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Antiallergenic 8-Azapurines. 2. Structural Characterization of 2-Phenyl-7-methyl-8-azahypoxanthine and 2-Phenyl-8-methyl-8-azahypoxanthine

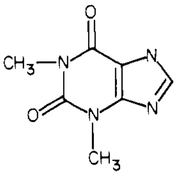
Susan J. Cline and Derek J. Hodgson*

Contribution from the Department of Chemistry, University of North Carolina, Chapel Hill, North Carolina 27514. *Received November 29, 1979*

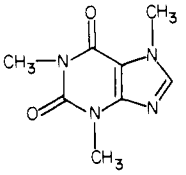
Abstract: The crystal and molecuar structures of 2-phenyl-7-methyl-8-azahypoxanthine and 2-phenyl-8-methyl-8-azahypoxanthine, $C_{11}H_9N_5O$, have been determined from three-dimensional counter X-ray data using Cu Kα radiation. The 7-methyl isomer crystallizes in the monoclinic space group $C2/c$ with eight molecules in a cell of dimensions $a = 11.084$ (7), $b = 8.214$ (5), $c = 23.431$ (10) Å; $\beta = 79.97$ (2)°. The structure has been refined by full-matrix least-squares methods to a final value of the conventional R factor of 0.038 based on 677 independent intensities. The 8-methyl isomer crystallizes in the monoclinic space group $P2_1/c$ with four molecules in a cell of dimensions $a = 7.490$ (2), $b = 12.891$ (7), $c = 10.976$ (4) Å; $\beta = 90.21$ (2)°. The structure has been refined by full-matrix least-squares methods to a value of the conventional R factor of 0.037 based on 1239 independent observations. In both isomers, the azapurine rings are planar. In the 7-methyl isomer, the phenyl ring is approximately coplanar with the azapurine ring, the dihedral angle between the two planes being 2.3°; in the 8-methyl isomer this angle is 29.5°. CNDO/2 molecuar orbital calculations show that, as in other 8-azapurines, ring atom N3 is very electron rich (−0.24 e) in both structures while the free triazole nitrogen atoms have smaller residual charges (−0.03 to −0.18 e). In both compounds, the molecules stack so that the phenyl ring of one molecule lies over the C4–C5 bond of the azapurine ring below, the interplanar separations being 3.45 Å in the 7-methyl isomer and 3.49 Å in the 8-methyl isomer.

Introduction

The antiallergenic properties[1,2] of the common methylxanthines such as theophylline (I) and caffeine (II) have effected efforts



I



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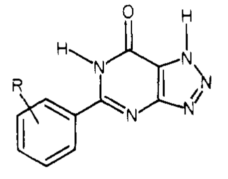

III

to determine the structural basis for the biochemical properties of these compounds in order to produce more potent antiallergic drugs;[3,4] moreover, the 8-azaxanthines have been shown to be consistently more potent than their xanthine analogs.[5] In a study of a series of 2-aryl-8-azahypoxanthines (III) the antiallergenic activity was shown to be correlated with the size and hydrogen-bonding capacity of the ortho substituent, R, on the phenyl ring.[4] As a consequence of this observation, it has been suggested that potent antiallergenic activity in this series is associated with the coplanarity of the phenyl ring with the azapurin-6-one portion of the molecule, which is favored by a strong intramolecular hydrogen bond between the proton on N1 and the ortho substituent on the phenyl ring. Structures of 2-phenyl-7-methyl-8-azahypoxanthine and 2-phenyl-8-methyl-8-azahypoxanthine were examined in order to determine whether this planarity is dependent upon the presence of this intramolecular hydrogen bond. In addition, molecular orbital calculations on these two molecules were performed to gain information on the relative basicities of the nitrogen atoms in the 8-azapurine ring. The results of these studies are presented here.

