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SYNTHESIS AND LIQUID CRYSTALLINE PROPERTIES OF THE *n*-ALKYL 1-THIO-α-D-GLUCOPYRANOSIDES, A NEW HOMOLOGOUS SERIES OF CARBOHYDRATE MESOGENS

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ABSTRACT

The *n*-alkyl 1-thio-α-D-glucopyranosides (*n*-propyl to *n*-dodecyl) were prepared by treating 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose with an alkanethiol in the presence of boron trifluoride etherate followed by deacetylation. The *n*-propyl and *n*-butyl derivatives are not thermotropic, the *n*-pentyl derivative is monotropic, and the compounds with *n*-hexyl and longer alkyl chains are enantiotropic, the largest liquid crystalline range being from ±100–175° for the *n*-undecyl derivative. The transition point data are typical for smectic behavior, and X-ray data and texture observations are indicative of a smectic A_d phase.

INTRODUCTION

There is growing interest in the synthesis and applications of long-chain alkyl 1-thio-D-glucopyranosides[1–5]. *n*-Heptyl and *n*-octyl 1-thio-β-D-glucopyranoside are commercially available and have been recommended as detergents for the solubilization and reconstitution of membrane proteins[4].

We are interested in these types of compounds for their potential for liquid crystalline (l.c.) behavior[6]. There are numerous descriptions in the literature of compounds that are probably carbohydrate mesogens, but which have not been so recognized[7]. An example is *n*-octyl 1-thio-β-D-glucopyranoside for which the Fluka catalogue cites m.p. 126–128°, whereas, in fact, the compound melts at 41.9–43.8° to form a viscous liquid crystalline phase, followed by transition to the isotropic liquid at 125–125.7°.

Jeffrey[8] was the first to point out that carbohydrate derivatives may be a vast source of mesogenic materials. We are currently investigating the scope and

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limitations of liquid crystalline behavior in monosaccharide derivatives and the relationship between configuration and thermal behavior[9].

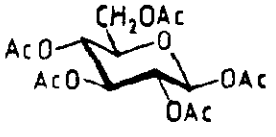
RESULTS AND DISCUSSION

Synthesis. — Several syntheses of *n*-alkyl 1-thioglycosides have been described[1,2,10,11], none of which was entirely satisfactory in our hands. The main problem was the deacetylation. The use of methanolic sodium methoxide[12] or aqueous methanolic sodium hydroxide[12] invariably gave a complex mixture of partly and wholly *O*-deacetylated products. However, treatment[13] with methanol–triethylamine–water (8:1:1) for 24 h at room temperature effected complete *O*-deacetylation.

The most straightforward route to *n*-alkyl 1-thio-β-D-glucopyranosides therefore seemed to be the method of Ferrier and Furneaux[10] followed by the procedure of Lubineau and Quenau[13].

However, when a solution of 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose in chloroform was treated[10] with 1.2 equiv. of *n*-alkanethiol and a five-fold excess of boron trifluoride etherate for 6 h at room temperature, preponderantly the *n*-alkyl 1-thio-α-D-glucopyranoside, not the β anomer, was obtained. This result was not surprising, since Erbing and Lindberg[14] reported the isomerization of *n*-alkyl 1-thio-β-D-glucopyranosides to give a 7:3 αβ-mixture under the influence of boron trifluoride.

When the reaction with *n*-nonanethiol was monitored by isolation of the product after 0.5, 1, 2, 4, 8, and 24 h, and determining its $[\alpha]_D^{20}$ value (*c* 1, chloroform), the following sequence of values was obtained: −23°, +2°, +18°, +51°, +66°, and +81°. The $[\alpha]_D^{20}$ values of *n*-nonyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α- and -β-D-glucopyranoside are +170° and −27°, respectively, and the results indicate that the β anomer was formed initially and that the αβ-equilibrium was established rather slowly. There was complete conversion of 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose into the thioglycoside after 30 min (determined by t.l.c.), and reaction times longer than 24 h resulted in decomposition of the product. The use of 1 equiv. of *n*-alkanethiol did not lower the yield significantly and was advantageous for the work-up and purification.



