# Characterization of some mesogenic alkyl 1-thioglycosides

**B. Henrissat, G.K. Hamer, M.G. Taylor, and R.H. Marchessault**

**Abstract**: A series of dodecyl 1-thio-β-D-glycosides has been synthesized and characterized (DSC, NMR, CP MAS, X-ray diffraction) as possible new marking materials with liquid-crystalline properties. These compounds undergo solid to liquid crystal phase transitions at various temperatures, which depend on the nature of the carbohydrate part of the structure. Their liquid-crystalline phases show extreme shear thinning behaviour.

*Key words*: liquid crystal, powder X-ray diffraction, phase transition, thioglycoside, solid-state NMR, marking material

**Résumé** : On a effectué la synthèse et on a caractérisé (DSC, RMN, CP MAS, diffraction des rayons X) une série de 1-thio-β-D-glycosides de dodécyle, de nouveaux marqueurs potentiels ayant des propriétés de cristaux liquides. Ces composés subissent des transitions de solide à cristal liquide à diverses températures qui dépendent de la nature de la portion hydrate de carbone de la structure. Leurs phases cristal liquide présentent un comportement extrême de fluidisation par cisaillement.

*Mots clés* : cristal liquide, diffraction de rayons X par des poudres, transition de phase, thioglycoside, RMN à l'état solide, marqueur.

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## Introduction

Alkyl glycosides have been shown to be thermotropic mesogens when the alkyl chain ranges from heptyl upwards (1). Because of the great variety of possible carbohydrates, alkyl chain length, type of linkage and its position of attachment to the sugar molecule, it has been predicted that several million carbohydrate liquid crystals could be obtained (2). A few of these amphiphilic carbohydrates have found biochemical applications as non-ionic detergents for membrane protein extraction (3). As part of a research program concerned with the evaluation of their liquid-crystalline phase as potential materials with advanced properties, we report here synthesis and the characterization of some dodecyl 1-thioglycosides.

## Experimental

### General methods

Solutions were evaporated below 45°C under diminished pressure. TLC was performed on silica gel F254 (Aldrich), eluent was ethyl acetate – hexane (1:2, v/v) and detection was done with 5% sulfuric acid in ethanol followed by heating. The $^{1}H$ and $^{13}C$ NMR spectra were recorded at 250 and 62.5 MHz, respectively, on a Bruker AM 250 spectrometer. Chemical shifts are given with respect to external tetramethylsilane. Differential scanning calorimetry was carried out with a PerkinElmer DSC-2C calorimeter on 12 mg samples sealed in aluminum capsules. The heating and cooling rates were 20°C $min^{-1}$. Powder X-ray diagrams were obtained in a Warhus flat-film camera by using Ni-filtered Cu Kα radiation on the sample loaded in 0.5-mm capillary tubes.

### Solid-state $^{13}C$ NMR

High resolution $^{13}C$ NMR spectra were acquired at 50.3 MHz with a Bruker CXP 200 instrument. Cross-polarization (CP) was performed with Hartmann–Hahn matched radio-frequency fields of about 60 Hz. Spectra were collected with a 1 ms contact time and 6 s recycle delay over a sweep width of 10 kHz. Magic-angle spinning (MAS) at about 2.5 kHz was achieved in a probe from Doty Scientific. A small chip of linear polyethylene (NBS Standard Reference Material 1475) was added to the samples to provide a chemical shift reference at 32.9 ppm (4) with respect to tetramethylsilane. The spectrum of the liquid-crystalline phase was not recorded because cross-polarization was ineffective due to high molecular mobility. Furthermore, the

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*Dedicated to the memory of Professor Raymond U. Lemieux.*

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**Table 1.** $^1$H NMR data for ring protons of 1-thio-β-D-glycosides **4**, **9**, **14**, and **15**.

