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Synthesis, purification and liquid-crystalline behaviour of several alkyl 1-thio-D-glycopyranosides

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Abstract

This paper describes the synthesis, purification, and liquid-crystalline behaviour of a series of alkyl 1-thioglycopyranosides. The synthesis of these derivatives was carried out via a Lewis acid mediated coupling of the fully acetylated monosaccharide with an alkanethiol. The choice of the Lewis acid depends on the configuration of AcO-2. The carbohydrate-derived surfactants exhibit thermotropic liquid-crystalline behaviour. The alkyl 1-thioglycopyranosides form the expected smectic A phases upon heating. The clearing temperatures vary with alkyl chain length which is in accordance with the accepted model for the S_A phase of amphiphilic carbohydrate mesogens. For the alkyl 1-thiotalopyranosides, the clearing points are much lower than expected, presumably due to the formation of an intramolecular hydrogen bond in the talose moiety. © 1997 Elsevier Science Ltd.

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1. Introduction

Interest in carbohydrate-derived surfactants has increased over the past decade, not only as a result of their potential commercial application in detergents, but also because these derivatives display liquid-crystalline behaviour [1]. Moreover, their potential use for selectively affecting cell surfaces and as enzymatic substrates has already been noted [2]. In addition, they can be applied in membrane protein reconstitution [3,4].

Previously the synthesis of anomerically pure alkyl 1-thioglucopyranosides was described [5]. In order to study the influence of stereochemistry on liquid-crystalline behaviour, a new set of alkyl 1-thioglycosides was synthesized. Earlier studies have shown that the stereochemistry of a carbohydrate has a significant effect on its hydration [6,7]. In the present study, the aldohexoses D-glucose, D-galactose, D-

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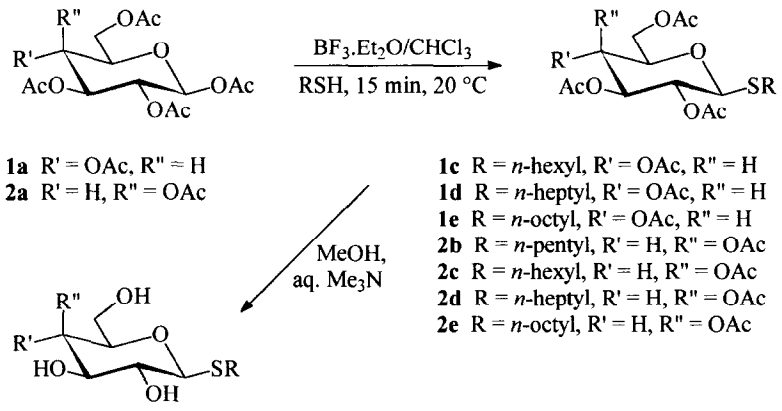
mannose and D-talose were chosen as carbohydrate starting materials and the corresponding hexyl, heptyl and octyl 1-thioglycopyranosides were prepared. An L-arabinose mesogen was also synthesized. The relatively short chain lengths were chosen to avoid complications due to high Krafft temperatures [8]. It was found that the method of purification for these compounds is dictated by the stereochemistry of the sugar moiety. The thermotropic liquid-crystalline behaviour of the pure compounds has been monitored as a function of the hydroxy topology of the carbohydrate moiety.

2. Results and discussion

Synthesis.—The *n*-alkyl 1-thio-β-D-glucopyranosides **1g–i** and the *n*-alkyl 1-thio-β-D-galactopyranosides **2f–i** can be synthesized from the respective peracetylated monosaccharides and the appropriate *n*-alkanethiol by using the $BF_3 \cdot Et_2O$ method [5]. This route (Scheme 1) has the advantage over a Königs–Knorr type of route [3,4,9,10] (which is often used for the synthesis of alkyl glycosides and 1-thioglycosides), in that it is shorter and more efficient. The $BF_3 \cdot Et_2O$ method can result in both the α and the β anomers. In the case of glucose and galactose, the β anomer is the kinetically controlled product, whereas the α anomer is the thermodynamically controlled product (an α:β ratio of ca. 7:3 is obtained after 24 h). The reaction proceeds through a cyclic intermediate in which the acetoxy group on C-2 provides anchimeric assistance for the loss of the acetoxy group at the anomeric centre. An acyloxonium ion intermediate is formed [11], which is most easily attacked by the thiol on the β-side.

For D-mannose peracetate (**3a**) we observed that the $BF_3 \cdot Et_2O$ method could not be used. No appreciable thioglycoside formation was observed even after prolonged reaction times. Although the acetoxy groups on the anomeric carbon and C-2 are related 1,2-*trans*, it appears that the required abstraction of the acetoxy anion does not take place. Therefore, an attempt was made to synthesize the *n*-alkyl 1-thio-D-mannopyranosides by S_N2 substitution of an *n*-alkanethiol on 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl chloride [12] using phase-transfer conditions [13]. However, this method also proved to be unsuccessful in our hands. A mixture of products ensued, probably due to the (partial) hydrolysis of the acetate protecting groups. Coupling of the *n*-alkanethiols with both the D-mannose and D-talose (**4a**) pentaacetates was successful in the presence of a different Lewis acid, $FeCl_3$ [14]. Mixtures of anomers were obtained (Scheme 2).

The L-arabinose derivative **5c** could be synthesized following the same route (Scheme 3) as for the

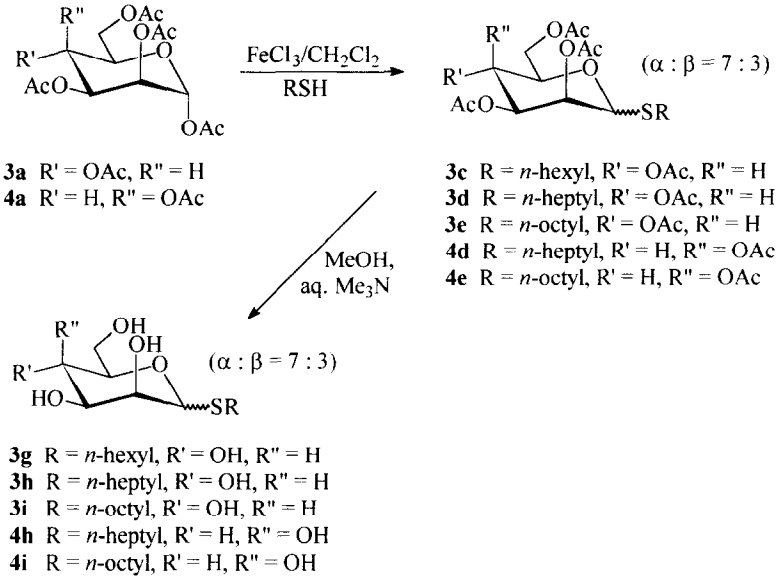


1a R' = OAc, R" = H
2a R' = H, R" = OAc

1c R = *n*-hexyl, R' = OAc, R" = H
1d R = *n*-heptyl, R' = OAc, R" = H
1e R = *n*-octyl, R' = OAc, R" = H
2b R = *n*-pentyl, R' = H, R" = OAc
2c R = *n*-hexyl, R' = H, R" = OAc
2d R = *n*-heptyl, R' = H, R" = OAc
2e R = *n*-octyl, R' = H, R" = OAc

1g R = *n*-hexyl, R' = OH, R" = H
1h R = *n*-heptyl, R' = OH, R" = H
1i R = *n*-octyl, R' = OH, R" = H
2f R = *n*-pentyl, R' = H, R" = OH
2g R = *n*-hexyl, R' = H, R" = OH
2h R = *n*-heptyl, R' = H, R" = OH
2i R = *n*-octyl, R' = H, R" = OH

Scheme 1.



