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Huber, Carol P.; Birnbaum, George I.; Post, Michael L.; Kulikowska, Ewa; Gajewska, Lucyna; Shugar, David

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Structure and properties of a *trans–anti* photodimer of 5-methylorotate[1]

CAROL P. HUBER,[2] GEORGE I. BIRNBAUM, AND MICHAEL L. POST

Division of Biological Sciences, National Research Council of Canada, Ottawa, Ont., Canada K1A 0R6

AND

EWA KULIKOWSKA, LUCYNA GAJEWSKA, AND DAVID SHUGAR

Department of Biophysics, Institute of Experimental Physics, University of Warsaw, 02-089 Warszawa, Poland

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5-Methylorotate is relatively radiation resistant in aqueous fluid medium, but readily photodimerizes in an ice matrix. Rapid formation of such a matrix made possible the preparative isolation of the photodimer in good yield. The potassium salt of the photodimer crystallizes as the hexahydrate, $C_{12}H_{10}N_4O_8K_2 \cdot 6H_2O$. The crystals are triclinic with space group $P\bar{1}$, $a = 8.139(3)$, $b = 9.759(3)$, $c = 7.398(3)$ Å, $\alpha = 100.28(7)$, $\beta = 74.22(5)$, $\gamma = 108.67(7)°$, and $V = 533.0$ Å^3, $Z = 1$. The structure was solved by Patterson and direct methods; refinement by block-diagonal least-squares converged at $R = 0.041$ for all 1671 observed reflections. The pyrimidine rings of the centrosymmetric photodimer are arranged in *trans–anti* configuration across the planar cyclobutane ring. The potassium ion is seven-coordinated. In aqueous medium the photodimer exhibits a pK_a of 12.8 due to dissociation of the ring N(3) hydrogen. Irradiation in aqueous medium at 254 nm leads to quantitative regeneration of the monomer with a quantum yield of 0.8. Thermal regeneration of the monomer also occurs in neutral and acid aqueous media, but at a slower rate than for the *trans–syn* orotate photodimer. In contrast to the orotate photodimer, which undergoes alkali-catalyzed opening of the 3,4 bonds of the pyrimidine rings, the 5-methylorotate photodimer under these conditions dissociates to the parent monomer.

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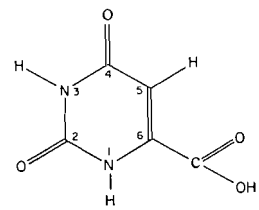
Dans l'eau liquide, le méthyl-5 orotate est assez résistant aux radiations; toutefois il subit facilement une photodimérisation dans une matrice de glace. La formation rapide d'une telle matrice permet d'isoler le photodimère avec de bons rendements à l'échelle préparative. Le sel du potassium du photodimère cristallise sous forme d'hexahydrate, $C_{12}H_{10}N_4O_8K_2 \cdot 6H_2O$. Les cristaux sont tricliniques avec un groupe d'espace $P\bar{1}$, $a = 8.139(3)$, $b = 9.759(3)$, $c = 7.398(3)$ Å, $\alpha = 100.28(7)$, $\beta = 74.22(5)$, $\gamma = 108.67(7)°$ et $V = 533.0$ Å^3, $Z = 1$. On a résolu la structure par les méthodes directes et de Patterson; un affinement par la méthode des moindres carrés (bloc diagonal) converge vers une valeur de R de 0.041 pour les 1671 réflexions observées. Les cycles de pyrimidine du photodimère centrosymétrique sont orientés dans une configuration *trans–anti* à travers le cycle planaire du cyclobutane. L'ion potassium est heptacoordonné. En solution aqueuse, le photodimère présente un pK_a de 12.8 qui est dû à une dissociation à l'hydrogène attaché en position N(3) du cycle. L'irradiation d'une solution aqueuse à 254 nm conduit à une regénération quantitative du monomère avec un rendement quantique de 0.8. La regénération thermique du monomère se produit aussi en milieu aqueux acide et neutre mais à une vitesse plus lente que pour le photodimère orotate *trans–syn*. Par opposition avec le photodimère orotate qui subit une ouverture catalysée par les bases des liens 3 et 4 du cycle pyrimidine, le photodimère du méthyl-5 orotate se dissocie, dans ces conditions, pour régénérer le monomère de base.