| Compound | Chemical shifts (ppm) and coupling constants (Hz) | | | | | | |
|---|---|---|---|---|---|---|---|
| | H-1 | H-2 | H-3 | H-4 | H-5 | H-6a | H-6b |
| **4** | 4.48<br>d<br>($J_{1,2}$ = 10.0) | 5.23<br>t<br>($J_{2,3}$ = 10.0) | 5.09<br>t<br>($J_{3,4}$ = 10.0) | 5.03<br>t<br>($J_{4,5}$ = 10.0) | 3.71<br>m<br>($J_{5,6a}$ = 5.0) | 4.25<br>dd<br>($J_{6a,6b}$ = 12.0) | 4.14<br>dd<br>($J_{5,6b}$ = 2.5) |
| **9** | 4.48<br>d<br>($J_{1,2}$ = 10.0) | 5.24<br>t<br>($J_{2,3}$ = 10.0) | 5.05<br>dd<br>($J_{3,4}$ = 4.0) | 5.43<br>dd<br>($J_{4,5}$ = 1.0) | 3.93<br>dt<br>($J_{5,6a}$ = 8.0) | | |
| | H-1 | H-2 | H-3 | H-4 | H-5a | H-5b | |
| **14** | 4.51<br>d<br>($J_{1,2}$ = 10.0) | 5.28<br>t<br>($J_{2,3}$ = 10.0) | 4.97<br>t<br>($J_{3,4}$ = 10.0) | 4.95<br>m<br>($J_{4,5a}$ = 10.0) | 4.23<br>dd<br>($J_{5a,5b}$ = 13.0) | 3.38<br>dd<br>($J_{4,5b}$ = 6.0) | |
| **15** | 4.24<br>d<br>($J_{1,2}$ = 10.0) | 3.04<br>t<br>($J_{2,3}$ = 10.0) | 3.18<br>t<br>($J_{3,4}$ = 10.0) | 3.34<br>m<br>($J_{4,5a}$ = 10.0) | 3.78<br>dd<br>($J_{5a,5b}$ = 12.0) | 3.08<br>dd<br>($J_{4,5b}$ = 6.0) | |

**Notes**: For each compound: 1st line, chemical shift; 2nd line, multiplicity; 3rd line, coupling constant (in parenthesis). d= doublet; t = triplet; dd = doublet of doublets; m = multiplet.

sample flowed under the rapid spinning conditions, leading to imbalance in the rotor and to magic angle spinning instabilities.

### Syntheses

Syntheses of the 2-thiopseudourea derivatives **2**, **7**, and **12** from the corresponding glycosyl bromides **1**, **6**, and **11** were done as previously described (5). *S*-alkylation was adapted from a classical procedure (6). In a typical experiment, the 2-thiopseudourea derivative (40 g) and potassium carbonate (70 g) in water (60 mL) are stirred with dichloromethane at room temperature, the extract is concentrated, and the residue is alkylated with an appropriate alkyl halide (75 mL). De-*O*-acetylation was effected with sodium methoxide in methanol.

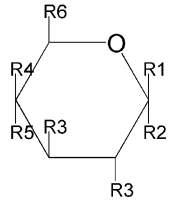
## Results and discussion

Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (7) **1** was converted into 2-*S*-(tetra-*O*-acetyl-β-D-glucopyranosyl)-2-thiopseudourea hydrobromide **2** according to standard procedures (5). 2,3,4,6-Tetra-*O*-acetyl-1-thio-β-D-glucopyranose **3** was generated from **2** and was *S*-alkylated in situ with 1-bromododecane in the presence of potassium carbonate (6). Treatment of the resulting dodecyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside **4** with a catalytic amount of sodium methoxide gave the expected dodecyl 1-thio-β-D-glucopyranoside **5**. An identical synthetic route was followed for the synthesis of dodecyl 1-thio-β-D-galacto- **10** and -xylo-pyranoside **15** starting, respectively, from tetra-*O*-acetyl-α-D-galactopyranosyl bromide (8) **6** and tri-*O*-acetyl-α-D-xylopyranosyl bromide (9) **11**.

