

## The Crystal Structure of *myo*-Inositol-2-phosphate Monohydrate

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The crystal and molecular structure of *myo*-inositol-2-phosphate monohydrate ( $C_6H_{13}O_9P \cdot H_2O$ ) has been determined from X-ray diffraction data. It crystallizes in the monoclinic space group  $P2_1/c$  with four molecules in a unit cell of dimensions  $a = 6.810$  (2),  $b = 16.548$  (4),  $c = 12.536$  (5) Å and  $\beta = 133.26$  (2)°. The intensities of 1680 reflections were measured on a four-circle automated diffractometer using Cu  $K\alpha$  radiation. The structure was refined by full-matrix least-squares methods to give  $R = 0.045$  for all reflections. The ring conformation in the molecule is found in the expected chair form, with one axial ester oxygen and five equatorial hydroxyl groups. The phosphate does not obey the  $m$  symmetry of the cyclohexane ring, nor does the hydrogen-bonding scheme. All of the hydroxyls are hydrogen-bond donors to acceptors situated on that side of the ring to which the phosphate is attached. The water molecule participates in four hydrogen bonds in an approximately tetrahedral arrangement.

### Introduction

*myo*-Inositol-2-phosphate is the terminal monophosphate produced by the enzymatic hydrolysis of phytic acid by plant enzymes (Tomlinson & Ballou, 1962), and exhibits more resistance to acid hydrolysis than its isomers (Cosgrove, 1963). *myo*-Inositol-1-phosphate occurs in phosphoinositides and can be produced from *myo*-inositol-2-phosphate by acid-catalyzed isomerization *via* a cyclic intermediate (Pizer & Ballou, 1959). To what extent this chemical chain is dependent upon the conformational and hydrogen-bonding properties of the molecule is uncertain. A precise description of these parameters was sought to help clarify their role in its chemistry.

### Experimental

*myo*-Inositol-2-phosphate monohydrate was prepared by the enzymatic hydrolysis of phytate according to the

procedure of McCormick & Carter (1952). White, acicular crystals elongated about **b** were obtained by cooling an ethanol–water solution to  $\sim 5^\circ\text{C}$ . Many of the crystals gave diffraction patterns showing extensive streaking. Oscillation and Weissenberg photographs showed monoclinic symmetry with systematic absences  $0k0$  ( $k = 2n + 1$ ) and  $h0l$  ( $l = 2n + 1$ ), uniquely determining that the crystal belongs to space group  $P2_1/c$ . The crystal used for collecting diffraction data had a length of 0.3 mm and cross-section of  $0.05 \times 0.02$  mm and was mounted on an automated FACS I Picker diffractometer with its **b** axis nearly parallel to the  $\varphi$  axis. The cell dimensions were determined from a least-squares analysis of the setting angles for 12 centered reflections ( $2\theta$  ranged from  $36$  to  $61^\circ$ ) measured on the diffractometer using the Picker DOS Software System (1972). Graphite-monochromated Cu  $K\alpha$  radiation was used throughout the analysis. Crystal data are given in Table 1. Integrated intensities were measured using a  $\theta:2\theta$  scan over a  $1.5^\circ$  range with a scan speed of  $1^\circ \text{min}^{-1}$  in  $2\theta$ . The background count was accumulated for 30 s at each end of the scan range. Three standard reflections, which were monitored after every 40 reflections, fluctuated within a 2% range during the data collection. The intensity data were corrected by means of the observed variations in the standards (Shiono, 1971a). All of the 1680 independent reflections with  $2\theta \leq 130^\circ$  were measured. As the intensities were being collected, the data were reduced simultaneously to structure amplitudes using the appropriate Lorentz–polarization factor for graphite-monochromated ( $2\theta_m = 26.16^\circ$ ) radiation (Picker DOS Software System, 1972). Of the independent reflections, 196 reflections were considered to be unobserved when  $|F| \leq 6\sigma(F)$  where  $|F|$  is the structure amplitude and  $\sigma(F)$  is given by  $(\frac{1}{2} L_p |F|) \sigma(I)$ ;  $L_p$  is the Lorentz–polarization factor,  $\sigma(I) = [I_t + K^2 B]^2$ ,  $I_t = I - B_t$ ,  $B_t = KB$ ,  $B = (b_1 + b_2)$ ,  $K = t_1/2t_2$ ,  $I_t = (10S + 5)$ ,  $b_1 = (10C_1 + 5)$ ,  $b_2 = (10C_2 + 5)$ ,

