

STRUCTURE OF S-(*p*-NITROBENZYL)-6-THIOGUANOSINE

SHARMILA S. MANDE, T. P. SESHADRI and M. A. VISWAMITRA

*Department of Physics and ICMR Centre on Genetics and Cell Biology,
Indian Institute of Science, Bangalore 560 012, India.*

ABSTRACT

The crystal structure of S-(*p*-nitrobenzyl)-6-thioguanosine has been determined. The crystal belongs to the monoclinic system with $a = 7.299(1)$, $b = 8.825(2)$, $c = 14.565(1)$ Å, $\beta = 94.78(1)^\circ$. There is one molecule in the asymmetric unit. The structure is solved by direct methods and refined to an R -factor of 0.031. The molecule has *syn* guanosine base, C(2')-*endo* sugar pucker and *gauche-gauche* conformation about the C(4')-C(5') bond. The torsion angle about S-C(9) bond bridging the base and the benzene ring is $-77.6(3)^\circ$. The crystal structure is stabilized by an N(3)...O(5') intramolecular hydrogen bond in addition to several intermolecular hydrogen bonds. Although the crystal structure shows no base-base stacking, the exocyclic atoms N(13) and O(1) of the phenyl ring show close stacking contacts with the guanosine base of the 2₁ related molecule.

INTRODUCTION

WE report here the structure of the title compound where a nitrobenzyl group is covalently linked to the guanosine base through a sulphur atom at the 6th position. S substituted derivatives of 6-thioguanosine and 6-thioinosine are important as potential inhibitors of nucleoside transport across the membrane in erythrocytes and other cells¹. The present structure is close to that of the thioinosine derivative already reported².

EXPERIMENTAL

Needle-shaped crystals were grown from water/ethanol solution of the compound (Sigma Chemicals) by slow evaporation. Table 1 summarizes the crystal data. Intensity data using a crystal of dimension $1.2 \times 0.05 \times 0.05$ mm were collected on a CAD-4 diffractometer using Cu K α radiation up to $\sin \theta/\lambda = 0.617$ Å⁻¹ using ω -2 θ scan. Lorentz and polarization corrections were made. Absorption corrections were not applied. A total of 2035 reflections were measured for $-9 \leq h \leq 9$, $0 \leq k \leq 10$ and $0 \leq l \leq 17$, of which 1416 were uniquely observed ($F > \sigma(F)$). The structure was solved by direct methods using MULTAN 80³. The E-map computed with CFOM = 1.89 revealed the positions of most of the non-hydrogen atoms. Rest of the structure was located from difference Fourier maps. Full matrix refinement of F with anisotropic temperature factors reduced R to 0.07. A difference

Fourier map computed at this stage revealed all hydrogens except one. Hydrogen atoms were refined isotropically. After the final cycles of refinement, R factor converged to $R = 0.031$. The function minimized during refinement is $\sum w(|F_o| - |F_c|)^2$ where $w = 1/\sigma^2(F)$. The residual electron density in the final difference Fourier synthesis is less than 0.2 eÅ^{-3} . The maximum shift/error is 0.24. All calculations were performed using Enraf Nonius structure determination package on a PDP 11/44 computer.

DISCUSSION

A perspective view of the molecule with numbering of atoms is shown in figure 1 and the packing diagram showing the hydrogen bonding is shown in figure 2. The final positional and thermal para-

Table 1 Crystal data for S-(*p*-nitrobenzyl)-6-thioguanosine

Molecular formula	C17 H19 S1 N6 O6
Molecular weight	435.3
Crystal system	Monoclinic
Space group	$P2_1$
Unit cell dimensions	$a = 7.299(1)$ Å $b = 8.825(2)$ Å $c = 14.565(1)$ Å $\beta = 94.78(1)^\circ$
Volume	934.9 Å ³
No. of molecules/cell, Z	2
Radiation used	Cu K α

