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## Magnesium Ion Binding to *myo*-Inositol: The Crystal Structure of *myo*-Inositol–Magnesium Chloride–Hydrate (1:1:4)

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The crystal structure of the complex *myo*-inositol–magnesium chloride–water (1:1:4) was studied as a model system for the carbohydrate–cation association. The complex crystallizes in the monoclinic space group  $P2_1/c$ ,  $a = 12.175$  (5),  $b = 7.643$  (1),  $c = 16.062$  (6) Å,  $\beta = 96.68^\circ$  (1) with  $Z = 4$ . The magnesium is coordinated to two *cis*-vicinal hydroxyl groups of inositol and four water molecules in an octahedral geometry. As a consequence of the cation binding, the cyclohexane ring geometry in the vicinity of the coordination site is distorted. Deviations of nearly  $15^\circ$  from the normal occur in some torsion angles. Structural features of the complex are discussed with regard to metal ion binding to phosphoinositides.

### Introduction

The transmission of nerve messages and changes in vesicular membrane structure can be depicted as processes based on stereospecific structural events accompanying the alternate binding of calcium and magnesium ions at anionic sites of membranes (Williams, 1970). Both mono- and polyphosphoinositides are constituents of the nerve myelin sheath (Dawson & Eichberg, 1965) and membrane systems of various tissues (Hawthorne & Michell, 1966). Phosphoinositides play a role in mitochondrial swelling (Vignais, Vignais & Lehninger, 1963) and the polyphosphoinositides may participate in ion transport across membranes (Galliard & Hawthorne, 1963; Hendrickson & Reinertsen, 1969). It has been suggested that the hydroxyl groups of the inositol moiety might act as secondary ligating sites for alkaline-earth metal ions (Hendrickson & Reinertsen, 1969).

Complexes between cyclitols and alkaline-earth metal ions are known to exist in solution (Angyal & Davies, 1971), (reviewed by Rendleman, 1966), and crystalline complexes have been prepared with *myo*-inositol (Bugg & Cook 1972; Windaus, 1907). The ability of *myo*-inositol to form such complexes is particularly relevant to its presence in phospholipids in view of the report that complexing of calcium with inositol is accompanied by conformational changes in the polyhydroxy moiety (Bugg & Cook, 1972). Precise data on the stereochemical features of complexes with other ions is pertinent to the understanding of the suspected role of this cyclitol as a lipid constituent active in ion transport and binding. A study of a complex between the magnesium ion and *myo*-inositol was therefore undertaken.

### Experimental

Equimolar amounts (2 mmoles) of *myo*-inositol and magnesium chloride hexahydrate were dissolved in

2 ml of an aqueous solution (saturated at  $25^\circ\text{C}$  with respect to both components) by heating. The cooled solution yielded large prismatic crystals, m.p.  $140$ – $142^\circ\text{C}$ . Crystallographic examination determined the composition to be a 1:1 complex with four molecules of hydration. Elemental analysis exhibited error attributable to the hygroscopic nature of the crystals ( $\text{C}_6\text{H}_{20}\text{O}_{10} \cdot \text{MgCl}_2$  requires: Cl, 20.40%, found: Cl, 20.00%). Crystal data for the monoclinic crystals are: space group  $P2_1/c$ ,  $a = 12.175$  (5),  $b = 7.643$  (1),  $c = 16.062$  (6) Å,  $\beta = 96.68^\circ$  (1),  $D_m = 1.55$  g cm $^{-3}$  (by flotation in dibromomethane: chloroform)  $D_c = 1.56$  g cm $^{-3}$  for  $Z = 4$ ,  $V = 1484.4$  Å $^3$ ; Cu  $K\alpha$ ,  $\lambda = 1.5418$  Å,  $\mu = 47.5$  cm $^{-1}$ .

A crystal was sealed in a glass capillary and the intensities were collected on a Picker FACS-1 automatic diffractometer by  $\theta/2\theta$  scans at  $2^\circ/\text{min}$  using monochromatic Cu  $K\alpha$  radiation (graphite monochromator). Background counts of 20 sec with both crystal and counter stationary were taken at the beginning and end of each scan. For the 2433 independent reflections measured for  $2\theta \leq 127^\circ$ , 193 had intensities less than the average intensity of those reflections absent due to space-group extinction and were designated unobserved. Three standard reflections monitored periodically indicated that the complex had undergone negligible degradation during the data collection (0.4% change). Following corrections for background and Lorentz–polarization, the intensities were reduced to structure amplitudes (FACS-1, 1972). No corrections were applied for absorption or extinction. An approximate absolute scale was obtained from a Wilson plot (Shiono, 1969).