Experimental Section

X-ray Data Collection: (*a*) 2-Phenyl-7-methyl-8-azahypoxanthine. A powdered sample of 2-phenyl-7-methyl-8-azahypoxanthine[6] was generously donated by Dr. K. R. H. Wooldridge and was recrystallized from THF. Colorless crystals of the sample were assigned to the monoclinic system on the basis of Weissenberg and precession photographs; the observed systematic absences of $(h + k)$ odd for hkl and l odd for $h0l$ are consistent with either $C2/c$ or its noncentrosymmetric equivalent Cc. The centrosymmetric choice was substantiated by the subsequent structure refinement. The cell constants, obtained by least-squares procedures, are $a = 11.084$ (7) Å, $b = 8.214$ (5) Å, $c = 23.431$ (10) Å, and $\beta = 79.97$ (2)°. The observed density of 1.42 (2) g cm^{-3} (flotation in carbon tetrachloride and pentane) is consistent with the density of 1.43 g cm^{-3} calculated for eight molecules in the unit cell.

Intensity data were collected from a prismatic crystal bounded by faces of the forms {001} and {110} with dimensions 0.09 × 0.19 × 0.19 mm. The crystal was mounted parallel to (100), and in this orientation intensity data were collected on a Picker FACS-1 four-circle automatic diffractometer using Cu Kα (1.54051 Å) radiation filtered with 0.5-mil nickel foil.

A unique data set having $2° \leq 2\theta \leq 95°$ was gathered; a total of 1953 intensities was recorded. The intensities of three standards, measured after every 100 reflections, showed no systematic decline as a function of exposure time. Data processing was carried out as described by Corfield et al.[7]

The data were corrected for Lorentz–polarization effects, but not for absorption. The linear absorption coefficient, μ, for these atoms with copper radiation is 8.31 cm^{-1}, and for the sample chosen the maximum effect of this term is estimated to be less than the esd for all data. Of the 1953 data collected only 677 were greater than three times their estimated standard deviations; only these data were used in the subsequent structure analysis and refinement.

(b) 2-Phenyl-8-methyl-8-azahypoxanthine.[6] A powdered sample of the complex was generously provided by Dr. K. R. H. Wooldridge and was recrystallized from ethanol. On the basis of Weissenberg and precession photographs, the colorless crystals were assigned to the monoclinic system; observed systematic absences of k odd for $0k0$ and l odd for $h0l$ are consistent only with space group $P2_1/c$. The cell constants, obtained as described above, are $a = 7.490$ (2) Å, $b = 12.891$ (7) Å, $c = 10.976$ (4) Å, and $\beta = 90.21$ (2)°. The observed density of 1.43 (1) g cm^{-3} (flotation in carbon tetrachloride and pentane) is in good agreement with the value

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Table I. Positional Parameters for 2-Phenyl-7-methyl-8-azahypoxanthine

atom	x	y	z
N1	0.192 33 (26)	0.525 32 (8)	0.486 29 (12)
N3	0.113 44 (26)	0.287 90 (38)	0.448 69 (14)
N7	0.264 70 (28)	0.505 21 (41)	0.329 52 (13)
N8	0.220 50 (34)	0.378 90 (48)	0.303 34 (14)
N9	0.158 07 (31)	0.283 22 (42)	0.343 21 (15)
O6	0.305 02 (22)	0.722 91 (33)	0.431 54 (9)
C2	0.129 12 (31)	0.379 37 (47)	0.492 68 (15)
C4	0.164 78 (37)	0.351 34 (48)	0.395 92 (17)
C5	0.231 75 (31)	0.491 36 (48)	0.387 56 (15)
C6	0.249 75 (33)	0.592 64 (51)	0.434 21 (15)
C7	0.338 20 (39)	0.631 01 (51)	0.296 17 (16)
C1P	0.077 17 (32)	0.325 96 (45)	0.552 26 (16)
C2P	0.007 02 (36)	0.183 54 (51)	0.559 35 (17)
C3P	−0.042 81 (38)	0.127 94 (53)	0.614 16 (22)
C4P	−0.024 62 (39)	0.213 11 (62)	0.662 58 (19)
C5P	0.044 13 (41)	0.354 26 (57)	0.656 28 (17)
C6P	0.094 90 (35)	0.409 88 (47)	0.601 55 (17)
N1H	0.197 0	0.582 9	0.519 3
C7H1	0.347 0	0.611 0	0.252 4
C7H2	0.420 9	0.635 9	0.305 2
C7H3	0.304 1	0.739 0	0.304 1
C2PH	−0.006 2	0.126 0	0.524 5
C3PH	−0.091 0	0.029 2	0.620 6
C4PH	−0.058 8	0.177 8	0.700 9
C5PH	0.056 0	0.417 6	0.689 7
C6PH	0.145 2	0.507 7	0.597 6

