

Synthesis and base-pairing properties of 5'-C-pyrenyl thymidine-modified fluorescent oligonucleotides

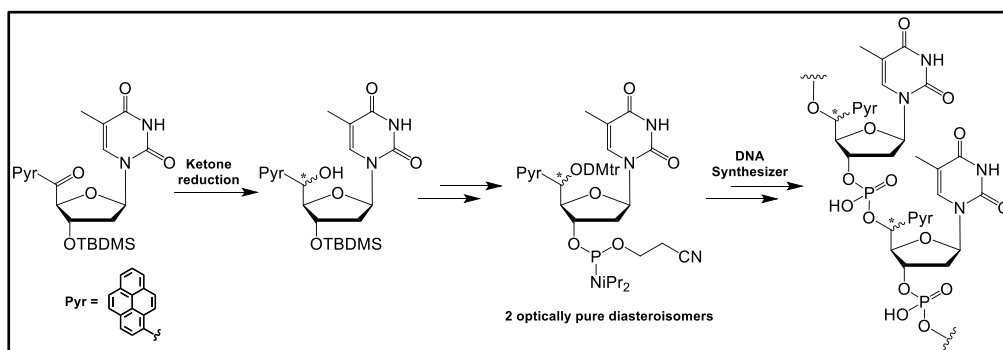


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In 2022, our group pioneered the development of 5'-C-ketone-modified nucleosides using the Liebeskind-Srogl (L-S) coupling reaction.¹ We demonstrated that Pd-catalyzed and Cu(I)-mediated cross-coupling between C-5'-thioester nucleosides and various aromatic, heteroaromatic and alkene boronic acids efficiently yielded the corresponding ketone in the presence of sensitive functions. The possible conversion of the carbonyl group into a secondary alcohol provides an outcome into the synthesis of new phosphoramidite building blocks for the synthesis of modified DNA/RNA.² In particular, pyrene-functionalized oligonucleotides have been attracting interest as tools for nucleic acid research, diagnostics and nanotechnology for some thirty years now.³ This is due to the remarkable properties of the pyrene group as a polarity-sensitive, quenchable fluorophore, excimer-generating unit, aromatic stacking group and nucleic acid intercalator.⁴ Pyrene-labeled oligonucleotides are mainly used as fluorescent biosensors for the detection of various targets such as metallic ions, gene sequences and oligonucleotide duplexes.⁵ The pyrene group has been introduced into various positions of the nucleoside scaffold, such as the nucleobase,⁶ the sugar (mostly in the 2' position)⁷ or the phosphate linker.⁸ To the best of our knowledge, only one example of a nucleoside carrying a pyrene in the 5' position, through a methyltriazole linker, that can be introduced into the core of an oligonucleotide has been reported.⁹

In this context, the use of 5'-C-pyrenyl nucleoside to introduce a pyrene moiety into oligonucleotides seems to be an interesting approach. Accordingly, in the present work, we describe the preparation of 5'-C-pyrenyl thymidine phosphoramidite from the corresponding 5'-C-keto nucleoside obtained with the L-S reaction. The incorporation of one or two modified thymidines into DNA oligonucleotides, the thermal stability and specificity, and the fluorescence properties of various DNA duplexes are detailed.



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