

<i>Cryst. Res. Technol.</i>	<b>36</b>	2001	4-5	485-492
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## **Crystal and Molecular Structure of 3'- Deoxyguanosine-N(2)-isobutyryl Dihydrate**

The crystal structure of the title compound has been determined from X-ray diffraction studies. The compound was crystallized from ethanol in the monoclinic system with the space group  $P2_1$ . The unit cell parameters are  $a = 9.650(2) \text{ \AA}$ ,  $b = 6.505(2) \text{ \AA}$ ,  $c = 14.251(2) \text{ \AA}$  and  $\beta = 93.70(2)^\circ$ . The number of molecules in the unit cell  $Z = 2$  and the volume of the cell is  $V = 892.7(4) \text{ \AA}^3$ . The structure was determined by direct methods and refined to a final R(F) factor of 0.062. The glycosyl torsion angle about  $C(1') - N(9)$  shows *anti* conformation. The furanose ring adopts  $C(3') - \textit{endo}$  puckering geometry.

Keywords: sugar modified nucleosides, X-ray structure, puckering, hydrogen bonds

(Received October 17, 2000; Accepted January 22, 2001)

### **Introduction**

3' Deoxy nucleosides are sugar modified nucleosides known for their anti bacterial (GUARINO, 1967), anti parasitic (RAINNY & SANTI, 1983) and anti cancer (JAGGER et al., 1961) activities. Some of the activities of these compounds are due to the lack of 3' hydroxyl group, which results in the inhibition of RNA synthesis (BAZIN & CHATTOPADHYAYA, 1985).

### **Experimental**

The compound was crystallized by slow evaporation from 40% ethanol in water. A colourless crystal of size  $0.3 \times 0.1 \times 0.1$  mm was used for intensity data collection in a graphite monochromated ( $\text{CuK}_\alpha = 1.5418 \text{ \AA}$ ) *Enraf-Nonius* four circle diffractometer. The intensity data were collected in the range  $3.11 < \theta < 67.93^\circ$  in  $\omega/2\theta$  scan mode. Three standard reflections were used to check the crystal orientation and decay for every 200 reflections and there was not any significant variation in the intensity over the entire duration of data collection. Of the 1792 reflections collected, 1696 for which  $I > 2\sigma(I)$  were used in the structure analysis. The relevant crystallographic details are listed in Table 1.

### **Structure Analysis**

The positions of all non hydrogen atoms of this compound were obtained through direct methods using the software SHELXS97-2 (SHELDRICK, 1997). The atomic parameters were initially refined isotropically and subsequently anisotropically by full matrix least square

refinement using the software SHELXL97-2 (SHELDRICK, 1997). All the hydrogen atoms except the methyl, hydroxyl and water hydrogen atoms were obtained from a difference Fourier map. Methyl and hydroxyl hydrogen atoms were fixed stereochemically while water hydrogen atoms were located using the software HYDROGEN (NARDELLI, 1999). The hydrogen atoms were refined in the initial cycles of refinement, but blocked from refinement in the final refinement cycles. The final  $R(F) = 0.0618$  ( $wR(F^2) = 0.1705$ ).

