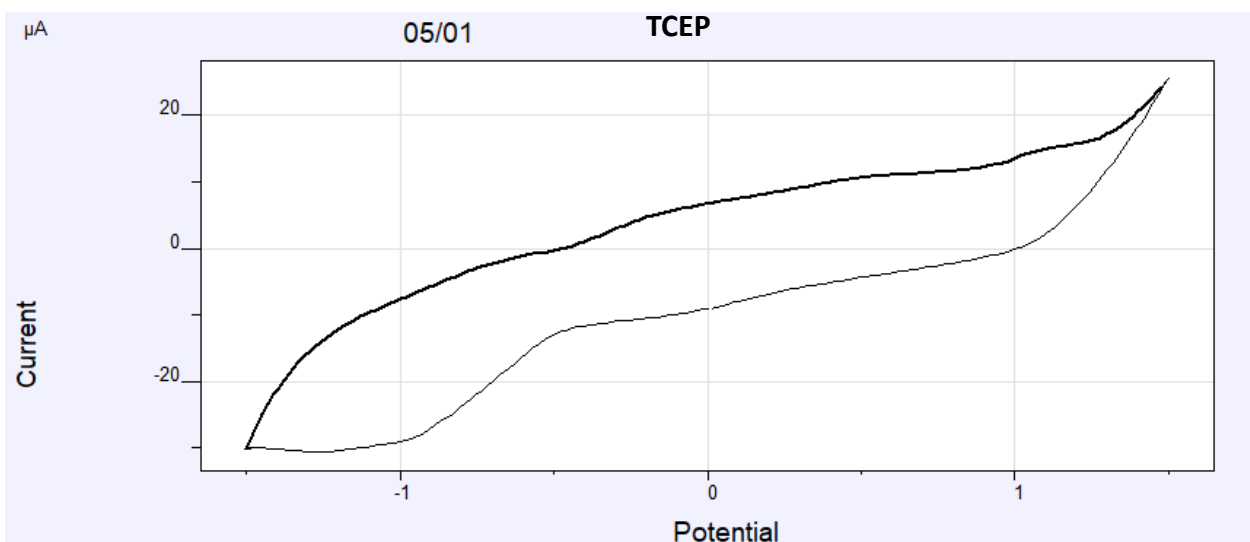
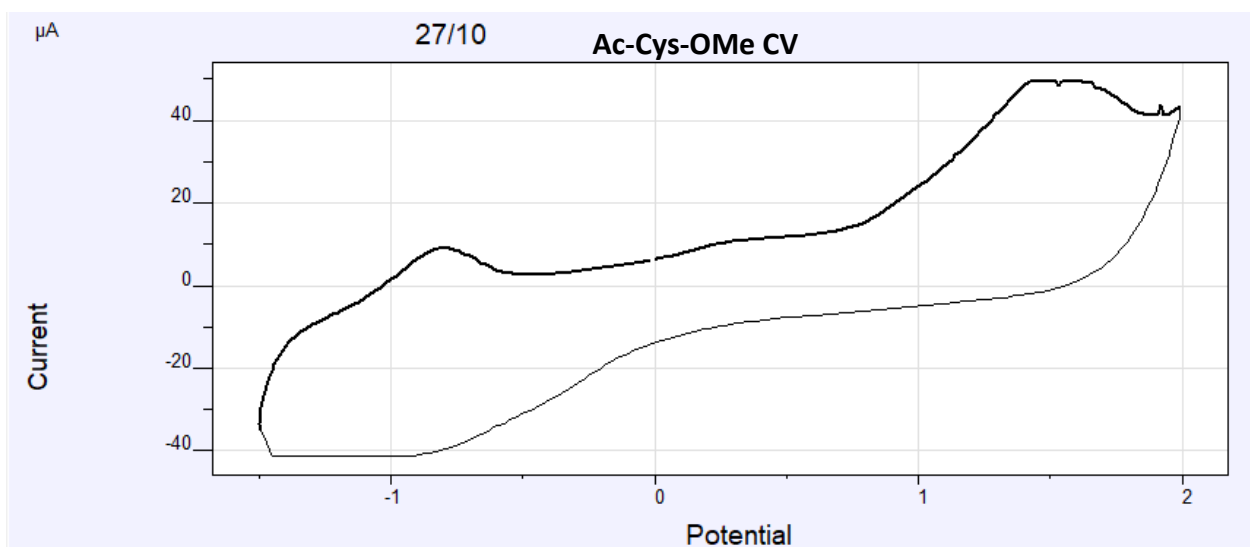


Novel electrochemically-mediated peptide dehylation in processes relevant to native chemical ligation

