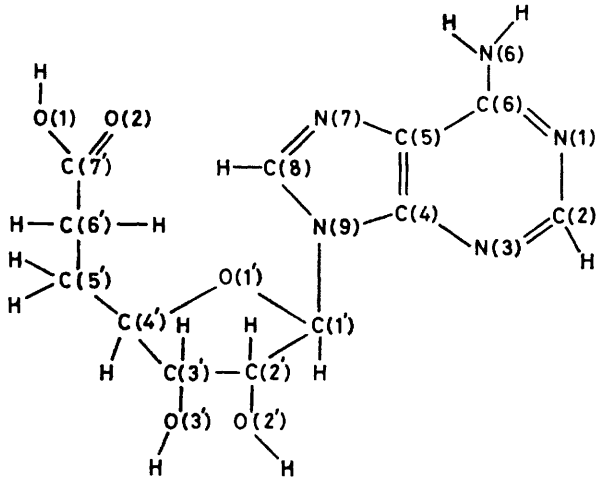
X-Ray Crystal Structure of 5′-Deoxy-5′-adenosineacetic Acid; a Model Nucleotide of Adenosine-5′-monophosphate

By TOSHIMASA ISHIDA,* MASATOSHI INOUE, ATSUTOSHI OTA, and TAKUSHI KURIHARA
(*Osaka College of Pharmacy, 2-10-65 Kawai, Matsubara-City, Osaka 580, Japan*)

Summary The conformation of 5′-deoxy-5′-adenosineacetic acid has been determined by *X*-ray crystal structure analysis *anti* for the glycosidic bond, *exo*-C(3′) for sugar puckering, *gauche–trans* for the orientation about the C(4′)–C(5′) bond, and the carboxy-group is linked to the N(6) and N(7) atoms of the neighbouring adenine ring by two hydrogen bonds

NUCLEOSIDE derivatives substituted at the exocyclic C(5′) atom of the ribose group are available for investigating structure–activity relationships of biochemically important mononucleotides, such as adenosine-5′-monophosphate (AMP) [1] To study the interactions with AMP utilizing enzymes, 5′-deoxy-5′-adenosineacetic acid (AAA) (**1**) could be used as a model nucleotide of AMP, because it has been shown that AAA can replace AMP as a building unit in oligonucleotides and as an enzyme substrate, such as AMP aminohydrolase [2] To determine the molecular structure of this nucleoside and to compare its conformation with that of AMP, we studied its crystal structure by *X*-ray diffraction



(1)

The acid AAA was synthesized by a procedure based on that reported by Walker *et al.*,[3] and transparent platelet crystals were obtained from aqueous solution *X*-Ray data were recorded with a Rigaku four-circle automated diffractometer using graphite-monochromated Cu-K_α radiation

Crystal data: $C_{12}H_{15}N_5O_5$, $M = 309{\cdot}28$, orthorhombic, space group $P2_12_12_1$, $a = 5{\cdot}197(1)$, $b = 10{\cdot}513(1)$, $c = 24{\cdot}258(5)$ Å, $U = 1325\ 4(4)$ Å^3, $D_m = 1\ 549(2)$, $D_c = 1{\cdot}550$ g cm^{-3}, $Z = 4$ The structure was solved by direct methods (MULTAN[4]) and refined by least-squares to $R = 0{\cdot}073$ using 1319 independent reflections ($2\theta_{max} < 130°$) †

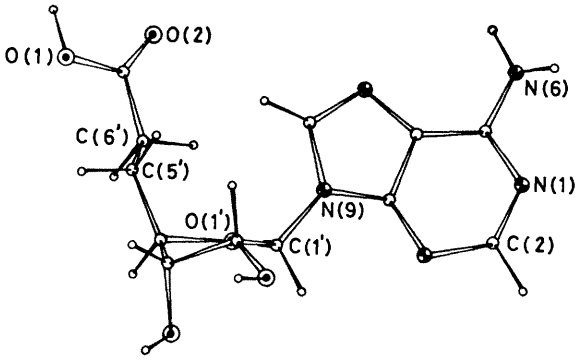


FIGURE 1 The conformation of the AAA molecule viewed along the C(1′)–O(1′)–C(4′) sugar plane

