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Synthesis of novel bis(glycosyl) ethers as bolaamphiphile surfactants

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Abstract

We have synthesized new bolaamphiphile carbohydrate derivatives having general structures A-O-$(CH_2)_n$-O-B or [A-O-$(CH_2)_n$]$_2$C(OH)R. The hydrophilic heads A and B (identical or different) are D-glucose, D-galactose, xylitol, or their respective protected derivatives, and R is an alkyl chain. The carbohydrate units A and B are condensed in the first step as di-*O*-isopropylidene derivatives with either α,ω-dibromo- or dimesyl-alkanes in the presence of powdered KOH in 9:1 or 4:1 toluene–Me_2SO. Appropriate choice of either selective or total deprotection of acetal groups and either regioselective esterification or regiospecific etherification allows modulation of either the hydrophilic or the lipophilic character of these new surfactants. The ether junctions between the alkyl chain and carbohydrate moiety proved resistant to severe acid-hydrolytic conditions.

Keywords: Bis(glycosyl) ethers, novel; Bolaamphiphile surfactants; Synthesis

1. Introduction

Compounds having two hydrophilic heads linked by either one or two alkyl chains fall into the class of surfactants known as bolaamphiphiles [1] (otherwise known as bolaform amphiphiles [2] or bolaform surfactants [3]). Such products, cited in the literature as vesicules and liquid-crystal generators, are categorized as either ionic [3,4] or non-ionic [4–10]. In the latter, the carbohydrate derivatives have two hydrophilic heads which can be *O*-glycoside, [8,10] thioglycoside [4], or glyconamide [9] groups.

We describe herein the synthesis and some surfactant properties of new bolaamphiphile carbohydrate derivatives having the general structures A-O-$(CH_2)_n$-O-B [namely,

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bis(glycosyl) ethers] and $[A\text{-}O\text{-}(CH_2)_n]_2C(OH)R$ in which R is an alkyl chain, and the hydrophilic groups A and B [identical (A = B) or different (A ≠ B)] are derived from D-galactose, D-glucose, or xylitol with either free or protected hydroxyl groups. The key step in their synthesis involves the reaction of a free hydroxyl group of a diacetalated sugar (A and/or B) with either an α,ω-dibromo- (**4**) or dimesyl-alkane (**5**). This reaction can be used to synthesize, in one step, symmetrical bis-molecules of the types **7**, **10**, and **13**. Alternatively, asymmetric molecules of the types **15** and **16** may be synthesized by first derivatizing either **4** or **5** with one sugar unit and then by substituting the remaining bromo or mesyl group by a second sugar unit.

An established method for effecting ether linkages in carbohydrate chemistry is to react the carbohydrate hydroxyl group with either an alkyl halide or corresponding sulfonate derivative using NaH as base and pure DMF as solvent. However such conditions are problematic on an industrial scale because of the hazardous nature of NaH, the toxicity of DMF, and the cost of operating with these reagents. Such disadvantages have prompted us to adopt alterative reaction conditions involving KOH as the base and toluene–Me_2SO as solvent. Dimethyl sulfoxide has the advantages of being relatively non-toxic [11] and an efficient solvent for polar and non-polar reagents. In particular it permits (as does DMF) dissociation of such bases as KOH, which is a weaker base than either NaH or potassium *t*-butoxide, by specifically solvating K^+ ions. Thus the availability of OH^- leads, in turn, to the carbohydrate alkoxide ions (sugar-O^-) required for nucleophilic substitution in accordance with the following equilibria:

$$KOH \rightleftharpoons [K\cdots(Me_2SO)_n]^+ + OH^-$$

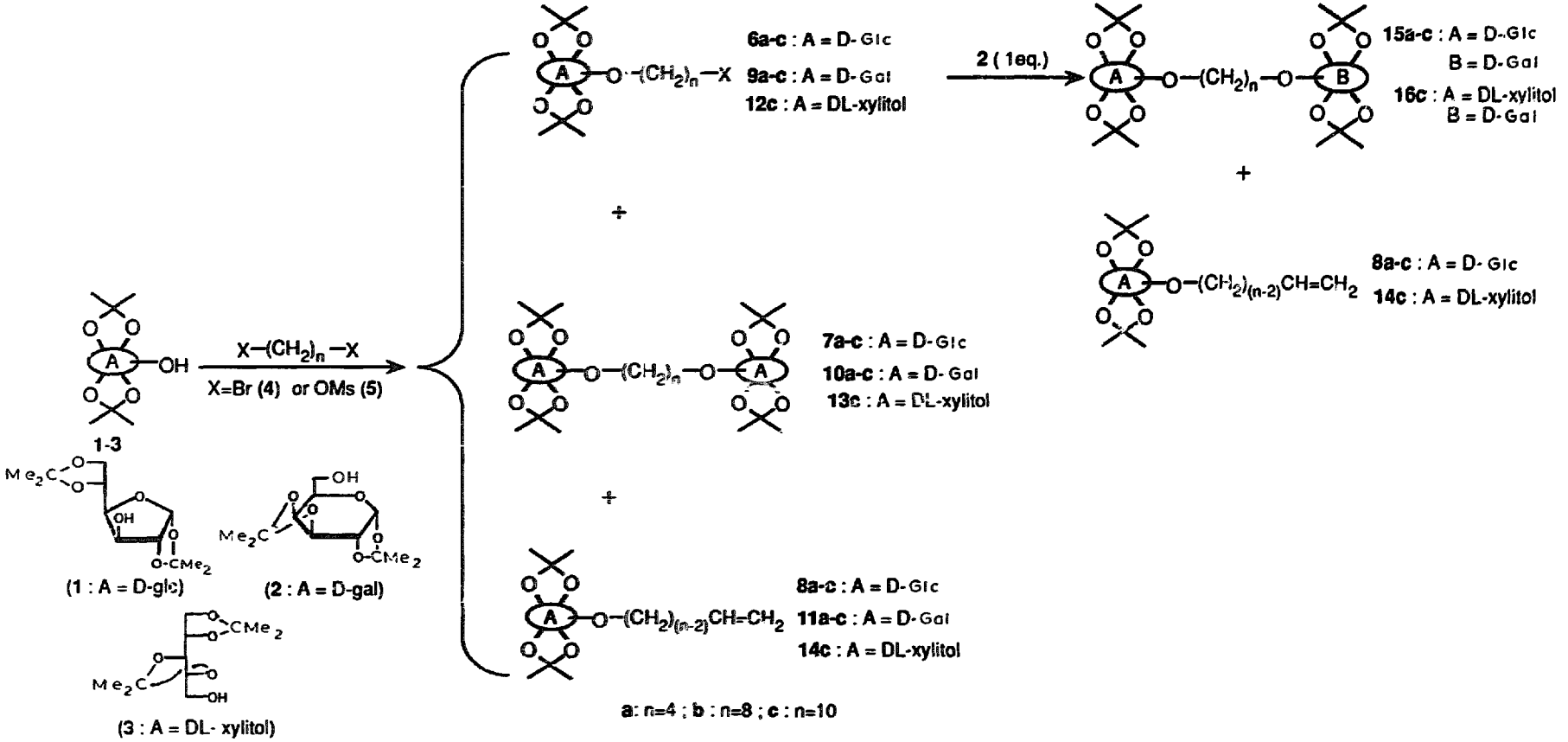
$$Sugar\text{-}OH + OH^- \rightleftharpoons Sugar\text{-}O^- + H_2O$$

Dimethyl sulfoxide can also solvate K^+ ions in the solvent mixture toluene–Me_2SO.

The design of the new bolaamphiphiles described herein, and the synthetic strategies involved took into account the choice of substrates, reagents and solvents with the objective of: (*a*) avoiding the use of the Koenigs–Knorr type of reaction which is used to obtain the analogous glucoside products [8,10], and less easy to implement; (*b*) effecting an ether junction between an alkyl chain and a specific non-anomeric site of a carbohydrate unit that is more resistant to hydrolysis than a carbohydrate glycosidic junction; (*c*) allowing the selective deprotection of *O*-isopropylidene groups according to the nature of the carbohydrate units A and B in order to either modulate the hydrophilicity of the products or attach, with the desired regiospecificity, additional functional groups such as lipophilic tails; and (*d*) permitting eventual industrial applications.

2. Results and discussion

All of the products described herein were obtained by condensation of di-*O*-isopropylidene derivatives of D-galactose, D-glucose, and xylitol, respectively, with either α,ω-dibromo- or dimesyl-alkanes in the presence of KOH. This was followed by either selective or total deprotection of the acetal groups and in some cases further derivatization of the partially deprotected compounds.


X–(CH2)n–X
X=Br (4) or OMs (5)
1-3
(1 : A = D-glc)
(2 : A = D-gal)
(3 : A = DL- xylitol)
6a-c : A = D-Glc
9a-c : A = D-Gal
12c : A = DL-xylitol
2 (1eq.)
15a-c : A = D-Glc
B = D-Gal
16c : A = DL-xylitol
B = D-Gal
8a-c : A = D- Glc
14c : A = DL-xylitol
7a-c : A = D-Glc
10a-c : A = D- Gal
13c : A = DL-xylitol
8a-c : A = D-Glc
11a-c : A = D-Gal
14c : A = DL-xylitol
a: n=4 ; b : n=8 ; c : n=10

Scheme 1.

