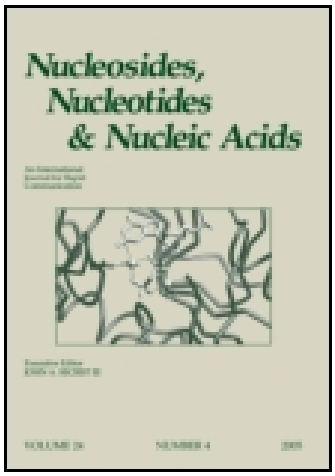

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Aryl-β-*C*-LNA Monomers as Universal Hybridization Probes[1,2]

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ABSTRACT

High-affinity universal hybridization is demonstrated for oligonucleotides containing the pyrenyl-LNA monomer **6b**, 2′-*O*-Me-RNA monomers and LNA monomers.

Key Words: Universal bases; Universal hybridization; LNA, locked nucleic acid.

Universal monomers that bind isoenergically with each of the natural nucleotides include non-hydrogen bonding, hydrophobic nucleotides.[3] Although there has been some success in the design of universal base analogues, examples that are able to hybridize without significant duplex destabilization are rare. We decided to synthesize the LNA[4] derivatives **6a** and **6b**, both based on the 2′-*O*,4′-*C*-methylene-β-D-ribofuranosyl moiety known to be preorganized in a locked C3′-*endo* (*N*-type) RNA-like furanose conformation.

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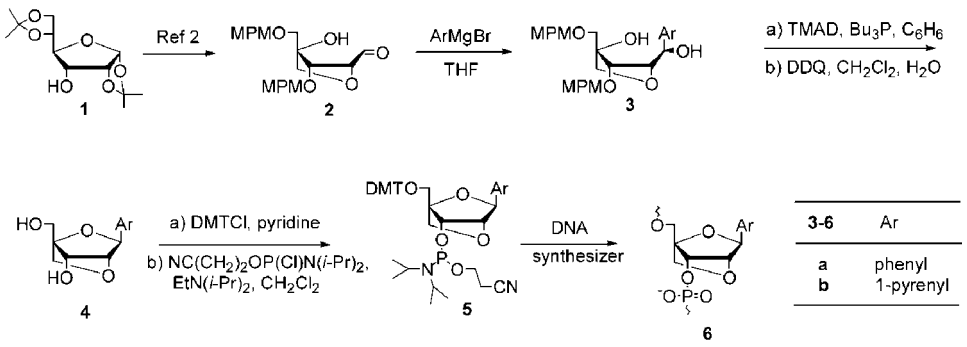
Table 1. Thermal denaturation experiments (T_m values shown) for **ON1-ON5** towards DNA complements with each of the four natural bases in the central position.

DNA target:	3′-d(CACTYTACG)	Y:	A	C	G	T
ON1	5′-d(GTGATATGC)		28	11	12	19
ON2	5′-d(GTGA**6a**ATGC)		12	5	6	7
ON3	5′-d(GTGA**6b**ATGC)		18	17	18	19
ON4	5′-d[2′-OMe(GTGATATGC)]		35	14	19	21
ON5	5′-d[2′-OMe(G$\mathbf{T^L}$GA**6b**A$\mathbf{T^L}$GC)]		39	38	37	40



Compared to the DNA reference **ON1**, introduction of the phenyl-LNA monomer **6a** (**ON2**) leads to reduced thermal stability of the resulting duplexes, and universal hybridization is not achieved due to the preferential binding to the target DNA with the central adenine monomer (Table 1). The pyrene-LNA monomer **6b** (**ON3**) displays more encouraging properties, i.e., increased binding affinity compared to **6a** (**ON2**) and universal hybridization (the four T_m values = 17–19°C). We then constructed **ON5** as a mixture of six 2′-*O*-Me-RNA monomers, one central pyrenyl-LNA monomer **6b**, and two affinity-enhancing LNA thymine monomers $\mathbf{T^L}$. Indeed, the 2-*O*-Me-RNA/LNA chimera **ON5** displays universal hybridization with binding affinities exceeding those of the references **ON1** and **ON4** (the T_m values of **ON5** = 37, 38, 39 and 40°C).

The obtained results show that high-affinity universal hybridization can be obtained by use of a combination of the pyrenyl-LNA monomer **6b**, 2′-*O*-Me-RNA monomers and LNA monomers.

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REFERENCES

1. Babu, B.R.; Wengel, J. Universal hybridization using LNA (locked nucleic acid) containing a novel pyrene LNA nucleotide monomer. Chem. Commun. **2001**, 2114 pp.
2. Babu, B.R.; Prasad, A.K.; Trikha, S.; Thorup, N.; Parmar, V.S.; Wengel, J. Conformationally locked aryl *C*-nucleosides: synthesis of phosphoramidite monomers and incorporation into single-stranded DNA and LNA (locked nucleic acid). J. Chem. Soc., Perkin Trans 1 **2002**, 2509 pp.
3. Loakes, D. The applications of universal DNA base analogues. Nucleic Acids Res. **2001**, *29*, 2437 pp.
4. Wengel, J. Synthesis of 3′-*C*- and 4′-*C*-branched oligodeoxynucleotides and the development of locked nucleic acid (LNA). Acc. Chem. Res. **1999**, *32*, 301 pp.

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