

A Photodimer of 1,2,3,6-Tetrahydro-5-methyl-2,6-dioxo-4-pyrimidinecarboxylic Acid (5-Methylorotic Acid); Crystal Structure of the Trihydrated Barium Salt

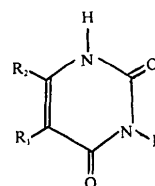
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Abstract. $C_{12}H_{10}O_8N_4Ba \cdot 3H_2O$. Monoclinic, $C2$, Cm or $C2/m$ ($C2$ found by structure analysis). $a = 14.407$ (2), $b = 7.094$ (1), $c = 9.888$ (3) Å, $\beta = 124.7$ (1)°. M.W. 529.45. $D_m = 2.13$ (3), D_c (for $Z = 2$) = 2.11 g cm⁻³. μ (Mo $K\alpha$) = 25.42 cm⁻¹. Crystals from solution are deposited as (+) and (-) forms. Molecules of the photodimer are of fused cyclobutane type, being *anti* isomers of *cis* configuration. The crystal structure is extensively hydrogen-bonded although no ketonic oxygens are involved. As in other known *cis-anti* dimers, the cyclobutane ring is buckled, but this is brought about by a twisting of the pyrimidinedione rings in the opposite sense to that found in both the uracil and 1,3-dimethylthymine photodimers. The absolute configuration was found for the molecules in the crystal chosen for examination.

Introduction. Frozen aqueous solutions of many pyrimidinediones such as uracil (I), thymine (II) and its derivatives give high yields of photoproducts, particularly dimers, under UV irradiation. Beukers & Berends (1960) suggested that these dimers have structures based on a cyclobutane ring formed by fusion of the R_1, R_2 positions. This has since been confirmed by X-ray analyses of a number of dimers. [For most earlier references, see Flippen & Karle (1971).]



(I) $R_1 = R_2 = H$; uracil
 (II) $R_1 = CH_3$; $R_2 = H$; thymine
 (III) $R_1 = CH_3$; $R_2 = COOH$
 methylorotic acid

Although 5-methylorotic acid (III) forms a photodimer on UV irradiation, by comparison with uracil and with thymine it is formed in exceptionally low yield. This raises some question as to its structure. We show here by structure analysis that this dimer is also formed by fusion to form a cyclobutane ring.

The dimer was prepared from frozen aqueous solutions of 5-methylorotic acid (Sigma Chemical Corp.). Details are given by Miskew (1970). Aqueous dimer solution was neutralized with $Ba(OH)_2$ solution, filtered and left in a desiccator over NaOH pellets. After three weeks, crystals suitable for X-ray analysis had formed.

A crystal $0.16 \times 0.32 \times 0.08$ mm was used to collect intensities of 1501 reflexions on a Canberra-automated four-circle diffractometer. Data collection was in 2θ scan mode at 1°min^{-1} , the base width being 2.2° adjusted for $\alpha_1\alpha_2$ splitting. After data collection, the intensities of about 100 reflexions were remeasured.

Table 1. Atomic fractional coordinates ($\times 10^4$, for H $\times 10^2$) and anisotropic thermal parameters ($\times 10^4$)

T.f. = exp $[-(h^2\beta_{11} + k^2\beta_{22} + l^2\beta_{33} + 2hk\beta_{12} + 2hl\beta_{13} + 2kl\beta_{23})]$. For H the isotropic B factor was taken as 6.0 \AA^2 .

