# New electrochemical method for Arylation of Cysteine containing peptides

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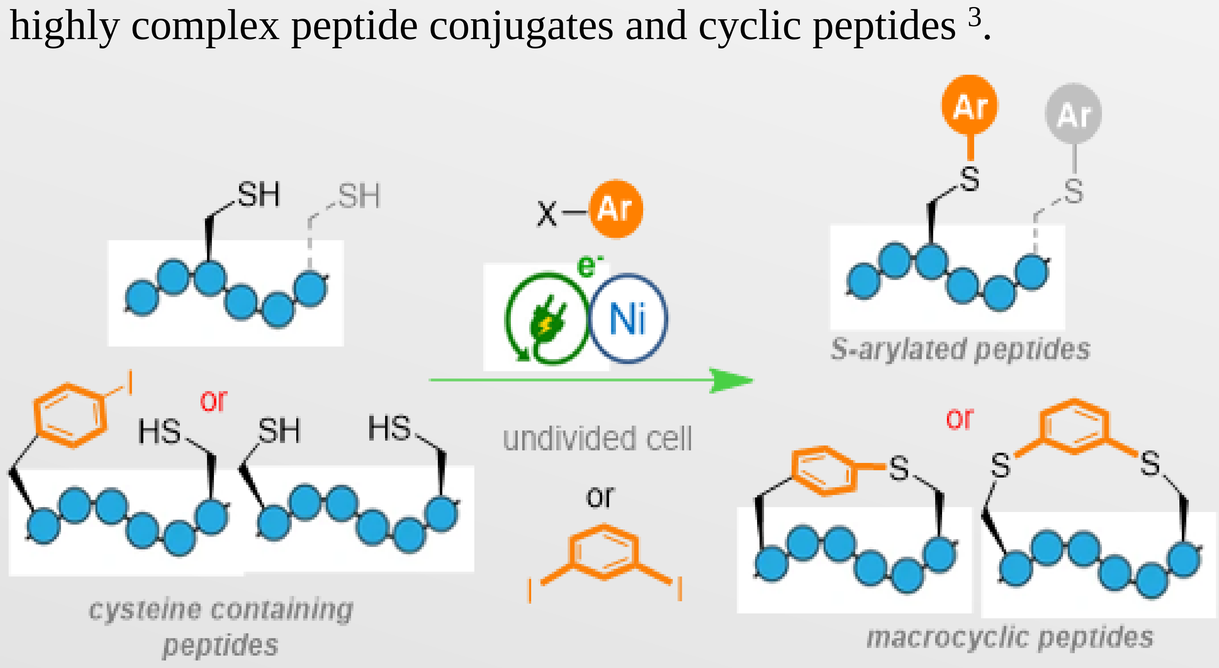
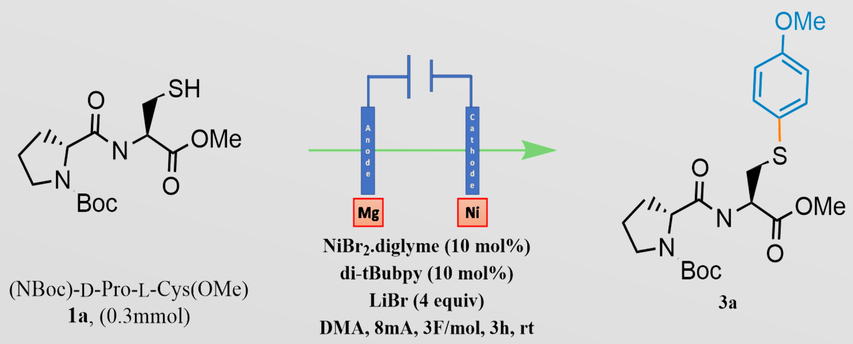
## INTRODUCTION

Functionalized peptides have emerged as a privileged class of bioconjugates with a diverse range of potential therapeutic applications, including cancer therapy, inflammation, and infection[1].
Thus, the development of peptide bioconjugates is a growing area of research and holds great potential for the treatment of various diseases. As a consequence, the need for new site-selective bioconjugation methods under biocompatible conditions is highly desirable.
Here we report a simple electrochemical route towards the synthesis of S-arylated peptides by a site selective coupling of Cysteine containing peptides with aryl halides under base free conditions. This approach demonstrates the power of electrochemistry to access both highly complex peptide conjugates and cyclic peptides [3].

