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FROM Y- TO SIAMESE-TWIN SHAPED GLYCOLIPIDS
Influence on the thermotropic phase behaviour

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A set of Y-shaped and Siamese-twin shaped carbohydrate based glycolipids was investigated using polarising microscopy. The structure was changed from the normal type (1 head, two chains) to complex inverted structures (2 heads outside 1 to 3 chains in the middle part). The carbohydrate headgroup was changed from mono- to disaccharide; also the alkyl chain length was varied systematically. The compounds displayed different thermotropic mesophases (Smectic A phases, columnar phases and cubic phases) depending on the type of carbohydrate headgroup and the alkyl chain length.

Keywords: *glycolipids, glyco glycero lipids, thermotropic liquid crystals*

Introduction

Glyco glycero lipids are known to be important constituents of many cell membranes. Naturally occurring glyco glycero lipids normally have an Y-shaped structure (Fig. 1a) with a polar carbohydrate head group linked to a 1,2- or 1,3-di-O-acyl or alkyl-*sn*-glycerol [1–11]. But only a few compounds with an inverse Y-shaped structure (Fig. 1b) were reported [2, 12] and no data are available about the phase behaviour of Siamese-twin compounds.

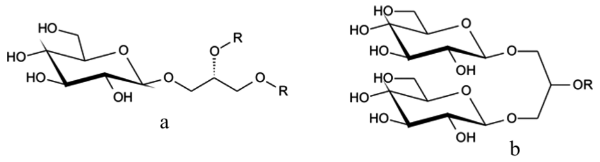

Fig. 1 a – normal Y-shaped glyco glycero lipid; b – inverted structure

All of these amphotropic molecules form both thermotropic liquid crystalline phases in their pure state upon heating and lyotropic polymorphism can be found on the addition of solvent. The driving force of the mesophase formation in case of amphiphiles is a micro phase separation leading to an aggregate structure with separated regions for the lipophilic and hydrophilic molecular parts.

The structures of the common lyotropic and thermotropic aggregates have been investigated extensively [13–16]. Depending on the molecular structure different mesophases will form. Normal Y-shaped glycolipids mainly form columnar phases, whereas inverse Y-shaped glycolipids will form smectic, columnar and cubic mesophases [15]. For Siamese-twin shaped glycolipids, where two lipid molecules are connected at the interface between the polar and non-polar molecular part, it is not clear whether they behave as Y-shaped or as rod-like molecules.

We investigated a series of glycolipids with a normal structure bearing β-*D*-gluco- and β-*D*-cellobiosyl carbohydrate headgroups and with an inverse structure with β-*D*-gluco- and β-*D*-cellobiosyl carbohydrate headgroups. The compounds bear from one (Y-shaped) up to three (Siamese-twin shaped) aliphatic chains in the middle part.

Experimental

Materials and methods

Compounds

The chemical structures of the investigated compounds are shown in Figs 1–6. Synthesis of the compounds is described elsewhere, compound **1** [17], compounds **7**–**10** [18, 19], compounds **11**–**25** [18], compounds **2**–**6** and **26**–**34** [20].

Polarising microscopy

An Olympus BH optical polarising microscope equipped with a Mettler FP 82 hot stage and a Mettler FP 80 central processor was used to identify thermal transitions and characterise anisotropic textures.