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Ba ²⁺	0	0	0	28 (0)	98 (1)	42 (1)	0	10 (0)	0
N(1)	-66 (5)	-3851 (9)	3391 (9)	24 (3)	79 (10)	73 (9)	-5 (4)	19 (4)	3 (8)
C(2)	882 (5)	-2804 (8)	3981 (7)	30 (3)	82 (9)	60 (7)	-1 (4)	24 (4)	9 (6)
N(3)	1828 (4)	-3324 (8)	5518 (6)	27 (3)	119 (9)	65 (6)	-12 (4)	21 (4)	9 (6)
C(4)	1881 (4)	-4779 (15)	6465 (7)	17 (2)	128 (24)	62 (5)	-1 (5)	20 (3)	3 (8)
C(5)	925 (4)	-6179 (8)	5707 (6)	18 (3)	74 (8)	50 (6)	-3 (4)	18 (3)	3 (6)
C(6)	-36 (5)	-5824 (11)	3856 (8)	19 (3)	77 (11)	63 (9)	1 (5)	23 (4)	9 (8)
C(7)	-41 (5)	-6997 (8)	2515 (6)	41 (4)	85 (9)	46 (6)	-2 (5)	27 (4)	-9 (6)
C(8)	1425 (5)	-8185 (9)	6066 (8)	42 (4)	98 (10)	81 (8)	21 (5)	36 (5)	16 (7)
O(1)	-913 (5)	-7859 (9)	1446 (7)	54 (3)	203 (11)	101 (7)	-23 (5)	40 (4)	-55 (7)
O(2)	919 (4)	-1402 (7)	3280 (6)	54 (3)	119 (8)	83 (6)	-31 (4)	36 (4)	3 (6)
O(3)	841 (4)	-6852 (8)	2558 (6)	50 (3)	167 (10)	109 (7)	16 (5)	52 (4)	2 (7)
O(4)	2699 (3)	-4883 (19)	7911 (5)	27 (2)	151 (15)	61 (4)	-12 (7)	13 (3)	7 (10)
O(5)	-1812 (8)	-1658 (13)	922 (11)	86 (6)	204 (18)	167 (13)	0 (9)	-24 (8)	57 (13)
O(6)	0	-3952 (16)	0	216 (19)	128 (20)	158 (18)	0	138 (17)	0

Table 1 (cont.)

	x	y	z
H(N1)	-8	-35	23
H(N3)	25	-22	60
H(C8A)	18	-83	55
H(C8B)	20	-81	70
H(C8C)	9	-92	60
H(O5A)	-26	-20	4
H(O5B)	-18	-4	9
H(O6)	5	-47	10

Reflexions of high 2θ had fallen (on average) more than those of low 2θ . Accordingly reflexions were divided into five 2θ ranges and for each range a different correction factor (linear with time) was applied.

Using the criterion $F \geq \sqrt{2}\sigma(F)$, 1271 reflexions were considered to have significant intensity, where $\sigma(F) = \{[\sigma(I)/Lp]^{1/2} + 0.02F^4\}^{1/2}/2F$, Lp being the Lorentz-polarization factor.

Ba positions were found from the Patterson function and the space group found to be $C2$. Anisotropic full-matrix least-squares refinement was carried out with scattering factors taken from Cromer & Mann (1968), the anomalous dispersion corrections assumed for Ba^{2+} being $\Delta f' = -0.613$ and $\Delta f'' = 2.282$ (*International Tables for X-ray Crystallography*, 1974). Balancing negative charges were assigned by scaling the scattering factors of O(1) and of O(3) by $(8\frac{1}{2}/8) = 1.063$. The ultimate cycle of refinement for all non-hydrogen atoms gave a conventional, unweighted residual of 0.037. All eight H atoms of the asymmetric unit were revealed on a difference map. Their inclusion in the structure factor calculation with temperature factor $B = 6.0 \text{ \AA}^2$ lowered R to 0.0343. Because the space group is $C2$ all the dimer molecules in one crystal must be of one chirality, the crystals having spontaneously resolved on deposition from solution. Accordingly the final y coordinates and those with sign reversed were compared for their effect on the residual. Sign reversal gave a lower R , 0.0326, and hence these

y coordinates are those listed in Table 1 giving the absolute configuration of the dimer molecules in the crystal which, by chance, was chosen for X-ray examination.*

* A list of structure factors and corresponding phase angles has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31743 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

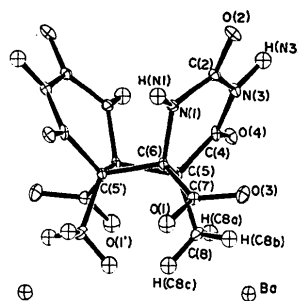


Fig. 1. Molecular conformation. Thermal ellipsoids represent 20% probability.

