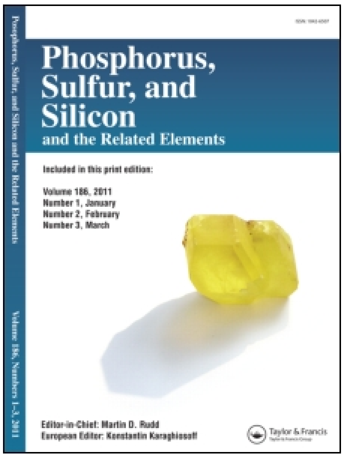

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Conformational Transmission in 5'-P^V and 5'-P^V TBP Phosphorylated Nucleosides. Implications For DNA Structure and Dynamics

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CONFORMATIONAL TRANSMISSION IN 5'-P^{IV} AND 5'-P^{V} TBP PHOSPHORYLATED NUCLEOSIDES. IMPLICATIONS FOR DNA STRUCTURE AND DYNAMICS

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Abstract Specific conformational changes in DNA and RNA can be induced via a transient pentacoordination of the phosphorus atoms in the helix backbone. The details of this conformational transmission mechanism are discussed briefly, using experimental data that were obtained with a set of 5'-P^{IV} and 5'-P^{V} phosphorylated tetrahydrofurfuryl systems. A conformational study on the more realistic model system, the dinucleotide **2** in which a stabilized pentacoordinated phosphorus forms the internucleoside linkage, is presented. Furthermore, it has been found that methylation of the phosphate groups in d($T_pT_pT_pT_pT_pT$) results in the formation of a non-Watson & Crick type parallel duplex DNA structure, in which the two strands are joined via hydrogen bonding between the thymidine bases. Various physico-chemical techniques (e.g. NMR methods and UV hyperchromicity) were used to elucidate the structural details of the parallel duplex. Characteristic properties (parallellity, slimness, symmetry) are presented.

Specific conformational changes in DNA and RNA can be generated by a transient pentacoordination of phosphorus in the sugar-phosphate helix backbone[1-4]. A very detailed insight in conformational transmission effects which occur on a coordinational change from P^{IV} into P^{V} was obtained with a set of 5'-P^{IV} and 5'-P^{V} trigonal bipyramidal (TBP) tetrahydrofurfuryl compounds.

From variable temperature 300 MHz ^{1}H NMR measurements on **1**, it could be deduced that the axial tetrahydrofurfuryl corresponds with a clear preference for the gauche(-) (g^-) rotamer around the $C_{4'}$-$C_{5'}$ bond (i.e. trans orientation of $O_{5'}$ and $O_{1'}$), which is due to a pronounced electrostatic repulsion between $O_{5'}$ and $O_{1'}$. On the other hand, gauche(+) (g^+) and

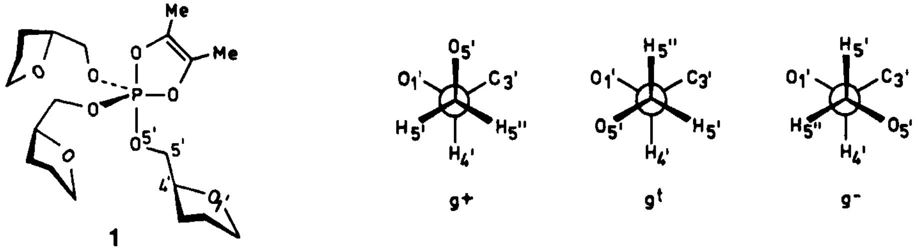

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FIGURE 1 Structural formula of **1** (left); Newman projections of the rotamers around the $C_{4'}$-$C_{5'}$ bond (right).

gauche(trans) (g^t), i.e. gauche arrangement of $O_{5'}$ and $O_{1'}$, are strongly preferred for the equatorial tetrahydrofurfuryls *and* for the P^{IV} counterpart model compound. Based on these observations it was concluded that: (i) the intrinsic bonding properties of the axial and equatorial sites in the TBP are reflected in the $C_{4'}$-$C_{5'}$ conformations of tetrahydrofurfuryl;

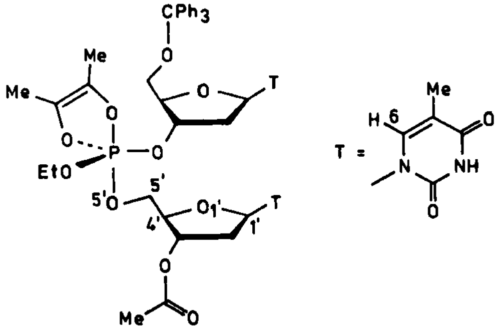

FIGURE 2 Structural formula of **2**.

