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THE CRYSTAL STRUCTURE OF HEPTYL 1-THIO-α-D-MANNOPYRANOSIDE, A LIQUID-CRYSTAL PRECURSOR

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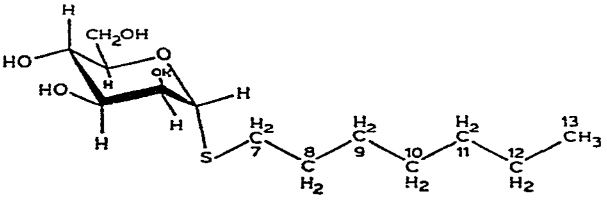
ABSTRACT

Heptyl 1-thio-α-D-mannopyranoside, $C_{13}H_{26}O_5S$, is orthorhombic, $P2_12_12_1$, with cell dimensions, at 123 K [20 °C], of a = 6.600(3) [6.611(2)], b = 7.624(5) [7.759(4)], c = 30.24(1) [30.47(1)] Å, V = 1520.9 [1563.0] Å^3, Z = 4, D_x = 1.286 [1.252] g.cm^{-3}, D_m = [1.245] g.cm^{-3}. The intensities of 2320 symmetry-independent reflections with $I > 2\sigma(I)$ were measured at 123 K with graphite-monochromated, MoKα radiation (λ = 0.7107 Å). The structure was solved by the direct method, and refined by full-matrix least-squares, to give agreement factors R = 0.030, R_w = 0.033, S = 1.61. The pyranoid conformation is $^4C_1$. The ring, C–O bond-lengths are significantly different, C-1–O-5 = 1.433(2), C-5–O-5 = 1.448(2) Å, but the C–S bond-lengths, 1.819(2), 1.824(2) Å, are not. The molecules pack in a bilayer arrangement, with the hexyl chains parallel, and head-to-tail in adjacent molecules. The hydrogen bonding of the pyranoside moieties consists of infinite chains cross-linked through bifurcated bonds to the ring-oxygen atoms. The compound has a liquid-crystal phase lying between 64 °C and the melting point at 151–152 °C, with a periodicity of 21 Å.

INTRODUCTION

Heptyl 1-thio-α-D-mannopyranoside (**1**), recrystallized from 2-propanol–diethyl ether, was obtained from Dr. P. L. Durette, Merck Sharp and Dohme Research Laboratories. It is one of a series of carbohydrate derivatives synthesized in order to evaluate their ability to affect cell-surface membranes selectively[1]. The structure was of interest because of its similarity to models postulated for membrane structures, and because it is a precursor to a liquid-crystal phase that occurs prior to melting.



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EXPERIMENTAL

Diffraction data consisting of 2320 symmetry-independent intensities with I $>2\sigma(I)$ were measured on a CAD-4 diffractometer at 123 K with graphite-monochromated, MoKα radiation (λ = 0.7107 Å). The crystal dimensions were 0.45 × 0.50 × 0.25 mm^3. The unit-cell parameters were determined from a least-squares fit of $\sin^2\theta$ values for $30.5° < 2\theta < 37.5°$. No corrections were made for absorption ($\mu_{MoK\alpha}$ = 2.26 cm^{-1}), or extinction.

The structure was solved by using the program MULTAN[2] from 190 reflections with E >1.68. All non-hydrogen atoms appeared on the E-maps, and all hydrogen atoms on difference-Fourier syntheses. Full-matrix refinement was of $w(F_o\text{-}kF_c)^2$, where $w = 1/\sigma^2$ from counting statistics. The non-hydrogen atoms were refined anisotropically, and the hydrogen atoms, isotropically. The positions for hydrogen atoms H-O-2, H-3, and H-5 were not well defined. These atoms were placed in the reasonable positions observed on the difference maps, and were not refined. The atomic scattering-factors used were those of Cromer and Waber[3] for C, O, and S, and of Stewart and co-workers[4] for hydrogen. Extinction was not serious, with only (020) affected such that $F_o = 0.91\ F_c$.