The structure was solved by the direct method using the program *MULTAN* (Germain, Main & Woolfson, 1971). The successful set of starting phases which led to the correct structure was as follows:  $65\bar{2}$ ,  $|E| = 3.73$ ,  $\varphi = 0$ ;  $42\bar{5}$ ,  $|E| = 3.31$ ,  $\varphi = 0$ ;  $339$ ,  $|E| = 3.26$ ,  $\varphi = 0$ ;  $25\bar{2}$ ,  $|E| = 2.72$ ,  $\varphi = 0$ ;  $212$ ,  $|E| = 2.67$ ,  $\varphi = 0$ ;  $8, 0, \bar{1}0$ ,  $|E| = 2.31$ ,  $\varphi = \pi$ ;  $127$ ,  $|E| = 2.30$ ,  $\varphi = 0$ . Phases for the 190

Table 1. Atomic positional and thermal parameters for the complex myo-inositol-magnesium chloride-hydrate

All  $x$ ,  $y$  and  $z$  parameters have been multiplied by  $10^4$  for the non-hydrogen atoms and  $10^3$  for hydrogens. The standard deviation of the least significant figure is in parentheses.

	$x$	$y$	$z$
Cl(1)	251 (1)	6463 (1)	6764 (1)
Cl(2)	4920 (1)	6341 (1)	6119 (1)
Mg	2564 (1)	1588 (2)	6363 (1)
O(W1)	4069 (2)	1875 (5)	7041 (2)
O(W2)	2277 (3)	-705 (5)	6965 (2)
O(W3)	2764 (3)	4033 (5)	5834 (2)
O(W4)	1526 (3)	2808 (5)	7086 (2)
O(1)	1314 (2)	857 (4)	5420 (2)
O(2)	3389 (2)	430 (4)	5391 (2)
O(3)	4461 (2)	-108 (4)	3978 (2)
O(4)	3617 (2)	-3264 (4)	3341 (2)
O(5)	1964 (2)	-4825 (4)	4232 (2)
O(6)	502 (2)	-2581 (4)	4937 (2)
C(1)	1621 (3)	-30 (5)	4701 (2)
C(2)	2779 (3)	580 (5)	4578 (2)
C(3)	3303 (3)	-495 (5)	3932 (2)
C(4)	3206 (3)	-2462 (5)	4045 (2)
C(5)	2015 (3)	-2965 (5)	4112 (2)
C(6)	1600 (3)	-2008 (5)	4845 (3)
H(1)	110 (4)	24 (6)	416 (3)
H(2)	276 (4)	175 (7)	444 (3)
H(3)	296 (4)	-15 (6)	335 (3)
H(4)	368 (4)	-283 (6)	466 (3)
H(5)	161 (4)	-259 (6)	354 (3)
H(6)	212 (4)	-239 (6)	541 (3)
H(O1)	140 (4)	74 (6)	585 (3)
H(O2)	337 (4)	41 (6)	582 (3)
H(O3)	454 (4)	113 (6)	391 (3)
H(O4)	340 (4)	-349 (7)	280 (3)
H(O5)	194 (3)	-481 (6)	495 (3)
H(O6)	53 (4)	-289 (6)	551 (3)
H(1W1)	428 (4)	183 (6)	762 (3)
H(1W2)	214 (5)	-77 (8)	666 (3)
H(2W2)	269 (4)	-105 (6)	746 (3)
H(1W3)	264 (4)	425 (6)	536 (3)
H(2W3)	280 (5)	371 (7)	621 (3)
H(1W4)	134 (4)	348 (7)	698 (3)

reflections with  $|E| \geq 1.77$  were generated from this starting set. These phased  $E$  factors were used as coefficients in the calculation of an  $E$  map (Karle, Hauptman, Karle & Wing, 1958), and all non-hydrogen atoms were identified. The non-hydrogen atom structure was refined by the full-matrix least-squares procedure (Shiono, 1966) to an  $R$  ( $R = \sum ||F_{\text{meas}}| - |F_{\text{calc}}|| / \sum |F_{\text{meas}}|$ ) of 0.10. Hydrogen atoms were located from a difference Fourier map, and assigned a thermal parameter comparable to that of the atom to which they were bonded. Positions for one of the pair of hydrogen atoms for water molecules O(W1) and O(W4) could not be determined. Thirteen reflections affected by extinction were removed from the refinement;

Table 2. Structure factors

Listed are  $l$ ,  $10|F_o|$ ,  $10A_c$ . Unobserved reflections or reflections affected by extinction as noted in the text are marked (\*).

