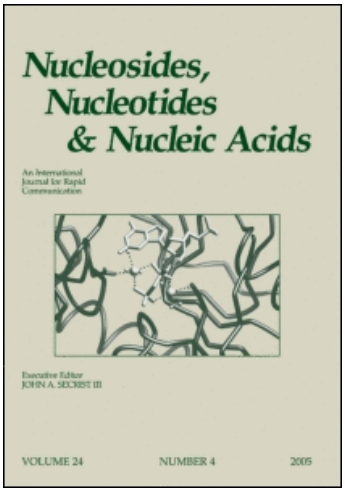

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Crystal Structure of Sodium Deoxyinosine Monophosphate

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CRYSTAL STRUCTURE OF SODIUM DEOXYINOSINE MONOPHOSPHATE

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Abstract: The crystal and molecular structure of sodium deoxyinosine monophosphate (5'-dIMP) has been determined by x-ray crystallographic methods. The crystals belong to orthorhombic space group $P2_12_12_1$, with a = 21.079(5) Å, b = 9.206(3) Å and c = 12.770(6) Å. This deoxynucleotide shows common nucleotide features namely anti conformation about the glycosyl bond, C2' endo pucker for the deoxyribose sugar and gauche-gauche orientation for the phosphate group. The sodium ion is directly coordinated to the O3' atom, a feature observed in many crystal structures of sodium salts of nucleotides.

Inosine is known to occur in alanine, serine and valine tRNA's[1]. We have been carrying out a systematic X-ray crystallographic investigations on deoxy and ribo nucleotides with a view to establishing the conformational differences between them[2-4]. As a part of the project we have now solved the crystal structure of sodium 5'-dIMP. This deoxynucleotide exhibits common nucleotide features : anti conformation of the inosine base about the glycosyl bond, C2' endo furanose ring puckering and g^+ conformation about the C4'-C5' bond. The Na^+ ion does not coordinate to the phosphate oxygens.

EXPERIMENTAL

Nucleotide crystals were grown by diffusion of acetone into aqueous solution of the compound (Sigma). Unit cell parameters were determined from measurements

made on the oscillation and Weissenberg photographs. Cu$K\alpha$ three dimensional intensity data upto $\sin\theta/\lambda = 0.60$ Å^{-1} was collected on a CAD4 diffractometer.

It was corrected for Lorentz, polarization and absorption[5] errors ($\mu = 17.98$ cm^{-1}) 2444 reflections out of 2709 reflections having I$\geq 3\sigma$(I) were considered observed. Two monitor reflections 3 3 2 and 2 3 5 showed negligible decay during data collection indicating crystal stability.

Crystal data are:

$C_{10}N_4O_7H_{11}$P.Na. $11H_2O$, M_w 551.22, orthorhombic , $P2_12_12_1$,

a = 21.079(5) Å, b = 9.206(3) Å, c = 12.770(6) Å, V = 2478.0 Å^3, Z = 4,

D_c = 1.47 g/cm^3, D_m = 1.49 g/cm^3 (bromoform/acetone mixtures),

The structure was solved using the RANTAN option in MULTAN[6]. The phosphate and the inosine base atoms were identified from the Fourier map. The remaining atoms of the molecule, an Na^+ ion and water oxygens were located from subsequent difference Fourier maps. After a few cycles of full matrix least squares refinement the thermal parameters of four water oxygens were found to be rather high. So, they were excluded from the structure factor calculations and redetermined from the difference Fourier map. They were considered as disordered since their thermal factors increased on refinement. Therefore, their thermal and occupancy factors were refined alternately. Two other disordered atoms were also located during the refinement of the structure. Isotropic temperature factor refinement of the structure dropped the R to 10%. The B_{eq} = 23Å^2 (OW13′) for disordered water oxygen is high but comparable to B_{eq} = 22Å^2 reported for ordered water oxygen in 5′- IMP.Na[7]. All the molecular hydrogen atoms were located from a difference Fourier map computed after several cycles of refinement with anisotropic thermal factors. Hydrogen atoms

