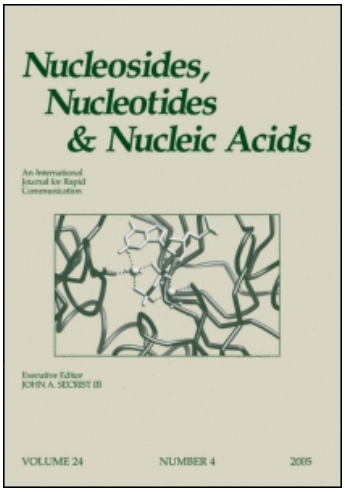

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Helmut Rosemeyer[a]; Frank Seela[a]
[a] Laboratorium für Organische und Bioorganische Chemie, Institut für Chemie, Universität Osnabrück, Osnabrück Deutschland

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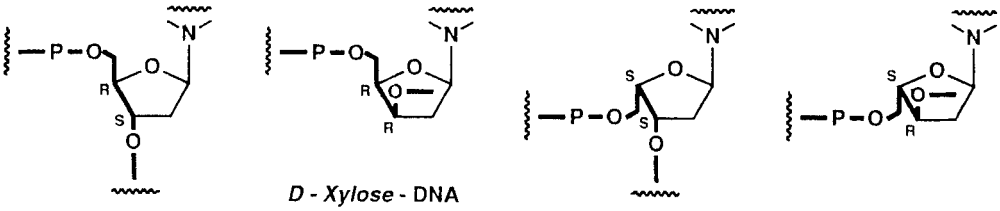
XYLOSE-DNA: SEQUENCE-DEPENDENT DUPLEX STABILITY AS FUNCTION OF BACKBONE CONFIGURATION

Helmut Rosemeyer and Frank Seela*

Laboratorium für Organische und Bioorganische Chemie, Institut für Chemie, Universität Osnabrück, Barbarastr. 7, D-49069 Osnabrück, Deutschland

Abstract: The base pairing of a series of homooligomeric or telomeric oligonucleotides built-up from 2'-deoxy-ß-*D*-xyloadenosine and/or -thymidine were synthesized and studied with respect to their thermodynamics of duplex formation. Oligo(2'-deoxyxylonucleotides) are more stable than the corresponding regular oligomers the more d(xA-xT) elements they contain.

Base pairing in DNA is not only defined by the donor-acceptor pattern of the nucleobases but also by the structure of the sugar-phosphate backbone. This has been demonstrated for *hexose-DNA* [1], which shows an altered base pairing pattern compared to regular *ribose-DNA*. Also the base pairing of *pentose*-DNA should be affected when the configuration of the sugar-phosphate backbone is changed. Recently, oligonucleotides built-up from 2'-deoxy-ß-*D*-xylonucleosides [oligo(2'-deoxy-ß-*D*-xylonucleotides)] have been synthesized [2]. Their backbone represents one of the conceivable alternative *pentose*-DNA structures (*Xylose*-DNA, *Scheme 1*).



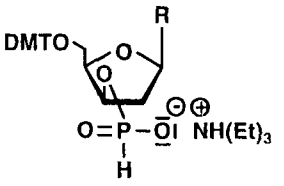
Scheme 1

Table 1. T_m-Values and Thermodynamic Data of Duplex Formation of Oligonucleotides

