worse R_B value of 0.054. The secondary phase Ni_3Al was also considered in the refinement. Further details on the crystal structure investigation may be obtained from the Fachinformationszentrum Karlsruhe, 6344 Eggenstein-Leopoldshafen, Germany (fax: (+49) 7247-808-666); e-mail: crysdata@fiz-karlsruhe.de), on quoting the depository number CSD-412238.

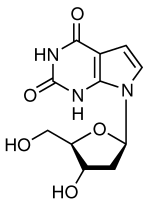
[20] Elemental analysis of **1** (%): Ni 50.65, Al 23.73, C 18.30, H 4.32. GC analysis of the condensed solution (%): butane 0.016, methylcyclohexane (hydrogenation product of toluene), 3.23, cyclooctane 2.00, butylcyclooctane 0.018, in addition 57 non-identified products with together 0.68%; residual toluene. Measurement apparatus: Carlo-Erba 4100 gas chromatograph, RTX-1 column (60 m); carrier gas H_2.

[21] Elemental analysis of **4** (%): Ni 59.7, Al 21.8, Ga 13.8, C 6.7, H 0.9.

7-Deaza-2′-deoxyxanthosine Dihydrate Forms Water-Filled Nanotubes with C–H···O Hydrogen Bonds**

Frank Seela,* Thomas Wiglenda, Helmut Rosemeyer, Henning Eickmeier, and Hans Reuter*

Inspection of an assembly of 7-deaza-2′-deoxyxanthosine dihydrate (**1**·2 H_2O) molecules[1] within a crystal discloses interesting structural features: Besides an intramolecular hydrogen bond (N3–H···OH–5′), an array of further hydrogen bonds stabilizes a supramolecular aggregate of four molecules of **1**. This arrangement results in the formation of an almost flat tetramer (Figure 1) with an oval cavity of approximate dimensions $9.5 \times 6.5 \times 3.0$ Å (±0.5 Å). A pile of completely stacked teramers forms a columnar nanotube-like structure (Figure 2).



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The synthesis of **1**[2] was performed as described previously.[3] It was crystallized from *i*PrOH/H_2O/MeOH (3/1/1), which was slightly acidified with glacial acetic acid, as a dihydrate in the monoclinic space group $P2_1$ (see Supporting Information).[4] The structure shows that **1** exists in the 2,4-dioxo form in the solid state (Figure 3); both oxo substituents lie slightly out of the ring plane.

The torsion angle χ^1 (O4′-C1′-N9-C4),[5] which defines the orientation of the base relative to the sugar group (*syn*/*anti*), amounts to 61.9°; thus the nucleoside **1** adopts the *syn* conformation. A literature survey[6] of nearly 300 X-ray structures of nucleosides reveals that **1** belongs to the minor group of about 50 structures showing this N-glycosylic *syn* conformation. The *syn* conformation around the N-glycosylic bond is unusual for 7-deazapurine nucleosides.[7] In the case of **1** it is fixed by an intramolecular hydrogen bond between the H atom on N3 and the O atom of the 5′-OH group (separation 1.98 Å)[8] forcing the exocyclic 5′-CH_2OH moiety into the +sc[(+)*g*]) conformation with a torsion angle γ of 52° for C3′-C4′-C5′-O5′. The sugar ring adopts the $^{2'}T_{3'}$ ("south") con-

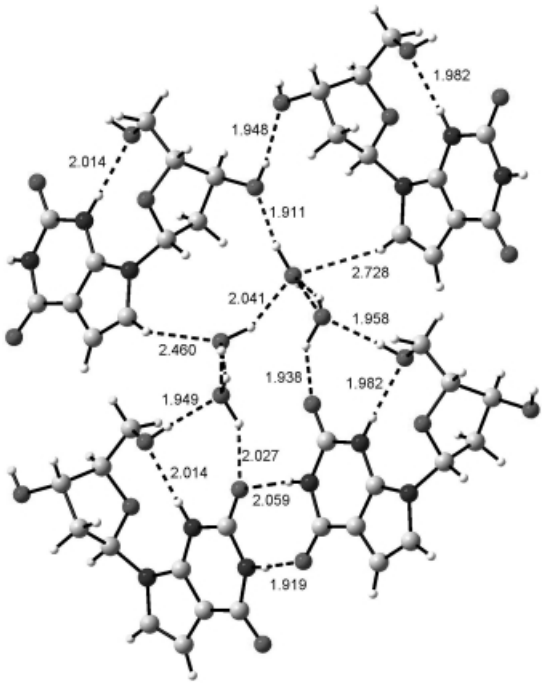

Figure 1. Length of the hydrogen bonds in a water-containing tetramer of **1**.

