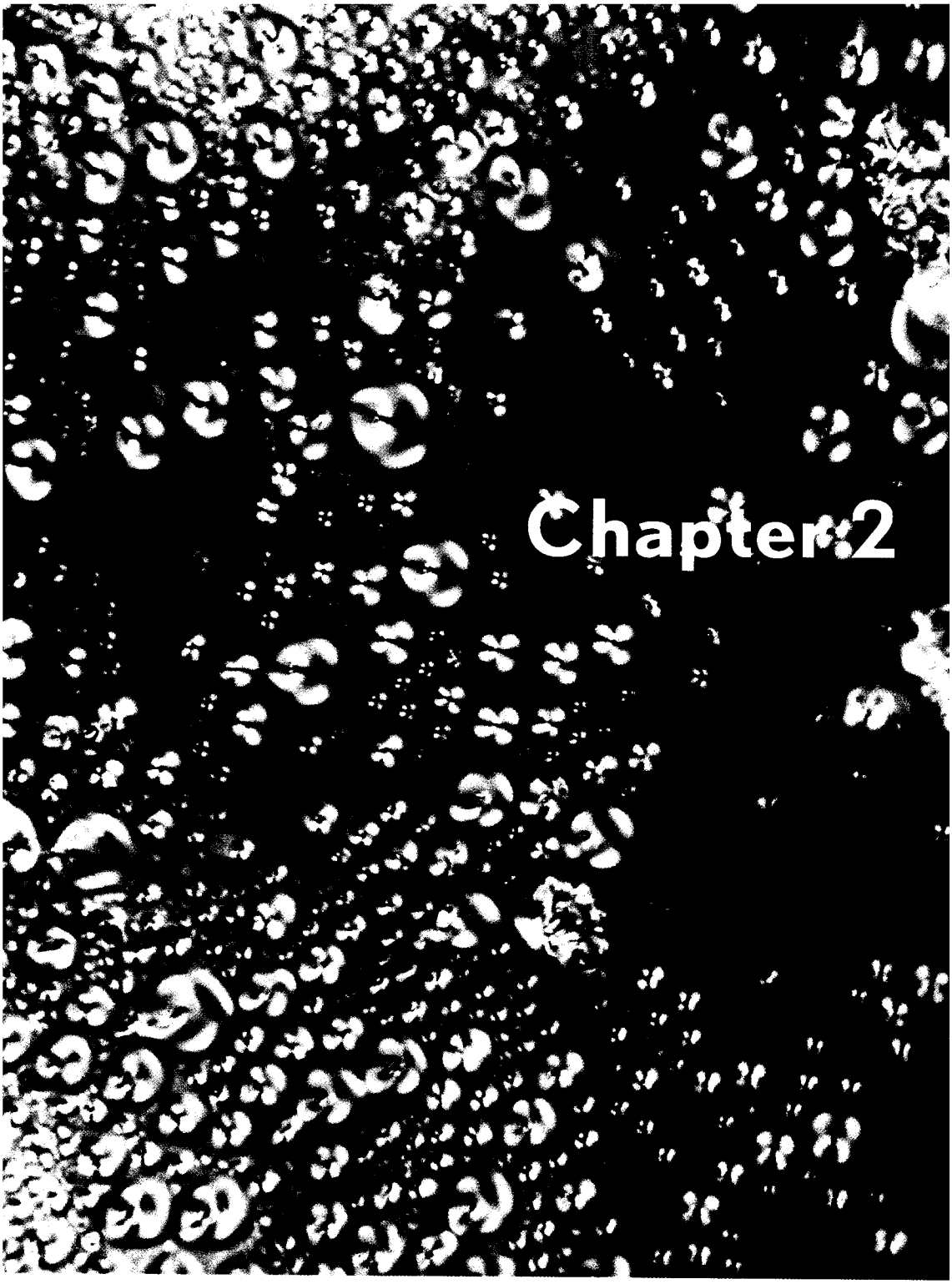
The sweet world of liquid crystals

Smits, E



Amphiphilic Carbohydrate-derived Liquid Crystals

2.1 Introduction

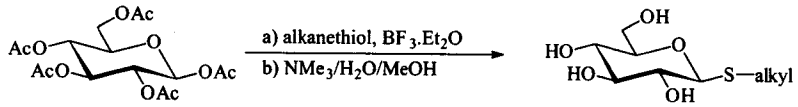
The interest in the liquid-crystalline (LC) behavior of amphiphilic carbohydrate derivatives stems largely from the fact that carbohydrates can be substituted relatively easily with one or more alkyl chains; hence, the products constitute a potentially large class of mesogenic compounds.[1,2,3] The occurrence of LC behavior and the phase transition temperatures are strongly dependent on the nature of the carbohydrate moiety (*e.g.*, cyclic or acyclic form, mono- or oligosaccharide), the hydrophobic alkyl chain(s), the type of linkage between the two parts (*e.g.*, (thio)ether, ester, or amide) and the presence of a rigid spacer unit.[4,5]

In the first part of this chapter, the LC-properties of a series of alkyl 1-thio-β-D-glucopyranosides (*n*-βSGPs, *n* is the number of carbon atoms in the alkyl chain) with the alkyl chain varying from pentyl to decyl and dodecyl are described. Although the LC-behavior of a complete series of alkyl 1-thio-α-D-glucopyranosides (*n*-αSGP) has been reported,[6] only a few members of the series of β-anomers have been prepared and described.[7] The thermotropic mesogenic behavior was studied using thermomicroscopy and differential scanning calorimetry (DSC) and was compared with the LC-behavior of alkyl α- and β-D-glucopyranosides (*n*-αOGPs and *n*-βOGPs).[8]

The second part of this chapter is concerned with the thermotropic and lyotropic LC behavior of a homologous series of 4-alkoxyphenyl β-D-glucopyranosides (alkoxy = methoxy to decyloxy and dodecyloxy, compounds **2.*n***, *n* is the number of carbon atoms in the alkoxy group). The compounds were prepared in a two-step synthetic procedure. The mesogenic behavior was studied using polarization microscopy and DSC.