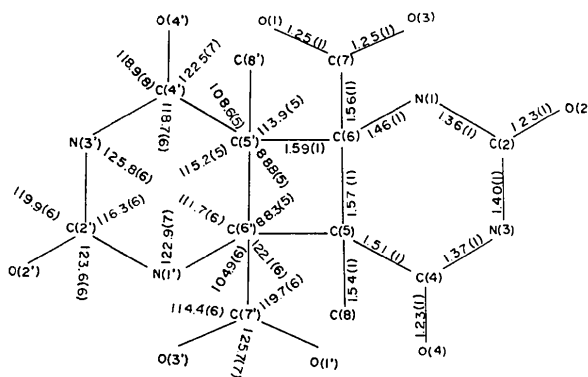


Fig. 2. Derived bond lengths and angles.

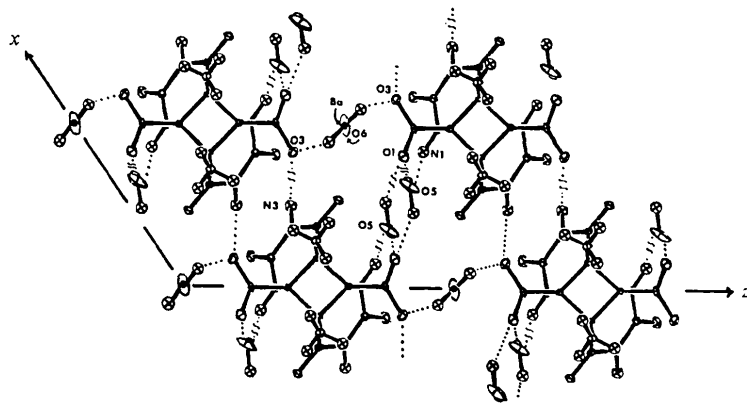


Fig. 3. Intermolecular hydrogen bonds in y projection. (Symbol $\lceil \rceil$ represents two separate bonds which overlap in y projection. One bond runs to an upper molecule, the other to a lower.)

Discussion. In space group $C2$, with two dimer molecules per unit cell, the molecular symmetry is 2. This is achieved by the dimer molecules having a twofold axis parallel to y through the centres of, and normal to the mean planes of the cyclobutane rings, (Fig. 1). The isomeric form is thus *cis-anti* [*cis* because the pyrimidine rings are on the same side of the cyclobutane ring, and *anti* because atom C(5) is fused to atom C(6') and not to C(5')]. Of the four *a priori* possible structures no example of a *trans-syn* isomer is yet known. Two other *cis-anti* dimers are however known, those of 1,3-dimethylthymine (Camerman, Weinblum & Nyburg, 1969) and of uracil (Konnert & Karle, 1971).

Derived bond lengths and angles are given in Fig. 2. The crystal structure is extensively intermolecularly hydrogen-bonded (Fig. 3) as follows. (i) Water molecule O atoms O(6) lie on twofold axes and are hydrogen-bonded to the two carboxylic O atoms, O(3), of molecules spanning the same twofold axis. (ii) These O(3) atoms are, in addition, hydrogen-bonded to N(3) atoms of adjacent dimer molecules. (iii) Water molecule O atoms O(5) are hydrogen-bonded to O atoms O(1) forming screw axis spirals along y . (iv) O atoms O(5) are also hydrogen-bonded to N(1) atoms of molecules spanning the same screw axis.

Detailed dimensions of these hydrogen bonds are given in Table 2. One striking feature of this table is that all the X-H-Y angles are around 150° . Kroon & Kanters (1974) found this to be the most common angle shown in polyalcohols, saccharides and related compounds. In the uracil dimer (Konnert & Karle, 1971) we calculate the average N-H-O angle as 159° .

