Carbohydrate Research, 241 (1993) 55–61
Elsevier Science Publishers B.V., Amsterdam

Crystal structure of 2,5-anhydro-1-*O*-(*p*-tolylsulfonyl)-D-mannitol

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(Received June 29th, 1992; accepted with revision, September 21st, 1992)

ABSTRACT

2,5-Anhydro-1-*O*-(*p*-tolylsulfonyl)-D-mannitol, $C_{13}H_{18}SO_7$, $M_r = 318.4$, monoclinic, $C2$, $a = 26.370(6)$, $b = 7.9741(11)$, $c = 6.6801(6)$ Å, $\beta = 91.401(11)°$, $V = 1404.3(6)$ Å^3, $Z = 4$, $D_X = 1.506$ g/cm^3, Cu$K\alpha$, $\lambda = 1.54184$ Å, $\mu = 23.03$ cm^{-1}, F(000) = 672, T = 296(1) K, $R = 0.042$ for 2832 observations with $I > 3\sigma(I)$ (of 2864 unique data). On the esterified side of the molecule, three bond lengths and three bond angles show small changes compared to the unesterified side, which is similar to the symmetrical parent compound, 2,5-anhydro-D-mannitol. The conformation of the five-membered ring is E_5 with P = 49.3° and $\tau_m = 38.1°$. The hydroxymethyl groups adopt g^+ and g^- dispositions similar to the parent molecule. The three hydroxyl groups are involved in a network of intermolecular hydrogen bonds both as donors and acceptors.

INTRODUCTION

The title compound, 2,5-anhydro-1-*O*-(*p*-tolylsulfonyl)-D-mannitol (**1**), is one of the few known unsymmetrical compounds derived from the symmetric parent 2,5-anhydro-D-mannitol (**2**)[1]. The parent compound has been shown to exhibit hypoglycemic properties[2,3]. Since **2** is symmetrical, it is difficult to modify unsymmetrically, and there are reasons to believe that unsymmetrical derivatives might retain hypoglycemic properties. The crystal structure analysis of **2** (ref. 1) indicated that the system is almost symmetric with the unexpected observation that the side chain torsion angles differ by 120°. The probable cause is the intermolecular hydrogen-bond network in **2**. Thus, it is of significance to investigate the effect of unsymmetric substitutions on the structure of **2**. One approach to reach this aim is to radically change one of the hydroxyls so as to remove its hydrogen bonding ability. With this goal in mind, we have prepared the title compound in crystalline form and determined its structure by X-ray diffraction analysis.

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EXPERIMENTAL

Preparation of 2,5-anhydro-1-*O*-(*p*-tolylsulfonyl)-D-mannitol (**1**) followed the procedure published in the literature[4], except that an ethyl acetate extraction was substituted for the PLC procedure, and the product was recrystallized (mp 108–110°C) from abs EtOH. A colorless plate was used for data collection on an Enraf–Nonius CAD-4 diffractometer equipped with Cu$K\alpha$ radiation and a graphite monochromator. Cell dimensions were determined from setting angles of 25 reflections having $30 > \theta > 20°$. Crystal data are given in Table I. The $\omega - 2\theta$ scans were designed for $I = 50\sigma(I)$, subject to a maximum scan time of 120 s, scan rates varied from 0.66–3.30° min^{-1}. Three quadrants of data having $2° < \theta < 75°$ were measured and corrected for background, Lorentz, polarization, and absorption. Three standard reflections (16 0 0, 0 4 0, 0 0 4) varied only randomly during data collection, and no decay correction was applied. Absorption corrections were based on ψ scans. A total of 4243 data points was measured. Equivalent data were averaged, $R_{\text{int}} = 0.021$, yielding 2864 unique data points. Systematic absences and the chirality of the compound indicated space group $C2$. The structure was solved by direct methods using MULTAN-80 (ref. 5), refined by full-matrix least-squares based upon F, using data for which $I > 3\sigma(I)$, weights $w = 4F_o^2[\sigma^2(I) + (0.02F_o^2)^2]^{-1}$ using the MolEN programs[6], scattering factors[7], and anomalous coefficients[8]. Heavy-atom coordinates were refined with anisotropic thermal parameters; H-atom coordinates were located by ΔF and, except for those of the methyl group, refined with isotropic thermal parameters. Final $R = 0.042$ for 2832

