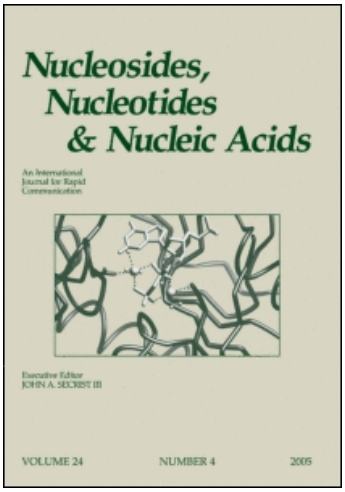

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The Three-Dimensional Structure of 3'-Deoxycytidine

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THE THREE-DIMENSIONAL STRUCTURE OF 3'-DEOXYCYTIDINE

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ABSTRACT: Structural analysis of 3'-deoxycytidine and comparison with 2'-deoxynucleosides reveals no noticeable effect on the conformation of the molecule due to the lack of 3'-oxygen atom. There are two crystallographically independent molecules and both adopt the *anti* conformation with C3'-*endo* sugar puckering. A 'head-to-tail' packing of the molecules along the *b* axis results in a 'virtual' 2'-5' polycytidylic acid chain.

Introduction

The lack of 3'-hydroxyl group in 3'-deoxyribonuclesides results in their inhibiting RNA synthesis, thus leading to their potential use as antibacterial, antiparasitic and anticancer agents[1-3]. Such functions could possibly arise out of the different conformations which may be adopted by the 3'-deoxyribose groups. The sugar ring has been shown to possess a high degree of flexibility[4] which manifests itself even in the presence of external cyclic constraints[5]. In addition, base-sugar interactions could lead to different conformations about the glycosyl bond as compared, say, to 2'-deoxynucleosides. To evaluate such conformational effects, it becomes necessary to determine the three-dimensional structure of 3'-deoxynucleosides. In this paper, we report the crystal structure of 3'-deoxycytidine.

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Results

There are two molecules present in the asymmetric unit of the crystal cell and are named A and B. Tables 1 & 2 give the final positional and thermal parameters of the non-hydrogen and hydrogen atoms respectively. Bond lengths and bond angles for the non-hydrogen atoms are given in tables 3 and 4 respectively. Thermal ellipsoid perspective views of the two independent molecules are given in figures 1a and 1b. Figure 1a also shows the numbering scheme adopted.

The molecular geometry is *anti* about the glycosidic bond, with *C3'-endo* sugar pucker in both the molecules. The conformation about the C4'-C5' bond is *gauche-gauche* in A and *gauche-trans* in B.

In molecule A the value of the glycosidic torsion angle χ_{CN} is 142.4°. In molecule B this is 172.1°. The difference of 30° notwithstanding, both molecules are squarely in the usual *anti* region of the conformational circle. Again in both molecules the C3' of atom the ribose moeity is displaced by 0.56 Å in the same direction as the C5' atom from the plane of C1', C4' and O4'. C2' also lies nearly in this plane (Table 5). The values of the pseudorotation phase angles[6] are 21.6° and 20.2° for the molecules A & B respectively. The pucker in both cases is thus C3'-*endo*. This is again a commonly observed conformation in conjunction with the *anti* geometry[7].

The conformation about the C4'-C5' bond is commonly *gauche-gauche*[8]. In the present structure the torsion angles ϕ_{OO} [O5'-C5'-C4'-O4'] and ϕ_{OC} [O5'-C5'-C4'-C3'] are 56.8(13)° and -60.7(13)° respectively for molecule A and -69.1(7)° and 173.7(5)° for molecule B. This means a g^+g^- conformation for A and g^+t conformation for B (Figure 2).

A possible rationale for this conformational difference lies in the different intermolecular interaction in which the two independent molecules take part. Both are stabilized in the crystal by hydrogen bonds. But molecule A forms more hydrogen bonds when compared with molecule B (Table 6). The exocylic atom N4 of the cytosine base of molecule A forms a hydrogen bond with O2 of molecule B related by (+x,+y-1,+z-1). The O2' hydroxyl group of molecule A participates in a reciprocal arrangement with O5' of molecule B, both atoms acting

TABLE 1. Atomic coordinates and equivalent isotropic thermal parameters ($Å^2$) for the non-hydrogen atoms of molecule A & molecule B E.s.d's (for coordinates) and anisotropicity (for Ueq) in parentheses.