$^1$H NMR (e.g., Table 1) has been used to characterize the stereochemistry of the synthetic intermediates **4**, **9**, and **14** as well as of the final products **5**, **10**, and **15**. The anomeric β configuration is unambiguously confirmed by the large coupling constants $J_{H\text{-}1,H\text{-}2}$ of about 10 Hz (Table 1).

The three dodecyl 1-thioglycosides **5**, **10**, and **15** have been examined under polarized light with an optical microscope equipped with a heating stage. Upon heating, all samples undergo melting to a birefringent liquid characteristic of a liquid-crystalline phase. When further heating is applied, they change to isotropic fluids and loose their birefringence. Upon cooling, the reverse succession of events is observed, i.e., the appearance of a liquid-crystalline phase and then, at lower temperatures, crystallization to a solid. The melting behavior of **5**, **10**, and **15** was examined by differential scanning calorimetry. A typical thermogram is shown in Fig. 1. The transition temperatures of the three dodecyl 1-thioglycosides **5**, **10**, and **15** are reported in Table 2. It is interesting to note that the crystal – liquid crystal transitions (K2-LC) occur at significantly higher temperatures on heating than on cooling. Also, while 1-thio-glycosides **10** and **15** both exhibit crystal-to-crystal transitions (K1-K2), glycoside **5** does not. It is possible that such a transition also occurs for the latter compound, but at a temperature lower than ambient.

A solid-state $^{13}$C NMR study was done with dodecyl 1-thio-β-D-xylopyranoside **15** because the two transitions of




1. $R^1$ = H; $R^2$ = Br; $R^3$ = $R^5$ = OAc; $R^4$ = H; $R^6$ = $CH_2OAc$
2. $R^1$ = S-C(=NH)-$NH_2$·HBr; $R^2$ = H; $R^3$ = $R^5$ = OAc; $R^4$ = H; $R^6$ = $CH_2OAc$
3. $R^1$ = SH; $R^2$ = H; $R^3$ = $R^5$ = OAc; $R^4$ = H; $R^6$ = $CH_2OAc$
4. $R^1$ = S-$(CH_2)_{11}$-$CH_3$; $R^2$ = H; $R^3$ = $R^5$ = OAc; $R^4$ = H; $R^6$ = $CH_2OAc$
5. $R^1$ = S$(CH_2)_{11}$-$CH_3$; $R^2$ = H; $R^3$ = $R^5$ = OH; $R^4$ = H; $R^6$ = $CH_2OH$
6. $R^1$ = H; $R^2$ = Br; $R^3$ = $R^4$ = OAc; $R^5$ = H; $R^6$ = $CH_2OAc$
7. $R^1$ = S-C(=NH)-$NH_2$·HBr; $R^2$ = H; $R^3$ = $R^4$ = OAc; $R^5$ = H; $R^6$ = $CH_2OAc$
8. $R^1$ =SH; $R^2$ = H; $R^3$ = $R^4$ = OAc; $R^5$ = H; $R^6$ = $CH_2OAc$
9. $R^1$ =S-$(CH_2)_{11}$-$CH_3$; $R^2$ = H; $R^3$ = $R^4$ = OAc; $R^5$ = H; $R^6$ = $CH_2OAc$
10. $R^1$ = S-$(CH_2)_{11}$-$CH_3$; $R^2$ = H; $R^3$ = $R^4$ = OH; $R^5$ = H; $R^6$ = $CH_2OH$
11. $R^1$ =H; $R^2$ = Br; $R^3$ = $R^5$ = OAc; $R^4$ = $R^6$ = H
12. $R^1$ = S-C(=NH)-$NH_2$·HBr; $R^2$ = H; $R^3$ = $R^5$ = OAc; $R^4$ = $R^6$ = H
13. $R^1$ = SH; $R^2$ = H; $R^3$ = $R^5$ = OAc; $R^4$ = $R^6$ = H
14. $R^1$ = S-$(CH_2)_{11}$-$CH_3$; $R^2$ = H; $R^3$ = $R^5$ = OAc; $R^4$ = $R^6$ = H
15. $R^1$ = S-$(CH_2)_{11}$-$CH_3$; $R^2$ = H; $R^3$ = $R^5$ = OH; $R^4$ = $R^6$ = H

**Fig. 1.** Differential scanning calorimetry thermogram of dodecyl 1-thio-β-D-xylopyranoside **15**. The top and bottom curves correspond to the heating and cooling cycles, respectively. (Endo) and (Exo) indicate *endo*- and *exo*-thermal transitions, respectively.