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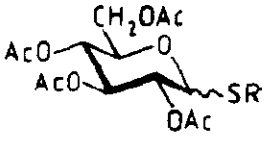

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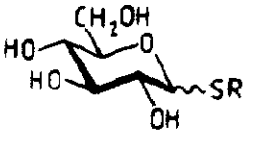

3 (αβ = 7:3)

3a	R = n-propyl	3f	R = n-octyl
3b	R = n-butyl	3g	R = n-nonyl
3c	R = n-pentyl	3h	R = n-decyl
3d	R = n-hexyl	3i	R = n-undecyl
3e	R = n-heptyl	3j	R = n-dodecyl

Deprotection of the crude $\alpha\beta$-mixture of acetylated glycoside (**2**) and repeated recrystallization from ethanol gave 20–30% of the *n*-alkyl 1-thio-α-D-glucopyranoside. However, for optimum yields, the α anomer should be removed by column chromatography[14] before *O*-deacetylation. The products (**3f**, **3h**, and **3j**) with an even number of carbon atoms in the *n*-alkyl chain were difficult to purify, whereas those (**3e**, **3g**, and **3i**) with an odd number of carbons readily gave crystals of the α anomer. The quality of the crystals of **3e** was such as to allow determination of the crystal structure[15].

The anomeric configuration of the α-glycosides was confirmed by the ^{1}H-n.m.r. spectra which revealed $J_{1,2}$ values of 5.9 and 5.4 Hz, respectively, for the acetylated and *O*-deacetylated products.

Thermal behavior. — The thermal behavior of **3a–j** was determined using a Perkin–Elmer DSC7 differential scanning calorimeter. The *n*-propyl (**3a**) and *n*-butyl (**3b**) derivatives exhibited no liquid crystal (l.c.) behavior. The *n*-pentyl derivative **3c** was monotropic (*i.e.*, there was no mesophase on heating, but, due to extensive supercooling of the isotropic phase, transition to a mesophase was observed prior to recrystallization). Compounds **3d–j** were enantiotropic (*i.e.*, a mesophase was observed upon heating and cooling).

Fig. 1 shows the d.s.c. curves for *n*-nonyl 1-thio-α-D-glucopyranoside (**3g**), and the d.s.c. data are compiled in Table I.

