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## Stereoelectronic Effects in Oxidative Transformations of Purines. III. Structure of 4,5-Ethylenedioxy-4,5-dihydro-3,7-dimethyluric Acid\*

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**Abstract.**  $C_9H_{12}N_4O_5$ ,  $M_r = 256.22$ , triclinic,  $P\bar{1}$ ,  $a = 10.172$  (4),  $b = 8.017$  (3),  $c = 7.524$  (5) Å,  $\alpha = 114.96$  (3),  $\beta = 103.09$  (5),  $\gamma = 89.94$  (4)°,  $V = 538.7$  (5) Å<sup>3</sup>,  $Z = 2$ ,  $D_x = 1.579$  g cm<sup>-3</sup>,  $\lambda(\text{Mo } K\alpha) = 0.7107$  Å,  $\mu = 1.41$  cm<sup>-1</sup>,  $F(000) = 268$ , room temperature,  $R = 0.036$  for 2590 observed reflections. N-containing rings of the hetero[4.4.3]propellane system adopt the ring-twisted conformation defined by the bridgehead torsion angle N(3)–C(4)–C(5)–N(7) of 83.9 (1)°; with the orthogonal N(3)–C(4)–N(9)–C(8) array [–89.7(1)°] and the O(4)–C(10) bond of the 1,4-dioxane chair antiperiplanar to the N(3)–C(4) bond, the ring opening in the conformationally rigid propellane is no longer stereoelectronically allowed.

**Introduction.** In the course of a study of the relationship between the molecular conformation and reactivity of appropriate chemical models it was shown that uric acid glycol, the key intermediate in oxidative breakdown of purines, can exist in two different ring-twisted conformations of the *cis*-fused bicyclic system. Regioselective ring opening requires that the  $\pi$ -type electron pair on one ureide N atom lies parallel and one non-bonded electron pair on the O atom antiperiplanar to the leaving N atom of the tetrahedral ester aminal array at C(4) (Poje & Vicković, 1987*a*, *b*).

In order to ascertain the stereoelectronic control in the cleavage of uric acid glycol, we have constructed a conformationally rigid propellane-type ether, 4,5-ethylenedioxy-4,5-dihydro-3,7-dimethyluric acid, in which non-bonded electrons on O(4) are oriented in such a way that the C–N bond cleavage of the ester aminal function cannot occur with the help of electronic

control. This derivative must, therefore, be unreactive and, indeed, it was completely stable under mild acidic conditions that are normally used for the hydrolysis of other uric acid glycol ethers.

**Experimental.** The title compound was synthesized by reaction of 5-chloro-3,7-dimethylisouric acid with cold anhydrous ethylene glycol. Recrystallization from water gave colourless prisms. Crystal size 0.21 × 0.25 × 0.38 mm, Philips PW 1100 diffractometer, graphite-monochromatized Mo  $K\alpha$  radiation, unit-cell parameters from 25 reflections ( $6 \leq \theta \leq 9^\circ$ ). Three standard reflections monitored every 2h showed no significant variation in intensity. A total of 2896 reflections were collected in the  $\theta$ - $2\theta$  mode, scan width 1.6°, scan speed 0.04° s<sup>-1</sup>,  $5 \leq 2\theta \leq 60.0^\circ$ ,  $0 \leq h \leq 14$ ,  $-11 \leq k \leq 11$ ,  $-10 \leq l \leq 10$ . From 2706 unique reflections 101 reflections with  $I \leq 3\sigma(I)$  and 15 reflections (20 $\bar{2}$ , 31 $\bar{2}$ , 2 $\bar{1}\bar{1}$ , 01 $\bar{1}$ , 11 $\bar{1}$ , 1 $\bar{1}$ 0, 200, 300, 110, 001, 101, 201, 011, 111, 211) due to secondary extinction were ignored. Data corrected for Lorentz and polarization effects but not for absorption. Structure solved by MULTAN80 (Main *et al.*, 1980). Six H atoms were located in a  $\Delta F$  map and used to calculate 12 H atoms at idealized positions (Vicković, 1985); ureide H atoms were relocated by a  $\Delta F$  synthesis to confirm their geometry; 2590 observed intensity data and 211 parameters in full-matrix least-squares refinement using  $F$  magnitudes;  $R = 0.036$ ,  $wR = 0.053$ ,  $\sum w(|F_o| - |F_c|)^2$ ,  $w = \sigma^{-2}(F_o)$  (derived from counting statistics),  $S = 1.96$ ,  $(\Delta/\sigma)_{\max} = 0.35$ ,  $(\Delta/\sigma)_{\text{av}} = 0.01$  for all refined parameters; maximum peak height in final  $\Delta F$  map  $\Delta\rho_{\max} = 0.36$  eÅ<sup>-3</sup>. Atomic scattering factors and anomalous-dispersion-correction coefficients as defined by XRAY76