Table II. Positional Parameters for 2-Phenyl-8-methyl-8-azahypoxanthine

atom	x	y	z
N1	0.202 46 (22)	−0.420 27 (13)	0.442 24 (13)
N3	0.485 51 (22)	−0.349 52 (13)	0.390 97 (13)
N7	0.477 29 (21)	−0.387 03 (12)	0.712 21 (14)
N8	0.637 30 (21)	−0.350 26 (13)	0.685 09 (13)
N9	0.672 00 (21)	−0.329 13 (13)	0.567 73 (14)
O6	0.108 35 (16)	−0.465 06 (13)	0.634 09 (11)
C2	0.327 39 (26)	−0.382 13 (15)	0.360 53 (16)
C4	0.518 21 (25)	−0.356 14 (14)	0.513 58 (16)
C5	0.398 43 (25)	−0.390 99 (14)	0.601 73 (16)
C6	0.225 41 (25)	−0.428 62 (16)	0.567 91 (16)
C8	0.771 41 (31)	−0.334 35 (23)	0.779 57 (21)
C1P	0.273 84 (27)	−0.379 48 (15)	0.230 68 (16)
C2P	0.096 66 (32)	−0.368 20 (19)	0.196 04 (21)
C3P	0.052 26 (41)	−0.365 07 (25)	0.073 02 (24)
C4P	0.182 53 (38)	−0.374 66 (21)	−0.014 59 (21)
C5P	0.357 84 (36)	−0.386 60 (18)	0.019 29 (19)
C6P	0.405 12 (32)	−0.388 52 (16)	0.141 18 (18)
N1H	0.094 7 (32)	−0.449 2 (17)	0.412 7 (20)
C8H1	0.892 6 (34)	−0.333 8 (19)	0.745 1 (21)
C8H2	0.765 3 (44)	−0.390 4 (27)	0.839 4 (32)
C8H3	0.754 1 (34)	−0.266 7 (21)	0.814 4 (23)
C2PH	0.001 4 (34)	−0.365 2 (18)	0.256 3 (22)
C3PH	−0.063 9 (45)	−0.357 8 (25)	0.056 0 (27)
C4PH	0.148 8 (34)	−0.372 4 (19)	−0.101 3 (24)
C5PH	0.456 3 (32)	−0.392 5 (16)	−0.036 7 (21)
C6PH	0.531 3 (36)	−0.397 3 (18)	0.171 6 (21)

1.42 g cm^{-3} calculated for four molecules per unit cell.

The intensity data were collected as described above. A unique data set having 2° ≤ 2θ ≤ 120° was gathered. The intensities of three standards, measured after every 100 reflections, showed no systematic decline as a function of exposure time. Of the 1778 data collected only 1258 were greater than three times their estimated standard deviation, and only these data were used to refine the structure. Absorption effects (μ = 8.25 cm^{-1}) were again neglected.

Solution and Refinement of the Structures. All least-squares refinements in these analyses were carried out on F, the function minimized being $\Sigma w(|F_o| - |F_c|)^2$; the weights w were taken as $4F_o^2/\sigma^2(F_o^2)$. In all calculations of F_c, the atomic scattering factors for all nonhydrogen atoms were from ref 8 and those for H from Stewart, Davidson, and Simpson.[9]

(a) 2-Phenyl-7-methyl-8-azahypoxanthine. The structure was solved by direct methods,[10] using the multiple solution program Multan.[11] An E map revealed the positions of all 17 nonhydrogen atoms, and isotropic least-squares refinement of these positions yielded values for the conventional agreement factors of $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o| = 0.105$ and $R_2 = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w F_o^2]^{1/2} = 0.135$. Anisotropic refinement of these atoms lowered the values of R_1 and R_2 to 0.077 and 0.100, respectively. All hydrogen atoms were found in a difference Fourier map, but because the data to variable ratio was not high enough to vary these parameters, the phenyl hydrogen atoms were put in calculated positions while the others were placed in their observed positions. The final least-squares calculations involved anisotropic refinement of the nonhydrogen atoms with 677 observations and 154 variables; no parameter shifted more than 0.2σ, which was taken as evidence of convergence. The final values of R_1 and R_2 are 0.038 and 0.043, respectively. The final difference Fourier map was featureless, with no peak higher than 0.061 e Å^{-3}. The atomic positional parameters, along with their standard deviations as estimated from the inverse matrix, are listed in Table I. The thermal parameters and a listing of observed and calculated structure amplitudes are available as supplementary material.

