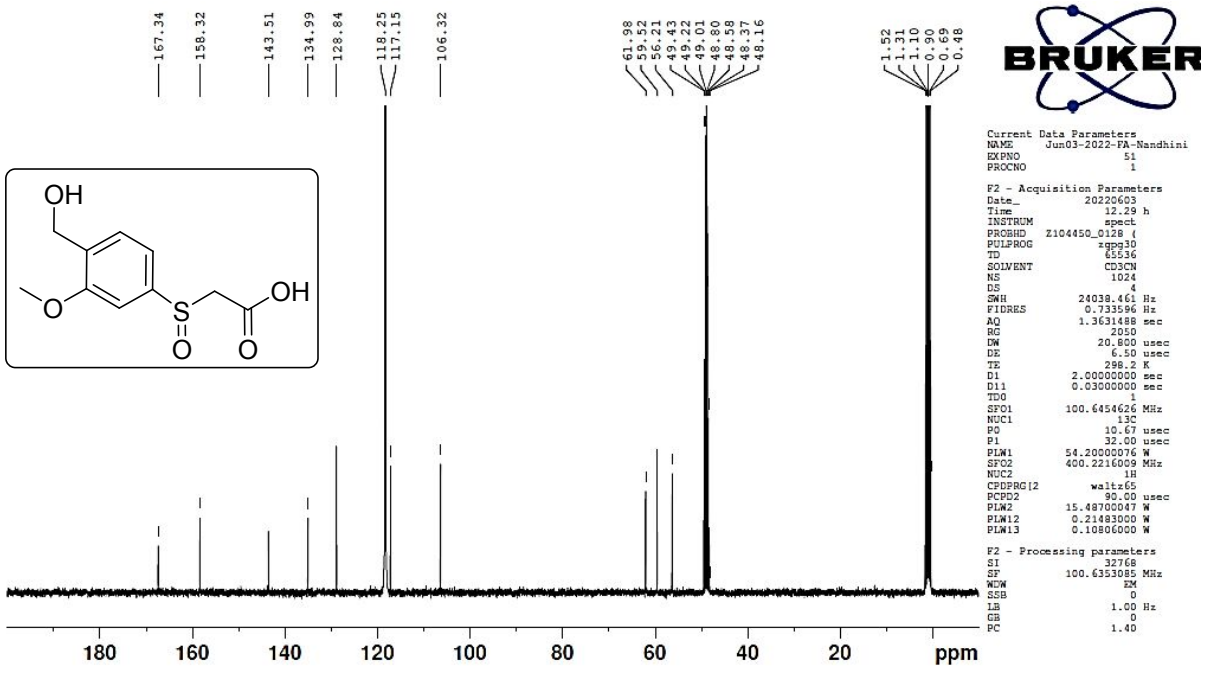

Figure S24: 13C{^{1}H} NMR spectra of Mmsb linker.

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