Electrochemical Reduction in an Aprotic Medium of New Functionalized Amphiphilic Molecules Derived from Sugars: Stereoselective Pinacolization and an Example of a Glycosidic Carbon-Oxygen Bond Cleavage

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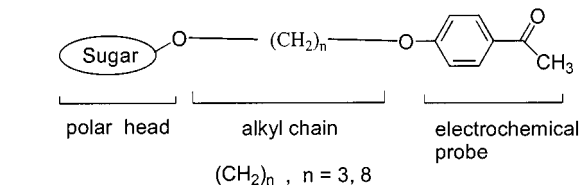
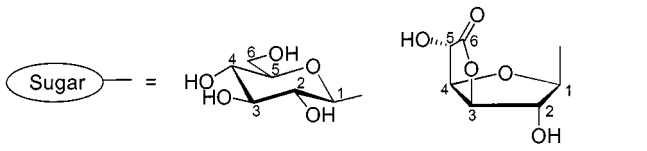
Electroreducible amphiphilic aromatic ketones derived from D-glucose and D-glucofuranurono-6,3-lactone (D-glucurone) have been synthesized by Schmidt condensation and reaction of the unprotected lactone with the appropriate substrates, respectively. The macroscale electrolyses of the glucose derivatives, performed in an aprotic solvent (DMF), yield the pinacols possessing two glycosidic side chains. Under the same conditions of electrolysis with the D-glucurone derivative, the glyosidic carbon-oxygen bond is cleaved. The use of a redox mediator (couple anthracene$^{-\bullet}$/anthracene) has demonstrated that a glucosidic bond can be reduced by a homogeneous electron transfer. In the presence of a proton donor the expected D-glucuronic pinacol is obtained. The radical-radical coupling involves the formation of two chiral centers. The diastereo- and the enantioselectivity of the reaction have been studied by ^{1}H- and ^{2}H-NMR spectroscopy, respectively.

Introduction

Alkyl glycosides and alkyl polyglucosides have gained wide interest during the past two decades. They have been used for miscellaneous applications in biological processes[1–3] for the isolation of membrane proteins or as nontoxic detergents produced in industry.[4,6] The presence of chiral centers in the sugar moiety coupled with their ability to form ordered systems (visicules, micelles) has been used for regioselective and enantioselective reduction of prochiral carbonyl derivatives.[7,8] In the context of electrochemistry in a micellar medium, we have synthesized new alkyl glycosides of the following general structure:





1 (GluAcO3, n = 3)
2 (GluAcO8, n = 8)

3 (LacAcO8, n = 8)

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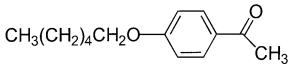
In previous work, we studied the electrochemical behavior of such surfactant molecules and their adsorption mode at the mercury electrolyte interface.[9] In the present article, we report the results of the macroscale electrolyses of glycosidic amphiphilic molecules derived from D-glucose **1** and **2** or from D-glucurone **3** performed in an aprotic medium. In the latter case, **3**, the electrolyses were achieved in the absence or in the presence of a proton donor. The influence of the sugar unit on the diastereo- and enantioselectivity has been analyzed by ^{1}H- and ^{2}H-NMR spectroscopy, respectively. A comparison with the nonglycosidic ketone **4** has also been made.



4 (HeAc)

The main aim of this study was to convert the two ketones into the corresponding bolaamphiphilic-type surfactants by carbon-carbon bond formation. Such bolaamphiphiles are of growing interest as models for lipids found in membranes of thermophilic archaebaceria,[10] for the preparation of monolayer stable vesicles[11] and the disruption of biological membranes.[12]

Results and Discussion

In a previous paper,[9] we described the syntheses of the glucopyranosides **1** and **2** according to the Schmidt glycosylation reaction.[13] The synthesis of the 1-*O*-[8-(4-acetylphenoxy)octyl] β-D-glucofuranosidurono-6,3-lactone **3** was performed in dry tetrahydrofuran in a single condensation

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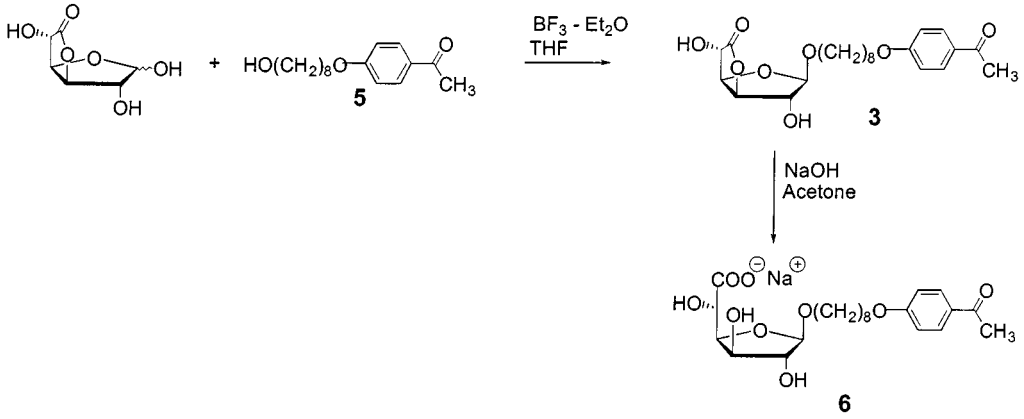


Scheme 1. Synthesis of glycosidic ketones **3** and **6**

step involving the ketone **5**, an excess of D-glucurone (4 equiv.) and boron trifluoride (10 equiv.) as a promoter (Scheme 1).

In an aprotic solvent (DMF), the cyclic voltammograms of the three ketones **1**, **2** and **3** present only one irreversible peak located at –2.18 V/SCE (Figure 1). The nonglycosidic aromatic ketone **4** exhibits a slightly reversible peak under the same conditions at –2.23 V/SCE.

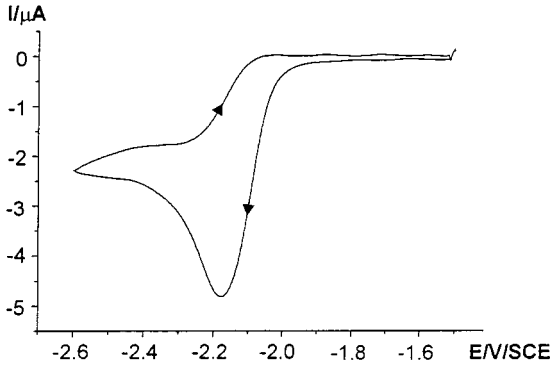


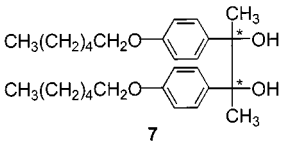
Figure 1. Voltammogram of 2×10^{-3} M **2** in 0.1 M Bu_4NPF_6/DMF, v = 0.05 V s^{-1}

The macroscale electrolyses of the two ketones derived from glucose (**1** and **2**), performed in dry DMF, consume 1 Faraday/mol (Table 1). With **4**, the electrolysis once more indicates an electricity consumption of one electron per molecule. Indeed, it is generally known that the electroreduction of aromatic ketones in an aprotic medium involves a one electron transfer and leads to an anion-radical that couples, resulting in the formation of the corresponding pinacol.[14]

At the end of every electrolysis, the reduction products were purified by chromatography on a silica gel column and characterized by ^1H, NMR spectroscopy and HRMS (FAB+) (see Experimental Section).

Electrolysis of the Model Compound 4

Electrolysis of **4** led to the formation of the pinacol **7**. Two chiral centers have been generated by the radical-radical coupling reaction, implying that the molecule may exist in two diastereomeric forms (*d,l* and *meso*). The ^1H, NMR spectrum of the crude electrolysis mixture shows, in the aromatic area, a set of doublets characteristic of two *p*-disubstituted benzene rings (Figure 2).