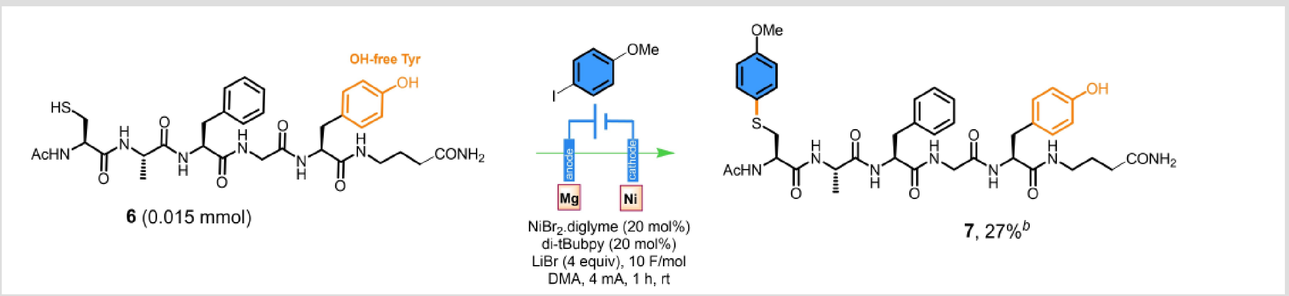


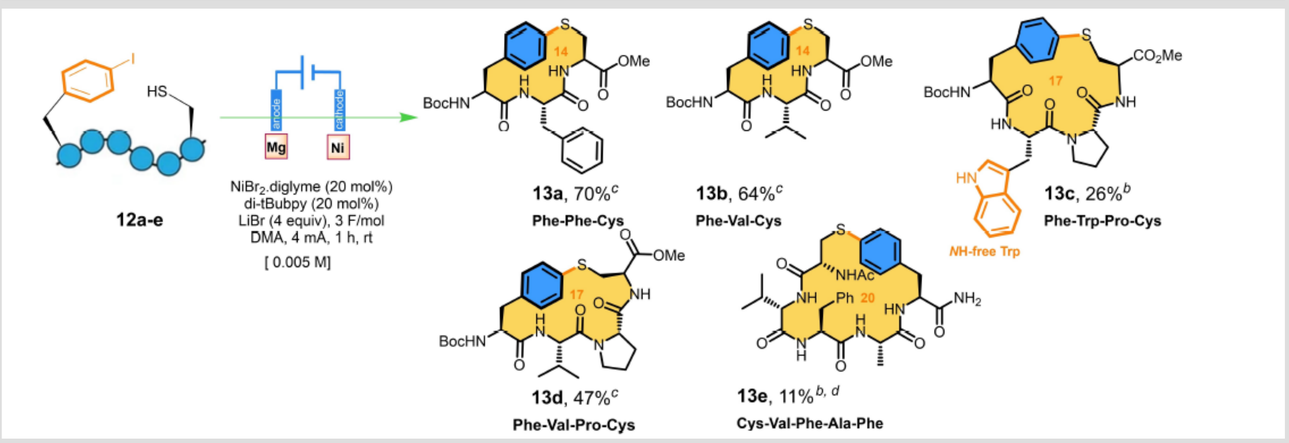

## Electrochemical S-arylylation of native Peptides



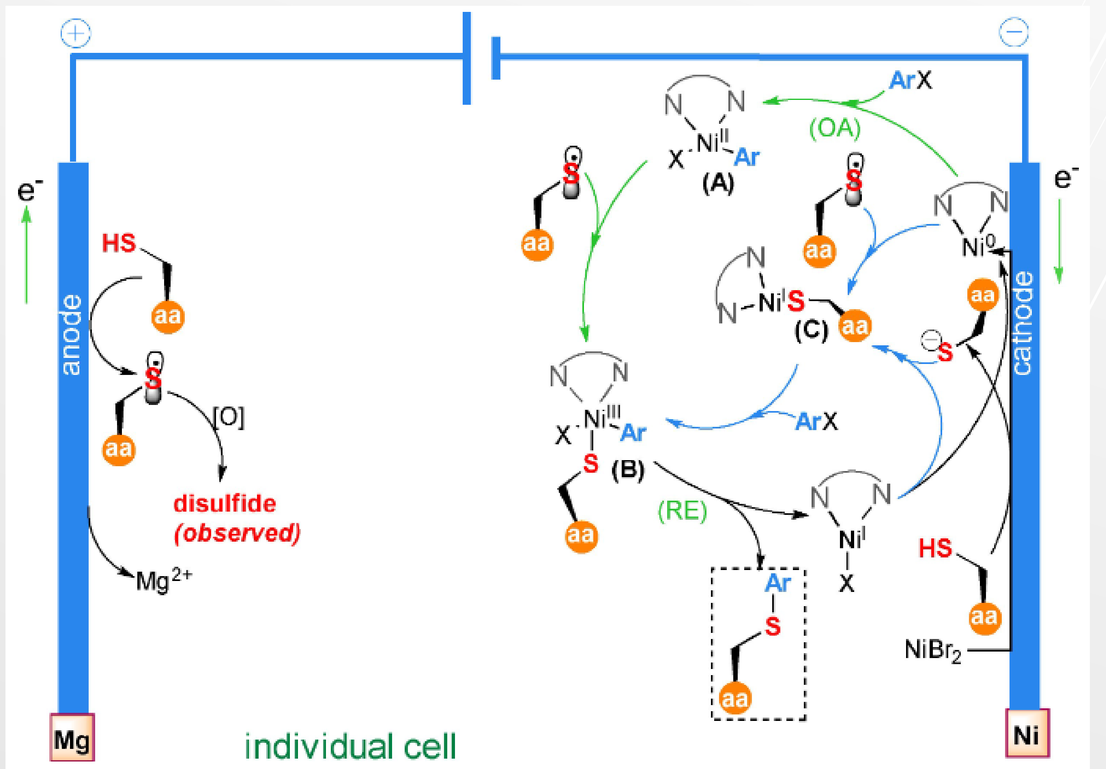

| Entry | Deviation from the standard conditions | Yield % |
|---|---|---|
| 1 | None | 89 |
| 2 | (4mA, 6h), instead of (8mA, 3h) | 84 |
| 3 | 4-Br-Anisole instead of 4-I Anisole | 57 |