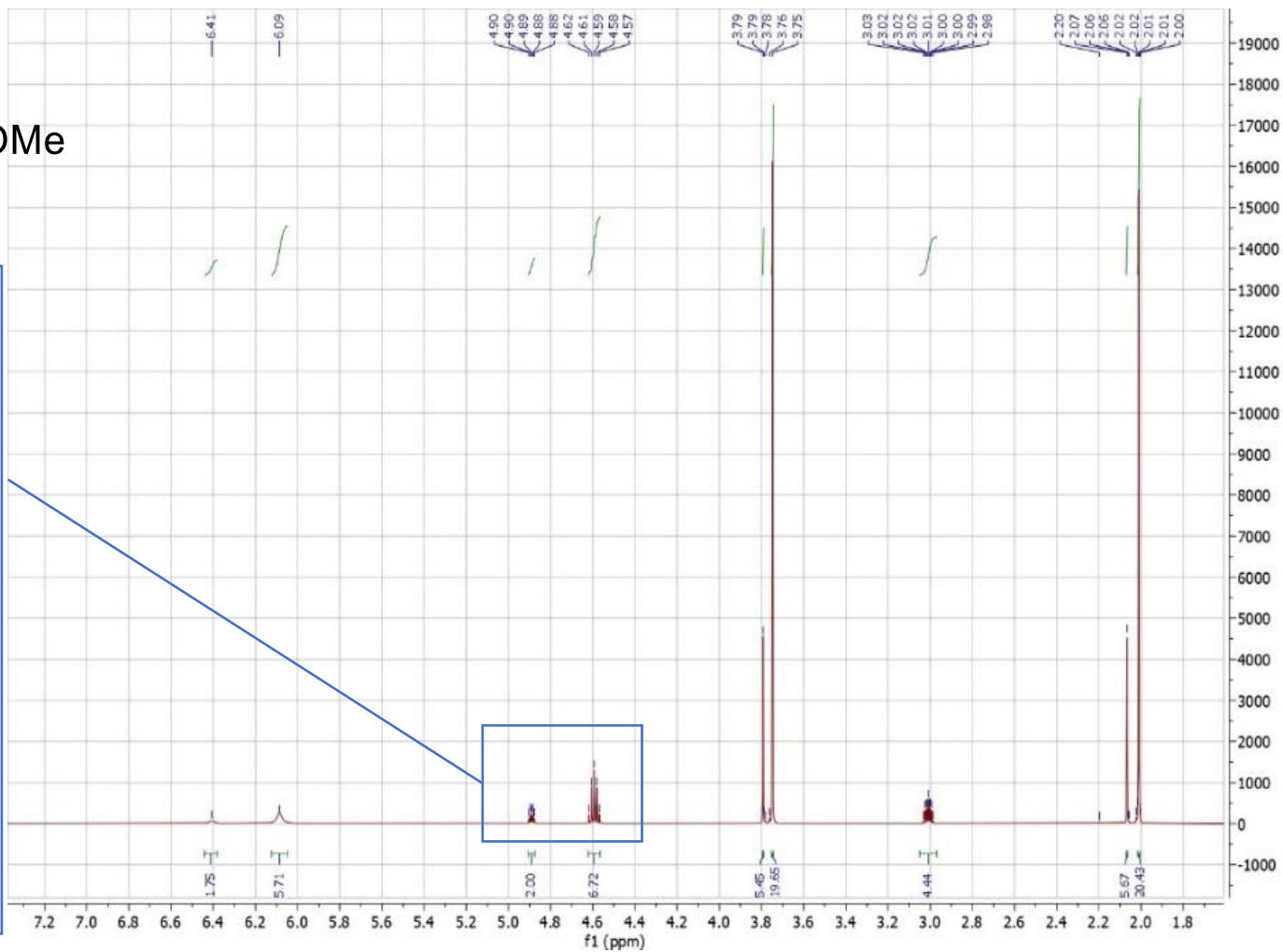
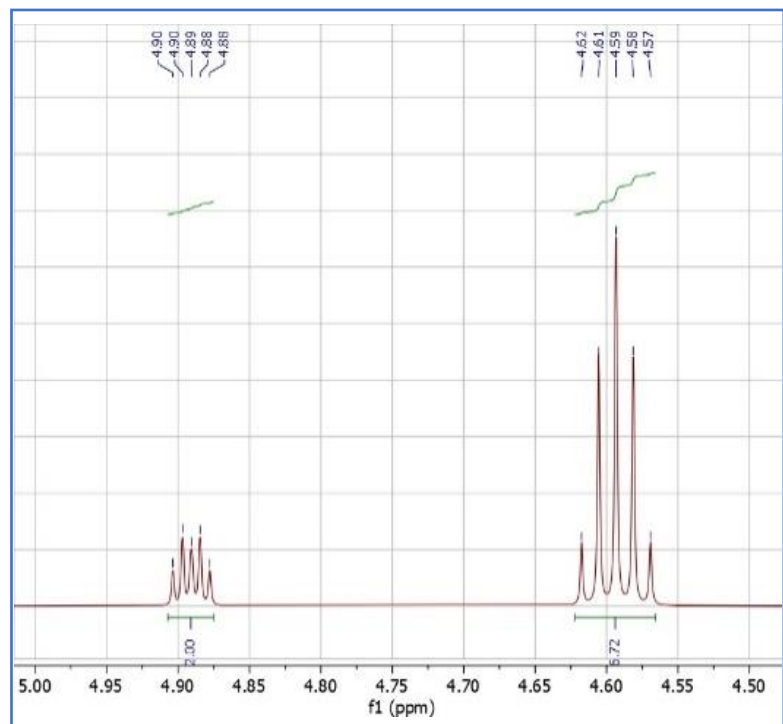
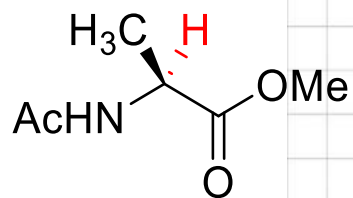
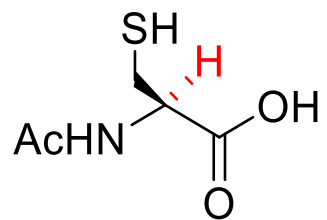
Charles M.G. Lamb, Jian Shi, Jonathan D. Wilden and Derek Macmillan*

