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Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597286>

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Online publication date: 09 August 2003

To cite this Article Babu, B. Ravindra , Keinicke, Lise and Wengel, Jesper(2003) 'Synthesis of 2'-Spiro Ribo- and Arabinonucleosides', *Nucleosides, Nucleotides and Nucleic Acids*, 22: 5, 1313 — 1315

To link to this Article: DOI: 10.1081/NCN-120022954

URL: <http://dx.doi.org/10.1081/NCN-120022954>

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Synthesis of 2'-Spiro Ribo- and Arabinonucleosides

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ABSTRACT

Four conformationally restricted bicyclic 2'-spiro nucleosides were synthesised and incorporated into oligonucleotides. These spiro nucleotides induced decreased duplex thermostabilities.

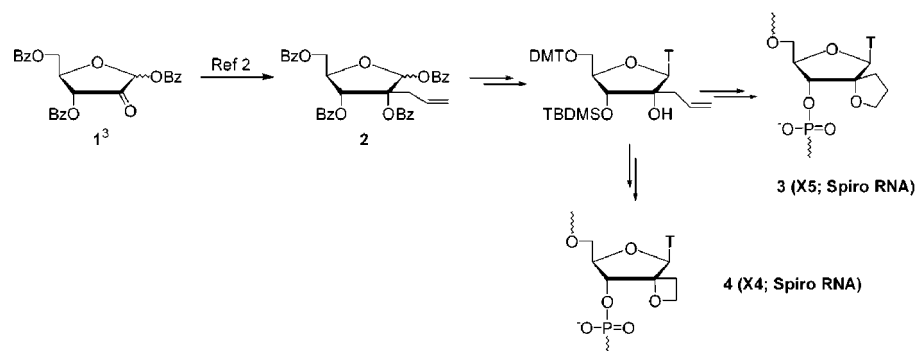
Key Words: Oligonucleotides; Spironucleosides; Arabinonucleosides; Ribonucleosides.

Introduction of an alkyl group at the 2'-C- or 2'-O-position of the ribose ring induces conformational rigidity of the furanose ring.^[1] We have now synthesized oligonucleotides containing conformationally restricted 2'-spiro nucleotides **3**, **4**, **7** and **8** with the hope of obtaining potent antisense oligonucleotides.

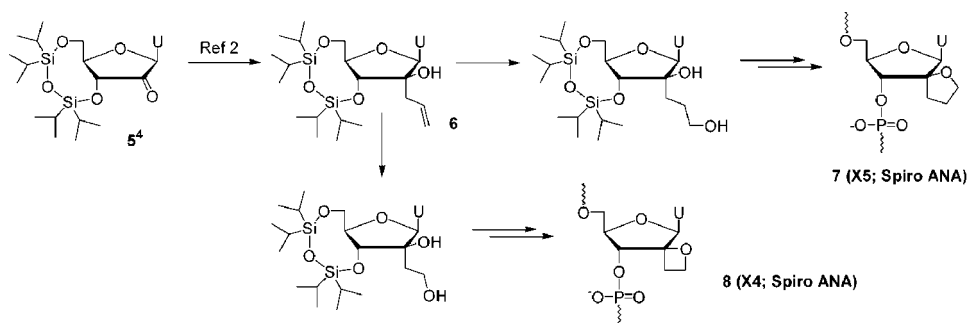
The key intermediates for the synthesis of the 2'-spiro nucleosides were 2'-C-allyl nucleosides **2** and **6** (Schs. 1 and 2).^[2] The allyl group was used because it via oxidative cleavage or hydration easily can be converted into a 2-hydroxyethyl or a 3-hydroxypropyl group, respectively.^[2]

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Scheme 1. Synthesis of 2'-spiro ribonucleosides and 2'-spiro RNA monomers.^[2]



Scheme 2. Synthesis of 2'-spiro arabinonucleosides and 2'-spiro ANA monomers.^[2]

Table 1. Thermal denaturation experiments ($T_m/^\circ\text{C}$).

Sequence	DNA complement		RNA complement	
	2'-Spiro RNA	2'-Spiro ANA	2'-Spiro RNA	2'-Spiro ANA
5'-T ₇ (X5)T ₆	19	17	19	18
5'-T ₇ (X4)T ₆	20	18	19	19
5'-T ₅ (X5) ₄ T ₅	9	<5	8	<5
5'-T ₅ (X4) ₄ T ₅	8	<5	8	<5
T ₁₄ (Reference)	32	32	29	29
5'-(X5) ₉ T	<5	<5	<5	<5
5'-(X4) ₉ T	<5	<5	<5	<5
T ₁₀ (Reference)	20	20	18	18
5'-d[G(X5)G A(X5)A (X5)GC]	12	<5	n.d.	<5
5'-d[G(X4)G A(X4)A (X4)GC]	12	<5	n.d.	<5
5'-d[GTG ATA TGC] (Reference)	29	29	28	28

Relative to the reference duplexes, incorporation of the 2'-spiro nucleoside monomers **3**, **4**, **7** and **8** into DNA strands induces destabilization of duplexes formed with complementary DNA and RNA strands (Table 1). We are currently by molecular modeling trying to determine possible steric and conformational effects induced by the 2'-spiro nucleoside monomers.

ACKNOWLEDGMENTS

The Danish National Research Foundation and The Danish Research Agency are thanked for financial support.

REFERENCES

1. Franchetti, P.; Cappellacci, L.; Marchetti, S.; Trincavelli, L.; Martini, C.; Mazzoni, M.R.; Lucacchini, A.; Grifantini, M. 2'-C-methyl analogues of selective adenosine receptor agonists; synthesis and binding studies. *J. Med. Chem.* **1998**, *41*, 1708 pp.
2. Babu, B.R.; Keinicke, L.; Wengel, J., *submitted*.