TABLE I

Crystal data for 2,5-anhydro-1-*O*-(*p*-tolylsulfonyl)-D-mannitol

Formula	$C_{13}H_{18}SO_7$
Formula weight	318.4
Cell constants	
a(Å)	26.370(6)
b(Å)	7.9741(11)
c(Å)	6.6801(6)
β(°)	91.401(11)
Volume (Å^3)	1404.3(6)
Z (molecules/cell)	4
Density calculated (g/cm^3)	1.506
Space group	$C2$
Crystal size (mm)	0.10×0.38×0.70
λ(Cu$K\alpha$) (Å)	1.54184
Minimum transmission	0.84
Unique reflections	2864
$I > 3\sigma(I)$	2832
R	0.042
R_w	0.056
S (250 variables)	3.463

TABLE II

Atomic coordinates and equivalent isotropic thermal parameters for 2,5-anhydro-1-*O*-(*p*-tolylsulfonyl)-D-mannitol

Atom	x	y	z	B_{eg} (Å^2) ^{a}
S	0.39298(1)	0	0.80432(6)	2.672(7)
O-1	0.39707(5)	0.1074(2)	0.6078(2)	3.17(2)
O-2	0.33850(5)	0.3600(2)	0.4162(2)	3.01(2)
O-3	0.23576(5)	0.1068(2)	0.3035(2)	3.10(2)
O-4	0.28144(5)	0.3284(2)	−0.0707(2)	3.27(2)
O-6	0.29372(5)	0.6819(2)	0.3022(2)	3.17(2)
O-7	0.34187(5)	−0.0498(2)	0.8302(3)	3.93(3)
O-8	0.41777(6)	0.1003(2)	0.9541(2)	4.11(3)
C-1	0.36317(7)	0.0694(3)	0.4356(3)	3.04(3)
C-2	0.31993(6)	0.1931(2)	0.4304(2)	2.45(3)
C-3	0.28449(6)	0.1620(3)	0.2455(2)	2.45(3)
C-4	0.28302(6)	0.3336(2)	0.1420(3)	2.44(3)
C-5	0.33253(6)	0.4137(3)	0.2127(3)	2.59(3)
C-6	0.33482(7)	0.6018(3)	0.2087(3)	3.05(3)
C-7	0.42986(6)	−0.1783(3)	0.7617(3)	2.47(3)
C-8	0.40679(7)	−0.3340(3)	0.7419(3)	2.80(3)
C-9	0.43652(7)	−0.4764(3)	0.7343(3)	3.11(3)
C-10	0.48940(7)	−0.4654(3)	0.7423(3)	3.10(3)
C-11	0.51146(7)	−0.3074(3)	0.7531(3)	3.35(4)
C-12	0.48272(7)	−0.1641(3)	0.7642(3)	3.02(3)
C-13	0.52151(9)	−0.6201(3)	0.7453(4)	4.23(4)
H-3OH	0.225(1)	0.022(4)	0.230(4)	4.6(6)
H-4OH	0.2555(9)	0.267(3)	−0.105(3)	3.1(5)
H-6OH	0.293(1)	0.636(5)	0.406(4)	4.7(6)

^{a} $B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$

observed data points (0.043 for all 2864 data points), $R_w = 0.056$, and $S = 3.463$ for 250 variables. Maximum shift 0.06σ in the final cycle, maximum residual density 0.99, minimum -0.66 e Å^{-3}, and extinction coefficient $g = 3.87(5) \times 10^{-5}$ where the factor $(1 + gI_c)^{-1}$ was applied to F_c. Atomic coordinates and equivalent isotropic thermal parameters are given in Table II *. The absolute configuration of the compound was confirmed to be D, as assumed based on the configuration of the starting compound. Refinement of the L-isomer under identical circumstances yielded $R = 0.059$, $R_w = 0.079$, and $S = 4.892$.