$hkl$	$10 F_o $	$10A_c$	$hkl$	$10 F_o $	$10A_c$	$hkl$	$10 F_o $	$10A_c$	$hkl$	$10 F_o $	$10A_c$	$hkl$	$10 F_o $	$10A_c$
000	1000	1000	100	100	100	200	200	200	300	300	300	400	400	400
100	100	100	110	110	110	120	120	120	130	130	130	140	140	140
200	200	200	210	210	210	220	220	220	230	230	230	240	240	240
300	300	300	310	310	310	320	320	320	330	330	330	340	340	340
400	400	400	410	410	410	420	420	420	430	430	430	440	440	440
500	500	500	510	510	510	520	520	520	530	530	530	540	540	540
600	600	600	610	610	610	620	620	620	630	630	630	640	640	640
700	700	700	710	710	710	720	720	720	730	730	730	740	740	740
800	800	800	810	810	810	820	820	820	830	830	830	840	840	840
900	900	900	910	910	910	920	920	920	930	930	930	940	940	940
1000	1000	1000	1010	1010	1010	1020	1020	1020	1030	1030	1030	1040	1040	1040
1100	1100	1100	1110	1110	1110	1120	1120	1120	1130	1130	1130	1140	1140	1140
1200	1200	1200	1210	1210	1210	1220	1220	1220	1230	1230	1230	1240	1240	1240
1300	1300	1300	1310	1310	1310	1320	1320	1320	1330	1330	1330	1340	1340	1340
1400	1400	1400	1410	1410	1410	1420	1420	1420	1430	1430	1430	1440	1440	1440
1500	1500	1500	1510	1510	1510	1520	1520	1520	1530	1530	1530	1540	1540	1540
1600	1600	1600	1610	1610	1610	1620	1620	1620	1630	1630	1630	1640	1640	1640
1700	1700	1700	1710	1710	1710	1720	1720	1720	1730	1730	1730	1740	1740	1740
1800	1800	1800	1810	1810	1810	1820	1820	1820	1830	1830	1830	1840	1840	1840
1900	1900	1900	1910	1910	1910	1920	1920	1920	1930	1930	1930	1940	1940	1940
2000	2000	2000	2010	2010	2010	2020	2020	2020	2030	2030	2030	2040	2040	2040
2100	2100	2100	2110	2110	2110	2120	2120	2120	2130	2130	2130	2140	2140	2140
2200	2200	2200	2210	2210	2210	2220	2220	2220	2230	2230	2230	2240	2240	2240
2300	2300	2300	2310	2310	2310	2320	2320	2320	2330	2330	2330	2340	2340	2340
2400	2400	2400	2410	2410	2410	2420	2420	2420	2430	2430	2430	2440	2440	2440
2500	2500	2500	2510	2510	2510	2520	2520	2520	2530	2530	2530	2540	2540	2540
2600	2600	2600	2610	2610	2610	2620	2620	2620	2630	2630	2630	2640	2640	2640
2700	2700	2700	2710	2710	2710	2720	2720	2720	2730	2730	2730	2740	2740	2740
2800	2800	2800	2810	2810	2810	2820	2820	2820	2830	2830	2830	2840	2840	2840
2900	2900	2900	2910	2910	2910	2920	2920	2920	2930	2930	2930	2940	2940	2940
3000	3000	3000	3010	3010	3010	3020	3020	3020	3030	3030	3030	3040	3040	3040
3100	3100	3100	3110	3110	3110	3120	3120	3120	3130	3130	3130	3140	3140	3140
3200	3200	3200	3210	3210	3210	3220	3220	3220	3230	3230	3230	3240	3240	3240
3300	3300	3300	3310	3310	3310	3320	3320	3320	3330	3330	3330	3340	3340	3340
3400	3400	3400	3410	3410	3410	3420	3420	3420	3430	3430	3430	3440	3440	3440
3500	3500	3500	3510	3510	3510	3520	3520	3520	3530	3530	3530	3540	3540	3540
3600	3600	3600	3610	3610	3610	3620	3620	3620	3630	3630	3630	3640	3640	3640
3700	3700	3700	3710	3710	3710	3720	3720	3720	3730	3730	3730	3740	3740	3740
3800	3800	3800	3810	3810	3810	3820	3820	3820	3830	3830	3830	3840	3840	3840
3900	3900	3900	3910	3910	3910	3920	3920	3920	3930	3930	3930	3940	3940	3940
4000	4000	4000	4010	4010	4010	4020	4020	4020	4030	4030	4030	4040	4040	4040
4100	4100	4100	4110	4110	4110	4120	4120	4120	4130	4130	4130	4140	4140	4140
4200	4200	4200	4210	4210	4210	4220	4220	4220	4230	4230	4230	4240	4240	4240
4300	4300	4300	4310	4310	4310	4320	4320	4320	4330	4330	4330	4340	4340	4340
4400	4400	4400	4410	4410	4410	4420	4420	4420	4430	4430	4430	4440	4440	4440
4500	4500	4500	4510	4510	4510	4520	4520	4520	4530	4530	4530	4540	4540	4540
4600	4600	4600	4610	4610	4610	4620	4620	4620	4630	4630	4630	4640	4640	4640
4700	4700	4700	4710	4710	4710	4720	4720	4720	4730	4730	4730	4740	4740	4740
4800	4800	4800	4810	4810	4810	4820	4820	4820	4830	4830	4830	4840	4840	4840
4900	4900	4900	4910	4910	4910	4920	4920	4920	4930	4930	4930	4940	4940	4940
5000	5000	5000	5010	5010	5010	5020	5020	5020	5030	5030	5030	5040	5040	5040
5100	5100	5100	5110	5110	5110	5120	5120	5120	5130	5130	5130	5140	5140	5140
5200	5200	5200	5210	5210	5210	5220	5220	5220	5230	5230	5230	5240	5240	5240
5300	5300	5300	5310	5310	5310	5320	5320	5320	5330	5330	5330	5340	5340	5340
5400	5400	5400	5410	5410	5410	5420	5420	5420	5430	5430	5430	5440	5440	5440
5500	5500	5500	5510	5510	5510	5520	5520	5520	5530	5530	5530	5540	5540	5540
5600	5600	5600	5610	5610	5610	5620	5620	5620	5630	5630	5630	5640	5640	5640
5700	5700	5700	5710	5710	5710	5720	5720	5720	5730	5730	5730	5740	5740	5740
5800	5800	5800	5810	5810	5810	5820	5820	5820	5830	5830	5830	5840	5840	5840
5900	5900	5900	5910	5910	5910	5920	5920	5920	5930	5930	5930	5940	5940	5940
6000	6000	6000	6010	6010	6010	6020	6020	6020	6030	6030	6030	6040	6040	6040
6100	6100	6100	6110	6110	6110	6120	6120	6120	6130	6130	6130	6140	6140	6140
6200	6200	6200	6210	6210	6210	6220	6220	6220	6230	6230	6230	6240	6240	6240
6300	6300	6300	6310	6310	6310	6320	6320	6320	6330	6330	6330	6340	6340	6340
6400	6400	6400	6410	6410	6410	6420	6420	6420	6430	6430	6430	6440	6440	6440
6500	6500	6500	6510	6510	6510	6520	6520	6520	6530	6530	6530	6540	6540	6540
6600	6600	6600	6610	6610	6610	6620	6620	6620	6630	6630	6630	6640	6640	6640
6700	6700	6700	6710	6710	6710	6720	6720	6720	6730	6730	6730	6740	6740	6740
6800	6800	6800	6810	6810	6810	6820	6820	6820	6830	6830	6830	6840	6840	6840
6900	6900	6900	6910	6910	6910	6920	6920	6920	6930	6930	6930	6940	6940	6940
7000	7000	7000	7010	7010	7010	7020	7020	7020	7030	7030	7030	7040	7040	7