## Reaction Optimization

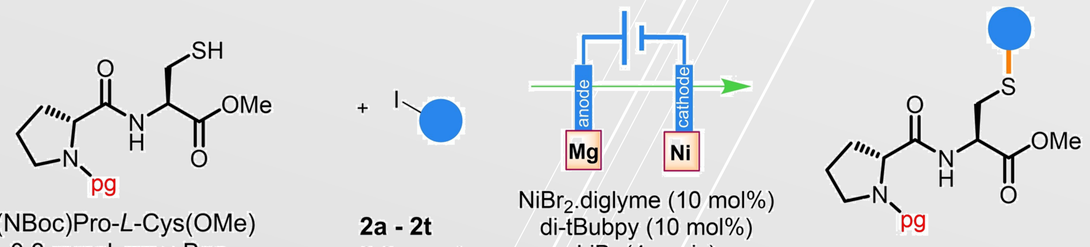


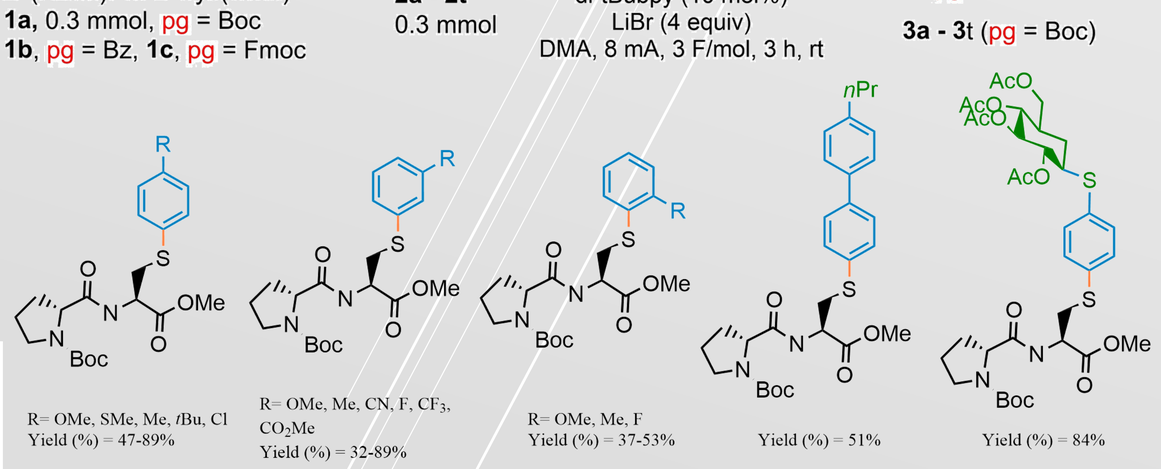




## Access to linear and cyclic peptides

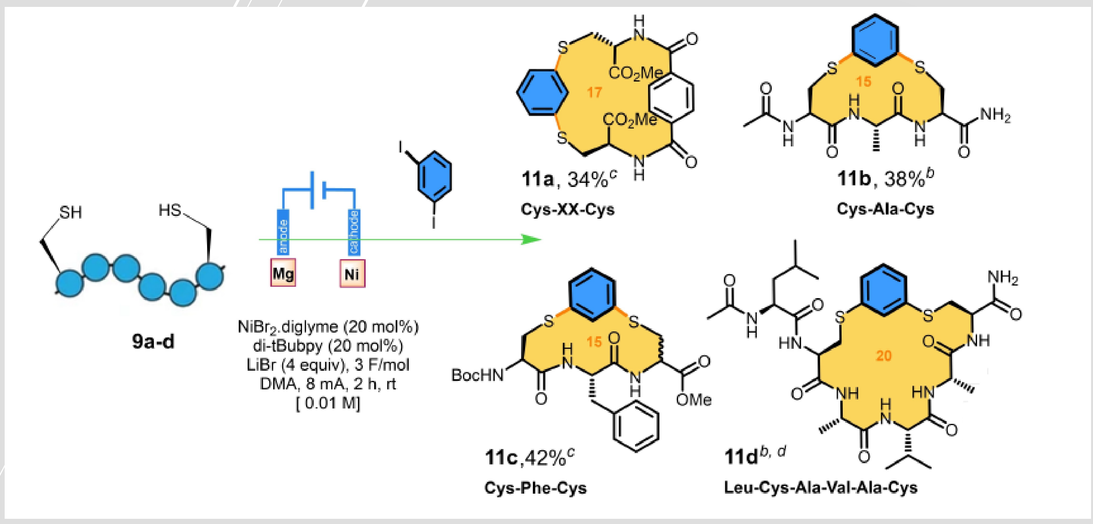



## Proposed Mechanism




## Aryl/Alkenyl/alkynyl halides Scope




## Access to stapled peptides

## CONCLUSION ET PERSPECTIVES

We developped the first electrochemical method for the coupling of cystein containing peptides with halides under mild reaction conditions, without precious metals or halide excess. We obtained linear, cyclic and stapled peptide, with or without protecting groups. Further studies on the applications of this method to obtain macrocyclic peptides are ongoing

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[3] L. Shen, O. Monasson, E. Peroni, F. Le Bideau, S. Messaoudi, Angew. Chem.Int. Ed.2023, 62, e2023157.