Ligation of Oligonucleotides Induced by Charge-Transfer Interactions

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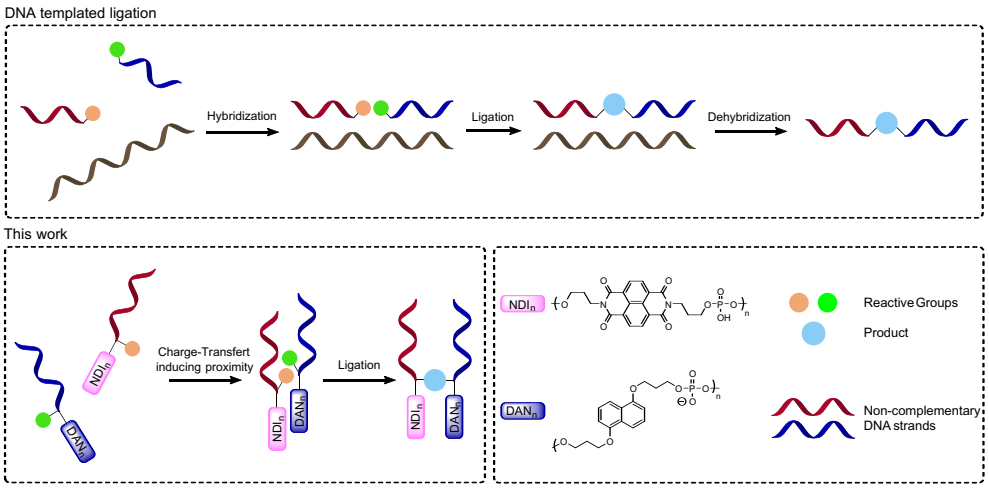
Intermolecular interactions, like hydrogen bonding or Van-Der-Waals forces, are ubiquitous in chemistry guiding both natural (DNA, proteins) and synthetic supramolecular assemblies. Among these interactions, charge-transfer (CT) interactions received a particular attention due to the wide range of potential applications.[1] Charge-transfer can be defined as the electrostatic attraction between an electron-rich entity, the donor (D), and an electron-poor unit, the acceptor (A). This attraction allowed an alternative stacking between these two species that can lead to strong supramolecular assemblies called CT complexes.[2] Among the various D and A pairs that have been identified, the most popular pair for forming CT complexes is naphthalene diimide (NDI) and dialkoxynaphtalene (DAN).[3] In this context, DAN/NDI interactions can be used to induce proximity effect between two biomolecules, such as oligonucleotides strands.[4] Usually, the ligation of two oligonucleotides carrying reactive functions proceeds through the use of a third strand, acting as a template to bring the reactive groups in close proximity.[5] In this project, we propose to use the charge transfer interaction to enhance the effective molarity of two non-complementary DNA strands in diluted media. We achieved this by synthesizing DAN and NDI phosphoramidite building blocks,[6] which were introduced into DNA sequences. We also applied this method to make oligonucleotide-peptide conjugates, developing an innovative and universal ligation approach that proceeds at submicromolar concentrations and in mild aqueous conditions.



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