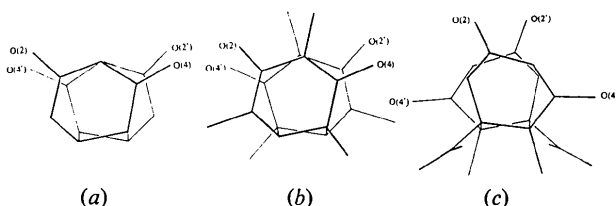


Fig. 4. Three *cis-anti* dimers viewed along a line joining the midpoints of C(5)-C(6) and C(5')-C(6'): (a) uracil dimer, (b) 1,3-dimethylthymine dimer, (c) 5-methylorotate dimer ion.

Table 2. Dimensions of hydrogen bonds

Donor lengths (Å)		Acceptor lengths (Å)	
O(6)-H(O6)	0.99	O(3)-H(O6)	2.02
O(5)-H(O5A)	1.04	O(3)-H(N3)	1.99
O(5)-H(O5B)	0.90	O(1)-H(O5A)	1.92
N(1)-H(N1)	0.99	O(1)-H(O5B)	2.06
N(3)-H(N3)	1.10	O(5)-H(N1)	1.88
Angles (°)		Angles (°)	
H(O6)-O(6)-H(O6)	114.8	O(6)-H(O6)-O(3)	152.6
H(O5A)-O(5)-H(O5B)	108.9	O(5)-H(O5A)-O(1)	150.3
		O(5)-H(O5B)-O(1)	156.0
		N(3)-H(N3)-O(3)	144.0
		N(1)-H(N1)-O(5)	149.0

It is worth noting that the ketonic O atoms O(2) and O(4) are not hydrogen-bonded at all. (There is also one ketonic O atom in the uracil dimer which is not hydrogen-bonded.)

As with the other *cis-anti* dimers of known structure, the cyclobutane ring is twisted away from the planar conformation. Thus when these dimers are viewed along a line joining the midpoint of C(5)-C(6) to the midpoint of C(5')-C(6') the two halves of the dimeric molecule do not closely overlap. This is shown in Fig. 4. There is a striking difference in the conformations of the uracil and 1,3-dimethylthymine dimers on the one hand and the 5-methylorotate dimer ion on the other. The first two dimers have the same sense of twist which, when viewed as in Fig. 4(a) and (b), brings O(2) of one ring close to O(4') of the other. In the 5-methylorotate dimer ion twisting, although of the same order of magnitude, is in the opposite sense, causing O(2) of one ring in the projection of Fig. 4(c) to move further away from O(4') of the other. The cause of this difference is not easily identified because not only may the substituents at the C(5) and C(6) positions affect the sense of buckling of the cyclobutane ring, but the different hydrogen-bonding scheme may also play a role.

Bond lengths and angles in the 5-methylorotate dimer ion closely resemble those found in other pyrimidinedione dimers and, although there are significant differences in some cases, there are no obvious trends. The pyrimidinedione rings in all the dimers of known structure show significant but usually small departures from coplanarity. Again the details of non-coplanarity differ from case to case without obvious trends. Best least-squares planes of interest in the 5-methylorotate dimer ion are given in Table 3.

Table 3. Best least-squares planes

	Coefficients*				Deviations of atoms from plane (Å)							
	A	B	C	D	C(5)	C(6)	C(5')	O(2)	N(3)			
Cyclobutane ring†	(0)	1.0	(0)	4.260	C(5)	0.126	C(6)	-0.127	C(5')	0.126	C(6')	-0.126
Pyrimidinedione ring†	0.775	0.514	-0.365	-0.912	N(1)	-0.248	C(2)	-0.002	O(2)	0.044	N(3)	0.119
					C(4)	0.012	O(4)	-0.095	C(5)	0.008	C(6)	0.162

* Equation to plane $AX+BY+CZ=D$ where X, Y, Z are orthogonal coordinates (in Å) with X along x and Z along z^* .