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Results and discussion

Normal structures

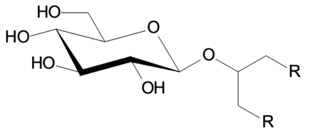
First a set of glyco glycero lipids with a normal structure was investigated (Fig. 2). The hydrophobic aglycon can be seen as a glycerol with different alkyl chains linked via a carbon atom to the glycerol moiety (compounds **1**–**6**). The compounds with a monosaccharide glucose headgroup do not show any liquid crystalline phase behaviour. Instead the melting temperature is lowered by 30°C if the alkyl chain length increases from three to five carbon atoms. This can be an indication of possible liquid crystalline phase behaviour with a further increase of the chain length. The disaccharide compounds **4**–**6** on the other hand show liquid crystalline phase behaviour at higher temperature. Compound **4** with three carbon atoms shows a Smectic A (SmA) phase. Also a glass is formed on cooling from the isotropic phase with a $T_g \sim 95$°C. Adding one carbon atom to the hydrophobic moiety (**5**) increases the clearing temperature by 19°C. Further increase of the alkyl chains (**6**) again raises the clearing temperature, but in this case no SmA phase is observed, instead a cubic phase forms on cooling. This result points on a change in the balance between the hydrophilic and hydrophobic moieties of the molecule. The balance is shifted with increasing chain length to the hydrophobic moiety. As a compromise for the slightly imbalance a cubic phase forms, with further increase of the alkyl chain length columnar phases will then form.

Inverted structures

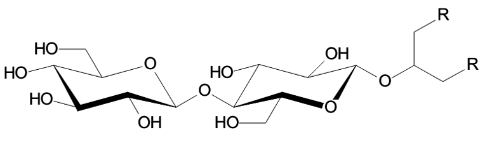
In Fig. 3 the thermotropic properties of the simple inverse glycolipids **7**–**10** are shown. All compounds bear glucose carbohydrate headgroups. The alkyl chains are linked via a carbon atom (**7**–**9**) or via an ether linkage (**10**) to the glycerol moiety. The melting temperatures of **7**–**10** are in the same temperature range. Compound **7** with a chain length of 12 carbon atoms shows only a columnar phase. Lipid **10** with a shorter alkyl chain, but an ether linkage also only forms columnar phases, despite the different linkages, the transition temperature of **10** fit in the line of compounds **7**–**9**. Compounds **8** and **9** form columnar phases with the hydrophilic/hydrophobic interface curved towards the hydrocarbon chain region. As a fact of frustration a cubic phase is formed between 126 and 173.3°C (**8**) and 125 and 175°C (**9**), since the columnar phase is already destabilised due to the increased volume of the fluid hydrocarbon chain region. A SmA phase cannot be formed, because the hydrocarbon chain length is too short to accommodate the hydrophilic headgroup, which is too broad compared to the hydrocarbon chain. The cubic mesophase of compound **8** was already described in the literature [12].

Next the hydrophobic moiety is increased by a second alkyloxy chain. As can be seen from Fig. 4 racemic and diastereomers were investigated. The monosaccharide **11** with a C6 chain shows no liquid crystalline phase behaviour, but a small melting region (4°C). With increasing chain length the compounds form lamellar SmA phases. The clearing temperatures rise steadily with increasing chain length for all compounds **11**–**14** (Fig. 7), also the data of the pure diastereomer fit in line with the racemic compounds.

If the monosaccharide headgroup is exchanged by the disaccharide cellobiose (compounds **15**–**18**) the clearing temperatures raise reaching a limit of stability between compounds **16** and **17** before the compound decomposes at the clearing point (see also Fig. 7). In this case the difference between the racemic compound **17** and the pure diastereomer **18** is obvious. The pure diastereomer shows a higher clearing temperature (22°C) than its racemic counterpart.



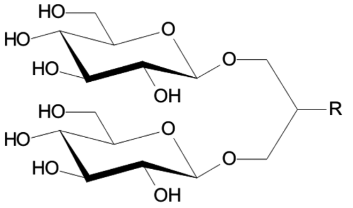
1 : R = C_3H_7
2 : R = C_4H_9
3 : R = C_5H_{11}



