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Crystal structures of (±)-1,2:4,5-di-*O*-isopropylidene-*myo*-inositol and (±)-1,2:5,6-di-*O*-isopropylidene-*myo*-inositol: a conformational analysis

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ABSTRACT

(±)-1,2:4,5-Di-*O*-isopropylidene-*myo*-inositol (**1**), $C_{12}H_{20}O_6$, crystallises in the monoclinic space group, $C2/c$ with unit-cell dimensions $a = 22.587(3)$, $b = 5.4204(3)$, and $c = 22.174(4)$ Å. (±)-1,2:5,6-di-*O*-isopropylidene-*myo*-inositol (**2**), $C_{12}H_{20}O_6$, crystallises in the monoclinic space group, $P2_1/n$ with $a = 11.543(3)$, $b = 6.860(1)$, and $c = 16.895(4)$ Å. The inositol ring of **1** and **2** has a chair and skew conformation, respectively. Based on the crystalline conformations of **1** and **2**, steric and hydrogen bonding features of the hydroxyl groups are discussed.

INTRODUCTION

We have recently investigated the regioselective functionalisation of (±)-1,2:4,5-di-*O*-isopropylidene-*myo*-inositol (**1**) and (±)-1,2:5,6-di-*O*-isopropylidene-*myo*-inositol (**2**) in various reactions[1]. According to previous reports[2] and our own results, the HO-3 group is generally more reactive than HO-6 and HO-4 for **1** and **2**, respectively. In our attempts to understand the origin of hydroxyl reactivity differences, it has been reasoned that the conformations of these compounds are probably associated with the regioselectivities they display. Thus, as a part of our efforts to deduce the conformational structures, the X-ray crystal structures of these two compounds were determined at room temperature.

RESULTS AND DISCUSSION

Large single crystals of **1** were grown by slow evaporation of an ethanol–dichloromethane solution. Single crystals of **2** were obtained by recrystallisation from

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TABLE I

Crystallographic data for **1** and **2** [a]

	1	**2**
Formula	$C_{12}H_{20}O_6$	$C_{12}H_{20}O_6$
Mol wt	260.29	260.29
Space group	$C2/c$	$P2_1/n$
a (Å)	22.587 (3)	11.543 (3)
b (Å)	5.4204 (3)	6.860 (1)
c (Å)	22.174 (4)	16.895 (4)
β (degrees)	110.406 (7)	97.64 (1)
Volume (Å^3)	2544.4 (7)	1326.6 (5)
Z	8	4
Temp (°C)	23	23
Density (calcd)(g/cm^3)	1.358	1.302
λ(Mo$K\alpha$) (Å)	0.70926	070926
Monochromator	Graphite	Graphite
Linear abs. coeff.(cm^{-1})	1.106	0.974
Crystal size (mm)	0.31×0.38×0.38	0.20×0.15×0.10
Take-off angle (degrees)	2.0	2.0
Scan mode	ω	$\omega/2\theta$
ω-scan width (degrees)	0.75+0.34 tan θ	0.80+0.34 tan θ
2θ limits (degrees)	50	44
Weighting scheme	$\omega = 4Fo^2/\sigma^2(Fo)^2$	$\omega = 4Fo^2/\sigma(Fo)^2$
Number of data collected	4077	1774
Number of unique data	2504	1680
Number of unique data with $Fo^2 > 3\sigma(Fo^2)$	1664	675
Number of variables	243	163
$R(F)$	0.028	0.060
$R_w(F)$	0.026	0.063
Diffractometer	Enraf–Nonius CAD4	

[a] Standard deviations in parentheses.

ethyl acetate. The relevant crystallographic data of **1** and **2** are given in Table I. The structures were solved by direct methods using SHELXS 86[3]. All the non-hydrogen atoms were refined anisotropically. For **1**, H atoms were located from a difference Fourier map and refined isotropically[4]. For **2**, the H atoms bonded to carbon were positioned according to idealised geometry (C–H distance 0.95 Å) and given isotropic thermal parameters of 1.2 times those of attached atoms. The final co-ordinates of C and O atoms for **1** and **2** are listed in Table II *. Selected torsional angles, as key conformational parameters, for **1** and **2** are given in Table III. ORTEP[5] drawings of **1** and **2** with the atom numbering schemes are shown in Figs. 1 and 2, respectively. Compound **1** was found to have a chair conformation and **2** a skew conformation in their crystalline phases. As shown in their crystal

* Atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Data Centre. The coordinates may be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

TABLE II

Fractional positional parameters of C and O atoms for **1** and **2** [a]

