Acta Cryst. (1981). B37, 294–296

Structure of 6-(2-Phenethyl)purine, a Synthetic Cytokinin

BY ALICE K. CHWANG* AND M. SUNDARALINGAM†

Department of Biochemistry, College of Agricultural and Life Sciences, University of Wisconsin–Madison, Madison, Wisconsin 53706, *USA*

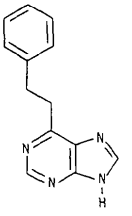
AND NELSON J. LEONARD

School of Chemical Sciences, University of Illinois, Urbana, Illinois 61801, *USA*

(*Received* 10 *July* 1980; *accepted* 22 *September* 1980)

Abstract. $C_{13}H_{12}N_4$, $M_r = 224$, monoclinic, $P2_1/c$, $a = 17{\cdot}903$ (2), $b = 5{\cdot}038$ (4), $c = 13{\cdot}193$ (3) Å, $\beta = 93{\cdot}89$ (2)°, $D_m = 1{\cdot}25$, $D_c = 1{\cdot}255$ Mg m^{-3}, $Z = 4$, $R = 0{\cdot}088$ on 1079 intensities. The molecule is extended with a *trans* conformation around the central C–C bond linking the purine and phenyl residues. The aromatic-ring planes are twisted roughly 90° with respect to the linking C–C bonds and the rings are twisted 14° to each other.

Introduction. Cytokinin activity is exhibited by a large variety of N^6-substituted adenine derivatives, natural and synthetic (Leonard, 1974). It has been demonstrated that compounds with the linking NH at C(6) replaced by CH_2, S, or O between the purine ring and, for example, the isopentenyl or benzyl side chain also possess cytokinin activity (Henderson, Frihart, Leonard, Schmitz & Skoog, 1975). The methylene analog of N^6-(2-isopentenyl)adenine is about 20% as active as the natural cytokinin in the tobacco bio-assay, while N^6-benzyladenine and 6-(2-phenethyl)purine (I) have nearly equal activity. Thus, an intact purine with an appropriate substituent at the 6 position is necessary and sufficient for cytokinin activity. It was of interest to compare the conformation of the phenethyl side chain directly attached to C(6) of the purine ring in (I) with the conformations that have been determined for the isopentenylamino C(6) substituent in the natural cytokinins: N^6-(2-isopentenyl)-2-methylthioadenine (McMullan & Sundaralingam, 1971*a*,*b*) and N^6-(2-isopentenyl)adenine (Bugg & Thewalt, 1972). Such a comparison of the flexible portion of the bases will hopefully provide some insight into any conformational limitations that define cytokinin-active compounds.



(I)

The title compound (I), which was synthesized as previously described, crystallized as thin needles from aqueous ethanol. Preliminary oscillation and Weissenberg photographs showed that the crystals were monoclinic, space group $P2_1/c$, with one molecule in the asymmetric unit. Unit-cell dimensions were determined by a least-squares fit of 12 reflections in the 2θ range 40–60° [λ(Cu $K\alpha$) = 1·5418 Å] carefully centered on a Picker FACS-1 diffractometer. The intensities of 1873 independent reflections were measured by the 2θ scan technique, and the usual Lorentz and polarization corrections were applied. The Wilson temperature factor of $B = 5{\cdot}3$ Å^2 was rather high.

The structure was solved by the program *MULTAN* (Germain, Main & Woolfson, 1971). The E map based on the phases of 256 reflections revealed all 17 nonhydrogen atoms, which gave an R index of 0·44. Three cycles of isotropic refinement followed by two cycles of anisotropic refinement of the atoms lowered the R index to 0·12. Further cycles of anisotropic refinement, fixing the H atoms at geometrically reasonable positions, resulted in convergence of the atomic parameters, at an R index of 0·088 for the highest 1079 intensities.‡ The weighting scheme adopted was: $w = 1/\sigma^2$, with $\sigma = 1$ for $F_o \leq 12$, and $\sigma = 1 + (F_o - 12)0{\cdot}067$ for $F_o > 12$.