3a R' = OAc, R" = H
4a R' = H, R" = OAc

3c R = *n*-hexyl, R' = OAc, R" = H
3d R = *n*-heptyl, R' = OAc, R" = H
3e R = *n*-octyl, R' = OAc, R" = H
4d R = *n*-heptyl, R' = H, R" = OAc
4e R = *n*-octyl, R' = H, R" = OAc

3g R = *n*-hexyl, R' = OH, R" = H
3h R = *n*-heptyl, R' = OH, R" = H
3i R = *n*-octyl, R' = OH, R" = H
4h R = *n*-heptyl, R' = H, R" = OH
4i R = *n*-octyl, R' = H, R" = OH

Scheme 2.

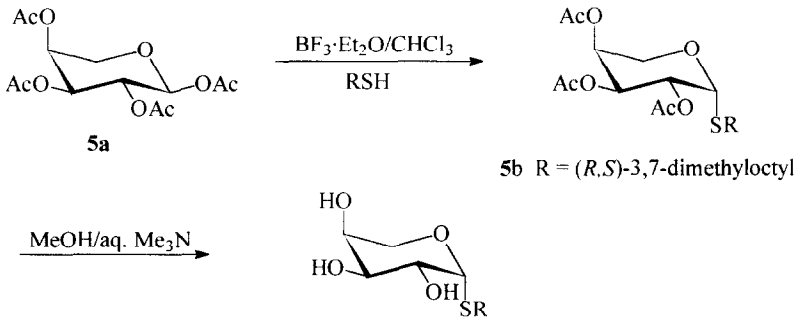
glucose derivatives. Only the β anomer was formed as shown by NMR spectral data ($J_{1,2}$ 4.03, $J_{2,3}$ 7.8 Hz).

Earlier attempts to couple a secondary thiol, (*R*,*S*)-2-heptanethiol (Synthesized according to a literature procedure, see [15]), under similar conditions, with the peracetylated arabinose **5a** were unsuccessful. The longer reaction time needed for the secondary alkanethiol resulted in the formation of a complex mixture of acetylated α- and β-arabinopyranosides and -furanosides as well as peracetylated arabinopyranosides/furanosides.

Deprotection was carried out with a mixture of methanol and a 45% solution of trimethylamine in water. Trimethylamine was chosen rather than triethylamine [5] because the subsequent evaporation of the former is more convenient.

Purification of the compounds.—Often, the most difficult aspect of the overall preparative procedure of carbohydrate-derived surfactants is the purification, particularly when the product has to be anomerically pure. There was no general method available to separate one anomer of a carbohydrate-derived surfactant from the other on a preparative scale. Therefore, we devoted considerable effort to resolving this problem.

The synthesis of the glucose and galactose derivatives can be nearly anomer-specific, because the substitution reaction goes to completion within ca. 10 min. However, trace amounts of the unwanted anomer are always present in the product mixture (glucose derivatives, 2–3%; galactose derivatives, ca. 5%). Both the mannose and the talose derivatives can only be synthesized as anomeric mixtures, $\alpha:\beta \approx 7:3$. For



5a

5b R = (*R*,*S*)-3,7-dimethyloctyl

5c R = (*R*,*S*)-3,7-dimethyloctyl

Scheme 3.

these compounds it is crucial to find a suitable purification method.

The first opportunity to purify the product is after the coupling reaction, when the hydroxy groups in the compound are still protected. By applying chromatography on silica gel with the eluent hexane–ethyl acetate (7:3, v:v) [16], the product mixture can be separated or enriched in one of its anomers and unreacted thiol can be removed conveniently. The second chance for purification is after deprotection. If trace amounts of the unwanted anomer are still present in the mixture, they can be removed by chromatography, depending on the hydroxy topology of the sugar moiety.

(*a*) *Alkyl 1-thio*-D-*glucopyranosides* (**1g–i**). The α and β anomers can be separated on silica gel using dichloromethane containing 5% of methanol as eluent. This method has been described previously by Saito and Tsuchiya [3,4]. The application of all the other column materials discussed in this section (vide infra) proved to be unsuccessful.

(*b*) *Alkyl 1-thio*-D-*galactopyranosides* (**2f–i**). The compounds can be purified on a Dowex 1-X2 anion-exchange resin in the OH^- form. Neither a cation-exchange column in the calcium form nor a Sephadex column were found to be suitable for purification. Previously, anion-exchange columns have been used for the purification of alkyl glycosides and separation of mixtures of aldoses [17–22]. Sephadex columns have been used previously to separate, for example, partially acetylated dextrans [23].

(*c*) *Alkyl 1-thio*-D-*mannopyranosides* (**3g–i**). These materials can be purified on Dowex 50-X4 (Ca^{2+}) cation-exchange resin as well as on a Sephadex column. The elution sequence of products was reversed going from one column to the other. The anion-exchange column was not applied.

(*d*) *Alkyl 1-thio*-D-*talopyranosides* (**4h,i**). The talose derivatives can be purified readily on Dowex 1-X2 (OH^-) anion-exchange resin; hence it was unnecessary to apply the calcium-ion column and the Sephadex column methods for their purification. The chemical shifts of the anomeric protons of the products are compiled in Table 1.

The present results show that ion-exchange columns can also be used successfully to separate anomeric mixtures of carbohydrate-derived surfactants.

In the case of the cation-exchange column in the calcium-ion form, one can take advantage of the fact that sugars can interact with calcium ions [24–26]. The strongest calcium-ion complex can be formed if there are three adjacent *cis*-hydroxy groups present in the carbohydrate moiety (in an axial–equatorial–axial sequence) as is the case for the D-talose derivatives **4h,i**. In addition, carbohydrates with two neighbouring *cis*-hydroxy groups are able to form weak complexes with calcium ions. For mannose these are HO-2 and HO-3, and for galactose they are HO-3 and HO-4. If the respective anomers possess a different affinity for calcium, the mixture can be purified on a calcium-ion column. The D-glucopyranosides have an all-*trans* arrangement of hydroxy groups and, therefore, show only a very weak interaction with the calcium ion. It was observed that the mannose derivatives have a different affinity for calcium ions depending on the relative position of the alkylthio chain. No affinity difference was observed for the α,β-galactose and α,β-glucose derivatives, respectively. The column was not tested for the talose derivatives.

The observation for the galactose derivatives was somewhat unexpected, particularly because the mannose derivatives could be purified successfully on a

Table 1
Chemical shift of the anomeric proton for alkyl 1-thioglycosides in CD_3OD at 25 °C [a]

Compound	Type of carbohydrate derivative	δ H-1 [b]	$J_{1,2}$ (Hz) [b]
1g–iα	alkyl 1-thio-α-D-glucopyranoside [c]	5.34	5.4
1g–iβ	alkyl 1-thio-β-D-glucopyranoside	4.35	9.8
2f–iα	alkyl 1-thio-α-D-galactopyranoside	5.37	–
2f–iβ	alkyl 1-thio-β-D-galactopyranoside	4.34	9.3
3g–iα	alkyl 1-thio-α-D-mannopyranoside	5.26	1.1
3g–iβ	alkyl 1-thio-β-D-mannopyranoside	4.75	1.0
4h,iα	alkyl 1-thio-α-D-talopyranoside	5.31	0.7
4h,iβ	alkyl 1-thio-β-D-talopyranoside	4.63	–

[a] Spectra were recorded in extremely dilute solution to avoid broadening and additional peaks as a result of aggregate formation.
[b] Average value.
[c] Taken from ref. [5].

calcium-ion column. The difference in affinity for the calcium ion in the case of the mannose derivatives may be caused by the fact that the alkyl chain can hinder the weak complex formation (with HO-2 and HO-3) when the alkyl chain is in the *cis*-position (i.e., the β anomer) with respect to the complex. In the α anomer, where the alkyl chain is *trans*, the complex formation is not hindered. For the *n*-alkyl 1-thio-β-D-mannopyranosides the retention time on the column is shorter than that for the α-D-mannopyranosides, consistent with the suggested mode of complexation. Possibly the alkyl chain of the galactose derivatives cannot hinder the complexation so effectively, because it is further away from the hydroxy groups which are involved in the interaction with calcium ions.