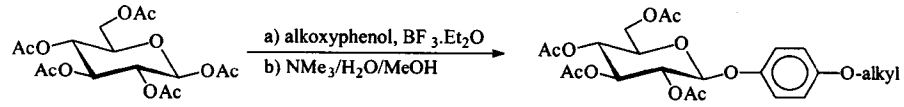
The incorporation of a rigid spacer unit (a phenyl ring) as a linking group between the carbohydrate and the alkyl chain stabilizes the mesophases of the compounds, as was reported by Baeyens-Volant *et al.*[9] for 4-alkylphenyl D-gluconamides. Tschierske *et al.*[10] reported a similar effect for the thermotropic LC behavior of octyl, 4-octylphenyl, and *trans*-4-butylcyclohexyl β-D-glucopyranosides (β-GPs); lyotropic mesophase formation was neglected. Jeffrey *et al.*[11] focused on the differences in the behavior of α- and β- anomers of 4-alkylphenyl GPs. Only three different alkyl chain lengths of each anomer were studied, and little attention was paid to the lyotropic LC behavior. The study of the lyotropic LC-behavior of a homologous series of carbohydrate amphiphiles is interesting because the size of the hydrated headgroup is relatively small compared to that of ionic surfactants and repulsive Coulomb interactions are absent. Consequently, variation of the alkyl chain length in a homologous series can have a large effect on the polymorphism of the lyotropic LC-behavior.

*Color Plate left: The texture of the smectic A phase of compound **2.6**. Uncovered droplet. Magnification 200x.*



β-SGPs
alkyl = pentyl/decyl and dodecyl

Scheme 2.1 Synthesis of alkyl 1-thio-β-D-glucopyranosides.



2.*n* alkyl = methyl/decyl and dodecyl

Scheme 2.2 Synthesis of 4-alkoxyphenyl β-D-glucopyranosides.

2.2 Synthesis

Alkyl 1-thio-β-D-glucopyranosides were synthesized from penta-*O*-acetyl-β-D-glucose and the corresponding alkanethiol, see Scheme 2.1, as described by Galema *et al.*[7] The glucosylation reaction is catalyzed by boron trifluoride diethyl ether ($BF_3.Et_2O$); when the reaction was quenched after 15 min. the β-products were isolated almost exclusively. The 4-alkoxyphenyl β-GPs were synthesized in two steps from penta-*O*-acetyl-β-D-glucose and the appropriate 4-alkoxyphenol as illustrated in Scheme 2.2. The glucosidic bond was formed in a Lewis acid-catalyzed ($BF_3.Et_2O$) reaction at room temperature to give the β-product exclusively.[12] The acetylated 4-alkoxyphenyl β-GPs were purified by crystallization from ethanol (yields: 62 - 85%) and deprotected quantitatively using trimethyl amine in aqueous methanol.[6] The crude 4-alkoxyphenyl β-GPs (**2.1-2.12**) were purified by crystallization from methanol/acetonitrile (1:2).

2.3 Thermotropic liquid-crystalline behavior of alkyl 1-thio-β-D-glucopyranosides

The *n*-βSGPs with an alkyl chain longer than pentyl display smectic A mesophases as was determined with polarization microscopy and DSC. The phase transition temperatures are compiled in Table 2.1 and plotted as a function of alkyl chain length in Figure 2.1. The melting transitions as recorded with DSC are relatively broad and in several cases crystal-to-crystal transitions were observed; the transitions from the mesophase to the isotropic state were recorded as sharp peaks. Compound 6-βSGP has a monotropic mesophase, whereas the longer homologs all have enantiotropic mesophases. The melting points do not show a clear odd-even effect as is the case for the α-SGPs. The clearing points of the *n*-βSGPs increase with increasing chain length.

Table 2.1. Thermotropic liquid-crystalline behavior of alkyl 1-thio β-D-glucopyranosides. Values in parentheses indicate crystal-to-crystal transitions.

compound	m.p. (°C)	$\Delta H_{melting}$ (kJ/mol)	c.p. (°C)	$\Delta H_{clearing}$ (kJ/mol)
5-βSGP	31.6-68.0	12.8		
6-βSGP	60.2-65.2	15.3	[65.4-66.5][a]	-1.0
7-βSGP	41.0-47.2	5.3	101.5-102.7	1.5
8-βSGP	37.1-41.4	30.5	127.7-128.8	1.6
9-βSGP	(47.2-53.4) 59.7-63.6	24.0 3.6	139.8-140.3	2.0
10-βSGP	62.4-68.0	36.5	159.7-160.7	2.3
12-βSGP	(55.7-58.0) 64.4-67.6	1.5 3.4	167.1-167.5	2.0

a) monotropic transition, measured upon cooling (enthalpy has a negative value).

With the thermal data of the *n*-βSGPs in hand, a comparison can be made of the LC-behavior of four homologous series: the thio-linked derivatives *n*-αSGPs[6] and *n*-βSGPs and the oxygen-linked analogs alkyl α- and β-D-glucopyranosides[8]. In Figure 2.1 and 2.2 the melting and clearing points of these four series of compounds are plotted. The melting points of the *n*-βSGPs are consistently lower (30-45°C) than those of the α-anomers. This suggests a better crystal packing of the *n*-αSGPs, in accordance with qualitative observations made during the purification of these products. The *n*-αSGPs were obtained nicely crystalline, in particular the compounds with an odd number of carbon atoms,[6] whereas the recrystallization of the *n*-βSGPs was troublesome. The clearing temperatures of the *n*-βSGPs are also lower but this difference is smaller (10-35°). The α- and β-anomers of the *n*-OGPs have almost identical melting points and lie in between those of the α- and β-anomers of the SGPs. The clearing points of the *n*-αOGPs are higher than those of the *n*-βOGPs, but this difference is smaller than for the α- and β-SGPs. The temperature ranges of the LC-phases of the *n*-SGPs are broader than those of the *n*-OGPs.

The reasons for the differences in thermal behavior of these four series of glucosides are not fully understood. Hydrogen bonding between the sugar headgroups plays an important role in the stability of both the liquid-crystalline and the solid phase.[13] Crystal structures should give information on differences in packing in the solid state, but only the crystal structures of 7-αSGP[14] and 8-αOGP[15] have been published. Unfortunately, even these cannot be compared because of the presence of water in the crystal of the latter. The differences in melting points of the oxygen- and thio-glucosides have been attributed to the larger size of the sulphur atom.[16] This changes the relative orientation of the sugar headgroup to the alkyl chain and, consequently, alters the hydrogen bonding between the sugar moieties, and the Van der Waals interactions between the alkyl chains.

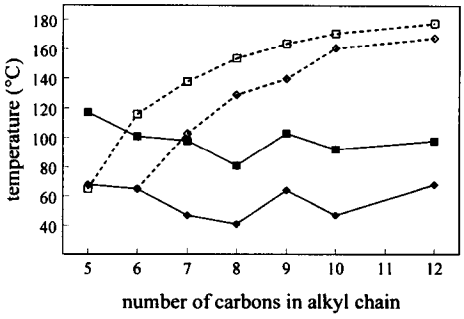


Figure 2.1 Melting and clearing temperatures of αSGPs (■,□) *and* β SGPs (◆,◇).