TABLE I

FRACTIONAL ATOMIC COORDINATES AND EQUIVALENT ISOTROPIC TEMPERATURE FACTORS FOR[a] HEPTYL 1-THIO-α-D-MANNOPYRANOSIDE AT 123 K

Atom	*x*	*y*	*z*	*B(iso) or B(eq) (Å²)*	*X-H (Å)*
S	31104(6)	24880(6)	−35011(1)	1.321	
C-1	3261(3)	2761(2)	−4099(1)	1.108	
C-2	1232(3)	3366(2)	−4289(1)	1.057	
C-3	−301(3)	1887(2)	−4258(1)	1.038	
C-4	463(3)	203(2)	−4470(1)	1.057	
C-5	2569(3)	−269(2)	−4294(1)	1.139	
C-6	3571(3)	−1738(2)	−4551(1)	1.349	
C-7	5807(2)	2261(2)	−3392(1)	1.405	
C-8	6194(3)	2224(2)	−2894(1)	1.552	
C-9	8461(3)	2155(3)	−2794(1)	1.501	
C-10	8926(3)	2146(3)	−2298(1)	1.634	
C-11	11191(3)	2144(3)	−2200(1)	1.637	
C-12	11655(4)	2124(3)	−1706(1)	2.068	
C-13	13918(4)	2154(3)	−1605(1)	2.552	
O-2	1530(2)	3969(2)	−4731(1)	1.378	
O-3	−2148(2)	2459(2)	−4457(1)	1.420	
O-4	−957(2)	−1123(2)	−4358(1)	1.523	
O-5	3925(2)	1219(2)	−4328(1)	1.153	
O-6	3635(2)	−1383(2)	−5014(1)	1.561	
H-O-2[b]	206	314	−494	3.0	0.96
H-O-3	−290(4)	175(4)	−441(1)	2.8(6)	0.75(3)

TABLE I *(continued)*

Atom	*x*	*y*	*z*	*B(iso) or B(eq) (Å²)*	*X-H (Å)*
H-O-4	−104(4)	174(3)	−457(1)	2.6(5)	0.78(2)
H-O-6	438(4)	−58(4)	−506(1)	3.2(6)	0.78(3)
H-1	430(3)	364(3)	−416(1)	0.6(4)	0.97(2)
H-2	75(3)	440(3)	−412(1)	1.2(4)	0.99(2)
H-3[b]	−55	165	−395	1.0	0.97
H-4	58(3)	34(2)	−478(1)	0.6(4)	0.95(2)
H-5[b]	239	−62	−399	1.0	0.97
H-61	491(3)	−199(2)	−445(1)	0.3(3)	0.96(2)
H-62	279(3)	−284(2)	−452(1)	0.5(3)	0.99(2)
H-71	627(4)	113(3)	−353(1)	1.7(5)	1.01(2)
H-72	657(4)	327(3)	−352(1)	1.7(4)	1.00(2)
H-81	548(4)	334(3)	−275(1)	2.2(5)	1.07(2)
H-82	552(4)	113(3)	−278(1)	1.7(5)	1.00(2)
H-91	900(4)	113(3)	−294(1)	1.5(4)	0.96(2)
H-92	917(4)	320(3)	−295(1)	3.1(6)	1.04(3)
H-101	831(4)	114(3)	−216(1)	2.3(5)	0.96(2)
H-102	823(4)	329(3)	−215(1)	2.2(5)	1.08(2)
H-111	1186(4)	107(3)	−235(1)	1.6(4)	1.03(2)
H-112	1180(4)	319(3)	−234(1)	2.2(5)	0.99(2)
H-121	1109(4)	107(4)	−157(1)	2.7(5)	0.98(3)
H-122	1095(4)	314(3)	−156(1)	1.8(5)	1.01(2)
H-131	1456(5)	116(4)	−174(1)	3.0(6)	0.96(3)
H-132	1412(5)	206(4)	−128(1)	3.8(6)	0.99(3)
H-133	1460(5)	322(4)	−170(1)	3.4(6)	0.97(3)

[a] Values are ×10⁵ for the sulfur atom, ×10⁴ for the carbon and oxygen atoms, and ×10³ for the hydrogen atoms. $B(eq) = \frac{1}{3} \Sigma_{i=1}^{3} B_{ii}$. The B(iso) values for H atoms are given according to the expression $\exp(-T) = \exp(-B\sin^2\theta/\lambda^2)$. Estimated standard deviations, given in parentheses, refer to the least significant digit. [b] These hydrogen positions were fixed, and not refined.