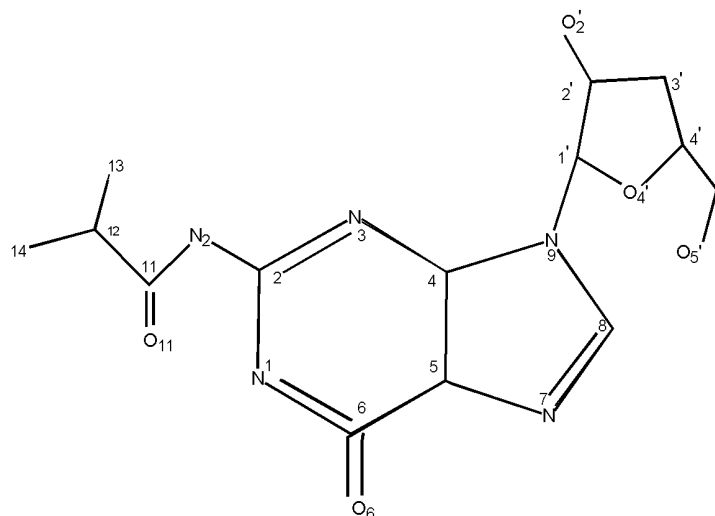


Fig 1: Chemical diagram of the molecular structure

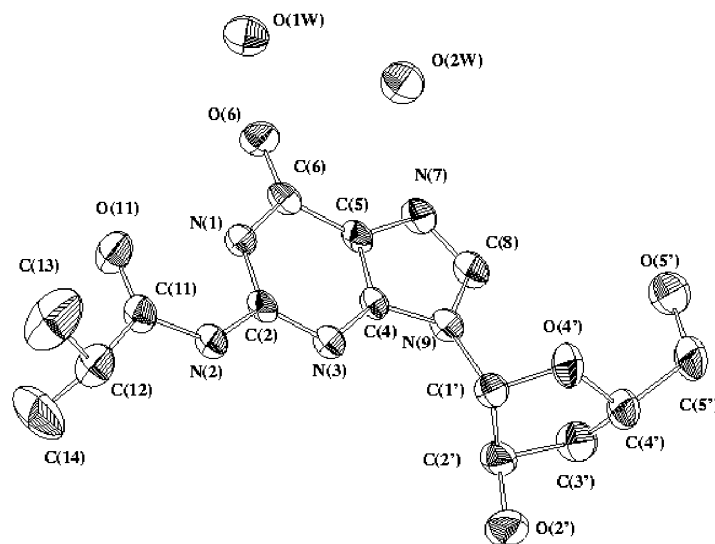


Fig 2: Molecular structure showing displacement ellipsoids at 30% probability level

## Results and Discussions

Figure 1 shows the chemical diagram and the numbering scheme adopted in the structure. Figure 2 shows the thermal ellipsoid plot drawn at 30% probability level using the program

ORTEP III (JOHNSON and BURNETT, 1998). Bond geometry calculations were made using the software PARST (NARDELLI, 1995). Table 2 gives the atomic parameters of the non hydrogen atoms.

Table 1: Crystal data and Refinement Details

Empirical formula	C14 H27 N5 O6
Formula weight	361.41
Temperature	293K
Wavelength	1.54180 Å
Crystal system, space group	Monoclinic, P2 <sub>1</sub>
Unit cell dimensions	a = 9.650(2) Å $\alpha$ = 90.00(2)° b = 6.505(2) Å $\beta$ = 93.70(2)° c = 14.251(2) Å $\gamma$ = 90.00(3)°
Volume	892.7(4) Å <sup>3</sup>
Z, Calculated density	2, 1.345 Mg/m <sup>3</sup>
Absorption coefficient	0.888 mm <sup>-1</sup>
F(000)	388
Crystal size	0.3 x 0.1 x 0.1 mm
Theta range for data collection	3.11 to 67.93°
Limiting indices	0 ≤ h ≤ 11, 0 ≤ k ≤ 7, -15 ≤ l ≤ 17
Reflections collected / unique	1792 / 1696 [R(int) = 0.0327]
Completeness to theta = 67.93	95.3 %
Data / restraints / parameters	1696 / 1 / 250
Goodness-of-fit on F <sup>2</sup>	1.058
Final R indices [I > 2σ(I)]	R1 = 0.0618, wR2 = 0.1705
R indices (all data)	R1 = 0.0691, wR2 = 0.1820
Extinction coefficient	0.012(3)
Largest diff. peak and hole	0.365 and -0.383 e.Å <sup>-3</sup>

Table 2: Atomic coordinates (x 10<sup>4</sup>) and Equivalent Isotropic Displacement parameters (Å<sup>2</sup> x 10<sup>3</sup>)

Atom	x	y	z	U(eq)
N(1)	-9823(3)	-1802(7)	1152(2)	31(1)
N(2)	-7419(3)	-1763(8)	1555(2)	36(1)
N(3)	-8181(3)	-1668(8)	-4(2)	34(1)
N(7)	-11577(3)	-1778(8)	-1229(2)	37(1)
N(9)	-9333(3)	-1608(7)	-1568(2)	35(1)
O(6)	-12175(3)	-1847(7)	889(2)	43(1)
O(11)	-8637(3)	-1729(8)	2865(2)	53(1)
O(2')	-6255(4)	-3291(9)	-2738(3)	62(1)
O(4')	-8376(4)	190(6)	-2792(2)	48(1)
O(5')	-10687(4)	98(9)	-4175(3)	65(1)
O(1W)	-14906(3)	-3011(8)	814(3)	60(1)
O(2W)	-14591(4)	-2251(8)	-1110(3)	62(1)
C(2)	-8528(4)	-1749(8)	868(3)	31(1)
C(4)	-9350(4)	-1702(8)	-615(2)	30(1)
C(5)	-10709(4)	-1781(9)	-403(3)	32(1)