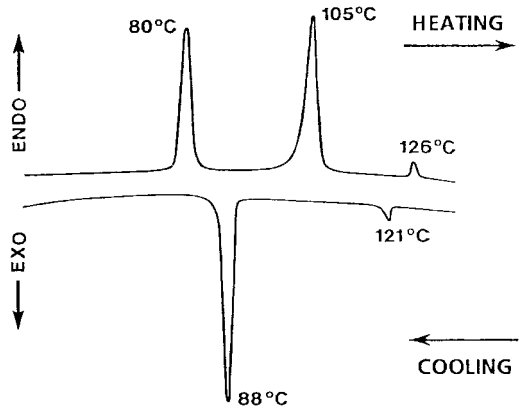



**Fig. 2.** Solid-state $^{13}C$ NMR spectra of dodecyl 1-thio-β-D-xylopyranoside **15** at 25°C (K1 form) (A) and 90°C (K2 form) (B).

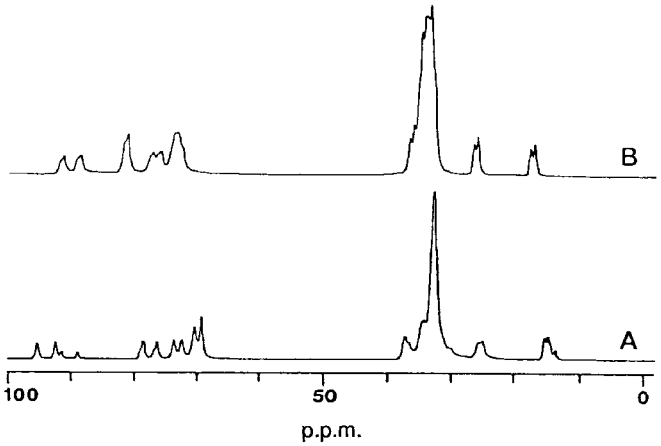



**Table 2.** Transition temperatures derived from differential scanning calorimetry.

| | | Transitions (°C)[a] | | |
|---|---|---|---|---|
| Compound | Conditions | K1↔K2 | K2↔LC | LC↔ISO |
| **5** | Heating | — | 60 | 164 |
| | Cooling | — | — | 158 |
| **10** | Heating | 88 | 115 | 171 |
| | Cooling | — | 50–60 | 171 |
| **15** | Heating | 80 | 105 | 126 |
| | Cooling | — | 88 | 121 |

[a]K1↔K2: crystal-to-crystal transition; K2↔LC: crystal-to-liquid crystal transition (melting point); LC↔ISO: liquid crystal-to-isotropic liquid transition (clearing point).