Sephadex separates on the basis of differences in hydrophobicity of similarly sized compounds. There will only be a difference in hydrophobicity between two anomers if the carbohydrate moiety interacts with the column material and if this affinity is influenced by the relative position (α or β) of the alkyl chain bound to the sugar moiety. Now the same reasoning can be followed as that used in the rationalization of the Ca^{2+} affinity. The carbohydrate moiety shows hydrophobic behaviour if there are several neighbouring *cis*-methine protons present in the carbohydrate moiety. The relative position of the alkyl chain can affect the interaction of this moiety with the column material. It was found that the galactose and the talose derivatives, which have three and four adjacent *cis*-methine groups, respectively, can be successfully purified on these columns. Glucose derivatives, which lack a *cis*-methine proton arrangement, cannot be purified under the same conditions. Mannose derivatives can be successfully purified on a Sephadex column because the (small) hydrophobic region in the carbohydrate headgroup is near the alkyl chain. For the Sephadex columns the elution sequence is the reverse of that observed on the Ca^{2+} columns. This indicates that the interaction with Sephadex takes place via the hydrophobic methine groups rather than via the hydroxy functionalities.

Although the general explanation for the column chromatographic results may seem somewhat speculative, it has been noted previously that a carbohydrate molecule possesses both a hydrophobic surface (or volume) and a hydrophilic surface (or volume) [27,28], the sizes of which depend on the detailed hydroxy topology of the carbohydrate. The dependence of calcium-ion affinity on stereochemistry is well documented [26–28].

Ion-exchange columns have previously been used in carbohydrate chemistry for separations [21–25,29–33] or as catalysts in the synthesis of carbohydrate-derived surfactants from unprotected sugars [34]. Differences in retention time between different sugars have been explained in terms of pK_a values [21,22].

Liquid-crystalline behaviour.—Emil Fischer [35] was the first to observe that long-chain alkyl glycosides possess a 'double melting point'. Noller and Rockwell [36] rationalized this phenomenon in terms of liquid-crystalline behaviour. In general, amphiphilic carbohydrate derivatives exhibit lyotropic as well as thermotropic liquid-crystalline properties. Self-association is driven by the energy gain that is obtained by favourable interactions in the ordered aggregates. It was not until the early 1980's [1,37] that the liquid-crystalline behaviour of carbohydrate-derived surfactants began to be studied more extensively [38–40]. It was concluded that most carbohydrate derivatives with one alkyl chain of sufficient length (usually C_6 or larger) form a smectic A phase upon heating [5,17,41–45].

Carbohydrate-derived surfactants are rodlike molecules. In a smectic A phase, they are ordered in a layered structure with alternating polar and apolar regions. The layer-spacing of the S_A phase corresponds to 1.2–1.4 times the length of one fully extended molecule [39]. Therefore, it is assumed that the molecules aggregate in interdigitated bilayers (S_{Ad}). The structure of the bilayers is believed to be similar to that of the lyotropic lamellar phase (L_α) [39]. The polar moieties are on the outside of each layer and the partially overlapping alkyl chains form the interior of each layer [39]. Stabilization of the mesophase is provided by van der Waals interactions between the alkyl groups on the one hand and hydrogen bonding between carbohydrates on the other. Interactions between the layers are also governed by hydrogen bonding.

The importance of the van der Waals interactions is clearly demonstrated by the fact that the clearing points rise rapidly with increasing alkyl chain length [1,5,16,38,39].

The melting points, clearing points, and heats of melting and clearing for the alkyl 1-thioglycopyranosides are summarized in Table 2. The typical mesophase textures of these derivatives are shown in Fig. 1. Generally, the melting points do not change regularly upon chain elongation, whereas the clearing

Table 2
Melting points (T_m), clearing points (T_c) and heats of melting (ΔH_m) and clearing (ΔH_c) for alkyl 1-thioglycopyranosides

Compound	T_m (°C)	T_c (°C)	ΔH_m (kJ mol^{-1})	ΔH_c (kJ mol^{-1})
Heptyl 1-thio-α-D-glucopyranoside [a]	97.2	137.9	34.6	2.2
Octyl 1-thio-α-D-glucopyranoside [a]	78.8	153.5	26.5	2.2
Pentyl 1-thio-β-D-galactopyranoside (**2f**)	109.6 [b]	–	28.7	–
Hexyl 1-thio-β-D-galactopyranoside (**2g**)	87.1	90.9	23.8	0.9
Heptyl 1-thio-β-D-galactopyranoside (**2h**)	62.4	112.0	40.9	1.0
Octyl 1-thio-β-D-galactopyranoside (**2i**)	91.7 [c]	140.5	26.4	2.2
Heptyl 1-thio-α-D-mannopyranoside (**3hα**)	62.1 [d,e]	152.4	25.2	2.2
Hexyl 1-thio-β-D-mannopyranoside (**3gβ**)	115.3	125.4	40.1	1.8
Octyl 1-thio-β-D-mannopyranoside (**3iβ**)	118.9	156.1	50.5	2.3
Heptyl 1-thio-α-D-talopyranoside (**4h**)	90.3	(85.6) [f]	34.5	(1.2)
Octyl 1-thio-α-D-talopyranoside (**4i**)	91.7	105.7	40.7	1.6
(*R,S*)-3,7-Dimethyloctyl 1-thio-β-L-arabinoside (**5c**)	149.8	> 170	44.0	–

[a] Ref. [5].
[b] A crystal transition at 73.2 °C, $\Delta H_{trans} = 2.3$ kJ mol^{-1}, no liquid-crystalline behaviour.
[c] A crystal transition at 60.5 °C, $\Delta H_{trans} = 6.3$ kJ mol^{-1}.
[d] A crystal transition at 43.9 °C, $\Delta H_{trans} = 3.6$ kJ mol^{-1}.
[e] Ref. [42]: $T_m = 60$, $T_c = 151$ °C.
[f] The phase transition is monotropic: only observed upon cooling.

points are higher for longer chain lengths. The heats of melting depend on both the hydroxy topology of the carbohydrate involved and the chain length. The heats of clearing do not show this dependence and are much smaller, which is in support of a smectic phase with liquid layers. The derivatives with a high Krafft temperature [8] have very large enthalpies of melting (Table 2). This suggests that the crystal packing is the main factor determining the solubility of a carbohydrate-derived surfactant in water. Nearly all the D-galactose derivatives show a crystal-to-crystal transition before melting, which signifies a rearrangement of the packing of the alkyl chains [16]. When the clearing points of the derivatives of α-D-glucose, α-D-mannose, and α-D-talose were measured, it was found that they are comparable for α-D-glucose and α-D-mannose derivatives, whereas the α-D-talose derivatives have a much lower clearing point. This difference can be explained by assuming the presence of an intramolecular hydrogen bond

Fig. 1. The texture of the smectic A phase of octyl 1-thio-β-D-galactopyranoside at 137 °C upon cooling from the isotropic melt.

between HO-2 and HO-4 in the case of D-talopyranose [46]. X-ray analysis of octyl 1-thio-α-D-talopyranoside [47] and an MD simulation of D-talose in aqueous solution [48] provide evidence for this interpretation. Due to the formation of an intramolecular hydrogen bond, the talose moieties are less capable of maintaining the hydrogen bond network which stabilizes the mesophase structure. The liquid-crystalline behaviour of alkyl 1-thio-α-D-glucopyranosides has been described and characterized previously [5]. The overall trend observed in the thermotropic behaviour of the compounds studied here is in good agreement with that of the glucose derivatives.

