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x-*O*-*n*-alkyl-itols. Substrate structure and alkyl chain position influences on their liquid crystalline properties

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Abstract

A range of 3-*O*-*n*-alkyl and 6-*O*-*n*-alkyl-D-galactitols, 2-*O*-*n*-alkyl-D-mannitols, 1-*O*-*n*-alkyl and 2-*O*-*n*-alkyl-D,L-erythritols and 1-*O*-*n*-alkyl and 2-*O*-*n*-alkyl-D,L-threitols was synthesized. Their thermotropic phase transition temperatures were compared with those of *x*-*O*-*n*-alkyl-D-glucitols ($x = 1$, 3, 4 and 6), *x*-*O*-*n*-alkyl-D-mannitols ($x = 1$ and 3) and *x*-*O*-*n*-alkyl-xylitols ($x = 1$, 2 and 3) in order to observe the influences of both the polyol structure and the alkyl chain *x*-position on the phase transition temperature. Lyotropic phase transition temperatures of all these compounds were also reported.

Keywords: Erythritol; Galactitol; Mannitol; Threitol derivatives; Thermotropic liquid crystals; Lyotropic liquid crystals

1. Introduction

In previous works, we reported that thermotropic phase transition temperatures of amphiphilic *x*-*O*-*n*-alkyl-xylitols depend on both the alkyl chain length (Goodby et al., 1997a) and the *x*-position on the saccharidic moiety (Harmouch et al., 1997, Goodby et al., 1997b). However, the latter effect varies with the itol structure, as is indicated by a comparison of values of *x*-*O*-*n*-alkyl-D-glucitols ($x = 1$, 3, 4 and 6) (Dahlhoff, 1990, 1991, Raaijmakers et al., 1995) and *x*-*O*-*n*-alkyl-D-mannitols ($x = 1$ and 3) (Dahlhoff, 1989, Raaijmakers et al., 1995). In order to develop this study, we synthesized a range of 3-*O*-*n*-alkyl and 6-*O*-*n*-alkyl-D-galactitols, 2-*O*-*n*-alkyl-D-mannitols, 1-*O*-*n*-alkyl and 2-*O*-*n*-alkyl-D,L-erythritols, and 1-*O*-*n*-alkyl and 2-*O*-*n*-alkyl-D,L-threitols. Thermotropic and lyotropic phase transition temperatures of all these compounds were measured.

2. General synthesis

3-*O*-*n*-alkyl and 6-*O*-*n*-alkyl-D-galactitols were obtained according to Scheme 1. The alkylation of diacetonide **1**, subsequent deprotection and sodium borohydride reduction gave the 3-*O*-*n*-alkyl-D-galactitols **4b** and **4d**. Similar reduction of 6-*O*-*n*-alkyl-α-D-galactopyranoses (Bault et al., 1998) led to the 6-*O*-*n*-alkyl-D-galactitols **5a–d**.

2-*O*-*n*-alkyl-D-mannitol synthesis is described in Scheme 2. Selective tritylation of monoacetal **6** (Spychala, 1997) followed by alkylation, simultaneous debenzylation–detritylation with H_2–Pd/C and sodium borohydride reduction gave the 2-*O*-*n*-alkyl-4,5-*O*-isopropylidene-D-mannitols **10b** and **10d**. Subsequent deacetalation led to the 2-*O*-*n*-alkyl-D-mannitols **11b** and **11d**.

1-*O*-*n*-alkyl and 2-*O*-*n*-alkyl-D,L-erythritols were prepared from the erythritol monoacetal **12** (Scheme 3). Selective tosylation allowed us to obtain the anhydro derivative **14** from which alkylation at the primary carbon with the corresponding alcoholate RO^- and subsequent deacetalation led to the 1-*O*-*n*-alkyl-D,L-erythritols **16a–d**. The 2-*O*-*n*-alkyl-D,L-erythritols **19b–d** were obtained by selective tritylation of **12** followed by alkylation at the C-2 position and deacetalation.

1-*O*-*n*-alkyl and 2-*O*-*n*-alkyl-D,L-threitol synthesis is described in Scheme 4. Selective deprotection of the 1-*O*-*n*-alkyl-2,3:4,5-di-*O*-isopropylidene-D,L-xylitols (Goodby et al., 1997a) followed by oxidative degradation with sodium periodate led to the D,L-threose derivatives **21b–d**; then, sodium borohydride reduction and deacetalation gave the 1-*O*-*n*-alkyl-D,L-threitols **23b–d**. 2-*O*-*n*-alkyl-D,L-threitols **27b, d** were obtained by selective tritylation of mono-

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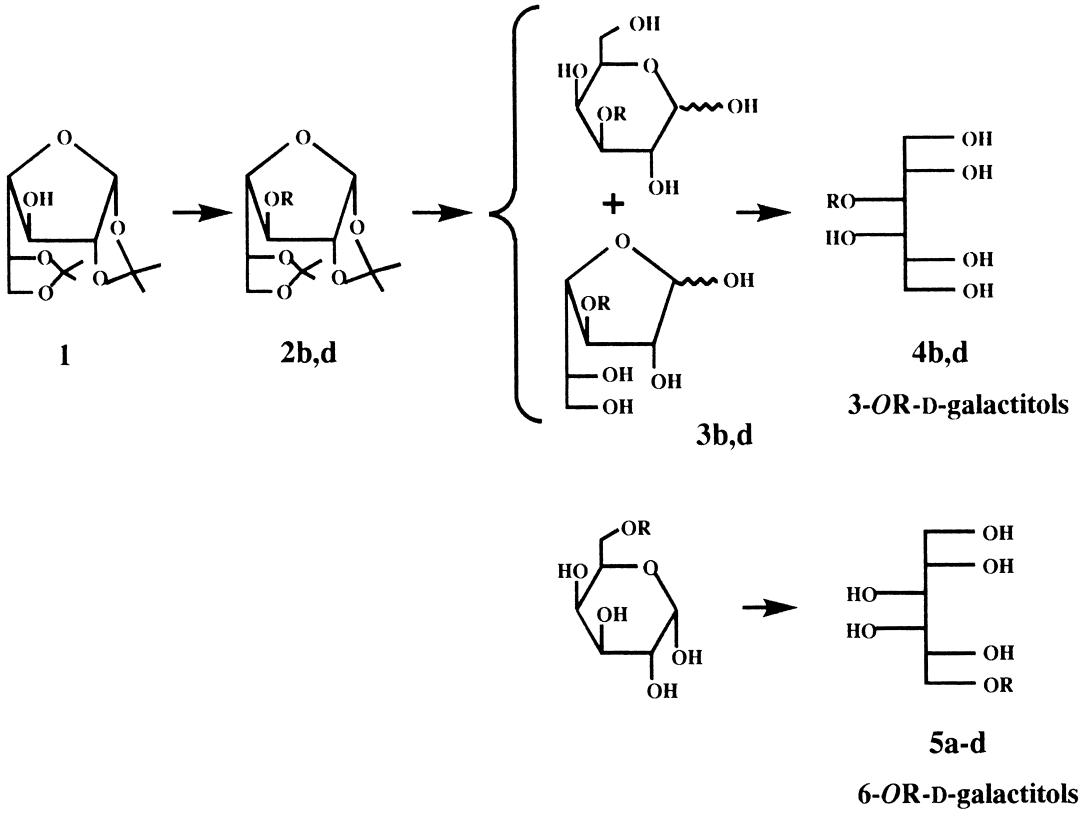


$R = n\text{-}C_nH_{2n+1}$ with n = 6 (**a**) ; n = 8 (**b**) ; n = 10 (**c**) ; n = 12 (**d**)

Scheme 1.

acetal **24** followed by alkylation at the C-2 position and deacetalation.

3. Results and discussion

Thermotropic and lyotropic phase transition temperatures are reported in Tables 1–3. These results show that all the x-*O*-*n*-alkyl itol series studied give thermotropic liquid crystals (smectic A*) except the 1-*O*-*n*-alkyl-erythritols (Table 3). Nevertheless, significant differences appear when the following structural factors are varied: (i) the alkyl chain length (carbon atom number *n*); (ii) the *x* position of the alkyl chain; (iii) the nature of the polyol substrate and the number of OH groups.

