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Fmoc-Based Synthesis of Peptide-$^{\alpha}$Thioesters: Application to the Total Chemical Synthesis of a Glycoprotein by Native Chemical Ligation
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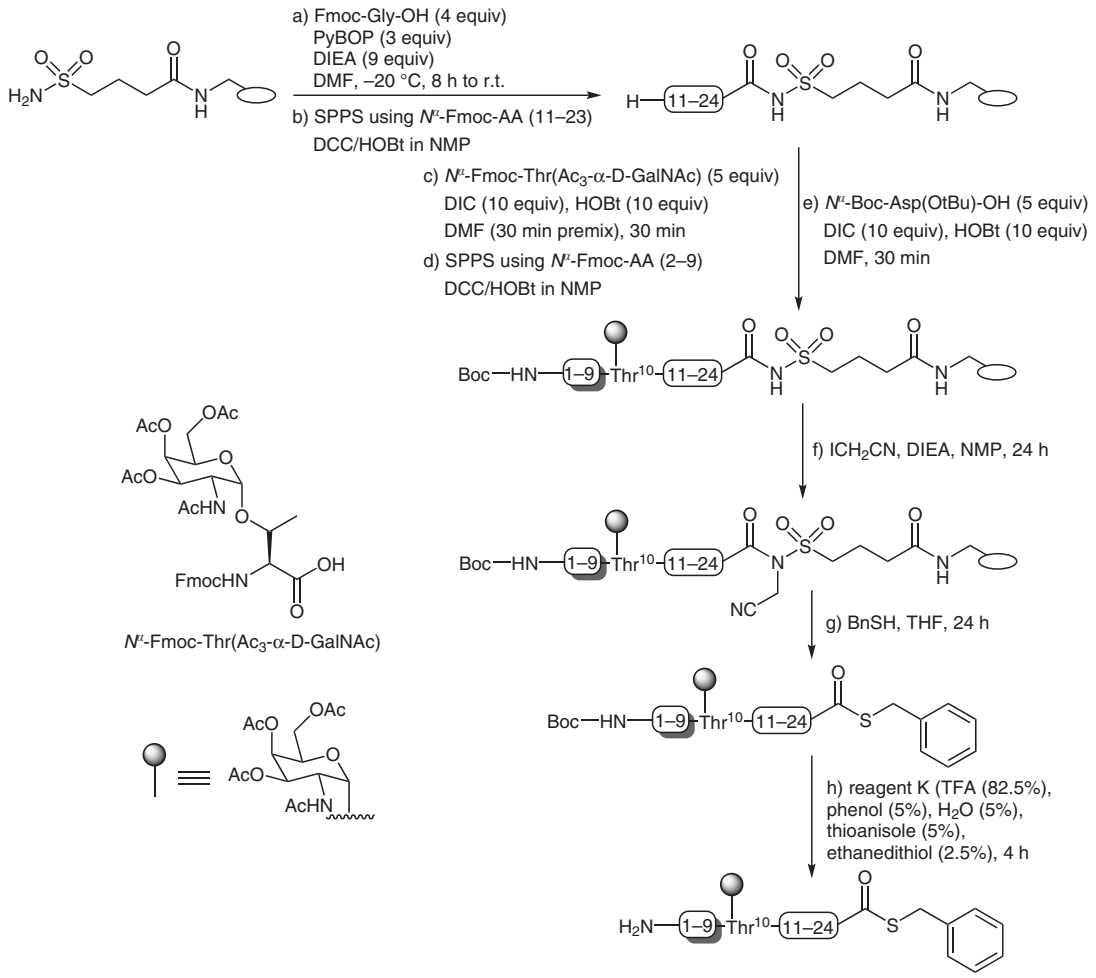
Total Chemical Synthesis of a Glycoprotein by Native Chemical Ligation

Synthesis of glycopeptide-$^{\alpha}$thioester using the alkanesulfonamide "safety-catch" linker:



Significance: The authors have developed a new approach for the synthesis of unprotected $^{\alpha}$thioesters by using Fmoc-based solid-phase peptide synthesis and have demonstrated its utility in the total synthesis of a glycosylated protein, the antimicrobial O-linked glycoprotein diptericin, by the native chemical ligation method. This method utilizes an alkanesulfonamide 'safety-catch' linker, which circumvented the problems associated with the incompatibility of glycosidic linkages with Boc chemistry and of thioesters with Fmoc chemistry.

Comment: The C-terminal residue of the peptide is attached to the resin through an acid- and base-stable *N*-acyl sulfonamide linkage. After peptide synthesis, the sulfonamide is activated by cyanomethylation and then cleaved with a thiol nucleophile. This general synthetic approach permits access to unprecedented quantities of homogeneous glycoproteins.

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