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These signals correspond to the presence of the racemic *d,l* and *meso* diastereoisomers. The assignment of each signal to the corresponding stereoisomer was based on a comparison with similar spectra recorded under the same conditions for authentic samples of the pinacols of the trifluoromethyl acetophenone and the methyl acetophenone. In these cases,

Table 1. Electrolysis in DMF

Substrate	Electrolysis Conditions[a]	Remaining ketone[b] (%)	Electricity consumption (F. mol^{-1})	Reduction product	*d,l*/*meso*	Electrolysis yield[c] (%)
4	A	20	1.00	**7**	9.53	80
2	B	<10	1.10	**8** (n = 8)	2.12	60
1	B	<10	1.05	**9** (n = 3)	2.45	60
3	C	<10	2.55	**5** and **10**	4.41	–
3	D	<10	1.44	**12**	4.26	40

[a] A: 0.1 M Bu_4NBF_4, E_{appl} = –2.20 V/SCE, 500 mg starting material; B: 0.1 M Bu_4NBF_4, E_{appl} = –2.10 V/SCE, 200–300 mg starting material; C: 0.1 M Bu_4NPF_6, E_{appl} = –2.15 V/SCE, 200 mg starting material; D: 0.1 M Bu_4NPF_6, 1.72×10^{-2} M Bu_4NHSO_4, E_{appl} = –2.15 V/SCE, 160 mg starting material. – [b] Remaining ketone: remaining amount of ketone/initial amount. – [c] Electrolysis yield: weight of isolated picacol/amount of initial ketone.

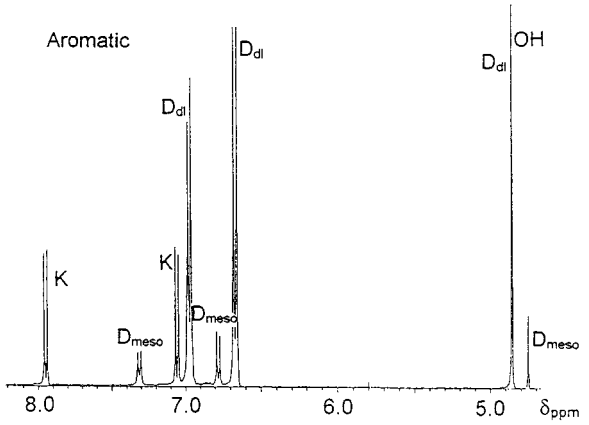
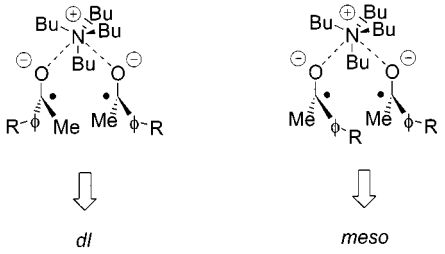


Figure 2. ^{1}H aromatic and hydroxyl NMR signals of pinacols **7** resulting from the electroreduction of **4** in an aprotic medium

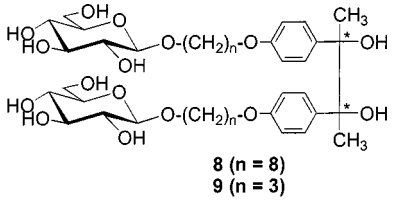
each diastereoisomer was characterized by gas chromatography on a chiral column (LIPODEX-E) and by ^{1}H, NMR spectroscopy (400 MHz, [D_6]DMSO). In the case of *meso* diastereoisomers, the set of doublets characteristic of *p*-disubstituted benzene rings is systematically situated at lower field as compared with that corresponding to the *d,l* diastereisomers. This sequence is inverted for the protons of the alcohol function (Figure 2).[15] The *d,l*/*meso* ratio of 9.5 for the two diastereomeric pinacols **7** is quite high. Bewick et al.[16,17] and Stocker et al.[18,19] have postulated that this diastereoselectivity can be explained by ion-pair formation between the anion-radical and BuN^+ from the supporting electrolyte. Thereby the less hindered radical pair with the methyl and phenyl groups facing each other (Scheme 2) leads to the favoured *d,l* diatereiosomer.



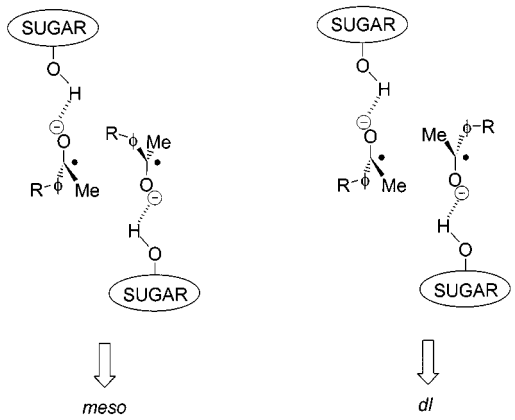
Scheme 2. Steric interactions involved in the case of ion pair formation[18,19]

Electrolysis of the Glycosidic Ketones 1 and 2

Electroreduction in DMF of the glycosidic ketones **2** and **1** leads to the formation of the expected pinacols **8** and **9**:



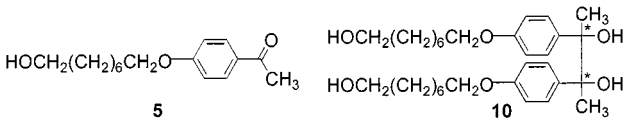
However, in these cases, the *d,l*/*meso* ratio decreases to 2, close to the value reported for an aqueous medium.[18,19] This shift can be explained by a solvation of the anion radicals by the hydroxyl groups of the carbohydrate that competes with the ion pair formation by BuN^+. The steric interactions of the carbohydrate groups promote a head-to-tail orientation of the two anion-radicals. Coupling from this configuration favors, as postulated by Stocker et al.,[18,19] the formation of the *meso* pinacol (Scheme 3).



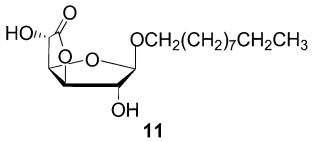
Scheme 3. Steric interactions postulated in the case of carbohydrate compounds

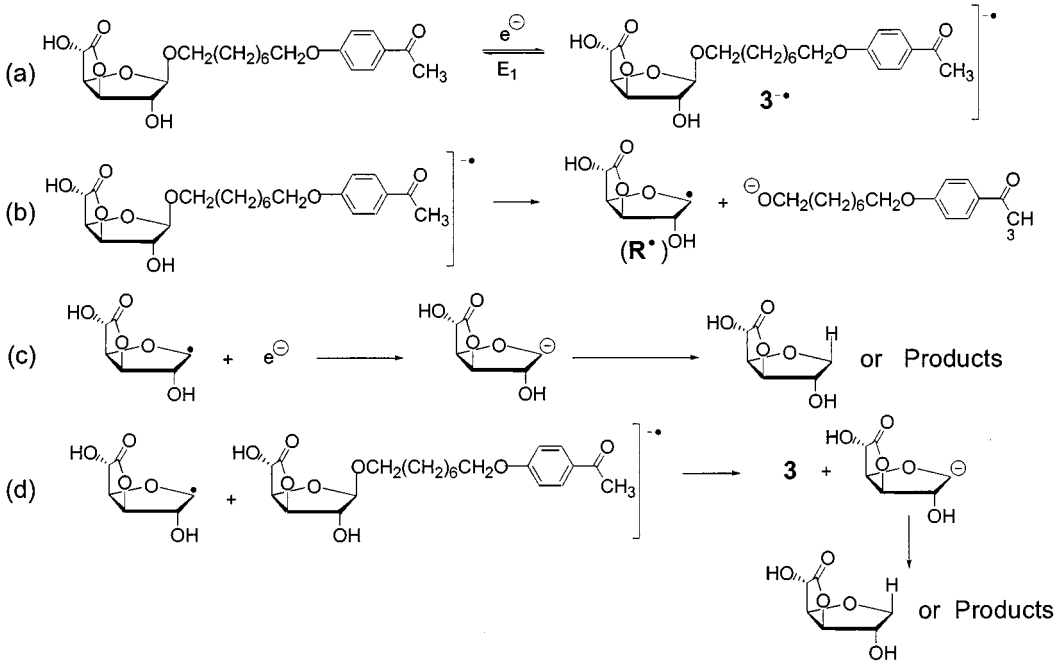
Electrolysis of the Ketone Derived from D-Glucurone 3

The results of the macroscale electrolysis of compound **3** (200 mg) performed at E = –2.15 V/SCE are different to those observed with the three others ketones. Firstly, the electricity consumption corresponds to 2.55 Faraday per mol of ketone and, secondly, the formation of three products is observed by thin layer chromatography. Two of these products, corresponding to the higher *Rf* values (0.77 and 0.65 in AcOEt), have been identified by ^{1}H, NMR spectroscopy and HRMS as ketone **5** (20 mg) and pinacol **10** (80 mg), respectively. These main reaction products (**5** and **10**) result from a cleavage of the carbon-oxygen glycosidic bond, the pinacol being formed by reduction of the ketone **5** at the fixed potential. The *d,l*/*meso* ratio for the pinacol **10** is 4.41, an intermediate value between those observed with **4** (*d,l*/*meso* = 9.53) and with the ketones **2** and **1** (*d,l*/*meso* = 2.12 and 2.45, respectively) (Table 1).