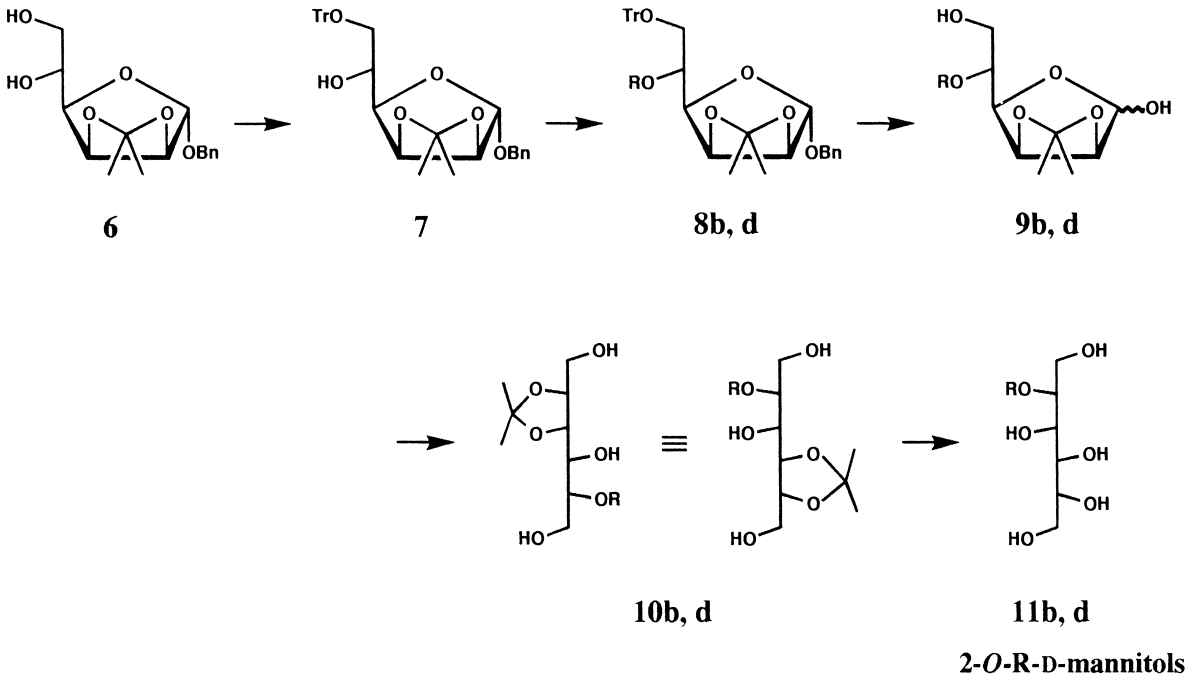
Generally the thermotropic phase appears when the alkyl chain has 6 or 8 carbon atoms and the phase transition temperatures increase with increasing carbon atom number *n*. However, for 3-*O*-*n*-alkyl-galactitols (Table 1), 2-*O*-*n*-alkyl-mannitols (Table 2) and 2-*O*-*n*-alkyl-erythritol (Table 3) the thermotropic phase is observed only with $n = 12$ (*n*-dodecyl derivatives) and the 1-*O*-*n*-alkyl-erythritol series never gave thermotropic liquid crystals.

The *x* position of the alkyl chain strongly affects the phase transition temperatures. With the *x*-*O*-*n*-alkyl-hexitols (Tables 1 and 2) these temperatures are ranged in the order:

6-*O*-*n*-alkyl- $\gg$ 3-*O*-*n*-alkyl-galactitols
1-*O*-*n*-alkyl- $\approx$ 6-*O*-*n*-alkyl- $>$ 3-*O*-*n*-alkyl- $>$ 4-*O*-*n*-alkyl-glucitols
1-*O*-*n*-alkyl- $>$ 3-*O*-*n*-alkyl- $\gg$ 2-*O*-*n*-alkyl-mannitols

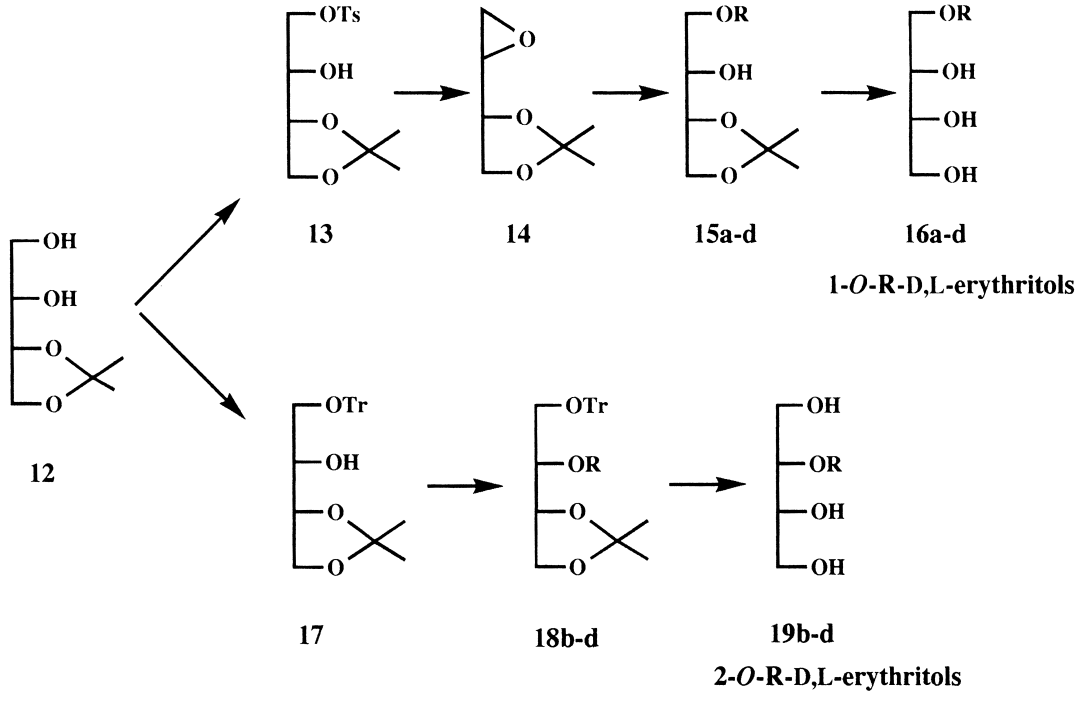
These hexitol data indicate that compounds with the alkyl chain at the terminal position (C-1 or C-6) have the highest phase transition temperatures. In contrast, for xylitol, erythritol and threitol series, compounds with the alkyl chain at this position have the lowest phase transition temperatures (Table 3).

Comparing 2-*O*-*n*-alkyl-mannitols (which have 5 hydroxyl groups) to the corresponding 2-*O*-*n*-alkyl-mannitol monoacetal (3 hydroxyl groups) (Table 2), and comparing xylitol derivatives (4 hydroxyl groups) to the corresponding erythritol and threitol (3 hydroxyl groups) derivatives (Table 3), it appears that both the solid–liquid crystal transition temperature M_p and the mesophasic domain $\Delta T = C_p - M_p$ are raised by the increased number of OH groups. But we can also observe that 3-*O*-*n*-dodecyl-galactitol (5 OH groups) has lower M_p and ΔT values



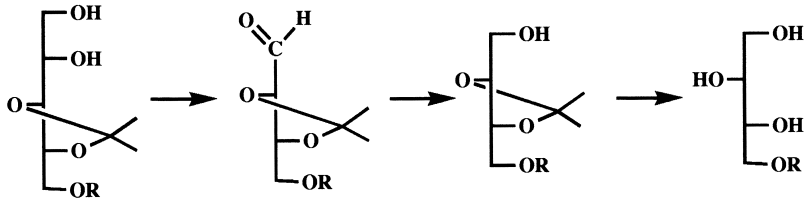
R = *n*-C_nH_{2n+1} with n = 8 (**b**) ; n = 12 (**d**)

Scheme 2.



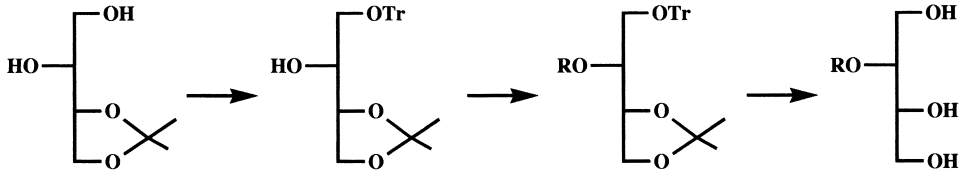
R = *n*-C_nH_{2n+1} with n = 6 (**a**) ; n = 8 (**b**) ; n = 10 (**c**) ; n = 12 (**d**)

Scheme 3.



20b-d **21b-d** **22b-d** **23b-d**

1-*O*-R-D,L-threitols



24 **25** **26b,d** **27b,d**

2-*O*-R-D,L-threitols

R = *n*-C_nH_{2n+1} with n = 6 (**a**) ; n = 8 (**b**) ; n = 10 (**c**) ; n = 12 (**d**)

Scheme 4.

than 1-*O*-*n*-dodecyl and 2-*O*-*n*-dodecyl-threitol (3 OH groups).