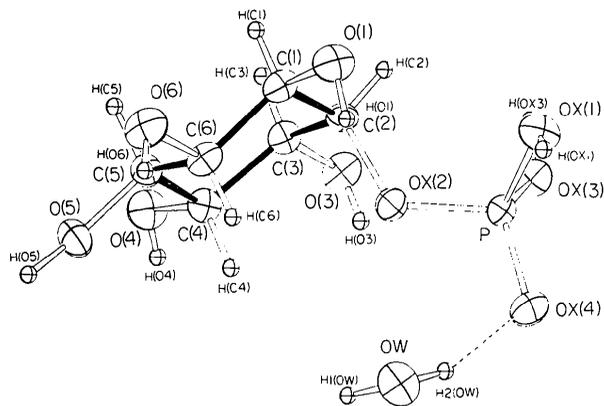


Fig. 1. A thermal-ellipsoid plot (Johnson, 1965) at the 50% probability level of *myo*-inositol-2-phosphate monohydrate showing the numbering scheme of the atoms.

$S$  = the number of decacounts accumulated during the scan requiring time  $t_1$ , and  $C_1$  and  $C_2$  = the background decacounts accumulated in time  $t_2$  at either end of the scan range. Absorption and extinction corrections were not applied to the data.

Table 1. *Crystal data*  
for *myo*-inositol-2-phosphate monohydrate

$C_6H_6(OH)_5 \cdot H_2PO_4 \cdot H_2O$	M.W. 278.18
$a = 6.810 (2) \text{ \AA}$	$\lambda(\text{Cu } K\alpha) = 1.5418 \text{ \AA}$
$b = 16.548 (4)$	$\mu(\text{Cu } K\alpha) = 28.8 \text{ cm}^{-1}$
$c = 12.536 (5)$	$\rho_o = 1.791 \text{ g cm}^{-3}$ (by flotation in a mixture of bromoform and n-hexane at 20°C)
$\beta = 133.26 (2)^\circ$	$\rho_c = 1.795 \text{ g cm}^{-3}$
$Z = 4$	m.p. $\approx 190^\circ$ (decomposed)
$V = 1028.8 \text{ \AA}^3$	
Space group: $P2_1/c$ from systematic absences $0k0$ for $k = 2n+1$ , $h0l$ for $l = 2n+1$	

### Structure determination and refinement

After the structure amplitudes were normalized to  $E$  values by means of a Wilson plot, the position of the

phosphorus atom was determined from a three-dimensional sharpened origin-removed Patterson function (Shiono, 1971*b*) synthesized with the  $(E^2 - 1)$  coefficients of 1484 observed reflections. Structure factors calculated with the contribution from the phosphorus atom alone gave an  $R$  value of 0.47. The electron density map phased on the phosphorus atom revealed oxygen atoms in the phosphate group and part of the cyclohexane ring. All remaining light atoms except for hydrogen atoms were then located unambiguously from a difference Fourier synthesis. One cycle of block-diagonal least-squares refinement on the IBM 1130 (Shiono, 1971*a*) gave an  $R$  value of 0.29 for all reflections, which was reduced to 0.10 by a full-matrix isotropic least-squares cycle. At this stage, all hydrogen atoms could be located in a difference Fourier map. Positional parameters for the hydrogen atoms were included as variables in subsequent cycles of refinement. However, the hydrogen thermal parameters were not refined but were set equal to those of atoms to which the hydrogen atoms were bonded. The refinement process was continued until no parameter shifted

