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Comparison of conformational propensities of peptide backbones containing 1,5- or 1,4- disubstituted [1,2,3] triazoles

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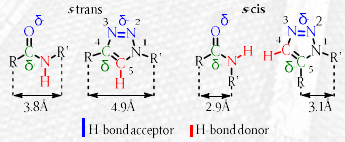
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1. Introduction

We previously obtained promising results using the side chain-to-side chain triazolyl bridge to stabilize specific conformation. These include the α-helical conformations of ACE2(24-42), the minimal peptide fragment containing all the residues involved in RBD binding to the SARS-CoV-2 spike glycoprotein,[1] and hPTHrP(11-19), fragment of antagonist of parathyroid hormone-related peptide.[2] We also demonstrated the stabilization of the β-turn in the melanocotin agonist MT-II[3] and oxytocin.[4]

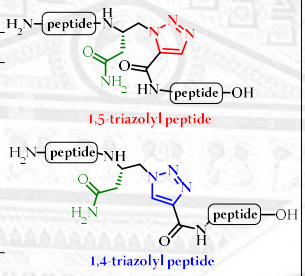
This project aims to evaluate the effects of **1,4- and 1,5-disubstituted [1,2,3]triazoles**, incorporated into the peptide backbone of model peptides, exploiting their ability to act as rigid, metabolically stable and structurally compatible amide bioisosteres.[5,6]



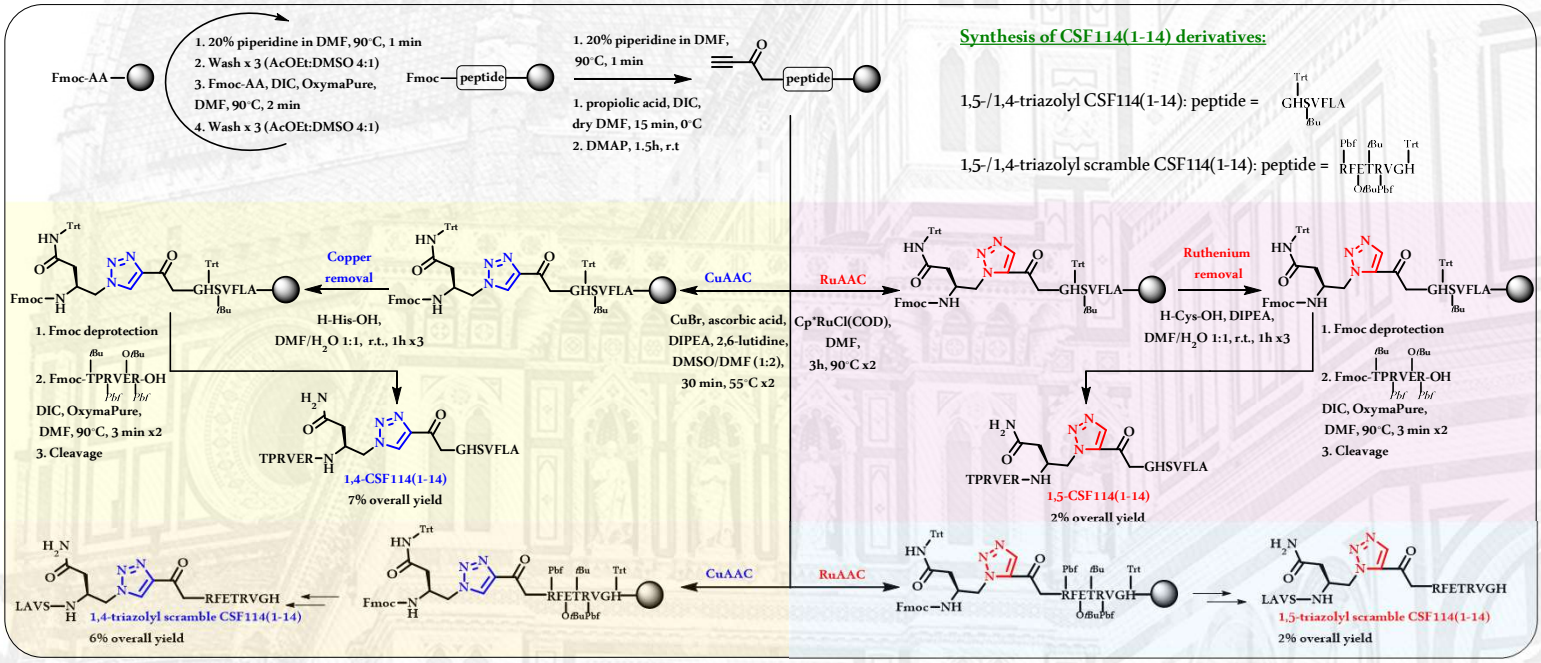
2. Objectives

The selected model peptides are: **CSF114**, a structure-based designed **β-turn** peptide and its scramble sequence, which does not induce a β-turn.[3,4] CSF114 presents a type I' β-turn, best exposing an asparagine residue at position 7.

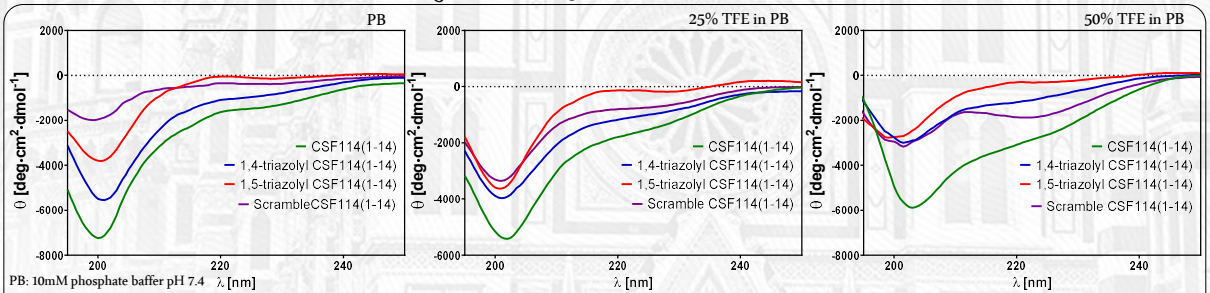
Peptide sequences	
CSF114(1-14)	TPRVERNGHSVFLA
Scramble CSF114(1-14)	PLAVSNRFETRVGH
1,5-triazolyl CSF114(1-14)	TPRVERN-1,5-Triazole-GHSVFLA
1,4-triazolyl CSF114(1-14)	TPRVERN-1,4-Triazole-GHSVFLA
1,5-triazolyl scrambleCSF114(1-14)	PLAVSN-1,5-Triazole-RFETRVGH
1,4-triazolyl scrambleCSF114(1-14)	PLAVSN-1,4-Triazole-RFETRVGH



3. Research and development



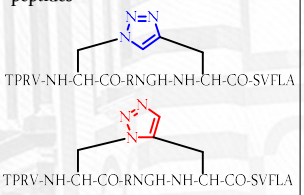
4. Results and Conclusion



➢ Both 1,5- and 1,4-disubstituted triazole replaced amide bond at positions i+1(Asn[7])-i+2 (Gly[8]) on the tip of the β-turn result β-turn disruptors in CSF114(1-14)

Future Perspectives

➢ Comparison with side chain-to-side chain 1,5- and 1,4-triazolyl bridged peptides



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