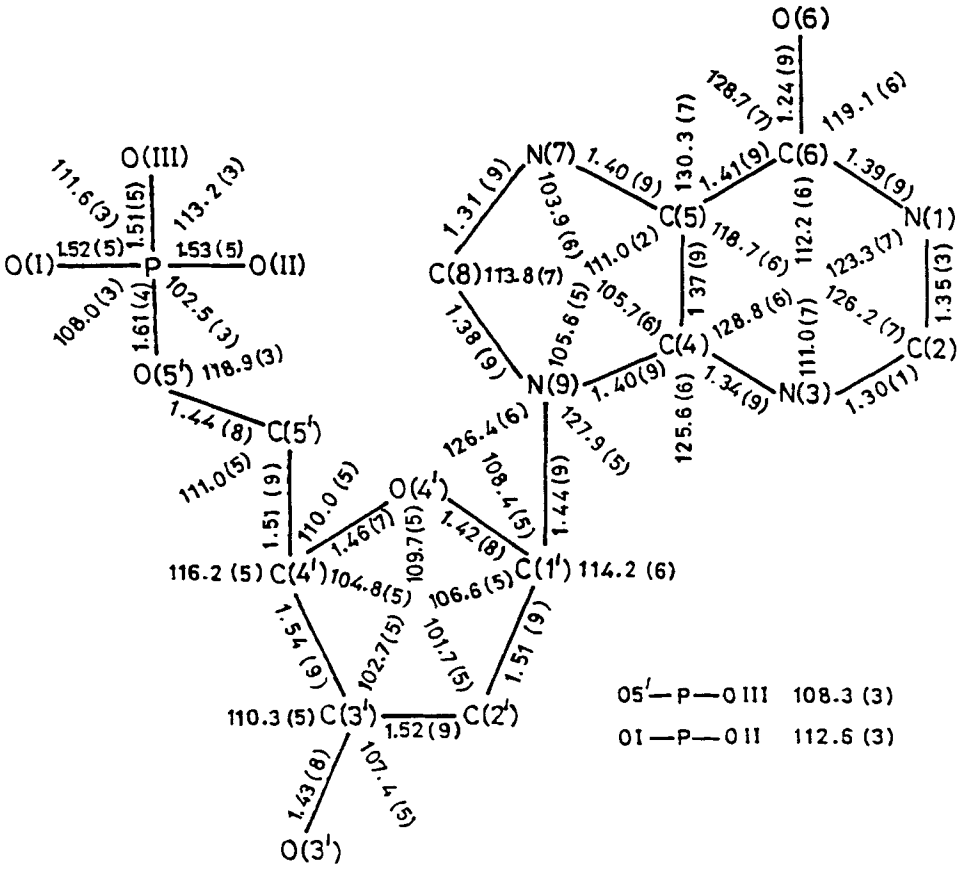

Fig. 1. Bond lengths and Bond angles in 5'–dIMP.Na

of some of the water molecules were located subsequently. The final R factor with hydrogen atoms and σ weighting scheme was 0.089. This rather high R for a structure of this size could be due to the disordered water molecules. Atomic numbering is shown in Fig. 1.

RESULTS AND DISCUSSION

Atomic coordinates are given in Table 1. The molecular conformation of 5'-dIMP.Na is shown in Fig. 2.

TABLE 1.

Final atomic coordinates with e.s.d's in parentheses and equivalent isotropic values of the anisotropic thermal parameters for non H atoms.