Supporting information

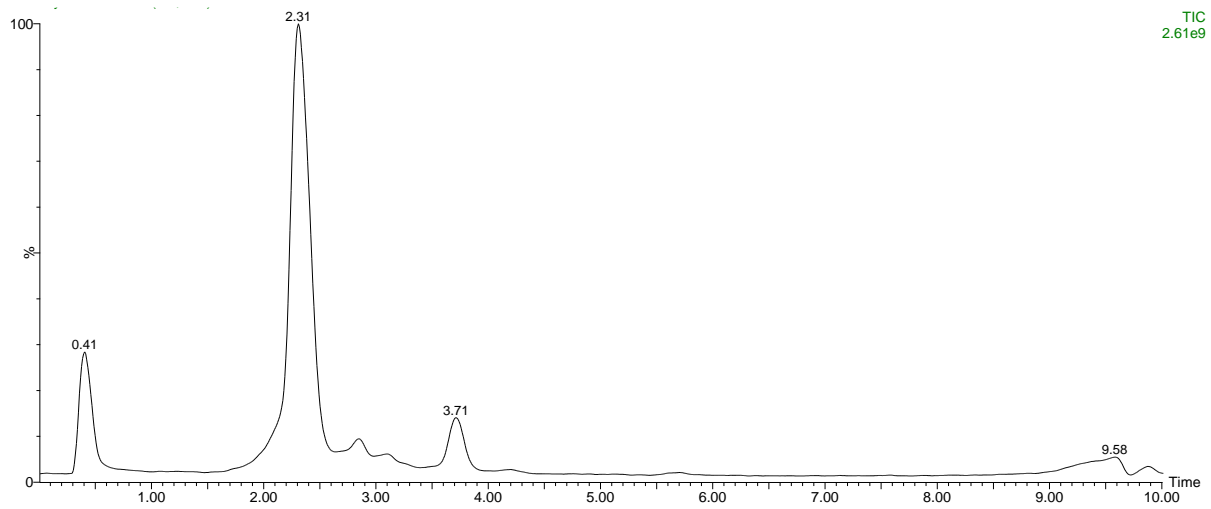
Cyclic voltammetry conditions: CV plots were measured on an Ivium Technologies Vertex model potentiostat operating with a glassy carbon working electrode, silver wire reference electrode and Pt wire counter electrode. The analyte was dissolved to a concentration of 1 mg/mL in deoxygenated 2:1 water/MeCN (10 mL) with 0.1 M LiClO₄ as the supporting electrolyte. Voltammograms were recorded at a scan rate of 100 mV/s.



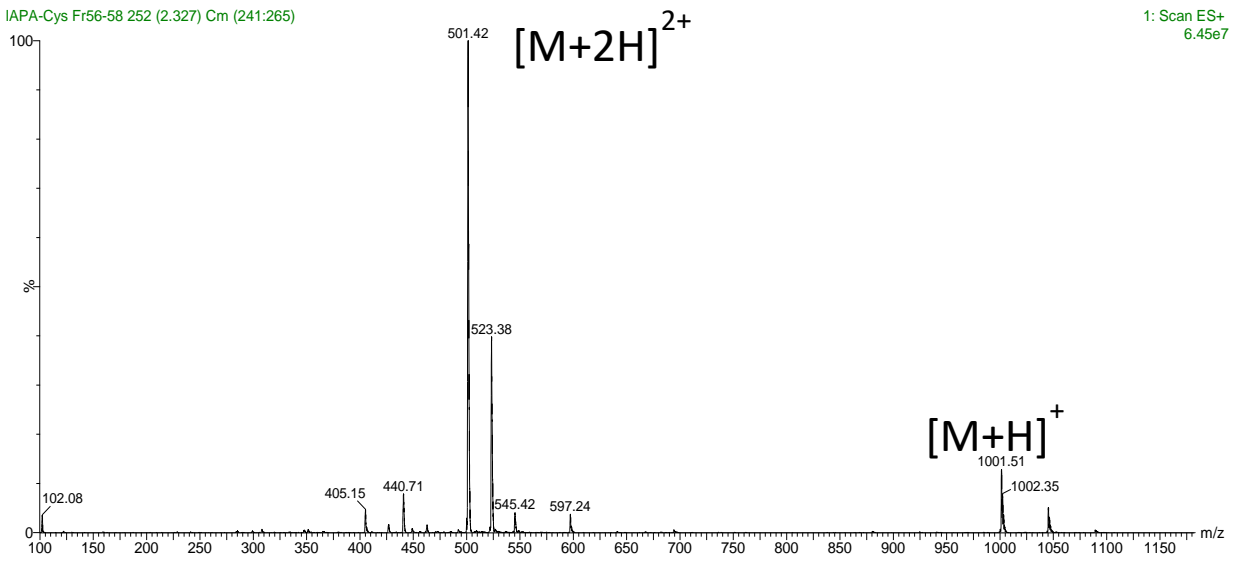
Example NMR after extraction, shows a 7:2 mixture of Alanine to Cysteine



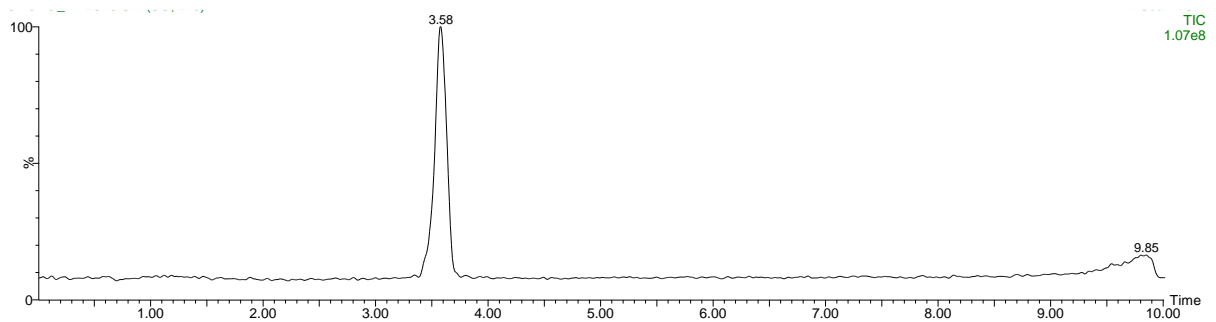
Linear peptide 3:

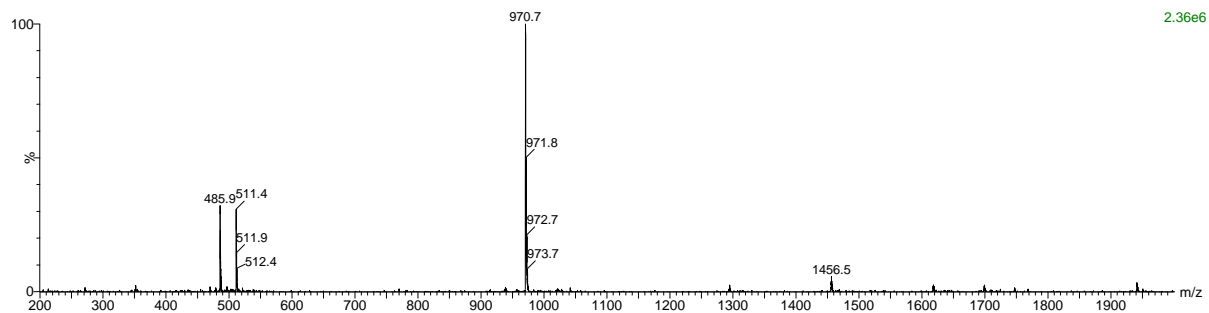


IAPA-Cys Fr56-58 252 (2.327) Cm (241:265)