RESULTS

The molecular structure and atomic numbering of 2,5-anhydro-1-*O*-(*p*-tolylsulfonyl)-D-mannitol (**1**) are illustrated in Fig. 1. Some of the bond lengths (Table

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* Lists of observed and calculated structure-amplitudes, anisotropic thermal parameters, hydrogen coordinates and isotropic thermal parameters, and torsion angles for **1** have been deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/520/*Carbohydr. Res.*, 241 (1993) 55–61.

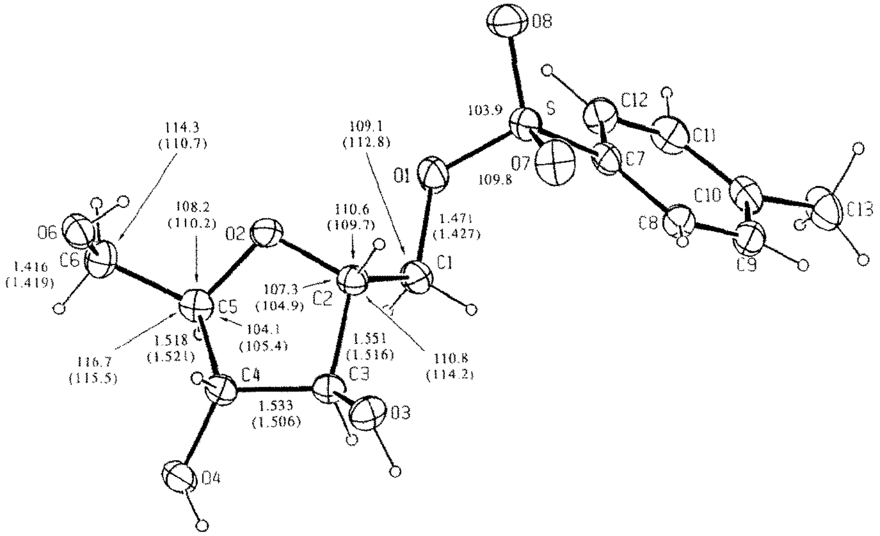

Fig. 1. Molecular structure, atomic numbering, selected bond lengths (in Å), and bond angles (in degrees) of 2,5-anhydro-1-*O*-(*p*-tolylsulfonyl)-D-mannitol (**1**) with the corresponding values of 2,5-anhydro-D-mannitol (**2**) in parenthesis.

III) and bond angles (Table IV) are also included in Fig. 1 for comparison with **2**. The bond lengths and angles of **1** are in the expected ranges with some distortions caused by the tosyl group. Two bond lengths (O-1–C-1 and C-2–C-3) on the esterified side are longer (0.033 and 0.055 Å, respectively) than the corresponding bonds on the unesterified side. On the other hand, the O-2–C-2 and C-1–C-2 values are similar to their corresponding values on the opposite side. The 5.9° closure of the C-1–C-2–C-3 bond angle is roughly compensated by the enlarging of the O-2–C-2–C-3 (3.2°) and O-2–C-2–C-1 (2.4°) angles. The exocyclic angle

TABLE III

Bond lengths for 2,5-anhydro-1-*O*-(*p*-tolylsulfonyl)-D-mannitol

Atom 1	Atom 2	Distance (Å)	Atom 1	Atom 2	Distance (Å)
S	O-1	1.574(1)	C-1	C-2	1.507(3)
S	O-7	1.420(1)	C-2	C-3	1.551(2)
S	O-8	1.427(2)	C-3	C-4	1.533(3)
S	C-7	1.750(2)	C-4	C-5	1.518(2)
O-1	C-1	1.471(2)	C-5	C-6	1.502(3)
O-2	C-2	1.423(2)	C-7	C-8	1.388(3)
O-2	C-5	1.431(2)	C-7	C-12	1.398(2)
O-3	C-3	1.421(2)	C-8	C-9	1.381(3)
O-3	H-3OH	0.88(3)	C-9	C-10	1.397(3)
O-4	C-4	1.421(2)	C-10	C-11	1.389(3)
O-4	H-4OH	0.87(2)	C-10	C-13	1.496(3)
O-6	C-6	1.416(2)	C-11	C-12	1.374(3)
O-6	H-6OH	0.78(3)			

