Synthesis and lyotropic phase behaviour of methyl 3',4'-di-*O*-hexyl- and -di-*O*-octyl-β-lactoside and partial O-acetylation of methyl 3',4'-di-*O*-octyl-β-lactoside

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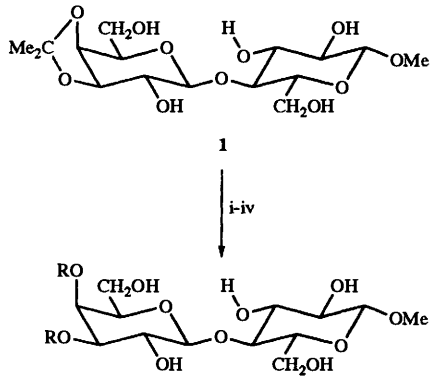
Methyl 3',4'-*O*-isopropylidene-β-lactoside was used as an intermediate in the synthesis of the 3',4'-di-*O*-hexyl- and 3',4'-di-*O*-octyl-β-lactoside. The following seven partially acetylated derivatives were prepared by partial *O*-acetylation of the dioctyllactoside: 6'- and 6-monoacetate, 2',6- and 6,6'-diacetate, 2,6,6'-triacetate, and 2,2',6,6'- and 2,3,6,6'-tetraacetate. The lyotropic phase behaviour of some of these derivatives was studied.

Introduction

As part of a study of the relationship between physical properties and structure of carbohydrate surfactants di-*O*-alkylated derivatives of disaccharides have been synthesized, and 4',6'-dialkylated methyl β-lactosides have recently been reported.[1] This paper reports the synthesis and lyotropic phase behaviour of isomeric 3',4'-dialkylated β-lactosides.

Results and discussion

The 3',4'-di-*O*-hexyl and -octyl derivatives of methyl β-lactoside were synthesized. The key intermediate was methyl 3',4'-*O*-isopropylidene-β-lactoside **1**, the thermodynamic product of the acetonation of methyl β-lactoside. Sequential *O*-benzylation, hydrolysis of the isopropylidene ketal, *O*-alkylation and debenzylation gave the 3',4'-di-*O*-alkylated lactosides **2** and **3** as crystalline solids (see Scheme 1).



2 R = hexyl
3 R = octyl

Scheme 1 *Reagents:* i, $PhCH_2Br$, NaH, DMF; ii, 90% TFA; iii, RBr, NaH, DMF; iv, H_2, Pd–C

Partial *O*-acetylation of methyl 3',4'-di-*O*-octyl-β-lactoside **3** was next studied in an attempt to form derivatives with different solubility. Reaction of the dioctyl lactoside with acetic anhydride (2.1 mol equiv.) in pyridine at −10 °C gave a crude product, which on fractionation on silica gel gave the 2,6,6'-triacetate (23%) containing a little 6,6'-diacetate, the 6,6'-diacetate (28%) containing a little 2,6,6'-triacetate, a trace of 2'6'-diacetate, and the 6'-monoacetate (3%). The acetylation was repeated with 3 mol equiv. of acetic anhydride, and five products were isolated by column chromatography: 2,2',6,6'-tetraacetate (2%), 2,6,6'-triacetate (18%), a mixture of 2,6- and 6,6'-diacetate (28%), 6'-monoacetate (15%) and 6-monoacetate (4%). These results were compared with the partial acetylations that resulted with acetyl chloride as the acetylating agent. The products from 2.1 mol equiv. of acetyl chloride were the 2,6,6'-triacetate (12%), and 6,6'-diacetate (51%), wereas 3 mol equiv. of acetyl chloride gave the 2,3,6,6'-tetraacetate (2%), 2,6,6'-triacetate (23%) and 6,6'-diacetate (44%).