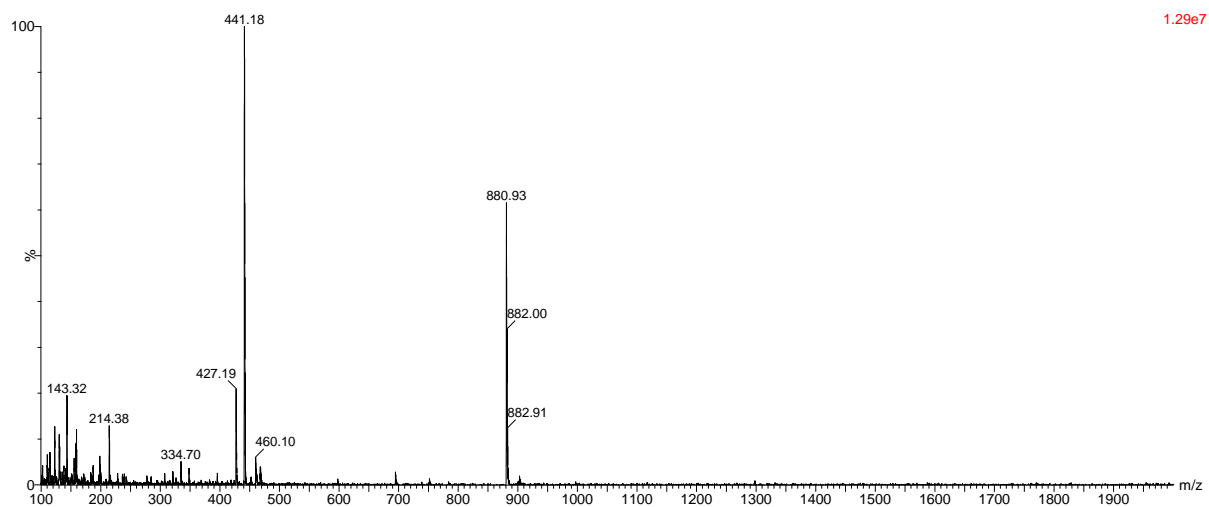


Linear Peptide 4.

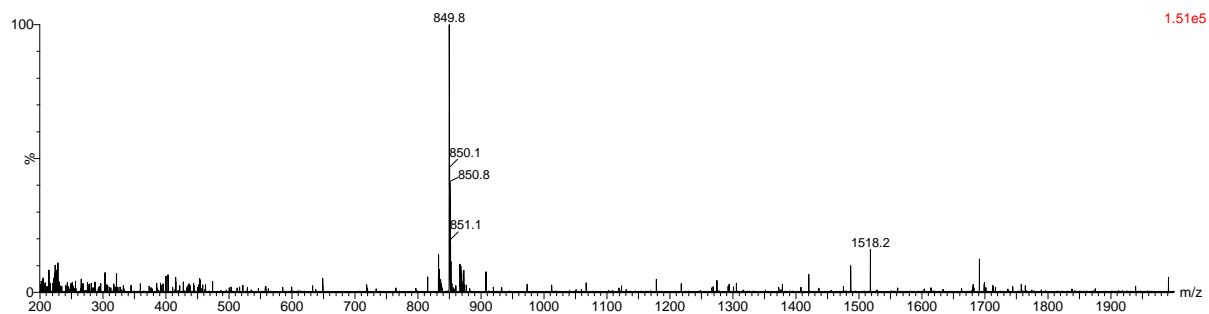
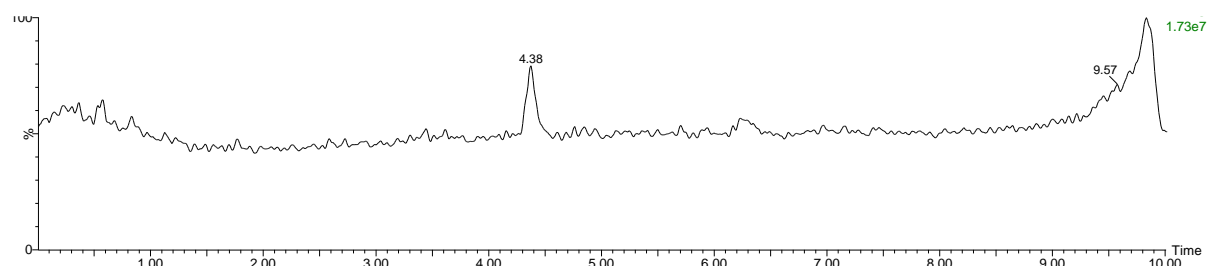