3. Experimental

Materials.—All the peracetylated hexoses [β-D-glucose pentaacetate (**1a**), β-D-galactose pentaacetate (**2a**), α-D-mannose pentaacetate (**3a**), (all 99 + %)] were purchased from Sigma. D-Talose was purchased from Sigma and L-arabinose was purchased from Janssen Chimica. Both 1-hexane- and 1-octane-thiol (purity > 98%) were purchased from Janssen Chimica, while 1-heptanethiol (purity > 97%) was purchased from Fluka AG. The Lewis acids were obtained from Janssen Chimica (48% $BF_3 \cdot Et_2O$ in ether) and Merck ($FeCl_3$). All solvents were distilled before use. The 45% aqueous trimethylamine solution was purchased from Merck.

Column materials.—Sephadex LH-20-100 (lipophilic Sephadex) was obtained from Pharmacia. Dowex 50-X4-400 ion-exchange resin (H^+ form) was purchased from Janssen Chimica. Dowex 1-X2 (Cl^-) (200/400 mesh) was purchased from Fluka AG.

Dowex 50 (H^+) was changed into the Ca^{2+} form by elution of the column with saturated aq $CaCl_2$. Thereafter the column was washed with demineralized water, until calcium ions were no longer present in the eluent (checked with aqueous ammonium oxalate).

Dowex 1 (Cl^-) was changed into the hydroxide form by elution with 1 M NaOH followed by washing with demineralized water to remove excess of hydroxide ions.

Liquid-crystalline behaviour.—The liquid-crystalline behaviour of the carbohydrate-derived surfactants was studied by heating samples of ca. 3 mg of each substance in a Perkin–Elmer differential scanning calorimeter (Perkin–Elmer DSC7 PC Series). The liquid-crystalline phase was identified by means of optical microscopy. A Mettler FP 82 hotstage mounted on a Nikon polarization microscope was used.

Chromatography.—Chromatography was performed using the column materials described above. When MeOH or MeOH/water mixtures were applied, fractions of ca. 10–15 mL were collected. The fraction collectors were an LKB 2112 Redirac and an LKB 17000 Minirac. The fractions were checked for the presence of carbohydrate-derived surfactants. Analytical TLC was performed on precoated silica gel F_{254} plates (Merck) with detection by charring with a 20% solution of H_2SO_4 in MeOH.

NMR spectroscopy.—All NMR spectra were recorded on a Varian Gemini 200 or VXR 300 spectrometer. The fully protected carbohydrate derivatives were dissolved in $CDCl_3$ and the carbohydrate-derived surfactants in CD_3OD, with tetramethylsilane as the reference. The spectra of the acetylated intermediates were derived from enriched anomeric mixtures; traces of the other anomer were usually observed.

Polarimetry.—Optical rotations were measured on a Perkin–Elmer 241 polarimeter with a sodium lamp.

α-D-Talose pentaacetate (**4a**).—Compound **4a** was synthesized in 65% yield from D-talose [49,50] and crystallized from EtOH. The NMR data were in agreement with the literature [49].

α-L-Arabinose tetraacetate (**5a**).—Compound **5a** was synthesized in 41% yield, after crystallization from 96% EtOH, according to the method described by Evelyn et al. [51], which, in our hands, gave a higher yield than the method described by Dasgupta et al. [52]. The NMR data were in accordance with literature data [51].

n-Alkyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranosides (**1c–1e**).—Compounds **1c–1e** were synthesized via the $BF_3 \cdot Et_2O$-method described previously [5]. In order to obtain the β anomer, the reaction was quenched with saturated aq $NaHCO_3$ after 15 min. Longer reaction times yielded considerable amounts of the α anomer. The alkyl chain length was varied from six to eight carbon atoms. The product could be purified by crystallization from *n*-hexane. The average yield was 70% after crystallization.

If a small amount of the α anomer was present in the mixture, this could not be removed by crystallization. However, chromatography over silica gel with

7:3 *n*-hexane–EtOAc resulted in a product mixture which was enriched in, if not purified completely, to the β anomer. Under these circumstances the α anomer was collected before the β anomer.

Hexyl 2, 3, 4, 6 - tetra - O - acetyl - 1 - thio - β - D - glucopyranoside (**1c**).—^{1}H NMR ($CDCl_3$): δ 0.86 (t, 3 H, H-6′); 1.30 (m, 6 H, H-3′/5′); 1.55 (m, 2 H, H-2′); 1.98, 2.00, 2.03, 2.05 (4 s, each 3 H, Ac); 2.64 (m, 2 H, H-1′); 3.68 (ddd, 1 H, H-5, $J_{4,5}$ 10.0, $J_{5,6a}$ 2.4, $J_{5,6b}$ 4.9 Hz); 4.10 (dd, 1 H, H-6a, $J_{6,6}$ 12.3 Hz); 4.22 (dd, 1 H, H-6b); 4.45 (d, 1 H, H-1, $J_{1,2}$ 10.0 Hz); 5.00, 5.05, 5.19 (3 t, each 1 H, H-2,3,4, $J_{2,3}/J_{3,4}$ ca. 9.5 Hz). ^{13}C NMR ($CDCl_3$): δ 11.9 (C-6′); 20.2–20.3 (4 CH_3CO); 22.1, 28.1, 29.2, 29.3 (C-1′, C-3′/5′); 31.1 (C-2′); 62.0 (C-6); 68.1, 68.8, 73.8, 75.7 (C-2/5); 83.4 (C-1); 169.1, 169.2, 169.9, 170.1 (4 CH_3CO).

Heptyl 2, 3, 4, 6 - tetra - O - acetyl - 1 - thio - β - D - glucopyranoside (**1d**).—^{1}H NMR ($CDCl_3$): δ 0.85 (t, 3 H, H-7′); 1.30 (m, 8 H, H-3′/6′); 1.57 (m, 2 H, H-2′); 1.98, 2.00, 2.03, 2.05 (4 s, each 3 H, Ac); 2.64 (m, 2 H, H-1′); 3.68 (ddd, 1 H, H-5, $J_{4,5}$ 10.0, $J_{5,6a}$ 2.4, $J_{5,6b}$ 4.9 Hz); 4.11 (dd, 1 H, H-6a, $J_{6,6}$ 12.3 Hz); 4.22 (dd, 1 H, H-6b); 4.46 (d, 1 H, H-1, $J_{1,2}$ 10.0 Hz); 5.00, 5.05, 5.19 (3 t, each 1 H, H-2,3,4, $J_{2,3}/J_{3,4}$ ca. 9.5 Hz). ^{13}C NMR ($CDCl_3$): δ 13.8 (C-7′); 20.4–20.5 (4 CH_3CO); 22.4, 28.5, 28.6, 29.4, 29.8 (C-1′, C-3′/6′); 31.5 (C-2′); 62.0 (C-6); 68.2, 69.7, 73.8, 75.7 (C-2/5); 83.5 (C-1); 169.2 (2 ×), 170.0, 170.4 (4 CH_3CO).