TABLE IV

Bond angles for 2,5-anhydro-1-*O*-(*p*-tolylsulfonyl)-D-mannitol

Atom 1	Atom 2	Atom 3	Angle(°)	Atom 1	Atom 2	Atom 3	Angle(°)
O-1	S	O-7	109.79(9)	O-4	C-4	C-3	115.1(2)
O-1	S	O-8	103.90(9)	O-4	C-4	C-5	109.1(1)
O-1	S	C-7	104.90(8)	C-3	C-4	C-5	102.9(1)
O-7	S	O-8	119.4(1)	O-2	C-5	C-4	104.1(1)
O-7	S	C-7	109.0(1)	O-2	C-5	C-6	108.2(2)
O-8	S	C-7	108.81(9)	C-4	C-5	C-6	116.7(1)
S	O-1	C-1	119.2(1)	O-6	C-6	C-5	114.3(2)
C-2	O-2	C-5	108.3(1)	S	C-7	C-8	119.9(1)
C-3	O-3	H-3OH	112(2)	S	C-7	C-12	119.4(2)
C-4	O-4	H-4OH	107(2)	C-8	C-7	C-12	120.5(2)
C-6	O-6	H-6OH	102(2)	C-7	C-8	C-9	119.4(2)
O-1	C-1	C-2	109.1(2)	C-8	C-9	C-10	120.9(2)
O-2	C-2	C-1	110.6(1)	C-9	C-10	C-11	118.4(2)
O-2	C-2	C-3	107.3(1)	C-9	C-10	C-13	120.9(2)
C-1	C-2	C-3	110.8(1)	C-11	C-10	C-13	120.8(2)
O-3	C-3	C-2	111.3(1)	C-10	C-11	C-12	121.8(2)
O-3	C-3	C-4	112.7(1)	C-7	C-12	C-11	118.9(2)
C-2	C-3	C-4	103.0(1)				

O-1–C-1–C-2 is 5.2° smaller than the angle O-6–C-6–C-5. The conformation of the tetrahydrofuran ring[9] is E_5, slightly distorted towards $^4T_5$, with a phase angle (P) of 49.3° and a pseudorotation amplitude (τ_m) of 38.1°. The side chain torsion angles O-2–C-2–C-1–O-1 [+58.7(2)°] and O-2–C-5–C-6–O-6 [−66.5(2)°] are such that the C-1–O-1 bond is directed parallel to the C-3–C-2 bond's direction but the C-6–O-6 bond is at an angle of 50° relative to the C-4–C-5 bond's direction. The tosyl group has bond lengths and angles in the expected ranges with the ring being nearly planar. A significant difference of about 6° exist between the O-1–S–O-7 [109.79(9)°] and O-1–S–O-8 [103.90(9)°] bond angles.

The data for the hexitol portion of **1** are compared to the symmetrical parent compound **2**. The data for the tosyl grouping are compared to those of the unsymmetrical ditosylated compound methyl 3,4-anhydro-1,6-di-*O*-(*p*-tolylsulfonyl)-β-D-tagatofuranoside (**3**) (ref. 10). A comparison of the selected bond lengths and angles of compounds **1** and **2** included in Fig. 1 shows that only the above-mentioned two bond lengths (O-1–C-1 and C-2–C-3) and C-3–C-4 (0.027 Å) are significantly longer in **1**. The values on the unesterified side of **1** mimic the values of **2**. A similar trend is noted for the bond angles of **1** as compared to **2**. Both compounds **1** and **2** have conformations in the same region of the pseudorotation itinerary with **2** being E_3, slightly distorted towards $^4T_3$, with $P = -11.7°$ and $\tau_m = 38.8°$. The torsion angles reported for **2** [+65.9(1)° and −66.5(1)°] indicate that O-1 and O-6 are in a similar conformation in the two molecules, with the exception of a minor difference (−7°) on the esterified side of the molecule. The tosyl group of **1** has bond lengths and angles similar to those of both tosyl

