Molecular Conformation of Inosine

INOSINE is one of the rare nucleosides found in nucleic acids. It occurs especially in transfer ribonucleic acid where it appears to form part of a number of anticodons[1,2]. It can form a base pair with any one of the bases adenine, uracil or cytidine in the third codon[1,2] position, and the possibility of atypical base pairs is part of the "wobble" hypothesis[2]. In addition, the action of mutagenic agents on ribonucleic acid can lead to the conversion of adenosine into inosine.

Inosine crystallizes in two distinct crystal forms, both of which are under examination in this laboratory. The results given here were obtained from crystals formed by slow evaporation from aqueous solution at 25° C. The unit cell is monoclinic, with cell dimensions $a = 4{\cdot}82$ Å, $b = 10{\cdot}45$ Å, $c = 10{\cdot}97$ Å and $\beta = 90°\ 43'$. The space group is $P2_1$ with two molecules in the unit cell. In all, 1,306 reflexions were observed using molybdenum Kα radiation and the Hilger and Watts linear diffractometer. The structure was solved by Patterson function interpretation using the $I(\theta\varphi)$ function[3], the rotation function[4] and the Q-functions[5]. The structure was refined by a least-squares process using anisotropic temperature parameters for the non-hydrogen atoms to a final R factor of 0·046, where

$$R = \frac{\Sigma||F_o| - |F_c||}{\Sigma|F_o|}$$

The positions of all the hydrogen atoms were confirmed from a three-dimensional difference synthesis. The details of the structure and the results obtained will be published later.

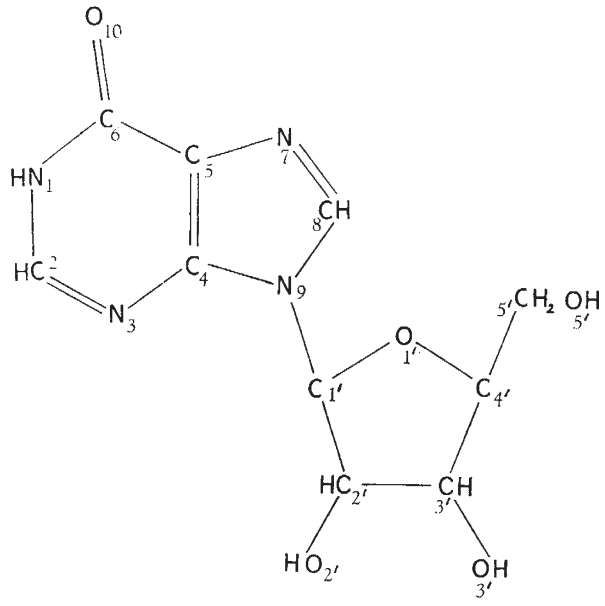

Fig. 1. The structural formula of inosine with the numbering system used.

The molecular formula of inosine and the conventional numbering system for the atoms are given in Fig. 1. The bond lengths and angles obtained from the structure determination are given in Table 1.

The purine ring in inosine is planar, but both O_{10} and C_1' are significantly displaced from this plane, the deviations being 0·16 Å and 0·15 Å respectively. The conformation of the sugar residue relative to the purine plane is best described by the torsion angle φ_{CN}[6], which in this case is −10·6°, the sugar being in the *anti* conformation. Atom C_3' of the ribose rings is displaced 0·63 Å from the plane of the remaining ring atoms and is in the *endo* conformation. The bond C_5'—O_5' is *gauche* with respect to the C_4'—O_1' bond and *trans* with respect to the C_4'—C_3' bond, the φ_{OO} and φ_{OC} angles[7] being 74·7° and 169° respectively. All available groups participate fully in the hydrogen bonding. The fact that the structure is strongly bonded is reflected in the relatively high calculated density of 1·61 g/cm^{-3}. In addition there are a number of close contacts between atoms of different molecules with distances between 3·0 and 3·2 Å. The possibility of a carbon–oxygen hydrogen bond has received some discussion[8,9] and some possible examples have been found[10]. One of the short intermolecular contacts in inosine is a short C—O distance of 3·09 Å between C_2 and an O_5' atom of a neighbouring molecule. The C—H and H—O distances are 0·98 Å and 2·34 Å respectively and the angle between the C—H bond and the line joining C_2 to O_5' is 34°.

Table 1. THE BOND LENGTHS AND ANGLES FOR INOSINE

N_1–C_2	1·355 Å	C_2–N_3	1·308 Å
N_3–C_4	1·365	C_4–C_5	1·374
C_4–N_9	1·372	C_5–C_6	1·433
C_6–N_1	1·397	C_6–O_{10}	1·233
C_5–N_7	1·371	N_7–C_8	1·307
C_8–N_9	1·372	N_9–C_1'	1·477
C_1'–O_1'	1·417	C_1'–C_2'	1·530
O_1'–C_4'	1·459	C_2'–O_2'	1·420
C_2'–C_3'	1·525	C_3'–O_3'	1·413
C_3'–C_4'	1·522	C_4'–C_5'	1·506
C_5'–O_5'	1·428		
N_1–C_2–N_3	124·6°	C_2–N_3–C_4	111·9°
N_3–C_4–C_5	128·5	C_4–C_5–C_6	118·3
C_5–C_6–N_1	111·0	C_6–N_1–C_2	125·4
N_1–C_6–O_{10}	120·6	C_5–C_6–O_{10}	128·4
C_6–C_5–N_7	130·1	C_4–C_5–N_7	111·6
N_7–C_8–N_9	113·6	C_5–N_7–C_8	103·8
N_9–C_4–C_5	105·4	C_8–N_9–C_4	105·7
C_8–N_9–C_1'	128·1	N_9–C_4–N_3	126·1
N_9–C_1'–O_1'	108·4	C_4–N_9–C_1'	126·0
O_1'–C_1'–C_2'	106·8	N_9–C_1'–C_2'	111·5
C_1'–C_2'–O_2'	109·6	C_1'–O_1'–C_4'	109·6
O_2'–C_2'–C_3'	107·5	C_1'–C_2'–C_3'	100·6
C_2'–C_3'–O_3'	115·9	C_2'–C_3'–C_4'	101·5
C_3'–C_4'–O_1'	104·0	O_3'–C_3'–C_4'	114·2
O_1'–C_4'–C_5'	110·0	C_3'–C_4'–C_5'	114·1
		C_4'–C_5'–O_5'	112·0

Estimated standard deviation in bond lengths is 0·004 Å, and in bond angles is 0·4°.

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In vitro Interaction of LSD with Purified Calf Thymus DNA

THE observation of broken chromosomes in test animals and humans treated with the hallucinogen lysergic acid diethylamide (LSD) has been well documented[1–8]. Although there has been some speculation about the mode of action of the drug, no specific studies of the mechanism of LSD-induced chromosomal damage have, as yet, been presented. Such studies would be most useful in determining whether LSD interacts directly with the chromo-