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A Metathesis Approach for the Preparation of Polyhydroxylated Compounds as Head Groups in Surfactant Synthesis

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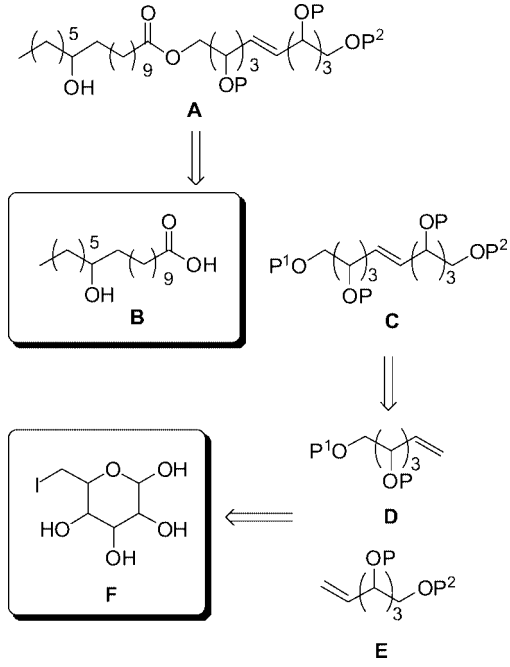
Starting from methyl-α-D-glucopyranoside, an efficient protocol for the preparation of polyhydroxylated surfactant head-groups is demonstrated and applied in the synthesis of a typical surfactant. The key transformation is a metathesis reaction between two monosaccharide residues to afford an octahydroxydecen. The importance of a strategic protecting-group constellation for a successful metathesis reaction is also investigated.

Introduction

Surfactants, also called tensides, belong to a class of compounds that carry a hydrophilic part (often called the head group) and a hydrophobic part (the tail group) in the same molecule. As a result the molecules assemble at interfaces between hydrophilic and hydrophobic media. Adsorption of the surfactant to the interface is spontaneous and the driving force is the lowering of interfacial energy.[1,2] The ability of surfactants to lower the energy of a surface in a system makes their use valuable in a wide variety of applications, such as solubilizers and emulsifying agents in pharmaceutical and food industry, as components in paints and detergents, as well as in the manufacturing of papers.[1] As the active component of a drug commonly suffers from low water solubility, surfactants are often employed as solubilizers for aqueous formulations.[3] This application requires the surfactant to be nontoxic and possess a low haemolytic activity, as well as having a high solubilizing capacity. Existing ethylene oxide-based surfactants for drug delivery are often complex mixtures of hundreds of different components. This might be beneficial for the function of the surfactant, but major drawbacks are large batch-to-batch variations and severe side-effects, among which histamine release might be the most acute.[4–6] Consequently, there is an obvious need for new efficient surfactants for drug-delivery applications that are free from adverse effects. With this in mind, we wanted to design and synthesize a surfactant with a defined composition and a low haemolytic activity. Several reasons exist for proposing a surfactant with the generic structure **A** shown in Scheme 1. First, hydroxy fatty acids have been successfully used as the hydrophobic part in commercial surfactants.[7] It has furthermore been reported that surfactants holding larger hydrophilic groups induce lower haemolysis compared to surfactants with the same length of the hydrophobic chain but with a smaller hydrophilic group,[4,8–10] the reason for why we required a strategy to easily control the length of the hydrophilic part.



Scheme 1. Retrosynthetic analysis.

Following the retrosynthetic pathway outlined in Scheme 1, surfactant **A** can be accessed by an ester coupling between 12-hydroxystearic acid (**B**) and olefin **C**, which contains a double bond that can be further derivatized. Since carbohydrates already encompass consecutive hydroxy groups with a defined stereochemistry, we speculated

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that monosaccharides would be a suitable starting point in the preparation of polyol **C**. We needed a simple and efficient way to extend the monosaccharide carbohydrate chain, and thus opted for a metathesis strategy combining the building blocks **D** and **E** to afford olefin **C**. Compounds **D** and **E** can be obtained from a Boord-type reaction[11] of a 6-deoxy-6-halo pyranose (**F**). This methodology presents a straightforward way to prepare polyhydroxy head-groups with high purity for surfactant synthesis, and can furthermore be applied in the synthesis of higher sugars, which are common structural motifs in various natural products.[12,13]