[Traduit par le journal]

Introduction

Various cyclobutane photodimers of 2,4-diketopyrimidines are involved in the lethal and mutagenic effects of ultraviolet irradiation, and orotic acid analogues have been extensively used as model systems in studies of the photodimerization reactions. Whereas orotic acid (I), in aqueous medium over the concentration range 10^{-2} *M* to 10^{-4} *M*, readily photodimerizes via a triplet state (1) to yield almost exclusively the *trans–syn* cyclobutane photodimer (2, 3), 5-methylorotate under these conditions is only slightly susceptible to photodimerization at



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[1]NRCC No. 16389.

[2]Author to whom correspondence should be addressed.

irradiation wavelengths to the red of 270 nm, and virtually fully resistant when irradiated at 254 nm (4). This situation is reversed in aqueous frozen medium, or in a KBr matrix. In the latter case (5) the quantum yields for photodimer formation from orotate and 5-methylorotate are 0.12 and 0.90, and probably depend on the extent of base stacking in the matrix. We have now found that the degree of photodimerization of 5-methylorotate in an ice matrix may be considerably enhanced by increasing the rate of formation of the matrix from the liquid phase. This has, in turn, made it possible to isolate the main photoproduct in adequate yield for crystallization on a preparative scale, and to examine some of its additional properties in solution, as well as to determine its structure by X-ray diffraction. A different (*cis–anti*) photodimer of 5-methylorotate has also been isolated, in very low yield, from frozen aqueous medium and analyzed crystallographically (6).

Experimental

5-Methylorotic acid was a product of Sigma Chemical Co. The photodimer of orotic acid was prepared as previously described (4).

Ultraviolet absorption spectra and spectral titrations made use of Zeiss (Jena, GDR) and Hilger UVISPEK instruments with 10-mm pathlength quartz cuvettes. ^{1}H nmr spectra were run on Varian 60 and 220 MHz instruments, using solutions in D_2O with sodium 2,2′-dimethyl-2-silapentane-5-sulphonate as internal standard. Infrared spectra were recorded on a Zeiss (Jena, GDR) UR-10 spectrophotometer, using variable pathlength cuvettes fitted with CaF_2 windows. Thin-layer chromatography made use of Merck cellulose F plates with the following solvent systems: (*A*) MeOH – conc. NH_4OH – H_2O (7:1:2), (*B*) *i*-ProOH – MeOH – conc. NH_4OH – H_2O (3:4:1:2), (*C*) *n*-BuOH – acetone – ether – H_2O (8:4.5:4.5:8), (*D*) EtOH – 1 *M* ammonium acetate (4:3). Quantum yields for photodimer dissociation were estimated by chemical actinometry, with the aid of the photohydration reaction of uridine, for which the quantum yield is 0.021.

Preparation of 5-Methylorotate Photodimer

A 10^{-2} *M* solution of 5-methylorotate in 0.01 *N* HCl was gently sprayed onto the surface of a 70 cm × 15 cm glass plate, the lower surface of which was in contact with finely powdered dry ice. Spraying was continued until an approximately 1-mm thick layer of frozen solution had been formed. This layer was then irradiated for a total of about 10–12 min with a Westinghouse 40-W germicidal lamp supported about 2 cm from the surface of the layer; at intervals of 2–3 min during irradiation, the surface of the layer was gently brushed to remove the opaque film formed by condensation from the atmosphere. Upon subsequent thawing of the irradiated frozen solution, a precipitate formed, due to the low solubility of the dimer photoproduct. The precipitate was collected by centrifugation, and the supernatant (the optical density of which was reduced to half of its initial level) concentrated twofold under reduced pressure and further irradiated as above. The final pooled product was extracted several times with small volumes of cold water to remove traces of monomer, dissolved in the minimum volume of 0.02 *N* NH_4OH and centrifuged to remove dust and other impurities. The clear solution was then brought to dryness and the ammonium salt of the 5-methylorotic acid dimer crystallized from water in the form of colourless needles (overall yield 30–35%). The ammonium salt was soluble in water, less so in ethanol and methanol. Suitable crystals for X-ray diffraction could not be obtained with this product, and it was therefore converted to the potassium salt by passage through a column of Dowex 50W-X8. Exposure of an aqueous solution of the potassium salt to ethanol vapour in a desiccator at atmospheric pressure led to precipitation of satisfactory crystals.

