Crystal structure and diffraction data for a polymorph of voglibose ($C_{10}H_{21}NO_7$)

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X-ray powder diffraction data of voglibose are reported, and its crystal and molecular structures were determined by simulated annealing and rigid-body Rietveld refinement methods. Voglibose was found to be crystallized in triclinic symmetry with space group *P*-1. The lattice parameters were determined to be $a=6.1974(6)$ Å, $b=6.9918(5)$ Å, $c=7.3955(9)$ Å, $\alpha=70.8628(3)$, $\beta=103.5312(4)$, $\gamma=94.3867(5)°$, $V=294.2(2)$ Å^3, and $\rho_{cal}=1.495$ g/cm^3. The crystal structure contains isolated $C_{10}H_{21}NO_7$ molecular. © *2010 International Centre for Diffraction Data.* [DOI: 10.1154/1.3478418]

Key words: voglibose, X-ray powder diffraction, crystal structure

I. INTRODUCTION

Voglibose, 5,6-didexoy-5-{[2-hydroxy-1-(hydroxymethyl) ethyl]amino}-1-*C*-(hydroxymethyl)-*D*-*epi*-inositol (as shown in Figure 1), has been the research focus due to its wide range of therapeutic and pharmacological properties, including its excellent inhibitory activity against α-glucosidase, hyperglycemia, and various disorders caused by hyperglycemia (Byrn *et al.*, 1995; Giordano *et al.*, 2001). Voglibose has shown strong antiobesity and antidiabetic activity as it is a new potent glucosidase inhibitor and is a drug used for type 2 diabetes in Japan and China (Morris *et al.*, 2000; Kariuki *et al.*, 1996). Voglibose obtained from organic synthesis processes is similar to the structure of the carbohydrates found naturally (Chen *et al.*, 2006). So far, single-crystal voglibose was not synthesized under current working conditions, but single-crystal 5,6-dideoxy-5-{[2-hydroxy-1-(hydroxymethyl)ethyl]-amino}-1-*C*-(methoxycyclohexyl-methyl)-*D* -*epi*-inositol can be synthesized as one of its by-products (Zhang *et al.*, 2004). Voglibose was usually obtained as a polycrystalline material in industry production. In this paper, the crystal structure of polycrystalline voglibose determined by *ab initio* X-ray powder diffraction (XRPD) methods is reported.

II. EXPERIMENTAL

The sample was obtained in the process of voglibose synthesized by the method reported by Ohtake and Ikegami (2000). Then, the obtained sample was crystallized and purified for XRPD analysis.

Diffraction data were recorded on a X'Pert PRO MPD diffractometer (40 kV, 40 mA, and Cu $K\alpha$ radiation with $\lambda=1.5406$ Å), equipped with a diffracted-beam graphite monochromator, an X'Celerator scintillation counter, and an automatic divergence slit. Carefully ground powders were filled into a glass capillary with 0.7 mm in diameter. Other experimental conditions were step scan mode, with $5<2\theta<130°$, $\Delta 2\theta=0.02°$, and $t=10$ s/step.

III. STRUCTURE SOLUTION

The first 20 diffraction peaks in the experimental X-ray diffraction pattern were first accurately estimated and then indexed using DICVOL program. The tile compound was determined to have a primitive triclinic cell with lattice parameters $a=6.1974(6)$ Å, $b=6.9918(5)$ Å, $c=7.3955(9)$ Å, $\alpha=70.8628(3)°$, $\beta=103.5312(4)°$, $\gamma=94.3867(5)°$, and $V=294.2(2)$ Å^3, and the values of figure of merit are $M(20)=40$, $F(20)=43$. The values of $2\theta_{obs}$, $2\theta_{cal}$, I/I_o, *hkl*, d_{obs}, and d_{cal} are listed in Table I. A survey of the Cambridge Structural Database (version 2009) showed no match of any compound with these lattice parameters (or one derived therefore by standard cell-reduction programs). We, therefore, decided to solve the structure by *ab initio* XRPD methods using the experimental data.

Systematic absences, density, and geometrical considerations indicated $Z=1$ and space group *P*-1, which are later confirmed by successful structure solution and refinement. Table II contains the relevant crystal data and data analysis parameters. The structural model employed in the final whole-pattern Rietveld refinement was determined by the simulated annealing technique implemented in DASH3.0 (David *et al.*, 2006). Based on the indexing results, the diffraction-peak intensities were first extracted by the Pawley refinement with values of figure of merit: $R_{wp}=16.0$, $R_{exp}=9.68$, and $\chi^2=2.52$. During structure solving, there were 11 degrees of freedom including three positional coordinates for the centre of mass of the molecule, three parameters describing orientation of the molecule within the unit cell, and five torsions angles for C13-N12-C4-C3, C14-C13-N12-C4, O16-C10-C6-C5, O17-C14-C13-N12, and O18-C15-C13-

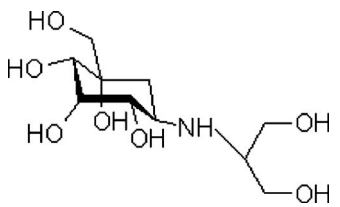

Figure 1. Structure formula for voglibose.