The structure of the third product (*Rf* = 0), or mixture of products, cannot be elucidated but it probably corresponds to the protonated form of the carbanion and/or the ammonium salt of the ring opened carbohydrate (Scheme 4).





Scheme 4. Electrocatalytic process involved in the cleavage of the glycosidic bond of the lactonic ketone **3**

Two hypotheses can be formulated to explain such a carbon-oxygen bond cleavage. The first explanation involves a direct electron transfer to the glycosidic bond occurring at the applied potential. A comparison with the alkyl glycoside **11** reveals that such a reduction process cannot take place at the applied potential used for macroscale electrolyses of our aromatic ketone. Indeed, the lactone **11** is reduced in an ill-defined wave that appears very close to the electrolyte discharge ($E \cong -2.8$ V/SCE) (Figure 3).

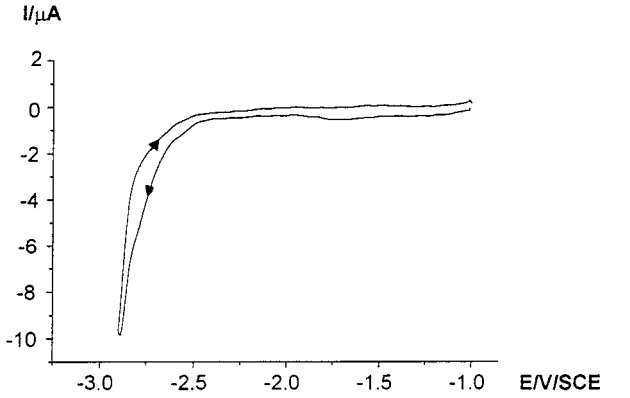


Figure 3. Voltammogram of 2×10^{-3} M lactone **11** in 0.1 M Bu_4NPF_6/DMF, v = 0.05 V s^{-1}

Secondly, the electricity consumption (2.55 F.mol^{-1}) suggests an electrocatalytic process involving the anion-radical of $\mathbf{3}^{-\bullet}$ playing the role of mediator in a homogeneous transfer to the glycosidic bond. This transfer can be either intra- or intermolecular with, as a consequence, the formation of a sugar radical $R^{\bullet}$ further reduced at the electrode or in solution by the anion-radical $\mathbf{3}^{-\bullet}$ (Scheme 4).

Taking into account the possibility of reducing the alkyl glycoside **11** at a more negative potential, we verified that the reductive cleavage of the glycosidic bond can be performed by a well adapted mediator. We chose anthracene (**A**), which gives a redox couple $\mathbf{A}^{-\bullet}/\mathbf{A}$ at $E_o = -1.97$ V/SCE. In spite of the fact that the cyclic voltammogram of pure anthracene is disturbed by interactions of $\mathbf{A}^{-\bullet}$ with the Hg electrode, Figure 4 shows that, in the presence of **11**, the signal becomes irreversible and a catalytic effect is observed on the cathodic response.

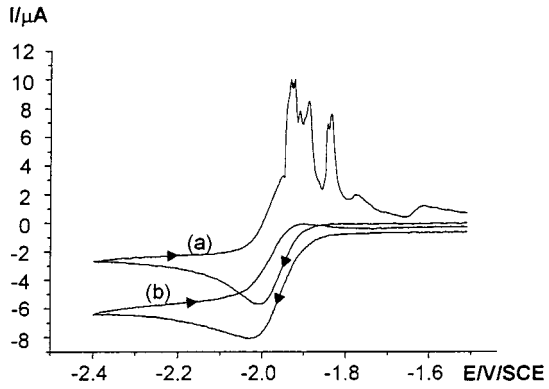
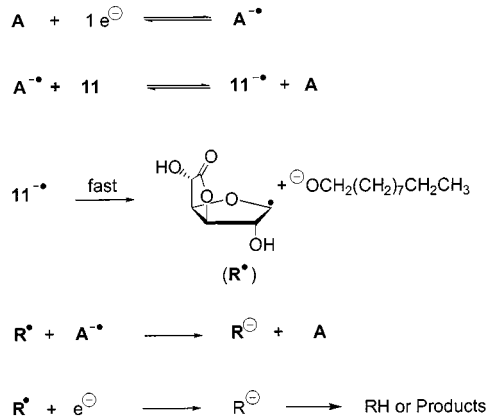


Figure 4. Voltammograms of 2×10^{-3} M anthracene (**A**) in 0.1 M Bu_4NPF_6/DMF, v = 0.02 V s^{-1}, (a) alone, (b) with 4×10^{-3} M lactone **11**

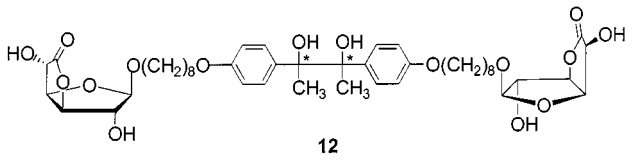
This result confirms the proposed electrocatalytic process involved in the cleavage of the glycosidic bond of the lactonic surfactant (Scheme 5).

In a homogeneous electron transfer implying an anion-radical, the presence of a proton donor can disturb the catalytic process by consumption of the mediator. In the presence of Bu_4NHSO_4, we noted that the intensity of the reduction peak of **3** is decreased compared to that observed in the absence of a proton donor, and the electricity consumption measured for macroscale electrolyses falls to 1.44 F ·mol^{-1}. The major product isolated under these condi-



Scheme 5. Electrocatalytic process, performed with anthracene as redox mediator, leading to the cleavage of the glycosidic bond of the lactone **11**

tions corresponds to the diastereomeric pinacols **12** still bearing the saccharidic groups:



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In this case, the ratio *d,l*/*meso* is 4.26, a value close to that obtained for pinacols **10**.

Study of the Enantioselectivity

As previously shown (vide supra), the electrochemical reduction of aromatic ketones in an aprotic medium leads mainly to the pinacols possessing two chiral centers. In our case, we wished to investigate whether the radical-radical coupling induces chirality due to the presence of the sugar moiety. Several methods, such as chromatography on a chiral support or NMR in the presence of chiral shift reagents, are commonly used to determine the enantiomeric excesses. Unfortunately these methods were unsuccessful for our products. Moreover, Mosher's method[20] for the determination of enantiomeric compositions was not applicable because of the steric hindrance of the tertiary alcohols. During the past decade, a very convenient technique based on the ^{2}H-NMR spectroscopy in liquid crystals has been developed.[21] The solvent used for the NMR experiments is a liquid crystal obtained by dissolution of poly-γ-benzyl-L-glutamate (PBLG) in dichloromethane. In such a chiral medium, the two enantiomers of the studied substrate can be set out differently and in this way give two quadrupolar splittings for the ^{2}H signal. The deuterium atoms were introduced in our pinacols by mean of an etherification reaction with CD_3I in the presence of NaH. A first experiment was performed with the pinacol **7** of the nonglycosidic model molecule. Two reaction products were isolated and identified to be the monoether **13** and the diether **14** (Scheme 6).