Octyl 2, 3, 4, 6 - tetra - O - acetyl - 1 - thio - β - D - glucopyranoside (**1e**).—^{1}H NMR ($CDCl_3$): δ 0.85 (t, 3 H, H-8′); 1.32 (m, 10 H, H-3′/7′); 1.58 (m, 2 H, H-2′); 2.00, 2.01, 2.04, 2,06 (4 s, each 3 H, Ac); 2.65 (m, 2 H, H-1′); 3.69 (ddd, 1 H, H-5, $J_{4,5}$ 10.0, $J_{5,6a}$ 2.4, $J_{5,6b}$ 4.9 Hz); 4.11 (dd, 1 H, H-6a, $J_{6,6}$ 12.3 Hz); 4.22 (dd, 1 H, H-6b); 4.46 (d, 1 H, H-1, $J_{1,2}$ 10.0 Hz); 5.00, 5.05, 5.20 (3 t, each 1 H, H-2,3,4, $J_{2,3}/J_{3,4}$ ca. 9.5 Hz). ^{13}C NMR ($CDCl_3$): δ 14.0 (C-8′); 20.5–20.6 (4 CH_3CO); 22.5, 28.7, 29.0 (2 ×), 29.5, 29.9 (C-1′, C-3′/7′); 31.7 (C-2′); 62.1 (C-6); 68.2, 69.8, 73.8, 75.8 (C-2/5); 83.5 (C-1); 169.3 (2 ×), 170.0, 170.5 (4 CH_3CO).

Alkyl 1-thio-β-D-glucopyranosides (**1g–1i**).—Deprotection was performed analogously to the method described previously [5], but using a 45% aqueous Me_3N:MeOH (2:8) mixture. After 24 h, the solvent was evaporated and a syrup remained. Purification of the compounds was realized by chromatography employing a silica gel column, with a 5% solution of MeOH in CH_2Cl_2 as eluent, as described by Saito and Tsuchiya [3,4]. With this method traces of the α anomer were removed. The β anomer migrated faster than the α anomer under these circumstances. All products were hygroscopic syrups.

Hexyl 1-thio-β-D-glucopyranoside (**1g**).—^{1}H NMR (CD_3OD): δ 0.91 (t, 3 H, H-6′); 1.38 (m, 6 H, H-3′/5′); 1.62 (m, 2 H, H-2′); 2.72 (m, 2 H, H-1′); 3.27 (m, 4 H and CD_3OD, H-2/5); 3.64 (dd, 1 H, H-6a, $J_{5,6a}$ 5.3, $J_{6a,6b}$ 12.1 Hz); 3.85 (dd, 1 H, H-6b, $J_{5,6b}$ 2.0 Hz); 4.34 (d, 1 H, H-1, $J_{1,2}$ 10 Hz). ^{13}C NMR (CD_3OD): δ 14.4 (C-6′); 23.6, 29.6, 30.8, 31.0 (C-1′, C-3′/5′); 32.5 (C-2′); 62.8 (C-6); 71.4, 74.3, 79.5, 81.9 (C-2/5); 87.1 (C-1).

Heptyl 1 - thio - β - D - glucopyranoside (**1h**).—^{1}H NMR (CD_3OD): δ 0.90 (t, 3 H, H-7′); 1.37 (m, 8 H, H-3′/6′); 1.62 (m, 2 H, H-2′); 2.71 (m, 2 H, H-1′); 3.27 (m, 4 H and CD_3OD, H-2/5); 3.66 (dd, 1 H, H-6a, $J_{5,6a}$ 5.2, $J_{6a,6b}$ 12.0 Hz); 3.85 (dd, 1 H, H-6b, $J_{5,6b}$ 1.8 Hz); 4.35 (d, 1 H, H-1, 9.8 Hz). ^{13}C NMR (CD_3OD): δ 14.4 (C-7′); 23.6, 29.9, 30.0, 30.8, 31.0 (C-1′, 3′/6′); 32.9 (C-2′); 62.8 (C-6); 71.3, 74.2, 79.5, 81.8 (C-2/5); 87.0 (C-1).

Octyl 1-thio-β-D-glucopyranoside (**1i**).—^{1}H NMR (CD_3OD): δ 0.91 (t, 3 H, H-8′); 1.33 (m, 10 H, H-3′/7′); 1.63 (m, 2 H, H-2′); 2.72 (m, 2 H, H-1′); 3.27 (m, 4 H and CD_3OD, H-2/5); 3.66 (dd, 1 H, H-6a, $J_{5,6a}$ 5.4, $J_{6a,6b}$ 12.2 Hz); 3.85 (dd, 1 H, H-6b, $J_{5,6b}$ 2.0 Hz); 4.35 (d, 1 H, H-1, $J_{1,2}$ 9.8 Hz). ^{13}C NMR (CD_3OD): δ 14.4 (C-8′); 23.7, 30.0, 30.3 (2 ×), 30.8, 31.0 (C-1′, C-3′–7′); 33.0 (C-2′); 62.9 (C-6); 71.4, 74.3, 79.6, 81.9 (C-2/5); 87.1 (C-1).

Alkyl 1-thio-β-D-galactopyranosides (**2f–2i**).—The alkyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranosides **2b–2e** were synthesized by the same method as used for the glucose derivatives. No suitable solvent mixture was found for crystallization of the protected adducts. Hence deprotection (as for glucose) was carried out with the products as such. Purification of the compounds (removing traces of the α anomer) was carried out by column chromatography on Dowex 1-X2 (OH^-) with MeOH as eluent. The α anomer was eluted from the column before the β anomer. All galactose derivatives were white crystalline compounds which could be recrystallized by dissolution of the compound in as little MeOH as possible, and addition of MeCN to turbidity. Crystallization ensued after prolonged cooling. Average yield from D-galactose pentaacetate (**2a**): 42%.

Pentyl 1 - thio - β - D - galactopyranoside (**2f**).—^{1}H NMR (CD_3OD): δ 0.95 (t, 3 H, H-5′); 1.42 (m, 4 H, H-3′/4′); 1.67 (m, 2 H, H-2′); 2.76 (m, 2 H, H-1′); 3.49 (dd, 1 H, H-3, $J_{2,3}$ 3.2, $J_{3,4}$ 9.1 Hz); 3.56 (m, 2

H); 3.67 (m, 2 H, H-6?); 3.92 (d, 1 H, H-5?, J 2.4 Hz); 4.33 (d, 1 H, H-1, $J_{1,2}$ 9.3 Hz). ^{13}C NMR (CD_3OD): δ 14.3 (C-5′); 23.3, 30.7, 30.8 (C-1′, C-3′/4′); 32.2 (C-2′); 62.6 (C-6); 70.5, 71.5, 76.3, 80.6 (C-2/5); 87.7 (C-1). $[\alpha]_D^{21}$ −34.8° (c 1.4, MeOH). Anal. Calcd for $C_{11}H_{22}O_5S$: C, 49.60; H, 8.33; S, 12.04. Found: C, 49.68; H, 8.40; S, 12.06.

Hexyl 1-thio-β-D-galactopyranoside (**2g**).—^{1}H NMR (CD_3OD): δ 0.94 (t, 3 H, H-6′); 1.36 (m, 6 H, H-3′/5′); 1.66 (m, 2 H, H-2′); 2.74 (m, 2 H, H-1′); 3.50 (dd, 1 H, H-3, $J_{2,3}$ 9.4, $J_{3,4}$ 3.1 Hz); 3.56 (m, 2 H, H-6?); 3.75 (m, 2 H); 3.92 (d, 1 H, H-5?, J 2.4 Hz); 4.33 (d, 1 H, H-1, $J_{1,2}$ 9.0 Hz). ^{13}C NMR (CD_3OD): δ 14.4 (C-6′); 23.6, 29.6, 30.8, 31.01 (C-1′,3′/5′); 32.5 (C-2′); 62.5 (C-6); 70.4, 71.4, 76.2, 80.5 (C-2/5); 87.6 (C-1). $[\alpha]_D^{21}$ −31.3° (c 1, MeOH). Anal. Calcd for $C_{12}H_{24}O_5S$: C, 51.41; H, 8.63; S, 11.44. Found: C, 51.29; H, 8.74; S, 11.25.