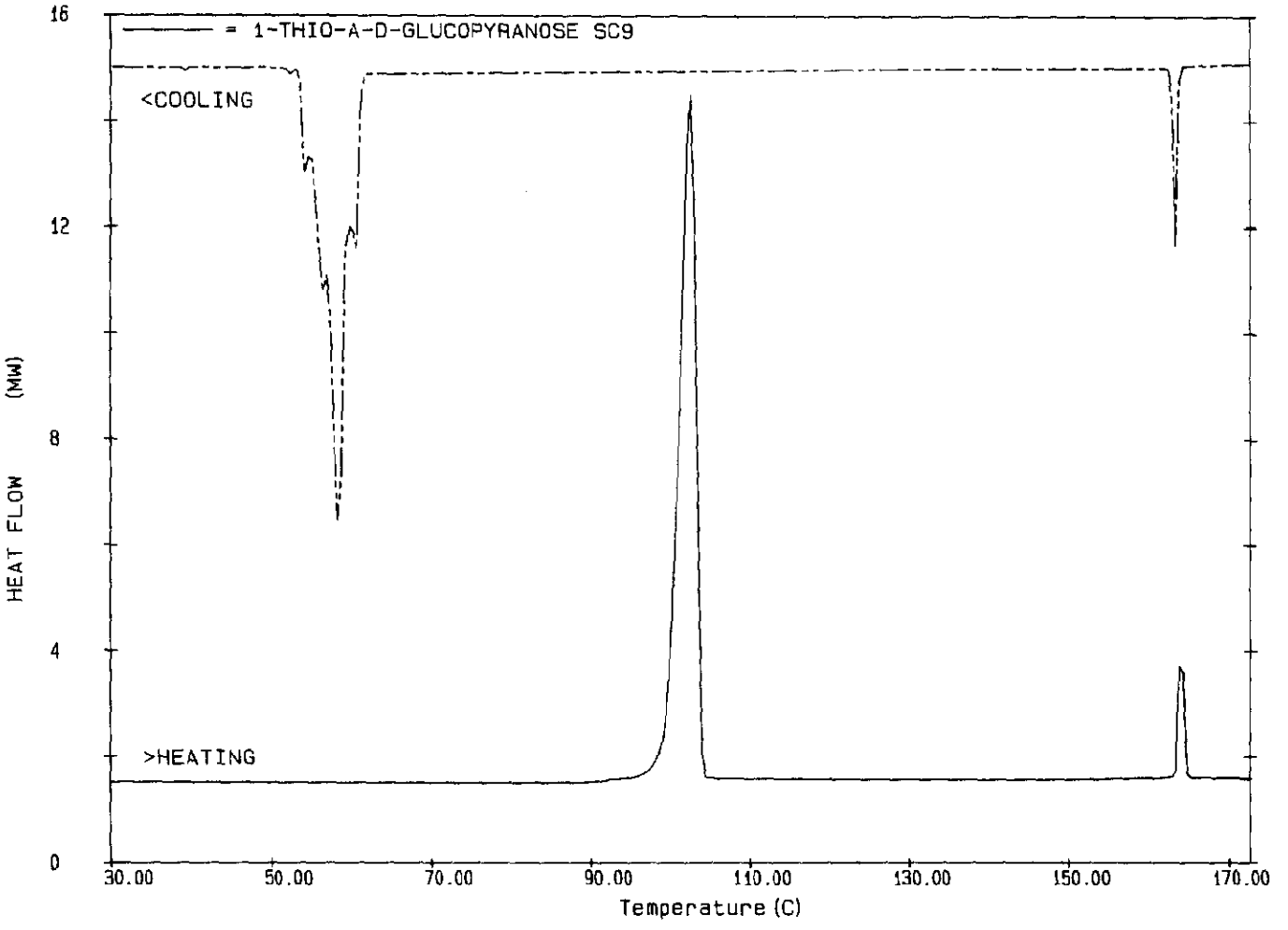

Fig. 1. The d.s.c. curves of *n*-nonyl 1-thio-α-D-glucopyranoside (**3g**).

TABLE I

TRANSITION TEMPERATURES AND ENTHALPIES[a], SPECIFIC OPTICAL ROTATIONS[b], AND COUPLING CONSTANTS OF THE ANOMERIC PROTON[c] OF A SERIES OF *n*-ALKYL 1-THIO-α-D-GLUCOPYRANOSIDES

Compound[d]	*M.p. (°)*	*ΔH (kJ mol⁻¹)*	*C.p. (°)*	*ΔH (kJ mol⁻¹)*	$[\alpha]_D^{20}$ *(°)*	$J_{1,2}$ *(Hz)*
3a	126.0–129.1	26.3	—	—	+302	5.3
3b	115.2–118.3	23.9	—	—	+269	5.4
3c	112.3–117.0	23.9	65.3	0.9	+250	5.5
3d	98.7–100.6	21.3	116.4	1.7	+256	5.4
3e	96.1–98.3	34.6	137.9	2.2	+239	5.5
3f	76.5–81.2	26.5	153.5	2.4	+217	5.4
3g	100.1–102.6	41.3	164.1	2.5	+211	5.4
3h	89.4–91.5	38.3	171.3	2.6	+200	5.4
3i	103.2–105.8	50.3	176.0	2.6	+197	5.5
3j	95.0–97.6	47.5	177.5	2.4	+179	5.5