Table 1
GPC determination of the product distribution and the diacetal conversion from the reaction of di-*O*-isopropylidene derivatives (**1–3**) with dibromo- (**4**) or dimesyl-alkane (**5**) in the presence of KOH

	Reaction conditions			Conversion of the diacetal (%)	Distribution of products (%)		
Diacetal A	4/5	Method	Time (h)	A	**6a–c**	**7a–c**	**8a–c**
1	**4a**	I	5	60	87	9	4
	4a	II	16	56	2	88	10
	5a	III	8	90	10	90	0
	4b	I	6	68	82	13	5
	4b	II	16	92	8	72	20
	4c	I	6	68	69	27	4
	4c	II	16	88	7	70	23
					9a–c	**10a–c**	**11a–c**
2	**4a**	I	6	66	78	18	4
	4a	II	16	54	3	85	12
	5a	III	9	88	11	89	0
	4b	I	6	70	73	22	5
	4b	II	16	81	10	69	21
	4c	I	6	75	65	30	5
	4c	II	16	79	7	66	27
					12c	**13c**	**14c**
3	**4c**	I	6	65	79	14	7
	4c	II	16	76	10	66	24

Condensation of the di-O-isopropylidene unit A on the alkyl derivatives X-(CH_2)$_n$-X.— The reaction led, as outlined in Scheme 1, to the monosubstitution of alkyl derivatives of the types **6**, **9**, and **12**, followed by bis-substitution products of the types **7**, **10**, and **13**, or the elimination of XH to give products of the types **8**, **11**, and **14**.

This reaction was, first of all, effected using Method I which involved the initial concentrations [**1–3**]$_0$:[**4**]$_0$:[KOH]$_0$ = 0.40 M:0.50 M:1.0 M in 9:1 toluene–Me_2SO at room temperature. The results given in Table 1 show that, after 5 or 6 h of reaction time, 60–75% of diacetal (**1–3**) had been consumed, while all of the alkyl substrate (**4**) had reacted to give the corresponding dialkyl derivative (corresponding to the substrate undergoing a double elimination reaction) and three di-*O*-isopropylidene derivatives illustrated in Scheme 1. It is noteworthy that these experimental conditions largely favored the formation of the monosubstituted product (relative proportions ranging from 65–87% for compounds of the types **6**, **9**, and **12**; yields after purification were 43–53%).

Method I gave in each case a satisfactory yield of the monosubstituted products (**6**, **9**, or **12**, respectively) which are precursors of bolaamphiphiles of the general structures A-O-(CH_2)$_n$-O-B or [A-O-(CH_2)$_n$]$_2$C(OH)R. Nevertheless, it was found possible to favor the formation of disubstituted derivatives with the same sugar head group (compounds of type **7**, **10**, and **13**) by changing the experimental conditions in this first step. For example, when, the initial concentration [**4a**]$_0$ was 0.25 M instead of 0.50 M, the disubstituted compound (**7a**) became the major product, but the diacetal **1** consumption was lowered (30% of diacetal **1** conversion after 16 h). This result can be explained by the relatively low initial concentration [**4a**]$_0$ which slows the formation of both the monosubstituted compound **6a**

Table 2
GPC determination of the product distribution and the diacetal conversion from the condensation of 1,2:3,4-di-*O*-isopropylidenegalactose (**2**) with the monosubstituted substrates **6a–c** and **12c** using Method I

Substrate	Time (h)	Substrate conversion (%)	Distribution of products (%) (isolated products %)	
			15	**8**
6a	17	92	69 (61)	31 (27)
6b	21	92	63 (54)	37 (30)
6c	28	94	67 (58)	33 (28)
			16	**14**
12c	15	84	81 (67)	19 (15)

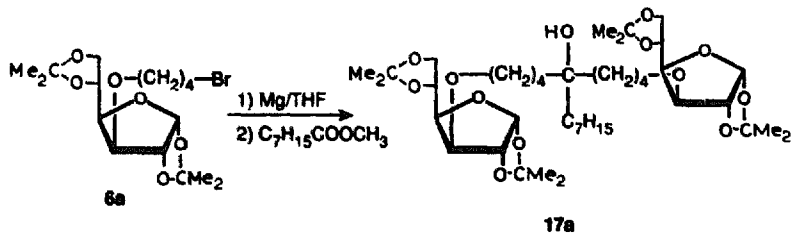
and disubstituted compound **7a**. However, the reaction was accelerated when the proportion of Me_2SO in the medium was increased: thus, the reaction conditions were modified in the form of Method II [initial concentration of reagents: $[\mathbf{1}\text{–}\mathbf{3}]_o$:$[\mathbf{4}]_o$:$[KOH]_o = 0.40$ M:0.25 M:1.0 M; 4:1 toluene–Me_2SO, at room temperature]. The results obtained using the latter are presented in Table 1. They show that, after 16 h of reaction, the percentage of the di-*O*-isopropylidene starting material consumed ranged from 54–92% and the relative proportion of the disubstituted product obtained, ranged from 66–88%.

Since it was found that the reactivity of the dihaloalkane decreased with an increase in the number of carbon atoms, it was surprising to observe that the percentage consumed of the diacetal for the same reaction time went in the reverse order using Methods I or II. However this result is probably because of the more-important contribution of the double elimination process for the 1,4-dibromobutane (**4a**), which is accelerated in the last step by the homoallylic assistance of the C-3–C-4 π-orbital. This is supported by the observation that a very low proportion of substituted product was obtained from 1,3-dibromopropane (the first elimination leading to allyl bromide) under the same reaction conditions. The elimination process is less favored with sulfonic esters than with the corresponding alkyl halides. For these reasons, we repeated the condensation using Method III. This involved a modification of Method II in which the dibromoalkane (**4a**) was replaced by dimesylalkane (**5a**), and the temperature was 50°C. The results in Table 1 show that, with the latter substrate, only mono- and di-substituted compounds were obtained.

*Condensation of the second di-*O*-isopropylidene unit B with the monosubstituted products* **6**, **9**, *and* **12**.—The condensation of the diacetal unit B with the monosubstituted derivatives (**6**, **9**, and **12**), according to the procedures outlined in Scheme 1, led to the diacetal precursors of the mixed bolaamphiphiles having the structure A-O-$(CH_2)_n$-O-B (**15a–c**, **16c**).

Using Method I, 1,2:3,4-di-*O*-isopropylidene-D-galactose (**2**) was condensed with the monosubstituted derivatives of 1,2:5,6-di-*O*-isopropylidene-D-glucose (**6a–c**), and 2,3:4,5-di-*O*-isopropylidenexylitol (**12c**), respectively. The byproduct of this reaction was the elimination product of the monosubstituted substrate (**8a–c** from **6a–c**; **14c** from **12c**). Table 2 gives the distribution of the products formed and their yields after purification.

*Condensation of the monosubstituted di-*O*-isopropylidene derivatives in their Grignard reagent forms, with either esters or acid chlorides.*—The condensation of the above monosubstituted compounds in the form of Grignard reagents were each treated with either an



Scheme 2.

ester or an acid chloride to give the respective precursors of a novel class of bolaamphiphiles having the structure $[A\text{-}O\text{-}(CH_2)_n]_2C(OH)R$ such as compound **17a** (Scheme 2).

The transformation of the monosubstituted derivative **6a** into the corresponding Grignard reagent was complete after 4 h at 70°C in THF. This was reacted with methyl octanoate for 20 h at 70°C, to give the expected product **17a** and three byproducts **18a**, **8a**, and **7b**. Compound **18a** was the 3-*O*-butyl diisopropylidene glucose derivative which resulted from the hydrolysis of the remaining Grignard reagent; compound **8a** resulted from the dehydrohalogenation of compound **6a** and compound **7b** resulted from a Wurtz reaction. The ratio of products **17a**:**18a**:**8a**:**7b**, estimated by GPC, was 57:28:9:6. Similar results were obtained when the ester was replaced by the corresponding acid chloride.

*Selective deprotection of the isopropylidene groups from the bis(glycosyl) ethers (***6a–c**, **15a**, *and* **16c**).—This step concerns disubstituted compounds in which the di-*O*-isopropylidene form of unit A was derived from either glucose or xylitol and unit B was the di-*O*-isopropylidene protected galactose. It was found that acid-catalyzed deprotection of the isopropylidene groups was more rapid at the 5,6-site of D-glucofuranose and at both acetal sites of xylitol than at the 1,2-site of D-glucofuranose and both sites of D-galactopyranose. We have performed the selective deprotection of symmetrical (A = B = D-glucose) and mixed (A = D-galactose; B = D-glucose and A = DL-xylitol; B = D-galactose) disubstituted derivatives following Scheme 3, operating in 19:1 ethanol–water at 50°C in the presence of dilute (0.05 or 0.1 M) sulfuric acid.

