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

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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:

Linear Peptide 4.

\[ [\text{M}+2\text{H}]^2^+ \]

\[ [\text{M}+\text{H}]^+ \]
**Electrochemical desulfurization of 6.**

2h

![Graph 1](image1.png)

6h

![Graph 2](image2.png)

**Methionine containing Agardhipeptin analogue:** The linear peptide (H-Cys-Trp-Pro-Trp-Gly-Met-His-Cys-OH) was synthesized 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 $C_{46}H_{58}N_{12}O_{9}S_3 [M]+ 1018.36$, observed $[M+H]^+ 1019.66$.

**Cyclisation via $N\rightarrow S$ acyl transfer:** was conducted as above for cyclic peptide 5. The product, obtained from (9.6 mg, 9.42 μmol) 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 μmol, 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 $[M+H]^+ 898.68$.

**Dethiylation 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%).
Detritylation 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 µmol, 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.