Thus this preliminary study indicates that it is difficult to explain the phase transition temperatures only as a consequence of both the *x*-*n*-alkyl chain position and the number of OH groups. The relative orientations of the OH groups in each polyol substrate can play a strong influence. Such structure parameters will be examined by a molecular modelization study.

In this work we examined also the lyotropic mesophases, except for 1-*O*-*n*-alkyl and 4-*O*-*n*-alkyl-glucitols. We do not observe a lyotropic mesophase with 3-*O*-*n*-alkyl and 6-*O*-*n*-alkyl-galactitols, whereas the other series generally have a large temperature mesophasic domain for lyotropic liquid crystals. However, in this study, liquid crystals were generated by water–crystal contact without water concentration control; for this reason it is difficult to discuss structural influences.

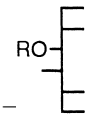
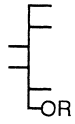
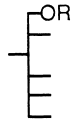
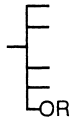
4. Experimental

4.1. General methods

Melting points were determined on an electrothermal automatic apparatus, and are uncorrected. Optical rotations, for solutions in $CHCl_3$ or methanol, were measured with a digital polarimeter JASCO model DIP-370 at 25°C. NMR spectra were recorded with a Bruker WB-300 instrument for solutions in $CDCl_3$, C_5D_5N or Me_2SO-d_6 (internal Me_4Si). Elemental analyses were performed by the Service Central de Micro-Analyse du Centre National de la Recherche Scientifique (Vernaison, France). Reactions were monitored either by HPLC (Waters 721), using either the reverse phase columns RP-18 (Merck) or PN 27-196 (Waters), or by CPG (Girdel) with either the columns OV 17 or SE 30. Column chromatography was performed on silica gel (60 mesh, Matrex) by usual gradient elution with hexane–acetone (in each case the ratio of silica gel to product mixture to be purified was 30:1).

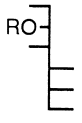
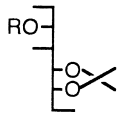
Phase transition temperatures were determined by DSC (differential scanning calorimetry) using a Mettler FP85 furnace and by thermal polarized light microscopy using an Olympus BX50 polarizing transmitted light equipped with a Mettler FP82 microfurnace. Readings from both Mettler apparatus were recorded on an FP90 central processor. For thermotropic liquid crystals, transition temperatures, denoted M_p (solid → liquid crystal) and C_p (liquid crystal → isotropic liquid), are T_{onset} (beginning temperature of the fusion pack) measured at 2°C min^{-1} by DSC. For lyotropic liquid crystals, transition temperatures, denoted T_1 (liquid

Table 1
Phase transition temperatures of *x*-*O*-*n*-alkyl-D-galactitols and D-glucitols

Structure	Code	*n*	Thermotropy		Lyotropy[a]	
			M_p (°C)	C_p (°C)	*T*1 (°C)	*T*2 (°C)
	3-*O*-*n*-alkyl-D-galactitol[a]	8	—	—	—	—
		12	< -20	< -11.9	—	
	6-*O*-*n*-alkyl-D-galactitol[a]	6	149[e]	—	—	—
		8	147	154	—	—
		10	145	170	—	—
		12	142	171	—	—
	1-*O*-*n*-alkyl-D-glucitol[b]	6	75.6	81		
		8	80.5	131.8		
		10	82.4	160.6		
	3-*O*-*n*-alkyl-D-glucitol[c]	6	< -8.9	2.1	—	—
		8	< -10	54	< RT	66.4
		10	56.9	144.3		
		12	64.7	164.2	< RT	> 96
	4-*O*-*n*-alkyl-D-glucitol[d]	6	—	—		
		8	< RT	61.8		
		10	33	136.2		
	6-*O*-*n*-alkyl-D-glucitol[d]	6	50.6	98.8	< RT	> 96
		8	72.6	135.3		
		10	78.8	147.7		
		12	< -11.6	93.5	< RT	> 96

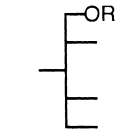
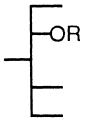
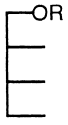
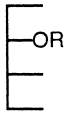
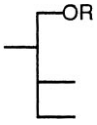
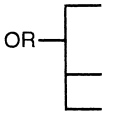
[a]This work. [b]Dahlhoff, 1990, for thermotropy. [c]Raaijmakers et al., 1995, for thermotropy. [d]Dahlhoff, 1991, for thermotropy. [e]Isotropic.

Table 2
Phase transition temperatures of *x*-*O*-*n*-alkyl-D-mannitols

Structure	Code	*n*	Thermotropy		Lyotropy[a]	
			M_p (°C)	C_p (°C)	*T*1 (°C)	*T*2 (°C)
	1-*O*-*n*-alkyl-D-mannitol[b]	6	95.0	102.0		
		8	103.7	144.4		
		10	107.5	162.0		
		12	111.2	167.0	65	> 96
	2-*O*-*n*-alkyl-D-mannitol[a]	8	36.3	148.0	—	—
		12[d]	30	176.5	< RT	> 96
	2-*O*-*n*-alkyl-D-mannitol monoacetal[a]	8	< -18.2	-0.6	—	—
		12	19.0	25.0	19.0	39.0
	3-*O*-*n*-alkyl-D-mannitol[c]	10	61.0	140.0		
		12	96.6	167.4	56.5	74.0

[a]This work. [b]Dahlhoff, 1989, for thermotropy. [c]Raaijmakers et al., 1995, for thermotropy. [d]Goodby et al., 1998.

Table 3
Phase transition temperatures of *x-O-n*-alkyl-xylitols, erythritols and threitols

Structure	Code	*n*	Thermotropy		Lyotropy[a]	
			M_p (°C)	C_p (°C)	*T*1 (°C)	*T*2 (°C)
	1-*O*-*n*-alkyl-D,L-xylitol[b]	6	21.4	49.3	< RT	58.6
		8	48.9	98	< RT	> 96
		10	56.2	109.8	30.0	> 96
		12	43.6	112	80.0	> 96
	2-*O*-*n*-alkyl-D-xylitol[c]	8	47.5	80.2	< RT	83
		12	69.1	120.3	61	> 96
	3-*O*-*n*-alkyl-xylitol[c]	12	101.3	137.3	79	95
	1-*O*-*n*-alkyl-D,L-erythritol[a]	6	39.1	—	< RT	38
		8	54.9[d]	—	42	89
		10	64.2[d]	—	26	> 96
		12	70.3[d]	—	44	> 96
	2-*O*-*n*-alkyl-D,L-erythritol[a]	8	10.4[d]	—	—	—
		10	40.2[d]	—	—	—
		12	39	77.1	< RT	> 96
	1-*O*-*n*-alkyl-D,L-threitol[a]	8	31.1	52	< RT	> 96
		10	42.5	61.9	< RT	> 96
		12	51.5	68.8	< RT	> 96
	2-*O*-*n*-alkyl-D,L-threitol[a]	8	29.5	52	< RT	> 83
		12	48.8	53.5	< RT	> 96

crystal apparition) and T_2 (liquid crystal disappearence) are determined by simply allowing crystals of the test material to dissolve in water, thereby creating a concentration gradient which supports mesophase formation.

4.2. Compounds synthesis

4.2.1. 1,2:5,6-di-O-isopropylidene-α-D-galactofuranose **1**

D-galactose (60 g, 0.33 mol) was dissolved at 80°C in DMF (500 ml). The stirred solution was cooled to 30°C, and 125 g (1.2 mol) of 2,2-dimethoxypropane and 4.8 g (25 mmol) of *p*-toluenesulfonic acid were added. After 24 h at room temperature, the same quantity of this acid was added again. The solution was neutralized 15 h later with an excess of CH_3COONa (15 g, 183 mmol) and concentrated under reduced pressure. 200 ml of water was added to extract the product by CH_2Cl_2 (200 ml, four times). The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. HPLC control (RP-18, 3:2 acetone–water, 1.2 ml min^{-1}) showed the formation of compound (**1**) and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose in 11:9 ratio. Column chromatography with 9:1 hexane–acetone gave 42.5 g (49%) of compound **1**: mp 92–93°C, and 34.7 g (40%) of 1,2:3,4-di-*O*-isopropylidène-α-D-galactopyranose: oil; $[\alpha]_D^{24}$ −56.4° (c 1.1, $CHCl_3$); lit. [(Chellé, 1992), $[\alpha]_D^{24}$ −55° (c 2.0, $CHCl_3$)].