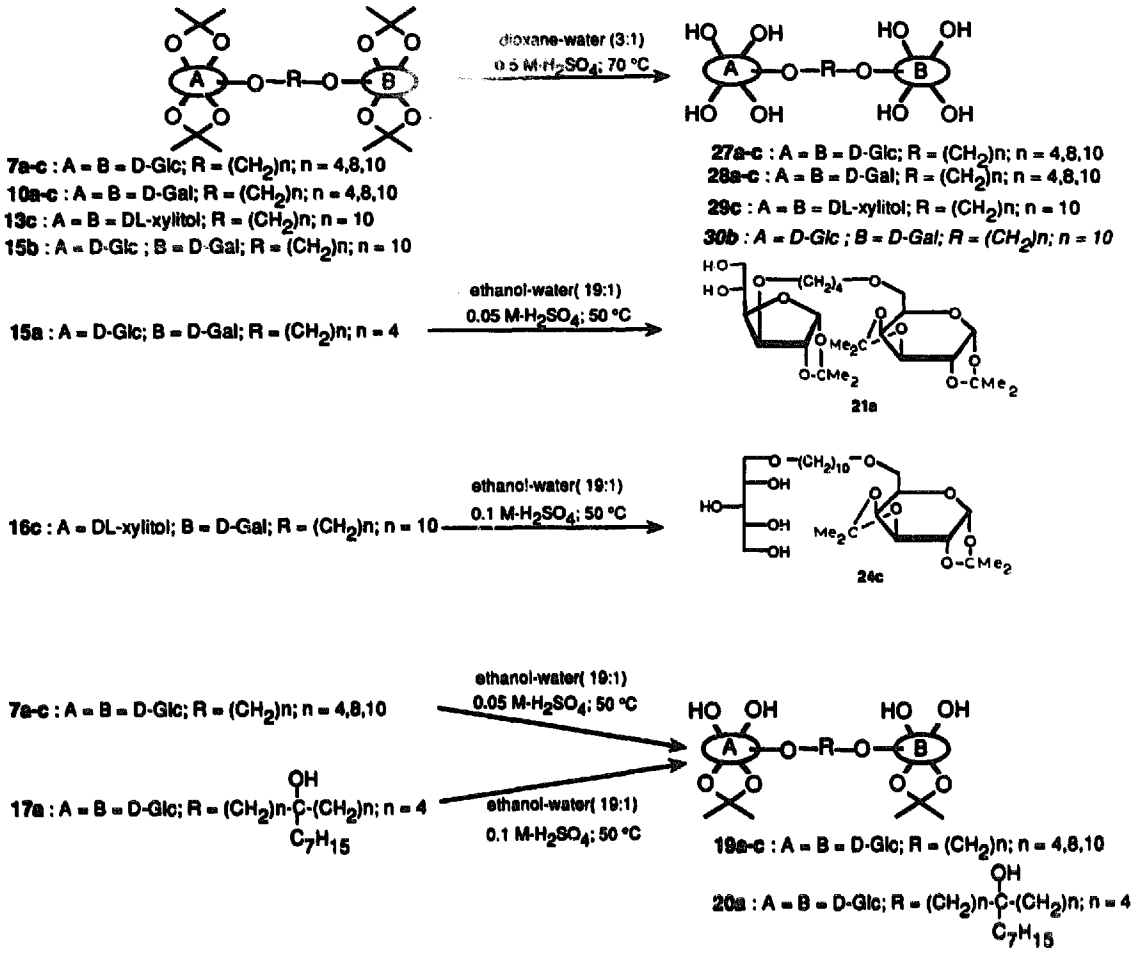
The results given in Table 3 show, for symmetrical derivatives of D-glucose (**6a–c** and **17a**), that yields of isolated compounds reached 80% when their alkyl moieties have four carbon atoms and decreased when the length of their alkyl moieties was increased. In the latter cases, there was also found to be a significant amount of a product corresponding to the deprotection of the 5,6-*O*-isopropylidene group on one of the D-glucose units.

Derivatization of the compounds of types **19** *and* **21**.—Compounds of the type **19a–c** and **21a** having two free OH groups on both D-glucose units and compound **21a** having two free OH groups on the sole D-glucose unit were found to be readily derivatized either regioselectively or regiospecifically.

Compound **19a** was esterified, regioselectively, following Scheme 4. After 4 h of reaction at room temperature, pure **25a** was isolated in 70% yield.

The regiospecific monoetherification of **21a** was effected according to Scheme 5. The overall yield obtained from this sequence of reactions was modest (20% of **26a**) because in step (c) the basic medium favored other competitive condensations on the anhydro derivative **23a**.

Total deprotection of products obtained in the previous steps.—In order to accelerate the deprotection of the *O*-isopropylidene group at the 1,2-site of D-glucofuranose and both



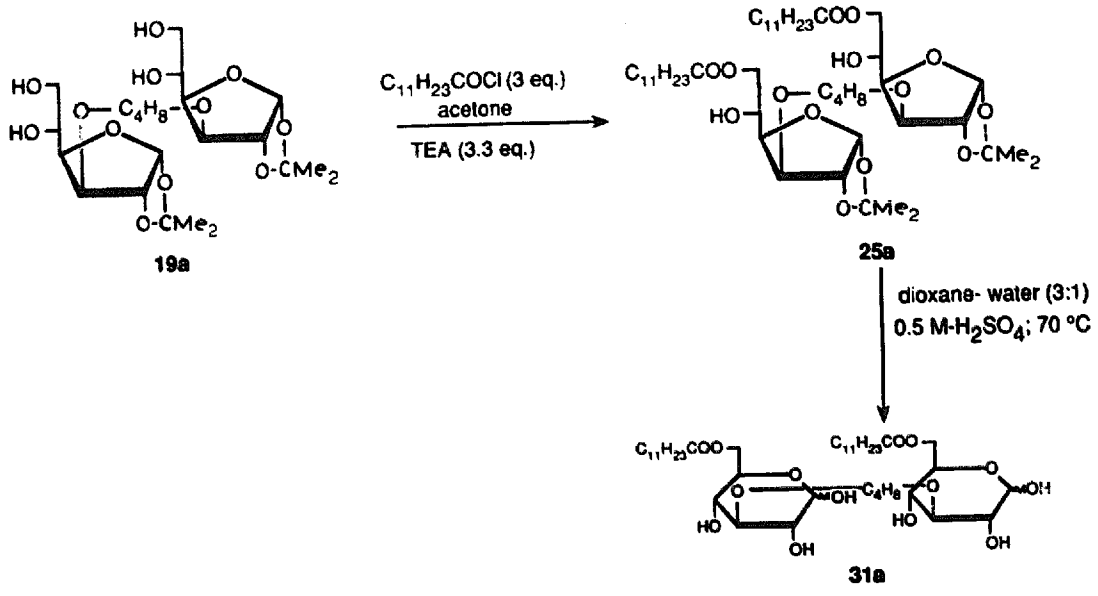
Scheme 3.

acetal groups of D-galactopyranose, we operated at 70°C, using 0.5 M H_2SO_4 in 3:1 dioxane–water instead of 19:1 ethanol–water to avoid the competing formation of ethyl glycoside derivatives (Scheme 3). The results are given in Table 4.

The low yield with the bis(dodecanoic) ester is because of the deacylation favored under our reaction conditions. For the other substrates, the yields were satisfactory. The decrease in the rate of deprotection with an increase in the alkyl chain length bridging two D-glucose units (**6a–c**), two D-galactose units (**9a–c**), or a D-glucose unit and a D-galactose unit, led