[a]The calibration of the instrument was checked before and after each series of measurements. The scanning rate was 5° min^{-1}. [b]In methanol (*c* 1). [c]Spectra recorded for solutions in CD_3OD with a Varian VXR 300. [d]*Anal.* Calc. for $C_9H_{18}O_5S$ (**3a**): C, 45.36; H, 7.61; S, 13.46. Found: C, 45.25; H, 7.59; S, 13.35. *Anal.* Calc. for $C_{10}H_{20}O_5S$ (**3b**): C, 47.60; H, 7.99; S, 12.71. Found: C, 47.72; H, 8.03; S, 12.62. *Anal.* Calc. for $C_{11}H_{22}O_5S$ (**3c**): C, 49.60; H, 8.33; S, 12.04. Found: C, 49.60; H, 8.27; S, 12.05. *Anal.* Calc. for $C_{12}H_{24}O_5S$ (**3d**): C, 51.41; H, 8.63; S, 11.44. Found: C, 51.48; H, 8.74; S, 11.53. *Anal.* Calc. for $C_{13}H_{26}O_5S$ (**3e**): C, 53.04; H, 8.90; S, 10.89. Found: C, 52.96; H, 8.80; S, 10.86. *Anal.* Calc. for $C_{14}H_{28}O_5S$ (**3f**): C, 54.52; H, 9.15; S, 10.40. Found: C, 54.74; H, 9.11; S, 10.23. *Anal.* Calc. for $C_{15}H_{30}O_5S$ (**3g**): C, 55.87; H, 9.38; S, 9.94. Found: C, 56.04; H, 9.35; S, 9.99. *Anal.* Calc. for $C_{16}H_{32}O_5S$ (**3h**): C, 57.11; H, 9.58; S, 9.53. Found: C, 57.02; H, 9.68; S, 9.55. *Anal.* Calc. for $C_{17}H_{34}O_5S$ (**3i**): C, 58.25; H, 9.78; S, 9.15. Found: C, 57.91; H, 9.73; S, 9.20. *Anal.* Calc. for $C_{18}H_{36}O_5S$ (**3j**): C, 59.31; H, 9.95; S, 8.80. Found: C, 59.10; H, 9.90; S, 8.86.

The mesophase of all carbohydrate mesogens reported (with the exception of the disc-like penta- and hexa-alkyl derivatives[16] and the aldose dialkyl dithioacetals[9,17]) has been determined tentatively as S_{Ad}[8,18], *i.e.*, a smectic A phase with bimolecular layers, with the sugar moieties partially overlapping in the core of the layers and the alkyl chains pointing outward at an angle. The *n*-alkyl 1-thio-α-D-glucopyranosides conform to this pattern.

For each compound, there is a single mesophase, and plotting the data from Table I leads to curves typical for a homologous series of compounds with a smectic mesophase[19] depicted in Fig. 2.

A temperature-dependent powder X-ray investigation[15] of **3e** yielded a single sharp line corresponding to a d-spacing of 23.5 Å in the l.c. phase.

The textures of the mesophases, usually pseudo-isotropic with small areas of fan-like focal-conics, were observed by means of a Mettler FP 82 hot-stage mounted on a Nikon microscope. Figs. 3a and 3b show some typical textures[20].

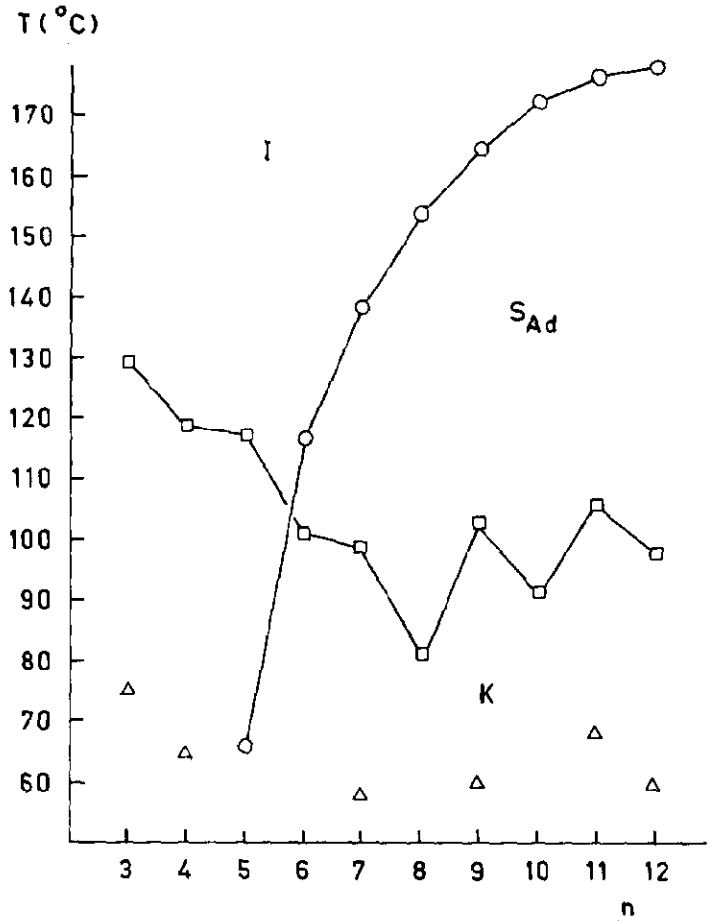

Fig. 2. The transition temperatures of a homologous series of *n*-alkyl 1-thio-α-D-glucopyranosides as a function of the number of carbon atoms in the alkyl chain: □, melting point; ○, clearing point; △, recrystallization point.

