

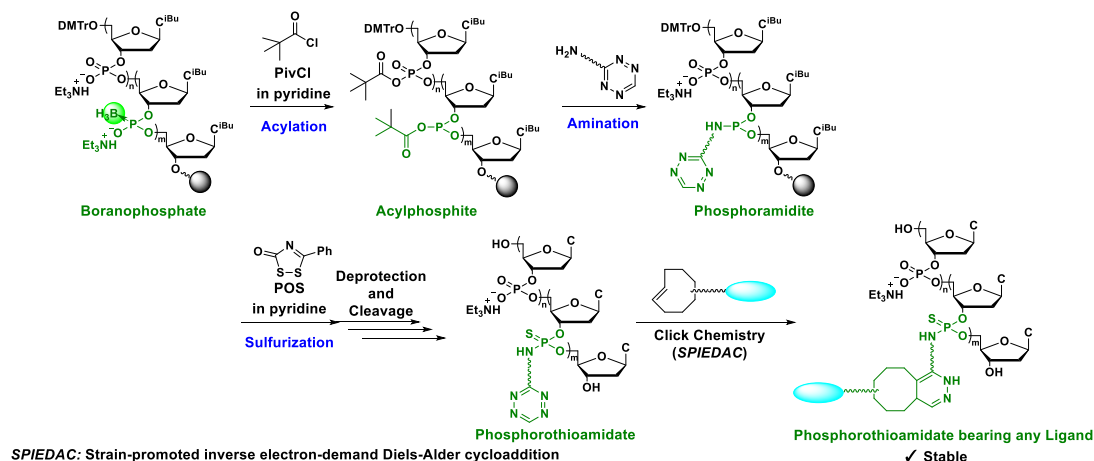
Development of a Post-Synthetic Modification Reaction for Oligodeoxynucleotides using a Boranophosphate as a Precursor

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Recently, delivery technologies for oligonucleotide therapeutics have been a major issue. To address this issue, introduction of a ligand to oligodeoxynucleotides (ODNs) has been vigorously investigated. However, the introduction site of a ligand is limited to the ends of ODNs due to the complexity of synthesis. We previously established a method for conversion of DNA, which is a *P*-modified DNA bearing a $P \rightarrow B$ bond, a boranophosphate, into the key intermediate, an acylphosphite. This intermediate is a useful precursor for the synthesis of various *P*-modified derivatives.¹ This study aims to introduce a chemical handle that enables efficient internal ligand modification of ODNs by utilising a boranophosphate as a synthetic precursor. A boranophosphate is introduced at an arbitrary position beforehand, and an amine bearing a click chemistry scaffold is used in the reaction. Then the boranophosphate is converted to phosphorothioamidate bearing a click chemistry scaffold via an acylphosphite. It allows a subsequent click reaction to readily introduce various modifications.

Previously, this conversion reaction was only achieved in the liquid-phase synthesis.² Therefore, we aim to adapt it to the solid-phase synthesis using propylamine as a model compound. The details will be discussed in the presentation.



1) K. Sato, *Org. Biomol. Chem.* **2016**, *14*, 11092-11095. 2) Y. Takahashi, *J. Org. Chem.* **2023**, *88*, 15, 10617–10631.