(b) 2-Phenyl-8-methyl-8-azahypoxanthine. The structure was solved as described above. Isotropic least-squares refinement of the positions of the 17 nonhydrogen atoms obtained from an E map yielded values of R_1 and R_2 of 0.120 and 0.166, respectively. Anisotropic refinement of these atoms lowered these values to 0.081 and 0.116. All hydrogen atoms were found in a difference Fourier map and included in subsequent least-squares cycles. The final least-squares calculations involved anisotropic refinement of the nonhydrogen and isotropic refinement of hydrogen atoms with 1239 observations and 191 variables; no parameter shifted by more than 0.2σ in this final cycle, which was taken as evidence of convergence. The final values of R_1 and R_2 are 0.037 and 0.049, respectively. The final difference Fourier map was featureless, with no peak higher than 0.140 e Å^{-3}.

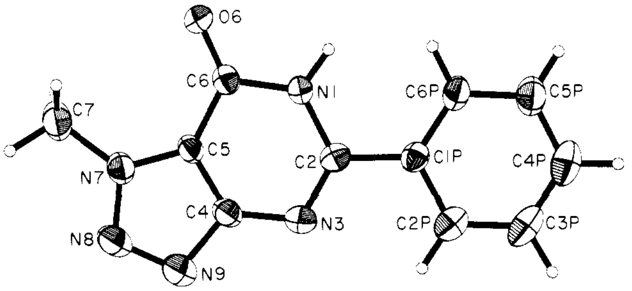

Figure 1. View of a single molecule of 2-phenyl-7-methyl-8-azahypoxanthine. Hydrogen atoms are shown as spheres of arbitrary size. Thermal ellipsoids are drawn at the 40% probability level.

The atomic positional parameters and estimated standard deviations are listed in Table II. The thermal parameters and a listing of observed and calculated structure amplitudes are available as supplementary materials.

Molecular Orbital Calculations. The MO calculations were performed by the CNDO/2 self-consistent-field method.[13] The calculations utilized the Quantum Chemistry Exchange Program No. 141 (University of Indiana, Bloomington, Ind.) as modified locally by Professor L. G. Pedersen. The molecular geometries of the 7- and 8-methyl isomers were taken from the X-ray diffraction results described in this paper. All C–H and N–H bond lengths in the molecule were changed to 1.08 and 1.01 Å, respectively, keeping their bond directions the same as those observed in the X-ray study. The net atomic charge is defined as the difference between the number of valence electrons and the nuclear charge, which is calculated as the sum of the diagonal elements in the density matrix for the particular atom.

Results and Discussion

The molecular structures of 2-phenyl-7-methyl-8-azahypoxanthine and 2-phenyl-8-methyl-8-azahypoxanthine are shown

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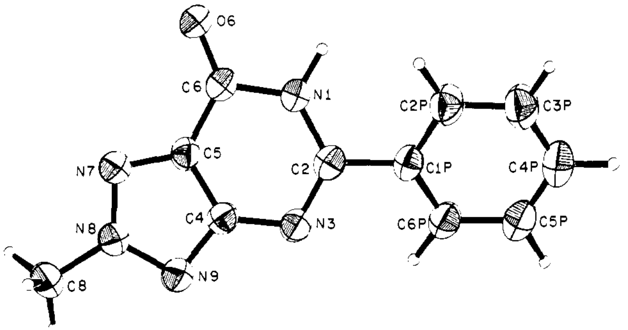

Figure 2. View of a single molecule of 2-phenyl-8-methyl-8-azahypoxanthine. Hydrogen atoms are shown as spheres of arbitrary size.