4 : R = C_3H_7
5 : R = C_4H_9
6 : R = C_5H_{11}

Fig. 2 Transition temperatures (in °C) and mesophases of compounds **1**–**6**

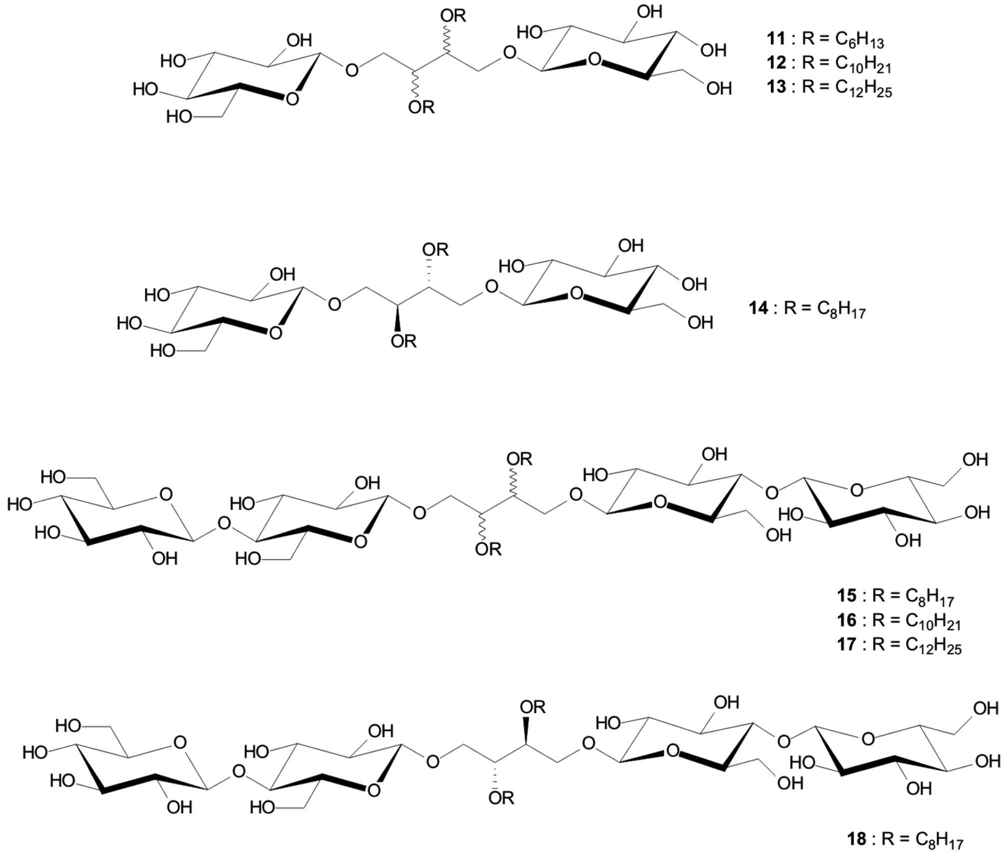
1	Cr	82.2					I
2	Cr	60					I
3	Cr	53.5					I
4	Cr	150	SmA	168			I
5	Cr	?	SmA	187			I
6	Cr	194			cub	148	I



7 : R = $C_{12}H_{25}$
8 : R = $C_{14}H_{29}$
9 : R = $C_{16}H_{33}$
10 : R = $OC_{10}H_{21}$

Fig. 3 Transition temperatures (in °C) and mesophases of compounds **7**–**10**. Data for compound 8 were taken from [12]

7	Cr	120	Col			173.3	I
8	Cr	<110	Col	126	cub	205	I
9	Cr	110	Col	126	cub	175	I
10	Cr	115	Col			149.5	I



11 : R = C_6H_{13}
12 : R = $C_{10}H_{21}$
13 : R = $C_{12}H_{25}$

14 : R = C_8H_{17}

15 : R = C_8H_{17}
16 : R = $C_{10}H_{21}$
17 : R = $C_{12}H_{25}$

18 : R = C_8H_{17}

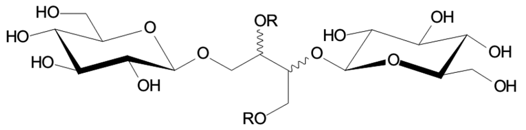
Fig. 4 Transition temperatures (in °C) and mesophases of compounds **11**–**18**