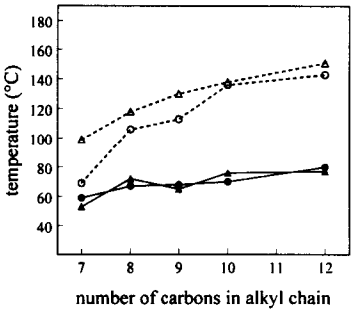


Figure 2.2 Melting and clearing temperatures of αOGPs (▲,△) *and* βOGPs (●,○).

For the *n*-βSGPs one might conclude that the larger size of the sulphur atom prevents the alkyl chains from getting as close together as they do in the *n*-βOGPs, reducing their mutual interactions and, consequently, lowering the melting points. But it is remarkable that for the *n*-OGPs, the configuration at the anomeric centre barely affects the melting points, whereas the melting points of the *n*-αSGPs are much higher than those of the *n*-βSGPs.

The conformation at the anomeric centre and the atom (O or S) linking the sugar and alkyl moieties also influences the stability of the LC-phase. The *n*-αSGPs have the highest clearing points, which suggests that these molecules have the best interactions in the LC-phase. But since there is no information available on the differences in, *e.g.*, the hydrogen bonding interactions in the LC-phases of these glucosides, we cannot yet relate sugar conformation and structure to thermal behavior.

2.4 Thermotropic liquid-crystalline behavior of 4-alkoxyphenyl β-D-glucopyranosides

The 4-alkoxyphenyl β-GPs with an alkoxy chain longer than butoxy (**2.5-2.12**) are enantiotropic liquid crystals (compound **2.4** displays a monotropic mesophase) as was established by polarization microscopy and DSC. The phase-transition temperatures and the corresponding enthalpies are given in Table 2.2. From the graphical presentation (Figure 2.3) an odd-even effect in the melting points is apparent which becomes smaller upon lengthening of the alkoxy chains to reach an almost constant melting temperature of 100°C for chain lengths greater than eight carbons (**2.9-2.12**). The **2.4** to 205°C for **2.12**. Based on their textures, the mesophases were characterized as smectic A and they are miscible with the S_A-phase of 9-βSGP.[6] When a sample was cooled from the isotropic

Table 2.2. Thermotropic liquid-crystalline behavior of 4-alkoxyphenyl β-D-glucopyranosides. Values in parentheses indicate crystal-to-crystal transitions.

	alkyl	m.p. (°C)	$\Delta H_{melting}$ (kJ/mol)	c.p. (°C)	$\Delta H_{clearing}$ (kJ/mol)
2.1	methyl	172.1-173.8	35.7		
2.2	ethyl	148.8-173.2	44.7		
2.3	propyl	(129.9-131.5) 155.4-159.4	(16.8) 21.1		
2.4	butyl	(121.7-123.2) 150.5-151.9	(17.5) 26.5	140.4-140.0	1.87
2.5	pentyl	(101.0-103.5) 109.2-112.4	(22.1) 3.2	159.8-161.4	2.48
2.6	hexyl	(90.1-93.4) 131.0-134.4	(15.6) 21.0	177.7-178.2	2.46
2.7	heptyl	(83.9-88.3) 90.2-96.0	(12.4) 6.5	182.9-185.0	2.59
2.8	octyl	89.0-94.0	14.3	195.4-196.3	2.18
2.9	nonyl	94.8-101.0	23.0	202.1-202.8	2.31
2.10	decyl	98.0-102.7	20.0	204.7-205.0	1.86
2.12	dodecyl	99.8-104.3	27.7	203.7-206.4	1.67

state, bâtonnets were formed at the transition from the isotropic to the liquid-crystalline phase. Further cooling gave a focal-conic fan-like texture with large homeotropic areas. Color plate preceeding this Chapter shows the texture of an uncovered droplet of compound **2.6**, (178°C).

Compound **2.3** is not liquid-crystalline, although the DSC cooling scan shows two exothermic peaks very close to each other. These peaks arise from crystallization followed by a crystal-to-crystal transition as was observed by light microscopy. Upon cooling of an uncovered droplet of **2.3** from the isotropic state, long, thin crystals were formed at 164°C, which curl like whiskers. Further cooling induces a crystal-to-crystal transition at 153°C. Apparently, the propoxy group of **2.3** is too short to induce mesophase formation.

The melting and particularly the clearing temperatures of the 4-alkoxyphenyl β-GPs (compound **2.8**: m.p.= 94°, c.p.= 196°C) are significantly higher than the transition temperatures of the alkyl β-GPs (octyl β-GP: m.p.= 69°, c.p.= 110°C);[10] the rigid 1,4-phenylene moiety stabilizes the thermotropic mesophase. A comparison of the two homologous series[8] shows that introduction of the phenylene unit increases the melting points by about 20°, and the clearing temperatures by 50°-90°C.

In non-amphiphilic calamitic liquid crystals it is generally observed that compounds with

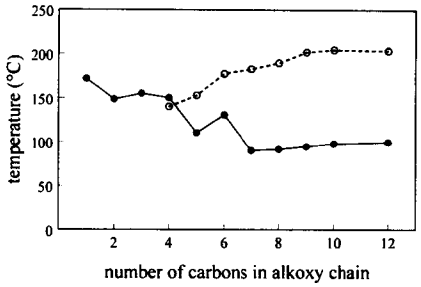


Figure 2.3 Melting (●) and clearing (○) temperatures for compounds **2.1-2.12** *plotted vs. number of carbons in the alkoxy chain.*

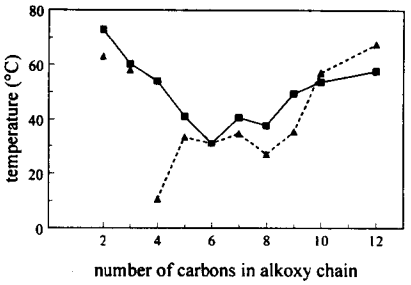


Figure 2.4 Krafft temperatures of compounds **2.2-2.12** *in 5% mixtures in water as measured with DSC. (■ first and ▲ second heating scans).*

In non-amphiphilic calamitic liquid crystals it is generally observed that compounds with alkoxy-substituted phenyl rings have higher clearing temperatures than the alkyl-substituted analogs. This phenomenon is not clear for the alkoxy- and alkyl-substituted aryl β-GPs. From a comparison between 4-heptyloxyphenyl β-GP (**K** *107* $\mathbf{S_A}$ *202* **I**) with 4-octylphenyl β-GP (**K** *108* $\mathbf{S_A}$ *192* **I**), Tschierske[10] concluded that replacement of a methylene group by an oxygen atom stabilizes the LC phase. But, whereas **2.2** and **2.3** are not LC (and **2.4** is monotropic LC), Jeffrey[11] reported enantiotropic S_A-phases for 4-propyl- and 4-butylphenyl βGP. The transition temperatures of 4-heptylphenyl βGP (m.p.=155°, c.p.= 207°C)[11] are significantly higher than those of **2.6**, which contradicts Tschierske's[10] observation. A relevant conclusion regarding the differences in behavior of amphiphilic mesogens with alkyl- and alkoxy-substituted phenyl rings cannot be drawn on the basis of these data.