Table III. Interatomic Distances (Å) in 2-Phenyl-7-methyl-8-azahypoxanthine and 2-Phenyl-8-methyl-8-azahypoxanthine

atoms	distance (7-Me)	distance (8-Me)
N1–C2	1.383 (4)	1.389 (3)
C2–N3	1.311 (4)	1.299 (3)
N3–C4	1.371 (4)	1.370 (2)
C4–C5	1.364 (5)	1.396 (3)
C5–C6	1.415 (5)	1.432 (3)
C6–N1	1.389 (4)	1.394 (2)
C6–O6	1.229 (4)	1.234 (2)
C4–N9	1.370 (4)	1.340 (3)
C5–N7	1.350 (4)	1.348 (2)
N7–N8	1.341 (4)	1.324 (2)
N8–N9	1.321 (4)	1.343 (2)
N7–C7	1.456 (5)	-
N8–C8	-	1.456 (3)
C2–C1P	1.481 (6)	1.480 (3)
C1P–C2P	1.398 (5)	1.387 (3)
C2P–C3P	1.384 (5)	1.390 (3)
C3P–C4P	1.377 (6)	1.378 (4)
C4P–C5P	1.381 (6)	1.372 (4)
C5P–C6P	1.385 (5)	1.383 (3)
C6P–C1P	1.388 (5)	1.397 (3)
N1–N1H	0.92[a]	0.95 (2)
C7–C7H1/C8–C8H1	1.03	0.98 (3)
C7–C7H2/C8–C8H2	0.98	0.98 (4)
C7–C7H3/C8–C8H3	0.97	0.96 (3)
C2P–C2PH	0.98	0.98 (3)
C3P–C3PH	0.97	0.89 (3)
C4P–C4PH	0.96	0.98 (3)
C5P–C5PH	0.97	0.96 (2)
C6P–C6PH	0.97	1.01 (3)

[a] H-atom parameters were not varied in the refinement of the 7-methyl isomer.

Table IV. Intramolecular Angles (deg) in 2-Phenyl-7-methyl-8-azahypoxanthine and 2-Phenyl-8-methyl-8-azahypoxanthine

atoms	angle (7-Me)	angle (8-Me)
C6–N1–C2	125.9 (3)	125.9 (2)
N1–C2–N3	123.1 (3)	124.4 (2)
N1–C2–C1P	117.7 (3)	116.7 (2)
N3–C2–C1P	119.2 (4)	118.9 (2)
C2–N3–C4	113.6 (3)	113.1 (2)
N3–C4–N9	125.4 (4)	125.7 (2)
N3–C4–C5	125.4 (4)	126.0 (2)
C5–C4–N9	109.2 (3)	109.2 (2)
C4–C5–C6	122.1 (4)	120.8 (2)
C4–C5–N7	105.1 (3)	109.3 (2)
N7–C5–C6	132.7 (4)	129.8 (2)
C5–C6–N1	109.9 (4)	109.8 (2)
C5–C6–O6	127.5 (4)	128.4 (2)
O6–C6–N1	122.6 (3)	121.8 (2)
C5–N7–N8	109.8 (3)	101.9 (2)
C5–N7–C7	128.9 (4)	
C7–N7–N8	121.2 (3)	
N7–N8–N9	109.0 (3)	117.8 (2)
N7–N8–C8		120.9 (2)
C8–N8–N9		121.3 (2)
N8–N9–C4	106.9 (3)	101.8 (1)
C2–C1P–C2P	118.5 (4)	121.5 (2)
C2–C1P–C6P	123.3 (4)	119.1 (2)
C2P–C1P–C6P	118.2 (3)	119.4 (2)
C1P–C2P–C3P	120.7 (4)	119.6 (2)
C2P–C3P–C4P	120.3 (4)	120.5 (3)
C3P–C4P–C5P	119.7 (4)	120.0 (2)
C4P–C5P–C6P	120.2 (4)	120.4 (2)
C5P–C6P–C1P	120.9 (4)	120.0 (2)

Table V. The 8-Azapurine and Phenyl Planes in 2-Phenyl-7-methyl-8-azahypoxanthine and 2-Phenyl-8-methyl-8-azahypoxanthine

atoms[a]	7-Me	8-Me	atoms[a]	7-Me	8-Me
N1	0.029	0.014	C1P	0.000	0.001
N3	−0.024	−0.009	C2P	0.002	−0.005
N7	−0.012	−0.008	C3P	−0.002	0.005
N8	0.011	0.015	C4P	0.000	−0.000
N9	0.025	0.010	C5P	0.002	−0.004
C2	−0.001	−0.001	C6P	−0.002	0.004
C4	−0.004	−0.005	C2*	−0.005	0.005
C5	−0.026	−0.025			
C6	0.002	0.009			
O6*	0.026	0.044			
C7*	−0.037	-			
C8*	-	0.057			

[a] An asterisk denotes atoms not included in the calculation of the least-squares plane.

in Figures 1 and 2, respectively. The bond distances for the two structures are listed in Table III; the bond angles are listed in Table IV.