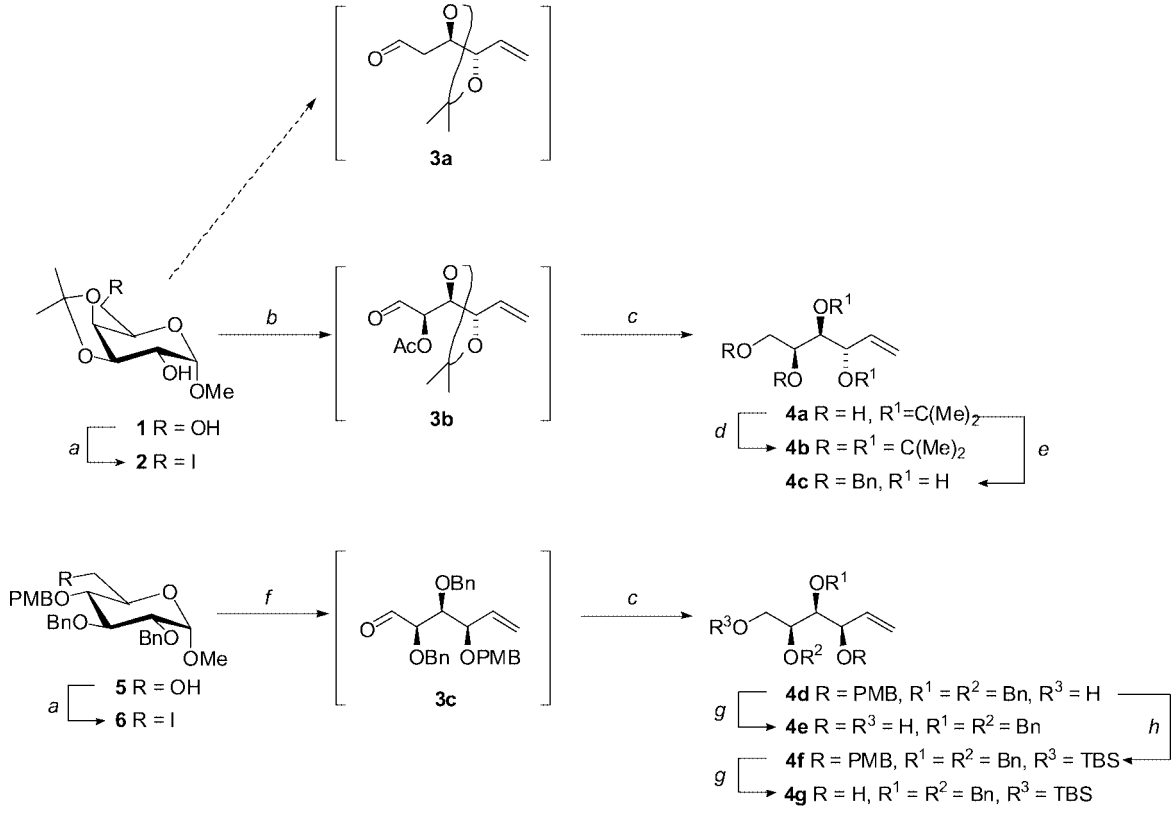
Results and Discussion

Preparation of Head-Group Building Blocks

The synthesis of surfactants is complicated by the often difficult purification of the target compounds, therefore the choice of protecting groups is critical for the success of the strategy − they should preferentially be removable without need for purification in the last step. Useful alcohol protecting groups are, for example, acetonide and benzyl groups.[14] We selected two monosaccharides − glucose and galactose − for preparation of building blocks **E** and **F**. Methyl-α-D-galactopyranoside was selectively protected as the corresponding 3,4-di-*O*-isopropylidene compound **1**[15] prior to 6-deoxyiodination, which furnished iodide **2**[16,17] (Scheme 2). The subsequent fragmentation of iodide **2** proceeded sluggishly and produced a mixture of by-products, from which the 2-deoxygenated aldehyde **3a** could be isolated.[11] To suppress formation of this 2-dexoygenated compound acetylation of the hydroxy group in iodide **2** therefore proved necessary. After screening several solvent systems for the fragmentation,[18–20] addition of four equivalents of NH_4Cl to the reaction mixture[21] and $LiAlH_4$ reduction of the intermediate aldehyde **3b** gave the desired olefin **4a** in modest yield. Several reports on cross metathesis with substrates containing allylic alcohols or ethers have been published lately, although it is unclear whether allylic alcohols or ethers facilitate the metathesis of the adjacent double bond or rather have an adverse effect on the reaction.[22–25] As part of our synthetic plan, we therefore decided to initiate a brief investigation on alcohol protecting-group strategies for the outcome of a metathesis reaction. Olefin **4a** therefore served as starting material for compounds **4b** and **4c**, which have different protecting-group constellations. To expand the number of possible metathesis substrates olefins **4d**–**g** were prepared from protected glucoside **5**,[26] which was iodinated and reductively fragmented as described for **1**.

Olefin Metathesis

With the seven hydroxylated olefins **4a**–**g** in hand a systematic investigation of Ru-catalyzed metathesis conditions

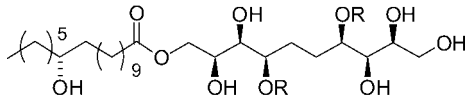


Scheme 2. Preparation of terminal olefins based on D-galactose and D-glucose. Reaction conditions: (a) PPh_3, I_2, imidazole, toluene, **2**: 48%, **6**: 94%; (b) *i*) Ac_2O, pyridine, DMAP, CH_2Cl_2, 100%; *ii*) Zn, NH_4Cl, THF/H_2O (10:1); (c) LAH, Et_2O, **4a**: 55% over two steps, **4d**: 71% over two steps; (d) 2-methoxypropene, *p*TsOH, DMF, 87%; (e) *i*) NaH, Bu_4NI, BnBr, THF, 61%. *ii*) HCl, THF, 85%; (f) Zn, NH_4Cl, THF/H_2O (10:1); (g) DDQ, CH_2Cl_2/H_2O (25:1), **4e**: 36%, **4g**: 81%; (h) TBSCl, imidazole, DMF, 69%.

was initiated, with the intention of dimerizing olefin **4** (Table 1). The two Ru catalysts **8** and **9** were chosen, of which **9** has been reported to be more active.[27] In this study, however, no significant differences between the two catalysts were experienced. Surprisingly, olefin **4a** was completely unreactive under the applied conditions (entries 1 and 2), and the starting material was recovered quantitatively even after repeated additions of catalyst and prolonged reaction times. Bis-acetonide **4b** was equally unreactive in refluxing CH_2Cl_2, while only decomposition products were isolated at 70 °C in toluene (entries 3 and 4). We speculated that this low reactivity might result from steric crowding in the *cis*-substituted five-membered acetonide present in compounds **4a** and **4b**, therefore olefin **4c**, which possesses a more flexible structure, was subjected to the same reaction conditions. The reactivity was, indeed, higher, however only by-products were isolated (entry 5). Continuing the investigation with the glucose-derived olefins **4d**–**g**, **4d** was unreactive in refluxing CH_2Cl_2 (entry 6), and when the solvent was changed to toluene and the temperature raised to 60 °C a mixture of unreacted olefin and decomposition products was isolated (entry 7). The deprotected diol **4e** proved to be even less suitable in the metathesis reaction as it resulted in a mixture of unidentified products even at room temp. (entry 8). We therefore speculated that the hydroxy groups at C1–C3 need to be protected, while a sterically demanding protecting group on the allylic hydroxy group cannot be tolerated in the metathesis reaction. To prove this theory, substrates **4f** and **4g** were subjected to the previously employed metathesis conditions, and, indeed, **4f** was recovered quantitatively even after stirring for several days, while **4g** was almost instantly converted into the desired dimer **7g** in good yield and as a single detected isomer (entries 9–11).

Completion of the Surfactants

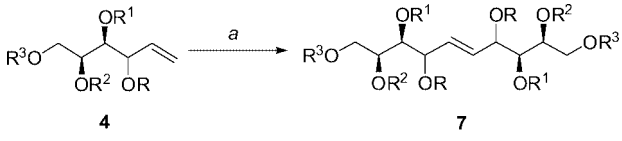
Delighted to have found a good dimerization protocol for olefin **4g**, we designed surfactants **10**–**12** with a head group based on polyol **7g** (Figure 1). It is well known that polyhydroxy-based surfactants might suffer from low water solubility due to favorable intermolecular hydrogen bonding and high crystallization energy. Therefore surfactants **11** and **12** were designed, which are similar to surfactant **10** but presumably have a lower affinity for intermolecular hydrogen bonding and crystallization due to the more bulky structure, which might aid the solubility.[28]



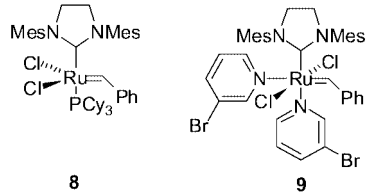
10 R = H
11 R = Ac
12 R = Me

Figure 1. Target surfactants.

Table 1. Olefin metathesis.[a]