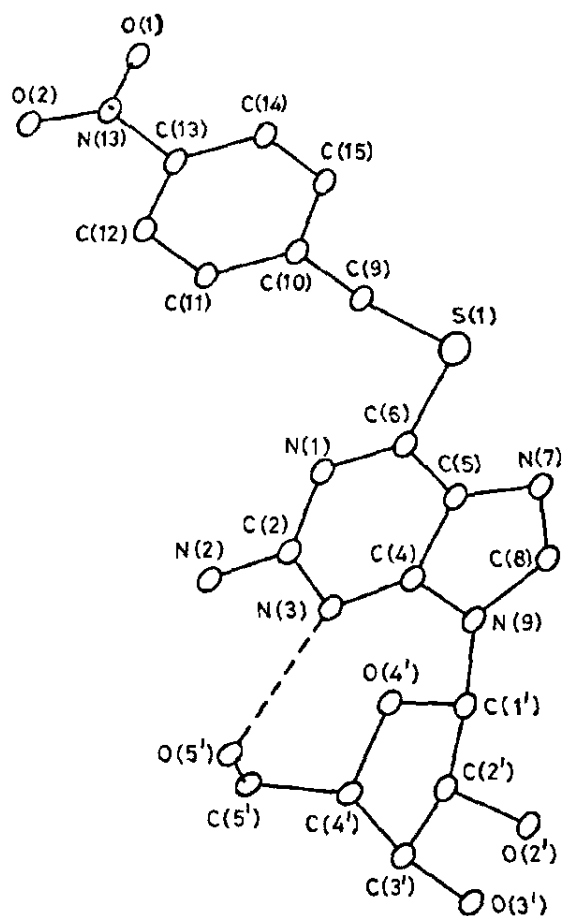


Figure 1. View of the molecule showing the intramolecular hydrogen bond between O(5') of the ribose and N(3) of the base.

meters of the non-hydrogen atoms are given in table 2.

Guanosine base

The base is essentially planar. The exocyclic sulphur atom deviates from the ring plane by 0.157(1) Å. χ_{CN} , the glycosidic torsion angle O(4')-C(1')-N(9)-C(4) is 61.7(5)° which falls in the range associated with the *syn* conformation⁴. The *syn* conformation has been observed previously in the crystal structures, 2'-3'-O-isopropylidene-5'-O-tosyluridine⁵, 6-(4-nitrobenzyl) thioinosine² and 2',3'-O-isopropylidene guanosine monohydrate⁶.

Ribose

The sugar pucker is C(2')-*endo*, a common geometry observed for the ribose furanose ring. P , the phase angle of pseudorotation and $\tau_{m \max}$, the maximum amplitude of pucker are equal to 157.7° and 37.79° respectively. The displacement of C(2') atom is -0.567(4) Å. The conformation about the

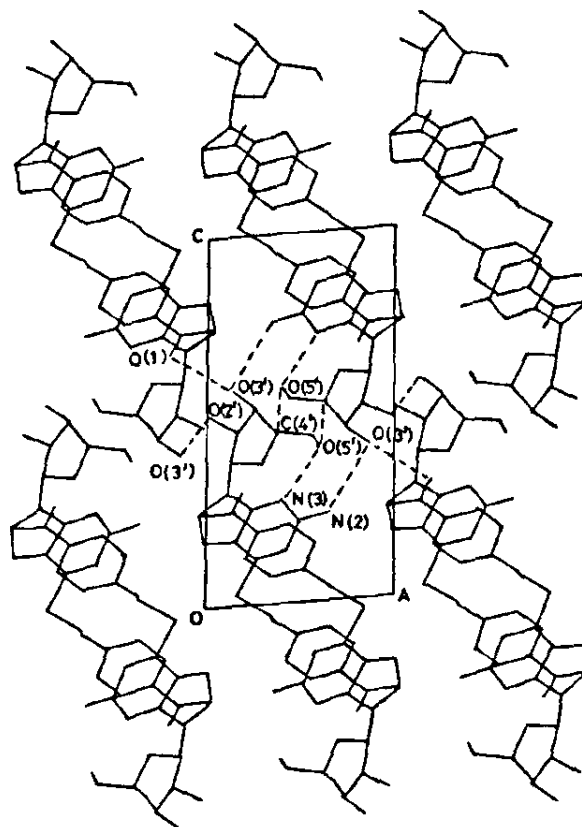


Figure 2. The crystal packing viewed down the a-axis showing hydrogen bonding between molecules in the unit cell.

exocyclic C(4')-C(5') bond is *gauche-gauche* with torsion angles ϕ_{OO} and ϕ_{OC} equal to -64.0(5) and 54.2(5)° respectively.

Benzoyl moiety

The benzoyl moiety is essentially planar. The maximum deviation is shown by the exocyclic atom C(9) [0.059(5) Å]. C(9)-C(10) is *cis* with respect to the C(6)-S bond with the C(6)-S-C(9)-C(10) = -77.6(3)°. The molecule has a somewhat folded shape as shown in figure 1.

Crystal packing

The presence of *syn* guanosine base, C2'-*endo* sugar pucker and *gauche-gauche* conformation about the C(4')-C(5') bond favours an intramolecular hydrogen bond between O(5') of the ribose and N(3) of the base (2.825(5) Å, 174.1°). There are several intermolecular hydrogen bonds which stabilize the crystal structure — O(2')-H...O(3') (2.808(5) Å, 161.75°), O(3')-H...O(1) (3.029(5) Å, 154.60°), N(2)-H...O(3') (3.179(5) Å, 153.28°) and C(4')-H...O(5') (3.293(6) Å, 153.28°).

