EFFECTS OF 3'-O-AMINOACYLATION AND 2'-O-METHYLATION ON THE CONFORMATION OF RIBONUCLEOSIDES. THE CRYSTAL STRUCTURE OF 3'-O-ACETYLADENOSINE

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SUMMARY

The molecular structure of 3'-O-acetyladenosine determined from the three-dimensional x-ray data is described. The glycosidic conformation is syn with an intramolecular hydrogen bond between the 5'-hydroxyl group and the N(3) atom of the base. The sugar is C(2')-endo puckered and the acetate group is only slightly twisted around the C(3')-O(3') bond.

The 2'-O-methylpurine ribonucleosides occur naturally in ribonucleic acids from a wide variety of sources (Biswas and Myers, 1960; Hall, 1963a; Hall, 1963b; Singh and Lane, 1964; Ogata et al., 1963) and in some transfer ribonucleic acids (Madison et al., 1966; Zachau et al., 1966), while the 3'-O-aminoacyladenate moiety occurs in the 3'-terminal of the charged t-RNAs. Precise structural knowledge on either the 2'-O- or 3'-O-substituted derivatives are of importance in better understanding their biochemical function. Recently, the three-dimensional structure of puromycin was described (Sundaralingam and Arora, 1969). We here report the molecular structure and conformation of 3'-O-acetyladenosine.

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METHOD

Well formed crystals of 3'-O-acetyladenosine were kindly supplied by Dr. C. B. Reese of Cambridge University, England. Crystal data for this compound are listed in Table 1.

Intensity data were collected on a Picker four circle automatic diffractometer using Ni filtered Cu radiation and a 2θ scan technique. A total of 1372 reflections were thus scanned with 2θ values less than 133°. 1189 reflections were considered observed based on the counting statistics and were used in the analysis.

The structure was solved by a straightforward application of symbolic addition method (Karle and Karle, 1966) and the phases so obtained were extended and refined by the tangent formula (Hauptman and Karle, 1956) to yield phase angles for 285 reflections with $E \geqslant 1.25$. A E-map using these reflections clearly revealed the positions of all the nonhydrogen atoms in the molecule.

The structure was refined by the method of least-squares varying the positional parameters of all atoms and anisotropic thermal parameters of the heavy atoms. The hydrogen atoms were located in a difference electron density map and their positions were also refined. The final R-index for 1189 reflections is 0.041.

Table 1

Stoichiometry	$C_{12}N_5O_5H_{15}$
Space group	$P2_12_12_1$
Z	4
Cell dimensions	a = 12.312Å, b = 12.609Å, c = 8.824Å, $\alpha = \beta = \gamma = 90°$
Calculated density	1.504 gm. cm^{-3}
Observed density	1.502 gm. cm^{-3}

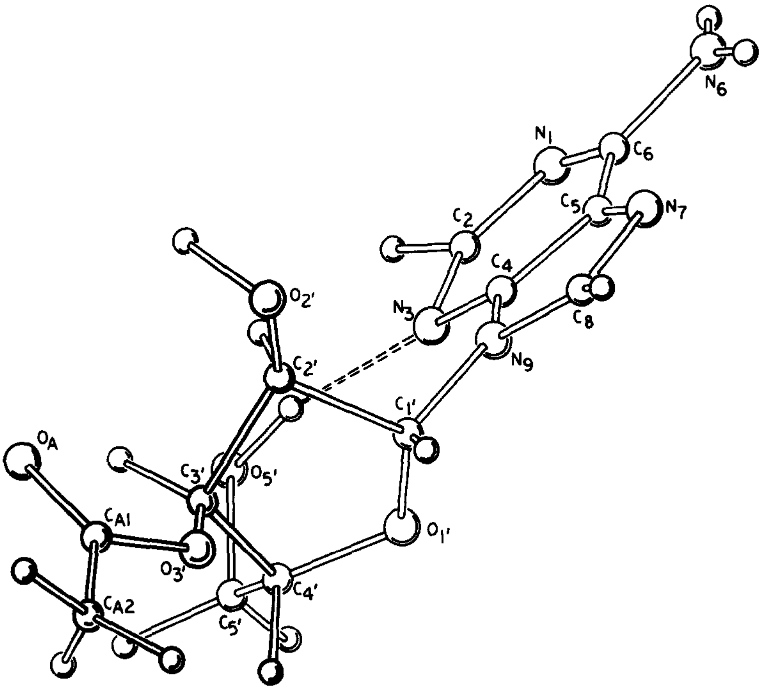

Figure 1. A view of the molecule of 3'-O-acetyladenosine down the c-axis showing the conformation and the intramolecular hydrogen bond.

RESULTS AND DISCUSSION

The conformation about the glycosidic linkage N(9)-C(1') is syn, the torsional angle being -139.9° (Sundaralingam, 1969). However, in puromycin (Sundaralingam and Arora, 1969) the nucleoside was observed to be in the anti conformation. The sugar exhibits C(2')-endo pucker and the O(5')-H...N(3) = 2.768Å (Fig. 1).

The carbonyl bond of the planar acetate group and the C(3')-H(3') are on the same side of the sugar and they are approximately parallel to each other. This is a characteristic conformation of the acylated and N-acylated derivatives (Sundaralingam and Arora, 1969). The acetate group is twisted by 6° around the C(3')-O(3') bond; the torsional angles are C(3')-O(3')-CA(1)-OA =

-6.6° and C(3')-O(3')-CA(1)-CA(2) = 173.9°. A similar conformation was observed in puromycin where O(3') is substituted by NH. Such a conformation is therefore very liekly for the aminoacyladenate moiety of t-RNAs.

The torsional angle H(3')-C(3')-O(3')-CA(1) is about -20°. Therefore, it is very likely that 2'-O-methylated ribonucleosides have a similar conformation for the bond sequence H(2')-C(2')-O(2')-CH_3.

Other than the intramolecular hydrogen bond, the crystal structure is stabilized by three intermolecular hydrogen bonds: N(6)...O(2') = 3.045Å, N(6)...O(5') = 2.894Å and O(2')...N(7) = 2.768Å. There are no hydrogen bonds involving the oxygen atom of the acetate group.

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