4 **7**

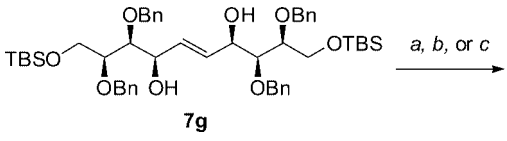


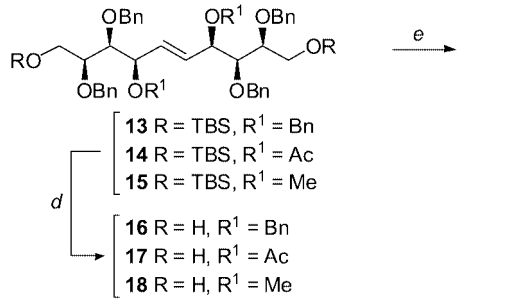
8 **9**

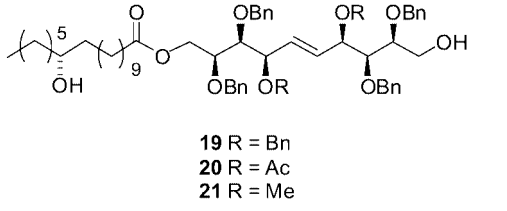
Entry	Olefin		Cat.	Solvent / temp. [°C]	Product / yield [%]
1	**4a**	R = R^1 = C(Me)$_2$, R^2 = R^3 = H, *S*,*S*	**9**	CH_2Cl_2 / 40	– / 0[b]
2	**4a**	R = R^1 = (CMe)$_2$, R^2 = R^3 = H, *S*,*S*	**8/9**	toluene / 70	– / 0[b]
3	**4b**	R = R^1 = R^2 = R^3 = C(Me)$_2$, *S*,*S*	**8/9**	CH_2Cl_2 / 40	– / 0[b]
4	**4b**	R = R^1 = R^2 = R^3 = (CMe)$_2$, *S*,*S*	**8/9**	toluene / 70	– / 0[c]
5	**4c**	R = R^1 = H, R^2 = R^3 = Bn, *S*,*S*	**8**	toluene / 70	– / 0[c]
6	**4d**	R = PMB, R^1 = R^2 = Bn, R^3 = H; *R*,*R*	**8**	CH_2Cl_2 / r.t.	– / 0[b]
7	**4d**	R = PMB, R^1 = R^2 = Bn, R^3 = H; *R*,*R*	**8**	toluene / 60	– / 0[d]
8	**4e**	R = R^3 = H, R^1 = R^2 = Bn; *R*,*R*	**8**	CH_2Cl_2 / r.t.	– / 0[c]
9	**4f**	R = PMB, R^1 = R^2 = Bn, R^3 = TBS; *R*,*R*	**8**	CH_2Cl_2 / r.t.	– / 0[b]
10	**4f**	R = PMB, R^1 = R^2 = Bn, R^3 = TBS; *R*,*R*	**8**	toluene / 60	– / 0[d]
11	**4g**	R = H, R^1 = R^2 = Bn, R^3 = TBS; *R*,*R*	**8**	CH_2Cl_2 / 40	**7g** / 67[e]

[a] Reaction conditions: (a) Catalysts **8** or **9**[27] (10–20 mol-%) in CH_2Cl_2 at room temp. to 40 °C or in toluene at 60–70 °C. No significant differences were seen between the two catalysts. [b] Starting material was recovered. [c] Starting material was consumed. [d] Starting material was recovered together with decomposition products. [e] *E*:*Z* > 99:1, Determined from coupling constants in compound **19**.

Starting from olefin **7g**, the allylic hydroxy groups were successfully benzylated,[29] acylated, and methylated to give **13**, **14**, and **15** respectively (Scheme 3). Cleavage of the TBS groups to deliver alcohols **16**, **17**, and **18**, respectively, was accomplished under acidic conditions,[30] which proved necessary in order to circumvent scrambling of the acetyl groups in **17**. To selectively obtain the monoester rather than the bis-ester in the subsequent esterification step, a fivefold excess of alcohols **16**–**18** to the (*R*)-12-hydroxystearic acid[31] was used. This stoichiometry, in combination with the Yamaguchi esterification protocol,[32] successfully provided the desired surfactant precursors **19**–**21**, together with recovered alcohols **16**–**18**. From the coupling constants of the vinylic protons in ester **19** it was furthermore possible to verify the stereochemistry of the double bond to be *E* (J = 15.5 Hz).

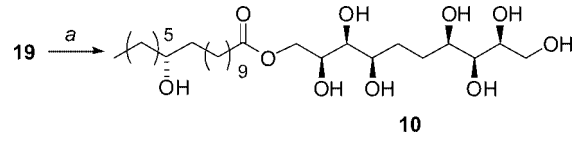






Scheme 3. Preparation of surfactant precursors **19**–**21**. Reaction conditions: (a) KHMDS, BnBr, THF, –78 °C → room temp., 71%; (b) Ac_2O, Et_3N, DMAP, CH_2Cl_2, 99%; (c) KHMDS, MeI, THF, –78 °C → room temp., 99%; (d) HOAc/H_2O/THF (1:3:3), 50 °C, **16**: 79%, **17**: 73%, **18**: 99%; (e) (*R*)-12-hydroxystearic acid, 2,4,6-trichlorobenzoyl chloride, Et_3N, DMAP, **19**: 73%, **20**: 84%, **21**: 82%.

Benzyl ethers are frequently used as hydroxy protecting groups since the hydrogenolytic deprotection usually only requires filtration and evaporation as workup.[14,33] This methodology was successfully applied to yield surfactant **10** (Scheme 4). A bit surprisingly, surfactant precursors **20** and **21** gave inseparable product mixtures when treated with H_2 and Pd/C in a variety of solvents and under different pressures, which forced us to temporarily leave those compounds.[34]



Scheme 4. Hydrogenolysis of compound **19**. Reaction conditions: (a) H_2, Pd/C, MeOH, 61%.

Conclusions

Using a Ru-catalyzed metathesis reaction as the key step we have developed an efficient synthesis of polyhydroxylated compounds to be used as surfactant headgroups. This strategy allows the synthesis of enantiomerically pure surfactants and should permit the synthesis of polyols with a different stereochemistry from other monosaccharides as starting materials. We have also demonstrated the importance of using a tactical protecting-group constellation to be successful in olefin metathesis of hydroxylated compounds. The surface chemical properties of surfactant **10** will be evaluated and presented in due course.

Experimental Section

General: ^1H and ^{13}C NMR spectra were recorded on Bruker dpx 400 MHz or avance 500 MHz spectrometers in $CDCl_3$ or CD_3OD using the residual peak of the corresponding solvent (^1H NMR: δ = 7.26 and 3.33 ppm, respectively; ^{13}C NMR: δ = 77.0 and 49.0 ppm, respectively) or added TMS (δ = 0.00 ppm), as internal standard. Optical rotations, $[\alpha]_D$ were measured on a Perkin–Elmer 343 polarimeter at the sodium D line at ambient temperature. Infrared spectra were recorded with an ATI Mattson FTIR spectrophotometer, and only the strongest/structurally most important peaks are listed. High-resolution mass spectra were recorded with a JEOL SX-102 spectrometer. Analytical thin-layer chromatography was performed on Merck silica gel 60 F_{254} plates, and visualized with UV light and phosphomolybdic acid staining reagent (5 wt.-% solution in EtOH) or H_2SO_4 (5 wt.-% solution in EtOH). Flash chromatography employed Grace Amicon silica gel 60 (35–70 μm) or Biotage SP4 flash system using Flash 12+M, 25+M and 40+M cartridges. Air- and moisture-sensitive reactions were carried out in flame-dried, septum-capped flasks under an atmospheric pressure of nitrogen. All liquid reagents were transferred with oven-dried syringes. THF and CH_2Cl_2 were taken from a GlassContour Seca Solvent system or freshly distilled from sodium-benzophenone ketyl and CaH_2, respectively. DMF and toluene were taken from a GlassContour Seca Solvent system.

(*S*)-1-[(4*R*,5*S*)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl]ethane-1,2-diol (4a). Acetylation of compound 2: Ac_2O (28 mL, 29.1 mmol), pyridine (1.17 mL, 14.55 mmol), and DMAP (cat.) were added to a solution of compound **2**[16,17] (1.9 g, 5.5 mmol) in CH_2Cl_2 (150 mL). The reaction mixture was stirred overnight and then washed with H_2O, dried ($MgSO_4$), and evaporated to give the acetate in 94% yield (2.0 g, 5.17 mmol). This material was immediately used for the Zn-promoted ring opening reaction.

