Research summary

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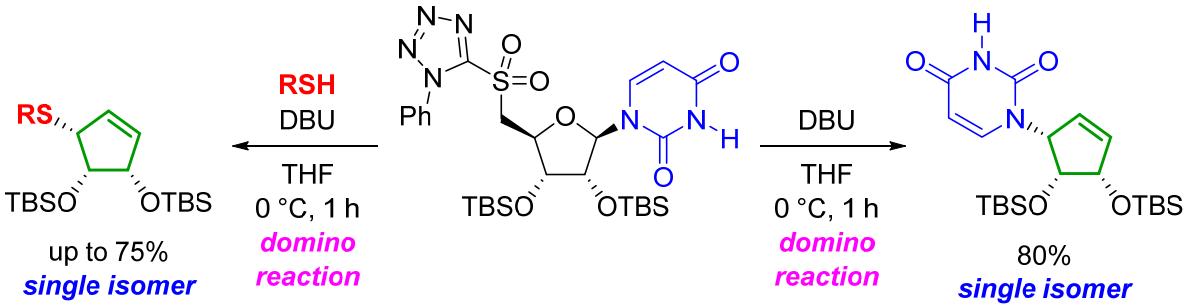
Synthesis of optically active cyclopentene derivatives by a novel domino reaction

Domino reactions are useful for the efficient synthesis of complex compounds. We have discovered that the treatment of Julia-Kocienski sulfones derived from nucleosides with bases such as DBU affords cyclopentene nucleosides in one step via a novel domino reaction. In addition, we discovered that the same reaction in the presence of a nucleophile such as a thiol or a thiocarboxylic acid provides cyclopentenes bearing the nucleophile in place of the nucleobase. The resulting cyclopentenes would be useful as synthetic intermediates for biologically active carbocyclic nucleosides and cyclopentanes.



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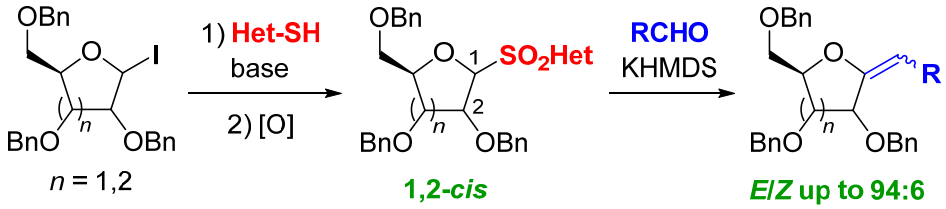
Stereoselective synthesis of 1,2-*cis*-glycosyl sulfones and their application

Glycosyl sulfones are useful as synthetic intermediates for various sugar derivatives and biologically active compounds. However, most of the previous research has used easily synthesized 1,2-*trans*-isomers, and little progress has been made in the study of 1,2-*cis*-isomers. We developed a novel method for the synthesis of 1,2-*cis*-glycosyl sulfones using glycosyl iodides as glycosyl donors. The resulting 1,2-*cis*-glycosyl sulfones were useful as Julia-Kocienski reagents to give *exo*-glycals in good yields from aldehydes. The 1,2-*cis*-glycosyl sulfones derived from ribose and glucose afforded the corresponding *exo*-glycals with higher *E*-selectivity than the 1,2-*trans*-isomers, and the difference was particularly large for the ribose derivatives. Thus, our study has revealed the usefulness of 1,2-*cis*-glycosyl sulfones.