Neither the ammonium nor potassium salts exhibited clearly defined melting points, both undergoing initial thermal conversion to the parent 5-methylorotate. For the potassium salt, 20 min heating at 305°C, followed by thin-layer chromatography, showed 90% conversion to monomer, which included some thymine resulting from decarboxylation of the 5-methylorotate. Attempts to thermally decarboxylate the product to thymine photodimer were unsuccessful.

Thin-layer chromatography of the crude ammonium and potassium salts of 5-methylorotate photodimer with solvent systems *A*, *B*, *C*, and *D* showed one major component with R_f values of 0.44, 0.10, 0.08, and 0.21, respectively. The corresponding R_f values for the parent 5-methylorotate were 0.56, 0.37, 0.24, and 0.50. In addition, there were up to three minor spots, amounting to less than 10% of the total, presumably photodimer isomers. Attempts to isolate these by gas chromatography of the trimethylsilylated derivatives were unsuccessful. However, all four isomers in aqueous medium exhibited similar spectral and photochemical characteristics (see below).

Collection and Reduction of X-Ray Data

Preliminary precession photographs indicated triclinic symmetry. The crystal used for data collection was a prism with approximately hexagonal cross section, 0.25 mm across, was 0.57 mm long, and was mounted with b^* as rotation axis; the direction of elongation was parallel to (101). Cell-parameter and intensity measurements were made with a card-controlled Picker four-circle diffractometer equipped with a scintillation counter and pulse-height analyser, using Ni-filtered Cu radiation. Cell dimensions were calculated from 2θ values of high-angle reflections.

$[C_{12}H_{10}N_4O_8]^{2-}\cdot 2K^+\cdot 6H_2O$ fw = 524.5

$P\bar{1}$ (confirmed by the structure analysis), a = 8.139(5), b = 9.759(5), c = 7.398(5) Å, α = 100.28(7), β = 74.22(5), γ = 108.67(7)°. (Delaunay reduced cell: a = 9.393, b = 10.518, c = 7.398 Å, α = 92.57, β = 123.50, γ = 112.20°.) V = 533.0 Å^3, ρ_o = 1.632(5), Z = 1, ρ_c = 1.634 g cm^{-3}. (Cu Kα_1, λ = 1.54051, Cu Kα_2, λ = 1.54433 Å; 20°C.)

One asymmetric unit contains half a dimer anion, one K^+ ion, and three water molecules.

Moving-crystal moving-counter (θ/2θ) scans were used for the intensity measurements; a 10-s background count was accumulated at the end of each scan. All 1818 independent reflections accessible to the diffractometer (2θ ≤ 130°) were measured, and of these, 1671 had net counts above a threshold level which was determined as 20 (deca) counts or 10% of the total background count, whichever was greater. The 147 reflections considered as 'unobservably weak' were excluded from the structure determination and refinement, but included in the final structure-factor calculation. The intensities of two check reflections were monitored periodically during the data collection; fluctuations were less than 2% and appeared to be random. Absorption corrections were applied using a Gaussian integration formula; maximum and minimum transmission factors were 0.428 and 0.136 respectively for μ(Cu Kα) = 46.2 cm^{-1}. The usual Lorentz and polarization corrections were also applied to obtain structure-factor amplitudes.