General Procedure for the Reductive Opening of 6-Deoxy-6-iodohexoses. Synthesis of Compounds 4a–4d: The protected sugar (2.0 g, 5.17 mmol) was redissolved in THF/H_2O (11:1, 220 mL). Zn dust (3.4 g, 52.3 mmol) and NH_4Cl (1.1 g, 20.9 mmol) were added and the reaction mixture heated at 50 °C until no starting material remained (<10 min, TLC). The reaction mixture was cooled to room

temp., and was then filtered through a plug of celite and concentrated to give the crude aldehyde. The oily residue was redissolved in Et_2O (80 mL) and then transferred through a cannula into a suspension of $LiAlH_4$ (595 mg, 15.7 mmol) in Et_2O (80 mL) at 0 °C. The cooling bath was removed and the reaction mixture allowed to reach room temp. over 30 min. The product was isolated by careful addition of $Na_2SO_4 \cdot 10H_2O$ until gas evolution ceased, followed by successive addition of H_2O (595 μL), NaOH (15%, 595 μL), and H_2O (1785 μL). After stirring for 1 h the formed white crystals were filtered off, and the eluent concentrated to give the crude product. Flash chromatography (EtOAc/MeOH, 6:1) gave the title compound **4a** as a clear oil in 55% yield (544 mg, 2.89 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.99 (ddd, J = 17.2, 10.2, 8.2 Hz, 1 H), 5.71 (d, J = 17.2 Hz, 1 H), 5.31 (d, J = 10.2 Hz, 1 H), 4.61 (t, J = 7.7 Hz, 1 H), 4.19 (dd, J = 6.8, 5.1 Hz, 1 H), 3.70–3.53 (m, 3 H), 3.14 (br. s, 2 H), 1.53 (s, 3 H), 1.39 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.1, 120.3, 109.3, 79.4, 78.2, 70.2, 64.6, 27.7, 25.4 ppm. IR (neat): $\tilde{\nu}$ = 3369 cm^{-1} (br), 2985, 1072, 883 cm^{-1}. $[\alpha]_D$ = +36.9 (c = 1.00, CH_2Cl_2). HRMS (FAB+): calcd. for $C_9H_{17}O_4$ [M + H] 189.1127; found 189.1128.

(*S*)-4-[(4*S*,5*S*)-2,2-Dimethyl-5-vinyl-1,3-dioxolan-4-yl]-2,2-dimethyl-1,3-dioxolane (4b): 2-Methoxypropene (44 μL, 0.465 mmol) was added to a solution of **4a** (21 mg, 0.116 mmol) and *p*TsOH (cat.) in DMF (1 mL). The reaction mixture was stirred at room temp. for 10 min, and then diluted with Et_2O (1.5 mL) and H_2O (0.5 mL) and filtered through an Extrelut® NT3 tube. The organic layer was eluted with CH_2Cl_2 (15 mL) and concentrated to give the title compound **4b** as a colorless oil in 87% yield (23 mg, 0.101 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.77 (ddd, J = 17.1, 10.2, 8.4 Hz, 1 H), 5.27 (d, J = 17.1 Hz, 1 H), 5.22 (d, J = 10.2 Hz, 1 H), 4.47 (dd, J = 8.4, 6.3 Hz, 1 H), 4.11–4.02 (m, 2 H), 3.93 (dd, J = 8.3, 6.3 Hz, 1 H), 3.51 (dd, J = 8.2, 7.0 Hz, 1 H), 1.48 (s, 3 H), 1.39 (s, 3 H), 1.34 (s, 3 H), 1.30 (s, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 134.0, 119.6, 109.69, 109.66, 80.1, 78.6, 75.1, 65.8, 27.7, 26.6, 25.29, 25.25 ppm. IR (neat): $\tilde{\nu}$ = 2983, 1371, 1066, 868 cm^{-1}. $[\alpha]_D$ = +6.3 (c = 0.95, CH_2Cl_2); m.p. 62.3–63.3 °C. HRMS (FAB+): calcd. for $C_{12}H_{20}O_4$ [M$^+$] 228.1362; found 228.1338.

(3*S*,4*S*,5*S*)-5,6-Bis(benzyloxy)hex-1-ene-3,4-diol (4c): NaH (5 mg, 0.124 mmol, 60 wt.-% dispersion in oil) was washed twice with pentane and then suspended in DMF (2 mL) and cooled to 0 °C. Compound **4a** (11 mg, 0.0606 mmol), BnBr (22 μL, 0.182 mmol), and Bu_4NI (2.2 mg, 0.00606 mmol) were added and the reaction mixture was allowed to reach room temp. overnight. The reaction was quenched by the addition of H_2O (5 mL) and the mixture was extracted with Et_2O (10 mL). The organic layer was dried ($MgSO_4$) and concentrated. Flash chromatography (pentane/EtOAc, 15:1) gave the corresponding bis-benzyl ether as a colorless oil in 61% yield (13.7 mg, 0.0371 mmol). This material was then stirred with HCl (1 M, 1.5 mL) in THF (1.5 mL) at 40 °C for 1 h. The THF was evaporated, Et_2O (1 mL) was added, and the biphasic mixture filtered through an Extrelut® NT3 tube. The organic phase was eluted with CH_2Cl_2 (15 mL). Concentration afforded the title compound **4c** as a colorless oil in 85% yield (10 mg, 0.0316 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.17 (m, 10 H), 5.86 (ddd, J = 17.2, 10.6, 5.5 Hz, 1 H), 5.26 (td, J = 17.2, 1.6 Hz, 1 H), 5.16 (td, J = 10.6, 1.5 Hz, 1 H), 4.70 (d, J = 11.3 Hz, 1 H), 4.52–4.45 (m, 3 H), 4.17–4.12 (m, 1 H), 3.81 (dt, J = 5.1, 3.0 Hz, 1 H), 3.71–3.60 (m, 3 H), 2.68 (d, J = 7.3 Hz, 1 H), 2.53 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.84, 137.78, 137.5, 128.6, 128.5, 128.2, 128.1, 127.8, 127.7, 116.3, 77.4, 74.2, 73.6, 73.5, 72.8, 70.4 ppm. IR (neat): $\tilde{\nu}$ = 3442 cm^{-1} (br), 2868, 1097, 737 cm^{-1}. $[\alpha]_D$ = +5.0 (c = 0.38, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{20}H_{25}O_4$ [M + H] 329.1754; found 329.1757.

Methyl-2,3-di-*O*-benzyl-6-iodo-4-*O*-(4-methoxybenzyl)-6-deoxy-α-D-glucopyranoside (6): This compound was prepared from **5**[26] as described previously[16,17] and obtained as a white powder in 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.29 (m, 10 H), 7.20 (d, J = 8.7 Hz, 2 H), 6.86 (d, J = 8.7 Hz, 2 H), 4.99 (d, J = 10.9 Hz, 1 H), 4.87–4.78 (m, 3 H), 4.68–4.60 (m, 3 H), 4.00 (t, J = 9.2 Hz, 1 H), 3.80 (s, 3 H), 3.53 (dd, J = 9.6, 3.6 Hz, 1 H), 3.47–3.42 (m, 2 H), 3.41 (s, 3 H), 3.34–3.24 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4, 138.5, 137.9, 130.1, 129.6, 128.5, 128.4, 128.1, 128.0, 127.9, 127.7, 113.9, 98.1, 81.6, 81.1, 80.0, 75.7, 75.0, 73.4, 69.3, 55.5, 55.3, 7.7 ppm. IR (neat): $\tilde{\nu}$ = 2908, 1514, 1250, 1068 cm^{-1}. $[\alpha]_D$ = +49.3 (c = 1.00, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{29}H_{33}O_6NaI$ [M + Na] 627.1220; found 627.1224.