Heptyl 1-thio-β-D-galactopyranoside (**2h**).—^{1}H NMR (CD_3OD): δ 0.94 (t, 3 H, H-7′); 1.36 (m, 8 H, H-3′/6′); 1.67 (m, 2 H, H-2′); 2.75 (m, 2 H, H-1′); 3.51 (dd, 1 H, H-3, $J_{2,3}$ 9.1, $J_{3,4}$ 3.2 Hz); 3.57 (m, 2 H); 3.76 (m, 2 H, H-6?); 3.93 (d, 1 H, H-5?, J 2.9 Hz); 4.35 (d, 1 H, $J_{1,2}$ 9.3 Hz). ^{13}C NMR (CD_3OD): δ 14.5 (C-7′); 23.7, 30.0 (2×), 30.9, 31.1 (C-1′,3′–6′); 32.9 (C-2′); 62.6 (C-6); 70.5, 71.5, 76.2, 80.5 (C-2′/5′); 86.7 (C-1). Anal. Calcd for $C_{13}H_{26}O_5S$: C, 53.04; H, 8.90; S, 10.89. Found: C, 52.56; H, 9.02; S, 10.51.

Octyl 1-thio-β-D-galactopyranoside (**2i**).—^{1}H NMR (CD_3OD): δ 0.94 (t, 3 H, H-8′); 1.40 (m, 10 H, H-3′/7′); 1.66 (m, 2 H, H-2′); 2.76 (m, 2 H, H-1′); 3.50 (dd, 1 H, H-3, $J_{2,3}$ 9.2, $J_{3,4}$ 3.3 Hz); 3.57 (m, 2 H, H-6?); 3.76 (m, 2 H); 3.93 (d, 1 H, H-5?, J 2.9 Hz); 4.35 (d, 1 H, H-1, $J_{1,2}$ 9.5 Hz). ^{13}C NMR (CD_3OD): δ 14.5 (C-8′); 23.7, 30.0, 30.3 (2×), 30.9, 31.1 (C-1′,3′/7′); 33.0 (C-2′); 62.5 (C-6); 70.4, 71.4, 76.2, 80.5 (C-2/5); 87.6 (C-1). $[\alpha]_D^{21}$ −32.3° (c 1.1, MeOH). Anal. Calcd for $C_{14}H_{28}O_5S$: C, 54.52; H, 9.15; S, 10.40. Found: C, 54.51; H, 9.02; S, 10.41.

Alkyl 2, 3, 4, 6-tetra-O-acetyl-1-thio-D-mannopyranosides (**3c–3e**).—The alkyl 2,3,4,6-tetra-*O*-acetyl-1-thio-D-mannopyranosides **3c–3e** were synthesized from **3a** and the appropriate *n*-alkanethiol via the $FeCl_3$ method as described by Dasgupta and Garegg [14]; a mixture of anomers was always produced. The fully protected products could be enriched in either α or β anomer by chromatography. The same conditions were used as for the fully protected glucose derivatives. Crystallization could be achieved using 96% EtOH, but crystallization did not yield an anomerically pure product. Average yield of anomer mixture: 20% (after crystallization).

Hexyl 2, 3, 4, 6-tetra-O-acetyl-1-thio-α-D-mannopyranoside (**3c**).—^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3 H, H-6′); 1.30 (m, 6 H, H-3′/5′); 1.62 (m, 2 H, H-2′); 1.99, 2.05, 2.09, 2.16 (4 s, each 3 H, acetyl CH_3); 2.63 (m, 2 H, H-1′); 4.08 (dd, 1 H); 4.31 (m, 2 H); 5.29 (m, 4 H). ^{13}C NMR ($CDCl_3$): δ 13.8 (C-6′); 20.4, 20.5 (2×), 20.7 ($COCH_3$); 22.3, 28.3, 29.2, 31.1 (C-1′,3′/5′); 31.2 (C-2′); 62.3 (C-6); 66.2, 68.7, 69.3, 71.0 (C-2/5); 82.3 (C-1); 169.5 (2×), 169.7, 170.3 ($COCH_3$). Anal. Calcd for $C_{20}H_{32}O_9S$: C, 53.56; H, 7.19; S, 7.15. Found: C, 53.53; H, 7.19; S, 7.22.

Heptyl 2, 3, 4, 6-tetra-O-acetyl-1-thio-α-D-mannopyranoside (**3d**).—^{1}H NMR ($CDCl_3$): δ 0.85 (t, 3 H, H-7′); 1.29 (m, 8 H, H-3′/6′); 1.58 (m, 2 H, H-2′); 1.96, 2.01, 2.06, 2.13 (4 s, each 3 H, acetyl CH_3); 2.50 (m, 2 H, H-1′); 4.04 (dd, 1 H, H-3); 4.28 (dd, 1 H), 4.35 (m, 2 H); 5.27 (m, 4 H). ^{13}C NMR ($CDCl_3$): δ 14.1 (C-7′); 20.6, 20.7 (2×), 20.9 ($COCH_3$); 22.6, 28.8, 29.4, 31.3 (C-1′/3′/6′); 31.7 (C-2′); 62.4 (C-6); 66.3, 68.8, 69.5, 71.2 (C-2/5); 82.5 (C-1); 169.7 (2×), 169.9, 170.5 ($COCH_3$). Anal. Calcd for $C_{21}H_{34}O_9S$: C, 54.53; H, 7.41; S, 6.93. Found: C, 54.36; H, 7.49; S, 6.85.

Octyl 2, 3, 4, 6-tetra-O-acetyl-1-thio-α-D-mannopyranoside (**3e**).—^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3 H, H-8′); 1.32 (m, 10 H, H-3′/7′); 1.60 (m, 2 H, H-2′); 1.98, 2.04, 2.09, 2.16 (4 s, each 3 H, $COCH_3$); 2.62 (m, 2 H, H-1′); 4.08 (dd, 1 H); 4.34 (m, 2 H); 5.40 (m, 4 H). ^{13}C NMR ($CDCl_3$): δ 13.9 (C-8′); 20.5, 20.6 (2×), 20.8 ($COCH_3$); 22.5, 28.6, 28.9, 29.0, 29.3, 31.2 (C-1′,3′/7′); 31.6 (C-2′); 62.3 (C-6); 66.2, 68.7, 69.3, 71.0 (C-2/5); 82.4 (C-1); 169.5 (2×), 169.7, 170.4 ($COCH_3$). Anal. Calcd for $C_{22}H_{36}O_9S$: C, 55.45; H, 7.61; S, 6.73. Found: C, 55.48; H, 7.55; S: 6.78.

Alkyl 1-thio-α-D-mannopyranosides (**3g–3i**).—After deprotection, which was quantitative (vide supra), and evaporation of the solvent mixture, the purification and separation of the anomers could be performed by chromatography either on Dowex 50-X4 (Ca^{2+}) or on a Sephadex column. In the first case a mixture of MeOH and water (7:3) was used as eluent; the β anomer had a shorter retention time than the α anomer. On Sephadex, MeOH was the eluent and the α anomer was eluted first. In addition, it was found that if the β anomer was present in the mixture in a proportion greater than 50% it could sometimes be crystallized specifically from MeOH.

