Structure of 1,2,3,4,5,6-Hexa-*O*-acetyl-*myo*-inositol

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Abstract. $C_{18}H_{24}O_{12}$, $M_r = 432 \cdot 4$, monoclinic, Cc, $a = 8 \cdot 996$ (3), $b = 20 \cdot 890$ (6), $c = 11 \cdot 872$ (4) Å, $\beta = 101 \cdot 11$ (2)°, $V = 2189$ (1) Å^3, $Z = 4$, $D_x = 1 \cdot 312$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0 \cdot 71069$ Å, $\mu = 1 \cdot 05$ cm^{-1}, $F(000) = 912$, $T = 163$ K, $R = 0 \cdot 041$, $wR = 0 \cdot 0375$ for 2158 reflections ($F_o \geq 6\sigma|F_o|$). The ring is in the chair conformation $^4C_1$ with five equatorial groups and one axial group bonded to C(2) as expected. The carbonyl bonds of the acetate groups at positions 2, 4, 5 and 6 are approximately coplanar with their respective ring C—H bonds. However, those at positions 1 and 3 are rotated towards the H(2) atom.

Introduction. The parent compound of this study, *myo*-inositol, has a configuration such that two different chair conformations are possible: one, the more stable, with five hydroxyl groups equatorial and one hydroxyl axial (5*e*/1*a*), and the other with five hydroxyls axial and one hydroxyl equatorial (5*a*/1*e*). The crystal structure of *myo*-inositol has been reported and the two molecules in the asymmetric unit exist in the 5*e*/1*a* conformation with only one small distortion from the perfect chair form (Rabinowitz & Kraut, 1964). Evidence of the physiological importance of *myo*-inositol derivatives is rapidly accumulating. These derivatives have been shown to act as second messengers of many processes (Pelech & Vance, 1989) and as cell-surface anchors (Ferguson & Williams, 1988). The majority of these systems are phosphate esters which may have lipid groups attached at various positions, consequently increasing the number of possible isomers and providing diverse conformations for the active effectors. The presence of a sterically large group on the single axial hydroxyl group would be expected to change the conformational distribution of the chair so as to orient the large group into the equatorial position. If other groups were located on any of the five now axial hydroxyl groups the distribution would then be subject to further distortion depending on the steric and ionic properties of all the

groups present. However, in one physiologically important derivative, *myo*-inositol-2-dihydrogenphosphate, the phosphate group, which is attached to the axial hydroxyl group, remains in the axial orientation and the molecule exists in the 5*e*/1*a* conformation (Yoo, Blank, Pletcher & Sax, 1974). Apparently, the dihydrogenphosphate group is not large enough to cause the other conformation to be the more stable one in the crystalline state. In contrast to these findings, the crystal structure of *myo*-inositol hexaphosphate (common name phytate) exists in the unexpected 5*a*/1*e* conformation (Blank, Pletcher & Sax, 1975). This compound was in the form of its dodecasodium salt and the sodium ions were shown to bridge the now axial phosphate groups and thus stabilize the 5*a*/1*e* conformation. We report here the results for the completely substituted compound 1,2,3,4,5,6-hexa-*O*-acetyl-*myo*-inositol (1). This is one of our continuing publications on the X-ray structures of physiological modulators and their analogues (Watkins, Abboud, Voll, Koerner & Younathan, 1983; Watkins, Abboud, Nghiem, Voll & Younathan, 1986).

(1)
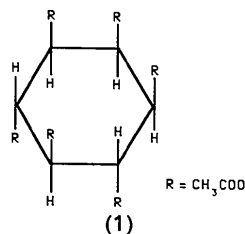
Experimental. Crystals of (1) were grown by sublimation in vacuum and a colorless plate of dimensions $0 \cdot 11 \times 0 \cdot 22 \times 0 \cdot 5$ mm was chosen for X-ray investigation. Data were collected on a Syntex $P2_1$ diffractometer equipped with a graphite monochromator utilizing Mo $K\alpha$ radiation ($\lambda = 0 \cdot 71069$ Å). 45 reflections with $13 \cdot 2 \leq 2\theta \leq 21 \cdot 5°$ were used to refine the cell parameters. 6287 reflections were collected using the ω-scan method ($h - 11$

→11, k −29→29, l 0→16, hkl reflections where $h +$ $k = 2n + 1$ were not collected), 3022 unique reflections, $R_{int} = 0\cdot027$; 2θ range 4→65°, 1° ω-scan at 3–6° min^{-1}, depending upon intensity. Four reflections (200, 112, 132, 080) were measured every 196 reflections to monitor instrument and crystal stability (maximum correction on I was $<1\cdot5\%$). Absorption corrections were applied based on measured crystal faces (Riley & Davis, 1976); minimum and maximum transmission 0·974, 0·982.

