Amphiphilic Carbohydrate-Based Mesogens, 4 [1]
Synthesis of a Homologous Series of Mesogenic 1-O-*n*-Alkyl-D-mannitols

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Dedicated to Prof. Dr. Roland Köster on the occasion of his 65th birthday

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Liquid Crystals, 1-O-*n*-Alkyl-D-mannitols, Glycoside Reductions

Regioselective reduction of a homologous series of O-*n*-hexyl to O-*n*-hexadecyl 2,3:5,6-bis-O-ethylboranediyl-β-D-mannofuranosides, **1a–k** is achieved with ethyldiboranes(6) in the presence of 9-methanesulfonyloxy-9-borabicyclo[3.3.1] nonane [MSBBN]. After deboronation the mesogenic 1-O-*n*-alkyl-D-mannitols **2a–k** are obtained, the liquid crystal ranges and solid state transitions of which are determined by D.S.C.

Introduction

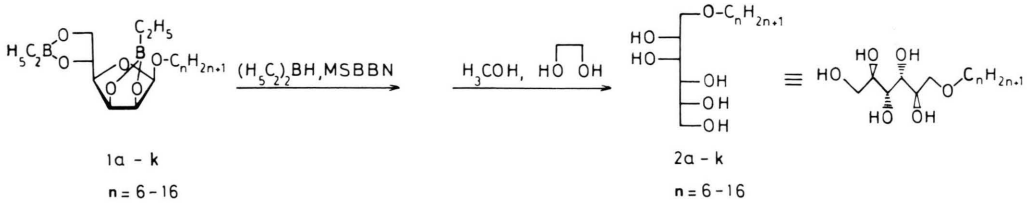
Alditols which are ether-linked to lipophilic moieties can have important biological functions. Thus, for example, the simple amphiphile 1-O-*n*-pentyl-D/L-glycerol can permeate the blood-brain-barrier [2]. Ether phospholipids are naturally occurring membrane components which have potent platelet activating ability [3] and unsymmetrical double-reacted alditol ethers have been found to be bacterial membrane components [4].

It has also been shown that amphiphilic carbohydrates which have acyclic head-groups can also form liquid crystals [5]. Certain 1-C-[6] [7], 1-O-[8] and 1-S-*n*-alkyl alditols [9] are mesogenic, as are the double-tailed aldose di-*n*-alkyl-dithioacetals [10] and double-headed mannitol ethers [1]. N-alkyl-aldonamides [11, 12] and *n*-alkyl-gluconates [13] are less stable and decompose in the mesophase. The *n*-alkyl-aldonamides have recently been reported to show interesting head-group dependent aggregation behaviour in water and xylene [14].

Below we report on the synthesis of a homologous series of stable amphiphilic 1-O-*n*-alkyl-D-mannitols by regioselective reductions of the ethylboranediyl protected *n*-alkyl-β-D-mannofuranosides.

Results and Discussion

O-*n*-Alkyl-2,3:5,6-bis-O-ethylboranediyl-mannofuranosides, **1a–k,** with aglycones ranging from *n*-hexyl to *n*-hexadecyl, served as educts in the reductions. **1a–k** are readily prepared and isolated in 60–70% yields by stereoselective glycosylations of 2,3:5,6-bis-O-ethylboranediyl-α-D-mannofuranosyl bromide with the sodium *n*-alkyl-oxytriethylborates [15]. The glycosides **1a–k** are quantitatively reduced under standard conditions [16] by heating them with ethyldiboranes(6) in the presence of 0.1 equivalent of 9-methanesulfonyloxy-9-borabicyclo[3.3.1]-nonane (MSBBN) [17]. Regioselective hydroborations of the endocyclic acetal linkages occur and the desired 1-O-*n*-alkyl-D-mannitols (**2a–k**) are obtained in 58–76% yields after concentrating the product mixtures *in vacuo* and then deboronating the residue with methanol and ethane-1,2-diol (see typical experiment and Table I).



Scheme 1.