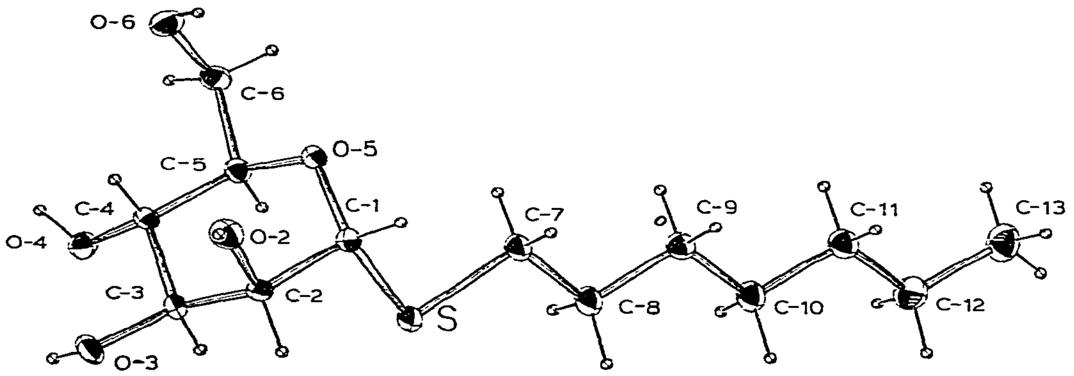

Fig. 1. Atomic notation and thermal ellipsoids (50% probability) for heptyl 1-thio-α-D-mannopyranoside at 123 K.

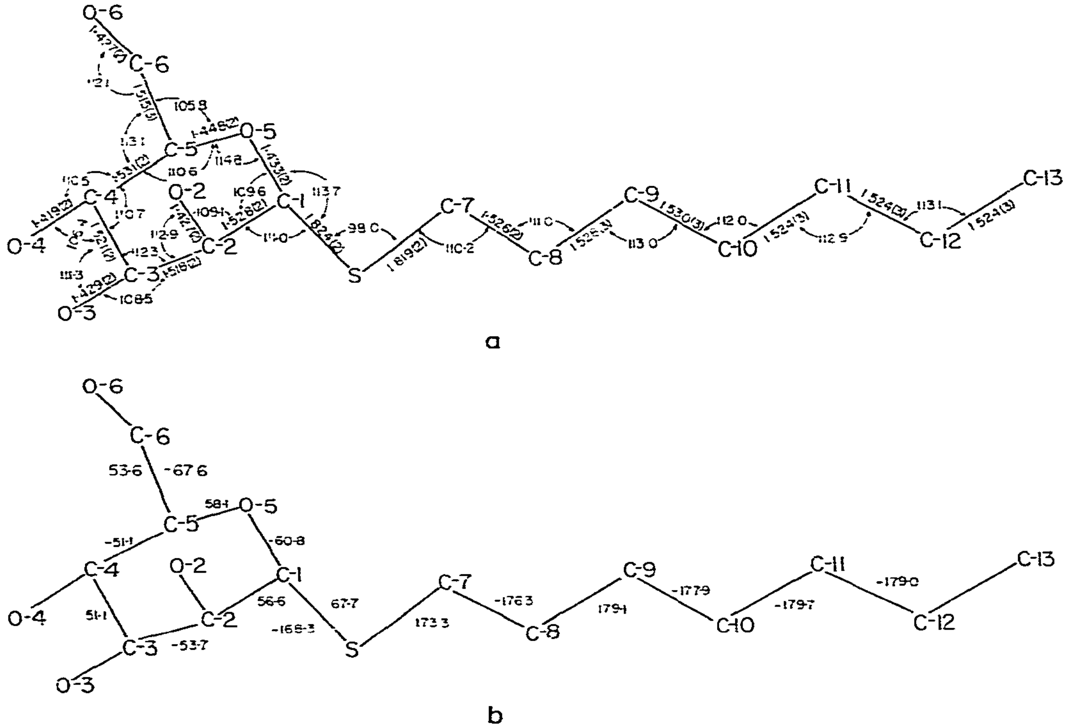

Fig. 2. Molecular dimensions of heptyl 1-thio-α-D-mannopyranoside at 123 K. [(a) Bond lengths (in Å, with estimated, standard deviations in parentheses), and valence bond-angles (in degrees; estimated, standard deviations are ±0.2°); (b) torsion angles (in degrees; estimated, standard deviations are ±0.2°).]