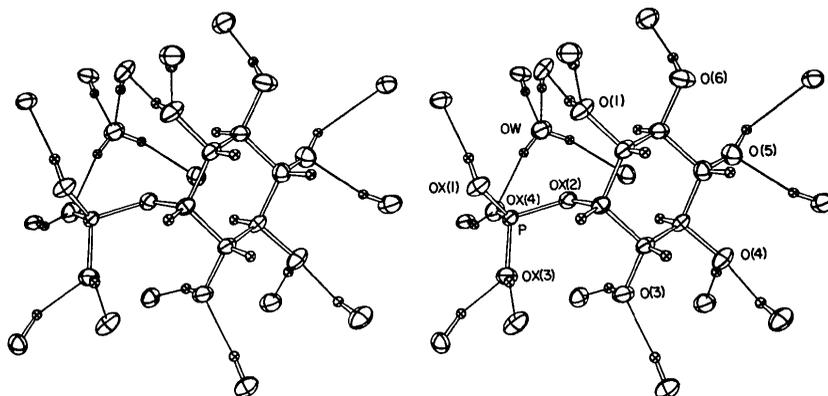


Fig. 2. A stereo drawing of the molecule and its closest neighbors.

Table 2. *Atomic parameters and their e.s.d.'s*

Fractional coordinates are  $\times 10^3$  for hydrogen atoms,  $\times 10^4$  for other atoms. Thermal parameters,  $\times 10^4$ , are in the form  $\exp[-(h^2\beta_{11} + \dots + 2kl\beta_{23})]$ .

	$x$	$y$	$z$	$\beta_{11}$	$\beta_{22}$	$\beta_{33}$	$\beta_{12}$	$\beta_{13}$	$\beta_{23}$
P	7947 (1)	1024 (0.3)	4768 (0.5)	125 (3)	14 (0.3)	46 (0.8)	0 (0.5)	56 (1)	1 (0.3)
OX(1)	6352 (3)	1690 (1)	4769 (2)	205 (7)	21 (0.7)	95 (2)	0 (2)	110 (4)	-4 (0.9)
OX(2)	7019 (3)	1045 (0.8)	3212 (2)	179 (7)	17 (0.6)	57 (2)	-2 (1)	72 (3)	1 (0.8)
OX(3)	10930 (3)	1306 (1)	5940 (2)	155 (7)	21 (0.7)	58 (2)	-6 (2)	56 (3)	0 (0.9)
OX(4)	7568 (3)	197 (1)	5027 (2)	249 (7)	19 (0.6)	81 (2)	-3 (2)	103 (3)	5 (0.9)
C(1)	4619 (4)	2026 (1)	1218 (3)	168 (9)	16 (0.8)	70 (3)	9 (2)	84 (5)	8 (1)
C(2)	7337 (4)	1772 (1)	2686 (2)	159 (9)	13 (0.8)	57 (3)	-6 (2)	69 (4)	-2 (1)
C(3)	9344 (4)	1586 (1)	2538 (2)	139 (8)	17 (0.8)	58 (3)	-3 (2)	65 (4)	1 (1)
C(4)	8242 (5)	990 (1)	1307 (3)	158 (9)	18 (0.8)	68 (3)	-2 (2)	85 (5)	-1 (1)
C(5)	5536 (5)	1273 (1)	-113 (2)	203 (9)	17 (0.8)	53 (3)	-4 (2)	71 (4)	-2 (1)
C(6)	3521 (4)	1384 (1)	43 (2)	134 (8)	18 (0.8)	57 (3)	5 (2)	54 (4)	7 (1)
O(1)	2741 (3)	2231 (1)	1346 (2)	216 (7)	21 (0.7)	102 (2)	15 (2)	121 (4)	5 (1)
O(3)	11834 (3)	1311 (1)	3893 (2)	141 (6)	23 (0.7)	69 (2)	1 (2)	63 (3)	5 (1)
O(4)	10087 (4)	940 (1)	1119 (2)	251 (8)	24 (0.7)	104 (3)	8 (2)	137 (4)	1 (1)
O(5)	4595 (3)	684 (1)	-1206 (2)	255 (7)	22 (0.7)	62 (2)	-3 (2)	83 (4)	-8 (1)
O(6)	1023 (3)	1635 (1)	-1326 (2)	160 (7)	26 (0.7)	69 (2)	8 (2)	47 (3)	8 (1)
OW	2833 (4)	-478 (1)	2232 (2)	227 (8)	31 (0.8)	89 (2)	3 (2)	99 (4)	6 (1)

Table 2 (cont.)