Determination and Refinement of the Crystal Structure

Positions for eight atoms were deduced from a sharpened

Patterson synthesis. Extension from this partial structure by tangent refinement (7) gave 17 more atom sites, and a difference synthesis revealed the rest of the structure. Intensity statistics had been inconclusive regarding the presence or absence of a centre of symmetry, and therefore the analysis was carried out in space group $P1$ until the existence of the symmetry centres became obvious. Refinement by block-diagonal least-squares converged at a final R value of 0.041 for all observed reflections. Scattering factors for K^+, O, N, and $C_{valence}$ were taken from International Tables for X-ray Crystallography, Vol. IV (8), and the real part ($\Delta f' = 0.365$) of the anomalous dispersion correction was applied to the K^+ curve. Scattering factor values for bonded H were taken from Stewart *et al.* (9). Non-hydrogen atoms were refined anisotropically and hydrogen atoms, which were all located on difference maps, were refined with isotropic thermal parameters. The function minimized was $\Sigma w(|F_o| - |F_c|)^2$, and the final weighting scheme used was

$$w = w_1 w_2$$

where

$$w_1 = 1 \Big/ \left(1 + \left[\frac{F_o - 10.0}{10.0}\right]^2\right)$$

$$1.25 \leq F_o \leq 73.25$$

and

$$w_2 = (\sin^2 \theta / 0.65)^2$$

if $\sin^2 \theta < 0.65$, otherwise $w_2 = 1.0$. An extinction correction (10) was applied near the end of the refinement. The largest (shift/estimated standard deviation) ratio in the final least-squares cycle was 0.30, and the mean (shift/σ) was less than 0.10. A difference synthesis computed[3] from the final structure factors[4] showed two small peaks and a trough (maximum height ± 0.45 e/Å^3) near the K^+ ion site plus a peak (0.38 e/Å^3) near the mid-point of the C(6)—C(5)′ bond, the latter possibly attributable to bonding electron density.

Results

Properties of 5-Methylorotate Photodimer

In neutral aqueous medium the photodimer exhibited only end absorption in the ultraviolet. Spectral titration in alkaline medium, accompanied by the appearance of a clearly defined band at 240 nm, demonstrated the existence of a pK_a of 12.8, corresponding to the known dissociation of the N(3) hydrogen of 2,4-diketopyrimidines with a saturated 5,6 bond (12, 13).

The infrared spectrum of the photodimer in a KBr matrix in the 1600–1700 cm^{-1} region showed two intense bands at 1690 and 1710 cm^{-1}. Similar carbonyl bands were exhibited by the orotate photodimer.

The 60 MHz ^{1}H nmr spectrum of 5-methylorotate in D_2O showed a single sharp singlet at 2.00 ppm, ascribed to the 5-methyl protons. The 220 MHz spectrum of the photodimer in D_2O showed a unique singlet at 1.44 ppm. This shift to higher field is similar to that observed for the 5-methyl protons in thymine photodimers (14) and is consistent, as are the other spectral properties, with a cyclobutane photodimer structure. However, the only noncrystallographic evidence regarding the nature of the isomer present comes from the titration in acid medium of the photodimers of orotate and of 5-methylorotate against the corresponding parent monomers as controls. Each photodimer gave a single titration curve, indicating that each photodimer must have the *trans* configuration.[5]

Lability in Aqueous Medium

Irradiation of a 10^{-4} M solution at 254 nm led to quantitative photodissociation to the parent monomer with a quantum yield of 0.8, as observed for other 2,4-diketopyrimidine cyclobutane photodimers (4). At neutral pH the photoproduct underwent thermal dissociation to the parent monomer. Heating for 15 h at 100°C, at a concentration of 10^{-4} M, led to 8% conversion to monomer at pH 6.5, and 22% conversion in 1 N HCl. Under analogous conditions the *trans–syn* orotate photodimer proved more labile; conversion to the monomer was 24% and 85% in neutral and acid media respectively. In strongly alkaline medium the 5-methylorotate photodimer was slowly converted to the parent monomer. In 1 N NaOH at 60°C the rate constant for this reaction was 6.3×10^{-2} min^{-1}, so that the $t_{1/2}$ was about 11 min. Under such conditions orotate photodimer is more reactive, but its reactivity is manifested by disappearance of the uv absorption band at about 240 nm (4), as in the case of 5,6-dihydro-2,4-diketopyrimidines (12), and appears to be due to opening of the 3,4 bonds in the pyrimidine rings, with retention of the cyclobutane ring as in the case of a thymine photodimer (15).