C(6)	-11053(4)	-1839(9)	555(3)	33(1)
C(8)	-10722(4)	-1656(10)	-1901(3)	39(1)
C(11)	-7524(4)	-1788(9)	2505(3)	38(1)
C(12)	-6160(4)	-1910(13)	3083(3)	55(2)
C(13)	-6161(6)	-565(12)	3933(4)	101(3)
C(14)	-5936(8)	-4183(12)	3337(4)	105(3)
C(1')	-8105(4)	-1345(8)	-2109(3)	37(1)
C(2')	-7699(5)	-3290(9)	-2627(3)	43(1)
C(3')	-8424(6)	-2939(11)	-3596(4)	52(2)
C(4')	-8262(6)	-660(11)	-3723(4)	47(1)
C(5')	-9295(6)	377(12)	-4400(4)	59(2)

Table 3: Least square plane calculations and puckering parameters of the furanose ring  
 Weighted least-squares planes; Equation of the plane:  $m1*X+m2*Y+m3*Z=d$ ;  
 $m1 = -0.95927(80)$ ;  $m2 = -0.27733(60)$ ;  $m3 = -0.05371(304)$ ;  $D = 7.70312(1057)$

Atom	d	s	d/s	(d/s)**2
C(1') *	0.0176	0.0042	4.220	17.810
C(2') *	-0.0140	0.0048	-2.885	8.326
O(4') *	-0.0154	0.0038	-4.030	16.238
C(4') *	0.0197	0.0056	3.547	12.585
C(3')	0.5837	0.0057	102.870	10582.192
C(5')	0.7812	0.0059	132.463	17546.422
Sum((d/s)**2) for starred atoms				54.959

\* - atoms forming the plane

Ring puckering coordinates of the furanose ring (CREMER, 1975)

Atom	Internal cartesian coordinates		
	X	Y	Z
C(1')	0.000(00)	1.549(4)	-0.262(5)
C(2')	-0.074(22)	1.128(6)	1.206(5)
O(4')	0.305(15)	0.396(5)	-1.007(4)
C(4')	0.350(06)	-0.761(5)	-0.136(5)
C(3')	-0.434(17)	-0.347(6)	1.080(9)
C(5')	-0.147(18)	-1.964(5)	-0.881(8)
q2 =	2.115(11)		
q3 =	-0.154(08)		
phi2 =	-99.370(16)		

Total puckering amplitude: QT = 2.121(11)

Asymmetry parameters (NARDELLI M., 1983).

DS(C1')	1.497(12)	DS(C1' -C5')	0.457(8)
D2(C1')	0.198(3)	D2(C1' -C5')	1.164(8)
DS(C2')	0.545(9)	DS(C2' -C1')	0.845(7)
D2(C2')	0.833(7)	D2(C2' -C1')	0.922(8)
DS(O4')	0.976(9)	DS(O4' -C2')	1.201(8)
D2(O4')	0.674(6)	D2(O4' -C2')	0.349(7)