$B_{eq} = 4/3 \sum_i \sum_j \beta_{ij} a_i a_j$

ATOM	x	y	z	B_{eq}	
P	0.2049(1)	0.1472(2)	0.2296(1)	1.81(3)	
O(I)	0.2728(2)	0.1098(5)	0.2600(4)	2.6(1)	
O(II)	0.1905(2)	0.3092(5)	0.2404(4)	2.9(1)	
O(III)	0.1578(2)	0.0518(6)	0.2856(4)	3.0(1)	
O(5')	0.1974(2)	0.1208(5)	0.1057(3)	2.4(1)	
C(5')	0.2094(3)	-0.0218(7)	0.0643(5)	2.4(2)	
C(4')	0.1897(3)	-0.0314(7)	-0.0487(5)	2.1(2)	
O(4')	0.1212(2)	-0.0097(5)	-0.0579(4)	2.5(1)	
C(3')	0.2190(3)	0.0817(7)	-0.1229(5)	2.0(2)	
O(3')	0.2232(2)	0.0245(6)	-0.2265(4)	3.0(1)	
C(2')	0.1695(3)	0.2011(7)	-0.1243(5)	2.4(1)	
C(1')	0.1088(3)	0.1146(7)	-0.1205(5)	2.2(1)	
N(9)	0.0559(3)	0.1918(7)	-0.0757(4)	2.6(1)	
C(8)	0.0530(3)	0.2509(0)	0.0230(6)	3.3(2)	
N(7)	-0.0001(3)	0.3187(9)	0.0427(5)	3.9(2)	
C(6)	-0.0952(3)	0.3569(8)	-0.0768(6)	2.8(2)	
O(6)	-0.1334(3)	0.4235(9)	-0.0214(5)	5.0(2)	
C(5)	-0.0344(3)	0.3064(8)	-0.0508(6)	2.7(2)	
C(4)	-0.0011(3)	0.2295(7)	-0.1239(5)	2.3(1)	
N(3)	-0.0180(3)	0.1943(8)	-0.2216(5)	3.2(1)	
C(2)	-0.0748(4)	0.2419(9)	-0.2427(6)	3.4(2)	
N(1)	-0.1124(3)	0.3194(7)	-0.1779(5)	2.8(1)	
Na	0.2527(2)	0.1525(3)	-0.3899(2)	3.4(1)	
OW(1)	0.1927(3)	0.3690(6)	-0.3694(5)	3.8(2)	
OW(2)	0.3232(3)	-0.0501(6)	-0.4217(4)	4.2(2)	
OW(3)	0.1696(3)	0.0445(7)	-0.4933(5)	4.4(2)	
OW(4)	0.3458(4)	0.2520(8)	-0.3118(6)	5.0(2)	
OW(5)	0.3122(4)	0.2402(8)	-0.5491(6)	4.2(2)	
OW(6)	0.3900(2)	0.0266(6)	0.8173(5)	3.7(1)	
OW(7)	0.4030(4)	0.1234(9)	-0.4549(6)	5.8(2)	
OW(8)	0.0601(9)	0.4457(6)	0.6184(8)	12.6(9)	0.644
OW(9)	0.5359(2)	0.2604(9)	-0.2811(8)	11.4(9)	0.600
OW(9')	0.0400(2)	0.1244(5)	0.3155(1)	13(2)	0.410
OW(10)	0.4485(9)	0.4715(9)	0.8211(3)	10.8(9)	0.487
OW(11)	0.5227(5)	0.0735(8)	-0.3636(6)	7.8(9)	0.326
OW(12)	0.0000( )	0.5000( )	0.1915(3)	3.6(2)	0.500
OW(13)	0.0736(7)	0.2196(0)	0.6030(1)	11.6(1)	0.450
OW(13')	0.0417(4)	0.0943(2)	0.5804(5)	23(3)	0.493

The occupancies of the disordered waters are given in the last column.

Inosine base

The hypoxanthine base is planar excluding the exocyclic O6 atom. The bond lengths and bond angles agree with the average values reported for purine structures[8]. The orientation of the inosine base with respect to the deoxyribose moiety is **anti** :

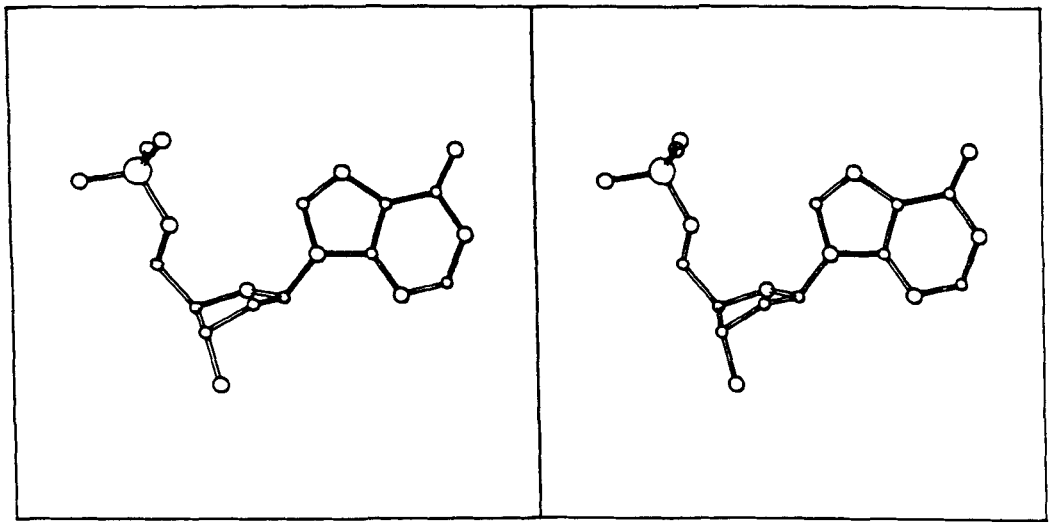

Fig. 2. A Stereoview of 5′-dIMP.Na showing its molecular conformation

the glycosyl torsion angle χ (O4′ –C1′–N9–C8) = 60.4°(9). The nitrogen atoms of the base do not participate in the Na^+ coordination as in 5′- dGMP.Na_2.[9,10]. The inosine bases partially stack on top of each other along b axis as shown in the Figure 2. Similar overlap of imidazole moiety has been observed in the structures of 5′-IMP.Na[7,11], 5′-IMP.Ba[12] and 5′-GMP.Na_2^+[13].