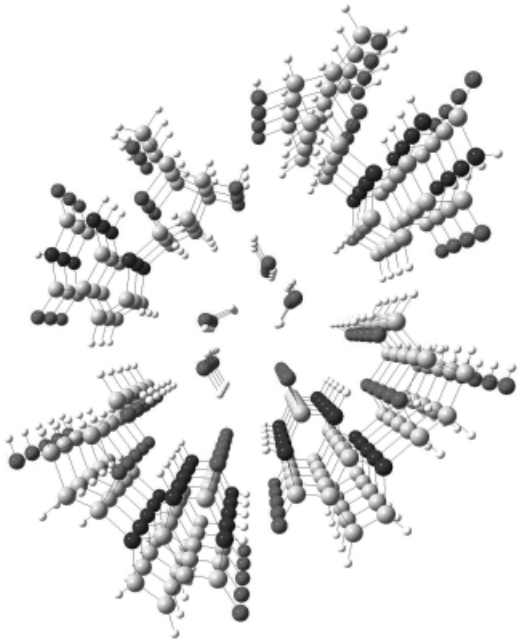

Figure 2. Nanotube of stacked tetramers (see Figure 1).

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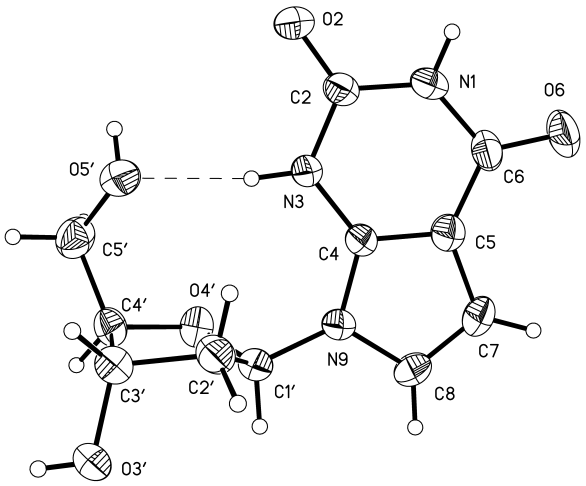

Figure 3. Molecular structure of $\mathbf{1}\cdot 2H_2O$. The intramolecular hydrogen bond that stabilizes the *syn* conformation is shown as a dashed line. Displacement ellipsoids for the atoms are drawn at the 50% probability level and H atoms are shown as spheres of an arbitrary size.

formation with a puckering amplitude $\phi_m = 35.9^\circ$ and a pseudorotation phase angle $P = 155.1^\circ$.[9] These conformational parameters are typical for most nucleosides in the *syn* conformation.[6] The discrete structure of **1** is maintained in aqueous solution, as determined by analysis of the vicinal ^{1}H,^{1}H NMR coupling constants of the sugar moiety of **1** as well as by [^{1}H,^{1}H]-NOE difference spectroscopy.[10]

Tetrameric assemblies of guanine and isoguanine derivatives containing various mono- or divalent cations have been identified as a fundamental structural element of supramolecular materials.[11] Such tetramers also form the elementary unit of guanine, isoguanine, and 7-deazaisoguanine-rich telomeric quadruplex DNA and RNA and of the so-called guanine wires.[12] Each oval-shaped tetramer cavity contains four water molecules of which two at any one time are interconnected by hydrogen bonds. The four guest molecules form a chain that bridges the nucleoside hosts. Two conventional types of hydrogen bond and an unconventional type were detected: conventional hydrogen bonds exist between the 3′- and 5′-OH groups of **1** and the O atom of a water molecule (O–H···O) and between the O2 atom of **1** and a H atom of a water molecule (=O···H–O). The O atoms of two of the H_2O molecules form unconventional hydrogen bonds to corresponding H atoms on C8 (Figure 1; 2.460 and 2.728 Å).[13] Both water oxygen atoms involved exhibit different coordination: one exhibits a distorted tetrahedral, the other one a distorted trigonal bipyramidal coordination sphere. As can be seen from Figure 2, all the H_2O molecules of the same type are arranged strictly in line along the nanotube.

The ability of the pyrrole hydrogen atoms of **1** to form attractive bonds such as hydrogen or anti-hydrogen[14] bonds is of particular importance for the structure, solvation, and stability of nucleic acids[15] containing such nucleoside units. This also concerns other analogous nucleosides, such as 7-deaza-2′-deoxyisoguanosine.[16] Being isosteric to the regular purine nucleosides, such base-modified nucleosides are well accommodated into a regular B-DNA double helix[17] and have been incorporated into triplex-forming oligonucleotides.[18] The pyrrole hydrogen atoms C7-H and C8-H are exposed to the major groove of the helix and are thus contact points for solvation by water molecules. Despite the common opinion, DNA double strands carrying stretches of 7-deazapurine bases do not necessarily contain a hydrophobic major groove, but might still bind water molecules in a similar manner as described for conventional DNA built-up from corresponding purine bases.