Molecule A:

Atom	x/a	y/b	z/c	Ueq
N1A	0.1990 (4)	-0.2054 (4)	-0.0556 (3)	0.033 (1)
C2A	0.0695 (5)	-0.1585 (5)	-0.0372 (5)	0.036 (1)
O2A	0.0393 (5)	-0.2015 (4)	0.0522 (4)	0.051 (1)
N3A	-0.0181 (5)	-0.0681 (4)	-0.1161 (5)	0.044 (1)
C4A	0.0193 (5)	-0.0260 (5)	-0.2107 (5)	0.037 (1)
N4A	-0.0607 (7)	0.0706 (6)	-0.2803 (6)	0.064 (2)
C5A	0.1413 (6)	-0.0799 (5)	-0.2402 (5)	0.040 (1)
C6A	0.2303 (5)	-0.1667 (5)	-0.1585 (4)	0.038 (1)
C1'A	0.3036 (5)	-0.2940 (5)	0.0403 (4)	0.033 (1)
C2'A	0.2722 (6)	-0.4324 (5)	0.0039 (5)	0.046 (1)
O2'A	0.2975 (4)	-0.5064 (5)	0.1131 (5)	0.063 (1)
C3'A	0.3990(10)	-0.4598 (6)	-0.0440 (6)	0.062 (2)
C4'A	0.5333 (7)	-0.3807 (6)	0.0359 (6)	0.051 (2)
O4'A	0.4607 (4)	-0.2678 (4)	0.0566 (4)	0.043 (1)
C5'A	0.6508(12)	-0.3452(11)	-0.0191(11)	0.114 (5)
O5'A	0.5920 (9)	-0.2746(10)	-0.1272 (8)	0.128 (3)
Molecule B:				
N1B	0.1900 (5)	-0.7844 (4)	0.4265 (4)	0.040 (1)
C2B	0.0915 (7)	-0.8468 (5)	0.4747 (5)	0.045 (1)
O2B	0.0735 (7)	-0.8007 (4)	0.5665 (5)	0.065 (1)
N3B	0.0251 (6)	-0.9554 (4)	0.4203 (5)	0.045 (1)
C4B	0.0476 (6)	-1.0005 (5)	0.3195 (5)	0.039 (1)
N4B	-0.0188 (6)	-1.1104 (5)	0.2697 (5)	0.051 (1)
C5B	0.1370 (6)	-0.9326 (5)	0.2629 (4)	0.039 (1)
C6B	0.2075 (6)	-0.8276 (5)	0.3206 (4)	0.039 (1)
C1'B	0.2738 (9)	-0.6693 (6)	0.4976 (6)	0.057 (2)
C2'B	0.4074(10)	-0.7092 (8)	0.6286 (6)	0.067 (2)
O2'B	0.4253(10)	-0.6150 (7)	0.7186 (6)	0.099 (2)
C3'B	0.5489 (9)	-0.7138 (9)	0.5983 (5)	0.074 (2)
C4'B	0.5161 (8)	-0.6081 (7)	0.4991 (5)	0.055 (2)
O4'B	0.3482 (5)	-0.6108 (6)	0.4260 (4)	0.050 (1)
C5'B	0.5997 (7)	-0.6250 (8)	0.4118 (6)	0.057 (2)
O5'B	0.5817 (5)	-0.5213 (7)	0.3313 (5)	0.077 (2)

TABLE 2. Atomic coordinates and isotropic thermal parameters ($Å^2$) for the hydrogen atoms of molecule A & molecule B.

Molecule A:

Atom	x/a	y/b	z/c	U_{iso}
H1NA	-0.0519	0.0935	-0.3550	0.101
H2NA	-0.0999	0.1192	-0.2404	0.071
HC5A	0.1647	-0.0307	-0.3162	0.036
HC6A	0.3204	-0.2395	-0.1435	0.067
H1'A	0.2959	-0.2905	0.1144	0.038
H2'A	0.1861	-0.4263	-0.0485	0.064
HO2A*	0.3322	-0.4603	0.1778	0.060
H3'A	0.4377	-0.5469	-0.0291	0.098
H3"A	0.3695	-0.4297	-0.1504	0.053
H4'A	0.5917	-0.4240	0.1008	0.034
H5'A*	0.7407	-0.2849	0.0514	0.120
H5"A*	0.7066	-0.4280	-0.0335	0.120
HO5'A	0.5205	-0.3567	-0.2000	0.050
Molecule B:				
H1NB*	0.0688	-1.1473	0.2908	0.050
H2NB*	-0.1339	-1.1425	0.2143	0.050
HC5B	0.1578	-0.9728	0.1877	0.128
HC6B	0.2749	-0.7831	0.3027	0.055
H1'B	0.1927	-0.6253	0.5009	0.083
H2'B	0.3323	-0.7883	0.6364	0.050
HO2B	0.3265	-0.5302	0.6600	0.050
H3'B	0.5490	-0.8107	0.5597	0.031
H3"B	0.6622	-0.6843	0.6819	0.061
H4'B	0.4604	-0.0322	0.4585	0.078
H5'B	0.7054	-0.6418	0.4658	0.085
H5"B	0.5830	-0.7035	0.3680	0.090
HO5'B*	0.4904	-0.5192	0.2770	0.070