H(C1)	489 (5)	250 (2)	98 (3)
H(C2)	800 (5)	219 (2)	335 (3)
H(C3)	979 (5)	211 (2)	238 (3)
H(C4)	802 (5)	47 (2)	158 (3)
H(C5)	571 (5)	182 (2)	-46 (3)
H(C6)	329 (5)	90 (2)	33 (3)
H(O1)	212 (6)	176 (2)	135 (3)
H(O3)	1164 (6)	90 (2)	408 (3)
H(O4)	1086 (6)	54 (2)	1456 (4)
H(O5)	316 (6)	36 (2)	-215 (3)
H(O6)	-23 (6)	127 (2)	-167 (3)
H(OX1)	489 (6)	155 (2)	444 (3)
H(OX3)	1110 (5)	180 (2)	592 (3)
H1(O $\bar{W}$ )	339 (6)	-59 (2)	178 (4)
H2(O $\bar{W}$ )	417 (6)	-35 (2)	314 (4)

by more than 1% of its estimated standard deviation. The final cycle gave an  $R$  value of 0.045 for all reflections and 0.041 for 1484 observed reflections. In the refinement, the Hughes (1941) weighting scheme was employed, with  $\sigma = F/11.0$  for  $F > 11.0$ ,  $\sigma = 1$  for  $F \leq 11.0$  and zero weight for unobserved reflections. The function minimized was  $\sum w(|F_o| - k|F_c|)^2$  where  $k$  is a single scale factor and  $w = 1/\sigma^2$ . Atomic form factors for P, O and C were taken from *International Tables for X-ray Crystallography* (1962) and hydrogen scattering factors were those of Stewart, Davidson & Simpson (1965).

The final positional and thermal parameters, and their estimated standard deviations are given in Table 2.\*

\* A list of observed and calculated structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30434 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

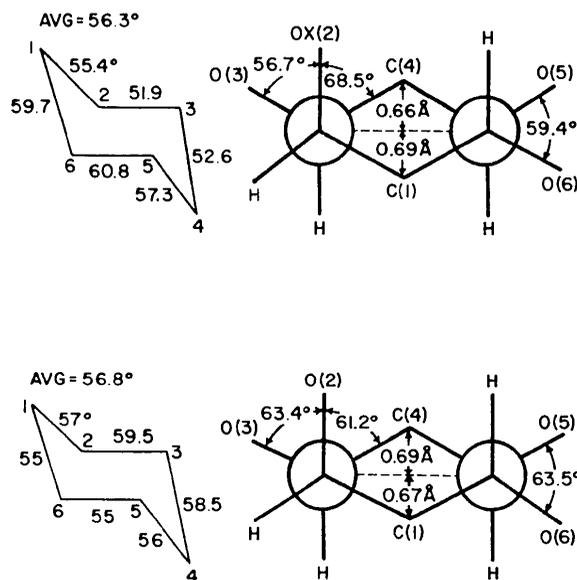


Fig. 3. Conformational angles for *myo*-inositol (lower diagram) and the *myo*-inositol moiety in *myo*-inositol-2-phosphate monohydrate (upper diagram).