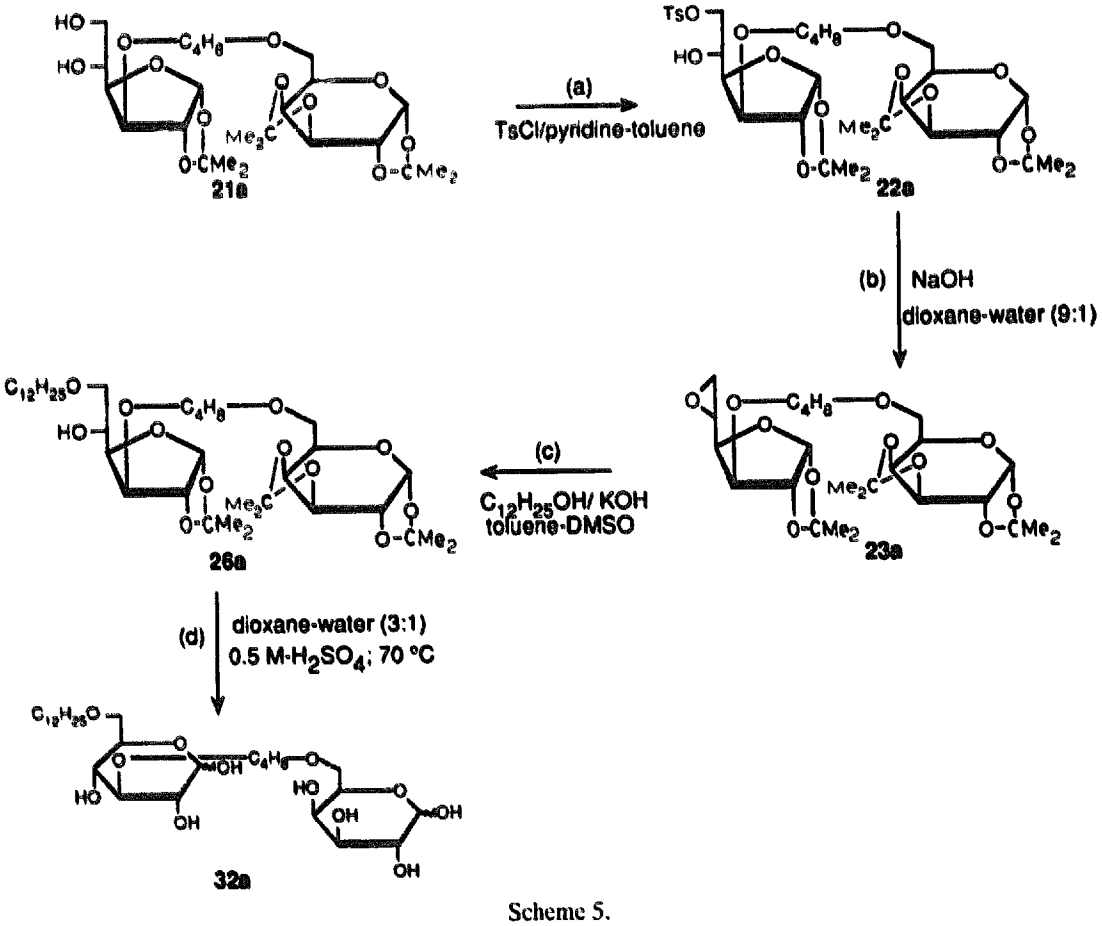
Table 3
Selective deprotection of di-*O*-isopropylidene protected glucose and xylitol moieties at 50°C in 19:1 ethanol–water, monitored by HPLC

Substrate	[H_2SO_4]	Time (min)	Substrate conversion (%)	Isolated yield (%)
7a	0.05 M	200	95	80 (**19a**)
7b	0.05 M	300	90	65 (**19b**)
7c	0.05 M	300	90	60 (**19c**)
15a	0.05 M	240	94	83 (**21a**)
16c	0.1 M	120	95	80 (**24c**)
17a	0.1 M	100	95	60 (**20a**)



Scheme 4.

to a decrease in the yield of totally deprotected compounds. This is because of incomplete deprotection such that only one of the two units is removed when 95% of the initial substrate had been consumed.



Scheme 5.

Table 4
Deacetalization in 0.5 M H_2SO_4 3:1 1,4-dioxane–water solution at 70°C

Substrate	Time (min)	Isolated yield (%)	Product
7a	80	78	**27a**
7b	150	60	**27b**
7c	150	57	**27c**
10a	190	76	**28a**
10b	250	52	**28b**
10c	250	50	**28c**
13c [a]	90	70	**29c**
15b	255	53	**30b**
25a [b]	50	22	**31a**
26a	270	76	**32a**

[a] 0.1 M H_2SO_4 3:1 1,4-dioxane–water.
[b] 40°C instead of 70°C.

It should be emphasized that the ether linkages between the alkyl chain and the carbohydrate derivatives were resistant to the severe acid hydrolytic conditions used, since we did not detect the presence of any byproducts resulting from the cleavage of these linkages.

Examination of surfactant properties.—In a preliminary surface-activity study, the surface tensions (γ) and critical micellar concentrations (CMC) of compounds of types **19c**, **20a**, **24c**, and **27c** were measured in water at 25°C (Table 5).

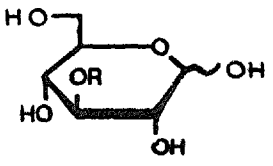
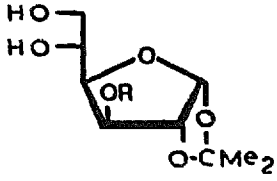
This compound range is too small to allow a meaningful correlation of structural effects on both γ and CMC values. Nevertheless, with the compounds **19c**, **24c**, and **27c** which have the same lipophilic chain ($R = C_{10}H_{20}$) and, respectively, 4, 4, and 8 free hydroxyl groups, CMC values were found to increase with an increase in the hydrophilic part of the sugar groups. Similar observations were made in a recent study [12] of two series of D-glucose derivatives: 3-*O*-alkyl-1,2-*O*-isopropylidene-α-D-glucofuranose and 3-*O*-alkyl-D-glucopyranose compounds (Table 6). Meanwhile, the decrease in CMC values is significant in relation to the increase in chain length (where R has 12–18 carbon atoms) in the D-glucose derivatives (Table 6).

It was also observed that 3-*O*-hexadecyl-D-glucose and compound **20a**, which both have 16 carbon atoms in the lipophilic part R, and which present only a small change in the hydrophilic moiety (4 and 5 free hydroxyl groups, respectively), show similar γ values but a greater difference in CMC values.

Table 5
Surface tension (γ) and critical micellar concentration (CMC) in water at 25°C of compounds **19c**, **20a**, **24c**, and **27c** measured by the Wilhelmy plate method [12]

Product	γ (mN m^{-1})	CMC (10^{-4} M)
19c	38	4.2
20a	35	4.7
24c	38	3.4
27c	32	6.5

Table 6
Surface tension (γ) and critical micellar concentration (CMC) in water at 25°C of D-glucose derivatives [12]

R				
	($mN\ m^{-1}$)	CMC (10^{-4} M)	γ ($mN\ m^{-1}$)	CMC (10^{-4} M)
n-C_8H_{17}	31	10	29.3	10.4
n-$C_{12}H_{25}$	30	0.33	31	2.3
n-$C_{16}H_{33}$	30	0.09	36	0.82
n-$C_{18}H_{37}$	34	0.08	37	0.81

This work should be extended to include the homologous series **19c**, **24c**, and **27c** longer alkyl chains to compare the influence on the CMC values to those observed for the D-glucose derivatives (e.g., Table 6) or other monosaccharide analogues. Further studies on the large range of bolaamphiphile compounds described herein are underway to better establish the relationships between structure and micelle formation. In parallel, vesicle and liquid-crystal aspects are being examined.

3. Experimental

General methods.—Reactions were monitored by (*i*) GPC (Girdel) with columns of either OV-17 or SE-30 (prepared using Girdel products), for condensation reactions; (*ii*) HPLC (Waters 721), using either reverse-phase columns RP-18 (Merck) or PN 27-196 (Waters) and 3:1 → 9:1 acetone–water for deprotection reactions. Preparative chromatography was performed on silica gel (Matrex 60 mesh) and monitored by TLC (D C Kieselgel 60 F_{254} ref. Merck 1.055 54). Specific rotations were determined with a Jasco-Dip 970 polarimeter (Prolabo) in $CHCl_3$ or MeOH. Melting points were determined with a digital melting-point apparatus (Electrothermal) and are uncorrected. ^1H and ^{13}C NMR spectra were performed in $CDCl_3$ unless stated otherwise (internal Me_4Si), using a Brüker WB-300 spectrometer. Surface tensions were measured using a Tensimat No. 3 apparatus (Prolabo). Elemental analyses were performed by the Service Central de Microanalyse du Centre National de la Recherche Scientifique (Vernaison, France). Acetone, hexane, toluene, and sulfuric acid (industrial grade) were supplied by CINAS (Amiens, France); the other reagents and solvents were from Janssen Chimica or Aldrich.

Analytical measurments of the compounds prepared here, and details of the product distribution under the various reaction conditions employed, appear in Tables 1–11, with elemental analyses in Table 10.

Condensation of di-O-isopropylidene units of type A and/or B with either dibromo- (**4**) *or dimesyl-alkane* (**5**) *to give compounds of types* **6**, **7**, **9**, **10**, **12**, **13**, **15**, **16**, *and* **17**.—

Table 7
^{1}H chemical shifts and coupling constants in $CDCl_3$ of compounds **6a**, **7a**, **9a**, and **10a**

Proton	**6a**		**7a**		**9a**		**10a**	
	δ (ppm)	J (Hz)	δ (ppm)	J (Hz)	δ (ppm)	J (Hz)	δ (ppm)	J (Hz)
H-1	5.80	$J_{1,2}$ 3.7	5.80	$J_{1,2}$ 3.7	5.50	$J_{1,2}$ 5.0	5.52	$J_{1,2}$ 5.1
H-2	4.47	$J_{2,3}$ 0	4.45	$J_{2,3}$ 0	4.27	$J_{2,3}$ 2.3	4.30	$J_{2,3}$ 2.4
H-3	3.80	$J_{3,4}$ 3.1	3.79	$J_{3,4}$ 3.1	4.54	$J_{3,4}$ 8.0	4.59	$J_{3,4}$ 7.9
H-4	4.03	$J_{4,5}$ 7.9	4.04	$J_{4,5}$ 7.7	4.23	$J_{4,5}$ 1.7	4.25	$J_{4,5}$ 1.7
H-5	4.21	$J_{5,6}$ 6.0	4.22	$J_{5,6}$ 6.1	3.93	$J_{5,6}$ 6.0	3.95	$J_{5,6}$ 6.2
H-6	4.03	$J_{5,6'}$	4.01	$J_{5,6'}$ 5.9	3.59	$J_{5,6'}$ 6.5	3.63	$J_{5,6'}$ 6.5
H-6′	3.91	$J_{6,6'}$ 8.6	3.91	$J_{6,6'}$ 8.5	3.51	[a]	3.55	[a]

[a] Unresolved.