The structure was solved by direct methods with *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978) from which the locations of all non-H atoms were obtained. The structure was refined (*SHELX*76; Sheldrick, 1976) using full-matrix least squares and the positions of all H atoms were determined from a difference Fourier map. Non-H atoms were treated anisotropically, whereas H atoms were refined with isotropic thermal parameters. 365 parameters were refined and $\sum w(|F_o| - |F_c|)^2$ was minimized; $w = 1/(\sigma|F_o|)^2$, $\sigma(F_o) = 0\cdot5kI^{-1/2}\{[\sigma(I)]^2 + (0\cdot02I)^2\}^{1/2}$, I(intensity) $=$ $(I_{peak} - I_{background})$(scan rate), and $\sigma(I) = (I_{peak} + I_{background})^{1/2}$(scan rate), where k is the correction due to decay and Lp effects, and 0·02 is a factor used to downweight intense reflections and to account for instrument instability. Final $R = 0\cdot041$, $wR = 0\cdot0375$ for 2158 reflections having $F_o \geq 6\sigma(F_o)$, and goodness of fit $S = 1\cdot58$. Maximum $\Delta/\sigma < 0\cdot04$ in the final refinement cycle, and the minimum and maximum peaks in the ΔF map were −0·27 and 0·34 e Å^{-3}, respectively. The linear absorption coefficient was calculated from values from *International Tables for X-ray Crystallography* (1974, Vol. IV, p. 55). Scattering factors for non-H atoms were taken from Cromer & Mann (1968) with anomalous-dispersion corrections from Cromer & Liberman (1970), while those of H atoms were from Stewart, Davidson & Simpson (1965). The least-squares-planes program was supplied by Cordes (1983) while other programs used are cited in Gadol & Davis (1982). The positional parameters and the equivalent isotropic thermal parameters of the non-H atoms are listed in Table 1, bond lengths and angles in Table 2. A thermal-ellipsoid drawing (*SHELXTL-Plus*; Sheldrick, 1987) of the molecule with the atom-labelling scheme is given in Fig. 1.*

Discussion. The six acetyl groups in (1) are in the expected $5e/1a$ configuration with the group on C(2)

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* Tables of crystallographic data, anisotropic thermal parameters, H-atom positional parameters and bond lengths and angles, torsion angles, and structure-factor amplitudes have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53046 (29 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Atomic coordinates of the non-*H *atoms* $(\times 10^4)$ *and equivalent isotropic displacement coefficients* $(\text{Å}^2 \times 10^3)$

	x	y	z	U_{eq}*
O(1a)	210	8409 (1)	4711	30 (1)
O(1b)	1734 (4)	7867 (1)	6108 (3)	52 (1)
C(1)	1383 (4)	8878 (1)	4704 (3)	25 (1)
C(1a)	544 (5)	7908 (2)	5449 (4)	38 (1)
C(1b)	−736 (6)	7445 (2)	5293 (5)	55 (2)
O(2a)	1606 (3)	8502 (1)	2832 (3)	27 (1)
O(2b)	1835 (4)	7447 (1)	3208 (3)	61 (1)
C(2)	2478 (4)	8640 (1)	3966 (3)	24 (1)
C(2a)	1347 (5)	7873 (2)	2566 (4)	36 (1)
C(2b)	344 (6)	7799 (2)	1420 (4)	47 (2)
O(3a)	4615 (3)	8948 (1)	3111 (3)	23 (1)
O(3b)	6138 (4)	8514 (1)	4645 (3)	41 (1)
C(3)	3610 (4)	9161 (1)	3843 (3)	22 (1)
C(3a)	5875 (4)	8632 (1)	3635 (4)	26 (1)
C(3b)	6832 (5)	8447 (2)	2786 (4)	32 (1)
O(4a)	3943 (3)	10265 (1)	3373 (2)	24 (1)
O(4b)	3854 (4)	10232 (1)	1469 (3)	41 (1)
C(4)	2833 (4)	9761 (2)	3314 (3)	22 (1)
C(4a)	4326 (4)	10469 (2)	2384 (3)	26 (1)
C(4b)	5366 (6)	11029 (2)	2602 (5)	43 (1)
O(5a)	814 (3)	10500 (1)	3370 (3)	31 (1)
O(5b)	1822 (6)	11240 (2)	4666 (5)	97 (2)
C(5)	1698 (5)	9997 (1)	4013 (3)	25 (1)
C(5a)	925 (6)	11094 (2)	3823 (5)	53 (2)
C(5b)	−174 (8)	11537 (2)	3101 (7)	70 (2)
O(6a)	−233 (3)	9723 (1)	5062 (3)	31 (1)
O(6b)	−2359 (4)	9849 (1)	3727 (3)	39 (1)
C(6)	583 (4)	9483 (2)	4219 (3)	24 (1)
C(6a)	−1707 (5)	9885 (2)	4700 (4)	30 (1)
C(6b)	−2354 (7)	10132 (3)	5689 (5)	55 (2)

* Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor.

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in the axial position. Moreover the ring is in the *myo* configuration where two acetyl groups, those bonded to C(4) and C(6), lie on one side of the cyclohexyl ring while those bonded to C(1), C(2), C(3) and C(5) are on the other side. The cyclohexyl ring is in the $^4C_1$ conformation with C(1) and C(4) lying at distances of 0·65 (1) Å on opposite sides of the least-squares plane passing through atoms C(2), C(3), C(5) and C(6). A range of 51·6 (4) to 58·5 (4)° is observed in the endocyclic torsion angles in (1) compared with an angle of 56° in a free cyclohexane ring (Bucourt, 1974), indicating a close similarity in puckering. The puckering of the ring in (1) is also similar to that of (1,3,5/2,4)-1,2,3,4-tetraacetyl-5-(acetoxymethyl)cyclohexane (2) (Watkins *et al.*, 1986), where a range of 52·8 (5) to 61·2 (4)° has been reported. It is somewhat different from the puckering of the ring in β-D-glucopyranose pentaacetate (3) (Jones, Sheldrick, Kirby & Glenn, 1982), where the torsion angles range from 45·7 (3) to 63·2 (3)°.

Table 3 lists torsion angles between the ring C—H bond and the C=O bond for each acetyl group in (1). The torsion angles involving the acetyl groups on C(2), C(4), C(5) and C(6) range from −12 to 13° and show that the C—H and C=O bonds point in the same direction and are approximately coplanar. This

Table 2. Bond lengths (Å) and angles (°) of the non-H atoms

O(1a)—C(1)	1·442 (4)	O(1a)—C(1a)	1·360 (4)
O(1b)—C(1a)	1·201 (5)	C(1)—C(2)	1·523 (6)
C(1)—C(6)	1·511 (5)	C(1a)—C(1b)	1·489 (6)
O(2a)—C(2)	1·450 (5)	O(2a)—C(2a)	1·362 (4)
O(2b)—C(2a)	1·198 (5)	C(2)—C(3)	1·517 (5)
C(2a)—C(2b)	1·488 (6)	O(3a)—C(3)	1·440 (5)
O(3a)—C(3a)	1·355 (4)	O(3b)—C(3a)	1·203 (5)
C(3)—C(4)	1·512 (4)	C(3a)—C(3b)	1·497 (7)
O(4a)—C(4)	1·444 (4)	O(4a)—C(4a)	1·355 (5)
O(4b)—C(4a)	1·196 (5)	C(4)—C(5)	1·517 (6)
C(4a)—C(4b)	1·488 (6)	O(5a)—C(5)	1·443 (4)
O(5a)—C(5a)	1·348 (5)	O(5b)—C(5a)	1·198 (7)
C(5)—C(6)	1·522 (5)	C(5a)—C(5b)	1·498 (8)
O(6a)—C(6)	1·440 (5)	O(6a)—C(6a)	1·357 (5)
O(6b)—C(6a)	1·193 (5)	C(6a)—C(6b)	1·499 (8)