## Discussion

The molecular configuration and conformation of *myo*-inositol-2-phosphate monohydrate are illustrated in Fig. 1. The ring conformation in the molecule, like that of *myo*-inositol (Rabinowitz & Kraut, 1964) and *myo*-inositol dihydrate (Lomer, Miller & Beevers, 1963), is found in the chair form, and all the hydroxyl groups are equatorial except for the ester oxygen atom OX(2). The mirror symmetry through C(2), OX(2), C(5) and O(5), which should be exact for the unesterified free *myo*-inositol molecule is approximately maintained in this structure if P, OX(1), OX(3) and OX(4) are not included. The least-squares planes for the planar part of the cyclohexane ring and the plane passing through C(2), OX(2), C(5) and O(5) are listed in Table 3. The dihedral angle between these two planes is  $89.8^\circ$ . The phosphate group is slightly rotated about the C(2)-OX(2) bond. This is probably due to the asymmetrical hydrogen-bonding environment around the phosphate group in the crystal as shown in Fig. 2. The torsion angles around the C(2)-OX(2) bond and OX(2)-P bond of one conformer are: C(1)-C(2)-OX(2)-P  $-123.7^\circ$ ; C(3)-C(2)-OX(2)-P  $115.3^\circ$ ; C(2)-OX(2)-P-OX(4)  $-175.5^\circ$ ; C(2)-OX(2)-P-OX(1)  $59.1^\circ$ ; and C(2)-OX(2)-P-OX(3)  $-53.0^\circ$ . The conformation angles in *myo*-inositol (Rabinowitz & Kraut, 1964) and the *myo*-inositol moiety for *myo*-inositol-2-phosphate monohydrate are compared in Fig. 3.

Table 3. The least-squares planes for two mutually perpendicular planes in *myo*-inositol-2-phosphate monohydrate

Coefficients  $\times 10^4$  in  $Ax + By + Cz - D = 0$ , referred to the crystallographic axes ( $x, y, z$  in Å). Atoms in bold type are included in the calculation of least-squares planes. Displacements from the plane are in Å  $\times 10^3$ .

Plane 1:  $A = 5120, B = 6903, C = -7232, D = 27949$

**C(1) 26, C(3) -26, C(4) 26, C(6) -26, C(2) -647, C(5) 693, O(1) -511, OX(2) -2065, O(3) -699, O(4) 782, O(5) 682, O(6) 632, H(C1) 870, H(C2) -540, H(C3) 871, H(C4) -897, H(C5) 1691, H(C6) -917**

Plane 2:  $A = 8372, B = 2615, C = -2241, D = 2653$

**OX(2) -5, C(2) 10, C(5) -15, O(5) 10, C(1) -1238, C(3) 1276, C(4) 1251, C(6) -1256, O(1) -2433, O(3) 2435, O(4) 2378, O(6) -2404, H(C1) -1220, H(C2) 23, H(C3) 1350, H(C4) 1273, H(C5) -51, H(C6) -1257, H(O1) -2582, H(O3) 2451, H(O4) 2895, H(O5) -407, H(O6) -2868, P 96, OX(1) -1102, OX(3) 1345, OX(4) 165**

Intramolecular bond distances and angles with their associated estimated standard deviations are shown in Fig. 4. The C-C bond lengths which range from 1.512 to 1.531 Å with a mean of 1.524 Å are not significantly different from those of *myo*-inositol (Rabinowitz & Kraut, 1964), where the range is 1.508 to 1.533 Å with a mean of 1.521 Å. The C-OH bonds vary from 1.418 to 1.434 Å. The shortest bond, C(6)-O(6) at 1.418 Å, is associated with the only hydroxyl which donates its hydrogen but does not accept a hydrogen bond. A

similar tendency is observed in *epi*-inositol (Jeffrey & Kim, 1971). The phosphate group is essentially tetrahedral, with O-P-O angles ranging from  $104.3$  to  $115.7^\circ$ . The distances P-OX(1) and P-OX(3),  $1.548$  and  $1.553 \text{ \AA}$  respectively, are normal for phosphorus-hydroxyl bonds. The P-OX(4) bond,  $1.468 \text{ \AA}$ , exhibits additional multiple-bond character expected for the nonprotonated oxygen.