(ii) a coordinational change from 5'-P^{IV} into 5'-P^{V} TBP will be transmitted in a $C_{4'}$-$C_{5'}$ conformational change towards g^-. The impact of this conformational transmission mechanism for structural changes in DNA is clearly illustrated with the dinucleotide **2**[5], for which it is found that in HMPT $x(g^+) = 0.26$, $x(g^t) = 0.20$, and $x(g^-) = 0.54$. These data substantiate our earlier proposal[3,4] that transient P^V structures may play a catalytic role in the structural interconversion from B into Z DNA for alternating d(G-C) duplices.

The reactivity of the backbone phosphate groups also comprises *alkylation*. For instance, reaction with methyl methane sulfonate results in the formation of electrostatically neutral phosphate triester internucleoside linkages. Using the hexanucleoside pentaphosphate $d(T_pT_pT_pT_pT_pT)$ it was established that methylation of the phosphate groups leads to the formation of a right-handed *parallel* duplex, as was confirmed by NMR measurements.

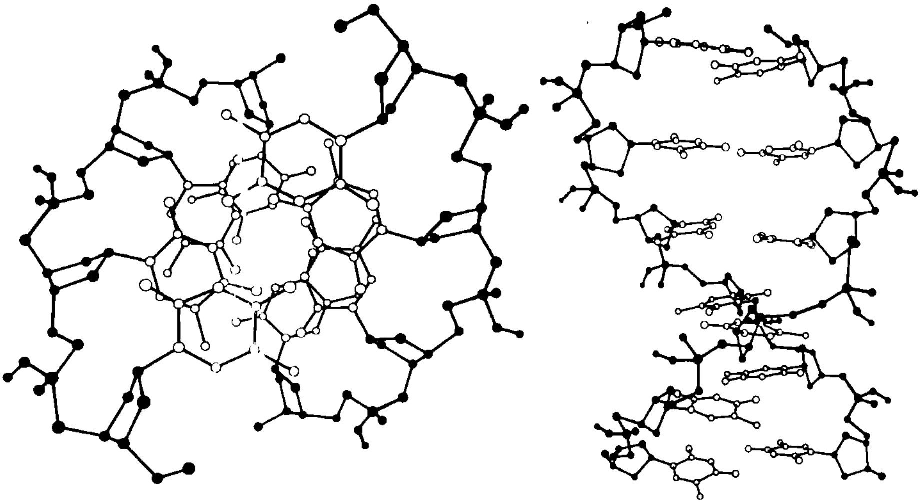

FIGURE 3 Computer-generated top and side view of the parallel duplex.

The imino protons resonate at a typical low field (13.3 ppm), proving the formation of thymine-thymine (T - T) base pairs. The subspectrum of the base methyl groups is consistent only with a symmetric parallel double helix structure (i.e. the 5' ⟶ 3' vectors run in the same direction). The double helix was also characterized with a UV hyperchromicity experiment, which established that the dissociation of the duplex occurs at a melting temperature (T_m) of 67 °C. Using the X-ray structure of 3',5'-di-O-acetyl thymidine[6,7] as a realistic conformation for extension in a polynucleotide, we obtained a parallel righthanded duplex with about 8 residues per turn. The structure is remarkably slim with a helix diameter of 15 Å, whereas the purine-pyrimidine base pairs in B DNA correspond with a helix diameter of 21 Å. Furthermore, the symmetry of the structure results in the formation of two identical grooves instead of the minor and major groove that are found in B DNA.

REFERENCES

1. H.M. Buck, Recl. Trav. Chim. Pays-Bas, 99, 181 (1980).
2. J.J.C. van Lier, M.T. Smits and H.M. Buck, Eur. J. Biochem., 132, 55 (1983).
3. L.H. Koole, E.J. Lanters and H.M. Buck, J. Am. Chem. Soc., 106, 5451 (1984).
4. L.H. Koole, R.J.L. van Kooyk and H.M. Buck, J. Am. Chem. Soc., 107, 4032 (1985).
5. L.H. Koole, H.M. Moody and H.M. Buck, Recl. Trav. Chim. Pays-Bas, 105, 196 (1986).
6. L.H. Koole, M.H.P. van Genderen, H. Frankena, H.J.M. Kocken, J.A. Kanters and H.M. Buck, Proc. Kon. Ned. Akad. van Wetensch., B89, 51 (1986).
7. C.C. Wilson, J.N. Low, P. Tollin and H.R. Wilson, Acta Cryst., C40, 1712 (1984).