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TABLE I. X-ray diffraction data for voglibose.

$2\theta_{obs}$ (deg)	$2\theta_{cal}$ (deg)	I/I_o	(h k l)	d_{obs} (Å)	d_{cal} (Å)	$\Delta 2\theta(2\theta_{obs}-2\theta_{cal})$
12.981	12.993	6.4	(0 1 0)	6.8142	6.8109	0.011
13.399	13.393	55.4	(1 0 0)	6.6029	6.6058	−0.006
14.698	14.705	31.5	(1 0 1)	6.0219	6.0197	0.007
15.400	15.397	12.8	(1 1 0)	5.7490	5.7491	−0.003
17.358	17.346	49.4	(1 −1 1)	5.1048	5.1064	−0.012
19.238	19.241	1.2	(0 −1 1)	4.6099	4.6095	0.003
19.939	19.926	100.0	(0 0 1)	4.4495	4.4487	−0.013
21.740	21.757	79.7	(1 1 1)	4.0847	4.0839	0.017
23.280	23.283	14.7	(2 1 1)	3.8178	3.8169	0.003
24.422	24.424	16	(2 −1 1)	3.6418	3.6401	0.002
25.299	25.283	5.0	(1 2 0)	3.5176	3.5200	−0.016
25.938	25.918	27.3	(2 1 0)	3.4323	3.4343	−0.02
27.020	27.052	18.8	(1 −2 1)	3.2973	3.2930	0.032
27.762	27.800	3.5	(0 1 1)	3.2109	3.2090	0.039
28.421	28.433	3.5	(−1 −1 1)	3.1378	3.1371	0.012
29.640	29.642	10.5	(2 −1 2)	3.0115	3.0105	0.001
30.841	30.833	13.5	(1 −1 2)	2.8969	2.8981	−0.008
31.100	31.082	11.5	(2 2 0)	2.8734	2.8745	3.2935
31.896	31.869	4.2	(−1 −2 1)	2.8035	2.8056	3.2065
32.222	32.244	5.2	(2 2 1)	2.7758	2.7746	−0.018

TABLE II. Crystal data and data analysis parameters for voglibose.

Formula	$C_{10}H_{21}NO_7$
F_w (g/mol)	267.3
System	Triclinic
Space group	P-1 (2)
Z	1
a (Å)	6.1974 (6)
b (Å)	6.9918 (5)
c (Å)	7.3955 (9)
α (deg)	70.8628 (3)
β (deg)	103.5312 (4)
γ (deg)	94.3867 (5)
V (Å^3)	294.2 (2)
ρ (g/cm^3)	1.495
$M(20)$	40
$F(20)$	43

N12. Simulating annealing finally ended with profile χ^2 =18.80. The crystal and molecular structures are shown in Figure 2, and the final Rietveld refinement plots are plotted in Figure 3. As shown in Figure 2, the molecular structure of voglibose contains one six-membered ring, and the ring (from C1 to C6) adopts chair conformation. The 2-hydroxy-1-[(hydroxymethyl) ethyl] amino group aligned with C5 by the way of an axial bond. The angles for C6-C10-C5, N12-C4-C3, and C13-N12-C4 are 108.998°, 130.526°, and 158.723°, respectively. The final fractional atomic coordinates, bond angles, and bond lengths are listed Tables III–V, respectively.

IV. CONCLUSION

In the absence of single crystals, the *ab initio* structure of a polymorph voglibose was determined from conventional laboratory X-ray powder diffraction data. The crystal model

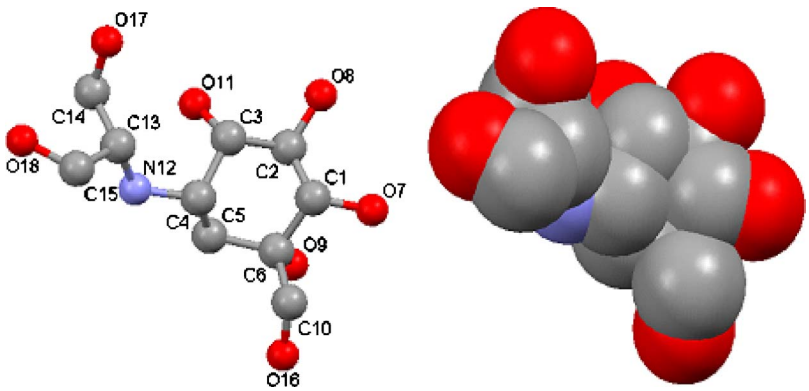

Figure 2. (Color online) Schematic illustration of voglibose molecule structure (left, ball and ticks; right, space filling model).