\* Uric acid is 7,9-dihydro-1*H*-purine-2,6,8(3*H*)-trione.

Table 1. Fractional atomic coordinates ( $\times 10^4$ ) and  $U_{eq}$  ( $\text{\AA}^2 \times 10^3$ ) values

	x	y	z	$U_{eq}^\dagger$
N(1)	8629 (1)	1549 (1)	6206 (2)	28 (<1)
C(2)	8699 (1)	97 (2)	6768 (2)	24 (<1)
O(2)	9326 (1)	-1203 (1)	5963 (2)	37 (<1)
N(3)	8036 (1)	187 (1)	8166 (1)	24 (<1)
C(3)	8176 (2)	-1267 (2)	8875 (2)	33 (<1)
C(4)	7542 (1)	1888 (1)	9414 (2)	20 (<1)
O(4)	8616 (1)	2806 (1)	11109 (1)	26 (<1)
C(5)	7013 (1)	3032 (1)	8225 (2)	20 (<1)
O(5)	6939 (1)	4889 (1)	9535 (1)	25 (<1)
C(6)	7834 (1)	2957 (2)	6721 (2)	24 (<1)
O(6)	7793 (1)	4109 (1)	6070 (2)	43 (<1)
N(7)	5648 (1)	2157 (1)	7219 (1)	25 (<1)
C(7)	4710 (1)	2861 (2)	5990 (2)	37 (<1)
C(8)	5208 (1)	1427 (2)	8379 (2)	26 (<1)
O(8)	4038 (1)	816 (1)	8098 (2)	37 (<1)
N(9)	6303 (1)	1477 (1)	9852 (2)	26 (<1)
C(10)	8446 (1)	4697 (2)	12373 (2)	31 (<1)
C(11)	8160 (1)	5745 (2)	11102 (2)	28 (<1)

$$\dagger U_{eq} = \frac{1}{3} [U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(cc^*)^2 + 2U_{12}aba^*b^*\cos\gamma + 2U_{13}aca^*c^*\cos\beta + 2U_{23}bcb^*c^*\cos\alpha].$$

(Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976). All calculations were carried out on a Univac 1110/42 computer.

**Discussion.** Final atomic coordinates and equivalent isotropic thermal parameters are given in Table 1,\* main bond lengths and angles and hydrogen-bond geometry in Table 2. An ORTEP drawing (Johnson, 1971) of the molecule is shown in Fig. 1 with the numbering scheme and the hydrogen-bonding pattern.

The ring-twisted conformation of the N-containing ring system of the hetero[4.4.3]propellane molecule defined by the bridgehead torsion angle  $N(3)-C(4)-C(5)-N(7)$  of  $83.9(1)^\circ$  corresponds to that found in the related 4,5-dihydro-4,5-dimethoxy-3,7-dimethyluric acid (Poje & Vicković, 1987b). The most important conformational feature is the orthogonal  $N(3)-C(4)-N(9)-C(8)$  array [ $-89.7(1)^\circ$ ] of the ester aminal function. The 1,4-dioxane ring has a slightly distorted chair conformation with the  $O(4)-C(10)$  bond oriented antiperiplanar to  $N(3)$ . It is interesting to note that this arrangement gives rise to the shorter non-bonded  $N(9)\cdots C(10)$  distance of  $3.004(3) \text{ \AA}$ , below the sum of their van der Waals radii ( $3.35 \text{ \AA}$ ). The  $N(3)$ ,  $N(7)$ , and  $N(9)$  atoms show a distinct pyramidalization; the distances from the planes through their adjacent atoms are  $0.132(1)$ ,  $0.245(1)$ , and  $-0.178(1) \text{ \AA}$ , respectively.