These reactions were performed using Method I. Diacetal (**1–3**), dibromoalkane (**4**), and powdered KOH in the corresponding concentrations 0.40 M:0.60 M:1.0 M, in 9:1 toluene–Me_2SO were stirred at room temperature. Before product extraction, the mixture was filtered and the filtrate neutralized with a saturated solution of NH_4Cl. The aqueous phase was extracted with toluene and the solvent evaporated. The products of the reaction were isolated by silica gel column chromatography using hexane–acetone mixtures as eluants.

Method II. This method involved modifying Method I by halving the molar concentration of the dibromoalkane (**4**) and changing the solvent to 4:1 toluene–Me_2SO.

Method III. This method involved modifying Method II by replacing the dibromoalkane (**4a**) by dimesylalkane (**5a**) and operating at 50°C.

Use of anhyd Na_2SO_4 as the dehydrating agent in the mixture was ineffective in increasing the yield.

Table 8
^{13}C NMR chemical shifts in $CDCl_3$ of compounds of types **6**, **7**, **9**, **10**, **12**, **13**, and **15–17**

Product	[a]	Glycosyl moiety						Alkyl linkage			
		C-1	C-2	C-3	C-4	C-5	C-6	OCH_2	OCH_2CH2	CH_2Br	R
6a	Glclp	105.2	82.4	82.0	81.1	72.4	67.1	69.3	29.4	33.5	
7a	2×Glclp	105.2	82.4	82.0	81.1	72.4	67.1	70.1	26.3		
9a	$Gallp_2$	96.3	70.5	70.5	71.1	66.7	69.4	71.4	29.2	34.0	
10a	2×$Gallp_2$	96.2	70.5	70.5	71.1	66.6	69.2	71.1	26.12		
12c	Xyl-ollp$_2$	71.3	75.7	78.6	76.3	65.6		71.3	25.9	32.7	
13c	2×Xyl-ollp$_2$	70.6	74.8	77.6	75.5	64.8		70.5	25.3		
15a	Glclp	105.2	82.4	82.0	81.1	72.4	67.1	71.0	25.9		
	$Gallp_2$	96.3	70.5	70.5	71.1	66.7	69.4				
16c	Xyl-ollp$_2$	70.5	74.8	77.7	75.4	64.7		70.5	25.2		
	$Gallp_2$	95.3	69.3	69.3	70.1	64.7	68.2	70.9			
17a	2×Glclp	105.2	82.4	82.1	81.0	72.5	67.1	70.2	30.2		39–14.0

[a] Glclp, 1,2-*O*-isopropylidene-α-D-glucofuranose; $Gallp_2$, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose; $Glclp_2$, 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose; Xyl-ollp$_2$, 2,3:4,5-di-*O*-isopropylidene-DL-xylitlol; R = C_8H_{17}.

Table 9
^{13}C NMR chemical shifts in $CDCl_3$ of compounds of types **19**, **20**, **21**, **24**, **25**, and **29** [a]

Product	[b]	Glycosyl moiety						Alkyl linkage			
		C-1	C-2	C-3	C-4	C-5	C-6	OCH_2	OCH_2CH2	C=O	R
19a	2×GlcIp	105.0	82.4	81.9	79.9	69.1	64.6	70.1	26.4		
19b	2×GlcIp	105.0	82.4	81.9	79.9	69.1	64.6	70.6	29.6		
19c	2×GlcIp	105.0	82.4	81.9	79.9	69.1	64.6	70.6	29.7		
20a	GlcIp	105.0	82.5	81.7	80.0	69.1	64.6	68.6	30.1		39.2
	GlcIp	105.1	82.6	81.7	80.1	69.1	64.8	68.9			14.0
21a	GlcIp	105.0	82.4	81.9	79.9	69.1	64.6	69.9	27.0		
	$GalIp_2$	96.3	70.6	70.3	71.1	66.7	69.4				
24c	Xylitol	70.5	70.2	70.2	71.9	62.8	–	71.1	28.5		
	$GalIp_2$	95.3	69.6	69.6	70.9	65.7	68.4	70.7			
25a	2×GlcIp	105.0	82.6	81.9	79.1	67.7	66.5	70.1	26.3	174.4	
29c	2×Xyl-olIp$_2$	71.6	72.2	72.2	74.2	64.4	–	71.6	26.4		

[a] Assignment was confirmed by selective proton decoupling and 2D ^1H–^1H homonuclear and ^{13}C–^1H heteronuclear COSY experiments.
[b] GlcIp, 1,2-*O*-isopropylidene-α-D-glucofuranose; $GalIp_2$, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose; R = C_8H_{17}.

Each reaction was monitored by GPC to quantify the diacetal conversion and the product distribution.

3-O-(4-Bromobutyl)-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**6a**).—Compound **1** (65.0 g, 250 mmol) was treated with 1,4-dibromobutane (64.8 g, 300 mmol) for 5 h using Method I. Initial elution with 24:1 hexane–acetone yielded 8.7 g of a 4:1 mixture of **6a** and **8a**. Further elution with 19:1 hexane–acetone gave 40.0 g (40%) of **6a** (syrup); $[\alpha]_D^{25}$ −24.6° (*c* 1.1, $CHCl_3$). The ^1H and ^{13}C NMR spectra ($CDCl_3$) are reported in Tables 7 and 8, respectively.

Finally, 4.9 g of **7a** was obtainedafter elution with 93:8 hexane–acetone and was found to be identical to that obtained using Method II.

3-O-(8-Bromooctyl)-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**6b**).—Compound**1** (22.0 g, 84.6 mmol) was treated with 1,8-dibromobutane (27.6 g, 101.5 mmol) for 6 h using Method I. Initial elution with 24:1 hexane–acetone yielded 3.3 g of a 1:1 mixture of **6b** and **8b**. Further elution with 19:1 hexane–acetone gave 26.6 g (50%) of **6b** (syrup); $[\alpha]_D^{25}$ −19.8° (*c* 1.2, $CHCl_3$). The ^1H and ^{13}C NMR spectra for the glucosyl moiety of **6b** were identical ($\Delta \approx 0.05$ ppm) to those of **6a**.

Finally 4.5 g of **7b** was obtained after elution with 23:2 hexane–acetone and was found to be identical to that obtained using Method II.

3-O-(10-Bromodecyl)-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**6c**).—Compound **1** (13.0 g, 50 mmol) was treated with 1,10-dibromodecane (18.0 g, 60 mmol) for 6 h using Method I. Initial elution with 24:1 hexane–acetone yielded 1.9 g of a 3:2 mixture of **6c** and **8c**. Further elution with 19:1 hexane–acetone gave 14.2 g (40%) of **6c** (syrup); $[\alpha]_D^{25}$ −16.9° (*c* 1.1, $CHCl_3$). The ^1H and ^{13}C NMR spectra for the glucosyl moiety were identical ($\Delta \approx 0.05$ ppm) to those of **6a**.

Finally, 5.5 g of **7c** was eluted with 23:2 hexane–acetone and was found to be identical to that obtained using Method II.

Table 10
Elemental analysis of compounds **6**, **7**, **9**, **10**, **12**, **13**, **15–17**, **19–22**, and **24–26**

Product	Calculated (%)		Found (%)	
	C	H	C	H
6a	48.74	6.65	49.00	7.23
6b	53.34	7.61	53.48	7.81
6c	55.22	8.00	55.85	8.28
7a	58.52	8.07	58.59	8.13
7b	60.93	8.6	261.05	8.61
7c	61.98	8.87	62.23	9.00
9a	48.74	6.65	48.90	6.93
9b	53.34	7.61	52.95	8.09
9c	55.22	8.00	56.05	8.34
10a	58.52	8.07	58.69	8.17
10b	60.93	8.62	60.86	8.55
10c	61.98	8.87	61.75	8.76
12c	55.87	8.65	55.99	8.64
13c	63.78	9.64	63.95	9.80
15a	58.52	8.07	58.69	8.17
15b	60.93	8.62	60.95	8.47
15c	61.98	8.87	61.05	8.61
16c	62.95	9.24	62.93	9.25
17a	63.33	9.23	63.17	9.45
19a	53.42	7.75	53.22	8.18
19b	56.71	8.42	56.12	8.52
19c	58.12	8.71	58.79	8.96
20a	60.16	9.20	58.09	7.40
21a	56.17	7.92	55.81	8.01
22a	55.80	7.02	55.22	7.07
24c	58.89	9.15	59.11	9.09
25a	64.31	9.62	64.26	9.36
26a	63.22	8.94	63.02	9.21

1,4-Bis[3-O-(1,2:5,6-di-O-isopropylidene-α-D-glucofuranos-3-yl)]butane (**7a**).— Compound **1** (13.0 g, 50 mmol) was treated with 1,4-dibromobutane (7.1 g, 30 mmol) for 16 h using Method II. Initial elution with 24:1 hexane–acetone yielded sequentially 0.4 g of **8a** (syrup); $[\alpha]_D^{25}$ −28.4° (*c* 1.0, $CHCl_3$); a second fraction (0.6 g) was a 3:1 mixture of **6a** and **8a**. Further elution with 19:1 hexane–acetone afforded 0.5 g of pure **6a** (syrup); $[\alpha]_D^{25}$ −24.6° (*c* 1.05, $CHCl_3$); and then elution with 93:7 hexane–acetone gave 6.5 g (44%) of **7a** (syrup); $[\alpha]_D^{25}$ −34.2° (*c* 1.0, $CHCl_3$). The ^1H and ^{13}C NMR spectra ($CDCl_3$) are reported in Tables 7 and 8, respectively.