The structures of the above acetate derivatives were established by mass spectrometry and proton NMR spectroscopy. The FAB mass spectrum of the 6'-monoacetate contained a fragment ion at *m/z* 429 due to a monoacetylated 3',4'-di-*O*-octyl-D-galactosyl cation. The position of the acetyl group was established by the increased deshielding of the protons at C-6' (δ 4.16 and 4.26). The mass spectrum of the 6-monoacetate contained an ion at *m/z* 387 corresponding to an acetate-free galactose unit, and no ion at *m/z* 429; hence the acetate was on the glucose unit. The deshielding of the protons at C-6 in the proton NMR spectrum (δ 4.5 and 4.3) established the position of the acetate at C-6. The 2',6'-diacetate was characterised by a fragment ion at *m/z* 471 and a double doublet in the proton NMR spectrum at δ 5.22 which was coupled to a proton (at δ 3.32) shown to be 3'-H by the coupling constants (*J* 2.7 and 10.1 Hz) and confirmed by spin decoupling. A characteristic feature of the proton NMR spectra of compounds possessing an acetate group at C-6 was a well resolved dd at δ 4.5, the other geminal proton often overlapping the 1-H and 1'-H doublets. Thus, the 6,6'-diacetate was characterised by the presence of four deshielded protons in the 4.18–4.5 region in addition to the two anomeric signals.

The triacetate contained one acetate group on the galactose unit (*m/z* 429) at C-6' and the other two at C-6 and C-2 of the glucose unit (2-H at δ 4.88). The acetate at C-2 also caused a slight shielding (0.08 ppm) of the anomeric methoxy-group protons. The 2,3,6,6'-tetraacetate was characterised by the proton NMR spectrum of an acetone solution (deshielded double doublets for 2-H and 3-H at δ 4.67 and 5.02, respectively). The 2,2',6,6'-tetraacetate contained two acetate groups on the galactose unit (*m/z* 471) and NMR spectra showed that the hydroxy group at position C-2 was acetylated (2-H at δ 4.87) in addition to that at C-6 of the glucose unit. Key diagnostic features of the NMR spectra were identified as follows:

dd at δ 5.2 for 2'-H when C-2' was acetylated;
dd at δ 4.9 for 2-H when C-2 was acetylated;
dd at δ 4.5 for 6-H when C-6 was acetylated;
dd at δ 3.2 for 3'-H when C-2' was not acetylated;
OMe at δ 3.49 when C-2 was acetylated;
OMe at δ 3.57 when C-2 was not acetylated.

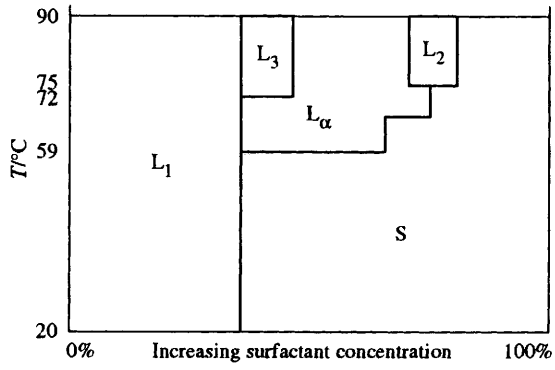


Fig. 1 Schematic diagram showing the lyotropic phase behaviour of methyl 3',4'-di-*O*-hexyl-β-D-lactoside

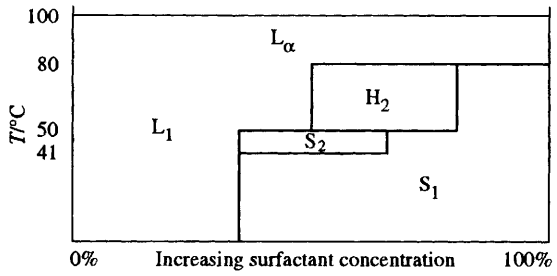


Fig. 2 Schematic diagram showing the lyotropic phase behaviour of methyl 3',4'-di-*O*-octyl-β-D-lactoside

The order of reactivity of the hydroxy groups in methyl β-lactoside towards *O*-acylation has been reported[2] to be 6' > 3' > 6 > 2 > 2',4' > 3, and the higher reactivity of the 3'-OH was attributed to an activating effect of the neighbouring *cis*-related 4'-OH group. When the 3'-OH group is alkylated the major products of dimolar and trimolar esterification would be expected to be the 6,6'-di- and 2,6,6'-tri-esters and these were indeed the major products.