(2*S*,3*S*,4*R*)-2,3-Bis(benzyloxy)-4-(4-methoxybenzyloxy)hex-5-en-1-ol (4d): This compound was prepared from **6** as described for **4a** and used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.26 (m, 10 H), 7.22 (d, J = 8.6 Hz, 2 H), 6.85 (d, J = 8.6 Hz, 2 H), 5.91–5.83 (m, 1 H), 5.31 (d, J = 6.0 Hz, 1 H), 5.27 (s, 1 H), 4.71 (s, 2 H), 4.60 (s, 2 H), 4.56 (d, J = 11.4 Hz, 1 H), 4.29 (d, J = 11.4 Hz, 1 H), 4.06 (dd, J = 7.3, 4.3 Hz, 1 H), 3.79 (s, 3 H), 3.72–3.61 (m, 3 H), 3.55–3.50 (m, 1 H), 2.19 (t, J = 6.3 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 259.7, 138.9, 138.7, 135.7, 130.4, 130.1, 128.9, 128.83, 128.78, 128.3, 128.2, 128.1, 119.2, 114.2, 82.2, 80.4, 80.0, 75.2, 73.2, 70.8, 61.8, 55.7 ppm. IR (neat): $\tilde{\nu}$ = 3469 cm^{-1} (br), 2872, 1066, 698 cm^{-1}. $[\alpha]_D$ = –7.2 (c = 0.29, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{28}H_{33}O_5$ [M + H] 449.2329; found 449.2328.

General Procedure for the PMB Deprotection Using DDQ. Synthesis of (2*S*,3*S*,4*R*)-2,3-Bis(benzyloxy)hex-5-ene-1,4-diol (4e): H_2O (0.4 mL) and DDQ (183 mg, 0.804 mmol) were added to a solution of compound **4d** (328 mg, 0.731 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was stirred vigorously for 1 h, and then quenched by the addition of $NaHCO_3$. The phases were separated and the organic layer was washed with brine, dried ($MgSO_4$), and the solvents evaporated. Flash chromatography (EtOAc/pentane 5% → 50%) gave **4e** in 84% yield (202 mg, 0.615 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.26 (m, 10 H), 5.91 (ddd, J = 17.1, 10.3, 5.0 Hz, 1 H), 5.34 (td, J = 17.1, 1.4 Hz, 1 H), 5.19 (td, J = 10.3, 1.4 Hz, 1 H), 4.66 (d, J = 11.3 Hz, 1 H), 4.65 (d, J = 11.7 Hz, 1 H), 4.60 (d, J = 11.3 Hz, 1 H), 4.59 (d, J = 11.7 Hz, 1 H), 4.40–4.35 (m, 1 H), 3.84–3.76 (m, 2 H). 3.68–3.61 (m, 1 H), 3.58 (dd, J = 5.8, 2.8 Hz, 1 H), 2.68 (d, J = 7.3 Hz, 1 H), 2.48 (dd, J = 6.5, 6.0 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.5, 138.1, 137.8, 128.5, 128.4, 128.2, 128.0, 127.9, 115.7, 80.8, 79.0, 74.5, 72.5, 71.1, 60.6 ppm; two carbon signals are overlapping at δ = 127.9 ppm. IR (neat): $\tilde{\nu}$ = 3415, 1095, 739, 698 cm^{-1}. $[\alpha]_D$ = +25.3 (c = 1.02, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{20}H_{25}O_4$ [M + H] 329.1754; found 329.1750.

***tert*-Butyl-[(2*S*,3*S*,4*R*)-2,3-bis(benzyloxy)-4-(4-methoxybenzyloxy)-hex-5-enyloxy]dimethylsilane (4f):** Compound **4d** (5.1 g, 11.4 mmol) was stirred with TBDMSCl (1.9 g, 12.5 mmol) and imidazole (1.55 g, 22.8 mmol) in DMF (250 mL) at room temp. overnight. The reaction mixture was diluted with Et_2O (300 mL) and washed with H_2O and brine. The organic phase was dried ($MgSO_4$) and concentrated. After purification with flash chromatography (EtOAc/pentane 5% → 50%) **4f** was obtained in 69% yield (4.42 g, 7.85 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.16 (m, 12 H), 6.80 (d, J = 8.8 Hz, 2 H) 5.76 (ddd, J = 17.1, 10.6, 7.8 Hz, 1 H) 5.23–5.15 (m, 2 H), 4.76 (d, J = 11.7 Hz, 1 H), 4.64 (d, J = 11.7 Hz, 2 H), 4.51 (d, J = 11.7 Hz, 2 H), 4.29 (d, J = 11.7 Hz, 1 H), 4.08 (dd, J = 7.6, 6.0 Hz, 1 H), 3.74 (s, 3 H), 3.66–3.54 (m, 4 H), 0.83 (s, 9 H), –0.055 (s, 3 H), –0.060 (s, 3 H) ppm. ^{13}C NMR

(100 MHz, $CDCl_3$): δ = 159.5, 139.44, 139.36, 136.3, 131.0, 130.1, 128.8, 128.63, 128.56, 128.3, 127.9, 127.8, 119.0, 114.1, 81.61, 81.58, 80.6, 75.6, 73.5, 70.8, 63.1, 55.7, 26.3, 18.6, –4.97, –5.0 ppm. IR (neat): $\tilde{\nu}$ = 1250, 1088, 837 cm^{-1}. $[\alpha]_D$ = –12.4 (c = 0.59, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{34}H_{47}O_5Si$ [M + H] 563.3194; found 563.3193.

(2*R*,3*S*,4*R*)-2,3-Bis(benzyloxy)-1-(*tert*-butyldimethylsilyloxy)hex-5-en-4-ol (4g): This compound was prepared as described for **4e** and obtained in 81% yield (2.8 g, 6.35 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.29 (m, 10 H), 5.94 (ddd, J = 17.2, 10.5, 5.6 Hz, 1 H), 5.35 (td, J = 17.2, 1.6 Hz, 1 H), 5.20 (td, J = 10.5, 1.6 Hz, 1 H), 4.75 (d, J = 11.3 Hz, 1 H), 4.73 (d, J = 11.8 Hz, 1 H), 4.66 (d, J = 11.3 Hz, 1 H), 4.62 (d, J = 11.8 Hz, 1 H), 4.40–4.36 (m, 1 H), 3.87 (AB-dd, J = 11.0, 5.1 Hz, 1 H), 3.85 (AB-dd, J = 11.0, 4.7 Hz, 1 H), 3.68 (q, J = 5.0 Hz, 1 H), 3.62 (dd, J = 5.1, 3.9 Hz, 1 H), 2.95 (d, J = 5.8 Hz, 1 H), 0.94 (s, 9 H), 0.10 (s, 3 H), 0.098 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.5, 138.4, 138.34, 128.32, 128.1, 127.9, 127.8, 127.6, 115.8, 81.6, 80.3, 74.8, 73.0, 71.9, 62.4, 25.9, 18.0, –5.39, –5.45 ppm. IR (neat): $\tilde{\nu}$ = 3450 cm^{-1} (br), 1256, 1093, 837 cm^{-1}. $[\alpha]_D$ = +18.0 (c = 1.00, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{26}H_{39}O_4Si$ [M + H] 443.2618; found 443.2623.