The α-anomer is crystalline when an odd number

of carbons is present in the alkyl chain and can be crystallized from MeOH/MeCN (see **2f–2i**). However, for an even number of carbon atoms in the alkyl chain it is exceedingly difficult to obtain crystals. For alkyl chain lengths of six and eight carbon atoms it was possible to obtain pure crystalline β anomer. The elemental analyses were performed for the anomer mixtures (before chromatography).

Hexyl 1-thio-α-D-mannopyranoside (**3gα**).—^{1}H NMR (CD_3OD): δ 0.94 (t, 3 H, H-6′); 1.40 (m, 6 H, H-3′/5′); 1.67 (m, 2 H, H-2′); 2.63 (m, 2 H, H-1′); 3.70 (m, 2 H, H-3,4); 3.78 (dd, 1 H, H-6a, $J_{5,6a}$ 5.5, $J_{6a,6b}$ 12 Hz); 3.85 (dd, 1 H, H-6b, $J_{5,6b}$ 2.5 Hz); 3.89 (m, 2 H, H-2,5); 5.26 (d, 1 H, H-1, $J_{1,2}$ 1.1 Hz). ^{13}C NMR (CD_3OD); δ 14.25 (C-6′); 23.5, 29.5, 30.7, 32.0 (C-1′,3′/5′); 32.5 (C-2′); 62.8 (C-6); 69.0, 73.3, 73.8, 74.8 (C-2/5); 86.5 (C-1). Anal. Calcd for $C_{12}H_{24}O_5S$: C, 51.41; H, 8.63; S, 11.44. Found: C, 50.26; H, 8.47; the values are too low because the sample is very hygroscopic. Therefore, the percentage S was not determined.

Hexyl 1-thio-β-D-mannopyranoside (**3gβ**).—^{1}H NMR (CD_3OD); δ 0.96 (t, 3 H, H-6′); 1.43 (m, 6 H, H-3′/5′); 1.66 (m, 2 H, H-2′); 2.75 (m, 2 H, H-1′); 3.27 (m, 1 H, H-5); 3.50 (dd, 1 H, H-3, $J_{2,3}$ 3.4, $J_{3,4}$ 9.5 Hz); 3.61 (t, 1 H, H-4, $J_{4,5}$ 9.4 Hz); 3.74 (dd, 1 H, H-6a, $J_{5,6a}$ 5.5, $J_{6a,6b}$ 11.9 Hz); 3.90 (dd, 1 H, H-6b, $J_{5,6b}$ 2.4 Hz); 3.92 (dd, 1 H, H-2); 4.75 (d, 1 H, H-1, $J_{1,2}$ 1.0 Hz). ^{13}C NMR (CD_3OD); δ 14.4 (C-6′); 23.6, 29.6, 31.1, 32.2 (C-1′,3′/5′); 32.6 (C-2′); 62.9 (C-6); 68.4, 74.0, 76.3, 82.3 (C-2/5); 86.2 (C-1).

Heptyl 1-thio-α-D-mannopyranoside (**3hα**).—^{1}H NMR (CD_3OD); δ 0.93 (t, 3 H, H-7′); 1.39 (m, 8 H, H-3′/6′); 1.65 (m, 2 H, H-2′); 2.65 (m, 2 H, H-1′); 3.70 (m, 2 H, H-3,4); 3.76 (dd, 1 H, H-6a, $J_{5,6a}$ 5.5, $J_{6a,6b}$ 12.1 Hz); 3.85 (dd, 1 H, H-6b, $J_{5,6b}$ 2.6 Hz); 3.93 (m, 2 H, H-2,5); 5.25 (d, 1 H, H-1, $J_{1,2}$ 1.1 Hz). ^{13}C NMR (CD_3OD); δ 14.4 (C-7′); 23.6, 29.8, 30.0, 30.7, 31.8 (C-1′,3′/6′); 32.9 (C-1′); 62.6 (C-6); 68.7, 73.1, 73.7, 74.7 (C-2/5); 86.3 (C-1). $[\alpha]_D^{21}$ +186.1° (*c* 1.4, MeOH), lit. +189° [42]. Anal. Calcd for $C_{13}H_{26}O_5S$: C, 53.04; H, 8.90; S, 10.89. Found: C, 52.77; H, 8.78; S, 10.89.

Octyl 1-thio-α-D-mannopyranoside (**3iα**).—^{1}H NMR (CD_3OD); δ 0.94 (t, 3 H, H-8′); 1.37 (m, 10 H, H-3′/7′); 1.66 (m, 2 H, H-2′); 2.67 (m, 2 H, H-1′); 3.70 (m, 2 H, H-3,4); 3.77 (dd, 1 H, H-6a, $J_{5,6a}$ 5.5, $J_{6a,6b}$ 11.9 Hz); 3.85 (dd, 1 H, H-6b, $J_{5,6b}$ 2.3 Hz); 3.93 (m, 2 H, H-2,5); 5.22 (d, 1 H, H-1, $J_{1,2}$ 1.1 Hz). ^{13}C NMR (CD_3OD); δ 14.4 (C-8′); 23.7, 29.8, 30.2, 30.3, 30.7, 31.8 (C-1′,3′/7′); 32.9 (C-2′); 62.7 (C-6); 68.8, 73.2, 73.7, 74.8 (C-2/5); 86.4 (C-1). $[\alpha]_D^{21}$ +125.3° (*c* 1, MeOH). Anal. Calcd for $C_{14}H_{28}O_5S$: C, 54.52; H, 9.15; S, 10.40. Found: C, 54.27; H, 8.98; S, 10.37.

Octyl 1-thio-β-D-mannopyranoside (**3iβ**).—^{1}H NMR (CD_3OD); δ 0.93 (t, 3 H, H-8′); 1.40 (m, 10 H, H-3′/7′); 1.68 (m, 2 H, H-2′); 2.75 (m, 2 H, H-1′); 3.28 (ddd, 1 H, H-5); 3.53 (dd, 1 H, H-3, $J_{2,3}$ 3.5, $J_{3,4}$ 9.3 Hz); 3.65 (t, 1 H, H-4, $J_{4,5}$ 9.5 Hz); 3.76 (dd, 1 H, H-6a, $J_{5,6a}$ 5.5, $J_{6a,6b}$ 11.9 Hz); 3.89 (dd, 1 H, H-6b, $J_{5,6b}$ 2.4 Hz); 3.93 (dd, 1 H, H-2); 4.74 (d, 1 H, $J_{1,2}$ 0.9 Hz). ^{13}C NMR (CD_3OD); δ 14.3 (C-8′); 23.5, 29.8, 30.2, 31.0, 32.2 (CH_2); 32.9 (C-2′); 63.0 (C-6); 68.5, 74.0, 76.3, 82.2 (C-2/5); 86.2 (C-1). $[\alpha]_D^{21}$ −45.8° (*c* 0.6, MeOH).

Alkyl 2, 3, 4, 6-tetra-O-acetyl-1-thio-α-D-talopyranosides (**4d,4e**).—Both heptyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-talopyranoside (**4d**) and octyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-talopyranoside (**4e**) were synthesized according to the method used for the mannose derivatives (**3c–3e**). The α anomer was obtained in pure form after chromatography of the product mixture over silica gel with *n*-hexane/EtOAc (7:3) as eluent. The α anomer was eluted first.

