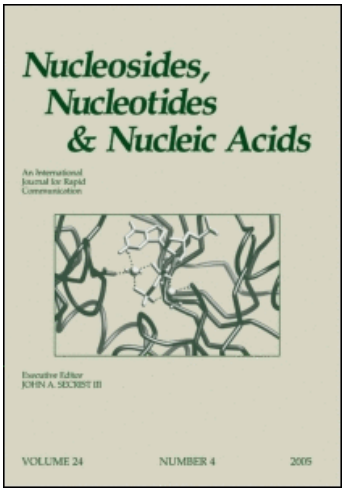

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xylo-Configured Oligonucleotides (XNA, Xylo Nucleic Acids): Synthesis and Hybridization Studies

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ABSTRACT

We report synthesis and high-affinity hybridization of fully modified home-thymine 2′-deoxy and 2′-deoxy-2′-fluoro xylo nucleic acids.

Key Words: XNA (xylo nucleic acids); Oligonucleotides; Hybridization.

Oligonucleotides containing 3′,4′-*threo*-configured phosphodiester backbone have attracted only limited attention.[1–4] We here report on novel *xylo*-configured oligonucleotides (XNA, Xylo Nucleic Acids). 1-(2-Deoxy-2-fluoro-β-D-xylofuranosyl) thymine was obtained starting from methyl 2-deoxy-2-fluoro-3,5-di-*O*-benzoyl-β-D-xylofuranoside[5] via Vorbrüggen-type condensation. The xylonucleosides were transformed into phosphoramidite building blocks **1**[1] and **2** (Sch. 1).

ON1 and XNAs **ON2**–**ON5** were synthesized using standard procedures except for modified coupling conditions as described for xylo-LNA synthesis.[4,6]

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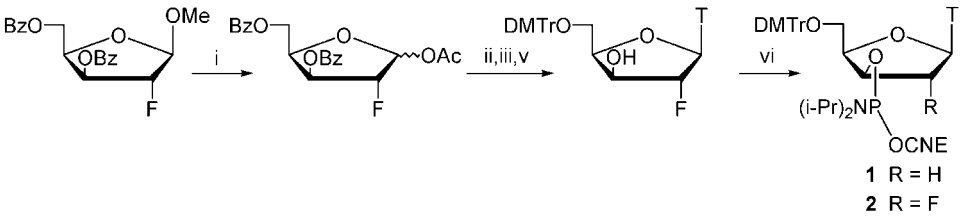
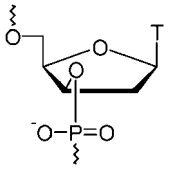


Scheme 1. i) AcOH, Ac_2O (3.8:1 v/v), conc. H_2SO_4, 75 min, 97%; ii) silylated thymine, TMSTf, 1,2-DCE, reflux, 3 h, 73% (α:β = 1:2); iii) NH_3, MeOH, 20 h; iv) DMTrCl, pyridine, 20 h, 90%; v) $NCCH_2CH_2OP(Cl)N(i\text{-}Pr)_2$, $(i\text{-}Pr)_2NEt$, DCM, 30 min, 81%.

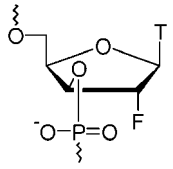
Table 1. Hybridization studies on XNAs **ON2**-**ON5**.[a]

Sequences	Complementary DNA [d(A_{14})] T_m/°C (ΔT_m vs. **ON1**)	Complementary RNA [r(A_{14})] T_m/°C (ΔT_m vs. **ON1**)
ON1 (T_{14})	33 (Reference)	29 (Reference)
ON2 (5′-T_7**dxT**T_6)	23 (−10)	25 (−4)
ON3 (5′-T_7**FxT**T_6)	23 (−10)	25 (−4)
ON4 (5′-(**dxT**)$_{13}$T)	33 (+/−0)	38 (+9)
ON5 (5′-(**FxT**)$_{13}$T)	36 (+3)	36 (+7)

[a]Medium salt buffer (10 mM sodium phosphate, 100 mM sodium chloride, 0.1 mM EDTA, pH 7.0).



dxT



FxT

Hybridization data are shown in the Table. A strong destabilizing effect of single incorporations of both XNA monomers is observed towards a DNA complement. The first data on hybridization of XNAs towards RNA complements are included in the Table. It is revealed that XNA is a class of molecules able to efficiently target RNA, and it is noteworthy that the almost fully modified XNAs (**ON4** and **ON5**) displays significantly increased binding affinity towards RNA compared to the reference (**ON1**). We are currently studying the structure of XNA-containing hybrids.

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REFERENCES

1. Rosemeyer, H.; Seela, F. 1-(2′-Deoxy-β-D-xylofuranosyl)thymine building blocks for solid-phase synthesis and properties of oligo(2′-deoxyxylonucleotides). Helv. Chim. Acta. **1991**, *74*, 748 pp.

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2. Seela, F.; Heckel, M.; Rosemeyer, H. Xylose-DNA containing the four natural bases. Helv. Chim. Acta. **1996**, *79*, 1451 pp.
3. Svendsen, M.L.; Wengel, J.; Dahl, O.; Kirpekar, F.; Roepstorff, P. Oligodeoxynucleotide analogues containing 3′-deoxy-3′-*C*-*threo*-hydroxymethylthymidine: synthesis, hybridization properties and enzymatic stability. Tetrahedron **1993**, *49* (11), 341 pp.
4. Rajwanshi, V.K.; Håkansson, A.E.; Kumar, R.; Wengel, J. High-affinity nucleic acid recognition using 'LNA' (locked nucleic acid, β-D-*ribo* configured LNA), '*xylo*'-LNA' (β-D-*xylo* configured LNA) or 'α-L-LNA' (α-L-*ribo* configured LNA). Chem. Commun. **1999**, 2073 pp.
5. Wright, J.A.; Wilson, D.P.; Fox, J.J. Nucleosides. LXIV. Fluoro sugar analogs of arabinosyl- and xylosylcytosines. J. Med. Chem. **1970**, *13*, 269 pp.
6. Rajwanshi, V.K.; Håkansson, A.E.; Dahl, B.M.; Wengel, J. LNA stereoisomers: *xylo*-LNA (β-D-*xylo* configured locked nucleic acid) and α-L-LNA (α-L-ribo configured locked nucleic acid). Chem. Commun. **1999**, 1395 pp.

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