(*E*,2*R*,3*S*,4*R*,7*R*,8*S*,9*R*)-2,3,8,9-tetra(Benzyloxy)-1,10-bis(*tert*-butyldimethylsilyloxy)dec-5-ene-4,7-diol (7g): Compound **4g** (5 mg, 0.0113 mmol) was dissolved in CH_2Cl_2 (0.5 mL) and Grubbs' second-generation catalyst (1 mg, 1.13 μmol) was added to this solution. The solution was heated to 40 °C and after 3 h the starting material had been consumed, as judged by TLC. Evaporation of the solvent and purification by flash chromatography (pentane/EtOAc, 4:1) provided olefin **7g** in 66% yield (3.2 mg, 3.73 μmol). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.17 (m, 20 H), 5.74 (dd, J = 2.8, 1.0 Hz, 2 H), 4.64 (d, J = 11.6 Hz, 4 H), 4.59–4.51 (m, 4 H), 4.31–4.26 (m, 2 H), 3.79 (dd, J = 11.1, 5.3 Hz, 2 H), 3.75 (dd, J = 11.1, 4.5 Hz, 2 H), 3.60 (app. q J = 5.0 Hz, 2 H), 3.49 (dd, J = 5.5, 3.8 Hz, 2 H), 2.72 (d, J = 6.0 Hz, 2 H), 0.86 (s, 18 H), 0.02 (s, 6 H), 0.01 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.5, 138.2, 131.7, 128.31, 128.28, 128.2, 127.9, 127.7, 127.6, 81.5, 80.4, 74.6, 73.0, 71.1, 62.7, 25.9, 18.2, –5.39, –5.42 ppm. IR (neat): $\tilde{\nu}$ = 3442 cm^{-1} (br), 1255, 1095, 837 cm^{-1}. $[\alpha]_D$ = +11.3 (c = 0.96, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{50}H_{72}O_8Si_2Na$ [M + Na] 879.4664; found 879.4664.

General Procedure for the *O*-Alkylation of Alcohol 7g. Synthesis of 13–15. (*E*,2*R*,3*S*,4*R*,7*R*,8*S*,9*R*)-2,3,4,7,8,9-Hexa(benzyloxy)-1,10-bis(*tert*-butyldimethylsilyloxy)dec-5-ene (13): KHMDS (0.187 mmol, 0.4 mL of a 0.5 M solution in toluene) was added dropwise to a solution of **7g** (40 mg, 0.0467 mmol) and alkyl halide (BnBr, 56 μL, 0.467 mmol) in THF (5 mL) at –78 °C. The reaction mixture was allowed to reach room temp. overnight, and the reaction was then quenched by the addition of Na_2CO_3 (sat.). The phases were separated and the aqueous phase was extracted three times with Et_2O. Drying ($MgSO_4$) and evaporation gave 108 mg of a crude oil that was purified with flash chromatography (EtOAc/pentane 5% → 10%) to give **13** as a clear oil in 86% yield (41.8 mg, 0.0403 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.24 (m, 30 H), 5.76 (dd, J = 4.3, 2.1 Hz, 2 H), 4.79 (d, J = 11.6 Hz, 2 H), 4.70 (d, J = 11.6 Hz, 2 H), 4.68 (d, J = 11.7 Hz, 2 H), 4.62 (d, J = 11.8 Hz, 2 H), 4.55 (d, J = 11.7 Hz, 2 H), 4.41 (d, J = 11.8 Hz, 2 H), 4.19–4.16 (m, 2 H) 3.76–3.62 (m, 8 H), 0.88 (s, 18 H), 0.01 (s, 6 H), 0.00 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.8, 138.7, 138.3, 131.7, 128.3, 128.2, 128.1, 127.9, 127.8, 127.5, 127.4, 81.3, 80.3, 80.1, 75.0, 73.0, 70.9, 63.0, 25.9, 18.2, –5.4 ppm. IR (neat): $\tilde{\nu}$ = 2927, 1092, 837 cm^{-1}. $[\alpha]_D$ = –9.1 (c = 0.7, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{64}H_{84}NaO_8Si_2$ [M + Na] 1059.5603; found 1059.5592.

(*E*,2*R*,3*S*,4*R*,7*R*,8*S*,9*R*)-4,7-Bis(acetoxy)-2,3,8,9-tetra(benzyloxy)-1,10-bis(*tert*-butyldimethylsilyloxy)dec-5-ene (14): Alcohol **7g** (43 mg, 0.498 mmol) was stirred together with Ac_2O (47 μL, 0.498 mmol), Et_3N (35 μL, 0.249 mmol), and DMAP (cat.) in CH_2Cl_2 (2 mL) for 14 h at room temp. The reaction mixture was then diluted with H_2O and filtered through an Extrelut® NT3 tube and eluted with CH_2Cl_2 (15 mL). Evaporation of the solvent gave **14** in 90% yield (42 mg, 0.0448 mmol). The compound was used without further purification. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.29–7.20 (m, 20 H), 5.68 (dd, J = 3.8, 1.9 Hz, 2 H), 5.55–5.49 (m, 2 H), 4.64–4.56 (m, 6 H), 4.51 (d, J = 12.0 Hz, 2 H), 3.70 (dd, J = 10.6, 5.7 Hz, 2 H), 3.64 (dd, J = 6.0, 4.4 Hz, 2 H), 3.56 (dd, J = 10.6, 5.4 Hz, 2 H), 3.49 (app. dd, J = 9.8, 5.4 Hz, 2 H), 1.87 (s, 6 H), 0.84 (s, 18 H), –0.02 (s, 6 H), –0.03 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.7, 138.7, 138.5, 129.5, 128.3, 128.2, 127.8, 127.50, 127.48, 80.1, 79.9, 74.9, 73.9, 73.1, 62.0, 25.9, 21.1, 18.2, –5.40, –5.43 ppm; two carbon signals are overlapping at δ = 127.8 ppm. IR (neat): $\tilde{\nu}$ = 2929, 1743, 1232, 1093, 837 cm^{-1}. $[\alpha]_D$ = –4.75 (c = 0.80, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{54}H_{76}NaO_{10}Si_2$ [M + Na] 963.4875; found 963.4877.

(*E*,2*R*,3*S*,4*R*,7*R*,8*S*,9*R*)-2,3,8,9-Tetra(benzyloxy)-1,10-bis(*tert*-butyldimethylsilyloxy)-4,7-bis(methoxy)-dec-5-ene (15): This compound was prepared from **7g** and MeI as described for **13**, and obtained in 99% yield. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.30–7.21 (m, 20 H), 5.64 (dd, J = 4.4, 2.2 Hz, 2 H), 4.70–4.61 (m, 6 H), 4.55 (d, J = 12.0 Hz, 2 H), 3.84 (ddd, J = 6.9, 4.7, 2.2 Hz, 2 H), 3.78 (dd, J = 10.7, 4.4 Hz, 2 H), 3.71 (dd, J = 10.7, 6.0 Hz, 2 H), 3.65 (app. dd, J = 10.1, 4.4 Hz, 2 H), 3.49 (t, J = 4.7 Hz, 2 H), 3.23 (s, 6 H), 0.87 (s, 18 H), 0.02 (s, 12 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.9, 138.7, 131.4, 128.22, 128.19, 128.17, 127.9, 127.5, 82.2, 81.5, 80.4, 74.9, 73.1, 63.1, 56.7, 25.9, 18.2, –5.37, –5.39 ppm; the two missing carbon signals are overlapping with the signals at δ = 127–129 ppm. IR (neat): $\tilde{\nu}$ = 2929, 2856, 1454, 1254, 1090, 837 cm^{-1}. $[\alpha]_D$ = –10.0 (c = 0.91, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{52}H_{76}NaO_8Si_2$ [M + Na] 907.4977; found 907.4971.