* indicates atoms fixed geometrically.

as both acceptor and donor, simultaneously. Apart from this, the O2' atom of molecule A also makes a close contact of 3.03Å with the O5' atom of a symmetry-related molecule A. This interaction is not a hydrogen bond, since the HO5' of symmetry-releted molecule A is pointed in a different direction. This close contact leads to infinite chains of cytosine molecules along the *b* axis, each making 2'-5' interaction with the next, in other words a 'virtual' (2'-5') polycytidilic acid, if we ignore the absence of the phosphate group (Figure 3). Molecule B does not participate in any such chain, owing to the unfavorable positioning of the O2'

TABLE 3. Bond lengths (Å) of molecule A & molecule B. E.s.d's in parentheses.

Atom 1	Atom 2	Molecule A	Molecule B
N1	C6	1.377 (6)	1.360 (6)
N1	C2	1.387 (6)	1.402 (6)
N1	C1'	1.476 (6)	1.502 (8)
C2	O2	1.245 (6)	1.225 (7)
C2	N3	1.345 (7)	1.339 (8)
N3	C4	1.333 (7)	1.335 (7)
C4	N4	1.328 (7)	1.337 (8)
C4	C5	1.419 (6)	1.428 (7)
C5	C6	1.337 (7)	1.328 (8)
C1'	O4'	1.416 (6)	1.404 (6)
C1'	C2'	1.526 (7)	1.570 (11)
C2'	O2'	1.411 (7)	1.395 (10)
C2'	C3'	1.504 (10)	1.480 (12)
C3'	C4'	1.476 (11)	1.536 (10)
C4'	O4'	1.440 (7)	1.440 (8)
C4'	C5'	1.501 (8)	1.493 (9)
C5'	O5'	1.358 (10)	1.402 (9)

TABLE 4. Bond angles (°) of molecule A & molecule B. E.s.d's in parentheses.

			Angle	
Atom 1	Atom 2	Atom 3	Molecule A	Molecule B
C6	N1	C2	120.4 (4)	120.8 (5)
C6	N1	C1'	121.6 (4)	122.5 (4)
C2	N1	C1'	117.9 (4)	116.8 (4)
O2	C2	N3	122.5 (4)	123.2 (5)
O2	C2	N1	118.6 (5)	118.3 (5)
N3	C2	N1	118.9 (4)	118.5 (4)
C4	N3	C2	120.0 (4)	120.6 (4)
N4	C4	N3	118.7 (5)	118.5 (5)
N4	C4	C5	118.5 (5)	120.0 (5)
N3	C4	C5	122.7 (5)	121.5 (5)
C6	C5	C4	116.2 (4)	117.4 (3)
C5	C6	N1	121.3 (4)	121.0 (4)
O4'	C1'	N1	107.9 (4)	108.3 (4)
O4'	C1'	C2'	107.4 (4)	106.9 (6)
N1	C1'	C2'	114.6 (4)	109.6 (5)
O2'	C2'	C3'	109.4 (5)	109.7 (7)
O2'	C2'	C1'	110.6 (5)	108.9 (7)
C3'	C2'	C1'	101.2 (5)	102.7 (5)
C4'	C3'	C2'	104.5 (5)	102.4 (7)
O4'	C4'	C3'	104.1 (5)	109.6 (5)
O4'	C4'	C5'	108.7 (6)	105.2 (5)
C3'	C4'	C5'	117.1 (7)	113.5 (7)
C1'	O4'	C4'	109.5 (4)	109.6 (5)
O5'	C5'	C4'	115.0 (7)	112.5 (6)