4.2.2. 3-O-n-alkyl-1,2:5,6-di-O-isopropylidene-α-D-galactofuranoses **2b** and **2d**

To a solution of **1** (10 g, 38.5 mmol) and 1.2 equiv of *n*-$C_nH_{2n+1}Br$ (n = 8 and 12) in 4:1 toluene–Me_2SO (100 ml) was added powdered KOH (5.2 g, 92.3 mmol). After two days at room temperature, the mixture was filtered and the filtrate neutralized with saturated aqueous NH_4Cl. The organic phase was separated, washed with water (twice), dried (Na_2SO_4) and concentrated under reduced pressure.

Table 4
Physicochemical and microanalytical data for D-galactose and D-galactitol derivatives **2-5**

Product	Yield (%)	M_p^a (°C)	$[\alpha]_D^{25}$	Formula	Calculated		Found	
					C	H	C	H
2b	96	oil	−27.3[b] (c 2.0)	$C_{20}H_{36}O_6$ (372.50)	64.48	9.74	64.18	9.87
2d	92	oil	−24.8[b] (c 1.8)	$C_{24}H_{44}O_6$ (428.61)	67.25	10.34	67.57	10.11
3b	84	oil	−16.9[c] (c 1.3)	$C_{14}H_{28}O_6$ (292.37)	57.51	9.65	57.32	9.52
3d	89	oil	−25.5[c] (c 1.5)	$C_{18}H_{36}O_6$ (348.48)	62.03	10.41	62.15	10.38
4b	54	oil	−2.7[c] (c 1.0)	$C_{14}H_{30}O_6$ (294.39)	57.12	10.27	56.89	10.31
4d	62	oil	−3.4[c] (c 0.9)	$C_{18}H_{38}O_6$ (350.49)	61.68	10.92	61.49	10.80
5a	89	149	−7.3[c] (c 1.1)	$C_{12}H_{26}O_6$ (266.33)	54.11	9.84	54.37	9.66
5b	89	147	−8.4[c] (c 1.2)	$C_{14}H_{30}O_6$ (294.39)	57.12	10.27	56.89	10.55
5c	94	145	−6.8[c] (c 1.0)	$C_{16}H_{34}O_6$ (322.44)	59.60	10.62	59.53	10.71
5d	96	142	−9.2[c] (c 1.1)	$C_{18}H_{38}O_6$ (350.49)	61.68	10.92	61.76	10.62

[a]Measured by thermal microscopy. [b]In $CHCl_3$. [c]In MeOH (stabilized during 5 days for 3-*O*-*n*-alkyl-D-galactoses).

The 3-*O*-alkyl-1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranoses **2** were isolated after purification by column chromatography with 49:1 hexane–acetone (Table 4). ^{1}H NMR ($CDCl_3$): 5.76 (d, 1H, J_{1-2} 4.0 Hz, H-1); 4.48 (dd, 1H, J_{2-3} 1.4 Hz, H-2); 4.25 (q, 1H, J_{5-6} 6.6 Hz, H-5); 3.95 (dd, 1H, J_{6a-6b} 8.3 Hz, H-6a); 3.79 (dd, 1H, J_{5-6b} 6.6 Hz, H-6b); 3.78 (dd, 1H, J_{4-5} 6.8 Hz, H-4); 3.58 (dd, 1H, J_{3-4} 5.2 Hz, H-3); 3.49 (dt, 1H, $J_{\alpha-\alpha'}$, 9.0 Hz, H-α); 3.36 (dt, 1H, $J_{\alpha-\beta}$ 6.6 Hz, H-α′); 1.59 (m, 2H, H-β, H-β′); 1.50 → 1.30 (4 s, 12 H, CH_3-*iso*); 1.25 → 1.20 (CH_2 chain); 0.83 (t, 3H, $J_{\omega-(\omega-1)'}$ 6.7 Hz, H-ω). ^{13}C NMR ($CDCl_3$): 113.5 and 109.6 (C-*iso*); 104.9 (C-1); 85.5 (C-2); 83.8 (C-3); 83.6 (C-4); 75.9 (C-5); 70.3 (C-α); 65.6 (C-6); 31.8 → 22.6 (CH_2 chain); 27.5, 26.8, 26.4 and 25.3 (CH_3-*iso*); 14.0 (C-ω).

*4.2.3. 3-O-n-alkyl-D-galactopyranoses **3b** and **3d***

2 was added to a stirred solution of 9:1 CF_3COOH–H_2O (100 g l^{-1}). After 1 h at room temperature, the solution was concentrated under reduced pressure. The 3-*O*-*n*-alkyl-D-galactopyranoses **3** were isolated after purification by column chromatography with 2:3 hexane–acetone (Table 4). ^{13}C NMR (Me_2SO-d_6): 102.1 (C-1 βfur); 97.4 (C-1 βpyr); 95.5 (C-1 αfur); 92.5 (C-1 αpyr); 84.8 (C-2 βfur); 82.9 (C-2 βpyr); 81.6 (C-2 αfur); 80.8 (C-2 αpyr); 68.5 and 69.3 (C-αpyr, C-αfur); 62.6, 62.3 and 60.4 (C-6); 31.2 → 22.0 (CH_2 chain, C-β to C-(ω − 1)); 13.8 (C-ω).

*4.2.4. 3-O-n-alkyl-D-galactitols **4b** and **4d***

3 was dissolved in methanol (50 g l^{-1}) and treated with $NaBH_4$ (6 equiv) at room temperature for 24 h. The excess of borohydride was destroyed by treatment with formic acid for 5 h at room temperature and the solution was concentrated under reduced pressure. The 3-*O*-*n*-alkyl-D-galactitols **4** were isolated after purification by column chromatography with 4:1 acetone–hexane (Table 4). ^{13}C NMR (Me_2SO-d_6): 60.3 (C-1); 62.5 (C-6); 64.6 and 63.0 (C-2, C-4); 68.5 and 68.3 (C-3, C-α); 62.6 (C-5); 31.2 → 21.9 (CH_2 chain, C-β to C-(ω − 1)); 13.7 (C-ω).

*4.2.5. 6-O-n-alkyl-D-galactitols **5a–d***

6-*O*-*n*-alkyl-α-D-galactopyranoses (Bault et al., 1998) were reduced in the conditions used for **4**. The 6-*O*-*n*-alkyl-D-galactitols **5** were isolated after crystallization from ethanol (Table 4). ^{1}H NMR (Me_2SO-d_6): 4.81 (dt, 1H, J_{4-5} 1.4 Hz, H-5); 4.74 (dt, 1H, J_{1-2} 5.8 Hz, H-2); 4.52 (dd, 1H, J_{3-4} 8.5 Hz, H-4); 4.43 (dd, 1H, J_{2-3} 1.9 Hz, H-3); 4.28 (d, 2H, H-1a, H-1b); 3.99 (m, 2H, J_{6a-6b} 14.7 Hz, H-6a, H-6b); 3.53 (t, 2H, $J_{\alpha-\beta}$ 6.6 Hz, H-α); 1.20 (m, CH_2 chain); 0.80 (t, $J_{\omega-(\omega-1)}$ 6.8, H-ω). ^{13}C NMR (Me_2SO-d6): 74.4 (C-6); 72.6 (C-3, C-2); 72.4 (C-4); 72.0 (C-α); 70.4 (C-5); 65.7 (C-1); 32.4 → 23.2 (CH_2 chain, C-β to C-(ω − 1)); 14.5 (C-ω).

*4.2.6. Benzyl 2,3-O-isopropylidene-6-O-trityl-α-D-mannofuranoside **7***

To a stirred solution of benzyl 2,3-*O*-isopropylidene-α-D-mannofuranoside (**6**) (Spychala, 1997) (10 g, 32.2 mmol) in pyridine (50 ml) was added trityl chloride (9.9 g, 35.5 mmol). After 24 h at room temperature, 200 ml of toluene was added and the mixture was filtered. The filtrate was neutralized with saturated aqueous NH_4Cl. The organic phase was separated, washed with water (twice), dried (Na_2SO_4) and concentrated under reduced pressure. The benzyl 2,3-*O*-isopropylidene-6-*O*-trityl-α-D-mannofuranoside (**7**) was isolated after purification by column chromatography with 19:1 hexane–acetone. Yielded 14.8 g (83%): mp 55.1–56.2°C; $[\alpha]_D^{24}$ + 51° (c 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$): 7.20 → 7.50 (m, 20H, H-ph); 5.05 (s, 1H, J_{1-2} 0 Hz, H-1); 4.85 (dd, 1H, J_{3-4} 2.7 Hz, H-3); 4.63 (d, 1H, J_{2-3} 5.9 Hz, H-2); 4.58 (dt, 1H, $J_{\alpha-\alpha'}$ 11.7 Hz, H-α); 4.39 (dt, 1H, H-α′); 4.11 (m, 2H, J_{5-6a} 3.0 Hz, H-4, H-5); 3.46 (dd, 1H, J_{6a-6b} 9.6 Hz, H-6a); 3.32 (dd, 1H, J_{5-6b} 4.0 Hz, H-6b); 2.94 (d, 1H, J_{5-OH-5} 6.3 Hz, OH-5); 1.31 and 1.44 (2s, CH_3-*iso*). ^{13}C NMR ($CDCl_3$): 143.9 (3 C-*ipso*trityle); 137.2 (C-*ipso*Bn); 127.1 → 128.7 (C-ph); 112.5 (C-*iso*); 105.2 (C-1); 86.6 (C-ph_3); 85.0 (C-2); 80.4 (C-3); 79.0 (C-4); 69.3 (C-5); 68.9 (CH_2-Bn); 65.0 (C-6); 26.0 and 24.6 (CH_3-*iso*).