\* Lists of structure factors, anisotropic thermal parameters, H-atom parameters, bond distances and angles involving H atoms and torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43420 (29 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Bond lengths ( $\text{\AA}$ ) and angles ( $^\circ$ ) and geometry of the hydrogen bonds (e.s.d.'s in parentheses)

$N(1)-C(2)$	1.393 (2)	$C(5)-O(5)$	1.410 (1)
$N(1)-C(6)$	1.360 (2)	$C(5)-C(6)$	1.534 (2)
$C(2)-O(2)$	1.225 (2)	$C(5)-N(7)$	1.439 (1)
$C(2)-N(3)$	1.350 (2)	$O(5)-C(11)$	1.435 (1)
$N(3)-C(3)$	1.468 (2)	$C(6)-O(6)$	1.211 (2)
$N(3)-C(4)$	1.458 (1)	$N(7)-C(7)$	1.457 (2)
$C(4)-O(4)$	1.393 (1)	$N(7)-C(8)$	1.383 (2)
$C(4)-C(5)$	1.551 (2)	$C(8)-O(8)$	1.225 (2)
$C(4)-N(9)$	1.444 (2)	$C(8)-N(9)$	1.369 (2)
$O(4)-C(10)$	1.446 (2)	$C(10)-C(11)$	1.502 (3)
$C(2)-N(1)-C(6)$	127.3 (1)	$O(5)-C(5)-C(6)$	109.9 (1)
$N(1)-C(2)-O(2)$	119.4 (1)	$O(5)-C(5)-N(7)$	107.9 (1)
$N(1)-C(2)-N(3)$	117.4 (1)	$C(6)-C(5)-N(7)$	112.0 (1)
$O(2)-C(2)-N(3)$	123.2 (1)	$C(5)-O(5)-C(11)$	113.6 (1)
$C(2)-N(3)-C(3)$	118.0 (1)	$N(1)-C(6)-C(5)$	115.9 (1)
$C(2)-N(3)-C(4)$	122.3 (1)	$N(1)-C(6)-O(6)$	122.4 (1)
$C(3)-N(3)-C(4)$	117.1 (1)	$C(5)-C(6)-O(6)$	121.7 (1)
$N(3)-C(4)-O(4)$	105.4 (1)	$C(5)-N(7)-C(7)$	121.0 (1)
$N(3)-C(4)-C(5)$	111.9 (1)	$C(5)-N(7)-C(8)$	108.8 (1)
$N(3)-C(4)-N(9)$	110.5 (1)	$C(7)-N(7)-C(8)$	121.4 (1)
$O(4)-C(4)-C(5)$	114.4 (1)	$N(7)-C(8)-O(8)$	125.2 (1)
$O(4)-C(4)-N(9)$	114.8 (1)	$N(7)-C(8)-N(9)$	108.3 (1)
$C(5)-C(4)-N(9)$	100.0 (1)	$O(8)-C(8)-N(9)$	126.4 (1)
$C(4)-O(4)-C(10)$	114.8 (1)	$C(4)-N(9)-C(8)$	109.8 (1)
$C(4)-C(5)-O(5)$	111.7 (1)	$O(4)-C(10)-C(11)$	109.2 (1)
$C(4)-C(5)-C(6)$	113.7 (1)	$O(5)-C(11)-C(10)$	109.1 (1)
$C(4)-C(5)-N(7)$	101.2 (1)		

N-H...O	N-H	H...O	N...O	N-H...O
$N(1)-H(1)\cdots O(2^i)$	0.92 (3) \text{ \AA}	1.98 (2) \text{ \AA}	2.867 (2) \text{ \AA}	163 (2)^\circ
$N(9)-H(9)\cdots O(8^h)$	0.92 (2)	2.01 (2)	2.918 (2)	175 (2)

Symmetry code: (i)  $2-x, -y, 1-z$ ; (ii)  $1-x, -y, 2-z$ .

