Thioacid-based strategy for the semi-synthesis of glycoproteins

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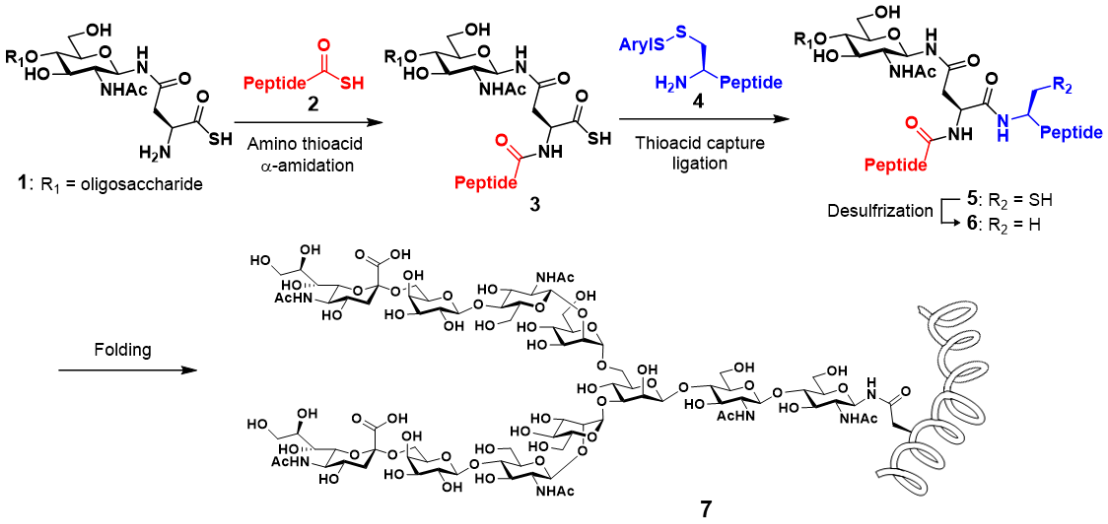
Keywords: Thioacid; Oligosaccharide; Glycoprotein; Amide; Peptide

Protein semisynthesis is a powerful approach for the synthesis of homogeneous glycoproteins, employing the coupling of recombinant peptides and glycopeptides prepared by chemical synthesis.

Herein we have developed a new semisynthetic strategy for glycoproteins using glycosyl asparagine thioacid. This strategy can selectively couple two peptides with both of N and C termini of glycosyl asparagine thioacid. As shown in figure, we employed glycosyl asparagine thioacid as the junction point for the coupling of N and C terminal peptides. The first coupling is designed to perform between peptide thioacid **2** and glycosyl asparagine thioacid **1** applying our chemoselective amide formation.[1] This amidation occurs through mild oxidation without drastic condensation reagents. Because the resultant glycopeptide **3** has thioacid form at its C-terminal, we could apply the thioacid capture ligation (TCL)[2] for the coupling of the resultant glycopeptide thioacid **3** and another peptide **4** having disulfide functional group at its N-terminal to afford glycopeptide **5**. The glycoprotein **7** can be efficiently obtained by the subsequent desulfurization and folding of **6**. In this presentation, we will discuss chemical characteristic nature of glycosyl asparagine thioacid. The approach for the semisynthesis of glycoproteins will also be discussed.



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