

## The Crystal and Molecular Structure of Propane-1,3-diol Cyclic Phosphate (C<sub>3</sub>H<sub>7</sub>PO<sub>4</sub>)

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The structure of propane-1,3-diol cyclic phosphate (C<sub>3</sub>H<sub>7</sub>PO<sub>4</sub>) has been solved by X-ray diffraction study. Crystals are orthorhombic, space group P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>,  $a = 5.98$ ,  $b = 7.92$ ,  $c = 12.47$  Å; four molecules per unit cell;  $d_{\text{obsd}} = 1.4$  g/cc;  $d_{\text{calcd}} = 1.551$  g/cc. Intensity data were collected visually from Weissenberg photographs. The structure was solved from the Patterson map and several subsequent Fourier maps. Refinement by least squares has proceeded to an  $R$  factor of 10.8 for 374 observed reflections, refining positional and anisotropic thermal parameters. The bond angles around phosphorus are nearly tetrahedral, ranging from 104.5 to 116.6°. The acyclic oxygen atoms of one molecule are hydrogen bonded to the other molecules related by a twofold screw axis, forming helical chains up the  $a$  axis. The O...O distance for this hydrogen bond is 2.44 Å, which is a very short hydrogen bond. The P=O and the P—OH bonds are nearly the same, 1.51 and 1.55 Å. The other P—O distances are 1.56 and 1.58 Å. The rest of the bond distances and angles are quite normal. The average standard deviations are 0.03 Å for bond distances and 0.9° for bond angles.

Cyclic organic phosphates have attracted much attention, particularly the relationship between the rates of hydrolysis and structure. Five-membered cyclic organic phosphates have been shown to hydrolyze at rates 10<sup>6</sup> to 10<sup>8</sup> times faster than noncyclic phosphates.<sup>1-3</sup> Reasons for this have been considered to be (1) ring strain and (2) ease of formation of the pentavalent intermediate due to the fact that the ring bond angles at phosphorus are near 90°.<sup>4-8</sup> Thus the thermodynamic stability of the five-membered cyclic phosphate is low, and there is a low activation energy between the five-membered cyclic phosphate and the trigonal bipyramid intermediate. To test some of the structural aspects presumed to account for the rapid hydrolysis of the five-membered cyclic phosphates, we have studied the structure of some six-membered cyclic phosphates, since six-membered cyclic phosphates are known to have hydrolysis rates essentially the same as their noncyclic analogs. We are here reporting the crystal and molecular structure of one of these.

### Experimental Section

Propane-1,3-diol cyclic phosphate was prepared according to the method described by Khorana, *et al.*<sup>9</sup> Purification and crystallization were accomplished from tetrahydrofuran by addition of ether and cooling. From the crystals formed, several were obtained which were satisfactory for collection of X-ray data. It was necessary to enclose the crystals of capillaries during collection of the intensity data. The density was measured by flotation in a mixture of CCl<sub>4</sub> and benzene. The crystals were soluble in this mixture and only an approximate value for the density was obtained.

The crystal chosen for collection of intensity data was approximately 0.3 mm in diameter and about 1 mm long, somewhat cylindrically shaped, but quite irregular. The crystal was enclosed in a Lindemann glass capillary; Weissenberg and precession photographs were taken with Cu K $\alpha$  radiation to determine the

TABLE I

$a$ , Å	5.98 ± 0.01
$b$ , Å	7.92 ± 0.01
$c$ , Å	12.47 ± 0.01
Space group	P2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>
Molecules per unit cell	4
Measured $d$ , g cm <sup>-3</sup>	1.40
Calculated $d$ , g cm <sup>-3</sup>	1.55
Observed reflections	374
$F(000)$	288
Linear absorption coefficient for Cu K $\alpha$ radiation, cm <sup>-1</sup>	36.0

space group and lattice parameters (Table I). The crystal was found to be orthorhombic. Systematic absences occurred for  $h00$ ,  $0k0$ , and  $00l$  reflections, when  $h$ ,  $k$ , and  $l \neq 2n$ , respectively, which indicates space group P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>.