Table 5
Physicochemical and microanalytical data for D-mannose and D-mannitol derivatives **8-11**

Product	Yield (%)	M_p^a (°C)	$[\alpha]_D^{25}$	Formula	Calculated		Found	
					C	H	C	H
8b	98	oil	9.4[b] (c 1.3)	$C_{43}H_{52}O_6$ (664.89)	77.71	7.83	77.71	7.92
8d	98	oil	6.2[b] (c 1.5)	$C_{47}H_{60}O_6$ (720.99)	78.29	8.38	78.15	8.42
9b	83	oil	−4.0[b] (c 1.0)	$C_{17}H_{32}O_6$ (332.44)	61.42	9.70	61.27	9.65
9d	91	oil	0.7[b] (c 1.1)	$C_{21}H_{40}O_6$ (388.55)	64.91	10.37	64.72	10.19
10b	94	oil	−16.8[b] (c 1.2)	$C_{17}H_{34}O_6$ (334.46)	61.05	10.24	60.78	10.15
10d	91	25.0	−17.9[b] (c 1.2)	$C_{21}H_{42}O_6$ (390.56)	64.58	10.84	64.70	10.75
11b	83	oil	−35.0[c] (c 0.8)	$C_{14}H_{30}O_6$ (294.39)	57.12	10.27	57.45	10.19
11d	78	30	−10.0[c] (c 0.9)	$C_{18}H_{38}O_6$ (350.50)	61.68	10.93	61.55	10.82

[a]Measured by thermal microscopy. [b]In $CHCl_3$. [c]In MeOH.

*4.2.7. Benzyl 5-O-n-alkyl-2,3-O-isopropylidene-6-O-trityl-α-D-mannofuranosides **8b** and **8d***

Benzyl 2,3-*O*-isopropylidene-6-*O*-trityl-α-D-mannofuranoside (**7**) (6 g, 10.9 mmol) was alkylated in the conditions used for **2**, with corresponding alkyl bromide (2 equiv). The benzyl 5-*O*-*n*-alkyl-2,3-*O*-isopropylidene-6-*O*-trityl-α-D-mannofuranosides **8** were isolated after purification by column chromatography with 99:1 hexane–acetone (Table 5). ^{1}H NMR ($CDCl_3$): 7.20 → 7.50 (m, 20H, H-ph); 4.94 (s, 1H, J_{1-2} 0 Hz, H-1); 4.86 (dd, 1H, J_{3-4} 3.4 Hz, H-3); 4.63 (d, 1H, J_{2-3} 5.8 Hz, H-2); 4.53 (d, 1H, $J_{\alpha a-\alpha b}$ 11.6 Hz, H-αa_{Bn}); 4.37 (dd, 1H, J_{4-5} 9.4 Hz, H-4); 4.33 (d, 1H, H-α′); 3.74 (m, 1H, J_{5-6a} 2.0 Hz, H-5); 3.68 (dt, 1H, $J_{\alpha-\alpha'}$ 8.9 Hz, H-α); 3.54 (dd, 1H, J_{6a-6b} 10.0 Hz, H-6a); 3.52 (dt, 1H, $J_{\alpha-\beta}$ 6.8 Hz, H-α′); 3.19 (dd, 1H, J_{5-6b} 4.0 Hz, H-6b); 1.40 to 1.20 (m, $J_{\alpha-\beta}$ 6.4 Hz, CH_2 chain, CH_3-*iso*); 0.88 (t, 3H, $J_{\omega-(\omega-1)}$ 6.5 Hz, H-ω). ^{13}C NMR ($CDCl_3$): 144.3 (3 C-*ipso*trityle); 137.1 (C-*ipso*Bn); 126.8 → 128.6 (C-ph); 112.0 (C-*iso*); 104.8 (C-1); 86.5 (C-trityl); 84.9 (C-2); 80.0 (C-3); 78.2 (C-4); 76.2 (C-5); 70.7 (C-α); 68.3 (CH_2-Bn); 62.9 (C-6); 26.1 and 24.9 (CH_3-*iso*); 22.7 → 31.9 (CH_2 chain C-β to C-(ω − 1)); 14.1 (C-ω).

*4.2.8. 5-O-n-alkyl-2,3-O-isopropylidene-α-D-mannofuranoses **9b** and **9d***

8 was dissolved in methanol (100 g l^{-1}). Pd/C-10% (240 g mol^{-1}) was added and the solution stirred under H_2 atmosphere. After 24 h, at room temperature, Pd/C was filtered and the filtrate concentrated under reduced pressure. The 5-*O*-*n*-alkyl-2,3-*O*-isopropylidene-D-mannofuranoses **9** were isolated after purification by column chromatography with 5:1 hexane–acetone (Table 5). ^{1}H NMR ($CDCl_3$): 5.26 (s, 1H, J_{1-2} 0 Hz, H-1); 4.73 (dd, 1H, J_{3-4} 3.5 Hz, H-3); 4.52 (d, 1H, J_{2-3} 5.8 Hz, H-2); 4.44 (s, 1H, OH-1); 4.13 (dd, 1H, J_{4-5} 8.8 Hz, H-4); 3.81 (dd, 1H, J_{6a-6b} 11.0 Hz, H-6a); 3.64 (dd, 1H, J_{5-6b} 2.8 Hz, H-6b); 3.59 (ddd, 1H, J_{5-6a} 5.9 Hz, H-5); 3.50 (dt, 1H, $J_{\alpha-\alpha'}$ 9.0 Hz, H-α); 3.49 (dt, 1H, $J_{\alpha-\beta}$ 6.7 Hz, H-α′); 2.93 (s, 1H, OH-6); 1.38 → 1.20 (m, CH_2 chain, CH_3-*iso*); 0.83 (t, 3H, $J_{\omega-(\omega-1)}$ 6.5 Hz, H-ω). ^{13}C NMR ($CDCl_3$): 112.1 (C-*iso*); 101.0 (C-1); 85.4 (C-2); 79.8 (C-3); 78.4 (C-4); 76.4 (C-5); 70.3 (C-α); 61.3 (C-6); 26.0 and 24.8 (CH_3-*iso*); 22.6 → 31.8 (CH_2 chain C-β to C-(ω − 1)); 14.0 (C-ω).

*4.2.9. 5-O-n-alkyl-2,3-O-isopropylidene D-mannitols **10b** and **10d***

Mannose derivatives **9** were reduced in the conditions used for **4**. The 5-*O*-*n*-alkyl-2,3-*O*-isopropylidene-D-mannitols **10** were isolated after purification by column chromatography with 7:3 hexane–acetone (Table 5). ^{1}H NMR ($CDCl_3$): 4.44 (s, 1H, OH); 4.30 (s, 1H, OH); 4.25 (dd, 1H, J_{3-4} 1.6 Hz, H-3); 4.11 (m, 1H, J_{2-3} 7.1 Hz, H-2); 3.67 (m, 1H, H-1a); 3.62 (m, 2H, H-6a, H-6b); 3.59 (m, 1H, H-α); 3.51 (m, 1H, H-4); 3.48 (m, 1H, H-1b); 3.37 (m, 1H, H-α′); 3.15 (m, 1H, J_{4-5} 7.9 Hz, H-5); 2.50 (s, 1H, OH); 1.46 (m, 1H, H-β); 1.39 and 1.26 (2s, 6H, CH_3-*iso*); 1.23 (m, CH_2 chain); 0.84 (t, 3H, $J_{\omega-(\omega-1)}$ 6.6 Hz, H-ω). ^{13}C NMR ($CDCl_3$): 106.7 (C-*iso*); 80.2 (C-5); 77.5 (C-2); 75.4 (C-3); 69.4 (C-α); 67.3 (C-4); 60.3 (C-1); 60.0 (C-6); 26.8 and 25.1 (CH_3-*iso*); 22.0 → 31.2 (CH2 chain C-β to C-(ω − 1)); 13.8 (C-ω).