cyclic peptide 5

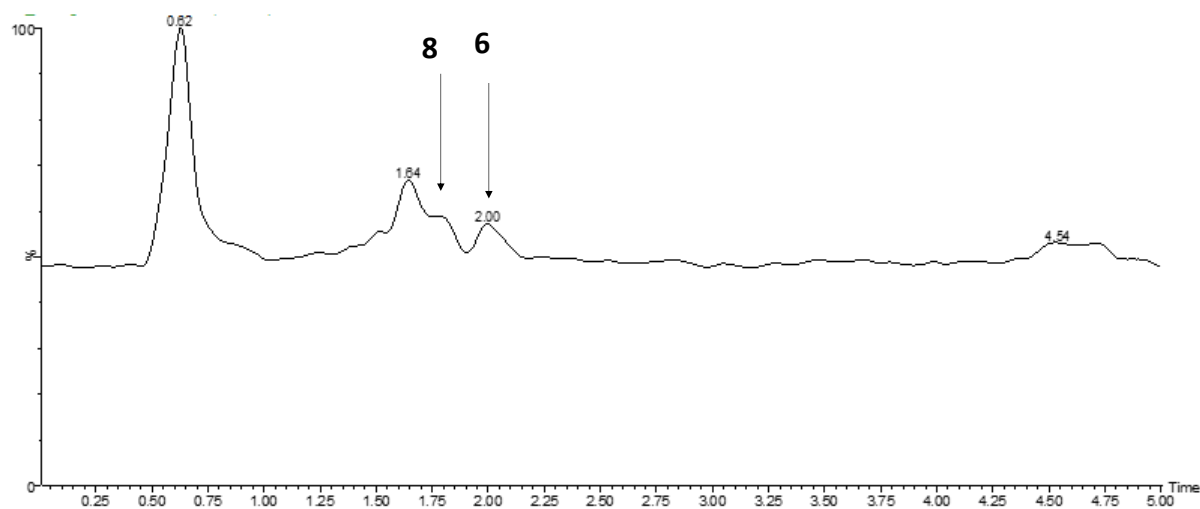


Cyclic peptide 6

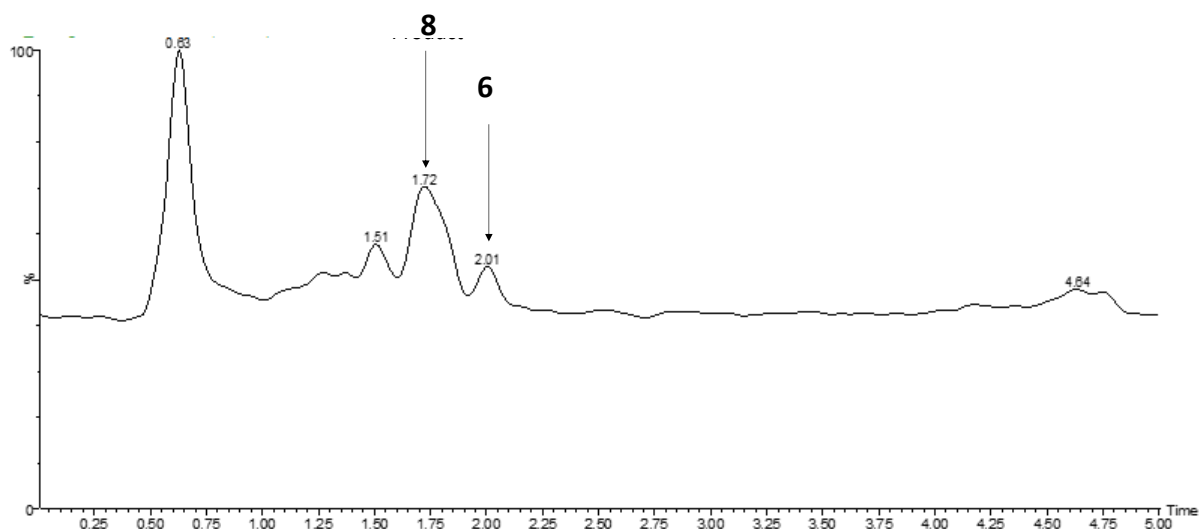


Electrochemical desulfurization of **6**.

2h



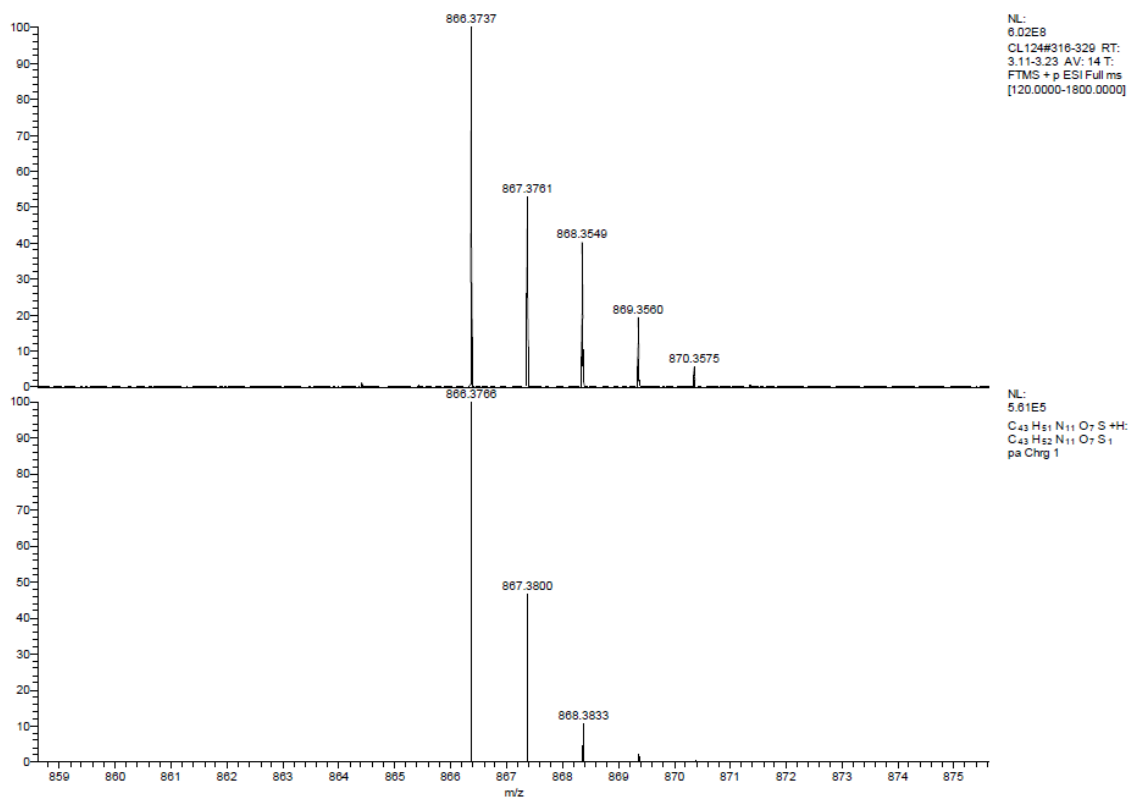
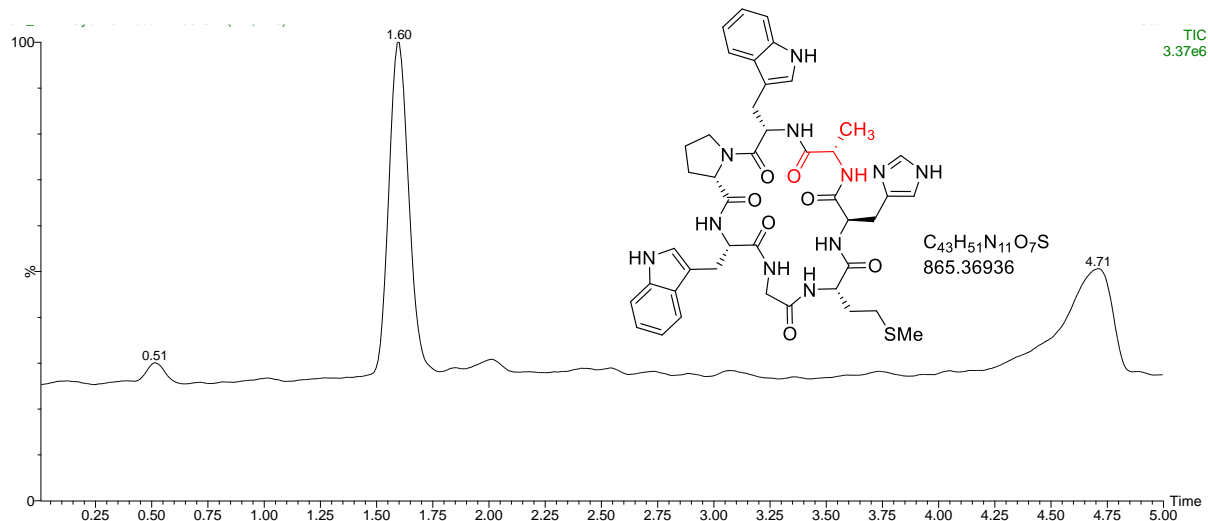
6h