Similarly **1** (13.0 g, 50 mmol) was treated with 1,4-dimesylbutane (6.8 g, 27.6 mmol) for 8 h using Method III. Elution with 93:7 hexane–acetone gave 10.5 g (75%) of **7a**.

Further elution with 22:3 hexane–acetone gave the unreacted compound **1**. Finally, elution with 4:1 hexane–acetone gave 3.2 g of **6a** (X = OMs).

1,8-Bis[3-O-(1,2:5,6-di-O-isopropylidene-α-D-glucofuranos-3-yl)]octane (**7b**).— Compound **1** (8.05 g, 30.9 mmol) was treated with 1,8-dibromooctane (5.4 g, 18.5 mmol) for 16 h using Method II. Initial elution with 24:1 hexane–acetone yielded 1.9 g of a 1:9

Table 11
Elemental analysis of compounds **27–32**

Product	Calculated (%)		Calculated + H_2O (%)		Found (%)	
	C	H	C	H	C	H
27a	46.37	7.30	44.49	7.45	44.96	7.45
27b	51.06	8.14	49.17	8.25	49.36	8.22
27c	53.00	8.49	51.15	8.58	52.69	8.49
28a	46.37	7.30	44.44	7.45	44.30	7.35
28b	51.06	8.14	49.17	8.14	48.97	8.01
28c	53.00	8.49	51.15	8.58	50.96	8.29
29c	54.28	9.56	52.16	9.63	53.85	9.59
30b	51.06	8.14	49.17	8.14	49.21	8.26
31a	61.67	9.57	60.28	9.61	59.75	9.35
32a	57.71	9.34	55.98	9.39	57.53	9.38

mixture of **6b** and **8b**. Further elution with 19:1 hexane–acetone gave sequentially 0.6 g of **6b** and 6.9 g (75%) of **7b** (syrup); $[\alpha]_D^{25}$ −29.2° (*c* 1.0, $CHCl_3$). The ^1H and ^{13}C NMR spectra for the glucosyl moiety were identical ($\Delta \approx 0.05$ ppm) to those of **7a**.

1,10-Bis[3-O-(1,2:5,6-di-O-isopropylidene-α-D-glucofuranos-3-yl)]decane (**7c**).—Compound **1** (26.0 g, 100 mmol) was treated with 1,10-dibromodecane (18.0 g, 60 mmol) for 16 h using Method II. Initial elution with 24:1 hexane–acetone yielded 8.0 g of a 1:4 mixture of **6c** and **8c**. Further stepwise elution with 19:1 hexane–acetone gave 1 g of pure **6c**; then, elution with 93:7 hexane–acetone gave 20.7 g (63%) of **7c** (syrup); $[\alpha]_D^{25}$ −26.7° (*c* 1.3, $CHCl_3$). The ^1H and ^{13}C NMR spectra for the glucosyl moiety were identical ($\Delta \approx 0.05$ ppm) to those of **7a**.

6-O-(4-Bromobutyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**9a**).—Compound **2** (39.0 g, 150 mmol) was treated with 1,4-dibromobutane (38.9 g, 180 mmol) for 6 h using Method I. Initial elution with 24:1 hexane–acetone yielded 3.4 g of a 3:2 mixture of **9a** and **11a**. Further elution with 19:1 hexane–acetone gave 23.7 g (40%) of pure **9a** (syrup); $[\alpha]_D^{25}$ −24.6° (*c* 1.1, $CHCl_3$). The ^1H and ^{13}C NMR spectra ($CDCl_3$) are reported in Tables 7 and 8, respectively.

Finally, 6.2 g of pure **10a** was obtained after elution with 93:7 hexane–acetone and was found to be identical to that obtained using Method II.

6-O-(8-Bromooctyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**9b**).—Compound **2** (13.2 g, 50.8 mmol) was treated with 1,8-dibromooctane (16.6 g, 60.9 mmol) for 6 h using Method I. Initial elution with 24:1 hexane–acetone yielded 1.7 g of a 1:2 mixture of **9b** and **11b**. Further elution with 19:1 hexane–acetone gave 15.7 g (49%) of **9b** (syrup); $[\alpha]_D^{25}$ −44.0° (*c* 1.2, $CHCl_3$). The ^1H and ^{13}C NMR spectra for the galactosyl moiety were identical ($\Delta \approx 0.05$ ppm) to those of **9a**.

Finally, 4.9 g of pure **10b** was obtained after elution with 23:2 hexane–acetone which was identical to that obtained using Method II.

6-O-(10-Bromodecyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**9c**).—Compound **2** (9.1 g, 35.5 mmol) was treated with 1,10-dibromodecane (12.8 g, 42.6 mmol) for 6 h using Method I. Initial elution with 24:1 hexane–acetone yielded 1.3 g of 7:13 mixture of **9c** and **11c**. Further elution with 19:1 hexane–acetone gave 10.5 g (45%) of **9c**

(syrup); $[\alpha]_D^{25}$ −41.1° (*c* 1.0, $CHCl_3$). The ^1H and ^{13}C NMR spectra for the galactosyl moiety were identical ($\Delta \approx 0.05$ ppm) to those of **9a**.

Finally, 5.0 g of pure **10c** was obtained after elution with 23:2 hexane–acetone which was identical to that obtained using Method II.

*1,4-Bis[6-*O*-(1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranos-6-yl)]butane* (**10a**).—Compound **2** (13.0 g, 50 mmol) was treated with 1,4-dibromobutane (6.5 g, 30 mmol) for 16 h using Method II. Initial elution with 93:7 hexane–acetone yielded 6.2 g (43%) of **10a**; mp 94–96°C; $[\alpha]_D^{25}$ −76.0° (*c* 1.05, $CHCl_3$). The ^1H and ^{13}C NMR spectra ($CDCl_3$) are reported in Tables 7 and 8, respectively.

Similarly **2** (19.5 g, 75 mmol) was treated with 1,4-dimesylbutane (10.2 g, 41.4 mmol) for 8 h using Method III. Elution with 93:7 hexane–acetone gave 15.5 g (72%) of **10a**.

Further elution with 22:3 hexane–acetone gave the unreacted compound **2**. Finally, elution with 4:1 hexane–acetone gave 3.2 g of **9a** (X = OMs).

*1,8-Bis[6-*O*-(1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranos-6-yl)]octane* (**10b**).—Compound **2** (9.1 g, 35 mmol) was treated with 1,8-dibromooctane (6.1 g, 21 mmol) for 16 h using Method II. Initial elution with 24:1 hexane–acetone yielded 2.5 g of a 1:4 mixture of **9b** and **11b**. Further elution with 19:1 hexane–acetone gave 0.6 g of **9b**; then elution with 93:7 hexane–acetone gave 7.2 g (65%) of **10b** (syrup); $[\alpha]_D^{25}$ −62.4° (*c* 1.25, $CHCl_3$). The ^1H and ^{13}C NMR spectra for the galactosyl moiety were identical ($\Delta \approx 0.05$ ppm) to those of **9a**.

*1,10-Bis[6-*O*-(1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranos-6-yl)]decane* (**10c**).—Compound **2** (26.0 g, 100 mmol) was treated with 1,10-dibromodecane (18.0 g, 60 mmol) for 16 h using Method II. Initial elution with 97:3 hexane–acetone yielded 9.1 g of a 1:8 mixture of **9c** and **11c**. Further elution with 19:1 hexane–acetone (19:1) gave 1.0 g of **9c**; then elution with 47:3 hexane–acetone gave 19.7 g (60%) of **10c** (syrup); $[\alpha]_D^{25}$ −61.2° (*c* 1.1, $CHCl_3$). The ^1H and ^{13}C NMR spectra for the galactosyl moiety were identical ($\Delta \approx 0.05$ ppm) to those of **10a**.