Table 3 (cont.)

(b) Angles (°)			
O(6)-C(6)-C(1)	110.5 (3)	C(6)-C(5)-H(5)	113 (3)
O(6)-C(6)-C(5)	109.4 (3)	C(4)-C(5)-H(5)	104 (2)
O(5)-C(5)-C(6)	110.4 (3)	O(5)-C(5)-H(5)	112 (3)
O(5)-C(5)-C(4)	108.5 (3)	C(5)-C(4)-H(4)	106 (2)
O(4)-C(4)-C(5)	112.0 (3)	C(3)-C(4)-H(4)	109 (2)
O(4)-C(4)-C(3)	107.0 (3)	O(4)-C(4)-H(4)	113 (2)
O(3)-C(3)-C(4)	106.7 (3)	C(4)-C(3)-H(3)	109 (3)
O(3)-C(3)-C(2)	110.0 (3)	C(2)-C(3)-H(3)	110 (3)
O(2)-C(2)-C(3)	111.4 (3)	O(3)-C(3)-H(3)	107 (3)
O(2)-C(2)-C(1)	104.3 (3)	C(3)-C(2)-H(2)	112 (3)
O(1)-C(1)-C(2)	107.1 (3)	C(1)-C(2)-H(2)	110 (3)
O(1)-C(1)-C(6)	109.7 (3)	O(2)-C(2)-H(2)	107 (3)
C(1)-C(6)-C(5)	110.2 (3)	C(2)-C(1)-H(1)	109 (2)
C(6)-C(5)-C(4)	109.9 (3)	C(6)-C(1)-H(1)	108 (2)
C(5)-C(4)-C(3)	110.3 (3)	O(1)-C(1)-H(1)	113 (2)
C(4)-C(3)-C(2)	114.2 (3)	C(6)-O(6)-H(O6)	104 (3)
C(3)-C(2)-C(1)	113.1 (3)	C(5)-O(5)-H(O5)	98 (2)
C(2)-C(1)-C(6)	110.9 (3)	C(4)-O(4)-H(O4)	139 (6)
C(1)-C(6)-H(6)	112 (2)	C(3)-O(3)-H(O3)	109 (3)
C(5)-C(6)-H(6)	108 (2)	C(2)-O(2)-H(O2)	147 (4)
O(6)-C(6)-H(6)	107 (2)	C(1)-O(1)-H(O1)	136 (4)