Furanose Ring Conformation

The best least square plane passes through the C1′– C3′–C4′–O4′ atoms of the furanose ring. The C2′ atom is displaced by 0.56Åon the same side of C5′ atom. Therefore, the furanose ring has the C2′ endo conformation. Altona and Sundaralingam puckering parameters[14] for the furanose ring are -τ_m = 37 and P = 171.0°. The conformation about the C4′-C5′ exocyclic bond is g^+ with ϕ = -63.5°(6) and ϕ = 55.3°(7) (Table 2).

TABLE 2

Selected torsion angles in 5′ -dIMP.Na

O5′	-C5′	-C4′	-O4′	-63.5(6)	05′	-C5′	-C4′	-C3′	55.3(7)
O4′	-C4′	-C3′	-C2′	27.5(6)	C3′	-C4′	-O4′	-C1′	-6.5(6)
C4′	-O4′	-C1′	-C2′	-17.5(6)	C4′	-C3′	-C2′	-C1′	-37.0(6)
C3′	-C2′	-C1′	-O4′	34.3(6)	O4′	-C1′	-N9	-C8	60.4(9)

TABLE 3

Na^+ ion coordination: distances (Å) and angles (°)

Na - O3′	2.48(5)	Na - OW1	2.38(7)
Na - OW2	2.42(7)	Na - OW3	2.41(7)
Na - OW4	2.39(9)	Na - OW5	2.52(8)
O3′ - Na - OW5	163.1(3)	O3′ - Na - OW4	92.1(2)
O3′ - Na - OW3	94.8(2)	O3′ - Na - OW2	86.0(2)
O3′ - Na - OW1	100.0(2)	OW4 - Na - OW5	78.7(3)
OW3 - Na - OW5	93.0(3)	OW3 - Na - OW4	170.6(3)
OW2 - Na - OW5	78.7(2)	OW2 - Na - OW4	81.9(3)
OW2 - Na - OW3	92.2(2)	OW1 - Na - OW5	95.0(3)
OW1 - Na - OW4	94.1(3)	OW1 - Na - OW3	91.0(2)
OW1 - Na - OW2	173.1(3)		

TABLE 4

Hydrogen bonding in 5′-dIMP.Na
distances (Å) and angles(°)

X - H....Y	X - H	H....Y	X...Y	X - H...Y	SYMM.	TRANS.		
N1 ..OI	-	-	2.72(7)		3	-1	0	0
N7 ..OW12	-	-	2.52(7)	-	2	0	1	0
O3' ..OII	-	-	2.69(6)	-	4	0	-1	0
OW1-1W1H..OW2	0.8	2.0	2.79(8)	154(10)	4	0	0	-1
OW1-2W1H..OI	0.9	1.9	2.72(7)	158(10)	4	0	0	0
OW2-1W2H..OII	1.1	1.6	2.67(7)	166(12)	4	0	-1	0
OW3-2W3H..OIII	1.0	1.9	2.83(8)	165(8)	1	0	0	-1
OW4-2W4H..OW6	0.8	2.2	2.80(9)	137(10)	1	0	0	-1
OW5 ..OI	-	-	2.8(8)	-	1	0	0	-1
OW6 ..OII	-	-	2.72(6)	-	4	0	0	1
OW6 ..O6	-	-	2.69(9)	-	3	0	0	1
OW7 ..OW11	-	-	2.66(3)	-	2	1	1	0
OW7 ..OW8	-	-	2.74(2)	-	4	0	-1	0
OW8 ..OW13	-	-	2.15(3)	-	1	0	0	0
OW9 ..OW10	-	-	2.23(2)	-	2	1	1	0

