Session I: Poster Abstract

A General and Automated Platform for the Synthesis of Small Molecules

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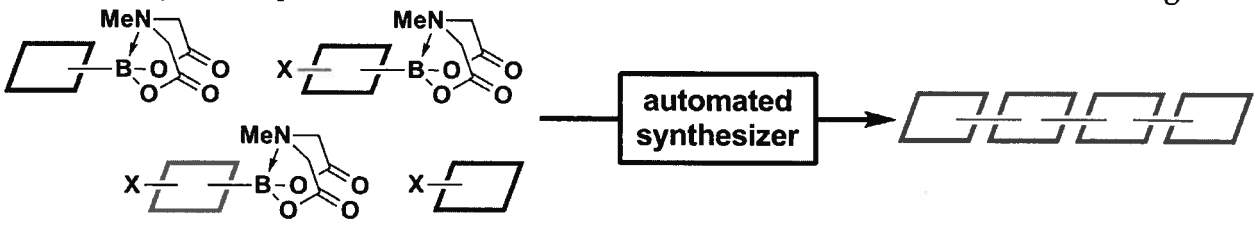
Small molecules have the potential to perform a wide variety of functions across all of science, but despite substantial methodological advances, their synthesis still remains the slow step in studying their functional capacity. This is due in large part to the necessity for a highly-trained specialist to perform the relatively complex, unsystematized, and time-intensive syntheses. In an effort to shift the rate-limiting step of small molecule science from synthesis to function study, we have developed a general and automated platform for the synthesis of small molecules. Our strategy harnesses the unique and universal property of the MIDA boronate functional group to act as both a protecting group and purification handle. The platform enables the iterative assembly of MIDA boronate building blocks into many different types of small molecules, including organic materials, pharmaceuticals, natural products, and polycycles. With thousands of applicable building blocks readily accessible, this simple, general, and fully automated synthesis platform stands to afford more efficient access to small molecule targets.



DNA-Catalyzed Conjugation of Nucleic Acids and Peptides

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We previously used in vitro selection to identify DNA catalysts (deoxyribozymes) that use DNA-anchored peptide substrates in forming peptide-RNA conjugates. However, the resulting deoxyribozymes require Watson-Crick binding to the anchor oligonucleotide, and therefore they either do not work with free peptides or require high (>mM) peptide concentration. Here, a new two-stage in vitro selection strategy was designed in which a free Tyr-containing peptide that incorporates an azido (N_3) group at the N-terminus was presented to the DNA pool during the selection step. Cu(I)-catalyzed azide-alkyne cycloaddition was utilized in the subsequent capture step with a 3'-alkyne-modified oligonucleotide to increase the mass of only the active DNA sequences and thereby enable their PAGE-shift separation. Via this strategy, several new deoxyribozymes were identified that catalyze the reaction between the hydroxyl group of Tyr and the α-phosphate of a 5'-triphosphorylated RNA. Additionally, we designed selections using phosphorimidazolide (Imp) instead of triphosphate as the electrophile, considering that Imp can be easily incorporated at the 5'-end or 3'-end of either DNA or RNA. The resulting deoxyribozymes catalyze the analogous reaction with 5'-ImpDNA as the oligonucleotide substrate. These findings demonstrate the feasibility of direct selections with free peptide substrates and provide a generalizable approach to DNA-catalyzed synthesis of peptide-nucleic acid conjugates.