Table 4: Bond lengths (Å) and angles (°) for non hydrogen atoms

N(3)-C(2)	1.308(5)	C(2)-N(3)-C(4)	110.5(3)
N(3)-C(4)	1.381(4)	C(2)-N(1)-C(6)	125.6(3)
N(1)-C(2)	1.338(5)	C(11)-N(2)-C(2)	126.2(3)
N(1)-C(6)	1.415(4)	C(8)-N(7)-C(5)	104.1(1)
N(2)-C(11)	1.363(5)	C(4)-N(9)-C(8)	105.4(3)
N(2)-C(2)	1.403(4)	C(4)-N(9)-C(1')	126.3(3)
N(7)-C(8)	1.307(5)	C(8)-N(9)-C(1')	128.1(3)
N(7)-C(5)	1.399(4)	C(1')-O(4')-C(4')	110.0(4)
N(9)-C(4)	1.360(5)	C(4)-C(5)-N(7)	110.2(3)
N(9)-C(8)	1.393(4)	C(4)-C(5)-C(6)	119.9(3)
N(9)-C(1P)	1.465(5)	N(7)-C(5)-C(6)	129.8(3)
O(6)-C(6)	1.210(5)	O(6)-C(6)-N(1)	120.0(4)
O(2)-C(11)	1.221(5)	O(6)-C(6)-C(5)	130.3(3)
O(5')-C(5')	1.411(7)	N(1)-C(6)-C(5)	109.7(3)
O(4)-C(1')	1.406(6)	N(3)-C(2)-N(1)	126.1(3)
O(4')-C(4')	1.449(6)	N(3)-C(2)-N(2)	115.6(3)
O(2')-C(2')	1.414(6)	N(1)-C(2)-N(2)	118.3(3)
C(5)-C(4)	1.366(5)	N(9)-C(4)-C(5)	107.2(3)
C(5)-C(6)	1.427(6)	N(9)-C(4)-N(3)	124.6(3)
C(11)-C(12)	1.509(5)	C(5)-C(4)-N(3)	128.2(3)
C(12)-C(13)	1.495(9)	O(2)-C(11)-N(2)	122.7(4)
C(12)-C(14)	1.537(11)	O(2)-C(11)-C(12)	122.2(4)
C(1')-C(2')	1.528(7)	N(2)-C(11)-C(12)	115.1(4)
C(5')-C(4')	1.500(7)	C(13)-C(12)-C(11)	111.5(5)
C(4')-C(3')	1.505(10)	C(13)-C(12)-C(14)	112.2(5)
C(3')-C(2')	1.523(7)	C(11)-C(12)-C(14)	106.5(5)
		O(4')-C(1')-N(9)	109.0(4)
		O(4')-C(1')-C(2')	107.1(3)
		N(9)-C(1')-C(2')	113.5(4)
		N(7)-C(8)-N(9)	113.0(3)
		O(5')-C(5')-C(4')	113.6(5)
		O(4')-C(4')-C(5')	109.3(5)
		O(4')-C(4')-C(3')	104.4(5)
		C(5')-C(4')-C(3')	116.7(5)
		C(4')-C(3')-C(2')	102.1(5)
		O(2')-C(2')-C(3')	107.4(4)
		O(2')-C(2')-C(1')	109.9(4)
		C(3')-C(2')-C(1')	101.5(4)

The glycosyl torsion angle takes up an *anti* conformation ( $O(4') - C(1') - N(9') - C(4') = -132.7(4)^\circ$ ) in contrast to the observations made by BRENNAN et al., (1972) and THEWALT et al., (1970) and in agreement with the observations made by KARTHE et al., (1997) on similar sugar modified nucleoside structures. The furanose ring shows a  $C(3')$  - *endo* puckering geometry. The phase angle of pseudorotation is  $13.36^\circ$  and the maximum amplitude of puckering is  $37.83^\circ$  (ALTONA & SUNDARALINGAM, 1973). Table 3 shows the least squares

plane calculations and puckering parameters. Table 4 gives bond lengths and bond angles for all the non hydrogen atoms. The partial double bond nature of the C(2) - N(2) (SAENGER, 1984) is altered probably because of the presence of isobutyryl group. The value of the C(2)-N(2) bond length in the present structure is 1.403(4) as compared to the average value of 1.34(1)Å in guanine structures (SAENGER, 1984; TAYLOR & KENNARD, 1982). Selected torsion angles are given in Table 5.

Table 5: Selected Torsion Angles(°)

Atoms	Symbol	Torsion angle
O(5')-C(5')-C(4')-O(4') -		60.9(7)
O(5)-C(5')-C(4')-C(3')		57.4(8)
C(1)-O(4)-C(4)-C(5)		146.1(5)
O(2)-C(11)-C(12)-C(13)		- 40.2(9)
N(2)-C(11)-C(12)-(13)		140.2(5)
O(2)-C(11)-C(12)-C(14)		82.5(7)
N(2)-C(11)-C(12)-(14)		-97.1(6)
O(5')-C(5')-C(4')-O(4')	$\phi_{oo}$	-60.6(6)
O(5)-C(5')-C(4')-C(3')	$\phi_{oc}$	57.6(7)
C(4)-N(9)-C(1)-O(4)	$\chi_{CN}$	-132.7(5)
C(4')-O(4')-C(1')C2')	$\nu_0$	3.6(5)
O(4')-C(1')-C(2')-C(3')	$\nu_1$	-25.6(5)
C(4)-C(3')-C(2')-C(1')	$\nu_2$	36.8(5)
O(4')-C(4')-C(3')-C(2')	$\nu_3$	-35.7(5)
C(1')-O(4')-C(4')-C(3')	$\nu_4$	20.4(5)