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Table I. Yields and analytical data for the 1-O-*n*-alkyl-D-mannitols **2a–k.**

Compound	Yield[a] [%]	Formula [mol.Wt.]	Analyses C calcd (found)	H calcd (found)	H^{+b} calcd (found)	$[\alpha]_D^{20}$ (c, DMSO)	MS[c]
2a	70	$C_{12}H_{26}O_6$ [266.3]	54.12 [53.53]	9.84 [9.37]	1.89 [1.92]	9° [0.7]	284
2b	76	$C_{13}H_{28}O_6$ [280.4]	55.69 [55.51]	10.00 [9.93]	1.80 [1.81]	4.8° [0.7]	298
2c	58	$C_{14}H_{30}O_6$ [294.4]	57.12 [57.03]	10.27 [10.19]	1.71 [1.75]	8.6° [0.6]	312
2d	60	$C_{15}H_{32}O_6$ [308.4]	58.42 [58.29]	10.46 [10.12]	1.63 [1.61]	2.9° [1.6]	326
2e	58	$C_{16}H_{34}O_6$ [322.5]	59.60 [60.38]	10.63 [10.85]	1.56 [1.50]	8.8° [2]	340
2f	67[d]	$C_{17}H_{36}O_6$ [336.5]	60.68 [61.02]	10.78 [10.50]	1.50 [1.47]	4.6° [1.5]	354
2g	71	$C_{18}H_{38}O_6$ [350.5]	61.68 [61.55]	10.93 [10.82]	1.44 [1.36]	6.3° [1.1]	368
2h	58	$C_{19}H_{40}O_6$ [364.5]	62.60 [62.27]	11.06 [10.93]	1.38 [1.30]	6.9° [1.3]	382
2i	68	$C_{20}H_{42}O_6$ [378.6]	63.46 [63.16]	11.18 [10.78]	1.33 [1.35]	5.5° [1.5]	396
2j	71	$C_{21}H_{44}O_6$ [392.6]	64.25 [63.84]	11.30 [10.95]	1.28 [1.24]	4.5° [1.9]	410
2k	75	$C_{22}H_{46}O_6$ [406.6]	64.99 [65.38]	11.40 [10.89]	1.24 [1.26]	3.7° [1.7]	424

[a] Yields of isolated products after reductions of **1a–k** and subsequent deboronations; [b] determined by using activated triethylborane [18]; [c] $[M+NH_4]$ parent ions were found by DCI-MS using ammonia as the reactant gas [19]; [d] after recrystallization from ethanol.

Table II. D.S.C. Data for **2a–k**[a].

Compound	Heating scan[b]	Solid-state Transition[c] [°C]	m.p. [°C]	ΔH [KJ mol^{-1}]	c.p. [°C]	ΔH [KJ mol^{-1}]
2a	1	–	95	39	102[d]	1[d]
	2	–	95	38.5	102[d]	1[d]
2b	1	24 [1.2]	100	45.8	132	2
	2	–	98.5	44.2	131	1.8
2c	1	96.7 [5.1]	103.7	50.8	144.4	1.6
	2	–	103.5	50.1	144.2	1.8
2d	1	90 [1.3]	102.3	46.7	155.4	1.8
	2	90 [1.8]	102.1	46.3	155.6	1.8
2e	1	92 [4.8], 103.5 [6], 107 [7.8]	107.5	61.5	162	1.7
	2	–	103.2	54.4	161.3	1.7
2f	1	102.3 [1.1]	114.0	51.7	165	0.8
	2	69 [1.8], 82 [0.4], 88 [0.4], 97.5 [0.6], 110.5 [2.3]	113	51	165	0.8
2g	1	89 [4], 106.4 [1.1]	111.2	57.5	167	1.3
	2	88 [4], 109 [3.7]	111.1	57.5	167	1.3
2h	1	70 [2.4], 80 [2.1]	113	60.4	166.3	1.1
	2	70 [2.7], 80 [2.4], 108 [24]	113	35	166	1.2
2i	1	68 [0.9], 75 [0.9], 100 [5]	105.3	51	158	1.5
	2	66 [1], 73 [1.3]	101	50	158.7	1.3
2j	1	–	111.5	61.8	161.5	0.8
	2	51 [1.3]	111.3	60.8	161.8	0.8
2k	1	–	114.3	80	162.6	0.9
	2	52[2.2]	114.5	78	162.7	0.9

[a] Determined with a DuPont 1090–910 calorimeter. Heating rate 10 °C min^{-1}; [b] all the first heating scans with samples which had been recrystallized from ethanol. Reheats were measured <1 h after the first heating scan; [c] enthalpies (KJ mol^{-1}) in brackets [ ]. The temperatures are given at the transition minima; [d] found on cooling the isotropic melt.

Any competing reductive cleavage of the glycosidic bonds of **1** gives 2,3:5,6-bis-*o*-ethylboranediyl-1,4-anhydro-D-mannitol and ethylborane derivatives of the aglycones, both of which are removed by concentrating the product mixture *in vacuo*.