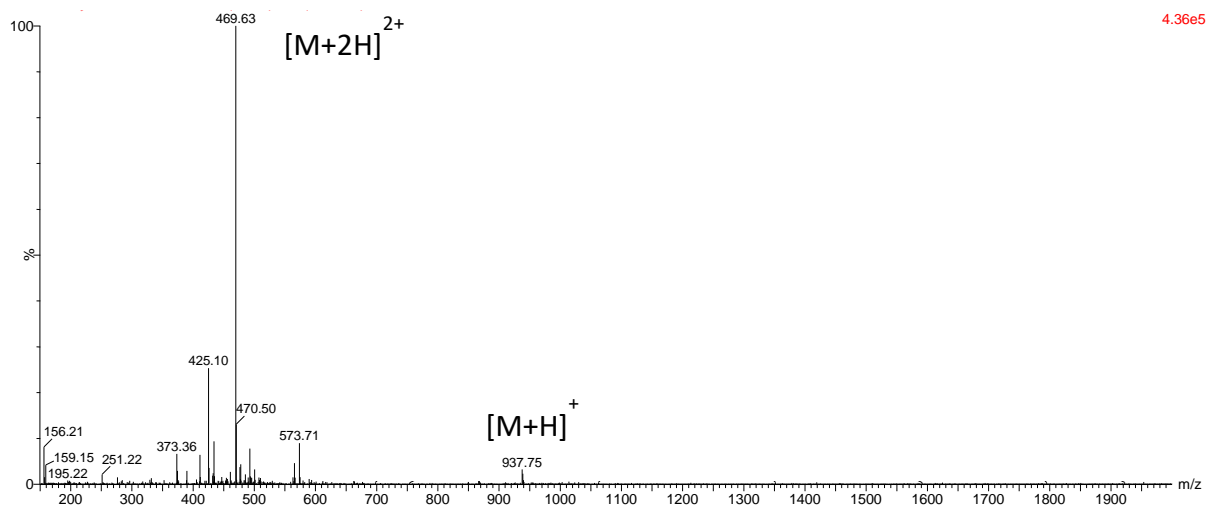
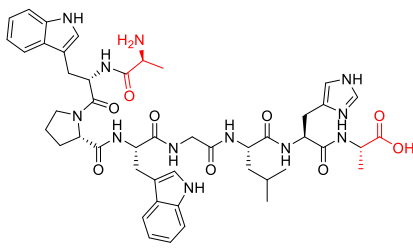
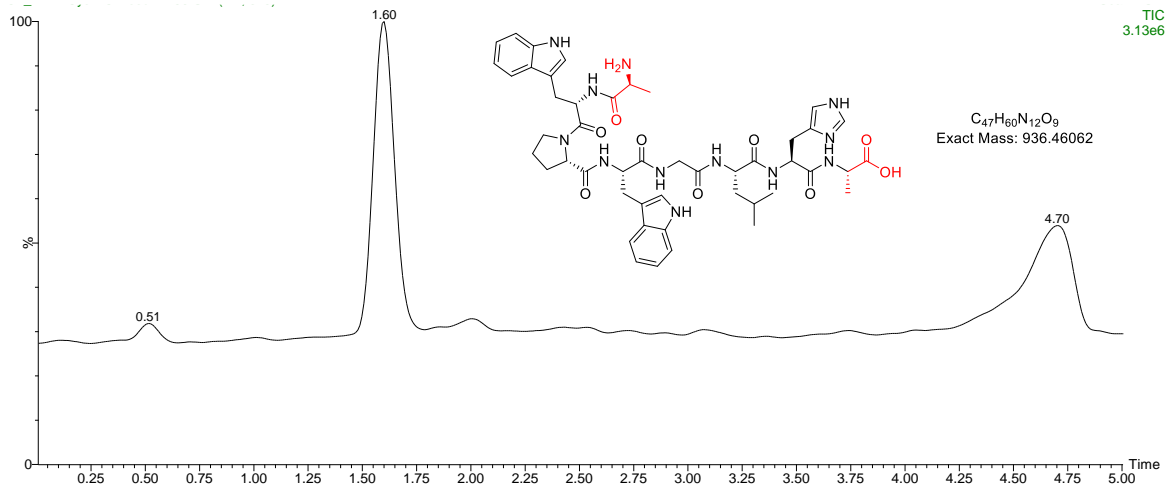
Methionine containing Agardhipeptin analogue: The linear peptide (H-Cys-Trp-Pro-Trp-Gly-Met-His-Cys-OH) was synthesised via our general solid phase peptide synthesis procedure, and isolated by semi-preparative HPLC and lyophilization to afford a white fluffy solid (9.6 mg, 19%), $t_R = 31.8$ min. **ESI-MS:** calculated m/z for $C_{46}H_{58}N_{12}O_9S_3$ $[M]^+$ 1018.36, observed $[M+H]^+$ 1019.66.