General Procedure for the TBS-Deprotection of Compounds 13–15. Synthesis of Alcohols 16–18. (*E*,2*S*,3*S*,4*R*,7*R*,8*S*,9*S*)-2,3,4,7,8,9-Hexa(benzyloxy)dec-5-ene-1,10-diol (16): Silyl ether **13** (359 mg, 0.346 mmol) was dissolved in THF (15 mL). H_2O (15 mL) and HOAc (5 mL) were added and the reaction mixture heated to 50 °C for 24 h. After cooling to room temp., the reaction mixture was transferred to a separation funnel containing Et_2O, and $NaHCO_3$ (aq) was added. The phases were separated and the aqueous layer was extracted twice with Et_2O. The combined organic phases were dried ($MgSO_4$) and evaporated to give 292 mg of a crude oil. Purification with flash chromatography (EtOAc/pentane 5% → 100%) gave **16** in 79% yield (222 mg, 0.274 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.27 (m, 30 H), 5.85 (dd, J = 4.3, 2.0 Hz, 2 H), 4.75 (d, J = 11.5 Hz, 2 H), 4.72 (d, J = 11.5 Hz, 2 H), 4.63 (d, J = 11.7 Hz, 2 H), 4.61 (s, 4 H), 4.43 (d, J = 11.7 Hz, 2 H), 4.18–4.14 (m, 2 H), 3.76–3.70 (m, 2 H), 3.67–3.57 (m, 6 H), 2.23 (dd, J = 7.3, 5.8 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.3, 138.2, 137.7, 131.2, 128.4, 128.39, 128.36, 128.3, 127.9, 127.83, 127.79, 127.7, 81.6, 79.6, 79.5, 74.7, 72.7, 71.0, 61.4 ppm; the two missing carbon signals are overlapping with the signals at δ = 127–129 ppm. IR (neat): $\tilde{\nu}$ = 3431 cm^{-1} (br), 2868, 1454, 1027, 1072, 735, 698 cm^{-1}. $[\alpha]_D$ = –0.42 (c = 0.48, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{52}H_{56}NaO_8$ [M + Na] 831.3873; found 831.3867.

(*E*,2*S*,3*S*,4*R*,7*R*,8*S*,9*S*)-4,7-Bis(acetoxy)-2,3,8,9-tetra(benzyloxy)-dec-5-ene-1,10-diol (17): This compound was prepared as described for **16** and obtained in 73% yield. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.30–7.16 (m, 20 H), 5.70 (dd, J = 3.3, 1.4 Hz, 2 H), 5.43 (app.

t, J = 3.9 Hz, 2 H), 4.60 (s, 4 H), 4.56 (d, J = 11.7 Hz, 2 H), 4.50 (d, J = 11.7 Hz, 2 H), 3.69–3.62 (m, 2 H), 3.60 (t, J = 5.4 Hz, 2 H), 3.52–3.44 (m, 4 H), 1.91 (s, 6 H), 1.83 (t, J = 6.3 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.8, 138.2, 137.9, 128.8, 128.5, 128.4, 128.0, 127.87, 127.86, 127.83, 80.2, 79.5 74.6, 73.2, 73.1, 61.4, 21.1 ppm. IR (neat): $\tilde{\nu}$ = 2875, 1739, 1232, 1078 cm^{-1}. $[\alpha]_D$ = +3.1 (c = 0.65, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{42}H_{48}NaO_{10}$ [M + Na] 735.3145; found 735.3149.

(*E*,2*S*,3*S*,4*R*,7*R*,8*S*,9*S*)-2,3,8,9-Tetra(benzyloxy)-4,7-bis(methoxy)-dec-5-ene-1,10-diol (18): This compound was prepared as described for **16** and obtained in 99% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27–7.19 (m, 20 H), 5.66 (dd, J = 4.3, 2.0 Hz, 2 H), 4.62 (d, J = 11.3 Hz, 2 H), 4.54 (d, J = 11.3 Hz, 2 H), 4.51 (s, 4 H), 3.79–3.76 (m, 2 H), 3.71–3.66 (m, 2 H), 3.59–3.49 (m, 4 H), 3.47 (dd, J = 5.7, 4.1 Hz, 2 H), 3.19 (s, 6 H), 2.24 (s, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.3, 138.1, 131.3, 128.43, 128.37, 128.3, 127.9, 127.82, 127.76, 81.7, 81.6, 79.7, 74.7, 72.7, 61.4, 56.8 ppm. IR (neat): $\tilde{\nu}$ = 3444, 2929, 1454, 1074 cm^{-1}. $[\alpha]_D$ = –3.4 (c = 0.58, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{40}H_{48}NaO_8$ [M + Na] 679.3247; found 679.3262.

General Procedure for the Esterification of Alcohols 16–18 with (*R*)-12-Hydroxystearic Acid. Synthesis of Esters 19–21. (*E*,2*S*,3*S*,4*R*,7*R*,8*S*,9*S*,12′*R*)-2,3,4,7,8,9-Hexa(benzyloxy)-10-hydroxydec-5-enyl 12-Hydroxystearate (19). Preparation of the Activated Anhydride: 2,4,6-Trichlorobenzoyl chloride (51.5 μL, 0.329 mmol) was added to a solution of (*R*)-12-hydroxystearic acid (99 mg, 0.329 mmol) and Et_3N (50 μL, 0.362 mmol) in THF (2.5 mL). The reaction mixture was allowed to stir for 20 h, and was then filtered through a small plug of cotton wool and evaporated to give 167 mg of a white powder. This was dissolved in CH_2Cl_2 (10.8 mL) to give a 15.4 mg/mL standard solution.

Esterification: Alcohol **16** (192 mg, 0.237 mmol) and DMAP (5.8 mg, 0.0475 mmol) were dissolved in CH_2Cl_2 (20 mL). To this solution was added 1.5 mL of the standard solution prepared above, and the reaction mixture was left stirring overnight. HCl (0.25 M, 10 mL) was added to quench the reaction and the phases were separated. The organic layer was collected, dried ($MgSO_4$), and evaporated to give a mixture of the title compound and unreacted starting material. This mixture was separated by flash chromatography (pentane/EtOAc, 4:1→ 1:1) to give **19** in 73% yield (36.4 mg, 0.0334 mmol) together with 74% of recovered alcohol **16**. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.20 (m, 30 H), 5.76 (dd, J = 15.9, 6.5 Hz, 1 H), 5.72 (dd, J = 15.9, 6.5 Hz, 1 H), 4.70 (d, J = 11.6 Hz, 1 H), 4.66–4.51 (m, 8 H), 4.48 (d, J = 11.6 Hz, 1 H), 4.36 (d, J = 11.8 Hz, 1 H), 4.32 (d, J = 11.8 Hz, 1 H), 4.22 (dd, J = 11.7, 4.5 Hz, 1 H), 4.16 (dd, J = 11.7, 6.0 Hz, 1 H), 4.10 (t, J = 6.2 Hz, 1 H), 4.07–4.01 (m, 1 H), 3.77 (app. q, J = 5.0 Hz, 1 H), 3.65 (s, 1 H), 3.60–3.48 (m, 5 H), 2.24–2.16 (m, 1 H), 2.15 (t, J = 7.6 Hz, 2 H), 1.58 (s, 1 H), 1.55–1.46 (m, 2 H), 1.45–1.33 (m, 6 H) 1.32–1.17 (m, 20 H), 0.86 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.5, 138.4, 138.20, 138.19, 138.0, 137.8, 131.5, 131.3, 128.43, 128.38, 128.37, 128.35, 128.32, 128.28, 128.27, 128.22, 127.91, 127.86, 127.81, 127.76, 127.70, 127.68, 127.62, 81.7, 80.9, 79.8, 79.6, 79.4, 74.8, 74.7, 72.9, 72.7, 72.0, 70.94, 70.93, 63.5, 61.4, 37.50, 37.49, 34.2, 31.8, 29.7, 29.6, 29.5, 29.44, 29.37, 29.27, 29.2, 25.7, 25.6, 24.9, 22.6, 14.1 ppm; one missing carbon signal is overlapping with the signals present at δ = 137–139 ppm, three missing carbon signals are overlapping with the signals present at δ = 127–129 ppm, and one benzylic carbon signal is overlapping with the signals present at δ = 70–76 ppm. IR (neat): $\tilde{\nu}$ = 2926, 1736, 1454, 1095, 733, 698 cm^{-1}. $[\alpha]_D$ = +3.1 (c = 0.16, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{70}H_{90}NaO_{10}$ [M + Na] 1113.6432; found 1113.6445.