The atomic parameters* are given in Table I. The atomic notation and thermal ellipsoids are given in Fig. 1, and the molecular dimensions are shown in Fig. 2. The liquid-crystal diffraction-patterns were taken with a flat-plate camera, with a film-to-specimen distance of 15.75 cm. The powder specimens were enclosed in glass capillaries in a heating chamber controlled to ±2°C.

DISCUSSION

The most interesting result of the structure analysis is the molecular packing, shown in Fig. 3. This is very similar to the packing of the molecules in 1-decyl α-D-glucopyranoside (illustrated in Fig. 2 of ref. 5), and in 1-*O*-β-D-glucosylphytosphingosine hydrochloride monohydrate [2-amino-2-deoxy-1-*O*-β-D-glucopyranosyl-D-*ribo*-

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*The Tables of observed, and calculated, structure factors and of anisotropic, thermal parameters may be obtained from the authors, or from: Elsevier Scientific Publishing Company, BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/212/*Carbohydr. Res.*, 102 (1982) 59–67.

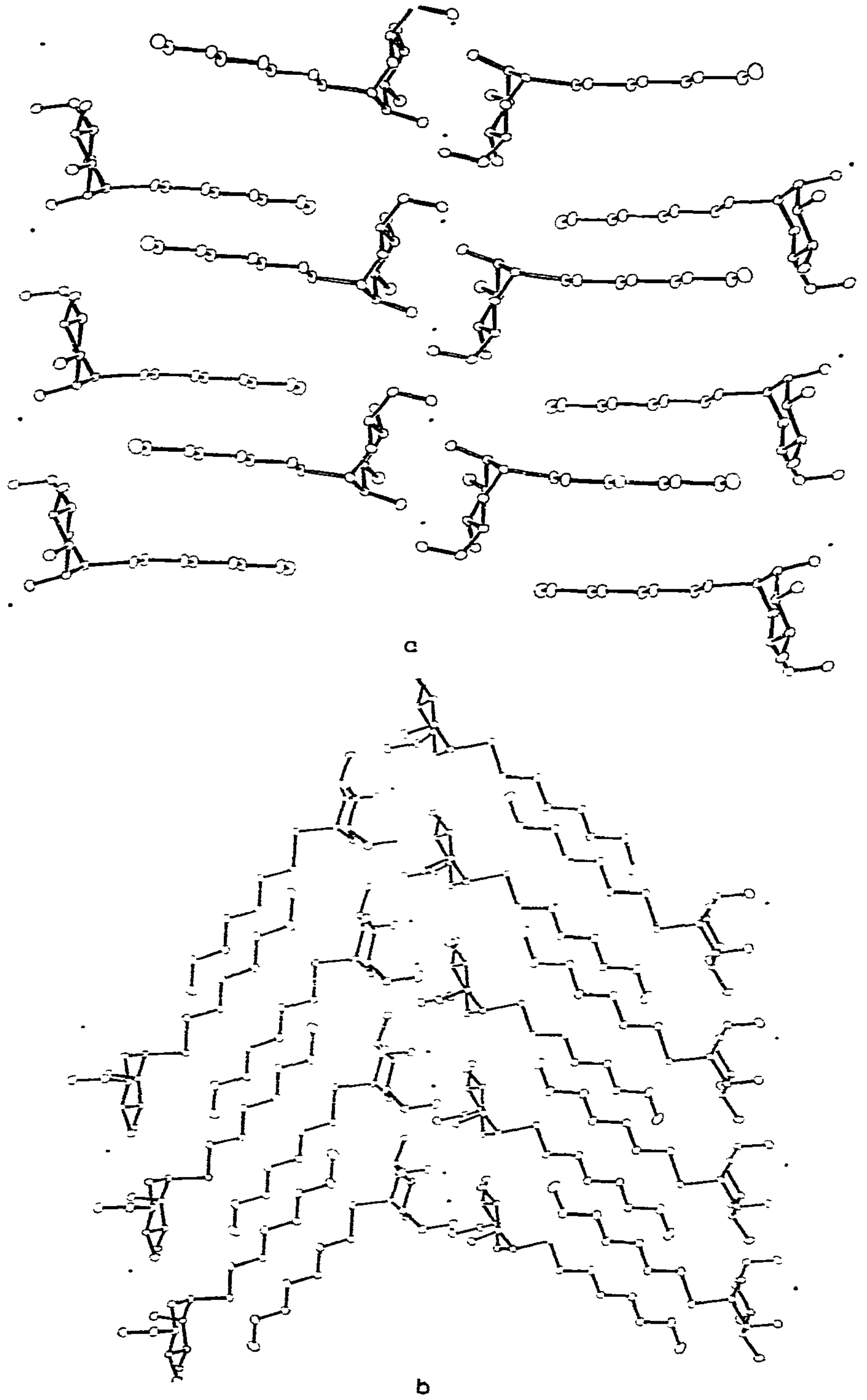


Fig. 3. Molecular packing in the crystal structure of heptyl 1-thio-α-D-mannopyranoside. [(a) Viewed down the *a* axis; the *b* axis is vertical; (b) viewed down the *b* axis; the *a* axis is vertical.]

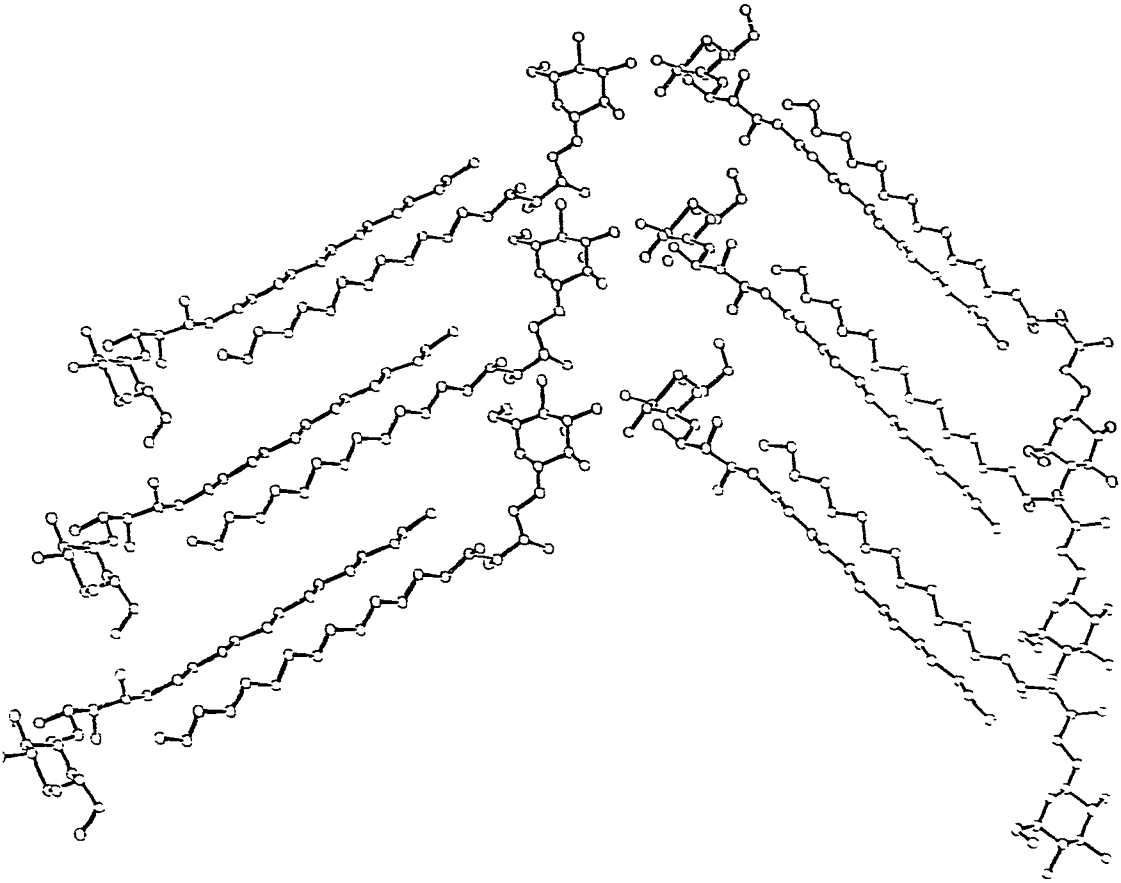


Fig. 4. Molecular packing in the crystal structure of 1-*O*-β-D-glucosylphytosphingosine hydrochloride[6], viewed down the *b* axis.