The water solubilities of methyl 3',4'-di-*O*-hexyl-β-lactoside and the dioctyl derivative were 1.5×10^{-3} mol dm^{-3} (at 20 °C) and less than 10^{-5} mol dm^{-3} (at 60 °C), respectively. Of the acetates tested three, the 6-monoacetate, 6'-monoacetate and 2,6,6'-triacetate, had solubilities less than 5×10^{-5} mol dm^{-3} (at 20 °C), and the 6,6'-diacetate had a solubility of 5×10^{-5} mol dm^{-3} (at 20 °C). There was insufficient of the 2',6'-diacetate to test.

The Krafft points of the methyl dialkyl lactosides did not show the expected increase with increasing alkyl chain length, values of 59 and 50 °C being found for the dihexyl and dioctyl lactoside, respectively. These values are significantly lower than those of the corresponding 4',6'-dialkylated lactosides. The acetates of the dioctyl lactoside had Kp 57 °C for the 6'-monoacetate and 71 °C for the 6,6'-diacetate, both values being higher than the Krafft point of the non-acetylated methyl 3',4'-di-*O*-octyl-β-lactoside.

Lyotropic phase behaviour was studied qualitatively by the 'penetration scan' method. The phase behaviour of methyl 3',4'-di-*O*-hexyl-β-lactoside is shown schematically in Fig. 1. The first myelins were seen at 59 °C, and at 72 °C a disordered phase of low viscosity (L3, the sponge phase) appeared at the micelle solution interface. A reversed micelle phase (L2) was also detected, at 75 °C. The dioctyl lactoside gave a different phase diagram (Fig. 2) which included a reversed hexagonal phase (H_2) and a second solid phase (S_2).

Experimental

General

See ref. 1. NMR data refer to 250 MHz for ^{1}H and 62.9 MHz for ^{13}C and $CDCl_3$ solutions unless otherwise stated. Spin decoupling or 2-D homonuclear chemical-shift correlation spectroscopy (COSY) measurements were used when necessary to confirm assignments.

Methyl 3',4'-*O*-isopropylidene-β-lactoside 1

This was prepared in 91% yield by reaction of methyl lactoside with 2,2-dimethoxypropane;[3] mp 210–214 °C (from EtOH) (lit.,[3] 219–221 °C); δ_H([$^2H_5$]pyridine) 7.79 (1 H, d, *J* 4.4, OH), 7.49 (1 H, br s, OH), 6.87 (1 H, br s, OH), 6.64 (1 H, br s, OH), 6.14 (1 H, br s, OH), 5.06 (1 H, d, *J* 8.2, 1- or 1'-H), 4.67 (1 H, d, *J* 7.7, 1'- or 1-H), 4.59–4.24 (9 H, m), 4.18 (1 H, m), 4.02 (1 H, t, *J* 8.5), 3.86 (1 H, m), 3.56 (3 H, s, OMe) and 1.52 and 1.38 (6 H, 2 s, 2 × Me).

Methyl 2,2',3,6,6'-penta-*O*-benzyl-3',4'-*O*-isopropylidene-β-lactoside

A solution of the isopropylidene lactoside (8.13 g) in anhydrous dimethylformamide (DMF) (100 cm^3) was added to oil-free NaH (12.3 g) under nitrogen, and the mixture was stirred for 1 h during which further DMF (500 cm^3) was added to maintain sufficient fluidity. Benzyl bromide (48.8 cm^3) was then added over a period of 30 min and more DMF (200 cm^3) was added. The mixture was stirred overnight and excess of NaH was destroyed by addition of methanol (100 cm^3). The mixture was poured into ice–water (1.6 dm^3) and the product was extracted with diethyl ether (3 × 1.5 dm^3). Washing with water (2 × 1 dm^3), drying ($MgSO_4$), and evaporation gave the crude product. Chromatography on silica gel with toluene–ethyl acetate (20:1) as eluent gave the *pentabenzyl derivative* as a syrup (8.5 g, 49%); δ_H 7.4–7.2 (25 H, m, ArH), 4.95–4.28 (12 H, m, 5 × CH_2Ph, 1-H and 1'-H), 4.09–3.3 (15 H, m) and 1.40 and 1.35 (6 H, 2 s, 2 × Me) [Found: *m/z* (CI) 864.426. $C_{51}H_{62}NO_{11}$ (M + NH_4) requires *m/z*, 864.432].