C(1)—O(1a)—C(1a)	117·1 (2)	O(1a)—C(1)—C(2)	109·7 (2)
O(1a)—C(1)—C(6)	106·0 (3)	C(2)—C(1)—C(6)	111·6 (3)
O(1a)—C(1a)—O(1b)	122·2 (3)	O(1a)—C(1a)—C(1b)	110·5 (3)
O(1b)—C(1a)—C(1b)	127·3 (4)	C(2)—O(2a)—C(2a)	116·4 (3)
C(1)—C(2)—O(2a)	107·7 (3)	C(1)—C(2)—C(3)	109·9 (3)
O(2a)—C(2)—C(3)	107·9 (3)	O(2a)—C(2a)—O(2b)	122·9 (4)
O(2a)—C(2a)—C(2b)	111·1 (3)	O(2b)—C(2a)—C(2b)	126·0 (4)
C(3)—O(3a)—C(3a)	116·1 (3)	C(2)—C(3)—O(3a)	110·3 (3)
C(2)—C(3)—C(4)	111·7 (3)	O(3a)—C(3)—C(4)	107·4 (3)
O(3a)—C(3a)—O(3b)	123·0 (4)	O(3a)—C(3a)—C(3b)	110·9 (3)
O(3b)—C(3a)—C(3b)	126·2 (3)	C(4)—O(4a)—C(4a)	118·5 (3)
C(3)—C(4)—O(4a)	108·9 (3)	C(3)—C(4)—C(5)	110·4 (3)
O(4a)—C(4)—C(5)	105·5 (3)	O(4a)—C(4a)—O(4b)	123·5 (3)
O(4a)—C(4a)—C(4b)	110·7 (3)	O(4b)—C(4a)—C(4b)	125·8 (4)
C(5)—O(5a)—C(5a)	117·9 (3)	C(4)—C(5)—O(5a)	108·0 (3)
C(4)—C(5)—C(6)	113·1 (3)	O(5a)—C(5)—C(6)	106·6 (3)
O(5a)—C(5a)—O(5b)	123·7 (4)	O(5a)—C(5a)—C(5b)	110·6 (4)
O(5b)—C(5a)—C(5b)	125·7 (4)	C(6)—O(6a)—C(6a)	117·7 (3)
C(1)—C(6)—C(5)	111·8 (3)	C(1)—C(6)—O(6a)	107·1 (3)
C(5)—C(6)—O(6a)	107·8 (3)	O(6a)—C(6a)—O(6b)	124·0 (4)
O(6a)—C(6a)—C(6b)	110·0 (4)	O(6b)—C(6a)—C(6b)	126·0 (4)

Table 3. Selected torsion angles (°)

C(6)—C(1)—C(2)—C(3)	56·5 (4)	C(3)—C(4)—C(5)—C(6)	−52·7 (4)
C(1)—C(2)—C(3)—C(4)	−58·5 (4)	C(4)—C(5)—C(6)—C(1)	51·6 (4)
C(2)—C(3)—C(4)—C(5)	56·3 (4)	C(5)—C(6)—C(1)—C(2)	−53·2 (4)
H(1)—C(1)···C(1a)—O(1b)	−31 (2)	H(4)—C(4)···C(4a)—O(4b)	−12 (2)
H(2)—C(2)···C(2a)—O(2b)	13 (2)	H(5)—C(5)···C(5a)—O(5b)	7 (2)
H(3)—C(3)···C(3a)—O(3b)	32 (2)	H(6)—C(6)···C(6a)—O(6b)	−12 (2)

The average endocyclic C—C bond of 1·517 (5) Å in (1) agrees well with an average of 1·514 (3) Å in (2) (Watkins *et al.*, 1986) and 1·517 (4) Å in (3) (Jones *et al.*, 1982). The average endocyclic angle is 111·4 (3)° compared with 111·5° in cyclohexane (Bucourt, 1974), 110·6 (3)° in (2) and 111·1 (3)° in (3). Bond lengths and angles of the six acetyl groups are in good agreement with each other and with those of (2) and (3).
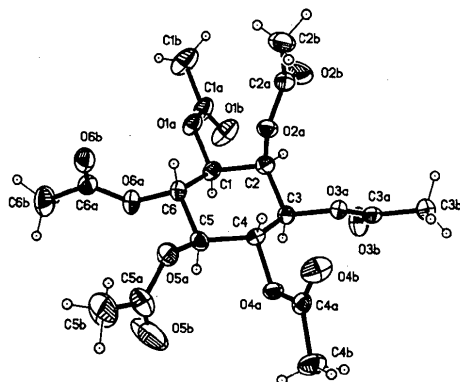
Fig. 1. Drawing of the molecule with the atom-labelling scheme (50% probability ellipsoids).

appears to be a general trend as evidenced by a search of similar compounds in the Cambridge Structural Database (1988). Such coplanarity, however, is not observed at C(1) and C(3) (−31, 32°, respectively). These two acetyl groups are on either side of the axial group and have the freedom to rotate in such a way as to move the carbonyl O atom towards the gap in the equatorial position on C(2).

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