The Azapurine Rings. The interatomic distances in the six-membered portion of the azapurine moiety agree with those tabulated by Ringertz[14] for a number of guanine drivatives and also with those reported for a variety of 8-azapurine derivatives.[15-19]

The bond lengths and angles in the triazole rings reflect the position of the methyl substituent. Thus, the C4–C5 bond in 7-methyl (1.364 (5) Å) indicates a strong double obnd, while the 1.396 (3) Å value for 8-methyl indicates a significant reduction in double-bond character. This difference is, of course, consistent with the predictions of simple valence bond theory.

It has been suggested by Ringertz[14] and Singh[20] that the internal angles in a purine ring are dependent on the nature of the exocyclic substituent atoms; increase in the bond order of an exocyclic bond decreases the internal ring angle at the site of attachment of the exocyclic atom. As has been noted elsewhere,[16,17] substitution of a sp^2-hybridized carbon atom for the exocyclic NH_2 group at C2 in guanine produces only a very slight change in the N1–C2–N3 bond angle; thus, this angle is 123.1 (3) and 124.4 (2)° for the 7- and 8-methyl isomers, respectively, as compared with the average value of 123.7° reported by Ringertz.[14] Protonation at a nitrogen site increases the internal bond angle associated with that nitrogen in both purines[14] and azapurines;[21] the 7- and 8-methyl compounds both have a C6–N1–C2 bond angle of 125.9° which is slightly smaller than the average value of 127.2° in protonated 8-azapurines[21] but considerably greater than the 120.3° angle observed for the unprotonated ones.[21,22]

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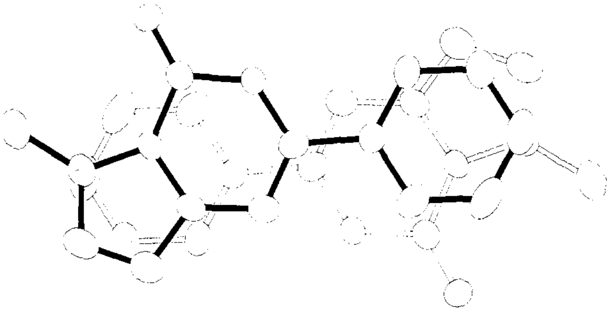


Figure 3. Stacking interactions in 2-phenyl-7-methyl-8-azahypoxanthine, viewed perpendicular to the molecular plane.

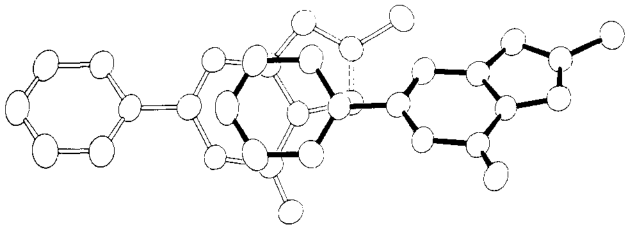


Figure 4. Stacking interactions in 2-phenyl-8-methyl-8-azahypoxanthine.

As shown in Table V, the 8-azapurine portion of both molecules is planar; the largest deviation from the nine-atom plane is 0.03 Å in both structures. The exocyclic atom O6 and C7 in the 7-methyl case are 0.026 Å above and 0.037 Å below the plane, respectively; in the 8-methyl structure O6 (0.044 Å) and C8 (0.057 Å) are on the same side of the plane of the azapurine.