Methyl 2,2',3,6,6'-penta-*O*-benzyl-β-lactoside

An ice-cooled solution of the isopropylidene lactoside (7.265 g) in 90% aq. trifluoroacetic acid (TFA) (35 cm^3) was kept at 0 °C for 1 h and was then poured into ice–water (150 cm^3). Extraction with diethyl ether (3 × 100 cm^3) followed by washing of the combined organic layers with saturated aq. $NaHCO_3$ (6 × 50 cm^3), drying ($MgSO_4$), and evaporation gave the *diol* as a solid (6.2 g), mp 108–109 °C (from EtOH) (Found: C, 71.4; H, 6.7. $C_{48}H_{54}O_{11}$ requires C, 71.4; H, 6.7%); δ_H 7.4–7.22 (25 H, m, ArH), 4.98 and 4.87 (2 H, 2 d, *J* 11, AB system in 2 × CH_2Ph), 4.83–4.38 (10 H, m), 4.04–3.3 (15 H, m, includes s at δ 3.56 for OMe) and 2.38–2.64 (2 H, br s, 2 × OH); δ_C 139.14, 138.68, 138.26 and 138.02 (quaternary ArC), 128.54–127.33 (11 peaks, ArCH), 104.72 and 102.63 (2 anomeric CH), 82.77, 81.82, 80.06, 76.59, 73.54, 72.88 and 68.79, (8 CH), 75.28, 74.92, 73.49, 73.21, 68.70 and 68.29 (7 × OCH_2) and 57.14 (OMe).

Methyl 2,2',3,6,6'-penta-*O*-benzyl-3',4'-di-*O*-hexyl-β-lactoside

A solution of the diol (4.5 g, 5.58 mmol) in dry DMF (80 cm^3) was stirred under nitrogen with oil-free NaH (1.34 g, 55.8 mmol). After 30 min, 1-bromohexane (3.13 cm^3, 22.3 mmol) was added and the suspension was stirred overnight. Methanol (20 cm^3) was added slowly to the stirred mixture, which was then poured into ice–water (150 cm^3) and extracted with diethyl ether (3 × 100 cm^3). The combined extracts were washed with water (2 × 200 cm^3), dried ($MgSO_4$), and evaporated. Chromatography on silica gel with toluene–ethyl acetate (9:1) gave the *protected dihexyl lactoside* as a soft solid (4.4 g, 81%), mp 55–57 °C (from aq. ethanol [Found: *m/z* (FAB) 997.5445. $C_{60}H_{78}NaO_{11}$ (M + Na) requires *m/z* 997.5442]; δ_H 7.43–7.21

(25 H, m, ArH), 5.05 (1 H, d, J 10.5, AB system in CH_2Ph), 4.88 (1 H, m, d, J 11.1, AB system in CH_2Ph), 4.83–4.27 (10 H, m, OCH_2Ph, 1-H and 1'-H), 3.94–3.33 (19 H, m), 1.57–1.55 (4 H, m, 2 × OCH_2CH_2Bu), 1.39–1.26 (12 H, m, 2 × $[CH_2]_3$) and 0.87 (6 H, t, J 6.4, 2 × Me); δ_C 138.99, 138.85, 138.59, 138.23 and 137.97 (quaternary ArC), 128.15, 128.06, 127.97, 127.77, 127.68, 127.53, 127.30 and 126.97 (9 × ArCH), 104.45 and 102.5 (2 × anomeric CH), 82.93, 82.73, 81.62, 79.63, 76.44, 75.09, 74.95 and 72.84 (8 × CH), 75.17, 74.91, 74.70, 73.25, 73.00, 72.79, 70.47, 68.15 and 67.88 (9 × OCH_2), 56.77 (OMe), 31.52, 30.15, 30.05, 25.75, 25.66, 22.50 and 22.44 (8 × alkyl CH_2) and 13.97 and 13.92 (2 × Me).