Atoms	**1**			**2**		
	x	*y*	*z*	*x*	*y*	*z*
O-1	0.87460(5)	0.5554(2)	0.41753(5)	1.1347(5)	−0.0111(9)	0.4163(3)
O-2	0.91888(5)	0.9148(2)	0.39973(5)	1.2195(5)	0.2685(9)	0.4648(3)
O-3	0.99256(5)	1.0358(3)	0.32846(5)	1.0099(6)	0.438(1)	0.4199(4)
O-4	0.89883(5)	0.9031(2)	0.19901(5)	1.1051(6)	0.6277(9)	0.2403(4)
O-5	0.81158(5)	0.6574(2)	0.18572(5)	0.9369(6)	0.2705(9)	0.1843(4)
O-6	0.80124(5)	0.3163(2)	0.28454(5)	0.9951(5)	−0.0221(9)	0.2424(3)
C-1	0.89295(7)	0.5206(3)	0.36219(7)	1.1447(8)	0.104(1)	0.3473(5)
C-2	0.94372(7)	0.7194(3)	0.37260(7)	1.1892(8)	0.305(1)	0.3810(5)
C-3	0.95730(7)	0.8134(3)	0.31370(7)	1.0992(8)	0.472(1)	0.3708(5)
C-4	0.89479(7)	0.8457(3)	0.26078(7)	1.0412(7)	0.494(1)	0.2826(5)
C-5	0.85925(7)	0.6070(3)	0.24701(7)	1.0381(8)	0.300(1)	0.2424(5)
C-6	0.83483(7)	0.5431(3)	0.29973(7)	1.0279(8)	0.130(1)	0.2974(5)
C-7	0.89086(7)	0.8027(3)	0.44141(7)	1.2203(8)	0.064(1)	0.4774(5)
C-8	0.93756(9)	0.7866(4)	0.50957(8)	1.3406(9)	−0.021(2)	0.4707(6)
C-9	0.83253(8)	0.9484(4)	0.43666(8)	1.177(1)	0.018(2)	0.5564(6)
C-10	0.84165(7)	0.8078(3)	0.15107(7)	0.9202(9)	0.062(1)	0.1743(6)
C-11	0.79760(9)	1.0142(4)	0.1201(1)	0.966(1)	−0.005(2)	0.1000(6)
C-12	0.86110(9)	0.6536(4)	0.10465(8)	0.794(1)	0.017(2)	0.1801(7)

[a] Standard deviations in parentheses.

TABLE III

Selected torsional angles (°) in **1** and **2** [a]

	1	**2**
Angles in the inositol ring		
C-1–C-2–C-3–C-4	42.3(2)	−52(1)
C-2–C-3–C-4–C-5	−58.4(2)	30(1)
C-3–C-4–C-5–C-6	72.6(2)	31(1)
C-4–C-5–C-6–C-1	−60.1(2)	−74.1(9)
C-5–C-6–C-1–C-2	42.8(2)	47.4(9)
C-6–C-1–C-2–C-3	−36.9(2)	11(1)
Angles between vicinal oxygens		
O-1–C-1–C-2–O-2	−36.5(1)	10.2(8)
O-2–C-2–C-3–O-3	49.3(2)	−46.9(9)
O-3–C-3–C-4–O-4	66.2(2)	147.5(7)
O-4–C-4–C-5–O-5	−42.5(1)	−92.9(8)
O-5–C-5–C-6–O-6	65.1(2)	42.2(8)
O-6–C-6–C-1–O-1	−83.5(2)	−85.4(9)
Angles between vicinal hydrogens		
H-1–C-1–C-2–H-2	−37(1)	13(1)
H-2–C-2–C-3–H-3	51(1)	−51(1)
H-3–C-3–C-4–H-4	180(1)	−93(1)
H-4–C-4–C-5–H-5	−171(1)	149.1(8)
H-5–C-5–C-6–H-6	180(1)	159.0(9)
H-6–C-6–C-1–H-1	157(1)	158.4(8)

[a] Standard deviations in parentheses.