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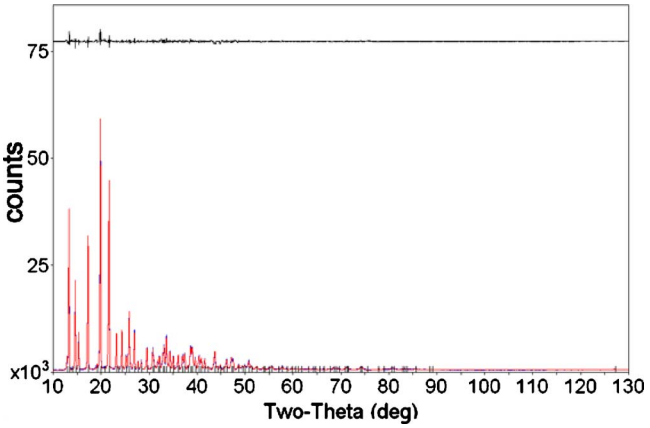

Figure 3. (Color online) Final Rietveld refinement plot (red line) with peak markers, raw experimental scan (blue line), and difference plot at the top.

TABLE III. Atomic coordinates for voglibose.

Number	Atom label	*x*	*y*	*z*
1	C1	0.166 88(2)	0.368 46(4)	0.618 18(1)
2	C2	0.258 16(1)	0.586 71(3)	0.641 38(3)
3	C3	0.425 59(4)	0.636 55(3)	0.502 91(2)
4	C4	0.524 34(3)	0.460 31(2)	0.523 34(2)
5	C5	0.539 37(2)	0.399 02(1)	0.755 08(1)
6	C6	0.321 05(3)	0.277 44(2)	0.776 27(2)
7	O7	−0.013 75(2)	0.285 96(4)	0.690 49(3)
8	O8	0.134 55(1)	0.706 56(5)	0.552 63(2)
9	O9	0.321 68(3)	0.295 37(4)	1.004 47(2)
10	C10	0.257 23(2)	0.052 97(1)	0.713 38(4)
11	O11	0.560 55(1)	0.827 41(4)	0.584 95(3)
12	N12	0.721 17(2)	0.541 04(3)	0.462 32(3)
13	C13	0.727 05(1)	0.631 87(2)	0.234 45(4)
14	C14	0.823 25(2)	0.862 54(3)	0.254 09(2)
15	C15	0.829 32(1)	0.543 29(2)	0.095 36(3)
16	O16	0.319 93(3)	−0.060 56(1)	0.899 82(4)
17	O17	0.733 01(2)	0.956 65(4)	0.066 24(2)
18	O18	1.005 06(1)	0.694 16(4)	0.062 22(4)

TABLE IV. Bond angles for voglibose.

Atoms			Bond angles (deg)
C5	-C4	-C3	120.088(4)
O11	-C3	-C4	95.787(1)
C6	-C5	-C4	90.253(3)
C13	-N12	-C4	158.723(2)
C1	-C2	-C3	126.871(1)
O8	-C2	-C3	74.358(3)
C2	-C3	-C4	104.304(2)
N12	-C4	-C3	130.526(3)
C10	-C6	-C5	108.998(4)
O17	-C14	-C13	134.996(1)
O18	-C15	-C13	119.347(3)
C15	-C13	-N12	129.347(4)
C14	-C13	-N12	116.730(2)
O7	-C1	-C2	174.183(3)
O16	-C10	-C6	100.003(1)
O9	-C6	-C5	68.145(2)

TABLE V. Bond lengths for voglibose.

Atoms		Bond lengths (Å)
C1	-C2	1.736
C2	-O8	1.852
C5	-C6	1.938
C3	-O11	2.307
C2	-C3	1.394
C6	-O9	1.514
N12	-C4	1.512
C3	-C4	1.585
C13	-C14	1.478
C6	-C10	2.126
C4	-C5	1.505
C13	-N12	1.406
C15	-C13	1.698
C1	-O7	1.755
C14	-O17	2.204
O16	-C10	1.330
O18	-C15	1.781

was solved by simulated annealing using rigid groups with flexible conformational freedoms including five torsion angles, and the final crystal structure parameters, including atomic coordinates, bond angles, and bond lengths, were refined by rigid-body Rietveld refinement method.

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