The scattering factors for C and N were from Cromer & Waber (1965), and for H from Stewart, Davidson & Simpson (1965).

* Present address: School of Dentistry, Case Western Reserve University, Cleveland, Ohio 44106, USA.

† Author to whom correspondence should be addressed.

‡ Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35674 (8 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

0567-7408/81/010294-03$01.00

Discussion. Atomic coordinates for 6-(2-phenethyl)-purine are given in Table 1, and an *ORTEP* drawing (Johnson, 1965) is shown in Fig. 1. It can be seen that there is considerable thermal anisotropy in the atoms of the phenyl ring. Indeed, the isotropic B's for C(14), C(15) and C(16) were greater than 9·0 Å^2. Some of the discrepancies from accepted values in the molecular geometry may be ascribed to the high thermal motion of the atoms. The molecule of 6-(2-phenethyl)purine displays an extended conformation. The conformations around the exocyclic C(6)–C(10) and C(11)–C(12) bonds are such that the C(10)–C(11) bond is rotated on average by 90° to the rings (Figs. 1, 2). Thus, the planes of the two rings are nearly parallel with an angle between them of 14·2°. The conformation around the central C(10)–C(11) bond is *trans*; the pertinent torsion angles for the molecule are: N(1)–C(6)–C(10)–C(11) = 92·8 (8), C(5)–C(6)–C(10)–C(11) = −87·4 (8), C(6)–C(10)–C(11)–C(12) = −176·1 (8), C(10)–C(11)–C(12)–C(13) = −77·7 (8), and C(10)–C(11)–C(12)–C(17) = 96·7 (8)°.

Table 1. *Positional parameters and isotropic thermal parameters for* 6-(2-*phenethyl*)*purine*

Positional parameters of non-hydrogen atoms are $\times 10^4$ and of hydrogen atoms are $\times 10^3$. B_{eq} for the non-hydrogen atoms was calculated using the relation $B_{eq} = \frac{4}{3}\sum_i\sum_j \beta_{ij}(\mathbf{a}_i.\mathbf{a}_j)$. The hydrogen atoms were all assigned a B value of 5 Å^2.

	x	y	z	B_{eq} (Å^2)
N(1)	9129 (3)	−1055 (11)	1712 (4)	4·67
C(2)	9672 (4)	674 (14)	1685 (5)	4·70
N(3)	9759 (3)	2443 (11)	919 (4)	3·99
C(4)	9229 (3)	2129 (12)	187 (5)	3·64
C(5)	8618 (5)	240 (15)	136 (6)	5·94
C(6)	8592 (5)	−1294 (16)	930 (7)	6·23
N(7)	8160 (3)	486 (13)	−783 (4)	5·29
C(8)	8502 (4)	2440 (18)	−1205 (6)	5·65
N(9)	9108 (3)	3503 (11)	−695 (4)	4·13
C(10)	7950 (4)	−3376 (14)	969 (6)	5·80
C(11)	7258 (4)	−2223 (19)	1401 (7)	7·35
C(12)	6662 (4)	−4259 (14)	1504 (6)	5·01
C(13)	6217 (5)	−5122 (19)	709 (7)	7·21
C(14)	5683 (5)	−7044 (23)	829 (12)	9·52
C(15)	5598 (7)	−8128 (22)	1710 (13)	9·56
C(16)	6030 (7)	−7459 (24)	2546 (9)	8·77
C(17)	6585 (5)	−5548 (21)	2445 (8)	7·15
H(2)	1012	91	230	
H(8)	820	349	−198	
H(9)	952	507	−80	
H(101)	817	−501	144	
H(102)	766	−382	20	
H(111)	700	−116	80	
H(112)	750	−133	213	
H(13)	616	−361	−8	
H(14)	535	−751	12	
H(15)	507	−967	156	
H(16)	582	−891	312	
H(17)	693	−432	306	