Figure 5a and 5b show the spectra obtained for the deuterium signal of the trideuteriomethyl monoether and of the trideuteriomethyl diether. The spectrum of the first one consists of two sets of doublets. The most important of these is attributed to the ether of the *d,l* pinacol and the other to that of pinacol *meso*. Each enantiomer of the racemic pinacol is characterized by a doublet with quadrupolar splittings $\Delta\nu_Q^1 = 65$ Hz and $\Delta\nu_Q^2 = 82$ Hz. As expected for this example, no asymmetric induction is observed. No quadrupolar splitting was observed for the diether **14** (Figure 5b).

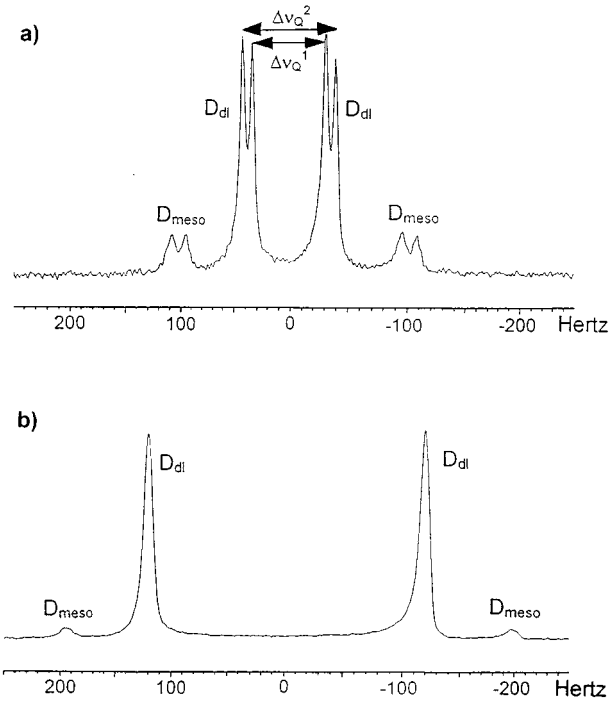
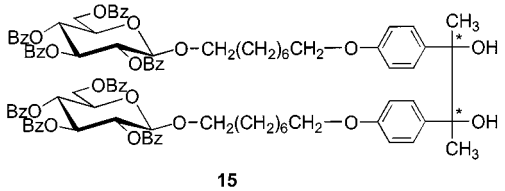


Figure 5. ^{2}H-NMR spectra in a polypeptide liquid crystal of (a) monoether **13**, (b) diether **14**

Application of the same method to the pinacol **8**, derived from glucose, required the selective protection of the hydroxyl groups of the sugar. Their esterification with benzoyl chloride is possible but the reaction product **15** does not react further with CD_3I.



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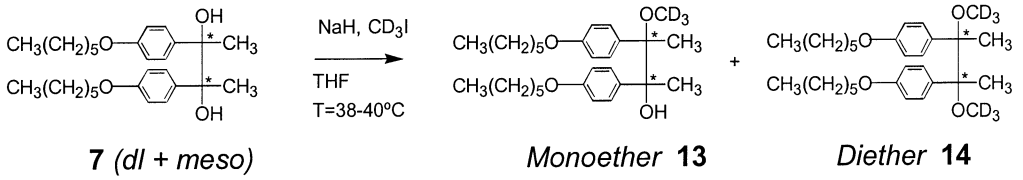
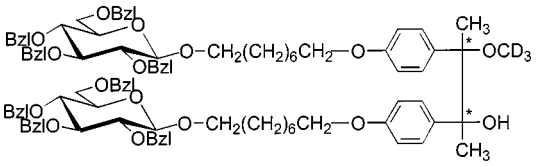


7 *(dl + meso)* *Monoether* **13** *Diether* **14**

Scheme 6

The protection of pinacol **8** can be successfully achieved with benzyl bromide in the presence of NaH. However, the reaction evolution must be carefully monitored by thin layer chromatography and stopped before the etherification of the tertiary hydroxyl functions of the pinacol. With this protecting group the monotrideuteriomethyl ether (**17**) can be obtained:



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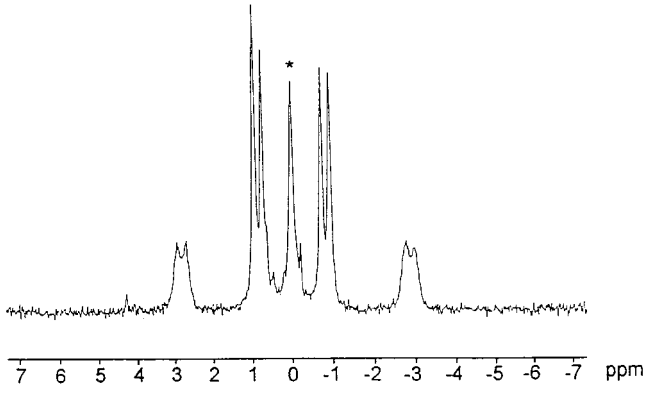
The NMR analysis (Figure 6) shows that no significant enantiomeric excess has been induced by the chiral auxiliary.



* : peak due to a lack of homogeneity of the sample

Figure 6. ^{2}H-NMR spectrum in a polypeptide liquid crystal of monoether **17**

Conclusion

In summary, the electrochemical reduction in an aprotic medium of glycosidic amphiphilic molecules derived from D-glucose and D-glucurone appears to be a convenient route to obtain two-chain surfactants. The carbon-carbon bond formation is performed with a high chemoselectivity. The presence of the nonprotected sugar unit therefore involves a decrease in the diastereoselectivity (*d,l*/*meso* ratio) compared to that observed under the same conditions for the nonglyosidic aromatic ketone. The radical-radical coupling generates two new stereogenic centers. A recent method based on ^{2}H-NMR spectroscopy has been applied for the first time, to the best of our knowledge, to the determination of enantiomeric excesses of diastereomeric pinacols. In the particular case of the glucurone derivative, an electrochemical cleavage of the glycosidic bond is observed in the absence of a proton donor while the expected pinacol is isolated in the presence of Bu_4NHSO_4. Further investigations, especially electrolyses in an aqueous medium of these ketones, are in progress in our group.[22]

Experimental Section

A Tacussel PRT 100-1X potentiostat coupled with a Tacussel IG5-N integrator was used for controlled-potential electrolyses, which were performed in a three compartment glass cell joined by two glass sinters. The cathodic cell contained the ketone (200–500 mg) dissolved in 60 mL of DMF in the presence of 0.1 M Bu_4NBF_4 or 0.1 M Bu_4NPF_6 as supporting electrolyte at 20 °C. The aqueous saturated calomel electrode (SCE) with an extension (DMF saturated with Bu_4NBF_4 or Bu_4NPF_6) was used as the reference electrode. The cathode was a mercury pool of 16 cm^2 and the anode a graphite electrode. In the case of glycosidic compounds **1**, **2** and **3**, 10 drops of water were also added to the cathodic solution after complete electrolysis in order to protonate the anions. The DMF was further distilled under reduced pressure at 50 °C. In the case of the nonglycosidic molecule **4**, the organic solution was poured into 400 mL of water and the products extracted with ether. The reduction products were chromatographed on a silica gel column (Merck, 70–230 mesh) and characterized by ^{1}H, and ^{13}C-NMR spectroscopy and mass spectrometry. The electrolysis yields are given in Table 1.

The ^{1}H- and ^{13}C-NMR spectra were recorded on Bruker AC 400 and ARX 400 spectrometers. Infrared spectra were obtained with Nicolet Impact 400 FT and Nicolet 205 FT spectrometers. The ^{2}H, NMR spectra were registered on Bruker AM 250 and MSL 300 spectrometers. The high resolution mass spectrometry (HRMS) was performed at the Centre National de la Recherche Scientifique (CNRS) at Vernaison (France). All the solvents were reagent grade and purchased from Aldrich.