Table 6: Hydrogen Bond Geometry

Donor-H...Acceptor	Donor-H (Å)	Donor...Acceptor (Å)	H...Acceptor* (Å)	Donor-H.....Acceptor (°)
N(1) -H(1N) ... O(11) (0)	0.821(3)	2.629(4)	2.073(3)	124.7(2)
O(1W) -H(1O1) ... O(6) (0)	0.835(3)	2.737(4)	1.952(3)	156.2(3)
O(2W) -H(12O) ... N(7) (0)	0.847(4)	2.940(5)	2.111(3)	166.4(3)
O(2W) -H(2O2) ... O(1W) (0)	0.842(4)	2.821(6)	2.433(4)	108.9(3)
O(5') -H(5') ... O(11) (1)	0.820(4)	2.886(7)	2.137(5)	151.7(3)
N(10) -H(1) ... O(1W) (2)	0.903(3)	2.827(5)	1.954(4)	161.9(2)
O(2') -H(15) ... O(2W) (2)	0.992(5)	2.828(5)	2.265(4)	114.0(2)

(\*) Values normalized following G.A.Jeffrey & L.Lewis, Carbohydr.Res. (1978).60,179; R.Taylor & O.Kennard, Acta Cryst.(1983).B39,133.

Equivalent positions: ( 0) x,y,z ; ( 1) -x-2,+y+1/2,-z ; ( 2) x+1,+y,+z ;

The conformation about C(2) – N(2) is *cis*. The torsion angles  $\phi_{oo}$  and  $\phi_{oc}$  are 60.5(6)° and 57.8(7)°. The geometry of the base about the exocyclic bond C(4') – C(5') is *gauche* – *gauche* (SHEFLER and TRUEBLOOD, 1965) Except the two methyl carbon atoms, all the other atoms of the isobutyryl group are in the plane of the base. The conformation is stabilized by an intramolecular hydrogen bond (N(1)-H(1). .O(11) ). The positions of hydrogen atoms

along with their equivalent isotropic displacement parameters are given in Table 6. The crystal packing is mainly due to the intermolecular hydrogen bonds (Figure 3). A list of possible hydrogen bonds is given in Table 7. Bases related by  $2_1$  screw stack along b-axis at a distance 3.25Å which is similar to the one observed by THEWALT et al., (1970).

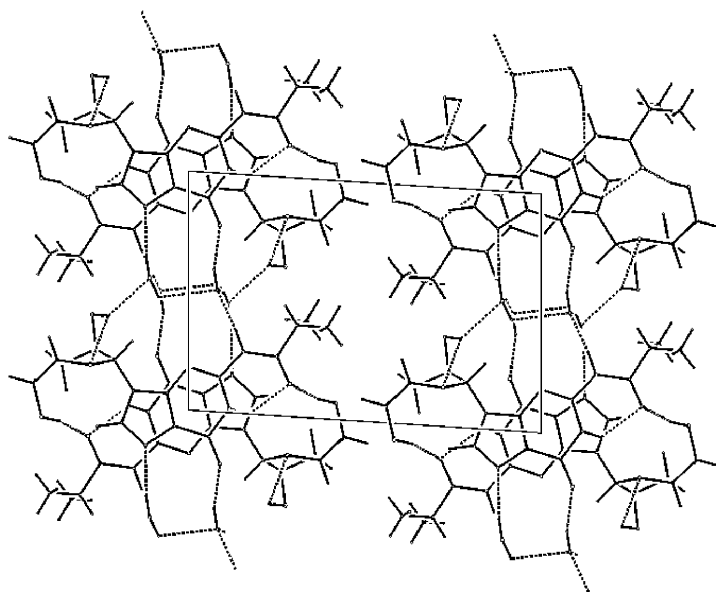


Fig. 3: Packing of molecules  
view down b-axis

#### *Acknowledgements*

ST thanks UGC for financial assistance

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