X-Ray Analysis Results

Final fractional coordinates and thermal parammeters are listed with their esd's in Table 1. Bond lengths and bond angles are shown for the organic anion in Fig. 1, and interatomic distances and angles for the coordination polyhedron around the potassium ion have been deposited.[4] The anisotropic thermal vibrations of the atoms comprising the anion were analysed (16) for rigid-body motion, and the translational and librational motion of the group was found to be very small. Bond length corrections

[3]Unless otherwise indicated, all computations were made with the NRCC set of Crystallographic Programs for the IBM/360 system (11).

[4]Copies of tables of observed and calculated structure factors and of interatomic distances and angles in the K—O coordination polyhedron are available, at a nominal charge, from the Depository of Unpublished Data, CISTI, National Research Council of Canada, Ottawa, Ont., Canada K1A 0S2.

[5]A *cis* configuration would have led to the known splitting of the pK values for neighbouring carboxyl groups in dicarboxylic acids.

TABLE 1. Final parameters and their standard deviations

(*a*) Nonhydrogen atoms[a]

Atom	x	y	z	U_{11}	U_{22}	U_{33}	$2U_{23}$	$2U_{13}$	$2U_{12}$
$K^+(1)$	6890(1)	3733(0)	−5723(1)	318(2)	298(2)	378(2)	113(3)	−73(4)	137(3)
N(1)	1797(2)	1464(2)	−2268(2)	222(7)	234(7)	204(7)	142(12)	48(12)	214(12)
C(2)	3187(2)	1011(2)	−3245(2)	187(8)	203(8)	211(8)	9(13)	−40(13)	81(13)
O(2)	4086(2)	1439(1)	−4781(2)	242(6)	294(7)	206(6)	135(10)	116(10)	194(10)
N(3)	3628(2)	9(2)	−2509(2)	201(7)	310(8)	273(8)	160(13)	112(12)	276(13)
C(4)	2660(2)	−709(2)	−977(3)	204(8)	252(9)	242(8)	81(14)	−40(14)	163(14)
O(4)	3081(2)	−1700(2)	−618(2)	335(7)	354(8)	373(8)	265(12)	60(12)	410(13)
C(5)	1199(2)	−116(2)	347(2)	193(8)	219(8)	183(8)	43(13)	−29(13)	128(13)
C(6)	773(2)	1121(2)	−394(2)	178(7)	217(8)	180(8)	42(13)	−3(12)	130(13)
C(7)	1705(3)	264(2)	2258(3)	321(10)	311(10)	225(9)	37(15)	−201(15)	150(16)
C(8)	964(2)	2529(2)	997(3)	221(8)	233(8)	253(9)	−3(14)	−69(14)	169(14)
O(9)	−194(2)	2492(2)	2491(2)	296(7)	359(8)	260(7)	−143(11)	24(11)	230(12)
O(10)	2320(2)	3564(2)	536(2)	361(8)	262(7)	397(8)	−57(12)	−46(13)	−40(12)
O(11)	7661(3)	3624(2)	−2145(2)	645(11)	395(9)	357(8)	108(14)	−22(16)	498(16)
O(12)	9049(2)	6526(2)	−5906(2)	413(8)	349(8)	350(8)	32(13)	−212(13)	251(13)
O(13)	4780(2)	5129(2)	−2490(3)	387(9)	503(10)	443(9)	233(15)	−234(15)	163(15)

(*b*) Hydrogen atoms[b]

Atom	x	y	z	B	Atom	x	y	z	B
H(11)	162(3)	207(3)	−272(3)	0.0(0.4)	H(111)	765(6)	446(5)	−149(6)	3.3(0.8)
H(31)	446(4)	−30(3)	−319(4)	0.5(0.5)	H(112)	733(6)	310(5)	−139(6)	3.4(0.8)
H(71)	85(4)	62(3)	323(4)	0.8(0.5)	H(121)	924(5)	683(4)	−489(5)	2.0(0.6)
H(72)	283(4)	94(4)	210(5)	1.6(0.6)	H(122)	1011(5)	651(4)	−658(5)	2.2(0.6)
H(73)	187(4)	−56(3)	258(4)	0.9(0.5)	H(131)	558(5)	556(4)	−198(6)	2.8(0.7)
					H(132)	411(6)	447(5)	−174(6)	3.5(0.8)

[a]These parameters were multiplied by 10^4. The thermal parameters are expressed as $\exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^2 + U_{33}l^2c^{*2} + 2U_{23}klb^*c^* + 2U_{13}hla^*c^* + 2U_{12}hka^*b^*)]$.
[b]The number of the atom to which the hydrogen is bonded is obtained by dropping the least significant digit of the hydrogen atom number. The coordinates were multiplied by 10^3.