(*E*,2*S*,3*S*,4*R*,7*R*,8*S*,9*S*,12′*R*)-4,7-Bisacetoxy-2,3,8,9-tetra(benzyloxy)-10-hydroxy-dec-5-enyl 12-Hydroxystearate (20): This compound was prepared from **17** as described for **19** and obtained in 84% yield together with 77% of unreacted alcohol **17**. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.24 (m, 20 H), 5.79–5.69 (m, 2 H), 5.49 (dd, J = 10.6, 5.0 Hz, 2 H), 4.67–4.60 (m, 6 H), 4.59–4.51 (m, 2 H), 4.33 (dd, J = 11.7, 4.0 Hz, 1 H), 4.09 (dd, J = 11.7, 6.0 Hz, 1 H), 3.75–3.69 (m, 2 H), 3.69–3.64 (m, 1 H), 3.62–3.53 (m, 4 H), 2.25 (t, J = 7.6 Hz, 2 H), 2.15–1.99 (m, 2 H), 1.98 (s, 3 H), 1.96 (s, 3 H), 1.65–1.52 (m, 2 H), 1.43 (s, 6 H), 1.35–1.20 (m, 20 H), 0.88 (t, J = 6.5 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.5, 169.8, 138.2, 138.1, 137.94, 137.88, 129.3, 128.7, 128.5, 128.41, 128.37, 128.0, 127.90, 127.88, 127.83, 127.80, 127.7, 80.1, 79.7, 79.4, 74.60, 74.56, 73.2, 73.1, 73.09, 73.06, 72.0, 63.4, 61.3, 37.5, 34.2, 31.8, 29.7, 29.6, 29.5, 29.43, 29.37, 29.3, 29.1, 25.6, 24.9, 22.6, 21.08, 21.05, 14.1 ppm; the two acetyl carbonyl carbon signals are overlapping at δ = 169.8 ppm, three missing aromatic carbon signals are overlapping with signals at δ = 127.5–128.5 ppm, one benzylic carbon signal is not visible, and two signals from the tail group are overlapping with signals at δ = 25.5–30.5 ppm. IR (neat): $\tilde{\nu}$ = 2926, 2854, 1739, 1230, 1093 cm^{-1}. $[\alpha]_D$ = ±0.0 (c = 0.20, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{60}H_{82}NaO_{12}$ [M + Na] 1017.5704; found 1017.5705.

(*E*,2*S*,3*S*,4*R*,7*R*,8*S*,9*S*,12′*R*)-2,3,8,9-Tetra(benzyloxy)-10-hydroxy-4,7-dimethoxydec-5-enyl 12-Hydroxystearate (21): This compound was prepared from **18** as described for **19** and obtained in 82% yield together with 84% of unreacted alcohol **18**. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.19 (m, 20 H), 5.72 (dd, J = 15.9, 6.8 Hz, 1 H), 5.66 (dd, J = 15.9, 7.1 Hz, 1 H), 4.73–4.49 (m, 8 H), 4.33 (dd, J = 11.8, 4.0 Hz, 1 H), 4.20 (dd, J = 11.8, 6.3 Hz, 1 H), 3.86–3.72 (m, 4 H), 3.69–3.56 (m, 3 H), 3.54 (dd, J = 5.8, 4.0 Hz, 1 H), 3.45 (t, J = 4.8 Hz, 1 H), 3.24 (s, 6 H), 2.33 (s, 2 H), 2.23 (t, J = 7.6 Hz, 2 H), 1.67–1.50 (m, 2 H), 1.50–1.35 (m, 6 H), 1.35–1.19 (m, 20 H), 0.88 (t, J = 6.5 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.6, 138.3, 138.23, 138.17, 138.1, 131.6, 131.1, 128.43, 128.37, 128.35, 128.30, 128.25, 128.0, 127.9, 127.81, 127.77, 127.7, 81.71, 81.69, 81.5, 81.0, 79.6, 77.4, 74.70, 74.68, 73.00, 72.7, 72.0, 63.8, 61.4, 56.8, 56.7, 37.50, 37.48, 34.3, 31.8, 29.7, 29.60, 29.55, 29.5, 29.4, 29.3, 29.2, 25.7, 25.6, 24.9, 22.6, 14.1 ppm; the two missing aromatic carbon signals are overlapping with the signals at δ = 127–129 ppm. IR (neat): $\tilde{\nu}$ = 2929, 2854, 1736, 1456, 1092 cm^{-1}. $[\alpha]_D$ = –8.7 (c = 0.15, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{58}H_{82}NaO_{10}$ [M + Na] 961.5806; found 961.5807.

(*E*,2*S*,3*S*,4*R*,7*R*,8*S*,9*S*,12′*R*)-2,3,4,7,8,9,10-Heptahydroxydec-5-enyl 12-Hydroxystearate (10): Surfactant precursor **19** (64 mg, 0.0586 mmol) was dissolved in MeOH (15 mL) and Pd/C (10 wt.-%, 25 mg) was added. The mixture was degassed at –78 °C for 30 min, and then connected to a H_2 gas balloon. The reaction mixture was hydrogenated at room temp. for 24 h. The H_2 gas balloon was then disconnected from the flask and the catalyst was removed by filtration through a small plug of RP silica, and washed with a few milliliters of fresh MeOH. Concentration of the filtrate and crystallization of the remaining powder from water gave the desired surfactant **10** in 61% yield (20 mg, 0.0354 mmol). ^{1}H NMR (400 MHz, MeOD): δ = 4.15–3.99 (m, 2 H), 3.88–3.78 (m, 1 H), 3.67–3.46 (m, 5 H), 3.44–3.34 (m, 2 H), 3.32 (t, J = 4.0 Hz, 1 H), 2.26 (t, J = 7.3 Hz, 2 H), 1.64–1.44 (m, 6 H), 1.41–1.11 (m, 26 H), 0.81 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 175.5, 74.6, 74.4, 74.0, 73.3, 73.1, 72.5, 71.5, 66.9, 64.4, 38.4, 35.0, 33.1, 30.9, 30.8, 30.7, 30.61, 30.58, 30.4, 30.2, 26.8, 26.0, 23.7, 14.4 ppm; two missing carbon signals are overlapping with the signals at δ = 30–31 ppm, two signals are overlapping at δ = 38.4 ppm, and two signals are overlapping at δ = 26.8 ppm. IR (neat): $\tilde{\nu}$ =

3340 cm^{-1} (br), 2920, 2850, 1730 cm^{-1}. $[a]_D$ = +4.8 (c = 0.98, CH_2Cl_2). HRMS (FAB+): calcd. for $C_{28}H_{56}NaO_{10}$ [M + Na] 575.3771; found 575.3773.

Supporting Information (see also the footnote on the first page of this article): ^1H and ^{13}C NMR spectra for compounds **4a**–**g**, **6**, **7g**, **10**, and **13**–**21**.

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