To minimize individual bond-angle deviations, torsional alterations about C(1)-C(2) and adjacent bonds contribute to the spatial displacement of O(1) and O(2) necessary for their accommodation in the magnesium coordination geometry. The torsion angles for bond C(1)-C(2) are given in Table 4 and differ by as much as 14° from those of *myo*-inositol. While the primary effects of the molecular association are on the geometries of C(1) and C(2), the stereochemical arrangements of atoms bonded to C(3) and C(6) show differences from uncomplexed *myo*-inositol primarily in their respective torsion angles, see Table 4. The

non-bonded distance between vicinal diequatorial oxygen atoms in *myo*-inositol is 2.841 (1) Å (Rabinowitz & Kraut, 1964). In this complex the O<sub>eq</sub>(3)⋯O<sub>eq</sub>(4) distance is reduced to 2.770 (4) Å and O<sub>eq</sub>(1)⋯O<sub>eq</sub>(6) lengthened to 2.882 (4) Å.

Bugg & Cook (1972) report that calcium binding to *cis* vicinal oxygen atoms results in a decrease of 0.2 Å in the O<sub>eq</sub> to O<sub>ax</sub> contact distance and 13–14° in the O<sub>eq</sub>-C-C-O<sub>ax</sub> torsion angle. The binding of magnesium to the *cis* hydroxyl groups of inositol induces conformational changes of equal or greater magnitude than found for calcium.

Table 4. Torsion angles for bonds to C(1) and C(2) of *myo*-inositol

The standard deviations of the least significant figures are in parentheses.

Bond sequence	Angle (°)	
	Mg complex	Uncomplexed*
C(6)-C(1)-C(2)-C(3)	49.8 (4)	57.3 (3)
C(6)-C(1)-C(2)-O(2)	-71.4 (4)	-63.8 (3)
O(1)-C(1)-C(2)-C(3)	169.4 (3)	176.4 (3)
O(1)-C(1)-C(2)-O(2)	48.2 (4)	62.6 (3)
O(1)-C(1)-C(6)-O(6)	63.5 (4)	59.3 (3)
O(1)-C(1)-C(6)-C(5)	-175.5 (3)	179.4 (3)
C(2)-C(1)-C(6)-O(6)	-178.4 (3)	-175.7 (3)
C(2)-C(1)-C(6)-C(5)	57.4 (4)	-55.0 (3)
O(2)-C(2)-C(3)-O(3)	-50.4 (4)	-63.5 (3)
O(2)-C(2)-C(3)-C(4)	69.4 (4)	61.2 (3)
C(1)-C(2)-C(3)-O(3)	-167.5 (3)	-176.0 (3)
C(1)-C(2)-C(3)-C(4)	-47.6 (4)	-59.4 (3)

\* Average angles for the two independent molecules in the structure of *myo*-inositol (Rabinowitz & Kraut, 1964) are listed.

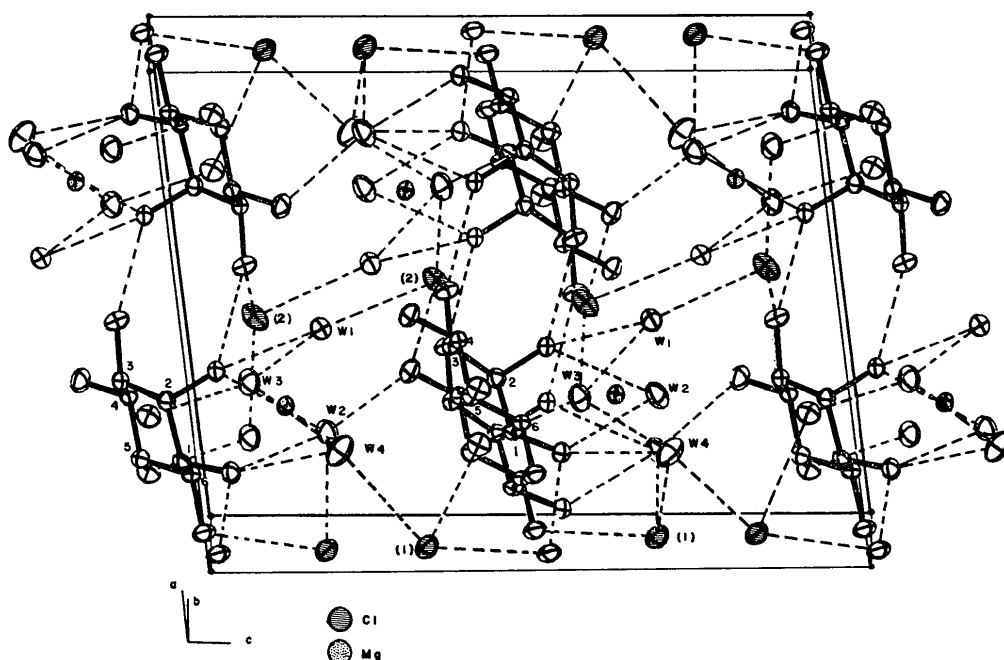


Fig. 2. Hydrogen bonding and close contacts in the crystalline complex.

