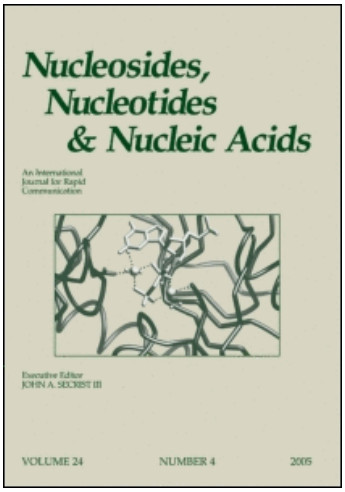

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Oligonucleotides Containing Disaccharide Nucleosides: Synthesis, Physicochemical, and Substrate Properties

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ABSTRACT

The efficient synthesis of oligonucleotides containing 2′-*O*-β-D-ribofuranosyl (and β-D-ribopyranosyl)nucleosides, 2′-*O*-α-D-arabinofuranosyl (and α-L-arabinofuranosyl)nucleosides, 2′-*O*-β-D-erythrofuranosylnucleosides, and 2′-*O*-(5′-amino-5-deoxy-β-D-ribofuranosyl)nucleosides have been developed.

Key Words: Oligonucleotides; Disaccharide nucleosides; Chemical synthesis; Substrate properties.

Recently we have developed a simple route for the preparation of disaccharide nucleosides, an important group of natural compounds. Disaccharide nucleosides with a 2′-*O*-β-D-ribofuranose, 2′-*O*-β-D-ribopyranose, 2′-*O*-α-D-arabinofuranose,

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2′-*O*-α-L-arabinofuranose, 2′-*O*-β-D-erythrofuranose, and 2′-*O*-(5-amino-5-deoxy-β-D-ribofuranose) substituents were synthesized. These modified nucleosides were incorporated into oligonucleotides.[1,2] Single substitution results in a ΔTm of +0.5°C to –0.4°C for DNA/RNA and a ΔTm of –0.8°C to –4.7°C for DNA/DNA duplexes. These disaccharide nucleosides can be accommodated well in RNA/DNA duplexes and the presence of a 5′′-amino group has a beneficial effect on duplex stability.[2] Previously the conformation of the self-complementary decaribonucleotide containing 2′-*O*-β-D-ribofuranosyladenosine was studied using high-resolution NMR spectroscopy and restrained molecular dynamics.[3] It was found that the duplex RNA maintains an A-type helical geometry with extra 2′-*O*-ribose moiety located in the minor groove.[3]

Several oligodeoxyribonucleotides containing 2′-*O*-β-D-ribofuranosyladenosine were used as modified primers in RNA-templated DNA synthesis catalyzed by HIV reverse transcriptase. It was shown that the additional 2′-ribofuranose residue in specific position (-4) of primer prevents its elongation due to the steric hindrances.[4] This finding might be of general value and such primers with bulky groups might be used for specific inhibition of different polymerases.

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