Replacement of a single (oxygen) atom linking group (odd) between two rigid units by O-CH_2 (even) has a stabilizing effect on the mesophase of calamitic liquid crystals.[10] This effect is not observed for amphiphilic carbohydrate liquid crystals. Hexyloxybenzyl β-GP melts at 115°C and its c.p. is 127°C,[10] for octyloxybenzyl β-GP the m.p.= 111.1°C and c.p.= 141.4°C. The mesophase ranges of alkoxybenzyl β-GPs (12°C and 30°C) are small compared to the ranges of 34°C and 104°C observed for compounds **2.6** and **2.8**, respectively.[17] This contrasting behavior of amphiphilic and calamitic LC most likely finds its origin in the different driving forces for mesophase formation, *i.e.*, microphase separation *vs.* anisotropic interactions.[18]

2.5 Lyotropic liquid-crystalline behavior of 4-alkoxyphenyl β-D-glucopyranosides

Amphiphilic carbohydrate derivatives not only display thermotropic LC phases; a wealth of lyotropic mesophases are often formed in the presence of water. The type of mesophase formed is

Table 2.3. Lyotropic liquid-crystalline behavior of compounds ***2.3-2.12****.*

	alkyl	T_{krafft} [a]	Hexagonal H_I [b]	Cubic V_I [b]	Lamellar L_α [b]
2.3	propyl	60.3-63.6			
2.4	butyl	54.0-55.5	61-75	71-89	85-97
2.5	pentyl	44.3-48.1[c]	37-76	53-95	40-97
2.6	hexyl	31.1-35.0	38-82	44-95	42-95
2.7	heptyl	40.7-43.2		36-80	51-95
2.8	octyl	43.3-45.3[c]		40-95	54-95
2.9	nonyl	49.5-52.8[c]		86-95	65-95
2.10	decyl	53.7-57.1			53-95
2.12	dodecyl	57.7-61.1			64-95

a) Measured with DSC, melting point of the anhydrous crystal in water.
b) Determined with polarization microscopy.
c) Broad transition (three non-separated peaks).

dependent on the temperature and the concentration, and also on the relative sizes of the hydrophobic and hydrophilic segments of the molecules.[19,20] The nonionic hydrophilic carbohydrate headgroup is relatively small. Therefore, increasing the alkoxy chain length, as in the series **2.1-2.12**, will have a significant effect on the lyotropic behavior.

A straightforward, qualitative method to study the lyotropic phase behavior of **2.1-2.12** is the water penetration method.[21,22] A minute amount of compound is heated to the isotropic phase on a microscope slide and covered with a cover slip. After the sample has cooled and solidified, water is added at the edge of the cover slip. Due to capillary action, water is brought into contact with the sample. A concentration gradient, ranging from pure water to pure compound, appears immediately or upon heating in the heating stage.

Water can only penetrate into the crystals to form lyotropic mesophases above the Krafft temperature (T_{Krafft}), the discontinuity in the solubility *vs.* temperature curve observed for surfactants.[23,24] Generally, T_{Krafft} increases with increasing alkyl chain length. Krafft temperatures can be measured conveniently by monitoring the heat effect when a sample containing ca. 5% of amphiphile in water is heated in the DSC. The melting points of the anhydrous crystals **2.1-2.12** in water first decrease with increasing chain length, with a minimum for **2.6**, and then increase when the alkoxy chain is lengthened further (see Table 2.3 and Figure 2.4, no transition was observed for compound **2.1**). However, with the exception of **2.2** and **2.3**, the transition temperatures measured in the second heating scans show normal behavior.[28,25] The higher melting points of the anhydrous crystals of **2.2-2.5** in water most likely arise from different crystal packings compared to the longer-

chain analogs. This is reflected by the enthalpies of melting, which are significantly higher for the short-chain compounds than for the higher homologs (Table 2.2). Upon cooling in the presence of water, compounds **2.4** and **2.5** apparently crystallize as their hydrates. These hydrates melt at a lower temperature than the anhydrous crystals. This most likely does not occur for compounds **2.2-2.3** since these do not form lyotropic mesophases in water.

Apparently, the hydrophobic moieties of **2.2** and **2.3** are too small to induce surface-active behavior. Compounds **2.4-2.12** form several mesophases in the presence of water when heated above T_{Krafft}. The temperature ranges of the different phases formed are listed in Table 2.3. Indeed, the shape of the hydrated molecules changes substantially as a function of alkyl chain length (from conical to cylindrical). [26,27] This is reflected by the hexagonal phases formed by compounds **2.4-2.6**, whereas compounds **2.10** and **2.12** only form lamellar phases. Compounds **2.4-2.9** also form a cubic phase;[28] a viscous isotropic band is formed in between the hexagonal (**2.4-2.6**) or isotropic (**2.7-2.9**) and the lamellar phase. Figure 2.5 shows the mesophases formed by **2.6** in a contact preparation. Compounds **2.7** and **2.8** form a cubic phase immediately after the crystalline hydrate has melted; in the contact preparation of compound **2.9** the cubic phase was formed at 86°C. Compounds **2.10** and **2.12** only form lamellar phases. At the interface between the super-cooled lamellar phase[13] and isotropic solution of compounds **2.9-2.12**, myelins are formed at ambient temperature, which is indicative for vesicle formation in dilute solutions.[29,30] We tried to visualize the vesicles using electron microscopy, and performed the experiments with compound **2.9**, because it has a lower T_{Krafft} than compounds **2.10** and **2.12**; the latter have not yet been examined. To our surprise, a 5% solution of **2.9** in water does not contain vesicles but long ribbons, see Figure 2.6.[31] The ribbons, consisting of 3-5 segments, each having a width of circa 8 nm, are several hundreds of micrometers long and most of the ribbons are twisted irregularly. The solution has a gel-like character and the aggregates are also visible in the light microscope as long threads. Tubular aggregates, which are used for the crystallization of membrane proteins, are generally formed from complex chiral amphiphilic molecules.[32] The driving forces for the formation of ribbons and their aggregation to tubules are not well-understood.[33,34,35] Various *N*-alkyl aldonamides are also known to form helical thread-like structures in water; the hydrogen bonds formed by the hydroxyl groups of the sugar moiety and the amide groups stabilize the aggregates and determine the morphology.[31,36,37] Compound **2.9** has only four hydroxyl groups, most likely π-π interactions between the phenyl groups play a dominant role in the aggregation behavior, since alkyl β-GPs do not display this special behavior. A more extensive electron-microscopy study on the aggregates of compound **2.9** and other long-chain 4-alkoxyphenyl β-GPs is needed to obtain further insight into their fascinating supramolecular behavior.