Table 5. *Least-squares planes*

		<i>A</i>	<i>B</i>	<i>C</i>	<i>D</i>	E.s.d. (Å)
I	C(4)C(5)O(4)O(5)	-0.5248	0.2246	-0.8210	-7.0708	0.003
IIa*	C(4)C(5)O(4)O(5)	-0.3548	0.5995	-0.7174	-0.5526	0.003
IIb*	C(4)C(5)O(4)O(5)	-0.3942	-0.4098	-0.8225	-4.9202	0.002

Table 5 (*cont.*)

	Deviation from the plane		
	I(Å)	II(Å)	
		<i>a</i>	<i>b</i>
C(1)	0.334	-0.276	0.332
C(2)	-0.152	0.350	-0.291
C(3)	0.111	-0.119	0.127
C(4)†	-0.302	0.300	-0.302
C(5)†	0.292	-0.296	0.298
C(6)	-0.166	0.112	-0.040
O(1)	-0.189	0.064	0.015
O(2)	-1.553	1.774	-1.720
O(3)	-0.618	0.389	-0.360
O(4)†	0.150	-0.148	0.148
O(5)†	-0.140	0.145	-0.145
O(6)	0.326	-0.542	0.684

\* Calculations IIa, IIb are for the two independent molecules of *myo*-inositol in the crystal structure by Rabinowitz & Kraut, (1964).

† Atoms used in the least-squares plane calculation. The equation for the plane is  $Ax + By + Cz = D$ .

Since the common four-atom arrangements used for least-squares plane calculations for cyclohexane rings encompass sites perturbed by the magnesium coordination, an unconventional location was chosen in order to have an undistorted reference for comparison with the uncomplexed molecule. The atomic displacements for atoms C(4), C(5), O(4), and O(5), see Table 5, are unaffected by complexing. The hydroxyl positions are particularly sensitive indicators that all other atoms are affected by the coordination at O(1) and O(2). The difference in the displacement of C(2) in the complexed and uncomplexed molecules is indicative of a decrease in pucker of that portion of the ring.

In the inositol complexes with both calcium (Bugg & Cook, 1972) and magnesium the cations are bound to their characteristic number of ligands, [8] and [6] respectively (Phillips & Williams, 1966). While calcium binds an equal number of hydroxyl groups and water molecules, the coordination geometry around magnesium is composed of the two hydroxyl groups from inositol and four water molecules. The oxygen atoms are arranged in an octahedral geometry around the magnesium atom, see Fig. 1. The bond distances and angles descriptive of this geometrical arrangement are given in Table 6. The distances and angles are normal (Andress & Gundermann, 1964; Sasvari & Jeffrey, 1966), except for some involving the hydroxyl groups, where constraints are imposed by the cyclohexane ring. Oxygen atoms alone constitute the primary coordination sphere of magnesium, and the chlorine atoms are 4.673 (2) Å, Cl(2) and 4.759 (2) Å, Cl(1) from the cation. The magnesium geometry is not appreciably different from that found in  $MgCl_2 \cdot 6H_2O$  (Andress & Gunder-

mann, 1964) or  $MgCl_2 \cdot 12H_2O$  (Sasvari & Jeffrey, 1966) where the cation is six-coordinated to oxygen at 2.06 Å. However, in the organic complex, as in  $MgCl_2 \cdot 12H_2O$ , hydration of the anions and subsequent steric considerations place the chlorine ions approximately 0.7 Å farther from the magnesium than in  $MgCl_2 \cdot 6H_2O$ .

Table 6. *Coordination distances and angles*

The standard deviations of the least significant figures are in parentheses.

(a) Coordination distances between magnesium and oxygen atoms (Å).

Mg-O(W1)	2.032 (4)
Mg-O(W2)	2.051 (4)
Mg-O(W3)	2.079 (4)
Mg-O(W4)	2.038 (4)
Mg-O(1)	2.094 (3)
Mg-O(2)	2.143 (3)

(b) Angles between oxygen atoms coordinated to the magnesium atom (°).