One also has to take into account the potential of such nucleosides to form base-pair motifs through the participation of C8/C7–H···N/O bonds. Analogous attractive C–H···O/N interactions have been described for U-U base pairs (the so-called Kalkutta base pair), A-A base pairs, and within Z-DNA from X-ray analysis of corresponding oligonucleotides and quantum chemical computations of model base pairs.[15] Despite the fact that the energy contribution of C–H···X bonds is low compared to that of standard hydrogen bonds,[15c] they have been postulated for the recognition of pyrimidine bases in a parallel DNA triple-helix motif[19] as well as for base pairs formed between guanine and ethenoadenine.[20] Such hydrogen bonding might also exist in nucleic acid duplexes incorporating other 7-deazapurine nucleosides. In this context the base-pairing properties of **1** as well as its potential of forming high molecular weight aggregates, such as triplexes or tetramers, at the oligonucleotide level are under current investigation. Additionally, compounds such as **1** allow the storage or the transport of various hydrophilic molecules.[21]

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[1] Systematic nomenclature: 7-(2-deoxy-β-D-*erythro*-pentofuranosyl)-7*H*-pyrrolo[2,3-*d*]pyrimidin-2,4-(1*H*,3*H*)-dione, c^7X_d; purine numbering is used throughout this manuscript.

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[4] Crystal data for $\mathbf{1}\cdot 2H_2O$ ($C_{11}H_{17}N_4O_7$; c^7X_d): $M_r = 303.28$, crystal dimensions $0.42 \times 0.30 \times 0.24$ mm, monoclinic, space group $P2_1$, $a = 4.891(2)$, $b = 17.746(4)$, $c = 15.467(4)$ Å, $\beta = 92.53(2)^\circ$, $V = 1341.3(6)$Å^3, $Z = 4$, $\rho_{calcd} = 1.502$ Mg m^{-3}, $\theta_{max} = 25.01^\circ$, $\mu = 0.126$ mm^{-1} ($Mo_{K\alpha}$ with $\lambda = 0.71073$ Å), $2\theta/\omega$ scans, $T = 293(2)$ K, 5418 measured reflections, 4698 independent reflections; 4698 reflections used for refinement, of which 4271 had $I > 2\sigma(I)$, $T_{min} = 0.1333$, $T_{max} = 0.1778$. Data were collected on a Siemens P4 diffractometer. The structure was determined by direct methods (SHELXS97: G. M. Sheldrick, *Program for the Solution of Crystal Structures*, Universität Göttingen, **1997**). Refinement on F^2 was performed with SHELXL (G. M. Sheldrick, *Program for the Refinement of Crystal Structures*, Universität Göttingen, **1997**), 404 free parameters, H atoms were treated by a mixture of independent and constrained refinement, $R = 0.0463$, $wR = 0.1609$, residual electron density min./max. $= -0.299/0.228$ e Å^{-3}. CCDC 169203 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

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RNA Two-State Conformation Equilibria and the Effect of Nucleobase Methylation**

Claudia Höbartner, Marc-Olivier Ebert, Bernhard Jaun, and Ronald Micura*

The constitutional diversity of RNA is impressively reflected in more than 90 chemically modified nucleosides.[1, 2] It was reported recently that the modified nucleosides of a human mitochondrial $tRNA^{Lys}$ are required for the formation of the correct cloverleaf three-dimensional structure.[3] In contrast, the corresponding unmodified in vitro transcript did not fold into a cloverleaf but into an extended bulged hairpin. To the best of our knowledge, these studies provide the first and so far only experimental data that document the significant influence of nucleoside modifications on RNA folding. These results encouraged us to investigate systematically the effect of nucleobase methylation in short palindromic oligoribonucleotide duplexes. We found that the replacement of single nucleosides with the corresponding methylated counterparts, such as 1-methylguanosine (m^1G), N^2,N^2-dimethylguanosine ($m^2{}_2G$), N^6,N^6-dimethyladenosine ($m^6{}_2A$), or 3-methyluridine (m^3U), led to the formation of a hairpin rather than of a duplex structure.[4] These remarkable changes in the secondary structure motif form the basis of our investigations. Herein we report on single-stranded oligoribonucleotides that exist in monomolecular two-state conformation equilibria. By methylation of selected nucleobases, it is possible to shift these equilibria to a significant extent.

The methylation pattern of the studied sequences corresponds to the naturally occurring helix 45 loop located at the 3′-end of ribosomal RNA of the small subunit (SSU) (Figure 1).[5] The two successive $m^6{}_2A$ nucleosides within the four-membered loop are conserved almost universally in bacteria and eukaryotes. These modified adenosines are functionally significant; however, the exact reason for their methylation is not yet understood. We have chosen 5′-…$CCm^2GGm^6{}_2A$-$m^6{}_2AGG$…-3′ as a lead sequence for a comparison of the conformation of methylated versus nonmethylated sequence constructs (Table 1, Figure 2). Two questions are important in the sequence design. First, is a complementary sequence partition such as 5′-…CCUUCC…-3′ able to break up the nonmethylated stem-loop structure of 5′-…CC*GGAA*GG…-3′?

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