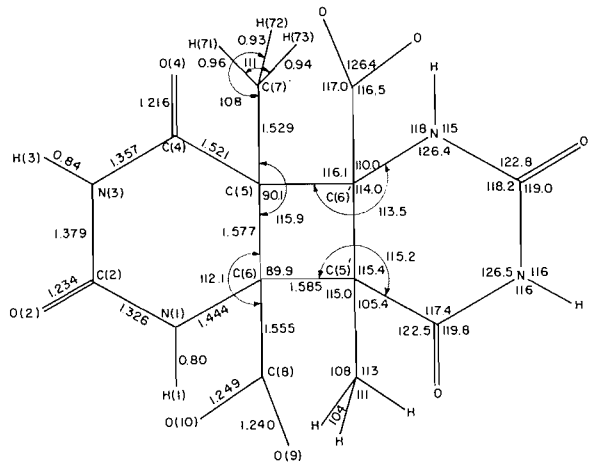

FIG. 1. Bond distances and angles in the 5-methylorotate photodimer anion. The esd's for the distances involving only nonhydrogen atoms are 0.002–0.003 Å; esd's for the corresponding angles are 0.13–0.19°. When hydrogen atoms are involved the esd's are about 10 times larger.

derived from the libration tensor were less than the individual esd's and were therefore not applied.

Discussion of the Crystal Structure

In this photodimer a crystallographic centre of symmetry lies in the centre of the cyclobutane ring, constraining it to be planar. The two pyrimidine rings are fused to the cyclobutane ring in *trans–anti* configuration and the dihedral angle between the cyclobutane ring and the mean pyrimidine ring plane is 121.6°. Each pyrimidine ring is significantly nonplanar, and the endocyclic torsional angles, given in Table 2, indicate that the distortions from planarity are in the direction of a slight twist-boat shape (17). Of the six atoms, C(4) deviates most (0.088 Å) from the mean pyrimidine ring plane, carrying O(4) 0.181 Å out of the plane, thereby increasing the separation between O(4) and C(7) which is, even so, only 2.84 Å. The C(7)···C(8) and C(7)···N(1)′ nonbonded distances, 2.83 and 2.81 Å respectively, are also rather short, indicating the severe overcrowding caused by the full substitution of C(5), C(6), C(5)′, C(6)′.

The bond lengths and angles in this structure are, in general, equal within experimental error to those in the *cis–anti* photodimer of 5-methylorotate (6). The few significant deviations are shown in Table 3, and it is interesting to note that where parameters involving only pyrimidine ring atoms differ, i.e. the N(1)—C(2) bond length and C(6)—N(1)—C(2), C(5)—C(6)—N(1) bond angles, the values found in the present *trans–anti* structure compare rather better with the values in the thymine *trans–anti* photodimer (18). Other significant deviations, involving the

TABLE 2. Torsional angles in the photodimer

(*a*) Endocyclic torsional angles in the pyrimidine ring

N(1)—C(2)—N(3)—C(4)	8.4
C(2)—N(3)—C(4)—C(5)	−16.0
N(3)—C(4)—C(5)—C(6)	9.5
C(4)—C(5)—C(6)—N(1)	2.4
C(5)—C(6)—N(1)—C(2)	−10.9
C(6)—N(1)—C(2)—N(3)	6.5

(*b*) Other torsional angles

C(7)—C(5)—C(6)—C(8)	0.3
C(8)—C(6)—C(5)′—C(4)′	3.6
N(1)—C(6)—C(5)′—C(7)′	2.5
N(1)—C(6)—C(8)—O(10)	−23.2
C(5)—C(6)—C(8)—O(9)	−71.8
C(5)—C(6)—C(8)—O(10)	104.9
C(5)′—C(6)—C(8)—O(9)	29.5

C(4)—C(5)—C(7), N(1)—C(6)—C(8), and C(5)′—C(6)—C(8) angles, probably can be explained as the result of the different distortions necessary to minimize interatomic repulsion in the two isomers.