*1-O-(10-Bromodecyl)-2,3:4,5-di-*O*-isopropylidene-*DL*-xylitol* (**12c**).—Compound **3** (5.0 g, 21.5 mmol) was treated with 1,10-dibromodecane (7.8 g, 26 mmol) for 6 h using Method I. Initial elution with hexane yielded 1.2 g of a 1:2 mixture of **12c** and **14c**. Further elution with 49:1 hexane–acetone gave 3.7 g (40%) of **12c** (syrup); $[\alpha]_D^{25}$ +1.2° (*c* 1.4, $CHCl_3$). The ^{13}C NMR spectrum ($CDCl_3$) is reported in Table 8.

Finally, 1.3 g of **13c** was obtained after elution with 19:1 hexane–acetone and was found to be identical to that obtained using Method II.

*1,10-Bis[1-*O*-(2,3:4,5-di-*O*-isopropylidene-*DL*-xylit-1-yl)]decane* (**13c**).—Compound **3** (5.0 g, 21.5 mmol) was treated with 1,10-dibromodecane (3.9 g, 13 mmol) for 16 h using Method II. Initial elution with 99:1 hexane–acetone yielded 2.8 g of a 8:1 mixture of **12c** and **14c**. Further elution with 19:1 hexane–acetone gave 4.0 g (62%) of **13c**; mp 73–74°C; $[\alpha]_D^{25}$ +0.53° (*c* 1.7, $CHCl_3$). The ^{13}C NMR spectrum ($CDCl_3$) is reported in Table 8.

*1-[3-*O*-(1,2:5,6-Di-*O*-isopropylidene-α-*D*-glucofuranos-3-yl)]-4-[6-*O*-(1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranos-6-yl)]butane* (**15a**).—Compound **6a** (12.4 g, 31.4 mmol) was treated with **2** (6.8 g, 26.2 mmol) for 17 h using Method I. Initial elution with 24:1 hexane–acetone yielded 2.66 g of **8a**. Further elution with 19:1 hexane–acetone gave 11.0 g (61%) of **15a** (syrup); $[\alpha]_D^{25}$ −50.0° (*c* 1.0, $CHCl_3$). The ^{13}C NMR spectrum ($CDCl_3$) is reported in Table 8.

1-[3-O-(1,2:5,6-Di-O-isopropylidene-α-D-glucofuranos-3-yl)]-8-[6-O-(1,2:3,4-di-O-isopropylidene-α-D-galactopyranos-6-yl)]octane (**15b**).—Compound **6b** (15.0 g, 33.3 mmol) was treated with **2** (7.2 g, 27.7 mmol) for 21 h using Method I. Initial elution with 24:1 hexane–acetone yielded 3.7 g of **8b**. Further elution with 41:4 hexane–acetone gave 11.3 g (54%) of pure **15b** (syrup); $[\alpha]_D^{25}$ −48.3° (*c* 0.9, $CHCl_3$). The ^{13}C NMR spectrum of the glycosyl moieties was identical ($\Delta \approx 0.05$ ppm) to that of **15a**.

1-[3-O-(1,2:5,6-Di-O-isopropylidene-α-D-glucofuranos-3-yl)]-10-[6-O-(1,2:3,4-di-O-isopropylidene-α-D-galactopyranos-6-yl)]decane (**15c**).—Compound **6c** (9.3 g, 19.2 mmol) was treated with **2** (4.2 g, 16.1 mmol) for 28 h using Method I. Initial elution with 24:1 hexane–acetone yielded 2.1 g of **8c**. Further elution with 91:9 hexane–acetone gave 7.3 g (58%) of **15c** (syrup); $[\alpha]_D^{25}$ −40.9° (*c* 1.3, $CHCl_3$). The ^{13}C NMR spectrum of the glycosyl moieties was identical ($\Delta \approx 0.05$ ppm) to that of **15a**.

1-[1-O-(2,3:4,5-Di-O-isopropylidene-DL-xylit-1-yl)]-10-[6-O-(1,2:3,4-di-O-isopropylidene-α-D-galactopyranos-6-yl)]decane (**16c**).—Compound **12c** (3.2 g, 7.1 mmol) was treated with **2** (1.5 g, 5.92 mmol) for 15 h using Method I. Initial elution with 49:1 hexane–acetone yielded 1.5 g of a 1:2 mixture of **12c** and **14c**. Further elution with 91:9 hexane–acetone gave 2.5 g (67%) of **16c** (syrup); $[\alpha]_D^{25}$ −33.5° (*c* 1.0, $CHCl_3$). The ^{13}C NMR spectrum ($CDCl_3$) is reported in Table 8.

1,9-Di-[3-O-(1,2:5,6-di-O-isopropylidene-α-D-glucofuranos-3-yl)]-5-heptylnonan-5-ol (**17a**).—A solution of **6a** (29.8 g, 76 mmol) in anhyd THF (100 mL) was slowly added to anhyd THF (20 mL), magnesium chips (1.9 g, 80 mmol), and a crystal of iodine. After refluxing for 4 h at 70°C, the magnesium chips disappeared and a solution of methyl octanoate (0.7 g, 49 mmol) in anhyd THF (10 mL) was slowly added to the mixture. The reaction was continued for 20 h and the mixture was neutralized with satd NH_4Cl, extracted with toluene, and concentrated under vacuum to give 27.9 g of a mixture of **17a**, **18a**, **8a**, and **7b** in the GPC-estimated ratio 57:28:9:6. Elution with 23:2 hexane–acetone yielded 14.0 g of a mixture of **8a**, **7c**, and **18a** in a 9:4:12 ratio. Further elution with 89:11 hexane–acetone gave 12.9 g (44%) of pure **17a** (syrup); $[\alpha]_D^{25}$ −23.2° (*c* 1.2, $CHCl_3$). The ^{13}C NMR spectrum ($CDCl_3$) is reported in Table 8.

Compounds of types **7**, **15**, **16**, and **17** were partially deprotected with a 0.05 M H_2SO_4 (or 0.1 M H_2SO_4 for **16c** and **17a**) 19:1 EtOH–water mixture at 50°C, in the proportion of 1.0 g for 9 mL of the solution. The reaction was monitored by HPLC until 95% conversion had been achieved. After neutralization with $NaHCO_3$, the mixture was filtered off and concentrated under vacuum. The resulting crude product was chromatographed on a silica gel column using a hexane–acetone gradient. The ^{13}C NMR chemical shifts ($CDCl_3$) are reported in Table 9.

1,4-Bis[3-O-(1,2-O-isopropylidene-α-D-glucofuranos-3-yl)]butane (**19a**).—Application of the foregoing procedure to **7a** (7.2 g, 12.5 mmol) yielded 5.0 g (80%) of **19a** (syrup) after elution of the crude product with 2:3 hexane–acetone; $[\alpha]_D^{25}$ −34.2° (*c* 1.3, $CHCl_3$).

1,8-Bis[3-O-(1,2-O-isopropylidene-α-D-glucofuranos-3-yl)]octane (**19b**).—Likewise, **7b** (3.25 g, 5.15 mmol) gave 1.65 g (65%) of **19b** (syrup) after elution of the crude product with 2:3 hexane–acetone; $[\alpha]_D^{25}$ −33.3° (*c* 1.1, $CHCl_3$).

1,10-Bis[3-O-(1,2-O-isopropylidene-α-D-glucofuranos-3-yl)]decane (**19c**).—Likewise, **7c** (10.0 g, 15.2 mmol) gave 5.7 g (65%) of pure **19c** (syrup) after elution of the crude product with 1:1 hexane–acetone; $[\alpha]_D^{25}$ −36.4° (*c* 1.3, $CHCl_3$).

1,9-Bis[3-O-(1,2-O-isopropylidene-α-D-glucofuranos-3-yl)]5-heptylnonan-5-ol (**20a**). —Likewise, **17a** (4.5 g, 5.9 mmol) in a 0.1 M H_2SO_4 solution gave 2.4 g (60%) of **20a** (syrup) after elution of the crude product with 1:1 hexane–acetone; $[\alpha]_D^{25}$ +19.3° (*c* 0.9, $CHCl_3$).

1-[3-O-(1,2-O-Isopropylidene-α-D-glucofuranos-3-yl)]-4-[6-O-(1,2:3,4-di-O-isopropylidene-α-D-galactopyranos-6-yl)]butane (**21a**).—Likewise, **15a** (9.2 g, 16 mmol) gave 8.5 g (83%) of **21a** (syrup) after elution of the crude product with 3:2 hexane–acetone; $[\alpha]_D^{25}$ −47.6° (*c* 1.4, $CHCl_3$).

1-[6-O-(1,2:3,4-Di-O-isopropylidene-α-D-galactopyranos-6-yl)]-1-(1-O-xylit-1-yl)-10-decane (**24c**).—Likewise, **16c** (2.0 g, 3.17 mmol) in a 0.1 M H_2SO_4 solution gave 1.4 g (80%) of **24c** (syrup) after elution of the crude product with 3:2 hexane–acetone; $[\alpha]_D^{25}$ −23.7° (*c* 1.1, $CHCl_3$). *Synthesis of compounds* **25a** *and* **26a** *by the respective derivatization of compounds* **19a** *and* **21a**.—The syntheses were as follows.