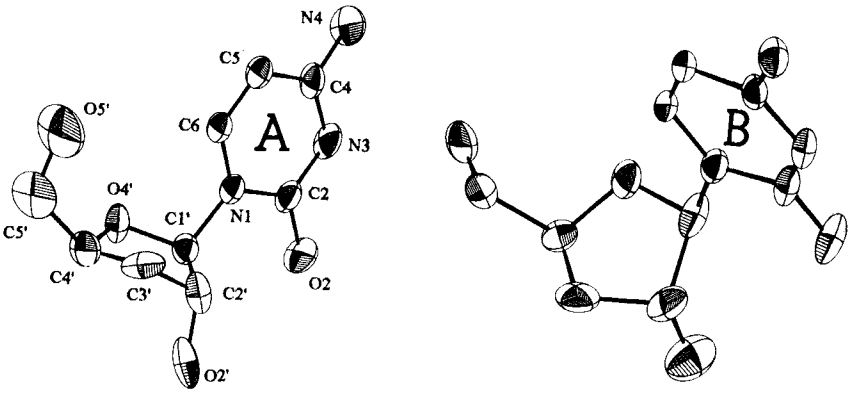

FIGURE 1a & 1b. Perspective view of ellipsoids (drawn at 50% probability) representing the anisotropic temperature parameters for molecule A & molecule B.

TABLE 5: Least-squares planes (x,y,z in crystal coordinates) and atomic deviations from them (* indicates atom used to define plane). E.s.d's in parentheses.

Ribose atom	Molecule A	Molecule B
	Deviation (Å)	
C1' *	0.000	0.000
C4' *	0.000	0.000
O4' *	0.000	0.000
C2'	-0.033 (0.013)	0.017 (0.018)
C3'	-0.559 (0.013)	0.560 (0.019)
C5'	-0.743 (0.012)	0.815 (0.013)

Equation of the plane:

For molecule A: - 0.691 (0.030) x + 2.368 (0.064) y + 10.502 (0.017) z = 0.910 (0.018)
For molecule B: 2.414 (0.038) x + 9.420 (0.034) y - 5.193 (0.075) z = 4.382 (0.057)

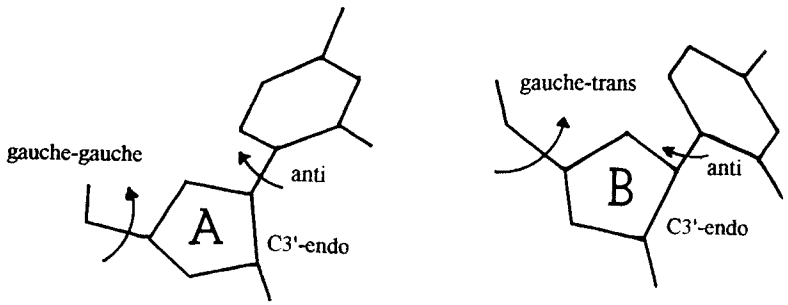

FIGURE 2. Conformational differences of the molecule A & molecule B. View perpendicular to C1', C2' & O4' atom plane.

TABLE 6. Possible intermolecular hydrogen bond distances (Å) and angles (°).

Donor-H	Donor... Acceptor	H...Acceptor	Donor-H ....Acceptor	Symmetry of Acceptor
N4A H1NA	N4A O2B	H1NA...O2B	N4A -H1NA...O2B	+x,+y-1,+z-1
0.919(8)	*2.861(10)*	2.060(6)	*144.9(5)*	
O2'A -H2'A	O2'A....O5'B	H2'A ..O5'B	O2'A -H2'A..O5'B	+x,+y,+z
0.837(5)	2.818(6)	2.366(5)	114.5(4)	
O5'B -HO5'B	O5'B....O2'A	HO5'B...O2'A	O5'B -HO5B...O2'A	+x,+y,+z
0.827(4)	2.818(6)	2.012(4)	164.7(5)	
C3'A -H3"A	C3'A....O2'B	H3"A...O2'B	C3'A -H3"A..O2'B	+x,+y,z-1
1.175(7)	3.259(11)	2.643(8)	111.4(4)	

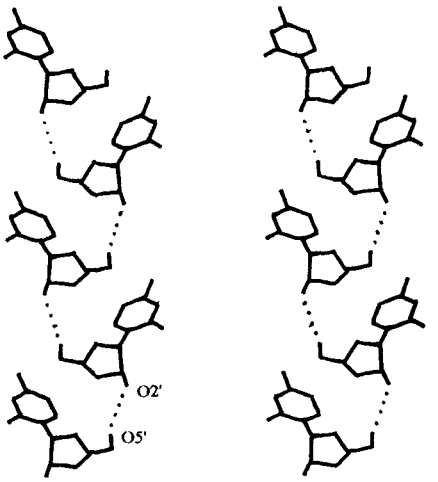

FIGURE 3. The 'head-to-tail' interaction between O2' and O5' of the symmetry releted molecules form a 'virtual' (2'-5') polycytidylic acid chain. (Stereo view).