Oligonucleotide	T_m [°C]	ΔH [kcal/mol]	ΔS [cal/K mol]
5'-d$(A)_{12}$·5'-d$(T)_{12}$	44	-89.1	-281
5'-d[$(xA)_{12}$A]·5'-d[$(xT)_{12}$T]	36	-46.0	-148
5'-d(AAAAAATTTTTT)	44	-81.0	-255
5'd(xAxAxAxAxAxAxTxTxTxTxTxTT)	45	-57.0	-175
5'-d(AAATTTAAATTT)	40	-85.6	-275
5'-d(xAxAxAxTxTxTxAxAxAxTxTxTT)	45	-46.8	-143
5'-d(AATTAATTAATT)	35	-107.8	-350
5'-d(xAxAxTxTxAxAxTxTxAxAxTxTT)	43	-55.3	-175
5'-d(ATATATATATAT)	33	-62.0	-203
5'-d(xAxTxAxTxAxTxAxTxAxTxAxTT)	53	-48.0	-148
5'-d(TATATATATATA)	31	-32.2	-106
5'-d(xTxAxTxAxTxAxTxAxTxAxTxAA)	47	-42.8	-132
5'-d(TTTTTTAAAAAA)	36	-68.6	-221
5'-d(xTxTxTxTxTxTxAxAxAxAxAxAA)	40	-36.1	-115
5'-d(TAATTTAAAATTTAAT)	27	-74.8	-221
5'-d(xAxTxTxAxAxAxTxTxTxTxAxAxAxTxTA)	52	-73.8	-201

60 mM Na-cacodylate, 1 M NaCl, 100 mM $MgCl_2$; 8 μM strand concentration.

Oligo(2'-deoxyxylonucleotides) were synthesized from the phosphonates **1-4** by conventional solid-phase techniques. Phosphoramidite synthesis is less efficient due to the steric hindrance of the 3'-hydroxyl group.



1: R = ib²Gua
2: R = bz⁶Ade
3: R = Thy
4: R = bz⁴Cyt

In this manuscript the duplex stability of oligonucleotides containing an increasing number of d(A-T) or d(xA-xT) elements (*Table 1*) is compared.

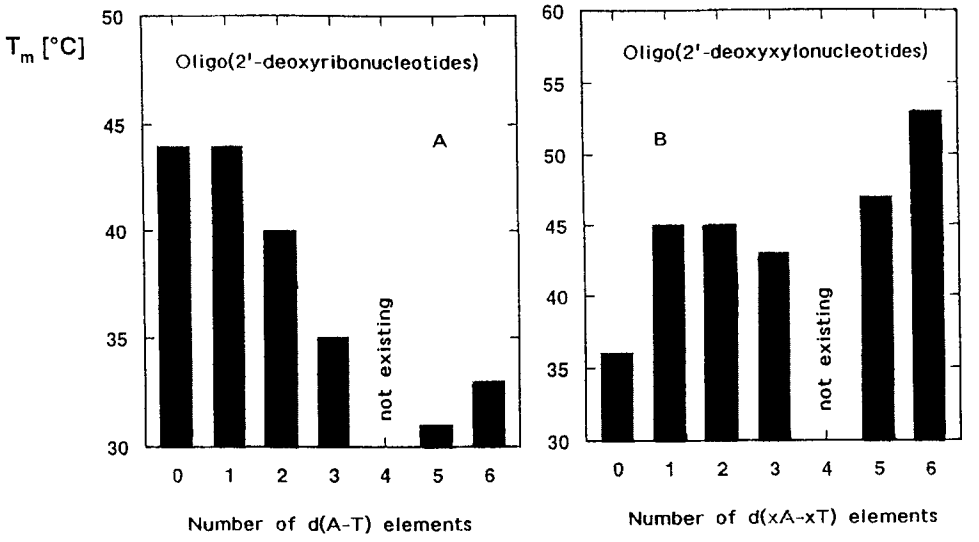


Figure 1. T_m Values of Dodecamers as a Function of d(A-T) (A) or d(xA-xT) (B) elements.

Table 1 presents the van't Hoff thermodynamic data of duplex formation of the various oligonucleotides. The data have been calculated by fitting the UV melting profiles to a two-state model.

From the table it can be seen that - with exception of $d(T\text{-}A)_6/d(xT\text{-}xA)_6$ - all modified dodecamers exhibit $\Delta H°$ values which are 30 - 50% smaller than the $\Delta H°$ values of the corresponding regular oligonucleotides. This is compensated by less unfavorable $\Delta S°$ values. Therefore, duplex formation of oligo(2'-deoxyxylonucleotides) is - in contrast to their regular counterparts - enthalpically less but entropically more favored.