11	Cr	139–143			I
12	Cr	?	SmA	163.3	I
13	Cr	96	SmA	198.0	I
14	Cr	?	SmA	155.5	I
15	Cr	?	SmA	171	I
16	Cr	135	SmA	230	I
17	Cr	?	SmA	250	decomp.
18	Cr	?	SmA	193	I

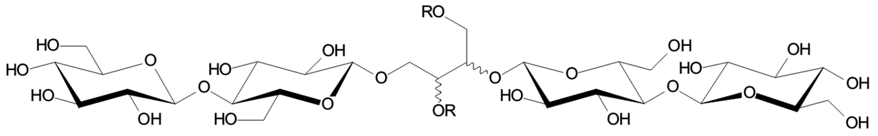
Figure 5 shows the thermotropic properties of unsymmetrical glycolipids with two alkyl chains and monosaccharide (**19**–**21**) and disaccharide carbohydrate headgroups (**22**–**25**). The monosaccharides show similar melting temperatures, although no exact transition temperature could be measured. The clearing temperatures rise steadily with increasing chain length (Fig. 7). The phase behaviour of the disaccharide compounds on the other hand is more complex. The melting temperatures of compounds **22**, **23** and **24** (C6, C8 and C10) are in the same region. For compound 25 a melting point could not be determined. **22** with the shortest alkyl chain (6 carbon atoms) shows no liquid crystalline phase behaviour, compounds **23** with two more methylene groups shows only a SmA phase on cooling from the isotropic phase. Additionally both compounds form a glass on cooling with T_g=138°C for **22** and T_g=160°C for **23**. Compounds **24** and **25** start to decompose at the clearing temperature. Nevertheless the SmA phase is stabilised with increasing chain length (Fig. 7).

The structures of the compounds shown in Fig. 6 are less Y-shaped as the compounds discussed before. Nevertheless the general principle of two polar heads at the terminus of the aglycon can still be applied. The aglycon is in this case very broad bearing three alkyl chains and monosaccharide (**26**–**29**) and disaccharide carbohydrate headgroups (**30**–**34**), respectively.

The monosaccharide compounds show no exact melting point but a SmA phase can be observed. Only compound **26** forms a glass on cooling from the isotropic phase (T_g=78°C). The clearing temperatures rise slightly with increasing alkyl chain length (Fig. 7), it can therefore be concluded that the stabil-



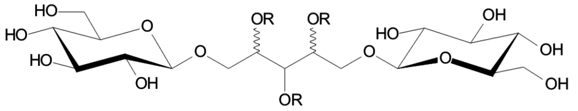
19 : R = C_8H_{17}
20 : R = $C_{10}H_{21}$
21 : R = $C_{12}H_{25}$



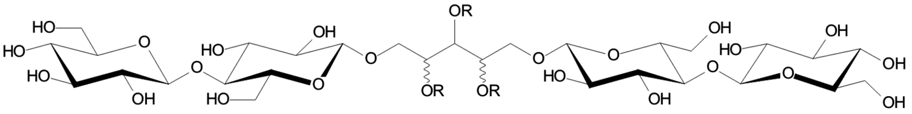
22 : R = C_6H_{13}
23 : R = C_8H_{17}
24 : R = $C_{10}H_{21}$
25 : R = $C_{12}H_{25}$

Fig. 5 Transition temperatures (in °C) and mesophases of compounds **19**–**25**

19	Cr	140	SmA	131	I
20	Cr	140	SmA	160	I
21	Cr	148	SmA	184	I
22	Cr	217			I
23	Cr	218	SmA	197	I
24	Cr	224	SmA	243	decomp.
25	Cr	?	SmA	274	decomp.