The general synthetic pathways to the ketones **1**, **2**, **4** and lactone **11** have been described in previous papers.[9][23][24]

1-*O*-[8-(4-Acetylphenoxy)octyl] β-D-Glucofuranosidurono-6,3-lactone (3): To a suspension of D-glucurone (3.06 g, 17.4 mmol, 4 equiv.) in dry THF (30 mL) was added the electroreducible alcohol **5** (1.15 g, 4.35 mmol, 1 equiv.) and then $BF_3{\cdot}Et_2O$ (48% BF_3, 5.35 mL, 43.5 mmol, 10 equiv.). The mixture was magnetically stirred and heated under reflux for 1 h 45 min. The solvent was evaporated under reduced pressure and the colored residue dissolved in ethyl acetate (30 mL). The organic layer was washed twice with water, dried over $MgSO_4$ and concentrated under reduced pressure. Product **3** was purified by chromatography on a silica gel column [eluent: ethyl acetate/petroleum ether (1:1 then 7:3 v/v), TLC: *Rf* (**3**) = 0.55 in ethyl acetate]. Compound **3** was obtained as a white powder in 55% yield (1 g), mp: 70–72 °C. – HRMS (FAB+) calcd. for $[C_{22}H_{30}O_8Li]^+$: 429.2100; found 429.2094. – $[a]_D^{20}$ = –32.7 (*c* = 1.01; $CHCl_3$). – ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.95 (d, 2 H, *J* = 8.9 Hz, aromatic), 7.06 (d, 2 H, *J* = 8.9 Hz, aromatic), 5.86 (d, 1 H, *J* = 6.4 Hz, OH), 5.71 (d, 1 H, *J* = 3.9 Hz, OH), 4.94 (s, 1 H, H_1), 4.79 (dd, 1 H, *J* = 6.4, 4.4 Hz, H_4), 4.73 (d, 1 H, *J* = 4.4 Hz, H_3), 4.47 (t, 1 H, *J* = 5.9 Hz, H_5), 4.09 (t, 2 H, *J* = 6.9 Hz, CH_2OAr), 4.08 (d, 1 H, *J* = 5.4 Hz, H_2), 3.72 (m, 1 H, OCH_2), 3.23 (mc, 1 H, OCH_2), 2.54 (s, 3 H, CH_3), 1.76 (quint, 2 H, *J* = 7.0 Hz, CH_2), 1.18–1.50 (m, 10 H, CH_2). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.67, 174.55, 163.32, 130.72, 129.88, 114.26, 109.17, 83.20, 77.54, 77.10, 69.13, 69.11, 68.27, 25.79–29.18.

Sodium 1-*O*-[8-(4-Acetylphenoxy)octyl]-β-D-glucofuranosiduronate (6): To a solution of compound **3** (0.93 g, 2.2 mmol, 1 equiv.) in acetone (30 mL) was added very slowly (30 min), at –10 °C, 4.4 mL

of a 0.5 N solution of NaOH in H_2O (2.2 mmol, 1 equiv.). The mixture was stirred at 15 °C for 2 h and then diluted with diethyl ether. The organic solution was extracted with water (2 × 15 mL). Ethyl acetate was added to the yellow aqueous phase and the solution concentrated under reduced pressure at 40–45 °C. The colored residue was dried under reduced pressure and chromatographed on a silica gel column [eluent: dichloromethane/methanol (4:1 then 3:2 v/v), TLC: *Rf* (**6**) = 0–0.30 in 3:2 v/v]. Compound **6** was obtained as a white powder in 55% yield (0.55 g), mp 130–135 °C. MS (ES); $C_{22}H_{31}O_9Na$ (462.47): *m/z* 439.5 ($[C_{22}H_{31}O_9]^{1-}$), 879.4 (dimer). – $[a]_D^{20}$ = –26.3 (*c* = 1.028; CH_3OH). – ^1H NMR (400 MHz, CD_3OD): δ = 7.92 (d, 2 H, aromatic), 6.95 (d, 2 H, aromatic), 4.87 (s, 1 H, H_1), 4.57 (dd, 1 H, *J* = 5.8, 3.1 Hz, H_4), 4.40 (d, 1 H, *J* = 3.1 Hz, H_5), 4.21 (d, 1 H, *J* = 3.7 Hz, H_3), 4.12 (s, 1 H, H_2), 4.03 (t, 2 H, *J* = 6.3 Hz, CH_2OAr), 3.79 (td, 1 H, OCH_2), 3.50 (td, 1 H, OCH_2), 2.51 (s, 3 H, CH_3), 1.76–1.77 (m, 2 H, CH_2), 1.60–1.62 (m, 1 H, CH_2), 1.45–1.47 (m, 1 H, CH_2), 1.35 (s, 8 H, CH_2). – ^{13}C NMR (100 MHz, CD_3OD): δ = 199.37, 195.00, 164.90, 131.81, 131.38, 115.44, 109.72, 83.19, 82.06, 78.21, 74.45, 70.23, 69.50, 27.03–30.59, 26.28.

Bis-1-[4-(1-hydroxyethyl)phenoxy]hexane (7): Chromatography: eluent; dichloromethane/ethyl acetate (19:1 then 9:1 v/v), *Rf* = 0.47. – HRMS (FAB+) calcd. for $[C_{28}H_{42}O_4Li]^+$: 449.3243; found 449.3224. – *d,l diastereoisomer*: ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 6.97 (d, 4 H, *J* = 8.9 Hz, aromatic), 6.67 (d, 4 H, *J* = 8.9 Hz, aromatic), 4.86 (s, 2 H, OH), 3.91 (t, 4 H, *J* = 6.6 Hz, CH_2OAr), 1.70 (quint, 4 H, *J* = 7.0 Hz, CH_2), 1.39–1.48 (m, 4 H, CH_2), 1.43 (s, 6 H, CH_3), 1.30–1.38 (m, 8 H, CH_2), 0.91 (t, 6 H, *J* = 6.9 Hz, CH_3). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.10, 135.53, 128.56, 112.98, 78.77, 67.97, 31.66, 29.53, 25.79, 22.66, 24.99, 14.10. – *meso diastereoisomer*: ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 7.32 (d, 4 H, *J* = 8.9 Hz, aromatic), 6.78 (d, 4 H, *J* = 8.4 Hz, aromatic), 4.75 (s, 2 H, OH), 3.95 (t, 4 H, *J* = 6.4 Hz, CH_2OAr), 1.70 (quint, 4 H, *J* = 7.0 Hz, CH_2), 1.39–1.48 (m, 4 H, CH_2), 1.30–1.38 (m, 8 H, CH_2), 1.28 (s, 6 H, CH_3), 0.91 (t, 6 H, *J* = 6.9 Hz, CH_3). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.00, 135.87, 128.12, 113.16, 78.56, 67.97, 31.66, 29.53, 25.79, 22.66, 25.14, 14.10.

Bis-1-*O*-{8-[4-(1-hydroxyethyl)phenoxy]octyl} β-D-Glucopyranoside (8): Chromatography: eluent; ethyl acetate/methanol (9:1 then 7:3 v/v), R_f = 0.34. – HRMS (FAB+) calcd. for $[C_{44}H_{70}O_{16}Na]^+$: 877.4561; found 877.4575. – *d,l diastereoisomer*: ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 6.98 (d, 4 H, *J* = 7.9 Hz, aromatic), 6.67 (d, 4 H, *J* = 7.9 Hz, aromatic), 5.00 (d, 2 H, *J* = 5.4 Hz, OH, sugar), 4.97 (d, 2 H, *J* = 5.9 Hz, OH, sugar), 4.93 (d, 2 H, *J* = 4.4 Hz, OH, sugar), 4.85 (s, 2 H, OH), 4.52 (t, 2 H, *J* = 5.9 Hz, OH, sugar), 4.13 (d, 2 H, *J* = 7.4 Hz, H_1), 3.91 (t, 4 H, *J* = 6.4 Hz, CH_2OAr), 3.79 (m, 2 H), 3.69 (ddd, 2 H, *J* = 11.3, 5.9, 1.5 Hz), 3.49 (m, 4 H), 3.01–3.19 (m, 6 H), 2.96 (m, 2 H), 1.65–1.78 (m, 4 H, CH_2), 1.50–1.62 (m, 4 H, CH_2), 1.21–1.49 (m, 22 H, CH_2 + CH_3). – *meso diastereoisomer*: ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 7.32 (d, 4 H, *J* = 8.9 Hz, aromatic), 6.78 (d, 4 H, *J* = 9.3 Hz, aromatic), 5.00 (d, 2 H, *J* = 5.4 Hz, OH, sugar), 4.97 (d, 2 H, *J* = 5.9 Hz, OH, sugar), 4.93 (d, 2 H, *J* = 4.4 Hz, OH, sugar), 4.74 (s, 2 H, OH), 4.52 (t, 2 H, *J* = 5.9 Hz, OH, sugar), 4.13 (d, 2 H, *J* = 7.4 Hz, H_1), 3.94 (t, 4 H, *J* = 6.6 Hz, CH_2OAr), 3.79 (m, 2 H), 3.69 (ddd, 2 H, *J* = 11.3, 5.9, 1.5 Hz), 3.49 (m, 4 H), 3.01–3.19 (m, 6 H), 2.96 (m, 2 H), 1.65–1.78 (m, 4 H, CH_2), 1.50–1.62 (m, 4 H, CH_2), 1.21–1.49 (m, 22 H, CH_2 + CH_3).