The molecules are linked by a system of intermolecular hydrogen bonds: four of the equatorial and one of the phosphate OH groups are involved both as donors and acceptors. The unprotonated oxygen in

the phosphate group accepts two hydrogen bonds, while the remaining equatorial hydroxyl and phosphate OH groups act as donors only. The hydrogens and the non-bonding oxygen electrons of the water molecule all participate in hydrogen bonds which form an approximately tetrahedral arrangement. The average of these angles is  $108.9^\circ$ . The hydrogen-bonding scheme around the molecule and overall packing scheme in the crystal are illustrated in Figs. 2 and 5. The hydrogen-bond distances and angles are given in Table 4. The intermolecular O-H...O distances range from  $2.535$  to  $2.907 \text{ \AA}$ .

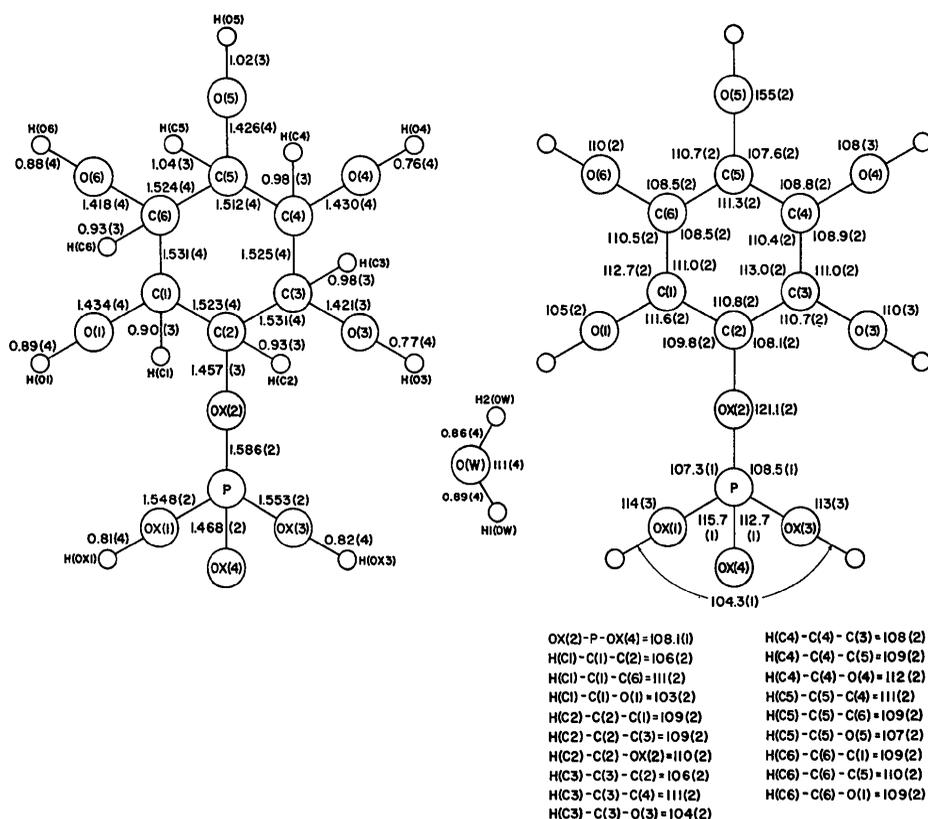


Fig. 4. Interatomic distances ( $\text{\AA}$ ) and angles ( $^\circ$ ) in the molecule. The estimated standard deviations are given in parentheses.

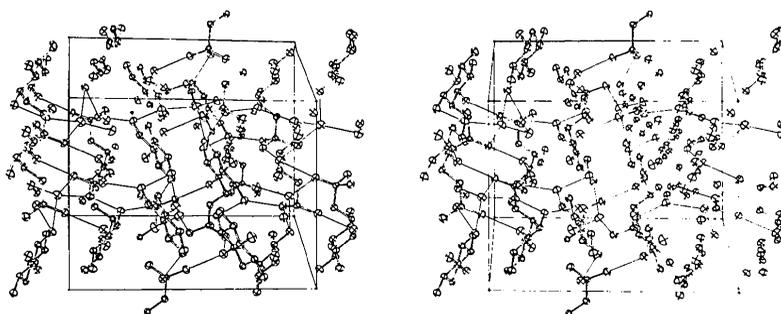


Fig. 5. Stereo diagram of *myo*-inositol-2-phosphate monohydrate as drawn by *ORTEP* (Johnson, 1965). View is down the *a* axis with hydrogen bonding shown by thin lines.