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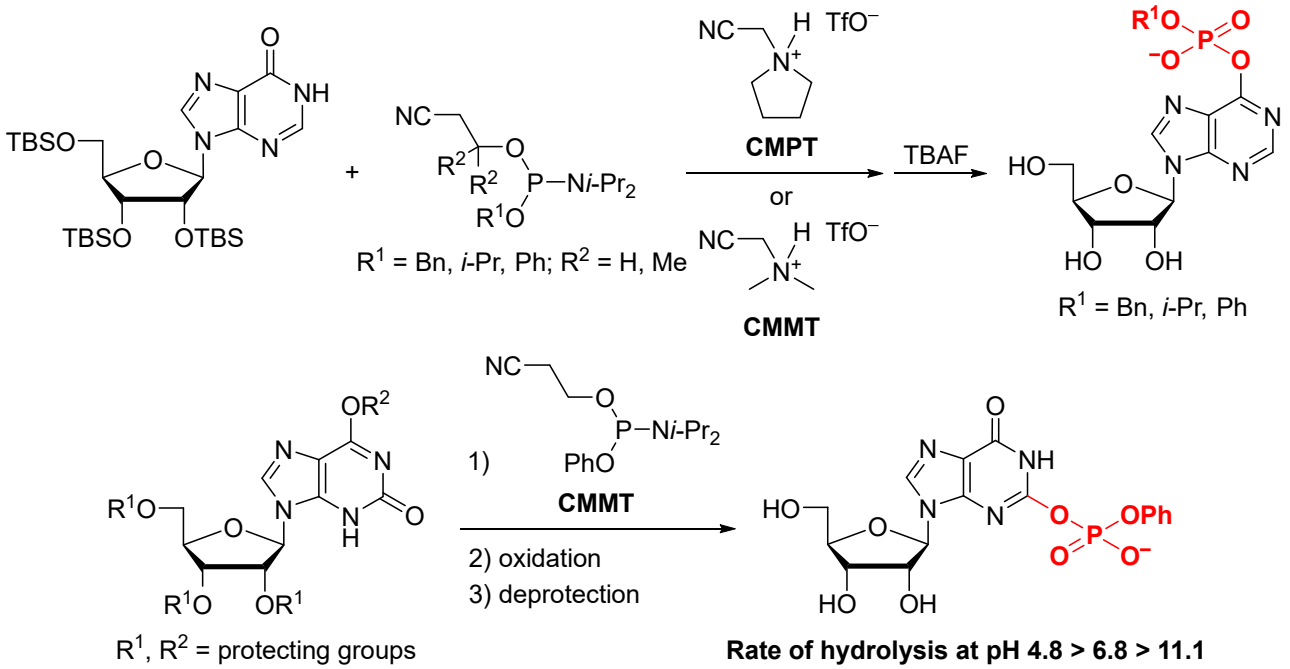
Synthesis of nucleosides phosphorylated at their carbonyl groups

In the biosynthetic pathways of nucleic acids, there are several reactions in which the carbonyl group of a nucleobase is activated by phosphorylation and replaced by an amino group or a sulfur atom. We developed a method for the synthesis of carbonyl-phosphorylated inosine, an active intermediate analog, to elucidate the reaction mechanism of the biosynthesis of adenylosuccinate. Such molecules would also be useful to develop enzyme-responsive molecules. Although the phosphorylation of nucleoside carbonyl groups is difficult to achieve using existing methods, we have succeeded in the synthesis of O^6-phosphorylinosines by using CMPT or CMMT, which are acidic activators with low nucleophilicity, to suppress the degradation of unstable synthetic intermediates. In addition, we succeeded in synthesizing an O^2-phosphorylxanthosine derivative as a simple model compound of adenosine monophosphorylated xanthosine monophosphate (AMP-XMP), which is known as a biosynthetic intermediate of guanosine monophosphate and clarified its hydrolytic stability.