2a–k are colourless solids which were crystallized from ethanol prior to their analyses. All of these 1-O-*n*-alkyl-D-mannitols are stable mectogens, as is easily established by polarizing microscopy [20] and both the liquid crystal ranges and any solid-state changes were determined by D.S.C. (Differential Scanning Calorimetry).

In contrast to the mesogenic O-*n*-alkyl-β-D-mannofuranosides, which have no solid state phase changes prior to melting, the 1-O-*n*-alkyl-D-mannitols, **2a–k,** exhibit a wide range of phase behaviour prior to the mesophase. **2a** is the only member of the homologous series that shows no solid-state transition in both the first and second heating scans using D.S.C. In most cases there are differences between the first heating cycle using recrystallized samples and the subsequent scans [see Table II]. The greatest differences in the first and second heating cycles are found for the 1-O-*n*-decyl- and 1-O-*n*-undecyl-D-mannitols **2e** and **2f,** respectively. Whereas **2e** has three crystal-to-crystal transitions in the first heating cycle, no solid phase changes are detected in the second and any further heating cycles. **2f,** on the other hand, has only one solid-state phase change within the first heating cycle but upon reheating, five solid-state transitions are detected by D.S.C. 1-O-*n*-tridecyl-D-mannitol, **2h** is exceptional in this series as a major solid-state phase change is brought about after the first heating scan.

The synthetic methodology for preparing 1-O-alkyl alditols by regioselective endocyclic acetal bond hydroborations of O-ethylborane protected glycosides, is not restricted to the mannityl ethers presented here. The same approach has been successfully applied to prepare 1-S-*n*-alkyl-D-mannitols in good yields [9] and also other amphiphilic 1-O-substituted alditols [21]. It is hoped that some of these stable amphiphiles will find usage for the solubilization and reconstitution of membrane proteins [22].

Experimental Section

All experiments were carried out under an atmosphere of dry argon. The O-ethylboranediyl protected *n*-alkyl-β-D-mannofuranosides (**1a–k**) were prepared as described previously [15].

Typical experiment: 1-O-*n*-alkyl-D-mannitols (**2a–k**) by reductions of 1-O-*n*-alkyl-β-D-mannofuranosides (**1a–k**) and subsequent deboronations.

MSBBN (~1 mmol) is added to the *n*-alkyl-β-mannofuranoside (~10 mmol) followed by addition of ethyldiboranes(6) (~40 mmol) and the stirred mixture is heated to 120 °C (bath) for *ca.* 4 h. The colourless mixture is concentrated *in vacuo* (10^{-3} torr) and the volatiles are distilled off (bath temperature 100–120 °C/10^{-3} torr). The viscous residue is then deboronated by adding methanol (10 ml) and 3 ml portions of ethane-1,2-diol and concentrating *in vacuo* (10^{-3} torr/70 °C). This process is repeated until the residue is boron-free [flame test]. Last traces of glycol are removed by adding ethanol (10 ml) and finally diethyl ether (10 ml) and concentrating *in vacuo* (10^{-3} torr) each time. The 1-O-*n*-alkyl-mannitols **2a–k** are obtained as colourless solids in 57–76% yields. **2a–k** are finally crystallized from hot ethanol. For yields and analytical data see Table I.

Typical ^{1}H and ^{13}C NMR data for the D-mannityl moieties in **2a–k** after per-O-acetylation with acetic anhydride in pyridine. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 5.47 (m, H-3, H-4), 5.08 (m, H-2, H-5), 4.22 (dd, $J_{5,6}$ = 2.9 Hz, $J_{6,6'}$ = 12.5 Hz, H-6), 4.07 (dd, $J_{5,6'}$ = 5.0 Hz, $J_{6,6'}$ = −12.5 Hz, H-6′), 3.53 (dd, $J_{1,2}$ = 4.1 Hz, $J_{1,1'}$ = −10.8 Hz, H-1), −3.45 (dd, $J_{1',2}$ = −5 Hz, $J_{1,1'}$ = −10.8 Hz, H-1). ^{13}C NMR ($CDCl_3$): δ = 71.8, 69.2 (C-1, $COCH_2$), 68.9, 68.5, 68.2, 67.9 (C-2–C-5), 62.1 (C-6).

[1] Part 3: see W. V. Dahlhoff, Z. Naturforsch. **43b,** 1367 (1988). A preliminary account of this work is given in [8].
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