O(W1)-Mg-O(W2)	91.8 (2)
O(W1)-Mg-O(W3)	88.9 (2)
O(W1)-Mg-O(W4)	103.0 (2)
O(W1)-Mg-O(1)	161.9 (2)
O(W1)-Mg-O(2)	88.0 (1)
O(W2)-Mg-O(W3)	174.4 (2)
O(W2)-Mg-O(W4)	88.4 (2)
O(W2)-Mg-O(1)	87.9 (1)
O(W2)-Mg-O(2)	96.3 (1)
O(W3)-Mg-O(W4)	86.0 (2)
O(W3)-Mg-O(1)	93.1 (1)
O(W3)-Mg-O(2)	89.2 (1)
O(W4)-Mg-O(1)	95.0 (1)
O(W4)-Mg-O(2)	167.9 (2)
O(1)-Mg-O(2)	74.1 (1)

Cl(1) is within van der Waals contact of five oxygen atoms and Cl(2) of four. The geometries of the hydration polyhedra are those of a distorted trigonal bipyramid and tetrahedron, respectively, see Table 7. Each anion is within hydrogen-bonding distance of two equatorial hydroxyl groups of different molecules. Thus, for a particular molecule of *myo*-inositol in the unit cell, any hydroxyl not coordinated to magnesium is hydrogen bonded to a chlorine anion. In the case of hydroxyl(5), the hydrogen-bond acceptor appears to be a water molecule.

Hydrogen bonding in the crystal structure is illustrated in Fig. 2. The dashed lines represent all contacts to the oxygen atoms which are less than the sum of the van der Waals radii. The hydrogen atoms have been excluded from the drawing. The dimensions and angular arrangement of the hydrogen bonds are given in Table 8. Although hydroxyl groups O(3) and O(6) are at less than the van der Waals distance from O(2)<sub>sym</sub>

Table 7. Distances and angles involving the chlorine ions and oxygen atoms

The standard deviations of the least significant figures are in parentheses.

## (a) Distances between chlorine ions and oxygen atoms (Å)\*

Cl(1)—O(W2)	3.268 (4)	Cl(2)—O(W1)	3.093 (3)
Cl(1)—O(W4)	3.209 (4)	Cl(2)—O(W3)	3.152 (4)
Cl(1)—O(W4)	3.175 (4)	Cl(2)—O(4)	3.015 (3)
Cl(1)—O(5)	3.224 (3)	Cl(2)—O(3)	2.986 (3)
Cl(1)—O(6)	3.074 (3)		

## (b) Angles between oxygen atoms bonded to chlorine ions (°)

O(W2)—Cl(1)—O(W4)	102.4 (1)	O(W1)—Cl(2)—O(W3)	116.4 (1)
O(W2)—Cl(1)—O(W4)	106.6 (1)	O(W1)—Cl(2)—O(4)	70.9 (1)
O(W2)—Cl(1)—O(5)	152.1 (1)	O(W1)—Cl(2)—O(3)	81.2 (1)
O(W2)—Cl(1)—O(6)	77.2 (1)	O(W3)—Cl(2)—O(4)	93.4 (1)
O(W4)—Cl(1)—O(W4)	122.6 (1)	O(W3)—Cl(2)—O(3)	138.0 (1)
O(W4)—Cl(1)—O(5)	95.9 (1)	O(4)—Cl(2)—O(3)	128.5 (1)
O(W4)—Cl(1)—O(6)	105.1 (1)		
O(W4)—Cl(1)—O(5)	80.1 (1)		
O(W4)—Cl(1)—O(6)	129.0 (1)		
O(5)—Cl(1)—O(6)	77.8 (1)		

and O(1)<sub>sym</sub> respectively, their preference to hydrogen bond to chlorine ions precludes the donation of hydrogen atoms to these oxygen atoms. The latter hydroxyl groups are hydrogen bonded to water molecules within the magnesium hydration polyhedra.

Table 8. Hydrogen bonds and close intermolecular contacts

The standard deviations of the least significant figures are in parentheses.

Acceptor (A)	Donor (D)	D—A(Å)	Hydrogen —A(Å)	Hydrogen —D—A(°)
O(1)	O(6 <sup>i</sup> )	2.580 (4)		
O(W4)	O(1)	3.048 (5)	2.53 (5)	37 (4)
O(W1)	O(2)	2.902 (4)	2.33 (5)	30 (4)
O(W2)	O(2)	3.126 (5)	2.53 (5)	28 (4)
O(2)	O(3 <sup>ii</sup> )	2.706 (4)		
Cl(2 <sup>iii</sup> )	O(3)	2.986 (3)	2.05 (5)	9 (3)
Cl(2 <sup>iv</sup> )	O(4)	3.015 (3)		
O(W2 <sup>v</sup> )	O(4)	2.708 (5)	1.90 (5)	21 (6)
O(4 <sup>vi</sup> )	O(W2)	2.708 (5)	1.78 (5)	5 (3)
O(5 <sup>vii</sup> )	O(W3)	2.783 (5)	2.02 (5)	11 (4)
O(W3 <sup>viii</sup> )	O(5)	2.783 (5)	1.86 (4)	
Cl(1 <sup>ix</sup> )	O(6)	3.074 (3)	2.14 (5)	
Cl(2 <sup>x</sup> )	O(W1)	3.093 (3)	2.17 (5)	9 (3)
O(1)	O(W2)	2.877 (5)	2.46 (6)	32 (6)
Cl(2)	O(W3)	3.152 (4)		
O(W4)	O(W3)	2.810 (5)	2.31 (6)	36 (5)
O(W1)	O(W3)	2.879 (5)	2.38 (6)	35 (5)
Cl(1)	O(W4)	3.209 (4)	2.64 (5)	9 (5)
Cl(1 <sup>xii</sup> )	O(W4)	3.175 (4)		