Methyl 2,2',3,6,6'-penta-*O*-benzyl-3',4'-di-*O*-octyl-β-lactoside

In a similar reaction the lactoside diol (5.2 g) was treated with 1-bromooctane (4.45 cm^3) to give, after chromatography, the *protected dioctyl lactoside* as a soft solid (6.77 g, 94%); δ_H 7.42–7.19 (25 H, m, ArH), 5.02 (1 H, d, J 10.5, AB system in CH_2Ph), 4.87 (1 H, d, J 11, AB system in CH_2Ph), 4.82–4.27 (10 H, m, OCH_2Ph, 1-H and 1'-H), 3.91–3.14 (19 H, m), 1.57–1.55 (4 H, m, 2 × OCH_2CH_2), 1.25 (20 H, m, 2 × $[CH_2]_5$) and 0.87 (6 H, m, 2 × Me) [Found: m/z (FAB) 1053.6032. $C_{64}H_{86}NaO_{11}$ $(M + Na)^+$ requires m/z 1053.6068].

Methyl 3',4'-di-*O*-alkyl-β-lactoside: general procedure

The pentabenzyl derivative was dissolved in a mixture of ethanol and cyclohexene (30-times excess, ethanol:cyclohexene ratio 2.5:1) and 20% $Pd(OH)_2$ on carbon (0.2 g per mmol) was added. The suspension was stirred under reflux for 6–20 h until debenzylation (monitored by TLC) was complete. Filtration and evaporation gave the deprotected lactosides.

Methyl 3',4'-di-O-*hexyl*-β-*lactoside* **2** (96%) had mp 146–147 °C (from EtOAc, then water); $\delta_H(CD_3OD)$ 4.34 (1 H, d, J 7.8, 1- or 1'-H), 4.20 (1 H, d, J 7.9, 1'- or 1-H), 2.89–3.21 (19 H, m), 1.59 (4 H, m, 2 × CH_2CH_2Bu), 1.33–1.31 (12 H, m, 2 × $[CH_2]_3$) and 0.91 (6 H, t, J 6.7, 2 × Me); δ_C 105.29 and 105.26 (2 × anomeric CH), 83.91, 81.01, 77.14, 76.43, 76.40, 75.44, 74.71 and 71.16 (8 × CH), 74.58, 71.95, 62.23 and 61.99 (4 × OCH_2), 57.51 (OMe), 33.04, 32.98, 31.38, 31.27, 27.11, 26.98 and 23.85 (8 × alkyl CH_2) and 14.61 (2 × Me) (Found: C, 57.2; H, 9.3. $C_{25}H_{48}O_{11}$ requires C, 57.2; H, 9.2%).

Methyl 3',4'-*di*-O-*octyl*-β-*lactoside* **3** (97%) had mp 147.3–148.6 °C (from EtOAc); $\delta_H(CD_3OD)$ 4.34 and 4.20 (2 H, 2 d, J 7.8, 1'- and 1-H), 3.89–3.21 (19 H, m), 1.56 (4 H, m, 2 × $CH_2CH_2CH_2$), 1.40–1.30 (20 H, m, 2 × $[CH_2]_5$) and 0.89 (6 H, t, J 6.6, 2 × Me); δ_C 105.29 (C-1 + -1'), 83.94, 81.09, 77.18, 76.41, 75.45, 74.69 and 72.16 (8 × CH), 74.64, 72.01, 62.26 and 62.05 (4 × OCH_2), 57.56 (OMe), 33.17, 31.44, 31.35, 30.80, 30.74, 30.63, 27.48, 27.33 and 23.89 (12 × CH_2) and 14.73 (2 × Me) (Found: C, 59.9; H, 9.8. $C_{29}H_{56}O_{11}$ requires C, 60.0; H, 9.7%).