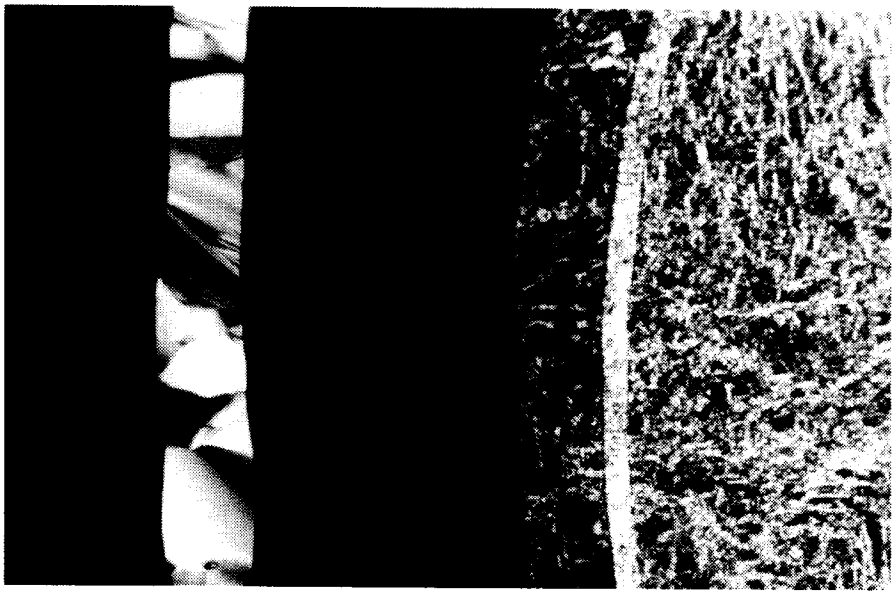


Figure 2.5 Lyotropic mesophases of compound **2.6**, *isotropic, hexagonal (H_I), cubic (V_I) and lamellar (Lα) phase. Contact preparation, 72°C, magnification 100x.*

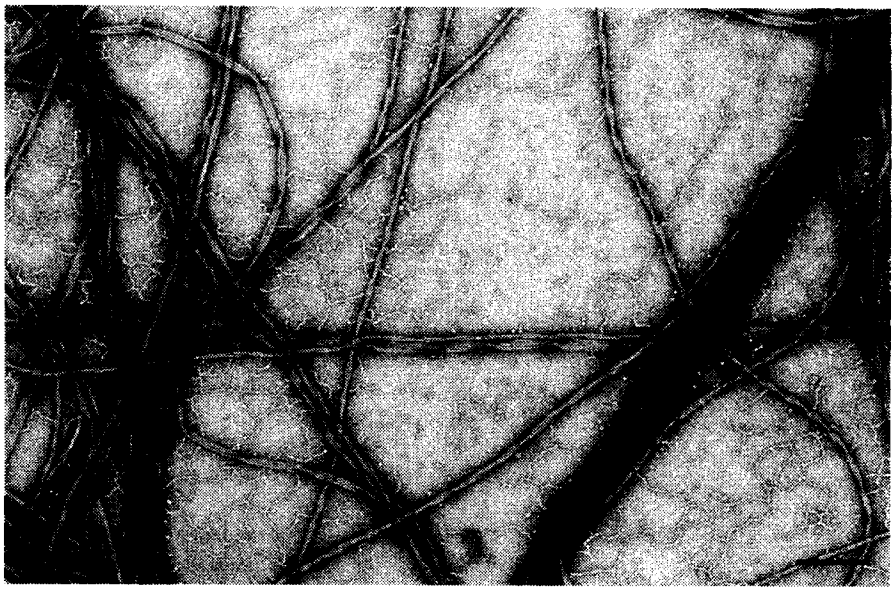


Figure 2.6 Ribbons formed by compound 2.9 (electron micrograph, negative staining, the bar represents 200 nm).

2.6 Conclusions

With the synthesis of a series of alkyl 1-thio-β-D-glucopyranosides, the possibility was created to compare the LC-behavior of the alkyl 1-thio-α- and β-D-glucopyranosides with the alkyl α- and β-D-glucopyranosides. The *n*-βSGPs with 6 or more carbon atoms in the alkyl chain form smectic A mesophases. Compound 6-βSGP has a monotropic mesophase. The differences found in the LC-behavior of the thio- and oxygen-linked compounds can possibly be attributed to the larger size of the sulphur atom, effecting an altered orientation of the alkyl chain relative to the sugar headgroup which has its consequences for the hydrogen bonding pattern in the sugar moieties. The clearing points of the *n*-αSGPs are higher than those of the *n*-βSGPs; similar effects have been found for the α- and βOGPs. The *n*-αSGPs have higher melting points than the *n*-βSGPs, whereas the α- and βOGPs have almost identical melting points. The *n*-αSGPs possess the most stable LC-phases.

Our study of the liquid-crystalline behavior of a homologous series of 4-alkoxyphenyl β-D-glucopyranosides has shown that compounds **2.4-2.12** display thermotropic S_A-phases; as a result of the rigid phenyl moiety, the mesophase stability is enhanced compared to that of alkyl β-D-glucopyranosides. In lyotropic systems, compounds **2.4-2.12** form several mesophases depending on the length of the alkoxy chain, similar to other homologous series of carbohydrate amphiphiles. The aggregation behavior of compound **2.9** is remarkable; ribbons are formed in dilute solution and most likely π-π interactions between the phenyl ring play a crucial role in the formation of these aggregates.