symmetry codes: 1. x, y, z 2. -x, -y, z 3. 0.5+x, 0.5-y, -z 4. 0.5-x, 0.5+y, -z

Na^+ ion coordination

The sodium ion has six nearest neighbours O3′, OW1, OW2, OW3, OW4 and OW5 at distances ranging from 2.38 to 2.52 Å(Table 3). Fig. 3 illustrates the arrangement of Na^+ coordination polyhedra in the orthorhombic lattice. The O3′ hydroxyl group is involved in the metal ion coordination just as in 5′-IMP.Na and 5′-IMP.Ba. The phosphate oxygens are not directly involved in Na^+ coordination just like in 5′-IMP.Na, 5′-dAMP.Na[15] and 5′-dGMP.Na, but are linked to the Na^+ ion through water oxygens. On the other hand in 5′- IMP.Ba and 5′-IMP.Ca[16] the metal ions are directly bound to the phosphate oxygens. Na^+ ion coordination in nucleotides has been discussed earlier[2,17].

Hydrogen bonding and Packing

The hydrogen bonding network in the orthorhombic 5′- dIMP lattice is given in Table 4. The phosphate oxygens are extensively involved in hydrogen bonds with water oxygens. The molecules pack as spirals parallel to the c axis (Fig. 3). N1 atom of the inosine base forms a hydrogen bond with OI of phosphate oxygen similar to that in Na.IMP. In addition, there are several short contacts ($\geq$ 3.4 Å) between O4′ and the inosine base atoms related by a twofold axis. Such short contacts between O4′ and purine bases have been reported in other crystal structures[18].

CONCLUSION

Deoxynucleotides are known to be far more conformationally flexible than ribonucleotides[19]. This is also borne out by the crystal structures of 5′-dGMP.Na_2, 5′-dUMP.Na_2 and 5′-dCMP.Na_2. They have shown conformational features not observed in any of the ribonucleotides studied so far. In contrast, 5′-dIMP has common nucleotide features.

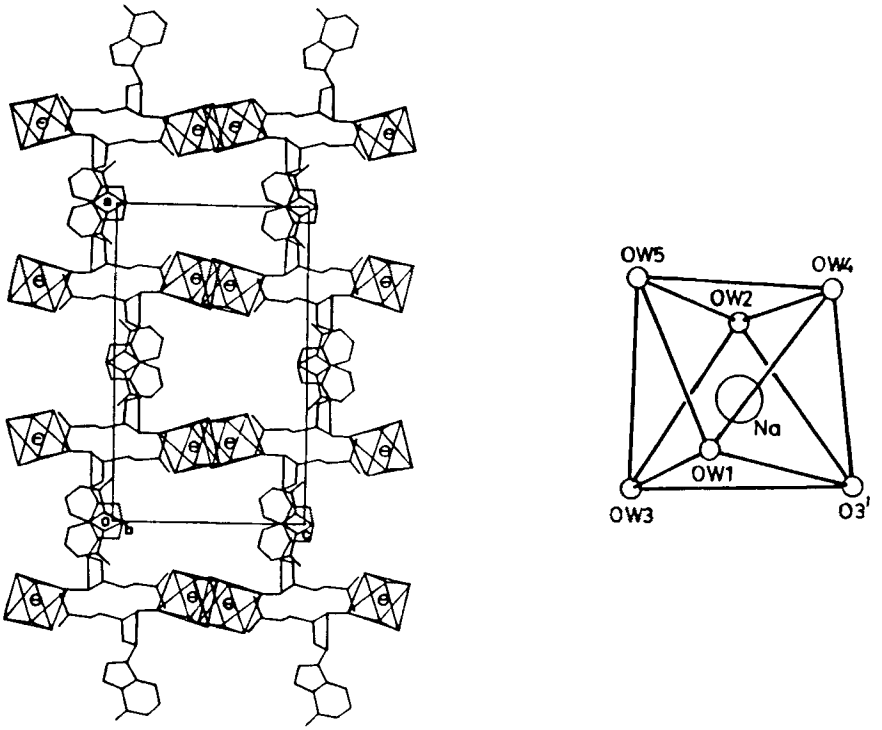

FIG. 3. Arrangement of Na^+ coordination polyhedra in the orthorhombic lattice of 5′-dIMP.Na

