Posttranslational glycan modification in *Thermococcus kodakarensis*: discovery and synthesis of *myo*-inositol containing *N*-glycan

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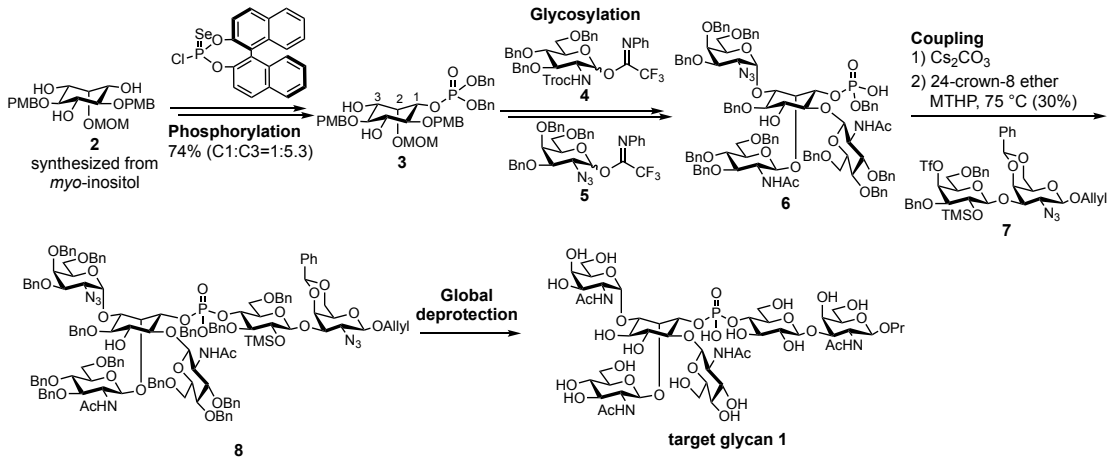
Archaea membrane proteins are glycosylated with asparagine-linked oligosaccharides (*N*-glycans), same as eukaryote proteins. However, their functions have not been well elucidated. To address this issue, we previously isolated *N*-glycan from the hyperthermophilic archaeon, *Thermococcus kodakarensis*, and determined its structure as **1** (scheme 1). *N*-Glycan **1** has highly glycosylated inositol, which is linked with the disaccharide via phosphate. We achieved the chemical synthesis of **1** (Scheme 1). According to our previous report,[1] **3** was synthesized via regioselective phosphorylation of **2** using an asymmetric phosphorylation reagent. Glycosylation of **3** with **4** followed by introduction of galactosamine using **5** afforded **6**. Coupling between the inositol phosphate and the disaccharide was then investigated under condensation conditions using various reagents, including CDI, DCC, PyBOP, and DIAD/PPh_3, but the reactions did not proceed. After the thorough investigation, S_N2 type reaction between cesium salt of phosphoric acid **6** and triflate **7** successfully gave the desired coupling product **8**. After global deprotection, we obtained the target glycan **1**. A comparison of the NMR data of the isolated *N*-glycan with that of synthetic **1** confirmed the structure of the *N*-glycan.



Scheme 1. Synthesis of target glycan **1**

1) Aiba, T. et al. *Chem. Eur. J.* **2017**, 23, 8304.