EXPERIMENTAL

n-*Alkyl 2,3,4,6-tetra*-O-*acetyl-1-thio*-α-D-*glucopyranosides* (**2a–j**). — To a solution of 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (3.9 g, 10 mmol) in dry chloroform (20 mL) were added *n*-alkanethiol (10 mmol) and $BF_3 \cdot Et_2O$ (50% solution in ether; 14 mL, 50 mmol), and the mixture was stirred for 8 h at room temperature (the color of the mixture became deep red). The mixture was then washed with aqueous 5% $NaHCO_3$ (2 × 50 mL) and water (50 mL), dried (Na_2SO_4), and concentrated to give **2a–j** (>95%, αβ-ratio 7:3) which was used without further purification.

The α anomers could be isolated (60–65%) by column chromatography on silica gel, using EtOAc–light petroleum (b.p. 40–60°).

N.m.r. data ($CDCl_3$) for nonyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-glucopyranoside: ^1H, δ 0.83 (t, 3 H, H-9′,9′,9′), 1.23 (bm, 12 H, H-3′,3′/8′,8′), 1.54 (m, 2 H, H-2′,2′), 1.90, 1.98, 2.02, 2.04 (4 s, each 3 H, 4 Ac), 2.48 (m, 2 H, H-1′,1′), 4.03 (dd, 1 H, $J_{5,6b}$ 2.2, $J_{6,6}$ 12.1 Hz, H-6b), 4.30 (dd, 1 H, $J_{5,6a}$ 4.4 Hz, H-6a), 4.38 (ddd, 1 H, H-5), 4.96 (dd, 1 H, $J_{2,3}$ 9.3 Hz, H-2), 5.01 (dd, 1 H, $J_{4,5}$ 10.1 Hz, H-4), 5.32 (t, 1 H, $J_{3,4}$ 10.3 Hz, H-3), 5.60 (d, 1 H, $J_{1,2}$ 5.9 Hz, H-1); ^{13}C, δ 13.97 (C-9′), 20.54–20.60 (4 CH_3CO), 22.55 (C-8′), 28.75, 28.99, 29.11, 29.36, 30.03 (C-1′/7′), 31.71 (C-2′), 61.83 (C-6), 67.93, 68.45, 70.41, 70.62 (C-2/5), 81.85 (C-1), 169.42, 169.72, 170.37 (4 CH_3CO).