Table 2 Positional parameters and equivalent temperature factors of non-hydrogen atoms

Atom	x	y	z	B(A ²)
N(1)	0.4225(4)	0.3700(4)	0.8613(2)	2.90(7)
C(2)	0.4879(5)	0.3180(5)	0.7829(3)	2.77(8)
N(2)	0.6513(4)	0.3765(5)	0.7631(2)	3.73(8)
N(3)	0.4063(4)	0.2198(4)	0.7218(2)	2.82(7)
C(4)	0.2392(5)	0.1786(5)	0.7446(3)	2.78(9)
C(5)	0.1549(5)	0.2240(6)	0.8229(3)	3.05(9)
C(6)	0.2547(5)	0.3247(5)	0.8802(3)	2.81(8)
N(7)	-0.0174(5)	0.1577(5)	0.8247(2)	3.47(8)
C(8)	-0.0350(6)	0.0764(6)	0.7498(3)	3.49(9)
N(9)	0.1158(4)	0.0825(5)	0.6974(2)	2.86(7)
C(1')	0.1323(5)	0.0069(5)	0.6113(3)	2.74(8)
C(2')	0.1703(6)	0.1109(5)	0.5317(3)	2.65(8)
O(2')	0.0099(5)	0.1732(4)	0.4848(2)	4.27(7)
C(3')	0.2629(6)	0.0044(5)	0.4689(3)	2.95(9)
O(3')	0.1293(4)	-0.0866(4)	0.4153(2)	3.18(6)
C(4')	0.3704(5)	-0.1016(6)	0.5351(3)	3.07(8)
O(4')	0.2856(4)	-0.0908(4)	0.6221(2)	3.15(6)
C(5')	0.5736(6)	-0.0656(6)	0.5549(3)	3.9(1)
O(5')	0.6066(4)	0.0843(4)	0.5857(2)	4.04(7)
S(1)	0.1535(1)	0.403	0.97436(7)	3.95(2)
C(9)	0.3417(6)	0.5068(6)	1.0332(3)	3.6(1)
C(10)	0.4751(5)	0.4054(6)	1.0885(2)	2.92(8)
C(11)	0.6598(6)	0.4070(7)	1.0727(3)	3.46(9)
C(12)	0.7851(6)	0.3187(6)	1.1258(3)	3.7(1)
C(13)	0.7232(6)	0.2312(6)	1.1942(3)	3.4(1)
N(13)	0.8568(6)	0.1416(5)	1.2529(3)	4.5(1)
O(1)	0.7989(5)	0.0496(5)	1.3057(2)	5.52(9)
O(2)	1.0202(5)	0.1634(6)	1.2469(3)	7.3(1)
C(14)	0.5398(6)	0.2265(6)	1.2118(3)	3.6(1)
C(15)	0.4182(6)	0.3164(6)	1.1583(3)	3.5(1)

Anisotropically refined atoms are given in the form of the isotropic equivalent displacement parameter defined as: $(4/3) \times [a^2 \times B(1,1) + b^2 \times B(2,2) + c^2 \times B(3,3) + ab \times (\cos \gamma) \times B(1,2) + ac (\cos \beta) \times B(1,3) + bc (\cos \alpha) \times B(2,3)]$; Figures in parentheses indicate estimated standard deviations.

Although the crystal structure has no base-base stacking, the exocyclic atoms N(13) and O(1) of the phenyl ring show close stacking contacts (3.40 Å and 2.99 Å) with the guanosine base of the 2₁ related molecule. The conformational features and the molecular interactions in the present structure are close to those found in the crystal structure of 6-(4-nitrobenzyl)thioinosine². We understand that the results obtained in the present study are close to those obtained in an independent investigation by Delbaere *et al* being reported elsewhere.

ACKNOWLEDGEMENT

The authors thank the Departments of Science and Technology and Biotechnology for financial support.

10 August 1988

1. Paul, B., Chen, M. F. and Paterson, R. P., *J. Med. Chem.*, 1975, **18**, 968.
2. Soriano-Garcia, M. and Parthasarathy, R., *Acta Crystallogr.*, 1984, **C40**, 1897.
3. Main, P., Fiske, S. J., Hull, S. E., Lessinger, L., Germain, G., Declercq, J. P. and Woolfson, M. M., *MULTAN 80. A system of computer programs for the automatic solution of crystal structures from X-ray diffraction data*, Universities of York, England, and Louvain, Belgium.
4. IUPAC-IUB Joint Commission on Biochemical Nomenclature, *Eur. J. Biochem.*, 1983, **131**, 9.
5. Gautham, N., Seshadri, T. P., Viswamitra, M. A. and Salisbury, S. A., *Acta Crystallogr.*, 1983, **C39**, 459.
6. Mande, S. S., Seshadri, T. P. and Viswamitra, M. A., *Acta Crystallogr.*, 1988, (in press).