Comparison of the T_m values of the oligo(2'-deoxy*ribo*nucleotides) shows a striking sequence dependence. The homooligomer $d(A)_{12}\cdot d(T)_{12}$ exhibits the highest (44°C), the alternating dodecamer $d(A\text{-}T)_6$ the lowest (33°C) T_m value. This is due to the fact that the first forms a stiff and unique B-DNA secondary structure (B'-DNA [3]), the latter, however, an extraordinarily flexible structure with dinucleotides as double-helical repeats ("alternating" B-DNA [3]). The transition between these two extremes is not abrupt but continuous,depending on the number of d(A-T) elements (***Figure 1A***).

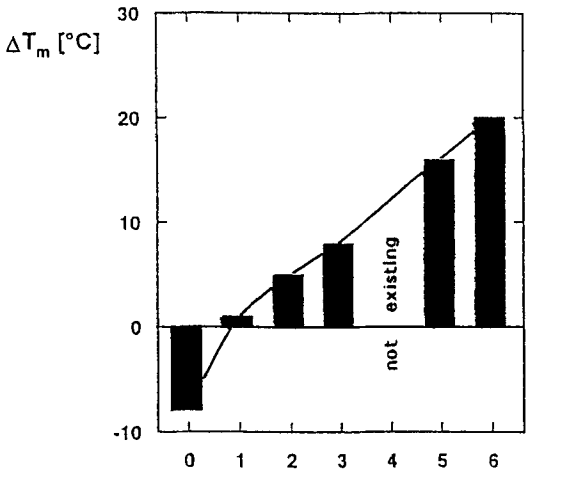


Figure 2. ΔT_m Values [= T_m(*xylose*-DNA) - T_m(*ribose*-DNA)] as a function of d(A-T) or d(xA-xT) elements.

Interestingly, d[$(xA)_{12}$-A]·d[$(xT)_{12}$-T] exhibits a T_m value which is 9° lower than that of the regular duplex while the self-complementary oligomers show an opposite behavior: d[$(xA\text{-}xT)_6$-T] exhibits a T_m value which is 20° higher than that of $d(A\text{-}T)_6$. In the case of the palindromic hexadecamers (*Table 1*, last line), which bear three d(A-T) or d(xA-xT) elements each and can form duplexes with a three-base overhang on both termini, the difference in T_m amounts even to 25° in favor of the oligo(2'-deoxyxylonucleotide). Therefore, the stability of both oligonucleotide systems is strongly sequence dependent - but in an opposite way (***Figure 1B***). This implies that the secondary structure of *xylose*-DNA is autonomous

Combining the sequence dependence of the T_m values of oligo*ribo*- and -*xylo*nucleotides by plotting ΔT_m [= T_m(*xylose*-DNA) - T_m(*ribose*-DNA)] vs. the number of d(A-T) or d(xA-xT) units a linear relation is found (***Figure 2***). This demonstrates a mirror-like behavior of the sequence dependence of duplex stability of *xylose*- and *ribose*-DNA. As a consequence the sequence specific base pairing and therewith the information of DNA is not only defined by the particular bases and the nearest neighbors but also by the structure of the

sugar-phosphate backbone. This has to be considered in designing antisense oligonucleotides with an altered backbone structure.

References

[1] A. Eschenmoser, M. Dobler, *Helv. Chim. Acta* **1992**, *75*, 218.
[2] F. Seela, K. Wörner, H. Rosemeyer, *Helv. Chim. Acta* **1994**, *77*, 883 and lit. cited therein.
[3] W. Saenger, *Principles of Nucleic Acid Structure*, Springer Verlag, New York, 1984, pp.253 ff.