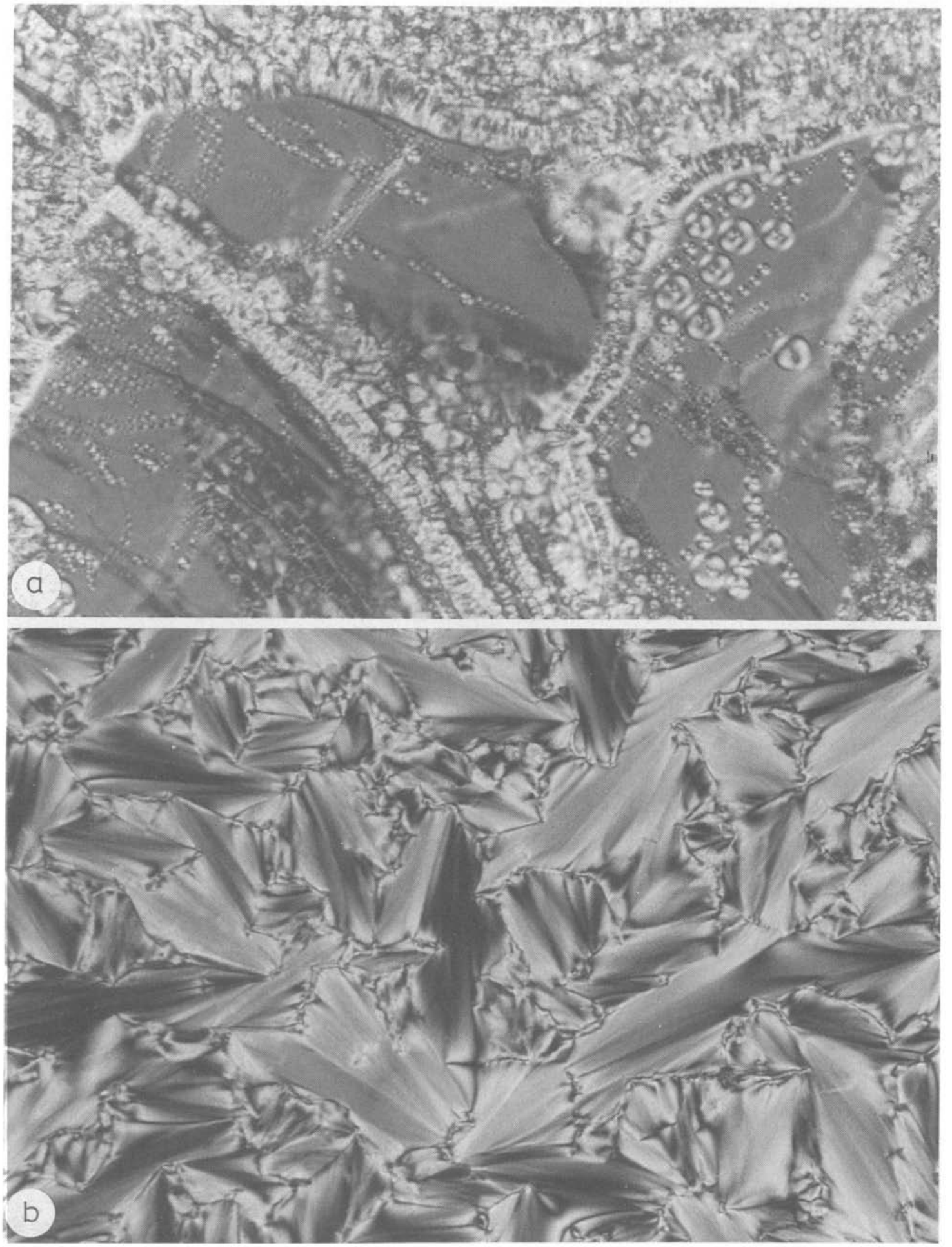

Fig. 3. The texture of the liquid crystalline phase of **3e** on (*a*) heating and (*b*) cooling, viewed through crossed polarizers [λ-wave plate used for (*a*) but not for (*b*)].

n-*Alkyl 1-thio-α-*D-*glucopyranosides (***3a–j***).* — A solution of each crude **2a–j** in methanol (80 mL), triethylamine (10 mL), and water (10 mL) was stirred for 24 h at room temperature and then concentrated, and water was evaporated repeatedly from the residue. Several recrystallizations of the residue from ethanol–ether (for **3a–d**) or ethanol (**3e–j**) yielded 20–30% of the pure products.

N.m.r. data (CD_3OD) for heptyl 1-thio-α-D-glucopyranoside (**3e**): ^1H, δ 0.95 (t, 3 H, H-7′,7′,7′), 1.3–1.5 (m, 8 H, H-3′,3′/6′,6′), 1.68 (m, 2 H, H-2′,2′), 2.62 (m, 2 H, H-1′,1′), 3.35 (dd, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 3.57 (t, 1 H, $J_{3,4}$ 8.6 Hz, H-3), 3.72 (dd, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 3.74 (dd, 1 H, $J_{5,6a}$ 5.3, $J_{6a,6b}$ 11.9 Hz, H-6a), 3.84 (dd, 1 H, $J_{5,6b}$ 2.3 Hz, H-6b), 3.99 (ddd, 1 H, H-5), 5.34 (d, 1 H, $J_{1,2}$ 5.4 Hz); ^{13}C, 14.43 (C-7′), 23.63 (C-6′), 29.94, 29.99, 30.74, 31.02 (C-1′,3′,4′,5′), 32.90 (C-2′), 62.45 (C-6), 71.60 (C-5), 73.06, 73.82, 75.59 (C-2,3,4), 87.08 (C-1).

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