Multiple film Weissenberg photographs were taken using Cu K $\alpha$  radiation. The intensities were measured visually by comparing them with a standard intensity strip. The films were originally indexed on a diagonal axis and an appropriate transformation was applied to give indices in the orthorhombic cell. Lorentz and polarization corrections were applied using data reductions program for the IBM 1620 computer.<sup>10</sup> This gave a preliminary scale factor and an overall temperature factor. No absorption corrections or corrections for extinction were made, since these did not appear necessary considering the size and shape of the crystals.

For structure factor calculations, form factors were used from the literature;<sup>11</sup> anomalous terms of the form factors were not included.

### Results and Discussion

**Structure Determination.**—Solution of the structure was accomplished by location of the phosphorus positions from the Harker section of the Patterson map, and subsequent Fourier syntheses from phases based on this partial structure. From the first Fourier, after location of the correct phosphorus positions,<sup>12</sup> three oxygen were found and the rest of the structure was found with two more three-dimensional Fourier maps. The  $R$  factor at this stage was 25%, and refinement was started.

(10) All programs used except the least-squares refinement were from Montana State University's crystallographic Program Library written for the IBM 1620 Model II by C. N. Caughlan, C. T. Li, G. W. Svetich, K. D. Watenpaugh, and R. D. Witters.

(11) "International Tables for Crystallography," Vol. III, Kynoch Press, Birmingham, England, 1962, Table 3.3 1A, p 202.

(12) Several false starts were made on the structure solution. The difficulty was location of the correct phosphorus-phosphorus vectors in the Patterson. Once the correct phosphorus position was found the solution and refinement proceeded smoothly.

(1) J. Kumamoto and F. H. Westheimer, *J. Amer. Chem. Soc.*, **77**, 2515 (1955).

(2) J. Kumamoto, J. R. Cox, Jr., and F. H. Westheimer, *ibid.*, **78**, 4858 (1956).

(3) J. R. Cox, Jr., R. E. Wall, and F. H. Westheimer, *Chem. Ind. (London)*, 929 (1959).

(4) P. C. Haake and F. H. Westheimer, *J. Amer. Chem. Soc.*, **83**, 1102 (1961).

(5) M. Ponar, E. R. Kaiser, and F. H. Westheimer, *ibid.*, **85**, 602 (1963).

(6) F. Covitz and F. H. Westheimer, *ibid.*, **85**, 1774 (1963).

(7) A. Eberhard and F. H. Westheimer, *ibid.*, **87**, 253 (1965).

(8) D. H. Usher, E. A. Dennis, and F. H. Westheimer, *ibid.*, **87**, 2320 (1965).

(9) H. G. Khorana, G. M. Tener, R. S. Wright, and J. F. Moffat, *ibid.*, **79**, 430 (1957).

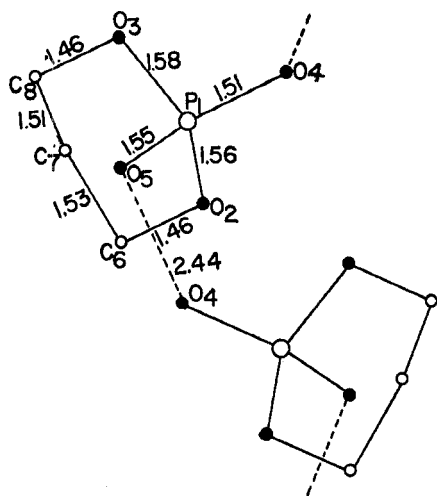


Figure 1.—Part of [010] projection of the structure of propane-1,3-diol cyclic phosphate and bond distances; the standard deviations are 0.02–0.05 Å.