## Symmetry code

i	—x,	—y,	—z
ii	1—x,	—y,	1—z
iii	1—x,	1—y,	1—z
iv	x,	—0.5—y,	0.5+z
v	x,	—1+y,	z
vi	1—x,	—0.5+y,	1.5—z
vii	—x,	—0.5+y,	1.5—z
viii	x,	1+y,	z
ix	x,	—0.5—y,	0.5+z

Presumably the forces between the magnesium ion and the oxygen atoms are ion-dipole interactions (Rendleman, 1966). Since the ratio of charge to atomic radius is greater for magnesium than calcium, and magnesium coordinates to fewer ligands than calcium, the magnesium-inositol complex may be a stronger association than that with calcium. The smaller stability constants found for magnesium than calcium carbohydrate complexes in aqueous solution (Angyal, 1972) may result from competitive ligation effects of the less sterically constraining water molecules.

Hydrogen bonding from the coordinated hydroxyl groups to water and from water to water within each polyhedron serves as a stabilizing influence for maintenance of the magnesium complex. No intrapolyhedral hydrogen bonding was found in the calcium-carbohydrate complexes examined (Bugg & Cook, 1972).

*cis* Vicinal hydroxyl groups possess more conformational flexibility than *trans*(eq/eq) groups. Coordination of an alkaline metal ion to vicinal hydroxyl groups causes a decrease in both the torsion angle O—C—C—O and intra-atomic oxygen to oxygen distance of the coordinated atoms. Angyal & MacDonald (1952) noted that such a deformation is energetically allowable for *cis* related groups, producing a decrease in pucker of the cyclohexane ring, and a lessening of 1,3-*syn*-diaxial steric interactions. In the case of *trans*-vicinal groups, the same motion increases ring pucker and produces unfavorable 1,3-*syn*-diaxial interactions. Although for the case in point such a structural alteration of the *cis* hydroxyl groups forces the coordinated oxygen atoms into steric opposition to one another, it serves to redirect the lone-pair electrons and minimize steric interference of the non-coordinated cyclitol atoms with components of the solvation polyhedron, e.g. H(6) with O(W2).

While the importance of cation binding to the hydroxyl groups of the *myo*-inositol moiety of phos-

phoinositides is uncertain, studies with synthetic bilayers have demonstrated that the negatively charged membrane components exhibit selective permeability for cations (Hopfer, Lehninger & Lennarz, 1970). Stability constants measured in aqueous solution cannot be realistically extended to membrane systems. Analysis of the structure of the inositol alkaline-earth metal complexes points up some interesting features.

Association of different alkaline-earth ions with myo-inositol in a complex induces specific stereochemical changes in the cyclitol. It has been noted that greater conformational flexibility exists for *cis*-vicinal hydroxyl groups than *trans* disposed groups. Thus, in the case of monophosphoinositides it may be difficult to discriminate between simultaneous coordination between the phosphate and either the axial hydroxyl at C(2) or the equatorial hydroxyl at C(6) from steric considerations alone. Alkaline-earth metal binding to polyphosphoinositides does not seem to involve ligation to hydroxyl groups if two vicinal phosphates are present (Hendrickson & Reinertsen, 1969).

Quantitative differences in stereochemical parameters of the magnesium and calcium complexes with inositol do not appear to be great. However, examination of the hydration habits of these ions reveals that magnesium prefers to remain hydrated in salts whereas calcium forms salts of lower hydration (Peacocke & Richards, 1969). The structures of the calcium complexes examined (Bugg & Cook, 1972; Bugg, 1973; Craig, Stephenson & Stevens, 1972) show a higher ratio of carbohydrate to water than for this magnesium complex. The stoichiometric associations exhibited in the solid-state complexes may reflect the preferred levels of hydration for the respective ions. Williams (1970) has outlined a mechanism for altering membrane structure utilizing the differential bonding characteristics of calcium and magnesium.

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