Partial *O*-acetylation: general procedure

A solution of either acetic anhydride in pyridine or acetyl chloride in dichloromethane was slowly added to a stirred solution of methyl 3',4'-di-*O*-octyl-β-lactoside **3** in dry pyridine (7.5% concentration) kept at −15 °C, and the reaction mixture was allowed to warm to room temp. After 4–12 h the mixture was poured into ice–water (5 volumes), and extracted with dichloromethane; the extracts were washed successively with dil. hydrochloric acid, saturated aq. $NaHCO_3$ and water, dried over $MgSO_4$ and evaporated to dryness.

First experiment. The dioctyl lactoside (0.15 g, 0.26 mmol) was treated with acetic anhydride (0.051 cm^3, 0.54 mmol) in pyridine (1 cm^3) to give a syrup (0.205 g) which, when chromatographed on silica gel [eluent: dichloromethane–acetone (10:1)] gave methyl 2,6,6'-tri-*O*-acetyl-3',4'-di-*O*-octyl-β-lactoside (42 mg, 23%); dichloromethane–acetone (10:3) next eluted methyl 6,6'-di-*O*-acetyl-3',4'-di-*O*-octyl-β-lactoside (data below; see **Third experiment**) contaminated with a little 2,6,6'-triacetate (48 mg) followed by methyl 2',6'-di-*O*-acetyl-3',4'-di-*O*-octyl-β-lactoside (1 mg); δ_H(400 MHz) 5.22 (1 H, dd, $J_{1',2'}$ 8.0, $J_{2',3'}$ 10.1, 2'-H), 4.47 (1 H, d, J 1.2, OH), 4.44 (1 H, d, $J_{1',2'}$ 8.0, 1'-H), 4.33 (1 H, dd, $J_{5',6'a}$ 3.8, $J_{6'a,6'b}$ −11.6, 6'-H),[a] 4.28 (1 H, d, $J_{1,2}$ 7.9, 1-H), 4.23 (1 H, dd, $J_{5',6'b}$ 8.5, 6'-H[b]), 3.91–3.33 (16 H, m, includes OMe at δ 3.56), 3.32 (1 H, dd, $J_{2',3'}$ 10.1, $J_{3',4'}$ 2.7, 3'-H), 2.51 (1 H, br s, OH), 2.11 and 2.10 (6 H, 2 s, 2 × Ac), 1.56 (4 H, m, 2 × OCH_2CH_2), 1.25 (20 H, m, 2 × $[CH_2]_5$) and 0.87 (6 H, t, J 6.9, 2 × Me); m/z (FAB 687 (M + Na); next eluted was *methyl* 6'-O-*acetyl*-3',4'-*di*-O-*octyl*-β-*lactoside* (5 mg, 3%), mp 113–115 °C (from aq. EtOH); δ_H(400 MHz) 4.31 (1 H, d, J 8.3, 1'-H), 4.29 (1 H, br s, OH), 4.26 (1 H, dd, $J_{5',6'a}$ 3.9, $J_{6'a,6'b}$ −11.7, 6'-H[a]), 4.21 (1 H, d, J 7.8, 1-H), 4.16 (1 H, dd, $J_{5',6'b}$ 8.3, $J_{6'a,6'b}$ −11.2, 6'-H[b]), 3.88–3.31 (16 H, m, includes s at δ 3.49 for OMe), 3.14 (1 H, dd, $J_{2',3'}$ 9.8, $J_{3',4'}$ 2.9, 3'-H), 2.81 (2 H, br s, 2 × OH), 2.53 (1 H, br s, OH), 2.04 (3 H, s, Ac), 1.52 (4 H, m, 2 × OCH_2CH_2), 1.20 (20 H, m, 2 × $[CH_2]_5$) and 0.81 (6 H, t, J 6.8, 2 × Me) [Found: m/z (FAB) 645.3794. $C_{31}H_{58}NaO_{12}$ (M + Na) requires m/z, 645.3826].