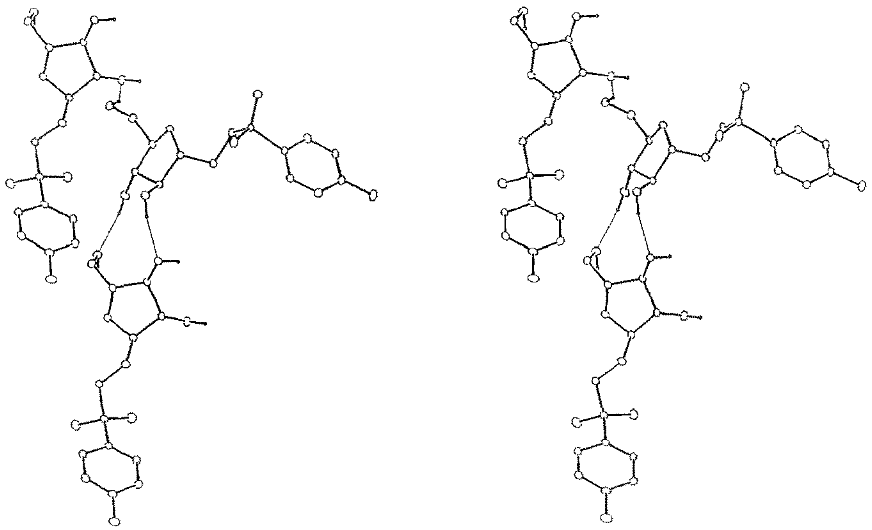

Fig. 2. Stereoview of the hydrogen bonding scheme of 2,5-anhydro-1-*O*-(*p*-tolylsulfonyl)-D-mannitol (**1**).

groups in **3**. The significant difference of about 6° in the bond angles about the sulfur atom is similar to those noted for both tosyl groups [109.6(3)°, 103.4(3)°, $\Delta = 6°$; 109.6(3)°, 102.2(3)°, $\Delta = 7°$] in **3**.

All three OH groups of **1** participate in intermolecular hydrogen bonds to other OH groups as indicated in the hydrogen-bonding diagram (Fig. 2). Substituents O-3 and O-4 donate to hydroxyl groups of the same molecule; the acceptors are O-4 of a second molecule, with an O–O distance of 2.742(2) Å and angle about H of 166(3)°, and O-6 of the same second molecule, with an O–O distance of 2.745(2) Å and an angle about H of 152(2)°, respectively. Hydroxyl group O-6 donates to O-3 of a third molecule, with an O–O distance of 2.828(2) Å and an angle about H of 151(3)°.

DISCUSSION

The data presented in this paper depict the changes in the 3D structure of a symmetrical anhydro-hexitol molecule, namely 2,5-anhydro-D-mannitol (**2**), by the introduction of a tosyl group at C-1. This single-sided tosylation results in an increase in the length of three bonds on the esterified side, namely O-1–C-1, C-2–C-3, and C-3–C-4, over the length of the corresponding bonds on the unesterified side. The latter remain similar to those in the parent compound (**2**). Concomitantly, three bond angles on the esterified side of the molecule show changes as compared to the unesterified side of **1**. Thus, whereas C-1–C-2–C-3 contracts, this is compensated for roughly by an increase in O-2–C-2–C-3 and O-2–C-2–C-1. A third angle O-1–C-1–C-2 decreases, and the corresponding angle C-5–C-6–O-6 on the unesterified side shows an increase over the parent compound.

Moreover, the change in the conformation of the tetrahydrofuran ring is noteworthy. Thus, the ring in **1** is E_5, slightly distorted towards $^4T_5$, and in the symmetric parent compound (**2**) it is E_3, slightly distorted towards $^4T_3$. We have reported[1] that crystalline **2** exists in an almost symmetric structure, except for the side chain torsion angles which differ by 120°. The present data indicate that this difference also exists in **1**. It would seem that the side-chain conformation on the unesterified portion of **1** is determined by the strong intermolecular hydrogen bond network, whereas the conformation on the esterified side is determined by steric crystal-packing effects. The limits of this effect will require the study of several other unsymmetrical derivatives of 2,5-anhydro-D-mannitol.

ACKNOWLEDGMENTS

The financial support of Louisiana Educational Quality Support Fund through Grant No. LEQSF(1990-92)-RD-B-09 and NIH Grant No. DK 40401 (to E.S.Y.), and support (to T.M.N.) from a grant to improve biomedical education from the Howard Hughes Medical Institute to Louisiana State University are gratefully acknowledged.

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