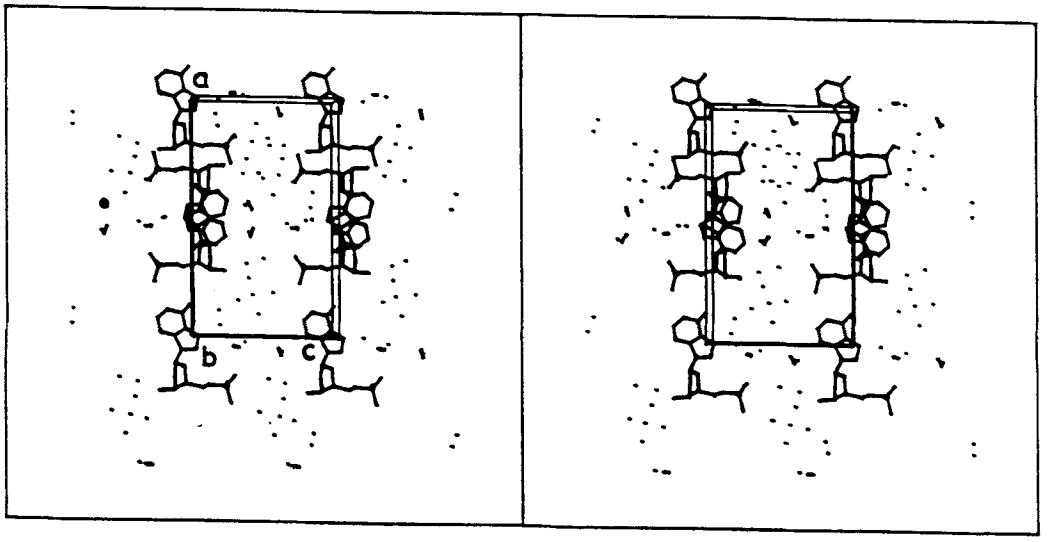

Fig. 4. A stereo view packing of 5′-dIMP.Na in the orthorhombic lattice viewed down b axis.

TABLE 5

Comparison of Structural features in 5′-dIMP.Na and 5′-IMP metal complexes.

Name	ϕ_{oo}	ϕ_{oc}	Base Conformation about glycosidic bond.	Sugar Pucker	Ref.
dIMP.Na	-63.5	55.3	Anti	C2′ endo	This work
IMP.Na(I)	-63.0	59.0	Anti	C2′ endo	11
IMP.Na(II)					
Mol. A	-60.1	60.3	Anti	C2′ endo	7
Mol. B	-62.7	59.3	Anti	C2′ endo	7
IMP.Ca	-62.5	58.3	Anti	C2′ endo	16
IMP.Ba	-58.6	61.4	Anti	C2′ endo	12

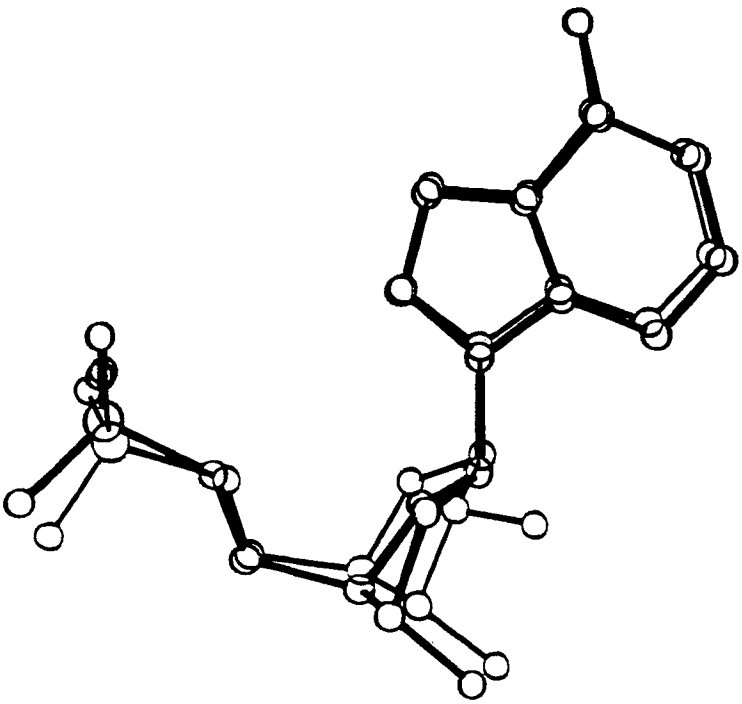

Fig. 5. Superposition of 5′-dIMP.Na (thick line) on 5′- IMP.Na[11] (thin line) showing their conformational similarities.

A comparison of conformational features of 5'-dIMP and several 5'-IMP structures is presented in Table 5. Evidently, this deoxynucleotide resembles its ribose analogue (Fig. 5).

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