tetritol-4-yltetradecane; 1-β-D-glucopyranosyloxy-(D-*ribo*-2-amino-3,4-octadecanediol) hydrochloride monohydrate][6], shown in Fig. 4. In all three structures, the hydrocarbon chains are aligned head-to-tail in adjacent molecules, with typical, hydrocarbon packing of zigzag, parallel chains. The sugar molecules are so hydrogen-bonded as to form polar, bilayer structures. In all three structures, the orientation of the zigzag hydrocarbon chain, relative to the hydrogen-bonded plane of the sugar molecules, is ~45°; this appears to be a general, structural type for the longer-chain-alkyl glycosides. In a series of alkyl 1-thio-D-xylopyranosides, the pentyl, heptyl, and octyl glycosides have related structures, and also have liquid-crystal phases[7].

The molecular conformation (**1**) of heptyl 1-thio-α-D-mannopyranoside is as expected[1], namely, $^4C_1$, with Cremer and Pople[8] puckering-parameters Q = 0.552 Å, $\theta = 3.9°$, and $\varphi = 61.8°$. The glycosidic torsion-angle O–C–S–C is +67.7°, which is normal for an α-glycosidic link. The primary alcohol group is gauche/gauche with O-5–C-5–C-6–O-6 = −67.6°. The ring C–C bond-lengths span the usual range,

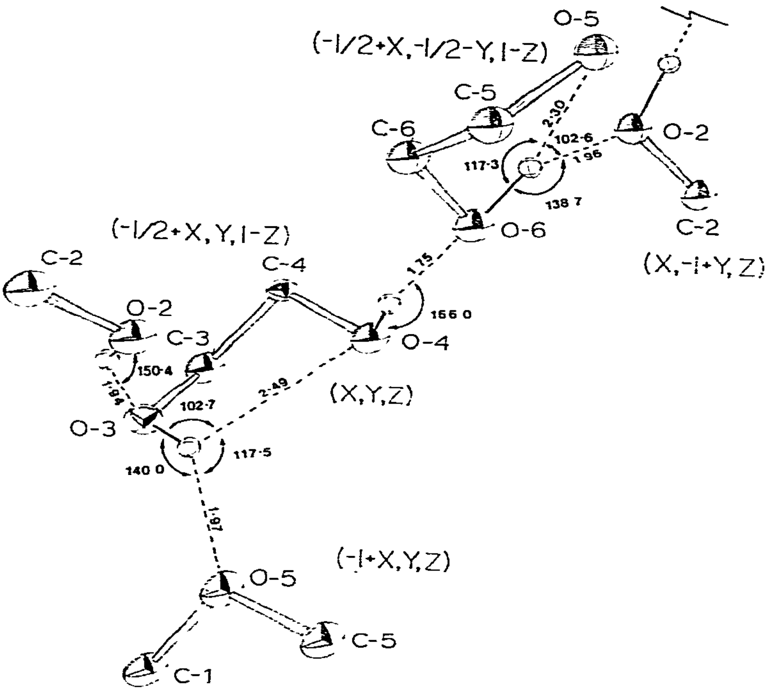
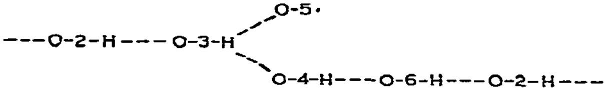


Fig. 5. Hydrogen bonding in the crystal structure of heptyl 1-thio-α-D-mannopyranoside.

1.518(2) to 1.531(2) Å, as do the C–OH bond-lengths, 1.419(2) to 1.429(2) Å. The ring-oxygen valence-angle is 114.8°, and the O-5–C-1–S valence-angle is 113.7°. These are all normal values for α-pyranosides.

The heptyl chain is non-sickle. From C-7 to C-13, the C–C–C–C torsion-angles are 180 ±2°. There are small departures from the ideal, chain conformation near the sulfur atom, with C-2–C-1–S–C-7 = −168°, C-1–S–C-7–C-8 = +173°, S–C-7–C-8–C-9 = −176°. The heptyl C–C bond-lengths range from 1.524 to 1.530 Å, with a mean value of 1.526 Å. The C–C–C valence angles range from 111.0(2) to 113.1(2)°, with a trend toward larger angles at the end of the chain.