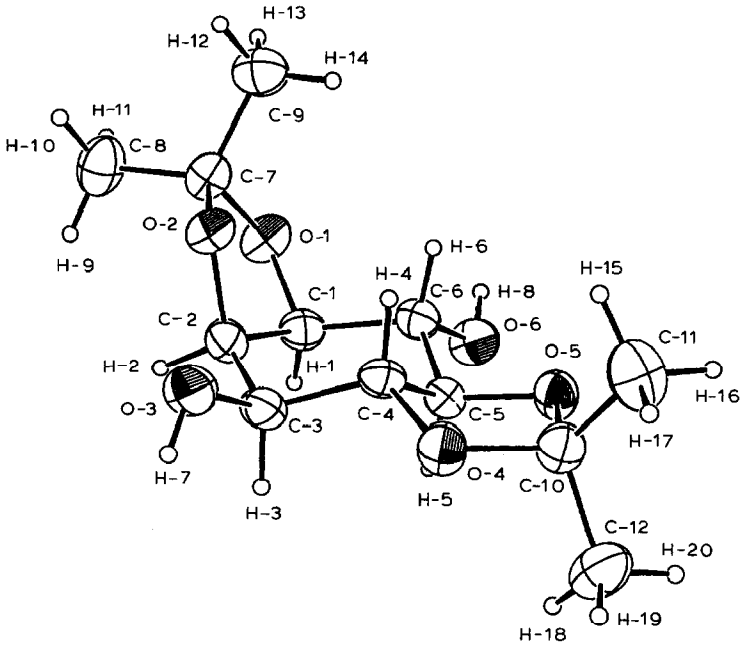

Fig. 1. ORTEP[5] drawing of 1 showing atom numbering.

structures, the HO-3 group for each of the diols 1 and 2 is more sterically hindered than HO-6 and HO-4, respectively, owing to the proximity of the adjacent *cis*-1,2-*O*-isopropylidene ring. In the skew conformation of 2, steric hindrance around HO-3 appears more severe because it is located in the *endo*-position of the

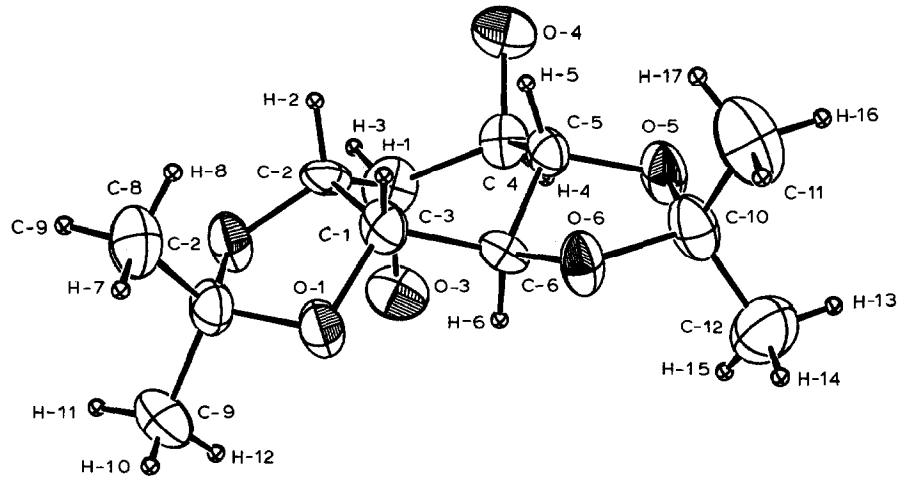

Fig. 2. ORTEP[5] drawing of 2 showing atom numbering.

TABLE IV

Selected interoxygen distances (Å) in 1 and 2

1		2	
O-1–O-3	4.6322	O-1–O-3	3.403
O-2–O-3	2.7456	O-2–O-3	2.702
O-4–O-6	4.6357	O-4–O-5	3.191
O-5–O-6	2.9382	O-4–O-6	4.635

inositol envelope while HO-4 is positioned *exo*. These results do not correlate with the fact that HO-3 is more reactive than HO-6 and HO-4 for **1** and **2**, respectively. Thus, steric effects are not likely to provide the hydroxyl-reactivity differences of these compounds.

Previous investigators working on the regioselectivity problems of carbohydrate molecules have suggested that intramolecular hydrogen bonding may enhance the reactivities of the associated hydroxyl group[6,7]. Hence, we tried to find the possibility of an intramolecular H-bond for **1** and **2** from their crystal structures. Direct evidence for the intramolecular H-bonds could not be found in the crystal structure of diol **1** because intermolecular H-bonds are apparently predominent in its unit cell. For diol **2**, the positions of the hydroxyl protons could not be positioned even by idealised geometry. For these reasons, interoxygen distances between the hydroxyl oxygen and ether oxygens were determined as useful parameters for estimating the possibility of intramolecular H-bonds under the assumption that crystalline conformations are similar to the solution conformations, and that the intramolecular H-bond becomes more dominant in a dilute solution[8]. These parameters are given in Table IV. The interatomic distance between O-2 and O-3 for each of **1** and **2** is ca. 2.7 Å while those of the other relationships are longer. The interoxygen distance of 2.7 Å may be reasonable for hydrogen bonding. In conclusion, an intramolecular H-bond between HO-3 and the cis-vicinal ether oxygen (O-2) for both **1** and **2** may be possible on the basis of crystal structure analysis.

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