Five cycles of refinement using Ahmed's<sup>13</sup> block-diagonal least-squares program, refining the atomic positions and individual temperature factors, reduced the *R* factor to 16.0%. The final nine cycles of refinement, refining positional parameters and individual anisotropic thermal parameters, reduced the *R* factor to 10.8%. A Hughes weighting scheme was used in the refinement.<sup>14</sup>

The final atomic positions with their standard deviations are given in Table II. The listing of anisotropic

TABLE II  
ATOMIC PARAMETERS AND THEIR STANDARD DEVIATIONS

Atom	<i>x</i>	<i>y</i>	<i>z</i>
P(1)	0.2019 (8) <sup>a</sup>	0.0610 (5)	-0.0479 (3)
O(2)	0.3822 (20)	-0.0795 (14)	-0.0316 (8)
O(3)	0.0161 (17)	-0.0250 (16)	-0.1194 (9)
O(4)	0.1046 (24)	0.1130 (20)	0.0593 (8)
O(5)	0.3001 (22)	0.2043 (16)	-0.1188 (9)
C(6)	0.4671 (29)	-0.1756 (32)	-0.1224 (14)
C(7)	0.2617 (31)	-0.2503 (21)	-0.1774 (18)
C(8)	0.0924 (31)	-0.1197 (31)	-0.2125 (15)

<sup>a</sup> The number in parentheses is the standard deviation and refers to the least significant digits.

thermal parameters, the principal axis of thermal vibration, and the final set of observed and calculated structure factors have been deposited with the American Documentation Institute.<sup>15</sup>

Table III gives the bond angles, with their standard deviation. Figure 1 shows a part of the [010] projection of the structure, giving an indication of the hydrogen-bonding arrangement and the interatomic distances.

Several interesting and significant features are apparent from the figures and tables. The P–O distances differ only slightly, the two esterified oxygens being 1.56 and 1.58 Å from the phosphorus atom, while the

(13) F. R. Ahmed, Structure Factor and Block-Diagonal Least-Squares Program, Division of Pure Physics, National Research Council, Ottawa, Ontario, Canada. This was adapted for use on the SDS Sigma 7 computer by Eric Enwall and David Smith.

(14) E. W. Hughes, *J. Amer. Chem. Soc.*, **63**, 1737 (1941).

(15) Document NAPS-00897 from ASIS National Auxiliary Publications Service, % CCM Information Corp., 909 3rd Ave., New York, N. Y., 10022. A copy may be secured by citing the document number and by remitting \$1.00 for microfilm or \$3.00 for photocopies. Advance payment is required. Make checks or money orders payable to CCMI-NAPS.

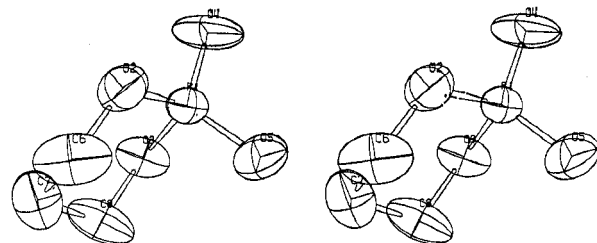


Figure 2.—The structure of the propane-1,3-diol cyclic phosphate molecule showing the chair form. P(1) is 0.17 Å below plane; O(2) and O(3) are 0.2 Å above plane; C(6) and C(8) are 0.24 and 0.25 Å below plane; C(7) is 0.25 Å above best least-squares plane formed by P(1)–O(2)–O(3)–C(6)–C(7)–C(8). The numbers for figures and on tables are consecutive and not consistent with the chemical nomenclature of propane-1,3-diol cyclic phosphate. This diagram was drawn using computer program ORTEP, written by Carrol K. Johnson of Oak Ridge National Laboratory, and adapted for computation at University of Washington.

TABLE III  
BOND ANGLES AND THEIR STANDARD DEVIATIONS

Atoms	Angle, degree
O(2)–P(1)–O(3)	104.6 (5) <sup>a</sup>
O(2)–P(1)–O(4)	110.1 (5)
O(2)–P(1)–O(5)	109.5 (6)
O(3)–P(1)–O(4)	110.2 (6)
O(3)–P(1)–O(5)	105.1 (7)
O(4)–P(1)–O(5)	116.6 (7)
P(1)–O(2)–C(6)	120.8 (9)
P(1)–O(3)–C(8)	116.9 (11)
O(2)–C(6)–C(7)	105.8 (14)
C(6)–C(7)–C(8)	113.8 (14)
C(7)–C(8)–O(3)	109.4 (16)