Bis-1-*O*-{3-[4-(1-hydroxyethyl)phenoxy]propyl} β-D-Glucopyranoside (9): Chromatography: eluent; dichloromethane/methanol (9:1 then 3:2 v/v), *Rf* = 0.22. – HRMS (FAB+) calcd. for $[C_{34}H_{50}O_{16}Li]^+$: 721.3258; found 721.3288. – *d,l diastereoisomer*: ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 6.99 (d, 4 H, *J* = 8.4 Hz, aromatic), 6.70 (d, 4 H, *J* = 8.9 Hz, aromatic), 5.06 (d, 2 H, *J* = 4.9 Hz, OH, sugar), 4.98 (d, 2 H, *J* = 4.4 Hz, OH, sugar), 4.95 (d, 2 H, *J* = 4.9 Hz, OH, sugar), 4.86 (s, 2 H, OH), 4.53 (t, 2 H, *J* = 5.9 Hz, OH, sugar), 4.17 (d, 2 H, *J* = 7.9 Hz, H_1), 4.03 (t, 4 H, *J* = 6.6 Hz, CH_2OAr), 3.93 (m, 2 H), 3.70 (ddd, 2 H, *J* = 11.3, 5.9, 1.5 Hz), 3.63 (m, 2 H), 3.47 (m, 2 H), 3.03–3.19 (m, 6 H), 2.98 (m, 2 H), 1.98 (quint, 4 H, *J* = 6.6 Hz, CH_2), 1.43 (s, 6 H, CH_3). – *meso diastereoisomer*: ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 7.34 (d, 4 H, *J* = 8.9 Hz, aromatic), 6.81 (d, 4 H, *J* = 8.9 Hz, aromatic), 5.06 (d, 2 H, *J* = 4.9 Hz, OH, sugar), 4.98 (d, 2 H, *J* = 4.4 Hz, OH, sugar), 4.95 (d, 2 H, *J* = 4.9 Hz, OH, sugar), 4.75 (s, 2 H, OH), 4.53 (t, 2 H, *J* = 5.9 Hz, OH, sugar), 4.17 (d, 2 H, *J* = 7.9 Hz, H_1), 4.07 (t, 4 H, *J* = 6.4 Hz, CH_2OAr), 3.93 (m, 2 H), 3.70 (ddd, 2 H, *J* = 11.3, 5.9, 1.5 Hz), 3.63 (m, 2 H), 3.47 (m, 2 H), 3.03–3.19 (m, 6 H), 2.98 (m, 2 H), 1.98 (quint, 4 H, *J* = 6.6 Hz, CH_2), 1.27 (s, 6 H, CH_3).

Bis-8-[4-(1-hydroxyethyl)phenoxy]octan-1-ol (10): Chromatography: eluent; dichloromethane/methanol (32:1 then 9:1 v/v), *Rf* = 0.65. – HRMS (FAB+) calcd. for $[C_{32}H_{50}O_6Li]^+$: 537.3767; found 537.3778. – *d,l diastereoisomer*: ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 6.98 (d, 4 H, *J* = 8.9 Hz, aromatic), 6.67 (d, 4 H, *J* = 8.9 Hz, aromatic), 4.84 (s, 2 H, OH), 4.37 (t, 2 H, *J* = 5.1 Hz, OH), 3.91 (t, 4 H, *J* = 6.4 Hz, CH_2OAr), 3.34–3.46 (m, 4 H, CH_2), 1.70 (quint, 4 H, *J* = 7.0 Hz, CH_2), 1.23–1.53 (m, 26 H, CH_2 + CH_3). – ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 156.79, 137.82, 128.41, 112.05, 77.26, 67.17, 60.76, 32.57, 28.98, 28.95, 28.82, 25.60, 25.52, 24.71. – *meso diastereoisomer*: ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 7.31 (d, 4 H, *J* = 8.4 Hz, aromatic), 6.78 (d, 4 H, *J* = 8.9 Hz, aromatic), 4.73 (s, 2 H, OH), 4.37 (t, 2 H, *J* = 5.1 Hz, OH), 3.95 (t, 4 H, *J* = 6.4 Hz, CH_2OAr), 3.34–3.46 (m, 4 H, CH_2), 1.70 (quint, 4 H, *J* = 7.0 Hz, CH_2), 1.23–1.53 (m, 26 H, CH_2 + CH_3). – ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 156.79, 138.72, 128.59, 112.26, 76.84, 67.17, 60.76, 32.57, 28.98, 28.95, 28.82, 25.60, 25.52, 25.15.

Bis-1-*O*-{8-[4-(1-hydroxyethyl)phenoxy]octyl} β-D-Glucofuranosid-urono-6,3-lactone (12): Chromatography: eluent; dichloromethane/methanol (19:1 then 4:1 v/v). – HRMS (FAB+) calcd. for $[C_{44}H_{62}O_{16}Li]^+$: 853.4197; found 853.4229. – *d,l diastereoisomer*: ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 6.98 (d, 4 H, *J* = 8.4 Hz, aromatic), 6.68 (d, 4 H, *J* = 8.4 Hz, aromatic), 5.86 (d, 2 H, *J* = 5.4 Hz, OH, sugar), 5.72 (s, 2 H, OH, sugar), 4.93 (s, 2 H, H_1), 4.85 (s, 2 H, OH), 4.79 (t, 2 H, *J* = 5.4 Hz, H_4), 4.73 (d, 2 H, *J* = 4.9 Hz, H_3), 4.46 (t, 2 H, *J* = 5.4 Hz, H_5), 4.08 (s, 2 H, H_2), 3.91 (t, 4 H, *J* = 6.4 Hz, CH_2OAr), 3.71 (m, 2 H, OCH_2), 3.23 (m, 2 H, OCH_2), 1.70 (m, 4 H, CH_2), 1.55–1.65 (m, 4 H, CH_2), 1.20–1.50 (m, 22 H, CH_2 + CH_3). – *meso diastereoisomer*: – ^1H NMR (400 MHz, $[D_6]$DMSO): δ = 7.32 (d, 4 H, *J* = 8.4 Hz, aromatic), 6.78 (d, 4 H, *J* = 8.9 Hz, aromatic), 5.86 (d, 2 H, *J* = 5.4 Hz, OH, sugar), 5.72 (s, 2 H, OH, sugar), 4.93 (s, 2 H, H_1), 4.79 (t, 2 H, *J* = 5.4 Hz, H_4), 4.73 (s, 2 H, OH), 4.73 (d, 2 H, *J* = 4.9 Hz, H_3), 4.46 (t, 2 H, *J* = 5.4 Hz, H_5), 4.08 (s, 2 H, H_2), 3.95 (t, 4 H, *J* = 5.9 Hz, CH_2OAr), 3.71 (m, 2 H, OCH_2), 3.23 (m, 2 H, OCH_2), 1.70 (m, 4 H, CH_2), 1.55–1.65 (m, 4 H, CH_2), 1.20–1.50 (m, 22 H, CH_2 + CH_3).