Second experiment. The dioctyl lactoside (0.5 g, 0.86 mmol) was treated with acetic anhydride (0.24 cm^3, 2.58 mmol) in pyridine (1 cm^3) to give a syrup (0.56 g), which when chromatographed on silica gel [eluent: dichloromethane–acetone (10:1)] gave *methyl* 2,2',6,6'-*tetra*-O-*acetyl*-3',4'-*di*-O-*octyl*-β-*lactoside* (15 mg, 2%); δ_H 5.22 (1 H, dd, $J_{1',2'}$ 7.9, $J_{2',3'}$ 9.9, 2'-H), 4.87 (1 H, dd, $J_{1,2}$ 8.1, $J_{2,3}$ 9.6, 2-H), 4.39 (1 H, d, $J_{1',2'}$ 8.1, 1'-H), 4.34–4.18 (4 H, m, 1-H, 6'-H_2 and 6-H)[a] 4.05 (1 H, dd, $J_{6a,6b}$ −11.8, $J_{5,6b}$ 5.0, 6-H)[b], 3.89–3.28 (14 H, m, includes s at δ 3.48 for OMe), 2.10 (9 H, s, 3 × Ac), 2.07 (3 H, s, Ac), 1.53 (4 H, m, 2 × OCH_2CH_2), 1.26 (20 H, m, 2 × $[CH_2]_5$) and 0.88 (6 H, t, J 6.5, 2 × Me) [Found: m/z (FAB) 771.4146. $C_{37}H_{64}NaO_{15}$ (M + Na) requires m/z, 771.4143] and *methyl* 2,6,6'-*tri*-O-*acetyl*-3',4'-*di*-O-*octyl*-β-*lactoside* (0.11 g, 18%), mp 55–57 °C; δ_H 4.88 (1 H, dd, $J_{1,2}$ 8.1, $J_{2,3}$ 9.6, 2-H), 4.53 (1 H, dd, $J_{5,6a}$ 1.8, $J_{6a,6b}$ −12, 6-H[a]), 4.36–4.24 (5 H, m), 4.29–3.39 (15 H, m), 3.18 (1 H, dd, $J_{3',4'}$ 2.7, $J_{2',3'}$ 9.7, 3'-H), 2.11, 2.09 and 2.07 (9 H, 3 s, 3 × Ac), 1.62–1.40 (4 H, m, 2 × OCH_2CH_2), 1.27 (20 H, m, 2 × $[CH_2]_5$) and 0.88 (6 H, t, J 6.6, 2 × Me) [Found: m/z (FAB) 729.4074. $C_{35}H_{62}NaO_{14}$ (M + Na) requires m/z 729.4037]; dichloromethane–acetone (5:1) next eluted a mixture of diacetates (162 mg, 28%) consisting of mainly the 6,6'-diacetate [δ_H 3.49 (s, OMe), 3.19 (dd, 3'-H) and 2.11 and 2.09 (2 s, Ac) and some 2,6-diacetate [δ_H 4.86 (dd, 2-H) and 3.58 (s, OMe); dichloromethane–acetone (2:1) then eluted methyl 6'-*O*-acetyl-3',4'-di-*O*-octyl-β-lactoside (0.08 g, 15%) and *methyl* 6-O-*acetyl*-3',4'-*di*-O-*octyl*-β-*lactoside* (0.02 g, 4%), mp 133–137 °C; δ_H 4.5 (1 H, d, J −10.7, 6-H[a]), 4.32–4.23 (3 H, m, 1-H, 1'-H and 6-H[b]), 3.93–3.38 (20 H, m, includes s at δ 3.56 for OMe), 3.20 (1 H, dd, $J_{2',3'}$ 9.9, $J_{3',4'}$ 2.3, 3'-H), 2.09 (3 H, s, Ac), 1.49 (4 H, m, 2 × OCH_2CH_2), 1.27 (20 H, m, 2 × $[CH_2]_5$) and 0.88 (6 H, t, J 6.5, 2 × Me) [Found: m/z (FAB) 645.3799. $C_{31}H_{58}NaO_{12}$ (M + Na) requires m/z 645.3826].