TABLE 7: Crystal data

Parameter		3'-deoxycytidine
Empirical formula	:	$C_9 H_{13} N_3 O_4$
Molecular weight	:	225.21
Crystal shape/colour	:	Cubic / Colourless
Crystal system	:	Monoclinic (*b* unique)
Space group	:	$P2_1$
Cell constant		
a (Å)	:	9.244(2)
b(Å)	:	10.642(3)
c(Å)	:	11.393(4)
α(°)	:	90.0
β(°)	:	113.24(4)
γ(°)	:	90.0
Cell measurement number of reflections	:	20
Cell measurement theta minimum and maximum	:	7 , 12
Volume ($Å^3$)	:	1028.4(5)
Z	:	4
F(000)	:	472
D_{cal} ($g\ cm^{-3}$)	:	1.454
Radiation type and wave length	:	Mo K_α , 0.7091 Å
Crystal dimension	:	0.7 X 0.7 X 0.7 mm
2 Theta maximum	:	26.90°.
Reflection limit minimum & maximum		
h	:	0 11
k	:	0 13
l	:	-14 13
Reflections measured	:	2352
Reflections observed [≥ 2 sigma(I)]	:	2198
Computer programs used for solving and refining the structure	:	SHELXS & SHELX93
Treatement of hydrogens	:	Not refined
Number of parameters	:	393
Weighting scheme	:	$1/[sigma^2(Fo^2)+(0.1332P)^2+1.18P]$ $P=(Fo^2+2Fc^2)/3$
Final residual (R)	:	0.073
Maximum & Minimum (Δρ) $e/Å^3$	:	0.81 & -0.69

atom. A few possible C-H...O type interactions also may contribute to the crystal stability.

As compared to both 2'-deoxynucleosides as well as ribonucleosides, the molecular conformations are little affected by the lack of 3'-oxygen atom. The 'head-to-tail' packing of the molecules A where the 2' end is the head and the 5' end is the tail, suggest that in the pre-biotic situation, crystallization could have acted as a catalyst for the formation of 2'-5' polynucleotides, perhaps as easily as for 3'-5' polynucleotides[9] and polypeptides[10].

Experimental section

Synthesis of the molecule has been described previously[11]. Cuboidal crystals were obtained by slow evaporation of a solution of the 3'-deoxycytidine in methanol-water mixture. Three dimensional X-ray intensity data were collected in an Enraf-Nonius CAD4 diffractometer using MoK_{α} radiation. Volume and symmetry comsiderations indicate two crystallographically independent molecules in the asymmetric unit. Table 7 gives details of the data collection, structure solution and refinement. The structure was solved by direct methods using the program SHELXS[12] and refined by a full matrix least-squares procedure using the program SHELX93[13]. Twenty hydrogens were located from the difference Fourier map and the six were fixed geometrically. The hydrogens located from the difference Fourier were refined isotropically for one cycle in the initial stage and at the final stages hydrogens were not refined. The final R_{factor} is 0.073 for 2198 reflections $\geq$ 2sigma(I).

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REFERENCES

1. Guarino, A. J. in "*Antibiotics*" (1987), **p 488**, Gottlieb, D. and Shaw, P. D. Eds., Springer Verlag, NewYork.
2. Rainny, P. and Santi, D. V. *Proc. Natl. Acad. Sci., USA.* (1983), **80**, 288.
3. Jagger, D.V., Kredich, N. M. and Guarino, A. J. *Cancer Res.* (1981), **21**, 218.

4 Sasisekharan, V. (1973), *Jerus. Symp. Quant. Chem. Biochem.*, **5**, 247.
5. Viswamitra, M. A. and Gautham, N. (1984), *Proc. Ind. Acad. Sci (Chem.Sci)*, **93**, 261.
6. Altona, C. and Sundaralingam, M. (1972), *J. Am. Chem. Soc.*, **94**, 8205.
7.. Haschemeyer, A. E. V. and Rich, A. (1967), *J. Mol. Biol.*, **27**, 369.
8.. Shefter, E. and Trueblood, K. N. (1965), *Acta Cryst.*, **18**,1067.
9. Dhingra, M. M. and Sarma, R. H. (1978), *Nature*, **272**, 798.
10. Vijayan, M. (1980), *FEBS Lett.*, **112**, 135.
11. Kumar, A., Khan, S. I., Manglani, A., Khan, K. and Katti, S. B. (1994), *Nucleosides and Nucleotides*, **13**, 1017.
12. Sheldrick, G. M. (1986), *SHELXS*. Program for the Solution of Crystal Structures, University of Gottingen, Germany.
13. Sheldrick, G. M. (1993), *SHELXL93*. Program for the Refinement of Crystal Structures, University of Gottingen, Germany.

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