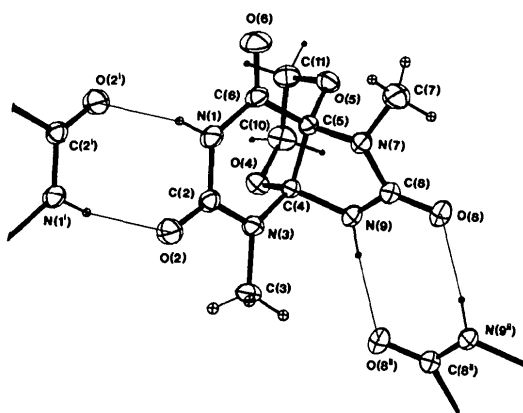


Fig. 1. Perspective view of the propellane molecule (*R,R*-configuration) showing 50% probability thermal ellipsoids.

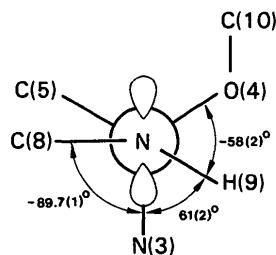


Fig. 2. Non-cooperative electronic effects in the ester aminal function [Newman projection along the  $N(9)-C(4)$  axis]; the ureide-N electron pair is depicted as  $sp^2$ -hybridized.

As a result of this conformationally rigid arrangement the O atom of the ester aminal function becomes locked into a configuration where cleavage of the N(3)–C(4) bond is no longer stereoelectronically allowed since the O(4) electron pair is no longer antiperiplanar to the N(3) atom (Fig. 2). The N(3)–C(4) bond is still longer than the C(4)–N(9) bond, but the O(4) atom with an electron pair now antiperiplanar to the C(4)–N(9) bond has a larger O(4)–C(4)–N(9) angle than the N(3)–C(4)–O(4) angle of the ester aminal function. It can be readily seen that this variation in bond lengths and angles is very simply related to the stereoelectronic effects and the rates of regiospecific ring openings of uric acid glycol ethers (Poje & Vicković, 1987*a,b*). An inspection of molecular models shows that the propellane molecule has no reasonable accessible conformation to develop a proper electron-pair orientation, and the remarkable stability of the ester aminal grouping under mild-acid conditions can be explained on the same stereoelectronic grounds.

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## Stereoelectronic Effects in Oxidative Transformations of Purines. IV. Structure of 4,5-Dihydro-4,5-dimethoxy-1,3,7-trimethyluric Acid\*

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**Abstract.** C<sub>10</sub>H<sub>16</sub>N<sub>4</sub>O<sub>5</sub>,  $M_r = 272.26$ , triclinic,  $P\bar{1}$ ,  $a = 8.780$  (4),  $b = 8.260$  (5),  $c = 8.997$  (5) Å,  $\alpha = 91.77$  (3),  $\beta = 89.65$  (5),  $\gamma = 103.54$  (4)°,  $V = 634.1$  (5) Å<sup>3</sup>,  $Z = 2$ ,  $D_x = 1.426$  g cm<sup>-3</sup>,  $\lambda(\text{Mo } K\alpha) = 0.7107$  Å,  $\mu = 1.24$  cm<sup>-1</sup>,  $F(000) = 288$ , room temperature,  $R = 0.043$  for 2678 observed reflections. The *cis*-fused bicyclic system has a ring-twisted conformation which is defined by the bridgehead torsion angle N(3)–C(4)–C(5)–N(7) of 91.4 (1)°. The nearly orthogonal N(3)–C(4)–N(9)–C(8) array [–93.5 (1)°] with N(9) antiperiplanar to the 4-methoxy group allows stereoelectronically controlled N(3)–C(4) bond breaking in the ring contractions to spiro[4.4]nonane systems.

**Introduction.** Uric acid glycol ethers offer an attractive means of determining stereochemistry and interactions which relate to structure and reactivity of tetrahedral intermediates in oxidative transformations of purines. Dramatic conformational changes effected by substitution at N atoms have been ascribed to repulsive Me↔O interactions, and at the same time the molecular structures indicated that the bond lengths and angles of the ester aminal function show strong stereoelectronic conformational dependence in complete agreement with the stereoelectronic principle (Poje & Vicković, 1987*a,b,c*). On the basis of this principle, the regiospecific ring-opening processes, involving two ring-twisted conformations of a *cis*-fused system, become intelligible.

More extensively alkylated uric acids, having both N(1) and N(7) alkylated, undergo an interesting

\* Uric acid is 7,9-dihydro-1*H*-purine-2,6,8(3*H*)-trione.