<sup>a</sup> The number in parentheses is the standard deviation and refers to the least significant digits.

shorter P–O distances are 1.51 and 1.55 Å. It is assumed that O(5) is the –OH oxygen, while P–O(4) is the phosphoryl bond, although its identity has nearly disappeared. The relatively long P–O(4) distance is probably due to the very strong hydrogen bond, which has significantly lengthened this distance. The distance between O(4) and O(5)' is only 2.44 Å, which is a very short hydrogen-bonded distance. The molecules form a helical chain up the *a* axis through these hydrogen bonds. The sum of the P–O bond distances is 6.20 Å. This compares with 6.14 Å in dibenzyl phosphate,<sup>16</sup> 6.20 Å in *L*-α-glycerolphosphocholin,<sup>17</sup> 6.25 Å in barium diethyl phosphate.<sup>18</sup> Most organic phosphate esters have the sum of P–O distances between 6.13 and 6.23 Å.

The C–O and the C–C distances are normal. The O–P–O angles are nearly tetrahedral and the P–O–C angles are about 120°, which is considered normal for such esterified oxygens.<sup>19</sup>

Figure 2 shows that the ring is in the chair form. The dihedral angle between the best least-squares plane through O(2), O(3), C(6), and C(8) and the plane defined by P(1), O(2), and O(3) is 40.4°. The corresponding dihedral angle with the plane of C(6), C(7), and C(8) is 54.2°.

(16) J. D. Dunitz and J. S. Rollet, *Acta Cryst.*, **9**, 327 (1956).

(17) S. Abrahamsson and I. Pascher, *ibid.*, **21**, 79 (1966).

(18) Y. Kyogogu and Y. Iitaka, *ibid.*, **21**, 79 (1966).

(19) M. G. Newton, J. R. Cox, Jr., and J. A. Bertrand, *J. Amer. Chem. Soc.*, **88** 1503 (1966); D. Swank, C. N. Caughlan, F. Ramirez, O. P. Madan, and C. P. Smith, *ibid.*, **89**, 6503 (1967); C. N. Caughlan and M. Ul-Haque, *Inorg. Chem.*, **6**, 1998 (1967).

Table IV gives the dihedral angles of the O-P-O planes and also the angle the O(4)-P-O(5) plane makes with the best least-squares plane of the ring.

TABLE IV  
DIHEDRAL ANGLE BETWEEN PLANES IN  
PROPANE-1,3-DIOL CYCLIC PHOSPHATE

Plane	Angle, degree
[O(4)-P(1)-O(5)] and [O(2)-P(1)-O(3)]	91.7
[O(4)-P(1)-O(5)] and [O(5)-P(1)-O(3)]	122.4
[O(4)-P(1)-O(5)] and [O(4)-P(1)-O(2)]	54.5
[O(3)-P(1)-O(5)] and [O(2)-P(1)-O(4)]	90.1
[O(2)-P(1)-O(5)] and [O(3)-P(1)-O(4)]	88.5
[O(4)-P(1)-O(5)] and [P(1)-O(2)-C(6)-C(7)-C(8)-O(3)]	92.3

Thus we have found that this six-membered cyclic phosphate has essentially no ring strain and has normal

tetrahedral bond angles around the phosphorus. These structural features should contribute to the stability of this molecule and give it a normally high activation energy for the formation of the five coordinated intermediate, thus accounting for the relatively slow rate of hydrolysis compared with five-membered cyclic phosphates.