Cyclisation via N→S acyl transfer: was conducted as above for cyclic peptide **5**. The product, obtained from (9.6 mg, 9.42 μ mol) linear starting material, was purified via semi-preparative HPLC and lyophilization to produce a fluffy white powder of peptide **11** (5.6 mg, 6.24 μ mol, 48%). $t_R = 30.6$ min. **ESI-MS:** calculated m/z for $C_{43}H_{51}N_{11}O_7S_2$ $[M]^+$ 897.34, observed $[M+H]^+$ 898.68.

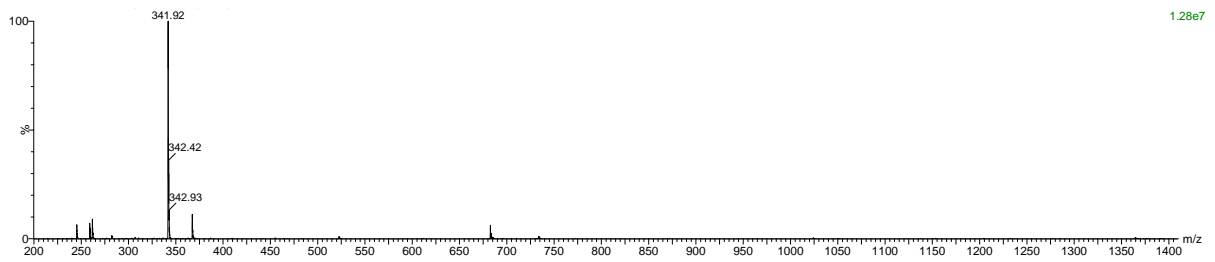
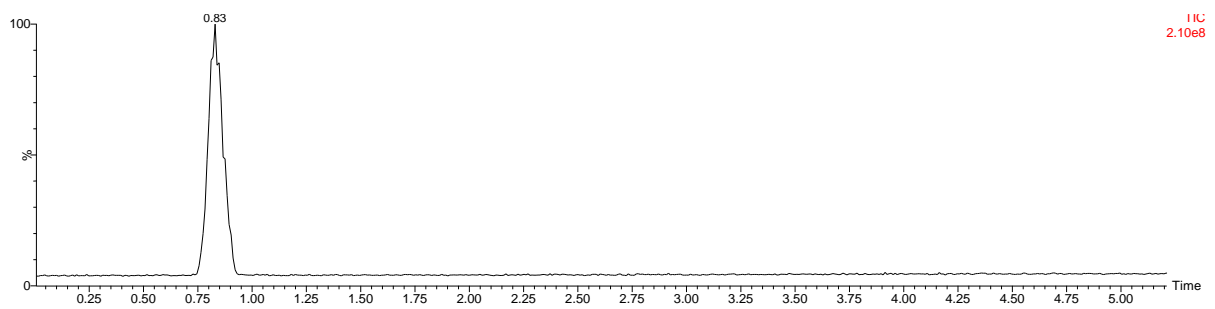
Dethylation of the Met analogue (5 mg) was desulfurized as described above for **5**. The product was purified directly from the reaction mixture via preparative HPLC and the eluted fractions freeze-dried to produce a fluffy white solid of the desulfurized peptide (1.2 mg, 25%).



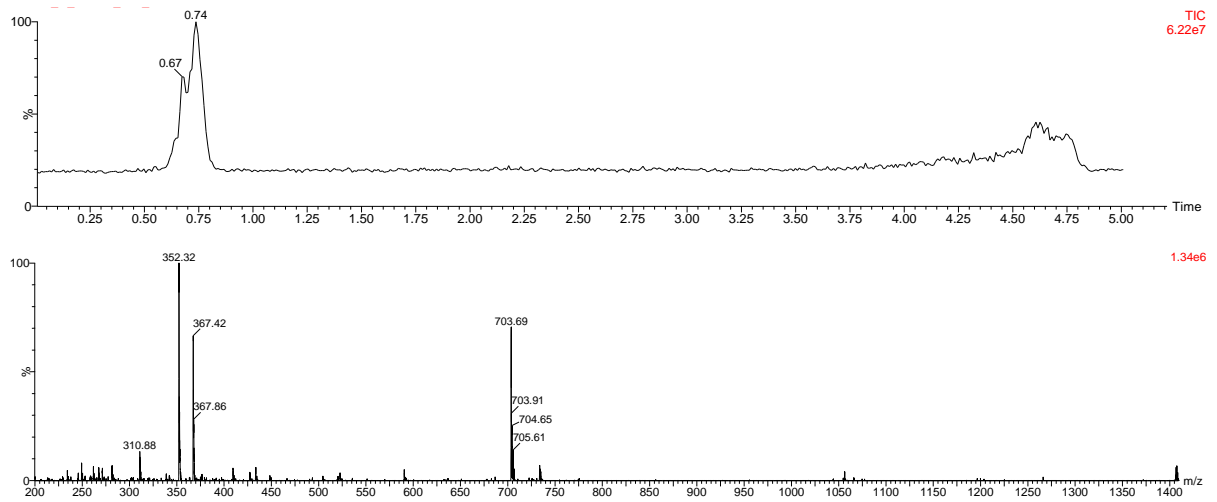
Dethylation of linear peptide 3. **3** (5 mg) was desulfurized as described above for **5**. After 8 h the product was purified directly from the reaction mixture via preparative HPLC and the eluted fractions freeze-dried to produce a fluffy white solid of the desulfurized peptide (0.6 mg, 0.65 μ mol, 13%).