26 : R = C_6H_{13}
27 : R = C_8H_{17}
28 : R = $C_{10}H_{21}$
29 : R = $C_{12}H_{25}$



30 : R = C_4H_9
30 : R = C_6H_{13}
31 : R = C_8H_{17}
32 : R = $C_{10}H_{21}$
33 : R = $C_{12}H_{25}$

Fig. 6 Transition temperatures (in °C) and mesophases of compounds **26**–**34**

26	Cr	?	SmA	102.5	I
27	Cr	?	SmA	112	I
28	Cr	?	SmA	123	I
29	Cr	?	SmA	129	I
30	Cr	?	SmA	147	I
31	Cr	?	SmA	213	I
32	Cr	135	SmA	247	I
33	Cr	?	SmA	254	I
34	Cr	178	SmA	240	I

ity of the liquid crystalline phases is only slightly affected by the increase of the chain length. Normally an increase of the chain length leads to significant changes in the clearing temperature [21].

Enlargement of the polar headgroup by a second sugar moiety (Fig. 6, compounds **30**–**34**) does not change the phase type, all compounds display thermotropic SmA phases. Defined melting temperatures were only obtained for **32** and **34**, unfortunately no predictions can be made from this values concerning the melting temperatures of the other compounds. The clearing temperature rises from compound **30**

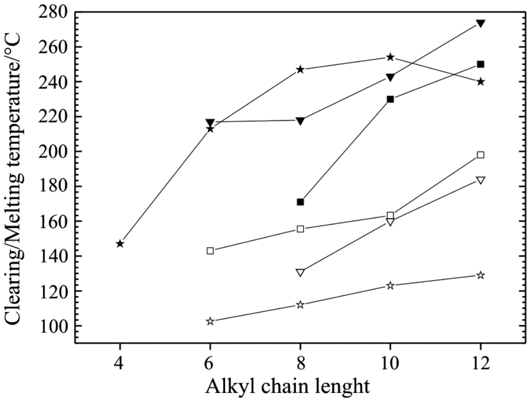


Fig. 7 Dependence of the clearing temperature/melting point on the alkyl chain length for inverted glycolipids: □ – compounds **11**–**14**; ■ – compounds **15**–**17**; ▽ – compounds **19**–**21**; ▼ – compounds **22**–**25**; ✩ – compounds **26**–**29**; ★ – compounds **30**–**34**

(C4-chain) and reaches a maximum for compound **33** (Fig. 7). Further increase of the chain length lowers the clearing temperature, also the SmA phase range is smaller than for compound **32** (112°C for **32** and ~60°C for **34**).

Conclusions

The thermotropic properties of a series of glycolipids with alkyl chains of short and medium length were investigated. The liquid crystalline phase behaviour strongly depends on the chemical structure.

Increase of the alkyl chain length raises the clearing temperature. An optimum of the alkyl chain length (Maximum of the phase stability) was only observed for the disaccharide compounds **15–18** and **30–33**. None of the monosaccharide compounds has reached this maximum yet. With further increase of the chain length (>12 carbon atoms) the maximum of the phase stability should be reached.

The molecular structure also influences the formation of mesophases. The structures with two monosaccharide headgroups and one alkyl chain display with short chains columnar phases (compound **7** and **10**), and with increasing chain length also cubic phases occur (compounds **8** and **9**) as a fact of packing frustration at higher temperature. A SmA phase was not observed, because the hydrocarbon chain length is too short to accommodate the hydrophilic headgroup, which is too broad compared to the hydrocarbon chain.

A second and third alkyl chain in the hydrophobic moiety simplifies the phase behaviour of these Siamese-twin shaped glycolipids (compounds **11–34**). The observed Smectic A phase points on a rod-like geometry of the compounds. If the monosaccharide headgroups are exchanged by the disaccharide cellobiose, the range of the SmA phase increases compared to the monosaccharide compounds. The connection of the chains at the polar/non-polar interface (Siamese-twins) compared to Y-shaped glycolipids changes the molecular shape hence this compounds show only a rod-like behaviour.

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