2.7 Experimental

General - Thermomicroscopy was performed with the Mettler FP 800 system, the hot stage was mounted on a Nikon microscope. Quantitative thermal analyses were performed using a Perkin Elmer PC Series DSC 7. The values reported are those of the first heating scans. For the measurements of the Krafft temperatures, DSC-pans were filled with 3 mg of anhydrous compound and 50 µl of water. Electron microscopy (EM) was performed on a Philips 201 electron microscope operating at 80 kV. A dispersion of 5% of **2.9** in water was sonicated with an ultrasonic horn at 60°C and negatively-stained on carbon-coated Formvar grids according to the two-droplet method with a 2% (w/v) solution of sodium phosphotungstate (PTA, pH 7.2).[38] The EM-experiments were performed by Monique Pestman. All reagents and solvents were purchased from any one of the large chemical suppliers and were used without further purification. Elemental analyses of the 4-alkoxyphenyl derivatives are compiled in Table 2.5. The structures of the products were confirmed by NMR-spectroscopy. NMR spectra were recorded on a 300 MHz Varian VTR-300 spectrometer. Chemical shifts are related to $CHCl_3$ (^{1}H: δ 7.24 ppm,^{13}C: 77.5) or CD_3OD (^{1}H: δ 3.35 ppm, ^{13}C: 49.0).

Alkyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranosides. The compounds were synthesized by reaction of penta-*O*-acetyl-β-D-glucose (7.8 g, 20 mmol) and an alkanethiol (20 mmol) in 40 ml of $CHCl_3$ with 5 equivalents of $BF_3.Et_2O$ (14 ml, 0.1 mol). The reaction mixture was stirred for 15 min. at room temperature and then poured into 100 ml of a 5% $NaHCO_3$ solution. The organic layer was separated, washed with aq. $NaHCO_3$ and once with water, dried over Na_2SO_4 and concentrated. The crude products were crystallized from hexane.

As a typical example some data and the ^{1}H- and ^{13}C-NMR spectra of decyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-gluco-

Table 2.4. Melting points of 4-alkoxyphenyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosides.
Values in parentheses indicate crystal-to-crystal transitions.

	m.p. (°C)	$\Delta H_{melting}$ (kJ/mol)
methyl	(93.2-95.5) 100.6-102.3	(5.5) 19.2
ethyl	110.1-111.4	36.1
propyl	109.3-115.7	25.3
butyl	113.3-114.7	30.3
pentyl	114.7-115.8	34.4
hexyl	101.6-102.9	30.9
heptyl	107.1-108.4	39.7
octyl	98.8-100.0	32.8
nonyl	(66.2-67.3) 97.2-101.6	(7.7) 28.5
decyl	88.0-89.3	1.8
dodecyl	99.3-101.1	67.2

pyranoside are given: Yield: 85% after recrystallization. m.p.= 71.5-73.3 °C. ^{1}H-NMR ($CDCl_3$): δ 0.86 (t, 3H, H-10'); 1.24 (br m, 14H, H-3'/9'); 1.57 (m, 2H, H-2'); 1.99, 2.01, 2.04, 2.26 (4×s, 12H, $COCH_3$); 3.68 (m, H-1'); 3.69 (ddd, 1H, H-5); 4.10 (dd, 1H, H-6b, $J_{5\text{-}6a}$= 2.4 Hz, $J_{6a\text{-}6b}$= 12.5 Hz); 4.22 (dd, 1H, $J_{5\text{-}6b}$= 4.9 Hz); 4.47 (d, 1H, H-1, $J_{1\text{-}2}$= 10 Hz); 5.01, 5.06, 5.20 (3×dd, 3H, H-2/4). ^{13}C-NMR: δ 13.9 (q, C-10"); 20.4, 20.5 (q's, CH_3, acetyl); 22.5 (t, C-1'); 28.6, 28.9, 29.1, 29.3, 29.4, 29.8, 31.7 (t's, C-2'/9'); 62.0 (d, C-1'); 68.1, 69.7, 73.7, 75.6 (4×d, C-2/5); 83.4 (d, C-1); 169.1, 169.2, 170.0, 170.4 (4×s, CO, acetyl).

Alkyl 1-thio-β-D-glucopyranosides. The acetylated alkyl 1-thio-β-D-glucopyranosides were deprotected quantitatively with trimethylamine in aqueous methanol.[6] This reagent was prepared by mixing a 45% solution of NMe_3 in water with 4 volumes of methanol. After stirring at room temperature for 24 h, the solvent was evaporated and the remaining syrup was crystallized from methanol.
As a typical example the ^{1}H and ^{13}C NMR spectra of decyl 1-thio-β-D-glucopyranoside are given: ^{1}H-NMR (CD_3OD) δ 0.94 (t, 3H, H-10'); 1.34 (m, 14 H, H-3'/9'); 1.67 (m, 2H, H-2'), 2.74 (m, 2H, H-1'); 3.33 (m, 4H, H-2/5); 3.70 (dd, 1H, H-6a, $J_{5\text{-}6a}$= 5.2 Hz, $J_{6a\text{-}6b}$= 12.1 Hz); 3.90 (dd, 1H, H-6b, $J_{5\text{-}6b}$= 2.1 Hz); 4.40 (d, 1H, H-1, $J_{1\text{-}2}$= 9.5 Hz). ^{13}C-NMR: δ 14.5 (q, C-10'), 23.7 (t, C-1'), 30.0, 30.3, 30.4, 30.7, 30.8, 31.0, 33.0 (t's, C-2'/9'); 62.9 (t, C-6); 71.4, 74.3, 79.5, 81.9 (4×d, C/2-5); 87.1 (d, C-1).

4-Alkoxyphenyl β-D-glucopyranoside.[12] Penta-*O*-acetyl-β-D-glucose (3.9 g, 10 mmol) and 10 mmol of 4-alkoxyphenol were dissolved in 20 ml of anhydrous CH_2Cl_2. Then $BF_3.Et_2O$ (1.25 ml, 10 mmol) was added. The reaction mixture was stirred at room temperature for 24 h and then poured into 40 ml of a 5 % aq. $NaHCO_3$ solution. The organic layer was separated, washed with aq. $NaHCO_3$ and subsequently with water, dried over Na_2SO_4 and concentrated. The crude

Table 2.4. Elemental analyses.

	alkoxyphenyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosides					alkoxyphenyl β-D-glucopyranosides				
		calculated		found			calculated		found	
		%C	%H	%C	%H		%C	%H	%C	%H
propyl	$C_{23}H_{30}O_{11}$	57.26	6.27	57.17	6.29	$C_{15}H_{22}O_7$	57.32	7.05	56.82	6.97
butyl	$C_{24}H_{32}O_{11}$	58.06	6.50	57.97	6.52	$C_{16}H_{24}O_7$	58.53	7.37	58.51	7.35
pentyl	$C_{25}H_{34}O_{11}$	58.82	6.71	58.70	6.72	$C_{17}H_{22}O_7$	59.64	7.65	59.34	7.87
hexyl	$C_{26}H_{36}O_{11}$	59.53	6.92	59.55	6.94	$C_{18}H_{28}O_7$	60.66	7.92	60.55	7.91
heptyl	$C_{27}H_{38}O_{11}$	60.21	7.11	60.07	7.06	$C_{19}H_{30}O_7$	61.60	8.16	61.21	8.06
octyl	$C_{28}H_{40}O_{11}$	60.86	7.30	60.78	7.24	$C_{20}H_{32}O_7$	62.48	8.39	62.25	8.32
nonyl	$C_{29}H_{42}O_{11}$	61.47	7.47	61.39	7.56	$C_{21}H_{34}O_7$	63.30	8.60	63.06	8.67
decyl	$C_{30}H_{44}O_{11}$	62.05	7.64	61.96	7.48	$C_{22}H_{36}O_7$	64.05	8.80	63.50	8.76
dodecyl	$C_{32}H_{48}O_{11}$	63.14	7.95	62.90	7.93	$C_{24}H_{40}O_7$	65.43	9.15	64.91	9.14

products were crystallized from ethanol (yields: 62 - 85%). The acetylated 4-alkoxyphenyl β-GPs were deprotected quantitatively with trimethylamine in aqueous methanol.[6] After stirring at room temperature for 24 h, the solvent was evaporated and the remaining syrup was crystallized from methanol/acetonitrile (1:2). The melting points of the acetylated 4-alkoxyphenyl β-GPs are given in Table 2.4, the elemental analyses of protected and deprotected products are given in Table 2.5.

As a typical example the ^{1}H- and ^{13}C-NMR spectra of 4-hexyloxyphenyl β-D-glucopyranoside are given: δ ^{1}H 0.92 (t, 3H, H-6'); 1.35 (m, 6H, H-3'/5'); 1.37 (m, 2H, H-2'); 3.4 (m, 2H, sugar); 3.7 (m,1H, H-6); 3.9 (m, 3H, sugar); 4.77 (d, 1H, $J_{1,2}$= 7.7 Hz); 6.82, 7.04 (2×d, 4H, arom.). δ ^{13}C: 14.3 (t,C-6'); 23.6, 26.8, 30.4, 32.7 (4×d, C-2'/5'); 62.5 (t, C-1); 69.5 (t, C-6'); 71.4, 74.9, 77.9, 78.0(4×d, C-2/5); 103.4 (d, C1); 116.2, 119.2 (2×d, arom. CH); 153.1, 156.0 (2×s, arom. CO).

4-Alkoxybenzyl β-D-glucopyranoside. A mixture of 4.1 g (10 mmol) of 2,3,4,6-tetra-*O*-acetyl-α-D-glucosyl bromide, 2.4 g (10 mmol) of 4-octyloxybenzylalcohol, 2.3 g (10 mmol) of Ag_2O, 3 g of $CaSO_4$ and 50 ml of diethyl ether was stirred in the dark for 48 h. The mixture was filtered over Cellite, which was washed with ether. The combined filtrates were concentrated. The product (5.5 g of a white solid) was dissolved in a small amount of $CHCl_3$ and purified over a silica gel column (220 g), $CHCl_3$ with an increasing amount of methanol was used as eluent. The first fractions contained unreacted 4-octyloxybenzylalcohol. Other fractions contained the desired product and unidentified byproducts. Attempts to crystallize the glucoside from these mixtures failed. Therefore, the mixtures were deacetylated using a mixture of NMe_3/MeOH/H_2O. Crystallization from benzene yielded 0.6 g 4-alkoxybenzyl β-D-glucopyranoside. ^{1}H NMR: δ 0.91 (t, 3H, H-8'); 1.34 (m, 8H, H-4'/7'); 1.47 (m, 2H, H-3'); 1.75 (m, 2H, H-2'); 3.21-3.38 (m, 4H, sugar); 3.70 (dd, H6a, $J_{5,6}$= 5.3 Hz, $J_{6a,b}$= 11.9 Hz); 3.90 (dd, 1H, H6b); 3.96 (t, 2H, H-1'); 4.34 (d, 1H, H-1, $J_{1,2}$= 7.7 Hz); 4.55 (d, 1H, benzyl, $J_{a,b}$= 11.3 Hz); 4.62 (br s, 4H, OH's); 4.83 (d, 1H, benzyl); 6.87 (d, 2H, arom.); 7.32 (d, 2H, arom.). ^{13}C NMR: δ 14.3 (q, C-8'); 23.6, 27.1, 30.3, 30.4, 32.9 (t, C-2'/7'); 62.9 (t, C-1'); 69.2 (t, C-6); 71.6 (t, OCH_2 benzyl); 71.8, 75.2, 78.0, 78.2 (4d, C-2/5); 103.1 (d, C-1); 115.4, 130.9 (2d, arom. CH); 130.9 (s, arom. C); 160.4 (s, CO).

(R)-4,6-O-Alkoxybenzylidene-D-glucopyranose. A mixture of 2 g (11 mmol) of glucose, 2.5 g (11 mmol) of 4-octyloxybenzaldehyde, 0.2 ml of $MeSO_3H$ and 20 ml of *N,N*-dimethylformamide was stirred for 48 h at room temperature. The mixture was poured into 6 ml of $NaHCO_3$ and ice. After centrifugation, the precipitate was isolated by decanting the supernatant. The product was crystallized from acetone. Yield: 0.51 g (1.3 mmol, 12%).
^{1}H-NMR: δ 0.90 (t, 3H, H-8"); 1.32 (m, 10H, H-3"/7"); 1.74 (m, 2H, H-2"); 3.27 (dd, 1H, sugar); 3.66 (m, 1H, sugar); 3.95 (t, 2H, H-1"); 4.20 (m, 1H, sugar); 4.58 (br s, 3H, OH's); 5.15 (d, 1H, H-1); 5.49 (s, 1H, benzylidene); 6.87 (d, 2H, arom.); 7.39 (d, 2H, arom.).