Table 4. *Hydrogen-bond distances and angles in myo-inositol-2-phosphate monohydrate*

<i>i</i>	<i>j</i>	<i>k</i>	<i>d</i> <sub>o...o</sub>	<i>d</i> <sub>o...H</sub>	$\angle_{ijk}$	Symmetry operation of <i>k</i> *
O(1)	H(O1)	O(4)	2.684 Å	1.82 Å	166°	455·1
O(1)	H(OX3)	OX(3)	2.603	1.82	159	454·3
O(3)	H(O3)	OX(4)	2.733	2.00	161	756·2
O(3)	H(OX1)	OX(1)	2.537	1.74	173	655·1
O(4)	H(O4)	OW	2.716	1.95	177	655·1
O(4)	H(O1)	O(1)	2.684	1.82	166	655·1
O(5)	H(O5)	OX(3)	2.802	2.35	106	454·1
O(5)	H1(OW)	OW	2.815	1.95	165	655·2
O(6)	H(O6)	OW	2.787	1.91	175	555·2
OX(1)	H(OX1)	O(3)	2.537	1.74	173	455·1
OX(3)	H(OX3)	O(1)	2.603	1.82	159	655·3
OX(3)	H(O5)	O(5)	2.802	2.35	106	656·1
OX(4)	H2(OW)	OW	2.905	2.07	163	555·1
OX(4)	H(O3)	O(3)	2.733	2.00	161	756·2
OW	H(O4)	O(4)	2.717	1.95	177	455·1
OW	H(O6)	O(6)	2.787	1.91	175	555·2
OW	H1(OW)	O(5)	2.815	1.95	165	655·2
OW	H2(OW)	OX(4)	2.905	2.07	163	555·1

\* Reference point is atom *i* at 555·1. The first three digits code a lattice translation, e.g. 466·1 is  $-a+b+c$  from 555·1. The last digit indicates one of the following operations:

- 1:  $x, y, z$                     2:  $\bar{x}, \bar{y}, \bar{z}$   
 3:  $x, \frac{1}{2}-y, \frac{1}{2}+z$

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Center of University of Pittsburgh were used throughout this research.

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## The Crystal and Molecular Structure of Diaquo- $\mu$ -triethylenetetraminehexaacetatodichromium(III) hexahydrate, [Cr<sub>2</sub>TTHA·2H<sub>2</sub>O]·6H<sub>2</sub>O

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The title compound crystallizes in space group  $P2_1/c$  with  $a = 8.634$  (5),  $b = 12.606$  (6),  $c = 13.867$  (7) Å,  $\beta = 99.67$  (8)°,  $D_m = 1.63$  (1),  $D_c = 1.64$  g cm<sup>-3</sup> for  $Z = 2$ . The structure has been determined by direct and Fourier methods, refined to  $R = 0.043$  from diffractometer data (1952 observed reflexions), and consists of discrete binuclear units which are required crystallographically to be centrosymmetric. The TTHA ion (triethylenetetraminehexaacetate) acts as a pentadentate ligand to each of the chromium atoms, the octahedra of which are completed by water molecules. The bond distances about each chromium are Cr-N, 2.120 and 2.042; Cr-OH<sub>2</sub>, 1.997; Cr-O, 1.946, 1.959 and 1.943 Å.

### Introduction

In the last decade many structural studies have been carried out on the coordinating ability of the potential hexadentate ligand EDTA (Richards, Pedersen, Silver-

ton & Hoard, 1964; Lin, Leggett & Wing, 1973; Hamor, Hamor & Hoard, 1964). It has been found that EDTA can act as a pentadentate ligand, one -CH<sub>2</sub>-COOH arm being free (Stephens, 1969; Smith & Hoard, 1959), as a hexadentate ligand in six- (Weakliem &