† Angle between planes: 59.14° .

The Ba ions, which lie on diad axes, are each surrounded by ten (*i.e.* five pairs of) O atoms. These are: O(4) (ketonic) at 2.73, O(6) (water) at 2.80, O(2) (ketonic) at 2.89, O(1) and O(3) (carboxylic) at 2.87 and 3.06 Å respectively.

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Sodium Neodymium Metaphosphate $\text{NaNdP}_4\text{O}_{12}$

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Abstract. Monoclinic, $P2_1/n$ (C_{2h}^5); $a=9.907$ (4), $b=13.10$ (1), $c=7.201$ (3) Å, $\beta=90.51$ (3)°; $Z=4$, $D_m=3.45$, $D_c=3.43$ g cm⁻³; $\mu(\text{Mo } K\alpha)=63.8$ cm⁻¹. The structural framework consists of helical chains of $(\text{PO}_3)_\infty$ along the c axis. Nd^{3+} and Na^+ ions alternate linearly in a direction surrounded by four $(\text{PO}_3)_\infty$ chains. NdO_8 dodecahedra and Na polyhedra form zigzag chains sharing faces. The refinement converged to $R=0.028$, $R_w=0.031$ for 2592 independent observed reflexions.

Introduction. Following the development of an efficient laser material $\text{LiNdP}_4\text{O}_{12}$ (Yamada, Otsuka & Nakano, 1974), another new Nd phosphate crystal $\text{NaNdP}_4\text{O}_{12}$ was found in our laboratory (Nakano, Otsuka & Yamada, 1976). The cell dimensions of the crystal are similar to those of the other alkaline Nd metaphosphate previously reported (Table 1).

Specimens were selected from crystals grown from

the melt of $33\text{Na}_2\text{O}-7\text{Nd}_2\text{O}_3-60\text{P}_2\text{O}_5$ by the Kyropoulos technique (Nakano *et al.*, 1976). Precession and Weissenberg photographs exhibited $2/m$ Laue symmetry with the following systematic absences: $h0l$ when $h+l=2n+1$, $0k0$ when $k=2n+1$.

A prismatic crystal $0.15 \times 0.20 \times 0.65$ mm was mounted with its c axis along the ϕ axis of the Rigaku Denki automatic four-circle X-ray diffractometer. Reflexions within $(\sin \theta/\lambda)=0.72$ Å⁻¹ were measured using the $\omega-2\theta$ scan technique with a Ge monochromator. The intensities were corrected for Lorentz-polarization, absorption and extinction effects.

The location of atoms, except oxygen, was determined by the three-dimensional Patterson method assuming a similarity to the $\text{LiNdP}_4\text{O}_{12}$ structure (Koizumi, 1976). Structure factors based on the Patterson coordinates gave the conventional R value of 0.283. Successive Fourier syntheses clearly revealed the oxygen positions indicating tetrahedral coordination around the P atom.

All the atomic parameters were refined by the full-matrix least-squares method (Busing, Martin & Levy, 1962) to give $R=0.028$, $R_w=0.031$. The final atomic parameters are listed in Table 2.*

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31747 (13 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 1. *The axial relations for three alkaline Nd metaphosphates*

Crystal	Space group	a	b	c	β	Z
$\text{LiNdP}_4\text{O}_{12}^{(a)}$	$I2/c$	9.844 Å	7.008 Å	13.25 Å	90.1°	4
$\text{LiNdP}_4\text{O}_{12}^{(b)}$	$C2/c$	16.408	7.035	9.729	126.38	4
$\text{NaNdP}_4\text{O}_{12}^{(c)}$	$P2_1/n$	9.907	13.10	7.201	90.51	4
$\text{KNdP}_4\text{O}_{12}^{(d)}$	$P2_1$	7.266	8.436	8.007	91.97	2

(a) Koizumi (1976); (b) Hong (1975a); (c) this work; (d) Hong (1975b).