Heptyl 2, 3, 4, 6-tetra-O-acetyl-1-thio-α-D-talopyranoside (**4d**).—^{1}H NMR ($CDCl_3$): δ 0.90 (t, 3 H, H-7′); 1.35 (m, 8 H, H-3′/6′); 1.67 (m, 2 H, H-2′); 2.02, 2.09, 2.18, 2.20 (4 s, each 3 H, $COCH_3$); 2.65 (m, 2 H, H-1′); 4.23 (d, 2 H); 4.66 (dt, 1 H); 5.23 (m, 2 H); 5.38 (dd, 2 H). ^{13}C NMR ($CDCl_3$): δ13.9 (C-7′); 20.4 (2×), 20.5 (2×) (4 CH_3CO); 22.5, 28.7, 29.2 (2×), 30.8 (C-1′,3′/6′); 31.6 (C-2′); 62.0 (C-6); 66.0, 67.1 (2×), 68.8 (C-2/5); 82.6 (C-1); 169.3, 169.7, 169.9, 170.2 (4 CH_3CO).

Octyl 2, 3, 4, 6-tetra-O-acetyl-1-thio-α-D-talopyranoside (**4e**).—^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3 H, H-8′); 1.33 (m, 10 H, H-3′/7′); 1.62 (m, 2 H, H-2′); 2.00, 2.06, 2.14, 2.15 (4 s, each 3 H); 2.62 (m, 2 H, H-1′); 4.19 (d, 2 H); 4.62 (dt, 1 H); 5.20 (m, 2 H); 5.34 (dd, 2 H). ^{13}C NMR ($CDCl_3$): δ 13.9 (C-8′); 20.5, 20.6 (2×), 20.8 (4 CH_3CO); 22.5, 28.6, 28.9, 29.0, 29.2, 31.2 (C-1′,3′/7′); 31.6 (C-2′); 62.0 (C-6); 66.0, 67.1 (2×), 68.8 (C-2/5); 82.6 (C-1); 169.3, 169.7, 169.9, 170.2 (CH_3CO).

Alkyl 1-thio-α-D-talopyranosides (**4h,4i**).—Compounds **4h** and **4i** were obtained from **4d** and **4e**, respectively, by hydrolysis in a solvent mixture of MeOH with aqueous trimethylamine (vide supra). The product was obtained by evaporation of the solvent mixture and purified by chromatography over a short column of Dowex 1-X2 (OH^-) with MeOH as eluent. The compounds were crystallized from a

MeOH/MeCN mixture (see **2f–2i**). Deprotection was quantitative. Average yield from **4a**: 30% (anomerically pure).

Heptyl 1-thio-α-D-talopyranoside (**4h**).—^{1}H NMR (CD_3OD): δ 0.90 (t, 3 H, H-7′); 1.37 (m, 8 H, H-3′/6′); 1.64 (m, 2 H, H-2′); 2.65 (m, 2 H, H-1′); 3.65 (t, 1 H, H-3, $J_{2,3} = J_{3,4} = 3.2$ Hz); 3.75 (d, 2 H, H-6, $J_{5,6}$ 6.1 Hz); 3.82 (2 d, 2 H, H-2,4); 4.11 (t, 1 H, H-5); 5.30 (d, 1 H, H-1, $J_{1,2}$ 0.7 Hz). ^{13}C NMR (CD_3OD): δ 14.2 (C-7′); 23.7, 29.9, 31.0, 30.7, 31.8 (C-1′,3′/6′); 32.9 (C-2′); 62.7 (C-6); 67.9, 71.8, 73.3, 74.2 (C-2/5); 87.1 (C-1). $[\alpha]_D^{21}$ +181.2° (*c* 1, MeOH). Anal. Calcd for $C_{13}H_{26}O_5S$: C, 53.04; H, 8.90; S, 10.89. Found: C, 52.52; H, 8.78; S, 10.85.

Octyl 1-thio-α-D-talopyranoside (**4i**).—^{1}H NMR (CD_3OD): δ 0.91 (t, 3 H, H-8′); 1.35 (m, 10 H, H-3′/7′); 1.63 (m, 2 H, H-2′); 2.65 (m, 2 H, H-1′); 3.68 (t, 1 H, H-3, $J_{2,3} = J_{3,4} = 3.2$ Hz); 3.77 (d, 2 H, H-6, $J_{5,6}$ 6.1 Hz); 3.85 (2 d, 2 H, H-2,4); 4.12 (t, 1 H, H-5); 5.32 (d, 1 H, H-1, $J_{1,2}$ 0.7 Hz). ^{13}C NMR (CD_3OD): δ 14.4 (C-8′); 23.7, 29.9, 30.2, 30.3, 30.7, 31.7 (C-1′,3′/7′); 32.9 (C-2′); 62.6 (C-6); 67.9, 71.6, 73.1, 74.1 (C-2/5); 86.9 (C-1). $[\alpha]_D^{21}$ +122° (*c* 1, MeOH). Anal. Calcd for $C_{14}H_{28}O_5S$: C, 54.52; H, 9.15; S, 10.40. Found: C, 54.58; H, 9.21; S, 10.36.

A crystal structure was solved for octyl 1-thio-α-D-talopyranoside [49].

(R,S)-3,7-Dimethyl-1-octanethiol (**6**).—(*R,S*)-3,7-Dimethyloctanethiol was synthesized from (*R,S*)-citronellol using a standard procedure [16]. ^{1}H NMR ($CDCl_3$): δ 0.87 (m, 9 H, 3 CH_3); 1.12 (m, 3 H); 1.26 (m, 4 H); 1.49 (m, 4 H); 2.53 (m, 2 H, H-1). ^{13}C NMR ($CDCl_3$): δ 19.1 (CH_3); 22.4 (CH_2); 22.5, 22.6 (2 CH_3); 24.5 (CH_2); 27.8 (CH); 31.7 (CH); 36.8 (CH_2); 39.1 (CH_2); 41.4 (CH_2).

(R,S)-3,7-Dimethyloctyl 1-thio-β-L-arabinopyranoside (**5c**).—Compound **5c** was synthesized by coupling α-L-arabinopyranose tetraacetate (**5a**) with the appropriate alkanethiol **6** under the same conditions used for the glucose and galactose derivatives described earlier, with a reaction time of 15 min. The acetylated adduct was deprotected by hydrolysis in the MeOH–Me_3N–H_2O mixture for 24 h. The yield from **5a** was 33%. ^{1}H NMR (CD_3OD): δ 0.93 (m, 9 H, H-3″,7″,8′); 1.20 (m, 4 H, H-5′,6′); 1.35 (m, 2 H, H-4′); 1.44–1.74 (m, 4 H, H-2′,3′,7′); 2.65 (m, 2 H, H-1′); 3.63 (dd, 1 H, H-5a, $J_{4,5a}$ 5.1, $J_{5a,5b}$ 11.7 Hz); 3.74 (dd, 1 H, H-3, $J_{3,4}$ 3.4 Hz); 3.91 (m, 1 H, H-4); 4.00 (dd, 1 H, H-2, $J_{2,3}$ 7.9 Hz); 4.07 (dd, 1 H, H-5b, $J_{4,5b}$ 3.0 Hz); 5.21 (d, 1 H, H-1, $J_{1,2}$ 4.0 Hz). ^{13}C NMR (CD_3OD): δ 19.7, 19.8, 22.9, 23.0 (C-3″,7″,8′); 29.1 (C-7′); 25.7, 29.4, 29.5 (C-6′, 4′ or 5′); 33.3 (C-3′); 38.0, 38.1, 38.2, 38.3 (C-1′, 4′ or 5′); 40.4 (C-2′); 65.5 (C-5), 68.9, 71.4, 71.9 (C-2/4); 86.8, 87.1 (C-1).

The extra signals in the NMR spectra are due to the presence of a diastereomeric mixture of compounds. Anal. Calcd for $C_{15}H_{30}O_4S$: C, 58.79; H, 9.87; S, 10.46. Found: C, 58.45; H, 9.69; S, 10.40.

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