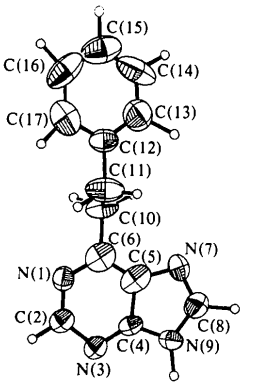


Fig. 1. An *ORTEP* (Johnson, 1965) drawing of the molecule with the atom numbering.

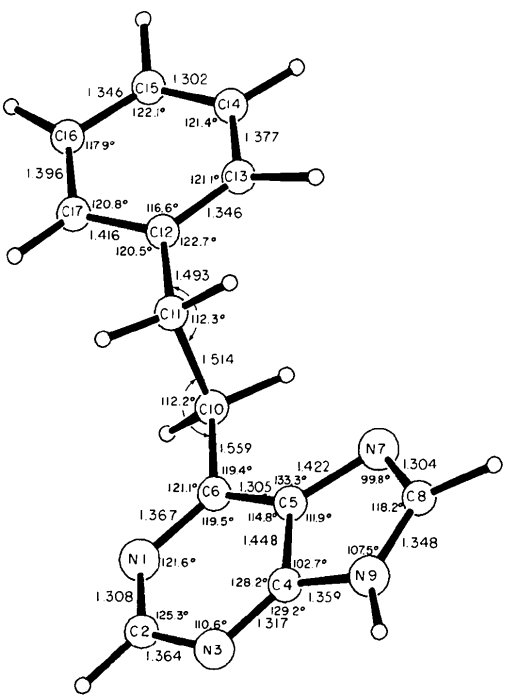


Fig. 2. Bond distances (Å) and bond angles (°) in 6-(2-phenethyl)purine. The estimated standard deviations in the bond distances and bond angles range from 0·006 to 0·020 Å (mean 0·012 Å) and 0·4 to 0·8° (mean 0·5°).

Fig. 3 is a view down the b axis showing the molecular packing and hydrogen-bonding scheme. Centrosymmetrically related adenine bases are paired to form N(9)–H···N(3) hydrogen bonds: N(9)···N(3) = 2·900 (6), H···N(3) = 1·81 Å. There is also a contact of 2·37 Å between N(1) and H(2) suggesting a possible weak C(2)–H···N(1) interaction between neighboring molecules. At the phenyl end of the molecule there are only van der Waals interactions and the somewhat loose packing in this region perhaps accounts for the relatively high thermal motion of the atoms. The N(9)–H···N(3) inter-

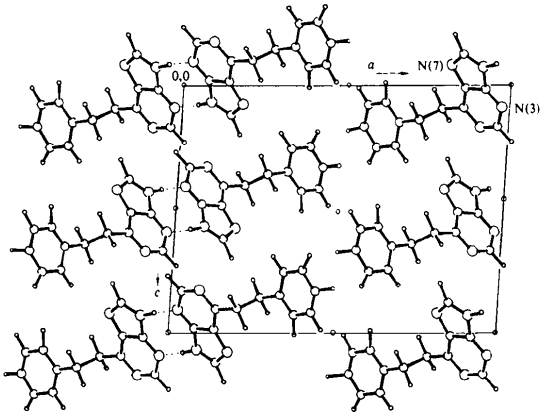


Fig. 3. The molecular packing and hydrogen bonding in the unit cell as viewed down the *b* axis.

molecular hydrogen-bonding pattern is similar to that observed for N^6-(2-isopentenyl)adenine (Bugg & Thewalt, 1972), in which N(1) is completely shielded, unlike the N(1) of 6-(2-phenethyl)purine.