The conformation of the AAA molecule is shown in Figure 1 The orientation of the adenine base with respect to the sugar ring is *anti*, because the torsion angle of C(8)–N(9)–C(1′)–O(1′) is 50 7° The C(3′) atom has a maximum deviation from the C(1′)–O(1′)–C(4′) plane of 0·481 Å, on the side opposite the C(5′) atom The sugar ring therefore has an *exo*-C(3′) envelope conformation clearly shown in Figure 1 The *pseudo*-rotational phase-angle *P* and the maximum amplitudes of puckering τ_{max}[5] are 191·3° and 37·6°, respectively The torsion angles about the exocyclic C(4′)–C(5′) sugar bond are C(6′)-C(5′)–C(4′)–O(1′) 47·1° and C(6′)–C(5′)–C(4′)–C(3′) 165·4° The conformation

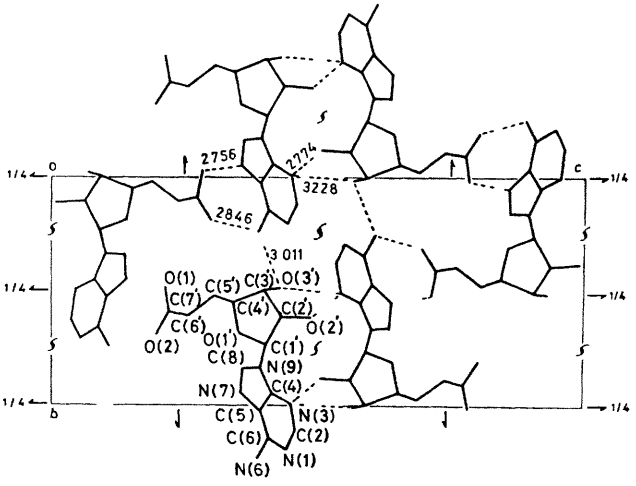


FIGURE 2 Hydrogen bonding diagram with the atomic numbering, shown as a projection on (1 0 0) Dashed lines represent possible hydrogen bonds E s d s of the interatomic distances are 0·008–0·011 Å

† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW Any request should be accompanied by the full literature citation for this communication

of the AAA molecule is therefore *gauche–trans* (*gt*). The torsion angle of C(7′)–C(6′)–C(5′)–C(4′) is −175·4° and is similar to that of P–O(5′)–C(5′)–C(4′) of numerous 5′-mononucleotides.[6]

Thus, in having the *anti* conformation about the glycosidic linkage, AAA is similar to both the monoclinic[7] and orthorhombic[8] forms of AMP. The other two characteristics, the *exo*-C(3′) puckering of the sugar bond and the *gt* conformation about the C(4′)–C(5′) bond, are different from those of AMP: *endo*-C(3′) and *gauche–gauche* (*gg*) for the monoclinic form and *endo*-C(2′) and *gg* for the orthorhombic form. This observed conformation of the AAA molecule is caused by the bulky methylene group replacing the O(5′) atom of the nucleoside.

The hydrogen bonding is shown in Figure 2. The carboxy-group is linked to the N(6) and N(7) atoms of the neighbouring adenine ring by the two hydrogen bonds. This interaction would be significant in specific binding with acidic amino-acids, because it is a model for the way in which an adenine, base-paired *via* the N(6) and N(1) atoms to uracil in the double stranded RNA, might form a hydrogen bond with a carboxy-group of glutamic or aspartic acid. This kind of hydrogen bond is also observed in the structure of *N*-(9-β-D-ribofuranosylpurin-6-yl)glycyl-L-alanine.[9]

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