1,4-Bis[3-O-(1,2-O-isopropylidene-6-O-lauroyl-α-D-glucofuranos-3-yl)]butane (**25a**). —To a stirred solution of **19a** (5.8 g, 12 mmol) and Et_3N (3.6 g, 36 mmol) in acetone (60 mL) was slowly added a solution of dodecanoyl chloride (7.9 g, 36 mmol) in acetone (40 mL). After 4 h at room temperature, 90% conversion had been achieved. The mixture was filtered and the filtrate evaporated to give a crude product which was purified on a column of silica gel to yield 7.2 g (70%) of **25a** (syrup) after elution 22:3 with hexane–acetone; $[\alpha]_D^{25}$ −24.9° (*c* 1.1, $CHCl_3$). The ^{13}C NMR spectrum ($CDCl_3$) is reported in Table 9.

1-[3-O-(1,2-O-Isopropylidene-6-O-tosyl-α-D-glucofuranos-3-yl)]-4-[6-O-(1,2:3,4-di-O-isopropylidene-α-D-galactopyranos-6-yl)]butane (**22a**).—The commonly used method [13] of tosylation was used to treat **21a** (8.0 g, 15 mmol) with tosyl chloride (3.4 g, 18 mmol) to give 7.25 g (70%) of **22a** (syrup) after elution on a column of silica gel with 3:1 hexane–acetone; $[\alpha]_D^{25}$ −37.3° (*c* 1.1, $CHCl_3$).

1-[3-O-(1,2-O-Isopropylidene-6-O-dodecyl-α-D-glucofuranos-3-yl)]-4-[6-O-(1,2:3,4-di-O-isopropylidene-α-D-galactopyranos-6-yl)]butane (**26a**).—Compound **22a** (7.1 g, 10.3 mmol) was treated with NaOH to give after extraction, 5.0 g of epoxide **23a**, which was treated for 24 h with *n*-dodecanol (6.0 g, 38.5 mmol) in the presence of KOH (5.15 g, 91.96 mmol) at 40°C. Chromatography on a silica gel column of the crude product gave 2.1 g (27%) of **26a** (syrup) after elution with 9:1 hexane–acetone; $[\alpha]_D^{25}$ −37.4° (*c* 1.0, $CHCl_3$).

Preparation of compounds of types **27–32**.—Compounds of the types **7**, **10**, **13**, **15**, **25**, and **26** were deprotected with a 0.5 M H_2SO_4 (or 0.1 M H_2SO_4 for **13c**) 3:1 1,4-dioxane–water solution at 70°C, in the proportion of 1.0 g for 9 mL of solution. The reaction was monitored by HPLC. Neutralization was effected with NaOH and completed with $NaHCO_3$. The mixture was then filtered and the filtrate concentrated under vacuum. The resulting crude product was chromatographed on a column of silica gel. The elemental analysis is reported in Table 11.

1,4-Bis[3-O-(D-glucopyranos-3-yl)]butane (**27a**).—Application of the foregoing procedure to **7a** (4.1 g, 7.14 mmol) gave 2.3 g (78%) of **27a** (syrup) after elution with 3:1 acetone–EtOH; $[\alpha]_D^{25}$ +45.0° (*c* 1.05, CH_3OH). The ^{13}C NMR spectrum (pyridine) showed the C-1 signals at δ 96.7 (β anomer) and 92.2 (α anomer).

1,8-Bis[3-O-(D-glucopyranos-3-yl)]octane (**27b**).—Likewise, **7b** (1.8 g, 2.91 mmol) gave 0.82 g (60%) of **27b** after elution with 4:1 acetone–EtOH; mp 143–145°C; $[\alpha]_D^{25}$

+27.8° (*c* 1.1, CH_3OH). The ^{13}C NMR spectrum of the glucosyl moieties was identical to that of **27a**.

1,10-Bis[3-O-(D-glucopyranos-3-yl)]decane (**27c**).—Likewise, **7c** (2.4 g, 3.71 mmol) gave 1.05 g (57%) of pure **27c** after elution with 9:1 acetone–EtOH; mp 148–150°C; $[\alpha]_D^{25}$ +17.1° (*c* 1.2, CH_3OH). The ^{13}C NMR spectrum of the glucosyl moieties was identical to that of **27a**.

1,4-Bis[6-O-(D-galactos-6-yl)]butane (**28a**).—Likewise, **10a** (4.1 g, 7.14 mmol) gave 2.3 g (76%) of **28a** (syrup) after elution with 3:1 acetone–EtOH; $[\alpha]_D^{25}$ +56.4° (*c* 1.1, CH_3OH). The ^{13}C NMR spectrum (pyridine) showed the C-1 signals at δ 101.5 (β-furanose anomer), 97.2 (β-pyranose anomer), and 92.5 (α-pyranose anomer).

1,8-Bis[6-O-(D-galactos-6-yl)]octane (**28b**).—Likewise, **10b** (4.2 g, 6.62 mmol) gave 1.6 g (52%) of **28b** after elution with 9:1 acetone–EtOH; mp 149–152°C; $[\alpha]_D^{25}$ +44.4° (*c* 1.3, CH_3OH). The ^{13}C NMR spectrum of the glycosyl moieties was identical to that of **28a**.

1,10-Bis[6-O-(D-galactos-6-yl)]decane (**28c**).—Likewise, **10c** (4.0 g, 6.08 mmol) gave 1.5 g (50%) of **28c** after elution with 9:1 acetone–EtOH; mp 147–149°C; $[\alpha]_D^{25}$ +28.5° (*c* 1.2, CH_3OH). The ^{13}C NMR spectrum of the glycosyl moieties was identical to that of **28a**.

1,10-Bis[1-O-xylit-1-yl]decane (**29c**).—Likewise, **13c** (2.0 g, 3.32 mmol) gave 1.3 g (90%) of **29c** following treatment with 0.1 M H_2SO_4 solution and elution with 1:1 water–EtOH; mp 70–71°C; $[\alpha]_D^{25}$ −16° (*c* 1.4, CH_3OH). The ^{13}C NMR spectrum (pyridine) is reported in Table 9.

8-[6-O-(D-Galactos-6-yl)]-1-[3-O-(D-glucopyranos-3-yl)]octane (**30b**).—Likewise, **15b** (1.86 g, 2.95 mmol) gave 0.73 g (53%) of **30b** (syrup) after elution with 9:1 acetone–EtOH; $[\alpha]_D^{25}$ +32.8° (*c* 0.8, CH_3OH). The ^{13}C NMR spectrum (pyridine) showed the C-1 signals at δ 101.6 (β-galactofuranose anomer), 97.2 (β-galactopyranose anomer), 92.5 α-galactopyranose anomer), 96.8 (β-glucopyranose anomer), and 92.2 (α-glucopyranose anomer).

1,4-Bis-[3-O-(6-O-dodecanoyl-D-glucopyranos-3-yl)]butane (**31a**).—In accordance with the foregoing procedure and by performing the deprotection reaction at 40°C instead of 70°C, **25a** (4.3 g, 5.01 mmol) gave 0.85 g (22%) of **31a** after elution with 1:1 hexane–acetone; mp 96–98°C; $[\alpha]_D^{25}$ +35.4° (*c* 1.1, CH_3OH). The ^{13}C NMR spectrum (pyridine) showed the C-1 signals at δ 96.6 (β anomer) and 92.4 (α anomer).

1-[3-O-(6-O-Dodecyl-D-glucofuranos-3-yl)]-4-[6-O-(D-galactopyranos-6-yl)]-butane (**32a**).—Using a similar procedure to that described for the deprotection of **7a**, **26a** (2 g, 2.85 mmol) gave 1.26 g (76%) of **32a** (syrup) after elution with 1:9 hexane–acetone; $[\alpha]_D^{25}$ +36.0° (*c* 0.6, CH_3OH). The ^{13}C NMR (pyridine) spectrum showed the C-1 signals at δ 101.6 (β-galactofuranosyl anomer), 97.2 (β-galactopyranosyl anomer), 92.4 (α-galactopyranosyl anomer), 96.7 (β-glucopyranosyl anomer), and 92.1 (α-glucopyranosyl anomer).

Surface tension and critical micellar concentration determinations.—An initial aqueous solution (S_o) at 25°C, corresponding to a concentration C_o, was prepared from **19c**, **20a**, **24c**, and **27c**, respectively. Several samples were obtained by diluting S_o in the concentration range C_o: $C_o/2$, $C_o/4$, $C_o/10$, $C_o/50$, and $C_o/100$. The surface tension (γ) of each sample was measured by the Wilhelmy plate method, after a period of more than 1 h in the

thermostated (25°C) cell. The critical micellar concentration (CMC) was determined from a plot of $\gamma = f(\log C)$. The classical slope change coordinates gave, respectively, the CMC values and the corresponding γ values reported in Table 5.

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