*4.2.10. 2-O-n-alkyl-D-mannitols **11b** and **11d***

Compounds **10** were deprotected in the conditions used for **4**. The 2-*O*-*n*-alkyl-D-mannitols **11** were isolated after purification by column chromatography with 17:3 ethyl acetate–hexane (Table 5). ^{1}H NMR (C_5D_5N): 5.70 (s, 5H, OH); 4.81 (d, 1H, J_{2-3} 7.9 Hz, H-3); 4.62 (d, 1H, J_{3-4} 0 Hz, H-4); 4.53 (m, 1H, J_{4-5} 7.1 Hz, H-5); 4.36 (dd, 1H, J_{1a-1b} 11.3 Hz, H-1a); 4.34 (m, 2H, H-6a, H-6b); 4.28 (dd, 1H, J_{1b-2} 3.6 Hz, H-1b); 4.01 (m, 1H, J_{1a-2} 3.2 Hz, H-2); 3.78 (dt, 1H, $J_{\alpha-\alpha'}$ 8.0 Hz, H-α); 3.59 (dt, 1H, $J_{\alpha-\beta}$ 7.2 Hz, H-α′); 1.51 (m, 1H, H-β); 1.18 (m, CH_2 chain); 0.82 (t, 3H, $J_{\omega-(\omega-1)}$ 7.0 Hz, H-ω). ^{13}C NMR ($CDCl_3$): 80.8 (C-2); 73.1 (C-5); 71.3 (C-4); 70.4 (C-α); 69.9 (C-3); 64.5 (C-6); 61.5 (C-1); 22.7 → 31.8 (CH_2 chain C-β to C-(ω − 1)); 14.0 (C-ω).

*4.2.11. 1,2-O-isopropylidene-D,L-erythritol **(12)***

To a stirred solution of *meso*-erythritol (60 g, 0.49 mol) in acetone (600 ml) H_2SO_4 (2 g) was added dropwise. After 140 min at room temperature the solution was filtered, cooled and neutralized with solid $NaHCO_3$. The mixture

Table 6
Physicochemical and microanalytical data for D,L-erythritol derivatives **15**, **16**, **18** and **19**

Product	Yield (%)	Mp[a] (°C)	Formula	Calculated		Found	
				C	H	C	H
15a	60[b]	—	—	—	—	—	—
15b	62[b]	—	—	—	—	—	—
15c	63[b]	—	—	—	—	—	—
15d	63[b]	—	—	—	—	—	—
16a	50	39.1	$C_{10}H_{21}O_4$ (205.27)	58.51	10.31	58.62	10.27
16b	82	54.9	$C_{12}H_{25}O_4$ (233.33)	61.77	10.80	61.85	10.82
16c	83	64.2	$C_{14}H_{29}O_4$ (261.38)	64.33	11.18	64.27	11.12
16d	82	70.3	$C_{16}H_{33}O_6$ (289.43)	66.39	11.49	66.25	11.32
18b	93	oil	$C_{34}H_{44}O_4$ (516.72)	79.03	8.58	78.85	8.47
18c	97	oil	$C_{36}H_{48}O_4$ (544.78)	79.37	8.88	79.21	8.79
18d	97	oil	$C_{38}H_{52}O_4$ (572.83)	79.68	9.15	79.55	9.05
19b	79	10.4	$C_{12}H_{25}O_4$ (233.33)	61.77	10.80	61.59	10.73
19c	70	40.2	$C_{14}H_{29}O_4$ (261.38)	64.33	11.18	64.42	11.22
19d	80	39	$C_{16}H_{33}O_6$ (289.43)	66.39	11.49	66.53	11.37

[a]Measured by thermal microscopy. [b]Determined by HPLC on crude product.

was filtered and the filtrate concentrated under reduced pressure. The 1,2-*O*-isopropylidene-D,L-erythritol (**12**) was isolated after purification by column chromatography with 7:3 hexane–acetone. Yielded 28.7 g (36%): mp 40–42°C. ^{1}H NMR ($CDCl_3$): 4.00 (dd, 1H, J_{4b-3} 6.0 Hz, H-4b); 3.96 (ddd, 1H, J_{4a-3} 4.2 Hz, H-3); 3.89 (dd, 1H, J_{4a-4b} 10.3 Hz, H-4a); 3.72 (dd, 1H, J_{1b-2} 2.7 Hz, J_{1a-1b} 10.9 Hz, H-1b); 3.62 (dd, 1H, J_{2-3} 8.9 Hz, H-2); 3.56 (dd, 1H, J_{1a-2} 5.8 Hz, H-1a); 1.36 and 1.29 (2s, CH_3-*iso*). ^{13}C NMR ($CDCl_3$): 109.2 (C-*iso*); 76.0 (C-2); 72.4 (C-3); 66.3 (C-1); 66.4 (C-4); 26.5 and 25.0 (CH_3-*iso*).

*4.2.12. 1,2-O-isopropylidene-4-O-tosyl-D,L-erythritol (**13**)*

To a stirred solution of **12** (6 g, 37 mmol) in 2:3 toluene–pyridine (50 ml) was added at −15°C *p*-toluenesulfonyl chloride (7.6 g, 39.8 mmol) dissolved in dry toluene (25 ml). After 72 h at 4°C the mixture was filtered and the filtrate neutralized with saturated aqueous NH_4Cl. The organic phase was separated, washed with water (twice), dried (Na_2SO_4) and concentrated under reduced pressure. The 1,2-*O*-isopropylidene-4-*O*-tosyl-D,L-erythritol (**13**) was isolated after purification by column chromatography with 17:3 hexane–acetone. Yielded 8.2 g (70%) as an oil. ^{1}H NMR ($CDCl_3$): 7.77 (d, 2H, $J_{ortho\text{-}meta}$ 8.2 Hz, H-*meta*); 7.30 (d, 2H, H-*ortho*); 4.22 (dd, 1H, J_{1a-1b} 10.6 Hz, J_{1b-2} 2.9 Hz, H-1b); 4.03 (dd, 1H, H-1a); 4.10 → 3.90 (m, 3H, H-2, H-4a, H-4b); 3.75 (m, 1H, H-3); 2.42 (s, 3H, CH_3-tosyl); 1.31 and 1.28 (2s, CH_3-*iso*). ^{13}C NMR ($CDCl_3$): 144.8 (C-*para*); 133.5 (C-*ipso*); 129.8 (C-*meta*); 127.9 (C-*ortho*); 109.2 (C-*iso*); 75.0 (C-3); 71.4 (C-4); 70.7 (C-2); 66.4 (C-1); 26.5 and 24.9 (CH_3-*iso*); 21.5 (CH_3-tosyl).

*4.2.13. 1,2-anhydro-3,4-O-isopropylidene-D,L-erythritol (**14**)*

To a stirred solution of **13** (6.3 g, 20 mmol) in 4:1 toluene–Me_2SO (63 ml) was added powdered KOH (2.7 g, 48 mmol). After 2 h at room temperature the mixture was filtered and the filtrate neutralized with saturated aqueous NH_4Cl. The organic phase was separated, washed with water (twice), dried (Na_2SO_4) and concentrated under reduced pressure. The 1,2-anhydro-3,4-*O*-isopropylidene-D,L-erythritol (**14**) was isolated after purification by column chromatography with 19:1 hexane–acetone. Yielded 2.3 g (81%) as an oil. ^{1}H NMR ($CDCl_3$): 4.06 (dd, 1H, J_{4b-3} 6.1 Hz, H-4b); 3.86 (dd, 1H, J_{4a-3} 5.6 Hz, J_{4a-4b} 8.1 Hz, H-4a); 3.81 (ddd, 1H, J_{2-3} 5.8 Hz, H-3); 2.96 (ddd, 1H, H-2); 2.78 (dd, 1H, J_{1b-2} 3.9 Hz, J_{1a-1b} 4.9 Hz, H-1b); 2.59 (dd, 1H, J_{1a-2} 2.6 Hz, H-1a); 1.39 and 1.30 (2s, CH_3-*iso*). ^{13}C NMR ($CDCl_3$): 109.2 (C-*iso*); 76.0 (C-2); 72.4 (C-3); 66.3 (C-1); 66.4 (C-4); 26.5 and 25.0 (CH_3-*iso*).