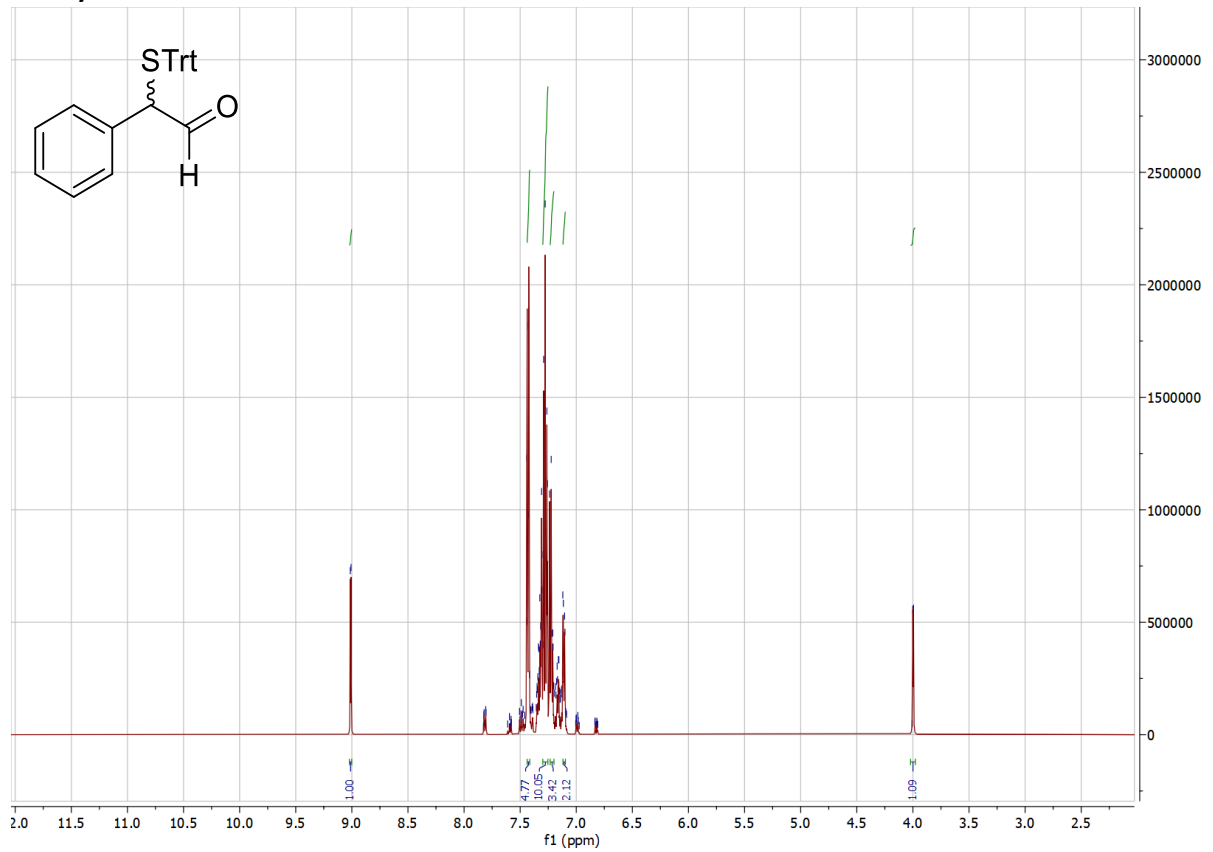
Linear Peptide H-LYRAGC-OH (14)



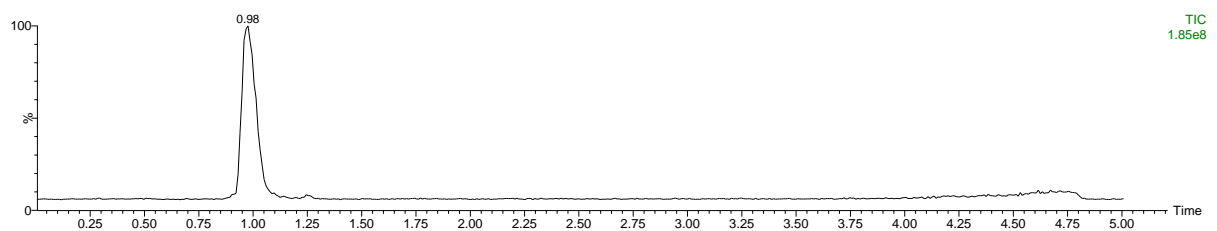
Linear Peptide thioester (15)

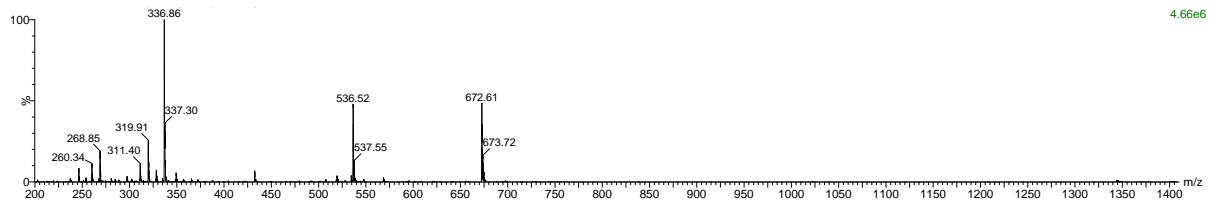


Aldehyde 12



Linear peptide Aux-GRAFS-NH₂ (13)





HRMS for peptide 17 calculated m/z for $C_{49}H_{78}N_{17}O_{12}$ $[M+H]^+$ 1096.6010, observed $[M+H]^+$ 1096.6019.