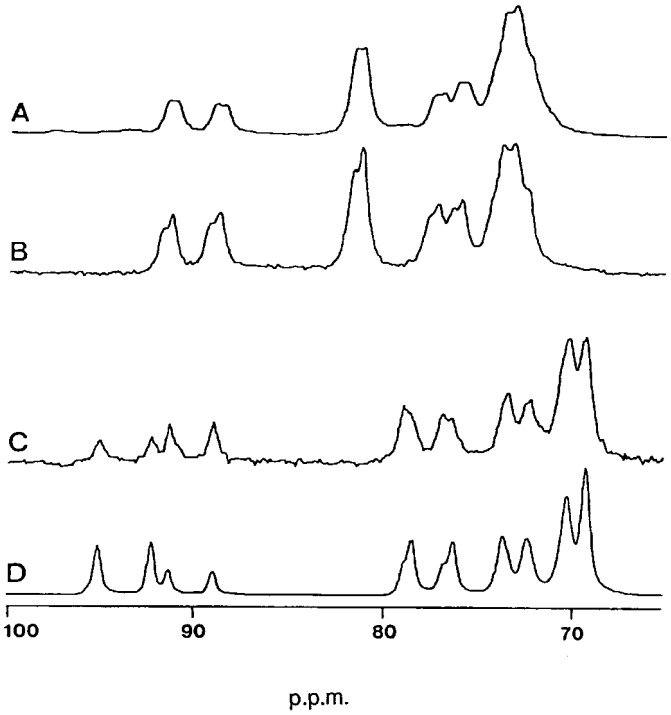
interest (K-K2 and K2-LC) occur at temperatures (80 and 105°C, respectively) compatible with the heating stage of our spectrometer. Figures 2A and 2B show the solid-state spectra recorded at 25 and 90°C, i.e., under and above the K1-K2 transition. In both forms, there are indications of multiple resonance for individual chemically equivalent carbons. This effect is more pronounced in the spectrum of the K1 form, where obvious splittings are observed for many resonances, especially for the terminal methyl group at 15 ppm and for the sugar C-1 carbon at 90 ppm. Specific resonance assignments are difficult since the peak positions change dramatically in the two forms. The peaks in the 87–95 ppm region can, however, be assigned with confidence to the C-1 carbon of the sugar ring. By analogy with the solution NMR spectrum, the remaining peaks can probably be assigned in order of decreasing chemical shift: C-3, C-2, C-4, C-5.

In the K1 form, the resonance assigned to C-1 of compound **15** clearly consists of four lines between 88 and 95 ppm with relative intensities of about 2:2:1:1. A similar situation is noted for the peaks at 77 and 79 ppm, each of which has a shoulder. Application of resolution enhancement shows four lines in this region with relative intensities of about 1:2:1:2. These observations indicate that there are four magnetically non-equivalent environments for the sugar ring in this crystal form. It is interesting to note that the X-ray crystal structure of octyl 1-thio-β-D-xylopyranoside (a lower homologue of compound **15** but with a shorter alkyl chain) shows a disordered structure where the carbohydrate moiety has two orientations with equal occupancy (10). The solid-state NMR results here show that a disordered structure could also be valid for dodecyl 1-thio-β-D-xylopyranoside **15**. A mixture of crystal polymorphs could also explain the peak multiplicity observed for **15**; however, in such a case the differential scanning calorimetry thermogram would show a more complex melting profile. The spectrum of the higher temperature form (K2), although of lower definition, also shows peak multiplicity, indicating at least two non-equivalent environments in the crystal (Fig. 2B).

The cooling behavior of the 1-thio-glycoside **15** was also investigated by solid-state NMR. Although it was not possible to record the spectrum of the material in the liquid crystal form, it was, however, heated in the spectrometer for one hour at 110°C and then cooled to 27°C. The differential scanning calorimetry data (Fig. 1 and Table 2) indicated that on cooling from the liquid-crystalline phase, **15** underwent only one transition to the intermediate crystal form (K2). Figure 3A shows the spectrum of the sugar-ring carbons obtained immediately after cooling the material. This spectrum clearly corresponds to the K2 form as seen by comparison with the spectrum obtained at 90°C (Fig. 3B). The sample was allowed to equilibrate at room temperature for 24 h before another spectrum was acquired at 27°C. In this case (Fig. 3C), it is seen that the material has returned to the K1 form by comparison with the original room temperature spectrum (Fig. 3D). It is interesting to note that the same number of lines is observed as in the original spectrum (Fig. 2A), but that there are differences in the relative intensities. These intensity variations may originate from a non-isotropic orientation of the crystals during the thermal transitions, which occurred under high-speed magic angle spinning conditions in the magnetic field of the NMR spectrometer.