*4.2.14. 1-O-n-alkyl-3,4-O-isopropylidene-D,L-erythritols **15a–d***

To a stirred solution of **14** (1 equiv) and corresponding alcohol ROH (4 equiv) in 1:1 toluene–Me_2SO (100 g l^{-1}) was added powdered KOH (3 equiv). After 24 h at 40°C the mixture was filtered and the filtrate neutralized with saturated aqueous NH_4Cl. The organic phase was separated, washed with water (twice), dried (Na_2SO_4) and concentrated under reduced pressure. The 1-*O*-alkyl-3,4-*O*-isopropylidene-D,L-erythritols **15** were directly deprotected without further purification because it was difficult to separate the remaining ROH (large excess).

*4.2.15. 1-O-alkyl-D,L-erythritols **16a–d***

To a stirred solution of crude **15** in ethanol (125 g l^{-1}) was added Amberlyst 15H$^+$ resin (weight ratio of resin to substrate 4:1). After 2–4 h at 50°C the mixture was filtered and the filtrate concentrated under reduced pressure. The 1-*O*-*n*-alkyl-D,L-erythritols **16** were isolated after purification by column chromatography with 7:3 hexane–acetone (Table 6). ^{1}H NMR ($CDCl_3$): 4.37 (dd, 1H, J_{4b-3} 6.3 Hz,

Table 7
Physicochemical and microanalytical data for D,L-threitol derivatives **22**, **23**, **26** and **27**

Product	Yield (%)	Mp[a] (°C)	Formula	Calculated		Found	
				C	H	C	H
22b	81	oil	$C_{15}H_{29}O_4$ (273.39)	65.90	10.69	65.82	10.63
22c	82	oil	$C_{17}H_{33}O_4$ (301.44)	67.73	11.03	67.59	10.98
22d	79	oil	$C_{19}H_{37}O_4$ (329.50)	69.26	11.32	69.37	11.28
23b	86	31.1	$C_{12}H_{25}O_4$ (233.33)	61.77	10.80	61.65	10.69
23c	90	42.5	$C_{14}H_{29}O_4$ (261.38)	64.33	11.18	64.48	11.25
23d	92	51.5	$C_{16}H_{33}O_6$ (289.43)	66.39	11.49	66.42	11.46
26b	100	oil	$C_{34}H_{44}O_4$ (516.72)	79.03	8.58	79.15	8.39
26d	99	oil	$C_{38}H_{52}O_4$ (572.83)	79.68	9.15	79.55	9.22
27b	81	29.5	$C_{12}H_{25}O_4$ (233.33)	61.77	10.80	61.64	10.76
27d	85	48.8	$C_{16}H_{33}O_6$ (289.43)	66.39	11.49	66.43	11.46

[a]Measured by thermal microscopy.

J_{4a-4b} 12.5 Hz, H-4b); 4.27 (m, 2H, J_{2-3} 5.0 Hz, J_{4a-3} 5.7 Hz, H-2, H-4a); 4.00 (dd, 1H, J_{1b-2} 6.6 Hz, J_{1a-1b} 9.8 Hz, H-1b); 3.85 (dd, 1H, J_{1a-2} 3.3 Hz, H-1a); 3.51 (dt, 1H, $J_{\alpha-\alpha'}$ 9.3 Hz, H-α'); 3.48 (dt, 1H, $J_{\alpha-\beta}$ 6.6 Hz, H-α); 1.20 → 1.06 (CH_2 chain, CH_3-*iso*); 0.72 (t, 3H, $J_{\omega-(\omega-1)}$ 6.6 Hz, H-ω). ^{13}C NMR ($CDCl_3$): 74.1 (C-1); 73.9 (C-2); 72.6 (C-3); 71.7 (C-α); 65.0 (C-4); 32.0 → 22.9 (CH_2 chain C-β to C-(ω − 1)); 14.2 (C-ω).

*4.2.16. 1,2-O-isopropylidene-4-O-trityl-D,L-erythritol (**17**)*

12 (20 g, 123 mmol) was tritylated in the conditions used for **7** to give the 1,2-*O*-isopropylidene-4-*O*-trityl-D,L-erythritol (**17**), isolated after purification by column chromatography with 4:1 hexane–acetone. Yielded 35 g (70%) as an oil. ^{1}H NMR ($CDCl_3$): 7.40 → 7.20 (H aromatic); 4.08 (ddd, 1H, J_{2-3} 6.8 Hz, H-2); 3.99 (dd, 1H, J_{1b-2} 6.1 Hz, J_{1a-1b} 8.3 Hz, H-1b); 3.93 (dd, 1H, J_{1a-2} 6.2 Hz, H-1a); 3.77 (ddd, 1H, H-3); 3.31 (dd, 1H, J_{4b-3} 4.1 Hz, J_{4a-4b} 9.7 Hz, H-4b); 3.24 (dd, 1H, J_{4a-3} 5.8 Hz, H-4a); 1.34 and 1.30 (2s, CH_3-*iso*). ^{13}C NMR ($CDCl_3$): 143.7 (C-*ipso*); 128.6 (C-*ortho*); 127.8 (C-*meta*); 127.1 (C-*para*); 109.0 (C-*iso*); 86.9 (C-trityl); 76.2 (C-2); 71.2 (C-3); 66.4 (C-1); 64.6 (C-4); 26.6 and 25.2 (CH_3-*iso*).

*4.2.17. 3-O-n-alkyl-1,2-O-isopropylidene-4-O-trityl-D,L-erythritols **18b–d***

17 was alkylated in the conditions used for **2**, with corresponding alkyl bromide (1.2 equiv). The 3-*O*-*n*-alkyl-1,2-*O*-isopropylidene-4-*O*-trityl-D,L-erythritols **18** were isolated after purification by column chromatography with 97:3 hexane–acetone (Table 6). ^{1}H NMR ($CDCl_3$): 7.40 → 7.20 (H aromatic); 4.10 (ddd, 1H, J_{2-3} 6.0 Hz, H-2); 3.98 (dd, 1H, J_{1b-2} 3.3 Hz, J_{1a-1b} 10.1 Hz, H-1b); 3.93 (dd, 1H, J_{1a-2} 5.3 Hz, H-1a); 3.63 (dt, 1H, $J_{\alpha-\alpha'}$ 9.1 Hz, $J_{\alpha-\beta}$ 6.6 Hz, H-α'); 3.47 (m, 2H, H-α, H-3); 3.28 (dd, 1H, J_{4b-3} 6.5 Hz, J_{4a-4b} 8.1 Hz, H-4b); 3.11 (dd, 1H, J_{4a-3} 6.3 Hz, H-4a); 1.60 → 1.25 (CH_2 chain, CH_3-*iso*); 0.85 (t, 3H, $J_{\omega-(\omega-1)}$ 6.7 Hz, H-ω). ^{13}C NMR ($CDCl_3$): 144.0 (C-*ipso*); 128.6 (C-*ortho*); 127.7 (C-*meta*); 126.8 (C-*para*); 108.8 (C-*iso*); 86.7 (C-trityl); 79.4 (C-3); 76.0 (C-2); 71.4 (C-α); 66.3 (C-1); 63.8 (C-4); 31.8 → 22.6 (CH_2 chain C-β to C-(ω − 1)); 26.5 and 25.4 (CH_3-*iso*), 14.0 (C-ω).

*4.2.18. 2-O-n-alkyl-D,L-erythritols **19b–d***

To a stirred solution of **18** (5 g) in 4:1 dioxane–water (50 ml) was added 13N HCl (5 ml). After 7 h at 50°C, the mixture was neutralized with $NaHCO_3$, filtered and the filtrate concentrated under reduced pressure. The 2-*O*-*n*-alkyl-D,L-erythritols **19** were isolated after purification by column chromatography with 3:1 hexane–acetone (Table 6). ^{1}H NMR ($CDCl_3$): 3.79 → 3.68 (m, 3H, H-1a, H-1b, H-3); 3.55 → 3.39 (m, 4H, H-4a, H-4b, H-α, H-α'); 3.24 (m, 1H, H-2); 1.51 → 1.22 (CH_2 chain); 0.84 (t, 3H, $J_{\omega-(\omega-1)}$ 6.5 Hz, H-ω). ^{13}C NMR ($CDCl_3$): 79.9 (C-2); 71.3 (C-3); 70.5 (C-α); 63.4 (C-4); 60.4 (C-1); 31.8 → 22.6 (CH_2 chain C-β to C-(ω − 1)); 14.0 (C-ω).

*4.2.19. 4-O-n-alkyl-2,3-O-isopropylidene-D,L-threoses **21b–d***

To a stirred solution of 1-*O*-*n*-alkyl-2,3-*O*-isopropylidene-D,L-xylitol **20** (Goodby et al., 1997a) in ethanol was added, at 0°C, an aqueous solution of $NaIO_4$ (1 equiv). After 1 h at room temperature the mixture was filtered and the filtrate concentrated under reduced pressure. Diethylether was added and the organic phase was separated, washed with water (twice), dried (Na_2SO_4) and concentrated under reduced pressure. The 4-*O*-*n*-alkyl-2,3-*O*-isopropylidene-D,L-threoses **21** were used in subsequent reactions without purification ($\nu_{c=0}$ = 1736 cm^{-1}).