The hydrogen bonding of the D-mannopyranosyl moieties is shown in Fig. 5; it forms an infinite chain, as shown diagrammatically.



$$\text{---O-2-H---O-3-H}\begin{matrix}\nearrow \text{O-5}\cdot \\ \searrow \text{O-4-H---O-6-H---O-2-H---}\end{matrix}$$

The three-centered (bifurcated), hydrogen bond at O-3-H includes a weak, intramolecular interaction to O-4, which completes the infinite chain.

Liquid-crystal phases

The crystals become opaque at 65°C without losing their morphology. The

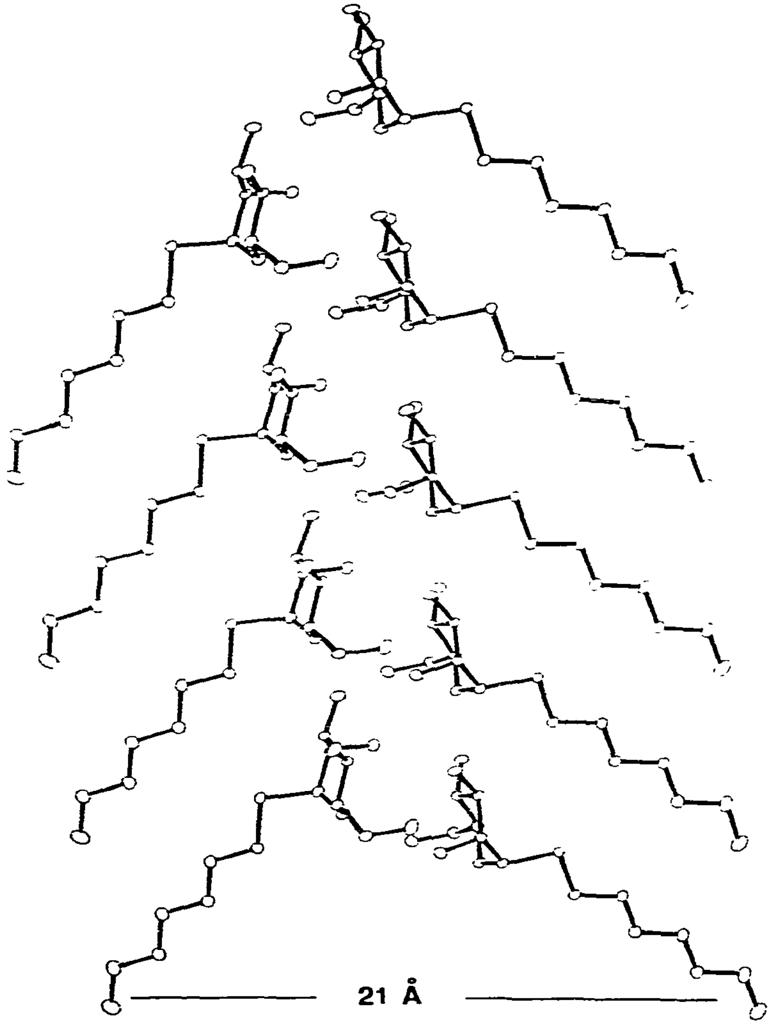


Fig. 6. Postulated structure for the molecular bundles in the liquid-crystal phase of heptyl 1-thio-α-D-mannopyranoside.

powder diffraction-pattern changes at that temperature from a normal Debye–Shearer type that is consistent with the single-crystal data to a single, strong ring corresponding to a *d* spacing of 20–21 Å. In the crystal structure, this distance of 21 Å corresponds to the separation between the terminal carbon atoms, C-13, of the hydrocarbon chains in the *c* axis direction, shown in Fig. 6. This suggests that the bundles of molecules that persist in the nematic, liquid-crystal phase are stacks of dimers hydrogen-bonded through the carbohydrate molecules, as shown in Fig. 6. The dimensions of the bundles will vary. The transition from crystalline to liquid-crystal phase, at 65 °C, involves the separation, *i.e.*, melting, of the hydrocarbon chains. The hydrogen bonding of the carbohydrate molecules persists, giving the short-range alignment of several hundred Ångström units into the molecular bundles, as shown in Fig. 6. The 21-Å periodicity will remain constant, but the short-range periodicity in the plane of the hydrogen bonding will vary, resulting in the characteristic, liquid-crystal diffraction-periodicity. At the melting point, 151 °C, the hydrogen-bonded structure between the D-mannosyl groups breaks down, and true melting of the crystals takes place.

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