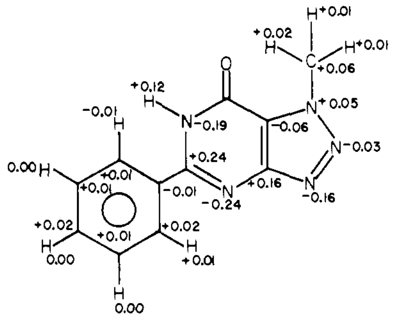
Other Aspects of the Structures

The bond lengths within the phenyl ring in the 7-methyl compound range from 1.377 Å to 1.398 Å (for C3P–C4P and C1P–C2P, respectively), and they average 1.386 Å. In the 8-methyl case the range is from 1.372 Å (C4P–C5P) to 1.397 (C1P–C6P), while the average is 1.385 Å. The six atoms deviate a maximum of 0.002 Å from the least-squares plane in the 7-methyl case, while the deviation in the 8-methyl compound is at most 0.005 Å (see Table V).

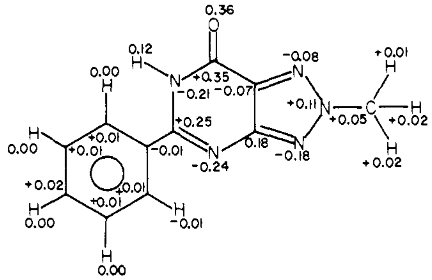
While the phenyl and azapurine rings are not entirely coplanar, the angle between the two moieties is only 2.3° in the 7-methyl case but is 29.5° in the 8-methyl case. This virtually planar structure in the 7-methyl case is presumably related to the fact that in the 7-methyl compound the 2-phenyl ring is directly conjugated with a *pseudo*-aromatic ring; in the 8-methyl case, there is only a cross-conjugated double-bond system. In each molecule the only potential hydrogen bond donor is N1. In the 8-methyl isomer this atom participates in an intermolecular N1—H···O6 hydrogen bond with N1···O6 and H1···O6 separations and N1—H···O6 angle of 2.880 (2) Å, 1.95(2) Å, and 168(2)°, respectively, but there is no hydrogen bonding in the 7-methyl compound. This latter result is presumably due to the approximate coplanarity of the azapurine and phenyl rings in this isomer, which effectively blocks close approach to H1 by the potential acceptors on adjacent molecules.

In the 7-methyl case, closest intermolecular approach between molecules is between molecules related by an inversion center. These molecules sit above one another as shown in Figure 3 with a 3.45-Å separation between the least-squares planes through the azapurines. Stacking of purine and pyrimidine molecules in crystals is common;[23] the molecules usually stack in such a way that the polar regions of one molecule overlap with the polarizable ring system of an adjacent base. In this case, the polar (see IV) C4–N9 and C4–N3 bonds overlap with the polarizable phenyl ring; there are, however no base stacking interactions. As illustrated in Figure 4, the stacking in the 4-methyl structure is substantially similar to that in the 7-methyl isomer. The molecues in this case stack along *b* and are related by the glide plane, and the average interplanar separation is 3.49 Å.

Electronic Charge Density. The net atomic charge densities as calculated by the CNDO/2 method[13] are shown below for the 7-methyl compound (IV) and the 8-methyl compound (V). The calculations indicate the most electron-rich site in the azapurine rings of both molecules is N3, −0.24 e in both cases. This charge density is very similar to those found in 8-azaadenosine[22] (−0.26 e), 7-methyl-8-azaadenine[18] (−0.23 e), 9-methyladenine[24] (−0.24 e), 2-(2-propoxyphenyl)-8-azapurin-6-one[17] (−0.28 e), and 9-diethylcarbamoyl-2-propoxyphenyl)-8-azahypoxanthine[16] (−0.28 e). The electron density at N9 in IV (−0.16 e) compares with the value for 7-methyl-8-azaadenine[18] (−0.16 e), while in V the value is slightly higher (−0.18 e). Carbon substitution at N7 in IV and at N8 in V reduces the electron density of these two atoms to +0.05 and +0.11 e, respectively. The enhanced electron density at N3 relative to that at the triazole nitrogen atoms provides further evidence for the contention[25] that N3 is relatively more basic in the 8-azapurines than in the purines, and helps explain why protonation at N3 is frequently observed in 8-azapurine cations[25-27] and that metal ion coordination to this site has been observed in the 8-azapurines.[21]



IV



V

Acknowledgment. We are very grateful to Dr. K. R. H. Wooldridge for providing the samples used in this study and for stimulating conversations.

Supplementary Material Available: Thermal parameters and a listing of observed and calculated structure amplitudes (13 pages). Ordering information is given on any current masthead page.

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