*4.2.20. 1-O-n-alkyl-2,3-O-isopropylidene-D,L-threitols **22b–d***

To a stirred solution of **21** in 3:1 ethanol–water (100 g l^{-1}) was added $NaBH_4$ (6 equiv). After 30 min at room temperature the solution was concentrated under reduced pressure. Water was added and the mixture extracted with CH_2Cl_2 (200 ml twice). The organic phase was separated, washed with water (twice), dried (Na_2SO_4)

and concentrated under reduced pressure. The 1-*O*-*n*-alkyl-2,3-*O*-isopropylidene-D,L-threitols **22** were isolated after purification by column chromatography with 99:1 hexane–acetone (Table 7). ^{1}H NMR ($CDCl_3$): 3.96 (ddd, 1H, J_{2-3} 8.1 Hz, J_{1b-2} 5.7 Hz, H-2); 3.87 (m, 1H, H-3); 3.75 → 3.51 (m, 3H, H-1a, H-4a, H-4b); 3.46 (dd, 1H, J_{1a-2} 4.6 Hz, J_{1a-1b} 9.7 Hz, H-1a); 3.42 (t, 2H, $J_{\alpha-\beta}$ 6.6 Hz, H-α); 1.53 → 1.21 (CH_2 chain, CH_3-*iso*); 0.83 (t, 3H, $J_{\omega-(\omega-1)}$ 6.6 Hz, H-ω). ^{13}C NMR ($CDCl_3$): 109.2 (C-*iso*); 79.9 (C-3); 76.8 (C-2); 72.0 (C-α); 71.0 (C-1); 62.5 (C-4); 31.6 → 22.6 (CH_2 chain C-β to C-($\omega-1$)); 26.8 (2 × CH_3-*iso*), 14.0 (C-ω).

*4.2.21. 1-O-n-alkyl-D,L-threitols **23b–d***

22 was deacetalized in the conditions used for **16**. The 1-*O*-*n*-alkyl-D,L-threitols **23** were isolated after purification by column chromatography with 7:3 hexane–acetone (Table 7). ^{1}H NMR (C_5D_5N): 4.47 (ddd, 1H, J_{1a-2} 6.4 Hz, J_{1b-2} 5.4 Hz, H-2); 4.34 (m, 1H, H-3); 4.27 (dd, 1H, J_{4b-3} 4.4 Hz, J_{4a-4b} 9.8 Hz, H-4b); 4.22 (dd, 1H, J_{4a-3} 5.6 Hz, H-4a); 4.00 (dd, 1H, J_{1a-1b} 9.6 Hz, H-1b); 3.91 (dd, 1H, H-1a); 3.50 (t, 2H, $J_{\alpha-\beta}$ 6.6 Hz, H-α) 1.61 → 1.17 (CH_2 chain); 0.83 (t, 3H, $J_{\omega-(\omega-1)}$ 6.8 Hz, H-ω). ^{13}C NMR (C_5D_5N): 73.9 (C-1); 73.6 (C-3); 72.0 (C-α); 71.6 (C-2); 64.9 (C-4); 32.4 → 23.2 (CH_2 chain C-β to C-($\omega-1$)); 14.6 (C-ω).

*4.2.22. 1,2-O-isopropylidene-D,L-threitol (**24**)*

To a stirred solution of D,L-threitol (15 g, 123 mmol) in acetone (200 ml) was added 600 mg of 36N H_2SO_4. After 80 min at room temperature the mixture was neutralized with solid $NaHCO_3$, filtered and the filtrate concentrated under reduced pressure. The 1,2-*O*-isopropylidene-D,L-threitol (**24**) was isolated after purification by column chromatography with 9:1 hexane–acetone. Yielded 7.8 g (39%) as an oil. ^{13}C NMR ($CDCl_3$): 108.6 (C-*iso*); 76.6 (C-3); 71.9 (C-2); 65.7 (C-1); 63.9 (C-4); 26.3 and 25.1 (CH_3-*iso*).

*4.2.23. 1,2-O-isopropylidene-4-O-trityl-D,L-threitol (**25**)*

24 (9.6 g, 59 mmol) was tritylated in the conditions used for **17**. The 1,2-*O*-isopropylidene-4-*O*-trityl-D,L-threitol (**25**) was isolated after purification by column chromatography with 4:1 hexane–acetone. Yielded 16.7 g (70%) as an oil. ^{1}H NMR ($CDCl_3$): 7.30 → 6.80 (H aromatic); 4.14 (m, 1H, J_{1b-2} 5.3 Hz, J_{1a-2} 3.9 Hz, H-2); 3.88 (ddd, 1H, J_{4a-3} 5.0 Hz, J_{4b-3} 4.5 Hz, H-3); 3.66 (dd, 1H, J_{4a-4b} 11.7 Hz, H-4b); 3.58 (dd, 1H, H-4a); 3.21 (dd, 1H, J_{1a-1b} 9.9 Hz, H-1b); 3.10 (dd, 1H, H-1a); 1.15 and 1.12 (2s, CH_3-*iso*). ^{13}C NMR ($CDCl_3$): 143.2 (C-*ipso*); 128.0 (C-*ortho*); 127.1 (C-*meta*); 126.3 (C-*para*); 108.2 (C-*iso*); 86.0 (C-trityl); 79.2 (C-3); 76.7 (C-2); 61.7 (C-4); 26.4 and 26.3 (CH_3-*iso*).

*4.2.24. 3-O-n-alkyl-1,2-O-isopropylidene-4-O-trityl-D,L-threitols **26b** and **26d***

25 was alkylated in the conditions used for **2** with the corresponding alkyl bromide (1.3 equiv) and powdered KOH (2.5 equiv). The 3-*O*-*n*-alkyl-1,2-*O*-isopropylidene-4-*O*-trityl-D,L-threitols **26** were isolated after purification by column chromatography with 49:1 hexane–acetone (Table 7). ^{1}H NMR ($CDCl_3$): 7.45 → 7.19 (H aromatic); 4.04 (ddd, 1H, J_{4a-3} 5.9 Hz, H-3); 3.95 (ddd, 1H, J_{1b-2} 4.9 Hz, H-2); 3.56 (dd, 1H, J_{4b-3} 3.6 Hz, H-4b); 3.50 (dd, 1H, J_{4a-4b} 10.4 Hz, H-4a); 3.42 (m, 2H, H-α, H-α'); 3.30 (dd, 1H, J_{1a-1b} 9.7 Hz, H-1b); 3.20 (dd, 1H, J_{1a-2} 5.0 Hz, H-1a); 1.52 → 1.24 (CH_2 chain, CH_3-*iso*); 0.86 (t, 3H, $J_{\omega-(\omega-1)}$ 6.6 Hz, H-ω). ^{13}C NMR ($CDCl_3$): 143.8 (C-*ipso*); 128.7 (C-*ortho*); 127.7 (C-*meta*); 127.0 (C-*para*); 109.4 (C-*iso*); 86.8 (C-trityl); 78.0 (C-3); 77.1 (C-2); 71.8 (C-α); 71.5 (C-4); 64.5 (C-1); 37.8 → 22.6 (CH_2 chain C-β to C-($\omega-1$)); 27.1 and 27.0 (CH_3-*iso*), 14.0 (C-ω).

*4.2.25. 2-O-n-alkyl-D,L-threitols **27b** and **27d***

26 was deacetalized in the conditions used for **16**. The 2-*O*-*n*-alkyl-D,L-threitols **27** were isolated after purification by column chromatography with 7:3 hexane–acetone (Table 7). ^{1}H NMR ($CDCl_3$): 3.75 (m, 1H, H-3); 3.74 → 3.67 (m, 3H, H-2, H-4a, H-4b); 3.64 (m, 1H, H-3); 3.51 (d, 2H, J_{1-2} 4.9 Hz, H-1a, H-1b); 3.42 (t, 3H, $J_{\alpha-\beta}$ 6.7 Hz, H-α); 1.55 → 1.21 (CH_2 chain); 0.83 (t, 3H, $J_{\omega-(\omega-1)}$ 6.6 Hz, H-ω). ^{13}C NMR ($CDCl_3$): 72.5 (C-1); 72.1 (C-2); 71.8 (C-α); 70.8 (C-3); 64.3 (C-4); 31.8 → 22.6 (CH_2 chain C-β to C-($\omega-1$)); 14.0 (C-ω).

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