A comparison of the crystal structure of the synthetic cytokinin (I) with those of the natural cytokinins, N^6-(2-isopentenyl)-2-methylthioadenine (McMullan & Sundaralingam, 1971*a*,*b*) and N^6-(2-isopentenyl)adenine (Bugg & Thewalt, 1972) indicates that in (I) neither H of the 6-CH_2 lies in the purine plane, as does the 6-NH. The side chain protrudes essentially straight out from C(6) in (I), whereas in N^6-monosubstituted adenines (Bugg & Sternglanz, 1974) the side chain is directed away from the imidazole ring of the base. Finally, the unsaturated portion of the side chain is nearly parallel to the purine ring in (I), in contrast to the dihedral angles of 91 and 72°, respectively, in the natural cytokinins in the order mentioned above. These comparisons indicate the latitude in side-chain conformation that is permitted for the expression of high cytokinin activity in substituted purines.

This research was supported at the University of Wisconsin by grant GM-17378 and at the University of Illinois by grant GM-05829 from the National Institutes of Health.

References

BUGG, C. E. & STERNGLANZ, H. (1974). *Molecular and Quantum Pharmacology*, edited by E. BERGMANN & B. PULLMAN, pp. 473–500. Dordrecht, Holland: Reidel.

BUGG, C. E. & THEWALT, U. (1972). *Biochem. Biophys. Res. Commun.* **46**, 779–784.

CROMER, D. T. & WABER, J. T. (1965). *Acta Cryst.* **18**, 104–109.

GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

HENDERSON, T. R., FRIHART, C. R., LEONARD, N. J., SCHMITZ, R. Y. & SKOOG, F. (1975). *Phytochemistry*, **14**, 1687–1690.

JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.

LEONARD, N. J. (1974). *Recent Advances in Phytochemistry*, Vol. 7, edited by V. C. RUNECKLES, E. SONDHEIMER & D. C. WALTON, pp. 21–56. New York; Academic Press.

MCMULLAN, R. K. & SUNDARALINGAM, M. (1971*a*). *Biochem. Biophys. Res. Commun.* **43**, 1158–1163.

MCMULLAN, R. K. & SUNDARALINGAM, M. (1971*b*). *J. Am. Chem. Soc.* **93**, 7050–7054.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

Acta Cryst. (1981). B**37**, 296–298

Structure of 1-(2-Isopentenyl)adenine

BY NELSON J. LEONARD,* EILEEN N. DUESLER AND BOŻENNA GOLANKIEWICZ†

School of Chemical Sciences, University of Illinois, Urbana, Illinois 61801, *USA*

(*Received* 10 *July* 1980; *accepted* 22 *September* 1980)

Abstract. $C_{10}H_{13}N_5$, $M_r = 203{\cdot}3$, monoclinic, $P2_1/c$, $a = 13{\cdot}577\,(4)$, $b = 6{\cdot}520\,(1)$, $c = 14{\cdot}546\,(4)$ Å, $\beta = 123{\cdot}97\,(2)°$, $V = 1068$ Å^3, $Z = 4$, $F(000) = 432$, $D_c = 1{\cdot}26$ Mg m^{-3}, μ(Mo $K\alpha$) = 0·09 mm^{-1}; $R = 0{\cdot}076$, $R_w = 0{\cdot}06$ for 1375 non-zero reflections. The tautomeric form in the crystal is 6-NH_2. The alkene side chain and the planar fused rings form a dihedral angle of 74°.

Introduction. 1-(2-Isopentenyl)adenine (I) (Leonard & Fujii, 1964) is of interest as a chemical precursor of the active cytokinin, N^6-(2-isopentenyl)adenine (Leonard, Achmatowicz, Loeppky, Carraway, Grimm, Szweykowska, Hamzi & Skoog, 1966). Determination

* Author to whom correspondence should be addressed.

† Present address: Instytut Chemii Organicznej PAN, Poznań, Poland.

0567-7408/81/010296-03$01.00