2-Hydroxy-2-(4-hexyloxyphenyl)-3-trideuteriomethoxy-3-(4'-hexyloxyphenyl)butane (13) and 2,3-Ditrideuteriomethoxy-2,3-bis(4-hexyloxyphenyl)butane (14): Dry tetrahydrofuran (15 mL) was placed in a dry, deaerated round-bottomed flask (equipped with a reflux condenser and a magnetic stirring bar). After deoxygenation with argon the THF was heated to 38 °C with stirring. Sodium hydride (15.5 mg of 60% dispersion in oil, 0.39 mmol, 3.25 equiv.), methyl iodide-d_3 (105 µL, 1.68 mmol, 14 equiv.) and then a solution

of pinacol **7** (54 mg, 0.12 mmol, 1 equiv.) in dry tetrahydrofuran (1 mL) was added. After 2 h heating, sodium hydride (15.5 mg, 0.39 mmol, 3.25 equiv.) and methyl iodide-d_3 (105 µL, 1.68 mmol, 14 equiv.) were added and then every hour (two or three times) methyl iodide-d_3 (105 µL). The successive formation of two products [TLC: eluent; cyclohexane/ethyl acetate (9:1 v/v); *Rf* = 0.51 (first observed) and 0.75] was observed. After 6 h heating, the reaction mixture was cooled and methanol was added dropwise until the evolution of hydrogen had ceased. The solvents were evaporated under reduced pressure and the residue treated with diethyl ether (10 mL). Insoluble compounds were filtered off and the organic solution was extracted with 5 mL of a 0.1 M aqueous solution of NH_4Cl, washed with water (2 × 2 mL), dried over $MgSO_4$, filtered then concentrated under reduced pressure. The yellow oil was purified by chromatography on a silica gel column [eluent; cyclohexane/ethyl acetate (19:1 v/v)]. Compounds **13** [TLC: eluent; cyclohexane/ethyl acetate (9:1 v/v); *Rf* = 0.51] and **14** [TLC: *Rf* = 0.75] were obtained as beige soaps in 42 and 53% yield, respectively (23 and 30 mg).

13: HRMS (FAB+) calcd. for $[C_{29}H_{41}O_4LiD_3]^+$: 466.3587; found 466.3573. – *d,l diastereoisomer*: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.90–7.01 (m, 4 H, aromatic), 6.78 (d, 2 H, *J* = 8.9 Hz, aromatic), 6.72 (d, 2 H, *J* = 8.9 Hz, aromatic), 3.90–3.99 (m, 4 H, CH_2OAr), 1.72–1.84 (m, 4 H, CH_2), 1.40–1.55 (m, 7 H, CH_2 + CH_3), 1.30–1.40 (m, 11 H, CH_2 + CH_3), 0.92 (m, 6 H, CH_3). – *meso diastereoisomer*: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.07 (d, 4 H, *J* = 8.4 Hz, aromatic), 6.76 (d, 2 H, *J* = 8.4 Hz, aromatic), 6.70 (d, 2 H, *J* = 8.4 Hz, aromatic), 3.90–3.99 (m, 4 H, CH_2OAr), 1.72–1.84 (m, 4 H, CH_2), 1.40–1.55 (m, 7 H, CH_2 + CH_3), 1.30–1.40 (m, 11 H, CH_2 + CH_3), 0.92 (m, 6 H, CH_3).

14: HRMS (FAB+) calcd. for $[C_{30}H_{40}O_4LiD_6]^+$: 483.3932; found 483.3965. – *d,l diastereoisomer*: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.70–6.85 (m, 4 H, aromatic), 6.65 (d, 4 H, *J* = 8.9 Hz, aromatic), 3.92 (t, 4 H, *J* = 6.4 Hz, CH_2OAr), 1.77 (m, 4 H, CH_2), 1.58 (s, 6 H, CH_3), 1.40–1.55 (m, 4 H, CH_2), 1.30–1.40 (m, 8 H, CH_2), 0.91 (t, 6 H, *J* = 7.7 Hz, CH_3).

Bis-1-*O*-{8-[4-(1-hydroxyethyl)phenoxy]octyl}-2,3,4,6-tetra-*O*-benzoyl β-D-Glucopyranoside (15): Dry dichloromethane (5 mL) and anhydrous pyridine (58 µL) (0.72 mmol, 8.8 equiv.) were introduced into a dry, deaerated round-bottomed flask. The reaction mixture was cooled to 5 °C. Benzoyl chloride (76 µL, 0.66 mmol, 8 equiv.) and pinacol **8** (70 mg, 0.082 mmol, 1 equiv.) were added successively with stirring. The temperature was maintained at around 5–10 °C and the reaction monitored by thin layer chromatography [eluent; cyclohexane/ethyl acetate (3:2 v/v)]. Every 30 min (five times) was added benzoyl chloride (19 µL, 0.16 mmol, 2 equiv.) and pyridine (15 µL, 0.18 mmol, 2.2 equiv.) and the reaction mixture was then stirred for 12 h at room temperature. A major component, characterized by *Rf* = 0.45, was observed by TLC. The organic phase was diluted with dichloromethane (10 mL), washed with a 0.015 M aqueous solution of H_2SO_4, water, a saturated aqueous solution of sodium hydrogencarbonate, and then water. The organic phase was dried over $MgSO_4$, filtered and then concentrated under reduced pressure. The crude product was purified by chromatography on a silica gel column [eluent; dichloromethane followed by dichloromethane/ethyl acetate (9:1 v/v)]. Product **15** [TLC: eluent; cyclohexane/ethyl acetate (3:2 v/v); *Rf* (**15**) = 0.45] was obtained as a sticky beige powder in 50% yield (70 mg). – HRMS (FAB+) calcd. for $[C_{100}H_{102}O_{24}Li]^+$: 1693.6921; found 1693.7036. – *d,l diastereoisomer*: ^{1}H NMR (400 MHz, $[D_6]$DMSO): δ = 8.01 (d, 4 H, *J* = 7.9 Hz, Ar-benzoyl), 7.89–7.94 (m, 4 H, Ar-benzoyl), 7.86 (d, 4 H, *J* = 7.4 Hz, Ar-benzoyl), 7.75 (d, 4 H, *J* = 7.9 Hz, Ar-benzoyl), 7.46–7.73 (m, 20 H, Ar-benzoyl), 7.39–7.45 (m, 4 H, Ar-benzoyl), 6.98 (d, 4 H, *J* = 8.4 Hz, aromatic), 6.65 (d, 4 H, *J* = 8.9 Hz, aromatic), 6.02 (t, 2 H, *J* = 9.6 Hz), 5.64 (t, 2 H, *J* = 9.3 Hz), 5.39 (t, 2 H, *J* = 8.9 Hz), 5.20 (dd, 2 H, *J* = 7.9, 2.5 Hz), 4.86 (s, 2 H, OH), 4.48–4.59 (m, 6 H), 3.82 (m, 6 H), 3.57 (m, 2 H), 1.55 (m, 4 H, CH_2), 1.40–1.50 (m, 10 H), 0.92–1.32 (m, 16 H). – *meso diastereoisomer*: ^{1}H NMR (400 MHz, $[D_6]$DMSO): δ = 8.01 (d, 4 H, *J* = 7.9 Hz, Ar-benzoyl), 7.89–7.94 (m, 4 H, Ar-benzoyl), 7.86 (d, 4 H, *J* = 7.4 Hz, Ar-benzoyl), 7.75 (d, 4 H, *J* = 7.9 Hz, Ar-benzoyl), 7.46–7.73 (m, 20 H, Ar-benzoyl), 7.39–7.45 (m, 4 H, Ar-benzoyl), 7.31 (d, 4 H, *J* = 8.9 Hz, aromatic), 6.77 (d, 4 H, *J* = 8.9 Hz, aromatic), 6.02 (t, 2 H, *J* = 9.6 Hz), 5.64 (t, 2 H, *J* = 9.3 Hz), 5.39 (t, 2 H, *J* = 8.9 Hz), 5.20 (dd, 2 H, *J* = 7.9, 2.5 Hz), 4.76 (s, 2 H, OH), 4.48–4.59 (m, 6 H), 3.82 (m, 6 H), 3.57 (m, 2 H), 1.55 (m, 4 H, CH_2), 1.40–1.50 (m, 10 H), 0.92–1.32 (m, 16 H).

