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Synthesis of nucleic acid - binding ligands

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The purpose of my project was to produce nucleic acid-targeting oligopeptides which contain non-natural amino acids as part of their sequence with the purpose of activating or inhibiting biological functions. Certain amino acids display selectivity for certain nucleobases. Arginine has a high propensity for being present at the binding interface of both protein-DNA and protein-RNA complexes. A torsional constraint for the guanidine group could be achieved by converting it into a bicyclic framework and then forming only a one-mode hydrogen bonding with its targets that would reduce the loss of the conformational entropy on its binding. The synthesis of differently-sized rings of bicyclic guanidine derivatives could be a means to control the hydrophobic interaction with DNA, with hydrophobicity increasing as the size of the ring of bicyclic guanidine increases. This project includes the novel strategy to generate a differently sized ring of bicyclic guanidine methylene alcohol in a high yield starting from an azido alkane amine and Boc-L-methionine as precursors. This modification to the route will open a promising way to produce the functionalized bicyclic guanidine.

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