2.8 References

1. E. Fischer, B, Helferich, *Liebigs Ann.*, **1911**, *383*, 68.
2. a) G.A. Jeffrey, *Mol. Cryst. Liq. Cryst.*, **1984**, *110*, 211. b) G.A.Jeffrey, L.M. Wingert, *Liq. Cryst.*, **1982**, *12*, 179.
3. a) H. Prade, R. Mietchen, V. Vill, *J. Prakt. Chem.*, **1955**, *337*, 427. b) R. Mietchen, D. Peters, *Wissenschaftliche Z. Wilhelm-Pieck-Univesität Rostock*, **1987**, *36*, 55.
4. a) R. Mietchen, J. Holz, H. Prade, *Colloid Polym. Sci.*, **1993**, *271*, 404. b) J.W. Goodby, M.A. Marcus, E. Chin, P.L. Finn, B. Pfannemüller, *Liq. Cryst.*, **1988**, *3*, 1569. c) W.V. Dahlhoff, K. Radkowski, K. Riehl, P. Zugenmaier, *Z. Naturforsch.*, **1995**, *50b*, 1079. d) W.V. Dahlhoff, K. Riehl, P. Zugenmaier, *Liebigs Ann.*, **1993**, 1079. e) G.A. Jeffrey, S. Bhattacharjee, *Carbohydr. Res.*, **1983**, *115*, 53.
5. a) M.A. Marcus, *Mol. Cryst. Liq. Cryst. Lett.*, **1986**, *3*, 85.b) T. HAnemann, E. Schumacher, W. Haase, F.W. Lichtenthaler, *Liq. Cryst.*, **1997**, *22*, 47. c) J.W. Goodby, J.A. Haley, M.J. Watson, G. Mackenzie, S.M. Kelly, P. Letellier, O. Douillet, P. Godé, G. Goethals, G. Ronco, P. Villa, *Liq. Cryst.*, **1997**, *22*, 367.
6. H.A. van Doren, R. van der Geest, R.M. Kellogg, H. Wynberg, *Carbohydr. Res.*, **1989**, *194*, 71.
7. S.A. Galema, J.B.F.N. Engberts, H.A. van Doren, *Carbohydr. Res.*, **1997**, *303*, 423.
8. V. Vill, T. Böcker, J. Thiem, F. Fischer, *Liq. Cryst.*, **1989**, *6*, 349.
9. M. Loos, D. Baeyens-Volant, C. David, G. Sigaud, M.F. Achard, *J. Colloid Interface Sci.*, **1990**, *138*, 128.
10. C. Tschierske, A. Lunow, H. Zaschke, *Liq. Cryst.*, **1990**, *8*, 885.
11. L.M. Wingert, G.A. Jeffrey, Jahangir, D.C. Baker, *Liq. Cryst.*, **1993**, *13*, 467.
12. E. Smits, J.B.F.N. Engberts, R.M. Kellogg, H.A. van Doren, *J. Chem. Soc., Perkin Trans. I*,**1996**, 2873.
13. H.A. van Doren, L.M. Wingert, *Mol. Cryst. Liq. Cryst.*, **1991**, *198*, 381.
14. H.A. van Doren, R. van der Geest, F. van Bolhuis, R.M. Kellogg, H. Wynberg, *Carbohydr. Res.*, **1989**, *194*, 79.
15. G.A. Jeffrey, Y. Yeon, J. Abola, *Carbohydr. Res.*, **1987**, *196*, 1.
16. P. Sakya, J.M. Seddon, R.H. Templer, *J. Phys, II France*, **1994**, *4*, 1311.
17. P. Letellier, D.F. Ewing, J.W. Goodby, J. Haley, S.M. Kelly, G. MacKenzie, *Liq. Cryst.*, **1997**, *22*, 609.
18. R.G. Laughlin, *The Aqueous Phase Behavior of Surfactants*, 1994, Ed. R.H. Ottewil and R.L. Rowell, (Academic Press, London), Chap. 8, 9 and 11.
19. M.A. Marcus, P.L. Finn, *Mol. Cryst. Liq. Cryst. Lett.*, **1985**, *2*, 159.
20. J. Charvolin, J.F. Seddon, *Micelles, Membranes, Microemulsions, and Monolayers*, 1994, Ed. W.M. Gelbart, A. Ben-Shaul and D. Roux, (Springer-Verlag), Chap. 4.
21. H.A. van Doren, Wingert, L.M., *Recl. Trav. Chim. Pays-Bas*, **1994**, *113*, 260.
22. H.A. van Doren, L.M. Wingert, *Liq. Cryst.*, **1991**, *9*, 41.
23. F. Krafft, *Ber. Deutsche Chem. Ges.*, **1899**, *32*, 1596.
24. K. Shinoda, N. Yamaguchi, A. Carlsson, *J. Phys. Chem.*, **1989**, *93*, 7316.
25. Galema, S.A., *Ph.D. Thesis*, 1992, University of Groningen, The Netherlands.
26. C. Hall, G.J.T. Tiddy, B. Pfannemüller, *Liq. Cryst.*, **1991**, *9*, 527.
27. K. Borisch, S. Diele, P. Göring, C. Tschierske, *J. Chem. Soc., Chem. Commun.*, **1996**, 237.
28. P. Sakya, J.M. Seddon, R.H. Templer, *J. Phys. II France*, **1994**, *4*, 1311.
29. H.A. van Doren, S.A. Galema, J.B.F.N. Engberts, *Langmuir*, **1995**, *11*, 687.
30. D.A. van Hall, J.A. Bouwstra, A. van Rensen, E. Jeremiasse, T. de Vringer, H.E. Junginger, *J. Colloid Interface Sci.*, **1996**, *178*, 263.

31. J.H. Fuhrhop, W. Helfrich, *Chem. Rev.*, **1993**, *93*, 1565.
32. N. Yamada, E. Koyama, M. Kaneko, H. Seki, H. Ohtsu, T. Furuse, *Chem. Lett.*, **1995**, 387.
33. J.H. Fuhrhop, S. Svenson, C. Boettcher, E. Rössler, H.M. Vieth, *J. Am. Chem. Soc.*, **1990**, *112*, 4307.
34. S. Svenson, B. Kirste, J.H. Fuhrhop, *J. Am. Chem. Soc.*, **1994**, *116*, 11969.
35. D.A. Frankel, D.F. O'Brien, *J. Am. Chem. Soc.*, **1994**, *116*, 10057.
36. J.H. Fuhrhop, C. Boettcher, *J. Am. Chem. Soc.*, **1990**, *112*, 1768.
37. R.J.H. Hafkamp, *Ph.D. Thesis*, 1996, University of Nijmegen, The Netherlands.
38. R.H. Haschemeyer, R.J. Meyers, *Principles and Techniques of Electron Microscopy*, **1972**, Ed. M.A. Hayat, (Van Nostrand Reinhold, New York) Vol. 2, Chap. 3.