Bis-1-*O*-{8-[4-(1-hydroxyethyl)phenoxy]octyl}-2,3,4,6-tetra-*O*-benzyl β-D-Glucopyranoside (16): Sodium hydride (68.1 mg of 60% dispersion in oil, 1.70 mmol, 16 equiv.) was introduced into a dry, deaerated round-bottomed flask (equipped with a magnetic stirring bar). After washing the dispersion with dry cyclohexane, DMF (5 mL) was added followed by a solution of pinacol **8** (97 mg, 0.11 mmol, 1 equiv.) in DMF (1 mL). After 30 min stirring at 20 °C, benzyl bromide (108 µL, 0.91 mmol, 8 equiv.) was introduced. The reaction was monitored by TLC [eluent; cyclohexane/ethyl acetate (7:3 v/v)]. Methanol was added dropwise when the reaction product (*Rf* = 0.40) was detected as the major component. The solution was concentrated and the DMF was distilled off under reduced pressure. The residue was dissolved in 10 mL of a diethyl ether/water mixture (1:1 v/v). The aqueous phase was separated and extracted with ether. The combined organic phases were washed with water, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by chromatography on a silica gel column [eluent; cyclohexane/ethyl acetate (4:1 v/v)]. Compound **16** [TLC: eluent; cyclohexane/ethyl acetate (7:3 v/v); *Rf* = 0.40] was obtained as a thick colorless oil in 30% yield (53 mg). – HRMS (FAB+) calcd. for $[C_{100}H_{118}O_{16}Li]^+$: 1581.8579; found 1581.8694. – *d,l diastereoisomer*: ^{1}H NMR (400 MHz, $[D_6]$DMSO): δ = 7.26–7.41 (m, 36 H, Ar-benzyl), 7.18–7.23 (m, 4 H, Ar-benzyl), 6.97 (d, 4 H, *J* = 8.4 Hz, aromatic), 6.65 (d, 4 H, *J* = 8.8 Hz, aromatic), 4.86–4.92 (m, 2 H, CH_2-benzyl), 4.81–4.86 (m, 4 H, CH_2-benzyl + OH), 4.72–4.78 (m, 4 H, CH_2-benzyl), 4.66–4.71 (m, 2 H, CH_2-benzyl), 4.48–4.60 (m, 8 H, CH_2-benzyl + H_1), 3.80–3.93 (m, 6 H), 3.60–3.74 (m, 6 H), 3.43–3.59 (m, 6 H), 3.29 (t, 2 H, *J* = 8.4 Hz), 1.66 (m, 4 H, CH_2), 1.59 (m, 4 H, CH_2), 1.23–1.46 (m, 22 H, CH_2 + CH_3). – *meso diastereoisomer*: ^{1}H NMR (400 MHz, $[D_6]$DMSO): δ = 7.26–7.41 (m, 40 H, Ar-benzyl + aromatic), 7.18–7.23 (m, 4 H, Ar-benzyl), 6.75 (d, 4 H, *J* = 8.9 Hz, aromatic), 4.86–4.92 (m, 2 H, CH_2-benzyl), 4.81–4.86 (m, 2 H, CH_2-benzyl), 4.72–4.78 (m, 6 H, CH_2-benzyl + OH), 4.66–4.71 (m, 2 H, CH_2-benzyl), 4.48–4.60 (m, 8 H, CH_2-benzyl + H_1), 3.80–3.93 (m, 6 H), 3.60–3.74 (m, 6 H), 3.43–3.59 (m, 6 H), 3.29 (t, 2 H, *J* = 8.4 Hz), 1.66 (m, 4 H, CH_2), 1.59 (m, 4 H, CH_2), 1.23–1.46 (m, 22 H, CH_2 + CH_3).

2-Hydroxy-2-[4-(1,8-octyldioxy)phenyl-1-*O*-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl]-3-trideuteriomethoxy-3-[4-(1,8-octyldioxy)-phenyl-1-*O*-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl]butane (17): Dry tetrahydrofuran (3 mL) was placed in a dry, deaerated round-bottomed flask (equipped with a reflux condenser and a magnetic stirring bar). After deoxygenation with argon the THF was heated to 38 °C with stirring. Sodium hydride (1.2 mg of 60% dispersion in oil, 0.03 mmol, 3 equiv.), methyl iodide-d_3 (10 µL, 0.16 mmol,

16 equiv.) and a solution of pinacol **16** (16 mg, 0.01 mmol, 1 equiv.) in dry tetrahydrofuran (1 mL) were added. After 1, 2 and 3 h heating, sodium hydride (1.2 mg, 0.03 mmol, 3 equiv.) and methyl iodide-d_3 (10 μL, 0.16 mmol, 16 equiv.) were added followed by methyl iodide-d_3 (15 μL) every hour until compound **17** was the major component [TLC: eluent; cyclohexane/ethyl acetate (4:1 v/v); *Rf* = 0.37]. The reaction mixture was cooled and methanol was added dropwise until hydrogen the evolution had ceased. The solvents were evaporated under reduced pressure and the residue dissolved in 10 mL of a mixture of diethyl ether/water (1:1 v/v). The aqueous phase was separated and extracted with diethyl ether. The combined organic phases were washed with water, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by chromatography on a silica gel column [eluent; cyclohexane/ethyl acetate (4:1 v/v)]. Compound **17** was obtained as a thick colorless oil in 65% yield (11 mg). – HRMS (FAB+) calcd. for $[C_{101}H_{117}O_{16}LiD_3]^+$: 1598.8924; found 1598.8970. – *d,l diastereoisomer*: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23–7.40 (m, 36 H, Ar-benzyl), 7.14–7.19 (m, 4 H, Ar-benzyl), 6.91–7.02 (m, 4 H, aromatic), 6.77 (d, 2 H, *J* = 9.4 Hz, aromatic), 6.71 (d, 2 H, *J* = 9.4 Hz, aromatic), 4.96 (d, 2 H, *J* = 11.8 Hz, CH_2-benzyl), 4.94 (d, 2 H, *J* = 10.8 Hz, CH_2-benzyl), 4.82 (d, 2 H, *J* = 10.8 Hz, CH_2-benzyl), 4.79 (d, 2 H, *J* = 10.8 Hz, CH_2-benzyl), 4.73 (d, 2 H, *J* = 11.3 Hz, CH_2-benzyl), 4.63 (d, 2 H, *J* = 12.3 Hz, CH_2-benzyl), 4.56 (d, 2 H, *J* = 12.3 Hz, CH_2-benzyl), 4.53 (d, 2 H, *J* = 10.8 Hz, CH_2-benzyl), 4.40 (d, 2 H, *J* = 7.9 Hz, H_1), 3.86–4.02 (m, 6 H), 3.75 (dd, 2 H, *J* = 10.6, 1.7 Hz), 3.50–3.71 (m, 6 H), 3.54 (m, 2 H), 3.42–3.50 (m, 4 H), 1.62–1.82 (m, 8 H, CH_2), 1.31–1.50 (m, 22 H, CH_2 + CH_3). – *meso diastereoisomer*: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23–7.40 (m, 36 H, Ar-benzyl), 7.14–7.19 (m, 4 H, Ar-benzyl), 7.10 (d, 4 H, *J* = 8.9 Hz, aromatic), 6.76 (d, 2 H, *J* = 8.9 Hz, aromatic), 6.70 (d, 2 H, *J* = 8.9 Hz, aromatic), 4.96 (d, 2 H, *J* = 11.8 Hz, CH_2-benzyl), 4.94 (d, 2 H, *J* = 10.8 Hz, CH_2-benzyl), 4.82 (d, 2 H, *J* = 10.8 Hz, CH_2-benzyl), 4.79 (d, 2 H, *J* = 10.8 Hz, CH_2-benzyl), 4.73 (d, 2 H, *J* = 11.3 Hz, CH_2-benzyl), 4.63 (d, 2 H, *J* = 12.3 Hz, CH_2-benzyl), 4.56 (d, 2 H, *J* = 12.3 Hz, CH_2-benzyl), 4.53 (d, 2 H, *J* = 10.8 Hz, CH_2-benzyl), 4.40 (d, 2 H, *J* = 7.9 Hz, H_1), 3.86–4.02 (m, 6 H), 3.75 (dd, 2 H, *J* = 10.6, 1.7 Hz), 3.50–3.71 (m, 6 H), 3.54 (m, 2 H), 3.42–3.50 (m, 4 H), 1.62–1.82 (m, 8 H, CH_2), 1.31–1.50 (m, 22 H, CH_2 + CH_3).

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