Third experiment. The dioctyl lactoside (0.75 g, 1.29 mmol) was treated with acetyl chloride (0.193 cm^3, 2.7 mmol) to give a syrup (0.8 g), which when chromatographed on silica gel (as above) gave the 2,6,6'-triacetate (0.11 g, 12%) and the 6,6'-*diacetate* (0.44 g, 50%), mp 93–94 °C (from ethyl acetate); δ_H (after D_2O exchange) 4.53 (1 H, dd, $J_{6a,6b}$ −11.8, $J_{5,6a}$ 1.7, 6-H[a]), 4.37–4.18 (5 H, m, 1- and 1'-H, 6-H[b] and 6'-H_2), 3.83–3.37 (14 H, m, includes s at δ 3.57 for OMe), 3.18 (1 H, dd, $J_{2',3'}$ 9.9, $J_{3',4'}$ 2.6, 3'-H), 2.11 and 2.09 (6 H, 2 s, 2 × Ac), 1.56 (4 H, m, 2 × OCH_2CH_2), 1.23 (20 H, m, 2 × $[CH_2]_5$) and 0.88 (6 H, t, J 6.5, 2 × Me); m/z (FAB) 687 (M + Na) (Found: C, 59.6; H, 9.2, $C_{33}H_{60}O_{13}$ requires C, 59.6; H, 9.1%).

Fourth experiment. Reaction of the dioctyl lactoside (0.72 g, 1.24 mmol) with acetyl chloride (0.26 cm^3, 3.7 mmol) gave, after chromatography (as above), *methyl* 2,3,6,6′-*tetra*-O-*acetyl*-3′,4′-*di*-O-*octyl*-β-*lactoside* (23 mg, 2%); δ_H(400 MHz; [$^2H_6$]acetone) 5.02 (1 H, dd, $J_{2,3}$ 9.7, $J_{3,4}$ 8.7, 3-H), 4.67 (1 H, dd, $J_{1,2}$ 8.0, $J_{2,3}$ 9.8, 2-H), 4.44 (1 H, dd, $J_{6a,6b}$ −11.9, $J_{5,6a}$ 1.9, 6-H^a), 4.43 (1 H, d, 1-H), 4.26 (1 H, dd, $J_{5,6b}$ 4.9, $J_{6a,6b}$ −11.9, 6-H^b), 4.17 (1 H, d, $J_{1',2'}$ 7.7, 1′-H), 4.10 (1 H, dd, $J_{6'a,6'}$ −10.8, $J_{5,6'a}$ 6.6, 6′-H^a), 4.00 (1 H, dd, $J_{5',6'b}$ 6.3, $J_{6'a,6'b}$ −10.9, 6′-H^b), 3.97–3.21 (13 H, m, includes s at δ 3.30 for OMe), 3.17 (1 H, dd, $J_{2',3'}$ 9.8, $J_{3',4'}$ 2.9, 3′-H), ~2.0 (Ac signals overlapping solvent signal), 1.41 (4 H, m, 2 × OCH_2CH_2), 1.13 (20 H, m, 2 × $[CH_2]_5$) and 0.75 (6 H, m, 2 × Me); *m/z* (FAB) 771 (M + Na) (Found: *m/z* 771.4148. $C_{37}H_{64}NaO_{15}$ requires *m/z*, 771.41437). The 2,6,6′-triacetate (0.20 g, 23%) was next eluted with acetone–dichloromethane (1:5), followed by the 6,6′-diacetate (0.36 g, 44%).

Penetration scan method

The solid was heated in contact with water on a glass slide, and the effect of increasing temperature was observed using an Olympic BH-2 polarising microscope. Lyotropic phases were identified from their texture when observed between crossed polars and from their relative viscosity.[4] The Krafft point was the temperature at which the first myelins, characteristic of the lamellar phase, appeared.

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