Partial relief of these forces of interatomic repulsion is also achieved by the lengthening of the C(5)—C(6) and C(6)—C(8) bonds. The C(5)—C(6) bond length in the present structure (1.577 Å), while essentially equal to the corresponding value (1.57 Å) in the *cis–anti* isomer, is significantly longer than in most other pyrimidine photodimers (3, 18–21). The C(6)—C(8) bond lengths in this structure (1.555 Å) and the *cis–anti* isomer (1.56 Å) are significantly longer than corresponding values in the orotic acid monohydrate structure (22) (1.498 Å) and in the *trans–syn* photodimer of methylorotate (3) (1.522 Å).

Differences in the interpyrimidine bond lengths in the present structure and in the *trans–syn* orotate photodimer help partially to explain the differences in lability of the two dimers. In the *trans–syn* crystal structure (3), the C(6)—C(6)′ bond, to which both carboxyl groups are bonded, is abnormally lengthened to 1.628 Å, while the C(5)—C(5)′ bond, 1.556 Å, is close to normal length, as are the intrapyrimidine bonds, 1.544 Å. In the present structure the strain induced by overcrowding is distributed more equally; the interpyrimidine bonds (1.585 Å) are essentially the same length as the intrapyrimidine bonds (1.577 Å). If we assume that the C(6)—C(6)′ bond in (nonesterified) *trans–syn* orotate photodimer has a fairly similar length to that observed in the crystal structure of the methyl ester (and the configurations of the dimer acid and ester have been shown to be identical (2)), then the increased lability in neutral and acid media of the orotate photodimer relative to the 5-methylorotate dimer

TABLE 3. Comparison of molecular geometry in the *trans–anti* (*A*) and *cis–anti* (*B*) photodimers of 5-methylorotate. Bond length and bond angle values given here are those showing significant differences in the two structures. Comparable values are shown also from the *trans–anti* thymine photodimer (*C*)

	A	*B*[a]	*C*[b]
N(1)—C(2)	1.326(3) Å	1.36(1) Å	1.334(3) Å
C(2)—N(1)—C(6)	126.4(2)°	122.9(7)°	125.7(2)°
N(1)—C(6)—C(5)	114.0(1)°	111.7(6)°	116.0(2)°
C(4)—C(5)—C(7)	105.4(2)°	108.6(5)°	110.5(2)°
N(1)—C(6)—C(8)	110.0(1)°	104.9(6)°	—
C(5)′—C(6)—C(8)	116.1(1)°	122.1(6)°	—

[a]From ref. 6.
[b]From ref. 18.

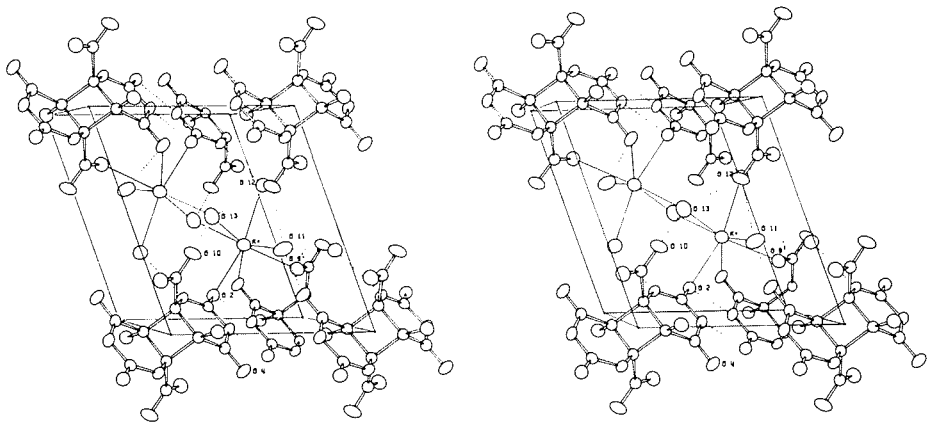

FIG. 2. Stereoscopic view of the packing arrangement drawn by the ORTEP program (23). $K^+\cdots O$ contacts are indicated by single solid lines, hydrogen bonds by dotted lines. Axial directions: $x\rightarrow$, $y\uparrow$, z pointing out of the plane toward the reader.

can be correlated with this longer bond. It is not so easy to understand why, in alkaline solution, the cyclobutane ring is preserved in the case of orotate photodimer (and also a *cis–syn* thymine photodimer (15)), and cleaved in the case of 5-methylorotate photodimer.