**Registry No.**—Propane-1,3-diol cyclic phosphate, 13507-10-3.

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## Structure and Absolute Configuration of Pulchellin. Crystal and Molecular Structure of 3-Bromoanhydrodehydrodihropulchellin<sup>1,2</sup>

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The structure and relative configuration of the sesquiterpene lactone pulchellin was established partially by X-ray crystallographic analysis of 3-bromoanhydrodehydrodihropulchellin (4), in which the asymmetric centers at C-2 and C-4 have been destroyed and the center at C-1 has been epimerized. Compound 4 crystallizes in an orthorhombic space group  $P2_12_12_1$  with lattice parameters  $a = 8.368$ ,  $b = 14.342$ , and  $c = 25.161$  Å. There are eight molecules in the unit cell and two molecules in the asymmetric unit. Bromine positions were located from a three-dimensional Patterson function. The first three-dimensional Fourier electron density map was calculated. The rest of the structure was found from four additional three-dimensional Fourier maps, and the structure was refined by anisotropic full-matrix least-squares refinement to a final  $R$  of 6.6%. The complete stereochemistry and absolute configuration of pulchellin was established by correlation with aromaticin and is in agreement with the hypothesis of a biogenetic pathway involving the guaianolide gaillardin.

Pulchellin, the main sesquiterpene lactone found in coastal races of *Gaillardia pulchella* Foug., has been formulated as 1,<sup>6</sup> the absolute configuration at C-2 and C-4 being based on applications of the Hudson-Klyne rule<sup>6</sup> and the Horeau method.<sup>7</sup> In this communication we present chemical and crystallographic evidence for its complete structure 2a.

Efforts at identification of some of the other asymmetric centers by chemical methods having proved unavailing, we decided to attack the problem by X-ray crystallography. However, attempts to prepare esters of pulchellin or dihydropulchellin containing heavy atoms consistently resulted in compounds which were

unsuitable for this purpose. Hence we decided to use a bromo derivative 4,<sup>8</sup> available (see Experimental Section) from dihydroanhydrodehydrodihropulchellin (3),<sup>6</sup> even though the centers at C-1 and C-3 were no longer present and the center at C-1 might have suffered epimerization as a consequence of the introduction of a carbonyl group at C-2.

**Crystal Data.**—3-Bromoanhydrodehydrodihropulchellin (4),  $C_{15}H_{19}O_3Br$ , mol wt 326.9, was orthorhombic with lattice parameters  $a = 8.368 \pm 0.005$ ,  $b = 14.342 \pm 0.006$ , and  $c = 25.161 \pm 0.006$  Å. The systematic absences were confined to  $h00$ ,  $0k0$ , and  $00l$  for  $h$ ,  $k$ , and  $l/2n$ ; the space group was therefore  $P2_12_12_1$ :  $V = 3020$  Å<sup>3</sup>,  $d_m = 1.432$  g cm<sup>-3</sup>,  $Z = 8$ ,  $d_c = 1.437$  g cm<sup>-3</sup>. The linear absorption coefficient for Cu K $\alpha$  radiation was  $\mu = 40.8$  cm<sup>-1</sup>. The total number of electrons in the unit cell was  $F(000) = 1344$ .

**Determination of the Structure.**—Diffraction data were collected on a crystal of dimensions  $0.10 \times 0.12 \times 1.2$  mm. The crystal was mounted with the  $a$  axis parallel to the  $\phi$  axis of the goniostat. Inten-

(1) Constituents of *Gaillardia* Species. X. Previous paper: H. Yoshioka, T. J. Mabry, N. Dennis, and W. Herz, *J. Org. Chem.*, **35**, 627 (1970).

(2) Supported in part by grants from the U. S. Public Health Service (GM-05814 and GM-12408).

(3) Florida State University.

(4) Montana State University.

(5) To whom correspondence should be addressed.

(6) W. Herz, K. Ueda, and S. Inayama, *Tetrahedron*, **19**, 483 (1963). Assignment of the secondary methyl group to C-10 rather than C-6 was based on biogenetic grounds. Since the publication of this paper, the absolute configuration of the C-7 side chain and the C-10 methyl group in a number of related compounds from *Helenium* and *Gaillardia* species has been shown to be  $\beta$  and  $\alpha$ , respectively. It was plausible to assume that this would also be true for pulchellin.

(7) W. Herz and H. B. Kagan, *J. Org. Chem.*, **32**, 216 (1967).

(8) Configurations of compounds, although unknown at the time, are depicted in the light of our final knowledge.