Powder X-ray diffraction diagrams of **15** were recorded to characterize its crystal-to-crystal transition at 80°C and to further identify the crystalline form obtained after standing 24 h at room temperature. Table 3 lists the main *d* spacings

**Fig. 3.** Solid-state $^{13}C$ NMR spectra of the carbohydrate part of dodecyl 1-thio-β-D-xylopyranoside **15** after different heat treatments. (A) Spectrum obtained at 27°C immediately after 1 h of treatment at 110°C; (B) spectrum of the K2 form obtained at 90°C; (C) same as (A) but after 24 h at room temperature; (D) spectrum of the K1 form (never heated).




measured for compound **15** at room temperature (A), immediately after heating two hours at 90°C (B), and 24 h later (C). One clearly observes different *d* spacings after heating above the transition temperature. After 24 h standing at room temperature, the material returns to its low temperature polymorph.

## Conclusions

This work covers part of an extensive program at Xerox Corporation on marking materials. The subject herein is described as hot-melt inks suitable for ink jet printing. A set of examples in a United States patent (11) makes use of the research described herein. The carbohydrate chemistry leading to synthesis of these liquid-crystalline materials is outlined schematically in the above referenced patent and their characterization was inspired by published data. However, while this work was in progress a related study by van Doren et al. (12) appeared, which reminded us of how Jeffrey (2) pioneered the field of carbohydrate mesogens. His basic crystal-line-packing model, for liquid-crystalline alkyl 1-glycosides, which can be applied to the compounds in this study, is a hydrogen-bonded layer of carbohydrate moieties with the alkyl chains pointing outwards in parallel arrangement (2). The latter are the first to melt, while the hydrogen-bonded layers resist the thermal motion up to a higher temperature. Jeffrey (2) predicted a staggering potential for easily available liquid-crystalline compounds from carbohydrate molecules.

**Table 3.** X-ray *d* spacings (Å) observed for dodecyl 1-thio-β-D-xylopranoside **15**.

| Conditions[a] | | |
|---|---|---|
| A | B | C |
| 12.70 | 15.60 | 12.65 |
| 7.35 | 7.68 | 7.33 |
| 6.54 | 5.43 | 6.56 |
| 4.77 | 4.60 | 4.75 |
| 4.02 | 4.36 | 4.00 |
| | 4.20 | |
| | 4.10 | |

[a](A) sample room temperature; (B) same as (A) but after 2 h at 90°C; (C) same as (B) but after 24 h at room temperature.

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## References

1. G.A. Jeffrey and S. Bhattacharjee. Carbohydr. Res. **115**, 53 (1983).
2. G.A. Jeffrey. Acc. Chem. Res. **19**, 168 (1986).
3. For example see: C. Baron and T.E. Thompson. Biochim. Biophys. Acta, **283**, 276 (1975); S.L. Wagner and R.D. Gray. Biochemistry, **24**, 3809 (1985); J. Cordoba, M.D. Reboiras, and M.N. Jones. Int. J. Biol. Macromol. **10**, 270 (1988).
4. D.L. VanderHart. J. Chem. Phys. **84**, 1196 (1986).
5. D. Horton. Methods Carbohydr. Chem. **2**, 433 (1963).
6. M. Cerny and J. Pacak. Chem. Listy, **52**, 2090 (1958).
7. R. U. Lemieux. Methods Carbohydr. Chem. **2**, 221 (1963).
8. J. Conchie and G.A. Levy. Methods Carbohydr. Chem. **2**, 335 (1963).
9. F. Weygand. Methods Carbohydr. Chem. **1**, 182 (1962).
10. S. Bhattacharjee and G.A. Jeffrey. Mol. Cryst. Liq. Cryst. **101**, 247 (1983).
11. W.M. Schwarz, R.H. Marchessault, L. Alexandru, and B. Henrissat. U.S. Patent 5 006 170 (1991).
12. H.A. van Doren, R. van der Geerst, R.H. Kellogg, and H. Wynberg. Carbohyd. Res. **194**, 71 (1989).