The carboxyl groups in the present dimer are both ionized, balancing the two K^+ ions per unit cell, and one would therefore expect delocalization to make the C—O bond lengths equal. The small difference, 0.009 Å, between the observed C(8)—O(9) and C(8)—O(10) bond lengths is possibly not significant, but could be ascribed to different hydrogen bonding patterns at O(9) and O(10) (see below).

The potassium ion is seven-coordinated, by three oxygen atoms from the dimer and by four contacts to water-molecule oxygens. Six of the $K^+\cdots O$ distances are in the range 2.67–2.94 Å, while the seventh is 3.057 Å. There are no other $K^+\cdots O$ distances less than 3.50 Å, and no short contacts to nonoxygen atoms. The six closer oxygens can be described as forming a distorted octahedron, with the seventh oxygen accommodated outside the largest octahedral face. Both the sevenfold coordination of the K^+ ion and the range of $K^+\cdots O$ distances are unexceptional.

Figure 2 gives a stereoscopic view of the packing arrangement and hydrogen bonding, and further geometrical details about the hydrogen bonds are listed in Table 4. All of the available hydrogen atoms are involved in hydrogen bond formation.

The dimer anions are linked into infinite chains along $[10\bar{1}]$ by pairs of hydrogen bonds joining N(3) and O(2) of one dimer to O(2) and N(3) respectively of an adjacent dimer. The pairs of pyrimidine rings joined by hydrogen bonds are coplanar within 0.2 Å. Dimer anions within a chain are also linked through participation of O(2), O(4), and O(9), from adjacent dimers, in each potassium coordination polyhedron.

The coordination polyhedra occur in pairs, sharing an edge of which the mid-point is a centre of symmetry. The only linkage of one dimer chain to another by the potassium coordination polyhedron is indirect, via centrosymmetrically related O(2), O(4), and O(9) atoms at opposite ends of each coordination pair.

TABLE 4. Geometrical details of the hydrogen bonds, *D*—H···*A*

D	*H*	*A*	*D*···*A* (Å)	*D*—H (Å)	H···*A* (Å)	*D*—H···*A* (deg)
N(1)	H(1)	O(12)	2.909	0.80	2.11	173
N(3)	H(3)	O(2)	2.849	0.84	2.04	163
O(11)	H(111)	O(10)	2.786	0.87	1.93	168
O(11)	H(112)	O(4)	2.835	0.76	2.08	169
O(12)	H(121)	O(9)	2.832	0.79	2.05	169
O(12)	H(122)	O(11)	2.711	0.88	1.83	176
O(13)	H(131)	O(10)	2.925	0.80	2.13	172
O(13)	H(132)	O(10)	2.859	0.87	2.03	160

Other cohesive forces are provided by the hydrogen bonds involving water molecules. Adjacent dimer chains in the *xz* plane are linked via O(12), while connections in the *y* direction are via O(11) and O(13).

The appearance of the report (6) on the *cis–anti* photodimer of 5-methylorotate, which followed completion of the present analysis, raises the question of why two different isomers were obtained under apparently very similar experimental conditions. (Both photodimers were prepared by irradiation of frozen aqueous solutions of 5-methylorotic acid, and then converted to the particular salts.) It seems possible that the different dimer may have resulted from differences in the procedure employed for preparation of the ice matrix, or that crystallization of the barium salt led to preferential isolation of one of the minor isomers referred to above. Unfortunately, Cheng *et al.* (6) give no quantitative data on yields or chromatographic behaviour of the crude photodimer solution prior to crystallization.

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