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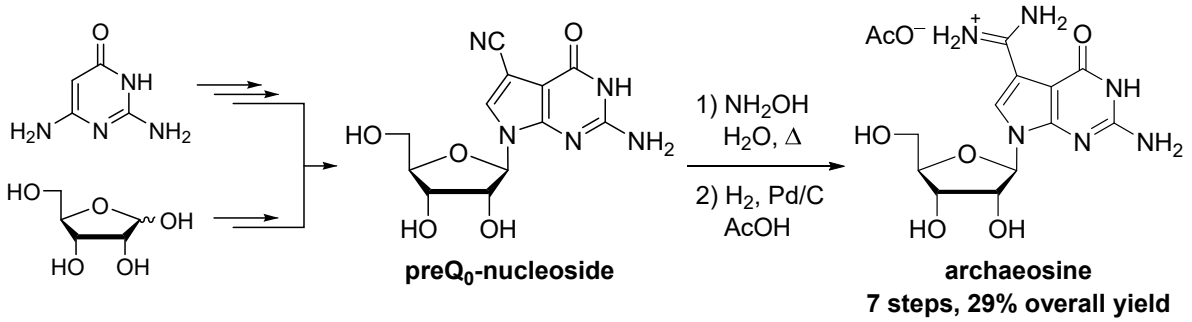
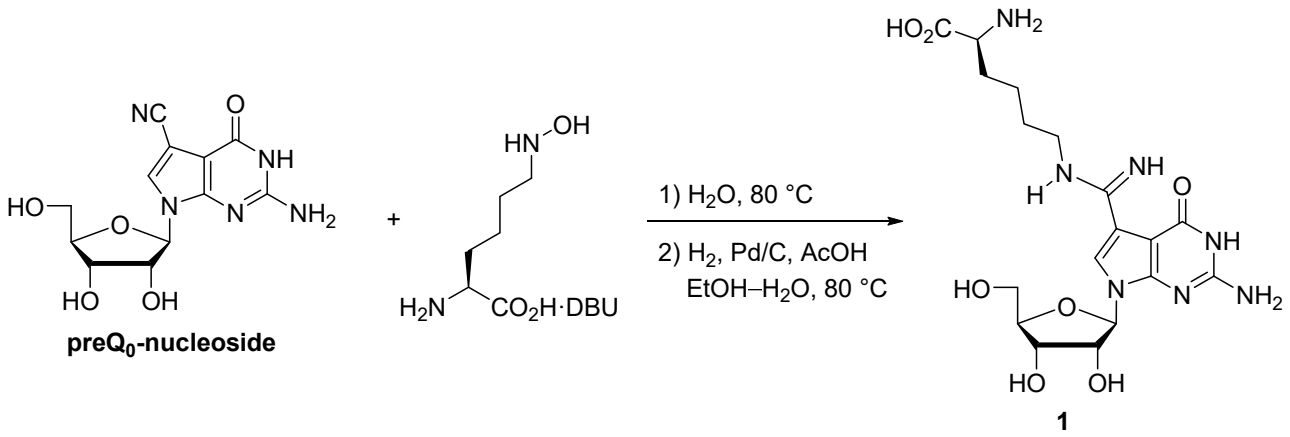
Chemical synthesis of archaeosine

Archaeosine is a hypermodified nucleoside found in archaeal tRNAs, and their biosynthesis and functions have been studied for a long time. The supply of pure archaeosine by chemical synthesis is important for promoting such research, but existing methods have shortcomings, such as low synthetic yields. We have developed an efficient method for the synthesis of archaeosine using $PreQ_0$-nucleoside as an intermediate. In addition, we applied this method to the synthesis of $PreQ_0$-nucleoside-lysine adduct **1**. Collaborative research with Prof. Yokogawa of our Department has revealed that **1** is a biosynthetic intermediate of archaeosine.





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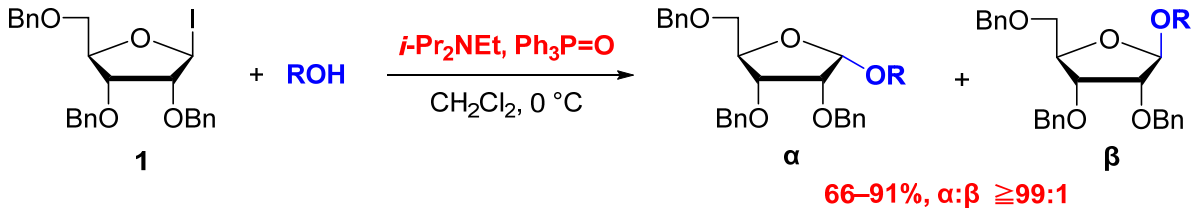
Development of α-selective ribofuranosylation reaction

Ribofuranosides are found in various biologically active natural products. Some of them are potentially useful as cosmetics, food additives, and medicines. Ribofuranosides have two stereoisomers, α- and β-ribofuranosides. While the synthesis of β-isomers is generally easy, it is still difficult to synthesize α-ribofuranosides completely stereoselectively. We developed a novel α-selective ribofuranosylation of alcohols using a ribofuranosyl iodide **1** as a glycosyl donor. The α-selectivity is up to >99:1 for various glycosyl acceptors.



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